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Madrid, 12-15 June 2019

Abstracts

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Speaker Abstracts

New avenues of OA & osteoporosis management

SP0001 WIN IN OA MANAGEMENT

Francis Berenbaum. *Sorbonne Universite, France*

All recommendations on the management of osteoarthritis (OA), including EULAR, consider that its treatment should include pharmacological and non-pharmacological treatments. In this lecture, the most recent advances in both fields will be addressed. Some of them can change our current practice like recommendations on physical activity or on the choice of analgesics.
Moreover, this lecture will highlight some of the drugs and cell therapies in development that could be on the market in the very close years
Disclosure of Interests None declared
DOI: 10.1136/annrheumdis-2019-eular.8428

SP0002 HOT: OSTEOPOROSIS @2019

Serge Ferrari. *Geneva University Hospital, Medecine, Geneva, Switzerland*

Background: The goal of osteoporosis therapy is to quickly prevent fragility fractures in subjects at risk and on the longer term to restore bone mass (Bone mineral density, BMD) to levels of appropriate bone strength.
Currently approved drugs for treatment of osteoporosis in Europe, namely bisphosphonates, denosumab, and teriparatide all decrease vertebral fracture risk within one year, whereas the benefits on non-vertebral fractures may take nearly two years to appear.
Objectives: To provide an update of recent trials regarding osteoporosis treatment.
Methods: Literature review and expert insights into recent analyses of clinical trials.
Results: New H2H trials, notably with teriparatide compared to risedronate, have shown the superiority of the anabolic therapy in preventing fractures in high risk patients. In GIOP, denosumab increased BMD more than risedronate. More importantly, romosozumab, a monoclonal Ab against sclerostin, was superior to alendronate to reduce fractures in high risk subjects, whereas the sequence of romosozumab and denosumab was superior to placebo followed by denosumab and increased BMD over just two years equivalent to seven years of continuous denosumab. New analyses of long-term denosumab, up to ten years of continuous therapy, have shown continuous BMD gains and further reduction in fracture rates, with T-scores at hip near -1.5 achieving the lowest fracture risk. However several case reports as well as a post-hoc analysis of subjects discontinuing denosumab in the FREEDOM trial have reported an increased risk of multiple vertebral fractures, which may be prevented by a 1-2 yrs consolidation by a bisphosphonate following denosumab therapy (guidelines).
Conclusion: In summary, while new data and more potent drugs are emerging (romosozumab), fueling the concept that anabolics should be used earlier in the course of therapy in high risk patients, additional long-term data with anti-resorptives indicate that continuous treatment, at least as long as treatment targets (T-scores >-2 and no fractures) are not reached, has a favourable benefits/risk profile.
Disclosure of interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8475

WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

Best practices in spondyloarthritis

SP0003 NSAIDS – HOW TO OPTIMALLY USE THEM? (SAFETY OF NSAIDS)

Victoria Navarro-Compán. *University Hospital La Paz, IdiPaz, Rheumatology, Madrid, Spain*

The management of patients with axial spondyloarthritis (axSpA) requires a combination of non-pharmacological and pharmacological treatment modalities. Among pharmacological treatment, nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended as first-line drug. NSAIDs have shown to be efficacious to reduce symptoms and signs in patients with axSpA.
Nevertheless, NSAIDs are not exepmt of side effects especially when administered chronically, as in patients with axSpA. These include gastrointestinal, cardiovascular and nephrological side effects. In addition, some situations may influence on the prescription of NSAIDs, such as the presence of some extrarheumatolgical manifestations of the disease (inflammatory bowel disease), comorbidities and family planning-decisions including pregnancy and breastfeeding. Therefore, it is essential taking risk and benefits of NSAIDs use to properly manage patients with axSpA. During this presentation, the optimal usage of NSAIDs in patients with axSpA will be analysed and discussed, taken into account all the possible side effects and the context of the patient.
Disclosure of Interests None declared
DOI: 10.1136/annrheumdis-2019-eular.8547

SP0004 MANAGING PATIENTS WITH AXSPA: WHAT ARE THE QUALITY STANDARDS?

Uta Kiltz. *Rheumazentrum Ruhrgebiet at Ruhr-University Bochum, Rheumatology, Herne, Germany*

Background: There is wide variation in the management of patients with axial spondyloarthritis (axSpA) worldwide with significant unmet needs such as delayed diagnosis and inequity in bMARD prescription.[1] Assessing the quality of care provided to patients with axSpA is important not only to patients and physicians, but also to providers and purchasers of health care. There is no agreed methodology to quantify quality of care but several approaches have been proposed aiming to assess quality in a measurable construct, e.g. quality indicators, performance measures or quality standards. Definition of quality standards (QS) enable society to identify resources and processes which may need to be optimized in patients with axSpA.
Objectives: A major goal of the international organization Assessment of SpondyloArthritis international Society (ASAS) is to improve quality of care and health outcomes in patients with axSpA. Recognized gaps in current care prompted ASAS in 2016 to start developing a quality standard set (ASAS QS) to optimize access, treatment and patient outcomes in axSpA.
Methods: An ASAS task force developed a set of ASAS QS step-wise. First, key areas for quality improvement were proposed, discussed, rated and agreed on. Thereafter, key areas were prioritized and statements for the most important key areas were phrased on consensus. Appropriate tools were selected and measures developed to be able to assess and quantify the quality of care on the community level.
Results: The ASAS task force, consisting of 20 rheumatologists, 2 physiotherapists and 2 patients, selected and proposed 34 potential key areas for quality improvement which were commented by 140 ASAS survey participants (86 physicians, 42 patients). Within that process 3 new key areas came up, which led to a reevaluation of all 37 key areas by 120 participants (86 physicians, 29 patients). Five key areas were identified as most important to determine quality of care: referral including rapid access, monitoring, treatment, education including patient information and comorbidities. On that background, 9 QS were agreed on and finally endorsed by ASAS.
Conclusion: ASAS successfully developed the first QS set for improvement of health care for adult patients with axSpA. All QS are measurable achievable in daily care in an optimized situation and intend to minimize variation in quality of care.

REFERENCE:

[1] Nikiphorou E, et al. Inequity in biological DMARD prescription for spondyloarthritis across the globe: results from the ASAS-COMOSPA study. Ann Rheum Dis 2018;77:405–411.

Disclosure of interests: Uta Kiltz Grant/research support from:
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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

How to maintain remission in vasculitis

SP0005 **CASE 1 DISCUSSANT: LONG TERM EFFICACY OF REMISSION-MAINTENANCE REGIMENS FOR AAV**

Loïc Guillevin. *National Referral Center for Rare Systemic and Autoimmune Diseases, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Université Paris Descartes, Department of Internal Medicine, Paris, France*

ANCA-associated vasculitides (AAVs) are a group of diseases with frequent relapses that can sometimes be severe. Treatment comprises an induction-remission phase followed by a maintenance regimen. Induction-remission therapy is effective and now well-established, mainly based on the combination of corticosteroids (CS) and cyclophosphamide or rituximab. For decades, maintenance therapy was compulsory and consisted of azathioprine or methotrexate, combined or not with low-dose CS. That regimen was prescribed for at least 18 months but was sometimes taken for several years. Criteria for stopping treatment have never been codified. Since rituximab has been widely prescribed for induction, the indication for azathioprine maintenance has been challenged because its relapse rate at 18 months (29%) was comparable to that of placebo (32%) given in its stead. However, we considered those relapse rates unacceptably high and have tried to devise a different therapeutic approach to maintenance, with semestrial evaluation of the indication of rituximab infusion over 18 months. MAINRITSAN1-trial results demonstrated the superiority of rituximab to maintain remission with a 5% relapse rate at 28 months vs 29% for azathioprine recipients. The 60-month follow-up of that trial confirmed the superiority of rituximab over azathioprine (37% vs 57%), even though rituximab did not abrogate relapses. Since the publication of those results, it is now clear that AAV remission-maintenance therapy should be rituximab—and not azathioprine or another equally effective immunosuppressant like methotrexate.

Maintaining remission should now also be based on other factors predictive of relapse: vasculitis type, ANCA subtype and/or ANCA presence or absence at the end of the induction regimen. Granulomatosis with polyangiitis relapses more frequently than microscopic polyangiitis or eosinophilic granulomatosis with polyangiitis. Relapse rates of the former two are probably linked mainly to ANCA type, anti-PR3 or anti-MPO, with the latter relapsing less frequently. The long-term MAINRITSAN1-trial results identified anti-PR3 presence 1 year after ending induction treatment and/or their persistence were predictor(s) of relapse.

We also designed a study comparing fixed-schedule rituximab infusions to re-infusions[JJ1] guided by ANCA titer and/or CD19+ circulating B lymphocytes. Results of that prospective study demonstrated that fewer rituximab infusions should be given but that ANCA titer and the circulating CD19+ B-cell level are not good predictors of relapse. ANCA presence—independently of their titer—is more frequently associated with relapse.

The optimal rituximab-administration duration has not yet been established. Our group is now awaiting the imminent results of a prospective trial comparing 4 vs 8 rituximab infusions at 6-month intervals after obtaining remission.

Conclusions: Major advances have been made in the therapeutic strategy for AAVs. After remission is obtained: 1) AAVs require maintenance therapy, 2) rituximab is superior to immunosuppressants, 3) the presence, persistence and/or reoccurrence of anti-PR3 ANCA predict relapses, 4) the 500-mg rituximab dose/infusion seems well-adapted. The optimal treatment duration remains to be elucidated.

Tailoring maintenance therapy is now the main therapeutic objective for AAV management. Future trials will attempt to evaluate very long-term maintenance treatment of AAVs with the goal of eradicating relapses.

Disclosure of Interests: None declared

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SP0006 **CASE 2 DISCUSSANT: LONG TERM EFFICACY OF REMISSION-MAINTENANCE REGIMENS FOR GPA**

Peter Villiger. *inselspital, Rheumatology, Immunology and Allergology, Bern, Switzerland*

Background: A case of Giant Cell Arteritis with different visual symptoms and delayed diagnosis will be presented. This 74 year-old patient was pulsed with Glucocorticoids (GC) and thereafter treated with Tocilizumab (TCZ). She rapidly achieved full and lasting remission. After 12 months of treatment with TCZ, infusions were stopped. The patient suffered minor relapse 4 months after treatment discontinuation and again responded to TCZ. The case raises several questions such as: How to dose and how long to treat with TCZ? How to reduce dose and when to stop GC? Are there variables to quantify subclinical diseases activity as CRP and ESR are unreliable under TCZ treatment? Are there predictive factors for relapse after treatment discontinuation? How to control development of disease damage over time?

Disclosure of Interests: None declared

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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

CPPD – a forgotten disease that requires more attention??!!!

SP0007 **IS ULTRASOUND A GOOD TOOL TO EVALUATE CPPD?**

Georgios Filippou. *University of Ferrara, Rheumatology Department, Ferrara, Italy*

CPPD is an arthropathy with high prevalence among the elderly and a multitude of clinical manifestations that can easily bring to misdiagnosis and therapeutic errors. The possibility to assess different aspects of the disease with only one tool can be of great help for clinicians.

Ultrasound (US) can help to address both the diagnosis and the inflammatory assessment of the disease. In the last years a lot of research has been carried out regarding the applications of US in CPPD. The special OMERACT US sub-task force that is working in CPPD has produced new definitions for identification of CPPD by US and has tested their reliability demonstrating that US can be used reliably at the knees and wrists for assessing CPPD[1,2]. Further, US has been tested also for assessment of inflammatory and structural changes in osteoarthritis demonstrating to be reliable also for this purpose[3].

During the lecture the potential of US in diagnosis and follow-up of patients with CPPD will be presented. Further, a deeper insight into possible pathogenetic mechanisms, based on observations made at US imaging, will be discussed.

REFERENCES:

[1] Filippou G., Scirè C.A., Damjanov N., et al. Definition and reliability assessment of elementary ultrasonographic findings in calcium pyrophosphate deposition disease: A study by the OMERACT calcium pyrophosphate deposition disease ultrasound subtask force. J Rheumatol 2017;44:1744–9. doi:10.3899/jrheum.161057

[2] Filippou G, Scirè CA, Adinolfi A, *et al.* Identification of calcium pyrophosphate deposition disease (CPPD) by ultrasound: reliability of the OMERACT definitions in an extended set of joints—an international multiobserver study by the OMERACT Calcium Pyrophosphate Deposition Disease Ultrasound Subtask Force. *Ann Rheum Dis* 2018;:annrheumdis-2017-212542. doi:10.1136/annrheumdis-2017-212542

[3] Bruyn GA, Naredo E, Damjanov N, et al. An OMERACT reliability exercise of inflammatory and structural abnormalities in patients with knee osteoarthritis using ultrasound assessment. Ann Rheum Dis Published Online First: 22 April 2015. doi:10.1136/annrheumdis-2014-206774

Disclosure of Interests: Georgios Filippou Speakers bureau: Laborest, Abbvie, BMS, Sanofi

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SP0008 **MANAGEMENT OF CPPD DISEASE**

Abhishek Abhishek. *The University of Nottingham, Academic Rheumatology, Nottingham, United Kingdom*

Background: Calcium pyrophosphate deposition (CPPD) is a common cause of arthritis. Its' prevalence increases with ageing, and it manifests with asymptomatic chondrocalcinosis, acute crystal synovitis, and chronic arthritis.

Objectives: The objectives of this talk are to summarize the treatment options for the management of CPPD, and, to review the evidence base supporting them.

Methods: A systematic literature search was performed to identify all studies published in the English language, and, reporting on the treatment of acute and chronic manifestations of CPPD. All published studies were included with the exception of case reports and conference abstracts. Similarly, a literature search was performed to identify the metabolic and hereditary risk-factors of CPPD. The findings of the systematic literature search are described in a narrative manner. Interventions for which there is no published data are recommended based on clinical experience and expert opinion.

Results: Based on clinical experience, oral or intra-articular corticosteroids are recommended for the management of CPPD. Colchicine and interleukin-1 antagonists are effective and recommended for the management of acute CPP crystal arthritis. Interleukin-1 antagonists should be reserved for use in refractory cases. Oral NSAIDs should be avoided as people with CPPD are frequently elderly. Low-

dose oral colchicine and hydroxychloroquine can be used in the management of recurrent acute CPP crystal arthritis to prevent recurrent flares. Based on current evidence, methotrexate cannot be recommended for the management of CPPD. However, there are anecdotal reports of beneficial effects of methotrexate in the management of chronic CPP crystal inflammatory arthritis, and, this agent holds promise for a role in the management of chronic CPP crystal arthritis which requires investigation in future studies. Radiosynovectomy may be effective in joints with chronic synovitis and CPPD. Individuals with young-onset CPPD, or polyarticular CPPD should be screened for inherited disorders such as ANKH gene mutations, Gitelman's syndrome; and for metabolic conditions such as hyperparathyroidism, haemochromatosis, hypomagnesemia and hypophosphatasia. When present, the underlying metabolic abnormality should be treated appropriately. In joints with end-stage osteoarthritis, the presence of CPPD does not adversely affect the outcomes of total joint replacement. There are anecdotal case-reports of radiographic articular chondrocalcinosis due to hyperparathyroidism or hypomagnesemia resolving after parathyroidectomy, or magnesium supplementation, to date, it has not been possible to dissolve CPPD in vivo with targeted drug therapy. Several candidate pharmaceutical agents that have the potential of dissolving CPPD have been identified, but, their clinical trial is generally precluded by the risk of systemic toxicity.
Conclusion: Although the pathogenesis of CPPD and CPP crystal mediated inflammation are well understood, its' management remains symptomatic. Expedited drug development programs and high quality randomised controlled trials are needed to advance the management of people with this disorder.
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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

Comorbidities in psoriatic arthritis

SP0009 **CARDIOVASCULAR RISK IN PSORIASIS AND PSORIATIC ARTHRITIS**

Iain McInnes. *University of Glasgow, Institute of Infection, Immunity, and Inflammation, Glasgow, United Kingdom*

Background: Psoriasis and psoriatic arthritis ar associated with increased cardiovascular and cardio metabolic risk.
Objectives: To describe the prevalence and magnitude CV risk in psoriasis and psoriatic arthritis and to comment on the clinical therapeutic implications of this risk in our practice.
Methods: Review of literature concerning CV risk and interpretation of the same.
Results: MACE are elevated over time in people with psoriasis and PsA. The mechanisms driving this are currently unclear but likely include both the impact of traditional risk factors e.g. dyslipidaemia, hypertension, obesity and novel risk factors e.g. mediated via increased inflammatory burden. Increased vigilance is required to detect this risk and a low index of suspicion should be introduced in practice. Aggressive management of CV risk should improve outcomes.
Conclusion: Recognising and treating factors mediating CV risk in psoriasis and psoriatic arthritis should comprise part of our routine clinical practice.
Disclosure of Interests: Iain McInnes Grant/research support from: AstraZeneca, Celgene, Compugen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Celgene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma
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SP0010 **INFECTIOUS RISK AND MANAGEMENT OF VACCINATION**

Nico Wulffraat. *Wilhelmina Children's hospital/UMC Utrecht, Pediatric rheumatology and Immunology, Utrecht, Netherlands*

Background: O ver the years, awareness of vaccine-preventable infection in rheumatic diseases has increased. At the same time, the safety of vaccines is still a hot topic in the public arena. Large-scale registries with data on juvenile idiopathic arthritis or RA taking the combination of methotrexate and biologics have demonstrated an increased incidence of infections. EULAR recommendations for both vaccination in pediatric patients and adults with rheumatic diseases, provide evidence-based guidance based on data from published studies on safety and efficacy of vaccinations in adults and children with rheumatic conditions. Especially in children, few data exist on safety and efficacy of live-attenuated vaccines such as MMR. This is relevant given the decreasing vaccination coverage and occurrence of measles outbreakes
Objectives: To provide an overview of vaccines used in patients groups with rheumatic conditions under medication such as MTX and or biologicals. Also we seek for evidence on adverse events, protection rates and persistence of protective antibody titers over time. From these studies general guidelines are proposed.
Methods: Literature review of vaccination studies performed in adults and children. In addition the clinical practice of boostering of MMR in JIA patients under immunosuppressive therapy was investigated in several large academic pediatric centers across Europe. Thus 234 JIA patients were identified that received a MMR booster under MTX and or biologicals.
Results: EULAR recommendations are updated for children and adults. For most vaccines it is adivised to follow the national vaccination guidelines. Non-live vaccines can be safely provided to AIIRD patients under immunomodulating treatments, whereas the administration of live attenuated vaccines should be avoided under immunomodulating treatment, with the possible exceptions of herpes zoster and MMR. In 234 children with JIA who received the MMR booster while using MTX and or a Biological only 7 of adverse events were reported. Adverse events reported were mild (skin reaction, mild fever, urinary tract infection. There was no relation between disease activity, disease type or duration, sex, age and outcome of vaccinations.
Vaccination status of patients with rheumatic conditions should be assessed annually. Live attenuated vaccines should be avoided during the first 6 months of life in newborns of mothers treated with biologics during the second half of pregnancy.
Conclusion: The EULAR recommendations of 2011 are currently updated and will provide an up-to-date guidance on the management of vaccinations in patients with inflammatory rheumatic conditions. There is still a scartity of data on safety and efficay of live attenuated vaccines under biologicals. The next challenge is the implementation into the clinical practice of health professionals across Europe.
Disclosure of Interests: None declared
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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

Environmental influences on disease development

SP0011 **HOW THE GUT INFLUENCES THE IMMUNE SYSTEM**

Mario Zaiss. *Friedrich-Alexander University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany*

Background: A disturbed gut microbiota composition has been associated with autoimmune diseases. Recent findings support the hypothesis that the onset of RA might be linked with the gut microbiota. Moreover, we could recently show that high fiber diets change the microbiota, increase SCFA levels and attenuate inflammatory arthritis and bone destruction [(1)]. However, direct mechanistic links between the gut microbiota and onset of autoimmune diseases remain largely unknown.
Objectives: Herein, we intended to identify if the intestinal barrier integrity could serve as a key checkpoint translating autoimmunity to inflammation.
Results: Restoration of the intestinal barrier in the pre-phase of arthritis using different approaches inhibited the development of arthritis.
Conclusion: In summary, our data identify a new preventive approach for the onset of autoimmune disease by specifically targeting impaired intestinal barrier function.

REFERENCE:

[1] Lucas S, Omata Y, Hofmann J, Böttcher M, Iljazovic A, Sarter K, Albrecht O, Schulz O, Krishnacoumar B, Krönke G, Herrmann M, Mougiakakos D, Strowig T, Schett G and Zaiss M M. (2018). Short-chain fatty acids regulate systemic bone mass and protect from pathological bone loss. Nat Commun 9: 55.

Disclosure of Interests: None declared
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SP0012 **THE HYGIENE HYPOTHESIS IN AUTOIMMUNITY**

Jean-Francois Bach. *Institut de France, Académie des Sciences, Paris, France*

Background and Aims: The frequency of autoimmune diseases has increased significantly in recent decades in developed countries. The hygiene hypothesis provides a possible explanation for this increase. The hypothesis is based on the observation of a concomitant decrease in the frequency of infectious diseases and an increase in the frequency of autoimmune diseases. It is also based on the geographical disparity in the frequency of autoimmune diseases, much more frequent in the north than in the south of the northern hemisphere, a disparity that is not explained by genetics.
Method: The disease frequency which is very low in southern countries increases from the first generation among subjects migrating northward. The causal relationship between the decline in infections and the increase in autoimmune diseases remains to be proven. Most of the evidence is based on spontaneous experimental models of autoimmune diseases that show the higher frequency of these diseases in a clean sanitary environment and their prevention through the administration of various bacteria, viruses or parasites.
Results: The underlying mechanisms are beginning to be revealed. An important place is given to pathogens and more particularly to their TLR ligands. Some arguments suggest that commensal bacteria in the intestinal microbiota also play a role. At the cellular level, the stimulation of certain regulatory cells and more particularly those producing TGF beta is well documented.
Conclusion: These considerations are important for understanding the epidemiology and pathophysiology of autoimmune diseases but can also provide new guidance on their treatment and especially their prevention. The problem is, however, complicated by the fact that the theory applies to varying degrees depending on the disease, for instance more in systemic lupus erythematosus than rheumatoid arthritis.
Disclosure of Interests: None declared
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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

Pharmaceutical pipeline in OA

SP0013 **GROWTH FACTORS AND CARTILAGE: FROM MECHANISMS TO DMOADS**

Marc Hochberg. *University of Maryland, School of Medicine, United States of America*

Background: Growth factors are biologically active molecules that can stimulate cellular division, growth and differentiation and, in articular cartilage, can regulate development, homeostasis and regeneration of matrix. These anabolic factors can stimulate synthesis of proteoglycans, aggrecan and type II collagen, induce mesenchymal stem cell (MSC) proliferation and drive differentiation of MSCs into chondrocytes and decrease catabolic effects of cytokines and matrix metalloproteinases (MMPs). Growth factors would not, however, be expected to have a direct analgesic effect in patients with symptomatic knee osteoarthritis.
Objectives: To review the role of growth factors in articular cartilage, identify specific growth factors and review data from phase 1 and 2 studies of selected growth factors in subjects with knee osteoarthritis.
Methods: A PubMed search was performed using key words “cartilage or chondrocyte” and “growth factor”. The search included both original manuscripts and review articles as well as clinical trials but was limited to English language. From these searches, I selected review articles and clinical trials and excluded articles that solely examined molecular mechanisms of action of growth factors on chondrocytes.
Results: Growth factors for articular cartilage include molecules in the transforming growth factor-β (TGF-ββ superfamily (including TGF-β1, bone morphogenic protein [BMP]-2 and BMP-7), insulin-like growth factor-I, fibroblast growth factor (FGF) family (including FGF-2 and FGF-18), platelet-derived growth factor (PDGF) and Wnt ligands as well as platelet rich plasma (PRP).
Conclusion: Data will be presented from phase 1 and 2 studies of rhFGF-18 and SM-04690, a Wnt signaling inhibitor, that demonstrate proof-of-concept and early efficacy of these growth factors for structure modifying effects in subjects with knee osteoarthritis (OA).

REFERENCES:

[1] Boehme KA, Rolauffs B: Onset and progression of human osteoarthritis - can growth factors, inflammatory cytokines, or differential miRNA expression concomitantly induce proliferation, ECM degradation, and inflammation in articular cartilage? Int J Mol Sci 2018;19:2282;doi:10.3390/ijms19082282.

[2] Zhu Z, Li J, Ruan G, Wang G, Huang C, Ding C: Investigational drugs for the treatment of osteoarthritis, an update on recent developments. Expert Opin Invest Drugs 2018. doi.org/10.1080/13543784.2018.1539075.

Disclosure of Interests: Marc Hochberg Shareholder of: BriOri Biotech, Theralogix LLC., Consultant for: Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis Pharma AG, Pfizer Inc., Samumed LLC, Symic Bio Inc., Theralogix LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., Zynerba, Galapagos, IQVIA, Hoffman LaRoche.
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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

What’s new: Latest news on biological treatment

SP0014 **THE LATEST NEWS ON BIOSIMILARS TREATMENT**

Jonathan Kay. *UMass Memorial Medical Center and University of Massachusetts Medical School, Division of Rheumatology, Department of Medicine, and Department of Population and Quantitative Health Sciences, Worcester, Massachusetts, United States of America*

Biologic medications have revolutionized the treatment of many rheumatologic diseases, but their high cost often limits patient access to these effective treatments. Biosimilars are legitimate copies of biopharmaceuticals, which no longer are protected by patent, that have undergone rigorous analytical and clinical assessment in comparison to their reference products and have been approved by a regulatory authority in a highly regulated area according to a specific pathway for biosimilar evaluation. In 2005, the European Medicines Agency (EMA) established a pathway for the review and approval of biosimilars and, one year later, approved the human growth hormone Omnitrope® as the first biosimilar. As of March 2019, 56 of 60 biosimilars approved by the EMA were commercially available in the European Union, of which 6 were of rituximab and 15 were of TNF inhibitors to treat rheumatologic diseases.
Commercially available lots of a reference product are not identical to one another. All biologic medications are subject to normal batch-to-batch variability and are monitored to ensure that this variation is within “proven acceptable ranges” so that patients are not subjected to risks of lesser safety or efficacy. Since biosimilars have been compared extensively to their reference products and been shown to have highly similar structure, equivalent efficacy, and comparable safety, an approved biosimilar can be considered to be like another batch of its reference product. Thus, patients need not be apprehensive about using an approved biosimilar in place of its reference product.
The “nocebo effect” refers to the misattribution of bodily symptoms to a medication and may result in discontinuation of a treatment that is not actually causing the perceived symptoms. Studies have suggested that the nocebo effect may result in discontinuation of treatment with a biosimilar because of subjective perceptions. This may be addressed by providing encouragement and reassurance through education and open collaborative discussion between providers and patients. By taking this approach to counseling patients, the rate of biosimilar discontinuation may be reduced.
The NOR-SWITCH study demonstrated that patients with inflammatory diseases controlled on treatment with reference infliximab do not experience greater worsening of disease activity when switched to biosimilar infliximab CT-P13 than when continued on treatment with the reference product. Thus, when the cost of the biosimilar is significantly lower than that of its reference product, substituting the biosimilar for the reference product may provide an economic advantage with no loss of clinical benefit. In Norway, where there is an annual “winner takes all” competitive tender process for hospital administered medications, the price of biosimilar infliximab in 2015 was 69% lower than that of its reference product. Thus, in most countries, it is safe, effective, and cost-effective to switch to a biosimilar. However, competition from biosimilars has occasionally driven down the price of a reference product, as in Sweden where the price of reference adalimumab was reduced by 80% in 2018 and became lower than that of adalimumab biosimilars.
The availability of lower-priced biosimilars should decrease the cost of treating patients by introducing market competition. Biosimilars should be more readily available to patients for whom the reference product had been inaccessible because of cost. Greater global access to effective biologic medications should reduce disability, morbidity, and mortality associated with rheumatologic diseases.
Disclosure of Interests: Jonathan Kay Grant/research support from: Gilead Sciences, Pfizer, UCB Pharma, Consultant for: AbbVie, Boehringer Ingelheim GmbH, Celltrion Healthcare, Merck Sharp & Dohme Corp., Novartis Pharmaceuticals, Pfizer, Samsung Bioepis, Sandoz, UCB Pharma
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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

How to perform low-budget high-quality research

SP0016 **YOUR VERY FIRST STEPS ON SYSTEMATIC REVIEW**

Loreto Carmona. *Instituto de Salud Musculoesquelética, Research, Madrid, Spain*

Systematic reviews (SR) are a type of clinical research, and thus they follow the hypothetical-deductive or scientific method. Their objective is to answer clinical questions and they do it based on a specific structure (protocol) and working through inferences. Interestingly, a SR is a type of study design that can answer all types of questions, from efficacy to incidence. They manage the information from previous studies in a pre-established reproducible way, as unbiased as possible. They provide quick answers. However, they should be performed and interpreted with caution: a poor systematic review is much worse than a narrative review, as it gives the false impression of "science". This is even worse if the studies were combined in a meta-analysis.

In this lecture, we will review the protocol of a SR, the importance of rephrasing the question, the search strategy, selection criteria, and procedures of studies selection, primary endpoints, and quality and risk of bias. The last part of any SR is the analysis, which is always qualitative, supported by the evidence table, and following a synthetic discourse with the PICO order, and sometimes quantitative (meta-analysis). We will review some methods to evaluate publication bias, to combine results, and to explore heterogeneity. In this sense, it is essential to note that if we cannot find a valid explanation for heterogeneity, our results may not be valid.

Disclosure of Interests: Loreto Carmona Grant/research support from: Abbvie, Actelion, Astellas, BMS, Eisay, Gebro Pharma, Grünenthal, Leo Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis and UCB Pharma, Paid instructor for: Novartis

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SP0017 **USING AVAILABLE DATASETS TO ANSWER NEW RESEARCH QUESTIONS**

Daniel Prieto-Alhambra. *University of Oxford, NDORMS, Oxford, United Kingdom*

Background: Clinical data are continuously recorded in clinical encounters in the form of electronic medical records, registries, audits ans similar databases. Such large datasets are available to researchers, and provide unique opportunities. However, challenges arise from the use of routinelly collected data, that need special attention and specific skills to minimise a waste in research.

Objectives: To discuss available data sources (data discovery), their advantages and limitations, their uses, and to cover examples of research conducted using routinely collected datasets.

Methods: We will discuss a list of data sources at high level (types of data), their main pros and cons, and then cover challenges and solutions through a number of previously published examples.

Disclosure of Interests: Daniel Prieto-Alhambra Grant/research support from: Grants from Amgen, UCB Biopharma and Servier outside the submitted work, Consultant for: UCB Biopharma, Speakers bureau: Amgen

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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

Health Professional Welcome session

SP0018 **WHAT YOU SHOULDN'T MISS FROM THE HPR PROGRAMME AS A CLINICIAN**

Maria Bergström. *Linköping University, Department of Social and Welfare Studies, Division of Occupational Therapy, Norrköping, Sweden*

As a health professional, the EULAR congress is the place where I can get access to new and fresh rheumatology research of good quality. My presentation will take you through the possibilities the congress offers clinicians when it comes to different topics within the area of rheumatology. Further, my aim and hope is to give you a sense of what is in store for you during this year's EULAR congress.

People with rheumatic diseases today live their lives to a great extent having the diagnosis affecting their everyday life. The ability to work, interact with others or engaging in activities they want to, can be limited. So what do we need to know about them in order to provide the best possible treatment and rehabilitation? As a health professional clinician, I look forward to finding some of the answers to this during this congress.

During the EULAR congress, we as health professionals have the possibility to contribute to and acquire research of good quality in rheumatology, on our way to give our patients the best possible treatment. Also, we have the possibility to contribute to the patientshealth, and I look forward to sessions touching health topics such as exercise. The quality of research and the variety of topics during this EULAR congress can give us a bigger set of tools to work with when we get back to our patients and continue our path towards the best possible treatment and health for this big and important group of patients. I hope that this session can provide an overview of what this years' congress can offer from a clinical perspective.

Disclosure of Interests: None declared

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SP0019 **PRES HPR: DONT DELAY, COLLABORATE TODAY**

Jeannette Cappon[1], PReS Committee for Health Professionals[1], Department pediatric rehabillitation, Reade Center for rehabilitation and rheumatology[2], Dutch Health Professionals in Pediatric Rheumatology[3]. [1]*Reade Center for Rehabilitation and Rheumatology, Pediatric Rehabilitation, 1056AB Amsterdam, Netherlands*

Background: The Pediatric Rheumatology European Society (PReS) is an international organization based in Europe which is dedicated to advance the care and improve the health and well-being of children and young people with rheumatic conditions, helping them to reach their full potential. Full PReS membership is extended to individuals from all European countries, whether they are within the EU or not, and includes countries in the middle east and from other parts of the world as associate members to enrich the collective experience and knowledge. PReS welcomes every practitioner/researcher in the field of pediatric rheumatology.

The PReS committee for Health Professionals in Pediatric Rheumatology aims to bring together nurses, physical therapists, occupational therapists, social workers, psychologists, podiatrists and other health professionals(HP) to foster dialogue, to set standards of clinical practice, education and research.

Collaboration between PReS and Eular Health Professionals starts today, here in Madrid.

Collaboration in general starts with a shared goal to work on together. Our young patients of today might be your patients of tomorrow: what should you know about what they have been through? Your patients of today might have been our young patients of yesterday: what can we learn from their experiences of the past being a child with a rheumatic condition? Did they receive comprehensive care that sustained into their adulthood?

Objectives: To find shared goals between HP Eular and HP PReS to deliver comprehensive care for people with rheumatic diseases during their full life.

To find common interests to discuss between HP Eular and HP PReS

Methods: Examples of common interests e.g. supporting self management of pain and health and illness education are presented.

Shared goals for collaboration are proposed and collected from the audience.

Opportunities to connect for Eular HP and PReS HP in Madrid and Prague September 2020 are listed and benefits are mentioned.

Results: Health Professionals from Eular and PReS experience common interests and shared goals. Positive relations are expected to develop upcoming years.

Conclusion: CollaboRelation between HP Eular and HP PReS can start today

Disclosure of Interests: None declared

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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

EULAR Projects in paediatric rheumatology

SP0020 **THE GLOBAL CHALLENGE AND OPPORTUNITY FOR PAEDIATRIC RHEUMATOLOGY**

Christian Scott. *University of Cape Town, Red Cross War Memorial Children's Hospital, Paediatric Rheumatology, Cape Town, South Africa*

Background: Poorly developed healthcare systems and the overwhelming burden of communicable diseases have limited the growth and development of Paediatric Rheumatology in non central and less resourced countries.[1,2] Most children on earth reside in these less resourced environments and suffer from disproportionately poor access to adequate care for paediatric rheumatic diseases. Emerging evidence suggests that rates of rheumatic diseases are not likely to be different to European and North American children but that diseases severity and

outcomes may be worse and that children in these countries face the additional burdens of poverty, socio-political instability and communicable diseases.[3,4]

Objectives: To review the current situation and challenges faced by the children in less resourced countries with rheumatic diseases and those who provide medical care for them, and to explore opportunities that will drive the global development of paediatric rheumatology to the benefit of all children with rheumatic diseases.

Methods: A thorough review of published literature and gaps in knowledge on the epidemiology and outcomes of childhood rheumatic diseases from less resourced countries. A review of current and planned global initiatives to improve Paediatric Rheumatology care in less resourced countries.

Results: Despite increasing emerging data on paediatric rheumatic diseases from less resourced countries, data on paediatric rheumatic diseases from less resourced countries are sparse. Paediatric rheumatology services in most countries remain inadequate or non-existent to serve the needs of the population, despite encouraging growth in some areas. Improvements in healthcare systems in these countries offer opportunities for the growth of paediatric rheumatology care. Greater genetic diversity and different disease profiles offer opportunities for the advancement of genetic and environmental influences on rheumatic diseases.

Conclusion: An organised effort from the paediatric rheumatology global community can play an important role in the development of education, networks, services and research capabilities that could lead to increased scientific growth and clinical benefits for all children with rheumatic diseases, regardless of their geographical or socio economic position.

REFERENCES:

[1] Scott C et al, Paediatric Rheumatology in Sub-Saharan Africa. Rheumatology (Oxford).2014, Jan 53(8):1357-1358
[2] Mody GM, et al. Improving musculoskeletal health: global issues. Best Pract Res Clin Rheumatol 26(2):237–249
[3] Consolaro A, et al. Paediatric Rheumatology International Trials Organisation. Phenotypic variability and disparities in treatment and outcomes of childhood arthritis throughout the world: an observational cohort study. Lancet Child Adolesc Health. 2019 Apr;3(4):255-263.
[4] Scott, C. et al. Juvenile arthritis management in less resourced countries (JAMLess): consensus recommendations from the Cradle of Humankind Clin Rheumatol. 2019, Feb 38(2):563-575

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SP0021 DELIVERING FUTURE GLOBAL RESEARCH CHALLENGES IN PAEDIATRIC RHEUMATOLOGY

Nicolino Ruperto. *Istituto Gaslini, Clinica Pediatrica e Reumatologia-PRINTO, Genoa, Italy*

The treatment of pediatric rheumatic diseases has improved tremendously in the last 20 years thanks to appropriate legislative initiatives, the existence of very large collaborative networks and the availability of new potent medications. In particular there has been a tremendous improvement in a sizable proportion of patients with juvenile idiopathic arthritis (JIA) with over 3500 children enrolled in trials with registrative purposes. For JIA now the tendency is to concentrate on oral therapies and on drugs targeting specific JIA categories. Also in juvenile systemic lupus erythematosus (SLE) the childhood counterpart of SLE there are several potential targets to be tested in children. In addition the field of paediatric rheumatology has provided an excellent example of large scale academic studies which, through the Paediatric Rheumatology International Trials Organisation (PRINTO) have enrolled over 38,000 children from over 60 countries

Further improvement in future years will stem from a better definition of the paediatric disease entities, the discovery of laboratory and imaging biomarkers that could help the tuning of therapy, a smoother implementation of future clinical trials, a more standardized link between academia (clinical and basic science), regulatory authorities, learned societies such as the Pediatric Rheumatology European Society (PRES) and family organisations for the planning of future trials.

This lecture will present a general overview and a perspective for the future (mainly academic) work to align clinical data collection with basic researchers, PRES, and family associations in order to foster and facilitate drug evaluation in pediatric rheumatic diseases as well as academic research.

REFERENCES:

[1] Ruperto N, Martini A. Current and future perspectives in the management of juvenile idiopathic arthritis. Lancet Child Adolesc Health 2018;2:360–370.
[2] Consolaro A, Giancane G, et al for PRINTO. Phenotypic variability and disparities in treatment and outcomes of childhood arthritis throughout the world: an observational cohort study. Lancet Child Adolesc Health. 2019 Feb 25. pii: S2352–4642(19)30027–6. doi: 10.1016/S2352–4642(19)30027–6. [Epub ahead of print].
[3] Ruperto N, Martini A, for PRINTO. Networking in pediatrics: the example of the Pediatric Rheumatology International Trials Organisation (PRINTO). Archives Dis Child 2011;96:596–601.
[4] Ruperto N*, Eichler I*, et al. A European network of paediatric research at the European Medicines Agency (Enpr–EMA). Archives Dis Child 2012;97 (3):185–188.
[5] Ruperto N, Vesely R, Saint–Raymond A, Martini A for PRINTO. Impact of the European paediatric legislation in pediatric rheumatology: past present and future. Ann Rheum Dis 2013; 72:1893–189.
[6] Brunner HI, Martini A, Lovell DJ, Ruperto N, on behalf of PRINTO–PRCSG. Clinical trials in children and adolescents with systemic lupus erythematosus –methodological aspects, regulatory landscape and future opportunities. Ann Rheum Dis 2019;78:162–170.

Disclosure of Interests: Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda.
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SP0022 PROJECT ABSTRACT 2: EMERGE – HELPING DELIVER OUR WORLDWIDE GOALS

Lovro Lamot. *The University of British Columbia and British Columbia Children's Hospital Research Institute, Department of Pediatrics, Division of Rheumatology, Vancouver, Canada*

EMERGE (EMErging Rheumatologist and rEsearchers) is a new group of young physicians and scientists from across the globe with a shared interest and passion for pediatric rheumatology. Amid numerous differences in education, research opportunities and healthcare systems across countries, the overarching aim of the group is to work closely together towards the same goal of providing a best possible care for children with rheumatic diseases. With the support of the Pediatric Rheumatology European Society (PReS), the group has created several compelling initiatives which could help the creation of a new generation of professionals who can deliver this goal. Therefore, one the paramount initiative of the group is the PReS EMERGE fellowship. This unique program enables clinicians and scientist from all over the world to come to the established pediatric rheumatology centers in Europe, receive clinical or translational research training, perform a short study and build a support network readily available after returning to their surroundings. Next, the Peer Review Mentoring Program has been recently started in order to provide a first structured peer review training in the field of pediatric rheumatology. The prevailing intention of this initiative is to improve the quality of published researches by education of the future peer reviewers. The important initiative of the group is also the organization of the Young Investigators Meeting (YIM), that takes place every year before the PReS congress. This meeting gathers many clinicians and scientist from all continents and provides them with an excellent opportunity of presenting their basic and clinical discoveries and compelling cases to their peers and "not so senior" faculty. Besides, the group is involved in the organization of many educational courses where world-leading experts are conveying their experience and knowledge of a particular topic. To succeed in these initiatives, the EMERGE group is working closely with other similar groups, such as CARRA young investigators from North America and EMEUNET group of young adult rheumatologist from Europe. Moreover, the group has a firm collaboration with Pediatric Task Force Global Musculoskeletal Health, a group dedicated to raising the awareness and improving access to right care for children with musculoskeletal diseases, and ENCA, a network of national associations working with children and young people with pediatric rheumatic diseases. Finally, in order to spread information about these initiatives and to attract new members, the group is actively using social media platforms, such as Facebook (https://www.facebook.com/PReSEMERGE/), Twitter (@PReSEMERGE), and bi-monthly newsletters (emerge.pres@gmail.com).

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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

Crystal I

SP0023 INTRODUCTORY TALK ON CRYSTAL ANALYSIS

Anne-Kathrin Tausche. *University Clinic Dresden, Rheumatology, Dresden, Germany*

Rheumatologists are used to do the arthrocentesis to diagnose (and treat) patients with joint effusions. Crystal arthropathies are the most common inflammatory joint diseases. So the prompt detection of (micro-) crystals in joint fluid by microscopic analysis is of outstanding importance to make the right diagnosis of the very common disease gout or CPPD-arthritis (1). Since many years the EULAR facilitates practical courses in microscopy of crystals to start the training of rheumatologists in that helpful technique. During the practical skill course the trainee will be shown how to properly prepare are slide of SF, analyze the preparation with ordinary light, simple and compensated microscope and learn to discriminate urate from CPPD-crystals[2,3].

REFERENCES:

[1] Zhang W, et al.; EULAR Standing Committee for International Clinical Studies Including Therapeutics. EULAR evidence based recommendations for gout. Part I: Diagnosis. Report of a task force of the Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2006 Oct;65(10):1301-11.
[2] Pascual E, et al. The ordinary light microscope: an appropriate tool for the detection and identification of crystals in synovial fluid. Ann Rheum Dis 1989; 48:983– 5.
[3] Tausche AK, et al. A 3-day delay in synovial fluid crystal identification did not hinder the reliable detection of monosodium urate and calcium pyrophosphate crystals. J Clin Rheumatol 2013.

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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

Capillaroscopy I

SP0024 STANDARDISATION OF NORMAL VERSUS ABNORMAL AND PATHOLOGICAL CAPILLAROSCOPIC IMAGES

Vanessa Smith. *Department of Rheumatology, Ghent University Hospital; 2Department of Internal Medicine, Ghent University; 3Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent, Belgium on behalf of the EULAR Study Group on Microcirculation in Rheumatic Diseases*

Abstract: Medical doctors frequently get patients with Raynaud's phenomenon (RP), a frequent symptom in the general population, referred. The importance of distinguishing normal capillaroscopic findings from (pathognomonic) abnormal (pathological) findings (scleroderma pattern), lies in the fact that this distinction allows the differentiation between a primary RP (not connected to any connective tissue disease [CTD]) from a secondary RP due to systemic sclerosis (SSc) and diseases of the scleroderma spectrum.
What is normal in primary RP?
A normal capillaroscopic pattern, by qualitative assessment, is characterized by a homogeneous distribution of hairpin shaped capillaries as a "comb-like structure", with a density of >7capillaries per mm, with a normal dimension and absence of large hemorrhages Yet, there exists a wide intra- and inter- individual variety in a normal population which will be discussed in this session.
What is pathognomonic abnormal in patients with RP due to SSc?
Patients with the RP who have an underlying clinically recognizable (= with skin involvement) SSc show a very characteristic combination of capillary abnormalities in the nailfold, which can easily be assessed through qualitative assessment (= pattern recognition). Maricq et al. described last century, with the widefield technique (magnification X12–14) the scleroderma pattern. This pathognomonic combination contains the following: a striking widening of all three segments of the capillary loop (arterial, venous and intermediate), loss of capillaries and disorganization of the nailfold capillary bed. Many branched "bushy" capillaries may also be observed.
In 2000, Cutolo et al. qualitatively assessed the nailfolds of an SSc cohort with patients fulfilling the American College of Rheumatology (ACR) criteria for SSc with the nailfold videocapillaroscopic (NVC) technique (magnification X200). According to the different proportions of the hallmark parameters of the scleroderma pattern (giants, capillary loss, hemorrhages and abnormal shapes: (neo) angiogenesis, Cutolo et al. defined three patterns "early", "active" and "late".
The central role of capillaroscopy in distinction between a primary and secondary RP due to SSc is reflected by the fact that capillaroscopy is one of the new ACR/EULAR criteria for classifying a patient as having SSc.
In this lecture the standard "FAST TRACK" recognition system of the EULAR Study Group on Microcirculation in Rheumatic Diseases to discern scleroderma patterns from non-scleroderma patterns will be taught to the attendees.
Suggested further reading:
Smith V, et al. Rheumatology (Oxford). 2016;55(5):883-90.
Cutolo M, et al. Rheumatology (Oxford). 2018;57(4):757-759.
Cutolo M, et al. Autoimmun Rev. 2018;17(4):344-352.
Disclosure of Interests: None declared
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SP0025 RELIABILITY IN THE LAST 10 YEARS: CAPILLAROSCOPIC CHARACTERISTICS VERSUS INSTRUMENTAL DETECTION

Ariane Herrick. *University of Manchester, Salford Royal Hospital NHS Foundation Trust, Division of Musculoskeletal and Dermatological Sciences, NIHR Manchester Musculoskeletal Biomedical Research Centre, Manchester, United Kingdom*

Background: With nailfold capillaroscopy there are different aspects of reliability to consider, including reliability of qualitative image grading (e.g. 'early', 'active' and 'late') and also of semi-quantitative and quantitative measures including capillary density, apical width and presence of giant capillaries. The reliability of image acquisition (i.e. test-retest reliability) is especially important if nailfold capillaroscopic parameters are to be used in longitudinal studies (e.g. clinical trials) which involve acquiring repeat images over time. Lastly when assessing reliability, it is important to recognise that the nailfold capillaries cannot always be clearly seen, and cannot therefore be evaluated.
Objectives: To highlight the different aspects of reliability relating to nailfold capillaroscopy and how these have been addressed in studies over the last 10 years.
Methods: Review of recent studies
Results: 1. Intra-observer reliability has been shown in several studies to be higher than inter-observer.
2. Assessment of 'evaluability' varies between observers and therefore also needs to be taken into account when assessing reliability.
3. Subject to evaluability, certain parameters demonstrate high intra- and inter-observer reliabilities. Reliability differs across different capillaroscopic parameters.
Conclusion: Recent studies examining reliability of capillaroscopy suggest that certain parameters, including image grade, capillary density and apex width have high intra-and inter-observer reliabilities (subject to nailfold image evaluability, which remains a major challenge). Standardised training is likely to improve reliability.

REFERENCES:

[1] Murray AK, Vail A, Moore TL, et al. The influence of measurement location on reliability of quantitative videocapillaroscopy in patients with SSc. Rheumatol 2012; 51 : 1323-30.
[2] Overbury R, Murtaugh MA, Fisher A, et al. Primary care assessment of capillary abnormalities in patients with Raynaud's phenomenon. Clin Rheumatol 2015; 34: 2135-40.
[3] Smith V, Beeckman S, Herrick AL, et al. An EULAR study group pilot study on reliability of simple capillaroscopic definitions to describe capillary morphology in rheumatic diseases. Rheumatol 2016; 55: 883-90.
[4] Dinsdale G, Moore T, O'Leary N, et al. Intra-and inter-observer reliability of nailfold videocapillaroscopy - A possible outcome measure for systemic sclerosis-related microangiopathy. Microvascular Research 2017; 112: 1-6.
[5] Dinsdale G, Moore T, O'Leary N, et al. Quantitative outcome measures for systemic sclerosis-related microangiopathy – reliability of image acquisition in nailfold capillaroscopy. Microvascular Research 2017;113:56-9.
[6] Boulon C, Devos S, Mangin M, et al. Reproducibility of capillaroscopic classifications of systemic sclerosis: results from the SCLEROCAP study. Rheumatology 2017; 56: 1713-20.
[7] Cutolo M, Melsens K, Herrick AL, et al. Reliability of simple capillaroscopic definitions in describing capillary morphology in rheumatic diseases. Rheumatology (Letter) 2018; 57: 757-9.

Disclosure of Interests: None declared
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SP0026 **METHODS AND TOOLS FOR QUANTIZATION OF CAPILLAROSCOPIC MORPHOLOGICAL CHANGES**

Alberto Sulli. *University of Genoa, Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS Polyclinic Hospital San Martino, Genova, Italy*

Capillaroscopy is routinely used in clinical practice to assess nailfold microvascular structure. Unlike laser techniques that give functional information, capillaroscopy allows a morphological assessment of nailfold capillary bed. It is a recognized tool to early differentiate primary from secondary Raynaud's phenomenon, as well as to follow scleroderma microangiopathy. As microangiopathy extent correlates with organ involvement degree, nailfold capillaroscopy abnormalities are also considered a possible biomarker in systemic sclerosis.[1,2]
Several tools may be used to quantitate morphological capillary changes, from devices with low magnification (20x), to instruments with high magnification (200x or more).[3] The instruments with low magnification allow a global evaluation of the entire nailfold area (wide-field capillaroscopy), and they provide a panoramic vision of the whole nailfold microvascular network. Magnifying glass, ophthalmoscope and dermatoscope are example of optical instruments with low magnification. Obtaining a high-quality documentation may be difficult by these tools, as well as the identification of early capillary changes; furthermore, storing capillary images is not possible.
Stereomicroscope, usb-microscope or videocapillaroscope allow a sequential higher magnification up to 600x which enable detailed observation of small nailfold areas or single capillaries. However, by using a microscope, patient‘s fingers must be placed under the lens, and this may make the exam sometimes difficult, for example in the presence of either finger contractures or arm disabilities.
The optical probe videocapillaroscope is currently considered the gold-standard for nailfold videocapillaroscopy, as it has the advantage to be moved to the finger of the patient at direct contact with the nailfold: this facilitates examination of patients with systemic sclerosis and finger flexion contractures, simply by moving the probe. The use of videocapillaroscope has a high sensitivity, a short time of execution after an easy operator training, allows early diagnosis of secondary Raynaud's phenomenon by very early detection of microvascular changes, and also allows the counting and scoring of capillaroscopic parameters. Connection of the instrument with a software enable image recording, report writing and automated capillary number counting.[4]
To quantitate capillaroscopic morphological changes (mainly capillary number, capillary dilations, giant capillaries, microhemorrhages, abnormal shape/ramified capillaries, capillary bed disorganization) a simple rating scale may be adopted to score each capillary abnormalities (score 0-3) (score 0 = no changes; score 1 = less than 33% of capillary alterations/reduction; score 2 = 33-66% of capillary alterations/reduction; score 3 = more than 67% of capillary alterations/reduction, per linear millimetre. Reduction = capillary number per linear millimetre <9).[5] The mean score value for each capillaroscopic parameter is calculated from the analysis of at least two millimetres in the centre of the nailfold, by evaluating the first row of capillaries in each finger from 2nd to 5th.
The Microangiopathy Evolution Score (MES) (sum of scores of progression parameters: capillary number, abnormal shaped/ramified capillaries, capillary bed disorganization - Score 0-9) may be calculated to follow the scleroderma microvascular damage.[5] However, at least the simple capillary number per linear millimetre should be counted, as well as larger capillary diameters measured, to monitor microangiopathy in systemic sclerosis.[4,6,7]

REFERENCES:

[1] Smith V, et al. J Rheumatol 2013;40:2023-8.
[2] Ingegnoli F, et al. Microvasc Res 2013;89:122-8.
[3] Cutolo M, et al. Best Pract Res Clin Rheumatol 2013;27:237-48.
[4] Cutolo M, et al. Microcirculation 2018;25:e12447.
[5] Sulli A, et al. Ann rheum Dis 2008;67:885-7.
[6] Cutolo M, et al. Arthritis Rheumatol 2016;68:2527-39.
[7] Trombetta AC, et al. J Rheumatol 2016;43:599-606.

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WEDNESDAY, 12 JUNE 2019

16:15:00 – 17:45:00

Bringing digital health care solutions to patients

SP0027 **E-HEALTH REDEFINES THE RELATIONSHIP BETWEEN PATIENTS WITH RMDS AND HEALTH CARE PROFESSIONALS**

Paul Studenic. *Medical University of Vienna, Internal Medicine 3, Division of Rheumatology, Vienna, Austria*

By definition of the World Health Organization (WHO), e-health relates to the use of information and communication technologies for health services. This incorporates digital patient charts, access to their respective health records by the patient and treating physicians as well as medical apps (applications) for monitoring of health parameters and interacting with health care professionals and peers. The use and initiatives and legislations concerning e-health have become increasingly wide spread across the world. With the continued popularity of smartphones in recent years, both smartphone applications and social media are progressively used. In 2018, worldwide users of social media were estimated at 3.196 billion, accounting for 42% of the global population. Social media use has grown enormously in the last decade, with a plus of 13% in 2017 alone. More than half and two thirds of the world's population are connected to the internet and having a mobile phone respectively. The roll-out of mobile solutions, affordable smartphones and broadband internet in remote areas on the globe allow for quicker and more specialised medical encounters. These developments enable people also to conveniently interact, access knowledge and take part in continued medical education regardless of geographical location. Mobile health (m-health) services range from toll free emergency numbers or health call centres (available in 75% of WHO countries) to treatment adherence and surveillance programs (48% of WHO countries). Fields, like radiology apply telehealth already very successfully, which leads to greater health equity globally. Therefore, e-health provides people with health conditions, particularly chronic conditions such as rheumatic and musculoskeletal diseases (RMDs), with new opportunities to identify information about their disease and treatment, as well as the ability to connect.
The use of e-health solutions for collecting patient reported outcomes (PRO) enables patients to more realistically depict on how they are doing over time, provides better comparisons and changes the dynamic of feedback and the potential most appropriate time point for clinical encounters. Online health users with rheumatoid arthritis do currently however not represent the general population of people with RA, since there are more often younger, do have shorter disease duration and live in rural areas. At the same time, they define an additional group for clinical trials and have a high willingness to participate, which outlines new avenues for recruitment of patients into trials. Still, continued constant use of m-health applications is less common. One third of people that started using a mobile health app are using it on daily or weekly basis. The use of apps does not always coincide with better outcomes as could be shown in a trial incorporating people with poorly controlled hypertension. This indicates, despite all positive developments and opportunities over the last decade, that there is still a long way ahead to tailor e-health initiatives to result in more optimised work flows for health care professionals and better health management for everyone.

Disclosure of Interests: None declared
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SP0028 **WHAT SHOULD MOBILE HEALTH APPLICATIONS FOR RMD PATIENTS BE LIKE?**

Aurelie Najm. *Nantes University Hospital, Rheumatology, Nantes, France*

Mobile health (mhealth) connects patients, their families and physicians by creating a network with mobile and specialized devices such as wearable sensors, recording health parameters and gathering health data converted and transferred to physicians via medical application interfaces. Apps for people with chronic health conditions have an important role to play in empowering those individuals to become more active in the self- and shared-management of their health. Since rheumatic and musculoskeletal diseases (RMDs) have multi-dimensional consequences on health, the increasing availability of apps have an important role to play in enabling people with RMDs to better self-manage their health. This talk provides insights into the most important aspects to be considered for apps designed for people living with RMDs: features, use, safety, and patient’s views and preferences.

Disclosure of Interests: None declared
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SP0029 **RHEVITAL: CONTROLLING YOUR DISEASE ACTIVITY WITH AN APP**

Corinna Elling-Audersch. *German Leage against Arthritis, NRW, Solingen, Germany*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease requiring long-term treatment with regular monitoring of the ongoing therapeutic process by a rheumatologist to achieve good health outcomes and prevent negative disease impacts.
Objectives: The RheVITAL App is the product of a new and multilayered concept of treatment.
A combination of a team of rheumatologists, physiotherapists, IT specialists and research partners from the German League against Arthritis have all contributed to the development of this research project.
Methods: The presentation will show how this monitoring system improves the treatment of RA individually, monitors the patients on their way to self-empowerment and promotes participative collaboration between patients and rheumatologists.
Results: The patients play an active role in the whole system. The patients are trained about their diseases, their treatment and the medicine they are taking. Furthermore they are given much more information about the German patient organisation.
Conclusion: My talk will consider the function and management of the app, the difficulties as well as the efforts of data security and the role of the patient organisation as a research partner involved in this project.
Disclosure of Interests: None declared
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SP0030 **DEVELOPING E-HEALTH SOLUTIONS FOR PATIENTS WITH PATIENTS**

Susanne Karlfeldt. *Karolinska Institutet, Academic Specialist Center, Center for Rheumatology, Stockholm, Sweden*

Background: At the Center for Rheumatology the Patient's voice and needs are always central in the planning and development of the organization and its' services and structure. The Patient Council at the unit, with representatives from 14 different patient organizations, is a core facility that is always addressed when decisions are to be made that affects the patients. The need of a structure for digital re-visits at the clinic was raised in the Patient Council meeting.
Objectives: To develop a structure for a fully digital re-visit where all the preparations, the actual visit and the documentation and follow up could be conducted using different e-Health solutions and digital tools.
Methods: By first asking the involved patient representatives about desired interfaces and features of the end solution, we could decide on which available tools and structures we could build the digitial re-visit around. A working group including patients, health care providers at the unit and technical staff, together formed the end product.
Results: A fully digitalized structure for re-visits to different health care providers (physicians, nurses, physiotherapists etc) is now up and running with an increasing number of visits every week.
Conclusion: By asking the patients about what is most important for them we focus on solutions and services that the patients really need and ask for. If we involve patients in the process from the very beginning, we know that we are doing the right thing and that we use our resources in the best way.
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WEDNESDAY, 12 JUNE 2019

16:15:00 – 17:45:00

Rehabilitation; opening Pandora's Box

SP0031 **NEWS IN THE WORLD OF REHABILITATION**

Ann Bremander. *RanD Spenshult, Sweden*

The ageing population and the increasing prevalence of chronic diseases is a great challenge for future health care systems. There will be a growing demand for rehabilitation services and a need to strengthen rehabilitation in the health system. According to the World Health Organization (WHO), rehabilitation is "the key for health in the 21st century". In the document *Rehabilitation in health systems* (2017), the WHO presents a number of overarching principles for rehabilitation services: the provision of person-centred care, the continuum of care across different levels of the health care system, and the importance of accessible, affordable care of high quality to everyone in need of rehabilitation. With reference to the WHO overarching principles, I will shortly address and discuss some achievements and challenges in the delivery of rehabilitation services supported by recent and ongoing studies. Rheumatic and musculoskeletal diseases (RMDs) include over 200 diagnoses why the talk will include examples from rehabilitation services given to people with inflammatory arthritis (IA).
Over the last decades, pharmacological interventions has contributed to improved quality of life for a large number of people with inflammatory arthritis (IA). However, a relatively large group of people with IA lives with a persistent disease and experience pain, fatigue, physical disability, impaired work ability and decreased quality of life, emphasizing the need of rehabilitation services. I will discuss advancements and challenges in providing person centered care, in bridging the gap between health care sectors, the challenge to provide evidence of an effective rehabilitation service of high quality and if we provide accessible rehabilitation services according to the need of people with rheumatic diseases.

REFERENCE:

[1] Rehabilitation in health systems. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.

Disclosure of Interests: None declared
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SP0032 **HOW TO MEASURE REHABILITATION**

Alison Hammond. *University of Salford, Centre for Health Sciences Research, Salford, United Kingdom*

Background: Measuring outcomes is fundamental to rehabilitation. A wide range of subjective and objective outcome are available to health professionals, with patient reported outcomes (PROs) being widely used. Fundamental to their use is understanding how to select appropriate measures and interpret results.
Objectives: This talk addresses: how to identify and select patient reported outcomes measures; the COSMIN taxonomy; understanding measurement properties; evaluating fitness for purpose; and understanding cross-cultural and linguistic validation of PROs, to enable PROs to be used across countries. This will be illustrated with an example of a Swedish – English-Dutch-German PRO, the Evaluation of Daily Activity Questionnaire.
Disclosure of Interests: None declared
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SP0033 **RHEUMATOLOGICAL REHABILITATION, WHAT'S NEXT**

Thea Vliet Vlieland. *Leiden University Medical Center, Orthopaedics, Rehabilitation and Physiotherapy, 2300 RC Leiden, Netherlands*

Over the past years, there have been major changes in the delivery of rheumatology rehabilitation and advances in its evidence base. To make rheumatology rehabilitation future-proof, a number of developments in the medical treatment of people with rheumatic and musculoskeletal diseases (RMDs), health systems and society as a whole need to be taken into account with the planning of services and their evaluation and the training of health professionals in rheumatology (HPRs).
Regarding the health status and needs of people with RMDs, their profile has changed markedly over the past decades, to a large extent due to improvements in the medical treatment. But some patients may not respond well to treatment, and for those who do, there may still be challenges to keep up with the increasing demands of our society.
For reasons of transparency, quality and efficiency there is a need to demonstrate the added value of rehabilitation, by working along defined rehabilitation care pathways. But care also needs to be personalized, tailored to a person's individual situation, abilities and needs. This includes, among others, that people with RMDs must be involved in any treatment decision, requiring a specific level of health literacy.
The actual delivery of rehabilitation services by means of extensive inpatient or outpatient trajectories is under pressure in many health care systems, for economic reasons but also because treatment in one's own environment whenever possible, is preferred by many people with RMDs. For that purpose, adequate use of digital interventions, but also seamless care involving primary care clinicians with specific expertise is needed.
All of the abovementioned developments require specific competences of HPRs, not only including the optimal assessment and treatment of individual people with RMD, but also makes a strong appeal to e.g. their communication, advocacy and organizational skills and abilities to monitor the quality of their practices and redesign when needed.
This presentation addresses current and future challenges for HPRs in rheumatology rehabilitation and how they can anticipate to be prepared for the next phase.

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WEDNESDAY, 12 JUNE 2019

18:15:00 – 19:45:00

Personalised medicine in rheumatic disease

SP0034 RA-MAP. PATIENT STRATIFICATION IN RA

John Isaacs. *Newcastle University, Institute of Cellular Medicine, Newcastle upon Tyne, United Kingdom*

Background: When we assess rheumatoid arthritis in the clinic we quantify inflammation. Apart from measuring auto-antibodies we do not assess the immune system.[
Objectives: The MRC/ABPI RA-MAP study was an academia-industry consortium designed to characterise the immune dysregulation that presents clinically as RA[1]. Key questions were:
o Are there baseline immune markers of prognosis/therapeutic response?
o What is the molecular signature of the disease state (is there an immune correlate of inflammation)?
o Can 'RA' be defined in terms of immune dysregulation and are there distinct subtypes?
Methods: RA-MAP was a systems immunology analysis of 275 patients with seropositive, treatment-naive early RA (the TACERA cohort). Patients were assessed at baseline and every 3 months for up to 18 months. At each visit, clinical samples were collected for transcriptomic (blood), proteomic (blood) and metabolomic (blood and urine) analyses. Peripheral blood mononuclear cells were characterised by flow cytometry. Clinical and demographic information was collected at each visit. Primary analyses addressed the key questions by seeking associations between immune parameters and disease activity or disease state.
Results: Latent class analysis of clinical data revealed three main disease trajectories[2]. Transcriptomic and systems approaches highlighted at least two subtypes of seropositive RA. Proteomic analyses also supported multiple RA subtypes. Metabolomic analyses revealed prognostic baseline signatures. Flow cytometry revealed a reduction in peripheral blood mononuclear cell complexity as disease became less active. Combinatorial analyses of different datasets is currently underway.
Conclusion: RA-MAP has provided important insights into the immunological and molecular heterogeneity of RA. Our findings require replication and validation, and some analyses are ongoing. RA is the consequence of dysregulated immunity characterized by distinct molecular 'endotypes'.

REFERENCES:

[1] Cope AP, et al. The RA-MAP Consortium: a working model for academia-industry collaboration. Nat Rev Rheumatol 2018;14:53-60. doi: 10.1038/nrrheum.2017.200
[2] Tom BDM, et al. Novel methodology to discern predictors of remission and patterns of disease activity over time using rheumatoid arthritis clinical trials data. RMD Open 2018;4:e000721. doi:10.1136/rmdopen-2018-000721

Disclosure of Interests: John Isaacs Grant/research support from: Pfizer, Grant/research support from: Pfizer, Consultant for: Abbvie, Pfizer, Roche, Galvani, Merck, Gilead, Eli Lilly, Amgen, Janssen, Celltrion, NAPP, Consultant for: Abbvie, Pfizer, Roche, Galvani, Merck, Gilead, Eli Lilly, Amgen, Janssen, Celltrion, NAPP, Speakers bureau: Abbvie, Pfizer, Eli Lilly, Speakers bureau: Abbvie, Pfizer, Eli Lilly
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SP0035 PRECISION MEDICINE IN PSA

Yoshiya Tanaka. *University of Occupational and Environmental Health, Japan, The First Department of Internal Medicine, KItakyushu, Japan*

Background: Biological DMARDs targeting particular molecules relevant to pathological processes have revolutionized the treatment of rheumatoid arthritis (RA) and clinical remission is now realistic targets. However, several issues to be addressed still remain. First, less than half of patients who are treated with methotrexate and biological DMARDs achieved remission defined by stringent composite measures. Second, from multiple biological DMARDs, how to select the most appropriate treatment in each patient remain unclear. Third, how to expand the treatment strategies learned from RA to other rheumatic and/or systemic autoimmune diseases are still under investigations.
Objectives: Psoriatic arthritis (PsA) is a typical complication of psoriasis that causes irreversible destruction and dysfunction of joints and/or the spine and appropriate and timely intervention is prerequisite to inhibit progress in the damages. Various cytokines including IL-12, IL-23, IL-17 and TNF play important roles in the pathogenesis of PsA. Therefore, biological DMARDs targeting these key effector cytokines are currently available and actually effective in supporting the resolution of enthesitis and subsequent arthritis as well as damages of spine/joint in PsA.
Methods: We have compared efficacies of biological DMARDs in PsA patients who were treated according to 2015 EULAR recommendations and whose biological DMARDs were strategically selected based on peripheral blood lymphocyte phenotyping using 8-colour flow cytometry with specific focus on helper T cell subsets.
Results: Patients with PsA were divided to 4 groups by the dominancy of Th1- and Th17-phenotypes and biological DMARDs were stratified in each subgroup: an anti-p40 antibody to the activated Th1 cell-predominant patients, anti-IL-17 antibodies to the activated Th17 cell-predominant, IL-17 inhibitors or TNF inhibitors to the Th1/Th17-high, and TNF inhibitors to the Th1/Th17-low patients. Significant improvement of simplified disease activity index (SDAI) and psoriasis area and severity index by both the standard treatment and the strategic selection of biological DMARDs after the 6-month treatments. It is noteworthy SDAI values were improved in the vast majority of patients in the strategic treatment group, whereas the values were sustained in some patients despite standard biological DMARDs.
Conclusion: Although accumulation of evidence and development of new markers are expected, the obtained results indicate potential for precision medicine via the strategic selection of different biological DMARDs for PsA based on the phenotypic differences in peripheral helper T cells.

REFERENCES:

[1] Miyagawa I, Nakayamada S, Nakano K, Kubo S, Iwata S, Miyazaki Y, Yoshikawa M, Yoshinari H, Tanaka Y. Precision medicine using different biological DMARDs based on characteristic phenotypes of peripheral T helper cells in psoriatic arthritis.Rheumatology (2019) 58: 336-344.
[2] Tanaka Y. Psoriatic arthritis in Japan: difference in clinical features and approach to precision medicine. Clin Exp Rheumatol (2016) 34, 49-52.

Disclosure of Interests: Yoshiya Tanaka Grant/research support from: Abbvie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Ono, Taisho-Toyama, Takeda, Speakers bureau: Abbvie, Asahi-kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Eisai, Glaxo-Smithkline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer Japan Inc, Sanofi, Takeda, UCB, YL Biologics
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SP0036 MASTERPLANS – TAILORING SLE FOR THERAPY

Ian N. Bruce. *University of Manchester, United Kingdom*

Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease which is highly heterogeneous in its clinical manifestations and also in its response to specific therapies. Across a number of trials of novel agents, overall response rates are approximately 40-60% and in the past almost 60 years only one drug (belimumab) has been licensed for use in SLE. Current therapy is therefore based on a 'trial and error' approach frequently involving glucocorticoid cotherapy. Delayed and poor control of inflammation results in organ damage, cardiovascular disease and glucocortocoid toxicity. We established a consortium of academia and industry partners (MAximizing Sle ThERapeutic PotentiaL by Application of Novel and Stratified approaches (MASTERPLANS) with the aim of identifying key endotypes associated with response and low disease activity on particular therapies.
Objectives: Our consortium is addressing the hypothesis that strata exist within SLE populations that will enable more targeted use of existing and novel therapeutic agents and improve response rates. Specifically, B-cell related biomarkers including dynamics and function predict responses to mycophenolate mofetil (MMF) and B-cell targeted biologics and interferon signature/pathway dynamics identifies patients with poorer responses to these agents.
Methods: Our approach will firstly be to re-analyse data already available from large studies and trials to identify key predictive factors of response. Also, using data from a large UK cohort, the BILAG-Biologics Register, we will assess clinical factors and biomarkers that predict response and low disease activity. Combining results from these studies with that gained from previous studies will enhance our ability to identify endotypes of response.
Conclusion: Identifying biomarkers of response will allow better selection of therapy for individual patients. Using the right drug at the right time will improve control of inflammation for patients with SLE and contribute to improving long-term outcomes.
Disclosure of Interests: Ian N. Bruce Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline,

ILTOO Pharma, MedImmune, Merck Serono, Speakers bureau: GlaxoSmithKline, UCB Pharma
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SP0037 **USING GENETICS IN PERSONALISED MEDICINE IN RHEUMATIC DISEASES**

Anne Barton. *University of Manchester, Centre for Musculoskeletal Research, Manchester, United Kingdom*

Background: For all treatments available for rheumatoid arthritis (RA), none are effective for all patients. For many drugs, patients are given 3-6 months of treatment before a decision is made regarding efficacy and, for those in whom the treatment does not work, that can be a period of on-going disease activity, exposure to the risk of side effects and possible accumulation of joint damage, all of which impact quality of life. Stratified medicine approaches aim to better target treatments to those most likely to respond. However, currently, CRP/ESR are the only biological markers (biomarkers) routinely used to inform whether therapy is required and RF/ACPA status are often considered.
Objectives: To update in progress of using genomic approaches to inform treatment selection in rheumatoid arthritis
Methods: National and international precision/stratified medicine programmes are investigating whether genetic and epigenetic biomarkers could help in the selection of therapies and progress will be reviewed.
Results: Recent studies have developed new outcome measures to assess treatment efficacy for controlling synovitis, confirming previous findings from genetic studies of heritability. Issues around the best tissue to sample, the predictive ability of a test and confounding factors including adherence will be considered and emerging biomarkers reviewed.
Conclusion: Matching the right treatments to the right patients is the goal of personalised medicine and potential biomarkers are starting to emerge. However, caution is required as none have so far been proven to be clinically useful or cost-effective.

REFERENCE:
[1] Hensor, et al. Rheumatology 2019; Plat et al, Arthritis and Rheumatol 2019.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8425

WEDNESDAY, 12 JUNE 2019

18:15:00 – 19:45:00

The riddle of adherence

SP0038 **FACTORS IMPORTANT FOR MEDICAL ADHERENCE**

Bart van den Bemt. *Sint Maartensliniek, Netherlands*

Factors important for medical adherence in rheumatic diseases
Disease-modifying antirheumatic drugs (DMARDs) are the cornerstone for the treatment of inflammatory arthritis and fundamental to prevent radiologic progression in patients with rheumatoid/psoriatic arthritis. However, the full benefit of DMARDs can only be achieved if patients follow prescribed treatment regimens. Adherence, or the extent to which patients take medications as prescribed, is however low in chronic medical conditions: approximately 50% of all people with chronic medical conditions do not adhere to their prescribed medication regimens [1,2]. Previous research in patients with rheumatic diseases vary from 30% to 107%, depending on the used measurement method [7].
Thus, improving adherence to DMARDs could dramatically improve the efficacy of drug therapy in rheumatic diseases and reduce costs. However, so far, interventions designed to improve medication adherence are only partly effective in changing medication-taking behaviour [2-5].
To be able to improve adherence, factors should be known that are associated with medication adherence in RA. This will help us to target non-adherent patients and design interventions to improve adherence. Although several studies have examined factors associated with adherence to treatment with DMARDs, hardly any variable was found to be consistently and strongly related to adherence. [6-7].
Despite this, there is evidence that especially patient's need to take medication, prior DMARD use, patient's self-efficacy and information delivered to the patient might be associated with medication adherence.
Overall, two types of non-adherent behaviour are commonly observed: unintentional (due to forgetfulness, regimen complexity or physical problems) and intentional (when the patient decides not to take the treatment as instructed). In case of intentional non-adherence, the decision to take medication is based on a cost benefit analysis weighing the costs/risks of the treatment against the perceived benefits. This implicates that health care professionals should individually assess patient's (un)intentional barriers to take medication and target medication adherence interventions on patient's individual barriers. Thus, besides tackling (unintentional) practical barriers, such as forgetfulness (with for example reminder services), clinicians should also be sensitive to patient's personal beliefs that might impact medication adherence, and should discuss with their patient any concerns that they raise about prescribed medications. This lecture will give insight in the latest insights in the research of factors important for medication adherence and their practical consequences for adherence improving interventions in clinical practice.

REFERENCE:
[1] Sabate E, ed. Adherence to long-term therapies: evidence for action. Geneva, World Health Organization, 2003.
[2] Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, Agoritsas T, Mistry N, Iorio A, Jack S, Sivaramalingam B, Iserman E, Mustafa RA, Jedraszewski D, Cotoi C, Haynes RB. Interventions for enhancing medication adherence. Cochrane Database Syst Rev. 2014; (11)
[3] Galo JS, Mehat P, Rai SK, Avina-zubieta A, Vera MA De. What are the effects of medication adherence interventions in rheumatic diseases: a systematic review. Ann rheum Dis. 2016;75: 667–673.
[4] Demonceau J, Ruppar T, Kristanto P, Hughes DA, Farger E, Kardas P, et al. Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: a systematic literature review and meta-analysis. Drugs. 2013;73: 545–562.
[5] Lavielle M, Puyraimond-zemmour D, Romand X, Gossec L, Senbel E, Pouplin S, et al. Methods to improve medication adherence in patients with chronic inflammatory rheumatic diseases: a systematic literature review. RMD Open. 2018;4: 1–8.
[6] Van den Bemt BJ, Zwikker HE, van den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Rev Clin Immunol. 2012;8(4):337-51.
[7] Pasma A, van't Spijker A, Hazes JM, Busschbach JJ, Luime JJ. Factors associated with adherence to pharmaceutical treatment for rheumatoid arthritis patients: a systematic review. Semin Arthritis Rheum. 2013 Aug;43 (1):18-28. doi: 10.1016/j.semarthrit.2012.12.001. Epub 2013 Jan 24.

Disclosure of Interests: Bart van den Bemt Grant/research support from: UCB, Pfizer, Abbvie; Speakers bureau: Pfizer, AbbVie, UCB, Biogen, Sandoz, Consultant for: UCB, Novartis and Pfizer
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THURSDAY, 13 JUNE 2019

10:15:00 – 11:45:00

Advances in understanding and treating of SLE

SP0039 **WIN: DE-CONVOLUTING THE COMPLEXITIES OF SLE – RECENT INSIGHTS INTO THE PATHOGENESIS**

Mary K. Crow. *Hospital for Special Surgery, Weill Cornell Medical College, Mary Kirkland Center for Lupus Research, United States of America*

Background: SLE remains one of the most complex diseases in medicine, with protean alterations in immune system function contributing to autoimmunity, tissue inflammation and damage, and diverse clinical manifestations. While considerable advances in understanding the molecular pathways and mediators involved in SLE have led to identification of rational therapeutic targets, a full understanding of the upstream etiologic drivers of the disease and how genetic risk and environmental stimuli shape the evolution of the disease and its clinical heterogeneity requires continued investigation.
Objectives: To review recent literature relevant to the etiology, pathogenesis and heterogeneity of SLE.
Methods: Review and synthesis of recent literature.
Results: Recent advances in characterizing the mechanisms of regulation and degradation of endogenous nucleic acids, particularly insights derived from disorders based on a variety of single gene mutations that result in production of type I interferon, suggest potential drivers of type I interferon production in SLE. The functional alterations in many aspects of T and B cell function in patients with SLE, some attributable to type I interferon, continue to be identified. Potential contributions of the microbiome expand our view of candidate disease-enhancing factors. Interest in defining patients at risk for evolving from pre-clinical to clinical disease

that fulfills classification criteria for SLE may help to identify the essential elements of lupus pathogenesis and suggest approaches for disease prevention.
Conclusion: Endogenous nucleic acids have emerged as compelling candidates for drivers of lupus pathogenesis, along with their traditional role as antigenic targets of lupus autoantibodies. Although the clinical heterogeneity of SLE has confounded efforts to successfully test new therapies, advances in identifying sources of nucleic acids stimulating type I interferon and alterations in adaptive immune system function help us move toward a synthetic understanding of disease pathogenesis and suggest that therapeutic regimens targeting both innate and adaptive immune systems might be required to control or prevent disease.

REFERENCES:

[1] Crow MK, Olferiev M, Kirou KA. Type I interferons in autoimmune disease. Annu Rev Pathol. 2019
[2] Uggenti C, Lepelley A, Crow YJ. Self-awareness: Nucleic acid-driven inflammation and the type I interferonopathies. Annu Rev Immunol. 2019.

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SP0040 **HOT: NOVEL PARADIGMS IN THE MANAGEMENT OF SLE**

Thomas Dörner. *Charite Berlin, Berlin, Germany*

Heterogeneity of systemic lupus erythematosus (SLE) remains challenging and, thus, many unmet needs remain, including the development of safer and more efficacious therapies to better control SLE activity resulting in improved outcomes. To develop innovative therapies, we need a far better understanding of its pathogenesis including delineation of clinical phenotypes. Recently, the the lupus community has developed new classification criteria, T2T principles as well as low lupus disease activity and remission definitions to overcome obstacles created by SLE heterogeneity and improve outcomes. New proposals for the histologic classification of lupus nephritis have also been put forward and undergo evaluation. Recent therapeutic advances and clinical developments hold promise for improved treatments in this challenging disease and will be discussed.
Disclosure of Interests: Thomas Dörner Grant/research support from: Eli Lilly, Janssen, Roche, UCB Pharma, Consultant for: Eli Lilly, Janssen, Roche, UCB Pharma, Speakers bureau: Eli Lilly, Janssen
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THURSDAY, 13 JUNE 2019

10:15:00 – 11:45:00

From child to adult care – breaking down the barriers of transition

SP0041 **TACKLING TRANSITION: THE CURRENT LANDSCAPE, AND WHERE WE ARE HEADING**

Stephen Ball. *Manchester University Foundation Trust, Specialist Medicine, Manchester, United Kingdom*

The transition from childhood to adulthood is a key life stage. While the time course of the bio-psycho-social development of young people is continuous, many of the health and social care services with which they may be involved have relatively fixed, rigid structures. This can be challenging for young adults: leading to a sense of marginalisation and alienation. Young people with long term health or social care needs and who require on-going support as they exit childhood are often further challenged by the requirement to move from a children's service (with which they are familiar) to an adult service: one requiring new relationships and with differing expectations.
Evidence supports the view that young people may be lost in the gap between children's and adult services, with a negative impact on longer-term health. Good practice in 'transitional' care (*'a multi-faceted, active process that attends to the medical, psychological and educational/vocational needs of adolescents as they move from child to adult-centred care'*, Blum 1993) can improve engagement and result in positive longer-term outcomes. Developmentally appropriate services recognise young people as a distinct group, subject to constantly changing circumstances. This model considers the young person as a whole: addressing their biological, psychological and social development in the broadest terms. Critically, the approach supports the young person to take an active role in the processes with which they are involved. While developmentally appropriate care and 'transition' are not equivalent, a developmentally appropriate approach to transition has clear benefits: seeing the process as being outcome and skills-based, rather than time-based.
Adolescence and early adulthood are times when life-long health behaviours are set in place; good health for young people is a foundation for good health in later life. There is a need to invest in age appropriate health promotion and youth-friendly health services if we are truly committed to improving young people's health outcomes and the health of the adult population they will go on to form. There is an opportunity to develop and sustain a generational shift in health literacy and health-related behaviours: a real legacy; and an investment in the future.

REFERENCE:

[1] Farre, A, Wood V, Radley T, et al. 2015. Developmentally appropriate healthcare for young people: a scoping study. Arch Dis Child 100: 144-151

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SP0042 **FROM PAEDIATRIC CARE TO ADULT CARE – THE NEEDS OF YOUNG PEOPLE, AND HOW HEALTHCARE PROFESSIONALS CAN FACILITATE OPTIMAL TRANSITION**

Judy Ammerlaan. *University Medical Center Utrecht, Rheumatology and Clinical Immunology, Utrecht, Netherlands*

In this presentation, the learning experiences and reflections of a healthcare team on redeveloping the transitional care for young adults with RMD's are shared.
In the process of redeveloping care, the healthcare team experienced that small steps, driven by patient stories and involvement of patients in all phases from development to evaluation, led to meaningful results.
The eHealth interventions, developed to support the transition and to increase self-management were found to be feasible and evaluated positively by the young adult group. But the healthcare team also experienced that the focus on the patient alone, is not enough to implement self-management interventions and sustain patient centered care in daily practice. How healthcare professionals personally think and feel about patient centered care is essential and needs to be discussed in daily care. It determines the way of being present with attention and commitment in daily health care. It affects the hands, head and heart.
A daily reflection on shared answers of the patient and the health care professional to the question 'what is the most important to you?' may help to implement patient centered care in health practice.
Disclosure of Interests: None declared
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SP0043 **MY IDEAL TRANSITION**

Indra Beer. *Rheuma – Liga Bundesverband e.V., Projekt "Mein Rheuma wird erwachsen!", 53111 Bonn, Germany*

In my lecture I will present the barriers of transition from the young patient's point of view and show possible solutions.
Every year 2.000 young people aged between 16 and 19 arrive at the transition phase in Germany. One third of these young rheumatic patients stop or interrupt their therapy when they have to change from the paediatric rheumatologist to the adult rheumatologist.
In my talk I will focus on significant changes in the lives of young people. This includes e.g. the changes due to education and training, the first partnership or just moving out of the parents' house.
Especially in the difficult phase of transition young people should be strengthened and be made aware of the differences between the doctors treating them and the barriers they will be facing. They should learn to manage themselves and be made sensitive that long-term damage can be avoided.
So, based on my experience I will outline the various support services that are necessary to prepare and accompany young people in that transition phase. Only then, in addition to evidence-based medical care, young people with a rheumatic disease can achieve a successful long-term healthcare outcome that will enable full participation in life.
Disclosure of Interests: None declared
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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Spondyloarthritides and vasculitis – new perspectives on outcome

SP0044 **WIN: VASCULITIS MAINTENANCE TREATMENT**

Raashid Luqmani. *University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*

Background: Cyclophosphamide and more recently rituximab have transformed the outcome for granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), resulting in survival in most cases. However, patients are at risk of frequent relapses, low grade grumbling disease, drug toxicity and worsening co-morbidity. Historically, prolonged courses of cyclophosphamide (used for both induction and maintenance) increased the risk of malignancy (especially bladder cancer). More limited use of cyclophosphamide, or the use of other agents including rituximab or methotrexate (for milder forms) offer safer but still effective options. The high relapse risk in AAV (especially in GPA) means that maintenance therapy is necessary but there is uncertainty over the most effective, safe long term choice. Maintenance RTX (fixed dose at fixed intervals of 4-6 months) is superior to azathioprine, but it is not clear if combination maintenance is superior to RTX alone. Long term side effects of RTX include hypogammaglobulinaemia and potential for reactivation of JC virus. Reducing the glucocorticoid burden in AAV remains a challenge. We still do not know how long to continue therapy in AAV. Two recent studies provide conflicting opinion on the duration of maintenance therapy using azathioprine on risk of future relapse. The use of low doses of rituximab has recently explored in AAV: in thyroid eye disease, 100mg rituximab is effective. Less frequent dose intervals, as used in rheumatoid arthritis, will not control AAV. Future studies could address optimal long term management of patients with AAV, in order to improve their quality of survival and well-being.
Objectives: To assess the risk of relapse of vasculitis and to review the evidence for the use, effectiveness and toxicity of different maintenance strategies in systemic vasculitis
Methods: A review of published studies of long term outcome in vasculitis and of maintenance therapy in systemic vasculitis
Results: Once remission has been achieved, relapse is increasingly common, perhaps over 70% in some forms of ANCA associated vasculitis such as GPA. A strategy of induction therapy for one year, without any maintenance results in relapse in most cases of limited GPA. A maintenance regimen is recommended in order to avoid recurrence of the disease, but the evidence base for use of maintenance therapies remains limited. Maintenance is different from treatment of a relapse, usually aiming to prevent recurrence of clinical evidence of disease. We will show the evidence for different types of maintenance regimens and the outcomes in terms of relapse and toxicity with a focus on recently completed clinical trials and observational cohorts in a variety of forms of systemic vasculitis
Conclusion: The management disease in systemic vasculitis requires induction therapy but increasingly recognised is the importance of a maintenance regimen. Current and future strategies should explore a mechanism based approach, to selectively modify the underlying immunopathogenic mechanisms.

REFERENCES:

[1] De Groot K, Rasmussen N, Bacon PA, Tervaert JW, Feighery C, Gregorini G, Gross WL, Luqmani R, Jayne DR. Randomized trial of cyclophosphamide versus methotrexate for induction of remission in early systemic antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Rheum. 2005 Aug;52(8):2461-9.
[2] Flossmann O, Berden A, de Groot K, Hagen C, Harper L, Heijl C, Höglund P, Jayne D, Luqmani R, Mahr A, Mukhtyar C, Pusey C, Rasmussen N, Stegeman C, Walsh M, Westman K; European Vasculitis Study Group. Long-term patient survival in ANCA-associated vasculitis. Ann Rheum Dis. 2011 Mar;70(3):488-94.
[3] Jayne D, Blockmans D, Luqmani R, Moiseev S, Ji B, Green Y, Hall L, Roth D, Henderson RB, Merkel PA; Collaborators, Lozano JA, Becker H, Quiroz AC, Carette S, Carrillo-Vazquez S, Cid MC, D'Cruz D, Deodhar A, Flossman O, Garibotto G, Gesualdo L, Hall S, Hauser T, Hellmich B, Kidder D, Kimmel M, Little M, Majdan M, Maksimowicz-McKinnon K, Marder G, Matsievskaia G, Meneses AS, Molloy E, Mueller R, Neuwelt C, Hernandez JR, Specks U, Tesar V, Walsh M. Efficacy and Safety of Belimumab and Azathioprine for Maintenance of Remission in ANCA-Associated Vasculitis: A Randomized Controlled Study. Arthritis Rheumatol. 2019 Jan 22.

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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Can imaging improve outcome in OA?

SP0045 **CAN IMAGING PREDICT PROGRESSORS?**

Jean-Pierre Raynauld. *Institut de Rhumatologie de Montreal, Medicine, Montreal, Canada*

Osteoarthritis (OA) is a highly heterogeneous disease with varying aetiologies, thus the manifestations of knee OA and response to treatment vary. This heterogeneity of clinical presentation and treatment response confounds interpretation of therapeutic clinical trials and complicates the care decisions for clinicians. Identifying factors to define patient profiles likely to progress more rapidly over time may help with subsequent therapeutic decision-making. Such characterisation could also help randomization strategies for clinical trials in attempting to balance comparator groups. Reasonable long-term goals among these rapid progressors would be to offer optimal quality of life and to postpone, if possible, the indication of joint replacement.
Quantitative magnetic resonance imaging (qMRI) can precisely and accurately assess and quantify joint structural changes seen in OA. Such technology should logically help to identify patients with rapid OA progression and some of its predictors. This short presentation shall address whether MRI structural markers can be used to predict knee OA patient hard outcomes such as the total joint replacement.
Data revealed that several articular tissue alterations have shown their potential for predicting patients with a rapid progression; global cartilage thickness/volume loss, presence and severity of meniscal damage, bone curvature, and presence of bone marrow lesions among others. However, clinical and demographics variables such as BMI, severe pain, and clinical knee synovitis and effusion are also strongly associated with articular tissue damage and should also be taken into careful consideration as they may independently also predict OA progression and potentially indication of joint replacement.
Optimizing the selection of patients for whom an intervention with a DMOAD could prevent the development of the disease should lead to better response to treatment. Imaging may assist us at identifying the rapid progressors but should be used in a context of an overall patient assessment that also integrate the co-existing demographic and clinical variables. Such context may assist us in the emergence of personalized or precision medicine for patients suffering from this disease.
Disclosure of Interests: Jean-Pierre Raynauld Consultant for: ArthroLab Inc.
DOI: 10.1136/annrheumdis-2019-eular.8571

SP0046 **CAN IMAGING MONITOR/DEMONSTRATE TREATMENT RESPONSE IN OA?**

Felix Eckstein. *Institute of Anatomy, Paracelsus Medical University, Imaging and Functional Musculoskeletal Research, Salzburg, Austria*

Background: Treatment for osteoarthritis (OA) should ideally not be limited to ameliorating symptoms, but should include the modification of synovial joint structures that are involved in the disease process (disease modification). Imaging, particularly MRI, has unparalleled ability to evaluate joint structures qualitatively or quantitatively.
Objectives: To discuss 1) Why one should care about structure (and its modification) in OA, 2) Which joint structures may be most relevant to modify, 3) Why quantification of tissue structure is beneficial, 4) To what extent tissue structure in OA can currently be modified by intervention, and 5) Whether translation of structure modification to clinical benefits is realistic?
Methods: Narrative literature review.
Results: A public meeting for the FDA, organized by the Arthritis Foundation in March 2017, concluded that "most importantly, patients want therapies which stop progression whilst alleviating pain and improving function, yet stopping disease progression is their utmost concern and desire for new therapies". Despite other notions, there is good evidence that structural damage of synovial tissues is related to joint pain. Quantification of synovial tissue from serial MRIs can detect longitudinal changes that are too small to be detected by the naked eye. There exist surgical (e.g. joint distraction[1] and high tibial osteotomy), and pharmacological approaches are in development (e.g. FGF 18 or sprifermin[2]), to modify joint structure. Finally, structural change of joint tissues has been shown to be related to knee replacement (KR) as a hard clinical outcome[3].
Conclusion: Quantitative imaging has become a powerful tool for demonstrating structure modification (treatment response) in OA. This may hopefully lead to regulatory approval of disease modifying therapy for OA in the not too distant future.

REFERENCES:

[1] van der Woude JAD, et al. Cartilage 2017: 263

[2] Hochberg M, et al. Osteoarthritis and Cartilage 2018; 26, S26-S27 [abstract]
[3] Eckstein et al. European Radiology 2016: 1942

Disclosure of Interests: Felix Eckstein Shareholder of: Shareholder of Chondrometrics GmbH, Consultant for: Consulting fees from Merck KGaA, Samumed LLC, Abbvie, Bioclinica, TissueGene, Servier, and Roche, Employee of: Employee of Chondrometrics GmbH
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SP0047 **NEW IMAGING TECHNOLOGIES IN OA: WHERE ARE THE ADDED VALUES?**

Philip G Conaghan. *University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*

The exact role for new imaging technologies in osteoarthritis (OA) depends in part on the setting (clinical trials or routine care) and also on the tissues we decide are important to be studied.
In clinical practice, modern imaging such as ultrasound provides a useful adjunct for patients where there is diagnostic uncertainty - the EULAR recommendations for the use of imaging in the clinical management of peripheral joint OA provide an evidence-based background to this use of imaging. The impact of imaging is minimal in guiding choice of therapy as our therapeutic options (outside of surgery) are very limited.
In clinical studies and trials, there are a number of imaging modalities that provide insights into a range of OA tissues, for both quantification and characterisation. Most techniques have been based on MRI because of its soft-tissue advantages. In OA trials, MRI-based quantification methods provide improved responsiveness advantages over semi-quantitative scores, which have served an important role in highlighting the multi-tissue nature of OA and frequency of pathology. Using appropriate sequences, manual segmentation of cartilage or contrast-enhancing synovitis can be quantified, and dynamic-contrast enhanced images can also be used to provide volumetric and pharmacokinetic assessments of the synovium. Using such information, we now know how to power studies for cartilage thickness endpoints.
A number of MRI techniques have been developed to study cartilage composition, such as T2mapping and T1rho. They have provided insights into structural deterioration, but are limited by technical aspects which make them difficult to apply in multicentre clinical trials.
Artificial intelligence and supervised machine learning have promised much in medicine, but in MSK imaging there has been some useful applications. Early technology applied 2D statistical shape models (SSMs) to X-rays, usually of the hip, providing novel information on bone shape. However the advent of 3D MRI or CT-based SSM technology has provided the ability to do automated quantification of large OA datasets. One of the most interesting tissues studied to date has been 3D bone shape. Studies have shown changes in bone shape are more responsive than radiographic joint space narrowing or even MRI quantitative cartilage thickness, predict incident radiographic OA, and that bone shape is associated with subsequent joint replacement. Recent work has shown a relationship between bone shape and bone marrow lesions, though these likely represent different elements of subchondral bone pathology. Work is just beginning on other relevant tissues such as the meniscus, and on other OA joints.
Disclosure of Interests: Philip G Conaghan Consultant for: Flexion Therapeutics, AbbVie, Medivir, Merck Serono, Novartis, GlaxoSmithKline
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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Can drugs and surgery help people with joint pain increase activity?

SP0048 **CASE 1 PRESENTER: ALL THESE PAINKILLERS AND STILL NOT GOING ANYWHERE**

Kristine Røren Nordén. *Diakonhjemmet hospital, Norwegian National Advisory Unit on Rehabilitation in Rheumatology and Norwegian National Unit for Rehabilitation for Rheuamtic Patients with Special Needs, Oslo, Norway*

Background: The session will present a case history of a 24 year-old male presenting with axial Spondyloarthritis and extensive pain problems. He had been treated with biological medication for a while, had a low inflammatory burden, but experienced persistent pain. Furthermore, he was on sick leave from his job as an electrician and had a very low physical activity level. The patient was admitted for a 3-week in-patient rehabilitation stay at the Norwegian National Unit for Rehabilitation for Rheumatic Patients with Special Needs. The unit offers person-centered, specialized interdisciplinary in-patient rehabilitation for patients with inflammatory rheumatic disease. Target group is patients with complex illness challenges and increasing function- or activity problems.
The rehabilitation was planned and organized through close cooperation between the patient and the specialized interdisciplinary team. Relationship between analgesics, pain and physical activity was a central issue in the rehabilitation process. The session will outline the patient response to comprehensive treatment modalities including changes in medication and participation in physical activity and exercise.
Objectives:
• To present the patient history
• To present results of the interdisciplinary examination
• To present the patient's specific goals for the rehabilitation process
• To present experiences with pharmacological and non-pharmacological treatment modalities for this patient
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8576

SP0049 **CASE 1 DISCUSSANT: DISCUSSION OF HOW ANALGESIC USE RARELY PROVIDES COMPLETE PAIN RELIEF, IS NOT SUFFICIENT TO ENABLE ACTIVITY, MAY BE A BARRIER TO ACTIVITY, AND CAN DETRACT FROM OTHER EFFECTIVE INTERVENTIONS**

Silje Halvorsen Sveaas. *Diakonhjemmet Hospital, Norwegian National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway*

All these painkillers and still not going anywhere: Pain is the cardinal symptom of rheumatic diseases, and is reported as the most important health aspect for this patient group.[1] Hence, analgesics is a part of the management for many patients with rheumatic diseases. Pain may be a barrier for physical activity, [2] and patients with rheumatic diseases is reported to have a lower physical activity level than the general population.[3]
At the same time, it is well known that physical activity has many benefits for this patient group. Physical activity may lower the burden of the disease[4], may prevent co-morbidities such as cardiovascular diseases, diabetes and osteoporosis, and has beneficial effects on psychological health.[2,3] The aim of this lesson will be to present a case history of a patient with extensive pain problems and discuss the treatment options based on relationship between analgesics, pain and physical activity.
Objectives:
• To discuss the effect of analgesics on activity
• To discuss the use of painkillers in connection with exercise
• To discuss pain tolerance during exercise
• To discuss the effect of physical activity on pain

REFERENCES:

[1] Heiberg T, Lie E, van der Heijde D, Kvien TK. Sleep problems are of higher priority for improvement for patients with ankylosing spondylitis than for patients with other inflammatory arthropathies. Ann Rheum Dis. 2011;70(5):872-873.
[2] Rausch Osthoff AK, Niedermann K, Braun J, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis. 2018;77(9):1251-1260.
[3] Cook MJ, Bellou E, Bowes J, et al. The prevalence of co-morbidities and their impact on physical activity in people with inflammatory rheumatic diseases compared with the general population: results from the UK Biobank. Rheumatology *(Oxford, England).* 2018;57(12):2172-2182.
[4] Sveaas SH, Smedslund G, Hagen KB, Dagfinrud H. Effect of cardiorespiratory and strength exercises on disease activity in patients with inflammatory rheumatic diseases: a systematic review and meta-analysis. Br. J. Sports Med. 2017;51(14):1065-1072.

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SP0050 **CASE 2 PRESENTER: SITTING AROUND ON A NEW JOINT**

Maaike Gademan. *LUMC, Orthopaedics and Clinical Epidemiology, Leiden, Netherlands*

The end-stage treatment for hip and knee osteoartritis is arthroplasty. The main aims of this treatment are to improve pain and joint functioning. It is thereby conceivable that patients should become more physically active after surgery.

Although the literature on the outcomes of total hip and knee arthroplasty (THA and TKA) is vast, relatively little is known about physical activity levels of OA patients undergoing surgery.
This presentations summarizes the state-of-the-art literature on the physical (in) activity level of patients with an indication for TKA or THA and its determinants, and the changes of physical (in)activity levels after surgery. These results are presented taking into account the activity levels of the general population. The presentation will end with an informal quiz on physcial (in)activity in THA and TKA patients.

REFERENCES:
[1] Meessen JM, et al. Rheumatol Int. 2017 Feb;37(2):219-227.
[2] Mills K, et al. Physiotherapy. 2019 MAR;105(1):35-45.
[3] Hammett T, et al. Arthritis Care Res. 2018 Jun;70(6):892-901.
[4] Lee J, et al. Artitis Care Res. 2015;67(3):366-373.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8482

SP0051 **CASE 2 DISCUSSANT: DISCUSSION OF HOW A LARGE PROPORTION OF PEOPLE DO NOT BECOME ACTIVE AFTER JOINT REPLACEMENT DESPITE ADEQUATE PAIN RELIEF, REASONS, NEGATIVE CONSEQUENCES OF REDUCED ACTIVITY AND POSSIBLE APPROACHES**

Thea Vliet Vlieland. *Leiden University Medical Center, Orthopaedics, Rehabilitation and Physiotherapy, 2300 RC Leiden, Netherlands*

The literature on the effect of total hip and knee arthroplasty (THA and TKA) on the amount of physical activity is scanty, with various studies suggesting that physical activity levels do not increase after surgery. These results raise several questions, such as: Are patients who will undergo or underwent THA or TKA more or less physically active than the general population? And, if not, should they become more physically active, what are barriers and facilitators for physical activity levels, what would be the potential benefits? Who are the stakeholders that should be involved in the promotion of physical activity in this patient group? These, and other questions will be highlighted in an interactive discussion with the attendees of the session.

REFERENCES:
[1] Pellegrini CA, et al. Disabil Rehabil. 2018;40:2004-2010.
[2] Naylor JM, et al. Arthritis Care Res (Hoboken). 2019;71:207-217.
[3] Hodges A, et al. Clin Rehabil. 2018;32:1271-1283.

Disclosure of Interests: None declared
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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

My joints hurt and I'm overwhelmingly tired – fatigue in rheumatoid arthritis

SP0052 **FATIGUE IN RHEUMATOID ARTHRITIS: WHAT IT IS AND HOW TO ASSESS IT?**

José Antonio P. da Silva. *Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal*

Background: Fatigue is a frequent and important symptom in rheumatoid arthritis (RA), and it is associated with significantly reduced health-related quality of life, thus contributing to the impact of disease upon patients' lives.
Objectives: To collect, summarise and interpret available evidence on the nature of fatigue and the best ways to assess it in Rheumatoid Arthritis
Methods: A systematic literature research was performed in trying to (i) to synthesize the role of fatigue in the global impact of rheumatoid arthritis; (ii) describe validated instruments and their psychometric properties as measures of fatigue among patients with RA; and finally (iii) propose a clinically meaningful, valid and feasible process to measure fatigue in clinical practice.
Results: Fatigue has a major relevance in the overall burden of disease in RA.
Several instruments have been validated o measure it, but no consensus has yet been reached to recommend a "gold-standard".
Conclusion: Although fatigue is recognized by the rheumatology community as an important consequence of RA and a major gap in its current management of the disease, it has not been easy to measure and grasp. The problem seems to reside in the multidimensional causality and subjetive nature of this phenomenon, which may warrant dedicated measures and interventions.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8454

SP0053 **HOW TO PREVENT AND MANAGE FATIGUE IN PATIENTS WITH RA**

James Galloway. *King's College London, Inflammation Biology, London, United Kingdom*

Background: Fatigue is, similar to pain, a subjective symptom that occurs in many different diseases, particularly in patients with RA. Indeed, RA patients consistently report fatigue as one of the most disabling features of the disease (second only to pain). Fatigue is multifactorial in origin and reflects a complex construct of psychological, biochemical and physiological processes.
Objectives: If we are to effectively support our patients with RA, we must address fatigue. This requires understanding of which of our interventions work. At the end of the talk you should be familiar with how you can help manage fatigue, know which non-pharmacological interventions have a robust evidence and be aware of the impact of our different mode of action targeted RA therapies upon fatigue. For most our patients, a multimodal approach is needed.
Methods: This talk will present a narrative review of the evidence base around fatigue interventions in RA.
Disclosure of Interests: James Galloway Consultant for: Pfizer Inc
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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Molecular fingerprinting

SP0054 **DECONVOLUTION OF THE IMMUNE RESPONSE**

Lars Rogge. *Institut Pasteur, Immunoregulation Unit, Immunology Department, 75015 Paris, France*

Background: Anti-TNF therapy has revolutionized treatment of many chronic inflammatory diseases, including rheumatoid arthritis, Crohn's disease and spondyloarthritis (SpA). However, clinical efficacy of TNF-inhibitors (TNFi) is limited by a high rate of non-responsiveness (30-40%) both in SpA and other diseases, which exposes a substantial fraction of patients to important side-effects without clinical benefit. Despite TNFi having been used extensively for many years, it is still not possible to determine which patients will respond to TNFi before treatment initiation.
Objectives: In this study, we have tested the hypothesis that the functional analysis of immune responses of patients before and after anti-TNF therapy may not only improve our understanding of the molecular mechanisms of TNF-blocker activity, but also identify correlates of therapeutic responses in SpA patients.
Methods: To facilitate the potential translation of our findings into a clinical setting, we have used standardized whole-blood stimulation assays ("TruCulture" assays; Duffy et al., 2014), and have minimized sources of pre-analytical variability, implementing a highly sensitive and robust pipeline to assess immune functions in patients.
Results: We show that anti-TNF therapy induces profound changes in patients' immune responses, affecting predominantly several innate immune pathways. Of note, all these effects could be measured in stimulated, but not in resting immune cells, and were already detectable early, after a single TNFi injection. Modular transcriptional repertoire analysis revealed that TNFi affect immune responses via multiple mechanisms, such as directing monocyte/macrophage polarization and the inhibition of a TNF- and IL-1-dependent feed-forward loop of NF-kB activation.
On the other hand, the action of anti-TNF treatment was surprisingly selective, in that it did not affect the IL-6/Th17 or Th1 arm of the patients' immune response. These findings have important implications for therapy, given the recent approval of anti-IL-17 antibodies as an alternative agent for the treatment of several chronic inflammatory diseases.
To investigate the concept that the immune status of a patient will define their response to TNFi treatment, we have used machine-learning algorithms to identify, in whole-blood stimulation assays, immunological transcripts that correlate with clinical efficacy of TNFi. We found that high expression, before treatment initiation, of molecules associated with leukocyte invasion/migration and inflammatory processes predisposes to favorable outcome of anti-TNF therapy, while high-level expression of cytotoxic molecules was associated with poor therapeutic responses to TNF-blockers.
Conclusion: These findings suggest that SpA patients whose immune response is characterized by strong, NF-kB-mediated inflammation are more likely to benefit

from TNFi treatment than patients with an active T/NK-cell component. This proof-of-concept study establishes a new framework to explore patient stratification in chronic inflammatory diseases according to the patients' immune phenotype.

REFERENCE:

[1] Duffy, D., et al. Functional Analysis via Standardized Whole-Blood Stimulation Systems Defines the Boundaries of a Healthy Immune Response to Complex Stimuli. Immunity 40, 436-450 (2014).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8574

SP0055 **CLINICAL MULTI-OMICS**

Timothy R. Radstake. *University Medical Center Utrecht, Netherlands*

It is becoming clear that the field of medicine needs to change to stay affordable. One way of doing that is by optimizing the patients journey with true personalized medicine approaches. In other words, how to give every patient the right drug, at the right moment for the optimal duration. Recent advances in molecular techniques have truly revolutionized research into molecular fingerprinting – classification of clinical phenomena on the basis of a molecular basis rather than a diagnosis based on organ, symptoms or clinical criteria. This makes personalized medicine reachable within the coming years.
In my presentation I will dive in to the various molecular technologies (multi-omics) to achieve molecular fingerprinting of patients. Next, I will explain the computational techniques necessary to process the big data originating from the molecular processes enabling researchers to visualize big data from clinicians and patients. Finally, I will provide several examples of how these exercises might improve care for patients covering the space of rheumatic and musculoskeletal diseases (RMDs).
At the end of my presentation I will show how big data can be used for drug discovery, immune monitoring in clinical trials and/or daily clinical practice as well as drug repurposing. Together, I will provide a glimpse of the future on personalized healthcare within the field of RMDs.
Disclosure of Interests: None declared
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SP0056 **MAPPING GENES TO IMMUNE CELLS**

Kazuhiko Yamamoto. *RIKEN Center for Integrative Medical Sciences, Laboratory for Autoimmune Diseases, Yokohama, Japan*

Background: Many disease susceptibility variants have been recently identified by genome wide association study (GWAS). Germline genetic variations exist before the disease onset and provide us with evidence into the causal relationship of the observed phenomenon and their pathogenesis. In this regards, the majority of GWAS risk variants have been found to function as an expression-quantitative trait locus (e-QTL).
Objectives: We need functional studies aiming at determining the causal genetic variants uncovered by GWAS and finding biological mechanisms underlying the observed statistical associations.
Methods: We established a system to evaluate various subtypes of leukocytes from peripheral blood mononuclear cells (PBMC) from healthy individuals. PBMC are separated with a fluorescence activated cell sorter and are analyzed in a steady state or activated conditions to capture the dynamic responses of gene regulation. Genotyping, RNA-seq, assay for transposase-accessible chromatin using sequencing (ATAC-seq) are performed on each subset. To further investigate the genetic determinants of promotor and enhancer activities, we also perform Cap Analysis of Gene Expression (CAGE) on the corresponding samples.
CAGE is a technology developed in our research center RIKEN in Japan. It relies on random priming and cap-trapping of cDNAs to capture the 5'ends of both polyadenylated and non- polyadenylated RNA transcripts. It thus enables genome-wide identification of transcription start sites (TSSs), which could be used as a portal to annotate and measure the activity of promoters and enhancers (Carninci P. et al Science 2005, Forrest ARR. et al Nature 2014 and other publications of the FANTOM project). Using CAGE, we can map the promoters, enhancers and lncRNAs active in each leukocyte subtypes and correlate their activities with genetic variants.
Results: I will present our ongoing data.

REFERENCES:

[1] Okada Y, et al. Genetics of rheumatoid arthritis contributes to biology and drug discovery. Nature 2014;506:376-381.
[2] Ishigaki K, et al. Polygenic burdens on cell-specific pathways underlie the risk of rheumatoid arthritis. Nat Genet 2017;49:1120-1125.

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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Adults are just grown up children! Discuss

SP0057 **EVERYTHING STARTS IN CHILDHOOD!**

Berent J. Prakken. *University Medical Center Utrecht, Biomedical education, Utrecht, Netherlands*

Background: While part of our future may be determined by our genes, the interaction of our immune system with the environment is crucial for the balance between health and disease. Most of these crucial interaction take place in the early years of life during which the developing immune system settles between self and non-self; danger and non danger or whatever paradigm you may want to apply. This early flexibility and early interactions between developing immunity and the environment hold the key for a health future; and ultimately will be the most effective way for true (very!) early prevention of chronic inflammatory disorders.
Disclosure of Interests: None declared
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SP0058 **GROWING UP CHANGES EVERYTHING!**

Iain McInnes. *University of Glasgow, Institute of Infection, Immunity, and Inflammation, Glasgow, United Kingdom*

Background: There is increasing interest in understanding the impact of age upon the emergence and clinical impact of immune mediated inflammatory diseases. In this lecture I will consider the similarities and distinctions between the presentation of inflammatory arthritis in children and adults.
Disclosure of Interests: Iain McInnes Grant/research support from: AstraZeneca, Celgene, Compugen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Celgene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma
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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Exercise – more than a wonderdrug

SP0059 **HELPING PEOPLE MAINTAIN PHYSICAL ACTIVITY**

Keegan Knittle. *University of Helsinki, Faculty of Social Sciences, Helsinki, Finland*

Background: Regular physical activity (PA) has clear benefits for individuals with rheumatic diseases, but PA levels among these individuals consistently fall below recommended levels. While interventions to increase PA are often successful in the short term, these effects are not generally maintained over time. Therefore, to be able to optimally support PA maintenance, rheumatology health professionals should be familiar with the relevant theory and evidence base for behavioral maintenance.
Objectives: This talk will outline several psychological theories of behavioral maintenance, and present evidence on the interventions and behavior change techniques most strongly associated with physical activity maintenance.
Methods: A review of the most recent and relevant health psychology and behavioral science literature surrounding issues of physical activity maintenance, particularly among individuals with rheumatic conditions.
Results: Theories of behavioral maintenance focus on social and environmental influences, motives, resources, self-regulation, and habits. Several studies will be presented to highlight the influence of these theoretical domains in PA maintenance among individuals with rheumatic disease. Physical activity interventions which specifically target these theoretical domains have the greatest likelihood to produce PA maintenance, and several case studies from successful interventions will be presented.
Conclusions: While helping patients to maintain PA is always a challenge, especially in the face of degenerative or progressive arthropathies, behavioral science

can offer health professionals in rheumatology some theory and evidence-based methods to support PA maintenance in practice.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8517

SP0060 **TOWARDS OPTIMAL INTENSITY**

George Metsios. *University of Glasgow, Institute of Infection, Immunity, and Inflammation, Glasgow, United Kingdom*

Background: There is ample evidence now to suggest that exercise can help ameliorate RMD symptoms and comorbidities. Similar to the prescription of medication, the dosage of exercise should be optimized to achieve the best health benefits. However, a consensus on the dosage of exercise prescription for RMD patients is currently missing.
Objectives: This talk will explore the data required from RMD patients to develop the best exercise prescription, exercise principles and current state-of-the-art, as well as how we can use the current evidence to identify the optimum dosage for the exercise prescription in people with RMDs.
Methods: Suggestions have been synthesized using existing evidence-based resources, including recent systematic reviews and meta-analyses (EULAR, Cochrane Library and peer-reviewed journals publications) as well as randomized controlled trials. Data for the effectiveness of exercise dosage on various different outcomes has been extracted and will be explored.
Results: Different dosages of exercise have differing effects on symptoms of RMDs. The optimal dosage depends on various factors and on the outcome that the exercise prescription aims to improve.
Conclusion: Despite the increasing research on exercise in RMDs, a currently a consensus for the optimal exercise dosage is currently missing. More interdisciplinary research, with a heavy patient involvement, is required in the area.
Disclosure of Interests: None declared
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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Getting a grip on the co-morbidities in gout

SP0061 **GOUT AND ASSOCIATED CO-MORBIDITIES – RELEVANCE TO CLINICAL PRACTICE**

Edward Roddy. *Keele University, Research Institute for Primary Care and Health Sciences, Keele, United Kingdom*

Patients with gout very commonly have multiple co-existent comorbidities. Associations between gout and hypertension, obesity, chronic kidney disease and cardiovascular disease have long been recognised whereas several new comorbid disease associations, such as sleep apnoea and mental health problems, have been described more recently, including lower risk of neurodegenerative diseases. These associations are complex with some comorbidities such as obesity and sleep apnoea predisposing to the development of gout, whereas gout is a risk factor for incident cardiovascular disease and erectile dysfunction. The management of gout is often more complex in the presence of comorbidity and can present a significant therapeutic challenge. This talk will provide an update on the comorbidities that are associated with gout and discuss their implications for the management of gout, in particular for long-term urate-lowering therapy.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8572

SP0062 **CARDIOVASCULAR MORBIDITY AND GOUT – FROM EPIDEMIOLOGY TO THERAPY**

Mariano Andrés. *Hospital General Universitario de Alicante-ISABIAL, Sección de Reumatología, Alicante, Spain*

Gout is an independent cardiovascular risk factor. Patients suffering from gout show a higher incidence of all forms of the atherosclerotic disease, as well as cardiovascular and all-cause mortality. This associates with both comorbidities and urate crystal-led inflammation. Thus, gout, along with being the most common form of inflammatory arthritis in rich countries, carries with significant morbidity and mortality. Proper management is essential. The purpose of this lecture is to analyze the potential strategies aimed to control the cardiovascular risk in patients with gout.
Disclosure of Interests: None declared
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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Treatment is more than drugs

SP0063 **NUTRITION AND RHEUMATIC DISEASES**

Elena Philippou. *University of Nicosia, Life and Health Sciences, Nicosia, Cyprus*

Background: Nutritional therapy could be a promising adjunct to pharmacological therapy in rheumatic disease (RMD).
Objectives: The aim of this talk is to provide evidence and recommendations on dietary management of rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythromatosus, psoriatric arthritis and osteoarthritis.
Methods: Research studies, systematic reviews and recommendations associating diet and RMDs were identified through MEDLINE.
Results: Maintenance or achievement of a healthy body weight is central to RMDs since weight gain is common and often results as a side-effect of pharmacotherapy, further increasing inflammation. Adherence to the Mediterranean diet (MD) by consumption of plant-based foods such as wholegrains, legumes, fruit, vegetables, daily consumption of extra virgin olive oil, and reduced (monthly) consumption of red meat and desserts, is beneficial for all RMDs. The MD should be supplemented with extra omega-3 polyunsaturated fatty acids (PUFAs) and thus consumption of 'fatty fish' such as seabeam, seabass, trout, salmon, sardines or mackerel $\geq$2/week, and walnuts, flaxseeds and chia seeds, daily is recommended, all providing different kinds of omega-3 fatty acids. The MD not only provides all the necessary vitamins and minerals with a balanced ratio of MUFA: PUFA to reduce inflammation, but also has long term benefits on the cardiovascular system. Additional recommendations to manage high cholesterol, include the consumption of plant stanols/sterols, oats, unsalted nuts and soy protein and limiting intake of foods high in saturated and trans fats. It is also recommended that plasma Vitamin D concentration, important for bone and cartilage health, is assessed and a daily supplement is taken if necessary especially during the winter months. Additionally, it is important to consume enough calcium daily, this being equivalent to 3-4 glasses of milk or slices of cheese (preferably low in fat). Finally, evidence on possible relationships between RMDs and diet is limited and inconclusive and dietary restrictions are not recommended. In psoriatric arthritis, a gluten-free diet is recommended only in patients who test positive for serologic markers of gluten sensitivity. Use of unnecessary supplements should be avoided.
Conclusion: In conclusion, adherence to a healthy diet can aid in disease management in RMDs by reducing inflammation and the risk of cardiovascular disease.

REFERENCES:

[1] Aparicio-Soto M, Sánchez-Hidalgo M and Alarcon-de-la Lastra C (2017) An update on diet and nutritional factors in systemic lupus erythematosus management Nutrition Research Reviews 30:118-137
[2] British Dietetic Association (2017) Diet and Osteoarthritis. Available at: https://www.bda.uk.com/foodfacts/OsteoArthritis.pdf. Accessed: 1.3.19
[3] Ford AR, Siegel M, Bagel J, et al. (2018) Dietary Recommendations for AdultsWith Psoriasis or Psoriatic Arthritis From the Medical Board of the National Psoriasis Foundation: A Systematic Review. JAMA Dermatol. doi:10.1001/jamadermatol.2018.1412.
[4] Macfarlane TV, Abbood HM, Pathan E, et al. (2018) Relationship between diet and ankylosing spondylitis: a systematic review. European Journal of Rheumatology 5: 45-52.
[5] Petersson S*, Philippou E*, Rodomar C, Nikiphorou E. (2018) The Mediterranean diet, fish oil supplements and Rheumatoid arthritis outcomes: evidence from clinical trials. Autoimmunity Reviews 17(11):1105 (*joint first authors).

Disclosure of Interests: None declared
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SP0064 **AKTIV-HOCH-R – COMBINING EXERCISE AND FUN**

Nicole Stefan-Schick. *Deutsche Rheuma-Liga Bundesverband e.V., Physical activity, 53111 Bonn, Germany*

Treatment is more than drugs: People with rheumatic diseases know about the health benefits of physical activity. But many studies show that integrating regular exercise into daily life is not always as easy as it seems, especially while experiencing rheumatic pain and feeling physical limitations.
Therefore the German Rheumatism League developed in association with leading experts in sports science and rehabilitation, at the Erlangen-Nürnberg University in Germany, "aktiv-hoch-r".

"aktiv-hoch-r" is an evidence-based exercise programme which imparts knowledge of sports science and motivational aspects. So "aktiv-hoch-r" is not just about the physical exercises, but also includes educational aspects to the programme.
The aim of "aktiv-hoch-r" is to inspire participants at an early stage to make a personal commitment to regular physical activity by helping them to understand the benefits for their long-term health. The programme should help them to self-motivate themselves to continue this for life.
To motivate people with rheumatic diseases to adopt an active lifestyle, "aktiv-hoch-r" uses a holistic approach, involving positive experiences of movement and playful tasks. The focus is on the individual capability of each participant.
So in "aktiv-hoch-r" classes participants learn how to move and how to exercise in a health-promoting way. They learn how to dose load in strength and endurance exercises. They also learn about the effects of regular physical activity on the body. There is a strong focus on self-efficacy, attitude and motivation: participants learn how to develop strategies to motivate themselves to do physical activity.
This presentation provides some theoretical and practical insights into "aktiv-hoch-r".

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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Challenging projects in education and training

SP0065 **EULAR SCHOOL OF RHEUMATOLOGY 2019: A NEW ERA FOR EDUCATION**

Annamaria Iagnocco. *Academic Rheumatology Unit Universita degli Studi di Torino, Academic Rheumatology Centre, Turin, Italy*

The first strategic aim of EULAR for the period 218-2023 is to be the leading provider of education in Rheumatic and Musculoskeletal Diseases (RMDs). The benefits that the rheumatology community gets from high levels of education in the field of RMDs result in an increased knowledge of them as well as in the optimization of their management. This leads to a significant relief to the lives of people with RMDs.
EULAR has traditionally been a strong supplier of education in rheumatology and the launch of the EULAR School of Rheumatology has further increased the EULAR's educational offering and its quality, by providing tailored learning materials, improving access to high quality education in the field of RMDs and developing innovative learning methods and recognised EULAR certifications.
The School of Rheumatology is as a fully integrated operational entity contained within EULAR which combines all educational offers, whether they are live courses, online courses, books, webinars or any other material, under one roof. In addition to the already existing offering, in the last years a team of experts in RMDs and with a solid experience in education has been working in the development of new activities and material addressed to rheumatologists, undergraduates, trainees, teachers, researchers, health professionals, and people with RMDs. Then, these new products, which integrate and further enrich the wide spectrum of existing offering, are tailored to the interests and fields of activity of different targets within the rheumatology community and are presented according to the most innovative educational methods. The use of a new learning management system which perfectly matches the current digital era, allows an optimized presentation and use of the new EULAR education opportunities.
With the modern and rapid developments of the Rheumatology discipline, the EULAR School of Rheumatology is today taking its educational offerings, services and products to a global audience worldwide.

Key Messages:

- The EULAR School of Rheumatology is an innovative educational model with new approaches, products and technologies which reflect the changing needs of the learners whether they are rheumatologists, undergraduates, trainees, teachers, researchers, health professionals, and people with RMDs.
- The EULAR School of Rheumatology represents a new era for education in RMDs.

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SP0066 **HOW TO IMPROVE YOUR TEACHING SKILLS**

Loreto Carmona. *Instituto de Salud Musculoesquelética, Research, Madrid, Spain*

This is not an easy task to do in 20 minutes, but we will try to engage the attendee and to pass the message through. The most important take home message of this lecture will be that "it is the learning, not the teaching, what we must master". Good teachers are, therefore, mere facilitators of the learning process, not the stars.
This lecture will have two parts, one dedicated to teaching in general and a second one on assessment (because assessment style drives learning behaviour).
Four are the principles of teaching in medicine: 1) orientation not only to knowledge but to problem solving, 2) adaptation to needs, 3) evaluation of the efficacy of teaching, and 4) learning should be enjoyable. We will review each one of these principles and how to implement them in our daily teaching. Things like preparing a lesson plan, or tips to engage learners, will be part of this lecture.
In the second part we will outline how to improve assessment and generate good questions.

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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Ultrasound basic I

SP0067 **HOW TO ASSESS US LESIONS FOR GOUT + DEMO**

Sara Nysom. *Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup., Copenhagen Center for Arthritis Research (COPECARE), Glostrup, Denmark*

Gout is the most common inflammatory joint disease in Western developed countries. Diagnosis and monitoring have historically been based upon clinical assessment combined with biochemical results (primarily p-urate) but over the last decade ultrasonography (US) has received increasing attention for these purposes. US has been shown able to detect monosodium urate deposits in both joints and tendons. In 2015 the Outcome Measures in Rheumatology (OMERACT) US Working Group developed definitions of structural lesions in gout. These include double contour sign (deposits of crystals on the surface of cartilage), tophus (larger hyper-echoic aggregation of crystals), aggregates (small hyperechoic deposits) and erosion (1). The double contour sign has been included in the ACR/EULAR 2015 gout classification criteria as a way to visualize urate deposits in joints (2). Furthermore, US can visualize potential concomitant inflammatory aspects of gout since it can visualize both joint inflammation and tenosynovitis.
In this talk the diagnostic properties of US will be described and the potential risk of false positive results due to artefacts or misinterpreted lesions will be discussed. Furthermore, the potential role of US in monitoring of treatment response will be explored.

REFERENCES:

[1] Gutierrez M, Schmidt WA, Thiele RG, Keen HI, Kaeley GS, Naredo E, Iagnocco A, Bruyn GA, Balint PV, Filippucci E, Mandl P, Kane D, Pineda C, Delle Sedie A, Hammer HB, Christensen R, D'Agostino MA, Terslev L; OMERACT Ultrasound Gout Task Force group. International Consensus for ultrasound lesions in gout: results of Delphi process and web-reliability exercise. Rheumatology (Oxford). 2015;54(10):1797-805.
[2] Neogi T, Jansen TLTA, Dalbeth N, Fransen J, Schumacher HR, et al. 2015 Gout Classification criteria: an American College of Rheumatology/ European Leaque Against Rheumatisme collaborative initiative. Ann Rheum Diss 2015; 74: 1789-1798.

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SP0068 US FOR TROCHANTERIC PAIN SYNDROME – CLINICAL USE + DEMO

Ingrid Möller. *University of Barcelona, Instituto Poal de Reumatologia, Barcelona 08022, Spain*

Background: Greater trochanteric pain syndrome (GTPS) is a clinical diagnosis with the typical presentation of chronic intermittent lateral hip/thigh/buttock pain, aggravated with activity and when lying on the affected side. There is a lack of valid/specific diagnostic criteria for GTPS. GTPS can be attributed to a multitude of causes ranging from tendinopathy and/or rupture of the gluteal tendons and/or bursitis, to pathological alterations of the iliotibial band/fascia lata and other nearby anatomical structures located on the lateral part of the hip. To further complicate the diagnostic process, according to different studies, the prevalence of GTPS in adults with lower back pain has been found to be between 20-30%. Alterations of the lumbar biomechanics may interfere in the range of internal rotation of the hip and consequently produce a GTPS and vice versa. Changes in hip range of motion will trigger changes in the dynamics of lower extremities and the spine. Generalized myofascial pain can also be a source of confusion when evaluating patients with GTPS.
Objectives: Understand the clinical anatomy of the lateral hip.
Interpret the US images of the lateral hip
Identify potential pain generators of the lateral hip.
Methods: The study of the static and dynamic sonoanatomy of the different components of the lateral region of the hip can contribute in a relevant way to clarify the diagnosis In the eular guidelines of sonographic musculoskeletal (MSUS) exam published in 2017, the sonographic exam of the lateral hip has been developed in detail and will be discussed during this lecture.
The anatomy against what is often thought is not stagnant knowledge but evolves over the years providing new and useful data applicable in daily clinical practice. The anatomy, both static and dynamic, of the trochanteric region, is complex. For example, the subgluteus maximus bursa, which is frequently incriminated in the GTPS, is located in the posterior facet of the greater trochanter and is related to the iliotibial tract, the fascial contributions of the gluteus maximus and the tensor of the fascia lata muscle to the iliotibial tract and the origin of the vastus lateralis. In order to understand the multifunction and relationships of the different structures of this region means one has to have seen images of them and for that purpose, the human cadaveric dissection is the best tool. Thanks to the fact that the speaker is involved as a professor in the anatomy department at the University of Barcelona, Bellvitge campus, directed by prof M Miguel, the clinical anatomy part will be developed with real dissections made specifically for this lecture.
Results:



Abstract SP0068 – Figure 1

Conclusion: Knowledge of the clinical anatomy needed to understand the relationships between the different structures, the clinical history, and physical examination of GTPS patients and the therapeutic possibilities including ultrasound-guided injections are other steps that lead to an accurate diagnosis of GTPS.

REFERENCES:

[1] anatomy and anthropology: Maribel Miguel, Mike Benjamin
[2] Clinical anatomy: Juan Canoso
[3] Regional musculoskeletal ultrasound: Carlo Martinoli
[4] Möller I, Bong D. Ultrasound-guided interventions in the hip joint. TechniquesIn Regional Anesthesia and PainManagement 2013; 17: 140–149
[5] Möller I, Janta I, Backhaus M, et al The 2017 EULAR standardized procedures for ultrasound imaging in rheumatology.
[6] Annals of the Rheumatic Diseases 2017;**76:**1974-1979.

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SP0069 HOW TO DIFFERENTIATE MINIMAL DISEASE ACTIVITY IN RA + DEMO

Ilfita Sahbudin. *Institute of Inflammation and Ageing, University of Birmingham, Rheumatology Research Group, Birmingham, United Kingdom*

Ultrasound (US) is increasingly utilised as a point-of-care tool to diagnose early inflammatory joint disease, monitor treatment response and detect subclinical inflammation. This is feasible as US can detect joint, and tendon, inflammation before it becomes clinically apparent. Despite the increasing use of US in Rheumatology, the key research question yet to be addressed is defining 'the normal reference value at the joint level.'
Improvement in US technology over the last decade results in acquisition of higher resolution images. US can now detect subtle abnormality in joints of healthy individuals who are asymptomatic. Consequently, the imaging boundary between US changes of normal joints (i.e *physiological changes*), and those of early arthritis joints (i.e. *early pathological changes*) has become unclear. In addition, a proportion of US-defined pathology observed in normal joints may be attributed to age-related changes.
Defining the concept of US-detected 'minimal disease' is crucial to enable investigators identify a threshold (or cut-off) to *differentiate normal physiological from minimal pathological changes* at the joint level. This threshold, subsequently, will be used to evaluate the best sensitivity to detect changes in therapeutic response and assess remission, as well as facilitate diagnosis of early disease.
In order to address this important research question, the OMERACT US SIG has formed the US Minimal Disease Taskforce at the OMERACT 2016 meeting. This collaboration between 24 OMERACT ultrasound centres in 11 countries has successfully recruited more than 600 subjects into the Minimal Disease Study. US data of healthy individuals encompassing synovial hypertrophy, synovial effusion, and Doppler enhancement will be presented.
Disclosure of Interests: None declared
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SP0070 HOW TO PERFORM US-GUIDED INTERVENTIONS + DEMO

Juhani Koski. *Mikkeli Central Hospital, Internal Medicin, Mikkeli, Finland*

Background: Aspiration and injection of joints and soft tissues is an indispensable skill used in everyday practice by the clinical rheumatologist. These tasks are usually conducted by palpation-guided techniques. These procedures are not always successful (1) and thus US -guided interventions have been developed.
Objectives: Are to explain the effect of needle and sound beam angle on needle visualization, describe different techniques of needle insertion under US guidance, to identify different approaches to the target under US guidance and finally to discuss about the accuracy and efficacy of the ultrasound guided technique.
Methods: There are two common methods for US puncturing: semi-guided or indirect method (skin surface marking) and needle guidance under direct sonographic vision (2,3). The scanning plane is optimized for visualization of the target and penetration of the needle should be at least 0.5cm from the transducer. The movement of the needle in the soft tissue should be followed on the screen during the procedure. The needle appears as a bright echoic line if the transducer is oriented longitudinally on the needle, and the needle tip may be followed as it reaches the target. If the ultrasound beam is transverse to the needle, the needle is seen as a bright echoic dot. In case of no visualization of the needle several means are available: steering of the ultrasound beam against the needle (in new machines), curved or virtual convex probe, toeing -in of the probe, shaken the needle slightly and moving the probe a bit from side to side.
Results: According to the clinical and cadaveric studies the ultrasound guided technique is more accurate than the landmark guided technique in the glenohumeral, acromioclavicular, wrist, hand, hip, knee and foot joints and in the tendons of the biceps, wrist, hand hip, knee and ankle (4). Synovial biopsies are more accurate using an ultrasound guided method (5).
Conclusion: Ultrasound is the most applicable and feasible imaging modality for routine clinical use in guiding musculoskeletal procedures. Though many studies have examined the role of imaging guidance for injection there needs to be more examination of how the use of ultrasound prior to injection can alter the pathological and anatomical diagnosis. There is a trend towards an expanded number of advanced applications of interventional musculoskeletal ultrasound which can also be performed by a rheumatologist like nerve blocks or needling of calcifications. Which ultrasound guided technique (direct or semi-guided) is the most appropriate in different anatomical areas and clinical settings remains to be studied. More studies are needed to show the accuracy and efficacy of ultrasound guided injections in different anatomical areas (4).

REFERENCES:

[1] Jones A, et al. Importance of placement of intra-articular steroid injections. BMJ 1993;307:1329-1330.

[2] Koski JM. Ultrasound guided injections in rheumatology. J Rheumatol 2000;7:2131-8.
[3] Fessell DP, et al. Using sonography to reveal and aspirate joint effusions. AJR 2000;174:1353-62.
[4] Kane D, Koski JM. Musculoskeletal interventional procedures: With or without imaging guidance? In Clinical Rheumatology. Best Practice & Research Clinical Rheumatology, 2016:736-750.
[5] Kelly S, et al. Ultrasound-guided synovial biopsy: a safe, well-tolerated and reliable technique for obtaining high-quality synovial tissue from both large and small joints in early arthritis patients. Ann Rheum Dis 2015;74:611-617.

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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Interstitial lung disease in rheumatic diseases and systemic sclerosis

SP0071 **WIN: SYSTEMIC SCLEROSIS – INNOVATIVE TREATMENT TARGETS OR "LOST IN TRANSLATION"?**

Yannick Allanore. *France*

Interstitial lung diseases (ILDs) are a group of heterogeneous disorders, either idiopathic (idiopathic pulmonary fibrosis-IPF) or associated with other diseases, particularly autoimmune diseases, from which systemic sclerosis is the leading disease at risk of developing ILD. It has been proposed that for clinical research and patient management various subsets of fibrosing ILD that have similar biological and clinical behaviours could be merged into a single entity although specificities within each disease remain, with various patterns of lung injury. Nevertheless, the shared part relates to progressive fibrosing ILD leading to progressive decline in lung function and early mortality. In SSc, a recent report from EUSTAR network showed that ILD was nowadays the first cause of death identified as contributing to 17% of deaths (1).

No drugs are licensed for the treatment of ILDs related to autoimmune diseases. Treatment guidelines issued by the European League Against Rheumatism (EULAR) recommend tailored therapy with cyclophosphamide (CYC) for SSc-ILD, in particular for patients with progressive ILD (2). Indeed, 3 randomized controlled trials showed some benefits of using CYC either orally or by infusion route although the effect size was small and the clinical translation of the findings was difficult to establish. The limitations of CYC trials in SSc-ILD led the experts to add that dose and duration of treatment need to be tailored individually dependent on the clinical condition and response. Furthermore, with regards to safety, potential risks of bone marrow suppression, teratogenicity, gonadal failure and haemorrhagic cystitis must be always considered. Beyond standard immunosuppression, the use of high dose CYC, with or without irradiation, but using rescue with stem cells showed some effects on ILD measured through lung function and imaging. Nevertheless, considering the risk of potential treatment-related mortality and morbidity, the EULAR experts recommend that HSCT should be considered for the treatment of selected patients with rapidly progressive SSc at risk of organ failure, two domains which remain to be delineated. Altogether these results suggest that immunosuppressants might be beneficial in the context of SSc-ILD although the right drug, the right dosing and the right patients still need to be defined. In practice, because of SLS2 trial, mycophenolate mofetil has emerged as the leading drug used when a physician aims at treating SSc-ILD. The understanding of SSc and SSc-ILD have improved in the recent years and subset at risk and candidate biomarkers have emerged. Indeed, interleukin 6 has been shown to predict some disease progression including lung involvement. Therefore, targeted therapy against IL6 is an appealing strategy to improve SSc outcomes. If the pivotal trials using tocilizumab had skin as a primary outcome and failed to meet the primary end-point, secondary analyses revealed stimulating lung results that will be showed during EULAR 2019 and discussed within the ILD session. B-cells role has also been scrutinized in SSc with promising data. Therefore, rituximab is used in some SSc patients with various indications according to physician views and experience. EUSTAR has assembled a large group of rituximab treated patients and performed a well-designed observational study that did not show clear evidence supporting some efficacy of rituximab on SSc-ILD although some clues emerged.

The role of antifibrotic drugs (nintedanib, pirfenidone), that showed to slow disease progression in patients with IPF, in patients in other forms of fibrosing ILD remains to be determined. However, several trials are ongoing and the results of the SENSCIS trial evaluating nintedanib in SSc-ILD will be presented during EULAR 2019 and discussed during the ILD session.

Altogether, the available results show some progresses made in the management of SSc-ILD, so far mainly through the use of treatment targeting immune disturbances. Considering the severity and the complexity of SSc pathogenesis and related lung complication, one might anticipate that if trials of antifibrotic therapies are positive, the treatment of SSc-ILD, and maybe of all fibrosing autoimmune ILDs, might involve combination of immunosuppression and antifibrotic therapies.

REFERENCES:

[1] Elhai, et al. Ann Rheum Dis. 2017;76(11):1897-1905.
[2] Kowal-Bielecka, et al. Ann Rheum Dis. 2017;76(8):1327-1339.

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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Diagnostic challenges in vasculitis

SP0072 **IMAGING IN THE DIAGNOSIS OF LARGE VESSEL VASCULITIS**

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Background: Giant cell arteritis (GCA) and Takayasu arteritis (TAK) are large-vessel vasculitides (LVV). Recommendations demanded so far to confirm the diagnosis histologically, particularly in suspected GCA. Biopsy is however invasive, and results are not immediately available. Technology has rapidly improved; and many recent studies suggest that imaging may have comparable diagnosic accuracy.

Objectives: To provide an overview of new developments for ultrasound, magnetic resonance imaging (MRI), computed tomography (CT) and 18-fluorodeoxyglucose positron emission tomography (PET) in diagnosis of LVV and to present new EULAR recommendations on imaging in LVV.

Methods: A systematic literature review and meta-analysis of diagnostic and prognostic studies enrolling >20 patients and investigating ultrasound, MRI, CT or PET in patients with suspected and/or established primary LVV was conducted (1). On this basis, a group of imaging experts, rheumatologists, patients and health care professionals developed EULAR recommendations on imaging in LVV (2). This review refers also to new data after the EULAR recommendations had been published.

Results: In suspected GCA, imaging should be done early, but without delaying treatment. No further diagnostic test (histology or other imaging) is necessary if results of imaging and clinical presentation correspond. Ultrasound of temporal and axillary artery arteries showing a non-compressible 'halo-sign' is the method of first choice in suspected cranial GCA. The meta-analysis showed positive and negative likelihood ratios of 19 and 0.2, respectively, for a final diagnosis of GCA. Good data is also available on MRI of cranial arteries. Ultrasound, MRI, CT or PET can be applied for confirming extracranial GCA. Ultrasound is of limited value for assessing particularly the thoracic aorta. MRI is first choice for suspected Takayasu arteritis, but ultrasound, CT or PET can be also applied. Conventional angiography is not recommended instead for interventions. Imaging might be useful in suspected flare and to monitor damage. There is no convincing evidence to recommend routine monitoring in remission. Imaging should be done by a trained specialist using appropriate equipment.

Particularly ultrasound of cranial arteries showed high diagnostic accuracy in a study for developing new classification criteria. Measuring intima thickness (cut-offs of around 0.4 mm for temporal and 1.0 mm for axillary arteries) may help to improve diagnostic accuracy and to use ultrasound for disease monitoring in trials (3). Reliabilities of sonographers both for evaluating videos and for examining patients directly were very high (4,5). Newer PET technology now allows to also show inflamed temporal, maxillary and vertebral arteries (6). The significance of positive imaging findings in follow-up studies still remains unclear. The incidence of vision loss decreased with the introduction of fast-track clinics. These clinics are increasingly established in centres. They include referral within one working day to a rheumatologist followed by immediate imaging for establishing the diagnosis. Imaging can be done by the rheumatologist (most commonly ultrasound) or by a collaborating department.

Conclusion: Ultrasound, MRI, CT and PET allow to confirm or exclude LVV provided that it is performed by a trained specialist using appropriate equipment. Fast-track clinics using ultrasound are increasingly established in rheumatology.

Ultrasound showed high diagnostic accuracy. Modern PET equipment may also delineate vasculitic temporal, maxillary and vertebral arteries. The significance of follow-up imaging studies in LVV still needs to be determined.

REFERENCES:

[1] Duftner C, et al. RMD Open 2018;4:e000612
[2] Dejaco C, et al. Ann Rheum Dis 2018;77:636-42
[3] Schäfer VS, et al. Rheumatology 2017;56:1479-83
[4] Chrysidis S, et al. RMD Open 2018;4:e000598
[5] Schäfer VS, et al. J Rheumatol 2018;45:1289-95
[6] Nielsen BD, et al. Eur J Nucl Med Mol Imaging 2019;46:184-93

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SP0073 DIAGNOSIS OF GASTROINTESTINAL VASCULITIS

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The gastrointestinal vasculature can be involved by a variety of vasculitis affecting large, medium, small or variable vessel size according to the 2012 revised Chapel Hill consensus nomenclature. Gastrointestinal involvement (GI) is one of the most severe complications of vasculitis requiring intensive immunosuppressive therapy and sometimes revascularization techniques or emergency surgery and may affect a variety of organs including large or small intestines, liver, biliary tract, pancreas, and less frequently, stomach or oesophagus. It can complicate the course of patient with known or with overt suspicion of vasculitis or be the main or even the only manifestation of these diseases.

Clinical manifestations range from abdominal pain, sometimes colicky, that usually worsens after eating to overt signs of bowel ischaemia or perforation with diffuse and constant abdominal pain, reduced peristaltism, abdominal defence and distension, and signs of peritoneal irritation. GI bleeding, frequently in the form of occult blood loss or haematochezia and less frequently melena or rectorragia, is common. Non-specific symptoms such as nausea, vomiting or diarrhoea may be observed. Pancreatitis, cholecystitis or appendicitis may also occur.

In large-vessel vasculitis, including giant-cell arteritis (GCA) and Takayasu disease (TAK), inflammation usually affects the proximal portion of the celiac trunk, hepatic or mesenteric arteries. GI involvement is rare in GCA with only isolated cases or small series having been reported. About 30% of patients with GCA have elevated hepatic enzymes as part of the acute phase response and rarely reflect involvement of the hepatic vasculature. Imaging techniques disclose stenotic or occlusive lesions in 25% of patients with TAK but clinically manifest involvement occur in about 16% of patients. Abdominal pain suggestive of vascular insufficiency is present in about 16% of patients; abdominal bruits can be perceived in 14% but only 4% present with overt signs of mesenteric ischemia. Due to the involvement of the proximal part of the GI branches, the ischemic territories may be extensive but usually progression of vascular occlusion is not abrupt, and due to the size of vessels involved, patients may benefit from percutaneous revascularization procedures if immunosuppressive treatments are not sufficient. Interestingly 5% of patients with TAK also suffer from inflammatory bowel disease, particularly Crohn's disease.

In medium sized vasculitis, such as polyarteritis nodosa (PAN) or Kawasaki disease (KD), multiple muscular artery branches of the GI vasculature can be involved. Abdominal pain is frequent in PAN (35-95% of cases). GI involvement is more frequent in HBV-associated PAN than in idiopathic PAN. About 61% of patient with KD may have GI symptoms but these are severe in 4.6% only. Gallbladder hydrops and appendicular vasculitis may occur. The presence of prominent GI manifestations is more frequent in patients with coronary aneurysms indicating more severe vasculitic disease.

In small-vessel vasculitis, including anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV)(granulomatosis with polyangiitis [GPA], microscopic polyangiitis [MPA], and eosinophilic granulomatosis with polyangiitis [EGPA]) and immune-complex-mediated vasculitis (IgA vasculitis [Henoch-Shönlein purpura] and cryoglobulinemic vasculitis) the microvasculature is segmentally affected and the severity of involvement may be variable in different areas. Among AAV, GI involvement is more frequent in patients with EGPA (35-50%), than MPA (5-30%) or GPA (5-11%). In EGPA, GI involvement can be vascular as in other vasculitis or may be in the form of eosinophilic gastroenteritis or esophagitis. In GPA, in addition to vascular involvement, granulomatous hepatitis or pancreatitis may occasionally occur. Among immune-complex vasculitis, GI involvement is typical in IgA vasculitis, occurring in 50-75% of patients. Although it is usually mild and self-limited, complications including bleeding, ischaemia, perforation or intussusception may appear in 3-5% of patients. Hepatobiliary involvement is uncommon (1.8%). GI involvement is rare in cryoglobulinemic vasculitis but is life-threatening when it occurs.

Among the category of variable vessel size vasculitis, GI involvement in Behçet's disease (BD) may consist of mucosal ulcers, frequently in the distal ileum, similar to inflammatory bowel disease, or involvement of mesenteric artery branches as in other vasculitis. Venous thrombosis involving the liver vasculature or GI tract may also occur in BD.

Vasculitis involvement may be restricted to different portions of the GI tract (gallbladder, appendix, intestines) in patients with no obvious evidence of systemic vasculitis. Gallbladder is the more frequent location and is usually incidentally discovered after surgery. Overt systemic vasculitis may develop in up to 25% of patients during follow-up.

Diagnosis of GI involvement in systemic vasculitis requires clinical suspicion. Imaging (computed tomography [CT]-angiography[CTA] or magnetic resonance angiography [MRA] are crucial in large vessel vasculitis evidencing concentric thickening with contrast enhancement of the vessel wall, along with lumen reduction. In medium vessel vasculitis CT may disclose hepatic, spleen or renal infarcts that reinforce clinical suspicion of vascular disease. However, CTA or MRA may not have enough resolution to evidence involvement of medium-sized branches and conventional angiography is usually needed, revealing vascular stenosis an occlusions as well as microaneurysms. In small-vessel vasculitis, and in all vasculitis conveying intestinal ischemia, CT may reveal thickening of the intestine wall, dilatation, and, in severe cases, pneumatosis of the intestine wall as well as gas in the portal system. Pneumo-peritoneum can be seen in the case of perforation. Ascites is not uncommon in medium and small vessel vasculitis. Occasionally, hemorrhage in the peritoneal cavity due to rupture of aneurysms can be observed. It is important to remark that imaging findings provide strong support to the clinical suspicion of vasculitis based on additional clinical, blood test or serologic findings or evidence of vasculitis elsewhere but similar findings can be observed in the context of a variety of vasculopathies or thrombophilic/embolic disorders that may mimic vasculitis.

Endoscopy is also a useful exploration in some settings. It may detect intestinal purpura, usually in IgA vasculitis, mucosal ulcers or mucosal inflammation. Endoscopic biopsies may reveal eosinophilic inflammation in EGPA but may not be deep enough to disclose inflamed blood vessels and its absence does not exclude vasculitis. In case of surgical complications, a throughout pathologic examination of the removed specimen should be requested in order to evidence of vascular inflammation.

GI involvement in systemic vasculitis is frequently a severe and potentially life-threating complication. Prompt detection and intense immunosuppressive, revascularization or surgical treatment in the appropriate settings are crucial for a successful recovery and prevention of irreversible damage.

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REFERENCES:

[1] Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013 Jan;65(1):1-11.
[2] Soowamber M, Weizman AV, Pagnoux C. Gastrointestinal aspects of vasculitides. Nat Rev Gastroenterol Hepatol. 2017 Mar;14(3):185-194.
[3] Chetty R, Serra S. A pragmatic approach to vasculitis in the gastrointestinal tract. J Clin Pathol. 2017 Jun;70(6):470-475
[4] Schmidt J, Kermani TA, Bacani AK, Crowson CS, Cooper LT, Matteson EL, et al. Diagnostic features, treatment, and outcomes of Takayasu arteritis in a US cohort of 126 patients. Mayo Clin Proc. 2013 Aug;88(8):822-30
[5] Kronzer VL, Larson DP, Crowson CS, Warrington KJ, Ytterberg SR, Makol A, et al. Occurrence and aetiology of gastrointestinal perforation in patients with vasculitis. Clin Exp Rheumatol. 2019 Jan 9. [Epub ahead of print]
[6] Fabi M, Corinaldesi E, Pierantoni L, Mazzoni E, Landini C, Bigucci B, et al. Gastrointestinal presentation of Kawasaki disease: A red flag for severe disease? PLoS One. 2018 Sep 4;13(9):e0202658.
[7] Retamozo S, Díaz-Lagares C, Bosch X, Bové A, Brito-Zerón P, Gómez ME, et al. Life-threatening cCryoglobulinemic patients with hepatitis C: clinical description and outcome of 279 patients. Medicine (Baltimore). 2013 Sep;92(5):273-284.
[8] Hernández-Rodríguez J, Hoffman GS. Updating single-organ vasculitis. Curr Opin Rheumatol. 2012 Jan;24(1):38-45. 9)
[9] Ghodasara N, Liddell R, Fishman EK, Johnson PT. High-value multidetector CT angiography of the superior mesenteric artery: what emergency medicine physicians and interventional radiologists need to know. Radiographics. 2019 Mar-Apr;39(2):559-577.

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SP0074 **DIAGNOSIS OF CEREBRAL VASCULITIS**

Leonard Calabrese. *Cleveland Clinic Foundation, United States of America*

Among all forms of vasculitis, perhaps that affecting the CNS (CNS-V) poses the greatest challenge in diagnosis given the lack of any non invasive high specificity test, the complex and extensive list of mimicking conditions, its inaccessibility for biopsy and its genuine rarity. The diagnosis still requires the presence of an unexplained neurologic sign or symptom(s) following an exhaustive evaluation, evidence of vascular involvement (by direct or indirect angiography) or biopsy and most importantly the meticulous exclusion of all those conditions capable of producing mimicking clinical, radiographic or histologic findings that would confound accurate diagnosis. Despite these challenges CNS-V has been increasingly reported due to a combination of increased diagnostic awareness and advances in diagnostics. Two of these major advances will be discussed including the use of direct vascular wall imaging to differentiate vascular inflammation from spasm or atherosclerosis and the use of next generations sequencing to identify infectious etiologies and obviate the use of biopsy. Clinical examples will be presented.

REFERENCES:

[1] Byram K, Hajj-Ali RA, Calabrese L CNS VasculitiByram K, Hajj-Ali RA, Calabrese L CNS Vasculitis: an Approach to Differential Diagnosis and Management. Review. Long-term outcomes of patients with primary angiitis of the central nervous system. Curr Rheumatol Rep. 2018 May 30;20 (7):37. doi: 10.1007/s11926-018-0747-zs: an Approach to Differential Diagnosis and Management. Review. Long-term outcomes of patients with primary angiitis of the central nervous system. Curr Rheumatol Rep. 2018 May 30;20(7):37. doi: 10.1007/s11926-018-0747-z

[2] Michael R. Wilson, M.D., M.A.S., Brian D. O'Donovan, M.S., Jeffrey M. Gelfand, M.D., M.A.S, Hannah A. Sample, B.S, Felicia C. Chow, M.D., John P. Betjemann, M.D.1,2, Maulik P. Shah, M.D., Megan B. Richie, M. D.1,2, Mark P. Gorman, M.D., Rula A. Hajj-Ali, M.D., Leonard H. Calabrese, D.O. et al. Metagenomic next-generation sequencing for chronic meningitis: a case series JAMA Neurology Published online April 16, 2018. doi:10.1001/jamaneurol.2018.0463

[3] Obusez EC, Hui F, Hajj-Ali RA, Cerejo R, Calabrese LH, Hammad T, Jones SE. High-resolution MRI vessel wall imaging: Spatial and temporal patterns of reversible cerebral vasoconstriction syndrome and central nervous system vasculitis. AJNR American Journal of Neuroradiology 2014 Aug;35(8):1527-32. doi: 10.3174/ajnr.A3909. Epub 2014 Apr 10.

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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

How to manage and treat childhood onset lupus? A multidisciplinary point of view

SP0075 **CASE PRESENTER: CHILDHOOD ONSET OF NEUROLUPUS**

Eve Smith. *Alder Hey Children's NHS Foundation Trust, Paediatric Rheumatology, Liverpool, United Kingdom*

Background: In the series of talks 'How to manage and treat childhood onset lupus? A multidisciplinary point of view' the first talk focuses on achievement of the initial diagnosis of Lupus within the childhood period, including some potential pitfalls and how these can be avoided. Initial and ongoing treatment within the childhood period, alongside paediatric specific therapeutic considerations will be discussed. The role of the multidisciplinary team of doctors, nurses, physiotherapists, occupational therapists, psychologists and sub-specialists will be highlighted. The impact of the diagnosis on the child, family, education and social activities will also be described. This talk will be followed by a subsequent talks following the patient through transition and into adulthood.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8590

SP0076 **CASE PRESENTER: TRANSITION OF NEUROLUPUS PHASE INTO ADULTHOOD**

Lovro Lamot. *The University of British Columbia and British Columbia Children's Hospital Research Institute, Department of Pediatrics, Division of Rheumatology, Vancouver, Canada*

Childhood-onset SLE (cSLE) accounts for approximately 20% of all SLE cases and is often regarded as one of the most complex rheumatic diseases. With the increase of five-year survival rate of cSLE patients to over 95%, there is a growing number of adolescents and young adults (AYA) transferring from pediatric to adult care. Even in the best-case scenario, there is often considerable challenges regarding this transition. Hence, it is not surprising that morbidity, mortality and disease activity in cSLE, as well as in many other chronic illnesses and conditions, worsen during or just after the transition. The reasons for these deteriorations are numerous, with most prominent arising from the nature of the disease and changes during the tumultuous period of adolescence, but also the differences between pediatric and adult clinical and healthcare settings. Besides, the AYA patients with chronic conditions often feel they are not well prepared for the transition to adult care, while the adult rheumatologists commonly report concerns about assuming the responsibility of patients with the pediatric-onset disease. Some of these concerns are probably motivated by increased vulnerability of AYA patients with cSLE, who are more likely than their adult counterparts to develop lupus nephritis and neuropsychiatric manifestations, as well as other organs involvement and atherosclerosis. Moreover, due to the severity of the disease, patients with cSLE are treated more aggressively, accumulating more drug-related toxicity than patients with adult-onset SLE, which results in significant SLE-related damage and complications such as osteoporosis during the childhood. On the other hand, there is decreased medication adherence in AYA, further complicated by the neurocognitive and memory impact of the disease, as well as high rates of comorbid depression and anxiety. Some additional problems in cSLE patients at transition age are sexuality, fertility, and pregnancy. All this makes patients with cSLE require specialized and multidisciplinary care at the transition, that is capable of addressing medical, psychosocial, educational and vocational needs.
This presentation will be part of the comprehensive session discussing distinct features of the SLE during the different phases of life. It will emphasize specific challenges of the transition from pediatric to adult care, with the use of a compelling clinical case as an example.

REFERENCES:

[1] Sadun RE,Schanberg LE. Transition and transfer of the patient with paediatric-onset lupus: a practical approach for paediatric and adult rheumatology practices. Lupus Science & Medicine 2018;5:e000282.

[2] Foster HE, Minden K, Clemente D, et al. EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases. Ann Rheum Dis 2017;76:639–46.

[3] Falcini F, Nacci F. Systemic lupus erythematosus in the young: the importance of a transition clinic. Lupus 2007;16:613–7.

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SP0077 **CASE DISCUSSANT**

Brigitte Bader-Meunier. *Hôpital Necker, Pediatric Immunology and Rheumatology, Paris, France*

Background: Pediadiatric-onset systemic lupus (pSLE) is a severe mulisystem autoimmune condition which mostly manifests after the age of 10 years. It is mainly a polygenic disorder, but a mutation in a single gene may predispose to the developementof SLE (« monogenic lupus »). We will describe some unusual presentations which may lead to a delayed diagnosis or misdiagnosis and provide clues for the diagnosis of monogenic lupus.
Objectives: To discuss the difficult diagnosis and pitffalls in pSLE
Results: The most common initial manifestations of pSLE are cutaneous, musculoskeletal, renal, hematologic, and fever. However, atypical symptoms may reveal the diagnosis or occur during the course of SLE. In a French retrospective study[1], thirty-two percent of children had atypical symptoms, mainly including abdominal involvement in 26 patients, which lead to negative laparotomy for presumed appendicitis before the diagnosis of SLE could be established. Abdominal pain was related to lupus pancreatitis or peritonitis. The diagnosis of pSLE should be systematically searched for in a teenager who presents with unexplained mood disorders, psychosis or depression, which may reveal pSLE. In a patient

with a suspected diagnosis of neuropsychiatric pSLE, underlying factors including infections, hypertension, metabolic abnormalities or adverse effects of medication should be excluded before considering a luous-related neurological involvement[2]. Finally, the diagnosis of pSLE should be also considered in case of severe complications such as macrophage activation syndrome or alveolar hemorrhage. Monogenic SLE should be suspected in early-onset SLE (< 5-year-old) and mainly comprise complement deficiencies, genetic overproduction of interferon-α, B-cell apoptosis defects and rare inherited immunodeficiencies. Each of these conditions is associated with specfic features : 1) Primary complement defects are associated with recurrent pyogenic or neisserial infections 2) type-1 interferonopathies are often associated with spasticity, cerebral calcifications, encephalopthy, skin ulcers and chilblains, and, in some cases, with a growth delay (spondylenchondrodysplasia) 3) B-cell apoptosis defects (mutation in *PRKCD* gene) is associated with a lymphoproliferative disease. A proper diagnosis of SLE must therefore be based upon a complete family medical history as well as on clinical evaluation with details history of both present and past illnesses, analysis of growth chart as well as laboratory tests for SLE. The search for auto-antibodies towards nuclear antigens is a key step in the diagnosis strategy, keeping in mind that antinuclear antibodies are not specific for SLE. Screening for complement deficiencies via CH50, AP50, C3 and C4 is recommended in order to facilitate adequate treatment of comorbidities including infections[2] in pSLE patients[2].
Conclusion: The diagnosis of pSLE should be suspected in teenagers with acute unexplained symptoms, especially in case of abdominal pain or neuropsychiratric involvement. A monogic predisposition to SLE should be considered in early-onset SLE, especially in patients with SLE family history, consanguinity, recurrent infections, and/or encephalopathy with spasticity.

REFERENCES:

[1] Bader-Meunier B, Armengaud JB, Haddad E, et al. Initial presentation of childhood-onset systemic lupus erythematosus: a French multicenter study. J Pediatr. 2005;146(5):648-53.
[2] Groot N, de Graeff N, Avcin T, et al. European evidence-based recommendations for diagnosis and treatment of childhood-onset systemic lupus erythematosus: the SHARE initiative. Ann Rheum Dis. 2017;76(11):1788-1796

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SP0078 CASE PRESENTER: LONGSTANDING NEURO LUPUS IN ADULT LIFE

Antonis Fanouriakis. *"Attikon" University Hospital, Rheumatology and Clinical Immunology, Athens, Greece*

Background: Juvenile-onset systemic lupus erythematosus (SLE) poses significant challenges for paediatric and adult rheumatologists. Longstanding disease in adult life carries the sequelae of the protracted course of the disease, as well as of the various treatments received.
Objectives: To present a didactic case of long-standing SLE of childhood onset, with the purpose to familiarise the audience with the multifaceted aspects of the disease, following transition from adolescence into adulthood.
Methods: Report of an illustrative juvenile-onset SLE patient after transition in adulthood.
Results: A 25-year old lady was diagnosed with SLE at the age of 9, due to generalised tonic-clonic seizures (status epilepticus), photosensitive rash and positive serology for SLE (ANA, anti-dsDNA, low complements). She was treated with high-dose glucocorticoids and cyclophosphamide with a good neurologic response. At the age of 15, she developed hematuria and nephrotic proteinuria; a kidney biopsy was compatible with class IV lupus nephritis (LN), with few crescents. She received mycophenolate mofetil (MMF), again with glucocorticoids, with complete response at 12 months. After entering adulthood, 5 years later, at the age of 21, she had a severe renal flare with recurrence of nephrotic proteinuria and active urinary sediment. A second kidney biopsy was performed, which showed histologic transformation into mixed class IV + V LN, and increase in chronicity index. Readministration of MMF failed to provide at least partial response; to this end, high-dose intravenous cyclophosphamide was administered, again with no response after 6 months. Finally, the patient was treated with rituximab, in combination with MMF, which managed to achieve partial remission, with proteinuria levels ~ 1.5 gr/day and normal renal function. Sixteen years following her initial diagnosis, apart from her ongoing renal inflammation, our patient has suffered significant side-effects from long-term glucocorticoid therapy and her quality of life is significantly affected.
Conclusion: This case illustrates the formidable challenges faced by both patients and treating physicians, for a patient diagnosed with SLE in childhood and had frequent flares during transition into adulthood and later in adult life.

Disclosure of Interests: Antonis Fanouriakis Paid instructor for: Amgen, GSK, Speakers bureau: Abbvie, Enorasis, Genesis Pharma
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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Radiographic progression in arthritides: still valid or a tale from the past!?

SP0079 STRUCTURAL DAMAGE PROGRESSION IN RA – DOES IT STILL MATTER WITH IMPROVED MEDICAL AND NON-MEDICAL TREATMENTS

Désirée van der Heijde. *Leiden University Medical Center, Department of Rheumatology, Leiden, Netherlands*

The distinction between symptomatic and disease modifying drugs is based on inhibition of structural damage and preservation of physical function. Radiographs of hands and feet are typically used to assess structural damage in RA. They provide a good representation of overall damage of all joints and bone erosions and joint space narrowing can be assessed reliably. Structural damage is the consequence of inflammation and is related to permanent loss of function and other outcomes important to patients such as work and quality of life. In cohorts of RA patients followed in the eighties of the twentieth century, the average progression rate was about 7 units of the modified Sharp score. This was still the case in the control arms of the RCTs in the nineties and early zeros. However, in recent trials the progression in the control arms is reduced to around 1 unit per year. There are several reasons for this reduced progression observed in clinical trials. First, the duration of placebo is limited to a maximum of 12-16 weeks for ethical reasons. Consequently, there is only restricted time to develop radiographic damage. Second, more frequently an active comparator is used instead of placebo. Third, there is better overall standard of care. Fourth, inclusion of patients with less severe disease in RCTs. Moreover, some speculate that there is a trend to a milder form of RA, however this is hard to proof. For all these reasons, it is essential to enrich the population with patients with a higher chance of showing radiographic progression over the (short) period of the RCT To enhance the probability of proving a reduction in radiographic progression. These factors include ACPA/RF-positivity, erosive disease and elevated CRP.
It is frequently asked if a reduction of the mean progression of 1 unit in the control arm to the mean progression of 0.5 unit in the treatment arm is clinically relevant. However, clinical relevance cannot be based on mean progression scores due to the skewness of the progression: many patients do not show progression, while a minority show (major) progression. A reduction in the likelihood of (significant) progression by treatment A over treatment B could already provide more useful information. Moreover, people tend to relate the '1 unit' to the maximum score of 448 units of the scale. Though, it is important to realise that a patient with a score of 50 already has major damage and that RA is a chronic disease with many patients suffering for many years. But true clinical relevance of structural damage needs to be established in observational cohorts over longer follow-up times.
Despite the limited radiographic progression in the control arms of RCTs, it was possible to show the disease modifying effect by inhibition of structural damage progression for csDMARDs (mainly MTX), all bDMARDs and tsDMARDs currently on the market.
Disclosure of Interests: Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge
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SP0080 STRUCTURAL DAMAGE PROGRESSION IN AXSPA

Denis Poddubnyy. *Charité – Universitätsmedizin Berlin, Department of Gastroenterology, Infectious diseases and Rheumatology, Berlin, Germany*

Structural damage in axial spondyloarthritis (axSpA) develops usually first in the sacroiliac joints and later in the spine. While development of structural damage in the sacroiliac joints is mostly relevant for diagnosis and classification (non-radiographic versus radiographic axSpA), structural damage in the spine has a relevance for the long-term outcome of the disease. Structural damage in the spine and inflammatory activity are two major determinant of functional status and spinal mobility in axSpA.
Structural damage in the spine in axSpA is mostly attributable to the process of new bone formation (development of syndesmophytes resulting in bony ankylosis) occurring in the areas affected by inflammation. Advanced ankylosis of the

spine is the worst long-term outcome of this disease, although this occurs less frequently nowadays if compared to former decades. This fact might be related either to the natural course of the disease that becomes milder over time or to a consequent anti-inflammatory treatment initiated earlier in patients with axSpA.
Structural damage in the spine in axSpA is usually assessed on plain radiographs of the spine and, therefore, is frequently referred to as radiographic spinal progression. In the presentation, pathophysiology, assessment and ways of prevention and/or retardation of structural damage progression in the spine in patients with axSpA will be discussed.
Disclosure of Interests: Denis Poddubnyy Grant/research support from: AbbVie, Merck Sharp & Dohme, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, UCB Pharma
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SP0081 **STRUCTURAL DAMAGE PROGRESSION IN PSA**

Philip Helliwell. *University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*

Psoriatic arthritis is a multifaceted disease in which the arthritis tends to be less frequent than in rheumatoid arthritis. This provides a challenge to measure radiographic progression using the simple and time-honoured fashion of assessing the hands and feet. Further, radiographic progression is slower in PsA and changes over a short time period, such as the placebo controlled phase of a trial, are minimal. Newer imaging, such as ultrasound and MRI may be more sensitive and responsive but data on these techniques are limited. These challenges, and how to overcome them, will be discussed.
Disclosure of Interests: Philip Helliwell Grant/research support from: Paid to charity: from AbbVie, Janssen and Novartis, Consultant for: Paid to charity: from AbbVie, Amgen, Pfizer, and UCB and Celgene. Paid to self: from Celgene and Galapagos
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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Difficult to manage Sjögren's syndrome and Myositis

SP0082 **SCREENING FOR MALIGNANCIES IN SJOGREN SYNDROME AND MYOSITIS**

Albert Selva-O'Callaghan. *Vall d'Hebron General Hospital. Universitat Autonoma de Barcelona, Internal Medicine Dept, Barcelona, Spain*

Both myositis and Sjögren syndrome may be associated with cancer. However, there are differences between the cancer-associated myositis and cancer that appears in patients with Sjogren syndrome, and these differences make for a distinct tumor screening approach. The fact that any type of cancer -mainly of the adenocarcinoma type- can be associated with myositis -dermatomyositis, either classical or amyopathic, immune-mediated necrotizing myopathy, or polymyositis phenotypes- makes more difficult to know if an occult malignancy is present. Nevertheless, in recent years biological markers such as several autoantibodies, essentially anti-TIF1γ, but also anti-NXP2 and to some extent anti-HMGCR, and combined techniques such as PET/CT that allow to detect structural and functional changes by means of ^{18}F- Fluorodeoxyglucose and whole CT have helped the clinician to screen for an occult cancer in patients with myositis. Alternatively, the clinical situation and screening approaches in Sjögren syndrome are more focused in the detection of lymphoproliferative disorders, mostly in salivary glands (MALT type lymphoma) but also marginal zone or diffuse large B cell lymphomas. Several approaches for detecting MALT-type lymphoma or generalized lymphomas, beyond the well-known parameters such as low complement levels, cytopenias, cryoglobulins or persistent enlargement of salivary glands, are also discussed.

REFERENCES:

[1] Selva-O'Callaghan A, Martínez-Gómez X, Trallero-Araguás E, Pinal-Fernández I. The diagnostic work-up of cancer-associated myositis. Curr Opin Rheumatol. 2018; 30:630-6
[2] Baldini C, Ferro F, Luciano N, Bombardieri S, Grossi E. Artificial neural networks help to identify disease subsets and to predict lymphoma in primary Sjögren syndrome. Clin Exp Rheumatol. 2018;36 (Suppl. 112): S137-S144

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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Anergy, exhaustion or post-activation in autoimmunity; Facts and future consequences

SP0083 **MOLECULAR AND METABOLIC EVENTS WHICH UNDERWRITE T CELL PHENOTYPES IN AUTOIMMUNITY**

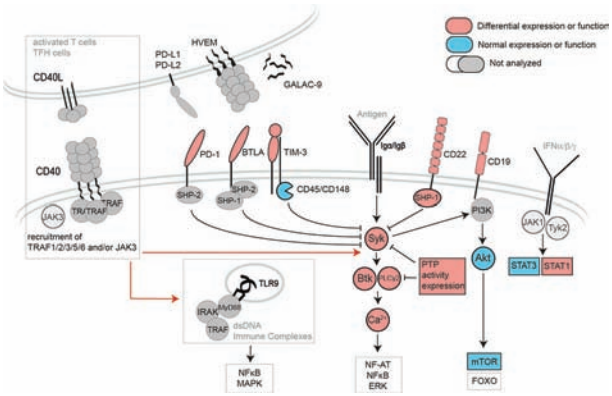
George Tsokos. *Beth Israel Deaconess Medical Center/Harvard Medical School, Medicine, Boston, United States of America*

The distribution and function of T cell subsets in patients with systemic lupus erythematosus (SLE) is aberrant. Distinct molecular and metabolic event dictate the numbers and function of T cells. Specifically, the transcriptional repressor cyclic AMP response element modulator alpha (CREMα), which is increased in cells from patients with SLE, accounts for the decreased expression of interleukin (IL)-2 and the increased expression of IL-17 through distinct epigenetic processes. CREMα promotes Th17 cell expansion by promoting the expression of Gls1, the first enzyme in glutaminolysis and by suppressing the expression of pyruvate dehydrogenase phosphatase catalytic subunit 2 that enables entry of pyruvate in to the Krebs cycle. In parallel, calcium calmodulin kinase 4 which is responsible for the increased binding of CREMα to cAMP response elements of the *IL-2*and *IL-17* loci, promotes the activity of pyruvate kinase M2 and promotes glycolysis and TH17 generation while suppressing the numbers of regulatory T cells. Understanding the exact molecular and metabolic processes that control T cell function in SLE enables therapeutic considerations.
Disclosure of Interests: George Tsokos Grant/research support from: Janssen Research & Development, LLC
DOI: 10.1136/annrheumdis-2019-eular.8604

SP0084 **POST-ACTIVATED B CELLS IN AUTOIMMUNITY**

Andreia Lino. *Rheumatology and Clinical Immunology, Department of Medicine, Charité Universitätsmedizin Berlin and German Rheumatism Research Center Berlin (DRFZ), Berlin, Germany*

Background: B cells are key players in autoimmune diseases such as systemic lupus erythematosus (SLE), primary Sjögren's syndrome (pSS) and rheumatoid arthritis (RA). In the past, it was believed that B cells from these patients were hyperresponsive to B cell receptor (BCR) and Toll-like receptor (TLR) signaling. New insights suggest that B cells from these patients present a post-activated *functiotype*.
Objectives: We aim at characterizing B cells and B cell responses of SLE, pSS and RA patients to understand which venues can be taken towards new therapies for these diseases.
Methods: B cells and B cell subsets from peripheral blood samples from SLE, pSS and RA patients and healthy donors (HD), as well as few autoimmune tissues, were analyzed for: phosphotyrosine kinase (PTK) phosphorylation kinetics, protein phosphatase activity, expression of phosphatases or of checkpoint molecules, such as *e.g.*PD-1, before and after BCR engagement, alone or together with TLR9 and CD40 stimulation, differentiation and proliferation. Expression of transcription factors, such as *e.g.*STAT1, and the effect of interferons in their expression in B cells from patients were also evaluated.
Results: B cell responses upon BCR engagement in SLE, pSS, RA patients were abnormal with diminished BCR downstream PTK phosphorylation. TLR9, but not CD40 responses were also abnormal. Part of the abnormality related to diffuse up-regulation of phosphatases that apparently counteracted PTK signaling. The abnormality was partially mimicked by repeated signaling through the BCR of HD B cells and could be overcome by CD40 engagement. Check-point molecules, such as *e.g.*PD-1, was differentially expressed in SLE naive and memory B cells. SLE naive and memory B cells expressed higher amounts of STAT1 compared to those of pSS, RA and HD.
Conclusion: Post-activated B cells are characterized by a phenotype of dysregulated expression of certain check-point molecules, such as PD-1, some transcription factors, like STAT1 and certain phosphatases (figure 1). Our data suggest that CD40 activation is involved in modulating BCR responses in post-activated B cells. This has implications for innovative therapies since blocking BCR signaling pathways and CD40 activation as well as targeting certain phosphatases may have synergistic value for treating systemic autoimmunity.



Abstract SP0084 Figure 1. Functiotypic characteristics of post-activated B cells from autoimmune patients.

Disclosure of Interests: None declared
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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Fracture liaison service: an opportunity for rheumatologists to focus on secondary fracture prevention

SP0085 **WHOM TO IDENTIFY AND INVITE TO AN FLS? WHO IS THAT FRACTURE PATIENT?**

Bo Abrahamsen. *x, x, x, Denmark*

Background: Though osteoporosis can be diagnosed through the presence of fragility fractures in the absence of other aetiology such as myeloma or metastases, patients with osteoporosis are also at increased risk of high impact traumatic fractures. Further, distinguishing between fracture mechanisms through chart review is often difficult and may lead to patients with osteoporosis being missed. On the other hand, focusing on identifying and treating patients at high imminent fracture risk rather than milder degrees of osteoporosis makes for better cost utility.
Objectives: To review the demographics of patients presenting with fragility fractures and the evidence for targeting osteoporosis assessment for each category of fracture in order to balance the need for maximum risk reduction with the requirement for an evidence based strategy.
Methods: Narrative review of recent epidemiology studies and national and international guidelines
Results: Based on epidemiology data from Iceland(1) and Denmark(2,3), the risk of subsequent fractures following a sentinel fracture event is critically dependent on the recency and the site of the initial fracture, with the risk of new fractures being particular high after major osteoporotic fractures(1) and pelvic fractures but less so after lower leg fractures(2).
In Danish women(2), 29.5% of patients suffering a pelvic fracture went on to sustain a hip fracture in the next ten years, compared with 25.9% after a vertebral fracture but only 12.5% after a lower leg fracture. Further, despite the high recurrent fracture risk in the FLS setting, it is important to appreciate that the majority of hip fracture patients have not consulted with a prior fracture in the last ten years prior to their hip fracture(3).
The following issues will be addressed in more detail
1) Demographics of fracture patients with particular emphasis on age, sex and BMD.
2) Which fracture types are indicators of elevated risk of subsequent major osteoporotic fractures?
3) Which fracture types will respond to osteoporosis treatment?
4) What is the role of DXA in FLS?
5) Identifying vertebral fractures
Conclusion: FLS patients are at elevated risk of sustaining additional fractures both in the long term and in the short term, with risks being particularly high in the first years after the sentinel fracture and especially if the initial fracture is a pelvic fracture or a major osteoporotic fracture.

REFERENCES:
[1] Kanis, Osteoporos Int 2018, 29:1747–1757
[2] Hansen, Osteoporos Int 2015, 26:513–519
[3] ***Frederiksen***, Osteoporos Int 2018; 29:109–114

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SP0086 **ASSESSMENT: HOW TO PERSONALIZE SECONDARY FRACTURE PREVENTION?**

Daniel Prieto-Alhambra. *University of Oxford, NDORMS, Oxford, United Kingdom*

Background: The existing armamentarium of therapeutic options to minimise fracture risk is growing. Different therapies have different properties, and can be used for different patient targets.
Objectives: To discuss data on short-term fracture risk following an index fracture, and on the short-term efficacy of different therapies.
Methods: Narrative review of recent literature.
Disclosure of Interests: Daniel Prieto-Alhambra Grant/research support from: Grants from Amgen, UCB Biopharma and Servier outside the submitted work, Consultant for: UCB Biopharma, Speakers bureau: Amgen
DOI: 10.1136/annrheumdis-2019-eular.8564

SP0087 **TREATMENT: HOW TO IMPLEMENT IT AND HOW TO MONITOR ADHERENCE?**

Kassim Javaid Muhammad. *University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, oxford, United Kingdom*

Background: The key to achieving the benefits of an FLS on the population and the patient level is to ensure enough high-risk patients are initiated and then adhere to therapy. There is a low rate of primary and secondary adherence by patients with osteoporosis. Treatment initiation requires co-developed decision making with patients and clinicians balancing locally agreed intervention thresholds with effective and efficient risk and treatment communication. Treatment adherence depends on patient, treatment and healthcare service characteristics.
Objectives: Describe the current status of treatment recommendation in the UK
Describe the current methods for imrpoving adherence globally
Methods: Review of the data from the UK Fracture Liaison Service Database and IOF Capture the Fracture audits.
Disclosure of Interests: Kassim Javaid Muhammad Shareholder of: Zebra Medical Vision, Grant/research support from: Amgen, Kyowa Kirin Hakin, Consultant for: Amgen, Internis, Consilient Health,Mereo Biopharma, Kyowa Kirin Hakin, UCB, Speakers bureau: Amgen, Lilly UK, Internis, UCB
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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

How not to smoke like a chimney

SP0088 **HOW YOU KNOW IT IS SMART NOT TO SMOKE LIKE A CHIMNEY**

Antonio Naranjo. *Hospital Universitario de Gran Canaria Dr Negrin, Rheumatology, Las Palmas de Gran Canaria, Spain*

Smoking is associated with a higher prevalence of many diseases. When a health professional is well informed of the risks of smoking in rheumatic diseases, the advice given to the patient about quitting smoking could be more effective.
It is known that smokers in the general population have an increased frequency of elevated rheumatoid factor (RF). Since 1987, we have known that cigarette smoking is a risk factor for rheumatoid arthritis (RA), especially in men with RF-positive who are heavy smokers. Later, it could be verified that cigarette smoking is implicated in the pathogenesis of RA particularly when associated with antibodies, cyclic citrullinated peptides (ACPA) and the shared epitope. Smoking increases the risk of both subsets of RA with a more pronounced influence on the risk of ACPA positive RA. The polyclonal immune response against modified antigens in patients with RA is not exclusively citrulline-specific, carbamylation of antigens like vimentin could be involved in the pathogenesis of the disease. Thus, smoking is a risk factor for breaking tolerance to multiple autoantigens in RA.
In RA patients, cigarette smoking correlated with an increased risk of joint erosions, extra-articular manifestations and cardiovascular disease, in addition to the established effects of longstanding disease activity on the risk of myocardial infarction and stroke.

Systemic lupus erythematosus (SLE) is also associated with smoking. A strong and specific connection of current smoking and >10 pack-years of smoking with dsDNA+ SLE has been observed. In patients with SLE, smoking exposure has deleterious effects on lupus morbidity and is related to cumulative chronic damage. In mucocutaneous SLE, smoking have a negative impact on the efficacy of belimumab and a 2-fold decrease in the proportion of patients achieving cutaneous improvement with antimalarials.

Published data indicate that smoking has a dose-dependent impact on structural damage progression in Ankylosing Spondylitis.

In a large UK cohort, smoking was positively associated with the risk of psoriatic arthritis in the general population, but negatively associated among patients with psoriasis. In addition, smokers with psoriatic arthritis had a poorer response to TNFi's compared to non-smokers.

Regarding osteoporosis, smoking has been identified as a predictor of ten-year fracture risk in men and women, largely independent of the densitometric results. This finding has eventually lead to incorporation of this risk factor into FRAX®. The impact of smoking on bone status is mainly associated with the number of smoking years.

In a few reports, it has been observed an association between smoking and carpal tunnel syndrome and inflammatory bowel disease. Finally, current smoking in patients with fibromyalgia is associated with greater pain, possibly as a function of depression.

Disclosure of Interests: Antonio Naranjo Grant/research support from: Amgen, Consultant for: UCB, Speakers bureau: Amgen, UCB

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SP0089 CONSEQUENCES OF SMOKING CESSATION IN RHEUMATOLOGY

Helen Harris. *Western General Hospital, NHS Lothian, Rheumatology, Edinburgh, United Kingdom*

Background: Cigarette smoking is a risk factor for many autoimmune and inflammatory conditions including rheumatoid arthritis (RA), psoriasis and psoriatic arthritis (PsO PsA), is linked with active skin disease in patients with systemic lupus erythematosis (SLE) and poorer outcomes in patients with ankylosing spondylitis (AS) and systemic sclerosis (SSc). In addition there are well established risks of cardiovascular and respiratory diseases and increased risk of at least 13 cancers in patients that smoke [1]. Patients continuing to smoke after RA is diagnosed often fail to respond or require higher doses of immunosuppressive medications [2]. When arthritis is in remission and biologic dose reduction is attempted, patients that continue to smoke are more likely to have a flare of arthritis after dose reduction [3]. Patients that quit smoking can reduce or stop immunosuppressive medications without experiencing a flare [4]. Smokers have higher rates of infection than non-smokers; immunosuppressive therapy has an increased risk of infection and smoking cessation when starting treatment such as methotrexate or anti-TNF inhibitors can reduce the risk of infection [5]. The five top reasons to deliver brief smoking cessation advice to rheumatology patients are: 1. Improve chances of response to therapy. 2. Reduce infective risks of immunosuppressive therapy. 3. Improve success of medication dose reduction. 4. Reduce cardiovascular and respiratory diseases and cancer risks. 5. Reduce mortality.

Objectives: To demonstrate how brief smoking cessation advice can be delivered in rheumatology outpatient clinics and to show the consequences that this has had for patients, the rheumatology team and the wider healthcare system.

Methods: Delivering a brief intervention on smoking cessation by saying to smokers "Do you know the best way to quit? Use Champix (Varenicline) or Nicotine Replacement Therapy" is an evidence based way to motivate a quit attempt that takes 30 seconds to deliver. A 50 minute talk was presented to the rheumatology team of doctors, nurses and allied health professionals explaining this method of delivering brief advice on smoking cessation. We have made brief advice easy to deliver in the rheumatology clinic by creating a pathway for referral of smokers to the community pharmacist and smoking cessation nurse. A questionnaire has been administered to the rheumatology team to explore their attitudes and beliefs about delivering smoking cessation advice in the rheumatology clinic.

Results: The referral figures for the smoking cessation pathway will be presented. The consequences of delivering brief advice on smoking cessation for the patients, rheumatology team and healthcare system will be reported.

Conclusion: This presentation will show that helping rheumatology smokers to quit is achievable and should be considered an essential part of the rheumatology outpatient consultation.

REFERENCES:

[1] Arnson Y, Shoenfeld Y, Amital H. Effects of tobacco smoke on immunity, inflammation and autoimmunity. Journal of Autoimmunity 34 (2010) J258eJ265.

[2] Harris H, Tweedie F, White M, Samson K. How to persuade patients with Rheumatoid Arthritis to quit smoking. J Rheumatol. 2016 Apr;43(4):691-8. doi: 10.3899/jrheum.141368. Epub 2016 Feb 15.

[3] Gibson J, Harris H, McLaren J. Dose reduction of biologic therapies. EULAR OP0161 June 2012

[4] Andersson M, Bergman S et al, for the BARFOT Study Group § The Effect of Stopping Smoking on Disease Activity in Rheumatoid Arthritis (RA). Data from BARFOT, a Multicenter Study of Early RA. Open Rheumatol J. 2012; 6: 303–309.

[5] Arcavi L, Benowitz NL. Cigarette smoking and infection. Arch Intern Med. 2004 Nov 8;164(20):2206-16.

Disclosure of Interests: None declared

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SP0090 INTENSIVE SMOKING CESSATION INTERVENTION

Ida Kristiane Roelsgaard. *Rigshospitalet, Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Glostrup, Denmark*

Smokers with an inflammatory joint disease (IJD) experience poorer health-related quality of life compared to non-smokers with IJD (1). Smoking may exacerbate the symptoms of the disease and cause a reduced response to antirheumatic treatment (2-4). Smoking cessation interventions have traditionally been designed for people without chronic diseases (5). The literature on smoking cessation interventions to people with IJDs is limited.

Initially, this lecture will focus on "state of the art" regarding smoking cessation interventions to people with IJD.

Firstly, results from a systematic review will be presented. Randomised controlled trials (RCT) were included if they tested any form of smoking cessation intervention for adult daily smokers diagnosed with an IJD (6).

Secondly, the lecture will focus on various interventions for smoking cessation e. g. brief advice, behavioural interventions, motivational interviewing and nicotine replacement therapy.

Finally, principles for an ongoing RCTs where daily smokers with rheumatoid arthritis (RA) are randomised to either an intervention group or to a control group will be presented (7). The intervention consists of motivational counselling combined with nicotine replacement therapy. One patient research partner with RA (former smoker) has been involved with all phases of the study.

The above indicate that smoking cessation may positively impact not only clinical outcomes but also patient reported outcomes. However, a limited number of studies on smoking cessation interventions and the effect of smoking cessation on clinical and patient reported outcomes to people with IJD have been published. The knowledge is therefore limited, and health professionals should focus on this subject to proactively support people with IJDs who wish to quit smoking.

REFERENCES:

[1] Bremander A, Jacobsson LT, Bergman S, Haglund E, Lofvendahl S, Petersson IF. Smoking is associated with a worse self-reported health status in patients with psoriatic arthritis: data from a Swedish population-based cohort. Clinical rheumatology. 2015;34(3):579-83.

[2] Chang K, Yang SM, Kim SH, Han KH, Park SJ, Shin JI. Smoking and rheumatoid arthritis. International journal of molecular sciences. 2014;15 (12):22279-95.

[3] Abhishek A, Butt S, Gadsby K, Zhang W, Deighton CM. Anti-TNF-alpha agents are less effective for the treatment of rheumatoid arthritis in current smokers. Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases. 2010;16(1):15-8.

[4] Soderlin MK, Petersson IF, Geborek P. The effect of smoking on response and drug survival in rheumatoid arthritis patients treated with their first anti-TNF drug. Scandinavian journal of rheumatology. 2012;41(1):1-9.

[5] Gritz ER, Vidrine DJ, Fingeret MC. Smoking cessation a critical component of medical management in chronic disease populations. American journal of preventive medicine. 2007;33(6 Suppl):S414-22.

[6] Roelsgaard IK, Esbensen BA, Østergaard M, Rollefstad S, Semb AG, Christensen R, et al. Smoking cessation intervention for reducing disease activity in chronic autoimmune inflammatory joint diseases. Cochrane Database of Systematic Reviews. 2018(2).

[7] Roelsgaard IK, Thomsen T, Ostergaard M, Christensen R, Hetland ML, Jacobsen S, et al. The effect of an intensive smoking cessation intervention on disease activity in patients with rheumatoid arthritis: study protocol for a randomised controlled trial. Trials. 2017;18(1):570.

Disclosure of Interests: None declared

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SP0091 **HOW TO SUPPORT YOURSELF QUITTING SMOKING**

Marios Kouloumas. *Cyprus League Against Rheumatism, Aglantzia, Patient Orgnanization, Nicosia, Cyprus*

Background: As a person living with Rheumatoid arthritis (RA) (a chronic inflammatory disease caused by both genetic and environmental factors) for the last 45 years (I have been diagnosed with RA at the age of 10 years old) I have been a smoker from the age of 14 years old. As I grew older, and was educated and involved concerning the management of my disease, I realized that smoking, besides its impact on my overall health, had a significant impact as one of the most important risk factors for RA that can increase the severity of the disease and to worsen symptoms. Smoking can also reduce the effect of treatments, including anti-TNF agents and disease-modifying anti-rheumatic drugs (DMARDs). Hence, quitting smoking will improve my overall health, reduce the severity of my disease and ensure that treatments work and reduce the risk for comorbidities e.g. cardiovascular disease and the progression of the disease (joint destructions).
Objectives: To quit smoking after 40 years of being a smoker and to regain my health and quality of life as well as increase the efficacy of the RA treatments.
Methods: To succeed I plan to be very well informed and to understand the reasons of quitting smoking as well as the negative impact of smoking and to realize that quitting smoking will improve my health and social life. To inform all people close to me including family members as well as friends and coworkers about my decision to quit smoking. Mentally being prepared to cope with the desire to smoke as well as ridding the thought of "just smoke one". It is also important to rid the mind and lose the connection of things associated with smoking, for example while drinking coffee. To ask for support if needed and to use tools to stop thoughts of smoking and to cope with the effects of nonsmoking and to try avoiding places that could increase my risk of starting to smoke again e.g. pubs
Results: I have started to cut down on smoking and to minimize it and finally to fully quit smoking for the last 2 years.
Conclusion: Although, if you ask all smokers how difficult it is to stop smoking, the answer will unanimously be "very hard", as a former smoker I can say that if you quit smoking, be aware of the reasons and the importance of quitting smoking and you will notice that after all it is not very difficult. Of course, when you set this goal it is important that in case of first time failure to not blame yourself and I can not stress enough how important a support system is for example that of your friends, family and especially your spouse.
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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Scientific data visualization: focus on (poster) presentation

SP0092 **'SCIENTIFIC DATA VISUALIZATION: FOCUS ON (POSTER) PRESENTATION**

Maarten Boers. *Amsterdam University Medical Centers; Vrije Universiteit, Epidemiology and Biostatistics; Amsterdam Rheumatology and immunology Center, Amsterdam, Netherlands*

This practical skills session introduces the principles of good graph and table design as pioneered by Cleveland[1]and Tufte[2]and updated by Few[3], this year focusing especially on (poster) presentation.
Its learning objectives include:

- choosing the data visualization that best fits the data
- identifying the basics of table and graph design
- choosing tables and graphs that tell the story in the data
- introduction to poster design

The session is linked to a special poster tour devoted to poster design on the next day:
Poster tour 'F00' (note: this may be a temporary number), Friday 14-06-19, 11:50-13:30 (signup required!).
Basics of table and graph design are also covered in my introductory YouTube clips on the ARD website (ard.com).
Direct link: https://www.youtube.com/playlist?list=PLXU14EQbU_V9JpmoIAKsaCC0VjJzbxzAN
Also, I've recently published two articles on table and graph design which are freely downloadable.[4,5]
When you download, don't forget the online appendices, because they contain many useful examples!

REFERENCES:
[1] Cleveland WS. The elements of graphing data: Hobart Press, Summit, NJ, USA; 1994.
[2] Tufte E. The visual display of quantitative information. 2nd ed: Graphics Press, Cheshire, CT, USA; 2001.
[3] Few S. Show me the numbers. Designing tables and graphs to enlighten. 2nd ed: Analytics Press, Oakland, CA, USA; 2012.
[4] Boers M. Graphics and statistics for cardiology: designing effective tables for presentation and publication. Heart 2018;104:192-200 direct link: http://heart.bmj.com/cgi/content/full/heartjnl-2017-311581.
[5] Boers M. Designing effective graphs to get your message across. Ann Rheum Dis 2018;77:833-9. direct link: http://ard.bmj.com/cgi/content/full/annrheumdis-2018-213396

Disclosure of Interests: None declared
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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Should we worry about anything else; also young people have multi-morbidities

SP0093 **MANAGING MORE THAN RMDS**

Kristien Van der Elst. *University Hospitals Leuven, Rheumatology, Leuven, Belgium*

Increasing emphasis has been placed on the concept of multi-morbidity or the coexistence of two or more chronic diseases in adult patients with rheumatic conditions. A few years ago a EULAR initiative raised some points to consider for management of comorbidities, such as cardiovascular diseases and depression, in chronic inflammatory rheumatic diseases in daily practice (1). Nevertheless, improved management of comorbidities, including prevention, remains a commonly identified unmet need in rheumatology (2). Multi-morbidity can be quite challenging to manage, while the perspective of the individuals having to cope with multiple chronic diseases could differ from that of health professionals taking care of them. Awareness and regular assessment are key, as well as a collaboration between health professionals and well-informed patients. This lecture aims to provide practical information about how to manage more than the rheumatic disease as such, focussing as well on topics of specific interest to young people.

REFERENCES:
[1] Baillet, et al. Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. Ann Rheum Dis. 2016
[2] Winthrop, et al. Unmet need in rheumatology: reports from the Targeted Therapies meeting 2018. Ann Rheum Dis. 2019

Disclosure of Interests: None declared
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SP0094 **DISEASES ON SALE – HOW I DEAL WITH ALL MY CONDITIONS**

Tanita-Christina Wilhelmer. *Österreichische Rheumaliga, Austria*

In her speech Tanita will explain how she experiences life with multiple conditions. There are a lot more than just symptoms of the main condition and emotions to deal with. Although being diagnosed with Adult Onset Stills Disease (AOSD), she suffers from additional morbidities. Like many other young people with RMD's she has to manage all conditions at once. The list of comorbidities to "choose from" is very long, but there are some that made it to the top three: fatigue, depression and anxiety.
The obstacles that come with this situation can be personal, interpersonal, concerning work, school or university. More illnesses lead to more doctors appointments, this results in missing work or private events. Helping others to understand the condition and communicating the needs is a big topic, as well as planning ahead and staying positive. Tanita will adress these issues and give best practice examples.
Disclosure of Interests: None declared
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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

EULAR Projects in investigative rheumatology

SP0095 **EULAR POINTS TO CONSIDER ON BIG DATA**

KEDRA Joanna. *Sorbonne Université, Institut Pierre Louis d'Epidémiologie et de Santé Publique (iPLESP), UMR S1136, Paris, France*

Background: There are tremendous opportunities for health research propelled by the recent expansion of big data and artificial intelligence. However, this is an emergent area where recommendations are needed.
Objectives: The objective was to develop points to consider for the use of big data by computational modelling, machine learning and artificial intelligence in rheumatic and musculoskeletal disorders (RMDs).
Methods: Based on a literature review of the current status of big data in RMDs and in other fields of medicine, on individual interviews of selected experts, and on the opinion of experts in a face-to-face meeting, points to consider were formulated, discussed and finalised by an international group of 14 experts from a range of disciplines including computer science and artificial intelligence. Levels of evidence and strengths of recommendations were allocated.
Results: The document comprises 5 overarching principles and 9 points to consider. The overarching principles address the definition of big data and artificial intelligence, types of big data, and ethical and general principles for dealing with big data in RMDs. The points to consider cover aspects of data sources and data collection, discussing privacy by design, use of specific data platforms, and data sharing; data analyses in particular through artificial intelligence and machine-learning; they refer to big data as a moving field in need of correct reporting of methods used and of benchmarking; and data interpretation and implementation in clinical practice.
Conclusion: These EULAR points to consider provide a framework for the use of big data in RMDs.
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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

MRI

SP0096 **MRI OF LARGE JOINTS IN ARTHRITIS: HOW TO DO AND HOW THEY ARE DIFFERENT FROM SMALL JOINTS?**

Iris Eshed. *Sheba Medical Center, Tel Aviv University, Department of Diagnostic Imaging, Ramat Gan, Israel*

The appendicular skeleton is frequently involved in patients with rheumatic diseases.
Involved joints are affected by inflammation of the synovium and joint's entheses.
Imaging depicts joint derangement and generally mirrors the pathophysiology of the disease.
MRI is considered the imaging modality of choice for the detection of acute joint inflammation as well as its structural sequela.
Thus, MRI plays an important role in identifying, monitoring disease activity and the patient follow-up.
The MRI features of inflammatory arthritis are well described, especially in the small appendicular joints of the hands and feet and include synovitis, erosions, osteitis, tenosynovitis and erosions.
In the current presentation, the typical MRI properties of large joints arthritis in different rheumatic entities will be presented with special focus on the difference from inflammatory findings in smaller appendicular joints.:
Disclosure of Interests: None declared
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SP0097 **MRI OF ENTHESITIS: HOW TO DO AND WHAT TO LOOK FOR**

Mikkel Østergaard. *Copenhagen Center for Arthritis Research (COPECARE), Rigshospitalet, University of Copenhagen, Center for Rheumatology and Spine Diseases, Glostrup, Denmark*

Enthesitis, inflammation at the insertion site of tendon, ligament or joint capsule into bone, is considered a key pathological feature in spondyloarthritis (SpA) and psoriatic arthritis (PsA)[1]. Compared to conventional assessment of enthesitis using clinical scores, MRI detects both soft tissue and intra-osseous abnormalities in active enthesitis, potentially aiding early diagnosis and outcome measurement in SpA and PsA[2]. With the advent of treat-to-target concept and novel therapies, objective and sensitive monitoring of response of enthesitis to therapy is desirable, and a validated MRI scoring system would be a useful adjunct to clinical practice as well as providing additional information as an outcome measure in clinical trials.
The Outcome Measures in Rheumatology (OMERACT) MRI in Arthritis Working Group recently undertook a systematic literature review (SLR) aiming to critically evaluate the published literature for available methods of evaluating enthesitis using MRI in SpA and PsA patients, describing the MRI variables, definitions and scoring systems used to diagnose and monitor enthesitis)[3]. Considerable limitations was found regarding standardisation of MRI enthesitis definitions across studies and validity of available semi-quantitative scores as outcome measures. The findings suggested a need for reliable and validated MRI scoring system for enthesitis.
Subsequently, The OMERACT MRI group developed consensus definitions of key pathologies and three heel enthesitis multi-reader scoring exercises were done, separated by discussion, training and calibration [4]. In a final exercise, median pairwise single-measures intra-class correlation coefficients (ICCs; patient-level) for entheseal inflammation status/change scores were 0.83/0.82 for all readers. For radiologists and selected rheumatologists ICCs were 0.91/0.84 and quadratic-weighted kappas (lesion-level) 0.57-0.91/0.45-0.81. It was concluded that the proposed definitions and heel enthesitis scoring system (OMERACT HEMRIS) are reliable among trained readers and promising for clinical trials [4].
This talk will briefly review the evidence behind the use of MRI for diagnosis and monitoring enthesitis, describe the recently developed OMERACT consensus definitions of key pathologies, and provide examples of these pathologies, aiming for the attendees to learn to be able to recognize them. Finally, an interactive quiz using cases for audience review will be undertaken to test this ability.

REFERENCES:

[1] Eshed I, Bollow M, McGonagle DG, Tan AL, Althoff CE, Asbach P, Hermann KG. MRI of enthesitis of the appendicular skeleton in spondyloarthritis. Ann Rheum Dis 2007;66:1553-9.
[2] Poggenborg RP, Eshed I, Østergaard M, Sorensen IJ, Moller JM, Madsen OR, Pedersen SJ. Enthesitis in patients with psoriatic arthritis, axial spondyloarthritis and healthy subjects assessed by 'head-to-toe' whole-body MRI and clinical examination. Ann Rheum Dis 2015;74:823-9.
[3] Mathew AJ, Krabbe S, Kirubakaran R, Barr AJ, Conaghan PG, Bird P, Østergaard M. Utility of Magnetic Resonance Imaging in Diagnosis and Monitoring Enthesitis in Patients with Spondyloarthritis: An OMERACT Systematic Literature Review. J Rheumatol 2019.
[4] Mathew AJ, Krabbe S, Eshed I, Gandjbakhch F, Bird P, Pedersen SJ, Stoenoiu MS, Foltz V, Glinatsi D, Lambert RG, Hermann KGA, Maksymowych WP, Haugen IK, Jaremko JL, Poggenborg RP, Paschke J, Laredo JD, Carron P, Conaghan PG, Østergaard M. The OMERACT MRI in Enthesitis Initiative: Definitions of Key Pathologies, Suggested MRI Sequences and Novel Heel Enthesitis Scoring System (HEMRIS). J Rheumatol 2019.

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SP0098 **CRYSTAL ARTHROPATHIES: IS THERE A ROLE FOR MRI?**

Kay-Geert Hermann. *Charite – Universitätsmedizin Berlin, Radiology, Germany*

The plain radiographic features of gout are well known. However, the sensitivity of plain radiographs alone for the detection of signs of gout is poor in acute disease. Dual-energy computed tomography (DECT) and ultrasonography fill the gap for early and specific detection. However, there are instances in which MRI of the painful joints was already acquired. Therefore, it is crucial to know the imaging findings of gout in MRI. MRI per se is not suitable for imaging the calcified bone or soft tissue calcifications. However, there are special techniques such as gradient echo sequences or susceptibility-weighted imaging (SWI) to visualize calcifications. Furthermore, the inflamed joint with all its characteristics such as synovitis, tenosynovitis, and erosions is easily accessible by MRI. Specific findings in the

differentiation of RA, PsA, and gout are presented. The presentation will be case-based, and participants will have the opportunity to test their knowledge.
Disclosure of Interests: Kay-Geert Hermann Paid instructor for: MSD, AbbVie, Novartis, but less than 10.000€
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SP0099 **MRI DIFFICULT CASES OF THE AXIAL SKELETON**

Lennart Jans. *Ghent University Hospital, Radiology, Gent, Belgium*

MRI has revolutionized the assessment of axial spondyloarthritis (SpA) in clinical practice. MRI of the sacroiliac joint is a cornerstone for diagnosis and classification, MRI of the spine may help with difficult cases as spinal changes may antedate sacroiliac changes and indicate disease burden. In daily practice, however, the interpretation of axial MRI is challenging. Experience has tempered the initial enthusiasm as the limitations of the ASAS criteria in daily practice become evident.
Firstly, the ASAS criteria are intended to classify patients with 'back pain' of more than 3 months' duration and with onset before 45 years of age as having axial SpA. In other patient groups, however, sacroiliitis on MRI as defined by ASAS has a lower sensitivity and specificity.
Secondly, the definition of a 'positive' MRI for sacroiliitis is validated to limited extend only. MRI of the sacroiliac joint requires inflammatory changes to meet the criteria, without a clear quantitative requirement. Bone marrow oedema lacks sensitivity and specificity as MRI findings suggestive of sacroiliitis may be produced by non-inflammatory disorders, a point that remains poorly investigated.
Thirdly, structural changes in the sacroiliac joints are not taken into account in the ASAS criteria. The diagnostic performance of MRI of the sacroiliac joint could be improved by including structural lesions, but to date this is not the case.
Fourthly, spinal imaging is not included in the ASAS criteria. MRI of the spine is considered 'positive' when at least 3 inflammatory or several structural lesions are present, with a sensitivity and specificity similar to those of the sacroiliac joints. The difficulty here is the lack of data. It has not been reliably shown that inflammation proceeds syndesmophyte formation and MRI seems uncapable of accurately evaluating treatment response. Only about 4% of patients with 'negative' sacroiliac MRI are reclassified based on positive spinal MRI findings.
Clinicians should be aware of unreasonable expectations on MRI. If MRI findings are considered in isolation the findings are not reliable. The diagnosis of SpA can only be made by an expert if patient's history, clinical examination, laboratory findings, and imaging studies converge. When solving difficult cases, collaboration is key: clear communication between rheumatologist and radiologist is mandatory. Radiologists should withstand the pressure to call if a patient has SpA or not based on MRI alone.

REFERENCE:
[1] Wendling D, Claudepierre P, Pham T, et al. MRI in axial spondyloarthritis: From light to shadow? Joint Bone Spine 2015;82:302-304.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8507

THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Ultrasound advanced I

SP0100 **US OF THE HAMSTRING – CLINICAL APPLICATION + DEMO**

David Andrew Bong. *Instituto Poal de Reumatologia, Universitat de Barcelona, Rheumatology; Anatomy, Barcelona, Spain*

Ultrasound of the Hamstring Muscle Complex-Clinical Application + DEMO
The hamstring muscle complex (HMC) are the "brakes" of human bipedal ambulation and are susceptible to injury during concentric contraction. Although common in sports medicine practice, a recent systematic review of severe hamstring injuries (grade II-III) suggests that greater than 10% of these severe injuries are non-sports related and disproportionately affect older women. Musculoskeletal ultrasound (MSKUS) is one of the basic imaging techniques utilized to detect and define these injuries and eliminate other potential causes of posterior thigh pain. This presentation will discuss the clinical application of MSKUS of the HMC in rheumatology/musculoskeletal medicine and offer a systematic anatomically-based method of examining this important non-articular region.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8432

SP0101 **US FOR ASSESSING LUNG INVOLVEMENT IN RHEUMATIC DISEASES – CLINICAL USE + DEMO**

Andrea Delle Sedie. *University of Pisa, Rheumatology Unit, Pisa, Italy*

Background: Evaluation of interstitial lung disease (ILD) is always difficult (low sensitivity for X-ray and pulmonary function tests or high level of radiation for HRCT): ultrasound (US) has recently shown interesting results on truth, discrimination and feasibility. Due to the thickening of interlobular septa for edema or fibrosis, US beam can interact with those structure and produce artifacts on the screen:
B-lines (BL) and pleural line irregularity (PLI). A positive correlation between BL and HRCT has been established both in systemic sclerosis patients and in other patients with ILD; more recently similar results have been published by using PLI as a finding for US assessment in patients.
BL has been recently defined by the OMERACT as a vertical hyperechoic reverberation artifact that arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with lung sliding, while PLI has been defined as a loss of regularity that may be associated with an increase in thickness, focal, diffuse, or nodular.
A low number of BLs has been described in healthy subjects but they are generally confined to the posterior and lower part of the thorax.
Up to now, many different scanning protocols have been used to assess BL or PLI in patients, providing similar results.
Conclusion: US lung evaluation is a usefull and feasible imaging technique.
Disclosure of Interests: Andrea Delle Sedie Speakers bureau: Abbvie, UCB, Celgene, MSD
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SP0102 **US FOR SYNOVIAL BIOPSIES – CLINICAL RELEVANCE AND SAFETY + DEMO**

Andrew Filer. *University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom*

Background: The introduction of ultrasound guidance to access synovial tissue samples has facilitated a rapid growth in tissue-related research. Ultrasound guidance enables operators to use less invasive approaches compared to a gold standard direct vision arthroscopy procedure while maintaining the quality of samples obtained. Patients find the procedures easy to tolerate and are willing to undergo repeat biopsy, facilitating the analysis of tissue samples in clinical trials and experimental medicine studies. Advanced analytic techniques including single cell analytics are now being used to exploit the tissue samples obtained in order to provide dramatic leaps in understanding of synovial pathology.
Objectives: In this session the key aspects of the dominant techniques in use will be presented, including safety, patient tolerability and quality of output. The research and clinical utility of synovial biopsy will be discussed. Sonographic approaches to the major techniques will then be illustrated through video demonstrations, and competencies required to undertake training will be discussed alongside current EULAR initiatives for training. Finally, examples of research outputs generated through synovial biopsy will be explored alongside the logistics required to deliver such clinical studies.
Disclosure of Interests: None declared
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THURSDAY, 13 JUNE 2019

17:30:00 – 19:00:00

Fighting and fixing: from initiation to resolution of inflammation

SP0103 **T LYMPHOCYTES AND INNATE IMMUNE CELLS BALANCE MUSCLE REGENERATION AND AUTOIMMUNITY**

Patrizia Rovere-Querini. *IRCCS Ospedale San Raffaele and Università Vita-Salute San Raffaele, Laboratory of Innate Immunity and Tissue Remodelling, Italy*

Background: The skeletal muscle is the largest cellular compartment of the organism. It represents an immunologically unique or a "non classical" immunological privileged site, being normally protected from the noxious effects of inflammation. The molecular events that control the homeostatic response to acute muscle injury are however poorly understood. The available information indicates that it involves the cross-talk among various cell populations, which i) perceive the muscle damage and release alert signals, which attract and activate inflammatory cells and progenitor cells ii) organize and maintain regeneration and tissue repair. The scenario is possibly even more complex during inflammatory idiopathic myositis (IIM) in which the immune privilege fails to proctect the environment and

muscle cells undergo continuous cycles of death and regeneration as a consequence of the pressure of the immune respose targeting antigens preferentially expressed within regenerating fibers (1, 2).
Objectives: I will review recent evidence on the relative role of unconventional cellular and molecular pathways activated in the tissues of subjects with IMM and in relevant experimental models of skeletal muscle regeneration and autoimmunity, focusing on the action of antigen-specific and regulatory T cells and immune cells populations of innate cells.
Methods: Review of available published data and of data recently generated on the topic.
Results: Muscle necrosis and the ensuing inflammation was consistently associated in mice with up-regulated expression of bona fide autoantigens targeted in patients with IIM, in particular of histidyl-transfer RNA synthetase (HisRS). Phagocytosis of HisRS-expressing apoptotic myoblasts and appropriate inflammatory costimuli are necessary to elicit the production of anti-HisRS autoantibodies and to jeopardize muscle regeneration. Soluble pattern recognition receptors, and in particular the prototypic long pentraxin PTX3 play a critical role in preventing the accumulation of cell debris in the inflamed skeletal muscle, restricting the immunogenic potential of dying and regenerating myofibers.
Conversely the local expression of type I IFN is necessary for the prolonged autoantibody response and for the maintenance and spreading of the immune-mediated muscle damage, as demonstrated using IFNα/βR-null mice (3-5). A specialized population of regulatory T (Treg) cells, has been recently characterized in the inflamed and regenerating muscle, which influence both the immune response, by promoting the M1-to-M2 switch, and the activation of precursor/stem muscle cells. Treg cells control the efficacy of muscle repair and might be involved in preventing the systemic effects of the autoimmune response generated as a consequence of the disruption of the immunologically protected environment of the skeletal muscle (6, 7).
Conclusion: Identification of the pathways that are physiologically involved in restricting the onset and accelerating the termination of autoimmune reponses targeting the skeletal muscle might be valuable for the identification of novel targets for molecular intervention in patients with IIM.

REFERENCES:

[1] Mammen AL, Casciola-Rosen LA, Hall JC, Christopher-Stine L, Corse AM, Rosen A. Expression of the dermatomyositis autoantigen Mi-2 in regenerating muscle. Arthritis Rheum. 2009 Dec;60(12):3784-93.
[2] Sciorati C, Rigamonti E, Manfredi AA, Rovere-Querini P. Cell death, clearance and immunity in the skeletal muscle. Cell Death Differ. 2016 Jun;23 (6):927-37.3.
[3] Sciorati C, Monno A, Ascherman DP, Seletti E, Manfredi AA, Rovere-Querini P. Required role of apoptotic myogenic precursors and toll-like receptor stimulation for the establishment of autoimmune myositis in experimental murine models. Arthritis Rheumatol. 2015 Mar;67(3):809-22.
[4] Vezzoli M, Sciorati C, Campana L, Monno A, Doglio MG, Rigamonti E, Corna G, Touvier T, Castiglioni A, Capobianco A, Mantovani A, Manfredi AA, Garlanda C, Rovere-Querini P. The clearance of cell remnants and the regeneration of the injured muscle depend on soluble pattern recognition receptor PTX3. Mol Med. 2017 Jan;22:809-820.
[5] Sciorati C, Monno A, Doglio MG, Rigamonti E, Ascherman DP, Manfredi AA, Rovere-Querini P. Exacerbation of Murine Experimental Autoimmune Myositis by Toll-Like Receptor 7/8. Arthritis Rheumatol. 2018 Aug;70(8):1276-1287.
[6] Schiaffino S, Pereira MG, Ciciliot S, Rovere-Querini P.Regulatory T cells and skeletal muscle regeneration. FEBS J. 2017 Feb;284(4):517-524. doi: 10.1111/febs.13827
[7] DiSpirito JR, Zemmour D, Ramanan D, Cho J, Zilionis R, Klein AM, Benoist C, Mathis D. Molecular diversification of regulatory T cells in nonlymphoid tissues. Sci Immunol. 2018 Sep 14;3(27).
[8] Panduro M, Benoist C, Mathis D. Treg cells limit IFN-γ production to control macrophage accrual and phenotype during skeletal muscle regeneration. Proc Natl Acad Sci U S A. 2018 Mar 13;115(11):E2585-E2593.

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DOI: 10.1136/annrheumdis-2019-eular.8577

SP0104 THE JANUS-FACED GLADIATOR: NEUTROPHILS IN STERILE INFLAMMATION AND AUTOIMMUNITY

Markus Hoffmann. *University of Maryland, School of Medicine, United States of America*

Background: Neutrophils, and particularly neutrophil extracellular traps (NETs), have been connected with inflammatory and autoimmune diseases, such as RA, SLE, gout and many others. However, the outcome of a deficiency of NET-formation can be observed in chronic granulomatous disease and Papillon-Lefèvre syndrome and is characterized by non-resolving inflammation and frequent autoimmunity.
Objectives: I will give an overview over pro- and anti-inflammatory effects of neutrophils and NETs, respectively, focusing on our results in gout and SLE.
Methods: We investigated the impact of NET-deficiency and/or neutrophil-depletion on animal models of SLE (pristane-induced lupus) and gout (MSU crystal-induced arthritis). Mechanistic studies were performed with isolated neutrophils from mice and humans.
Results: In experimental lupus and gouty arthritis neutrophil depletion or neutropenia worsens disease. Also mice strains with normal neutrophil numbers but defects in NET formation (NOX2 or PAD4-defieicnet mice) have exacerbated and unresolving inflammation.
Release of inflammatory mediators by stimulated neutrophils was highest at intermediate cell densities (20–40 $\times$ 10^6 cells/cm^3). Above such densities, mediator release by normal neutrophils was outweighed by proteolytic degradation via proteases expressed on aggregated NETs. Additionally, binding to aggregated NETs conferred protection of the serine protease neutrophil elastase (NE) against inactivation by α1-antitrypsin (A1AT).
Conclusion: Although neutrophils are often regarded as archetypical pro-inflammatory cells, evidence is increasing that they can also exert anti- inflammatory and immunoregulatory function. Formation and aggregation of NETs and degradation of inflammatory mediators by serine proteases are important neutrophil tools to resolve gouty arthritis and other forms of localized inflammatory conditions. On the downside, NETs come at the price of collateral tissue damage and may cause occlusion of ductal structures.

REFERENCES:

[1] Schauer, et al. Nature Med 2014, 20(5):511-7.
[2] Kienhöfer *et al*. JCI Insight, 2(10).
[3] Hahn *et al*. FASEB J 2019, 33(1):1401-1414.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8501

SP0105 REGULATION OF AUTOANTIBODY ACTIVITY BY T CELL SUBSETS

Gerhard Krönke. *University Hospital Erlangen, Internal Medicine 3, Erlangen, Germany*

Our recent data show that the IL-23–T_H17 axis controls the intrinsic inflammatory activity of autoantibodies and thereby triggers the clinical onset of autoimmune arthritis in mice and humans suffering from rheumatoid arthritis. TH17 cells regulate expression of sialyltransferases in newly differentiating antibody-producing cells and determine the glycosylation profile and activity of immunoglobulin G (IgG) that is produced by the consecutively emerging plasma cells.
Disclosure of Interests: Gerhard Krönke Grant/research support from: Lilly, Pfizer, Speakers bureau: Novartis
DOI: 10.1136/annrheumdis-2019-eular.8521

FRIDAY, 14 JUNE 2019

08:15:00 – 09:45:00

Seeing is believing: Nanotechnologies in tissue imaging

SP0106 LOOKING THROUGH MY BACK BONE

Matthias Gunzer. *University Hospital, University Duisburg-Essen, Institute for Experimental Immunology and Imaging, Essen, Germany*

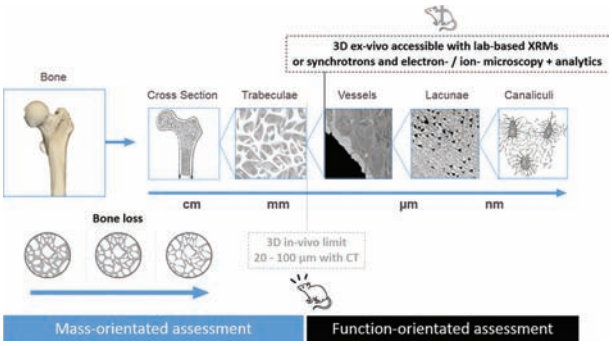
Background: Because bone marrow is the source of all immune cells, knowing the blood supply of bones is essential to understand diverse mechanisms such as arthritic bone inflammation, anti-infectious immune defense or sterile inflammation.
Objectives: We wanted to clarify, how immune cells are able to function inside of the bone and also leave bones for peripheral functions.
Methods: Using an array of different imaging approaches and innovative animal models as well as insights from clinical studies in humans we have made the bone open to ways of studying, that have not previously possible.
Results: Using these methods we have defined an entirely new concept of how a closed circulatory loop is established in long bones. Thereby we show the mechanistic role of osteoclasts and define, how T cells and neutrophils use the system to fight against viral infection or invade ischemic tissue. This allows an integrated

view how the blood circulation inside and outside of bones are interconnected to mediate functional or dysfunctional immunity.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8490

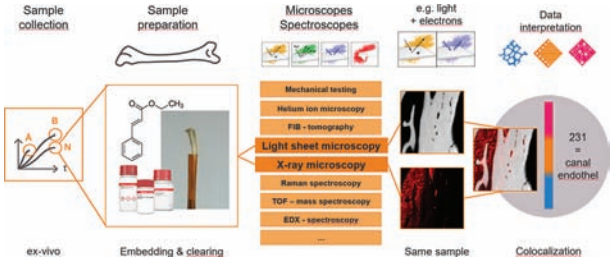
SP0107 THE 4-D+ NANOSCOPE: THE RESOLUTION FOR BIOLOGICAL SAMPLES

L. Kling[1,3], L. Mill[3,5], A. Grüneboom[5], G. Sarau[1,3], M. Herrmann[4], G. Schett[4], A. Maier[5], S.H. Christiansen[1,2,3]. *[1]Helmholtz-Zentrum Berlin für Materialien und Energie, Forschergruppe Christiansen, Berlin, Germany*; *[1]Christiansen Research Group, Helmholtz Zentrum Berlin für Materialien und Energie, Hahn-Meitner-Platz 1, 14109 Berlin, Germany*; *[2]Physics Department, Free University, Berlin, Arnimallee 14, 14195 Berlin, Germany*; *[3]Max Planck Institute for the Science of Light, Günther-Scharowsky-Str. 1, 91058 Erlangen, Germany*; *[4]Universitätsklinikum der Friedrich-Alexander-Universität Erlangen-Nürnberg, Med. 3, Ulmenweg 18, 91054 Erlangen, Germany*; *[5]Friedrich-Alexander-Universität Erlangen-Nürnberg, Pattern Recognition Lab, Martensstr. 3, 91058 Erlangen, Germany*

Background: In ageing societies all over the globe, the number of people suffering from bone disease, e.g. osteoporosis (OP) in the first place, has increased dramatically. OP considerably impairs patients' life quality, and results in high societal costs. However, current understanding of OP is still insufficient due to the lack of appropriate high resolution tools that permit a thorough analysis of scale bridging bone architectures from macro to nano with statistical significance to support the development of better treatments by drugs or surgical intervention.
Objectives: To revolutionize our knowledge of bone diseases based on an increase in understanding of the underlying bone anatomy, cutting-edge correlative high-resolution microscopy and spectroscopy together with advanced data analysis including machine learning approaches permit reaching the next, so far unprecedented level of understanding.
Methods: Correlative workflows starting from X-ray microscopy (XRM) volume analysis, with voxel sizes of <1µm, over light-sheet fluorescence microscopy and large scale scanning electron microscopy data acquisition, to dual beam microscope analysis (focused electron- and ion beams) permit the scale bridging investigation of bone architectures and thus merging the "big picture" and the underlying ultrastructure with statistical significance. In combination with additional analytical add-ons to these microscopes, physical properties such as optical, mechanical, compositional, structural etc. deliver a highly detailed correlative dataset of bone (cf. Figure 2).
The present paper demonstrates novel findings related to various partly age related bone diseases using advanced correlative data acquisition (cf. Figure 2).
Results: Figure 1 shows the different bone fine structures, composed of trabecular and vascular networks as well as a three-dimensional arrangement of osteolacunae that host osteocytes, as obtained by volume analysis in a new generation of lab-based x-ray microscope (Zeiss XRM Versa 520). These fine structures can be assessed quantitatively with statistical significance and can be correlated with additional modalities as shown in Figure 2. Elucidating examples demonstrating the power of such an approach will be given [ref 1, ref 2, ref 3, ref 4].
Figure 2 shows the an example correlative workflow from sample collection over sample preparation and the acquisition of various image modalities utilizing correlated data from electron-, ion-beam imaging and analytics, probes and focused laser light to study scale bridging bone architectures. We will demonstrate how these correlative workflows will permit to advance the current understanding of bone architectures and function substantially and will show some first systematic correlative microscopy and spectroscopy studies on mouse tibia and human bone [ref1, ref2, ref3, ref 4].



Abstract SP0107 Figure 1. Bone anatomy with scale – bridging architecture: mass oriented assessment with conventional methods such as DEXA and µCT and function-oriented assessment using correlative microscopy including volume analysis of trans-cortical vessels, osteo-lacunae and canaliculi by XRM and FIB/SEM.



Abstract SP0107 Figure 2. Correlative microscopy/spectroscopy workflow in bone research including (i) the challenges of sample preparation, (ii) the interplay of various image and data modalities, (iii) data evaluation, resolution enhancement and data analysis based on deep learning strategies; finally, new insights in open questions related to bone remodelling and bone structure at various length scales in relation to vasculature will be extracted from statistical correlative microscopy data.

Conclusion: Based on our correlative analytics and the data availability, the advanced data interpretation using machine learning approaches will be discussed. Using this approach, all details of bone micro-/nano-architecture can be used to provide a novel clinical tool-set for future for early detection of bone diseases.

REFERENCES:

[1] P. Milovanovic, et al., Bone tissue aging affects mineralization of cement lines, bone 110, 187 (2018).
[2] A. Grüneboom, et al., A network of trans-cortical capillaries forms the mainstay for blood circulation in long bones, Nature Metab. Published online (02/2019).
[3] P. Milovanovic, et al., The Formation of Calcified Nanospherites during Micropetrosis Represents a Unique Mineralization Mechanism in Aged Human Bone, small 13(3), 1602215 (2017).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8516

SP0108 LSFM AND CATCHING UP IN JOINT IMAGING

Anika Grueneboom[1].

Background: Bone tissue differs from other organs by its hardness and high optical density. These physical characteristics are challenging in the context of fluorescence based imaging studies addressing bone anatomy and physiology. The development of novel imaging technologies, such as light-sheet fluorescence microscopy and X-ray microscopy, and tissue-specific preparation procedures like optical clearing allowed us to reveal a so far overseen network of blood vessels in the cortical bone. These trans-cortical vessels (TCVs) directly connect the bone marrow vascularization with the periosteum and make the major contribution to total blood flow in long bones. Furthermore, we could show that immune cells are recruited to the peripheral circulation via TCVs and that TCVs are highly remodeled und inflammatory conditions. In case of chronic arthritis we observed a massive increase in TCV numbers, especially at the metaphysis of long bones. This increase in bone vascularization confirms observations of previous studies describing increasing numbers of microcanals in the bare area of metacarpal heads in the hands of rheumatoid arthritis patients. These alterations in bone anatomy might hint to an alternative mechanism by which immune cells are recruited into inflamed joint tissue. While current concepts describe the recruitment of immune cells from the systemic circulation, immune cells can potentially infiltrate the arthritic joints directly from the underlying bone marrow.
Objectives: Clarifying the anatomical routes of cell recruitment as well as exploring the regulatory mechanism guiding immune cells from the bone marrow to the site of inflammation might bear novel therapeutic strategies to resolve inflammation and tissue injury in rheumatoid arthritis.
Methods: 3D optical imaging approaches like Light-sheet fluorescence microscopy and 2-Photon laser-scanning microscopy enable the visualization of entire bones and joints. In combination with tissue-specific preparation procedures and labeling strategies inflammatory mediated changes in vascularization and cell recruitment can be analyzed.
Results: The joint tissue architecture is massively affected by inflammatory arthritic processes leading to changes in vascularization, permeability and cellular tissue composition. These processes are directly connected to the onset as well as the resolution of inflammatory arthritis.
Conclusion: Newly available imaging techniques as light-sheet fluorescence microscopy facilitate new insights into bone and joint tissue architecture, function and inflammatory processes. These findings might guide the identification of novel

proresolving mediators to develop therapeutic strategies for managing tissue-damage-induced inflammation.

REFERENCE:
[1] Grüneboom, A. et al., A network of trans-cortical capillaries as mainstay for blood circulation in long bones. *Nature Metabolism* 1, 236-250, doi:10.1038/s42255-018-0016-5 (2019)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8487

FRIDAY, 14 JUNE 2019

10:15:00 – 11:45:00

Paradigm shifts in arthritides

SP0109 **HOT: DIAGNOSIS AND TREATMENT OF INFECTION RELATED ARTHRITIDES**

Robert Schoen. *Yale School of Medicine, Rheumatology, Allergy, Clinical Immunology, New Haven, United States of America*

Background: Management of infectious arthritis has evolved because of empiric knowledge, clinical studies, and emerging pathogens. For patients with bacterial arthritis, organism specific, effective anti-microbial therapy is essential, but assessment of co-morbidities, adequate joint drainage, and supportive care are also required. For patients with infectious arthritis an acute intervention is usually necessary, since delay in diagnosis often leads to unsatisfactory outcome. In some situations, the distinction between infection and a post-infectious inflammatory process may be challenging.
Objectives: The goal of this lecture is to review management of septic arthritis in native joints. In addition, I will discuss Lyme arthritis and chronic chikungunya arthritis as examples of the broadening spectrum of infectious arthritis.
Methods: This lecture will rely on my clinical experience and a Pubmed literature search.
Results: In this HOT lecture, I will provide practical, up to date information about the diagnosis and management of septic (bacterial) arthritis of native joints. I will discuss longstanding treatment paradigms, as well as advances in management and areas of uncertainty. I will then consider two emerging infections, Lyme arthritis and chronic chikungunya arthritis, that illustrate the changing spectrum of infectious arthritis.
Conclusion: It is the intention of this lecture to assist rheumatologists in management of patients across the spectrum of infectious arthritis. Accurate diagnosis and treatment are often challenging, but critical to satisfactory patient outcome.

REFERENCES:
[1] Ross JJ: Septic arthritis of native joints. Infect Dis Clin North Am 2017; 31: 203-218.
[2] Schoen RT: Musculoskeletal manifestations of Lyme disease. In: Basow DS (ed): UptoDate 2019. Waltham, MA.
[3] Kennedy Amaral Pereira J, Schoen RT: Management of chikungunya arthritis. Clin Rheumatol 2017; 36: 2179-2186.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8583

FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

Safety First! Infectious complications and pregnancy issues in patients with rheumatic diseases

SP0110 **WIN: PREGNANCY ISSUES IN PATIENTS WITH RHEUMATIC DISEASES: THE OB PERSPECTIVE FOR RHEUMATOLOGISTS**

Catherine Nelson-Piercy. *Guy's and St. Thomas' Foundation Trust and Queen Charlotte's and Chelsea Hospital London, United Kingdom*

Pregnancy issues in patients with rheumatic diseases: the OB perspective for rheumatologists
Learning Objectives:

- Understand the importance of pre pregnancy counselling for women with rheumatic disease in pregnancy
- Understand the risk factors for adverse pregnancy outcome in women with rheumatic disease
- Understand the medications which are compatible with use in pregnancy and lactation
- Understand the management of rheumatic disease in pregnancy

Abstract: Rheumatic disease predominantly affects women of child-bearing age and are commonly encountered in obstetric practice. Pregnancy poses an important challenge for doctors looking after these women. Knowledge about medication safety, the effect of pregnancy on the disease, and vice versa, together with pre-conception counselling and multidisciplinary team care, are important to provide the best obstetric and medical care to these women.
Women with rheumatic have increased risks of miscarriage, preterm delivery, pre-eclampsia, fetal growth restriction, and disease flare in pregnancy. The main risk factor for adverse pregnancy outcomes in inflammatory arthritides is active disease/flare. For women with SLE the risks are lupus nephritis, particularly with CKD class 3-5, anti Ro/La antibodies, active disease and antiphospholipid antibodies. The most important issues of delaying pregnancy until there is quiescent disease, ensuring continued remission by continuation of drugs that are safe in pregnancy and adequately and promptly treating any flare of disease will be discussed. Adequate surveillance of the mother and fetus is imperative, but stratification of women is important to ensure that those with low risk pregnancies are not over medicalized.
There is an understandable reluctance to prescribe drugs, particularly immunosuppressant drugs, in pregnancy and in breast feeding mothers. However much harm can result if drugs are withdrawn, omitted or the dose reduced inappropriately. Active disease has an adverse effect on female fertility and time to pregnancy aw well as impacting adversely on pregnancy outcomes.
Guidelines from the British Society of Rheumatology and EULAR have reviewed the safety data for antirheumatic drugs in pregnancy. These publications include recommendations for which drugs are compatible with pregnancy and during lactation. These guidelines should reduce errors of omission where important medication for disease control are discontinued prior to or in pregnancy and empower rheumatologists to help women to time their pregnancies during disease remission and with continuation of medications including biologics compatible with pregnancy.

REFERENCES:
[1] Ateka-Barrutia O, Nelson-Piercy C. ***Connective tissue disease in pregnancy***. Clin Med. 2013; 13: 580-4. Soh MC, Nelson-Piercy C. ***High-risk pregnancy and the rheumatologist***. Rheumatology (Oxford). 2015 Apr;54(4):572-87. doi: 10.1093/rheumatology/keu394. Epub 2014 Dec 3.
[2] Flint J, Panchal S, Hurrell A, van de Venne M, Gayed M, Schreiber K, Arthanari S, Cunningham J, Flanders L, Moore L, Crossley A, Purushotham N, Desai A, Piper M, Nisar M, Khamashta M, Williams D, Gordon C, Giles I*; BSR and BHPR Standards, Guidelines and* Audit Working Group. BSR ***and BHPR guideline on prescribing drugs in pregnancy and breastfeeding****-Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. Part II: analgesics and other drugs used in rheumatology practice.* Rheumatology (Oxford). 2016 Jan 10. *pii: kev405.*
[3] Götestam Skorpen C, Hoeltzenbein M, Tincani A, Fischer-Betz R, Elefant E, Chambers C, da Silva J, Nelson-Piercy C, Cetin I, Costedoat-Chalumeau N, Dolhain R, Förger F, Khamashta M, Ruiz-Irastorza G, Zink A, Vencovsky J, Cutolo M, Caeyers N, Zumbühl C, Østensen M. *The* **EULAR points to consider** *for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation.* Ann Rheum Dis. 2016 May;75(5):795-810. doi: 10.1136/annrheumdis-2015-208840. Epub 2016 Feb 17.

Disclosure of Interests: Catherine Nelson-Piercy Consultant for: UCB, Speakers bureau: UCB
DOI: 10.1136/annrheumdis-2019-eular.8549

FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

Immunosuppression in SSc – a matter of timing!

SP0111 **POTENTIAL CELLULAR AND MOLECULAR TARGETS**

Jörg Distler. *University of Erlangen-Nuremberg, Department of Internal Medicine 3, Erlangen, Germany*

The pathophysiology of systemic sclerosis (SSc) is characterized by a cascade of microvascular injury with apoptosis of endothelial cells, Th2/M2 biased

inflammation and autoimmunity and aberrant fibroblast activation with excessive matrix deposition. We increasingly recognize that physiological wound healing and the initial stages of SSc share many commonalities. However, in contrast to physiological repair, these tissue repair programs are not effectively terminated in SSc resulting in progressive matrix deposition and tissue damage. The mechanisms of fibroblast activation may change during the cause of SSc; Profibrotic mediators released from infiltrating leukocytes, activated endothelial cells and degranulated platelets may drive fibroblast activation and collagen release in particular in early stages, whereas endogenous activation loops with activation of fibroblasts by epigenetic changes and biomechanical or physical factors may be of increasing importance in later stages of SSc.
In my presentation, I will discuss novel insights into the pathogenesis of SSc with a particular focus on the interplay of inflammation and fibroblast activation. I will focus on translational aspects and highlight mechanisms with high potential for transfer from bench-to-bedside.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8460

SP0112 **IMMUNOSUPPRESSION – ONE FITS ALL VS. INDIVIDUALIZED SELECTION?**

Marco Matucci-Cerinic. *University of Florence, Division of Rheumatology AOUC, florence 50139, Italy*

Systemic sclerosis (SSc) is an autoimmune disease characterised by skin, vascular and internal organ involvement leading eventually to tissue fibrosis and atrophy. The best control of the disease is usually achieved in the early phase which is characterised by a diffuse tissue inflammation and vasculopathy. of the tissues. In this phase an immunosppressive stragey can in fact lead to disease remission even if some cases may escape control and progress inesorably to fibrosis.
Classically, the clinical profile of the patient needs to be achieved. The subset, the disease activity and the main clinical features should be defined in order to have the precise profile of the disease. The knowledge of the clinical conditions may therefore help in deciding the drug and shaping the therapeutic regimen and its intensity. Usually, the use of Cyclophosphamide (CYC) and Micophenolate (MMF) may fit the necessity of the largest part of the SSc population. In practice, CYC may be employed as an induction treatment, eithe rorally or intravenous, while MMF may be used as a maintenance therapy. Both drugs have been demonstrated to be useful in the treatment of SSc either on the cutaneous or on the lung involvement.
However, the most severe and refractory cases may be today considered for a hematopietic stem cell transplantation (HSCT). In this case, an individualised selection is performed before a patient can be considered fit to receive this kind of therapeutic regimen. Therefore, the treatment is strictly individualised and only after having a thorough clinical evaluation the patient can be accepted for the systemic conditioning with high doses of CYC for bone marrow ablation. In conclusion, the treatment of SSc is today mainly centered on immunesuppression whose intensity must be decided and individualized according to the disease activity. New innovative targeted drugs are on the horizon in the effort to find the right immunosuppressive and antifibrotic therapeutic approach clinically tailored on the SSc patient.
Disclosure of Interests: Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS; MSD, Janssen
DOI: 10.1136/annrheumdis-2019-eular.8534

SP0113 **STEM CELL TRANSPLANTATION – ALL SCIENTIFIC QUESTIONS ANSWERED?**

Jacob M. van Laar. *University Medical Center Utrecht, Netherlands*

Hematopoietic stem cell transplantation (HSCT) currently is the only disease modifying treatment for patients with poor prognosis diffuse cutaneous systemic sclerosis (dcSSc) based on three controlled clinical trials (ASSIST, ASTIS, SCOT). Nevertheless uptake of this intensive treatment modality is slow in most countries, due to funding issues, lack of medical experience, and concerns over toxicities including the risk of transplant-related mortality (TRM). Over the years, safety of HSCT has improved and TRM has dropped due to more stringent patient selection and better supportive care. Nevertheless, dcSSc remains a high-risk condition for HSCT, and even a minimum degree of risk remains unavoidable. The decision to opt for HSCT therefore requires a thorough discussion of potential benefits and possible risks with a patient and their family and ultimately hinges on shared decision making and informed consent. Apart from such clinical issues there are still plenty of scientific questions to be answered. First, should HSCT be offered as first-line immunosuppressive or chemotherapy in high-risk patients, or is it better to reserve HSCT as salvage-therapy for those who failed a course of routine immunosuppression or i.v. pulse cyclophosphamide? And if so, on the basis of what criteria should treatment intensity be stepped up? Second, how can patient selection be optimised so as to avoid transplanting dcSSc patients with little chance of responding? Third, is there a window of opportunity where the immune system can be rebooted? Last but not least, how can potentially eligible dcSSc patients get access to HSCT? The latter may be the most (de)pressing one, as HSCT is only available in a small number of centres. Until efficacious disease-modifying drugs with a better risk-benefit ratio become available, HSCT will continue to be the only therapeutic option to reverse the disease course in dcSSc patients.
Disclosure of Interests: Jacob M. van Laar Grant/research support from: Genentech, Consultant for: F. Hoffmann-La Roche
DOI: 10.1136/annrheumdis-2019-eular.8611

FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

Predicting short-term fracture risk: can we foresee the (close) future?

SP0114 **CASE 1 PRESENTER: IMMINENT FRACTURE RISK: ASSESSMENT AND DOES IT HELP CLINICAL MANAGEMENT**

Nicholas Fuggle. *University of Southampton, MRC Lifecourse Epidemiology Unit, Southampton, United Kingdom*

A 60 year old female was under long-term follow-up for rheumatoid arthritis, for which she took methotrexate. Ten years previously she had been found to have a single vertebral fracture and her fracture risk, assessed using The WHO Fracture Risk Assessment Tool (FRAX®), was calculated as a 13% risk of major osteoporotic fracture over the next 10 years. According to The National Osteoporosis Guideline Group (NOGG) recommendations, she underwent Dual X-ray Absorptiometry (DXA) which demonstrated a bone mineral density T-score of -1.7 at the femoral neck. Lifestyle, vitamin D and calcium intake were optimised and follow-up was arranged for 6 months.
Prior to her next appointment she fell and sustained a fracture of the distal radius. On fracture liaison review her FRAX® risk of fracture was 14% (rising due to an increased year of age) despite the recent change in clinical circumstances.
This case serves to emphasise the clinical conundra associated with imminent fracture risk (the 2 years after a fracture when the patient is at a significantly higher risk of fracture) and the difficulties with the decision to treat.
Disclosure of Interests: None declared
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SP0115 **CASE 1 DISCUSSANT: IMMINENT FRACTURE RISK: ASSESSMENT AND DOES IT HELP CLINICAL MANAGEMENT**

Cyrus Cooper. *University of Southampton, MRC Lifecourse Epidemiology Unit, Southampton, United Kingdom*

With an estimated 520,000 fragility fractures every year in the UK, delivering effective and efficient healthcare for this patient group has significant consequences for patients, families, the NHS, and society. A fragility fracture is a major risk factor for further fractures, and healthcare systems are now beginning to recognise the benefits of secondary fracture prevention. Despite this, less than 50% of patients receive effective secondary fracture prevention after a fragility fracture. This has led to national and international initiatives to improve clinical services by implementing fracture liaison services (FLSs). Successful funding of a new FLS is usually influenced by the number of fractures it is expected to prevent in the first few years after an index fracture. The expected number of fractures prevented is in turn determined by the baseline risk of subsequent fracture, the number of patients at high enough fracture risk to warrant anti-osteoporosis medication (AOM), and the degree of fracture risk reduction by AOMs. Underestimating fracture risk in the post-fracture period will lead to fewer expected fractures prevented and lower perceived benefit of the FLS by payers, and importantly also by patients, families, healthcare providers, and payers. Tools are available to determine the long-term risk of fracture based on patient factors, including previous fracture. Of these, FRAX and QFracture have been incorporated within UK NICE clinical guidance, and the FRAX-derived intervention threshold is used to guide recommendations for AOM in the NHS.
Disclosure of Interests: Cyrus Cooper Consultant for: Personal fees from Alliance for Better Bone Health, Amgen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB.
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SP0116 **CASE 2 PRESENTER: BREAKING BAD AND TRAGICALLY HIP. A CASE OF A MISSED OPPORTUNITY AFTER VERTEBRAL FRACTURE**

Michael Skjødt. *Norwegian University of Science and Technology (NTNU), Department of Public Health and Nursing, Trondheim, Norway*

Mrs A is a 78-year old woman, admitted to the emergency room after a same level fall in her home earlier the same day. She has a history of Chronic Obstructive Pulmonary Disease with recurrent exacerbations, and hysterectomy at the age of 41.
At admittance, she is complaining of agonising pain localised to her right hip, and she is unable to move the leg. Upon the physical examination, the right leg is shortened and outwardly rotated. Upon further questioning, Mrs A reveals that she has lost four or five cm of height during the past years.
An X-ray of the hip demonstrates a neck of the femur fracture. Mrs A has surgery the following day and two screws are inserted. Due to a hospital-acquired pneumonia, Mrs A stays in the hospital for an additional 9 days after the operation, upon which she is discharged for a temporary placement at a nursing home for further rehabilitation.
Two months following discharge, Mrs A was called for a clinical evaluation by the hospital Fracture Liaison Service. Assessment with DXA confirms the osteoporosis diagnosis and VFA shows lower thoracic vertebral fractures. The FLS coordinator noted that Mrs A, related to a hospital admission for an acute exacerbation of her COPD 3 years before, had had a chest x-ray performed, on which vertebral fractures of the thoracic spine could be seen to be present. Mrs A has never previously been assessed nor treated for osteoporosis.

Disclosure of Interests: None declared
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SP0117 **CASE 2 DISCUSSANT: AUTOMATED (IMPLEMENTED IN ELECTRONIC MEDICAL RECORD SYSTEMS) SHORT-TERM FRACTURE RISK PREDICTION**

Bo Abrahamsen. *x, x, x, Denmark*

Identification of patients at high risk of osteoporotic fractures is commonly based on fracture history, bone mineral density or a combination of the two. However, vertebral fractures are very often either missed or not acted upon by our health systems and DXA scanning to measure BMD in itself requires a coherent case finding strategy.
Current EPR systems may have built-in features to capture signs of sepsis or warnings to alert clinicians to cases with a diagnosis of atrial fibrillation with no apparent prescription for anti-coagulation. Building on the same principle, EPR systems or even national databases can be set up with appropriate decision rules to alert physicians to diagnoses such as RA, AS or COPD that we know strongly increases the risk of osteoporosis and to flag out medication patterns known to predict a high risk of osteoporotic fractures. This can then be checked against the presence of referrals for DXA and/or prescriptions for anti-osteoporosis medications and a clinical decision aid triggered to alert healthcare professionals. The mechanism powering such a tool can be an existing clinical risk algorithm such as qFracture, FRAX, FREM, Garvan FRC or others, depending on the nature of routinely collected data, the setting and the timescale required, or a bespoke risk tool developed for the healthcare system in question. It is important to appreciate that risk tools need careful calibration to be appropriate across countries and clinics and that the trigger risk level is ultimately a trade-off between clinical judgment and health economics.
Vertebral fractures represent a particular challenge. It has been established in the past that vertebral fractures often are not mentioned in radiology reports even if clearly present, or reported using unclear terminology that does not make it sufficiently clear to clinicians that a vertebral fracture is present. Moreover, even when vertebral fractures are called out in the radiology report it is not uncommon for this to go unnoticed. Opportunistic identification of vertebral fractures by software tools is a possible new avenue for narrowing the treatment gap in osteoporosis. With increasing integration of DICOM images into EPR systems, DICOMs of CT scans and other modalities containing spine images could be used either for automated case finding with alert boxes in the EPR system itself or employed in radiology departments to automatically populate reports with additional information about the presence of vertebral fractures.

REFERENCES:

[1] ***Rubin KH*** *A New Fracture Risk Assessment Tool (FREM) Based on Public Health Registries.* J Bone Miner Res. 2018 Nov;33(11):1967-1979.
[2] ***Reber KC*** *Development of a risk assessment tool for osteoporotic fracture prevention: A claims data approach.* Bone. 2018 May;110:170-176.
[3] ***Hippisley-Cox J*** *Predicting risk of osteoporotic fracture in men and women in England and Wales: prospective derivation and validation of QFractureScores.* BMJ. 2009 Nov 19;339:b4229.
[4] ***Moon RJ***. *Identification of patient profile for treatment. Best Pract Res Clin Endocrinol Metab. 2014 Dec;28(6):767-82.*
[5] ***Rubin KH*** *Risk assessment tools to identify women with increased risk of osteoporotic fracture: complexity or simplicity? A systematic review. J Bone Miner Res. 2013 Aug;28(8):1701-17.*

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FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

Primary and secondary fibromyalgia; are they different?

SP0118 **FIBROMYALGIA; AN ACCEPTABLE DIAGNOSIS?**

Rinie Geenen. *Utrecht University, Department of Psychology, Utrecht, Netherlands*

Background: Neither patients nor clinicians and researchers fully embrace the fibromyalgia diagnosis. A core objection relates to the huge overlap with other polysymptomatic distress disorders such as somatic symptom disorder and chronic fatigue syndrome. Another objection has to do with the classification of fibromyalgia as a rheumatic disease, which may hamper research and treatment of psychosocial factors.
Objectives: To get insight into the pros and cons of the fibromyalgia diagnosis.
Methods: The scientific literature was reviewed with a focus on homogeneity and heterogeneity within the group diagnosed as fibromyalgia.
Results: That fibromyalgia is not a stable diagnosis of a homogeneous group is reflected in the ongoing development of new classification and diagnostic criteria; the newest including diagnostic criteria, common features, comorbidities, consequences, and putative mechanisms (Arnold et al., 2019). Moreover, treatment recommendations progressed from a focus on pharmacological treatment in 2008 to a focus on nonpharmacological therapies in 2017 (Macfarlane et al., 2017). Also, several studies showed that the group is quite heterogeneous with respect to type, number and severity of symptoms and comorbidities (e.g., Davis et al., 2018) as well as with respect to adaptation profiles covering a spectrum of severely maladjusted to quite well adjusted in terms of objective and subjective management (Estevez-Lopez et al., 2018).
Conclusion: Although diagnostic classifications such as fibromyalgia help to examine underlying mechanisms and interventions and to define treatment recommendations, in clinical practice and research account should be taken of heterogeneity of patients in terms of symptoms and disorder-transcending biopsychosocial factors that influence the disorder. This suggests that fibromyalgia is an acceptable diagnosis to the extent that individuality is accepted as part of the diagnosis.

REFERENCES:

[1] Arnold, et al. AAPT Diagnostic Criteria for Fibromyalgia. J Pain 2019, in press.
[2] Davis, et al. Characterizing classes of fibromyalgia within the continuum of central sensitization syndrome. J Pain Res 2018;11:2551-60.
[3] Estevez-Lopez, et al. Adaptation profiles comprising objective and subjective measures in fibromyalgia: the al-Andalus project. Rheumatology (Oxford) 2017;56:2015-24
[4] Macfarlane, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis 2017;76:318-28.

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SP0119 **SEARCHING FOR PATHOLOGY; HOW HARD SHOULD WE LOOK?**

Ernest Choy. *CREATE Centre, United Kingdom*

Background: The 1990 American College of Rheumatology (ACR) classification criteria for Fibromyalgia (FM) was intended to facilitate research by defining a homogenous patient population [1]. Two key features of the criteria are tender point examination and exclusion of other conditions that may cause widespread pain. This led to the view that FM is a diagnosis of exclusion. This is no longer the case in 2019.
Results: In 2010, the ACR published provisional criteria for the diagnosis of FM [2]. These allowed FM to be diagnosed by using questionnaire removing the need for tender point examination. One of the major advantages of the criteria is that the diagnosis of FM can be made by primary care physician and the first-line treatment be initiated without referral to secondary care. Such an approach was

recommended by the Canadian guidelines [3], which recommended "patients should undergo a physical examination which should be within normal limits except for tenderness on pressure of soft tissues however the specific tender point examination according to the 1990 ACR diagnostic criteria is not required to confirm a clinical diagnosis of fibromyalgia". Furthermore, it stated that "Fibromyalgia should be diagnosed as a clinical construct, without any confirmatory laboratory test, and with testing limited to simple blood testing including a full blood count, erythrocyte sedimentation rate, C-reactive protein, creatine kinase, and thyroid stimulating hormone. Any additional laboratory or radiographic testing should depend on the clinical evaluation in an individual patient that may suggest some other medical condition." However, many primary care physicians do not feel competent/confident to exclude other rheumatic conditions by physician examination.

Over the last decade, comorbid FM is increasingly recognized in many chronic musculoskeletal diseases including patients with inflammatory arthritis. A systematic review found that the prevalence of FM is 21%, 13% and 18% in RA, axSpA and PsA respectively [4]. Patients with comorbid FM have higher diseases activity score and more severe pain.

In 2016, the ACR diagnostic criteria for FM were modified and stated that "A diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses." [5].

Conclusion: The motion that "FM is a diagnosis of exclusion" is no longer valid. FM should be a positive diagnosis and does not exclude other rheumatic diagnosis.

REFERENCES:

[1] Wolfe F, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum. 1990;33:160-72.
[2] Wolfe F, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res. 2010;62:600-10.
[3] Fitzcharles MA, et al. 2012 Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome: executive summary. Pain Res Manag. 2013;18(3):119-26.
[4] Duffield SJ, Miller N, Zhao S, Goodson N. Concomitant fibromyalgia complicating chronic inflammatory arthritis: a systematic review and meta-analysis. Rheumatol (Oxford). 2018;57:1453-1460.
[5] Wolfe F, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016;46:319-329.

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SP0120 **PERSONALISED TREATMENT FOR FIBROMYALGIA; THE IMPACT OF COMORBIDITIES**

Serge Perrot. *France, France*

Background: The heterogeneity of the clinical presentation, the co-morbidities and the pathophysiologic mechanisms associated with fibromyalgia (FM), and the modest results on average for any therapy, call for a more individualized management strategy.

How to develop personalized treatment?

Individualized treatment can be developed on the basis of subgrouping of patients according to associated conditions and co-morbidities (mental health problems, chronic overlapping pain conditions, other somatic diseases) or on disease severity. Personalizing treatment needs to classify FM in specific subgroups. It can be proposed on the basis of clinical assessment (eg, degree of daily functioning), on co-morbidities or on dedicated questionnaires. Lastly, shared decision-making regarding treatment options can be directed according to patient preferences, co-morbidities, and availability in various health care settings.

What is currently recommended as a personalized approach?

The European League Against Rheumatism guidelines recommend a tailored approach directed by FM key symptoms (pain, sleep disorders, fatigue, depression, disability), whereas the German guidelines recommend management tailored to disease severity, with mild disease not requiring any specific treatment, and more severe disease requiring multicomponent therapy (combination of drug treatment with aerobic exercise and psychological treatments). When indicated, treatments should follow a stepwise approach beginning with easily available therapies such as aerobic exercise and amitriptyline. We will present how successful application of a tailored treatment approach that is informed by individual patient characteristics should improve outcome of FM.

Key points: This presentation will presents suggestions for an individualized treatment strategy for FM patients on the basis of symptoms, disease severity and co-morbidities.

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FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

Joint EULAR – EFIS: Combatting or harnessing ILC in the battle against autoimmunity

SP0121 **DEBATE: ILC AS INNOCENT BYSTANDER**

Mikael Ebbo. *Hopital de la Timone, AP-HM, Aix-Marseille Université, Internal Medicine, Marseille, France*

Innate lymphoid cells (ILC) are recently (10 years ago) described tissue-resident lymphoid populations [1]. They lack adaptive antigen receptor (generated by the recombination of genetic elements) and are innate counterparts of T lymphocytes. Indeed ILC1s, ILC2s, and ILC3s mirror $CD4^+$ T helper (Th)1, Th2, and Th17 cells, respectively, in terms of transcription factor expression and cytokine production.

In this lecture, an overview of the different protective immunological functions of these helper ILC will be provided, in particular their role for maintenance of gut homeostasis, for control of parasitic, bacterial or viral infections, for anti-tumor immune responses, for metabolism, or for tissue repair mechanisms. The concept of ILC plasticity, which represents the capacity of these cells to change their phenotype and functional capacities in response to diverse microenvironment stimuli, will be also addressed. It directs the heterogeneity of these cells in the tissues, and may be important for their effective immune responses.

In this context, targeting ILC for therapeutic use, for example in the battle against autoimmune or inflammatory diseases in which they may also play roles [2], could be associated with deleterious consequences. However, recent data concerning patients with a profound and selective ILC deficiency and no susceptibility to disease will be also presented here. This last observation suggests that most protective functions mentioned above may be redundant and potentially dispensable for human health, at least in modern conditions of hygiene and medicine, when T cell and B cell functions are preserved.

REFERENCES:

[1] Innate Lymphoid Cells: 10 Years On. Vivier E, et al. Cell. 2018 Aug 23;174(5):1054-1066.
[2] Innate lymphoid cells: major players in inflammatory diseases. Ebbo M, et al. Nat Rev Immunol. 2017 Nov;17(11):665-678.
3] . Evidence of innate lymphoid cell redundancy in humans. Vély F, et al. Nat Immunol. 2016 Nov;17(11):1291-1299.

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FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

Optimizing the access to new treatments for RMD patients

SP0122 **OPTIMIZING HOLLISTIC TREATMENTS: THE CHALLENGE OF IMPLEMENTATION**

Krysia Dziedzic. *Keele University, School for Primary, Community and Social Care, Stoke on Trent, United Kingdom*

International guidelines present recommendations for holistic care for RMDs, building upon best evidence. However, there is still a gap between what we know about best care and what we do to implement best care in our clinical services. Having EULAR guidelines alone (and multiple updates and revisions) is not enough to change complex systems. European funders are now investing in projects to accelerate the uptake of best care across multiple European partners.

Using one example of a completed EIT-Health funded implementation project, JIGSAW-E (Joint Implementation of Guidelines for oSteoArthritis in Western Europe), this presentation will highlight some of the challenges of implementation such as: understanding the context; competing priorities; lack of time and funding; stability of the workforce; and differing health care systems. It will describe the use of Knowledge Mobilization and Communities of Practice as methods for overcoming these challenges and optimizing holistic treatments.
The presentation will offer some of the key factors for implementation such as 'leading from the middle' and brokering across silos; working with patients and the public '*Patients are the most under-used resource in any health care system';* using theories, models and frameworks to plan, understand and evaluate implementation; using pilot sites to build momentum with dedicated Communities of Practice; and agreeing what success should look like.
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SP0123 **NEW TREATMENTS: WHY SHOULD WE WAIT?**

Daniel Morales. *University of Dundee, Population Health and Genomics, Dundee, United Kingdom*

Background: Improving access to new and established medicines for rheumatological disease is of public health importance. However, drug development processes, medicines regulation and health technology requirements may significantly impact on when a new medicine become available to be used by health care professionals.
Objectives: The objectives of this session are to present some of the challenges and opportunities for accessing new and established medicines for rheumatological disease.
Methods: Drug development processes, medicines regulation and health technology requirements may significantly impact on when a new medicine become available to be used by health care professionals. Although these requirements may be perceived as barriers, many of these requirements are in place to ensure a medicines benefit risk profile is favorable and is cost effective in terms of quality of life. This session will briefly discuss issues around the process of making medicines newly available from drug development to gaining new market approvals with an emphasis on rheumatological disease, including the post-authorization safety requirements that are in place to safe guard public health.
Disclosure of Interests: None declared
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FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

New assessments in clinical practice

SP0124 **WHICH MEASURES TO USE TO ASSESS REMISSION IN RHEUMATOID ARTHRITIS**

Annamaria Iagnocco. *Academic Rheumatology Unit Universita degli Studi di Torino, Academic Rheumatology Centre, Turin, Italy*

Remission is the ideal target of treatment in rheumatoid arthritis (RA) patients. However, the definition and characterization of remission is still a theme of discussion and its assessment can be a challenging issue in RA clinical practice. Indeed, nonetheless the new treatments and therapeutic strategies for RA make remission possible, sub-clinical inflammation can still be present both at the joint site and at the patient level, leading to damage progression and to occurrence of flares.
Clinically, remission entails persistent absence of any sign of joint and systemic inflammation. However, the presence of some residual joint inflammatory activity can be accepted by current clinical indexes such as DAS28, SDAI, CDAI and Boolean remission, although the latter is clearly based on more stringent parameters (1,2). Based on those criteria, and particularly with the use of SDAI and Boolean cut-offs, complete and persistent remission is then quite uncommon in late RA, while it seems to be more easily possible in early disease (3). Another interesting issue to consider in clinical practice is the presence of sustained remission which seems to occur less frequently than remission at different point times and with only a minority of cases reaching a complete disease recovery (4).
Depending on the modality that is used, the assessment of remission by imaging encompasses the evaluation of a wide spectrum of lesions. While ultrasound is able to show intra- and peri-articular signs of inflammation and to differentiate active from inactive synovitis with the use of Doppler modes, MR shows also bone marrow inflammatory-related abnormalities. Moreover, ultrasound detects inflammation at multi-site level and allows the measurement of stable remission over time on longitudinal evaluation. Interestingly, also tenosynovial Doppler inflammation has been demonstrated to be a frequent finding in patients in clinical remission and, compared to joint synovitis, it is more associated with self-perceived unstable remission (5). In addition, tenosynovial and joint Doppler positivity has been demonstrated to be an independent risk factor of flare in RA patients in remission (6). Residual joint inflammation in patients in remission can be demonstrated also by other imaging techniques, such as PET which shows enhanced tracer uptake at different joint sites (3). Basically, the capability of imaging to demonstrate sub-clinical disease activity even in patients in clinical remission, by allowing the detection of residual inflammation at different joint sites and at different disease stages gives it an added value compared to clinical assessment alone.
In conclusions, clinical evaluation of remission alone appears frequently inadequate to capture a real persistent lack of inflammation at different joint sites. Imaging can complement the assessment of patients in clinical remission, offering additional data that may still reveal a certain amount of sub-clinical disease activity. With new therapeutic strategies RA management has become increasingly complex over the last years (7). The relevance of this information is then substantial, being structural damage the result of both previous and current phases of disease activity.

REFERENCES:
[1] Felson, et al. Ann Rheum Dis 2011;70: 404–13.
[2] Chandrashekara, et al. International Journal of Rheumatic Diseases 2013; 16: 291–6.
[3] Bugatti, et al. Front Med (Lausanne)2018; 15: 140-8.
[4] Pope, et al. Athritis Care Res (Hoboken) 2019 Mar 1. doi: 10.1002/acr.23862.
[5] Bellis, et al. Rheumatology 2016; 55: 1826-36.
[6] Filippou, et al. Ann Rheum Dis 2018; 77: 1283-9.
[7] Smolen, et al. Ann Rheum Dis 2017; 76: 960-77.

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SP0125 **HOW TO ASSESS PATIENT WITH SUSPECTED VASCULITIS**

Raashid Luqmani. *University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*

Background: Systemic vasculitides are multi-organ, multi-system conditions which can mimic many other diseases. They are rare but very significant because they can rapidly lead to end organ damage or death if left untreated. The difficulty faced by clinicians in diagnosing a patient with vasculitis is further compounded by the presentation of limited forms of vasculitis, which can be difficult to recognise as due to vasculitis, the effects of co-existing co-morbidity and the use of drugs either for medicinal or recreational purposes. Giant cell arteritis is one of the most common serious forms of vasculitis in adults, leading to blindness if untreated. In view of this risk, many clinicians will initiate treatment of any patients with suspected giant cell arteritis before definitive investigations have been performed. Unfortunately this can result in inadequate outcomes form diagnostic tests such as ultrasound or biopsy of the temporal artery. There are no diagnostic criteria for most forms of vasculitis apart from Behcet's syndrome. Some tests can be very useful in ruling out other causes as well as helping to confirm a diagnosis of vasculitis. We will review some of the strategies for diagnosing vasculitis, complementing a thorough history and examination with selected investigations to improve diagnostic certainty.
Objectives: To consider the strategies used to assist the diagnosis of systemic vasculitis; to assess the frequency of multi-system involvement in systemic vasculitis; to critically evaluate the role of diagnostic testing in systemic vasculitis.
Methods: A review of current literature on the approach to diagnosis and classification of vasculitis.
Results: Table 1 summarises the clinical manifestations of some forms of primary systemic vasculitis, comparing the different frequencies of the common presenting features. Patients with large vessel vasculitis are usually more distinct as a clinical group from other forms of vasculitis but increasingly we see an overlap between GCA and older patients (especially males) with Takayasu arteritis. There is considerable overlap of clinical features amongst the small vessel vasculitides, despite different immuno-pathogenetic pathways. Amongst the anti-neutrophil cytoplasm antibody (ANCA) associated vasculitides (AAV), the presence of active nephritis characterises most patients with MPA; it is less common in GPA and least common in EGPA. Lung involvement is prevalent in all three forms of AAV, but has different characteristics: bronchial wall inflammation with ulceration plus nodules and infiltrates in GPA; transient infiltrates and bronchospasm in EGPA; lung haemorrhage at presentation in MPA, with subsequent risk of developing lung fibrosis. The different patterns of disease activity help in differentiating

Abstract SP0125 – Table 1. Clinical features of some forms of systemic vasculitis

Type of vasculitis	Systemic	Eye	Skin	ENT	Lung	Heart	Gut	Renal	PNS	CNS
Takayasu arteritis	<65%	30%	3-28%	-	50-86%	5-55%	7-9%	0- 50%	-	33%
Giant cell arteritis	40%	20-50%	<5%	<50%	<10%	10%	-	-	14%	0 - 90%
Polyarteritis nodosa	<66%	10-20%	8-27%	-	-	10-40%	40-60%	30-50%	50-75%	1%
Granulomatosis with polyangiitis	30-97%	28-58%	10-50%	75-98%	52-94%	0-12%	5-11%	40-100%	15-41%	6-13%
Microscopic polyangiitis	73-92%	28-30%	35-60%	20-30%	25-55%	9-18%	30-56%	up to 100%	14-58%	0-40%
Eosinophilic granulomatosis with polyangiitis	69-100%	10%	51-69%	0-80%	100%	28-49%	8-59%	16-27%	65-76%	9-11%

individual forms of vasculitis, but it is important to remember that many features associated with medication and co-morbidity may make this patient group more homogeneous, especially if the original disease manifestations are now quiescent.

We will explore the potential use of classification criteria as substitutes for diagnostic criteria in different forms of vasculitis and evaluate the role of specific tests to assist in the diagnosis, with a focus on ANCA testing in small vessel vasculitis and on imaging in large vessel vasculitis.

Conclusion: A rational approach to diagnosis in vasculitis is required, based on a combination of clinical features together with relevant investigations. Diagnostic certainty can vary in the absence of definitive evidence from investigations, especially if patients have already been partly treated prior to completing all relevant investigations. Diagnostic testing is improving and with the development of new criteria for classification, this forms a stronger basis to develop a more sound approach to diagnosis. However, we should always be prepared to apply a provisional diagnosis and reconsider any emerging evidence to suggest an alternative condition.

REFERENCES:

[1] Monti S, Águeda AF, Luqmani R. The use of ultrasound in the management of large-vessel vasculitis: an evolving concept. Clin Exp Rheumatol. 2018 Sep-Oct;36 Suppl 114(5):96-102
[2] Ponte C, Águeda AF, Luqmani RA. Clinical features and structured clinical evaluation of vasculitis. Best Pract Res Clin Rheumatol. 2018 Feb;32 (1):31-51.
[3] Seeliger B, Sznajd J, Robson JC, Judge A, Craven A, Grayson PC, Suppiah RS, Watts RA, Merkel PA, Luqmani RA. Are the 1990 American College of Rheumatology vasculitis classification criteria still valid? Rheumatology (Oxford). 2017 Jul 1;56(7):1154-1161
[4] Slart RHJA; Writing group; Reviewer group; Members of EANM Cardiovascular; Members of EANM Infection & Inflammation; Members of Committees, SNMMI Cardiovascular; Members of Council, PET Interest Group; Members of ASNC; EANM Committee Coordinator. FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (PIG), and endorsed by the ASNC. Eur J Nucl Med Mol Imaging. 2018 Jul;45 (7):1250-1269.

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SP0126 **CLINICAL IMPORTANCE OF ANA ANTI-DSF70 ANTIBODIES**

Johan Rönnelid. *Uppsala University, Department of Immunology, Genetics and Pathology, Uppsala, Sweden*

Background: Analysis of anti-nuclear antibodies (ANA) is a hallmark in the classification criteria for many systemic rheumatic diseases, including systemic lupus erythematosus (SLE). ANA investigations performed with indirect immune fluorescence (IF) on HEp-2 cells detect autoantibodies against a large number of nuclear autoantigens, and is often followed by, or done in parallel to, investigations which determine the autoantibody specificities causing the IF ANA staining. Two IF ANA-associated SLE-specific autoantibodies, anti-double stranded DNA and anti-Sm, are included both in previous as well as emerging SLE classification criteria. But IF ANA itself is also included in all of these classification criteria (1-3). This is because a positive IF-ANA is regarded as an independent risk factor for SLE, irrespective of what autoantibody specificity determines the nuclear staining. Antibodies against lens epithelium-derived growth factor 70/75 kD autoantigen creates a specific dense fine speckled IF-ANA pattern, and the autoantibodies are generally called anti-DFS70. The rather recently described anti-DFS70 pattern is unique and has obtained the AC-2 pattern in the recent universally accepted International Consensus on ANA Patterns (ICAP) classification system (www.anapatterns.com), but was not previously recognised and might be misinterpreted. In contrary to other IF-ANA patterns/specificities, isolated anti-DFS70 is not associated with systemic rheumatic diseases, and might even be more common among healthy individuals than among diseased populations (4). However, when anti-DFS70 occur together with other ANA specificities, different IF-ANA patterns may predominate.

Objectives: The European Consensus Finding Study Group on autoantibodies (ECFSG), a.k.a. the EULAR autoantibody study group, regularly investigate autoantibody content in new autoantibody reference standards produced to obtain consistent results between clinical laboratories.

Methods: In the 2018 ECFSG serum investigation, a newly produced pooled anti-DFS70 reference standard was investigated blindly concerning IF ANA patterns and autoantibody specificities by 38 participating laboratories.

Results: Most laboratories correctly described the IF-ANA pattern correctly as the dense fine speckled AC-2 pattern; however 5/38 laboratories reported the pattern as homogenous (AC-1). Concerning autoantibody specificities, the standard was determined to be monospecific for anti-DFS70. This new reference standard has recently been described (5), and will be available via www.autoab.org.

Conclusion: In my talk I will give a background on the emergence of anti-DFS70 antibodies, and report on the outcome of the ECFSG investigation of the anti-DFS70 reference standard. Moreover, I will present an algorithm for how to incorporate investigations for anti-DFS70 in ANA investigations in a cost efficient way.

REFERENCES:

[1] E. M. Tan, et al. Arthritis Rheum. 25, 1271 (1982).
[2] M. Petri, et al. Arthritis Rheum 64, 2677 (2012).
[3] S. K. Tedeschi, et al. Ann Rheum Dis (2019).
[4] M. Mahler, et al. J Rheumatol 39, 2104 (2012).
[5] A. Dellavance, et al. Clin Chem Lab Med in press (2019).

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FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

The benefits of involving patients in health technology assessment

SP0127 **PATIENT ENGAGEMENT WITHIN THE EUROPEAN MEDICINES AGENCY**

Nathalie Bere. *European Medicines Agency (EMA), Public engagement Department, London, United Kingdom*

The European Medicines Agency (EMA) is the European regulatory body whose role is to evaluate and supervise medicines across the European Union.

EMA has been engaging with patients and consumers for many years and today, patient involvement is an integral part of the work at EMA, with a diverse range of opportunities in place to include the patient‘s voice at various stages along the medicines regulatory life-cycle. Key to successful engagement has been the need for flexibility, a range of well-tested methodologies and a robust system of support and training.

Patients and caregivers’ real-life perspectives and unique insights complement the scientific data within EMA reviews; they provide input on proposed protocol designs and participate in expert meetings and written consultations on medicines evaluation. They are voting members of EMA committees and they review medical information written for the public. Evidence has shown their contributions make a difference and ultimately help ensure that the Agency’s outcomes are as meaningful and relevant as possible for all concerned.

Some of the key challenges and conclusions of our journey will be highlighted to serve as a guide to those considering a similar, rewarding path.

Disclosure of Interests: None declared
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SP0128 **THE VARIOUS ROLES OF PATIENT PARTICIPATION IN HTA BY THE EXAMPLE OF IQWIG**

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Background: The involvement of affected persons in preparing systematic reviews and HTA represents an established international standard of benefit assessment. The Institute of Quality and Efficiency in Health Care (IQWiG) is a professionally independent scientific Institute founded within the framework of the German Health Care Reform of 2004 as an establishment of the Foundation for Quality and Efficiency in Health Care. IQWiG provides benefit assessments addressing issues concerning the statutory health insurance services. Its responsibilities include among others the preparation of scientific reports, expert opinions and comments on quality and efficiency issues taking age, gender, and personal circumstances into account.
Objectives: The goal of this presentation is to provide an overview on different paths of involvement of patients and affected persons at IQWiG.
Methods: IQWiG's legal basis and responsibilities are anchored in the Social Code Book Fifth Book – Statutory Health Insurance (SGB V) and have been adapted and extended several times in the course of further health care reforms. The Institute's work is commissioned by the Federal Joint Committee or by the Federal Ministry of Health. The information for this presentation stems from IQWiG's General Methods (currently in version 5.0), a publicly available paper provided on the Institute's website, which explains the groundwork for its assessments.
Results: The involvement of affected persons at IQWiG primarily takes place during the initial work on a report within the framework of patient-relevant outcomes and relevant subgroups. Moreover, involvement can also include partaking in hearings. Affected persons include in particular patients (represented by parents or relatives, when appropriate) as well as potential participants in prevention measures. Affected persons are found via the patient representation of the Federal Joint Committee, as well as national or local self-help organizations or groups, hospitals or medical practices, external experts or other routes. The involvement can consist of a personal consultation or providing information in writing (through questionnaires or reports on personal experience), in both cases with documenting potential conflicts of interest.
Conclusion: As representatives of patients or self-help groups are sometimes not patients themselves and cannot directly account for symptoms or their impact on the quality of life, focus is placed on involving persons directly affected. Different assessments require distinct types of involvement depending on the available time and the confidentiality of the topic.
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SP0129 **A PATIENT'S VIEW ON PATIENT INVOLVEMENT**

Souzi Makri. *CYPLAR, Limassol, Cyprus*

Background: • HTA as defined by the EUPATI:
Health technology assessment aims to inform decision making by health care policy makers. It is a systematic process that considers health technologies (such as medicines) and can involve a review of: Clinical evidence compared to existing models of care, Cost effectiveness, Social and ethical impacts on the health care system and the lives of patients EUPATI Overarching principle: "We recommend close cooperation and partnership between the various stakeholders including healthcare professionals' organisations, contract research organisations, patients' and consumers' organisations, academia, scientific and academic societies, regulatory authorities and HTA bodies and the pharmaceutical industry. Experience to date demonstrates that the involvement of patients has resulted in increased transparency, trust and mutual respect between them and other stakeholders. It is acknowledged that the patients' contribution to the discovery, development and evaluation of medicines enriches the quality of the evidence and opinion available."
Objectives: Inform decision making by health care policy makers. It is a systematic process that considers health technologies (such as medicines) and can involve a review of:

1. Clinical evidence compared to existing models of care,
2. Cost effectiveness,
3. Social and ethical impacts on the health care system and the lives of patients

EUPATI Overarching principle:
"We recommend close cooperation and partnership between the various stakeholders including healthcare professionals' organisations, contract research organisations, patients' and consumers' organisations, academia, scientific and academic societies, regulatory authorities and HTA bodies and the pharmaceutical industry. Experience to date demonstrates that the involvement of patients has resulted in increased transparency, trust and mutual respect between them and other stakeholders. It is acknowledged that the patients' contribution to the discovery, development and evaluation of medicines enriches the quality of the evidence and opinion available."
Objectives: Areas of patient involvement: Data, Decision problem (context), Scientific judgment and analysis,Value, Recommendation, Decision, Governance EUPATI guidance: (an exercise with 150 responders from 39 countries (Academia, HTA agencies, Patients industry : Knowledge and experience of patients are unique and contribute to essential knowledge - Fairness : Patients have the same rights as any other stakeholders to be part of the process -Equity: patient perspective helps to seek equity, by bringing into the process the true needs of patients, versus fairness of distribution of resources -Legitimacy : facilitates those affected by HTA decisions to participate contributing to the transparency and equability and credibility of the process - Capacity building : addresses barriers and helps building capacity for patients and HTA Organizations to work together
Methods: EPF Survey contacted 2010-2011 which produced a report among HTA agencies, decision makers and patient Organizations. The aim of the research was to assess the state of patient involvement in HTA. Responses collected from 40 HTA agencies, 18 decision makers and 23 patient organizations through on line questionnaires. The type of involvement varies. Few HTA agencies currently involve patients perspectives in their reports and contact formal evaluation of the impact of patient involvement in HTA. Out of the 40 HTA agencies that responded, nearly half of them (18) involve patients in HTA. Out of the 23 patient organisations that completed the questionnaire, 10 indicated that their organisations have been involved in HTA. Out of 18 decision-makers, four stated that they are planning to involve patients in decision-making for health technologies and three said that they already involve patients. On the other hand, five respondents stated that they do not intend to involve patients in the future and the remaining six either stated that they did not know or did not respond to the question.
Results: There are four main challenges according to all three stakeholders to involve patients in HTA: (1) lack of an agreed and good method to obtain/provide patient evidence, (2) not knowing the stage at which patient engagement is needed and most useful, (3) patient involvement process being time intensive, and (4) lack of capacity (HTA agencies, decision-making bodies, patient organisations). These themes represent all different forms of capacity that need to be in place for a meaningful patient involvement in HTA. According to the responses from the HTA agencies, high to moderate involvement is mainly seen in the phases of diffusion and dissemination, assessment, production of information, and external review. Low to no involvement is seen in the phases of identification, filtration, and prioritization.
Conclusions: The role of patient is very important in HTA in all aspects of the process. Before the medicine is developed, within HTA and when recommendations are made.
As patients' life and health state will be a affected by new technology, their input is vital in all stages of evaluating a new technology or medicinal product. Patients should be part of the process to explain WHY and HOW important is the proposed technology for the health. If there no involvement in all stages there is a risk of not deciding on the most appropriate technology and for crucial needs remain unmet. Recommendations for patient Organizations and HTA agencies exist in the EPF guide

REFERENCES:
[1] Results of the EPF Survey
[2] Patient involvement in the HTA decision-making process

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FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

Capillaroscopy II

SP0130 **STANDARDISATION OF NORMAL VERSUS ABNORMAL AND PATHOLOGICAL CAPILLAROSCOPIC IMAGES**

V. Smith[1,2,3], on behalf of the EULAR Study Group on Microcirculation in Rheumatic Diseases. [1]*Department of Rheumatology, Ghent University Hospital*; [2]*Department of Internal Medicine, Ghent University*; [3]*Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent, Belgium*

Medical doctors frequently get patients with Raynaud's phenomenon (RP), a frequent symptom in the general population, referred. The importance of

distinguishing normal capillaroscopic findings from (pathognomonic) abnormal (pathological) findings (scleroderma pattern), lies in the fact that this distinction allows the differentiation between a primary RP (not connected to any connective tissue disease [CTD]) from a secondary RP due to systemic sclerosis (SSc) and diseases of the scleroderma spectrum.

What is normal in primary RP?

A normal capillaroscopic pattern, by qualitative assessment, is characterized by a homogeneous distribution of hairpin shaped capillaries as a "comb-like structure", with a density of >7capillaries per mm, with a normal dimension and absence of large hemorrhages Yet, there exists a wide intra- and inter- individual variety in a normal population which will be discussed in this session.

What is pathognomonic abnormal in patients with RP due to SSc?

Patients with the RP who have an underlying clinically recognizable (= with skin involvement) SSc show a very characteristic combination of capillary abnormalities in the nailfold, which can easily be assessed through qualitative assessment (= pattern recognition). Maricq et al. described last century, with the widefield technique (magnification X12–14) the scleroderma pattern. This pathognomonic combination contains the following: a striking widening of all three segments of the capillary loop (arterial, venous and intermediate), loss of capillaries and disorganization of the nailfold capillary bed. Many branched "bushy" capillaries may also be observed.

In 2000, Cutolo et al. qualitatively assessed the nailfolds of an SSc cohort with patients fulfilling the American College of Rheumatology (ACR) criteria for SSc with the nailfold videocapillaroscopic (NVC) technique (magnification X200). According to the different proportions of the hallmark parameters of the scleroderma pattern (giants, capillary loss, hemorrhages and abnormal shapes: (neo) angiogenesis, Cutolo et al. defined three patterns "early", "active" and "late".

The central role of capillaroscopy in distinction between a primary and secondary RP due to SSc is reflected by the fact that capillaroscopy is one of the new ACR/EULAR criteria for classifying a patient as having SSc.

In this lecture the standard "FAST TRACK" recognition system of the EULAR Study Group on Microcirculation in Rheumatic Diseases to discern scleroderma patterns from non-scleroderma patterns will be taught to the attendees.

Suggested further reading:

[1] Smith V, et al. Rheumatology (Oxford). 2016;55(5):883-90.
[2] Cutolo M, et al. Rheumatology (Oxford). 2018;57(4):757-759.
[3] Cutolo M, et al. Autoimmun Rev. 2018;17(4):344-352.

Disclosure of Interests: None declared
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SP0131 RELIABILITY IN THE LAST 10 YEARS: CAPILLAROSCOPIC CHARACTERISTICS VERSUS INSTRUMENTAL DETECTION

Ariane Herrick. *University of Manchester, Salford Royal Hospital NHS Foundation Trust, Division of Musculoskeletal and Dermatological Sciences, NIHR Manchester Musculoskeletal Biomedical Research Centre, Manchester, United Kingdom*

Background: With nailfold capillaroscopy there are different aspects of reliability to consider, including reliability of qualitative image grading (e.g. 'early', 'active' and 'late') and also of semi-quantitative and quantitative measures including capillary density, apical width and presence of giant capillaries. The reliability of image acquisition (i.e. test-retest reliability) is especially important if nailfold capillaroscopic parameters are to be used in longitudinal studies (e.g. clinical trials) which involve acquiring repeat images over time. Lastly when assessing reliability, it is important to recognise that the nailfold capillaries cannot always be clearly seen, and cannot therefore be evaluated.

Objectives: To highlight the different aspects of reliability relating to nailfold capillaroscopy and how these have been addressed in studies over the last 10 years.

Methods: Review of recent studies.

Results:

1. Intra–observer reliability has been shown in several studies to be higher than inter–observer.
2. Assessment of 'evaluability' varies between observers and therefore also needs to be taken into account when assessing reliability.
3. Subject to evaluability, certain parameters demonstrate high intra– and inter–observer reliabilities. Reliability differs across different capillaroscopic parameters.

Conclusion: Recent studies examining reliability of capillaroscopy suggest that certain parameters, including image grade, capillary density and apex width have high intra-and inter-observer reliabilities (subject to nailfold image evaluability, which remains a major challenge). Standardised training is likely to improve reliability.

REFERENCES:

[1] Murray AK, Vail A, Moore TL, et al. The influence of measurement location on reliability of quantitative videocapillaroscopy in patients with SSc. Rheumatol 2012; 51 : 1323-30.
[2] Overbury R, Murtaugh MA, Fisher A, et al. Primary care assessment of capillary abnormalities in patients with Raynaud's phenomenon. Clin Rheumatol 2015; 34: 2135-40.
[3] Smith V, Beeckman S, Herrick AL, et al. An EULAR study group pilot study on reliability of simple capillaroscopic definitions to describe capillary morphology in rheumatic diseases. Rheumatol 2016; 55: 883-90.
[4] Dinsdale G, Moore T, O'Leary N, et al. Intra-and inter-observer reliability of nailfold videocapillaroscopy - A possible outcome measure for systemic sclerosis-related microangiopathy. Microvascular Research 2017; 112: 1-6.
[5] Dinsdale G, Moore T, O'Leary N, et al. Quantitative outcome measures for systemic sclerosis-related microangiopathy – reliability of image acquisition in nailfold capillaroscopy. Microvascular Research 2017;113:56-9.
[6] Boulon C, Devos S, Mangin M, et al. Reproducibility of capillaroscopic classifications of systemic sclerosis: results from the SCLEROCAP study. Rheumatology 2017; 56: 1713-20.
[7] Cutolo M, Melsens K, Herrick AL, et al. Reliability of simple capillaroscopic definitions in describing capillary morphology in rheumatic diseases. Rheumatology (Letter) 2018; 57: 757-9.

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SP0132 METHODS AND TOOLS FOR QUANTIZATION OF CAPILLAROSCOPIC MORPHOLOGICAL CHANGES

Francesca Ingegnoli. *Academic Rheumatology Unit Universita degli Studi di Torino, Academic Rheumatology Centre, Turin, Italy*

Nailfold capillaroscopy is the one most used technique in both clinical and research settings by adult physicians and paediatric rheumatologists to assess patients with Raynaud's phenomenon as shown by an international survey on non-invasive techniques to assess the microcirculation performed under the aegis of members of the EULAR Study Group on Microcirculation in Rheumatic diseases [1].

Nailfold capillaroscopy is a simple non-invasive imaging technique mainly used to observe capillaries on the skin surface. After application of a drop of immersion oil, capillaries can be observed with a magnification lens because they run parallel to the epidermis at the nailbed area [2].

A number of different instruments can be used to perform the exam. They have different characteristics in terms of their cost, quality of images, magnifications, training period, portability, software for image analysis and storage.

Some of these instruments can be used both in clinical and research settings such as the stereomicroscope and the videocapillaroscope. The stereomicroscope allows the widefield visualization of the nailfold with low magnifications, the training is relatively short, but the examination is difficult to perform in patients with digital flexion contractures.

There appears to be consensus regarding the use of videocapillaroscopy that allows a detailed visualization of capillary morphology using higher magnifications (100-300x). Contact probe with polarized light microscopy permits easier observation of the skin surface, and the training period is briefer. Specific software are available for images analysis, storage, and complete medical reports (text + images) can be produced. By contrast, in a clinical setting, nailfold capillaries can generally be visualized using more simple, but also efficient tools such as a dermatoscope, USB microscope, ophtamloscope or smartphone device. The quality of images can be quite good, although the lower magnification means that some details are unlikely to be seen, and they often lack the possibility of image storage and measurement. In particular, the dermatoscope with magnification of the order of x10 is a small, inexpensive and easily portable piece of equipment that has been suggested to be comparable to videocapillaroscopy in routine clinical practice. As the study of capillary morphology provides clinically relevant information in the management of patients with scleroderma-spectrum diseases, the development of specific software to standardize and automatize the analysis is ongoing [3-4].

REFERENCES:

[1] Ingegnoli F, Smith V, Sulli A, Cutolo M. Capillaroscopy in Routine Diagnostics: Potentials and Limitations. Curr Rheumatol Rev. 2018 20;14(1):5-11
[2] Ingegnoli F, Ughi N, Dinsdale G, Orenti A, Boracchi P, Allanore Y, et al.; EULAR Study Group on Microcirculation in RheumaticDiseases. An international SUrvey on non-iNvaSive tecHniques to assess the mIcrocirculation in patients with RayNaud's phEnomenon (SUNSHINE survey). Rheumatol Int. 2017;37(11):1879-1890.

[3] Cutolo M, Trombetta AC, Melsens K, Pizzorni C, Sulli A, Ruaro B, et al. Automated assessment of absolute nailfold capillary number on videocapillaroscopic images: Proof of principle and validation in systemic sclerosis. Microcirculation. 2018;25(4):e12447.
[4] Berks M, Dinsdale G, Murray A, Moore T, Manning J, Taylor C, Herrick AL. Automated structure and flow measurement - a promising tool in nailfold capillaroscopy. Microvasc Res. 2018;118:173-177.

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FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:00

Ultrasound basic II

SP0133 HOW TO ASSESS US LESIONS FOR GOUT + DEMO

Sara Nysom. *Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup., Copenhagen Center for Arthritis Research (COPECARE), Glostrup, Denmark*

Gout is the most common inflammatory joint disease in Western developed countries. Diagnosis and monitoring have historically been based upon clinical assessment combined with biochemical results (primarily p-urate) but over the last decade ultrasonography (US) has received increasing attention for these purposes. US has been shown able to detect monosodium urate deposits in both joints and tendons. In 2015 the Outcome Measures in Rheumatology (OMERACT) US Working Group developed definitions of structural lesions in gout. These include double contour sign (deposits of crystals on the surface of cartilage), tophus (larger hyper-echoic aggregation of crystals), aggregates (small hyperechoic deposits) and erosion (1). The double contour sign has been included in the ACR/EULAR 2015 gout classification criteria as a way to visualize urate deposits in joints (2). Furthermore, US can visualize potential concomitant inflammatory aspects of gout since it can visualize both joint inflammation and tenosynovitis.
In this talk the diagnostic properties of US will be described and the potential risk of false positive results due to artefacts or misinterpreted lesions will be discussed. Furthermore, the potential role of US in monitoring of treatment response will be explored.

REFERENCES:

[1] Gutierrez M, Schmidt WA, Thiele RG, Keen HI, Kaeley GS, Naredo E, Iagnocco A, Bruyn GA, Balint PV, Filippucci E, Mandl P, Kane D, Pineda C, Delle Sedie A, Hammer HB, Christensen R, D'Agostino MA, Terslev L; OMERACT Ultrasound Gout Task Force group. International Consensus for ultrasound lesions in gout: results of Delphi process and web-reliability exercise. Rheumatology (Oxford). 2015;54(10):1797-805.
[2] Neogi T, Jansen TLTA, Dalbeth N, Fransen J, Schumacher HR, et al. 2015 Gout Classification criteria: an American College of Rheumatology/ European Leaque Against Rheumatisme collaborative initiative. Ann Rheum Diss 2015; 74: 1789-1798.

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SP0134 US FOR TROCHANTERIC PAIN SYNDROME – CLINICAL USE + DEMO

Ingrid Möller. *University of Barcelona, Instituto Poal de Reumatologia, Barcelona 08022, Spain*

Background: Greater trochanteric pain syndrome (GTPS) is a clinical diagnosis with the typical presentation of chronic intermittent lateral hip/thigh/buttock pain, aggravated with activity and when lying on the affected side. There is a lack of valid/specific diagnostic criteria for GTPS. GTPS can be attributed to a multitude of causes ranging from tendinopathy and/or rupture of the gluteal tendons and/or bursitis, to pathological alterations of the iliotibial band/fascia lata and other nearby anatomical structures located on the lateral part of the hip. To further complicate the diagnostic process, according to different studies, the prevalence of GTPS in adults with lower back pain has been found to be between 20-30%. Alterations of the lumbar biomechanics may interfere in the range of internal rotation of the hip and consequently produce a GTPS and vice versa. Changes in hip range of motion will trigger changes in the dynamics of lower extremities and the spine. Generalized myofascial pain can also be a source of confusion when evaluating patients with GTPS.
Objectives: Understand the clinical anatomy of the lateral hip.
Interpret the US images of the lateral hip
Identify potential pain generators of the lateral hip.
Methods: The study of the static and dynamic sonoanatomy of the different components of the lateral region of the hip can contribute in a relevant way to clarify the diagnosis In the eular guidelines of sonographic musculoskeletal (MSUS) exam published in 2017, the sonographic exam of the lateral hip has been developed in detail and will be discussed during this lecture.
The anatomy against what is often thought is not stagnant knowledge but evolves over the years providing new and useful data applicable in daily clinical practice. The anatomy, both static and dynamic, of the trochanteric region, is complex. For example, the subgluteus maximus bursa, which is frequently incriminated in the GTPS, is located in the posterior facet of the greater trochanter and is related to the iliotibial tract, the fascial contributions of the gluteus maximus and the tensor of the fascia lata muscle to the iliotibial tract and the origin of the vastus lateralis. In order to understand the multifunction and relationships of the different structures of this region means one has to have seen images of them and for that purpose, the human cadaveric dissection is the best tool. Thanks to the fact that the speaker is involved as a professor in the anatomy department at the University of Barcelona, Bellvitge campus, directed by prof M Miguel, the clinical anatomy part will be developed with real dissections made specifically for this lecture.
Results:



Conclusion: Knowledge of the clinical anatomy needed to understand the relationships between the different structures, the clinical history, and physical examination of GTPS patients and the therapeutic possibilities including ultrasound-guided injections are other steps that lead to an accurate diagnosis of GTPS

REFERENCES:

[1] anatomy and anthropology: Maribel Miguel, Mike Benjamin
[2] Clinical anatomy: Juan Canoso
[3] Regional musculoskeletal ultrasound: Carlo Martinoli
[4] Möller I, Bong D. Ultrasound-guided interventions in the hip joint. TechniquesIn Regional Anesthesia and PainManagement 2013; 17: 140–149
[5] Möller I, Janta I, Backhaus M, et al The 2017 EULAR standardized procedures for ultrasound imaging in rheumatology. Annals of the Rheumatic Diseases 2017;**76:**1974-1979.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8541

SP0135 HOW TO DIFFERENTIATE MINIMAL DISEASE ACTIVITY IN RA + DEMO

Ilfita Sahbudin[1]. [1]*Institute of Inflammation and Ageing, University of Birmingham, Rheumatology Research Group, Birmingham, United Kingdom*

Ultrasound (US) is increasingly utilised as a point-of-care tool to diagnose early inflammatory joint disease, monitor treatment response and detect subclinical inflammation. This is feasible as US can detect joint, and tendon, inflammation before it becomes clinically apparent. Despite the increasing use of US in Rheumatology, the key research question yet to be addressed is defining 'the normal reference value at the joint level.'
Improvement in US technology over the last decade results in acquisition of higher resolution images. US can now detect subtle abnormality in joints of healthy individuals who are asymptomatic. Consequently, the imaging boundary between US changes of normal joints (i.e *physiological changes*), and those of early arthritis joints (i.e. *early pathological changes*) has become unclear. In addition, a proportion of US-defined pathology observed in normal joints may be attributed to age-related changes.

Defining the concept of US-detected 'minimal disease' is crucial to enable investigators identify a threshold (or cut-off) to *differentiate normal physiological from minimal pathological changes* at the joint level. This threshold, subsequently, will be used to evaluate the best sensitivity to detect changes in therapeutic response and assess remission, as well as facilitate diagnosis of early disease.
In order to address this important research question, the OMERACT US SIG has formed the US Minimal Disease Taskforce at the OMERACT 2016 meeting. This collaboration between 24 OMERACT ultrasound centres in 11 countries has successfully recruited more than 600 subjects into the Minimal Disease Study. US data of healthy individuals encompassing synovial hypertrophy, synovial effusion, and Doppler enhancement will be presented.
Disclosure of Interests: None declared
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SP0136 HOW TO PERFORM US-GUIDED INTERVENTIONS + DEMO

Juhani Koski. *Mikkeli Central Hospital, Internal Medicin, Mikkeli, Finland*

Background: Aspiration and injection of joints and soft tissues is an indispensable skill used in everyday practice by the clinical rheumatologist. These tasks are usually conducted by palpation-guided techniques. These procedures are not always successful (1) and thus US -guided interventions have been developed.
Objectives: are to explain the effect of needle and sound beam angle on needle visualization, describe different techniques of needle insertion under US guidance, to identify different approaches to the target under US guidance and finally to discuss about the accuracy and efficacy of the ultrasound guided technique.
Methods: There are two common methods for US puncturing: semi-guided or indirect method (skin surface marking) and needle guidance under direct sonographic vision (2,3). The scanning plane is optimized for visualization of the target and penetration of the needle should be at least 0.5cm from the transducer. The movement of the needle in the soft tissue should be followed on the screen during the procedure. The needle appears as a bright echoic line if the transducer is oriented longitudinally on the needle, and the needle tip may be followed as it reaches the target. If the ultrasound beam is transverse to the needle, the needle is seen as a bright echoic dot. In case of no visualization of the needle several means are available: steering of the ultrasound beam against the needle (in new machines), curved or virtual convex probe, toeing -in of the probe, shaken the needle slightly and moving the probe a bit from side to side.
Results: According to the clinical and cadaveric studies the ultrasound guided technique is more accurate than the landmark guided technique in the glenohumeral, acromioclavicular, wrist, hand, hip, knee and foot joints and in the tendons of the biceps, wrist, hand hip, knee and ankle (4). Synovial biopsies are more accurate using an ultrasound guided method (5).
Conclusion: Ultrasound is the most applicable and feasible imaging modality for routine clinical use in guiding musculoskeletal procedures. Though many studies have examined the role of imaging guidance for injection there needs to be more examination of how the use of ultrasound prior to injection can alter the pathological and anatomical diagnosis. There is a trend towards an expanded number of advanced applications of interventional musculoskeletal ultrasound which can also be performed by a rheumatologist like nerve blocks or needling of calcifications. Which ultrasound guided technique (direct or semi-guided) is the most appropriate in different anatomical areas and clinical settings remains to be studied. More studies are needed to show the accuracy and efficacy of ultrasound guided injections in different anatomical areas (4).

REFERENCES:

[1] Jones A, et al. Importance of placement of intra-articular steroid injections. BMJ 1993;307:1329-1330.
[2] Koski JM. Ultrasound guided injections in rheumatology. J Rheumatol 2000;7:2131-8.
[3] Fessell DP, et al. Using sonography to reveal and aspirate joint effusions. AJR 2000;174:1353-62.
[4] Kane D, Koski JM. Musculoskeletal interventional procedures: With or without imaging guidance? In Clinical Rheumatology. Best Practice & Research Clinical Rheumatology, 2016:736-750.
[5] Kelly S, et al. Ultrasound-guided synovial biopsy: a safe, well-tolerated and reliable technique for obtaining high-quality synovial tissue from both large and small joints in early arthritis patients. Ann Rheum Dis 2015;74:611-617.

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FRIDAY, 14 JUNE 2019

13:30:00 – 15:00:05

Jewels in the crown of health professionals

SP0137 CORE COMPETENCIES

Thea Vliet Vlieland. *Leiden University Medical Center, Orthopaedics, Rehabilitation and Physiotherapy, 2300 RC Leiden, Netherlands*

Background: To maintain and optimize the quality of care provided by health professionals in rheumatology (HPRs), adequate educational offerings are needed. Ideally, these are based on defined core competences.
Objectives: A task force (TF) aimed to develop evidence-based recommendations for the generic core competences of nurses, physical therapists (PTs) and occupational therapists (OTs) to serve as a basis for their postgraduate education.
Methods: The EULAR standardised operating procedures for the development of recommendations were followed. A TF including rheumatologists, nurses, PTs, OTs, patient-representatives, an educationalist, methodologists and researchers from 12 countries met twice. In the first TF meeting, 13 research questions were defined to support a systematic literature review (SLR). In the second meeting, the SLR evidence was discussed and recommendations formulated. Subsequently, level of evidence and strength of recommendation were assigned and level of agreement (LoA) determined (0-10 rating scale).
Results: Three overarching principles and 10 recommendations for the generic core competences of HPRs were developed supported by the SLR and expert opinion. The SLR included 79 full-text papers, 20 of which addressed the competences, knowledge, skills, attitudes or educational needs of HPRs from multiple professions. The average LoA for each recommendation ranged from 9.42 to 9.79. Consensus was reached on education and research agendas.
Conclusion: Evidence and expert opinion informed a set of recommendations providing guidance on the generic core competences of nurses, PTs and OTs in rheumatology. Implementation of these recommendations in the postgraduate education of HPRs at the international and national level is advised, considering variation in health care systems and professional roles.
Task Force Members: L.M. Edelaar, E. Nikiphorou, G.E. Fragoulis, A. Iagnocco, C. Haines, M. Bakkers, L. Barbosa, N. Cikes, M. Ndosi, J. Primdahl, Y. Prior, P. Pchelnikova, V. Ritschl, V.S. Schäfer, H. Smucrova, I. Storrønning, M. Testa, D. Wiek, T.P.M. Vliet Vlieland

REFERENCE:

[1] Van der Heijde D, Aletaha D, Carmona L, et al. 2014 Update of the EULAR standardised operating procedures for EULAR-endorsed recommendations. Ann Rheum Dis. 2014;74:8-13.

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SP0138 WHAT WE ARE BRILLIANT AT; OT PERSPECTIVE

Ingvild Kjeken. *Norwegian Advisory Unit on Rehabilitation in Rheumatology, Department of Rheumatology, Dlakonhjemmet Hospital, 0370 Oslo, Norway*

The unique contribution of occupational therapy is its focus on occupation, which may be defined as *"groups of activities and tasks of everyday life, named, organized and given value and meaning by individuals and a culture. Occupation is everything people do to occupy themselves, including looking after themselves (self-care), enjoying life (leisure), and contributing to the social and economic fabric of their communities (productivity)".* Occupation is further being influenced by the environment, one's social roles and one's developmental level; being client-defined; and consisting of both a performance (objective) dimension and a satisfaction (subjective) dimension (1).
Using the terminology of the International Classification of Functioning (ICF), occupational performance covers the domain of Activity and Participation in the ICF model.
In clinical practice, occupational therapists use assessment and interventions to develop, recover, or maintain the meaningful occupations of individuals, groups, or communities. Lately, occupational therapists have also been increasingly concerned with occupational injustice, which relates to conditions wherein people are deprived, excluded or denied of occupations that are meaningful to them.
Within rheumatology, the most frequently applied occupational therapy interventions are patient education concerning ergonomic principles and activity pacing, therapeutic exercise and activity programs, provision of orthoses and assistive technology, and environmental and task modifications.

In the presentation, patient cases will be used to illustrate how occupational therapists may work to enhance occupation in individual clients with a rheumatic condition, and evidence for some of the core interventions will be discussed.

REFERENCE:

[1] Townsend EA, Polatajko HJ. Enabling occupation II: advancing an occupational therapy vision for health, well-being, & justice through occupation. Ottawa: Canadian Association of Occupational Therapists; 2007.

Disclosure of Interests: None declared
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SP0139 **WHAT WE ARE BRILLIANT AT; NURSING PERSPECTIVE**

Ricardo Ferreira. *Centro Hospitalar e Universitário de Coimbra, EPE, Rheumatology, Coimbra, Portugal*

The challenges confronting health care delivery systems worldwide are rapidly changing, and this calls for practice-defined competencies for nurses and other health care workers (Zhang, Luk, Arthur, & Wong, 2001). The definition of competency or competence in nursing has been a subject of debate (Axley, 2008; Fukada, 2018; Zhang et al., 2001). Its clarification is important and still needed to establish a foundation for realistic working behaviours, for nursing education and management.
Although there has been an extensive and valuable work in the definition of core competencies of nursing profession, which includes both autonomous and interdependent activities within the multidisciplinary team, little scientific research has been done to clarify the way in which nursing profession is unique.
This presentation will address the following questions:

- What are nurses (collectively) really brilliant at?
- What leads them to develop unique characteristics?
- How do they bring into care, that matches or complements other health professions to result in better quality care?

The presentation is informed by a scoping review, a survey of international nurse leaders and researchers.

REFERENCES:

[1] Axley, L. (2008). Competency: a concept analysis. Nurs Forum, 43(4), 214-222. doi:10.1111/j.1744-6198.2008.00115.
[2] Fukada, M. (2018). Nursing Competency: Definition, Structure and Development. Yonago Acta Medica, 61(1), 1-7.
[3] Zhang, Z., Luk, W., Arthur, D., & Wong, T. (2001). Nursing competencies: personal characteristics contributing to effective nursing performance. Journal of Advanced Nursing, 33(4), 467-474.

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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

New insights into JIA and autoinflammatory diseases

SP0140 **HOT: MANAGEMENT OF JUVENILE IDIOPATHIC ARTHRITIS 2019 AND BEYOND**

Michael Beresford. *University of Liverpool, University of Liverpool/Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom*

Background: Improvements in our care and understanding of paediatric rheumatic disorders has undergone tremendous advances in the last decade. The transformative therapeutic armamentarium now available in targeting treatments for juvenile idiopathic arthritis (JIA) combined with a step change in addressing a holistic approach to our multi-disciplinary management of children and young people, seeks to make a real difference to the lives of the patients we care for.
Objectives: To provide an overview on best management of juvenile idiopathic arthritis, an outlook for new treatment possibilities and JIA outcome with a focus on adults.
Methods: The advances in our understanding of disease mechanisms, coupled with legislative changes across the EU and North America have led to an increase in clinical trials and evidence based new therapies for children with JIA. This progress continues to accelerate, fostered by major international collaborative efforts in clinical and translational research, and stratified/personalised medicine. Our greater understanding of the genetic, molecular and mechanistic pathways underpinning JIA in children, in whom there is less accumulation of significant co-morbidities and organ damage, have offered new opportunities for this advancement.
Results: The shared knowledge between paediatric and adult clinical research communities and international collaboration has ensured the management of JIA has been transformed. However, we must not be complacent. Future progress will depend upon ensuring that appropriate clinical trials, using methodology and trial design appropriate for and including the insights and perspectives of children and young people care carried out in paediatric rheumatology. This is especially important with the advent of newer molecules and therapies that are relevant to our patients and clinicians treating them, and not just in meeting regulatory requirements.
Conclusion: As the management of JIA continues to evolve and develop, equitable access to the very best care and new and effective treatments and therapies is critical across the world.
Disclosure of Interests: None declared
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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Overdiagnosis and overtreatment in inflammatory arthritis

SP0141 **DOES IMAGING LEAD TO OVERDIAGNOSIS AND OVERTREATMENT?**

Duncan Porter. *Gartnavel General Hospital, Rheumatology, Glasgow, United Kingdom*

Background: The use of musculoskeletal ultrasound (MSUS) and magnetic resonance (MR) imaging is widespread in the diagnosis and management of patients with rheumatic disease. Interpreting the images, and their implication for clinical management is challenging, particularly in the community, in mild/early disease, when there is discordance between clinical and imaging findings, and in the presence of co-morbid joint disease.
Objectives: – to review the evidence about whether the use of imaging results in over-diagnosis and over-treatment
Specifically, the following issues will be addressed, using rheumatoid arthritis as the exemplar:

- To review the prevalence of 'abnormal' MSUS and MR findings in the general population
- To understand the prevalence and significance of sub–clinical joint inflammation
- To summarise the evidence from clinical trials about the risks/benefits of treating to a target of imaging (rather than clinical) remission

Methods: If clinicians are to interpret the available imaging correctly, several issues are pertinent. Firstly, it is important to understand the prevalence of erosions, synovitis and bone marrow oedema in the general population, in different joints, at different ages and in the presence of co-morbid conditions such as osteoarthritis. Secondly, in RA what are the implications of sub-clinical inflammatory changes for disease progression? Thirdly, do clinical trials support the hypothesis that 'treat to target' strategies should aim at a target of 'imaging remission' rather than clinical remission? The results of the TaSER, ARCTIC and RA-IMAGINE trials will be reviewed to identify if the systematic, routine use of imaging results in over-treatment or clinical harm. Lastly, the possibility that imaging could have a role in reducing over-treatment will be discussed.
Conclusion: It is impossible to interpret the results of imaging correctly, without knowing the clinical context. Clinicians need to understand the value and the limitations of imaging, and should not pursue a simplistic or binary approach when interpreting the results - otherwise over-diagnosis and over-treatment will be the result. To date, the evidence from RCTs in the management of RA suggest that a 'treat-to-target' approach should aim for clinical and not imaging remission.

REFERENCES:

[1] Dale J, Stirling A, Zhang R, Purves D, Foley J, Sambrook M, et al. Targeting ultrasound remission in early rheumatoid arthritis: the results of the TaSER study, a randomised clinical trial. Ann Rheum Dis. 2016 Jun;75 (6):1043–50
[2] Haavardsholm EA, Aga A-B, Olsen IC, Lillegraven S, Hammer HB, Uhlig T, et al. Ultrasound in management of rheumatoid arthritis: ARCTIC randomised controlled strategy trial. BMJ. 2016 Aug 16;:i4205.
[3] Møller-Bisgaard S, Hørslev-Petersen K, Ejbjerg B, Hetland ML, Ørnbjerg LM, Glinatsi D, et al. Effect of Magnetic Resonance Imaging vs

Conventional Treat-to-Target Strategies on Disease Activity Remission and Radiographic Progression in Rheumatoid Arthritis: The IMAGINE-RA Randomized Clinical TrialEffect of MRI vs Conventional Treat-to-Target Strategies on Disease Activity Remission in RAEffect of MRI vs Conventional Treat-to-Target Strategies on Disease Activity Remission in RA. JAMA. 2019 Feb 5;321(5):461–72

[4] Mangnus L, van Steenbergen HW, Reijnierse M, van der Helm-van Mil AHM. Magnetic Resonance Imaging–Detected Features of Inflammation and Erosions in Symptom-Free Persons From the General Population. Arthritis & Rheumatology. 2016;68(11):2593–602

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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

The multiple rheumatological faces of PsA (or PsA is more than just poly-arthritis? – Consequences for management in daily practice)

SP0142 CASE 1 PRESENTER: A PATIENT WITH PERSISTING MONO/OLIGO-ARTHRITIS (EITHER AT START OR REMAINING AFTER TREATMENT OF POLY-ARTICULAR DISEASE)

William Tillett. *Royal National Hospital for Rheumatic Diseases, Rheumatology, Bath, United Kingdom*

Background: The varied clinical phenotypes of psoriatic arthritis present treatment challenges in clinical practice. The dominant phenotype represented in clinical trials is polyarthritis with little representation of oligoarticular or monoarticular disease.
Objectives: To review the phenotypes of psoriatic disease and treatment of resistant oligo/monoarthritis in the context of a clinical case.
Methods: Clinical case history
Conclusion: The clinical phenotype of articular disease in psoriatic arthritis can evolve over time. There is limited data to inform the treatment of resistant oligo/monoarthritis
Disclosure of Interests: William Tillett Grant/research support from: AbbVie, Celgene, and Lilly, Consultant for: AbbVie, Celgene, Lilly, Novartis, and Pfizer, Speakers bureau: Abbvie, Celgene, Lilly, Janssen, Novartis, UCB, and Pfizer
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SP0143 CASE 1 DISCUSSANT: HOW IS TACKLING OLIGO-ARTICULAR DISEASE DIFFERENT FROM POLYARTHRITIS? CAN WE USE TRIAL RESULTS FROM POLY-ARTICULAR PSA IN A PATIENT WITH MONO/OLIGO-ARTHRITIS?

Laura C Coates. *University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*

Background: Oligoarthritis is a well recognised phenotype in psoriatic arthritis (PsA) where less than 5 joints are involved with active arthritis. In cohort studies, the proportion of patients presenting with mono/oligoarthritis varies from 20-70% depending on the timeframe studied and duration of disease. However most studies of therapeutic agents in PsA have focused on polyarticular disease. Although the majority of studies accept a minimum of 3 active joints for inclusion, the average tender and swollen joint counts are usually over 10 at baseline.
Objectives: To review data supporting treatment of psoriatic mono/oligoarthritis including comparisons of response rates in therapeutic trials in PsA and the differential performance of outcome measures in this subtypes of disease.
Results: When considering the applicability of RCT data to mono/oligoarthritis in PsA it is important to address the populations included in these studies. Nearly all large therapeutic studies exclude monoarthritis, and while some oligoarthritis patients are eligible for inclusion in most RCTs, the demographics of the population included suggest that this is a minority. Unfortunately most clinical trials have not reported the efficacy results separately for oligoarthritis and polyarthritis patients. The other key consideration is that the outcome measures used in the majority of trials are developed and validated on patients with polyarticular PsA. Thus assessing effectiveness of therapies may be limited in the oligoarthritis population as the response measures are less sensitive to change.
Conclusion: Although data from polyarticular RCT populations is often used to choose therapies in oligoarticular PsA, there is a real paucity of data to ensure that we are treating these patients optimally. Future research is needed to address the variable prognosis seen in mono/oligoarticular PsA, to ensure that appropriate outcome measures are used to test different therapies and to provide clear evidence on the efficacy of drugs in this important subtype of disease.
Disclosure of Interests: Laura C Coates Grant/research support from: AbbVie, Celgene, Lilly, Novartis and Pfizer, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead Sciences Inc., Janssen, Lilly, Novartis, Pfizer, Prothena Corp and UCB
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SP0144 CASE 2: SOLITARY ENTHESITIS AS A THERAPEUTIC CHALLENGE

Philippe Carron. *Ghent University Hospital, Rheumatology, Gent, Belgium*

The enthesis is a site crucial for mobility of the musculoskeletal system yet it is also commonly a target of inflammation, especially in spondyloarthritis. Because the enthesis is prone to high biomechanical forces, it has been hypothesized that biomechanical forces may be implicated in the onset of the enthesitis and spondyloarthritis in general. However, treatment recommendations involve exercise therapy which at first glance appears to pose a paradox. Using a case, we will discuss the current knowledge on enthesitis, the link with mechanical stress and the implications thereof in diagnosis and management of spondyloarthritis.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8442

SP0145 CASE 2 DISCUSSANT: ENTHESITIS AND THE CONCEPT OF MECHANICAL STRESS

Dirk Elewaut. *Ghent University Hospital, Rheumatology, Ghent, Belgium Philippe Carron and Dirk Elewaut, VIB Inflammation Research Institute, Ghent University and Department of Rheumatology, Ghent University Hospital*

The enthesis is a site crucial for mobility of the musculoskeletal system yet it is also commonly a target of inflammation, especially in spondyloarthritis. Because the enthesis is prone to high biomechanical forces, it has been hypothesized that biomechanical forces may be implicated in the onset of the enthesitis and spondyloarthritis in general. However, treatment recommendations involve exercise therapy which at first glance appears to pose a paradox. Using a case, we will discuss the current knowledge on enthesitis, the link with mechanical stress and the implications thereof in diagnosis and management of spondyloarthritis
Disclosure of Interests: None declared
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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Cannabis for arthritis: hype or hope?

SP0146 BENEFITS OF CANNABIS TO YOUR JOINTS: HYPE OR HOPE?

Serge Perrot. *France, France*

Cannabis-based medicines have been approved for pain management in a number of countries. However, there are uncertainties and controversies about their role and the appropriate use of these medicines for the management of chronic pain, particularly in musculoskeletal conditions. These ancient drugs are now being rediscovered and considered as modern analgesic approaches in the context of cannabis legalization in more and more countries. The fight for cannabis legalization is frequently confused with the search for new analgesics in a medical context. Furthermore, there is a confusion between herbal cannabis, medical cannabis and cannabinoids. Therefore, it is important to differentiate products and

situations and look beyond prejudice and misconceptions, to discover whether there are pharmacological and clinical data to support the use of medical cannabis and cannabinoids in musculoskeletal conditions and arthritis. Aside from media and social discussions, we will try to answer to the current hot question for a clinician is "Is it possible to recommend medical cannabis as a new analgesic option in musculoskeletal conditions?"

Disclosure of Interests: None declared

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SP0147 **ETHICAL ISSUES IN MEDICAL CANNABIS USE**

Steve Alexander. *University of Nottingham, School of Life Sciences, Nottingham, United Kingdom*

Background: The human history of *Cannabis* is chequered.

We have evidence from the Ebers papyrus of ancient Egypt (1450 BCE) that 'shm-shm-t' was used as a medication for what appears to have been topical inflammatory issues. In the Atharva Veda (~1500 BCE), 'bhang' was considered one of the five sacred plants of India. The Old Testament refers to 'kaneh-bosm' as a component of a ceremonial anointing oil. In the UK's Elizabethan era, *Cannabis,* as hemp, was grown widely for fibre to make rope and sail for the Royal Navy. In Victorian times, WB O'Shaughnessy brought back from India to the UK the medicinal use of *Cannabis* preparations for its reputed analgesic, anti-emetic, anti-inflammatory and anti-convulsant properties. In the modern era, *Cannabis* is a Schedule 1 drug in many countries - a legal status defined as having high abuse potential with no currently accepted medical value.

Objectives: To consider the ethical issues associated with the use of Cannabis-derived preparations for medicinal purposes.

Conclusion: *Cannabis* is unique among the Schedule 1 list, because extracts from the plant are licensed medicines in different parts of the world. The two most widely-researched metabolites from the plant are Δ^9-tetrahydrocannabinol and cannabidiol (THC and CBD). The clinical uses of nabiximols (THC:CBD 1:1, combined with other minor cannabinoids) and nabilone (a synthetic THC analogue) for multiple sclerosis and antiemesis, respectively, as well as cannabidiol and dronabinol ((-)-*trans*-THC) for childhood intractable epilepsy and cachexia, respectively, identify that *Cannabis*-derived medicinal products have therapeutic value.

Cannabis or THC in acute administration has a remarkably low association with mortality, however, there are a number of potential issues in the use of *Cannabis* itself rather than the above-mentioned extracts/compounds. Long-term heavy use of *Cannabis* is associated with the risk of addiction in about 10% of individuals. Severe anxiety attacks and psychotic episodes have been linked to higher doses of THC, although this has not been systematically identified. Both THC and CBD have identified metabolic profiles which might influence the turnover of other drugs.

A major feature of the use of *Cannabis* itself is the variability observed. In part, this derives from the natural product nature of the plant and the associated variation in the metabolites between different parts of the plant, different plants, different methods of harvesting, storage as well as method, dose and frequency of administration, the subject's prior exposure to *Cannabis* and the immediate environmental context. Even with the well-controlled clinical trials, there has been identified a variability in plasma levels of the administered agents. In those countries where medicinal *Cannabis* is more freely available, there are also concerns about patient use of black market sources.

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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Reproductive issues in rheumatology

SP0148 **DOES PREGNANCY REALLY AMELIORATE DISEASE ACTIVITY OF WOMEN WITH CHRONIC ARTHRITIS? OLD BELIEFS VS NEW PARADIGMS**

Laura Andreoli. *University of Brescia, Spedali Civili of Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy*

Rheumatoid arthritis (RA) and Spondyloarthritis (SpA) are chronic inflammatory diseases whose onset can occur during childbearing age. Juvenile Idiopathic Arthritis (JIA) can be active still during adulthood. Therefore, the disease course during pregnancy has been a topic of interest over the decades [1]. The approach towards the management of pregnancy in the rheumatic diseases has greatly changed in the last 30 years, as it became evident that active maternal disease is associated with adverse pregnancy outcomes, such as miscarriage, pre-term birth, small-for-gestational age babies. A well-controlled maternal disease during pregnancy is associated with a better pregnancy outcome: the key-point is the treatment of maternal disease with drugs which are not harmful for the fetus. To achieve this "ideal setting" is of fundamental importance to perform a preconception counselling a tailor the management of the patient according to the individual risk stratification [2].

Historically, pregnancy has been considered to have a beneficial effect upon RA, with around 90% of women improving and up to 75% going into remission, followed by flares in puerperium in about 80% [3]. Modern prospective studies using validated measures of disease activity reveal less impressive ameliorative effects of pregnancy on RA [4]. A recent systematic review of prospective studies, using serial and objective evaluations of inflammatory disease, reported that RA improves in 60% of patients through pregnancy and flares in 46.7% of cases after delivery [5].

What are the possible explanations for this shift in the course of RA during pregnancy over decades? 1) methodological issues are obviously present (different study design; different patient population in terms of disease subset, duration, and severity); 2) disease activity as a "self-reported outcome" vs use of validated indices [6]; 3) change in treatment strategies over time: in the '80s women with RA were likely to be treated with steroids only and probably those women with active disease despite treatment were not able to carry out a pregnancy, therefore it is possible that only patients with mild-moderate form of RA were observed during pregnancy. Conversely, the current wide therapeutic armamentarium allows to reach disease remission also in patients with aggressive forms of RA, therefore it is likely to observe disease flares (rather than amelioration) during pregnancy if the drug is stopped at conception. Interestingly, among 75 prospectively-followed RA pregnancies, in patients treated with tumor necrosis factors inhibitors (TNFi) before conception, the discontinuation of the TNFi early in pregnancy resulted in increased risk for disease flares during pregnancy [7]. On the other hand, if disease is well controlled with drugs which are maintained during pregnancy, then there is little room to detect any improvement during pregnancy.

Spondyloarthritis (SpA) is a heterogeneous group of diseases and limited data are available about the disease course of different subsets (axial SpA –axSpA- and Psoriatic Arthritis –PsA-) during pregnancy. Recently, prospective data from the RevNatus registry showed that the majority of women with r-axSpA had stable or low disease activity from preconception period to 1 year after delivery with a small increase in the second trimester [8]. Previous studies reported that axSpA tend to be stable or to get worse [9]. Only one small retrospective work showed that the majority of women with AS displayed a decrease in disease activity during pregnancy [10]. In a recent report of 61 pregnant women with axSpA prospectively followed the discontinuation of TNFi early in pregnancy was a risk factor for flare [7]. Regarding PsA, data are scarce. The only two prospective studies demonstrated improvement during pregnancy and deterioration in the postpartum period [11, 12]. Similarly to axSpA, discontinuation of TNFi at conception is associated with an increased number of flares during pregnancy [13].

In general, it seems that the changes in management of chronic arthritis has determined a shift in paradigm in the disease course during pregnancy. The major determinant of this change has been the growing confidence in using anti-rheumatic drugs during pregnancy and breastfeeding. The increasing evidence about the safety of the majority of anti-rheumatic drugs has been recognized by many national and international working groups under the umbrella of scientific societies which endorsed guidelines and points to consider about this topic [14, 15].

Regarding biologic agents (bDMARDs), they can differ in molecular structure; however, they are all big size proteins which cannot passively diffuse and reach the fetus during the first trimester of gestation. Based on this assumption, unintended pregnancies exposed to these drugs are not a problem. As the active transport of IgG immunoglobulins across the placenta becomes significant after week 16 of gestation, it is understood that those bDMARDs which are IgG monoclonal antibodies will be transferred to the fetus. It was demonstrated that the drug concentration of monoclonal antibodies was higher in the newborn as compared to the mother, as expected for any IgG. Therefore, it is recommended to stop bDMARDs (with different timing according to their structure) in the second trimester – early third trimester in order to minimize the exposure to the drug and avoid that the new born will be immunosuppressed because of the drug received from the mother [14, 15]. Among TNFi, certolizumab pegol (CTZ) does not have the Fc portion needed for transplacental passage and no to minimal drug was detectable in the blood of neonates whose mothers received the drug until delivery [16]. Regarding breastfeeding, it is possible to consider bDMARDs as a homogenous class. They are all large proteins, which are unlikely excreted into breastmilk due to their high molecular weight. But even if they were present in breastmilk, bDMARDs will be degraded in the newborn's digestive tract with no chance for absorption (consider that bDMARDs are administered intravenously or subcutaneously, not orally). CTZ was shown to be absent in the breastmilk and breastfed children did not show any particular adverse event [17].

The exposure to immunosuppressive drugs, especially to bDMARDs, during late pregnancy poses the question about the immune competence of the neonate and the approach towards vaccinations. Data from large administrative US databases showed that children exposed during the third trimester to TNFi did not have an

increased risk for serious infections during the first year of life [18]. The only concern about vaccinations is about live vaccines; it is recommended to postpone these vaccinations after 4-6 months after the last administration of drug during pregnancy.

REFERENCES:

[1] Clowse ME, 2019
[2] Ostensen M, 2017.
[3] Da Silva JA, 1992.
[4] de Man YA, 2008.
[5] Jethwa H, 2019.
[6] Andreoli L, 2019.
[7] van de Brandt S, 2017.
[8] Ursin K, 2018.
[9] Ostensen M, 2004.
[10] Timur H, 2016.
[11] Ursin K, 2018 (epub ahead of print).
[12] Ostensen M, 1992.
[13] Berman M 2018.
[14] Flint J, 2016.
[15] Gotestam-Skorpen C, 2016.
[16] Mariette X, 2018.
[17] Clowse ME, 2017.
[18] Vinet E, 2018

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SP0149 ASSISTED REPRODUCTION TECHNIQUES: WHAT CAN WE TELL TO WOMEN WITH RHEUMATIC DISEASES?

Nathalie Costedoat-Chalumeau. *Université Paris-Descartes and Hopital Cochin, internal medicine, Paris, France*

Assisted medical procreation includes all the techniques based on the manipulation of reproductive cells that will allow infertile couples to conceive a child. Main techniques are ovulation induction with or without intrauterine insemination, controlled ovarian stimulation and in vitro fertilization (IVF).

Intrauterine insemination: sperm (from partner or donor) is inserted directly into woman's cervix, or uterus at the time of ovulation.

Controlled ovarian stimulation is aimed at stimulate ovarian to allow egg retrieval few hours later. Protocols usually include gonadotropin-releasing hormone agonist or antagonists associated with recombinant follicle-stimulating hormone (with concomitant close ovarian monitoring).

Controlled ovarian stimulation is generally followed by egg retrieval and then by IVF, which is performed in the laboratory by putting into contact collected oocytes with sperm (partner or donor). Intracytoplasmic sperm injection (ICSI) is performed in case of inadequate quality of the partner's sperm (oligospermia notably). One or 2 embryos are transferred in utero 2/3 or 5 days later (or during the next cycle), while other good quality embryos are cryopreserved for later use. There is no difference in the rates of ongoing pregnancy between transfers of frozen or fresh embryos [1].

By definition, an IVF procedure is defined by the transvaginal egg retrieval: even if the X obtained embryos are implanted Y times, this is still counted as the same procedure. A retrospective study of 14,469 women undergoing IVF, found that the cumulative live birth rates by procedure steadily increased with the number of collected oocytes, reaching 70% when $\geq$25 oocytes had been retrieved [2].

Women with auto-immune diseases or inflammatory chronic rheumatisms may have infertility as in the general population or because of previous gonadotoxic treatment as cyclophosphamide. While artificial inseminations and oocyte or embryo donations can be considered equivalent to a natural conception in terms of risk, particular attention is needed during IVF in women with systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS) and/or biology (APL) because of the increased level of estradiol after ovarian stimulation (risk of lupus flare and of thrombosis) [3].

Ovulation induction treatments with in vitro fertilization can be safely used in patients with SLE with stable/inactive disease [4]. Similarly, women with rheumatoid arthritis or spondyloarthritis can underwent IVF safely. In case of APS or APL, an adaptation of the treatment is usually required, especially around the egg retrieval. Management of pregnancy (both treatment and monitoring) must be planned before IVF [4].

As for a natural pregnancy, pre-counselling is important to adapt the treatment (interruption of contraindicated drugs in pregnancy as mycophenolate mofetil or methotrexate before conception due to their potential teratogenicity or at the end of the second trimester for anti TNF agents) [4]. Some treatments, especially hydroxychloroquine in SLE, have to be maintained during all this period and during pregnancy. In women with APS or APL, prophylactic dose of low weight molecular heparin (LWMH) is recommended during the period of stimulation. In case of treatment with coumadine, switch for curative LWMH is needed. In both cases, short interruption is required for the oocyte puncture. Low dose of aspirin is added after the embryo implantation. Folic supplement is recommended, especially in cases of recent treatment with methotrexate of current treatment with sulfasalazine. Immunizations are also important.

Given its potential to reduce the miscarriage rate, LT4 supplementation is recommended for infertile women with subclinical hypothyroidism or thyroid autoimmunity who are undergoing IVF [5].

Finally, a key role of inflammatory immune response has been shown in reproductive failures but a recent meta-analysis did not find any positive effect of immunotherapy (especially anti-TNF) in improving the live birth rate in women undergoing IVF treatment [6].

REFERENCES

[1] Vuong LN, Dang VQ, Ho TM, Huynh BG, Ha DT, Pham TD, et al. IVF Transfer of Fresh or Frozen Embryos in Women without Polycystic Ovaries. N Engl J Med 2018;378:137–47.
[2] Polyzos NP, Drakopoulos P, Parra J, Pellicer A, Santos–Ribeiro S, Tournaye H, et al. Cumulative live birth rates according to the number of oocytes retrieved after the first ovarian stimulation for in vitro fertilization/intracytoplasmic sperm injection: a multicenter multinational analysis including approximately 15,000 women. Fertil Steril 2018;110:661–70 e1.
[3] Sennstrom M, Rova K, Hellgren M, Hjertberg R, Nord E, Thurn L, et al. Thromboembolism and in vitro fertilization – a systematic review. Acta Obstet Gynecol Scand 2017;96:1045–52.
[4] Andreoli L, Bertsias GK, Agmon–Levin N, Brown S, Cervera R, Costedoat–Chalumeau N, et al. EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome. Ann Rheum Dis 2017;76:476–85.
[5] Rao M, Zeng Z, Zhao S, Tang L. Effect of levothyroxine supplementation on pregnancy outcomes in women with subclinical hypothyroidism and thyroid autoimmuneity undergoing in vitro fertilization/intracytoplasmic sperm injection: an updated meta–analysis of randomized controlled trials. Reprod Biol Endocrinol 2018;16:92.
[6] Achilli C, Duran–Retamal M, Saab W, Serhal P, Seshadri S. The role of immunotherapy in in vitro fertilization and recurrent pregnancy loss: a systematic review and meta–analysis. Fertil Steril 2018;110:1089–100.

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SP0150 THE IMPACT OF RHEUMATIC DISEASES AND ANTI-RHEUMATIC DRUGS ON MALE FERTILITY IN ADULT AND YOUNG PEOPLE

Monika Østensen. *Sorlandet Hospital Kristiansand, Rheumatology, Kristiansand, Norway*

Background: The chronic, systemic inflammation in rheumatic diseases can impair male fertility by direct effects on the gonads or by affecting the hypothalamic-pituitary-gonadal (HPG) axis resulting in hypogonadism. Impaired gonadal function is reflected by reduced sperm quality and sometimes lowered testosterone levels. Drugs may impair fertility by impairing spermatogenesis or interfere with the HPG axis.

Objectives: To summarize the knowledge on the impact of rheumatic disease and its therapy on fertility in adult and pediatric patients

Methods: Search of the literature

Results: No impairment of spermatogenesis has been shown for azathioprine, cyclosporine, and mycophenolate mofetil. Risk of permanent infertility is associated with cytotoxic drugs, particularly the alkylating agent cyclophosphamide.

Effects of methotrexate (MTX) on male fertility are related to dose. There is no indication that low-dose MTX 5 – 25 mg/week impairs male fertility. Case reports of men with psoriasis treated with low-dose MTX have either found completely normal sperm quality or detected oligo- and azoospermia.

Cyclophosphamide (CYC) is administered to adult and pediatric patients with systemic lupus erythematosus, other connective tissue disease and vasculitides. Gonadal damage by CYC is dose-dependent revealed by oligo-and azoospermia

as well as low testosterone, low inhibin B and elevated FSH levels. Cumulative doses of > 7.5g/m^2 carry a high risk of permanent infertility in adults. In survivors of childhood cancer treated with CYC recovery of spermatogenesis was sometimes seen after many years.
Sulfasalazine (SZ) can induce transient infertility with oligospermia, abnormal morphology of sperm cells and reduced sperm motility in about 40-86% of treated men. Plasma levels of steroids and gonadotropins remain normal during SZ therapy. Recovery of normal sperm quality is observed one to three months after discontinuation of SZ.
Studies comparing men treated with TNF inhibitors (TNFi) with disease-matched and/or healthy controls did not find impairment of sperm quality neither after short term or long-term treatment. Several studies found significantly better sperm quality in patients receiving long-term TNFi therapy than untreated disease matched controls.
Conclusion: Rheumatic disease has an impact on male fertility both by the disease process and by therapy. Most antirheumatic drugs have no negative effect on reproduction, however, treatment with cyclophosphamide increases the risk of infertility both in adults and pediatric patients. Increasing awareness about reproduction issues and infertility risk is needed among adult and pediatric rheumatologists. Clinicians should actively involve themselves in counseling their patients.

REFERENCES:

[1] Østensen M. Sexual and reproductive health in rheumatic disease. Nat Rev Rheumatol. 2017;13(8):485-493.
[2] Micu MC & Ostensen M, Villiger PM, Micu R, Ionescu R. Paternal exposure to antirheumatic drugs –– what physicians should know. Review of the literature. Semin Arthritis Rheum. 2018; 48(2):343-355.

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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

The future of therapeutic strategies

SP0151 MICROFABRICATION TECHNOLOGIES FOR CARTILAGE REPAIR

Marcel Karperien. *Technical Medical Centre University of Twente, Developmental BioEngineering, 7522 NB, Netherlands*

Background: Cartilage trauma is a major risk factor for the development of post-traumatic osteoarthritis. Treatment options are limited, are ineffective in the long run or come with disadvantages. Hence unconventional new strategies need to be explored to address this problem.
Objectives: In this lecture, I will present three strategies that are currently explored in my lab and that rely on the integration of biology with micro- and nanotechnologies to solve this problem.
Results and Methods: In a first strategy, we invested in the development of injectable and in situ gelating hydrogels that can be used as fillers of a cartilage defect stimulating its regeneration. We developed a panel of natural polymer (e.g. hyaluronic acid, dextran, heparin, gelatin, collagens) – tyramine conjugates which crosslink in a macromolecular network in an enzymatic reaction. The reaction is fast, can be tuned and using this method a wide variety of extracellular matrix mimics can be engineered. Moreover, the crosslinking reaction fixates the gel in the surrounding tissue through covalent bonding between tyramine residues in the hydrogel with tyrosine residues in extracellular matrix proteins, effectively acting as a glue. The hydrogel can be applied during an arthroscopic procedure. We tested the potential of the hydrogel to facilitate the repair of an acute focal cartilage defect in an equine chondral defect model and evaluated the repair process after 2 weeks, 3 months and 7 months. We compared the repair of a hydrogel-filled defect with the microfracture procedure, a frequently used but largely ineffective procedure due to the formation of fibrous cartilage instead of hyaline cartilage. After two weeks massive cell ingrowth in the hydrogel was observed. This continued and after 3 months hydrogel treated defects resulted in near complete defect filling with predominantly hyaline cartilage and without noticeable reactions in the subchondral bone. This was in marked contrast to the defects treated with microfracture, which showed a massive response in subchondral bone and the formation of fibrous tissue. The repair was consolidated after 7 months. Defect filling might be a viable solution for treatment of focal cartilage defects to prevent early onset, post-traumatic osteoarthritis.
In a second strategy, we use the same material platform for cell delivery in the joint. Co-injection of cells with the in situ gelating hydrogels might be beneficial in the repair of particularly large (osteo)chondral defects. We have developed microfluidic-based systems for the encapsulation of 10-15 cells in microgels of approximately 100μm or even at the single cell level in microgels with a diameter of 30μm slightly larger than the cell itself. We postulated that encapsulation of Mesenchymal Stromal Cells (MSCs) could prolong the retention time in the joint after an intra-articular injection over "naked" MSCs and may, therefore, improve the therapeutic benefit of these cells. We tested this hypothesis in a rat model and indeed showed that, while "naked" near infrared labeled MSC rapidly disappeared from the injected joint, encapsulated cells remained present up to 4 months. We are currently exploring its potential to improve the therapeutic efficacy of the MSCs.
In a third strategy, we use the material platform in combination with cytokine neutralizing antibodies to generate easily injectable microgels that can sequester pro-inflammatory cytokines from the synovial fluid. Rather than using conventional antibodies, we rely on the variable domain of single chain, heavy chain-only antibody fragments such as found in Camelidae. These antibody fragments can be easily produced using recombinant DNA technology and are open for a wide variety of chemical reactions without impacting its biological activity. These microgels can effectively neutralize cytokines in cell assays in vitro and are currently explored for its potential to neutralize cytokines in synovial fluid and after intra-articular injection.
Conclusion: In conclusion, the integration of biology with microfabrication technologies has the potential to generate the next generation of therapies for the treatment of cartilage defects and osteoarthritis.
Disclosure of Interests: None declared
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SP0152 3D PRINTED DRUGS

Matthew Peak. *Alder Hey Children's Foundation NHS Trust, Paediatric Medicines Research Unit, Liverpool, United Kingdom*

Background: With the advent of personalised medicine, the need for flexible dosing is increasingly important. Conventional pharmaceutical manufacturing processes can be constrained in their ability to offer flexible dosing options to meet patient need. This is particularly important in specific populations, for example children, where available formulations are frequently not age-appropriate and need to be modified to achieve an intended dose. 3D-printing of solid dosage forms offers a disruptive technology which enables solid-dosage forms of medicines to be manufactured at flexible, precise doses meeting the needs of individual patients. This technology has relevance for manufacture of existing active pharmaceutical ingredients for a range of conditions including inflammatory diseases.
Objectives: To develop 3D-printed oral solid dosage forms of medicines which are age-appropriate for children and young people. To determine the acceptability of 3D-printed medicines to children and young people by conducting interventional studies of tablet administration.
Methods: Tablets containing a range of active pharmaceutical ingredients (API) were produced using two stages: (i) holt melt extrusion of a filament containing API and excipients; (ii) 3D printing of the filament using fused deposition modelling (FDM) to produce the desired shape in a layer-by-layer pattern. Acceptability of 3D-printed tablets to children and young people (CYP) aged 4-12 years was assessed by the swallowability and mouthfeel following administration of different size 3D-printed placebo tablets.
Results: Using hydrocortisone as an exemplar API, Tablets were successfully produced by the FDM 3D printing process. Thermal analysis indicated that HC remained stable below 160°C and the tablets had very high mechanical strength with friability of 0%. This illustrates the ability of the printer to produce a ready-to-use-tablet without the need for a drying or finishing step. The disintegration took 9.2–14 min confirming immediate release properties. We administered for the first time globally an ingestible 3D-printed tablet to a child. CYP were able to swallow and ingest 3D-printed bi-convex tablets of either 6mm, 8mm or 10mm diameter. The 3D tablets were reported by CYP to have a slightly more discernible mouthfeel than placebo tablets of the same size manufactured in a GMP facility.
Conclusion: FDM 3D printing offers a disruptive technology for the manufacture of solid dosage forms of medicines of flexible doses with excellent dose precision and pharmacopeial properties. In circumstances where modification of existing dosage forms is needed, this offers an alternative reliable means of achieving the intended dose. This technology is also suited to the manufacture of solid dosage forms of small molecules which may be particularly important in the treatment of inflammatory disease.
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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Calming the cytokine storm in children and adults

SP0153 **CALMING THE STORM IN ADULT MAS/HLH IN RHEUMATIC DISORDERS**

Jan van Laar. *Erasmus MC, University Medical Center Rotterdam, Internal Medicine, Division of Clinical Immunology, Netherlands*

Background: Hemofagocytic lymfohistiocytosis (HLH) is a rare and often overlooked clinical manifestation of an aberrant hyper inflammatory immune response leading to a fatal cytokine storm(1). Diagnostic criteria according to The HLH Study Group of the Histiocyte Society include fever, splenomegaly, bicytopenia, hypertriglyceridemia and/or hypofibrinogenemia, hyperferritinemia, low/or absent NK activity, increased soluble CD-25 levels and hemophagocytosis(2). Prompt recognition and differentiation from severe sepsis is essential to improve the outcome. HLH reflects a disbalanced immune system in response to infectious, malignancy, or autoinflammatory/autoimmune mediated triggers(1). The latter group of patients are regarded as having Macrophage Activation Syndrome (MAS-HLH)() In adults MAS-HLH comprises 12.5% of all HLH causing triggers(4). The most frequent immunological disorders associated with adult HLH-MAS are systemic lupus erythematosus and adult onset Still´s disease, but every other immunological disorder can be involved(4, 5).
Treatment: Treatment of adults HLH patients requires swift recognition and an experienced team of specialists that are acquainted with the critical factors influencing the balance between co-morbidity, cytokine storm induced septic-like symptoms and toxicity of chemo-immunotherapy(6). In general, adult patients do not tolerate doses of etoposide that are given in (HLH-94 based) chemo-immunotherapy schedules that have been shown effective in children(7,8). Dose and frequency modifications of etoposide may avoid prolonged neutropenia, infectious complications or hepatic toxicity. The same precautions account for adults patients with MAS-HLH in which treatment differs from the HLH schedules. A step up approach depending on clinical features and severity is warranted(9, 10). High doses of corticosteroids are recognized as first-line treatment(9, 10). In patients with MAS-HLH and SLE steroids, cyclophosphamide or etoposide are given (10). Cyclosporine can be added in patients with insufficient immediate response(9). The cytokine blocking agent anakinra (anti-IL-1β) given in high doses is emerging as an alternative or additional treatment of adult MAS-HLH(11, 12, 13). Another promising cytokine blocker is anti-IL-6 (tocilizumab). Etoposide at a reduced dose can be initiated in patients with severe non-responsive and active disease or CNS-involvement(10).
Conclusion: Awareness of the clinical emergency MAS-HLH in patients with autoinflammatory/autoimmune mediated disorders is essential for timely recognition and potential life-saving treatment. The management of MASH-HLH in adults requires a team of dedicated specialists with experience in the treatment of critically ill patients with immunological disorders and anticipation on its rapidly changing and deteriorating nature.

REFERENCES:

[1] Janka GE. Familial and acquired hemophagocytic lymphohistiocytosis. Annu Rev Med. 2012;63:233-46
[2] Henter JI, Horne A, Arico M, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007;48:124-131
[3] Carter SJ, Tattersall RS, Ramanan AV. Macrophage activation syndrome in adults: recent advances in pathophysiology, diagnosis and treatment. Rheumatology (Oxford). 2019;58(1):5-17.
[4] Ramos-Casals M, Brito-Zerón P, López-Guillermo A, Khamashta MA, Bosch X. Adult haemophagocytic syndrome. Lancet. 2014;383:1503-1516
[5] Fukaya S, Yasuda S, Hashimoto T, et al. Clinical features of haemophagocytic syndrome in patients with systemic autoimmune diseases: analysis of 30 cases. Rheumatology (Oxford) 2008;47: 1686–91
[6] Halyabar O, Chang MH, Schoettler ML, et al. Calm in the midst of cytokine storm: a collaborative approach to the diagnosis and treatment of hemophagocytic lymphohistiocytosis and macrophage activation syndrome. Pediatr Rheumatol Online J. 2019;17:7
[7] La Rosee P. Treatment of hemophagocytic lymphohistiocytosis in adults. Hematology Am Soc Hematol Educ Program. 2015;2015:190-196
[8] Ehl S, Astigarraga I, von Bahr Greenwood T, et al. Recommendations for the Use of Etoposide-Based Therapy and Bone Marrow Transplantation for the Treatment of HLH: Consensus Statements by the HLH Steering Committee of the Histiocyte Society. J Allergy Clin Immunol Pract. 2018;6:1508-1517
[9] Kumar B, Aleem S, Saleh H, Petts J, Ballas ZK. A Personalized Diagnostic and Treatment Approach for Macrophage Activation Syndrome and Secondary Hemophagocytic Lymphohistiocytosis in Adults. J Clin Immunol. 2017;37:638-643
[10] Gavand PE, Serio I, Arnaud L, et al. Clinical spectrum and therapeutic management of systemic lupus erythematosus-associated macrophage activation syndrome: A study of 103 episodes in 89 adult patients. Autoimmun Rev. 2017;16:743-749
[11] Wohlfarth P, Agis H, Gualdoni GA, et al. Interleukin 1 Receptor Antagonist Anakinra, Intravenous Immunoglobulin, and Corticosteroids in the Management of Critically Ill Adult Patients With Hemophagocytic Lymphohistiocytosis. J Intensive Care Med. 2017:885066617711386
[12] Schulert GS, Minoia F, Bohnsack J, et al. Effect of Biologic Therapy on Clinical and Laboratory Features of Macrophage Activation Syndrome Associated With Systemic Juvenile Idiopathic Arthritis. Arthritis Care Res (Hoboken). 2018;70:409-419
[13] Zhou S, Qiao J, Bai J, Wu Y, Fang H. Biological therapy of traditional therapy-resistant adult-onset Still's disease: an evidence-based review. Ther Clin Risk Manag. 2018;14:167-171

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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Know your methods! Interactive discussion

SP0154 **REASONS FOR QUALITATIVE RESEARCH FOR HPR**

Romualdo Ramos. *University Medical Center Utrecht, Netherlands*

Qualitative research plays a pivotal role in clinical practice by providing insights from the patient's perspective. This becomes all the more relevant, as we move into the era of patient-centered care. In this presentation, we shed light on the different approaches to qualitative data collection and analysis, as well as systematic literature reviews of qualitative research. We will also elaborate on how qualitative research methods are used to better understand which outcomes are relevant to patients, self-management of symptoms, non-adherence to medication and non-pharmacological methods, the doctor-patient relationship, and to evaluate policy and interventions within the realm of RMDs. Finally, in an open panel, we will discuss how qualitative and quantitative methods triangulate, contributing to mixed methods approaches.

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SP0155 **REASONS FOR QUANTITATIVE RESEARCH FOR HPR**

Mwidimi Ndosi. *University of the West of England, Nursing and Midwifery, Bristol, United Kingdom*

Health professionals in rheumatology are expected to provide care that is evidence-based. Evidence-based practice is the careful integration of best research evidence with clinical expertise, patient values and needs in the delivery of high-quality, cost-effective health care.[1] A sound understanding of quantitative methods is essential for correct evaluation of research and appropriate implementation into clinical practice.
Quantitative methods are used in a wide range of topics, from validating patient-reported outcome measures, sample size estimation, assessing associations between variables or predicting risk factors and evaluating the effectiveness of interventions. Furthermore, quantitative methods can be used to pool the results of several studies into a meta-analysis and thus provide better estimates of effectiveness than what can be achieved in individual studies.
This presentation will debate the case for quantitative research using examples of research conducted by health professionals in rheumatology. It is hoped that delegates will gain more confidence in using quantitative methods in their own research or evaluating evidence for clinical practice.

REFERENCE:

[1] Sackett, D.L.; Straus, S.E.; Richardson, W.S.; Rosenberg, W.; Haynes, R. B. (2000). *Evidence-based medicine: How to practice and teach EBM.* **2**. London: Churchill Livingstone.

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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Missing data in clinical research: to impute or not to impute, that is the question

SP0156 **MISSING DATA: IS IT ALL THE SAME?**

Stian Lydersen. *Norwegian University of Science and Technology, Department of mental health, Trondheim, Norway*

Introduction: In most studies, there are "holes" in the data set, such that data are missing partly or completely for some of the subjects. This results in reduced statistical power. More seriously, missing data may cause biased results, since data are usually not missing completely at random.
Missing data mechanisms: In which way, and to what extent, does the probability that data are missing, depend on observed and/or unobserved data values? This is called the missing data mechanism, and is important for an appropriate choice of analysis method. Three types of missing data mechanisms have been defined, see for example (Sterne et al. 2009).
MCAR: *Missing completely at random*. There are no systematic differences between the missing values and the observed values. The probability that values are missing does not depend on any of the data, observed or unobserved.
MAR: *Missing at random*. The probability that values are missing may depend on observed data values, but not on unobserved data values. For example, some variables are missing more frequentely for patients with higher age. Data are missing at random *conditionally* on observed data.
MNAR: *Missing not at random.*
Even after the observed data are taken into account, systematic differences remain between the missing values and the observed values: The probability that values are missing depends on unobserved data values as well.
It is possible to distinguish between MCAR and MAR by inspecting the data at hand. But it is never possible to determine whether data are MNAR from your data.
Methods for handling missing data
Some commonly used methods, from the less to the more complex ones, are listed below, with an indication of when they give unbiased estimates:

- Complete case analysis (disregarding cases with partially missing data) (MCAR)
- Single imputation methods (sometimes under MAR but underestimates uncertainty)
- Multiple imputation (MAR)
- Full information maximum likelihood (MAR)
- Linear mixed models in longitudinal studies (MAR)

In longitudinal studies, Last observation carried forward (LOCF) is a simple method for imputing missing values. But it is not unbiased under any sensible assumptions, and should not be used (Lydersen 2019).
Reporting: In general, report the amount of missing data in the different variables, and how this was handled in the analysis. This is recommended in the Consort Guidelines (Moher et al. 2010) as well as the STROBE Statement (STROBE 2014), see also (Lydersen 2015)

REFERENCES:

[1] Lydersen, S. 2015. Statistical review: frequently given comments. Ann. Rheum.Dis., 74, (2) 323-325. Lydersen, S. 2019.Last observation carried forward - simple but not recommended. In press,Tidsskrift for Den norskelegeforening
[2] Moher, D., Hopewell, S., Schulz, K.F., Montori, V., Gotzsche, P.C., Devereaux, P.J., Elbourne, D., Egger, M., & Altman, D.G. 2010. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ, 340, c869
[3] Sterne, J.A., White, I.R., Carlin, J.B., Spratt, M., Royston, P., Kenward, M. G., Wood, A.M., & Carpenter, J.R. 2009. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ, 338, b2393
[4] STROBE Statement 2014. Strengthening the reporting of observational studies in epidemiology.

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SP0157 **PRO SESSION: IMPUTATION IS A POWERFUL ANALYTICAL TOOL, WHEN APPROPRIATELY USED**

Loreto Carmona. *Instituto de Salud Musculoesquelética, Research, Madrid, Spain*

Analysing a study with missing data very likely will yield biased results. Of course, the first principle is to avoid missing data by designing the study and the data collection very thoughtfully. If the study is already done and data collected, then one needs to study how important, and what type of missingness is affecting our data. Simple *ad hoc* methods, such as LOCF, or imputing the mean or other value are generally invalid. Multiple imputations need additional work and expertise, but generally yield better results, closer to reality.
Many statistical programmes have macros available for imputing missing values and analysing imputed data. We will review how these work. Understanding what multiple imputations do will make the decision clearer.
Disclosure of Interests: Loreto Carmona Grant/research support from: Abbvie, Actelion, Astellas, BMS, Eisay, Gebro Pharma, Grünenthal, Leo Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis and UCB Pharma, Paid instructor for: Novartis
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SP0158 **CON SESSION: PREPARE YOUR DATA COLLECTION WELL: IMPUTATION DOES NOT REPLACE 'REAL DATA'**

DOUGADOS Maxime.

The recently proposed sophisticated statistical methods to impute missing data are very attractive.
For the clinical researchers in charge of data collection, it might be tempting to "neglect" the quality of data collection in favor of the time spent by one database manager/statistician to impute missing data.
This presentation will be a plea in favor to make all the possible efforts to collect appropriately the data in clinical research studies/trials. In particular, emphasis will be placed on the importance of writing a specific section in any research protocol describing the technics used to avoid these missing data and also the a priori decided technic that will be used to manage the missing data. One point of importance in this section: to specify in advance the maximum percentage of missing data over which no imputation can be made.
Two different situations:
- Cross-sectional studies. Any item (for example HLA B27, MRI SIJ inflammation positivity) should be considered as mandatory or not before running the study.
- Longitudinal studies: any longitudinal protocol should include a section detailing the technic to appropriately follow the patients in order to avoid the "lost of follow-up patients". This is particularly important in longitudinal follow-up of patients suffering from a recent onset disease (e.g. early synovitis cohorts, early inflammatory back pain cohorts) since it is well known that the "lost of follow-up" have specific baseline characteristics suggesting a less severe disease. It is also important to decrease at a minimum level the "lost of follow-up" patients participating at a therapeutical trial/registry since the reason of "lost of follow-up" might be related to a specific drug effect.
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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Don't panic – round table discussion on risk perception

SP0159 **WHAT DO WE KNOW – WHAT SHALL WE DO – WHAT DO WE TELL**

Timothy R. Radstake. *University Medical Center Utrecht, Netherlands*

There is an increasing need for patients to be involved in research as well as matters that can influence their own clinical journey. One aspect of science that links optimal clinical care is the increased use of biomarkers for so-called personalized medicine approaches.

In my presentation I will showcase the State of the Art technologies of biomarker research and how the information that comes from this can be implemented for improving clinical care. I will discuss the revolution of molecular profiling and how the large amount of data coming from these approaches is used to molecularly classify patients into molecular fingerprints. How this technology leads to a disruptive change in medicine for the coming 5-10 years. I will close of with the role of biomarkers in the treatment of diseases, trial design and drug development for the coming 5 years.

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SP0160 DISEASE REMISSION: DO WE AIM FOR THE SAME THING?

Ricardo Ferreira. *Centro Hospitalar e Universitário de Coimbra, EPE, Rheumatology, Coimbra, Portugal*

It is consensually accepted that the most important therapeutic goals for treating rheumatoid arthritis (as well as other inflammatory arthritis) are eliminating signs and symptoms (such as joint pain, swelling, and stiffness); preventing joint damage or its progression; and maximizing physical function and quality of life (Aletaha & Smolen, 2019). According to current medical knowledge, these aims are believed to be best accomplished by achieving disease remission, a state in which no or only minimal residual inflammation is discernible (Aletaha & Smolen, 2019). However, different studies have been providing evidence that achieving inflammatory remission is not enough as a considerable proportion of patients with no or minimal inflammation remain with high levels of pain, fatigue, functional impairment, mental health problems, among other symptoms (Boone et al., 2019; Ferreira et al., 2019; Ferreira et al., 2017). The perfect path to achieve good results is still to be defined, namely, regarding the T2T strategy (van Vollenhoven, 2019). Recent studies still show that despite a high level of patient agreement with RA T2T, patient engagement in this process needs to be improved in order to individualize therapy adjustments, make shared decisions and decide on targets that accurately reflect disease control according to patients (Benham et al, 2019).
In this session I would address the following questions:

- Is aiming for one target enough nowadays?
- Do health professionals and patients aim for the same thing when defining treatment strategies?
- Do the current treatment targets pose a risk of overtreatment with immunosuppressive therapy?

This presentation is informed by current research in this area including research from our own group (Ferreira et al., 2018; Santos et al., 2018).

REFERENCES:

[1] Aletaha, D., & Smolen, J. S. (2019). Achieving Clinical Remission for Patients With Rheumatoid Arthritis. JAMA, 321(5), 457-458. doi:10.1001/jama.2018.21249
[2] Benham, H., Rutherford, M., Kirby, S., Stebbings, S., White, D., Sim, D., & Harrison, A. (2019). Treat-to-target in rheumatoid arthritis: Evaluating the patient perspective using the Patient Opinion Real-Time Anonymous Liaison system: The RA T2T PORTAL study. International Journal of Rheumatic Diseases. doi:10.1111/1756-185x.13514
[3] Boone, N. W., Sepriano, A., van der Kuy, P. H., Janknegt, R., Peeters, R., & Landewe, R. B. M. (2019). Cotreatment with methotrexate in routine care patients with rheumatoid arthritis receiving biological treatment yields better outcomes over time. *RMD Open,* 5(1), e000836. doi:10.1136/rmdopen-2018-000836
[4] Ferreira, R. J. O., Carvalho, P. D., Ndosi, M., Duarte, C., Chopra, A., Murphy, E.,. . . da Silva, J. A. P. (2019). Impact of patient global assessment on achieving remission in patients with rheumatoid arthritis: a multinational study using the METEOR database. *Arthritis Care Res (Hoboken)*. doi:10.1002/acr.23866
[5] Ferreira, R. J. O., Dougados, M., Kirwan, J., Duarte, C., de Wit, M., Soubrier, M.,. . . Gossec, L. (2017). Drivers of patient global assessment in patients with rheumatoid arthritis who are close to remission: an analysis of 1588 patients *Rheumatology*. doi:10.1093/rheumatology/kex211
[6] Ferreira, R. J. O., Ndosi, M., de Wit, M., Santos, E. J. F., Duarte, C., Jacobs, J. W. G.,. . . da Silva, J. A. P. (2018). Dual target strategy: a proposal to mitigate the risk of overtreatment and enhance patient satisfaction in rheumatoid arthritis. Annals of the Rheumatic Diseases. doi:10.1136/annrheumdis-2018-214199
[7] Santos, E. J. F., Duarte, C., Ferreira, R. J. O., Pinto, A. M., Geenen, R., & da Silva, J. A. P. (2018). Determinants of happiness and quality of life in patients with rheumatoid arthritis: a structural equation modelling approach. Annals of the Rheumatic Diseases, 77(8), 1118-1124. doi:10.1136/annrheumdis-2017-212934
[8] van Vollenhoven, R. (2019). Treat-to-target in rheumatoid arthritis - are we there yet? *Nature Reviews*. Rheumatology, 15(3), 180-186. doi:10.1038/s41584-019-0170-5

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SP0161 LOOKING FOR A NEEDLE IN A HAYSTACK: HELPING YOUNG PEOPLE TO MAKE SENSE OF EVIDENCE BASED HEALTH CARE

Simon Stones. *University of Leeds, School of Healthcare, Leeds, United Kingdom*

While it has been suggested that there are no differences in the occurrence of risk-taking behaviours in young people with chronic conditions compared with healthy peers, young people with chronic conditions often face the dilemma of balancing twice the amount of risk to that of other young people, owing to their condition and treatment. For example, young people with juvenile idiopathic arthritis taking methotrexate face the risks of alcohol consumption plus the increased risk of toxicity from consuming alcohol while taking methotrexate. However, such issues are often ignored or overlooked (1).Research has suggested that a lack of experience with, and not worrying about serious health consequences may desensitise young people with chronic conditions to potential health risks (2). It is also recognised that young people's perceived focus of health and wellbeing can often be on short-term goals; which is often paradoxical to the focus of families and healthcare professionals thinking about longer-term outcomes and prognosis.
It has been demonstrated that young people with chronic conditions value interventions that enable them to live a "normal" life – extending beyond the clinical management of their condition (3). The emotional, social, and vocational consequences of condition management can be profound (4). When this is coupled with the challenges of accessing accurate, trusted and individualised information and support, it can often leave young people and their families feeling as though they are looking for a 'needle in a haystack'. Finding the best evidence requires knowledge of the best quality and most appropriate sources, as well as the ability to use and navigate such resources appropriately (5). In an era where health information is easier and faster to find than ever before, it is often a challenge for young people to be able to filter the 'good' from the 'not so good'. There are significant amounts of unreliable and irrelevant content on the internet, which ultimately places the responsibility for interpretation of information and advice onto young people and their families.
Therefore, age- and developmentally- appropriate opportunities to discuss health, wellbeing and the effects of treatment need to be provided early and regularly, across the lifecourse, in multiple formats to suit individual needs and circumstances. Attempts have already been made to make health information more accessible, for example, with the introduction of the Accessible Information Standard within the National Health Service (6). However, this is not necessarily enough to engage and support young people with chronic conditions in making sense of evidence-based healthcare. Information needs to be taken, in the right formats, to where young people are interacting, such as on certain social media platforms. This needs to be multifaceted, using peer- and community-driven approaches to enhance engagement. Furthermore, periodic consideration of the long-term risks and benefits of health and wellbeing interventions needs to happen across the lifecourse, both as a prompt for young people to air their concerns, but to also check their understanding. Only through understanding young people's values, preferences, and concerns can a sustainable balance between condition control, treatment burden and quality of life be achieved.

REFERENCES:

[1] McDonagh JE. Getting It Right For Young People: Developing Adolescent Rheumatology Services. Future Rheumatol 2008; 3(2):133-41.
[2] Greening L, et al. Predictors of children's and adolescents' risk perception. *J Ped Psych* 2005; 30(5):425-35.
[3] van Houtum L, et al. Do everyday problems of people with chronic illness interfere with their disease management? BMC Public Health 2015;15:1000.
[4] Hart RI, et al. Being as normal as possible: how young people ages 16–25 years evaluate the risks and benefits of treatment for inflammatory arthritis. Arthritis Care Res 2016; 68(9):1288-94.
[5] NHS England. Accessible information: Specification v1.1. 2017.

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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Remission – the holy grail? Looking across diseases

SP0162 REMISSION IN RA: DOES THE DEFINITION MATTER?

Daniel Aletaha. *Medical University of Vienna, Department of Medicine III, Division of Rheumatology, Austria*

Remission is the ultimate target for chronic inflammatory rheumatic disease, and so also for rheumatoid arthritis (RA). In this presentation, we will review the challenges in defining and assessing remission. Further, we will discuss if remission should be a clinical target, or whether imaging results, e.g. from ultrasound or MRI examinations, should be included in the concept of remission. Many symptoms in patients with RA may mimick RA disease activity, while they are not directly a consequence of the disease process, with secondary pain syndromes being a typical example. FInally, patients are the most important stakeholders on the question of whether or not a musculoskeletal disease is in remission. Patient reported outcomes have been critizised for their subjectivity and their role in remission indices has been questioned. We will also explore the influence and Pro's and Con's of these measures on remission assessment.
Disclosure of Interests: Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB
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SP0163 REMISSION IN SLE: WHAT TO AIM FOR?

Marta Mosca. *Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy*

It is generally acknowledged that, in SLE, disease activity is associated with poor prognosis, high glucocorticoid use, damage development and increased mortality; therefore reaching low level of disease activity or remission are main treatment targets for SLE.
Definitions for disease remission and low disease activity are being proposed and validated as meaningful targets to be pursued in SLE management.
In detail an international task force has recently developed a definition of remission in SLE (DORIS) taking in consideration four different domains: clinical activity, serological activity, treatment and duration. This approach led to the development of different levels of remission i.e. clinical remission on/off treatment and complete remission on/off treatment.
Recently data from different cohorts have been published, showing that remission is an achievable target in SLE. Achieving remission appears associated with reduced damage accrual, however persistence in remission is rare being maintained in an average of 7% of patients over 5 years. In addition, the more stringent is the definition, the more difficult is to achieve remission and a longer time to remission is observed in patients with high activity, high therapy, hematological activity, African-American ethnicity.
Low disease activity may represent another target in SLE treatment and a definition of (lupus low disease activity state (LLDAS) has been developed by Franklyn et al. LLDAS is defined based on three domains which are SLEDAI-2k 4, physician global assessment (PGA) 1, absence of new manifestations and stable and well tolerated treatment with a prednisolone (or equivalent) dose of 7.5 mg/day.
Interestingly, LLDAS is achieved by a high percentage of patients over follow up, ranging between 33 and 88% in different cohorts and it is maintained over follow up in up to 50% of patients for 50% of follow up time. Predictive factors for LLDAS attainment are shorter disease duration, lower disease activity score, lower mean PGA, lower mean SLEDAI, older age; while persistent LLDAS is less frequent in patients with vasculitis, neurological, renal, cardiopulmonary and mucocutaneous manifestations.
Achievement and persistence of LLDAS are associated with lower prednisone dose during follow up, reduction of disease flares, lower damage accrual, better quality of life.
In conclusion, definitions of remission and low disease activity in SLE have been proposed and validated against outcomes such as glucorticoids usage, damage accrual, quality of life.
Both targets are associated with improved outcomes, however at present persistence in remission is not common. The achievement of LLDAS is not rare, persistence in LLDAS is achievable.

REFERENCES:

[1] van Vollenhoven RF, Mosca M, Bertsias G, et al. Treat-to-target in systemic lupus erythematosus: recommendations from an international task force. Ann Rheum Dis 2014;73:958-67.
[2] van Vollenhoven R, Voskuyl A, Bertsias G, et al. A framework for remission in SLE: consensus findings from a large international task force on definitions of remission in SLE (DORIS). Ann Rheum Dis 2017;76:554-561.
[3] Franklyn K, Lau CS, Navarra SV, et al. Asia-Pacific Lupus Collaboration. Definition and initial validation of a Lupus Low Disease Activity State (LLDAS). Ann Rheum Dis 2016;75:1615-21.
[4] Petri M, Magder LS. Comparison of Remission and Lupus Low Disease Activity State in Damage Prevention in a United States Systemic Lupus Erythematosus Cohort. Arthritis Rheumatol 2018.
[5] . Tsang-A-Sjoe MW, Bultink IE, Heslinga M, et al. Both prolonged remission and Lupus Low Disease Activity State are associated with reduced damage accrual in systemic lupus erythematosus. Rheumatology 2017;56:121-28.
[6] Zen M, Iaccarino L, Gatto M, et al. Lupus low disease activity state is associated with a decrease in damage progression in Caucasian patients with SLE, but overlaps with remission. Ann Rheum Dis 2018;77:104-10.
[7] Zen M, Iaccarino L, Gatto M, et al. The effect of different durations of remission on damage accrual: results from a prospective monocentric cohort of Caucasian patients. Ann Rheum Dis 2017;76:562-65.
[8] Tselios K, Gladman DD, Touma Z, et al. Clinical remission and low disease activity have comparable outcomes over 10 years in systemic lupus erythematosus. Arthritis Care Res 2018.

Disclosure of Interests: Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB
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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Laboratory course – from the clinic to the lab and back (from translation to prescription)

SP0164 ANA DIAGNOSTIC AND ANTIPHOSPHOLIPID SYNDROME (APS) AS INHERITED COAGULATION DISORDER

Thomas Dörner. *Charite Berlin, Berlin, Germany*

Use of ANA diagnostic is key for systemic autoimmune diseases. ANA is an overarching term and the underlying specificities are important for defined diagnosis of SLE, Sjögren's, systemic sclerosis etc. Diagnostic algorithms of ANA and new semi-automated procedures are discussed in the context of case discussions. Subsequently, the value and limitations of the diagnostics of lupus anticoagulant and antiphospholipid antibodies as key serologic findings in antiphospholipid syndrome are discussed in the context of instructive cases.
Disclosure of Interests: Thomas Dörner Grant/research support from: Eli Lilly, Janssen, Roche, UCB Pharma, Consultant for: Eli Lilly, Janssen, Roche, UCB Pharma, Speakers bureau: Eli Lilly, Janssen
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SP0165 **NEW TRENDS IN BIOMARKERS IN INFLAMMATORY JOINT DISEASE**

Eugen Feist. *Charité Universitätsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany*

This lecture provides an overview on new developments in biomarker research and standardization in inflammatory joint diseases. The presentation includes an introduction of established and new biomarkers in serum and synovial fluid as well as methods for their detection. Furthermore, an overview on different modifications of auto-antigens (including citrullinated, carbamylated and acetylated isoforms) and their role in immune response and pathogenesis of disease will be given. The diagnostic performance of new and established biomarkers will be discussed including antibodies against modified antigens also illustrated by difficult to diagnose cases. In this context, special attention will be attributed to the predictive value of biomarkers for diagnosis of disease and treatment response.
Disclosure of Interests: Eugen Feist Grant/research support from: Pfizer, Roche, Novartis, BMS, Sanofi, Lilly, Consultant for: Pfizer, Roche, Novartis, BMS, Abbvie, Celgene, Sanofi, MSD, Lilly, Speakers bureau: Pfizer, Roche, Novartis, BMS, Abbvie, Celgene, Sanofi, Lilly
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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Ultrasound advanced II

SP0166 **ULTRASOUND OF THE HAMSTRING MUSCLE COMPLEX-CLINICAL APPLICATION + DEMO**

David Andrew Bong. *Instituto Poal de Reumatologia, Universitat de Barcelona, Rheumatology; Anatomy, Barcelona, Spain*

The hamstring muscle complex (HMC) are the "brakes" of human bipedal ambulation and are susceptible to injury during concentric contraction. Although common in sports medicine practice, a recent systematic review of severe hamstring injuries (grade II-III) suggests that greater than 10% of these severe injuries are non-sports related and disproportionately affect older women.
Musculoskeletal ultrasound (MSKUS) is one of the basic imaging techniques utilized to detect and define these injuries and eliminate other potential causes of posterior thigh pain. This presentation will discuss the clinical application of MSKUS of the HMC in rheumatology/musculoskeletal medicine and offer a systematic anatomically-based method of examining this important non-articular region.
Disclosure of Interests: None declared
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SP0167 **US FOR ASSESSING LUNG INVOLVEMENT IN RHEUMATIC DISEASES – CLINICAL USE + DEMO**

Andrea Delle Sedie. *University of Pisa, Rheumatology Unit, Pisa, Italy*

Background: Evaluation of interstitial lung disease (ILD) is always difficult (low sensitivity for X-ray and pulmonary function tests or high level of radiation for HRCT): ultrasound (US) has recently shown interesting results on truth, discrimination and feasibility. Due to the thickening of interlobular septa for edema or fibrosis, US beam can interact with those structure and produce artifacts on the screen:
B-lines (BL) and pleural line irregularity (PLI). A positive correlation between BL and HRCT has been established both in systemic sclerosis patients and in other patients with ILD; more recently similar results have been published by using PLI as a finding for US assessment in patients.
BL has been recently defined by the OMERACT as a vertical hyperechoic reverberation artifact that arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with lung sliding, while PLI has been defined as a loss of regularity that may be associated with an increase in thickness, focal, diffuse, or nodular.
A low number of BLs has been described in healthy subjects but they are generally confined to the posterior and lower part of the thorax.
Up to now, many different scanning protocols have been used to assess BL or PLI in patients, providing similar results.
Conclusion: US lung evaluation is a usefull and feasible imaging technique.
Disclosure of Interests: Andrea Delle Sedie Speakers bureau: Abbvie, UCB, Celgene, MSD
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SP0168 **US FOR SYNOVIAL BIOPSIES – CLINICAL RELEVANCE AND SAFETY + DEMO**

Andrew Filer. *University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom*

Background: The introduction of ultrasound guidance to access synovial tissue samples has facilitated a rapid growth in tissue-related research. Ultrasound guidance enables operators to use less invasive approaches compared to a gold standard direct vision arthroscopy procedure while maintaining the quality of samples obtained. Patients find the procedures easy to tolerate and are willing to undergo repeat biopsy, facilitating the analysis of tissue samples in clinical trials and experimental medicine studies. Advanced analytic techniques including single cell analytics are now being used to exploit the tissue samples obtained in order to provide dramatic leaps in understanding of synovial pathology.
Objectives: In this session the key aspects of the dominant techniques in use will be presented, including safety, patient tolerability and quality of output. The research and clinical utility of synovial biopsy will be discussed. Sonographic approaches to the major techniques will then be illustrated through video demonstrations, and competencies required to undertake training will be discussed alongside current EULAR initiatives for training. Finally, examples of research outputs generated through synovial biopsy will be explored alongside the logistics required to deliver such clinical studies.
Disclosure of Interests: None declared
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FRIDAY, 14 JUNE 2019

17:30:00 – 19:00:00

Complement and autoimmunity – emerging therapeutic opportunities

SP0169 **COMPLEMENT AND LUPUS IN THE YOUNG AND THE OLD**

Marina Botto. *Imperial College London, Centre for Inflammatory Disease/ Immunology and Inflammation, London, United Kingdom*

Complement component C1q is known to play an important recognition role in adaptive and innate immunity. More recently evidence has emerged that C1q may have roles outside the complement system and the relevance of these functions may change with ageing. Homozygous deficiency of the first component of the complement system, C1q, is one of the most powerful susceptibility genetic factors for the development of systemic lupus erythematosus (SLE). The vast majority of patients with C1q deficiency develop a syndrome closely related to SLE. The disease is typically of early onset and is often very severe. Although the phenotype of disease varies between patients, the fact that C1q deficiency is sufficient to cause SLE in almost all humans identifies a pivotal role for this molecule. The challenge is to identify the relevant physiological activity that can explain this strong association.
On the other hand, C1q seems to play a different role in old people. The concentration of C1q rises with aging and can be modulated by exercises. Of note, increased levels of C1q have been reported in the central nervous systemof old people, with the highest levels being seen in close proximity to synapses and central regions of the brainsuggesting that C1q may play a role in the development of problems associated with aging. Consistent with this hypothesis aged C1q-deficient mice showed less cognitive and memory decline in hippocampus-dependent behaviour tests compared to their wild-type litter mates.
In summary,the traditional view of the role of C1q as just initiator of the classical complement pathway needs revision. Evidence is emerging that C1q has roles outside the complement system and these will be discussed.
Disclosure of Interests: None declared
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SP0170 **IS COMPLEMENT A CRITICAL INGREDIENT IN THE DEVELOPMENT OF RA?**

V. Michael Holers. *University of Colorado Denver, Rheumatology, Aurora, CO, United States of America*

Background: Prior studies of patients with classified rheumatoid arthritis (RA) have demonstrated in synovial fluid, on cartilage surfaces and in the synovium the presence of pro-inflammatory complement activation fragments C3a and C5a, the membrane attack complex (MAC), and C3 fragment-bound immune complexes. Ex vivo studies of RA-related autoantibodies have shown the capacity to activate complement pathways, and also demonstrated the presence of disease-

associated changes in antibody glycosylation that promote engagement of the complement system. In contrast, clinical trials in patients with classified RA utilizing inhibitors of complement C5 have demonstrated minimal improvement. Nevertheless, recent translational research studies of patients during the natural history of RA have opened up new avenues for therapeutic intervention. Specifically, there exists in seropositive RA a prolonged asymptomatic preclinical stage wherein mucosal autoantibody production in the lung is associated with NETosis, elevated cytokines and evidence of activated innate immunity, with the capacity of each to interact and promote localized inflammation. Beyond this, murine studies have strongly suggested that complement C3d generation promotes autoimmunity and therapeutic pathway inhibitory strategies should encompass all of the effector mechanisms and not just those at C5 and beyond.
Objectives: The presentation objective is to explore the evidence for involvement of the complement system in the preclinical development of RA, and what mechanisms may be involved to promote autoimmunity and ultimate joint damage.
Methods: The presentation will review studies of the natural history of human RA, with an emphasis on the potential roles for complement in multiple stages of disease. In addition, the results of informative murine studies which have explored the mechanisms by which the complement system can modulate the development of experimental autoimmune arthritis will be summarized.
Results: Studies of preclinical RA in subjects have suggested the potential for complement and NETs to interact and promote localized mucosal inflammation in the lung. In addition, murine studies of the roles of complement have supported that all components of the pathway, including C3d linked to antigens, the anaphylatoxins C5a and C3a, as well as the MAC, are centrally involved in promoting arthritis.
Conclusion: Complement likely plays a role in multiple phases of RA development, including: 1) mucosal inflammation and the break in systemic tolerance to citrullinated antigens, 2) initial inflammation following targeting of ACPA to the synovium in early RA, and 3) regulation of RA-related autoantibody production. In addition, it is likely that inhibition of C3 and C5 convertases in tandem will be necessary to see major clinical effects in patients with active synovitis. Finally, the use of a complement inhibitor or modulator in the pre-clinical, transitioning and/or early RA populations are all intriguing approaches.

REFERENCE:

[1] Holers, V.M., et al. 2018. Rheumatoid arthritis and the mucosal origins hypothesis: protection turns to destruction. Nature Reviews Rheumatology 14:542-557. 2. Holers, V.M., and Banda, N.K. 2018. Complement in the initiation and evolution of rheumatoid arthritis. Front. Immunol. 9:1057.

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SP0171 **THE NEW COMPLEMENT THERAPEUTICS**

Claire Harris. *Newcastle University, School of Medicine, Newcastle-upon-Tyne, United Kingdom*

Despite a wealth of knowledge in the complexities of the complement cascade, and many decades of endeavour, very few drugs have progressed to the clinic. Recently, strong genetic associations of complement with common diseases have emerged and fuelled the fire of complement drug discovery leading to an explosion in complement therapies in development; while many of these agents and others before them have failed to progress, their legacy is key to future success. Obstacles to successful drug development include target concentration and turnover rates, and ability to target to the appropriate site. The drug development landscape is littered with agents that have failed at the preclinical or early clinical stage; their modes of action and modalities are wide-ranging. It is becoming increasingly clear that an understanding of disease mechanism and matching of drug modality and mode of action to the right disease and patient population (or stratified sub-population) is critical to success. A number of drugs are now in phase 3 clinical development for a number of different diseases. In this talk, innovative approaches that are emerging to overcome obstacles blocking success will be explored, highlighting drugs in development which employ new state-of-the-art strategies. These include 'homing' drugs and a new generation of orally bioavailable molecules.
Complement biomarkers that can decipher disease mechanism and be applied for patient stratification will be discussed. It is clear that a range of different drugs, or combination of drugs, will be needed for effective management of the many and diverse complement-mediated diseases.
Disclosure of Interests: None declared
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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Lights at both ends of the tunnel? Advances in GI Involvement in SSc

SP0172 **CASE 2 PRESENTER: ALWAYS AT THE EDGE: SEVERE GI COMPLICATIONS**

Kristina Clark. *University College London, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom*

The clinical impact of lower gastrointestinal tract involvement in systemic sclerosis will be illustrated through a case presentation. This will describe the challenges of managing patients with systemic sclerosis presenting with pseudo-obstruction, severe malnutrition, and electrolyte imbalance and how these were managed to optimise patient care.
Disclosure of Interests: None declared
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SP0173 **CASE 2 DISCUSSANT: IMMUNOSUPPRESSION OR ANTIBIOTICS – WHEN TO CHOOSE WHAT?**

Christopher Denton. *Royal Free Campus, x, x, United Kingdom*

Gastrointestinal tract involvement is almost universal in systemic sclerosis but in most patients is relatively mild with symptoms of gastro-oesophageal dysmotility and reflux or lower bowel symptoms of constipation. A minority of cases have severe involvement, and this can be life-threatening. The key issues related to severe disease are attacks of pseudo-obstruction with complications such as pneumatosis coli and perforation of infection. Additional issues include malnutrition and intestinal failure that may require long term home parenteral supplementation. Finally, the most severe lower tract involvement can result in intractable diarrhoea, persistent anorectal incompetence and complications of severe chronic constipation such as sigmoid volvulus. Management is challenging and requires interaction with gastroenterology and nutritional expert colleagues. Some newer approaches that have been beneficial include long term intravenous immunoglobulin therapy although in general response to immunosuppression are relatively modest. This discussion will focus on treatment with immunomodulation and use of antibiotic therapy to treat small intestinal bacterial overgrowth and also to manage other infective problems and the potential impact on intestinal dysbiosis.
Disclosure of Interests: Christopher Denton Grant/research support from: GlaxoSmithKline, Inventiva, CSF Behring, Consultant for: Roche-Genentech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Bayer
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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Novel autoantibodies in RMD: a neverending quest?

SP0174 **ADVANCES IN THE DETECTION OF PATHOGENIC AUTOANTIBODIES IN SLE**

Luis Munoz. *Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Internal Medicine 3, Erlangen, Germany*

Background: The accumulation of late apoptotic or so-called Secondary NEcrotic Cells (SNEC) in germinal centers challenges B and T cell tolerance and leads to the development of autoimmunity and the production of autoantibodies.
Objectives: Determine the test performance of immobilized SNEC autoantigens for the diagnosis of Systemic Lupus Erythematosus.
Methods: SNEC ELISA of sera from patients with SLE and test performance statistics were deployed to evaluate the diagnostic potential SNEC-derived autoantigens. Functional assays confirmed its pathophysiological relevance.
Results: SNEC contains nuclear autoantigens bearing apoptosis-associated modifications such as histone H3 K27me3, histone H2A/H4AcK8,12,16, and histone H2B-AcK12. The SNEC ELISA clearly discriminated patients with SLE from patients with Rheumatoid Arthritis (RA), Primary Anti-Phospholipid Syndrome (PAPS), Spondyloarthropathy (SpA), Psoriatic Arthritis (PsA), and Systemic Sclerosis (SSc). A positive test result in SNEC ELISA significantly correlated with

serological variables and reflected the uptake of opsonized SNEC by neutrophils in the blood.
Conclusion: SNEC ELISA allows for the sensitive detection of pathologically relevant autoantibodies in the serum of patients with SLE. The clearance of nuclear remnants by neutrophils enhances inflammatory responses supporting the role of clearance deficiency in the etiopathogenesis of SLE.

REFERENCE:

[1] Biermann MHC, Boeltz S, Pieterse E, Knopf J, Rech J, Bilyy R, van der Vlag J, Tincani A, Distler JHW, Krönke G, Schett GA, Herrmann M and Muñoz LE (2018) Autoantibodies Recognizing Secondary NEcrotic Cells Promote Neutrophilic Phagocytosis and Identify Patients With Systemic Lupus Erythematosus. Front. Immunol. 9:989. doi: 10.3389/fimmu.2018.00989

Disclosure of Interests: None declared
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SP0175 POST-TRANSLATIONAL MODIFICATIONS OF ANTIBODIES: WHERE THERE'S SMOKE THERE'S FIRE

Rene Toes. *Leiden University Medical Center, Rheumatology, Leiden, Netherlands*

Rheumatoid arthritis (RA) is a prototype autoimmune disease, with the hallmark signs of synovial inflammation and the presence of autoantibodies. One of the most prominent examples of such autoantibodies are anti-citrullinated protein antibodies (ACPA), which are directed against a wide-array of citrullinated proteins. The immune response to citrullinated antigens is a dynamic response that expands before the onset of disease and generates antibodies that are extensively glycosylated in the variable domain. This feature of ACPAs is remarkable and might be involved in the breach of tolerance to citrullinated proteins as well as function as an additional biomarker to predict disease onset in subjects at risk.
Next to ACPA, it has become clear that the autoantibody response in RA extends towards several other modified proteins, such as proteins modified by carbamylation or acetylation. Carbamylation leads to the formation of homocitrulline. Structurally, homocitrulline greatly resembles citrulline but is one methylene group longer. In contrast, acetylation is mediated by intracellular acetyltransferases and is structurally less related to citrulline or homo-citrulline. Although the presence of autoantibodies against these post-translationally modified proteins (Anti-Modified Protein Antibodies; AMPA) hallmark RA, at present, there is no conceptual framework explaining the concordant presence of different AMPA-responses in RA. In the context of this presentation, the latest insights into the development of humoral response against citrullinated-, carbamylated and acetylated proteins in relation to their role as biomarkers to predict the development of RA will be discussed.
Disclosure of Interests: Rene Toes Grant/research support from: Sanofi
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SP0176 PATHOGENIC ANTIBODIES IN PHOSPHOLIPID SYNDROM

Sasa Cucnik. *University Medical Center Ljubljana, Department of Rheumatology, Immunology Laboratory, Ljubljana, Slovenia*

Antiphospholipid syndrome (APS) is prothrombotic systemic autoimmune disorder characterized with multisystem manifestation, most commonly venous and arterial thromboembolism and/or recurrent pregnancy loss. The varying clinical phenotype is associated with heterogeneity in the pathogenic antiphospholipid antibodies (aPL) that are central to the diagnosis of APS. According to the international consensus statement on classification criteria, APS is classified when persistently elevated levels of specific aPL, such as lupus anticoagulant (LA), anticardiolipin (aCL) and anti-β2 glycoprotein I (anti-β2GPI) antibodies, are confirmed in addition to clinical manifestations (1, 2). The exact pathogenesis of APS is unknown, but aPL have been described to activate monocytes, neutrophils, dendritic cells and placental tissue (3). Despite the fact that many different proteins have been identified as being involved in the pathogenesis of APS, accumulating evidence from in vitro experiments as well as animal studies has revealed that β2GPI is the main target for aPL. It was also shown that triple aPL positivity, defined by detection LA, high titres of aCL and anti-β2GPI antibodies, correlates better with both thrombosis and pregnancy morbidity than any other aPL profile (4).
Several autoantibodies outside those included in APS classification criteria could be also relevant to APS pathogenesis (5) and therefore, antibodies against other antigen targets have been investigated. Current evidence shows that some of these antibodies, particularly antibodies against domain I of β2GPI (anti-DI-β2GPI) and phosphatidylserine dependent anti-prothrombin antibodies (aPS/PT) might be relevant in the better recognition of APS patients. These antibodies are commonly referred as non-criteria aPL (6) because they have not been yet accepted as laboratory criterion for the diagnosis of APS. The DI of β2GPI has been identified as the most relevant antigenic target involved in β2GPI/anti-β2GPI antibody binding. Anti-DI-β2GPI antibodies were found to be strongly related to thrombosis and pregnancy complication and are more frequently detected in patients with APS than in asymptomatic aPL carriers (7). High titres of anti-DI-β2GPI are also frequently present in triple aPL positive patients. Nevertheless, it is far too soon to recommend replacement of anti-β2GPI testing with an anti-DI-β2GPI antibody assay because it was shown that about 30% of patients with anti-β2GPI antibodies are negative for anti-DI-β2GPI antibodies (8). The clinical significance of autoantibodies reacting with epitopes other than DI was also investigated in multicenter study (9). The results showed a diverse clinical association with reactivity to different epitopes on β2GPI, suggesting all domains were relevant. Therefore, more detailed profiling of domain specificity and avidity of anti-β2GPI antibodies may be useful as risk stratification for clinical events.
aPS/PT antibodies also represent strong risk factor for thrombosis. Results of multicenter study demonstrated that IgG aPS/PT detection might contribute to a better and more reliable identification of APS patients (10).
Due to the heterogeneity of aPL (criteria and non-criteria) the interpretation of aPL results is huge challenge in daily routine practice and should always be related to clinical symptoms and therefore, interaction between the laboratory and clinician is essential.

REFERENCES:

[1] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4(2):295-306.
[2] Wilson WA, Gharavi AE, Koike T, Lockshin MD, Branch DW, Piette JC, et al. International consensus statement on preliminary classification criteria for definite antiphospholipid syndrome: report of an international workshop. Arthritis Rheum. 1999;42(7):1309-11.
[3] Yin D, de Laat B, Devreese KM, Kelchtermans. The clinical value of assays detecting antibodies against domain I of β2-glycoprotein I in the antiphospholipid syndrome. Autoimmunity Reviews 2018;17:1210-1218.
[4] Pengo V, Ruffatti A, Legnani C, Gresele P, Barcellona D, Erba N, Testa S, Marongiu F, Bison E, Denas G, Banzato A, Padayattil JS, Iliceto S. Clinical course of high-riskmpatients diagnosed with antiphospholipid syndrome. J Thromb Haemost 2010;8:237–242.
[5] Sciascia S, Amigo MC, Roccatello D, Khamashta M. Diagnosing antiphospholipid syndrome: 'extra-criteria' manifestations and technical advances. Natural reviews 2017;13:548-560.
[6] Amengual O, Atsumi T. Antiphospholipid syndrome: "the best prophet of the future". Modern Rheumatology 2018; 409-416.
[7] Chighizola CB, Gerosa M, Meroni PL. New Tests to Detect Antiphospholipid Antibodies: Anti-Domain I Beta-2-Glycoprotein-I Antibodies. Curr Rheumatol Rep 2014;16:402-410.
[8] Pengo V, Ruffatti A, Tonello M, Cuffaro S, Banzato A, Bison E, Denas G, Padayattil JS. Antiphospholipid syndrome: antibodies to Domain 1 of beta2-glycoprotein 1 correctly classify patients at risk. J Thromb Haemos 2015;13:782–787.
[9] . Artenjak A, Locatelli I, Brelih H, Simonic DM, Ulcova-Gallova Z, Swadzba J, et al. Immunoreactivity and avidity of IgG anti-beta2-glycoprotein I antibodies from patients with autoimmune diseases to different peptide clusters of beta2-glycoprotein I. Immunologic Research 2015;61:35–44.
[10] Amengual O, Forastiero R, Sugiura-Ogasawara M, Otomo K, Oku K, Favas C, et al. Evaluation of phosphatidylserine-dependent antiprothrombin antibody testing for the diagnosis of antiphospholipid syndrome: results of an international multicentre study. Lupus 2017;26:266-76.

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Lessons learned from checkpoint inhibitors

SP0177 IMPACT OF CHECKPOINT INHIBITORS ON B CELLS

David Pisetsky. *Duke University Medical Center, Medicine/Immunology, Durham, North Carolina, United States of America*

Immune checkpoint inhibitors (ICI) are a new class of biological agents that has revolutionized the treatment of cancer. Unlike conventional cytotoxic agents that

are designed to kill cells, ICI block interactions that regulate the T cell response to cancer. At present, two classes of ICI are available to treat a wide variety of malignancies: antibodies to cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and antibodies directed to the programmed death-1 (PD-1) and PD-1 ligand (PD-L1) axis, either to PD-1 or PD-L1. While both anti-CTLA-4 and antibodies to PD-1/PD-L1 are effective, these systems differ in the T cell populations affected, the location of these cells and the downstream signaling pathways involved. ICI can be used alone or in combination. Despite differences in mechanism of action, treatment with both types of ICI is associated with severe side effects that have been termed immune-related adverse reactions (irAE). irAE include, among other manifestations, dermatitis, colitis, pneumonitis, endocrinopathy (hypothyroidism, hypophysitis, adrenal insufficiency) and arthritis and related conditions. Because of the goal of ICI therapy is the induction or stimulation of cytotoxic T cells, the effect of these agents on B cells has received much less attention. In general, effects of ICI on tumors are considered the action of T cells. irAE, however, may result from B cell effects and the induction of autoantibodies. Thus, autoantibodies to thyroid antigens may lead to thyroiditis and subsequent hypothyroidism. Similarly, ICI can lead to the production of antibodies to islet antigens as well as glutamic acid decarboxylase 65 and induction of diabetes. On the other hand, while arthritis can be an irAE, affected patients usually do not show antibodies to citrullinated proteins (ACPA). Importantly, functional and phenotypic properties of B cells following ICI may help predict the emergence of irAE. Much of the data on this issue comes from a detailed analysis of patients with melanoma treated with anti-CTLA-4, anti-PD-1 or the combination. With this combination, B cells of treated patients showed characteristic changes that include a decrease in the number of circulating B cells in conjunction with an increase in plasmablasts and a population of B cells characterized by low expression of CD21. Furthermore, in treated patients, the $CD21^{lo}$ B cells population showed greater clonality as well as a higher frequency of clones in comparison to the $CD21^{hi}$ population. These changes, which may resemble those seen in patients haploinsufficent for CTLA-4, may predict the development of irAE. The $CD21^{lo}$ B cell population may have a particular role in the development of irAE since these cells appear to be recent emigrants from germinal centers and may undergo rapid activation. The effects of ICI on B cell populations is also relevant for ICI use in the setting of pre-existent inflammatory or autoimmune disease marked by autoantibody production. While ICI, either alone or in combination, can lead to the exacerbation of these conditions, the effect on autoantibody production has not yet been well studied. These exacerbations, however, can respond to agents such as glucocorticoids or TNF blockers whose B cell effects are not clear. Since B cells can express PD-1 as well as PD-L1, the effects of ICI may direct actions or the indirect effects on other cell populations. Future studies are needed to delineate more precisely the contribution of B cells to the response of cancer to ICI as well as the development of irAE.

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Orthotic treatment: is it in or out?

SP0178 **LOWER LIMB ORTHOSES**

Martin van der Esch. *Amsterdam Rehabilitation Research Center | Reade, Rehabilitation, Amsterdam, Netherlands*

Background: Osteoarthritis (OA) is the most common rheumatic disease of the musculoskeletal system, with the knee as the most affected joint. The number of people with OA of the knee is likely to increase due to the ageing society and the obesity epidemic. The predominant clinical symptom of knee OA is pain, which is described as worsening by activity and relieving by rest. Knee instability has been recognized as an important clinical feature in persons with knee OA. Pain and knee instability are associated with limitations in performing daily activities. Non-pharmacological options in the management of knee OA consist of education, weight loss, exercise, braces and physical therapy. Knee bracing has been recommended by the Osteoarthritis Research Society International (OARSI). Valgus knee braces designed to decrease loads on the medial compartment of the knee for patients with varus alignment are the most common. It has been shown however, that valgus bracing may have little or no effect on pain and physical functioning, and adherence to this treatment in patients with knee OA is low.
Because of ease of use and access, lack of complications and low cost, soft knee braces are commonly used in persons with knee OA. However, the evidence for efficacy of soft knee bracing on pain and activity limitations in knee OA is limited. Therefore, it is important to strengthen the evidence of using a soft brace to reduce pain and activity limitations as well as to evaluate the efficacy of soft knee bracing on knee instability in persons with knee OA. There is also debate about the effectiveness of soft braces in other affected joints of the lower extremity and in conditions other than OA such as rheumatoid arthritis.
Objectives: The aim of the study will be to evaluate the effect of wearing a soft brace on dynamic knee instability in patients with OA of the knee.
Methods: Persons with knee OA and self-reported knee instability from the Amsterdam Osteoarthritis cohort participated in a single-session lab-experimental study. A within-subject design was used, comparing no brace versus brace, and comparing a non-tight versus a tight brace (standard fit). The primary outcome measure was dynamic knee instability, expressed by the Perturbation Response (PR), i.e., a biomechanics based measure reflecting deviation in the mean knee varus-valgus angle after a controlled mechanical perturbation, standardized to the mean (SD) varus-valgus angle during level walking. Linear mixed-effect model analysis was used to evaluate the effect of a brace on dynamic knee instability.
Results: The wearing of a soft brace reduced the knee instability significantly during perturbed walking. Results will also be presented from the literature search and from the lab-experimental study.
Conclusion: Wearing a soft brace reduces dynamic knee instability in patients with knee OA. However, longitudinal studies are needed to evaluate the clinical implications of wearing a soft brace.

REFERENCE:

[1] Cudejko T, van der Esch M, Schrijvers J, Richards R, van den Noort JC, Wrigley T, van der Leeden M, Roorda LD, Lems W, Harlaar J, Dekker J. The immediate effect of a soft knee brace on dynamic knee instability in persons with knee osteoarthritis. Rheumatology (Oxford). 2018 Oct 1;57 (10):1735-1742.

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SP0179 **ORTHOSES AND ASSISTIVE DEVICES FOR THE HAND**

Nina Osteras. *Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway*

This presentation will summarize the scientific evidence for the effects of orthoses and assistive devices for the hand. The main focus will be on hand osteoarthritis. The presentation will shed light on how orthoses and assistive devices may facilitate participation.

Disclosure of Interests: None declared
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SP0180 **FOOT ORTHOSES IN RA**

Jim Woodburn. *Glasgow Caledonian University, School of Health and Life Sciences, Glasgow, United Kingdom*

In this presentation I will: (1) Provide a general overview of the indications and use of foot orthoses in rheumatoid arthritis (RA) [1], (2) Explore mechanisms of action with respect to preserving, maintaining and restoring foot biomechanics [2], (3) Summarise current evidence on the use of foot orthoses for managing foot pain, disability, deformity and quality of life by drawing on recently published systematic reviews and meta-analyses[3]. Further I will direct delegates to national, European and International evidence-based clinical guidelines where they exist[1,4], and (4) Introduce new technology advances with regards to materials and digital design and manufacturing concepts[2].
I will conclude the presentation by setting out future directions and priorities for both clinical practice and research and innovation.

REFERENCES:

[1] Hennessy K, Woodburn J, Steultjens M. Clinical practice guidelines for the foot and ankle in rheumatoid arthritis: a critical appraisal. J Foot Ankle Res. 2016 Aug 19;9:31.
[2] Gibson KS, Woodburn J, Porter D, Telfer S. Functionally optimized orthoses for early rheumatoid arthritis foot disease: a study of mechanisms and patient experience. Arthritis Care Res (Hoboken). 2014 Oct;66(10):1456-64.
[3] Hennessy K, Woodburn J, Steultjens MP. Custom foot orthoses for rheumatoid arthritis: A systematic review. Arthritis Care Res (Hoboken). 2012 Mar;64(3):311-20.
[4] Chapman LS, Redmond AC, Landorf KB, Rome K, Keenan AM, Waxman R, Alcacer-Pitarch B, Siddle HJ, Backhouse MR. Foot orthoses for people with rheumatoid arthritis: a survey of prescription habits among podiatrists. J Foot Ankle Res. 2019 Jan 25;12:7.

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Current treatment of vasculitis

SP0181 **TREATMENT OF GCA**

John H. Stone. *USA*

The treatment of giant cell arteritis (GCA) has taken a dramatic leap forward over the past 18 months, with the start of the era of interleukin-6 inhibition for the treatment of this disease. For the first time in 70 years, rheumatologists now have a highly-effective alternative to continuous therapy with doses of glucocorticoids that are often unacceptably high, leading inevitably to steroid-related toxicity. Clinicians now have many questions about the optimal approach to treatment in this new era: When should IL-6 inhibition begin? How quickly should glucocorticoids be tapered? Should prednisone be stopped completely? Can tocilizumab ever be discontinued? How does one monitor for the possibility of disease flare? This session will address all of these questions using a data-driven approach, with reference to new data from the GiACTA trial

Disclosure of Interests: John H. Stone Grant/research support from: F. Hoffmann-La Roche, Genentech, Xencor, Consultant for: Chugain, F. Hoffmann-La Roche, Genentech, Xencor
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SP0182 **TREATMENT OF AAV**

David Jayne. *University of Cambridge, Department of Medicine, Cambridge, United Kingdom*

Background: ANCA associated vasculitis is an autoimmune disease classified by clinical phenotype and serology. A genetic predisposition has been determined which differs between PR3-ANCA and MPO-ANCA patients. Experimental models have confirmed the pathogenicity of ANCA for certain aspects of pathology and have defined a role for alternative complement pathway activation but have failed to explain granuloma formation or gain insights into the origin of breakdown of tolerance. Therapy has emerged empirically to include the combination of high dose glucocorticoids and immunosuppression with B cell depletion, Rituximab, emerging as an alternative immunomodulator over the last 20 years. Studies have evaluated the role of Rituximab in induction, in refractory and relapsing disease and in the prevention of relapse and have explored the role of b biomarkers in monitoring therapy. AAV patients continue to suffer poor outcomes especially if renal, cardiac or gastrointestinal features are present at diagnosis. Adverse event rates remain high and the majority of patients pursue a relapsing course. Inhibition of the alternative complement component C5a is emerging as a new therapeutic opportunity.
Objectives: To define the outcomes and predictors for adverse outcomes in AAV. To review recent clinical trial data in the context of established guideline statements and to discuss the treatment of more complex clinical scenarios.
Methods: A description of current approaches to classification and subgrouping by severity. Review of recent clinical trial data and guidelines and application of learned knowledge to clinical scenarios.
Conclusion: AAV remains a disease with poor outcomes. There is a need for further understanding of the barriers to early diagnosis and access to specialist care. Treatment decisions are now well supported by evidence from clinical trials. Rituximab has had a major influence on current management strategies and is leading to improved outcomes and reduced glucocorticoid exposure. Complement inhibition is a potential new therapy for AAV.

REFERENCES:

[1] Jayne DR, Rasmussen N, Andrassy K, Bacon P, Tervaert JW, Dadoniene J, Ekstrand A, Gaskin G, Gregorini G, de Groot K, Gross W, Hagen EC, Mirapeix E, Pettersson E, Siegert C, Sinico A, Tesar V, Westman K, Pusey C. A randomized trial of maintenance therapy for vasculitis associated with antineutrophil cytoplasmic autoantibodies. N Engl J Med. 2003;349:36-44.
[2] De Groot K, Rasmussen N, Bacon PA, Tervaert JW, Feighery C, Gregorini G, Gross WL, Luqmani R, Jayne DR (senior author). Randomized trial of cyclophosphamide versus methotrexate for induction of remission in early systemic antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Rheum. 2005;52:2461-2469.
[3] Jayne DR, Gaskin G, Rasmussen N, Abramowicz D, Ferrario F, Guillevin L, Mirapeix E, Savage CO, Sinico RA, Stegeman CA, Westman KW, van der Woude FJ, de Lind van Wijngaarden RA, Pusey CD. Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. J Am Soc Nephrol. 2007;18:2180-2188.
[4] de Groot K, Harper L, Jayne DR, Flores Suarez LF, Gregorini G, Gross WL, Luqmani R, Pusey CD, Rasmussen N, Sinico RA, Tesar V, Vanhille P, Westman K, Savage CO. Pulse versus daily oral cyclophosphamide for induction of remission in antineutrophil cytoplasmic antibody-associated vasculitis: a randomized trial. Ann Intern Med. 2009;150:670-680.
[5] Hiemstra TF, Walsh M, Mahr A, Savage CO, de Groot K, Harper L, Hauser T, Neumann I, Tesar V, Wissing KM, Pagnoux C, Schmitt W, Jayne DR. Mycophenolate Mofetil vs Azathioprine for Remission Maintenance in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: A Randomized Controlled Trial. JAMA. 2010;304:2381-8.
[6] Jones RB, Cohen Tervaert JW, Hauser T, Luqmani R, Morgan MD, Peh CA, Savage CO, Segelmark M, Tesar V, van Paassen P, Walsh D, Walsh M, Westman K, Jayne DR (senior author). Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. N Engl J Med. 2010;363:211-220.
[7] Jones RB, Furuta S, Cohen Tervaert JW, Hauser T, Luqmani R, Morgan MD, Peh CA, Savage CO, Segelmark M, Tesar V, Jayne DR. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis: 2-year results of a randomised trial. Ann Rheum Dis. 2015;74(6):1178-82
[8] Yates M, Watts RA, Bajema IM, Cid MC, Crestani B, Hauser T, Hellmich B, Holle JU, Laudien M, Little MA, Luqmani RA, Mahr A, Merkel PA, Mills J, Mooney J, Segelmark M, Tesar V, Westman K, Vaglio A, Yalçindağ N, Jayne DR, Mukhtyar C. EULAR/ERA-EDTA recommendations for the management of ANCA associated vasculitis. Ann Rheum Dis. 2016 Sep;75 (9):1583-94.
[9] Hiemstra TF, Walsh M, Mahr A, Savage CO, de Groot K, Harper L, Hauser T, Neumann I, Tesar V, Wissing KM, Pagnoux C, Schmitt W, Jayne DR; European Vasculitis Study Group (EUVAS). Mycophenolate mofetil vs azathioprine for remission maintenance in antineutrophil ectoplasmic antibody associated vasculitis. JAMA. 2010 Dec 1;304(21):2381-8.

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SP0183 **DIAGNOSIS AND TREATMENT OF HCV RELATED VASCULITIS**

Peter Lamprecht. *University of Lubeck, Department of Rheumatology and Clinical Immunology, Lubeck, Germany*

Chronic hepatitis C virus (HCV) infection is the most common cause of cryoglobulinemic vasculitis. In contrast, non-cryoglobulinemic vasculitis is rare in chronic HCV infection. Cryoglobulinemic vasculitis is a systemic immune complex-mediated vasculitis predominantly affecting small vessels and associated with the presence of serum cryoglobulins, i.e. cold-precipitable immunoglobulins. HCV is a hepato- and lymphotropic virus. Notably, secondary transition from benign lymphoproliferative disease to malignant non-Hodgkin lymphoma (NHL) as well as primary co-manifestation of cryoglobulinemic vasculitis and NHL has been reported in chronic hepatitis C. While cryoglobulinemia is detected in 50% or more of the patients with chronic hepatitis C, less than 5% develop related vasculitis. In this disorder, HCV induces clonal proliferation of memory phenotype marginal zone-like B-lymphocytes with restricted Ig heavy chain variable (V_H) 1-69 gene expression encoding for the IgM rheumatoid factor (RF) WA idiotype. Monoclonal IgM RF binding to the Fc region of polyclonal IgG with anti-HCV reactivity facilitate the formation of cryoprecipitable multi-molecular immune-complexes. Cryoglobulins are preferentially deposited in tissues with high blood flow per unit mass of tissues, *e.g.* skin, synovium, choroid plexus and glomerulus, where they bind to endothelial cells via the C1q receptor.
Endothelial cryoglobulin deposition induces the activation and recruitment of circulating neutrophil granulocytes and other immune cells to the endothelial lesion eventually resulting in complement-consuming vasculitis.
The histopathologic changes in HCV-related vasculitis range from cutaneous leukocytoclastic vasculitis to severe necrotizing arteritis. Type I membranoproliferative glomerulonephritis is frequently found in patients with renal involvement. Clinical features of HCV-associated vasculitis comprise purpura, Meltzer`s triad (purpura, arthralgia, asthenia), polyneuropathy, renal involvement and Raynaud`s

phenomenon. Hemorrhagic alveolitis, interstitial lung disease, gastrointestinal vasculitis, cardiac involvement, osteosclerosis and hyperviscosity syndrome are less common manifestations. Diagnostic criteria have been developed for HCV-associated cryoglobulinemic vasculitis.

International therapeutic guidelines recommend treatment of HCV-related vasculitis to be guided according to the severity of disease. In patients with mild to moderate disease, interferon-free therapy regimens with direct acting antivirals (DAA) are considered as first-line treatment. In patients with severe manifestations, rituximab is given for the control of vasculitic manifestations, followed by HCV eradication using DAA. High rates of clinical responses and sustained virologic responses (SVR) have been reported for DAA treatment in HCV-associated cryoglobulinemic vasculitis. However, relapse of cryoglobulinemic vasculitis may occur in patients despite earlier treatment-induced clinical response and SVR. Persistence of clonal B-lymphocyte proliferation and perseverance of perturbations of the immune homeostasis have been shown in HCV-cured patients with relapse of cryoglobulinemic vasculitis.

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Workshop: #ConnectToday and tomorrow: the campaigning continues

SP0184 **DON'T DELAY, CONNECT TODAY IN FINLAND: A VIDEO TO PROMOTE EARLY DIAGNOSIS**

Maria Ekroth. *Institute of Anatomy, Paracelsus Medical University, Imaging and Functional Musculoskeletal Research, Salzburg, Austria*

Positive Encounter - Don't Delay Connect Today

Background: Too often people suffer the symptoms of rheumatoid arthritis for too long before they visit a doctor.

The positive encounter between physician and patient can lead to a good relationship, follow-up care and positive health outcomes. We conducted a survey about the need for a treatment plan and found that less than 30% of patients know their treatment plan and patients who do know their plan are better committed and more satisfied with their physicians. 72% of survey respondents who know their treatment plan are happy with their treatment as whole. Of the remainder, only 33% are satisfied.

Objectives:

1. The aim of this campaign is to illustrate and inform people of the symptoms of rheumatoid arthritis and encourage them to visit a doctor, enabling the doctor to assist the patient.
2. To give advice to patients on how to prepare for a doctor's appointment.
3. The campaign also includes a section directed at rheumatologists and rheumatology nurses, that advises on the importance of the encounter and the creation of the treatment plan.
4. To increase awareness about our association, and to recruit new members

Methods: Video for patients and the wider public. Video for rheumatologists and rheumatism professionals. Mailing of brochures on the importance of the treatment plan to all Finnish rheumatologists and arthritis treatment units. We also thanked doctors and attached a fruit gift card.

We sent flyers and posters to our member associations. Members have handed out materials directed at patients locally. They have distributed them to libraries, municipalities, sports centres… and given away fliers at the events.

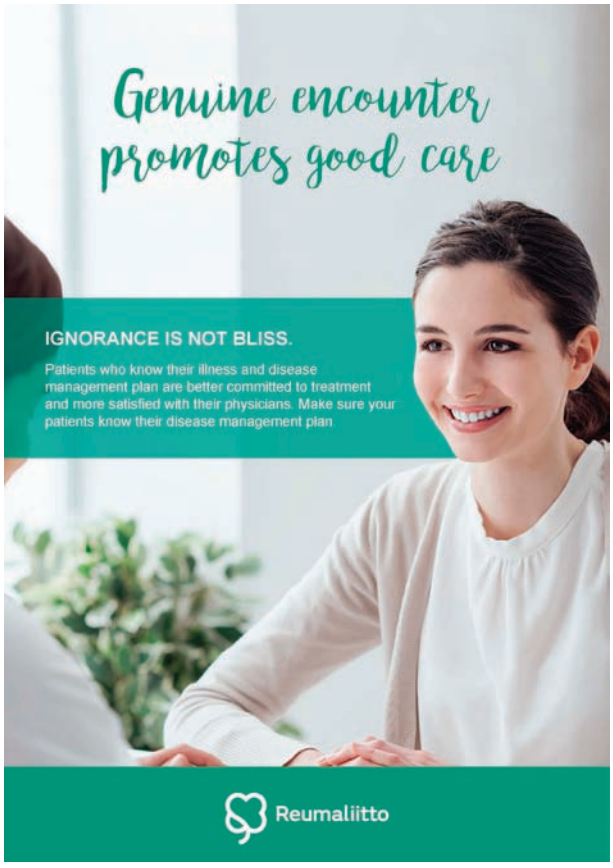
Results: Patients have reported being better prepared for the visits and having written down important questions in advance. We achieved attention value amongst professionals and were invited to design a national treatment path with rheumatism professionals for children with JIA. All the main hospitals are involved and will start to use it. Free TV air time was offered for the patient video on the national main TV channel.

The Finnish Society for Rheumatology offered us the possibility of promoting our campaign at the Scandinavian Congress of Rheumatology.

Conclusion: The campaign was successful.

REFERENCES:

[1] www.youtube.com/watch?v=Y2_z8cxDvaA
[2] https://www.youtube.com/watch?v=vkDf7C-VPoY
[3] https://www.reumaliitto.fi/fi/reumaliitto/uutiset/reumaliiton-tilaisuus-eduskunnassa-viestit-vaaleihin-2019
[4] https://www.reumaliitto.fi/fi/hoidonlaatu





Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8467

SP0185 **DON'T DELAY, CONNECT TODAY IN TWELVE VIDEO'S: HOW TO GET EARLY DIAGNOSIS OF RMD'S ON THE TABLE IN POLAND**

Jolanta Grygielska. *Polish Rheuma Federation 'REF', National Board, Warsaw, Poland*

Background: Early diagnosis and appropriate treatment is a mile stone in future progress of rheumatic and musculoskeletal disease (RMD), especially inflammatory. We know from our experiences that delays of diagnosis are connected with knowledge and attitude of patient, of primary care physician (fast referral to rheumatologist) and with access to rheumatologist. New EULAR campaign "Don't delay, connect today" gives an opportunity to pay attention to the problem of RMDs, increase public awareness and remind persons about responsibility for their own health.
Objectives: Aim of our project was to increase public awareness about RMDs and self-awareness of patients, to present how important is a role of everybody being face to face with progressing disease. It was most important to reach to younger people believing that rheumatic diseases are typical only for older people. Lack of knowledge about RMDs and faith in myths are a first step to loose a time from first symptoms of diseases to appropriate diagnosis. The first step was translation of EULAR campaign slogan into Polish and preparing of Polish version of logo. It was done very fast after launching EULAR campaign.
Methods: We have many ideas which subject are more important for people around diagnosis. We decided to start with choice of subjects and connecting them with the first letter of Polish names of months. We tried to order them in logical process: from self-awareness to the sin of neglect though subject like for example medicine, physician, medication, choice, love, return. After decision about subjects we invited speakers for every subject. There were rheumatologists from National Institute of Geriatrics, Rheumatology and Rehabilitation in Warsaw and from other rheumatological clinics in Poland, mainly co-operating with our member associations. Every invited speaker received only a subject and main message to present in his/her film. Form, place and comments were suggested by speaker and discussed with a team preparing videos. Part of films were supported with our regional member associations. Forms of videos prepared in regions were decided by associations. In two films members of associations present their opinions and experiences to give a strength for new rheumatic persons to live with RMD and avoid unnecessary health situations. One video was enriched by physical exercises presented by students of physiotherapy under supervise of rheumatologist. All videos were filmed and prepared by our member, translation was done by another our member - both are professionals on their fields and with experiences of living with RMD. It gives added value to our campaign. After that videos were posted on our channel on YouTube and information about them was shared by our websites, facebook and Twitter. We sent information by e-mail to our colleagues and supporters. We invite every viewer to subscribe our channel to have easy access to our newest films.
Results: "Video for every month" is a series but every video can be used separately. Order of videos watching can be optional according to the viewer's choice. At the same time when videos were posted one by one, project on early diagnosis of rheumatoid arthritis supported by European founds and with our partnership start in Poland. Thanks to this our message "Don't delay, connect today" is stronger. Parallel our new project "RA - don't resign" starts from World Arthritis Day 2018. All actions give an occasion to focus on early diagnosis and appropriate treatment of RMDs.
Conclusion: Every aim can be achieve in co-operation and engagement of main players. We involve in our project members of regional associations, rheumatologists, students. During realization of other projects we used every occasion to share information about our videos. All subjects of videos are overtime. Every patient with RMD can receive new knowledge about her/his disease from reliable source everywhere and at every time in two languages versions Polish (voice) and English (subtitles). We are planning to use this form of information in next project.
Disclosure of Interests: None declared
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SP0186 **WHAT DO GP'S KNOW ABOUT RMD'S? #CONNECTTODAY IN MALTA**

Mary Vella. *Arthritis and Rheumatism Association Malta (ARAM), NGO, Mgarr, Malta*

Background: The Arthritis and Rheumatism Association Malta known as ARAM has been established these last eleven years since 2007. Through this experience as a support group working very closely with RMDs patients through various talks and seminars, and participating on Live Radio and Television to bring awareness on RMDs, ARAM became aware that there is Lack of Knowledge on the subject by the GPs and this needed to be addressed. Patients were being given the idea that once one develops arthritis there was nothing that can be done to embrace an independent and good quality of life. Obviously, with so much research and studies, this is not so!
I can confirm this myself being a patient who developed Rheumatoid Arthritis sixteen years ago. It was then that ARAM was established and being the President of the Association I advocated strongly for RMD Patients throughout the island. I believed that education and Knowledge on Arthritis should be a basic step both for the Patients as well as for the GPS and the General Public.
Objectives: When Eular announced the award for national campaign Don't delay Connect today' for early signs and symptoms and early referral, ARAM applied for the award in collaboration with the College of Family Doctors to educate the GPs on arthritis. This was possible after a number of meetings and discussion.
Methods: ARAM approached the Synapse which is an E-platform led by a medical doctor for Health Professionals based on sharing academic research and other articles to people that matter. With such a professional body ARAM produced four videos by Rheumatologist specialist on RMDs focusing on different aspects of these chronic conditions.

1. General Rheumatology Introduction –Dr Michaela Frendo
2. Juvenile Arthritis – Dr Cecilia Mercieca
3. Scleroderma– Dr Bernard Coleiro
4. Fibromyalgia– Prof Andrew Borg

Another two educational Talks for GPs led by Prof Andrew Borg, Head of Rheumatology Department of Mater Dei Hospital were held in a specific venue and were well attended. Topics delivered focused on:

1. Management of Inflammatory Joints
2. Management of Metabolic Bone diseases

Conclusion: To this effect, ARAM believes that GPs are now better informed and educated and more aware of possible early interventions that could mitigate the seriousness on the condition.
The general outcome of these talks include:

1. GPs became more educated and informed which will translate into
2. Better outcomes for the patients.

Results: Evaluation was carried out following both interventions by asking GPs for their feedback on both the Synapse e-platform and the two seminars.
Conclusion: To this effect, ARAM believes that GPs are now better informed and educated and more aware of possible early interventions that could mitigate the seriousness on the condition.
Disclosure of Interests: None declared
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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Tackling inflammatory bone disorders in children and adults

SP0187 **PATHOPHYSIOLOGY AND THERAPEUTIC CONSEQUENCES AUTO-INFLAMMATORY BONE DISORDERS**

Christian Hedrich. *Institute of Translational Medicine, University of Liverpool, Department of Women's and Children's Health, Liverpool, United Kingdom*

Chronic nonbacterial osteomyelitis (CNO) is an autoinflammatory bone disorder, covering a clinical spectrum with asymptomatic inflammation of single bones at the one end, and chronic recurrent multifocal osteomyelitis (CRMO) at the other end. Bone inflammation, however, can also be a symptom of other autoimmune/inflammatory conditions. Rare monogenic autoinflammatory diseases with bone involvement have informed research and provide models for the more common and pathophysiologically complex disorder CNO/CRMO.
Despite recent efforts, the exact molecular pathophysiology of CNO remains incompletely understood. Profound dysregulation of cytokine responses was demonstrated in CNO/CRMO. Failure to produce antiinflammatory cytokines interleukin (IL)-10 and IL-19 contributes to activation of inflammasomes and subsequent IL-1β release. In IL-10-deficient and in CNO-prone chronic multifocal osteomyelitis mice, IL-1β was linked to bone inflammation. Recently, increased inflammasome component expression and inflammasome assembly have been linked with CNO/CRMO in humans. Furthermore, alterations to the gut microbiome were suggested in contributing to IL-1β release from innate immune cells in mice, offering an interesting target in the search for molecular mechanisms in CNO.
This presentation will review molecular alterations in autoinflammatory bone disease, focussing on CNO and discuss therapeutic consequences.

REFERENCES:

[1] Brandt D, Sohr E, et al. CD14+ monocytes contribute to inflammation in chronic nonbacterial osteomyelitis (CNO) through increased NLRP3 inflammasome expression. Clin Immunol. 2018 Nov;196:77-84.

[2] Hofmann SR, Schnabel A, *et al*. Chronic Nonbacterial Osteomyelitis: Pathophysiological Concepts and Current Treatment Strategies. J Rheumatol. 2016 Nov;43(11):1956-1964.

[3] Hofmann SR, Kubasch AS, *et al*. Altered expression of IL-10 family cytokines in monocytes from CRMO patients result in enhanced IL-1β expression and release. Clin Immunol. 2015 Dec;161(2):300-7.

[4] Zhao Y, Wu EY, *et al*. Consensus Treatment Plans for Chronic Nonbacterial Osteomyelitis Refractory to Nonsteroidal Antiinflammatory Drugs and/or With Active Spinal Lesions. Arthritis Care Res (Hoboken). 2018 Aug;70 (8):1228-1237.

[5] Ferguson PJ, Laxer RM. New discoveries in CRMO: IL-1β, the neutrophil, and the microbiome implicated in disease pathogenesis in Pstpip2-deficient mice. Semin Immunopathol. 2015 Jul;37(4):407-12.

[6] Cox AJ, Darbro BW, *et al*. Recessive coding and regulatory mutations in FBLIM1 underlie the pathogenesis of chronic recurrent multifocal osteomyelitis (CRMO). PLoS One. 2017 Mar 16;12(3):e0169687.

Disclosure of Interests: Christian Hedrich Grant/research support from: Novartis Pharmaceuticas for Research study on effector T cells in psoriasis, Speakers bureau: In 2016: Roche Pharmaceuticals, RheumatoLogisch, Dresden, Germany; Novartis, Advisory board > Travel costs.

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SP0188 **SAPHO – AN ADULT PERSPECTIVE**

Gunter Assmann. *University Medical School of Saarland, Medicine I, Oncology and Rheumatology, Homburg, Germany*

Background: The acronym SAPHO has been introduced to describe a syndrome in adolescents and adults suffering from synovitis (arthritis), acne, pustulosis, hyperostosis, and non-bacterial osteitis preferentially in the sternal region. Currently, this also includes the entity CNO with non-bacterial chronic recurrent multifocal osteomyelitis (CRMO) in cases which primarily occur in adult age.

Objectives: The diagnostic certainty of SAPHO syndrome in case of incomplete presentation of the clinical features has been unclear so far. Furthermore, the treatment approach of SAPHO syndrome is difficult because the etiology remains unknown, although a reactive infectious osteitis in genetic predisposed subjects seems appealing.

Methods: Here we present relevant case series of SAPHO patients which should elucidate the relevance of different diagnostic procedures and treatment options. It has been noted, however, that particularly in respect of the use of antirheumatic drugs case series with predominantly small numbers of SAPHO patients suggest different treatment approaches.

Results: The diagnosis of SAPHO syndrome is made not only in the full picture of the disease according to the acronym, but also in non-bacterial and non-malignant osteitis with hyperostosis with simultaneous or delayed onset of acne, psoriasis and/or PPP. In addition, the primary manifestation of CNO in adulthood is nowadays classified as SAPHO syndrome. Recent studies have previously confirmed the usefulness of skeletal scintigraphy in 2 phases as a diagnostic. Imaging with MRI is frequently used preferentially for the assessment of osteitis activity, CT for the assessment of destruction and hyperostosis. The CT-guided biopsy of the lesion should be performed in solitary manifestation of osteitis. Basically, SAPHO syndrome has a high impact on patients' general health resulting in high burden of disease. There are many approaches to drug therapy, but only a few have been investigated in larger case series - none of them as controlled studies. Smaller case series of less than 10 patients reported limited efficacy of DMARD with MTX, azathioprine, or ciclosporin. Studies with larger case numbers show a moderate efficacy of bisphophonates as well as TNF-alpha blockers. A short-term but not sustained effect has been demonstrated for the antibiotic azithromycin, as well as for steroids per os or as infiltration into osteitis. Referring to the treatment approach in SpA newly approved biologicals with IL-17 or IL-12/23 blocking effects demonstrated promising results in individual case reports of SAPHO patients.

Conclusion: Modern diagnostic imaging methods are increasingly being used for SAPHO syndrome. The selection of potentially effective drugs for SAPHO syndrome has increased. However, prospective studies to develop guidelines for the diagnosis and therapy of SAPHO syndrome are still lacking. Until further notice, the therapy is based on the recommendations for psoriatic arthritis or spondyloarthritis.

Disclosure of Interests: None declared

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:50:00

EULAR Projects in clinical affairs

SP0189 **UPDATE ON EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF SLE**

Antonis Fanouriakis. *"Attikon" University Hospital, Rheumatology and Clinical Immunology, Athens, Greece*

Background: Recent advances in treatment strategies and goals of treatment in systemic lupus erythematosus (SLE) called for an update of the EULAR recommendations for the disease, capitalizing on the strengths of and experience from similar previous projects.

Objectives: To update the EULAR recommendations for the management of SLE

Methods: Systematic literature review (01/2007-12/2017) followed by modified Delphi method to form questions, elicit expert opinions and reach consensus.

Results: Treatment in SLE aims at remission or low disease activity and prevention of flares. Hydroxychloroquine is recommended in all lupus patients, at a dose not exceeding 5mg/kg real body weight. During chronic maintenance treatment, glucocorticoids should be minimized to less than 7.5 mg/day (prednisone equivalent) and, when possible, withdrawn. Appropriate initiation of immunomodulatory agents (methotrexate, azathioprine, mycophenolate) can expedite the tapering/discontinuation of glucocorticoids. In persistently active or flaring extrarenal disease, add-on belimumab should be considered; rituximab may be considered in organ-threatening, refractory disease. Updated specific recommendations are also provided for cutaneous, neuropsychiatric, haematological and renal disease. SLE patients should be assessed for their antiphospholipid antibody status, infectious and cardiovascular diseases risk profile, and preventative strategies be tailored accordingly.

Conclusion: The recommendations provide physicians and patients with updated consensus guidance on the management of SLE, combining evidence-base and expert-opinion.

Disclosure of Interests: Antonis Fanouriakis Paid instructor for: Amgen, GSK, Speakers bureau: Abbvie, Enorasis, Genesis Pharma

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SP0190

2019 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF SJÖGREN'S SYNDROME WITH TOPICAL AND SYSTEMIC THERAPIES

Manuel Ramos-Casals[1]. [1]*Hospital Clinic, Autoimmune Diseases, Barcelona, Spain*
Manuel Ramos-Casals[1,2,3], Pilar Brito-Zerón[2,4], Stefano Bombardieri[5], Hendrika Bootsma[6], Salvatore De Vita[7], Thomas Dörner[8], Benjamin A. Fisher[9], Jacques-Eric Gottenberg[10], Gabriela Hernández-Molina[11], Agnes Kocher[12], Belchin Kostov[13], Aike A. Kruize[14], Thomas Mandl[15], Wan-Fai Ng[16], Soledad Retamozo[17], Raphaèle Seror[18], Yehuda Shoenfeld[19], Antoni Sisó-Almirall[13,20], Athanasios G. Tzioufas[21], Claudio Vitali[22], Simon Bowman[9], Xavier Mariette[18], on behalf of the EULAR-Sjögren Syndrome Task Force Group.
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Aims: The therapeutic management of Sjögren syndrome (SjS) has not changed substantially over the past decades: treatment decisions remain challenging in clinical practice, without a specific therapeutic target beyond the relief of symptoms as the most important goal. In view of this scenario, the European League Against Rheumatism (EULAR) promoted and supported an international collaborative study (EULAR SS Task Force) aimed to develop the first EULAR evidence-, consensus-based recommendations for the management of patients with SjS with topical and systemic medications. The aim was to develop a rational therapeutic approach to SjS patients useful for healthcare professionals, doctors in specialist training, medical students, pharmaceutical industries and drug regulatory organizations following the 2014 EULAR standardized operating procedures.
Methods: The Task Force included rheumatologists, specialists in internal medicine, oral care specialists, ophthalmologists, gynaecologists, dermatologists, epidemiologists, statisticians, GPs, nurses and patient representatives from 30 countries of the 5 continents. Evidence was collected from studies including primary SjS patients fulfilling the 2002/2016 criteria; when no evidence was available, evidence from studies including associated SjS or patients fulfilling previous sets of criteria was considered and extrapolated. On the basis of the research questions, a systematic literature search between January 1986 and December 2017 was carried out. Summary-of-findings tables were generated and levels of evidence were determined according to the study design using the standards of the Oxford CEBM. A web-based Delphi procedure was carried out in order to reach consensus. For each statement, the grade of recommendation was based on the maximum level of evidence achieved in the SLR using the 4-point scale CEBM categorization. Consensus for endorsement was defined as an agreement score of at least 8 on a 0-10 scale by more than 80% of participants.
Results: The Task Force endorsed the presentation of general principles for the management of patients with SjS as 3 overarching, general consensus-based recommendations and 12 specific recommendations that form a logical sequence starting with the management of the central triplet of symptoms (dryness, fatigue and pain) followed by the management of systemic, extraglandular disease (**Table 1**).
Conclusion: The 2019 EULAR recommendations are based on the evidence collected in the last 16 years in the area of management of primary 2002 SjS patients and on discussions by a large and broadly international Task Force. The recommendations synthesise the current thinking on approaching SjS treatment in a set of overarching principles and recommendations. We hope that the current recommendations will be broadly applied in clinical practice and/or serve as a template for national societies to develop local recommendations.

Abstract SP0190 – Table 1. Overarching and specific recommendations.

	LoA (% endorsement)	LoE	GoR
A. Patients with SjS should be managed at, or in close collaboration with, centres of expertise following a multidisciplinary approach	90,7	na	Na
B. The first therapeutic approach for dryness should be symptomatic relief using topical therapies	93,3	na	Na
C. Systemic therapies may be considered for treating active systemic disease	90,7	na	Na
1. Baseline evaluation of salivary gland function is recommended before starting treatment for oral dryness	81,3	5	D
2. The preferred first therapeutic approach for oral dryness according to salivary gland function may be: **2.1. Non-pharmacological stimulation for mild dysfunction;** **2.2. Pharmacological stimulation* for moderate dysfunction;** **2.3. Saliva substitution for severe dysfunction**	88,0	1a/ *1b	B
3. First-line therapeutic approach of ocular dryness includes the use of artificial tears and ocular gels/ ointments	98,7	1a	B
4. Refractory/severe ocular dryness may be managed using topical immunosuppressive-containing drops* and autologous serum eye drops	94,7	1a/ *1b	B/D
5. Concomitant diseases should be evaluated in patients presenting with fatigue/pain, whose severity should be scored using specific tools	93,3	5	D
6. Consider analgesics or other pain-modifying agents for musculoskeletal pain considering the balance between potential benefits and side-effects	89,3	4	C
7. Treatment of systemic disease should be tailored to organ-specific severity using the ESSDAI definitions	89,3	4	C
8. Glucocorticoids should be used at the minimum dose and length of time necessary to control active systemic disease	85,3	4	C
9. Immunosuppressive agents should be mainly used as GC-sparing agents, with no evidence supporting the choice of one agent over the others	82,7	4	C
10. B-cell targeted therapies may be considered in patients with severe, refractory systemic disease	98,7	1b	D
11. Systemic organ-specific therapeutic approach may follow as a general rule the sequential (or combined) use of glucocorticoids, immunosuppressive agents and biologics	98,7	5	D
12. Treatment of B-cell lymphoma should be individualized according to the specific histological subtype and disease stage	88,0	4	C

Disclosure of Interests: None declared
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SP0191

MANAGEMENT OF ADULT APS: RECOMMENDATIONS FROM AN EULAR TASK FORCE

Maria Tektonidou. *National and Kapodistrian University of Athens, Joint Rheumatology Program, Greece*

Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by arterial and venous thrombotic events or pregnancy morbidity in the presence of persistently positive antiphospholipid antibodies. There is a great heterogeneity in clinical and laboratory classification of the syndrome and treatement approaches over the past four decades.
Objectives: To develop evidence-based recommendations for the prevention and management of adult APS that will help guide clinical practice.
Methods: EULAR standardised operating procedures were followed. A task force was formed including 21 physicians, 1 healthcare professional, and 2 patients, from 11 countries. Research questions were developed using the Delphi method. A systematic literature review of published articles up to January 2018 was performed.
Results: Based on the evidence and experts opinion, a set of 3 overarching principles and 12 recommendations including their level of evidence and grade of recommendation was developed and voted. The level of agreement for each recommendation was high. The overarching principles include the risk stratification, general measures, and education/counselling of patients with APS.
Recommendations for primary prevention address the primary thromboprophylaxis (low dose aspirin vs no treatment) in antiphospholipid antibody individuals

including asymptomatic carriers, patients with systemic lupus erythematosus without history of thrombotic or obstetric APS, and non-pregnant women with a history of obstetric APS only. Recommendations for the management of thrombotic manifestations address different types of anticoagulation in patients with definite APS and first provoked or unprovoked venous thrombosis and the management of recurrent venous thrombosis, as well as the type and intensity of anticoagulation in patients with first or recurrent arterial thrombosis.
Recommendations for the management of obstetric APS describe the management of various types of pregnancy complications in APS and of refractory to treatment cases. Recommendations for catastrophic APS refer to precipitating factors, first-line treatment of catastrophic APS, and management of refractory cases.
Conclusion: These recommendations based on evidence and expert opinion aim to guide practice and improve quality of care in patients with APS.

REFERENCE:

[1] Tektonidou MG, Andreoli L, Limper M, et al. EULAR Recommendations for the management of Antiphospholipid Syndrome in adults. Ann Rheum Dis. 2019

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8601

SP0192 **UPDATE OF THE EULAR RECOMMENDATIONS LAGE VESSEL VASCULITIS MANAGEMENT**

Bernhard Hellmich. *Medius Kliniken, Klinik für Innere Medizin, Rheumatologie und Immunologie, Kirchheim-Teck, Germany*

Background: Since the publication of the European League Against Rheumatism (EULAR) recommendations for the management of large vessel vasculitis (LVV) in 2009, several relevant randomized clinical trials and cohort analyses have been published, which have the potential to change clinical care and therefore supporting the need to update the original recommendations.
Objectives: To update the 2009 EULAR recommendations for the management of LVV.
Methods: Using EULAR standardized operating procedures for EULAR-endorsed recommendations, the EULAR task force undertook a systematic literature review and sought opinion from 20 experts from 13 countries. We modified existing recommendations and created new recommendations.
Results: Three overarching principles and 10 recommendations were formulated. We recommend that a suspected diagnosis of LVV should be confirmed by imaging or histology. High dose glucocorticoid therapy (40-60 mg/day prednisone-equivalent) should be initiated immediately for induction of remission in active giant cell arteritis (GCA) or Takayasu arteritis (TAK). We recommend adjunctive therapy in selected patients with GCA (refractory or relapsing disease, presence of an increased risk for glucocorticoid-related adverse events or complications) using tocilizumab. Methotrexate may be used as an alternative. Non-biologic glucocorticoid-sparing agents should be given in combination with glucocorticoids in all patients with TAK and biologic agents may be used in refractory or relapsing patients. We no longer recommend the routine use of antiplatelet or anticoagulant therapy for treatment of LVV unless it is indicated for other reasons.
Conclusion: We have updated the recommendations for the management of LVV to facilitate the translation of current scientific evidence and expert opinion into better management and improved outcome of patients in clinical practice.
Disclosure of Interests: Bernhard Hellmich Consultant for: Roche, Speakers bureau: Abbvie, MSD, Roche, Novartis, Pfizer
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SATURDAY, 15 JUNE 2019

12:00:00 – 13:30:00

Skin and eye manifestations in rheumatic diseases

SP0193 **WIN: SKIN AND RHEUMATIC DISEASES**

Annegret Kuhn. *University Hospital Muenster, Executive Department of the University Hospital, Muenster, Germany*

Background: The main underlying mechanisms of skin manifestations in rheumatic diseases include autoimmune responses, auto-inflammatory processes, and tissue-specific alterations. In psoriasis, therapies targeting T cell activation, T cell migration, or neutralization of disease-related cytokines are highly effective. However, targeted therapies still need to be developed in less frequent autoimmune diseases, such as systemic lupus erythematosus (SLE), systemic sclerosis (SSc), or dematomyositis (DM).
Objectives: To provide an update for rheumatologists on the management of skin manifestations in autoimmune diseaes based on recent insights into the pathogenesis.
Methods: Several agents are approved for the treatment of SLE, including the monoclonal antibody belimumab, a B lymphozyte stimulator-specific inhibitor, but no drugs have been licensed specifically for the treatment of skin manifestations in this disease. The aim of the European guideline was to achieve a broad consensus on treatment strategies for patients with cutaneous lupus erythematosus (CLE) by a European subcommittee. In total, 16 European participants were included in this project and agreed on all recommendations.
Results: First-line treatment options in CLE include topical corticosteroids or calcineurin inhibitors; in patients with disfiguring and widespread disease, systemic agents need to be applied. The first-line systemic treatment is antimalarials, but some patients are therapy-resistant and immunosuppressive agents, such as methotrexate, are used as alternative therapeutic option. In 2011, the monoclonal antibody belimumab was introduced for SLE as an adjunct therapy for patients with autoantibody-positive disease who despite standard therapy show high disease activity, intolerance of other treatments, or an unacceptably high need for corticosteroids. So far, a validated skin score has not been used to confirm the efficacy of belimumab on mucocutaneous manifestations. In SSc, the therapeutic modalities are even more limited. Treatment with endothelin-receptor antagonists has been proven to reduce the occurrence of new digital ulcers in SSc patients but has no or limited effect on healing of digital ulcers. DM is a further idiopathic autoimmune disease characterized by inflammation of the muscles and skin, which is treated with immunosuppressives. Corticosteroids are still the first-line treatment for muscle involvement in DM, but skin lesions often flare by reduction or discontinuation.
Conclusion: In summary, there is a high unmet need for new therapeutic strategies focusing on skin involvement in systemic autoimmune diseases. Therefore, innovative designs of randomized controlled trials based on the pathogenesis are warranted to develop new therapies for patients with skin manifestations in rheumatic diseases.

REFERENCES:

[1] Kuhn A, Landmann A, Bonsmann G. The skin in autoimmune diseases - unmet needs. Autoimmun Rev 2016;15:948-954
[2] Kuhn A, Aberer E, Bata-Csoergő Z, et al. S2k guideline for treatment of cutaneous lupus erythematosus - guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV). J Eur Acad Dermatol Venereol 2017;31:389-404
[3] Smith V, Scirè CA, Talarico R, et al. Systemic sclerosis: state of the art on clinical practice guidelines. RMD Open 2018;4:e000782
[4] Sunderkoetter C, Nast A, Worm M, et al. Guidelines on dermatomyositis - excerpt from the interdisciplinary S2k guidelines on myositis syndromes by the German Society of Neurology. J Dtsch Dermatol Ges 2016;14:321-338
[5] Tamirou F, Arnaud L, Talarico R, et al. Systemic lupus erythematosus: state of the art on clinical practice guidelines. RMD Open 2018;4:e000793

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SATURDAY, 15 JUNE 2019

12:00:00 – 13:30:00

To image or not to image in spondyloarthritis?

SP0194 **WHEN AND HOW TO USE AND NOT USE IMAGING FOR DIAGNOSIS?**

Floris A. van Gaalen. *Leiden University Medical Center, Rheumatology, Leiden, Netherlands*

Since axial spondyloarthritis (axSpA) has no single shared distinguishing feature that distinguishes the disease from other causes of back pain, diagnosis of axSpA requires recognition by the clinician of a pattern of features that taken together are characteristic of axSpA. Information from patient history and physical examination, laboratory, and imaging findings may all aid in recognition of axSpA and the diagnosis of axSpA requires exclusion of other potential causes for these abnormalities/differences.
Traditionally, plain radiography is used to assess sacroiliac and spinal involvement of disease. A weakness of radiography in assessing sacroiliac involvement - apart from its inability to detect early disease - is reader variability. Additionally, involvement of the spine (i.e detection of syndesmophytes) is very uncommon in early disease.
The use of MRI in diagnosing axSpA has increased over the past ten years and MRI greatly facilitates earlier diagnosis of axSpA. However, it has also become increasingly clear that MRI detectable lesions associated with SpA -including bone marrow edema and fatty lesions- may also occur in patients without axSpA.

The aim of this presentation is to provide insight into the pitfalls of imaging in diagnosing SpA, with a particular focus on false positives in imaging as well as the importance of interpretation of the clinical context.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8610

SP0195 **IMAGING IN DISEASE AND TREATMENT MONITORING – DOES IT MATTER?**

Xenofon Baraliakos. *Rheumazentrum Ruhrgebiet, Ruhr University Bochum, Rheumatology, 44649 Herne, Germany*

Background: Imaging of the axial skeleton is a crucial step in classification and diagnosis of axial Spondyloarthritis. After diagnosis, patients with axSpA are being treated with non-steroidal anti-inflammatory drugs (NSAIDs) or with disease-modifying anti-rheumatic drug (bDMARD). Despite the fact, that the latter treatment is referred to as disease-modifying and modification of the disease is supposed to be relating to the objective course of the disease, as assessed by imaging, recommendations for monitoring of the course of axSpA by imaging are still lacking mostly due to the lack of data. Nevertheless, this aspect is mentioned in the treat-to-target principle for axSpAOverall, earlier data have shown that the course of lesions documented by magnetic resonance imaging (MRI) is correlating well with other objective measures of changes of systemic inflammation such as c-reactive protein (CRP), than with patient-reported measures of disease activity. Similarly, conventional radiographs (CR) are being used for documenting of the development of structural changes over many years.
Objectives: The objective of this presentation is to show the current evidence of the possibilities of different imaging techniques used in axSpA for assessment of the course of the disease (both for the inflammatory and chronic changes) and give practical tips about when imaging would be advised for monitoring the disease course or where this can be avoided.
Disclosure of Interests: Xenofon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma
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SP0196 **IS THERE ROOM FOR OTHER IMAGING MODALITIES BEYOND CONVENTIONAL X-RAYS AND MRI?**

C.J. van der Laken. *Amsterdam UMC location VUmc, Rheumatology, Amsterdam, Netherlands*

Early diagnosis of spondyloarthritis is still tempting since objective measures to assess disease activity are often negative. MRI provides highly sensitive visualization of inflammation, but detection levels in early spondyloarthritis are varying. Another clinical temptation is early treatment evaluation of spondyloarthritis. An important outcome measure is therapeutic efficacy on bone formation in vertebral column and sacro-iliac joints. Conventional X-rays only allow for assessment of bone formation over a time span of at least 2 years. In this presentation, opportunities with new upcoming imaging techniques to address above mentioned clinical issues will be discussed in relation to longer existing imaging techniques.
Disclosure of Interests: None declared
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SATURDAY, 15 JUNE 2019

12:00:00 – 13:30:00

The lung in rheumatoid arthritis

SP0197 **CASE 1 PRESENTER: EARLY RA WITH LUNG PROBLEMS IN THE CONTEXT OF BIOLOGICAL TREATMENT**

Ana Milena Millán Arciniegas. *Santa Creu i Sant Pau Hospital, Rheumatology, Barcelona, Spain*

We present a 77-year-old male patient with a history of former smoker, arterial hypertension and dyslipidaemia, whose diagnosis of Rheumatoid Arthritis was made in July 2017 by arthritis of metacarpophalangeal joints, wrists and knees and positivity for anticyclic citrullinated peptide antibodies (ACPA) and rheumatoid factor (RF). Treatment with Methotrexate and prednisone was started but the patient did not achieve adequate control of joint symptoms, so we decided to add Etanercept to the treatment. A good joint response was obtained but in a follow-up control he explained breathlessness with cough and low grade fever. The chest X-Ray was not conclusive and we decided to perform a high resolution computerized tomography (HRCT) scan. An interstitial involvement was detected and an accurate differential diagnosis was made.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8538

SP0198 **CASE 1 DISCUSSANT: HOW TO DIFFERENTIATE ILD FROM OTHER CAUSES OF LUNG INVOLVEMENT IN RA**

Ivan Castellvi. *Hospital Universitari de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain*

The lung in Rheumatoid Arthritis (RA) can be affected by different manifestations and Interstitial Lung Disease (ILD) related to RA is one of the most devastating complications that we can find in the disease. The lung parenchyma involvement can be present with different patterns. As opposite with other forms of connective tissue diseases the usual interstitial pneumonia pattern (UIP) is more frequent than nonspecific interstitial pneumonia pattern (NSIP) in RA. Currently high-resolution computed tomography (**HRCT**) and pulmonary function test are the best tools to detect and to follow ILD in RA. Nevertheless, other lung involvements, infections and drug toxicity of nonbiological and biological disease-modifying anti-rheumatic drugs (DMARDs) can affect patients with rheumatoid arthritis and simulate ILD. To know which affectation are present in our patients with interstitial lung compromise is crucial to proceed against the problem. Patient characteristics, clinical presentation, radiological distribution or bronchoalveolar lavage would be helpful to discriminate ILD from other causes of lung involvement. An individual and multidisciplinary approach is very important to do the best management in these patients.
Disclosure of Interests: None declared
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SP0199 **CASE 2 DISCUSSANT: HOW TO TREAT DIFFICULT ILD**

Toby Maher. *Imperial College London and Royal Brompton Hospital, National Heart and Lung Institute, London, United Kingdom*

Background: ILD frequently results in progressive and irreversible destruction of the lung through scarring. Prompt therapy can help rescue lung function and prevent subsequent respiratory decline. This case will demonstrate the challenges inherent in diagnosing and managing interstitial lung disease in the context of connective tissue disease
Objectives: To discuss typical presentation of CTD-ILD
Review challenge of making diagnosis and choosing best treatment.
Assess treatment options, duration of therapy and measurement of treatment response.
Conclusion: A range of therapeutic options exist for CTD-ILD albeit with a paucity of trial data to support best practice. Accurate diagnosis of systemic disease, paired with careful assessment and monitoring of the respiratory system are vital in ensuring optimal management. Intravenous therapy is often necessary in advanced disease or for disease which proves refractory to oral immunosuppression.

REFERENCES:

[1] Saunders P, Tsipouri V, Keir GJ, Ashby D, Flather MD, Parfrey H, Babalis D, Renzoni EA, Denton CP, Wells AU, Maher TM. Rituximab versus cyclophosphamide for the treatment of connective tissue disease-associated interstitial lung disease (RECITAL): study protocol for a randomised controlled trial. Trials 2017; 18: 275.
[2] Maher TM. Immunosuppression for connective tissue disease-related pulmonary disease. Seminars in respiratory and critical care medicine 2014; 35: 265-273.

Disclosure of Interests: Toby Maher Grant/research support from: Received funds from BI advisory board participation and conference travel. Received research funding and/or consulting fees or other remuneration from GSK, UCB, AstraZeneca, Roche, Bayer, Biogen Idec, Cipla, Prometic, and Sanumed. Toby Maher has, via his institution, received industry-academic funding from GlaxoSmithKline R&D and UCB., Consultant for: Toby Maher has received consultancy or speakers fees from Apellis, AstraZeneca, Bayer, Biogen Idec, Boehringer Ingelheim, Galapagos, GlaxoSmithKline R&D, Indalo, Pliant, ProMetic, Roche, Samumed and UCB; and has received consultancy fees from Galecto.
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SATURDAY, 15 JUNE 2019

12:00:00 – 13:30:00

Novel treatments and old challenges: where do we stand in the management of antiphospholipid syndrome

SP0200 TARGETED TREATMENTS: WHAT'S ON THE HORIZON FOR OBSTETRIC ANTIPHOSPHOLIPID SYNDROME?

Jane E. Salmon. *Hospital for Special Surgery – Weill Cornell Medicine, Rheumatology, New York, United States of America*

Pregnancy in women with APS and/or lupus is dangerous both for mother and offspring, and, in the past, patients were advised not to have children. Among complications frequently seen in women with lupus are preeclampsia (also known as toxemia of pregnancy), preterm birth, markedly underweight newborns, and fetal death. Identifying women destined for complications remains challenging and limits our ability to counsel and care for pregnant lupus patients.

There is currently no effective treatment for women with these high-risk pregnancies; treatments to prevent poor pregnancy outcomes require an understanding of mechanisms of injury. Our research in an animal model that mimics the human condition shows that blockade of well-established mediators of inflammation, specifically complement and TNF-alpha, prevents adverse outcomes. To translate these discoveries to lupus patients, we launched the **PROMISSE** Study (**P**redictors of p**R**egnancy **O**utcome: bio**M**arkers **I**n antiphospholipid antibody **S**yndrome and **S**ystemic lupus **E**rythematosus) to determine which pregnancies were at highest risk for adverse outcomes. Over 20% of pregnancies in patients with SLE resulted in an adverse pregnancy outcome. We discovered that the presence of a lupus anticoagulant which can be detected in the blood before pregnancy or in the first trimester, confers a 10-fold increase in risk of complications. Furthermore, we found that early in pregnancy, measurable alterations in the balance of angiogenic factors (proteins that circulate in blood, promote proper placenta development, and are required to maintain the health of the mother's vascular system) are highly predictive of preeclampsia and other pregnancy complications.

The results of the PROMISSE Study provide models for early risk stratification to allow physicians to identify patients early in pregnancy who are at low risk and reassure them that their pregnancies were likely to be uncomplicated and their babies healthy. Conversely and importantly, we can reliably predict which patients are destined to have poor pregnancy outcomes, and we conducting a trial with a TNF-alpha inhibitor that does not cross the placenta in patients at highest risk an experimental therapy to prevent placental dysfunction. Treatments to prevent poor pregnancy outcomes require an understanding of mechanisms of injury. Experiments in mouse models have enabled us to embark upon a trial of a potential treatment.

Disclosure of Interests: Jane E. Salmon Shareholder of: Biogen-Idec, BMS, Johnson & Johnson, Regeneron, Merck, Grant/research support from: UCB, Consultant for: BMS, Ionis

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SP0201 CATASTROPHIC APS TREATMENT GUIDELINES

Ricard Cervera. *Hospital Clinic, Barcelona, Department of Autoimmune Diseases, Barcelona, Spain*

The current recommendation for specific therapy of catastrophic antiphospholipid syndrome (CAPS) is the triple therapy with anticoagulation, glucocorticoids, plasma exchange and/or intravenous immunoglobulins. Of note, only anticoagulation had a significant effect improving the vital prognosis of these patients. From the experimental point of view, there is only indirect evidence to advocate the use of these immunomodulatory therapies in CAPS.

Recently, two monoclonal antibodies, rituximab and eculizumab, have been successfully used in some cases of severe or refractory CAPS. The first decreases the generation of pathogenic autoantibodies such as antiphospholipid. The second prevents the generation of C5b-C9 complex.

The current presentation will describe the conventional and recent modalities of CAPS treatment, discussing the rationale for each one.

REFERENCES:

[1] Cervera R, Rodríguez-Pintó I, Espinosa G. The diagnosis and clinical management of the catastrophic antiphospholipid syndrome: A comprehensive review. J Autoimmun 2018; 92: 1-11.

[2] Rodríguez-Pintó I, Espinosa G, Cervera R. Catastrophic antiphospholipid syndrome: The current management approach. Best Pract Res Clin Rheumatol 2016; 30: 239-249.

[3] Rodriguez-Pintó I, Santacreu I, Cervera R, Espinosa G. What is the best strategy in treating catastrophic antiphospholipid syndrome? Int J Clin Rheumtol 2015;10: 245–255.

[4] Rodríguez-Pintó I, Espinosa G, Erkan D, Shoenfeld Y, Cervera R, for the CAPS Registry Project Group. The effect of triple therapy on the mortality of catastrophic antiphospholipid syndrome. Rheumatol 2018; 57: 1264-1270.

Disclosure of Interests: None declared

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SATURDAY, 15 JUNE 2019

12:00:00 – 13:30:00

How low should you go? What is the relevant target in T2T in rheumatoid arthritis?

SP0202 WHAT DOES REMISSION MEAN FOR PHYSICIANS?

Laure Gossec. *Sorbonne Universite and Pitie-Salpetriere Hospital, Rheumatology, Paris, France*

Remission is the announced objective is rheumatoid arthritis. However, there are several definitions of remission. In this talk, we will review different health professional based definitions of remission, the components of these definitions, and their advantages and drawbacks.

Disclosure of Interests: Laure Gossec Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB, Consultant for: L Gossec has received honoraria from Celgene as investigator for this study

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SP0203 WHAT DOES REMISSION MEAN FOR PATIENTS?

Ruth Williams. *Kings College London, Department of Inflammation Biology, London, United Kingdom*

What does remission in Rheumatoid arthritis mean to patient?

This session discusses what remission means to patients. Remission holds different meaning for researchers, clinicians and patients. In addition it holds different meaning for individual patients and for individual patients at different points of time in their lives. I shall reflect on over fifty years living with Rheumatoid arthritis, as both a patient and a doctor. To consider the changes in my care, my therapy and in my own and my clinicians objectives and treatment aims, at different points in time. Looking at how things have progressed from pain relief, splinting, physical therapy, rehabilitation and surgery. To progressively more effective DMARD's, antI-TNF's & Biologics and an aim of complete 'clinical remission'.

However commonly 'clinical remission' can conflict with a patients concept of remission, as patients are individuals and the tools used to define remission are research based and consider populations not people. 'Disease activity scoring' and 'Treat to Target' has had significant impact on patients, clinicians and their rheumatology consultations. The absence of inflammation does not equal remission for many patients and it is important to consider the differing needs of patients who were diagnosed pre and post- biologic therapies and those with refractory disease. Currently maximal energy appears to be concentrated on the newly diagnosed and even pre-diagnosis, but has this been at the detriment of those with long established disease?

I will share my own and different patients viewpoints of what 'remission' means and consider the benefits of progress in effective 'therapies' but also to reflect upon some of the important things that may have been lost from clinical 'care' along the way. To list simple things that can help patients achieve remission that can easily be forgotten. I will explain the phenomenon of 'DAS blindness' and the potential failings it can lead to. Discuss how improved shared decision making of treatment aims might improve outcomes for patients whilst reducing risk and possibly costs; aiming to increase patient autonomy and improve the doctor patient dynamic.

In order to achieve 'remission' for patients we need to have a clear shared understanding of what 'remission' means to each individual and only then can we aim to achieve it.

Disclosure of Interests: None declared

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SATURDAY, 15 JUNE 2019

12:00:00 – 13:30:00

Behaviour change in fibromyalgia

SP0204 **CASE1 PRESENTATION: FACILITATING BEHAVIOUR CHANGE IN FIBROMYALGIA: A CASE STUDY FROM THE UK**

Yeliz Prior. *University of Salford, Centre for Health Sciences Research, Manchester, United Kingdom*

Background: Fibromyalgia is a chronic pain condition which, is commonly accompanied by the symptoms of fatigue, sleep disturbance, low mood and cognitive dyscognition. EULAR Revised Recommendations for the management of Fibromyalgia suggests initial management should involve patient education and focus on non-pharmacological therapies [1]. Occupational Therapists at the Rheumatology Outpatients Department, Leighton Hospital, Mid Cheshire NHS Hospitals Foundation Trust developed the Fibromyalgia Self-Management Education (FAMe) Group Programme, based on the current evidence-base and patient partner involvement. The primary aim of this programme is to support self-management of Fibromyalgia using behaviour change interventions as outlined in the NICE recommendations. FAMe comprises 2.5 hrs weekly sessions over six weeks (6-Wks) and core components include education about Fibromyalgia, pain, fatigue, sleep and mood management, dealing with dyscognition, physical exercise and practicing mindfulness, based on Cognitive Behavioural Therapy (CBT) and Motivational Interview (MI) approaches.
Objectives: Service evaluation aims to assess how well a service is achieving its objectives. This service evaluation was undertaken with a view to benefit patients using the FAMe Group Programme and is designed and conducted with the sole purpose of defining and examining the current occupational therapy service provision for people with Fibromyalgia at the Mid Cheshire NHS Trust Hospitals. This Case Study will report on the findings of this service evaluation with reference to patient outcomes and discuss the barriers and facilitators of implementing this programme at an NHS Hospital setting.
Methods: Patients with a primary diagnosis of FM were screened and recruited from the rheumatology department of the Mid-Cheshire NHS Hospitals. Patients self-completed postal questionnaires at home [including socio-demographic characteristics; General Health Questionnaire SF-12; Revised Fibromyalgia Impact Questionnaire; Arthritis Self Efficacy Scale; Multidimensional Assessment of Fatigue Scale) at baseline, and again at 6 and 12-week follow-up. Focus groups were held at the hospital following the completion of the FAMe Group Programme, to obtain patients' views on the programme content, delivery and the impact on their self-management. Quantitative data from the baseline, 6 and 12-week follow-up questionnaires were analysed using paired t-tests and effect sizes calculated using eta-squared. Focus groups were transcribed and analysed by three independent researchers, not involved in the initial design or the delivery of this programme, using Thematic Analysis [2].
Results: As the service evaluation is in progress at the time of submitting this abstract, the results will be presented and discussed at the annual meeting.
Conclusion: To be discussed at the meeting.

REFERENCES:

[1] Corless L, Ching A, Mayana K, Walker N, Prior Y (2019) Occupational Therapy-led Fibromyalgia Self-Management Education Group Programme: Patients' Perspectives. *Rheumatology Vol 58 Issue Suppl 1* April 2019
[2] Macfarlane GJ, Kronisch C, Dean LE, et al. (2017) EULAR revised recommendations for the management of fibromyalgia. Annals of the Rheumatic Diseases 76:318-328.

Disclosure of Interests: None declared
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SATURDAY, 15 JUNE 2019

12:00:00 – 13:30:00

How to build a clinical scientist

SP0205 **SCIENCE CARRIER AND MENTAL HEALTH**

Annet van Royen. **Background:** Clinician scientists are at the heart of the transitional medicine process. Over the last decades many reports and studies have showed that they risk becoming extinct, and that efficient career pathways are lacking. Recently more reports show that alarming numbers of clinicians and clinical scientists suffer from burn out and depression.
To address this issue, next to thorough study of the root factors leading to mental problems it is important to develop career pathways for clinician scientists and educational programs to improve resilience.
New educational programs such as those offered by the Eureka Institute help to build networks of translational scientists and help to strengthen resilience, needs to overcome the challenges they face while pursuing translational research.
Disclosure of Interests: None declared
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SATURDAY, 15 JUNE 2019

12:00:00 – 13:30:00

Restless lives: managing fatigue, sleep and pain

SP0206 **LINKS BETWEEN SLEEP QUALITY AND IMMUNITY IN RMDS**

Tanja Lange. *University of Lübeck, Department of Rheumatology and Clinical Immunology, Lübeck, Germany*

Summary: Sleep and the immune system are bi-directionally linked. An immune activation induces fatigue, sleepiness and changes in sleep architecture. These range from a deepening of sleep to severe sleep disturbances with shallow and fragmented sleep. Patients with rheumatic and musculoskeletal diseases (RMDs) often complain about feelings of debilitating fatigue, of problems initiating and maintaining sleep and of unrefreshing sleep. Chronic low-grade inflammation due to the RMD, disease symptoms such as pain, concurrent diseases such as depression and medication such as glucocorticoids are potential triggers of poor sleep. Often it is demanding to delineate the exact cause(s) of sleep impairments in patients with RMDs and attempts to improve sleep quality therefore often fail. However, as fatigue and sleep problems can substantially impair quality of life and as poor sleep may further aggravate RMDs and their symptoms it is key to unravel the pathophysiology of fatigue and poor sleep in these patients. A deeper understanding of sleep-immune interactions in RMDs will advance targeted interventions that presumably will encompass a combination of immunomodulatory drugs, chronopharmacology and cognitive behavioral therapy.

REFERENCES:

[1] Besedovsky L, Lange T, Born J. Sleep and immune function (2012) Pflugers Arch 463(1):121-37.
[2] Tan X, van Egmond L, Partinen M, Lange T, Benedict C. A narrative review of interventions for improving sleep and reducing circadian disruption in medical inpatients (2018) Sleep Med pii: S1389-9457(18)30314-9.
[3] Lacourt TE, Vichaya EG, Chiu GS, Dantzer R, Heijnen CJ. The high costs of low-grade inflammation: persistent fatigue as a consequence of reduced cellular-energy availability and non-adaptive energy expenditure (2018) Front Behav Neurosci 12:78.

Disclosure of Interests: None declared
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SP0207 **PHYSICAL ACTIVITY, CHRONIC MUSCULOSKELETAL PAIN AND INSOMNIA**

Eivind Skarpsno. *Norwegian University of Science and Technology (NTNU), Department of Public Health and Nursing, Trondheim, Norway*

The interplay between physical activity, chronic musculoskeletal pain and insomnia
The unfavourable consequences of insomnia and musculoskeletal pain for both individuals and society underscore the importance of identifying modifiable factors for prevention and treatment. Prospective studies have shown that there exists a bidirectional relation between insomnia and musculoskeletal pain, i.e., insomnia is associated with risk of chronic musculoskeletal pain and vice versa. This suggests that management of insomnia symptoms may be an efficient treatment objective for people with musculoskeletal pain and that management of musculoskeletal pain has the potential to improve sleep quality. Furthermore, some evidence shows that physical activity may represent an efficient initiative that can improve both sleep quality and chronic pain, potentially leading to effects as beneficial as pharmacological treatment. However, many unresolved questions need to be resolved before physical activity can be prescribed as an optimal treatment

option for these conditions. For instance, in contrast to leisure-time physical activity, recent evidence has shown that occupational physical activity seems to be associated with more insomnia symptoms, and that this association is particularly evident among people who also report musculoskeletal pain. These latter findings therefore call attention to the domain-dependent association between physical activity and health related outcomes, including musculoskeletal pain and insomnia. As methods to deal with physical activity have improved the recent years, the intention of this presentation is to provide an updated review of the interplay between domains of physical activity, insomnia and chronic musculoskeletal pain

Learning objectives:

- To understand the bidirectional relationship between insomnia and musculoskeletal pain
- To understand the interplay between domains of physical activity, chronic musculoskeletal pain and insomnia

REFERENCES:

[1] Uhlig BL, Sand T, Nilsen TI, Mork PJ, Hagen K. Insomnia and risk of chronic musculoskeletal complaints: longitudinal data from the HUNT study, Norway. BMC Musculoskeletal Disorders. 2018;19 (1):128.

[2] Skarpsno ES, Nilsen TIL, Sand T, Hagen K, Mork PJ. Do physical activity and body mass index modify the association between chronic musculoskeletal pain and insomnia? Longitudinal data from the HUNT study, Norway. Journal of Sleep Research. 2018;27(1):32-39.

[3] Youngstedt S, Kline C. Epidemiology of exercise and sleep. Sleep and Biological Rhythms. 2006;4(3):215-221.

[4] Ambrose KR, Golightly YM. Physical exercise as non-pharmacological treatment of chronic pain: Why and when. Best Practice & Research Clinical Rheumatology. 2015; 29(1):120-130.

[5] Chennaoui M, Arnal PJ, Sauvet F, Leger D. Sleep and exercise: a reciprocal issue? Sleep Medicine Reviews. 2015;20:59-72.

[6] Skarpsno ES, Mork PJ, Nilsen TIL, Jorgensen MB, Holtermann A. Objectively measured occupational and leisure-time physical activity: cross-sectional associations with sleep problems. Scandinavian Journal of Work Environment &Health. 2018;44(2):202-211.

[7] Skarpsno ES, Mork PJ, Nilsen TIL, Jorgensen MB, Holtermann A. The joint association of musculoskeletal pain and domains of physical activity with sleep problems: cross-sectional data from the DPhacto study, Denmark. International Archives of Occupational and Environmental Health. 2018.

Disclosure of Interests: None declared
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SP0208 **UNDERSTANDING THE IMPACT OF PAIN, SLEEP AND FATIGUE ON PATIENTS LIVES**

Savia de Souza. *King's College London, Centre for Rheumatic Diseases, London, United Kingdom*

Pain is well known to be a common dominant symptom in people with rheumatic musculoskeletal diseases (RMDs). Perhaps less well acknowledged by healthcare professionals are fatigue and sleep disturbances in these patients. Individually these symptoms are problematic but when combined their effect and impact on patients' lives is greatly amplified; often leaving people in a vicious cycle whereby being in pain results in poor sleep leading to fatigue the next day, which lowers patients' pain tolerance resulting in a poorer night's sleep, more fatigue and increased pain.

Pain, fatigue and sleep disturbance greatly reduce quality of life for people with RMDs. Patients have to adapt their daily and leisure activities, or give them up altogether with negative psychological consequences such as anxiety and depression. Patients can end up feeling helpless and sometimes suicidal. Relationships with partners and friends are often altered affecting their sexual and social lives. Major life decisions, such as having a baby, can be put on hold or shelved.

People with RMDs may also have to reduce their working hours or stop working, which has financial repercussions for them and their families. This can exacerbate stress, anxiety and depression leading to poorer health outcomes. It is therefore of great importance that healthcare professionals understand the extent to which pain, fatigue and sleep difficulties impact on patients' lives so that priority can be given to addressing these distressing symptoms as part of any management strategy.

Disclosure of Interests: None declared
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SATURDAY, 15 JUNE 2019

12:00:00 – 13:30:00

EULAR Projects in musculoskeletal imaging

SP0209 **EULAR RECOMMENDATIONS FOR REPORTING IN MSK ULTRASOUND STUDIES**

Maria-Antonietta d'Agostino. *APHP Hôpital Ambroise Paré, Versailles Saint-Quentin University, Rheumatology, Boulogne-Billancourt, France*

Background: Ultrasound is now considered as an established imaging modality for the management of rheumatic and musculoskeletal diseases (RMDs). However, the reporting of ultrasound information in clinical studies is often inadequate and/or incomplete which hampers the assessment of the generalizability and applicability of their results.

Objectives: to develop European League Against Rheumatism (EULAR) recommendations for the reporting of ultrasound studies in RMDs with the ultimate goal to produce a "reporting checklist" containing a minimal list of items that should be checked when a study using ultrasound is submitted for publication.

Methods: Following the standardised operating procedures for EULAR-endorsed recommendations, a task force has been created, including ultrasound experts, methodologists, patients and health professionals. After a first face-to-face meeting, preliminary recommendations were formulated together with research questions to drive the literature reviews. Based on the results of the literature reviews and on the results of several DELPHI rounds with the participation of external experts, these preliminary recommendations were then refined during a second face-to-face meeting in November 2018.

Results: The current checklist comprises 21 items (19 mandatory and two optional) divided into 13 sections. For helping the interpretation of some specific terms, a glossary has also been created, including 12 definitions. The checklist is currently evaluated by external experts to assess its comprehensiveness. Finally, all the members of the task force will be asked to give their level of agreement with each of the items.

Conclusion: this checklist will help to improve quality and completeness in reporting of ultrasound studies in RMDs.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8455

SP0210 **IMPLEMENTATION AND ROLE OF MODERN MUSCULOSKELETAL IMAGING (US, MRI AND PET) IN RHEUMATOLOGICAL PRACTICE IN EUROPE – A EULAR SURVEY**

Peter Mandl. *Medical University of Vienna, Rheumatology, Vienna, Austria*

Objectives: To document the current training, implementation and role of modern musculoskeletal imaging techniques, i.e. ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) among rheumatologists in the member countries of the European League Against Rheumatism (EULAR).

Methods: English-language questionnaires for each imaging modality developed by aEULAR Taskforce were sent out to national and international scientific societies as well as imaging experts in the given modalities involved in research and/or training. The surveys were distributed via an online survey tool (Surveymonkey). Simple descriptive and summary statistics were calculated from the responses.

Results: More than 90% of US experts reported the availability of an US unit in their department. Suspicion of rheumatoid arthritis and spondyloarthritides were the main clinical indications for performing US for diagnostic purposes. Suspicion of sacroiliitis and degenerative spine disease were the most common indications to perform MRI or CT for diagnostic purposes, while PET was mainly performed to diagnose large vessel vasculitis and to investigate fever of unknown origin. The reported percentage of rheumatologists performing US was highly variable, ranging from more than 80% in 6% of countries to less than 10% in 15% of countries. The majority of experts (77%) reported that their national rheumatology societies organize US courses, while courses in MRI or CT organized by the national rheumatology societies were less commonly reported (29% and 8% respectively).

Conclusions: Rheumatologists in Europe utilise modern imaging techniques, however access to the techniques and training offered is varied.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8533

SP0211 **DEVELOPMENT OF A STANDARDIZED TRAINING MODEL FOR ULTRASOUND-GUIDED SYNOVIAL BIOPSY'S IN SMALL AND LARGE JOINTS**

Ingrid Möller. *University of Barcelona, Instituto Poal de Reumatologia, Barcelona 08022, Spain*

Background: Ultrasound-guided needle biopsy of synovium is a minimally invasive tool to complete the study and in the investigation of the therapeutic response in some patients with arthritis. As a consequence, there is a need to have a didactic material and a form of training. This EULAR project: Development of a standardized training model for ultrasound-guided synovial biopsy's in small and large joints, covers these objectives

Objectives:

1. To develop educational material on the procedures for ultrasound–guided minimally–invasive synovial biopsy in small and large joints.
2. To test the consistency, reliability and feasibility of these procedures on cadaveric specimens (Barcelona University, Barcelona, Spain).
3. To validate these procedures by assessing the synovial tissue quality (i.e. number of graded tissue samples per biopsy procedure, amount of RNA extraction) obtained by this biopsy modality in patients (5 patients) from the participating centres. Tissue will be analyzed in a central laboratory (Joint and Bone Laboratory, Fundación Jiménez Díaz, Madrid, Spain).

Methods: Meeting in Barcelona was in January 2019 from the 21 to the 25.
During the meeting, part of the educational material was produced and the exercise to test the consistency, reliability, and feasibility of these procedures on cadaveric specimens (Barcelona University, Barcelona, Spain) was done. Then the material was circulated among the experts.
The validation of these procedures by assessing the synovial tissue quality (i.e. number of graded tissue samples per biopsy procedure, amount of RNA extraction) obtained by this biopsy modality in patients (5 patients) from the participating centres and Tissue analysis in a central laboratory (Joint and Bone Laboratory, Fundación Jiménez Díaz, Madrid, Spain) is ongoing
Results: Here is presented the teaching material produced by the members of this EULAR task force in animal model and cadaver as a basis for learning the ultrasound-guided synovial biopsy technique.
Conclusion: The animal model and the cadaver, having the appropriate anatomical and musculoskeletal ultrasound knowledge, are useful for learning ultrasound-guided biopsy. As a complement, you can include the stay with an expert to face the problems of the technique with the real patient. The visualization of the produced video is a useful tool for this learning.

REFERENCES:

[1] Gerlag D, Tak PP. Synovial biopsy. Best practice & research. 2005;19:387-400
[2] Vordenbaumen S, Joosten LA, Friemann J, et al. Utility of synovial biopsy. Arthritis research & therapy. 2009;11:256.
[3] Bresnihan B, Pontifex E, Thurlings RM, et al. Synovial tissue sublining CD68 expression is a biomarker of therapeutic response in rheumatoid arthritis clinical trials: consistency across centers. The Journal of rheumatology. 2009;36:1800-1802.
[4] Kraan MC, van Kuijk AW, Dinant HJ, et al.Alefacept treatment in psoriatic arthritis: reduction of the effector T cell population in peripheral blood and synovial tissue is associated with improvement of clinical signs of arthritis. Arthritis and rheumatism. 2002;46:2776-2784.
[5] Tak PP. Analyzing synovial tissue samples. What can we learn about early rheumatoid arthritis, the heterogeneity of the disease, and the effects of treatment? J Rheumatol Suppl. 2005;72:25-26.
[6] van de Sande MG, Gerlag DM, Lodde BM, et al. Evaluating antirheumatic treatments using synovial biopsy: a recommendation for standardisation to be used in clinical trials. Annals of the rheumatic diseases. 2011;70:423-427.
[7] Vos K, Thurlings RM, Wijbrandts CA, et al. Early effects of rituximab on the synovial cell infiltrate in patients with rheumatoid arthritis. Arthritis and rheumatism. 2007;56:772-778.
[8] Saaibi DL, Schumacher HR, Jr. Percutaneous needle biopsy and synovial histology. Bailliere's clinical rheumatology. 1996;10:535-554.
[9] Koski JM, Helle M. Ultrasound guided synovial biopsy using portal and forceps. Annals of the rheumatic diseases. 2005;64:926-929.
[10] van Vugt RM, van Dalen A, Bijlsma JW. Ultrasound guided synovial biopsy of the wrist. Scand J Rheumatol. 1997;26:212-214.
[11] Kelly S, Humby F, Filer A, et al. Ultrasound-guided synovial biopsy: a safe, well-tolerated and reliable technique for obtaining high-quality synovial tissue from both large and small joints in early arthritis patients. Annals of the rheumatic diseases. 2013.

Disclosure of Interests: None declared
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SATURDAY, 15 JUNE 2019

13:45:00 – 14:45:00

HPR Highlight session

SP0212 **HIGHLIGHTS FROM THE SCIENTIFIC PROGRAMME**

Daniel Aletaha. *Medical University of Vienna, Department of Medicine III, Division of Rheumatology, Austria*

In this presentation we will review the most interesting findings from the scientific programme of this year's EULAR meeting for for Health Care Professionals.
Disclosure of Interests: Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB
DOI: 10.1136/annrheumdis-2019-eular.8414

SATURDAY, 15 JUNE 2019

13:45:00 – 14:45:00

PARE Highlight session

SP0213 **HIGHLIGHTS FROM THE SCIENTIFIC PROGRAMME**

Alexandre Sepriano. *Leiden University Medical Center, Rheumatology, Leiden, Netherlands*

This talk will cover highlights from the Congress Scientific Programme, encompassing a wide range of topics in the field of rheumatology
Disclosure of Interests: None declared
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Oral Presentations

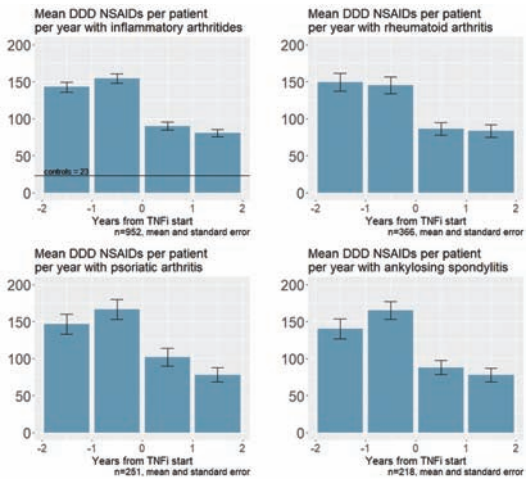
WEDNESDAY, 12 JUNE 2019

Best practices in spondyloarthritis

OP0001 THE PRESCRIPTION OF NSAIDS FOR PATIENTS WITH INFLAMMATORY ARTHRITIS IS ASSOCIATED WITH PATIENT BUT NOT PHYSICIAN ASSESSED DISEASE ACTIVITY MEASURES AND DECREASES WITH INITATION OF TNF INHIBITOR THERAPY

Olafur Palsson[1,2,3], Johan K Wallman[2,3], Thorvardur Jon Love[4,5], Meliha C Kapetanovic[2,3], Petur S Gunnarsson[6,7], Björn Gudbjornsson[1,5]. *[1]Centre for Rheumatology Research, University Hospital, Reykjavik, Iceland*; *[2]Lund University, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden*; *[3]Skåne University Hospital, Lund, Sweden*; *[4]University Hospital, Department of Science, Reykjavik, Iceland*; *[5]University of Iceland, Faculty of Medicine, Reykjavik, Iceland*; *[6]University of Iceland, Faculty of Pharmaceutical Sciences, Reykjavik, Iceland*; *[7]University Hospital, Hospital Pharmacy, Reykjavik, Iceland*

Background: TNFα-inhibitor therapy is effective in controlling several rheumatic diseases and has been shown to reduce pain. Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for treatment of pain and stiffness in inflammatory arthritides and are the first treatment line in axial spondyloarthritis.
Objectives: To study the prescriptions of NSAIDs in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) registered in ICEBIO and matched controls, and explore their relationship with disease activity measures. In addition, to explore the impact of initial TNFα-inhibitor therapy on NSAID prescription rates.
Methods: All patients receiving biologic DMARD therapy in Iceland for rheumatic diseases are registered in a nationwide database; ICEBIO. The Icelandic Directorate of Health operates a prescription database that includes over 90% of all drug prescriptions in Iceland. On February 1st2016 we extracted data for all patients with RA, PsA and AS from ICEBIO along with all filled prescriptions for NSAIDs made two years before and after the initiation of TNFα-inhibitor therapy. We then extracted NSAID prescriptions for five randomly selected individuals matched on age, sex, and calendar time of TNF inhibition for each patient.
Results: Data from 366 patients with RA, 218 with AS, 251 with PsA and 4760 controls was included. Control group was prescribed a mean of 23 defined daily doses (DDD) of NSAIDs per year. In total the ICEBIO patients were prescribed 6.7 times more DDDs of NSAIDs than the controls or a mean of 149 per year. After initiation of TNFα-inhibitor therapy the use of NSAIDs was reduced to a mean of 85 DDD per year, or 3.9 times that of the controls.
Among the patients with RA, consumption was reduced by 43% (mean 148 to 85 DDD/year), 47% in the AS group (154 to 83 DDD/year) and 43% in the PsA group (157 to 90 DDD/year). The 20% of patients who used the largest amounts of NSAIDs over the 4 year period reported worse visual analogue scale (VAS) pain scores (mean ±SD 65±20 to 60±23), VAS global health scores (70±19 to 65±23), and HAQ scores (1.19±0.64 to 1.03±0.67) when TNFα-inhibitor therapy was initiated compared to the rest of the ICEBIO group ($p<0.05$ by students t-test), though there was no statistically significant difference in the number of swollen (4.5±4.7 vs 4.2±4.4) or tender (5.4±4.8 vs 5.5±5.4) joints or in the physician global VAS assessment (56±17 vs 57±18).



Conclusion: Patients with inflammatory arthritidies requiring TNFα-inhibitor therapy use more NSAIDs than general population controls, but consumption is significantly reduced following the initiation of the first-line biologic drug. The patients with the highest NSAID use have worse patient reported outcome measures but physician outcome measures are similar, which may suggest a non-inflammatory etiology of the pain.
Disclosure of Interests: Olafur Palsson: None declared, Johan K Wallman Consultant for: Consultant for AbbVie, Celgene, Eli Lilly, Novartis, and UCB Pharma., Thorvardur Jon Love Consultant for: Received reimbursment from Celgene for speaking about guidelines for the treatment of psoriatic arthritis, Meliha C Kapetanovic: None declared, Petur S Gunnarsson: None declared, Björn Gudbjornsson: None declared
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OP0002 EARLY INFLAMMATORY BACK PAIN SERVICE – REDUCING TIME TO DIAGNOSIS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS – THE FIRST 8 YEARS

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Background: Specialist axial spondyloarthritis (axial SpA) clinics are advocated to promote early diagnosis and treatment and provide essential support and guidance to patients suffering with axial SpA[1]. In 2010, we set up an early inflammatory back pain service (EIBPS) to target early diagnosis and management to prevent the consequences of delayed diagnosis.
Objectives: We established an EIBPS to reduce time to diagnosis and initiation of biologic therapy. This was accompanied by an education campaign (Back on Track) to local GP's, allied health practitioners (AHP's)and secondary care colleagues and to the general public to focus raising awareness of Inflammatory Back Pain (IBP) and axial SpA.
Methods:

- Referred patients with suspected IBP were screened by a specialist physiotherapist.
- Each patient was assessed for IBP (Berlin Criteria) and other SpA features.
- Bloods including HLA–B27 were taken for those with IBP or suspected axial SpA.
- Sacroiliac Joint (SIJ) X–Rays were taken in suspected axial SpA patients and if normal spinal and SIJ MRI's taken.
- An educational campaign was undertaken with formal education on axial SpA for AHP's and doctors, in addition to a suite of promotional and training materials developed and disseminated.

Results: Between 2010-2018, 599 patients had an initial assessment appointment in the EIBPS. 312 (52%) were female, mean age 39.6 years (at data collection). Of the 599 referrals, 413 (69%) had symptoms of IBP and fulfilled the Berlin IBP criteria. These were referred for formal screening. 238 (40%) patients had confirmed axial SpA fulfilling ASAS criteria. Of these 238, 59 (10%) had a pre-existing diagnosis from another hospital. The remaining 179 (30%) patients received a new diagnosis, with 128 patients fulfilling radiographic axial SpA criteria and 51 patients fulfilling non-radiographic ASAS criteria. The time between the onset of back pain and diagnosis of axial SpA was 3.0 (0.3-30 years). Of those patients who fulfilled the criteria for biologic therapy, treatment was initiated within a mean 5.6 months of their initial EIBPS appointment.
Conclusion: Establishing an EIBPS with an awareness campaign has resulted in a significant reduction in time to diagnosis to a median of 3yrs, with biologic initiation within 5.6 months of their initial EIBPS appointment in appropriate patients. The long term advantage of early patient diagnosis and access to biologic therapy on reducing structural damage, and positive benefits in terms of functional, emotional and socioeconomic factors is well known[2]. We advocate the replication of our specialist EIBPS service within the UK.

REFERENCES:

[1] National Ankylosing Spondylitis Society. Looking Ahead: Best practice for the care of people with ankylosing spondylitis. 2010. Available at: http://www.nass.co.uk/campaigning/looking-ahead/. Last accessed: 23 May 2014.
[2] Weiß A, et al. Good correlation between changes in objective and subjective signs of inflammation in patients with short- but not long duration of axial spondyloarthritis treated with tumor necrosis factor-blockers. Arthritis Res Ther. 2014;16:R35.

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WEDNESDAY, 12 JUNE 2019

CPPD – a forgotten disease that requires more attention??!!!

OP0003 CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION IN A COHORT OF 52 PATIENTS WITH GITELMAN SYNDROME

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Background: Gitelman syndrome (GS) is a rare recessively inherited tubulopathy, caused by inactive mutations in *SLC12A3* gene encoding the thiazide-sensitive-sodium-chloride transporter. It is characterized by an hypokalemic metabolic alkalosis with hypomagnesemia and hypocalciuria. Calcium pyrophosphate (CPP) crystal deposition is frequently described in GS case-reports but its prevalence and clinical phenotype are unknown.
Objectives: The aim is to describe clinical, biological and radiological features of CPP in a cohort of patients with genetically proven GS.
Methods: All patients (pts) with genetically proven GS in the French national reference center of rare diseases were proposed to have a consultation with a senior rheumatologist. Demographic data, history of joint pain and flare and biology disorders were recorded. Other causes of CPP disease were systematically ruled out. CPP crystal deposition was assessed by X-rays (all peripheral joints and cervical spine) and ultrasonography (US) (wrist, knee, ankle joints and symptomatic joints). Patients with history of cervical pain underwent computed tomography (CT) of the full cervical spine from occipital bone to C1-T1 disk, including temporomandibular joints.
Results: Fifty-two GS pts (21 men, mean age 46.5± 12.2 years) have been examined by a rheumatologist. Almost all patients had an heterozygous mutation on SLC12A3 gene. Forty-four pts experienced joint pain (84.6%), 23 joint flares (44,2%) and 25 cervical pain (48.1%). X-rays were performed in 42 pts, US in 38 and CT in 23. CPP depositions were observed in 36 (85.7%), 27 (71.1%) and 15 pts (65.2%) by X-rays, US and CT, respectively. All techniques combined, chondrocalcinosis was discovered in 42 patients. Deposits occurred in knees (n=32), wrists (n=29), cervical spine (n=23), ankles and feet (n=22) and shoulders (n=16). CPP depositions were widespread involving at least 3 joints in 27 (55.1%) pts. In knees, CPP depositions involved menisci (n=24), hyaline cartilages (n=16) and ligament or joint capsule (n=15). Cervical spine CT demonstrated CPP deposition in vertebral discs (n=17), transverse ligament (n=13), other ligament (n=13), vertebral facets (n=3) and temporomandibular joints (n=5).
Patients with CPP crystal deposition in more than 3 joints were significantly older (52.8±10.5 years) than patients with 2 or 3 affected joints (40.8±11.6 years, p=0.02) or patients without any affected joint (36.6±8.1 years, p=0.001). They were also more symptomatic with significantly more joint flares (p<0.0001). Magnesemia was inversely correlated with the number of affected joints: patients with >3 or 2-3 affected joints had a significantly lower magnesemia (0.57±0.1 and 0.59 ±0.1 mM, respectively) than patients with only 1 affected joint (0.83±0.1 mM). CPP crystal deposition was not associated with potassium level.

Table 1. Patients characteristics

Male sex, n (%)	21 (40.4)
Mean age ± SD (years)	46.5± 12.2
Heterozygous mutation on SLC12A3 gene, n (%)	36 (69.2)
Arthralgia, n (%)	44 (84.6%)
Recurrent joint flares, n (%)	23 (44.2%)
Cervicalgia, n (%)	25 (48.1%)
Kaliemia at GS diagnosis, mean ± SD (mM)	2.7± 1.1
Magnesemia at visit, mean ± SD (mM)	0.6± 0.3
Calcemia at visit, mean ± SD (mM)	2.4± 1.0

Conclusion: CPP crystal deposition occurred in more than 80% of patients with GS, was widespread and often symptomatic. The most affected sites were wrists, knees and the cervical spine. CPP crystal deposition was associated with long-standing GS, older age and lower serum magnesium level. Further studies are necessary to understand how GS favors CPP crystal deposition.
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OP0004 IS DUAL-ENERGY COMPUTED TOMOGRAPHY ABLE TO IDENTIFY EARLY-STAGE CALCIUM CRYSTAL DEPOSITION IN VIVO? INITIAL CLINICAL EXPERIENCE IN 132 PATIENTS WITH AND WITHOUT KNEE CHONDROCALCINOSIS

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Background: Calcium crystals are below the spatial resolution limit of currently available imaging techniques, and only aggregates can be identified in vivo at more advanced stages of the disease. Although dual-energy computed tomography (DECT) has the potential to discriminate the various calcium crystal types owing to its biochemical signature assessment capabilities, it remains to be seen whether this technique would be able to identify early-stage calcium crystal deposition in vivo.
Objectives: We aimed to assess whether DECT was able to identify calcium crystal deposition in the knee prior to the onset of chondrocalcinosis (CC), more specifically if DECT attenuation properties differed between patients with CC and controls without CC on DECT.
Methods: Consecutive patients with clinical suspicion of crystal arthritis and knee DECT scans were retrospectively reviewed and assigned to either CPPD (n=50) or control (n=82) groups depending on the presence/absence of CC on DECT. Regions of interest (ROI) were drawn in the following knee zones on a specific coronal DECT image: hyaline cartilage of the patellofemoral and medial and lateral tibiofemoral joint spaces, as well as medial and lateral menisci. The presence or absence of CC in these predefined ROIs were noted. Five DECT parameters were obtained: CT numbers (HU) at 80 and 140 kV, dual-energy index (DEI), electron density (ρe), and effective atomic number (Zeff). Knee zones were compared between groups using mixed linear models adjusting for age and the presence of osteoarthritis. A subgroup analysis was performed excluding zones were calcifications were visible on DECT images.
Results: Menisci from CPPD patients and controls had a mean Zeff of 7.9±0.4 and 7.6±0.2 (p<0.0001), mean ρe of 85±23 and 74±14 (p<0.0001) and mean DEI of 0.0036±0.0046 and -0.0001±0.0042 (p<0.001), respectively. DEI values differed significantly between patients and controls in tibiofemoral cartilage (0.0026 ±0.0041 in CPPD and 0.0023±0.0045)(p=0.013) but not in patellofemoral cartilage (p=0.57). When considering only the various regions from CPPD patients without CC in the selected ROIs, the ρe in menisci (n=79/185) did not differ between groups and differences in Zeff (p=0.15) and DEI (p=0.09) did not reach statistical significance after adjustment for age and osteoarthritis.
Conclusion: DECT has the potential to discriminate between meniscal fibrocartilage and articular cartilage of CPPD patients and controls in predefined regions of interest. DECT's ability to improve the sensitivity of conventional CT to identify invisible CPP deposits remains unclear as the trend did not reach statistical significance.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7383

WEDNESDAY, 12 JUNE 2019

Comorbidities in psoriatic arthritis

OP0005 INCIDENCE OF OVERALL AND SITE-SPECIFIC CANCERS IN TNF INHIBITOR TREATED PATIENTS WITH PSORIATIC ARTHRITIS: A POPULATION-BASED COHORT STUDY FROM 4 NORDIC COUNTRIES

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Background: Tumour necrosis factor inhibitors (TNFi) effectively reduce inflammation in Psoriatic arthritis (PsA). However, a possible association between treatment with TNFi and an increased cancer risk has previously been suggested.

Objectives: To investigate the risk of cancer in TNFi treated PsA patients compared with standardized rates from the general population in Denmark, Finland, Iceland and Sweden.
Methods: TNFi-treated PsA patients were followed from first registration with TNFi-treatment in ARTIS (Sweden), DANBIO (Denmark), ICEBIO (Iceland) or ROB-FIN (Finland) and linked to the national Cancer Registry in each country. Patients with a cancer history prior to start of follow-up were excluded. We investigated the risk of primary cancer among TNFi-treated PsA patients compared with general population cancer rates standardized to age, sex and calendar period within each country. Standardized incidence ratios (SIRs) were estimated for each country and pooled SIRs were subsequently calculated for both any cancer and site-specific cancers of interest.
Results: A total of 5218, 2039, 270 and 526 patients were registered as ever TNFi-treated in ARTIS, DANBIO, ICEBIO and ROB-FIN, respectively, contributing a total of 44 041 patient years of follow-up across all 4 countries.
For all cancers, the SIRs of TNFi-treated patients from ARTIS, DANBIO, ICEBIO and ROB-FIN were 0.94 (0.80 to 1.10), 0.99 (0.77 to 1.26), 1.71 (0.88 to 2.99) and 1.28 (0.82 to 1.90), respectively. The number of observed and expected cancers and the SIRs of any and selected site-specific cancers are listed in **table 1**.

Table 1. Standardized incidence ratios (SIR) of TNFi-treated patients from 4 Nordic countries compared with the general population.

	Observed cancers	Expected cancers	SIR (95% confidence interval)
All cancers	282	281.6	1.00 (0.89 to 1.13)
Colorectal	32	26.5	1.21 (0.85 to 1.71)
Hodgkin's and non-Hodgkin's lymphoma	21	11.4	1.84 (1.20 to 2.82)
Lung	20	25.4	0.79 (0.51 to 1.22)
Malignant melanoma	20	18.6	1.07 (0.69 to 1.66)
Pancreas	8	6.6	1.21 (0.60 to 2.41)
Brain	7	7.4	0.95 (0.45 to 1.99)
Female breast	58	48.4	1.20 (0.93 to 1.55)
Corpus uteri	6	9.0	0.67 (0.30 to 1.49)
Prostate	34	48.8	0.70 (0.50 to 0.98)

Only included sites with >5 cancer outcomes.

Conclusion: Our results suggest that the overall cancer risk for TNFi-treated PsA patients is not increased compared to the general population. Further analysis of the risk of malignant lymphomas will inform on whether the increased risk we observed is attributed to the PsA disease or treatment with TNFi.
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Disclosure of Interests: Christine Ballegaard Speakers bureau: Janssen Pharmaceuticals., Karin Hellgren: None declared, René Cordtz: None declared, Bénédicte Delcoigne: None declared, Björn Gudbjornsson: None declared, Thorvardur Jon Love Consultant for: Received reimbursment from Celgene for speaking about guidelines for the treatment of psoriatic arthritis, Kalle Aaltonen: None declared, Dan Nordström Grant/research support from: MSD, Pfizer, Consultant for: AbbVie, BMS, MSD, Novartis, Roche, Pfizer, UCB, Speakers bureau: Novartis, UCB, Sella Aarrestad Provan Consultant for: Novartis, Speakers bureau: Lilly, Johan Askling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer., Kristian Zobbe: None declared, Lars Erik Kristensen Grant/research support from: UCB, Biogen, Janssen Pharmaceuticals, and Novartis, Consultant for: Consultant for AbbVie, Amgen, Biogen, BMS, Celgene, Eli Lilly, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB Pharma., Speakers bureau: Pfizer, AbbVie, Amgen, UCB, BMS, Biogen, MSD, Novartis, Eli Lilly and Company, and Janssen Pharmaceuticals, Lene Dreyer Consultant for: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: UCB, MSD, Eli Lilly and Janssen Pharmaceuticals.
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OP0006 IMPROVEMENT OF ENDOTHELIAL DYSFUNCTION AND INFLAMMATION IN PSORIATIC ARTHRITIS: IMPROVE – PSA STUDY

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Background: Cardiovascular (CV) disease is leading cause of death in Psoriatic Arthritis (PsA)[1]. Chronic inflammation in PsA is associated with vascular endothelial dysfunction and enhanced CV risk. However, the therapeutic options to treat this enhanced CV risk are limited.
Objectives: To investigate the impact of Olmesartan and Rosuvastatin on endothelial dysfunction and inflammation in PsA.
Methods: 54 PsA patients randomized to receive 24 weeks of treatment with Olmesartan (OLME) (10mg/day, n=18), Rosuvastatin (Rvs) (10mg/day, n=18), and placebo (PL) (n=18) as an adjunct to existing stable antirheumatic drugs. FMD assessed by AngioDefender. EPCs estimated by flow cytometry. Serum nitrite, TBARS, ICAM-1, VCAM-1 and lipids levels estimated at baseline and after treatment. Inflammatory measures included DAS28, DAPSA, ESR and CRP, pro-inflammatory cytokines. Quality of life and CV 10-year risk (SCORE high risk charts) were estimated using standard tools.
Results: Baseline levels of FMD and EPC population were impaired indicating endothelial dysfunction. Basal concentrations of inflammatory markers, pro-inflammatory cytokines and markers of endothelial dysfunction were elevated among three groups. After 24 weeks treatment, FMD improved significantly in rosuvastatin and olmesartan group as compared to placebo. {OLME vs. PL ($p \leq 0.01$), Rvs vs. PL ($p < 0.01$), Rvs vs. OLME ($p = 0.10$)} (Fig.1A). EPCs and nitrite (Fig.1B) levels improved significantly in both rosuvastatin and olmesartan groups. Significant reduction found in ICAM-1 after rosuvastatin treatment ($p < 0.01$) where as olmesartan significantly decreased VCAM-1 ($p = 0.04$) and TBAR levels ($p \leq 0.05$). Both rosuvastatin and olmesartan resulted in significant reductions of DAS28, DAPSA, ESR, CRP, IL-6 (Fig.1C) and TNF-α (Fig.1D) as compared to placebo. There was a significant reduction in SCORE, HAQ-DI and SF-36 (PH) score after treatment with rosuvastatin and olmesartan.

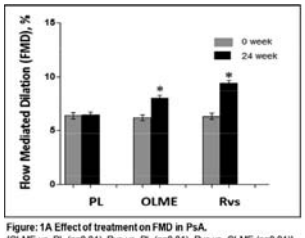


Figure: 1A Effect of treatment on FMD in PsA. {OLME vs. PL (p=0.01), Rvs vs. PL (p=0.01), Rvs vs. OLME (p=0.01)} after 24 weeks.

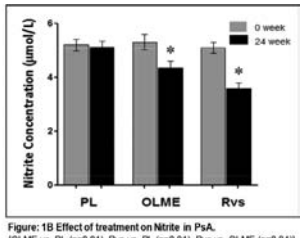


Figure: 1B Effect of treatment on Nitrite in PsA. {OLME vs. PL (p=0.01), Rvs vs. PL (p=0.01), Rvs vs. OLME (p=0.04)} after 24 weeks.

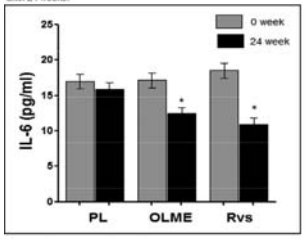


Figure: 1C Effect of treatment on IL-6 in PsA. {OLME vs. PL (p=0.02), Rvs vs. PL (p=0.01), Rvs vs. OLME (p=0.40)} after 24 weeks.

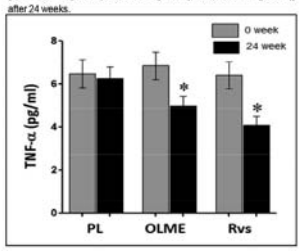


Figure: 1D Effect of treatment on TNF-α in PsA. {OLME vs. PL (p=0.02), Rvs vs. PL (p=0.01), Rvs vs. OLME (p=0.37)} after 24 weeks.

Conclusion: Olmesartan and rosuvastatin improve endothelial dysfunction, inflammation, CV risk and quality of life in PsA patients. Olmesartan and Rosuvastatin lower the proinflammatory cytokines, especially TNF-α, that down regulates production of CRP, adhesion molecules and nitric oxide which in turn improves endothelial dysfunction. Both drugs also decrease nitrite concentration and improve the EPC population in PsA patients. The augmentation of EPCs by olmesartan and rosuvastatin represents a fascinating new approach for the management of PsA. However, Rosuvastatin in addition also favourably impacted ICAM-1 and lipid abnormalities. In contrast, olmesartan has beneficial effect on blood pressure. Thus, both rosuvastatin and olmesartan demonstrate immunomodulatory, vasculoprotective and cardioprotective potential in PsA mediated through anti-proinflammatory cytokine action.

REFERENCE:
[1] Haroon M, Gallagher P, Heffernan E and FitzGerald O. The Journal of Rheumatology. 2014; 41:7.

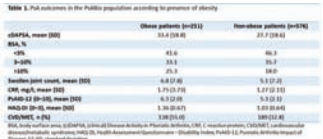
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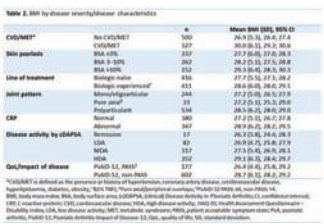
OP0007

HIGH BODY MASS INDEX (BMI) IN PSORIATIC ARTHRITIS (PSA) IS ASSOCIATED WITH HIGHER DISEASE ACTIVITY IN JOINTS AND SKIN, IMPAIRED QUALITY OF LIFE AND MORE DISABILITY: RESULTS FROM THE PSABIO STUDY

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Background: The link between obesity and disease activity in PsA is unclear. Obesity has been associated with a poorer therapeutic response and higher treatment discontinuation rates in patients with PsA being treated with tumour necrosis factor inhibitors (TNFi). Recent data confirm the favourable effect of weight reduction on these factors. There are no data available for other biologics.
Objectives: To investigate the relationship between baseline overweight/obesity and disease activity, patient-reported outcomes and disability, in a large real-world cohort of patients with PsA starting biologic treatment with either ustekinumab (UST) or TNFi.
Methods: The PsABio study (ClinicalTrials.gov: NCT02627768) is an ongoing observational study evaluating efficacy, tolerability and persistence of 1st, 2nd- and 3rd-line UST or TNFi in PsA in 8 European countries[1] when introduced as part of standard clinical care. Baseline data of the study population were collected and analysed for BMI, disease activity (cDAPSA, psoriasis BSA), patient-perceived impact (PsAID-12), disability (HAQ-DI) and presence or history of CVD/MET. Descriptive statistics on available data and 3 exploratory multiple regression models are shown, to investigate the relationship of cDAPSA, PsAID-12 and HAQ-DI (dependent variables) with BMI, adjusted for age, sex, smoking, BSA, CRP, disease duration and biologic treatment.
Results: In all, 917 patients were included, starting either UST (n=450) or TNFi (n=467): mean (SD) age 49.7 (12.5) years, 55.5% female. The mean (SD) baseline BMI (N=827) was 28.1 (5.8) kg/m^2, with 40.0% and 30.4% in BMI categories overweight (>25–30) and obese (>30), respectively. In univariate analyses, obesity was linked to worse outcomes (Table 1). More severe disease was associated with higher BMI (Table 2). In multiple regression modelling, higher BMI was independently linked to higher cDAPSA (BMI: β=0.09 p=0.026); to higher patient-perceived disease impact measured by PsAID-12 (BMI: β=0.16, p<0.0001) and to higher disability measured by HAQ-DI (BMI: β=0.21, p<0.0001).
Conclusion: This multi-country routine-care PsA cohort of patients in need of biologic treatment confirms the high prevalence of overweight/obesity and indicates an independent association between high BMI and disease activity as well as patient-reported impact of disease and disability. These results emphasize the need for lifestyle-directed approaches in PsA, such as overweight management in parallel with joint- and skin-focused treatment.





REFERENCE:
[1] Gossec L, et al. Ann Rheum Dis. 2018;77(Suppl):A1033.

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OP0008

SUSTAINED LOW DISEASE ACTIVITY AFTER WEIGHT LOSS TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS AND OBESITY; A 12-MONTHS FOLLOW-UP

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Background: Obesity is over-represented in patients with psoriatic arthritis (PsA) and associated with increased disease activity. We have previously shown in 41 patients with PsA (Caspar criteria) and obesity (body mass index BMI $\geq$33 kg/m^2) that weight loss treatment with Very Low Energy Liquid Diet (VLED), 640 kcal/day during 12-16 weeks, followed by a structured reintroduction of an energy restricted diet resulted in a median weight loss of 18.6% and concomitantly a significant improvement of the disease activity in joints, entheses and skin. At 6-months follow-up Psoriatic Arthritis Response Criteria (PsARC) was reached by 46.3% and American College of Rheumatology (ACR) 20, 50, 70 criteria for treatment response by 51.2%, 34.1% and 7.3% of the patients.
Objectives: To study the effects of the weight loss treatment on disease activity in longer term (12 months) in patients with PsA and obesity, when the patients are on a weight loss maintenance diet.
Methods: The patients were assessed with 66/68 joints count, Leeds enthesitis index, body surface area (BSA), questionnaires, CRP and BMI at the 12-months follow-up.
Results: Totally 39 PsA patients, median age 56 (IQR 49-63) years, 64% women were examined at the 12-month follow-up. The median weight reduction since baseline was 16.1 kg (IQR 10.5–22.8) or 16.0% (10.5–22.4). A majority of the disease activity parameters remained significantly improved (Table). At the 12-months follow-up PsARC was still fulfilled by 35.9% (n=14) and ACR 20, 50, 70 response criteria by 53.8% (n=21), 35.9% (n=14) and 15.5% (n=6) respectively.

Conclusion: Weight loss treatment with VLED in patients with PsA and obesity was associated with sustained weight reduction and lowered disease activity at 12-months follow-up.

N=39	Baseline Median (IQR)	12-months Median (IQR)	p-value
Weight, kg	106 (93.5–112.5)	87.5 (80.6–95.5)	<0.001
Body Mass Index kg/m^2	35.2 (33.9–37.9)	30.5 (28.1–32.9)	<0.001
Tender joints 68, count	4 (1–14)	3 (0-6)	0.001
Swollen joints 66, count	0 (0–1)	0 (0–0)	0.015
Leeds enthesitis index	1 (0–4)	0 (0–2)	<0.001
Psoriasis Body Surface Area, %	0.75 (0–2)	0.25 (0–1)	0.018
CRP, mg/L	5 (3–9)	2 (1–5)	0.009
VAS Pain, mm	30 (17–62)	29 (10–55)	0.251
VAS Global health, mm	34 (18–58)	23 (9.5–38)	0.009
VAS Fatigue, mm	57 (21–67)	32.5 (16–62)	0.007
HAQ, score	0.63 (0.13–1.00)	0.25 (0–0.63)	0.002
DAS-28CRP, score	2.9 (2.2–3.5)	2.2 (1.7–3.0)	<0.001
DAPSA, score	15.3 (6.5–28.2)	10.2 (4.2–16.6)	0.001

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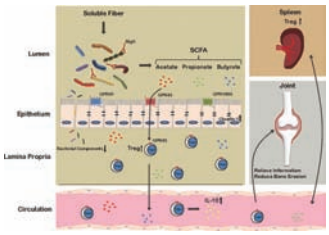
WEDNESDAY, 12 JUNE 2019

Environmental influences on disease development

OP0009 **RESISTANT STARCH INTAKE ALLEVIATES COLLAGEN-INDUCED ARTHRITIS IN MICE BY MODULATING GUT MICROBIOTA AND PROMOTING SCFA PRODUCTION**

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Background: Dietary intervention has been an auxiliary therapy in many diseases treatment[1]. Increasing evidences indicate that dietary compositions vary in their impacts on gut microbial constitution and function capable of affecting the systemic immune status of the host[2, 3]. Recently, a high fiber diet (HFD) receives close attention due to its effective improvement in symptoms in metabolic diseases and inflammatory diseases. It is also reported that intake of fruits and vegetables can improve the clinical symptoms of rheumatoid arthritis (RA) to a moderate extent. However, it remains unclear how a high fiber diet cross-talks with gut flora and RA initiation or remission.
Objectives: To systemically evaluate the effect of a high fiber diet mainly composed of resistant starch, a new resource of soluble fiber, on collagen-induced arthritis (CIA) mice and gut microbial composition. Meanwhile, the relative mechanisms was explored in this study.
Methods: CIA was established by immunization mice with collagen on day 0 and 21. Arthritis severity was evaluated by clinical score, histological staining and micro CT. Fresh stool was collected and gut microbiota analyses were performed by 16s RNA sequencing. Gut barrier dysfuction was evaluated by detecting the genes expression of intestine epithelial tight junction protein Zonulin-1 (ZO-1), Claudin-1 and Occludin. Flow cytometry was applied to measure the proportions of T cell subsets in various immune organs. Short chain fatty acids (SCFA) levels in the circulation and their receptor GPR41, 43 and 109A gene expressions were examined via GC-TOFMS and real-time PCR, respectively.
Results: High fiber feeding accelerated the arthritis remission in CIA mice, evidenced by the inflammatory cell infiltration reduction in the joints and bone erosion improvement. Th1, 2 and 17 cell population were not affected by HFD. While, regulatory T cell (Treg) percentages in the intestinal lamina propria and spleen were significantly higher in HFD-treated CIA mice, accompanied with an increase of interleukin-10 (IL-10) in the blood. Importantly, HFD modified gut dysbiosis in CIA mice, in particular, promoted the ratio of *Bacteroidetes* to *Firmicutes* and the prevalence of *Bacteroides acidifaciens*. Claudin-1 gene expression in the intestine was significantly increased with the gut flora alteration. Meanwhile, HFD-treated CIA mice had much higher levels of SCFAs in the blood and GPR43 gene expression in the intestine. Blocking SCFAs production by adding hops extract β-acids into drinking water completely eliminated the beneficial effect of HFD on joint swelling, bone erosion and Treg cell expansion in CIA mice.
Conclusion: Intake of resistant starch drives the significant modifications of the gut microbial composition and SCFAs production capable of triggering Treg cells differentiation and IL-10 production, which favorable to the alleviation of RA.



REFERENCES:
[1] Complex Relationships Between Food, Diet, and the Microbiome. Pace LA, Crowe SE. Gastroenterol Clin North Am. 2016 45:253-65.
[2] The Gut Microbiota, Food Science, and Human Nutrition: A Timely Marriage. Barratt MJ, Lebrilla C, Shapiro HY, Gordon JI. Cell Host Microbe. 2017 22:134-141.
[3] Food and microbiota in the FDA regulatory framework. Green JM, Barratt MJ, Kinch M, Gordon JI. Science. 2017 357:39-40.

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Pharmaceutical pipeline in OA

OP0010 **CARTILAGE THICKNESS MODIFICATION WITH SPRIFERMIN IN KNEE OSTEOARTHRITIS PATIENTS TRANSLATES INTO SYMPTOMATIC IMPROVEMENT OVER PLACEBO IN PATIENTS AT RISK OF FURTHER STRUCTURAL AND SYMPTOMATIC PROGRESSION: POST-HOC ANALYSIS OF THE PHASE II FORWARD TRIAL**

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Background: Results from the 5-year Phase II FORWARD study showed significant dose-dependent modification of total femorotibial joint (TFTJ) cartilage thickness change with sprifermin at 2 and 3 years, by quantitative MRI. Total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores improved by ~50% in all treatment groups, including placebo (PBO). Selection of a patient (pt) subgroup with higher pain scores and lower joint space width (JSW) at baseline (BL), to identify pts who are at risk of further structural and symptomatic progression, may facilitate better WOMAC discrimination.
Objectives: Post-hoc analysis to evaluate cartilage thickness changes and symptomatic outcomes in an "at risk" subgroup of pts (BL medial or lateral minimum [m]JSW 1.5–3.5 mm and BL WOMAC pain score of 40–90).
Methods: Pts in FORWARD were randomized 1:1:1:1:1 to: sprifermin 100 µg every 6 months (q6mo); 100 µg q12mo; 30 µg q6mo; 30 µg q12mo; and PBO. The treatment period was 2 years, with an extended follow up at 3 years. Post-hoc analysis was conducted in the "at risk" subgroup.
Treatment effects were estimated using a repeated measures model, controlling for BL, treatment, time, country and treatment by time interaction. Linear dose-effect trend tests were performed exploratively at each timepoint. Confidence intervals (CIs) were adjusted for multiplicity of treatments using Dunnett adjustment.
Results: 161/549 (29%) pts met criteria for the "at risk" subgroup. In this subgroup, BL characteristics were balanced between treatment arms. Pts in the PBO arm had more cartilage loss at 2 and 3 years vs the modified intent-to-treat (mITT) PBO arm (mean change from BL in mm [SD]: Year 2 -0.05 [0.10] vs -0.02 [0.07]; Year 3 -0.07 [0.09] vs -0.05 [0.07]), but TFTJ net cartilage modification with sprifermin 100 µg q6mo vs PBO was similar (adjusted mean difference from PBO [95% CI] in the at risk subgroup vs the mITT group: Year 2 0.06 [0.01, 0.11] vs 0.05 [0.02, 0.08]; Year 3 0.05 [-0.01, 0.12] vs 0.05 [0.02, 0.09]). Having both medial or lateral mJSW 1.5–

3.5 mm AND pain score ≥40 at BL led to greater differentiation in WOMAC total and pain scores for sprifermin 100 μg q6mo vs PBO than having either BL characteristic alone. At Year 3 (18 mos after last injection), the exploratory dose-effect trend test had a nominal p-value of <0.05 (**Fig 1; Table 1**).

Conclusion: Despite substantial structural and symptomatic progression in the "at risk" subgroup, structural improvement with sprifermin was maintained, and WOMAC score improvements vs PBO increased over time and were significant at Year 3. This supports further investigation of sprifermin as a potential disease-modifying osteoarthritis drug in a targeted population where structural improvement may translate into symptomatic benefit vs PBO within a reasonable timeframe.

Table 1. Observed and adjusted mean difference [95% CI] in WOMAC pain scores for sprifermin vs PBO in the "at risk" subgroup

	Sprifermin 100 μg q6mo (N=33) vs PBO (N=34)		
	Obs mean diff [95% CI]	Adj mean diff [95% CI]	Trend test* (nominal p value)
Y1	-5.81 [-15.96, 4.35]	-3.65 [-15.73, 8.43]	>0.05
Y2	-10.45 [-22.76, 1.85]	-5.82 [-18.87, 7.23]	>0.05
Y3	-14.51 [-26.16, -2.85]	-8.75 [-22.42, 4.92]	**<0.05**

*Across 4 sprifermin groups and PBO

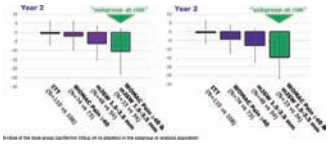


Figure 1. Observed mean differences [95% CI] in WOMAC pain scores for sprifermin 100 μg q6mo vs PBO across different risk subgroups at 2 and 3 years

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OP0011

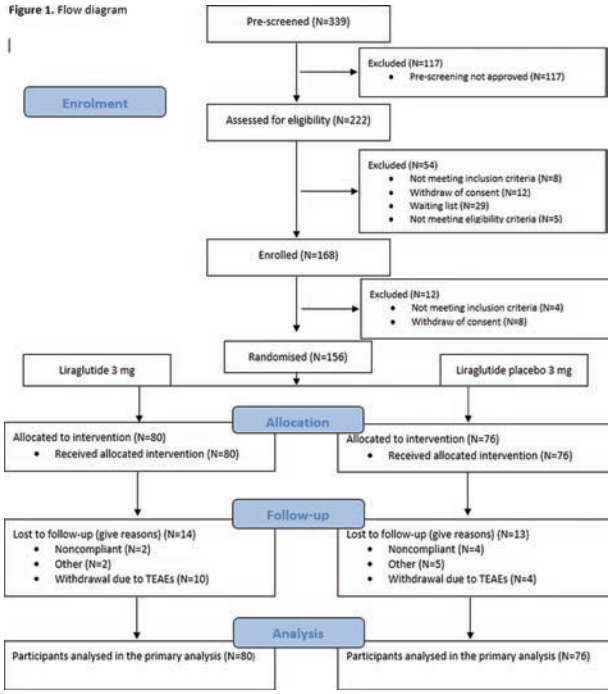
EFFECT OF LIRAGLUTIDE ON BODY WEIGHT AND PAIN IN THE TREATMENT OF OVERWEIGHT AND KNEE OSTEOARTHRITIS: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

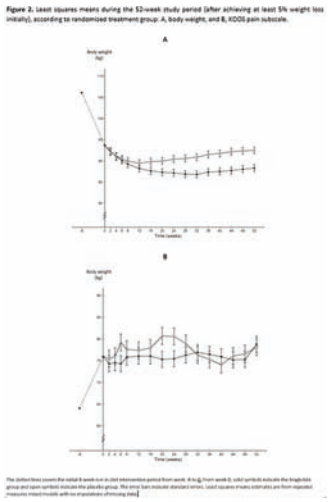
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Background: Weight loss is recommended as treatment of concomitant knee osteoarthritis (OA) and overweight. The GLP-1 receptor agonist liraglutide has been shown effective in maintaining or even further reducing weight loss, but the compound has not been tested in a population of patients with overweight and knee OA.

Objectives: The objective of this trial was to investigate if liraglutide in a 3 mg/day dosage was effective in maintaining weight loss and symptomatic effects 52 weeks after an initial 8-week dietary-based weight loss intervention dosing in patients with overweight and knee OA.

Methods: Patients with overweight or obesity and knee OA participated in a randomised, double blind, placebo-controlled, parallel group, single-centre trial. Patients were provided an initial 8-week run-in diet intervention (week -8 to 0) including a low-calorie diet from Cambridge Weight Plan and dietetic counselling. At week 0 patients who had lost at least 5% of their initial body weight were randomised to liraglutide 3 mg/day or placebo for 52 weeks. The co-primary outcomes were changes in body weight and the KOOS pain subscale from week 0 to 52. Trial registration: NCT02905864. Analyses were based on the intention-to-treat population.





Results: 168 patients (Kellgren-Lawrence grade 1-3) were enrolled in the initial 8-week diet intervention and 156 patients were randomised (Figure 1). Before randomisation the 156 patients had lost 12.46 kg (SD:3.82) (≈12%) and improved in KOOS pain corresponding to 11.86 points (SD:15.13) (≈19%). Baseline characteristics were similar in the intervention and control groups. From baseline to 52 weeks there was a statistically and clinically significant difference in the weight loss between the liraglutide and the placebo groups (mean -2.76 and 1.17 kg, respectively; group difference, 3.93 kg; 95%CI -6.85 to -1.02; p=0.008), there was no difference between groups in change in KOOS pain (mean changes: 0.35 and

-0.55 points, respectively; group difference, 0.89 points; 95%CI -3.89 to 5.68; p=0.713). Week 52 least squares means for body weight and KOOS pain showed similar results (Figure 2). 4 patients in the intervention and 4 patients in the control groups experienced serious adverse events, and no deaths were observed.
Conclusion: In overweight patients with knee OA, an 8-week low-calorie diet intervention significantly reduced body weight and knee pain. Liraglutide treatment added after the initial diet-induced weight loss provided further weight loss over 1 year but did not reduce knee pain any further compared to placebo.
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WEDNESDAY, 12 JUNE 2019

What's new: Latest news on biological treatment

OP0012 EFFECTIVENESS OF TNFI AFTER A FIRST SWITCH IS LOWER IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: A LONGITUDINAL ANALYSIS OF THE DESIR COHORT

Marion Pons[1,2], Sylvie Chevret[2], Karine Briot[1,2], Maria-Antonietta D'agostino[3], Christian Roux[1,2], Maxime Dougados[1,2], Anna Moltó[1,2]. *[1]University Paris Descartes, Cochin Hospital, Rheumatology, Paris, France*; *[2]INSERM U-1153, CRESS Paris-Sorbonne, Paris, France*; *[3]Ambroise-Paré Hospital, Boulogne-Billancourt, France*

Background: Some contradictory data has been reported on the effectiveness of a second and third line of TNFi in early axial spondyloarthritis (axSpA).
Objectives: To evaluate the effectiveness after a first and second TNFi switch, in real life conditions, over 5 years of follow-up in an early axSpa population.
Methods: Observational prospective French cohort (DESIR) with 5 years of follow-up, including 708 TNFi-naïve early axSpA patients. Study visits were scheduled every 6 months in the first two years of follow up then yearly up to 5 years. Treatment (TNFi or other) was at the discretion of the treating rheumatologist's. The characteristics of patients who received a second and a third TNFi were compared to those who never switched. Effectiveness was defined by the drug survival of the first, second and third TNFi were estimated by the Kaplan-Meier method, and compared using the log-rank test.
Results: Of the 708 patients included in the analysis, 258 (36.4%) patients initiated a first TNFi during the 5 years of follow up. Of these, 127/258 (49.2%) switched to a second TNFi, and among them 59/127(46.5%) switched to a third TNFi. Patients who switched to a second or a third TNFi were more frequently older, predominantly females, HLA-B27 negative, with MRI and radiographic sacroiliitis negative, without history of peripheral arthritis, and with higher BASFI and BASDAI scores at baseline of the DESIR cohort (see table). Estimated median drug survival for the first, second and third TNFi was 21.7 months [95%CI 17.6-33.6], 18.8 months [95%CI 15.1-24.4] and 25.0 months [95%CI 11.8-NA] respectively. Drug survival was significantly extended for the first TNFi compared to the second one (p=0.04), but no differences were observed between the 2nd and the 3rd TNFi.
Conclusion: Our study suggests a poorer TNFi effectiveness after a first switch in real-life conditions in early axial spondyloarthritis.

Baseline characteristics	Patients remaining in their first TNFi N=88	Patients switching to a 2nd TNFi N=127	Patients switching to a 3rd TNFi N=59
Age (years)	33.6(9.4)	35.3(8.7)	35.4(8.5)
Sex (male)	52(59.1)	40(31.5)	17(28.8)
HLA-B27 positive	57(64.8)	62(48.8)	26(44.1)
MRI sacroiliitis positive	46/85(55.1)	39/125(31.2)	16/57(28.1)
Radiographic sacroiliitis positive	27/85(31.8)	17(13.4)	9(15.3)
History of arthritis	31(35.2)	37/125(29.6)	17/58(29.3)
BASDAI (range 0-10)	4.5(1.8)	5.9(1.5)	6.0(1.4)
BASFI (range 0-10)	3.1(2.1)	4.6(2.1)	4.8(2.1)

Disclosure of Interests: Marion Pons: None declared, Sylvie Chevret: None declared, Karine Briot Consultant for: Karine Briot has received consultancy honoraria and conference fees from UCB, Amgen, Lilly and MSD, Maria-Antonietta d'Agostino: None declared, Christian Roux Grant/research support from: Alexion, Amgen, UCB, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Anna Moltó: None declared
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OP0013-PARE AFLAR'S – FRENCH LEAGUE AGAINST RHEUMATISM –POSITION AND PATIENT INFORMATION ACTION ABOUT BIOSIMILAR MEDICINES IN FRANCE

Laurence Carton[1], Claire Cardon[1], Francoise Alliot Launois[1], Gerard Chales[1], Brigitte Liesse[1], Laurent Grange[2,3], PATIENT's of AFLAR. *[1]Association Française de Lutte Antirhumatismale A.F.L.A.R, Paris, France*; *[1]Association Française de Lutte Antirhumatismale A.F.L.A.R, Paris, France*; *[3]University hospital of Grenoble Alpes/SUD hospital, Rheumatology, Échirolles, France*

Background: 20 years after biotherapies were introduced in rheumatic diseases treatment in France, biosimilars are a new medical and economic issue in terms of therapeutic opportunities, and innovative treatment spreading and development. Patients' rights - quality of life, information on treatment and safety - as well as public health cost management, medical and other caregivers 'practices are involved.
Objectives: AFLAR wants to play an active role in these fields, as about one million of patients with inflammatory rheumatic diseases, and next other diseases, are concerned.
Methods: AFLAR's patient led board (1), medical and scientific experts and especially expert patients have been working together to:

1. state AFLAR's position about biosimilars
2. define the most adapted association's actions in the field of biosimilars
3. create the most proper tool to inform and empower patients to their rights, especially in the field of treatment efficacy and safety.

Results: A position paper leading to a press release dated Dec. 7th, 2018 prior to national rheumatology medical congress opening has been achieved. An informative tool to be used for shared medical decision when biosimilars are involved, is currently in progress. AFLAR'S position on biosimilars includes 2 statements and 6 advices addressed to patients, caregivers and other stakeholders:
Statements:

1. Biosimilars are a medical and healthcare cost reduction effective solution in rheumatic diseases treatment;
2. Biosimilars have scientifically proved their efficacy and safety in past and ongoing studies; drug safety monitoring is ensured by national and European drug safety agencies.

Advices:

1. Further continuous clinical post–marketing studies should be achieved, and their results easily available to patients.
2. Patient should be properly informed each time a biosimilar is proposed if has not been tested versus original biotherapy in his/her own specific disease
3. Biosimilar drug can be prescribed for cost reduction reason as initial biotherapy treatment, when not contraindicated
4. Blind random switch from originator to biosimilar and among biosimilar products should not be done, based on precautionary principle
5. Patient should be precisely informed of product with biosimilar name (not only international non–proprietary name), and batch number, as this allows

mandatory pharmacovigilance by professionals and patients. As per law (2) and professional ethics, patient preference and right to informed consent must prevail.
6. Self–assessment surveys, and patient reported outcomes using studies, should be encouraged. These are facilitated by new information technologies practices and devices.

Conclusion: The information tool will be proposed in the form of an information letter to be remitted by professionals to patient when biosimilar prescription or initiation is planned. The process includes:

1. creation of document by expert patients
2. user testing of tool (assessment about understandability and usefulness), in hospital departments, patient groups and on–line
3. knowledge assessment and opinion gathering among patients about biosimilars.

REFERENCES:

[1] According to its current by-laws, AFLAR board consists of at least 2/3 of persons affected with/concerned by rheumatic diseases, and/or presidents of affiliated patient associations.
[2] Articles L1111-2 and L2002-303 Code de Santé Publique

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WEDNESDAY, 12 JUNE 2019

How to perform low-budget high-quality research

OP0014

NO ASSOCIATION BETWEEN THE PROPORTION OF ELDERLY PEOPLE AND TRIAL RETENTION IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS TRIALS: A SYSTEMATIC REVIEW WITH META-REGRESSION ANALYSES

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Background: The elderly (defined by an age of ≥65 years) are underrepresented in current rheumatoid arthritis (RA) and osteoarthritis (OA) trials.[1] This is partly due to age-related exclusion criteria. Investigators might be reluctant to include more elderly people because they fear reduced trial retention.

Objectives: To evaluate whether the proportion of included elderly individuals (PE) is associated with trial retention in current RA and OA trials.
Methods: This study is registered with protocols.io (*dx.doi.org/10.17504/protocols.io.uhaet2e*). In our previous study,[1] two systematic searches in *MEDLINE* had yielded randomized controlled trials (RCTs) in rheumatoid arthritis (RA) and osteoarthritis (OA) on any intervention published in 2016 and 2017. Here we included all trials reporting data on retention. We either extracted the PE from the research manuscript or estimated it from an assumed (truncated) normal distribution. We coded retention into proportional effect sizes (logit-transformed for analysis and back-transformed for reporting). Subsequently, multiple mixed effects meta-regression models with several covariates assessed whether there is an association between the PE and trial retention. Sensitivity analyses evaluated whether associations were connected to attrition due to lack of efficacy (LoE) or adverse events (AE).
Results: 243 RCTs comprising 48,288 participants were deemed eligible, and 227 RCTs provided complete data on overall retention and all covariates. Pooled trial retention (random effects) was 88% (95%-CI 87% to 90%; I^2 = 90%). The PE was not associated with trial retention in the unadjusted (slope β = 0.0 [–0.0 to 0.0]; p = 0.97; **Figure 1**). or any protocolized adjusted model (p-values depending on the adjustment: 0.14 to 0.90). Of all included covariates, only study duration (longer study duration being associated with inferior retention: $p < 0.001$) and the type of intervention (surgical interventions averaging the highest retention; psychological interventions averaging the lowest retention: $p < 0.001$) were associated with trial retention. Post hoc analyses allowing for interaction revealed a small statistically significant association between the PE and trial retention in pharmacological (retention increasing with the PE) and physical/physiotherapeutic (retention decreasing with the PE) interventions. Further sensitivity analyses showed no significant associations between attrition due to LoE or AE and the PE in any model.
Conclusion: Trial retention in RA and OA trials is very high, and unaffected by the proportion of elderly.

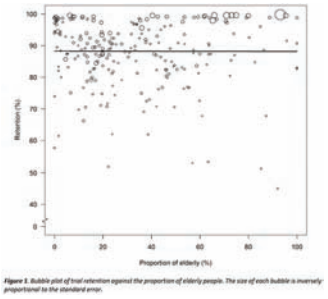


Figure 1. Bubble plot of trial retention against the proportion of elderly people. The size of each bubble is inversely proportional to the standard error.

REFERENCES:

[1] Palmowski A, Buttgereit T, Palmowski Y, et al. Applicability of trials in rheumatoid arthritis and osteoarthritis: A systematic review and meta-analysis of trial populations showing adequate proportion of women, but underrepresentation of elderly people. Semin Arthritis Rheum 2018 [ePub ahead of print].

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OP0015

INCIDENCE, RISK FACTORS AND VALIDATION OF THE RABBIT SCORE FOR SERIOUS INFECTIONS IN A REAL LIFE PROSPECTIVE STUDY OF PATIENTSWITH RHEUMATOID ARTHRITIS: DATA FROM 1.549 PATIENTS

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Background: Identification of the risk factors for the development of serious infections in patients with rheumatoid arthritis (RA) is critical for designing preventive measures and early treatment.
Objectives: To identify risk factors for serious infections and to validate the RABBIT risk score in RA patients in daily clinical practice.
Methods: Multicenter, prospective study of RA patients in Greece. Demographics, disease characteristics, treatments and co-morbidities were prospectively collected via a web-based platform at baseline and one year later. The observed incidence of serious infections was compared to the one estimated by the RABBIT score.
Results: 1.549 RA patients were included (women: 78%, mean age: 63 years, mean disease duration: 10.4 years, RF and/or anti-CCP positive: 54%, mean DAS28: 3.4, mean HAQ: 0.5, bDMARD use: 46%, corticosteroid use: 36%). During follow-up, 38 serious infections were recorded (incidence: 2.3/100 patient-years). Patients who developed a serious infection had longer disease duration (14.2 vs. 10.3 years, p=0.02), higher HAQ at baseline (0.85 vs. 0.5, p=0.006), a history of previous serious infection (26% vs. 10%, p=0.002) and were more likely to have chronic lung disease (23% vs. 9%, p=0.008) or cardiovascular disease (23% vs. 11%, p=0.04). Disease duration (OR: 1.04, CI: 1.01-1.08, p=0.025), history of previous infection (OR: 3.3, CI: 1.3-8.1, p=0.01) and chronic lung disease (OR: 3.03, CI: 1.17-7.85, p=0.023) remained statistical significant in multivariate logistic regression analysis. bDMARD use was not associated with increased risk in uni-or multi-variate analysis. Data for RABBIT score calculation were available in 1.349 patients. Estimated incidence per 100 patient-years was divided in Q1-Q4 quartiles (25-50-75th percentiles: 0.94-1.35-2.15). Estimated and observed incidence rates were in Q1: 0.8 and 0.54, Q2: 1.14 and 0.79, Q3: 1.76 and 1.84 and Q4: 3.7 and 5.6, respectively (Hosmer Lemeshaw test, p=0.9).
Conclusion: In this large, real life, prospective study of RA patients, the incidence of serious infections was 2.3/100 patient-years. Longer disease duration, history of previous serious infections and chronic lung disease were independently associated with the development of serious infections. RABBIT score predicted rather accurately the risk for serious infections in our cohort.



REFERENCES:

[1] Zink et al, Ann Rheum Dis. 2014 Sep; 73(9): 1673–1676.

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Opening Plenary Abstract session

OP0016

WHAT TO CHOOSE: A SECOND TNFI OR AN ALTERNATIVE CLASS OF BIOLOGIC FOR PATIENTS WITH JIA WHO HAVE FAILED THEIR FIRST TNFI

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Background: Biologic therapies, second-line treatment after failure of methotrexate, have revolutionised treatment pathways and outcomes for patients with juvenile idiopathic arthritis (JIA). The expanding choice allows patients to switch biologic if current treatment is not working. Current NHS England guidelines recommend most patients with JIA to start a tumour necrosis factor inhibitor (TNFi), and if that fails switch to a second TNFi rather than change class. The evidence base for this in JIA is limited.
Objectives: The aim of this study was to compare the effectiveness of a second TNFi versus an alternative class of biologic therapy in patients with polyarticular JIA following initial TNFi therapy in routine clinical practice.
Methods: Analysis included patients with JIA starting a second biologic following initial TNFi therapy in two UK cohort studies; BSPAR-ETN and BCRD. Within the studies, data were collected at start of biologic, 6 months, 1 year, then annually on patient characteristics and anti-rheumatic therapy. Patients with extended oligoarticular and polyarticular (rheumatoid factor positive and negative) JIA were included. Patients with a history of uveitis at start of second biologic were excluded. Patient characteristics at start of second biologic were compared between patients starting a second TNFi versus an alternative class. Kaplan-Meier drug survival was used to assess drug survival on second biologic. Stop reasons of second biologic were described. Change in core outcome variables, JADAS-71, American College of Rheumatology Paediatric 50% response (ACR Pedi 50), and Minimal Clinically Important Difference (MCID; ≤0.13 reduction in CHAQ) from baseline to one year was compared between the two cohorts. Multiple imputation and propensity scores were used to account for missing baseline co-variate data and adjust for confounding by indication.
Results: 151 patients with polyarticular JIA starting a second biologic up to 13-Nov-2018 were included; 115 (76%) a second TNFi, 36 (24%) an alternative class. Patient characteristics at the start of second biologic were mostly similar except patients starting a non-TNFi had lower CRP levels (p<0.001). There was no difference in second biologic drug survival between the two cohorts of patients (p=0.8), with approximately 60% remaining on drug by one year. The majority reported inefficacy as stop reason (51%). There was no difference between one year improvement in core outcome variables or JADAS-71 after start of second biologic, and no difference in the odds of achieving ACR Pedi 50 response (odds ratio [OR] 0.8; 95% confidence interval [CI] 0.3, 2.3; p=0.7) or MCID (OR 1.0; 95% CI 0.3, 3.1; p=0.9) between patients starting a second TNFi versus a non-TNFi.
Conclusion: In this real-world cohort of children and young people with JIA starting a second biologic following initial TNFi therapy failure, there appears to be no difference between drug survival and effectiveness outcomes in those patients switching to a second TNFi compared with a non-TNFi biologic. Further research on larger sample sizes is required to know whether there is any initial advantage to switching class of drug following failure of a first TNFi.

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OP0017 NINTEDANIB REDUCED DECLINE IN FORCED VITAL CAPACITY ACROSS SUBGROUPS OF PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: DATA FROM THE SENSCIS TRIAL

Oliver Distler[1], Kristin Highland[2], Martina Gahlemann[3], Arata Azuma[4], Aryeh Fischer[5], Maureen Mayes[6], Ganesh Raghu[7], Wiebke Sauter[8], Mannaig Girard[9], Margarida Alves[10], Emmanuelle Clerisme-Beaty[10], Susanne Stowasser[10], Masataka Kuwana[11], Toby M Maher[12], SENSCIS trial investigators. *[1]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland*; *[2]Respiratory Institute, Cleveland Clinic, Cleveland, Ohio, United States of America*; *[3]Boehringer Ingelheim (Schweiz) GmbH, Basel, Switzerland*; *[4]Department of Pulmonary Medicine and Oncology, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan*; *[5]University of Colorado School of Medicine, Denver, Colorado, United States of America*; *[6]Division of Rheumatology and Clinical Immunogenetics, University of Texas McGovern Medical School, Houston, Texas, United States of America*; *[7]University of Washington, Seattle, United States of America*; *[8]Boehringer Ingelheim Pharma GmbH and Co. KG, Biberach an der Riss, Germany*; *[9]Boehringer Ingelheim France S.A.S., Reims, France*; *[10]Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany*; *[11]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan*; *[12]National Heart and Lung Institute, Imperial College London, UK, and National Institute for Health Research Clinical Research Facility, Royal Brompton Hospital, London, United Kingdom*

Background: In the SENSCIS trial, nintedanib reduced the progression of interstitial lung disease associated with systemic sclerosis (SSc-ILD) compared with placebo, as demonstrated by a significantly lower rate of decline in forced vital capacity (FVC) over 52 weeks (primary endpoint).
Objectives: To assess the effect of nintedanib on the rate of decline in FVC in the SENSCIS trial across pre-specified subgroups defined by baseline characteristics.
Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom <7 years before screening and ≥10% fibrosis of the lungs on a high-resolution computed tomography scan were randomised to receive nintedanib 150 mg bid or placebo double-blind. The annual rate of decline in FVC (ml/year) assessed over 52 weeks (primary endpoint) was analysed in the overall population using a random coefficient regression model (with random slopes and intercepts) including anti-topoisomerase I antibody (ATA) status, age, height, gender and baseline FVC as covariates. Analyses in subgroups by baseline characteristics included additional terms for treatment-by-subgroup and treatment-by-subgroup-by-time interaction.
Results: A total of 576 patients were treated (288 in each group). Most (75.2%) of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were aged ≥65 years. Nintedanib had a consistent effect on reducing the rate of FVC decline across pre-specified subgroups defined by baseline characteristics (p>0.05 for all treatment-by-time-by-subgroup interactions) (figure).
Conclusion: Nintedanib is effective at reducing ILD progression in a broad range of patients with SSc-ILD.

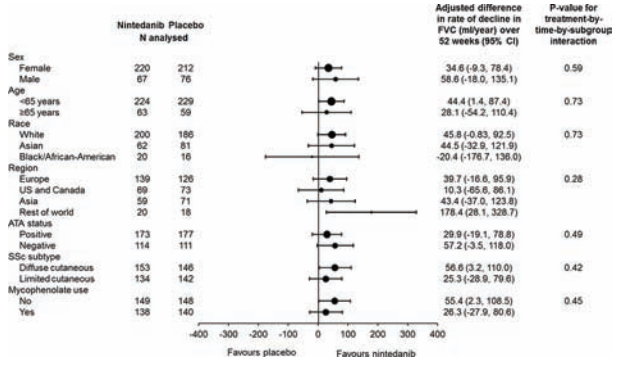


Figure 1

Disclosure of Interests: Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Kristin Highland Grant/research support from: Kristin Highland is a site PI for the SENSCIS trial (Dr Highland's institution has the contract for the study) which is funded by Boehringer Ingelheim., Consultant for: Kristin Highland is a paid consultant for Boehringer Ingelheim through her role sitting on the steering committee., Speakers bureau: Kristin Highland is on the speakers' bureau for Boehringer Ingelheim., Martina Gahlemann Employee of: Employee of Boehringer Ingelheim
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OP0018 MIR-34A IS A POTENTIAL THERAPEUTIC TARGET IN OSTEOARTHRITIS

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Background: We have previously reported that microRNA-34a (miR-34a) is expressed at significantly higher levels in the synovial fluid of late-stage radiographic knee osteoarthritis (OA) compared to early-stage radiographic knee OA. Despite increased levels of miR-34a, its exact role in OA pathogenesis is largely unknown. The aim of this study was to comprehensively elucidate the role and therapeutic potential of microRNA-34 in OA.
Objectives: The aim of this study was to comprehensively elucidate the role and therapeutic potential of microRNA-34 in OA.
Methods: Human plasma, cartilage and synovium were obtained from total knee replacement (TKR) patients. Chondrocytes and synovial fibroblasts were transfected with miR-34a mimic or inhibitor for qRT-PCR or Western blot. For *in-vivo* studies, mice were injected once with a *in-vivo* grade mir-34a mimic or control oligonucleotide and joints were collected 8 weeks post-injection for histology. Mice were subjected to destabilization of the medial meniscus (DMM) to induce OA and injected 2, 4, and 6 weeks post-surgery with miR-34a inhibitor and joints were collected 10 weeks post-surgery for histology. Heterozygous miR-34a knock out

(KO) mice were bred to generate homozygous KOs and mouse articular cartilage was isolated to culture chondrocytes.
Results: miR-34a expression was significantly elevated in the plasma as well as cartilage and synovium of TKR patients (KL IV) compared to healthy controls and early OA patients (KL-I), respectively. Similarly, miR-34a was significantly overexpressed in mouse knee joints (cartilage and synovium) at 10 weeks post OA surgery compared to sham. To identify the biological effects of miR-34a on chondrocyte and synovial fibroblast (SF), functional studies were conducted *in-vitro*. Chondrocytes treated with miR-34a mimic had a significant reduction of SIRT1 (a direct target of miR-34a), anabolic (type II collagen and aggrecan) and autophagy markers, as well as, elevated catabolic markers (MMP13), suggesting that miR-34a contributes to cartilage degeneration. Chondrocytes treated with mir-34a inhibitor reversed these destructive effects. SFs treated with miR-34a mimic expressed elevated inflammatory (TNF-α, IL-6), fibrotic (TGF-β, Type 1 Collagen), and autophagy markers, suggesting that miR-34a is involved in mediating synovial inflammation and fibrosis. SFs treated with miR-34a inhibitor reversed these effects.
In vivo, intra-articular injection of miR-34a mimic induced cartilage damage, loss of proteoglycan content, and elevated cell death markers (PARP p85 and Caspase 3) in the articular cartilage. To confirm the destructive effects of miR-34a in the articular cartilage, we used miR-34a KO mice. MiR-34a KO mice further confirmed that genetic ablation of miR-34a resulted in marked elevation in the expression of anabolic markers (type II collagen and aggrecan) and decreased expression of catabolic ADAMTS-5 in the articular cartilage.
To test the therapeutic potential of blocking miR-34a, we intra-articularly injected mir-34a inhibitor in mice subjected to OA surgery. Results showed marked reduction in the severity of cartilage degeneration in mice treated with miR-34a inhibitor.
Conclusion: This study, for the first time, demonstrates miR-34a as a crucial mediator involved in OA pathogenesis and as a potential therapeutic target for limiting cartilage destruction during OA.
Disclosure of Interests: None declared
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OP0019-HPR A SYSTEMATIC REVIEW AND META-ANALYSIS ASSESSING GASTROINTESTINAL, LIVER, RENAL AND CARDIOVASCULAR ADVERSE EVENTS OF PARACETAMOL

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Background: Despite its modest efficacy, guidelines consistently recommend paracetamol as a first-line analgesic for osteoarthritis (OA) based on its perceived safety. However, there is growing controversy, highlighted in the National Institute for Health and Care Excellence OA (NICE) 2014 guidance on OA, that paracetamol is not as safe as previously thought, especially at the highest therapeutic dose of 4gm/day.
Objectives: To investigate the association between paracetamol and gastrointestinal, liver, renal and cardiovascular adverse events both in randomised controlled trials (RCTs) and observational studies.
Methods: We systematically searched MEDLINE, EMBASE, PUBMED, AHMED, CINAHL, Web of Science, and Google Scholar for published literature in any language to the end of November 2018 for (1) RCTs of paracetamol in symptomatic OA, and (2) observational studies irrespective of any underlying condition, to determine the risk of gastrointestinal, liver, renal and cardiovascular adverse events. We included studies assessing oral paracetamol in people aged $\geq$18 years and reporting on clinically relevant adverse effects. Risk ratio (RR) and 95% confidence interval (CI) were estimated for RCT and cohort studies, whereas odds ratio (OR) and 95% CI were used for case-control studies. Results were pooled as appropriate using random effects model. The risk of bias was assessed using modified Cochrane tool for RCTS and Newcastle Ottawa scale for observational studies.
Results: We reviewed titles and abstracts of 3,622 records in the systematic search (1,997 RCTs and 1,635 observational studies). After examining full papers 23 RCTs (7,863 participants), 15 cohort studies (2,262,517 participants) and 34 case-control studies (441,638 participants) met inclusion criteria.
Compared to placebo, paracetamol was associated with increased incidence of treatment-related adverse events (RR 1.35, 95% CI 1.04 to 1.75), especially diarrhoea (RR 2.14, 95% CI 1.35 to 3.37) and abnormal liver function (RR 3.99, 95% CI 2.05 to 7.77). The pooled OR from twelve age and gender matched case-control studies (7894 participants) was 1.36 (95% CI 1.13 to 1.64) for upper gastrointestinal bleeding. In addition, a dose response relationship was observed in a cohort study (382,404 participants) for this outcome. The RR was 1.11 (95% CI 1.04 to 1.21) with low dose paracetamol (measured as medication possession rate) and 1.49 (95% CI 1.29 to 1.71) with high dose paracetamol. Paracetamol was not associated with cardiovascular events in two RCTs (775 participants) (RR 1.27, 95% CI 0.06 to 27.77) and three case-control studies (42,180 participants) (OR 0.97, 95% CI 0.77 to 1.21), but in three cohort studies (208,926 participants) (RR 1.35, 95% CI 1.14 to 1.59). There were insufficient data in RCTs and case-control studies for renal adverse events. However, three cohort studies (7,360 participants) demonstrated a dose response relationship between paracetamol and renal function impairment (defined as $\geq$30 percentage decrease in estimated glomerular filtration rate). The data of these three cohort studies could not be pooled due to different doses of paracetamol. One cohort study (1697 participants) reported RR of 1.40 (95% CI 0.79 to 2.48) for renal impairment for paracetamol 100-499g, and 2.19 (95% CI 1.4 to 3.43) for paracetamol >3000g.
Conclusion: Paracetamol is associated with diarrhoea and abnormal liver function in short-term trial data, and with upper GI bleeding and renal impairment in long-term observational data. Methodological limitations of observational data, such as channelling bias, may confound the results. Large-scale well-designed prospective studies are needed to ascertain the long-term safety of paracetamol.
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OP0020 LESS IS MORE: ANA-LYSING THE IMPACT OF REPEATED ANTINUCLEAR ANTIBODY TESTING

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Background: Minimising unnecessary tests is a global health economic priority with multiple initiatives in place to avoid inappropriate healthcare utilisation(1) and harm. Anti-nuclear antibody (ANA) testing is frequently performed as a diagnostic test for autoimmune conditions, such as systemic lupus erythematosus (SLE) or as a screening test in patients with inflammatory or musculoskeletal symptoms. The value of serial testing in the monitoring of such conditions is unclear and false positive tests can lead to unnecessary further investigation and increased patient anxiety(2)
Objectives: To evaluate the frequency of repeated ANA testing as a prelude to Electronic Medical Record (EMR) test alert design in an Australian healthcare network. The primary endpoint was calculation of the total cost associated with repeated testing and whether a longitudinal change in ANA resulted in any new ANA associated rheumatological diagnoses. Our secondary endpoint was the examination of baseline ANA testing behaviours.
Methods: We retrospectively analysed data from a multi-centre tertiary health network in Melbourne, Australia across a 7-year period (19 March 2011 to 23 July 2018). ANA and other autoimmune test results were obtained from the hospital pathology system with a positive ANA cut off set at 1:160. Clinical information was sourced from clinical information systems on patients who had a change in ANA result from negative to positive on repeat testing. The associated cost of repeated ANA testing was calculated based on the baseline cost to the public system.
Results: A total of 36,715 ANA tests (excluding 980 cancelled same-day requests) were performed in 28,840 patients. Of these, 14,058 (38.3%) were positive with females accounting for 9,265 (65.9%, p<0.001). The most frequent ANA patterns were homogenous (47.4%) and nucleolar (23.3%). ANA titres were as follows; 1:160 (41.4%), 1:320 (15.3%), 1:640 (13.1%) and 1:1280 (29.2%). 7,875 (21.4%) of tests were repeat tests. Of these 511 (6.5%) results changed from negative to positive. The median time between a negative ANA result to the first positive result was 1.71 years (IQR 0.50-3.55). Clinical information was captured for a median duration of 1.24 years (IQR 0.50-2.07) following a positive ANA result. A change to positive ANA was associated with a new ANA-associated rheumatological diagnosis in only 5 cases (2 SLE, 1 scleroderma and 2 undifferentiated connective tissue disease) with a positive predictive value calculated at 0.01. When comparing patients who with a new diagnosis to those with no new diagnosis, there was no difference between ANA titre, pattern, duration to first positive ANA, ordering location or clinician, or age of first positive ANA test. The direct total cost for the government of all ANA testing was AUD$903,189, of which repeat testing contributed AUD$193,725.
Conclusion: Repeat ANA testing after a negative result had limited utility in the diagnosis of ANA associated rheumatological conditions with a positive predictive value of only 0.01, and resulted in high cost. New technology and clinical alert systems may help reduce unnecessary testing with potential significant direct cost savings when extrapolated across the Australian healthcare system.

REFERENCES:
[1] Levinson W, Kallewaard M, Bhatia RS, Wolfson D, Shortt S, Kerr EA. 'Choosing Wisely': a growing international campaign. BMJ Qual Saf. 2015;24(2):167-74.
[2] Abeles AM, Abeles M. The clinical utility of a positive antinuclear antibody test result. The American journal of medicine. 2013;126(4):342-8.

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OP0021 PREDICTING SEVERE INFECTION IN REPEAT CYCLES OF RITUXIMAB AND EFFECTS OF HYPOGAMMAGLOBULINAEMIA FOR THE TREATMENT OF RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Rituximab (RTX) is effective in treating various rheumatic and musculoskeletal diseases (RMDs). Repeat cycles are often required for disease control but may lead to hypogammaglobulinaemia. Low IgG at baseline has been associated with increased risk of severe infection event (SIE) post-RTX. However, there are limited data on predictors of SIEs in repeat cycles including immunoglobulin levels and B-cell numbers as well as outcomes of hypogammaglobulinaemia.
Objectives: To assess predictors of SIEs in repeat RTX cycles and effects of hypogammaglobulinaemia in terms of SIEs rates, humoral response and its persistence post-cessation of RTX.
Methods: A retrospective study was conducted in the first 700 consecutive ARD patients treated with at least a cycle of RTX in Leeds. IgM, IgA and IgG levels were measured at baseline and 4-6 months after each cycle. For cycles 2-4 (C2-4), predictors for SIEs were analysed using mixed-effects logistic regression analysis.
Results: 550 patients were female, mean(SD) age 56(16) years and median (IQR) disease duration 7.9(3.4-15.0) years. 507(72%) had RA, 94(13%) SLE, 49 (7%) AAV, 14(2%) inflammatory myopathies, 9(1%) pSS, 5(1%) APS, 6(1%) SSc and 16(3%) other CTDs. 364(52%) were biologic-naïve and 514(73%) were on concomitant DMARDs. Total follow-up: 2880 patient-years (PY). 281 SIEs were recorded in 176 patients (9.8/100 PY). In C1, we had validated that low IgG was predictive of SIE within 12 months of C1. For cycles 2-4, in multivariable analysis, non-RTX-specific comorbidities [chronic lung OR (95% CI) 2.4 (1.3-4.4), diabetes 2.9 (1.2-6.9), heart failure 6.3 (1.4-28.1), previous cancer 3.0 (1.3-6.7) and severe infection 6.3 (3.0-13.4)] and RTX-specific variables [higher corticosteroid dose 1.08 (1.02-1.14), higher IgM 1.3 (1-1.7) and longer retreatment time 1.01 (1-1.02)] were associated with increased odds of SIEs, but not B-cell numbers or depletion status. Higher IgG reduced the risk 0.88 (0.8-0.96). Of 103 patients with low IgG for at least 4 months duration, SIEs rates were higher in those with low baseline IgG (16.4 PY) or acquired it during/post-RTX (21.3 PY) versus those with normal IgG (9.7 PY), 5/8(64%) had impaired humoral response to pneumococcal and haemophilus following vaccination challenge and only 4/11(36%) had IgG normalised after switching therapies. Overall, 7(1%) of the patients required Ig replacement based on recurrent sino-pulmonary SIEs and/or low IgG.
Conclusion: Immunoglobulin should be monitored at baseline and before each RTX cycle to identify patients at risk of SIEs. Vigilance is needed for those with lower IgG as this is a consistent predictor of SIE and may affect infection outcomes when patients are switched to a different bDMARD. For those at risk of SIEs, reduction of corticosteroid dose could reduce risk. Low B-cell numbers were not predictive of SIEs.
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OP0022 DO MRI-DETECTED EROSIONS IN PATIENTS WITH CLINICALLY SUSPECT ARTHRALGIA PREDICT PROGRESSION TO RHEUMATOID ARTHRITIS? A LONGITUDINAL STUDY

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Background: Radiographic joint erosions are a hallmark of Rheumatoid Arthritis (RA). MRI is more sensitive than radiographs in detecting erosions. It is unknown if MRI-detected erosions are predictive for RA-development in patients with Clinically Suspect Arthralgia (CSA).
Objectives: We investigated the prognostic value of MRI-detected erosions (any MRI-erosion, or MRI-erosion characteristics that were recently identified as specific for RA) in CSA.
Methods: Patients presenting with CSA (n=491) underwent contrast-enhanced 1.5T MRI of the wrist, metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints at baseline. MRIs were scored according to RAMRIS. Presence of any MRI-erosion (erosion score $\geq$1) and RA-specific erosion characteristics as identified previously (grade $\geq$2 erosions, erosions in MTP5, erosions in MTP1 if aged <40) were studied with clinically apparent inflammatory arthritis development as outcome (median follow-up 17 months). Analyses were corrected for age, CRP, ACPA and MRI-detected inflammation.
Results: Erosions were present in 20.6% of patients. Presence of erosions was not associated with arthritis development (HR multivariable analysis 0.85 (95% CI 0.52-1.40)). Also the different erosion characteristics were not predictive in CSA-patients (grade $\geq$2 HR 1.29 (95% CI 0.40-4.14), erosions in MTP5 HR 0.89 (95% CI 0.38-2.09) and MTP1 if aged <40 HR 0.98 (95% CI 0.23-4.21)). MRI-erosions were more prevalent in ACPA-positive than in ACPA-negative patients (32.3% versus 18.8%, p=0.02). However, no association with arthritis development was observed in both subgroups.
Conclusion: MRI-detected erosions in hands and feet of patients with CSA were not predictive for arthritis development. These data warn against overinterpretation of MRI-detected erosions in CSA.
Disclosure of Interests: Fenne Wouters: None declared, Xanthe Matthijssen: None declared, Debbie Boeters: None declared, Robin ten Brinck: None declared, Annette van der Helm - van Mil Grant/research support from: The research leading to these results has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (Starting grant, agreement No 714312) and from the Dutch Arthritis Foundation.
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LB0001 EFFICACY AND SAFETY OF FILGOTINIB FOR PATIENTS WITH RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO METHOTREXATE: FINCH1 PRIMARY OUTCOME RESULTS

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Background: Filgotinib (FIL) is an orally administered, potent and selective inhibitor of Janus kinase 1 (JAK1) that has shown good efficacy and was well tolerated for treatment of rheumatoid arthritis (RA).
Objectives: To evaluate efficacy and safety of FIL treatment in patients with RA who have had an inadequate response to methotrexate (MTX).

Methods: This phase 3, double-blind, active- and placebo (PBO)-controlled study randomized patients with active RA (3:3:2:3) to FIL 200 mg, FIL 100 mg, active comparator (adalimumab [ADA] 40mg every 2 weeks), or PBO daily for up to 52 weeks; results through week 24 are presented. Patients were also receiving MTX for ≥12 weeks with a stable dose of MTX for ≥4 weeks before initiation of study drug. Primary efficacy endpoint was proportion of patients achieving ACR20 response at week 12; additional clinical assessments were ACR50 and ACR70 responses, DAS28-CRP score ≤3.2 and <2.6, van der Heijde modified total Sharp score (mTSS), and patient-reported outcomes were HAQ-DI, SF-36 PCS, and FACIT-Fatigue. Safety endpoints included types and rates of adverse events. Logistic regression adjusting for stratification factors with nonresponder imputation was used for superiority test of FIL vs PBO for ACR response and other binary endpoints. Mixed-effect model adjusting for baseline value, stratification factors, treatment, visit, and treatment by visit interaction as fixed effects with observed cases was used for continuous endpoints. Non-inferiority test of FIL to ADA (preserving >50% of ADA response) was performed for DAS28-CRP ≤3.2 and <2.6.
Results: Of 1,759 patients randomized, 1,755 received study drug and were analyzed, with 475 FIL 200mg; 480 FIL 100mg; 325 ADA; and 475 PBO, of which 89.5%, 90.4%, 88.9%, and 81.3%, respectively, completed week 24 study drug. Most patients (81.8%) were female, mean (standard deviation [SD]) duration of RA was 7.8 (7.6) years, and mean (SD) DAS28-CRP was 5.7 (0.9). At week 12, significantly more patients in the FIL 200mg and 100mg arms achieved an ACR20 response compared to PBO (Table 1). Similarly, compared to PBO, more patients receiving FIL achieved ACR50 and ACR70 responses, DAS28-CRP scores ≤3.2 and <2.6, had lower radiographic progression, and reported improvements in HAQ-DI, SF-36 PCS, and FACIT-Fatigue scores (Table 1). Non-inferiority of FIL 200mg to ADA was met based on DAS28-CRP ≤3.2. The FIL safety profile was consistent with prior studies through week 24 (Table 2).

Table 1. Efficacy at Week 12 (Primary Analysis) and Week 24*

	FIL 200 mg (N = 475)		FIL 100 mg (N = 480)		ADA 40 mg Q2W (N = 325)		PBO (N = 475)	
	Week 12	Week 24	Week 12	Week 24	Week 12	Week 24	Week 12	Week 24
ACR20, %	76.6***	78.1	69.8***	77.7	70.8	74.5	49.9	59.2
ACR50, %	47.2***#	57.9	36.3***#	52.7	35.1	52.6	19.8	33.3
ACR70, %	26.3***#	36.2	18.5***#	29.4	14.2	29.5	6.7	14.9
DAS28-CRP ≤ 3.2, %	49.7***#	60.6	38.8***	53.1	43.4	50.5	23.4	33.7
DAS28-CRP < 2.6, %	33.9***#	48.4	23.8***#	35.2	23.7	35.7	9.3	16.2
mTSS, mean change from BL	0.08	0.13***	0.11	0.17***	0.13	0.16	0.25	0.38
HAQ-DI, mean change from BL	−0.69***	−0.82	−0.56***	−0.75	−0.61	−0.78	−0.42	−0.62
SF-36 PCS, mean change from BL	9.2***#	10.4	8.5***#	10.3	8.4	10.4	5.8	7.7
FACIT-Fatigue, mean change from BL	9.2***#	10.5	9.1***#	10.8	8.8	10.3	6.8	8.4

*All patients who were randomized and received at least 1 dose of study drug were included in efficacy analyses. P-values are shown only for primary time points (all at week 12 except mTSS, which was at week 24).
***P<0.001 vs PBO; #P<0.01 vs ADA non-inferiority test; †P<0.001 vs ADA non-inferiority test; ‡P<0.01 vs ADA superiority test; §Comparison not adjusted for multiplicity.
ACR20/50/70, 20%/50%/70% improvement in American College of Rheumatology criteria; ADA, adalimumab; BL, baseline; DAS28-CRP, Disease Activity Score based in 28 joints with C-reactive protein; FIL, filgotinib; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; mTSS, modified total Sharp score; SD, standard deviation; SF-36 PCS, Short-Form 36 Physical Component Summary; Q2W every 2 weeks.

Table 2. Safety Events of Interest through Week 24

Patient with event, n (%)	FIL 200 mg (N = 475)	FIL 100 mg (N = 480)	ADA 40 mg Q2W (N = 325)	PBO (N = 475)
Serious AEs	21 (4.4)	24 (5.0)	14 (4.3)	20 (4.2)
Serious infections	8 (1.7)	8 (1.7)	8 (2.5)	4 (0.8)
Herpes zoster	2 (0.4)	2 (0.4)	2 (0.6)	2 (0.4)
Adjudicated MACEs	0	1 (0.2)	1 (0.3)	2 (0.4)
Venous thrombotic events	1 (0.2)	0	0	2 (0.4)
Malignancies	0	1 (0.2)	1 (0.3)	3 (0.6)
Deaths	2 (0.4)	1 (0.2)	0	2 (0.4)

AE, adverse event; MACE, major adverse cardiovascular event

Conclusions: The selective JAK1 inhibitor FIL, at doses of 200mg and 100mg led to significant improvement in signs and symptoms of RA, prevented radiographic progression, and improved physical function compared to PBO, and was well tolerated among patients with RA with prior inadequate response to MTX. Efficacy of FIL 200mg was non-inferior to ADA based on DAS28-CRP ≤3.2.
Disclosure of Interests: Bernard Combe Consultant for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB, Alan Kivitz Shareholder of: Novartis, Consultant for: Abbvie, Janssen, Pfizer, UCB, Genzyme, Sanofi, Regeneron, Boehringer Ingelheim, Sun Pharma Advanced Research, Flexion., Paid instructor for: Celgene, Horizon, Merck, Novartis, Pfizer, Genzyme, Sanofi, Regeneron, Speakers bureau: Celgene, Horizon, Merck and Genetech, Flexion, Yoshiya Tanaka Grant/research support from: Abbvie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Ono, Taisho-Toyama, Takeda, Speakers bureau: Abbvie, Asahikasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Eisai, Glaxo-Smithkline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer Japan Inc, Sanofi, Takeda, UCB, YL Biologics, Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Franziska Matzkies Shareholder of: Gilead, Employee of: Gilead, Beatrix Bartok Shareholder of: Gilead, Employee of: Gilead, Lei Ye Shareholder of: Gilead, Employee of: Gilead, Ying Guo Shareholder of: Gilead, Employee of: Gilead, Chantal Tasset Shareholder of: Warrants from Galapagos, Employee of: Galapagos, John Sundy Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Neelufar Mozaffarian Shareholder of: Gilead, Employee of: Gilead (former employee), Robert B.M. Landewé: None declared, Sang-Cheol Bae: None declared, Edward C. Keystone Grant/research support from: AbbVie, Amgen, Gilead Sciences, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, PuraPharm, Sanofi, Consultant for: AbbVie, Amgen, AstraZeneca Pharma, Bristol-Myers Squibb Company, Celltrion, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis, Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, MSD, Celgene, Gilead, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, MSD, Celgene, Gilead, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, MSD, Celgene, Gilead
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LB0002

RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTIPLE-DOSE, PHASE 2B STUDY TO DEMONSTRATE THE SAFETY AND EFFICACY OF TILDRAKIZUMAB, A HIGH-AFFINITY ANTI-INTERLEUKIN-23P19 MONOCLONAL ANTIBODY, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Tildrakizumab (TIL), a high-affinity anti–interleukin-23p19 monoclonal antibody, is approved for moderate-to-severe plaque psoriasis treatment and is under investigation for psoriatic arthritis (PsA).
Objectives: To evaluate the 24-week efficacy and safety results from the randomised, double-blind, placebo-controlled, multiple-dose, phase 2b TIL study in patients with active PsA (NCT02980692).
Methods: Patients with active PsA were randomised 1:1:1:1:1 to receive TIL (200 mg once every 4 weeks [Q4W] [n = 78], 200 mg every 12 weeks [Q12W] [n = 79], 100 mg Q12W [n = 77], 20 mg Q12W to week 24 [n = 78]), or placebo (PBO) Q4W to week 24 (n = 79). Stable concomitant methotrexate or leflunomide use was permitted but not mandated. The primary efficacy endpoint was the proportion of patients who achieved a 20% reduction from baseline in American College of Rheumatology response criteria (ACR20) at week 24. Other outcome measurements included proportion of patients achieving ACR50/70 response and Psoriasis Area and Severity Index (PASI) 75, PASI 90, and changes in swollen and

Table 1. Demographics and baseline disease characteristics

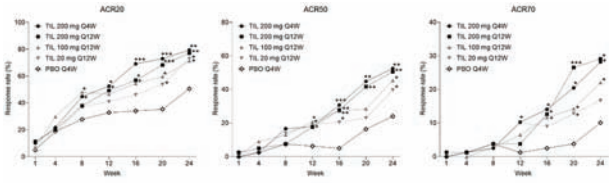
	TIL 200 mg Q4W (N = 78)	TIL 200 mg Q12W (N = 79)	TIL 100 mg Q12W (N = 77)	TIL 20 mg Q12W (N = 78)	PBO (N = 79)
Patient demographics					
Age, years, median	50.0	49.0	50.0	47.5	47.0
Female, n (%)	46 (59.0)	37 (46.8)	47 (61.0)	41 (52.6)	44 (55.7)
White, n (%)	76 (97.4)	78 (98.7)	75 (97.4)	75 (96.2)	74 (93.7)
BMI, kg/m², median	30.0	29.3	27.8	28.9	27.8
Baseline disease characteristics					
Swollen joint count, median (range)	8.0 (3.0–35)	7.0 (3.0–45)	8.0 (0–38)	8.0 (3.0–38)	8.0 (3.0–42)
Tender joint count, median (range)	13.5 (3.0–64)	15.0 (4.0–63)	19.0 (3.0–59)	14.0 (4.0–54)	15.0 (3.0–64)
BSA ≥3%, n (%)	53 (67.9)	44 (55.7)	54 (70.1)	41 (52.6)	42 (53.2)
Physician GADA, mean ± SD	54.0 ± 16.1	55.4 ± 16.2	57.3 ± 17.3	59.4 ± 14.4	59.5 ± 15.6
Patient GADA, mean ± SD	57.8 ± 18.3	61.1 ± 20.7	60.3 ± 20.2	61.9 ± 17.4	65.2 ± 18.1
Patient's pain assessment, mean ± SD	55.4 ± 19.1	59.6 ± 23.5	59.2 ± 22.1	60.9 ± 19.7	64.2 ± 20.4

BMI, body mass index; BSA, body surface area; GADA, global assessment of disease activity; Q4W, every 4 weeks; Q12W, every 12 weeks; PBO, placebo; SD, standard deviation; TIL, tildrakizumab.

Table 2. Efficacy endpoints at week 24

	TIL 200 mg Q4W (N = 78)	TIL 200 mg Q12W (N = 79)	TIL 100 mg Q12W (N = 77)	TIL 20 mg Q12W (N = 78)	PBO (N = 79)
PASI 75*, %	64.2***	79.6***	55.6***	46.3*	16.7
PASI 90*, %	47.2***	50.0***	38.9**	36.6*	7.1
Swollen joint count, median change from BL	−6.0*	−6.0	−6.0*	−6.0	−5.0
Tender joint count, median change from BL	−9.0	−10.0*	−11.0*	−10.0	−8.5

*Response rates only calculated in patients with BSA ≥3% at baseline, missing responses were imputed as nonresponses. *P <0.05; **P <0.001; ***P <0.0001 vs PBO.
BL, baseline; BSA, Body Surface Area; PASI, Psoriasis Area and Severity Index; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.



*P <0.05; **P <0.001; ***P <0.0001 vs PBO.
ACR, American College of Rheumatology response criteria; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

Figure 1. ACR20/50/70 response rates

tender joint count at week 24. Safety assessments included monitoring of treatment-emergent adverse events (TEAEs).

Results: Of 500 patients screened, 391 patients met inclusion criteria (including =18 years old, PsA diagnosis with symptoms for 6 months, and =3 tender and =3 swollen joints). Demographics and baseline disease characteristics are shown in Table 1. There were significantly greater proportions of ACR20/50/70 and PASI 75/90 responders with TIL vs PBO at week 24, and in some cases differences in parameters were noted as early as week 8 (Figure 1 and Table 2).

The most frequent TEAEs through week 24 included nasopharyngitis (pooled TIL arms: 5.4% [17/312]; PBO: 6.3% [5/79]); and diarrhoea (TIL: 1.3% [4/312]; PBO: 0). There were no reports of candidiasis, inflammatory bowel disease, major adverse cardiac events, or malignancy. No patients discontinued treatment due to TEAEs and no deaths were reported. Serious TEAEs occurred in 2.2% (7/312) of TIL-treated patients vs 2.5% (2/79) in PBO-treated patients.

Conclusion: By week 24, TIL was significantly more efficacious than PBO in treatment of joint and skin manifestations of PsA. Furthermore, there was a clear separation between TIL and PBO as early as 8 weeks for ACR20 (TIL 200 mg Q4W and 100 mg) and 12 weeks for ACR50 (all TIL groups). Shortening the dosing interval from Q12W to Q4W for the 200-mg dose did not result in a measurable increase in skin or joint response scores. There was a low rate of TEAEs in the TIL-treated group.

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WEDNESDAY, 12 JUNE 2019

RA therapy –JAK inhibitors and beyond

OP0023

ACPA-POSITIVE RHEUMATOID ARTHRITIS PATIENTS BENEFITED MORE FROM ADVANCED TREATMENT STRATEGIES THAN ACPA-NEGATIVE RHEUMATOID ARTHRITISPATIENTS: 25-YEAR RESULTS OF A LONGITUDINAL COHORT STUDY

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Background: Over the last 25 years, treatment of rheumatoid arthritis (RA) has changed considerably, and clinically relevant joint damage and deformations have become infrequent. It is unclear to what extent the long-term outcomes mortality, sustained drug-free remission (DFR) and physical functioning have improved, and whether ACPA+ and ACPA- patients have benefited equally from treatment-improvements.

Objectives: To investigate the influence of treatment strategies that have been improved for 25-years on mortality, DFR and functionality, and whether these effects differed for ACPA+ and ACPA- RA-patients.

Methods: In the Leiden early arthritis cohort, 1291 patients with RA (1987 criteria) were included between 1993-2016. Patients were treated in routine care; initial and subsequent treatment changed over time; divided in 5 inclusion periods. Patients included between 1993-1996 (n=168) received initial NSAIDs and started DMARDs with delay, patients included 1997-2000 (n=185) were treated early with mild DMARDs (e.g. hydroxychloroquine, penicillamine), in 2001-2005 (n=210) patients started early with methotrexate, in 2006-2010 (n=338) early methotrexate was followed by treat to target treatment adjustments; in 2011-2016 (n=390) this was similar and additional efforts were undertaken for very early referral. Patients were followed yearly including assessments of swollen joints, DAS28-ESR and health assessment questionnaires (HAQ). Mortality data were obtained from the civic registry. DFR was defined as the persistent absence of synovitis after cessation of DMARD-therapy during all available follow-up ($\geq$ 1 year). DAS28-ESR and HAQ data were analysed with linear mixed models; mortality and time to DFR with multivariable and univariable Cox regression. Inclusion period 1993-1996 was used as reference. Analyses were stratified for ACPA-status (anti-CCP2).

Results: Baseline age, sex and antibody status did not differ between inclusion periods. With 1993-1996 as reference, the DAS28-ESR decreased in the first year and thereafter remained lower in all inclusion periods (all p<0.05).

Compared to 1993-1996, mortality was decreased in all inclusion periods (1997-2000 HR 0.67 (0.46;0.99); 2001-2005 HR 0.66 (0.45;0.97); 2006-2010 HR 0.64 (0.42;0.98); 2011-2016 HR 0.31 (0.14;0.68)). DFR achievement was faster in 2006-2010 (HR 2.68 (1.68;4.29)) and 2011-2016 (3.37 (1.97,5.74)), compared to 1993-1996. Additionally, HAQ over time was lower in 2006-2010 (-0.25 (-0.36;-0.14)) and 2011-2016 (-0.21 (-0.32;-0.10)).

Stratification for ACPA revealed that ACPA+ patients in the first two inclusion periods remained to have a higher DAS28-ESR over time (1993-1996 β 0.76 (0.42;1.10); 1997-2000 β 0.40 (0.07;0.74)); thereafter there was no difference in DAS28-ESR between ACPA+ and ACPA- patients. The decrease in mortality was similar for ACPA+ and ACPA- patients. The increased rate of DFR was more prominent in ACPA+ patients than ACPA- patients in the two most recent inclusion periods (2006-2010 HR ACPA+: 3.85 (1.25;11.9); ACPA- 2.27 (1.34;3.83); 2011-2016 HR ACPA+: 6.48 (1.89;22.2); ACPA-: 3.04 (1.66;5.55)). Within ACPA+ RA, the HAQ over time had improved in 2001-2005 (-0.19 (-0.34;-0.04)), 2006-2010 (-0.35 (-0.49;-0.22)) and 2011-2016 (-0.26 (-0.40;-0.13)), compared to 1993-1996. This effect was absent ACPA- RA.

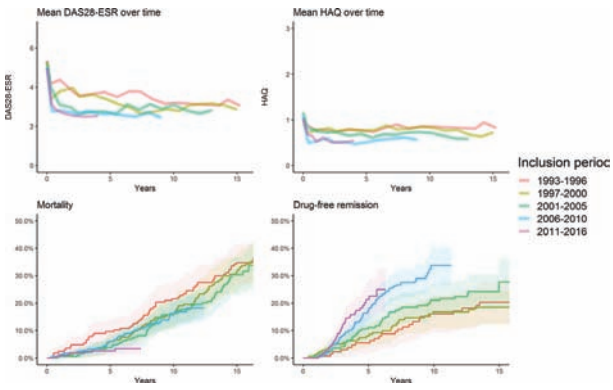


Figure 1. Disease outcomes over time stratified for inclusion period

Conclusion: Improvements in treatment strategies during the last 25 years have resulted in lower disease activity, less mortality, more DFR and better physical functioning of RA-patients. ACPA+ patients, traditionally the most severe subset, benefited most from these improvements and have become more similar to ACPA- patients.

Disclosure of Interests: Xanthe Matthijssen: None declared, Ellis Niemantsverdriet: None declared, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringher, Takeda, Zydus, Epirus, Eli Lilly, Annette van der Helm - van Mil Grant/research support from: The research leading to these results has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (Starting grant, agreement No 714312) and from the Dutch Arthritis Foundation.

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OP0024 PATIENT DISCUSSIONS OF GLUCOCORTICOID-RELATED SIDE EFFECTS WITHIN AN ONLINE HEALTH COMMUNITY FORUM

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Background: Social media websites are an important, largely untapped source of data about patients' experience of living with disease and its treatment. This includes information on drugs such as the occurrence, nature and impact of side effects. However, there are few published studies reporting drug safety profiles using such data.

Health Unlocked (HU), Europe's largest social media network for health that supports patients and health care providers, hosts over 200 communities including the UK's National Rheumatoid Arthritis Society (NRAS). Using the example of glucocorticoid (GC) therapy, this study aims to explore the potential of HU posts in providing information about the occurrence and nature of drug side effects.

Objectives:

1. Evaluate the accuracy of a computerised system for automated suspected adverse drug reaction (sADR) detection from posts from HU compared to human annotation.
2. Explore themes of discussion about GC–related ADRs within posts from HU.

Methods: HU provided a dataset of de-identified posts from the NRAS community from December 2015 to December 2016. Posts mentioning GCs were processed by automated Natural Language Processing software, which identified the drug and health issues, mapped them to the Medical Dictionary for Regulatory Activities (MedDRA®) dictionary and categorised as a sADR or not. A sample (n=50) of sADR posts were randomly selected and manually reviewed to determine whether they were true ADRs. Additionally, a sample (n=50) of the posts that included GC and were labelled as having a health issue but not thought to have an ADR, were also assessed for true ADRs.

Posts identified as containing GC ADRs from manual analysis were reviewed to identify themes.

Results: Of the 35,904 posts from 1,998 users, 2,409 posts mentioned GCs, of which 324 posts were identified as containing information representing a sADR. After manual review of the 50 sampled sADRs, only 36% (18/50) of these posts contained a true ADR. Of the 50 sampled posts that included a mention of GCs and a health issue but were not a sADR, 28% (14/50) were found to contain true ADRs. Thematic analysis of the 32 posts containing true GC ADRs found the most frequently mentioned ADRs were fractures (n=6), infection (n=5), headaches (n=3) and weight gain (n=3). Posts included rich descriptions about the nature of side effects ("my weight tripled in size with steroids"). This included experiences of how side effects changed with time ("huge mood swings settles after a while"). Users also described how ADRs impacted on their quality of life ("with steroid induced diabetes, I lost a stone in three days, it was grim"), and their value judgements about the importance of side effects ("my taste buds are making everything taste strange, either salty, metallic, or plain awful … but I cope with it, as hardly any pain with steroids.") Posts also described frustrations about how well informed they were about side effects ("I had two eye ops for cataracts, no one told me steroids caused cataracts"). Within posts where ADRs were discussed, patients also commented on the benefits of treatment ("my pain subsided with steroids") and the difficult balance between benefits and harms ("wonderful to not feel like I had RA in the first month of having [pred], but now I have more acne then when I was a teenager").

Conclusion: Current machine learning models for ADR detection in social media still need further improvements to identify sADRs in health forum data. Nonetheless, manual review shows there are important themes relating to patients' experiences and perceptions of using GC that may not be obtained using traditional methods such as analysis of health records or spontaneous pharmacovigilance. With improved automated ADR detection, this rich data source may be useful to identify ADRs most important to patients and the impact on quality of life.

Disclosure of Interests: None declared

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OP0025 FENEBRUTINIB COMPARED TO PLACEBO AND ADALIMUMAB IN PATIENTS WITH INADEQUATE RESPONSE TO EITHER METHOTREXATE THERAPY OR PRIOR TNF THERAPY: PHASE 2 STUDY

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Background: Fenebrutinib (GDC-0853, FEN) is a small molecule inhibitor of Bruton's Tyrosine Kinase (BTK) that is orally administered, highly selective, non-covalent, and reversible.

Table 1. Endpoints

	Cohort 1, MTX-IR					Cohort 2, TNF-IR	
	FEN-50 50 mg QD (*n*=40)	**FEN-150** 150 mg QD (*n*=109)	**FEN-200** 200 mg BID (*n*=110)	**PBO** (*n*=110)	**ADA** 40 mg Q2W (*n*=111)	**FEN-200** 200 mg BID (*n*=48)	**PBO** (*n*=50)
ACR50 responders at W12	7 (18%)	30 (28%)	38 (35%)	16 (15%)	40 (36%)	12 (25%)	6 (12%)
95% confidence interval (CI)	(6%, 29%)	(19%, 36%)	(26%, 43%)	(8%, 21%)	(27%, 45%)	(13%, 37%)	(3%, 21%)
Weighted difference vs. PBO	8.0%	12.9%	20.0%	-	21.6%	13.9%	-
95% CI of weighted difference*	(-6%, 22%)	(2%, 23%)	(9%, 31%)	-	(11%, 33%)	(-1%, 29%)	-
P-value**	0.2503	0.0164	0.0003	-	0.0001	0.0650	-
Weighted difference vs. ADA	-17.8%	-8.6%	-1.5%	-21.6%	-	-	-
95% CI of weighted difference*	(-34%, -2%)	(-21%, 4%)	(-14%, 11%)	(-33%, -11%)	-	-	-
P-value**	0.0268	0.1694	0.8132	0.0001	-	-	-
DAS28-CRP at W12							
Change from baseline							
Pts (*n*) completing W12	36	95	95	99	104	47	44
Adjusted mean*	-1.74	-1.96	-1.96	-1.33	-2.11	-1.96	-1.20
95% CI of weighted difference*	(-0.93, -0.11)	(-1.00, -0.25)	(-1.00, -0.24)	-	(-1.15, -0.41)	(-1.14, -0.37)	-
P-value vs. PBO**	0.1674	0.0002	0.0002	-	<0.0001	0.0002	-
Safety							
AEs	15 (37.5)	45 (41.3)	56 (50.9)	50 (45.5)	50 (45.0)	11 (22.4)^	22 (44.9)^
Pts with ≥1 event, *n* (%)							
Serious AEs:	-	1 (0.9)	3 (2.7)	1 (0.9)	2 (1.8)	-	-
Pts with ≥1 event, *n* (%)							
Deaths, *n* (%)	-	-	1 (0.9)***	-	-	-	-

*Adjusted for geographic region (Eastern Europe, Latin America, and USA) for Cohort 1, and geographic region and prior exposure to a non-TNF biologic for Cohort 2

**Not adjusted for multiplicity

***Death was due to myocardial infarction

^One PBO pt was treated with FEN-200 in error

Objectives: This study evaluated the efficacy and safety of FEN compared with placebo (PBO) and adalimumab (ADA), in combination with background methotrexate (MTX), in patients (pts) with rheumatoid arthritis (RA).
Methods: This multicenter, randomized, double-blind Phase 2 study included pts with moderate-to-severe active RA with an inadequate response to MTX (MTX-IR, Cohort 1) or TNF inhibitors (TNF-IR, Cohort 2). Cohort 1 pts were randomized to FEN at 50 mg QD (FEN-50), 150 mg QD (FEN-150), 200 mg BID (FEN-200), 40 mg ADA injections SC Q2W, or PBO. Cohort 2 pts were randomized to FEN-200 or PBO. Key efficacy endpoints evaluated the proportion of pts with an ACR50 response at Week 12 (W12), comparing FEN doses to PBO (both cohorts) and to ADA (Cohort 1).
Results: Cohort 1 (FEN-50, n=40; FEN-150, n=109; FEN-200, n=110; PBO, n=110; ADA, n=111) and Cohort 2 (FEN-200, n=48; PBO, n=50) demographics and disease characteristics were balanced, and ~90% of pts per arm completed the study. In Cohort 1, ACR50 response rates increased with increasing FEN dose (18%, 28%, and 35% for FEN-50, FEN-150, and FEN-200, respectively). FEN-150 (28%, p=0.0164) and FEN-200 (35%, p=0.0003) were superior to PBO (15%), and numerically similar to ADA (36%). In Cohort 2, the response for FEN-200 was higher than PBO (25% vs. 12%) (Table 1). Adverse events (AEs) were generally balanced across Cohort 1; there were 9 serious AEs in 7 pts and one death in the FEN-200 group. In Cohort 2, more pts in the PBO arm reported AEs, and no serious AEs were reported.
Conclusion: FEN demonstrated higher efficacy rates than PBO for ACR50 at W12 in both MTX-IR and TNF-IR populations, and was similar to ADA in MTX-IR pts. The overall safety profile of FEN was acceptable.
Disclosure of Interests: Stanley Cohen Grant/research support from: AbbVie, Amgen Inc., AstraZeneca, Biogen-IDEC, Bristol Meyer Squibb, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Merck, and Roche, Consultant for: Abbvie, Amgen, AstraZeneca, Biogen-IDEC, Bristol Meyer Squibb, Genentech, Janssen, Lilly, Novartis Pfizer, Merck and Roche, Katie Tuckwell Shareholder of: Genentech/Roche, Employee of: Genentech/Roche, Tamiko R. Katsumoto Shareholder of: Genentech, Inc., Consultant for: Roche/Genentech, Principia Biopharma, Abbvie, Employee of: Former employee of Genentech, Inc., Rui Zhao Shareholder of: Genentech, Inc., Employee of: Genentech, Inc., Chin Lee Shareholder of: Roche/Genentech and of Eli Lilly & Co., Employee of: Genetech, Inc. and Eli Lilly & Co., Alberto Berman Grant/research support from: Grants/research support: Roche/Genentech, Bristol-Myers Squibb, Merck Serono, AbbVie, Amgen, Eli Lilly, Janssen, Nemanja Damjanov Grant/research support from: AbbVie, Pfizer and Roche, Consultant for: Abbvie, Gedeon Richter, Merck, Novartis, Pfizer and Roche., Speakers bureau: Abbvie, Gedeon Richter, Merck, Novartis, Pfizer and Roche., Dmytro Fedkov Grant/research support from: MSD, AbbVie, ProPharma, Laboratoires Expanscience; Consultant for: MSD, AbbVie, ProPharma, Laboratoires Expanscience; Speakers bureau: Janssen, Sławomir Jeka: None declared, Mark C. Genovese Grant/research support from: Sanofi/Genzyme, Genentech/Roche, RPharm, Consultant for: Sanofi/Genzyme, Genentech/Roche, RPharm
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OP0026

A PHASE 3 STUDY OF THE EFFICACY AND SAFETY OF PEFICITINIB (ASP015K) IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAD AN INADEQUATE RESPONSE TO METHOTREXATE

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Background: Peficitinib (ASP015K), a novel oral JAK inhibitor, demonstrated efficacy as once-daily monotherapy in patients with moderate-to-severe rheumatoid arthritis (RA) in a phase 2b study (NCT01649999)[1].
Objectives: To evaluate the efficacy and safety of peficitinib–methotrexate (MTX) combination in patients with RA who had an inadequate response to MTX.
Methods: This multicentre, randomised, double-blind, parallel-group, placebo (PBO)-controlled, phase 3 study (NCT02305849) was conducted in Japan. Patients had RA diagnosed within the past 10 years (1987 ACR or 2010 ACR/EULAR criteria), active disease (≥6 tender and painful joints and ≥6 swollen joints, using 68 and 66-joint assessment respectively; CRP ≥1.0 mg/dL; bone erosion; and ACPA or RF positivity) and inadequate response to MTX (administered for ≥90 days; ≥8 mg/week for ≥28 days prior to baseline). Patients were randomised 1:1:1 to 52-week MTX plus PBO, peficitinib 100 mg/day or peficitinib 150 mg/day. At week 12, inadequate responders in the PBO group (<20% improvement from baseline in tender and swollen joint counts) were switched (under blinded conditions) to peficitinib 100/150 mg until end of treatment. Remaining patients in the PBO group were switched (under blinded conditions) to peficitinib at week 28. Concomitant stable MTX dose (≤16 mg/week) was mandatory. Primary efficacy variables were ACR20 response rate at week 12/early termination (ET) and change from baseline in modified Total Sharp score (mTSS) at week 28/ET.

Table 1 Primary and selected secondary efficacy endpoints at week 12/ET

Result	Week 12/ET			Week 28/ET		
	PBO	Peficitinib 100 mg/day	Peficitinib 150 mg/day	PBO	Peficitinib 100 mg/day	Peficitinib 150 mg/day
ACR20, n/N (%)	37/170 (21.8)	102/174 (58.6)***	112/174 (64.4)***	50/170 (29.4)	129/174 (74.1)***	137/174 (78.7)***
ACR50, n/N (%)	13/170 (7.6)	52/174 (29.9)***	80/174 (46.0)***	19/170 (11.2)	88/174 (50.6)***	103/174 (59.2)***
ACR70, n/N (%)	4/170 (2.4)	21/174 (12.1)***	41/174 (23.6)***	10/170 (5.9)	47/174 (27.0)***	70/174 (40.2)***
Mean (SD) CRP change from baseline, mg/dL	-0.001 (2.038)	-1.499 (1.855)***	-1.421 (2.182)***	-0.041 (2.399)	-1.649 (2.165)***	-1.625 (2.236)***
Mean (SD) ESR change from baseline, mm/h	-2.42 (19.71)	-18.90 (19.85)***	-22.17 (22.79)***	-3.26 (22.68)	-24.51 (23.67)***	-26.21 (24.58)***
DAS28-CRP <2.6, n/N (%)	13/169 (7.7)	54/172 (31.4)***	60/171 (35.1)***	20/169 (11.8)	86/172 (50.0)***	86/171 (50.3)***
Mean (SD) DAS28-CRP change from baseline	-0.51 (1.10)	-1.70 (1.20)***	-2.09 (1.33)***	-0.64 (1.33)	-2.27 (1.31)***	-2.56 (1.38)***
Mean (SD) change from baseline in patient's assessment of pain, 100 mm VAS	-6.64 (25.22)	-21.09 (27.04)***	-26.87 (26.65)***	-7.61 (27.81)	-26.33 (28.22)***	-32.23 (27.59)***
SDAI remission (SDAI score ≤3.3), n/N (%)	1/169 (0.6)	12/172 (7.0)**	24/171 (14.0)***	6/169 (3.6)	36/172 (20.9)***	37/171 (21.6)***
	Week 28/ET			Week 52/ET		
	PBO	Peficitinib 100 mg/day	Peficitinib 150 mg/day	PBO	Peficitinib 100 mg/day	Peficitinib 150 mg/day
Mean (SD) mTSS change from baseline[a]	3.37 (5.46)	1.62 (4.23)***	1.03 (2.86)***	6.27 (10.18)	2.12 (5.83)***	1.54 (4.11)***
Patients achieving mean mTSS change from baseline ≤0.5[a], n/N (%)	70/153 (45.8)	110/164 (67.1)***	119/164 (72.6)***	65/153 (42.5)	105/164 (64.0)***	113/164 (68.9)***

Last Observation Carried Forward imputation method was used, except for mTSS. Statistical testing was performed for peficitinib 100 mg, and 150 mg, compared with PBO.
**p<0.01 vs PBO; ***p<0.001 vs PBO, according to Fisher's Exact test for ACR20, ACR50, ACR70, DAS28-CRP <2.6, SDAI remission, and mTSS change from baseline ≤0.5; analysis of covariance for CRP, ESR, DAS28-CRP, and patient's assessment of pain; and rank analysis of covariance for mTSS change from baseline. Closed testing procedure was used for multiplicity adjustment in the primary analysis.
[a]For the calculation of mTSS, patients who discontinued at or before week 28 or were switched from PBO to peficitinib at week 12 due to lack of efficacy, week 28/ET mTSS was extrapolated using linear extrapolation method based on the mTSS at baseline and early termination or week 12 (day 85) (before switching). For patients who discontinued at or before week 52 or switched to receive peficitinib instead of placebo at week 12 or week 28, mTSS at week 52/ET was extrapolated using a linear extrapolation method based on mTSS at baseline and early termination, week 12 (Day 85) or week 28 (Day 197) (before switching).
mTSS=modified Total Sharp score; SD=standard deviation; SDAI=simplified disease activity index; VAS=visual analog scale.

Table 2 Treatment-emergent adverse events

	PBO (N=170)	Peficitinib 100 mg/day (N=174)	Peficitinib 150 mg/day (N=174)	Peficitinib 100 mg/day + 150 mg/day (N=348)
Event, n (%), Week 0–12				
Any AE	84 (49.4)	89 (51.1)	104 (59.8)	193 (55.5)
Drug-related AE[a]	47 (27.6)	57 (32.8)	80 (46.0)	137 (39.4)
Death	0	0	0	0
SAE	4 (2.4)	5 (2.9)	3 (1.7)	8 (2.3)
Drug-related SAE[a]	2 (1.2)	3 (1.7)	3 (1.7)	6 (1.7)
Grade ≥3 AE[b]	8 (4.7)	9 (5.2)	16 (9.2)	25 (7.2)
AE leading to permanent discontinuation of study drug	7 (4.1)	5 (2.9)	5 (2.9)	10 (2.9)
Serious infection	0	3 (1.7)	1 (0.6)	4 (1.1)
Herpes zoster-related disease	0	2 (1.1)	3 (1.7)	5 (1.4)
Malignancy	0	0	0	0
Incidence rate per 100 patient-years (95% confidence interval), overall study period[c]	**PBO (N=170)**	**Peficitinib 100 mg/day (N=174)**	**Peficitinib 150 mg/day (N=174)**	**Peficitinib total (N=496)[d]**
Serious infection[e]	0.0	3.8 (1.7, 8.4)	3.7 (1.7, 8.3)	3.4 (2.0, 5.8)
Herpes zoster-related disease	3.2 (0.8, 12.8)	8.3 (4.8, 14.3)	3.8 (1.7, 8.4)	5.7 (3.8, 8.6)
Malignancy	1.6 (0.2, 11.3)	0.6 (0.1, 4.4)	0.0	0.2 (0.0, 1.7)

[a]Possibly or probably related to study drug, as assessed by the investigator, or records where relationship is missing.
[b]Based on NCI-CTCAE grade: grade 3=severe or medically significant, grade 4=life threatening, grade 5=death related to AE.
[c]Patient-years covers from initial dose up to first incidence of AE for patients who had at least one event, otherwise, the duration of the patients are summed as from initial dose through follow-up. Incidence rate was calculated as (100 x number of patients who had at least one incidence / total patient-year).
[d]Includes AEs that occurred after initial peficitinib dosing, and after switching from PBO to peficitinib 100 mg/day or 150 mg/day.
[e]Defined as an AE belonging to the system organ class of 'Infections and infestations' and regarded as serious.
AE=adverse event; SAE=serious adverse event.

Results: 519 patients were treated: PBO (n=170), peficitinib 100 mg (n=175) and peficitinib 150 mg (n=174). At week 12, 75 PBO-treated patients were switched to peficitinib 100 mg (n=37) and 150 mg (n=38) due to inadequate response. At week 12/ET, peficitinib showed superior efficacy vs PBO with respect to symptoms and inflammatory markers (**Table 1**). At weeks 28 and 52, peficitinib significantly reduced the mean mTSS change from baseline vs PBO (**Table 1**). Week 0–12 safety results were similar for PBO and peficitinib (**Table 2**). For the overall study period, incidence rate of serious infections per 100 patient-years was higher with peficitinib 100 mg/150 mg than PBO (**Table 2**).
Conclusion: In patients with RA who had an inadequate response to MTX, peficitinib 100 mg/day and 150 mg/day demonstrated significant superiority vs PBO in reducing RA symptoms and suppressing joint destruction, according to primary efficacy variables (ACR response and change in mTSS). Peficitinib 100 mg and 150 mg showed acceptable safety and tolerability, with no new safety signals compared with other JAK inhibitors.

REFERENCE:
[1] Takeuchi T, et al. Ann Rheum Dis 2016; 75: 1057–64

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OP0027 EFFECT OF SHORT-TERM METHOTREXATE DISCONTINUATION ON THE DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: POSTHOC-ANALYSIS OF TWO RANDOMIZED CLINICAL TRIALS

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Background: Patients with rheumatoid arthritis (RA) require a continuous, potentially life-long immune suppression with disease modifying antirheumatic drugs (DMARDs) including methotrexate (MTX). However, in special circumstances such as life-threatening infections, vaccinations or major surgeries, use of MTX should be minimized to restore the treatment-associated immune suppression. While a long-term or permanent discontinuation of MTX is associated with a disease flare or relapse, the effect of short-term discontinuation on disease activity has not been fully elucidated.
Objectives: To investigate the effect of short-term discontinuation of MTX on the disease activity in patients with RA on stable dose of MTX.
Methods: This is a posthoc analysis of 2 randomized controlled studies investigating effect of MTX discontinuation for 2 weeks or 4 weeks on vaccine response to seasonal influenza vaccination in patients with RA. In the 4-week discontinuation study, 54 patients continued MTX and 44 patients discontinued it for 4 weeks before vaccination with trivalent seasonal influenza vaccine. In the 2-week discontinuation study, 159 patients continued MTX and 161 patients held it for 2 weeks after a seasonal quadrivalent influenza vaccine. Disease activity (DAS28 change, DAS28 flare rate and flare-free survival) was compared between the patients who continued MTX and those held it. A RA flare was defined as an increase in DAS28 of >1.2 or >0.6 if the baseline DAS28 was $\geq$3.2.
Results: In the 4-week MTX-hold group, the mean DAS28 increased at the 4 weeks after MTX discontinuation by 0.38 ± 0.94 and then improved back to baseline after reintroduction of MTX, whereas the mean DAS28 in the MTX-continue group remained stable over time (Figure 1A). The overall flare-free survival during 20 weeks did not differ between the groups (log rank p=0.142) (Figure 1B). However, numerically more patients in the MTX-hold group experienced a flare than those in the MTX-continue group during the 4-weeks MTX discontinuation (20.5% vs. 7.4%, p=0.058). After resuming MTX, the flare rate did not differ between the groups up to 20 weeks of observations (Figure 1C). A temporary MTX discontinuation for 2 weeks was not associated with any clinically meaningful change in disease activity.

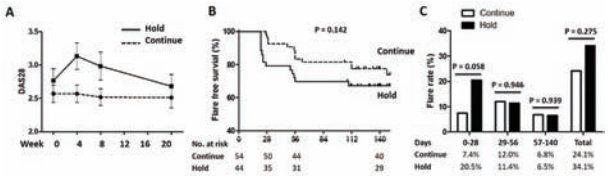


Figure 1. Changes in disease activity of rheumatoid arthritis after MTX discontinuation over time. (A) DAS28-CRP and (B) RA flare free survival in the MTX continue and the MTX hold group were depicted. (C) RA flare rates over time were shown. MTX, methotrexate.

Conclusion: A short-term MTX discontinuation for 2 weeks is safe without any change in disease activity. A 4-week MTX discontinuation is associated with transient increase in disease activity without affecting long-term outcomes.

REFERENCES:
[1] Park JK, Lee MA, Lee EY, Song YW, Choi Y, Winthrop KL, et al. Effect of methotrexate discontinuation on efficacy of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis. 2017 May 03.
[2] Park JK, Lee YJ, Shin K, Ha YJ, Lee EY, Song YW, et al. Impact of temporary methotrexate discontinuation for 2 weeks on immunogenicity of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. Ann Rheum Dis. 2018 Jun; 77(6):898-904.
[3] Haschka J, Englbrecht M, Hueber AJ, Manger B, Kleyer A, Reiser M, et al. Relapse rates in patients with rheumatoid arthritis in stable remission tapering or stopping antirheumatic therapy: interim results from the prospective randomised controlled RETRO study. Ann Rheum Dis. 2016 Jan; 75(1):45-51.

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OP0028 POST-APPROVAL COMPARATIVE SAFETY STUDY OF TOFACITINIB AND BIOLOGIC DMARDS: FIVE–YEAR RESULTS FROM A US-BASED RHEUMATOID ARTHRITIS REGISTRY

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Real-world data (RWD) complement clinical trial data in assessing

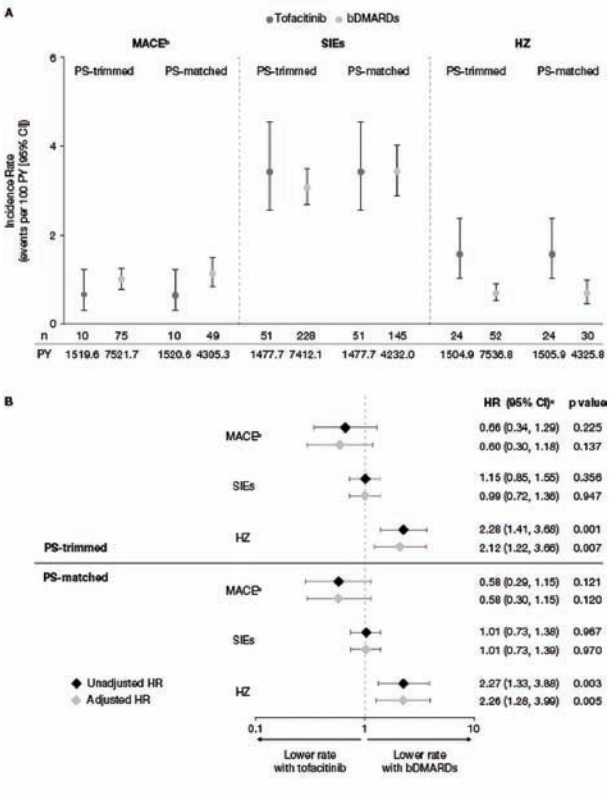
long-term safety. To our knowledge, this is the first long-term comparative RWD analysis of tofacitinib.

Objectives: To compare 5-year adverse event (AE) incidence rates (IRs) in patients (pts) starting tofacitinib vs biological (b)DMARDs using cohorts from the US Corrona RA registry.

Methods: This prospective, observational 5-year study embedded in the ongoing US Corrona RA registry routinely collected 9 categories of predefined AEs from participating physicians. Real-world safety event rates of major adverse cardiovascular events (MACE), serious infectious events (SIEs) and herpes zoster (HZ; serious and non-serious) were compared in pts with RA who started tofacitinib or a bDMARD regardless of dose/schedule between 6 Nov 2012 (US FDA approval) and 30 Jun 2017 (follow-up through 31 Dec 2017). Endpoints were selected *a priori* as having sufficient power to detect a 2-fold difference between cohorts at this datacut; there was insufficient power to assess malignancy. Baseline variables with a standardised difference >|0.10| between tofacitinib and bDMARD initiators, and *a priori* selected covariates (gender, age, line of therapy, history of AE of interest) were used to construct propensity scores (PS) to derive a PS-trimmed (primary) population and a PS–matched population for sensitivity analysis (ratio: max. 4 bDMARD:1 tofacitinib; calliper=0.05). Pts were followed from initiation until an AE of interest, discontinuation and/or start of a new therapy +90 days, death or end of follow-up, whichever came first. Crude IRs (events/100 pt–years [PY]) were estimated; multivariable-adjusted Cox regression was used to estimate hazard ratios (HRs) comparing rates of first events between cohorts.

Results: In total, 1544 tofacitinib (2138.2 PY) and 7083 bDMARD (9904.9 PY) initiators were included. PS–trimming resulted in 1117 tofacitinib and 5542 bDMARD initiators. Rates of MACE and SIEs were similar in both cohorts (Fig 1A); adjusted HRs (95% confidence intervals [CIs]) were: MACE 0.60 (0.30, 1.18); SIEs 0.99 (0.72, 1.36; Fig 1B). HZ IR was higher for tofacitinib vs bDMARDs (Fig 1A); HRs for HZ were significantly increased with tofacitinib vs bDMARDs (adjusted HR 2.12 [1.22, 3.66]; Fig 1B); all HZ events were non-serious with tofacitinib. Similar results were observed in PS-matched populations.

FIG 1: A. Crude incidence rates* for MACE, SIEs and HZ; and B. Hazard ratios for MACE, SIEs and HZ



*Incidence rates are events per 100 PY; †MACE is defined as any myocardial infarction, stroke/transient ischaemic attack or cardiovascular death; ‡bDMARD initiators were the reference population for calculation of HRs

bDMARD, biological disease-modifying antirheumatic drug; CI, confidence interval; HR, hazard ratio; HZ, herpes zoster; MACE, major adverse cardiovascular event; PS, propensity score; PY, patient-years; SIEs, serious infection events

Conclusion: This is the first comparative analysis of RWD for tofacitinib and bDMARDs to use PS-trimmed and PS-matched analyses to adjust for channelling/prescribing patterns for newly approved therapies. Pts starting tofacitinib or bDMARDs for RA had similar rates of MACE and SIEs. Tofacitinib initiators had higher HZ IRs vs bDMARD initiators. These results are consistent with long-term clinical trial findings.

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OP0029

SWITCHING BETWEEN THE JAK1-SELECTIVE INHIBITOR-UPADACITINIB AND ADALIMUMAB FOLLOWING INITIAL NON-RESPONSE: CLINICAL AND FUNCTIONAL OUTCOMES AMONG RHEUMATOID ARTHRITIS PATIENTS

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Background: Initiating advanced therapy for rheumatoid arthritis (RA) patients (pts) with a bDMARD or a Janus kinase (JAK) inhibitor is recommended if remission or low disease activity (LDA) is not achieved with csDMARDs.[1,2] While data show that pts are switched alternately between bDMARD and JAK treatments, there is lack of evidence for pts with inadequate response (IR) to a JAK inhibitor switching to a bDMARD. Recently, the JAK1-selective inhibitor-upadacitinib (UPA) demonstrated superior clinical and functional outcomes through 26 wks to the standard of care-adalimumab (ADA) with continued background methotrexate (MTX).[3]

Objectives: To describe outcomes associated with treatment switch from UPA to ADA and vice-versa among RA pts who do not achieve initial response.

Methods: This phase 3, double-blind, placebo (PBO)-controlled, head-to-head study of UPA 15 mg q.d. vs PBO or ADA 40 mg injection every other wk included MTX-IR patients; all pts continued stable background MTX through 26 wks. Pts without ≥20% improvements from bl in tender (68) and swollen (66) joint counts by wks 14, 18, or 22 were considered non-responders (NR) and switched without washout to either ADA (UPA group) or UPA (ADA group) in a bl fashion. Post-hoc analysis assessed clinical outcomes - DAS28 (CRP), CDAI, SDAI, and ACR responses (from baseline), and HAQ-DI at 3 and 6 mos (±2 wks) post-switch. Adverse events (infections) were summarized as n% (95% CI) through 6 mos post-switch (ps). Data were as observed.

	UPA 15 mg QD Non-responders Switched to ADA 40 mg eow (N=126)		ADA 40 mg eow Non-responders Switched to UPA 15 mg QD (N=77)	
n/N (%)	3 months post-switch	6 months post-switch	3 months post-switch	6 months post-switch
ACR20*	68/118 (58)	67/111 (59)	49/75 (65)	53/71 (75)
ACR50*	33/120 (28)	29/112 (26)	26/73 (36)	34/69 (49)
ACR70*	10/120 (8)	14/114 (12)	13/74 (18)	17/73 (24)
DAS28(CRP) ≤3.2	30/119 (25)	38/109 (35)	31/74 (42)	38/70 (54)
DAS28(CRP) <2.6	15/119 (13)	21/109 (19)	19/74 (26)	22/70 (31)
CDAI ≤10	33/120 (28)	41/114 (36)	24/72 (33)	33/70 (47)
CDAI ≤2.8	5/120 (4)	6/114 (5)	6/72 (8)	10/70 (14)
SDAI ≤11	32/119 (27)	41/109 (38)	26/73 (37)	33/69 (48)
SDAI ≤3.3	5/119 (4)	4/109 (4)	5/73 (7)	12/69 (17)
Mean change from baseline (95% CI)†				
HAQ-DI	-0.49 (-0.60, -0.38)	-0.52 (-0.64, -0.41)	-0.63 (-0.76, -0.50)	-0.67 (-0.81, -0.53)
DAS28(CRP)	-1.29 (-1.03, -1.55)	-2.10 (-2.36, -1.84)	-2.36 (-2.66, -2.06)	-2.56 (-2.90, -2.22)
CDAI	-20.87 (-23.62, -18.11)	-23.61 (-26.49, -20.73)	-22.45 (-25.79, -19.12)	-24.95 (-28.35, -21.55)
SDAI	-21.70 (-24.46, -18.94)	-24.52 (-27.47, -21.56)	-23.49 (-27.03, -19.95)	-26.07 (-29.59, -22.59)

*Responses are based on percent improvement in American College of Rheumatology criteria from baseline at randomization; †mean change from baseline at randomization.

UPA: upadacitinib; QD: once daily; ADA: adalimumab; eow: every other week; ACR: American College of Rheumatology; DAS28(CRP): 28-joint disease activity score based on C-reactive protein; CDAI: clinical disease activity index; SDAI: simplified disease activity index; CI: confidence interval; TJC68: tender joint count based on 68 joints; SJC66: swollen joint count based on 66 joints; HAQ-DI: health assessment questionnaire disability index.

Results: Of the 651 and 327 pts randomized to receive UPA and ADA, 126 (19%) and 77 (24%), were considered NR and switched to ADA and UPA respectively. NR demographics were consistent with the overall randomized population. Of the switched pts, ~90% remained in the study through 6 mo ps. Patients switched to ADA (UPA-NR) achieved 59%/26%/12% improvements in ACR20/50/70 responses, and 35% achieved DAS28(CRP) ≤3.2 at 6 mos ps (**Table**). Patients switched to UPA (ADA-NR) achieved 75%/49%/24% improvements in ACR20/50/70, and 54% achieved DAS28(CRP) ≤3.2 at 6 mo- consistent with data observed in a phase 3 study of UPA in bDMARD-IR RA pts.[4] The proportion (95% CI) of pts with infection and serious infection through 6 mos ps appeared consistent with those observed for ADA and UPA during comparable periods (ADA, switched from UPA: infection: 34.1 [26.43, 42.77], serious infection: 1.6 [0.44, 5.60]; UPA, switched from ADA: infection: 40.3 [30.02, 51.42], serious infection: 3.9 [1.33, 10.84]

Conclusion: Data from this blinded, controlled study indicate that pts with initial non-response to either UPA or ADA can benefit from switching to the other therapy. No additional safety concerns were observed. These are the first data to demonstrate effectiveness of a TNF inhibitor following failure of a JAK inhibitor.

REFERENCES:

[1] Smolen, et al. Ann Rheum Dis, 2017;76:1113-36.
[2] Singh, et al. *Arthritis Rheumatol*, 2016;68:1-26.
[3] Fleischmann, et al. *Arthritis Rheumatol*, 2018;70(Suppl 10).
[4] Genovese, et al. Lancet, 2018;391:2513-24.

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OP0030

RANDOMIZED CONTROLLED 24-WEEK TRIAL EVALUATING THE SAFETY AND EFFICACY OF BLINDED TAPERING VERSUS CONTINUATION OF LONG-TERM PREDNISONE (5 MG/D) IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVED LOW DISEASE ACTIVITY OR REMISSION ON TOCILIZUMAB

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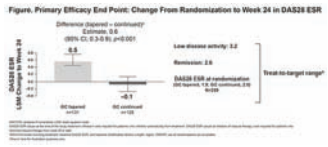
Background: Guidelines recommend low-dose, short-term glucocorticoid (GC) treatment for rheumatoid arthritis (RA).[1,2] Long-term use, especially at prednisone-equivalent doses >5 mg/d, should be avoided,[2] but many patients (pts) with early established RA receive long-term GCs, often ≥5 mg/d.[3]

Objectives: Compare GC tapering vs continuation to maintain disease control in RA pts with chronic GC exposure receiving tocilizumab (TCZ) in a randomized controlled trial.

Methods: Before randomization pts had to receive TCZ ± conventional synthetic (cs)DMARDs and GC (prednisone-equivalent dose 5-15 mg/d) for ≥24 wks. At randomization pts had to be in at least low disease activity (LDA: DAS28-ESR ≤3.2) and receiving stable concomitant therapy (prednisone 5 mg/d [GC5mg]) and TCZ ± csDMARDs) for ≥4 wks. Pts were randomized to continue blinded GC5mg for 24 wks or undergo blinded taper (GCtaper, from 4 mg/d with 1-mg reduction every 4 wks to 0 mg/d at wks 16-24) while receiving stable TCZ and csDMARD doses. Pts with RA flare (DAS28-ESR >3.2 and increase >0.6 vs baseline) received open-label rescue GC5mg for 2 wks and continued blinded treatment. Primary outcome was mean change in DAS28-ESR at wk 24. Key secondary outcome was treatment success—DAS28-ESR ≤3.2 at wk 24 **and** no RA flare during 24 wks **and** no adrenal insufficiency necessitating replacement therapy.

Results: 259 pts were randomized to GCtaper (n=131) or GC5mg (n=128); 114 and 112, respectively, completed 24 wks. Mean baseline DAS28-ESR was 1.9. Mean RA duration was 9.2 y. For the primary endpoint, the between-arm difference was 0.6 DAS28-ESR units (95% CI, 0.3, 0.9; $p<0.001$, ANCOVA) favoring GC5mg (Figure). Results were consistent for key subgroups (DAS28-ESR between-arm difference 0.5 [95% CI –0.1, 1.0] for TCZ monotherapy, 0.7 [0.4-1.0] for TCZ + csDMARDs, 0.6 [0.2-1.0] for baseline DAS28 <2, and 0.6 [0.2-1.0] for baseline DAS28 ≥2). Most pts in both arms achieved treatment success (65% GCtaper vs 77% GC5mg; relative risk, 0.83 [0.71-0.97]; $p=0.021$, Cochran-Mantel-Haenszel test); 11% of GC5mg pts and 26% of GCtaper pts experienced RA flare. One GC5mg pt and no GCtaper pts discontinued blinded treatment due to insufficient flare control. Serious adverse events (no deaths) were reported for 5% of GC5mg vs 3% of GCtaper pts. No pts had symptomatic adrenal insufficiency.

Conclusion: Continued GC5mg provided better DAS28-ESR control than GC taper in RA pts in LDA or remission. The 0.6 DAS28-ESR unit between-arm difference should be interpreted in the context of approximately two-thirds of tapered pts experiencing treatment success and no tapered pts discontinuing due to lack of flare control. The taper schedule was safe regarding adrenal insufficiency. The results suggest that all pts achieving LDA or remission with TCZ and receiving long-term low-dose GC should be considered for GC tapering, ideally targeting discontinuation.



REFERENCES:

[1] Singh JA et al. *Arthritis Rheum.* 2016;68:1.
[2] Smolen JS et al. *Ann Rheum Dis.* 2017;76:960.
[3] Buttgereit F, Bijlsma JW. *Ann Rheum Dis.* 2017;76:1785.

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WEDNESDAY, 12 JUNE 2019

Spondyloarthritis on the move: Thrilling developments

OP0031

ARE THE MODIFIED NEW YORK AND ASAS AXIAL SPONDYLOARTHRITIS CRITERIA INTERCHANGEABLE IN THE CLASSIFICATION OF SPONDYLOARTHRITIS PATIENTS WITH RADIOGRAPHIC SACROILIITIS: COMPARISON IN 8 COHORTS?

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Background: Axial spondyloarthritis (axSpA) patients with radiographic sacroiliitis may be classified using the modified New York (mNY) criteria) and the more recent ASAS criteria. In the mNY criteria these patients are referred to as ankylosing spondylitis (AS) patients and in the ASAS criteria as radiographic axSpA (r-axSpA) patients.
In both the mNY and the ASAS r–axSpA classification sets the radiographic criterion is the same but the additionally required features differ (figure), for example patients with age at onset of back pain ≥45 cannot fulfil the ASAS criteria. This raises the question whether the two sets can be used interchangeably in the classification of axSpA patients with radiographic sacroiliitis.

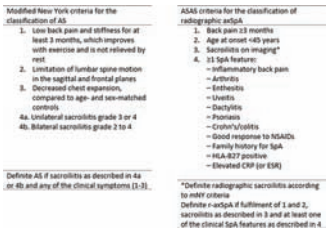


Figure 1. mNY and ASAS r–axSpA criteria for the classification of patients with axSpA and radiographic sacroiliitis.

Objectives: To investigate to what degree patients with axSpA and radiographic sacroiliitis who fulfil the mNY criteria also fulfil the ASAS criteria for r–axSpA and vice–versa.
Methods: Patients diagnosed with axSpA who had back pain longer than 3 months and definite radiographic sacroiliitis (i.e. common and mandatory features for both classification criteria sets (figure)) were selected from several cohorts (ASAS, Esperanza, GESPIC, OASIS, Reuma.pt, SCQM, SPACE, and UCSF). Subsequently we calculated how many patients fulfil the mNY criteria and/or the ASAS r–axSpA criteria. For the Esperanza and OASIS cohorts specific information on the individual items of the mNY criteria was unavailable, which restricted data analysis for these cohorts.
Results: Of the 3882 patients fulfilling the mNY criteria, 93% also fulfilled the ASAS r–axSpA criteria. Inversely, of the 3434 patients fulfilling the ASAS r–axSpA criteria, 96% also fulfilled the mNY criteria (table). In total, 89% (3607/4041) of patients with axSpA and radiographic sacroiliitis fulfilled both criteria sets; 7% only the mNY criteria; 3% only the ASAS criteria and 1% neither set.

Table 1. Percentage of patients fulfilling ASAS r–axSpA within subgroup fulfilling mNY criteria and vice–versa (per cohort and overall)

	ASAS+ within mNY+ subgroup	mNY+ within ASAS+ subgroup
ASAS	97% (98/101)	90% (98/109)
Esperanza	97% (106/109)	NA
GESPIC	98% (78/80)	93% (78/84)
OASIS	95% (201/211)	NA
Reuma.pt	93% (1156/1249)	95% (1156/1211)
SCQM	92% (1612/1760)	98% (1612/1652)
SPACE	100% (77/77)	84% (77/92)
UCSF	98% (279/286)	98% (279/286)
Total	93% (3607/3882)	96% (3300/3434)

The main difference between the two criteria sets was caused by reported age at onset of back pain. Out of 275 mNY+ patients not fulfilling the ASAS criteria (7% of all included patients), 265 (96%) cases were due to the age criterion and 10 (4%) due to the absence of SpA features. Of the 3434 ASAS+ patients, 90% fulfilled the mNY criteria because they had IBP, another 6% despite not having IBP fulfilled the mNY criteria due to a mobility restriction; and the remainder 4% had neither but fulfilled the ASAS criteria because of other SpA features.

Conclusion: AxSpA patients classified as AS according to mNY criteria and those classified as r–axSpA according to ASAS criteria are mostly the same: 93% of mNY positive patients also fulfil the ASAS r-axSpA criteria while 96% of ASAS r–axSpA positive patients also fulfil the mNY criteria. These findings support the interchangeable use of the terms r–axSpA and AS, which was also approved by a vote of ASAS members at the 2019 annual workshop in Amsterdam.
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OP0032

LOCALIZATION AND MORPHOLOGY OF MAGNETIC RESONANCE IMAGING FEATURES OF PATHOLOGIC CHANGES IN THE SACROILIAC JOINTS SUGGESTIVE OF AXIAL SPONDYLOARTHRITIS – A SYSTEMATIC COMPARISON OF PATIENTS AND CONTROLS WITH CHRONIC BACK PAIN

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Background: Bone marrow edema (BME), fat metaplasia (FL) and erosions have been identified as relevant for magnetic resonance imaging (MRI) changes in the sacroiliac joints (SIJ) of patients with axial spondyloarthritis (axSpA). However, a high prevalence of MRI changes has recently also been reported in subjects with no evidence of axSpA (1,2).
Objectives: To map the MRI lesions suspicious of axSpA in patients diagnosed with axSpA and compare them to those in patients with chronic back pain (cBP, non-SpA).
Methods: Consecutive patients with cBP < 45 years were included if they had at least one pathologic lesion of any type in the SIJ-MRI performed at the time point of cBP symptoms. AxSpA patients diagnosed by 2 experienced rheumatologists in consensus also had to fulfil ASAS classification criteria. Two experienced readers, blinded for diagnosis and patient´s demographics, evaluated all MRIs independently. Lesions were only counted as positive if both readers were in agreement and mean values of both readers were calculated for the final analysis. Both the coronal (assessing the upper and lower sacral and iliac SIJ part) and axial (assessing the ventral, middle and retroauricular as well as the upper and lower sacral and iliac SIJ part) MRI orientations were analyzed for the localization of BME, FL, sclerosis and erosions. In addition, length and width were digitally measured for BME, FL and sclerosis, and signal intensity was measured electronically in each individual patient in comparison to the cerebrospinal fluid signal for BME and the subcutaneous fat for FL (no units).
Comparisons were calculated by Mann-Whitney-U-test for patients classified as positive by both readers for the respective lesions.
Results: A total of 200 consecutive patients (100 axSpA, 100 non-SpA), mean age 36.1±11.3 and 40.3±11.0 years, respectively, were analyzed. BME was found in 85% vs. 80% of patients, while 80% vs. 69% had FL, 54% vs. 40% had sclerosis and 64% vs. 12% had erosions, respectively. The largest surface area covered by BME in axSpA vs. non-SpA was found in the lower and dorsal SIJ: 60±10.1 mm^3 in the iliac and 47.3±9.4 mm^3 in the sacral part vs. the upper and ventral SIJ: 18.7 ±3.4 mm^3 in the sacral and 5.2±0.1 mm^3 in the iliac part.
Patients with axSpA showed a larger surface area covered by FL was found in the upper and anterior sacral SIJ (305.5±56.3 mm^3), whereas patients with non-SpA showed larger FL areas in the lower and posterior sacral SIJ (197.9±1.2 mm^3).
Regarding sclerosis, the upper and anterior iliac part had more surface involvement in both SpA (139.3±11.6 mm^3) and non-SpA (81.8±2.8 mm^3) patients.

The mean signal intensity of all lesions and MRI planes differed between axSpA (102.385 *units?*) and non-SpA (48.995) patients for BME (p<0.001) but not for FL. Overall, axSpA patients also had significantly more SIJ quadrants with pathologic changes, except for BME and sclerosis in the ventral and fat located in the retro-auricular part of the SIJ. The occurrence of erosions in the mid (61 vs. 7) and the ventral (51 vs. 8) part of the SIJ could discriminate best between axSpA and non-SpA (both p<0.001).

Conclusion: These data show that although all types of lesions may be found in both patient groups, the anatomic pattern of SIJ involvement can still distinguish axSpA from non-SpA. The localization and morphological appearance of SIJ-MRI features suggestive of axSpA may serve as an additional feature in the definition of a 'positive' MRI both for diagnosis and classification.

REFERENCES:

[1] Weber U, et al. Arthritis Rheumatol 2018
[2] De Winter, et al. Arthritis Rheumatol 2018

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OP0033

WHAT IS AXIAL SPONDYLOARTHRITIS? A LATENT CLASS AND TRANSITION ANALYSIS IN THE SPACE AND DESIR COHORTS

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Background: Axial spondyloarthritis (axSpA) is a disease with a rather heterogeneous presentation that may be difficult to diagnose. Classification criteria, such as the ASAS criteria, which have been developed and validated against the gold-standard 'expert diagnosis', exist, but may suffer from inappropriate circularity because features deemed important by experts (e.g. sacroiliitis on MRI) may have easily got a too prominent, and therefore biased, role. If classification criteria are used inappropriately to confirm a diagnosis, overdiagnosis ('too much SpA') may be an unwarranted consequence.

Objectives: To gain an unbiased insight into the concept of axSpA, by circumventing expert opinion and investigating its 'latent constructs': We examined the SpA-features' mutual statistical coherence, established the unbiased 'Gestalt' of SpA, and evaluated how well the ASAS axSpA classification criteria capture these 'latent constructs'.

Methods: Two independent cohorts of patients (pts) with early onset chronic back pain (SPACE cohort) and inflammatory back pain (IBP) (DESIR cohort) were included. Latent class analysis (LCA) (different than a cluster analysis) was used to estimate the latent (i.e. unobserved) 'Gestalt' of axSpA by modelling the covariance of the observed SpA features (without 'a priori' assumptions on their 'weights'). The selected best LCA model splits axSpA into a number of (clinically meaningful) classes with best data fit. Each class was labelled by us and named according to most prominent features. The latent axSpA classes were then used as 'gold-standard' against which the ASAS axSpA, pSpA (ignoring IBP) and both (SpA criteria) were tested. Finally, 5-year follow-up data from DESIR were used to perform a latent transition analysis (LTA) in order to examine if patients change classes over 5-year time.

Table 1. Latent class analysis model in SPACE (N=465)

	'Axial' (P*=15.9%)	'IBP+Peripheral' (P*=20.0%)	'At risk' (P*=24.3%)	'No SpA' (P*=39.7%)
	Estimated probability (95% CI)	Estimated probability (95% CI)	Estimated probability (95% CI)	Estimated probability (95% CI)
Inflammation on MRI-SIJ (ASAS)	***0.74 (0.52; 0.88)***	0.04 (0.01; 0.14)	0.00 (0.00; 1.00)	0.03 (0.01; 0.08)
Radiographic sacroiliitis (mNY)	**0.32 (0.19; 0.49)**	0.09 (0.04; 0.20)	0.01 (0.00; 0.32)	0.03 (0.01; 0.08)
Elevated CRP (≥ 6 mg/dL)	**0.49 (0.32; 0.65)**	0.22 (0.13; 0.34)	0.21 (0.13; 0.32)	0.20 (0.15; 0.28)
BME on MRI-Spine (≥ 5 lesions)	**0.25 (0.14; 0.42)**	0.02 (0.00; 0.18)	0.00 (0.00; 1.00)	0.00 (0.00; 0.11)
≥ 1 syndesmophyte on X-spine	0.03 (0.01; 0.11)	0.06 (0.03; 0.14)	0.00 (0.00; 1.00)	0.04 (0.02; 0.08)
Good response to NSAIDs (ever)	*0.59 (0.41; 0.75)*	***0.85 (0.72; 0.93)***	0.25 (0.14; 0.42)	0.20 (0.14; 0.29)
Peripheral arthritis (ever)	0.17 (0.09; 0.30)	**0.44 (0.30; 0.58)**	0.04 (0.01; 0.15)	0.10 (0.06; 0.17)
Dactylitis (ever)	0.02 (0.00; 0.17)	**0.18 (0.11; 0.29)**	0.00 (0.00; 1.00)	0.03 (0.01; 0.07)
Heel enthesitis (ever)	0.10 (0.04; 0.25)	***0.66 (0.50; 0.79)***	0.13 (0.06; 0.24)	0.04 (0.01; 0.11)
HLA-B27	***0.84 (0.67; 0.93)***	0.33 (0.23; 0.46)	*0.69 (0.24; 0.94)*	0.00 (0.00; 1.00)
Family history of SpA	0.38 (0.24; 0.54)	0.50 (0.38; 0.62)	***0.71 (0.56; 0.82)***	0.21 (0.10; 0.38)
Psoriasis (ever)	0.10 (0.04; 0.22)	**0.31 (0.21; 0.43)**	0.02 (0.00; 0.23)	0.08 (0.05; 0.14)
Uveitis (ever)	**0.13 (0.06; 0.24)**	0.07 (0.03; 0.17)	0.12 (0.06; 0.22)	0.02 (0.00; 0.11)
IBD (ever)	0.03 (0.01; 0.16)	**0.15 (0.08; 0.25)**	0.00 (0.00; 1.00)	0.10 (0.06; 0.17)
Inflammatory back pain	*0.68 (0.55; 0.79)*	***1.00 (0.00; 1.00)***	*0.66 (0.53; 0.76)*	0.49 (0.39; 0.59)

* Probability of the latent class. Values are the conditional probability (95% confidence interval) for each SpA feature positivity within each latent class (range: 0-1). Values in **bold** highlight dominant features between latent classes. Values in *italic* highlight dominant features (probability >50%) within each class. BME, bone marrow edema; IBD, Inflammatory bowel disease.

Table 2. Latent class analysis model in DESIR (N=576)

	'Axial' (P*=18.8%)	'IBP+Peripheral' (P*=26.7%)	'At risk' (P*=54.5%)
	Estimated probability (95% CI)	Estimated probability (95% CI)	Estimated probability (95% CI)
Inflammation on MRI-SIJ (ASAS)	***0.83 (0.69; 0.92)***	0.22 (0.15; 0.30)	0.09 (0.06; 0.16)
Radiographic sacroiliitis (mNY)	***0.58 (0.45; 0.70)***	0.06 (0.02; 0.13)	0.02 (0.01; 0.08)
Elevated CRP (≥ 6 mg/dL)	***0.56 (0.44; 0.67)***	0.41 (0.32; 0.51)	0.14 (0.10; 0.20)
BME on MRI-Spine (≥ 5 lesions)	**0.20 (0.13; 0.30)**	0.00 (0.00; 1.00)	0.01 (0.00; 0.03)
≥ 1 syndesmophyte on X-spine	**0.11 (0.06; 0.20)**	0.05 (0.02; 0.11)	0.06 (0.04; 0.10)
Good response to NSAIDs (ever)	***0.97 (0.90; 0.99)***	*0.84 (0.76; 0.90)*	*0.82 (0.77; 0.86)*
Peripheral arthritis (ever)	0.09 (0.04; 0.20)	***0.73 (0.49; 0.88)***	0.00 (0.00; 1.00)
Dactylitis (ever)	0.03 (0.01; 0.15)	**0.46 (0.36; 0.55)**	0.01 (0.00; 0.31)
Heel enthesitis (ever)	0.26 (0.18; 0.37)	***0.60 (0.51; 0.69)***	0.45 (0.39; 0.51)
HLA-B27	***0.90 (0.79; 0.96)***	*0.52 (0.43; 0.61)*	*0.53 (0.47; 0.59)*
Family history of SpA	**0.48 (0.37; 0.58)**	0.44 (0.36; 0.53)	0.41 (0.36; 0.48)
Psoriasis (ever)	0.09 (0.04; 0.18)	**0.29 (0.22; 0.38)**	0.14 (0.10; 0.19)
Uveitis (ever)	0.08 (0.04; 0.18)	**0.12 (0.07; 0.20)**	0.08 (0.05; 0.12)
IBD (ever)	0.02 (0.00; 0.10)	0.05 (0.02; 0.11)	0.05 (0.03; 0.08)

* Probability of the latent class. Values are the conditional probability (95% confidence interval) for each SpA feature positivity within each latent class (range: 0-1). Values in **bold** highlight dominant features between latent classes. Values in *italic* highlight dominant features (probability >50%) within each class. BME, bone marrow edema; IBD, Inflammatory bowel disease.

Results: In total, data of 465 (SPACE) and 576 (DESIR) pts were analyzed. SPACE yielded 4 latent classes (Table 1). The 'Axial' class characterized by highest likelihood on abnormal imaging and HLA-B27-positivity; the 'IBP+Peripheral' class had 100% likelihood of IBP in association with peripheral signs. The 'At risk' class is anchored on a positive family history and HLA-B27 positivity in association with IBP; and the 'No SpA' class had very low likelihoods for all SpA-features which were correlated. The independent analysis in DESIR (without 'no-SpA' patients) yielded identical latent classes ('Axial':19%; 'IBP+Peripheral':27% and 'At risk':55%) (Table 2). The ASAS axSpA criteria, tested in SPACE ('No SpA' absent in DESIR), captured 67% of the patients in the 'Axial' and 'IBP+Peripheral' classes ('latent gold-standard'), but sensitivity was better (87%) if axSpA and pSpA criteria were combined. Of note, the axSpA criteria captured only 4% of the patients from the 'No SpA' class. Importantly, the LTA suggests that transition between classes over time was highly unlikely. 'Axial' and 'IBP+Peripheral' patients did not switch and only 11% of 'At risk' pts had switched to 'IBP+Peripheral' after 5 years.

Conclusion: The 'Gestalt' of axial spondyloarthritis comprises three distinguishable clinical entities ('pure axial SpA', 'axial SpA with peripheral signs, and 'axial SpA at risk'). Patients keep their clinical entity over 5 years and transition is very rare. The 'Axial' and 'IBP+Peripheral' entities are best captured by combining the ASAS axSpA and pSpA criteria.

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OP0034

DO SMOKING AND SOCIO-ECONOMIC FACTORS INDEPENDENTLY INFLUENCE IMAGING OUTCOMES IN AXIAL SPONDYLOARTHRITIS? FIVE-YEAR DATA FROM THE DESIR COHORT

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Background: Smoking and systemic inflammation have been shown to independently associate with radiographic spinal progression in patients with axSpA. Furthermore, evidence suggests that certain socioeconomic (SE) factors (e.g. physically demanding jobs) may modify these associations, but clarity on the intricate relationships between smoking, axial damage and SE factors is yet to be achieved. Moreover, the impact of smoking and SE factors and their interplay on axial inflammation have not been thoroughly investigated to date.
Objectives: To investigate the relationship between smoking and imaging outcomes (SI joints, spine, MRI and radiographs) over time in axSpA and to assess if SE factors first modify and if not, confound, such a relationship.
Methods: Patients with axSpA from the DESIR cohort who fulfil the ASAS axSpA classification criteria were included. Four imaging continuous outcomes (X-ray spine [mSASSS, range 0-72]; X-ray SIJs modified New York grading [mNY, 0-8]; MRI-Spine [SPARCC, range 0-414] and MRI-SIJ [SPARCC, range 0-72]) have been scored by 3 central readers independently (average score used) in one session, blinded for time order (baseline, 2 and 5 years). Smoking, the main variable of interest, was tested as a binary variable to indicate smoking status since last visit. SE variables tested were: age, gender, ethnicity (Caucasian vs other), job type based on 'collar' (blue [manual labour work] vs white [office-based work]); educational status (low vs high [university]); marital status (married vs not) and parental (number of children) status. Potential interactions between smoking and SE factors were first investigated and, if statistically ($p<0.15$) and clinically relevant, models were stratified. The effect of smoking on imaging outcomes was assessed in multivariable time-varying models using generalized estimating equations making use of all available observations and adjusted for other known possible confounders (see table).
Results: In total, 425 axSpA patients were included: 225 [53%] male, 167 [40%] smokers and 287 [68%] blue collar. The mean baseline (SD) MRI-SIJ SPARCC was 4.67 (7.85), MRI-spine SPARCC: 2.73 (7.95)); mSASSS: 0.39(1.66); mNY: 1.70(1.84)). A significant interaction was found between smoking and job type with MRI-SIJ inflammation as the outcome ($p=0.031$) as well as with mNY grading ($p=0.096$). Similarly, educational status also proved to modify the association between smoking and MRI-SIJ inflammation ($p=0.026$). In the multivariable models, smoking was significantly associated with more MRI-SIJ inflammation over 5 years of follow-up but only in patients with a blue-collar job (β [95% CI]: 3.35 [0.54,6.17]) (table). Results were similar in the low education stratum (β [95% CI]: 2.69 [0.48, 4.91]. Smoking was not significantly associated with any of the other imaging outcomes over time. Male gender was positively associated with MRI-SIJ inflammation regardless of job type, and also with MRI-Spine inflammation and structural damage although only for blue-collar patients in the case of SIJ damage.

Table. (Time-varying) relationship between smoking and imaging outcomes across all patients or in strata according to type of job.

OUTCOME	MRI-SIJ (SPARCC)		mNY-SIJs		MRI-Spine (SPARCC)	mSASSS-Spine
STRATA	EVER BLUE COLLAR	NEVER BLUE COLLAR	EVER BLUE COLLAR	NEVER BLUE COLLAR	ALL PATIENTS	ALL PATIENTS
	β Coefficient (95% CI)	β Coefficient (95% CI)	β Coefficient (95% CI)	β Coefficient (95% CI)	β Coefficient (95% CI)	β Coefficient (95% CI)
Model numbers	N=64	N=198	N=85	N=209	N=281	N=403
Smoking (vs not)	3.35(0.54,6.17)	0.47(-1.08,2.02)	0.43(-0.04,0.90)	0.05(-0.08,0.18)	1.32(-0.04,2.67)	0.49(-0.11,1.08)
Age	-0.15(-0.34,0.01)	-0.10(-0.20,-0.00)	-0.00(-0.05,0.04)	0.01(-0.01,-0.02)	0.07(-0.03,0.17)	0.06(0.02,0.10)
Gender (M vs F)	3.95(0.89,7.01)	1.61(0.24,2.98)	1.38(0.56,2.20)	0.59(0.05,1.07)	2.48(1.34,3.62)	0.55(0.04,1.06)
Married (vs not)	-3.45(-9.38,2.49)^	-0.60(-2.15,0.96)				
CRP abnormal at visit (vs not)	8.09(2.97,13.20)	3.03(0.98,5.09)			4.18(2.13,6.23)	
NSAID score (last 6months)			0.00(-0.00,0.00) ^	-0.00(-0.00,0.00)		-0.00(-0.00,0.00) ^
csDMARD use last 6m (vs no)	-4.43(-7.47,-1.39)	-2.15(-3.46,-0.84)	-0.35(-0.60,-0.10)	0.01(-0.07,0.10)	-2.46(-3.58,-1.34)	
TNF use					-1.46(-2.64,-0.28)	
Presence of uveitis					-1.81(-2.91,-0.72)	

Other independent variables tested in models included HLA B27 status, all SE variables of interest, ASDAS or BASDAI, presence of psoriasis, inflammatory bowel disease and peripheral arthritis. ^Indicates confounding effect on the association between smoking and the outcome.

Conclusion: There is a strong association between smoking and MRI-SIJ inflammation over time in axSpA patients with blue collar job type or with low education, irrespective of other socio-economic factors, systemic inflammation and treatment. These findings suggest a possible role for mechanical stress (seen with manual jobs) amplifying the effect of smoking on axial inflammation in axSpA. No significant relationship was found between smoking and spinal inflammation or axial damage, possibly also due to the limited imaging changes in this cohort.
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OP0035

DEPRESSION IN ANKYLOSING SPONDYLITIS AND THE ROLE OF DISEASE-RELATED AND CONTEXTUAL FACTORS: A STRUCTURAL EQUATION MODELLING APPROACH

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Background: Patients with ankylosing spondylitis (AS) are at increased risk of depression compared to the general population. Comorbid depression in AS likely has a multifactorial origin. While several disease-related and contextual factors have been associated with depressive symptoms in AS, a comprehensive model of their interrelations is currently lacking. Such a model could help understand the mechanisms leading to, or maintaining, depression in AS.
Objectives: To determine which factors contribute to depressive symptoms in AS, and to understand the relationships between relevant factors.
Methods: Data from patients with AS participating in the Dutch cross-sectional multicentre survey-based Social Participation in Ankylosing Spondylitis Study (SPASS) were used. Potential determinants included both contextual and disease-related factors. Depressive symptoms were assessed by the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D). A latent 'depression' variable was constructed by regressing the 7 manifest items of the HADS-D questionnaire on the outcome 'depression', to represent it more accurately. Candidate variables for the model were selected using univariable negative binomial regression. Direct and indirect associations between risk factors and the dimensional latent depression outcome were explored using structural equation modelling. Both theory-driven and data-driven approaches were explored. A final model was selected based on model fit criteria, clinical plausibility and explained variance in the outcome.
Results: Among 245 patients, median (interquartile range) HADS-D was 3 (1-6) and 44 patients (18%) had a HADS-D >=8, indicating possible depression. The theory-driven model had poor fit and was rejected. The data-driven approach led to a model with good fit. In this final model (see Figure), contextual factors associated with depressive symptoms were male gender, a history of depression, being employed, lower income, lower mastery and worse satisfaction with social role participation. Regarding disease-related factors, Bath AS Disease Activity Index (BASDAI) was the only determinant in the final explanatory model, acted only indirectly, and had less effect on depressive symptoms than several of the contextual factors. Mastery had a central role in the path diagram and was a mediator for the effects of BASDAI, income and satisfaction with social role participation on depressive symptoms. The final model explained 64% of the variance in the latent depressive symptoms outcome.

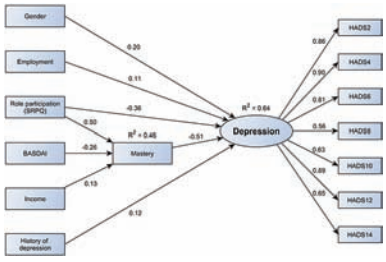


Figure 1. The final model of depression in AS, based on model fit criteria. Numbers above the arrows represent the standardized regression coefficients of direct paths. Standardized regression coefficients can be interpreted as the change in y (dependent variable) in y standard deviation units for a standard deviation change in x (independent variable). The numbered HADS items represent the individual corresponding items on the HADS questionnaire.

Conclusion: Both contextual and disease-related factors contribute to depressive symptoms in AS, but contextual factors have a larger contribution. Mastery, the extent to which one feels in control over life and disease, has a key role in this process. These results support a relevance of self-efficacy in disease management and patient education. In order to improve patients' mental health, research is warranted whether mastery and its relation with depression can be modified.
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OP0036 EROSIONS ARE THE MOST OFTEN REPORTED STRUCTURAL LESION ON MRI OF THE SACROILIAC JOINTS IN AXSPA PATIENTS WITH IBP

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Background: HLA-B27 and sacroiliitis on MRI form the basis of the Assessment of SpondyloArthritis international Society (ASAS) axial spondyloarthritis (axSpA) classification criteria. In addition, while not an entry criterion of the classification criteria, inflammatory back pain (IBP) is fundamental in the axSpA diagnostic process and it is endorsed as referral parameter in primary care. Besides inflammation on MRI, which is the hallmark of axSpA, there is still debate on the value of structural MRI lesions in these patients.
Objectives: To report on MRI of the sacroiliac joints (MRI-SIJ) findings in newly diagnosed axSpA patients stratified for the presence of IBP and HLA-B27 positivity.
Methods: Newly diagnosed and anti-TNF naive axSpA patients of an ongoing Belgian (Be-Giant) cohort were included in this study. MRI-SIJ assessment was performed independently by 3 calibrated readers according to an adapted method of the Spondyloarthritis Research Consortium of Canada score, evaluating erosions, fatty lesions, sclerosis and ankylosis (T1-weighted and STIR images viewed simultaneously). Also, the ASAS definition of a positive MRI-SIJ was evaluated. MRI sum scores were calculated as 2 out of 3 (median) reader scores.
Results: In 138 axSpA patients MRI-SIJ data was available; 68 (49.3%) patients were male, 104 (75.4%) HLA-B27 positive and 131 (94.9%) patients fulfilled the IBP criteria according to ASAS. In the IBP+ patient groups, a large amount of structural MRI lesions were seen. In these groups, erosions are most frequently reported, with an average extent of 5 erosions. IBP- patients were rarely seen in this cohort and erosions and fatty lesions were the only structural lesions observed in these patients, with a much lower extent compared to the IBP+ patients (see table 1). There were no axSpA patients with negative MRI-SIJ, negative HLA-B27 and without IBP.
Conclusion: In this cohort of newly diagnosed anti-TNF naïve axSpA patients, structural lesions are frequently and with a high extent seen in IBP+ patients. Only in the IBP+ axSpA patients the previously reported threshold for axSpA patients of ≥3 erosions and ≥3 fatty lesions is maintained, as IBP- axSpA patients have far fewer lesions. IBP seems to be an indicator for the presence of structural MRI-SI lesions in newly diagnosed axSpA patients.

Table 1. Structural lesions seen on MRI in axSpA patients stratified for IBP, HLA-B27 and a positive MRI-SIJ

Structural MRI lesions	IBP+ HLAB27+ MRI-SI+ n=77	IBP+ HLAB27+ MRI-SI- n=22	IBP+ HLAB27- MRI-SI+ n=27	IBP+ HLAB27- MRI-SI- n=5	IBP- HLAB27+ MRI-SI+ n=3	IBP- HLAB27+ MRI-SI- n=2	IBP- HLAB27- MRI-SI+ n=2	IBP- HLAB27 - MRI-SI- n=0
Gender, n(%) male	41 (53.2%)	13 (59.1%)	9 (33.3%)	2 (40.0%)	1 (33.3%)	1 (50.0%)	1 (50.0%)	-
Erosions*	61 (79.2%); 5.3±4.9	8 (36.4%); 4.9±6.6	20 (74.1%); 5.2±4.4	2 (40.0%); 5.0±5.7	1 (33.3%); 1.0±NA	1 (50%); 2.0±NA	1 (50%); 1.0±NA	0
Fatty lesions*	23 (29.9%); 8.6±7.0	5 (22.7%); 12.0±7.7	4 (14.8%); 13.0±5.3	3 (60.0%); 2.3±0.6	1 (50%); 2.0±NA	1 (50%); 2.0±NA	1 (50%); 3.0±NA	0
Sclerosis*	13 (16.9%); 4.4 ±3.1;	0	5 (18.5%); 3.0±1.6	2 (40.0%); 11.5±5.0	0	0	0	0
Ankylosis*	10 (13.0%); 11.2±8.6	2 (9.1%); 32.0±11.3	2 (7.4%); 8.0±5.7	0	0	0	0	0

*numbers reported are: number of patients with 1 or more of the given structural lesion (% from group total); mean±standard deviation of patients with 1 or more of the given structural lesion.

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OP0037 ASSOCIATION BETWEEN BONE MARROW EDEMA AND STRUCTURAL PROGRESSION IN THE SAME QUADRANT IN AXIAL SPONDYLOARTHRITIS – 5-YEAR DATA FROM THE DESIR COHORT

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Background: The overall presence of inflammation in the MRI-SIJ is associated with overall 5-year radiographic damage in patients with axSpA[1]. But we do not know if a bone marrow edema (BME) lesion leads to a structural lesion at the same place (i.e. in the same quadrant).
Objectives: To investigate the association between BME and structural progression in the same quadrant of the SIJ, over time.
Methods: Patients from the DESIR cohort (early axSpA according to the rheumatologist) with ≥2 consecutive MRI-SIJ (out of baseline, 2 and 5 years), were included. Each image was independently scored by 3 trained central readers blinded to chronological order. BME was considered present in a time point if detected in ≥1/6 slices in each of the 8 quadrants. The prevalence of BME (yes/no) and structural lesions (sclerosis, erosions, fatty lesions and ankylosis; all yes/no) defined, per quadrant, by the agreement of ≥2 out of 3 readers, was described at BL and at 5 years. The longitudinal association between BME and each of the structural lesions in the same quadrant was tested in time-lagged multilevel Generalized Estimating Equation (GEE) models with autoregression, taking individual reader data into account, and adjusting for clinical variables selected a priori on clinical grounds (age, gender, disease activity and treatment).
Results: In total, 197 patients were included (age 34 (SD 9) years, 48% male and 61% HLA-B27 positive). While BME and fatty lesions were evenly distributed across quadrants, erosions and sclerosis occurred preferably in the iliac side (i.e. Q1 and Q4) (Table 1). The prevalence of BME decreased over time (baseline range: 11%-16%; 5-year range: 7%-14%), while erosions (baseline range: 2%-23%; 5-year range: 3%-28%) and especially fatty lesions (baseline range: 4%-14%; 5-year range: 9%-21%) increased. Ankylosis and sclerosis were rare in this early axSpA cohort. In the multivariable models, BME was longitudinally associated with sclerosis (OR:1.7 (95% CI: 1.0;3.2)), erosions (2.0 (1.5;2.5)) and fatty lesions (1.7 (1.1;2.5)). The possible association with ankylosis could not be tested due to too low number of lesions (Table 2).

Table 1- Prevalence of the different imaging lesions* per Quadrant – at BL and 5 years

Baseline (n=197)				
Left side	**BME - %**	**Sclerosis - %**	**Erosions - %**	**Fatty lesion - %**	**Ankylosis - %**
Q1	14.2	4.1	23.4	9.6	1.5
Q2	12.7	0	4.1	12.7	1.5
Q3	11.7	0	1.5	7.6	2.2
Q4	14.7	2.5	13.7	10.7	2.2
Right side	**BME - %**	**Sclerosis - %**	**Erosions - %**	**Fatty lesion - %**	**Ankylosis - %**
Q1	13.7	3.1	19.8	3.6	0.5
Q2	13.7	0	6.1	14.2	0.5
Q3	10.7	0	1.5	8.1	1.5
Q4	16.2	1.0	11.7	7.1	1.5
At 5 years (n=136)					
Left side	**BME - %**	**Sclerosis - %**	**Erosions - %**	**Fatty lesion - %**	**Ankylosis - %**
Q1	7.9	5.0	28.1	13.7	2.9
Q2	11.5	0	5.8	18.7	2.9
Q3	6.5	0	2.9	18.0	2.9
Q4	10.8	1.4	13.0	13.7	2.9
Right side	**BME - %**	**Sclerosis - %**	**Erosions - %**	**Fatty lesion - %**	**Ankylosis - %**
Q1	11.8	3.6	25.9	8.6	2.2
Q2	14.0	0	7.2	20.9	2.2
Q3	7.4	0	5.8	15.1	5.0
Q4	11.0	1.4	12.2	10.1	5.0

* Agreement between ≥ 2 out of the 3 readers. Q= quadrant; BME: Bone Marrow Edema

Table 2 – Longitudinal association between BME and structural outcomes in the same quadrant

Outcome	Binomial GEE - OR [95% CI]*
Sclerosis	1.7 (1.0;3.2)
Erosion	2.0 (1.5;2.5)
Fatty	1.7 (1.2;2.5)
Ankylosis	*(not convergent)*

*: Multilevel (reader, time, side, quadrant) with auto-regression and adjusted for the following variables: age, sex, ASDAS and treatment (NSAIDs, steroids, csDMARDs, and TNFi). ASDAS and treatment are time-lagged

Conclusion: We here demonstrate that in early axSpA-patients inflammation in one SIJ quadrant leads to structural damage in the same quadrant. This finding reinforces the pathophysiological implications of inflammation in axSpA.

REFERENCE:

[1] Dougados, et al. Ann Rheum Dis. 2017;76(11):1823–1828.

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OP0038

HIGH PREVALENCE OF SACROILIAC BONE MARROW EDEMA ON MRI IN POSTPARTUM WOMEN: A TEMPORARY PHENOMENON

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Background: Magnetic Resonance Imaging (MRI) is a sensitive method for detection of sacroiliitis. However, recently, concerns have been raised about its specificity. In contrast to radiographic spondyloarthritis (SpA), non-radiographic SpA has a more equal sex distribution. Hence, in young women with back pain a broad differential diagnosis has to be considered. In clinical practice, women occasionally present with inflammatory(-like) low back pain, following pregnancy and childbirth. Up until now, little is known regarding the presence of SpA-like MRI lesions in postpartum women. We hypothesized that physical stress on the pelvis during pregnancy may lead to signs of bone marrow edema on MRI.
Objectives: To explore (A) the association between pregnancy and giving birth on the one hand, and the occurrence of MRI lesions compatible with SpA on the other hand; and (B) if these lesions are transient.
Methods: Twenty-five women underwent an MRI of the sacroiliac joints (SIJ) in the first 10 days after vaginal delivery. The scan was repeated after 6 months. Both time points were scored in pairs by 3 trained readers, blinded for time sequence and subject characteristics. MRI assessment was done on 6 consecutive slices for inflammatory and structural SpA-like lesions; bone marrow edema (BME), capsulitis, enthesitis, high signal intensity in joint space, erosions, fatty lesions, sclerosis and (partial) ankylosis. In addition, the Assessment of SpondyloArthritis international Society (ASAS) definition of a positive MRI-SIJ was applied. MRI reader scores were reported as 2 out of 3 (median) scores.
Results: Twenty out of 25 (80.0%) subjects displayed BME; the median SPARCC score was 5 (IQR 1-11) (see table). One subject was lost to follow-up. After 6 months, 11 out of 24 (45.8%) subjects still showed BME; however, median SPARCC score dropped to 0 (IQR 0-1) (p = 0.002). At baseline, 16 out of 25 (64.0%) participants had a positive MRI-SIJ according to the ASAS definition, reducing to 4 out of 24 (16.7%) after 6 months (p = 0.002). 75.5% of the baseline lesions were located in the anterior part of the SIJ; 57.3% situated on the iliac side. Structural lesions were rarely detected in this study population (see table).

Table: Number of MRI-SIJ lesions in 25 postpartum women.

	Baseline			6 months		
Inflammatory lesions	Median	IQR	95% CI	Median	IQR	95% CI
SPARCC (/72)	5	1 – 11	1 – 8	0	0 – 1	0 – 1
Capsulitis (/12)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Enthesitis (/12)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
High signal intensity (/12)	0	0 – 4	0 – 3	0	0 – 0	0 – 0
Structural lesions	Median	IQR	95% CI	Median	IQR	95% CI
Erosions (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Fatty lesions (/48)	0	0 – 1	0 – 0	0	0 – 0	0 – 0
Sclerosis (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Partial ankylosis (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0
Ankylosis (/48)	0	0 – 0	0 – 0	0	0 – 0	0 – 0

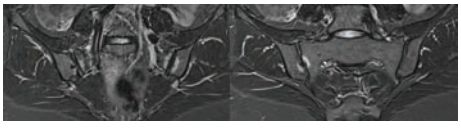


Figure: Baseline MRI T2 short tau inversion recovery (STIR) images of sacroiliac bone marrow edema in a 33-year old postpartum woman.

Conclusion: A very high prevalence of sacroiliac BME on MRI was seen in women immediately postpartum with 64.0% even having a positive MRI for sacroiliitis according to the ASAS definition. A significant decrease in BME was seen over 6 months time, yet a substantial fraction continued to display BME after follow up. History of a recent pregnancy is crucial to take into account when interpreting an MRI-SIJ. In case of a recent pregnancy and clinical suspicion of SpA, it may be wise to postpone MRI-SIJ imaging until at least 6 months after the delivery.
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SLE, Sjögren's and APS – treatment

OP0039

EFFICACY AND SAFETY OF ABATACEPT IN ACTIVE PRIMARY SJÖGREN'S SYNDROME: RESULTS OF A RANDOMISED PLACEBO-CONTROLLED PHASE III TRIAL

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Background: Traditional DMARDs have limited efficacy in primary Sjögren's syndrome (pSS) and, so far, no biologic DMARDs are approved for its systemic treatment. Two open-label studies suggested abatacept (ABA) may have a beneficial effect on disease activity and had an acceptable safety profile in pSS.[1,2]
Objectives: To examine the efficacy and safety of ABA vs placebo (PBO) in patients (pts) with moderate-to-severe pSS.
Methods: In this Phase III, double-blind, PBO-controlled study (NCT02915159), adult pts meeting the 2016 ACR-EULAR criteria for pSS with EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) $\geq$5 were randomised to receive ABA 125 mg SC weekly or PBO for 168 days (24 weeks), followed by a 197-day (365-day in Japan) open-label period of ABA treatment. All pts had a 168-day post-treatment follow-up period. Randomisation was stratified by corticosteroid (CS) and hydroxychloroquine (HCQ) use, enrolment in Japan (yes/no) and stimulated whole salivary flow (SWSF; < or $\geq$0.1 mL/min). The primary endpoint was mean change in ESSDAI at Day 169. Key secondary endpoints included mean changes in EULAR Sjögren's Syndrome Patient Reported Index and SWSF at Day 169. Other secondary endpoints included objective measures of eye and mouth dryness, DAS28 (CRP), patient-reported outcomes and biomarkers. Hierarchical testing for the primary and two key secondary endpoints was done to preserve overall type I error of 5%.
Results: A total of 187 (ABA, 92; PBO, 95) pts were randomised and received $\geq$1 dose of study drug. Baseline characteristics were comparable between treatment groups: mean (SD) age was 52 (12.9) years, 95% of pts were female, 64% were white, 40% were receiving concomitant stable-dose HCQ and 25% oral CS (≤10 mg/day prednisone equivalent). Mean (SD) baseline ESSDAI score was 9.4 (4.3) (ABA, 8.7 [3.4] vs PBO, 10.1 [5.0]). At Day 169, no significant differences were seen between ABA- and PBO-treated pts for the primary or key secondary efficacy outcomes (Table 1). Applying the Benjamini–Hochberg method (with a false discovery rate of 5%) at Day 169, significant treatment differences were observed for 5/12 biomarkers (post hoc analysis) (Table 1). Serious AEs related to the study drug occurred in 3% of ABA- and 1% of PBO-treated pts. Related AEs occurred in

Table 1. Adjusted mean change from baseline (SE) in disease activity and biomarkers at Day 169

	ABA (n=92)	PBO (n=95)	Adjusted mean difference (95% CI)	p value*
Disease activity				
ESSDAI	−3.2 (0.7)	−3.7 (0.7)	0.5 (−0.7, 1.6)	0.4421
ESSPRI	−1.3 (0.3)	−1.5 (0.3)	0.3 (−0.3, 0.8)	0.3367†
SWSF‡ (mL/min)	0.06 (0.09)	0.1 (0.09)	−0.05 (−0.2, 0.1)	0.5641†
Schirmer's Test, mm/5 minutes	1.7 (1.1)	1.0 (1.1)	0.7 (−1.5, 2.9)	NA
Tear break-up time, seconds	−0.2 (0.4)	−0.3 (0.4)	0.1 (−0.8, 0.9)	NA
Ocular staining score, range 0–12	−1.5 (0.4)	−0.7 (0.4)	−0.7 (−1.6, 0.1)	NA
Biomarkers				
C4 complement, g/L	0.01 (0.0)	−0.01 (0.0)	0.02 (0.01, 0.03)	0.0003
IgM-RF autoantibodies§	−10.4 (2.2)	−1.5 (2.1)	−8.9 (−14.7, −3.1)	0.0028
IgG, g/L	−0.9 (0.3)	0.3 (0.3)	−1.2 (−2.0, −0.4)	0.0041
Kappa light chain, mg/L	−4.7 (1.1)	−0.4 (1.1)	−4.2 (−7.2, −1.2)	0.0062
IgA, mg/L	−57.1 (54.6)	133.6 (52.3)	−190.7 (−336.5, −44.9)	0.0106

*Longitudinal repeated measures model adjusting for the four randomization stratification variables (oral CS use, HCQ use, enrolment in Japan [yes/no], SWSF <0.1 or ≥0.1 mL/min) and baseline value. For biomarker analyses, the Benjamini–Hochberg procedure was applied to control the false discovery rate at an alpha level of 5% (post hoc analysis)
†Nominal p values are shown since the primary endpoint was not met
‡n pts with SWSF ≥0.1 mL/min at baseline
§Units are calibrated against standard curves derived from a WHO international reference
ABA=abatacept; CS=corticosteroid; ESSDAI=EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI=EULAR Sjögren's Syndrome Patient Reported Index; HCQ=hydroxychloroquine; IgA=immunoglobulin A; IgG=immunoglobulin G; IgM=immunoglobulin M; NA=not available; PBO=placebo; pt=patient; SWSF=stimulated whole salivary flow

46% and 25% of ABA- and PBO-treated pts, respectively, but this was not enriched for any specific event and there were no new ABA safety signals.
Conclusion: Despite favourably impacting biomarkers of disease activity, abatacept therapy was no better than PBO for improving the clinical measures of disease. These results do not indicate a clinical benefit of abatacept in pSS.

REFERENCES:

[1] Meiners PM, et al. Ann Rheum Dis 2014;73:1393–6.
[2] Adler S, et al. *Arthritis Care Res (Hoboken)* 2013;65:1862–8.

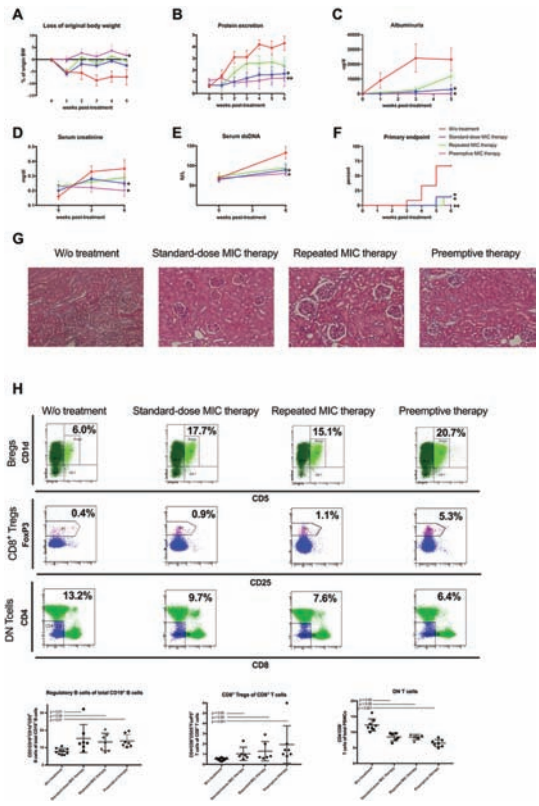
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OP0040

MODIFIED IMMUNE CELL THERAPY AMELIORATES MURINE LUPUS NEPHRITIS AND INDUCES REGULATORY CELL SUBSETS

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Background: Modified immune cells (MICs) are mononuclear cells that gain immunosuppressive properties after incubation with the proliferation inhibitor mitomycin C. We recently showed that syngeneic MIC therapy controlled experimental autoimmune encephalitis (EAE) (1). In addition, allogeneic MIC therapy prevented rejection in rat heart and hindlimb as well as pig kidney transplantation (2).
Objectives: We now wanted to translate these encouraging findings to the prevention and treatment of lupus nephritis.
Methods: Splenocytes of syngeneic NZB/W F1 (BWF1) donor mice were incubated with mitomycin C and injected into recipient's tail vein after matching for age and disease activity. Group 1 received no MIC therapy, group 2 standard-dose MIC therapy with $1.5x10^8$/kg BW once and group 3 repeated MIC therapy with $1.5x10^8$/kg BW at weeks 1, 2 and 3. Group 4 received MIC infusions before disease onset as preemptive treatment approach. Disease activity was monitored by loss of body weight, protein excretion, serum creatinine and dsDNA antibodies. Combined primary endpoint was day 40 post-treatment, protein excretion $\geq$3g/l for 2 consecutive weeks and >30% loss of original body weight. Histopathology with PAS and HE staining was performed to assess degree of lupus nephritis. Regulatory cell subsets were measured in peripheral blood.
Results: MIC therapy prevented the progression of fatal lupus nephritis in BWF1 mice. Protein excretion, serum creatinine and dsDNA antibodies were lower in standard-dose (group 2) and preemptive (group 4) groups compared to control group (group 1) whereas repeated MIC therapy after disease onset had no effect (Figure 1A-E). The primary endpoint was reached significantly more often in control group (group 1, 67%) compared to treatment groups 2 (14%), 3 (14%) and 4 (0%) (Figure 1F). Renal architecture was preserved in different MIC treatment



groups (groups 2-4) with decreased glomerular and tubular damage scores (Figure 1G). Most importantly, frequencies of $CD8^+CD25^+FoxP3^+$ regulatory T cells and $CD19^+CD5^+CD1d^{high}$ regulatory B cells were significantly higher in MIC-treated (groups 2-4) compared to control animals of group 1, whereas double negative T cells were markedly reduced (Figure 1H).

Conclusion: MIC therapy inhibits progression of active lupus nephritis. Interestingly, preemptive MIC therapy was even able to prevent onset of disease with no significant disease activity at completion of the study. In accordance with our previous pre-clinical EAE experiments (1) and a first in-human clinical trial in living-donor kidney transplantation (TOL-1 study), MIC therapy was able to induce an in-vivo induction of regulatory cell subsets. This clinically applicable cell therapeutic approach may control lupus nephritis by specifically silencing deleterious autoimmune responses.

REFERENCES:

[1] Terness P, Oelert T, et al. Mitomycin C-treated dendritic cells inactivate autoreactive T cells: toward the development of a tolerogenic vaccine in autoimmune diseases. Proc Natl Acad Sci USA. 2008 Nov 25;105 (47):18442–7.

[2] Jiga LP, Ehser S, Kleist C, Opelz G, Terness P. Inhibition of heart allograft rejection with mitomycin C-treated donor dendritic cells. Transplantation. 2007 Feb 15;83(3):347–50.

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OP0041 MAINTENANCE OF EFFICACY AND SAFETY AND REDUCTION OF BILAG FLARES WITH USTEKINUMAB, AN INTERLEUKIN-12/23 INHIBITOR, IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): 1-YEAR RESULTS OF A PHASE 2, RANDOMIZED PLACEBO-CONTROLLED, CROSSOVER STUDY

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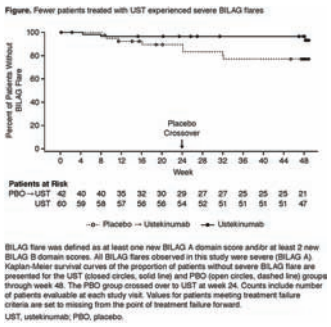
Background: Both IL-12 and IL-23 have been implicated in the pathogenesis of SLE. We have previously reported that treatment with an anti-IL-12/23 p40 monoclonal antibody ustekinumab (UST) resulted in greater improvement in several SLE disease measures through week 24 compared with placebo (PBO).[1]

Objectives: Results of global and organ-specific disease measures and flares through 1 year are reported here.

Methods: We conducted a PBO-controlled phase 2 study in 102 patients with seropositive active SLE (defined by SLICC criteria, SLEDAI score $\geq$6, and $\geq$1 BILAG A and/or $\geq$2 BILAG B scores). Patients were randomized (3:2) to UST (6 mg/kg single IV infusion, then 90 mg SC q8w beginning at week 8, n=60) or PBO (n=42), both added to standard background therapy. Patients receiving PBO crossed over to UST (90 mg SC q8w) at week 24. The primary endpoint was the proportion of patients achieving SLE Responder Index (SRI)-4 response at week 24. Modified intention-to-treat (mITT) analyses across SLE disease measures were performed to evaluate maintenance of response with UST between week 24 and week 48 and severe BILAG flares ($\geq$1 new BILAG A score). Safety was assessed through week 56.

Results: As previously reported, SRI-4 response rate at week 24 was significantly greater (p=0.0057) in patients receiving UST (62%) vs PBO (33%).1 In the UST group, SRI-4 (week 24: 62% vs week 48: 63%), SRI-5 (week 24: 43% vs week 48: 48%), and SRI-6 (week 24: 43% vs week 48: 47%) response rates were sustained at 1 year. Proportions of patients with $\geq$4-point improvement from baseline in SLEDAI-2K score (week 24: 65% vs week 48: 67%) and with $\geq$30% improvement from baseline in Physician's Global Assessment score (week 24: 68% vs week 48: 75%) were also maintained in the UST group. UST response rates were also sustained through 1 year in organ-specific disease measures ($\geq$50% improvement in active joint counts: week 24: 87% vs week 48: 87%; $\geq$50% improvement in CLASI activity score: week 24: 53% vs week 48: 69%). In PBO patients who crossed over to UST at week 24 (n=33), response rates across outcomes studied were 10-20% higher at week 48 vs week 24. Flare rates for patients with severe BILAG flares were 2.1/10,000 patient-days in week 0-24 and 1.1/10,000 patient-days in week 24-48 in the UST group. In the PBO group, severe BILAG flare rates were 8.4/10,000 patient-days in week 0-24 and, following UST crossover, were 4.6/10,000 patient-days in week 24-48. The occurrence of severe BILAG flares seemed to diminish after approximately 8 weeks (week 8 in UST arm, week 32 in PBO arm) of treatment with UST (Figure). No deaths, malignancies, opportunistic infections, tuberculosis cases, or unexpected serious AEs (SAEs) were observed. Incidences of $\geq$1 SAE were UST (week 0-24) 8.3%, PBO (week 0-24) 9.5%, UST (week 24-48) 8.9%, and PBO-UST (week 24-48) 12.1%. Safety events were consistent with the known UST safety profile.

Conclusion: UST provided sustained clinical benefit in global and organ-specific SLE-activity measures and reduced flares through 1 year, with a safety profile consistent with other indications. Thus, UST may have durable therapeutic benefit in SLE.



REFERENCE:

[1] van Vollenhoven RF, et al. Lancet 2018;392:1330.

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OP0042 LONG-TERM EFFECTS OF SYNERGETIC B CELL IMMUNOMODULATION WITH RITUXIMAB AND BELIMUMAB COMBINATION TREATMENT IN SEVERE, REFRACTORY SLE: TWO YEAR RESULTS

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Background: We conducted a phase 2, proof-of-concept study (SynBioSe study) in which we combined rituximab and belimumab (RTX+BLM) for treatment of SLE patients with severe, refractory disease. We have previously reported that RTX +BLM effectively reduced relevant anti-nuclear autoantibodies (ANAs) and showed a clinical response at 24 weeks[1].

Objectives: The aim of the present study is to investigate the long-term immunological and clinical effects of RTX+BLM in severe, refractory SLE patients.

Methods: Fifteen severe, refractory SLE patients were included and followed for 2 years. Patients received RTX at week 0 and 2 and BLM at week 4, 6, 8 and then 4-weekly until week 104. Clinical response was assessed by achievement of low level of disease activity (LLDAS). By using specific antibody assays and high sensitivity flowcytometry (HS-FACS), we longitudinally followed, respectively, levels of SLE-specific ANAs and B-cell subsets.
Results: Ten patients (67%) showed a good clinical response after 24 weeks, referred to as 'responders'. Two of these patients (13%) switched treatment after 24 weeks due to a pregnancy wish and 8 patients (53%) continued study treatment throughout the complete 2 years of follow-up. Five patients (33%) discontinued treatment due to persistent LN (n=2), major flare (n=2) or relapsing minor flare (n=1), together referred to as 'non-responders'. Responders achieved LLDAS at a median of 24 weeks [range 12-36] and remained in LLDAS for 76 weeks [56-92] out of 104 weeks of follow-up. In 7 patients with active LN, 6 attained a complete renal response. In responders, ANAs showed significant and specific reduction throughout 2 years with achievement of seronegative anti-dsDNA immunofluorescence in 6 out of 6 anti-dsDNA positive patients at baseline while total IgG, anti-tetanus and anti-rubella antibodies remained stable. By using HS-FACS, a median decrease of 97% [-99;+35] CD19+ B-cell depletion was achieved at 24 weeks. Long-term follow-up showed that B-cell repopulation was inhibited throughout 2 years with a persistent median decrease of 84% [-92;+22] compared to baseline. Further analysis of B-cell subsets revealed that in the responders, double negative (DN) B cells (CD27-IgD-) reached maximum depletion at 4 weeks (median $1.09*10^6$ cells/liter [range $0.23*10^6$-$4.31*10^6$]), which lasted up to week 72 with a median of $1.26*10^6$ cells/liter [$0.79*10^6$-$4.11*10^6$] at week 72, similar to values at nadir. This was in contrast to non-responders, where maximum depletion of DN B-cells was reached at 12 weeks ($0.48*10^6$ [$0.17*10^6$-$5.86*10^6$], after which these cells increased to $2.29*10^6$ [$0.49*10^6$-$4.39*10^6$] at 24 weeks.
Conclusion: Over 2 years follow-up, RTX+BLM for severe, refractory SLE patients prevented complete B-cell repopulation with persistent and specific reduction of ANAs. Clinical response was observed in 67% of patients and treatment discontinuation due to high disease activity was associated with early repopulation of DN B-cells. These data warrant further studies on clinical and immunological benefits of combination treatment RTX+BLM.

REFERENCE:

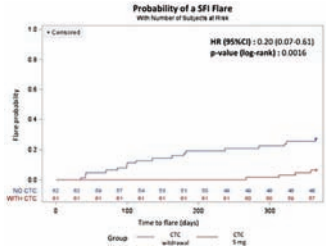
[1] Kraaij T, Kamerling SWA, de Rooij ENM, et al. The NET-effect of combining rituximab with belimumab in severe systemic lupus erythematosus. J Autoimmun 2018;91:45-54.doi: 10.1016/j.jaut.2018.03.003.

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OP0043 WITHDRAWAL OF A LOW DOSE (5 MG) OF CORTICOSTEROIDS IN SYSTEMIC LUPUS IN REMISSION FOR MORE THAN A YEAR IS AT RISK OF RELAPSE – THE CORTICOLUP TRIAL

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Background: Glucocorticoids (GCs) are a mainstay of treatment for patients with SLE but are associated with significant adverse effects. Some SLE patients are maintained for a long-term under a low dose of prednisone to prevent relapse. There is no scientific data to sustain this therapeutic strategy.
Objectives: We hypothesized that maintaining a daily dose of 5 mg prednisone in patients with an inactive SLE for at least a year would prevent the risk of relapse.
Methods: The CORTICOLUP study (NCT02558517) was a prospective randomized, open-labeled, controlled, monocentric study sought to compare maintenance vs withdrawing of low-dose of prednisone (5mg) to reduce SLE flares, conducted from January 2014 to March 2017. Inclusion criteria were SLE patients **who during the year** preceding the inclusion had 1/an inactive SLE defined by a SLEDAI-2K score ≤ 4, a BILAG-2004 index C, D or E in all systems and a PGA =0 and 2/a stable SLE treatment including prednisone 5 mg daily. The primary end point was the number of patients with flares during 12 months of follow-up defined by the revised-SELENA SLEDAI Flare Index (rSFI). Secondary outcomes were occurrence of a BILAG scores A or B ≥1, clinical SLEDAI-2k >0, PGA ≥0.5 and increase of the SLICC damage index (SDI). All patients were included in the intention-to-treat analysis.
Results: A total of 124 patients (61 in the maintenance group and 63 in the withdrawal group) were included. No patients were lost to follow up. At baseline There were no significant differences between the maintenance and the withdrawal group with respect to: duration of SLE [mean (±standard deviation) duration of 11.8 (±0.9) versus 13.1 (±1.0) years], duration of remission [55.7 (±5.8) vs 67.5 (±6.8) months], HCQ treatment [98.2% vs 100.0%], immunosuppressive drugs [27.9% vs 25.4%], previous renal involvement [34.4% vs 41.3%], low C3 [16.4% vs 15.9%], positive Farr test [47.5% vs 46.0%], and SDI [mean index of 0.5 (±0.1) vs 0.7 (±0.2)].



There were significantly more flares in the withdrawal group compared to the maintenance group (17 flares versus 4, p=0.0034 using the Fisher's exact test). Mild or moderate flares were more frequent in the withdrawal group compared to the maintenance group (12 vs 3, p=0.029). The occurrence of severe flare was not significantly different between the two groups (5 vs 1, p = 0.208). More than two-thirds of the flares in the withdrawal group occurred within the first six months. Within the withdrawal group, using forest plot analysis, no significant association was found between the occurrence of a flare and age, sex, duration of SLE, duration of SLE remission, duration of GCs treatment, immunosuppressants and serological SLE activity at randomization. Four patients in the withdrawal group and none in the maintenance group experienced damage: 2 osteoporosis bone fractures, 1 hydroxychloroquine retinopathy and 1 cataract.
Conclusion: Withdrawal of low dose of steroids in patients with inactive SLE and stable therapeutic regimen for more than a year is associated with a high risk of relapse.
Disclosure of Interests: None declared
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OP0044 A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE GONADOTOXIC EFFECTS OF CYCLOPHOSPHAMIDE AND BENEFITS OF GONADOTROPIN RELEASING HORMONE ANALOGUES IN WOMEN OF CHILD-BEARING AGE WITH AUTOIMMUNE RHEUMATIC DISEASE

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Background: Premature ovarian insufficiency (POI) is a side effect of intravenous cyclophosphamide (i.v.CYC), which is the treatment of choice for many severe manifestations of autoimmune rheumatic disease (ARD) (1). The risk of POI post-CYC appears to be dependent on cumulative dose and patient age but has not been precisely quantified. Gonadotropin Releasing Hormone Analogues (GnRHa) may reduce this risk (2). Studies however, on GnRHa and CYC use in ARD patients have been limited in size and/or by combined analysis with patients receiving CYC for malignancies.
Objectives: In order to more precisely categorise the risk of POI in ARD patients, and determine whether GnRHa are effective in reducing this risk, we performed a systematic review to assess the risk of sustained amenorrhoea with i.v.CYC in ARD and a meta-analysis of the efficacy of GnRHa in reducing this risk.
Methods: Using Preferred Reporting Items for Systematic Reviews and Meta-Analyses principles, we searched English language papers using Pubmed, MEDLINE, EMBASE and the Cochrane Library to April 2018. We included all studies

that reported the incidence of sustained amenorrhoea (defined as at least 12 months of amenorrhoea) during i.v.CYC treatment in patients with ARD; and those that assessed sustained amenorrhoea in patients receiving GnRHa and i.v.CYC, compared to controls receiving i.v.CYC alone.

Results: 1099 articles were identified and their titles and abstracts screened, following which 81 papers were selected for full text review. 31 studies were then identified that addressed the risk of sustained amenorrhoea with i.v.CYC in n=1382 patients with ARD. The majority of these patients had systemic lupus erythematosus (1326 out of 1382 patients, 96.0%). The mean age was 24.9 (range 13-36.1) years. Sustained amenorrhoea occurred in 269 patients (19.5%, range 0-54% depending on age and cumulative cyclophosphamide dose). The rate of sustained amenorrhoea significantly positively correlated with increasing cumulative cyclophosphamide dose, and occurred in patients with a mean age ranging from 13-36.1 years at mean cumulative doses ranging from 1-20.1g. A further 3 studies assessed ARD patients given i.v.CYC +/- GnRHa, including 56 patients (mean age range 23.9-25.6 years) receiving GnRHa and i.v.CYC, and 37 controls (mean age range 25-29.4 years) given i.v.CYC only. Sustained amenorrhoea occurred in 2/56 (3.6%) patients treated with GnRHa, compared to 15/37 (40.5%) of controls. The pooled odds ratio of sustained amenorrhoea with GnRHa and i.v.CYC compared to i.v.CYC alone was 0.0543 (95%CI 0.0115-0.2576, p=0.0002). The number needed to treat was 2.7 (95%CI 2.0-4.4) and the absolute risk reduction was 37.0% (95%CI 35.6-38.4%).

Conclusion: Although the risk of POI with i.v.CYC was associated with increasing age, it was observed across all age groups and from cumulative doses of 1g or more. GnRHa markedly reduced this risk in ARD, and therefore should be considered for concomitant use with i.v.CYC in all women of child-bearing age with ARD.

REFERENCES:

[1] Marder W, Fisseha S, Ganser MA, Somers EC. Ovarian damage during chemotherapy in autoimmune diseases broad health implications beyond fertility. Clin Med Insights Reprod Health 2012;6:9-18.

[2] Marder W, McCune WJ, Wang L, Wing JJ, Fisseha S, McConnell DS, et al. Adjunctive GnRH-a treatment attenuates depletion of ovarian reserve associated with cyclophosphamide therapy in premenopausal SLE patients. Gynecol Endocrinol 2012;28(8):624-7.

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OP0045 ABATACEPT TREATMENT OF PATIENTS WITH EARLY ACTIVE PRIMARY SJÖGREN'S SYNDROME – A RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED PHASEFRED K.L. SPIJKERVETY. K. ONNO TENGE.J. ARENDS III-STUDY (ASAP-III)

Jolien F. van Nimwegen[1], Greetje S. van Zuiden[1], Suzanne Arends[1], Esther Mossel[1], Robin F. Wijnsma[1], Alja J. Stel[1], Konstantina Delli[2], Bert van der Vegt[3], Erlin A. Haacke[1,3], Lisette Olie[4], Leonie I. Los[4], Janita Bulthuis-Kuiper[1], Gwenny M. Verstappen[1], Sarah A. Pringle[1], Fred K.L. SpijkervetFrans G. M. Kroese[2], Frans G.M. Kroese[1], Arjan Vissink[2], Hendrika Bootsma[1]. *[1]University Medical Center Groningen, University of Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*; *[2]University Medical Center Groningen, University of Groningen, Oral and Maxillofacial Surgery, Groningen, Netherlands*; *[3]University Medical Center Groningen, University of Groningen, Pathology and Medical Biology, Groningen, Netherlands*; *[4]University Medical Center Groningen, University of Groningen, Ophthalmology, Groningen, Netherlands*

Background: Effective systemic treatment is not yet available for primary Sjögren syndrome (pSS). Abatacept (CTLA-4-Ig) targets the CD80/CD86:CD28 co-stimulatory pathway required for full T-cell activation and T-cell dependent activation of B-cells. IV abatacept was shown to be safe, well tolerated, and to decrease disease activity in an open-label study of 15 pSS patients.[1]

Objectives: To assess the efficacy and safety of subcutaneous (SC) abatacept vs. placebo in patients with early active pSS.

Methods: The Abatacept Sjögren Active Patients phase III (ASAP-III) study is a monocenter, investigator-initiated, double-blind, placebo-controlled trial (NCT02067910). ASAP-III included 80 adult patients with biopsy-proven pSS, fulfilling the AECG and ACR/EULAR criteria, with a disease duration of ≤7 years and moderate to high EULAR Sjögren's syndrome disease activity score (ESSDAI ≥5). Patients were randomized in a 1:1 ratio to receive weekly SC abatacept (125 mg) or placebo for 24 weeks (figure 1). After the double-blind phase, all patients were treated with abatacept in a 24-week open label phase. Concomitant use of other DMARDs was not permitted, with the exception of a stable dose of prednisone (≤10mg). Rescue therapy with prednisone or cyclophosphamide was permitted after week 12. Participants visited our pSS tertiary referral center nine times, to be evaluated by a multidisciplinary team of rheumatologists, ophthalmologists, and oral and maxillofacial surgeons.

The primary endpoint is ESSDAI at 24 weeks. Secondary outcomes over 24 and 48 weeks include clinical, patient reported, functional, histological, laboratory, ultrasound, and microbiome parameters, and the occurrence of (serious) adverse events and treatment discontinuation.

Results: Baseline characteristics of participants are shown in table 1. Database lock for the blinded stage is planned in March 2019. Subsequently, the first intention-to-treat analyses will be performed, focusing on the ESSDAI and EULAR Sjögren Syndrome Patient Reported Index (ESSPRI), quality of life (EQ-5D), unstimulated and stimulated whole salivary flow (UWS, SWS), Schirmer test, Ocular Staining Score (OSS), serological parameters (RF, IgG), and safety parameters.

Conclusion: The ASAP-III trial was designed to assess the clinical efficacy and safety of SC abatacept in pSS patients with short disease duration and active disease. The 24-week results will be available during the EULAR congress 2019.

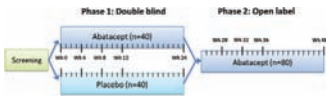


Figure 1. Design of the ASAPIII study.

REFERENCE:

[1] Meiners, et al. Ann Rheum Dis 2014;73:1393-6.

Table 1:. Baseline characteristics of participants (n=80)

Characteristics	Value
Age (years), mean±SD	48.8±15.6
Female, n (%)	74 (93)
Disease duration (years), median (IQR)	2.0 (1.0–4.0)
Anti-Ro/SSA, n (%)	71 (89)
Previous use of DMARDS, n (%)	34 (42.5)
Use of prednisone, n (%)	1 (2)
ESSDAI, median (IQR)	13 (8-17)
ESSPRI, mean±SD	6.7±1.6
EQ-5D index, median (IQR)	0.71 (0.57-0.84)
UWS (ml/min), median (IQR)	0.05 (0.01-0.13)
SWS (ml/min), median (IQR)	0.16 (0.04-0.35)
OSS*, mean±SD	4.5±3.4
Schirmer* (mm/5 min), median (IQR)	3 (0-10)
IgG (g/L), median (IQR)	18.2 (14.4-25.9)
RF (IU/ml), median (IQR)	25 (5-71)

* Average of left and right eye.

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OP0046 MULTICENTRIC STUDY COMPARING CYCLOSPORINE, MYCOPHENOLATE MOFETIL AND AZATHIOPRINE IN THE MAINTENANCE THERAPY OF LUPUS NEPHRITIS: 10 YEARS FOLLOW UP

Lorenza Maria Argolini[1,2], Elena Elefante[3], Francesca Saccon[4], Valentina Binda[5], Maria Gerosa[1,2], Luigi Sinigaglia[2], Piergiorgio Messa[5], Andrea Doria[4], Marta Mosca[3], Gabriella Moroni[5]. *[1]University of Milan, Clinical Sciences and Community Health, Milan, Italy*; *[2]ASST Istituto Gaetano Pini – CTO, Clinical Rheumatology, Milan, Italy*; *[3]Rheumatology Unit, University of Pisa, Clinical and Experimental Medicine, Pisa, Italy*; *[4]University of Padua, Rheumatology, Padova, Italy*; *[5]Fondazione Ca' Granda IRCCS Ospedale Maggiore Policlinico Milano, Nephrology, Milan, Italy*

Background: The most effective drug for the maintenance therapy of severe forms of lupus nephritis (LN) is still a matter of debate.

Objectives: To compare efficacy and safety of cyclosporine (CYA) with mycophenolate mofetil (MMF) and with azathioprine (AZA) in the long-term maintenance therapy of LN.

Methods: Ninety-six patients (pts) (93 females, mean age 31.98±12.78 years) with SLE and biopsy proven LN (16 pts:class III; 64 pts:class IV; 16 pts:class V ISN/RPS). Fifty-six pts entered this study at diagnosis of LN and 40 during a course of a LN flare. Twenty-five pts (30%) had Glomerular Filtration Rate (eGFR) <60ml/min (MDRD) and proteinuria was 3.88±2.89 gr/day. Induction therapy: 3 methylprednisolone pulses followed by oral prednisone in 92 pts and oral prednisone in 4 pts; cyclophosphamide in 74% of pts, MMF in 9.4%, AZA in 5.2%, and other immunosuppressors in 11.4%. After six months, 30 pts started maintenance therapy with CYA, 32 with MMF and 34 with AZA. At induction therapy there were not significant differences between the three groups in histological classes at renal biopsy, mean serum creatinine, eGFR and proteinuria, and type of induction therapy. The mean follow-up after the beginning of the study was 15.9 years for CYA, 10.5 for MMF, 14.1 AZA. Primary endpoint was renal response at 1, 5 and 10 years defined as complete renal response: eGFR>60ml/min and proteinuria <0.5g/die, partial response: eGFR>60ml/min and proteinuria ≥0.5/die, no response: eGFR<60ml/min. Secondary endpoint: incidence of flare and safety.

Results: At the beginning of maintenance therapy**,** the mean serum creatinine and eGFR were similar in the 3 groups (0.92±0.26mg/dl, eGFR 109,9±49,5ml/min in CYA, 0.86±0.4mg/dl, eGFR 119±44,6 in MMF, 0.85±0.3mg/dl, eGFR 106,6 ±43,9ml/min in AZA). Proteinuria was higher in CYA group (CYA:2.03±1.7g/day; MMF:0.77±0.8g/day; AZA:1.2±1.1g/day). At the beginning of maintenance therapy, complete, partial and no response were 26.6%, 60%, and 13.4% in CYA, 53.1%, 43.8% and 3.1% in MMF and 38.2%, 58.8% and 3% in AZA group (Fig 1). At 1 year, after 6 months of maintenance therapy, in CYA group the percentage of pts in complete remission increased to 73% (vs 65.6% in MMF and 40% in AZA), at 5 years it was 80% (vs 83% in AZA and in MMF) and 88% at 10 years vs 70% in MMF and 68% in AZA (Fig 2,3,4). The percentage of non-responsive pts was stable from 1 to 10 years in the CYA group (around 13%), it slightly increased in MMF group (from 3.1 to 13,5%) and in AZA group (from 15 to 24%). During the study, SLE flares occurred in 30% of CYA group, 41% in MMF and 32% of the AZA. The average time from the beginning of the study and the first flare was 3.95 ±2.76years in CYA, 3.62±1.60 in MMF and 5.9±2.37 in AZA. No side effects were reported in 90% of pts treated with CYA, in 81.3% with MMF and in 85.3% with AZA group.

Conclusion: This is the first study comparing these 3 drugs as maintenance therapy in the long term. After 10 years of observation, CYA, AZA and MMF have proven to be effective in consolidating and maintaining the remission of LN. Of interest are the results achieved in the CYA group. Despite worse clinical conditions at the beginning of maintenance therapy, CYA allowed a rapid achievement of LN remission in the great majority of pts compared to AZA and MMF. Remission persisted over 10 years of observation. The number and type of flares and of side effects were not different between groups.

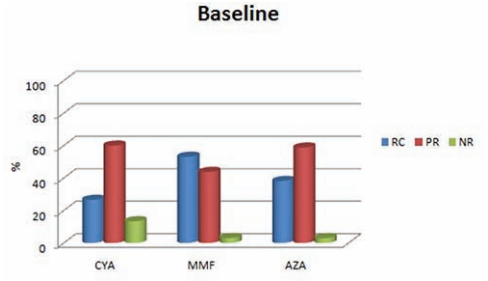


Figure 1

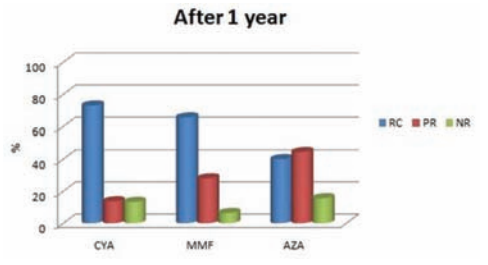


Figure 2

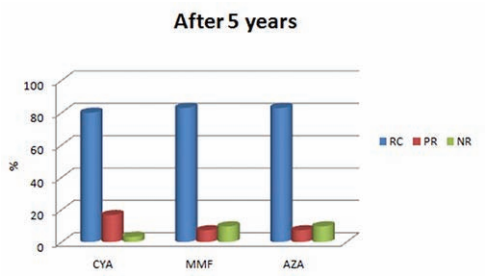


Figure 3

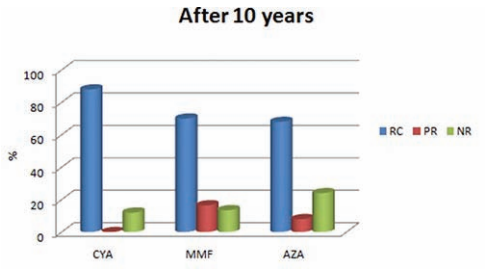


Figure 4

REFERENCE:

[1] Moroni G, et al. 2006

Disclosure of Interests: Lorenza Maria Argolini: None declared, Elena Elefante: None declared, Francesca Saccon: None declared, Valentina Binda: None declared, Maria Gerosa: None declared, Luigi Sinigaglia Speakers bureau: Yes, I, ve been invited speaker by Amgen, Ely Lilly, UCB, Abbvie, Roche and BMS., Piergiorgio Messa: None declared, Andrea Doria: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB, Gabriella Moroni: None declared

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WEDNESDAY, 12 JUNE 2019

Crystals

OP0047

A GENOME-WIDE ASSOCIATION STUDY IDENTIFIED NOVEL LOCI ASSOCIATED WITH THE PROGRESSION FROM ASYMPTOMATIC HYPERURICEMIA TO GOUT

Yusuke Kawamura[1], Hirofumi Nakaoka[2], Akiyoshi Nakayama[1], Yukinori Okada[3], Ken Yamamoto[4], Hiroshi Ooyama[5], Blanka Stiburkova[6], Tony Merriman[7], Masahiro Nakatochi[8], Kenji Wakai[9], Michiaki Kubo[10], Kimiyoshi Ichida[11], Nariyoshi Shinomiya[1], Hirotaka Matsuo[1]. *[1]National Defense Medical College, Department of Integrative Physiology and Bio-Nano Medicine, Tokorozawa, Japan*; *[2]National Institute of Genetics, Division of Human Genetics, Department of Integrated Genetics, Mishima, Japan*; *[3]Osaka University Graduate School of Medicine, Department of Statistical Genetics, Suita, Japan*; *[4]Kurume University School of Medicine, Department of Medical Biochemistry, Kurume, Japan*; *[5]Ryougoku East Gate Clinic, Tokyo, Japan*; *[6]Institute of Rheumatology, Prague, Czech Republic*; *[7]University of Otago, Department of Biochemisty, Dunedin, New Zealand*; *[8]Nagoya University Hospital, Data Science Division, Data Coordinating Center, Department of Advanced, Nagoya, Japan*; *[9]Nagoya University Graduate School of Medicine, Department of Preventive Medicine, Nagoya, Japan*; *[10]RIKEN Center for Integrative Medical Sciences, Yokohama, Japan*; *[11]Tokyo University of Pharmacy and Life Sciences, Department of Pathophysiology, Tokyo, Japan*

Background: Gout is one of the commonest forms of inflammatory arthritis induced by monosodium urate (MSU) crystals that result from elevated serum uric acid (SUA) level. Thus far, we and others have performed genome-wide association studies (GWASs) of gout by comparing the genetic differences between gout cases and normouricemia controls[1-3] and have identified gout risk loci such as *ABCG2* and *SLC2A9*: these are similar results to those from GWASs of SUA. Meanwhile, not all hyperuricemia cases develop gout: the reason, we consider, is that there are at least two steps (Figure 1) by which normouricemic individuals develop gout.

Objectives: The first ever GWAS of clinically defined gout cases and asymptomatic hyperuricemia (AHUA) controls was performed to identify novel gout loci that aggravate AHUA into gout, as distinct from loci causing SUA elevation.
Methods: We carried out a GWAS of 945 clinically-defined gout cases and 1,003 AHUA controls followed by two replication studies. In total, 2,860 gout cases and 3,279 AHUA controls (all Japanese males) were analyzed. And also, we compared the odds ratios (ORs) for each locus in the present GWAS (gout vs. AHUA) with those in the previous GWAS (gout vs. normouricemia). Furthermore, we investigated the effect of each locus on SUA using the results from our recent GWAS meta-analysis of SUA with a total of 121,745 Japanese subjects[4].
Results: This new approach enabled us to identify two novel gout loci (rs7927466 of *CNTN5* and rs9952962 of *MIR302F*) and one suggestive locus (rs12980365 of *ZNF724*) at the genome-wide significance level ($P<5.0\times10^{-8}$) (Figure 2). The present study also identified the loci of *ABCG2*, *ALDH2* and *SLC2A9*. One of them, rs671 of *ALDH2*, was identified as a gout locus by GWAS for the first time. Comparing ORs for each locus in the present vs. the previous GWAS revealed three "gout vs. AHUA GWAS" specific loci (*CNTN5*, *MIR302F* and *ZNF724*) to be clearly associated with mechanisms of gout development which distinctly differ from the known gout risk loci that basically elevate serum uric acid (SUA) level. The effect of each locus on SUA using the results from our recent GWAS meta-analysis of SUA are consistent with those of the present study.
Conclusion: This first discovery of "AHUA to Gout" loci using a new GWAS strategy will lead to elucidation of the molecular mechanism of the last step of gout development and to the prevention of gout attacks in high-risk AHUA individuals.

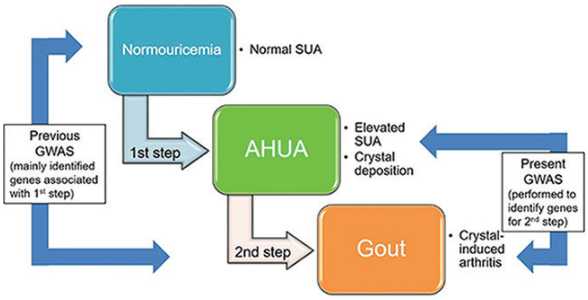


Figure 1. Two steps in the development of gout.

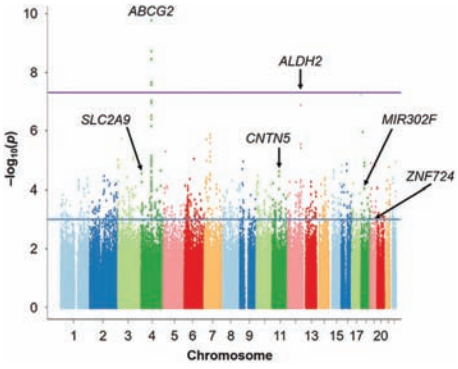


Figure 2. Manhattan plots of the present GWAS (Gout vs. AHUA).

REFERENCES:
[1] Matsuo, H. et al. Ann Rheum Dis 75, 652-9 (2016).
[2] Nakayama, A. et al. Ann Rheum Dis 76, 869-77 (2017).
[3] Li, C. et al. Nat Commun 6, 7041 (2015).
[4] Nakatochi, M. et al. *Commun Biol,* in press.

Disclosure of Interests: Yusuke Kawamura: None declared, Hirofumi Nakaoka: None declared, Akiyoshi Nakayama: None declared, Yukinori Okada: None declared, Ken Yamamoto: None declared, Hiroshi Ooyama: None declared, Blanka Stiburkova: None declared, Tony Merriman Grant/research support from: Ardeabiosciences, Ironwood Pharmaceuticals, Consultant for: Ardeabiosciences, Ironwood Pharmaceuticals, Masahiro Nakatochi: None declared, Kenji Wakai: None declared, Michiaki Kubo: None declared, Kimiyoshi Ichida: None declared, Nariyoshi Shinomiya: None declared, Hirotaka Matsuo: None declared
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OP0048

GENOME-WIDE META-ANALYSIS REVEALED MULTIPLE NOVEL LOCI ASSOCIATED WITH SERUM URIC ACIDLEVELS IN JAPANESE

Hirotaka Matsuo[1], Masahiro Nakatochi[2], Masahiro Kanai[3], Akiyoshi Nakayama[1], Asahi Hishida[4], Yusuke Kawamura[1], Mayuko Nakajima[1], Yoichiro Kamatani[5], Nariyoshi Shinomiya[1], Mitsuhiro Yokota[6], Kenji Wakai[4], Yukinori Okada[3,5].
[1]National Defense Medical College, Department of Integrative Physiology and Bio-Nano Medicine, Tokorozawa, Japan; [2]Nagoya University Hospital, Data Science Division, Data Coordinating Center, Department of Advanced Medicine, Nagoya, Japan; [3]Osaka University Graduate School of Medicine, Department of Statistical Genetics, Suita, Japan; [4]Nagoya University Graduate School of Medicine, Department of Preventive Medicine, Nagoya, Japan; [5]RIKEN Center for Integrative Medical Sciences, Laboratory for Statistical Analysis, Yokohama, Japan; [6]Aichi Gakuin University, Department of Genome Science, School of Dentistry, Nagoya, Japan

Background: Uric acid is an end metabolite of purines which is produced predominantly in the liver and is excreted by the kidneys and the intestine. Genes for urate transporters and proteins associated with cell metabolism might therefore be expected to be associated with serum uric acid (SUA). Indeed, urate transporter genes such as SLC22A12 (also known as URAT1), SLC2A9 (GLUT9), and ABCG2 (BCRP) have been markedly associated with SUA[1,2], hyperuricemia, and gout[3-5]. To date, several genome-wide association studies (GWASs) of SUA have been performed with some populations including Japanese.
Objectives: We have investigated the genetic loci that influence SUA with more than 120,000 Japanese individuals with a genome-wide meta-analysis and have compared our findings with those of previous GWASs.
Methods: We performed a genome-wide meta-analysis based on three Japanese cohorts including those of the Japan Multi-institutional Collaborative Cohort (J-MICC) Study, the Kita-Nagoya Genomic Epidemiology (KING) Study, and the BioBank Japan (BBJ). We also performed the trans-ethnic meta-analysis across the present study and the Global Urate Genetics Consortium (GUGC)-based study to carry out fine-mapping analysis.
Results: We identified 8,948 variants at 36 genomic loci ($P<5\times10^{-8}$) including eight novel loci (Figure 1). Of these, missense variants of *SESN2* and *PNPLA3* were predicted to be damaging to the function of these proteins; another five loci—*TMEM18*, *TM4SF4*, *MXD3-LMAN2*, *PSORS1C1-PSORS1C2*, *HNF4A*—are related to cell metabolism, proliferation, or oxidative stress; and the remaining locus, *LINC01578*, is unknown. We also identified 132 correlated genes whose expression levels are associated with SUA-increasing alleles. These genes are enriched for the UniProt transport term, suggesting the importance of transport-related genes in SUA regulation. Furthermore, trans-ethnic meta-analysis across our own meta-analysis and the GUGC has revealed 15 more novel loci associated with SUA (Figure 2).

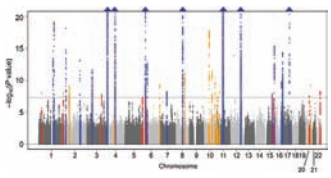


Figure 1. Manhattan plot for the meta-analysis of SUA in Japanese.

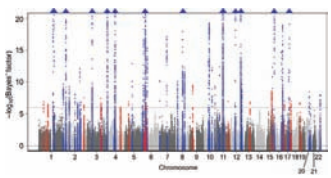


Figure 2. Manhattan plot for the trans-ethnic meta-analysis of SUA.

Conclusion: Our findings thus provide important insight into SUA regulation and the pathogenesis of hyperuricemia and gout, and they provide a potential basis for the development of new treatments for these diseases.

REFERENCES:
[1] Köttgen, A. et al. Nat Genet 45, 145-54 (2013).
[2] Kanai, M. et al. Nat Genet 50, 390-400 (2018).
[3] Matsuo, H. et al. Sci Transl Med 1, 5ra11 (2009).
[4] Woodward, O.M. et al. Proc Natl Acad Sci U S A 106, 10338-42 (2009).
[5] Nakayama, A. et al. Ann Rheum Dis 76, 869-877 (2017).

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OP0049 FACTORS ASSOCIATED WITH EARLY FLARES WHEN INITIATING URATE LOWERING THERAPIES. POST HOC ANALYSIS OF CLEAR 1,2 AND CRYSTAL TRIALS

Pascal Richette[1], Fernando Perez-Ruiz[2], Ravi Karra[3], Augustin Latourte[1], Imane Wild[3], Prashanth Kandaswamy[3], Heiko Hagedorn[3], Thomas Bardin[1]. *[1]Hopital Lariboisière, Paris, France*; *[2]Servicio de Reumatología, Hospital Universitario Cruces, Cruces, Spain*; *[3]Grunenthal, Aachen, Germany*

Background: Initiation of urate lowering therapies (ULT) in patients with gout can trigger flares which could contribute to poor treatment adherence. The EULAR guidelines recommend a prophylactic treatment with colchicine or low dose NSAIDs for up to 6 months. However, long term treatment with either NSAIDs or colchicine can be poorly tolerated or contra-indicated. Thus, identification of risk factors for flares to identify patients who would benefit more from a prophylactic treatment could improve patients care.
Objectives: To investigate the influence of patient and treatment related factors on the occurrence of flares 1 month after the initiation of ULT.
Methods: Data are from n=1018 patients (mean age 52.0 (SD 11.1) years; 95.2% male) not responding to allopurinol or febuxostat monotherapy and who received lesinurad (200 mg or 400 mg) in the CLEAR and CRYSTAL trials. Patients were prescribed colchicine (84%) or NSAIDs (12.9%) as prophylactic treatment. Data from 3 trials were pooled and the following covariates were considered in the main analysis using a Generalized Estimation Equation (GEE) model: age, gender, serum uric acid (SUA) levels, baseline body mass index, renal function, and presence of tophus, type of gout flare prophylaxis, triglycerides, comorbidities (smoking, tobacco, diabetes, hypertension, hyperlipidemia) antihypertensive and lipid lowering medications at baseline and newly started and change in SUA levels. A multivariate analysis was conducted using the occurrence of flares as response measured from baseline until month 1
Results: In the multivariate analysis, tophus at baseline and gender (female) were both associated with an increased risk of early flares: OR=2.7 (95% CI: 1.7-4.2) and OR=1.8 (95%: CI 1.0-3.4), respectively, whereas hyperlipidemia and hypertension were associated with a decreased risk of flares: OR=0.64 (95%: CI 0.45-0.91) and OR= 0.62 (95%: CI 0.39-0.99). There was a trend toward a reduced risk of flares with colchicine versus NSAIDs: OR=0.71 (95%: CI 0.47-1.05). Neither the duration of gout nor the change in SUA levels modified the risk of flares.
Conclusion: This analysis shows that gender (female) and tophus are independent risk factors of early flares when initiating ULT, and suggests that colchicine might be more effective than low dose NSAIDs as prophylactic treatment.
Disclosure of Interests: Pascal Richette Consultant for: Grunenthal, Horizon, Speakers bureau: AstraZeneca, Grunenthal, Fernando Perez-Ruiz Grant/ research support from: Cruces Rheumatology Association, Consultant for: Grunenthal, Menarini, Horizon, Speakers bureau: Menarini, Grunenthal; Spanish foundation for rheumatology, Ravi Karra Employee of: Grunenthal, Augustin Latourte: None declared, Imane Wild Employee of: Grunenthal, Prashanth Kandaswamy Employee of: Grunenthal, Heiko Hagedorn Employee of: Grunenthal, Thomas Bardin Consultant for: Astrazeneca, Grunenthal, Horizon, Novartis, Speakers bureau: Astella, AstraZeneca, Grunenthal.
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OP0050 ADDITIVE VALUE AND DIAGNOSTIC ACCURACY OF DUAL-ENERGY CT FOR THE DIAGNOSIS OF GOUT: A PROSPECTIVE STUDY IN SUBJECTS WITH UNCLASSIFIED MONO OR OLIGOARTHRITIS

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Background: The latest diagnostic technique to visualize monosodium uric acid (MSU) depositions is Dual Energy CT scan (DECT).[1]
Objectives: To assess the additive value and accuracy of DECT in diagnosing gout in a prospective study in subjects with unclassified arthritis.
Methods: We included 100 consecutive patients with acute unclassified mono or oligo arthritis who presented to the outpatient clinic of the Department of Rheumatology of Meander Medical Centre, Amersfoort, the Netherlands, ClinicalTrials.gov NCT03038386. Eleven patients dropped out, see Figure. Patients underwent aspiration of the arthritic joint (see Table) and a DECT scan of hands and wrists, knees, ankles and feet bilaterally. The 2015 EULAR/ACR gout classification criteria were used to score the subjects, with and without DECT result, to determine the additive value of DECT. Sensitivity and specificity of DECT for diagnosing gout were calculated separately for at the joint and at individual persons' level, using as reference standards microscopy of synovial fluid (SF) and the gout classification criteria.
Results: For demographic and clinical characteristics of the patients see Table 1, and for study data and outcomes see Figure and Table 2. Sixty-eight of 89 patients (76.4%) fulfilled the 2015 EULAR/ACR criteria for gout. Of the 98 patients with SF aspiration, 55 (56%) were positive for MSU; of these, 89 subjects underwent DECT, of whom 38 had a negative microscopy result. Of these 38 subjects, 14 (37%) met the gout classification criteria only after a positive DECT result.
Conclusion: Our findings suggested that DECT could have an additive value to clinical algorithms in subjects with undifferentiated arthritis when microscopy of SF fails to demonstrate the presence of MSU crystals.

REFERENCES:

[1] Choi HK, et al. Dual energy CT in gout: a prospectieve validation study. Ann Rheum Dis 2012; 71:1466-71.

Table 1. The characteristics of the patients (n=89) in the analysis

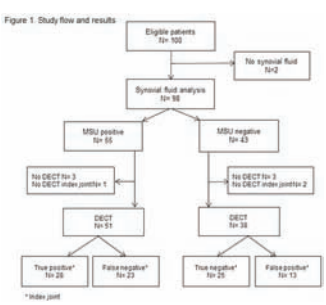
	Patients MSU positive (n=51)	Patients MSU negative (n=38)
Age, years, mean (SD)	60 (16)	64 (12)
Gender, N (%)		
Male	44 (86.3)	38 (73.7)
Arthritic joint aspirated (N,%)		
MTP1	32 (66.7)	8 (21.1.)
Other joints	19 (33.3)	31 (78.9)
Period between 1th arthritis attack and baseline visit in months, median (IQR)*	12 (0.9-48)	5.5 (0.2-36)
Serum uric acid (µmol/L) mean (SD)	499 (88)	411 (101)

* according to patient

Table 2. Diagnostic accuracy of DECT

DECT evaluation method	Reference standard	TP	FP	FN	TN	Sensitivity (95%CI)	Specificity (95% CI)	Diagnostic accuracy (95%CI)
joint/ localisation based	MSU	28	13	23	25	0.55 (0.40- 0.69)	0.66 (0.49 - 0.80)	0.60 (0.49-0.70)
patient based	MSU	39	20	12	18	0.77 (0.63- 0.87)	0.47 (0.31- 0.64)	0.64 (0.53-0.74)
joint/ localisation based	EULAR/ ACR 2015	41	0	27	21	0.60 (0.48 -0.72)	1 (0.84-1)	0.70 (0.59 - 0.79)
patient based	EULAR/ ACR 2015	56	3	12	18	0.82 (0.71- 0.91)	0.86 (0.64-0.97)	0.83 (0.74-0.90)
joint/ localisation based	MSU	11	7	9	12	0.55 (0.32- 0.76)	0.63 (0.38-0.84)	0.59 (0.42-0.74)
patient based	MSU	16	10	4	9	0.80 (0.56- 0.94)	0.47 (0.24-0.70)	0.64 (0.46-0.78)
joint/ localisation based	EULAR/ ACR 2015	18	0	11	10	0. 60 (0.42- 0.79)	1 (0.69-1)	0.72 (0.55-0.85)
patient based	EULAR/ ACR 2015	25	1	4	9	0.86 (0.68- 0.96)	0.90 (0.56-0.99)	0.87 (0.73-0.96)

joint-/localisation-based evaluation, person based evaluation: imaging results positive for gout if green pixilation were observed at the index joint, at the index joint and/or in other locations, respectively.



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OP0051 DEVELOPMENT OF A MULTIVARIABLE IMPROVEMENT MEASURE FOR GOUT

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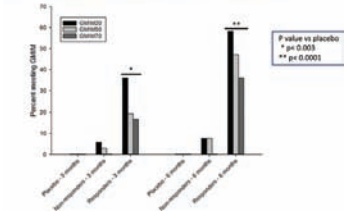
Background: Inflammatory rheumatic diseases are generally multifaceted disorders and the complex pathology underlying these conditions makes it difficult to assess patient status and the efficacy of therapy with a single outcome measure. This has prompted the development of composite measures for many rheumatic diseases. Gout is also a multifactorial inflammatory disease in which patients experience a wide range of signs and symptoms, including intermittent and persistent pain and inflammatory arthritis, tophi and disability. Most assessments of gout and response to urate-lowering therapy (ULT) have focused primarily on the ability to lower serum urate and decrease the frequency of flares. Recognition that assessment of ULT and other treatments for gout could be facilitated by endpoints that more closely reflect the multidimensional impact of the disease has prompted an interest in developing composite measures, although there is no consensus on the most appropriate composite measure to employ.

Objectives: To develop an evidence-based gout multivariable improvement measure (GMIM) that captures the spectrum of gout manifestations and is sensitive to change.

Methods: Databases from patients with chronic refractory gout who participated in two randomized 6 month clinical trials (RCTs) of pegloticase were reviewed[1]. Sub-sets who had persistent urate lowering (responders) to biweekly pegloticase (n=36) and those who had only transient urate lowering (non-responders, n=49) were identified and compared to those who received placebo (n=43). Initially individual patients were assessed for achievement of previously reported criteria for remission[2]: serum urate <6 mg/dL, absence of tophi and flares, patient global assessment, and pain (each <2 on a 10-point visual analog scale). A repeated measures mixed effects model controlling for repeated observations with backward elimination using data from these patients was employed to determine the model components that best correlated with time to maximum benefit[3]. This analysis resulted in the addition of swollen and tender joints to the outcome measure. In order to assess the degree of improvement, each subject was scored based upon a serum urate <6 mg/dL and 20, 50 or 70% improvement in ≥4 of the 6 clinical evaluations and termed GMIM20, 50, 70.

Results: GMIM was able to capture gradation of change in the treated populations and also distinguish responses in those with persistent versus those with transient urate lowering and subjects treated with placebo (Figure 1). At 3 and 6 months, achievement of GMIM20, 50 and 70 in persistent responders occurred significantly more often vs placebo and versus non-responders without persistent urate lowering. Sensitivity analysis indicated that flares contributed minimally to the model.

Figure 1: Percentage of Subjects Meeting GMIM Response Criteria



Conclusion: GMIM effectively captures changes in disease severity in response to treatment in patients with advanced gout treated with pegloticase. GMIM20,50,70 may serve as an evidence-based tool for assessment of the quality of response to therapies in subjects with gout in medical practice or in clinical trials.

REFERENCES:

[1] Sundy JS, et al. JAMA. 2011; 306 (7):711-20
[2] deLatour H, et al. *Arthritis Care Res (Hoboken)*. 2016; 68(5):667-72
[3] Schlesinger N, et al. *Arthritis Rheumatol*. 2017; 69 (Supple 10)

Disclosure of Interests: Naomi Schlesinger Consultant for: Astra Zeneca, Novartis, Horizon Pharma, N. Lawrence Edwards Consultant for: Horizon Pharma, Astra Zeneca, Selecta Biosciences, Anthony Yeo Employee of: Horizon Pharma, Peter Lipsky Consultant for: Consulting fees from Horizon Pharma

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OP0052 FAILURE TO REACH SERUM URATE TARGET IS ASSOCIATED WITH ELEVATED MORTALITY IN GOUT

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Background: Gout is associated with an increased risk of cardiovascular events and death. It has been shown that both overall and risk of death are associated with increasing gout severity, as reflected by the number of tophi. It remains to be proven whether better control of gout through lowering of serum uric acid (sUA) confers a survival advantage.

Objectives: To determine the impact of achieving sUA less than 6 mg/dl (vs greater) on mortality risk among gout patients.

Methods: Analysis of data from a prospective follow-up cohort (1992 to 2017) of patients attending a gout clinic (85% of patients with microscope or ultrasound diagnosis) and with at least one follow-up visit. Mortality was confirmed from medical records, patients' families, or local death registries if needed. sUA levels were monitored during follow-up and the average sUA until sUA was stable was used as the primary exposure dichotomized as < 6 mg/dl (versus ≥ 6 mg/dl). Descriptive variables and potential confounders included: age, gender, body mass index, previous treatment with urate-lowering drugs (ULDs), number of joints affected at entry, presence of subcutaneous tophi, radiographic evidence of articular damage, number of gout flares in the year preceding evaluation, previous diagnosis of cardiovascular (CV) disease, loop diuretic use, alcohol intake, diabetes, hypertension, hyperlipidemia, and renal function impairment. In addition, the Kaiser Permanente stratification of comorbidity was further used to risk stratify patients from low to high risk of death. Univariate and multivariate Cox proportional hazards models were used to determine mortality risks expressed a hazard ratios (HR) and 95% Confidence Intervals (CI).

Results: The study cohort included 1,193 patients (92% men, mean age 60, 6.8 years disease duration, with an average of 3-4 flares in the previous year). Mean follow-up was 48 (median 30, IQR 12-66), with 4,830 patient-year observation. Mean sUA at baseline was 9.1 mg/dl and 16.3% of the patients maintained sUA levels ≥6 mg/dl despite treatment. A total of 158 deaths occurred (13% overall mortality), with loss to follow-up in 286 cases (24%). Overall crude mortality rate was 32.7 per 1,000 patient-years, (95% CI: 28.0-38.2) and was significantly higher for patients with sUA ≥ 6 mg/dl, 80.9 per 1, 000 person years (95% CI 59.4-110.3) compared to patients with sUA <6 mg/dl, 25.7 per 1,000 person-years (95% CI: 21.3-30.9). With adjustment for age, sex, previous CV events, and baseline sUA concentration, a sUA ≥ 6 mg/dl was associated with a HR of 2.39 (1.64 - 3.50).

Conclusion: Failure to reach a target sUA level of 6 mg/dl is an independent predictor of mortality in gout patients. Control of gout with achievement of sUA target <6 mg/dl should be considered in order to improve patient survival.

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OP0053 CERAMIDES AND DIHYDROCERAMIDES LEVELS ARE ASSOCIATED WITH THE INFLAMMATORY RESPONSE IN A MURINE MODEL OF GOUT

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Background: The metabolic syndrome is strongly associated with gout and hyperuricemia in man. Patients with gout commonly report acute flares after eating particular foods and it is suspected that metabolic changes, apart from serum urate levels, influence the triggering of the inflammatory response to MSU crystals.

Objectives: By studying the metabolic changes that impact on the response to MSU crystals in a murine model of gout, we hope to identify the dietary effect on metabolites that are associated with the inflammatory response to MSU crystals.
Methods: Male mice (C57Bl/6) were fed either a normal diet (ND) or high fat diet HFD (DIO D12492) for >6 weeks. During the last 4 weeks of feeding, half the mice in each group were treated with antibiotics (Enrofloxacin 0.25% + co-amoxicillin) to induce a germ-free state. At day 0, mice were injected i-p with 1mg of MSU crystals. Mice were sacrificed 6h after i-p injection. Serum, plasma and peritoneal exudate samples were collected at sacrifice and plasma obtained 3 weeks before sacrifice. Untargeted and targeted liquid chromatography – mass spectrometry based-metabolomics approach was performed on serum and plasma samples. IL1 and IL6 were measured in serum and peritoneal exudates by ELISA. Animal experimental authorization was obtained for these experiments.
Results: Mice fed a HFD had a greater serum and peritoneal IL6 response to MSU. In an untargeted analysis, multiple metabolic alterations were observed related to diet. Targeted analyses of sphingolipids were performed. Both diet and inflammation (MSU injection) altered plasma sphingolipid levels. No effect of antibiotics was observed. MSU injection induced marked changes in the sphingolipid profile (38.2% of explained variance), while diet had a lesser effect (16.2% of explained variance). Mice fed an HFD had significantly higher serum IL6 before and peritoneal IL6 levels after MSU injection than mice fed a ND. DhCer C16:0 and Cer C16:0 levels decreased significantly after MSU injection. Pre-MSU levels of DhCer C16:0 and Cer C16:0 showed significantly negative correlations with IL6p levels after i-p injection in HFD animals.
Conclusion: The sphingolipid profile was significantly changed by diet and inflammation. In mice given a HFD, the levels of particular ceramides were significantly correlated with subsequent inflammatory response as assessed by IL6 secretion, suggesting that they may play a role in modulating the inflammatory response to MSU. These same ceramides and their derivatives have been linked to susceptibility to diabetes and cardiovascular diseases1,2. Further investigation of these sphingolipids in gout in man is warranted.

REFERENCES:

[1] Wigger L, et al. Cell Rep. 2017 Feb 28;18(9):2269-2279. doi: 10.1016/j.celrep.2017.02.019
[2] Summers SA. Cell Metab. 2018 Feb 6;27(2):276-280. doi: 10.1016/j.cmet.2017.12.003

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OP0054 OCCUPATIONAL EXPOSURE TO INORGANIC DUST – A NOVEL RISK FACTOR FOR INCIDENT GOUT?

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Background: Hyperuricemia and factors contributing to it are strong risk factors for gout but it is still unexplained why only some individuals with hyperuricemia develop gout. Additional risk factors for gout could be genetic or related to comorbidity, lifestyle or occupation. Occupational exposure to inorganic dust has previously been linked to an increased occurrence of inflammatory rheumatic diseases such as rheumatoid arthritis and could possibly increase the risk of gout.
Objectives: To evaluate if occupational exposure to inorganic dust increases the risk of incident gout.
Methods: Gout was defined as having at least one ICD-10 code for gout (M10 or M14.0) in the population based health care database of the Western Swedish Health Care Region (VEGA), during the years 2006-2012, without any gout diagnosis during at least 6 years previously. Individuals with gout that were employed in the 5-year period prior to first diagnosis were included for analysis. Population controls without gout were identified in the census register by Statistics Sweden, matching up to 5 controls per case on the basis of age, sex and place of residence, excluding controls that were not employed during the predictor period. Data on occupation (coded by the ISCO-88 standard) for the 5 years prior to inclusion were collected from official registries and were used to assign exposure status using a job exposure matrix for inorganic dust previously developed.[1] Data on predefined comorbidities (psoriasis, renal disease, alcohol abuse, obesity and diuretic treatment) considered to be possibly relevant confounders for the analyses were collected from VEGA, defined by ICD-10 codes. Alcohol abuse and obesity were found to be related both to gout and exposure to inorganic dusts and were therefore adjusted for in multivariate analyses. The effect of exposure to inorganic dust on risk of gout was described with odds ratios, calculated using conditional logistic regression, for the whole population and stratified by sex.
Results: 6120 gout cases and 25074 controls were included. Frequencies of exposures (n (%)) and odds ratios (OR (95% conf. int.) for association of risk factors with incident gout are shown in the table below.

		Exposed to inorganic dust	Alcohol abuse	Obesity
Whole population	Gout cases, n=6120	1836 (30)	299 (5)	671 (11)
	Controls, n=25074	7074 (28)	538 (2)	821 (3)
	OR univariable	1.10 (1.04 to 1.17)	2.37 (2.04 to 2.74)	3.81 (3.42 to 4.26)
	OR multivariable*	**1.07 (0.99 to 1.14)**	2.26 (1.94 to 2.62)	3.75 (3.36 to 4.19)
Men	Gout cases, n=4751	1615 (34)	267 (6)	489 (10)
	Population controls, n=19339	6343 (33)	471 (2)	576 (3)
	OR univariable	1.07 (1.00 to 1.15)	2.42 (2.07 to 2.82)	3.93 (3.45 to 4.48)
	OR multivariable*	**1.03 (0.97 to 1.11)**	2.29 (1.95 to 2.69)	3.85 (3.38 to 4.39)
Women	Gout cases, n=1369	221 (16)	32 (2)	182 (13)
	Population controls, n=5735	731 (13)	67 (1)	245 (4)
	OR univariable	1.33 (1.12 to 1.57)	2.02 (1.31 to 3.11)	3.53 (2.87 to 4.34)
	OR multivariable*	**1.27 (1.07 to 1.51)**	2.03 (1.31 to 3.14)	3.50 (2.85 to 4.31)

*includes inorganic dust, alcohol abuse and obesity as covariates.

Conclusion: As expected, previously known risk factors for gout such as obesity and alcoholism were strongly associated with incident gout. In univariate analyses, exposure to inorganic dust was also associated with gout. After adjusting for alcohol abuse and obesity, the relationship was attenuated in men but remained in women, providing evidence that occupational exposure to inorganic dust might be a previously unknown risk factor for gout.

REFERENCE:

[1] Lillienberg L, et al. Occupational exposure and new-onset asthma in a population-based study in Northern Europe (RHINE). Ann Occup Hyg. 2013;57:482-92.

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WEDNESDAY, 12 JUNE 2019

JIA: From new horizons of treatment to perspectives of current ones

OP0055 EFFICACY OF CANAKINUMAB, ON A REDUCED DOSE OR A PROLONGED DOSE INTERVAL WITHOUT CONCOMITANT CORTICOSTEROIDS AND METHOTREXATE, IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Canakinumab (CAN), a selective, human anti-IL-1β mAb, has shown sustained therapeutic effect along with corticosteroid (CS) dose reduction/discontinuation in patients (pts) with systemic juvenile idiopathic arthritis (SJIA), in a long-term extension study (NCT00891046).[1]
Objectives: To evaluate the efficacy and safety of 2 different CAN tapering regimens in SJIA pts who were in clinical remission (NCT02296424).

Methods: This Phase 3b/4 study had 2 parts. Of 182 enrolled pts, 166 pts with inactive disease (ID) (cohort 1; 68pts)[1] and CAN-naïve pts (cohort 2; 98pts) were administered subcutaneous CAN 4mg/kg q4w in Part I. Per protocol titration off CS and/or methotrexate (MTX) was attempted during Part I. Eligible pts (ID for 24 weeks[wks] and being CS- and MTX-free for at least 4 wks) advanced to Part II wherein, pts were randomised to either a 3-step CAN dose reduction (2mg/kg/q4w, followed by tapering to 1 mg/kg/q4w and then discontinuation) or dose interval prolongation (4mg/kg q8w, followed by tapering to 4mg/kg/q12w and then discontinuation); pts advanced to the next tapering step if ID was maintained for 24 wks. Adapted American College of Rheumatology (ACR) paediatric criteria, its individual components and Juvenile Arthritis Disease Activity Score (JADAS) were assessed.
Results: In total, 75 pts were randomised to a dose reduction (n=38) or dose interval prolongation (n=37) CAN tapering regimen in part II. The pts who maintained ID for 24 wks exceeded the predefined threshold of 40% for the reduced CAN dose arm (71%) and prolonged dose interval (84%) treatment arm of Step 1 (primary endpoint). A total of 68.4% (26/38) and 81.1% (30/37) pts in the dose reduction and interval prolongation arms, respectively were successful in Step 2; 33% (25/75) of pts successfully discontinued CAN and maintained ID for 24 wks. ID, ACR 90/100 and JADAS 27 C-reactive protein (CRP) scores are summarised in the table. Adverse events (AEs) and serious AEs observed within the 2 cohorts and across Parts I and II were similar. The most frequent AEs were common infections (nasopharyngitis, upper respiratory tract infection, pharyngitis) followed by SJIA-related events (rash, pyrexia and arthralgia).

Table 1. Efficacy responses of Part I over 24 Wks

	Cohort 1 N=68	Cohort 2 N=98
Inactive disease, n (%)		
BL	56 (82.4)	0.0
Wk 4	61 (89.7)	45 (45.9)
Wk 24	67 (98.5)	67 (68.4)
Median JADAS27-CRP, range (min, max)		
BL	1.1 (0.0, 35.5)	22.8 (4.9, 48.0)
Wk 4	5.05 (0.0, 12.97)	2.6 (0.0, 41.7)
Wk 24	1.0 (0.0, 27.8)	2.0 (0.0, 31.5)
ACR 90, n (%)		
BL	17 (25)	
Wk 4	0 (0.0)	13 (13.3)
Wk 24	13 (19.1)	15 (15.3)
ACR 100, n (%)		
BL	38 (55.9)	
Wk 4	2 (2.9)	31 (31.6)
Wk 24	34 (50)	44 (44.9)

N, total number of patients; n, number of patients

Conclusion: SJIA pts with ID for 24 wks on CAN monotherapy can successfully taper CAN by either reducing the dose or prolonging the dosing interval. However, only a minority of pts overall successfully discontinued CAN treatment and maintained ID for 24 wks. The safety profile was similar and consistent with other CAN SJIA studies. No new safety signals were identified.

REFERENCE:

[1] *Arthritis Rheumatol.*2016; 68 (S10).

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OP0056

MAINTENANCE OF CLINICAL RESPONSE IN INDIVIDUAL CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH SUBCUTANEOUS ABATACEPT

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Background: The efficacy of SC abatacept (ABA) in patients (pts) with polyarticular-course juvenile idiopathic arthritis (pJIA) was shown in a 2-year (yr), Phase III, open-label international study (NCT01844518).[1] However, it is unknown whether each individual pt within a treatment group consistently achieves the same efficacy endpoint at all time points.
Objectives: To investigate whether ABA efficacy is maintained by individual pts with pJIA over time.
Methods: In this subgroup analysis, pts in two age cohorts (2–5 yrs and 6–17 yrs) who achieved clinical response to weekly SC ABA (10 to <25 kg [50 mg], 25 to <50 kg [87.5 mg], ≥50 kg [125 mg]) at Day 113 (time point of primary pharmacokinetics endpoint[1]) were followed for 2 yrs. Stringent efficacy outcomes selected for analysis included JIA-ACR70, JIA-ACR100, Juvenile Arthritis Disease Activity Score 71 (JADAS71) minimal disease activity (MDA; ≤3.8) and JADAS71 inactive disease (ID; ≤1) rates. Prognostic factors for sustained response were investigated using logistic regression.
Results: A total of 219 pts entered the study (46 [21.0%] 2–5 yrs; 173 [79.0%] 6–17 yrs) and a subgroup of these pts achieved a clinical response at Day 113 (Table). Most pts who achieved JIA-ACR70, JIA-ACR100, JADAS71 MDA and JADAS71 ID at Day 113 sustained their response at Day 393 and at Days 393 and 645 in the 2–5-yr and 6–17-yr cohorts (Figure). Across cohorts, more than 75% and 60% of pts maintained a JIA-ACR 70 and JADAS71 MDA response through Day 645, respectively. Prior biologic (b)DMARD use was an important prognostic factor. In pts aged 6–17 yrs, sustained JIA-ACR70 response rate at Days 393 and 645 was 81% (57/70) in pts who did not have prior bDMARDs vs 57% (12/21) in pts who had prior bDMARDs (p=0.0715); sustained JADAS71 MDA response rate was 71% (37/52) vs 37% (7/19; p=0.0320). Prognostic factors for JIA-ACR100 response and JADAS71 ID in pts aged 6–17 yrs and for all outcomes in pts aged 2–5 yrs could not be determined due to low pt numbers.
Conclusion: The majority of individuals with pJIA who achieved stringent efficacy endpoints with weekly SC abatacept by Day 113 sustained that clinical endpoint over time. Prior bDMARD use may be a prognostic factor for sustained response over 2 yrs.

Table. Proportion of pts who achieved a clinical response at Day 113

Endpoint	Pts with response at Day 113	
	2–5 yrs (n=46)	6–17 y (n=173)
JIA-ACR70	34 (74)	91 (53)
JIA-ACR100	19 (41)	25 (15)
JADAS71 MDA	28 (61)	71 (41)
JADAS71 ID	17 (37)	28 (16)

Data are expressed as n (%)
ID=inactive disease; JADAS71=Juvenile Arthritis Disease Activity Score 71; MDA=minimal disease activity; pt=patient; yr=year

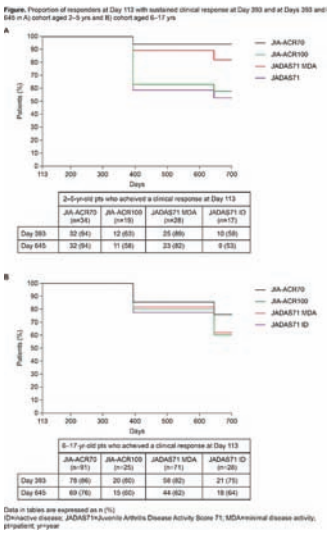


Figure. Proportion of responders at Day 113 with sustained clinical response at Day 393 and at Days 393 and 645 in A) cohort aged 2–5 yrs and B) cohort aged 6–17 yrs

A) 2–5-yr-old pts who achieved a clinical response at Day 113

	JIA-ACR70 (n=34)	JIA-ACR100 (n=19)	JADAS71 MDA (n=28)	JADAS71 ID (n=17)
Day 393	32 (94)	12 (63)	25 (89)	10 (59)
Day 645	32 (94)	11 (58)	23 (82)	9 (53)

B) 6–17 yr-old pts who achieved a clinical response at Day 113

	JIA-ACR70 (n=91)	JIA-ACR100 (n=25)	JADAS71 MDA (n=71)	JADAS71 ID (n=28)
Day 393	78 (86)	20 (80)	58 (82)	21 (75)
Day 645	69 (76)	15 (60)	44 (62)	18 (64)

Data in tables are expressed as n (%)
ID=inactive disease; JADAS71=Juvenile Arthritis Disease Activity Score 71; MDA=minimal disease activity; pt=patient; yr=year

REFERENCE:
[1] Brunner HI, et al. *Arthritis Rheumatol* 2018;70:1144–54.

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OP0057 EARLY TREATMENT WITH ANAKINRA IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Systemic juvenile idiopathic arthritis (sJIA) accounts for 10-20% of all patients with JIA. The prominent systemic clinical features, the marked elevation of inflammatory markers and the absence of autoantibodies make this disease different from other JIA forms. sJIA should be considered as a polygenic autoinflammatory disease. Interleukin 1 (IL-1) has been shown to be a major mediator of the inflammatory cascade that underlies sJIA. Treatment with anakinra has been reported to be effective in a sizable portion of patients with sJIA.
Objectives: To assess clinical response rate and disease course in sJIA patients treated with anakinra. To evaluated whether the response to anakinra was related to baseline variables.
Methods: We reviewed 56 (28 F) consecutive patients with sJIA treated with anakinra for at least 6 months in our institution. The diagnosis of sJIA was established according to the International League of Associations for Rheumatology (ILAR) classification criteria. We analyzed the effect of anakinra on fever, rash, number of active joints, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cells count, platelets count and ferritin levels. Clinically inactive disease (CID) was defined according to Wallace criteria. Clinical and laboratory data were obtained using a standard data collection form.
Results: The median age at the disease onset was 5.7 (IQR 2.9-10.2) years. The median time from onset to received anakinra was 1.9 (IQR 0.7-9.7) months. At baseline 52/56 (93%) of patients had fever and median number of active joints was 2 (IQR 1-4). After 6 months of treatment 39 patients (69.6%) met criteria for inactive disease. Among 56 patients 17 (30.3%) received anakinra in monotherapy and 39 (69.6%) received anakinra with glucocorticoids. There were no statistically significant differences between the two groups for demographic, clinical and laboratory features. 13/17 (76.4%) patients treated with anakinra alone and 26/39 (66.6%) patients treated with anakinra and glucocorticoids met criteria for CID off glucocorticoids at 6 months (p=0.54). Among the 56 patients, 29 (51.7%) received anakinra within 2 months from disease onset. There were no statistically significant differences for demographic, clinical and laboratory features among patients who started anakinra in the first 2 months from disease onset compared to those that started anakinra after 2 months. At 6 months after beginning of anakinra treatment, 27/29 patients (93.1%) who started anakinra within 2 months from disease onset and 12/27 (44.4%) who started anakinra after 2 months from disease onset reached clinical inactive disease off glucocorticoids (p=0.0001). Patients who started anakinra after the first 2 months from disease onset have a significantly higher risk of non-response (OR=8.06, 95% CI: 2.03-32.0).
Conclusion: According with several observations, anakinra is effective in a significant proportion of patients with sJIA. A possible approach to introduce IL-1 inhibitor, with or without concomitant glucocorticoids, early in the disease course taking advantage of a "window of opportunity" has been suggested. Our observation confirms that earlier treatment with anakinra is associated with a better short-term outcome. Moreover, our results show that beginning of treatment after two months of disease is correlated with a high risk of non-response.

REFERENCE:
[1] Nigrovic PA. Review: is there a window of opportunity for treatment of systemic juvenile idiopathic arthritis? Arthritis Rheumatol 2014;66:1405-13.

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OP0058 DEVELOPMENT OF INFLAMMATORY BOWEL DISEASE DURING TREATMENT WITH ETANERCEPT IN PATIENTSWITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) has a reported prevalence varying from 16 to 150 per 100,000 patients and it thereby is the most frequent chronic rheumatologic disease presenting in childhood. Inflammatory bowel disease (IBD) is an auto-inflammatory disease that can develop in patients with JIA. Results from multiple studies suggest an association between therapy with Etanercept (ETN) and occurrence of IBD in patients with JIA, which may or may not be counteracted by methotrexate.
Objectives: The aim of this study was to describe characteristics of JIA patients who developed IBD and to evaluate a possible relationship between IBD onset and medication use at IBD onset.
Methods: Pharmachild, the largest international JIA registry, was used for this study. Patients were enrolled via members of the Paediatric Rheumatology

INternational Trials Organisation (PRINTO). The registry contains both retrospective and prospective data.

Results: A total of 8,309 patients were included in this study. 290 gastrointestinal disorders were reported in 260 patients. 50 cases in 47 patients were classified as IBD or suspected IBD.

Age at JIA onset was significantly higher in patients who developed IBD (9.1 vs 7.1 years p=0.002), and female predominance was lower (48.9% versus 67.6% p=0.011). Enthesitis related arthritis (ERA) was the JIA subtype in 40.4% of the patients who developed IBD.

In 14 out of 47 patients more detailed information about IBD disease onset was available, such as date of disease onset and medication used at that time. 71.4% of all 14 patients used etanercept and 50.0% used MTX 3 months prior or at IBD onset. Etanercept exposure prior to IBD onset varied from no exposure to 6.39 years with a median of 1.3 years. Methotrexate exposure prior to disease onset varied from no exposure to 8.10 years with a median of 2.9 years.

Information regarding quality of life was available for 2,752 patients of which 17 IBD patients. Quality of life, both physical and psychosocial, was significantly lower in patients who developed IBD patients (p=0.018 and p=0.046 respectively).

Conclusion: In this study ERA patients were more at risk of developing IBD and 71.4% used etanercept while developing IBD. We did not find a protective role of MTX since 50.0% of patients with available data developed IBD while using MTX. Lastly, IBD has an important physical and psychosocial impact on quality of life.

REFERENCE:

[1] Swart JF; Giancane G; Horneff G; Magnusson B; Hofer M; Alexeeva E; Panaviene V; Bader-Meunier B; Anton J; Nielsen S; De Benedetti F; Kamphuis S; Stanevicha V; Trachana M; Ailioaie LM; Tsitsami E; Klein A; Minden K; Foeldvari I; Haas JP; Klotsche J; Horne. Pharmacovigilance in juvenile idiopathic arthritis patients treated with biologic or synthetic drugs: combined data of more than 15,000 patients from pharmachild and national registries. Arthritis Res Ther. 2018;

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OP0059

PERIARTICULAR GLUCOCORTICOID INJECTIONS: DELINEATING THEIR USE IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Glucocorticoid injections in periarticular sites (PAGI) such as tendons and bursae often complete the local treatment of active disease in juvenile idiopathic arthritis (JIA). However, the use of PAGI and their role in the achievement of disease remission has seldom been studied.

Objectives: To identify the clinical features of JIA patients treated with PAGI at the study center in a 6 years period, the sites most frequently injected, the frequency of and the time for achieving local remission.

Methods: Records of JIA patients treated with PAGI at the study center from 2012 were retrospectively reviewed. Demographic and clinical features, including ongoing systemic treatment, sites of injection, procedure setting, type and dosage of glucocorticoid injected, time to achieve local remission (complete or partial when one/some of the injected sites were in remission and one/some showed persistent synovitis), frequency of remission of the injected sites at the last follow-up and side-effects were recorded.

Results: In a total of 293 procedures 647 tendons and 26 bursae were injected in 191 patients. Most of the patients were females (74%), with ILAR oligoarticular JIA subtype (50% persistent, 23% extended), followed by RF-negative polyarthritis (23.2%), RF-positive polyarthritis (0.7%) and systemic JIA (1.3%), with a median age of 8.2 years (IQ 4.7-11.3) at the PAGI. All procedures were ultrasound-guided, 281 (96%) under general sedation. Acetate methylprednisolone was used in 96% of the procedures (average dosage 0.45 mg/kg/tendon, 0.89 mg/kg/bursa), whereas trimcinolone exacetonide in 4%. In 255 procedures (87%) patients experienced remission in the injected sites after a median of 2.6 months (IQ 1.9-3.5). Forthy-seven patients (24.6%) underwent to repeated injections in the same sites after at least 3 months from the 1st procedure. A total of 96 tendons and 9 bursae were re-injected during 69 procedures (23.5%). At the last follow up, after a median period of 29.4 months (IQ 15-45.48) from PAGI, patients experienced complete local remission in 259 (88.4%) injected procedures and partial local remission in 23 (7.8%). In 53 procedures with repeated injection(s) in the same site(s) (77%), patients were in local remission at the last follow up. In 77 procedures (26.3%) patients presented flare of disease in periarticular sites. Concerning concomitant therapy, at the time of each PAGI 115 patients (39.2%) were not on treatment, 137 (46.7%) were on methotrexate, 29 (9.9%) on methotrexate and biologics, 8 (2.7%) on biologics and 4 (1.5%) received others. Patients were started with a new treatment in around three months following 139 (47.4) procedures due to poor control of disease. In 156 (53.2%) procedures, patients experienced complete/local remission and maintained the same treatment before or after the injection at the last follow up in a median period of 20.8 months (IQ 12.67-39.35). Of notice, 81.4% of patients who experienced complete remission following the injection were not on concomitant treatment; 85.9% of patients who experienced complete remission at the last follow up did not receive concomitant treatment. In 24 injection procedures (8.2%) patients showed only mild local side effects (atrophy and hypopigmentation).

Periarticular sites	N. injections (%)
Total	673(100%)
Tendons	647 (96.1%)
Posterior tibialis tendon	194 (30%)
Flexor digiti propri tendons (I-V)	152 (23.5%)
Peroneals	123 (19%)
Others	178 (27.5%)
Bursae	26 (3.9%)
Deep infrapatellar bursa	11 (42.3%)
Retrocalcaneal bursa	4 (15.4%)
Baker's cyst	4 (15.4%)
Others	7 (26.9%)

Conclusion: PAGI are a safe option in the management of JIA. In our cohort, patients treated with PAGI had more frequently persistent oligoarticular JIA subtype; acetate methylprednisolone was by far the most frequently used glucocorticoid. In 88.4% procedures patients experienced remission at last follow up. However, further investigations are mandatory to assess the role of concomitant therapy in achieving and maintaining remission.

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OP0060

SAFETY PROFILE OF ETANERCEPT IN LONG-TERM USE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: Etanercept is the most frequently used biologic drug in patients with JIA. Children and adolescents with JIA are treated with etanercept often over long periods of time, sometimes even into adulthood. The knowledge about its long-term safety, especially with regard to the occurrence of new-onset immune-mediated diseases and malignancies, is still limited.
Objectives: To investigate the exposure-adjusted rates of adverse events (AE) and serious AE (SAE) in patients with JIA with long-term use of etanercept.
Methods: Patients with JIA who were enrolled in the German biologic register BiKeR and were born before 30.05.2000 (at least 18 years of age at this date) were considered for this analysis. The follow-up register JuMBO ensures the long-term follow-up into adulthood. An AE or SAE was attributed to etanercept when the treatment was either ongoing or terminated in less than 3 month prior to the event. The incidence of malignancies was estimated in patients who were ever exposed to etanercept with at least one dose.
Results: Of 4546 patients who were currently enrolled in BiKeR a total of 2584 JIA patients were eligible for the JuMBO register (>18 years). Among those, 1765 (68%) were ever exposed to etanercept and observed for a mean of 6.8±4.9 years (including 1101 into adulthood). The majority of them had polyarthritis (35%), followed by enthesitis-related arthritis (20%) and extended oligoarthritis (17%). The patients were exposed to etanercept for a total of 4.2 years (mean, 6,726 exposure years, EY); 518 patients were continuously treated with etanercept for at least 5 years (4,534 EY). In total, 124 autoimmune events (1.84/100EY) and 7 other immune disorders (0.10/100EY) were reported in 102 (5.8%) and 7 (0.4%) patients with onset on average 10.2 years after JIA onset, and 6.8 years after start with etanercept, respectively. The number of selected immune-mediated events and the exposure-adjusted rates are given in the table. In addition, 11 malignancies (0.10 events/100 person-years) were reported in patients ever exposed to etanercept. Among those (mean age at onset 20.3 years), 4 malignancies were reported in childhood and 7 in young adulthood. Three patients were also exposed to other biologics before the incidence of malignancy. The malignancies occurred on average 12.1 years after JIA onset, 10.4 years after start with a first DMARD and 7.5 years after first exposure to etanercept.
Conclusion: This is the first long-term large safety study in prospectively followed JIA patients with focus on new-onset immune-mediated diseases and malignancies in etanercept. The study also highlights that it is important to prospectively collect data on adverse events under treatment with biologics in JIA, particular with respect to the risk of malignancies in young adulthood.

Table 1. Adverse and serious adverse events under treatment with etanercept

	All patients ever treated with etanercept, n=1765		Patients continuously treated with etanercept for at least 5 years, n=516	
	Number of patients	Number of reported events (rate / 100 EY)	Number of patients	Number of reported events (rate / 100 EY)
Serious adverse events	218 (7.3%)	320 (4.76)	116 (22.4%)	189 (4.17)
All infections	285 (16.1%)	469 (6.97)	124 (23.9%)	238 (5.25)
Medically important infections	56 (3.2%)	69 (1.03)	31 (6.0%)	43 (0.95)
Autoimmune disorder events	102 (5.8%)	124 (1.84)	49 (9.5%)	59 (1.30)
Uveitis	72 (4.1%)	87 (1.29)	37 (7.1%)	43 (0.95)
Inflammatory bowel diseases	22 (1.2%)	28 (0.42)	8 (1.5%)	11 (0.24)
Demyelinating disorders	3 (0.2%)	3 (0.04)	2 (0.4%)	2 (0.04)
Autoimmune hepatitis	1 (0.1%)	1 (0.01)	1 (0.2%)	1 (0.02)
Autoimmune thyroiditis	1 (0.1%)	1 (0.01)	1 (0.2%)	1 (0.02)
Encephalitis autoimmune	1 (0.1%)	1 (0.01)	0	0 (0.00)
Histiocytosis haematophagic	1 (0.1%)	1 (0.01)	0	0 (0.00)
Incident immune disorders	7 (0.4%)	7 (0.10)	6 (1.2%)	6 (0.13)
Vasculitides	2 (0.1%)	2 (0.03)	2 (0.4%)	2 (0.04)
Psoriasis	4 (0.2%)	4 (0.06)	3 (0.6%)	3 (0.07)
Erythema nodosum	1 (0.1%)	1 (0.01)	1 (0.2%)	1 (0.02)

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OP0061

CONSUMER PERSPECTIVE ON PAEDIATRIC RHEUMATOLOGY CARE AND SERVICE DELIVERY: RESULTS FROM AN EARLY JUVENILE IDIOPATHIC ARTHRITIS (JIA) COHORT STUDY

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Background: Timely access to specialized and multidisciplinary care is a core principle in the management of JIA patients and crucial to achieve the best possible outcome for children and adolescents with JIA.
Objectives: To assess satisfaction with access to specialized care and used health care services of families with children with JIA and to identify factors associated with unmet needs.
Methods: Parents of JIA patients enrolled in the early JIA cohort study ICON completed the Child Healthcare Questionnaire on Satisfaction, Utilisation and Needs (CHC-SUN)[1] and the Family Burden Questionnaire (FaBel) 3 months after enrolment. The socioeconomic status, disease activity, patients´ functional ability and quality of life were also assessed. Factors associated with unmet needs were identified by logistic regression analysis.
Results: Data were available from 835 families with children diagnosed with JIA 3 months (median, IQR 1-6) after symptom onset and cared for by paediatric rheumatologists (68% females). At assessment (4.6 months after diagnosis, median), 67% of patients received non-steroidal anti-inflammatory drugs, 50% received conventional synthetic DMARDs and 8% biologic DMARDs. In addition, the following health care services were utilized: 84% physiotherapy, 23% occupational therapy, 21% supply with physical aids, 17% telephone counselling, 15% health education, 13% social worker services, and 11% psychological counselling. Unmet needs were most frequently reported for health education (19%), rehabilitation services (11%), psychological counselling (11%), self-help groups (10%), and lowest for physiotherapy (2%). Unmet needs varied depending on the type of service and JIA category (Table). They were more frequently observed in families with higher burden as indicated by FaBel, but were not associated with migration background and socioeconomic status. Most parents were generally satisfied with their child's health care (satisfied 30%, very satisfied 42%, extremely satisfied 23%). Satisfaction was highest with the behaviour of doctors and lowest with school-related services (e.g. 36% not or partly satisfied with teachers´ knowledge about the child´s illness) and diagnosis/information (e.g. 29% not or partly satisfied with the time required for the diagnosis).

Table: Unmet needs reported by parents of children with various JIA categories

	OA	RF- PA	RF+ PA	ERA	PsA	SoJA	Other JIA	P-value
N	389	228	13	87	32	29	57	
Age at assessment, years*	5.1 (6.6)	7.2 (8.6)	12.7 (3.7)	12.8 (4.1)	10.8 (7.0)	6.9 (8.4)	10.9 (10.2)	<0.001
cJADAS-10*	7.0 (6.0)	13.5 (10.0)	11.0 (14.0)	7.5 (9.0)	10.5 (13.0)	10.5 (14)	9.8 (8)	<0.001
CHAQ*	0.0 (0.0)	0.3 (1.0)	0.4 (1.0)	0.1 (0.0)	0.13 (1.0)	0.13 (1.0)	0.13 (3.0)	<0.001
Most frequently reported unmet needs (in %)								
Health education	16.2	21.1	46.2	16.7	13.8	25.9	20.0	0.11
Psychological counselling	7.5	12.9	15.4	13.0	10.3	12.0	16.0	0.31
Rehabilitation services	10.5	11.2	33.3	7.6	3.4	15.4	14.3	0.13
Self-help groups	9.3	11.5	7.7	7.6	10.3	14.8	14.0	0.84
Telephone counselling	7.8	7.5	7.7	6.4	13.3	11.5	8.0	0.92
Occupational therapy	7.8	9.1	7.7	6.3	6.7	7.4	6.1	0.99

*median (IQR)

Conclusion: There are, although infrequently, unmet needs and dissatisfaction with health services among families with children who have JIA and receive specialized care. Whether these deficits are relevant for long-term JIA outcomes will be further investigated in the ICON study.

REFERENCE:

[1] Schmidt S, Thyen U, Chaplin J, Mueller-Godeffroy E; European DISABKIDS Group. Cross-cultural development of a child health care questionnaire on satisfaction, utilization, and needs. Ambul Pediatr. 2007;7:374-82.

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Myositis and SSc: Clinical highlights 2019

OP0062 IDENTIFICATION OF SIX DERMATOMYOSITIS SUBGROUPS USING PRINCIPAL COMPONENT ANALYSIS-BASED CLUSTER ANALYSIS

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Background: Dermatomyositis (DM) is a heterogeneous disease with a wide range of clinical manifestations. Bohan and Peter suggested four subtypes of DM: idiopathic DM, juvenile DM, DM associated with cancer, and DM associated with other connective tissue diseases. Different DM subtypes have distinct clinical manifestations, responses to therapy and prognoses.
Objectives: The aim of the present study was to identify the clinical subtypes of DM by applying cluster analysis.
Methods: We retrospectively reviewed the medical records of 720 DM patients and selected 21 variables for analysis, including clinical characteristics, laboratory findings, and comorbidities. Principal component analysis (PCA) was first conducted to transform the 21 variables into independent principal components. Patient classification was then performed using cluster analysis based on the PCA-transformed data. The relationships among the clinical variables were also assessed.
Results: We transformed the 21 clinical variables into 9 independent principal components by PCA and identified 6 distinct subgroups. Cluster A was composed of two sub-clusters of patients with classical or moderate DM. Cluster-B patients were older and had malignancies. Cluster C was characterized by interstitial lung disease (ILD), skin ulcer, and minimal muscle involvement. Cluster D included patients with prominent lung, muscle, and skin involvement. Cluster E contained DM patients with other connective tissue diseases. Cluster F included all patients with myocarditis and prominent myositis and ILD. We found significant differences in treatment across the six clusters, with clusters C, D, and E being more likely to receive aggressive immunosuppressive therapy.
Conclusion: We applied cluster analysis to a large group of DM patients and identified six clinical subgroups, underscoring the need for better phenotypic characterization to help develop individualized treatments and improve prognosis.

REFERENCES:

[1] Bohan, A. and J.B. Peter, Polymyositis and dermatomyositis (first of two parts). N Engl J Med, 1975. 292(7): p. 344-7.
[2] Bohan, A. and J.B. Peter, Polymyositis and dermatomyositis (second of two parts). N Engl J Med, 1975. 292(8): p. 403-7.
[3] Marie, I., Morbidity and mortality in adult polymyositis and dermatomyositis. Curr Rheumatol Rep, 2012. 14(3): p. 275-85.
[4] Callen, J.P., Dermatomyositis. The Lancet, 2000. 355(9197): p. 53-57.

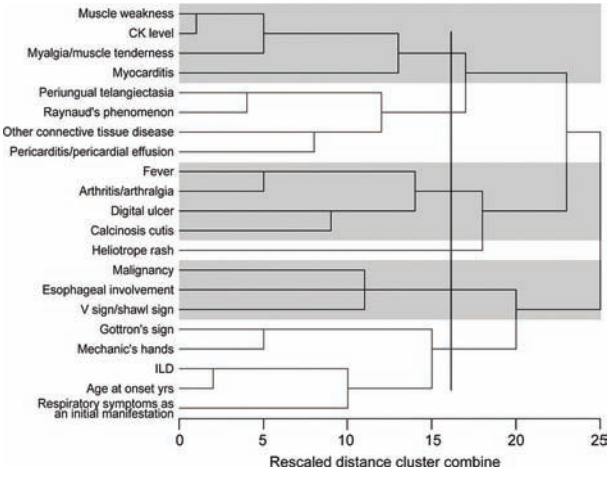


Fig. 1

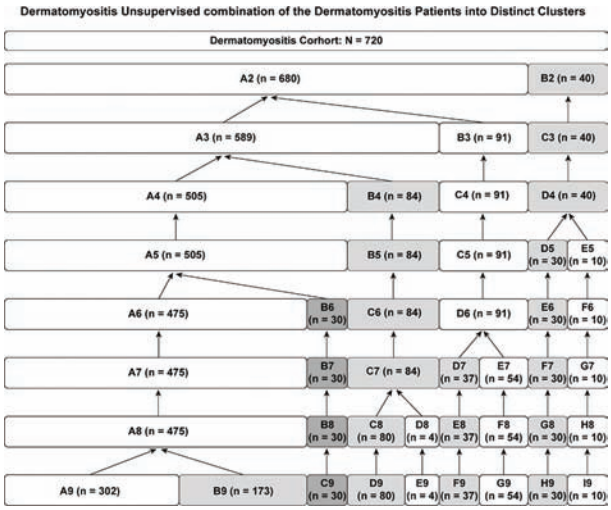


Fig. 2

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OP0063 SAFETY OF MYCOPHENOLATE MOFETIL TREATMENT IN SYSTEMIC SCLEROSIS IN REAL LIFE: REPORT FROM A SINGLE CENTER LARGE COHORT OBSERVATIONAL STUDY

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Background: Mycophenolate mofetil (MMF) has been increasingly used in the treatment of early diffuse cutaneous Systemic Sclerosis (dcSSc) and SSc-associated interstitial lung disease (SSc-ILD), and a recent Randomized Controlled Trial confirmed its efficacy and safety in SSc-ILD. However, the safety of this drug in the long term use has not been assessed in a real life setting.
Objectives: We aimed to analyze the period prevalence and the type of adverse events (AEs) associated to MMF treatment in a single center large cohort.
Methods: Charts of all SSc patients meeting the 2013 ACR/EULAR classification criteria consecutively visited at our outpatient clinic from January 1st 2017 to December 31st 2017 were retrospectively analyzed. Demographics, clinical, serological, functional, imaging data, treatments, and AEs were recorded. Patients were subgrouped according to the immunosuppressant (IS) taken during the observation period (e.g. MMF, azathiprine- AZA, or cyclophosphamide- CYC, no IS). The period prevalence of AEs was calculated and correlations of between AEs and patient features were investigated by univariate and multivariate analyses.
Results: Two-hundred and thirty-seven patients were included (92.4% were females, aged 56.4±11.3 years, with a median disease duration of 17 years, range 1-60). Among them, 85 (35.9%) were taking MMF, 34 (14.3%) AZA or CYC, 118 (49.8%) had no current IS treatment. Prevalence of the dcSSc subset was higher in the MMF group (34.1% versus 17.6% in the AZA/CYC group and 5.9% in the no IS group; $p < 0.05$), while prevalence of ILD was similar in the MMF and in the AZA/CYC group and higher than the no IS group (89.4% and 82.3% versus 41.5%; $p<0.05$ for both), as well as the prevalence of the anti-topoisomerase I antibody positivity (60.7% and 52.9% versus 26.3%; $p<0.05$). Both patients treated with MMF and AZA/CYC had more frequently concomitant low-dose glucocorticoid (GC) therapy than patients without IS (76.5% for both groups versus 39%; $p<0.05$). In regard of total AEs, their prevalence was higher in the MMF group (71.7% versus 67% in the AZA/CYC group and 49% in the no IS group; $p<0.05$ MMF vs no IS). In particular, patients treated with MMF had a higher prevalence of total infectious AEs (55.7% versus 30.4% in the AZA/CYC group and 27.6% in the no IS group; $p<0.05$), predominantly airway infections (41.2% of all infectious AEs). Given so, we investigated the correlations of the infectious AEs in the MMF group with ILD, smoking history, and concurrent GC. However, we didn't find any significant association with these variables. When we looked for correlations of infectious AEs in the MMF group with other disease features, we found that they were correlated with the duration of the disease (median= 4 years; $r=0.25$; $p=0.02$) and with the presence of digital ulcers and/or pitting scars ($r=0.22$; $p=0.03$). No AE required hospitalization and resolved after treatment suspension.

Conclusion: The period prevalence of AEs recorded during MMF treatment appeared as high as 71.7% in our real life setting. Even though we did not record any serious AE, our analysis suggests a close monitoring of this therapy in SSc.
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OP0064 EVIDENCE-BASED CONSENSUS RECOMMENDATIONS FOR THE IDENTIFICATION AND MANAGEMENT OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS

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Background: Interstitial lung disease in systemic sclerosis (SSc-ILD) occurs frequently and carries a high burden of morbidity and mortality. To date, there are no existing guidelines for screening, diagnosis and management of SSc-ILD that would aid early recognition and treatment and improve the care of these patients.
Objectives: To develop expert consensus recommendations for the identification and management of SSc-ILD.
Methods: Based on the results of a comprehensive systematic literature analysis conducted in line with NICE/CRD and IQWiG guidelines and PRISMA methodology, evidence-based statements on SSc-ILD risk, screening, diagnosis, treatment and follow-up were developed. A modified Delphi process was then used to establish consensus statements for the identification and management of SSc-ILD. Briefly, an expert panel of 27 European-based pulmonologists, rheumatologists and internists with experience in treating SSc-ILD was established. Between July and November 2018, the panel took part in 3 rounds of online surveys, a face-to-face discussion and a WebEx meeting to establish consensus-based recommendations for the management of SSc-ILD. Statements were categorised by topic: risk factors (including biomarkers); screening; diagnosis; assessment of severity; treatment initiation; treatment options; disease progression; treatment escalation; other management options. Panellists indicated their level of agreement with proposed statements on a scale of 1 (strong disagreement) to 7 (strong agreement), and consensus was considered achieved when $\geq$80% either disagreed (score of 1–3) or agreed (score of 5–7) with a statement. Based on panel feedback, statements that did not reach consensus were modified and re-voted in later rounds.
Results: At the close of the Delphi process, the panel agreed on the following:

1. Risk factors: The presence of anti–topoisomerase I antibodies, male gender and diffuse cutaneous SSc all increase risk for ILD
2. Screening: All SSc patients should undergo screening for ILD, using HRCT and lung function testing. Frequency of screening using HRCT should be guided by risk of developing ILD, in combination with clinical symptoms and lung function
3. Diagnosis and assessment of severity: Use of HRCT to diagnose SSc–ILD and assess severity, with supporting findings from lung function testing and clinical assessment, is also recommended
4. Treatment initiation and options: All patients with severe or progressive SSc–ILD should be considered for pharmacotherapy, with mycophenolate mofetil and cyclophosphamide recommended as treatments. Patients not receiving treatment should be followed closely for signs of disease progression
5. Disease progression: Indicators of progression include sustained decline in lung function, worsening of clinical symptoms, and change in extent and/or pattern of fibrosis on HRCT
6. Treatment escalation: Patients with inadequate treatment responses should be considered for treatment escalation. Suitability for lung transplant should be evaluated early, especially for patients diagnosed with advanced disease. Autologous haematopoietic stem cell transplant may be considered in carefully selected patients

Conclusion: These evidence-based expert consensus recommendations, developed using a modified Delphi process, provide important guidance for the identification and management of SSc-ILD.
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OP0065 THE VERY EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS (VEDOSS) PROJECT: PREDICTORS TO DEVELOP DEFINITE DISEASE FROM AN INTERNATIONAL MULTICENTRE STUDY

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Background: Early identification of patients is of key importance for the management and treatment of inflammatory rheumatic diseases.
Objectives: The aim of the VEDOSS project (1) is to determine through an at-risk population the predictive factors for the progression toward a definite systemic sclerosis (SSc).
Methods: VEDOSS investigators prospectively recruited patients with Raynaud phenomenon (RP), with or without anti-nuclear antibodies (ANA)for this longitudinal, observational study. Fulfilling the 2013 classification criteria at baseline was an exclusion criterion. Patients with primary Raynaud syndrome were recruited as controls. Patients had an annual assessment according to EUSTAR standards to determine organ involvement and severity. The endpoint was defined as fulfilment of the 2013 classification criteria. The time to fulfilling 2013 classification criteria was evaluated with Kaplan-Meier analysis, and predictors of evolution were determined by univariate and multivariate Cox regression.

Figure 1: A matrix was built to show the PPV of various variables alone or in combination to predict subsequent progression of VEDOSS patients toward definite SSc after 3 years

	alone	Disease specic atb	scleroderma patten on NVC	puffy fingers
	PPV%	PPV%	PPV%	PPV%
Disease specific atb	70.2		82.2	94.1
scleroderma patten on NVC	75.0	82.2		77.8
puffy fingers	78.9	94.1	77.8	

Results: 735 patients with RP were recruited into the study. The sample is distributed as follows: i) *237* patients (143 with follow up) RP/ANA negative (ANA^-/pRP) as the control group, ii) *498 patients* (401 with follow up) RP/ANA positive (ANA^+/pRP)): 87 had puffy fingers (PF), 199 had anti-centromere antibodies (atb) positive, 45 had anti-topoisomerase I atb positive and 182 had nailfold videocapillaroscopy (NVC) abnormalities at baseline. Out of 401 ANA^+/pRP patients, 7.4% within 1 year, 29.3% within3 and 44.1% within 5 years satisfied the 2013 classification criteria. Out of the 143 ANA^-/pRP patients, none (0%) within 1 year, 4.6% within 3 years, and 4,6% within 5 years satisfied SSc criteria. After adjustment for age, the following baseline parameters were identified as independent predictors for progression into definite SSc by multivariate analysis: puffy fingers (OR=3.4 [2.0;5.6]), anti-centromere atb (OR=2.6 [1.6;4.1]) and anti-topoisomerase 1 atb (OR=3.1 [1.6;5.8]), and NVC abnormalities (OR=1.9 [1.3;2.9]) The presence of PF had a positive predictive value (PPV) of 79% and combination of PF + specific auto-antibodies showed 94% PPV to satisfy ACR/EULAR 2013 criteria within 5 years (figure 1).
Conclusion: the data show that patients with very early SSc develop definite, classification criteria fulfilling SSc within 5 years of follow up. The VEDOSS study

identified PF and SSc auto-antibodies at first visit as independent parameters predicting the development of definite SSc. These data are of key importance for the risk stratification of patients with very early SSc in clinical practice and clinical studies.

REFERENCE:

[1] Avouac J, et al. Ann Rheum Dis 2011;70:476

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OP0066

EFFECTIVENESS OF SPECIALIZED HAND/FACE PHYSICAL-OCCUPATIONAL THERAPY IN PATIENTS WITH SYSTEMIC SCLEROSIS – PRELIMINARY RESULTS OF A ONE-YEAR CONTROLLED STUDY

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Background: Systemic sclerosis (SSc) is characterized by stiffness and contraction of tissues, which leads to a limitation in the execution of day-to-day activities. The aim of our study was to investigate the impact of specialized physical-occupational therapy (POT) focused on the hands/face and QoL of SSc patients.

Objectives: Fifty five patients fulfilled the EULAR/ACR criteria for SSc and had skin involvement leading to hand/face function impairment. 25 patients were recruited into the intervention group (IG) and 30 patients into the control group (CG). Both groups received an educational material for home exercise, but only the IG underwent a 6-month intervention with a subsequent 6-month follow-up period.

Methods: Patients were assessed by a physician and a physiotherapist blinded to intervention at months 0, 3, 6, and 12. Patients also filled out patient reported outcomes questionnaires and provided blood for routine laboratory analysis and bio-banking. Data analysis was done between groups and within the group.

Results: Compared to the observed statistically significant deterioration in the CG, we found a statistically significant improvement in the IG in objectively assessed function and strength of hand, distance between incisors and functional ability (SHAQ) (Table). Only numerical improvements in the IG during the intervention compared to numerical deterioration in CG that did not reach statistical significance were observed in subjectively assessed hand function and mouth handicap, functional ability (HAQ) and in some domains of QoL (SF-36) and fatigue (FIS – cognitive function). During the follow-up period, there was a significant deterioration or stagnation of the achieved positive results in the IG.

Conclusion: Our program led to a significant improvement in the observed parameters that was clinically significant in a substantial proportion of patients, and prevention of the expected worsening of hand/face handicap and QoL.

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OP0067

UTILITY OF RISK STRATIFICATION IN PREDICTING OUTCOMES OF INITIAL MONOTHERAPY VERSUS COMBINATION THERAPY IN PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH CONNECTIVE TISSUE DISEASE: A POST-HOC ANALYSIS OF THE AMBITION STUDY

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Background: The AMBITION study (NCT01178073, sponsored by GSK and Gilead) demonstrated a reduced risk of clinical failure event in patients receiving initial combination therapy of ambrisentan and tadalafil (COMB) compared with initial monotherapy of either agent (MONO) in treatment-naive patients with pulmonary arterial hypertension (PAH)[1)]. A similar treatment outcome was observed in connective tissue disease (CTD)-PAH or systemic sclerosis (SSc)-PAH subgroups in both the primary analysis set and modified intention to treat (mITT) population[2,3)]. The 2015 ESC/ERS guidelines[4)] and 2018 WSPH consensus recommended the use of risk assessment (classified as low, intermediate, and high risk) based on the variables to predict prognosis, but the clinical utility of risk stratification in patients with CTD- or SSc-PAH has not been established.

Parameter (unit)	Intervention group Mean ± SEM	Control group Mean ± SEM	Intra-group analysis (Friedman+Dunn) Interevention gr.	Intra-group analysis (Friedman+Dunn) Control group	Inter-group analysis (2WA)
dFTP, dominant hand (cm)	m0: 5.7 ± 0.5 m3: 6.2 ± 0.5 m6: 6.8 ± 0.6 m12: 6.0 ± 0.6	m0: 6.8 ± 0.5 m3: 6.2 ± 0.4 m6: 5.9 ± 0.4 m12: 5.6 ± 0.4	m0-3: p<0.01 m3-6: p<0.05 m0-6: p<0.0001 m6-12: p<0.0001	m0-3: NS m3-6: NS m0-6: p<0.0001 m6-12:NS	p<0.0001
Hand grip strength, dominant hand (kg)	m0: 17.2 ± 1.8 m3: 19.2 ± 1.9 m6: 19.7 ± 1.9 m12: 17.5 ± 2.0	m0: 16.5 ± 1.2 m3: 14.9 ± 1.3 m6: 13.8 ± 1.2 m12: 14.2 ± 1.3	m0-3: p<0.05 m3-6: NS m0-6: p<0.001 m6-12: p<0.05	m0-3: NS m3-6: NS m0-6: p<0.01 m6-12: NS	p<0.0001
HAMIS, dominant hand	m0: 9.8 ± 1.3 m3: 7.1 ± 1.3 m6: 4.1 ± 0.9 m12: 7.2 ± 1.2	m0: 3.9 ± 1.1 m3: 6.3 ± 1.2 m6: 8.9 ± 1.1 m12: 9.8 ± 1.2	m0-3: p<0.01 m3-6: p<0.001 m0-6: p<0.0001 m6-12: p<0.001	m0-3: NS m3-6: p<0.001 m0-6: p<0.0001 m6-12: NS	p<0.0001
Inter-incisor distance (cm)	m0: 2.9 ± 0.2 m3: 3.2 ± 0.2 m6: 3.5 ± 0.2 m12: 3.2 ± 0.2	m0: 3.3 ± 0.1 m3: 3.1 ± 0.1 m6: 3.0 ± 0.1 m12: 3.0 ± 0.1	m0-3: p<0.01 m3-6: NS m0-6: p<0.0001 m6-12: p<0.01	m0-3: p<0.01 m3-6: NS m0-6: p<0.001 m6-12: NS	p<0.0001
SHAQ (mm)	m0: 28.8 ± 3.9 m3: 21.5 ± 3.4 m6: 22.0 ± 3.5 m12: 23.4 ± 3.7	m0: 21.5 ± 2.1 m3: 24.6 ± 2.6 m6: 24.9 ± 2.9 m12: 27.5 ± 3.3	m0-3: NS m3-6: NS m0-6: p<0.05 m6-12: NS	m0-3: NS m3-6: NS m0-6: NS m6-12: NS	p=0.0015

Objectives: To evaluate utility of risk stratification strategy in predicting outcomes in CTD-PAH patients by post-hoc analysis of prospectively collected AMBITION data.
Methods: This study examined 216 patients with CTD (COMB; n=117: MONO n=99) enrolled in the AMBITION study mITT population. The most common underlying CTD etiology was SSc (n=137). Abbreviated average risk score[5)] was determined at baseline and at 16 weeks based on 6-minute walking distance, NT-proBNP, and WHO-FC. Time to clinical failure (TtCF) was compared between groups stratified by the risk stratification and/or treatment assignment using the log-rank test.
Results: At baseline, CTD patients were divided into low (n=27, 12.5%), intermediate (n=179, 82.9%), and high risk (n=10, 4.6%) and at Week 16, subjects were classified as low (n=55, 27.9%), intermediate (n=135, 68.5%), and high risk (n=7, 3.6%). Risk of clinical failure was lowest for subjects in the baseline low risk group and highest in the baseline high risk group. When TtCF was compared between COMB and MONO arms of CTD-PAH patients in individual risk groups at baseline, risk of clinical failure event was lower in COMB than in MONO in the low and the intermediate risk groups (P=0.05, hazard ratio [HR] NA due to no event in COMB, and P= 0.02, HR 0.519, 95%CI 0.297-0.905, respectively), however, no difference in the high risk group was observed. The same analysis was conducted using risk stratification at week 16, resulting in a 93% risk reduction in TtCF after Week 16 in COMB, compared with MONO in the low risk group (P<0.001, HR 0.069, 95%CI 0.009-0.548), but no difference between COMB and MONO in the intermediate risk group (P=0.3). Risk of clinical failure event was comparable between patients with low and intermediate risk after 16 weeks of treatment with MONO.
Conclusion: A simplified risk stratification at baseline and week 16 may be useful in predicting PAH related outcomes in patients with CTD-PAH. Among those achieving a low risk status at week 16, which could be considered a treatment goal, COMBO was associated with an improved outcome, when compared to MONO.

REFERENCES:

[1] Galie N, et al. N Engl J Med 2015; 373:834-44.
[2] Kuwana M, et al. J Scleroderma Relat Disord 2018 ;3: suppl.
[3] Coghlan JG, et al. Ann Rheum Dis. 2017; 76:1219-27.
[4] Galie N, et al. Eur Heart J. 2016; 37:67-119.
[5] Kylhammar D, et al. Eur Heart J. 2017 (e-pub).

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OP0068

ABATACEPT IN EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS— RESULTS OF A PHASE 2 INVESTIGATOR-INITIATED, MULTICENTER, DOUBLE-BLIND RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Background: Abatacept (ABA) is a recombinant fusion protein including extracellular domain of human CTLA4 and hinge– CH2–CH3 of the Fc domain of human IgG.

Objectives: This phase 2 trial assessed the safety and efficacy of ABA 125 mg subcutaneous (SC) versus placebo SC given every week on skin fibrosis using the modified Rodnan skin score (mRSS) in diffuse cutaneous SSc (dcSSc; clinicaltrials.gov NCT02161406).
Methods: A 12-month, investigator-initiated, multicenter double-blind, randomized placebo-controlled trial was conducted between September 2014 and February 2018 at 27 US, Canadian and UK sites. Eligible subjects were randomized in a 1:1 ratio to either ABA or matching placebo, stratified by duration of dcSSc (≤18 vs >18 to ≤36 months). Key inclusion criteria included dcSSc with disease duration of ≤ 36 months (defined as first non–Raynaud phenomenon) and mRSS ≥ 10 and ≤ 35 units for disease duration of ≤ 18 months and mRSS ≥ 15 and ≤ 45 units with evidence of active disease for disease duration of >18-36 months. Escape therapy was allowed at 6 months for worsening SSc. Primary outcomes include safety and change in mRSS over 12 months (ΔmRSS). Secondary endpoints include ΔFVC%, ΔHAQ-DI, Δpatient and Δphysician global assessment, and ACR CRISS[1] (composite measure in dcSSc). The primary endpoint of ΔmRSS was assessed using a linear mixed model (see Table) with primary end point data censored after initiation of escape therapy.
Results: 88 subjects were randomized (44/group) and formed the mITT group; 34 (77%) and 35 (80%) completed the 12-month double-blind treatment period in ABA and placebo groups, respectively. At baseline, the mean age was 49 years, 75% were female, mean disease duration was 1.59 years, 60% had disease duration ≤ 18 months, mRSS was 22.4, mean FVC% was 84.3%, and mean HAQ-DI was 1.0. Compliance with both drugs was >98%. ABA was well tolerated with comparable adverse events (AEs), serious AEs, and AEs of special interest (e.g., infections and malignancies) between treatments. There were 3 deaths during the treatment— 2 in ABA (both scleroderma renal crisis-days 11 and 46) and 1 in placebo (sudden cardiac arrest- day 310). The primary endpoint showed an adjusted mean improvement of mRSS of -6.24 in ABA vs. -4.49 in placebo, p= 0.28 (Table). The secondary outcome measures were statistically significant and clinically meaningful (HAQ-DI and physician global assessment) or showed numerical results favoring ABA (Table). A larger proportion of placebo subjects required escape immunosuppressive therapy vs. ABA (36% vs. 16%, p=0.03).

Outcome at Month 12	Abatacept N=44	Placebo N=44	Difference (ABA - Placebo)	P-value
ΔmRSS, 0-51, mean	-6.24	-4.49	-1.75	0.28
ΔPatient Global Assessment, 0-10, mean	-0.31	-0.09	-0.22	0.73
ΔPhysician Global Assessment, 0-10, mean	-1.30	-0.35	-0.95	0.03
ΔFVC% predicted, mean	-1.34	-4.13	2.79	0.11
ΔHAQ-DI, mean	-0.17	0.11	-0.28	0.005
ACR CRISS index, median (IQR)	0.68 (1.00)	0.01 (0.86)		0.03

Estimates are from a linear mixed model with treatment group, month (3, 6, and 12), treatment x month interaction, duration of dcSSc (≤18 vs >18 to ≤36 months), and baseline outcome measure as fixed effects and participant as a random effect (except for ACR CRISS). For ACR CRISS, treatment differences were assessed by the non-parametric Van Elteren test. Multiple imputation was used for ACR CRISS analysis.
Conclusion: In patients with early dcSSc, ABA was well tolerated, but ΔmRSS was not statistically significant. Secondary outcome measures showed evidence in favor of ABA, including greater requirement of escape therapy in the placebo group. mRSS showed large variability, despite recruiting an early dcSSc population.

REFERENCES:

[1] Khanna D, et al. Arthritis Rheumatol 2016, 68:299-311

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OP0069

PERFORMANCE OF AMERICAN COLLEGE OF RHEUMATOLOGY (ACR) COMBINED RESPONSE INDEX IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (CRISS) SCORE IN PHASE 2 TRIAL OF LENABASUM IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSS)

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Background: Change in modified Rodnan skin score (mRSS) has been used as primary efficacy outcome in at least 13 failed controlled studies in dcSSc. In 2016, the CRISS score was provisionally accepted by ACR as a primary efficacy outcome for clinical trials in dcSSc. Its performance as a primary efficacy outcome has not been tested in a clinical trial.
Objectives: To evaluate performance of ACR CRISS outcome measure in the lenabasum Phase 2 study in dcSSc, the first study in which it was used prospectively as the primary efficacy outcome.
Methods: The Phase 2 study JBT101-SSc-001 (NCT02465437) included a 16-week, double-blinded, randomized, placebo-controlled Part A followed by an open-label extension (OLE). ACR CRISS score is calculated from a weighted exponential formula that includes change in mRSS, Patient Global Assessment (PtGA), HAQ-DI, Physician Global Assessment (MDGA), and FVC% predicted. Spearman correlations were determined for: pairs of core items at Baseline; change in pairs of core items; and change in a given core item and calculated ACR CRISS score. Median ACR CRISS scores were determined in subjects with different levels of improvement in patient-reported outcomes (PROs).
Results: Correlations among pairs of CRISS core items at baseline and change in core items were all < 0.80 at 4 and 12 months. The strongest correlations ($r \geq 0.60$, $P \leq 0.0001$) for core items at baseline were between PtGA and HAQ-DI, HAQ-DI and MDGA, and PTGA and MDGA. The strongest correlations ($r \geq 0.50$, $P \leq 0.001$) for changes in pairs of core items were between PtGA and HAQ-DI, HAQ-DI and MDGA, and MDGA and mRSS, all others were ≤ 0.30 (**Table 1**). Correlations between change in each core item and ACR CRISS score were all statistically significant, $p \leq 0.05$ at both 4 and 12 months and very strong for change in mRSS and ACR CRISS (**Table 1**).
Median ACR CRISS scores increased with increasing levels of improvement in PROs that were core items (HAQ-DI and PtGA) and even PROs (PROMIS-29 domains) that were not core items. Median ACR CRISS score associated with improvement in HAQ-DI at least -0.250 points was 0.82 and associated with at least 1-point improvement in PtGA was 0.53 at 12 months.

Table 1. Correlation of ACR CRISS with Change in Core Item, r

Time	Correlation of ACR CRISS with Change in Core Item, r				
	mRSS	PtGA	HAQ-DI	MDGA	FVC% predicted
4 months	-0.91	-0.37	-0.45	-0.66	0.38
12 months	-0.76	-0.38	-0.39	-0.38	0.54

Conclusion: In the context of the lenabasum Phase 2 clinical trial, ACR CRISS core items at baseline and change in ACR core items were not redundant ($r < 0.80$). Change in each core item correlated with ACR CRISS score, indicating each contributed to the score at both 4 and 12 months. The 12-month median ACR CRISS score was higher in subjects with greater levels of improvement in PROs, even PRO that were not core items, showing that ACR CRISS score reflects long-term clinical benefit in how the patent feels and functions. These data provide preliminary evaluation of the ACR CRISS score as a clinical trial endpoint in dcSSc.
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WEDNESDAY, 12 JUNE 2019

Bringing digital health care solutions to patients

OP0070-PARE

GEOCACHING AS AN ENCOURAGEMENT FOR BEING ACTIVE

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Background: The Finnish Rheumatism Association and Novartis started a project in 2017 to energise our local associations, members and their families by adapting an active lifestyle. Geocaching is a fun, family-friendly way to exercise both mind and body. It is for everybody to enjoy.
Geocaching is an outdoor recreational activity, in which participants use a Global Positioning System (GPS) receiver or mobile device and other navigational techniques to hide and seek containers, called “geocaches” or “caches”, at specific locations marked by coordinates all over the world.
There are about three million geocaches hidden around the world. A typical cache is a small waterproof container containing a logbook and sometimes a pen or pencil. The geocacher signs the log with their established code name and dates it to prove that they found the cache. After signing the log, the cache must be placed back exactly where it was found.
Objectives: The main goal of the project was to hide 70 new caches all over Finland to create an enjoyable experience for other geocachers. Those caches were named “Reumageo” at the beginning of the cachename. For all the associations that were involved in this project received money allocated to sport and physical activity out of the 15,000 euro project budget. The project ended on 12 october 2018, and all logged caches were included in the game.
Methods: We started our project by training association representatives. The training included the basics of geocaching: how to find caches, how to hide your cache and create your cache page, different geocachetypes and everything you should know geocaching. The trained representatives told about geocaching in their own associations, and they were responsible for creating at least 2-3 new caches and handling the new caches. The main idea was that when you have found about 15-20 caches you would start to hide your own caches. Together with local associations our aim was to create 70 caches all over Finland to celebrate the 70-year-old Finnish Rheumatism Association.
Outdoor geocaching adventure starts indoors with preparation and online research. You need a Global Positioning System (GPS) receiver or a mobile device, your own account at the site geocaching.com. The site offers a completely free access to the caching data and all the site features. The site offers also a “premium” member status to access certain features. You can also download the Geocaching intro app onto your smartphone, like Geocaching.

Results: There were 43 members from 30 local associations in Oulu, Mikkeli, Helsinki and Turku in these geocaching trainings. All these members are suffering from rheumatic and other musculoskeletal diseases (RMDs) and work as volunteers for sport and physical activity, and now for geocaching. By 12 october 2018 there were 48 reumageocaches made by 13 local associations. The caches were logged 6593 times. So local associations earned 173-4303 euros each to be used for promoting sport and physical activity programmes and active lifestyles.
Conclusion: Promoting an active lifestyle is part of the health and wellbeing policy in The Finnish Rheumatism Association. The goal is to encourage people of all ages to stay healthy by getting enough exercise.
The geocaching project shows that it is easy to some of local associations to start projects like this. Some associations thought that it is too difficult to learn new methods especially when their members are elderly people. Geocaching is increasingly popular, inclusive, a fun and healthy pastime for individuals of all ages. It is also great for groups like local associatons, families, friends, and youth groups working as teams. Those local associations that were involved in this project received a great budget for their local sport and physical activity programmes. It is great to see something evolving from the beginning and come into being.
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WEDNESDAY, 12 JUNE 2019

Cartilage, synovium and bone

OP0071 REVEALING THE LINK BETWEEN OSTEOARTHRITIS DEVELOPMENT AND MESENCHYMAL STEM CELL SENESCENCE

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Background: Tissue accumulation of $p16^{INK4A}$-positive senescent cells is associated with age-related disorders such as osteoarthritis (OA). These senescent cells induce a tissue loss of function through a particular secretory phenotype called SASP (senescence-associated secretory phenotype).
Objectives: Links between OA onset and cellular senescence remain poorly detailed. We wanted to determine the localization of articular senescent cells in *in vivo* OA mouse models and study the involvement of mesenchymal stem cells (MSC) senescence in OA pathogenesis.
Methods: Wild-type mice C57BL/6, SAMP8/R1 (senescence accelerated mouse-prone and resistant), transgenic $p16^{INK4A\ +/Luc}$ and $p16^{INK4A\ Luc/Luc}$ were used. Experimental OA was induced by intraarticular injections of collagenase (CIOA). Cartilage, synovial tissue and subchondral bone were analyzed by histology, RT-qPCR and micro-tomography. MSCs come from healthy human donors and primary chondrocytes from OA patients.
Results: (1) CIOA was induced in senescence-driven luciferase transgenic mice. Under CCD camera, a peak in luminescence was detected at day 24 post-injection revealing the presence of senescent cells in the joint. Remarkably, articular senescence is not only a marker of the pathology but contributes to OA onset: mice deficient in $p16^{INK4a}$, a main senescence-driving known cell cycle inhibitor, were partially protected against CIOA. These results were confirmed in C57Bl/6 mice after CIOA by showing an increase in gene expression for senescence, catabolic and inflammatory markers in the synovial tissue preceding cartilage degradation.
(2) MSCs found in synovial, cartilage, fat pad and bone marrow participate in joint homeostasis. Because MSC are proposed to be at the root of OA development, we hypothesize that cellular senescence onset in these progenitor cells would be a possible etiological factor for OA. We have established an *in vitro* $p16^{INK4A}$-induced senescence model on human primary MSC: their intrinsic properties such as self-renewing are altered during senescence onset. Furthermore, in co-culture conditions with chondrocytes from OA patients, senescent MSC lost their extrinsic chondroprotective properties.
(3) To *in vivo* challenge these findings, we rely on the mouse model of accelerated senescence SAMP8, which develop spontaneous OA at the age of 6 months with cartilage degradation, synovial hypertrophy, osteophytosis and subchondral bone remodeling associated to meniscal calcification. Isolated MSC from these mice express senescence but non-inflammatory markers ($p16^{INK4a}$, p21waf1, MMP13, TGF-β1). Remarkably, intra-articular injection of these isolated SAMP8-derived MSC compared to SAMR1-derived control MSC, in young wid-type C57Bl/6 mice, was suffisant by its own, to induce significant articular cartilage degradation (OA score of 12.2 ± 1.5 vs 6.1 ± 3.5 for SAMP8 and SAMR1 MSC respectively. $p < 0.05$).
Conclusion: $p16^{INK4A}$-induced cellular senescence in MSC played a causative role in cartilage loss of function and OA pathogeny. *In vitro*, senescent MSC show altered intrinsic and extrinsic supportive tissue functions. *In vivo*, intra-articular injection of senescent MSC was sufficient to induce cartilage degradation. Specific targeting of such deleterious senescent cells could be an innovating and promising treatment in OA.
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OP0072 INHIBITION OF CLK2 AND DYRK1A BY SM04690 AS A NOVEL MOLECULAR REGULATOR OF WNT SIGNALING, CHONDROGENESIS, AND INFLAMMATION, A POTENTIAL DISEASE-MODIFYING TREATMENT FOR KNEE OSTEOARTHRITIS

Vishal Deshmukh, Alyssa O'green, Carine Bossard, Tim Seo, Lisa Lamangan, Maureen Ibanez, Abdullah Ghias, Carolyn Lai, Long Do, Shawn Cho, Joseph Cahiwat, Kevin Chiu, Melinda Pedraza, Yusuf Yazici. *Samumed, LLC, San Diego, United States of America*

Background: In the synovial joint, Wnt pathway upregulation contributes to osteoarthritis (OA) by increasing osteocyte differentiation, cartilage thinning, and inflammation. SM04690, a novel small molecule, has previously demonstrated potential OA disease-modifying effects through Wnt pathway inhibition *in vitro* and *in vivo*.
Objectives: To elucidate the novel mechanism of action for SM04690 on Wnt pathway inhibition, chondrocyte differentiation, and anti-inflammation.
Methods: Wnt pathway activity was measured using a cell-based TCF/LEF luciferase reporter in SW480 colon cancer cells. A kinome screen (318 kinases) was performed. The effects of SM04690 on protein phosphorylation of serine and arginine rich splicing factors (SRSF proteins), Sirt1, and FoxO1 in hMSCs, chondrocytes, and synovial fibroblasts were measured by Western blot. The effects of SM04690 and siRNA knockdown (KD) on chondrogenic and Wnt pathway gene expression were measured by NanoString gene expression panels and effects on LPS-induced inflammatory cytokines (IL-6, IL-8, TNF-α) in BEAS-2B cells were measured by qPCR and ELISA. *In vivo*, the pharmacodynamic effects of SM04690 were evaluated in monosodium iodoacetate injection-induced and anterior cruciate ligament transection with partial medial meniscectomy rat knee OA models in which a single intra-articular SM04690 (0.1 μg, 0.3 μg, 1.0 μg) or vehicle injection was administered. Cartilage was isolated at Day 10 and 35; phosphorylation and expression of SRSF proteins, Sirt1, FoxO1, STAT3, and NF-κB were measured by Western blot.
Results: SM04690 was a potent (EC_{50}=11nM) inhibitor of Wnt signaling. Cdc-like kinases (CLKs) and dual-specificity tyrosine kinase (DYRK1A) were identified as molecular targets of SM04690. In hMSCs and chondrocytes, compared to DMSO, SM04690 potently inhibited CLK-mediated phosphorylation of SRSF proteins. SM04690 also inhibited DYRK1A-mediated Sirt1 and FoxO1 phosphorylation, thus increasing total and nuclear FoxO1 levels. Compared to siRNA control, DYRK1A/CLK2 dual KD increased expression of chondrogenic genes (*COL2A1, ACAN, COMP, CD44* [all $P<0.05$]). CLK2 and DYRK1A KDs each inhibited Wnt pathway genes (*AXIN2, TCF7, TCF4, LRP5, FZD6, FZD7, PITX2* [all $P<0.05$]) with no effects on β-catenin levels, compared to siRNA control. In synovial fibroblasts, compared to DMSO, SM04690 decreased phosphorylation of NF-kB and STAT3. In BEAS-2B cells, compared to siRNA control, DYRK1A KD inhibited inflammatory cytokine production (IL-6, IL-8, TNF-α [all $P<0.05$]), while DYRK1A/CLK2 dual KD enhanced anti-inflammatory effects of DYRK1A KD. In cartilage from rat OA models, compared to vehicle, SM04690 inhibited phosphorylation of SRSF proteins, Sirt1, FoxO1, and STAT3, as well as expression of NF-κB.

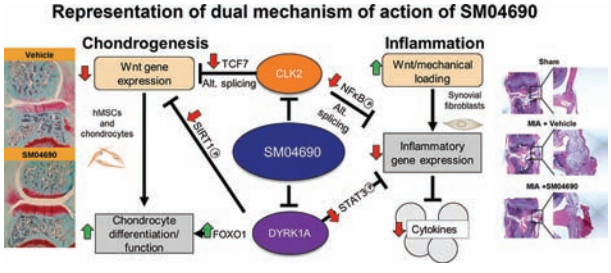


Figure 1. Schematic representation of SM04690's proposed mechanism of action via CLK2 and DYRK1A inhibition in OA

Conclusion: To our knowledge, this is the first report of SM04690 inhibition of nuclear kinases CLK2 and DYRK1A, leading to effects on the Wnt pathway, chondrocytes, and inflammation **(Figure 1)**. This dual mechanism of SM04690 potentially modifies OA through increased chondrocyte differentiation and function and benefits symptoms through anti-inflammatory activity. Human trials are ongoing.
Disclosure of Interests: Vishal Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Alyssa O'Green Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Carine Bossard Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Tim Seo Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Lisa Lamangan Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Maureen Ibanez Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Abdullah Ghias Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Carolyn Lai Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Long Do Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Shawn Cho Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Joseph Cahiwat Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Kevin Chiu Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Melinda Pedraza Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Yusuf Yazici Shareholder of: Samumed, LLC, Consultant for: Celgene Corporation, BMS, Genentech, Sanofi, Employee of: Samumed, LLC
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OP0073 ESTABLISHMENT OF HUMAN INDUCED PLURIPOTENT STEM CELL-LINES (IPSC) FOR IN VITRO MODELLING HAND OSTHEOARTHRITIS

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Background: Research results in the field of hand OA are currently limited due to the unavailability of tissue samples and lack of animal models replicating the features of the disease in humans. Cellular *in vitro* models are important tools to elucidate molecular mechanisms and pathways that are involved in hand OA. Specifically, induced pluripotent stem cells (iPSc) are considered ideal tools for this purpose since they allow the use of unlimited cells with chondrogenic differentiation potential. However, there are not studies published generating iPSc from patients with hand OA.
Objectives: To generate and characterize iPSc-lines from patients with radiographic hand OA and healthy donors, which can be used as cellular models of the disease, for studying the pathogenesis of the disease *in vitro* and for testing new drugs.
Methods: Patients with hand OA (non erosive hand OA with right thumb OA) and a healthy control were selected for the study. Using the explant culture technique, fibroblasts from skin biopsies of these patients were isolated. Transcriptional factors Oct4, Sox2, Klf4 and c-Myc were used for the reprogramming process; which was performed by using a non-integrating method, the Sendai virus. Cell lines obtained were morphologically, phenotypically and functionally characterized. To evaluate weather these iPSc lines could be used as cellular model of hand OA, presence of single nucleotide polymorphisms (SNPs) within the genes ALDH1A2 and SMAD3 were studied by Sanger sequencing, before and after reprogramming. Variants rs3204689 and rs12901499 respectively have been associated with severe OA of the hand (Styrkarsdottir *et al.*, 2014; Shu-Thao Gao *et al.*, 2018). Finally, chondrogenic differentiation capacity of the "healthy" and "ill" iPSc-lines was studied by means of histological techniques.

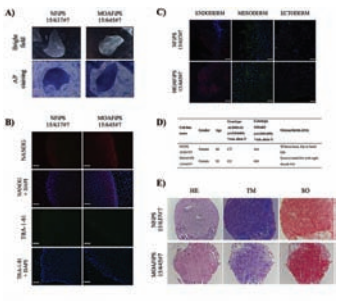


Figure 1. (A) Bright field images and images after alkaline phosphatase staining (AP staining) of iPSc colonies from each cell line. x4 magnification. (B) Immunofluorescence images of pluripotency markers (NANOG and TRA-1-81) of representative clones from each cell line. Escale 100 µm. (C) Immunofluorescence images of endoderm, mesoderm and ectoderm markers in each one of the cell lines. Escale 100 µm. (D) Summarize of the results obtained after single nucleotide polymorphism analysis. (E) Haematoxilin-Eosin (HE), Masson's Tricromic (TM) and Safranin-O (SO) staining after chondrogenic differentiation of the iPSc lines. x10 magnification.

Results: Fibroblasts were isolated from one patient with radiographic hand OA and one healthy donor. Three weeks after reprogramming, embryonic stem cell-like colonies emerged in culture. These cells showed positivity for alkaline phosphatase activity (fig. 1A) and the pluripotency markers Tra1-81 and Nanog (fig. 1B). Molecular analyses showed high relative expression levels of the pluripotency-related genes OCT4, SOX2, NANOG and CRIPTO in the iPSc. These cells were also able to give rise to cells from the three germ layers (fig. 1C). Indeed, during mesodermal differentiation, spontaneously beating cardiomyocytes were seen in culture. Regarding SNPs studies, cells from the patient with hand OA were homozygous for the at-risk allele in both genes studied, both before and after reprogramming (fig. 1D). The "ill" iPSc-line (MOAFiPS 15/645#7) showed worse chondrogenic differentiation than the "healthy" iPSc-line (NFiPS 15/637#7), as shown by the micromasses collagen and proteoglycan content (fig. 1E).
Conclusion: The generation of one iPSc-line form patients with hand OA is reported for the first time. The presence of the at-risk alleles within the ALDH1A2 and SMAD3 genes were maintained after fibroblast reprogramming. The iPSC lines obtained shown differences in their chondrogenic differentiation capacity, showing their usefulness to model hand OA *in vitro*, and to deeper study the role of these genetic variants in the pathogenesis of hand OA.
REFERENCES:
[1] Styrkarsdottir U, et al. (2014). Nat Genet. 46(5):498-502.
[2] Shu-Tao Gao, et al. (2018) Ther Clin Risk Manag. 14: 929–936.

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Disclosure of Interests: Rocío Castro-Viñuelas: None declared, Clara Sanjurjo-Rodríguez: None declared, María Piñeiro-Ramil: None declared, Tamara Hermida Gómez: None declared, Isaac Fuentes-Boquete: None declared, Javier de Toro-Santos: None declared, Francisco J. Blanco Consultant for: AbbVie, Bioiberica, BMS, GSK, Grünenthal, Janssen, Lilly, Pfizer, Regeneron, Roche, Sanofi, TRB Chemedica, and UCB, SILVIA MARIA DÍAZ-PRADO: None declared
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OP0074 TOFACITINIB PROMOTES FUNDAMENTAL PROCESSES OF BONE HEALING

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Background: Inflammatory diseases like rheumatoid arthritis (RA) and anti-inflammatory treatment of RA with glucocorticoids (GC) or NSAIDS negatively influence bone metabolism and fracture healing. Janus kinase (Jak) inhibition with tofacitinib has been demonstrated as a potent anti-inflammatory therapeutic agent in the treatment of RA but its impact on the fundamental processes of bone regeneration such as recruitment of human mesenchymal stromal cells (hMSCs) and chondrogenesis, osteogenesis and osteoclastogenesis is still controversial and in part elusive.
Objectives: Therefore, in this study, we aim to examine the effects of Tofacitinib on processes of bone healing under reduced oxygen availability mimicking the in vivo situation of the fracture gap.
Methods: To this end, we analyzed the influence of Tofacitinib on the (i) invasion of hMSCs towards TNFα using a trans-well assay, (ii) chondrogenic differentiation of hMSCs in a 3D-micro-mass culture under hypoxic conditions, (iii) osteogenic differentiation of hMSCs, (iv) M-CSF/RANKL-mediated differentiation of isolated monocytes towards osteoclasts and (v) hypoxia-mediated target gene expression in non-differentiated, osteogenic and chondrogenic differentiated hMSCs.
Results: We demonstrate that Tofacitinib dose-dependently promotes the recruitment of hMSCs under hypoxia but inhibits recruitment of hMSCs under normoxia. With regard to the chondrogenic differentiation of hMSCs, we observed that Tofacitinib did not inhibit survival and at therapeutic relevant doses of 10-100nM. Moreover, Tofacitinib dose-dependently enhances osteogenic differentiation of hMSCs and reduces osteoclast survival and differentiation under hypoxic conditions. We show that Tofacitinib does not affect chondrogenic HIF target gene expression but increases HIF target gene expression in human osteogenic differentiated MSCs.
Conclusion: We conclude from our data, that Tofacitinib may influence bone healing by promotion MSC recruitment into the hypoxic microenvironment of the fracture gap, does not interfere with the cartilaginous phase of the soft callus phase of fracture healing process. We assume that Tofacitinib may promote bone

formation and reduce bone resorption which could in part explain the positive impact on bone erosions by Tofacitinib. Thus, we hypothesize that it will be unnecessary to stop this medication in case of fracture and suggest that positive effects on osteoporosis are likely.

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OP0075 PAR2 ACCELERATES OSTEOARTHRITIS-LIKE JOINT CHANGES IN A MURINE MODEL OF POST-TRAUMATIC OSTEOARTHRITIS

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Background: Post-traumatic osteoarthritis (PTOA) is associated with articular cartilage damage and represents a major clinical challenge due to the poor regenerative capability of cartilage. We have recently developed a novel and robust dual injury murine model of PTOA, which combines destabilisation of the medial meniscus (DMM) and cartilage scratch[1]. This model results in accelerated OA-like symptoms including enhanced osteophyogenesis. Prior studies in the DMM model have demonstrated that absence of proteinase-activated receptor 2 (PAR2) in mice results in significant protection from early OA-like symptoms[2,3].

Objectives: To investigate if the absence of PAR2 confers protection in a dual injury PTOA murine model.

Methods: PTOA was induced in both male C57BL/6 wild-type (WT) and PAR2$^{-/-}$ mice, via combined destabilisation of the medial meniscus and cartilage scratch (DCS). Twenty-eight days post-surgery, osteophytogenesis and bone changes were monitored using microcomputed tomography. Dynamic weight bearing was assessed as an indirect measurement of pain at day 14.

Results: Evaluation of the presence and number of osteophyte revealed no significant differences between WT and PAR2$^{-/-}$ mice at day 28. However, quantification of osteophytes revealed that PAR2$^{-/-}$ mice had significantly smaller osteophytes (p=0.006) with less mineralised bone (p=0.003). Moreover, analysis of metaphyseal trabecular bone on the operated leg showed a significant decrease in% bone volume/tissue volume (BV/TV) (p=0.025). Assessment of pain-related behaviour, using dynamic weight bearing at day 14, demonstrated that PAR2$^{-/-}$ mice exerted less load on their front paws.

Conclusion: The findings in this study show that PAR2 plays a role in accelerated OA-like symptoms (i.e., osteophyte formation) in a dual injury model of OA, where both destabilisation of the medial meniscus and cartilage damage drive disease pathology. Furthermore, the loss of PAR2 decreases pain behaviour suggesting that PAR2 is involved in pain sensing. Taken together, these results support the future exploration of PAR2 as a therapeutic target for PTOA.

REFERENCES:

[1] McCulloch K, Huesa C, Dunning L, van 't Hof R, Lockhart J, Goodyear CS. Accelerated Osteoarthritic-like Symptoms in a Novel Dual Injury Model Combining Destabilisation of the Medial Meniscus and Cartilage Damage. Journal of Bone and Mineral Research. 2018; 33:155

[2] Huesa C, Ortiz AC, Dunning L, McGavin L, Bennett L, McIntosh K, Crilly A, Kurowska-Stolarska M, Plevin R, van 't Hof RJ, et al. Proteinase-activated receptor 2 modulates OA-related pain, cartilage and bone pathology. Ann Rheum Dis. 2016;75:1989-97.

[3] Ferrell WR, Kelso EB, Lockhart JC, Plevin R, and McInnes IB. Protease-activated receptor 2: a novel pathogenic pathway in a murine model of osteoarthritis. Annals of the Rheumatic Diseases. 2010;69:2051.

Disclosure of Interests: Kendal McCulloch: None declared, Carmen Huesa: None declared, Lynette Dunning: None declared, Rob van't Hof Shareholder of: OsteoRx Ltd, John Lockhart: None declared, Carl Goodyear Grant/research support from: AstraZeneca, BMS, Celgene, Janssen, MedAnnex, Pfizer and UCB, Speakers bureau: Abbvie

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OP0076 JAK-INHIBITORS TOFACITINIB AND BARICITINIB IMPROVE PATHOLOGICAL BONE LOSS IN VIVO

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Background: Targeting cytokines relevant to rheumatoid arthritis (RA) has proven efficient in clinical practice, but there is still demand for therapies that rebuild joint tissues which have been subjected to deterioration. Since many cytokines involved in RA rely on the intracellular janus kinase - signal transducer and activator of transcription (JAK-STAT) signaling pathway, targeting them presents itself as option. For this approach, JAK-inhibitors such as Tofacitinib and Baricitinib, targeting JAK1/JAK3 and JAK1/JAK2 respectively, seem favorable, as they have been approved for the treatment of RA[1]. Moreover, preliminary data indicates an impact of JAK inhibition on local bone formation.

Objectives: To investigate the influence of JAK-inhibition on structural bone damage *in vivo* and its impact on osteoclast/osteoblast-mediated bone homeostasis *in vitro*.

Methods: *In vivo* analysis comprised unchallenged steady-state, the ovariectomy-induced mouse model of postmenopausal osteoporosis (OVX) and the serum-induced arthritis (SIA) mouse model. For steady-state analysis C57BL/6 (WT) mice obtained tofacitinib QD by oral gavage for 6 weeks. For OVX, WT mice received tofacitinib BID by oral gavage for 6 weeks. WT mice of the SIA model were fed tofacitinib or baricitinib BID for 14 days. Experimental readout included clinical parameters, ELISA (RANKL/OPG levels in serum), qPCR (mRNA expression in bone) and μCT. For *in vitro* analysis, murine osteoclasts (OC) were analyzed with TRAP staining (osteoclastogenesis) and von Kossa staining (Resorptive capacity). Murine osteoblasts (OB), derived from mesenchymal stem cells (MSC) and calvariae were assessed with qPCR (differentiation) and Alizarin red staining (mineralization capacity).

Results: In steady-state conditions, JAK-inhibition by tofacitinib enhanced tibial trabecular bone density and decreased RANKL/OPG fraction in blood serum. These findings, and increased trabeculae numbers, were also applicable to spinal bone of tofacitinib-treated OVX mice. In SIA, both baricitinib and tofacitinib improved clinical symptoms and halted trabecular and cortical bone loss. *In vitro* OC-differentiation and function were not affected by JAK-inhibition. However, tofacitinib and baricitinib amplified OCN expression in MSC-derived OBs at day 1 after osteogenic induction, together with reduced Igf1 and elevated Dkk1 levels at day 7. Moreover, as a result of JAK-inhibition RANKL expression was decreased in calvaria-derived OBs. Accordingly, both MSC- and calvaria-derived OBs showed increased mineralization when treated with JAK-inhibitors.

Conclusion: Our results suggest that JAK-inhibition by tofacitinib and baricitinib causes increased mineralization by osteoblasts, resulting in enhanced bone density *in vivo*, in both unchallenged and pathological mouse models.

REFERENCE:

[1] Baker KF, Isaacs JD, ARD, 2018

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Disclosure of Interests: Susanne Adam: None declared, Nils Simon: None declared, Ulrike Steffen (née Harre): None declared, Fabian Andes: None declared, Dorothea Müller: None declared, Stephan Culemann: None declared, Darja Andreev: None declared, Madelaine Hahn: None declared, Carina Scholtysek: None declared, Georg Schett: None declared, Gerhard Krönke Grant/research support from: Lilly, Pfizer, Speakers bureau: Novartis, Silke Frey: None declared, Axel Hueber Grant/research support from: Novartis, Pfizer, Lilly, Consultant for: Lilly, GSK, Novartis, Janssen, Celgene, Abbvie, Roche, Speakers bureau: Lilly, Janssen, Novartis, Celgene, Biogen, Abbvie, BMS

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OP0077 INNOVATIVE TRANSLATIONAL MODELS TO STUDY HUMAN SYNOVIAL PATHOLOGY: TARGET VALIDATION AND PRECLINICAL IMAGING

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Background: Many experiments to study inflammation, hyperplasia, and fibrosis in the synovium have been performed in animal models of RA and OA. However, the predictive value of these models for the screening of potential drugs in RA is variable and for OA, none were sufficiently effective in clinical trials. Translational

arthritis research with human cells is often performed in monolayer culture where the absence of extracellular matrix and other cell types results in alterations of cell functions and loss of phenotype.
Objectives: To improve the predictive value of preclinical arthritis research by developing and optimizing innovative translational models to study human synovial pathology in vitro and in vivo.
Methods: Synovial biopsies from RA patients were obtained during joint replacement surgery and processed for either (1) explant cultures, (2) 3D-synovial micromasses, (3) RA-SCID transplantation studies, and/or (4) a biobank for corresponding mRNA and IHC profiling. For explant culture, 3mm biopsies were cultured for 24hr w/o various inhibitors, and cytokine production was analyzed by Luminex. 3D-micromasses were generated from primary RA FLS and CD14+ PBMCs, stimulated for 3 weeks with 10 ng/ml TNFα or TGFβ and analyzed by histology, IHC and QPCR. For target validation and preclinical imaging, 6mm biopsies were engrafted SC into SCID mice. Radionuclide- and fluorescently-labelled anti-CD64 antibodies were injected IV, and targeting was determined by biodistribution, μSPECT/CT and IVIS imaging analysis.
Results: Our first assay with RA synovium explants demonstrated to be highly suitable to test the therapeutic efficacy of inhibitors for TNFα, TLR4, p38 and the JAK-pathway, resulting in significantly reduced production of proinflammatory mediators after 24hr of culture.
In contrast to the explant cultures, our 3D synovial micromasses could be followed for weeks. In this second translational model, lining formation was observed at day 7 and the micromasses could be stimulated to mimic RA- or OA-like features of synovial hyperplasia or fibrosis respectively. Long-term exposure to the RA-related cytokine TNFα lead to hyperplasia of the lining and an altered macrophage phenotype characterized by reduced CD163 expression. Conversely, the repair-related growth factor TGFβ induced fibrosis-like changes in the micromass lining, a hallmark of OA. This was accompanied by an increased expression of *PLOD2*, *COL1A1* and αSMA.
Our third preclinical model, the RA synovium SCID mouse, was previously validated using adalimumab, secukinumab, and rituximab, and was now used to study CD64 as a potential marker to image synovitis. Gene expression of *FCGRI (CD64)* in synovial explants from RA patients was shown to correlate positively to gene expression of pro-inflammatory factors *IL1B, TNFA, IL8, S100A8, MCP1,* and with damage-associated genes *MMP2* and *MMP13*. Interestingly, dual-labelled ^{111}In-DTPA-IrDye800CW-anti-CD64 antibody showed high uptake in the synovial transplants of the SCID mice, and specifically visualized the subcutaneous synovial grafts by both μSPECT/CT and IVIS imaging.
Conclusion: The development of these translational models allows us to bridge the gap between preclinical and clinical drug development research. Whereas our synovial explant assay is ideal for short-term interventions, and the RA-SCID mouse a great translational model for in vivo preclinical studies, donor variability and access to sufficient tissue may be challenging. In such cases, the 3D synovial micromass model may be an excellent alternative. Especially in combined setting, these 3 translational approaches will improve target validation and preclinical development of novel anti-rheumatic drugs.

REFERENCE:

[1] Abdollahi-Roodsaz, J Clin Invest 2008; Koenders, Arthritis Rheum 2012; Broeren, ALTEX 2019

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OP0078

LINKING LIPID MARKERS TO SYNOVIAL HYPERPLASIA AND VASCULARIZATION IN OSTEOARTHRITIS BY MALDI-MSI

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Background: Synovial inflammation or synovitis causes severe histological changes in the tissue affecting its normal functioning. These morphological changes are one of the most characteristic events in the OA pathology. Additionally, lipid species are recognized as important key factors in the development and regulation of inflammatory processes. Therefore, the lipid signature of the synovial membrane can provide new markers involved in the synovitis process undergoing the OA disease
Objectives: To define the specific lipid profile and distribution in human control and OA synovial membranes.
Methods: Human synovial membrane samples of OA patients (n=13) and controls (n=10) were compared by matrix-assisted laser desorption ionization mass spectrometry imaging (MALDI-MSI). Tissue sections at 10 μm thickness were mounted on conductive slides and coated with norharmane matrix (7mg/ml, 2:1 chlorophorm/methanol) for lipid extraction. MALDI images were acquired using a MALDI TOF-TOF instrument (Rapiflex MALDI Tissuetyper, Bruker, Germany) in reflectron positive and negative ionization mode at a pixel size of 50 μm. Multivariate statistical analysis was used to search for the lipids with the highest differences between OA and control synovial membranes. Then, lipid spatial distribution was investigated with FlexImaging 4.1 software. Identifications were based on tandem mass spectrometry analyses in comparison to LIPID MAPS Structure Database.

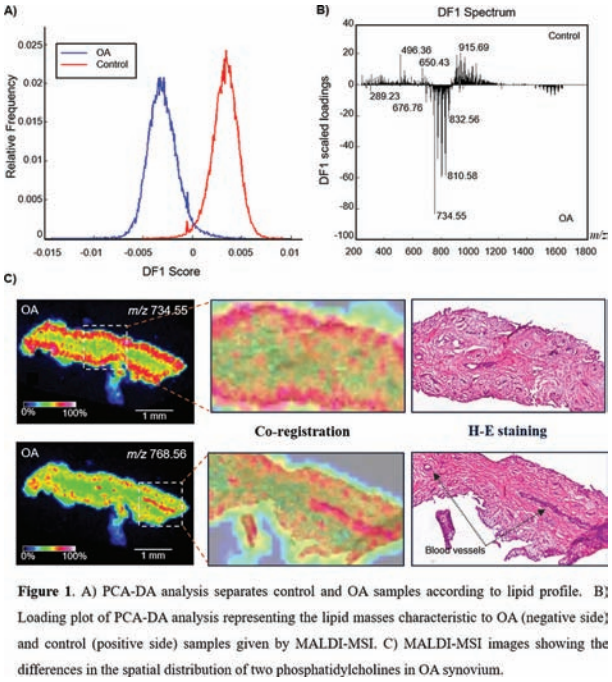


Figure 1. A) PCA-DA analysis separates control and OA samples according to lipid profile. B) Loading plot of PCA-DA analysis representing the lipid masses characteristic to OA (negative side) and control (positive side) samples given by MALDI-MSI. C) MALDI-MSI images showing the differences in the spatial distribution of two phosphatidylcholines in OA synovium.

Results: MALDI-MSI in combination with principal component analysis (PCA) and discriminant analysis (DA) revealed differential lipid profile between OA and control samples. Data acquired in positive ion mode showed a good separation of OA patients and controls (Figure 1A). OA tissues showed higher lipid content in the mass/charge (*m/z*) range 600-800, compared to controls (Figure 1B). Among identified lipid species, we found 35 phospholipids significant differentially expressed between OA and controls, mainly classified in phosphatidylcholines (30%), phosphatidylethanolamines (26%), phosphatidylinositols (26%), phosphatidylserines (14%) and lysophosphatylcholines (6%). Some of them showed a specific localization within tissue. For instance, the phosphatidylcholine (PC) *m/z* 734.55 showed a specific localization in the lining layer of hyperplastic OA synovium, whereas PC *m/z* 768.56 were located in the sublining layer characterized by high vascularity and inflammatory cell infiltrations (Figure 1C). The PCA-DA analysis also showed a higher presence of phosphatidylinositols (PIs) and phosphatidylethanolamines specifically in OA samples, whereas lysophosphatidylcholines were more abundant in control samples compared to OA. Most of these molecules, mainly PIs, were also spatially distributed in the lining layer of the OA synovium.
Conclusion: OA synovial tissues were characterized by a higher content of phospholipids, mainly PCs and PIs, compared to control synovial biopsies. Specific phospholipids related to morphological features of the synovial membrane have been described for the first time by MALDI-MSI. These molecules could have an important role in the synovitis associated with the pathogenesis of OA and constitute relevant molecular disease classifiers for the OA diagnosis.
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WEDNESDAY, 12 JUNE 2019

Rehabilitation; opening Pandora's Box

OP0079-HPR NON-PHARMACOLOGICAL CARE IN SYSTEMIC SCLEROSIS: OPENING THE BLACK BOX

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Background: Although health professional (HP) treatments are considered to be a corner stone in the management of systemic sclerosis (SSc), little is known about the referral process to and the content of non-pharmacological care in SSc.
Objectives: To describe non-pharmacological care in SSc from the perspective of Dutch HPs, including referral reasons, diagnostic focus, interventions used and alignment in the communication between HPs and rheumatologists.
Methods: Dutch HPs were invited through their SSc patients to complete an anonymous online survey provided by the Dutch ARCH (Arthritis Research and Collaboration Hub) working group. The survey comprised multiple response and open questions covering six topics: sociodemographic questions, referral reasons, diagnostic focus, treatment targets, interventions and the assessment of quality of communication between HPs and rheumatologists based on the Consumer Quality Index (CQI) (rheumatoid arthritis, version 2.0). Referral reasons and treatment targets were examined by means of open questions, and then linked to the ICF (International Classification of Functioning, Disability and Health) following the refined ICF Linking Rules (Cieza, 2016).
Results: A total of 79 HPs, 65.8% women (N=52), with a mean age of 41.2 (SD=13.6) from 8 different professions completed the survey. Physiotherapists were the largest group represented (73%, N=58). All in all 133 different referral reasons were reported that yielded 58 different ICF codes, of which 70.7% (N = 41) could be linked to the ICF domain "body structures and functions". The reported interventions focus on body functions and structures, training of daily activities, education and advices and psychosocial interventions (Table 1). The quality of communication between HPs and rheumatologists as perceived by the HPs is shown in Table 2.

Table 1. Interventions applied by the 79 health professionals, top 4 per topic

Interventions	N (%)
Treatments focus on bodily functions and/ or structures	
Physical activity promotion	38 (48.1)
Training of body functions (e.g. muscular strength, range of motion)	34 (43.0)
Aerobic capacity training	25 (31.7)
Balance/coordination training	14 (17.7)
Training of activities	
Walking/biking	45 (57.0)
Movement activities/ sports	45 (57.0)
Leisure	19 (24.1)
Household	16 (20.3)
Education/advice/instruction	
Graded activity	44 (55.7)
Physical activity	42 (53.2)
Lifestyle (e.g. smoking, cold, silver gloves)	14 (17.7)
Energy conservation	12 (15.2)
Psychosocial interventions	
Self-management/ self-monitoring	53 (67.1)
Relaxation strategies/ stress management/ biofeedback therapy	23 (29.1)
Motivational Interviewing	13 (16.5)
Problem-solving training	10 (12.7)

Table 2. Quality of communication between HPs and rheumatologists, N (%)

	always/ mostly	sometimes/ never	N/A	don't know
Do you think that the treatments for SSc patients were well coordinated between you and the rheumatologist?	32 (42.7%)	20 (26.7%)	14 (18.7%)	9 (12.0%)
Do you think that the advice you and the rheumatologist gave to the SSc patients were well coordinated?	39 (52.0%)	16 (21.3%)	13 (17.3%)	7 (9.3%)
Did you and the rheumatologist, in your opinion, make good agreements with each other?	19 (25.4%)	26 (34.7%)	26 (34.7%)	4 (5.3%)
Did you inform the rheumatologist about the goals, progress and outcomes of your treatment?	31 (41.4%)	29 (38.6%)	14 (18.7%)	1 (1.3%)

Conclusion: The results of this study show clear discrepancies between referral reasons and applied interventions, visible in the clear focus on body functions and structures on one hand and the broad spectrum of applied interventions on the other hand. It is possible that HPs make a translation of the reasons given for referral to the needs of the individual patient. Viewed from this perspective, it is questionable whether the referrals by the rheumatologists are sufficiently targeted. Further, the results describe a suboptimal communication between rheumatologists and HPs that should be targeted in practice and further research.

REFERENCE:

[1] Cieza, et al., (2016). Refinements of the ICF Linking Rules to strengthen their potential for establishing comparability of health information. Disability and rehabilitation, 1-10.

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Osteoporosis

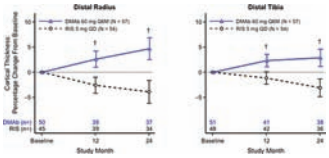
OP0080 EFFECT OF DENOSUMAB VERSUS RISEDRONATE ON CORTICAL AND TRABECULAR BONE MICROARCHITECTURE BY HIGH RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (HR-PQCT) IN GLUCOCORTICOID-TREATED INDIVIDUALS

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Background: In a study of patients initiating or continuing GC, 12 and 24 months gains in lumbar spine and total hip areal bone mineral density (aBMD) were greater with DMAb vs RIS.[1,2]
Objectives: Evaluate the effects of DMAb vs RIS on cortical and trabecular bone.
Methods: Phase 3, double-blind, double-dummy, active-controlled study randomised women and men ≥18 years, receiving GC (≥7.5 mg prednisone daily or equivalent) for <3 (GC-initiating [GC-I]) or ≥3 months (GC-continuing [GC–C]), to DMAb 60 mg every 6 months or RIS 5 mg daily for 24 months. Subjects <50 years had a history of osteoporosis (OP) fracture. GC-C subjects ≥50 years had lumbar spine, total hip or femoral neck BMD T–score ≤–2.0; or T-score ≤–1.0 with history of OP fracture. All subjects were to receive daily calcium (≥1000 mg) and vitamin D (≥800 IU). In a subset, HR-pQCT scans of the distal radius and distal tibia were performed at baseline and Months 12 and 24. Treatment differences (DMAb–RIS) were estimated using analysis of covariance (ANCOVA).
Results: The substudy enrolled 111 subjects (57 DMAb, 54 RIS). DMAb was associated with significantly greater increases than RIS in cortical thickness, total volumetric BMD (vBMD) and cortical vBMD at the radius and tibia at 12 and 24 months, and in trabecular vBMD at the radius at 12 months and tibia at 24 months (Table). Change in cortical porosity did not differ between DMAb and RIS (Table).
Percentage Change From Baseline and Treatment Difference in vBMD and Cortical Microarchitecture

		Distal Radius		Distal Tibia	
		Month 12	Month 24	Month 12	Month 24
Total vBMD	DMAb	1.8 (0.7, 2.8)	4.1 (2.6, 5.6)	1.3 (0.4, 2.2)	2.2 (1.2, 3.1)
	RIS	-1.1 (-2.2, -0.1)	-1.7 (-3.3, -0.1)	-0.8 (-1.8, 0.1)	-1.4 (-2.4, -0.4)
	DMAb—RIS	2.9 (1.4, 4.4)†	5.8 (3.6, 7.9)†	2.2 (0.9, 3.5)†	3.6 (2.2, 5.0)†
Cortical vBMD	DMAb	0.2 (-0.4, 0.8)	1.2 (0.4, 1.9)	0.5 (-0.1, 1.1)	1.0 (0.4, 1.5)
	RIS	-0.7 (-1.3, -0.1)	-1.4 (-2.2, -0.6)	-0.7 (-1.3, -0.1)	-1.3 (-1.8, -0.7)
	DMAb—RIS	0.9 (0.1, 1.8)*	2.6 (1.5, 3.6)†	1.2 (0.4, 2.1)*	2.2 (1.4, 3.1)†
Trabecular vBMD	DMAb	2.3 (0.2, 4.3)	9.4 (1.4, 17.3)	0.8 (-0.3, 1.8)	1.7 (0.7, 2.8)
	RIS	-0.9 (-3.0, 1.1)	-0.7 (-9.0, 7.6)	-0.3 (-1.3, 0.7)	-0.4 (-1.5, 0.6)
	DMAb—RIS	3.2 (0.3, 6.1)*	10.1 (-1.4, 21.6)	1.1 (-0.4, 2.5)	2.1 (0.7, 3.6)*
Cortical porosity	DMAb	2.3 (-2.9, 7.5)	8.5 (1.1, 15.9)	1.3 (-2.5, 5.2)	3.0 (-0.7, 6.6)
	RIS	2.2 (-3.1, 7.6)	10.2 (2.5, 18.0)	2.0 (-1.9, 5.9)	1.7 (-2.1, 5.5)
	DMAb—RIS	0.1 (-7.3, 7.5)	-1.7 (-12.4, 9.0)	-0.7 (-6.1, 4.8)	1.3 (-4.0, 6.6)
Cortical thickness	DMAb—RIS	5.2 (2.9, 7.4)†	8.6 (5.4, 11.8)†	3.5 (1.7, 5.2)†	6.0 (3.5, 8.5)†

Reported as LS mean (95% CI); p-value based on ANCOVA that included treatment, baseline value, and duration of prior GC use (<12 vs ≥12 months) as covariates
N = no. of subjects enrolled in substudy; n = no. of subjects with observed data p-value for treatment difference: *p<0.05; †p≤0.001



Conclusion: Compared with RIS, DMAb was associated with sustained improvements in cortical bone structure, assessed by HR–pQCT of the radius and tibia. It remains to be confirmed whether increased cortical thickness with DMAb is associated with improved bone strength in GIOP. These results further support DMAb as a treatment for GC-treated patients at increased fracture risk.

REFERENCES:

[1] Saag KG, et al. Lancet Diabetes Endocrinol. 2018;6(6)
[2] Saag KG, et al. Ann Rheum Dis. 2018;77 (Suppl 2)

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OP0081 RELATIONSHIP BETWEEN DIFFUSE IDIOPATHIC SKELETAL HYPERSOSTOSIS AND FRAGILITY VERTEBRAL FRACTURE – A PROSPECTIVE STUDY IN OLDER MEN

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Background: Diffuse idiopathic skeletal hyperostosis (DISH) is a common disorder of unknown cause characterized by ossifications of entheses with spinal and extraspinal manifestations(1). The prevalence ranges from 4% to 35%, depending on the diagnostic criteria (2). An increased risk of vertebral fracture in DISH has been suggested, due to the loss of flexibility of the fused spine, reminiscent of what is observed in ankylosing spondylitis(3–6).
Objectives: The aim of this study was to prospectively analyze the risk of vertebral fracture in men with DISH, compared with men without DISH.
Methods: Men older than 50 (n = 782) had coronal and lateral spine radiographs along with DXA and were monitored prospectively. We analyzed the risk of incident vertebral fractures (over 7.5 years) in men with DISH defined by flowing ossification alongside the anterolateral aspect of at least four contiguous vertebral bodies, relative intervertebral disc preservation and the absence of apophyseal ankylosis and inflammatory changes of the SI joints, according to Resnick'criteria (7). Incident vertebral fracture was defined by a decrease of at least 20% or 4 mm in any vertebral height (anterior, central or posterior) between the follow-up and the baseline radiographs.
Results: DISH was present in 21,7% (170/782) of men (mean age=). Among the 782 examined at baseline, 761 had at least one spine X-ray after baseline and 164/170 men with DISH had enough available data to be analyzed. Vertebral fracture incidence was higher in men with DISH compared with those without DISH (mean 10/164 (6.1%) vs. 16/597 (2.7%); p<0.05). DISH was also associated with the risk of vertebral fracture after adjustment for age, BMI, lumbar spine bone mineral density (BMD), prevalent vertebral fractures (Grade 2&3), disc space narrowing and endplate irregularity (OR = 2.89, [95%CI : 1.15 – 7.28]; p<0.05). 6.3% (10/149) of men with DISH had both normal BMD ($\geq$0.912 g/cm^2) and increased risk of vertebral fracture (OR 6.54 [95%CI : 2.13 - 20.26]; p<0.05).
Conclusion: DISH is associated with higher risk of vertebral fracture, independently of BMD. The risk of vertebral fracture of men with DISH but normal BMD may be underestimated.

REFERENCES:

[1] Mader R, Verlaan J-J, Buskila D. Diffuse idiopathic skeletal hyperostosis: clinical features and pathogenic mechanisms. Nat Rev Rheumatol. 2013;9(12):741–50.
[2] Diederichs G, Engelken F, Marshall LM, Peters K, Black DM, Issever AS, et al. Diffuse idiopathic skeletal hyperostosis (DISH): relation to vertebral fractures and bone density. Osteoporos Int. juin 2011;22(6):1789–97.
[3] Ghozlani I, Ghazi M, Nouijai A, Mounach A, Rezqi A, Achemlal L, et al. Prevalence and risk factors of osteoporosis and vertebral fractures in patients with ankylosing spondylitis. Bone. mai 2009;44(5):772–6.
[4] Davey-Ranasinghe N, Deodhar A. Osteoporosis and vertebral fractures in ankylosing spondylitis. Curr Opin Rheumatol. juill 2013;25(4):509–16.
[5] Leone A, Marino M, Dell'Atti C, Zecchi V, Magarelli N, Colosimo C. Spinal fractures in patients with ankylosing spondylitis. Rheumatol Int. oct 2016;36(10):1335–46.
[6] Caron T, Bransford R, Nguyen Q, Agel J, Chapman J, Bellabarba C. Spine fractures in patients with ankylosing spinal disorders. Spine. 15 mai 2010;35(11):E458-464.
[7] Resnick D, Niwayama G. Radiographic and pathologic features of spinal involvement in diffuse idiopathic skeletal hyperostosis (DISH). Radiology. juin 1976;119(3):559–68.

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OP0082 TEMPORAL TRENDS OF BISPHOSPHONATE DISCONTINUATION AND FACTORS ASSOCIATED WITH ALENDRONATE DISCONTINUATION AND RESTART AT POPULATION LEVEL

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Background: Bisphosphonates are the most commonly used class of osteoporosis medication worldwide. Rare adverse events related to long-term use of bisphosphonates have raised interest in planned temporary drug discontinuation. Due to chronicity of osteoporosis, restarting osteoporosis medication is likely to be needed after such a discontinuation. Trends in the discontinuation and the restart of bisphosphonates and their reasons are not fully understood.
Objectives: We investigated the temporal trends of bisphosphonate discontinuation from 2010 to 2015 and evaluated the factors associated with alendronate only discontinuation and restart of any osteoporosis medication at a population level.
Methods: To determine the temporal trends of discontinuation (at least 12 months without prescription claims) from 2010 to 2015, we identified a cohort of women with long-term bisphosphonate therapy (medication possession ratio (MPR) $\geq$ 80% for at least 3 continuous years) derived from the enhanced 5% Medicare sample and a cohort of beneficiaries with evidence of osteoporosis (defined using diagnosis and fracture codes, and medication claims). We used a case-crossover design, nested within the cohort study, to identify factors associated with discontinuation of long-term alendronate therapy and restart of any osteoporosis medication. We used conditional logistic regression adjusted for potential confounders to compare factors associated with alendronate discontinuation and osteoporosis therapy restart in the hazard period (120 days) referent to the preceding control periods (120 days).
Results: We identified a total of 73,800 women with exclusive long-term alendronate (59,251), risedronate (6,806), or zoledronic acid (7,743) use, respectively, of which 26,281 (35.6%) women discontinued therapy. The proportion of long-term bisphosphonate users who discontinued therapy increased from 1.7% in 2010 to 14.0% in 2012, and remained relatively stable thereafter (**Figure 1**). After adjustment, factors most strongly associated with the discontinuation of alendronate included: a new prescription of benzodiazepines (adjusted Odds Ratio [aOR] = 2.5, 95% CI [2.1, 3.0]), prior dual-energy X-ray absorptiometry (DXA) scan (aOR = 1.8, 95% CI [1.7, 2.0]), skilled nursing facility care utilization (aOR = 1.8, 95% CI [1.6, 2.1]). Factors most strongly associated with the restart of any osteoporosis

medication were: performing DXA scan (aOR = 9.9, 95% CI [7.7, 12.6]), fragility fracture (aOR = 2.8, 95% CI [1.8, 4.5]), and osteoporosis or osteopenia diagnosis (aOR = 2.5, 95% CI [2.0, 3.1]).

Conclusion: We describe temporal trends in bisphosphonate discontinuations and factors associated with discontinuation of alendronate and restart of osteoporosis therapy. From 2010 to 2015, approximately one-third of women with long-term bisphosphonate treatment discontinued treatment for ≥12 months. We observed an increasing trend in discontinuation from 2010 to 2012, which remained steady through 2015. Factors associated with discontinuation of alendronate were associated with worsening of overall health status, while factors traditionally associated with worsening bone health were associated with restart of osteoporosis medication.

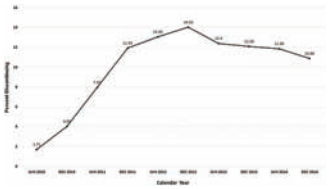


Figure 1. Temporal trends of Bisphosphonate Discontinuation in U.S. Medicare women beneficiaries by calendar year

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OP0083

PREVALENCE OF VERTEBRAL FRACTURES IN POSMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a risk factor for the development of fragility fractures, but there is little quality data on its prevalence. Conversely, osteoporosis is one of the most frequent comorbidities of RA.

Objectives: To determine the prevalence of vertebral fractures in postmenopausal women with RA and to analyse their characteristics and associated risk factors.

Methods: We included 346 postmenopausal women diagnosed with RA according to the ACR/EULAR 2010 criteria in 19 Spanish Rheumatology Departments, randomly selected from the registry of RA patients in each center, recruited during 2018. Lateral radiographs of the dorsal and lumbar spine were obtained from all patients, to evaluate morphometric vertebral fractures. Expert rheumatologists identified vertebral fractures and classified them into mild (grade 1: reduction of height of 20-25%), moderate (grade 2: reduction of 26-40%) and severe (grade 3: reduction > 40%), according to the Genant grading scale. The spinal deformity index (SDI) was calculated by assigning numbers 1, 2 and 3 to each fractured vertebra and adding the total score of each patient. The study variables were: a) age, body mass index (BMI), b) factors related to RA: time of evolution, FR, ACPA, and c) fracture risk factors: prior fragility fracture, parental hip fracture, glucocorticoids, smoking, alcohol intake ≥3 units daily, secondary osteoporosis and time since menopause.

Results: The mean age was 66.8 (SD: 10.1) years and the median evolution of the disease, 8.00 [RIQ: 3.00-15.5] years. 77.2% (n: 267) and 75.7% (n: 252) had FR and ACPA +, respectively. The mean duration of the postmenopausal period was 15.0 (SD: 9.6) years. 23.4% (n: 79) of patients had at least one vertebral fracture; 10.7% (n: 36) had a single fracture and 12.7% (n: 43), multiple fractures. The most fractured vertebrae were D12, L1 and L2 (fractured in > 5% of patients). The median SDI was 3 [RIQ: 2-5]. The vertebrae with the highest mean IDE were D8, D10, D11 and L1 (all mean IDE ≥ 2).An association was found between the presence of vertebral fractures and age, height, postmenopausal period, time of disease progression, glucocorticoid treatment and parental hip. No linear association was found between SDI and age, time of evolution of the disease, BMI and time since menopause.

Conclusion: One out of every 4 postmenopausal women with RA has at least one vertebral fracture. Vertebrae of the dorso-lumbar hinge are the most frequently involved and the magnitude of the spinal deformity is relevant. Vertebral fractures are related to the time of evolution of RA and to the risk factors for fracture.

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OP0084

FRAGILITY HIP FRACTURES – DOES DESTINATION AFTER HOSPITAL DISCHARGE HAVE AN IMPACT ON PATIENT'S OUTCOME?

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Background: In Osteoporosis, hip fractures account for significant disease burden, with increased morbi-mortality. Because of this, patients are referred to rehabilitation and specific health care units, in order to regain autonomy and health. However, there is few evidence about patients' outcome, considering destination after inpatient discharge.

Objectives: To evaluate if destination after hospital discharge for a osteoporotic hip fracture has impact in the outcome (mortality and new fracture).

Methods: Patients referred to a Fracture Liaison Service from March 2015 until March 2017 with a fragility hip fracture were considered for this study. Clinical/demographic variables were retrospectively collected until January 2018, including destination at discharge (home, nursing home (NH), inpatient rehabilitation unit (RU)) and outcome (death, new fracture, lost to follow-up). Kaplan Meyer curves with log-rank test were used for statistical analysis (SPSS statistics 23); p<=0.05 was considered statistically significant.

Results: From a total of 522 patients, 437 patients were discharged with a known destination: 58.1% to home (n=254), 27.7% to a RU and the remaining to a NH. Table 1 summarizes clinical and demographic characteristics of the sample. Seventy-four patients died (median time = 264 days, range 22-1049) and 43 suffered a new fracture (median time 301, 15-946); 129 patients maintained follow-up. Mortality rates within each group of discharged patients were: 15.4% in the group destined home, 22.6% in the group forwarded to a NH and 17.4% in those referred to a RU. No statistically significant difference was found in cumulative survivals between groups (figure 1A). The event refracture was observed in 10.2% of those discharged home, 6.5% in the group forwarded to a NH and 10.7% of those referred to a RU. Again, no statistically significant difference was observed (figure 1B).

Table 1. sample's characteristics

Total (N)	437
Age at admission, y (median, min-max)	83 (65-101)
Sex, female (n,%)	368, 79.7
Degree of dependence (N)	288
Totally dependent (n,%)	20, 7.0
Partially dependent (n,%)	76, 26.4
Autonomous (n,%)	192, 66.7
Type of fracture (N)	437
Subtrochanteric (n,%)	36, 8.2
Femoral neck (n,%)	176, 40.3
Transtrochanteric (n,%)	225, 51.5
Type of intervention (N)	437
Girdlestone (n,%)	1, 0.2
No surgery (n,%)	6, 1.4
Total hip replacement (n,%)	68, 15.6
Partial hip replacement (n,%)	68, 15.6
Osteosynthesis (n,%)	292, 66.8
Destination at discharge (N)	437
Home (n,%)	254, 58.1
NH (n,%)	62, 14.2
RU (n,%)	121, 27.7
Vertebral fracture (N)	229
0 (n,%)	96, 41.9
1 fracture (n,%)	54, 23.5
$\geq$ 2 fractures (n,%)	79, 34.5
Femur neck BMD, g/cm^2 (mean, SD, N)	0.7, ±0.12, 205
Femur neck T score (mean, SD, N)	-2.8, ±1.04, 205
≤2.5 (n,%)	144, 70.0%
vitD, ng/ml (mean, SD, N)	23.5, ±11.69, 210

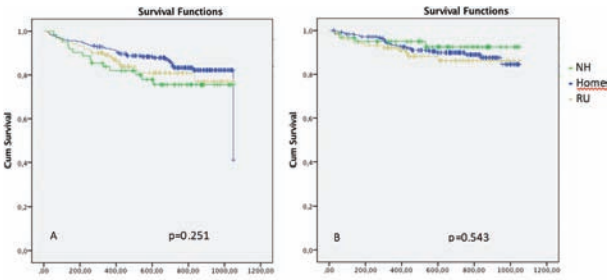


Figure 1. Panel A - outcome mortality; Panel B - outcome refracture.

Conclusion: Previous studies showed lower survival in patients discharged for conventional home care (1,2). In our cohort, despite more than half the sample was discharged home, no difference was found in mortality or re-fracture. Further studies will assist to clarify this matter.

REFERENCE:

[1] Pitzul KB, et al. Arch Osteoporos. 2017 Sep 30;12(1):87.

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OP0085 CAN WE AVOID THE LOSS OF BONE MINERAL DENSITY ONE YEAR AFTER DENOSUMAB DISCONTINUATION? THE REOLAUS BONE PROJECT

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Background: Denosumab discontinuation (DD) induces bone turnover markers (BTMs) increase, bone mineral density (BMD) decrease, and increased risk of spontaneous vertebral fractures. Prescribing a bisphosphonate after DD could avoid this rebound effect.
Objectives: The objective of the ReoLaus (Rebound Effect Observatory in Lausanne) Bone Project is to follow bone parameters after DD. We report the determinants associated to BMD loss 1 year after DD.
Methods: 170 patients are followed in ReoLaus. Patients with a BMD follow-up ≥ 1 year after DD with a standardized management were included. We defined as significant a lumbar spine BMD loss (Loosers group) over 3.96% at one year after DD as compared with values at the end of the denosumab treatment 18 months after last injection.
Results: 71 post-menopausal women stopped denosumab after 7.7±2.2 injections: age 63.8±8.1 years, BMI 23.8±4.5, 0.96 prevalent fractures/patient, 8.45% previously exposed to corticoids, 22.54% to anti-aromatases. 17.25 months after last denosumab injection 30 patients were classified as Loosers and 41 as Stable. At denosumab introduction Loosers were younger (61.4±7.3 vs 65.5±8.2 years, p=0.034) with higher sCTX level (644.7 vs. 474.1 ng/ml, p=0.005). The rate of BP given less than 2 years before denosumab was not different, but none of the Loosers had received zoledronate vs. 12% of the Stable (p=0.047). Other pre-denosumab characteristics were not different. Number of denosumab injections, BTMs and BMD values were comparable in both groups during denosumab treatment. First BTMs values measured 7.5 months (median) after last denosumab injection and before bisphosphonates were not different (sCTX: Loosers, 592 ng/ml; Stable, 379 ng/ml, p=0.06). At DD 59% received zoledronate, 24% alendronate, 3% others, and 14% nothing (p=0.39 between groups). BTMs 12.8 months post-BP were higher in Loosers as compared to Stable (sCTX 537 vs. 336 ng/ml, p=0.009). Incidence of new fractures was low (0.18/patient) without between group's difference.
Conclusion: In our sub-cohort, being younger, having high BMTs and not having received zoledronate before denosumab introduction increases the risk of a BMD loss, even if a bisphosphonate is prescribed at DD. Our results support the use of denosumab after a bisphosphonate to restrain the BMD loss at its discontinuation.
Disclosure of Interests: Bérengère Aubry-Rozier Speakers bureau: Lilly Pfizer Amgen Novartis, Giovanni Liebich: None declared, Delphine Stoll: None declared, Elena Gonzalez-Rodriguez: None declared, Didier Hans Shareholder of: co owner of TBS, medimaps group, Speakers bureau: Amgen Lilly, Olivier Lamy Speakers bureau: Amgen Lilly

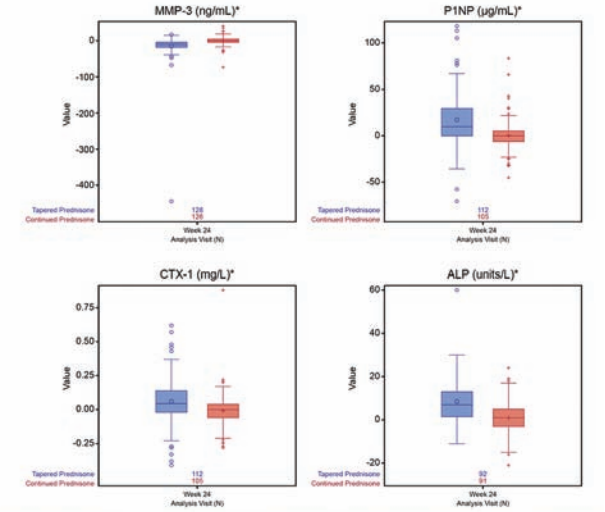
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OP0086 IMPACT OF GLUCOCORTICOID TAPERING ON MARKERS OF BONE METABOLISM IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVED LOW DISEASE ACTIVITY OR REMISSION ON TOCILIZUMAB: EXPLORATORY ANALYIS FROM A RANDOMIZED CONTROLLED TRIAL

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Background: Glucocorticoids (GCs) directly impact bone metabolism via increased bone resorption and inhibited bone formation[1]; hence, systemic fracture risk increases with daily and cumulative GC doses.[2] However, many patients with established rheumatoid arthritis (RA) receive long-term treatment with GCs to suppress inflammation, which confers some benefit in delaying bone erosion.[3]
Objectives: This exploratory analysis of the SEMIRA (Steroid EliMination In RA) study[4] compared changes in markers of bone and cartilage metabolism in RA patients with low disease activity (LDA) or remission on tocilizumab (TCZ) + GC ± conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) who received either slow GC tapering (GCtaper) or continuation (5 mg; GC5mg).
Methods: Patients had at least stable LDA (DAS28-ESR ≤3.2) for ≥4 weeks, were receiving a stable prednisone regimen (5 mg/day) + TCZ ± csDMARDs for ≥4 weeks, and received TCZ + GCs (prednisone equivalent 5-15 mg/day) for ≥6 months before randomization. Patients were randomly assigned to GC5mg (n=128) or GCtaper (n=131; starting at 4 mg/day with 1-mg reduction every 4 weeks to 0 mg/day at weeks 16-24) for 24 weeks, during which TCZ ± csDMARDs remained stable. Change between baseline (BL) and week 24 in serum levels of markers of bone and cartilage metabolism—including N-terminal propeptide of type 1 collagen (P1NP), C-terminal telopeptide of type 1 collagen (CTX1), alkaline phosphatase (ALP), matrix metalloproteinase 3 (MMP3), calcium, phosphorus, and albumin—were exploratory outcomes. Within-group and between-group changes from baseline were evaluated by Wilcoxon paired rank test and Wilcoxon signed rank test, respectively.
Results: Figure 1 shows changes from BL to week 24 in bone and cartilage biomarkers. MMP3 (marker of cartilage degradation) was reduced at week 24 in the GCtaper group compared with GC5mg. Change from BL at week 24 in P1NP (bone formation) and CTX1 (bone resorption) favored the GCtaper arm, with P1NP increasing relatively more than CTX1 (44% and 24%, respectively, compared with GC5mg), indicating net anabolism. The increase in ALP from BL to week 24 was greater for the GCtaper arm than for the GC5mg arm, suggesting neomineralization. There was no difference in the change from BL to week 24 in calcium, phosphorus, or albumin (not shown).

Figure 1. Box plots of change from baseline to week 24 in biomarkers of bone metabolism observed values



ALP, alkaline phosphatase; CTX-1, C-terminal telopeptide of type 1 collagen; MMP-3, matrix metalloproteinase 3; P1NP, N-terminal propeptide of type 1 collagen
*p<0.001 for tapered prednisone vs continued prednisone based on Wilcoxon signed rank test

Conclusion: The findings of this biochemical marker analysis suggest that withdrawal from GC after achievement of LDA or remission with TCZ results in increased bone remodeling, with a trend toward an anabolic window and reduced cartilage degradation. Given that it could take a year to recover from increased fracture risk after cessation of GC therapy,[5] our results offer further insight on the reversible risk of systemic harm to noninflamed bone versus benefits for inflamed joints in the context of LDA or remission.

REFERENCES:

[1] Canalis E, Delany AM. Ann N Y Acad Sci 2002;966:73.
[2] Van Staa TP, et al. Rheumatology 2000;39:1383.
[3] Kavanaugh A, Wells AF. Rheumatology 2014;53:1742.
[4] Burmester GR, et al. Arthritis Rheumatol 2018;70(suppl 10).
[5] Vestergaard P, et al. Calcif Tissue Int 2008;82:249.

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OP0087 TRENDS IN HIP FRACTURE INCIDENCE IN WOMEN AND MEN OVER 1980-2015 IN OLMSTED COUNTY, MINNESOTA, USA

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Background: Hip fracture incidence, which has been generally declining in North America, may have recently plateaued in women (Lewiecki, et al 2018).
Objectives: We examined the trends in hip fracture incidence over 1980-2015, in both women and men, from Olmsted County, Minnesota, USA.
Methods: Using the Rochester Epidemiology Project, a unique medical records linkage system that allows access to all (inpatient and outpatient) community medical records for Olmsted County residents, we identified all incident hip fractures among residents age ≥18 years between 1980-2015. Available medical records were reviewed by trained nurse abstractors to validate hip fractures identified and to determine their antecedent cause (pathological process [e.g., malignancy], severe trauma [e.g., motor vehicle accidents] and those due to no more than moderate trauma [by convention, equivalent to a fall from standing height or less]). Overall incidence rates were summarized separately for women and men, as well as by 5 year strata for different age groups (ages 18-39, 40-59, 60-79 and ≥ 80 yrs). Rates for women and men were each directly age-adjusted to the population distribution of US whites in 2010.
Results: Between 1980-2015, we identified 2488 hip fractures in women (73%, median age 84 yrs) and 918 hip fractures in men (27%, median age 80 yrs), 97.4% of which were in whites. The majority of hip fractures were due to no more than moderate trauma (88% in women; 81% in men). The overall age-adjusted annual incidence of first hip fracture over 1980-2015 was 154 per 100,000 person-years (p-y) for women and 98 per 100,000 p-y for men. Hip fracture rates have decreased overall in women since 1980 (Table), however since 2005, there has been a trend for increasing hip fractures among women age 40-59 yrs and since 2010, a possible plateau vs. slight increase in hip fracture rate for women age ≥ 80 yrs. In men, there has been a general decrease in rates among those age 60-79 yrs and, at least since 2005, in men age ≥ 80 yrs, but there may be a trend for increasing hip fractures since 2010 in men age 40-59 (Table).

	Hip Fracture Incidence per 100,000 p-y by Age Group							
	18-39 yrs		40-59 yrs		60-79 yrs		≥ 80 yrs	
Years	Women	Men	Women	Men	Women	Men	Women	Men
1980-84	2	4	43	7	345	175	1954	1173
1985-89	4	4	32	11	329	163	1892	1188
1990-94	2	3	26	19	282	122	1914	771
1995-99	4	3	20	17	302	168	2117	1116
2000-04	2	6	10	9	199	132	1788	1300
2005-09	5	4	27	10	203	134	1320	1148
2010-15	4	4	27	29	162	125	1413	811

Conclusion: There appears to be different trends in hip fracture rates for women and men and by age groups. The factors contributing to the observed recent increases in hip fracture rates among women and men ages 40-59 yrs warrant further attention. As suggested by others, there may be a recent plateau vs. slight increase in hip fracture rates in older women, which we noted in women age ≥ 80 yrs since 2010. The decrease in hip fractures in older men, particularly in those age ≥ 80 yrs, may reflect improved awareness in recent years of osteoporosis in men with initiation of treatment or better mitigation of risk factors, but warrants further review.

REFERENCE:

[1] Lewiecki E.M., et al. Hip fracture trends in the United States, 2002 to 2015. Osteoporos Int 29(3):717-722, 2018.

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WEDNESDAY, 12 JUNE 2019

When rheumatoid arthritis (RA) does not walk alone: new data on comorbidities in RA

OP0088 COMORBIDITIES AS RISK FACTORS FOR RHEUMATOID ARTHRITIS (RA) AND ACCRUAL AFTER RA DIAGNOSIS

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Background: Understanding the timeline of comorbidity development in patients with RA may inform disease pathogenesis and help identify targets for improving outcomes (1).
Objectives: We first aimed to compare the prevalence of a comprehensive list of comorbidities in RA cases versus controls. Second, we aimed to investigate the time association of comorbidity development relative to RA onset to identify which comorbidities might predispose to developing RA and comorbidities that might result from RA.
Methods: We performed a case-control study using a biobank at a single center, identifying 821 cases of RA (143 incident) using a rules-based algorithm combining two diagnosis codes with use of a DMARD (PPV = 95%). We matched each case to three controls based on age, sex, and location of residence at the time of the biobank survey. Participants self-reported the presence or absence and age of onset for 77 comorbidities on the survey.
Results: Among the 3,276 RA cases and controls, mean age was 62 years, and 73% were female. Cases with RA had the same number of comorbidities as controls before RA diagnosis (median 1.0 vs 1.0, P = 0.49) but had more comorbidities by the time of the survey (median 5.0 vs 4.0, p < 0.001). At the time of the survey, several comorbidities were more common in participants with RA than controls (Table1). Cancer was not more common in RA cases than controls (31% vs 32%, p = 0.80), even among all cancer subtypes. The only comorbidities that tended to develop in the time period before RA diagnosis more often than controls were inflammatory bowel disease (1.9% vs 0.5%, p < 0.001) and type 1 diabetes (1.3% vs 0.4%, p = 0.01). In contrast, in the time period after RA diagnosis, myocardial infarctions were more common in cases with RA (3.8% vs 1.2%, p < 0.001) and hyperlipidemia was less common (11.4% vs 16.4%, p = 0.004) compared to controls.

Table 1. Comorbidities that were more prevalent in RA cases than controls at the time of baseline survey*

Comorbidity	N (%) RA cases (N = 821)	Controls (N = 2455)	p-value
Osteoarthritis	370 (50)	915 (38)	< 0.001
Fibromyalgia	114 (15)	144 (6)	< 0.001
Autoimmune disorder	123 (16)	95 (4)	< 0.001
Epilepsy	22 (3)	29 (1)	0.003
Cataracts	278 (35)	699 (29)	0.003
Myocardial infarction	63 (8)	88 (4)	< 0.001
COPD	47 (6)	88 (4)	< 0.001
Sleep apnea	164 (20)	352 (15)	< 0.001
Pulmonary fibrosis	16 (2)	10 (0.4)	< 0.001
Gastroesophageal reflux disease	304 (38)	675 (28)	< 0.001
Inflammatory bowel disease	37 (5)	40 (2)	< 0.001

*significance threshold was set at p < 0.01 given multiple comparisons
COPD = chronic obstructive pulmonary disease

Conclusion: Many comorbidities were associated with RA, including several potentially novel comorbidities such as COPD, epilepsy, and acid reflux. RA was not associated with an increased risk of cancer. The increased occurrence of inflammatory bowel disease and type 1 diabetes prior to RA suggests either a predisposition to RA development or a shared immunological defect, meriting further study.

REFERENCES:

[1] Gabriel SE, Michaud K. Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis Res Ther. 2009;11(3):229.

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OP0089 METABOLIC SYNDROME IS COMMON AROUND THE TIME OF EARLY RHEUMATOID ARTHRITIS DIAGNOSIS AND ASSOCIATIONS VARY BY SEX AND MENOPAUSAL STATUS: RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT

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Background: Prevalence studies of metabolic syndrome (MetS) in early rheumatoid arthritis (ERA) are sparse and estimates are variable. Differences by sex and menopausal status have not been formally assessed.
Objectives: We estimated prevalence and factors associated with MetS in ERA patients treated in routine practice settings. Variations by sex, and by menopausal status were also examined.
Methods: Cross-sectional data were analyzed from patients meeting 1987 or 2010 ACR/EULAR RA criteria enrolled in the Canadian Early Arthritis Cohort (CATCH) from January 2007-March 2017. CATCH is a prospective multicenter observational study of patients diagnosed and treated for early inflammatory arthritis (symptoms < 1 year) by a rheumatologist. Participants completed standardized clinical assessments and patient-reported outcome measures. Laboratory testing of metabolic parameters was encouraged, but left to the discretion of the rheumatologist. MetS was defined according to modified WHO criteria[1] as $\geq$ 2 of the following: body mass index (BMI) $\geq$ 30, hypertension, low high-density lipoprotein (HDL) cholesterol, dyslipidemia, or impaired glucose intolerance (IGT)[1]. Univariate and multivariable logistic regression was used to estimate crude and adjusted associations between baseline demographic, clinical and lifestyle variables with prevalent MetS in men and in women, respectively.
Results: The sample included 1543 participants; 71% were female and mean (SD) age was 54 (15) years. 476 (31%) of the total sample met criteria for MetS. Participants with MetS were older, more frequently past smokers and reported more comorbid conditions, including cardiovascular disease (CVD) (p<0.0001). MetS prevalence was higher in men (42%) than women (26%, p<0.0001) and higher in post-menopausal (33%) vs. pre-menopausal women (15%, p<0.0001). Post-menopausal women had a higher frequency of hypertension (65%), IGT (32%) and dyslipidemia (21%) compared to pre-menopausal women (p<0.001). In multivariable logistic regression MetS was negatively associated with seropositivity and pulmonary disease in men; with corticosteroid use in menopausal women; and with psychiatric comorbidity in pre-menopausal women.
Conclusion: Approximately 1 in 3 ERA patients met crietria for MetS. Though men had a higher prevalence of MetS and individual MetS components, post-menopausal women had a similar MetS profile as men, and should equally be considered high risk for CVD development. Characteristics and associations with MetS differed in men and women suggesting sex-specific variations are important considerations for comorbidity screening and surveillance of CVD outcomes in ERA.

REFERENCE:

[1] Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998;15 (7):539-53.

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Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, UCB., Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Vivian Bykerk Grant/research support from: Mallinckrodt, BMS, Crescendo Biosciences, Sanofi/Regeneron., Consultant for: Amgen, Pfizer, UCB, Scipher, Sanofi/Genzyme/Regeneron, Lillian Barra: None declared
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OP0090 THE OCCURRENCE OF SUBCLINICAL AND CLINICAL ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS, RESULTS FROM THE 3-YEAR, MULTICENTER, PROSPECTIVE, OBSERVATIONAL, GIRRCS STUDY

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Background: The systemic inflammatory process and the "traditional" cardiovascular (CV) risk factors could synergize the enhancement of CV burden in rheumatoid arthritis (RA) [1].

Objectives: To assess the occurrence and the predictive factors of subclinical and clinical atherosclerosis in patients with RA.
Methods: During 2015, consecutive patients, admitted to Italian Rheumatology Units, were assessed in GIRRCS (*Gruppo Italiano di Ricerca in Reumatologia Clinica e Sperimentale*) cohort [2]. After that, patients were followed-up in a 3-year, prospective, observational study, assessing the occurrence of subclinical (carotid and/or peripheral arteries atherosclerotic lesions detected by ultrasound imaging) and clinical atherosclerosis (myocardial infarction and/or congestive heart failure and/or cerebrovascular accidents) and possible predictive factors. McNemar test was employed to assess the changes in subclinical and clinical atherosclerosis and regression analyses exploited the ORs for the occurrence of those comorbidities.
Results: After 3 years of prospective follow-up, 797 patients (82.7% female, median age of 60 years, range 21-89) were assessed. We also observed a median RA duration of 8.35 years (range 0.1-35), 70.9% of patients showed rheumatoid factor and 55.7% ACPA. Among "traditional" CV risk factors, we observed that BMI was 27.21 ± 4.05, 33% of patients reported smoking habit, 49.3% were affected by high blood pressure (HBP) and 12.3% by type 2 diabetes (T2D). Corticosteroids were administered in 75.5% of patients (low dosage 66.8%), methotrexate in 86.8%, hydroxychloroquine in 28.1% and biologic DMARDs in 60.7%. The remission was reached and maintained in 42.6% of patients, during the follow-up. We recorded an increased rate of subclinical atherosclerosis (70 vs 130 patients p<0.0001) and clinical atherosclerosis (30 vs 46 patients, p<0.001), at the end of follow-up. The multivariate regression analysis showed that T2D (OR: 4.50, 95%CI:1.74-11.62, p=0.002), HBP (OR: 2.03, 95%CI:1.04-4.14, p=0.042), ACPA (OR: 2.36, 95%CI:1.19-4.69, p=0.002) and mean values of CRP during the follow-up (OR: 1.07, 95%CI: 1.03-1.14, p=0.040) were associated with subclinical atherosclerosis. Differently, the maintenance of remission was associated with a reduced risk of subclinical atherosclerosis (OR: 0.25, 95%CI: 0.11-0.56, p=0.001). The multivariate regression analysis showed that T2D was associated with clinical atherosclerosis (OR:6.21, 95%CI:2.19-17.71, p=0.001). Conversely, the maintenance of remission was associated with a reduced risk of clinical atherosclerosis (OR:0.20, 95%CI: 0.09-0.95, p=0.041).
Conclusion: The maintenance of remission was strongly associated with a reduced risk of clinical and subclinical atherosclerosis in 3-year prospective follow-up. Among "traditional" CV risk factors, T2D was significantly associated with both clinical and subclinical atherosclerosis.

REFERENCES:

[1] Nurmohamed MT, et al. Nat Rev Rheumatol. 201511:693-704
[2] Ruscitti P, et al. Medicine (Baltimore). 2017;96:e8180.

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OP0091 RISK OF MEDICAL COMPLICATIONS FOLLOWING TOTAL HIP OR KNEE ARTHROPLASTY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE REGISTER-BASED COHORT STUDY

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Background: Total hip and total knee arthroplasty (THA/TKA) are major surgeries carrying a risk of complications. Patients with rheumatoid arthritis (RA) are at increased risk of venous thromboembolism (VTE), arterial thromboembolic events (ATE), and infections in a non-surgical setting.
Objectives: To investigate the risk of VTE, ATE, and non-surgical infection following THA/TKA in patients with RA compared with osteoarthritis (OA); and to explore the impact of biologics treatment.
Methods: In a nationwide register-based study, patients with RA and OA who had elective THA/TKA in 2000-2014 were identified in the Danish Hip Arthroplasty Register/Danish Knee Arthroplasty Register and followed up to 90 days after surgery for the occurrence of VTE, ATE, and infections. Cox models stratified on sex and type of surgery (THA vs TKA) and adjusted for age, calendar period, history of chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), cancer, VTE and CVD were carried out. Outcome information was obtained through linkage with the Danish National Patient Registry.
In DANBIO, we identified RA patients treated with biologics within 90 days preceding surgery and estimated their risk of each outcome compared with non-biologics treated RA patients in a Cox model adjusted for the propensity score (PS) of receiving biologics as a restricted cubic spline covariate. The PS was conditional on age, sex, calendar period, use of methotrexate, other csDMARDs, and/or glucocorticoids, pre-surgical DAS28, HAQ-DI, VAS physician, and COPD, DM, cancer and/or VTE.
Results: In total, 2899 and 112,571 patients with RA and OA were followed-up (Table).
Conclusion: In this nationwide cohort study, RA patients were at increased risk of infection after THA/TKA compared to OA patients, but treatment with biologics did not further increase the risk.
As seen in other studies RA patients had a lower risk of VTE following TKA when compared with OA patients, but our finding of an increased incidence of VTE in biologics-treated patients warrants further studies.
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Table. Patient characteristics and risk of venous thromboembolism (VTE), arterial thromboembolism (ATE), and non-surgical infection following total hip or total knee arthroplasty (THA/TKA) among patients with rheumatoid arthritis (RA) compared with osteoarthritis (OA), and biologics treated compared with non-biologics treated RA patients.

	RA	OA	p	Biologics treated	Non-biologics treated	p
N	2899	112,571		411	1391	
Female	73%	58%	<0.001	73%	74%	0.43
Age at surgery, mean (s.d.)	66 (11)	69 (10)	<0.001	62 (12)	65 (10)	<0.001
Had TKA surgery	63%	44%	<0.001	67%	63%	0.09
Received thromboprophylaxis	99%	99%	0.53	97%	99%	0.002
History of VTE	3%	2%	0.001	3%	4%	0.31
Prevalent CVD	17%	15%	0.01	11%	15%	0.07
History of cancer	6%	7%	0.03	4%	6%	0.05
History of hospitalisation due to infection	10%	4%	<0.001	12%	8%	0.02
Outcome	**Events, n (%)**		**HR (95%CI)**	**Events, n (%)**		**HR (95%CI)**
VTE	25 (1.0)	1167 (1.3)	0.7 (0.5 to 1.1)	8 (1.9)	7 (0.5)	5.5 (1.7 to 18.4)
ATE	22 (0.8)	849 (0.7)	1.2 (0.8 to 1.8)	4 (1.0)	8 (0.6)	2.8 (0.7 to 11.1)
Infection	73 (2.5)	2224 (2.0)	1.3 (1.0 to 1.6)	11 (2.7)	35 (2.5)	0.9 (0.4 to 1.9)

Abbreviations: HR, hazard ratio, 95%CI, 95% confidence interval.
RA was associated with an increased risk of infection, but a lower risk of VTE (HR_{TKA}=0.6, 0.3 to 1.0,p=0.04). Compared with non-biologics treated, biologics-treated patients were not at increased risk of infection but had a 5-fold increased risk of VTE.

Eli Lilly, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB Pharma., Speakers bureau: Pfizer, AbbVie, Amgen, UCB, BMS, Biogen, MSD, Novartis, Eli Lilly and Company, and Janssen Pharmaceuticals, Anders Odgaard: None declared, Søren Overgaard: None declared, Lene Dreyer Consultant for: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: UCB, MSD, Eli Lilly and Janssen Pharmaceuticals.

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OP0092 ASSOCIATIONS BETWEEN CLINICAL VARIABLES AND PSYCHOLOGICAL SYMPTOMS IN RHEUMATOID ARTHRITIS: A NETWORK SCIENCE PERSPECTIVE

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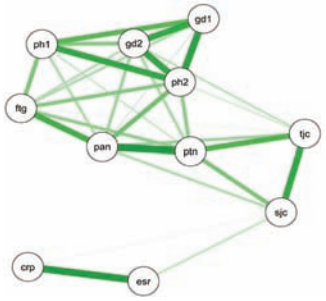
Background: Rheumatoid arthritis (RA) is associated with an increased prevalence of common mental disorders, including anxiety and depression (Matcham et al. 2013). Borsboom's (2017) network theory of mental illness is gaining traction as a model for depression which incorporates biological, social and psychological aspects of depression by looking at interactions between individual symptoms and other variables within a wider network. Currently applications have been restricted to psychiatric samples, however, this model may potentially help gain a clearer understanding of the causal links clinical variables and mental health symptoms in RA.

Objectives: To study the prescriptions of NSAIDs in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) registered in ICEBIO and matched controls, and explore their relationship with disease activity measures. In addition, to explore the impact of initial TNFα-inhibitor therapy on NSAID prescription rates.

Objectives: To test the feasibility of a network analysis approach to examine associations between clinical variables and mental health symptoms in RA.

Methods: The data used are from patients attending rheumatology clinics at King's College Hospital who completed patient reported outcomes (PROs) electronically via the Integrating Mental and Physical Healthcare (IMPARTS) system. Over 1,000 patients completed PROs via IMPARTS, with a subsample of 211 extracted for this analysis where psychological screening and inflammatory markers were recorded concurrently (<14days). The screening tools used were the two-item Patient Health Questionnaire (PHQ2) and the two-item Generalised Anxiety Disorder (GAD2), which assess the core symptoms of depression and anxiety: low pleasure/interest, low mood, high anxiety, uncontrollability of worry. Additional data recorded were joint counts and visual analogue scales for pain, fatigue and global disease activity. Missing data were imputed using multiple imputation. Network analysis was conducted using the *ggraph* package in R based on the regularised correlations between variables. With a graphical network model of variables created to calculate centrality values.

Results: Figure 1 below illustrates that the symptoms with the most connections were PHQ1 (low pleasure/interest), GAD2 (uncontrollable worry), pain and global disease activity. As expected the strongest connections were between PHQ1 (low pleasure/interest) with PHQ2 (low mood), GAD1 (high anxiety) with GAD2 (uncontrollable worry), pain with patient global, tender joints with swollen joints, and ESR with CRP.



The results highlight pain and PHQ2 (low mood) as having both the highest degree (3.9 & 3.8, respectively) and betweenness centrality (22 & 10, respectively). This indicates that these are the variables with both the highest number of connections and providing the shortest pathway between other symptoms and so may act as key variables linking inflammation and mental health. Pain and global disease activity had the highest closeness centrality (0.033 & 0.032, respectively), illustrating that they have the shortest path with all other symptoms and capture the influence of both inflammation and mental health. Tender and swollen joints have weak connections to the mental health variables, suggesting that that extra-articular aspects of pain may be important.

Conclusion: Inflammation in RA does not appear to have a strong influence on mental health, with pain providing the main connection between these areas of the network. Concerning the symptoms of mental health considered, all were strongly connected but low mood provided the main connection between clinical and psychological variables. This indicates mood as potentially a key variable in RA, which is easy to monitor in routine care.

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REFERENCES:

Borsboom, D. (2017). A network theory of mental disorders. *World Psychiatry, 16*(1), 5-13. doi:10.1002/wps.20375Matcham, F., Rayner, L., Steer, S., & Hotopf, M. (2013). The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis. *Rheumatology (Oxford), 52*(12), 2136-2148. doi:10.1093/rheumatology/ket169

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OP0093 THE INCIDENCE AND RISK FACTOR OF NEW CAROTID PLAQUES AND THE PROGRESSION RATE OF CAROTID PLAQUES IN PATIENTS WITH RHEUMATOID ARTHRITIS IN 6 YEARS PROSPECTIVE CASE CONTROL STUDY. -TOMORROW STUDY-

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Background: Cardiovascular disease is one of the complications of rheumatoid arthritis (RA). Patients with RA show higher rates of cardiovascular disease mortality and overall mortality compared with individuals without RA. The presence of an abnormally increased intima–media thickness (IMT) in the carotid artery and carotid plaques on carotid ultrasound are useful for assessing the presence of subclinical atherosclerosis. A greater presence of carotid artery IMT and carotid plaques is a predictor of cardiovascular disease events.

Objectives: The objective of this study was to evaluate progression of carotid plaques in 6 years by comparing 2011 and 2017, and to assess the risk factors of progression.

Methods: This study included 208 patients with RA and 204 age- and sex-matched controls (Co) in the TOtal Management Of Risk factors in Rheumatoid arthritis patients to lOWer morbidity and mortality (TOMORROW) study. This was a 10-year cohort study that started in 2010. Carotid ultrasound was performed in 2011 and 2017. Ultrasound examination of bilateral carotid arteries was performed using high-resolution B-mode ultrasound (HI VISION Avius; Hitachi Aloka Medical, Tokyo, Japan) with a 6- to 18-MHz liner array transducer. IMT was evaluated as the distance between the luminal–intimal interface and the medial–adventitial interface. IMT was measured using two calipers on the frozen frame of a suitable longitudinal image. The upper limit of normal for IMT was defined as 1.0 mm. Lesions with any focal structure that protruded into the vessel lumen for at least an IMT $\geq$ 1.1 mm were defined as atherosclerotic plaques. Subsequently, the plaque score was assessed as the sum of the maximal thicknesses of all plaques in bilateral carotid arteries in the scanning area. Plaque scores were categorized as follows: none, no plaques; mild, score of 1.1–5.0; moderate, score of 5.1–10.0; and severe, score of > 10.0.

Results: A total of 175 patients with RA (mean age: 58.9 ± 12.7 years, female ratio: 85.7%, mean disease duration: 15.0 ± 11.7 years) and 185 Co (mean age: 58.5 ± 12.5 years, female ratio: 84.3%) were finally analyzed. Carotid plaques were observed more frequently in the RA group than in the Co group in 2011 (n = 82 vs n = 66, p = 0.04). However, the incidence of new plaques was not significantly different between the RA and Co groups (n = 33 vs n = 44, p = 0.94). Age (p = 0.015) and the presence of diabetes (p = 0.009) were higher in patients with RA and new plaques than in those without new plaques. Multivariate logistic regression analysis did not show that RA was a risk factor for the incidence of new plaques (OR: 0.90, 95% CI: 0.47–1.73, p = 0.750). However, the presence of hypertension (OR: 3.11, 95% CI: 1.43–6.74, p = 0.004), the presence of diabetes (OR: 6.13, 95% CI: 1.13–33.4, p = 0.036) were risk factors for the incidence of new plaques. The plaque score became advanced in the RA and Co groups (both p < 0.001) in 6 years.

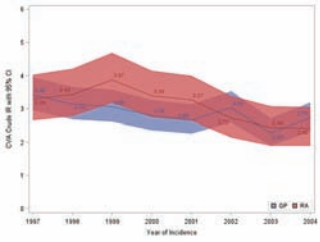
Conclusion: There are no significant differences in the incidence of new plaques and the progression rate of the plaque score between patients with RA and Co. This finding might due to the recent advances in RA treatment, such as methotrexate or biologic DMARDs. In patients with RA, the presence of hypertension and diabetes represents a risk factor for the incidence of new plaques.

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OP0094 SECULAR TRENDS IN THE INCIDENT RISK OF CEREBROVASCULAR ACCIDENT IN RHEUMATOID ARTHRITIS RELATIVE TO THE GENERAL POPULATION

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Background: Recent studies have demonstrated a declining trend in RA mortality relative to the general population (1). This improvement in mortality could be due to improvement in incident risk of cardiovascular events that are the leading cause of excess deaths in RA (2).
Objectives: Our objective was to assess secular trends in ten-year incident risk of cerebrovascular accident (CVA) in incident cohorts of RA versus general population controls, using administrative health data.
Methods: We conducted a retrospective study of a population-based cohort of incident RA cases who first met previously published RA criteria between 01/01/1997 and 31/12/2004 in British Columbia followed until 31/12/2014, with general population controls matched 2:1 on gender, age, and index year. Individuals were excluded if they had a diagnosis of CVA prior to index date. Incident CVA was defined as first CVA during follow-up using ICD codes 9 code 433, 434/ICD-10 code I64, I63) in Hospital Discharge data or death certificate in Vital Statistics data. RA and general population cohorts were stratified according to year of RA incidence, defined according to first RA visit, using a 7-year wash-out period. Incident rates (IRs) of CVA for RA and general population cohorts, as well as incident rate ratios (IRRs), with 95% confidence intervals (CI) were calculated per calendar years of incidence. Multivariable Cox Proportional Hazard models with left truncation were used to estimate risk of CVA in RA relative to general population while controlling for potential confounders, with contribution of person time of follow-up starting from index date (second RA visit) to avoid immortal time bias and censoring at ten years from incident year, or last health care utilization. To examine whether secular trends differed in RA relative to general population, an interaction term was tested between the RA indicator and year of RA incidence. To account for non-linear effect of cohort year, we compared cox regression models with linear, quadratic, and flexible spline forms of the cohort-year effects and the model with the best AIC was used to interpret the data.



Results: 23,545 RA individuals (65.7% female; mean [SD] age 58.11[16.82] years) and 47,090 controls experienced 658 and 1,220 incident CVA respectively. A linear spline Cox model with a knot at year 1999 was selected to fit the CVA events. The change in CVA risk over time differed significantly in RA vs. general population after 1999 [p=0.0488], but not before 1999 [p=0.06]. A significant decline in risk of CVA was observed over the calendar years of incidence after 1999 in RA [0.91 (0.86, 0.96); p=.0003] but not in the general population [0.97 (0.93, 1.01); p=0.1019].
Conclusion: Our findings suggest that the risk of CVA has significantly declined over time in people with RA onset from 1999 onwards, but not in the general population.

REFERENCES:
[1] Lacaille, D., et al., *Improvement in 5-year mortality in incident rheumatoid arthritis compared with the general population—closing the mortality gap*. Annals of the Rheumatic Diseases, 2016.
[2] Myasoedova, E. and S.E. Gabriel, *Overview of rheumatoid arthritis and mortality in relation to cardiovascular disease*, in *Handbook of Cardiovascular Disease Management in Rheumatoid Arthritis*, A.G. Semb, Editor. 2017, Springer International Publishing: Cham. p. 1-17.

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OP0095 INFLUENCE OF PERIODONTITIS ON DISEASE ACTIVITY, PHYSICAL FUNCTION, AND SAFETY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A OBSERVATIONAL STUDY USING THE IORRA COHORT

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Background: Periodontitis (PD) is considered to be one of the triggers for rheumatoid arthritis (RA) [1]. Several reports demonstrated the associations between the disease activity of RA and presence of PD, however, most of them are based on small population, and results are inconsistent [2, 3]. Furthermore, impact of PD on physical function and safety is not known. Thus, a study using a large cohort database is warranted to clarify the relationship between patients' outcomes and PD among patients with RA.
Objectives: To demonstrate the influence of PD on the outcome of RA, an established cohort IORRA database was used to compare the disease activity, physical function and prevalence of infection between patients with PD and those without.
Methods: IORRA database is an established cohort database with RA in our institute since 2000. Trough biannual data collection including patient's questionnaire, physician's evaluations and laboratory data in more than 5,000 RA patients, a database with a total 91,884 patient-year observation period was established by 2018. In this IORRA database, RA patients who answered to all the questionnaires about PD in October 2016 were extracted. Among those, we defined patients with PD (PD group) as having diagnosis of PD during the last 6 months, and those without PD (non-PD group) as having no present and previous PD. Using the data set from April 2016 to October 2016, we compared Disease Activity Score 28 (DAS28), Japanese Health Assessment Questionnaire (J-HAQ) score, and the prevalence of patients self- reported infections required hospitalizations or hospital visits between the two groups. For background data comparisons, we used chi-squared test for categorical data and Mann-Whitney U-test for continuous data. To investigate associations between PD and remission or PD and infection, we calculated adjusted odds ratio (OR) of PD using a logistic regression model.
Results: At baseline, patients in the PD group (n=925) were significantly older, had higher DAS28 and J-HAQ than those in the non-PD group (n=2,583). DAS28 and J-HAQ at 6 month in the PD group were significantly higher than those of the non-PD group (DAS28, 2.60 in PD group, 2.42 in non-PD group, p<0.001; J-HAQ score, 0.25 in PD group, 0.13 in non-PD group, p<0.001). Median of delta DAS28 and delta J-HAQ in the both groups were similar and adjusted ORs of PD for DAS28 remission (0.85 [0.69-1.04]) and for J-HAQ remission (0.99 [0.67-1.45]) at 6 month were not statistically significant. There were significant differences in the percentage of patients who developed infections between the two groups (5.8% in PD group, 3.4% in non-PD group, p=0.002). Adjusted OR of PD for infections was 1.72 [1.10-2.69], which was significantly elevated.
Conclusion: RA patients with PD had similar treatment response with those in the non-PD group, however, had higher disease activity, poorer physical function, and higher risk of infections compared to those without. These results may indicate that oral management is important for the better outcomes of patients with RA in the daily practice.

REFERENCES:
[1] Nat Rev Rheumatol. 2017:606-20
[2] J Clin Rheumatl. 2012:180-4
[3] Med J Islam Repub. Iran. 2017:44

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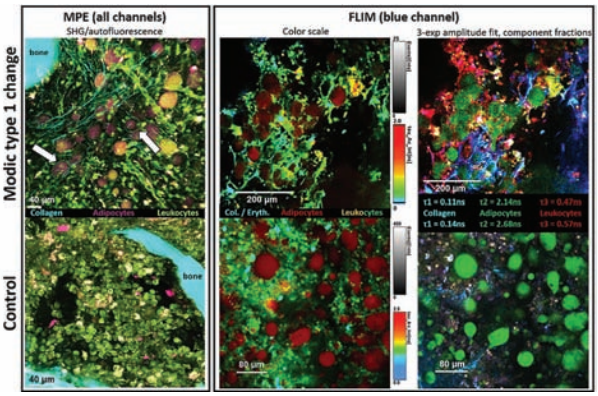
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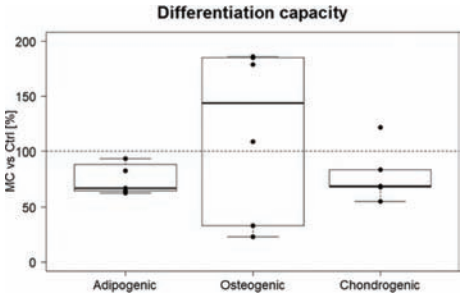
Tackling chronic pain; fibromyalgia and back pain

OP0096 **DYSREGULATED BONE MARROW STROMAL CELLS IN MODIC TYPE 1 CHANGES**

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Background: Modic type 1 changes (MC1) are fibrotic-inflammatory vertebral bone marrow lesions adjacent to degenerating discs. Patient with MC1 often develop low back pain [1]. In MC1, extra-cellular collagen is deposited, myelopoiesis is dysregulated, and bone is rapidly remodeled. These are signs of a chronic inflammation. The cellular mechanisms are unknown, yet bone marrow stromal cells (BMSC) are key regulators of myelopoiesis, can differentiate into collagen-producing cells, and modulate inflammation [2].
Objectives: To link BMSC phenotype and function to molecular changes in MC1.
Methods: From patients undergoing lumbar spondylodesis, bone marrow aspirates (n=5 MC1+5 controls, adjacent level healthy bone marrow (Ctrl)) or biopsies (n=2 MC1+2 Ctrl) were taken through pedicle screw trajectory before screw insertion.
Biopsies were fixed, dehydrated, and imaged with multiphoton fluorescence microscopy (MPE). Tissue auto-fluorescence and second-harmonics-generation (SHG) of collagen were recorded of full-length biopsies with up to 200 µm penetration depth and qualitatively evaluated. Fluorescence-life-time-imaging-microscopy (FLIM) of the auto-fluorescence signal was performed in key areas of biopsies and single-photon-counting histograms were fitted with a triple-exponential decay function.
BMSC were isolated from aspirates by plastic adherence and characterized (passage 2): Sequencing of ribosomal depleted RNA (Illumina Novaseq) with pathway analysis was performed, differentiation capacity was quantified histologically (Wilcoxon test), duplication rate was measured with CellTrace™ (t-test), and stem cell surface marker expression was quantified by flow cytometry (CD14, CD16, CD19, CD34, CD45, CD73, CD90, CD105, CD284 (t-test).





Results: Biopsies: Collagen was qualitatively more abundant in MC1 than in Ctrl bone marrow, particularly in areas of adipocyte clusters and around adipocytes (Figure 1, arrows). FLIM was able to distinguish adipocytes (T =2.1-2.7ns), leukocytes (T =0.4-0.8ns), erythrocytes (T =0.2-0.4ns), and collagen (T <0.15ns) based on their different auto-fluorescent life-times (Figure 1, right).
BMSCs: By RNA sequencing 154 genes were differentially expressed between MC1 and Ctrl BMSCs ($p \leq 0.01$; log2 ratio ≥ 0.5). Pathway analysis revealed significant alterations in processes important for 'cell adhesion' (p<9.3e-13) and 'extracellular matrix organization' (p<1.8e-7). Aggrecan (fold change=0.25, p<1e-7) and osteopontin (fold change=5.26, p<1e-5) were the first and third top-most differentially regulated genes, indicating a shift away from chondrogenic polarization towards osteogenic polarization. A shift in BMSC polarization was corroborated with differentiation assays: MC1 vs. Ctrl BMSCs had a reduced adipogenic (mean ±sd: -33±13%, p=0.03) and chondrogenic (-31±25%, p=0.18) differentiation capacity (Figure 2). In addition, an increased duplication rate of MC1 vs. Ctrl BMSCs (29.3±1.7 vs. 26.2±1.0 hours, p=0.07) was observed, also indicate a change in phenotype. There were no changes in the expression of surface markers.
Conclusion: These data suggest that MPE-FLIM is a prime technology to investigate fibrotic pathologies and it allows to morphologically study the importance of BMSCs in MC1. The BMSC/adipocyte axis seem to play a pivotal role in the fibrotic pathomechanism. Adipocytes have not been regarded as pathomechanistically relevant yet and hence open novel targets for therapeutic approaches.

REFERENCE:

[1] Dudli, et al. Eur Spine J. 2017;26(5):1362-1373. [2] García-García A, et al. Immunol Lett. 2015;168(2):129-135.

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OP0097

CHRONIC PAIN AND SICK LEAVE IN A 21-YEAR FOLLOW UP

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Background: Chronic musculoskeletal pain (CMP) is a common cause of disability and impaired quality of life. In Sweden, chronic pain and mental illness are major causes of sick leave. But sick leave itself is also proposed as a risk factor for prolonged sick leave and disability pension.
Objectives: To study CMP and sick leave as potential risk factors for long term sick leave or disability pension in a 21 year follow up of a general population cohort.
Methods: In a cohort study, with a baseline survey in 1995, 1466 individuals aged 20-67 years were followed for 3 years and 691 for 21 years, or up to the age of 67. CMP (>3 months duration) was reported on a pain mannequin. Sick leave and disability pension were self-reported. Mental health was measured by the mental health (MH) score of the SF-36 health status, and categorized into tertiaries (best, medium and worst). CMP, sick leave, and mental health at baseline, were studied as potential predictors for long term sick leave (disability pension or sick leave >3 months) at a 3 and 21 year follow up. Other potential predictors (socioeconomic group, education, and immigrant status) were introduced in multiple regression analyzes but did not add to the results and were removed from the final models, which were controlled for age and sex.
Results: CMP and mental health predicted long term sick leave at the 3 year follow up (OR 2.11, p=0.010 and OR 3.52, p<0.001). Mental health (OR 1.92, p=0.046), but not CMP (OR 0.77, p=0.409), was also a predictor at the 21 year follow up. Sick leave >3 months, irrespectively if due to pain or not, predicted long term sick leave both at the 3 and the 21 year follow up (Table). Sick leave for ≤3 months also predicted long term sick leave at both follow ups when due to pain (OR 2.70, p=0.008 and OR 2.78, p=0.012), but not when due to other causes (OR 1.52, p=0.212 and OR 1.17, p=0.606).

	Long term sick-leave or disability pension at 3 year follow up vs. all other		Long term sick-leave or disability pension at 21 year follow up vs. all other	
	OR (95% CI)	p	OR (95% CI)	p
Sick leave 1995				
No sick leave	1		1	
≤3 months due to pain	2.70 (1.29-5.63)	0.008	2.78 (1.26-6.14)	0.012
>3 months due to pain	7.81 (2.66-22.94)	<0.001	15.60 (2.28-106.50)	0.005
≤3 months other cause	1.52 (0.79-2.96)	0.212	1.17 (0.65-2.09)	0.606
>3 months other cause	4.60 (1.13-18.60)	0.033	9.22 (1.21-70.30)	0.032
CMP in 1995				
no	1		1	
yes	2.11 (1.19-3.71)	0.010	0.77 (0.42-1.42)	0.409
SF-36 MH 1995				
Best	1		1	
Medium	1.63 (0.73-3.61)	0.231	1.63 (0.87-3.09)	0.128
Worst	3.52 (1.75-7.10)	<0.001	1.92 (1.01-3.66)	0.046

Conclusion: Sick leave and especially sick leave due to pain predicted long term sick leave up to 21 years later, independently of pain status or mental health at baseline. It is thus important to early identify individuals at risk and minimize sick leave by providing proper rehabilitation.
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OP0098

SUICIDAL BEHAVIOUR IN FIBROMYALGIA PATIENTS: META-ANALYSIS AND SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Suicide is a leading cause of death worldwide, with approximately 800,000 people dying every year. Fibromyalgia is the second most common rheumatic disease, affecting 0.2-6.6% of the population worldwide and fibromyalgia patients suffer from anxiety and depression, which are known to be risk factors for suicidal behaviour. Suicidality related to chronic pain conditions has been studied, but there is a dearth of information specifically concerning suicidality among patients with fibromyalgia.
Objectives: To investigate the risk of suicidal ideation and attempts in patients with fibromyalgia.
Methods: A systematic review and meta-analysis was conducted and reported according to the "Preferred Reporting Items for Systematic reviews and Meta-analyses" (PRISMA) standards. Also, the gray literature was extensively searched.
Results: Thirteen studies were included in the present systematic review and meta-analysis, of 394,087 fibromyalgia patients. Sample size ranged from 44 to 199,739 subjects: mean age ranged from 45.8 to 54.5 years while female percentage went from 17.1% to 100.0%. Fibromyalgia diagnosis was based on the 1999 ACR criteria and 2010 ACR criteria in one study. The overall suicide ideation prevalence was 29.57% (95%CI 1.84-72.07), with an OR 9.12 of (95%CI 1.42-58.77), ranging from 2.34 (95%CI 1.49-3.66) to 26.89 (95%CI 5.72-126.42). Pooled suicide attempt prevalence was 5.69% [95%CI 1.26-31.34], with an OR of 3.12 [95% CI 1.37-7.12]. Suicide risk was higher with respect to the general population with an OR of 36.77 (95%CI 15.55-96.94), as well as suicide events with an HR of 1.38 (95%CI 1.17–1.71). Determinants of suicidality were found to be: employment status, disease severity, obesity and drug dependence, chronic pain and co-morbidities, in particular depression, anxiety, poor sleep, and global mental health.
Conclusion: Fibromyalgia patients are particularly prone to suicide, in terms of ideation, attempt, risk and events, warranting a pre-emptive screening of their mental health status. However, in some cases, after adjusting for psychiatric conditions, the threshold of statistical significance was not achieved. Given the few studies available, the high amount of heterogeneity and the evidence of publications bias, further high-quality studies should be conducted.

Table 1. The main findings of the systematic review and meta-analysis on suicidality among fibromyalgia patients.

Variable	Results
Suicide ideation	Overall suicide ideation prevalence 29.57% [95%CI 1.84-72.07]; 1.08-54.6% Passive suicide ideation prevalence 39.86% [95%CI 35.14-44.72]; 39.7-41.0% Active suicide ideation prevalence 9.00% [95%CI 6.44-12.16]; 8.3-13.6% OR 9.12 [95%CI 1.42-58.77]; 2.34 [95%CI 1.49-3.66]-26.89 [95%CI 5.72-126.42] OR 7.60 [95%CI 0.72-80.17] adjusted for psychiatric conditions
Suicide attempt	Prevalence 5.69% [95%CI 1.26-31.34]; 0.38-16.67% OR 3.12 [95%CI 1.37-7.12] OR 1.27 [95%CI 0.54-3.01] adjusted for psychiatric conditions
Suicide risk	OR from 36.77 [95%CI 15.55-96.94]; 30.06 [95%CI 10.25–100.27] to 48.0 [95%CI 12.93–178.21] HR 1.45 [95%CI 1.16-1.81] HR 1.16 [95%CI 0.92-1.44] adjusted for psychiatric conditions
Suicide event	HR 1.38 [95%CI 1.17–1.71] Incidence 31/100,000 person/years Mortality OR 3.31 [95%CI 2.15-5.11] SMR 10.5 [95%CI 4.5-20.7]

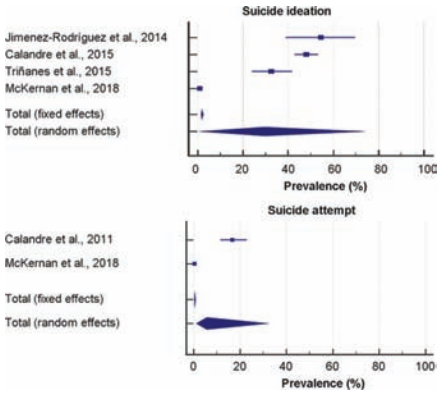


Figure 1. Forest plots of suicide ideation and attempt rates among fibromyalgia patients.

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OP0099

EFFECTIVENESS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN PATIENTS WITH FAILED BACK SURGERY SYNDROME

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Background: Failed back surgery syndrome (FBSS) is the term of persistent back and/or leg pain after lumbar surgery (1). Repetitive transcranial magnetic stimulation (r-TMS) is a technique that allows non-invasive and relatively painless stimulation of cerebral cortex. It can reduce the experience of chronic pain by using magnetic field to produce small electrical currents in the cortex (2).
Objectives: The aim of this study is to determine the effectiveness of r-TMS treatment on patients with FBSS.
Methods: In this double-blinded, randomized, placebo-controlled trial, 20 patients (aged 34-65 years) clinically diagnosed as FBSS, who had a history of surgery for lumbar disk herniation with persistent back and leg pain. Only patients with no root compression in postoperative magnetic resonance imaging of lumbar spine were included. Patients were randomly assigned to r-TMS (n:10) and sham (n:10) groups. Patients in r-TMS group received 5 Hz of r-TMS, as a 20-min (1000 pulses) daily session, 5 days per weeks, for a total of 10 sessions. R-TMS applied with MagVenture device (MagPro X100, Denmark, 2009) and figure eight coil (MMC 140 parabolic, MagVenture). Control group received sham r-TMS with the same protocol. Patients were assessed before and after the 1st and 5th sessions, at the end of the treatment and at 2 weeks, 1 month and 3 months after treatment. Visual Analogue Scale (VAS), DN-4, Oswestry Disability Index (ODI), Beck Depression Inventory (BDI), Pittsburgh Sleep Quality Index (PSQI) were used for evaluation.
Results: There were no statistically significant differences between the groups for age, sex, number of surgery, pain duration, working status and drug usage. Significant improvements were achieved in DN4, ODI, BDI and PSQI scores in r-TMS group in comparison to sham group. Both groups displayed improvements in VAS scores while improvement in the sham group was limited to first month. Achieved improvements in r-TMS group in terms of VAS, DN4, ODI, BDI and PSQI scores were sustained at third month.
Conclusion: Repetitive transcranial magnetic stimulation might be an effective treatment alternative in patients with FBSS, further studies with larger groups are needed.

REFERENCES:

[1] Al Kaisy, A., Pang, D., Desai, M. J., Pries, P., North, R., Taylor, R. S.,. .. & Rigoard, P. (2015). Failed back surgery syndrome: who has failed?. Neurochirurgie, 61, S6-S14.
[2] Johnson, S., Summers, J., & Pridmore, S. (2006). Changes to somatosensory detection and pain thresholds following high frequency repetitive TMS of the motor cortex in individuals suffering from chronic pain. Pain, 123(1-2), 187-192.

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OP0100

THE EFFECT OF COMBINED PREGABALIN AND DULOXETINE IN FUNCTIONAL STATUS, QUALITY OF LIFE AND PSYCHOLOGICAL STATUS IN FIBROMYALGIA

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Background: Fibromyalgia syndrome (FMS) is a chronic pain syndrome that characterized by chronic widespread pain, muscle tenderness and is often accompanied by fatigue, sleep disturbance, and depressive moods[1]. Pregabalin and duloxetine are thought to reduce pain by different pharmacological actions, and the studies for combining different treatments in FMS are limited[2].
Objectives: Assessment of the effectiveness of combined pregabalin and duloxetine in functional status, quality of life and psychological status in fibromyalgia
Methods: One hundred and twenty adult patients of primary FMS (according to the 2010 ACR criteria for FMS) participated in this study. Patients with other source of chronic pain as inflammatory or degenerative rheumatic diseases, severe debilitating systemic diseases were excluded; also we excluded patients with any previous psychiatric disorders and patients who had any contraindications for the used treatments. After written consent; the patients were randomly divided into 4 equal groups; group I were given pregabaline (200 mg divided twice daily) for 6 months, group II were given duloxetine (60 mg divided twice daily) for 6 months, group III were given combined therapy (200 mg divided twice daily of pregabaline plus 30 mg daily single dose of duloxetine) for 6 months, group IV were given placebo treatment, any other previous treatments were stopped before starting this study. The patients were assessed at baseline, after 3 and 6 months of treatment by Fibromyalgia Impact Questionnaire (FIQ), Medical Outcomes Study Questionnaire Short Form 36 Health Survey (SF-36), Hospital Anxiety and Depression Scale (HADS) and serum beta endorphin.

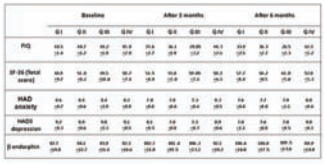


Table 1: Pre- and post-treatment clinical measurement of the patient groups

Results: In this study 115 patients completed the study. There was no significant difference between all groups in demographic data or educational status. At baseline there were no significant differences between all groups regarding FIQ, SF-36, HADS. Patients in all groups had low levels of β-Endorphin at baseline (82.7 ±14.8, 84.1±12.7, 83.9±11.4, and 82.3±16.6 respectively). There was significant improvement($P<0.05$) in FIQ, SF-36 and HADS in groups I, II and III after 3 and 6 months of treatment, while there was no significant improvement($P>0.05$) in group IV. There was significant better improvement ($P<0.05$) in group III than in group I and II. The levels of serum β- Endorphin were significantly elevated in the first 3 groups only ($P<0.05$) with no significant difference between the 3 groups ($P>0.05$). The results of the study are summarized in table 1.
Conclusion: The combination therapy of pregabalin and duloxetine is more effective than monotherapy in treatment of fibromyalgia

REFERENCES:

[1] Egunsola O, Wylie CE, Chitty KM, Buckley NA. Systematic Review of the Efficacy and Safety of Gabapentin and Pregabalin for Pain in Children and Adolescents. Anesth Analg. 2018 Nov 16. doi: 10.1213/ANE.0000000000003936. [Epub ahead of print]
[2] Gilron I, Chaparro LE, Tu D, Holden RR, et al. Combination of pregabalin with duloxetine for fibromyalgia: a randomized controlled trial. Pain. 2016 Jul;157(7):1532-40.

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OP0101

COMPARATIVE EFFECTIVENESS OF LAND AND WATER-BASED EXERCISE ON QUALITY OF LIFE OF PATIENTS WITH FIBROMYALGIA: PRELIMINARY FINDINGS FROM THE AL-ÁNDALUS RANDOMISED CONTROLLED TRIAL

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Background: Compelling evidence supports the efficacy of physical exercise in the management of fibromyalgia (FM)[1]. Although exercise interventions have typically focused on either land or water-based programs, research comparing the efficacy of both protocols is limited.
Objectives: The aim of this study was to compare the effect of two exercise interventions (land-based and water-based training) on quality of life (QOL) of patients with FM.
Methods: Among the 272 participants initially randomized, a total of 151 (age:50.6 ±7.6 years, 98%women) completed all the assessments with an attendance $\geq$70% (land-based n=48, water-based n=42, control n=61). The intervention groups trained 3 non-consecutive days/week (60 minutes per session) during 24 weeks. Each session involved exercises to improve cardiorespiratory fitness, muscular strength, and flexibility. Physical and mental domains of QOL were assessed

through the *36-item Short Form Health Survey* (SF-36). Participants were evaluated at baseline (pre-test), at the end of the intervention (post-test) and following a detraining period of 12 weeks after the end of the intervention (re-test). Land-based, water-based, and control groups were comparable in sex, sociodemographic characteristics, disease duration, drugs intake, and BMI. Age, tenderness, and baseline outcomes values were used as covariates in the comparisons of the changes from baseline (post-test vs. pre-test and re-test vs. pre-test) between groups

Results: Post-intervention changes from baseline in QOL dimensions in the land-based exercise group were better for physical role (compared to the control and water-based groups; all, $p<0.01$), bodily pain, general health, social function, emotional role, mental health, and mental component (compared to the control group; all, $p\leq0.05$). Post-intervention changes from baseline in the water-based exercise group were not statistically significant compared to land-based or control groups ($p>0.05$). After a detraining period of 12 weeks, changes in QOL from baseline in the land-based exercise group were better for physical role, bodily pain (compared to the control and water-based exercise groups; all, $p<0.01$), physical function and physical component (compared to the water-based exercise group; all $p<0.05$). No significant changes in QOL after the detraining period from baseline were observed in the water-based exercise group compared to land-based or control groups ($p>0.05$).

Conclusion: A land-based exercise intervention improved FM patients' QOL, whereas a water-based exercise intervention showed no significant effect. Improvements in the physical role and bodily pain domains of QOL were sustained in a 12-week detraining period. Land-based exercise might be an easily accessible treatment option that improves QOL to a greater extent than water-based exercise for FM patients.

REFERENCE:

[1] Macfarlane GJ, et al. Ann Rheum Dis, 2018; 76(2), 318-328.

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Disclosure of Interests: None declared

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OP0102 INTERVERTEBRAL DISC THERAPIES FOR NON-SPECIFIC CHRONIC LOW BACK PAIN: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Intervertebral disc therapies (IDT) for the management of non-specific chronic low back (NScLBP) pain are raising interest (1).

Objectives: To review evidence on the benefits and harms of IDT in people with NScLBP.

Methods: We searched 4 databases and conference abstracts, from inception to July 2018, for randomized trials of IDT *versus* placebo interventions, active comparators or usual care. Two independent investigators extracted data and assessed the risk of bias. The primary outcome was LBP intensity at short, intermediate and long terms (2). Secondary outcomes were LBP-specific activity limitation and safety (3). Our review was registered with the International Prospective Register of Systematic Reviews (CRD42019106336).

Results: Of 17 eligible trials, 5 trials (436 patients) assessed glucocorticoid (GC) IDT and were included in a quantitative synthesis. Twelve trials assessed IDT of other products including ozone (n=2, 140 patients), methylene blue (n=1, 72 patients), stems cells (n=1, 24 patients), glycerol (n=1, 11 patients), etanercept (n=2, 96 patients), tocilizumab (n=1, 60 patients), platelet-rich plasma (n=1, 47 patients), chymopapaine (n=1, 39 patients) and rhGDF-5 (n=2, 55 patients) and were included in a narrative synthesis. Standardized mean differences (SMD) of GC IDT for LBP intensity and activity limitations were -1.33 (-2.34;-0.32) and -0.76 (-1.85;0.34) at short-term, -2.22 (-5.34;0.90) and -1.60 (-3.51;0.32) at intermediate-term and -1.11 (-2.91;0.70) and -0.63 (-1.68;0.42) at long-term, respectively. OR of GC IDT for serious and minor adverse events were 1.13 (0.20; 4.59) and 0.97 (0.49;1.91).

Conclusion: GC IDT are associated with a reduction in LBP intensity at short-term in people with NScLBP. Positive effects are not sustained. There is no effect on activity limitations.

REFERENCES:

[1] Knezevic NN, Mandalia S, Raasch J, Knezevic I, Candido KD. Treatment of chronic low back pain - new approaches on the horizon. J Pain Res. 2017;10:1111-23.

[2] Chiarotto A, Boers M, Deyo RA, Buchbinder R, Corbin TP, Costa LOP, et al. Core outcome measurement instruments for clinical trials in nonspecific low back pain. Pain. 2018;159(3):481-95.

[3] Team QAaSM. Safety of medicines : a guide to detecting and reporting adverse drug reactions : why health professionals need to take action. In: Organization WH, ed. Geneva; 2002.

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OP0103 EFFECTS ON A FRENCH MASS MEDIA CAMPAIGN ON BACK PAIN BELIEFS AND BEHAVIORS

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Background: Low back pain (LBP) in general and chronic LBP specifically is frequent with high impact on both individuals and Society. In 2017, the French national public health insurance (CNAMTS, Caisse Nationale d'Assurance Maladie des Travailleurs Salariés) has decided to launch a countrywide mass media campaign to improve general population (POP) and general practitioners (GPs) beliefs and behaviors about LBP and tend to reduce its impact on health resource use and including sick leaves.

Objectives: To evaluate the impact on population and physician beliefs and behaviors of the nationwide population-based campaign on LBP.

Methods: A campaign was conducted by the CNAMTS with the help of health experts (rheumatologists, rehabilitation specialists, algologists, GP and physiotherapists). It ran between November 2017 and November 2018, using multi media: booklets for POP and GPs available on CNAMTS website, TV and radio spots, large size wall posters hanged in public areas, videos on social networks, publicity articles and a smartphone application. The campaign main messages were: "LBP is not a severe disease" and "rest doesn't help to heal" with a tagline: "Low back pain? The right treatment is the movement". The impact of the campaign was assessed by internet surveys conducted by a private polling company (BVA, Brulé, Ville et Associés), in random samples of the two populations (POP and GP). The respondents were selected according to the quota method, which enabled adequate representativeness based on sex, age, region of living and socio-economic status. The pre-test survey was performed on June 2017 and the post-test in May 2018, 6 months after beginning of the campaign. The questions explored different domains: 1) memorization, understanding and perception of the campaign, 2) knowledge and beliefs about LBP, and 3) repercussions on behaviors. Statistical significance at 5% was assessed with student test for means and sd, and chI2 test for categorical variables.

Results: Among the 2000 POP, 92% have already experienced LBP with mean pain intensity of 5.7/10 on VAS. Among the 400 GPs, 74% reported to be consulted for LBP almost every day. 35% of the POP and 74% of GPs saw, read or listened to the campaign. Overall, it was well perceived with an average rating of 7.0 and 7.3/10, respectively. POP and GP beliefs and behaviors about LBP are summarized in the table 1. There were statistically significant improvements in beliefs and behaviors related to activity in both populations. GPs are more confidence in preventing chronicization of back pain and declare to prescribe less sick leave superior to 5 days.

Table 1. Evolution in beliefs and behaviors concerning LBP in GPs and POP before and after campaign

Questions		% of agreement		p
		Pre-test	Post-test	
POP		n=2000	n=2000	
Beliefs	We have to maintain activity	56%	74%	<.001
	The best treatment is rest	68%	45%	<.001
Behaviors	You try to continue daily life independently of pain	46%	54%	<.001
	You practice activity to heal	15%	25%	<.001
GPs		n=400	N=400	
Beliefs	We have to maintain activity	88%	95%	=.001
	The best treatment is rest	33%	14%	<.001
	It is easy to prevent chronicization	31%	43%	<.001
Behaviors	% of sick leaves >5 days prescribed last year	51%	33%	<.001

Conclusion: The French media campaign appears to have significant impact on public and physicians beliefs, mainly related to the message of staying active. An additional campaign focused on employers and occupational therapists is

currently conducted. Other outcomes, of which health resource use and sick leave, will be assessed at the end of the program.

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WEDNESDAY, 12 JUNE 2019

Personalised medicine in rheumatic disease

OP0104 THE PRESENCE OF BLOOD IN THE JOINT AND THE IMMEDIATE MOLECULAR RESPONSE IN SYNOVIAL FLUID ARE INDEPENDENTLY ASSOCIATED WITH WORSE CLINICAL OUTCOMES AT 2 YEARS AFTER HUMAN KNEE INJURY

Cesar Garriga[1,2], Megan Goff[1], Kirsten Leyland[3,4], Erin Paterson[1], Renata Hrusecka[1], Benjamin Hamid[1], Lesley Honeyfield[5], Keshthra Satchithananda[5], Adrian Lim[5], Nigel Arden[3], Andrew Judge[3,6], Andy Williams[1,7], Tonia Vincent[1], Fiona Watt[1]. *[1]University of Oxford, Arthritis Research UK Centre for Osteoarthritis Pathogenesis Kennedy Institute of Rheumatology Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; *[2]University of Oxford, Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom*; *[3]University of Oxford, Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Nuffield Orthopaedic Centre, Oxford, United Kingdom*; *[4]University of Bristol, Southmead Hospital, National Institute for Health Research Bristol Biomedical Research Centre (NIHR Bristol BRC), University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom*; *[5]Imperial College Healthcare NHS Trust, St Mary's Hospital, London, United Kingdom*; *[6]University of Bristol, Musculoskeletal Research Unit, Translational Health Sciences, Bristol Medical School, Bristol, United Kingdom*; *[7]Fortius Clinic, London, United Kingdom*

Background: Knee injury increases the risk of knee osteoarthritis at least 7 fold. We have shown an immediate inflammatory response to acute knee injury which is measurable both in mouse joint tissues and also in human synovial fluid (SF).

Objectives: We set out to test whether the measured immediate inflammatory protein response in SF or plasma/serum was associated with knee symptoms at 2 years after knee injury.

Methods: 150 individuals were recruited within 8 weeks of a significant acute knee injury to the Knee Injury Cohort at the Kennedy (KICK; REC 10/H0805/39; NCT02667756) from 2011-2014. The primary outcome was the Knee Injury and Osteoarthritis Outcome Score (KOOS)-4 at 2 years (a composite measure of 4 KOOS domains, where 100 is normal knee health). Baseline covariates were sex, age, body mass index (BMI), clinical effusion, SF blood staining, radiographic Kellgren/Lawrence (KL) Grade. 14 SF and 4 plasma/serum biomarkers were defined based on our prior translational studies. Regression models assessed association of biomarkers with 2 year KOOS4, adjusting for significant covariates.

Results: 123/150 (82%) were male, mean age (SD) 27(8) years and BMI 26(4) kg/m^2. Mean KOOS4 increased from 38(18) at baseline to 70(18) at 2 years. 64 (43%) had KL 0/1, 24 (16%) KL 2 and 11 (7%) KL 3, 75 (50%) medium/large effusion and 50 (39%) moderate/severe SF blood staining.

Medium/large knee effusion (-7.2(-13.5,-0.9)P=0.025) and moderate/severe SF blood staining (-10.1(-18.6,-1.6)P=0.02) were significant. Significant biomarkers adjusted for these covariates are shown in Table. MCP-1 and IL-6 were each significantly associated with 2 year KOOS4 independently in the fully adjusted model and in the multivariable model.

	Adjusted simple linear model (by baseline KOOS4)		Fully adjusted model (by baseline KOOS4, blood staining and effusion)	
SF biomarker (pg/ml)	coef (95% CI)	*P*	coef (95% CI)	*P*
MCP-1	-0.020 (-0.029, -0.011)	0.00005	-0.015 (-0.027, -0.004)	0.01
FGF-2	-0.047 (-0.087, -0.007)	0.02	-0.021 (-0.059, -0.017)	0.28
IL-6	-0.0006 (-0.0010, -0.0003)	0.001	-0.0005 (-0.0009, -0.0001)	0.02
TGFβ	-0.0028 (-0.0053, -0.0003)	0.03	-0.0018 (-0.0042, 0.0006)	0.14
IL-18	-0.078 (-0.147, -0.008)	0.03	-0.02 (-0.11, 0.08)	0.75

Conclusion: Those with higher levels of SF MCP-1 and IL-6 at the time of injury had a significantly worse outcome at 2 years. The presence of haemarthrosis, clinical effusion and impairment/pain at the time of injury were also independent predictors of outcome. In contrast, no baseline plasma/serum markers were associated with outcome. Stratifying individuals at high risk of persistent symptoms after knee injury may enable clinical trials of interventions to prevent or treat PTOA.

Disclosure of Interests:: Cesar Garriga: None declared, Megan Goff: None declared, Kirsten Leyland: None declared, Erin Paterson: None declared, Renata Hrusecka: None declared, Benjamin Hamid: None declared, Lesley Honeyfield: None declared, Keshthra Satchithananda: None declared, Adrian Lim: None declared, Nigel Arden Grant/research support from: Grants from BIOIBERICA, and from MERCK., Consultant for: Personal fees from Flexion, from Regeneron, from Freshfields Bruckhaus Deringer, outside the submitted work., Andrew Judge Grant/research support from: Consortium research grants from Roche, Consultant for: Received consultancy fees, lecture fees and honoraria from Servier, UK Renal Registry, Oxford Craniofacial Unit, IDIAP Jordi Gol and Freshfields Bruckhaus. Member of Deringer Data Safety and Monitoring Board for Anthera Pharmaceuticals, Inc. Consultancy for Freshfields Bruckhaus Deringer, Andy Williams: None declared, Tonia Vincent: None declared, Fiona Watt Grant/research support from: Pfizer and Astellas clinical study grants (not in this area)

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WEDNESDAY, 12 JUNE 2019

The riddle of adherence

OP0105-HPR DO MOBILE APPS IMPROVE SHARED DECISION MAKING AND DISEASE MANAGEMENT IN THE RHEUMATIC DISEASES? AN EVALUATION OF APPS IN A SWISS RHEUMATOLOGY REGISTRY

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Background: From 2015 to 2018, the Swiss Clinical Quality Management in Rheumatic Diseases registry (SCQM) offered two mobile apps, iDialog and COmPASS, allowing patients to track disease and health status between rheumatology visits. Both apps are linked to the registry database, providing patients and physicians extra information to guide disease management decisions.

Objectives: To investigate the effect of SCQM app use on shared decision making (SDM) and disease management.

Methods: Patients were administered a cross sectional survey about satisfaction with SDM [1], disease management, and app use (February-December 2018). Patients' demographic data and longitudinal data on disease status, health status, and medication use was extracted from the SCQM database.

Analyses included patients diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA), or axial spondyloarthritis (axSpA) who had 1) used an SCQM app for at least 6 months and discussed app data with their physician (app + discussion group), 2) used an SCQM app for at least 6 months and did not discuss app data with their physician (app only group), or 3) did not use any SCQM app (non-app users).

We compared the 3 groups by conducting logistic regressions for the following dichotomized outcomes: maximum satisfaction with SDM and physician following the evolution of the disease, low disease activity at the most recent SCQM visit, disease activity improvement in the last year of followup, and treatment intensification (adding/increasing the dose of a disease-modifying antirheumatic drug) in the last 6 months of followup. Regressions were weighted using multinomial propensity scores to balance differences in baseline characteristics between the 3 groups.

Results: 1924 patients were included in the analyses. App users were younger than non-app users (Table 1). In adjusted analyses (Table 2), satisfaction rates were higher in the app + discussion group (p<0.05) compared to non-app users, but not for the app only group. The app only group had higher rates of treatment intensification in the last 6 months of followup (p=0.02) compared to non-app users. Although the app only and app + discussion groups had higher adjusted rates of other disease management outcomes compared to non-app users, the effects were not statistically significant.

Conclusion: App users who communicated with their rheumatologist about their app data were more satisfied with their physicians than app users who did not communicate about their app data and non-app users. Provision of apps that increase the frequency of disease monitoring may have limited impact on patient satisfaction with care and disease management processes without integration of app use into existing care processes.

REFERENCES:
[1] Elwyn G, et al. Developing CollaboRATE: A fast and frugal patient-reported measure of shared decision making in clinical encounters. Patient Education and Counseling 2013;93:102-107.
[2] Coates LC, et al. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis 2010;69:48-53.

Table 1. Baseline characteristics

	Mean (standard deviation) or %			
	App use (n=128)	App use + discussion (n=158)	No app use (n=1638)	P-value#
Age in years	42.44 (12.11)	43.62 (13.15)	47.77 (13.21)	<0.001
% Male	44.5%	45.9%	42.0%	0.572
Diagnosis				0.030
% RA	35.9%	38.2%	43.8%	
% PsA	21.1%	16.6%	21.6%	
% axSpA	43.0%	45.2%	43.8%	
Disease duration in years	16.10 (4.28)	16.49 (4.19)	16.53 (4.69)	0.596
Low disease activity at baseline	35.8%	40.3%	34.3%	0.356

#Test of difference between groups
*Low disease activity was defined as DAS28 < 3.2 in RA and BASDAI ≤ 4 in axSpA. In PsA, it was defined as fulfilling at least 5 of 7 criteria for minimal disease activity [2].

Table 2. Association of app use with patient satisfaction and disease management

Outcome	Odds Ratio [95% CI] (reference group: no app use)	
	App use only	App use + discussion
Satisfaction with shared decision making*	0.79 [0.53, 1.17]	1.74 [1.14, 2.66]
Satisfaction with following evolution of disease*	0.73 [0.49, 1.09]	2.07 [1.36, 3.14]
Low disease activity at last visit*	1.08 [0.67, 1.72]	1.30 [0.82, 2.08]
Improved disease activity*	1.10 [0.69, 1.76]	1.54 [0.98, 2.40]
Treatment intensification*	1.82 [1.10, 3.01]	1.08 [0.66, 1.95]

*Total=1924 (app use only=128, app use + discussion=158, no app use=1638) & Total=1141 (app use only=106, app use + discussion=114, no app use=921)

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THURSDAY, 13 JUNE 2019

From the cradle to the grave – what does paediatric disease teach us about adult disease?

OP0106 A NOVEL KNOCK-IN MOUSE MODEL OF CAPS THAT DEVELOPS AMYLOIDOSIS: THERAPEUTIC EFFICACY OF PROTON PUMP INHIBITORS

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Background: Cryopyrin associated periodic syndromes (CAPS) are a group of autoinflammatory diseases linked to gain-of-function mutations in the NLRP3 gene that cause uncontrolled IL-1β secretion. CINCA syndrome is the most severe CAPS disease characterized by central nervous system disabilities with a long-term risk of secondary amyloidosis.
Proton pump inhibitors (PPIs), commonly used as inhibitors of gastric acid production, also display anti-inflammatory properties, making them promising drugs in sepsis and in inflammatory disorders.
Objectives: To develop a novel NLRP3 knock-in (KI) mouse model of CAPS to evaluate amyloid deposition and to test alternative therapeutic approaches.
Methods: We generated KI mice by engineering N475K mutation associated with CAPS phenotype into mouse *Nlrp3* gene. KI and Wild Type (WT) mice received PPIs or PBS intraperitoneally and were analyzed for survival, inflammation, cytokine secretion, and amyloidosis development. Cytokines secretion from bone marrow derived dendritic cells (BMDCs) and peritoneal macrophages (PMs) was evaluated by ELISA. Hystological analysis of all organs was evaluated by hematoxylin and eosin staining. Amyloid deposition was quantified through Congo Red staining.
Results: Mutant NLRP3 KI mice displayed features that recapitulates the immunological and clinical phenotype of CAPS. These mice had systemic inflammation, with high levels of serum pro-inflammatory cytokines compared to WT controls. Hystological analysis revealed the presence of acute and chronic inflammatory cell infiltrates and amyloid deposits in spleen, liver and kidneys. As in CAPS monocytes, BMDCs and PM from KI mice showed a strong increase in IL-1β, IL-18, and IL-1α secretion and decreased levels in interleukin-1 receptor antagonist (IL-1Ra), the naturally occurring IL-1b inhibitor.
PPIs treatment of KI mice showed a clear clinical impact with improvement of inflammatory conditions and regression of amyloid deposits. Remarkably, BMDCs and PMs from PPI-treated mice presented reduced secretion of pro-inflammatory cytokines and re-established the levels of IL-1RA.
Conclusion: NLRP3 KI mice display a CAPS phenotype with many characteristics of autoinflammation, including amyloidosis. The therapeutic effectiveness associated with lack of toxicity indicates that PPIs could represent relevant adjuvants to the anti-IL-1 drugs in IL-1 driven diseases.

REFERENCES:
[1] Gattorno M, Martini A. Beyond the NLRP3 inflammasome: autoinflammatory diseases reach adolescence. Arthritis Rheum. 2013;
[2] Brydges SD, Mueller JL, McGeough MD, Pena CA, Misaghi A, Gandhi C Putnam CD, et al. Inflammasome-mediated disease animal models reveal roles for innate but not adaptive immunity. Immunity. 2009;
[3] Balza E, Piccioli P, Carta S, Lavieri R, Gattorno M, Semino Cet al. Proton pump inhibitors protect mice from acute sistemic inflammation and induce long-term cross-tolerance. Cell Death Dis. 2016.

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I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:
AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.
The money received for these activities are directly transferred to the Gaslini Institute's bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Isabella Ceccherini: None declared, Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis, Anna Rubartelli: None declared, Sabrina Chiesa: None declared
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OP0107 **HETEROZYGOUS MUTATIONS IN COPA ARE ASSOCIATED WITH ENHANCED TYPE I INTERFERON SIGNALLING**

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Background: Heterozygous mutations in *COPA*, encoding coatomer protein subunit alpha, cause an autosomal dominant inflammatory syndrome associating lung, joint and renal disease, showing some overlap with STING-associated vasculopathy with onset in infancy (SAVI). Mutations were originally described to cause endoplasmic reticulum (ER) stress and priming of a T helper 17 response. More recently, increased transcription of interferon (IFN)-stimulated genes (ISGs) was reported in blood circulating cells of affected individuals. However, the precise pathophysiology of this disease remains unclear.
Objectives: To better decipher the mechanism of COPA syndrome.
Methods: We studied 8 patients from 3 unrelated families, each segregating a heterozygous mutation in *COPA*. We assessed type I IFN status by IFNα ultra-sensitive digital quantification in plasma, STAT1 phosphorylation and RNA expression of ISGs in whole blood from patients. *In vitro* assays also were performed in HEK293T and THP-1 cells to study IFN signalling in the context of COPA mutations.
Results: We observed commonalities in the lung pathology between COPA and SAVI, as well as an IFN signature, raised levels of IFNα protein in the serum and phosphorylation of STAT1 in patient T cells. In a cellular model of HEK293T, phosphorylation of IRF3 and increased ISG expression were observed in cells co-transfected with wild type STING and mutant COPA plasmids. In THP-1 cells, short hairpin RNA knockdown of COPA induced IFN signalling that was abrogated in the absence of STING.
Conclusion: Our data suggest that mutations in *COPA* lead to constitutive activation of type I IFN signalling through STING. Based on these results, one patient has been treated with the JAK1/2 inhibitor ruxolitinib for the last 12 months. How COPA interacts with ER-resident STING remains to be investigated.

REFERENCES:
[1] Watkin et al, Nat Genet 2015;47:654-60.
[2] Volpi et al, Clin Immunol 2018;187:33-36.

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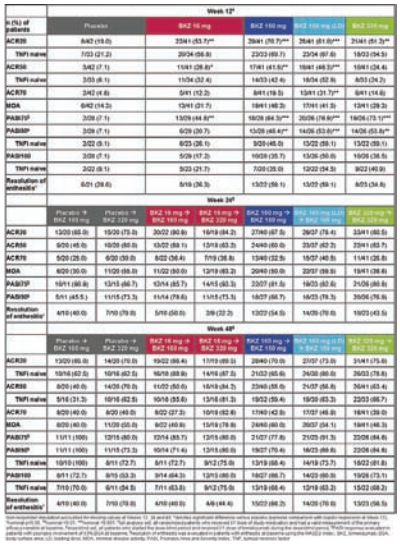
THURSDAY, 13 JUNE 2019

Psoriatic arthritis: old and new drugs and how to deal with them?

OP0108 **DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH BIMEKIZUMAB IN PATIENTS WITH ACTIVE PSA: OVERALL AND TNF-INHIBITOR-NAÏVE POPULATION RESULTS FROM A 48-WEEK PHASE 2B RANDOMISED STUDY**

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Background: IL-17F shares structural homology and pro-inflammatory function with IL–17A. Preclinical and early clinical data support neutralisation of IL-17F, in addition to IL–17A, as a novel targeting approach in psoriatic disease.
Objectives: The objective of this Phase 2b study (NCT02969525) was to assess the dose response, long-term efficacy and safety of bimekizumab (BKZ), a mAb that potently and selectively neutralises IL-17A and IL-17F, over 48 weeks in patients (pts) with active PsA.
Methods: 206 pts with active PsA, ≥3/76 swollen joint count, ≥3/78 tender joint count and CASPAR score ≥3, were randomised (1:1:1:1:1) to receive subcutaneous BKZ 16mg, 160mg, 160mg with 320mg loading dose (160mg [LD]), 320mg or placebo (PBO) Q4W, for 12 weeks (double-blind period). After Week 12, pts receiving PBO or BKZ 16mg were re-randomised (1:1) to BKZ 160mg or 320mg; all other pts continued on their initial dose (dose-blind period). The primary endpoint was ACR50 response at Week 12.



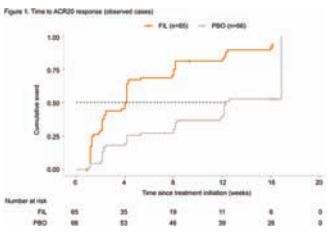
Results: 203/206 and 189/206 pts completed the double- and dose-blind periods, respectively. Overall, demographics and baseline disease characteristics were balanced across groups. 19% of pts had prior exposure to TNF inhibitors (TNFi). There was a statistically significant ($p<0.05$) dose-response at Week 12 for ACR50 response rates. At Week 12, significantly more pts receiving BKZ versus PBO achieved ACR50 (primary endpoint: 16–160mg [LD] doses), ACR20 and PASI90 (in those pts with baseline body surface area ≥3%; 160–320mg doses) (table). ACR20/50/70, PASI75/90/100, MDA and resolution of enthesitis response rates increased between Week 12 and Week 24 in those continuing on their initial BKZ dose; Week 24 responses were maintained through the study; responses were similar across the three highest dose groups at Week 48 (PASI100 analyses were *post hoc*). Rapid improvements were observed across all response criteria in pts re–allocated to BKZ 160 or 320mg (table). BKZ-treated pts naïve to TNFi achieved ACR20/50 and PASI90/100 at comparable rates to the overall population at Week 12 and 48. There was no apparent relationship between dose and TEAEs. Serious AEs were reported by 9/206 (4.4%) pts up to Week 48 (8/206 [3.9%] patients were receiving BKZ). The most common TEAE up to Week 48 was nasopharyngitis 25/206 [12.1%]). Oral candidiasis was reported at Week 48 by 10/206 (4.9%) pts (all cases during BKZ treatment). No deaths, or cases of IBD or MACE were reported.
Conclusion: Dual neutralisation of IL-17A and IL-17F with BKZ provided substantial improvements in both musculoskeletal and skin outcomes; response rates increased after Week 12 (primary analysis) and were sustained from Week 24 to 48, with a safety profile consistent with previous BKZ studies. These data provide further support that neutralising IL–17F in addition to IL-17A with BKZ is a promising therapeutic approach in pts with active PsA.
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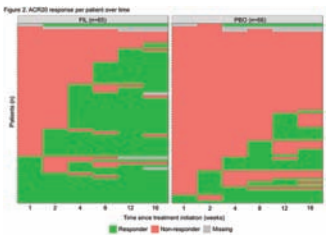
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OP0109 EFFICACY OF FILGOTINIB VS PLACEBO IN ACTIVE PSORIATIC ARTHRITIS: PATIENT-LEVEL DATA FROM EQUATOR, A RANDOMIZED, PHASE 2 STUDY

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Background: Filgotinib (FIL) is an oral, selective Janus kinase 1 inhibitor in development for the treatment of several inflammatory diseases. In the phase 2 EQUATOR trial (NCT03101670), FIL was efficacious vs placebo (PBO) in patients with active psoriatic arthritis (PsA), and was well tolerated [1].
Objectives: To evaluate the onset and maintenance of response to FIL vs PBO in EQUATOR by evaluating patient–level response over time.
Methods: EQUATOR was a 16-week, multicenter, double-blind study in which patients with active PsA were randomized 1:1 to FIL 200 mg or PBO once daily [1]. Disease activity was assessed at screening, day 1 and weeks 1, 2, 4, 8, 12 and 16, and the primary efficacy endpoint was the proportion of patients achieving 20% American College of Rheumatology (ACR20) response. The onset of response was assessed by calculating the median time to ACR20 response using the Kaplan-Meier method and compared between FIL and PBO using the log-rank test. Maintenance of response was assessed by analysing ACR20 response patterns over time in the FIL and PBO groups.
Results: Of 131 patients randomized (FIL: n=65; PBO: n=66), 124 (95%) completed the study. Demographics and baseline disease characteristics were similar between groups. The onset of response to FIL was early, with a median (95% confidence interval) time to first ACR20 response of 4.07 weeks (2.29, 4.14) in the FIL group compared with 12.29 weeks (12, not reached) in the PBO group (p<0.0001; Figure 1). ACR20 responses were achieved at week 16 in 80.0% (52/65) and 33.3% (22/66) of patients in the FIL and PBO groups, respectively, using the non-responder imputation method, and 86.7% (52/60) and 34.4% (22/64), respectively, using observed cases. The number of patients who presented with a stable ACR20 response (i.e. the response was maintained once initially achieved regardless of the time point at which the patient first became a responder) among those who were responders at week 16 (i.e. the primary endpoint) was higher in the FIL group than in the PBO group (80.8% [42/52] vs 68.2% [15/22]) (**Figure 2**). Similar trends were observed for other efficacy endpoints representing various manifestations of PsA.
Conclusion: In general, patients treated with FIL achieved an ACR20 response earlier than those on PBO and these responses appeared to be more stable. In the PBO group, there were more occurrences of the response being lost over time and fewer cases of regaining a lost response.





REFERENCE:
[1] Mease P, et al. Lancet 2018;392:2367–77.

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OP0110 IXEKIZUMAB IMPROVES SIGNS AND SYMPTOMS OF PSORIATIC ARTHRITIS IN PATIENTS WHO HAVE HAD INADEQUATE RESPONSE TO 1 OR 2 TUMOR NECROSIS FACTOR INHIBITORS

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Background: Psoriatic arthritis (PsA) is a progressive, chronic inflammatory disease often treated with tumor necrosis factor inhibitors (TNFi) when conventional treatments fail. Patients with inadequate response to TNFi represent a more difficult-to-treat population.
Objectives: To report the efficacy of ixekizumab (IXE), a monoclonal antibody that selectively targets interleukin-17A, in patients with inadequate response to 1 TNFi or 2 TNFi.
Methods: In a Phase 3 study (SPIRIT-P2; NCT02349295), patients who had an inadequate response or intolerance to 1 or 2 TNFi were randomized to receive subcutaneous IXE 80 mg every 2 weeks (IXEQ2W; N=123) or every 4 weeks (IXEQ4W; N=122), after a 160-mg starting dose, or placebo (PBO; N=118) for up to 24 weeks. At Week 16, patients not meeting predefined criteria (<20% improvement in tender joint count [TJC] and swollen joint count [SJC]) received rescue therapy and were imputed as nonresponders at Weeks 20 and 24. At Week 24, PBO patients were rerandomized to IXEQ2W or IXEQ4W through Week 52 and excluded from the 52-week analysis. At Week 32 or any subsequent visit, patients were discontinued if they did not reach ≥20% improvement from baseline in both TJC and SJC. These ad-hoc data were derived from patients in the intent-to-treat population with prior inadequate response to TNFi; intolerant patients were excluded from the analysis. Efficacy was measured by percentage of patients who attained ≥50% improvement in American College of Rheumatology response criteria (ACR50), an improvement in Health Assessment Questionnaire-Disability Index (HAQ-DI) ≥0.35, minimal disease activity (MDA), Disease Activity Score 28 – C-reactive protein (DAS28-CRP) EULAR Good Response criteria, and Disease Activity in Psoriatic Arthritis (DAPSA) ≤14.
Results: At baseline, 1-TNFi inadequate responders were, on average, 52 years of age with a PsA diagnosis for 10 years; 40% were using MTX, and HAQ-DI was 1.2. 2-TNFi inadequate responders were 52 years of age with a PsA diagnosis for 11 years; 42% were using MTX, and HAQ-DI was 1.3. Regardless of inadequate response to 1 or 2 TNFi, at Week 24 significantly more patients receiving Q4W or

Q2W than PBO attained ACR50, improvement in HAQ-DI ≥0.35, MDA, DAS28-CRP, and DAPSA ≤14. Improvement persisted on all measures through Week 52.

	1-TNFi Inadequate Responder n/N (%)			2-TNFi Inadequate Responder n/N (%)		
	PBO	Q4W	Q2W	PBO	Q4W	Q2W
ACR50						
Week 24	2/68 (2.9%)	24/71 (33.8%)**	19/65 (29.2%)**	3/41 (7.3%)	15/41 (36.6%)*	16/46 (34.8%)*
Week 52	–	29/71 (40.8%)	20/65 (30.8%)	–	18/41 (43.9%)	13/46 (28.3%)
Improvement in HAQ-DI ≥0.35[a]						
Week 24	9/61 (14.8%)	28/61 (45.9%)**	19/58 (32.8%)*	7/38 (18.4%)	16/36 (44.4%)*	20/41 (48.8%)*
Week 52	–	32/61 (52.5%)	18/58 (31.0%)	–	14/36 (38.9%)	13/41 (31.7%)
MDA						
Week 24	3/68 (4.4%)	22/71 (31.0%)**	14/65 (21.5%)*	1/41 (2.4%)	8/41 (19.5%)*	13/46 (28.3%)**
Week 52	–	26/71 (36.6%)	17/65 (26.2%)	–	11/41 (26.8%)	7/46 (15.2%)
DAPSA ≤14						
Week 24	11/68 (16.2%)	30/71 (42.3%)**	24/65 (36.9%)*	2/41 (4.9%)	14/41 (34.1%)*	12/46 (26.1%)*
Week 52	–	41/71 (57.7%)	26/65 (40.0%)	–	18/41 (43.9%)	14/46 (30.4%)
DAS28-CRP Good Response Criteria[b]						
Week 24	7/68 (10.3%)	33/71 (46.5%)**	24/65 (36.9%)**	2/41 (4.9%)	17/41 (41.5%)**	16/46 (34.8%)**
Week 52	–	38/71 (53.5%)	27/65 (41.5%)	–	19/41 (46.3%)	15/46 (32.6%)

*P<0.05 vs. PBO, **P<0.001 vs. PBO, Fisher's exact test. Missing values imputed using nonresponder imputation.
[a]Patients with ≥0.35 HAQ-DI at baseline.
[b]Good response criteria defined as >1.2 improvement and ≤3.2 present DAS28-CRP.

Conclusion: Both IXE Q4W and Q2W improved the signs and symptoms of PsA in a population of difficult-to-treat patients who have had inadequate response to 1 or 2 TNFi.

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OP0111 A RANDOMIZED, PHASE 3, DOUBLE-BLIND TRIAL EXAMINING METHOTREXATE AND ETANERCEPT AS MONOTHERAPY OR IN COMBINATION FOR TREATING PSORIATIC ARTHRITIS: A COMPARISON OF THE COMPOSITE MEASURES USED TO EVALUATE DISEASE ACTIVITY

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Background: Optimal treatment regimens and measuring outcomes in psoriatic arthritis (PsA) remain key areas of research.
Objectives: To examine methotrexate (MTX) and etanercept (ETN) as monotherapy or in combination in a randomized trial and assess the relative performance of PsA-specific composite measures using trial efficacy data.
Methods: Patients with active PsA naïve to biologic drugs (no prior MTX for PsA) were randomized to 3 groups for 48 weeks: ETN 50mg+MTX 20mg weekly (Combo; N=283); ETN 50mg+placebo weekly (ETN-mono; N=284); or MTX 20mg+placebo weekly (MTX-mono; N=284). At week 24, the American College of Rheumatology (ACR)20 and Minimal Disease Activity (MDA) responses were the primary and key secondary endpoints, respectively. Other PsA-specific composite measures used for disease activity included the Psoriatic Arthritis Disease Activity Score (PASDAS) and Disease Activity Index for Psoriatic Arthritis (DAPSA).
Results: Baseline characteristics were well balanced in the 3 arms. Mean (SD) age was 48.4 (13.1) years and mean/median PsA duration 3.2/0.6 years. ACR20 and MDA responses at week 24 were significantly greater with ETN-mono vs MTX-mono and Combo vs MTX-mono; ETN-mono and Combo had similar results (Table). PASDAS also showed differences between each ETN-containing arm vs MTX-mono and no difference for ETN-mono vs Combo, whereas study arm differences were not seen with DAPSA. PASDAS had a greater effect size and standardized response than DAPSA.
Conclusion: In this large randomized, controlled PsA trial, ETN-mono or Combo had greater efficacy than MTX-mono. Combining ETN and MTX did not improve ETN efficacy. Compared with the joint-focused DAPSA, PASDAS captured a wider range of PsA manifestations and performed better in this trial.

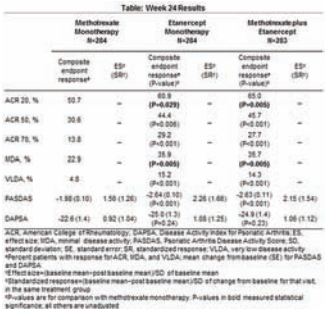


Table: Week 24 Results

	Methotrexate Monotherapy N=284		Etanercept Monotherapy N=284		Methotrexate plus Etanercept N=283	
	Composite endpoint response*	ES† (SRM)	Composite endpoint response* (P-value)‡	ES† (SRM)	Composite endpoint response* (P-value)‡	ES† (SRM)
ACR 20, %	50.7	–	60.9 (P=0.029)	–	65.0 (P=0.005)	–
ACR 50, %	30.6	–	44.4 (P=0.006)	–	45.7 (P<0.001)	–
ACR 70, %	13.8	–	29.2 (P<0.001)	–	27.7 (P<0.001)	–
MDA, %	22.9	–	38.9 (P=0.005)	–	36.7 (P=0.005)	–
VLDA, %	4.8	–	15.2 (P<0.001)	–	14.3 (P<0.001)	–
PASDAS	-1.98 (0.10)	1.58 (1.26)	-2.64 (0.10) (P<0.001)	2.26 (1.68)	-2.63 (0.11) (P<0.001)	2.15 (1.54)
DAPSA	-22.6 (1.4)	0.92 (1.04)	-25.0 (1.3) (P=0.24)	1.66 (1.25)	-24.9 (1.4) (P=0.23)	1.06 (1.12)

ACR, American College of Rheumatology; DAPSA, Disease Activity Index for Psoriatic Arthritis; ES, effect size; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; SD, standard deviation; SE, standard error; SR, standardized response; VLDA, very low disease activity.
*Percent patients with response for ACR, MDA, and VLDA; mean change from baseline (SE) for PASDAS and DAPSA.
†Effect size=(baseline mean−post baseline mean)/SD of baseline mean
‡Standardized response=(baseline mean−post baseline mean)/SD of change from baseline for that visit, in the same treatment group.
§P-values are for comparison with methotrexate monotherapy. P-values in bold measured statistical significance; all others are unadjusted

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OP0112 UNACCEPTABLE PAIN DESPITE INFLAMMATION CONTROL AFTER START OF A FIRST ANTI-TNF THERAPY IN PATIENTS WITH PSORIATIC ARTHRITIS AND ITS RELATION TO TREATMENT RESPONSE

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Background: Pain is a major concern of patients with inflammatory arthritides, but while considerable focus has been put on the occurrence and

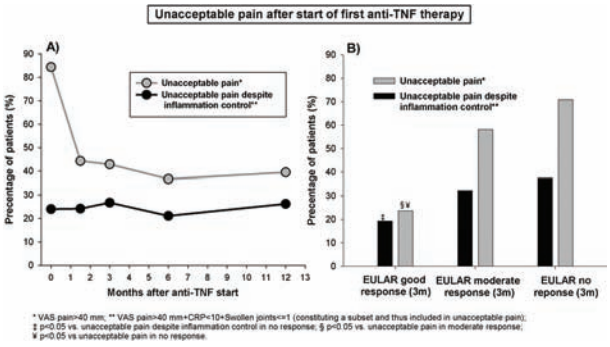
management of pain due to inflammation, less is reported on pain despite inflammation control, with most such reports addressing rheumatoid arthritis (RA).

Objectives: To investigate the prevalence of pain despite inflammation control after start of a first anti-TNF therapy in psoriatic arthritis (PsA) patients and its relation to EULAR treatment response.

To test the feasibility of a network analysis approach to examine associations between clinical variables and mental health symptoms in RA.

Methods: PsA patients starting a first anti-TNF therapy 2004-2010 were identified in the prospective, observational South Swedish Arthritis Group register (n= 352, 48% women), with mean age 47 years and mean disease duration 10 years. At anti-TNF start, 63% of patients had ongoing methotrexate and 68% were on any conventional DMARD(s). Based on the patient acceptable symptom state (PASS) 1, unacceptable pain was defined as >40 mm on a Visual Analogue Scale (VAS) of pain (scale 0-100 mm), and concomitant inflammation control (as in earlier RA studies) was captured through CRP<10 mg/L,2 in combination with <1 swollen joint (of 28).3 Assessments were performed at baseline, 1.5, 3, 6 and 12 months after anti-TNF start. Furthermore, analyses were conducted in relation to EULAR treatment response after 3 months (good, moderate, no response). Differences in pain measures between treatment response groups were estimated by logistic regression.

Results: At start of a first anti-TNF therapy, 84.5% of PsA patients reported unacceptable pain, which declined to 42.9% after 3 months and then remained stable during the rest of the study period, being 39.5% at 12 months (Figure 1A). In contrast, the fraction showing unacceptable pain despite inflammation control was largely unchanged over the study period (24.0 % at treatment start, 26.7% at 3 months and 26.2% at 12 months). Unacceptable pain at 3 months was strongly related to EULAR 3-month response (23.7% of good responders vs. 70.8% of non-responders; p<0.001), whereas for unacceptable pain despite inflammation control the relation was less pronounced (19.3% of EULAR good responders vs 37.5% of non-responders, p=0.016). Among EULAR good responders, unacceptable pain despite inflammation control constituted 81% of all unacceptable pain at 3 months (Figure 1B).



Conclusion: A considerable proportion of PsA patients starting their first biological treatment reported unacceptable pain throughout the first treatment year. Among EULAR good responders non-inflammatory pain made up more than 4/5 of this pain load at 3 months, indicating insufficient effects of biologics on a subset of patients with inflammation-independent pain, and strongly warrants alternative treatment strategies in affected patients.

REFERENCES:

[1] Tubach et al. *Arthritis Care Res* 2012;64:1699-72.
[2] Lourdudoss et al. *Arthritis Care Res.* 2018;70:205-12.
[3] Olofsson et al. *Ann Rheum Dis* 2018;77:S2.

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OP0113

HISTOLOGICAL AND MOLECULAR PORTRAIT OF THE SYNOVIAL TISSUE IN EARLY TREATMENT-NAÏVE PSORIATIC ARTHRITIS IN COMPARISON WITH RHEUMATOID ARTHRITIS

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Background: Psoriatic Arthritis (PsA) and Rheumatoid Arthritis (RA) are autoimmune joint diseases characterised by chronic inflammation of the synovial tissue (ST). It has been previously suggested that PsA-ST has less marked hyperplasia of the synovial lining and fewer infiltrating T/B cells in comparison with RA. However, several confounders such as treatment, disease duration, sampling techniques and predominance of large joints samples may have influenced these findings.

Objectives: To compare the synovial features of PsA/RA at the beginning of the disease process and prior to any treatment for defining their histological/molecular individual characteristics, and to correlate the histological pattern with clinical parameters.

Methods: 183 consecutive treatment-naïve patients with <12 months symptoms and active synovitis of at least one joint were enrolled into the Pathobiology of Early Arthritis Cohort (PEAC) at the Barts Health NHS Trust, and underwent a baseline US-guided synovial biopsy of an inflamed joint. ST inflammatory infiltrate was evaluated by semi-quantitative score (0-4) of the immunostaining for CD68 (macrophages), CD3 (T cells), CD20 (B cells) and CD138 (plasma cells). Patients were classified as: pauci-immune if CD68sublining (SL)<2 and/or CD3-CD20-CD138<1; diffuse-myeloid if CD68SL≥2, CD20<2 or CD138<2; lymphoid-myeloid if CD20≥2 or CD138>2. RNA sequencing of the ST was performed on 93RA/15PsA patients.

Results: 39/183 patients were diagnosed with PsA (32 polyarticular, 7 oligoarticular) and 144/183 with RA (2010 ACR/EULAR criteria). Age was significantly lower in PsA patients. The comparison of the age-adjusted baseline variables showed: significantly higher number of tender and swollen joints in RA, but no significant differences between ESR, CRP and DAS28; higher US synovial thickening score of the biopsied joint in PsA, but comparable power-doppler. ST was obtained from small joints in 74.4% of PsA and 82% of RA. Histological comparison is summarised in Table 1 and 2. Only in RA, the pauci-immune pathotype associated with significantly lower ESR, CRP and DAS28 compared to lymphoid-myeloid; this association was maintained in a subset of 26 RA patients age- and gender-matched with the PsA population. Transcriptomic profiling showed that PsA-ST has significantly higher expression of the skin fibroblasts, eosinophils and neutrophils cellular gene modules. Genes significantly up regulated in PsA clustered in neutrophil recruitment/enrichment, cell migration and cytoskeleton remodelling modules.

	PsA (n=37)	RA (n=125)	*p value*
CD3	0.9 (1)	1.7 (1.3)	**0.0045***
CD20	0.8 (1.1)	1.4 (1.5)	**0.03***
CD68L	1.5 (1.3)	1.8 (1.2)	0.16
CD68SL	1.8 (1.2)	2.3 (1.2)	**0.04***
CD138	0.8 (1.2)	1.4 (1.5)	**0.02***

	PsA (n=37)	RA (n=125)	*p value*
Pauci-immune	16 (43.2%)	31 (24.8%)	0.056
Diffuse-Myeloid	12 (32.4%)	40 (32%)	
Lymphoid-Myeloid	9 (24.4%)	54 (43.2%)	

Conclusion: The identification of specific histological and molecular signatures characterising early-untreated PsA will help to better understand the disease pathogenesis and explore novel therapeutic targets.

REFERENCE:

[1] van Kuijk AW, Tak PP. Synovitis in psoriatic arthritis: immunohistochemistry, comparisons with rheumatoid arthritis, and effects of therapy. Curr Rheumatol Rep. 2011 Aug;13(4):353-9

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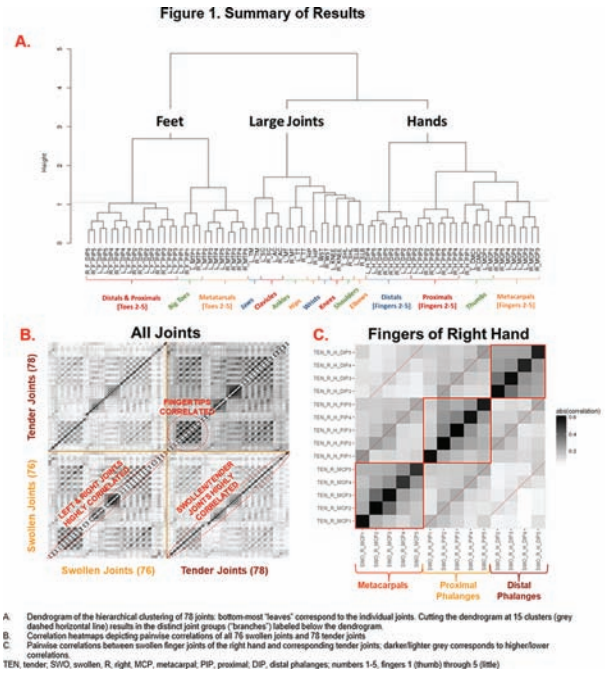
OP0114

MACHINE LEARNING TOOLS IDENTIFY PATIENT CLUSTERS AND SWOLLEN AND TENDER JOINT CORRELATION PATTERNS IN A LARGE DATABASE FROM THE SECUKINUMAB PSORIATIC ARTHRITIS CLINICAL DEVELOPMENT PROGRAM

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Background: Identifying patient phenotypes using machine-learning (ML) techniques amidst the variability and heterogeneity of the clinical manifestations of psoriatic arthritis (PsA) could be the first critical step towards better understanding of the disease eventually leading to individualized medicine.[1]
Objectives: To identify distinct clusters of patients with PsA based on patients' tender joint (TJ) and swollen joint (SJ) counts and correlation patterns among TJ and SJ counts at baseline as captured in the secukinumab FUTURE trials program.
Methods: Pairwise correlations were explored among 76 SJ and 78 TJ measurements of >2,700 patients with PsA across 5 phase III studies with ≈425,000 data entries at baseline and were visualized using heatmaps. Due to high correlations between SJs and corresponding TJs, a composite variable "swollen/tender joint count" was constructed for each joint. Hierarchical clustering was then performed on the composite using "1-correlation" as the dissimilarity metric and Ward's agglomeration method for pairwise grouping of joints. A dendrogram was used to visualize and assess the resulting joint groupings.
Results: The hierarchical clustering algorithm grouped the 78 individual joints into distinct and natural clusters (Figure 1A). At higher level of the dendrogram, the algorithm grouped separately all foot, larger (jaws, clavicles, ankles, hips, wrists, knees, shoulders, elbows), and hand joints. Cutting the dendrogram at 15 clusters separated all the joints into distinct groups; hand joints (distal and proximal phalanges, metacarpals and thumbs), and foot joints (distal and proximal phalanges, metatarsals and big toes). Similar clustering algorithms were explored to identify patient clusters at baseline with distinct swelling and tenderness patterns across the identified joint groups. High correlation between swelling/tenderness of the left and swelling/tenderness of the corresponding right joint was observed across all individual joints (Figure 1B); a high correlation was also observed between swelling and tenderness at all individual joints. More localized patterns showed that there is a gradual decrease in correlation (from highest to lowest) among TJs and SJs in adjacent vs non-adjacent fingers, which is evident from grey-scale patterns (Figure 1C). Specifically, a gradual decrease in correlation between the swelling of 2nd distal interphalangeal joint and the tenderness of the 2nd–5th distal phalanges was noted.
Conclusion: Machine learning methodology confirmed a natural grouping of joints in patients with psoriatic arthritis based on baseline swelling and tenderness and revealed complex correlation patterns. Additional cluster analyses have demonstrated distinct patient clusters across the identified joint groups. Further investigating potential associations of other disease manifestations such as skin and nail involvement to define additional phenotypes may explain differences in disease pathogenesis and treatment outcomes.

Figure 1. Summary of Results



A. Dendrogram of the hierarchical clustering of 78 joints: bottom-most "leaves" correspond to the individual joints. Cutting the dendrogram at 15 clusters (grey dashed horizontal line) results in the distinct joint groups ("branches") labeled below the dendrogram.
B. Correlation heatmaps depicting pairwise correlations of all 76 swollen joints and 78 tender joints
C. Pairwise correlations between swollen finger joints of the right hand and corresponding tender joints; darker/lighter grey corresponds to higher/lower correlations.
TEN, tender; SWO, swollen, R, right, MCP, metacarpal; PIP, proximal; DIP, distal phalanges; numbers 1-5, fingers 1 (thumb) through 5 (little)

REFERENCE:
[1] Grys BT, et al., J Cell Biol. 2017; 216(1): 65-71.

Disclosure of Interests: Matthias Kormaksson Shareholder of: Novartis, Employee of: Novartis, Effie Pournara Shareholder of: Novartis, Employee of: Novartis, Gregory Ligozio Shareholder of: Novartis, Employee of: Novartis, Luminita Pricop Shareholder of: Novartis, Employee of: Novartis, Ken Abrams Shareholder of: Novartis, Employee of: Novartis, Bruce Kirkham Grant/research support from: Abbvie, Janssen, Lilly, Novartis, Roche, UCB, Consultant for: Abbvie, Janssen, Lilly, Novartis, Roche, UCB, Speakers bureau: Abbvie, Janssen, Lilly, Novartis, Roche, UCB, Kristian Reich Consultant for: Abbvie, Affibody, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward Pharma, Fresenius Medical Care, GlaxoSmithKline, Janssen-Cilag, Kyowa Kirin, Leo, Lilly, Medac, Merck Sharp & Dohme Corp., Novartis, Miltenyi Biotec, Ocean Pharma, Pfizer, Regeneron, Samsung Bioepis, Sanofi, Takeda, UCB Pharma, Valeant, Xenoport; Speakers bureau: Abbvie, Affibody, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward Pharma, Fresenius Medical Care, GlaxoSmithKline, Janssen-Cilag, Kyowa Kirin, Leo, Lilly, Medac, Merck Sharp & Dohme Corp., Novartis, Miltenyi Biotec, Ocean Pharma, Pfizer, Regeneron, Samsung Bioepis, Sanofi, Takeda, UCB Pharma, Valeant, Xenoport, Iain McInnes Grant/research support from: AstraZeneca, Celgene, Compugen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Celgene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma
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OP0115

GENERAL AND SEX-SPECIFIC PREDICTORS OF PSA AMONG PATIENTS WITH PSORIASIS

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Background: Risk prediction models in electronic health record (EHR) databases may assist in early identification of patients with psoriasis likely to develop psoriatic arthritis (PsA).[1] A better understanding of potential predictors and whether stratification by sex would be needed in building such algorithms is required.[1]
Objectives: Examine general and sex-specific predictors of PsA in an EHR dataset among patients with psoriasis
Methods: A retrospective cohort study was performed within the OptumInsights EHR Database (United States) between 2006-2017. Patients with two or more ICD codes for psoriasis and ages 16-90 were identified. The outcome was PsA (defined by a single ICD code). Potential predictors, in particular comorbidities and infections, were also identified using ICD codes. Hazard ratios were calculated using Cox proportional hazards models between individual predictors and development of incident PsA in univariate models and those that were significant ($p<0.1$) were entered into a multivariable model. A final model was achieved using automated stepwise regression. Separate models were developed for each sex as some predictors (e.g., polycystic ovarian syndrome, prostatitis) are sex-specific.
Results: Among 215,386 patients with psoriasis, mean age was 50 (SD 15.6) and 55% were female. At index date (one year after date of first psoriasis code), 4.6% and 4.2% of patients had been prescribed a biologic therapy or oral therapy in the past year. Mean follow up time was 5.6 years (SD 2.8) and 4,288 patients developed incident PsA (incidence 3.5 cases/1,000 person years). Previously identified predictors were significant in univariate models (depression, fatigue, inflammatory bowel disease, uveitis, hyperlipidemia, fracture; data not shown due to space restrictions) but several new predictors were also identified (diabetes, hidradenitis suppurativa, celiac disease, irritable bowel syndrome, sepsis, post-traumatic stress disorder, anxiety, anemia) (Table). Automated regression identified subsets of these factors in multivariable models; these models differed by sex.
Conclusion: Predictors of developing PsA differed by sex but obesity, depression, and fatigue were statistically significant predictors in both groups. Infections were also associated with development of PsA but the type of infection differed by sex.

REFERENCES:
[1] Scher, et al. Nat Rev Rheum 2019 In Press.

Table. Multivariable HRs for the risk for PsA among patients with psoriasis.

	All*	Women	Men
Age	0.99 (0.99-1.00)	1.00 (0.99-1.00)	0.99 (0.99-0.99)
Male Sex	1.09 (1.02-1.16)		
Obesity	1.31 (1.16-1.48)	1.30 (1.11-1.53)	1.35 (1.12-1.64)
Depression	1.19 (1.06-1.33)	1.19 (1.04-1.37)	1.23 (1.01-1.49)
Fatigue	1.61 (1.43-1.81)	1.50 (1.30-1.75)	1.91 (1.59-2.29)
Anemia	1.48 (1.29-1.70)	1.62 (1.37-1.92)	
Uveitis	2.48 (1.41-4.38)	2.90 (1.38-6.08)	
Sepsis	1.64 (1.07-2.52)	2.39 (1.41-4.03)	
Liver Disease	1.31 (1.06-1.62)		1.40 (1.04-1.88)
Hiddradenitis Suppertiva	2.16 (1.16-4.02)		4.04 (1.68-9.74)
Hypertension	1.16 (1.07-1.26)		1.18 (1.05-1.33)
Osteomyelitis	2.17 (1.29-3.67)		2.70 (1.38-5.29)
Celiac Disease	1.98 (1.10-3.58)		
HIV	0.24 (0.06-0.96)		
Any infection	1.13 (1.04-1.22)		
Restless Leg Syndrome		1.55 (1.06-2.28)	
Salmonella		9.30 (1.30-66.27)	
Cellulitis		1.36 (1.09-1.70)	
Diabetes		1.23 (1.06-1.43)	
Irritable Bowel Syndrome			1.62 (1.00-2.62)
Venous Thromboembolism			1.58 (1.04-2.43)
Encephalitis			4.40 (1.10-17.62)
Gangrene			4.33 (1.05-17.85)

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THURSDAY, 13 JUNE 2019

"Rheumatoid arthritis – looking before, looking forward!"

OP0116

JOINT EROSIONS VISIBLE ON ULTRASOUND PREDICT ARTHRITIS DEVELOPMENT IN PATIENTS WITH ACPA AND MUSCULOSKELETAL PAIN BUT NO SWOLLEN JOINTS

Michael Ziegelasch[1], Emma Eloff[1], Hilde Berner Hammer[2], Jan Cedergren[1], Klara Martinsson[1], Åsa Reckner[1], Thomas Skogh[1], Mattias Magnusson[1], Alf Kastbom[1]. *[1]Linköping University, Dpt of Rheumatology and Dpt of Clinical and Experimental Medicine, Linköping, Sweden; [2]Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway*

Background: Anti-citrullinated protein antibodies (ACPA) are associated with an increased risk of developing rheumatoid arthritis (RA), and in particular erosive disease. Detection of joint inflammation prior to clinical synovitis may improve treatment decisions in early disease.
Objectives: We sought to determine the value of ultrasound (US) to predict arthritis development among ACPA positive patients with musculoskeletal (MSK) pain.
Methods: We prospectively followed 82 ACPA-positive patients with MSK pain but without arthritis upon baseline clinical examination (mean follow-up 68 months, range 23-91). US at baseline assessed joint erosions, synovial hypertrophy in grey scale (GS), and inflammatory activity judged by power Doppler (PD) in 36 small joints in hands and feet. We used a ProFocus system (BK Medical) with pulse repetition frequency 0.8 kHz for PD grading. The US and PD results were blinded to patients and treating rheumatologists during the initial 3 years. US findings among patients were compared to 100 age-matched healthy blood donors. Arthritis development during follow-up of patients was determined by clinical examination by an experienced rheumatologist. Associations between baseline US findings and arthritis development were tested by Cox regression analysis with adjustment for sex, age, symptom duration, smoking habits, erythrocyte sedimentation rate, C-reactive protein level, rheumatoid factor, and ACPA levels.
Results: Significantly more patient joints had synovial hypertrophy (GS score >0) compared to control joints in metacarpophalangeal (MCP) (5.2% vs. 2.5%; p<0.001) and proximal interphalangeal (PIP) joints 2-5 (6.6 vs. 1.5%; p<0.001). In contrast, metatarsophalangeal (MTP) joints 1-5 of the controls were more often scored GS>0 compared to patient joints (49% vs. 24%; p<0.001). Positive PD (>0) occurred significantly more often in patient joints compared to the controls in all joint areas (p<0.05). At patient level, the mean sum score of all investigated joints was higher among patients than controls, regarding GS as well as PD (p<0.001 for both). 13 patients (16%), but none of the controls, had erosions detected on US (p<0.001). During follow-up of patients, 39 (48%) developed arthritis after median 25 weeks (range 5-302). Arthritis development was significantly more common among patients with baseline US erosions (10 out of 13; 77%) compared to those without (29 out of 69; 42%, p=0.032). This remained significant also in Cox regression adjusting for potential confounders (Hazard ratio =4.2, 95% CI 1.7-10.4, p=0.002). Out of the 13 erosions detected on US, 4 could be identified on conventional radiographs. Neither GS nor PD findings were significantly associated with arthritis development.
Conclusion: Arthritis-related US findings are more common among patients at increased risk of RA compared to healthy controls, but with site-specific differences. Erosions detected on US predicted arthritis development. Thus, US assessment of erosions improves risk-stratification of ACPA-positive patients without swollen joints, and potentially identifies patients eligible for very early pharmacotherapy.

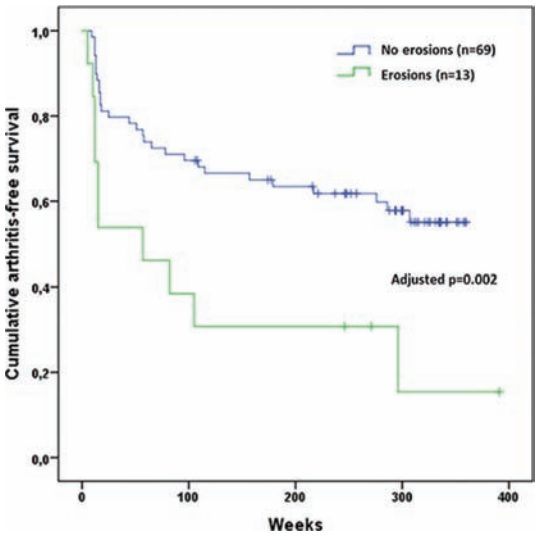


Figure 1. Survival plot illustrating progression to arthritis during follow-up in relation to the presence of ultrasound erosions at baseline among patients with anti-citrullinated protein antibodies and musculoskeletal pain.

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Squibb, Roche, UCB Pharma and Pfizer, Jan Cedergren: None declared, Klara Martinsson: None declared, Åsa Reckner: None declared, Thomas Skogh: None declared, Mattias Magnusson: None declared, Alf Kastbom Consultant for: Roche and Pfizer, Employee of: Sanofi, Speakers bureau: UCB and BMS
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OP0117

MICRO-STRUCTURAL CHANGES ASSOCIATED WITH ANTI-CITRULLINATED VIMENTIN AUTOIMMUNITY IN RA-AT-RISK INDIVIDUALS PRECIPITATE THE ONSET OF RHEUMATOID ARTHRITIS

Arnd Kleyer[1], David Simon[1], Cong Duy Bui[1], Axel Hueber[1], Holger Bang[2], Andreas Ramming[1], Jürgen Rech[1], Gerhard Krönke[1], Georg Schett[1]. *[1]Friedrich-Alexander University Erlangen-Nuremberg (FAU) and Universitätsklinikum Erlangen, Department of Internal Medicine 3, Rheumatology and Immunology, 91054 Erlangen, Germany; [2]Orgentec Diagnostika, 55129 Mainz, Germany*

Background: Development of rheumatoid arthritis (RA) is characterized by a several years lasting phase of autoimmunity, characterized by the presence of anti-modified protein antibodies (AMPA), recognizing citrullinated, carbamylated or acetylated proteins, as well as rheumatoid factor (RF) which precedes the onset of clinical disease (1,2).High resolution peripheral quantitative (HR-pQCT) technique enables the depiction of small cortical changes in peripheral joints (3).
Objectives: To describe microstructural bone lesions in rheumatoid arthritis (RA) at-risk individuals using HR-pQCT technique, their relation to rheumatoid arthritis specific autoimmunity, particularly osteoclast-inducing citrullinated vimentin (cVIM) antibodies and their impact on the later development of RA.
Methods: Cortical micro-channels (CoMiCs) as well as volumetric cortical and trabecular bone densities were analyzed by high-resolution computed tomography in the hand joints of RA at-risk individuals. Anti-modified protein antibody (AMPA) response was profiled including reactivities against citrullinated proteins (vimentin, enolase, fibrinogen) as well as carbamylated and acetylated vimentin. All subjects were followed for the development of RA.
Results: RA at-risk subjects (all N=75) with high-level (>1000U) cVIM antibodies showed a broader AMPA response and significantly more severe microstructural changes (higher CoMiCs, lower cortical and trabecular bone volume) compared to subjects with low/no cVIM reactivity. High cVIM antibodies and microstructural changes (>15 radial CoMiCs/joint) were associated with the presence of arthralgia. Furthermore, progression to RA was high in subjects with high cVIM (53%) vs. those with low (22%) or no (5%) antibodies and those with microstructural changes (46%) vs. those without such changes (16%).
Conclusion: cVIM antibodies are associated to microstructural changes in RA at-risk individuals and predict the onset of RA. These data support the concept of structural priming of joints by autoimmunity before the onset of RA.

REFERENCES:

[1] McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med. 2011;365:2205-19.
[2] Catrina AI, Svensson CI, Malmström V, Schett G, Klareskog L. Mechanisms leading from systemic autoimmunity to joint-specific disease in rheumatoid arthritis. Nat Rev Rheumatol. 2017;13:79-86.
[3] Werner D, Simon D, Englbrecht M, et al. Early Changes of the Cortical Micro-Channel System in the Bare Area of the Joints of Patients With Rheumatoid Arthritis. Arthritis Rheumatol. 2017;69:1580-7.

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OP0118

DISCRETE PATTERNS OF CITRULLINATED PEPTIDE AUTOANTIBODY REACTIVITIES EMERGE DURING PROGRESSION FROM PRE-DISEASE STATE TO DIAGNOSIS OF RHEUMATOID ARTHRITIS

Matthew J Loza[1], Sunil Nagpal[1], Renee Laird[2], Suzanne Cole[1], Frederic Baribaud[1], Ian Anderson[1], Navin Rao[1], Mark Riddle[3], Chad Porter[2]. *[1]Janssen Research and Development, LLC, Spring House, PA, United States of America; [2]Navy Medical Research Center, Enteric Diseases Department, Silver Springs, MD, United States of America; [3]F. Edward Hebert School of Medicine, Uniformed Services University, Bethesda, MD, United States of America*

Background: Rheumatoid Arthritis (RA) patients with established disease can have autoantibodies reactive to a broad array of citrullinated antigens. Autoantibodies reactive against several citrullinated proteins can develop 10-15 years before the clinical onset of disease.
Objectives: We aimed to identify common patterns of citrullinated peptide reactivities that emerge among subjects during progression from a pre-disease state through diagnosis of RA.
Methods: 500 subjects with RA (based on ICD9-CM code) were identified from the Defense Medical Surveillance System. For each subject, up to four serum samples were obtained from the Department of Defense (DoD) serum repository: 1 from earliest time point before diagnosis (9.2 ± 2.0 years before, mean ± SD); one proximal to (immediately prior to or after) disease diagnosis (127 ± 125 days before diagnosis); plus 2 intermediate time points. A discovery subset of serum samples from 88 RA subjects confirmed to be positive for anti-citrullinated protein antibodies (ACPA) at the diagnosis-proximal time point (>5 U/mL for cyclic citrullinated peptide (CCP)-II test) was assessed for IgG antibodies to 36 antigens (24 citrullinated-peptide antigens among 14 proteins and 12 non-citrullinated antigens among 9 proteins) using a custom Luminex-based assay. Subjects testing above the upper limit of detection for the CCP-II test (300 U/mL) were considered ACPA-high (n=28), with the remainder considered moderate (n=60).
Results: For the group of ACPA-high subjects at the diagnosis-proximal time point, average IgG autoantibody binding to 9 citrullinated peptide antigens (from 7 proteins: clusterin, enolase, fibrinogen A, fibrinogen B, fibronectin, filaggrin, vimentin) showed significant increases from the earliest through diagnosis-proximal time points at the population level (FDR<0.05). In ACPA-moderate subjects, IgG levels to only one antigen (citrullinated-fibronectin) had a nominally significant but small increase (mean +8%) during this time frame. Significant reactivity to the non-citrullinated antigens was not observed. In ACPA -high but not -moderate subjects, group averages for a composite score of the 9 citrullinated peptide antigens increased relative to the earliest time points, with increased average levels observable 6-years before diagnosis that steadily increased as approaching diagnosis. Patterns of increases in IgG to specific citrullinated peptides differed among subjects, for both ACPA -high and -moderate groups. In the ACPA-high group, 46% of subjects had ≥50% increase in a majority (≥5) of the 9 citrullinated-peptide antigen set and the remaining had ≥50% increase for at least 1 of the antigens. In contrast, in the ACPA-moderate group, 58% of subject did not achieve ≥50% increase for any of the 9 antigens and only 8% of subjects had ≥50% increase in a majority of the 9-antigen set. The most commonly increased IgG reactivities were for citrullinated -filaggrin and -fibrinogen A, with ≥50% increase in 64% of ACPA-high and 20% of ACPA-moderate subjects.
Conclusion: Novel patterns of citrullinated peptide autoantibody reactivities that begin to emerge on average about 6 years before diagnosis of RA have been identified in samples from the US DoD serum repository. Evaluation of specific anti-citrullinated peptide autoantibodies could potentially provide sensitive, patient-tailored biomarkers to monitor disease trajectories as at-risk individuals progress to clinically-defined RA.
Disclosure of Interests: : Matthew J Loza Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Sunil Nagpal Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Renee Laird: None declared, Suzanne Cole Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Frederic Baribaud Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Ian Anderson Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Navin Rao Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Mark Riddle: None declared, Chad Porter: None declared
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OP0119

THE PRE-TREATMENT GUT MICROBIOME PREDICTS EARLY RESPONSE TO RHEUMATOID ARTHRITIS THERAPY

Sandrine Isaac[1], Alejandro Artacho[1], Renuka Nayak[2], Alejandra Flor[1], Steven Abramson[3], Pamela Rosenthal[3], Leonor Puchades[4], Andrew Patterson[5], Antonio Pineda-Lucena[6], Peter Turnbaugh[2], Carles Ubeda[1], Jose Scher[3]. *[1]FISABIO, Valencia, Spain; [2]University of California, San Francisco, United States of America; [3]New York University, New York, United States of America; [4]Centro de Investigación Príncipe Felipe, Valencia, Spain; [5]Penn State University, Pennsylvania, United States of America; [6]Instituto de Investigación Sanitaria La Fe, Valencia, Spain*

Background: Early treatment initiation in rheumatoid arthritis (RA) is fundamental to avoid chronic joint destruction and disability. Despite remarkable advances in RA therapeutics, oral methotrexate (MTX) remains the anchor drug and mainstay of treatment worldwide (1,2). However, MTX bioavailability has a wide inter-individual variability and >50% of patients with moderate or severe RA show no or suboptimal improvement in their symptoms in response to MTX (1,3). The reasons for these disparities in treatment response remain unclear. Prior studies have shown that the biotransformation of MTX is altered in germ-free and microbiome-

depleted mice (4), prompting us to hypothesize that inter-individual differences in the human gut microbiome could impact drug bioavailability and thus clinical efficacy.
Objectives: To determine differences in the microbiome of drug-naïve, new onset RA (NORA) patients that could predict response to MTX therapy.
Methods: We performed 16S rRNA gene and shotgun metagenomic sequencing on the baseline gut microbiomes of 27 drug-naïve, NORA patients.
Results: Our analysis revealed significant associations between the abundance of gut bacterial taxa and genes including gene families related with purine and methotrexate metabolism. Machine learning techniques were applied to this metagenomic data, resulting in a robust predictive model based on bacterial gene abundance that accurately predicted response to MTX therapy in an independent group of patients. Finally, MTX available levels remaining after *ex vivo* incubation with distal gut samples from pre-treatment RA patients significantly correlated with the magnitude of future clinical response, suggesting a direct effect of the gut microbiome on MTX bioavailability and response to therapy.
Conclusion: Together, these results provide the first step towards predicting response to oral MTX in NORA patients and support the utility of the gut microbiome as a prognostic tool and perhaps even as a target for manipulation in the treatment of rheumatic and autoimmune disease.

REFERENCES:

[1] Detert, J. et al. Ann Rheum Dis 72, 844-850, doi:10.1136/annrheumdis-2012-201612 (2013).
[2] Favalli, E. G. et al. Autoimmunity reviews 13, 1102-1108, doi:10.1016/j.autrev.2014.08.026 (2014).
[3] Emery, P. et al. Lancet 372, 375-382, doi:10.1016/S0140-6736(08)61000-4 (2008).
[4] Valerino, D. M. et al. Biochem Pharmacol 21, 821-831 (1972).

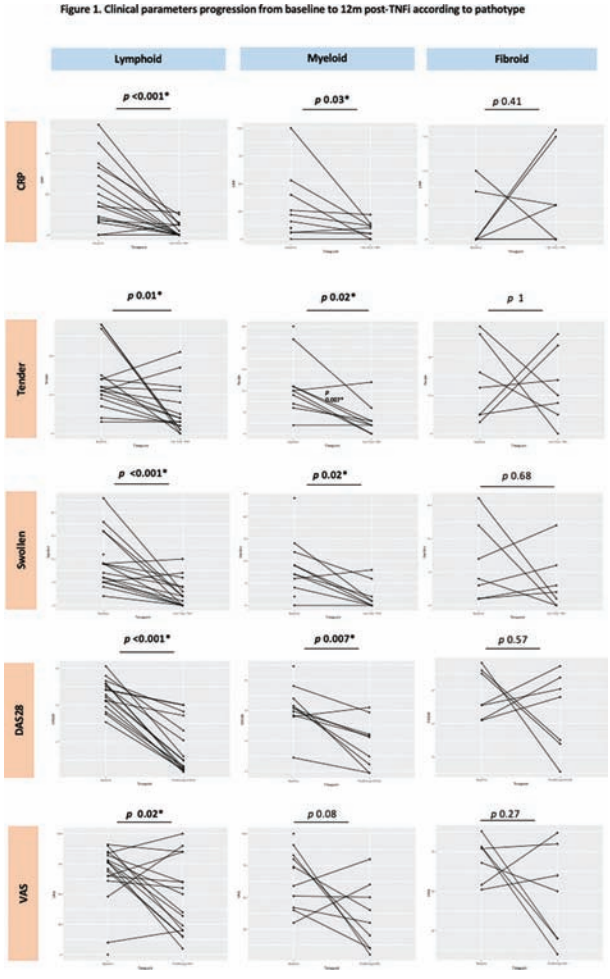
Disclosure of Interests: Sandrine Isaac: None declared, Alejandro Artacho: None declared, Renuka Nayak: None declared, Alejandra Flor: None declared, Steven Abramson: None declared, Pamela Rosenthal: None declared, Leonor Puchades: None declared, Andrew Patterson: None declared, Antonio Pineda-Lucena: None declared, Peter Turnbaugh Consultant for: P.J.T is on the scientific advisory board for Kaleido, Seres, SNIPRbiome, uBiome, and WholeBiome; there is no direct overlap between the current study and these consulting duties., Carles Ubeda: None declared, Jose Scher Grant/research support from: Pfizer, Novartis, Consultant for: Janssen, UCB, Novartis, Amgen
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OP0120

BASELINE CELLULAR AND MOLECULAR CHARACTERISTICS OF SYNOVIAL TISSUE AND RELATION WITH TNFI RESPONSE. RESULTS FROM THE PATHOBIOLOGY OF THE EARLY ARTHRITIS COHORT (PEAC)

Gloria Lliso Ribera[1], Frances Humby[1], Alessandra Nerviani[1], Myles Lewis[1], Stephen Kelly[2], Michele Bombardieri[1], Katriona Goldmann[1], Rebecca Hands[1], Chris Buckley[3], Peter C. Taylor[4], Iain B Mcinnes[5], Costantino Pitzalis[1]. *[1]William Harvey Research Institute, Experimental Medicine and Rheumatology, London, United Kingdom; [2]Barts Health. Mile End Hospital, Rheumatology, London, United Kingdom; [3]Division of Immunity and Infection, The University of Birmingham, Birmingham, United Kingdom; [4]Kennedy Institute of Rheumatology, University of Oxford Botnar Research Centre, Oxford, United Kingdom; [5]Glasgow Biomedical Research Centre, University of Glasgow, Glasgow, United Kingdom*

Background: Despite early intervention with disease modifying therapy a high percentage of patients (~30%) fail to respond and require escalation to advanced therapies such as TNFi, with no available biomarkers to predict response. Whether synovial signatures predicting subsequent response to TNFi therapy can be identified at disease onset remains an unanswered question although critical for long term prevention of disease progression and overall health economic impact.
Objectives: The aim of this study was to evaluate in a cohort of treatment naïve early RA patients, whether baseline synovial cellular and molecular signatures predict subsequent response or not to anti-TNF therapy.
Methods: A total of 186 consecutive DMARD naïve inflammatory arthritis patients (disease duration <1 year) recruited as part of the multicentre PEAC study at Barts Health NHS Trust were evaluated. After 12 months 35 patients commenced therapy with a TNFi (DAS28>5.1, failed 2 x cDMARDs as per UK NICE guidelines). EULAR response (DAS28 and DAS improvement from baseline) was calculated 12 months after TNFi was initiated. All patients underwent an US guided baseline synovial biopsy of a clinically active joint along with collection of clinical characteristics. Following H&E staining, sections underwent immunohistochemical staining and semi-quantitative scoring (0-4) to determine the degree of CD20+Bcells, CD3+T cells, CD68+ lining (l) and sublining (sl) macrophage and CD138+ plasma cell infiltration. Sections were categorised into three pathotypes: (i) Fibroid: (CD68 SL<2 and or CD3, CD20, CD138<1), (ii) Myeloid: (CD68SL>2, CD20<1 and or CD3>1) and (iii) Lymphoid: (grade 2-3 CD20+ aggregates, CD20>2). Synovial gene expression was evaluated with Nanostring and RNA sequencing.
Results: 12 months after TNFi was initiated 17/35 (48%) patients responded to therapy (TNFi good EULAR response) and 18/35 (52%) had a moderate or non-response to TNFi. Baseline demographic or US characteristics did not differentiate between the 2 groups. Although we saw no significant differences between groups there was a trend for higher levels of B (CD20+) and T (CD3+) cells, sublining macrophages (CD68+) and plasma cells (CD138+) in the TNFi response group. The cohort was segregated by pathotype and each clinical parameter was compared from baseline to 12months. Interestingly, we observed a significant reduction of levels of CRP, VAS and DAS28 and number of tender and swollen joints in those patients with Lymphoid and Myeloid pathotype ($p<0.05$), but not in those with Fibroid pathotype (Figure 1). We also evaluated gene expression (using Nanostring and RNA-sequencing) and observed increased expression of genes related to macrophages, plasma cells and B/T regulatory cells expression/activation and/or stimulation at baseline in patients who responded to TNFi.
Conclusion: This study demonstrates first evidence of potential novel signatures/biomarkers of TNFi response in treatment naïve early RA. Clinical or US assessment cannot discriminate between responders to TNFi. Lymphoid and Myeloid pathotypes associated with significant falls in clinical outcome. Finally, molecular signatures including differential upregulation of T cells, B cells and macrophage associated genes are associated with good response to TNFi therapy.
Disclosure of Interests: Gloria Lliso Ribera: None declared, Frances Humby: None declared, Alessandra Nerviani: None declared, Myles Lewis Grant/research support from: Celgene, Stephen Kelly: None declared, Michele Bombardieri Grant/research support from: Celgene, Consultant for: Medimmune, Katriona Goldmann: None declared, Rebecca Hands: None declared, Chris Buckley Consultant for: GlaxoSmithKline, Peter C. Taylor Grant/research support from: Celgene, Galapagos, Eli Lilly, UCB, Consultant for: AbbVie, Galapagos, Gilead, Eli Lilly, Pfizer Inc, Iain B McInnes: None declared, Costantino Pitzalis Grant/research support from: Celgene
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OP0121

PATIENT CHARACTERISTICS AND INCIDENCE OF SIGNS OF INFLAMMATION IN PATIENTSWITH NEW ONSET OF NON-SPECIFIC MUSCULOSKELETAL SYMPTOMS AND POSITIVE ANTI-CITRULLINATED PEPTIDE POINT-OF-CARE TEST IN GERMANY – THE PANORA TRIAL

Michaela Koehm[1,2], Ulf Henkemeier[1], Tanja Rossmanith[1], Karola Mergenthal[3], Juliana J. Petersen[3], Harald Burkhardt[1,2], Frank Behrens[1,2], PANORA Working Group. *[1]Frauhofer IME-TMP, Clinical Research, Frankfurt, Germany*; *[2]Goethe-University Frankfurt, Rheumatology, Frankfurt, Germany*; *[3]Goethe-University Frankfurt, Institute for General Practice, Frankfurt, Germany*

Background: Rheumatoid Arthritis (RA) is a chronic inflammatory joint disease affecting approx. 1% of the adult population of Northern Europe. Strategies for its early detection and diagnosis are of high importance as prompt treatment improves clinical and structural outcome. Formation of autoantibodies against cyclic citrullinated proteins (anti-CCP) are identified to be associated to RA-development. Non-specific musculoskeletal (nsMSK) pain often precedes early RA-development. Often, patients with initial symptoms are referred to General Practitioners (GP) without access to a sensitive rheumatologic assessment.
Objectives: To evaluate incidence of patients with positivity in anti-CCP rapid-test and signs and symptoms of subclinical and clinical inflammation in a on risk-population for RA.
Methods: In this prospective study (PANORA), 980 patients with new onset of nsMSK pain at GP were included in 77 GP sites in Germany. In case of positivity in anti-CCP rapid-test (CCPoint®), patients were referred to Rheumatology Department (RD) for assessment and RA-evaluation. At RD, validation of anti-CCP testing (using ELISA) and a rheumatological examination including ultrasound was performed. Subclinical signs of inflammation defined as increase of microvascularisation were monitored by Fluorescence-optical imaging (FOI). In case of ELISA positivity but missing clinical evidence of RA, patients are monitored every 6 months for a total follow-up of 36 months or until RA-diagnosis.
Results: Data from 980 patients with completion of visits at GP and/or RD was analyzed from which 9.8% (n=94) of the patients showed a positive anti-CCP rapid-test at GP. At RD, 21% (n=25) of the rapid-test positive patients were confirmed anti-CCP-positive by ELISA. 10 patients were diagnosed with RA (1 in the ELISA negative group), thereof one case of a newly detected RA at month 6 of the follow-up period. In the three groups at baseline (figure 1), age was well balanced, the proportion of female patients was highest in the RA-diagnosis cohort (80%) as well as the proportion of patient with current or past smoking-status (40% vs. 22.2% in the RA-/ELISA- group).
Conclusion: Here, for the first time data from patients suspect for RA development (non-specific musculoskeletal pain within the last 6 months) and screened using anti-CCP point-of-care test at GP are reported. Within the group re-evaluated at RD due to positive point-of-care test, only 21% were confirmed positive using ELISA testing. In the screened population, already 10 patients were diagnosed as RA at RD including 1 patient in the follow-up period until now. The continuation of the PANORA patients in the follow-up period will give more insights in specific characteristics of the RA-risk population at early stages of the disease when combining serological and imaging markers using ultrasound and FOI.

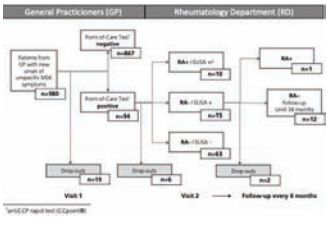


Figure 1. Study Flow Chart

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OP0122

EXPLORING HETEROGENEITY IN RHEUMATOID ARTHRITIS: PATIENT PROFILING THROUGH PRINCIPAL COMPONENT AND CLUSTER ANALYSIS OF THE BRASS REGISTRY

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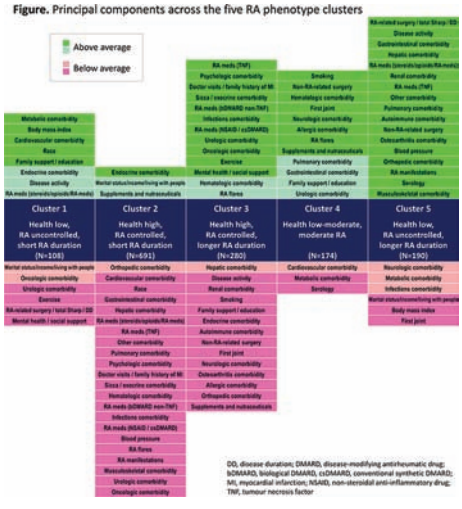
Background: Data-driven principal component (PC) and cluster analysis has the potential to identify previously unknown patient subgroups within a rheumatoid arthritis (RA) registry to establish prognosis, predict disease trajectory, and help inform treatment.
Objectives: The Brigham and Women's Rheumatoid Arthritis Sequential Study (BRASS), established in 2003, is a single-center, prospective observational registry cohort providing a comprehensive set of clinical disease activity measures in >1400 patients with RA. Our objective was to use PC and cluster analysis of baseline demographic, socio-economic, health and disease characteristics in BRASS to identify and characterize distinct patient clusters in RA.
Methods: Patient variables recorded at entry into BRASS were refined and combined using PC analysis to reduce dimensionality and collinearity. The number of PCs was established by eigenvalue >1, cumulative variance, and interpretability. Patients were clustered using a k-means approach with non-hierarchical, exclusive, and complete clustering, with minimum cluster size 5% of population, and maximum 19 clusters. The final number of clusters was determined according to the cubic clustering criterion and pseudo F.
Results: Analysis of baseline data from 1443 patients identified 41 PCs that capture the fundamental characteristics involved in RA. Cluster analysis distinguished 5 patient clusters. Each cluster reflected a different profile of PCs, and can be described based on overall health, RA disease activity and duration (Table). Key differentiators between clusters include comorbidity PCs (metabolic comorbidities predominate in cluster 1, neurologic in cluster 4, and orthopedic in cluster 5) and patient characteristics/social PCs (greatest number of doctor visits and family history of MI in cluster 3, greatest BMI in cluster 1, highest income in cluster 2, lowest income in cluster 5, and least emotional support in cluster 1).

Summary of clusters

	N	Summary descriptor	Patients, %				
			≥1 comorb-idity*	CDAI ≤10	RA duration, years <5	5–20	>20
1	108	Health low, RA uncontrolled, short RA duration	30%	28%	37%	38%	25%
2	693	Health high, RA controlled, short RA duration	59%	43%	46%	37%	17%
3	280	Health high, RA controlled, longer RA duration	48%	46%	24%	45%	31%
4	174	Health low-moderate, moderate RA	36%	36%	26%	50%	24%
5	190	Health low, RA uncontrolled, longer RA duration	7%	24%	12%	33%	55%

*Charlson Comorbidity Index

Figure. Principal components across the five RA phenotype clusters



Conclusion: Data-driven cluster analysis of RA patient characteristics at entry into the BRASS registry identified five distinct patient phenotypes, providing a convenient method to potentially derive novel insights into the multifactorial drivers, commonly co-occurring health conditions, and manifestations of RA. Investigation of longitudinal outcomes in these different clusters in the BRASS registry and validation in an independent dataset is ongoing.

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OP0123

SYMPTOMS IN FIRST DEGREE RELATIVES OF PATIENTS WITH RHEUMATOID ARTHRITIS: EVALUATION OF DATA FROM THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITISQUESTIONNAIRE

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Background: First degree relatives (FDRs) of people with rheumatoid arthritis (RA) have a four-fold increased risk of developing RA. The Symptoms in Persons At Risk of Rheumatoid Arthritis (SPARRA) questionnaire was developed to document symptoms in persons at risk of RA.

Objectives: To describe i) symptoms in a cohort of FDRs of patients with RA using the SPARRA questionnaire and (ii) the proportion of these symptoms in participants with detectable autoantibodies or elevated CRP.

Methods: The PRe-clinical EValuation of Novel Targets in RA (PREVeNT-RA) study is a cohort of FDRs of patients with RA, who are without inflammatory arthritis and aged ≥30 years at recruitment. Consented participants completed a study questionnaire and provided a blood sample for measurement of Rheumatoid factor (RF), anti-cyclic citrullinated peptide antibodies (anti-CCP) and C-reactive protein (CRP). Those who agreed to future contact were asked to complete the SPARRA questionnaire. This questionnaire asks about a variety of joint symptoms, other symptoms and severity of joint pain in specific parts of the body, allowing identification of symmetrical, small and large joint pain. We identified subjects with moderate/severe symptoms and rheumatoid distribution (symmetrical, small and large joints). We also stratified these groups by 1) seropositivity (RF or anti-CCP positive) and 2) elevated CRP.

Table 1. Participants reporting moderate or severe symptoms by seropositivity status and elevated CRP (N=870)

		Seropositive (RF or anti-CCP positive)			Elevated CRP		
	Overall %	Yes %	No%	Difference in proportion (95% confidence interval)	Yes %	No%	Difference in proportion (95% confidence interval)
Symmetrical joint pain	17.1	27.9	16.6	11.3 (-2.3 to 25.0)	27.0	15.5	11.5 (3.2 to 19.8)
Small joint pain	22.8	34.9	22.1	12.8 (-1.8 to 27.3)	32.0	21.3	10.7 (1.9 to 19.5)
Large joint pain	31.0	32.6	31.0	1.6 (-12.8 to 16.0)	39.3	29.7	9.7 (0.4 to 18.9)

Results: By July 2018, 1866 participants had completed the study questionnaire and provided a blood sample. Of those 870 (47%) returned the SPARRA questionnaire and in this subgroup, 43 (5%) were seropositive and 122 (14%) had elevated CRP. The most frequently reported symptoms were sleep problems (20%), joint pain (18%) and fatigue (17%). The proportion with joint stiffness, symmetrical joint pain or small joint pain was higher in the seropositive and elevated CRP groups. This difference was statistically significant in those with elevated CRP, respective difference in proportions (95% CI) of small and symmetrical joint involvement were 10.7 (1.9 to 19.5) and 11.5 (3.2 to 19.8) (Table 1).

Conclusion: This is the first time the SPARRA questionnaire has been applied in FDRs of patients with RA. Some of the most prevalent symptoms e.g. sleep problems or fatigue, did not identify patterns suggestive of progression to RA. However, the distribution of joint involvement (symmetrical, small joint pain), was in keeping with RA features. This part of the questionnaire may be useful in identifying individuals most likely to develop RA.

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THURSDAY, 13 JUNE 2019

SLE, Sjogren and APS: systemic autoimmunity in the real life

OP0124

DO ALL ANTIPHOSPHOLIPID ANTIBODIES CONFER THE SAME RISK FOR MAJOR ORGAN INVOLVEMENT IN SLE PATIENTS?

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Background: Antiphospholipid antibodies (aPL) have been associated with organ damage and certain features in SLE patients.

Objectives: To investigate the association between the different aPL and SLE manifestations as well as to elucidate the influence of the load of antibodies.
Methods: Patients from the RELESSER-T registry were included. RELESSER-T is a multicenter, hospital-based registry, with retrospective cross-sectional collection of data adult non-selected patients with SLE attending Spanish rheumatology services from the public national health system.
Results: Out of a total of 3651 SLE patients, 1368 were positive for aPL (44.9% of patients were positive for anticardiolipin (aCL) antibodies, 27.3% for anti b2glycoprotein I (aB2GPI) and 24% for lupus anticoagulant (LA)). Regarding the load of antibodies, 20.6%, 12.1% and 4.8% were positive for one, two and three antibodies, respectively. The association between the different aPL, the number of positive antibodies and antiphospholipid syndrome related manifestations is showed in **Table 1**. Overall, all types of aPL were associated with classic APS manifestations, although LA, IgG isotypes, and patients with more than one aPL display a higher risk to develop clinical APS.

Table 1. Association between the different aPL and the number of positive antibodies and APS related features.

	Arterial thrombosis	Venous thrombosis	Small vessel thrombosis	Fetal death	≥3 pregnancy losses	Thrombocytopenia
LA	4.45 (3.2-6.3) p<0.001	4.9 (3.8-6.3) p<0.001	4.7 (3.2-7) p<0.001	1.7 (1.2-2.5) p<0.001	4.1 (2.2-7.3) p<0.001	2.3 (1.9-2.8) p<0.001
aB2GP IgM	3.5 (2.3-5.2) p<0.001	1.8 (1.3-2.3) p=0.001	2.7 (1.6-4.3) p<0.001	2.2 (1.4-3.5)p=0.001	4.6 (2.3-9)p<0.001	1.7 (1.3-2.2) p<0.001
aB2GP IgG	6.5 (4.4-9.5) p<0.001	3.2 (2.3-4.4) p<0.001	3.7 (2.3-5.8) p<0.001	1.8(1.1-2.9) p=0.024	5.2 (2.7-10) p<0.001	1.6 (1.2-2.1) p=0.001
aCL IgM	2.4 (1.8-3.4) p<0.001	2.4 (1.9-3.0) p<0.001	4 (2.8-5.8) p<0.001	1.7 (1.2-2.4) p=0.006	3.1 (1.8-5.3) p< 0.001	1.8 (1.5-2.1) p<0.001
aCL IgG	7.3 (5.2-10.2) p<0.001	4 (3.2-5.0) p<0.001	4 (2.8-5.7) p<0.001	1.9 (1.4-2.6) p<0.001	3.8 (2.2-6.6) p<0.001	1.8 (1.5-2.1) p<0.001
Nº of positive antibodies	2.5 (2.2-2.9) p<0.001	2.2 (1.9-2.4) p< 0.001	2.3 (1.9-2.4) p<0.001	1.4 (1.2-1.7) p<0.001	2.3 (1.8-2.9) p<0.001	1.4 (1.3-1.6) p<0.001

Regarding specific lupus manifestations, all aPL types showed a significant negative association with cutaneous manifestations. LA and aCL were associated with an increased risk of cardiac, respiratory and neuropsychiatric manifestations (p<0.001). Furthermore, LA was also associated with an increased risk of renal disease (p<0.001). aCL IgG was associated with a higher risk of specific lupus manifestations compared with aCL IgM. Interestingly, aB2GP IgG were only associated with an increased risk of seizures (p< 0.001). When evaluating the influence of the load of antibodies, we found that the risk of neuropsychiatric manifestations (p<0.001), as well as the cardiac (p=0.003), and pulmonary manifestations (p=0.001), significantly increased with a higher number of positive antibodies. Inversely, the risk of cutaneous symptoms decreased while the number of positive antibodies increased (OR 0.89, 95% CI 0.82-0.96, p=0.003).
Conclusion: There is a hierarchy for aPL and the risk of APS and lupus manifestations. aCL, and especially LA, confer a higher risk for major organ involvement in SLE patients. IgG isotypes and the load of aPL antibodies increase the risk for clinical APS and major lupus manifestations.
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OP0125

REAL WORLD LONGITUDINAL DATA USING EULAR OUTCOME ASSESSMENT TOOLS FOR PRIMARY SJÖGREN'S SYNDROME (PSS) PATIENTS IN A UK CLINIC

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Background: The EULAR Sjögren's Syndrome Study Group has developed standardised outcome assessment tools for pSS, which are used in clinical trials and routine clinical assessment. While there has been a growing body of data on the use of these outcome assessment tools, data on their application in routine clinical practice, particularly over time, remains scarce.
Objectives: This paper aims to investigate how EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) scores change at multiple timepoints in a large cohort of pSS patients.
Methods: ESSDAI and ESSPRI scores were collected from patients with a confirmed diagnosis of pSS attending a pSS clinic at a single UK centre over a ten-year time-period. Anonymised data from 2009 to 2019 were analysed for patterns of change in the (overall and domain-specific) ESSDAI and ESSPRI scores over time. Time between clinic visits was also plotted against each patient's ESSDAI and ESSPRI score at each clinic visit to give an idea of real-world fluctuations in these assessment outcomes over a period time in this large group of patients. Baseline characteristics were also analysed to determine predictors in ESSPRI and ESSDAI changes.
Results: 634 patients used the clinic with 467 of them had more than one visit and 297 of them having three or more clinic visits. 32% had an ESSPRI at least 1 point higher at the last compared to the first visit (ESSPRI-worse group). 16% had an ESSPRI at least 1 point lower (ESSPRI-improved group) and 48% had a change of less than 1 in ESSPRI between the first and last visits (ESSPRI-unchanged group). The ESSPRI-worse group had a lower mean initial ESSPRI (4.59), compared to the ESSPRI-unchanged and ESSPRI-Improved group (6.27 and 6.29 respectively). There were no significant differences in age, sex and anti-Ro positivity between the three groups; age, percentage female and percentage anti-Ro+ were 60 years, 89%, 66% (ESSPRI-worse); 60 years; 86%, 60% (ESSPRI-unchanged); 62 years, 91%, 73% (ESSPRI-improved). 16% had an ESSDAI at least 3 points higher at the last visit (ESSDAI-worse group); 19% patients had an ESSDAI at least 3 points lower (ESSDAI-improved); and 62% of patients had a difference of less than 3 in ESSDAI between the first and last visits (ESSDAI-unchanged). The mean ESSDAI at first visit was significantly higher in the ESSDAI-improved group (9.2) compared to the ESSDAI-unchanged and ESSDAI-worse groups (3.1 and 2.4 respectively). There was no difference in age between the 3 ESSDAI groups. The ESSDAI-worse group had more female subjects and less anti-Ro positivity (93% & 54% respectively) compared to the ESSDAI-improved (84% & 59%) and ESSDAI-unchanged 86% & 65%) groups.
Conclusion: ESSPRI and ESSDAI scores did not change significantly over time when looking at an overall cohort level. However, there were significant changes in these outcomes on an individual level. Worsening ESSPRI was associated with lower baseline score whereas improvement in ESSDAI was associated with higher baseline score. Given the lack of proven treatment available for pSS, our data may reflect natural history of the disease course rather than treatment effects.

REFERENCES:

[1] Seror R. et al. EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI): development of a consenus patient index for primary Sjogren's syndrome. Ann Rheum Dis. **70,** 968-972 9 (2011).
[2] Seror R. et al. EULAR Sjogren's syndrome disease activity index: development of a consensus systemic disease activity index for primary Sjogren's syndrome. Ann Rheum Dis 69, 1103–1109 (2010).

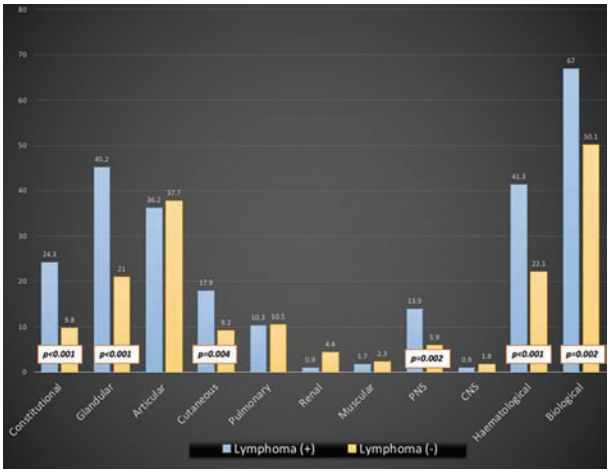
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OP0126

LYMPHOMA ARISING AT THE TIME OF DIAGNOSIS OF PRIMARY SJÖGREN SYNDROME: A HIGHLY-ACTIVE SYSTEMIC SUBSET OF THE DISEASE

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Objectives: To analyse the phenotype of patients with primary Sjogren syndrome (SjS) in whom a lymphoproliferative disease is diagnosed concomitantly.
Methods: By January 2019, The Big Data Sjögren Project included 11,420 consecutive patients with primary SjS recruited from 24 countries of the five continents.
Results: 117 (1%) patients were diagnosed with lymphoma and primary SjS synchronously. Age-gender adjusted multivariate analysis identified the following features associated with lymphoma (OR; CI95%): male gender (4.61; 2.88-7.18), White ethnicity (3.51; 1.78-7.91), abnormal oral tests (3.4; 1.38-10.88), positive biopsy (3.2; 1.3-10.17), positive RF (2.27; 1.48-3.53), hypocomplementemia (3.39; 2.06-5.54), and cryoglobulins (4.74; 2.57-8.38). Activity (score > 1) in the constitutional (2.97; 1.86-4.62), glandular (3.11; 2.1-4.57), cutaneous (2.17; 1.28-3.52), peripheral nerve (2.56; 1.4-4.41) and hematological (2.49; 1.64-3.75) ESSDAI domains was associated with lymphoma (frequencies summarized in the Figure).



Conclusion: Patients diagnosed concomitantly with primary SjS and lymphoma have a very specific, highly-active phenotype (men, White, severe oral involvement, cryoglobulinemic-related immunological markers, and high systemic activity).
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OP0127

DISEASE PRESENTATION OF 1,312 CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: INFLUENCE OF ETHNICITY

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Background: To our knowledge the influence of ethnic background in childhood-onset SLE (cSLE) presentation was not evaluated in a large population of Latin American country.
Objectives: To assess demographic data, clinical manifestations, laboratory abnormalities and disease activity score in cSLE patients according to ethnic groups at diagnosis
Methods: This multicenter study included cSLE patients(ACR criteria) followed in 27 Pediatric Rheumatology services of Brazil. Ethnicities were classified in four groups according to the parents´ and all four grandparents´ self-reported ethnicity. The statistical analysis was performed using the Bonferroni's correction ($p<0.0027$).
Results: According to ethnic groups, 1,537 cSLE patients were classified in: Caucasian (n=786), African-Latin American(n=526), Asian(n=8) and others/unknown (n=217). Comparisons between 1,312 African-Latin American and Caucasian

revealed similar median age at cSLE diagnosis[12.2(2.6-18) vs. 12.1(0.3-18) years,p=0.234], time interval to diagnosis[0.25(0-12) vs. 0.3(0-10) years,p=0.034] and SLEDAI-2K score[14(0-55) vs. 14(0-63),p=0.781] in both groups. The mean number of diagnostic criteria according to SLICC(6.47±1.911 vs. 5.81±1.631, p<0.0001) and frequencies of maculopapular lupus rash (8% vs. 3%, p<0.0001), palate oral ulcers(17% vs. 11%,p=0.001), tongue oral ulcers (4% vs. 1%, p=0.001) and nonscarring alopecia(29% vs. 16%,p<0.0001) were significantly higher in African-Latin American, whereas malar rash(45% vs. 58%,p<0.0001) was more frequent in Caucasian. The presence of antiphospholipid antibody(23% vs. 12%,p<0.0001), low complement levels(58% vs. 41%, p<0.0001) and isolated direct Coombs test (10% vs. 5%,p=0.001) were also significantly higher in the former group.

Conclusion: Our study demonstrated that disease presentation severity of African-Latin American cSLE patients is comparable to Caucasian. Mucocutaneous manifestations and autoantibodies profile were the only distinctive features of the former group. The unique mixed background of Brazilian patients probably minimized race diversity spectrum of these patients.

Disclosure of Interests: None declared

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OP0128 SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE CHARACTERISTICS ASSOCIATED WITH THE TYPE I INTERFERON GENE SIGNATURE: BASELINE DATA OF THE SLE PROSPECTIVE OBSERVATIONAL COHORT STUDY (SPOCS)

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Background: Despite accumulating data on the role of type I interferons (IFN) in the pathogenesis of SLE, real-world, longitudinal clinical data on the type I IFN gene signature (IFNGS) collected from patients with SLE are limited.

Objectives: This initial analysis of the SLE Prospective Observational Cohort Study (SPOCS; NCT03189875) examined the prevalence of the type I IFNGS (high vs low) and its association with baseline SLE disease characteristics in patients with moderately to severely active SLE receiving standard-of-care treatment.

Methods: SPOCS is an international, multicenter, prospective observational cohort study of patients enrolled with moderately to severely active SLE (SLEDAI-2K $\geq$6 at entry) from Australia, Canada, France, Germany, Italy, Spain, the United Kingdom, and the United States; a completion date of 2022 is planned. Patients are evaluated biannually during a 3-year follow-up period. At each visit, data are collected on disease activity and damage, treatment received, type I IFNGS (stratified high or low IFNGS based on a predefined cutoff), and several patient-reported outcomes.

Baseline Demographics and Clinical Characteristics

Variable	Total population (N=307)	IFNGS-high (N=210)	IFNGS-low (N=83)	*P*-value[a]
Age (years), median (min–max)	46.0 (18–88)	42.5 (18–82)	50.0 (19–88)	<0.0001
18–29, n (%)	45 (14.7)	38 (18.1)	5 (6.0)	
30–39, n (%)	71 (23.1)	61 (29.0)	9 (10.8)	
40–49, n (%)	68 (22.1)	37 (17.6)	26 (31.3)	
50–59, n (%)	70 (22.8)	42 (20.0)	23 (27.7)	
≥60, n (%)	53 (17.3)	32 (15.2)	20 (24.1)	
BMI (kg/m^2), median (min–max)	26.8 (17–58)	25.5 (17–52)	28.9 (17–58)	0.0029
Age at SLE diagnosis (years), median (min–max)	34 (8–76)	30 (8–76)	42 (8–73)	<0.0001
Age at first SLE manifestation (years), median (min–max)	31.0 (5–75)	28.5 (7–75)	37.0 (5–66)	0.0005
SLEDAI-2K, total score, median (min–max)	8.0 (4–29)	8.0 (4–29)	6.0 (4–26)	0.0002
SDI, median (min–max)	1.0 (0–10)	1.0 (0–10)	1.0 (0–5)	0.8502
PtGA VAS score, median (min–max)	50.0 (0–100)	48.5 (0–100)	58.5 (5–98)	0.0131
Medical history, n (%)				
Any comorbidity	254 (82.7)	167 (79.5)	76 (91.6)	0.0136
CNS disorders	28 (9.1)	24 (11.4)	1 (1.2)	0.0048
CV risk factors and CBV disease	101 (32.9)	60 (28.6)	36 (43.4)	0.0150
Joint disease (SLE and non-SLE)	196 (63.8)	123 (58.6)	65 (78.3)	0.0015
Diabetes mellitus	28 (9.1)	14 (6.7)	13 (15.7)	0.0164
Laboratory tests				
Complement C3, (mg/dL) median (min–max), n	96.5 (31–191), 142	90.5 (31–191), 100	104.0 (60–171), 35	0.0026
Complement C4, (mg/dL) median (min–max), n	17.0 (2–177), 138	14.0 (2–177), 97	21.0 (8–164), 34	0.0005
ANA positive, n (%)[b]	37 (75.5)	30 (93.8)	6 (42.9)	0.0004
Sm, RNP autoantibody positive, n (%)[b]	12 (36.4)	12 (50.0)	0 (0.0)	0.0261
dsDNA antibody positive, n (%)[b]	15 (26.8)	14 (37.8)	1 (7.1)	0.0411

ANA, antinuclear antibody; BMI, body mass index; CBV, cerebrovascular; CNS, central nervous system; CV, cardiovascular; dsDNA, double-stranded deoxyribonucleic acid; IFNGS, interferon gene signature; max, maximum; min, minimum; PtGA, Patient Global Assessment of Disease Activity; SDI, Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) Damage Index; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index-2000; Sm, Smith antibody; RNP, ribonucleoprotein antibody; VAS, visual analog scale.
[a]IFNGS-high vs IFNGS-low, determined by chi-square test, Mann-Whitney U test, or Fisher exact test. [b]Total number of patients tested (total, high, low): ANA: 49, 32, 14; Sm, RNP: 32, 24, 6; dsDNA: 56, 37, 14.

Results: As of November 15, 2018, a total of 307 patients were enrolled in SPOCS (North America, n=184; Europe, n=123), of whom 96.1% (n=295) were female, with a median age of 46 years (range: 18–88). At study entry, the prevalence of high type I IFNGS was 70.5% (n=210) vs 27.9% (n=83) for low type I IFNGS, with 1.7% (n=5) unknown (table, 9 missing data). IFNGS-high patients were younger than IFNGS-low patients (median: 42.5 years [range: 18–82] vs 50 [19–88], *P*<0.0001) and diagnosed with SLE at an earlier age (*P*<0.0001). SLEDAI-2K scores were greater for IFNGS-high patients vs IFNGS-low patients (*P*=0.0002), while SDI scores were similar between the two groups. Fewer comorbidities were reported for IFNGS-high patients than for IFNGS-low patients (79.5% [n=167] vs 91.6% [n=76], *P*=0.0136). Lower complement C3 and C4 levels were observed in IFNGS-high vs -low patients. At study entry, antinuclear antibodies and ribonucleoprotein antibodies were more frequent in the IFNGS-high vs IFNGS-low subset of patients. A greater percentage of IFNGS-high patients were dsDNA antibody positive vs IFNGS-low patients (*P*=0.0411).

Conclusion: The profile of patients with a baseline high type I IFNGS differed from those with a low type I IFNGS, in that those with a high type I IFNGS comprised a group that were on average younger, had greater SLEDAI-2K scores, were more serologically active, and seemed to have fewer comorbidities. As the lupus community evolves from using a classical clinical classification of patients to one based on molecular signatures, it is important to understand the role of the type I interferon pathway on disease activity, treatment, and outcomes. SPOCS recruitment and follow-up are ongoing.

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OP0129 CAPS CRITERIA FAIL TO IDENTIFY MOST SEVERE PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME ADMITTED TO THE INTENSIVE CARE UNITWITH A NEW THROMBOTIC MANIFESTATION

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Background: Catastrophic antiphospholipid syndrome (CAPS) is the most severe manifestation of antiphospholipid syndrome (APS), characterized by the simultaneous occurrence of thrombosis in multiple organs.

Objectives: The objectives of this study were to evaluate the distribution and the prognosis of CAPS criteria in APS patients admitted to the intensive care unit (ICU) with acute thrombotic manifestation.

Methods: We conducted a multicentre retrospective study, from January 2000 to September 2018, including all APS patient admitted to 24 French ICUs with any new thrombotic (arterial, venous or microvascular) manifestation.

Results: 134 single patients were admitted to the ICU for 152 episodes. The number of patients with definite CAPS, probable CAPS and no CAPS was: 11 (7.2%), 60 (39.5%) and 81 (53.5%) respectively. We compared patients with definite/probable CAPS (group 1, n=61) and no CAPS (group 2, n=73). General characteristics and APS-involved organs are reported in Table 1. APS characteristics and biological findings before admission were comparable between both groups. In-ICU and in-hospital length of stay, day-0 SAPS II and day-0 SOFA in-ICU severity scores

and Charlson comorbidity score were not different between group 1 and 2. The median [IQR25-75] number of organs involved (4 [3-4] vs. 2 [1-3], p<0.0001) and the frequency of proven microvascular thrombosis (23 (37.7%) vs. 8 (11%), p<0.0001) were higher in group 1. Treatment and outcomes are reported in Table 2. Aside plasmapheresis there was no difference in terms of APS treatments between both groups. The in-hospital mortality was not different between patient with definite/probable CAPS and no CAPS (23% vs. 28.8% respectively, p=0.4). The Kaplan-Meier curve of cumulative probability of survival retrieve no difference of survival between both groups (log-rank test p=0.5, Figure 1).

Table 1

Variable	Every patients' last episode n=134	Group 1 n=61	Group 2 n=73	p-value
Female	96/134 (71.6)	38 (62.3)	58 (79.5)	0.03
Age, years	46.0±15.1	47.5±13.9	44.7±16.1	0.3
Venous APS	93 (69.4)	46 (75.4)	47 (64.4)	0.2
Arterial APS	61 (45.5)	28 (45.9)	33 (45.2)	0.9
Triple positivity	71 (53.0)	31 (50.8)	40 (54.8)	0.6
Defined APS	123 (91.8)	57 (93.4)	66 (90.4)	0.8
SLE	46 (34.3)	17 (27.9)	29 (39.7)	0.1
Organ involved				
Kidney	77 (57.5)	46 (75.4)	31 (42.5)	<0.0001
Heart	64 (47.8)	33 (54.1)	31 (42.5)	0.2
Central nervous system	49 (36.6)	28 (45.9)	21 (28.8)	0.04
Skin	33 (24.6)	26 (42.6)	7 (9.6)	<0.0001
Adrenal gland	30 (22.4)	22 (36.1)	8 (11.0)	0.001
Gastrointestinal tract	15 (11.2)	11 (18.0)	4 (5.5)	0.02
Anemia	126 (94.0)	57 (93.4)	69 (94.5)	0.8
Thrombocytopenia	118 (88.1)	56 (91.8)	62 (84.9)	0.2

Table 2

Variable	Every patients' last episode n=134	Group 1 n=61	Group 2 n=73	p-value
Specific APS treatment				
Anticoagulant	128 (95.5)	58 (95.1)	70 (95.9)	0.8
Antiplatelet therapy	36 (36.9)	18 (29.5)	18 (24.7)	0.5
Corticosteroids	108 (80.6)	51 (83.6)	57 (78.1)	0.4
Ivlg	46 (34.3)	19 (31.1)	27 (37)	0.5
Plasmapheresis	50 (37.3)	29 (47.5)	21 (28.8)	0.02
Rituximab	18 (13.4)	11 (18.0)	7 (9.6)	0.1
Triple therapy	75 (56.0)	38 (62.3)	37 (50.7)	0.2
Outcome				
In-ICU mortality	27 (20.1)	12 (19.7)	15 (20.5)	0.9
In-hospital mortality	35 (26.1)	14 (23.0)	21 (28.8)	0.4

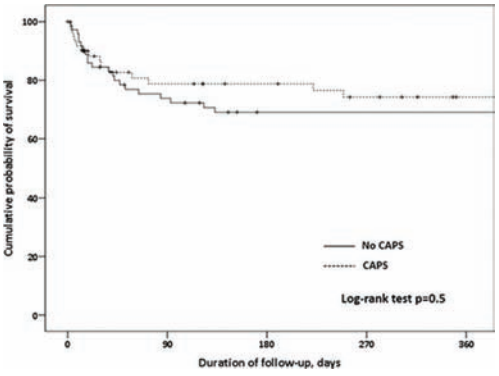


Figure 1

Conclusion: In this study**,** CAPS criteria were not associated with mortality in APS patients admitted to the ICU with new thrombotic manifestations. Further studies are needed to evaluate the accuracy of CAPS criteria in this population.
Disclosure of Interests: None declared
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OP0130

PREMATURE OVARIAN FAILURE IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS: A CROSS-SECTIONAL CASE CONTROL STUDY

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Background: Women suffering from autoimmune diseases, such as Systemic Lupus Erythematosus (SLE), could develop menopause at a younger age in comparison with healthy population. In particular, a higher frequency of abnormal ovarian function has been described in SLE cohorts[1-4]. The presence of a cause-effect link between the disease and such modifications remains poorly understood. The role of disease activity and chronic damage, combined with the intake of some drugs, such as cyclophosphamide (CYC), has been suggested[2].
Objectives: We evaluated the age at natural menopause and the prevalence of premature ovarian failure (POF) in a monocentric Caucasian SLE cohort. Additionally, we analyzed the possible association with the disease features.
Methods: We performed a cross-sectional case-control study, enrolling consecutive SLE women and reporting their clinical and laboratory data. As control group (healthy controls - HC), women without autoimmune diseases were enrolled. By using an interview, gynecological characteristics were investigated in patients and controls: in particular, we registered age at menarche, occurrence and age of menopause, history of hysterectomy. Natural menopause was defined as the absence of menses for at least 12 months in women aged ≥40 years and POF as amenorrhea of at least 12 months in women < 40 years.
Results: We enrolled 196 Caucasian women with SLE (median age 47.0 years, IQR 16.7; median disease duration 132 months, IQR 180) and 90 HC (median age 49.9 years, IQR 15.0). Ninety-four SLE patients (48.0%) and 26 HC (23.4%) referred a condition of menopause: the median age at occurrence was significantly lower in SLE than HC (47 years, IQR 8.0 *versus* 50.5 years, IQR 4; P=0.0001). Among the SLE patients, a natural menopause was observed in 70 subjects (74.4%), surgical in 7 (7.4%), iatrogenic in 17 (18.1%). In particular, 13 (13.8%) SLE patients referred the occurrence of menopause after CYC exposure. Excluding SLE patients with surgical menopause, we registered POF in 16 patients (17%); this prevalence was significantly higher in comparison with HC group, in which none of subjects experienced POF (P=0.0001). The comparison between SLE patients developing POF and those with natural menopause history demonstrated a significant higher prevalence of anti-Sm (31.2% *versus* 10.2%; P=0.0004), anti-RNP (25.0% versus 12.8%; P=0.02), anti-cardiolipin (aCL) IgG/IgM (50.0% versus 26.9%; P=0.0008) and lupus anticoagulant (37.5% versus 17.9%; P=0.002). As expected, a significant more frequent CYC treatment was identified in patients developing POF (56.0% *versus* 11.0%; P=0.0001). Moreover, POF subjects showed a significant more frequent history of treatment with azathioprine (62.5% *versus* 30.7; P=0.0001), mycophenolate mofetil (50% *versus* 20.5%; P=0.0001) and cyclosporine A (37.5% *versus* 19.2%; P=007). No significant differences were found in terms of clinical manifestations and mean SLICC/ACR damage index (SDI).
Conclusion: In the present study, we observed a significantly lower age at menopause in SLE patients in comparison with HC; in addition, a significantly higher frequency of POF was observed. POF was associated with a more active disease, in terms of autoantibodies prevalence and use of immunosuppressant drugs. Finally, for the first time, it was found an association between POF and antiphospholipid positivity, suggesting a possible role of these antibodies, in particular aCL, in POF development.

REFERENCES:

[1] Mayorga J, et al. Lupus 2016
[2] Malheiro, et al. *Gynecol Endocrinol* 2014
[3] Fatnoon NN, et al. *Singapore Med J* 2008
[4] Lawrenz, et al. Lupus 2011.

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OP0131

COMPARISON OF CLINICAL PHENOTYPE, SEROLOGICAL CHARACTERISTICS AND HISTOLOGIC FEATURES OF MALES VS FEMALES PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME (PSS)

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Background: Primary Sjögren's syndrome (pSS) is a female predominant autoimmune disease and very few studies have been conducted to address the phenotypic and laboratory differences of the disease between the two genders.
Objectives: To investigate whether gender in pSS interferes with clinical manifestations, serology, disease course and lymphoma development, in the largest cohort of pSS males in Greece.
Methods: From a cohort of 588 consecutive pSS patients who fulfill the 2016 ACR/EULAR criteria for Sjögren's, 33 males were included in the study. Every male was matched with a female in a 1:2 ratio, according to age of disease onset and disease duration. A 3 year age deviation was permitted. Glandular (dry mouth, dry eyes, parotid gland enlargement) and extra-glandular manifestations (Raynaud's phenomenon, lymphadenopathy, arthralgias/arthritis, palpable purpura, liver involvement, kidney involvement, lymphoma) as well as serology (anti Ro/SSA, anti La/SSB, rheumatoid factor, cryoglobulinemia, low C4 complement levels) and histologic features (focus score, presence of germinal centers) were recorded and compared. Statistical analysis for categorical data was performed by Fisher exact test in SPSS software version 22.0.
Results: The median age of disease onset was 52 years (range: 15-71 years) for the male group and 50 years (range: 15-73 years) for the females. The median disease duration was 8 years (range: 0-26 years) and 7 years (range: 0-26 years) for males and females respectively. Anti-La/SSB antibodies were found in statistically significant higher frequency in males compared to female patients [21/33 (63.3%) vs 23/66 (34.8%), respectively, p=0.009]. A similar trend was observed regarding anti-Ro/SSA antibodies [26/32 (81%) for males vs 44/64 (68%) for females] and rheumatoid factor [18/26 (69%) for males vs 28/57 (49%) for females], however without reaching statistical significance. Furthermore, males with pSS had less frequently Raynaud's phenomenon [3/33 (9%) vs 17/64 (26.5%) respectively] and a tendency to develop lymphomas [6/33 (18%) for males vs 6/65 (9%) for females] compared to females.
Conclusion: This is the first study comparing males and females with pSS after applying the 2016 ACR/EULAR classification criteria. The difference in the prevalence of anti-La/SSB antibodies and to a lesser extend of anti-Ro/SSA and rheumatoid factors implies a potential role of gender and hormones in the production of autoantibodies. Furthermore, higher frequency of lymphoma among males without classical risk factors may suggest distinct lymphomagenesis mechanisms between the 2 genders.
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Diagnostics and imaging procedures

OP0132

HOW ACCURATE IS PHYSICAL JOINT EXAMINATION OF THE MTP-JOINTS, AND WHAT CAN WE LEARN FROM ADDITIONAL MAGNETIC RESONANCE IMAGING ON FOREFOOT INVOLVEMENT IN EARLY ARTHRITIS?

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Background: Magnetic resonance imaging (MRI) is known to be more sensitive than physical examination in detecting inflammation, and has predominantly been studied in metacarpophalangeal-(MCP) and wrist-joints. Data on the concordance and discordance of physical examination and MRI-detected inflammation of metatarsophalangeal-(MTP)joints is scarce, which is surprising as physical examination of these joints is generally considered more challenging than of MCP-joints.
Objectives: We aimed to study the concordance and discordance of arthritis upon physical examination with MRI-detected inflammation of MTP-joints. Analyses on MCP-joints were included for comparison.
Methods: 1764 MTP(2-5)-joints and 1764 MCP(2-5)-joints of 441 consecutive patients presenting with early inflammatory arthritis (36% RA, 64% other inflammatory arthritides) underwent physical examination (PE) of joint swelling and 1.5T contrast-enhanced MRI of unilateral MCP- and MTP-joints. MRI-detected synovitis and bone marrow oedema were scored according to the RA MRI score (RAMRIS), and tenosynovitis according to Haavardsholm by two experienced readers (scores ranged 0-3). Analyses were done on joint level and joints were grouped as PE+MRI+, PE–MRI–, PE+MRI– and PE–MRI+. MRI-positivity required the presence of the same MRI-inflammatory feature on joint level that was scored by both readers$\geq$1. In addition, to be classified as PE+MRI–, the joints required to have clinical swelling as objectified by two independent observers. After categorisation, the MRIs of the joints that were PE+MRI– were further studied by two other, independent observers among whom an experienced musculoskeletal radiologist, to investigate the presence of contrast-enhancement that was not scored according to RAMRIS guidelines.
Results: Physical examination of joints and MRI were concordant in 79% of MTP-joints (6% PE+MRI+, 74% PE–MRI–). For the MCP-joints this was 71% (15% and 56% respectively). Next discordance was studied. Subclinical joint inflammation (PE–MRI+) was present in 14% (n=248) of MTP-joints. This was less frequent than in MCP-joints, where subclinical inflammation was present in 27% joints (n=465, p<0.001). Discordance in the opposite direction (PE+MRI–) was present in 5% of MTP-joints (n=78). This was observed more frequent than in MCP-joints (3%, n=44 joints, p<0.001).
Subsequently, the MRIs of the joints that were clinically inflamed and scored negative according to RAMRIS were studied for other MRI-abnormalities. Out of the 78 MTP-joints that were PE+MRI–, 54% (n=42) showed no MRI abnormalities, whereas in 46% (n=36) extra-articular contrast-enhanced lesions were observed that were predominantly identified as peri-arthritis and intermetatarsal bursitis. Within this category, extra articular inflammation was more prevalent in RA than in other inflammatory arthritides (58% vs 26%, p=0.005). At the MCPs no extra-articular inflammation was found.
Conclusion: Joint examination and MRI were mostly concordant in MTP- and MCP-joints. In MTP-joints MRI-detected subclinical joint inflammation was infrequent (14%), especially when compared to MCP-joints (27%). Clinical joint swelling without MRI-detected joint inflammation according to RAMRIS was also infrequent (5% of MTP-joints) and in part caused by extra-articular inflammation such as intermetatarsal bursitis. Further detailed imaging studies are needed to determine if extra-articular inflammation at the level of MTP-joints, with or without concomitant intra-articular inflammation, is a novel finding that is characteristic for early RA.
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OP0133

ONE-YEAR PROGRESSION OF EROSIVE DISEASE EVALUATED WITH HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY IN PATIENTS WITH ANTI-CITRULLINATED PEPTIDE ANTIBODIES AND ARTHRALGIA

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Background: Bone erosions are common at diagnosis of rheumatoid arthritis (RA). However, bone erosions in preclinical RA (pre-RA) are not well described, and have not been studied prospectively.
High resolution peripheral quantitative computed tomography (HR-pQCT) has a spatial resolution of 82 µm and may therefore be ideal to detect bone erosions.
Objectives: To evaluate erosive progression with HR-pQCT in anti-citrullinated peptide antibody (ACPA) positive patients with arthralgia compared with healthy subjects.

Methods: Patients were recruited by specialists in rheumatology at hospital clinics and in private practice, and healthy controls were recruited from a website for research subjects. Patients with arthralgia, ACPA and no rheumatic disease, and controls without arthralgia, ACPA, or rheumatic disease were included. Medical history, ACPA, clinical examination and ultrasound of symptomatic joints were performed in all patients and controls. A 2.7-cm-long volume of interest in the 2nd and 3rd MCP joint of the right hand was HR-pQCT scanned at a spatial resolution of 82 μm at baseline and after one year. Cortical and trabecular bone structure were evaluated in a 12.3-mm-long volume of interest proximal to the MCP head using the provided scanner software. Erosions were defined as cortical breaks in two consecutive slices, in two planes, non-linear in shape, and with loss of underlying trabecular structure. Number, depth, width, and volume of erosions were measured using the Osirix DICOM viewer. Intra observer agreement for erosions was evaluated with Cohens *Kappa* and coefficient of variance (CV). Values are median(interquartile range).
Results: Twenty-two patients (aged 53(36-63) years) and 23 controls (aged 48 (42-57) years) were evaluated. Ten patients were diagnosed with RA after 86(24-200) days. There was a significant increase in the number of patients with erosions during follow-up in the patient group (4 vs. 10, p=0.031), but not in the control group (1 vs. 4, p=0.083). In addition, at follow-up more erosions per individual were demonstrated in patients compared to controls (p=0.031).
The increase in average and total volume of erosions from baseline to follow-up were larger in patients compared with controls (Fig. 1) (p=0.031 and p=0.027). At follow-up average and total width, depth and volume of erosions were larger in patients compared with controls (p between 0.031 and 0.045).
Percent change in bone density, cortical, as well as trabecular parameters did not differ between patients and controls. Agreement was 95% equivalent to a *kappa* of 0.89 for erosions. CV for width, depth, and volume of erosions were 8%, 23%, and 39%.

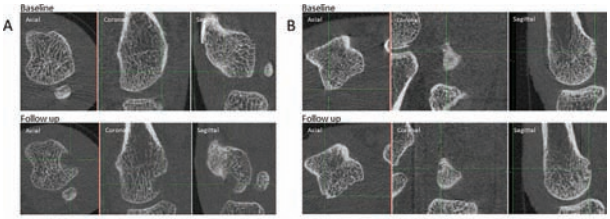


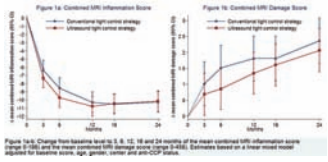
Fig. 1 High resolution peripheral quantitative computed tomography images of bone changes. **(A)** New active erosion at follow up in a patient characterized by diffuse/wolly lining. **(B)** New active erosion at follow up in a control.

Conclusion: Progression of erosive disease in ACPA positive patients with arthralgia using HR-pQCT is reported for the first time. The results highlight that an even earlier diagnosis of RA is crucial to prevent erosive disease.
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OP0134 ULTRASOUND IN THE MANAGEMENT OF EARLY RHEUMATOID ARTHRITIS: MRI OUTCOME DATA FROM THE ARCTIC RANDOMIZED CONTROLLED STRATEGY TRIAL

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Background: It has been debated whether treatment outcomes in early RA would be improved by targeting imaging remission, assessed by ultrasound or MRI, in addition to clinical remission. The primary analyses of the ARCTIC and TaSER trials (1, 2) did not show a beneficial effect of adding structured ultrasound assessment to a treat-to-target tight control strategy. However, both studies reported a trend toward less radiographic progression in the ultrasound arm.
Objectives: We aimed to investigate whether management of early RA by a tight control strategy incorporating ultrasound information in treatment decision-making would lead to improvement in MRI inflammation or less structural damage, compared to a conventional tight control strategy.
Methods: The ARCTIC trial was a 24-month RCT with inclusion criteria age 18-75 years, fulfillment of ACR/EULAR criteria for RA, DMARD-naivety, < 2 years from first patient reported swollen joint, and indication for DMARD treatment. Patients were randomized to an ultrasound tight control strategy targeting DAS < 1.6, no swollen joints and no power-Doppler signal in any joint, or a conventional strategy targeting DAS < 1.6 and no swollen joints. Patients in both arms were treated by the same treat-to-target drug escalation algorithm starting with MTX, then triple combination therapy MTX/SSZ/HCQ, then biologic DMARD. In the ultrasound arm, treatment was stepped up if indicated by the ultrasound score, overruling the DAS and swollen joint count. MRI of dominant wrist and hand was performed at 6 times and scored in chronological order by a reader blinded to study arm and clinical data. MRI acquisitions and scoring were done according to the RAMRIS (3) recommendations. Of the 230 patients in ARCTIC, 218 (ultrasound n=116, conventional n=102) had MRI at baseline and ≥ 1 follow-up visit, and were included in the analyses. RAMRIS synovitis, tenosynovitis and bone marrow edema scores were summarized to a combined inflammation score; scores for erosions and joint space narrowing to a combined damage score. Mean change from baseline to each follow-up was estimated by a linear mixed model adjusted for baseline score, age, gender, center and anti-CCP status. The proportion of patients in each treatment arm with MRI erosive progression after 2 years was calculated, using the smallest detectable change (0.61) as cut-off.
Results: Demographic composition was comparable to the ARCTIC primary sample. There were no statistically significant baseline differences between the arms in either of the combined MRI scores. The mean combined MRI inflammation score decreased during the first year (1-year change in ultrasound arm −10.8 (95% CI: −12.0 to −9.6), conventional arm −10.3 (95% CI: −11.5 to −9.0), p=0.56), and maintained at the same level throughout the 2nd year. There were no significant differences in changes from baseline between the study arms at any time (figure 1a). The mean combined MRI damage score showed a small increase over time, without any significant differences between study arms (figure 1b). In the ultrasound arm 45% of patients had MRI erosive progression vs. 39% in the conventional arm (OR: 1.26 (95% CI: 0.73 to 2.16), p=0.40).



Conclusion: A tight control strategy incorporating ultrasound information in treatment decisions did not lead to improved MRI inflammation or less structural damage, compared to a conventional tight control strategy. The findings support the conclusion of the ARCTIC trial that systematic use of ultrasound does not provide added value in the follow-up of patients with early RA treated according to current recommendations.

REFERENCES:
[1] E. A. Haavardsholm, et al. BMJ 2016; 354: i4205
[2] J. Dale, et al. ARD 2016; 75: 1043-50
[3] M. Østergaard, et al. J Rheum 2017; 44: 1706-12

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OP0135

HOW WELL DOES WHOLE BODY MAGNETIC RESONANCE IMAGING AGREE WITH WHOLE BODY ULTRASOUND IN THE ASSESSMENT OF JOINT INFLAMMATION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Whole body MRI (WBMRI) is a new promising tool for assessing synovitis in the whole body in one session, but is less validated. Ultrasound (US) is another sensitive and well-validated imaging technique that can assess the whole body in one session.

Objectives: To evaluate the agreement between US, WBMRI and clinical assessment of joint inflammation in rheumatoid arthritis (RA) patients on joint and patient level.

Methods: US, WBMRI and clinical assessment for tender joints (TJ) and swollen joints (SwJ) were performed in 19 RA patients (90% Women, median age 55 (26-73), diseases duration 5.5 years (1-42), SwJ(28) 5 (1-13), TJ(28) 7 (2-24) and DAS28-CRP 4.66 (3.48 -6.66))) fulfilling ACR 1987 criteria for RA. The 28 conventional joints, bilateral ankles and MTP 1-5 were assessed by WBMRI and US.

Joint inflammation by US was graded 0-3 on both B-mode and colour Doppler (CD), and subsequently converted to +/- by defining US synovitis as B mode ≥2 or CD ≥1, and scored for individual joint. For WBMRI, joint inflammation was defined in two ways; 1) as presence of synovitis and/or osteitis, 2) as the presence of synovitis only.

The total inflammatory burden was established as sum scores for the 28 conventional joints for US (US28) and for 26 joints (WBMRI26) for WMBRI - same 28 joints except elbows (due to poor image quality). The max score of a joint in US and WBMRI including osteitis was 2, while WMBRI excluding osteitis was 1. The agreement between the clinical joint assessment, US and WBMRI for joint inflammation was calculated with Cohen's kappa (κ). The correlations between US28, WBMRI26 and DAS28-CRP were calculated by Spearman correlation coefficient (rho).

Results: When considering joint inflammation by WBMRI as synovitis and/or osteitis, US28 for synovitis and WBMRI26 sum scores showed good correlation rho= 0.72 (p=0.003) (Fig. 1), whereas US28 and WBMRI26 did not correlate with DAS28 CRP (rho=-0.26, p=0.28; rho=0.20, p=0.47 respectively). Moderate-good agreement was found between US and WBMRI in wrists and MCP 1, 2 and 5(κ= 0.42–0.62) but poor in other joints (κ ≤ 0.37).

By comparing WBMRI synovitis (excluding osteitis) with US synovitis, US28 and WBMRI26 sum scores showed weakened correlation rho= 0.46 (p=0.049) (Fig. 2), and without correlation between WBMRI26 and DAS28 CRP (rho=-0.07, p=0.78). At joint level, moderate-good agreement was found between US and WBMRI in wrists, MCP 2 and 5, and PIP 5(κ= 0.41–0.62) but poor in other joints (κ ≤ 0.37).

Agreement between US and clinical joint tenderness was poor (all κ<0.31; except κ=0.42 for wrist), but better between US and clinical swelling for shoulders, elbows, MCP1 and PIP5 (κ=0.42–0.66) while ≤0.36 for other joints. Agreement between WBMRI and clinical joint swelling or tenderness showed κ<0.38 in all joints irrespective of counting osteitis as one of the features or not.

Conclusion: WBMRI and US sum scores of joint inflammation showed good correlation in RA patients for the overall inflammatory burden. The agreement at joint level was variable.

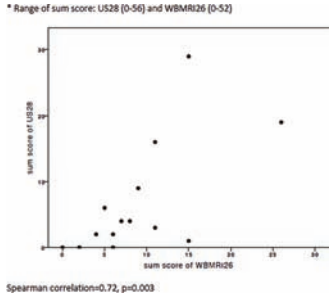


Figure 1. Correlation between US sum score for 28 joints (US28) & whole body MRI sum score for 26 joints (WBMRI26), which included osteitis, for assessing joint inflammation

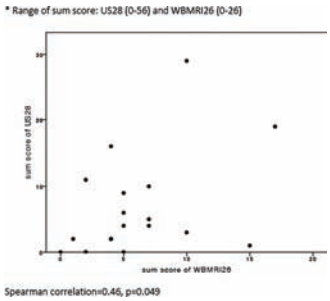


Figure 2. Correlation between US28 & WBMRI26, which excluded osteitis, for assessing joint inflammation

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OP0136

DIAGNOSTIC VALUE OF ULTRASOUND IN CALCIUM PYROPHOSPHATE DEPOSITION DISEASE OF THE KNEE JOINT

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Background: The Outcome Measures in Rheumatology (OMERACT) US subtask force published a new definition for calcium pyrophosphate deposition (CPPD) at the knee level.

Objectives: To assess the diagnostic performance of ultrasound (US) for CPPD at the level of menisci, hyaline cartilage (HC), tendons, and synovial fluid (SF) of the knee, and to examine inter- and intra-observer reliability.

Methods: We consecutively included patients with knee effusion over a 2-year period (43 patients with CPPD and 131 controls). All patients underwent SF analysis, conventional radiography (CR), and US examination using the Outcome Measures in Rheumatology (OMERACT) definition of the US characteristics of CPPD. Two independent operators performed the US, and inter-observer agreement was calculated. Intra-observer agreement was examined with static images obtained for all enrolled patients.

Results: US revealed calcium pyrophosphate (CPP) deposits in menisci, HC, and tendon more frequently in patients with CPPD than in control patients. The presence of US CPP deposits in SF was not significantly different between the two groups. Combined US evaluation of the 3 components (menisci, HC, and tendon) showed the best diagnostic performance. The sensitivity and specificity for US evaluation of the three components were 74.4% and 77.1%, respectively, while for CR evaluation, the sensitivity and specificity were 44.2% and 96.9%, respectively. Inter- and intra-observer agreement were excellent for medial (κ=0.930, 0.972) and lateral menisci (κ=0.905, 0.942), HC (κ=0.844, 0.957), and SF (κ=0.817, 0.925). Tendon showed fair inter-observer (κ=0.532) and good intra-observer reliability (κ=0.788).

Conclusion: Based on the OMERACT definition, US demonstrated better diagnostic capacity than CR to diagnose CPPD, with excellent reliability. Combined evaluation of menisci, HC, and tendon showed the best diagnostic accuracy.

REFERENCE:

[1] Filippou G, Scire CA, Damjanov N, Adinolfi A, Carrara G, Picerno V, et al. Definition and Reliability Assessment of Elementary Ultrasonographic Findings in Calcium Pyrophosphate Deposition Disease: A Study by the OMERACT Calcium Pyrophosphate Deposition Disease Ultrasound Subtask Force. J Rheumatol 2017; 44: 1744-1749.

Acknowledgement: This research was supported by the Basic Science Research Programs through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science, and Technology

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Disclosure of Interests: None declared
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OP0137 OPTIMIZING SUBJECT SELECTION IN KNEE OSTEOARTHRITIS CLINICAL TRIALS BY RADIOGRAPHIC JOINT SPACE WIDTH: POST-HOC CLINICAL RESPONSE ANALYSIS FROM A PHASE 2B TRIAL OF WNT PATHWAY INHIBITOR, SM04690

Sarah Kennedy[1], Christopher Swearingen[1], Jeyanesh Tambiah[1], Philip G. Conaghan[2]. [1]*Samumed, LLC, San Diego, United States of America*; [2]*University of Leeds, Leeds, United Kingdom*

Background: Knee osteoarthritis (OA) trial radiographic inclusion criteria usually comprises Kellgren-Lawrence (KL) grading, which mixes features such as osteophytes and joint space narrowing and leads to study population heterogeneity. Selecting subjects with baseline medial joint space width (mJSW) 2-4 mm has been shown to reduce heterogeneity and improve responsiveness to radiographic change in comparison to broader knee OA populations.[1,2] However, effects of baseline-fixed mJSW on symptom responsiveness are unknown.
Objectives: To evaluate the impact of baseline mJSW 2-4 mm on patient-reported outcomes (PROs) as measured by effect size in a 24-week phase 2b trial of SM04690, a Wnt pathway inhibitor in development as a potential disease-modifying OA drug (DMOAD).
Methods: Knee OA subjects with KL grades 2-3 and Pain Numerical Rating Scale (NRS, [0-10]) ≥4 and ≤ 8 in the target knee and <4 in the contralateral knee received a single IA 2 mL SM04690 injection (0.03, 0.07, 0.15, 0.23 mg), vehicle placebo (PBO), or sham (dry needle) in the target knee at baseline. PRO 24-week endpoints included change from baseline in weekly average of daily OA target knee pain by NRS, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain [0-100], WOMAC Physical Function [0-100], and Patient Global Assessment (PtGA) [0-100]. Primary results are presented elsewhere[3]. A post-hoc completer analysis of subject results with baseline mJSW 2-4 mm is reported.

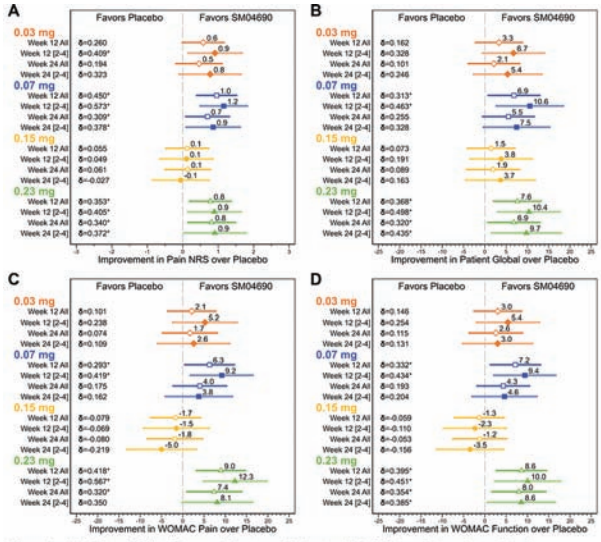


Figure. Ladder Plots of Effect Sizes and Treatment Estimates (with 95% confidence intervals) of Improvement over Placebo from Baseline-Adjusted ANCOVAs for All Subjects as well as All Subjects with baseline mJSW between 2 and 4 mm ([2-4]).
A) Pain NRS **B)** Patient Global **C)** WOMAC Pain **D)** WOMAC Function δ : Effect Size *P<0.05

Results: 635 subjects (91.4%) completed the study (mean age 59.0 [±8.5] years, BMI 29.0 [±4.0] kg/m^2, female 58.4%, KL3 57.3%). In both full analysis set (FAS, all dosed subjects) and mJSW 2-4 mm subjects, significant improvements compared to PBO (P<0.05) were seen in pain NRS, WOMAC Pain, WOMAC Function, and PtGA for 0.07 mg and 0.23 mg SM04690 dose groups at Week 12 (**Figure 1**). The. effect sizes were improved in the mJSW 2-4 mm group in comparison to FAS for most doses at weeks 12 and 24.
Conclusion: In this post-hoc analysis of SM04690-treated knee OA subjects, those with baseline mJSW 2-4 mm showed increased PRO effect sizes compared to those in the FAS. Previous data also demonstrated SM04690-treated subjects with mJSW 2-4 mm had improved radiographic sensitivity to change. Data from SM04690 studies suggest mJSW 2-4 mm should be considered as an inclusion criterion for trials of potential knee DMOADs.
Image: Schematic representation of SM04690's proposed mechanism of action via CLK2 and DYRK1A inhibition in OA

REFERENCES:
[1] Bowes M, et al. ARD 2017
[2] Yazici Y, et al. *Arthritis Rheumatol.* 2017
[3] Yazici Y, et al. *Arthritis Rheumatol.* 2018

Disclosure of Interests: Sarah Kennedy Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Christopher Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Jeyanesh Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Philip G Conaghan Consultant for: Flexion Therapeutics, AbbVie, Medivir, Merck Serono, Novartis, GlaxoSmithKline
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OP0138 THE ROLE OF ULTRASOUND IN THE DIAGNOSIS OF PRIMARY SJÖGREN SYNDROME AND ITS CONCORDANCE WITH SALIVARY GLAND BIOPSY

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Background: Minor salivary gland biopsy (MSGB) is the gold-standard technique for primary Sjögren Syndrome (SSp) but nowadays the use of mayor salivary gland ultrasonography (MSGUS) is increasing because it is a fast and non-invasive technique and with no adverse events for the patient.
Objectives: To assess the utility of MSGUS as a diagnostic tool for SSp and to study the concordance with MSGB.
Methods: 72 patients were recruited consecutively with clinical and/or analytical suspicion of SSp, from the Rheumatology outpatient consultations at the Príncipe de Asturias Hospital (2015-2018). Demographics, clinical and serological data and validated activity indexes, ESSPRI and ESSDAI, were recorded. All patients underwent a MSGB and blindly, both for clinical and histological results, a MSGUS. The histological results were classified according to *Chisholm and Mason scores* (pathological grades 3/4), and the US results according to the system by *Cornec et al.* (pathological grade ≥2). The final SSp diagnosis was made using both the 2002 and the 2016 ACR/EULAR classification criteria. The data was analyzed using the software STATA. The validity of the US and the MSGB to diagnose SSp according to the 2002 and 2016 ACR/EULAR classification criteria was evaluated by calculating the percentage of agreement between the tests, along with the specificity (Sp), sensitivity (S), positive and negative predictive values (PPV and NPV) and area under the curve (AUC).
Results: Descriptive analysis of the main variables is shown in *Table 1*. Using the MSGB as a gold-standard, the total% of agreement was 78% with a good AUC (0.75) (IC95%0.65-0.84). Using the 2002 classification criteria as a gold-standard, the total% of agreement was 82% for US and 79% for MSGB with an AUC of 0.78 (IC95%0.67-0.88) and 0.80 (IC95%0.70-0.89) respectively. In this case, US had a S of 93% (IC95%0.82-0.99) and a Sp of 62% (IC95%0.41-0.80) whereas MSGB had a S of 78% (IC95%0.64-0.89) and a Sp of 81% (IC95%0.61-0.93). Similar results were obtained using ACR/EULAR criteria: US% of agreement 83%, AUC 0.78 (IC95%0.67-0.90), S 90% (IC95%0.79-0.97) and Sp 67% (IC95%0.43-0.85); while MSGB% agreement 81%, AUC 0.83 (IC95%0.75-0.92), S 76% (IC95% 0.63-0.87) and Sp 90% (IC95%0.70-0.99). In addition, 9 patients who fullfilled the 2002 classification criteria with a negative histological result had a pathological US.
Conclusion: MSGUS has a similar diagnostic value compared to MSGB in patients with SSp, which could be part of the classification criteria used to date. In this series of patients and compared to MSGB, it has a higher sensitivity and a lower specificity, so it could be used as an initial diagnostic method in patients with high suspicion of disease, leaving the MSGB for those cases in which US and other clinical and serological data are inconclusive. With this approach, the disadvantages derived from an invasive technique such as MSGB would be avoided.

REFERENCES:
[1] Zhou M. Diagnostic accuracy of salivary gland ultrasonography with different scoring systems in Sjögren's syndrome: a systematic review and meta-analysis. Sci Rep. 2018 Nov 20;8(1):17128.
[2] Ultrasonography of major salivary glands compared with parotid and labial gland biopsy and classification criteria in patients with clinically suspected primary Sjögren's syndrome Esther MosselMossel E, et al. Ann Rheum Dis 2017.

Table 1. Demographic, clinical and serological characteristics

Sex%	♀97 ♂3
Mean age	57.5
Smoking%	**Active** 8, **non** 68 **and former smoker** 24
Classification Criteria%	**2002** 64 **ACR/EULAR** 49
Shirmer test +%	83
Extraglandular features%	74
Serologies +%	**ANA** 82 **AntiRo52** 43 **AntiRo60** 46 **AntiLa** 32
Hypergammaglobulinemia%	50
Rheumatoid factor +%	42
Hypocomplementemia%	**C3** 7 **C4** 13
Acute phase reactants mean	**ESR** 35 **CRP** 1.85
ESSPRI mean	5.6
ESSDAI mean	2

Disclosure of Interests: None declared
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OP0139

ASSESSMENT OF ULTRASOUND DEFINITIONS AND A SCORING SYSTEM FOR SALIVARY GLAND DISEASE IN PRIMARY SJÖGREN'S SYNDROME: AN OMERACT PATIENT RELIABILITY EXERCISE

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Background: Salivary gland ultrasound (SGUS) may have the potential of facilitating diagnosis and therapy monitoring of salivary gland disease in patients with primary Sjögren's syndrome (pSS). The aim of the Outcome Measures in Rheumatology Clinical Trials (OMERACT) US subgroup on SG is to validate US as an outcome measurement instrument in pSS. Following the OMERACT US stepwise validation approach, preliminary consensus definitions for elementary lesions based on a systematic literature review were developed and subsequently a scoring system has been agreed upon and tested through a web-based Delphi exercise.
Objectives: To assess the reliability of consensus based SGUS scoring system in patients with SS.
Methods: Nine sonographers conducted an US reliability exercise of the parotid and submandibular glands (PG, SMG) of 9 patients with primary and secondary SS in 3 rounds. A 4-grade semi-quantitative scoring was applied in B-mode for structural lesions as follows: Grade 0: normal, grade 1: mild inhomogeneity without anechoic or hypoechoic areas, grade 2: moderate inhomogeneity with focal anechoic or hypoechoic areas, grade 3: severe; diffuse inhomogeneity with an-/hypoechoic areas occupying all the surface of the gland. Next, presence or absence of typical pSS-lesions was scored in binary fashion. Intrareader and interreader reliability were computed by Cohen and Light kappa. Weighted k coefficients with absolute weighting were calculated for B-mode abnormalities.

Weighted kappa for intra-reader reliability (Kappa: mean (min-max):		
Grading	PG	0.75 (0.49-0.93)
	SMG	0.79 (0.58-0.94)
presence / absence of typical pSS-lesions	PG	0.91 (0.80-0.98
	SMG	0.92 (0.85-0.99)
Weighted kappa for inter-reader reliability (Kappa: mean (min-max):		
Grading	PG	0.63 (0.49-0.73)
	SMG	0.63 (0.50-0.72)
presence / absence of typical pSS-lesions	PG	0.86 (0.75-0.92)
	SMG	0.87 (0.77-0.93)

Results: Light weighted kappa for grading and diagnostic evaluation for intra- and inter-reader reliability was moderate to excellent (see Table for details).
Conclusion: The developed US definitions and the scoring system for salivary gland lesions in pSS showed a good to excellent reliability in patients with SS. Next step is to apply the scoring system in clinical trials.
Disclosure of Interests: Stephanie Finzel: None declared, Sandrine Jousse-Joulin: None declared, Annamaria Iagnocco: None declared, Esperanza Naredo Consultant for: Abbvie, Speakers bureau: AbbVie, Roche, Bristol-Myers Squibb, Pfizer, UCB, Lilly, Novartis, Janssen, and Celgene GmbH, ALOJZIJA HOCEVAR: None declared, Sarah Ohrndorf: None declared, Petra Hanova: None declared, Maria-Antonietta d'Agostino: None declared, Felicie Costantino: None declared, Lene Terslev Speakers bureau: Speakers fee from : Roche, Novartis, Pfizer, MSD, BMS, Celgene, Helen Keen: None declared, George Bruyn : None declared
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THURSDAY, 13 JUNE 2019

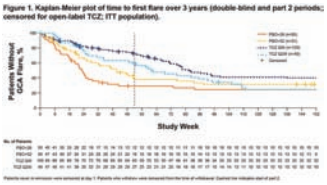
Vasculitis

OP0140

LONG-TERM OUTCOME OF TOCILIZUMAB FOR PATIENTS WITH GIANT CELL ARTERITIS: RESULTS FROM PART 2 OF THE GIACTA TRIAL

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Background: Tocilizumab (TCZ) 162 mg administered subcutaneously weekly (QW) or every-other-week (Q2W) plus 26-wk prednisone tapering resulted in higher rates of sustained glucocorticoid (GC)–free remission in patients (pts) with giant cell arteritis (GCA) than placebo plus 26-wk (PBO+26) or 52-wk (PBO+52) prednisone tapering in the 52-wk, double-blind, randomized controlled GiACTA trial.[1]
Objectives: Determine long-term safety and explore maintenance of efficacy in GCA pts in a 2-year long-term extension (part 2) of this trial.
Methods: At the end of the double-blind period, pts in clinical remission (CR) were instructed to stop double-blind TCZ treatment upon entering part 2. CR was defined as absence of flare per investigator assessment. GCA therapy, which could include initiation/termination of open-label TCZ and/or GC, was at the investigator's discretion per disease status. Outcomes included maintenance of CR (no flare during part 2), flare, time to first flare, treatments received, cumulative GC dose, and safety. Treatment groups refer to originally assigned treatment (PBO or TCZ).



Results: Among 250 pts treated in the double-blind period, 215 entered part 2 and 197 (92%) completed 3 years in the trial. Among the 81 TCZ QW and 36 TCZ Q2W pts in CR at wk 52, 38 (47%) and 13 (36%) pts, respectively, maintained CR during part 2. Of these 51 original TCZ pts, 33 (65%) were treatment-free (no TCZ and no GC treatment), which was higher than the treatment-free proportion of original PBO pts who maintained CR in part 2 (17/38; 45%). Median time to first flare while not receiving TCZ was longer for pts in the original TCZ groups (TCZ QW, 575 days; TCZ Q2W, 428 days) than for pts in the original PBO groups (PBO+26, 162 days; PBO+52, 295 days); TCZ QW pts remained flare-free the longest (Figure 1). Retreatment with TCZ (with or without GC) for flare was effective for restoring CR in part 2. Cumulative GC dose over the 3-year study was lowest in the TCZ QW group (median dose [mg/day]: TCZ QW, 2372.8; TCZ Q2W, 2863.0; PBO +26, 5006.0; PBO+52, 5322.5). Rates of serious adverse events per 100 pt-years over 3 years (double-blind period + part 2) were comparable for pts who never received TCZ (23.2) and who did receive ≥1 dose of TCZ (25.4), and rates of

serious infections were 4.6 and 3.5 per 100 pt-years, respectively. Additional results will be presented for original PBO pts.
Conclusion: Nearly half the pts treated with TCZ QW maintained CR for the entirety of part 2, though flares still occurred in the remaining pts once they discontinued TCZ treatment. Among pts who maintained CR in part 2, higher proportions of those originally assigned to TCZ were treatment-free compared with those originally assigned to PBO. Retreatment with TCZ restored CR in pts who experienced flare. Cumulative GC doses over 3 years were lower in pts originally assigned to TCZ than in those originally assigned to PBO. No new safety signals were observed with TCZ exposure in GCA pts during the 3-year study.

REFERENCES:
[1] Stone JH, et al. N Engl J Med. 2017;377:317-328.

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OP0141 CD28 AS A POTENTIAL THERAPEUTIC TARGET FOR GIANT CELL ARTERITIS

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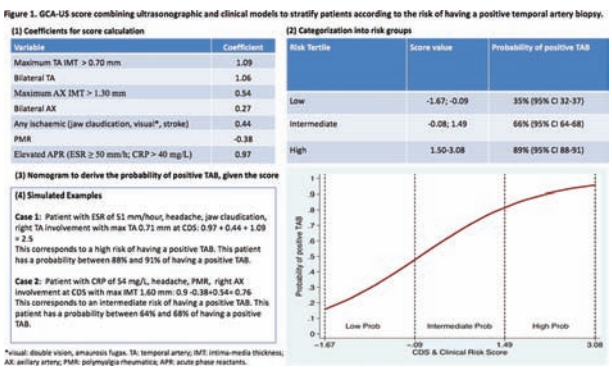
Background: Giant cell arteritis (GCA) is a granulomatous vasculitis of medium and large arteries. In GCA-affected arteries, vascular wall is destroyed by tissue-infiltrating CD4 T cells and macrophages, which leads to intramural neoangiogenesis, intimal hyperplasia and luminal occlusion.
Objectives: This study aimed to examine how CD28 signaling plays a role in vasculitis induction and maintenance and which pathogenic processes are dependent on CD28-mediated T-cell activation.
Methods: We engrafted human arteries into immunodeficient NSG mice and induced vasculitis by transferring GCA immune cells. Human artery-NSG chimeras were treated with anti-CD28 domain antibody or control Ab. Using tissue transcriptome analysis, immunohistochemistry, flow cytometry and immunometabolic analysis, treatment effects were examined in vivo and in vitro.
Results: Treating such humanized mice with an anti-CD28 domain antibody profoundly reduced tissue-infiltrating T-cells and effectively suppressed vasculitis. Mechanistic studies revealed that CD28 regulated AKT signaling, T-cell proliferation and differentiation of IFN-γ and IL-21-producing effector T-cells. Blocking CD28 signaling disrupted T-cell metabolic fitness; particularly, glucose utilization. Expression of the glucose transporter Glut1 and of glycolytic enzymes as well as mitochondrial oxygen consumption all rely on CD28 signaling. CD28 blockade effectively suppressed vessel wall remodeling processes such as adventitial microvessel formation and intimal hyperplasia as well as induction and maintenance of $CD4^+CD103^+$ tissue-resident memory T cells.
Conclusion: CD28 stimulation provides a metabolic signal required for pathogenic effector functions in GCA, implicating CD28 signaling as a promising therapeutic target.

REFERENCES:
[1] MMP (Matrix Metalloprotease)-9-Producing Monocytes Enable T Cells to Invade the Vessel Wall and Cause Vasculitis.
[2] Watanabe R, Maeda T, Zhang H, Berry GJ, Zeisbrich M, Brockett R, Greenstein AE, Tian L, Goronzy JJ, Weyand CM.
[3] Circ Res. 2018 Aug 31;123(6):700-715.
[4] Inhibition of JAK-STAT Signaling Suppresses Pathogenic Immune Responses in Medium and Large Vessel Vasculitis.
[5] Zhang H, Watanabe R, Berry GJ, Tian L, Goronzy JJ, Weyand CM. Circulation. 2018 May 1;137(18):1934-1948.
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OP0142 THE IMPACT OF DISEASE EXTENT AND SEVERITY DETECTED BY QUANTITATIVE ULTRASOUND ANALYSIS IN THE DIAGNOSIS AND OUTCOME OF GIANT CELL ARTERITIS: RESULTS FROM THE TEMPORAL ARTERYBIOPSY VERSUS ULTRASOUND (TABUL) STUDY AND VALIDATION IN AN INDEPENDENT COHORT

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Background: Colour duplex sonography (CDS) is used in patients with giant cell arteritis (GCA) to detect inflammatory oedema of the vascular wall, known as "halo". A quantitative analysis of halo characteristics to grade the severity and extension of vascular involvement detected by CDS could improve GCA assessment.
Objectives: To develop a quantitative CDS score to improve the diagnosis of GCA, and to correlate the score with histologic findings and clinical outcome. To determine the additional role of clinical signs/symptoms to the CDS score.
Methods: We selected patients with a positive CDS and a diagnosis of GCA recruited into the Temporal Artery (TA) Biopsy (TAB) vs Ultrasound in Diagnosis of GCA (TABUL) study. Due to collinearity we fitted 4 different CDS models including combinations of the following items: number of sites and distribution of halos, average and maximum intima-media thickness (IMT) at the level of the TA and axillary arteries (AX) and halos bilaterality. We fitted 4 models with clinical and laboratory findings. We combined the best CDS and clinical models (according to the Akaike Information Criterium) to identify independent correlates of a TAB diagnostic for GCA and of clinical outcome at 6 months (visual loss + VDI ocular + glucocorticoids > 10 mg/day and/or need for immunosuppressants) and performed a 10-fold cross-validation of the model. We validated the clinical outcome model on an independent cohort referred to the fast-track ultrasound clinics of two European rheumatology centres.
Results: We included 135 patients with GCA from TABUL (female: 68%, age 73 ±8) and 72 patients from an independent cohort (female: 46%, age 75±7). The


Figure 1. GCA-US score combining ultrasonographic and clinical models to stratify patients according to the risk of having a positive temporal artery biopsy.

(1) Coefficients for score calculation

Variable	Coefficient
Maximum TA IMT > 0.70 mm	1.09
Bilateral TA	1.06
Maximum AX IMT > 1.30 mm	0.54
Bilateral AX	0.27
Any ischaemic (jaw claudication, visual*, stroke)	0.44
PMR	-0.38
Elevated APR (ESR ≥ 50 mm/h; CRP > 40 mg/L)	0.97

(2) Categorization into risk groups

Risk Tertile	Score value	Probability of positive TAB
Low	-1.67; -0.09	35% (95% CI 32-37)
Intermediate	-0.08; 1.49	66% (95% CI 64-68)
High	1.50-3.08	89% (95% CI 88-91)

(3) Nomogram to derive the probability of positive TAB, given the score

(4) Simulated Examples

Case 1: Patient with ESR of 51 mm/hour, headache, jaw claudication, right TA involvement with max TA 0.71 mm at CDS: 0.97 + 0.44 + 1.09 = 2.5
This corresponds to a high risk of having a positive TAB. This patient has a probability between 88% and 91% of having a positive TAB.

Case 2: Patient with CRP of 54 mg/L, headache, PMR, right AX involvement at CDS with max IMT 1.60 mm: 0.9 -0.38+0.34+ 0.76
This corresponds to an intermediate risk of having a positive TAB. This patient has a probability between 64% and 68% of having a positive TAB.

*visual: double vision, amaurosis fugax. TA: temporal artery; IMT: intima-media thickness; AX: axillary artery; PMR: polymyalgia rheumatica; APR: acute phase reactants.

best fitting CDS model for TAB used maximum IMT size and bilaterality of halos at the level of the TA and AX. The best fitting clinical model included raised ESR/CRP, polymyalgia rheumatica, headache and ischaemic symptoms (jaw/tongue claudication, amaurosis, double vision, stroke). The coefficients from the combined models (CDS and clinical) allowed to produce a comprehensive score (GCA-US score) to stratify patients according to the probability of having a positive TAB (Figure 1). Model discrimination was fair (AUC-ROC 0.77, 95%CI 0.68-0.84). None of the considered variables was associated with clinical outcome expressing worse prognosis at 6 months.

Conclusion: We demonstrated that a quantitative analysis of CDS findings adds important diagnostic information with a computable estimate of the probability of positive histology, supporting the use of CDS as a surrogate diagnostic tool to replace TAB. A few CDS and clinical findings can be combined into a simple computable risk score to support a diagnosis of GCA.

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OP0143 PREDICTORS OF SEVERE CRANIAL ISCHEMIC COMPLICATIONS IN GIANT CELL ARTERITIS

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Background: Vision disturbances and ischemic stroke represent severe ischemic complications of giant cell arteritis (GCA). Despite the fast track GCA pathway since 2011 at our secondary/tertiary rheumatology center, about 10% of patients still develop permanent vision loss (PVL) or stroke.

Objectives: We aimed to determine markers predicting severe cranial ischemic complications in GCA.

Methods: We analyzed medical records of prospectively collected GCA patients diagnosed between 01.09.2011 and 31.12.2018 and compared clinical and laboratory characteristics of patients with and without vision disturbances (diplopia, transient vision loss (TVL), PVL) or ischemic stroke.

Results: During the 88-month observation period, we identified 250 new GCA patients (63.2% female, median (IQR) age 74.9 (67.8-79.9) years, 83.3% histologically proven, 79.8% with positive temporal artery ultrasound, 30.3% with extracranial large vessel involvement). Fifty (20.0%) patients developed either vision disturbances (16 diplopia, 10 TVL or 19 PVL) or ischemic stroke (8); isolated vision disturbances in 42, and isolated stroke in 5 patients. Conventional cardiovascular risk factors (obesity, arterial hypertension, hyperlipidemia, diabetes mellitus, and smoking were not associated with severe cranial ischemic complications (Table 1). The patients with severe cranial ischemic complications had more frequently had atrial fibrillation (RR 2.4 (95%CI 1.3-4.4), p=0.011). Twenty-five from 35 patients with atrial fibrillation were already treated with anticoagulants (10/13 in the group with cranial ischemic complication and 15/22 without them). Besides, GCA cases with severe cranial ischemic complications were significantly older (p=0.006) and more commonly reported jaw claudication (RR 1.8 (95%CI 1.4-2.3), p <0.001). We found no significant differences in the median level of C-reactive protein between the compared groups, whereas the erythrocyte sedimentation rate was slightly lower (p=0.032) and haemoglobin concentration higher (p=0.030) in cases with severe cranial ischemic complications.

Table 1. Characteristics of GCA patients with and without severe cranial ischemic complications

Characteristics	With complications (N=50)	Without complications (N=200)	P value
Female,%	52.0	66.0	ns
Age (yrs) #	77.9 (72.1-81.5)	74.0 (66.9-79.1)	0.006
Symptom duration#	26 (14-60)	30 (21-60)	ns
BMI*,#	25.2 (23.6-27.3)	25.5 (23.4-28.7)	ns
Ever smokers,%	48.0	35.5	ns
Diabetes,%	10.0	14.0	ns
Arterial hypertension,%	66.0	53.5	ns
Hyperlipidemia,%	30.0	30.5	ns
Ischemic heart disease	6.0	7.5	ns
Previous stroke	4.0	5.0	ns
Atrial fibrillation,%	26.0	11.0	0.011
Low dose Aspirin,%	26.0	18.0	ns
Anticoagulant treatment,%	22.0	10.5	ns (0.055)
Constitutional symptoms,%	62.0	77.0	ns
Jaw claudication,%	66.0	37.0	<0.001
ESR (mm/h) #	75 (58-94)	83 (61-110)	0.032
CRP (mg/l) #	60 (40-105)	84 (42-143)	ns (0.054)
Haemoglobin (g/l) #	121 (107-132)	116 (104-127)	0.030

Legend: # Median and interquartile range; BMI body mass index; * prior disease onset; CDS Colour Doppler sonography; ESR erythrocyte sedimentation rate; CRP C-reactive protein; ns not significant;

Conclusion: Increasing age and jaw claudication predicted severe cranial ischemic complications in our GCA cohort. Atrial fibrillation might represent an additional risk factor. **Disclosure of Interests:** None declared

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OP0144 MORTALITY IN GIANT-CELL ARTERITIS PATIENTS: A NATIONWIDE POPULATION-BASED STUDY

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Background: Giant cell arteritis (GCA), is the most common type of chronic systemic vasculitis over the age of 50. So far, studies regarding mortality in giant-cell arteritis (GCA) patients had yielded conflicting results.

Objectives: In this large population-based study we aimed to examine whether GCA is associated with increased mortality in different time periods, and in patients diagnosed ≤ 70 years of age.

Methods: We utilized the medical database of the Clalit-Health-Services in a retrospective cohort study. Follow-up was from January 1st, 2002 and continued until death or end of study follow-up at September 1st, 2018. Incident GCA patients were compared with age- and sex-matched controls. Estimated median survival-times were calculated using Kaplan-Meyer (KM) method and Risk for all-cause mortality in different follow-up periods was obtained by Cox proportional-hazard model, adjusted for age, gender, socio-demographic variables and traditional risk factors.

Results: Our study included 7,294 GCA patients and 34,156 age- and sex-matched controls. The mean age at the start of follow-up was 72.11±9.90 years with 69.2% females. The crude mortality rates for the entire follow-up period was 33.4% amongst GCA patients and 30.2% amongst controls. In KM analysis estimated median survival-time was 13.08 years (95% CI, 12.64-13.52 years) in GCA patients compared to 14.35 years (95% CI, 14.09-14.61) in controls (*P*-value < 0.001). Cox regression demonstrated increased mortality risk in the first 2 years after diagnosis (HR 1.15; 95% CI 1.04-1.26) and >10 years after diagnosis (HR 1.13; 95% CI 1.02-1.32). Risk was higher in patients diagnosed ≤70 years of age [HR 1.66 (95% CI 1.22-2.13) 0-2 years; HR 1.44 (95% CI 1.16-1.79) > 10 years].

Conclusion: GCA patients have a minor decrease in long-term survival compared to age-and-sex matched controls. The seen difference is due to excess mortality in the first 2 years, and >10 years after diagnosis of GCA, especially in patients diagnosed ≤70 years of age.

REFERENCES:

[1] Mohammad AJ, Nilsson J-Å, Jacobsson LTH, Merkel PA, Turesson C. Incidence and mortality rates of biopsy-proven giant cell arteritis in southern Sweden. Ann Rheum Dis [Internet]. 2015 Jun 1 [cited 2018 Aug 10];74 (6):993–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24442881

[2] Salvarani C, Cantini F, Boiardi L, Hunder GG. Polymyalgia Rheumatica and Giant-Cell Arteritis. N Engl J Med [Internet]. 2002 Jul 25 [cited 2018 Aug 3];347(4):261–71. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMra011913

[3] Hill CL, Black RJ, Nossent JC, Ruediger C, Nguyen L, Ninan J V., et al. Risk of mortality in patients with giant cell arteritis: A systematic review and meta-analysis. Semin Arthritis Rheum [Internet]. 2017 Feb 1 [cited 2018 Aug 4];46(4):513–9. Available from: https://www.sciencedirect.com/science/article/pii/S0049017216301433?via%3Dihub

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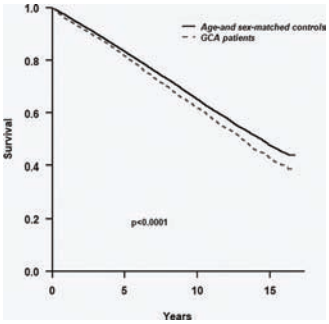


Figure 1. Kaplan-Meyer survival curve showing cumulative survival over time in years

speaker for AbbVie; Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Perrigo; Pfizer; Rafa; Sanofi, Doron Comanesther: None declared, Shmuel Tiosano: None declared.
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OP0145 NORMAL VERSUS ELEVATED ACUTE PHASE REACTANTS IN PATIENTS WITH POLYMYALGIA RHEUMATICA: ARE THESE DIFFERENT SUBSETS?

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Background: Systemic signs of inflammation such as raised CRP or ESR are a classical feature of PMR, but some patients present with normal acute phase reactants (APR).[1,2] It is not known whether these patients represent milder forms of PMR, whether their disease is not yet fully expressed, or whether they represent another pathophysiological subset of PMR or another disease. Data on demographic and clinical differences between PMR patients with normal versus elevated APR might provide some answers.
Objectives: To explore baseline differences in demographics and clinical characteristics in PMR patients with and without elevated APR.
Methods: We conducted a retrospective cohort study of clinical characteristics of newly diagnosed PMR patients (clinical diagnosis) who visited our outpatient clinic between April 2012 and September 2017. Patient with concomitant inflammatory rheumatic disease were excluded. Data on patient-, disease,- and treatment characteristics were extracted from the electronic health record. Descriptive statistics were used [using mean (SD), median (p25-p75) or n (%) as appropriate], and differences between patients with high APR(CRP>10 mg/L and/or ESR >30mm/hour) were tested using Fischer's exact test for categorical data, t-test for normally and Wilcoxon test for non-normally distributed data.
Results: 454 patients were included (table 1). Sixty-two patients had normal, and 392 had elevated APR. In the group with normal APR, fewer patients had peripheral arthritis (2 versus 9%; p=0.044) and fewer had anemia at diagnosis (17 versus 43%; p= 0.001). Furthermore, patients had a longer median duration of symptoms before diagnosis (13 versus 10 weeks; p= 0.0196) and were more likely to have a history of PMR (16 versus 8%; p= 0.057). No significant differences were found in other clinical characteristics.
Conclusion: The results of this cohort indeed suggest that patients with normal APR are a different subset of PMR patients. Fewer cases have peripheral arthritis and anemia at diagnosis, suggesting a milder form of PMR. Secondly, our results do not support the hypothesis that PMR of those with normal APR is not yet fully expressed, as they have a longer symptom duration prior to diagnosis.

Table 1. Baseline characteristics of patients with normal versus elevated APR

Characteristic	Normal APR (N= 62; 14%)	Elevated APR (N= 392; 86%)
Female (%)	32 (52)	218 (56)
Age in years at diagnosis (SD)	66.0 (7.5)	66.6 (8.9)
History of previous PMR (%)	10 (16)	32 (8)
RR systolic (SD) diastolic (SD) mmHg[#]	146 / 85 (18;11)	145 / 84 (18;10)
Weeks with PMR symptoms before diagnosis (median, IQR)*	13 (7-20)	10 (6-16)
Neckpain	27 (44)	175 (45)
Bilateral shoulderpain /stiffness (%)	57 (92)	361 (92)
No shoulderpain/stiffness (%)	2 (3)	20 (5)
Bilateral hippain/stiffness (%)	55 (87)	327 (83)
No hippain/stiffness (%)	7 (11)	51 (13)
Both bilateral shoulder- and hippain/stiffness (%)	52 (84)	310 (79)
Peripheral arthritis (%) *	1 (2)	35 (9)
Dubious (%)	4 (6)	22 (6)
Distal swelling pitting edema (%)	1 (2)	11 (3)
Systemic symptoms [#] (%)	27 (44)	172 (44)
BSE (median, IQR)	19 (12-25)	42 (21-53)
CRP (median, IQR)**	5 (2-7)	24 (21-57)
Anemia (%)*	8 (17)	132 (43)
Morning stiffness>45 min (%)	29 (73)	206 (68)
Rheumatoid factor present*** (%)	4 (11)	24 (13)
Anti-CCP present*** (%)	0 (0)	3 (1)

[1] N=32 in normal APR group; N= 247 in elevated APR group
* Significant with appropriate test
#Fever, night sweats, weight loss, anorexia
**N=46 in normal APR group; N= 358 in elevated APR group
***Rheumatoid factor: N= 36 versus N= 257; anti-CCP: N= 33 versus N= 242

REFERENCES:

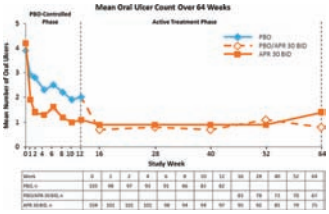
[1] Buttgereit F, Dejaco C, Matteson EL, Dasgupta B. Polymyalgia Rheumatica and Giant Cell Arteritis: A Systematic Review. JAMA. 2016 Jun;315:2442-58.
[2] González-Gay MA[1], Matteson EL[2] Castaneda S[3]. Polymyalgia rheumatica. Lancet. 2017 Oct Oct 7;390(10103):1700-1712

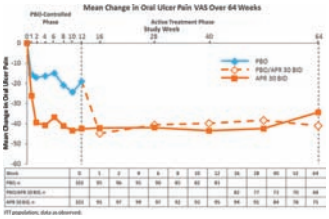
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OP0146 EFFICACY OF APREMILAST FOR ORAL ULCERS ASSOCIATED WITH ACTIVE BEHÇET'S SYNDROME OVER 64 WEEKS: RESULTS FROM A PHASE III STUDY

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Background: Behçet's syndrome is a chronic, relapsing, multi-system inflammatory disorder characterized by recurrent oral ulcers (OU) that can impact quality of life (QoL).
Objectives: To assess apremilast (APR) efficacy and safety for the treatment of OU associated with Behçet's syndrome in the phase III RELIEF study for up to 64 wks and at 4-wk follow-up (after APR discontinuation).
Methods: Adult patients (pts) with active Behçet's syndrome (defined by $\geq$3 OU at randomization or $\geq$2 OU at screening and at randomization without active major organ involvement) were randomized (1:1) to placebo (PBO) or APR 30 mg twice daily for 12 wks. All pts then received APR through Wk 64. Pts who completed the Wk 64 visit or discontinued treatment at any time and for any reason in the study entered a 4-wk posttreatment observational follow-up. The primary endpoint was area under the curve for the number of OU over 12 wks (AUC_{Wk0-12}), which reflects the number of OU over time and accounts for the recurring-remitting course of OU. Other outcomes included change from baseline in OU pain VAS, complete response (% of pts with no OU) or partial response (% of pts with $\geq$50% reduction in number of OU), disease activity (Behçet's Disease Current Activity Form [BDCAF], composed of the Behçet's Disease Current Activity Index [BDCAI], Pt's and Clinician's Perception of Disease Activity and Behçet's Syndrome Activity Score [BSAS]), and QoL (Behçet's Disease QoL [BDQoL]).
Results: A total of 207 pts were randomized and received $\geq$1 dose of study medication (PBO: n=103; APR: n=104); 178 pts entered the active treatment phase (PBO/APR: n=83; APR: n=95) and 143 pts (PBO/APR: n=68; APR: n=75) completed Wk 64. The primary endpoint of AUC_{Wk0-12} was achieved; significantly lower AUC_{Wk0-12} was observed for APR vs PBO (P<0.0001). Significantly lower OU counts ($P\leq$0.0015) and OU pain ($P\leq$0.0035) were observed with APR vs PBO from Wks 1 through 12; APR efficacy was sustained up to 64 wks (Figure). Significantly greater improvements with APR were observed in complete and partial response of OU at Wk 12 (P<0.0001); effects were maintained through Wk 64 (53.3% and 76.0%, respectively). Pts initially randomized to PBO and switched to APR at Wk 12 showed comparable benefits through Wk 64 (Figure). Improvements in disease activity (BDCAI: P=0.0335; BSAS: P<0.0001) and QoL (BDQoL: P=0.0003) were significant in pts receiving APR vs PBO at Wk 12 and maintained at Wk 64. Comparable effects in pts who switched from PBO to APR were observed at Wk 64. After APR was discontinued before or at Wk 64, the improvements in OU assessments decreased within 4 wks. Disease activity measures and BDQoL similarly indicated recurrence of symptoms at the 4-wk follow-up. Incidence of any adverse event (AE) was comparable for pts initially randomized to APR vs PBO during the PBO-controlled period (78.8% vs 71.8%) and through Wk 64 for pts who continued APR vs pts who switched from PBO to APR (84.3% vs 86.5%). The most common AEs with APR were diarrhea, nausea, headache and upper respiratory tract infection; most AEs were mild/moderate in severity, and no new safety concerns were identified.





Conclusion: APR demonstrated efficacy in the treatment of OU in pts with active Behçet's syndrome. Benefits were sustained for up to 64 wks with continued treatment. APR was well tolerated, and safety was consistent with the known safety profile of APR.

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OP0147

KAWAKINRA: A PHASE IIA MULTICENTER TRIAL TO ASSESS THE EFFICACY, AND SAFETY OF ANAKINRA IN PATIENTS WITH INTRAVENOUS IMMUNOGLOBULIN-RESISTANT KAWASAKI DISEASE

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Background: The development of more potent therapeutic approaches of KD is an urgent need because intravenous immunoglobulin (IVIg) treatment is not effective in 20% of patients, increasing the risk of coronary dilatations/aneurysms. The combination of genetic and transcriptomic data revealed the key role of interleukin-1 (IL-1) signaling in KD vasculitis and mouse model of KD has shown that anakinra (IL1RA: IL-1R1receptor antagonist) could prevent the development of vascular aneurysms.

Objectives:

- To assess as primary objective, the efficacy of anakinra in patients with KD who fail to respond to at least one infusion of 2g/kg of IVIg.
- To assess its safety and tolerability and its effect on disease activity, systemic inflammation and coronary lesions.

Methods: A 45-day, phase IIa proof of concept study open labeled with anakinra dose escalation, with a target of at least 12 patients completing the study Eligible patients had KD according to the AHA criteria, duration of fever ≤ 14 days, and were ≥ 3 months and 5 Kg. They had persistent (or relapsing) fever (≥38°C) within 48h of the last IVIG infusion, had not received other alternative treatment including steroids, and had no others exclusion criteria. After informed consent, they received a starting dose of 2mg/kg *(patients <10kg and/or <8 months: 4mg/kg)* of anakinra, which could be increased every 24h of 2mg/kg until a maximum of 6mg/kg *(patients <10kg and/or <8 months: 8mg/kg)*, in case of persistent fever. Anakinra treatment duration was 15 days. Outcome measures were fever, KD symptoms, blood inflammation and cardiac echography. Total study duration was 45 days. **Clinical trials: NCT02390596**. The study is supported by a grant from the French ministry of health, APHP, national PHRC 2014. IRB approval was obtained and all patients (parents) gave informed consent.

Results: 18 patients were screened and 16 were included and 13 have completed the study. Anakinra was started in 16 patients (14 boys, 2 girls) at a median age 2 years (3 months to 6 years) and at a median of 9.5 days after the onset of fever. 4 patients escaped early for SAE, and 1 had sJIA final diagnosis. The maximum dose of anakinra was 6mg/kg in 6 patients, 4mg/kg in 6, and 2mg/kg in 4. Mean PGA decreased from 7.80 (4-10) to 1.2 (0-3) at D14. Median temperature was 37.6°C (36.7-39.7) at day 3 and 37.2°C at D7 (36.7- 37.9)). Median CRP was 135mg/L at screening and decreased to 9.5 mg/L at D7. 8/14 evaluated patients had coronary dilatation (Z score max ≥2.5mm) at inclusion, 5/14 at D14 and 3/14 at D45. 3/14 patients who increased Z score at D14 decreased it at J45. We observed 3 severe adverse events (SAE) where treatment was discontinued: anakinra overdose, MAS in a patient evolving to sJIA and increase of coronary dilatation. Others AE included cytolytic hepatitis (2 patients), hypereosinophilia (1), injection site reaction (1) and pancreatitis (1) without treatment discontinuation.

Conclusion: We have realized the first experimental study assessing IL-1 blockade in severe refractory KD. 15 days-duration of anakinra treatment, given early in the course of IVIG-resistant KD, was rapidly effective on KD symptoms, biologic inflammation and coronary dilatations in almost all patients, with a good tolerability. This study calls for further investigation of IL1 blockade in KD

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THURSDAY, 13 JUNE 2019

Journeys from bench to bedside in paediatric rheumatology

OP0148

METABOLOMICS IN JUVENILE-ONSET SLE: IDENTIFYING NEW BIOMARKERS TO PREDICT CARDIOVASCULAR RISK

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Background: Juvenile-onset systemic lupus erythematosus (JSLE) is an autoimmune disorder characterised by immune dysregulation, chronic inflammation and increased cardiovascular risk (CVR). Cardiovascular disease is the leading cause of mortality in JSLE not attributable to lupus flare. Our findings in adult-onset SLE link immune cell dysregulation with dyslipidaemia but little is known about the immune profile or whether abnormal lipid metabolism contributes to disease pathogenesis in JSLE.

Objectives: The objective of this study was to investigate dyslipidaemia and CVR in a cohort of JSLE patients using in depth metabolomics and relate this to clinical and immune cell profiles and to identify novel biomarkers to predict CVR in these patients.

Methods: Metabolic biomarker analysis (NMR) and in-depth immune cell phenotyping (30 subsets by flow cytometry) was performed on serum and PBMCs respectively from a discovery cohort of 35 JSLE patients (median age 19 (14-25), 12 males, 23 females) compared with 39 age/sex matched healthy donors (HCs) (median age 18 (16-25), 17 males, 22 females). Data was analysed using cluster and correlation-correlation and receiver operating characteristic (ROC) analysis. Results were validated in a second cohort of 31 JSLE patients.

Results: Patient stratification by metabolomic profile using unbiased hierarchical clustering revealed 3 groups that each had a unique lipoprotein profile, immune cell phenotype and clinical presentation. Group-1 had decreased atheroprotective high density lipoproteins (HDL) and increased atherogenic very low and low density lipoproteins (VLDL/LDL) and Group-2 had elevated HDL but reduced VLDL/LDL indicating that these groups could be at high and low CVR respectively. This hypothesis was validated by previously recognised markers of CVR including the atherogenic index of plasma, ApoB:A1 ratios and lipid biomarkers we previously identified to be associated with pre-clinical atherosclerotic plaque in adult SLE patients. Patients in Group-1 had a significant increase in plasmablasts and activated T-cells compared to HCs and had clinical features associated with increased disease activity. These immunopathogenic properties were not seen in

low CVR Group-2. Patients in Group-3 displayed an intermediate CVR but a pro-inflammatory immune cell profile. This metabolomic patient stratification was validated in a separate JSLE cohort. Importantly ApoB:A1 ratio was identified as a highly predictive biomarker (ROC area under the curve>0.99) distinguishing between JSLE patients in Group-1 and 2, indicating high and low CVR respectively. Finally, longitudinal analysis revealed that the ApoB:A1 ratio biomarker remained stable over time.

Conclusion: ApoB:A1 ratio and metabolomic lipoprotein signatures could be new biomarkers to predict CVR in JSLE patients. Patient stratification using these biomarkers could provide an opportunity for tailored disease treatments using lipid modification therapy and/or diet/lifestyle interventions.

REFERENCES:

[1] Kone-Paut, I., et al., Lupus in adolescence. Lupus, 2007. 16(8): p. 606-12.
[2] Ambrose, N., et al., Differences in disease phenotype and severity in SLE across age groups. Lupus, 2016.
[3] McDonald, G., et al., Normalizing glycosphingolipids restores function in CD4+ T cells from lupus patients. J Clin Invest, 2014. 124(2): p. 712-24.
[4] McMahon, M., et al., Dysfunctional proinflammatory high-density lipoproteins confer increased risk of atherosclerosis in women with systemic lupus erythematosus. Arthritis & Rheumatism, 2009. 60(8): p. 2428-2437.

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OP0149 CD4+ T CELLS FROM CHILDREN WITH ACTIVE JUVENILE IDIOPATHIC ARTHRITIS SHOW ABERRANT CHROMATIN ORGANIZATION AND CTCF LOCALIZATION ASSOCIATED WITH TRANSCRIPTIONAL ABNORMALITIES

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Background: Our group and others have shown that peripheral blood cells of children with juvenile idiopathic arthritis (JIA) display numerous transcriptional abnormalities. However, most of these studies have been performed on mixed cell types (peripheral blood mononuclear cells, whole blood). Little cell type specific data is available, making mechanistic inferences and links to disease pathogenesis difficult.

Objectives: To define transcriptional patterns in CD4+ T cells from children with polyarticular JIA and query mechanisms underlying transcriptional abnormalities.

Methods: We studied CD4+ T cells obtained from children with active polyarticular onset JIA and sought to identify epigenetic features associated with altered gene expression. We performed RNA-seq and ATAC-seq on a cohort of patients who had the active disease and were under treatment with methotrexate and etanercept (ADT), patients who fit criteria for clinical remission on medication (CRM), and healthy control children (HC). We used standard used the common dispersion protocol in EdgeR to identify differential gene expression. We used our recently developed and validated Hidden Markov ModeleR for ATAC-seq doftware to identify differentially accessible regions, comparing ADT, CRM, and HC samples. We integrated ATACseq and RNAseq data using the BETA software package. After preliminary analysis revealed a potential role for the transcriptional regulator, CCCTC binding factor (CTCF) in the observed transcriptional patterns, we performed ChIPseq and HiChIP studies on an independent group of JIA CD4+ T cell samples.

Results: We found widespread transcriptomic differences between ADT and either HC or CRM patients. We identified 4,062 genes that showed differential expression between ADT and HC samples. Gene expression patterns from CRM samples were nearly identical to healthy controls, suggesting that remission largely results in normalization of CD4+ T cell transcriptomes. We performed transcription factor motif analysis on the ATAC-seq identified accessible regions that were associated with differentially expressed genes. We identified the motif for the CCCTC-binding factor (CTCF) as being enriched within these accessible regions, compared to accessible regions associated with non-differentially expressed genes. We performed CTCF ChIP-seq and HiChIP on a second cohort of ADT and HC patients and were able to identify differential binding events, mediated by genetic alterations that interacted with differentially expressed genes.

Conclusion: Transcriptional abnormalities in CD4+ T cells of children with polyarticular JIA are associated with aberrant chromatin organization compared to healthy children. Some of this organization is due to aberrant localization of the transcriptional regulator CTCF, which is due, in some patients, to genetic variance.

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OP0150 MONOCYTE AND MACROPHAGE TRANSCRIPTIONAL PHENOTYPES IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS REVEAL TRIM8 AS A MEDIATOR OF IFNGAMMA HYPERRESPONSIVENESS AND RISK FOR MACROPHAGE ACTIVATION SYNDROME

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Background: Systemic juvenile idiopathic arthritis (SJIA) is a severe and distinct subtype of childhood arthritis. Children with SJIA are at risk for macrophage activation syndrome (MAS), a life-threatening episode of hyperinflammation driven by interferon-gamma (IFNγ). Previous work has suggested that monocytes in SJIA display hyperrsponsiveness to IFNγ, but the molecular basis of this remains unclear.

Objectives: Utilize transcriptional profiling of monocytes and macrophages in SJIA to identify polarization phenotypes including features of interferon response

Methods: Bulk RNA-sequencing (RNA-seq) was performed on purified monocytes from 26 patients with SJIA without over MAS. In addition, single-cell RNA-seq was performed on isolated bone marrow macrophages from control patients and patients with SJIA and MAS. THP-1 monocytic cells and primary human monocyte-derived macrophages (MDM) were transfected with TRIM8-specific or negative control small-interfering RNA prior to stimulation with IFNγ.

Results: RNA-seq of purified SJIA monocytes revealed marked transcriptional changes between cells from patients with high vs low serum ferritin levels. Pathway analysis demonstrated enriched upregulated gene ontology pathways including Response to External Stimulus ($p=2.73x10^{-17}$), Defense Response ($p=2.66x10^{-14}$) and Inflammatory Response ($p=1.95x10^{-11}$). When comparing the SJIA monocyte signature to well-characterized polarization phenotypes, we identified substantial overlap with multiple polarization states, most notably M1 and M2b, but little evidence of IFNγ-induced signature. Among the most highly upregulated genes in SJIA monocytes was tripartite motif containing 8 (TRIM8), an E3 ubiquitin-ligase involved in activation of IFNγ through promoting degradation of the suppressor of cytokine signaling 1 (SOCS1). Elevated TRIM8 expression was found in monocytes from both active and inactive SJIA patients, with the highest levels in those with subclinical MAS features (n=3). Furthermore, we utilized single cell RNA-seq to determine gene expression profiles of bone marrow macrophages from a patient with subclinical MAS. This identified a distinct subpopulation of bone marrow macrophages which exhibited markedly altered transcriptional profiles, with alterations in gene pathways predicted for hemophagocytes in MAS, including cellular response to interferon gamma (p=1.35e-14), endocytic vesicle membranes (p=8.44E-14), and phagosome (p=2.98e-9). These bone marrow macrophage also showed significantly increased TRIM8 expression (6.4-fold increase, p=0.02). To confirm the role of TRIM8 in augmenting macrophage responses to IFNγ, RNA interference was use to knock-down TRIM8 expression in THP-1 cells and MDM. TRIM8 knockdown macrophages showed significant reductions in both early (4 hour) and late (24-48 hours) response to IFNγ, as determined by production of CXCL9, a biomarker for MAS activity in both humans and animal models.

Conclusion: Peripheral blood monocytes in SJIA display markers of multiple polarization states, while during MAS tissue macrophages demonstrate a clear IFNγ response phenotype. TRIM8 is highly expressed in both monocytes and macrophages in SJIA, and in vitro knockdown of TRIM8 impairs IFNγ responses in macrophages. Together these data provide a molecular mechanism for monocyte hyperresponsiveness to IFNγ in SJIA, as well as a novel therapeutic target for MAS.

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OP0151

MIRNAS CONTRIBUTE TO DYSREGULATED ROS METABOLISM OF IMMUNE CELLS IN THE INFLAMED JOINT

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Background: In the last years miRNAs have emerged as critical regulators of innate and adaptive immune responses and an altered expression or function is associated with several inflammatory and autoimmune diseases. Therefore miRNAs are also believed to promote inflammatory processes within the inflamed joint of juvenile idiopathic arthritis (JIA) patients. It is furthermore known that oxidative stress is associated with JIA. Free radicals are implicated in joint damage and play an important role as secondary messengers in immunological responses. How and if miRNAs contribute to dysregulated reactive oxygen species (ROS) metabolism in JIA remains to be elucidated.
Objectives: We aimed to identify miRNAs and miRNA regulated pathways, which contribute to dysregulated immune cell responses within the inflamed joint.
Methods: miRNA profiling was performed on peripheral blood mononuclear cells (PBMCs) from healthy children, PBMCS from 9 JIA patients and synovial fluid mononuclear cells (SFMCs) from the same JIA patients. Subsequently, GO and pathway enrichment analyses were performed on predicted target genes. Upregulation of miRNAs was confirmed *in vitro* after incubation with synovial fluid by qRT-PCR. Mitochondrial integrity, cellular ROS and Nrf2 protein expression were measured by flow cytometry.
Results: Transcriptome analysis of JIA SFMCs compared to HC PBMCs revealed strongly enhanced expression of *miR23a* and *miR23a*, *miR27a*, *miR146a*, and *miR155*, which are involved in oxidative stress responses. In addition, expression of those could be induced in healthy control PBMCs by synovial fluid *ex vivo*. ROS level in synovial fluid T cells were enhanced, while expression of Nrf2, the main regulator of anti-oxidative responses and a target of *miR27a*, remained low. Furthermore mitochondrial cyclophilin, which regulates ROS escape from mitochondria and is suppressed by *miR23a*, was downregulated in SFMCs as well.
Conclusion: SFMCs within the inflamed joint reveal a distinct miRNA expression profile. Especially miRNAs that are involved in regulation of ROS metabolism are upregulated. In line with this, expression of Nrf2 and mitochondrial cyclophilin which are important regulators of cellular ROS metabolism are reduced while production of ROS is enhanced. We suggest that higher abundance of miRNAs, that are involved in oxidative stress pathways, contribute to redox dysregulations within the inflamed joint and thereby contribute to inflammatory processes.
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OP0152

OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS DOES NOT SHOW SIGNS OF T-CELL EXHAUSTION, IN SPITE OF INCREASED EXPRESSION OF CO-INHIBITORY RECEPTORS

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Background: Oligoarticular Juvenile idiopathic arthritis (O-JIA) is a common inflammatory joint disease in children, driven by continuous local T-cell activation. [1] T cell activation is counter-balanced via signals generated by co-inhibitory receptors (co-IRs) such CTLA-4, PD-1, LAG-3, and TIM-3.[2]
Objectives: Here we identify the role of co-IRs in the pathogenesis of O-JIA.
Methods: Paired synovial fluid (SF) and plasma, PBMCs and SFMCs, were obtained from O-JIA patients together with clinical data (n=14). Plasma from healthy controls (HC, n=14); paired SF and plasma from 5 non-arthritis juvenile orthopedic patients (OC, n=5) served as controls. Soluble levels of co-IRs were measured by ELISA and their cellular expression by flow cytometry. Spontaneously differentiated fibroblast like synoviocytes (FLS) from SFMCs were co-cultured with autologous PBMCs/SFMCs and used as an *ex-vivo* disease model. Functional effects of co-IRs were evaluated via blocking them with checkpoint inhibitors in these *ex-vivo* disease models.
Results: In O-JIA patients, increased levels of sPD-1, sLAG-3 and sTIM-3, but not sCTLA-4, were present in the SF compared with plasma. (Figure 1A) There was a close correlation between sPD-1 levels in the plasma and SF (r=0.65, p=0.029). In plasma, sTIM-3 levels correlated with sPD-1 levels (r=0.84, p=0.001) and sLAG-3 levels (r=0.68, p=0.021). In the SF, there was a significant correlation between sLAG-3 levels and sPD-1 levels (r=0.54, p=0.047). None of the soluble co-IR levels correlated with disease activity scores. Plasma and SF levels of sLAG-3 and sTIM-3 were higher in O-JIA patients when compared with HC and OC. (Figure 1A) On the CD3+CD4+CD45RO+ T cells, the surface expression of PD-1 (p=0.02), LAG-3 (p=0.001), TIM-3 (p<0.001), but not CTLA-4 (p=0.48), were higher in the SFMC compared with PBMC.
MHC class II expression was induced on FLS when these were co-cultured with autologous PBMCs and SFMCs, together with an increased Monocyte Chemoattractant Protein-1 (MCP-1) production. (Figure 1B) Only addition of neutralizing anti-LAG3 antibodies significantly increased the MCP-1 production in PBMC monocultures (p<0.01) and FLS+PBMC co-cultures (p<0.01). PBMCs and SFMCs produced significantly higher levels of IFN-γ after CD3/CD28 activation both in monocultures and co-cultures (p<0.001), but they were not affected from addition of any of the checkpoint inhibitor.

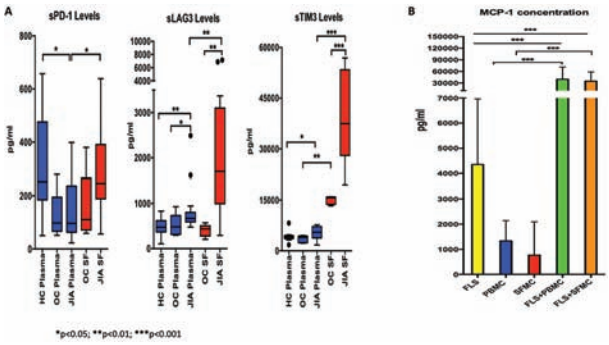


Figure 1

Conclusion: This is the first report studying the effects of different co-IRs in O-JIA. Both the soluble levels and the surface expressions of the co-IRs were higher at the site of inflammation in O-JIA. SFMCs and PBMCs of O-JIA patients are not exhausted, based on their ability to respond to CD3/CD28 activation. This is opposite to what has been shown in adult inflammatory arthritis.[3] Co-cultures of autologous FLSs and PBMCs/SFMCs may serve as an *ex-vivo* arthritis model to perform functional analysis. LAG-3 stands out among the co-IRs and might play a role in O-JIA pathogenesis and a potential therapeutic option for O-JIA.

REFERENCES:

[1] Wedderburn, L.R., et al., Int Immunol, 2001. 13(12): p. 1541-50.
[2] Wherry, E.J. and M. Kurachi, Nat Rev Immunol, 2015. 15(8): p. 486-99.
[3] Frenz, T., et al., J Allergy Clin Immunol, 2016. **138**(2): p. 586-589 e10.

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OP0153

BROADENING OUR UNDERSTANDING OF THE GENETICS OF JUVENILE IDIOPATHIC ARTHRITIS: INTERROGATION OF THREE DIMENSIONAL CHROMATIN STRUCTURES WITHIN JIA-ASSOCIATED RISK LOCI

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Background: Our group has shown that, like most complex traits, the risk loci for juvenile idiopathic arthritis (JIA) identified on genome-wide association studies (GWAS) and genetic fine mapping studies are highly enriched for enhancers. Enhancers are regulatory elements that fine-tune gene expression to specific

physiologic circumstances. Enhancers do not always regulate the nearest gene, and may regulate more than one gene. Enhancers typically regulate genes within the same chromatin loop, or topologically associated domain (TAD).
Objectives: To gain a better understanding of the genetics of JIA by examining the broader chromatin architecture that encompasses the known risk haplotypes.
Methods: We used publically available chromatin conformation HiC data and the online JuiceBox software suite to query known JIA risk haplotypes for evidence of physical interactions between putative enhancers within the haplotypes and immunologically relevant genes. We specifically queried 20 haplotypes in which H3K4me1/H3K27ac marks were prominent within both lymphoid and myeloid cells. We queried data from GM12787 (B cell), K562 (lymphoblast), and THP-1 (monocyte/macrophage) cells, as well as human cord blood T cells. To identify TADs associated with specific enhancers, we used a 5KB resolution (which allowed us to visualize chromatin loops as peaks), setting the cursor at the center of each putative enhancer. We also identified the genes within the identified chromatin loop domains and used gene ontology (GO) analyses to identify functional associations among genes within the TADs incorporating the JIA risk loci.
Results: We identified at least one chromatin loop structure in all 20 of the JIA risk haplotypes for each of the 4 cell lines we queried. These loops were not cell type specific. That is, almost identical loops structures could be seen in each of the cell lines at each of the loci, suggesting that these enhancers regulate a broad range of common leukocyte functions. The TADs incorporating the JIA haplotypes invariably included genes of immunologic interest. For example, the TAD incorporating the *IL2RA* haplotype including *IL15R* (the alpha chain of the IL15 receptor) and *PKCQ*, a protein kinase C-family enzyme important in both T and B cell activation. The most complex locus was *C5orf56* which encompassed 23 genes (including *IL3*, *IL4*, and *IL13*) and 3 miRNA within 4 loops and sub-loops. Genes within the TADs were highly enriched for multiple GO terms for processes involved in leukocyte activation (e.g., MAP kinase signaling cascade), JAK-STAT responses, chemotaxis, and cytokine-mediated signaling pathways.
Conclusion: These 20 JIA-associated risk loci are situated within complex chromatin regions that show similar features in both lymphoid and myeloid cells. HiC data demonstrate direct physical contacts between putative enhancers within the risk loci and multiple genes of immunologic interest. We hypothesize that at least some of the genes within the haplotype-associated TADs are the long sought "target genes" of JIA-associated genetic variants. This work emphasizes the importance of broadening our focus beyond the "nearest gene" to the GWAS-identified tag SNPs.
Disclosure of Interests: None declared
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OP0154 **A NOVEL RELA TRUNCATION IN A 3-GENERATION FAMILY WITH BEHCET'S DISEASE ALTERS THE APOPTOTIC RESPONSE TO INFLAMMATORY STIMULANTS**

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Background: Bechet's disease (BD) is a heterogeneous multifactorial auto-inflammatory condition characterised by recurrent episodes of oral and genital ulceration, uveitis and skin lesions, with less frequent involvement of the gastrointestinal tract, large blood vessels and central nervous system. The NF-κB pathway is a 'master-regulator' of immune and inflammatory signaling, with the ability to control the expression of key inflammatory genes and genes associated with apoptosis and proliferation.
Objectives: To identify the pathobiology associated with a novel genetic mutation identified in a 3-generation family with Behçet's-like mucocutaneous ulceration syndrome, primarily involving childhood-onset chronic oral and genital ulcers.
Methods: The novel RELA mutation was identified using whole exome sequencing. Immunoblot of peripheral blood mononuclear cell (PBMCs) lysates from affected family members was used to determine if the predicted truncated protein was expressed. PBMCs were stimulated with TNF; NFkB phosphorylation was measured relative to unstimulated cells form affected and unaffected family members. HEK293T cells transfected with plasmids encoding either wild-type or the novel RELA-mutant and overexpression confirmed via immunoblot. An in vitro model of the RELA truncation was used to observe the effect of the RELA truncation on response to TNF stimulation. Apoptosis protein arrays, western blots, and ELISA assays were used to investigate the effect of TNF on wild-type RELA compared to the mutant protein. Mouse Embryonic Fibroblasts (MEFs) isolated from $RELA^{-/-}$ mice, which do not express endogenous RELA, were transfected with plasmids encoding either wild-type or the novel RELA-mutant. Wild Type MEF cells (with endogenous RELA) were used as a control. Cells were stimulated with LPS (2.5ug/ml) or no treatment control for 12 hours.
Results: A heterozygous cysteine deletion at position 1459 in RELA was detected in all affected individuals as previously reported. This mutation results in a frameshift His487ThrfsTer7, producing a truncated protein of 492 amino acids. RELA-His487ThrfsTer7 heterozygotes have different phosphorylation kinetics of key NFkB pathway proteins in response to TNF compared to wild-type controls. Cells overexpressing RELAHis487ThrfsTer7, had increased pro-apoptotic proteins (BAD, cleaved caspase 3 and SMAC) whereas anti-apoptotic proteins (BCL2, CLASPIN) were decreased compared to cells transfected with wildtype RELA. Cells transfected with RELAHis487ThrfsTer7 were less sensitive to TNF stimulation compared to wild-type controls, as measured by induction of TNF-sensitive proteins.
Conclusion: This study gives novel information on both the genetic basis and biological mechanisms of BD in individual families. Familial mutations that induce haploinsufficiency of RELA have recently been associated with BD. However, the His487ThrfsTer7 results in protein truncation rather than haploinsufficiency. Our study supports several recently published studies that loss-of-function mutations in the NF-κB pathway are linked with the development of familial early-onset BD-like syndromes. We propose that RELAHis487ThrfsTer7 causes altered NFκB signaling resulting in reduced mucosal cell recovery and the observed Behçet's-like mucocutaneous ulceration syndrome.
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Transformative care – the future

OP0155-HPR **TARGETS FOR REDUCING PREMATURE MORTALITY IN OLDER ADULTS WITH OSTEOARTHRITIS: RESULTS FROM A NOVEL PATH ANALYSIS WITHIN A COX PROPORTIONAL HAZARDS MODEL**

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Background: There is increasing evidence that it is the impact of osteoarthritis rather than the osteoarthritis itself that explains an excess risk of mortality. This indicates that potentially modifiable targets may reduce mortality for those with osteoarthritis. Mediation analysis can be used to investigate pathways, although this has rarely been undertaken using survival analysis due to the challenge of accounting for time. The study uses a novel approach to examine mediation using path analysis with Cox proportional hazard modelling (survival analysis).
Objectives: The objectives of this study were to identify potential mechanisms of the impact of osteoarthritis on mortality and examine the role of modifiable targets (anxiety, depression, insomnia and walking frequency) for health professionals in rheumatology (HPRs).
Methods: A population-based prospective cohort study was conducted using data from the North Staffordshire Osteoarthritis Project (NorStOP), in which primary care medical record data was linked to self-report information collected by questionnaire in adults aged 50 years and over (n=8066). Individuals were defined as having osteoarthritis if they had consulted general practice for osteoarthritis, identified by Read codes in the primary care medical record, and indicated moderate to severe pain interference in daily life in the Medical Outcomes Short Form 36 at baseline (2002). A Cox proportional hazards analysis was performed to determine the total effect (TE) of osteoarthritis on mortality, both with adjustment for confounding variables (age, sex, education, occupation, smoking status, ischaemic heart disease, chronic obstructive pulmonary disease, non-steroidal anti-inflammatories, obesity, cognitive impairment). Within the Cox model, path analysis was used to decompose the TE to assess the indirect (IE) and direct effects (DE) for each of four potential mediators (anxiety, depression, insomnia, walking frequency; all measured by questionnaire) with adjustment for confounders. Results are expressed as adjusted hazard ratios (aHR); bootstrap resampling was used to generate 95% confidence intervals (95% CIs).
Results: Mean age of participants was 65.2 (SD 9.8) years and 51.6% were female. 2396 (29.7%) had osteoarthritis. Participants were followed up over 10 years during which time 1188 (14.7%) died. The rate of mortality was greater in those with osteoarthritis (52 deaths per 1000 person years) compared to those without (38 deaths per 1000 person years). Osteoarthritis was significantly associated with mortality (aHR 1.14; 1.00, 1.28). The relationship between osteoarthritis and mortality was mediated by walking frequency, depression and insomnia (anxiety did not mediate the relationship (IE HR 1.00; 0.98, 1.02)). The strongest mediator was walking frequency (TE 1.14; 1.00, 1.29: DE 1.04; 0.91, 1.18: IE 1.08; 1.06, 1.11), followed by depression (IE 1.06; 1.03, 1.08) and insomnia (IE 1.01; 1.00, 1.03).

Conclusion: This is the first study to examine mediation and highlights the importance of potentially modifiable targets for HPRs to reduce mortality in older adults with osteoarthritis. Encouraging people to maintain levels of physical activity at a population level and targeting a reduction in physical limitation in clinical practice to allow this, is important.
Disclosure of Interests: None declared
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OP0156-HPR THE FEASIBILITY AND EFFECTIVENESS OF TELEMEDICINE FOR KNEE OSTEOARTHRITIS IN DISEASE MANAGEMENT: A RANDOMISED CONTROL TRIAL

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Background: Osteoarthritis (OA) is a serious health concern worldwide, and patients with OA are in urgent need of proper long-term disease management to prevent disability and improve the quality of life. Research has started to investigate the feasibility and effectiveness of telemedicine in providing disease management for patients with chronic diseases. Guangdong Online Hospital (GOH) is the first officially recognized web-based hospital that widely provides telemedicine services in southern China.
Objectives: This study aimed to establish the feasibility and effectiveness of GOH in providing long-term disease management for patients with knee OA via a 6-month, randomised control trial (RCT).
Methods: 40 patients with knee OA were randomly assigned to receive conventional therapy (CT) in the clinic or conventional therapy plus a brief GOH-based intervention (CT-GOHT). GOH-based intervention included educational lectures, medical suggestions and psychotherapy. The primary outcome was the drop-out rates and the secondary outcomes included the mean change of the self-reported total score of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the Multidimensional Fatigue Inventory (MFI), the Hospital Anxiety and Depression Scale (HADS) and the Pittsburgh Sleep Quality Index (PSQI) from baseline to endpoint.

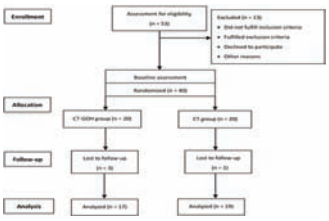


Figure 1. Flow chat of trial participation



Figure 2. A telemedicine intervention to patients with knee OA

Results: The baseline characteristics were comparable between the two groups. 3 patients in CT group and 1 patient in CT-GOHT group lost to follow-up during the study (P = 0.598). A statistically significant difference was observed in the mean change of WOMAC recommended index of joint pain (8.82 ± 5.02 vs. 13.90 ± 7.63, P = 0.026), morning stiffness (3.12 ± 1.50 vs. 4.42 ± 2.06, P = 0.039), functional limitation (27.65 ± 9.91 vs. 38.84 ± 17.28, P = 0.025), HADS-Anxiety (3.24 ± 2.41 vs. 5.32 ± 3.23, P = 0.037), and PSQI global score (2.35 ± 1.54 vs. 4.21 ± 3.34, P = 0.043) from baseline to endpoint when comparing the CT group to the CT-GOHT group. In addition, Guangdong Online Hospital was widely accepted by the including OA patients for their disease management.
Conclusion: Delivering a telemedicine intervention to patients with knee OA via GOH is a feasible and potentially effective method in long-term disease management, especially for patients living in remote areas. The results provide preliminary experiences and guidance for an upcoming full-scale RCT in disease management via telemedicine.

Trial registration: ChiCTR1800014465.

REFERENCE:

[1] Huang Z, et al. Implementation of telemedicine for knee osteoarthritis: study protocol for a randomized controlled trial. Trials, 2018, 19(1):232.

Table 1. Baseline characteristics of the two study groups

Variable	CT group (n = 20)	CT-GOH group (n = 20)
Age	72.25 ± 8.84	67.25 ± 10.97
Female, n	15	15
Education, n	12	14
Primary school	8	6
High school		
Han Chinese, n	20	20
Income, n	8	5
<¥2000	10	13
¥2000 -¥5000	2	2
>¥5000		
BMI, kg/m^2	25.85 ± 3.87	26.29 ± 2.96
Distance to hospital, kilometre	105.83 ± 100.35	111.33 ± 92.54
Kellgren-Lawrence grade, n	8	6
Grade I	10	13
Grade II	2	1
Grade III		
WOMAC pain, 0-10	18.90 ± 10.08	21.00 ± 8.38
WOMAC morning stiffness, 0-10	8.45 ± 4.89	9.25 ± 4.68
WOMAC function, 0-10	58.05 ± 20.55	63.30 ± 25.31
MIF	43.55 ± 19.77	45.70 ± 20.43
HADS-A	8.90 ± 5.55	8.30 ± 4.64
HADS-D	7.10 ± 5.28	6.85 ± 4.55
PSQI global score	7.35 ± 4.56	7.70 ± 5.13

Table 2. Mean change of outcome measures from baseline to endpoint

Results	CT group (n = 17),	CT-GOH group, (n = 19)	*P* value
WOMAC pain	8.82 ± 5.02	13.90 ± 7.63	0.026
WOMAC morning stiffness	3.12 ± 1.50	4.42 ± 2.06	0.039
WOMAC function	27.65 ± 9.91	38.84 ± 17.28	0.025
MIF	17.53 ± 7.73	20.95 ± 8.75	0.225
HADS-A	3.24 ± 2.41	5.32 ± 3.23	0.037
HADS-D	2.12 ± 2.06	2.36 ± 2.01	0.714
PSQI global score	2.35 ± 1.54	4.21 ± 3.34	0.043

Disclosure of Interests: None declared
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OP0157-HPR EUROPEAN PATIENT VOICE IN GOUT SURVEY – SUBJECTIVE SATISFACTION IN GOUT PATIENTS VERSUS OBJECTIVE SUBOPTIMAL GOUT CARE

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Background: Gout is the most common form of inflammatory arthritis with an increasing prevalence and incidence in many countries (1). Few information is available about current management of gout and satisfaction of patients living with gout.
Objectives: To evaluate diagnosis and treatment of gout from patient perspective to improve treatment outcomes for gout patients in Europe.
Methods: A 15 minute online survey with gout patients from 14 European countries (Austria, Belgium, France, Denmark, Germany, Italy, Ireland, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland) was conducted in 2018. The design and content of the survey has been developed together with several patient and clinical experts
Results: 1,100 gout patients (78% males, mean age 55 years) with a mean number of 2.9 flares in the past 12 months completed the survey. 77% percentage of patients are suffering from co-morbidities (hypertension 52%, dyslipidemia 41%, overweight 40%, type 2 diabetes 23%, long-term illness of kidney/renal insufficiency 17%). It was reported that mainly general practitioners are involved in the diagnosis of the disease (73%), discussion of gout (68%) and treatment of last gout flare (59%), whereas rheumatologists are less involved in diagnosis (8%), discussion (15%) and treatment (11%) of last gout flare. 22% of patients were not diagnosed until they have had 4 or more flares. 71% of patients had flares in the past 12 months (thereof 33% ≥3 flares) which seemed to be particularly an issue for younger patients. 58% of patients receive uric acid lowering therapies, 43% pain killers, 25% colchicine, 13% non-medical pain relief and 12% corticosteroids. 59% of patients do not have regular follow up appointments for their gout and 53%

are monitored for serum uric acid less than twice per year. But 79% of patients claim to be satisfied with their current treatment and do not expect better management of their disease.
Conclusion: The results of the survey demonstrate that gout patients in Europe are diagnosed late, their disease is not well controlled and not regularly monitored. It seems that their doctors are not aware of the pain and impact of gout on their patients' quality of life as patients are not telling them about it. Nevertheless, most of the patients feel their current treatment is the best they can get. There is a clear need to educate patients and their doctors about adequate management of gout.

REFERENCE:

[1] Kuo C-F, Grainge MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. Nat Rev Rheumatol. 2015 Nov;11 (11):649–62.

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OP0158-HPR THE BARRIERS AND FACILITATORS TO REQUESTING AND RECEIVING PSYCHOLOGICAL SUPPORT FOR PEOPLE WITH RHEUMATOID ARTHRITIS AND ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: UK guidelines[1-3] state that psychological interventions should be offered to people with rheumatoid arthirtis (RA) to help them adjust. Although rheumatology units recognise that providing psychological support is part of their role, 3 in 4 rate their overall provision as inadequate.[4] The reasons being a lack of time, a lack of trained clinicians and available training and the costs of delivering this type of service. However, little is known about the barriers to requesting psychological support from the patient perspective.
Objectives: To establish the full range of barriers and facilitators to requesting psychological support.
Methods: The 2018 National Rheumatoid Arthirtis Society (NRAS) 'Emotional Health and Well-being Matters' survey was designed by patients and researchers. This included a questionnaire designed to capture the barriers to accessing psychological support, using an established theoretical framework.[5] The questionnaire consisted of 41 items covering a range of barriers, with responses on a 5-point Likert scale. Participants were recruited by NRAS via their social media platforms, membership and non-membership lists through direct mail and in newsletters and the NRAS HealthUnlocked forum. The survey was open from May-July 2018. Recruitment was those diagnosed with RA and AJIA, aged 18 years and over and living in the UK.
Results: A final sample of 1650 participants took part in the survey, 97% of the sample had RA and 3% AJIA. 1 in 5 people with RA and 1 in 10 with AJIA were unlikely or extremely unlikely to seek psychological or emotional support in the future, even if they felt they needed it. The most frequently reported barriers to requesting psychological support from their healthcare team were (i) lack of optimism about their future with RA or AJIA (ii) not knowing what support they can access (iii) finding it difficult to talk about their emotions and asking for help (iv) believing healthcare professionals lack the time and ability to help them (v) believing that discussing emotions and providing psychological support is on not on their healthcare team's agenda, evidenced by a focus on physical rather than psychological health in consultations and (vi) never or rarely being asked about their emotions.
Conclusion: Exploring the potential barriers to requesting psychological support has given us unique insight into the complex journal of receiving psychological support. To overcome the most influential barriers steps need to be taken to encourage hope for the future, empower patients with RA and AJIA to talk about their emotions and instigate these discussions with their healthcare team, as well as providing more information and guidance about what support they can access and from where.

REFERENCES:

[1] National Institute for Health and Care Excellence. Rheumatoid arthritis in adults: management NG100. 2018. London, NICE.
[2] Luqmani R, Hennell S, Estrach C, Birrell F, Bosworth A, Davenport G, et al. British Society for Rheumatology and British Health Professionals in Rheumatology guideline for the management of rheumatoid arthritis (the first two years). Rheumatol 2006; 45(9):1167-1169.
[3] Luqmani R, Hennell S, Estrach C, Basher D, Birrell F, Bosworth A, et al. British Society for Rheumatology and British Health Professionals in Rheumatology guideline for the management of rheumatoid arthritis (after the first 2 years). Rheumatol 2009; 48(4):436-439.
[4] Dures E, Almeida C, Caesley J, Peterson A, Ambler N, Morris M, et al. A survey of psychological support provision for people with inflammatory arthritis in secondary care in England. Musculoskeletal Care 2014; 12 (3):173-181.
[5] Francis JJ, O'Connor D, Curran J. Theories of behaviour change synthesised into a set of theoretical groupings: introducing a thematic series on the theoretical domains framework. Implement Sci. 2012;7:24.

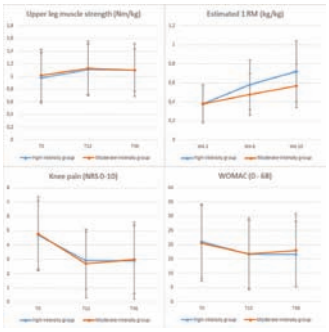
Disclosure of Interests: None declared
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OP0159 THE EFFECT OF HIGH-INTENSITY RESISTANCE TRAINING AND VITAMIN D SUPPLEMENTATION ON MUSCLE STRENGTH IN PATIENTS WITH KNEE OSTEOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

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Background: Exercise therapy is the cornerstone of knee osteoarthritis (OA) management. In particular muscle strengthening exercise, targeting the characteristic loss of muscle strength present in knee OA, is a key factor for the beneficial effects reported for exercise therapy. The optimal training intensity for resistance training in patients with knee OA, however, is not known to date. Besides resistance training, vitamin D supplementation in patients with vitamin deficiency may optimize muscle strength.
Objectives: To assess (i) whether high-intensity resistance training leads to greater improvements in muscle strength compared to moderate-intensity resistance training in patients with knee OA; and (ii) whether vitamin D supplementation in combination with strength training leads to greater improvements in muscle strength compared to placebo in combination with strength training in patients with knee OA and vitamin D deficiency (25 (OH)D level > 15 nmol/L and < 50 nmol/L (in winter) or <70 nmol/L (in summer)).
Methods: In a randomized controlled trial, 177 patients with a clinical diagnosis of knee OA were included. All patients were randomly allocated to a high-intensity (70-80% of the Repetition Maximum (1RM)) or a moderate-intensity (40-50% of the 1RM) resistance training program of 12 weeks. Both groups were supervised by a physical therapist twice a week and performed home exercises once a week. In addition, 50 out 177 patients had vitamin D deficiency and received supplementation of vitamin D (1200 IU vitamin D3 per day) or placebo in the 12 weeks prior to and during the resistance training program. The primary outcome measure was isokinetic (60 °/s) upper leg muscle strength (Nm/kg). In addition, the estimated 1 RM for leg press, leg curl and hip abduction were used as measures for muscle strength. Other outcome measures included severity of knee pain (NRS), self-reported and performance based activity limitations (WOMAC physical functioning (WOMAC), Get-up-and-go-test (GUG)). Measurements were performed by a blinded assessor prior to the exercise program (T0), directly after the program (T12) and at 6 months follow-up (T36). Additionally, for patients with vitamin D deficiency, measurements were also taken prior to vitamin supplementation or placebo (T-12).
Results: Both the high-intensity group and moderate-intensity group improved in upper leg muscle strength over time. No significant differences between groups were found for isokinetic upper leg muscle strength (p = 0.646) (see *figure 1).* However, when measured by the estimated 1 RM, significant differences were found between groups in favor of the high–intensity group (p = 0.001) (see *figure 1).* No between-group differences were found on pain (p = 0.885), or on self-reported and performance-based activity limitations (WOMAC p = 0.968; GUG p = 0.800), although both groups improved (see *figure 1).* An unexpected finding was that, in the (small sample of) patients with vitamin D deficiency, the placebo group showed significant greater isokinetic upper leg muscle strength over time compared to the vitamin D group (p = 0.001).
Conclusion: No differences between groups were found for isokinetic upper leg muscle strength. With the estimated 1 RM as a measure of muscle strength, high-

intensity resistance training led to greater improvements in muscle strength compared to moderate-intensity resistance training in patients with knee OA. This did not result in greater improvements in pain and physical functioning in the high-intensity resistance group; both groups showed similar clinically important improvements. The added value of vitamin D supplementation on muscle strength in knee OA patients with vitamin D deficiency need further study.



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OP0160-HPR

DOES OCCUPATIONAL THERAPY DELAY OR REDUCE THE PROPORTION OF PATIENTS WHO RECEIVES THUMB CARPOMETACARPAL SURGERY? A RANDOMIZED CONTROLLED TRIAL

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Background: The 2018 update of the EULAR recommendations for the management of hand osteoarthritis (OA) states that every patient with hand OA should be offered patient education, hand exercises and provision of assistive devices. Orthoses should be considered for symptom relief in patients with thumb carpometacarpal (CMC1) OA. Surgery should only be considered when other treatment modalities have not been sufficiently effective in relieving pain (1).
Objectives: The main aim was to evaluate whether occupational therapy in the waiting period prior to surgical consultation can reduce or delay the need for surgery in CMC1 OA. A secondary aim was to explore potential predictors for CMC1 surgery.
Methods: This is a multicentre parallel-group randomized controlled trial including patients referred by their general practitioner for surgical consultation due to CMC1 OA at three Norwegian departments of rheumatology. After baseline assessments, participants were randomized into an occupational therapy group or a control group and reassessed after 4, 18 and 24 months. Both groups received written and oral information on hand OA. In addition, the occupational therapy group received a hand exercise program, day and night orthoses, assistive devices and a treatment diary.
Intention-to-treat analyses were conducted fitting multivariate logistic regression analyses to compare the proportion of participants in the two groups who had received CMC1 surgery after two years. Time to surgery was examined in a Kaplan-Meier survival plot, whereas crude and adjusted logistic regression analyses were performed to investigate predictors for CMC1 surgery using a predefined set of covariates of demographic and clinical variables.
Results: Of 214 patients screened for eligibility, 180 (84%) were randomized. The mean age was 63 years (SD 7.6) and 79% were women. Eighty-four (93%) participants in the occupational therapy group and 82 (91%) in the control group completed 24 months follow-up assessments. Fifty-eight (64%) participants in the occupation therapy group were categorized as having high treatment adherence. Twenty-two (24%) participants in the occupational therapy group and 31 (34%) in the control group received surgery before the two year follow-up. The odds for receiving surgery were 50 percent lower in the occupational therapy group (p=0.10). Median time to surgery was 349 days (IQR 210 to 540) in the occupational therapy group and 267 days (IQR 181 to 406) in the control group (p=0.07). Previous non-pharmacological treatment (OR 2.70, 95% CI 1.16 to 6.27) and higher motivation for surgery (OR 1.22, 95% CI 1.07 to 1.38) were significant predictors for CMC1 surgery
Conclusion: In participants receiving occupational therapy there was a clear, but not statistically significant trend towards reduction and delay in CMC1 surgery as compared to the control group. Previously received non-pharmacological treatment and higher motivation for surgery significantly predicted surgery. The results support that patients with CMC1 OA should be referred to occupational therapy before surgery is considered.

REFERENCE:

[1] Kloppenburg M, Kroon FP, Blanco FJ, Doherty M, Dziedzic KS, Greibrokk E, et al. 2018 update of the EULAR recommendations for the management of hand osteoarthritis. Ann Rheum Dis. 2019;78(1):16-24.

Disclosure of Interests: : Else Marit H. Gravås: None declared, Nina Østerås: None declared, Randi Nossum: None declared, Ruth Else Mehl Eide: None declared, Åse Klokkeide: None declared, Karin Hoegh Matre: None declared, Monika Olsen: None declared, Øyvor Andreassen: None declared, Ida Kristin Haugen Grant/research support from: ADVANCE research grant from Pfizer, Consultant for: Advisory board Abbvie, Anne Therese Tveter: None declared, Ingvild Kjeken: None declared
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OP0161-HPR

SHORT-TERM EFFECT OF OCCUPATIONAL THERAPY INTERVENTION ON HAND FUNCTION AND PAIN IN PATIENTS WITH THUMB BASE OSTEOARTHRITIS – SECONDARY ANALYSES OF A RANDOMIZED CONTROLLED TRIAL

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Background: Carpometacarpal joint osteoarthritis (CMC1 OA) is a subset of hand osteoarthritis (HOA), presenting symptoms of pain and functional limitations. No cure for OA exists, and the EULAR recommendations highlight conservative treatment as first-line treatment for patients with HOA. Although several studies have assessed the effect of different treatments on pain and function in patients with HOA, there is a lack of high quality studies assessing these effects in patients with CMC1 OA. A recent systematic review showed that multimodal treatments (i.e. patient education, exercises, orthoses) improved pain but not function; however, the two studies included had short intervention periods and small samples. Thus, additional studies are warranted.
Objectives: To assess the short-term effect of a 3-month multimodal occupational therapy intervention on pain and function in patients referred to surgical consultation for CMC1 OA.
Methods: This study presents secondary analyses of a multicenter randomized controlled trial. Patients referred to surgical consultation due to CMC1 OA at three departments of rheumatology in Norway between 2013 and 2015 were considered eligible if they could speak Norwegian and did not have cognitive dysfunction. During the waiting period between referral and actual surgical consultation, the 180 included patients were randomized to either usual care (information about hand OA) or multimodal occupational therapy consisting of patient education, hand exercises, orthoses and assistive devices. Patients were instructed in conducting hand exercises three times per week for 12 weeks. They were given both day and night orthoses and were instructed to use them as much as possible. They were also given five commonly used assistive devices for use at home. The patients answered questionnaires and were assessed at baseline and in conjunction with the surgical consultation (follow-up). Pain at rest and during pinch- and grip strength was self-reported on a 10-point numeric rating scale. Function was self-reported in MAP-Hand (1-4, 1= no problems) and QuickDASH (0-100, 0=no disability) and measured as grip- and pinch strength (% of reference values) and range of motion (flexion deficit 2.-5.finger, palmar abduction and abduction in the CMC1). Within-group difference from baseline to follow-up was analyzed with paired sample t-test, while between-group difference at follow-up was estimated with multiple linear regression, adjusting for baseline value and time to follow-up. Due to multiple analyses of secondary outcomes, the p-value was set to p<0.01.
Results: The 180 included patients' mean (SD) age was 63 (8) years and most were women (81%). At baseline, there were no significant differences between

groups in any of the included variables. Most patients reported mild pain (NRS median 3) and moderate disability. Thirty-six had additional affection of interphalangeal joints. At follow-up, the control group showed no improvements, while the intervention group showed significant improvement in all pain and functional measures, except flexion deficit. When adjusting for baseline value and time to follow-up, there were significant differences between the two groups at follow-up for pain at rest, pain following grip, self-reported function (MAP-Hand and Quick-DASH) and grip strength, with the intervention group showing greater improvement ($p<0.01$).

Conclusion: Occupational therapy had significant positive short-term effects on pain and function in patients referred to surgical consultation for CMC1 OA.

Disclosure of Interests: None declared

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OP0162-HPR

THE NEED FOR PERSONALIZED, NON-PHARMACOLOGICAL INTERVENTION PROGRAMMES IN AUTOIMMUNE CONNECTIVE TISSUE DISORDERS: RESULTS OF A EULAR-FUNDED SCOPING REVIEW WITH A NESTED, DESCRIPTIVE META-ANALYSIS

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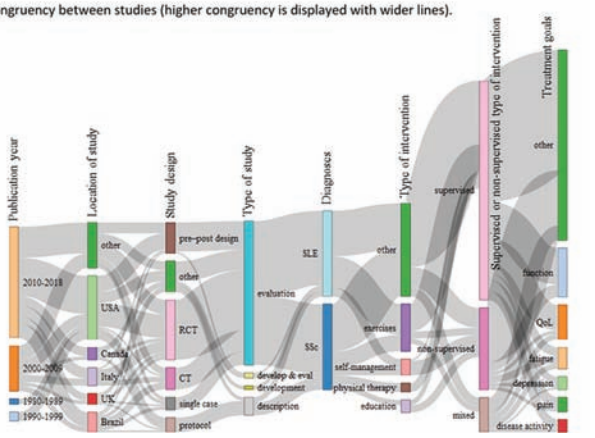
Background: Autoimmune Connective Tissue Disorders (CTDs), including Mixed Connective Tissue Disease (MCTD), systemic sclerosis (SSc) and systemic lupus erythematous (SLE) can lead to Raynaud phenomenon, involvement of internal organs, pain in joints, skin abnormalities and muscle weakness. Consequently, people with CTDs experience limitations in activities of daily life and restrictions in participation. Programmes promoting patient education, self-management, physical activity, and healthy life style, provided by health professionals are therefore essential to these patients. However, there is a substantial gap of knowledge about the content which should be included in non-pharmacological intervention programmes.

Objectives: To identify, map and appraise the content of existent face-to-face, digital and/or distance-learning non-pharmacological intervention programmes for patients with MCTD, SSc and/or SLE to inform a EULAR funded project with the overall aim to develop a new distance learning programme realizable with digital technologies.

Methods: A scoping literature review with a nested descriptive meta-analysis was performed in MEDLINE [Pubmed], EMBASE [OVID], CINAHL [EBSCO], PsycINFO [ProQUEST], the Cochrane Database of Systematic Reviews, OTSeeker, PEDro, and SciELO in September 2018. Furthermore, an international task-force identified additional grey literature and ongoing research projects. Eligibility checks of the articles based on pre-defined in- and exclusion criteria and data extractions were done independently by two researchers. The interventions contained in these programmes were extracted using the "Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide". A Sankey diagram and descriptive statistics were used to illustrate the relationships between the interventions and other characteristics of the studies. The protocol was pre-published on ResearchGate.

Results: Of 6667 identified records, 94 papers were eligible. Sixty-one studies (65%) were conducted between 2000 and 2018, mainly in the USA (35 [37%]), Brazil (11 [12%]) and Italy (10 [11%]). Thirty-three studies (35%) were randomised controlled trials, 17 (18%) were one-group pre-post-test designs and 12 (16%) clinical trials without randomisation (Figure 1). Overall, 4274 patients participated; 2955 had SLE [69%] and 1319 had SSc [31%], thus no studies with MCTD where found. The main content of the intervention programmes included exercises (22 [23%]), self-management (9 [10%]) and education (7 [7%]), with treatment goals focusing mainly on physical function (27 [29%]), quality of life (19 [20%]) and fatigue (12 [16%]). The interventions (67 [72%]) included or were based on an initial face-to-face component.

Figure 1. Sankey diagram. This diagram illustrates the relationships between the different study characteristics. The width of the grey connections lines between the bars are reflecting a higher congruency between studies (higher congruency is displayed with wider lines).



Conclusion: There was a variety of programmes content and interventions due to different consequences regarding activity limitations and participation restrictions in autoimmune CTDs. This highlights the need for personalized, multicomponent, non-pharmacological interventions.

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THURSDAY, 13 JUNE 2019

Other orphan diseases

OP0163

LONG-TERM EFFECTIVENESS OF CANAKINUMAB IN PATIENTS WITH CRYOPYRIN-ASSOCIATED PERIODIC SYNDROME

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Background: Treatment options for autoinflammatory diseases include anti-interleukin (IL)-1 therapies since the IL-1 pathway is crucial in immune dysregulation in patients with monogenic periodic fever syndromes.

Objectives: To gain further insights from routine clinical practice with respect to long-term effectiveness and safety of canakinumab (CAN) in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndrome, including Muckle-Wells syndrome [MWS], familial cold autoinflammatory syndrome [FCAS], neonatal onset multisystem inflammatory disease [NOMID]/chronic infantile neurological cutaneous and articular syndrome [CINCA]), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up enrolling patients aged $\geq$2 years with clinically confirmed diagnoses who routinely received CAN. 6-monthly clinical assessment and evaluation of patient-reported outcomes is aligned with routine clinic visits. CAPS disease activity was determined by physicians' and patients' assessment. Endpoints were effectiveness and safety of CAN under standard clinical practice conditions.

Results: The interim analysis includes 52 CAPS patients with prior long-term CAN treatment (43.1% females) enrolled by September 2018. 44.2% of the patients participated in the β-Confident study previously. The mean age was 20.7 years (4.0–79.0 years) at baseline and the mean duration of prior CAN treatment was 5.4 years (0.0–11.0 years). 40 patients (76.9%) were diagnosed with MWS, the other patients had FCAS (2), NOMID/CINCA (7) or atypical CAPS (1) (subtype diagnosis of 2 patients not available). Mutations in Nod-like receptor family pyrin domain-containing-3 were identified in 34 patients (68.0%) including E311K (7), Q703K (5), V198M (5), T348M (5), A439V (4). A baseline screening revealed sensorineural hearing loss (62.0%), papillitis (84.0%) and neurological symptoms (71.4%) in patients which had not been detected previously. The majority of patients had no disease related symptoms at baseline and 6 months demonstrating sustained remission in patients receiving long-term CAN treatment. The following disease related symptoms (mild/moderate and severe) were observed in the analysis cohort (N=31) at baseline and 6 months, respectively – disease symptom: baseline (mild/moderate, severe) vs. 6 months (mild/moderate, severe) – urticarial skin rash: 19.4%, 6.5% vs. 25.8%, 0.0%, arthralgia: 32.3%, 0.0% vs. 29.0%, 9.7%, myalgia: 9.7%, 0.0% vs. 16.1%, 0.0%, headaches: 22.6%, 9.7% vs. 19.4%, 19.4%, conjunctivitis: 32.3%, 3.2% vs. 12.9%, 6.5%, abdominal pain: 9.7%, 6.5% vs. 22.6%, 9.7%. Patients' assessment of disease activity and fatigue did not change between baseline and 6 months. However, at baseline 45.5% and after 6 months 76.0% of patients had no impairment of social life by the disease. Serious adverse events were reported for 2 patients (tonsillitis, delivery at week 31).

Conclusion: The RELIANCE study longitudinally monitors the stability of effectiveness of CAN in patients with monogenic periodic fever syndromes. An initial interim analysis including the CAPS subgroup which had prior CAN treatment showed that CAN is an effective and safe treatment in those patients.

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OP0164

LEFLUNOMIDE IN COMBINATION WITH GLUCOCORTICOIDS IS SUPERIOR TO CONVENTIONAL GLUCOCORTICOIDS MONOTHERAPY IN PREVENTING RELAPSE IN IGG4-RELATED DISEASE: A RANDOMIZED, OPEN-LABEL, CONTROLLED TRIAL

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Background: Glucocorticoids (GCs) was recommended as first-line therapy for the induction of remission of IgG4-related disease (IgG4-RD), whereas, a large proportion of patients may fail to maintain remission with GCs monotherapy. Considering that recurrent flares might lead to irreversible organ damage, immunosuppressive agents should be added. However, opinions among the experts were split on this issue [1]. Previously, we preliminarily reported the efficacy and safety of GCs and leflunomide (LEF) combination therapy for maintaining the remission of IgG4-RD [2].

Objectives: To evaluate the efficacy and safety of GCs and LEF combination therapy compared with GCs monotherapy for the management of IgG4-RD.

Methods: This study was a 12-month, randomized, open-label, controlled trial (NCT02703194). Patients were randomly allocated to GCs and LEF combination therapy or GCs monotherapy with 1:1 group allocation ratio. The dosage of LEF was 20 mg/d. All received GCs with a predefined taper regimen from a starting dosage of 0.5-0.8mg/kg/d. The primary outcome was time to relapse and the main secondary outcomes were time to complete response (CR) and time to remission.

Results: A total of 66 patients were randomly assigned (33 in each group) (Figure 1). The demographic and disease characteristics of the patients in the ITT population were similar between the treatment groups. The mean initial dosages of GCs were similar (GCs and LEF: 0.68 mg/kg/d, GCs: 0.70mg/kg/d, P=0.529). The cumulative relapse rates at 12 months were 21.2% in the GCs and LEF group and 50.0% in the GCs group (P=0.023). GCs and LEF combination therapy was significantly superior to GCs monotherapy with respect to the time to relapse (HR, 0.35; 95% CI, 0.13 to 0.90; P=0.030) (Figure 2), and was superior to GCs monotherapy with respect to the time to remission (HR, 1.74 95% CI, 0.97 to 3.10; P=0.063). These two groups were similar when analyzing the time to CR (HR, 1.57 95% CI, 0.91 to 2.74; P=0.108). At 12 months, 14 (42.4%) patients in the GCs group and 22 (66.7%) patients in the GCs and LEF group successfully tapered GCs to 10 mg/d or less with no relapse (P=0.048), 6 (18.2%) patients in the GCs group and 18 (54.5%) patients in the GCs and LEF group to 5 mg/d or less with no relapse (P=0.002). The relapsing organs of these relapsing patients were salivary glands (n=5), pancreas (n=5), bile ducts (n=5), retroperitoneal fibrosis (n=3), lacrimal gland (n=1), and skin (n=1). The incidences of new-onset diabetes mellitus (GCs and LEF: 21.21%, GCs: 27.27%, P=0.566) and the infections (GCs and LEF: 18.18%, GCs: 12.12%, P=0.566) were similar between two treatment groups.

Conclusion: The efficacy of LEF in combination with GCs therapy was significantly superior to conventional GCs monotherapy in preventing relapse in patients with IgG4-RD. LEF can be used as a steroid-sparing agent in the management of IgG4-RD.

REFERENCES:

[1] Khosroshahi A, Wallace ZS, Crowe JL, et al. International Consensus Guidance Statement on the Management and Treatment of IgG4-Related Disease. Arthritis Rheumatol. 2015 67: 1688-99.

[2] Wang Y, Li K, Gao D, et al. Combination therapy of leflunomide and glucocorticoids for the maintenance of remission in patients with IgG4-related disease: a retrospective study and literature review. Intern Med J 2017; 47: 680-9.

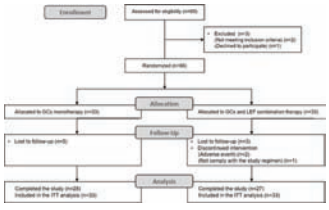


Figure 1. Treatment Assignments and Withdrawal in the Intention-to-Treat Population.

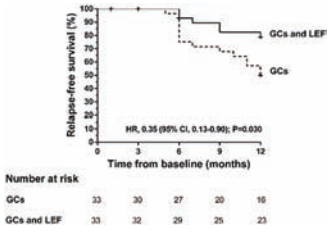


Figure 2. Kaplan-Meier Analysis for Time to Relapse.

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OP0165

EULAR RECOMMENDATIONS FOR THE DIAGNOSIS AND THE MANAGEMENT OF RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS DUE TO CANCER IMMUNOTHERAPY

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Background: Rheumatic immune-related adverse events (irAEs) are increasingly recognized musculoskeletal manifestations in cancer patients receiving immune checkpoint targeted immunotherapy (1). Since they represent a spectrum of new clinical entities and a robust evidence base is lacking, a task force was convened to harmonize expert consensus regarding their identification and management due to the lack of dedicated clinical trials.

Objectives: To develop EULAR recommendations for the diagnosis and the management of rheumatic irAEs due to cancer immunotherapy, based on literature and expert opinion.

Methods: Recommendations were developed according to the 2014 EULAR Standard Operating Procedures. The task force consisted of 19 clinical experts from Europe and North America (14 rheumatologists, 2 internists and 3 oncologists), 1 clinical epidemiologist, 1 allied health professional and 2 patient representatives. During the first meeting, the group defined the focus of the task force, the target population, and formulated research questions. A systematic literature research was performed by one fellow (MK) with the help of a librarian. Based on available evidence and using a consensus procedure, recommendations were developed during a second meeting. The level of agreement was determined by an anonymous voting process.

Results: 4 overarching principles and 10 recommendations were developed. The overarching principles define the role of rheumatologists and highlight the shared decision-making process between patients, oncologists and rheumatologists. One recommendation addresses the referral process, two address the diagnosis, and five address the therapeutic strategy of cancer patients experiencing rheumatic, musculoskeletal, and systemic signs or symptoms while receiving immunotherapy. An additional recommendation was included to address pre-existing rheumatic conditions and the last focuses on the diagnostic approach before immunotherapy.

Conclusion: These recommendations provide the basis of a EULAR consensus on the diagnosis and the management of rheumatic irAEs.

REFERENCE:

[1] Calabrese LH, Calabrese C, Cappelli LC. Rheumatic immune-related adverse events from cancer immunotherapy. Nat Rev Rheumatol. 2018 Oct;14(10):569-579.

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OP0166

THE EFFICACY OF CALCINEURIN INHIBITORS IN PATIENTSWITH ADULT-ONSET STILL'S DISEASE: MULTI-CENTRE HISTORICAL COHORT STUDY

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Background: Adult-onset Still's disease (AOSD) is a systemic inflammatory disorder generally responsive to corticosteroid (CS) therapy, whereas cases not responding CS monotherapy are frequently found in clinical practice. In such cases, methotrexate and/or biologics including TNF-α, IL-1, or IL-6 inhibitors are used [1]. However, further treatment options are required for refractory AOSD patients who are intolerant to methotrexate and/or biologics. Calcineurin inhibitors (CNI) downregulate T cell activation through inhibiting IL-2 transcription and signal transduction. Therefore, they are reasonable therapeutic medication for AOSD considering T cells and subsequently activated macrophages play a pathophysiological role in AOSD [2]. Nevertheless, only a few case series have indicated effects of CNI for difficult AOSD.

Objectives: To evaluate the efficacy of CNI in patients with AOSD.

Methods: This is a multi-centre historical cohort study comprised the consecutive patients with AOSD in accordance with Yamaguchi classification criteria. The primary endpoint was set as the time from the initiation of treatment to event defined as death of any causes or relapse of AOSD requiring an increase of CS dose. Secondary endpoints were set as persistency rate of CNI and safety. Based on the recurrent event data analysis, these endpoints were evaluated for each event. We compared the frequency of events between two groups according to the treatment that included calcineurin inhibitors (CNI+) or conventional therapy without calcineurin inhibitors (CNI-).

Results: One hundred seventy-eight patients were enrolled in this study. Mean age was 46 year-old, and median follow-up period 36 months. Seventy-one events in 56 patients were treated with therapeutic regimen including CNI (CNI+, cyclosporine: 14, tacrolimus: 60), and 176 events in 138 patients were treated with the conventional therapy excluding CNI (CNI-). CNI were used in AOSD patients with recurrent history, high ferritin level, serositis, hemophagocytic syndrome (HPS) and/or disseminated intravascular coagulation (DIC). The CNI+ group had longer event-free survival than the CNI- group (83% versus 75% at 5th

year). The hazard ratio (HR) was 0.57 (95% CI, 0.32-0.99) after adjustment of initial dose of CS and other concomitant medications. Subgroup analysis showed that CNI were more effective for AOSD patients with high ALT levels ($\geq$ 80 IU/L) and/or severe complications such as HPS and DIC. The persistency rate of CNI was 71% at 5th year. Adverse events occurred more frequently in the CNI+ group than in the CNI- group (18% versus 8%, p = 0.04); however, serious adverse events did not increase in the CNI+ group (3% versus 2%). AOSD-related mortality had never been found in the observation period. One patient had a fatal course due to septic shock in the CNI+ group.
Conclusion: Our retrospective analysis suggested that CNI could be an additional option for treating AOSD with acceptable safety.

REFERENCES:
[1] Efthimiou P, et al. Diagnosis and management of adult onset Still's disease. Ann Rheum Dis. 2006.
[2] Chen DY, et al. Predominance of Th1 cytokine in peripheral blood and pathological tissues of patients with active untreated adult onset Still's disease Ann Rheum Dis. 2004.

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OP0167 B LYMPHOCYTES DIRECTLY CONTRIBUTE TO TISSUE FIBROSIS IN IGG4-RELATED DISEASE

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Background: IgG4-related disease (IgG4-RD) is a fibro-inflammatory condition marked by rapid clinical improvement after selective depletion of B lymphocytes with rituximab. This feature suggests that B cells might participate in fibrogenesis and wound healing (1-3).
Objectives: In the present work we aimed to demonstrate that B lymphocytes contribute directly to tissue fibrosis in IgG4-RD.
Methods: Total circulating CD19+ B-lymphocytes, naïve B cells, memory B cells, or plasmablasts from IgG4-RD patients were cultivated with human fibroblasts. Pro-fibrotic soluble factors and collagen production in the co-cultures were assessed by ELISA and Luminex assays. RNA-sequencing and quantitative RT-PCR were used to assess fibroblast activation in the presence of B cells, as well as the induction of pro-fibrotic pathways in B cell subsets. Relevant pro-fibrotic and inflammatory molecules were confirmed in vitro by functional experiments and on IgG4-RD tissue sections by multi-color immunofluorescence studies.
Results: B cells from IgG4-RD patients (i) produced the pro-fibrotic molecule PDGF-B and stimulated collagen production by fibroblasts; (ii) expressed enzymes implicated in extracellular matrix remodeling such as LOXL2; (iii) produced the chemotactic factors CCL-4, CCL-5, and CCL-11; and (iv) induced the production of these same chemokines by activated fibroblasts. Plasmablasts expressed sets of genes implicated in fibroblast activation and proliferation, and therefore represent cells with intrinsic pro-fibrotic properties
Conclusion: We have demonstrated that B cells, contribute directly to tissue fibrosis in IgG4-RD. These unanticipated pro-fibrotic properties of B lymphocytes, particularly of plasmablasts, might be relevant for fibrogenesis in other fibro-inflammatory disorders and for wound healing processes in physiological conditions.

REFERENCES:
[1] Della-Torre E, Lanzillotta M, Doglioni C. Immunology of IgG4-related disease. Clin Exp Immunol 2015;181:191-206.
[2] Carruthers MN, Topazian MD, Khosroshahi A, Witzig TE, Wallace ZS, Hart PA, et al. Rituximab for IgG4-related disease: a prospective, open-label trial. Ann Rheum Dis. 2015;74:1171-7.
[3] Della-Torre E, Feeney E, Deshpande V, Mattoo H, Mahajan V, Kulikova M, et al. B-cell depletion attenuates serological biomarkers of fibrosis and myofibroblast activation in IgG4-related disease. Ann Rheum Dis 2015;74:2236-43.

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OP0168 DERIVATION AND VALIDATION OF A NEW STILL ACTIVITY SCORE (SAS)

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Background: Adult-onset Still's disease (AOSD) is a rare, chronic, multisystem and auto-inflammatory disorder. Although several classification criteria exist for the diagnosis of AOSD, there is no valid method for the assessment of disease activity for these patients.
Objectives: To determine a simple method for the assessment of AOSD activity.
Methods: We conducted a cross-sectional, multicenter study for assessment of disease activity in AOSD patients. All AOSD patients were fulfilled the Yamaguchi criteria. Age, sex, disease duration and current symptoms were recorded. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), leukocyte count, and ferritin levels were also recorded. Visual analog scale (VAS) (0–10 cm) and likert scale (as remission, low, moderate, severe, and more severe disease activity) were used for physician's (PhGA) and patient's (PtGA) global assessment of disease activity. Patients were enrolled to ''derivation cohort'' (n=125) and subsequently ''validation cohort'' (n=72). Ordinal logistic regression model was used to derive Still Activity score (SAS).
Results: Overall, 197 (66.5% female) AOSD patients were enrolled. Mean age was 39 (13) years and median disease duration was 2 (0–30) years. Cross-sectional frequency of AOSD findings were as follow; fever 69 (35%), rash 55 (27.9%), arthritis 57 (28.9%), arthralgia 112 (56.9%), sore throat 58 (29.4), myalgia 80 (40.6), lymphadenopathy 25 (12.7%), splenomegaly 37 (18.8%), hepatomegaly 23 (11.7%), abdominal pain 8 (4.1%), pleuritic pain 8 (4.1%), pericarditis 4 (2%), hemophagocytic syndrome 4 (2%). Mean (SD) ESR (mm/h), CRP (mg/dl), ferritin and leukocyte count were 32.5 (31), 43.4 (65.3), 1169 (3088) and 10356 (4821), respectively. Mean PtGA and PhGA was 3.86 (3.29), and 3.05 (3.06). SAS derived for the assessment of AOSD disease activity is given in Table 1.

SAS were correlated with the PtGA of disease activity as 83% for the derivation cohort and 75% for the validation cohort, also, correlation of this score and patient's global VAS assessments were 79% and 73%, respectively. Sensitivity and specificity of SAS equal and/or higher than 4 to predict '' active (severe) and highly active (more severe) AOSD activity'' are 100% and 82.6%, respectively (Figure 1).

Conclusion: In this study, we created a Still activity score (SAS) with the routine clinical and laboratory features of patients. This score can detect patients who have high likelihood of being in active disease status. In the future perspective, SAS should be assessed in the clinical trials and routine practice.

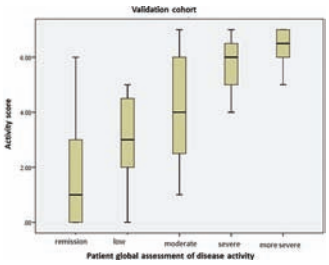


Figure 1. Boxplot of SAS and patients' global assessment of disease activity

Table 1. Still activity score (SAS)

	0 point	1 point	2 points
Fever	Absent		Present
Arthralgia	Absent		Present *
Neutrophilia% ≥65	No	Yes	
Ferritin ≥ 350 ng/ml	No	Yes	

*If number of swollen joints ≥2, add 1 point.

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OP0169 LONG-TERM SURVIVAL IN LUNG TRANSPLANTATION FOR INTERSTITIAL LUNG DISEASE ASSOCIATED WITH CONECTIVE TISSUE DISEASES. STUDY OF 26 CASES OF A SINGLE CENTER

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Background: Interstitial lung disease (ILD) is one of the most serious complications associated with connective tissue diseases (CTD). Patients with ILD have increased mortality and limited treatment options. Lung transplant has been recognized as an option for patients with end-stage CTD-ILD. However, rheumatic diseases are still sometimes considered a contraindication for lung transplant because of concerns for worse outcomes.

Objectives: Our aims were to: **a)** assess long-term post-transplant survival in patients with CTD-ILD and **b)** compare post post-transplant survival of patients with CTD-ILD with patients with idiopathic pulmonary fibrosis (IPF).

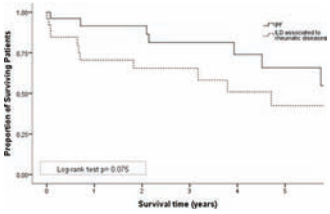
Methods: Single center study in a referral center for lung transplant of all patients who underwent lung transplantation for CTD-ILD between 1998 and 2017. This cohort was compared with patients with IPF (group-matched for age, transplant year and basiliximab induction). Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test.

Results: We studied 26 patients with CTD-ILD matched to 26 patients with IPF. The underlying diseases of patients with CTD-ILD were: Rheumatoid arthritis (n=9), Scleroderma (n=6), Sjögren syndrome (n= 4), ANCA-vasculitis (n=3), Anti synthetase syndrome (n=2), Dermatomyositis (n=1), Systemic lupus erythematosus (n=1). The comparative study of baseline characteristics between both groups is shown in the TABLE. All of RA patients undergoing transplantation in our study had the histologic subtype of usual interstitial pneumonia (UIP) whereas non-specific interstitial pneumonia (NSIP) was the most common histologic subtype of ILD associated with the rest of CTD. Cumulative survival rates at 5 year post-transplant did no differ significantly between CTD-ILD and IFP [42.4% vs 65.8% (p=0.075)] (FIGURE 1).

TABLE

	IPF (n=26)	CTD-ILD (n=26)	P
Age *(years)*, mean ± SD	60.4 ± 5.3	56.5 ± 8.3	0.06
Sex *(women), n (%)*	6 (23.1)	18 (69.2)	0.001
Time on waiting list (*days*), median [IQR]	86.0 [35.5-268.3]	82.0 [37.0-212.3]	0.78
Smokers, n (%)	19 (73.1)	11 (42.3)	0.07
Type of transplant (*bilateral*), n (%)	8 (30.8)	13 (50.0)	0.16
Donor CMV + and recipient CMV -, n (%)	4 (15.3)	2 (7.7)	0.72
Basiliximab induction, n (%)	9 (34.6)	9 (34.6)	0.99
Variables at transplant			
FEV 1 (%), median [IQR]	57 [35.5-71.3]	50 [41.0-60.0]	0.34
FVC (%), median [IQR]	54 [36.0-65.8]	51 [44.0-61.0]	0.55
FEV1/FVC, median [IQR]	82 [75.9-88.5]	80 [72.0-89.1]	0.52
DLCO	24 [18.7-42.0]	30 [23.0-43.5]	0.49
KCO	66 [49.5-82.5]	68 [42.9-78.0]	0.54
Serum creatinine (*mg/dL*), mean ± SD	0.78 ± 0.14	0.80 ± 0.31	0.74
Right catheterization, n (%)	11 (42.3)	16 (61.5)	0.07
mPAP (*mm Hg*), mean ± SD	23.3 ± 3.8	26.5 ± 8.6	0.15
PCP (*mm Hg*), mean ± SD	13.3 ± 2.7	12.0 ± 4.7	0.44
Treatment pre-transplant			
Glucocorticoids, n (%)	20 (76.9)	23 (88.5)	0.22
Immunosuppressive drugs, n (%)	7 (26.9)	21 (80.8)	0.001
Allograft dysfunction			
Acute rejection	15 (62.5)	8 (32.0)	0.032
Chronic rejection	2 (8.3)	5 (20.0)	0.417

CTD-ILD: interstitial lung disease related with connective tissue diseases; DLCO: diffusing capacity of lung for carbon monoxide; IFP: idiopathic pulmonary fibrosis; KCO: transfer coefficient of the lung for carbon monoxide; RA-ILD: interstitial lung disease related with rheumatoid arthritis; mPAP: mean pulmonary arterial pressure; PCP: pulmonary capillary pressure.



Conclusion: Our retrospective analysis showed a trend to lower long-term post-transplant survival than in those with IPF, however no statistical differences were found in cumulative survival rates at 5-years post-transplant. These data support that lung transplantation should be considered in patients with end-stage CTD-ILD.

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OP0170 **USE OF THE PROVISIONAL EULAR/ACR IGG4-RD CLASSIFICATION CRITERIA IN A COHORT OF SPANISH PATIENTS**

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Background: The ACR/EULAR IgG4-related disease (IgG4-RD) provisional classification criteria were presented at the ACR conference in 2018. The performance of these criteria in a fully non-Asian cohort is unknown.
Objectives: To explore the performance of these provisional criteria in a cohort of Spanish patients with IgG4-RD.
Methods: Data were obtained from the Spanish IgG4-RD registry (REERIgG4) from October 2013 to December 2018, including 9 centers. Patients needed to fulfill almost 1 of the available diagnostic criteria sets (pathology consensus and/or comprehensive). N provisional ACR/EULAR classification criteria (PAECC) were applied based on the public information disclosed at the abovementioned meeting.
Results: One-hundred patients were included. Thirty-four (34%) were females, median age at diagnosis was 54.8 years (IQR 20.7). The ethnicity of the participants was: Caucasian 83%, Hispanic 12% and North-African/Middle-East 5%. Ninety-two percent were diagnosed with a biopsy. Regarding the diagnostic criteria, 85% met consensus pathology criteria and 94% comprehensive criteria.
Fifty-one patients (51%) had systemic IgG4-RD involving >1 tissue. The most commonly involved tissues were: retroperitoneum (35%), lymph nodes (19%), orbit pseudotumor (18%), salivary glands (16%) and pancreas (14%). Forty-two patients (42%) had elevated serum IgG4.
Seventy-one individuals (71%) met the PAECC including entry criteria, exclusion criteria with an inclusion criteria score equal or >19 points. From the 29 cases that did not meet the PAECC, 9 (31%) did not fulfill the first step (entry). Those patients had rarer organs involved as hypophysis, mesenterium or jaw. Eight patients (28%) met one of the exclusion items. Two had positive antineutrophil cytoplasmic antibodies, 2 steroid resistance, 2 double-stranded antideoxyribonucleic acid antibodies, 1 other specific autoantibodies, 1 eosinophilia and fever. None of them had evidence of active connective tissue disease, vasculitis, malignancy or infection. Finally, 16 of the patients who did not meet the PAECC (55%) had an inclusion criteria score under 19 points (median 12): 3 (19%) did not have a biopsy, 8 (50%) biopsies had partial reports, and 10 subjects (62.5%) had normal serum IgG4 levels. Six (38%) of them had involvement limited to the head and neck and 3 (19%) had retroperitoneal or aortic involvement.
Conclusion: Seventy-one percent of the Spanish patients participating in the REERIgG4 met the 2018 PAECC, while all of them met almost one of the previous diagnostic criteria. Populations with non-Asian ancestry might get lower scores, as they would make less points in significant domains (serum IgG4, pancreatic-biliary) or have presentations that may grant lower scores or exclusion. Enforcing complete pathology reports might increase the scores. Nevertheless, the new classification criteria are provisional and primarily intended for clinical trial recruitment, focusing in the most common manifestations. Therefore, the preexisting diagnostic criteria should be used for standard clinical purposes.

REFERENCE:

[1] Wallace Zs, Naden RP, Choi H. The 2018 ACR/EULAR Classification Criteria for igG4- Related Disease. Submitted 2018.

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THURSDAY, 13 JUNE 2019

From child to adult care – breaking down the barriers of transition

OP0171-PARE **THE SWEDISH YOUNG RHEUMATICS REPORT – THE MOST URGENT MATTERS AND THE MOST PROMISING DEVELOPMENT AREAS FOR YOUNG PEOPLE WITH RMD'S IN SWEDEN**

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Background: In May 2017, the Swedish National Organization for Young Rheumatics (Unga Reumatiker) adopted its first political program. The program is composed by six areas and within every section we have stated what our organization want and what changes we see as necessary. To make sure we are working with the most urgent matters for our members and all of the young people with RMD's in Sweden, we wanted to do a survey, based on our political wills, amongst our members. The survey was conducted in the Autumn of 2017, with support by Pfizer, and the results were presented in the Swedish Young Rheumatics Report (Unga Reumatiker-rapporten) in April 2018.
Objectives: By conducting a survey and presenting a report, we wanted to highlight what are the largest obstacles for young people with RMD's in Sweden today. What areas need change, and what great solutions already exists? Answering these questions has been of great help for us as an organization, because we now know what matters the most to our members and what we need to focus on, but it is also of great help to others. It is for example much easier for healthcare professionals to work on fixing existing issues, now that they know what issues are of most concern for their patients. We also wanted to raise awareness about the situation for young people with RMD's in Sweden today, and inspire these people to follow their dreams.
Methods: The survey was conducted digitally and was sent out to our 1550 members and 425 people answered the survey, which consisted of 40 questions. After analyzing what stood out the most and seemed most urgent and important to the respondents, the report was composed with the most remarkable survey results, divided into four headlines; *education and support*, *from child to adult*, *healthcare and treatment*, and *sex and family planning*. We created www.ungareumatikerrapporten.se where the results are presented, and also personalized by four members telling their stories and sharing their dreams. As another part of the report, we also developed a new tool called the Dream Scale (Drömskalan). It is our response to the standard pain scale, VAS, and it is a tool meant to help inspire our members to dare to follow their dreams.
Results: We launched the report the 10th of April with the campaign hashtag #wearenotourdisease (#viärintevårsjukdom). We wanted to make sure to focus on joy of life and dreams to inspire our members, while at the same time highlight some problematic areas that needs to be adjusted. With the hashtag, we also wanted to create a sense of community, and invite people to share their own stories and dreams. We published the results and shared the videos from the report website on our social media for two weeks, including popular takeovers, and got a lot of attention. We published a debate article in Dagens Medicin, Sweden's leading health care newspaper, about how it is time for a focus shift within the healthcare system. And we have sent out printed copies of the report to all clinics in Sweden, and have also lectured and keep on lecturing about the report and our work at clinics all over Sweden.
Conclusion: There is still a lot to do and a lot of changes still have to be made if all young rheumatics shall be able to experience joy of life and fulfill their dreams – but the report helped us take a giant step in the right direction. We have raised awareness about what problems young people with RMD's in Sweden face on a daily basis. We know what the most urgent matters are and also what solutions we need to push for when working and talking with politicians and other decision makers. And we have been able to shift the conversation and the focus from just talking about what's bad, to talking about joy of life, hopes and dreams. We have empowered our members and others, telling them to share their own stories and dare to pursue their dreams. Having a rheumatic disease should never prevent you from living your life to the fullest!

REFERENCE:

[1] www.ungareumatikerrapporten.se

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OP0172-PARE

WORKING TOGETHER FOR CHILDREN AND FAMILIES LIVING WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES: THE EUROPEAN NETWORK FOR CHILDREN WITH ARTHRITIS (ENCA)

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Background: The European Network for Children with Arthritis (ENCA) is a pan-European network led for and by parents and young people with rheumatic and musculoskeletal diseases (RMDs). ENCA's activities are delivered voluntarily by parents and young people passionate about improving the care and treatment of children and young people (CYP) with RMDs. This is done through education, innovation, networking and empowerment. ENCA is associated with the Paediatric Rheumatology European Society (PReS).
Objectives: ENCA aims to facilitate the exchange and dissemination of information, knowledge and best practice with regards to paediatric RMDs across Europe, working in partnership with national patient organisations for CYP and families living with RMDs. ENCA also aims to provide international awareness, engagement and research opportunities.
Methods: ENCA is managed by a board of elected members, who are all volunteers with national patient organisations. ENCA hosts an annual conference in conjunction with PReS, inviting attendance from national patient organisations. Aside from a newly refreshed website, ENCA hosts a closed Facebook and WhatsApp group for national patient organisation representatives, enabling real-time communication and the instant sharing of knowledge and best practice. ENCA hosts an annual 'Fun with JIA challenge', aimed at empowering CYP with RMDs to share their story; and has been involved in establishing a new international awareness campaign for 2019, titled 'World young Rheumatic Disease (WORD) day'. In addition, ENCA cooperates with a number of international organisations with shared goals in rheumatology, representing the paediatric voice.
Results: Since its inception in 2002, ENCA has enhanced the communication and shared learning between national patient organisations, by embedding the voice of CYP and families into research and advocacy activities. The 'Fun with JIA challenge' delivered since 2017 has provided CYP with RMDs across Europe with the opportunity to share their stories through film. In addition, ENCAs' cooperation with PReS has recently facilitated the planning and launch of WORD day on March 18th, 2019. The need for a specific paediatric RMD awareness day was identified as a priority from national representatives, in light of the relatively limited attention that paediatric RMDs receive. WORD day helped to raise parental and professional awareness about paediatric RMDs.
Conclusion: As parents and young people living with RMDs, ENCA has enabled individuals and national patient organisations to develop their knowledge in relation to paediatric RMDs. ENCA provides several opportunities for networking and the sharing of best practices between national patient organisations and professionals, through informal and formal activities focused on paediatric RMDs. International networking helps individuals and communities to navigate through challenges with the support of others with a shared-goal.

REFERENCE:

[1] Egert Y, et al. PARE0005|Brief Overview of ENCA (European Network for Children with Arthritis). Ann Rheum Dis 2016; 75:1321.

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THURSDAY, 13 JUNE 2019

OSTEOARTHRITIS: RESEARCH IN MOTION

OP0173

EROSIVE HAND OSTEOARTHRITIS ASSOCIATES WITH LOW OCCURRENCE OF KNEE OSTEOARTHRITIS

Natividad Oreiro[1], Ignacio Rego-Perez[1], Sara Relaño-Fernandez[1], Maria Teresa Silva[1], Paula Ramos-Louro[1], Alejandro Durán-Sotuela[1], Sonia Pertega[2], Francisco J. Blanco[1]. *[1]Instituto de Investigación Biomédica de A Coruña (INIBIC), Servicio de Reumatología, A Coruña, Spain; [2]Instituto de Investigación Biomédica de A Coruña (INIBIC), Unidad de Epidemiología Clínica y Bioestadística, A Coruña, Spain*

Background: Erosive hand osteoarthritis (OA) is considered a more severe form of hand OA that includes pain and inflammation (1,2). However, more data are needed regarding the different hand OA phenotypes, especially erosive and non-erosive, to conclude if they represent two different subsets of hand OA or even different degrees of affectation of the same disease (1,3,4)
Objectives: To compare the clinical pattern of patients with erosive hand OA with those that do not show this phenotype
Methods: The study was conducted in the Prospective Cohort of Osteoarthritis A Coruna (PROCOAC). This cohort consists of 1107 subjects, of which 747 suffered from radiographic hand OA. We split the cohort into patients with and without erosive hand OA, and analyzed both clinical and demographic data within each group, together with the assessment of the AUStralian CANadian Osteoarthritis Hand (AUSCAN) index. The study consisted in a univariate analysis comparing different variables between both groups, followed by a stepwise logistic regression analysis taking into account the significant confounder variables analyzed in the Univariate approach
Results: The mean age of the cohort was 63.23±8.85 years and consisted of 627 females and 120 males. Of the 747 OA patients, 179 had erosive hand OA and 568 did not. The univariate analysis revealed that patients with erosive hand OA were younger (60.25±8.10 vs 64.16±8.88;p<0.001), smokers (p=0.005), with lower body mass index (p=0.005), increased inflammatory episodes (p<0.001), with family history or suffering from psoriasis (p=0.021) and less number of damaged joints (p<0.001). In addition, metabolic syndrome (MetS) was not associated with erosive hand OA and, despite the higher number of females suffering from hand OA, no significant differences between erosive and non-erosive phenotypes in terms of gender were detected.
The regression model confirmed the strong association of age (OR=0.9734; 95% CI=0.947-0.999; p=0.044), inflammation (OR=5.096; 95% CI=2.868-9.058; p<0.001), number of damaged joints (OR=0.490; 95% CI=0.307-0.782; p=0.003) and, interestingly, showed MetS as a risk factor too (OR=2.146; 95% CI=1.250-3.682; p=0.006). Regarding the number of damaged joints, a lower frequency of both knee and hip OA was detected in patients with erosive hand OA compared with non-erosive patients (24.4% vs 54.7% for knee OA prevalence and 11.6% vs 16.7% for hip OA prevalence); however, only knee OA occurred at a significant lower frequency (OR=0.267; 95% CI=0.182-0.393; p<0.001). In addition, the three subscales of the AUSCAN score showed significantly higher mean values in patients with the erosive phenotype: pain (57.67±29.30 vs 43.86±31.45; p<0.001), function (55.61±27.68 vs 40.53±29.48; p<0.001) and stiffness (55.40 ±32.26 vs 40.95±36.23;p=0.001)
Conclusion: The erosive hand OA phenotype is associated with more inflammation in younger patients, and worst AUSCAN score. Contrarily to the non-erosive phenotype, the presence of erosions associates with a lower occurrence of other forms of OA, specially knee OA. In our cohort, erosive hand OA seems to be more localized in the hand and it also seems to be associated with psoriasis. This different profile could serve the clinicians to provide personalized prevention strategies, and the researchers to investigate the pathogenesis of this specific phenotype

REFERENCES:

[1] Haugen, et al. Osteoarthritis Cartilage 2016;24:647-654
[2] Marshall, et al. Ann Rheum Dis 2015;74:136-141
[3] Dolzani, et al. Clin Exp Rheumatol 2011;29:1006-1009
[4] Punzi, et al. Ann Rheum Dis 2005;64:955-957

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OP0174

PARTIAL KNEE REPLACEMENT IS ASSOCIATED WITH A LOWER RISK OF VENOUS THROMBOEMBOLISM AND OPIOID USE THAN TOTAL KNEE REPLACEMENT BUT INCREASED RISK OF LONG-TERM REVISION: A MULTINATIONAL, MULTI-DATABASE, PROPENSITY SCORE-MATCHED, COHORT ANALYSIS INCLUDING OVER 280,000 PATIENTS

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Background: Knee replacement is one of the few effective treatments for severe knee osteoarthritis. A number of surgical interventions are available, including two main types: partial or total knee replacement.
Objectives: We aimed to assess the outcomes of partial compared to total knee replacement.
Methods: We conducted a multi-database propensity score-matched cohort study. Data was obtained from 4 US claims databases (IBM MarketScan® Commercial Database (CCAE), IBM MarketScan® Medicare Supplemental Database (MDCR), Optum ® de-identified Clinformatics ® Datamart, Extended - Date of Death (Optum), and Pharmetrics), and 1 UK primary care electronic medical record database (THIN).
All people aged 40 years or older at the time of knee replacement surgery were included. Data were mapped to a common data model (OMOP), and processed using analytical tools developed by the OHDSI community.
Participants were followed up from the date of their first knee replacement and for up to 5 years. Outcomes included short-term (60-day) post-operative complications (infection, venous thromboembolism, mortality, readmission), opioid use in the 3-12 months post-surgery as a proxy for persistent pain, and 5-year revision risk.
Propensity score matching (up to 1:10) was used to control for all available confounders, and negative control outcomes and calibration to minimize the impact of residual confounding. Separate Cox regression models were fitted for each outcome to estimate calibrated HR (cHR) and 95% confidence intervals related to partial, using total knee replacement as a reference group.
Results: A total of 32,379 and 250,377 patients receiving partial and total knee replacement respectively were matched. Short-term risk of venous thromboembolism was consistently lower in the former, with cHR ranging from 0.47 [0.32-0.71] in MDCR to 0.76 [0.59-0.99] in CCAE. No differences were observed in the risk of other complications. The use of opioids in months 3 to 12 after surgery was also lower in subjects receiving partial knee replacement, with cHR ranging from 0.70 [0.57-0.90] in THIN to 0.86 [0.78-0.96] in Optum.
Conversely, risk of 5-year revision was consistently higher amongst those undergoing partial compared to total knee replacement: cHR ranged from 1.51 [1.24-1.88] in CCAE to 2.16 [1.63-3.15] in MDCR.
Conclusion: Partial knee replacement is associated with a 25% to 50% reduction in short-term risk of venous thromboembolism, and a 15%-30% lower risk of persistent pain post-surgery. In contrast, partial knee replacement results in a 50% to >100% excess risk of revision in the longer term. This information should be used to individualize surgical indications for patients with severe knee osteoarthritis.
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OP0175

METHOTREXATE IN PATIENTS WITH HAND OSTEOARTHRITIS REFRACTORY TO ANALGESICS: A RANDOMISED, DOUBLE-BLIND, PLACEBO CONTROLLED TRIAL

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Background: To date, no studies have been published on the effect of Methotrexate (MTX) in hand osteoarthritis (HOA).
Objectives: The aim of our study is to examine the effect of methotrexate on pain in symptomatic erosive HOA, as well as its functional and structural effect using MRI and radiography.
Methods: This prospective, single-center, randomized, double-blind, placebo-controlled study followed patients with HOA over 12 months. Patients were randomized to Methotrexate 10 mg per week or placebo.
The primary endpoint was pain assessment at 3 months, and secondary endpoints were clinical (Visual Analogue Scale "VAS" pain at 12 months), and radiographic (radiographic anatomical score, then the Ghent University Score System "GUSS" and MRI).
All subjects aged between 45 and 85 years, who had apparent NSAIDs and pain traitement failure with an VAS greater than 4/10, and at least one erosive joint were included.
Results: Out of 71 evalued patients with symptomatic erosive HOA, and 64 matched the inclusion criteria and were randomized. Among them, 32 patients were randomized in the placebo group and 32 in the Methotrexate group. There was no significant difference between the two groups on the primary endpoint at 3 months, with an average decrease in VAS in the placebo group of 8.36 mm (+/- 25.15), and 17.47 mm (+/- 28.37) in the treatment group (p = 0.1797). At 12 months, no difference was found in the evolution of pain between the two groups (p = 0.6045) as well as in the functional evolution. In subjects taking Methotrexate, erosive joints move more to a remodeling phase undergoing treatment (27%) than placebo subjects (15%) (p = 0.0278). They also seem to evolve less towards erosion when their joints present a space loss (29% become erosive under placebo, against 8% in the Methotrexate group) (p = 0.0879). No predictor of erosive outcome was found in patients with non-erosive hand osteoarthritis.
Conclusion: Our study does not show superior efficacy of MTX over placebo over pain and function in subjects with erosive HOA. Our results suggest a possible structural effect on the radiological evolution of HOA under Methotrexate.
Disclosure of Interests: None declared
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OP0176

HEALTH-RELATED QUALITY OF LIFE IN HAND OSTEOARTHRITIS PATIENTS FROM THE GENERAL POPULATION AND THE OUTPATIENT CLINIC

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Background: In osteoarthritis (OA) patients health-related quality of life (HRQoL) is decreased. Whether patients with OA seeking care in a rheumatology outpatient clinic experience more impact on HRQoL than those in the general population is unknown.
Objectives: To investigate the impact of hand OA on physical and mental HRQoL in the general population, and to investigate the difference in impact between patients who have, and who have not been referred to a medical specialist.
Methods: In the population-based Netherlands Epidemiology of Obesity (NEO) study, middle-aged participants were recruited from the greater area of Leiden. In the Hand OSTeoArthritis in Secondary care (HOSTAS) study, patients with a rheumatologist's diagnosis of primary hand OA were recruited from the outpatient clinic at the Leiden University Medical Center, a secondary and tertiary referral center. In both cohorts, hand and knee OA was defined by the ACR clinical classification criteria. Patients with fibromyalgia or inflammatory rheumatic conditions were excluded. Fur the current analyses, only patients classified with hand OA alone were included. HRQoL was measured with the SF-36 questionnaire; we calculated standardized scores on a scale of 0 to 100 with subsequent application of a norm-based transformation (mean 50, standard deviation 10). Linear regression analyses, corrected for age, sex, education, ethnicity and BMI, were used to study cross-sectional associations between OA and HRQoL. Data are presented as regression coefficients with 95% confidence intervals (CI). Because a suitable reference group without OA was lacking in the HOSTAS study, these patients were compared to the normative value of 50. Previous research concluded a minimal clinically important difference of 2 points on the SF-36 scale, which was used to assess clinical relevance of differences in scores.
Results: Of the 6,334 NEO participants 8% were classified with only hand OA and 4% were classified concurrent hand and knee OA. The HOSTAS cohort consisted of a total of 538 patients with hand OA, of whom 57% fulfilled the ACR criteria for only hand OA and 32% was defined with concurrent hand and knee OA. In the population-based NEO study, mean PCS was reduced with -2.4 (-3.6; -1.3) in participants with only hand OA, compared to participants without hand or knee OA (table 1). The subscales bodily pain and physical functioning were affected the most with mean differences of –3.4 (-4.6; -2.2) and -2.1 (-3.0; -1.1). Mental HRQoL was not reduced in participants with only hand OA, compared to participants without OA. In the population-based cohort 14% of participants with hand OA reported to have visited a medical specialist for OA. Participants with hand OA that have been referred to a medical specialist showed a lower physical HRQoL with a

mean difference in the PCS of –3.9 (-6.7; -1.2), but no difference in mental HRQoL, compared with participants with hand OA that have not reported consulting secondary care for OA (table 2). In patients with only hand OA from the outpatient clinic, the PCS (-3.5), bodily pain (-4.9), vitality (-2.5) and role functioning – physical (-2.2) scales were clinically relevantly reduced, but mental HRQOL was not affected.

Table 1. Health-related quality of life of hand osteoarthritis patients in the general population

	NEO n = 6,334		
	No hand OA 78%	Hand OA 8%	Mean difference (95% CI)
Physical component score	**55.1 (7.6)**	**52.0 (8.7)**	**-2.4 (-3.6; -1.3)**
General health	53.8 (8.1)	52.1 (8.6)	-1.5 (-2.6; -0.3)
Bodily pain	55.3 (8.4)	51.5 (8.9)	-3.4 (-4.6; -2.2)
Vitality	51.0 (8.8)	50.6 (8.6)	-0.6 (-1.6; 0.5)
Physical functioning	55.0 (7.0)	51.8 (8.0)	-2.1 (-3.0; -1.1)
Role functioning - physical	53.9 (7.6)	52.6 (8.8)	-0.9 (-2.0; 0.2)
Mental component score	**51.3 (8.9)**	**51.3 (8.9)**	**0.2 (-1.0; 1.3)**
Mental health	52.4 (7.8)	51.3 (7.8)	-0.8 (-1.7; 0.2)
Social functioning	52.6 (8.0)	51.6 (8.4)	-0.6 (-1.7; 0.4)
Role functioning - emotional	52.7 (8.0)	52.3 (8.6)	-0.2 (-1.3; 0.8)

Higher SF-36 scores represent a better HRQoL. Numbers represent mean (SD). Results are adjusted for age, sex, BMI, education and ethnicity. CI = confidence interval

Table 2. Health-related quality of life of hand osteoarthritis patients in secondary care

	NEO n = 6,334			HOSTAS n = 538	
	Hand OA spec° 6.6%	Hand OA spec* 1.0%	Mean difference (95% CI)	Hand OA 57%	Δ
Physical component score	**52.6 (8.4)**	**48.5 (9.4)**	**-3.9 (-6.7; -1.2)**	**46.5 (8.1)**	**-3.5**
General health	52.5 (8.3)	49.5 (10.0)	-2.6 (-6.2; 0.9)	49.2 (6.3)	-0.8
Bodily pain	52.2 (8.8)	47.5 (8.9)	-4.9 (-7.6; -2.1)	45.1 (7.7)	-4.9
Vitality	50.7 (8.7)	50.2 (8.1)	-0.6 (-3.2; 1.9)	47.5 (8.8)	-2.5
Physical functioning	52.5 (7.6)	47.9 (9.5)	-4.3 (-7.0; -1.7)	48.8 (9.4)	-1.2
Role functioning - physical	52.9 (8.6)	50.7 (9.9)	-2.1 (-5.0; 0.8)	47.8 (10.2)	-2.2
Mental component score	**51.3 (8.5**	**50.9 (11.3)**	**-0.6 (-5.0; 3.8)**	**51.7 (8.8)**	**1.7**
Mental health	51.5 (7.4)	50.1 (9.8)	-1.5 (-5.2; 2.1)	51.0 (8.3)	1.0
Social functioning	51.8 (8.2)	50.4 (9.6)	-1.4 (-4.8; 2.0)	50.0 (9.1)	0
Role functioning - emotional	52.6 (8.2)	50.0 (10.8)	-2.5 (-6.3; 1.3)	51.1 (9.5)	1.1

Higher SF-36 scores represent a better HRQoL. Numbers represent mean (SD). Results are adjusted for age, sex, BMI, education and ethnicity. In HOSTAS the delta (Δ) between population scores and norm scores were calculated. CI = confidence interval

Conclusion: Participants with hand OA from the general population had a clinically relevant lower physical HRQoL, but not mental HRQoL. Physical HRQoL was further reduced in patients consulting secondary care and in co-occurrence with knee OA. Hence, patients with hand OA in secondary care experience more impact on physical HRQoL than patients in the general population.

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OP0177 ASSOCIATION BETWEEN METABOLIC SYNDROME AND KNEE STRUCTURAL CHANGE ON MRI: A 10.7-YEAR FOLLOW-UP STUDY

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Background: Metabolic syndrome (MetS) has been suggested a crucial role in the pathophysiology of osteoarthritis (OA); however, currently none of studies have examined the associations between MetS and structural changes on MRI.
Objectives: To describe the associations between MetS and its components and strucutral changes on MRI including knee cartilage volume (CV) loss and bone marrow lesion (BML) change over 10.7 years.
Methods: Longitudinal data on 435 participants (mean age 61 years, 50% of females) from a population-based cohort study were analysed. Blood pressure, glucose, triglycerides, and high-density lipoprotein (HDL) were collected. MetS was defined based on the National Cholesterol Education Program-Adult Treatment Panel III criteria. MRI of the right knee was performed to measure CV and BML. Radiographic knee osteoarthritis (ROA) was assessed by X-ray.
Results: 32% of participants had MetS and 60% had ROA. In multivariable analysis, the following were independently associated with medial tibial CV loss [MetS: β=-0.30%; central obesity: β=-0.26%; low HDL: β=-0.26% per annum]. MetS, hypertriglyceridemia and low HDL were also associated with higher risk of BML size increase in the medial compartment [MetS: relative risk (RR) 1.72, 95%CI 1.22-2.43; Hypertriglyceridemia: RR 1.43, 95%CI 1.01-2.02; low HDL: RR 1.67, 95%CI 1.18-2.36]. After further adjustment for central obesity, MetS and low HDL remained significant with both medial tibial CV loss and BML size increase. The number of components of MetS correlated with greater CV loss and BML size increase (both P for trend <0.05). There were no statistically significant associations in the lateral compartment.
Conclusion: MetS and low HDL are associated with medial compartment CV loss and BML worsening, suggesting that targeting MetS has the potential to prevent or slow structural change in knee osteoarthritis.
Disclosure of Interests: None declared
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OP0178 CARDIOVASCULAR COMORBIDITIES HAVE A DELETERIOUS IMPACT ON KNEE OSTEOARTHRITIS PROGNOSIS AT 5 YEARS: DATA FROM THE PROSPECTIVE KHOALA COHORT

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Background: The long-term effect of comorbidities on progression of structural changes in osteoarthritis (OA) remains poorly understood. Patients with knee OA have been reported to be at increased risk of several comorbidities including cardiovascular diseases (CVD). Nevertheless, the impact of all comorbidities on structural progression and on arthroplasty, not only in knee but also in hip OA, should be further defined.
Objectives: The objective of our study was to explore the relationship between comorbidities and the progression of structural changes in symptomatic knee and/or hip OA patients over 5 years.
Methods: The KHOALA (Knee and Hip OsteoArthritis Long-term Assessment) cohort is a French prospective multicenter observational cohort that included 878 subjects, aged 40 to 75 years, with symptomatic hip and/or knee OA at baseline (Kellgren and Lawrence (KL) $\geq$2). The structural progression was defined by the increase of one point of KL (ΔKL $\geq$1) or incidence of total knee or hip replacement at 5 years. Various comorbidities were analyzed: cardiovascular diseases excluding hypertension (coronary artery disease, heart failure, stroke, lower limb arteriopathy), hypertension, diabetes, smoking, dyslipidemia, metabolic syndrome, osteoporosis, neurological (e.g. Parkinson's disease, dementia), digestive (e.g. gastroesophageal reflux disease, ulcer), pulmonary (e.g. asthma, COPD), and psychiatric (depression, anxiety) diseases. Multivariate analysis was performed separately in hip and knee OA adjusted on age, sex and body mass index (BMI). Subjects with a BMI> 30 kg/m² were excluded from the analysis given the close relationship between obesity and the different comorbidities analyzed. Subjects with KL = 4 at the time of inclusion were also excluded from the analysis.
Results: Data from 631 non-obese subjects (BMI <30 kg/m²) were analyzed. At 5 years, cardiovascular diseases were significantly associated with the 5-year KL change in knee OA (OR = 2.6 [1.13-5.76], p=0.02) and with knee arthroplasty (OR = 3.4 [1.1-11.2], p=0.04). Such associations were not found at the hip. Other comorbidities had no significant impact on knee OA structural progression. No significant relationship was found between any type of comorbidities and hip OA structural progression.
Conclusion: This 5-year data analysis of the KHOALA cohort revealed a significant association between cardiovascular comorbidities and structural progression of knee OA in subjects without obesity (BMI <30 kg/m²). Other types of comorbidities do not appear to influence the structural prognosis of OA. These results argue for an integrated management of cardiovascular comorbidities in knee OA patients and highlight the differences between hip and knee OA.
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OP0179

DO DISTINCT PAIN PHENOTYPES HAVE DIFFERENT RISK OF KNEE REPLACEMENT: A 13.7-YEAR FOLLOW-UP STUDY?

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Background: Pain is the main impetus for osteoarthritis (OA) patients to seek healthcare including joint replacement. The pain experience is very heterogeneous and affected by factors across multiple domains–peripheral, psychological, and neurological, which suggests the existence of homogenous subgroups/phenotypes within OA patients with pain. We recently identified three pain phenotypes using a wide spectrum of factors including main pain dimensions (structural damage on MRI, body mass index (BMI), comorbidities, psychological and multi-site pain (a surrogate of neurological factor)).
Objectives: To examine whether the risk of knee replacement (KR) varied when these three pain subgroups were compared.
Methods: 1099 participants (mean age 63 years; range 51-81 years) from a population-based cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Demographic, psychological, lifestyle and comorbidities data were obtained at baseline. T1-weighted or T2-weighted MRI of the right knee was performed to measure knee structural pathology–cartilage defects, bone marrow lesions (BMLs) and effusion-synovitis at baseline. Knee pain was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain questionnaire at each time-point. Presence of pain (yes/no) in the neck, back, hands, shoulders, hips, knees and feet was also assessed by questionnaire at each time-point. KR up to 13.7 years after recruitment was identified by linking to the Australian Orthopaedic Association National Joint Replacement Registry. Latent class analysis was used to differentiate pain phenotypes by considering sex, BMI, emotional problems, education level, comorbidities, number of painful sites and knee structural damage on MRI. Log-binomial regression was used to evaluate the association between three pain phenotypes and risk of KR.
Results: 963 participants were included in the analysis (BMI 27.7 kg/m^2, 50% female). Three distinct phenotypes were identified: Class 1: high prevalence of emotional problems and low revalence of structural damage (25%); Class 2: high prevalence of structural damage and low prevalence of emotional problems (20%); Class 3: low prevalence of emotional problems and low prevalence of structural damage (55%). Participants in Class 1 had greater pain severity than those in Class 2 and 3. During a follow-up of 13.7 years, There were 46 right and 51 left TKR's in 79 participants In multivariable analyses, participants in Class 1 and 2 had higher risk of requiring KR on the right [Class 1 vs. Class 3: relative risk (RR) 6.66, 95%confidence interval (CI) 2.17-20.49; Class 2 vs. Class 3: RR 14.14, 95CI% 4.85-41.22], left (Class 1 vs. Class 3: RR 2.75, 95%CI 1.22-6.19; Class 2 vs. Class 3: RR 5.46, 95CI% 2.64-11.32), and any knee joints (Class 1 vs. Class 3: RR 3.65, 95%CI 1.88-7.09; Class 2 vs. Class 3: RR 6.81, 95CI% 3.68, 12.60) compared to Class 3, but the associations were stronger with Class 2 than Class 1.
Conclusion: Participants with distinct pain phenotype groups have different risks of KR. This suggests that the identified phenotypes reflect distinct clinical subgroups with different prognoses. As expected the highest risk of KR was found in those with the most structural damage (Class 2). However, those participants with low structural damage have an increased risk of KR when they have high compared to low emotional problems, indicating that selection of subjects for KR could be improved by screening out those in Class 1.
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OP0180

LOW-DOSE PREDNISOLONE IN PATIENTS WITH HAND OSTEOARTHRITIS (HOPE): RESULTS FROM A RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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Background: Hand osteoarthritis (OA) is a prevalent joint disease with high disease-burden in need for effective therapeutic options. Studies have shown that synovial inflammation is often present in hand OA and a main determinant of pain and radiographic disease progression.
Objectives: To investigate the efficacy and safety of short-term low-dose prednisolone in patients with painful hand OA.
Methods: This randomised, double-blind, placebo-controlled trial enrolled patients with painful hand OA, fulfilling American College of Rheumatology criteria, and signs of synovial inflammation. Patients with ≥4 interphalangeal joints (IPJ) with osteoarthritic nodes, ≥1 IPJ with soft swelling or erythema and ≥1 IPJ with positive power Doppler signal (PDS) or synovitis grade ≥2 on ultrasound, were eligible. Key exclusion criteria were chronic inflammatory rheumatic diseases, psoriasis, using immune modulating drugs within 90 days before baseline, and predominant thumb base pain. Eligible patients with visual analogue scale (VAS) finger pain ≥30 mm, flaring ≥20 mm upon non-steroidal anti-inflammatory drug washout, were randomised to receive prednisolone 10 mg daily for 6 weeks or placebo, followed by a two-week tapering scheme and 6 weeks without study medication. Outcomes were assessed at 2, 4, 6, 8 and 14 weeks. Primary endpoint was VAS finger pain at week 6 in intention-to-treat analysis. Secondary clinical endpoints included fulfilment of OMERACT-OARSI responder criteria, Australian/Canadian Hand OA Index (AUSCAN) pain/function, Functional Index for Hand OA (FIHOA), VAS patient global assessment, Short-Form 36 and grip strength. Imaging endpoints included ultrasound synovitis and PDS.

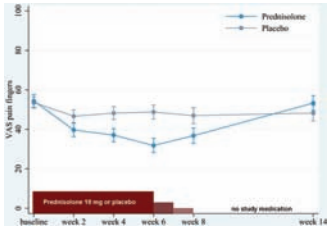


Table. Baseline characteristics and results of secondary endpoints at week 6 of HOPE study.

	Mean (SD) at baseline		Mean (SD) change from baseline		Adjusted mean between-group difference (95% CI)*	p-value
	Prednisolone	Placebo	Prednisolone	Placebo		
Pain						
AUSCAN pain, 0-20	11.3 (3.3)	10.2 (3.1)	-4.7 (3.5)	-1.1 (3.1)	-3.5 (-4.9 to -2.1)	<0.001
Function						
AUSCAN function, 0-36	18.6 (7.8)	19.0 (7.1)	-6.5 (7.4)	-2.7 (4.7)	-3.7 (-6.2 to -1.1)	0.01
FIHOA, 0-30	12.4 (5.4)	11.0 (4.7)	-2.6 (5.1)	-0.5 (4.0)	-2.1 (-4.0 to -0.2)	0.03
SF-36 physical component scale†	44.6 (7.9)	46.2 (6.8)	3.1 (6.7)	-0.3 (6.3)	3.5 (0.8 to 6.2)	0.01
VAS patient global assessment, 0-100	55.5 (21.7)	55.7 (22.0)	-23.6 (23.5)	-8.0 (25.3)	-15.4 (-25.6 to -5.2)	0.003
Grip strength, kg	20.4 (11.3)	20.4 (11.8)	3.5 (4.1)	2.2 (5.5)	1.2 (-0.8 to 3.2)	0.24
Ultrasound (sum scores)						
Synovitis, 0-90	16.4 (6.3)	17.8 (6.3)	-2.8 (4.7)	-0.3 (5.0)	-2.5 (-4.5 to -0.5)	0.02
Power Doppler Signal, 0-90	5.3 (4.1)	7.0 (4.3)	-1.7 (4.3)	-1.3 (4.2)	-0.4 (-2.2 to 1.4)	0.68

*Adjusted for baseline value and study center. †Norm-based scores with a standardized mean of 50 and SD of 10 using age- and sex-specific Dutch population-based norms. AUSCAN=Australian/Canadian Hand Osteoarthritis Index. FIHOA=Functional Index for Hand Osteoarthritis. SF-36=Short Form-36. VAS=visual analogue scale.

Results: Of 92 patients (mean (SD) age 63.9 (8.8), 79% women) randomised to prednisolone (n=46) or placebo (n=46), 42 patients in each group completed the study. Baseline characteristics were well-balanced between the groups. The mean (SD) change from baseline to week 6 in VAS finger pain was -21.5 (21.7) in the prednisolone and -5.2 (24.3) in the placebo group, with a mean between-group difference of -16.5 (95% confidence interval (CI) -26.1 to -6.9; figure). At week 6, 33 (72%) patients in the prednisolone versus 15 (33%) in the placebo group fulfilled OARSI responder criteria (odds ratio 5.3, 95% CI 2.0 to 13.6, p=0.001). In analogy with the primary endpoint, prednisolone was superior to placebo in most other secondary clinical endpoints (table). Ultrasound synovitis significantly improved at week 6 in the prednisolone compared to the placebo group, while no difference was observed in PDS (table). After tapering, between-group

differences disappeared. Adverse events were mostly mild and comparable between groups.
Conclusion: Six-week treatment with low-dose oral prednisolone led to a substantial improvement of symptoms in patients with painful hand OA and signs of inflammation. This trial provides evidence that local inflammation is a suitable target for drug-treatment in hand OA.
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The funding source had no role in the design and conduct of the study., Frits Rosendaal: None declared, Naghmeh Riyazi: None declared, Mirian Starmans: None declared, Franktien Turkstra: None declared, Jende van Zeben: None declared, Cornelia Allaart: None declared, Margreet Kloppenburg Grant/research support from: Pfizer, IMI-APPROACH (Grant Agreement n° 115770), Consultant for: GlaxoSmithKline, Merck-Serono, Abbvie, Levicept, Pfizer
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Systemic sclerosis, myositis and related syndromes – etiology, pathogenesis and animal models

OP0181 MOLECULAR CHARACTERIZATION AND STRATIFICATION OF IDIOPATHIC INFLAMMATORY MYOPATHIES: ON THE BASIS OF SKELETAL MUSCLE TRANSCRIPTOME STUDY

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Background: Idiopathic inflammatory myopathies (IIM) are a group of complicated heterogenous autoimmune diseases, to date, little is known about its skeletal muscle transcriptomic features.
Objectives: Here, we performed skeletal muscle RNA-sequencing (RNA-seq) to discover the global muscle transcriptional signature of IIM based on myositis-specific antibodies (MSA) profiles and investigate the potential molecular pathway of IIM.
Methods: Muscle specimen were taken from 60 patients with IIM, 6 patients with non-IIM myopathies and 9 healthy controls. The serum and PBMC samples were also obtained from the IIM patients at the time of muscle biopsy. For RNA-seq, IIM was dissected into eight groups based on their MSA profiles: MSA and ANA negative (n = 4), anti-synthetase antibodies positive (n= 13), -MDA5 positive (n = 6), -NXP-2 positive (n = 7), -TIF-1γ positive (n = 10), -SRP or anti-HMGCR positive (n = 6), -Mi-2 positive (n = 7), MSA negative but anti-Ro-52 positive (n = 7). RNA from muscle specimen were extracted according to manufactory guide and sequenced using Illumina HiSeq2500. Quantitative real-time reverse transcription-polymerase chain reaction (qRT-PCR) was performed on sequencing cohorts and expanding cohorts to validate the results of RNA-seq. Immunohistochemistry was also performed on muscle biopsy to determine the MxA expression in different MSA subgroups.
Results: To define the global muscle signature of IIM, all IIM samples were compared to NC and total of 1637 transcripts were differentially expressed (log2 Fold Change > 1, Padj < 0.05). Unsupervised hierarchical clustering of these differentially expressed transcripts (DETs) revealed a prevalent interferon (IFN) signature and showed that 68 interferon-stimulated genes (ISGs) were significantly up-regulated in IIM. Then these 68 ISGs were used to cluster different MSA subgroups and distinct ISG expression was found. The mRNA expression levels of several ISGs (MX1, IFIH1, LAMP3, CMPK2, HERC6) in sequencing cohorts and expanding cohorts also confirmed the diverse ISG expression between different MSA subgroups. An IFN signature scoring system was established to quantify the IFN activity and subsequently IIM could be classified into IFN-Dominant, IFN-Moderate and IFN-Weak respectively based on the IFN intensity and different MSA subgroup. Moreover, the IFN-Dominant group showed much higher MxA expression on muscle biopsy than the IFN-Moderate and IFN-Weak group by immunohistochemistry.
Conclusion: We revealed a prominent IFN signature and MSA-based ISG expression heterogeneity in IIM through muscle transcriptomics. Preliminary results showed that the IFN muscle signature may play a predominant role in some subgroups but not all IIM groups in the pathogenesis of IIM.

REFERENCES:
[1] Miller FW, Lamb JA, Schmidt J, Nagaraju K. Nat Rev Rheumatol. 2018 Apr 20;14(5):255-268.
[2] Mariampillai K, Granger B, Amelin D, Guiguet M, Hachulla E, Maurier F, Meyer A. JAMA Neurol. 2018 Dec 1;75(12):1528-1537.
[3] Banchereau R, Hong S, Cantarel B, Baldwin N, Baisch J, Edens M, Cepika AM. Cell. 2016 Apr 21;165(3):551-65.

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OP0182 SYNTHETIC PEPTIDES TARGETING CD206 INHIBIT PATHOGENIC MACROPHAGES IN SYSTEMIC SCLEROSIS

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Background: In systemic sclerosis, activated macrophages having M2-like properties are believed to contribute to the fibrotic pathology by secreting profibrotic factors such as TGFβ. Certain synthetic peptides (10-12mers) studied here coopt the mechanism used by macrophages to detect bacteria by binding to certain regions of CD206, a receptor highly expressed in the M2 macrophages, and repolarise them to an M1 phenotype.
Objectives: We aimed to determine the macrophage activation signature in SSc, assess CD206 as a biomarker of ongoing fibrotic activity, and measure the effect of the peptides on macrophage activation and macrophage-fibroblast cross-talk.
Methods: sCD206 was assayed in plasma (n=50 healthy, 50 limited SSc, 50 diffuse SSc), and suction blister fluid (BF) obtained over active lesions by ELISA. sSIGLEC (monocyte interferon signature) and IL-31 (Th2 signature) were assayed for comparison. Cell surface CD206 and DAMP receptor P2X7, were assayed by flow cytometry. The macrophage activation signature was investigated further by qPCR for inflammatory M1, as well as M2-like gene expression (*IFNγ, Arg1, CD2106*). Macrophage-fibroblast cross talk was assessed using media transfer following heat activation to SSc dermal fibroblasts assayed by qPCR for collagen I. The macrophage secretome was determined by Luminex and ELISA.
Results: CD206 was significantly elevated in SSc BF (SSc median sCD206 42, HC 31 pg/ml, p<0.041). Plasma sCD206 was raised in diffuse versus limited SSc (P<0.0103) and was correlated with ESR (R=0.364, p<0.009) and sSIGLEC (R=0.244, p<0.05), but not disease duration or IL-31. By flow cytometry both CD206 and P2X7 were highly expressed by SSc macrophages (mean fluorescence SSc, 776.1 SD=409.1, 724.4 SD=455.3 vs HC 632.2 SD=73.7, 472.9 SD=25.4), correlating with modified Rodnan Skin Score (mRSS) (p<0.05, r=0.51). Double positive P2X7 and CD206 cells were seen in a subgroup with higher mRSS. Four RP peptides (RP182, 185, 832 & 837) were assessed for effect on growth of SSc and control macrophages. In general, the RP peptides selectively inhibited SSc macrophage growth, with RP185 and RP832 reaching significance (p<0.05) for 1 and 10μM concentrations at 96 hours. Pro-fibrotic cross-talk leading to elevated fibroblast collagen I, was characteristic of 4 out of 9 SSc macrophage cell lines examined. A mixed activation signature was identified by qPCR of the fibroblast-stimulating macrophages (elevated Arginase1, CD206 and IFNγ) but not the non-fibroblast inducing cell lines. Pre-treatment of the pro-fibrotic SSc macrophages with RP832, but not the others, eliminated the pro-fibrotic cross-talk (fibroblasts treated with SSc macrophage media mean collagen I, 1995 (SEM 149), RP832 treated macrophages 1551 (SEM 133) p<0.038 relative expression units, paired t test), and suppressed the macrophage activation signature (reduced mean Arg1 p<0.030, CD206 p<0.058, IFNγ p=0.058, paired t test). Secretome analysis confirmed the mixed activation signature of SSc macrophages including elevated total TGFβ, PDGF-BB, sCD40L as well as inflammatory factors IL-6, IL-1β, TNFα and type I cytokine IFNγ. Treatment with RP 832c reduced TGFβ in 6 out of 9 SSc macrophage cell lines but this did not reach statistical significance.
Conclusion: A macrophage activation signature is identified in SSc patients, in proportion to the severity of disease. A mixed activation signature with inflammatory as well as pro-fibrotic M2-like properties is seen. RP peptides, which target the cells via CD206, reduce the activation signature and inhibit pro-fibrotic cross talk in these cells.
Disclosure of Interests: : Henry Lopez Shareholder of: Murigenics, Riptide Bioscience, Employee of: Pfizer, Kimti Kumar: None declared, George Martin

Shareholder of: Riptide Bioscience, Jesse Jaynes Shareholder of: Riptide Bioscience, James Stanway: None declared, Bahja Ahmed Abdi: None declared, Nikita Arumalla: None declared, Sarah Karrar: None declared, Sian Morris: None declared, Christopher Denton Grant/research support from: GlaxoSmithKline, Inventiva, CSF Behring, Consultant for: Roche-Genentech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Bayer, David Abraham: None declared, Xu Shiwen: None declared, Richard Stratton: None declared

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OP0183 EFFICACY AND SAFETY OF RIOCIGUAT IN PATIENTS WITH EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS AND INTERSTITIAL LUNG DISEASE (SSC-ILD): RESULTS FROM THE PHASE IIB RISE-SSC STUDY

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Background: Diffuse cutaneous systemic sclerosis (dcSSc) is an autoimmune connective tissue disease characterised by fibrosis and, in some patients, interstitial lung disease (ILD). Riociguat is a soluble guanylate cyclase (sGC) stimulator with vasoactive, anti-proliferative and anti-fibrotic effects. We hypothesised that riociguat may preserve lung function in patients with dcSSc.

Objectives: To evaluate the effect of riociguat on lung function in patients with early dcSSc from the multicentre, randomised, double-blind, placebo-controlled Phase IIb RISE-SSc study (NCT02283762).

Methods: Patients had dcSSc of duration ≤18 months, modified Rodnan skin score (mRSS) 10–22 units, forced vital capacity (FVC) ≥45% predicted (%pred) and lung diffusion capacity for carbon monoxide (DLCO) ≥40%pred at screening. Patients were randomised to riociguat (n=60) or placebo (n=61) in individually adjusted doses of 0.5 mg up to 2.5 mg tid. The primary endpoint was the change in mRSS from baseline to Week 52. Secondary endpoints included change in FVC%pred from baseline to Week 52. Effects on lung function (FVC%pred) were assessed in the overall population and in post-hoc analyses in patients with FVC %pred 50-75% or medical history of ILD at baseline. Between groups, differences were in least-squares [LS] means.

Results: Although the study did not meet its primary endpoint, there was a reduction in mRSS with riociguat vs placebo (−2.34; 95% CI: −4.99 to 0.30; p=0.08). There were no significant differences between treatment groups in the changes in FVC%pred (−0.20; 95% CI, −3.40 to +3.00; p=0.90) or DLCO%pred (2.01; 95% CI: −4.99 to 6.25; p=0.35) which included all patients irrespective of the presence of SSc-ILD. However, differences between riociguat and placebo were observed when patients with SSc-ILD were analysed: At baseline, 11/60 (18%) patients in the riociguat group and 12/61 (20%) in the placebo group had medical history suggesting ILD (SSc-ILD); 11/60 (18%), and 7/61 (11%), respectively, had restrictive lung disease (FVC%pred 50–75%). Results in subgroups were expressed as within-group mean change (SD). In patients with SSc-ILD, the decline in FVC% pred between baseline and Week 52 was smaller in the riociguat group (–2.7[4.0]) than the placebo group (–8.9[13.1]). The changes in DLCO%pred were –0.11 (0.22) and +0.87(0.71), respectively. In patients with restrictive lung disease, FVC %pred decreased by –8.7 (14.0) at Week 52 with placebo but was almost unchanged (+0.7[5.7]) with riociguat. The changes in DLCO%pred were +0.42 (0.85) and –0.27(0.39), respectively.

Patients with SSc-ILD receiving riociguat had lower incidences of adverse events and serious adverse events [82% (n=9) and 9% (n=1) respectively] compared with placebo [92% (n=11) and 25% (n=3) respectively] with no differences between treatment groups in the incidence of respiratory adverse events. No deaths occurred in the SSc-ILD subgroup, and no new safety signals were observed.

Conclusion: These results suggest that in an exploratory analysis, riociguat may be associated with preservation of lung function and good tolerability in patients with dcSSc and evidence of ILD on medical history.

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OP0184 PROFIBROTIC LNCRNA H19X: UNRAVELLING THE EFFECTS ON CHROMATIN REMODELING IN SYSTEMIC SCLEROSIS FIBROBLASTS

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Background: Long noncoding RNAs (lncRNAs) are noncoding transcripts involved in the regulation of gene expression in health and disease. LncRNAs function via different mechanisms either acting cis, regulating the expression of nearby genes, or in trans, modulating the expression of distant genes. We identified a novel TGFβ regulated lncRNA, H19X, which was strongly upregulated in a wide variety of fibrotic disorders. Moreover, we were able to demonstrate that H19X is a key driver of myofibroblast formation and extracellular matrix (ECM) overproduction.

Objectives: To define the mode of action of H19X (cis or trans) and to assess H19X function on chromatin rearrangements that may drive myofibroblast differentiation and ECM production.

Methods: The function of H19X was investigated in SSc dermal fibroblasts (n=5) by knocking down H19X with locked nucleic acid oligonucleotides followed by TGF-β stimulation and microarray analysis with Illumina HT-12 arrays. In situ hybridization for H19X was performed using Stellaris FISH probes. Chromatin remodeling was investigated by Assay for Transposase-Accessible Chromatin using sequencing (ATAC-seq).

Results: As analyzed by microarray, none of the 16 genes belonging to the same genomic region as H19X locus was affected by its downregulation, indicating that in-cis regulation is not a major mechanism of H19X activity. Cellular localization can give a first indication about lncRNA trans function: FISH staining of SSc fibroblasts stimulated with TGF-β revealed tightly localized nuclear foci in TGF-β treated cells. H19X nuclear localization was confirmed by cell fractionation, where H19X expression was peaking in the nucleus of cells after 6h of treatment with TGF-β. We next hypothesized that H19X nuclear expression might induce chromatin rearrangements. We assessed whether chromatin changes caused by H19X knockdown might be correlated with changes in expression profile seen by microarray. Therefore, we analyzed the differences in the chromatin conformation flanking transcription start sites (TSSs) by ATAC-seq. A clear separation between the two experimental groups (scrambled vs H19X knockdown) was observed and 450 differentially accessible regions were identified ($p<0.05$, $Log2FC>0.5$).

After focusing on genes that displayed significant variations and $Log2FC>0.5$ for both the array and ATAC-seq analysis, eight candidates genes were found both upregulated by microarray and showed increased accessibility at their TSSs by ATAC-Seq. Similarly, three candidate genes were identified as being downregulated by microarray and showed decreased TSS accessibility by ATAC-Seq. These genes included histones HIST1H2BD and HIST1H1C, suggesting a direct regulation of chromatin organization as a mode of action for H19X. Moreover, the cell cycle progression inhibitors FABP3 and PTTG1 were pointing to a role of H19X in proliferation.

In addition, analysis for transcription factor motif enrichment in the differentially accessible peaks of the ATAC-Seq analysis revealed that motifs for TEAD2, RUNX family, and NFKB2 were less accessible, while motifs for JUN::FOS, NF2L2 and EHF were more accessible due to the chromatin changes. These results indicate that H19X could promote or repress the activity of these candidate transcription factors by changing chromatin conformation at the sites of their consensus sequence.

Conclusion: ATAC-Seq in combination with microarray analysis identified candidate mechanism for the TGFβ regulated profibrotic effects of H19 X including direct effects on chromatin organization and on transcription factors associated with fibrotic pathways.

Disclosure of Interests: Elena Pachera: None declared, Shervin Assassi: None declared, Gloria Salazar: None declared, Mojca Frank-Bertoncelj : None declared, Jörg Distler: None declared, Gabriela Kania: None declared, Oliver Distler Grant/ research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders

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OP0185 INFLAMMATION-DEPENDENT DECREASED EXPRESSION OF CD52 ON CIRCULATING CD14+ MONOCYTES FACILITATES ADHESION IN SYSTEMIC SCLEROSIS

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Background: During the course of systemic sclerosis (SSc), infiltration of inflammatory cells, including monocytes, into the organs is a major process leading to fatal fibrosis, remodelling and organ dysfunction.

CD52 protein is highly expressed on $CD4^+$ T-cells and plays an important role in the modulation of T-cell receptor signalling. Nevertheless, the function of this protein on monocytes is not completely understood.

Objectives: We aimed to functionally investigate the role of circulating $CD14^+$ monocytes in the course of SSc with a special focus on monocyte adhesion and the influence of CD52 expression.

Methods: Biopsies from the heart, lungs and skin of SSc patients (n=11, 7, 7 respectively) and healthy controls (HC) (n=10, 7, 9 respectively) were analysed by immunohistochemistry for the presence of $CD14^+$ cells. PolyA RNA sequencing of $CD14^+$ monocytes isolated from peripheral blood of lcSSc (n=5, age=54.4 ±6.7), dcSSc patients (n=5, age=51.8±7.2) and age- and sex-matched HC (n=5, age=50.8±9.7) was performed using Illumina HiSeq 4000 platform. Differentially expressed genes were computed using DeSEQ2 algorithm. Gene ontology and pathway analysis were performed using Metacore software and ShinyApp. Expression of adhesion molecules was confirmed on the protein level using flow cytometry (HC n=8, SSc n =22). Adhesion of $CD14^+$ monocytes to immobilized ICAM1 and TNFα-stimulated endothelial cells was checked using the 96-well plate adhesion assay (HC n=8, SSc n=22). CD52 regulation in $CD14^+$ monocytes from HC (n=4) was analysed on mRNA level upon stimulation with different concentrations of LPS, IFNγ, IL-4 and IL-13. THP-1 cell lines with overexpression and silencing of CD52 were generated using lentiviral vectors, and further, their adhesion was investigated (n=4).

Results: Immunochemistry confirmed higher infiltration of $CD14^+$ cells in the heart ($p<0.01$), lung ($p<0.05$), and skin ($p<0.001$) of SSc patients. We detected 1440 differentially expressed genes between dcSSc vs HC and 225 between lcSSc and HC CD14+ monocytes respectively ($p\leq0.01$; log2 ratio$\geq$0.5). Pathway analysis revealed significant alterations in processes important for tissue infiltration, including adhesion. Flow cytometry analysis showed upregulation of adhesion molecules: integrin α_M (CD11b) ($p<0.01$) and integrin β_2 (CD18) ($p<0.01$On the other hand, expression of CD52 was downregulated in SSc patients ($p<0.05$). SSc CD14+ monocytes exhibited increased adhesion both to ICAM1-coated plates ($p<0.01$) and to TNFα-stimulated endothelial cells ($p<0.05$). CD52 mRNA was significantly increased in a dose-dependent manner after anti-inflammatory stimulation (IL-4, IL-13) and significantly decreased after inflammatory stimulation (LPS, IFN-γ) ($p<0.05$). Overexpression of CD52 in THP-1 monocytes decreased adhesion to TNFα-stimulated endothelial cells ($p<0.01$). Accordingly, silencing of CD52 increased adhesion of THP-1 monocytes ($p<0.01$).

Conclusion: This is the first report pointing to an increased adhesion of peripheral blood $CD14^+$ monocytes to ICAM1 and endothelial cells in SSc. Our results suggest the primary activation of monocytes in peripheral blood, which translates into higher organ infiltration in SSc patients. Finally yet importantly, we characterised a novel function of CD52 molecule on monocytes and its possible contribution during the course of the disease.

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OP0186 LIN-GP38+ STROMAL CELLS ARE KEY EFFECTOR CELLS IN MYOCARDIAL FIBROSIS AND DEFECTS OF THE CONDUCTION SYSTEM

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Background: Cardiac dysfunction is a significant cause of mortality in SSc due to inflammation, vasculopathy and fibrosis. In fibrotic conditions, the excessive number of fibroblasts, myofibroblasts and extracellular matrix in the myocardium may directly or indirectly affect the cardiac conduction system by different mechanisms. Myofibroblasts are the main players in cardiac fibrogenesis, but their origin in SSc remains unknown.

Objectives: To unravel the role of Fos-related antigen 2 (Fra2) in stromal cell activation, cardiac fibrosis and alteration of the conduction system.

Methods: Fra2 transgenic (tg) mice and $Rag2^{-/-}$ Fra2 tg mice were studied. Hearts from Fra2 tg and WT mice were analysed by immunohistochemistry (IHC) and immunofluorescence (IF). Cardiac function was assessed by echocardiography, electrocardiogram (ECG) and telemetry. Myocardial stromal ($Ter119^-CD45^-CD31^-$, hereafter Lin^-) $gp38^+$ stromal cells were sorted and cultured *in vitro*. The cellular phenotype was evaluated by qPCR, α-smooth muscle actin (αSMA) and stress fibre staining, secreted collagens and contraction assay.

Results: Echocardiography of 20-week-old Fra2 tg mice displayed increased ejection fraction ($p=0.02$) and fractional shortening ($p=0.02$) with decreased left ventricle end-diameter and end-volume in systole ($p=0.006$, $p=0.008$) and in diastole ($p=0.007$, $p=0.008$). ECG in conscious mice revealed lower heart rate (HR) (WT 741 ± 33 BPM, tg 644 ± 37 BPM, $p<0.0001$) and prolonged QRS, ST and QTc parameters ($p=0.001$, $p=0.01$, $p=0.01$), which may predispose to arrhythmias. Telemetry recording showed the presence of atrio-ventricular (AV) blocks that correlated with disease severity ($R=0.9$, $p=0.02$). The myocardium of Fra2 tg mice presented mild inflammation and fibrosis with higher expression of collagen ($p=0.03$, n=7) and periostin ($p=0.001$, n=7), increased number of αSMA^+ myofibroblasts and expansion of stromal Lin^-gp38^+ cells compared to WT mice (1.4% ± 1.4, n=15 and Fra-2 tg: 6% ± 4.5, n=14, $p=0.001$). Fibrosis disrupts the conductivity of cardiac tissue. Therefore, we investigated whether these stromal cells might be responsible for fibrosis. The majority of Lin^-gp38^+ cells co-expressed αSMA, collagen, ADAM12 and periostin, indicating that myocardial Lin^-gp38^+ cells might acquire a myofibroblast-like phenotype. Moreover, gp38 expression correlated with collagen deposition ($R=0.9$, $p< 0.0001$). The comparison between Lin^-gp38^+ cells isolated from WT and Fra2 tg showed that both αSMA total protein and αSMA fibres were increased in Fra2 cells. Importantly, αSMA fibres co-localized with stress fibres, resulting in a faster and stronger contraction capacity of Fra2 cells ($p<0.0001$, n=3). Proliferation of Fra2 cells was increased compared to WT ($p=0.007$, n=5), while apoptosis was unchanged ($p=0.335$, n=5). Interestingly,

$Rag2^{-/-}$Fra2 tg mice showed no fibrosis or $Lin^{-}gp38^{+}$ cell expansion. ECG parameters of $Rag2^{-/-}$Fra2 tg mice were not changed compared to control mice, indicating that inflammation is necessary to acquire Fra2-driven fibrotic phenotype and defects in the conduction system.

Conclusion: Fra2 overexpression and inflammation foster stromal cell-to-myofibroblast differentiation, leading to cardiac fibrosis and defects of the conduction system. Targeting this process might be a therapeutic strategy for SSc patients with disorders of cardiac involvement.

Disclosure of Interests: Mara Stellato: None declared, Michal Rudnik: None declared, Florian Renoux: None declared, Przemyslaw Blyszczuk: None declared, Elena Osto: None declared, Matthias Dewenter: None declared, Petra Seebeck: None declared, Elena Pachera: None declared, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Gabriela Kania: None declared

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OP0187 RITUXIMAB AND CYCLOPHOSPHAMIDE COMPARISON FOR EFFICACY AND SAFETY IN THE PATIENTS WITH SYSTEMIC SCLEROSIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE

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Background: Cyclophosphamide (CyP) is considered as a drug of choice for the treatment of interstitial lung disease (ILD) in the patients with systemic sclerosis (SSc). However, according to the literature, the use of CyP leads to rather limited and transient improvement of the pulmonary fibrosis. In this context the search for novel, more efficacious agents has been continued, such as attracting much attention retuximab (RTM).

Objectives: To compare the impact of CyP and RTM on SSc clinical manifestation and activity, and the safety of these agents in the open-label prospective non-randomized study.

Methods: 107 patients with the confirmed SSc diagnosis and ILD evidence based on HRCT findings were enrolled into the study. All patients received low-dose and moderate-dose prednisolone regimens. 36 patients (**Group A) received parenteral CyP** for 12±6 months at total dose 10.6±5 g (the average age 47±12 years, females 92%, SSc duration 5.0±4.8 years, diffused/localized forms 1.6/1). 71 patients (**Group B) received RTM** at total dose 1.43±0.66 g over the follow-up period 13.2±2 months (the average age 46±13 years, females 83%, SSc duration 5.6±4.4 years, diffused/localized forms 1.4/1); to 32 (45%) of them RTM was added to immunosupressants due to inadequate efficacy of the latter. The time courses FVC(%), modified skin count (mRss, points), activity index (EScSG, points), left ventricle ejection fraction (LVEF,%), mean pulmonary arterial pressure (EchoCG), and cardiac rhythm and conductivity disorders (ECG) were evaluated.

Results: In Groups A and B the therapy was associated with significant decrease in mRss (p=0.009 and 0,001, respectively) and EScSG (p=0.000165 and 0.001, respectively). Increase in LVEF (61.8±7.3 и 63.6±7.3. p=0.02) was observed only in RTM-treated patients.

Evaluation of FVC time course in Groups A and B revealed significant FVC increase (p= 0.034 and 0.000045, respectively), with median increment about 5%. In Group A FVC 10% FVC increase was found in the third of the patients thus exceeding respective parameter in Group B (p=0.2). The patient percentage with FVC decrease by ≥10% was similar in both groups.

During the follow-up period no change of the other studied parameters was observed.

The therapy was better tolerated in RTM-treated group: during RTM therapy adverse reactions emerged in significantly lower proportion of the patients (11/14%) compared with CyP-treated group (19/53%), p=0,0000.

Parameters	Group A	Group B
EScSG 1 *M ± SD*	2.8±2*	2.8±1.8*
EScSG 2 *M ± SD*	1.4±1.17*	1.3±1.1*
mRss 1 *M ± SD*	11.2±9.8 *	11.3±9.6 *
mRss 2 *M ± SD*	7.9±6.8. *	8.0±6.6*
FVC 1 *M ± SD*	80.5±20.1*	77.3±20 *
FVC 2 *M ± SD*	85.9±20.5*	82.6±21.*
Δ FVC%	5.4 [-0.6; 12.3]	5.3 [0.1; 10.2]
FVC increment by ≥10%, n/%	11/31	14/19.7
FVC decrement by ≥10% n/%	2/5.6	4/5.6

Notes: *in Parameters column 1 = before treatment, 2 = after treatment; M ± SD = mean value and standard deviation; * = significant difference between the vales measured before and after the treatment*

Conclusion: Both agents effectively alleviated skin induration and EScSG, and significantly improved FVC. However, CyP use for a year slightly more frequently resulted in clinically significant FVC increase, probably due to low RTM cumulative dose. RTM was better tolerated compared to CyP. The study findings substantiate potential use of anti-B-cell therapy both as a first-line agent for ILD treatment in the patients with SSc, and in the event of CyP inefficacy of poor tolerability, especially in the patients with cardiopathy.

Disclosure of Interests: None declared

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OP0188 PATHOGENICITY OF FUNCTIONAL AUTOANTIBODIES AGAINST AT1R IN A MOUSE MODEL OF SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune connective tissue disease featured by autoimmunity, fibrosis and vasculopathy. Although many autoantibodies have been detected in the sera of patients with SSc, it is not clear whether they play a role in the pathogenesis of disease. It has been reported that autoantibodies against the angiotensin-II receptor type 1 (AT1R) are present in the sera of SSc patients and are associated with several clinical symptoms of the disease, suggesting that these autoantibodies may act as pathogenic drivers. Recently, our group has developed a novel mouse model for SSc by immunizing mice with human AT1R (hAT1R). From this model we were able to generate functional monoclonal antibodies agonizing AT1R.

Objectives: In the current study, we aim to clarify, whether B cells and antibodies directed against AT1R are involved in the pathogenesis of experimental SSc *in vivo.*

Methods: To investigate the role of B cells in the hAT1R-induced mouse model of SSc, we immunized B-cell deficient mice with hAT1R. Nine weeks after the first immunization, mice were sacrificed and sera and tissues were collected for further evaluation. To investigate the pathogenicity of anti-AT1R antibodies in the disease, monoclonal autoantibodies against hAT1R were applied to the ear of C57Bl/6 mice by single or repetitive injection. Mice were sacrificed 24 hours or 14 days after the first injection for single and repeated application, respectively, and ear and lung tissues were collected for further evaluation.

Results: Compared to the wild type C57Bl/6 mice, hAT1R-immunized B-cell deficient mice were resistant against experimental SSc with regard to autoantibody production, inflammation in the lung and skin, and skin fibrosis. Furthermore, both single and repetitive injection of monoclonal antibodies against hAT1R induced inflammation in ears of mice. Despite this local effect, repetitive injection of anti-AT1R monoclonal antibodies provoked also inflammation in the lung of mice.

Conclusion: Our data demonstrate that i) B cells are indispensable for the pathogenesis of the hAT1R-induced mouse model for SSc and ii) monoclonal antibodies against hAT1R can induce inflammation in mice. Therefore, our results support a role of autoantibodies against AT1R in the pathogenesis of SSc.

REFERENCES:

[1] Yannick Allanore, et al. Nat Rev Dis Primers 2015.

[2] Gabriela Riemekasten, et al. Ann Rheum Dis 2011.
[3] Mike O. Becker, et al. Am J Respir Crit Care Med 2014.

Disclosure of Interests: Junping Yin: None declared, Xiaoqing Wang: None declared, Xiaoyang Yue: None declared, Gabriela Riemekasten Consultant for: Chugai, F. Hoffmann-La Roche, Speakers bureau: Chugai, F. Hoffmann-La Roche, Xinhua Yu: None declared, Frank Petersen: None declared
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THURSDAY, 13 JUNE 2019

Genetics, epigenetics and immunity

OP0189 GENETICS OF JUVENILE IDIOPATHIC ARTHRITIS: THE IDENTIFICATION OF A NOVEL RISK LOCUS AND CLINICAL SUBGROUP ANALYSIS

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Background: Juvenile idiopathic arthritis (JIA) is a clinically heterogeneous group of childhood onset inflammatory joint diseases with strong evidence to support a genetic contribution to susceptibility. JIA is divided into seven clinical subgroups based on observed patterns of clinical symptoms using the International League of Associations for Rheumatology (ILAR) classification system. The genetic overlap between these groups is not completely understood and this lack of knowledge typically leads to the different ILAR groups being analysed as discrete entities and reducing the overall power of genetic association studies.
Objectives: The aim of this study was to conduct a large case-control association study on susceptibility to JIA to identify novel susceptibility loci and to investigate differences of these associations between the ILAR groups.
Methods: JIA participants were genotyped on the Illumina Infinium CoreExome or OmniExpress arrays at The University of Manchester. UK population control genotype data was obtained from the Understanding Society Longitudinal Study. Quality control of data was performed conforming to conventional standards based on call rate, cryptic relatedness and ancestry outliers. Imputation was performed using the Haplotype Reference Consortium panel on the Michigan Imputation Server followed by exclusion of SNPs with low imputation accuracy ($r^2 < 0.5$) and low minor allele frequency (< 1%). Association testing of all SNPs was performed with an additive model incorporating imputation uncertainty using SNPTEST. A subset of SNPs independently associated with all JIA (p-value < $5x10^{-6}$) were tested to evaluate if they were specific to a particular ILAR group or shared across multiple ILAR groups using Bayesian multinomial regression and model selection methods implemented in the Trinculo software package.
Results: Following quality control the dataset consisted of > 7.4 million SNPs for 3305 JIA cases and 9196 controls. Association testing in a combined dataset of all ILAR groups identified seven SNPs associated at genome-wide significance ($5x10^{-8}$); six of these have previously been reported for JIA while one is a novel association. The novel association (rs497523, p-value = $7.12x10^{-9}$, OR 0.85, 95% CI 0.8:0.9) maps to chromosome 16p11 and is located within intron one of the *CCDC101* gene. In a subset of 44 independently associated SNPs we found no strong evidence to support association of any SNP to a specific ILAR group with the majority of the SNPs showing evidence for sharing across multiple groups.
Conclusion: In the largest case control association study for susceptibility to JIA performed to date, we identified a novel association to a SNP in the intron of *CCDC101.* This gene is involved in transcriptional regulation through histone acetyltransferase. *CCDC101* may be the causal gene at this locus; however introns contain enhancer elements that regulate other genes in the transcriptional domain. Therefore fine mapping with the integration of genomic data is currently being performed for this locus. The results provide little evidence to support ILAR subgroup specificity for any of the associated variants; on the contrary the results support a general model of sharing across multiple groups. The combined analysis of data across subgroups, informed by model sharing, will maximise power to identify novel associations.
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OP0190 META-ANALYSIS OF IMMUNOCHIP DATA OF FOUR AUTOIMMUNE DISEASES REVEALS NOVEL SINGLE-DISEASE AND CROSS-PHENOTYPE ASSOCIATIONS

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Background: In recent years, research has consistently proven the occurrence of genetic overlap across autoimmune diseases, which supports the existence of common pathogenic mechanisms in autoimmunity.
Objectives: The objective of this study was to further investigate this shared genetic component.
Methods: We performed a cross-disease meta-analysis of Immunochip data from 37,159 patients diagnosed with a seropositive autoimmune disease (11,489 celiac disease (CeD), 15,523 rheumatoid arthritis (RA), 3,477 systemic sclerosis (SSc), and 6,670 type 1 diabetes (T1D)) and 22,308 healthy controls of European origin using the R package ASSET.
Results: We identified 38 risk variants shared by at least two of the conditions analyzed, five of which represent new pleiotropic loci in autoimmunity. We also identified six novel genome-wide associations for the diseases studied. Cell-specific functional annotations and biological pathway enrichment analyses suggested that pleiotropic variants may deregulate gene expression in different subsets of T cells, especially Th17 and regulatory T cells. Finally, drug repositioning analysis evidenced several drugs that could represent promising candidates for CeD, RA, SSc and T1D treatment.
Conclusion: We have been able to advance in the knowledge of the genetic overlap existing in autoimmunity, thus shedding light on common molecular mechanisms of disease and suggesting novel drug targets that could be explored for the treatment of the autoimmune diseases studied.

REFERENCES:

[1] Richard-Miceli C, Criswell LA. Emerging patterns of genetic overlap across autoimmune disorders. Genome Med. 2012;4(1):6.
[2] Bhattacharjee S, Rajaraman P, Jacobs KB, et al. A subset-based approach improves power and interpretation for the combined analysis of genetic association studies of heterogeneous traits. Am J Hum Genet. 2012;90(5):821-35

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OP0191

EPIGENETIC PROFILING OF SYNOVIAL FIBROBLASTS REVEALS STRUCTURAL DNA DYNAMICS AT DISEASE IMPLICATED CHROMOSOME REGIONS

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Background: One of the more striking findings from genome-wide association studies (GWAS) is how the majority of disease associated genetic variants are found within gene regulatory regions, known as enhancers. It is now well established that these enhancers regulate target genes through physical interactions. We, and others, have shown that these interactions can vary between cell types and act over long distances. Therefore, if we are to fully translate GWAS findings, we need link disease associated enhancers to their target genes, in the relevant cell types. So far we only have a limited picture in rheumatoid arthritis (RA) relevant cell types, since synovial fibroblasts (SF) have been omitted from this type of chromatin interaction analysis.
Objectives: Investigate dynamic Hi-C interactions in unstimulated and stimulated SF, mapping RA enhancers to their target genes, and correlating with gene expression.
Methods: We cultured SF from synovial tissues of RA patients. After stimulation of the SF (n=6) with 10 ng/ul TNF for 24h, Hi-C and RNA libraries were generated and sequenced on the Illumina HiSeq 4000. We called dynamic active and inactive regions of the genome (A/B compartments), mapped on RA associated enhancers, linked these to target genes and correlated the interactions with dynamic expression.
Results: We found a region on the chromosome 6q23, intergenic between *OLIG3* and *TNFAIP3*, with an enhancer containing SNPs associated with RA to be dynamically linked to the *TNFAIP3* gene through DNA activity, interactions and corresponding gene expression.
As shown in figure 1a, the genomic region containing the RA associated variants (red square) only resides in an open, active region of DNA (black bar, compartment A) upon TNF-stimulation of the SF. This region then makes a strong interaction with the promoter of *TNFAIP3* (figure 1a) in stimulated cells, which corresponds to a more than 100-fold increase in *TNFAIP3* gene expression (figure 1b).
Conclusion: Using independent data, we have indicated how the RA region on 6q23 could influence the expression of *TNFAIP3*, under stimulatory conditions in SF cells. This supports previous work, where this particular 6q23 enhancer is preferentially active in RA synovium, compared to osteoarthritis, reflecting the different stimulatory conditions in each disease (Ai *et al. 2018*). We have successfully linked an RA associated enhancer to its target gene in SF, indicating how the enhancer works over a large distance to interact with and regulate the *TNFAIP3* gene. Furthermore we show that this enhancer containing RA associated SNPs is only active upon stimulation with TNF in SF.

REFERENCE:

[1] Ai R, et al. Nat Commun. 2018 May 15;9(1):1921

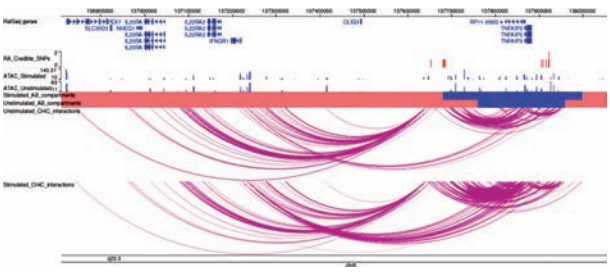


Figure 1a

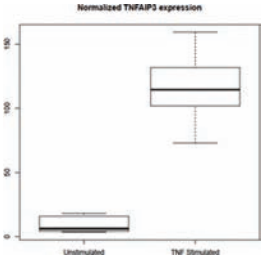


Figure 1b

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OP0192

DISSECTING THE LONG-RANGE GENE REGULATION OF RHEUMATOID ARTHRITISRISK ENHANCERS AT THE 5Q11 LOCUS USING THE COMPLEMENTARY APPROACHES OF CRISPRA AND CRISPRI

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Background: Large-scale genome wide association studies (GWAS) in rheumatoid arthritis (RA) have revealed that the majority of associated risk variants lie in non-coding regions of the genome. For RA it has been demonstrated that risk variants are significantly enriched in T cell specific enhancers. One such susceptibility locus known as 5q11 is the third strongest association with RA. At this locus the lead risk variants lie in two distinct active enhancer elements intronic to the *ANKRD55* gene. Previous work using chromatin conformation has shown these enhancers make physical contact with the promoter of *IL6ST*, 150 kb away on the linear chromosome[1]. Whilst *ANKRD55* is a gene of unknown function, *IL6ST* is part of the IL6R complex which regulates the IL6 signalling pathway. Tocilizumab is already an approved drug for RA, which works against the IL6R. CRISPR is an ideal tool to dissect this enhancer-gene relationship to provide us with empirical evidence that the intronic enhancer within *ANKRD55* regulates the expression of *IL6ST*. Understanding how RA risk genetic background affects gene regulation will give us a better understanding of the underlying biology of the disease and can ultimately be used to help repurpose or discover novel drug therapies.
Objectives: To use CRISPR interference (CRISPRi) and CRISPR activation (CRISPRa) to perturb the ANKRD55 intronic enhancer and measure the downstream effect on the expression of *IL31RA, IL6ST, ANKRD55*).
Methods: We used dead (dCas9) a modified CRISPR Cas9 enzyme that is catalytically inactive, that precisely targets DNA, but does not cut. Instead, effector molecules are fused to the dCas9 (VP64 for activation and KRAB for repression) to alter the transcription of the targeted genes.Two lead functional risk SNPs at the 5q11 risk locus rs10065637 and rs7731626 (R^2 = 0.4472) lie in two distinct enhancer elements separated by 5.5kb. We designed 4 guides across each enhancer, and transduced a T cell line (Jurkat) using lentiviral delivery; first dCas9-KRAB and dCas9-VP64 and subsequently the pool of guides for each enhancer alongside controls. We cultured the cells until confluent and then sorted the top 60% expression of BFP-GFP (KRAB) or MCherry-GFP (VP64). RNA was extracted and then a qPCR was performed (Quantstudio) for *IL31RA*, *IL6ST* and *ANKRD55*.
Results: In the CRISPRa Jurkat cells the guides targeted to both SNP containing enhancers significantly increased the expression of *ANKRD55*: rs7731626 (p=<0.0001) and rs6859219 (p=0.0003) respectively. They also increased the expression of *IL6ST* rs7731626 (p 0.0023) and rs6859219 (p= 0.01). In CRISPRi Jurkat cells the guides targeted to both SNP containing enhancers significantly decreased the expression of *ANKRD55*: rs7731626 (p=<0.001) and rs6859219 p=(0.0071). When guides were simultaneously used for both enhancers rs6859219+rs7731626 there was also a significant decrease in expression of *ANKRD55*. (p=<0.0001). Only the pool guides against both enhancers significantly decreased the expression of *IL6ST* (p=<0.0001). In both systems no significant effect was seen on the expression of *IL31RA* **(Figure 1).**

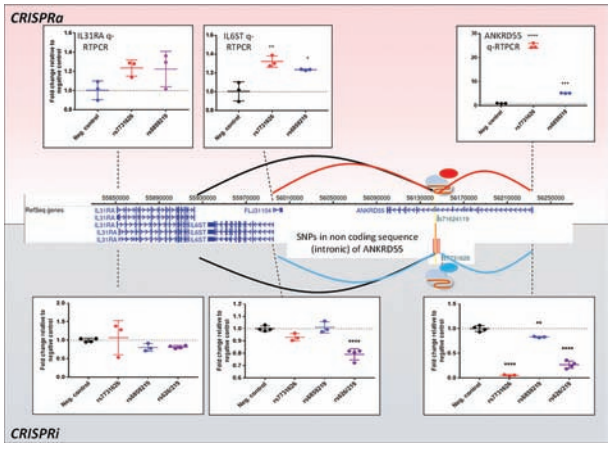


Figure 1

Conclusion: Results from CRISPRi and CRISPRa are concordant and support the idea that intronic enhancers within *ANKRD55*, containing SNPs associated with RA susceptibility, can regulate the expression of both *ANKRD55* and also modulate long range gene regulation with *IL6ST* to influence disease risk. These techniques are crucial to begin to dissect and translate GWAS findings.

REFERENCE:

[1] Capture Hi-C reveals novel candidate genes and complex long-range interactions.

Disclosure of Interests: None declared

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OP0193 CAMP RESPONSE ELEMENT MODULATOR (CREM)A INDUCES DUAL SPECIFICITY PROTEIN PHOSPHATASE (DUSP)4 THROUGH EPIGENETIC REMODELING, PROMOTING IL-17A AND REDUCING IL-2 EXPRESSION IN T CELLS

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Background: Tissue inflammation and organ damage in systemic lupus erythematosus (SLE) have been linked to effector T cells that are characterized by increased IL-17A and reduced IL-2 production(1). T cells from patients with SLE express increased levels of the transcription factor cAMP response element modulator (CREM)α that contributes to altered cytokine expression(1-3). However, the exact molecular events contributing to dysregulated IL-17A and IL-2 expression are incompletely understood.

Objectives: To investigate molecular events that promote effector T cells in health and disease. The definition of molecular regulators of effector T cell generation and activity may deliver new biomarkers and potential therapeutic targets in disorders characterized by altered effector T cell function, including (but not limited to) SLE.

Methods: Using CRISPR/Cas9 genome editing and lentiviral transduction, we generated CREMα deficient or overexpressing Jurkat T cells. Gene expression profiles in Jurkat and primary human CD4+ T cells were assessed by qRT-PCR and mRNA probe-based hybridization techniques. Gene regulation events were investigated using luciferase reporter assays (*trans*-activation) and ChIP. Interactions between CREMα and the transcriptional co-activator p300 were assessed using proximity ligation assays and p300 knock-down with siRNAs.

Results: We link CREMα production in effector $CD4^+$ T cells with increased expression of dual specificity protein phosphatase (DUSP)4. Using genetically modified Jurkat T cells, we demonstrate that CREMα induces DUSP4 through recruitment of the transcriptional co-activator p300 and histone H3K18 acetylation. Using DUSP4 transfection models and genetically modified Jurkat T cells, we support previous reports suggesting that DUSP4 induces IL-17A while limiting IL-2 expression. Furthermore, we demonstrate that $CD4^+$ T cells from patients with juvenile-onset SLE share the phenotype with CREMα over-expressing $CD4^+$ T cells with increased DUSP4 expression that contributes to imbalanced IL-17A and IL-2 production.

Conclusion: Collectively, our results deliver previously unknown CREMα-mediated molecular mechanisms promoting effector T cells and support the central involvement of CREMα in the pathophysiology of SLE. CREMα and DUSP4 may prove valuable as disease biomarkers and/or targets in the search for individualized and target-directed treatments.

REFERENCES:

[1] SLE-Associated Defects Promote Altered T Cell Function. Crispin JC, Hedrich CM, *et al*. Crit Rev Immunol. 2017;37(1):39-58.

[2] cAMP responsive element modulator: a critical regulator of cytokine production. Rauen T, Hedrich CM, *et al*. Trends Mol Med. 2013 Apr;19 (4):262-9.

[3] cAMP response element modulator α controls IL2 and IL17A expression during CD4 lineage commitment and subset distribution in lupus. Hedrich CM, Crispin JC, *et al*. Proc Natl Acad Sci U S A. 2012 Oct 9;109 (41):16606-11.

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OP0194 HISTONE DEACETYLASE 1 (HDAC1): A KEY MEDIATOR OF T CELLS FOR THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

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Background: Despite enormous efforts to develop new therapeutic strategies for treatment of rheumatoid arthritis (RA), the large number of non responding patients to currently available drugs underlies the unmet need to identify new therapeutic targets. Certain $CD4^+$T cell subsets, especially those polarized toward the T helper (Th) subsets Th1 andTh17, have been shown to be major drivers of inflammation in patients with RA. The expression of their key transcription factors is controlled by histone modifications which includes acetylation of *lysine residues* mediated by histone deacetylases (HDAC). Indeed, pan HDAC inhibitors have been shown to be a potential therapeutic strategy. However, major side effects limited the clinical use and underline the need of more specific HDAC inhibitors.

Objectives: We addressed the individual role of HDAC1 on the development of collagen-induced arthritis model (CIA), which partially reflects human RA.

Methods: Mice with a T cell specific deletion of HDAC1 (HDAC1 cKO) were generated by using the CD4Cre/LoxP system. At week 8 of age arthritis was induced in wild type (WT) and HDAC1 cKO mice by immunizing with chicken collagen II (CII), emulsified in complete Freund´s adjuvant. After 21 days mice received a booster injection of CII. The animals were 3 times per week scored for paw swelling and grip strength. Anti-CII antibody levels were determined by ELISA. Various cell subsets, including Th cells, where detected in the blood, the spleen and the draining lymph node by FACS analysis. To test antigen-specific T cell activation we performed in vitro restimulation of spleen and lymph node cells with collagen II followed by assessment of cytokine production and quantification of the proliferation rate using 3Hthymidine incorporation.

After 4 and after 10 weeks mice were sacrificed and paraffin sections of the affected joints were analyzed for histomorphologic signs of inflammation, cartilage and bone destruction.

Results: Eighty percent of the animals developed serum anti-CII anibodies (IgM and IgG) whereby the antibody levels were a day 21 of disease similar between the HDAC1 cKO and the WT mice. Furthermore, no differences in the production of antibody subclasses, especially of pathogenic IgG2c antibodies, were observed. Enhanced percentages of Th1 and Th17 cells among HDAC1-null $CD4^+$T cells were detected after immunization in the HDAC1 cKO mice. Nonetheless and unexpectedly, these mice did not develop any signs of disease at the clinical level while WT mice developed pronounced paw swelling and loss of grip strength. In accordance with the clinical data, histological analysis revealed no signs of inflammation, no bone erosion and no appearance of osteoclasts in the joints of HDAC1 cKO mice. This appeared to be mainly caused by an impaired migratory capacity of HDAC1 cKO $CD4^+$ T cells, so that they were unable to invade the joints.

Conclusion: Our data show the importance of HDAC1 as a key immune regulator in the pathogenesis of T cell driven collagen induced arthritis. Therefore it might be considered as an interesting novel therapeutic target in RA.

Disclosure of Interests: None declared

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OP0195 SELECTIVE EXPANSION OF REGULATORY T-CELLS IN HUMANS BY A NOVEL IL-2 CONJUGATE T-REG STIMULATOR, NKTR-358, BEING DEVELOPED FOR THE TREATMENT OF AUTOIMMUNE DISEASES

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Background: Impaired IL-2 production and dysfunction of regulatory T cells (Tregs) have been identified as key immunological defects leading to the

breakdown of immune self-tolerance, a causative mechanism implicated in multiple autoimmune diseases. Enhanced sensitivity of Tregs to IL-2 supports the use of low-dose IL-2 therapy; however, this treatment is limited by its short half-life and relatively poor selectivity for stimulation of Tregs versus other T cell types. NKTR-358 is a polyethylene glycol (PEG) conjugate of recombinant human IL-2 (aldesleukin sequence with no additional amino acid mutation or substitution). It is differentiated from native IL-2 by its prolonged biological activity as well as its marked and selective stimulation of Tregs in different animal species, including non-human primates.

Objectives: Study objectives assessed the safety and tolerability of NKTR-358 in humans administered single ascending doses subcutaneously (SC). In addition, time course and extent of changes in the numbers and percentages of Tregs, conventional CD4+ and CD8+ T cells, NK cells, cytokine levels, and the pharmacokinetics (PK) of NKTR-358 in peripheral blood were investigated.

Methods: In this first-in-human, double-blind, single ascending dose study, healthy volunteers received SC doses ranging from 0.3 to 28 ug/kg (9 active:3 placebo per cohort) and subjects were followed for 50 days.

Results: All 8 planned cohorts completed dosing. There were no dose-limiting toxicities, serious adverse events, deaths, or clinically significant abnormalities in vital signs, electrocardiograms, or laboratory test values. Adverse events attributed to NKTR-358 were primarily limited to mild (grade 1) injection site reactions. One subject at the highest dose tested demonstrated transient and mild (grade 1) symptoms of elevated cytokine levels and lymphopenia, which resolved without treatment. No other individual at any dose level had systemic signs or symptoms known to be associated with IL-2 therapy. The first 6 cohorts have been tested for anti-drug antibodies to date and none have been detected. NKTR-358 reached maximum plasma levels 4-6 days after administration, with little change for ~2 weeks, and then decreased with a half-life of ~ 8-9 days. NKTR-358 exhibited linear PK above the 1.0 ug/kg dose.

The primary effect of NKTR 358 was seen on Tregs. In the 3.0 to 28.0 ug/kg dose cohorts, a dose-dependent and sustained increase in the absolute numbers and percentages of circulating CD4+FoxP3+CD25bright Tregs were observed. The elevated levels peaked at Days 10-12 and did not return to baseline until ~ 20 to 25 days following administration. At 28.0 ug/kg, the mean peak increase in numbers of these CD25bright Tregs was 17-fold above baseline, and the mean peak percentage increased from 0.5% to 7.4%. In addition, there was an increase in Treg activation markers at doses $\geq$13.5 ug/kg. There was a mean increase of 3.5-fold in the percentages and numbers of NK cells at the highest dose tested, but no changes in percentages or numbers of conventional CD4+ or CD8+ T cells were observed. NKTR-358 selectively induced Tregs, evidenced by a 15-fold increase in the mean peak Treg:CD8 ratio over baseline in the 28.0 ug/kg group.

Conclusion: Single doses of the IL-2 conjugate T-reg stimulator, NKTR-358, in the dose range tested were well tolerated and safe. NKTR-358 led to a striking and selective dose-dependent increase in circulating CD25bright Tregs with minimal effects on conventional T cells and with relatively small effects on NK cells. These clinical results extend previous animal studies showing the prolonged and Treg selective action of NKTR-358, and provide strong support for testing NKTR-358 as a new therapeutic in autoimmune diseases, such as systemic lupus.

Disclosure of Interests: Christie Fanton Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Suresh Siddhanti Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Neha Dixit Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Lin Lu Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Toufigh Gordi Shareholder of: Nektar Therapeutics, Consultant for: Rosa & Co LLC, Employee of: Nektar Therapeutics, Daniel Dickerson Speakers bureau: Last speaking engagement was 2013, Jonathan Zalevsky Shareholder of: Nektar Therapeutics, Employee of: Nektar Therapeutics, Brian Kotzin Shareholder of: Nektar Therapeutics, Gilead Sciences, Amgen, Rigel Pharmaceuticals, Consultant for: Nektar Therapeutics, Employee of: Nektar Therapeutics

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OP0196

IMBALANCE BETWEEN MEMORY TH1 AND TH1-TREG CELLS DEPENDS ON DIFFERENTIAL REGULATION OF CELL METABOLISM IN PATIENTS WITH SLE

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Background: T helper 1 (Th1) cells play an important role in Systemic Lupus Erythematosus (SLE). However, which abnormalities generated in Th1 cells may be related to the pathogenesis of SLE remains elusive. “Immunometabolism” has recently attracted much attention. We previously reported that both IFN-γ and T-bet positively regulated aerobic glycolysis, leading to activation of Th1 cells in mice (**REF1**). This suggests a potentially important role for metabolic reprograming in human Th1 cells and the pathogenesis of SLE which requires further investigation.

Objectives: In this study, we assessed the abnormality of metabolism in Th1 cells in patients with SLE. In addition, we investigated which abnormalities of Th1 cells are generated via metabolic reprograming in vitro.

Methods: Peripheral blood mononuclear cells (PBMCs) were obtained from 31 age-matched healthy donors (HDs) and 60 patients with SLE. Th1- and metabolism-related markers in $CD4^+$ T cells were measured by flow cytometry. In addition, the correlation of these markers with clinical characteristics was investigated. Next, $CD4^+CD45RA^-$ cells were purified from peripheral of HDs, and the effect of mTORC1 inhibitor Rapamycin (Rapa) or glycolysis inhibitor 2DG on characteristic changes in Th1 cells were assessed in vitro.

Results: Baseline characteristics of patients with SLE were males: females=5:55, age 41.1 years, disease duration 142.3 months, SLEDAI 11.5 and BILAG 12.9 at the timing of admission due to exacerbation of SLE. Activated effector memory $CD4^+$T-bet^{hi} cells in patients with SLE were higher than HCs. The $CD4^+$T-bet^{hi} cells had high potential for IFN-γ production. mTORC1 acts as a regulator of cell growth through the phosphorylation of substrates that potentiate anabolic processes such as aerobic glycolysis. The $CD4^+$T-bet^{hi} cells highly expressed p-mTORC1, and this was closely related to treatment-resistance, but not disease activity and autoantibodies such as anti ds-DNA Abs (Treatment resistance was defined as refractory to >3 kinds of immunosupressants and/or 2> re-increase to high dose corticosteroid). Therefore, we examined the effect of Rapa or 2DG to such memory mTORC1$^+$T-bet$^+$IFNγ^+CD4$^+$ cells in vitro. When $CD45RA^-CD4^+$ cells were isolated from peripheral blood of HDs and stimulated with anti-CD3/CD28 Abs, T-bet expression and IFN-γ production as well as p-mTOC1 expression and glycolysis were induced. Interestingly, 2DG, but not Rapa, suppressed IFN-γ production and, in contrast, enhanced IL-2 production. Therefore, we hypothesized that 2DG induced Th1-Treg cells, reported as one of Treg cell subsets (**REF2**). 2DG induced FoxP3^{hi}T-bet$^+$IFN-γ^- (Th1-Treg like) cells and suppressed FoxP3$^-$T-bet$^+$IFN-γ^+ (Th1 like) cells. Meanwhile, Rapa induced FoxP3^{int}T-bet$^+$IFN-γ^+ (non-Treg like) cells and did not affect to FoxP3$^-$T-bet$^+$IFN-γ^+ (Th1 like) cells. Finally, we examined the involvement of Th1-Treg cells to the pathogenesis of SLE. $CD45RA^-$FoxP3^{int}IFN-γ^+ (non-Treg) cells as well as T-bet^{hi} (Th1 like) cells were increased, whereas $CD45RA^-$FoxP3^{hi}CXCR3$^+$T-bet^{hi} (Th1-Treg) cells were decreased in SLE.

Conclusion: These results indicate that activated effector memory Th1 cells were increased while memory Th1-Treg cells were decreased in patients with SLE. Importantly, metabolic modulators redressing the imbalance of helper T subsets have potential as a new therapeutic strategy.

REFERENCES:

[1] Iwata S, et al. Immunity. 2017;46:983-91.
[2] Levine AG, et al. Nature. 2017;546:421-25.

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THURSDAY, 13 JUNE 2019

Can imaging improve outcome in OA?

OP0197 EVALUATING THE RELATION OF STRUCTURAL DAMAGE BY MRI TO CLINICAL PAIN SCORES, PAIN SENSITISATION AND TYPE II COLLAGEN DEGRADATION IN KNEE OSTEOARTHRITIS

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Background: The evolution of pain in relation to damage in the synovium, bone and cartilage in osteoarthritis (OA), coupled with their relation to wet biochemical markers are not well understood.
Objectives: In this study we evaluated the relation between structural damage by MRI, clinical and pain sensitisation measures and wet biochemical biomarkers in knee OA.
Methods: We recruited 130 participants fulfilling ACR criteria with advanced OA requiring total knee replacement (TKR) (n=80), mild OA having standard care (n=42) and non-OA controls (n=8). Knee MRI in 90 subjects (72 F, 18 M) was acquired and assessed by two radiologists with the MRI Knee Osteoarthritis Score (MOAKS). Overall MOAKS scores were created for Bone Marrow Lesions (BML), Cartilage Degradation (CD) and effusion/Hoffa synovitis (tSyn). Type II collagen cleavage products (CTX-II) were determined by ELISA. Clinical scoring was performed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for pain levels (WOMAC_P), Hospital Anxiety and Depression Scale (HADS), Body mass index (BMI) and pain sensitisation with pain pressure thresholds (PPT) of the patella by Quantitative Sensory Testing (QST).
Results: The mild OA group had a mean age of 63 +/-9 yr and the advanced OA group 69 +/- 9 yr. The advanced OA group had higher levels of pain, with a mean WOMAC_P of 58 +/- 22 compared with the mild OA group who had a mean WOMAC_P of 40 +/-22. WOMAC_P correlated with the total number of regions with cartilage damage (nCD) (R=0.225, p=0.033) and total number of BMLs (nBML) (R=0.195, p=0.065) using BMI, age and HADS as covariates. Levels of CTX-II correlated with tSyn (R=0.313, p=0.03), nBML (R=0.252, p=0.019), number of osteophytes (R=0.33, p=0.002) and nCD (R=0.218, p=0.042), using BMI and age as covariates. The correlation for urinary CTX-II with tSyn (p=0.006) is shown in Figure 1 using a partial linear regression analysis of MOAKS, BMI and age. We also found CTX-II correlated with lesion load scores (total number of lesions multiplied by MOAKS size by% damage scores) for CD (R=0.277, p=0.009) and BML (r=0.308, p=0.004). PPT correlated with patella MOAKS scores for nBML (R=-0.221, p=0.038) and nCD (R=-0.279, p=0.009), with HADS, BMI and age as covariates.
Conclusion: There is a direct correlation between the degree of cartilage damage and BMLs with pain in OA. Type II collagen degradation products were higher when there was more severe MRI-detected synovitis, BMLs and cartilage damage in the knee joint, suggesting that the source of enzymes degrading type II collagen in OA, including matrix metalloproteinases, are also likely to be produced by synovium and bone (1) and not just cartilage, as previously hypothesised in other studies. There was also a correlation between pain sensitisation and frequency of BMLs and cartilage degradation, suggesting that molecular mediators of pain sensitisation, which we have shown are produced by BMLs (1), are a cause of patient-reported OA pain.

REFERENCES:

[1] Kuttapitya, et al. Annals Rheumatic Diseases, 2017; 76(10): 1764-73

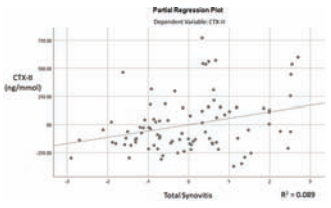


Figure 1

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OP0198 MRI-DETECTED STRUCTURAL ABNORMALITIES AND DEVELOPMENT OF INCIDENT RADIOGRAPHIC KNEE OSTEOARTHRITIS OVER 10 YEARS OF FOLLOW-UP

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Background: Structural joint pathology on MRI has been found in knees without radiographic evidence of osteoarthritis (OA). We have previously shown that structural abnormalities on MRI may be precursors of disease and associated with the detection of incident radiographic knee OA (ROA) up to 2 years later, and in some circumstances up to seven years later. The prognostic value of structural abnormalities on MRI for knee OA, however, is unknown.
Objectives: Estimate the probability of incident ROA over 10 years of follow-up, according to structural abnormalities detected on baseline MRIs.
Methods: A subcohort of participants (862 knees, one knee/person) from the Osteoarthritis Initiative (OAI) with at least one knee at risk of developing ROA (i.e., Kellgren-Lawrence (KL) 0,1 at baseline) was randomly selected. MRI-detected structural features of the knee were assessed by expert readers using the MRI Osteoarthritis Knee Score (MOAKS). Participants underwent bilateral posteroanterior fixed-flexion weight-bearing knee radiography at baseline and annually through year 4, and then every two years until year 10. Radiographs were centrally read for KL grade, with ROA defined as KL$\geq$2. Survival was estimated with the Turnbull non-parametric maximum likelihood estimator, a generalization of Kaplan Meier curves for interval censored data. Survival curves were compared using a log rank permutation test available in the R package interval. Hazard ratios were estimated using Cox models fit using the R package icenReg, designed for interval censored data. Features were considered one at a time, with no adjustments.
Results: Knees with any of the following structural abnormalities had higher estimated probabilities for the development of radiographic OA within two, four and 10 years of follow-up: effusion-synovitis, Hoffa-synovitis, bone marrow lesions in the medial compartment and whole knee, surface area and full thickness cartilage damage in the medial compartment and whole knee, and medial meniscal extrusion (Table 1). Differences in the probability for the development of ROA within two, four, and 10 years of follow-up were significant (pointwise 95% confidence intervals did not include 0), between knees without the abnormality and knees in the most severe category for all features, with one exception at the two-year follow-up. All of these abnormalities were significantly associated with time to ROA over 10 years of follow-up.

Table 1. Baseline MRI-Detected Structural Abnormalities and Incident Radiographic Osteoarthritis

MRI-detected abnormalities at baseline	Knees	Estimated Probability of Radiographic OA			P value*	Hazard Ratio	(95% CI)
		Within 2 years	Within 4 years	Within 10 years			
Effusion-Synovitis					<.0001		
Physiologic amount	692	0.06	0.10	0.27		1.00	ref
Small	146	0.15	0.31	0.46		2.11	(1.81, 2.46)
Medium/Large	24	0.48	0.62	0.67		5.10	(3.55, 7.34)
Hoffa-Synovitis					<.0001		
Normal	593	0.05	0.11	0.25		1.00	ref
Mild	248	0.16	0.24	0.44		1.97	(1.72, 2.26)
Moderate/Severe	21	0.43	0.43	0.54		4.09	(2.75, 6.07)
BML, Medial Max Score					<.0001		
0: none	733	0.08	0.13	0.27		1.00	ref
1: <33%	110	0.12	0.19	0.49		1.82	(1.54, 2.15)
2/3: >=33%	19	0.39	0.57	0.59		3.82	(2.49, 5.86)
BML, Whole knee Max Score					<.0001		
0: none	339	0.06	0.10	0.21		1.00	ref
1: <33%	333	0.08	0.13	0.33		1.43	(1.22, 1.67)
2: 33-66%	143	0.14	0.25	0.43		2.14	(1.78, 2.57)
3: >66%	47	0.24	0.41	0.56		3.25	(2.49, 4.24)
Cartilage Damage, Surface Area, Medial Max Score					<.0001		
0: none	558	0.08	0.12	0.23		1.00	ref
1: <10%	146	0.05	0.12	0.36		1.63	(1.38, 1.94)
2: 10-75%	158	0.19	0.28	0.56		2.85	(2.45, 3.32)
Cartilage Damage, Full Thickness, Medial Max Score					<.0001		
0: none	834	0.09	0.15	0.30		1.00	ref
1/2: Any	48	0.18	0.35	0.57		2.70	(2.17, 3.36)
Cartilage Damage, Surface Area, Whole Knee Max Score					<.0001		
0: none	148	0.04	0.06	0.13		1.00	ref
1: <10%	235	0.03	0.06	0.16		1.41	(1.05, 1.90)
2: 10-75%	454	0.13	0.21	0.43		3.67	(2.81, 4.80)
3: >75%	27	0.43	0.43	0.66		8.66	(5.40, 13.86)
Cartilage Damage, Full Thickness, Whole Knee Max Score					<.0001		
0: none	574	0.07	0.11	0.25		1.00	ref
1: <10%	167	0.11	0.20	0.39		1.73	(1.47, 2.02)
2/3: >10%	121	0.18	0.28	0.52		2.43	(2.04, 2.90)
Meniscus Extrusion, Medial					<.0001		
0: <2 mm	677	0.06	0.12	0.24		1.00	ref
1: 2-2.9 mm	141	0.19	0.32	0.55		2.51	(2.15, 2.92)
2/3: >3 mm	44	0.20	0.25	0.55		2.88	(2.27, 3.66)

* Asymptotic Logrank k-sample test (permutation form), Sun's scores

Conclusion: Our results demonstrate the prognostic value of effusion-synovitis, Hoffa-synovitis, bone marrow lesions, cartilage damage, and meniscal extrusion

for the development of ROA up to 10 years later. Future directions include developing a predictive model that incorporates multiple features.

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THURSDAY, 13 JUNE 2019

Different pathophysiological pathways in axial and peripheral disease: Peripheral and axial spondyloarthritis: to split or to lump?

OP0199 THE HUMAN ENTHESIS HARBOURS RESIDENT ADAPTIVE CD4+ AND CD8+ T-CELLS WITH INDUCIBLE IL-17A AND TNF PROTEIN THAT IS PHARMACOLOGICALLY SUPPRESSED BY RORγT AND PDE4 INHIBITORS BUT NOT METHOTREXATE IN A NOVEL IN VITRO ENTHESITIS MODEL

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Background: Animal models have demonstrated that enthesitis is the primary lesion in experimental spondyloarthritis (SpA). In mice, innate lymphocytes were suggested as the major cytokine producers at the enthesis.

Objectives: We tested the hypothesis that the human enthesis harbours tissue resident conventional T-cells. We also assessed their ability to express SpA-related cytokines including TNF and IL-17A and if this could be blocked using psoriasis therapeutic agents (methotrexate (MTX), and phosphodiesterase type 4 inhibitor (PDE4i)) and experimental RORγt inhibitors (RORγti).

Methods: Entheseal spinous process was obtained from patients undergoing elective orthopedic procedures (n=20) and mechanically digested or processed for confocal staining and flow cytometry. CD4+ and CD8+ T-cells were sorted and RNA was isolated and analysed by qPCR. Magnetically isolated cells were stimulated using an anti-CD3/CD2/CD28 bead with and without the presence of MTX, RORγti and PDE4i. Following stimulation IL-17A and TNF were measured by ELISA and intracellular flow cytometry.

Results: CD4+ and CD8+ T-cells represent 35.7% and 23.7% of T-cells in the enthesis, respectively, with topographic confirmation by anti-CD3 immunofluorescence staining. Entheseal tissue contained a higher proportion of CD4+ and CD8 + T-cells expressing a resident memory phenotype (CD69+/CD45RA-) compared to matched blood. Sorted T-cells from entheseal tissue had a gene expression profile consistent with a tissue resident phenotype and CD4+ and CD8+ T-cells showed increased expression immunomodulatory genes including IL-10 and TGF-β compared to peripheral blood T-cells ($p<0.001$). Following stimulation CD4 + T-cells produced more TNF than CD8+ T-cells ($p<0.05$), IL-17A was robustly detected in CD4+ but not CD8+ T-cells. TNF and IL-17A production from CD4+ T-cells was effectively inhibited by PDE4i ($p<0.05$), while RORγti only reduced IL-17 secretion ($p<0.001$). MTX had no significant impact on both TNF and IL-17A production in either cell population. This pattern of inhibition was mirrored in TNF secretion from CD8+ T-cells.

Conclusion: This is the first description of conventional CD4+ and CD8+ enthesis resident T-cells. PDE4i was effective in abrogating induced TNF production and IL-17, whereas RORγti is highly effective for IL-17A production but not TNF. In contrast, MTX had little effect on *in vitro* enthesitis model cytokine production. These findings may have some practical implications in the treatment of subclinical enthesitis.

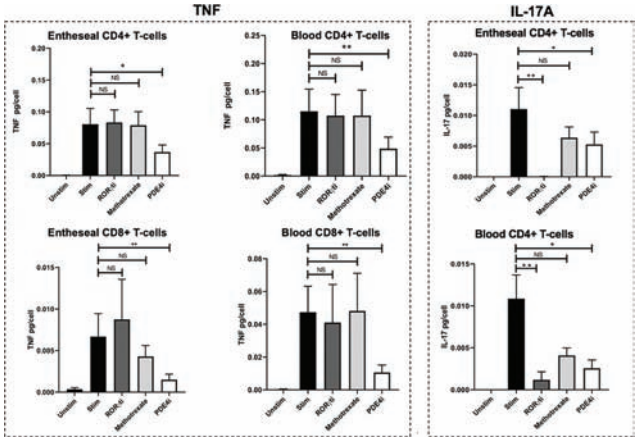
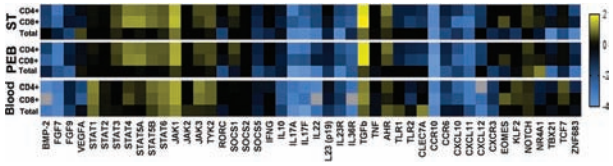


Figure 1. Effect of different therapeutic agents on the TNF and IL-17A production by resident entheseasl T -cells and matched peripheral blood

Figure 2. Gene expression profile of entheseal T-cells (soft tissue and adjacent bone) compared to peripheral blood



Abbreviations: ST, entheseal soft tissue; PEB, peri-entheseal bone.

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OP0200 A SET OF INFLAMMATORY MARKERS ALLOWING TO DETECT SYSTEMIC INFLAMMATION IN PSORIATIC SKIN, ENTHESEAL AND JOINT DISEASE IN THE ABSENCE OF CRP AND THEIR LINK TO CLINICAL DISEASE MANIFESTATION

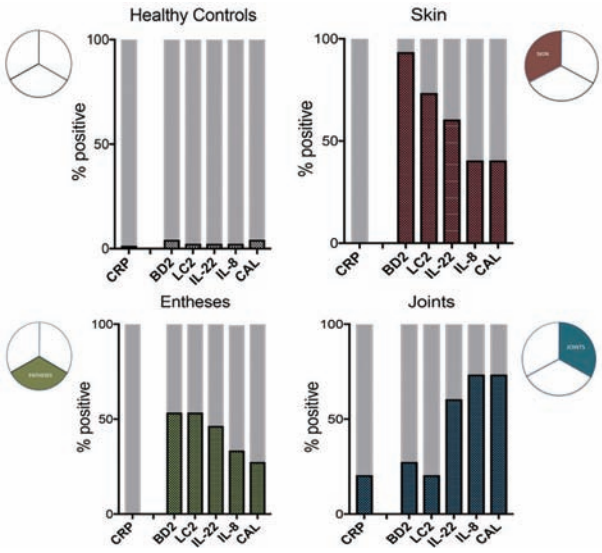
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Background: Psoriatic disease is composed of skin, entheseal and joint disease, which can manifest isolated or combined. Little is known about the systemic inflammation levels in psoriatic disease as a robust IL-6 signal is missing and therefore acute phase reactants such as C-reactive protein are often normal. Measuring systemic inflammation in the different manifestations of psoriatic disease is therefore a continuous unmet need.

Objectives: To better define systemic inflammation in patients with psoriatic disease limited to the skin (S), the entheses (E) or the joints (arthritis, A) or with a combination of these disease manifestations (SE, SA, EA, SEA).

Methods: Hypothesis-driven approach selecting markers that are (i) either targets of IL-23/IL-17 pathway activation (b-defensin 2, lipocalin 2, IL-22), (ii) associated with neutrophil/monocyte activation (calprotectin, IL-8) and (iii) achieve serum concentrations sufficient for reliable detection by standard ELISA. Parameters were assessed in 210 individuals comprising 105 healthy controls and 105 patients with psoriatic disease (each 15 for isolated (S, E, A) and composed disease manifestations SE, SA, EA, SEA). Results are expressed as percent positive patients with levels above three standard deviations over the mean level in healthy controls. In addition, 6-months sequential data on levels of these markers were collected in 20 patients treated with secukinumab or adalimumab to test treatment effects.

Results: CRP levels were normal in the majority of individuals. The respective percentages of patients with normal CRP (<5mg/L) were as follows: S: 100%, E: 100%, A: 80%, SE: 93%, SA: 67%, EA: 73%, SEA: 67% (Figure). Thus, CRP is only elevated in a subset of patients with arthritis. In sharp contrast, beta-defensin 2 levels (>1.88 ng/mL) and lipocalin-2 (>24.7 ng/mL) were elevated in the majority of patients with isolated skin and entheseal, but not joint disease. Conversely, elevations of calprotectin (>3.58 mig/mL) and IL-8 (>10.3 pg/mL) were found in the majority of patients with isolated joint disease. IL-22 was elevated (>17.1 pg/mL) in all three manifestations of psoriatic disease. Reflecting a combination of the findings the vast majority of patients with composed disease manifestation (SE, SA, EA, SEA) showed widespread marker elevation. IL-17 and TNF inhibition differentially lowered and partially normalized elevated markers of inflammation.



Conclusion: Systemic inflammation is detectable in the majority of patients with psoriatic disease, even if CRP is normal. The respective marker pattern depends on the manifestation (skin, entheses, joints) of psoriatic disease, with beta-defensin 2 and lipocalin-2 reflecting skin and entheseal disease, calprotectin and IL-8 joint disease and IL-22 a combination of these disease manifestations.

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My joints hurt and I'm overwhelmingly tired – fatigue in rheumatoid arthritis

OP0201 FATIGUE IN JUVENILE IDIOPATIC ARTHRITIS AFTER 18 YEARS OF FOLLOW-UP

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Background: Fatigue is common in adults with rheumatic disease and has also been shown in adolescents with juvenile idiopathic arthritis (JIA). Knowledge on fatigue in JIA in long-term follow-up is limited.

Objectives: To study the prevalence and severity of fatigue 18 years after onset of JIA.

Methods: In this close to population-based cohort study from defined geographical areas of Norway, Sweden, Denmark and Finland, consecutive cases of JIA with disease onset in 1997 to 2000 were prospectively enrolled (1). At 18-year follow-up, fatigue was measured using Fatigue Severity Scale (FSS, range 0-7) (2), and severe fatigue was defined as FSS $\geq$4. General health status was measured with Health Assessment Questionnaire (HAQ) and 36-Item Short Form Health Survey (SF-36). Reduced health was defined as HAQ >0, and SF-36 <40 (according to the physical component summary score/mental component summary score (PCS/MCS)). Pain was measured with 10 cm visual analogue scale (VAS), 0 = no pain, >0 = pain. Remission was defined according to the preliminary criteria described by Wallace. A Norwegian healthy cohort was used for comparison. Multivariable logistic regression analyses were performed.

Results: Among 434 eligible JIA participants 377 completed a Fatigue Severity Scale (FSS) measurement at the 18-year follow-up and were included. Of these 72% were girls, 53% had oligoarticular disease six months after onset, median age at onset was 5.6 (IQR 2.6-9.7) years, and age at the 18-year visit was 23.1 (IQR 20.3-27.2). Mean total FSS (±SD) was 3.2 (±1.5), and participants with active disease scored 3.6 (±1.6) compared to 2.9 (±1.4) for those in remission off medication. The highest total FSS was found in those with SF-36 PCS and/or MCS <40 (4.7 (±1.6) and 4.6 (±1.6), respectively). Severe fatigue was considerably more frequent in participants with active disease (36%, odds ratio (OR) 2.5) compared to those in remission off medication (19%), HAQ score >0 (47%, OR 4.1) compared to HAQ score =0 (18%), SF-36 PCS/MCS <40 (64/61%, OR 7.1/6.9) compared to SF-36 PCS/MCS $\geq$40 (20/19%), and VAS pain >0 (36%, OR 3.8) compared to VAS pain =0 (13%). The proportion of severe fatigue in a healthy Norwegian control cohort was 12%.

Conclusion: At 18-year follow-up fatigue was a prominent symptom in JIA, and we found consistently higher fatigue burden and considerably more severe fatigue among participants with active disease, pain and self-reported health problems, compared to those without. We suggest fatigue to be measured at long-term follow-up both in clinical and research settings.

REFERENCES:

[1] Nordal E, et al. Arthritis Rheum 2011;63:2809-18

[2] Krupp LB, et al. Arch Neurol 1989;46:1121-23

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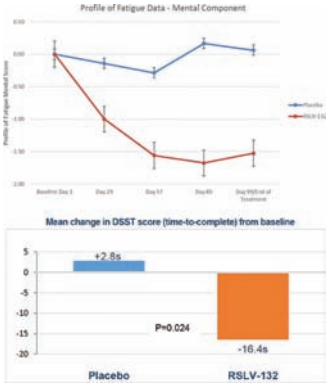
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OP0202

EFFECT OF RSLV-132 ON FATIGUE IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME – RESULTS OF A PHASE II RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PROOF OF CONCEPT STUDY

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Background: Fatigue is the key symptom that leads to poor health related quality of life and loss of work productivity in patients with primary Sjogren's syndrome (pSS). RSLV-132 is a first-in-class drug comprising RNase1 fused to the Fc region of IgG1. It is designed to increase serum RNase activity to digest RNA associated immune complexes, thereby reducing Toll-like receptor (TLR) activation and subsequent production of type 1 interferon (IFN), B-cell proliferation, and autoantibody production – mechanisms that are key to pSS pathogenesis. IFN pathway dysregulation has also been implicated in fatigue.
Objectives: To explore the clinical efficacy of RSLV-132 in improving patient-reported outcomes (PRO), particularly fatigue among patients with pSS.
Methods: PSS patients with positive anti-Ro and IFN gene expression signature were randomised 3:1 to RSLV-132 10 mg/kg IV or placebo (PBO) at weeks 0,1, 2, and then fortnightly until week 12. Use of hydroxycholoroquine, other immunomodulatory therapies or prednisolone > 10mg daily were not permitted. There was no minimum entry criteria for EULAR Sjogren's syndrome disease activity (ESSDAI) or EULAR Sjogren's syndrome patient reported index (ESSPRI). The primary endpoint was changes in gene or protein expression levels in blood indicative of reduced inflammation. Secondary endpoints, among others, included safety and tolerability, and changes in PRO between baseline and week 14 including ESSPRI, FACIT, Fatigue visual analogue score (0-100), Profile of fatigue (PRO-F (0-7)) and Neuropsychological tests.
Results: Thirty patients were randomised (RSLV=22, PBO=8). Baseline clinical and demographic characteristics were comparable between groups. Two subjects randomised to active drug withdrew from the study before dosing.
Among the patients receiving RSLV-132, the mental component of PRO-F improved by 1.53 points compared to worsening of 0.06 points in the PBO group (p=0.046). Consistently, there was a significant improvement in the RSLV-132 group in their Digital Symbol Substitution Test performance with a reduction of 16.4s in completing the test compared to an increase of 2.8s in the PBO group (p=0.024). The physical component of PRO-F improved by 0.8 points in the RSLV-132 group compared to improvement of 0.06 points in the PBO group (p=0.142). Similar trends were observed for ESSPRI and FACIT-F scores.



There was no drug effect on ESSDAI but the baseline median ESSDAI scores were low for both groups (RSLV=3 (IQR (0,11), PBO=5 (IQR (0,18)).
Treatment Emergent Adverse Events were reported by all participants and similar between arms; overall RSLV-132 was safe and well-tolerated. One SAE of parotitis in the RSLV-132 arm occurred 88 days after last dose of study drug and was considered unrelated to the RSLV-132.
Analyses of the primary endpoints and other secondary endpoints are ongoing.
Conclusion: RSLV-132 is a promising therapy to improve the symptoms of fatigue in patients with pSS, with a good safety profile. Further investigation of its use in pSS is warranted.

REFERENCE:
[1] Study supported by Resolve Therapeutics

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UCB Pharma (to University of Birmingham) and Roche, Consultant for: 2016-7: Novartis, Mitsubishi Tanabe Pharma
2017-8: AstraZeneca, MedImmune, GFK, Xtlbio, ONO Pharmaceutical
2018-9: Novartis, AstraZeneca, UCB Pharma, Jessica Tarn: None declared, Dennis Lendrem: None declared, Daniel Burge Employee of: Resolve Therapeutics, Medical Monitor for the clinical trial, James Posada Shareholder of: Owns equity of Resolve Therapeutics, Employee of: Founder and CEO of Resolve Therapeutics, Wan-fai Ng Grant/research support from: I have research collaborations with Resolve Therapeutics, electroCore, GSK, and Abbvie., Consultant for: Novartis, GSK, Abbvie, MedImmune, Pfizer, BMS
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THURSDAY, 13 JUNE 2019

Molecular fingerprinting

OP0203

CHARACTERIZING THE EPIGENOMIC LANDSCAPE OF PSORIASIS PATIENTS DESTINED TO DEVELOP PSORIATIC ARTHRITIS

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Background: Approximately 30% of psoriasis patients develop psoriatic arthritis (PsA), typically within 10 years of psoriasis onset. A large proportion of individuals with PsA remain undiagnosed. Epigenetics is potentially a major mechanism through which environmental factors influence PsA risk. An understanding of how the epigenome changes during the transition to PsA could yield predictive biomarkers and facilitate PsA diagnosis. We hypothesize that epigenetic deregulation at the level of DNA methylation occurs early in PsA pathogenesis, prior to overt clinical symptoms, and epigenetic marks can be used as biomarkers for disease prediction.
Objectives: To discover predictive biomarkers of PsA and gain an understanding of the pathogenesis of PsA by characterizing the epigenomic landscape of psoriasis patients who later developed PsA (converters) and comparing it to psoriasis patients who did not develop PsA (non-converters).
Methods: We performed an epigenome-wide comparison of DNA methylation in baseline whole blood samples from psoriasis converters (n=60) and non-converters (n=60) from a longitudinal cohort. Converters and non-converters were matched for age, sex, psoriasis duration, and duration of follow-up. DNA was analyzed on Human MethylationEPIC BeadChips using the ChAMP package. Cell type heterogeneity was corrected using RefbaseEWAS. Differentially methylated probes and regions were identified using limma and DMRcate, respectively. The FEM package was used to infer differentially methylated gene modules within a protein-protein interaction network.
Results: Converter baseline samples were collected a median of 4.2 (interquartile range 1.9-6.3) years prior to the onset of PsA, while non-converters samples were collected a median of 4.3 (1.2-7.3) years prior to the most recent clinic visit. The RefbaseEWAS method estimated that converters had slightly higher proportions of CD4+ T cells and granulocytes compared to non-converters, however the differences were not statistically significant. After adjustment for cell type heterogeneity, 68 individual CpG sites were found to be differentially methylated between converters and non-converters (FDR<0.05). Differentially methylated regions (DMRs) containing at least 4 significant CpGs were identified in genes such as *FBXO27* (beta fold change [FC]=0.06, region-wise adjusted $p=4.1x10^{-4}$), a ubiquitin ligase involved in lysosomal degradation, *RCAN1* (FC=0.05, $p=5.2x10^{-3}$), a protein which inhibits calcineurin-dependent signaling pathways and is involved in bone homeostasis, and *PMAIP1* (FC=0.04, $p=6.71x10^{-3}$), which encodes the NOXA protein involved in mediating apoptosis of activated B cells. Several significant CpG sites mapped to protein-protein interaction subnetworks involved in Th17 differentiation (*IRF4* and *MAF*), TNF alpha signaling (*IKBKE*, *REL*, *MAVS*,

TRAF7, MAFB), and Toll-like receptor signaling (*TLR1, IRAK2 MYD88, TOLLIP, TICAM1, TRAM1*).

Conclusion: Changes in individual CpGs, DMRs, and inflammatory pathways were detected in baseline samples of psoriasis converters compared to non-converters. These preliminary data support our hypothesis that DNA methylation changes occur early in PsA pathogenesis and can potentially serve as prognostic biomarkers of future onset of arthritis in psoriasis patients.

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THURSDAY, 13 JUNE 2019

Adults are just grown up children! Discuss

OP0204 EMAPALUMAB, AN INTERFERON GAMMA (IFN-Y)-BLOCKING MONOCLONAL ANTIBODY, IN PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME (MAS) COMPLICATING SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA)

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Background: MAS is a severe complication of rheumatic diseases, most frequently sJIA, caused by excessive activation and expansion of T cells and macrophages. It is characterized by fever, hepatosplenomegaly, liver dysfunction, cytopenias, coagulation abnormalities and hyperferritinemia, possibly progressing to multiple organ failure and death. MAS is categorized as a secondary form of HLH. A vast body of evidence points to uncontrolled overproduction of IFNγ as a major driver of hyperinflammation and hypercytokinemia in MAS and HLH. Emapalumab has been shown to effectively control disease activity in patients with primary HLH.

Objectives: To assess the pharmacokinetics (PK), efficacy and safety of intravenous (IV) emapalumab in patients with MAS and confirm the proposed dose regimen.

Methods: This is a pilot open-label single arm international study (NCT03311854). Patients had to have MAS (defined according to the 2016 ACR/EULAR classification criteria), on a background of confirmed, or high presumption of, sJIA, and inadequate response to high-dose IV glucocorticoids. Emapalumab initial dose was 6 mg/kg and treatment was continued at 3 mg/kg, twice weekly for a total of 4 weeks or less upon achievement of complete response. Serum concentrations of emapalumab, IFNγ-induced chemokine CXCL9 and sIL2R were measured. Safety assessments included adverse events (AEs) and laboratory abnormalities. Efficacy was defined as complete response by week 8, i.e. absence of MAS clinical signs plus white blood cell and platelet counts above lower limit of normal, LDH, AST/ALT<1.5 x upper limit of normal, fibrinogen >100 mg/dL, and ferritin decreased by ≥80% or to <2000 ng/mL, whichever was lower. Twin protocols are in place to recruit 5 patients each in Europe and North America (trial not started yet). We report data on the 6 patients recruited in the European protocol.

PK/PD parameters	Baseline	Week 1	Week 2	EOT	Week 8
Emapalumab (ug/mL) Median (range) trough levels	n.a.	48 (35-84)	88 (49-156)	112 (88-247)	58 (2-120)
CXCL9 (r.r. ≤ 300 pg/mL) Median (range) serum levels	8,506 (1,518-98,121)	465 (192-768)	134 (80-499)	109 (80-156)	120 (80-249)
sIL2R (r.r. ≤ 2000 pg/mL) Median (range) serum levels	4,350 (1,664-20,954)	4,161 (1,883-17,059)	2,184 (909-8,090)	1,095 (571-2,045)	1,083 (442-1,271)

Laboratory parameters	Baseline	EOT	Week 8
Platelet count < LLN, n. pts Median (range)	5 132.5 (70-229)	1 269.5 (133-455)	None 387.5 (214-455)
Ferritin > 2,000 ng/mL, n. pts Median (range)	5 21,668 (716-192,548)	None 322 (49-1222)	None 116 (38-258)
AST (IU/L) > 1.5 x ULN, n. pts Median (range)	4 136.5 (43-1507)	None 25.5 (19-39)	None 30.5 (18-43)
ALT (IU/L) > 1.5 x ULN, n. pts Median (range)	6 176.0 (95-852)	2 44.0 (23-76)	None 37.5 (27-48)
LDH (IU/L) > 1.5 x ULN, n. pts Median (range)	6 2,063 (727-12,734)	1 662 (423-810)	None 542 (423-579)
Fibrinogen (mg/dL) < LLN, n. pts Median (range)	3 203.5 (110-465)	None 240 (200-302)	None 271 (210-361)

EOT: end of treatment; LLN: lower limit of normal; ULN: upper limit of normal; r.r.: reference range

Results: Six patients (5 females, median age 11 years, range: 2-25 years) received emapalumab according to the prescribed dose regimen. Treatment duration ranged from 3 (2 patients) to 4 weeks. Prior to emapalumab, all patients failed methylprednisolone pulses, in 2 patients plus cyclosporine A (CsA) and in 2 patients plus CsA and anakinra. The achieved emapalumab concentrations led to rapid neutralization of IFNγ as indicated by CXCL9 levels and subsequent deactivation of T cells as indicated by sIL2R levels. In all patients, complete response was achieved by week 8, in 4 patients by end of treatment (Table). Systemic glucocorticoids were weaned in all patients. Emapalumab infusions were well tolerated and none of the patients discontinued emapalumab. A CMV reactivation was reported by investigator as a serious event possibly related to emapalumab, but resolved completely with treatment.

Conclusion: Emapalumab administration with the tested dosing regimen led to rapid neutralization of IFNγ as shown by normalization of CXCL9, associated with evidence of decreased T cell activation. In all patients, emapalumab treatment was effective in controlling MAS with a favourable safety profile.

REFERENCE:

[1] Ravelli A, et al. Ann Rheum Dis. 2016;75:481-9.

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OP0205 LIVE ATTENUATED VACCINES IN PEDIATRIC RHEUMATIC DISEASES ARE SAFE: MULTICENTER, RETROSPECTIVE DATA COLLECTION

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Background: Common practice is to withhold vaccination with live-attenuated vaccines in patients with rheumatic diseases on high-dose DMARDs, glucocorticosteroids or biological agents, due to limited safety data, and the (theoretical) risk of introducing an infectious disease to the patient. Evidence for this approach is low. We collected data from pediatric rheumatologists who vaccinate these patients, to obtain additional safety data, which might update and revise this approach.

Objectives: To collect retrospective data in patients with JIA and other diseases who received live booster MMR or MMRV while on DMARDs, glucocorticosteroids or biological agents.

Methods: Data from 13 pediatric rheumatology centers in 10 countries were collected.

Results: 234 patients were reported; mean age 5± 2.7, 70% girls. 206 had JIA;. 46% oligoarticular, 36% polyarticular, 8% systemic, 5% SPA types, 5% JIA and uveitis. 48% of JIA patients were in remission on medication. Disease activity was low in 38%, high in 2%, moderate in 7%; 11 patients had juvenile dermatomyositis, 3 systemic and 2 localized scleroderma, 4 isolated idiopathic uveitis, 1 CINCA syndrome, 1 MKD, and 1 FMF.

110 patients had MMR/V booster while on MTX; 3 reported mild side-effects of local skin reaction and pain, none had disease flare. 76 had booster while on MTX + anti-TNF; 7 reported mild and transient adverse events of local skin reaction, fever and URTI. 39 had booster while on anti-TNF alone; 1 reported fever. 3 had

booster while on tocilizumab, 7 on anakinra, and 5 on canakinumab. There was no relation between disease activity, type or duration, sex, age and outcome of vaccinations. No vaccine infection related to measles, rubella, mumps and varicella were reported.

Conclusion: This large, retrospective data collection demonstrates that live-attenuated booster vaccine is probably safe in children with rheumatic diseases, on immunosuppressive therapies. This strengthens the new PRES recommendation: "Vaccination of live-attenuated vaccines in patients on high-dose DMARD, high-dose glucocorticosteroids or biological agents can be considered on a case-by-case basis, weighing the risk of infections against the hypothetical risk of inducing infection through vaccination." These data provide the basis for a large, prospective data collection study that is planned by the PReS vaccination study group. It will increase the current level of evidence for the safety of vaccinations in our pediatric rheumatology population.

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THURSDAY, 13 JUNE 2019

Exercise – more than a wonderdrug

OP0206-HPR

BENEFICIAL LONG-TERM EFFECT OF A SUPERVISED EXERCISE PROGRAM ON PHYSICAL ACTIVITY LEVEL IN PATIENTS WITH AXIAL SPONDYLOARTHRTIS: 12 MONTHS FOLLOW-UP OF A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Background: Exercise is recommended in the management of axial spondyloarthritis (axSpA)[1] as it may reduce the burden of the disease.[2] Despite this, patients with axSpA tend to have a low physical activity (PA) level[3] and few patients engage in high intensities of exercise[4].

Objectives: To investigate the long-term effect of a three months supervised exercise program on PA-level in patients with axSpA.

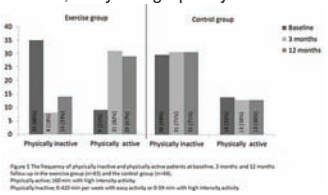
Methods: 100 patients with axSpA were randomized to either an exercise group (EG) or a no-intervention control group (CG). The exercise group participated in a three months high intensity cardiorespiratory and strength exercise program supervised by a physiotherapist. PA-level was a secondary outcome measured at 12 months follow-up with a standardised questionnaire (frequency, duration, intensity and mode)[5]. Being physically active was defined as $\geq$1 hour/week with high intensity PA. Statistical analyses were performed on an intention-to-treat basis using chi-square tests and logistic regression.

Results: A total of 87 of 100 (87%) patients were included in the analyses (table 1). At 12 months follow-up, significantly more patients in the EG than in the CG were physically active, p<0.001 (figure 1). Further, significantly more patients in the EG than in the CG exercised 2-3 times per week (25 [58%] vs. 15 [34%], p=0.02). Fewer patients in the EG reported to exercise at a low intensity level (low intensity reported by 3 [8%] in the EG vs. 14 [44%] in the CG, p=0.002). The regression analysis showed that participating in the exercise program (p<0.001) and earlier exercise experience (p=0.01) were the factors most associated with being physically active at 12 months follow-up (table 2).

Table 1. Baseline descriptive of the exercise group and the control group

	Exercise group (n=43)	Control group (n=44)
Age, years, mean (min-max)	45.5 (23-68)	47.4 (24-69)
Sex, male, n (%)	22 (51%)	20 (46%)
Radiographic axSpA	32 (74%)	28 (64%)
TNF-inhibitor, n (%)	38 (44%)	20 (46%)
ASDAS, mean (SD)	2.6 (0.7)	2.5 (0.7)

ASDAS, Ankylosing Spondylitis Disease Activity Score



Conclusion: A three month supervised exercise program delivered by physiotherapists had a significant long-term beneficial effect on PA-level in patients with axSpA. As regular exercise is an important part of the treatment recommendations for patients with axSpA[1], the results indicate that a time-limited supervised exercise program may be used as an effective intervention to succeed in reaching this recommendation.

REFERENCES:

[1] van der Heijde D, Ramiro S, Landewe R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017;76(6):978-991.
[2] Pecourneau V, Degboe Y, Barnetche T, Cantagrel A, Constantin A, Ruyssen-Witrand A. Effectiveness of Exercise Programs in Ankylosing Spondylitis: A Meta-Analysis of Randomized Controlled Trials. Archives of physical medicine and rehabilitation. 2018;99(2):383-389.e381.
[3] O'Dwyer T, O'Shea F, Wilson F. Physical activity in spondyloarthritis: a systematic review. Rheumatology international. 2015;35(3):393-404.
[4] van Genderen S, Boonen A, van der Heijde D, et al. Accelerometer Quantification of Physical Activity and Activity Patterns in Patients with Ankylosing Spondylitis and Population Controls. J Rheumatol. 2015;42(12):2369-2375.

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Getting a grip on the co-morbidities in gout

OP0207

URATE-LOWERING THERAPY WITH VERINURAD AND FEBUXOSTAT REDUCES SERUM URIC ACID AND ALBUMINURIA IN HYPERURICEMIC PATIENTS WITH DIABETES

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Background: Hyperuricemia is implicated as a major risk factor for chronic kidney disease (CKD), and emerging clinical data suggest that lowering serum uric acid (sUA) may protect kidney function by reducing albuminuria and slowing the rate of CKD progression. We evaluated the efficacy and safety of an intensive sUA-lowering strategy of verinurad (RDEA3170), a novel urate transport inhibitor of URAT1, and febuxostat in patients with Type 2 diabetes mellitus (T2DM) and albuminuria (clinicaltrials.gov: NCT03118739).

Objectives: To compare the efficacy of verinurad + febuxostat to placebo in reducing albuminuria in patients with T2DM.

Methods: A Phase 2 parallel group, randomised, double-blind, placebo-controlled clinical trial. Patients were assigned 1:1 to either verinurad 9 mg + febuxostat 80 mg (n=32) or placebo (n=28). Inclusion criteria: aged $\geq$18 years, sUA concentration $\geq$6.0 mg/dL, estimated glomerular filtration rate (eGFR) $\geq$30 mL/min/1.73 m^2, urinary albumin-to-creatinine ratio (UACR) 30–3500 mg/g and T2DM diagnosis. Exclusion criteria: history of gout or recent treatment with urate-lowering therapy. The primary endpoint was change in UACR. Secondary endpoints included sUA, renal function biomarkers, and eGFR.

Results: Baseline characteristics were similar between groups. For treatment vs placebo, respectively, mean (SD) sUA was 7.5 (1.6) vs 7.0 (0.8) mg/dL, eGFR was 59.2 (25.3) vs 68.1 (23.2) mL/min/1.73 m^2, and UACR was 459 (825) vs 412 (548) mg/g at baseline. The study met the primary endpoint as verinurad/febuxostat reduced UACR by 39% vs placebo after 12 weeks of treatment (p=0.07,

predetermined α=0.1). Least squares (LS) mean% change in eGFR at 24 weeks from baseline was
–1.73% for verinurad/febuxostat vs +0.55% for placebo (p=0.71). LS mean% change in sUA was –57% in the verinurad/febuxostat vs an increase of 7% in the placebo group at 12 weeks (p<0.0001). This effect was sustained at 24 weeks (62% reduction with verinurad/febuxostat vs 5% increase with placebo; p<0.0001). Excluding patients with prior gout avoided the need to administer gout prophylaxis, and only one gout flare-up (3%) was reported in the verinurad/febuxostat group. Most adverse events (AEs) observed were mild to moderate. AEs reported in more than one patient on active treatment were diarrhoea, dizziness, and nasopharyngitis.
Conclusion: Treatment with verinurad + febuxostat significantly reduced hyperuricemia and albuminuria in patients with T2DM. The effect was rapid, and the improvement was sustained through Week 24, suggesting that an intensive urate-lowering strategy that combines a URAT1 inhibitor with a xanthine oxidoreductase inhibitor may protect against the progression of diabetic kidney disease. Further studies are planned to confirm the efficacy of a verinurad-led urate-lowering strategy in preventing CKD progression.
Disclosure of Interests: Robert Terkeltaub Consultant for: AstraZeneca, Horizon, SOBI, and Selecta, Nalina Dronamraju Employee of: AstraZeneca, Susanne A Johansson Employee of: AstraZeneca, Joanna Parkinson Shareholder of: AstraZeneca, Employee of: AstraZeneca, Eva Johnsson Employee of: AstraZeneca, Fredrik Erlandsson Employee of: AstraZeneca, Austin Stack Consultant for: AstraZeneca, Grunenthal, and Menarini
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OP0208 EFFECT OF SERUM URATE LOWERING WITH ALLOPURINOL ON BLOOD PRESSURE IN YOUNG ADULTS

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Background: The association between serum urate and hypertension continues to be controversial. Animal models and studies in adolescents provided strong support of urate- lowering therapy (ULT) efficacy to improve early hypertension (1), while one recent randomized-controlled study in adults failed to find benefit (2).
Objectives: To test the hypothesis that serum urate reduction with allopurinol would lead to blood pressure reductions in young adults with pre-hypertension.
Methods: Single center, double-blinded, crossover trial in which participants were randomly assigned to allopurinol (300 daily mg) or placebo for a period of one month each. Adults ages 18-40, with baseline systolic blood pressure (SBP) $\geq$ 120 and < 160 mm Hg or diastolic blood pressure $\geq$ 80 and < 100 mm Hg, and serum urate $\geq$ 5.0 mg/dL (>297.4 μmol/L) or $\geq$ 4.0 mg/dL (237.9 μmol/L) (men or women, respectively) were enrolled. Main exclusion criteria included chronic kidney disease, gout, or use of ULTs. The primary outcome was change from baseline in SBP assessed by 24 hour ambulatory blood pressure monitoring. Safety assessments were also conducted.
Results: 99 participants were randomized, and 82 completed study participation (Table 1). Serum urate decreased by -1.33 ± 1.21 mg/dL (-79.1 ± 72.0 μmol/L) during the allopurinol period (p<0.001) and by a non-significant -0.04 ± 0.75 mg/dL (2.4 ± 44.6 μmol/L) while taking placebo. SBP changed by -0.71 ± 8.21 mmHg during the period assigned to allopurinol versus -0.16 ± 7.33 mmHg during the period assigned to placebo. The difference between these changes in SBP was not significant (p=0.52) (Table 2). Changes in diastolic blood pressure and mean ambulatory blood pressure also were not significantly different during allopurinol and placebo exposure periods. In post hoc analyses, there was a trend towards significant blood pressure decreases in the small participant subgroup with serum urate of > 6.5 mg/dL (> 386.7 μmol/L) at baseline visit. No allopurinol hypersensitivity events or other serious adverse events were observed.
Conclusion: In the intention-to-treat analysis, urate -lowering therapy with allopurinol in young adults did not lead to reductions in blood pressure when compared with placebo. Blood pressure reductions with allopurinol may be limited only to participants with higher baseline serum urate levels.

Table 1. Baseline characteristics of participants (n =99)

	Mean or frequency
Age (years)	28.0 ± 7.0
Sex	62 (63%)
Men	37 (37%)
Women	
Race/Ethnicity	40 (40%)
African American	59 (60%)
Not African American	
Serum urate	6.4 ± 1.0 mg/dL (380.7 ± 59.5 μmol/L)
Men	4.9 ± 0.7 mg/dL (291.5 ± 41.6 μmol/L)
Women	
Blood pressure at screening	133.8 ± 10.0
Mean systolic (mmHg)	84.3 ± 8.8
Mean diastolic (mmHg)	

Table 2. Change in blood pressure parameters during allopurinol and placebo treatment phases (n=99). Mean (SD)

Outcomes (mmHg)	Placebo	Allopurinol	p
Systolic blood pressure	- 0.16 (7.33)	-0.71 (8.21)	0.52
Diastolic blood pressure	-0.22 (5.81)	-0.28 (6.58)	0.68
Mean arterial pressure	-0.43 (5.63)	-0.54 (6.86)	0.54

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THURSDAY, 13 JUNE 2019

Treatment is more than drugs

OP0209-PARE IMPROVING MENTAL WELLBEING - COACHING PEERS TO USE TOOLKIT FOR MIND

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Background: The theme for the Finnish Rheumatism Association for 2019 is Mind and Me. The Age Institute in Finland launched a project called Mental Wellbeing to Promote Older People's Knowhow to Face Life's Challenges and the project was piloted at the Finnish Rheumatism Association in 2018. During the pilot project, staff members from the Finnish Rheumatism Association and volunteers from its member organisations were trained as Tools for Mind Coaches. This training gave new tools for peer support targeting older people and their mental wellbeing. The Cocahes may use the tools developed by the Age Institute, and these include Mind Tools, Senior Mind Pack of 52 cards, Nature Attraction Path, A Guide for Life Skills Coaches and a pocket book on Mental Wellbeing. The project especially targeted older people and their families in challenging life situations by promoting their mental wellbeing.
Objectives: To disseminate the theme and activities of mental wellbeing in member associations. To utilise the trained mental wellbeing coaches for tutoring in older people groups. To utilise the Tools for Mind in the activities of the Finnish Rheumatism Association and its member associations. To promote mental wellbeing to members
Methods: In the pilot project in 2018 the Age Institute organized three mental wellbeing training sessions for peer support group coaches, each lasted 1-2 days. The Finnish Rheumatism Association provided the coaches with some of the Tools for Mind. The training sessions included theory and practices. Participants were introduced how to use the Tools for Mind and they were encouraged to think for other applications of the tools. Also the themes discussed included elements of mental wellbeing, solution-focused approach, organising peer support groups for old people with chronical illnesses and ethical principles for group activities.
Results: There were altogether 11 people from the Finnish Rheumatism Association and its member associations that finished the training for Mind Coaches. Feedback from the participants was positive and the Tools for Mind were not only considered as useful practical tools but they also increased self-confidence and enthusiasm for peer led support groups. Senior Mind Pack of 52 cards were described as multipurpose and having good visual quality. All Tools for Mind were considered as thought-provoking tools to start conversation. Practical tools help

REFERENCES:
[1] Feig DI, Soletsky B, Johnson RJ. JAMA. 2008;300:924-32.
[2] McMullan CJ, Borgi L, Fisher N, et al. Clin J Am Soc Nephrol. 2017;12:807-16.

to recognise new aspects of one's own illness and they can be used to give support to people in different stages of their illness. Participants felt that forming groups and increasing cooperation between trained coaches and local associations need to be supported by the umbrella organisation, Finnish Rheumatism Association. Tools for Mind have successfully been used in a Fibromyalgia group and in senior groups for veterans (who did not have any RMDs).

Conclusion: The Finnish Rheumatism Association is creating new activities to endorse mental wellbeing. The training in 2018 will be used as a model for training coaches in mental wellbeing and it will be introduced in member organisations in 2019. Four training sessions will be arranged around Finland in the spring 2019. The programme will follow the pilot project programme. Training includes learning how to use the tools for mental wellbeing, going through the elements of mental wellbeing, solution-focused practices, organising peer support groups for old people with chronical illnesses and ethical principles. If possible, it is always good to have a trained Coach in the training, to tell about his/her experiences of using the Tools for Mind, how people have reacted to using the tools, and what kind of challenges and good moments the coach has experienced in group work. In 2019, the tools are utilised for example in monthly tasks concerning mental wellbeing and the Senior Mind Pack of 52 cards are being used in the member organisation visits to start conversation.

REFERENCE:

[1] https://www.ikainstituutti.fi/content/uploads/2018/05/Improving-older-peoples-mental-wellbeing_hires.pdf

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THURSDAY, 13 JUNE 2019

Diagnostic challenges in vasculitis

OP0210 FALSE POSITIVES OF ULTRASOUND IN GIANT CELL ARTERITIS. SOME DISEASES CAN ALSO HAVE HALO SIGN

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Background: Giant cell arteritis (GCA) is the most common systemic vasculitis in the elderly. The halo sign has been shown as an accepted valid test in the diagnosis of GCA in trained units[1-2]. However, to further improve the specificity, the sonographer should know some pathologies that can mimic halo signs since they also produce a hypoechoic increase of the arterial wall thickness.

Objectives: The aim of our study was to identify the causes and diseases that could be associated with the false positive diagnoses of GCA made by color Doppler ultrasound (CDUS).

Methods: Observational study of 305 patients with temporal artery CDUS findings compatible with GCA. The medical histories of these patients were reviewed and demographic, physical examination, clinical and analytical data were collected. The clinical diagnosis based on the long term follow-up of the patient was established as the definitive true diagnosis.

Results: 13 of the 305 cases included (4.3%) were false positives. The characteristics of these 13 patients and their final diagnoses are shown in table 1. 69.2% were women, while 30.8% were men. The mean age was 73.3 ± 8.0 years. Analytically, the mean ESR was 64.8 ± 42.3 mm/h, CRP 50.8 ± 60.0 mg/L and hemoglobin 12.6 ± 2.0 g/dL. Five patients (38.5%) fulfilled the ACR GCA classification criteria and eight did not (61.5%). A temporal artery biopsy was performed in 8 of the 13 patients (61.5%), with negative results in all of them. Eleven patients had CDUS involvement of superficial temporal arteries. Five had 1 branch involved (38.5%), three 2 branches (23.1%), one 3 branches (7.7%) and two 4 branches (15.4%). In addition, two patients (15.4%) had isolated halo sign in the axillary arteries, one unilateral and the other bilateral. Regarding the definitive diagnosis, four patients were polymyalgia rheumatica (30.8%), three atherosclerosis (23.1%), and there was one case of non-Hodgkin's Lymphoma type T, osteomyelitis of the skull base, primary amyloidosis associated with multiple myeloma, granulomatosis with polyangiitis, urinary sepsis and narrow-angle glaucoma. Some of these cases were false positives probably due to exam errors. However, others were due to diseases that increase the arterial wall thickness probably caused by cell infiltration and related edema (as Hodgkin's Lymphoma type T and ANCA-associated vasculitis) or by hypoechoic material deposit (as atherosclerosis and primary amyloidosis/multiple myeloma).

Table 1. Final diagnoses for false positive halo signs and associated ultrasound findings

Patient	Definitive diagnosis	Biopsy result	Artery involved	Number of arterial branches
1	Non-Hodgkin's T lymphoma	Negative	Temporal	3
2	Narrow-angle glaucoma	No done	Temporal	1
3	Osteomyelitis of the skull base	No done	Temporal	4
4	Polymyalgia rheumatica	Negative	Temporal	2
5	Urinary sepsis	Negative	Temporal	1
6	Polymyalgia rheumatica	Negative	Temporal	1
7	Polymyalgia rheumatica	Negative	Temporal	1
8	Amyloidosis due to multiple mieloma	Negative (deposit of amyloid material)	Temporal	4
9	Atherosclerosis	No done	Axilar	
10	Atherosclerosis	No done	Axilar	
11	Polymyalgia rheumatica	Negative	Temporal	1
12	Atherosclerosis	Negative	Temporal	2
13	ANCA-associated vasculitis	No done	Temporal	2

Conclusion: The percentage of false positives in the CDUS for the diagnosis of GCA is low. Nevertheless, some other diseases can also produce halo sign and the clinician should be aware of this to improve the accuracy of the ultrasound test.

REFERENCES:

[1] Chrysidis S, et al. Definitions and reliability assessment of elementary ultrasound lesions in giant cell arteritis: A study from the OMERACT large vessel vasculitis ultrasound working group. RMD Open. 2018;4(1):1–9.
[2] Aranda-Valera IC, et al. Diagnostic validity of Doppler ultrasound in giant cell arteritis. Clin Exp Rheumatol. 2017;35(1):123–7.

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OP0211 ULTRASONOGRAPHY CAN POTENTIALLY BE THE FIRST CHOICE OF IMAGING IN SUSPECTED EXTRA-CRANIAL GCA

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Background: Color duplex ultrasonography (CDU) is recommended as first line of imaging in patients suspected for cranial GCA [1]. However, extra-cranial involvement without temporal artery involvement is found in up to 40% of GCA patients [2]. CDU is very suitable to also assess extra-cranial artery inflammation, of which the axillary artery is relatively easy to assess. However, data on the value of CDU in extra-cranial GCA is limited [3].

Objectives: We aimed to (1) evaluate the performance of axillary artery CDU in patients with extra-cranial GCA by comparing CDU findings with [18F]-FDG PET/CT findings. Furthermore, to (2) compare the sensitivity and specificity of adding assessment of axillary arteries to temporal artery CDU, over temporal artery CDU only.

Methods: Consecutive patients suspected of GCA who underwent CDU examination of the temporal and axillary arties between 2013 and 2017 were

retrospectively included. The presence of a halo or occlusion was considered a positive CDU finding for GCA. In patients with PET-proven extra-cranial GCA, an axillary FDG uptake higher than liver uptake was considered positive. The reference was the clinical diagnosis (GCA or not) after 6 months.

Results: Of the 113 included patients, GCA was diagnosed in 41 and excluded in 72 patients at 6 months reference. PET-proven extra-cranial involvement was present in 20/41 GCA patients, of which 13 showed axillary involvement. An axillary halo was found in 8/13 of these patients, consistent with an increased FDG uptake. In 5/13, axillary involvement on PET was missed with axillary CDU (1/5 on steroids). However, in 4/5 of these an halo was found in the temporal arteries. Additionally, 6/20 patients with extra-cranial involvement did not show axillary involvement on both CDU and PET. All 6 had isolated involvement of a single artery on PET (2 aorta; 4 vertebral). CDU found a temporal halo in 3 of them. Overall, CDU of only the temporal arteries resulted in a sensitivity of 52% (95CI 35-67) and a specificity of 93% (95CI 84-97) for the reference diagnosis at 6 months. Adding CDU results of axillary arteries improved sensitivity to 71% (95CI 55-84), while specificity did not change. Although not systematically assessed, adding CDU assessment of the subclavian arteries improved sensitivity to 76% (95CI 59 – 87).

Conclusion: In case of an axillary halo no further FDG PET/CT scanning is required to diagnose extra-cranial GCA. In this study, investigation of both temporal and axillary arteries substantially increased the diagnostic performance of CDU. Furthermore, CDU and FDG PET arterial involvement is not always congruent, and occasionally arterial involvement is restricted to vessels not systematically assessed with CDU in our center. In patients in whom the axillary CDU is negative, a targeted CDU of selected vessels (e.g. subclavian, carotid or vertebral), or an FDG PET/CT is mandatory.

REFERENCES:

[1] Dejaco C, Ramiro S, Duftner C, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheum Dis. 2018;77(5):636-643.
[2] Schmidt WA, Seifert A, Gromnica-Ihle E, et al. Ultrasound of proximal upper extremity arteries to increase the diagnostic yield in large-vessel giant cell arteritis. Rheumatology (Oxford). 2008;47(1):96-101.
[3] Duftner C, Dejaco C, Sepriano A, et al. Imaging in diagnosis, outcome prediction and monitoring of large vessel vasculitis: A systematic literature review and meta-analysis informing the EULAR recommendations. *RMD Open*. 2018;4(1):e000612-2017-000612. eCollection 2018.

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THURSDAY, 13 JUNE 2019

Difficult to manage Sjögren's syndrome and Myositis

OP0212 DIGESTIVE INVOLVEMENT IN PATIENTS WITH PRIMARY SJÖGREN SYNDROME FROM THE SJOGRENSER SPANISH REGISTRY

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands. Among the extraglandular manifestations, digestive involvement (DI) is frequent, and may condition the quality of life of these patients. There are few studies that systematically analyze gastrointestinal involvement in pSS.

Objectives: To describe the prevalence of DI in patients with pSS included in SJOGRENSER Spanish registry and the phenotype of these patients, and to analyze their association with other clinical manifestations, serological markers, activity index and treatments used.

Methods: Transversal multicenter study that includes all patients of SJOGRENSER registry (patients who meet 2002 pSS classification criteria), a study conducted in 33 units of rheumatology in Spain between 2014-2016, which collected demographic and clinical and serological data (1). Patients were classified according to the presence of DI (that included esophagus, stomach, intestine, liver and pancreas). A descriptive analysis was done, with means and standard deviations, frequencies and proportions. Student t for quantitative variables and Chi2 for qualitative ones were performed to evaluate differences between groups. The association of DI with other variables was analyzed by bivariate and multivariate binomial logistic regression analysis. In the multivariate model all variables with p <0.2 in the bivariate were included, and the effect of age and sex was controlled.

Results: From 437 patients included (95% women, median age of 58 years), 59 (13.5%) had some DI (21 (36%) chronic atrophic gastritis, 12 (20%) esophageal dismotility, 3 (5%) lymphocytic colitis, 23 (39%) other). 54% of patients developed DI at the time of pSS diagnosis or later, and 45% before the diagnosis, with a mean age of 49 years at the onset of pSS symptoms. Patients with DI were older, both at diagnosis, onset of pSS symptoms and inclusion in the cohort, than those without it. There were no differences in the ESSDAI index between both groups.

Comparison regarding clinical and serological characteristics is shown in Table 1. Patients with DI had more thyroid involvement and C3 hypocomplementemia. In addition, patients with DI had been treated more frequently with glucocorticoids and immunosuppressants.

In the multivariate analysis, DI was significantly associated with older age at diagnosis (OR 1.03 (1.00-1.05); p=.005), more C3 hypocomplementemia (OR 2.40 (1.10-5.26) p=.027) and absence of anti-Ro antibodies (OR 0.33 (0.12-0.87) p=.025).

Conclusion: In patients with pSS from the SJOGRENSER cohort, the prevalence of digestive involvement is 13.5%. These patients are older at diagnosis, have more C3 hypocomplementemia and negative anti-Ro antibodies. These patients need more frequently glucocorticoids and immunosuppressants, suggesting a more severe disease phenotype.

REFERENCE:

[1] Fernandez Castro M, Reum Clin 2016; 12:184-9

	WITH DI (n=59; 13.5%)	WITHOUT DI (n=378; 86%)	P value
Age symptoms pSS onset	49 ± 13	45 ±13	**0.006***
Age diagnosis pSS	54 ±12	49 ±12	**0.008***
Age cohort inclusion	62 ±10	58 ±13	**0.036***
sex	57F (96%), 2M	359F (95%), 19M	0.585
Glandular involvement	23 (39%)	119 (31%)	0.253
Lung involvement	9 (15%)	34 (9%)	0.121
Thyroid involvement	13 (22%)	66 (17%)	**0.017***
Raynaud	17 (28%)	75 (19%)	0.116
anti-Ro antibodies	52 (88%)	357 (94%)	0.066
Hypocomplementemia C3	14 (25%)	51 (14%)	**0.034***
Hypocomplementemia C4	12 (21%)	50 (14%)	0.131
Glucocorticoid treatment	36 (63%)	177 (47%)	**0.026***
DMARD treatment	36 (64%)	180 (49%)	**0.035***

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OP0213 MYOFASCIA-DOMINANT: INFLAMMATION DETECTED ON WHOLE BODY MRI PREDICTS RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE IN PATIENTS WITH DERMATOMYOSITIS

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Background: Rapidly progressive interstitial lung disease (RPILD) is a major cause of death in patients with dermatomyositis (DM). Early diagnosis and aggressive immunosuppressive therapy are required in RPILD to improve the prognosis. Clinically amyopathic dermatomyositis (CADM) and anti-melanoma differentiation-associated gene 5 antibody are known as the risk factors for RPILD. However, 70% of the patients with CADM do not develop RPILD[1]. Whole-body magnetic resonance imaging (WB-MRI) can detect inflammation of whole muscle and myofascia. Although recent studies have indicated that MRI could be

useful for assessing disease activity[2], the relation between MRI findings and RPILD has not been investigated.
Objectives: In this study, we assessed whether WB-MRI findings are related with RPILD in patients with DM.
Methods: This retrospective study comprised 33 patients with DM who underwent WB-MRI in our hospital before the initiation of treatment for myositis. Muscular and myofascial signal abnormalities were scored on 42 muscular groups. The ratio of myofascial score to muscular score (myofascia/muscle ratio) was calculated and used to evaluate myofascia-dominant inflammation. RPILD was defined as the acute onset and rapid worsening of dyspnea, hypoxemia and radiographic ILD/fibrosis within 1 month.
Results: Of 33 patients, 16 were CADM, and 24 had ILD, including 8 patients with RPILD. All patients including CADM showed abnormal signal intensity in muscle and myofascia (scores median: 15 and 21, respectively). Muscle scores positively correlated with serum level of creatine kinase ($r=0.672$, $p<0.001$). The patients with RPILD showed a significantly higher myofascia/muscle ratio compared with that in the non-RPILD patients (2.167 vs 1.000; $p=0.018$). Logistic regression analysis identified myofascia/muscle ratio >1.53 (odds ratio: 141.90, $p=0.042$) and older age (odds ratio: 1.15, $p=0.041$) as independent risk factors for RPILD.
Conclusion: We newly defined myofascia-dominant inflammation using WB-MRI as a predictor to develop RPILD in patients with dermatomyositis.

REFERENCES:

[1] Moghadam-Kia S, et al. Anti-Melanoma Differentiation-Associated Gene 5 Is Associated With Rapidly Progressive Lung Disease and Poor Survival in US Patients With Amyopathic and Myopathic Dermatomyositis. Arthritis Care Res. 2016.
[2] Malattia C, et al. Whole-body MRI in the assessment of disease activity in juvenile dermatomyositis. Ann Rheum Dis. 2014.

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THURSDAY, 13 JUNE 2019

Anergy, exhaustion or post-activation in autoimmunity – facts and future consequences

OP0214 DISTURBED PD-L1 UPREGULATION IS CHARACTERISTIC OF ANERGIC B CELLS IN SLE

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Background: Prior studies on systemic lupus erythematosus (SLE) B cells reported an altered responsiveness to TLR9 stimulation, such as proliferation, cytokine production as well as indications for impaired T and B cell interaction [1]. The role of co-inhibitory and co-stimulatory (check-point) molecules in this setting has not been delineated in detail so far.
Objectives: Assess the expression of co-inhibitory (PD-1, PD-L1 and PD-L2) and co-stimulatory molecules (CD86 and CD40) by SLE B cells after *in vitro* stimulation and their potential contribution for B cell hyporesponsiveness in SLE.
Methods: PBMCs from 10 SLE patients and 10 healthy donors (HD) were stimulated with IL-2/IL-10, anti (α) - B cell receptor (BCR), CpG and CD40L alone or in combination. Expression of PD-1, PD-L1, PD-L2 as well as CD86, CD40 on CD19 +CD20+ B cell subsets after 48h stimulation was analyzed by FACS. CD71 was employed to measure proliferation of $CD19^{+}CD20^{+}$ B cells after 48h stimulation.
Results: SLE B cells exhibited a substantially decreased upregulation of PD-L1 ($p = 0{,}0006$) and CD86 ($p = 0{,}0188$, Fig.1) associated with significantly reduced B cell proliferation ($p = 0{,}0039$) after 48h stimulation with CpG alone and in combination compared with HD. While TLR9 engagement in SLE B cells appeared to be abnormal, activation of CD40 resulted into a consistent upregulation of both, inhibitory and stimulatory molecules. PD-L1 was positively correlated with B cell proliferation ($p = 0.003$). Notably, the expression of PD-L1 and CD86 correlated inversely with Siglec-1, as surrogate marker for interferon signature ($p < 0{,}0001$ and $p = 0.0021$ respectively). PD-L1 expression correlated inversely with cSLEDAI ($p = 0.0087$).

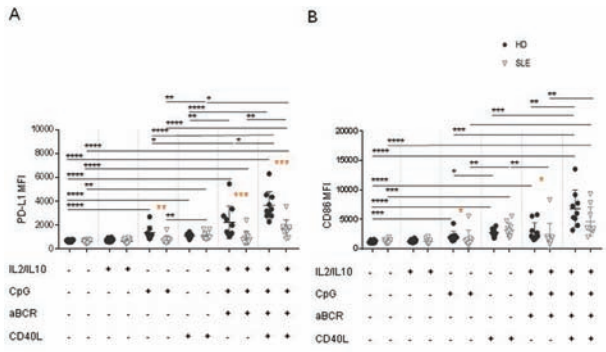


Fig. 1 PD-L1 and CD86 expression by SLE B cells upon stimulation is lower than in healthy donors. A. PD-L1 and B. CD86 expression by CD19+CD20+ B cells after stimulation with IL2/IL10, CpG, anti-BCR and CD40L in healthy donors and SLE patients.

Conclusion: Hyporesponsive/anergic lupus B cells are characterized by a functionally diminished PD-L1 and CD86 upregulation associated with reduced proliferation and clinical activity. The data mandate evaluations of innovative therapeutic interventions in SLE.

REFERENCE:

[1] Schrezenmeier, E., et al., *Postactivated B cells in systemic lupus erythematosus: update on translational aspects and therapeutic considerations*. Curr Opin Rheumatol, 2018.

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Fracture liaison service: an opportunity for rheumatologists to focus on secondary fracture prevention

OP0215 THE RISK OF FIRST AND SUBSEQUENT FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THE UK

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Background: Osteoporosis is a well-known complication of rheumatoid arthritis (RA) (1). NICE advises that health providers do not routinely assess fracture risk in people with RA aged under 50 years unless they have other major risk factors. However, studies suggest that young people with RA are at increased fracture risk even before age 50 years (2-4).
Objectives: To measure the incidence and risk of first and subsequent fracture in adults with RA aged under 50 in the UK.
Methods: A retrospective observational cohort study with matched control using data from Clinical Practice Research Datalink (CPRD) of adults ≥18 years with diagnosis of RA recorded from 1987 to 2016. Patients were followed from index date to the first fracture and subsequent fracture. Cases were adults with a new diagnosis of RA with at least one day of follow-up during the period. These cases were matched to 3 controls by age, sex, GP surgery and calendar year. The date of RA diagnosis date is the index date for cases and their matched controls.
CPRD data has a high level of data validity in reporting of fractures but subsequent fractures may be recorded more than once. In this analysis when subsequent fractures were of the same body part the fracture had to occur at least 6 months after the previous fracture to be classified as a "subsequent fracture". "First fracture" is the first fracture occurring after the index. "Subsequent fracture" is the fracture occurring after the first fracture. "Pre-index fracture" is a fracture that occurs before the index date.
Results: The characteristics of the study population are shown in Table 1.

Variable	Case (n=11,120)	Control (n=33,364)
	N (%)	N (%)
Age group 0-9	1,542 (13.87)	4,654 (13.95)
40-49	3,430 (30.85)	10,308 (30.90)
	6,148 (55.29)	18,402 (55.16)
Gender (female)	8,232 (74.03)	24,676 (73.96)
Glucocorticoid prescription <=6 months before index	830 (7.46)	371 (1.11)
Pre-index fracture	1,648 (14.82)	4,251 (12.74)
First fracture	954 (8.57)	1,995 (5.97)
Subsequent fracture	197 (1.77)	354 (1.06)

The incidence rate of first fracture for cases was 9.02 per 1000-person years (95% CI 8.46-9.61), for controls 6.85 per 1000-person years (95% CI 6.55-7.15). The incidence rate ratio (IRR) for first fracture was 1.32 (95% CI 1.220-1.426; p=0.00). The incidence rate of subsequent fracture was 1.78 (95% CI 1.55-2.05) per 1000-person years for cases and 1.17 (1.05-1.29) per 1000 -person years for controls. The IRR for subsequent fracture was 1.53 (95% CI 1.283-1.833; p=0.00). A Cox's proportional hazards model was used to estimate the hazard (or risk) of first and subsequent fracture for cases and controls stratified by age. Those with a pre-index fracture and with a glucocorticoid prescription prior to the index date had significantly higher hazard ratios for first and subsequent fracture. Women had a higher hazard ratio for first fracture.
Conclusion: This study shows that the incidence of fracture in patients with RA aged under 50 is significantly higher than in matched controls. This is true for the first fracture and for the subsequent fracture and is significantly higher for women in those under 50 for first fractures.

REFERENCES:

[1] Van Staa TP, Geusens P, Bijlsma JWJ, et al. Clinical assessment of the longterm risk of fracture in patients with rheumatoid arthritis. Arthritis & Rheumatism. 2006; 54(10): 3104–3112.
[2] Amin S, Gabriel SE, Achenbach SJ, et al. Are Young Women and Men with Rheumatoid Arthritis at Risk for Fragility Fractures? A Population-Based Study. J Rheumatol. 2013; 40(10): 1669–1676.
[3] Kim SY, Schneeweiss S, Liu J, et al. Risk of osteoporotic fracture in a large population-based cohort of patients with rheumatoid arthritis. Arthritis Research & Therapy. 2010; 12(4):R154.
[4] El Maghraoui A, Rezqi A, Mounach A, et al. Prevalence and risk factors of vertebral fractures in women with rheumatoid arthritis using vertebral fracture assessment. Rheumatology. 2010; 49(7):1303–1310.

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OP0216 IDENTIFICATION AND MANAGEMENT OF PATIENTSAT INCREASED RISK OF OSTEOPOROTIC FRACTURE: IMPLEMENTATION OF IMMINENT RISK FACTOR IN STANDARD DAILY PRACTICE FOR BONE MINERAL DENSITY ASSESSMENT AND PATIENT MANAGEMENT

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Background: Osteoporotic fractures are common and associated with significant morbidity, mortality, and healthcare resource use. The role of the recency of fracture has been shown for both vertebral and non-vertebral fracture risk. However, several patient characteristics contributing to imminent risk for fracture have not been well defined. Furthermore, the inclusion of imminent fracture risk in standard practice remains a challenge.
Objectives: to evaluate electronic recording of osteoporosis patients' data using online proforma to request DXA scan, analyse the correlations and the applicability of imminent fracture risk (ImFR) identification and the WHO fracture risk assessment tool (FRAX) for the prediction of osteoporotic fractures in standard practice and its implication on the patients' management.
Methods: 368 patients referred for DXA scanning were included in this work. The online referral form for DXA scanning includes 4 main components: Risk factors for osteoporosis (6 factors) to be completed by the referring doctor; 2. the 8 fracture risk factors identified in FRAX; 3. Risk factors for falls (5 factors) [1] and its score graded as low, moderate and high; 4. Risk factors for ImFR and a question Yes/No regarding the presence of ImFR. For the patients who had fracture in the last 24-months, potential risk factors during the period before fracture were assessed. The BMD as well as 10-years probability of fracture risk were analysed in patients with ImFR and those without. Risk stratification and correlation analyses were applied to analyse the associations between ImFR and FRAX-based probabilities versus BMD at different sites. Data from patients with and without recent fracture were used to identify factors associated with imminent risk for fracture.
Results: Of the 368 subjects, 181 (46.9%) were diagnosed as osteoporotic, and 158 (40.9%) were diagnosed as osteopenic. There was no significant difference on comparing the FRAX-based 10-year major osteoporotic fracture probability and hip osteoporotic fracture probability estimated with and without considering the BMD. Keeping the other factors constant, patient with ImFR had significantly ($p < 0.01$) lower BMD at both spine and hip in contrast with those without history of ImFR or history of fracture more than 10-years ago. Using data from 24- months before fracture, factors significantly associated with ImFR were high falls risk, older age, poorer functional disability and hand grip, specific comorbidities (central nervous system disease, inflammatory arthritis, Alzheimer's disease, parkinsonism, psychosis) steroid therapy and intake of drugs targeting CNS,. There was no significant difference ($p > 0.05$) on comparing FRAX estimated 10-year fracture probabilities in those with ImFR compared to those who had previous fracture more than 2-years ago.
Conclusion: It is important to include the ImFR in the referral for BMD assessment. In patients with osteoporosis or osteopenia and no recent fracture, high falls risk, older age, poorer health status, comorbidities were predictive of imminent risk for fracture. Identification of patients with imminent fracture risk may help identify and risk stratify those patients most in need of immediate and appropriate treatment to decrease fracture risk.

REFERENCES:

[1] El Miedany, et al. Falls risk assessment score (FRAS): Time to rethink. J clin Gerontology Geriatrics 2011;2: 21-26

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How not to smoke like a chimney

OP0217-HPR **EVALUATION OF PATIENTS' EXPERIENCES OF AN INTENSIVE SMOKING CESSATION INTERVENTION FOR PEOPLE WITH RHEUMATOID ARTHRITIS**

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Background: Smoking is considered one of the most important modifiable environmental risk factors to the pathogenesis of rheumatoid arthritis (RA). Smoking may also exacerbate the symptoms of RA. A randomized controlled trial (RCT) testing the effect of an intensive smoking cessation intervention on smoking cessation and disease activity in people with RA is currently being carried out (1).
Objectives: To evaluate how people with RA experienced an intensive smoking cessation intervention.
Methods: We conducted a qualitative study with individual interviews. Participants were recruited consecutively from the intervention group in a smoking cessation RCT after having completed both the smoking cessation intervention and the three-month follow-up visit. The analysis was based on thematic analysis (2). One patient research partner was involved in all phases of the study.
Results: In total 12 patients with RA were included (6 female, mean age 58 years (range 33-71)). We identified seven themes illustrating participants' experiences of the smoking cessation intervention. The themes were; ***Instilling hope for smoking cessation*** referring to the initial invitation to participate in the RCT and the allocation to the intervention group, which participants seized as a chance to stop smoking, ***Having a fellow traveler on the road to smoking cessation*** referring to their cooperation with the smoking cessation counselor which was important for maintaining motivation for smoking cessation, ***Tangible evidence that smoking cessation makes a difference*** referring to improved carbon monoxide levels which motivated endeavors to quit smoking, ***Apprehension – fear of a new dependence*** referring to participants' fear of becoming addicted to nicotine replacement therapy instead of smoking, ***Breaking habits*** referring to ongoing reflection on and efforts to quit smoking using the tools and knowledge obtained from the smoking cessation intervention, ***Why wasn't I told?*** Referring to the lacking provision of information on smoking and RA from health professionals, and ***Denial*** referring to neglect of the detrimental impact of smoking on RA symptoms and overall health.
Conclusion: The participants were grateful for the offer to participate in a RCT and a smoking cessation intervention because it created an opportunity for them to stop smoking. They valued getting concrete information about detrimental effects of smoking on RA and RA treatment. Many requested that health professionals focus more proactively on smoking and smoking cessation.

REFERENCES:

[1] Roelsgaard et al. The effect of an intensive smoking cessation intervention on disease activity in patients with rheumatoid arthritis: study protocol for a randomised controlled trial. Trials. 2017;18(1):570.
[2] Braun V et al. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101.

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THURSDAY, 13 JUNE 2019

Should we worry about anything else – also young people have multi-morbidities

OP0218-PARE **PREVENTATIVE MEDICINE THROUGH IDENTIFYING AND ADDRESSING COMORBIDITIES OF SPONDYLOARTHRITIS (SPA*) TO IMPROVE PATIENT OUTCOMES THROUGH PATIENT ORGANIZATION PARTNERSHIPS AND ALLIED HEALTHCARE OUTREACH**

Wendy Gerhart[1], Gerald Major[2], Austin Gerhart[2], Marilyn Walsh[2]. *[1]Canadian Spondylitis Association, Phelpston, Canada*; *[1]Canadian Spondylitis Association, Phelpston, Canada*

Background: Many patients are not aware of the common comorbidities they may experience. We need to understand if by educating patients and managing or preventing comorbidities, will patient outcomes be improved and the impact on healthcare system.
Objectives: To determine what type and number of comorbidities patients commonly experience in addition to their diagnosed SpA condition. This will help identify how collaboration with other patient organizations and allied healthcare professionals can better raise awareness, educate and support the community. It will convey the conditions, symptoms and importance of early diagnosis and treatment. This will reduce the impact on the Canadian healthcare system and improve patient outcomes
Methods: Canadian patients were surveyed from February through June 2018. Respondents were asked a variety of questions to gain insights on the comorbidities and how many they experience and live with in addition to their SpA diagnosis.
Results: The most common comorbidities respondents reported included: chronic pain (55%), mental health (depressions & anxiety) (54%), gut (Crohn's and ulcerative colitis)(35%), eye inflammation (uveitis/iritis) (33%), sleep issues (30%) and chronic fatigue (26%). Interestingly, these results are different from other studies where osteoporosis and cardiovascular disease were most commonly experienced. In addition to the more prevalent comorbidities, a significant number of people experienced skin (psoriasis), fibromyalgia, hypertension and lung disease.
There were 406 respondents who completed the survey. Only 3.7% reported to not have any comorbidities.
42.6% of patients were diagnosed with another condition in advance of being diagnosed with a SpA disease. There were 44.6% of respondents who had a healthcare professional other than their GP or Rheumatologist suggest they may have a SpA condition. Recommendation for further assessment was initiated by a physiotherapist (12%), a chiropractor 11%), ophthalmologist (7%) or massager therapist (5%).
Conclusion: A significant number of patients diagnosed with a SpA condition experience comorbidities and often have more than one condition. On average, people live with 4 different comorbidities. The survey results have confirmed the significance depression and anxiety impacts patients with SpA.
Through partnerships with trusted patient organizations, we can provide resources to educate and support our SpA community on the comorbidities commonly experienced. This will empower patients to manage symptoms sooner, thus contributing to a quicker recovery, reduced damage or prevent the complication from occurring all together.
Expanding outreach and collaborating with allied healthcare professionals through Canadian professional associations including family physicians, physiotherapists, chiropractors, ophthalmologists and massage therapists can further educate practicing healthcare professionals on SpA conditions and symptoms to recognize with patients contributing to prevention or earlier diagnosis and treatment intervention
The CSA will form collaborative agreements by leveraging existing partnerships and creating new partnerships with Canadian organizations and professional associations to support and educate people with credible and valuable resources on the comorbidities identified through this survey with the intended purpose to treat earlier or prevent complications that adds unnecessary financial strain on the Canadian healthcare system.
Together we are stronger.

REFERENCES:

[1] Molto, A., Nikiphorou, E. Comorbidities in Spondyloarthritis. Frontiers in Medicine. March 2018. Volume 5. Article 62
[2] Danve, A., Raychaudhuri, S. Comorbidities in Spondyloarthritis. Curr Treat Options in Rheum (2017) 3:63-74

Disclosure of Interests: Wendy Gerhart Grant/research support from: The Canadian Spondylitis Association received funding from multiple pharmaceutical companies for the comorbidity awareness campaign., Employee of: I was employed by Janssen Canada until October 2016. I have been working with the Canadian Spondylitis Association since March 1, 2017. Janssen did not provide support for the awareness campaign., Gerald Major: None declared, Austin Gerhart: None declared, Marilyn Walsh: None declared
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OP0219-PARE **LUPUS EUROPE YOUTH PANEL – WHAT WE LEARNED FROM YOUNG PEOPLE LIVING WITH LUPUS**

Alain Cornet[1,2], Jeanette Andersen[1]. [1]*Lupus Europe, Romford, essex, United Kingdom*; [2]*CLAIR, St Maur, Belgium*

Background: Since 2014, Lupus Europe conducts patient panels, where 10 to 12 persons from all over Europe living with lupus discuss the selected topic guided by facilitators living with lupus themselves. This allows to capture qualitative feedback of relevance, without the obstacle of the "white blouse". In 2018, 10 Young (18-27) European Lupus patients (8 female, 2 male) with diverse Lupus types met to discuss "Lupus and youth".
Objectives: Understand specificity of being young with lupus to better include young patients in Lupus groups action plans
Methods: 11 young patients, mostly with little or no involvement in patient groups were recruited through Lupus Europe's network. They were asked to send ahead of time their top challenges/issues living with lupus as well as their key questions for the panel. this input was used to build the 2 days program itself. Mid May, 10 of the 11 met face-to-face in Brussels, and explored multiple aspects of their input though 7 specifically designed interactive workshops
Results: While they considered taking pills every day as a key problem, they preferred to focus on the collective issues of being understood by friends and family and having to live with limitations.
A big "Wow" was the feeling of guilt expressed by several female participants (guilt of imposing limits to their partners, guilt of not being able to do as much as others, …), a very important underlying dimension of their social and affective life, which is likely much misunderstood by doctors and patient organizations;
young people with lupus remain fundamentally more positive on their life with lupus than the average patients. While they perceive lupus as being "all over their lives", they refuse to be ruled by it …
They view the future of a LUPUS EUROPE youth group as a "virtual group" on social media, with minimal commitment required, but bringing together "friends" around highly visual messages, short stories and the exchange of ideas that could lead to small group gatherings.
On the medical front, when we probed what would drive them to consider joining a clinical trial, clear first media is their lupus doctor, second are national lupus groups and LUPUS EUROPE. Other medias have a very limited impact.
Conclusion: Young patients needs must be addressed in a more aspirational way and using more virtual tools than average patients (more focused on health issues and geographic proximity).
The feeling of guilt of young women with regards to their affective life must be further explored to give them confidence and reassurance.

REFERENCE:

[1] Lupus Europe Patient panel 3 project report, acvailable on request at secretariat@lupus-europe.org

Disclosure of Interests: Alain Cornet Grant/research support from: No direct financial grants from Pharmaceutical companies, but some grants accrued LUPUS EUROPE does, in the form of Grants or payment for attending advisory boards or providing patient views, Speakers bureau: I have been involved in GSK panels to provide patient perspective. However, the minor service fee obtained accrued to LUPUS EUROPE ratyher than the company, Jeanette Andersen: None declared
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THURSDAY, 13 JUNE 2019

Fighting and fixing: from initiation to resolution of inflammation

OP0220 **SINGLE-CELL TRANSCRIPTOMIC AND FUNCTIONAL ANALYSES REVEAL NOVEL HETEROGENEITY IN PATHOGENIC PATHWAYS MEDIATED BY HUMAN SYNOVIAL TISSUE MACROPHAGES**

Samuel Finlay[1,2], Lucy MacDonald[1,2]*, Barbara Tolusso[3], Aziza Elmesmari[1,2], Maria Rita Gigante[4], Clara DI Mario[3],Luca Petricca[3], Andrew Filer[2,5], Neal L Millar[1], Elisa Gremese[3,4], Iain Mcinnes[1,2], Thomas Otto[1,2], Stefano Alivernini[3,4], Mariola Kurowska-Stolarska[1,2]. [1]*University of Glasgow, Institute of Infection Immunity and Inflammation, Glasgow, United Kingdom*; [2]*Rheumatoid Arthritis Pathogenesis Centre of Excellence (RACE), Glasgow, Birmingham, Newcastle, United Kingdom*; [3]*Fondazione Policlinico Universitario A. Gemelli IRCCS, Division of Rheumatology, Rome, Italy*; [4]*Università Cattolica del Sacro Cuore, Rome, Italy*; [5]*University of Birmingham, Institute of Infection, Inflammation and Ageing, Birmingham, United Kingdom*

Background: We hypothesise that synovial tissue macrophages (STM) are heterogeneous and mediate discrete pathogenic pathways that may underlie partial or absent therapeutic responses in RA patients. Better understanding of STMs will provide novel targets for re-instating synovial homeostasis. We have shown that the human synovium contains at least two major populations of STMs (CD206/MerTK^{neg} and CD206/MerTK^{pos}) with transcriptomes suggesting different function.
Objectives: To dissect the phenotypic and functional heterogeneity of STMs using single-cell transcriptomics and associated functional assays.
Methods: The relative proportions of the two major populations of STMs were quantified in 64 RA synovial biopsies (including 26 from RA patients in sustained remission), and in 8 healthy synovial tissues by flow cytometry. To uncover STM phenotypes, single-cell RNA sequencing of STMs from healthy donors (n=4), active RA (n=7; DAS28 $\geq$5.1) and RA in remission (n=4; DAS28$\leq$2.6) was performed with 10X Genomics. 21,000 STMs were sequenced and analysed (Seurat). For functional analysis, CD206/MerTK^{neg} and CD206/MerTK^{pos} STMs were sorted from biopsies of active RA (n=15) and RA in remission (n=8). These were stimulated *in vitro* with LPS (to mimic activation by joint damage) or with LPS plus the MerTK agonist GAS6 to activate MerTK^{pos} STMs; or co-cultured with FLS.
Results: The synovium of healthy subjects and RA patients in remission contain predominantly CD206/MerTK^{pos} STMs, whereas RA patients with any disease activity additionally contain substantial proportions of CD206/MerTK^{neg} STMs. In active RA, the CD206/MerTK^{neg} STMs produce TNF while CD206/MerTK^{pos} STMs produce type I interferon following TLR4 activation. Interestingly, CD206/MerTK^{pos} STMs from RA patients in remission showed a limited response to TLR stimulation, and their cytokine production was further inhibited by GAS6. This regulatory function of GAS6/MerTK was confirmed in macrophage-fibroblast co-culture assays: inhibition of MerTK in macrophages increased macrophage-induced cytokine production by FLS. STM single-cell transcriptomic analysis uncovered further STM heterogeneity in healthy, active RA and RA in remission (5 distinct subpopulations). These included three subpopulations that were not present in healthy and remission RA. These inflammatory subpopulations differ in their expression of surface receptors, spectrum of activated pathways and in their frequency in the synovium of patients with similar high DAS28. One of the subpopulations, characterised by increase metabolism, pro-inflammatory cytokines (e.g. IL-1β, BAFF) and chemokines, dominated in 3 out of 7 RA patients with active RA analysed; the second, characterised by high levels of MHC II and GPR receptors in 2 out of 7 patients while the third one characterised by high levels of alarmins (e.g. S100A8, 9 and 12) dominated in the remaining 2 inflamed RA synovia.
Conclusion: Pathogenic diversity of inflammatory synovial tissue macrophage subpopulations may partially account for unpredictable clinical responses in RA. Identifying and targeting the predominant STM subpopulation may facilitate novel therapeutic development and eventually patient stratification.
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OP0221 **OLIGOMERIC S100A4 INDUCES MONOCYTE INNATE IMMUNE MEMORY**

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Background: Trained immunity is a process of innate immune memory in which a primary stimulus such as beta-glucan can enhance the response of monocytes to secondary stimuli. The concept that specific damage associated molecular patterns (DAMPs) in rheumatoid arthritis (RA) could cause trained immunity which is involved in the disease pathogenesis has not been investigated so far. The oligomeric form of S100A4 (oS100A4) is a potent inducer of proinflammatory cytokines which is found in the plasma of patients with rheumatoid arthritis (RA).
Objectives: Aims are to investigate whether oS100A4 induces trained immunity in monocytes and characterize the molecular pathways involved in this process.
Methods: Monocytes were isolated from peripheral blood of healthy donors using anti-CD14 magnetic beads. To induce training, monocytes were stimulated with 2 μg/ml of oS100A4 and 1 μg/ml β-glucan for 24 hours (n=8). We searched for differential gene expression by RNA sequencing in order to identify factors that play a role in the initial stages of trained immunity. On day 4, LPS (10 ng/ml) was added. After 24 hours, IL-6 and TNFalpha were measured in cell culture supernatants by ELISA. The training protocol was repeated in monocytes transfected with PRDM8 siRNA using Lipofectamine (n=4). In addition, plasma levels of S100A4, CCL5 and IL-6 were measured in a cohort of RA patients (n=36) and healthy controls (n=18) by ELISA and PRDM8 transcripts in RA peripheral blood monocytes were quantified by RT-PCR.
Results: Monocytes primed with oS100A4 showed increased releases of IL-6 and TNFalpha in response to a subsequent LPS stimulation. RNA-Seq revealed the differential expression of 902 genes upon oS100A4 and 667 upon beta-glucan (mean and median > 2 fold, $p<0.01$). Among the differential genes, 601 were upregulated in S100A4 and 447 in beta-glucan stimulated cells. Upregulated genes included chemokine/cytokine and epigenetic factors. When we compared the upregulated genes from oS100A4 and beta-glucan stimulated cells, 83% of chemokines/cytokines and 50% epigenetic factors were identical. Interestingly, the histone methyltransferase PRDM8 was found to be a major regulator of proinflammatory mediators by both stimuli. siRNA knockdown of PRDM8 abolished the training effect of oS100A4 by decreasing the LPS induced release of IL-6 and TNFalpha ($p<0.01$). Furthermore, we analyzed a cohort of monocytes taken from RA patients. Higher PRDM8 transcription in RA monocytes was associated with increased plasma levels of CCL5 and IL-6 ($r = 0.52$ and 0.55, $p < 0.01$). RA patients in remission versus active patients showed significantly lower PRDM8 transcripts ($p < 0.05$).
Conclusion: Oligomeric S100A4 induced trained immunity in monocytes similarly to beta-glucan. PRDM8 histone methyltransferase is involved in this process that appears to be activated in monocytes of RA patients.
Disclosure of Interests: Emmanuel Karouzakis: None declared, Agnieszka Pajak: None declared, Niels Riksen: None declared, Leo Joosten: None declared, Mihai Netea: None declared, Esther Lutgens: None declared, Eric Stroes: None declared, Adrian Ciurea Consultant for: AbbVie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Mariam Grigorian: None declared, Michel Neidhart: None declared
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FRIDAY, 14 JUNE 2019

Seeing is believing: nanotechnologies in tissue imaging

OP0222 **STUDY OF VERTEBRAL FRACTURE PREVALENCE AND SCANOGRAPHIC BONE ATTENUATION COEFFICIENT (SBAC-L1) IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS VS. CONTROLS**

FAUNY Marine[1]*, Eliane Albuisson[2], Elodie Bauer[1], Julia Perrier Cornet[1], Isabelle Chary Valckenaere[1], Damien Loeuille[1]. *[1]CHRU Nancy, Rheumatology, VANDOEUVRE LES NANCY, France*; *[2]CHRU Nancy, VANDOEUVRE LES NANCY, France*

Background: Osteoporosis is a common disease whose prognosis can be seriously impacted by the development of fractures that lead to functional limitations and may even have life-threatening sequelae. This disease is often underscreened, especially in at-risk populations that require multidisciplinary care such as patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS) [1,2,3,4,5,6]. Moreover, a recent study showed that the scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1) with a threshold at 145 Hounsfield Units (HU) identified 96.6% of patients in the general population with a vertebral fracture (VF), whereas DEXA (with a T-score ≤ -2,5) identified only 39% of these patients [7].
Objectives: The aim of the study was to identify the prevalence of vertebral fractures (VFs) and to measure the scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1) based on CT-scan examinations of patients with rheumatoid arthritis (RA), patients with ankylosing spondylitis (AS) and in a control group.
Methods: This monocentric and retrospective study included patients who were evaluated between 2009 and 2017 with a diagnosis of RA based on the ACR/EULAR criteria, those with a diagnosis of AS based on the New-York criteria, and a RA-matched control group. All of the patients received a CT-scan. The osteoporosis risk factors, data from dual energy X-ray absorptiometry (DEXA) and clinical characteristics were collected. VFs were determined via CT-scans according to the Genant classification, and the SBAC-L1 was measured in Hounsfield units (HU). SBAC-L1 ≤ 145 HU (fracture threshold) defined patients at risk of VFs.
Results: A total of 244 patients were included (105 RA, 83 AS, 56 controls). The AS group was younger and primarily consisted of males. Of the 4,365 vertebrae studied, 66 osteoporotic VFs were found in 36 patients: 18 (17.1%) patients with RA, 13 (15.7%) patients with AS and 5 (8.9%) controls. The SBAC-L1 was 142.2 (±48.4) HU for the RA group and 142.8 (±48.2) for the AS group, both of which were significantly lower than that of the control group (161.8 (±42.7) HU). Of the 36 patients with VFs and rheumatism, 28% had a T-score ≤ -2.5 SD, and 71.4% had a SBAC-L1 ≤ 145 HU. A T-score ≤ -2.5 SD and a SBAC-L1 ≤ 145 HU were associated with the presence of a VF (OR = 2.35 [CI95%: 1.12-4.92] and 2.06 [CI95%: 1.04-4.10]), respectively.
Conclusion: The SBAC-L1 was significantly lower in the RA and AS groups than in the control group. Furthermore, SBAC-L1 ≤ 145 HU was associated with a higher risk of VFs, with an odds ratio similar to that of a DEXA.

REFERENCES:
[1] Toledano E. Reumatol Clin. 2012 Nov-Dec;8(6):334-41.
[2] Dougado M. Ann Rheum Dis. 2014;73:62-8.
[3] McKeown E. Rheumatol Oxf Engl. 2012;51:1662-9.
[4] Van der Weijden MA. Clin Rheumatol. 2012 Nov;31(11):1529-35.
[5] Ghozlani I. Bone. 2009 May;44(5):772-6.
[6] Ardizzone M. Rev Med Interne. 2006 May;27(5):392-9.
[7] Pickhardt PJ. Ann Intern Med. 2013;158(8):588–95.

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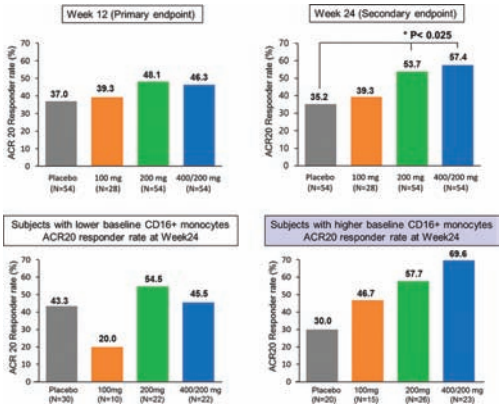
FRIDAY, 14 JUNE 2019

Rheumatoid arthritis – biological DMARDs

OP0223 **EFFICACY AND SAFETY OF E6011, AN ANTI-FRACTALKINE MONOCLONAL ANTIBODY, IN MTX-IR PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. We have conducted clinical trials of E6011, a novel humanized anti-FKN monoclonal antibody, for patients with rheumatoid arthritis (RA) in Japan[1]. This is the first report of efficacy and safety results of E6011 from a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group comparison study in RA patients inadequately responding to methotrexate (NCT02960438).
Objectives: To evaluate efficacy and safety of three dose of E6011 compared with placebo.
Methods: During the 24-week double-blind period, patients with moderately to severely active RA of inadequate response to MTX were randomly assigned to E6011 100 mg, 200 mg, 400/200 mg, or placebo groups at a 1:2:2:2 ratio. In the E6011 100 mg, 200 mg, and placebo groups, subjects received 100 mg, 200 mg, or placebo at Weeks 0, 1, 2, and every 2 weeks subsequently. In the E6011 400/200 mg group, subjects received 400 mg at Weeks 0, 1, 2, 4, 6, 8, 10 and then 200 mg every 2 weeks subsequently.
Results: A total of 190 subjects (54 in the placebo group, 28 in the 100 mg group, 54 in the 200 mg group, 54 in the 400/200 mg group) received study drug. Of the 190 subjects, 169 completed and 21 discontinued study treatment prematurely during the 24-week double-blind period. The ACR20 response rate at Week 12 (non-responder imputation), the primary endpoint, was 37.0% in the placebo group, 39.3% in the 100 mg group, 48.1% in the 200 mg group, and 46.3% in the 400/200 mg group (not statistically significant), and statistically significant difference from placebo in ACR20 response rate was found in the 200 mg and 400/200 mg groups at Week 24 (35.2% for placebo, 39.3% for 100 mg, 53.7% for 200 mg, 57.4% for 400/200 mg). In addition, we focused on CD16+ monocytes which highly expressing FKN receptor/CX3CR1 as a blood biomarker that linked to the clinical response to E6011. The whole patient population was divided into 2 groups according to the median value of baseline CD16+ monocyte percentage (Median: 10.35%). Much clearer ACR20 response was observed in a dose dependent manner in the subjects who showed higher baseline CD16+ monocytes over the median at Week 24 (NRI) (30.0% for placebo, 46.7% for 100 mg, 57.7% for 200 mg, and 69.6% for 400/200 mg) although such fashion was obscure in the subjects below the median value. Adverse events that occurred in ≥5% of subjects in any E6011 group were nasopharyngitis, upper respiratory tract infection, stomatitis, bronchitis, back pain, pharyngitis, and dental caries. As a results, E6011 was well tolerated with no notable safety concerns at doses of 100, 200, and 400/200 mg when administered subcutaneously for 24 weeks.



Conclusion: E6011 provided clinical improvements with a good safety profile in RA patients with inadequately responding to MTX. Especially, a higher efficacy of E6011 was suggested in patients with higher baseline CD16+ monocytes (%). This is the world-first evidence suggesting that a novel approach to target FKN/CX3CR1 interaction could be beneficial for RA.

REFERENCES:

[1] Tanaka Y, et al., Mod Rheumatol (2018) 28, 58-65

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OP0224

RESULTS OF A PHASE 2 STUDY OF RG6125, AN ANTI-CADHERIN-11 MONOCLONAL ANTIBODY, IN RHEUMATOID ARTHRITIS PATIENTS WITH AN INADEQUATE RESPONSE TO ANTI-TNFALPHA THERAPY

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Background: Cadherin-11 is expressed on fibroblasts in joints of RA patients and augments local fibroblast–mediated inflammation, pannus formation and tissue invasion (1). RG6125 is a novel humanized monoclonal antibody directed against Cadherin-11.
Objectives: To assess the safety, tolerability and efficacy of RG6125 as adjunctive treatment in patients with moderately to severely active RA and an inadequate response to anti-TNF-α therapy.
Methods: The Phase 2 study was conducted as a multicenter, randomized, double-blind, placebo-controlled study. Patients were randomly assigned (2:1) to receive 810 mg of RG6125 or placebo by IV infusion. In the treatment period, patients received RG6125 or placebo IV infusions twice every two weeks and then monthly for a total of 4 dose administrations up to Week 12. The primary efficacy endpoint was the proportion of patients with ACR50 response at Week 12.
Results: Demographics: 109 patients were randomized (98 female) to either placebo (N=37) or RG6125 (N=72) and were included in the efficacy analysis population. 107 patients were included in the safety analysis population (37 placebo, 70 RG6125). The median age was 55 years (22 – 78), and median RA disease duration was 12.4 years (1.0 – 42.4).
Efficacy: Overall, there was little to no difference between RG6125 and placebo arms in the primary and secondary efficacy assessments (Table 1).
Safety: More frequent musculoskeletal/connective tissue (14.3% vs. 8.1%) and gastrointestinal adverse events (12.9% vs. 8.1%) were noted on RG6125 compared to placebo, respectively. Two serious AEs were noted, one on RG6125 (intervertebral disc protrusion) and one on placebo (bacterial arthritis). No deaths occurred during the study.
PK/PD: Pharmacokinetics of RG6125 appears linear at the dose range tested. There was no significant relationship identified between exposure groups, defined by Cavg, and the efficacy endpoints at week 12. The kinetics of continuous endpoints was not significantly different across the exposure groups.

Table 1. Summary of Efficacy Results (Efficacy Analysis Population)

	RG6125 810 mg (N=72)	Placebo (N=37)	Difference - (90% CI)
ACR50 Responders - n(%)	8 (11.1%)	6 (16.2%)	-5.1% (-19.8%, 6.9%)
ACR20 Responders - n(%)	20 (27.8%)	16 (43.2%)	-15.5% (-32.4%, 1.6%)
ACR70 Responders - n(%)	1 (1.4%)	0 (0.0%)	1.4% (-7.9%, 7.0%)
Change from Baseline in DAS28 – adjusted mean*	-1.18 (n=65)	-1.65 (n=36)	0.48 (-0.84, -0.12)
Change from Baseline in CDAI – adjusted mean*	-14.67 (n=65)	-17.94 (n=36)	3.27 (-7.47, 0.94)
Change from Baseline in SDAI – mean (SD)	-20.69 (35.29) (n=63)	-21.31 (33.82) (n=33)	-
Change from Baseline in HAQ-DI – mean (SD)	-0.24 (0.51) (n=65)	-0.15 (0.52) (n=37)	-
RAMRIS Synovitis Score – median (range)	0.00 (-6.3 – 4.5) (n=59)	-0.25 (-4.0 – 2.7) (n=27)	-
RAMRIS Osteitis Score – median (range)	0.00 (-15.3 – 8.0) (n=59)	0.00 (-13.0 – 1.3) (n=27)	-
RAMRIS Bone Erosion Score – median (range)	0.00 (-6.0 – 3.5) (n=59)	0.00 (-1.0 – 2.5) (n=27)	-

Non-responder imputation used for missing ACR responses. LOCF used for missing SJC/TJC. For ACR missing CRP has been imputed with ESR if available. No imputation for other missing components. No imputation for missing DAS28, CDAI, SDAI, HAQ-DI or MRI RAMRIS scores.
* ANCOVA adjusted for baseline score and prior anti-TNFα therapy duration. MRI RAMRIS score is combination of the wrist and 1-5 MCP joints, and are exploratory endpoints.
Conclusion: RG6125 was well tolerated with only mild to moderate AEs. RG6125 did not show a discernible treatment effect in RA patients in combination with anti-TNFα-blockers over placebo.

REFERENCE:
[1] Lee DM, et al. Science 2007;315:1006-10.

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OP0225

SERIOUS INFECTIONS IN OFFSPRING EXPOSED IN UTERO TO NON-TNFI BIOLOGICS AND TOFACITINIB

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Background: During pregnancy, maternal circulating immunoglobulins G (IgG) are actively transported across the placenta through their Fc portion. Thus, TNFi and other biologics harbouring an Fc part have the potential to transfer across the placenta, often reaching higher fetal than maternal levels.[1] In addition, it is postulated that small-molecule drugs may cross the placenta, although this remains unconfirmed. As fetuses could be exposed to therapeutic (or potentially supra-therapeutic) levels of biologics and small molecules, there are concerns that these agents could cause immunosuppression in exposed offspring.
Objectives: We compared the risk of serious infections in children born to mothers with chronic inflammatory diseases who used non-TNFi biologics or tofacitinib during pregnancy, versus unexposed offspring and children exposed to TNFi in utero.
Methods: We identified all women with $\geq$1 hospitalization for delivery after a diagnosis of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriasis (PsO), psoriatic arthritis (PsA), or inflammatory bowel diseases (IBD), and a randomly selected group of unaffected mothers, matched $\geq$4:1 for age, year of delivery, and state of residence, using MarketScan data (2011-2016). Only women continuously enrolled within MarketScan for $\geq$12 months prior to delivery and with available child linkage were included. We defined tofacitinib, TNFi and non-TNFi biologic (i.e. abatacept, rituximab, tocilizumab, ustekinumab, vedolizumab) exposure based on $\geq$1 filled prescription and/or infusion procedure code during pregnancy and/or the preconception period. We ascertained serious infections in the offspring based on $\geq$1 hospitalization with infection as a primary diagnosis, within the first year of life. We also characterized all exposure groups according to maternal demographics, disease type, co-morbidities, pregnancy complications, and drug use (i.e. corticosteroids, DMARDs, biologics).
Results: We identified 16,490 offspring of mothers with RA (4,142), AS (381), PsO/PsA(5,743), and IBD (6,731), as well as 164,553 children born to unaffected matched mothers. Among offspring whose mothers had inflammatory diseases, 108 were exposed to tofacitinib or non-TNFi biologics (tofacitinib 4, abatacept 34, rituximab 6, tocilizumab 12, ustekinumab 42) and 1,611 to TNFi during pregnancy. We observed 2 cases of serious infections in children exposed to tofacitinib or non-TNFi biologics (1.9%; 95% CI 0.3, 7.2): one case was exposed to tofacitinib, while the other was exposed to abatacept. The percent of serious infections in offspring of inflammatory disease mothers with no TNFi exposure was 2.1% (95% CI 1.9, 2.3), while for those with TNFi in utero exposure, it was 2.3% (95% CI 1.6, 3.0). In children born to unaffected mothers, the percent of serious infections was 1.6% (95% CI 1.6, 1.7).
Conclusion: In the largest cohort of inflammatory disease offspring ever assembled, we detected very few serious infections in children exposed to non-TNFi biologics or tofacitinib. More studies are necessary to precisely determine the specific effects of individual non-TNFi biologic and small-molecule drugs on the risk of serious infections in exposed offspring.

REFERENCE:
[1] Vinet É, De Moura C, Pineau CA, Abrahamowicz M, Curtis JR, Bernatsky S. Serious Infections in Rheumatoid Arthritis Offspring Exposed to Tumor Necrosis Factor Inhibitors: A Cohort Study. Arthritis Rheumatol. 2018 Oct;70(10):1565-1571.

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OP0226

SOLID TUMOUR OUTCOMES IN PATIENTS WITH RA TREATED WITH ABATACEPT AND OTHER DMARDS: RESULTS FROM A 10-YEAR INTERNATIONAL POST-APPROVAL STUDY

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Background: The abatacept global post-marketing epidemiology programme includes observational studies based on biologic disease registries and healthcare claims database studies to evaluate infection and malignancy risks associated with abatacept treatment, as used in routine clinical practice.
Objectives: To assess the risk of solid tumour malignancies in patients with RA treated with abatacept vs conventional synthetic (cs)DMARDs and other biologic (b) or targeted synthetic (ts)DMARDs.
Methods: Data were analysed from four cohorts: two biologic registries (the Anti-Rheumatic Therapy in Sweden [ARTIS] register and the Rheumatoid Arthritis Observation of Biologic Therapy [RABBIT] German registry), a disease registry (FORWARD, The National Databank for Rheumatic Diseases in the USA) and a healthcare claims database (the population-based British Columbia Canadian RA Cohort [BC]). Exposure defined as "ever exposed" unless specified. Crude incidence rates (per 1000 patient-years of exposure) with 95% CIs were calculated for overall malignancy, breast cancer, lung cancer and lymphoma. Adjusted risk ratios (RRs) with 95% CIs were estimated using multivariate models adjusting for demographics, comorbidities and other potential cofounders within each database and were subsequently pooled using a random-effects model for meta-analyses.[1]
Results: Patients treated with abatacept (~5100), csDMARDs (~74K) and other b/tsDMARDs (~37K) were followed up for a mean of 3.0–3.7, 3.0–6.2 and 3.0–4.7 years, respectively. Patients were mainly female (71–86%), with a mean age ranging from 55–63 years, and 4–34% had a history of malignancy. A greater number of abatacept-treated patients had been treated with ≥2 prior biologics (abatacept, 44–85%; csDMARDs, 11% [FORWARD] and other b/tsDMARDs, 0–19%). The incidence rate of overall malignancy in abatacept-treated patients was low (Table). Adjusted RRs (95% CIs) for abatacept vs csDMARDs (range: 0.8 [0.2, 3.4] to 1.3 [0.5, 3.3]; pooled estimate: 1.1 [0.8, 1.5]) and abatacept vs other b/tsDMARDs (range: 1.0 [0.4, 2.6] to 1.2 [0.6, 2.3]; pooled estimate: 1.0 [0.8, 1.3]) showed no increased risk in overall malignancy. Although individual registries showed a slight increase in breast (BC), lung (RABBIT) and lymphoma (ARTIS) cancers in patients treated with abatacept, numbers were too low to make an accurate comparative risk assessment.
Conclusion: While the development of malignancy is a potential risk associated with the use of immunomodulators, data from this large, international, post-marketing epidemiology programme suggest that the risks of overall malignancy and breast, lung or lymphoma cancers were not significantly increased in patients treated with abatacept. These data are consistent with the established safety profile of abatacept.

Table. IRs per 1000 PY (95% CI) for malignancies

	Overall malignancy			Breast			Lung			Lymphoma		
	Abatacept	csDMARDs	Other b/tsDMARDs	Abatacept	csDMARDs	Other b/tsDMARDs	Abatacept	csDMARDs	Other b/tsDMARDs	Abatacept	csDMARDs	Other b/tsDMARDs
ARTIS	11 (9, 14)	13 (13, 14)[a]	10 (9, 11)	2.5 (1.5, 4.1)	2.5 (2.4, 2.7)	2.3 (2.0, 2.7)	0.7 (0.2, 1.6)	2.0 (1.8, 2.1)	1.4 (1.1 1.6)	1.1 (0.5, 2.0)	0.9 (0.8, 1.0)	0.6 (0.4, 0.7)
BC	11 (6, 18)	10 (8, 13)	12 (10, 13)[a]	4.4 (1.6, 9.6)[b]	2.3 (1.2, 4.0)[b]	2.5 (1.9, 3.4)[b,c]	NR	3.7 (2.4, 5.4)	2.9 (2.2, 3.6)[c]	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)[c]
FORWARD	8 (5, 12)	9 (6, 13)	5 (3, 7)	0.0 (0.0, 0.4)	0.0 (0.0, 1.3)	0.0 (0.0, 0.7)	0.1 (0.0, 0.7)	0.0 (0.0, 1.3)	0.0 (0.0, 1.9)	0.0 (0.0, 0.4)	0.0 (0.0, 1.3)	0.0 (0.0, 0.7)
RABBIT	9 (7, 13)	12 (10, 15)[a]	9 (6, 10)	1.3 (0.5, 2.5)	3.3 (2.1, 4.9)[a]	1.9 (1.4, 2.4)	2.5 (1.5, 4.0)	2.3 (1.3, 3.7)[a]	1.7 (1.3, 2.3)	0.2 (0.01, 1.2)	0.7 (0.2, 1.7)[a]	0.5 (0.3, 0.9)

[a]Biologic-naive patients (most of whom had been receiving csDMARDs)
[b]Other biologic group in BC only included anti-TNF inhibitors
[c]Female only
ARTIS=Anti-Rheumatic Therapy in Sweden; b/tsDMARD=biologic/targeted synthetic DMARD; BC=British Columbia Canadian RA Cohort; csDMARD=conventional synthetic DMARD; FORWARD=FORWARD, The National Databank for Rheumatic Diseases in the USA; IR=incidence rate; NR=not reported; PY=patient-years; RABBIT=Rheumatoid Arthritis Observation of Biologic Therapy German registry

REFERENCE:

[1] DerSimonian R, Laird N. Control Clin Trials 1986;7:177–88.

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OP0227

EFFECTS OF SUCCESSIVE SWITCHES TO DIFFERENT BIOSIMILARS INFLIXIMAB ON IMMUNOGENICITY IN CHRONIC INFLAMMATORY DISEASES IN DAILY CLINICAL PRACTICE

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Background:
Objectives: To determine whether the successive switches from innovator infliximab to a first then a second biosimilar infliximab increase the risk of immunogenicity during a 3-year observation period.
Methods: This is a usual care study performed in Cochin Hospital, Paris, France. First switch from innovator infliximab to a first biosimilar infliximab occurred in October/December 2015 and the second switch from the first to the second biosimilar infliximab started in December 2017. The end of the observation period was December 2018. Immunogenicity was defined by the detection of positive anti-drug antibodies (ADA >10 ng/mL), at least at two consecutive time points. The primary outcome of the study was the development of immunogenicity during the observation period. Secondary outcomes were i) the point prevalence of positive ADA at baseline, ii) the influence of the successive switches to biosimilars on the risk of immunogenicity and iii) the retention rate of biosimilar infliximab at the end of the observation period.
Results: Our prospective cohort consisted on 265 patients on maintenance therapy with innovator infliximab (135 axSpA, 64 with inflammatory bowel diseases, IBD, 31 with RA, 21 with PsA, 8 with uveitis and 6 with other chronic inflammatory diseases) who switched to biosimilar infliximab. Then, 140 patients switched to the second biosimilar infliximab, 26 remained treated with the first biosimilar, and innovator infliximab was re-established in 55 patients. 29 patients (15 females, 14 males) had positive ADA at baseline (point prevalence: 12.4%), before the switch to biosimilar infliximab. Among these 29 patients, 15 had axSpA (11%), 6 RA (19%), 6 IBD (9%) and 2 PSa (10%). Among the 236 patients with no ADA at baseline, 20 patients developed ADA during the observation period, corresponding to a rate of 3 for 100 patient years. The mean time to positive ADA detection was 21.2±13.7 months. Kaplan Meyer curve showed no influence of the number of biosimilars infliximab received on immunogenicity (Figure 1A). Among the 20 patients with positive ADA, 4 were back to innovator infliximab at the time of ADA detection, 10 patients were exposed to the first biosimilar and 6 to the second. The risk of treatment discontinuation was significantly higher in patients with positive ADA at baseline or during follow-up compared to patients without ADA (Figure 1B, Hazard Ratio 2.27, 95% confidence interval 1.33-3.89). No predictive factor of immunogenicity was identified (including type of disease, age, sex, BMI or concomitant DMARD intake). The retention rate of biosimilar infliximab (Figure 1C) was 58% (154/265) at the end of observation period, including 131 patients treated with the second biosimilar and 23 who remained treated with the first biosimilar.
Conclusion: In this usual care study with a 3-year observation period, the development of immunogenicity was low (3 for 100 patient years) and not favored by the switch to biosimilars infliximab. Thus, immunogenicity does not constitute a barrier to interchangeability between biosimilars infliximab in chronic inflammatory diseases.

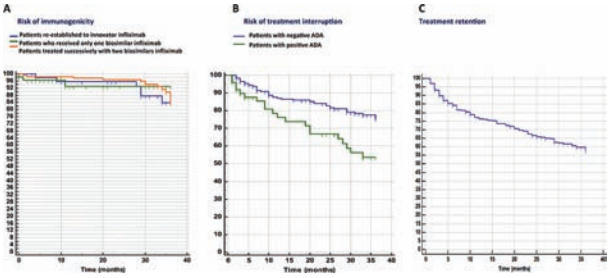


Figure 1. Kaplan Meyer Survival Analyses. A, risk of immunogenicity according to the number of biosimilars infliximab received; B, risk of treatment interruption according to the presence of anti-drug antibodies (ADA); and C, treatment retention within the observation period

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OP0228

GSK3196165 AN INVESTIGATIONAL ANTI-GM-CSF MONOCLONAL ANTIBODY, IMPROVES PATIENT REPORTED OUTCOMES IN A PHASE IIB STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: GSK3196165 is a human mAb that inhibits GM-CSF, a key driver in a broad range of immune-mediated conditions (Hamilton, 2016). In trials of patients with RA, inhibition of GM-CSF signaling has resulted in clinical benefit. GM-CSF is not only a key mediator of inflammation, but emerging science suggests it is also an important regulator of pain.
Objectives: To evaluate the treatment effect of GSK3196165 on pain, fatigue, physical functioning, mental functioning and global assessment of disease, in patients with moderate-to-severely active RA.
Methods: 222 adult patients with active, moderate-severe RA (ACR 2010 criteria), ≥4 each of swollen and tender joints, DAS28(CRP) ≥3.2 and CRP ≥5.0 mg/L, were randomized equally to placebo or GSK3196165 22.5mg, 45mg, 90mg, 135mg or 180mg SC weekly for 5 injections, then every other week until Week 50. The Patient Reported Outcomes (PROs) measured throughout the study included, pain Visual Analogue Scale (VAS), Patient's Global Assessment of Arthritis (PtGA), Health Assessment Questionnaire - Disability Index (HAQ-DI), Brief Fatigue Inventory (BFI) Question 3, the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F), and the 36-item short form health survey (SF-36). The primary outcome was the proportion of patients who achieved remission (DAS28(CRP) <2.6) at Week 24 and the data has been previously reported (Buckley, 2018).
Results: 37 patients were randomised to each treatment group. The observed GSK3196165 pharmacokinetic exposures were lower than anticipated but despite this, there was a rapid and substantial improvement in RA symptoms in patients treated with GSK3196165 compared with placebo.
The table below summarizes the change from baseline data for the GSK3196165 180 mg dose and placebo at Week 12. An increase in the FACIT-F and SF-36 scores and a decrease in all other scores indicate an improvement in RA symptoms.

PRO endpoint at Week 12	Placebo (N=37)	GSK3196165 180mg (N=37)	
	Least squares mean change from baseline (SE)		Difference from placebo (95% CI, p Value)
Pain VAS	-7.07 (3.705)	-25.01 (3.650)	-17.94 (-28.18, -7.70, p<0.001)
PtGA	-6.72 (3.660)	-23.90 (3.606)	-17.18 (-27.27, -7.10, p<0.001)
HAQ-DI	-0.26 (0.091)	-0.50 (0.090)	-0.24 (-0.49, 0.01, p=0.059)
BFI Question 3	-0.63 (0.346)	-2.20 (0.339)	-1.57 (-2.53, -0.62, p=0.001)
FACIT-F	3.37 (1.291)	8.70 (1.262)	5.33 (1.77, 8.89, p=0.004)
SF-36 Physical Component	3.42 (1.203)	6.97 (1.182)	3.55 (0.22, 6.88, p=0.037)
SF-36 Mental Component	3.54 (1.558)	6.79 (1.521)	3.25 (-1.05, 7.54, p=0.138

Conclusion: The results of this Phase IIb study showed that GSK3196165 substantially improved the scores of a range of PRO measures among RA patients. In particular, there was a highly significant improvement in pain; a key symptom of RA. These effects were observed despite achieving much lower drug exposure than predicted. Further studies are required to confirm the additional patient relevant benefits that are expected to arise from increased exposure to GSK3196165.

REFERENCES:

[1] Hamilton JA, Cook AD, Tak PP. Anti-colony-stimulating factor therapies for inflammatory and autoimmune diseases. Nat Rev Drug Discov 2016; 16:53-70
[2] Buckley C, et al. A Phase IIb Dose-Ranging Study of Anti-GM-CSF with Methotrexate Treatment in Patients with Rheumatoid Arthritis (RA) and an Inadequate Response to Methotrexate. Arthritis Rheumatol. 2018;70 (Suppl 10): abs 1938

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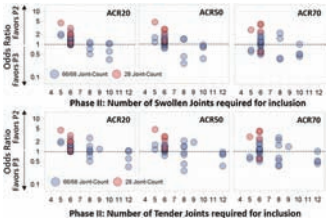
OP0229

PHASEII CLINICAL TRIALS SYSTEMATICALLY OVERESTIMATE TREATMENT EFFECTS OF SUBSEQUENT PHASE III TRIALS IN RHEUMATOID ARTHRITIS

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Background: Phase 3 (P3) clinical trials are the mainstay of drug development in all areas of medicine, including rheumatology, allowing to determine safety and efficacy of new drugs on their way to approval. Historically, efficacy results of P3 trials have often been disappointing with respect to the expectations set by phase 2 (P2) trials. It is unclear whether these observations are reflection of a true bias or merely a play of chance.
Objectives: To systematically compare efficacy results of P2 versus P3 trials in RA and investigate potential determinants of efficacy differences.
Methods: We performed a systematic review of disease modifying anti-rheumatic drugs (DMARDs) tested in P2 trials in rheumatoid arthritis (RA) over the last 20 years for which also P3 trials exist. We searched Medline, EMBASE, and the

Cochrane Library to identify all randomized controlled double-blind trials investigating biological (b) and targeted synthetic DMARDs in RA. The criteria for inclusion in the analyses were defined as follows: (i) treatment arms in P2 and P3 used the same treatment regimen; (ii) the same RA population was studied (DMARD naïve; conventional DMARD insufficient responders (IR); bDMARD IR). The treatment regimen was regarded the same when a DMARD was used at the same dose, interval and route in P2 and P3. Multilevel mixed model logistic regression was used to determine a summary estimate for comparison of P2 versus P3 results on the outcomes of American College of Rheumatology (ACR)20, ACR50, and ACR70 responses (in separate models). Results are expressed as Odds Ratio (OR) and 95% confidence intervals (95% CI). Possible determinants of systematic overestimation were explored using the same statistical technique, investigating study and baseline characteristics of the individual trials and study arms, respectively.



Results: In total 1290 abstracts were screened of which 133 were regarded as potentially relevant, with 44 trials (19 agents, 48 regimens, 17476 patients) finally included in the analysis. Summary estimates revealed that outcomes of P2 trials were systematically overestimating the subsequent P3 results for ACR20 (OR: 1.40; 95% CI: 1.15-1.57; p≤0.001), ACR50 (OR: 1.36; 95% CI: 1.21-1.54; p≤0.001) and ACR70 (OR: 1.39; 95% CI: 1.02-1.90; p=0.037).

Exploration of determinants of this systematic bias revealed that inclusion criteria for minimum number of required swollen (IC-SJC) and tender joints (IC-TJC) as well as the joint count used for inclusion (28 vs. 66/68 joint count) were significant determinants of P2/P3 efficacy differences. Figure 2 shows scatter plots of efficacy differences (shown as OR), revealing that higher IC-SJC and IC-TJC, as well as using the 66-JC instead of the 28-JC for study inclusion lead to a significantly lower chance of efficacy overestimation.

Conclusion: Our results reveal that Phase 2 clinical trials overestimate the treatment effects when compared with subsequent Phase 3 trials in RA. The identification of this systematic bias towards overestimation of efficacy by Phase 2 studies has implications for considerations of clinical investigators, sponsors, and regulatory agencies during the development and licencing process of new compounds, as well as potential ethical implications.

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Disclosure of Interests: Andreas Kerschbaumer Speakers bureau: Bristol-Myers-Squibb, Celgene, Pfizer, Harald Herkner: None declared, Josef S. Smolen Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB

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OP0230 EFFECTIVENESS OF INFLUENZA VACCINE IN TNF INHIBITORS TREATED PATIENTS

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Background: Tumor Necrosis Factor-α inhibitors (TNFi) are immunosuppressive therapies that are known to increase infectious risk. Indeed, patients affected by TNFi requiring conditions are at higher risk of influenza compared with healthy controls. Furthermore, mildly reduced seroconversion rate after influenza vaccination had been reported in TNFi-treated patients. Nonetheless the immune response is considered large enough to recommend influenza vaccination in all patients affected by rheumatoid arthritis, regardless of treatment. However, there are data showing that patients are not being vaccinated as recommended. In addition, given that subjects with autoimmune conditions treated with TNFi are at higher risk for influenza, the exact number needed to vaccinate (NNV) for this condition is still unknown.

Objectives: We sought to determine the NNV for influenza in TNFi treated patients and the cost for preventing one case of influenza compared with general population.

Methods: The present analysis included data from cohorts of healthy subjects [1] and TNFi treated patients [2]. We calculated NNV for preventing one case of influenza in each cohort. NNV is the required number of patients receiving vaccination to prevent one case of a given infectious disease. NNV is the inverse of the absolute risk reduction (ARR), which is calculated as following: Control Event Rate (CER) – Experimental Event Rate (EER). In addition, the NNV gives us the opportunity to calculate the cost for preventing one case of influenza, assuming a cost per vaccine from 20 to 40 $.

Results: In 71,221 healthy individuals influenza vaccination reduced influenza rate from 2.3% in individuals without vaccination (CER = 0.023) to 0.9% in vaccinated individuals (EER = 0.009). The calculated NNV is 71 (NNV = 1/ARR, ARR = 0.023 – 0.009), namely 71 healthy adults need to be vaccinated to prevent one of them experiencing influenza. The costs to prevent a case of clinical influenza in healthy controls would range from 1,420 to 2,840 $. On 15,132 patients exposed to adalimumab, influenza-related adverse events have been reported in 55 of 382 not-vaccinated patients (CER = 0.14) and in 8 of 179 vaccinated patients (EER = 0.04). In this population (mean age 53.5 years, predominantly white women) the NNV of influenza vaccines is 10 (NNV = 1/ARR, ARR = 0.144 – 0.045) and preventing a case of influenza would cost approximately from 200 to 400 $, which is largely lower when compared to healthy controls' costs. The relative risk of influenza vaccination in healthy individuals (2.3% to 0.9%, RR 0.41, 95% confidence interval (CI) 0.36 to 0.47) and rheumatoid arthritis patients treated with TNFi (14.4% to 4.5%, RR 0.31, 95% CI 0.15 to 0.64) are similar, while there is a large difference between NNVs (71 vs 10) (**Figure 1**).

Conclusion: When estimating the effectiveness of vaccinations, clinicians should always include the calculation of the NNV and not only the calculation of relative risk, which might be misleading. The difference in NNV for influenza between healthy individuals and TNFi treated patients is due to a greater absolute risk for influenza in the latter group. The present analysis provides further evidences on the effectiveness of influenza vaccination in patients affected by rheumatoid arthritis receiving treatment with TNFi and should represent a call-to-action for all rheumatologists to consider vaccination in such patients.

REFERENCES:

[1] Burmester GR, et al. Adalimumab long-term safety: infections, vaccination response and pregnancy outcomes in patients with rheumatoid arthritis. Ann Rheum Dis 2017;76:414–7

[2] Demicheli V, et al. Vaccines for preventing influenza in healthy adults. Cochrane Database Syst Rev 2018;2:CD001269

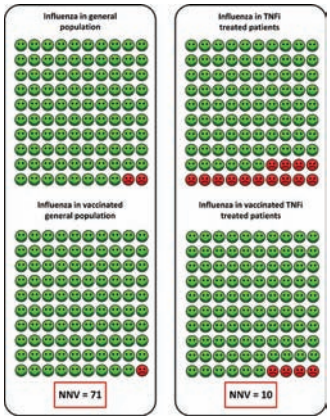


Figure 1. Number Needed to Vaccinate (NNT) for influenza in the general population and in patients treated with Tumor Necrosis Factor-α inhibitors (TNFi)

Disclosure of Interests: Giovanni Adami: None declared, Angelo Fassio Speakers bureau: Abiogen Pharma, Giovanni Orsolini Speakers bureau: Grunenthal, Alessandro Giollo: None declared, Davide Gatti Speakers bureau: Abiogen, Amgen, Janssen-Cilag, Mundipharma, Pfeizer, Maurizio Rossini: None declared

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FRIDAY, 14 JUNE 2019

How to treat SpA? From physiotherapy to new IL-17 blocking drugs

OP0231

DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH BIMEKIZUMAB WAS ASSOCIATED WITH IMPROVEMENTS IN PATIENT-REPORTED AND QUALITY-OF-LIFE OUTCOMES IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

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Background: Ankylosing spondylitis (AS) is a chronic immune-mediated inflammatory disease primarily affecting the sacroiliac joints and spine, causing pain, stiffness and loss of mobility and function. These manifestations can severely impair patients' quality of life (QoL).[1] Dual neutralisation of IL–17F in addition to IL-17A has been shown to reduce inflammation to a greater extent than inhibition of IL-17A alone in disease–relevant cell models.[2] Results previously reported from this Phase 2b study (NCT02963506) demonstrated that, during the 12-week double-blind treatment period, bimekizumab provided substantial clinical improvements in disease outcome measures, including Assessment of SpondyloArthritis international Society 40% (ASAS40), in patients with active AS.[3]

Objectives: To assess the impact of bimekizumab on patient-reported and QoL outcomes at Week 12 in patients with active AS.

Methods: In this 48-week Phase 2b study (double blind to Week 12 then dose blind to Week 48), 303 patients with active AS (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] $\geq$4; spinal pain $\geq$4 [0–10 numerical rating scale]), fulfilling the modified New York criteria, were randomised 1:1:1:1:1 to receive subcutaneous bimekizumab 16mg, 64mg, 160mg, 320mg or placebo Q4W for 12 weeks. Prior exposure to one anti-TNF therapy was permitted. Secondary and other endpoints included: BASDAI, $\geq$50% improvement in BASDAI (BASDAI 50), Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Quality of Life (ASQoL) and Patient's Global Assessment of Disease Activity (PGADA) at Week 12. Safety was also assessed.

Results: Overall, 297 (98.0%) patients completed the 12-week double-blind period. Baseline scores on patient-reported and QoL outcomes were similar across treatment groups (Table). At Week 12, BASDAI 50 was achieved by 23.7–47.5% of bimekizumab-treated patients versus 11.9% receiving placebo. All bimekizumab doses were associated with greater reductions in individual BASDAI components, including: fatigue (range: -1.6 to –2.5 vs -0.8); neck, back or hip pain (-2.0 to -3.3 vs -1.2); discomfort due to tenderness to touch or pressure (-1.6 to -3.0 vs -1.1); level of morning stiffness (-2.5 to -3.5 vs -1.2) and duration of morning stiffness (-1.7 to -3.3 vs -1.4) (Table). Compared with placebo, greater reductions from baseline were also achieved with bimekizumab for BASFI (-1.4 to -2.2 vs –0.6), ASQoL (-2.3 to -4.6 vs -1.3) and PGADA (-1.9 to -3.3 vs -1.0). The overall incidence of treatment-emergent adverse events was 89/243 (36.6%) for bimekizumab-treated patients versus 23/60 (38.3%) for placebo; the majority were of mild or moderate intensity. No unexpected safety findings were observed.

Table. Disease outcome measures at baseline and Week 12 (full analysis set)

Mean (SD)	Placebo (n=60)	Bimekizumab 16mg (n=61)	Bimekizumab 64mg (n=61)	Bimekizumab 160mg (n=62)	Bimekizumab 320mg (n=61)
BASDAI: fatigue					
Baseline	6.7 (1.6)	7.1 (1.6)	6.8 (1.3)	6.3 (1.8)	6.4 (1.9)
Week 12	5.8 (3.1)	5.5 (2.2)	4.3 (2.5)	4.3 (2.5)	4.4 (2.4)
BASDAI: neck/back/hip pain					
Baseline	7.4 (1.6)	7.7 (1.2)	7.7 (1.2)	7.0 (1.7)	7.5 (1.5)
Week 12	6.3 (2.5)	5.8 (2.4)	4.5 (2.4)	4.4 (2.5)	4.2 (2.4)
BASDAI: discomfort due to tenderness to touch/pressure					
Baseline	5.9 (2.1)	6.2 (2.4)	6.2 (2.0)	5.5 (2.3)	6.2 (2.3)
Week 12	4.9 (2.8)	4.6 (2.5)	3.6 (2.4)	3.3 (2.5)	3.2 (2.5)
BASDAI: level of morning stiffness					
Baseline	7.3 (1.8)	7.3 (2.0)	7.3 (1.9)	6.8 (2.0)	7.1 (2.1)
Week 12	6.2 (2.4)	4.8 (2.6)	4.0 (2.5)	4.1 (2.4)	3.6 (2.4)
BASDAI: duration of morning stiffness					
Baseline	6.3 (2.4)	5.9 (2.5)	6.4 (2.6)	6.0 (2.3)	6.1 (2.6)
Week 12	5.0 (2.6)	4.1 (2.6)	3.4 (2.4)	3.3 (2.3)	2.9 (2.0)
BASFI: overall score					
Baseline	5.6 (2.3)	5.9 (1.7)	6.0 (1.9)	5.9 (2.2)	5.9 (2.0)
Week 12	5.0 (3.4)	4.5 (2.4)	4.1 (2.4)	3.8 (2.2)	3.7 (2.5)
ASQoL					
Baseline	8.9 (4.7)	8.9 (4.2)	8.6 (4.1)	8.5 (4.3)	8.7 (4.3)
Week 12	7.6 (5.2)	6.6 (5.5)	4.5 (3.5)	4.9 (4.5)	4.1 (4.1)
PGADA					
Baseline	7.0 (1.7)	7.1 (1.5)	7.3 (1.6)	6.9 (1.4)	7.1 (1.6)
Week 12	6.0 (2.4)	5.3 (2.3)	4.0 (2.2)	4.3 (2.5)	3.9 (2.2)

In numbers shown are group totals or randomisation. Multiple imputation data presented for ASQoL, observed data are presented for BASDAI, BASFI and PGADA. ASQoL, Ankylosing Spondylitis Quality of Life; BASDAI, Bath Ankylosing Spondylitis Disease Severity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; PGADA, Patient's Global Assessment of Disease Activity; SD, standard deviation.

Conclusion: Dual neutralisation of IL-17A and IL-17F with bimekizumab was associated with improvements in patient-reported and QoL outcomes including pain, fatigue and tenderness in patients with active AS after 12 weeks of treatment. No new safety findings were observed versus previous studies of bimekizumab.[3,4]

REFERENCE:

[1] Kotsis *Expert Rev Pharmacoecon Outcomes Res* 2014;14:857–72; 2Glatt *Ann Rheum Dis* 2018;77:523–32; 3van der Heijde *Ann Rheum Med* 2018;77(Suppl 2):70.

Disclosure of Interests:

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OP0232

NETAKIMAB REDUCES THE DISEASE ACTIVITY OF RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS. RESULTS OF ASTERA STUDY

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Background: Efficacy and safety of netakimab (NTK), a humanized anti-IL17A antibody, was established in phase 2 clinical trials in patients (pts) with radiographic axial spondyloarthritis (r-axSpA)[1] and psoriasis[2].

Objectives: The abstract presents 16-week data from ongoing ASTERA study (NCT03447704) in pts with active r-axSpA.

Methods: ASTERA is a phase 3 international double-blind placebo (PBO)-controlled study. 228 adult pts with r-axSpA, active (BASDAI $\geq$ 4) despite the standard NSAIDs, were randomly assigned (1:1) to receive 120 mg NTK or PBO SC at Week (Wk) 0,1,2 and then q2w through Wk 16. After Wk 16 all pts will start to receive NTK up to Wk 52. Primary endpoint was ASAS40 rate at Wk 16.

Results: The mean age at baseline was 39.14±9.9 years, the mean symptoms duration was 4.3±4.5 years. 76.8% of pts were naïve to biological treatment. At Wk 16 ASAS40 rate was higher in NTK arm compared to PBO: 40.35% versus (vs.) 2.63% pts (95% CI for the difference in ASAS40 rate was [27.37%; 48.07%] (p<0.0001, Figure 1). Efficacy of NTK was also proved by comparison of secondary endpoints (Figure 2); improvement in BASDAI, MASES, BASFI became significant from Wk 4 and remained during the study (no data presented). Most reported adverse events (AE) and treatment-related AEs (TRAE) were mild/moderate (Table 1). The most frequent AEs were anemia, neutropenia, ALT increase. One serious AE (SAE), not related to the treatment (bone fracture), was reported in NTK arm.

Conclusion: NTK at a dose 120 mg is well-tolerated drug with favorable safety profile that leads to decline in r-axSpA activity, function improvement and axial mobility in 16 Wks.

REFERENCES:

[1] Mazurov V, *et al. Ann Rheum Dis* 2018;77:A64. 2Samtsov A, *et al. Vestn Dermatol Venerol* 2017;0(5):52-63.

Table 1. Safety data

% of patients with	NTK (n = 114)	PBO (n = 114)	p-value
AE/SAE	33.3% (38)	25.4% (29)	0.245
TRAE	17.5% (20)	14.0% (16)	0.586
SAE	0.9% (1)	0	1.0
Grade 3-4 AEs	2.6% (3)	3.5% (4)	1.0
Grade 3-4 TRAEs	1.8% (2)	1.8% (2)	1.0
Local reactions	1.8% (2)	0.9% (1)	1.0

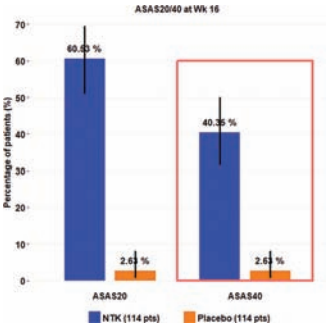


Figure 1

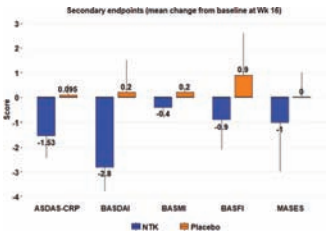


Figure 2

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OP0233

THE IMPACT OF EXTRA-ARTICULAR MANIFESTATIONS ON THE CHOICE OF TNF INHIBITOR IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN THE BSRBR-AS REGISTER

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Background: Axial spondyloarthritis (axSpA) is associated with important extra-articular manifestations (EAMS), most notably acute anterior uveitis (AAU), inflammatory bowel disease (IBD) and psoriasis, which may influence the choice of biologic agent used to treat axSpA.

Objectives: To examine the factors associated with choice of 1st TNF inhibitor (TNFi) for the treatment of axSpA.

Methods: Clinical and patients-reported outcomes of 2420 patients with axSpA from 83 rheumatology centres in the United Kingdom were collected as part of the British Society for Rheumatology Biologics Register in Ankylosing Spondylitis (BSRBR-AS). History of pre-treatment AAU, IBD and psoriasis were analysed to explore their association with the choice of 1st TNFi. This preference was also examined in relation to other demographic and background factors. These associations were analysed using univariable and multivariable logistic regression models, considering necessary interaction terms.

Results: First-line biologic data was available for 441 patients, compromising of 284 (64.4%) adalimumab (ADA), 109 (24,7%) etanercept (ETA) and 48 (10.9%) certolizumab (CZP). Pre-treatment EAMS in the entire cohort were 568 cases of AAU, 247 IBD and 264 psoriasis.

Prior diagnosis of AAU was associated with a choice of ADA over the other TNFi (ETA and CZP) [OR=3.13, 95% CI: 1.78 – 5.52). Conversely, a diagnosis of AAU was associated with less preference for ETA (OR=0.16, 95% CI: 0.07 – 0.37) compared with ADA and CZP.

The choice of a particular TNFi was not associated with HLA-B27, age, gender, axSpA disease duration, BASDAI or BASFI scores.

When IBD and psoriasis, and interactions with AAU, were considered in multivariable models (Table), a diagnosis of either AAU or IBD was associated with more preference of ADA versus other TNFi. In contrast, diagnosis of either AAU or IBD was associated with significantly less preference of ETA over other TNFi. The preference of CZP was not associated with presence any pre-treatment extra-articular manifestations.

Table 1. Pre-treatment extra-articular manifestations and the choice of 1st TNFi

		Wald	*p* value	OR	95% CI for OR
ADA vs. others	Acute Anterior Uveitis (AAU)	19.91	<0.001	3.79	2.11 - 6.80
	Inflammatory Bowel Diseases (IBD)	11.93	0.001	5.50	2.09 - 14.46
	Psoriasis	0.17	0.684	1.15	0.58 - 2.28
	Constant	3.08	0.079	1.23	
ETA vs. others	AAU	20.41	<0.001	0.14	0.06 - 0.33
	IBD	8.34	0.004	0.17	0.05 - 0.57
	Psoriasis	1.02	0.313	0.67	0.30 - 1.47
	Constant	27.38	<0.001	0.52	
CZP vs. others	AAU	0.01	0.959	1.02	0.48 - 2.16
	IBD	1.50	0.221	0.40	0.09 - 1.74
	Psoriasis	0.65	0.420	1.47	0.58 - 3.73
	Constant	126.09	<0.001	0.12	

Conclusion: EAMs appear to play an important role in the choice of TNFi in axSpA. Patients with previous AAU and IBD are more likely to be prescribed ADA

and less likely to receive ETA, consistent with the superior efficacy of monoclonal TNFi for these conditions. The presence or absence of EAMS did not influence the use of CZP, although small sample size might explain the lack of associations. Future work will determine whether EAMS influence TNFi survival, or effectiveness, and whether this varies between agents.

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OP0234 EFFICACY AND SAFETY OF BRODALUMAB, AN ANTI-INTERLEUKIN-17 RECEPTOR A MONOCLONAL ANTIBODY, IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A 16 WEEK RESULTS OF A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Background: It is known that clinical features and pathophysiological pathways of ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) have similarities. Recent reports suggest that IL-17 signaling pathway may be involved in development of axial spondyloarthritis (axSpA). Here we reported the confirmatory phase 3 trial of brodalumab, a human anti-interleukin-17 receptor A monoclonal antibody, in patients with axSpA (4827-006 Study, NCT02985983).
Objectives: To evaluate the efficacy and safety of brodalumab in axSpA (including AS and nr-axSpA) patients at week 16.
Methods: In this phase 3, multicenter, randomized, double-blind, placebo-controlled study conducted in Japan, South Korea and Taiwan, eligible axSpA patients were randomized 1:1 to brodalumab subcutaneously (s.c.) 210 mg or placebo at baseline, weeks 1 and 2, every 2 weeks thereafter. At week 16, all subjects entered an open label extension phase and received brodalumab 210 mg s.c. Q2W. ASAS 40 (Assessment of SpondyloArthritis international Society) response rate at week 16 was the primary endpoint. Secondary outcomes and safety profiles were also assessed.
Results: A total of 159 patients were randomized, and 77/80 patients in brodalumab arm and 69/79 patients in placebo arm were completed the 16 weeks' double-blind phase study. The ASAS 40 response rate at week 16 was significantly higher in brodalumab group (35/80, 43.8%, p=0.018) compared to placebo group (19/79, 24.1%). Other disease activity parameters demonstrated trend to improvement in therapeutic arm (Table). Brodalumab 210 mg had good safety profile. Most commonly reported adverse event was nasopharyngitis observed in both brodalumab (11.1%) and placebo (10.3%) arms. AE rates including SAE rates were comparable between groups. No suicidal ideation or behavior were observed.
Conclusion: Brodalumab s.c. 210 mg Q2W treatment was effective and tolerable in axSpA patients in this 16 week phase 3 clinical trial. Based on the ongoing trial results, brodalumab could be considered as a future therapeutic option for patients with axSpA.

Table 1. Summary of efficacy result at Week 16 (FAS)

Efficacy End Points	axSpA (N=159)	
	Placebo (N=79)	210 mg Brodalumab (N=80)
ASAS 40 Response at Week 16 (NRI), n (%)	19 (24.1)	35 (43.8, p=0.018)
ASAS 20 Response at Week 16 (NRI), n (%)	33 (41.8)	54 (67.5)
ASDAS-CRP change from baseline at Week 16 (BOCF), LS mean	-0.672	-1.127
BASDAI change from baseline at Week 16, Mean	-2.4	-2.9
BASFI change from baseline at Week 16, Mean	-0.7	-1.1

FAS, Full Analysis Set; NRI, Non responder inputation; BOCF, Baseline Observation Carried Forward; LS mean is based on ANCOVA model adjusted with the baseline, treatment group, strata of CRP level at screening (>= ULN and < ULN), region (Japan, Korea, Taiwan), and disease subpopulations (AS, nr-axSpA).

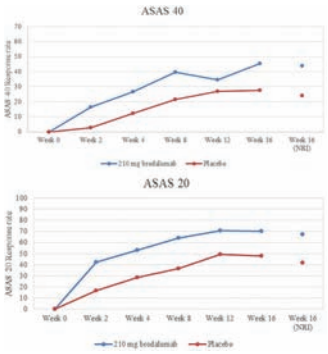


Figure. ASAS 20/40 response rate

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OP0235 SECUKINUMAB IMPROVES AXIAL MANIFESTATIONS IN PATIENTS WITH PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO NSAIDS: PRIMARY ANALYSIS OF THE MAXIMISE TRIAL

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Background: Secukinumab (SEC) has provided significant and sustained improvement in the signs and symptoms of active psoriatic arthritis (PsA) and ankylosing spondylitis [1]. Evidence on the efficacy of biologics in the treatment of PsA patients (pts) with axial manifestations affecting 30–70% of PsA pts is limited[2], particularly as validated classification criteria for this subtype of PsA are not yet available; an effort to develop criteria is being undertaken by ASAS/GRAPPA. MAXIMISE is an ongoing study evaluating the efficacy and safety of secukinumab 300 or 150mg in managing axial manifestations in PsA pts
Objectives: To report the primary analysis results at Week (Wk) 12 from MAXIMISE (NCT02721966) trial
Methods: This phase 3b, double blind, placebo (PBO)-controlled, multicentre 52-wk trial included 498 pts (aged ≥18 years) with PsA (CASPAR criteria), clinician-

diagnosed axial involvements, spinal pain VAS >40/100 and BASDAI >4 despite trial of at least two NSAIDs. Pts were randomised to subcutaneous (SC) SEC (300/150 mg) or PBO weekly for 4 wks and every 4 wks thereafter. At Wk 12, PBO pts were re-randomised to SC SEC 300/150 mg. The primary endpoint was proportion of pts achieving ASAS20 response with SEC 300 mg at Wk 12. The key secondary endpoint was ASAS20 response with SEC 150 mg at Wk 12 after superiority of 300 mg was established. Analyses used multiple imputation

Results: Demographic and baseline (BL) disease characteristics were comparable across groups (**Table**). Primary and key secondary endpoints were met; ASAS20 response rates at Wk 12 were 63.1% (SEC 300 mg; P<0.0001) and 66.3% (150 mg; P<0.0001) vs 31.3% (PBO; **Figure**). ASAS20 responses in pts using concomitant MTX were 65.1% [300 mg], 67.3% [150 mg] vs 33.9% [PBO] and corresponding values in No MTX group were 60.5%, 64.4% vs 27.1%. The safety profile was similar across groups through Wk 12

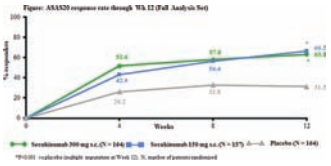
Conclusion: MAXIMISE is the first randomised controlled trial evaluating the efficacy of a biologic in the management of the axial manifestations of PsA. SEC 300 and 150 mg provided rapid and significant improvement in ASAS20 responses through Wk 12 in PsA pts with axial manifestations and inadequate responses to NSAIDs

REFERENCES:

[1] Lubrano E and Perrotta FM. Ther Clin Risk Manag. 2016;12:1587-92
[2] Feld J, et al. *Rheum Rev.*2018;14:363

Demographics/BL Characteristics			
Mean (SD) unless specified	**SEC 300 mg SC (N = 167)**	**SEC 150 mg SC (N = 165)**	**PBO (N = 166)**
Age (yrs)	46.2 (12.3)	46.9 (11.5)	46.6 (11.5)
Male, n (%)	77 (46.1)	81 (49.1)	88 (53.0)
Evidence of current psoriasis, n (%)	152 (91.0)	147 (89.1)	153 (92.2)
Time since first axial symptoms (yrs)	6.8 (7.7)	7.4 (7.6)	7.7 (9.5)
Total back pain score, VAS	72.5 (13.8)	73.6 (15.3)	74.0 (13.7)
Inflammatory back pain parameters, n (%)			
Onset of back pain is insidious	150 (89.8)	147 (89.1)	152 (91.6)
Back pain improving with exercise	148 (88.6)	139 (84.2)	146 (88.0)
Back pain worsening with rest	152 (91.0)	151 (91.5)	157 (94.6)
Night pain with improvement upon getting up	147 (88.0)	147 (89.1)	143 (86.1)
Awakening due to back pain in 2nd half of night	143 (85.6)	145 (87.9)	137 (82.5)
Alternating buttock pain	102 (61.1)	98 (59.4)	101 (60.8)
Back pain improved after NSAID intake in past	136 (81.4)	134 (81.2)	138 (83.1)
BASDAI	7.3 (1.2)	7.2 (1.4)	7.3 (1.2)
HLA-B27 positive, n/M (%)	31/85 (36.5)	24/82 (29.3)	26/74 (35.1)

M, number of pts with available HLA-B27 status



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OP0236

SIMILAR ONE-YEAR TREATMENT RETENTION OF ORIGINATOR AND BIOSIMILAR ETANERCEPT. RESULTS OF A NORDIC COLLABORATION INCLUDING 1015 PATIENTS WITH SPONDYLOARTHRITIS

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Background: The marketing approval of the etanercept biosimilar SB4 was based on phase III studies on patients with rheumatoid arthritis, but extended to all etanercept indications. Currently, no randomized controlled trials have compared etanercept originator (ETN) with SB4 in patients with spondyloarthritis (SpA). However, the uptake of etanercept biosimilars in the treatment of SpA has been exponential in the Nordic countries, with marked differences across the countries [1].

Objectives: To compare the one-year treatment retention in bio-naïve patients with SpA treated with ETN versus SB4. Furthermore, to explore baseline characteristics in the two patient groups.

Methods: Observational cohort study. Patients with SpA (ankylosing spondylitis (AS), non-radiographic axial SpA (nrax-SpA) or uSpA)), starting etanercept as their first ever TNFi Jan 2014 through Jun 2017 were identified in biologics registers in the five Nordic countries. Baseline characteristics were retrieved from each biological register and comorbidity data through linkage to national registers. The country-specific data were then pooled for further analysis. Comparisons of treatment retention between ETN and SB4 were assessed through survival probability curves and one-year retention rates.

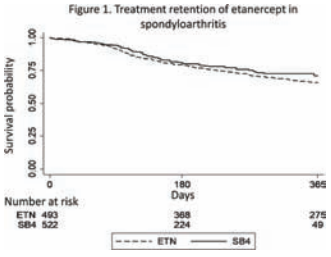
Results: In total, 1015 patients were included, whereof 49% started ETN and 51% SB4. Baseline characteristics were similar in the two patient groups (Table 1).

Table 1. Baseline characteristics of etanercept treated SpA patients

	ETN (N=493)	SB4 (N=522)
Age, years	41 (14)	41 (14)
Disease duration, years	12 (12)	11 (12)
Sex, men,%	48	50
AS,%	41	38
nrax-SpA or uSpA,%	59	62
Psoriasis*,%	7	5
Inflammatory bowel disease*,%	2	2
CRP, mg/L	11 (18)	10 (15)
VAS-pain, mm	59 (24)	59 (22)
ASDAS	3.05 (0.90)	2.98 (0.94)
BASDAI, mm	5.4(2.0)	5. 4 (1.9)
BASFI	4.1 (2.4)	4.1 (2.5)
Concomitant csDMARD,%	29	22

Numbers are means (standard deviations) unless otherwise stated
ETN=etanercept originator; SB4= etanercept biosimilar.
*) comorbidities only available from Sweden, Denmark and Finland.
csDMARD = conventional synthetic Disease Modifying anti-Rheumatic Drugs.

One-year survival probability curves were similar for ETN compared to SB4 (Figure 1), and the proportions of patients remaining on drug after one year were comparable: ETN 66% (95%CI: 61-70%) and SB4 73% (95%CI: 68-78%). Further confounder-adjusted analyses are planned and will be presented at the conference.



Conclusion: In this observational study of 1015 patients with SpA from five Nordic countries, biologics-naïve patients starting treatment with originator versus biosimilar etanercept had similar baseline characteristics and similar one-year treatment retention rates, suggesting similar effectiveness and tolerability of the two drugs.

REFERENCE:

[1] Glintborg, et al. Biological treatment in ankylosing spondylitis in the Nordic countries during 2010-2016: a collaboration between five biological registries. Scand J Rheumatol. 2018;47:465-74.

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OP0237 INTERLEUKIN-17 OR TNF BLOCKADE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AFTER WITHDRAWAL OF AT LEAST ONE TNF INHIBITOR

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Background: Secukinumab (SEC), an interleukin-17A inhibitor, is approved for the treatment of ankylosing spondylitis (AS) and has been integrated into the current treatment recommendations of patients with axial spondyloarthritis (axSpA) as an alternative to tumor necrosis factor inhibitors (TNFi). The optimal use of one mode of action over the other remains unclear and longitudinal real-life data are lacking to date.

Objectives: To compare drug survival of SEC versus TNFi in axSpA patients having previously stopped at least one TNFi in a large prospective cohort.

Methods: Patients with a clinical diagnosis of axSpA in the Swiss Clinical Quality Management cohort were included if they had previously stopped treatment with at least one TNFi, initiated therapy with either SEC or a next TNFi after approval of SEC and had a baseline clinical visit. Drug survival was evaluated by Cox proportional hazards models adjusted for sex, age, Bath ankylosing spondylitis disease activity index (BASDAI), Maastricht ankylosing spondylitis enthesitis score (MASES), proportion of patients with elevated CRP, number of previous TNFi and interaction between mode of action and number of previous TNFi.

Results: Baseline characteristics of 382 axSpA patients included (N=107 for SEC and N=275 for next TNFi) are shown in Table 1. The proportion of patients with $\geq$2 TNFi administered previously was significantly higher in the SEC group. Patients starting SEC had higher baseline disease activity, more enthesitis and greater impairment of spinal mobility, function and quality of life. A history of uveitis was more prevalent in the TNFi group. No differences between the groups could be detected with regards to the reason for discontinuation of the previous TNFi. Unadjusted median (interquartile range) drug maintenance was 1.1 (0.9; 1.3) years for SEC and 2.0 (1.7; 2.2) years for TNFi (p=0.03). The adjusted hazard ratio to stop SEC vs. TNFi in patients without missing data (N=233, 61%) was 1.05 (95% CI 0.42; 2.61; p=0.91) (Table 2).

Table 1. Baseline characteristics of axSpA patients having stopped $\geq$1 TNFi at start of a next biologic after approval of SEC in Switzerland, stratified by the mode of action.

Parameter	N	TNFi	SEC	p
	382	N=275	N=107	
Male sex,%	374	43.3	43.0	1.00
Age, years	382	45.3 (12.6)	45.7 (11.5)	0.81
Symptom duration, years	369	14.0 (10.8)	14.8 (11.3)	0.47
HLA-B27 positive,%	338	58.9	60.0	0.90
BASDAI	276	4.8 (2.1)	6.1 (1.9)	<0.001
ASDAS	239	2.7 (0.9)	3.5 (1.0)	<0.001
Elevated CRP,%	336	31.5	41.0	0.13
BASFI	266	3.0 (2.4)	4.9 (2.6)	<0.001
BASMI	205	1.8 (1.6)	2.6 (1.9)	0.01
Number of swollen joints	348	1.0 (3.0)	1.4 (3.7)	0.32
MASES	352	2.8 (3.3)	3.9 (3.9)	0.02
Uveitis ever,%	369	16.9	8.7	0.05
Psoriasis ever,%	366	9.8	13.0	0.45
Inflammatory bowel disease ever, %	371	10.6	4.7	0.10
$\geq$2 previous TNFi used,%	382	37.8	77.6	<0.001
Ineffectiveness of previous TNFi, %	334	60.7	67.3	0.24

Table 2. Multivariable adjusted cox regression model for drug survival of next biologic DMARD.

	HR	95% CI	p
Secukinumab vs. TNFi	1.05	0.42; 2.61	0.91
Age	1.01	0.99; 1.03	0.42
Female sex	1.60	0.98; 2.61	0.06
BASDAI	1.15	1.02; 1.31	0.03
Elevated CRP	1.15	0.71; 1.86	0.56
Number of previous TNFi	0.83	0.61; 1.13	0.23
Interaction between bDMARD mode of action and number of previous TNFi	1.20	0.83; 1.73	0.34

Conclusion: SEC was predominantly initiated in axSpA after use of at least 2 TNFi. Patients starting SEC had a higher mean disease activity than patients starting a next TNFi. Adjusted drug survival after previous withdrawal of TNFi was comparable for SEC or a next TNFi.

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OP0238 WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT AMONG PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS/RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND TREATED WITH IXEKIZUMAB FOR 16 WEEKS: RESULTS FROM COAST-V AND COAST-W

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Background: Axial spondyloarthritis (axSpA) negatively impacts work productivity and IL-17A antagonists, such as ixekizumab (IXE), may improve paid and unpaid work productivity.[1,2] Also, it is unknown if improvements with IXE differ between biologic-naïve and TNF inhibitor (TNFi) experienced patients.

Objectives: We investigated the effect of IXE treatment for 16-weeks on work productivity and activity impairment among patients with radiographic axSpA (r-axSpA) using data from the biologic-naïve and TNFi-experienced patients receiving either placebo (PBO), IXE, or adalimumab (ADA; if biologic-naïve).

Methods: Both COAST-V and COAST-W investigated the efficacy and safety of IXE among patients with r-axSpA that either were biologic-naïve patients (COAST-V, NCT02696785) or TNFi-experienced patients (COAST-W, NCT02696798), as defined by prior inadequate response or intolerance to 1 or 2 TNFi. Patients were required to have a diagnosis of axSpA. Patients fulfilled ASAS criteria for r-axSpA and mNY criteria for ankylosing spondylitis. Active disease was defined by BASDAI $\geq$4 and back pain $\geq$4 on a numeric ratings scale (NRS).[1,2] Full eligibility criteria were previously reported.[1,2]Patients were treated with placebo (PBO), 40-mg adalimumab (ADA) every 2 weeks (Q2W; COAST-V only), 80-mg IXE Q2W (IXEQ2W) or every 4 weeks (IXEQ4W) for 16 weeks. Work productivity was investigated using the Work Productivity and Activity Impairment Questionnaire for Ankylosing Spondylitis (WPAI:SpA). Individual and integrated

study data were analyzed using analysis of covariance models. Results reported as least squares mean (LSM) change from baseline±standard error (SE). Integrated data of COAST-V and -W were analyzed for inferential statistics due to small sample sizes in the individual studies. ADA was included in COAST-V as an active reference arm only, and the study was not powered to allow comparisons between the IXE and ADA arms.

Results: Overall, 365 (64.5%) PBO- and IXE-treated patients reported paid work (part-time or full-time) at baseline in COAST-V and COAST-W. Based on integrated data, Absenteeism was significantly lower in IXEQ2W treated patients than PBO and Presenteeism, Work Productivity Loss, and Activity Impairment were significantly reduced in IXEQ2W and IXEQ4W treated patients versus PBO (Table 1). WPAI-SpA outcomes for biologic-naïve and TNFi-experienced were similar with some exceptions (Table 2). The active reference arm (ADA) exhibited numerical improvements for presenteeism, work productivity, and activity impairment versus PBO.

Table 1. Integrated WPAI:SpA results for patients with r-axSpA

	PBO	IXEQ2W	IXEQ4W
Absenteeism	-1.7±1.7 n=107	-7.3±1.8* n=96	-1.5±1.7 n=104
Presenteeism	-14.0±2.3 n=104	-24.0±2.4** n=90	-22.0±2.3* n=99
Work Productivity Loss	-14.7±2.4 n=104	-24.9±2.5** n=90	-22.0±2.4* n=99
Activity Impairment	-13.2±1.7 n=185	-22.4±1.7*** n=179	-20.8±1.7** n=192

*p<.05, **p<.01, ***p<.001, all vs PBO

IXEQ2W = ixekizumab every 2 weeks; IXEQ4W = ixekizumab every 4 weeks; n = number of patients in the analysis category; PBO = placebo

Table 2. WPAI:SpA results for biologic-naïve and TNFi-experienced patients with r-axSpA

	PBO	IXEQ2W	IXEQ4W	ADA
Biologic Naive (COAST-V)				
Absenteeism	-1.3±2.3 n=50	-6.7±2.3 n=49	1.2±2.2 n=57	-1.2±2.0 n=65
Presenteeism	-17.7±3.1 n=50	-23.3±3.1 n=47	-22.7±2.9 n=55	-20.9±2.8 n=60
Work Productivity Loss	-17.8±3.3 n=50	-24.1±3.3 n=47	-21.4±3.1 n=55	-21.4±2.9 n=60
Activity Impairment	-14.1±2.3 n=86	-23.4±2.3 n=83	-23.0±2.4 n=80	-21.1±2.2 n=88
TNFi Experienced (COAST-W)				
Absenteeism	-1.2±2.8 n=57	-6.9±3.1 n=46	-4.7±2.9 n=47	
Presenteeism	-8.9±3.6 n=54	-22.2±4.1 n=43	-19.5±3.9 n=44	
Work Productivity Loss	-9.8±3.7 n=54	-23.5±4.2 n=43	-21.0±4.0 n=44	
Activity Impairment	-10.1±2.6 n=99	-18.4±2.7 n=96	-16.5±2.4 n=112	

IXEQ2W = ixekizumab every 2 weeks; IXEQ4W = ixekizumab every 4 weeks; n = number of patients in the analysis category; PBO = placebo

Conclusion: In this integrated analysis of patients with active r-axSpA, IXE treatment for 16 weeks yielded significant improvements in work productivity and activity impairment versus PBO. The effect is similar in biologic-naïve and TNFi-experienced patients. A limitation for evaluations of work productivity in the individual studies was the relatively low number of employed patients.

REFERENCES:

[1] Van der Heijde, et al. Lancet. 2018.
[2] Deodhar, et al. Arthritis Rheumatol. 2018.

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FRIDAY, 14 JUNE 2019

SSc and Myositis – novel therapeutic options

OP0239

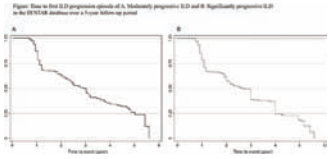
PROGRESSIVE LUNG FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE IN THE EUSTAR DATABASE

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Background: Some patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) develop progressive ILD, but the prevalence is unknown and no validated algorithms for early detection exist.

Objectives: To assess the frequency of, and parameters associated with, progressive SSc-ILD in the EUSTAR database.

Methods: Patients from the EUSTAR database registered after 2010, ≥18 yrs old, fulfilling SSc classification criteria, with serial lung function, HRCT assessments and disease duration recordings were eligible. Progressive ILD, assessed as absolute changes in%predicted, was defined as: significantly progressive (FVC decline >10% or FVC decline 5−10% and DL_{CO} decline ≥15%); moderately progressive (FVC decline 5−10%); or stable (<5% FVC change in either direction). Lung fibrosis changes from baseline to 12±3 months, disease course and cumulative frequency of progressive ILD during the 5-yr follow-up were assessed. Candidate predictors of significant progressive ILD were selected by expert opinion, and logistic regression applied. Time to event was evaluated by Kaplan-Meier estimates.



Results: 826 SSc-ILD patients were included; 219/826 (26.5%) showed moderate/significant ILD progression at 12±3 months' follow-up. Baseline FVC, erythrocyte sedimentation rate, modified Rodnan skin score (mRSS), GERD and disease duration were significantly associated with significant progressive fibrosis in uni- and multivariable modelling (area under curve 0.67). Serial lung function data with median follow-up of 5 yrs were available in 411/826 (49.8%) patients. In 128/411 with initial progressive ILD at 12±3 months, 59/128 (46.1%) showed further progression, while 69/128 (53.9%) were stable. Baseline FVC, mRSS and disease duration were significantly associated with further ILD progression. The incident cumulative frequency of moderate and significant ILD progression was 22.9% (n=189/826) and 28.5% (n=235/826) during the median 5-yr follow-up and time to first progressive event (Figure).

Conclusion: This study provides novel insights into the frequency, severity and association of progressive fibrosis in patients with SSc-ILD in the EUSTAR database.

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Actelion, Bayer, BMS, Boehringer, Roche, Sanofi, Margarida Alves Employee of: Employee of Boehringer Ingelheim, Nicole Graf Grant/research support from: Received consulting fees or other remuneration from Astellas and Biotronik, Paolo Airò: None declared, Lidia P. Ananyeva: None declared, László Czirják: None declared, Serena Guiducci: None declared, Eric Hachulla Consultant for: Received consulting fees or other remuneration from Actelion, GSK, Pfizer, and Bayer, Mengtao Li: None declared, Carina Mihai Consultant for: Received consulting fees or other remuneration from Actelion, Geneva, Roche, and Rofarm, Consultant for: F. Hoffmann-La Roche, Actelion, Geneva Romfarm, Gabriela Riemekasten Consultant for: Chugai, F. Hoffmann-La Roche, Speakers bureau: Chugai, F. Hoffmann-La Roche, Petros Sfikakis: None declared, Gabriele Valentini Grant/research support from: Received research funding and other remuneration from AbbVie, BMS, Lilly, Pfizer, and Sanofi, Consultant for: Received consulting fees and other remuneration from AbbVie, BMS, Lilly, Pfizer, and Sanofi, Otylia Kowal-Bielecka Consultant for: Received consulting fees or other remuneration from Bayer, Boehringer Ingelheim, Inventiva, Medac, Novartis, and Roche, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders

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OP0240

ASSESSMENT OF PULSE WAVE VELOCITY IN SYSTEMIC SCLEROSIS: POTENTIAL BENEFICIAL EFFECTS OF BOSENTAN ON FOREARM ARTERIAL STIFFNESS? AN EXPLORATORY STUDY

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Background: Systemic sclerosis (SSc)-related vasculopathy is generally thought to occur on a microvascular level. However, some observations also suggest involvement of arterial vessels. Macrovascular involvement (e.g., aorta or upper extremity) can be non-invasively assessed by measuring pulse wave velocity (PWV). Although, several studies have assessed aortic and upper extremity PWV in SSc, studies have not reached a consensus regarding this matter. Furthermore, we hypothesized that the endothelin antagonist bosentan may improve arterial stiffness by its direct endothelial and potential anti-fibrotic effects.

Objectives: The aim of this exploratory study was two-fold. First, we aimed to compare arterial stiffness in patients with SSc and age and sex-matched healthy controls (HC). Secondly, we will investigate the effect of bosentan on both short-term (three month) and long-term (one year) PWV.

Methods: Baseline differences between HC and SSc patients were studied in a case-control design. The follow-up of SSc patients was a randomized, prospective, 2-arm parallel group, open-label, (usual care with bosentan versus usual care only), blinded endpoint, intervention study. PWV (Sphygmocor) in meters/second, was measured to assess arterial stiffness in the aorta (carotid-femoral PWV), upper arm (carotid-brachial PWV), and forearm (brachial-radial PWV), adjusted for mean arterial pressure.

Results: Baseline characteristics are shown in table 1. No significant differences were observed in PWV (at all sites) between HC and SSc patients. No effect of bosentan on aortic, and upper arm PWV was found. The change in forearm PWV was different between the groups, with a decrease (e.g. lowering arterial stiffness) in the bosentan group (figure 1).

Table 1. Baseline characteristics

	Healthy controls (n=19)	Systemic sclerosis patients (n=19)	Bosentan group (n=9)	Usual care group (n=7)
Female, n (%)	13 (69)	13 (69)	5 (56)	6 (86)
Age in years, median (IQR)	53 (47–63)	50 (44–54)	52 (49–66)	44 (43–54)
Pack years, median (IQR)	0 (0–7.5)*	2.5 (0–30.6)*	17.3 (0.7–34.1)	0.8 (0–2.75)
Body mass index in kg/m², median (IQR)	25 (23–27)	25 (21–29)	25 (22–27)	26 (20–37)
Systolic blood pressure in mm Hg, median (IQR)	130 (121–137)	127 (123–134)	126 (117–142)	127 (123–132)
Diastolic blood pressure in mm Hg, median (IQR)	81 (72–88)	85 (79–89)	84 (76–87)	83 (79–85)
Raynaud's phenomenon duration in years, median (IQR)	N/A	8.0 (4.0-13.0)	1.0 (1.0–7.0)	13.0 (6.0–16.0)
Systemic sclerosis disease duration since first non-Raynaud symptom in years, median (IQR)	N/A	2.0 (1.0–7.0)	1.0 (1.0–7.5)	5.0 (2.0–14.0)

*difference between groups with a p<0.05

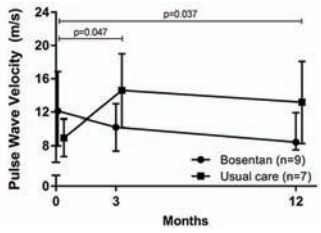


Figure 1. The median (IQR) of the brachial-radial pulse wave velocity over time of the bosentan and usual care group

Conclusion: This small study shows that aortic, upper arm, and forearm arterial stiffness does not appear to be increased in patients with SSc, as compared to age- and sex-matched healthy controls. To the best of our knowledge, this is the first study to investigate the concept of potential effects of an endothelin receptor antagonist on macrovascular involvement in SSc. Although the results demonstrate no effects on aorta and upper arm arterial stiffness, they may indicate a beneficial effect on the stiffness of the smaller arteries of the forearm. Future studies are needed to further investigate the potential effect of bosentan on these smaller arteries.

Acknowledgement: Actelion for co-funding the study

Disclosure of Interests: Anniek van Roon: None declared, Amaal Eman Abdulle : None declared, Saskia van de Zande: None declared, Arie Van Roon: None declared, Dan Zhang: None declared, Reinhard Bos Grant/research support from: SUN Pharma, Hendrika Bootsma Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant for: Roche, Bristol-Myers Squibb, Novartis, Medimmune, Union Chimique Belge, Speakers bureau: Bristol-Myers Squibb, Novartis, Andries Smit Shareholder of: Has been co-founder, and is still shareholder of Diagnoptics Technologies, the company which developed the AGE reader., Douwe J Mulder Grant/research support from: My University has received research grants for my research from: Boehringer Ingelheim and Actelion, Speakers bureau: My University has received speakers fee from: Sanofi

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OP0241

SAFETY AND EFFICACY OF LENABASUM IN AN OPEN-LABEL EXTENSION OF A PHASE 2 STUDY OF LENABASUM IN REFRACTORY SKIN-PREDOMINANT DERMATOMYOSITIS (DM) SUBJECTS

Victoria Werth[1,2], David Pearson[1,2], Joyce Owaka[1,2], Rui Feng[2], Josef Simon Concha[1,2], Basil Patel[1,2], Emily Hejazi[1,2], Caitlin Cornwall[3], Scott Constantine[3], Nancy Dgetluck[3], Barbara White[3]. *[1]Philadelphia Veteran Affairs Medical Center, Philadelphia, United States of America*; *[2]University of Pennsylvania, Philadelphia, United States of America*; *[3]Corbus Pharmaceuticals, Inc., Norwood, United States of America*

Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses. Lenabasum had acceptable safety and tolerability and improved efficacy outcomes in the initial 16-week double-blinded, randomized, placebo-controlled Part A of Phase 2 trial JBT101-DM-001 (NCT02466243) in dermatomyositis (DM) subjects with refractory, skin-predominant involvement.

Objectives: To provide long-term safety and efficacy data in DM subjects in this study.

Methods: Subjects who completed Part A were eligible to receive oral lenabasum 20 mg BID in an open-label extension (OLE) that assessed safety and efficacy at 4 weeks, then every 8 weeks.

Results: 20/22 (90.9%) eligible subjects received open-label lenabasum, following a mean interval of 31 weeks from end of Part A, during which when they received only standard-of care, to start of OLE during which lenabasum 20 mg BID was added. 17/20 (85.0%) subjects were on stable baseline

immunosuppressive drugs. At the time of data cut-off, all subjects who entered OLE completed 12 months of dosing.

Nineteen/20 (95%) of subjects experienced at least 1 AE, with 59 AEs occurring among the subjects during the OLE to date. The majority of AEs were mild (n = 16, 80%), with 1 severe AE (fatigue) considered unrelated to lenabasum reported. AEs occurring in ≥ 2 subjects were: dermatomyositis worsening, dizziness, fatigue, herpes zoster, nasopharyngitis, nausea, upper respiratory tract infection, and urinary tract infection. No serious AEs related to lenabasum have been reported.

Improvement was seen in multiple physician- and patient-reported efficacy outcomes; selected outcomes are presented in Figure 1. Mean (SE) changes from study start at Week 52 in the OLE were: CDASI activity score = -17.6 (SD), Patient Skin Activity VAS = -2.6 (SD); Skindex-29 Symptoms Domain = -21.6 (SD); Patient Itch VAS = -2.8 (SD); Physician Overall Disease VAS = -3.0 (SD); and Patient Pain VAS = - 2.3 (SD). Improvements were seen in other efficacy outcomes. 12 subjects had no changes in immunosuppressive drugs during the OLE, 3 reduced chronic steroids, 2 reduced mycophenolate, 3 were switched from methotrexate to mycophenolate, 1 started methotrexate, and 1 had a burst and taper of steroids.

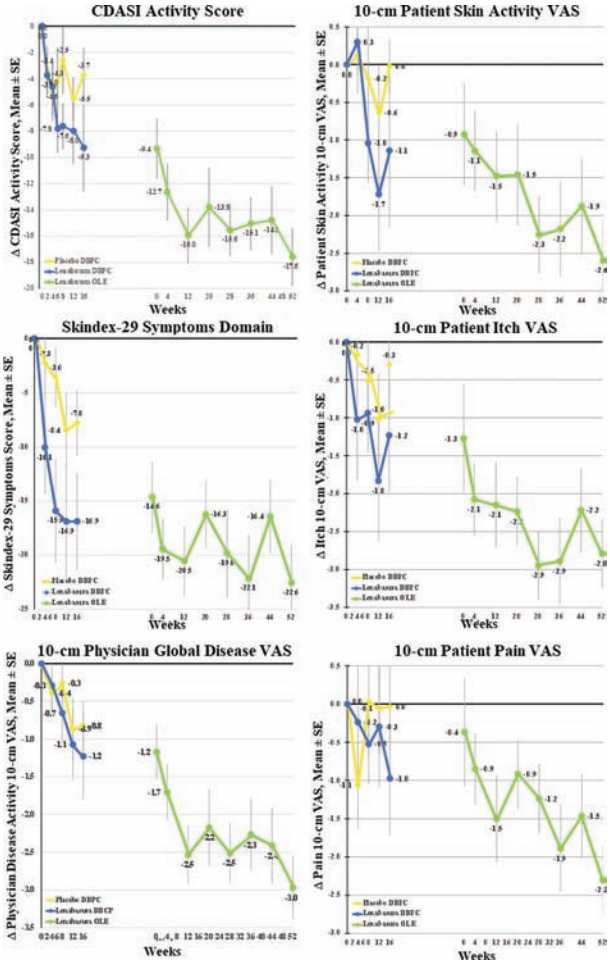


Figure 1. Change from Baseline in Selected Efficacy Outcomes in OLE of Phase 2 Trial JBT101-DM-001

Conclusion: : Lenabasum continues to have a favorable safety and tolerability profile in the OLE of the Phase 2 trial JBT101-DM-001 with no serious AEs or study discontinuations related to lenabasum. The CDASI activity score and multiple other physician and patient-reported outcomes improved, although limitations of attributing efficacy to lenabasum in the setting of open-label dosing is acknowledged. These data support further testing of lenabasum for the treatment of DM, and a Phase 3 study of lenabasum in DM has started.

Disclosure of Interests: : Victoria Werth: None declared, David Pearson: None declared, Joyce Owaka: None declared, Rui Feng: None declared, Josef Simon Concha: None declared, Basil Patel: None declared, Emily Hejazi: None declared, Caitlin Cornwall Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc., Scott Constantine Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc., Nancy Dgetluck Employee of: Corbus Pharmaceuticals, Inc., Barbara White Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc.

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OP0242 SAFETY PROFILE OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE AND IDIOPATHIC PULMONARY FIBROSIS

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Background: Nintedanib has been investigated in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) in the SENSCIS trial and idiopathic pulmonary fibrosis (IPF) in the two INPULSIS trials. These patient populations differ in age, sex, disease characteristics and comorbidities.

Objectives: To compare the safety and tolerability of nintedanib in patients with SSc-ILD and IPF.

Methods: Adverse events that occurred over 52 weeks of treatment in the SENSCIS and INPULSIS trials were assessed descriptively in subjects who received ≥1 dose of trial drug.

Results: A total of 576 subjects were treated in the SENSCIS trial (288 nintedanib; 288 placebo) and 1061 in the INPULSIS trials (638 nintedanib; 423 placebo). At baseline, mean (SD) age was 54.0 (12.2) and 66.8 (8.0) years in SENSCIS and INPULSIS, respectively. The proportion of males was 24.8% and 79.3%, respectively. Over 52 weeks, 19.4% and 10.8% of patients treated with nintedanib and placebo discontinued treatment in SENSCIS, compared with 24.5% and 18.9% of patients treated with nintedanib and placebo in INPULSIS. Gastrointestinal adverse events were the most frequently reported adverse events with nintedanib and, as expected based on the underlying disease, were more frequent in patients with SSc-ILD than IPF in both treatment groups (Table). Diarrhoea adverse events were reported in 75.7% and 31.6% of patients treated with nintedanib and placebo in SENSCIS, and 62.4% and 18.4% of patients treated with nintedanib and placebo in INPULSIS, respectively.

	SENSCIS		INPULSIS	
	Nintedanib (n=288)	Placebo (n=288)	Nintedanib (n=638)	Placebo (n=423)
Diarrhoea	218 (75.7)	91 (31.6)	398 (62.4)	78 (18.4)
Nausea	81 (31.6)	39 (13.5)	156 (24.5)	26 (6.1)
Vomiting	71 (24.7)	30 (10.4)	74 (11.6)	11 (2.6)
Nasopharyngitis	36 (12.5)	49 (17.0)	87 (13.6)	69 (16.3)
Cough	34 (11.8)	50 (18.1)	85 (13.3)	57 (13.5)
Weight decreased	34 (11.8)	12 (4.2)	62 (9.7)	15 (3.5)
Decreased appetite	27 (9.4)	12 (4.2)	69 (10.7)	24 (5.7)
Upper respiratory tract infection	33 (11.5)	35 (12.2)	58 (9.1)	42 (9.9)
Abdominal pain	33 (11.5)	21 (7.3)	56 (8.8)	10 (2.4)
Bronchitis	16 (5.6)	24 (8.3)	67 (10.5)	45 (10.6)
Fatigue	31 (10.8)	20 (6.9)	40 (6.3)	33 (7.8)
Dyspnoea	21 (7.3)	25 (8.7)	49 (7.7)	48 (11.3)
Progression of IPF*	0	0	64 (10.0)	61 (14.4)
Skin ulcer	53 (18.4)	50 (17.4)	1 (0.2)	0

Data shown are n (%) of patients with ≥1 such event. Table shows adverse events reported in >10% of patients in any of the treatment groups shown. Adverse events are listed by preferred term in the Medical Dictionary for Regulatory Activities (MedDRA). *Corresponds to MedDRA term 'IPF', which included disease worsening and acute exacerbations.

Conclusion: The safety and tolerability profile of nintedanib in patients with SSc-ILD is similar to that observed in patients with IPF.

Disclosure of Interests: DOI: 10.1136/annrheumdis-2019-eular.3237

OP0243 EFFICACY OF PIRFENIDONE IN SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE – A RANDOMISED CONTROLLED TRIAL

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Background: Interstitial lung disease (ILD) is a major cause of morbidity and mortality in systemic sclerosis(SSc).(1) Lung fibrosis in systemic sclerosis shares

similar pathogenesis as idiopathic pulmonary fibrosis.(2) Pirfenidone slows the decline in lung functions in idiopathic pulmonary fibrosis.(3) Therefore, pirfenidone may be efficacious in SSc-ILD.

Objectives: To compare the efficacy and safety of pirfenidone with placebo in SSc-ILD.

Methods: This was a double-blind, randomised, placebo controlled trial. We enrolled 34 consecutive subjects of SSc-ILD with forced vital capacity (FVC) >50% of predicted value and diffusing capacity of lung for carbon monoxide > 30% of predicted value. Subjects were randomly assigned in a ratio of 1:1 to receive either pirfenidone (n = 17) or placebo (n = 17) and followed up for 6 months. Pirfenidone was started at 600 mg/day and increased to 2400 mg/day over one month and continued for the trial period. Primary outcome was to compare the proportion of patients with stabilisation or improvement in lung functions (FVC). Secondary outcome was to compare the change in FVC, Mahler's dyspnea index, 6 minute walk distance (6MWD), modified Rodnan skin score (MRSS) and change in serum levels of tumour necrosis factor α (TNF-α) and tissue growth factor β (TGF-β) at the end of 6 months. Trial was registered with clinical trials registry of India (CTRI/2018/01/011449).

Results: By intention-to-treat analysis, 16 (94.1%) patients in treatment group showed stabilisation of lung function compared to 13 (76.5%) in control group (p = 0.335). The median change in FVC was -0.55% (IQR = -4.75% to 1.75%) and 1.0% (IQR = -8.5% to 5%) in the treatment and control groups respectively (p = 0.654). The median change in 6MWD was -15 (IQR = -42.5 – 13.75) meters and 0.0 (IQR = -50 – 30) meters in treatment and control groups respectively (p = 0.601). The median of focal scores for transitional dyspnea index in both the treatment and control groups were 3.0 (IQR = 0 – 3) (p = 0.838). Median change in MRSS was 0.0 (IQR = -2.0 – 1.0) and -1.0 (IQR = -4.0 – 0.0) in treatment and control groups (p = 0.828). Difference in TNF-α levels were -5.14 (IQR = -14.6 – 0.29) pg/ml in the treatment and -2.94 (IQR = -5.51 – -2.35) pg/ml control group (p = 0.918). Difference in TGF-β levels in the treatment and control groups were -186.73 (IQR = -731.43 – -64.6) pg/ml and 24.29 (IQR = -233.21 – 362.0) pg/ml respectively (p = 0.093). The mean tolerated dose of pirfenidone was 1700 ±644 mg/day. Adverse events were mild, most common among them were gastrointestinal followed by skin rashes. Only one serious gastrointestinal adverse effect was documented.

Conclusion: We failed to demonstrate a beneficial effect of pirfenidone over placebo in stabilising FVC, functional status, or skin disease after 6 months of therapy. A larger study with longer follow up period may be further required.

REFERENCES:

[1] Steen VD, Medsger TA. Changes in causes of death in systemic sclerosis, 1972–2002. Annals of the Rheumatic Diseases. 2007;66:940–4.

[2] Herzog EL, Mathur A, Tager AM, Feghali-Bostwick C, Schneider F, Varga J. Interstitial Lung Disease Associated With Systemic Sclerosis and Idiopathic Pulmonary Fibrosis. Arthritis Rheumatol. 2014;66:1967–78.

[3] Noble PW, Albera C, Bradford WZ, Costabel U, Glassberg MK, Kardatzke D, et al. Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomised trials. The Lancet. 2011;377:1760–9.

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Disclosure of Interests: None declared

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OP0244

EFFICACY AND SAFETY OF LOW-DOSE IL-2 IN PATIENTS WITH MULTIPLE MYOSITIS/ DERMATOMYOSITIS

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Background: Dermatomyositis (DM) and polymyositis (PM) are rare chronicinflammatory disorders with significant associated morbidityand mortality despite treatment [1, 2], characterized by subacute onset of proximal muscle weakness, elevated muscle enzymes, and inflammatory infiltrates on muscle biopsy. Although several hypotheses have been proposed for triggers of inflammation in the diseases [3], growing evidences have focused on the immune disorders [4]. However, the quantitative changes of lymphocyte subsets in DM/PM are unclear and whether low-dose IL-2 could rebalance the lymphocyte subsets and further benefit to remission disease activity of DM/PM patients is unknown.

Objectives: To investigate the quantitative status of peripheral blood lymphocyte subsets in the patients for the exploration of pathogenesis and evaluate the safety and efficacy of low-dose IL-2 therapy in patients with DM/PM.

Methods: From February 2016 to October 2018, total 147 patients with PM/DM and 128 gender and age matched healthy individuals were enrolled in this study. The absolute numbers of T, B, NK, CD4+T, CD8+T, Th1, Th2, Th17 and Treg cells in peripheral blood of these individuals were detected by flow cytometry combined with standard absolute counting beads. Patients in IL-2 group (n=31) were not only given traditional treatments, but injected subcutaneously human IL-2 (aldesleukin) at 50 WIU per day for a 5-day course. The demographic features, clinical manifestations and laboratory indicators were compared before and after the treatment.

Results: Patients with PM/DM had lower levels of Treg cells as well as T, CD4+T, CD8+T, Th1, Th2, and Th17 compared with those of the healthy controls (P < 0.05), which was correlated with disease activity(P < 0.05). After IL-2 administration, the absolute numbers of peripheral lymphocyte subsets in patients were significantly increased (P < 0.05), leading to a better remission compared with the patients received conventional therapy (P < 0.05).

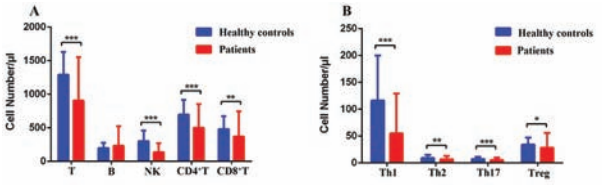


Figure 1: Comparison of absolute numbers of peripheral lymphocyte subsets between patients with PM/DM (n=147) and health controls (n=128). All the lymphocytes subpopulations were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired *t*-test. Patients had lower levels of T, NK,CD4+T, CD8+T, Th1, Th2, Th17 and Treg cells in PB compared with those of healthy controls. *P < 0.05, **P <0.01, ***P <0.001.

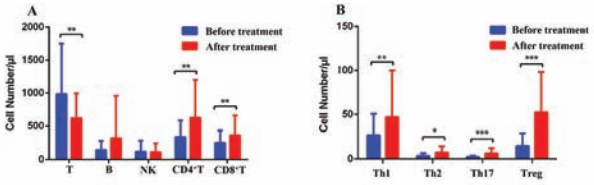


Figure 2: Changes of peripheral lymphocyte subsets after different treatments (n=31). Absolute numbers of T, CD4+T, CD8+T, Th1, Th2, Th17 and Treg cells in patients were significantly increased after treatment. *P<0.05, **P <0.01, ***P <0.001.

Conclusion: The difference status of peripheral lymphocyte subsets, especially Tregs, between PM/DM patients and healthy individuals suggests that lymphocyte subsets may be involved in and play an important role in the pathogenesis of patients. Low-dose IL-2 can effectively increase the level of Treg cells as well as other lymphocytes to some degree and maintain the immunologic balance, which may help for PM/DM patients' symptoms remission without over-treatment and evaluated side effect. But long-term benefits of IL-2 therapy are required to further study.

REFERENCES:

[1] Erin, V. and L. T. Sarah, et al. (2015). "The evidence for immunotherapy in dermatomyositis and polymyositis: a systematic review." Clin Rheumatol 34 (12): 2089-95.

[2] Thomas, B. and F. Romain, et al. (2018). "Treatment of idiopathic inflammatory myositis associated interstitial lung disease: A systematic review and meta-analysis." Autoimmun Rev.

[3] Angela, C. and D. S. Maria, et al. (2017). "The Immune Response and the Pathogenesis of Idiopathic Inflammatory Myositis: a Critical Review." Clin Rev Allergy Immunol 52 (1): 58-70.

[4] V, P. and C. E (2018). "Dermatomyositis: a slow path towards targeted therapies or will conventional therapies prevail?" Br J Dermatol 179 (6): 1233-1234.

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Disclosure of Interests: None declared

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OP0245

PRESERVATION OF LUNG FUNCTION OBSERVED IN A PHASE 3 RANDOMIZED CONTROLLED TRIAL OF TOCILIZUMAB FOR THE TREATMENT OF EARLY SSC

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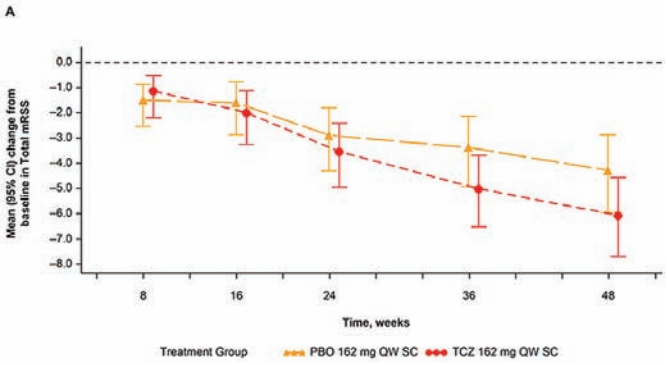
Background: The anti–IL6 receptor-α antibody tocilizumab (TCZ) demonstrated numerical improvement in modified Rodnan skin score (mRSS) and clinically relevant preservation of lung function (LF) (assessed by forced vital capacity [FVC]) in systemic sclerosis (SSc) patients (pts) in a ph 2 trial.[1]

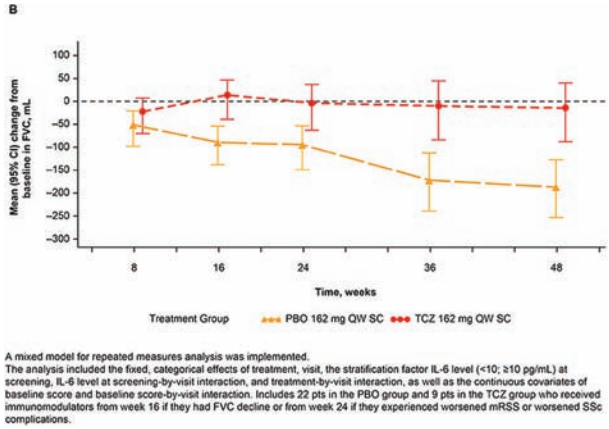
Objectives: Report the efficacy and safety (sft) of TCZ vs placebo (PBO) in SSc pts from the double-blind period of ph 3 trial (NCT02453256).

Methods: SSc pts were randomly assigned 1:1 to weekly subcutaneous TCZ 162 mg or PBO for 48 wks. Primary endpoint was mean difference (diff) in change (Δ) from baseline (BL) to wk 48 in mRSS for TCZ vs PBO. Key secondary endpoints were ΔBL%-predicted FVC (ppFVC) and time to Tx failure (time from first study treatment (Tx) to first occurrence of death, decline in FVC >10%, increase in mRSS >20% and mRSS ≥5, or occurrence of predefined SSc-related Cx). Chest high-resolution computed tomography (HRCT) and ACR Combined Response in SSc (CRISS) were exploratory endpoints.

Results: Of 106 PBO- and 104 TCZ-treated pts, 81% were women and 31% had previous or concurrent interstitial lung disease based on history. BL mean values were age 48 yrs, SSc duration 23 mts, mRSS 20.4, ppFVC 82.1%, and ppDLCO 75.6%. Mean BL computer-assisted quantitative lung fibrosis of the most affected lobe (QLF-LM) was 4.7% for the PBO group and 5.5% for the TCZ group. At wk 48, the primary endpoint was not significant (ΔBL mRSS: PBO, −4.4; TCZ, −6.1; adjusted least squares mean diff, −1.7 [95% CI: −3.8, 0.3]; p=0.098) (Fig 1A). All p values for other endpoints were nominal. The cumulative distribution of wk 48 ΔBL ppFVC favored TCZ over PBO (median [IQR]: PBO, −3.9 [−7.2, 0.6] vs TCZ, −0.6 [−5.3, 3.9]; van Elteren nominal p=0.0015). The diff in mean ΔBL FVC at wk 48 between Tx groups was 167 mL (95% CI: 83, 250), favoring TCZ (Fig 1B). At wk 48, 5 (5.4%) TCZ-treated pts experienced ≥10% absolute decline in ppFVC compared with 15 (16.5%) for PBO. The HR (95% CI) for time to Tx failure was 0.6 (0.4, 1.1), numerically favoring TCZ (Cox proportional hazards model; p=0.082). ACR CRISS scores favored TCZ over PBO at wk 48: median (IQR), 0.89 (0.09-1.00) vs 0.25 (0.00-0.99) (p=0.023). HRCT showed less progression of lung fibrosis for TCZ than for PBO, which supports the FVC results. Sft results were consistent with Cx of SSc and the established TCZ sft profile; SAEs were reported by 17% of PBO pts and 13% of TCZ pts; serious infections were reported by 7% and 2% of pts, respectively.

Figure 1. Change from baseline in (A) mRSS and (B) FVC





A mixed model for repeated measures analysis was implemented.
The analysis included the fixed, categorical effects of treatment, visit, the stratification factor IL-6 level (<10; ≥10 pg/mL) at screening, IL-6 level at screening-by-visit interaction, and treatment-by-visit interaction, as well as the continuous covariates of baseline score and baseline score-by-visit interaction. Includes 22 pts in the PBO group and 9 pts in the TCZ group who received immunomodulators from week 16 if they had FVC decline or from week 24 if they experienced worsened mRSS or worsened SSc complications.

Conclusion: The primary mRSS endpoint was not met; however, TCZ Tx resulted in clinically relevant differences in FVC with preservation of LFS and improvement in fibrosis, measured by HRCT, in SSc pts.

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SLE news

OP0246 ATTAINMENT OF THE LUPUS LOW DISEASE ACTIVITY STATE IS ASSOCIATED WITH PROTECTION FROM DAMAGE ACCRUAL IN PATIENTS WITH ACTIVE DISEASE AT BASELINE

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Background: The recently validated Lupus Low Disease Activity State (LLDAS) definition has been shown to have utility as a treat to target endpoint in SLE, whereby LLDAS attainment is associated with reduction in permanent damage accrual. Robust evaluation is required to ensure this protective association is not simply reflective of milder disease phenotypes being over-represented among LLDAS attainers.
Objectives: To assess the effect of attainment of LLDAS on damage accrual in patients with active disease at baseline. SLEDAI-2K$\geq$6 was chosen as this reflects clinical trial entry criteria.
Methods: A prospective multinational cohort study was undertaken in 13 centres between 2013-2017. Patients with SLE were recruited, SLEDAI-2k, SELENA flare index, PGA, and medication data collected at every visit, and damage score (SLICC-ACR damage index (SDI)) collected annually. Subgroup analyses were performed to assess the effect of LLDAS on damage accrual in patients who had active disease at baseline (SLEDAI-2K$\geq$6). Time-dependent hazards regression models were used to assess the association of attainment of LLDAS at any time point, and proportion of time in LLDAS at the 50% observed time cut-off, with accrual of irreversible end-organ damage.
Results: 1,735 patients were followed for (mean ± SD) 2.2 ± 0.9 years, totalling 12,717 visits. LLDAS attainment was less frequent in patients with active disease at baseline (901 of 3835 visits in LLDAS, 23.5%), compared to patients with SLEDAI2-K<6 at baseline (5190 of 8845 visits in LLDAS, 58.7%), p<0.001. In contrast, compared to those with baseline SLEDAI-2K<6, patients with active disease at baseline demonstrated a stronger association of LLDAS attainment with reduction in risk of damage accrual, in visit by visit analysis (HR 0.49, 95% CI 0.28-0.86, p 0.01 vs HR 0.72, 95% CI 0.52-0.99, p 0.05), and in analysis of cumulative time spent in LLDAS (HR 0.52, 95% CI 0.33-0.83, p 0.01 vs HR 0.65, 95% CI 0.47-0.91, p 0.01).
Conclusion: Despite lower attainment of LLDAS in patients with higher disease activity at baseline, the magnitude of association of LLDAS attainment with lower damage accrual was greater in this subgroup of patients compared to those less active baseline disease. This supports the validity of LLDAS as an outcome measure, in a population similar to that typically selected into clinical trials, and further highlights the potential impact of achieving a target outcome in SLE patients with active disease.
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OP0247 EFFECT OF IMMUNOSUPPRESSIVE DRUG WITHDRAWAL ON DAMAGE PROGRESSION AND FLARE OCCURRENCE IN SLE PATIENTS IN REMISSION

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Background: Patients with Systemic Lupus Erythematosus (SLE) are often treated with prolonged maintenance therapy with immunosuppressants (ISs) after remission achievement, with the aim of avoiding disease flares and subsequent organ damage. Data on the risk of flare after IS discontinuation and the effect of IS discontinuation on damage accrual are scanty.
Objectives: Our aims were to analyze damage progression in remitted SLE patients who did or did not discontinued ISs, to assess flare rate after IS withdrawal and to compare damage accrual in patients who did or did not flare after IS discontinuation.
Methods: We considered all SLE patients included in our lupus database, diagnosed between 1990 and 2018 (ACR criteria), treated with immunosuppressants over their disease course, who discontinued IS due to remission. IS discontinuation was defined as complete withdrawal of any immunosuppressive drug, and remission as clinical SLE Disease Activity Index (SLEDAI)-2K=0. Flares were defined according to SLEDAI Flare Index, and damage according to SLICC damage Index (SDI).
Results: Eligible patients ever treated with ISs were 319 out of 456 (69.9%) currently in follow-up. Remission lasting at least 6 months was achieved by 206 patients treated with IS (64.6%) (Table 1); among them 105 (51%) discontinued ISs during the follow-up. Mean±SD follow-up after IS withdrawal was 91±71 months (range 6-372). No difference in damage accrual between remitted patients who discontinued or did not discontinue ISs was observed at the end of follow-up, after adjusting for disease duration: median (range) SDI 1 (0-6) and 0 (0-4), respectively. Accordingly, the proportion of remitted patients who accrued damage during the follow-up was similar between those who did or did not discontinue ISs (55% vs. 48%). Among patients who discontinued ISs, 26 (24.7%) experienced a flare after a median (range) of 57 (6-264) months from IS discontinuation. Flares were severe in 50% of cases (Table 2). No difference in damage progression between patients who flared and did not flare after IS withdrawal was found at the end of follow-up: median (range) SDI 1 (0-5) and 1 (0-6), respectively. Moreover, the proportion of patients with damage accrual was similar among patients with and without flare after IS discontinuation (56% vs. 54%).

Table 1. Characteristics of remitted patients according to the discontinuation of ISs. Data are expressed as mean±SD or number (%).

	Remitted patients		P value
	IS discontinued (105)	IS not discontinued (101)	
Female, N (%)	93 (88.6)	85 (84.1)	n.s.
Age at 2018, years	44±11	40±12	0.035
SLE duration at 2018, years	19.5±9.2	12.3±8.7	0.027
SLE duration at remission, years	5.2±6.1	6.3±4.2	n.s.
Remission lasting at IS discontinuation > 2 consecutive years, N (%)	66 (63)	36 (35.6)	0.001
Reason for IS therapy, N (%)			
Lupus Nephritis	68 (64.8)	57 (56.4)	n.s.
Skin involvement	6 (5.7)	7 (6.9)	
Arthritis	12 (11.4)	15 (14.4)	
Haematological involvement	5 (4.7)	8 (7.9)	
Neuropsychiatric involvement	3 (2.9)	2 (1.9)	
Vasculitis	3 (2.9)	1 (0.9)	
Multisystemic involvement	8 (7.6)	11 (11)	
Type of last IS*, N (%)			
Mycophenolate	48 (45.7)	73 (72.2)	0.001
Azathioprine	30 (28.6)	18 (17.8)	0.04
Methotrexate	14 (13.3)	5 (4.9)	0.008
Cyclosporine	7 (6.7)	4(3.9)	n.s.
Cyclophosphamide	6 (5.7)	1 (0.9)	0.001

* last IS used before withdrawal or at last visit. Multisystemic: involvement of more than 2 organs requiring IS therapy.

Table 2. Type of flare after IS discontinuation in 105 SLE remitted patients.

Type of flare	Number (%)	Severe flare, number (% of all flares)
Arthritis	5 (19.2)	2 (7.7)
Skin manifestations	6 (23.1)	1 (3.9)
Serosal involvement	2 (7.7)	0
Haematological involvement	5 (19.2)	2 (7.7)
Lupus nephritis	8 (30.8)	8 (30.8)
Total	26	13 (50)

Conclusion: In our SLE cohort, the withdrawal of IS therapy in remitted patients did not seem to influence damage progression in the medium-term.
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OP0248 THE IMPACT OF EXERCISE ON HAND FUNCTION AND QUALITY OF LIFE OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RANDOMIZED CONTROLLED TRIAL

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Background: Systemic Lupus Erythematosus (SLE) has a significant impact on the ability to perform daily activities and patients' quality of life. To date, no studies have examined the effect of exercise on hand function and quality of life of SLE patients.
Objectives: To determine the effect of exercise on hand strength, dexterity and performance of daily activities, and the quality of life of SLE patients.
Methods: A randomized, 24-week follow-up trial was designed. A total of 240 consecutive SLE patients fulfilling the SLICC classification criteria were evaluated. Sixty two patients who met the inclusion criteria [age>18 years, upper limb arthralgias, DASH (Disabilities of the Arm, Shoulder, and Hand) score>10 and stable drug regimen for $\geq$3 months], were randomly assigned to the exercise group (n=32) or the routine care (control) group (n=30).
Patients in the exercise group received by the hand therapist a 30 min daily program at home of strengthening and stretching upper limb exercises for 12 weeks. Performance of daily activities was evaluated with the DASH and HAQ questionnaires, the grip and pinch strength with the Jamar dynamometer and pinch gauge tools respectively, the dexterity with the Purdue pegboard test, and the quality of life with the LUPUSQoL questionnaire, at 0, 6, 12 (end of the exercise program) and 24 weeks for both groups. SLE activity and cumulative organ damage were evaluated with the SLEDAI and SLICC/ACR-DI, respectively.
Results: There were no statistically significant differences between two groups in age (p=0.062), sex (p=0.346), disease duration (p=0.065), SLEDAI (p=0.937), SLICC/ACR-DI (p=0.242), number of tender joints (p=0.703), and use of corticosteroids (p=0.640), hydroxycloroquine (p=0.985) or immunosupressives (p=0.806). Thirty patients (93.75%) from the exercise group completed the 12-week exercise program and 28 (87.5%) were re-evaluated at 24 weeks; 30 patients (100%) of control group completed the 24-week study.
The percent changes of DASH and HAQ scores were significantly lower (improvement) in the exercise group compared to control group at all-time points. Moreover, all percent changes of grip strength, pinch strength hand dexterity and the LupusQol score were significantly higher in the exercise group compared to control group at all-time points (Table 1).

Table 1. Comparison between groups of percent changes from baseline to 6, 12 and 24 weeks for all parameters.

	Evaluation time (weeks)	Exercise Group	Control Group	P-value
DASH score	6	-33.7 (28.4)	-1.3(33.8)	<0.001
	12	-43.4 (31.5)	-11.2 (34.5)	<0.001
	24	-51.9 (47.8)	-7.1 (54.1)	<0.001
HAQ score	6	-20 (49.8)	49.77 (39.9)	0.013
	12	-55 (70.4)	-9.72 (42.2)	<0.001
	24	-69.8 (56.3)	-9.13 (60.4)	<0.001
Grip strength (DH)	6	9.9 (32.8)	2.39 (35.5)	0.044
	12	20.9 (43.4)	4.10 (30.2)	<0.001
	24	23.1 (41)	13.51 (36.8)	0.020
Pinch strength (JAW)	6	17.2 (50)	5.98 (37.4)	0.049
	12	27.1 (55.8)	0 (48.5)	0.002
	24	34.2 (57.6)	2.04 (56.7)	<0.001
Dexterity (COM)	6	17.4 (19.4)	0 (18.6)	<0.001
	12	23.6 (32)	3.13 (31.1)	0.004
	24	22.2 (30.3)	9.55 (22.5)	0.003
LUPUSQoL score (PH)	6	9.5 (49.9)	-5.62 (30.5)	0.010
	12	32.5 (53.8)	5.59 (28.4)	<0.001
	24	28.6 (74.8)	2.38 (48.8)	0.002

All values are presented as median (interquartile range). DASH=Disabilities of the Arm, Shoulder, and Hand), HAQ=Health Assessment Questionnaire, LUPUSQoL=Lupus Quality of Life, PH=physical health domain, DH=dominant hand, JAW=tripoid pinch, COM=combination.
Conclusion: Upper limb exercise, significantly improves hand function and quality of life in SLE patients.
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OP0249 ANTIPHOSPHOLIPID SYNDROME (APS) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) LEADS TO A MORE SEVERE DISEASE

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Background: Antiphospholipid antibodies (aPL) have been associated with organ damage and certain features in SLE patients.
Objectives: Our aim was to investigate the differences between SLE patients according to the presence of aPL and/or clinical antiphospholipid syndrome.
Methods: Patients from the RELESSER-T registry were included. RELESSER-T is a multicenter, hospital-based registry, with retrospective cross-sectional collection of data from a large representative sample of adult non-selected patients with SLE attending Spanish rheumatology services from the public national health system.
Results: We included 3651 SLE patients and 1368 were positive for aPL (44.9% of patients were positive for anticardiolipin antibodies, 27.3% showed positivity for anti b2glycoprotein I and 24% for lupus anticoagulant). Overall 2283 patients were classified as SLE no aPL, 528 as SLE-APS and 840 as SLE-aPL. Demographic data, clinical and laboratory features in the different groups are showed in **Table 1**. Regarding cardiovascular risk factors, SLE-APS patients had higher rates of hypertension, dyslipidemia and diabetes than SLE-aPL and SLE no aPL patients (p< 0.001, p< 0.001 and p=0,022, respectively). SLE-APS patients showed a lower prevalence of photosensitivity and higher frequencies of serositis, proteinuria (>0.5 grs), urinary cell casts, seizures and psychosis ($p\leq$0.001). Overall, SLE-APS patients showed a lower rate of cutaneous manifestations and higher rates of neuropsychiatric, cardiac, pulmonary, renal, joint and ophthalmological manifestations (**Table 1**). In accordance with a more severe clinical profile, higher frequency of anti-DNA antibodies and hypocomplementemia were observed in the SLE-APS group (p<0.001). In addition to a higher disease activity (SLEDAI), SLE APS patients presented more damage accrual with higher values in SLICC (1.9±2.2 in SLE APS, 0.9±1. 4 in SLE aPL and 1.1±1.6, p<0.001) and Katz indexes (3±1.8 in SLE APS, 2.7±1.7 in SLE aPL and 2.6±1.6 in SLE no aPL, p <0.001).

Table 1. Main demographic data, clinical and laboratory features in the studied group.

	SLE no aPL, n (%)	SLE APS, n (%)	SLE aPL, n (%)	p
Female sex	2075 (90.9%)	455 (89.3%)	757 (90.1%)	0.179
Age, mean±SD (yr)	47.0±15.1	46.5±14.4	45.3±14.3	<0.001
Disease duration, mean±SD (mo)	141.5±100.7	156.8±109.8	136.4±94.0	0.001
Tobacco use: •Current •Former	335 (16.3) 494 (24.1)	91 (18.6) 119 (24.3)	125 (16.6) 189 (25.2)	0.743
High blood pressure	647 (28.6)	211 (40.1)	203 (24.4)	<0.001
Dyslipidemia	664 (30.1)	216 (41.9)	221 (27.3)	<0.001
Diabetes: •Without organ damage •With organ damage	97 (4.3) 17 (0.8)	29 (5.6) 8 (1.5)	25 (3) 3 (0.4)	0.022
Cutaneous manifestations	1700 (74.4)	358 (67.4)	611 (72.7)	0.005
Joint symptoms	636 (27.8)	164 (30.9)	204 (24.3)	0.022
Respiratory manifestations	241 (10.5)	125 (23.5)	70 (8.3)	<0.001
Cardiac manifestations	379 (16.6)	159 (29.9)	125 (14.9)	<0.001
Renal manifestations	862 (37.7)	249 (46.9)	298 (35.4)	<0.001
Neuropsychiatric manifestations	655 (28.7)	235 (44.3)	238 (28.3)	<0.001
Ophthalmological manifestations	315 (13.8)	111 (20.9)	103 (12.2)	<0.001
Positive anti DNA antibodies	1049 (46.9)	258 (50)	367 (45.1)	<0.001
Hypocomplementemia	1716 (76.7)	424 (82.6)	645 (77.9)	0.011

Conclusion: SLE-APS patients show a more severe clinical profile with higher frequency of major organ involvement and more damage accrual than SLE-aPL and SLE no APL.

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OP0250 INFLUENTIAL FACTORS IN PROMOTING TREAT-TO-TARGET FOR SYSTEMIC LUPUS ERYTHEMATOSUS VIA EMPOWERING PATIENTS: A COHORT STUDY FROM CHINA BY SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: T2T is routine in RA, but no comparable standard has been defined for SLE. In 2015, the definition of Lupus Low Disease Activity State (LLDAS) was generated by Asia-Pacific Lupus Collaboration, and the preliminary validation demonstrated its attainment to be associated with improved outcomes in SLE. A SLEDAI-2K score lower than 4 is the main criteria for LLDAS. SSDM is an interactive mobile disease management application, including application systems for both the doctors and patients. The patients can perform self-assessment, including SLEDAI and medical records entry through the mobile application. The data is synchronized to the SSDM of authorized rheumatologists and stored in cloud database.

Objectives: To evaluate the patterns of T2T and related influential factors among SLE patients after applying SSDM in real world.

Methods: Patients were trained to master SSDM by rheumatologists in clinics. The first assessment for SLEDAI was performed as the baseline. Patients were required to perform repeated assessments after leaving the clinics.

Results: From July 2015 to Jan 2019, 1,090 SLE patients from 88 hospitals were followed up for more than 12 months through SSDM, and the results were summarized in Table 1. The ratio of T2T achievers was 52.84% (576/1,090) at the baseline and improved significantly to 68.35% (745/1,090) after a 12-month follow-up, p<0.01. Among T2T achievers at the baseline, 77.08% (444/576) maintained T2T, and 22.92% (132/576) relapsed. Of patients who didn' t achieve T2Tat baseline, 58.56% (301/514) of the them achieve T2T after 12-month follow-up.

The impact of the times of self-assessment for SLEDAI on T2T has been analyzed. The more frequent of the self-assessments being conducted by patients, the higher improvement of T2T rate will be. We performed linear regression analysis of variables in statistics and parameter estimation by least square method. The improvement of T2T rate(y) was positively correlated with times of self-assessment for SLEDAI(x) independently. The regression equation as "y = 0.0324x + 0.0226 R2 = 0.7717", p<0.01. (Figure 1)

Conclusion: After proactive disease management via SSDM, the rate of T2T in SLE patients increased significantly. Patients with SLEDAI-2K≤4 score at baseline had a significantly higher retention rate. The patients who performed more self-assessments through SSDM had lower probability of relapse and higher rate of T2T maintaining and achievement. SSDM is a valuable tool for long term SLE follow-up through empowering patients.

Table1:

Baseline\Last follow-up	Number	%	SLEDAI≤4	%	SLEDAI≥5	%
SLEDAI≤4	576	52.84%	444	77.08%	132	22.92%
SLEDAI≥5	514	47.16%	301	58.56%	213	41.44%
Total	1090	100%	745	68.35%	345	31.65%

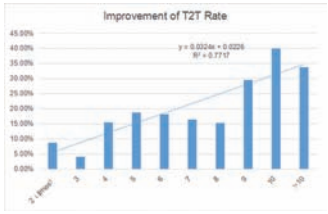


Figure 1

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OP0251 SLE PATIENTS FROM NORTH AMERICA ARE OLDER WITH LESS SEROLOGIC ACTIVITY THAN OTHER POPULATIONS IN INTERNATIONAL CLINICAL TRIALS

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Background: Regional differences have been identified as potential confounders of SLE clinical trial results. Recently, no difference between treatment and placebo was observed in the US lupus patients when a significant treatment effect was observed in Europe[1].

Objectives: To compare SLE serologic features/markers of active disease between different geographic regions in recent multinational clinical trials.

Methods: Laboratory data of 1005 subjects from four global randomized SLE clinical trials at baseline were examined. Mean/median C3 and C4 complement levels, prevalence of low C3 or C4 (**Low C3**/**C4**), positive anti-double stranded DNA (**DNA**), anti-Extractable Nuclear Antibodies (**ENA**), and high-titer Antinuclear Antibody (**ANA≥1:640**) in North America (**NA**) patients were compared to Asia (**AS**), Latin America (**LA**), Africa (**AF**), Western Europe (**WE**), and Eastern Europe (**EE**)

Results: NA patients were significantly older than patients in LA, AF, or AS but not WE or EE. Not surprisingly, they also had higher complement levels and the lowest rates of low C3/C4, DNA, ENA, and ANA ≥1:640. Our data confirm that age is an important factor in the prevalence of low complement and autoantibodies. However, there remained a marked difference in serologic activity between NA and EE, despite being close in age.

Table: Comparison of serologic features between NA and other regions and in different age groups.

Region/Age Group		NA	LA	WE	EE	AF	AS	18-29	30-39	40-49	50-59	≥60	Total
N		164	395	27	202	58	159	237	271	259	167	71	1005
Age	Mean	44.5	37.9	39.7	42.3	40.6	36.8	24.4	34.4	44.5	53.5	63.9	39.9
	Med	45.5	36	36	43	49.5	39.5	25	34	44	53	63	39
	p	*C	<0.001	*ns*	*ns*	<0.05	<0.05			-			-
C3	Mean	1250	1053	956	1044	1193	880	950	1011	1121	1158	1189	1062
	Med	1200	850	920	1040	1170	840	940	1000	1100	1130	1190	1050
	p	*C	<0.001	<0.001	<0.001	*ns*	<0.001			#<0.001			-
C4	Mean	244	180	160	171	216	163	160	173	207	210	218	189
	Med	233.5	176	165	170	200	160	156	167	190	210	210	180
	p	*C	<0.001	<0.001	<0.001	*ns*	<0.001			#<0.001			-
Low C3/C4	N	25	137	13	80	10	91	116	116	70	44	10	356
	%	15.2	34.7	48.1	39.6	17.2	57.2	48.9	42.8	27.0	26.3	14.1	35.4
	p	**C	<0.001	<0.001	<0.001	*ns*	<0.001			**<0.001			-
DNA	N	44	161	9	80	17	89	144	115	72	44	16	391
	%	26.8	40.8	33.3	39.6	29.3	56.0	60.8	42.4	27.8	26.3	22.5	38.9
	p	**C	<0.01	*ns*	<0.05	*ns*	<0.001			**<0.001			-
ENA	N	83	277	18	131	40	112	175	187	157	100	42	661
	%	50.6	70.1	66.7	64.9	69.0	70.4	73.8	69.0	60.6	59.9	59.2	65.8
	p	**C	<0.001	<0.05	<0.001	<0.001	<0.001			**<0.01			-
ANA≥	N	21	222	8	68	30	63	140	149	111	82	28	510
1:640	%	12.8	56.2	29.6	33.7	51.7	39.6	59.1	55.0	42.9	49.1	39.4	50.7
	p	**C	<0.001	*ns*	<0.001	<0.001	<0.001			**<0.001			-

Asian patients were the youngest, had the lowest complement levels and the highest rate of ENA & DNA consistent with high disease activity. Low complement, but not DNA, was relatively common in Europe. LA patients, like Asians, had high rates of serologic activity but less incidence of low C3/C4, suggesting that this population may have intrinsic disease severity without being as acutely active.

*Mann-Whitney Rank Sum **Chi-square #One-way ANOVA on ranks; Med-median **p**-p value C-comparator *ns*-not significant; Data not corrected for multiple comparisons

Conclusion: SLE patients entering studies from North America are strikingly less likely to have markers of active disease than other regions, raising concerns for their suitability for trials. This appears to be associated, at least in part, with age, although more aggressive treatments cannot be ruled out.

Asian subjects have the greatest prevalence of autoantibodies and low complement. Latin American patients have high prevalence of ANA≥1:640 and other autoantibodies, but less evidence of low complements.

These findings may help to explain regional differences in treatment/placebo responses and emphasize the importance of geographical stratification and improved methods to screen out patients unsuitable for SLE trials.

REFERENCE:

[1] www.immupharma.co.uk

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OP0252

NEUROPATHIES IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM AN INTERNATIONAL, INCEPTION COHORT STUDY

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Background: Central nervous system (CNS) involvement accounts for over 90% of neuropsychiatric (NP) events compared to involvement of the peripheral nervous system (PNS) which accounts for most of the other events. Although there is a large body of work on CNS disease in SLE patients, involvement of the PNS is less well established.

Objectives: In a multi-ethnic/racial, prospective SLE inception cohort, to determine the clinical characteristics, associations and outcomes in different types of peripheral nervous system (PNS) disease.

Methods: Patients were evaluated annually for 19 NP events including seven types of PNS disease. Standardized case definitions and attribution models for each type of PNS event were used. SLE disease activity (SLEDAI-2K), organ damage (SLICC/ACR damage index), autoantibodies, patient (SF-36) and physician (Likert score) assessment of outcome were measured. Time to event and linear regressions were used as appropriate.

Results: Of 1,827 SLE patients, 88.8% were female, 48.8% Caucasian. The mean±SD age was 35.1±13.3 years, disease duration at enrollment 5.6±4.2 months and follow-up 7.6±4.6 years. There were 161 PNS events in 139/1,827 (7.6%) patients. The predominant events were peripheral neuropathy [66/161 (41.0%)], mononeuropathy [44/161 (27.3%)] and cranial neuropathy [39/161 (24.2%)] and the majority were attributed to SLE. Multivariate Cox regressions suggested longer time to resolution in patients with prior history of neuropathy, older age at SLE diagnosis, higher SLEDAI-2K scores, and for peripheral neuropathy versus other neuropathies. Neuropathy was associated with significantly lower SF-36 physical and mental component summary scores versus patients without NP events. By physician assessment, the majority of neuropathies

resolved or improved over time and this was associated with improvements in SF-36 summary scores for peripheral neuropathy and mononeuropathy.
Conclusion: PNS disease is an important component of total NPSLE and has a significant negative impact on health related quality of life. The outcome is favourable for most patients, but several factors associated with longer time to resolution were identified.
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OP0253

WORLDWIDE TRENDS IN MORTALITY OF SYSTEMIC LUPUS ERYTHEMATOSUS BETWEEN 2000 AND 2015: ANALYSIS OF THE WORLD HEALTH ORGANIZATION DATABASE

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Background: Although diagnosis, treatment and prevention strategies of Systemic Lupus Erythematosus (SLE) have further improved during the last two decades, the net benefit in term of global SLE-related mortality remains unknown.
Objectives: To describe the worldwide trends in SLE mortality between 2000 and 2015 using data of 125 countries from the World Health Organization (WHO) mortality database. To modelize SLE-related deaths taking into account temporal changes, geographical localization and country wealth.
Methods: We analyzed the WHO mortality database containing cause-specific mortality of participating countries. SLE-related deaths were identified using the international classification of disease 10 (ICD-10, code M32). In all countries which provided data between 2000 and 2015, sex-specific mortality rate was calculated for each year using the WHO reference population database. To have a better understanding of mortality fluctuations, countries were grouped geographically by continents and their nominal gross domestic product (GDP) per capita were retrieved from the United Nation database. A mixed regression model for repeated measures was used to take into account the time factor, GDP per capita and continent in SLE-related death.
Results: Between 2000 and 2015, a total of 97,008 SLE-related deaths occurred in 125 countries, which accounted for 0.021% of all deaths during the same period. World-wide, the overall mortality rate attributed to SLE remained stable (p=0.86) over the study years. However, we detected significant differences between continents (p=0.0006) with the mortality rate of Africa being significantly higher than that of Europe (p=0.004). There was a significant interaction between the continents and the study years (p=0.01) revealing a strong increase in the mortality rate attributed to SLE in Africa. We found a very strong association between SLE-attributed mortality and the GDP per capita (p<0.0001).
Conclusion: We observed drastic differences in the evolution of SLE-related mortality due to country geographic localization, wealth and ethnic factors. SLE-related remained stable as a whole but strongly increased in the African continent.
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FRIDAY, 14 JUNE 2019

Tackling the challenges of autoimmune/autoinflammatory conditions in children and young people

OP0254

CANAKINUMAB IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RECURRENT FEVER SYNDROMES: RESULTS FROM A PHASE 3 TRIAL (CLUSTER)

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Background: Recurrent fever syndromes have a significant impact on health-related quality of life (HRQoL).[1] Canakinumab (CAN) has demonstrated efficacy and safety in patients with colchicine-resistant familial Mediterranean fever (crFMF), hyper-immunoglobulin D syndrome/mevalonate kinase deficiency (HIDS/MKD) and tumour necrosis factor receptor-associated periodic syndrome (TRAPS) in the pivotal, Phase 3, CLUSTER trial (NCT02059291),[2] but there are limited published data on the impact of CAN on the HRQoL, work/school and social life of these patients.
Objectives: To evaluate effect of CAN on HRQoL, work/school and social life of patients in the 3 disease cohorts (crFMF, HIDS/MKD, and TRAPS) in a double blinded randomised study.
Methods: The detailed study design was reported previously.[2] The HRQoL of patients treated with CAN was assessed at Baseline (BL), Week 17 (Wk17) and Week 41 (Wk41) in patients who fully responded (absence of flares), either to 150 mg q4w CAN, or to 300 mg q4w CAN after up dosing. Methods used were the Child Health Questionnaire (CHQ)-PF50 physical (PhS) and psychosocial (PsS) summary scores (children >5–<18 years), Short-Form health survey (SF-12) physical component summary (PCS) and mental component summary (MCS; adults $\geq$18 years) scores. An increase from baseline of 2, 5, and 8 points in the CHQ-PF50 physical and psychological component summary scores corresponds to a small, moderate and large treatment effect, respectively. Functional impairment related to work/school, social life and family life/home responsibilities was assessed by Sheehan Disability Scale (SDS). A score of 5 or higher in SDS is associated with significant impairment.
Results: Patients showed a high impairment of HRQoL at baseline in all 3 cohorts (crFMF n=31, HIDS/MKD n=37 and TRAPS n=22). At Wk17, a moderate to large

treatment effect, either with 150 mg or 300 mg q4w CAN, was observed by an improvement in the CHQ-PF50 PhS and PsS (increased >5),
SF-12 PCS (increased >5) and SDS scores (decreased below 2). At Wk41, the number of patients on CAN was limited (crFMF n=9, HIDS/MKD n=6 and TRAPS n=4) due to the design of the trial (randomised withdrawal part). For the patients who remained on CAN, the improvement in HRQoL, work/school and social life was sustained.
Conclusion: Treatment with CAN led to sustained improvement of HRQoL, work/school and social life in patients with crFMF, HIDS/MKD and TRAPS.

REFERENCES:

[1] Sahin, et al. Eur Rev Med Pharmacol Sci. 2013;17:958–963.
[2] De Benedetti, et al. *NEJM* 2018;378:1908–1990.

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OP0255 MICROBIOTA TRANSPLANT TO CONTROL INFLAMMATION IN A NLRC4-RELATED DISEASE PATIENT WITH RECURRENT HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

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Background: The NLRC4 inflammasome activation is essential in host defence, particularly against enteric pathogens. Gain-of-function mutations in *NLRC4* are associated with a distinct autoinflammatory syndrome characterized by enterocolitis and recurrent HLH.
Objectives: To report safety and efficacy of faecal microbiota transplantation (FMT) in a patient carrying a *de novo* missense mutations in *NLRC4*, with gut inflammation and gut colonization by multi-drug resistant (MDR) pathogens.
Methods: Subject and donors were screened for potential FMT according to Cammarota *et al.* (1) with modifications introduced by Ospedale Pediatrico Bambino Gesù Committee for paediatric FMT procedures. Culture-based and NGS-based microbiota profiling were performed to address MDR persistence and microbial associated communities coupled to inflammatory profiling. After wide donor screening, a universal adult donor was selected and infusion performed twice by colonoscopy from fresh and frozen faeces, respectively. A one year FMT follow up was ensured to address clinical outcomes.
Results: A Caucasian 16 months old boy presented, from 1 month of life, with recurrent HLH, diarrhoea and vasculitic skin lesions, secondary to a de novo missense mutation in *NLRC4* (I343N). His disease was not controlled despite treatment with repeated high dose of intravenous methylprednisolone pulses and chronic daily glucocorticoid therapy, cyclosporine-A (5 mg/kg) and anakinra (ranging from 5 to 25 mg/kg/day). Because of recurrent HLH episodes, the patient was treated with emapalumab (anti-IFNgamma antibody) for three months, with HLH control. However, the patient presented persistent diarrhoea with gut inflammation and colonization by MDR pathogens (*Enterobacter cloacae* and *Enterococcus faecalis*), leading by translocation to systemic infections and, hence, HLH reactivation. Moreover, he developed severe intestinal meteorism with subsequent paralytic-ileus that required ileostomy. Based on the hypothesis that his intestinal dysbiosis concurred in the persistent gut inflammation related to his underlying disease, he received a first FMT with initial clinical improvement. Therefore, ileal anastomosis was performed with recanalization, and a second FMT was performed a month later. The patient did not develop any complication. The stool cultures no longer showed the presence of enteropathogenic germs and since the last FMT (12 months of follow-up) he did not present any symptom of gut inflammation or HLH reactivations.
Conclusion: *NLRC4*-related disease is typically characterized by enterocolitis and *NLRC4*, highly expressed in intestinal macrophages, is critical for pathogen restriction by phagocytes in the gut lamina propria. The chronic gut inflammation of *NLRC4*-patients is a stimulus for systemic inflammation. Moreover, pathogens present in the gut can trigger HLH episodes. A presence of a selected microbiota from appropriate donor can decrease gut inflammation. FMT may represent a valid and safe therapeutic option in *NLRC4*-patients in order to reduce chronic inflammatory *stimuli*.

REFERENCE:

[1] Cammarota G. et al. European consensus conference on faecal microbiota transplantation in clinical practice. Gut. 2017 Apr;66(4):569-580.

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OP0256 IN MEDIUM TO LONG-TERM JUVENILE DERMATOMYOSITIS, PROINFLAMMATORY AND PROFIBROTIC CYTOKINES ARE DIFFERENTLY ASSOCIATED WITH PULMONARY INVOLVEMENT IN ACTIVE VS INACTIVE DISEASE

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Background: Knowledge about associations between cytokines and lung involvement in juvenile dermatomyositis (JDM) is scarce.
Objectives: To examine associations between cytokines and pulmonary involvement in JDM assessed after medium to long-term follow-up.
Methods: 58 JDM patients examined median 17y after disease onset were stratified in active and inactive disease by the updated PRINTO criteria (Ref 1). Serum levels of cytokines were analyzed by Luminex or ELISA. Pulmonary function tests (PFT) included forced vital capacity (FVC), total lung capacity (TLC) and diffusing capacity for carbon monoxide (DLCO) (hgb adjusted). PFT variables are expressed as% of predicted. High resolution computed tomography (HRCT) scans were scored for interstitial lung disease (ILD), calcinosis in chest wall and airway disease. Associations between lung involvement and cytokines are presented as Spearman's correlation coefficient (r_s).

Results: **Table 1**. Characteristics, PFT, HRCT findings and cytokines

	Total (n=58)	Active (n=37)	Inactive (n=21)
Age, y, median (IQ range)	21 (15-34.8)	20 (14-34)	26 (17-37)
Female, n (%)	35 (60)	25 (68)	10 (48)
Disease duration, y (IQ range)	17 (7-27)	16 (6-26)	17 (8-28)
TLC[a]	93 (11)	91 (10)	94 (11)
FVC[a]	96 (12)	94 (12)	99 (12)
DLCO[a]	82 (15)	79 (13)	87 (16)
Any HRCT findings, n (%)	21 (36)	15 (40)	6 (29)
HRCT ILD, n (%)	8 (14)	6 (16)	2 (10)
HRCT calcinosis, n (%)	8 (14)	6 (16)	2 (10)
HRCT airways disease, n (%)	9 (15)	7 (18)	2 (10)
TGFb1[b]	29252 (8868)	29698 (9623)	28467 (7513)
PDGF[b]	9083 (2799)	8990 (2979)	9248 (2511)
IP-10 [b]	1448 (1281)	1491 (1438)	1371 (972)
MCP-1 [b]	34 (21)	34 (19)	34 (26)
Eotaxin [b]	138 (103)	142 (108)	132 (95)
IL-17 [b]	15 (14)	15 (15)	15 (10)
IL-5 [b]	1.4 (1.3)	1.6 (1.6)	1.2 (0.5)
MIP1a [b]	2.5 (1.4)	2.7 (1.5)	2.3 (1.1)

Numbers are mean (SD) if not stated otherwise; [a]PFT variables are% of predicted; [b] unit: pg/ml

No significant differences were found between active and inactive patients in tbl. 1.
Associations between cytokines and PFT/HRCT findings
Numbers are r_s, all p`s < 0.05
In patients total, TGFb1 and PDGF correlated with TLC and FVC (- 0.38 - -0.30). For TGFb1 correlations with TLC and FVC were - 0.62 and -0.59 in the inactive group, whereas PDGF correlated with FVC in the active group (- 0.48). IP-10 correlated with TLC in active patients only (- 0.35).

In patients total and active patients, eotaxin correlated with DLCO% (0.39 and 0.52). In inactive patients, MIP1b correlated with DLCO% (0.47).
In patients total, IP-10 correlated with any HRCT finding and airways disease (0.37 and 0.44); which were also present in active patients (0.34 and 0.61). In patients total, MCP-1 correlated with any HRCT finding and calcinosis (0.34 and 0.40); in active patients MCP-1 and calcinosis correlated (0.34). Eotaxin correlated with ILD in both patients total and active patients (0.37 and 0.38).
The following cytokines correlated with HRCT findings in inactive patients only; IL-17 with any HRCT findings and ILD (0.61 and 0.52), MIP1a with any HRCT findings (0.63) and IL-5 with ILD (-0.42).
Conclusion: In JDM, lung involvement was associated with mainly proinflammatory cytokines in active and profibrotic/proinflammatory cytokines in inactive patients. The association between higher eotaxin and better gas diffusion was interesting, since we have previously demonstrated an association between higher eotaxin and cardiac dysfunction (Ref 2).

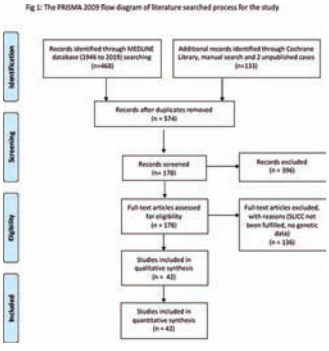
REFERENCES:
[1] Almeida, A&R 2015;67(9)
[2] Schwartz, Rheumatology, 2014;53(12)

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OP0257 CHILDHOOD-ONSET MONOGENIC SYSTEMIC LUPUS ERYTHEMATOSUS NOT DUE TO COMPLEMENT DEFICIENCY: ASYSTEMATIC REVIEW OF 90 CASES

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Background: The paediatric SLE (pSLE) are estimated 10 to 17% of SLE (1). Studies comparing pSLE with adult-onset SLE reported high prevalence of pre-existing organ damage at diagnosis due to the diagnosis delay, more severe disease clinical course with high disease activity resulting in worse prognosis in pSLE (1,2). Recently, whole exome sequencing and next-gene sequencing have facilitated the identification of rare monogenic variants associated with SLE and lupus-like phenotypes with high penetrance (3,4)
Objectives: To reporting the whole spectrum of monogenic pSLE according to pathway abnormalities, using a meta-analysis (MA) approach.
Methods: A systematic review of studies focused on monogenic pSLE were analysed. To be included in the systematic review, studies had to meet simultaneously all the following criteria: (i) reported at least 1 case of SLE (ii) started before the age of 16 (iii) with clearly description of the diagnosis criteria and (iv) provided genetic data of the case.
We pooled the genes into three main groups of signalling pathways: (i) genes that affect adaptive immunity pathways including the lymphocyte apoptosis (FAS, KRAS, PTPN11, SHOC2) and the B and T cell development checkpoints (PRKCD, RAG2, IKZF1,DOCK8, WASP), (ii) genes containing type I interferon (IFN) pathways (ACP5, TREX1, SAMHD1, RNASEH2A, RNASEH2B, RNASEH2C, IFIH1, DNASE1L3, DNASE1, TMEM173, Tetrasomy 9), and (iii) metabolism pathways including both amino acid metabolism (PEPD, SLC7A7, MAN2B1) and oxidative metabolism (NCF2). Clinical and laboratory data were analysed according to the SLICC classification.



Results: We included 42 articles encompassing 88 patients, plus 2 additional unpublished cases of one author (AB). The MA process were carried out according to the PRISMA statement.
According to the SLICC classification, the blood disorders were significantly higher in the group of the metabolism pathway as well as the positivity of direct Coombs test. The positivity of antibodies anti-Sm was also a distinguishing element for this group, while the positivity of ALP antibodies was the lonely manifestation to distinguish the adaptive immunity pathway from the others. Fever, recurrent infections, hepatosplenomegaly, and pulmonary diseases were significantly predominant in the metabolism pathways. In the group of the IFN pathway, the most distinctive criteria were the neurological manifestations and bone changes. There were no statistically significant differences in all groups concerning all other clinical or immunological criteria.

Conclusion: This is the first quantitative analysis of multiples cases reports, comparing the whole spectrum of monogenic pSLE according to three different pathways. Our results suggest that abnormalities in signaling pathway delimitate different SLE juvenile subset. The clinical and biological differing between the three signaling pathway were not specific, but our results may help to detect phenotypes requiring targeted genetic investigations. Subsets of SLE syndrome have to be identified to drive the treatment and propose personalized medicine.

REFERENCES:
[1] Livingston B, Bonner A, Pope J. Differences in clinical manifestations between childhood-onset lupus and adult-onset lupus: a meta-analysis. Lupus. 2011 Nov;20(13):1345–55.
[2] Hedrich CM, Smith EMD, Beresford MW. Juvenile-onset systemic lupus erythematosus (jSLE) – Pathophysiological concepts and treatment options. Best Pract Res Clin Rheumatol. 2017 Aug;31(4):488–504.
[3] Tsokos GC, Lo MS, Reis PC, Sullivan KE. New insights into the immunopathogenesis of systemic lupus erythematosus. Nat Rev Rheumatol. 2016 Dec;12(12):716–30.
[4] Chung SA, Shum AK. Rare variants, autoimmune disease, and arthritis: Curr Opin Rheumatol. 2016 Jul;28(4):346–51.

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OP0258 LESSON FROM EUROFEVER REGISTRY AFTER THE FIRST TEN YEARS OF ENROLLMENT

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Background: In 2008 the Paediatric Rheumatology European Society (PReS) promoted an International Project for the study of Autoinflammatory Diseases (AIDs) named Eurofever, whose main purpose is to create a web-based registry for the collection of information in AIDs patients.
Objectives: To assess the impact of the Eurofever Registry on scientific community with particular interest in the geographical coverage, diagnostic delay, access to treatment and pubblications.
Methods: The data analyzed in the study were extracted from the Eurofever registry, which is hosted in the PRINTO website.
Results: Up to date 4175 patients have been enrolled from 62 countries (3843 of them with complete demographic data). Most of patients (72%) are resident in Western Europe, 8% in Central-Eastern Europe, 11% in Southern-Eastern Mediterranean, 2% in South America and 7% in other countries. Compared to the first Eurofever report (Toplak et al, 2012) we have observed an increase of enrolled patients from 1388 to 2651 in Western Europe, from 106 to 313 in Central-Eastern Europe, from 294 to 406 in Southern-Eastern Mediterranean. The median onset age is 4 years (range 1 month – 75 years), the median diagnosis age is 8 years (range 1 month – 78 years). The median diagnostic delay observed in 2012 was 7.3 years (range 0.3–76), from patients enrolled after 2012 it was 1.9 years (range 0-57). Comparing the mean diagnostic delay from 1980 to 2018, we have observed an encouraging constant reduction of period between AIDs onset e diagnosis (from a mean diagnostic delay value of 20 years for patients born before 1980, to a mean value of 1 year for patients born after 2011, Figure 1). Complete information on access to treatment were available in 2430 patients. DMARDs were used in 1031 (42%), biologics in 396 (16%) patients. According to the number of enrolled patients, biologics were used in 361/1782 (20%) of Western europeans, 17/342 (5%) of Central-Eastern europeans, 6/259 (2%) of Southern-Eastern Mediterranean patients. Regarding Eurofever impact on Scientific Community, during this first 10 years the Registry provided 12 papers with more than 800 citations. Detailed analysis of clinical features collected in Eurofever database allowed to perform studies with large cohort of patients, to purpose new classification criteria (Federici et al, 2015), to validate damage and activity score (Piram et

al, 2014 and N Ter Haar et al, 2017) and to evaluated genotype/phenotype correlation (Papa et al, 2017).

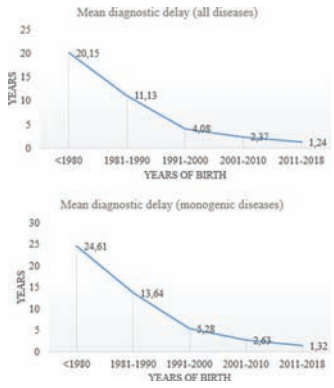


Figure 1. Diagnostic delay (years) according the year of birth

Conclusion: In the last years we have observed an encouraging increase of involved Countries, with a greater number of patients coming from geographic area poorly represented in the first epidemiologic study of Toplak et al. Eurofever data analysis has confirmed an improvement of diagnostic ability during the last years, with a significant reduction of mean diagnostic delay. Longterm studies will help understand the efficacy and safety of different treatments used in these rare conditions.

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I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:
AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.
The money received for these activities are directly transferred to the Gaslini Institute's bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis

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OP0259

OVERWEIGHT AND OBESITY IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ENROLLED IN THE GERMAN NATIONAL PAEDIATRIC RHEUMATOLOGIC DATABASE (NPRD)

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Background: Patients with juvenile idiopathic arthritis (JIA) may have a different body composition associated with reduced muscle mass and increased fat mass [1]. They display decreased physical fitness, perform less strenuous physical activities, and spend more time sleeping than do healthy children. A lower level of physical activity is associated with deconditioning and functional deterioration, favoring an inactive lifestyle. The risk of overweight might be further increased by the glucocorticoid treatment.
Objectives: Since obesity can increase inflammatory processes, cause early atherosclerotic changes and promote metabolic disorders, the objectives were a) to determine the prevalence of overweight and obesity in children and adolescents with JIA, and b) to examine the association between overweight and health-related parameters in this population.
Methods: A cross-sectional analysis of physicians' recorded body weights and heights of patients with JIA enrolled in the NPRD in the year 2016 was performed. Overweight was defined as BMI >90th sex- and age-specific percentile and obesity as BMI >97th percentile. For comparison with data from the general German population [2], patients aged 3 to 17 years were considered. A linear regression model was used to explore the association between overweight and both clinical as well as self-reported outcomes.
Results: In total, data from 6.860 children and adolescents with JIA (age 11.5 ± 4 years, disease duration 4.6 ± 3.6 years, 67% girls, 39% persistent oligoarthritis) were analyzed. Overweight was found in 14% (including 6% obesity) of JIA cases. Comparative data from the German general population report an overweight prevalence of 15% (including 6% obesity). In contrast to the general population, overweight rates in JIA differed between girls and boys (girls 14% vs. boys 16%, $p<0.05$). Patients with psoriatic arthritis (20%) and systemic JIA (18%) showed the highest overweight rates. In multivariate analyses, age (OR 1.06; 95%CI: 1.04-1.09), male sex (OR 1.21; 95%CI: 1.01-1.44), functional limitations (OR 1.29; 95%CI: 1.04-1.59), as well as therapy with biological DMARDs (OR 1.48; 95%CI: 1.22-1.80) and systemic glucocorticoids (OR 1.40; 95%CI: 1.14-1.71) were significantly associated with overweight.
Conclusion: The prevalence of overweight and obesity in young patients with JIA is similar to that of children and adolescents in the general population. The overweight rate increases with age and is strongly associated with functional restrictions and treatment with glucocorticoids. The role of overweight in the long-term outcome of JIA is an issue that still needs to be addressed.

REFERENCES:

[1] Grönlund MM, et al. Juvenile idiopathic arthritis patients with low inflammatory activity have increased adiposity. Scand J Rheumatol 2014;43:488–92.
[2] Schienkiewitz A, et al. Übergewicht und Adipositas im Kindes- und Jugendalter in Deutschland. Journal of Health Monitoring 2018; 3:16–23.

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Disclosure of Interests: Florian Milatz: None declared, Jens Klotsche: None declared, Martina Niewerth: None declared, Nils Geisemeyer: None declared, Jana Hörstermann: None declared, Gerd Ganser: None declared, Ivan Foeldvari Consultant for: Chugai, Novartis, Angelika Thon: None declared, Rainer Berendes: None declared, Markus Hufnagel: None declared, Toni Hospach Speakers bureau: Chugai, Roche, Novartis, Kirsten Minden Consultant for: AbbVie

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OP0260 **VACCINATION SAFETY AND COVERAGE IN AN ITALIAN COHORT OF AUTOINFLAMMATORY DISEASES**

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Background: Vaccine-preventable diseases are again emerging in our population after anti-vaccine campaign has started. In autoinflammatory diseases (AID), vaccine triggered-disease is a well known phenomenon for Hyper-IgD/Mevalonate-Kinase Deficiency (MKD). In CAPS, severe flares have been experienced after pneumococcus vaccine, while PFAPA patients did not achieve sufficient and protective levels of antibodies. This evidence has raised doubts in physicians and families about the safety of vaccines.
Objectives: To evaluate, in a cohort of italian AID, the vaccination coverage of the Italian Vaccination Schedule and the prevalence of adverse reactions and disease flares induced by vaccinations.
Methods: An anamnestic questionnaire was applied to AID patients refering to the AID Unit of the Istituto Giannina Gaslini from August 2017 to August 2018. Acquired data were revised for quality of information. Data about disease triggers in AID were obtained from the EUROFEVER registry for statistical reference.
Results: Triggers in AID Eurofever Registry: In august 2018 a total of 3783 patients were enrolled in the EUROFEVER registry (1908 female, 50,43%). The mean age of symptoms at disease onset was 7.04 +/- 9,48 SD yrs, (minimal 0 - maximum 75,92 yrs). The distribution among the periodic hereditary fevers was: 28,75% FMF (n=1081); 17,66% PFAPA (n=666); 9% Undefined inflammatory disease (UND n = 347); 7,85% CAPS (n=297); 7,16% TRAPS (n=271) and 5,39% MKD (n=204). Vaccines triggered the disease in 70% of the MKD, while PFAPA, TRAPS and UND had a rate of reactions of 20%. This was also found in 12.34% of CAPS, whereas FMF and inflammatory bone disorders had a rate of 6% and 3%, respectively. Excluding other causes of reactions, and isolating just vaccines as a cause, MKD had a higher percentage of reactions (7,14%), while PFAPA and UND had 1% and CAPS, TRAPS, FMF and inflammatory bone disorders had less than 1%. Triggers in IGG cohort: 150 questionnaires were distributed with 70% rate of response. Quality of data was 100% for coverage and adverse reactions. 105 patients were identified: PFAPA (n=26); CAPS (n=5); TRAPS (n=6); FMF (n=14); MKD (n=8); Inflammatory Bone Disorders (CRMO and PAPA, n=4) and UND (n=41). Rate of coverage was lower than 90% for Hib3 (83,11%), MMR/MMRV (88,9%) and for Rota C (1,85%). For DTP3, Hep3, PCV3 and IPV the rate of coverage was higher than 90% for all vaccines. 11 moderate/severe reactions were observed as following: 5 after DTPA+IPV (1 PFAPA; 2 TRAPS, 1 MKD and 1 UND); 1 after Hib (PFAPA); 1 after P10/13 (PFAPA); 4 after MPR (1 PFAPA, 1 TRAPS, 1 MKD and 1 UND). The general rate of severe reactions/shot was 6,36 for 1000 shots and no severe infection, death, persistent or significant disability or life-threatening condition was observed. Just one MKD patient had a severe disease flare requiring hospitalization following pneumococcal vaccine.
Conclusion: Data show that in AID patients vaccines may more frequently trigger the disease. Therefore, vaccination in AID may be cosidered a peculiar public health problem. Specific recommendations for vaccination in AID are warranted as well as further investigations for immunologic protection.

REFERENCES:

[1] Ter Haar, et al. The phenotype and genotype of mevalonate kinase deficiency.Arthritis Rheumatol. 2016 Nov;68(11):2795-2805.
[2] Walker A, et al. Severe inflammation following vaccination against Streptococcus Pneumoniae in patients with cryopyrin-associated periodic syndrome.Arthritis Rheumatol. 2016 Nov;68(2):516-520.

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FRIDAY, 14 JUNE 2019

Epidemiology

OP0261 **RISK OF NEUROLOGICAL ADVERSE EVENTS DURING TUMOUR NECROSIS FACTOR INHIBITOR TREATMENT FOR ARTHRITIS: A POPULATION-BASED COHORT STUDY FROM DANBIO AND ARTIS**

Tine Iskov Kopp[1], Elizabeth Arkema[2], René Cordtz[3], Bénédicte Delcoigne[2], Johan Askling[2], Lene Dreyer[4]. *[1]Copenhagen University Hospital, Rigshospitalet, Danish Multiple Sclerosis Registry, Department of Neurology, Copenhagen, Denmark*; *[2]Karolinska Institutet, Department of Medicine Solna, Stockholm, Sweden*; *[3]Center for Rheumatology and Spine Diseases, The Parker Institute, Gentofte-Rigshospitalet, Denmark*; *[4]Aalborg University Hospital and Aalborg University, DANBIO, Department of Rheumatology, Aalborg, Denmark*

Background: Tumor necrosis factor alpha inhibitors (TNFi) have successfully been used for the treatment of immune-mediated inflammatory disorders including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) since 1998. However, several case reports and series have indicated that different neurological disorders including multiple sclerosis (MS), inflammatory neuropathies, demyelinating diseases and optic neuritis may be a serious, although rare, adverse event following TNFi treatment. The relationship is complex, as some studies show that RA is protective of MS and vice versa.
Objectives: To investigate the association between new-onset neurological events following TNFi treatment in arthritis patients compared to non-TNFi-treated arthritis patients from Denmark and Sweden.
Methods: 40,927/62,702 patients registered with a diagnosis of either RA, AS or PsA in DANBIO/ARTIS between January 1, 2000 and January 20, 2017 were included. Complete follow-up on mortality, emigration and incident neurological diseases suspected to be associated with use of TNFi until May 10, 2017 were obtained by linkage to the Danish and Swedish National Patient Registry and the Civil Registration Systems. Cox proportional hazard models were used to examine the association between use of TNFi and risk of a neurological event.
Results: The DANBIO/ARTIS arthritis cohorts contributed 612,347 person-years of observation and 221 patients were diagnosed with demyelinating disease or inflammatory neuropathy during follow-up with 117 cases among TNFi-treated patients and 104 cases among non-TNFi-treated patients. TNFi treatment among RA patients was not associated with an increased risk of a neurological event (DANBIO: HR=1.09, 95% Confidence Interval (CI) 0.60-1.99)/(ARTIS:HR=0.83, 95%CI 0.52-1.35) adjusted for age, gender and year of inclusion. However, TNFi-treated PsA and AS patients had an increased risk of neurological events (DANBIO:HR=2.57, 95%CI 1.17-5.65)/(ARTIS:HR=2.17, 95%CI 0.88-5.35). In TNFi-treated PsA/AS patients, 7 cases of inflammatory polyneuropathies were observed in DANBIO/ARTIS respectively versus 1 and 0 cases among non-TNFi treated. In on-drug models, the HR for neurologic events was 1.17 (ARTIS 95% CI: 0.41-3.35) and 1.66 (DANBIO 95% CI: 0.70-3.92) in PsA/AS.
Conclusion: The use of TNFi for the treatment of arthritis may be associated with increased risk of demyelinating disease or inflammatory neuropathies among patients with PsA and AS. Since these events are rare, larger multicentre studies are warranted to further characterize the risk.
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Disclosure of Interests: Tine Iskov Kopp : None declared, Elizabeth Arkema: None declared, René Cordtz: None declared, Bénédicte Delcoigne: None declared, Johan Askling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer., Lene Dreyer Consultant for: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: UCB, MSD, Eli Lilly and Janssen Pharmaceuticals.
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OP0262

FACTORS ASSOCIATED WITH ACUTE ANTERIOR UVEITIS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: ANALYSIS OF THE BSRBR-AS REGISTER DATABASE

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Background: Acute anterior uveitis (AAU) is one of the key extra-articular manifestations in axial spondyloarthritis (axSpA). The presence of AAU may influence the decision to start and the choice of biological therapy.
Objectives: To examine the factors associated with AAU in patients with axSpA in the British Society for Rheumatology Biologics Register in Ankylosing Spondylitis (BSRBR-AS).
Methods: Clinical and patients-reported outcomes of 2420 patients with axSpA from 83 rheumatology centres in the United Kingdom were collected as part of the BSRBR-AS. Patients with AAU diagnosed by an ophthalmologist were compared to those without AAU in relation to demographic and lifestyle factors. The associations were analysed using univariable and multivariable logistic regression models, considering necessary interaction terms and sensitivity analyses.
Results: 568 (23.5%) patients in the cohort had at least one episode of AAU. The male/female ratio was 2.0:1 and group's median (IQR) age was 51 (41 – 61) years. Factors associated with higher odds of AAU in univariable analyses were HLA-B27 positivity [OR 2.32 (95%CI: 1.66 – 3.23)], university degree [OR 1.44 (95%CI: 1.53 – 1.79)], age [OR (per year) 1.02 (95%CI: 1.01 – 1.03)] and axSpA disease duration [OR (per year) 1.02 (95%CI: 1.02 – 1.03)]. Ever-smoking was inversely associated with AAU [(OR 0.71 (95%CI: 0.59 – 0.89)]. Ever-alcohol drinking (p=0.213), BMI (p=0.325) and gender (p=0.317) did not show any associations.
In multivariable analysis, the magnitude of associations remained significant for HLA-B27 positivity, age, and axSpA disease duration, as did the inverse association with smoking (see Table). Analysis restricted to patients with inflammatory bowel disease did not alter the relationship between AAU and the above risk factors.

Table 1. Factors associational with AAU in axSpA, multivariable analysis

	Wald	df	P value	OR	95% CI for OR
Ever Smoking (vs never)	9.76	1	0.002	0.614	0.452 - 0.834
University Degree (vs lower)	2.27	1	0.132	1.325	0.919 - 1.912
HLA-B27 positive (vs negative)	21.12	1	<0.001	2.399	1.652 - 3.484
Age	17.25	1	<0.001	1.038	1.020 - 1.056
AxSpA Disease Duration	15.77	1	<0.001	1.093	1.046- 1.142

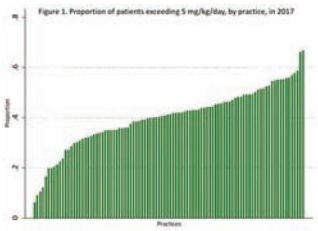
Conclusion: The odds of having a diagnosis of AAU is high in axSpA patients with positive HLA-B27, and longer disease duration (having controlled for age). The negative association with smoking in this large cohort contrasts with previous published data and warrants further evaluation.
Acknowledgement: British Society of Rheumatology
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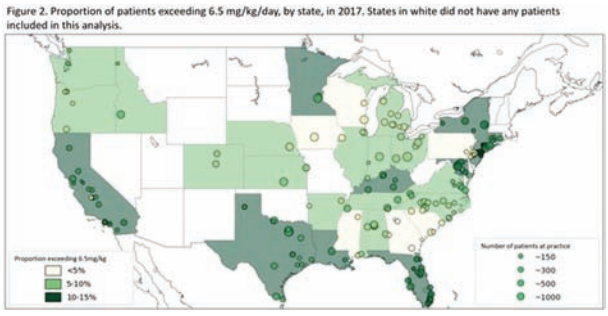
OP0263

HYDROXYCHLOROQUINE DOSING IN PATIENTS WITH RHEUMATIC DISEASE ACROSS THE U.S.: DATA FROM THE RHEUMATOLOGY INFORMATICS SYSTEM FOR EFFECTIVENESS (RISE) REGISTRY

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Background: The risk of retinal toxicity and subsequent visual loss from hydroxychloroquine (HCQ) is dependent on daily dose and duration of use. Although further efficacy and safety studies are required to understand optimal dosing strategies, real-world application of existing American Academy of Ophthalmology (AAO) recommendations in a population-based sample of patients with rheumatic disease has never been described.
Objectives: The objectives of this study were to assess application of AAO dosing recommendations across the U.S. and identify patient and practice-level risk factors for receiving higher than recommended doses using data from the ACR's RISE registry.
Methods: RISE is a national, EHR-enabled registry that passively collects data on all patients seen by participating practices, reducing the selection bias present in single-insurer claims databases. As of December 2017, RISE held validated data from 1,257 providers in 236 practices, representing about 36% of the U.S. clinical rheumatology workforce. We included adult patients with at least one order for HCQ in 2017. For patients with multiple orders, the most recent order was included in the analysis. We excluded weights that appeared to be outliers and practices with <30 patients receiving HCQ. Instructions were interpreted to yield an average daily dose per patient. We investigated practice-level and state-level variation by calculating the proportion of patients who received a dose >5 mg/kg/day by practice and the proportion of patients who received a dose >6.5 mg/kg/day (AAO's 2011 recommendation) by state. We tested whether prescribing a dose exceeding the AAO recommendations was associated with patient-level demographics (age, sex, race/ethnicity, insurance) or practice characteristics (type, size) using multivariate mixed-effects regression.
Results: We included 49,712 patients (85% female, 53% Caucasian, with mean age 57±15) from 96 practices (34% single specialty group practice, 76% with 1-5 providers). The patient average daily dose of HCQ ranged from 57 mg to 800 mg, with a median of 400 mg. Overall, 40% and 9% of patients received a HCQ dose >5 mg/kg/day and >6.5 mg/kg/day, respectively. Practice-level variation ranged from 6-66% for receiving a dose >5 mg/kg/day (Figure 1) and 0-28% for receiving a dose >6.5 mg/kg/day. State-level variation was also significant (p<0.0001, Figure 2). After adjusting for demographics and practice characteristics, low body weight (<78 kg, the sample median) was strongly associated with receiving doses >5 mg/kg/day (+64%, p<0.001) and >6.5 mg/kg/day (+18%, p<0.001). In the same model, female gender was also associated with doses >6.5 mg/kg/day (+5%, p<0.001). Practice characteristics were not statistically significantly associated with receiving a higher dose.





Conclusion: A significant fraction of patients with rheumatic disease on HCQ received doses greater than those recommended by the AAO, with large differences across practices and states. Patients with low body weight are consistently at increased risk of receiving a higher dose. Although further studies are required to

achieve consensus on optimal dosing of HCQ, these data suggest that patients with low body weight should be targeted for toxicity monitoring regardless of the dosing cut-off used.

Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

REFERENCE:

[1] Marmor MF, Kellner U, Lai TY, et al. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (2016 revision).; American Academy of Ophthalmology. Ophthalmology 2016; 123:1386–1394.

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OP0264 REFINING THE PRIMARY CARE CCP+ PATIENT PATHWAY

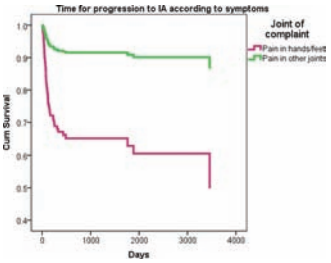
Leticia Garcia-Montoya, Jacqueline Nam, Kulveer Mankia, Laurence Duquenne, Peta Pentony, Andrea Dimatteo, Paul Emery. *NIHR Leeds Biomedical Research Centre, Chapel Allerton Hospital, Leeds, United Kingdom*

Background: It is known that the presence of anti-CCP antibodies (CCP+) is associated with the development of rheumatoid arthritis (RA). Between 0-9% of the general population test positive [1], but only a small percentage of them will develop the disease. Previous work [2] showed that the selection of individuals with non-specific musculoskeletal symptoms, without clinical synovitis enriched the prevalence of anti-CCP positivity and also the likelihood of imminent progression to inflammatory arthritis.

Objectives: To assess for other factors which are associated with disease progression in patients testing CCP+ in order to optimise primary care referrals to Rheumatology.

Methods: A prospective observational study recruiting patients over 18 years old with a new musculoskeletal complaint and no clinical synovitis was conducted. Patients were recruited from primary care centres across the UK from July 2007 until February 2018. Those testing CCP+ in anti-CCP2 assay (immunocap method, Phadia assay) were invited to come to Leeds for assessment and follow-up including a baseline musculoskeletal ultrasound. Patients unable to attend were sent questionnaires 12 months later and were contacted in January 2019 to assess their status.

Results: 5702 eligible patients were recruited from primary care. 2.99% (171/5702) patients tested CCP+ and data from 150 patients was available for analysis: 42.7% (64/150) progressed to inflammatory arthritis (IA), predominantly RA. The mean time of progression was 242 days and 91% progressed in less than 12 months. The absence of pain in the hands or feet had a negative predictive value of 91% for the development of IA (p=0.001) (fig.1); indeed, the RR for progression to IA in patients with a new complaint in hands or feet was 1.6 (95% CI 1.02-2.36, p=0.025). Regarding the presence of antibodies, CCP+ high titre patients had a RR of 2.1(95% CI 1.63-2.68, p<0.001) for the development of IA and 93% of all progressors were CCP+ high titre.



Only 9% (4/43) of patients with CCP+ low titre progressed to IA vs the 57% (55/97) of patients with CCP+ high titre (p<0.001). All low titre progressors had pain in hands and feet and history of smoking exposure. 114 patients came to secondary care for assessment and a baseline musculoskeletal ultrasound scan was performed in 72 of them: the presence of PD in hands/feet was associated with progression to IA with a RR 2.4 (95%CI 1.27-4.58, p=0.01).

Conclusion: CCP+ patients without clinical synovitis who do not have pain in the hands or feet are unlikely to progress to IA especially if they have low titre antibodies. A high anti-CCP titre, new pain in hands/feet and PD in these joints are associated with rapid progression. These data may help optimise the primary care referrals to Rheumatology.

REFERENCES:

[1] Generali, et al., ACR congress 2017
[2] Nam JL, Ann Rheum Dis 2016;75:1452-1456

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Disclosure of Interests: Leticia Garcia-Montoya: None declared, Jacqueline Nam: None declared, Kulveer Mankia Grant/research support from: Research support from BMS and Lilly, Speakers bureau: Honoraria from Abbvie, UCB, Laurence Duquenne: None declared, Peta Pentony: None declared, Andrea DiMatteo: None declared, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead,Samsung, Sandoz and Lilly
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OP0265 FRAILTY, DISABILITY, AND WORK DISABILITY IN PEOPLE WITH OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

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Background: Frailty is a clinical syndrome associated with adverse health outcomes. Frailty and disability can co-occur though are distinct entities. There are few prospective data looking at the occurrence and development of frailty, disability, and work disability in people with osteoarthritis (OA) and rheumatoid arthritis (RA).

Objectives: To determine the odds of prevalent and incident frailty, disability, and work disability in people with OA or RA, compared to people without these diseases.

Methods: Subjects aged 40-69 were recruited to the UK Biobank cohort. Data, including self-reported physician-diagnosed OA and RA, were collected at baseline (2007-10) and, in a subset, at follow up (2012-16). Frailty was measured using a modified Fried phenotype comprising five components: self-reported weight loss, exhaustion, low physical activity, slow usual walking pace, and low measured grip-strength (1). Participants were classified as robust if none of the components were present, pre-frail if 1-2 components were present and frail if $\geq$3 components were present. Participants were classified as having a disability if they indicated receiving a disability allowance/benefit. Participants indicating that they were unable to work due to disability or illness were classified as work disabled. Incident frailty was defined as frail at follow up and robust or pre-frail at baseline. Incident disability or work disability, respectively was defined as receiving a disability benefit or indicating work disability at follow up but not at baseline.

Results: The mean (SD) age of the 465,379 participants at baseline was 56.5 (8.1) years and 54.3% were female. At baseline, 8.0% of the cohort reported that they had OA and 1.1% RA. At baseline, the prevalence of pre-frailty and frailty was 45.9% and 3.1%, respectively. 3.4% of the cohort indicated receiving a disability benefit, and 3.6% being work disabled. In a model adjusted for age, sex, smoking status and deprivation, compared to those without OA, those with OA were more likely to be pre-frail, odds ratio (OR) (95% CI), 1.8 (1.7,1.8), or frail, OR 4.5 (4.3,4.7), than robust. The adjusted OR (95% CI) for pre-frailty and frailty in those with RA (vs no RA) was 2.8 (2.6, 3.0) and 10.6 (9.7, 11.6), respectively. The adjusted OR (95% CI) for disability benefit was 3.9 (3.8, 4.1) in people with OA (vs no OA) and 7.7 (7.2, 8.2) in people with RA (vs no RA). The adjusted OR (95% CI) for work disability at baseline was 3.5 (3.3, 3.6) in people with OA and 4.8 (4.4, 5.2) in people with RA.

Data were available for 26,932 participants at follow up. The mean (SD) follow up time was 5.3 (1.5) years. Of those without frailty at baseline, 573 participants developed frailty during follow up. There were 292 incident cases of disability benefit and 137 incident cases of work disability. The adjusted OR (95% CI) for incident frailty in people with OA and RA at baseline was 2.3 (1.8, 2.9) and 3.3 (1.9, 5.7), respectively. The adjusted OR (95% CI) for incident disability benefit in people with OA and RA at baseline, was 2.7 (2.0, 3.6) and 3.2, (1.7, 6.2), respectively. The adjusted OR (95% CI) for incident work disability in people with OA and RA at baseline was 2.3 (1.3, 3.9) and 3.7 (1.3, 10.1), respectively.

Conclusion: People with OA and RA have an increased risk of being, or becoming, frail, disabled, or work disabled. Further work is needed to determine effective

strategies for preventing or delaying the occurrence of frailty, disability, and work disability in people with OA and RA.

REFERENCES:

[1] Hanlon P, Nicholl BI, Jani BD, Lee D, McQueenie R, Mair FS. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: A prospective analysis of 493 737 UK biobank participants. The Lancet Public health 2018;3:e323-e32

Disclosure of Interests: None declared
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OP0266 RISK OF HOSPITALIZED INFECTION IN PATIENTS WITH CHRONIC INFLAMMATORY ARTHRITIS TREATED WITH BIOLOGICAL DRUGS – A MATCHED COHORT STUDY

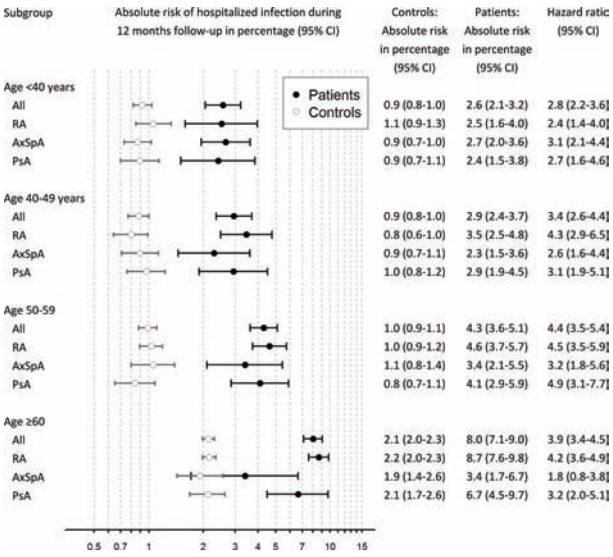
Simon Krabbe[1,2], Kathrine L. Grøn[1,2], Bente Glintborg[1,3], Frank Mehnert[4], Dorte E. Jarbøl[5], Mikkel Østergaard[1,2], Merete L. Hetland[1,2]. [1]*The DANBIO Registry and Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark*; [2]*Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*; [3]*Center for Rheumatology and Spine Diseases, Gentofte Hospital, Hellerup, Denmark*; [4]*Department of Clinical Epidemiology, Aarhus University, Aarhus, Denmark*; [5]*Department of Public Health, University of Southern Denmark, Odense, Denmark*

Background: Patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) treated with biological drugs (bDMARDs) have increased risk of hospitalized infection (i.e. infection causing admission to hospital) compared to the general population. Since patients with RA, axSpA and PsA have different age distributions, and age is an important predictor for infection, we found it of interest to quantify the excess burden of hospitalized infection in patients with inflammatory arthritis treated with bDMARDs compared to the general population and to investigate whether risk depended on age and diagnosis.
Objectives: To compare the risk of hospitalized infection in bio-naïve patients with inflammatory arthritis, who started treatment with a bDMARD with that of the general population, and to explore how this risk was influenced by age and diagnosis.
Methods: Matched cohort study based on data from The Danish Rheumatology Register (DANBIO) linked with The Danish National Patient Register and The Danish National Prescription Register. Patients with a diagnosis of RA, PsA or axSpA in DANBIO initiating first bDMARD January 2006-December 2016 were included. For each patient, 10 controls from the general population, matched by age, sex, postal code and date were obtained. Infection risk in patients and matched controls were compared in analyses stratified by age and diagnosis, with Cox proportional hazards models accounting for matching. Follow-up time was 12 months irrespective of whether treatment was continued or changed during follow-up. Clinicaltrials.gov: NCT03496831.
Results: In total, 11,372 patients and 113,715 controls were included. Overall, hospitalized infection was observed during follow-up in 4.6% of patients and 1.3% of controls; hazard ratio 3.7 (95% confidence interval (CI): 3.4-4.1).

Table 1. Baseline characteristics and risk of hospitalized infection.

	RA		AxSpA		PsA	
	Patients (n=5985)	Matched cohort (n=59848)	Patients (n=2958)	Matched cohort (n=29579)	Patients (n=2429)	Matched cohort (n=24288)
Age <40	11.9%	11.9%	49.6%	49.6%	29.0%	29.0%
40-49	16.9%	16.9%	26.5%	26.5%	28.1%	28.1%
50-59	28.9%	28.9%	16.0%	16.0%	28.0%	28.0%
≥60	42.3%	42.3%	7.9%	7.9%	14.9%	14.9%
Men	25.0%	25.0%	60.9%	60.9%	45.6%	45.6%
No. of persons with hospitalized infection during 12 months of follow-up	352	880	81	292	89	262
Absolute risk of hospitalized infection during 12 months of follow-up (95% CI)	5.9% (5.3-6.5%)	1.5% (1.4-1.6%)	2.7% (2.2-3.4%)	1.0% (0.9-1.1%)	3.7% (3.0-4.5%)	1.1% (1.0-1.2%)

The absolute risk was highest in RA patients, followed by PsA, axSpA and controls (unadjusted comparison). When stratified by age, the absolute risk increased with age, but was largely similar across diagnoses (Figure). In the stratum ≥60 years, RA patients appeared to have higher risk than axSpA patients, but the subgroup of axSpA patients ≥60 years was small.



Conclusion: The risk of hospitalized infection during 12 months of follow-up was approximately four times higher in bio-naïve patients with inflammatory arthritis who started treatment with a biological drug (bDMARD) compared to matched controls from the general population. When stratified by age, the absolute risk was largely similar across the diagnoses RA, axSpA and PsA. Thus, attention to preventive strategies such as vaccination seems prudent in these patients, especially those ≥60 years of age.
Disclosure of Interests: Simon Krabbe: None declared, Kathrine L. Grøn: None declared, Bente Glintborg Grant/research support from: Biogen, Pfizer, AbbVie, Frank Mehnert: None declared, Dorte E. Jarbøl: None declared, Mikkel Østergaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Merete L. Hetland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Bioepis
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OP0267 INACTIVATED INFLUENZA VACCINATION DOES NOT ASSOCIATE WITH DISEASE FLARES IN AUTOIMMUNE RHEUMATIC DISEASES: A SELF-CONTROLLED CASE SERIES STUDY USING DATA FROM THE CLINICAL PRACTICE RESEARCH DATALINK

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Background: Concerns about vaccination with the seasonal flu vaccine associating with increased risk of autoimmune rheumatic disease (AIRD) activity, and anecdotal reports of the seasonal flu vaccine triggering diseases such as vasculitis are barriers to flu vaccination in this population[1-2]. This is despite reports of stable disease activity following flu vaccination provided disease modifying antirheumatic drug therapy is continued in the peri-vaccination period[3]. Previous studies generally include patients with stable disease activity, and as far as we are aware, a real world study evaluating the association between inactivated influenza vaccine (IIV) administration and AIRD activity has not been conducted.
Objectives: To examine the association between IIV administration and primary care consultation for joint pain, fatigue, rheumatoid arthritis (RA) flare, corticosteroid prescription, and incident vasculitis in people with AIRDs.

Methods: We undertook within-person comparisons using self-controlled case-series (SCCS). AIRD cases who received IIV and had an outcome of interest in the same influenza cycle, between 1st September of one year and 31st August of the next year, between 2006 and 2016 were ascertained within the Clinical Practice Research Datalink. The influenza cycle (1st September of one year to 31st December of the next year) was partitioned into five exposure periods (1-15 days pre-vaccination, and 0-14, 15-30, 31-60, and 61-90 days post-vaccination), with the remaining time period classified as non-exposed. Incidence rate ratios (IRRs) and 95% confidence intervals (CI) were calculated to compare the frequency of outcomes in different periods.

Results: Data for 14,928 AIRD cases (69% women, 80% with RA) were included. There was no association between IIV administration and primary-care consultation for RA flare, corticosteroid prescription, and vasculitis (Table 1). Vaccination associated with reduced primary-care consultation for joint pain in the 90-day post-vaccination period (IRR (95%CI) 0.91(0.87-0.94)), and fatigue (IRR (95%CI) 0.40(0.22-0.71)) in the 61-90 days post vaccination (Table 1).

Abstract Table 1. Association between IIV and AIRD flare and vasculitis

	IRRs(95% CI)				
Risk period	**Joint pain**	**Corticosteroid prescription***	**Fatigue**	**RA flare**	**Vasculitis**
Baseline	1.00	1.00	1.00	1.00	1.00
Upto 15 days pre vaccination	**1.29 (1.20-1.39)**	1.17 (0.73-1.89)	1.09 (0.67-1.79)	0.95 (0.64-1.41)	0.95 (0.38-2.33)
Post-vaccination					
0-14 days	**0.84 (0.77-0.92)**	1.11 (0.67-1.84)	0.62 (0.32-1.20)	0.97 (0.65-1.45)	0.41 (0.10-1.65)
15-30 days	0.94 (0.86-1.02)	1.31 (0.83-2.06)	0.90 (0.52-1.54)	1.12 (0.78-1.62	0.95 (0.38-2.33)
31-60 days	**0.93 (0.88-0.99)**	1.02 (0.70-1.48)	0.87 (0.59-1.30)	1.06 (0.80-1.39)	0.76 (0.37-1.56)
61-90 days	**0.90 (0.84-0.96)**	0.76 (0.49-1.16)	**0.40 (0.22-0.71)**	0.81(0.59-1.10)	1.14 (0.62-2.08)

*New corticosteroid prescription on the same date as consultation for either RA flare, or joint pain, or fatigue.

Conclusion: The administration of IIV was not associated with flare of the underlying AIRD and its association with reduced disease activity warrants further investigation. Nevertheless, these data add to the accumulating evidence to support seasonal influenza vaccination in people with AIRDs.

REFERENCES:

[1] Loubet P, et al. Vaccine. 2015; 33(31):3703-8.
[2] Birck R, et al. Journal of clinical rheumatology: practical reports on rheumatic & musculoskeletal diseases. 2009; 15(6):289-91.
[3] Park JK, et al. Annals of the Rheumatic Diseases. 2018; 77(6):898-904.

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FRIDAY, 14 JUNE 2019

HPR Abstract session II

OP0268-HPR

THE PREVALENCE AND IMPACT OF FATIGUE IN PEOPLE WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME: A MIXED METHODS STUDY

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Background: Primary antiphospholipid syndrome (pAPS) is a prothrombotic disorder associated with increased morbidity and mortality[1]. Symptoms include fatigue but the prevalence and impact of fatigue is unknown.

Objectives: To explore the prevalence, relationships and impact of fatigue in adults with pAPS.

Methods: This mixed methods study recruited participants from one public hospital, UK. Inclusion criteria comprised: adults with ≥6 month history of pAPS (Sydney classification criteria) and sufficient written and spoken English. Exclusion criteria included: other autoimmune rheumatic/inflammatory disorders; cancer; active chronic infections, positive Antinuclear antibody, pregnancy/breast-feeding, drugs/alcohol dependency and BMI>30.

Consenting participants completed seven questionnaires to record sociodemographc characteristics, fatigue (Fatigue Severity Scale (FSS), FACIT-Fatigue subscale, (FS)), social support (Multi-Dimensional Perceived Social Support Scale (MDPSS), mood (Patient Health Questionnaire (PHQ-9), quality of life (EQ-5D-5L), sleep quality (Pittsburgh Sleep Quality Index (PSQI) and physical activity (International Physical Activity Questionnaire (IPAQMETS)). The relationship between fatigue (FSS) and predictor variables were explored using Spearman's Rho correlation coefficients and backward stepwise regression analyses.

Audio recorded, semi structured interviews were conducted with a subset of participants by two researchers with an agreed topic guide. Interviews were transcribed verbatim, anonymised, and analysed thematically with NVivo 10. The data was validated by a subsample of participants, cross-referencing the emergent codes and themes.

Results: 103 participants were recruited (87 complete datasets; mean (standard deviation) 50.3 (10.4) years, 8 men, 49 thrombotic APS). 69% of participants reported clinically relevant fatigue (FSS>3) and 62% of participants indicated severe fatigue (FSS>4). FSS was positively associated with PSQI ($r_s(67)=0.269$ $p=0.025$), PHQ9 ($r_s(83)=0.602$ $p<.001$) and negatively associated with EQ-5D-5L ($r_s(83)=-0.505$ $p<0.001$), FS ($r_s(82)=-0.656$ $p<0.001$) and IPAQMETS ($r_s(80)=-0.243$ $p=0.028$) but not MSPSS.

The best fit model explained 62% of the variance in FSS (adjusted $R^2=0.617$, $F_{(5,62)}=22.63$,$p>0.001$) and included FS, MSPSS, PHQ9, and IPAQMETS as significant predictors. For every 1 unit increase in FS, MSPSS, IPAQMETS and PHQ9, FSS decreased by -0.087 points, -0.084 points and $-9.7*10^{-5}$ MET/minutes or increased by 0.090 points respectively.

Twenty participants (10 obstetric/10 thrombotic pAPS) completed interviews (duration 20-50 minutes). Participants with obstetric pAPS were younger. Five themes were identified across both subgroups: 1. Unpredictability of fatigue 2. Impact on daily life 3. Physical activity matters 4. Individual coping strategies 5. Acknowledgement and help with fatigue from clinicians.

Conclusion: Fatigue is a common, overwhelming, unpredictable symptom of pAPS which is a challenge to manage. Social support, mood and physical activity predicted fatigue severity. Interviewees tended not to discuss fatigue with clinicians due to lack of observed response or empathy. Participants perceived physical activity as important but difficult to complete regularly. Interventions to manage fatigue and support physical activity are needed for adults with pAPS.

REFERENCE:

[1] Cervera R, et al. Annals of the rheumatic diseases. 2015 Jun 1;74 (6):1011-8

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OP0269-HPR PATTERNS OF FATIGUE AND PREDICTORS OF SIGNIFICANT IMPROVEMENT IN THE 1ST YEAR OF RA: RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT (CATCH)

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Background: Fatigue is common in early RA(ERA) and though some patients experience improvement in fatigue when disease is well controlled, others experience persistent fatigue associated with work disability, poor QOL, and depression.

Objectives: To compare patterns and predictors of improved vs. persistent fatigue in the first year of ERA.

Methods: Data were from ERA patients (symptoms <1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) from 01-2007 to 03-2017. All met ACR1987 or 2010 ACR/EULAR criteria, had active disease, were on DMARDS, and complete fatigue (0-10) data over ≥ 12 months. Patients were classified at baseline with **low** (<4) or **high** (≥4) fatigue; high fatigue patients were categorized at 12-months as **improved** (↓ ≥2) or **persistent** (↓ <2). Multivariable logistic regression was used to identify predictors of improved vs. persistent fatigue at 12 months in those with high baseline fatigue.

Results: The 1002 pts were mostly white (81%), female (71%), with a mean (SD) age of 54 (15); 32% were obese. 70% had high fatigue at baseline; these patients were more obese, had OA/backpain, poor sleep, depression, major stress, and higher disease activity (Table 1). Among those with initial high fatigue, 30% had persistent fatigue at 12 months and was associated with obesity, comorbidities, FM, longer symptom duration, and slightly lower baseline fatigue.

Mean (SD) or N (%)	LOW FATIGUE	HIGH FATIGUE		p-value	
	Low (n=301)	Improved (n=493)	Persistent (n=208)	Low v. High	Imp v. Persist
Age	55 (15)	54 (15)	54 (15)	0.13	0.97
Female sex	202 (67%)	360 (73%)	152 (73%)	0.06	0.99
>High School	169 (56%)	267 (54%)	103 (50%)	0.33	0.26
Personal/health					
Work (full/part time)	161 (53%)	274 (56%)	115 (55%)	0.56	0.94
RD Comorbidity Index	1.1 (1.3)	**1.1 (1.3)**	**1.4 (1.4)**	0.42	**0.001**
OA or backpain	**52 (17%)**	**114 (23%)**	**55 (26%)**	**0.02**	0.35
Fibromyalgia	3 (1%)	**10 (2%)**	**10 (5%)**	0.07	**0.04**
Poor sleep	**2.6 (2.7)**	**6.3 (2.9)**	**6.1 (2.7)**	**<0.001**	0.38
Cognitive/Behavioral					
Obese (BMI≥30)	**78 (26%)**	**152 (31%)**	**86 (41%)**	**0.01**	**0.01**
Smoking	48 (16%)	83 (17%)	33 (16%)	0.81	0.75
Depression (SF12 MCS<45.6)	**62 (22%)**	**273 (59%)**	**113 (57%)**	**<0.001**	0.59
Major stress past year	**138 (46%)**	**268 (54%)**	**118 (57%)**	**0.01**	0.58
RA					
Symptom duration (mth)	5.7 (2.9)	**5.5 (3.0)**	**6.1 (3.2)**	0.79	**0.02**
RF+/ACPA+	221 (85%)	349 (81%)	133 (76%)	0.07	0.21
DAS28 (MDA/HDA v. LDA/REM)	**280 (93%)**	**481 (98%)**	**199 (96%)**	**<0.01**	0.18
Pain (0-10)	**3.8 (2.6)**	**6.7 (2.4)**	**6.4 (2.2)**	**<0.001**	0.08
HAQ-DI	**0.7 (0.6)**	**1.3 (0.7)**	**1.2 (0.7)**	**<0.001**	0.15
Baseline fatigue (0-10)	**1.6 (1.2)**	**7.2 (1.9)**	**6.6 (1.7)**	**<0.001**	**<0.001**

Predictors of improved fatigue in multivariable models were BMI<30 (OR 0.6; 95% CI 0.4, 0.9), MTX≥20 mg (OR 1.7; 95% CI 1.0, 2.7) and higher pain (OR 1.1; 95% CI 1.0, 1.2) after controlling for other variables.

Conclusion: Fatigue is common in ERA and associated with active disease, worse pain and disability, obesity, depression, major stressors, poor sleep and OA/backpain. In high fatigue pts, those who are not obese, have higher pain, and take ≥20 mg MTX are more likely to improve over the first year. Optimizing weight, sleep, physical and emotional health and MTX use may improve persistent fatigue beyond control of RA inflammation.

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OP0270-HPR COMPARISON OF THE REASONS FOR NOT GOING TO SCHOOL BETWEEN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS AND THEIR FAMILIES:

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Background: Chronic physical illnesses may disrupt school attendance which possibly causes academic and social problems in children. Decreased school attendance and poor educational performance are shown to be related to poor self-esteem (1). In addition, family life is affected by the consequences of chronic diseases. Family reinforcement has an important effect on children's behaviors and function (2). In this psychosocial combination, daily routines like school attendance may be affected by family and children's behavior to disease symptoms.

Objectives: The aim of this study was to compare the reasons for not going to school between children with juvenile idiopathic arthritis and their families.

Methods: The study included 181 juvenile idiopathic arthritis children who do not attend school and their families who applied to Hacettepe University, Faculty of Medicine, Department of Pediatric Rheumatology. The reasons for not attending school was assessed with one of the questions of Juvenile Arthritis Biopsychosocial Questionnaire (JAB-Q)(3) with three answers. Functional status of the children was assessed with the functional score of JAB-Q and Child Health Assessment Questionnaire (CHAQ) and psychosocial status with the psychosocial score of JAB-Q. Mean and standard deviations were used for descriptives and Chi-Square test was used to compare the family and children responses.

Results: Mean age of children was 12,65±3,736 and mean scores of CHAQ, JAB-Q function and JAB-Q psychosocial were 0,48±0,59, 4,36±7,7 and 13.74 ±8,13, respectively (Table 1). Children and families gave the same answer with% 92,4 to the question about the reason for not attending school (Table 2). There wasn't any difference between children's and family's answers (p>0,05). Functional status of children was good according to JAB-Q and CHAQ, and psychosocial status was good according to JAB-Q.

Table 1. Descriptive Statistics

	Mean	Std. Deviation
Age (year)	12,65	3,73
CHAQ–Total (between 0-3 points)	0,48	0,59
JAB-Q Function (between 0-66 points)	4,36	5,70
JAB-Q Psychosocial (between 0-52 points)	13,74	8,13

Table 2. Children's and Parent's Answers

			Parent's Answers			Total
			He/she couldn't go because he/she felt unwell.	I didn't let them go.	He/she was worried about attending school. He/she was concerned about doing well in exams.	
Children's Answers	I was ill and felt unwell.	Count	159	9	4	172
		% within	92,4%	5,2%	2,3%	100,0%
	My parents didn't let me go.	Count	2	1	0	3
		% within	66,7%	33,3%	0,0%	100,0%
	I'm worried/scared about going to school. I can't go because I'm scared I won't do well in exams.	Count	6	0	0	6
		% within	100,0%	0,0%	0,0%	100,0%
Total		Count	167	10	4	181
		% within	92,3%	5,5%	2,2%	100,0%

Conclusion: Child's psychosocial adjustment is likely to be related with school attendance. When the attendance decreases, problems such as social functioning and isolation can occur. The fact that families and children agreed on the reasons about not to go to school but their functional and psychosocial status were good may have been due to different reasons. It was thought to normalize and encourage children to go to school. In addition, families should motivate their children with positive reinforcements.

REFERENCES:

[1] C Sturge, M E Garralda, M Boissin, C J Doré, P Woo; School attendance and juvenile chronic arthritis., Rheumatology, Volume 36, Issue 11, 1 November 1997, Pages 1218–1223

[2] Catherine Cant Peterson, Tonya Mizell Palermo; Parental Reinforcement of Recurrent Pain: The Moderating Impact of Child Depression and Anxiety on Functional Disability, Journal of Pediatric Psychology, Volume 29, Issue 5, 1 July 2004, Pages 331–341, https://doi.org/10.1093/jpepsy/jsh037

[3] UNAL, Edibe, et al. A new biopsychosocial and clinical questionnaire to assess juvenile idiopathic arthritis: JAB-Q. Rheumatology international, 2018, 1-8.

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OP0271-HPR ASSESSMENT OF MUSCLE MASS RELATIVE TO FAT MASS AND ITS ASSOCIATION WITH DISEASE ACTIVITY STATUS AND PHYSICAL FUNCTIONING IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune, chronic, progressive, inflammatory disease characterized by symmetrical, destructive polyarthritis and is accompanied by systemic manifestations. RA patients show low appendicular lean mass index (ALMI) and higher fat mass index. Impaired physical function is associated greater with fat mass and the adiposity is an important confounder that may mask true relationships between physical functioning and ALMI (1).
Objectives: To assess muscle mass relative to fat mass and verify associations this parameter with disease activity status, functional capacity and biologics treatments.
Methods: 90 RA patients, aged between 40 and 70 years, were recruited and followed for 12 months. Body composition was assessed by total body dual-energy x-ray absorptiometry for measurement of appendicular lean mass index (ALMI, kg/m2) and fat mass index (FMI, kg/m2). Age-, sex-, and race-specific Z- Scores and T-Scores were determined by comparison to published reference ranges. ALMI values were adjusted for FMI (ALMIZ/FMIZ) using a published method. Disease activity was assessed by Disease Activity Score-28 with erythrocyte sedimentation rate (DAS28). RA patients were divided in non-remission (DAS28<2.6) and in remission (DAS28>2.6). Physical functioning was assessed by Health Assessment Questionnaire (HAQ). Pharmacological treatment used by patients were assessed in patient medical records and the RA were divided in RA patients treated with biologic disease modifying antirheumatic drugs (bDMARDs) and non-treated with bDMARDs. Frequency analysis, Pearson Correlations and GEE analyses were used and statistical significance was considered as $p<0.05$.
Results: Of the 90 patients analyzed, most were women (86.7%,78/91), with mean age of 56.5±7.3 and median disease duration time of 8.5 (3-18) years. At baseline, the mean±SD DAS28 score was 3.7±1.4 and thirty percent of the RA patients (27/90) were treated with bDMARDs. After 12 months, the use of bDMARD did not change ($p>0.05$), however, mean DAS28 increased over time (mean and SD of 4.0±1.3; $p<0.05$). Eleven RA patients (12.2%) showed low ALMI/FMI for age (Z-score ≤-1) at baseline, and 13 (16.0%) after 12 months. After 12 months, ALMIZ/FMIZ was inversely associated with HAQ ($r=-0.3$; $p<0.05$). At, baseline, women in remission had higher ALMIZ, lower FMIZ and higher ALMIZ/FMIZ, while men had lower ALMIZ, lower FMIZ and higher ALMIZ/FMIZ. In men, remission was associated with decreases in FMIZ ($p<0.05$). The use of bDMARDs was not related with alterations in ALMIZ, FMIz and ALMIZ/FMIZ ($p>0.05$).
Conclusion: Low skeletal muscle mass relative to adiposity was common in RA patients. This condition was associated with low physical functioning and its changes over time are associated with disease activity status. The observations that skeletal muscle mass relative to adiposity was affected by remission state stresses and that associated negatively with poor physical functioning demonstrate the importance of adequate control of disease activity in RA established. In addition, from our results, further studies are necessary to elucidate the direct impact of bDMARDs on body composition in RA patients.

REFERENCES:

[1] Weber D, Long J, Leonard MB, Zemel B, Baker JF. PLoS One. 2016; 10;11(10):e0164385

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OP0272-HPR FITNESS STATUS OF PEOPLE WITH AXIAL SPONDYLOARTHRITIS (AXSPA): FIRST RESULTS AFTER IMPLEMENTATION OF FITNESS ASSESSMENTS IN AXSPA EXERCISE GROUPS

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Background: Public health recommendations for physical activity (PA) advice that exercise programs include all four fitness dimensions, i.e. cardiorespiratory, muscle strength, flexibility and neuromotor exercise training at well-defined

frequency, intensity and duration/repetitions, and regular evaluations (1). The 2018 EULAR recommendations for PA (2) state that this is also effective, feasible and safe for people with rheumatic diseases. Therefore, the Ankylosing Spondylitis Association of Switzerland (SVMB) has started to implement assessments of all four fitness dimensions in their exercise groups (n=68). Criteria for selection of an assessment were its psychometric properties and feasibility for group setting, i.e. low costs and material requirements: Chester step test (CST) for cardiorespiratory fitness (3); adapted Core Strength Endurance test battery (CSE) for muscle strength (4); Bath AS Metrology Index (BASMI) for flexibility (5); Single-Leg-Stance test (SLS) for balance (as proxy for neuromotor activities) (6). For all assessments, except CSE, norm values for healthy people are available.

Objectives: To assess the fitness status of people with axSpA across four volunteering pilot groups and evaluate if between-subject variables of interest are associated with fitness status.

Methods: Participants were assessed at baseline and after 6 months on all four fitness dimensions. For each dimension, a linear mixed model with random intercept was fitted to the data with the within-subject variables time and measurement condition and the between-subject variables age, disease duration, disease activity (Bath AS Disease Activity Index, BASDAI) and PA level (weekly Metabolic Equivalent of Task MET) as explanatory variables.

Results: Of 30 patients assessed, 10 (33%) were women, mean age was 58.8 (SD 9.68) years, mean disease duration was 32.6 (SD 9.68) years, mean disease activity was 3.1. (SD 2.36) and mean PA per week was 5013 (SD 3479.77) METs. Mean estimated VO^2max for cardiorespiratory fitness was 35.2 (SD 6.59). Disease activity was negatively (slope=-1.49, p=0.01) and PA level positively (slope=3.28, p=0.01) associated with cardiorespiratory fitness. Mean core muscle strength endurance was 78.8 (SD 51.98) seconds. PA level was positively associated with core muscle strength (slope= 8.62, p=0.05). Mean flexibility score was 3.1 (SD 2.36), with age being positively associated with flexibility (slope=0.100, p=0.04). Mean balance was 43.1 (SD 21.09) and 7.7 (SD 5.84) seconds with open and closed eyes respectively. Age was negatively associated with balance (slope = -0.84 (p=0.00).

Conclusion: The SVMB has made an important step by implementing regular fitness evaluations in their axSpA exercise groups. The test scores of the assessed people with axSpA were lower than in healthy people but within the norms. PA level was positively associated with cardiorespiratory fitness and core muscle strength. Disease duration and disease activity were negatively associated with cardiorespiratory fitness only, but not with the other fitness dimensions, which may be different from what is usually assumed.

REFERENCES:

[1] Garber CE, et al. MedSciSportsExerc 2011;43:1334–59.
[2] Rausch AK, et al. AnnRheumDis 2018; 9(77): 1251-1260.
[3] Buckley JP. B J Sports Med, 2004;38(2);197-205
[4] Rausch AK, et al. Intra-rater reliability and construct validity of a core strength-endurance test battery in people with axial Spondyloarthritis (manuscript in preparation)
[5] Jenkinson TR. 1994;21(9):1694-8. Epub 1994/09/01
[6] Springer BA. J Ger Phys Ther. 2007;30(1);8-15

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OP0273-HPR FUNCTIONAL EXERCISE FOR ADULTS WITH CHRONIC NON-SPECIFIC LOW BACK PAIN: A RANDOMIZED CONTROLLED TRIAL

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Background: Exercise therapy is part of the recommendation for the treatment of chronic non-specific low back pain (LBP). Functional exercise may be an alternative for the treatment, no studies assessing its effectiveness were found.

Objectives: To assess the effectiveness of the functional exercise program for pain, functional capacity, general health, kinesiophobia and perceived exertion in adults with chronic nonspecific LBP.

Methods: A randomized controlled clinical trial with intention-to-treat analysis and 24-week follow-up was performed. Eighty-four patients were randomly assigned to an experimental group (EG) or control group (CG). The EG participated in the functional exercises program performed twice a week for twelve weeks. The functional exercise program was composed by global exercise that worked the group of muscles of the trunk and lower and upper limbs with progression every 4 weeks. The two groups received an informative class on the disease and were advised to use analgesic if necessary. Primary outcome was LBP measured by numeric rating scale (NRS). Secondary outcomes included was functional capacity by Oswestry and Roland Morris questionnaires, 6-minute walk and TUG tests, kinesiophobia (FABQ), general health (SF-36), perceived exertion (BORG). Evaluations were performed at baseline, after 6, 12 (end of intervention) and 24 weeks by a blind evaluator.

Results: The groups were homogeneous for all parameters at baseline. Compared with the CG, the EG statistically improved pain, functional capacity, kinesiophobia, some domains of general health and peceived exertion - Table 1.

Conclusion: The functional exercise program was effective to improve pain, functional capacity, kinesiophobia, general health and percepived exertion in adults with chronic nonspecific LBP.

REFERENCES:

[1] Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, et al. A systematic review of the global prevalence of low back pain. Arthritis and Rheumatism. 2012.
[2] Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, et al. What low back pain is and why we need to pay attention. The Lancet. 2018.

Abstract OP0273HPR Table 1. Between-groups evaluations

	T0		T6		T12		T24		p Value (GLM)
	EG	CG	EG	CG	EG	CG	EG	CG	
NSR	6.2 (1.3)	6.0 (1.7)	3.1 (1.8)	5.5 (1.7)	2.3 (1.9)	5.5 (1.8)	2.3 (1.8)	5.5 (1.6)	<0.001*
ODI	20.7 (10.8)	25.5 (11.3)	12.0 (7.0)	22.1 (10.3)	9.5 (6.3)	22.5 (10.5)	8.9 (6.4)	22.8 (10.9)	<0.001*
RMDQ	6.9 (5.0)	8.4 (5.3)	4.1 (3.3)	7.6 (4.7)	2.8 (2.6)	7.3 (4.7)	2.6 (2.4)	8.1 (5.2)	<0.001*
TUG	8.3 (1.1)	8.7 (2.6)	8.27 (1.94)	8.69 (1.90)	7.84 (1.08)	8.99 (2.14)	7.86 (0.83)	9.08 (2.49)	0.005*
FABQ work	18.6 (15.7)	17.6 (12.0)	12.4 (9.0)	16.8 (12.0)	10.5 (9.3)	16.6 (11.1)	7.5 (7.4)	17.6 (11.4)	<0.001*
FABQ phys	11.9 (6.2)	13.0 (6.3)	7.1 (6.5)	13.0 (7.1)	7.0 (6.0)	13.2 (7.3)	6.9 (6.1)	13.0 (7.5)	<0.001*
SF-36 Physical functioning	66.1 (21.3)	60.1 (25.7)	77.7 (16.5)	61.8 (24.2)	83.8 (13.8)	58.2 (26.4)	82.4 (14.3)	60.1 (26.7)	<0.001*
Role physical	55.4 (40.8)	45.8 (39.8)	78.1 (31.2)	48.8 (38.2)	86.3 (24.8)	49.4 (42.9)	87.7 (17.6)	47.0 (39.9)	0.046*
Bodily pain	45.8 (17.0)	40.0 (14.9)	65.1 (19.8)	55.7 (20.4)	76.7 (16.0)	62.0 (21.7)	66.7 (21.6)	61.1 (24.7)	<0.001*
General health	64.8 (21.3)	62.0 (20.1)	68.3 (18.9)	65.6 (17.2)	77.2 (15.6)	62.0 (17.2)	76.0 (15.2)	62.0 (17.4)	<0.001*
Vitality	46.4 (19.1)	48.0 (22.3)	58.8 (17.2)	46.5 (21.2)	64.1 (15.4)	48.6 (18.9)	62.7 (17.6)	47.6 (19.9)	<0.001*
Social functioning	68.6 (24.7)	65.7 (41.8)	80.2 (18.6)	64.8 (25.0)	87.5 (17.0)	69.6 (26.9)	87.4 (17.1)	68.3 (27.1)	<0.001*
Role emotional	55.4 (41.5)	61.7 (41.8)	72.1 (36.8)	55.5 (42.1)	82.4 (29.8)	56.3 (46.3)	82.2 (27.0)	64.2 (43.2)	<0.001*
Borg (0-10)	2.4 (0.9)	2.4 (1.5)	2.17 (1.06)	2.38 (1.01)	1.9 (0.76)	2.60 (1.40)	1.88 (0.77)	2.62 (1.96)	0.012*

Data expressed as mean (standard deviation); GLM, Generalized Linear Models; *Statistically significant p value (<0,05).

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OP0274-HPR DEVELOPMENT OF GENERIC CORE COMPETENCES OF HEALTH PROFESSIONALS IN RHEUMATOLOGY: A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2018 EULAR RECOMMENDATIONS

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Background: Acquisition and maintenance of competences by Health Professionals in Rheumatology (HPRs) is important to ensure the best care for people with

rheumatic and musculoskeletal diseases (RMDs). HPRs' competencies have never been systematically evaluated, nor international recommendations provided. A EULAR Task Force (TF) was formed for this purpose.
Objectives: To perform a systematic literature review (SLR) on the core competences of HPRs with a focus on nurses, physiotherapists (PT) and occupational therapists (OT) to inform the "EULAR recommendations for the generic core competences of Health Professionals in Rheumatology"
Methods: Thirteen main themes identified by the TF and translated into research questions, formed the basis of the SLR. Existing literature was systematically evaluated using the following databases (PubMed/Medline, Embase, Cochrane library, CENTRAL, Emcare, PsycINFO, Academic Search Premier, Web of Science, Google Scholar, ERIC and National Science Digital Library) from 1/1/1990 to 20/02/2018. Relevant search terms for competences, RMDs and HPRs were used. In addition, EULAR HPR national presidents were invited to share any documents describing HPRs' competences. Inclusion criteria were: studies on competences or roles, knowledge, attitudes, skills or educational needs relevant for the management of people with RMDs, of HPRs in general or specifically of nurses, PTs or OTs, at post-graduate level. Exclusion criteria were: HPRs' competences for children's care or for concurring co-morbidities; extended roles of HPRs; a very specific clinical intervention or an intervention clearly attributable to only one profession or studies written in a language other than English or Dutch. All abstracts were screened to identify eligible studies for full text inclusion. The methodological quality of the studies was scored using appropriate tools (Table).

Authors/Year	Type of study	Quality score of papers used*
Bergsten et al. / 2011	Qualitative study (Interviews, ground theory)	Medium (8)
Brodin et al. / 2015	Questionnaire-based study	High (10)
Darlow et al. / 2012	Systemic review	Moderate.^
Duers et al. / 2014	Qualitative study (semi-structured interviews)	High (12)
Erwin et al. / 2018 (a)	Qualitative study (face to face groups)	Medium (9)
Erwin et al. / 2018 (b)	Qualitative study (Delphi survey)	High (12)
Health Education England, NHS England Medical Directorate and Skills for Health / 2018	Descriptive Framework informed by Delphi project and focus groups of patients	High (12)
Helland et al. / 2013	Quantitative study (Questionnaire)	83.3%^
Hurkmans et al. /2011	Questionnaire-based study	High (10)
Hurkmans et al. / 2013	Qualitative study (consensus meetings, face to face group, phone conference)	Low (6)
Larkin et al. / 2017	Qualitative study (Interviews)	High (12)
Lillie et al. / 2013	Focus groups and Online survey-based study	Low (5)
Lundon et al. / 2009	Qualitative and quantitative arms (Survey and interviews)	62.5%^
Maycock / 1991	Opinion paper	NA^
Moe et al. / 2018	Survey-based study	Medium (9)
Taal et al. / 2006	Review	Critically Low^
Vlieland et al. / 2016	Qualitative study (Structured interviews and online survey)	High (11)
Willems et al. / 2015	Observational (online survey)	High (11)
Woolf et al. / 2007	Descriptive study – recommendations	Low (6)
Zangi et al. / 2015	Recommendations	High (10)

*Scoring of qualitative studies was performed using a modified version of the criteria presented in Harden et al (BMJ. 2009 Nov 12;339:b4254). Quality is being scored as low, medium or high. Score values (range: 1-12) are reported in brackets. ^Scoring of reviews was performed using the AMSTAR criteria (Shea BJ et al. BMJ. 2017 Sep 21;358:j4008). Quality is being scored as critically low, low, moderate and high. ^ this source has not been scored as this is an opinion paper. ^MMAT score was used for the quality assessment for quantitative studies or for studies of mixed methods (Pluye et al. Int J Nurs Stud. 2009;46:529-546)

Table: Methodological quality assessment of the 20 studies addressing the competences of multiple HPRs (nurses, physical therapists and occupational therapists).

Results: From 591 unique references reviewed, 79 studies were included. Twenty studies addressed competences of multiple HPRs. The methodological quality of most papers was high to medium (Table). The identified studies underpinned a range of HPRs' competences, including: communication skills, promotion of physical activity, basic knowledge about RMDs and education of patients and other health providers. Competences more relevant to specific professions (e.g musculoskeletal system examination skills for PTs and assessment of house and work environment for OTs) were also recorded. Heterogeneity in the HPR desired competences and practice across countries highlighted the need for further education of HPRs to acquire certain competences.
Conclusion: High-quality literature is available on the competences of HPRs for the management of people with RMDs. This literature supports the formulation of evidence-based recommendations for the core competences for HRPs by a EULAR Task Force.
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FRIDAY, 14 JUNE 2019

SLE, Sjögren's and APS – etiology, pathogenesis and animal models

OP0275 **THE PI3KΔ INHIBITOR INCB050465 AMELIORATES SALIVARY GLAND PATHOLOGY AND REDUCES AUTOANTIBODY FORMATION IN A MURINE MODEL OF SJÖGREN'S SYNDROME**

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Background: Sjögren's syndrome (SS) is a chronic autoimmune exocrinopathy affecting the glands that produce tears, saliva and vaginal and bronchial secretions. SS represents a complex interaction between the adaptive immune system and specific tissue regions of exocrine glands. Germinal ectopic lymphoid structures that are rich in autoimmune B-cells are thought to play an important role in local chronic B-cell activation and clonal expansion, autoantibody production, and Ig class switching in SS[1]. Genetic deletion or pharmacological inhibition of PI3Kδ leads to defective B-cell activation, reduced proliferation and functional suppression. INCB050465, an oral small molecule selective PI3Kδ inhibitor, is currently being evaluated in clinical trials for the treatment of B-cell driven autoimmune diseases: SS and autoimmune hemolytic anemia (NCT03627065 & NCT03538041).
Objectives: To evaluate INCB050465 efficacy as a monotherapy in a spontaneous murine model of Sjögren's syndrome.
Methods: The NOD.ShiLtJ mice develop progressive autoimmunity primarily targeting salivary glands that share many disease characteristics with SS. Histological assessment of salivary glands constituted a primary efficacy endpoint. Additional readouts included autoantibody and cytokine quantification in serum and saliva. INCB050465 efficacy was also assessed in a mechanistic dinitrophenol-keyhole limpet hemocyanin (DNP-KLH) mouse model of B-cell activation and *de novo* anti-specific immunoglobulin production. Serum was collected to quantify DNP-specific immunoglobulin levels. Spleen tissue was investigated for B-cell subsets using flow cytometry.
Results: INCB050465 treatment (0.1-1 mg/kg, b.i.d.) dose-dependently ameliorated the severity of salivary gland inflammation ($p<0.0001$) and reduced circulating levels of anti-SS-related antigen A (anti-SSA/Ro) and anti-SS-related antigen B (anti-SSB/La) ($p<0.0001$). Reduced lymphocytic infiltration of salivary glands in INCB050465-treated groups coincided with lowered B-cell activating cytokine (BAFF) levels in saliva ($p<0.05$). In the DNP-KLH model, INCB050465 treatment dose-dependently reduced the proportion of germinal center B-cells ($CD19^{+}PNA^{+}CD95^{++}$ cell subset) ($p<0.0001$) and decreased DNP-specific IgM and IgG antibody titers ($p<0.0001$).
Conclusion: INCB050465 administration ameliorated germinal center formation, inhibited salivary gland inflammation and reduced autoantibody titers as a single agent in a dose-dependent manner. Together, the data suggest that INCB050465, a selective PI3Kδ inhibitor, may have potential as a therapeutic agent for the treatment of Sjögren's syndrome.

REFERENCE:

[1] Salomonsson, et al. Cellular basis of ectopic germinal center formation and autoantibody production in the target organ of patients with Sjögren's syndrome. Arthritis Rheum. 2003; 48(11): 3187-3201.

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OP0276

DENDRITIC CELL-DERIVED IL-27 REGULATES THE MAGNITUDE OF INDUCIBLE ECTOPIC GERMINAL CENTRES BUT FAILS TO DOWNMODULATE IL-17 PRODUCTION IN CD4 T CELLS FROM PATIENTS WITH SJÖGREN'S SYNDROME

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Background: Approximately 30% of Sjögren's Syndrome (SS) patients develop Ectopic Lymphoid Structures (ELS) in their salivary glands (SG). ELS play an active role in autoimmunity and contribute to the development of MALT lymphoma. Interleukin 27 (IL-27) exerts key immunomodulatory actions on CD4 T cells with both pro and anti-inflammatory roles but its role in the formation and regulation of ELS in the salivary glands of SS is unknown.
Objectives: We first used a murine model of inducible SG ELS to elucidate the role of IL-27 and its interaction with IL-17 in the regulation of ELS formation and function. We then extended our observations on a cohort of SS patients to identify IL-27 cellular source, target cells and functional properties in modulating peripheral and lesional CD4 T cells function.
Methods: To trigger ELS formation a single dose of reporter-encoding adenovirus was delivered directly to the SG of wild-type (WT) and IL-27RA-deficient (KO) mice. For IL-17 blockade anti-mouse IL-17A antibody was administered systemically. ELS development and peripheral immune responses were tracked by immuno-histopathology, FACS, and qPCR. Minor SG biopsies were collected from SS and non-specific sialadenitis (sicca) patients. Peripheral blood mononuclear cells (PBMC) isolated from patients and age/sex matched healthy donors (HD). For in vitro experiments PBMCs, isolated CD4 T cells and parotid gland MCs were incubated with IL-27 and analysed by FACS for CD4 T cell subsets while cytokines levels were measured intracellularly by FACS and in culture supernatants. Tissue IL-27 was assessed in SS SG sections by multicolour immunofluorescence to identify IL-27 producing cells.
Results: In WT mice, SG ELS formation was preceded by an upregulation of IL-27p28 and infiltration of IL-27 producing cells (CD11b+ first followed by CD4 and CD8 T cells). KO mice displayed larger, more abundant ELS in the SG with more germinal centres and higher levels of ELS-related genes (*Cxcl13*, *Ccl19, Ltb, Aid*) compared to WT mice. During ELS formation, KO mice had an uncontrolled SG Th17 response and systemic IL-17A blockade caused reduction in ELS size and in the expression of ELS-related genes. In SS patients SG and serum, we observed higher expression levels of IL-27 transcripts and protein, respectively, compared to sicca, while SG IL-27 was selectively increased in the ELS+ subset of SS. Immunofluorescence staining for IL-27 revealed its presence primarily in the T cell rich areas of SG ELS with frequent co-localization with DC-LAMP+ dendritic cells. Finally, while IL-27 was able to significantly downregulate IL-17 production in HD, CD4 T cells from patients with SS failed to downregulate IL-17 but showed an aberrant IFNγ release upon IL-27 incubation. We did not observe any difference in IL-27R expression or downstream STAT1/3 phosphorylation between SS and HD.
Conclusion: IL-27 is a critical regulator of the magnitude of the germinal centre response in the SG by restricting Th17 expansion. Both in murine inducible ELS and in patients with SS, dendritic cells appear as the main cellular source of IL-27. Although SG IL-27 was increased in the ELS+ subset of SS, it consistently failed to downregulate IL-17 release in CD4 T cells from SS patients suggesting that a profound dysregulation of the IL-27/IL-17 axis play an important role in ELS formation in this condition.
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OP0277

RNA SEQUENCING AND MACHINE LEARNING TECHNIQUES PREDICT MAJOR ORGAN INVOLVEMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Both clinically and molecularly, Systemic Lupus Erythematosus (SLE) is a heterogeneous disease with non-synchronous multi-organ involvement of varying severity, and alternating periods of remission and flares. There is an unmet need for a blood-based- "liquid biopsy" to predict prognosis of the disease.
Objectives: To detect the smallest set of genes predicting SLE organ involvement and disease activity using RNA-sequencing data derived from whole blood cells from 150 SLE patients and machine learning techniques.
Methods: Disease activity was measured by the SLE disease activity index-2000 (SLEDAI-2K) and by organ involvement (treated as binary outcomes). SLEDAI-2K: mild-moderate disease (SLEDAI 0-8), severe (SLEDAI $\geq$8). Organ involvement: major (renal, heart, lung, central nervous system & SLEDAI-2K$\geq$6) and minor (all others). The RNA-sequencing dataset was pre-processed to assemble 20,368 genes and then split in training/validation data. Two feature selection steps (edgeR and recursive feature elimination) were used to remove noise and keep the smallest set of genes which best predicts each outcome. Different prediction models were fit to identify which one performs best using the gene signature selected in the previous step.
Results: Two gene signatures were kept after feature selection to predict each of the two outcomes (25 genes for organ involvement; 50 genes for SLEDAI-2K). Organ involvement was predicted with high accuracy (accuracy=0.89, sensitivity=0.89, specificity=0.88 in the validation data) using the elastic net generalised linear model. Among the 25 best predictors were *MPO, ITGA3* and *CD38*. SLEDAI-2K could not be predicted with high accuracy (accuracy 0.75, sensitivity=0.79, specificity=0.67) using the neural network model. Performance was still the same even when 1648 genes (after first feature selection step) were used as predictors of SLEDAI-2K. The performance of these models will also be tested in an independent test dataset once available (currently undergoing sequencing).
Conclusion: The model predicting organ involvement performed better compared to the model predicting SLEDAI-2K. This could be attributed to the fact that certain disease manifestations are not currently included in SLEDAI-2K. Further analysis and functional laboratory experiments of those genes will help to identify biomarkers for more accurate assessment of disease activity and prognosis in the clinic.
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OP0278

BIOMARKER PROFILING REVEALS NOVEL MECHANISTIC INSIGHTS INTO USTEKINUMAB THERAPEUTIC RESPONSES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a heterogenous autoimmune disease that causes progressive organ damage. The cytokines type I interferon (IFN-I), IL-12 and IL-23 have all been shown to contribute to SLE pathogenesis. We previously reported that treatment with ustekinumab (UST), an anti-IL-12/23 p40 neutralizing monoclonal antibody, improved global and organ-specific measures of disease activity in a randomized, placebo (PBO)-controlled study of patients with active SLE (NCT02349061).[1] Here, we utilized biomarker data from this clinical study to elucidate the mechanism of action of UST in SLE.
Objectives: We aimed to determine whether modulation of IL-12, IL-23, or both cytokines was associated with clinical efficacy, and to ascertain whether UST treatment could modulate IFN-I or improve disease activity in patients exhibiting an elevated IFN-I signature at baseline.
Methods: A Phase 2, placebo (PBO)-controlled study enrolled 102 patients with seropositive SLE and active disease despite standard-of-care therapy.[1]Patients were randomized 3:2 to receive UST IV ~6 mg/kg or PBO at week 0, then subcutaneous injections of 90mg UST q8w or PBO. Whole blood RNA from PAXgene tubes and serum were collected over 24 weeks. Age and sex-matched healthy controls were also studied. Serum IFN-γ, and IL-17A, IL-17F and IL-22 levels were quantified by ELISA as indicative of the IL-12 and IL-23 pathways, respectively, and an IFN-α ELISA was utilized to quantify the IFN-I pathway. Whole blood RNA was assessed for gene expression by microarray. Two Th17[2,3], an IFN-γ[4] gene signature and 21-gene IFN-I signature (IGS)[5] were analyzed. SLE Responder Index (SRI)-4 at week 24 was used to define UST response (UST-R) and non-response (UST-NR).
Results: Serum IL-17A, IL-17F and IL-22 levels and Th17 gene signature levels in blood remained largely stable over the course of 24 weeks in all treatment groups. In contrast, UST-R was associated with a durable reduction in IFN-γ protein and IFN-γ gene signature levels relative to baseline, which was not observed

in UST-NR or PBO patients. IGS levels were elevated in 67% of patients at baseline versus healthy controls. Serum IFN-α levels and IGS levels in blood were not modulated by UST treatment through week 24. Baseline IFN-I signature status did not associate with response to UST, as the treatment effect size (UST vs PBO) was similar in IGS low (Δ=27%) and high (Δ=28%) patients.
Conclusion: Response to UST was associated with reductions in IFN-γ levels, whereas IL-17A, IL-17F, IL-22 and IFN-I remained largely unchanged. While these findings require confirmation in an ongoing Phase 3 study, these data implicate the involvement of the IL-12 pathway and suggest a novel mechanism of action for UST-R in SLE.

REFERENCES:

[1] VanVollenhovenR. Lancet. 2018;392:1330.
[2] ZhangW. PLoS One. 2012;7:e38510.
[3] ZhangH. JAllergyClinImmunol. 2013;132:1005.
[4] WelcherAA. ArthritisRheumatol. 2015;67:2713.
[5] YaoY. HumGenomicsProteomics. 2009;doi:10.4061/2009/374312.

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OP0279

A UNIQUE IL-21 SIGNATURE CHARACTERIZES LESIONAL AND CIRCULATING T-FOLLICULAR HELPER CELLS IN SJÖGREN'S SYNDROME PATIENTS WITH ECTOPIC GERMINAL CENTRES AND MALT LYMPHOMA

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Background: B/T cell aggregates in the salivary glands (SG) of Sjögren's syndrome (SS) can form ectopic lymphoid structures (ELS) with germinal centers (GC), which are linked to MALT lymphoma (MALT-L) development. T follicular-helper cells (Tfh), main producers of IL21, are crucial for affinity maturation and class-switching of GC B cells, and may be responsible for onset of autoimmunity.
Objectives: To characterize the cytokine production in circulating T cells alongside the Tfh infiltration and the expression of IL21/IL21 receptor (IL21R) in the SGs of SS patients, in the context of ectopic GCs and MALT-L.
Methods: SG biopsies with matching histology and RNA from 37 SS and 38 non-specific chronic sialadenitis (NSCS) patients were stratified as ELS-/ELS+ based on CD3/CD20/CD21/CD138 immunostaining (IHC). Histological samples and mRNA from 12 parotid MALT-L were also analyzed. Gene expression was measured by Taqman RT-PCR. Multicolor immunofluorescence/confocal microscopy for CD3, CD4, CD45RO, ICOS, PD1, BCL6 identify Tfh cells in SG and MALT-L tissues. FACS analysis for CD4, CD8, INFγ, IL17, IL21, Granzyme-B, IL10, CD25, Foxp3, CXCR5, ICOS, PD1, was performed on peripheral blood mononuclear cells from 20 SS and 10 NSCS patients with matched SG histology for the characterization of T CD4+ cells cytokines production.
Results: IL21 and IL21R expression, together with $CD4^+CD45RO^+PD1^+ICOS^+$ Tfh cells were strongly enriched in ELS+ vs ELS- SS SGs. Tfh cells densely infiltrated B cell rich areas and, within ectopic GC, acquired BCL6 expression, both in ELS+ and MALT-L. Tfh infiltration significantly correlated with SG IL21 mRNA level, which in turn was associated with high T (CD3+), B (CD20+) and plasma cells (CD138+) IHC scores and significantly correlated with CXCL13, LTβ, BAFF, AID and Pax5 gene expression. MALT-L samples displayed 10-fold higher IL21 mRNA and twice as much $PD1^+ICOS^+BCL6^+$ Tfh-cells/field in comparison to ELS + SS samples. Within the SGs, IL21 and INFγ were the most abundant cytokines produced by infiltrating CD4 T cells and CXCR5+ Tfh cells frequently displayed double IL21/INFγ production. Similarly, IL21, IL17 and IFNγ producing ICOS +CXCR5+ circulating Tfh cells were significantly increased in the peripheral blood of SS patients compared to sicca, but only IL21+ Tfh cells were associated with the presence of ectopic GC in SG. IL21, IL17 and IFNγ production by Tfh in the peripheral compartment showed a positive correlation with IgG serum levels.
Conclusion: Within the SG of SS patients Tfh cells closely segregate with lesional IL21 expression, localize within ELS and are strongly enriched during MALT-L development, which is supporting their role in sustaining B cell activation and malignant transformation. High production of IL21 by Tfh in peripheral blood selectively identifies SS patient with ectopic GC in the SG, suggesting a role for IL21+ Tfh cells as surrogate markers of SG histopathology in SS.
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OP0280

THE SELECTIVE JAK1 INHIBITOR INCB054707 AMELIORATES CUTANEOUS LESIONS IN A SPONTANEOUS MURINE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that can affect multiple organs, including the skin, joints and kidneys. The disease is characterized by the development of skin lesions, autoantibody production and inflammation-induced glomerulonephritis. The skin is involved in up to 85% of SLE cases[1]. In the MRL/lpr spontaneous mouse model of SLE, disease symptoms also include lymphocyte hyper-proliferation, resulting in lymphadenopathy and splenomegaly. The evolutionary conserved Janus kinase-signal transducer of activators of transcription (JAK-STAT) pathway constitutes a rapid membrane to nucleus signaling modality that affects key biological aspects of the mammalian immune system[2]. Janus kinase 1 (JAK1) is involved in the downstream signaling pathway of type I interferons (IFNs), and high levels of type I IFNs are associated with SLE[3]. INCB054707 is an oral small molecule JAK1 selective inhibitor currently being evaluated in clinical trials for the dermatological disease hidradenitis suppurativa (NCT03569371 & NCT03607487). We hypothesized that INCB054707 should reduce IFN signaling and ameliorate cutaneous lesions in SLE.
Objectives: To determine the effectiveness of INCB054707, a selective JAK1 inhibitor, in a preclinical model of cutaneous lupus erythematosus.
Methods: Female MRL/lpr mice were randomized to treatment groups at 11 weeks old to receive twice daily oral doses of vehicle (0.5% methyl cellulose) or INCB054707 at 10, 30, or 90 mg/kg for 10 weeks. Efficacy was determined by weekly scoring of the changes in skin, lymph node size, and proteinuria. At study termination (week 21), inguinal lymph nodes and spleens were excised and weighed, skin lesions and kidneys were excised and fixed for histopathologic analysis, and serum was collected for pharmacokinetic analysis and ELISA. Autoantibody presence in the serum was detected using a commercial anti-dsDNA ELISA kit.
Results: In vitro enzymatic selectivity screening of INCB054707 revealed JAK1 IC50 = 8.9 nM versus JAK2 IC50 = 463 nM, resulting in a JAK1/JAK2 selectivity

ratio of approximately 52-fold. Spontaneous skin lesions were observed in 90%+ of vehicle treated mice by 18 weeks of age, with the majority located around the head and nape of the neck. Histologically, lesions were characterized by combined lymphocyte infiltration and epidermal thickening. In contrast, therapeutic INCB054707 treatment dose-dependently reduced the incidence and severity of cutaneous lesions ($p < 0.05$). In addition, INCB054707 treatment abrogated lymphoid tissue and spleen enlargement ($p < 0.0001$) in a dose-dependent manner. Kidney damage was only partially improved by INCB054707 at the highest (90 mg/kg) dose. Quantification of anti-dsDNA antibodies by ELISA revealed a profound, statistically significant reduction of antigen-specific autoreactive IgG immunoglobulins in the serum ($p < 0.0001$). Total immunoglobulin titers were not reduced.

Conclusion: These data are consistent with immunomodulation and show that oral INCB054707 treatment, resulting in JAK1-specific inhibition, has the potential to modulate ongoing inflammatory (autoimmune) cutaneous skin disease.

REFERENCES:

[1] Luis Uva, et al. Cutaneous Manifestations of Systemic Lupus Erythematosus. Autoimmune Dis. 2012; 2012: 834291.
[2] O'Shea, et al. The JAK-STAT Pathway: Impact on Human Disease and Therapeutic Intervention. Annu Rev Med. 2015; 66: 311–328.
[3] Ivashkiv, et al. Regulation of type I interferon responses. Nat Rev Immunol. 2014; 14(1): 36–49.

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OP0281 ELEVATED EXPRESSION OF BAFF-RECEPTOR IN PERIPHERAL MONOCYTES PROMOTES B CELL ACTIVATION AND CORRELATES WITH CLINICAL MANIFESTATIONS OF PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is an idiopathic autoimmune disease whose major clinical manifestations are xerostomia and keratoconjunctive sicca, and is often accompanied with hypergammaglobulinemia. Several lines of evidence suggest that a focal lymphocytic infiltrate of the exocrine glands is responsible for lesion formation, IgG production and subsequent dysfunction of the glands. It is well known that B cell activating factor (BAFF) and its receptor, BR3, are deeply involved in the pathogenesis of pSS, and hence BAFF and BR3 are promising targets to treat the disease. We have reported that the abnormally elevated expression of BR3 in monocytes is associated with overproduction of inflammatory cytokines, such as IL-6, by monocytes of pSS patients. Our in vitro experiments suggest that BAFF-stimulated monocytes contribute to IgG overproduction by pSS B cells. We also found that the population of a specific subset of B cells overexpressing BR3 was abnormally increased in pSS patients and that the proportion of the subset was positively and significantly correlated with serum levels of autoantibodies and total IgG as well as ESSDAI, one of the indicators of disease activity of pSS. Our results collectively suggest that the elevated expression of BR3 in pSS monocytes results in B cell activation and subsequent overproduction of IgG. However, the relationship between the abnormalities of peripheral cells and clinical manifestations of pSS has not been fully understood.

Objectives: To elucidate possible roles of abnormal monocytes in the development of clinical manifestations of pSS.

Methods: The expression level of BR3 in peripheral monocytes of patients with pSS (n = 65) and healthy controls (HC: n = 38) was analyzed by FACS. Peripheral B cells were cultured with BAFF-stimulated monocytes in the presence or absence of an anti-IL-6 receptor antibody, and the proportion of $CD38^{high}IgD^{low}$ cells among $CD19^{+}$ cells, and IgG production were analyzed by FACS and ELISA, respectively. The serological data and focus scores by lip biopsy of the patients were collected by clinical records.

Results: FACS analysis revealed that the expression level of BR3 in pSS monocytes was significantly higher than that of HC ($p < 0.001$). Moreover, the expression level of BR3 in peripheral monocytes was positively and significantly correlated with serum levels of IgG ($p = 0.01$) and IgM ($p = 0.02$) of the patients. Notably, BR3 expression in monocytes from focus score-positive pSS patients was significantly higher than that from negative patients ($p = 0.006$). In addition, BR3 expression in pSS monocytes was elevated in anti-SS-A and/or anti-SS-B positive patients as compared to negative patients. When B cells prepared from pSS patients were mixed with autologous monocytes and co-cultured in vitro in the presence of BAFF, 1) the proportion of $CD38^{high}IgD^{low}$ cells, which are plasmablasts and/or plasma cells, among CD19 positive cells and 2) the amounts of IgG produced by the cells were drastically enhanced by BAFF-stimulation, whereas the stimulation showed only marginal effects when B cells were solely cultured in vitro. In addition, an anti-human sIL-6R antibody significantly inhibited the proportion of $CD38^{high}IgD^{low}$ cells and IgG production. These data strongly suggest that IL-6 produced by BAFF-stimulated monocyte plays a pivotal role in B cell differentiation and the IgG overproduction in pSS patients.

Conclusion: Our data strongly suggest that accelerated signal transduction through a BAFF-BR3 axis in monocytes is involved in the pathogenesis of pSS and associates with clinical manifestations of the disease. These results also suggest that BAFF and the BAFF signaling pathways through BR3 are the possible therapeutic targets for pSS.

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OP0282 **OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (OAPS) VS. WITH OBSTETRIC MORBIDITY RELATED WITH ANTIPHOSPHOLIPID ANTIBODIES (OMAPS): A SURVEY OF 1650 CASES FROM EUROAPS REGISTRY**

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Background: The obstetric antiphospholipid syndrome is an autoimmune systemic disorder related to antiphospholipid antibodies and pregnancy morbidity. There exist many patients that do not fulfill the Sydney classification criteria. Those cases may be defined as Obstetric Morbidity related with antiphospholipid antibodies (OMAPS).
Objectives: To compare clinical features, laboratory data and foetal-maternal outcomes, between 1000 women with obstetric antiphospholipid syndrome and 640 women with aPL-related obstetric complications not fulfilling Sydney criteria.
Methods: Retrospective and prospective multicenter study from the European Registry on Obstetric Antiphospholipid Syndrome.
Results: 1650 women with 5251 episodes were included of which 3601 were historical and 1650 were latest episodes. 1000 cases (OAPS group) fulfilled the classification criteria and 650 (OMAPS group) did not. Ten OMAPS cases were excluded because they presented a thrombosis during follow-up. In the OMAPS group, 172/640 (26.87%) did not fulfil Sydney clinical criteria (subgroup A), 179/640 (27.96%) had a low titer and/or non-persistent aPL-positivity but fulfilled clinical criteria (subgroup B), and 289/640 (45.15%) had a medium or high aPL titer but did not fulfil Sydney clinical criteria (subgroup C).
Conclusion: Significant clinical and laboratory differences were found between groups. Foetal-maternal outcomes were similar in both groups when they were treated. The results suggest that we could improve our clinical practice with closed defining and monitoring OMAPS patients.

REFERENCES:

[1] Cervera R, Piette JC, Font J, Khamashta MA, Shoenfeld Y, Camps MT, et al. Antiphospholipid syndrome: clinical and immunologic manifestations and patterns of disease expression in a cohort of 1,000 patients. Arthritis Rheum 2002;46:1019-27.
[2] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. Interna-tional consensus statement on an update of the classification criteria for definiteantiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295-306.
[3] Esteve-Valverde E, Ferrer-Oliveras R, Alijotas-Reig J. Obstetric antiphospholipid syndrome. Rev Clin Esp 2016;216:135-45.

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FRIDAY, 14 JUNE 2019

PARE Abstract session

OP0283-PARE **A DUTCH RESEARCH AGENDA DEVELOPED BY PEOPLE WITH RMDS: WHAT ARE THE MAIN PROBLEMS PEOPLE WITH RMDS FACE AND WHAT ARE THEIR MAIN WISHES FOR RESEARCH AND DEVELOPMENT?**

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Background: In the Netherlands much progress has been made with regard to patient participation in research. More and more researchers are finding their way to patient organizations for collaboration. This is also the case for the National Association ReumaZorg Nederland where more and more researchers are asking for the opinion of our patient-experts on their written research proposals. However, this happens mostly because 'asking for the patient's view' is an obligatory (last) part of the submission process of their proposal. ReumaZorg Nederland wants to take patient participation in research to the next level. A level where 'what matters most to patients' is taken into account before a proposal is written. Only then will the patient's voice really be heard in the very heart of a research project.
Objectives: To identify the main problems people with RMDs face in their daily lives and to prioritize their wishes for future research and development. To investigate whether these problems and wishes vary between patients with different types of RMDs. To encourage researchers and product-developers to take these wishes into account at the very start of their research proposal or product-plan.
Methods: Independent and professional research was needed to develop this research agenda. NIVEL, the Dutch Institute for Health Services Research, performed a 7 month research project which consisted of several steps. First, a literature search was performed on scientific publications in PubMed, Embase and PsychInfo on search strings focusing on living with RMDs, problems and wishes of people with RMDs and other known research agenda's for people with RMDs. The second step consisted of 3 focus group sessions: inflammatory RMDs (group 1), osteoarthritis & fibromyalgia (group 2) and soft tissue- & systemic RMDs (group 3). In addition, a combined session of representatives of each focus group (12 participants) was organized to compare and complement the results of the 3 focus groups. In the third step, an online survey (277 respondents) was held to explore how these problems and research wishes were recognized and prioritized within the Dutch community of people with RMDs. After data-analysis in step 4, a stakeholders session was held in step 5 to discuss results amongst patients, researchers, rheumatologists and project-developers.
Results: Among the 89 problems that were recognized, the main problems people with RMDs face are:
1. Uncertainty about their future.
2. Having to cope with fatigue.
3. Having to cope with the unpredictability of RMDs.
4. Preserving boundaries/staying balanced.
5. Having to cope with the impact of RMDs on social life with family and friends.

Among the 85 wishes for research and development, the main wishes of people with RMDs are:
1. To develop treatments of RMDs other than surgery.
2. To develop an accessible and affordable network of physical exercise activities under professional supervision.
3. To investigate the cause of inflammatory RMDs.
4. To investigate the cause of fatigue with RMDs and how to cope.
5. To investigate alternative forms of therapy and their effect on specific types of RMDs.

All results were described in the first Dutch research agenda made by people with RMDs.[1]
Conclusion: Remarkably, the main problems people face with RMDs are not necessarily the same as the wishes they have for further research or development. The problems people face have to do with issues regarding living and coping with RMDs in everyday life, whereas their research-wishes are more medical. Fatigue is, however, an issue that is highly prioritized as a problem as well as a subject for further research. This goes for people with all types of RMDs.

REFERENCES:

[1] Verkaik, R., Kappen, H., Boeije, H. Kennisagenda van mensen met reuma: welke onderwerpen vinden mensen met reuma belangrijk voor toekomstig onderzoek en ontwikkeling? Utrecht; NIVEL, November 24th, 2018

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OP0284-PARE THE INFLUENCE OF FUNCTIONAL TRAINING AND PSYCHO-SOCIAL SUPPORT

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Background: Treatment of chronic noncontagious diseases in which we include RMD implies usage of medicines and non medicine (changing bad lifestyle habits like losing nutrition, physical activity, smoking…).[1] Unwanted cardiovascular and cerebrovascular states are the most common cause of shortening of live of people with RMD.[2] None of the chemical drugs can replace physical activity. Physical activity dosage is individual, and depends on aerobic capability and heart rate increase, taking in account age, type of noncontagious diseases, level of tissue and organs damage as well as the type of work the person is engaged in.

Patients with RMD have common symptoms, such as stiffness, fatigue, poor mobility, joint pain and muscle pain, anxiety and depression, and lack of fitness. In addition to physical medicine and rehabilitation and balneoklimatology, various forms of physical activity are recommended, such as walking, swimming, functional training. Today, moderate physical activity is known to help reduce fatigue, strengthen muscles and bones, improve flexibility and endurance of the joints, and improve general health. It is necessary to find the best combination of rest, activities and exercise programs to prevent deformities of the joints, the development of disability, improve the quality of life, and the mental health of patients with RMD.[3]

Objectives: 1. By practicing Cigong, an increase in the volume of movement in the joint, the strengthening of joint muscles and the improvement of general condition, pain relief, fatigue reduction is achieved and also, it helps patients look and feel better.

2. The goal of Yoga is to neutralize and remove all obstacles that stand in the way and disturb the function of the body and the mind and achieves inner peace.

3. Changing the psychological state during exercise also led to a positive way of thinking.

4. Psycho-physical support for the people with RMD

Methods: From 2011, we organize two times a week functional training of Cigong.[4]

Since January 2016, twice a week persons with RMD have been practicing Yoga.[5]

From 2015, one per week four psychologists volunteer hold workshops for psycho-social support for persons with RMD.[6,7]

Participants of the training and psycho-social sessions took a survey.

Results: 1. Joint pain reduction – 50% of total number of participants

2. Joint mobility increase – 95% of total number of participants

3. General fitness improvement – 73% of total number of participants

4. Less pronounced negative emotions – 59% of total number of participants

Conclusion: Practicing cigong, yoga and psycho-social support workshops help patients look better and feel better. Changing the psychological state during exercise also led to a positive way of thinking. All of this increased the effectiveness of drug treatment and improved the quality of life of patients with RMD.

REFERENCES:

[1] Dragojević R. Vodič za zdrav život: preporuke medicine i pouke mudrosti, Beograd 2017.

[2] Lapcević M., Vuković M. Dimitrijevic I. Et all Uticaj medikamentnog I nemedikamentnog lečenja na smanjenje faktora rizika za kardiovaskularne I cerebrovaskularne događaje u interventnoj studiji. Srp Arh Celok Lek 2007.

[3] Lapčević M, Prvanov D, Đorđević S. Procena kvaliteta života obolelih od hroničnih reumatskih oboljenja. Opšta medicina 2010.

[4] Ilinka Acimovic, "The Influence of Health Qigong on the Subjectively Expressed Psychophysical State of Patients with Rheumatoid Arthritis, Rheum, Osteoporosis, Osteopenia" CHINESE MEDICINE AND CULTURE

[5] Swami Kriyananda, "Demystifying Patanjali: The Yoga Sutras - The Wisdom of Paramhansa Yogananda". Crystal Clarity Publishers, Nevada City, CA, 2013.

[6] Lapčević M, et al. Socioeconomic and therapy factor influence on self-reported fatigue, anxiety and depression in rheumatoid arthritis patients. Rev Bras Reumatol. 2017.

[7] Milić V. Analiza ličnosti I uticaj optimizma na pozitivan ishod lečenja; 2018.

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OP0285-PARE SARCOPENIA IN PATIENTS WITH RHEUMATIC DISEASES

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Background: Sarcopenia is a rather new term, coined in 1989: only in 2016 the International Classification of Disease (ICD) code was established for this disease. Sarcopenia describes a state of reduced muscle mass together with reduced muscle strength and reduced muscle performance that comes with aging. The topic is of great relevance for people with rheumatic diseases, because chronic inflammations and lack of exercise, among others, have been identified as risk factors for the development of sarcopenia. To shed additional light on this emerging field, the German Rheumatism League has funded a participatory research project for the investigation of sarcopenia.

Objectives: The aim of the study was to investigate the prevalence of sarcopenia in patients with rheumatoid arthritis. In addition, the study aimed at identifying risk factors and biomarkers for the development/diagnosis of sarcopenia. The results of the study are intended to enhance the diagnostic tools for recognising sarcopenia in patients with rheumatoid arthritis and to allow the formulation of specific exercise recommendations for the prevention of sarcopenia. Based on the results of the study and additional information from the literature, an information leaflet or brochure for patients will be prepared.

Methods: Participants were screened by medical questionnaires. Blood chemistry was analysed. Body composition was assessed by dual-energy X-ray absorptiometry (DXA). Muscle area and muscle density were measured using peripheral quantitative computed tomography (pQCT). Various neuromuscular tests were performed to assess muscle performance, muscle strength and sense of balance. Additional information on treatment options, prevention and detection were retrieved in a comprehensive literature search. Two "Patient Research Partners" are involved in the study.

Results: The study has not yet been completed. So far, 269 patients (age 18 and older; 216 female, 53 male) were recruited until December 2018. Mean age of participants was 59 years, mean DAS-28 was 2.4 (remission). The control group consisted of an existing cohort of 280 individuals without chronic inflammatory diseases or muscle paralysis (153 females, 127 males, mean age 63 years). Preliminary data show that prevalence of sarcopenia is higher in patients with rheumatoid arthritis compared to the control group. Literature revealed that physical exercise has a positive effect on sarcopenia. In addition, amino acid supplementation, nutritional interventions and hormones might be effective in the treatment of sarcopenia.

Conclusion: The higher prevalence of sarcopenia in patients with rheumatoid arthritis illustrates the urgent need to provide education on sarcopenia for patients with rheumatic diseases.

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OP0286-PARE DEVELOPING A VIRTUAL ASSISTANT TO PROMOTE EDUCATION ON OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is one of the most prevalent chronic rheumatic diseases (24% in Portugal, according to the Portuguese Society of Rheumatology) accounting for significant years of disability. Optimal management of OA requires active patient participation. A recent systematic review concluded that more effective information strategies are needed to respond to the needs of OA patients.[1]

Interactive computational simulation with Virtual Humans (VH) has been used with the purpose of educating or promoting lifestyle change in healthy people or in

the management of chronic illnesses, such as diabetes treatment, including good users' acceptance and an increase in their knowledge.[2] Knowledge acquisition is generally seen as a necessary condition for behavioral change. Applications with virtual humans offer a dynamic, interactive and easily accessible approach to enhance users' knowledge. We did not find published literature on the use of virtual humans to educate people with OA.

Objectives: To develop a web application to support education of caregivers and people with OA.

Methods: This is a proof of concept study, which builds on our previous experience with virtual assistant applications. For example, "Virtual Pharmacy"[4] is intended to improve self-medication consultation skills between students/pharmacy professionals and community pharmacy clients, whilst "VASelfCare"[3] aims to facilitate self-care of older people with type 2 diabetes (REF?).

The main principle underpinning the development of our application is the use of gamification embedded in a narrative with a double purpose of maintaining user engagement and enhancing the play experience. This option has in consideration that OA is more prevalent among the seniors and is supported by a study showing that embedding narratives in mobile games enhances the play experience of this age group.[5]

In our approach, the narrative comprises dialogues aiming to ease and stimulate the search for new knowledge, and to educate for disease management and health promotion.

Results: So far, we have developed NOA, a virtual assistant that interacts with users through speech (voice and subtitles) plus facial and body animations. NOA is a 2D cartoon female model that plays the role of a character who suffers from OA and provides information about her own experiences with the disease. At the end of each dialogue, a quiz tests users' knowledge. Awarding points and digital badges for correct answers, or showing the right answers when the user fails, are expected to motivate users to play and learn more. This application will be placed in the "Portuguese League Against Rheumatic Diseases" website to convey easy access.

Conclusion: Development of a virtual assistant web application to promote education on OA, resorting to a narrative approach and gamification principles, is ongoing. Future work includes testing the application with experts and patients.

REFERENCES:

[1] Chou, L., et al. (2018). Patients' perceived needs of osteoarthritis health information: A systematic scoping review. PloS one, 13(4), e0195489
[2] Finkelstein, J., & Bedra, M. (2014). Avatar-based Interactive Diabetes Education in Older Adults. Journal of the American Geriatrics Society, 62(S1), S64
[3] http://vaselfcare.rd.ciencias.ulisboa.pt/
[4] Cláudio, A. P., et al. (2016). Virtual Humans Playing the Role of Patients in Self-medication Consultations: Perspectives of Undergraduate Pharmacy Students. GRAPP 2016, pp 296-303
[5] Yee, S. L. C. Y., et al. (2010). Investigating narrative in mobile games for seniors. CHI 2010, pp 669-672

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OP0287-PARE SETTING UP A EUROPEAN FEDERATION OF SJÖGREN'S SYNDROME PATIENT ASSOCIATIONS: HOW WE BUILT UP SJÖGREN EUROPE IN LESS THAN ONE YEAR

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Background: Despite its considerable prevalence among CTDs, SS has been devoted less research, interest, time and effort compared with other close conditions. Active and synergistic involvement of patients, clinicians and scientists in the definition of unmet needs and areas of future research is crucial.

Objectives: To set up a perennial European Federation of SS patient associations to address the lack of visibility and the unmet needs, foster patient training and involvement in research and articulate patient voices throughout Europe.

Methods: Sjögren Europe was conceived during the 2018 ISSS and the decision to materialize the Federation was launched during the EULAR 2018 congress, where several meetings with key entities representatives were organized to get advice on various aspects. A medical advisory board was also set up. By-laws, a logo and a website were created. The task force is composed of patients already involved in patient advocacy at a national and international level. The first step was to set a mindset and to communicate on a regular basis to ensure a common spirit. We set priorities and down-to-earth objectives and focus on them. Although there is a leader for supervision and to take final decisions, the governance is mainly based on shared leadership sustained by trusted connections. Personal initiatives are encouraged, and failure is considered as a learning experience. We build a culture of compromise. As members experience debilitating fatigue, they achieve the tasks they can, whenever they have time and energy, and report them to the others: Sjögren Europe adapts to its members. We also welcome anyone sharing our mission principles and wanting to be involved in the project.

Results: On the 23rd of February 2019, Sjögren Europe was officially set up with more than 8 countries as founders. Being flexible not only allows patients with debilitating fatigue to work for the federation but also leads to lean and efficient procedures and tasks. An enthusiastic and supportive environment makes the commitment sustainable and meaningful. Face to face meetings, a good network and collaboration are imperative. The way we respond to mistakes is also crucial for motivation.

Conclusion: This project empowers the SS patient community, brings hope, injects a new energy in patient advocacy and breathes motivation for collaboration to researchers, scientists and clinicians. This presentation aims to share our story and the key learning points about the way we work and to spread the positive atmosphere.

REFERENCE:

[1] Romão V. C., Talarico R., Scirè C. A., et al. *Sjögren's syndrome: state of the art on clinical practice guidelines* RMD Open 2018; 4:e000789. doi: 10.1136/rmdopen-2018-000789

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OP0288-PARE WHAT DO YOUNG PEOPLE THINK ABOUT CONTINUOUS DATA COLLECTION IN CLINICAL RESEARCH AND THE TYPES OF ELECTRONIC DEVICES?

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Background: The use of wearable devices are of increasing interest to enable continuous data collection during drug trials. This is particularly pertinent when involving young people who are "digital natives" and have grown up with such technologies.

Objectives: To ascertain opinions from young people regarding the design of wearable devices and the use of continuous data collection for a future clinical drug trial for juvenile idiopathic arthritis (JIA).

Methods: A three hour face-to-face patient involvement session was held in a young person friendly venue in central Manchester on the 8th December 2018. Young people with a rheumatic disease were invited to participate using event flyers provided in local rheumatology clinics. Members of a national youth advisory panel, Your Rheum, were also invited to attend. Data was collected in both large and small group discussions and included a ranking exercise involving the use of voting cards, emojis and pictures of electronic devices to aid conversations. In addition, an online survey was also developed and uploaded to http://yourrheum.org for young people to complete if they could not attend the event in person. Open questions (requesting free text answers) ranged from general thoughts and concerns about continuous data collection, device preferences and features, to examples of unattractive devices.

Results: Eight young people attended the event (M=5, F=3, 11-19 age range). All males were under 14 years of age. One young person completed the online survey (F=1). All participants regularly used some form of an electronic device and were generally willing to use a wearable device for continuous data collection, although consideration of school regulations (e.g. uniform policies) and potential bullying was necessary. Participants reported that they would choose a device based on its viability, look, comfort and functionality. For instance, the device would need to be discrete in terms of size, muted (no sounds or vibrations) and removable. The preference of device type differed by gender though a watch and patch were in the top three favourite devices for all. Key features included the

ability to switch devices on and off, send reminders, chat to other young people and to track their own data. Some caution was expressed about a device monitoring sleep (or other behaviours that parents may want to know about). It was important for participants to know where the data will be stored, who had access to it and what the information will be used for.
Conclusion: Young people have clear opinions as to what they like and don't like with respect to wearable data collection devices. As well as personal preferences, age specific considerations were highlighted by the young people. It is therefore imperative not only to involve young people as research participants but also to involve them at early stages of research including trial design to ensure acceptability of data collection methods including the design of any devices proposed.
Acknowledgement: Your Rheum is the national youth advisory panel of the Barbara Ansell National Network for Adolescent Rheumatology BANNAR. We would like to thank all of the young people who took part and other individuals who facilitated their involvement including BANNAR members and Versus Arthritis Young People Coordinators.
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OP0289-PARE **THE ROLE OF PATIENTORGANISATIONS ON THE EDUCATION AND ESTABLISHMENT OF RHEUMATOLOGY NURSE**

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Background: Rheumatology Nurse is a practitioner well educated or with a specialty on Rheumatology diseases who help people with RMD's to live as fully independently as possible. A Big Part of the rheumatology nurse's job is to help patients with rheumatic diseases to release their pain and manage their symptoms. In Europe, the use of rheumatology nurses for the treatment of rheumatism is becoming more and more popular. In my country, this is not the case. There is still a lot of work to be done to apply the rheumatology practitioner. That's why our organization is pushing the government to implement in the system Rheumatology Nurse.
Objectives: During discussions between our organization and the Ministry of Health for asking the use of rheumatology nurse in the rheumatology outpatient clinic, since we don't have a rheumatology inpatient clinic, Ministry refused to give the authorisation with the justification of not having any nurse specialist, educated or interested to be educated on the rheumatology fields. So this was a challenge for our organization: The "Nurse Education on Rheumatology".
Methods: The aim had various steps to achieve. The first step was to inform Government Nursing Services the significant of Rheumatology Nurse. The second step was to discuss with them the need for educated Nurses on rheumatology and their opinion. Third to persuade them to educate nurses on Rheumatology by organizing an Education Program. And the Last one but Very Important, part of the Education Program to be our organization not only as a presenter but to have an actual role as an associate with opinion, on the structure and themes of the program.
Results: The organisation had many meetings with the Government Nursing Services. The officers become very excited about the idea of having a New Education Program on such an interesting theme. After having a number of meetings about the development of the Program and after escaping the barriers, the program was done: Educational Program title "**Patient Care with Rheumatic Diseases"**. Duration of the training: 3 months, 1 day per week, with 3 days of Clinical Exercise on outpatient Rheumatology Clinic and 1 Day on the Care Department-preparation and delivery of biological and biosimilar factors. Success in the Program requires Final Written Evaluation (60%) and Case study (Presentation). Patient Organization: 5 Lectures- Workshops. The education took place from October to December 2018. 27 Nurses have been educated. The program includes between a lot of Lectures, Patient Raise Awareness and Patient Perspective which were given by our Patient Organization. The lectures were given from Organizations'Psychologist staff and from Volunteers Patient Experts for giving the patient perception for the treatment and for the self-management of their condition and Organization's Big Role regarding the disease awareness, treatment, and management. Organization conducted a survey among the participants and the results are very encouragingly to continue the tries to implement the Rheumatology Nurse in the outpatient and inpatient Rheumatology Clinics of the Country. At the question "after training will you be interested in working as a Rheumatology Nurse in a Rheumatology Clinic?'**The answer was YES for the 100% of the participants**.
Conclusion: The importance of nurses' involvement in the treatment of rheumatic diseases is enormous. This has been demonstrated in Europe. Our Organization shows the significant role of nurses for achieve the maximum results on the patient treatment. Also the organization has been able to prove the importance of the contribution of patients to better treatment of the disease. It has also demonstrated to the state the need for a Rheumatology Nurse and refutes their excuses.
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FRIDAY, 14 JUNE 2019

Rheumatoid arthritis – etiology, pathogenesis and animal models

OP0290 **HOTAIR IS INVOLVED IN JOINT PATTERNING BY REGULATING FGFR2, BMP2 AND WNT PATHWAYS**

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Background: Different forms of chronic arthritis such as rheumatoid arthritis (RA) or spondyloarthritis show a typical pattern of joint involvement. However, mechanisms involved in this patterning remain unknown. Synovial fibroblasts (SF) isolated from different joint regions, differ in their epigenetic landscape, their gene expression and their function. The long non-coding RNA HOTAIR, which is an important regulator of the epigenetic landscape, was found to be exclusively expressed in joints of the lower extremity.
Objectives: We aim to clarify the role of HOTAIR in SF.
Methods: HOTAIR was silenced in knee SF isolated from patients with osteoarthritis (OA) by HOTAIR GapmeR using Lipofectamine, and changes in gene expression were measured by next generation RNA sequencing (Illumina NovaSeq 6000) after 48h (n=3). Pathway analysis was performed using STRING protein network, and regulated genes were confirmed by real-time PCR in SF silenced for HOTAIR from OA and RA-patients (n=8) and compared with control SF transfected with Antisense LNA GapmeR negative control. The time course of targeted genes was studied with and without cycloheximide (10ug/ml 6h and 24h) (n=2). To assess the effect of HOTAIR silencing on the canonical Wnt pathway, we employed the TOP/FOP reporter system using the dual-luciferase kit (n=3). Regulation of HOTAIR and targeted genes expression was studied after stimulation with TNF-α (n=17), IL1, LPS, TLR2, TLR4 and poly I:C (n=5). The expression of HOTAIR and TNF-α were measured in synovial tissue from RA-patients (n=7) by qPCR.
Results: STRING analysis identified among others three significantly enriched pathways, namely FGF, BMP and Wnt, including 19 genes differentially expressed between SF silenced for HOTAIR and controls according to p-value (<0.05) and log ratio (>2.5 or <-2.5). Real-time PCR confirmed 6 genes: FGFR2 (5 ± 0.1-fold downregulated; p<0.01), FGF7 (1.9± 0.4-fold downregulated; p=0.02), BMP2 (1.7± 0.5-fold upregulated; p<0.01), LGR5 (3.4±0.3-fold downregulated; p=0.02), CTNNB1 (beta-catenin) (1.5±0.5-fold upregulated; p<0.01) and GSK3β (1.8± 0.2-fold downregulated; p=0.03). There was a trend for LRP6 (p=0.06). HOTAIR expression and FGFR2 and FGF7 expression were correlated (r= 0.67 and 0.55; p<0.01) as well as HOTAIR and BMP2 (r=-0.45; p<0.05). Time course of gene expression peaked after 30-48 hours. Adjunction of cycloheximide, blocking translation, did not change gene expression of BMP2 and CTNNB1 in SF silenced for HOTAIR, suggesting a direct effect of HOTAIR on these genes. FGFR2, FGF7, LGR5, LRP6 and GSK3β expression were normalized with cycloheximidine indicating the need of a protein to mediate HOTAIR effect on FGF pathway and on Wnt pathway. TopFlash assay confirmed the role of HOTAIR in regulation of Wnt pathway by 1.7± 0.2-fold decrease in Wnt activation after HOTAIR silencing (p=0.02). Stimulation by TNF-α led to a 2.1± 0.3 decrease in HOTAIR expression (p<0.0001). Following TNF-α stimulation, FGFR2 and LGR5 expression decreased (p=0.0001 and 0.0004, respectively), whereas there was an increase in BMP2 expression (p<0.0001), consistent with the effect of silencing HOTAIR on these genes. There was a decrease in HOTAIR expression following LPS (p=0.006), and poly I:C (p=0.003). HOTAIR and TNF-α were inversely correlated in the synovium of RA patients (r=-0.79; p<0.05).
Conclusion: Our study highlights three main pathways regulated by HOTAIR and involved in joint patterning: FGFR2/FGF7, BMP2 and LRP6/LGR5/GSK3β/

beta-catenin (Wnt). These pathways are known to play a role in normal joint development, but are also involved in inflammation, proliferation and apoptosis. Consistently, we observed that HOTAIR and targeted genes were selectively downregulated by TNF-α suggesting a role of HOTAIR in the joint specific regulation of TNF-α mediated inflammatory arthritis.

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OP0291

ACTIVATION OF THE DEACETYLASE SIRTUIN-1 COUNTERACTS THE ACTIVATED AND PROANGIOGENIC PROFILE OF ENDOTHELIAL CELLS IN RHEUMATOID ARTHRITIS AND ALLEVIATES EXPERIMENTAL ARTHRITIS

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Background: Angiogenesis through the recruitment and activation of endothelial cells (ECs) is a crucial event to promote the development of the hyperplasic proliferative synovium in rheumatoid arthritis (RA).

Objectives: Our aim was to decipher the phenotype of ECs derived from circulating progenitors issued from patients with RA.

Methods: Proliferation capacities between RA and control ECs was compared using the xCELLigence™ RTCA System. rh-TNFα-induced EC activation was analyzed by adhesion cell expression, VEGF synthesis and stress fiber formation. Angiogenic properties of ECs were assessed *in vitro* by tube formation on Matrigel and migration capacities through VEGF stimulation in modified Boyden chambers, and *in vivo* in a mouse model of tumoral neovascularization. Microarray experiments were then performed on Affymetrix GeneChip® Human Exon 1.0 ST Arrays in ECs issued from 18 RA patients compared to 11 age and sex-matched healthy controls to identify gene candidates relevant to pathological angiogenesis. Expression of identified candidates was assessed by RT-PCR and western blots in ECs and by immunohistochemistry in the synovial tissue of RA patients and controls. Their functional importance was then evaluated *in vitro* after gene invalidation by siRNA and gene overexpression via adenovirus, and *in vivo* in the mouse model of methyl-BSA-induced arthritis.

Results: EPC-derived ECs issued from RA patients displayed higher proliferation rate, greater sensitization to TNFα, with increased VEGF production, ICAM/VCAM expression, and more prominent stress fiber formation, as well as enhanced angiogenic capacities, characterized by accelerated tube formation and increased migration capacities through VEGF stimulation, compared co control ECs. The subcutaneous transplantation of murine colon carcinoma (CT-26) cells with RA ECs in CB17-SCID mice markedly amplified tumor growth and intratumoral neovessel density, compared to the transplantation of control ECs.

Supervised microarray analyses identified the NAD^+-dependent protein deacetylase sirtuin-1 (SIRT1) as a relevant gene candidate. A strikingly decreased SIRT1 gene/protein expression and enzyme activity was detected in RA ECs. A markedly decreased SIRT1 expression was also observed in RA synovium, and more particularly in blood vessels.

Invalidation of SIRT1 with specific siRNA in control ECs was associated with a proliferative and activated profile upon TNFα stimulation, trough the acetylation of p53 and p65, and with the proangiogenic capacities through the upregulation of the matricellular protein CYR61. Conditional deletion of SIRT1 in ECs trough a Cre-LoxP recombination system increased angiogenesis and worsened signs of arthritis and in experimental models of tumor angiogenesis and methyl-BSA-induced arthritis. Conversely, overexpression of SIRT1 via adenovirus in RA ECs reversed this activated and proangiogenic phenotype, and activation of SIRT1 with resveratrol alleviated signs of experimental methyl-BSA-induced arthritis.

Conclusion: SIRT1 expression is reduced in synovial blood vessels of patients with RA. SIRT1 invalidation in control ECs reproduces the proliferative, activated and proangiogenic profile of RA ECs, and these effects were reversed by SIRT1 overexpression in RA ECs. These results support the implication of SIRT1 in RA synovial neoangiogenesis and may have direct therapeutic implications, since targeting angiogenesis, and especially SIRT1, might be used as a complementary therapeutic approach in RA.

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OP0292

THE HELPFUL EIGHT: KEY SPLICING MACHINERY ELEMENTS IN LEUKOCYTE SUBSETS MAY IMPROVE THE TYPIFICATION OF THE DISEASE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: The Splicing, a process of removing introns of RNA to produce mature messenger RNA, is exerted by an intricate macromolecular complex, the spliceosome. The alternative splicing, key mechanism that provides transcription and protein diversity, is dysregulated in various genetic, metabolic and inflammatory diseases. Splicing variants could contribute to the development and severity of pathologies of crucial importance.

Objectives: The aim of this study was the identification and characterization of alterations in the splicing machinery of leukocyte subsets of Rheumatoid Arthritis (RA) patients, as well as their influence on the activity of the disease and its atherothrombotic profile.

Methods: Monocytes, lymphocytes and neutrophils from 74 RA patients and 29 healthy donors (HD) were purified, and 45 elements of the splicing machinery were evaluated using a microfluidic qPCR array (Fluidigm). In parallel, the clinical status of the patients and the carotid intima-media thickness (CIMT) were assessed, along with an extensive serological evaluation, including autoantibodies, oxidative stress markers, inflammatory molecules and prothrombotic mediators. Correlation and association studies and logistic models among those clinical and analytical parameters were performed. Finally, leukocytes from HD were incubated with purified ACPAs-IgG from RA patients and changes promoted in both, splicing machinery and leukocyte inflammatory profile, were assessed.

Results: A significantly altered expression of spliceosome components was found in all the leukocyte subsets: 21, 17 and 27 components were differentially expressed in monocytes, lymphocytes and neutrophils, respectively, in RA patient's vs HD. The levels of those altered components were associated to ACPA positivity, high disease activity (DAS28>5.1), early atherosclerosis and radiological involvement. Correlations with inflammatory mediators, oxidative stress markers and NETosis were further identified. Interestingly, eight components, belonging to the major spliceosome (SNRNP70, SNRNP200 and U2AF2), minor spliceosome (RNU4ATAC), and splicing factors (RBM3, RBM17, KHDRS1 and SRSF10) were found simultaneously altered in the three leukocyte subtypes. Logistic regression models, built with levels of simultaneously altered spliceosome components, generated several signatures related to RA disease features that were able to: i) discriminate between RA patients and HD; ii) classify patients with high disease activity (DAS28>5.1); iii) recognize patients with radiological involvement; and iv) identify patients showing atheroma plaques. *In vitro* studies showed that the purified ACPAs of RA patients modulated the expression of these components.

Conclusion: 1) The splicing machinery is profoundly altered in leukocytes from RA patients and closely related to the activity of the disease, including inflammation, autoimmunity and articular involvement, as well as with the occurrence of early atherosclerosis. 2) Evaluation of the common altered components of the spliceosome in leukocytes subsets might be used to typify the disease, avoiding complementary ultrasound or radiological tests.

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OP0293 A FIRST-IN-CLASS METABOLIC REPROGRAMMING AGENT, MBS2320, SELECTIVELY MODULATES IMMUNE CELL FUNCTION AND IMPROVES OSTEOID FORMATION AND BONE PROTECTION VERSUS ETANERCEPT IN THE MOUSE COLLAGEN-INDUCED ARTHRITIS MODEL

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Background: Despite the availability of several treatment options, some Rheumatoid Arthritis (RA) patients do not reach low disease activity. There thus remains a need for differentiated new therapies. Prior studies identified a series of biphenylsulphonamides with bone protecting and anti-inflammatory activity[1,2] which might meet this need.
Objectives: To evaluate the selectivity of a novel small molecule, MBS2320, in myeloid and lymphoid cells, characterise its selectivity for osteoclasts versus osteoblasts and characterise its effects on synovitis and osteoprotection compared to an anti-TNFα agent in a therapeutically administered collagen-induced arthritis (CIA) mouse model.
Methods: Viability, proliferation or cytokine production were assessed in human primary monocytes, lymphocytes or a Mixed Lymphocytes Reaction (MLR). Human primary osteoclasts (OCs) were differentiated from CD14+ monocytes with M-CSF and RANK–L. Mature OCs were stained with tartrate-resistant acid phosphatase (TRAP) and quantified by light microscopy. Osteolytic activity was assessed on mineral-coated surfaces. Osteoblasts were derived from mesenchymal stem cells by differentiation in the presence of MBS2320; mineralisation was assessed by Alizarin Red S staining. CIA was induced in DBA/1J mice by collagen immunisation. MBS2320 and etanercept were dosed once daily after onset of disease. Arthritic Index (AI) was scored throughout the dosing period after which serial paw sections were assessed for inflammation, synovitis, stromal cavity osteolysis, pannus hyperplasia, osteoid layering and bone resorption foci.
Results: MBS2320 reduced the production of cytokine from monocytes and inhibited T-cell proliferation, and cytokine production in a MLR. MBS2320 also reduced primary OC differentiation and function *in vitro* to a greater degree than alendronate but showed no effect on the differentiation of primary osteoblasts. MBS2320 (0.3 mpk/d) and etanercept (10 mpk/d) inhibited the onset and severity of CIA arthropathy, and synovitis, pannus infiltration and osteolysis, with equivalent efficacy. In addition MBS2320 showed anatomically appropriate osteoid layering with conservation of the tide mark, and the bone marrow showed no cell atypia, with all progenitor classes present although reduced in number and distribution. In contrast, osteoid formation in the etanercept group was multi-focal with an often erratic tide-mark morphology and was localised to areas of reduced osteoclastic resorption and osteolysis with erratic osteocyte distribution.
Conclusion: MBS2320 selectively inhibits myeloid and lymphoid activity/differentiation, whilst sparing mesenchymal cells, in vitro. In murine CIA, MBS2320 treatment led to the formation of anatomically appropriate osteoid layering indicating an ongoing process of osteogenesis conditioned by biomechanics. By contrast osteoid formation due to etanercept was more 'reactive' and secondary to suppression of inflammation. The data suggest that MBS2320 offers equivalent anti-inflammatory activity, but a broader spectrum of osteoprotective efficacy in CIA compared to TNFα inhibition and may offer an alternative therapeutic approach to improving bone quality in RA.

REFERENCES:

[1] Greig IR, et al. Development and Characterization of Biphenylsulfonamides as Novel Inhibitors of Bone Resorption *J Med Chem* 2006;49:7487-7492
[2] Coste E, et al. Identification of small molecule inhibitors of RANKL and TNF signaling as anti-inflammatory and antiresorptive agents in mice Ann Rheum Dis 2015;74:220–6

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OP0294 TRANSCRIPTIONAL PROFILING OF RA PATIENTS SYNOVIAL TISSUE REVEALS TARGETS FOR PRECISION MEDICINE

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Background: We were the first in the United States to demonstrate the applicability of performing transcriptional profiling of macrophages cells isolated from ultrasound guided synovial biopsies on RA patients (Mandelin et al, *A&R* 2018[1]). While the numbers of macrophages are known to corelate with response to therapy in RA patients, little is known about macrophage heterogeneity or dendritic cell (DC) involvement in disease.
Objectives: Here, we performed single cell RNA seq and bulk population RNA-seq on RA synovium and peripheral blood (classical monocytes, non-classical monocytes, and DCs) from RA patients in order to compare their genome-wide transcriptional profile within and across individuals.
Methods: We obtained blood samples and ultrasound-guided minimally invasive synovial biopsy tissue from RA patients with active disease. Using Fluorescence-Activated Cell Sorting (FACS), we isolated classical monocytes (MHCII+CD14+ +CD16-), non-classical monocytes (MHCII+CD14+CD16+), and dendritic cells (MHCII+CD1c+) from blood. After processing synovial tissue for single-cell suspension, we isolated CD45+ cells for single cell RNA seq and macrophages (MHCII+CD14+CD11b+CD206+) and dendritic cells (MHCII+CD1c+) by FACS. We extracted RNA from these cell populations and prepared libraries for RNA-seq. These libraries were sequenced on an Illumina NextSeq 500 and assessed for quality of RNA, sequencing, and gene detection.
Results: For each cell population, we assessed the variability of gene expression across patients. We identified 5 different populations of macrophages that differ in their origin, response to methotrexate, differentiation status, and activation status. Additionally, as expected, the bulk population of DCs were highly variable across individuals, which this is likely due to the heterogeneity of subtypes within this population as shown in the single cell RNA seq for macrophages. In circulating monocytes, we observed varying levels of common cytokines and chemokines, such as TNF and CCL1. We also compared gene expression across cell populations to characterize transcriptional signatures that were distinctive to a given cell population. In addition to the genes previously known to be unique to dendritic cells vs. monocytes/macrophages in health, we also identified potential pathogenic factors that varied in their expression across cell types. Finally, to explore the relationship between circulating and tissue cell populations, we asked whether there were pathways that were turned on in the blood prior to extravasation into the synovium. For example, we identified genes that maintained their expression across monocytes and synovial macrophages in RA patients supporting the differentiation of the former into the latter.
Conclusion: Together, these results provide a survey of myeloid cells in the blood and synovial tissue of RA patients. We aim to understand how these cells vary across patients and what clinical variables and medication status influence their transcriptional profile across individuals. Our long-term goal is to use these studies to better understand the underlying mechanisms of pathogenesis and response to current treatments of RA as well as to identify potential targets for future therapies.

REFERENCE:

[1] Mandelin, A.M., 2nd, et al. Transcriptional Profiling of Synovial Macrophages Using Minimally Invasive Ultrasound-Guided Synovial Biopsies in Rheumatoid Arthritis. Arthritis & rheumatology (Hoboken, N.J.) 70, 841-854 (2018).

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OP0295 N-LINKED GLYCANS IN THE VARIABLE DOMAIN OF ACPA-IGG IN THE DEVELOPMENT OF RHEUMATOID ARTHRITIS

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Background: Anti-citrullinated protein antibodies (ACPA) are disease-specific biomarkers in rheumatoid arthritis (RA). Recently, we described that more than

90% of ACPA-IgGs harbour N-linked glycans in the antibody variable (V) domain. The corresponding N-glycosylation sites in the amino acid backbone of ACPA V-regions result from somatic hypermutation, a T cell-dependent process. Notably, both genetic evidence and data obtained from the analysis of serum ACPA indicate that T-cells drive the maturation of the ACPA-response prior to the onset of arthritis.

Objectives: We investigated whether ACPA-IgG carry V-domain N-glycans prior to the development of arthritis and whether the occurrence of such glycans predicts the transition from pre-disease autoimmunity to overt RA.

Methods: Two independent sets of serum samples were obtained from RA patients and from ACPA-positive first-degree relatives (FDR) of RA-patients (n=126) of an Indigenous North American (INA) population with high incidence rates of ACPA-positive RA. These samples comprised cross-sectional and longitudinal samples of individuals who did or did not transition to inflammatory arthritis. Serum ACPA-IgG were affinity-purified and subjected to enzymatic glycan release and UHPLC-based glycan analysis.

Results: ACPA-IgG V-domain glycosylation could be detected in RA patients and in FDR of RA patients. In both datasets, FDR-derived ACPA-IgG displayed markedly lower levels of V-domain glycans (<50%) compared to ACPA-IgG from RA-patients. Notably, FDRs that later developed RA showed extensive V-domain glycosylation before the onset of arthritis. Moreover, the degree of ACPA-IgG V-domain glycosylation in FDRs was strongly associated with future development of RA (HR: 6.07 [95% CI: 1.46-25.2]; p=0.013).

Conclusion: Glycosylation of the ACPA-IgG V-domain can be detected prior to the onset of disease. Extensive glycosylation is present in a subset of predisposed FDRs of INA RA patients. The presence of this feature substantially increases the risk of RA development. These observations fit well with a pivotal role for T cells in the selection and expansion of ACPA-expressing B cells, possibly by facilitating the introduction of N-glycosylation sites in ACPA-IgG V-domains. Moreover, glycosylation of the ACPA-IgG V-domain represents a predictive marker for RA development in ACPA-positive individuals and may serve to better time and target preventive therapeutic interventions.

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OP0296 COMPARISON OF TRANSCRIPTOMIC PROFILES BETWEEN PAIRED JOINT BIOPSIES FROM RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid Arthritis (RA) is a chronic and heterogenous condition characterized by inflammatory involvement of the synovial membrane in multiple joints. Synovial biopsies are used in research setting in order to identify diagnostic and theranostic markers. Many studies have shown a high degree of heterogeneity in histological and transcriptomic profiles between patients.

Objectives: We wanted to explore histological and transcriptomic profile of synovial biopsies across pairs of joints in the same patients to assess heterogeneity at the individual level.

Methods: Synovial biopsies were performed simultaneously in one small and one large joint per patient using needle-arthroscopy for the knee and US-guided needle biopsy for the hand or foot. Synovium from individuals with osteoarthritis (OA) were used as control. Paraffine-embedded samples were stained for CD3, CD 20, CD 68 and CD138. Whole-tissue RNA was extracted and hybridized on GeneChip Human Genome U133 Plus 2.0 Array (Affymetrix). The samples were tested for RNA integrity by Bioanalyzer (Agilent). Normalization and statistical analyzes were performed on Genespring. Pathway analysis were performed using DAVID.

Results: 10 RA patients were included (females: 10/10, ACPA/RF positivity: 8/10, mean age (± SEM): 54.4 (± 4.4) years, mean disease duration (± SEM): 13.3 (± 3.7) years, mean DAS28CRP (± SEM): 5.01 (± 0,34), mean HAQ (± SEM): 1.7 (± 0.28)).

Quantification of histological markers did not show differences in population of macrophages, plasmocytes, T and B Cells, across pairs of joints.

After correction for multiple comparisons, no transcripts were differentially expressed between large and small joints. Similarly, we did not find any significant difference in the expression of transcripts involved in pathways (TCR-activation and cell-division) specifically overexpressed in RA compared to OA synovial tissue.

In order to increase our ability to observe pair-wise differences in gene expression profiles, we studied correlations between transcripts significantly overexpressed in RA compared to OA joints with a fold change > 2 (n = 581) and clinical or biological markers of disease activity (DAS28-CRP, CRP, Physician Global Assessment of disease activity). Similar patterns of correlations indicated that disease activity was not driven by different pathways in small versus large joints.

Conclusion: This study is an important methodological milestone in the field of synovial biopsies, as it indicates that cellular and molecular alterations occurring in RA synovitis are similar across small and large joints from the same patient. Hence, biopsy of a single joint is representative and can be used to explore pathogenic processes or potential biomarkers in RA.

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OP0297 ABERRANT ADENOSINE TO INOSINE RNA EDITING IN ACTIVE RHEUMATOID ARTHRITIS

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Background: Adenosine to inosine (A-to-I) RNA editing is a widespread post-transcriptional RNA modification mainly located in repetitive *Alu* elements and mediated by the enzyme adenosine deaminase acting on RNA-1 (ADAR1). A-to-I RNA editing controls various aspects of RNA metabolism, which may affect tissue-specific gene expression. Although deregulation of RNA editing has been previously reported in various human diseases including cardiovascular disease and cancer (Stellos et al., *Nat Med*, 2017; Liu et al., *Nat Med*, 2019 and Ishizuka et al., *Nature*, 2019), its role in autoimmune diseases and especially in rheumatoid arthritis (RA) remains unknown.

Objectives: To study whether A-to-I RNA editing is involved in the pathogenesis of RA and to determine the impact of anti-rheumatic treatment on RNA editing.

Methods: We first analysed the expression of ADAR1 in 185 RA synovial tissues versus 76 healthy/osteoarthritic synovia derived from 4 independent RNA-sequencing and microarray datasets. We validated the findings in peripheral blood mononuclear cells (PBMCs) derived from 19 patients with active RA vs 14 controls and performed an additional ADAR1-isoform analysis (ADAR1p110/ADAR1p150) by RT-qPCR. Further, we studied in single nucleotide level the A-to-I RNA editing levels of the pro-inflammatory gene cathepsin S (CTSS) 3'-untranslated region (3'UTR), a matrix degradation enzyme which is a well-established target of ADAR1, by *Alu* Sanger sequencing and RNA editing analysis. Last, we examined the effect of anti-rheumatic treatment on RNA editing.

Results: Expression of the RNA editor ADAR1 was significantly increased in RA synovium compared to healthy or osteoarthritic synovium. Similarly, a significant increase of ADAR1, mainly due to an increase of the interferon-inducible ADAR1p150 isoform, was observed in PBMCs from active RA. Next, we studied the RNA editing levels in PBMCs from active RA patients before and after 12-week treatment versus controls. RNA editing of CTSS 3'UTR *AluSx*$^{+}$ was increased in active RA (6-47% increase in editing rate of 8 individual adenosines, all P<0.05). Increased CTSS mRNA expression in RA PBMCs was associated with both ADAR1p150 expression (r=0.623, P=0.004) and RNA editing rate of 12 individual adenosines (r=range 0.45-0.72, P<0.05 for all) located within the CTSS 3' UTR *AluSx*$^{+}$. The correlation between CTSS and ADAR1 was also observed in synovial tissue. Notably, ADAR1p150 expression and RNA editing rate reached control levels after 12-week treatment with methotrexate ± corticosteroids and/or biologics in patients with good clinical response (EULAR responders) but remained unchanged in the EULAR moderate/non-responders.

Conclusion: ADAR1-mediated RNA editing is increased in active RA inducing the expression of pro-inflammatory genes thus representing a novel drug response biomarker and a potential therapeutic target in EULAR moderate/non-responders.

REFERENCES:
[1] Stellos, et al., Nat Med 2016;22:1140–50. doi:10.1038/nm.4172
[2] Liu, et al., Nat Med 2019;25:95–102. doi:10.1038/s41591-018-0302-5
[3] Ishizuka, et al., Nature 2019;565:43–8. doi:10.1038/s41586-018-0768-9

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FRIDAY, 14 JUNE 2019

Novel biomarkers in RMDs – next steps towards clinical implementation

OP0298

PCSK9 IN ATHEROSCLEROTIC INFLAMMATION OF LUPUS PATIENTS AND MURINE MODEL OF LUPUS WITH ATHEROSCLEROSIS

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Background: Systemic lupus erythematosus (SLE) patients have tendencies of accelerated atherosclerosis (AS), which is refractory to statins. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a new therapeutic target for AS for its dual mechanisms in lipids metabolism and inflammation. PCSK9 inhibitors had proved to be highly promising cardiovascular disease (CVD) drugs [1]. Our previous study suggested that Toll-like recetor 4(TLR4) signal participates in the atherosclerotic inflammation of murine model of lupus with AS [2].
Objectives: To investigate the role of PCSK9 in atherosclerotic process of lupus and the association between TLR4 and PCSK9 in athergenic inflammation of murine model of lupus with AS.

Table 1 Characteristics of SLE patients and controls.

Variables	*SLE*	*Healthy controls*	*p-value*
Number	90	50	NA
Female/Male	82/8	43/7	>0.05
Age(years)	33(29-42)	32(28-44)	>0.05
Disease duration(years)	6(3-10)	NA	NA
SLEDAI	6(2-8)	NA	NA
Cholesterol(mmol/l)	4.52(3.85-5.37)	4.52(3.93-5.60)	>0.05
LDL cholesterol(mmol/l)	2.47(1.84-3.16)	2.58(2.03-3.06)	>0.05
Triglycerides(mmol/l)	1.16(0.79-1.61)	1.34(0.87-1.56)	>0.05
HDL cholesterol(mmol/l)	1.47(1.23-1.73)	1.61(1.36-1.91)	>0.05
cIMT thickening	27/90(30.00%)	7/50(14.00%)	0.03
Treatment			
HCQ use	90/90(100%)		
Steroid use	75/90(83.33%)		
AZA use	15/90(16.67%)	NA	
CsA use	9/90(10.00%)		
MMF use	16/90(17.78%)		

Data are shown as number or median (interquartile range), respectively. SLE: systemic lupus erythematosus; SLEDAI: systemic lupus erythematosus disease activity index; LDL: low-density lipoprotein; HDL: high-density lipoprotein; cIMT: carotid intima-media thickness; HCQ: Hydroxychloroquine; AZA: Azathioprine; CsA: Cyclosporin A; MMF: Mycophenolate Mofetil.

Methods: 90 SLE patients and 50 healthy controls were included. According to carotid intima-media thickness (cIMT), SLE patients were further divided into SLE-AS and SLE-NonAS subgroups (cut-off point: 1.0mm). Traditional CVD risk factors, inflammatory biomarkers and PCSK9 concentrations were compared between: (I) SLE patients and controls; (II) SLE-AS subgroup and SLE-NonAS subgroup. Correlational analysis and multivariate linear regression analysis were applied to analyze the association between PCSK9 levels and disease parameter, and the predictors of PCSK9 levels in SLE patients. Effects on PCSK9 concentrations by monotherapy with hydroxychloroquine (HCQ), which is thought having protective effects against CVD in SLE, were investigated by follow-up analysis in 15 SLE patients with inactive disease (SLEDAI=2). In animal experiment, murine model of SLE with AS was set up by intraperitoneally injection of lipopolysaccharides (LPS) in ApoE-/- mice. 30 female ApoE-/- mice were respectively administrated with LPS (SLE+AS group, n=10), saline (AS group, n=10) and LPS plus injection of lentiviruse-PCSK9 small hairpin RNA targeting the mouse PCSK9 gene into the tail vein to interfere PCSK9 expression (SLE+AS+PCSK9i group, n=10). 10 female C57BL/6 mice were included as controls. Serum concentrations of PCSK9 and inflammatory biomarkers including TNF-α and IL-1β, atherosclerotic lesion, lipids parameters, expression of PCSK9, TLR4 and NF-κB p65 in atherosclerotic plaque were assessed.
Results: Characteristics of SLE patients and controls were listed in Table 1. SLE patients had significantly elevated serum PCSK9 levels than controls, especially in SLE-AS subgroup, accompanied with higher ratio of cIMT thickening. Correlational analysis showed PCSK9 concentrations correlated with C-reactive protein (CRP) levels, age and erythrocyte sedimentation rate (ESR), but not lipids parameters. Univariate and multivariate linear regression revealed that only CRP, but not age or ESR was positive predictors of PCSK9. Monotherapy with HCQ for 3 months significantly reduced PCSK9 levels in inactive SLE patients (Table 2, Figure 1). Mice in SLE+AS group had significantly higher serum PCSK9 concentrations than mice in AS group and C57BL/6 mice. Immunohistochemistry showed that PCSK9 overexpression was observed in SLE+AS mice than those in AS group and SLE+AS +PCSK9i group. Mice in SLE+AS+PCSK9i group exhibited decreased inflammatory cell infiltration in atherosclerotic plaque, alleviated atherosclerotic lesion, lower serum TNF-α and IL-1β levels and attenuated expression of TLR4 and NF-κB p65 in atherosclerotic plaque than SLE+AS group. PCSK9 silencing had no significant effects on lipids parameters in SLE+AS mice (Figure 2).

Table 2 Multivariate linear regression of CRP, ESR, age (independent variable) and PCSK9 (dependent variable) in SLE patients

	Unstandardized Coefficients		Standardized Coefficients		
Model	B	Std. Error	Beta	t	p
(Constant)	280.339	72.128		3.887	<0.001
CRP	4.040	0.972	0.408	4.158	<0.001
ESR	1.028	0.974	0.103	1.055	0.294
Age	2.931	1.767	0.159	1.659	0.101

SLE: systemic lupus erythematosus; PCSK9: Proprotein convertase subtilisin/kexin type 9; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

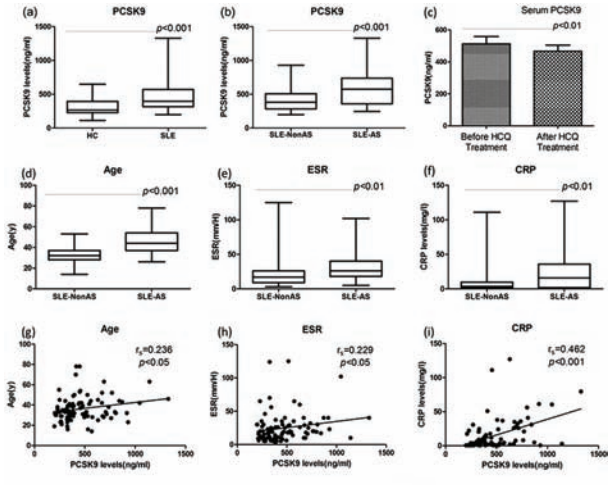


Figure 1. (a)-(b) SLE patients had significantly elevated serum PCSK9 concentrations than controls, especially in those with AS; (c) Monotherapy with HCQ for three months significantly reduced PCSK9 levels in SLE patients with inactive disease(n=15); (d)-(f) Difference of age, ESR and CRP levels between patients in SLE-AS subgroup and those in SLE-NonAS subgroup had statitical significance; (g)-(i) Correlational analysis showed that serum PCSK9 levels correlated with age, CRP levels and ESR in SLE patients.

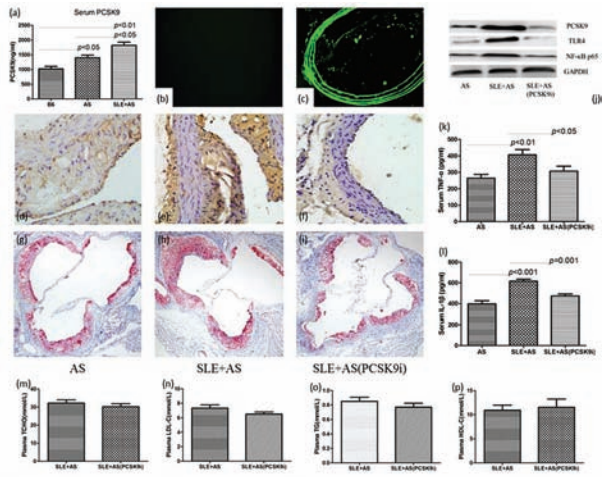


Figure 2. (a) SLE+AS mice had significantly higher serum PCSK9 concentrations than mice in AS group and C57BL/6 mice; (b)-(c) Expression of PCSK9 was interfered via injection of lentiviruse-PCSK9 small hairpin RNA targeting the mouse PCSK9 gene into the tail vein. Compared with SLE+AS group(b), SLE+AS+PCSK9i group(c) exhibits bright green fluorescence in atherosclerotic plaque; (d)-(i) Immunohistochemistry showed that PCSK9 overexpression was observed in SLE+AS mice than those in AS group and SLE+AS+PCSK9i group. Mice in SLE+AS+PCSK9i group showed alleviated inflammatory cell infiltration and atherosclerotic lesion than those in SLE+AS group and AS group(d-f: Immunohistochemistry of PCSK9, ×200; g-i: Oil red O stain, ×40); (j)-(l) Mice in SLE+AS+PCSK9i group exhibited lower serum TNF-α and IL-1β levels and attenuated expression of TLR4 and NF-κB p65 in atherosclerotic plaque than those in SLE+AS group; (m)-(p) PCSK9 silencing had no significant effect on lipids parameters(TCHO, LDL-C, TG and HDL-C) in SLE+AS mice($p>0.05$).

Conclusion: PCSK9 participates in atherogenic inflammation in SLE patients and murine model of SLE with AS. This process is associated with TLR4-NF-κB pathway, probably independent of lipids parameters alteration. HCQ can effectively reduce PCSK9 levels in SLE patients.

REFERENCES:

[1] Sabatine MS, et al. N Engl J Med. 2017, 376(18):1713-1722.
[2] Ni JQ, et al. Clin Dev Immunol. 2013;2013:476856.

Disclosure of Interests: None declared
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OP0299 ASSESSMENT OF ROLE OF URINARY HEPARANASE IN LUPUS NEPHRITIS PATIENTS AND ITS CORRELATION WITH DISEASE ACTIVITY

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Background: Lupus nephritis (LN) is one of the most common and serious complication of Systemic Lupus Erythrematosus (SLE) and assessment of its activity is crucial. Heparanase has been proposed to be important in the pathogenesis of proteinuria in various forms of glomerulonephritis.
Objectives: To assess the ability of urinary heparanase to identify SLE with nephritis and the relation of this marker to lupus activity.
Methods: This cross sectional study was carried out on 90 subjects; 70 patients with SLE and 20 healthy volunteers as a control. All patients and controls were subjected to full history taking and complete clinical examination, routine investigations. Immunological assay and assessment of disease activity by systemic lupus erythematosus disease activity index (SLEDAI) score, renal SLEDAI (r-SLEDAI) were done for lupus nephritis group. The lupus patients were divided according to SLEDAI score into 4 groups; 20 with active lupus nephritis, 17 with non-active LN, 18 with active lupus without renal involvement, 15 with non-active lupus without renal involvement. Urinary Heparanase levels were measured by using ELISA for all groups.
Results: The level of urinary heparanase was significantly higher in LN groups than non-LN groups and control. It was also significantly higher in active LN than non-active LN patients. There was a significant positive correlation between urinary heparanase and 24 hours urinary proteins, total SLEDAI, and r-SLEDAI, and significant negative correlation between urinary heparanase and C3 & C4. ROC curve analysis revealed that urinary heparanase predicted presence of lupus nephritis activity with a sensitivity of 80%, and a specificity of 91.43%.
Conclusion: Urinary heparanase levels are increased in patients with active LN and correlate with disease activity markers, indicating that it can serve as a new useful biomarker for lupus nephritis activity.

REFERENCES:

[1] Kim K-J, Kim J-Y, Park S-J, Baek I-W, Yoon C-H, Kim W-U, et al. SAT0227 Urinary heparanase activity is elevated in patients with lupus nephritis and correlate with protein excretion. Annals of the Rheumatic Diseases. 2013;71(Suppl 3):548-9.
[2] Cho C, Kim K, In-Woon B. 206 Increased urinary heparanase levels are associated with active lupus nephritis. Archives of Disease in childhood; 2017.

Table (1). : Comparison between the different studied groups regarding HPSE (ng/ml)

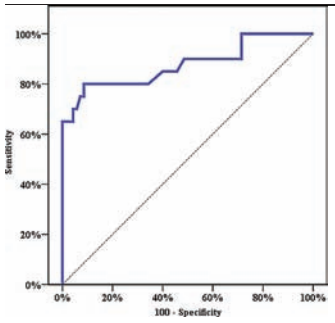
	Group I Active LN (n=20)	Group II Non active LN (n=17)	Group III Active lupus Without nephritis (n=18)	Group IV Non-active lupus Without nephritis (n=15)	Group V Control (n=20)	F	P
HPSE (ng/ml)	2.36 ± 0.62	1.44 ± 0.11	1.23 ± 0.07	1.31 ± 0.07	0.29 ± 0.13	115.716*	<0.001*
p_1 Sig. bet. Grps	<0.001*	<0.001*	<0.001*	<0.001*			
	p_2<0.001*, p_3=0.914, p_4<0.001*, p_5=0.719, p_6<0.001*, p_7=0.230						

F: **F for ANOVA test**, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)
– p: p value for comparing between the different groups
– p_1: p value for comparing between group V and each other group
– p_2: p value for comparing between group I and group II
– p_3: p value for comparing between group III and group IV
– p_4: p value for comparing between group I and group III
– p_5: p value for comparing between group II and group IV
– p_6: p value for comparing between group I and group IV
– p_7: p value for comparing between group II and group III

Table 2. Agreement (sensitivity, specificity) for HPSE (ng/ml) to diagnose active lupus nephritis

	Cut off	Sensitivity	Specificity	PPV	NPV
HPSE (ng/ml)	**>1.48**	80.0	91.43	72.7	94.1

	HPSE (ng/ml)
AUC	0.877
p	<0.001*
95% C.I	0.771 – 0.982



Disclosure of Interests: None declared
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OP0300 A NEUTROPHIL SIGNATURE IS STRONGLY ASSOCIATED WITH CARDIOVASCULAR RISK IN GOUT

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Background: Similar to other rheumatic diseases, patients with gout have an increased cardiovascular morbidity and mortality, not fully explained by traditional cardiovascular risk factors. Instead, gout-specific factors, including xanthine oxidase induced oxidative stress, increased lipid oxidization and chronic low-grade inflammation, have been suggested as important contributors.(1) Neutrophils, through formation of neutrophil extracellular traps (NETs), partake in pro-

thrombotic and atherogenic processes contributing to cardiovascular disease.(2) However, the role of NETs in cardiovascular disease in human gout is not known.
Objectives: Our objective is to investigate the association between neutrophil activation and cardiovascular risk in gout patients. We hypothesize that neutrophil activation mediates inflammation, as well as activation and damage to endothelial cells, partaking in atherosclerosis development.
Methods: Plasma samples from 75 gout patients participating in the 'Reade gout cohort Amsterdam' were analyzed. Patient data was collected on disease activity, demographics, gout history, comorbidities, medication use and cardiovascular risk assessments. Measurements included anthropometry, vital parameters (RR, HF), ECG and lab variables. Levels of NETs, and NET-derived markers (cell-free DNA and peroxidase activity) were analyzed using a MPO-DNA ELISA, as well as fluorimetry. Levels of calprotectin (S100A8/A9) were analyzed by ELISA. Markers of NETosis were related to clinical markers of cardiovascular risk, including BMI, smoking, blood pressure, lipid profile and 10 year risk of cardiovascular mortality (SCORE EU).
Results: No associations were found between markers of cell death (cfDNA and NETs) and cardiovascular risk. However, markers of neutrophil activation, including peroxidase activity correlated with BMI (r=0.31, p=0.008), waist-hip ratio (r=0.52, p<0.001), cholesterol ratio (r=0.51, p<0.001), and triglycerides (r=0.42, p<0.001). These associations were even stronger in patients with chronic, polyarticular gout. Peroxidase activity was associated with the 10 year risk of cardiovascular comorbidity (r=0.47, p<0.001, Figure 1A). Calprotectin levels were elevated in hypertension (p=0.005) and diabetes (p=0.02), with calprotectin levels associating with diabetes independently on BMI (OR=6.2, p=0.04). Finally, we constructed a neutrophil risk score ranging from 0-2 based on positivity for peroxidase and/or calprotectin to identify patients with a 'neutrophil activation signature'. The neutrophil risk score strongly associated with CVD risk (Figure 1B). Patients with neutrophil activation signature (risk score 1-2) had markedly elevated cardiovascular risk score (p=0.001), with 67.7% of the patients having high cardiovascular risk, versus 32.3% of the patients without a neutrophil activation signature (OR=2.9, p=0.03).
Conclusion: We have demonstrated, for the first time, that neutrophil activation markers are associated with several risk factors of cardiovascular disease, including hyperlipidemia, hypertension and diabetes in a large cohort of gout patients. Furthermore, the presence of a neutrophil activation signature is strongly associated with a 10-year risk of cardiovascular comorbidity.

Figure 1A

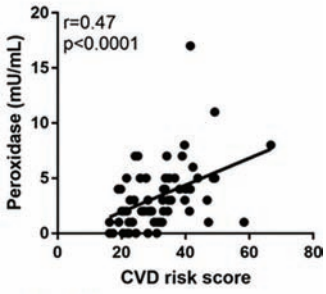
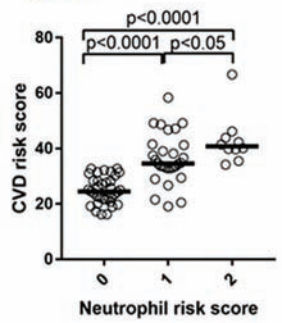


Figure 1B



REFERENCES:

[1] Krishnan E. Inflammation, oxidative stress and lipids: the risk triad for atherosclerosis in gout. Rheumatology (Oxford). 2010;49(7):1229-38.
[2] Doring Y, et al. Neutrophil Extracellular Traps in Atherosclerosis and Atherothrombosis. Circ Res. 2017;120(4):736-43.

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OP0301 C-X-C MOTIF CHEMOKINE 10 (CXCL10) IS A POTENTIAL BIOMARKER OF DISEASE ACTIVITY IN PSORIATIC ARTHRITIS (PSA)

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Background: Assessment of Psoriatic Arthritis (PsA) disease activity requires detailed clinical evaluation complemented by imaging. Current laboratory markers such as CRP do not accurately reflect PsA disease activity. Identifying soluble biomarkers of PsA disease activity is an important perceived clinical need.
Objectives: We aimed to identify markers that correlates with PsA disease activity and change with treatment.
Methods: Serum samples were obtained from a cohort of patients with PsA not on DMARD treatment assessed clinically every 6 months according to a standard protocol including several measures of disease activity: physician and patient global assessment, tender and swollen joint counts, skin scores (BSA, PASI) and the composite measures- Disease Activity Score for PsA (DAPSA) and PsA Disease Activity Score (PASDAS). In the discovery phase, we mined our clinical and biomarker database that has linked biomarker and disease activity measures and identified markers that potentially reflect PsA disease activity. In verification phase 1 we measured the selected 17 markers in 80 PsA samples. 8 Markers that significantly correlated with disease activity were identified based on Spearman correlation coefficients. In the verification phase 2 these 8 markers were further assayed in an inception cohort of 80 patients. In this phase, physician global assessment of disease activity (including skin and joints-MDGA) was used as the primary measure of disease activity; other skin, MSK and patient reported measures were considered secondary measures. In verification phase 3 with the hypothesis that markers associated with disease activity would decrease with treatment, the markers that correlated with MDGA where further assayed in 40 patients before and after 6 months of treatment (26 biologics and methotrexate, 14 methotrexate). All assays were done using commercially available ELISA.
Results: In verification phase 1 8 markers of 17 tested were found to be associated with measures of disease activity in 80 PsA patients (mean age 47, males 58%, swollen joint count [SJC] 2, tender joint count [TJC] 3.6, PASI 2.9). In verification phase 2 2 markers [CXCL10 (ρ=0.25, p =0.03) and CRP (ρ=0.26, p =0.02)] tested in 80 patients (mean age 49, males 54%, SJC 1.5, TJC 3.3, PASI 5.6) correlated with MDGA, and did not correlate with each other. Three other markers correlated with secondary measures; COMP correlated with PASDAS (ρ=0.22, p =0.04), MMP3 correlated with PASI (ρ=0.27, p =0.01) and CPII-C2C ratio correlated with active joints (ρ= -0.27, p =0.02). In verification phase 3 CXCL10 (baseline mean =246.7(standard deviation 190.79) - 6 month 177.7 (163.8)); (p=0.0008) and CRP (18.5 (19.1) - 9.5 (8.9)); (p=0.002)] significantly decreased 6 months post treatment.
Conclusion: CXCL10, a marker previously associated with PsA, may also be a marker of PsA disease activity. Identifying a robust outcome measure for disease activity to conduct biomarker studies in a heterogeneous disease like PsA remains a significant challenge.
Disclosure of Interests: None declared
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OP0302 MUCOSAL-ASSOCIATED INVARIANT T (MAIT)-CELL-DERIVED IL-17A AND IL-17F PRODUCTION IS IL-23-INDEPENDENT AND BIASED TOWARDS IL-17F

Suzanne Cole, Catherine Simpson, Remi Okoye, Meryn Griffiths, Dominique Baeten, Stevan Shaw, Ash Maroof. *UCB Pharma, Slough, United Kingdom*

Background: The requirement for IL-23 in driving IL-17A and IL-17F production in humans is incompletely understood. Preclinical data support IL-17F, together with IL-17A, as a key driver of chronic tissue inflammation.[1] MAIT cells, an innate-like T cell population, uniformly express RORγt but only a minority have been shown to produce IL-17A.[2] Dysregulation in frequency and function of MAIT cells

has been associated with IL-17A-mediated inflammatory diseases, including PsA and AS.[3,4] IL-17F production in MAIT cells remains largely unexplored.
Objectives: To explore the importance of IL-23 signalling in MAIT cell-derived IL-17A and IL-17F production, examine the presence of MAIT cells in psoriatic lesional skin and assess the contribution of MAIT cell-derived IL-17A and IL-17F using *in vitro* models of skin inflammation.
Methods: IL-17A and IL-17F production by MAIT cells was assessed by flow cytometry, ELISA, qPCR and CyTOF upon activation by anti-CD3/CD28 or fixed *E. coli* via MR1–presented riboflavin metabolites, with or without disease-relevant recombinant cytokines or an IL-23-neutralising antibody. RNAscope was utilised to observe MAIT cells in psoriatic lesional skin. MAIT cell supernatant, generated from FACS sorted activated MAIT cells, was cultured with normal human dermal fibroblasts (NHDFs) in the presence of IL-17-isoform-specific antibodies, including bimekizumab, a monoclonal antibody that potently and selectively neutralises both IL-17A and IL-17F.
Results: Optimal MAIT cell IL-17A and IL-17F production occurred upon T cell receptor triggering with IL-12 and IL-18, independently of IL-23. IL-17F expression was greater at both gene and protein levels than IL-17A. The kinetics and threshold of activation for IL-17A and IL-17F suggest tighter regulation compared with other inflammatory cytokines, including IFNγ and TNF. Optimal MAIT cell IL-17A and IL-17F production requires monocytes, which contribute to IL-12 production upon IL-18 stimulation. MAIT cells were abundant in psoriatic lesional skin. NHDFs cultured with supernatant generated from activated MAIT cells produced inflammatory mediators IL-6, IL-8 and CCL2, which were reduced upon inhibition of either IL–17A or IL-17F, with optimal suppression achieved following dual neutralisation with bimekizumab.
Conclusion: IL-17A and IL-17F can be produced from MAIT cells independently of IL-23, and contribute to inflammatory responses in NHDFs. These results support dual neutralisation of IL-17A and IL-17F as a complete and targeted approach to supress IL–17–driven inflammatory responses.

REFERENCE:

[1] Glatt *Ann Rheum Dis* 2018;77:523–32, 2Dusseaux *Blood* 2011;117:1250–59, 3Menon *Arthritis Rheumatol* 2014;66:1272–81, 4Gracey *Ann Rheum Dis* 2016;75:2124–32

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OP0303 MONOSODIUM URATE AND CALCIUM PYROPHOSPHATE CRYSTAL-INDUCED INTERLEUKIN 1 PRODUCTION DEPENDS ON GLUCOSE UPTAKE THROUGH GLUT1 TRANSPORTER

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Background: Monosodium urate (MSU) and monoclinic calcium pyrophosphate dihydrated (mCPPD)crystals are responsible for relapsing acute arthritis which is driven by interleukin 1β (IL-1β).IL-1β production relies on NLRP3 inflammasome activation leading to ASC and caspase-1 recruitment. In tumor cells and in LPS-stimulated macrophages a switch of cell metabolisms toward glycolysis favors IL-1β production.
Objectives: The aims of this study were to assess 1/whether crystal-induced NLRP3 activation and IL-1β production involved glucose metabolism and 2/how MSU and mCPPD crystals induced glucose uptake focusing on the role of glucose transporter Glut1.
Methods: Synthetic and pyrogen-free MSU and mCPPD crystals were used to stimulate THP-1 cells and mouse bone marrow-derived macrophages (BMDM). Cells were stimulated in presence or absence of glucose (2g/L) and pyruvate (10mM). Glycolysis was inhibited by 2-deoxy-glucose (2DG) and the role of glucose transporter 1 (Glut1) was assessed by pharmacological inhibitor (STF-31) and siRNA. IL-1β production was quantified by ELISA.Metabolomic analysis was performed by mass spectrometry. Glucose uptake was determined using ^{18}F-DG (Fluor18 labeled-2DG) and positron emission tomography (PET). Glut1 membrane localization was assessed by flux cytometry and confocal microscopy, ASC speck formation by confocal microscopy. *In vivo*, we used murine air pouch model to assess the effects of 2DG and Glut1 inhibition in crystal-mediated inflammation.Glut1 membrane localization of circulating neutrophils was compared to synovial fluid neutrophils harvested during gout flare.
Results: *In vitro*, both MSU and mCPPD crystal-induced IL-1β secretion and ASC speck formation were inhibited when cells were cultured in glucose-free medium or in presence of 2DG.Similarly,MSU and mCPPD crystal-induced inflammation was abrogated in mice treated with 2DG.In THP-1 cells stimulated by MSU and mCPPD crystals, metabolomic analysis displayed alteration of glycolysis pathway and Krebs cycle and decrease of intracellular ATP production. Interestingly, MSU and mCPPD crystals increased glucose uptake*in vitro, ex vivo and in vivo*. Crystal-induced IL-β secretion was decreased by STF-31 and in THP-1 cells transfected with Glut1 siRNA. Next, we observed that MSU and mCPPD crystals increased membrane localization of Glut1 in THP-1, BMDM and neutrophils infiltrated in air pouch lavages and membranes. Glut1 membrane localization was positively correlated with IL-1β production. Moreover, during gout flare, the proportion of Glut1 positive neutrophils was higher in synovial fluid neutrophils than in circulating neutrophils. Finally, STF-31 treatment decreased, *in vitro,* glucose uptake induced by MSU and mCPPD crystals, and *in vivo* MSU and mCPPD crystal-induced inflammation.
Conclusion: Glucose uptake through Glut1 transporter enhanced IL-1β production induced by MSU and mCPPD crystals. Studies to decipher how these crystals induced Glut1 membrane localization are ongoing. Similarly, we investigate how glycolysis regulates NLRP3 and ASC activation. Decreasing Glut1 membrane localization might be a potential target to dampen crystal-induced inflammation.
References: **Disclosure of Interests:** Félix Renaudin: None declared, Laure Campillo-Gimenez: None declared, Florence Castelli: None declared, François Fenaille: None declared, Aurélie Prignon: None declared, Christèle Combes: None declared, martine Cohen Solal Speakers bureau: Amgen and Lilly, Frederic Lioté Grant/research support from: institutional grants from Grunenthal, Ipsen Pharma/Menarini, Novartis, SOBI for the European Crystal Network Workshops, Consultant for: Grunenthal, Novartis, Hang Korng Ea: None declared
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OP0304 GENETIC AND FUNCTIONAL STUDY OF OMENTIN REGARDING CARDIOVASCULAR RISK IN AXIAL SPONDYLOARTHRITIS

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Background: Cardiovascular (CV) disease is one of the main causes of mortality in axial spondyloarthritis (axSpA). The higher incidence of CV risk factors and systemic chronic inflammation increase CV risk in axSpA.[1] This is enhanced by a dysregulation of adipokines. Low levels of omentin, an anti-inflammatory adipokine, have been associated with metabolic dysfunction and CV disease in general population and conditions different from axSpA.[2,3]
Objectives: To evaluate the implication of omentin in CV risk and subclinical atherosclerosis in axSpA at the genetic and functional (mRNA and protein) level.
Methods: 382 patients fulfilling the ASAS classification criteria for axSpA[4] and 84 controls were included. Carotid ultrasound was performed to evaluate the presence of subclinical atherosclerosis. Serum omentin levels were assessed by ELISA. mRNA expression of *ITLN1*, coding omentin, was evaluated by RT-qPCR. *ITLN1* rs12409609 (C/T), in complete linkage disequilibrium with a polymorphism

previously associated with coronary artery disease,[5] was genotyped by TaqMan probes. Results were adjusted by potential confounding factors (STATA® v.11.1).
Results: Serum and mRNA levels of omentin were lower in axSpA compared to controls (p<0.001). Low omentin serum levels were observed in obese patients, patients with inflammatory bowel disease (IBD) and in those with an atherogenic index indicative of dyslipidemia (p=0.002, 0.006 and 0.004, respectively). Interestingly, the C allele of rs12409609 (both when alleles and genotypes were assessed) was associated with low mRNA levels of omentin in axSpA (p<0.001). No association was observed between omentin and markers of subclinical atherosclerosis at the DNA, mRNA and protein level.
Conclusion: style="font-family: 'Times New Roman','serif'; font-size: 10.0pt; margin: 0cm; margin-bottom: 8.0pt; line-height: 106%; margin-left: 0cm; margin-right: 0cm; margin-top: 0cm; mso-style-name: Normal_0; text-align: justify;" font-size="11.0" data-pos-index="15" class-name="Deleted">Omentin is linked to obesity and adverse lipid profiles in axSpA. Additionally, low serum levels of omentin are associated with the presence of IBD in axSpA. These data support a role of omentin as a CV risk biomarker in axSpA.

REFERENCES:
[1] Joint Bone Spine.2014;81:57-63.
[2] Cardiovasc Hematol Disord Drug Targets.2013;13:59-72.
[3] Curr Issues Pharm Med Sci.2015;28:176-80.
[4] Ann Rheum Dis.2009;68:777-83.
[5] Asian Cardiovasc Thorac Ann.2017;25:199-203.

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OP0305

THE ALARMIN S100A9 HAMPERS OSTEOCLAST DIFFERENTIATION FROM CIRCULATING PRECURSORS BY REDUCING THE EXPRESSION OF RANK

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Background: High levels of the damage-associated molecular pattern (DAMP) S100A8/A9 are produced in the inflamed synovium during experimental and human rheumatoid arthritis (RA), which have been implicated in sterile inflammation-induced bone resorption. We and others have previously shown that stimulation of mature osteoclasts with S100A8/A9 increases their bone-resorptive capacity. In agreement, reduced bone destruction was observed after induction of experimental RA models in *S100a9-/-* mice. However, its effects on the differentiation of osteoclasts from their precursors remains elusive.
Objectives: Here, we investigated the effects of S100A9 on osteoclast differentiation from $CD14^+$ circulating precursors.
Methods: $CD14^+$ monocytes were isolated from buffy coats of healthy donors and differentiated towards osteoclasts with macrophage colony-stimulating factor (M-CSF) and receptor activator of nuclear factor kappa-B (RANK) ligand in the presence or absence of S100A9. Differentiation state of osteoclasts was determined by tartrate-resistant acid phosphatase (TRAP) staining and resorption capacity was quantified using hydroxyapatite-like-coated plates. RNA expression was analyzed with RNA sequencing and qPCR. RANK expression was assessed using FACS. Underlying epigenetic programming was studied using chromatin immunoprecipitation. Secretion of pro-/anti-inflammatory mediators was analyzed with Luminex analysis.
Results: S100A9 stimulation during monocyte-to-osteoclast differentiation resulted in a strong decrease in the numbers of multinucleated osteoclasts, underlined by a decreased resorptive capacity. The thus differentiated cells showed a high production of pro-inflammatory factors, such as interleukin (IL)-1β, IL-6, IL-8, and tumor necrosis factor-α (TNFα) after 16h of stimulation. In contrast, at day 4, the cells showed a decreased expression of the osteoclast-promoting factor TNFα. Interestingly, we showed that S100A9 stimulation only during the first 16h of culture was sufficient to reduce osteoclastogenesis. To determine the mechanism of how this short S100A9 stimulation might reduce the osteoclast differentiation, we determined the protein expression of RANK. We observed that within this 16h time frame, S100A9 inhibited the M-CSF-mediated induction of RANK, which we found to be associated with changes in various histone marks at the epigenetic level. This S100A9-induced reduction in RANK could be partially reversed by blocking TNFα using etanercept, but not by blocking interleukin-1 (IL-1) with the IL-1 receptor antagonist.
Conclusion: Whereas S100A8/A9 was previously shown to stimulate the resorptive capacity of mature osteoclasts, we here show that early S100A9 stimulation impedes monocyte-to-osteoclast differentiation via reduction of RANK expression that is partially TNFα-mediated. This suggests that the timing of exposure to S100A8/A9 is an important determinant for monocyte-to-osteoclast differentiation.
Disclosure of Interests: Martijn van den Bosch: None declared, Irene Di Ceglie: None declared, Arjen Blom: None declared, Robab Davar: None declared, Colin Logie: None declared, Ehsan Habibi: None declared, Johannes Roth: None declared, Thomas Vogl: None declared, Carl Goodyear Grant/research support from: AstraZeneca, BMS, Celgene, Janssen, MedAnnex, Pfizer and UCB, Speakers bureau: Abbvie, Peter van der Kraan: None declared, Peter van Lent: None declared
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Public health, health services research, and health economics

OP0306

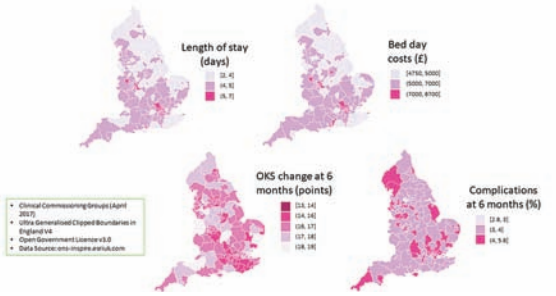
GEOGRAPHICAL VARIATION IN PATIENT OUTCOMES OF PRIMARY KNEE REPLACEMENT ACROSS CLINICAL COMMISSIONING GROUPS: STUDY FROM "THE NATIONAL JOINT REGISTRY OF ENGLAND, WALES, NORTHERN IRELAND AND THE ISLE OF MAN"

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Background: In the UK, the Health and Social Care Act 2012, places duties on the NHS Commissioning Board and Clinical Commissioning Groups (CCG) to have regard to the need to reduce variations in access to, and outcomes from, health care services for patients[1]. There are well known geographical variations in the uptake of common surgical procedures including knee replacement[2]. Much less is known about variations in outcomes of surgery and factors that can explain why such variation exists.
Objectives: Our aim was to explore variation in patients' outcomes for primary total or unicomparmental knee replacement (TKR/UKR) surgery across CCGs, and to identify whether patient, surgical and hospital factors can explain why such variation exists.
Methods: We used the National Joint Registry, which incorporates data on knee replacement surgeries. Primary operations were linked with Hospital Episode Statistics data which contains records of all inpatient episodes undertaken in NHS hospitals, and Patient Reported Outcome Measures (PROMs). Primary TKR/UKR in people aged 18 years or over between 2014 and 2016 were identified. Multilevel regression models were generated for the following outcomes: length of stay (LOS), bed costs, change in Oxford knee score (OKS) 6-months after surgery, and complication by 6 months. Models included a wide range of patient, surgical

and hospital organisation factors. Geographical Information Systems are used to display maps describing adjusted estimates of variation in outcomes across NHS CCG areas.

Variation in outcome of surgery across Clinical Commissioning Groups (2014-2016)



Results: 210,725 primary TKR/UKR were identified nested in 207 clinical commissioning group areas. 57% of patients were women, with an average age 70 years (SD ±9 years). Whilst we identified a number of factors that predicted outcomes of surgery (e.g. age, gender, co-morbidity, deprivation, baseline function, surgical volume, numbers of orthopaedic surgeons, beds, operating theatres), these factors did not explain the observed geographical variations in outcomes of surgery across CCGs. The absolute predicted change in OKS varied from 13.0 to 18.8, predicted 6-month complication rate from 2.9% to 5.8%, predicted revision from primary TKR/UKR undertaken in 2014-2016 0.7% to 1.8%, predicted mean length of stay 2.9 to 6.6 days, bed-day cost £4758 to £8693 (Figure).
Conclusion: We have identified potentially unwarranted variations in patient outcomes of knee replacement surgery. This variation cannot be explained by differences in patients case mix, surgical factors, or hospital organisational factors. This information is informative to patients in making a decision in where they have their surgery, and to commissioners in monitoring variations in outcomes of surgery.

REFERENCES:

[1] Geographic Variations in Health Care. What Do We Know and What Can Be Done to Improve Health System Performance?2014:23.
[2] Judge A, Welton NJ, Sandhu J, et al. Equity in access to total joint replacement of the hip and knee in England: cross sectional study. BMJ 2010;341 doi: 10.1136/bmj.c4092

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OP0307

STANDARDS OF CARE FOR RHEUMATOID ARTHRITIS: GAPS IN IMPLEMENTATION EXPERIENCED BY PATIENTS AND RHEUMATOLOGISTS ACROSS 33 EUROPEAN COUNTRIES

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Background: Eumusc.net, a EULAR and EU supported initiative (which took place from 2008 to 2013) aimed to raise and harmonize quality of care for patients with rheumatic and musculoskeletal diseases across European countries. As part of Eumusc.net, 16 user-focused standards of care (SoC) for rheumatoid arthritis (RA) were developed.
Objectives: To evaluate gaps in quality of care using the Eumusc.net SoCs among patients and rheumatologists across Europe and to investigate the contribution of individual- and country-level characteristics to care gaps
Methods: Fifty RA patients and 50 rheumatologists from each of 34 countries were invited to participate in a survey. For each SoC, levels of importance and care were rated for received by patients or provided by rheumatologists on a scale from 0 to 10 (=best). Care gaps were calculated as difference from the maximum score for care received multiplied by the score for importance of care [0 (no gap) - 100], and defined as 'problematic' when the gap was >30 and importance $\geq$6. Individual- and country-level (GDP in tertiles) determinants of care gaps were analysed in multilevel logistic regression models, with patients clustered in country of residence. For patients, individual factors included gender, age, disease duration (years), level of education (low, high), work status (retired, disabled, working, not working), literacy, patient organisation membership and overall health (0-10). For rheumatologists, individual factors were gender, age, years of experience and work setting (university hospital and non-university hospital/private practice).
Results: In total, 1,422 patients from 27 and 1,044 rheumatologists from 33 European countries, respectively, were included. Patients had a mean (SD) age of 57.2 (13.2) years and 74% were female. For rheumatologists, the mean age was 47.7 (10.5) and 53% were female. After ranking the SoCs on percentage of problematic gap, the 7 SoCs in the top 10-ranks for both patients and rheumatologists (Table) were: *diagnosis within 6 weeks*, *information about patient organisations*, *availability of treatment plan*, *receiving a schedule of regular assessment*, *vaccination-related information*, *information about adequate physical exercise* and *training on aids, devices and ergonomic principles*. The least frequent problematic SoC for both patients and rheumatologists was *adequate DMARD received (*6% and 3%*)*.
Multilevel analyses revealed large variation across countries for patients (all models p<0.01) and for the majority of analyses for rheumatologists, despite adjustment for individual characteristics. In addition, patients with higher education and lower self-reported health experienced problematic gaps more frequently. Among rheumatologists, patterns in determinants across SoCs were less consistent. For about half of the SoCs, rheumatologists from lower GDP countries identified problematic gaps more often compared to those from medium or high GDP countries (see Table).

Table. Frequency and determinants of care gaps perceived by patients and rheumatologists (top-7 SoCs with highest % of respondents reporting a problematic gap)

SoC description	(rank)	% (n) of respondents indicating problematic gap**	Gender: fem vs male	Education: high vs low	Overall health	GDP: low vs high	GDP: medium vs high
			Odds ratio from multilevel logistic regression (>1 indicates higher odds for problematic gap)				
Diagnosis within 6 weeks	Patient (1)	50% (811)	ns	1.97*	0.92*	2.24*	ns
	Rheum (1)	57% (622)	ns	na	na	ns	ns
Info about relevant patients organisations and trusted sources	Patient (5)	38% (587)	ns	1.44	0.88*	ns	ns
	Rheum (2)	35% (362)	ns	na	na	4.71*	2.26*
Availability of a treatment plan	Patient (8)	36% (587)	ns	2.18*	0.83*	ns	ns
	Rheum (9)	19% (205)	ns	na	na	ns	ns
Patients are informed about vaccination	Patient (6)	37% (490)	1.48*	1.69*	0.87*	ns	ns
	Rheum (6)	24% (252)	0.52*	na	na	4.81*	1.41
Schedule of regular assessment of disease received	Patient (9)	36% (560)	1.39*	1.87*	0.79*	ns	ns
	Rheum (7)	22% (233)	0.67*	na	na	2.47*	1.83*
Info on adequate physical exercise	Patient (10)	36% (563)	1.45*	1.56*	0.88*	ns	ns
	Rheum (8)	20% (216)	ns	na	na	ns	ns
Training on aids, devices, and ergonomic principles	Patient (3)	38% (521)	ns	ns	0.83*	ns	ns
	Rheum (4)	31% (324)	ns	na	na	4.72*	4.97*

SoC: Standard of Care; GDP: gross domestic product; rheum: rheumatologist; ns: not significant; na: not applicable; * p-value<0.05; ** data presented for only complete pairs (i.e. when both importance and level of implementation were rated by the respondent)

Conclusion: For most SoCs, problematic gaps were identified in essential aspects of RA care, and substantial differences across countries were observed.

In general, patients identified problematic gaps in SoCs more frequently than rheumatologists did. These findings can help to evaluate quality of care and to work towards improvement of care for RA patients in Europe.

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OP0308 QUALITY OF CARE PREDICTS OUTCOME IN SYSTEMIC LUPUS ERYTHEMATOSUS – CROSS SECTIONAL ANALYSIS OF A GERMAN LONG-TERM STUDY (LULA COHORT, 2011–2015)

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Background: Systemic lupus erythematosus (SLE) is a chronic disease, which is still associated with significant morbidity and mortality[1]. Recommendations for the management of SLE patients exist[2-5], but information on its implementation and the resulting impact on long-term outcome remain unclear.

Objectives: Our aim was to study the quality of SLE medical care in Germany to understand gaps and to analyze the association to long-term outcome parameters.

Methods: In the LuLa-study information on demographics, clinical and medical care parameters are assessed annually by self-reported questionnaires among a representative sample of SLE patients in Germany (LuLa cohort, n=572). In 2013 additional questions on the management of care, as mentioned in current guidelines and recommendations, were surveyed. Ten items predicting a good clinical care (quality measures) were evaluated and an overall score with a minimum of 0 points and a maximum of 10 points was calculated. The ten items are taking antimalarials, osteoporosis protection at a dose above 7.5mg prednisolone equivalent per day or taking ≤ 7.5mg per day, vaccination, blood pressure, fat metabolism counseling, urine examination and blood test once a year, treatment of comorbidity fat metabolism disorder, osteoporosis and hypertension. Health related quality of life (Short Form Survey, SF-12/36), damage (Brief Index of Lupus Damage, BILD) and disease activity (Systemic Lupus Activity Questionnaire, SLAQ) were chosen as relevant proxies for long-term outcome.

Using linear regression, we examined the relationship between the quality measures and outcome parameters, adjusted for age, disease duration and gender.

Results: 65.5% of the patients consulted a rheumatologist as a main contact for their disease. On average 6.1 points of the 10 quality measures were met (SD 1.7). The fulfillment of these quality measures varied between 22.8% (fat metabolism counseling) and 97.6% (osteoporosis protection at a dose above 7.5mg prednisolone equivalent per day or ≤ 7.5mg per day). Fulfilling more clinical care items in 2013 was predictive for high disease-related quality of life (SF-36, p=0.004), low progress in disease-related damage (BILD, p=0.048) and low disease activity (SLAQ, p=0.046) in the subsequent years.

Conclusion: Our study illustrates a strong link between the quality of care and important SLE outcome parameters: quality of life, disease-related damage and disease activity assessed by a self-reported questionnaire. Consistent considerations of these care parameters, which are recommended in several management guidelines, yield a positive effect on outcome. An interdisciplinary approach with general practitioners and other specialists is certainly beneficial and warranted.

German Clinical Trial Register, www.germanctr.de, DRKS00011052

REFERENCES:

[1] Borchers, A. T., Keen, C. L., Shoenfeld, Y. & Gershwin, M. E. Surviving the butterfly and the wolf: mortality trends in systemic lupus erythematosus. *Autoimmun. Rev.* **3**, 423–453 (2004).

[2] Bertsias,G. *et al.* EULAR recommendations for the management of systemic lupus erythematosus. Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics. *Ann. Rheum. Dis.* **67**, 195–205 (2008).

[3] Mosca, M. *et al.* European League Against Rheumatism recommendations for monitoring patients with systemic lupus erythematosus in clinical practice and in observational studies. *Ann. Rheum. Dis.* **69**, 1269–1274 (2010).

[4] Guidelines for referral and management of systemic lupus erythematosus in adults. American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus Guidelines. *Arthritis Rheum.* **42**, 1785–1796 (1999).

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OP0309 OPTIMIZATION OF FLARE MANAGEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Background: Flares in rheumatoid arthritis (RA) are common [1]. The shortage of readily available specialized care may hinder early detection and timely management of RA flares. Engaging non-physician rheumatology providers in care of RA flares may be beneficial.

Objectives: To evaluate the effect of a nurse-led flare management intervention versus usual care between rheumatology visits on flare occurrence and RA disease activity in patients with RA.

Methods: Patients with established RA (2010 ACR criteria) were randomized to the intervention versus usual care. The Flare Assessment in Rheumatoid Arthritis (FLARE-RA) questionnaire was administered monthly during the 24-month follow-up to all patients in the intervention arm to assess flare status. The results of the FLARE-RA questionnaire and patient's response to the question "Are you currently in a flare of your RA?" were recorded. Telephone nurse-led counseling or a visit with a mid-level rheumatology provider within 7 days of detection of flare was offered to patients in the intervention arm who indicated they were in flare. Patients in the usual care arm were followed by their rheumatology providers according to standards of care. OMERACT9 definition of flare was used to compare flare occurrence between the study arms. All patients completed satisfaction surveys at baseline and at the end of the follow-up.

Results: 150 patients with RA were randomized to intervention (n=75) versus usual care (n=75). At baseline, the majority of patients in the intervention arm (51%) and in the usual care (60%, p=0.32) were interested in expedited appointments with a rheumatology provider if in RA flare. There were no differences between the study arms at baseline in age, sex, tender joint counts, pain intensity, patient and physician global assessments, C-reactive protein levels, DAS28-CRP, CDAI, or SDAI. Despite randomization, patients in the intervention arm had lower swollen joint counts (1.1±2.7 vs 2.4, p=0.003) and Health Assessment Questionnaire (HAQ) score (0.6±0.6 vs 0.9±0.6, p=0.005) than those in the usual care arm. The number of patients in the intervention arm who completed the FLARE-RA questionnaires at baseline, 6, 12, 18, and 24 months was 75, 37, 27, 13, and 23, respectively. Patients in the intervention arm completed a median of 8.5 (range 1-24) questionnaires. RA flare was reported on 122 (19%) of these questionnaires; average FLARE-RA score: 2.57. Patients agreed to have an expedited clinic visit with a rheumatology provider during 39 (32%) of flares. The majority of patients preferred to self-manage their flare (76, 62%) or receive nursing advice over the phone 7 (6%). There were no differences in DAS28-CRP, CDAI, SDAI, anti-rheumatic treatment change by rheumatology provider, RA flare by OMERACT9 definition, or remission by CDAI between the study arms over 24-month follow-up. At the end of the study, a higher proportion of patients in the intervention arm (44%) versus the usual care arm (21%, p=0.04) reported positive effect of participation in the study on the management of RA flares.

Conclusion: The majority of patients expressed interest in expedited rheumatology appointments for their RA flares on their baseline patient-satisfaction survey. However, during the study, patients in the intervention arm largely preferred self-management and/or over-the-phone counseling. The nurse-led flare

management intervention had no major effect on RA disease activity metrics over the 24-month follow-up. However, patients in the intervention arm reported a positive effect of the intervention. More studies are needed to further understand patient preferences for optimal RA flare management and to design interventions to meaningfully address these preferences.

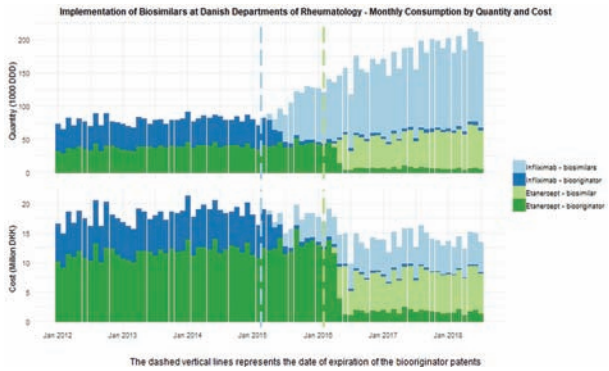
REFERENCE:
[1] Bechman, K., et al. J Rheumatol, 2018. **45**(11): p. 1515-21.

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OP0310 IMPLEMENTATION OF TNF-BIOSIMILARS (INFLIXIMAB AND ETANERCEPT) IN DANISH DEPARTMENTS OF RHEUMATOLOGY

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Background: The use of expensive biological drugs in rheumatology is rapidly increasing and has led to substantial increases in drug expenditures. A considerable reduction of drug costs is possible by using biosimilars as soon as they become available and carrying out non-medical shifts to biosimilars (i.e. switching a patient well treated on a biooriginator to the biosimilar). Research on biosimilars has focused on interchangeability and safety outcomes, but little focus has been on nationwide implementation and the direct economic consequences on drug expenses.
In Denmark, TNF-inhibitors are solely given in an in-hospital setting and bought through national tenders. The Danish in-hospital organization includes Regional Drug and Therapeutics Committees that ensures regional implementation of treatment guidelines and close collaboration between hospital pharmacies and regional clinical pharmacologists. Furthermore, the implementation of TNF-inhibitor biosimilars was preceded by careful preparations from among others a newly established national biosimilar task force.
Objectives: The aim of this study was to describe the implementation of the two first TNF-inhibitor biosimilars (infliximab and etanercept) in Danish departments of rheumatology.
Methods: Monthly data on drug sales to Danish rheumatology departments were used to assess the biosimilar uptake rate and subsequent changes in the drug expenditures during the implementation in Denmark.
Results: Shifts to biosimilars were begun within a few months following end of biooriginator patent, vertical lines in the figure. Use of the infliximab biosimilar was begun in April 2015, and in August 2015 biosimilar uptake was 92.9% of total infliximab use. Similarly use of etanercept biosimilar was begun in April 2016, and in June 2016 the biosimilar uptake was 91.6% of total etanercept use. In January 2015 the total use in Defined Daily Doses (DDD) were 42.4 thousand DDD's for infliximab and 37.3 thousand DDD's for etanercept. The use increased steadily and was in January 2018 138.4 thousand DDD's for infliximab and 62.1 thousand DDD's for etanercept (equivalent to increases of 226.6% and 66.8%). The increases in DDD's were not reflected in total drug costs due to the shift to biosimilars. The total drug cost for infliximab in January 2015 was 6.7 million DKK but was reduced to 5.4 million DKK in January 2018 (-19.4%). A corresponding cost reduction was seen for etanercept (11.3 million DKK in January 2015, 8.1 million DKK in January 2018, -28.7%).



Conclusion: Danish departments of rheumatology experienced a fast and near-complete switch of infliximab and etanercept biooriginators to biosimilars. At the same time the use of the drugs increased substantially, but due to large price reductions the total drug cost decreased despite the increasing use. We believe that a thorough preparation and an organizational setting supporting the implementation was crucial for the successful implementation. The Danish structure, with its national tendering, probably contributed to the substantial drug discounts obtained. The implementation will be used for future biosimilars in Denmark.
Disclosure of Interests: None declared
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OP0311 RETROSPECTIVE ANALYSIS OF PRESCRIPTION DYNAMICS OF ETANERCEPT AFTER INTRODUCTION OF BIOSIMILARS BASED ON NORWEGIAN PRESCRIPTION DATABASE. AN INTERIM ANALYSIS

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Background: In Norway, several high quality data registries are available that can be used to generate "real life" data. All individuals living in Norway are given a unique ID number which makes it possible to trace individuals. The Norwegian Prescription Database (NorPD) is one of the central public registers that are available for research purposes. All prescriptions being collected by individuals are recorded, including reimbursement code, dispensing date, name and dose of the prescribed drug. Following loss of exclusivity of some biologics, biosimilars are competing in the Norwegian tender.
Objectives: Both efficacy, bio-chemical features and patient satisfaction with biosimilars have been debated since they were introduced to replace originator. However, there is only sparse evidence as to how many patients were switched and how many are switched back to the originator so large, registry based studies are warranted.
Therefore, our aim was to follow all patients on originator receiving maintenance treatment (drug prescription being collected and registered in NorPD) after biosimilar entry (BE) in order to retrospectively describe the pattern of switch and monitor dynamics, assumed to be economically motivated from patients stable on originator to biosimilars or other preferred drug.
Methods: We included all patients on etanercept maintenance treatment for 9 months prior to BE with maximum gap of 4 months from previous prescription retrieval. Switch was defined as discontinuation of use for at least 4 consecutive months.
Prescription data scans from NorPD started March 2016 (BE) and data scans were performed every 3 months during the first 6 months of this project and every 6 months for 2 years. Final data extraction will be performed within July 2019. This abstract covers the interim analysis and the time period from 9 months prior to BE and 18 months thereafter.
Results: We have identified 8149 individuals on biologics prescribed in Norway. Of those, 4799 collected at least two prescriptions of etanercept before BE and are included in further analyses. The proportion of originator etanercept users declined sharply after biosimilar entry as expected for the first three months after BE and kept decreasing for the consecutive 9 months, however it changed little thereafter.
A great majority of former etanercept users was switched to SB4 (70.5%) and continued with this medication, however some switched back to etanercept or other

medication. A small proportion of individuals switched shortly to SB4 and then later to other medication. 5.7% of former etanercept users switched to other medication at the time of Switch date. For details, see Figure 1.
Many patients switched back and forth several times, also using other medication at short time intervals. The method of distribution (pen versus injection) was associated with higher odds for being switched. Patients using etanercept pen were more likely to switch to biosimilar etanercept after BE (Figure 2).
For patients who switched to SB4 the 18 months cumulative incidence of drug survival was 72%; 95%CI [65-79]%. At 2 years follow-up the drug survival in switchers will be matched with historic drug survival rate of etanercept estimated using data from NorPD.
Conclusion: The Norwegian Prescription Database is a useful tool that enables to monitor use, changes and trends in use of selected drugs. A longer follow-up is warranted in order to describe drug survival after switch from etanercept to biosimilar etanercept. However, close collaboration between pharmacists, clinicians and statisticians is warranted.

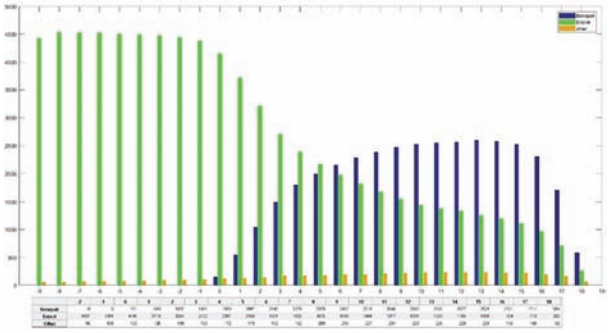


Figure 1

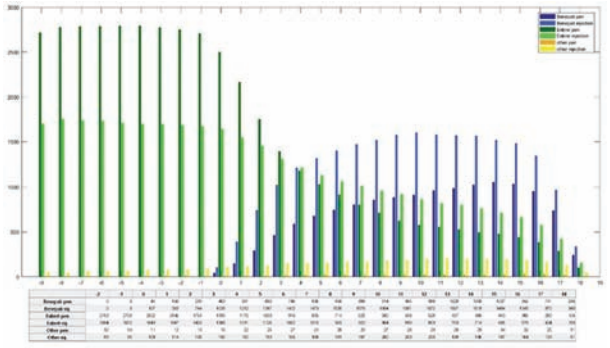


Figure 2

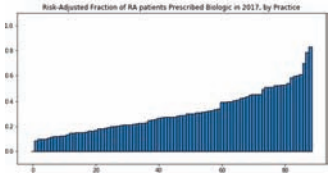
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OP0312 VARIABILITY IN BIOLOGIC PRESCRIPTION PATTERNS FOR RHEUMATOID ARTHRITIS PATIENTS IN THE AMERICAN COLLEGE OF RHEUMATOLOGY INFORMATICS SYSTEM FOR EFFECTIVENESS (RISE) REGISTRY

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Background: Biologics account for a substantial portion of drug spending in rheumatoid arthritis (RA). Variability in the U.S. in biologic prescribing patterns (and therefore variability in cost of care), and factors that correlate with that variability, remain largely undefined.
Objectives: We used data from the RISE registry to perform a cross-sectional analysis among U.S. rheumatologists of prescription patterns for biologic DMARDs and tofacitinib and their relationship to RA disease activity.
Methods: RISE is a U.S. registry that passively collects data on all patients seen by participating practices, thereby reducing selection bias present in single-insurer claims databases. As of December 2017, RISE held validated data from 1.257 providers in 236 practices, representing an estimated 25% of the U.S. clinical rheumatology workforce. We identified patients with available demographic and disease activity information who were assigned $\geq$2 codes for RA $\geq$30 days apart between January and December 2017. Practices with <20 RA patients (15/104 practices providing all necessary data) were excluded. We tallied the proportion of patients in each practice prescribed a TNF inhibitor, abatacept, rituximab, tocilizumab, or tofacitinib at least once during 2017. Patients prescribed >1 of these drugs were assigned to the first drug prescribed and therefore counted only once. We used a hierarchical linear model to predict the probability of receiving a prescription for a biologic based on the patient's most recent disease activity score (moderate or high disease activity vs. low disease activity or remission) and age from 2016, accounting for clustering by practice.
Results: We analyzed 53.850 patients from 104 practices. Overall, 29% of patients were prescribed a biologic DMARD or tofacitinib in 2017. TNF inhibitors were most commonly prescribed, followed by abatacept (4.5% of patients), tofacitinib (4.2%), tocilizumab (3.4%), and rituximab (2.5%). We found significant variation within practices in the proportion of patients prescribed any of these drugs (range 0%-100%). In the adjusted analysis, we found that patients with higher disease activity in 2016 were more likely to receive biologics in 2017 (OR 1.56, 95% CI (1.51, 1.62)). Within a practice, as shown in the figure, the risk-adjusted likelihood of receiving a biologic prescription still showed significant variation (between 0%-83% of patients in each practice received a biologic; model c-statistic 0.61).

Figure. Proportion of RA patients prescribed biologics or tofacitinib, aggregated by practice and adjusted for disease activity and age, for practices with at least 20 patients with RA, between January and December 2017.



Conclusion: In this large sample of U.S. rheumatology practices, higher RA disease activity correlated with the likelihood that a patient would receive a prescription for a biologic, but did not account for all of the variability in biologic prescription patterns. These results suggest that there may be other factors in addition to RA disease activity that account for practice-to-practice variability in biologic prescription patterns. Disclaimer: These data were collected from the ACR's RISE Registry; however, the views expressed represent those of the authors, not necessarily those of the ACR.
Disclosure of Interests: Douglas White Grant/research support from: Abbott 2006-2009, Pfizer 2017-2019 (unrelated to this work), Consultant for: Crescendo advisory board 2013-2014, Employee of: Genomyx (Genentech) 1991, Speakers bureau: None since 2008, Michael Evans: None declared, Tracy Johansson: None declared, Rachel Myslinski: None declared, Jinoos Yazdany Grant/research support from: Pfizer, Consultant for: AstraZeneca, Gabriela Schmajuk Grant/research support from: Investigator initiated award from Pfizer from 2015-2018, unrelated to this work
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OP0313 COST-EFFECTIVENESS OF A JAK1/JAK2-INHIBITOR VS. A BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG IN A TREAT-TO-TARGET STRATEGY FOR RHEUMATOID ARTHRITIS

Celine van de Laar[1], Martijn Oude Voshaar[1], Walid Fakhouri[2], Liliana Zaremba-Pechmann[2], Francesco de Leonardis[2], Inmaculada De La Torre[2], Mart van de Laar[1,3]. [1]*Transparency in Healthcare, Hengelo, Netherlands*; [2]*Eli Lilly and Company, Indianapolis, United States of America*; [3]*Arthritis Center Twente, Enschede, Netherlands*

Background: Treating Rheumatoid Arthritis (RA) to an a priori defined disease activity target (T2T) is recommended in EULAR guidelines. This involves a step-up approach in which it is first attempted to achieve the target with a combination of conventional synthetic (cs) DMARDs. Baricitinib is a JAK1/JAK2-inhibitor approved for treatment of patients suffering from RA. EULAR and ACR guidelines currently position JAK1/JAK2-inhibitors and bDMARDs at the same level in the therapeutic treatment sequence for csDMARD Inadequate Responders (IR). Cost-effectiveness assessment of different T2T strategies, especially ones

including new treatments, and integrating health economic considerations is of importance to the decision-making process as it incorporates the societal perspective in the longer run.

Objectives: To compare the cost-effectiveness of the previously evaluated DREAM T2T strategy csDMARD combination therapy (csDMARDs)→ first bDMARD (adalimumab)→ next bDMARD (TNFi/non-TNFi) with the comparable strategy in which baricitinib is placed instead of adalimumab in csDMARDs IR using a Markov model. All analyses were performed from the societal perspective. Costs and effects over five years were compared between the two strategies to provide insight into the differences in economic considerations between treating patients with strategies including either JAK1/JAK2-inhibitor (baricitinib) or 1st bDMARD (adalimumab).

Methods: A Monte Carlo microsimulation model was developed to conduct cost-utility analysis from the societal perspective over 5 years. Health states were based on the DAS28-ESR categories. Effectiveness of baricitinib was retrieved from clinical trials (1) and corrected for differences between RCT and real-world setting. Effectiveness of all other treatments, health state utilities, medical costs, and productivity loss were retrieved from DREAM cohorts (2) and the Dutch Institute for Health. Annual discount rates of 1.5% for utility and 4% for costs were used, as advised in Dutch guidelines. All analyses were run using probabilistic sensitivity analysis (PSA) to incorporate uncertainty around all parameters and assess result robustness.

Results: PSA results showed the baricitinib strategy yielded lower costs and higher utility over a 5-year period and is cost-effective and dominant over the DREAM T2T strategy. Scenario analyses showed the baricitinib strategy to be cost-effective in both the moderate and severe at baseline RA populations analysed together and separately.

Table 1. Probabilistic Sensitivity Analysis Results

	Costs (€) (CI)	Effects (QALY) (CI)	ΔC	ΔE	ICER
DREAM T2T	14288.36 (10104.68-19053.39)	3.5607 (2.4028-4.7236)			
Baricitinib strategy	13430.57 (9475.10-17848.92)	3.5643 (2.4042-4.7315)	-857.79	0.0036	Dominant

CI= 95% Confidence Interval, QALY = Quality-Adjusted Life Year, ΔC = Cost difference, ΔE = Effect Difference, ICER = Incremental Cost-Effectiveness Ratio

Conclusion: Results suggest the use of a JAK1/JAK2-inhibitor (baricitinib) instead of a 1st bDMARD (adalimumab) in a T2T strategy is cost-effective in treating RA patients.

REFERENCES:

[1] Taylor, P. C., Keystone, E. C., van der Heijde, D., Weinblatt, M. E., del Carmen Morales, L., ... & Arora, V. (2017). Baricitinib versus placebo or adalimumab in rheumatoid arthritis. *New England Journal of Medicine*, *376* (7), 652-662.

[2] M., Versteeg, G. A., Vonkeman, H. E., Ten Klooster, P. M., Kuper, H. H., ... & van de Laar, M. A. (2016). Initial combination therapy versus step-up therapy in treatment to the target of remission in daily cl. Steunebrink, L. inical practice in early rheumatoid arthritis patients: results from the DREAM registry. *Arthritis Research & Therapy*, *18*(1), 60.

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FRIDAY, 14 JUNE 2019

Primary and secondary fibromyalgia; are they different?

OP0314

LONG TERM TRAJECTORIES OF CHRONIC WIDESPREAD PAIN: A 21-YEAR PROSPECTIVE COHORT LATENT CLASS ANALYSIS

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Background: Chronic widespread pain (CWP) is common (population prevalence of approximately 10%) and has a significant impact on the individual, healthcare, and society. Currently little is known about the actual course of CWP over time, in particular the pathways to the development and maintenance of CWP. One useful way to understand these pathways is to identify common clusters of people who share pain trajectories. Such information is clinically useful to identify factors that predict development, persistence, and resolution of CWP.

Objectives: To identify different longitudinal pain trajectories over a period of 21 years.

Methods: A 21-year longitudinal open-population cohort of n=1858 adults (aged 20-74) who completed surveys relating to their pain status in at least three of the five time points 1995, 1998, 2003, 2007, and 2016. Pain status (presence of persistent pain) was ascertained from a report of painful regions (0-18) on a pain mannequin and categorised into: NCP (No chronic pain), CRP (Chronic regional pain) and CWP (chronic widespread pain). Latent Class Growth Analysis (LCGA) was carried out based on these categories. Participants were assigned to a trajectory cluster where the posterior probability was the highest. Model fit was assessed by statistical indices and clinical interpretations of clusters.

Results: LCGA identified five clusters describing different pathways of NCP, CRP and CWP over the 21 years. The cluster "Persistent NCP" was the most common pathway (n = 1052, 57%) representing those with no chronic pain over the whole time period. The "Persistent CRP or Migration from CRP to NCP" cluster included 411 individuals (22%) representing a group with stable or improving regional pain. In the groups who were shown to increase pain status, the "Migration from NCP to CRP or CWP" cluster included 92 individuals (5%), and there were 184 individuals (10%) in the cluster "Migration from CRP to CWP" representing a group with regional pain who developed CWP. The final cluster "Persistent CWP" included 119 individuals (6%) representing those with stable CWP throughout the time period. Figure 1 presents the mean number of pain sites over time by cluster.

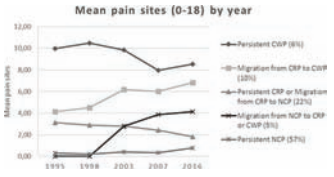


Figure 1. Mean pain sites for each cluster for each point in time.

Conclusion: This study showed that whilst half of adults report no chronic pain over 21 years, a substantial proportion develop CWP or have persistent CWP over this time period. Whilst a common trajectory was movement from chronic regional pain to no chronic pain, a pattern of improving CWP was not seen suggesting this is an uncommon trajectory. This is the first study to show long-term trajectories for CWP, and further work is now required to understand factors that may identify individuals at risk of worsening pain status and factors that might promote improvement. These identified pathways of chronic pain over a lifespan improve the understanding of long-term development of chronic pain and chronic widespread pain.

Disclosure of Interests: None declared

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OP0315

ACHIEVING A LOW DISEASE STATE WITHIN FIRST 3 MONTHS IN EARLY RHEUMATOID ARTHRITIS RESULTS IN LOWER FATIGUE OVER 5 YEARS

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Background: Up to 80% of rheumatoid arthritis patients report clinically relevant fatigue.[1] Fatigue is complex multi-factorial process that can result in adverse affects on patients' physical and emotional well-being.[2]
Objectives: To examine the relationship between disease activity and fatigue over time in early rheumatoid arthritis (ERA).
Methods: Data were from patients with ERA (symptoms ≤ 12 months) enrolled in the Canadian Early Arthritis Cohort (CATCH). CATCH participants completed repeat clinical assessments, laboratory investigations and self-reported questionnaires including rating their fatigue over the past week using a 10 point numerical rating scale (NRS). Fatigue severity was classified as low (≤2); moderate (>2 but <5) and high (≥5) based on other published RA studies. Bivariate relationships between disease activity measures and fatigue over 5 years of follow-up were estimated using the Pearson correlation coefficient. T-tests and repeated measures anova were used to compare differences in fatigue ratings in patient who did vs. did not achieve a low disease state (DAS28 <3.2) within 3-months of cohort entry.
Results: Of the 1864 patients included, 1640 (88%) met criteria for RA, 1342 (72%) were women and most had moderate-high baseline disease with a mean (SD) DAS28 of 4.9 (1.5). Fatigue was common with 19% reporting moderate and 59% severe fatigue at baseline. Fatigue was positively and strongly correlated with pain and patient global ratings (r 0.56-0.67, p<0.001), positively and moderately correlated with DAS28 (r 0.35-0.49, p<0.001), and positively but more weakly correlated with tender/swollen joint count, physician global assessment, ESR and CRP (r 0.10-0.39, p<0.01) throughout the first year of follow-up. Patients who reported low fatigue severity by three months continued to have significantly lower fatigue throughout follow-up compared to those with moderate or high fatigue (p<0.001). Patients who achieved DAS28 REM or LDA within 3-months of cohort entry had significantly lower mean fatigue compared to those with more active disease throughout 5 years of follow-up (p<0.001) (Figure 1).

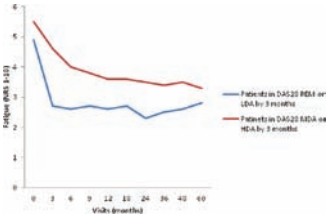


Figure 1. Mean patient fatigue scores based on NRS of 1-10 over subsequent visits, split based on DAS28 score at 3 months.

DAS28: disease activity score in 28 joints; REM: remission; LDA: low disease activity; MDA: moderate disease activity; HDA: high disease activity.
Conclusion: Fatigue is common in ERA and is most strongly correlated with pain and disease activity. Early treatment response within 3-months was associated with short and long-term improvements in fatigue over time. Further longitudinal research examining the time-varing effects of both clinical and psychosocial factors on fatigue is needed.

REFERENCES:

[1] Pollard, LC., Choy, HE., Gonzalez, J., Khoshaba, B., and Scott, DL. Fatigue in rheumatoid arthritis reflects pain, not disease activity. Rheumatology. 2006;45:885-889.
[2] Nikolaus, S., Bode, C., Taal, E., and Van De Laar, MA. Fatigue and Factors Relating to Fatigue in Rheumatoid Arthritis: A systematic Review. American College of Rheumatology. 2013;65:1128-1146.

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FRIDAY, 14 JUNE 2019

Optimizing the access to new treatments for RMD patients

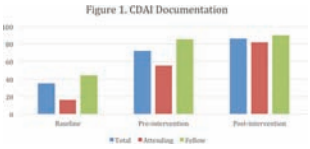
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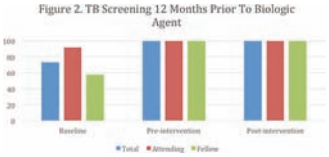
COST EFFECTIVE INTERVENTION TO IMPROVE QUALITY OF CARE MEASURES FOR RHEUMATOID ARTHRITIS PATIENTS IN AN UNDERSERVED COMMUNITY

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Background: Quality of care measures for rheumatoid arthritis (RA) have been endorsed by the American College of Rheumatology and the CDC. Similar quality indicators have been studied and recommended by the European League Against Rheumatism. Improving quality metrics in an underserved community is a problem given the lack of resources.
Objectives: To identify quality metrics for RA patients with need for improvement in our underserved urban public hospital, and to establish an effective intervention.
Methods: An initial retrospective chart review established baseline data from patients with RA seen in our clinic (July 2015 - July 2016), they were identified by ICD-9/10 coding. We identified 3 RA measures needing improvement: (a) tuberculosis screening (TBsc) 12 months prior to starting a new biologic agent, b) documentation of clinical disease activity index (CDAI) in >/=50% of encounters, c) appropriate pneumococcal vaccination. We then planned an intervention by placing index cards at computer stations to remind providers to check these measures. We collected data on these 3 variables prior to the intervention (December 2016 - July 2017) and 30+ days after (August 2017 - December 2017). We also compared these results by provider type (attendings and fellows). For statistical analysis we used Chi-Square test and SPSS 24.
Results: Baseline data included 240 patients, analysis prior to the intervention included 86 patients, and after the intervention included 131 patients. CDAI documentation was improved from 72.1% to 86.3% (Figure 1, p=0.01), however when stratifying the analysis by provider type, this improvement was only significant in attendings (p=0.005) and not in fellows (p=0.43). Further analysis by including only the same fellows in both pre and post intervention moments (some fellows graduated) showed a significant difference in both groups (attendings: p=0.005; fellows: p=0.024). In terms of TBsc, baseline data showed 73.1% compliance, however we already found a compliance of 100% prior to the intervention (Figure 2, p=0.002 when compared with baseline data). Finally, there was no difference in

compliance with pneumococcal vaccination between baseline data, prior and post intervention (p=0.895).





Conclusion: Placing a card reminding providers to check 3 RA quality measures significantly improved CDAI documentation after 30 days of starting the intervention. The compliance with TBsc prior to starting a new biologic agent was 100% even before the intervention, which was better compared to baseline data, likely due to providers being aware there was a problem after initial data was collected. We did not find improvement in pneumococcal immunization rate, most likely because there are multifactorial components to motivating patients to get the vaccine. Our results suggest that interventions as simple as raising provider awareness to a problem such as TB screening, and an index card to remind people to document CDAI can be effective to improve QI measures in RA patients in underserved communities.

REFERENCES:
[1] Yazdany K, et al. Development of the American College of Rheumatology's RA Electronic Clinical Quality Measures. Arthritis Care & Research. 2016; 68 (11): 1579–1590.
[2] Petersson I, et al. Development of healthcare quality indicators for RA in Europe. Ann. Rheum. Dis. 2014;73(5):906-8.
[3] Lai Q, Johnson B. Improving Quality of Care for RA Patients in an Underserved Area. Arthritis Rheumatol. 2017; 69 (suppl 10).

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OP0317

ASSOCIATION OF PATIENT SATISFACTION WITH HEALTHCARE UTILIZATION, COST, AND QUALITY OF LIFE IN RHEUMATOID ARTHRITIS

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Background: Patient satisfaction and experience with care is being used as a surrogate marker of quality and value of healthcare delivery. No study has evaluated the association of patient satisfaction with healthcare utilization and cost, and quality of life in RA patients.
Objectives: To examine the association of RA patient satisfaction with healthcare utilization and cost, and quality of life.
Methods: 2010-2015 longitudinal files from the Medical Expenditure Panel Survey (MEPS), a nationally representative survey of the US civilian non-institutionalized population were used to identify patients with self-reported RA diagnosis. MEPS has overlapping panel design with participants interviewed up to 5 rounds over a 2- year period. In rounds 2 and 4, patient satisfaction is assessed by the four items about physician interaction – listened carefully, explained things well, showed respect, and spent enough time; and one item for overall satisfaction with quality of care received. A patient satisfaction score was constructed from standardized composite score of these items, and classified as most satisfied (patient satisfaction quartile 4) and less satisfied (patient satisfaction quartiles 1-3). The outcome measures were assessed in year 2: healthcare utilization (any emergency department visit, any inpatient stay, number of visits to office-based providers, outpatient department, and prescription drugs); total healthcare expenditures (measured in 2015 dollars), and quality of life (QoL, measure using 12-item Short Form healthy survey (SF-12)). Two statistical approaches were used: a standard logistic regression comparing most satisfied with less satisfied, and propensity score matching. Propensity scores were estimated using a logistic regression to model most satisfied quartile (vs. lower) as a function of covariates (satisfaction score in year 1 were matched 1 to 1 without replacement using a greedy matching algorithm. After matching, means of outcomes in year 2 were compared among matched pairs. Standard errors were estimated using bootstrapping method with 200 repetitions. Covariates included socio-demographic measures, health behaviors, health status (Charlson Comorbidity Index, general health, activity limitation, and pain affecting activities); RA measures (DMARDs, corticosteroids, and analgesics use); and the Year 1 outcome measures (utilization, total expenditure, QoL).
Results: 568 patients had a self-reported RA diagnosis. 1025 (65.4%) patients were analyzed (326 patients excluded for missing satisfaction response; 201 patients for missing information on other study variables; and 16 for not having data in all 5 rounds). The results using the propensity score matching approach are presented in the Table (202 most satisfied matched to 202 less satisfied patients). There were no differences in the healthcare utilization, cost and QoL among the two groups. Logistic regression approach yielded similar results.

Outcome	Most satisfied, Q4	Less satisfied, Q1-Q3	Difference	Bootstrapped SE (reps 200)	P Value
Total expenditure, $	13452	14695	-1243	2607	0.633
Number of Office Visits	13.24	12.73	0.51	1.55	0.741
Number of Outpatient Visits	1.06	1.24	-0.17	0.35	0.622
Number of Inpatient Visits	0.23	0.34	-0.09	0.085	0.267
Number of ER visits	0.460	0.525	-0.064	0.107	0.547
Number of Prescriptions	48.936	51.465	-2.530	4.351	0.561
QoL - Mental health summary scores	47.557	47.186	0.371	1.116	0.739
QoL - Physical health summary scores	36.526	34.840	1.686	0.969	0.082

Conclusion: Patient satisfaction score of RA patients was not associated with healthcare utilization and cost, and quality of life measures.

REFERENCE:
[1] Fenton JJ et al. Arch Intern Med. 2012;172(5):405-411

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Teenage look in the mirror (sexuality and body image meeting health care)

OP0318-HPR

IS PSYCHOLOGICAL SUPPORT REACHING THOSE IN MOST NEED? A SURVEY OF PEOPLE WITH RHEUMATOID ARTHRITIS AND ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS:

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Background: Rheumatoid arthirtis (RA) and adult juvenile idiopathic arthirtis (AJIA) is associated with a significant impact on psychological well-being.[1-2] UK guidelines for the management of RA[3-5] state that psychological interventions should be offered to people with RA to help them adjust to living with their condition and manage their psychological well-being. Three in four rheumatology units in the UK however, rate their overall provision of psychological support as inadequate.[6]
Objectives: To establish levels of anxiety and depression in people with RA or AJIA and how this relates to the prevalence of diagnosed mood disorders and receipt of psychological support.
Methods: The 2018 National Rheumatoid Arthirtis Society (NRAS) 'Emotional Health and Well-being Matters' survey was designed by patients and researchers. This included a questionnaire designed to capture self-reported comorbidities, receipt of psychosocial support and the Hospital Anxiety and Depression Scale (HADS).[7] Participants were recruited by NRAS via their social media platforms, membership and non-membership lists and in newsletters and forum. The survey was open from May-July 2018. Recruitment was focused on those diagnosed with RA or AJIA aged 18 years and over and living in the UK.
Results: A total of 1565 people with RA and 55 AJIA completed the survey. Although mean scores on the HADS were within the normal range in both populations, over 25% of the samples were experiencing clinical levels of anxiety or depression. Over half of those reporting clinical levels of anxiety or depression had never received a formal diagnosis. Most concerning however, was that 1 in 2

respondents with RA and 1 in 3 AJIA who had either clinical levels or a formal diagnosis of anxiety or depression had never received any psychological support.
Conclusion: This survey indicates that despite meeting the criteria for anxiety or depression a majority of people with RA and AJIA have not been formally diagnosed with a mental health condition and many are not receiving the support they should. It is therefore an imperative for rheumatology services to routinely measure anxiety and depression in order to intervene before the individual is in crisis. Acting early by sign-posting and referring on to specialist services has the potential to improve a person's physical and psychological well-being.

REFERENCES:

[1] Packham JC, Hall MA, Pimm TJ. Long−term follow−up of 246 adults with juvenile idiopathic arthritis: predictive factors for mood and pain. Rheumatology 2002; 41(12):1444-1449.
[2] Covic T, Cumming SR, Pallant JF, Manolios N, Emery P, Conaghan PG et al. Depression and anxiety in patients with rheumatoid arthritis: prevalence rates based on a comparison of the Depression, Anxiety and Stress Scale (DASS) and the hospital, Anxiety and Depression Scale (HADS). BMC Psychiatry 2012; 12(1):6.
[3] National Institute for Health and Care Excellence. Rheumatoid arthritis in adults: management NG100. 2018. London, NICE.
[4] Luqmani R, Hennell S, Estrach C, Birrell F, Bosworth A, Davenport G et al. British Society for Rheumatology and British Health Professionals in Rheumatology guideline for the management of rheumatoid arthritis (the first two years). Rheumatology 2006; 45(9):1167-1169.
[5] Luqmani R, Hennell S, Estrach C, Basher D, Birrell F, Bosworth A et al. British Society for Rheumatology and British Health Professionals in Rheumatology guideline for the management of rheumatoid arthritis (after the first 2 years). Rheumatology 2009; 48(4):436-439.
[6] Dures E, Almeida C, Caesley J, Peterson A, Ambler N, Morris M et al. A survey of psychological support provision for people with inflammatory arthritis in secondary care in England. Musculoskeletal Care 2014; 12 (3):173-181.
[7] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatrica Scandinavica 1983; 67(6):361-370.

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New assessments in clinical practice

OP0319 **DIAGNOSTIC ACCURACY OF ULTRASOUND IN CALCIUM PYROPHOSPHATE DEPOSITION DISEASE: PRELIMINARY RESULTS OF THE OMERACT US IN CPPD SUB-GROUP**

Georgios Filippou[1], Anna Scanu[2], Antonella Adinolfi[3], Carmela Toscano[3], Raquel Largo-Carazo[4], Esperanza Naredo[4], Emilio Calvo[4], Gabriel Herrero-Beaumont[4], Pascal Zufferey[5], Christel Madelaine-Bonjour[5], Daryl Maccarter[6], Stanley Makman[6], Zachary Weber[6], Ingrid Möller[7], Marwin Gutierrez[8], Carlos Pineda[8], Denise Clavijo Cornejo[8], Héctor García[8], Victor Ilizaliturri[8], Jaime Mendoza Torres[8], Raul Pichardo[8], Luis Carlos Rodriguez Delgado[8], Emilio Filippucci[9], Edoardo Cipolletta[9], Teodora Serban[10], Florentin Ananu Vreju[11], Gael Mouterde[12], Maria-Antonietta D'agostino[13], Marcello Govoni[1], Leonardo Punzi[14], Nemanja Damjanov[15], Lene Terslev[16], Irene Azzolin[17], Giulio Guerrini[1], Carlo Alberto Scirè[1], Annamaria Iagnocco[17]. *[1]University of Ferrara, Ferrara, Italy*; *[2]University of Padua, Padua, Italy*; *[3]University of Siena, Siena, Italy*; *[4]Hospital Fundación Jiménez Díaz, Madrid, Spain*; *[5]rhu/dal/chuv, Lausanne, Switzerland*; *[6]North Valley Hospital, Whitefish, Montana, United States of America*; *[7]Instituto Poal, Barcelona, Spain*; *[8]Instituto Nacional de Rehabilitacion, Mexico City, Mexico*; *[9]Università Politecnica delle Marche, Jesi, Italy*; *[10]ASL3 – Azienda Sanitaria Genovese, Genova, Italy*; *[11]University of Medicine and Pharmacy, Craiova, Romania*; *[12]Lapeyronie hospital, Montpellier, France*; *[13]APHP Hôpital Ambroise Paré, Boulogne-Billancourt, Paris, France*; *[14]Venice Hospital, Venice, Italy*; *[15]University of Belgrade, Belgrade, Serbia*; *[16]Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark*; *[17]Università degli Studi di Torino, Turin, Italy*

Background: 9The OMERACT Ultrasound (US) in calcium pyrophosphate deposition disease (CPPD) sub-task force has been working on the assessment of the utility of US in CPPD since 2014 first creating definitions for CPPD identification and then demonstrating that US is a reliable tool[1].
Objectives: Objective of this study is to assess the diagnostic accuracy of US in CPPD
Methods: This is a multicentre international diagnostic accuracy study involving 17 centres from 9 countries. We enrolled in this study consecutive patients waiting to undergo knee replacement surgery due to severe osteoarthritis. Each patient underwent US examination of the knee, focusing on the menisci and the hyaline cartilage, the day prior to surgery, scoring each site according to the presence/absence of CPP as defined by OMERACT[1]. After surgery, the menisci and the condyles were collected and examined microscopically. Six samples were collected, both from the surface and from the internal part of menisci and cartilage trying to cover a large part of the structure. All slides were observed under transmitted light microscopy and by compensated polarised microscopy. A dichotomous score was given for the presence/absence of CPP crystals. US and microscopic analysis were performed by blinded operators. Sensitivity and specificity of US were calculated using microscopic findings of the menisci and cartilage as the gold standard.

		[95% Confidence Interval]	
Prevalence	40%	23%	59.4%
Sensitivity	83.3%	51.6%	97.9%
Specificity	61.1%	35.7%	82.7%
ROC area	.722	.562	.882
Likelihood ratio (+)	2.14	1.14	4.03
Likelihood ratio (-)	.273	.073	1.02
Odds ratio	7.86	1.42	43.2
Positive predictive value	58.8%	32.9%	81.6%
Negative predictive value	84.6%	54.6%	98.1%

Results: These preliminary analyses include 30 patients. The mean age was 71yrs (SD±9.1), 19 (63%) were females. 17 patients were positive at US analysis and 12 at microscopic analysis. Diagnostic accuracy results of US at patient level, are presented in figure 1.
Conclusion: These preliminary results demonstrate that US is a sensitive exam for identification of CPPD with acceptable specificity. US is the first diagnostic technique with consistent reliability and validity to be applied for non-invasive screening for CPPD in clinical practice.

REFERENCES:

[1] Filippou G, Scirè CA, Adinolfi A, *et al.* Identification of calcium pyrophosphate deposition disease (CPPD) by ultrasound: reliability of the OMERACT definitions in an extended set of joints—an international multiobserver study by the OMERACT Calcium Pyrophosphate Deposition Disease Ultrasound Subtask Force. *Ann Rheum Dis* 2018;:annrheumdis-2017-212542. doi:10.1136/annrheumdis-2017-212542

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OP0320 **SUCCESSFUL EVALUATION OF A PREDEFINED SET OF ANATOMIC SITES IN THE PELVIS OF PATIENTS WITH POLYMYALGIA RHEUMATICA SHOWING EXTRACAPSULAR INFLAMMATION AS VISUALIZED BY CONTRAST ENHANCED MAGNETIC RESONANCE IMAGING:**

Martin Fruth[1], J Kozik[1], P Martin-Seidel[1], Annika Seggewiss[1], Xenofon Baraliakos[2,3], Juergen Braun[2,3]. [1]*Radiology, Herne, Germany*; [2]*Rheumazenrum Ruhrgebiet, Herne, Germany*; [3]*Ruhr-University, Bochum, Germany*

Background: The diagnosis of polymyalgia rheumatica (PMR) is based on a thorough clinical evaluation of the patient - including exclusion of other diseases, since there is no decisive diagnostic test. A characteristic pattern of extracapsular inflammation in the pelvis of patients with PMR as assessed by contrast enhanced magnetic resonance imaging (MRI) has been recently described (1)
Objectives: To evaluate the performance of a predefined set of anatomic sites in the pelvis of patients with PMR vs. controls.
Methods: A total of 120 pelvic MRI scans of patients who had presented to our tertiary center with pelvic girdle pain in the last 3 years, including 40 patients with an expert rheumatologist diagnosis of PMR and 80 controls with other reasons of pelvic pain was evaluated by 3 radiologists blinded to clinical diagnosis and patient demographics. The experts scored the presence or absence of contrast enhancement at 19 predefined tendinous and capsular pelvic structures. Different patterns of involvement were compared and statistically evaluated by ROC analysis. Kappa statistics were applied to calculate inter- and intrareader agreement.
Results: Mostly bilateral peritendinitis and capsulitis including uncommon sites such as the proximal origins of the muscles rectus femoris and adductor longus were found almost exclusively and, thus, typically in PMR patients: the difference in the mean number of sites showing contrast enhancement was significantly different with 13.4±2.7 for PMR vs 4.0±2.3 for controls. A cut-off of $\geq$10 inflamed sites discriminated very well between the groups resulting in a sensitivity and specificity of 95.8% and 97.1%, respectively. Just concentrating on the most frequently involved anatomic sites bilateral inflammation of proximal M. rectus femoris or adductor longus tendons together with at least 3 other bilaterally inflamed sites performed even better with a sensitivity and specificity of 100% and 97.5%, respectively.
Conclusion: This study strongly confirms that the previously described pattern of extracapsular pelvic inflammation as assessed by contrast enhanced MRI is very typical for patients with PMR. In addition, the high sensitivity and specificity of the set of anatomic sites evaluated suggest their definite potential for use as a confirmatory diagnostic test.

REFERENCE:

[1] Fruth M, Buehring B, Baraliakos X, Braun J. Use of contrast-enhanced magnetic resonance imaging of the pelvis to describe changes at different anatomic sites which are potentially specific for polymyalgia rheumatica. Clin Exp Rheumatol. 2018; 36 Suppl 114(5):86-95.

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The benefits of involving patients in health technology assessment

OP0321-PARE **A NOVEL APPROACH TO REACH PATIENTS FOR EDUCATIONAL PURPOSES – VIRTUAL CONFERENCE REUMANET**

Mitchell Silva, Nele Caeyers. *ReumaNet, zaventem, Belgium*

Background: Every two years, ReumaNet organises a physical conference for patients addressing various topics of rheumatic and musculoskeletal diseases (RMD). Traditionally, about 200 individuals attend this event. For the last edition however, ReumaNet swapped the physical event with a virtual one. This allowed us to reach far more people, who could attend the 'conference' online whenever they wanted, over a period of four weeks.
Objectives: The objective was to assess the impact, reach and patient experience of such a virtual event.
Methods: In this virtual event, more than twenty presentations were pre-recorded and put into an online system. Virtual booths were offered to partner organisations to offer educational material in pdf's or in video format.
The board of ReumaNet set up an interesting program, covering the following aspects:

- Medical evolution in RMD's: explanation about new treatments in various indications, information on new medication
- Living with an RMD: information about the psychological, vocational, social and physical aspects of having an RMD
- The future of healthcare: information on the changing technology in healthcare and sustainability of the healthcare system
- Testimonials: video testimonials of patient advocates

All information was pre-recorded and integrated into an online portal. The lectures showed both speaker and the slide set, moving along with the presentation. Registration was free and anonymous. Only email was required in order to validate the registration. Visitors also had the option to answer surveys on various topics and score every video presentation. All material could be downloaded (PowerPoint presentations, brochures, videos).
This virtual symposium was accessible from mid-September till mid-October, covering four weeks around World Arthritis Day. People could come and go, and log in at any other point in time from different devices, so it was not necessary to view all at once.
Results: The results were very promising, having over 1.300 registrations (compared to 200 registrations at a physical event). The social media reach was over 140.000 and the event also increased the visibility of the Facebook page of ReumaNet. On the platform itself there were over 5000 video views and over 3000 visits of the virtual booths of partner organisations. General satisfaction rates were high: 96% of the visitors indicated they were most likely to visit a similar event in the future. Over 80% gave the event a + 4 star rating out of 5.
Conclusion: This event was considered to be very successful. The results showed that this virtual event exceeded our expectations and had an impact on the visibility of our organisation via social media. This type of event has been expanded towards sister organisations in rheumatology, such as the Belgian organisation for healthcare professionals and can serve as an innovative way for other European patient organisations to attract new profiles and increase awareness of RMDs among the broad public.
Disclosure of Interests: Mitchell Silva Consultant for: For Pfizer, MSD, Janssen, Merck, BMS, Sanofi, Novartis, AstraZeneca, Speakers bureau: For Pfizer, MSD, Janssen, Merck, BMS, Sanofi, Novartis, AstraZeneca, Nele Caeyers: None declared **DOI:** 10.1136/annrheumdis-2019-eular.3281

OP0322-PARE **GRASSROOTS CAMPAIGN FOR DUTCH RMD-FRIENDLY MUNICIPALITIES**

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Background: Following the decentralisation of healthcare in 2014, Dutch municipalities were assigned a key role in providing healthcare support to local residents. ReumaNederland used the 2018 council elections to start a campaign to raise awareness for RMD-friendly council policies.
Objectives: The campaign aimed to raise awareness for suitable RMD healthcare policies across municipalities.

Methods: Patient consultation – We asked people with RMD to complete an online survey about council policies. The survey asked whether, and how, these policies restricted them, in addition to what could be done to address and solve these restrictions. The questions focused on healthcare, support and the provision of medical aids. After identifying the three greatest challenges for residents, the Dutch Arthritis Society (DAS) focused on three main recommendations, which were sent via letter to local politicians. This letter included a clear call to action for better local arthritis care.
Online tool - We also created an online tool that linked the letter to the email addresses of all local party leaders in the 380 Dutch municipalities. The online tool enabled local residents to simply forward the letter to the party leaders in their council. The tool also allowed residents to include their personal experiences.
Results: Patient consultation: More than 2,200 people with RMD completed the survey. The three greatest points of improvement included:

- Sports and leisure facilities for people with RMD – 80% of all respondents were interested in sport facilities that suit their needs. However, 75% were unsure if there were any available in their council.
- Better communication and information – 40% of all respondents indicated that it was unclear where and how they could apply for care with their council. Respondents also indicated that councils lacked expertise regarding the impact of RMD.
- A threshold–free and accessible RMD–friendly environment – Municipalities must consider RMD–friendly access to roads, public transport and public buildings.

Online tool: A total of 10,000 emails were sent to party leaders, reaching over half of all municipalities. The majority of feedback from party leaders was positive. Some residents were invited to introduce themselves, attend a meeting or take a seat on a client advisory board. RMD-friendly policies are also now featured on the political agenda of many local councils.
Conclusion: This campaign has put RMD-friendly policies on the council agenda in many municipalities. Clearly, using the momentum of local political developments is an effective tool to create attention. It is also a way to build the network and voice of the movement. Following the campaign, it has become easier for us to speak to the councillors responsible for healthcare and to address the issues raised by people with RMD. For instance, in the autumn of 2018, local RMD patient associations met with the council for the first time. The online tool has allowed for nation-wide participation in this campaign.
Disclosure of Interests: None declared
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FRIDAY, 14 JUNE 2019

Overdiagnosis and overtreatment in inflammatory arthritis

OP0323 USEFULNESS OF UNIVERSAL ANTINUCLEAR ANTIBODIES TESTING IN EARLY ARTHRITIS REFERRALS

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Background: The CHUC Early Arthritis Clinic, founded in 2011, intends to provide a prompt response to patients with recent onset of symptoms suggestive of an inflammatory rheumatic disease (IRD). By research protocol, all patients are screened at baseline for the presence of antinuclear antibodies (ANA). An analysis was performed to evaluate the usefulness of universal ANA testing in these patients.
Objectives: To evaluate the prevalence and clinical correlates of ANA positivity in early arthritis referrals.
Methods: A retrospective study of consecutive patients referred to the Early Arthritis Clinic between 2011 and 2018 was conducted. Referral is based on the fulfillment of specific criteria: presence of arthritis or clinically suspected arthralgia beginning in the previous 12 months plus suggestive laboratorial abnormalities (rheumatoid factor, C-reactive protein or erythrocyte sedimentation rate). ANA titer (positive= $\geq$1:160) and cellular staining patterns were assessed by indirect immunofluorescence (Hep-2 cells). Positive (PPV) and negative predictive values (NPV) of an ANA positive test for the diagnosis of an IRD or an ANA-related rheumatic disease (ARD) were determined, along with PPV for the other referral criteria.
Results: 207 patients were included in the analysis (64.3% female, aged 53.9 ± 18.2 years). The diagnosis of an IRD was confirmed by the rheumatologist in 61.4% of cases, including 11.8% cases of ARD. The most prevalent diagnosis was rheumatoid arthritis (21.7%), followed by unclassified arthritis (8.7%), psoriatic arthritis, osteoarthritis and fibromyalgia (6.8% each). The prevalence of ANA positivity in our cohort was 64.2%, most frequently in low titration (1:160 in 33.8%, 1:320 in 19.3%, 1:640 in 8.7% and 1:1280 in 2.4%) and with a dense fine speckled pattern (45.1%). ANA-positive patients were older (53.7 ± 17.9 versus 47.9 ± 18.5, p=0.05), more likely to have an IRD (72.9% versus 40.5%, p<0.001) but not an ARD (9.0% versus 4.1%, p=0.186). PPV for ARD was 9.0% for the 1:160 cut-off titration and 15.6% for the 1:320. Squeeze test (PPV 13.5%), erythrocyte sedimentation rate (PPV 9.9%) and rheumatoid factor (PPV 20.0%), as referral criteria, all performed better at predicting an ARD, compared to an ANA positive testing.
Conclusion: Early Arthritis Clinic referred cohort has a high prevalence of IRD but a low prevalence of ARD which explains the poor predictive value of ANA in this setting, especially when considering lower titters and when compared with specific referral criteria. Thus, universal ANA testing in Early Arthritis Clinic referrals seems unjustified, given its costs and added value. Studies designed to optimize the use of ANA in this context are warranted.
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FRIDAY, 14 JUNE 2019

Cannabis for arthritis: Hype or hope?

OP0324 CANNABIDIOL ELEVATES INTRACELLULAR CALCIUM AND INDUCES APOPTOSIS IN HUMAN ARTICULAR CHONDROCYTES

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Background: Osteoarthritis (OA) is a major public health problem among the increasing aged and obese population, therefore development and investigation of new therapeutics is a major focus of OA research. Endocannabinoids (ECs), cannabinoids derived from the *Cannabis sativa* plant and synthetic cannabinoids have been attributed anti-inflammatory, antitumorigenic, analgesic and psychoactive effects. Over recent years increasing interest in the EC system as a target for therapeutic treatment of joint diseases has emerged [1].
Objectives: Cannabidiol (CBD) is the most abundant non psychoactive compound of *Cannabis sativa* extracts and has been shown to have anti-arthritic potency in animal models [2, 3]. In the present study we investigated the effects of CBD on the cell viability and Ca^{2+} homeostasis in human articular chondrocytes.
Methods: Cell viability, discrimination of intact, apoptotic and necrotic cells and caspase 3/7 activity were determined by Resazurin assays, Annexin-V/7-AAD staining followed by flow cytometry and caspase-Glo 3/7 assay respectively. Intracellular Ca^{2+} was monitored by time-lapse fluorescence imaging. The perforated whole-cell patch clamp technique was used for measuring the cell membrane potential. Western blot analysis was performed for the quantification of Erk1/2 phosphorylation.
Results: C28/i2 and human primary chondrocytes showed a significantly reduced viability with an apoptosis maximum at 10µM CBD after treatment with rising amounts of CBD. This apoptotic effect was accompanied by an increase of caspase 3/7 activity. Flow cytometry analysis of Annexin-V/7-AAD stained cells revealed a decline of intact cells and a significant dose dependent increase of the early apoptotic cell population after treatment with CBD.
CBD significantly elevated intracellular $Ca^{2+}{}_i$ accompanied by a depolarization of the cell membrane. This increase of $Ca^{2+}{}_i$was abrogated, when Ca^{2+} was omitted from the bath solution indicating an influx of extracellular Ca^{2+} rather than depletion of internal stores. Several blocking substances were tested to identify the channel/receptor responsible for this Ca^{2+} influx. Cannabinoid receptor1 (CB1) antagonist AM251 significantly inhibited the Ca^{2+} influx triggered by CBD. Moreover, preincubation of chondrocytes with AM251 significantly reduced the toxic effects of CBD. Looking for mediators of the apoptotic CBD effect downstream of the CB1 receptor enhanced Erk1/2 phosphorylation could be detected. However this Erk1/2 activation proved to be unaffected by CB1 receptor blockage.
Conclusion: Micromolar concentrations CBD induce apoptosis in human articular chondrocytes. CBD also triggers an influx of extracellular Ca^{2+} and potentiates Erk1/2 phosphorylation. The apoptotic effects are at least partially

mediated by the CB1 receptor indicated by an increased cell viability and reduction of caspase activity after combined treatment with CBD and CB1 antagonist AM251. Since CBD induced Erk1/2 phosphorylation seems to be independent of CB1 signalling, the involvement of other signalling pathways and/or a crosstalk with other Ca^{2+} channels or receptors seems likely and will be the focus of further investigations.

REFERENCES:

[1] Staunton, C.A., A. Mobasheri, and R. Barrett-Jolley, *High hopes for cannabinoid agonists in the treatment of rheumatic diseases.* BMC Musculoskelet Disord, 2014. **15**: p. 410.
[2] Malfait, A.M., et al., *The nonpsychoactive cannabis constituent cannabidiol is an oral anti-arthritic therapeutic in murine collagen-induced arthritis.* Proc Natl Acad Sci U S A, 2000. **97**(17): p. 9561-6.
[3] Hammell, D.C., et al., *Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis.* Eur J Pain, 2015.

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OP0325

SAFETY AND EFFICACY OF LENABASUM IN AN OPEN-LABEL EXTENSION OF A PHASE 2 STUDY IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS SUBJECTS (DCSSC)

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Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses and limits fibrosis in animal models of SSc. Lenabasum had acceptable safety and tolerability, and improved efficacy outcomes in the 16-week, double-blinded, randomized, placebo-controlled Part A of Phase 2 trial JBT101-SSc-001 (NCT02465437) in dcSSc subjects.
Objectives: To provide long-term open-label safety and efficacy data in dcSSc subjects in study JBT101-SSc-001.
Methods: Subjects who completed Part A were eligible to receive oral lenabasum 20 mg BID in an open-label extension (OLE) that assessed safety and efficacy at 4 weeks, then every 8 weeks.
Results: 36/38 (95%) eligible subjects enrolled in the OLE, with mean interval of 134 (range 33-392) days or 19.1 weeks from end of dosing in Part A to start of OLE when subjects received only standard-of care drugs. 34/36 (94%) subjects were on stable doses of immunosuppressive drugs. At safety data cut-off, 31 (86%) subjects finished 1 year, 30 (83%) finished 18 months, and 24 finished $\geq$ 2 years in the OLE. Thirty-five (97%) subjects experienced at least 1 AE; 239 AEs have occurred during the OLE to date. Seven (19%) subjects had $\geq$ 1 AE considered related to lenabasum in the OLE. Only fatigue (1 subject) was considered definitely-related, none of the related AEs were serious or severe. Most subjects experienced AEs that were mild (n = 6, 17%) to moderate (n = 24, 67%) in maximum severity. Four (11%) had severe AEs and 1 (3%) had a life-threating AE of renal crisis caused by high-dose steroids. AEs in $\geq$ 10% of subjects: upper respiratory tract infection (n = 11, 31%), skin ulcer and arthralgia (each n = 6, 17%), urinary tract infection (n = 5, 14%), and diarrhea, nasopharyngitis, and cough (each n = 4, 11%). Dizziness and fatigue occurred in 3 (8.3%) subjects each.
At the time of efficacy data cut-off, 30/36 (83%) subjects had completed $\geq$ 18 months in the OLE. Improvement was seen in multiple physician- and patient-reported efficacy outcomes; selected outcomes are shown in **Figure 1**. Compared to Baseline at study start, the CRISS median score (primary efficacy outcome) was 0.99 (0.43 IQR) at Week 76 and mRSS declined by mean (SD) = -10.7 (7.2) points. HAQ-DI, Physician Global Assessment, Patient Global Assessment, skin symptoms, itch, and multiple PROMIS-29 domains also improved. FVC% predicted was relatively stable during the OLE; mean (SD) FVC% predicted decreased by 2.5% from study start.

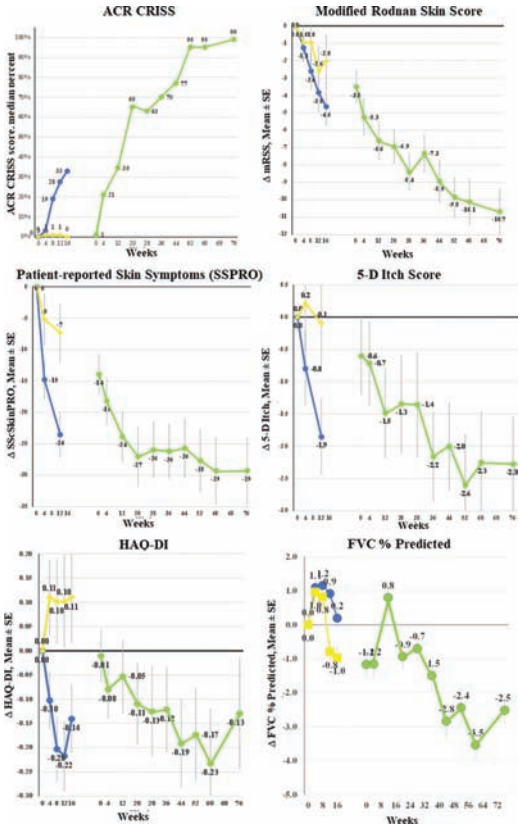


Figure 1. Change from Baseline in Selected Efficacy Outcomes in OLE of Phase 2 Trial JBT101-SSc-001

Conclusion: Lenabasum continues to have a favorable safety and tolerability profile in the OLE of Phase 2 trial JBT101-SSc-001 with no lenabasum-related serious AEs or study discontinuations. Only 7 (19%) subjects had an AE related to lenabasum in $\geq$ 18 months of OLE dosing. ACR CRISS score, mRSS, Physician Global Assessment, and multiple patient-reported outcomes show continued improvement, although background therapy, potential for spontaneous improvement, and open-label dosing limit what can be definitely attributed to lenabasum.
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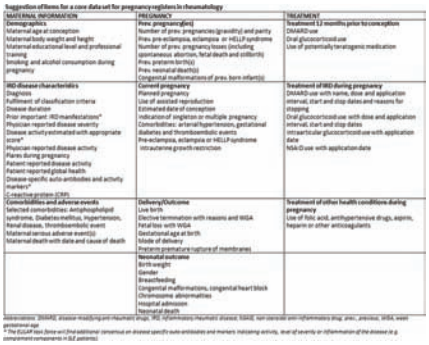
FRIDAY, 14 JUNE 2019

Reproductive issues in rheumatology

OP0326 **DEVELOPMENT OF A STANDARDIZED MINIMAL CORE DATA SET FOR PREGNANCY REGISTERS IN RHEUMATOLOGY – RESULTS OF A EULAR TASK FORCE**

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Background: Results from individual data collections on drug safety during pregnancy and outcomes of pregnancy in patients with inflammatory rheumatic diseases (IRD) are often limited due to small number of cases. Joint data analyses from different data sources could solve this problem.
Objectives: The aim of this EULAR task force was to define a core data set to facilitate joint analysis of pregnancy registers in rheumatology.
Methods: Scope and core areas of the core data set have been developed according to COS-STAD recommendations[1] by consensus. An initial list of data items possibly relevant for pregnancy registers was generated based on (I) a systematic literature search, (II) data items already collected by European pregnancy registers and (III) a survey amongst patient representatives. Consensus about the importance of each data item to be included in a core data set was reached by applying a 2-round Delphi survey where each item was rated on a numeric scale (1-3 = low importance, 4-6 = important but not critical, 7-9 = critical importance). Any data item that was considered as 'critical important' by at least 70% of responders in Delphi round 2 was included in the core set. During a face-to-face meeting of the EULAR task force, the inclusion or exclusion of data items with no consensus was finally decided.
Results: The scope was defined as follows: 'To develop a standardized core data set for data collection in prospective observational research and clinical care of pregnant women with IRD including the neonatal phase. All interventions the women receive will be covered. Patients should be enrolled at the earliest possible moment during pregnancy, and data should ideally be collected once every trimester. An additional visit should capture the neonatal phase'. Three core areas were described: 'Maternal information' (including demographics, IRD disease characteristics and comorbidities), 'Pregnancy' (including prior and current pregnancy(ies), delivery and neonatal outcomes) and 'Treatment' (including medication of IRD and other health conditions).
64 experts from 14 different European countries participated in the 2 rounds of Delphi (68% female; 84% physicians, 5% obstetricians, 5% epidemiologists, 3% patients, 3% midwives). Of the 148 data items, 85 were included in the final core set. The figure shows included items within the core areas.



Conclusion: The consensus process resulted in an extensive list of data items recommended by experts to be collected as a minimum by pregnancy registers in rheumatology. This core data set applies to all pregnant women irrespective of the underlying IRD. The EULAR task force plans to find consensus on additional disease specific advice.

REFERENCE:
[1] Kirkham et. al. PLoS med.2017;14(11):e1002447.

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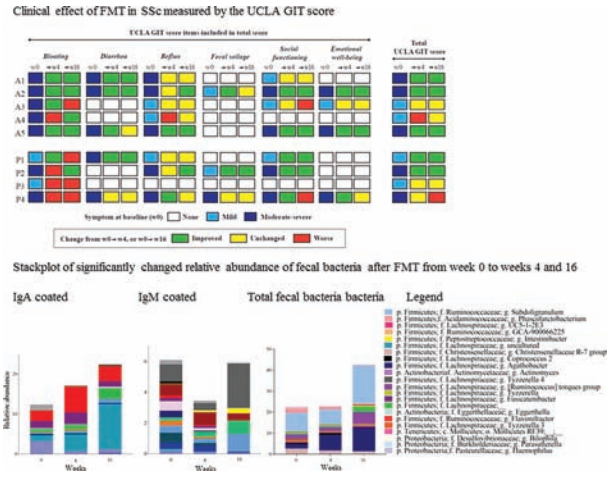
FRIDAY, 14 JUNE 2019

The future of therapeutic strategies

OP0327 **FECAL MICROBIOTA TRANSPLANTATION IN SYSTEMIC SCLEROSIS: A DOUBLE-BLIND, PLACEBO-CONTROLLED RANDOMIZED PILOT TRIAL**

Anna-Maria Hoffmann-Vold, Håvard Fretheim, Brian K Chung, Henriette Didriksen, Espen S Bækkevold, Øyvind Midtvedt, Cathrine Brunborg, Torhild Garen, Tore Midtvedt, Johannes R Hov, Knut Ea Lundin, Øyvind Molberg. *Oslo University Hospital, Oslo, Norway*

Background: Systemic sclerosis (SSc) is a progressive, multi organ, autoimmune disease marked by frequent and severe gastrointestinal (GI) afflictions and gut dysbiosis.
Objectives: Determine the safety and efficacy of fecal microbiota transplantation (FMT) using commercially-available anaerobic cultivated human intestinal microbiota (ACHIM) in patients with SSc.
Methods: The trial was a single-center, randomized, double-blind, placebo-controlled 16-week pilot of FMT by gastroduodenoscopy of ACHIM in SSc conducted at Oslo University Hospital. Primary endpoints were safety and clinical efficacy on GI symptoms assessed at weeks 4 and 16. Safety was assessed by observation, interviews and standardized safety form. Efficacy on GI symptoms was measured using the UCLA GIT 2.0 score questionnaire. Patients were defined as responders if reported symptom improvement was equivalent to the UCLA GIT definition of "minimally clinically important difference". Secondary and explorative endpoints included changes in relative abundance of total, immunoglobulin (Ig)A- and IgM-coated fecal bacteria measured by 16s rRNA sequencing; changes in modified Rodnan skin score, lung function, CRP, ESR, and patient and physician global. Descriptive statistics were applied for clinical endpoints and linear mixed models for microbial analysis.
Results: Ten patients with limited cutaneous SSc randomized to ACHIM (n=5) or placebo (n=5) were included. All patients were female with clinical apparent GI symptoms, mean age of 62 years and mean time from diagnosis of 12 yrs. Two placebo controls experienced procedure-related serious adverse events; one developed laryngospasms at first gastroduodenoscopy necessitating study exclusion, one duodenal perforation at final gastroduodenoscopy. Improvement in total GIT score was reported by 3/5 FMT patients compared to 2/4 placebo controls at weeks 4 and 16 (Figure 1). FMT effects were most pronounced on lower GI symptoms, with improvement reported by 5/5 FMT patients with diarrhea, distention/bloating and/or fecal incontinence at baseline compared to 2/4 placebo controls (Figure). Clinical secondary endpoints showed no differences and other side effects (stomach discomfort, bloating and diarrhea) were mild and transient. Fecal microbiota diversity (observed number of operational taxonomic units) was increased after FMT compared to placebo treatment at week 16 ($p<0.006$). Moreover, abundant bacterial genera in ACHIM were present within the total, and IgA- and IgM-coated fecal bacteria at both week 4 and 16 in the FMT group (Figure 2) but not in the placebo controls.



Conclusion: FMT of commercially-available ACHIM in patients with SSc appeared safe, effectively reduced lower GI symptoms, altered gut microbiota composition, richness and diversity and appeared to affect the mucosal immune system

Disclosure of Interests: Anna-Maria Hoffmann-Vold Grant/research support from: Received research funding or other remuneration from Boehringer Ingelheim, GSK, and Actelion, Consultant for: Received consulting fees or other remuneration from Boehringer Ingelheim, GSK, and Actelion, Speakers bureau: Actelion and Boehringer Ingelheim, Håvard Fretheim Consultant for: Received consulting fees or other remuneration from GSK, and Actelion, Brian K Chung: None declared, Henriette Didriksen Consultant for: Received consulting fees or other remuneration from GSK, and Actelion, Espen S Bækkevold: None declared, Øyvind Midtvedt: None declared, Cathrine Brunborg: None declared, Torhild Garen: None declared, Tore Midtvedt Shareholder of: Owner of ACHIM, Johannes R Hov: None declared, Knut EA Lundin: None declared, Øyvind Molberg: None declared

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FRIDAY, 14 JUNE 2019

Calming the cytokine storm in children and adults

OP0328 COMPARISON OF SERUM CYTOKINE PROFILE IN MACROPHAGE ACTIVATION SYNDROME AMONG DIFFERENT BACKGROUND RHEUMATIC DISEASES IN CHILDREN:

Mao Mizuta, Masaki Shimizu, Masaaki Usami, Naoto Sakumura, Hitoshi Irabu, Maiko Takakuwa, Natsumi Inoue, Yasuo Nakagishi, Akihiro Yachie. *Graduate School of Medical Sciences, Kanazawa University, Department of Pediatrics, Kanazawa, Japan*

Background: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening complication of pediatric rheumatic diseases. MAS occurs most often in children with systemic juvenile idiopathic arthritis (s-JIA) and less commonly in children with systemic lupus erythematosus (SLE), Kawasaki disease (KD) and juvenile dermatomyositis (JDM). The hallmark of MAS includes uncontrolled and dysfunctional immune responses involving continual activation and expansion of T lymphocytes and macrophages, which in turn lead to marked hypercytokinemia. However, it is still unknown which cytokines play a key role in the pathogenesis of MAS among different backgrounds.

Objectives: This study was aimed to clarify cytokines involved in the development of MAS among different background rheumatic diseases and to identify the serum biomarkers for the diagnosis of MAS.

Methods: Serum neopterin, interleukin (IL)-18, IL-6, tumor necrosis factor (TNF)-α and soluble TNF receptor type I (sTNFR-I) and sTNFR-II levels were determined using enzyme-linked immunosorbent assay in 112 s-JIA patients including 30 with MAS, 8 SLE patients including 3 with MAS, 67 KD patients including 4 with MAS, and 7 JDM patients including 3 with MAS. Cytokine profiles in MAS phase of each disease were compared to those in active phase.

Results: Serum neopterin levels in patients with s-JIA, SLE and KD were significantly elevated in MAS phase compared to those in active phase. Serum neopterin levels in patients with JDM were also elevated in MAS phase compared to those in active phase, although statistically significant. Serum sTNFR-I levels in patients with s-JIA and SLE were significantly elevated in MAS phase compared to those in active phase. Serum sTNFR-I levels in patients with KD and JDM were also elevated in MAS phase compared to those in active phase, although statistically significant. Serum sTNFR-II levels in patients with s-JIA and KD were significantly elevated in MAS phase compared to those in active phase. Serum sTNFR-II levels in patients with JDM were also elevated in MAS phase compared to those in active phase, although statistically significant. Serum IL-18 levels in patients with s-JIA were significantly elevated in both active and MAS phase compared to those in patients with other diseases. There were no significant differences of serum IL-6 and TNF-α levels among different backgrounds.

Conclusion: The elevation of serum neopterin levels was the common finding in patients with MAS even in different backgrounds. These findings indicate that overproduction of interferon (IFN)-γ might be closely related to the development of MAS. Serum neopterin levels which reflect IFN-γ production might be a promising biomarker for the disease activity of MAS.

REFERENCES:

[1] Huber C, et al. J Exp Med 1984;160:310-6.
[2] Bracaglia C, et al. Ann Rheum Dis 2017;76:166-72.

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OP0329 PLCGAMMA2/TMEM178 DEPENDENT PATHWAY IN MYELOID CELLS MODULATES THE PATHOGENESIS OFCYTOKINE STORM SYNDROME

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Background: Cytokine storm syndrome (CSS) is a life-threatening condition, observed in several rheumatic diseases, and a well-known complication of systemic juvenile idiopathic arthritis (sJIA) (1). Defects in T cell cytotoxicity leading to their excessive activation are major contributors to CSS development. However, dysregulated innate immune responses are also observed (2). The role of monocytes and macrophages as drivers of CSS, regardless of T cells, and the signaling pathways regulating monocyte/macrophage responses, have not been formally investigated.

Objectives: The goal of this study was to determine the contribution of monocytes/macrophages to the development of CSS and analyze the signaling pathways that lead to aberrant monocyte/macrophage pro-inflammatory responses using animal models of the disease and patient samples.

Methods: To study the involvement of monocytes/macrophages in a T cell-dependent model of CSS we treated LCMV-infected Perforin-/- mice with clodronate-liposomes or neutralizing anti-CSF1Ab prior to disease initiation. Similar depletion experiments were performed in a T-cell independent CSS model consisting of five injections of the TLR9 agonist CpG-1826 into WT mice. Myeloid cell contribution to CSS was assessed in mice with LysMCre-driven deletion of Plcγ2 or global deletion of Tmem178, a downstream Plcγ2 target gene specifically expressed in macrophages. Presence of immune infiltrates in liver and spleen was evaluated by FACS analysis and immunohistochemistry, circulating inflammatory cytokine levels were detected by ELISA, multi-organ damage was evaluated by histology.

Results: Depletion of monocytes/macrophages during early stages of CSS reduces mortality and inflammatory cytokine levels in both T-cell dependent and independent CSS models. Activation of Plcγ2 in myeloid cells controls CSS development by driving macrophage pro-inflammatory responses. Intriguingly, the Plcγ2 downstream effector Tmem178 acts in a negative feedback loop to restrain inflammatory cytokine production and protect from CSS development. Highlighting the clinical relevance, Tmem178 levels are reduced in macrophages from mice with CSS or exposed to sJIA patient plasma with active disease.

Conclusion: Macrophages are key drivers of CSS initiation. We identified a novel Plcγ2/Tmem178 axis as a modulator of inflammatory cytokine production by monocytes/macrophages in CSS. Reduced Tmem178 levels are observed in sJIA and might be responsible for the increased macrophage pro-inflammatory responses.

REFERENCES:

[1] Canna SW, Behrens EM. Making sense of the cytokine storm: a conceptual framework for understanding, diagnosing, and treating hemophagocytic syndromes. Pediatr Clin North Am. 2012;59:329-44.
[2] Grom AA, Horne A, De Benedetti F. Macrophage activation syndrome in the era of biologic therapy. Nat Rev Rheumatol. 2016;12:259-68.

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FRIDAY, 14 JUNE 2019

Remission – the holy grail? Looking across diseases

OP0330 COMPARISON OF THE EFFECTS OF DORIS REMISSION AND LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) ON DISEASE OUTCOMES IN A MULTINATIONAL PROSPECTIVE STUDY

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Background: The Definitions of Remission in SLE (DORIS) group has proposed multiple definitions of remission, but these are infrequently attained and have not been prospectively evaluated in relation to protection from damage accrual. In contrast, the Lupus Low Disease Activity State (LLDAS) is more attainable, and has been shown to be associated with improved patient outcomes.
Objectives: To compare the attainability, and association with outcomes, of LLDAS and remission in a prospective multicentre study.
Methods: A prospective multinational cohort study was undertaken in 13 centres between 2013-2017. Time dependent Cox proportional hazards models were used to compare LLDAS and DORIS definitions of remission in terms of impact on disease flares and damage accrual.
Results: 1735 SLE patients were recruited, and followed for (mean±SD) 2.2±0.9 years, totalling 12,717 visits. LLDAS was achieved in 47.2% of observed visits. In contrast, remission was achieved in 1.1%-15.4% of visits depending on the stringency of remission definition. LLDAS attainment at any visit was associated with significantly reduced subsequent flare (HR 0.65, 95%CI 0.56-0.75, p<0.001) and damage accrual (HR 0.59, 95%CI 0.45-0.76, p<0.001). In contrast, only the least stringent remission definition was associated with reduced damage accrual (HR 0.58, 95%CI 0.39-0.88, p 0.01). Only remission definitions including serological remission were significantly associated with reduction in subsequent flares. Patients who spent ≥50% of their observed time in LLDAS had reduction in damage accrual (HR 0.54, 95% CI 0.42- 0.70, p<0.001) compared to patients with <50% of observed time in LLDAS; again, only the least stringent remission definition, or the related definition excluding serology, were associated with reduced damage (HR 0.59, 95% CI 0.42-0.83, p 0.003; HR 0.69, 95% CI 0.48-0.99, p 0.05, respectively).
Conclusion: LLDAS was more attainable than any remission definition, whilst still conferring significant reduction in flares and damage accrual. Only the least stringent remission definitions could be shown to be associated with significantly lower damage accrual, likely reflecting a low frequency of remission attainment overall. LLDAS is a valid treatment target for SLE and is more achievable than remission.
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OP0331 MAGNETIC RESONANCE IMAGING TENOSYNOVITIS AND OSTEITIS ARE INDEPENDENT PREDICTORS OF RADIOGRAPHIC AND MRI DAMAGE PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION

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Background: Progression of structural joint damage occurs in 20-30 % of patients with rheumatoid arthritis (RA) in clinical remission[1]. Magnetic resonance imaging (MRI)-detected synovitis and in particular osteitis/bone marrow edema (BME) are known predictors of structural progression in both active RA and in remission, but the predictive value of adding MRI tenosynovitis assessment as potential predictor in patients in clinical remission has not been investigated.
Objectives: To investigate the predictive value of baseline MRI inflammatory and damage parameters on 2 year MRI and X-ray damage progression in an RA cohort in clinical remission, following MRI and conventional treat-to-target (T2T) strategies.
Methods: 200 RA patients in clinical remission (DAS28-CRP<3.2 and no swollen joints) on conventional DMARDs, included in the randomized IMAGINE-RA trial[2] (conventional DAS28 + MRI-guided T2T strategy targeting absence of BME vs conventional DAS28 guided T2T strategy) had baseline and 2 years contrast-enhanced MRIs of the dominant wrist and 2nd-5th MCP joints and X-rays of hands and feet performed, which were evaluated with known chronology by two experienced readers according to the OMERACT RAMRIS scoring system and Sharp/van der Heijde method, respectively.
The following potentially predictive baseline variables: MRI BME, synovitis, tenosynovitis, MRI and X-ray erosion and joint space narrowing (JSN) score, CRP, DAS28, smoking status, gender, age and patient group were tested in univariate logistic regression analyses with 2-year progression in MRI combined damage score, Total Sharp Score (TSS), and MRI and X-ray JSN and erosion scores as dependent variables. Variables with p<0.1, age, gender and patient group were included in multivariable logistic regression analyses with backward selection.
Results: Based on univariate analyses MRI BME, synovitis, tenosynovitis, x-ray erosion and JSN, gender and age were included in subsequent multivariable analyses. Independent MRI predictors of structural progression were BME (MRI progression) and tenosynovitis (MRI and X-ray progression), see table.

		Dependent variables, progression ≥1 from baseline to month 24[a]					
		MRI			**X-ray**		
		MRI Erosion	MRI JSN	MRI combined damage score	X-ray Erosion	X-ray JSN	TSS
Explanatory variables	MRI BME	1.13 (1.06-1.21) p<0.001	1.18 (1.08-1.29) p<0.001	1.22 (1.12-1.33) p<0.001			
	MRI Tenosynovitis	1.13 (1.03-1.25) p=0.01	1.21 (1.04-1.40) p=0.01	1.13 (1.02-1.26) p=0.02		1.10 (1.00-1.21) p=0.04	
	Age				0.96 (0.93-0.99) p=0.007		

[a]: Odds Ratio (95% confidence interval; CI) p-value;
MRI combined damage score: sum score of MRI erosion and JSN scores.

Conclusion: This trial is the first to report that MRI tenosynovitis independently predicts both X-ray and MRI damage progression in RA patients in clinical remission. Further studies are needed to confirm MRI-determined tenosynovitis as predictor of progressive joint destruction in RA clinical remission.

REFERENCES:
[1] Lillegraven, et al. Ann Rheum Dis 2012
[2] Møller-Bisgaard et al. JAMA, accepted Dec 2018

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FRIDAY, 14 JUNE 2019

Complement and autoimmunity – emerging therapeutic opportunities

OP0332 COMPLEMENT FACTOR EXPRESSION AND ACTIVATION IN OSTEOARTHRITIS JOINT COMPARTMENTS

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Background: Several studies have identified a central role for the activation of the complement system in the pathogenesis of OA, finding an abnormally high expression and activation of complement in human osteoarthritic joints and the specific contribution of complement (C) components 5 and 6 and the membrane attack complex (MAC) (1). The complement system consists of several proteins which contribute to an enzymatic cascade ending in lysis. Two main, different pathways converge into C3 factor activation. In the classical pathway C4 is involved, while in alternative pathways Factor-b (FB) is involved.
Objectives: The aim of this study was to investigate the expression of complement factors (C3, C4 and FB) and activation fragments (C3a, C5a, FBa, MAC) in OA joint tissues.
Methods: Osteochondral biopsies from 33 patients (16 OA, 12 Rheumatoid Arthritis-RA and 15 Postraumatic cases-PT) who underwent knee, hip or shoulder arthroplasty were collected. Immunohistochemistry and quantitative Imaging analysis were perfomed to analyze C3, C4 and CFB expression. Cartilage pathology was evaluated utilizing Mankin score. Chondrocytes, synoviocytes, cartilage and synovial biopsies were obtained from 11 OA patients undergoing joint replacement surgery. Cultures were set up with or without pro-inflammatory (IL-1beta) stimulus. Culture supernatants were analyzed for C3a, C5a, CFBa and C5b-9 production using enzyme-linked immuno-sorbent assay (ELISA). Statistical analysis was performed utilizing Wilcoxon matched pairs test and Mann Whitney's test, using Graph Pad Prism software.
Results: In osteochondral biopsies, C factor expression was located in bone marrow and in a few subchondral bone cells. C3 was the most expressed factor in all patient subtypes while factor C4 had a very low expression, except for some sporadic cases. (OA: C3 vs FactorB p=0.0280, C3 vs C4 p=0.0005; RA: C3 vs FactorB p= 0.0269, C3 vs C4 p=0.0005; PT: C3 vs FactorB p=ns, C3 vs C4 p=0.0001) CFB was significantly augmented in PT and was not significantly different between OA and RA. C factors expression did not correlate with Mankin score or with the joint type (knee, hip or shoulder). Cell positivity was mainly present in the subchondral bone (bone marrow) whereas cartilage was almost negative. As to activation fragments, C3a was the most produced factor (vs C5a and CFBa p<0.0005) but no differences were found between cultured chondrocytes and synoviocytes (vs synovial tissue p<0.0005) and its production was not stimulated by proinflammatory stimulus. C5a production in cartilage was significantly higher than in chondrocytes and synovial tissue (both p<0.0005) but no differences were found between cartilage and synoviocytes. CFBa was induced by IL-1beta in synovial tissue. C5b-9 production was undetactable in chondrocytes and synoviocytes cell culture supernatants. In cartilage C5b-9 production was decreased by IL-1 beta stimulus while in synovium it was increased, although not significantly.
Conclusion: Complement factors were expressed mainly in bone marrow and in a few subchondral bone cells, but not in cartilage. Complement activating fragments are produced by chondrocytes and synoviocytes. The dissimilar expression of activating fragments by different cell types could suggest various C activating mechanisms in joint tissues.

REFERENCE:
[1] Wang Q, et al. Nat Med 2011;17:1674-1679.

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SATURDAY, 15 JUNE 2019

Novel autoantibodies in RMD: a neverending quest?

OP0333 RISING ACPA IGG VARIABLE DOMAIN GLYCOSYLATION PRE-DISEASE ASSOCIATES WITH AN INCREASE IN AUTOANTIBODY LEVELS AND THE DEVELOPMENT OF RHEUMATOID ARTHRITIS

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Background: Anti-citrullinated protein antibodies (ACPA) are present in the majority of rheumatoid arthritis (RA) patients (60-70%) and play a pivotal role in disease development[1]. ACPA IgGs are unique in a way that they are abundantly N-glycosylated within their variable regions[2]. These variable domain (V-domain) glycans are found on over 90% of ACPAs present in sera from RA-patients[3]. To undergo N-linked glycosylation, a consensus sequence in the protein backbone is required (N-X-S/T, where $X \neq P$)[4]. Recently, it was shown that the N-linked glycosylation sites in ACPA-IgG V-domains are introduced during somatic hypermutation and that the introduction of such sites likely conveys a selective advantage to ACPA expressing B-cells[5]. However, it is currently unknown, whether ACPA-expressing B-cells already introduced glycosylation-sites into their V-domains before disease onset or when ACPA-V-domain glycosylation occurs.
Objectives: Investigate the appearance of ACPA V-domain glycosylation in pre-symptomatic individuals and RA patients.
Methods: In a case-control study, individuals (n=201) from the Medical Biobank, who were sampled before onset of symptoms (mean±SEM predating time; 5.8 ±0.3 years) (140 aCCP+ and 61 aCCP-), and after diagnosis of RA (n=99, 94 aCCP+ and 5 aCCP-) and randomly selected control samples (n=43, 3 aCCP+ and 40 aCCP-) were analyzed for their ACPA IgG V-domain glycosylation levels. ACPA IgGs were affinity purified, N-linked glycans released, and 2-AA labeled for further analysis using UHPLC[6]. Data calibration and integration was performed and a cut-off defined. Samples below the cut-off were determined as non-detectable and excluded from the analysis. The percentage V-domain glycosylation was calculated as described previously[3]. Statistical calculations were performed using SPSS.
Results: Our data indicated that ACPA IgG V-domain glycans are already present years before symptom onset, in pre-symptomatic individuals who subsequently will develop RA. Analysis of matched pairs showed a significant increase of ACPA V-domain glycosylation in RA patients compared to individuals pre-disease (p<0.001). The results showed that ACPA N-glycosylation was correlated with anti-CCP concentrations pre-disease (r_s =0.504, p<0.001), while no such association can be found after RA onset. Further, V-domain glycosylation levels increase closer to symptom onset.

Table 1. Impact of serologic features on markers of active SLE

	Subset	N	Mean/Median C3	p value	Mean/Median C4	p value	% with Low C3/C4	p value	% DNA +	p value
Baseline	ALL	1019	1056		186		39.2%		35.8%	
N=1019	ENA+	670	990	**	162	**	42.1%	#0.001	43.6%	#0.001
	ENA-	349	1130	0.001	210	0.001	23.8%		30.7%	
	DNA+	399	890	**	130	**	63.9%	#0.001	-	na
	DNA-	620	1130	0.001	210	0.001	22.9%		-	
	ENA+ DNA-	378	1117	**	198	**	25.9%	**	-	na
	ENA- DNA-	242	1211	0.001	237	0.001	18.2%	0.001	-	
Screen N=783	ALL	783		***		***	32.1%		24.9%	
	ANA neg	190	1230	<0.001	230	<0.001	15.3%	#0.073	7.4%	#0.026
	ANA=1:80	74	1130		228		25.7%	comp	17.6%	comp
	ANA=1:160	104	1110		210		25.0%	*ns*	19.2%	*ns*
	ANA=1:320	97	1110		190		29.9%	*ns*	22.7%	*ns*
	ANA=1:640	104	960		152		47.1%	#0.006	34.6%	#0.019
	ANA=1:1280	88	924		160		45.4%	#0.015	35.2%	#0.019
	ANA=1:2560	52	920		160		48.1%	#0.016	44.2%	#0.002
	ANA≥1:5120	74	959		135		45.9%	#0.016	48.6%	#0.001
	ANA - ENA +	61	1122	*	203	**	21.3%	*ns*	13.1%	*ns*
	ANA - ENA -	129	1254	0.007	258	0.001	12.4%		4.7%	
	ANA≥1:80 or DNA+	607	1020	**	170	**	37.7%	#0.012	-	na
	DNA+ or ENA+ or ANA≥1:640	318	940	0.001	152	0.001	46.5%		-	

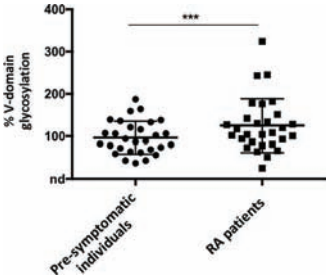


Figure 1%Variable. domain glycosylation of matched paired samples before and after disease onset.

Conclusion: Our analysis revealed that ACPA IgG molecules can harbor V-domain glycans already relatively long time before disease onset. An increase in ACPA V-domain glycosylation, presumably due to the generation of de-novo N-glycosylation sites or the expansion of N-glycosylation site-bearing clones was associated with an increase in ACPA levels. These results suggest that ACPA-expressing B cells gain a selective advantage through the generation V-domain N-glycosylation in parallel with rising ACPA-levels in serum in the phase prior to the development of arthritis.

REFERENCES:

[1] https://doi.org/10.1038/nrrheum.2011.204
[2] https://doi.org/10.1136/annrheumdis-2014-206598
[3] https://doi.org/10.1074/mcp.M116.062919
[4] J. Biol. Chem. 1996, 271 (11), 6363–6366, PMID: 8626433
[5] https://doi.org/10.1136/annrheumdis-2017-212052
[6] https//doi.org/10.1371/journal.pone.0200280

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OP0334 WHAT SEROLOGIC PROFILING PROVIDES OPTIMAL ENTRY CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS CLINICAL TRIALS?

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Background: A major concern for SLE clinical trials is the possibility that some patients who technically meet entry criteria may not have active disease. Antinuclear antibody (**ANA**) is known to lack specificity for SLE, permitting inclusion of inappropriate patients. Typically, ANA≥1:80 and/or positive anti-double stranded DNA (**DNA**) are required screening elements, but lately other autoantibody variables have been utilized.

Objectives: To examine serologic features that promote entry of active SLE patients into trials while supporting reasonable recruitment rates.

Methods: Serologic features of 1411 individual subjects who had full laboratory data at screening (N=783) and/or baseline (N=1019) in 4 phase 2 multicenter SLE trials were examined. Complement levels, percent of patients with low C3 or C4, and elevated DNA were used as markers of active disease. Serological profiles consistent with active SLE were tested on screened population for effects on potential screen failure rates.

Results: Of 1019 patients who qualified for the studies (baseline population), 399 (39.2%) were positive for DNA and 670 (65.8%) had anti-Extractable Nuclear Antibodies (**ENA**). Patients with positive DNA or ENA (even in absence of DNA) had lower complement levels and were more likely to have low C3/C4. (Table 1)

In patients at screening, higher titers of ANA were associated with lower complement levels and higher rates of patients with low C3/C4 and elevated DNA. ENA impacted complement levels even in the absence of ANA. Compared to traditional entry criteria (ANA≥1:80 and/or DNA), patients defined by positive DNA or ENA or ANA≥1:640 had significantly lower complement levels and greater rates of low C3/C4, suggesting a more active patient population. (Table 1)

*t test **ranks ***one way ANOVA on ranks #chi square (comp=comparator) na=not applicable *ns*=not significant. Data not adjusted for multiple comparisons

Compared to a 22.5% screen failure rate with the typical requirement for ANA≥1:80 or DNA, testing DNA or ENA or low C3/C4 as entry criteria resulted in 30.7% exclusion. Adding high titer (≥1:640) ANA as an additional optional criterion would decrease the screen failure to 25.7%. (Table 2)

Table 2. Impact of serological profiles as entry criteria on potential screen failure rate (N = 783)

Entry Criteria	N	Screen Failure Rate
ANA≥1:80 or DNA	607	22.5%
ANA≥1:80 or DNA or anti-Smith	614	21.6%
DNA or ENA	495	36.8%
DNA or ENA or low C3/C4	543	30.7%
DNA or ENA or ANA≥1:640	552	29.5%
DNA or ENA or low C3/C4 or ANA≥1:640	582	25.7%

Conclusion: The following entry criteria may help increase the likelihood that trial subjects have active SLE: **ANA≥1:640, or DNA, or ENA, or low C3 or C4**. To the extent that a modest loss of recruitment increases the probability of entering true, active SLE patients, these alternative constructs should be considered in future SLE trials.

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Exagen, Bristol Myers Squibb, Medimmune/Astra Zeneca, Lilly, Immupharma, Amgen, Janssen, Sanofi, Neovacs, Anthera, Speakers bureau: UCB, GSK, EMD Serono, Bristol Myers Squibb, Medimmune/Astra Zeneca, Janssen
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SATURDAY, 15 JUNE 2019

Lessons learned from checkpoint inhibitors

OP0335 **A PROSPECTIVE CLINICAL AND MRI STUDY OF IMMUNE CHECKPOINT INHIBITOR (ICI)-INDUCED MUSCULOSKELETAL MANIFESTATIONS MYO-FASCIITIS AND NOT SYNOVITIS IS THE PROMINENT IMAGING FINDING**

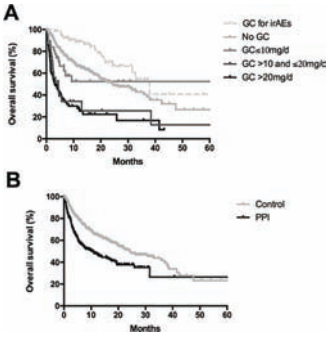
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Background: Immune check point inhibitors (ICI) were a breakthrough in cancer therapeutics. These agents target certain "brakes" of the immune system aiming at activating T cells to fight cancer. Taking into account their mechanism of action it is no surprise that they have been associated with immune related adverse events
Objectives: To assess the prevalence, clinical and imaging characteristics of ICI-induced musculoskeletal manifestations in a prospective manner
Methods: This is a prospective, clinical and MRI study conducted from Jan 2016 to Oct 2018. All patients treated with ICI who developed musculoskeletal manifestations were referred to the Rheumatology Department and subjected to a full clinical assessment and laboratory workup. An MRI of the involved area(s) was performed within one week of the initial clinical evaluation. In 2 patients MRI was not performed due to claustrophobia (n=1) and presence of non compatible metal implant (n=1).
Results: During the study period a total of 130 patients were treated with ICI. Of those, 10 (7.7%) developed ICI-induced musculoskeletal manifestations. They suffered from lung (n=4), bladder (n=3), renal cancer (n=2) or melanoma (n=1) and received treatment with nivolumab (n=7), pembrolizumab (n=1), durvalumab (n=1) and atezolizumab (n=1). They were mostly male (n=8) with a mean ± SEM age of 66.7 ± 2.6 years. The median (range) time from ICI treatment since development of symptoms was 2.5 (1-22) months. Autoantibodies (RF/ACPA/ANA) were negative in all patients and only 3/10 had a mild/moderate increase of inflammatory markers at disease onset. Three different patterns of musculoskeletal manifestations were found: i) Prominent joint involvement (n=3). Areas involved were the small joints of the hands (n=2) and knee/ankle (n=1). The MRI of the latter patient depicted not only synovitis but also myositis of the muscles surrounding the involved joints, ii) Prominent "periarticular" involvement (n=4). These patients had diffuse swelling of the hands (n=4) feet (n=3) or knees (n=1). Joints retained a good and relatively painless range of motion. MRI depicted mild synovitis with more prominent myositis and/or fasciitis in the surrounding tissues in all cases, iii) Myo-fasciitis (n=3). In all 3 such cases the involved area was the knee. Clinically, these patients presented with pain in the knee and either no objective signs of arthritis (n=2) or swelling with non inflammatory synovial fluid. MRI depicted myo-fasciitis of the surrounding muscles in all cases; a partial tear of the quadriceps tendon was also found in the patient with knee swelling. Overall, symptoms were mild/moderate and responded well to treatment (low dose steroids in 6 and NSAIDs/analgesics in 4) with no need for ICI discontinuation.
Conclusion: In our cohort ICI-induced musculoskeletal manifestations were not uncommon and developed in 7.7% of patients. Imaging evidence of myo-fasciitis was found in all patients indicating that the muscle/fascia is more frequently involved than the synovium. Our clinical and imaging data point to the direction that ICI-induced musculoskeletal manifestations mostly involve periarticular structures and associate mainly with myo-fasciitis and not synovium based pathology
Disclosure of Interests: None declared
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OP0336 **COMMONLY USED DRUGS IN RHEUMATOLOGY MAY ALTER ANTI-TUMORAL RESPONSE TO IMMUNE CHECKPOINT INHIBITORS**

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Background: Immune checkpoint inhibitors (ICIs) are revolutionizing the treatment of some advanced cancers. Gut microbiota has emerged as an important component of anti-tumoral response and can also be related to the occurrence of immune-related adverse events (irAEs). It has recently been shown that antibiotic treatment given at the initiation of ICI therapy had a dramatic impact on microbiota that compromised the anti-tumoral effect of ICIs (1).
Objectives: To evaluate whether co-medications known to have a potential impact on gut microbiota may alter ICI efficacy and/or irAE occurrence when given at ICI onset.



Methods: This was a retrospective cohort study including all cancer patients who received ICIs at our institution from May 2015 to September 2017. Co-medications given to the patients within one month before or one month after the first administration of ICI were extracted from medical records on the basis of a predefined list of medications known to impact gut microbiota. The tumour response, occurrence of irAEs and patient outcomes were assessed on a regular basis. Overall survival (OS) has been considered from the start of ICI therapy.
Results: 635 patients (70% male, mean age 64.5 years) were included, of whom 293 had melanoma, 150 had advanced non-small cell lung cancer and 83 had renal carcinoma. A previous autoimmune disorder was present in 8% of patients, mainly rheumatic and endocrine diseases. Psychotropic drugs (41.1%), proton pump inhibitors (PPIs) (37.3%), angiotensin-converting enzyme (ACE) inhibitors and/or angiotensin II receptor blockers (ARBs) (32%), glucocorticoids (GC) (24.2%), antibiotics (21.4%), statins (20.8%) and morphine (20.6%) were the most co-prescribed medications. Baseline GC use, when $\geq$ 10mg of prednisone equivalent, was associated with a significant decrease in OS (median 4.5 months versus 24.3 months; p<0.0001) and a less frequent tumour response (55% versus 73%; p=0.0001). When given after ICI onset for the management of irAEs, GC did not influence ICI efficacy (**Figure A**). Baseline PPIs use also altered both OS (median 10.9 versus 24.3 months; p<0.0001) and tumour response (62% versus 71%; p=0.02) (**Figure B**). We confirmed the detrimental impact of antibiotics when given at ICI onset, and also found worse outcomes for patients receiving baseline psychotropic drugs (median OS 9.3 versus 19.4 months; p=0.0001). No significant difference was observed with baseline use of NSAIDs, aspirin, statins and ARBs/ACE. Furthermore, co-medication with antibiotics, GC, PPIs, morphine, NSAIDs, aspirin and psychotropic drugs was associated with decreased occurrence of irAEs.
Conclusion: As many of these treatments are used by rheumatologists, one should be aware of their potential detrimental effect when used at ICI initiation, that sometimes could have been avoided.

REFERENCE:

[1] Routy B *et al.* Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors. Science. 2018 Jan 5;359(6371):91-97.

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SATURDAY, 15 JUNE 2019

Orthotic treatment: is it in or out?

OP0337-HPR EFFECTIVENESS OF CUSTOMIZED INSOLES IN PATIENTS WITH MORTON'S NEUROMA: A RANDOMIZED, CONTROLLED, DOUBLE-BLIND CLINICAL TRIAL

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Background: Morton's neuroma (MN) is a benign enlargement of the third common digital branch of the medial plantar nerve The most common symptom is burning pain in the plantar foot, located between the metatarsal heads, often radiating to the two corresponding toes. Treatment can be surgical or conservative, which consists of decreasing nerve pressure and irritation through therapies that promote analgesia, patient education, and plantar orthosis. The custom insole prescriptions are aimed at relieving the pressure in the MN region, and to redistribute pressure throughout the sole of the foot. There is no study evaluating the effect of insoles in patients with MN.
Objectives: The aim of the present study was to assess the effectiveness of a customized insole with metatarsal and arch support on pain in patients with Morton's neuroma and the impact of this insole on function, load distribution in the plantar region, gait, quality of life and satisfaction with insole use.
Methods: A randomized, controlled, double-blind, clinical trial was carried out with intent-to-treat analysis. Seventy-two patients with NM were randomly allocated into a study group (n=36) and control group (n=36). One week following the baseline evaluation, the study group received a customized insole with metatarsal and arch support made of ethyl vinyl acetate and the control group received a flat insole of the same material, color and density. The groups were evaluated after 6, 12 and 24 weeks of insole use. The following assessment parameters were employed: pain when walking, on palpation and at rest (END); paresthesia (ENP); quality of life (SF-36); foot function (FFI and FHSQ); six-minute walk test (6MWT) and foot pressure analysis using the AM Cube FootWalk Pro program.
Results: The groups were homogeneous regarding the majority of variables at baseline. In the comparisons over time, statistically significant differences between groups were found for pain when walking (p=0.048), in the general health domain (p <0.001) and physical activity (p = 0.025) in the FHSQ questionnaire, in the general FFI questionnaire score (p = 0.012) and in the functional capacity domain of the SF-36 questionnaire (p = 0.046). For pain at rest and palpation, in the domains of the FFI, some parameters of the FHSQ (vigor, pain, function and general health of the foot) and quality of life (limitation by physical aspects, bodily pain and vitality), we observed improvement in both groups with no statistically significant difference between them. No change was observed in the baropodometry parameters with the use of the insole.
Conclusion: A customized insole with metatarsal and arch support reduce pain when walking and improve function of patients with NM.

REFERENCES:

[1] Bennett GL, Graham CE, mauldin DM. Morton`s interdigital neuroma: a comprehensive treatment protocol. Foot Ankle Int 1995;16:760-763.
[2] Adams WR 2nd. Morton's neuroma Clin Podiatr Med Surg. 2010 Oct;27 (4):535-45.
[3] Lee KS. Musculoskeletal ultrasound: how to evaluate for Morton's neuroma. AJR Am J Roentgenol. 2009 Sep;193(3):W172.

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SATURDAY, 15 JUNE 2019

Current treatment of vasculitis

OP0338 LOW-DOSE IL-2 SELECTIVELY RESTORES REGULATORY T CELLS IN PATIENTS WITH BEHCET'S DISEASE

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Background: The lack of CD4+CD25+Foxp3+ T regulatory cell (Treg) has been associated with human systemic autoimmune diseases, such as rheumatoid arthritis (RA). IL-2 is an essential growth and survival factor for Treg cells. However, the significance of Treg cells in the pathogenesis and the effect of low dose IL-2 on Behcet's disease (BD) are rarely reported.
Objectives: To investigate the significance of Treg cells and the effect of low dose IL-2 on BD.
Methods: Eighty patients with BD and seventy healthy donors were enrolled. $CD4^+$T cell subsets in peripheral blood mononuclear cells from these people were measured by multicolour flow cytometry. Twenty-six patients were treated daily with subcutaneous injections of 0.5 million IU of human IL-2 for five consecutive days, $CD4^+$T cell subsets were analysed before and after treatment by flow cytometry.
Results: Compared to health control, the absolute counts of circulating Treg cells were significantanty decreased in patients with BD (median:29.93 cells/ul VS median:33.16 cells/ul, P=0.039) and it is negative correlation with disease activity. While the ratios of Th17/Treg in patients with BD (median:0.29) were significantly higher than those of health control (median:0.2). No diffrernce in the absolute counts of circulating Th17 cells ($CD4^+IL\text{-}17^+$) between patients with BD and health control. Treatment of patients with BD with a low-dose IL-2 selectively increased the absolute counts of Treg cells, from a median of 18.97 cells/ul to 74.68 cells/ul (at 5 days) (P<0.001). No significant difference was observed in the absolute counts of circulating Th17, Th1 and Th2 cells after IL-2 treatment.
Conclusion: Th17/Treg cells may play a role in the pathogenesis of patients with BD, low-dose IL-2 proposes a selective biological treatment strategy by restoring immune tolerance.

REFERENCES:

[1] Zeidan M J, Saadoun D, Garrido M, et al. Behcet's disease physiopathology: a contemporary review[J]. Auto Immun Highlights,2016,7(1):4.
[2] Malek T R, Castro I. Interleukin-2 receptor signaling: at the interface between tolerance and immunity[J]. Immunity,2010,33(2):153-165.
[3] Klatzmann D, Abbas A K. The promise of low-dose interleukin-2 therapy for autoimmune and inflammatory diseases[J]. Nat Rev Immunol,2015,15 (5):283-294.

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OP0339 TOCILIZUMAB IN GIANT CELL ARTERITIS. MONOTHERAPY VERSUS COMBINED WITH CONVENTIONAL IMMUNOSUPPRESSIVE DRUGS

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Background: Giant cell arteritis (GCA) can be refractory to corticosteroid therapy. Tocilizumab (TCZ) has been approved in the treatment of GCA. There are no studies comparing the efficacy and safety when using TCZ as monotherapy or in combination with conventional immunosuppressive drugs in GCA.
Objectives: Our aim was to compare efficacy and safety of TCZ combined or in monotherapy in GCA.
Methods: Multicenter study on 134 patients with refractory GCA who received TCZ therapy as monotherapy or combined with conventional immunosuppressants. Prolonged remission, absence of clinical symptoms and signs and normalization of the acute phase reactants for at least 6 months. Relapse, recurrence of signs or symptoms of GCA and/or ESR >20 mm/h in men or >25 mm/h in women, and/or serum CRP >0.5 mg/dL related to GCA, both before and after starting TCZ therapy.
Results: We evaluated 134 patients (101 w/33 m) with a mean age of 73.0±8.8 years. TCZ was prescribed as monotherapy in 82 (62.2%) cases and combined with conventional immunosuppressants in 52 (38.8%) patients: MTX (n=48), AZA (n=3), and LFN (n=1). A comparative study between both groups is summarized in **TABLE**. Patients who received combined TCZ were younger and had a higher C-reactive protein (CRP) and a higher presence of aortitis in imaging techniques. After TCZ was started, prolonged remission was reached with combined therapy (statistical significance at 12 and 24 months). The corticosteroids sparing effect

was similar in both groups. And in terms of side effects no significant difference was seen between TCZ as monotherapy or combined with conventional immunosuppressants.

TABLE

	TCZ IN MONOTHERAPY (n=82)	TCZ COMBINED (n=52)	p
BASAL FEATURES AT TCZ ONSET			
GENERAL FEATURES			
Age, years, mean± SD	71.2 ± 9.0	68.8 ± 8.0	**0.04**
Sex, female/male n (%)	62/20	39/13	0.93
Time from GCA diagnosis to TCZ onset (months), median [IQR]	13.0 [7.75-33.5]	18.5 [6.25-34.0]	0.333
SYSTEMIC MANIFESTATIONS			
Fever, n (%)	6 (7.3%)	3 (5.8%)	0.72
Constitutional syndrome, n (%)	18 (22.0%)	13 (25.0%)	0.68
PMR, n (%)	40 (48.8%)	33 (63.5%)	0.096
ISCHEMIC MANIFESTATIONS			
Visual involvement, n (%)	20 (24.4%)	8 (15.4%)	0.21
Headache, n (%)	42 (51.2%)	28 (53.8%)	0.76
Jaw claudication, n (%)	7 (8.5%)	7 (13.5%)	0.36
AORTITIS AND ANOTHER LVV involvement, n (%)	28 (34.1%)	30 (57.7%)	**0.007**
ACUTE PHASE REACTANTS			
ESR, mm/1st hour, mean (SD)	39.4 ± 32.5	42.3 ± 29.6	0.6
CRP, mg/dL mean (SD)	2.1 ± 3.0	4.4 ± 7.5	**0.014**
Hemoglobin, g/dL, mean (SD)	12.2 ± 1.5	12.4 ± 1.4	0.41
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d	23.9±17.3	19.4 ±14.0	0.11
EFFICACY AND SAFETY AFTER TCZ			
Prolonged remission n (%)			
Month 6	31 (50.8)	27 (69.2)	0.160
Month 12	18 (51.4)	28 (82.4)	**0.006**
Month 24	10 (50)	17 (85)	**0.018**
Relapses n (%)			
Month 1	3 (3.8)	1 (2)	0.579
Month3	4 (5.4)	3 (6.3)	0.845
Month 6	3 (4.9)	2 (5.1)	0.962
Month 12	6 (17.1)	3 (8.8)	0.305
Month 24	6 (30)	1 (5)	**0.037**
CORTICOSTEROIDS SPARING EFFECTS, median [IQR]	15 [7.5-21.25]	10 [7.5-20]	0.457
Month 1	10 [5-15]	7.5 [5-10]	0.179
Month3	5 [2.5-10]	5 [2.5-7.5]	0.146
Month 6	5 [0-5]	2.5 [0-5]	0.064
Month 12	1.3 [0-5]	0 [0-1.25]	0.095
Month 24			
SIDE EFFECTS, n (%)			
Relevant adverse events	23 (28)	9 (17.3)	0.155
Serious infections	12 (14.6)	4 (7.7)	0.227

Conclusion: Patients receiving combined conventional immunosuppressants with TCZ in the clinical practice study showed a higher prolonged remission. The incidence of serious infections and/or relevant adverse events was not affected according to the treatment. As well as the corticoid-sparing effect was achieved in the same way in both groups.

REFERENCES:

[1] Goercke .Calderón-M. Tocilizumab in giant cell arteritis. Observational, open-label multicenter study of 134 patients in clinical practice. Semin Arthritis Rheum. 2019 Jan 5. pii: S0049-0172(18)30571-7. doi: 10.1016/j.semarthrit.2019.01.003. [Epub ahead of print]
[2] Loricera J et al. Semin Arthritis Rheum.2015;44:717-723

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SATURDAY, 15 JUNE 2019

Workshop: #ConnectToday and tomorrow: The campaigning continues

OP0340-PARE THE USE OF INTERACTIVE AUGMENTED REALITYPOSTERS AS PUBLIC ENGAGEMENT TOOLS TO ENHANCE THE EULAR 'DON'T DELAY, CONNECT TODAY' CAMPAIGN

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Background: Musculoskeletal conditions (MSC), such as Rheumatoid arthritis (RA), place a heavy burden on society and have severe consequences for the individuals affected. In order to limit this burden of disease, early diagnosis and implementation of treatment are essential and result in a significantly increased chance of achieving long-term sustained remission. The European League Against Rheumatism (EULAR) campaign 'Don't Delay Connect Today' (DDCT) was created in order to educate the general public and primary healthcare providers (such as General Practitioners) about the importance of recognising the early warning signs of MSC's. Many countries have adopted the campaign across Europe, with groups using new and creative ways to engage local communities with this essential message. In Scotland, the Rheumatosphere team have worked to develop interesting and impactful ways of disseminating this message to the public. Augmented reality (AR) is a potential tool to enhance learning and has already been successfully used as a new and exciting tool for teaching[1]. However, its role in less formal educational setting, such as public engagement, is still relatively unknown.

Objectives: The primary objective of this study was to test a new AR modality, assessing its effectiveness in increasing knowledge pertaining to RA and the central message of the DDCT campaign.

Methods: An interactive AR application was designed for a lay audience, incorporating aspects of RA disease pathogenesis along with the importance of early diagnosis and treatment of disease. The modality consisted of printed posters that were enhanced by an interactive AR application accessed through a hand-held tablet device. Members of the public, visiting the Glasgow Science Centre, were asked to assess our AR application by completing a 5 point Likert scale questionnaire before and after interacting with our posters and AR application.

Results: In total 27 participants took part in the testing, with the majority being between the age of 25-34 years old, a key target audience for the campaign, as this demographic commonly believe that they are 'too young' to develop arthritis[2]. Overall the testing revealed that the AR application was easy to use, engaging and enjoyable. Further evaluation conducted using a 5-point Likert scale, showed that the AR application was successful in raising awareness of RA, with 81% of the participants reporting that they felt more aware about the pathogenesis, symptoms and treatment of RA after use. Moreover, 55% of the participants thought that they would inform friends and family about the causes, symptoms and treatments of RA, helping to disseminate the campaign message further, enhancing it's overall reach from a single event.

Conclusion: Overall the application was well received and indicates that this tool could be used to enhance public engagement moving forward. It would therefore be worthwhile to invest in the development of similar modalities for the EULAR 'Don't Delay, Connect Today' campaign.

REFERENCES:

[1] Sommerauer, P. and Müller, O. (2014) 'Augmented reality in informal learning environments: A field experiment in a mathematics exhibition', Computers and Education. Elsevier Ltd, 79(2014), pp. 59–68. doi: 10.1016/j.compedu.2014.07.013.
[2] Doran MF, Pond GR, Crowson CS, O'Fallon WM, Gabriel SE. Trends in incidence and mortality in rheumatoid arthritis in Rochester, Minnesota, over a forty-year period. Arthritis Rheum 2002;46:625-31.3.

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OP0341-PARE #SEEME – RAISING AWARENESS AND UNDERSTANDING OF JUVENILE IDIOPATHIC ARTHRITIS IN IRELAND

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Background: For those living with juvenile idiopathic arthritis (JIA), it is a doubly confounding condition. The popular perception that arthritis is an old person's disease leaves little room for understanding that children can also get the disease or its impact. There are 1,200 children and young people under 16 living with JIA in Ireland.

In this campaign, Arthritis Ireland sought to capture people's attention by subverting typical associations around arthritis. The campaign had to speak to and draw upon youth culture. Once people's attention was captured, this created an opportunity to communicate key pieces of information about the disease and highlight the challenging situation regarding access to Irish paediatric rheumatology services.

Objectives:

- To raise awareness that children and young people can get arthritis;
- To increase awareness and understanding of what it's like to live with JIA;
- To increase political support for the provision of enhanced paediatric rheumatology services.

Methods: #SeeMe was launched during Ireland's National Arthritis Week (9-15 April 2018) and encompassed social media, public affairs and media relations.

A key element of the campaign was the creation of a unique media asset, a short music video, which would speak directly to young people and encourage them to get involved in the campaign. The video communicated how JIA can impact enjoyable, everyday teenage activities such as dancing.

A dedicated microsite was created which housed all of the campaign assets.

A campaign petition called on the Government to implement the Model of Care for Paediatric Rheumatology. It was extremely successful, gathering more than 17,000 signatures and far exceeding the target of 5,000. The petition also harvested powerful testimony from supporters who were able to share their own stories of living with JIA.

Personal patient stories were leveraged throughout the campaign by the involvement of #SeeMe Ambassadors. These were children and young people living with JIA who were willing to share their experience publicly. National and regional media were successfully targeted, securing considerable coverage. Subsequently, the campaign progressed to a third phase of activity as young people raised awareness of JIA through their own schools, social clubs and social media networks.

An infographic was developed to communicate key medical information about JIA and paediatric rheumatology services in a clear, accessible way.

Results: #SeeMe received an overwhelmingly positive response, not just from those affected by JIA, but from the general public, the medical community and political stakeholders. The campaign was successful in the following measurable ways:

- 87,000 people viewed the campaign video;
- 17,000 people signed the #SeeMe petition;
- 820,000 people were reached by the social media campaign;
- 35 pieces of media coverage on television, radio and print were achieved;
- Lobbying of politicians by patients and their families prompted 12 TDs and senators to raise this issue;
- In May 2018, the Government committed to the appointment of an additional paediatric rheumatologist in 2019, with plans to recruit a multidisciplinary team.

Conclusion: This campaign set out to give a voice to those living with JIA and to increase awareness and understanding of the disease. The campaign highlighted the challenges in paediatric rheumatology services and proved an effective vehicle in harnessing public opinion; resulting in over 17,000 people signing the petition calling for the implementation of the Model of Care for Paediatric Rheumatology.

In the wake of the campaign, the announcement by the Irish Government to invest in paediatric rheumatology services represents an important step forward. While much remains to be done, this is progress and highlights the important role played by patient organisations, and their public education and advocacy work.

Disclosure of Interests: None declared

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SATURDAY, 15 JUNE 2019

Tackling inflammatory bone disorders in children and adults

OP0342

IDENTIFYING CANDIDATE ITEMS TOWARDS THE DEVELOPMENT OF CLASSIFICATION CRITERIA FOR CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO) AND CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CRMO)

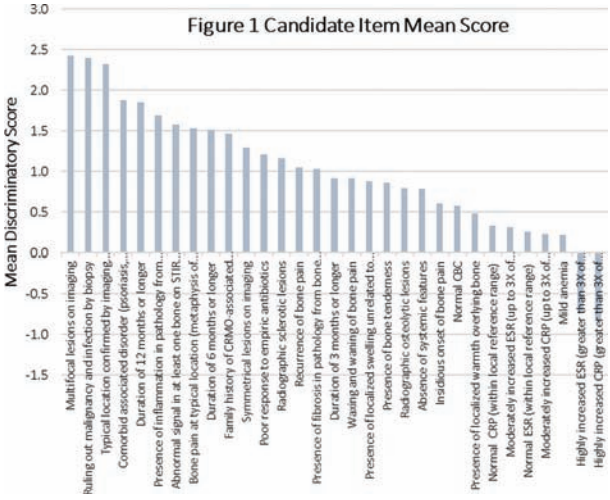
Melissa Oliver[1], Eveline Wu[2], Raymond Naden[3], Matthew Hollander[4], Polly Ferguson[5], Fatma Dedeoglu[6], Seza Özen[7], Yongdong Zhao[8]. *[1]Riley Hospital for Children at Indiana University Health, Indianapolis, United States of America*; *[2]University of North Carolina at Chapel Hill, Chapel Hill, United States of America*; *[3]McMaster University Medical Centre – Hamilton Health Sciences, Hamilton, Canada*; *[4]University of Vermont Children's Hospital, Burlington, United States of America*; *[5]University of Iowa Stead Family Children's Hospital, Iowa City, United States of America*; *[6]Boston Children's Hospital, Boston, United States of America*; *[7]Hacettepe University, Ankara, Turkey*; *[8]Seattle Children's Hospital, Seattle, United States of America*

Background: Chronic nonbacterial osteomyelitis (CNO) is a severe and occult autoinflammatory bone disease of unknown cause. Early diagnosis is challenging, and CNO may debilitate affected children when left untreated. Currently, evidence-based and validated diagnostic and classification criteria for CRMO/CNO are lacking. The insidious disease course, increasing disease incidence, and significant delay in diagnosis highlight the need for the development of classification criteria that leads to more precise and early selection of patients for clinical trials[1,2].

Objectives: To identify candidate items towards developing classification criteria for CNO using anonymous survey and nominal group technique.

Methods: An international collaborative effort was formed within the pediatric and adult rheumatology communities to conduct the following phases: 1) to generate candidate criteria items by a Delphi survey among international rheumatologists; 2) to reduce candidate criteria items through consensus processes involving physicians managing CNO and patients or caregivers of children with CNO. This study was approved by Seattle Children's Hospital Institutional Review Board.

Results: In Phase 1, 259 pediatric rheumatologists (30%, N=865) participated in an online questionnaire about features most relevant to the classification of CNO. Of those, 77 (30%) practiced in Europe, 132 (51%) in North America, and 50 (19%) in other continents. A total of 138 (53%) responders had >10 years of practicing experience and 108 (42%) had managed >10 CNO patients. There were 33 candidate criteria items initially identified. In Phase 2, candidate items were presented to 39 rheumatologists and 7 parents and items were refined or eliminated through item reduction techniques. Seventy-seven (94%, N=82) workgroup members then participated in a second survey to rank the remaining items by their distinguishing power of CNO from mimicking conditions. Figure 1 shows the mean score for the remaining 31 candidate criteria. Multifocal lesions, ruling out malignancy and infection and typical location on imaging had the greatest means. CRP and/or ESR greater than 3x the normal upper limit had the greatest negative means.



Discriminatory Score: +3/-3 (increases/decreases the likelihood of CRMO the most)
+2/-2 (increases/decreases the likelihood of CRMO moderately)
+1/-1 (increases/decreases the likelihood of CRMO slightly)
0 (no difference)

Conclusion: Through surveys and consensus technique, candidate items towards developing classification criteria for CNO were identified. This list of items will guide the design of a feasible patient data collection form towards weighting of each item in the classification criteria.

REFERENCES:

[1] Roderick MR, Shah R, Rogers V, Finn A, Ramanan AV. Chronic recurrent multifocal osteomyelitis (CRMO)–advancing the diagnosis. Pediatric Rheumatology. 2016 Dec;14(1):47.

[2] Jansson A, Renner ED, Ramser J, Mayer A, Haban M, Meindl A, et al. Classification of non-bacterial osteitis: retrospective study of clinical, immunological and genetic aspects in 89 patients. Rheumatology. 2006 Jun 17;46(1):154-60.

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To image or not to image in spondyloarthritis?

OP0343 LONGITUDINAL ASSESSMENT OF MRI OF THE SACROILIAC JOINTS IN THE ASAS CLASSIFICATION COHORT: EVOLUTION OF DIAGNOSTIC FEATURES AND PREDICTIVE UTILITY FOR AXIAL SPONDYLOARTHRITIS:

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Background: Follow up of the ASAS Classification Cohort (CC) indicated a high positive predictive value for the ASAS classification criteria derived from baseline patient and imaging data[1]. Moreover, diagnosis of axSpA was changed by the rheumatologist in only 11.2% of patients after 4.4 years. This has raised potential concerns regarding diagnostic ascertainment bias.
Objectives: To determine the evolution of MRI features of axSpA in ASAS-CC cases by central readers, whether this reflects diagnostic assignment by the rheumatologist, and the predictive utility of baseline MRI features of axSpA.
Methods: MR images were available from 108 cases in the ASAS-CC at baseline and follow up (mean 4.4 years) and also had a rheumatologist diagnosis at both time points. Eight readers from the ASAS MRI group recorded MRI lesions that comprised global assessment (MRI indicative of axSpA (yes/no), active and/or structural lesion typical of axSpA (yes/no) according to ASAS definitions), ASAS definition of positive MRI, and detailed scoring of lesions per SIJ quadrant (SPARCC SIJ method). MRI data from ≥2 readers and from the majority of readers (≥5/8) was used to calculate positive and negative predictive values (PPV, NPV).

Table 1

Rheumatologist's diagnosis	MRI is indicative of axSpA (≥ 2 readers)			
	Yes at baseline and yes at follow up (N =48)	Yes at baseline and no at follow up (N = 4)	No at baseline and yes at follow up (N =6)	No at baseline and No at follow up (N = 50)
SpA yes at baseline and follow up (N= 82)	46 (56.1%)	2 (2.4%)	4 (4.9%)	30 (36.6%)
SpA yes at baseline and no at follow up (N = 4)	1 (25%)	1 (25%)	0 (0%)	2 (50%)
SpA no at baseline and yes at follow up (N =5)	1 (20%)	0 (0%)	1 (20%)	3 (60%)
SpA no at baseline and no at follow up (N =17)	0 (0%)	1 (5.9%)	1 (5.9%)	15 (88.2%)

Taleb 2

MRI scan at baseline	Rheumatologist Diagnosis of axSpA at follow up n=108			
	Sensitivity	Specificity	PPV (%)	NPV (%)
Active lesions typical of axSpA (≥2 readers)	48.3 (37.4-59.2)	100.0 (83.9-100.0)	100.0	31.8
Active lesions typical of axSpA (≥5/8 readers)	40.2 (29.9-51.3)	100.0 (83.9-100.0)	100.0	28.8
Structural lesions typical of axSpA (≥2 readers)	48.3 (37.4-59.2)	90.48 (69.6-98.9)	95.5	29.7
Structural lesions typical of axSpA (≥5/8 readers)	31.0 (21.5-41.9)	95.2 (76.2-99.9)	96.4	25.0
ASAS positive MRI (≥2 readers)	46.0 (35.2-57.0)	100.0 (83.9-100.0)	100.0	30.9
ASAS positive MRI (≥5/8 readers)	40.23 (29.9-51.3)	100.0 (83.9-100.0)	100.0	28.8
MRI indicative of axSpA (≥2 readers)	56.3 (45.3-66.9)	85.7 (63.7-97.0)	94.2	32.1
MRI indicative of axSpA (≥5/8 readers)	50.6 (39.6-61.5)	100.0 (83.9-100.0)	100.0	32.8

Results: MRI was considered diagnostic of axSpA in 52/108 (48.1%) cases at baseline and in 47/86 (54.7%) diagnosed at baseline as axSpA by the rheumatologist. Change in MRI diagnosis was recorded in 10/108 (9.3%) of cases (2 from yes to no, and 4 from no to yes for axSpA) according to agreement by ≥2 readers and in only 3 cases according to ≥5/8 readers (Table 1). Change in rheumatologist diagnosis was recorded in 9/108 (8.3%), 2 of which had a change in MRI diagnosis. Baseline MRI lesions considered typical of axSpA had very high PPV for follow up diagnosis of axSpA (Table 2).
Conclusion: The infrequent change in diagnostic ascertainment of rheumatologists over follow up of the ASAS-CC is supported by this central reader evaluation of MRI scans. A positive MRI at baseline had very high PPV for a follow up diagnosis of axSpA.

REFERENCE:

[1] Sepriano et al. ARD 2016;75:1034-42

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OP0344 WHICH MAGNETIC RESONANCE IMAGING LESIONS OF THE SACROILIAC JOINTS ARE OF DIAGNOSTIC VALUE FOR AXIAL SPONDYLOARTHRITIS?

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Background: Classification of patients as having axial spondyloarthritis (axSpA) by the imaging arm of the ASAS criteria relies partly on the detection of bone marrow edema (BME) suspicious of SpA on magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ). Fatty lesions (FL) and erosions on SIJ-MRI have been suggested to be genuinely related to SpA in the context of interpretation of a 'positive' MRI in case of doubtful BME cases (1).
Objectives: Evaluate the role of different SIJ-MRI lesions for diagnosing axSpA in daily routine practice.
Methods: Consecutive patients with chronic back pain (duration >3 months) starting before age 45 and clinical suspicion of axSpA underwent a complete diagnostic workup including SIJ-MRI. All clinical, laboratory and imaging data were available to experienced rheumatologists for diagnosing axSpA or not (non-SpA). In parallel, two experienced readers, blinded to all patients´ information and diagnosis, evaluated the MRIs and made a diagnostic judgement based only on imaging. Furthermore, radiologists quantitatively assessed MRIs for BME (Berlin Score), FL, erosions, sclerosis and ankylosis.
Results: A total of 300 consecutive patients were recruited. AxSpA was diagnosed by the rheumatologist in 131 patients (43.7%) with mean age of 34.5±7.2 years, 73% HLA-B27+, mean symptom duration 58.6±69.5 months, vs. 169 non-SpA patients with mean age of 34.5±7.4 years, 21.3% HLA-B27+, mean symptom duration 33.9±45.1 months. The ASAS classification criteria were fulfilled by 99/131 patients diagnosed with axSpA (75.6%) vs. 70/169 patients diagnosed vs. non-SpA non-SpA (41.4%).

In 97/162 patients, rheumatologists and radiologists agreed on a diagnosis of axSpA and non-SpA (overall agreement: 86.3%). However, 34/131 (28.1%) patients were diagnosed with axSpA by rheumatologists but not by radiologists.
According to radiologists, BME alone was critical for diagnosis in only 7/97 patients (7.2%) with axSpA as agreed by both, rheumatologists and radiologists, in contrast to chronic lesions alone (30/97, 30.9%) or the combination of both lesion types (60/97, 61.9%).
While the sensitivity of BME for diagnosing axSpA did not change, the specificity improved when chronic lesions were also present (Tab.1). In addition, based on rheumatologists´ diagnosis, the respective odds ratio (OR) for identifying axSpA by MRI was higher when chronic lesions were present (Tab.1). MRI scores were significantly higher in axSpA vs. non-SpA patients, indicating that axSpA is associated with deeper BME or chronic lesions (Tab.2).

Table 1. Odds ratios for MRI lesions and combinations used for diagnosing axSpA.

Lesion type	Sensitivity	Specificity	OR	95% CI	p-value
BME	72.5%	63.3%	4.6	2.8-7.5	0.001
BME + any chronic lesion	71.8%	72.8%	16.0	7.5-34.0	0.001
FL	56.5%	89.3%	10.9	6.0-19.8	0.001
Erosion	59.5%	88.8%	11.6	6.4-21.0	0.001
Sclerosis	81.7%	43.2%	3.4	2.0-5.8	0.001
Ankylosis	12.2%	99.4%	23.4	3.1-178.7	0.002
BME+FL	36.6%	95.3%	11.6	5.3-25.7	0.001
BME+Erosion	48.9%	94.1%	15.2	7.4-31.4	0.001
BME+Sclerosis	64.1%	75.1%			0.001
BME+Ankylosis	5.3%	99.4%	9.5	1.2-78.1	0.036

Table 2. Mean/median Berlin SIJ scores ± standard deviation for inflammatory and chronic lesions.

	Lesion type	axSpA	non-SpA	p-value
Mean ±SD	Total score	14.8 ±10.8	2.7±3.4	p<0.001
	BME (0-24)	3.3±3.6	0.8±1.3	
	FL (0-24)	5.2±6.8	0.5±1.9	
	Erosions (0-24)	4.5±5.4	0.4±1.4	
Median	Sclerosis or Ankylosis (0-2)	0	0	–

Conclusion: The combination of structural changes and BME lesions as assessed by MRI performed best in the process of diagnosing axSpA in consecutive patients in a real-life setting presenting to our center. The discrepancy in diagnosis between rheumatologists and radiologists reflects the increasing insecurity of including only BME of SIJ as the major criterium for diagnosing axSpA.

REFERENCE:

[1] Lambert R et al. Ann Rheum Dis 2016

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SATURDAY, 15 JUNE 2019

How low should you go? What is the relevant target in T2T in rheumatoid arthritis?

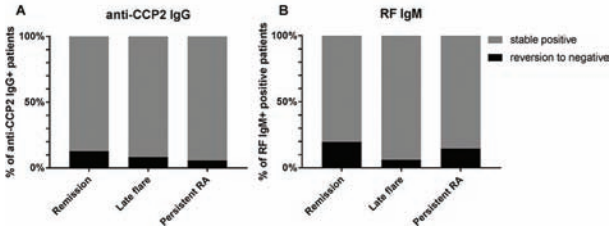
OP0345

DOES IMMUNOLOGICAL REMISSION, DEFINED AS DISAPPEARANCE OF AUTOANTIBODIES, OCCUR WITH CURRENT TREATMENT STRATEGIES? A LONG-TERM FOLLOW-UP STUDY IN RHEUMATOID ARTHRITIS PATIENTS WHO ACHIEVED A SUSTAINED DMARD-FREE STATUS

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Background: Sustained disease modifying antirheumatic drug (DMARD)-free status, the sustained absence of synovitis after cessation of DMARD-therapy, is infrequent in autoantibody-positive RA, but approximates cure (i.e. disappearance of signs and symptoms). It was recently suggested that immunological remission, defined as disappearance of anticitrullinated protein antibodies (ACPA) and rheumatoid factor (RF), underlies this outcome.[1] However, the association between seroreversion and cure of disease has not been extensively studied before.
Objectives: To determine in a long-term observational study if autoantibodies disappear in RA-patients who achieved sustained DMARD-free remission.
Methods: We studied 95 ACPA- and/or RF-positive RA-patients who achieved DMARD-free remission after median 4.8 years and kept this status for the remaining follow-up (median 4.2 years). Additionally, 21 autoantibody-positive RA-patients with a late flare, defined as recurrence of clinical synovitis after a DMARD-free status of $\geq$1 year, and 45 autoantibody-positive RA-patients who were unable to stop DMARD-therapy (during median 10 years) were studied. Anti-CCP2 IgG, IgM and RF IgM levels were measured in 587 samples obtained at diagnosis, before and after achieving DMARD-free remission.
Results: 12.8% of anti-CCP2 IgG positive RA-patients had seroreverted when achieving remission. In RA-patients with a late flare and with persistent disease this was 8.3% and 5.7%, respectively (p=0.63, Figure). For anti-CCP2 IgM and RF IgM similar results were observed. Evaluating the estimated slope of serially measured levels revealed that RF-levels decreased more in patients with than without remission (p<0.001); the course of anti-CCP2 levels was not different (p=0.66).

Figure Reversion to anti-CCP2 IgG (A) and RF IgM (B) seronegativity in autoantibody positive RA-patients who achieved sustained DMARD-free remission, who had a late flare and in patients with persistent RA



Conclusion: Sustained DMARD-free status in autoantibody-positive RA was not paralleled by an increased frequency of reversion to autoantibody-negativity. This form of immunological remission should therefore not be a treatment target.

REFERENCE:

[1] Schett G, Emery P, Tanaka Y, *et al.* Tapering biologic and conventional DMARD therapy in rheumatoid arthritis: current evidence and future directions. *Ann Rheum Dis* 2016;**75**:1428–37. doi:10.1136/annrheumdis-2016-209201

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OP0346

MRI OF THE WRIST IN EARLY RHEUMATOID ARTHRITIS AFTER 1-YEAR TREAT-TO-TARGET STRATEGY

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Background: There are two types of remission in rheumatoid arthritis. The first, and most commonly applied, is clinical remission. Imaging remission is another aspect to consider given that (a) the correlation between clinical and imaging at presentation is only modest, (b) imaging can show subclinical inflammation not evident clinically and (c) imaging evidence of inflammation can predict structural damage (1). In this study, we compared clinical and imaging remission in early rheumatoid arthritis (ERA) patients after one year of standard treatment.
Objectives: To semi-quantitatively and quantitatively measure the degree of inflammation (synovitis, tenosynovitis, bone marrow oedema) and structural change (erosions, joint space narrowing) on MRI in early RA patients following treat-to-target strategy treatment for one year and to compare this with changes in clinical parameters.
Methods: Prospective cross-sectional study of 70 ERA patients underwent treat-to-target strategy treatment for one year. DAS28-ESR remission (DAS28-ESR score ≤3.2), 2011 ACR/EULAR definition of remission, SDAI remission (SDAI ≤ 3.3) and Boolean remission was measured before and after treatment. High resolution MRI of the most symptomatic wrist was performed before and after treatment. MRI parameters including RAMRIS subscores, synovial volume (synovitis and tenosynovitis), synovial perfusion (max enhancement, enhancement slope) were measured.
Results: 55 (%) out of 70 ERA patients completed baseline and one-year clinical and MRI assessments. Remission rates for DAS28-ESR, SDAI and Boolean were 60% (33), 44% (24) and 33% (18) respectively. Eight (24%) out of 33 patients with DAS28-ESR remission, showed progression in bone erosion. Four (16.7%) of 24 patients with SDAI remission showed progression in bone erosion while 1 (5%) of 18 patients with Boolean remission showed progression in bone erosion. Patients who achieved remission after treatment had a greater reduction in all MRI-evident inflammation as well as bone erosion. At month 12, MRI-evident joint synovitis, tenosynovitis and bone marrow oedema was still frequently seen in ERA patients with clinical remission though patients who achieved Boolean remission had the lowest levels of joint synovitis (RAMRIS Synovitis= 2.6±0.8 (2.9±1.3 for SDAI remission and 3±1.2 for DAS28-ESR remission); synovitis volume= 1298±1217 mm^3 (1480±1367 mm^3 for SDAI remission and 1520±1584 mm^3 for DAS28-ESR remission); synovitis perfusion of max enhancement= 38±22% (41±24% for SDAI remission and 41±25% for DAS28-ESR remission)), bone marrow oedema (RAMRIS BME score= 0.9±1.1 (1.3±2.6 for SDAI remission and 1.4±2.3 for DAS28-ESR remission)) as well as bone erosion (RAMRIS bone erosion score= 4±5.8 (4.6±5.5 for SDAI remission and 4.3±4.9 for DAS28-ESR remission)) for all patients at one year.
Conclusion: MRI detected inflammation is common even in patients with clinical remission. Patients with Boolean remission had overall less residual inflammation than DAS28-ESR or SDAI remission patients as well as lowest number of patients who had bone erosion progression in remission group at month 12. Treat to target protocols should ideally target Boolean remission.

REFERENCE:

[1] Anandarajah A, Thiele R, Giampoli E et al. Patients with rheumatoid arthritis in clinical remission manifest persistent joint inflammation on histology and imaging studies. J Rheumatol. 2014 Nov;41(11):2153-60.

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SATURDAY, 15 JUNE 2019

Restless lives: Managing fatigue, sleep and pain

OP0347-PARE

THE INFLUENCE OF PAIN ON SLEEP PROBLEMS, MENTAL HEALTH AND USE OF STRONG PAINKILLERS AMONG PATIENTS WITH ARTHRITIS

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Background: Chronic pain is a part of daily life for many people with RMD and leads to reduced quality of life, high risk of losing work ability, impaired functions and a poor social life. The chronic pain also means that many patients need painkillers. In Denmark there is a very high consumption of strong painkillers (opioids) compared to the other countries in Scandinavia. Therefore, the authorities have a great focus on reducing this and are urging the doctors to reduce the prescription of strong painkillers to patients with chronic pain, including patients with RMDs.
In the Danish Rheumatism Association, we have many inquiries to our professional helpline from patients regarding pain. Especially about the use of painkillers, sleeping problems caused by pain, and the negative influence that pain has on one's mood. The patients experience side effects and discomfort associated with the painkillers. Some must phase out their consumption of strong painkillers, because of the authorities' focus on this - and have problems with this.
In order to get a more detailed knowledge about the influence of pain among patients with RMD, the Danish Rheumatism Association made this study.
Objectives: To investigate the influence of pain on sleeping problems, mental health and the use of strong painkillers among members of a user-panel.
Methods: The study was carried out in November 2018 as an online questionnaire survey sent to 1328 members of a user-panel in The Danish Rheumatism Association. 69% answered the questionnaire. The user-panel consists of people with at least one RMD. It is not representative of patients with RMD in Denmark.
Results: The most important results are:
Sleep: 67% rarely or never feel fully rested when they wake up in the morning, and 36% takes painkillers to improve their sleep. 69% have experienced that the quality of their sleep has affected their pain negatively.
Mental health: During the past four weeks, 58% have felt that everything is unmanageable for them due to pain, 11% indicated having had thoughts of taking their own life due to pain, and 45% have not wanted to be together with other people because of their pain.
Use of strong painkillers: 83% have pain on a daily basis or several times a week. Among these, 46% have received strong painkillers over the last year, and 78% have not been offered alternatives to strong painkillers.
More results from the survey will be presented on EULAR.
Conclusion: The study indicates that pain and poor quality of sleep, has surprisingly large influence on patient's daily life. More than one third takes painkillers to improve their sleep. Pain seems to have a severe negative influence on their sleep and reversed - poor sleep worsens their pain. Surprisingly many are still using strong painkillers, despite the authorities focus on reducing prescription of strong painkillers, and the patients' state, that they are not been given an alternative to strong painkillers. Finally, the study shows that pain has a surprisingly negative influence on mental health and the patients' hope for the future. In general, it has been a surprise for the Danish Rheumatism Association, that pain has such a huge impact on the participants' daily life, especially on their mental health. Therefore, the organization has been using the result of this study in our political work for better treatment and support to patients with chronic pain in our healthcare system, and in our political campaigning about the importance of a focus on pain among patients with RMDs. It is to be explained on EULAR, how we more concrete have applied the results of the study in our political work.
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OP0348-PARE

FACE ARTHRITIS: WHAT SITUATIONS AFFECT EMOTIONALLY THE PATIENT WITH RHEUMATOID ARTHRITIS AND HOW TO RESOLVE THEM EFFECTIVELY

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Background: WHO defines health as a state of physical, psychological and social well-being. However, patients with rheumatoid arthritis (RA) declare that

treatment is mainly aimed at combating physical affectation and hardly focusses on emotional and social aspects.
Objectives: To identify the situations that produce the greatest negative emotional impact in RA patients and to assess the coping strategies used.
Methods: A previous phase (Project OpinAR) (1) identified situations with negative emotional and social impact. In this project, 2 stages were developed: a) A nominal group of patients, following the McMillan method, selected the most emotionally affected situations from the previous list; b) Voting of patients and rheumatologists to assess the assumed effectiveness of 8 coping strategies for each situation with a Likert scale of 1 to 10 (minimum and maximum): proactive resolution, self-criticism, emotional expression, desiderative thinking, social support, cognitive restructuring, avoidance of problems and social withdrawal. The median, interquartile range (IQR), and statistical significance of the differences between patients and physicians (Student's T test) were calculated with a cut-off value of p=0.05. The strategies valued with 8, 9 and 10 were recommended and those valued as 1, 2 or 3 were discouraged. The study was approved by the Ethical Research Committee of the Hospital of La Princesa.
Results: 107 patients from all the Autonomous Communities and 31 expert rheumatologists from 13 Autonomous Communities were recruited, of which 100 (93%) and 17 (55%) participated in the study in a valid way, respectively.
The four situations that most negatively affect them, in the opinion of patients and their doctors are: i) The patient feels that his disease evolves worse than what the doctor says, ii) The patient does not know aspects of the control and monitoring of his disease, iii) The patient feels that he does not really participate in the decision making, and iv) The patient is dissatisfied with the overall treatment received. Regarding coping strategies, doctors recommended using proactive resolution in all situations more frequently than patients ($p<0.05$ for all situations, low variability, with IQR ≤ 2 among physicians) as well as emotional expression ($p<0.05$ for 3 situations, high variability, with IQR ≥ 3). Other strategies were less valued by doctors and patients, but with similar responses. There was a lot of dispersion (IQR >1) in most cases.
Conclusion: The situations with the greatest negative emotional impact on RA are those that put the doctor and the patient at odds with regard to the perception of the disease and its control and should be treated during visits. The most recommended strategies are proactive resolution and emotional expression. The most discouraged are self-criticism and the avoidance of the problem. Anyway, there is a great variability of opinions and doctors tend to give more extreme responses. Doctors and patients should have a space and willingness to discuss and exchange opinions on how they emotionally face RA.

REFERENCE:

[1] Castañeda S, et al. National Barometer to assess the emotional aspect of the patient with Rheumatoid Arthritis (Spanish). Science and Evidence. Bate Scientia Salus (ISSN 2174-8101). Madrid 2016; vol 3: pp 3-11.

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SATURDAY, 15 JUNE 2019

EULAR Projects in musculoskeletal imaging

OP0349 NEURAL NETWORKS FOR AUTOMATED SCORING OF JOINT DISEASE ACTIVITY ON DOPPLER ULTRASOUND IMAGES

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Background: The development of standardized methods for ultrasound (US) scanning and evaluation of synovitis activity by the
OMERACT-EULAR Synovitis Scoring (OESS) system, is a major step forward in the use of US in the diagnosis and monitoring of patients with inflammatory arthritis. The variation in interpretation of disease activity on US images can affect diagnosis, treatment and outcomes in clinical trials.
Objectives: To investigate if we could utilize neural network architecture for the interpretation of disease activity on Doppler US images, using the OESS scoring system.
Methods: Two state-of-the-art neural networks were used to extract information from 1342 Doppler US images from Rheumatoid Arthritis (RA) patients. One neural network that divided images as either healthy (Doppler OESS score 0 or 1) or diseased (Doppler OESS score 2 or 3). The other to score images across all four of the OESS systems Doppler US scores (0-3). The neural networks were hereafter tested on a new set of RA Doppler US images (n=176). Agreement between rheumatologist's scores and network scores was measured with the kappa statistic.
Results: For the neural network assessing healthy/diseased score, the highest accuracies compared to an expert rheumatologist were 86.4% and 86.9% with a sensitivity of 0.864 and 0.875 and specificity of 0.864 and 0.864, respectively. The other neural network developed to four class Doppler OESS scoring achieved an average per class accuracy of 75.0%, and a quadratically weighted kappa score of 0.84.
Conclusion: This study is the first to show that neural network technology can be used in the scoring of disease activity on Doppler US images according to the OESS system.
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OP0350 ULTRASOUND POWER DOPPLER SEMI-QUANTITATIVE SCORING, IS IT TIME WE MOVED TO A RED PIXEL DENSITY ALGORITHMIC PROGRAM TO DETERMINE TRUE TREATMENT RESPONSE?

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Background: The introduction of the semi-quantitative (SQ) grey-scale and power Doppler (PD) 0-3 scoring system, as agreed by the EULAR-OMERACT ultrasound (US) working group (1, 2), has undoubtedly been the most recognised and accepted method in both clinical practice and trials. Studies have suggested that the SQ scoring method is reliable as the quantitative when scoring the grey-scale (3, 4). Additional studies have shown that the use of red pixels in determining the PD signal in tenosynovitis, compared to SQ scoring was not different (5). However, the distribution of the SQ PD score over estimated the percentage compared to the quantitative score, which could reflect treatment responses inaccurately (6).
Objectives:
1. To describe how a quantitative pixel density score maps to a SQ PD score.
2. Can using a 0–4 PD grading scale better distribute the PD percentages, as determined by pixel count, than 0–3 scale?

Methods: Patients were selected from an observational study of 122 DMARD naïve patients (PEAC study REC: 05/Q0703/198; IRAS Project ID:60271) and 60 DMARD failure patients treated with anti-TNF (THERAPIST study, MREC: 15/SC/0045; IRAS Project ID:147240). All patients were classified according to the 1987 ACR or 2010 ACR/EULAR criteria for rheumatoid arthritis. In total 334 images were analysed, from a total of 127 patients. The calculator for the US PD signal/synovial area ratio was created on software MATLAB 2018b. PD was scored according to the SQ definitions for the visual grade 0-3 and 0-4 scoring systems (Figure 1A). Agreement between two readers using 80 US images: ICC SH —0.82 (interval 0.79–0.9), ICC PD —0.93 (interval 0.9–0.95), calculated using SPSS software. The results were analysed using R v3.4.2.
Results: The SQ grade 3 score was shown to over estimate PD signal/synovial area ratio, with a mean ratio of only 40.8%. Figure 2A, illustrates how the spread in PD signal varied within a single grade, in this case SQ grade 3. Figure 1B showed that adding a SQ grade 4 reduced the SD in the SQ grade 3 group but increased the SD overall by causing a larger SD in SQ grade 1, 2 and 4 grades.
A k-means (KM) clustering algorithm was used to find the most efficient ratio cut off points for a SQ grade 3 scoring system. The SQ grades are not taken into account for this scoring system, it is based on the mathematically optimum cut off points (Figure 1C). It is seen that the SD dramatically reduced in the KM score and the 95% confidence interval and grade overlaps.
When comparing the KM score with the SQ score it was shown to be significantly dependent (Pearson's Chi squared p-value <2.2e-16) and strongly positively correlated (Spearman's 0.84, p–value <2.2e-16), this is illustrated in Figure 2B and C. Furthermore, the KM score was seen to have a stronger linear correlation (Pearson's 0.95, p-value <2.2e-16) when compared to the SQ score (0.82, p-value <2.2e-16).

Conclusion: The 0-4 SQ grade was not equivalent to that of the 0-3 SQ grade used PD scoring and it increased the variance in the majority of SQ grades. This study does show that the PD pixel algorithm has a stronger linear correlation when compared to the SQ grading, suggesting a more accurate method at interpreting treatment response, as the intervals between grades are more equal. Therefore, built in algorithms to detect PD signal in US machines are the future for drug monitoring in inflammatory arthritis.

REFERENCES:

[1] D'Agostino et al. RMD 2017.

Figure 1. A) Definitions of US PD scoring scale 0-3 using the OMERACT grading system and a revised 0-4 score. B) Comparison between SQ 0-3 and 0-4 PD score, with the mean and standard deviation and 95% confidence intervals of PD signal/synovial area ratio. C) Scoring system found by K-means clustering algorithm showing the optimum ratio boundaries and the mean standard deviation and 95% confidence intervals of the ratio in each quantitative grade 0-3.

A

Synovitis grade	Power Doppler OMERACT score	Power Doppler revised score
Grade 0 (normal)	No Doppler signal	No Doppler signal
Grade 1 (minimal)	Up to three single Doppler spots OR up to one confluent spot and two single spots OR up to two confluent spots	1-2 Doppler spots OR up to one confluent spot
Grade 2 (mild)	>Grade 1 but ≤50% Doppler signals in the total greyscale background	More than 2 Doppler spots or scattered single spots or <25% Doppler signals in the total greyscale background
Grade 3 (moderate)	>Grade 2 (>50% of the total greyscale background)	25-50% Doppler signals in the total greyscale background
Grade 4 (severe)		>50% of the total greyscale background

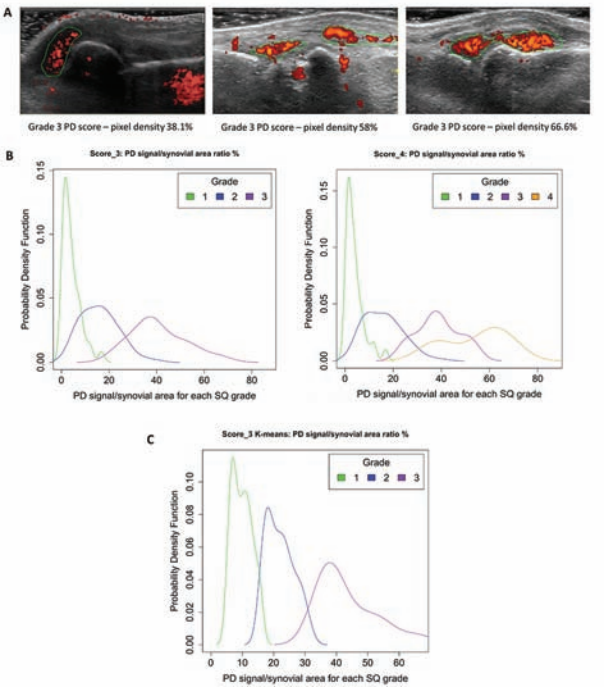
B

SQ PD Grade	0	1	2	3	4
3-Score					
Mean	0.02%	4.14%	16.02%	40.8%	
SD	0.09%	3.71%	8.14%	11.74%	
95% CI Upper	0.20%	11.56%	32.30%	64.28%	
95% CI Lower	-0.16%	-3.28%	-0.26%	17.32%	
4-Score					
Mean	0.02%	3.92%	15.82%	38.72%	54.25%
SD	0.09%	3.69%	8.19%	9.01%	14.63%
95% CI Upper	0.20%	11.30%	32.20%	56.74%	83.51%
95% CI Lower	-0.16%	-3.46%	-0.56%	20.70%	24.99%

C

K-means Grade	0	1	2	3
Ratio Boundaries	[0,5.30)	[5.30, 15.97)	[15.97,32.79)	[32.79,100)
Mean	0.7%	9.9%	22.03%	43.55%
SD	1.33%	3.10%	4.38%	9.47%
95% CI Upper	-1.96%	3.70%	13.27%	24.61%
95% CI Lower	3.36%	16.10%	30.79%	62.49%

Figure 2. A) US images demonstrating the spread in PD signal/synovial area ratio with the same SQ PD grade 3 score. B) Comparison between SQ 0-3 and 0-4 PD grading, illustrating the spread of the PD signal/synovial area percentage ratio in each SQ grade category. C) Density graph using K-means statistical test demonstrating how the spread between the individual grades can be minimised compared to the 3 score PD signal/synovial area ratio in Figure 2B.



[2] Terslev et al. RMD 2017.
[3] Terslev et al. Rheum 2012.
[4] Dougadous et al. ARD 2010.
[5] Ammitzboll-Danielsen et al. Rheum 2016.
[6] Schmidt et al. Rheum 2015.

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Late breaking abstract session

LB0003

EFFICACY AND SAFETY OF FILGOTINIB FOR PATIENTS WITH RHEUMATOID ARTHRITIS NAÏVE TO METHOTREXATE THERAPY: FINCH3 PRIMARY OUTCOME RESULTS

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Background: Filgotinib (FIL), an orally administered, potent, selective inhibitor of Janus kinase 1 (JAK1), has shown good efficacy and was well tolerated for treatment of rheumatoid arthritis (RA).
Objectives: To compare efficacy and safety of FIL with and without methotrexate (MTX) in patients with RA who were naïve to MTX therapy.
Methods: This phase 3, double-blind, active-controlled study randomized patients with moderately to severely active RA (2:1:1:2) to FIL 200mg daily + MTX weekly (up to 20mg), FIL 100mg + MTX, FIL 200mg (+placebo [PBO]), or MTX (+PBO) for up to 52 weeks; results through week 24 are presented. Primary efficacy endpoint was proportion of patients achieving ACR20 response at week 24; additional assessments included ACR50 and ACR70 responses; DAS28-CRP score ≤3.2 and <2.6, and changes in van der Heijde mTSS, HAQ-DI, SF-36 PCS, and FACIT-Fatigue. Safety endpoints included types and rates of adverse events (AEs). Logistic regression adjusting for stratification factors with nonresponder imputation was used for treatment comparisons for ACR response and other binary endpoints. Mixed-effect model adjusting for baseline value, stratification factors, treatment, visit, and treatment by visit interaction as fixed effects with observed cases was used for continuous endpoints.
Results: Of 1,252 randomized patients, 1,249 received study drug (416 FIL 200mg+MTX; 207 FIL 100mg+MTX; 210 FIL 200mg monotherapy; 416 MTX monotherapy) and were analyzed; 1,130 completed week 24. Most (76.9%) were female; mean time since RA diagnosis was 2.2 years (median 0.4 years); mean (standard deviation [SD]) DAS28-CRP was 5.7 (1.0); and 35.9% were using oral steroids at baseline. At week 24, significantly more patients in the FIL 200mg +MTX (81.0%; *P*<0.001) and FIL 100mg+MTX (80.2%; *P*<0.05) arms achieved an ACR20 response compared to MTX monotherapy (71.4%)(Table 1). Compared to MTX monotherapy, more patients receiving FIL with or without MTX achieved

Table 1. Efficacy Outcomes at Week 24[a]

	FIL 200 mg + MTX (N = 416)	FIL 100 mg + MTX (N = 207)	FIL 200 mg Monotherapy (N = 210)	MTX Monotherapy (N = 416)
ACR20, %	81.0***	80.2*	78.1	71.4
ACR50, %	61.5***	57.0**	58.1**#	45.7
ACR70, %	43.8***	40.1***	40.0***#	26.0
DAS28-CRP ≤ 3.2, %	68.8***#	62.8***#	60.0***#	46.2
DAS28-CRP < 2.6, %	54.1***	42.5***	42.4***#	29.1
mTSS, mean change from BL	0.20	0.22	−0.04**#	0.52
HAQ-DI, mean change from BL	−0.94***	−0.90**	−0.89**#	−0.79
SF-36 PCS, mean change from BL	12.3***#	11.1*#	10.4	9.7
FACIT-Fatigue, mean change from BL	10.6	11.4	10.2	10.1

[a]All patients who were randomized and received at least 1 dose of study drug were included in efficacy analyses.
*P<0.05 vs MTX monotherapy; **P<0.01 vs MTX monotherapy; ***P<0.001 vs MTX monotherapy; #Comparison not adjusted for multiplicity.
ACR20/50/70, 20%/50%/70% improvement in American College of Rheumatology criteria; BL, baseline; DAS28-CRP, Disease Activity Score based in 28 joints with C-reactive protein; FACIT, Functional Assessment of Chronic Illness Therapy; FIL, filgotinib; HAQ-DI, Health Assessment Questionnaire Disability Index; mTSS, modified total Sharp score; MTX, methotrexate; PBO, placebo; SF-36 PCS, Short-Form 36 Physical Component Summary.

Table 2. Safety Events of Interest through Week 24

Patients with event, n (%)	FIL 200 mg + MTX (N = 416)	FIL 100 mg + MTX (N = 207)	FIL 200 mg Monotherapy (N = 210)	MTX Monotherapy (N = 416)
Serious AEs	17 (4.1)	5 (2.4)	10 (4.8)	12 (2.9)
Serious infections	4 (1.0)	2 (1.0)	3 (1.4)	4 (1.0)
Herpes zoster	2 (0.5)	1 (0.5)	1 (0.5)	2 (0.5)
Adjudicated MACEs	2 (0.5)	0	1 (0.5)	2 (0.5)
Venous thrombotic events	0	0	0	1 (0.2)
Malignancies	0	0	0	1 (0.2)
Deaths	1 (0.2)[a]	0	0	0

[a]Cause of death was lupus myocardiopathy.
AE, adverse event; MACE, major adverse cardiovascular event

ACR50 and ACR70 responses, DAS28-CRP <2.6 and ≤3.2, and reported improvements in SF-36 PCS (Table 1). The onset of activity was rapid, with significantly more patients achieving ACR50 and DAS28-CRP <2.6 with FIL than MTX at week 2. The FIL safety profile was consistent with prior studies through week 24 (Table 2).

Conclusion: The JAK1 inhibitor FIL in combination with MTX led to significant improvements in RA signs and symptoms, physical function, and patient-reported outcomes compared to MTX alone and was well tolerated in patients with early active RA naïve to MTX. Clinically meaningful response to FIL occurred as early as 2 weeks after treatment initiation.

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LB0004 METHOTREXATE WITHDRAWAL IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVE LOW DISEASE ACTIVITY WITH TOFACITINIB MODIFIED-RELEASE 11 MG ONCE DAILY + METHOTREXATE: A RANDOMISED NON-INFERIORITY PHASE 3B/4 STUDY

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). The impact of methotrexate (MTX) withdrawal in patients (pts) with RA who achieve low disease activity (LDA) or remission following treatment with tofacitinib in combination with MTX is unclear.

Objectives: To compare the efficacy and safety of tofacitinib modified-release (MR) 11 mg once daily (QD) with and without MTX in pts with RA who have achieved LDA with tofacitinib and MTX.

Methods: ORAL Shift (NCT02831855) was a global Phase 3b/4 study in pts aged ≥18 years with moderate to severe RA and an inadequate response to MTX. Pts received open-label (OL) tofacitinib MR 11 mg QD with MTX (tofacitinib + MTX) for 24 weeks. Pts achieving LDA (CDAI ≤10) at Week (W)24 entered the 24-week double-blind (DB) MTX withdrawal phase and were randomised 1:1 to receive tofacitinib MR 11 mg QD with placebo (tofacitinib monotherapy; ie underwent blinded MTX withdrawal) or continue tofacitinib + MTX. The primary endpoint was least squares mean change from W24 to W48 (Δ; DB phase) in DAS28 4(ESR). Non inferiority of tofacitinib monotherapy vs tofacitinib + MTX was declared if the upper bound of the 95% two-sided confidence interval (CI) for the difference in ΔDAS28-4(ESR) between arms was <0.6. Secondary endpoints included ΔDAS28-4(CRP), ΔSDAI, ΔCDAI, ΔHAQ-DI; rates of ACR20/50/70 response, HAQ-DI response, DAS28-4(ESR)- and CDAI-defined LDA and remission, and ACR-EULAR Boolean-defined[1] remission (W48); and safety (OL and DB phases).

Results: Of 694 pts in the OL phase, 530 achieved CDAI-defined LDA at W24 and were treated in the DB phase (tofacitinib monotherapy: n=264; tofacitinib + MTX: n=266). Demographics and pt characteristics at OL-phase baseline were similar between treatment arms. The difference (95% CI) between arms in ΔDAS28 4(ESR) (primary endpoint) was 0.30 (0.12, 0.48; Table 1) at W48, demonstrating that tofacitinib monotherapy was non-inferior to tofacitinib + MTX. Consistent with the primary endpoint, ΔDAS28-4(CRP)/SDAI/CDAI were greater for tofacitinib monotherapy vs tofacitinib + MTX, but these differences were not clinically meaningful; ACR/HAQ-DI response and LDA rates were generally similar between arms (Table). Remission rates were also similar between arms and generally did not change after MTX withdrawal. In the DB phase, rates of AEs, serious AEs, discontinuations due to AEs and AEs of special interest were generally comparable between arms (Table 1).

Table: Efficacy and safety outcomes during the double-blind MTX withdrawal phase (W24 [randomisation] to W48)

	Tofacitinib MR 11 mg QD monotherapy N=264[a]		Tofacitinib MR 11 mg QD + MTX N=266[a]	
Efficacy				
Change from W24 to W48, least squares mean (95% CI)				
DAS28-4(ESR) (primary endpoint)	0.33 (0.20, 0.46)		0.03 (-0.10, 0.16)	
Least squares mean (95% CI) difference, tofacitinib monotherapy minus tofacitinib + MTX	0.30 (0.12, 0.48)[b]			
DAS28-4(CRP)	0.29 (0.16, 0.41)		0.01 (-0.11, 0.13)	
SDAI	3.16 (2.18, 4.15)		0.94 (-0.03, 1.91)	
CDAI	2.97 (2.03, 3.90)		0.84 (-0.09, 1.76)	
HAQ-DI	0.01 (-0.04, 0.07)		-0.00 (-0.06, 0.05)	
Response, n (%)	**W24**	**W48**	**W24**	**W48**
ACR20[c]	250 (94.7)	193 (73.1)	250 (94.0)	212 (79.7)
ACR50[c]	205 (76.9)	146 (55.3)	213 (80.1)	179 (67.3)
ACR70[c]	122 (46.2)	100 (37.9)	122 (45.9)	114 (42.9)
HAQ-DI[d]	200 (75.8)	181 (68.6)	209 (78.6)	200 (75.2)
LDA, n (%)	**W24**	**W48**	**W24**	**W48**
DAS28-4(ESR) ≤3.2	134 (50.8)	119 (45.1)	137 (51.5)	132 (49.6)
CDAI ≤10[e]	262 (99.2)	172 (65.2)	262 (98.5)	205 (77.1)
Remission, n (%)	**W24**	**W48**	**W24**	**W48**
DAS28-4(ESR) <2.6	80 (30.3)	63 (23.9)	76 (28.6)	80 (30.1)
CDAI ≤2.8	72 (27.3)	75 (28.4)	74 (27.8)	82 (30.8)
ACR-EULAR Boolean[f]	62 (23.5)	59 (22.4)	60 (22.6)	63 (23.7)
Safety				
AEs, n (%)	107 (40.5)		109 (41.0)	
SAEs, n (%)	10 (3.8)		5 (1.9)	
Discontinuations due to AEs, n (%)	5 (1.9)		5 (1.9)	
Deaths, n (%)	0		2 (0.8)	
Most common (≥2%) AEs by MedDRA PT, n (%)				
Arthralgia	7 (2.7)		2 (0.8)	
ALT increased	5 (1.9)		10 (3.8)	
AST increased	5 (1.9)		6 (2.3)	
Nasopharyngitis	5 (1.9)		7 (2.6)	
URTI	4 (1.5)		6 (2.3)	
Bronchitis	3 (1.1)		7 (2.6)	
AEs of special interest, n (%)				
Serious infections	2 (0.8)		2 (0.8)	
Herpes zoster[g]	2 (0.8)		3 (1.1)	
Malignancies excluding NMSC[h]	1 (0.4)		0	
NMSC[i]	1 (0.4)		1 (0.4)	
MACE[j]	0		1 (0.4)[k]	

[a]Efficacy data are from the full analysis set (all patients who received at least one dose of tofacitinib + MTX during the open-label phase, and were randomised and received at least one dose of tofacitinib + MTX or tofacitinib monotherapy in the double-blind phase). Continuous endpoint results are from a mixed-effect model of repeated measures. Binary data are calculated using non-responder imputation. The number of patients who completed each efficacy outcome measure (n) may be less than the overall N. The safety analysis set during the double-blind phase is the same as that for efficacy. [b]Non-inferiority criteria were met; upper bound of 95% CI was <0.6. [c]20/50/70% improvement in tender and swollen joint counts and 20/50/70% improvement in three of the five other criteria (PtGA, PGA, HAQ-DI, Pain [VAS], ESR), relative to open-label phase baseline; [d]HAQ-DI decrease of ≥0.22, relative to open-label phase baseline; [e]Due to protocol deviations, some patients who had not achieved LDA at W24 (randomisation) were randomised and received study treatment; they were therefore included in the analysis; [f]At herpes zoster events reported involved one or two adjacent dermatomes and were non-serious; [g]Adjudicated events; [h]Occurred >28 days after the last dose of the study treatment

ACR, American College of Rheumatology; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CDAI, Clinical Disease Activity Index; CI, confidence interval; DAS28-4(CRP), Disease Activity Score in 28 joints, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDA, low disease activity; MACE, major adverse cardiovascular event; MedDRA, Medical Dictionary for Regulatory Activities; MR, modified-release; MTX, methotrexate; NMSC, non-melanoma skin cancer; PGA, Physician Global Assessment; PT, preferred term; PtGA, Patient Global Assessment; QD, once daily; SAE, serious adverse event; SDAI, Simplified Disease Activity Index; URTI, upper respiratory tract infection; VAS, visual analogue scale; W, Week

Conclusion: Pts receiving tofacitinib MR 11 mg QD + MTX who achieve LDA may withdraw MTX up to W48 without significant worsening of disease activity. Pts in remission tend to remain in remission after MTX withdrawal. Safety appeared consistent with the known profile of tofacitinib.

REFERENCE

[1] Felson DT *et al. Arthritis Rheum* 2011;63:573-586

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LB0005

MULTICENTRE, RANDOMISED, OPEN-LABEL, ASSESSOR-BLINDED, PARALLEL-GROUP HEAD-TO-HEAD COMPARISON OF THE EFFICACY AND SAFETY OF IXEKIZUMAB VERSUS ADALIMUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS NAIVE TO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS: 24-WEEK RESULTS

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Background: There have been few head-to-head clinical trials comparing different biologic disease-modifying anti-rheumatic drugs (bDMARDs) in patients (pts) with psoriatic arthritis (PsA).

Objectives: To report 24-week (wk) results of a study directly comparing efficacy and safety of ixekizumab (IXE), an IL-17A inhibitor, and adalimumab (ADA), a TNF inhibitor, in bDMARD-naive pts with PsA.

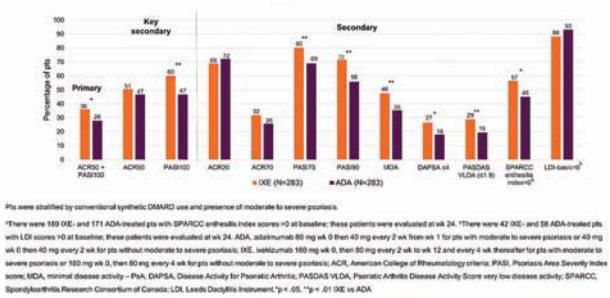
Methods: The study (NCT03151551; SPIRIT-H2H) included pts with active PsA (≥3 TJC + ≥3SJC) and plaque psoriasis (BSA ≥3%) who were bDMARD naive and inadequate responders to csDMARD therapy. Patients were randomised (1:1) to IXE or ADA for 52 wks (on-label dosing based on presence/absence of moderate to severe psoriasis). The primary objective was superiority of IXE vs ADA measured by the proportion of pts achieving both ACR50 and PASI100 responses at wk 24. Key secondary objectives versus ADA at wk 24 were (1) non-inferiority of IXE for ACR50 (noninferiority margin -12%) and (2) superiority of IXE for PASI100. Additional PsA, skin, composite treat-to-target (T2T: MDA, DAPSA 4), PASDAS remission and patient-reported outcomes, and safety were assessed. Nine pts had PASI=0 and BSA≥3% (a medical inconsistency) at baseline; these pts were considered PASI100 responders if PASI=0 and BSA=0 at wk 24. Categorical variables were evaluated using logistic regression analyses with NRI in the ITT population. Continuous variables were analysed using mixed models for repeated measure analysis.

Results: 566 pts were randomised (283 to IXE and 283 to ADA). Baseline demographics and disease characteristics were generally well balanced between groups (Table 1). All primary and key secondary efficacy endpoints at wk 24 were met (Figure). The proportion of pts achieving both ACR50 and PASI100 was significantly greater for IXE than ADA (36% vs 28%; p<0.05). IXE was non-inferior to ADA for ACR50 response and superior for PASI100 response (Figure). While improvements from baseline were achieved with both treatments, significantly better results were seen with IXE vs ADA for skin and composite T2T outcomes, enthesitis resolution (Figure 1), and skin-related quality of life (Table 2). No unexpected safety signals were observed.

Table 1. Patient baseline demographics/characteristics

	IXE (N=283)	ADA (N=283)
Age, years	47.5 (12.0)	48.3 (12.3)
Male, n (%)	162 (57)	150 (53)
PsA duration since diagnosis, years	6.6 (7.4)	5.9 (6.4)
Concomitant csDMARD use, n (%)	193 (68)	199 (70)
TJC	19.1 (12.7)	21.3 (15.4)
SJC	10.1 (7.5)	10.7 (8.1)
PASI	7.9 (8.7)	7.7 (7.3)
Data are mean (SD), unless stated otherwise		

Figure



Pts were stratified by conventional synthetic DMARD use and presence of moderate to severe psoriasis.

*There were 189 IXE- and 171 ADA-treated pts with SPARCC enthesitis index scores >0 at baseline; these patients were evaluated at wk 24. †There were 42 IXE- and 58 ADA-treated pts with LDI scores >0 at baseline; these patients were evaluated at wk 24. ADA, adalimumab 80 mg wk 0 then 40 mg every 2 wk from wk 1 for pts with moderate to severe psoriasis or 40 mg wk 0 then 40 mg every 2 wk for pts without moderate to severe psoriasis; IXE, ixekizumab 160 mg wk 0, then 80 mg every 2 wk to wk 12 and every 4 wk thereafter for pts with moderate to severe psoriasis or 160 mg wk 0, then 80 mg every 4 wk for pts without moderate to severe psoriasis; ACR, American College of Rheumatology criteria; PASI, Psoriasis Area Severity Index score; MDA, minimal disease activity – PsA; DAPSA, Disease Activity for Psoriatic Arthritis; PASDAS VLDA, Psoriatic Arthritis Disease Activity Score very low disease activity; SPARCC, Spondyloarthritis Research Consortium of Canada; LDI, Leeds Dactylitis Instrument. †p < .05, ‡p < .01 IXE vs ADA

Table 2. Patient reported outcomes

	IXE (N=283)		ADA (N=283)	
	Baseline	LS mean change at wk 24	Baseline	LS mean change at wk 24
HAQ-DI	1.20	-.63	1.27	-.56
SF-36 PCS	36.80	9.96	36.12	8.82
SF-36 MCS	45.40	4.47	44.85	3.93
Dermatology Life Quality Index	9.77	-7.81*	9.82	-6.48
Fatigue Severity Numeric Rating Scale	5.87	-2.66	6.46	-2.53
LS, least square; *p<.001 vs ADA				

Conclusion: In bDMARD naive pts with active PsA and skin disease, IXE showed superior efficacy to ADA based on simultaneous achievement of ACR50 and PASI100 responses at wk 24. Greater improvements with IXE vs ADA were also attained in individual PsA domains and composite T2T outcomes.

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LB0006 SUBCUTANEOUS SECUKINUMAB 300MG AND 150MG PROVIDES SUSTAINED INHIBITION OF RADIOGRAPHIC PROGRESSION IN PSORIATIC ARTHRITIS OVER 2 YEARS: RESULTS FROM THE PHASE 3 FUTURE-5 TRIAL

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Background: Secukinumab (SEC) provided sustained clinical efficacy, and inhibition of radiographic progression over 52 Weeks (Wks) in patients (pts) with psoriatic arthritis (PsA) in the FUTURE 5 study[1].
Objectives: To report the effect of SEC on radiographic progression at Wk 104 (2 years) in PsA pts in the FUTURE 5 study.
Methods: Adults (N=996) with active PsA, stratified by prior anti-TNF therapy (naïve and inadequate response/intolerance [IR]) were randomised 2:2:2:3 to subcutaneous SEC 300mg with loading dose (LD; 300mg), 150mg LD (150mg), 150mg no LD, or placebo at baseline (BL), Wks 1, 2, 3, 4, and every 4 wks thereafter. Pts could have SEC dose escalated from 150 to 300 mg starting from Wk 52, based on physicians' judgement. Data are shown for pts originally randomised to SEC; 150mg groups include pts who had dose escalated to 300mg. Concomitant MTX (≤25 mg/week) was allowed. Radiographic progression (mean change in van der Heijde-modified total Sharp score [vdH-mTSS] and its components: erosion and joint space narrowing [JSN] scores, was based on hand/wrist/foot X-rays obtained at BL and Wk 104, and assessed by two blinded readers (plus an adjudicator if required). Other efficacy endpoints included ACR20/50, PASI90 and resolution of dactylitis and enthesitis.

Table. Summary of Efficacy Results

Mean change in vdH-mTSS scores from BL to Wk 104 (BL score)			
	300mg N=222 n=191	**150mg group* N=220 n=181**	**150mg no LD group* N=222 n=169**
vdH-mTSS	0.37 (12.07)	0.52 (11.47)	0.41 (13.99)
Erosion	0.27 (7.15)	0.27 (6.67)	0.38 (8.07)
JSN	0.11 (4.92)	0.24 (4.79)	0.03 (5.92)
Clinical responses at Wk 104 (% responders [n])			
	300 mg N = 222	**150 mg group* N = 220**	**150 mg no LD group* N = 222**
ACR20	77.0 (187)	79.4 (175)	78.0 (168)
ACR50	51.9 (187)	52.6 (175)	57.7 (168)
PASI90[1]	70.1 (97)	59.2 (103)	62.6 (91)
Resolution of enthesitis[2]	78.0 (118)	80.3 (117)	69.5 (95)
Resolution of dactylitis[3]	82.8 (64)	85.5 (62)	89.3 (75)

Observed data

*150mg and 150mg no load arms include 86 and 92 pts, respectively, who were dose escalated at Wk 52 or later.

N, number of pts randomised; n, number of pts with data at BL and Wk 104.

Data from pts with: [1]BL psoriasis ≥3% body surface area, [2]enthesitis at BL, [3]dactylitis at BL

Results: Overall, 84.7% (300mg), 82.3% (150mg) and 75.2% (150mg no LD) pts completed 2 years of treatment. A total of 86 (39%) and 92 (41%) pts had their dose escalated to 300mg in the 150mg and 150mg no LD groups, respectively. Inhibition of radiographic progression was sustained with SEC through 2 years (Table 1). Proportions of pts with no radiographic progression (change from BL in mTSS ≤0.5) with SEC were 89.5% (300 mg), 82.3% (150 mg), and 81.1% (150 mg no LD) at 2 years; corresponding proportion of pts for change from BL in mTSS ≤0.0 were: 81.2%, 69.1% and 73.4%, respectively. Clinical responses were also sustained through 2 years (Table 1).
Conclusion: Subcutaneous secukinumab provided sustained inhibition of radiographic progression and sustained clinical responses through 2 years of treatment in pts with active PsA.

REFERENCE

[1] Mease PJ *et al. Arthritis Rheumatol* 2018;70(suppl 10).

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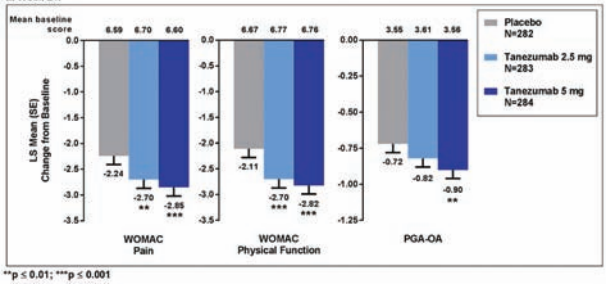
LB0007 SUBCUTANEOUS TANEZUMAB FOR OSTEOARTHRITIS PAIN: A 24-WEEK PHASE 3 STUDY WITH A 24-WEEK FOLLOW UP

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Background: Tanezumab, a monoclonal antibody against nerve growth factor, is in development for treatment of osteoarthritis (OA) pain.
Objectives: To assess efficacy and safety of tanezumab in patients with moderate to severe OA pain who have not responded to or cannot tolerate standard of care analgesics.
Methods: A randomized, double-blind, placebo-controlled study (24 week treatment; 24 week follow-up) was conducted in patients in Europe and Japan with moderate to severe OA pain of the knee or hip and history of insufficient pain relief or intolerance to acetaminophen, oral nonsteroidal anti-inflammatory drug, and either tramadol or opioids (or unwilling to take opioids). Patients received subcutaneous tanezumab (2.5 or 5 mg) or placebo at baseline, week 8, and week 16. Co-primary endpoints were change from baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Physical Function, and Patient Global Assessment of OA (PGA-OA) scores at week 24. Safety, including independent adjudication of joint safety events, was assessed.
Results: Tanezumab 5 mg met all co-primary endpoints (Fig. 1). Tanezumab 2.5 mg met WOMAC Pain and Physical Function endpoints but not the PGA-OA endpoint; thus, this dose did not meet pre-specified efficacy criteria. The occurrence

of adverse events (AEs) and discontinuations due to AEs were similar across groups, though serious AEs occurred more frequently in both tanezumab groups relative to placebo. Two deaths in the 5 mg tanezumab group were deemed unrelated to treatment. The only AE occurring in =3% of patients in any group, and more frequently (>1% difference) in both tanezumab groups relative to placebo, was OA. Total joint replacements (TJR) occurred in 6.7%, 7.8%, and 7.0% of patients in the placebo, tanezumab 2.5 mg, and tanezumab 5 mg groups, respectively. Joint safety events, including TJRs, were mostly adjudicated as normal progression of OA (58/79; 73.4%). Pre-specified joint safety events occurred in 0% and 2.5% (n = 14) of patients in the placebo and tanezumab (2.5 mg = 1.8%; 5 mg = 3.2%) groups, respectively. These 14 events in the tanezumab groups included rapidly progressive OA (2.5 mg n = 4; 5 mg n = 8), subchondral insufficiency fracture (2.5 mg n = 1), and primary osteonecrosis (5 mg n = 1).

Figure 1. Change from baseline in WOMAC Pain, WOMAC Physical Function, and Patient Global Asessment of OA scores at Week 24.



**p ≤ 0.01; ***p ≤ 0.001

Table 2. Treatment-Emergent AEs During the Treatment Period (All Causalities)

N (%) of patients	Placebo N=282	Tanezumab 2.5 mg N= 283	Tanezumab 5 mg N= 284
AE	155 (55.0)	150 (53.0)	162 (57.0)
Serious AE	3 (1.1)	8 (2.8)	9 (3.2)
Discontinued study due to AE	2 (0.7)	5 (1.8)	1 (0.4)
Discontinued treatment but continued study	7 (2.5)	3 (1.1)	4 (1.4)
Common AEs[a]			
Arthralgia	34 (12.1)	27 (9.5)	23 (8.1)
Nasopharyngitis	25 (8.9)	31 (11.0)	22 (7.7)
Back pain	15 (5.3)	16 (5.7)	17 (6.0)
Headache	18 (6.4)	15 (5.3)	14 (4.9)
Osteoarthritis	5 (1.8)	9 (3.2)	13 (4.6)
Paraesthesia	5 (1.8)	5 (1.8)	12 (4.2)
Influenza	5 (1.8)	5 (1.8)	9 (3.2)
Fall	8 (2.8)	12 (4.2)	7 (2.5)
Pain in extremity	7 (2.5)	9 (3.2)	5 (1.8)

[a] Occurring in ≥3% of patients in any group.

Conclusion: Tanezumab 5 mg significantly improved all co-primary endpoints of pain, physical function, and PGA-OA. Tanezumab 2.5 mg significantly improved pain and physical function, but did not reach significance on PGA-OA. AEs are consistent with previous studies of tanezumab in OA. A similar number of TJRs were reported across groups, though overall joint safety events were more frequent with tanezumab than placebo.

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LB0008

THE EFFECT OF HLA-DRB1 RISK ALLELES ON THE CLINICALEFFICACY OF ABATACEPT AND ADALIMUMAB IN SEROPOSITIVE BIOLOGIC-NAÏVE PATIENTSWITH EARLY, MODERATE-TO-SEVERE RA: DATA FROM A HEAD-TO-HEAD SINGLE-BLINDEDTRIAL

William Rigby[1], Jane Buckner[2], Lou Bridges[3], Marleen Nys[4], Sheng Gao[5], Martin Polinsky[5], Alyssa Johnsen[5], Neelanjana Ray[5], Vivian Bykerk[6]*[1]Dartmouth-Hitchcock Medical Center, Lebanon, United States of America*; *[2]Benaroya Research Institute, Seattle, United States of America*; *[3]University of Alabama School of Medicine, Birmingham, United States of America*; *[4]Bristol-Myers Squibb, Braine-l'Alleud, Belgium*; *[5]Bristol-Myers Squibb, Princeton, United States of America*; *[6]Hospital for Special Surgery, New York, United States of America*

Background: Mechanistic differences between biologics are poorly understood. *HLA-DRB1* alleles containing the shared epitope (SE), which are strongly associated with RA, are present in 85% of anti-cyclic citrullinated protein 2 (anti-CCP2) + patients (pts) with RA (Jiang *et al. Arthritis Rheumatol* 2015). In a prior retrospective exploratory analysis, abatacept (ABA) was more effective in SE+ vs SE- pts (Oryoji *et al. Ann Rheum Dis* 2017). Head-to-head (H2H) comparisons with other agents are lacking.

Objectives: This H2H, single-blinded trial (NCT02557100) in biologic-naïve pts with early, active RA prospectively explored the relationship between *HLA-DRB1* SE and the clinical efficacy of ABA or adalimumab (ADA).

Methods: Adults with early (=12 mths from symptom onset), moderate-to-severe RA (ACR/EULAR 2010 criteria) seropositive for anti-CCP2 (>3x ULN) and RF, were randomised 1:1 to SC ABA 125mg wkly or SC ADA 40mg every 2 wks (both with stable, oral MTX wkly) for 24 wks. Pts were grouped by SE status (+/-) based on *HLA-DRB1* genotype (-: no SE allele; +: =1 SE allele). Safety was analysed throughout the trial and up to 8 wks post last study drug dose. Clinical efficacy was assessed at Wk24 to determine the proportion of ACR20/50/70 responders in ABA vs ADA arms, and the adjusted mean changes from baseline in DAS28 (CRP), SDAI and CDAI. Treatment (tmt) differences between ABA and ADA in SE + and SE– pts were assessed for ACR20/50/70 responders and DAS28 (CRP) remission at Wk24.

Results: 80 pts were treated: 40 ABA (9 SE-, 30 SE+, 1 SE unknown) and 40 ADA (9 SE-, 31 SE+). Baseline characteristics were balanced. Mean (SD) age, disease duration and DAS28 (CRP) were 46.0 (14.4) years, 5.5 (2.6) mths and 5.2 (1.1), respectively; 75% were female. No new safety signals were identified. In each arm, related AEs (ABA: 12 [30%]; ADA: 11 [27.5%]) and related serious AEs (ABA: 0; ADA: 1 [2.5%]) were similar. Numerically higher efficacy responses were seen with ABA vs ADA at Wk24 (Table 1). Similar results were observed for DAS28 (CRP), SDAI and CDAI. In SE+ pts, numerically higher efficacy responses were seen with ABA vs ADA at Wk24; 95% CI for estimated tmt differences for ACR20/50/70 responses and DAS28 (CRP) remission did not cross 0 (Figure 1).

Conclusion: In this seropositive early RA population, numerically higher efficacy responses were seen with abatacept vs adalimumab after 24wks of tmt, with more pronounced tmt differences in SE+ pts. Results are consistent with a previous

Table 1. Clinical outcomes at Wk24: as-treated analysis population

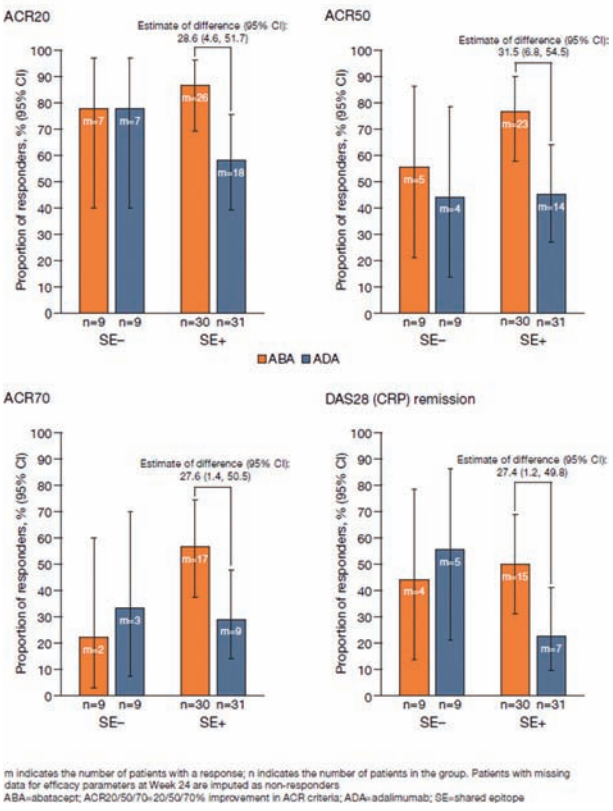
Clinical outcome	ABA (n=40)	ADA (n=40)	Estimate of difference for ABA vs ADA (95% CI)
ACR responses			
ACR20	83 (67, 93)	63 (46, 77)	20 (−3, 42)
ACR50	70 (54, 83)	45 (29, 62)	25 (2, 46)
ACR70	48 (32, 64)	30 (17, 47)	17.5 (−6, 39)
DAS28 (CRP)			
Adjusted mean change* (95% CI)	−2.6 (−2.9, −2.2)	−2.4 (−2.7, −2.1)	0.2 (−0.6, 0.3)†
Remission	48 (32, 64)	30 (17, 47)	17.5 (−6, 39)
SDAI			
Adjusted mean change* (95% CI)	−27.4 (−29.9, −24.9)	−26.1 (−28.7, −23.5)	−1 (−5, 2)†
Remission	35 (21, 52)	23 (11, 39)	12.5 (−11, 35)
CDAI			
Adjusted mean change* (95% CI)	−27.1 (−29.5, −24.7)	−25.0 (−27.5, −22.6)	−2 (−5.5, 1)†

Data are % (95% CI) unless stated otherwise. Estimates of adjusted mean change are from a repeated measures mixed model which includes baseline value, treatment group, time and time by treatment group interaction. Missing values were imputed as non-responders. DAS28 (CRP) remission: DAS28 (CRP) <2.6. SDAI remission: SDAI ≤3.3

*From baseline. †Adjusted mean difference for ABA vs ADA (95% CI).

ABA=abatacept; ACR20/50/70=20/50/70% improvement in ACR criteria; ADA=adalimumab

Figure 1. Clinical outcomes in ABA- vs ADA-treated pts at Wk 24 by SE genotype: as-treated analysis population



m indicates the number of patients with a response; n indicates the number of patients in the group. Patients with missing data for efficacy parameters at Week 24 are imputed as non-responders
ABA=abatacept; ACR20/50/70=20/50/70% improvement in ACR criteria; ADA=adalimumab; SE=shared epitope

study in which greater efficacy was seen with abatacept, but not TNF inhibitors, in anti-CCP2+ vs anti-CCP2- pts with RA (Harrold *et al. J Rheumatol* 2018).

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LB0009 FIRST-IN-HUMAN STUDY OF NOVEL IMPLANTED VAGUS NERVE STIMULATION DEVICE TO TREAT RHEUMATOID ARTHRITIS

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Background: The inflammatory reflex plays a role in regulating innate and adaptive immunity through cellular and molecular pathways[1]. Activation of this neuroimmune reflex by electrical vagus nerve stimulation (VNS) reduced systemic inflammation and improved disease activity in a 17 subject rheumatoid arthritis (RA) proof-of-concept study using a reprogrammed epilepsy stimulator[2]. A novel miniaturized neurostimulator, the "MicroRegulator" (MR), was developed for a first-in-human pilot study in multi-drug refractory RA.

Objectives: To assess the safety and efficacy of the MR in a double-blind study in active RA patients.

Methods: The MR was implanted in 14 patients with active RA and prior insufficient response to =2 bDMARDS or JAK inhibitors with =2 different modes of action; all patients remained on stable background of methotrexate. Three weeks after implantation, the first 3 subjects were stimulated 1 min QD and, following safety review board approval, the remaining 11 patients were implanted with the MR and randomized to 1 min of sham, QD, or QID stimulations for 12 weeks. Patients, rheumatologists, joint assessors and monitors were fully blinded to treatment arm. Subjects randomized to sham had their devices activated after the primary endpoint at 12 weeks. Clinical efficacy was measured by DAS28-CRP response and contrast-enhanced MRI (RAMRIS OMERACT). The pharmacodynamic response to VNS was assessed in blood using cytokine production in an ex-vivo bioassay (TruCulture).

Results: 14 patients were enrolled (mean prior bDMARDs= 4.8, mean DAS28-CRP= 5.94). Implantation and stimulation were generally well tolerated. There were no device or treatment-related SAEs and 2 surgery related adverse events (left vocal cord paralysis, Horner's syndrome) that resolved without clinically significant sequelae. DAS28-CRP change at week 12 was (mean ± SEM): Open label QD= -1.44 ± 0.64, QD= -1.24 ± 0.88, QID= 0.38 ± 0.71, Sham=0.16 ± 0.21. Of QD stimulated patients, 4 of 6 had a EULAR good or moderate response. MRI measures of synovitis or osteitis did not change after 12 weeks of stimulation. RAMRIS erosion scores correlated with EULAR response (change ± SEM in erosion scores in EULAR responders = -2.2 ± 1.4 vs. 2.4 ± 0.96 in EULAR non-responders). The pharmacodynamic response to VNS was confirmed in actively stimulated groups with >30% decrease from baseline in bioassay levels of IL-1β, IL-6, and TNF-a at week 12.

Conclusion: The novel MR device and stimulation was well tolerated independent of the two surgery-related events. MR associated stimulation reduced signs and symptoms of RA in a meaningful number of highly drug-refractory subjects. No clinical improvement was observed in the sham group. These initial pilot data support the use of the MR in a larger blinded sham-controlled study in patients who have failed biologics or targeted oral therapies as a novel approach for treatment of RA and other chronic inflammatory diseases.

REFERENCES:

[1] Andersson U, Tracey K, Annu. Rev. Immunol. 2012; 30:313.
[2] Koopman, F, et. al. PNAS. 2016; 113(29):8284

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LB0010 ULTRA-LOW DOSES OF RITUXIMAB OR RETREATMENT OF RHEUMATOID ARTHRITIS: A RANDOMISED CONTROLLED NON-INFERIORITY TRIAL

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Background: Rituximab (RTX) is an effective treatment for patients with Rheumatoid Arthritis (RA). 1000mg (1 × 1000mg or 2 × 500mg) has similar 6-month efficacy as the registered dose of 2 × 1000mg. Based on several case reports and a

case series even lower doses might be sufficient for maintenance treatment, potentially improving safety and decreasing costs.(1)

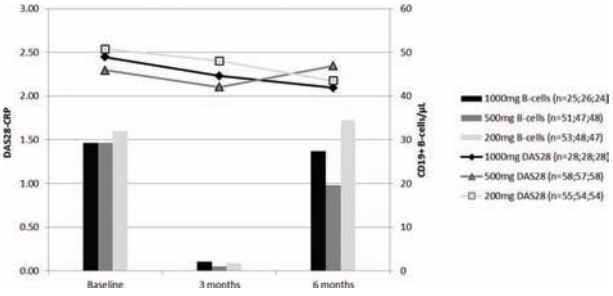
Objectives: To compare effectiveness of RTX retreatment with ultra-low doses (1 × 500mg or 1 × 200mg) to standard low dose (1 × 1000mg).

Methods: A 6-month double-blind randomised controlled non-inferiority trial (REDO study (2)) was performed in 5 centres in the Netherlands. Patients with RA responding well to RTX (based on DAS28-CRP<2.9 or clinical judgement) were randomised (1:2:2) to 1 × 1000mg, 1 × 500mg or 1 × 200mg RTX respectively. DAS28-CRP and peripheral CD19+ B-cells were measured at baseline, 3 and 6 months. Primary analysis (per protocol with LOCF) consisted of a hierarchical testing procedure comparing ultra-low doses (1 × 500mg at 3 and 6 months, then 1 × 200mg at 3 and 6 months) to 1 × 1000mg using a non-inferiority margin of 0.6 (on DAS28-CRP). DAS28-CRP change of study groups was compared using linear regression, adjusted for baseline DAS28-CRP, RF/ACPA status and concomitant csDMARD use.

Results: The projected inclusion was met (n=142, table 1a). In both ultra-low dose groups 2 patients received an extra dose of 1000mg RTX due to a flare. The 500mg dose was non-inferior to 1000mg at 3 months (-0.04 (95% CI -0.39 to 0.30)), but not at 6 months (0.31 (95% CI -0.05 to 0.68). The 200mg dose was non-inferior to 1000mg at both time points. Because of our pre-defined hierarchical testing, non-inferiority could not formally be inferred for the 200mg dose. Mean DAS28-CRP scores remained low in all groups throughout the study, and B-cell counts decreased similarly at 3 months (figure 1). In the 200mg group, more patients received intramuscular corticosteroid injection(s) compared to the 1000mg group (table 1b).

1a. Baseline characteristics (mean (sd) or n(%))			
	1000mg (n=29)	500mg (n=58)	200mg (n=55)
Age	63.8 (9.0)	64.0 (10.9)	64.2 (12.2)
Female	18 (62%)	37 (64%)	40 (73%)
Disease duration in years	17.1 (11.1)	14.9 (10.7)	13.5 (7.2)
RF/ACPA positive	27 (93%)	54 (93%)	49 (89%)
Concomitant csDMARD	18 (62%)	35 (60%)	32 (58%)
1b. Flares, co-medication and SAEs (n(%))			
Flare(s)	3 (10%)	14 (24%)	10 (18%)
Extra 1000mg RTX received*	0 (0%)	2 (3%)	2 (4%)
im gc injection(s)	4 (14%)	7 (12%)	16 (29%)
SAE(s)	3 (10%)	5 (9%)	5 (9%)

*2 patients with regular RTX accidently given before study end (protocol violation) not included



Conclusion: Non-inferiority of retreatment with 1 × 500mg or 1 × 200mg rituximab versus 1 × 1000mg after 6 months could not formally be established. However, ultra-low doses appear similarly effective in the majority of RA patients, judged by DAS28-CRP course over time and B-cell results, with use of slightly more co-medication.

REFERENCES

[1] Shenoy *et al. Arthritis Rheumatol* 2015;67(suppl 10).
[2] Den Broeder *et al. Trials* 2017;30;18(1):403.

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LB0011 A PHASE II SINGLE ARM (ADAPTIVE DESIGN) TRIAL OF TOCILIZUMAB IN ANTI-TNF REFRACTORY PATIENTS WITH JIA-ASSOCIATED UVEITIS (APTITUDE TRIAL)

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Background: Children with severe uveitis or those who have not responded to anti-tumour necrosis factor agents and methotrexate (MTX) are at significant risk of sight loss[1-3]. Evidence on alternative therapies is needed.

Objectives: To evaluate the clinical response to Tocilizumab with MTX in children with Juvenile Idiopathic Arthritis (JIA)-associated uveitis who failed anti-TNF therapy to determine the need for further research.

Methods: Multi-centre, open label, single arm trial using a two-stage Simon design[4].

Setting: 7 UK sites

Participants: Children aged 2-18 years with JIA-associated uveitis defined as "2 readings of cellular infiltrate in anterior chamber of SUN criteria grade ≤1+ or more during the preceding 6 weeks, the latest reading must be at the time of screening."

Intervention: Treatment with MTX and those weighing ≤30 kg treated with 162 mg of Tocilizumab every 2 weeks and those weighing <30 kg every 3 weeks.

Main Outcome Measures: Primary outcome was treatment response at 12 weeks defined as per SUN criteria as a 2 step decrease in the level of inflammation or decrease to 0 between baseline and 12 weeks of treatment. Data on safety, topical corticosteroid usage, tolerability, compliance, optic and ocular measurements, American College of Rheumatology Pedi core set criteria measurements, changes in biologic/Disease-modifying anti-rheumatic drugs therapy and flares of arthritis collected.

Results: 22 participants were registered; 1 was removed as found to be ineligible soon after registration. A total of 7 were classified as a pre-specified treatment response, the median unbiased estimate of proportion was 34% 95% CI (25% to 57%), p=0.11. 4 had macular oedema at baseline and this was resolved in 3 participants. Post-hoc analysis showed that there were 4 (19%) who were classified as a non-treatment response but had at least a one-step improvement at 3 months, leaving 10 (48%) showing no response, the mean (SD) number of steroid drops at baseline was 4.48 (3.11) and which reduced to 4.33 (2.29) at 12 weeks. Safety results were consistent with the known safety profile of Tocilizumab; no SAEs were reported.

Conclusion: Whilst this study did not pass the pre-specified criterion, the data shows almost a half of the participants including 7 (33%) with a 2-step improvement, and a further 3 (14%) with 1-step improvement, responded to Tocilizumab.

REFERENCES

[1] Foeldvari I, Wierk A. Methotrexate is an effective treatment for chronic uveitis associated with juvenile idiopathic arthritis. *J Rheumatol* 2005;32:362-365.
[2] Weiss AH, Wallace CA, Sherry DD. Methotrexate for resistant chronic uveitis in children with juvenile rheumatoid arthritis. *J Pediatr* 1998;133:266-8.
[3] Yu EN, Meniconi ME, Tufail F, Baltatzis S, Foster CS. Outcomes of treatment with immunomodulatory therapy in patients with corticosteroid-resistant juvenile idiopathic arthritis-associated chronic iridocyclitis. *Ocul Immunol Inflamm* 2005;13:353-60.
[4] Simon R. Optimal Two-Stage Designs for Phase II Clinical Trials. *Control Clin Trials* 1989;10:1-10.

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LB0012

HEADLINE RESULTS FOR A PHASE 4, 52-WEEK, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS ADVERSE EVENTS OF SPECIAL INTEREST (AESI) IN ADULTS WITH ACTIVE, AUTOANTIBODY-POSITIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) RECEIVING BELIMUMAB

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Background: Belimumab (BEL) is approved in adults with active, autoantibody-positive SLE. Phase 2, 3 and long-term extension studies showed a favourable benefit-risk profile. However, numerical differences in the incidence of mortality, infections, hypersensitivity reactions and some psychiatric events warranted a large, focused safety study to assess these events, along with potential for malignancy.

Objectives: To evaluate all-cause mortality and AESI in patients with SLE receiving intravenous (IV) BEL vs placebo (PBO) over 52 weeks.

Methods: This study (BASE; BEL115467; NCT01705977) randomised adults with SLE (1:1) to monthly BEL 10 mg/kg IV or PBO, plus standard of care, for 48 weeks. No minimum SELENA-SLEDAI disease activity was required and no exclusions for previous psychiatric conditions were made. Differences in rates (95% CI) of mortality and other pre-specified AESI (malignancies, serious infections, opportunistic infections and other infections of interest, serious depression, suicidality [C-SSRS], and serious infusion/hypersensitivity reactions) on-treatment (first to last dose +28 days) were assessed. For on-treatment serious suicidal ideation/behaviour and self-injury events (per sponsor adjudication), and on-study (first dose to end of Week 52 study follow-up) suicidal ideation/behaviour (C-SSRS), differences (95% CI) vs PBO were calculated post hoc.

Results: 4003 patients received ≤1 dose. Baseline demographics and disease characteristics were similar between groups. On-treatment mortality and pre-specified AESI rates are shown in the Table 1 below. Overall rates of on-treatment AESIs were similar between groups, except for serious depression and serious infusion/hypersensitivity reactions.

On-treatment deaths were most frequently caused by infection (3 [0.15%] PBO vs 9 [0.45%] BEL); on-study deaths occurred in 22 (1.10%) PBO and 13 (0.65%) BEL patients (difference [95% CI]: -0.45 [-1.03, 0.13]). On-treatment serious suicidal ideation/behaviour and self-injury events were reported for 5 (0.25%) PBO and 15 (0.75%) BEL patients (difference [95% CI]: 0.50 [0.06, 0.94]); on-study suicidal ideation/behaviour (C-SSRS) occurred in 39 (1.96%) PBO and 48 (2.43%) BEL patients (difference [95% CI]: 0.47 [-0.44, 1.38]). No suicide-related deaths were reported.

Conclusion: In this double-blind, placebo-controlled (1:1) safety study, which is the largest SLE clinical study to date with 4003 patients, on-treatment all-cause mortality, infection and malignancy AESI rates were similar between BEL and PBO, with imbalances observed in serious depression, serious suicidal ideation/behaviour and self-injury events, and serious infusion/hypersensitivity reactions.

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Table. Prespecified AESI endpoints in the BASE study (on-treatment period)

	PBO (n=2001) n (%)	BEL 10 mg/kg IV (n=2002) n (%)	Difference in % vs PBO (95% CI)
Deaths	8 (0.40)	10 (0.50)	0.10 (−0.31, 0.51)
Serious infections	82 (4.10)	75 (3.75)	−0.35 (−1.55, 0.85)
Opportunistic infections and other infections of interest	50 (2.50)	36 (1.80)	−0.70 (−1.60, 0.20)
Malignancies (excluding NMSC)	5 (0.25)	5 (0.25)	0 (−0.31, 0.31)
NMSC	3 (0.15)	4 (0.20)	0.05 (−0.21, 0.31)
Serious depression	1 (0.05)	7 (0.35)	0.30 (0.02, 0.58)
Suicidality (C-SSRS)[a]	23 (1.16)	28 (1.42)	0.26 (−0.44, 0.96)
Serious infusion/hypersensitivity reactions	2 (0.10)	8 (0.40)	0.30 (−0.01, 0.61)

[a]Treatment-emergent suicidal ideation/behaviour.

CI, confidence interval; C-SSRS, Columbia-Suicide Severity Rating Scale; NMSC, non-melanoma skin cancer.

THURSDAY, 13 JUNE 2019

Innate immunity in rheumatic diseases

THU0001 CIRCULATING INNATE LYMPHOID CELLS IN IGG4-RELATED DISEASE

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Background: IgG4-related disease (IgG4-RD) is characterized by lymphoplasmacytic infiltrates, $IgG4^+$ plasma cells, fibrosis and frequent ectopic lymphoid structures (ELS). Excessive Th2 cytokines production and role of T follicular helper (Tfh) cells have been reported. Innate cells (ILCs), a heterogeneous population of non-B non-T lymphocytes lacking antigen-specific receptors, are able to produce type 2 cytokines (ILC2s) or to participate to ELS formation (ILC3s) and could contribute to IgG4-RD lesions.
Objectives: To analyze circulating blood ILCs in IgG4-RD.
Methods: IgG4-RD patients were identified according to the Comprehensive Diagnostic Criteria. Patients treated with steroids or DMARDs within 3 months or rituximab within 6 months prior inclusion were excluded. Peripheral blood mononuclear cells were isolated and analyzed by flow cytometry. ILCs were defined as lymphoid $CD45^+$Lineage(Lin)$^-CD127^+$ cells. Among ILCs, 3 subsets were defined according to CRTH2 and CD117 expression. In some patients, transcription factor expression (T-bet, GATA3, RORγt) as well as cytokine production (IFNγ, IL-4/IL-13, IL-17/IL-22) after different stimulations were analyzed in ILC subsets. Results were compared to healthy controls (HC), correlated to clinical and biological characteristics, and compared before and after treatment.
Results: Twenty patients with active untreated IgG4-RD and 30 HC were included. In IgG4-RD group, mean age was 64 years and sex ratio 4:1. Serum IgG4 levels were >1.35 g/l for 85% of patients and median eosinophil count 410/mm^3. Most patients (65%) were analyzed at diagnosis. Main organs involved were lymph nodes (n=15), pancreas (n=9), salivary glands (n=8), biliary tree and kidney (n=5), lung and retroperitoneum (n=4), with ≥3 organs involved in 65%. Number of blood ILCs was not modified in IgG4-RD patients (1.2 ± 2.6 x10^3/ml *vs* 1.5 ± 1.3 x10^3/ml in HC, *p=0.29*; 0.07 ± 0.06% of $CD45^+$ lymphocytes *vs* 0.09 ± 0.05% in HC, *p=0.35*). ILC1s, ILC2s, and ILC3s represented respectively 30%, 29% and 32% of total ILCs in HC. IgG4-RD patients presented a decrease in ILC2s (23.8% [12.4-29.3], *p=0.04*) and ILC3s (21.2% [8.8-28.1], *p=0.002*) and an increase in ILC1s (54.1% [33.8-68.7], *p=0.0009*) proportions. ILC2s (274/ml [152-594] *vs* 554/ml [62-1000], *p=0.045*) and ILC3s (214/ml [120-620] *vs* 509/ml [336-908], *p=0.04*) numbers were decreased in IgG4-RD patients. No correlation was found between number or proportion of total ILCs or any ILCs subsets and clinical or biological characteristics such as age, number of organ involved, IgG4-RD Responder Index or serum IgG4. No correlation was found between Tfh and ILC3s, or between eosinophils and ILC2s numbers. As human ILC3s and ILC2s can convert *in vitro* into IFNγ producing cells, we explore if ILC plasticity could contribute to ILCs subset distribution observed. GATA3 or RORγT expression by ILC1s was not modified (*p=0.29*, respectively) in IgG4-RD patients compared to HC. As previously reported, no cytokine production (IFNγ, IL-4/IL-13, IL-17/IL-22) was observed after different stimulations of blood ILCs. Analyzes before and after treatment found no difference in proportion or absolute number of total or subsets of circulating ILCs.
Conclusion: Circulating ILC2s and ILC3s are decreased in IgG4-RD. Recruitment of ILC2s or ILC3s in tissues, where they could participate to Th2 cytokine production, ELS formation and fibrosis, needs further investigations.
Disclosure of Interests: None declared
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THU0002 THERAPEUTIC ANTI-TNF BIOLOGIC AGENTS EXHIBIT FUNCTIONAL DIFFERENCES IN BLOCKING TNF-INDUCED EFFECTS ON HUMAN MONOCYTES IN VITRO

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Background: Therapeutic anti-TNF biologic agents can be distinct in their structure, such as etanercept, a human TNFRII- Fc fusion protein, as compared to adalimumab, a human IgG molecule, and/or in their binding to TNF as shown by crystal structures of adalimumab as compared to infliximab in the presence of TNF. Whether these differences can affect the functional properties of these biologics in direct comparison to each other has not been thoroughly investigated.
Objectives: To determine the equivalency of all anti-TNF biologic agents currently approved for the treatment of RA in preventing a variety of TNF-induced effects on human monocytes *in vitro*.
Methods: Human monocytic U937 NF-kB luciferase reporter cell line was incubated with 100 ng/mL TNF +/- increasing conc. (0.15-338 nM) of adalimumab (ADA), etanercept (ETN), infliximab (IFX), golimumab (GOL) or certolizumab pegol (CZP) as pre-formed complexes generated for 1 h. at 37°C. Surface TNF-RI and –RII levels were monitored by flow cytometry following 1 h. incubation. Luciferase activity was measured in cell lysate after 4 h. to assess NF-kB activation. After 24 h., U937 cells were analyzed by flow cytometry for surface levels of ICAM-1, an NF-kB-induced adhesion molecule shown to contribute to monocyte migration and arthritis. Apoptosis was assessed by time-lapsed microscopy and flow cytometry using caspase 3/7 fluorescent substrate. Alpha-2,6 sialylation (Sia), a glycosylation modification shown to regulate TNF-RI internalization and apoptosis induction, was evaluated by flow cytometry using FITC-labeled Sambucus nigra lectin (SNA). Human PBMC were incubated with TNF +/- pre-formed complex with anti-TNF biologics for 24 h. and then stained with CD14 and ICAM-1 Abs for flow cytometry.
Results: Surface levels of TNF-RI and –RII on U937 cells were both reduced by 2.4-fold in presence of TNF. TNF-RI was maintained at baseline levels by 16.7 nM ADA or CZP as pre-formed complexes with TNF; however, those complexes with ETN, IFX or GOL could only preserve a fraction of this receptor on the surface (43%, 52% and 62%, respectively). All anti-TNF biologics were equally effective in preventing loss of surface TNF-RII. TNF stimulation of U937 NF-kB reporter cells led to a 122-fold increase in luciferase activity which was reduced to baseline by only ADA or CZP with largest conc. range tested. Partial reduction by 3, 7 and 11-fold was observed with ETN, IFX or GOL, respectively. TNF-enhanced ICAM-1 surface expression (3-fold increase) on U937 cells was reduced to baseline by 16.7 nM ADA or CZP, whereas ETN, IFX or GOL were only partially effective (48%, 61% and 59% reduction, respectively). Exposure of CD14+ primary monocytes to ADA:TNF or CZP:TNF complexes not only prevented TNF induction of ICAM-1 but significantly reduced its level below that of baseline, whereas those with GOL or IFX brought ICAM-1 levels to baseline and those with ETN were only 46% effective. Both ADA:TNF and CZP:TNF complexes also completely inhibited TNF-induced apoptosis in a dose dependent manner unlike ETN, IFX and GOL, which were less effective (42%, 32% & 42% reduction, respectively). According to SNA staining, alpha-2,6 Sia surface levels dropped in presence of TNF specifically on the subset of cells undergoing apoptosis, and this subset was reduced proportionately to the inhibitory properties of anti-TNF biologics on apoptosis.
Conclusion: For each of the conditions tested *in vitro*, many resembling features associated with RA pathogenesis, the pre-formed complexes of ADA:TNF and CZP:TNF were significantly more effective in preventing the TNF-induced effects (decrease of surface TNF-RI expression and alpha-2,6 Sia; increase in NF-kB activation, ICAM-1 surface expression, and apoptosis) on human monocytes than those complexes of TNF with ETN, IFX or GOL. Additional *in vitro* and *in vivo* studies need to be done to further elucidate the mechanism responsible for these differences.
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THU0003 CRYSTALLINE SILICA IMPAIRS EFFEROCYTOSIS CAPACITIES OF HUMAN MONOCYTE-DERIVED MACROPHAGES THROUGH RHOA-ROCK ACTIVATION

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Background: Inhalation of crystalline silica can lead to pulmonary diseases and systemic autoimmune disorders, such as systemic sclerosis (SSc), systemic lupus erythematosus or rheumatoid arthritis (1). A failure of apoptotic cell clearance, also called efferocytosis, is reported in autoimmune diseases and, impaired efferocytosis in macrophages from SSc patients has especially been described recently (2). However, the precise

mechanisms linking crystalline silica exposure and autoimmune disorders is still to be determined.

Objectives: This study explored the effects of crystalline silica on efferocytosis abilities of human macrophages.

Methods: Monocyte-derived macrophages (MDM) were exposed *in vitro* to crystalline silica for 4 hours. Their ability to phagocyte CFSE-positive apoptotic and non-apoptotic Jurkat cells and their polarization profile after silica exposure were assessed by flow cytometry. Efferocytosis capacities of MDM from SSc were also evaluated using the same methods.

Results: Crystalline silica exposure impaired efferocytosis capacities of human MDM in a specific and dose-dependent manner. This effect of silica required the expression of SR-B1 and, was associated with a decreased membrane expression of the M2 polarization markers CD206, CD204 and CD163. Their expressions after silica exposure were similar to those of M1 polarized MDM. Silica increased F-actin staining, RhoA activation and phosphorylation of myosin phosphatase subunit 1 (MYPT1), a known ROCK target. Y27632, a Rho kinase (ROCK) inhibitor, reversed the F-actin staining, the phosphorylation of MYPT1 and, at least in part, the silica-induced impairment of efferocytosis. Moreover, efferocytosis abilities of MDM from SSc patients were similar to those of silica-exposed MDM and, a treatment of SSc-MDM with Y27632 significantly increase their efferocytosis capacities, suggesting an activation of the RhoA/ROCK pathway in SSc MDM also.

Conclusion: These findings demonstrate that silica impairs efferocytosis in MDM via an activation of RhoA/ROCK pathway **(Figure 1)**. These results also suggest a therapeutic potential of drugs targeting this pathway and advance the hypothesis that silica exposure may contribute to the impaired efferocytosis capacities of macrophages from SSc patients, a silica-associated systemic disorder still without curative treatment to date.



Abstract THU0003 Figure 1. Crystalline silica alters polarization of human monocyte-derived macrophages and impairs their efferocytosis capacities through RhoA-ROCK activation

REFERENCES:

[1] Blanc PD, Järvholm B, Torén K. Prospective risk of rheumatologic disease associated with occupational exposure in a cohort of male construction workers. Am J Med. 2015 Oct;128(10):1094-101.

[2] Ballerie A, Lescoat A, Augagneur Y, Lelong M, Morzadec C, Cazalets C, Jouneau S, Fardel O, Vernhet L, Jégo P, Lecureur V. Efferocytosis capacities of blood monocyte-derived macrophages in systemic sclerosis. Immunol Cell Biol. 2018 Nov 13.

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THU0004 MICRORNA-223 NEGATIVELY REGULATE GOUTY INFLAMMATION BY TARGETING THE NLRP3 INFLAMMASOME WITHOUT INFLUENCING IL-37 AND TGF-B1

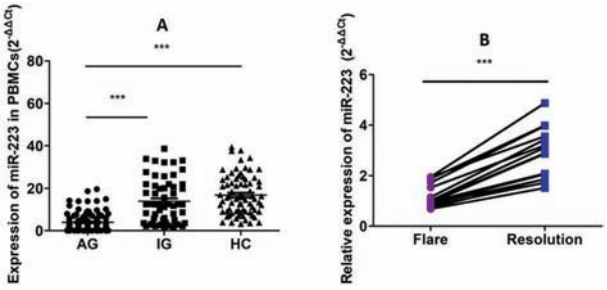
Yu-Feng Qing[1,2], Dan Zhu[2], Ting Yi[2], Jian-Xiong Zheng[2], Qin Xiong[3], Quan-Bo Zhang[3]. *[1]Institute of Rheumatology and Immunology, Affiliated Hospital of North Sichuan Medical College, Department of Rheumatology and Immunology, nanchong, China; [2]Institute of Rheumatology and Immunology, Affiliated Hospital of North Sichuan Medical College, Department of Rheumatology and Immunology, Affiliated Hospital of North Sichuan Medical College, nanchong, China; [3]Institute of Rheumatology and Immunology, Department of Geriatrics, affiliated Hospital of North Sichuan Medical College, nanchong, China*

Background: MicroRNA-223 (miR-223) serves as an important regulator of inflammatory and immune responses and is implicated in several autoinflammatory disorders[1]. To date, no relevant studies have reported the expression levels of miR-223 in gout patients or assessed whether miR-223 participates in negatively regulating gouty inflammation via regulating cytokines (such as IL-1β, tumor necrosis factor (TNF)-α, IL-37 and TGF-β 1) by targeting the NLRP3 inflammasome.

Objectives: To determine the function of miR-223 in monosodium urate (MSU)-induced gouty inflammation.

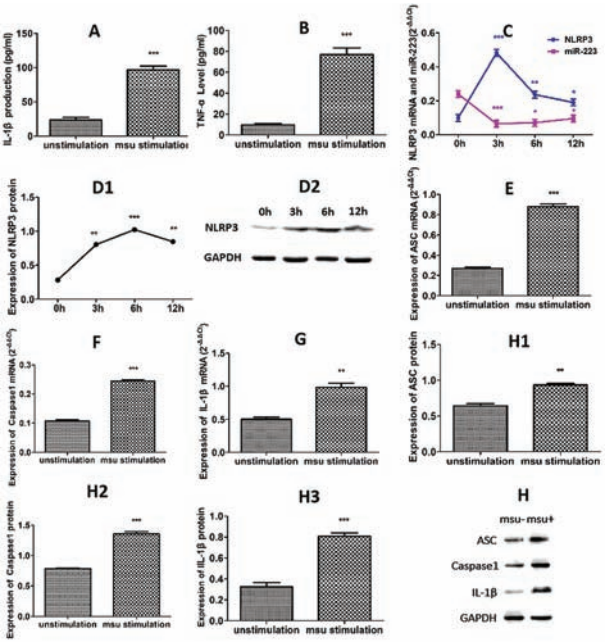
Methods: miR-223 was detected among 107 acute gout patients (AG), 58 intercritical gout patients (IG), and 75 healthy subjects (HC). RAW264.7 macrophages were cultured and treated with MSU. Over-expression or under-expression of miR-223 was inducted in RAW264.7 macrophages to investigate the function of miR-223. Real-time quantitative PCR, ELISA and western blotting were used to determine the expression levels of miR-223, cytokines and the NLRP3 inflammasome.

Results: 1. *Expression of miR-223 in PBMCs among the AG, IG and HC groups(Figure1)*



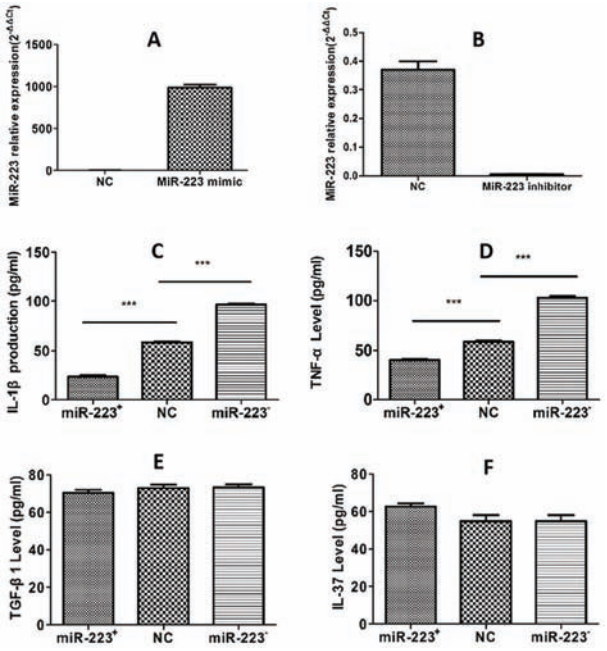
Abstract THU0004 Figure 1.

2. 2.*Altered expression of miR-223, the NLRP3 inflammasome and cytokines in MSU-induced RAW264.7 murine macrophage inflammation (Figure2)*



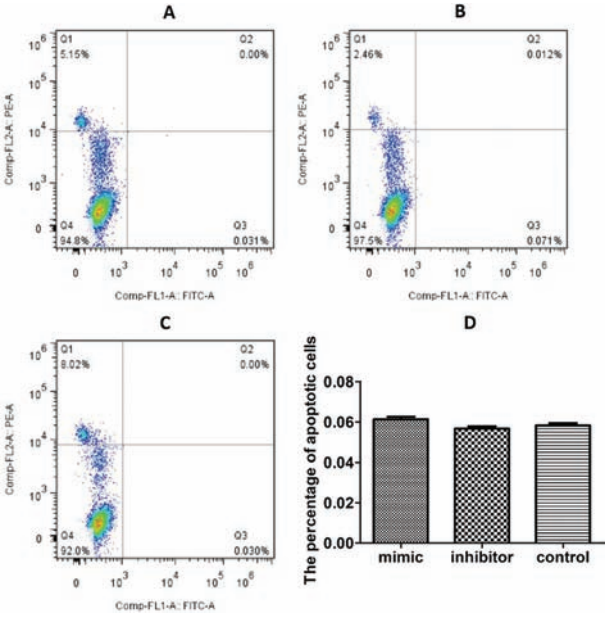
Abstract THU0004 Figure 2.

3. Effect of miR-223 on cytokine secretion from RAW264.7 macrophages treated with MSU(Figure3)



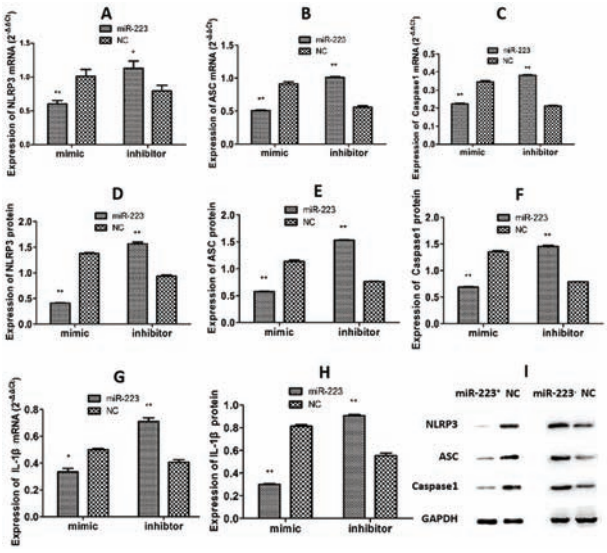
Abstract THU0004 Figure 3.

4. No effect on RAW264.7 macrophage apoptosis(Figure4)



Abstract THU0004 Figure 4.

5. Effect of miR-223 on NLRP3 inflammasome expression in RAW264.7 macrophages treated with MSU(Figure5)



Abstract THU0004 Figure 5.

Conclusion: Our findings suggest that miR-223 provides negative feedback regulation of gouty inflammation development by suppressing production of IL-1β and TNF-α, but not by regulating IL-37 and TGF-β1, and that miR-223 regulates cytokine production by targeting the NLRP3 inflammasome. These findings provide novel insight into the regulatory role of miR-223 in the spontaneous resolution of acute gouty inflammation. Finally, these results suggest that targeting miR-223 in macrophages might be an effective therapeutic strategy for the treatment of gout flare.

REFERENCES:

[1] Henshall DC, Hamer HM, Pasterkamp RJ, Goldstein DB, Kjems J, Prehn JHM, Schorge S, Lamottke K, Rosenow F: MicroRNAs in epilepsy: pathophysiology and clinical utility. Lancet Neurol 2016; 15:1368-1376.

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THU0005 PTX3 AS A UNIVERSAL MARKER OF VASCULAR INFLAMMATION IN MULTIPLE IMMUNE-MEDIATED DISEASES

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Background: Pentraxin-3 (PTX3) is a prototypic innate humoral pattern recognition receptor with a multi-functional role in tissue homeostasis from host defence to fertility, cancer biology, autoimmunity, regulation of angiogenesis and tissue repair. PTX3 is selectively expressed at sites of inflammation and rises in the circulating blood during disease activity in many (but not all) immune-mediated inflammatory conditions. Research on PTX3 as a biomarker has so far focused on single diseases.

Objectives: To identify correlations among PTX3 elevation in plasma and clinical and pathophysiological phenotypes in multiple immune-mediated diseases.
Methods: Three-hundred-sixty-six subjects encompassing 79 healthy controls and 287 patients with autoimmune diseases were enrolled. Autoimmune diseases included systemic lupus erythematosus (SLE, n=55), rheumatoid arthritis (RA, n=21), polymyalgia rheumatica (PMR, n=10), ANCA-associated vasculitides (AAV, n=63), giant cell arteritis (GCA, n=96) and Takayasu's arteritis (TA, n=42). Plasma PTX3 concentrations were measured by ELISA. Basic demographics (including gender, age at sampling and disease duration), disease activity and accrued irreversible damage, dose of prednisone or equivalents, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values at time of sampling were recorded. Disease activity and damage scores were made homogeneous by calculating Z-scores (i.e. (x-mean)/(standard deviation): Z-activity and Z-damage).
Results: Patients with SLE, AAV, TA and GCA, but not patients with RA and PMR, had higher PTX3 levels than HC (2.33 ng/ml, IQR: 1.26-4.89 vs 1.22 ng/ml, IQR: 0.80-1.98; p<0.001). PTX3 concentration correlated with Z-activity (p=0.016), ESR and CRP (p<0.001 and p=0.035 respectively) and prednisone dose (p=0.001). It was higher in females (p=0.018), in patients with disease onset within 6 months from sampling (p=0.041) and in those with previous or current active vasculitis (both p<0.001) at univariate analysis. Active small-(B=6.706, Std.Err=1.473, p<0.001), or large- vessel vasculitis (B=4.269, Std.Err=0.844, p=0.008) were the main independent variables influencing PTX3 levels at multivariate analysis.
Conclusion: High levels of PTX3 in the blood can contribute to identify an increased risk of vascular involvement in patients with systemic immune-mediated diseases.

REFERENCES:
[1] Erreni M, et al. Immunological reviews. 2017
[2] Ramirez GA, et al. Arthritis research & therapy. 2015
[3] Rovere P, et al. Blood. 2000

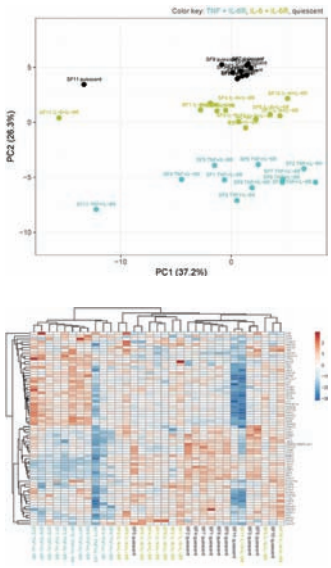
Disclosure of Interests: Giuseppe Alvise Ramirez: None declared, Enrico Tombetti: None declared, Patrizia Rovere-Querini Grant/research support from: Adienne Pharma & Biotech, Miriam Blasi: None declared, Mattia Baldini: None declared, Rebecca De Lorenzo Grant/research support from: Adienne Pharma & Biotech, Enrica Bozzolo: None declared, Roberto Leone: None declared, Alessandro Ambrosi: None declared, Alberto Mantovani: None declared, Angelo Manfredi: None declared
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4. Cytokines and inflammatory mediators

THU0006 PROINFLAMMATORY RESPONSES IN THE JAK-STAT PATHWAY IN SYNOVIAL FIBROBLASTS ARE STIMULUS-SPECIFIC AND ONLY PARTIALLY INHIBITED BY THERAPEUTIC DOSES OF TOFACITINIB

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Background: The Jak-STAT signalling pathway has a key role in the pathogenesis of rheumatoid arthritis (RA). First Jak inhibitors, including tofacitinib, have been approved for the treatment of RA. Whereas Jak inhibitors exhibit pleiotropic effects on the immune system, their "in situ" activities on synovial fibroblasts (SF), the resident synovial cells, are less well understood.
Objectives: To characterise the Jak-STAT pathway and its inhibition by tofacitinib in RA synovial tissues and SF from different joints across diverse pro-inflammatory stimuli.
Methods: Synovial tissues and SF were isolated from knee (n=4), shoulder (n=4) and hand (n=4-6) joints of RA patients undergoing joint replacement surgery. To activate and inhibit the Jak-STAT pathway, SF were stimulated with TNF (0.1 ng/ml, 1ng/ml) ± IL-6 receptor (IL-6R, 50ng/ml) or IL-6 (50ng/ml) + IL-6R for 24h in the presence or absence of 80nM, 180nM and 1000nM tofacitinib. 80nM and 180nM tofacitinib mimic the plasma drug concentrations in subjects on therapeutic doses of tofacitinib. 1000nM is the *in vitro* used tofacitinib concentration. Gene expression in synovial tissues and SF (n=12 each) was measured using the low-density gene expression arrays containing 6 housekeeper genes and 90 probes for the core components, inhibitors and target genes of the Jak-STAT pathway. Clustering analysis of the array data [principal component analysis (PCA), heatmap] was performed using the ClustVis web tool. PCA identified one outlier SF sample, driven by distinct housekeeper gene expression that was omitted from further analysis. The production of IL-6 was determined by ELISA.
Results: RA synovial tissues and quiescent SF exhibited highly similar expression of the core components of the Jak-STAT signalling pathway, suggesting that SF contribute significantly to the synovial expression of JAK and STAT genes. Clustering analysis of the array data showed that SF stimulated with 0.1ng/ml TNF+IL-6R, SF treated with IL-6+IL-6R and quiescent SF formed separate clusters (Figure 1), pointing towards stimulus-specific transcriptional outputs in the Jak-STAT pathway. Moreover, TNF+IL-6R increased the expression of multiple core components in the Jak-STAT pathway (IL6ST, JAK2, JAK3, STAT3, STAT4) with simultaneous downregulation of pathway inhibitors (PIAS1, PIAS2) (p<0.05). SF produced different amounts of IL-6 under distinct proinflammatory stimuli, including 0.1ng/ml TNF (IL-6 mean±SD: 1.1±0.8 ng/ml), 0.1ng/ml TNF + IL-6R (2.7±1.5 ng/ml), 1ng/ml TNF (2.8±1.7 ng/ml) and 1ng/ml TNF + IL-6R (5.0±2.7 ng/ml). Specifically, the addition of IL-6R to 0.1 ng/ml TNF increased the production of IL-6 in SF to the levels observed with 1ng/ml TNF alone and this response was further exacerbated in the presence of IL-6R + 1 ng/ml TNF. 80nM, 180nM and 1000nM tofacitinib decreased the IL-6 production by 20-30%, 50% and 60% respectively, suggesting a limited anti-inflammatory effect at average plasma concentrations (80nM). The inhibitory effect of tofacitinib on IL-6 production in SF was thus dose dependent, however highly similar across distinct proinflammatory conditions (0.1ng/ml or 1ng/ml TNF ± IL-6R).



Abstract THU0006 Figure 1. Clustering analysis of the Jak-STAT transcriptional signatures in SF

Conclusion: Here we show that soluble IL-6R strongly augments the pro-inflammatory effects of TNF in SF. Furthermore, percent inhibition of the IL-6 production by tofacitinib remained constant across diverse proinflammatory conditions despite different amounts of IL-6 being produced. Thus, higher pre-treatment inflammatory responses to TNF ± IL-6R predict higher residual inflammatory activity in SF following Tofacitinib therapy, pointing towards a saturation of anti-inflammatory effects of Tofacitinib in SF in RA.
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GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Caroline Ospelt: None declared, Mojca Frank-Bertoncelj : None declared

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THU0007 IL-26 PROMOTES OSTEOCLASTOGENESIS IN RHEUMATOID ARTHRITIS

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Background: IL-26 is a 171-amino acid protein, which is classified as a member of the Th17 cytokine family. The role of IL-26 in osteoclastogenesis in RA is needed to be clarified to understand the pathogenesis of RA.

Objectives: To examine the functional role of interleukin-26 (IL-26) in the expression of RANKL and induction of osteoclastogenesis in rheumatoid arthritis (RA).

Methods: The expression of IL-20Rα, CD55 and RANKL in RA synovial fibroblasts was analyzed using confocal microscopy. RA Fibroblasts like synoviocytes (RA-FLS) were treated with recombinant human IL-26, and the expression of RANKL messenger RNA (mRNA) and protein was measured using real-time polymerase chain reaction and ELISA. Human peripheral blood monocytes were cultured with macrophage colony-stimulating factor and IL-26, after which osteoclastogenesis was evaluated by counting the number of tartrateresistant acid phosphataseepositive multinucleated cells. Osteoclastogenesis was also evaluated after monocytes were co-cultured with IL-26-prestimulated FLS.

Results: The IL-26 concentration in the FLS was higher in RA patients than in patients with osteoarthritis (OA). In RA-FLS treated with rhIL-26, the expression of RANKL mRNA and protein was increased in a dose-dependent manner. IL-26 increased the expression of RANKL in RA-FLS, and the IL-26-induced RANKL expression decreased by the inhibition of IL-20Rα. IL-26–induced RANKL expression was down-regulated significantly by the inhibition of SHP-1, ERK, JNK, stat1, c-jun or p38 MAPK/NF-κB signaling. When monocytes isolated from human peripheral blood were cultured with IL-26, they were differentiated into osteoclasts in the absence of RANKL. Monocytes were also differentiated into osteoclasts when they were cocultured with IL-26–pretreated RA-FLS

Conclusion: IL-26 has a dual effect on osteoclastogenesis in RA: 1) direct induction of osteoclastogenesis from monocytes and 2) up-regulation of RANKL production in RA-FLS. This IL-26/RANKL axis could be a potential therapeutic target for bone destruction in RA.

REFERENCE:

[1] Corvaisier M, Delneste Y, Jeanvoine H, et al. IL-26 Is Overexpressed in Rheumatoid Arthritis and Induces Proinflammatory Cytokine Production and Th17 Cell Generation. PLoS Biol. 2012;10(9):e1001395.

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Disclosure of Interests: None declared

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THU0008 GM-CSF PATHWAY SIGNATURE IDENTIFIED IN TEMPORAL ARTERY BIOPSIES OF PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant Cell Arteritis (GCA) is a type of large vessel vasculitis that can cause blindness and aortic aneurysms. A significant unmet medical need remains in GCA, as current treatment options are limited, and relapse increases corticosteroid (CS) exposure and toxicity.

The primary role of macrophages/dendritic cells (DCs) and T_H1/T_H17 lymphocytes in GCA pathogenesis has been highlighted previously. Granulocyte-macrophage colony stimulating factor (GM-CSF) may contribute to GCA pathogenesis by stimulating giant cell formation.[1] GM-CSF produced by $CD4^+$ T helper T_H1 and T_H17 cells can stimulate conventional DCs and promote differentiation of monocyte-derived DCs.[2] GM-CSF may drive DCs to program naïve $CD4^+$ cells to T_H1, T_H17, and T follicular helper phenotypes (IFNγ/IL-17/IL-21). Notably GM-CSF RNA has been reported in GCA lesions[3] and in peripheral blood mononuclear cells of symptomatic patients.[4]

Objectives: We hypothesized elevation of the GM-CSF pathway signature in GCA vessels versus controls.

Methods: Two independent sources of temporal artery biopsies were utilized. First, GCA (n=17) and control (symptomatic patients suspected for GCA, but with a normal temporary artery biopsy; n=5) biopsies were analyzed for 15 mRNA transcripts representing T_H1, T_H17, and GM-CSF signaling (RNAscope; RS) and for mRNA transcripts representing the autoimmune panel (Nanostring; NS). Semi-quantitative scoring was performed on RS images, and fold-change of representative T_H1, T_H17 and GM-CSF related mRNA transcripts were calculated via NS nCounter analysis. Additional GCA and control biopsies were obtained and analyzed by RT-PCR for a subset of transcripts (n=10 each) and by confocal microscopy for GM-CSF and GM-CSF-Rα protein (n=2 each).

Results: The GM-CSF signaling pathway molecular signature was confirmed to be upregulated by 4 independent analyses.

GM-CSF-associated and T_H1-associated genes were upregulated in GCA biopsies versus control (GMCSF: 3-4x RS; GM-CSF-Rα: 6.7x NS, 6x RS; and CD83: 3.9x NS, 6x RS; TNFα: 2x NS, 3x RS; IFNγ: 2x RS; IL-1β: 6x RS). T_H17 associated genes were not elevated, potentially due to concomitant CS treatment.

Upregulation of both GM-CSF (12x) and GM-CSF-Rα (3x) mRNA was confirmed in a separate cohort of biopsies from GCA patients vs. controls by RT-PCR (Figure). GM-CSF and GM-CSFRα proteins were detected in the luminal endothelium, neovessels and inflammatory cells of GCA patients. In normal temporal arteries, GM-CSF protein was not detected, and some GM-CSFRα expression was observed in the luminal endothelium.

Pu.1, a transcription factor downstream of GM-CSF signaling, was increased 8x in GCA vs. controls (RS, NS) (Figure).

Conclusion: GM-CSF and T_H1 pathway signatures were demonstrated in GCA patient temporal arteries by independent analytical techniques. Active GM-CSF signaling in diseased tissue is evidenced by increased expression of Pu.1 in the vessel wall. These data implicate the GM-CSF pathway in GCA pathophysiology and increase confidence in rationale for targeting GM-CSF in GCA.

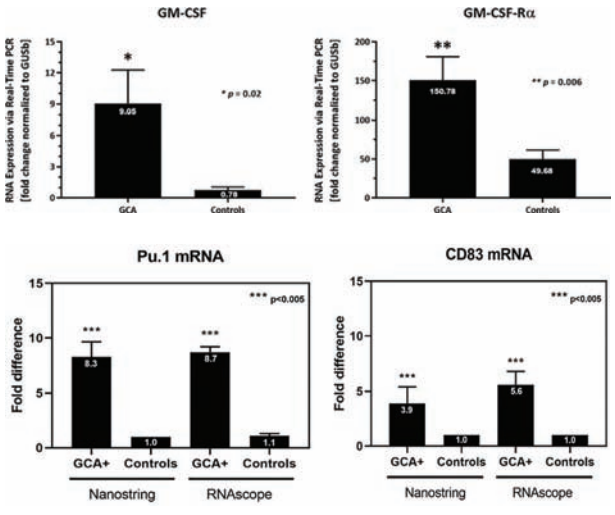
REFERENCES:

[1] M-CSF and GM-CSF promote alveolar macrophage differentiation into multinucleated giant cells with distinct phenotypes. Lemaire *et al,* 1996. Journal of leukocyte biology, 60(4):509-18.

[2] Targeting GM-CSF in inflammatory diseases. Wicks & Roberts, 2016. Nature reviews. Rheumatology, 12(1):37-48.

[3] Tissue cytokine patterns in patients with polymyalgia rheumatica and giant cell arteritis. Weyand *et al,* 1994. Annals of internal medicine, 121(7):484-91.

[4] Interleukin-21 modulates TH1 and TH17 responses in giant cell arteritis. Terrier *et al*, 2012. Arthritis and rheumatism, 64(6):2001-11.



Abstract THU0008 Figure 1.

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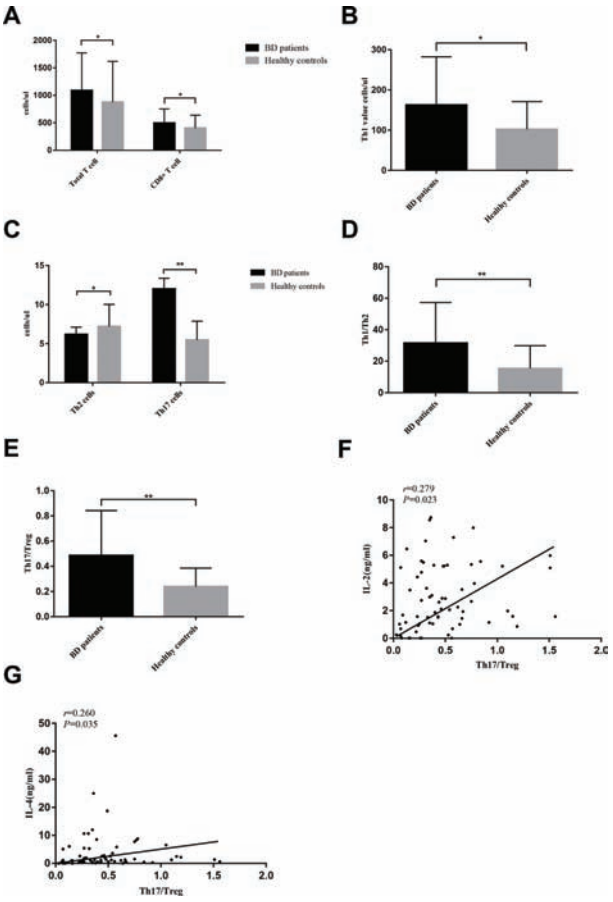
THU0009 ASSOCIATIONS BETWEEN CYTOKINE LEVELS AND TH17/TREG IMMUNE BALANCE IN PATIENTS WITH BEHCET'S DISEASE

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Background: Behcet's disease(BD) is a chronic systemic vascular inflammatory disease.Autoimmune imbalance associated with genetic and infectious factors promotes the immune response of neutrophils and T cells, which is BD's important pathogenesis. Several studies indicate the Th17/Treg immune imbalance may play an important role in BD pathogenesis[1-2].Although the proportion of Th17 cells was notably increased, which was accompanied by an increased levels of IL-17, IL-23[1], whether other cytokines are associated with Th17/Treg immune balance is unclear.
Objectives: The aim of this study was to examine associations between levels of a broad selection of cytokines and Th17/Treg immune balance in patients with BD.
Methods: The study included 66 BD patients and 66 healthy controls. The absolute counts of lymphocyte subsets and CD4+T cell subsets were detected by flow cytometry for all participants.Serum levels of the following 6 cytokines were determined in the same samples using a cytometric beads array:Interleukin-2(IL-2),Interleukin-4(IL-4), Interleukin-6(IL-6), Interleukin-10(IL-10),Interferon-γ(INF-γ)and Tumor necrosis factor-α(TNF-α) for all BD patients.T tests was used to compare continuous measures. Correlations between levels of cytokines and Th17/Treg were assessed by Spearman's rank correlation tests.
Results: (1)Compared to healthy controls, the absolute counts of T cells were increased(P=0.048),the absolute counts of $CD8^+$T cells were also increased (P=0.031) in BD group, the absolute counts of Th1 and Th17 cells were significantly increased(P< 0.05)in BD group,the absolute counts of Th2 cells were decreased (P< 0.05)in BD group,the ratio of Th1/Th2 was increased (P< 0.001), and the ratio of Th17/Treg were increased (P< 0.001) in BD group.There were no differences between the absolute counts of the two groups of B, NK, T+B+NK, CD4+T and Treg cells. (2) Among the investigated cytokines,the differences between the levels of IL-2,IL-6,INF-γ and normal range have statistical significance(P< 0.001). Finally,two cytokines were positively correlated with Th17/Treg:i.e.,IL-2 (r=0.279,P=0.023) and IL-4(r=0.260,P=0.035)($P\geq$ 0.2 for all other cytokines).
Conclusion: Our research shows that T cell homeostasis perturbation, especially Th1 and Th17 expansion and Th17/Treg immune imbalance,is the cornerstone of BD pathogenesis.These findings suggest that immune responses associated with increased levels of IL-2 and IL-4 may promote Th17/Treg immune imbalance. This also highlights the role of IL-2 and IL-4 in maintaining a balance in the Th17/Treg ratio. Further studies are required to evaluate these preliminary findings in different patient populations and also examine the possible molecular mechanisms behind our observations.

REFERENCES:

[1] Ahmadi M, Yousefi M, Abbaspour-Aghdam S, et al. Disturbed Th17/Treg balance, cytokines, and miRNAs in peripheral blood of patients with Behcet's disease[J]. Journal of Cellular Physiology, 2018.234(4)3985-3994. DOI:10.1002/jcp.27207.
[2] Greco A, De Virgilio A, Ralli M, et al. Behcet's disease: New insights into pathophysiology, clinical features and treatment options[J]. Autoimmun Rev, 2018,17(6):567-575. DOI: 10.1016/j.autrev.2017.12.006.



Abstract THU0009 Figure 1. Figure:The absolute counts of lymphocyte subsets in RA patients and healthy controls. Data are expressed as means ±SD(ABCDE).Correlation coefficient and regression line of Th17/Treg with IL-2 and IL-4 serum levels were represented as scatter plots(FG).

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THU0010 THE ANTI-INFLAMMATORY CYTOKINE INTERLEUKIN 37 IS AN ENDOGENOUS INHIBITOR OF TRAINED IMMUNITY

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Background: Trained immunity (TI) is a *de-facto* innate immune memory program induced in monocytes/macrophages by exposure to pathogens or vaccines, which evolved as a protective mechanism against infections. TI is characterized by rewiring of functional, epigenetic and metabolic programs of innate immune cells such as monocytes and macrophages, which sustain enhanced production of pro-inflammatory cytokines. Since aberrant activation of TI is implicated in inflammatory diseases, tight regulatory mechanisms are likely in place, but the mechanisms responsible for this modulation remain elusive.
Objectives: Scope of this study was to evaluated the role of IL-37, an anti-inflammatory cytokine that curbs inflammation as well as modulates metabolic pathways, as an endogenous regulator of trained immunity.
Methods: The effects of recombinant IL-37 were evaluated in a mouse model of TI induced by the administration of beta-glucan in vivo (survival to a lethal inoculum of infectious agents, production of inflammatory cytokines, recruitment of inflammatory cells at the sites of infection). Subsequently, the effects of IL-37 were evaluated *ex vivo* on bone marrow monocytes (production of inflammatory cytokines, metabolomic analysis of the activation status of the main pathways of cellular energy metabolism).

Finally, we evaluated the association between IL-37 gene polymorphisms and the induction of TI in monocytes of healthy donors with *in vitro* functional studies.

Results: The exogenous administration of IL-37 abrogated the pro-inflammatory effects of TI, significantly reducing the production of pro-inflammatory cytokines and the survival of experimental animals subjected to a model of disseminated infection. The inhibitory effects of IL-37 on TI were also associated with reduced recruitment of neutrophils at sites of inflammation. IL-37 and TI programs had differential and opposite effects on the modulation of cellular energy metabolism of monocytes. In humans, polymorphisms in the IL-37 gene were associated with reduced activation of TI programs and reduced production of inflammatory cytokines by healthy donor monocytes.

Conclusion: In conclusion, IL-37 emerges as an endogenous regulator of TI, which makes this cytokine a potential therapeutic target in immune-mediated pathologies.

REFERENCES:

[1] M. G. Netea, et al., Trained immunity: A program of innate immune memory in health and disease. Science. (2016).
[2] G. Cavalli, C. A. Dinarello, Suppression of inflammation and acquired immunity by IL-37. Immunol Rev (2018).

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THU0011 PEFICITINIB (ASP015K) INHIBITS MONOCYTE CHEMOTACTIC ACTIVITY VIA PROINFLAMMATORY CYTOKINE PRODUCTION IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

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Background: Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway has been identified as an important signaling pathway in rheumatoid arthritis (RA) of various cytokines (eg, IL-6). Janus kinase (JAK) is a cytoplasmic protein tyrosine kinase associated with various cytokine receptors. Molecules of signaling pathways such as the JAK family are thought to be promising targets for RA treatment. Peficitinib (ASP015K) is a novel JAK inhibitor in development for the treatment of RA. Peficitinib has been suggested for its effectiveness in clinical trials, but clarification of the mechanism of RA for the inflammatory pathology is still inadequate.

Objectives: We clarified the effect of peficitinib on RA fibroblast-like synoviocytes (FLS).

Methods: To determine whether JAK1, JAK2 and JAK3 were expressed in RA ST and FLS, immunohistochemistry was performed. In order to confirm if IL-6 and IL-6 receptor (IL-6R) activate JAK-STAT pathway in FLS, western blot analysis was performed. RA FLS were stimulated with IL-6 (100 ng/ml) and IL-6R (100 ng/ml) for 10 minutes or 30 minutes. Next, we investigated effect of peficitinib on IL-6 and IL-6R responses in RA FLS. RA FLS were stimulated with IL-6 (100 ng/ml) and IL-6R (100 ng/ml) after treated peficitinib (0.1, 1, 5μM) for 24 h. Furthermore, we performed a proliferation assay of FLS and chemotaxis assay using THP-1 (human acute monocyte leukemia cell line) and peripheral blood mononuclear cells (PBMC) to perform functional analysis by peficitinib. In the same procedure as Western blot analysis, peficitinib (5 μM) was added to FLS and stimulate with IL-6 and IL-6R. Finally, we investigated whether peficitinib suppresses the secretion of FLS inflammatory mediator using ELISA. The amounts of RANTES/CCL5, MCP-1/CCL2, MMP-3, fractalkine/CX3CL1, ENA78/CXCL5 and IL-8 in IL-6 and IL-6R stimulated peficitinib treated RA FLS conditioned medium were determined compared with IL-6 and IL-6R stimulated non treated RA FLS conditioned medium.

Results: We found JAK1, JAK2 and JAK3 were expressed in RA STs and FLS. JAK1 and JAK3 were observed in RA ST lining layers. JAK2 was expressed entirely in RA ST cell nucleus. JAK1, JAK2 and JAK3 were detected in RA FLSs. It was confirmed that JAK1, JAK2 and JAK3 is expressed in FLSs of ST. Representative western blotting showing expression of phospho STAT1, phospho STAT3 and phospho STAT5 were increased 10 minutes after stimulation with IL-6 and IL-6R. Phosphorylation of STAT1, STAT3 and STAT5 in RA FLS was suppressed by concentration dependence of peficitinib. It was proved that peficitiib suppress the activation of JAK-STAT pathway. Furthermore, peficitinib treated RA FLS conditioned medium reduced THP-1 migration compared to non-treated RA FLS conditioned medium (number of THP-1 cells migrated ± SEM; 42 ± 3 and 66 ± 6 cells migrated, respectively, p<0.05). Peficitinib treated RA FLS conditioned medium also reduced PBMC migration compared to nontreated RA FLS conditioned medium (number of PBMC migrated ± SEM; 36 ± 5 and 63 ± 9 cells migrated, respectively, p<0.05). In addition, peficitinib treated RA FLS showed a 14 ± 2% decrease in proliferation of RA FLS compared with nontreated RA FLS. Finally, we found peficitinib suppress the secretion of inflammatory mediators in RA FLS. MCP-1/CCL2 in RA FLS supernatant was suppressed in peficitinib compared to nontreated(mean ± SEM; 160.1 ± 65.6 and 846.0 ± 107.1 pg/ml, respectively, p<0.05). From these results, suppression of chemotaxis of THP-1 and PBMC was also observed through suppression of MCP-1/CCL2 in RA FLS supernatant.

Conclusion: Peficitinib suppressed the JAK-STAT pathway of RA FLS and was involved in the suppress of monocyte chemotaxis and the proliferation of FLS through suppress of inflammatory cytokines. These results suggest that peficitinib acts on FLS and suppresses inflammatory pathology.

Disclosure of Interests: None declared
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THU0012 ESTROGEN REGULATES MICRO RNA BIOPROCESSING AND PRODUCTION OF IL9 CYTOKINE WITHIN LEUKOCYTES IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is more prevalent in females. It is reported to be alleviated during pregnancy, and increase in severity during menopause, which implies estrogen as an important contributor in RA pathogenesis. Micro-RNA (miR) are short, non-coding RNAs, that act within a RNA-induced silencing complex. miRs have recently emerged as important epigenetic controls of leukocyte maturation and function.

Objectives: To study the epigenetic effect of estrogen on the transcription of microRNA and their bio-processor enzymes in RA patients.

Methods: The leukocytes of 145 female RA patients split for estrogen receptor alpha (ERα) (dCT 9.57) were analyzed for the expression of Dicer, Drosha and DGCR8 mRNA by RT-PCR and serum levels of TGFb-dependent cytokines IL4 and IL9. Micro-RNA transcription array was performed by 3D-Gene™ microarray measuring >2560 miRs (TATAA Biocenter, Gothenburg) in human primary leukocytes, fat tissue and plasma. The samples were split by expression of estrogen receptor alpha (ERα, dCT 9.57), a proxy of an active estrogen signaling, and used to identify miRs of interest. Bioinformatic analysis was performed using DIANA, miRDB, miRTarBase and Ensembl, using microRNA nucleotide sequences obtained from miRBase, to predict signaling pathways and gene targets of miR. To confirm estrogens effect on miR processing, leukocyte cultures of RA patients were exposed to estrogen and subjected to miR, gene and protein analysis.

Results: Comparing leukocytes with different ERα, we identified 214 miRs with high and 7 miRs with low expression when ERα was high. Cross-analysis in the fat and serum sample miR array identified most of those miRs. Bioinformatic analysis of the upregulated miRs confirmed that 16miRs were involved in the estrogen signaling pathway (p=0.0063) and 15 TGFb signaling pathway (p=<0.0001), where these miRs had 61 common predicted gene targets.

To study if transcription of these predicted targets was dependent on estrogen signaling, we took advantage of the clinical RA material. Patients with high ERα were significantly younger (51y vs 61y, p<0.00001), which confirmed active estrogen signaling. High ERα had significantly higher expression of miR bioprocessing enzymes Dicer (p=0.0197), Drosha (p=0.0454), DGCR8 (P=0.0192) and lower disease activity (DAS28, p=0.0023; ESR p=0.005, IL6, p=0.0129).

Exposure of leukocytes to estrogen in culture induced a significant reduction in IL9 (p=0.0078), which suggests a suppression of TGFb signaling.

Conclusion: High ERα expression can be considered a significant regulator of miR transcription in leukocytes. miR and bio-processors regulated by estrogen could be of importance in the pathogenesis on RA by targeting genes responsible for regulation of inflammation and the non-protective elements of RA development; explaining the ameliorating effects of estrogen.

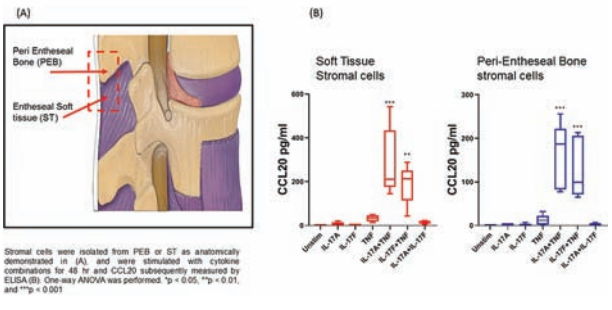
Disclosure of Interests: None declared
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THU0013 IL-17A AND IL-17F ARE SECRETED BY ENTHESIS T CELLS AND SYNERGIZE WITH TNF TO INDUCE CCL20 FROM ENTHESEAL STROMAL CELLS

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Background: Enthesitis or inflammation of tendon/ligament anchorage points is the cardinal lesion in spondyloarthritis (SpA)[1]. Human SpA is thought to be driven by IL-17 producing T-cells and can be successfully therapeutically targeted with anti-IL-17A and more recently anti-IL-17F[2]. The CCR6-CCL20 axis is thought to be crucial to tissue recruitment of IL-17 producing T-cells into tissues, however it is presently unknown if CCR6+ T-cells reside at the healthy human enthesis[3]. Moreover, the ability of IL-17 to drive CCL20 production and hence to promote further T-cell migration to the enthesis has not been tested.
Objectives: To determine if enthesis T cells secrete IL-17A and IL-17F. To determine if CCR6+ T-cells reside at the normal human enthesis. To study the effect of both IL-17A and IL-17F on CCL20 induction from entheseal stromal cells.
Methods: Normal spinous process enthesis was obtained from patients undergoing spinal decompression or surgery for scoliosis correction. Following enzymatic digestion, CD4+ and CD8+ T cells were stimulated with anti CD3/CD28 and IL-17A and IL-17F measured by intracellular FACS. Stromal cells were isolated from both the peri-entheseal bone (PEB) and enthesis soft tissue (ST). Stromal cells were stimulated with combinations of IL-17A or IL-17F and TNF and subsequently CCL20 was measured by ELISA. Normal PEB and ST were also analysed for the presence CCR6 + T-cells by multiparameter FACS including CD4+ and CD8
Results: Entheseal CD4+ cells secreted IL-17A and IL-17F following stimulation. When used as single agents IL-17A, IL-17F and TNF were able to induce minimal CCL20 from entheseal stromal cells, but great synergy was reported between IL-17A/TNF and IL-17F/TNF. No synergy was reported for IL-17A/IL-17F. CCR6+ CD4+ and CD8+ cells were also confirmed in the enthesis.

Figure 1: IL-17A and IL-17F synergize with TNF to induce CCL20 from Entheseal stromal cells



Abstract THU0013 Figure 1.

Conclusion: Resident CD4+ T cells at the enthesis secrete IL-17A and IL-17F following stimulation. The normal human enthesis contains CCR6+ T cell populations, suggesting a CCR6/CCL20 axis is important to entheseal homeostasis. IL-17A/F dramatically synergize with TNF to induce CCL20 from enthesis stromal cells, which would be well placed to mediate further migration of IL-17 producing lymphocytes to entheseal tissues.

REFERENCES:

[1] Bridgewood, C., et al., *Spondyloarthritis: new insights into clinical aspects, translational immunology and therapeutics*. Current opinion in rheumatology, 2018. 30(5): p. 526-532.
[2] Hall, A.O.H., J.E. Towne, and S.E. Plevy, *Get the IL-17F outta here!* Nature immunology, 2018: p. 1.
[3] Singh, S.P., et al., *Human T cells that are able to produce IL-17 express the chemokine receptor CCR6*. The Journal of Immunology, 2008. 180(1): p. 214-221.

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THU0014 TARGETING ACTIVATED ASK1 IN SYNOVIAL FIBROBLASTS IN COMBINATION WITH JAK1 INHIBITION ENHANCES EFFICACY IN RAT CIA

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Background: Despite improved therapy, rheumatoid arthritis (RA) remains an area of unmet medical need. Current therapies have improved disease control by targeting inflammatory pathways. However, treatments rarely induce remission, highlighting the need for new therapies. Filgotinib (FIL) is an oral selective JAK1 inhibitor that has demonstrated clinical efficacy in RA trials.[1-3] Apoptosis signal-regulating kinase 1 (ASK1) is a member of the MAP3K family that activates p38 and c-jun and has recently been shown to modulate human RA fibroblast-like synoviocyte (FLS) invasion, proliferation, and migration in vitro.[4] We hypothesize that by dual targeting of JAK-dependent inflammatory pathways with FIL, and ASK1 signaling in FLS with an ASK1 inhibitor, we can demonstrate an increase in efficacy in a rat collagen-induced arthritis (CIA) model.
Objectives: To evaluate the individual and combination activity of JAK1 and ASK1 inhibition in the rat CIA model by oral dosing with FIL and an ASK1 inhibitor.
Methods: The in vivo efficacy of FIL and an ASK1 inhibitor were tested individually or in combination in a therapeutic rat CIA model. Dosing was initiated at the onset of disease (day 11) and continued until day 18. Efficacy evaluations were based on animal body weights, daily ankle caliper measurements, ankle diameter (expressed as area under the curve), terminal hind paw weights, and histopathology of the ankles and knees.
Results: Administration of FIL individually significantly reduced ankle diameter and final paw weights by 51% and 52%, respectively ($p<0.05$). There was no change in body weight loss or in histological measurements with treatment. Conversely, ASK1 inhibition did not reduce inflammation as measured by ankle diameter or paw swelling, but resulted in a 48% reduction in ankle histopathological score ($p<0.05$). The combination of FIL and the ASK1 inhibitor showed significantly greater effects on all measured parameters including paw weight (81% reduction), ankle diameter (78% reduction), and ankle and knee histopathology scores (69% and 87% reduction, respectively) than either agent alone. Body weight loss was also significantly reduced with the combination, and increased toward normal weight gain compared to the monotherapy arms.
Conclusion: Combining FIL with ASK1 inhibition significantly improved clinical and histopathology scores, and reduced body weight loss in this model. These data suggest that simultaneously targeting JAK and ASK1 pathways can provide orthogonal activities that can enhance overall disease control.

REFERENCES:

[1] Kavanaugh A, et al. Ann Rheum Dis. 2017;76:1009-1019.
[2] Westhovens R, et al. Ann Rheum Dis. 2017;76:998-1008.
[3] MC Genovese, et al. ACR 2018, Abstract L06.
[4] Nygaard G, et al. Biochem Pharm. 2018;151:282-290.

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THU0015

VARIATION IN MACROPHAGES DIFFERENTIATION AND SREBF1 EXPRESSION BETWEEN INFRAPATELLAR FAT PAD AND SUBCUTANEOUS TISSUES FROM RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS PATIENTS

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Background: Sterol regulatory element-binding protein 1 (SREBP1) has been known to upregulate the expression levels of regulators of ω-3 fatty acids in the resolution phase of macrophages, and this would in turn repress the production of pro-inflammatory cytokines.[1, 2] In OA joints, adipocytes might participate in inflammatory process.[3] We are interested in the proportion of M1 and M2 macrophages in stromal vascular fraction (SVF) from both tissues in both diseases. And to investigate how *srebf1* works in infrapatellar fat pad (IFP, or Hoffa) or subcutaneous (SC) tissue, we studied the expression levels of *srebf1*, pro-inflammatory cytokines and regulators of fatty acids.

Objectives: To investigate the proportion of CD14 positive cells as well as M1 and M2 macrophages in SVF of Hoffa and SC; and to explore contribution of SREBP1 to rheumatic disease pathological processes of RA and OA.

Methods: After treated with collagenase, macrophages (CD14 positive cells) in SVF were counted by flow cytometry. Then they were divided, half for calculating the ratio between CD80 positive cells (M1 macrophages) and CD163 positive cells (M2 macrophages), and half for performing qRT-PCR.

Results: Characteristics of the patients

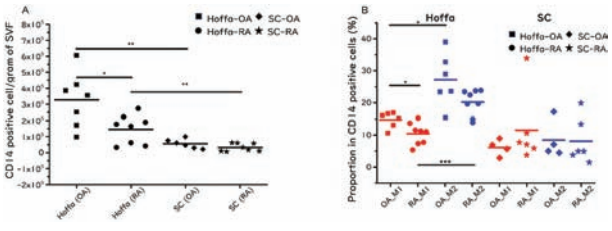
Table 1. Characteristics of the patients

		OA (n=7)	RA (n=8)	*p* value
Age (years)		72 (62-79)	63 (49-76)	0.055
Female patients (n)		6	7	
Male patients (n)		1	1	
Height (cm)		155 (151-164)	157 (147-161)	0.341
Body weight (kg)		62.7 (48.7-74.1)	58.7 (48.8-72.2)	0.386
pre-ope CRP (mg/L)		0.75 (0-2)	12.8 (0-17)	0.064
BMI	Underweight	0%	0%	
	Normal	42.9%	50.0%	0.234
	Overweight	42.9%	37.5%	0.05
	Obese	14.3%	12.5%	

OA: osteoarthritis; RA: rheumatoid arthritis; CRP: C-reactive protein; BMI: body mass index; BMI: <18,5 underweight; BMI: 18.5–24.99 normal; BMI: 25.0–29.99 overweight; BMI >30.0 obesity[4]

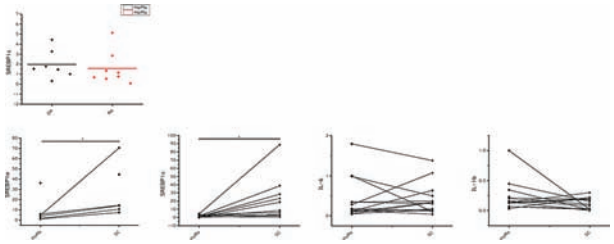
More CD14 positive cells exist in Hoffa comparing to SC, and M2 macrophages show higher proportion.

A comparison of proportion of CD14 positive cells between Hoffa and SC showed significance both from OA and from RA. To M2 macrophages proportion, higher percentages of M2 macrophages (OA: 26.3±5.5%, RA: 22.5±2.4%) exist in Hoffa from both OA and RA patients, but no significance was found between the diseases. However, the proportion of M1 macrophages (OA: 15.6±1.7%, RA: 11.3±2.1%) indicated significance.



Abstract THU0015 Figure 1. (A) Proportion of CD14 positive cells per gram of SVF from OA and RA patients. (B) Proportion of M1 and M2 macrophages in CD14 positive cells from OA and RA patients. (*p<0.05, **p<0.01, ***p<0.001, as determined by One-Way ANOVA.)

Srebf1 expressed less in Hoffa than in SC



Abstract THU0015 Figure 2. qRT-PCR analysis of cytokine and *srebf1* expression levels displayed among total patients. (*p<0.05, as determined by One-Way ANOVA.)

Results show that in Hoffa, *srebf1c* expressed less in RA patients than that in OA patients, but no significance was indicated. In the comparison of expression levels between Hoffa and SC, both *srebf1a* and *srebf1c* showed significance, and more *IL-6* and *IL-1*β expressed in Hoffa than in SC.

Conclusion: In RA patients, more M2 macrophages exist in Hoffa than in SC. Lower expression levels of *srebf1c* in Hoffa from RA patients suggests that macrophages differentiation can be reprogrammed by fatty acid metabolism.

REFERENCES:

[1] Oishi, Y., et al., Cell Metab, 2017. 25(2): p. 412-427
[2] Shimano, H. and R. Sato, Nat Rev Endocrinol, 2017. 13(12): p. 710-730.
[3] Shimano, H., et al., The Journal of Clinical Investigation, 1997. 99(5): p. 846-854.
[4] Plebanczyk, M., et al., Inflammation, 2018.

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THU0016

ALTERED EXPRESSION AND FUNCTION OF P2X7 RECEPTOR IN PATIENTSAFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Extracellular ATP (eATP) is one of the most diffuse danger associated molecular patterns (DAMPs) released actively through specific mechanisms from intact cells, or passively from damaged or dying cells[1]. An implication for eATP has been found in SLE[2]. Among receptors for eATP, P2X7R is deeply involved in inflammatory and immune processes and its activation drives different intracellular pathways such as NLRP3-inflammasome activation, IL-1β maturation and release, IL-6 and TNF-α production, regulation of lymphocyte proliferation and cell apoptosis[3]. Previous studies pointed out a possible relationship between P2X7R signaling pathways and SLE pathogenesis[4 5]. A marked inflammatory condition characterize serositis, that are among the most common manifestations of SLE, and chloroquine is one of the main drugs employed.

Objectives: The aim of this study was to investigate P2X7R expression and activity in SLE.

Methods: 48 SLE patients, and 20 healthy control (HC) subjects were enrolled. Among SLE patients, 16 (SLE-S) presented, and 32 (SLE-NS) did not present history of serositis. All subjects gave written informed consent to peripheral venous blood withdrawal after approval by the local ethic committee. Plasma samples were used to measure IL-1β, IL-6 and TNF-α levels by ELISA. Mononuclear cells were isolated from blood samples by Ficoll gradient sedimentation and employed as follow: i) assessment of IL-1β, IL-6 and TNF-α release after stimulation with lipopolysaccharide (LPS) and/or Benzoyl ATP (BzATP); ii) evaluation of P2X7R mRNA expression by RT-PCR; iii) measurement of P2X7R activity as BzATP-induced increase of intracellular Ca^{2+} concentration using the Fura2/AM probe.

Results: In SLE patients respect to HC, plasma IL-1β levels were unmodified whereas IL-6 was higher, resulting significantly increased in SLE-S. Monocytes isolated from SLE patients released lower quantities of IL-1β after stimulation with BzATP, whereas the release of both IL-6 and TNF-α was significantly augmented in SLE-NS respect to both HC and SLE-S subjects after all types of stimulation. RT-PCR showed reduced P2X7R and augmented NLRP3 mRNA expression in SLE patients. Accordingly, P2X7R activity was significantly reduced in all SLE patients and did not appear to be influenced by a chloroquine pre-treatment.
Conclusion: In SLE patients, compared to HC subjects, we found reduced P2X7R mRNA expression, increased NLRP3 mRNA, as a possible compensating mechanism, and correspondingly, significantly lower BzATP-induced intracellular Ca^{2+} increase, without an apparent influence by chloroquine, one of the drugs most diffusely used for SLE treatment. The in vitro IL-1β release was reduced, whereas plasma IL-1β was unaltered, indicating an alternative source, other than monocytes, of this cytokine. Conversely, IL-6 and TNF-α levels were increased in vitro, and IL-6 was present in plasma at higher levels. The possible consequences of reduced P2X7R, mainly on cytokines network deregulation and lymphocyte proliferation, will be further investigated as well as the role of IL-6 and TNF-α as possible therapeutic targets.

REFERENCES:

[1] Giuliani, A.L. et al. Extracellular nucleotides and nucleosides as signalling molecules. Immunol Lett, doi:10.1016/j.imlet.2018.11.006 (2018).
[2] Magna, M. & Pisetsky, D.S. The Role of Cell Death in the Pathogenesis of SLE: Is Pyroptosis the Missing Link? Scand J Immunol 82, 218-224, (2015).
[3] Di Virgilio, F. et al. The P2X7 Receptor in Infection and Inflammation. Immunity 47, 15-31, (2017).
[4] Di Virgilio, F. & Giuliani, A.L. Purinergic signalling in autoimmunity: A role for the P2X7R in systemic lupus erythematosus? Biomed J 39, 326-338, (2016).
[5] Faliti, C.E. et al. P2X7 receptor restrains pathogenic Tfh cell generation in systemic lupus erythematosus. J Exp Med, (2019).

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THU0017 IN VITRO MECHANISTIC STUDIES DEMONSTRATE FILGOTINIB ACTIVITY THAT HAS POTENTIAL IMPLICATIONS FOR DIFFERENTIATION AMONG JAK INHIBITORS

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Background: Inhibition of the Janus kinase-signal transducers and activators of transcription (JAK-STAT) pathway has demonstrated efficacy in immune-mediated diseases and has been identified as a therapeutic target for the treatment of rheumatoid arthritis (RA). Differences in JAK inhibitor specificity for JAK1, JAK2, JAK3, and TYK2 may influence their safety profiles, but the mechanism is not known. Selective JAK1 inhibition by filgotinib (FIL) may modulate a subset of proinflammatory cytokines associated with RA pathogenesis and improve the risk-benefit profile by minimizing other non–JAK1-related adverse events. JAK2 inhibition is associated with cytopenias, while JAK3 inhibition has been associated with increased risk for opportunistic infections (eg, tuberculosis and herpes zoster) and chronic low-grade inflammation. In clinical trials, FIL did not negatively impact hemoglobin, LDL/HDL ratios, or natural killer (NK) cell counts.[1-3]
Objectives: To compare the in vitro profile of JAK inhibitors with different JAK selectivity profiles, for effects on erythroid progenitor cell expansion, NK cell proliferation, and liver X receptor (LXR) agonist-induced cholesteryl ester transfer protein (CETP) expression, an enzyme responsible for the conversion of HDL to LDL.
Methods: JAK inhibitors (FIL, FIL metabolite [GS-829845], baricitinib [BARI], tofacitinib [TOFA], and upadacitinib [UPA]) were evaluated in vitro in human cell-based assays: growth of erythroid progenitors from human cord blood $CD34^+$ cells using a HemaTox™ liquid expansion assay, IL-15–induced NK cell proliferation, and LXR agonist-induced CETP expression in the hepatic cell line (HepG2). Using IC_{50}s generated from these assays and the reported human plasma concentrations of the JAK inhibitors from clinical studies,[4-6] we calculated the target coverage for each compound at clinically relevant doses. The activity of FIL in humans was based on a PK-PD modeling algorithm[7] of FIL + GS-829845.
Results: In vitro assay results are described in the table. Based on these results, human exposure data, and modeled PK-PD relationships, FIL 100 mg and FIL 200 mg result in lower calculated cellular inhibition than the other JAK inhibitors at clinical exposures. Notably, FIL 100 mg and FIL 200 mg, but not the other inhibitors, are calculated to reduce CETP expression by 17% and 27%, respectively, while BARI, TOFA, and UPA are not expected to alter CETP levels.

Abstract THU0017 Table 1. IC_{50} ± SD in in vitro assays (nM, unless otherwise noted).

Assay	FIL	GS-829845	BARI	TOFA	UPA
Early erythroid progenitors	1960 ±137	19300 ±1730	38.6±2.9	210 ±15.2	42 ±2.9
Mature erythroid progenitors	1140 ±112	10600 ±1270	25.7±2.9	110 ±10	24.5 ±2.75
NK cell proliferation	314.8 ±53	9697 ±8100	6.6±1.9	12.2 ±2.1	4.1 ±1.7
Inhibition of LXR agonist-induced CETP expression	15.3 ±7.1 μM	19.4 ±4.2 μM	>1 μM weak induction[a]	No effect	

[a] Weak stimulation of LXR agonist-induced CETP expression.
Conclusion: JAK1 selectivity of FIL and GS-829845 resulted in less inhibition of erythroid progenitor expansion and NK cell proliferation compared with BARI, TOFA, and UPA. FIL also reduced LXR agonist-induced CETP expression, while the other inhibitors did not alter these levels. These results provide a potential mechanistic link to the observed reduction of CETP concentration and activity following FIL treatment, and the observed reduction in LDL:HDL in RA patients.[8]

REFERENCES:

[1] Kavanaugh A, et al. Ann Rheum Dis. 2017;76:1009-1019.
[2] Westhovens R, et al. Ann Rheum Dis. 2017;76:998-1008.
[3] MC Genovese, et al. ACR 2018. Abstract L06.
[4] Shi JG. J Clin Pharmacol. 2014;54:1354-1361.
[5] Lamba M. J Clin Pharmacol. 2016;56:1362-1371.
[6] Mohamed MF, et al. Clin Pharmacokinet. 2016;55:1547-1558.
[7] Tuk B. J Pharmacol Exp Ther. 1999;289:1067-1074.
[8] Galien R. Arthritis Rheumatol. 2015;67(suppl 10).

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THU0018 ANTI-GALECTIN-9 ANTIBODY AS A NOVEL TREATMENT OPTION IN RHEUMATOID ARTHRITIS TARGETING PATHOGENIC FIBROBLAST-LIKE SYNOVIOCYTES

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Background: Fibroblasts-like synoviocytes (FLS) present in the stromal environment are key effector cells in the persistence of synovial inflammation and joint damage in rheumatoid arthritis (RA). A particular subset of FLS characterized as $Thy\text{-}1^+Podoplanin^+CD34^-$ is significantly expanded in RA patients and has been described to be disease-associated[1]. Currently, no treatment targeting the stromal environment in RA is available[2].
Objectives: To identify a novel treatment option targeting the stromal environment in RA to modify the disease-associated subset of fibroblasts.
Methods: An *in vitro* model was established with FLS derived from synovial fluid mononuclear cells (SFMC) from RA and osteoarthritis (OA) patients (n=6). FLS between passage 2-5 were used for further analyses. Untreated FLS in cultures were analyzed by flow cytometry for expression

of the surface proteins CD34, CD45, Thy-1 and Podoplanin. The potential effect of cell detachment solutions on the expression of the surface proteins was examined by applying either trypsin or lidocaine. To evaluate on the inflammation status of the FLS, MCP-1 levels in supernatants from FLS in mono-cultures stimulated with either antibodies targeting galectin-9 (Gal-9), an anti-Gal-9 antibody-matched isotype control, LPS or steroid were analyzed by ELISA and compared to culture medium alone. Cell viability were examined using an MTT assay. Data are expressed as mean (95% CI) and analysed by a paired t-test. P-values <0.05 were considered statistically significant.

Results: FLS derived from SFMC were characterized as $CD34^{-}CD45^{-}$ and the majority co-expressed Thy-1 and Podoplanin [80.5%, (66.3-94.7%)] confirming the pathogenic phenotype of these cells. This phenotype was not altered by using different methods to detach the cells from the cell-culture plates. FLS receiving anti-Gal-9 antibody treatment showed a significant decreased fold change in MCP-1 secretion (0.84, [0.70;0.98]) compared with unstimulated cells (p=0.036). Treatment with an isotype control did not result in a significant decrease in MCP-1 secretion. This tendency was specific to FLS derived from RA patients as FLS derived from OA patients showed no significant decrease in MCP-1 secretion upon anti-Gal-9 antibody treatment. FLS derived from both RA or OA patients showed a significant increased fold change in secretion of MCP-1 upon LPS stimulation and significantly decreased levels of MCP-1 upon steroid treatment, consistent with the pathogenic phenotype of these cells. None of the different stimulations resulted in morphological changes of the FLS examined by light microscopy. Further, no significant changes in cell viability were detected after anti-Gal-9 antibody treatment.

Conclusion: FLS cultures derived from RA patients at passage 2-5 consist mainly of disease-associated fibroblasts and secrete significantly lower amounts of MCP-1 when treated with an anti-Gal-9 antibody whitout affecting cell viability. Thus suggesting that Gal-9 neutralization may represent a novel treatment option targeting the stromal environment and inflammation in RA.

REFERENCES:

[1] Mizoguchi, F. et al. Functionally distinct disease-associated fibroblast subsets in rheumatoid arthritis. Nat. Commun. 9, 789 (2018).
[2] Dakin, S. G. et al. Pathogenic stromal cells as therapeutic targets in joint inflammation. Nat. Rev. Rheumatol. 14, 714–726 (2018).

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THU0019 INHIBITION OF FUCOSYLATION IN ENDOTHELIAL CELLS REDUCES RHEUMATOID ARTHRITIS ANGIOGENESIS

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Background: Glycosylation has been reported to associate with tumor invasion and metastasis. Fucosylation is involved the biological functions of adhesion molecules and growth factor receptors. In regards to arthritis, we have previously reported that fucosylated proteins were expressed in rheumatoid arthritis (RA) synovial tissues. However, a direct role for fucosylated cytokines in RA has not been demonstrated.

Objectives: To confirm that fucosylated proteins are expressed in RA and are involved in RA angiogenesis.

Methods: Total glycans were determined in serum from normal (NL) subjects and RA patients using mass spectrometry. N-glycans from 10 RA or 10 healthy controls, and 10 pretreatment with tocilizumab (TCZ) or after treatment sera at 24 weeks were purified by glycoblotting using BlotGlycoH.To determine whether fcosylated proteins involved with RA inflammation, the correlation with disease activity score (DAS) 28 (ESR) was measured. 2-deoxy-D-galactose (2-dGal) is an analog of hexose that inhibits fucosylation. In order to confirm the role of fucosylation in RA angiogenesis, we did Matrigel assays *in vitro*. To block the expression of fcosylated proteins, human umbilical vein endothelial cells (HUVECs) were treated with 2-dGal (15 mM) for 5 days. After treatment with 2-dGal, HUVECs were plated on Matrigel and were incubated with phosphate buffered saline (PBS) or RA synovial fluids. In addition, chemotaxis assays were performed to determine the role of fucosylation in HUVEC migration. Finally, expression of proangiogenic cytokines such as fractalkine/CX3CL1, CXCL16, interleukin (IL)-8/CXCL8, monocyte chemotactic protein 1 (MCP-1)/CCL2, epithelial neutrophil-activating protein 78 (ENA-78)/CXCL5 and vascular endothelial growth factor (VEGF) in 2-dGal treated HUVEC conditioned medium were measured by ELISA.

Results: Total glycans in RA serum were significantly higher than in NL serum [mean ± SEM; 477 ± 24 pmol/µl (n=10) and 339 ± 14 pmol/µl (n=10), p<0.05, respectively]. In addition, total glycans in RA serum were significantly decreased with tocilizumab treatment at 24 weeks. Total glycans in RA serum were also correlated with DAS28 (ESR). Percent of fucosylated proteins in total glycans were decreased with TCZ treatment at 24 weeks. 2-d Gal treated HUVEC tube formed towards RA synovial fluids (n=6 patients) were decreased compared with nontreated HUVEC tube formed (number of tube formed; 7 ± 1 and 25 ± 2, p<0.05, respectively). We found that 2dGal treated HUVECs showed decreased migration compared with nontreated HUVECs, towards RA SF (numbers of HUVEC migrated; 3 ± 1 and 34 ± 4, n=5 patients, p<0.05). Fractalkine/CX3CL1, CXCL16, or IL-8/CXCL8 in 2-d Gal treated HUVEC conditioned medium were decreased compared with in non-treated HUVEC conditioned medium but not MCP-1/CCL2, ENA-78/CXCL5, or VEGF.

Conclusion: These data indicate that glycoproteins are involved with RA, and play a role in angiogenesis in RA and suggest that targeting glycosylation especially fucosylation may provide a method by which to decrease inflammation and potentially treat other inflammatory diseases.

Disclosure of Interests: None declared
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THU0020 COMPARATIVE STUDY OF THE PHOSPHODIESTERASE TYPE 5 INHIBITOR SILDENAFIL AND THE PROSTACYCLIN ANALOGUE ILOPROST ON IP10 MODULATION IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease ending in multiorgan fibrosis. Vascular damage, responsible for the vascular alteration and disruption, has been suggested to play a key role in disease maintenance and progression [1]. Recent data demonstrated that high serum levels of the interferon (IFN)-γ-induced protein 10 (IP-10) in SSc patients correlated with peripheral vascular injure and increased in association with nailfold capillaroscopic pattern worsening and digital ulcers presence [2, 3]. Between the vasoactive drugs used for SSc treatment, the prostacyclin analogue iloprost (I) and PDE-5 inhibitor sildenafil (S) seem to have high vasodilatatory and immunomodulatory actions [4-6].

Objectives: To investigate and compare the ability of S and I to modulate: IP-10 circulating levels in SSc patients under different treatments; IP-10 release by human endothelial (Hfaec) cells subjected to Th1-related inflammatory stimuli.

Methods: Sera of 28 patients satisfying ACR/EULAR 2013 classification criteria for SSc were analyzed by ELISA. IFNγ+TNFα-induced activation of NFkB, STAT1, JNK, ERK1/2 and AKT in Hfaec after S or I was tested by Western blot.

Results: The treatment with S significantly reduced IP-10 serum levels vs. treatment with (DMARDS) and corticosteroids (CCs) (184.1±65.10 vs. 880.9±339.0 pg/ml and vs. 426.5±101.7, respectively, P<0.01); while no significant difference has been found vs. I (184.1±65.10 vs. 282.7±46.6 pg/ml). In Hfaec, S and I differently counteracted the IFN-γ/TNF-α-induced phosphorylation of JNKs (respectively 61.6.0±20.1% and 9.5±13.1% of phosphorylation vs. I+T-induced taken as 100%), STAT1 (respectively 49.2±15.8% and 93.4±1.2% of phosphorylation vs. I+T-induced taken as 100%), NFkB (respectively 72.6±8.3% and 92.2±3.3% of phosphorylation vs. I+T-induced taken as 100%), ERK1/2 (respectively 31.6±7.9% and 27.3±4.4% of phosphorylation vs. I+T-induced taken as 100%), and AKT (respectively 85.7±5.6% and 3.8±7.4% of phosphorylation vs. I+T-induced taken as 100%).

Conclusion: In vivo results show that S and I have more effect in targeting serum IP-10 in SSc patients than other therapeutic treatments. In vitro data show different inhibitory drug-induced effects onto paths underlying IP-10 production, depending on intracellular targets. S could be a potential pharmacological tool as effective as I to control IP-10 in blood or at endothelial cell level in SSc.

REFERENCES:

[1] Varga J, et al., 2007.
[2] Antonelli A, et al., 2008.
[3] Crescioli C, et al., 2018.

[4] Scorza R, et al., 2001.
[5] Higuchi T, et al., 2015.
[6] Hassoun PM, et al. 2015.

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THU0021 CLINICAL SIGNIFICANCE OF WEIGHT LOSS ON THE LEVEL OF PROINFLAMMATORY CYTOKINES IN PATIENTS WITH OSTEOARTHRITIS

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Background: Obesity is a condition that prolongs chronic inflammation and promotes synthesis and secretion of pro-inflammatory factors by adipose tissue, such as classical cytokines, tumor necrosis factor-α (TNF-α), adipokines (leptin, adiponektin, resistin) and other newly identified proinflammatory factors (hemerin, lipokain, serum amyloid protein 3) [1,2,3,4,5]. Nowadays one of the most actively studied adipokines is nicotinamide phosphoribosyltransferase (visfatin, Nampt).
Objectives: We investigated the relationship the effect of weight loss over 5 kg on the clinical manifestations of OA and Nampt serum levels in patients with OA.
Methods: We observed 160 patients with different forms of OA ranged in age from 36 to 78 years, of whom there were 104 (65%) women (mean age 52.08 ± 1,58 years), and 56 (35%) of men (mean age - 54.07 ± 2,0 years) and the control group (60 healthy persons) with no complaints of pain in the joints over a lifetime, and without clinical signs of OA. Nampt level in serum was determined by ELISA using a commercial test systems.
Results: As overweight patients were recruited in the study, hypocaloric diet low in animal fats and physiotherapy has been recommended to all participants. The positive dynamics in body weight loss over 5kg within 3 months has been achieved by 36 patients (23%). All patients were divided into two groups to study the effect of weight loss on the clinical manifestations of OA. These data proves that obesity may be an important risk factor for OA progression. As a result, weight loss results in decreasing metabolic disorder severity. In the second group of patients we have seen a decrease in all the parameters, but a significant difference has been observed only in the level of CRP, level of pain at rest and during walking according to VAS scale and total index on the WOMAC. However, patients with weight loss over 5 kg had significantly greater positive dynamics of clinical parameters than in the second group without weight loss. This fact is probably explained by the decreased activity of inflammatory process after OA therapy and weight reduction.
Conclusion: Thus, as a result of our study patients with OA with weight loss of more than 5 kg had more obvious pain relief than patients with the original weight. These findings suggest that there is a possible role of visfatin in the pathogenesis of osteoarthritis. All patients with OA with a BMI over 25 kg/m 2 are recommended to lower their weight to decrease the mechanical stress on the joints, and also to reduce the severity of inflammation and metabolic disorders.

REFERENCES:

[1] Akhverdyan, Y. et al. Adipokines as new laboratory markers in osteoarthritis//Ann Rheum Dis 2013. – Vol.72 (Suppls. 3):702.
[2] Degtiarev, V.K.; Aleksandrov, A.V. et al. The influence of general magnetic therapy on the psychological status of the patients presenting with osteoarthrosis//Voprosy kurortologii, fizioterapii, i lechebno fizicheskoy kultury 2013, №3, P.27-30.
[3] Zavodovsky, B. V. et al. The efficacy and safety of etoricoxib versus meloxicam in the treatment of patients with gonarthrosis//Terapevticheskii Arkhiv Volume: 88 (12), P.: 78-81.
[4] Papichev, E. V. et al. Fetuin-a level and secondary osteoporosis in women with rheumatoid arthritis//Osteoporosis International, 2018, Vol.:29 S.239.
[5] Polyakova J. et al. Pathogenic relationship between osteoarthritis, overweight and inflammation//Annals of the Rheumatic Diseases. 2015. :. 74. №S2. C. 372.

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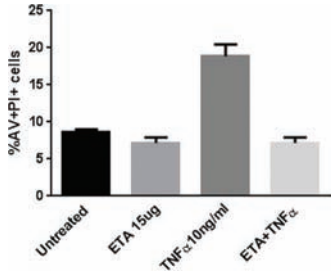
THU0022 ETANERCEPT INCREASES AUTOPHAGY AND REDUCES APOPTOSIS INDUCED BY TNF-ALPHA EXPOSURE IN ENDOTHELIAL CELLS IN VITRO

Alessandra Ida Celia, Cristiana Barbati, Fulvia Ceccarelli, Tania Colasanti, Annacarla Finucci, Carlo Perricone, Mariangela Speziali, Francesca Romana Spinelli, Marta Vomero, Fabrizio Conti, Guido Valesini, Cristiano Alessandri. *Sapienza University of Rome, Roma, Italy*

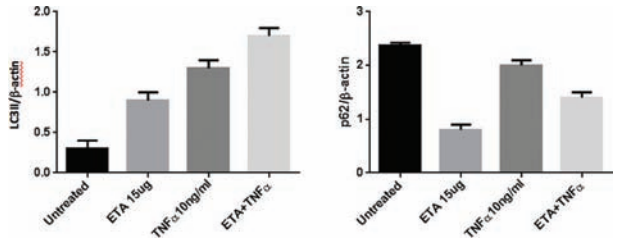
Background: Rheumatoid arthritis (RA) is associated with high incidence of cardiovascular events, mainly due to accelerated atherosclerosis and endothelial dysfunction (1). Apoptosis in endothelial cells has been associated with vascular wall damage, contributing to atherosclerotic plaque formation (2). At the contrary, autophagy may play a protective role in preventing development of atherosclerosis. However, the exact mechanism which controls the autophagy of endothelial cells is still unknown. Tumor necrosis factor alpha (TNF-α) is one of the leading cytokines involved in the pathogenesis of RA. Several evidences suggest a pro-atherogenic effect of TNF-α in patients with RA. Etanercept (ETA) and other TNF-α inhibitors are effective treatments for joint inflammation in RA, but their effect on endothelial dysfunction is still not well understood.
Objectives: The aim of this study was to investigate in *vitro,* the effects of ETA treatment on endothelial cells exposed to TNF-α, with particular attention on apoptosis levels and autophagy pathway.
Methods: *In vitro* effects of ETA and TNF-α on endothelium were evaluated using human umbilical vein cell line EA.hy926. Cells were treated with ETA (15μg), TNF-α (10 ng/ml), alone or in combination. An untreated control cell culture was also performed. After 24 hours, apoptosis levels and autophagy have been evaluated. Apoptosis was analyzed by flow cytometry using a FITC-conjugated annexin V and propidium iodide apoptosis detection kit (3); autophagy was analyzed by western blot for the expression level of the autophagic markers LC3-II and p-62 (4).
Results: TNF-α treatment significantly increased apoptosis in endothelial cells compared both to untreated and ETA-treated cells (p= 0.0067 and p= 0.00187 respectively) [Figure 1]. The co-treatment with TNF-α and ETA significantly reverted the increase of apoptosis levels (p= 0.001 versus TNFα alone). Both ETA and TNFα treatments significantly increased the expression level of LC3II in treated cells when compared to untreated cells (p=.18 and p=.3 respectively). The co-treatment induced an additive effect on autophagy levels (p< 0.0001 versus untreated cells). At last, the expression level of p-62 showed an inversely proportional trend to LC3II levels [ETA (p=0.0001), TNF-α p=.1), ETA+TNF-α p=5) versus untreated cells, respectively] [Figure 2].
Conclusion: Our results show that treatment with Etanercept have a protective effect on endothelial cells *in vitro*, reversing the apoptosis induced by TNF-α. Moreover, this is the first study that supports a possible effect of Etanercept in increasing autophagy level in endothelial cells. Reducing TNFα-induced apoptosis, Etanercept treatment may lead to an improvement of endothelial function and to a reduction of accelerated atherosclerosis.

REFERENCES:

[1] Hürlimann D, Forster A, Noll G, Enseleit F, Chenevard R, Distler O, et al. Anti-tumor necrosis factor-a treatment improves endothelial function in patients with rheumatoid arthritis. Circulation. 2002;106:2184–2187
[2] Fukuo K, Nakahashi T, Nomura S, Hata S, Suhara T, Shimizu M, et al. Possible participation of Fas-mediated apoptosis in the mechanism of atherosclerosis. Gerontology. 1997;1:35–42.
[3] Alessandri C, Barbati C, Vacirca D, Piscopo P, Confaloni A, Sanchez M, et al. T lymphocytes from patients with systemic lupus erythematosus are resistant to induction of autophagy. FASEB J. 2012;26:4722–4732.
[4] Barbati C, Alessandri C, Vomero M, Vona R, Colasanti T, Vacirca D, et al. Autoantibodies specific to D4GDI modulate Rho GTPase mediated cytoskeleton remodeling and induce autophagy in T lymphocytes. J Autoimmun. 2015;58:78–89.



Abstract THU0022 Figure 1.



Abstract THU0022 Figure 1.

Disclosure of Interests: None declared
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THU0023 PARADOXICAL EFFECT OF INTERLEUKIN 1 BETA CYTOKINE ON COLLAGEN TYPE I SYNTHESIS IN OSTEOBLAST-LIKE CELLS

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Background: Osteoblasts are the bone forming cells that responsible for the synthesis of collagen type I and mineralization of bone during initial bone formation and later bone remodeling. Abnormalities in osteoblasts phenotype and activity occur in common bone diseases including osteoarthritis (OA). Studies showed that osteoarthritic osteoblasts secrete a collagen type I homotrimer of α1 chains, which is phenotypically distinct from the normal heterotrimer formed by two α1 chains and one α2 chain.
Cytokines released during OA initiation or progression may interfere with osteoblastic function in the bone matrix. Interleukin 1 beta (IL-1β) is one of the major inflammatory cytokines implicated in the pathogenesis of OA; however, the biological response of osteoblasts to the cytokine is only partly understood.
Objectives: Our aims were to clarify the effects of IL-1β on collagen type I synthesis in osteoblast-like cells and to explore further possible relationship between collagen type I synthesis and mineralization.
Methods: At confluence, MG63 osteoblast-like cells in osteogenic media were stimulated with low (1 ng/ml) or high (10 ng/ml) dose of recombinant human IL-1β at several incubation times; 1, 2, 3, 4 and 5 hours. Non-stimulated MG63 cells were grown as control at indicated time points. Cell viability was tested by using the PrestoBlue reagent. Total collagen production was evaluated by Picro-sirius red precipitation method. Secretion of homotrimer collagen type I alpha 1 (COL1A1) and mineralization at exposure time of 1-, 3- and 5- hour were determined by immunofluorescence staining of COL1A1 antibody and Alizarin Red S staining, respectively.
Results: IL-1β showed no statistical evidence in influencing cell viability at the time and dose tested compared to control. We found that IL-1β significantly ($p<0.05$) increased collagen content at short exposure time (1-hour), while significantly ($p<0.05$) decreased collagen content at longer exposure time (5-hour), in a dose-dependent manner. Immunofluorescence staining showed increased of homotrimer COL1A1 at 1-hour exposure and decreased of homotrimer COL1A1 at 5-hour exposure of IL-1β in the MG63 cells. IL-1β stimulated the formation of mineralized nodules at all exposure time.
Conclusion: We demonstrated for the first time of the paradoxical effect of IL-1β on collagen type I synthesis in osteoblast-like cells. Increased mineralization in low and high homotrimer type I collagen condition may possibly explain the abnormal mineralization in osteoarthritic bone. Paradoxical role of IL-1β in osteoblast may generate a different signal that regulates osteoblast markers expressed in the heterogenous subchondral bone changes in OA. Understanding these mechanisms could pave the way towards targeted therapeutic interventions.
Acknowledgement: This study was supported by the Academy of Medical Sciences and the Material Science Institute Lancaster University.
Disclosure of Interests: None declared
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THU0024 INHIBITION OF CELL PROLIFERATION AND PROMOTION OF INTERLEUKIN-8 PRODUCTION BY T-614 IN CULTURED HUMAN AORTIC ADVENTITIAL FIBROBLASTS

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Background: Takayasu's arteritis (TA) is an inflammatory fibrosing arteritis that affects predominantly the aorta and its main branches. Recently, growing evidence supports that adventitial fibroblasts play an essential role in vascular inflammation [1].Tumor necrosis factor-α (TNF-α) can reportedly induce inflammation of vascular adventitial fibroblasts[2]. T-614 (iguratimod), a novel disease-modifying antirheumatic drug, has been widely used in rheumatoid arthritis in China and Japan [3]. However, the effect and mechanism of T-614 on TA have received little attention.
Objectives: We report the effects of T-614 on cell proliferation and interleukin-8 (IL-8) production in cultured human aortic adventitial fibroblasts (HAAF), and explored its possible effect on the treatment of TA.
Methods: HAAF were cultured with 0, 5, 50, 100, or 250 μg/ml T-614 in the absence or presence of 10 ng/ml TNF-α in vitro. Cell viability of HAAF was determined by a modified MTT assay. Supernatant IL-8 level was measured by enzyme linked immunosorbent assay.
Results: (1)After subculture, HAAF were polygonal or spindle-shaped under the microscope (Figure 1A, B).(2)In the presence of TNF-α, compared with the contrast group, cell viability of HAAF significantly decreased in 50, 100, and 250 μg/ml T-614 treatment groups (OD value: $P<0.01$, $P<0.001$, $P<0.001$, respectively; survival fraction (SF): $P<0.05$, $P<0.001$, $P<0.001$, respectively) (Table I, Figure 2). However, there was no significant difference in cell viability between TNF-α stimulated and unstimulated groups at the same concentration of T-614. In the absence and presence of TNF-α, T-614 suppressed HAAF cell viability dose-dependently (OD value: r = -0.915, P =0.000 and r = -0.926, P =0.000, respectively; SF: r = -0.897, P =0.000; r = -0.885, P =0.000, respectively). (3)In the absence of TNF-α, compared with the contrast group, IL-8 level in 5 and 100 μg/ml T-614 treated groups were significantly higher($P<0.05$); in the presence of TNF-α, IL-8 level in 5, 50, and 100 μg/ml T-614 treated groups were significantly higher ($P<0.001$, $P<0.001$, $P<0.01$, respectively); (Figure 3). There was a negative correlation between supernatant IL-8 level and the concentration of T-614 in groups stimulated with TNF-α (r = -0.670, P =0.000). TNF-α increased IL-8 level in the control group and various concentrations of T-614 treated groups (all $P<0.001$).

Table I. Effects of T-614 on TNF-α stimulated cell viability of HAAF (OD value)

T-614(μg/ml)	OD value	
	0 ng/ml TNF-α	10 ng/ml TNF-α
0	0.424±0.038	0.414±0.042
5	0.404±0.050	0.440±0.054
50	0.347±0.061***	0.358±0.040**
100	0.267±0.034***	0.302±0.039***
250	0.096±0.019***	0.092±0.009***

TNF-α, tumor necrosis factor-α; HAAF, human aortic adventitial fibroblasts. Data are shown as mean ± SD of 3 independent experiments, each in triplicate. $^{***}P < 0.001$, $^{**}P < 0.01$ vs. control group(0μg/ml T-614) within each group alone.
Conclusion: T-614 can inhibit the proliferation of HAAF and promote IL-8 production; therefore, it may provide a new immunotherapeutic intervention for TA.

REFERENCES:

[1] Maiellaro, K. and W.R. Taylor, *The role of the adventitia in vascular inflammation.* Cardiovasc Res, 2007. 75(4): p. 640-8.

[2] He, Y., et al., *SIRT6 inhibits TNF-alpha-induced inflammation of vascular adventitial fibroblasts through ROS and Akt signaling pathway*. Exp Cell Res, 2017. 357(1): p. 88-97.
[3] Wei, Y., et al., *Inhibitory Effect of a Novel Antirheumatic Drug T-614 on the IL-6-Induced RANKL/OPG, IL-17, and MMP-3 Expression in Synovial Fibroblasts from Rheumatoid Arthritis Patients*. Biomed Res Int, 2015. 2015: p. 214683.

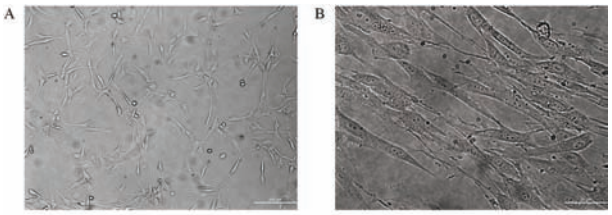


Figure 1.Clutured human aortic adventitial fibroblasts(HAAF) in vitro. HAAF were polygonal or spindle-shaped under the microscope. (A) Appearance of HAAF at generation 5, x100; (B) Appearance of HAAF at generation 5, x400.

Abstract THU0024 Figure 1.

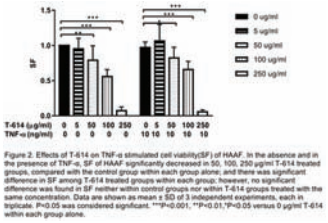


Figure 2. Effects of T-614 on TNF-α stimulated cell viability(SF) of HAAF. In the absence and in the presence of TNF-α, SF of HAAF significantly decreased in 50, 100, 250 μg/ml T-614 treated groups, compared with the control group within each group alone; and there was significant difference in SF among T-614 treated groups within each group; however, no significant difference was found in SF neither within control groups nor within T-614 groups treated with the same concentration. Data are shown as mean ± SD of 3 independent experiments, each in triplicate. P<0.05 was considered significant. ***P<0.001, **P<0.01,*P<0.05 versus 0 μg/ml T-614 within each group alone.

Abstract THU0024 Figure 2.

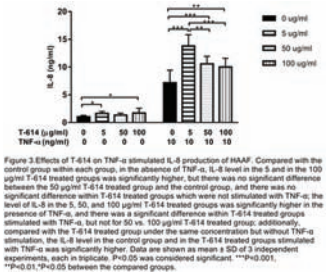


Figure 3.Effects of T-614 on TNF-α stimulated IL-8 production of HAAF. Compared with the control group within each group, in the absence of TNF-α, IL-8 level in the 5 and in the 100 μg/ml T-614 treated groups was significantly higher, but there was no significant difference between the 50 μg/ml T-614 treated group and the control group, and there was no significant difference within T-614 treated groups which were not stimulated with TNF-α; the level of IL-8 in the 5, 50, and 100 μg/ml T-614 treated groups was significantly higher in the presence of TNF-α, and there was a significant difference within T-614 treated groups stimulated with TNF-α, but not for 50 vs. 100 μg/ml T-614 treated group; additionally, compared with the T-614 treated group under the same concentration but without TNF-α stimulation, the IL-8 level in the control group and in the T-614 treated groups stimulated with TNF-α was significantly higher. Data are shown as mean ± SD of 3 independent experiments, each in triplicate. P<0.05 was considered significant. ***P<0.001, **P<0.01,*P<0.05 between the compared groups.

Abstract THU0025 Figure 2.

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THU0025 ANALYSIS OF POTENTIAL INTERACTIONS BETWEEN TENOCYTES AND SYNOVIAL FIBROBLASTS AFTER STIMULATION WITH CYTOKINES EXPRESSED WITHIN THE SYNOVIO-ENTHESAL COMPLEX

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Background: Psoriatic arthritis (PsA) is frequently associated with enthesitis. It has been proposed that inflammatory processes at the synovio-enthesal complex are involved in the pathogenesis of inflammatory arthritides including especially PsA. Besides IL-1β and TNF-α, IL-15, IL-23 and IFN-γ are cytokines expressed within the synovium, tendons and entheses and some of which are already used as therapeutic targets. While synovial fibroblasts (SF) are known key effector cells of cartilage destruction in inflammatory arthritides such as RA, tenocytes are a major component of tendons and entheses and play a central role in tendon inflammation observed in PsA.
Objectives: To investigate whether PsASF and tenocytes show significant interactions while being stimulated with the above cytokines alone as well as in combination with the aim to find out whether these may contribute to the pathogenesis of PsA.
Methods: SF were isolated from patients with PsA undergoing joint surgery. Human tenocytes were acquired commercially and isolated from hamstring tendon tissue of patients undergoing hamstring tendon ACL reconstruction. PsASF and tenocytes were stimulated with IL-1β, TNF-α, IFN-γ, IL-15 and IL-23 alone and in combination. Direct cell co-culture experiments were performed at a 1:1 ratio of both cell types in parallel to experiments with single cell type cultures. IL-6 levels were measured by ELISA to quantify the immunological activation of the cells.
Results: PsASF as well as tenocytes showed strong responses to IL-1β (tenocytes ↑173-fold, n=3; PsASF ↑56-fold, n=3) and TNF-α (tenocytes ↑10-fold, n=3; PsASF ↑9-fold, n=3) stimulation regarding IL-6 secretion. IFN-γ alone had only minimal effects on both cell types but acted synergistically when applied together with IL-1β (tenocytes ↑218-fold, n=3; PsASF ↑129-fold, n=3) and TNF-α (tenocytes ↑24-fold, n=3; PsASF ↑19-fold, n=3). IL-15 and IL-23 alone showed no effect but the data suggest a small antagonistic effect against IL-1β (tenocytes IL-15 ↓21%/IL-23 ↓27%, n=3; PsASF IL-23 ↓19%, n=3) and TNF-α induced IL-6 secretion. Overall, PsASF and tenocytes showed similar responses in the single cell type stimulation experiments. Co-culturing PsASF and tenocytes did not reveal any synergistic or antagonistic interactions in regards to any of the cytokines used.
Conclusion: Our data suggest that tenocytes and PsASF do not interact in a way that would promote inflammation within the synovio-enthesal complex. Also, as far as the induction of IL-6 is concerned, PsASF and tenocytes are not major target cells of IL-15 and IL-23. IFN-γ, however, may be able to promote inflammation in combination with other cytokines in both cell types.
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THU0026 TARGETING SYNOVIAL FIBROBLASTS IN RHEUMATOID ARTHRITIS BY PEFICITINIB AND FILGOTINIB

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Background: The Janus kinase inhibitors (JAKi) peficitinib and filgotinib are currently examined in clinical trials for treatment of rheumatoid arthritis. Both inhibitors are well tolerated up to doses causing Cmax values higher than 1 μM [1,2]. This is in contrast to the approved dosages of tofacitinib and baricitinib reaching Cmax values below 0.5 μM [3,4]. However, it is not known if the higher concentrations of peficitinib or filgotinib offer a benefit in treatment of rheumatoid arthritis.
Objectives: The aim of the study compared the effect of different JAKi on inflammatory response and functional behavior of fibroblast-like synoviocytes from patients with RA (RASF).
Methods: Human RASF were isolated and pretreated with JAKi. After stimulation with IL-1β and JAKi with/without soluble IL-6 receptor (sIL-6R) the levels of IL-6 and MMP-3 were measured in supernatants by ELISA. The effect of different JAKi on proliferation of RASF was determined by a BrdU-incorporation assay. The influence of peficitinib on migration of RASF towards a FCS gradient was examined. For short-term adhesion assays, cells were treated with JAKi, detached and seeded in culture plates. The plates were extensively shaken and adherent RASF quantified by counting crystal violet stained cells. Cell viability, cytotoxicity and apoptosis were measured using commercially available assays.
Results: The IL-1β (10 ng/ml) dependant IL-6 release of RASF was decreased by peficitinib (62%, p<0.001) and by filgotinib (30%, p<0.05, n=7) at 5 μM. Peficitinib also decreased the IL-6 release at 1 μM (24%, n=7). In contrast to filgotinib, the JAK-inhibition with peficitinib reduced

the MMP-3 levels induced by IL-1β by 88% (n=7, p<0.001) at 5 μM and by 31% at 1 μM (n=7, ns). In direct comparison to tofacitinib and baricitinb the IL-1β (20 ng/ml) induced IL-6 increase was only decreased by peficitinib and filgotinib but not by tofacitinib or baricitinib even at 10 μM. Tofacitinib only blocked the specific IL-6 effect e.g. induced by the combination of the soluble IL-6 receptor (sIL-6R) and low doses of IL-1β (p<0.01).

The proliferation of RASF was attenuated by tofacitinib, baricitinib and peficitinib at 5 μM. Peficitinib exerted the strongest decrease of about 70% (p<0.001, n=4) and it was the only inhibitor attenuating the proliferation at 1 μM (23%, p<0.05, n=4). Peficitinib also decreased the migration of RASF by 38% at 1 μM and by 92% at 5 μM. The observed effects were not mediated by apoptosis and even after 48h peficitinib did not act cytotoxic on RASF. In contrast to migration, short-term adhesion onto a plastic surface was not affected by peficitinib.

Conclusion: Peficitinib and filgotinib modulated the IL-1β-induced response of RASF. Peficitinib also inhibited the proliferation and the migration of RASF. Therefore, especially peficitinib could be able to reduce the aggressive pannus formation in RA patients.

REFERENCES:

[1] Cao YJ, et al.: Pharmacokinetics, Pharmacodynamics, and Safety of ASP015K (Peficitinib), a New Janus Kinase Inhibitor, in Healthy Subjects. Clin Pharmacol Drug Dev 2016;5:435-449.

[2] Vanhoutte F, et al.: Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Filgotinib, a Selective JAK-1 Inhibitor, After Short-Term Treatment of Rheumatoid Arthritis: Results of Two Randomized Phase IIa Trials. Arthritis Rheumatol 2017;69:1949-1959.

[3] Lamba M, et al.: Evaluation of Pharmacokinetics Compared With Immediate-Release Tofacitinib and Impact of Food. J Clin Pharmacol 2016;56:1362-1371.

[4] Shi JG, et al.: The pharmacokinetics, pharmacodynamics, and safety of baricitinib, an oral JAK 1/2 inhibitor, in healthy volunteers. J Clin Pharmacol 2014;54:1354-1361.

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THU0027 INHIBITION OF TH17 CELLS IN PSORIATIC ARTHRITIS THROUGH ACTIVATION OF THE ARYL HYDROCARBON RECEPTOR IS DEPENDENT UPON DISEASE ACTIVITY

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Background: Th17 cells have been implicated in the development of psoriatic arthritis (PsA) and psoriasis and are a major target for therapy. Th17 cells exhibit plasticity and can transdifferentiate to other effector cell types. Th17 cells that lose expression of IL-17 in favour of IFN-γ (non-classical Th1 cells) contribute to the pathogenesis of autoimmune diseases and are found in the joints of patients with inflammatory arthritis. Conversely, induction of IL-10 in Th17 cells has been shown to suppress their pathogenic potential. The Aryl Hydrocarbon Receptor (AhR) is a nuclear receptor with pleiotropic effects on immune function. The AhR ligand, 6-formylindolo[3,2-b]carbazole (FICZ) has been shown to induce or suppress Th17 cell differentiation and promote generation of tolerogenic FoxP3+ T regs or Type 1 regulatory cells (Tr1) that produce IL-10. FICZ also reduces psoriaform inflammation in a model of skin inflammation through AhR activation[1]. FICZ could thus play a regulatory role to control inflammation in PsA.

Objectives: To evaluate the immunomodulatory effects of FICZ on IL-17, IL-10 and IFN-γ production from human CD4+ T cells in PsA and healthy controls (HCs)

Methods: Whole PBMCs and purified CD4+ T cells were isolated from HCs, untreated or DMARD treated (UNT/DMARD) PsA patients and anti-TNFα (adalimumab and etanercept) treated patients. Cells were stimulated with anti-CD3/CD28 (αCD3/28) (1μg/ml) and cultured for 3-5 days in the presence or absence of FICZ (250nM). To some cultures 2,3,7,8-Tetrachlorodibenzodioxin (TCDD) (10nM) was used as a control AhR ligand, and IL-21 (30ng/ml) as a positive control for IL-10 production. Cells were then re-stimulated with PMA/ionomycin and intracellular production of IL-17, IFN-γ and IL-10 measured by FACS.

Results: The percentage of IL-17+ CD4+ T cells was reduced in the peripheral blood of HCs and PsA patients after 3 days (healthy p=0.0098, UNT/DMARD p=0.0004, anti-TNFα p=0.0012) and 5 days (healthy p=0.0005, UNT/DMARD p=0.0012, anti-TNFα p=0.0012). The percentage of IFN-γ+ CD4+ T cells was reduced in HCs and PsA patients (HC p=0.016, UNT/DMARD p=0.001, anti-TNFα p=0.001) after 3 days culture with FICZ but this effect was only sustained for HCs (p=0.02) and anti-TNFα treated patients (p=0.01) after 5 days of culture. No ligand specific difference in IL-17 suppression was seen between FICZ and TCCD. No difference in baseline IL-10 expression was seen between treatment groups. However, IL-10 production was significantly enhanced by FICZ in the anti-TNFα patients group (p=0.02). This effect was not seen with TCDD nor IL-21 alone. The addition of IL-21 to cultures from anti-TNFα patients treated with FICZ further enhanced IL-10 expression (p<0.05). Increase in Il-10 by FICZ was associated with a reduction in IL-17. Upon stratifying patients by swollen joint count (SJC) and Psoriasis Area Severity Index (PASI) into high (SJC≥3, PASI≥5) and low (SJC<3, PASI<5) disease activity, the percentage of IL-17+ CD4+ T cells after 3 days culture with FICZ was reduced for patients with low PASI score (p=0.02). A similar trend was seen for those with low SJC (p=0.06). In contrast, stimulation with FICZ did not regulate Th17 cells in patients with high PASI score or SJC.

Conclusion: The AhR ligand FICZ suppresses IL-17 production in CD4+ T cells of PsA patients and HCs and IFN-γ in HCs and anti-TNFα treated patients. FICZ promotes IL-10 production in CD4+ T cells from anti-TNFα treated patients and this effect is enhanced in the presence of IL-21. CD4+ T cells from patients with high disease activity are more resistant to FICZ mediated IL-17 suppression. Use of AhR ligands may thus be a useful therapeutic adjunct to conventional and biological therapy in PsA.

REFERENCE:

[1] Di Meglio P, et al. Activation of the AhR dampens the severity of inflammatory skin conditions, Immunity, 2014, Jun 19;40(6):989-1001.

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THU0028 COMPARISON OF IL-17A AND TNF INDUCED CYTOKINE SECRETION BY RHEUMATOID AND PSORIATIC ARTHRITIS SYNOVIAL FIBROBLASTS AND THEIR INHIBITION BY BIOLOGICS

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Background: Rheumatoid arthritis (RA) and psoriatic arthritis (PsA), although similar in several respects, display clinical as well as therapeutic differences. This includes, for example, the higher effectiveness of the anti-IL17A biologic secukinumab in PsA than in RA patients. Synovial fibroblasts (SF) are one of the key effector cell types in the pathophysiology of RA and PsA. We hypothesized that RASF and PsASF respond differentially to IL-17A and its biologic secukinumab and that this might contribute to the difference seen in the therapeutic response.

Objectives: To examine the effect of the two cytokines IL-17A and TNF-α on RASF in comparison to PsASF as well as the effect of their corresponding biologics. To analyze the effect of the IL-17A homolog IL-17F.

Methods: SF were isolated from synovium from PsA or RA patients undergoing surgery. SF from RA and PsA patients were stimulated with recombinant IL-17A, IL-17F and TNF-α alone or with respective combinations. Dose-response curve analysis was performed with IL-17A. The biologics secukinumab and adalimumab were used to block the effects on the SF. As a measure of the proinflammatory response, secretion of the cytokine IL–6 was quantified using an immunoassay.

Results: IL-6 secretion was induced by IL-17A in RASF as well as PsASF (IL-17A: 13.7-fold ↑ vs 6.9–fold ↑; n=3). Although sharing the same receptor, the IL-17A homolog IL-17F alone caused no induction of IL-6 secretion in SF. However, when combined with TNF-α, both IL-17 isoforms, IL–17A and IL-17F, increased IL-6 secretion due to a strong synergistic effect with TNF-α. RASF (n=3) responded more strongly than PsASF (n=3) to the combined stimulation (IL-17A: 544-fold ↑ vs 127-fold ↑, IL-17F: 54-fold ↑ vs 27-fold ↑). Adalimumab and secukinumab were

similarly effective in abolishing the synergistic effect of IL-17A + TNF-α in RASF and PsASF.
Conclusion: According to our data, the differences in the therapeutic effectiveness of the anti-IL17A biologic secukinumab cannot be attributed to differential SF responses since the response to IL-17A alone and IL-17A together with TNF–α is not stronger for PsASF than for RASF and since secukinumab was similarly effective for both SF types. Furthermore, in a proinflammatory milieu with increased TNF levels, both IL-17A and IL-17F can contribute to promoting inflammation in the pathophysiology of PsA and RA.
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THU0029 FAS LIGAND REGULATES THE GENE EXPRESSIONS OF VARIOUS KEY MOLECULES IN RHEUMATOID SYNOVIAL FIBROBLASTS

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Background: Fas ligand (FasL) is a member of tumor necrosis factor superfamily (TNFSF6) and reported to contribute to synovial hyperplasia of rheumatoid arthritis (RA). Apoptosis of RA synovial cells through Fas/FasL pathway was inhibited by pro-inflammatory cytokines present within the synovium [1]. We previously reported that decoy receptor 3 overexpressed in rheumatoid synovial fibroblasts (RA-FLS) stimulated by TNFα protects the cells from Fas-induced apoptosis [2].
Objectives: In this study, we investigated the gene expression profiles regulated by FasL in RA-FLS to reveal how FasL is involved in the pathogenesis of RA.
Methods: RA-FLS were obtained during total knee replacement surgery from patients with RA. Four individual lines of primary cultured RA-FLS were incubated either with 1000 ng/ml of recombinant human FasL protein or the same volume of phosphate buffered saline as unstimulated control in reduced serum medium for 12h. Gene expressions were detected by microarray assay (Human Genome U133 Plus 2.0, GeneChip® 3' Expression Array; Thermo Fisher Scientific).
Results: Microarray data analysis revealed that FasL up-regulated or down-regulated the expression of various genes in RA-FLS. The function of regulated genes included transcriptional activator activity, positive regulation of metabolic process, positive regulation of cellular metabolic process, positive regulation of macromolecule metabolic process, positive regulation of nitrogen compound metabolic process, regulation of phosphorylation, positive regulation of biological process, regulation of phosphate metabolic process, regulation of MAPK cascade, and regulation of multicellular organismal process. The most up-regulated 3 genes by FasL were dual specificity phosphatase 6 (DUSP6), epiregulin (EREG) and interleukin11 (IL-11). The most down-regulated 3 genes by FasL were angiopoietin-like 7 (ANGPTL7), protein inhibitor of activated STAT2 (PIAS2) and growth differentiation factor 5 (GDF5).
Conclusion: DUSP6 regulates CD4+ T-cell activation and differentiation by inhibiting the T-cell receptor-dependent extracellular signal-regulated kinases 1 and 2 activations [3]. EREG is increased in patients with RA and associated with the development of cytokine-induced arthritis [4]. IL-11 regulates the growth and development of hematopoietic stem cells and decreases the pro-inflammatory cytokines and nitric oxide productions [5]. ANGPTL7 is pro-angiogenic factor [6] and promotes pro-inflammatory responses through the P38 signaling pathway [7]. PIAS proteins inhibit the activated STAT and are involved in the pathogenesis of RA [8]. GDF5 is associated with joint destruction of patients with OA and RA [9]. FasL regulates the expression of various genes in RA-FLS. Therefore, FasL may affect the pathogenesis of RA by regulating gene expressions of these molecules in RA-FLS.

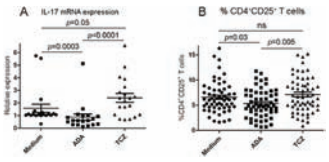
REFERENCES:
[1] Wakisaka S. et al., Clin Exp Immunol. 1998;114:119-128.
[2] Hayashi S. et al., Arthritis Rheum. 2007;56:1067-1074.
[3] Bertin S. et al., Mucosal Immunol. 2015;8:505-515.
[4] Harada M. et al., J Immunol. 2015;194:1039-1046.
[5] Moreland L. et al., Arthritis Res. 2001;3:247-252.
[6] Katoh Y, et al., Int J Mol Med. 2006;17:1145-1149.
[7] Quian T, et al., Inflammation. 2016;39:974-985.
[8] Lao M. et al., J Immunol. 2016;196:596-606.
[9] Martinez A. et al., Ann Rheum Dis. 2008;67:1352-1353.

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THU0030 THE DIFFERENTIAL EFFECT OF TNF-A AND IL-6R BLOCKERS ON THE EXPRESSION OF IL-17 AND ACTIVATED CD4+CD25+ T CELLS IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: TNF-α blockers are effective drugs for the treatment of psoriatic arthritis (PsA) and rheumatoid arthritis (RA). On the other hand, while interleukin-6 receptor (IL-6R) blockers have emerged as effective drugs in the treatment of RA, their effect in PsA has been disappointing. We hypothesized that the differential effect of TNF-α and IL-6R blockers in PsA may be mediated by the effect of these drugs on IL-17 expression, a cytokine profoundly involved in PsA and by their influence on activated $CD4^+CD25^+$ T cells.
Objectives: To evaluate the differential effect of adalimumab (ADA) (representing TNF-α blockers) and tocilizumab (TCZ) (IL-6R blocker) on the expression level of IL-17 and on the frequency of activated $CD4^+CD25^+$ T cells.
Methods: Levels of IL-17 mRNA expression were measured following *in vitro* co-culture of peripheral blood mononuclear cells (PBMC) derived from PsA patients with, ADA, TCZ at 10ug/ml or with medium alone as control for 3 days. Next, RNA was extracted and real-time PCR for IL-17 mRNA expression was performed. In addition, after 5 days incubation with the biologic agents the frequency of activated $CD4^+CD25^+$ T cells were analyzed by flow cytometry.
Results: The differential effect of ADA and TCZ on IL-17 mRNA expression and modulation of activated $CD4^+CD25^+$ T cells in culture of PBMC derived from PsA patients is shown in Figure 1. We found that IL-17 mRNA expression in PsA patients derived PBMC (n=20) was down-regulated by ADA. This down grading was significant in comparison with TCZ and medium control respectively ($p<0.0001$, $p=0.0003$). On the other hand, TCZ significantly up-regulated the expression of IL-17 as compared to medium control ($p=0.05$) (Figure 1A). The frequency of activated $CD4^+CD25^+$ T cells was down-regulated by ADA as compared to medium and TCZ, respectively ($p=0.03$, $p=0.005$). whereas activated $CD4^+CD25^+$ T cells were up-regulated by TCZ (although not significantly) as compared to medium control (n=60) (Figure 1B).



Abstract THU0030 – Figure 1. ADA and TCZ differentially modulates IL-17 mRNA expression and activated $CD4^+CD25^+$ T cells in PBMC derived from PsA patients. PBMC were co-cultured in the presence of ADA,TCZ or medium alone as a control. (A) After 72 h incubation RNA was extracted and real-time PCR for quantification of IL-17 was performed. (n=20). (B) After 5 days incubation change in%$CD4^+CD25^+$ T cells was determined by flow cytometry (n=60), ns=not significant.

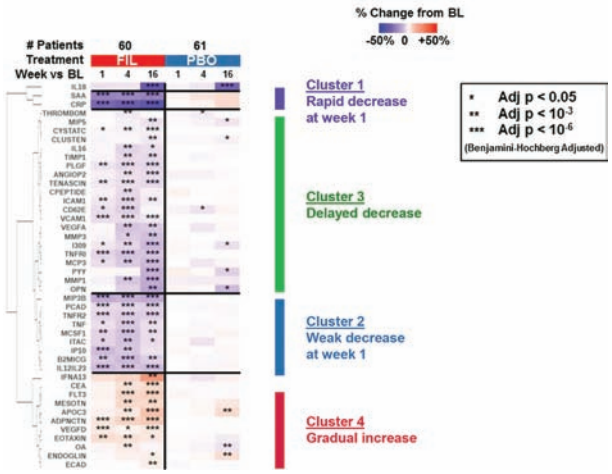
Conclusion: Our data highlight the differential effect of ADA and TCZ on IL-17 expression level and on frequency of activated $CD4^+CD25^+$ T cells in culture of peripheral immune cells derived from PsA patients. This data suggest a new mechanism of action of ADA and provide a possible explanation of the inefficacy of TCZ in PsA.
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THU0031 FILGOTINIB TREATMENT PROVIDES RAPID AND SUSTAINED REDUCTION OF INFLAMMATORY BIOMARKERS IN MODERATE TO SEVERE PSORIATIC ARTHRITIS (PSA) PATIENTS

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Background: PsA is a chronic inflammatory musculoskeletal disease characterized by joint and skin inflammation, enthesitis, dactylitis, and nail lesions. In the recent EQUATOR study, filgotinib (FIL), an oral, selective Janus kinase 1 (JAK1) inhibitor, produced significant and sustained improvements on the signs and symptoms of PsA compared to placebo (PBO).[1] As targeted JAK1 inhibition by FIL has potential to simultaneously block multiple inflammatory pathways, we analyzed biomarker samples from EQUATOR using exploratory multiplex biomarker panels.
Objectives: To evaluate the impact of targeted JAK1 inhibition on the circulating biomarkers in patients with active PsA.
Methods: Design and results of the EQUATOR study—a 16-week, double-blind, multicenter, phase 2 study in subjects with active PsA (NCT03101670)—have been published.[1] Subjects were randomized 1:1 to 200 mg FIL (n=65) or PBO (n=66) once daily. Serum samples (FIL n=60 and PBO n=61) were collected at baseline (BL), week 1, week 4, and week 16, and analyzed using 135 multiplex biomarker screening panels. Biomarker changes from BL were analyzed on all time-paired subject data and reported for weeks 1, 4, and 16.
Results: FIL treatment produced significant reductions serum concentration of multiple biomarkers associated with PsA disease activity. We identified 4 clusters of biomarker response based on the kinetics and magnitude of changes from BL (Figure); Cluster 1: rapid, substantial and sustained reduction (>25% from BL by week 1); Cluster 2: rapid and moderate reduction (5%–15% from BL by week 1); Cluster 3: delayed reduction (significant reduction by week 4); and Cluster 4: moderate increase (5%–10% from BL). Although initial grouping was based on the speed and magnitude of biomarker response, a number of biomarkers formed subclusters representing discrete biological functions. Cluster 1 included 2 acute phase reactants (CRP, SAA) while Cluster 2 included inflammatory mediators (TNFR1, CXCL10, IL-12/-23; CXCL10 and IL-12/-23 reached full reduction by week 1). Cluster 3 was the largest group and represented biomarkers of matrix remodeling (MMP1, TIMP1), cell adhesion (ICAM-1, E-selectin), and angiogenesis (VEGF-A). Cluster 4 had biomarkers related to diverse functions (Eotaxin, CEA, adiponectin).
Conclusion: In patients with active PsA, FIL treatment significantly decreased levels of circulating biomarkers, including acute-phase reactants, proinflammatory cytokines and chemokines, and various adhesion molecules. These data support the idea that FIL treatment results in rapid and sustained reduction of the inflammatory milieu present in autoimmune inflammatory diseases, consistent with efficacy previously reported for this study.[1]

Figure. Heatmap with % change and p values.



Abstract THU0031 – Figure 1

REFERENCE:
[1] Mease PJ, et al. Lancet. 2018;392:2367-2377.

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THU0032 DYNAMICS OF ADIPOCYTOKINES IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS IN DIFFERENT TREATMENT REGIMENS

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Background: Adipose tissue is a highly active endocrine organ that produces a large number of various pro-inflammatory cytokines and adipocytokines (adiponectin, leptin, etc.) involved in the pathogenesis of rheumatoid arthritis (RA). The relationship of adipokines with activity markers and inflammation in RA and the effect of antirheumatic therapy on adipocytokine levels in patients with early RA is discussed.
Objectives: To assess the dynamics of adipocytokine levels (adiponectin, leptin) in patients with early RA (initial and after 24 weeks) using various treatment regimens: methotrexate monotherapy (MT) and combination therapy (MT + adalimumab (ADA).
Methods: The study included 47 patients with early RA (criteria ACR/EULAR, 2010.), 57 [46.5; 62.0] years, disease duration 6.0 [5.5;15.5] months, seropositive for IgM RF and anti-CCP, with highly active RA (DAS28 5,5 [5,1; 5,9]; SDAI 32,4 [22,4; 41,7], CDAI 29,0 [19,7; 39,5]). At study entry, all patients received methotrexate (MTX) (10 [10-15] mg/week), after 12 weeks, with inefficiency of MT, adalimumab (ADA) was administered 40 mg 1 time in 2 weeks. Serum concentration of adipokines (adiponectin, leptin) was measured with ELISA.
Results: By the 24th week of therapy, 23 (49%) patients with early RA received a combination therapy (adalimumab and methotrexate), 24 (51%) patients with RA received methotrexate monotherapy. In patients with RA, after 24 weeks, a significant decrease in adiponectin levels by 44 and 49% and an increase in the concentration of leptin by 39 and 43% were observed both against the background of MT monotherapy and with the use of combination therapy ($p < 0.05$ in all cases). By the end of the study, adiponectin levels were higher in the MT monotherapy group, and leptin in the combination therapy group.
Table 1:

	Monotherapy MT (n=24)			Combination therapy MT+ADA (n=23)		
	0 point	24 weeks	Δ,%	0 point	24 weeks	Δ,%
Adiponectin, ng/ml	23,0 [12,6;77,0]	12,8[8,0;19,6]*/**	–44	20,0[13;34]	10,2[7,0;12,1] *	–49
Leptin, ng/ml	15,6 [7,8;27,5]	21,7[12,5;40,4] */**	+39	20,0 [11;39,2]	28,1 [12,4;58,3]*	+43

* -p <0,05 reliability of differences in factors before treatment and after 6 months (Wilcoxon); ** -p <0.05 difference in the indices between the groups by the 6th month of therapy; Δ,% -the difference between the indices between the groups by the 6th month of therapy.
Conclusion: After 24 weeks of therapy, the adipocytokine levels in the two groups changed: the adiponectin concentration decreased, and the leptin level increased. MT monotherapy and combination therapy (MT + ADA) acted on changes in adipocytokine levels unidirectionally, although the changes were more pronounced in patients on combination therapy.
Disclosure of Interests:
None declared
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THU0033 RNA PROFILING OF HEALTHY AND RHEUMATOID ARTHRITIS SUBJECTS TREATED WITH TOFACITINIB MONOTHERAPY

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Background: The Janus kinase (JAK) family of tyrosine kinases includes JAK1, JAK2, JAK3 and TYK2 which signals through type I and type II cytokine receptors. Tofacitinib is an oral JAK inhibitor approved for the treatment of rheumatoid arthritis (RA). In cellular settings where JAKs signal in pairs, tofacitinib preferentially inhibits signalling by heterodimeric receptors associated with JAK1 and/or JAK3 and has functional selectivity over JAK2. Next generation sequencing (i.e. RNA sequencing) offers an unbiased analysis of whole transcriptome pharmacology.
Objectives: To profile the transcriptome in whole blood samples collected in a Phase 1 healthy volunteer (HV) study and a Phase 2 study with RA subjects treated with placebo, 5 mg, 10 mg or 15 mg of tofacitinib monotherapy.
Methods: In the HV study, a total of 93 Paxgene RNA tubes were obtained from 30 subjects collected at screening, at baseline on day 1, and at 2 hours post dosing on day 15. HVs were treated daily with tofacitinib (10 mg BID) for 15 days. In the RA study (NCT00550446), a total of 239 RNA samples were obtained from 25–31 subjects at baseline and day 28 who were treated with tofacitinib 5 mg BID, 10 mg BID or 15 mg BID daily for 84 days. RNAseq libraries were generated using a polyA based mRNA kit and sequenced to a depth of 40 million paired-end reads. Upstream processing included alignment of sequences, gene quantification and data quality control. The raw reads were normalised using the Trimmed Mean of M values (TMM) method in the edgeR package. Log2 fold-changes (FC) and corresponding false discovery rate (FDR)-adjusted p-values (padj) were calculated using the voom function in the Limma package (vers 3.8) in R 3.5.1. In particular, the correlations between baseline and measurements at each visit per patient were estimated by Limma's duplicateCorrelation function. Genes were considered significant after multiple test correction with FDR, or padj <0.1 within each study.
Results: Modulation of the JAK-STAT signalling pathways was observed as exemplified by gene expression differences in cytokine-inducible SH2-containing protein (CISH) (p value=4.64E-41 in the HV study and p value=1.2E-8 in the RA study) and suppressor of cytokine signalling (SOCS2) protein (p value=1.38E-18 in HV study and p value=2.27E-7 in the RA study). Gene expression of CISH, a member of the SOCS family, was decreased from its baseline value at day 15 in HV (FC from baseline=0.18) and at day 28 in RA subjects (FC from baseline=0.42) when comparing tofacitinib treatment (HV:10 mg, RA:15 mg) to baseline or placebo, respectively. SOCS2 gene expression was also decreased at day 15 in HV (FC from baseline=0.40) and at day 28 in RA subjects (FC from baseline=0.52) when comparing tofacitinib treatment (HV:10 mg, RA:15 mg) to baseline or placebo, respectively. Other changes observed in the HV study: 301 genes were upregulated and 169 genes were downregulated when comparing 2 hours post dose on day 15 to baseline. In the RA study, 643 genes were upregulated and 801 genes were downregulated when comparing the 15 mg dose to placebo at week 4. Preliminary pathway level analysis shows overall a broader modulation of cytokine and chemokine signalling pathways by tofacitinib treatment in RA compared to what we observe in HV.
Conclusion: The results of this post hoc analysis demonstrate that tofacitinib induces measureable changes in the modulation of the JAK-STAT signalling pathway as well as effects on inflammatory cytokines and chemokines. The existence of overlapping but also unique JAK-STAT pathway inhibition due to tofacitinib between the HV and RA studies, as well as ongoing work, will provide a better understanding of response/non-response to tofacitinib and future drug developments.
Disclosure of Interests: Angela Hadjipanayis Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Xing Chen Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Julie Lee Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Shanrong Zhao Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Weidong Zhang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, David Martin Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Mateusz Maciejewski Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Daniel Ziemek Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lori Fitz Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Craig Hyde Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, David von Schack Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
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THU0034 IRAK4 INHIBITION SUPPRESSES TLR7, TLR9, AND SLE SERUM-INDUCED IFNA PRODUCTION IN PRIMARY HUMAN PLASMACYTOID DENDRITIC CELLS

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Background: A hallmark of lupus is the presence of antinuclear autoantibodies, including those against RNA-protein complexes and double-stranded DNA (dsDNA).[1,2] FcγR-mediated internalization of these nucleic acid:autoantibody immune complexes results in endosomal activation of TLR7 and TLR9, respectively, and the production of IFNα from plasmacytoid dendritic cells (pDC).[3,4] The importance of this pathway is underscored by the majority of SLE patients having a peripheral interferon-stimulated gene (ISG) signature.[5] IRAK4 is a serine/threonine kinase at the top of the signaling cascade downstream of TLRs, including TLR7 and TLR9. As such, inhibition of IRAK4 represents a promising therapeutic target for lupus.
Objectives: To investigate the effect of a highly selective IRAK4 inhibitor on IFNα production from pDCs stimulated with TLR7 and TLR9 agonists, SLE serum, and nucleic acid:autoantibody immune complexes.
Methods: Primary human pDCs were precultured with an IRAK4 inhibitor followed by stimulation for 24 hours. Stimulation agents included TLR7 and TLR9 agonists, human SLE serum, and nucleic acid:autoantibody immune complexes. Culture supernatants were then assessed for secretion of IFNα by MSD.
Results: TLR7 and TLR9 stimulation of pDCs resulted in the secretion of IFNα from pDCs as expected. Treatment with an IRAK4 inhibitor resulted in dose-dependent inhibition of TLR7- and TLR9-induced IFNα with high potency. Human SLE serum was tested to extend findings to physiological SLE-relevant stimuli. Several SLE serum samples, which had positive ELISA titers to the antinuclear antibodies, stimulated production of IFNα in pDCs after 24 hours in culture. No induction of IFNα was observed with healthy volunteer serum samples. Treatment with an IRAK4 inhibitor effectively blocked secretion of IFNα from SLE serum-stimulated pDCs in a dose-dependent manner. Additional antigen (either RNP or dsDNA) was added to SLE samples that yielded titers for autoantibodies but failed to elicit IFNα production. Addition of RNP or dsDNA to anti–RNP and anti–dsDNA-positive SLE sera induced strong IFNα production, and this response was blocked with IRAK4 inhibition. No induction was seen with SLE serum that was negative for both anti–RNP and anti–dsDNA.
Conclusion: This work demonstrates the effects of IRAK4 inhibition on IFNα production in primary pDCs downstream of disease-relevant stimuli and highlights the potential for IRAK4 inhibition as a promising treatment for lupus.

REFERENCES:
[1] Rose T, Dorner T. Best Pract Res Clin Rheumatol. 2017;31:321-333.
[2] Zharkova O, et al. Rheumatology. 2017;56:i55-i66.
[3] Barrat FJ, et al. J Exp Med. 2005;202(8):1131-1139.
[4] Means TK, et al. J Clin Invest. 2005;115(2):407-417.
[5] Yao Y, et al. Hum Genomics Proteomics. 2009. 2009(374312):1-16.

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THU0035 DOMINANCE OF DRUG TARGET MECHANISMS IN RHEUMATOID ARTHRITIS

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Background: Biological and Targeted Synthetic Disease-Modifying Anti-Rheumatic Drugs (b- and tsDMARDs) have been developed over the years for patients with rheumatoid arthritis (RA). They can be grouped into families of drugs according to their mechanisms of action. Here we focus specifically on anti-TNFs, anti-IL6s, anti-IL1s, T or B Cells inhibitors and JAK inhibitors. There is still a significant proportion of patients

inadequately responding to RA treatments. Lacking predictive biomarkers of response or personalised medicine approaches to guide use of targeted therapies in RA patients, EULAR and ACR guidelines [1,2] both recommend to loop over available ts- and bDMARDs as long as the patient's response is considered as inadequate. Meanwhile, for historical reasons and despite the similar clinical efficacy of these drugs, anti-TNFs have a large dominance in medical practice.

Objectives: Determine in what proportions the different mechanisms targeted by existing DMARDs families are dominant in RA patients synovial tissue.

Methods: Retrospective analysis of 7 private or public datasets of 300 rheumatoid arthritis patients, consisting in all cases of transcriptomic data from synovial biopsies. Three datasets come from the RheumaKit platform [3,4] (low-density microarrays or qPCR). Four other datasets are publicly available on Gene Expression Omnibus (GSE89408, GSE45867, GSE97165, GSE21537, produced on Illumina, KTH or Affymetrix platforms). Each mechanism of action is associated to a « drug target complex » (DTC), consisting of the genes coding for proteins directly targeted by the DMARDs of interest. For a given dataset, computations are made in four steps: 1) each patient is described by its different DTC values (an average of the expression values of the members of each DTC) 2) each patient is scored for each of its DTC value. Each of these DTCs are scored as a percentile of the corresponding DTC distribution over the full dataset from which a given patient's data is extracted. This gives, for a single patient, as many percentiles as defined DTCs. 3) for each individual patient, a ranking of DTC values is then operated. This allows to overcome the fact that absolute numerical values of two different DTCs should not be compared. 4) A summary statistic is then computed over each dataset separately, to conclude which DTC is dominant in which proportion of the cases among this dataset.

Results: This analysis exhibits different dominance patterns for RA-related mechanisms of action in individual patients. Statistically, no unique mechanism is shown dominant in a majority of patients; On the four public datasets, where all DTCs of interest are available, averaged dominance proportions across datasets are : IL1 15%, IL6 20%, TNF 11%, B Cells 20%, JAK 17%, T Cells 7%. About 10% of the patients exhibit equivalent dominance patterns between multiple DTCs. On all seven datasets, this analysis also outputs weak or moderate correlations between the dominance levels of multiple DTCs.

Conclusion: These results highlight large variability in metabolic patterns underlying RA; such observation is consistent with the similar efficacy observed for b or tsDMARDs when evaluated in clinical trials. Herein we show that TNF-dependent pathways is dominant in only a relatively small proportion of RA patients, whereas non-TNF-dependent pathways (e.g. IL-6 or JAK-dependent pathways) are more dominant. This work pleads for a more balanced use of available treatments. In addition, these results support further investigations towards precision medicine-oriented approaches, namely based on biomarkers from synovium, in the treatment of RA.

Data analyses included in this work have been financially supported by Sanofi Genzyme.

REFERENCES:

[1] Smolen J.S. et al., Ann. Rheum. Dis. 2017
[2] Singh J.A. et al., Arthritis Care & Res. 2015
[3] www.rheumakit.com : for founding work & detailed description, see Lauwerys B. *et al.*, PloS ONE 2015
[4] Helleputte Th. et al., Ann. Rheum. Dis. 2016.

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THU0036 ACTIVATED MEMORY T CELLS PRODUCE LIGANDS THAT CAUSE NF-KB-DEPENDENT INFLAMMATORY ACTIVATION OF THE ENDOTHELIUM: IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS

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Background: Endothelial cells (EC) are important contributors to inflammation via expression of inflammatory mediators, including cytokines, chemokines and adhesion molecules. Production of these inflammatory mediators can be induced via canonical and NF-κB-inducing kinase (NIK)-dependent noncanonical NF-κB signalling. The ligands activating these pathways are well studied, but less is known about the cells producing ligands that can activate NF-κB signalling in EC.

Objectives: To study the effects of factors produced by activated memory T (T_m) cells on NF-κB dependent inflammatory activation of EC.

Methods: $CD4^+CD45RO^+$ memory T cells were isolated from healthy PBMC using MACS sorting and cultured in presence of anti-CD3 and anti-CD28 for 72h, after which supernatant was harvested. Endothelial cells were stimulated for 72h with 50% T_m supernatant (T_m sup) after which protein and RNA was harvested followed by analysis of NF-κB signalling and downstream expression of inflammatory mediators using qPCR and western blot. Culture supernatants were analysed by ELISA for various inflammatory mediators. To repress canonical NF-κB signalling an inhibitor of IKKβ (iIKKβ) was used and to repress NIK-dependent NF-κB signaling an inhibitor of NIK (iNIK) was used in the EC cultures.

Results: Stimulation with T_m sup led to activation of both canonical NF-κB signalling (increased levels of phosphorylated IκBα) and noncanonical NF-κB signalling (increased p100 to p52 processing). After stimulation with T_m sup EC had increased mRNA levels of all tested inflammatory mediators compared to non-treated cells. Gene expression of chemokines, cytokines, and growth factors (CXCL1, CXCL5, IL6, IL8 and GM-CSF) in T_m sup stimulated EC was significantly reduced after treatment with iIKKβ and to a lesser, but still significant, extent after treatment with iNIK. Treatment with iIKKβ also led to a reduction in mRNA levels of the adhesion molecules VCAM-1 and ICAM-1, while this effect was less pronounced after iNIK treatment. Of note, treatment with either IKKβ or iNIK led to a significant reduction of CXCL5 in the culture supernatant of T_m sup stimulated EC.

Conclusion: This study provides new insights into the cellular interactions leading to production of inflammatory mediators by EC. Our findings demonstrate that activated T_m cells produce factors that can cause NF-κB-dependent inflammatory activation of EC. Targeting canonical NF-κB signaling via IKKβ or NIK-dependent NF-κB signaling reduces inflammatory activation of the endothelium and may be a potential novel therapeutic target.

Disclosure of Interests:
None declared

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THU0037 ASSOCIATION BETWEEN PRO-INFLAMMATORY CYTOKINE POLYMORPHISMS AND JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic arthritis of childhood and has a variety of subtypes, but the etiology is unclear. Proinflammatory cytokines such as interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-α play a major role in the development of JIA. Single nucleotide polymorphisms (SNPs) may be associated with susceptibility, phenotype, progression, and treatment of JIA, and the relevance of more than 20 SNPs and JIA has been studied.

Objectives: We investigated whether IL-1, IL-6, and TNF-α polymorphisms were associated with susceptibility to JIA.

Methods: A meta-analysis was conducted on the associations between IL-1α-899 C/T, IL-1β-511 C/T, IL-6-174 G/C, and TNF-α-308 G/A and -238 G/A polymorphisms, and JIA. A literature search was performed using PubMed and Embase. The strength of the association between these cytokine polymorphisms and risk of JIA was estimated using the crude odds ratio (OR) and 95% confidential interval (CI). We performed meta-analyses using 1) allelic contrast, 2) recessive, 3) dominant, and 4) additive models. The heterogeneity between studies was assessed with the Cochran Q test, and the heterogeneity among studies was tested with the I^2 statistic.

Results: A total of 27 studies included 4,678 JIA cases and 7,634 control subjects. There were 23 studies on Caucasians, 3 on Asians, and 1 on Africans. Seven studies were on IL-1α-899 C/T, 5 were on IL-1β-511 C/T, 6 were on IL-6-174 G/C, 19 were on TNF-α-308 G/A, and 14 were on TNF-α -238 G/A polymorphisms. Meta-analysis of IL-1α-899 C/T, IL-1β-511 C/T, IL-6-174 G/C, and TNF-α-308 G/A and -238 G/A polymorphisms revealed no significant associations between JIA and minor alleles (OR 0.99, 95% CI 0.87–1.12, *P* =0.84; OR 1.10, 95% CI 0.97–1.25, *P* =0.15; OR 1.04, 95% CI 0.91–1.19, *P* =0.57; OR 1.09, 95% CI 0.87–1.37, *P* =0.46; OR 0.85, 95% CI 0.63–1.13, *P* =0.26). Subgroup analysis was conducted on the relationship between JIA and proinflammatory cytokines based on ethnicity. In Caucasians, there was no significant association between IL-1α-899 C/T, IL-6-174 G/C, and TNF-α-308 G/A and -238 G/A polymorphisms and JIA; however, there were significant relationships between JIA and recessive (TT vs. CT + CC) and additive (TT vs. CC) models of IL-1β-511 C/T polymorphisms (OR 1.48, 95% CI 1.09–2.00, *P* =0.01; OR 1.46, 95% CI 1.05–2.03, *P* =0.02).
Conclusion: IL-1α-899 C/T, IL-1β-511 C/T, IL-6-174 G/C, and TNF-α-308 G/A and -238 G/A polymorphisms were not significantly associated with overall JIA susceptibility in all ethnicities. However, differences according to ethnicity were observed, and the TT genotype of IL-1β-511 C/T was associated with a high prevalence of JIA in Caucasians.

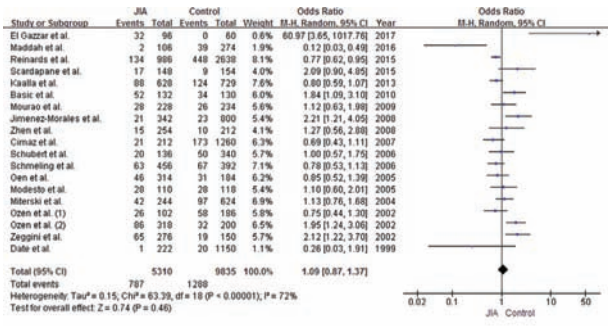


Figure 1. OR and 95% CI of individual studies and pooled data for the association between minor alleles of TNF-α-308 G/A and JIA in all study subjects.

Abstract THU0037 – Figure 1

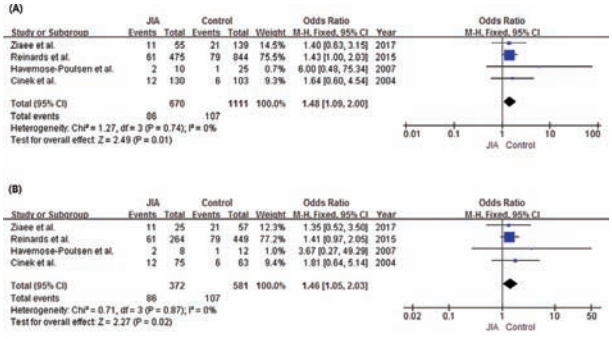


Figure 2. OR and 95% CI of individual studies and pooled data for the association between the IL-1β-511 C/T polymorphisms and JIA in Caucasian subjects. **(A)** recessive and **(B)** additive models.

Abstract THU0037 – Figure 2

REFERENCES:

[1] Cimaz R, Cazalis MA, Reynaud C, Gerloni V, Zulian F, Biggioggero M, Martini G, Pontikaki I, Fantini F, Mougin B, Miossec P (2007) IL1 and TNF gene polymorphisms in patients with juvenile idiopathic arthritis treated with TNF inhibitors. Ann Rheum Dis 66:900-904.
[2] Donn RP, Barrett JH, Farhan A, Stopford A, Pepper L, Shelley E, Davies N, Ollier WER, Thomson W (2001) Cytokine gene polymorphisms and susceptibility to juvenile idiopathic arthritis. British Paediatric Rheumatology Study Group. Arthritis Rheum 44:802-810.
[3] McDowell TL, Symons JA, Ploski R, Førre Ø, Duff GW (1995) A genetic association between juvenile rheumatoid arthritis and a novel interleukin-1α polymorphism. Arthritis Rheumatism 38:221-228.

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THU0038

INDIVIDUAL FUNCTIONS OF THE HISTONE-ACETYLTRANSFERASES CBP AND P300 IN REGULATING THE INFLAMMATORY RESPONSE OF RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: The two coactivators of transcription cAMP-response element binding protein (CREB) binding protein (CBP) and p300 are close homologues. They are widely accepted as redundant proteins and unique functions have not been investigated in depth. Both proteins contain a histone acetyltransferase (HAT) activity for writing of cell type specific activating H3K27 histone acetylation marks, and a bromodomain, which functions as a reader of acetylated lysine residues on histone tails. Inhibitors targeting the bromodomains are in drug development for inflammatory and malignant diseases.
Objectives: To analyze individual functions of CBP and p300 in regulating the inflammatory response of rheumatoid arthritis (RA) synovial fibroblasts (SF).
Methods: SF were isolated from knee, shoulder and hand joints of RA patients undergoing joint replacement surgery. The expression of CBP and p300 was silenced by transfection of antisense LNA gapmeRs (12.5 nM). 24h after transfection, cells were stimulated with TNF-α (10 ng/ml, 24h). The levels of H3K27ac in SF were analyzed by Western blotting (n=7). Transcriptomes were determined by RNA-seq (Illumina NovaSeq 6000, n=6). Pathway enrichment analysis of RNAseq data was performed using DAVID bioinformatic resources (fold change > 1.5, FDR < 0.05, top 3000 genes included). Changes in the mRNA expression of potential target genes were confirmed by quantitative Real-time PCR (n=12-14).
Results: Silencing of p300 reduced the levels of H3K27ac by 30% in unstimulated SF, and by 61.4% ($p<0.05$) in presence of TNF-α, whereas silencing of CBP reduced H3K27ac by 43.5% only in presence of TNF-α. In line with the changes in the H3K27ac, silencing of p300 affected the expression of 6026 and 5138 genes in unstimulated and stimulated SF, respectively. In contrast, only 285 and 1911 genes were affected by CBP silencing in unstimulated and stimulated SF, respectively. 184 genes were affected by both, CBP and p300, in unstimulated SF, with 9.2% of genes being regulated in opposite directions. 13.5% of overlapping genes affected by CBP and p300 were regulated in opposite directions in TNF-α-stimulated SF. Principal component (PC) analysis of RNAseq data separated TNF-α-stimulated from unstimulated SF (PC1) and p300 gapmeR-transfected SF (PC2) from controls and CBP gapmeR-transfected SF, which clustered together. The top pathways regulated by CBP were 'cell cycle' and 'focal adhesion' in unstimulated cells and 'DNA replication' and 'cell cycle' after stimulation with TNF-α. Top pathways regulated by p300 in presence and absence of TNF-α were 'proteasome', 'spliceosome' and 'focal adhesion'. The expression of 16 chemokines and cytokines was changed in RNAseq data (fold change >1.5, $p<0.05$) by either silencing of CBP or p300. Whereas silencing of CBP reduced the expression of all of them, silencing of p300 had pro- and anti-inflammatory effects. We further confirmed expression changes in cytokine and chemokine expression by Real-time PCR. Silencing of CBP reduced the expression of IL6, CCL2 ($p<0.01$), CXC3L1 ($p<0.05$), and CXCL10. Silencing of p300 reduced the expression of CCL2 and CXC3L1 ($p<0.001$) but increased the expression of IL8 ($p<0.001$) and CXCL2 ($p<0.05$).
Conclusion: Our results suggest that p300 is the major writer for H3K27ac marks in SF. We have identified overlapping and distinct functions for CBP and p300 in SF. CBP inhibition has anti-inflammatory effects. In contrast, p300 inhibition has pro- and anti-inflammatory functions.
Disclosure of Interests: Marcel Gabathuler: None declared, Monika Krosel: None declared, Christoph Kolling: None declared, Matija Tomsic: None declared, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications.

In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Caroline Ospelt: None declared, Kerstin Klein: None declared

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THU0039 THE RELATION BETWEEN THE INFLAMMATORY STATUS OF HUMAN END STAGE OSTEOARTHRITIC SYNOVIUM AND LEVELS OF LOW DENSITY LIPOPROTEIN

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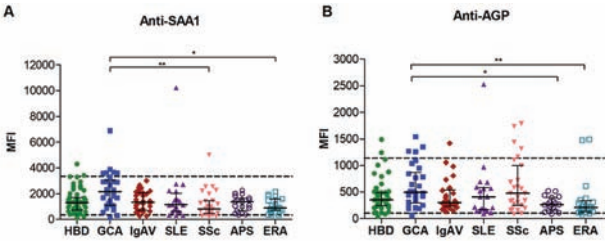
Background: High systemic levels of low density lipoprotein (LDL) is a shared metabolic risk factor for osteoarthritis (OA) and cardiovascular disease (CVD), which may point to common biochemical pathways. One of the key events in atherosclerosis is formation and uptake of oxidized LDL (oxLDL) as a consequence of macrophage-mediated inflammation. Studies performed in our lab have previously shown that in mice, high LDL levels enhance synovial activation and ectopic bone formation during development of collagenase-induced OA. Furthermore, injection of oxLDL in naïve macrophage depleted joints led to infiltration of myeloid progenitor cells. Although these results strongly indicate towards (ox)LDL-mediated events that enhance OA severity, these processes have not yet been shown to occur in human osteoarthritic synovium.
Objectives: In the present study, we investigated whether the inflammatory status of OA synovium is associated to systemic and local levels of (ox)LDL.
Methods: Blood was collected from patients planned to undergo total knee replacement and LDL serum levels were determined (n=16). After surgery, synovial explants from the same patients (2-8 per patient) were collected and incubated at 37˚C for 24 hours in presence of LDL (50 μg ApoB/mL), oxLDL (50 μg ApoB/mL) or control medium. Levels of IL-1β, TNF-α, IL-10 and MCP-1 secreted in the conditioned medium were measured using Luminex. Levels of S100A8/A9 were measured using ELISA. Concentrations of secreted factors were normalized for tissue sample weight. Synovial explants were further processed for histological analysis. Immunohistochemical staining of ApoB was performed to assess presence and uptake of (ox)LDL in the synovium. Hematoxylin & eosin-stained sections were used to arbitrarily score cellular infiltration and synovial hyperplasia.
Results: Around 50% of the patients in our cohort showed synovial activation exemplified by high secretion levels of IL-1β, TNF-α and IL-10. Cellular infiltration and synovial hyperplasia was observed in the majority of synovial tissue samples, their grades did however not correlate with cytokine secretion. Secretion levels of IL-1β positively correlated with serum levels of LDL and total cholesterol and did not correlate with BMI, suggesting a link that runs via systemic metabolic processes rather than increased weight-mediated joint loading. Considering that around 50% of OA patients suffers from synovitis characterized by increased macrophage presence and activity, high LDL in these patients may trigger oxLDL formation and uptake in the synovium. Staining of LDL-associated protein ApoB in histological sections of synovia showed distinct speck-like staining within macrophages and endothelial cells especially, suggesting oxLDL accumulation in these cells. Unexpectedly, presence of high concentrations of LDL or oxLDL during incubation of synovial explants did not significantly affect secretion of IL-1β, TNF-α, IL-10 and MCP-1, whereas presence of LDL but not oxLDL negatively affected secretion of S100A8/A9.
Conclusion: IL-1β secretion by end stage OA synovium is associated to systemic levels of LDL. Intervention with high concentrations of LDL or oxLDL for 24-hours after synovium extraction did however not alter cytokine secretion, suggesting that LDL and synovitis are linked through more long-term local interactions, or alternatively via systemic inflammatory factors.
Disclosure of Interests:
None declared

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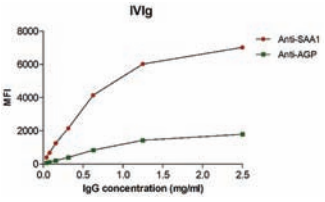
THU0040 USING A NOVEL BEAD-BASED IMMUNOASSAY FOR SIMULTANEOUS DETECTION OF AUTOANTIBODIES AGAINST SERUM AMYLOID A1 AND ALPHA1 ACID GLYCOPROTEIN

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Background: Naturally occurring autoantibodies (Abs) against acute phase proteins (APPs), such as anti-serum amyloid A1 (SAA1) Abs have already been identified in sera of healthy individuals, as well as in patients with autoimmune diseases (1). Currently however, no method exists for simultaneous detection of multiple Abs against APPs.
Objectives: To develop a bead-based duplex immunoassay for simultaneous detection of IgG anti-SAA1 and anti-alpha 1 acid glycoprotein (AGP) Abs and quantify their levels in sera of healthy blood donors (HBD), and patients with systemic autoimmune diseases, as well as in intravenous immunoglobulin preparation (IVIg).
Methods: Fluorescently labeled MagPlex microspheres (Luminex Corp) were used to covalently bind SAA1 and AGP. Sera samples (diluted 1:20) were added to a 96-well microtiter plate and incubated with SAA1- and AGP-coupled microspheres for 2h. Subsequently, PE-conjugated anti-human IgG Abs were added to each well, incubated for 30 min, resuspended in PBS-1%BSA and analysed using the MagPix system (Biomedica, GmbH).



Abstract THU0040 – Figure 1. Levels of antibodies against SAA1 (A) and AGP (B) in HBD as compared to patients with systemic autoimmune diseases. Shown is median and IQR. 5th and 95th percentile of MFI values in HBD are indicated with dotted lines; *p<0.05; **p<0.01. SAA1, serum amyloid A1; AGP, alpha 1 acid glycoprotein; MFI, median fluorescence intensity; HBD, healthy blood donors; GCA, patients with giant cell arteritis; IgAV, immunoglobulin A vasculitis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; APS, antiphospholipid syndrome; ERA, early rheumatoid arthritis.



Abstract THU0040 – Figure 2. Presence of antibodies against SAA1 and AGP in IVIg. IVIg, intravenous immunoglobulin G; SAA1, serum amyloid A1; AGP, alpha 1 acid gycoprotein; MFI, median fluorescence intensity.

Sera samples were collected from HBD (n=55), patients with giant cell arteritis (GCA; n=30), immunoglobulin A vasculitis (IgAV; n=30), systemic lupus erythematosus (SLE; n=20), systemic sclerosis (SSc; n=27), antiphospholipid syndrome (APS; n=19) and early rheumatoid arthritis (ERA; n=20). Ab levels were determined also in IVIg (Octapharma AG).
Results: We observed the presence of both, anti-SAA1, and anti-AGP Abs in sera of HBD, as well as in patients with GCA, IgAV, SLE, SSc, APS and ERA.
GCA patients had significantly higher anti-SAA1 levels (median (IQR) MFI was 2163 (1113- 3048)) as compared to SSc (816 (480-1462); p<0.01) and ERA (886 (722-1596); p<0.05) patients. Levels of anti-AGP Abs were also significantly higher in sera of GCA patients (495 (298-872)) as compared to ERA (213 (130-338); p<0.01) and APS (264 (154-399); p<0.05) patients. No difference in anti-SAA1 or anti-AGP levels was observed between HBD and the tested groups of patients (Figure 1).

Substantial amounts of anti-SAA1 Abs were observed in serially diluted IVIg, while there were 4-fold less anti-AGP Abs detected (Figure 2), which corresponds also to the ratio found in HBD (Figure 1).
Conclusion: Serum IgG Abs against SAA1 and AGP present in HBD, patients with systemic autoimmune diseases and in IVIg can be simultaneously quantified using a customized bead-based multiplex assay. These natural autoAbs found in IVIg could be endogenous immune-regulators of the acute phase response.
Acknowledgement: The authors would like to acknowledge funding from the Slovenian Research Agency (ARRS) for the National Research Program P3-0314.

REFERENCE:
[1] Lakota K, et al. Could antibodies against serum amyloid A function as physiological regulators in humans? Autoimmunity 2011;44: 149-58.

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THU0041 MESENCHYMAL STEM CELLS OF DIFFERENT ORIGINS EXHIBIT UNIQUE RESPONSES TO DIFFERENT INFLAMMATORY STIMULI

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Background: Mesenchymal stromal/stem cell (MSC) - based therapies represent promising avenues for treatment of various inflammatory and autoimmune diseases. Currently, a variety of fetal and adult tissues represent a good source of MSC, however further characterization of their effects, especially in an inflammatory environment, is needed.
Objectives: Firstly, to characterize MSC from different origins, namely bone marrow (BM), adipose tissue (AT) and umbilical cord (UC), after stimulation with TNFα, IL-1β and serum amyloid A (SAA). Secondly, to determine the effects of MSC secretome on migration, proliferation and apoptosis of lung fibroblasts.
Methods: BM-, AT- or UC-MSC were isolated each from 3 healthy donors. The expression and secretion of analytes were studied in each cell type at basal level and followingTNFα- (1 ng/ml), IL-1β- (1 ng/ml) and SAA- (12 μg/ml) stimulation using qPCR (SDF, CCL5, VCAM, PDE, PGC, IDO, VEGF, IGF) and Luminex technology (IL-6, IL8, MCP-1, ICAM, CH3L1, MMP1, MMP3, tenascin, uPA, HGF, VEGF), respectively. Normal healthy lung fibroblasts (NHLF) were used in the wound scratch assay and treated for 24h with 20% of MSC-conditioned media. For evaluation of BM-, AT- and UC conditioned media effects on proliferative and apoptotic activity, Ki-67-immunolabeled mitotic cells and caspase-3-immunolabeled cells were counted using fluorescence microscopy.
Results: Treatment of MSC with pro-inflammatory cytokines increased mRNA levels of SDF, CCL5, VCAM1, PGC and IDO, while levels of PDE-5A were down-regulated. The greatest increase in expression was observed in TNFα-stimulated MSCs, namely of two immunomodulatory molecules, CCL5 and IDO in AT-MSC (4396- and 928-fold change increase respectively). Secretome analysis showed highest secretion levels of IL-6, IL-8 and MCP1 after IL-1β-activation in all 3 tissue sources. AT- and BM-derived conditioned media increased NHLF scratch closure, while UC-MSC decreased it. In non-inflammatory conditions, UC-, BM- and AT-MSCs conditioned media decreased the number of mitotic events in NHLF by an average of 40%. Importantly, only the conditioned medium derived from inflammatory cytokine-treated AT- and BM-MSC significantly decreased the mitotic rate of NHLF ($p<0.01$). The number of apoptotic cells increased 3- to 8-fold after treatment with all MSC conditioned media, with UC-MSC showing the highest effect ($p<0.01$).
Conclusion: Our results highlight specific roles of MSC from different tissue origins, as well as their response to environmental inflammatory stimuli and suggest that source selection might be critical for the success of treatment approaches in different diagnoses.
Disclosure of Interests: None declared
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THU0042 EFFECT OF SPLEEN TYROSIN KINASE (SYK)-INHIBITORS ON RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: The spleen tyrosine kinase (syk) is an intracellular protein kinase involved in signal transmission processes of immune cells and non-hematopoietic cells, such as fibroblasts. Various syk-inhibitors are therefore currently being tested in preclinical and clinical studies, e.g. for the treatment of different types of cancer as well as autoimmune diseases. In preclinical studies, the syk inhibitor fostamatinib showed a pronounced anti-inflammatory effect on synovial fibroblasts (SF) from patients with rheumatoid arthritis (RA). These cells play an important role in the pathogenesis of RA by mediating matrix destructive processes. On the other hand, clinical trials have been only moderately successful due to the side effects and the limitation regarding increase in dosage. However, further inhibitors such as RO9021 or TAK-659 have been developed. They are characterized by a more specific kinase profile and therefore side effects could potentially be less severe. Whether these inhibitors also convey an anti-inflammatory effect on RASF has not yet been investigated.
Objectives: This study examines the effect of syk-inhibitors on the inflammatory response and functional behavior of activated RASF.
Methods: RASF were isolated from synovial tissue of patients with known rheumatoid arthritis during joint replacement surgery. RASF were pretreated with different concentrations of RO9021 and TAK-659 and their vehicle control for 2h and additionally stimulated with IL-1β (10 ng/ml) for 17h or with oncostatin M (OSM, 100 ng/ml) for 24h. Supernatants were collected and the concentration of IL-6 and MMP3 were determinate by ELISA. The measurement of cell viability, cytotoxicity and apoptosis was performed to exclude possible cytotoxic or apoptotic effects of the syk-inhibitors. The RASF proliferation was detected by a BrdU-incorporation assay. The effect of syk-inhibitors on cell migration towards a FCS-gradient was measured by cell culture inserts.
Results: Both TAK-659 and RO9021 showed a significant reduction of the release of the pro-inflammatory cytokine IL-6 and the production of MMP3 in IL-1β stimulated RASF. However TAK-659 showed a stronger effect on IL-6 reduction (48%, $p<0.005$) than RO9021 (25%, $p<0.05$) at 10μM. MMP3 decrease was also stronger with TAK-659 (92%, $p<0.001$) than with RO9021 (59%, $p<0.001$). This effect was apparently not restricted to IL-1β because both inhibitors also decreased the OSM-induced IL-6 release of RASF by 85% ($p< 0.01$) with TAK-659 and 30% with RO9021 at 10μM. The proliferation of RASF was also reduced by both syk-inhibitors at 5μM and higher. The highest effect could be observed with TAK-659 for 80% and with RO9021 by 50% both at 15μM. The migration of RASF was also decreased by TAK-659 at 10μM ($p<0.01$, n=3). The effects were not mediated by induction of apoptosis or by cytotoxicity.
Conclusion: The syk-inhibitors TAK-659 und RO9021 at concentrations above 5μM reduce the inflammatory response, the migration and proliferation of RASF. If appropriate concentrations can be reached in vivo, these syk-inhibitors could offer a possibility to modulate the aggressive phenotype of RASF.

DISCLOSURE OF INTERESTS:
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THU0043 IL-25 ALLEVIATES RHEUMATOID ARTHRITIS BY INHIBITING TH17 IMMUNE RESPONSE

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Background: Rheumatoid arthritis (RA) is a prevalent common autoimmune disease characterized by chronic inflammation of the joint and synovial hyperplasia and progressive destruction of articular cartilage and bon. Accumulating evidence highlighted that an imbalance between pro-

and anti-inflammatory cytokines maybe a key mechanism for disease progression in RA. IL-25 is reported to play an anti-inflammatory role in autoimmune and inflammatory diseases through the downregulation of Th1 and Th17 cell responses However, the exact role of IL-25 in the pathogenesis of RA remains to be elucidated.

Objectives: Explore the role of IL-25 in the pathogenesis of RA, and provide the scientific evidence of IL-25 relevant biological agent.

Methods: 1.The study was first to analyze the relationship between IL-25 and DAS28 score, CRP and anti-CCP in RA patients. Test IL-1β, IL-6, IL-17A, TNF-α and IFN-γ through ELISA, then analyze the relationship with IL-25. $CD4^+$ T cells from PBMCs of the 5 RA patients and 5 HCs were isolated under the manual of EasySep™ Human $CD4^+$ T Cell Isolation Kit and stimulated with anti-CD3 plus anti-CD28 in the presence or absence of rhIL-25. 2.CIA model was established to explore the mechanism of IL-25. The expression of CII specific IgG1 and IgG2a, as well as IL-1β, IL-6, IL-17A and TNF-α in CIA serum were examined using ELISA assay. The ROR-γ,T-bet, GATA-3 mRNA levels in knee joints and spleen were assessed by real-time qPCR analysis. In vitro, $CD4^+$ T cells from spleen were isolated from CIA mice and cultured with or without recombinant mouse (rm)IL-25 for 24h to control the expression IL-17A. Cells were stimulated with plate-bound anti-CD3 plus anti-CD28 in the presence or absence of recombinant mouse (rm) IL-25 with different dose for 24 h.

Results: 1.The expression of IL-25 were upregulated in the serum and synovial fluid in RA patients. Serum IL-25 levels were positively associated with DAS28 score, ESR and C-reactive protein. However, no significant correlation was observed between serum IL-25 levels, RF and anti-CCP. IL-25 serum levels was positively correlated with the concentrations of IL-1β, IL-6, IL-17A and TNF-α, respectively. However, no significant correlation was observed between serum IL-25 and IFN-γ level. 2. IL-25 can alleviate inflammatory response of CIA mouse and inhibite IL-17 differentiation. The serum levels of IL-1β, IL-6, IL-17A and TNF-α in IL-25-treated mice were markedly reduced compared with those in WT mice, except IFN-γ. RT-qPCR also demonstrated that the transcription levels of IL-17A and ROR-γt were decreased in the synovial tissue of IL-25-treated mice. RmIL-25 treatment significantly inhibited IL-17A production in a dose-dependent manner, and the mRNA level of the key TFs for Th17 cells (ROR-γt), as well as IL-17A, were also decreased.

Conclusion: IL-25 is upregulated in the serum and synovial fluid of RA patients. High levels of IL-25 was associated with disease severity and inflammation response in RA patients. IL-25 inhibits CD4+ T-cell activation and differentiation into Th17 cells, without affecting Th1 cells in RA. Systemic administration of IL-25 attenuates arthritis onset and joint damage in CIA mice. IL-25 of multi - target regulation further be used in the clinical treatment of RA.

Disclosure of Interests: None declared

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THU0044 PRO- AND ANTI-INFLAMMATORY MEDIATORS OF SYSTEMIC INFLAMMATION AND ARTHRITIS IN THE ELDERLY

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Background: Elderly-onset RA (EORA), which is defined as rheumatoid arthritis (RA) with an onset at >60 years of age, and polymyalgia rheumatica (PMR) are common rheumatic diseases in the elderly. Eicosanoids are biological lipids that serve a specific role as either activators or suppressors of systemic inflammation and have been involved in the development and progression of arthritis.

Objectives: We hypothesized that eicosanoid-related perturbations are related to arthritic symptoms in the elderly, and that by defining this eicosanoid profile, we might be able to define elements of inflammation pathobiology in this population.

Methods: Arthritis in the Elderly (ARTIEL) is a recent collection cohort with patients older than 60 years of age who have newly diagnosed arthritis. Blood samples were collected from these patients at baseline (pre-treatment) and 3 months after treatment, along with physician and patient outcome measures through 12 months. These patients were also compared with randomly-selected control individuals of the same age and gender. A thorough clinical examination was conducted and patients completed a health assessment questionnaire (HAQ). Disease activity score (DAS)28CRP was also calculated. Serum eicosanoids were determined by mass spectrometry at baseline and after 3 months of treatment and were classified into groups according to their eicosanoid precursors: eicosapentaenoic acid (EPA), docosohexanoic acid (DHA) or arachidonic acid (AA). Data processing and statistical analysis were performed in R.

Results: 64 patients (average: 75.15, standard deviation (SD) 6.80) and 18 controls (average: 75.39, SD, 6.04) were analyzed. Of these, 44 were diagnosed with RA and 20 with PMR. At the start of the study, patients had a mean DAS28CRP of 5.72 (SD, 1.05) and a mean HAQ of 1.64 (SD, 0.73). In addition, 84% of the patients reported scapular pain and 56% reported pelvic pain at baseline. After three months of treatment, patients had a mean DAS28CRP of 2.38 (SD, 1.23) and a mean HAQ of 0.36 (SD, 0.41). Several eicosanoids, especially anti-inflammatory species derived from EPA and DHA, were significantly downregulated in both RA and PMR patients at the start of the study as compared to normal controls (Figure 1). Three months after treatment, the levels of anti-inflammatory eicosanoid species derived from EPA and DHA went back to normal only in patients who responded to therapy.

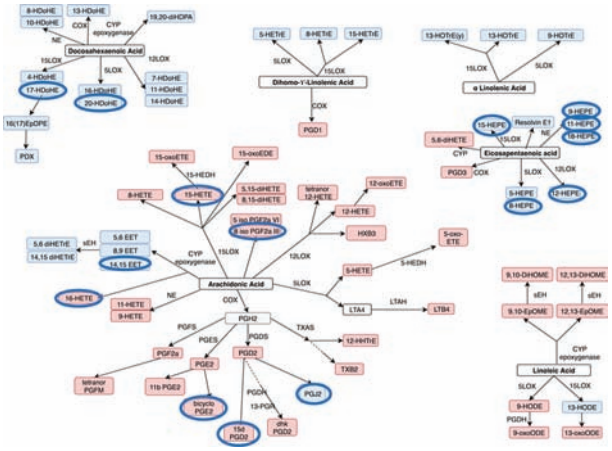
Conclusion: These results suggest that certain eicosanoids may be key effectors in arthritis in the elderly and that the imbalance between pro and anti-inflammatory eicosanoids before and after treatment might be related to clinical and therapeutic outcomes in this population.

REFERENCES:

[1] A systematic review on the role of eicosanoid pathways in rheumatoid arthritis. Hoxha M. Adv Med Sci. 2018 Mar;63(1):22-29.

[2] Kobak S, Bes C. An autumn tale: geriatric rheumatoid arthritis. Therapeutic advances in musculoskeletal disease. 2018 Jan;10(1):3-11. PMID: 29290762

[3] Quehenberger O, Dennis EA. The human plasma lipidome. New England Journal of Medicine. 2011 Nov 10;365(19):1812-23. PMID: 22070478



Abstract THU0044 – Figure 1. Anti-inflammatory species derived from EPA and DHA are significantly downregulated in patients at baseline. Pro-inflammatory (in red) and anti-inflammatory eicosanoids (in blue) detected in our patients are represented by pathways and origin PUFA. Significant eicosanoids ($p < 0.05$) are circled in blue if downregulated in patients compared to controls at baseline.

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THU0045 IL-25/IL-17RB AXIS IS ACTIVATED AND ASSOCIATED WITH ILC2 EXPANSION IN GRANULOMATOSIS WITH POLYANGIITIS (GPA)

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Background: Pathogenesis of Granulomatosis with polyangiitis (GPA) is still unknown. However, it has been observed a skewing of circulating CD4+ T cells toward the Th17 and Th2 phenotype. The pro-inflammatory cytokine interleukin 25 (IL-25) is a member of IL-17 cytokine family associated to the Th2 immune phenotype. Through the receptor IL17RB, IL-25 further sustains the Th2-type immune response and elicits the expansion of the type 2 innate lymphoid cells (ILC2) and M2 macrophages. A pathogenic role of the innate lymphoid cells in GPA has been recently demonstrated; however, the relevance of IL-25 in this condition remains unexplored.

Objectives: Aim of the study was to evaluate the expression of IL-25/IL-25R axis and its functional relevance in patients with granulomatosis with polyangiitis (GPA).

Methods: Thirty patients with a diagnosis of GPA fulfilling the Chapel Hill Consensus Conference and ACR classification criteria, and 20 age-matched healthy controls (HC) were included in this study: age range 30-66 years, 40% female in GPA group and 32-63 years, 20% female in HC. IL-25 and IL-33 serum levels were measured by ELISA at the diagnosis and after Rituximab (RTX) therapy (n=15). Immunohistochemical staining for IL-25, IL-33, IL-17B was performed on sections of renal biopsies obtained from GPA patients (n=10). Kidney ILC2 infiltration was assessed by confocal microscopy. Frequencies ILC1, ILC2 and ILC3 were evaluated by flow cytometry analysis by CD45, Lyn, CRTH2, GATA3, Tbet, CD56, NKp44, IL-22, IL-23R, RORc. Expression levels of IL-5 and IL-13 in kidney were quantified by quantitative real-time PCR (qRT-PCR).

Results: Increased pre-RTX serum levels of IL-25 and IL-33 at baseline were observed in GPA compared to HC ($p<0.0001$). Both serum IL-25 and IL-33 correlated with the Birmingham Vasculitis Activity Score (BVAS) ($r^2 0.51$ $p<0.0001$ and $r^2 0.14$ $p<0.05$ respectively). IL-25, IL-17RB and IL-33 expressing cells were increased in GPA renal biopsies vs HC ($p<0.0001$). Frequencies of circulating ILC1 and ILC3 were not significantly increased in GPA. Conversely, the frequency of ILC2 was expanded in GPA vs HC ($p<0.0001$) and correlated with BVAS ($r^2 0.60$ $p<0.0001$). The number of ILC2 and the levels of expression of IL-5 and IL-13 in GPA kidney were increased ($p<0.0001$). RTX therapy led to a reduction in IL-25 and IL-33 serum levels and in the frequency of circulating ILC2.

Conclusion: Our data confirm the increases in IL-33 levels previously reported by other authors. The increased circulating and tissue levels of IL-25 and IL-25 receptor-expressing cells, including ILC2, suggests a role for the IL-25/IL-17RB axis in GPA pathogenesis. Treatment with anti-CD20 Rituximab may lead to modulation of IL-25/IL-17RB axis and reduction in ILC2.

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THU0046 FRACTALKINE PROMOTES DIFFERENTIATION INTO OSTEOCLASTS FROM HUMAN PERIPHERAL BLOOD MONOCYTES

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Background: Fractalkine (FKN) also known as chemokine (C-X3-C motif) ligand 1 plays important roles in the pathogenesis of rheumatoid arthritis (RA). Clinical trials of monoclonal antibody against FKN for RA are currently in progress. Although FKN has been reported to be involved in the migration of osteoclast precursor cells, the direct effect of FKN on osteoclast differentiation is not clear.

Objectives: In this study, we aimed to clarify the effect of FKN on differentiation into osteoclasts from human peripheral blood monocytes.

Methods: CD14-positive monocytes were purified from peripheral blood obtained from healthy donors by magnetic beads. CD16-positive and CD16-negative peripheral blood monocytes were isolated from the CD14-positive monocytes. The purified peripheral blood monocytes were incubated with M-CSF + RANKL with or without FKN for 1 week. The cells were stained for tartrate-resistant acid phosphatase (TRAP). TRAP-positive multinucleated (three or more nuclei) cells were counted as osteoclasts. The cells were seeded onto plates coated with calcium phosphate thin films, and the resorption lacunae were examined. Next, CD14-positive monocytes were incubated with GM-CSF + IL-4 with or without FKN for 1 week to differentiate into dendritic cells. The surface markers of these cells were analyzed by flow cytometry. In addition, the monocyte-derived dendritic cells were further incubated with M-CSF + RANKL with or without FKN. Then the cells were stained for TRAP. The research procedure has been approved by the ethics committee of Toho University School of Medicine (Approval number: 27060).

Results: CD16-negative peripheral blood monocytes differentiated into osteoclasts by incubation with M-CSF + RANKL. The osteoclast differentiation was enhanced by additional stimulation with FKN in a concentration-dependent manner. In addition, calcium resorption was also enhanced by addition of FKN. On the other hand, CD16-positive monocytes treated with M-CSF + RANKL did not differentiate into osteoclasts with or without FKN. CD14-positive monocytes differentiated into dendritic cells by stimulation with GM-CSF + IL-4. Expression of CD14 was decreased and CD1a expression was increased on the monocyte-derived dendritic cells. CD16-negative monocyte-derived dendritic cells differentiated into osteoclasts by further stimulation with M-CSF + RANKL. By co-stimulation with FKN, the osteoclast differentiation from CD16-negative monocyte-derived dendritic cells was also enhanced.

Conclusion: FKN promotes osteoclast differentiation from human peripheral blood CD16-negative monocytes and also from CD16-negative monocyte-derived dendritic cells. FKN might contribute bone destruction in the affected joints of RA as well as inflammatory cell accumulation into the synovial tissue.

REFERENCES:

[1] Tanaka Y, Takeuchi T, Umehara H, Nanki T, et al. Safety, pharmacokinetics, and efficacy of E6011, an antifractalkine monoclonal antibody, in a first-in-patient phase 1/2 study on rheumatoid arthritis. Mod Rheumatol. 2018; 28: 58.

[2] Nanki T, Imai T, Kawai S. Fractalkine/CX3CL1 in rheumatoid arthritis. Mod Rheumatol. 2017; 27: 392.

[3] Nanki T, et al. Inhibition of fractalkine ameliorates murine collagen-induced arthritis. J Immunol. 2004; 173: 7010.

[4] Nanki T, et al. Migration of CX3CR1-positive T cells producing type 1 cytokines and cytotoxic molecules into the synovium of patients with rheumatoid arthritis. Arthritis Rheum. 2002; 46: 2878.

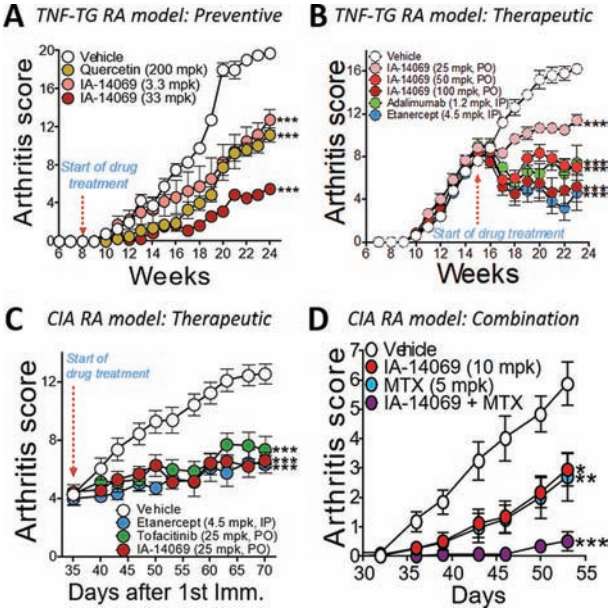
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THU0047 IA-14069, A NOVEL SMALL-MOLECULE INHIBITOR DIRECT-TARGETING TUMOR NECROSIS FACTOR-α, ATTENUATES COLLAGEN INDUCED ARTHRITIS

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Background: Rheumatoid arthritis (RA) is systemic autoimmune disease that is characterized by autoreactive immune cells and various cytokines-mediated inflammation in multiple joints, leading to cartilage degradation, bone erosion and finally irreversible joint destruction[1]. The inflammatory cytokine tumor necrosis factor-α (TNF-α) is known to play a central role in several chronic immune-mediated inflammatory disorders[2].
Objectives: Despite the great success of anti-TNF-α biological drugs in the treatment of RA, no chemical drug targeting TNF-α is available. Here we report that IA-14069, a novel small molecule inhibitor, binds directly to TNF-α and inhibits TNF-α activities both *in vitro* and *in vivo*.
Methods: IA-14069 was screened and identified by competitive binding assay using TNF-α and TNF receptor. *In vitro* neutralization activity of IA-14069 against TNF-α was determined using MTT assay. The direct binding IA-14069 to TNF-α was demonstrated by surface plasmon resonance and bead pull-down assays. The inhibition of TNF-α-TNFR interactions by direct binding of IA-14069 to TNF-α was analyzed by flow cytometry. Levels of phosphorylated IκBα (p-IκBα) and NF-κB p65 were analyzed by western blot. IA-14069 was orally administrated to TNF-α-transgenic (TNF-α-TG) RA mice at 3.3 or 33 mg/kg twice per week or at 25, 50 or 100 mg/kg 3 times per week for preventive or therapeutic effect, respectively. *In vivo* therapeutic efficacy of IA-14069 or methotrexate was evaluated in collagen-induced arthritis (CIA) mice immunized with bovine type II collagen (CII) emulsified in complete Freund's adjuvant, and boosted with CII emulsified in incomplete Freund's adjuvant.
Results: IA-14069 potently inhibits both TNF-α-induced cytotoxicity (IC_{50} < 0.7 μM) which directly binds to TNF-α and TNF-α-triggered signaling (p-IκBα and NF-κB p65) activities. The therapeutic as well as preventive anti-RA effects of IA-14069 were demonstrated in TNF-α-TG and CIA models. IA-14069 and MTX had synergistic effects in the CIA therapeutic model. According to pharmacokinetic analysis, IA-14069 showed significant bioavailability. In addition, no *in vivo* toxicity was observed even under treatment of excessive amount of IA-14069.



Abstract THU0047 – Figure 1

Conclusion: The data indicate that IA-14069 can be a novel and potential TNF-α inhibitor for the treatment of RA and other inflammatory diseases.

REFERENCES:
[1] Choy EH, et al. N Engl J Med. 2001;344:907-16.
[2] Wong M, et al. Clin Immunol. 2008;126:121-36.

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THU0048 2ND LINE TREATMENT WITH LESINURAD AND ALLOPURINOL VERSUS FEBUXOSTAT FOR MANAGEMENT OF HYPERURICEMIA: A COST-EFFECTIVENESS ANALYSIS FOR SPANISH PATIENTS

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Background: Lesinurad, a medication that inhibits uric acid reabsorption, has been recently approved in combination for the treatment of patients with gout which do not reach therapeutic serum urate target with xanthineoxidase inhibitors monotherapy
Objectives: To assess the incremental cost-effectiveness ratio of adding lesinurad to allopurinol as 2nd line therapy, compared to febuxostat for the management of patients with gout in Spain.
Methods: A Markov model comprising 6 health-states representing the disease evolution was used to estimate in 6-months cycles, the lifetime accumulated cost and benefits in terms of quality-adjusted-life-year (QALY) in an hypothetical cohort of patients stratified according to serum uric acid levels observed on pooled CLEAR trials: 18.8% (<6 mg/dL); 63.7% (6-8 mg/dL); 15.2% (8-10 mg/dL) and 2.3% (≥10 mg/dL). During the simulation, patients could either continue with 2nd line treatment with lesinurad (200mg/daily) plus allopurinol (400mg/daily) or febuxostat (80mg/daily), switch to allopurinol monotherapy (271mg/daily) in case of intolerance or discontinue treatment. Proportion of tophaceous gout (18.9%) was considered at each health-state. The efficacy of treatments was captured in the transition probabilities between health states which were derived from findings on CLEAR 1, CLEAR 2 and EXCEL clinical trials. Quality of life related to gout severity (tophaceous or non-tophaceous) and flare frequency was considered by means of utilities estimated from SF-36 scores of the pooled CLEAR trials which were mapped to EQ-5D values. The total cost estimation (€, 2018) included drug acquisition cost (retail prices with mandatory deduction applied), disease monitoring (€ 377.03 for first 6-month period, € 329.95/subsequent year) and flare management cost (€ 301.69). Unitary costs derived from local cost databases and literature. A 3% annual discount rate was applied for cost and outcomes. Sensitivity analyses (SA) were carried out.
Results: Lesinurad added to allopurinol provided higher QALYs (14.79) than febuxostat (14.69). Total accrued cost per patient were lower (€ -6,819.13) with lesinurad and allopurinol (€ 49,659.27) compared to febuxostat (€ 56,478.40). Lesinurad plus allopurinol resulted a dominant option (more effective and less costly) compared to febuxostat. SA results confirmed the model robustness.
Conclusion: These results suggest that treatment with lesinurad 200 mg/day plus allopurinol 400 mg/day compared to febuxostat 80 mg/day is an effective second option for the management of hyperuricemia in patients with gout who did not reach therapeutic srum urate target to previous allopurinol monotherapy, associated to cost-savings for the Spanish National Health System.

REFERENCES:
[1] Bardin T, *et al.* Ann Rheum Dis. 2017;76:811-20.
[2] Becker MA, *et al.* J Rheumatol. 2009;36:1273-82.
[3] Pérez-Ruiz F, *et al.* J Med Econ. 2016;19:604-10.
[4] Saag K, *et al.* Arthritis Rheumatol. 2017;69:203-12.

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THU0049 CORRELATION BETWEEN IL-6 AND OSTEOCALCIN SERUM LEVELS WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS (RA) PATIENTS

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Background: IL-6 plays a significant role in RA pathophysiology. It is considered nowadays as an important inflammation marker and it is responsible for a wide range of articular and extra-articular manifestations in RA patients. Osteocalcin is a protein (non collagenous) that can be found in the bones extracellular matrix, as well as in the circulating blood serum. This protein is a marker of bone formation and turnover.
Objectives: Evaluating IL-6 and osteocalcin serum levels in RA patients and their correlation with disease activity.
Methods: We examined 126 patients previously diagnosed with RA according to the ACR/EULAR 2010 criteria. To all patients it was measured the IL-6 serum level (<4.0 pg/mL), and also the osteocalcin serum level using the ELISA-OSTEO kit method (13-46ng/ml) and the disease activity was defined according to the DAS28. By using this activity score index the patients were divided in three groups: group I with active disease scoring > 5.1 (43 patients); group II with moderate disease activity scoring between 3.2 - 5.1 (52 patients); and group III with no disease activity scoring <3.2 (31 patients).
Results: IL-6 serum level resulted elevated in patients group I (1.9±0.6pg/ml;) and group II (0.9±0.3pg/ml) and normal in patients group III (0.35 ±0.1pg/ml). Osteocalcin serum level resulted elevated in the three groups but with higher serum levels in patients group I and II (62±1.9ng/ml; 49.2±2.6ng/ml) and less higher serum levels in group III (44.5±1.7ng/ml). IL-6 serum level correlates best with osteocalcin serum level in patients group I and II (r=0.9). IL-6 serum level correlates with disease activity (r=1). Osteocalcin serum level correlates with disease activity in group I and II (r=0.9) but not with disease activity in group III (r=0.4).
Conclusion: There is a significant correlation between IL-6 serum level and disease activity according to DAS 28 in RA patients. The elevation of osteocalcin serum level correlates with disease activity in RA patients with high and moderate disease activity which is an important finding of the intense bone remodeling, whereas in patients with no disease activity bone remodeling tents to slow down.
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THU0050 IMPLICATIONS OF THE DIFFERENT RESPONSES OF NK CELLS AND MONOCYTES TO IL-6 AND IL-10 IN THE PATHOGENESIS OF ADULT-ONSET STILL'S DISEASE

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Background: Adult-onset Still's disease (AOSD) is a systemic inflammatory disease, the cause of which is largely unknown. AOSD has recently been classified as one of the autoinflammatory diseases in which innate rather than acquired immunity plays an important role in the pathogenesis. Serum IL-18 has been shown to be highly elevated in AOSD patients [1,2].
Objectives: We attempted to quantify the levels of multiple cytokines in the serum of AOSD patients and to evaluate the effects of the cytokines detectable in the AOSD serum on natural killer (NK) cells and monocytes, since these are cells critical to innate immunity.
Methods: Our patients fulfilled Yamaguchi's criteria for the diagnosis of AOSD. We quantified the serum levels of 10 cytokines (IFN-α, IFN-γ, IL-1β, IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-17A and TNF-α) using multiplex bead array assays and IL-18 using ELISA. We next sorted NK cells or monocytes from peripheral blood mononuclear cells of healthy controls and stimulated each of the cell populations *in vitro* in the presence of the cytokines that had been detected in the AOSD serum. We quantified the level of IFN-γ in the culture supernatant by ELISA and assessed the surface expression level of tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) on NK cells by flow cytometry. Intracellular staining of proinflammatory cytokines in monocytes was performed after stimulation with the same combinations of cytokines.
Results: The level of IL-18 was high in all of the AOSD samples tested. IL-6 was detectable in 8 out of 16 patients and IL-10 in 3 out of 16. In contrast, serum IFN-γ was not detected in any of the samples. When NK cells were stimulated *in vitro* with IL-18 alone, IFN-γ was undetectable in the culture supernatant. The combination of IL-10 and IL-18, but not IL-6 and IL-18, induced IFN-γ. We evaluated the expression of the receptors for IL-6 and IL-10 on NK cells and found that IL-10R and IL-10Rβ were present, while IL-6R and gp130 were absent. The combination of IL-10 and IL-18 also induced TRAIL expression on NK cells in an IFN-γ-independent manner. In contrast, monocytes expressed both the IL-6 and IL-10 receptors. Monocytes stimulated with IL-6 expressed IL-1β and those stimulated with IL-18 expressed IL-6; L-10 exhibited inhibitory rather than stimulatory effects on monocytes.
Conclusion: IL-18 alone did not induce the production of IFN-γ from NK cells *in vitro*. The combination of IL-10 and IL-18, but not IL-6 and IL-18, induced the production of IFN-γ and the surface expression of TRAIL on NK cells. In contrast, monocytes did express IL-6 receptors, and when stimulated with IL-6 or IL-18, produced various inflammatory cytokines, which were inhibited, not stimulated, in the presence of IL-10. Thus, the same cytokines can exert very different effects on inflammation, which is partly explained by the specific expression of corresponding receptors.

REFERENCES:

[1] Kawashima M, et al., Arthritis Rheum. 2001;44(3):550-60.
[2] Yoshida Y, et al., Intern Med. 2011;50(16):1757-60.

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THU0051 OFF-LICENCE USE OF ANAKINRA IN CRITICALLY ILL ADULTS WITH SUSPECTED HAEMOPHAGOCYTOSIS – A SINGLE CENTRE EXPERIENCE

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Background: Anakinra is a recombinant interleukin-1 receptor antagonist licensed in Europe for the treatment of rheumatoid arthritis, periodic fever and auto-inflammatory syndromes[1]. It is increasingly recognised as an adjunct in the treatment of macrophage activation syndrome/secondary haemophagocytic lymphohistiocytosis (HLH)[2].
Objectives: To analyse the indication, patient demographic and outcomes of critically unwell patients receiving anakinra for suspected HLH.
Methods: Retrospective cohort analysis of adult patients who received anakinra over a 12-month period at Imperial College Healthcare NHS Trust, London.
Results: Eleven patients received anakinra (both sub-cutaneous and intravenous, dose range 100– 460 mg daily), ten alongside conventional treatments for HLH. 64% were male. Median age at presentation was 32 years (range 27-73 years). Serum ferritin was significantly elevated (median 17371 (range 4335 – 160,664 micrograms per litre) in all cases. Ten of eleven cases underwent bone marrow examination which showed haemophagocytosis in all cases. Underlying diagnoses were: T-cell Lymphoma (n=3), Mantle Cell Lymphoma (n=1), gastric MALT Lymphoma (n=1), infection (n =3: Group A streptococcus in a patient with inflammatory arthritis (bone marrow not performed), EBV and CMV), retained products of conception (n=1), post-transplant-related lymphoproliferative disorder in a case of systemic lupus with renal transplant (n=1), unknown (n=1).
Overall mortality was 55%. The underlying diagnosis were: T –cell Lymphoma (n=3), gastric MALT Lymphoma (n=1), CMV infection in a post-renal transplant immunosuppressed patient (n=1, sarcoidosis underlying diagnosis), unknown (n=1). 100% of cases with T-cell lymphoma as the cause of HLH died, despite two of the three receiving standard chemotherapy to treat the lymphoma. The third case was diagnosed with non-hepatosplenic gamma delta T-cell lymphoma post-mortem.
In the five cases that survived, anakinra led to rapid recovery in three cases (underlying diagnoses: Mantle Cell lymphoma (managed entirely steroid free), HLH secondary to retained products of conception, and inflammatory arthritis with Group A Streptococcal pneumonia). The two remaining cases had underlying PTLV and EBV-driven HLH. Anakinra led to rapid resolution of fever, improvement in respiration and dramatic decreases in serum ferritin (up to 98% reduction in three weeks).
There were no identifiable complications from anakinra use. One case remains on anakinra, a young male with inflammatory arthritis and Group A Streptococcus pneumonia, who rapidly flared again two days after cessation with full recovery once anakinra was re-instigated.
Conclusion: Anakinra can be a useful adjunct in the treatment of suspected HLH but appears to be less efficacious in those with underlying haematological malignancy, where mortality remains high. In critically ill

patients we have used it intravenously, and in higher doses, where the half-life is shorter and twice daily dosing is required.
Anakinra was well tolerated and its short half-life makes it ideal for use in suspected sepsis-driven HLH. One case was managed entirely steroid-free using anakinra. This allowed for the identification of an underlying lymphoma which may have missed had high-dose steroids been used.
Larger studies will help us ascertain whether earlier anakinra use may spare steroid and chemotherapy side-effects and improve patient outcomes.

REFERENCES:

[1] Clinical Commissioning Policy: NHS England Reference: 170062P. 2018.
[2] Grom AA, et al. Nat Rev Rheumatol. 2016; 12(5): 259–268.

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THU0052 USTEKINUMAB AND GUSELKUMAB TREATMENT RESULTS IN DIFFERENCES IN SERUM IL17A, IL17F AND CRP LEVELS IN PSORIATIC ARTHRITIS PATIENTS: A COMPARISON FROM USTEKINUMAB PH3 AND GUSELKUMAB PH2 PROGRAMS

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Background: Ustekinumab (UST) is a monoclonal antibody (mAb) that binds the p40 epitope which is shared by IL12 and IL23, whereas guselkumab (GUS) is a mAb that selectively binds the p19 subunit of IL23. In recent studies, both UST (Phase 3 programs)[1] and GUS (Phase 2 program)[2] have demonstrated a reduction in musculoskeletal clinical signs and symptoms and improvement of psoriatic lesions in patients with active psoriatic arthritis (PsA), implicating the IL12/23 pathway in disease pathogenesis.
Objectives: To explore the post-treatment pharmacodynamic changes of IL17A, IL17F, and CRP with GUS and UST in the context of PsA.
Methods: Serum protein levels of IL17A, IL17F, and CRP were measured in 142 subjects and 38 matched healthy controls from the GUS Ph2 study[2] at Weeks 0, 4, and 16. In the UST Ph3 studies[1], biomarkers were assayed at Weeks 0, 4, and 24 as follows: IL17A (n=474), IL17F (n=237), CRP (n=927). IL17A and IL17F were assayed using Single Molecule CountingTM Human Immunoassay Kits (formerly Singulex). CRP was measured using CardioPhase hsCRP assay (UST studies) or Meso Scale Discovery Platform (GUS study).
Results: At baseline, the Th17 effector cytokines IL17A and IL17F were elevated in the serum of PsA subjects in the GUS Ph2 cohort compared to healthy controls. IL17A and IL17F levels significantly correlated with affected skin body surface area, but not swollen or tender joint scores, in both studies. While none of the baseline levels of evaluated cytokines were associated with American College of Rheumatology (ACR) or Psoriasis Area Severity Index (PASI) clinical responses to UST, baseline IL17F levels were modestly associated with ACR20 response to GUS at week 24. Both UST and GUS treatment resulted in pharmacodynamic decreases in IL17A, IL17F, and CRP levels, with GUS treatment restoring IL17A and IL17F levels to that of healthy controls by week 16. Consistent with being a component of ACR scores, CRP changes were significantly associated with ACR20 responses to both UST and GUS treatment. Weeks 4 and 16 changes in IL17F with GUS treatment were significantly associated with ACR20 response at week 24. Week 24 PASI75 response to GUS was significantly associated with week 4 changes in IL17A, with a similar trend observed at Week 16.
Conclusion: These results underscore the relevance of the IL23/Th17 pathway in PsA, with GUS treatment providing a stronger suppression of the pathway than UST treatment. The significant associations of changes in IL17A and IL17F levels with GUS treatment with PASI75 and ACR20 response, respectively, support the importance of the IL23/Th17 pathway for both skin and joint pathologies. The associations of reduction in CRP levels with both UST and GUS treatment also reinforce the role of acute phase inflammation in joint pathology.

REFERENCES:

[1] Deodhar A, Kavanaugh A, et al. Lancet. 2013; 382(9894):780-9.
[2] Deodhar A, Gottlieb AB, et al. Lancet. 2018; 391(10136):2213-2224.

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THU0053 APREMILAST INHIBITS THE TGFB1 MEDIATED TRANSITION OF CULTURED HUMAN SKIN FIBROBLASTS INTO PROFIBROTIC MYOFIBROBLASTS: IN VITRO STUDY

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Background: Fibroblast-to-myofibroblast transition and extracellular matrix (ECM) overproduction represent fundamental events in chronic inflammation, that characterise several diseases, including psoriasis (1,2). Transforming growth factor-β1 (TGFβ1), plays an important role as a profibrotic mediator (3).
Phosphodiesterases (PDE)4 act as proinflammatory enzymes via degradation of cAMP. PDE4 are expressed in normal skin fibroblasts (Fbs) and overexpressed in psoriatic skin Fbs and myofibroblasts (2).
Objectives: This study investigated how apremilast (an oral PDE4 inhibitor small molecule used for the treatment of psoriasis and psoriatic arthritis) might interfere with intracellular signalling for the fibroblast-to-myofibroblast transition and the synthesis of profibrotic ECM proteins induced by TGFβ1 in primary cultures of healthy human skin Fbs.
Methods: Human skin Fbs were isolated from 7 voluntary healthy subjects after signing informed consent and EC approval. The cultured Fbs were stimulated with TGFβ1 10ng/ml alone or in combination with apremilast 1μM and 10μM for 4, 16 and 24 hours. Other aliquots of Fbs were also previously stimulated with TGFβ1 for 4 hours and then treated with apremilast 1μM and 10μM for 4, 16 and 24 hours always in the presence of TGFβ1. Genes and related protein expression of α-smooth muscle actin (αSMA), type I collagen (COL-1) and fibronectin (FN) were investigated by qRT-PCR and Western blotting (WB). Smad proteins (the main signal transducers for receptors of TGFβ1) and extracellular signal–regulated kinases (ERKs), which are implicated in mediating TGFβ1 effects, were investigated by WB after 15, 30 and 60 minutes of apremilast treatment combined with TGFβ1 stimulation.
Results: Apremilast significantly downregulated the phosphorylation of Smad 2 and 3, at 15 minutes, and that of Erk1/2, after 30 minutes ($p<0.05$), both induced by TGFβ1 stimulation in cultured skin Fbs. Apremilast significantly downregulated the TGFβ1-induced increase in the gene expression of αSMA, COL-1 and FN at 4 and 16 hours, and the related protein synthesis at 24 hours ($p<0.05$) in cultured skin Fbs (treated in combination with TGFβ1). Similar effects were observed in differentiated myofibroblasts treated with apremilast.
Conclusion: Apremilast inhibited the fibroblast-to-myofibroblast transition *in vitro*, as well as the profibrotic activity induced by TGFβ1 in cultured skin Fbs by downregulating specific intracellular signalling pathways Smad 2/3 and Erk 1/2. These results might partially explain some of the downregulating effects on skin Fbs overactivity during treatment of skin lesions of psoriasis and that of psoriatic patients with apremilast.

REFERENCE:
[1] Clarke DL, et al. Fibrogenesis & Tissue Repair 2013, 6:20. 2. Schafer PH, et al. Cell Signal. 2016;28:753-63. 3. Carthy JM. J Cell Physiol.2018;233:98-106.

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THU0054 THE SYNOVIAL FLUID FROM RHEUMATOID ARTHRITIS PATIENTSCONTAINS SOLUBLE TAM RECEPTOR TYROSINE KINASES OF WHICH SOLUBLE TYRO3 AND ITS LIGAND GAS6 CORRELATES WITH THE PROINFLAMMATORY CYTOKINE LEVELS

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Background: We recently showed that the tyrosine-protein kinase receptors MER and AXL, both members of the TAM (including TYRO3) receptor family, play a protective role in mouse models of rheumatoid arthritis (RA) [1, 2]. In both humans and mice, TAM receptors can be proteolytically cleaved from the cell membrane and shed as a soluble (s) receptors. These sTAM receptors may act as decoy receptors, bind their ligands Growth Arrest-Specific 6 (GAS6) and Protein S (PROS1), and thereby inhibit the immunoregulatory and anti-inflammatory effect of TAM receptor activation, and prevent TAM receptor-mediated phagocytic clearance of dying cells.
Objectives: To determine the soluble TAM receptor levels in synovial fluids from RA and osteoarthritis (OA) patients and correlate this to the inflammatory process.
Methods: The level of sMER, sAXL, sTYRO3, GAS6, IL-8, TNFα and IL-1β was measured in synovial fluids of RA (n = 28) and OA patients (n = 12) by ELISA or multiplex array. Synovial explants were cultured for 24 hrs and the release of sMER and GAS6 was measured by ELISA. Human synovial explants of RA (n = 15) and osteoarthritis (OA) (n = 17) patients were immunostained for MER.
Results: Soluble MER and sTYRO3 were significantly enhanced in synovial fluids (P<0.0001 and P=0.0042) of RA patients as compared to OA patients. The sAXL and GAS6 levels in synovial fluid of RA and OA patients was equally high (P = 0.267 and P = 0.074). In RA patients, but not in OA patients, the synovial fluid levels of sTYRO3 and GAS6 (a ligand for all three TAM receptors) positively correlated with TNFα (r=0.555, r=0.477), IL-1β (r=0.597, r=0.481) and IL-8 (r=0.567, r=0.529). Soluble MER levels, however, did not correlated with local inflammatory markers. Although synovial explants from RA released more sMER into the culture media than explants from OA (P = 0.0045), the explants of both RA and OA patients contained comparable amounts of immunopositive MER cells.
Conclusion: We showed that synovial fluid sTYRO3 and GAS6 levels correlates with higher proinflammatory cytokine levels in RA but not in OA patients. This is in line with the recent observation done by Xu et al. [3], that circulating levels of sTYRO3, but not sMER or sAXL, correlates with disease activity and bone destruction in RA patients. In accordance to serum, the synovial sMER levels were significantly higher in RA - than in OA patients with sAXL levels comparable between both patient groups. Interestingly, only for sMER the synovial fluid levels were much higher than in serum suggesting local production as we confirmed in the synovial explants cultures. This illustrates that release of soluble TAM receptors is either the results of different processes (enzymatic shedding or alternative splicing isoforms) or reflects the different cell populations in the arthritic joint. We found that naïve macrophages express high MER and inducible AXL, while synovial fibroblast express high AXL and TYRO3. Further studies are warranted to determine if sMER levels impair the clearance of apoptotic cells in the arthritic joint as we have found in our mice studies. Our study shows that synovial sTYRO3 is a marker for joint inflammation and possibly a novel therapeutic target for RA.

REFERENCES:
[1] Waterborg, C.E., et al., *Protective role of the Mer Tyrosine Kinase via efferocytosis in rheumatoid arthritis Models*. Frontiers in immunology, 2018. 9.
[2] Waterborg, C.E., et al., *03.05 The tam receptors axl and mer play a protective role in a temporal and spatial manner in inflammatory arthritis*. 2017, BMJ Publishing Group Ltd.
[3] Xu, L., et al., *Soluble TAM receptor tyrosine kinases in rheumatoid arthritis: correlation with disease activity and bone destruction.* Clinical & Experimental Immunology, 2018. 192(1): p. 95-103.

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THU0055 TPL2 INHIBITION SUPPRESSES MEK-ERK INFLAMMATORY SIGNALING AND PROINFLAMMATORY CYTOKINE PRODUCTION IN PRIMARY HUMAN MONOCYTES

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Background: Tumor progression locus 2 (TPL2, also known as MAP3K8) is a mitogen-activated protein kinase kinase kinase and the primary regulator of ERK-mediated gene transcription downstream of multiple proinflammatory stimuli including bacterial products (eg, LPS and bacterial peptidoglycans), damage-associated molecular patterns (DAMPs), TNFα, and IL-1β.[1] Dysregulated signaling downstream of these inflammatory signals can drive uncontrolled immune cell activation and inflammation, which is associated with multiple chronic inflammatory and autoimmune diseases. As such, TPL2 inhibition represents a strategy to modulate inflammation in a variety of disease settings.
Objectives: We evaluated the effect of a highly selective TPL2 inhibitor on inflammatory signaling and cytokine production in LPS and TNFα-stimulated primary human monocytes.
Methods: Monocytes were precultured with a TPL2 inhibitor and stimulated with LPS or TNFα, and phosphosignaling and cytokine production were then evaluated at 30 minutes and 4 hours poststimulation. A431 cells (human epidermoid carcinoma cell line) were stimulated with TNFα or EGF and phospho–ERK was evaluated after 30 minutes.
Results: TPL2 inhibition selectively inhibited LPS and TNFα-stimulated phosphorylation of TPL2, MEK, and ERK, with little to no inhibition of phosphorylated p38, JNK, or p65 observed. TPL2 inhibition similarly inhibited both the RNA production and secretion of TNFα, IL-1β, IL-6, and IL-8 following LPS stimulation in primary human monocytes. To confirm TPL2 requirement for inflammatory, but not Ras-mediated (growth factor stimulated) ERK signaling, A431 cells were stimulated with either TNFα or EGF. Although TPL2 inhibition reduced TNFα-stimulated pERK, no effect on ERK activation downstream of EGF was observed.
Conclusion: This work demonstrates the selective effects of TPL2 inhibition on ERK-mediated signaling and proinflammatory cytokine gene transcription in primary human monocytes and highlights the potential for TPL2 inhibition to treat diseases associated with dysregulated inflammatory signaling and chronic inflammation.

REFERENCE:
[1] Gantke T, Sriskantharajah S, Ley S. Cell Res. 2011;21:131-145.

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THU0056 EFFECTS OF CX3CL1 INHIBITION ON MURINE BLEOMYCIN-INDUCED INTERSTITIAL PNEUMONIA

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Background: Pathological findings of interstitial pneumonia (IP) reveal the accumulation of inflammatory cells and proliferation of fibroblasts in lung tissue. Although a treatment has not yet been established for IP, particularly for IP with collagen diseases, chemokines may play a role in the pathogenesis of IP for inflammatory cell infiltration. We previously reported that chemokine (C-X3-C motif) ligand 1 (CX3CL1, also known as fractalkine) has potential as a therapeutic target for rheumatoid arthritis (RA).[1,2,3]Humanized anti-human CX3CL1 monoclonal antibody (mAb) is currently undergoing clinical trials for RA.[4]

Objectives: In the present study, we examined the therapeutic effects of CX3CL1 blockade in a murine model of IP.

Methods: Bleomycin (BLM)-induced IP was developed by the intratracheal administration of BLM to C57BL/6 mice. The murine lung was stained with hematoxylin and eosin, and the expression of CX3CL1 and CX3CR1, a receptor for CX3CL1, was analyzed by immunohistochemistry. Mice were treated with anti-CX3CL1 mAb for 2 weeks. Collagen eluted from the lung was quantified using the Sircol™ Collagen Assay. The expression of CX3CL1 and CX3CR1 by mouse lung fibroblasts (MLFs) was examined with quantitative RT-PCR and Western blotting, respectively. Cell movement was investigated using the scrape motility assay.

Results: The expression of CX3CL1 and CX3CR1 was upregulated in BLM-induced IP. The treatment with anti-CX3CL1 mAb did not significantly alter inflammatory cell infiltration. However, collagen in the lung was decreased by the treatment with anti-CX3CL1 mAb. Stimulation with CX3CL1 did not alter the *in vitro* production of collagen by MLFs, but significantly enhanced cell movement.

Conclusion: CX3CL1 may be involved in increasing collagen in IP and the cell movement of MLFs. The present results suggest that CX3CL1 plays an important role in fibrosis in IP.

REFERENCES:

[1] Nanki T, et al. Inhibition of fractalkine ameliorates murine collagen-induced arthritis. J Immunol. 2004;173(11):7010-6.
[2] Nanki T, et al. Migration of CX3CR1-positive T cells producing type 1 cytokines and cytotoxic molecules into the synovium of patients with rheumatoid arthritis. Arthritis Rheum. 2002;46(11):2878-83.
[3] Nanki T, et al. Fractalkine/CX3CL1 in rheumatoid arthritis. Mod Rheumatol. 2017 May;27(3):392-397.
[4] Tanaka Y, et al. Safety, pharmacokinetics, and efficacy of E6011, an anti-fractalkine monoclonal antibody, in a first-in-patient phase 1/2 study on rheumatoid arthritis. Modern rheumatology. 2018;28(1):58-65.

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THU0057 PLASMACYTOID DENDRITIC CELLS IN THE ENTHESIS: PHENOTYPING AND FUNCTION INVESTIGATION

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Background: Plasmacytoid dendritic cells (pDCs) play an important role in linking innate and adaptive immune responses and selectively express Toll-like receptor (TLR) 7 and TLR9 that sense RNA and DNA respectively thus regulating the secretion of type I interferons (IFN) and other inflammatory cytokines such as TNF [1]. pDCs have been directly implicated in psoriasis immunopathology and are activated following anti-viral vaccination, with vaccination also linked to psoriatic arthritis onset [2-3]. Inflammation of the enthesis (enthesitis) is a cardinal spondyloarthritis associated lesion so we hypothesized the presence of enthesis resident pDCs

Objectives: To investigate whether the human enthesis contains a resident pDC population and to compare the responses of TLR7/9 agonists on entheseal pDCs function relative to peripheral blood derived pDCs.

Methods: Normal interspinous process enthesis and matched peripheral blood (PB) were obtained from patients (n=11) undergoing spinal decompression or scolosis corrective surgery. Cells were isolated from perientheseal bone by mechanical digestion. Cells were stimulated with either TLR7 agonist (imiquimod) or TLR9 agonist (ODN-2216). Flow cytometry was used to phenotype pDCs, and intracellular staining used to measure IFNα and TNF. IFNα from supernatant was also measured by ELISA.

Results: pDCs were identified in the human enthesis with a typical phenotype (CD45+HLA-DR+CD123+CD303+CD11c-). By intracellular FACS, following ODN or imiquimod stimulation, IFNα and TNF was detected in entheseal pDCs and also PB. IFNα and TNF induction trended upwards in entheseal pDC when compared with unstimulated pDCs. IFNα was also detected by ELISA following ODN or imiquimod stimulation of entheseal derived pDCs.

Conclusion: The human enthesis contains a resident population of pDCs that produce IFNα and TNF following induction with relevant TLR agonists. For the first time, our findings provide a link between viral illness and vaccination and pivotal innate immune cell production of IFNα and TNF.

REFERENCES:

[1] Melissa Swiecki and Marco Colonna, *The multifaceted biology of plasmacytoid dendritic cells*. Nat Rev Immunol. 2015 Aug;15(8):471-85.
[2] Gunes AT, Fetil E, Akarsu S, et al., Possible Triggering Effect of Influenza Vaccination on Psoriasis. J Immunol Res. 2015;2015:258430.
[3] Nestle FO, Conrad C, Tun-Kyi A, et al., Plasmacytoid predendritic cells initiate psoriasis through interferon-alpha production. J Exp Med. 2005 Jul 4;202(1):135-43.

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THU0057B **TNF-ALPHA INDUCES NECROPTOSIS-LIKE DEATH OF MACROPHAGES AND PROMOTES EXTRACELLULAR RELEASE OF 14–3–3ETA**

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Background: 14-3-3η is an intracellular protein detected in the serum and synovial fluid of patients with rheumatoid arthritis (RA) [1]. While presence of 14-3-3η is both diagnostic for early and established RA [2] and prognostic for radiographic progression [3], the mechanism of 14-3-3η externalization in RA remains unclear.
Objectives: To clarify the mechanism of externalization of 14-3-3η into the extracellular space using human PBMC-derived macrophages (Mφ).
Methods: Distribution of 14-3-3η in synovial tissue of patients with RA or osteoarthritis (OA) was examined by immunohistochemistry; cellular morphology was studied by confocal microscopy and electron microscopy (EM). Mφ were stimulated with TNF-α, Diamide (induces ligand-independent TNFR signaling) or IL-6/sIL-6R. Western blotting was used to detect S-358-phosphorylated MLKL (a mediator of necroptosis) and presence of 14-3-3η in Mφ culture supernatants.
Results: Dense and widespread staining of 14-3-3η was detected in Mφ of RA, but not OA, synovial tissues. 14-3-3η and peptidylarginine deiminase 4 (PAD4) co-localized in $CD68^+$ cells (Mφ) from RA synovial tissue; 14-3-3η was not detected in $CD68^+$ cells from RA lung tissue or $CD4^+$ cells (T cells) from RA synovium. The outer space around the nucleus of healthy control Mφ treated with TNF-α or Diamide, but not IL-6/sIL-6R, demonstrated abnormal actin distribution by phalloidin staining and presence of cellular and organelle swelling by EM. Further, magnified images showed partial destruction of the cell membrane in TNF-α and Diamide-treated cells. Phosphorylation of MLKL was observed between 20 min and 24 h after stimulation of healthy control Mφ with TNF-α, with maximum signal at 8 h post-stimulation, but was not observed upon IL-6/sIL-6R stimulation at any time point. After 8 h of stimulation no 14-3-3η was detected in the culture supernatant of healthy control Mφ endogenously expressing 14-3-3η or Mφ stimulated with IL-6/sIL-6R, while a high concentration of 14-3-3η was detected in culture supernatants in Mφ treated with TNF-α or Diamide.
Conclusion: 14-3-3η protein was abundant in RA, but not OA, synovial tissues and co-localized with PAD4 in $CD68^+$ synovial Mφ; this close proximity to PAD4 may promote citrullination of 14-3-3η *in vivo*. Treatment of healthy control Mφ with TNF-α induced phosphorylation of MLKL and cell swelling and disintegration of the plasma membrane characteristic of necroptosis, correlated with the release of intracellular 14-3-3η protein into cellular supernatants. Our results shed light on mechanism of externalization of 14-3-3η and how it achieves elevated levels in RA synovial fluid.

REFERENCES:

[1] Kilani RT, et al. J Rheumatol 2007; 34:1650–7.
[2] Maksymowych W, et al. J Rheumatol 2014; 41:2104-13.
[3] Carrier N, et al. Arthritis Res Ther 2016; 18:50.

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Rheumatoid arthritis – prognosis, predictors and outcome

THU0058 **B CELL SYNOVITIS AND CLINICAL PHENOTYPES IN RHEUMATOID ARTHRITIS AT DIFFERENT DISEASE STAGES**

Felice Rivellese[1], Frances Humby[1], Serena Bugatti[2], Liliane Fossati-Jimack[1], Hasan Rizvi[3], Davide Lucchesi[1], Gloria Lliso Ribera[1], Alessandra Nerviani[1], Rebecca Hands[1], Giovanni Giorli[1], Barbara Frias[1], Edyta Jaworska[1], Katriona Goldmann[1], Myles Lewis[1], Antonio Manzo[2], Michele Bombardieri[1], Costantino Pitzalis[1]. *[1]Queen Mary University of London, Centre for Experimental Medicine and Rheumatology, London, United Kingdom*; *[2]University of Pavia, IRCCS Policlinico San Matteo Foundation, Pavia, Italy*; *[3]Barts Health NHS Trust, Department of Pathology, London, United Kingdom*

Background: The role of B cells in the pathogenesis of Rheumatoid Arthritis (RA) is well recognised and has been reinforced by the established efficacy of B cell depleting treatments. However, B cell infiltration in synovia is highly variable and their association with clinical disease activity has been inconsistently reported, with contradicting results possibly linked to the lack of standardization in quantitative and qualitative assessment of B cell synovitis. In particular, the presence of B cells in synovia has never been systematically assessed in large cohorts.
Objectives: To evaluate B cells and their association with clinical phenotypes in the synovia of patients with RA at various disease stages.
Methods: A total of 432 synovial biopsies from the following cohorts of RA patients were analysed: i. early (<1 year) treatment-naïve RA (n=165), ii. Synthetic Disease Modifying Anti-Rheumatic Drugs inadequate responders (sDMARDs-ir) (n=103), iii. TNF-inhibitors inadequate responders (TNFi-ir) (n=164). Haematoxylin and eosin staining was used for the assessment of synovitis according to a previously validated score (Krenn). Upon immunohistochemical staining for CD20, semi-quantitative (Sq) scoring (0-4) was used to classify patients into B cell rich ($\geq$ 2) and poor (< 2) and automated digital image analysis (DIA) to calculate the B cell area fraction. B cell expression markers, including CD20 mRNA counts and a composite B cell module, were obtained by RNA-sequencing from early RA synovial biopsies (n=91).
Results: Semi-quantitative synovial B cell scores positively correlated with the B cell area fraction obtained by DIA (Spearman r 0.93 in early RA and 0.88 in TNFi-ir, p<0.0001). Accordingly, B cell rich patients (Sq score $\geq$ 2) had a significantly higher B cell area fraction (p<0.0001). RNA-sequencing from 91 patients with early RA showed a positive correlation between the Sq B cell scores and CD20 mRNA counts and the B cell module (Spearman r=0.6 and 0.67, respectively, p<0.0001). Similarly, a positive correlation was found between the B cell area fraction obtained by DIA and CD20 mRNA counts and B cell module (r=0.67 and 0.69, respectively, p<0.0001) When comparing B cell presence in the three cohorts, B cell-rich synovitis was present in 35% of early RA, 36% of sDMARDs-ir and 47.1% of TNFi-ir (p=0.025 comparing early RA vs late-stage TNFi-ir patients). Finally, while B cell-rich patients showed significantly higher synovial inflammatory scores across all cohorts, higher disease activity (number of swollen joints, DAS28) and higher prevalence of autoantibody positivity (ACPA and RF) in B cell-rich patients were observed exclusively in the early RA cohort.
Conclusion: We here describe a robust and validated synovial B cell score that can potentially contribute to patient stratification in RA, as it helps identifying an enrichment of B cell synovitis in established disease, uncoupled from clinical disease activity.
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THU0059 INCIDENCE OF JOINT REPLACEMENT SURGERY AMONG BIOLOGICS AND NON-BIOLOGICS TREATED PATIENTS WITH RHEUMATOID ARTHRITIS: A PROPENSITY SCORE MATCHED COHORT STUDY FROM DENMARK

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Background: Biologics have improved several clinical, patient-reported and radiological outcomes in patients with rheumatoid arthritis (RA), but little is known about the potential impact on the need for joint replacement surgery.

Objectives: To investigate the incidence of joint replacement surgery among biologics treated compared with biologics naïve patients with RA.

Methods: A nationwide, register-based propensity score matched cohort study. RA patients registered between 2006 and 2016 in the DANBIO register with a disease duration ≤ 2 years were identified. Patients initiating their first treatment series with biologics were followed up to 10 years for a first joint replacement of the hip, knee, shoulder, elbow and finger/wrist. Biologics naïve patients were followed up for the same outcome from their first clinical visit registered in DANBIO. Following a 1:n propensity score matching, Cox-models were undertaken to calculate the hazard ratio (HR) for a first joint replacement surgery among biologics compared with non-biologics treated RA patients. Further, subgroup analyses based on within-strata propensity score matched patients were carried out. All information on surgical outcomes was obtained in the Danish National Patient Registry.

Results: In total, 1187 biologics treated were matched with 3666 non-biologics treated patients (See Table).

Abstract THU0059 – Table1. Baseline characteristics of biologics treated and biologics naïve patients with rheumatoid arthritis and a disease duration < 2 years registered in DANBIO between 2006 and 2016.

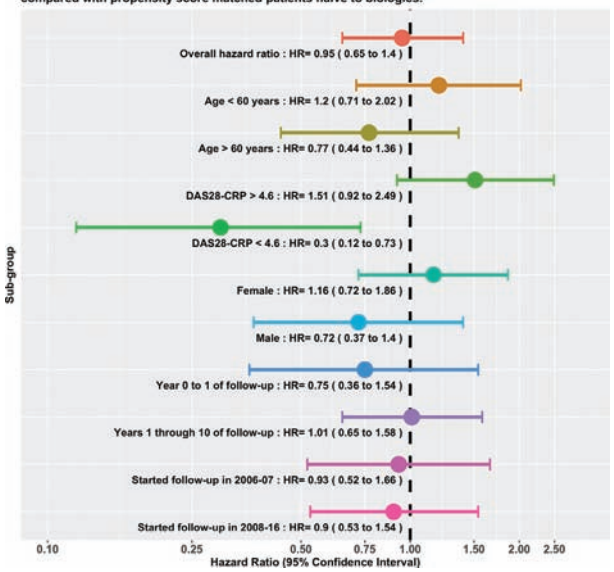
	Biologics treated	Biologics naive	SMD
N Total	1187	3666	
Female, n (%)	828 (70)	2546 (69)	0.01
Age at start of follow-up, mean (s.d)	53.8 (13.5)	54.1 (15.1)	0.02
Age at diagnosis, mean (s.d)	52.7 (13.5)	52.9 (15.1)	0.02
IgM-RF and/or ACPA positive at start of follow-up, n (%)	686 (58)	2042 (56)	0.04
DAS28-CRP	4.5 [3.6 to 5.4]	4.5 [3.4 to 5.4]	0.03
HAQ-DI	1.00 [0.50 to 1.62]	1.00 [0.50 to 1.62]	0.03
CRP mg/ml	9 [3 to 22]	9 [3 to 20]	0.02
VAS physician global	32 [18 to 49]	30 [16 to 50]	0.04
VAS pain	53 [31 to 73]	52 [30 to 74]	0.01
Methotrexate, n (%)	1044 (88)	3160 (86)	0.06
Glucocorticoid, n (%)	246 (21)	718 (20)	0.04
Chronic obstructive pulmonary disease, n (%)	168 (5)	57 (5)	0.01
Cardiovascular disease, n (%)	322 (9)	97 (8)	0.02
Hospitalised with infection in previous 5 years, n (%)	128 (4)	43 (4)	0.01

Abbreviations: SMD, absolute standardized mean difference; s.d., standard deviation; VAS, visual analogue scale. All values are median [interquartile range] unless otherwise stated.

During follow-up, 43 biologics-treated and 124 naive patients had a first joint replacement surgery corresponding to an overall HR of 0.95 (0.65 to 1.40) for biologics treated compared with naïve patients (Figure 1). Patients with a DAS28-CRP < 4.6 at start of follow-up (low and moderate disease activity)[1], biologics treated had a lower risk of joint replacements compared with biologics naïve patients.

Conclusion: In this nationwide Danish cohort study, there was no difference in the incidence of joint replacement surgery among newly diagnosed RA patients selected for treatment with biologics compared with patients naïve to biologics.

Figure 1. Overall and sub-group hazard ratios for a first joint replacement surgery among newly-diagnosed patients with rheumatoid arthritis and treated with biologics compared with propensity score matched patients naive to biologics.



Abstract THU0059 – Figure 1

References:

[1] Fleischmann, et al. DAS28-CRP and DAS28-ESR cut-offs for high disease activity in rheumatoid arthritis are not interchangeable. RMD Open 2017;3:2–6.

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THU0060 ELEVATED SYNOVIAL MUC1 EXPRESSION IS ASSOCIATED WITH JOINT DAMAGE AND ONE-YEAR RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: The tumor-like transformation of synovium, especially the lining layer, play a critical role in joint damage in rheumatoid arthritis (RA) by forming aggressive and invasive rheumatoid pannus, but the underlying mechanisms remains unknown. Mucin1(MUC1), an O-glycosylated protein participating in forming protective mucous barriers on epithelial surfaces and intracellular signaling, has been found aberrantly expressed in many cancers and implicated in tumor progression and metastasis. However, the expression of MUC1 in synovium and its role in RA is unclear.

Objectives: We aimed to investigate the expression of MUC1 in RA synovium and its correlation with joint destruction in RA patients.

Methods: Synovial tissue (ST) were sampled by Parker-Pearson needle biopsy from 67 RA patients who had completed one year follow-up from a prospective RA cohort [1]. ST from 13 patients with orthopedic arthropathies (Orth. A) with arthroplasty or arthroscopy were used as control. Expression of MUC1 in ST was assessed by immunohistochemistry (IHC). Radiographic assessments of hand/wrist at baseline and month 12 were performed with the Sharp/van der Heijde-modified sharp score. Radiographic joint damage (RJD) was defined as total modified Sharp score (mTSS) >10. Radiographic progression (RP) was defined as a change of mTSS more than 0.5 units.

Results: 1. Both nuclear and cytoplasmic MUC1 expression were observed in lining and sublining cells of synovium. The percentage of MUC1+ lining cells was significantly higher in RA (median 65.4%, IQR 53.6% 73.2%) than that in Orth. A (median 43.1%, IQR 3.4% 68.4%, P <0.05).

2. Thirty-five (52%) RA patients showed RJD at baseline and their MUC1expression in lining layer was significantly enhanced compared with RA patients without RJD (median 69.6%, IQR64.5% 76.8% vs. median 58.9%, IQR 39.8% 67.9%, P <0.01). Spearman's rank order correlation test showed significantly positive correlations between the percentage of MUC1+ lining cells with mTSS, joint space narrowing (JSN) subscore and joint erosion (JE) subscore at baseline (r =0.303~0.426, all P < 0.05).

3. Furthermore, twenty-two(33%) patients suffered from one-year RP and they showed significantly higher percentage of MUC1+ lining cells than non-progressive patients (median 71.2%, IQR 55.2% 75.2 vs. median 64.1%, IQR 55.2% 75.2%, r < 0.01). The percentage of MUC1+ lining cells was positively correlated with mTSS, JSN and JE subscores at month 12 (r =0.310 0.405, all P < 0.05). ROC curve analysis showed that the tradeoff value of MUC1+ lining cells for predicting one-year RP was 69% with sensitivity 72% and specificity 71% (AUC=0.661, 95% CI~0.516 0.805, P=0.034). Univariate logistic regression analysis showed that high MUC1+ lining cells was a significant predictor of one-year radiographic progression (OR: 5.893, 95%CI: 1.934 17.956, P=0.002).

Conclusion: Our data showed elevated MUC1expression in RA synovial lining cells was positively correlated with joint damage and predicted one-year radiographic progression, which imply that MUC1 might be involved in the pathogenesis of RA joint destruction.

REFERENCE:

[1] Chen Y, et al. Deleterious role of hepatitis B virus infection in therapeutic response among patients with rheumatoid arthritis in a clinical practice setting: a case-control study. Arthritis Research & Therapy. 2018, 20(1).

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THU0061 IN OVERWEIGHT SUBJECTS, SERUM ADIPONECTIN PREDICTS THE DEVELOPMENT OF RHEUMATOID ARTHRITIS INDEPENDENTLY OF OTHER ADIPOKINES

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Background: Adipokines, such as adiponectin, leptin, resistin and visfatin, are cytokines produced by the adipose tissue and involved in metabolism and inflammation[1]. Adiponectin is elevated in both serum and synovial fluid of subjects with rheumatoid arthritis (RA), suggesting a possible role of this adipokine in the pathogenesis of RA [2,3]. Circulating levels of leptin, resistin, and visfatin are also higher in subjects with RA compared to controls [2,4].

Objectives: Aim of this study was to determine if adiponectin, leptin, resistin, and visfatin predict the development of RA.

Methods: Two nested-case control studies were performed including pre-symptomatic participants of two cohorts from Sweden: the Swedish Obese Subjects (SOS) study and a cohort of individuals identified within the Medical Biobank of northern Sweden. The SOS is a clinical trial including 4047 subjects with obesity[6]. During a follow-up for up to 29 years, 92 subjects developed RA. Among those 92 subjects, 82 subjects with available serum at baseline were matched 1:5 with 410 subjects who did not develop RA during follow-up. Matching was based on baseline age, sex, body-mass index (BMI), bariatric surgery yes/no, year of inclusion, and smoking. A nested case-control study of 88 sex- and age-matched pairs was performed within the Medical Biobank of Northern Sweden using blood samples donated before the onset of the first RA symptoms. The pre-dating time before onset of symptoms of RA was 8.5±5.0 years[7].

Baseline serum levels of adiponectin, leptin, resistin, and visfatin were measured using the Quantikine ELISA kit from R&D Systems (Wiesbaden, Germany). Visfatin could not be measured in the Biobank cohort, due to lack of serum. Both binary logistic as well as conditional logistic regression analyses were used to determine if adipokines were elevated years before the onset of RA.

Results: In a multivariable analysis including adiponectin, leptin, resistin, visfatin performed in the SOS cohort, serum adiponectin was associated with a higher risk for RA independently of other adipokines (Odds ratio, OR, 1.1, 95% confidence interval, CI, 1.0-1.1, p value=0.01). Leptin, resistin and visfatin levels were not associated with the risk of RA.

In the Biobank cohort, no association between adipokines and risk for RA was detected. However, when stratifying the population according to BMI, in the subgroup having BMI>25 (n=109), adiponectin levels were associated with higher risk for RA (OR 1.2, 95% CI 1.0-1.36, p=0.03), independently of leptin and resistin levels. Virtually the same results were obtained in both the SOS and the Biobank cohorts when conditional logistic regression analysis was used.

Conclusion: Our results suggest that higher serum adiponectin levels predict the development of RA in subjects with overweight/obesity.

REFERENCES:

[1] Kwon H, Pessin JE. Adipokines mediate inflammation and insulin resistance. Front Endocrinol (Lausanne) 2013;4:71.

[2] Otero M, et al. Changes in plasma levels of fat-derived hormones adiponectin, leptin, resistin and visfatin in patients with rheumatoid arthritis. Ann Rheum Dis 2006;65:1198-201.

[3] Fantuzzi G. Adiponectin in inflammatory and immune-mediated diseases. Cytokine 2013;64:1-10.

[4] Huang Q, et al. Serum resistin levels in patients with rheumatoid arthritis and systemic lupus erythematosus: a meta-analysis. Clin Rheumatol 2015;34:1713-20.

[5] Sjöström L, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med 2007;357:741-52.

[6] Johansson L, et al. Antibodies directed against endogenous and exogenous citrullinated antigens pre-date the onset of rheumatoid arthritis. Arthritis Res Ther 2016;18:127.

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THU0062 THE DYSREGULATION OF NK CELLS AND NON-CLASSICAL AND CLASSICAL MONOCYTE SUBPOPULATIONS IN INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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Background: Antibodies against citrullinated proteins (ACPA) are present months to years before the clinical manifestation of rheumatoid arthritis (RA). ACPA+ individuals are at 8-10x higher risk of developing RA compared to seronegative individuals. EULAR characterised individuals with arthralgia suspicious for progression to RA based on their clinical features (clinically suspect arthralgia, CSA).

Objectives: The alteration of natural killer (NK) cells and monocyte subpopulations in patients with established RA has been previously described. We therefore aimed to study the lymphocyte and monocyte subpopulations in individuals in the preclinical phase of RA.

Methods: Our study included 49 individuals with arthralgia (mean age 45.97±11.95 years; 92% females) and 80 age and gender matched healthy controls (HC). Leukocytes from peripheral blood were analysed by flow cytometry. Lymphocyte subpopulations were defined as B (CD19

+CD3-), T (CD3+CD4+, CD3+CD8+) and NK (CD16/56+CD3-) cells. Monocytes were further classified to classical (CD14++CD16-), intermediate (CD14++CD16+/++) and non-classical (CD14-/+CD16++) subsets. Data were analysed using Mann Whitney test and expressed as median and interquartile range [IQR].

Results: Out of 49 individuals with arthralgia, 36 were ACPA+ and 28 met CSA definition (15 of them were ACPA+), with symptoms duration 21 months [IQR=53], CRP 3.18 mg/L [IQR=3.6], DAS28 score 2.28 [IQR=1.31]. As per definition, there was no evidence of clinical arthritis on examination of 66 joints at baseline. Ten individuals developed RA within a median of 4 months of follow up.

Individuals with arthralgia had higher%CD3+ T cells (78.10 [8.10] vs. 75.04 [9.26], p=0.001) and lower%NK (11.20 [7.20] vs. 12.89 [6.62], p≤0.001) as well as absolute count of NK cells (0.18 [0.13] vs. 0.24 [0.17], p≤0.001) compared to HC. Similarly, higher%CD3+ T cells (77.95 [8.65] vs. 75.04 [9.26], p=0.003) and lower%NK (10.85 [7.81] vs. 12.89 [6.62], p=0.003) and absolute count of NK cells (0.20 [0.14] vs. 0.24 [0.17], p=0.003) was confirmed in a subgroup of ACPA+ individuals compared to HC. Moreover, individuals who developed RA during follow up, had a lower baseline absolute count of NK cells (0.14 [0.10] vs. 0.19 [0.15], p=0.039).

Analysis of monocyte subpopulations revealed higher count of non-classical (5.99 [4.87] vs. 4.03; IQR [3.28], p=0.022) and intermediate (5.82 [2.93] vs. 4.31 [2.08], p=0.034) monocytes and lower count of classical monocytes (86.06 [7.69] vs. 89.41 [3.52], p=0.005) in individuals with arthralgia compared to HC. Specifically, also ACPA+ patients had higher count of non-classical (6.07 [5.84 vs. 4.03 [3.28, p=0.020) and intermediate (5.86 [3.05] vs. 4.31 [2.08], p=0.036) and lower count of classical (85.43 [8.34] vs. 89.41 [3.59], p=0.005) monocytes compared to HC. There was no difference in% or absolute count of lymphocytes and monocytes subpopulations at the time of manifestation of RA and between ACPA+ and ACPA- individuals.

Conclusion: We show lower numbers of NK cells and classical monocytes and expansion of intermediate and non-classical monocytes in individuals in the preclinical phase of RA, especially in ACPA+ individuals. Such disproportion or pro-inflammatory potential of these cells was previously shown in the pathogenesis of established RA. We hypothesize that the dysregulation observed in at-risk individuals may be a prognostic marker and a predisposition leading to further development of RA.

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THU0063 PRE-MRNA SPLICING ALTERATIONS IN FOLYLPOLYGLUTAMATE SYNTHETASE IN BLOOD CELLS OF EARLY RHEUMATOID ARTHRITIS PATIENTS ARE ASSOCIATED WITH UNRESPONSIVENESS TO METHOTREXATE

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Background: Low-dose methotrexate (MTX) serves as the first-line treatment for rheumatoid arthritis (RA). Conversely, for hematological malignancies, high-dose MTX treatment is indicated in combination with folinic acid/leucovorin to prevent untoward toxicity. For both disease modalities, efficient pharmacological response critically depends on the retention and accumulation of intracellular MTX. The latter process is mediated by the enzyme folylpolyglutamate synthetase (FPGS) through MTX conversion into MTX-polyglutamates (MTX-PG). As such, decreased FPGS activity has been recognized as a mode of MTX resistance, but the underlying molecular mechanism has not yet been pinpointed [1,2]. Recently, aberrant pre-mRNA splicing of FPGS in acute lymphoblastic leukemia cells was associated with reduced FPGS activity, decreased MTX-PG accumulation and lower overall survival. Specifically, a partial retention of FPGS intron 8 (8PR) was identified as a prominent splice variant causing FPGS dysfunction [3].

Objectives: To investigate whether the expression of the FPGS pre-mRNA variant partial retention of intron 8 is associated with MTX unresponsiveness in RA patients over 3-6 months of MTX therapy.

Methods: Patients were enrolled from the COBRA-light trial comprising MTX treatment [4]. After informed consent, blood was obtained from 38 patients in either the COBRA (n=15) or the COBRA-light (n=21) treatment arm [4] and collected in Paxgene tubes for RNA isolation. Two patients were excluded due to insufficient sample quality. Quantitative PCR techniques were used to assess the ratios of FPGS 8PR over wild type FPGS (8WT) expression in whole blood RNA. Remission was defined as a DAS44 < 1.6.

Results: Baseline ratios of 8PR/8WT were associated with a decline in DAS44 at T3 (p=0.001) and T6 (p=0.13) in the COBRA-light patients. T3 ratios were also associated with DAS44 at T6 (p=0.001) and ΔDAS44 at T6 (p=0.26). Logistic regression analysis showed that in COBRA-light patients baseline ratios of 8PR/8WT were associated (p=0.05) with the probability of T3 remission but not T6 remission. T3 ratios of 8PR/8WT in COBRA-light patients were similarly associated with T6 remission but not with T3 remission. COBRA patients also showed a significant association between baseline 8PR/8WT ratios and DAS44 at T6 (p=0.04) while T3 ratios of 8WT/8PR were significantly associated with DAS44 at T3 (p=0.03) and T6 (p=0.05). However, analysis of COBRA patients showed no significant associations between baseline 8PR/8WT ratios and T3/T6 remission, nor associations between T3 ratios and T3/T6 remission.

Conclusion: These results demonstrate that a higher expression of an intron 8 retention of FPGS mRNA is associated with a higher DAS44 at T3 and T6 in COBRA-light patients, and at T6 for COBRA patients. Moreover, in COBRA-light patients, baseline expression of 8WT/8PR is significantly associated with remission at T3 or T6. This study is the first to show the impact of FPGS pre-mRNA splicing alterations in relation to unresponsiveness to MTX treatment in RA.

REFERENCE:

[1] PM Brown et al, Nat Rev Rheumatol. 2016;12:731-742. [2] S Raz et al, Drug Resist Updat. 2016;28:43-64. [3] A Wojtuszkiewicz et al, Haematologica. 2016;101:e291-294. [4] D den Uyl et al, Ann Rheum Dis 2014;73:1071–1078.

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THU0064 COMPARISON OF MORTALITY IN RHEUMATOID ARTHRITIS AND DIABETES – THE HUNT POPULATION-BASED STUDY

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Background: Patients with rheumatoid arthritis (RA) have higher mortality rates than the general population, primarily from cardiovascular disease (CVD). Diabetes is an acknowledged risk factor for early death, mainly due to CVD. The reported risk for CVD is increased for both patients with RA and diabetes, however the effect of diabetes appears to be greater than that of RA (1).

Objectives: To assess whether the increase in all-cause mortality rates in patients with RA and patients with diabetes are similar, compared to the general population.

Methods: Data were obtained from the 2nd and 3rd survey of the population-based Nord Trøndelag Health Study (HUNT) and the Norwegian National Cause of Death Registry. The RA diagnoses have previously been validated (2). The definition of diabetes was self-reported diabetes, self-reported use of antidiabetica, or non-fasting blood glucose level >11.1 mmol/L. The participants were followed from their participation in HUNT to death or to 31.12.2014, whichever came first. Participants with other types of inflammatory arthritis or missing data for any of the variables in

the model were excluded. Furthermore, the patients with both RA and diabetes were not included in the analysis (n=33). Participants with neither RA nor diabetes were defined as controls.

RA patients, diabetes patients and controls were compared using Cox proportional hazard regression modelling, with age as the time scale. The model was adjusted for sex, smoking status, previous CVD, body mass index (BMI), hypertension, total cholesterol and creatinine. To obtain proportional hazards, an interaction term with age ≤75 years vs >75 years was included for diabetes, smoking and previous CVD. The effects of the groups were compared using overlap of confidence intervals.

Results: **Table 1**. Participant characteristics

	RA N=387	Diabetes N=2,898	Controls N=63,903
Female sex, n (%)	261 (67)	1,369 (47)	33,781 (53)
Age (yrs), median (IQR)	58 (49-68)	63 (51-73)	46 (34-60)
Never smoker, n (%)	132 (34)	1,263 (44)	29,426 (46)
Former smoker, n (%)	129 (33)	682 (23)	19,010 (30)
Current smoker, n (%)	126 (33)	953 (33)	15,467 (24)
Previous CVD, n (%)	41 (11)	594 (20)	4,094 (6)
BMI (kg/m²), median (IQR)	26.0 (23.7-29.1)	28.7 (25.9-32.0)	25.7 (23.4-28.4)
Hypertension, n (%)	199 (51)	2,098 (72)	25,333 (40)
Total cholesterol (mmol/l), median (IQR)	6.0 (5.3-6.8)	6.0 (5.1-6.9)	5.7 (4.9-6.5)
Creatinine (µmol/l), median (IQR)	84 (77, 92)	89 (80, 99)	85 (77, 94)
RA duration (yrs), median (IQR)	6 (3-9)		
Seropositive RA, n (%)	277 (72)		
Diabetes duration (yrs), median (IQR)		5 (2-11)	
Observation time (yrs), median (IQR)	18 (13-19)	17 (8-19)	18 (13-19)

There were 123 (32%) deaths in the RA group, 1280 (44%) deaths in the diabetes groups and 11,641 (18%) deaths in the control group. The hazard ratio (HR) for RA was 1.24 (95% confidence interval: CI 1.02-1.46, p-value 0.013). The HR for diabetes was 1.82 (CI 1.60-2.05, p-value <0.001) for those aged ≤75 years and 1.48 (CI 1.39-1.58, p-value 0.004) for those aged >75 years. RA patients had a significantly lower HR compared to diabetes patients for age ≤75 years, but not for age >75 years.

Conclusion: Patients with RA or diabetes had significantly higher mortality rates than controls, with larger HR for diabetes than for RA. The HR for RA was significantly lower than for diabetes for patients ≤75 years, but not for patients >75 years. This may be due to survival bias in diabetes patients >75 years.

REFERENCES:

1 Curtis, J. R. et al., Is Rheumatoid Arthritis a Cardiovascular Risk-Equivalent to Diabetes Mellitus? Arthritis Care Res, 2018. 70(11): p.1694-1699

2 Videm, V, et al., Self-reported Diagnosis of Rheumatoid Arthritis or Ankylosing Spondylitis has Low Accuracy: Data from the Nord-Trondelag Health Study. J Reumatol, 2017. 44(8):p.1134-1141

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THU0065 VALIDATION OF THE ADJUSTED MULTI-BIOMARKER DISEASE ACTIVITY SCORE FOR PREDICTING RISK OF RADIOGRAPHIC PROGRESSION FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The multi-biomarker disease activity (MBDA) test has been adjusted to account for the effects of age, sex, and leptin (a surrogate for adiposity) in patients with rheumatoid arthritis (RA).[1] Using data from two cohorts (OPERA study and BRASS registry), this adjusted MBDA score was shown to be the best individual disease activity measure for predicting radiographic progression, and to provide significant additional information to DAS28-CRP in predicting radiographic progression.

Objectives: To validate the association between the adjusted MBDA score and radiographic progression in two additional cohorts, and to evaluate the MBDA score for predicting risk of radiographic progression in four cohorts combined.

Methods: Four cohorts with requisite data were identified: BRASS registry (N=424), OPERA study (N=164), SWEFOT study (N=235), and Leiden registry (N=163). For the SWEFOT and Leiden cohorts, association of disease activity measures and other factors with radiographic progression (change per year in total Sharp score [TSS]), was evaluated using linear regression. These variables included the adjusted MBDA score, seropositivity (RF and/or ACPA positive), DAS28-CRP, SDAI, CDAI, CRP, baseline total TSS, age, and sex, as available for each cohort. Estimates of risk for radiographic progression (change in TSS >5) as a function of the adjusted MBDA score were calculated using logistic regression in separate and pooled analyses.

Results: Among the tested measures of disease activity, the leptin-adjusted MBDA score was the most statistically significant univariate predicator of radiographic progression in the SWEFOT (P<0.0001) and Leiden (P<0.00001) cohorts, followed by CRP (p<0.01, in each) (Table). No significant predictive ability was observed for DAS28-CRP, SDAI or CDAI in SWEFOT. DAS28-CRP was a weak predictor in the Leiden cohort (P<0.05), (SDAI, CDAI unavailable). Among non-disease activity variables, baseline TSS and seropositivity were statistically significant predictors, to varying degrees. Neither age nor sex was significant (Table). When DAS28-CRP and the adjusted MBDA score were covariates in the same regression model in the Leiden cohort, DAS28-CRP was not a significant predictor, whereas the adjusted MBDA score remained significant (p=0.000054). When the SWEFOT, Leiden, OPERA and BRASS cohorts were combined (N=986), the adjusted MBDA score remained a significant predictor of radiographic progression, enabling the creation of a risk curve for radiographic progression relative to the continuous adjusted MBDA score.

Conclusion: In two population-based observational cohorts, the adjusted MBDA score was validated and shown to be a more significant predictor of radiographic progression than conventional measures of RA disease activity. Four cohorts were combined to predict risk of radiographic progression using the continuous adjusted MBDA score for the first time.

Table: Univariate linear regression of radiographic progression in the SWEFOT and Leiden cohorts.

	SWEFOT			Leiden		
Variable	N	Coefficient (95% CI)	p-value	N	Coefficient (95% CI)	p-value
MBDA score	235	0.11 (0.057, 0.15)	0.000026	163	0.12 (0.069, 0.16)	0.000002
log(CRP + 1)	235	1.1 (0.35, 1.9)	0.0046	156	1.0 (0.28, 1.8)	0.0076
Seropositivity	181/235	2.7 (0.87, 4.5)	0.004	118/162	1.6 (0.064, 3.2)	0.041
Baseline TSS	235	0.11 (0.012, 0.20)	0.028	163	0.042 (0.024, 0.059)	0.000004
DAS28-CRP	235	0.57 (-0.22, 1.4)	0.16	156	0.67 (0.13, 1.2)	0.016
SDAI	233	0.038 (-0.026, 0.10)	0.24	n/a	n/a	n/a
Male sex	66/235	-0.80 (-2.5, 0.94)	0.37	54/163	-0.36 (-1.9, 1.1)	0.64
CDAI	233	0.016 (-0.058, 0.90)	0.67	n/a	n/a	n/a
Age	235	-0.0094 (-0.067, 0.048)	0.74	163	-0.020 (-0.072, 0.033)	0.46

n/a: not applicable because data needed to compute that variable were not available.

Abstract THU0059 – Table 1

REFERENCE:

[1] Curtis JR, Flake IIDD, Weinblatt ME, et al. Adjustment of the multi-biomarker disease activity score to account for age, sex and adiposity in patients with rheumatoid arthritis. Rheumatology (Oxford). 2018:key367-key367.

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Samsung, Scipher, Set Point, Nancy Shadick Grant/research support from: Bristol-Myers Squibb, Sanofi/Regeneron, Crescendo Biosciences, Mallinckrodt, Amgen, Consultant for: Consulting work for Bristol-Myers Squibb for under $10,000., Cecilie Heegaard Brahe Grant/research support from: Unrestricted grant: Novartis, Mikkel Østergaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Merete L. Hetland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Bioepis, Saedis Saevarsdottir Employee of: Part-time employee at deCODE Genetics/Amgen Inc, working on genetic research unrelated to this project., Megan Horton Employee of: Myriad Genetics, Inc., Brent Mabey Employee of: Myriad Genetics, Inc., Darl Flake Shareholder of: Myriad Genetics, Inc., Employee of: Myriad Genetics, Inc., Eric H. Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience, Inc., Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringher, Takeda, Zydus, Epirus, Eli Lilly

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THU0066

IN EARLY RHEUMATOID ARTHRITIS ANTI-CITRULLINATED PEPTIDE ANTIBODIES ASSOCIATE WITH LOWER NUMBER OF AFFECTED JOINTS, AND IGM RHEUMATOID FACTOR WITH SYSTEMIC INFLAMMATION IN AN ANTI-CITRULLINE DEPENDENT MANNER

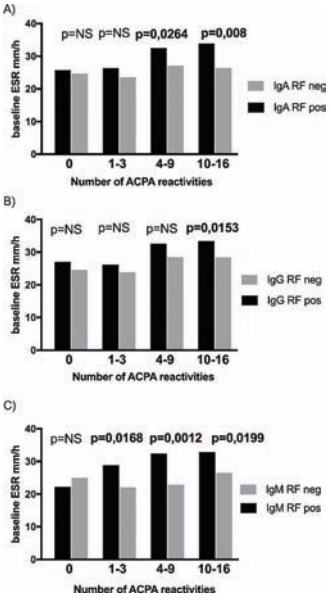
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Background: Recent studies have shown divergent associations between rheumatoid arthritis (RA)-associated autoantibodies and RA onset phenotype. Whereas some studies report more inflammation in seronegative patients [1, 2], others report that rheumatoid factor (RF) associates with high baseline disease activity [3].

Objectives: To define how individual RA-associated autoantibodies associate with individual disease activity score (DAS28, DAS28CRP) components at the time of RA diagnosis.

Methods: Sixteen individual ACPA reactivities, anti-CCP2, IgA-, IgG- and IgM-RF were analyzed centrally in baseline sera from 1600 RA patients classified according to the 1987 ACR criteria. All antibody cut-offs were determined as the 98th percentile among controls. The results were related to CRP, ESR, number of swollen and tender joints, DAS28, DAS28CRP, global disease activity (visual analogue scale), and health assessment questionnaire obtained at baseline.

Results: Individually, anti-CCP2, IgA RF and IgM RF associated with low counts of swollen and tender joints, with strongest association to anti-CCP2, and with high ESR. The association to low joint counts was stronger to number of individual ACPA reactivities than to anti-CCP2 levels (table). In multiple regression adjusted for age, sex and inclusion year, ACPA number associated strictly with low joint counts whereas IgM RF level associated with increased inflammatory markers, especially ESR (table). Also among IgM RF negative patients, occurrence of ACPA associated with low swollen and tender joint counts. Contrary, among ACPA negative patients, IgM showed no association to elevated ESR. The effect of RF on ESR increased with the number of individual ACPA reactivities present, most prominently for IgM RF (figure).



Abstract THU0066 – Figure 1

Conclusion: In early RA, ACPA associate with low counts of affected joints and IgM RF associates with elevated ESR in an ACPA-dependent manner. The latter finding relates to in vitro studies showing enhanced inflammatory effect of ACPA immune complexes with addition of RF[4, 5]. Future RA studies relating autoantibodies to disease activity may benefit from evaluating the impact of individual antibodies as well as distinct DAS components separately.

REFERENCES:

[1] Barra L, et al. J Rheumatol 2014;41:2361.
[2] Nordberg LB, et al. Ann Rheum Dis 2017;76:341.
[3] Aletaha D, et al. Arthritis Res Ther 2015;17:229.
[4] Laurent L, et al. Ann Rheum Dis 2015;74:1425.
[5] Sokolove J, et al. *Arthritis Rheumatol* 2014;66:813.

	IgA RF	IgG RF	IgM RF	ACPA
N (%) antibody positive	692 (43.2)	529 (33.1)	916 (57.2)	1020 (63.8)
Multiple regression:				
CRP P value (β)	0.6914 (0.011)	0.3162 (-0.026)	**0.0106** (0.071)	0.6889 (0.011)
ESR P value (β)	**0.0215** (0.062)	0.1237 (0.039)	**<0.0001** (0.108)	**0.0380 (**0.057)
SJC P value (β)	0.6175 (0.013)	0.2110 (-0.032)	0.0645 (0.051)	**<0.0001** (-0.122)
TJC P value (β)	0.6168 (0.014)	0.4120 (-0.021)	0.8712 (0.005)	**0.0007** (-0.094)

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THU0067

THREE-MONTH RADIOLOGICAL CHANGES IN WRIST JOINT MEASURED BY MRI AND HR-PQCT CAN PREDICT 12-MONTH CHANGES IN EROSION AND FUNCTIONAL OUTCOMES AFTER MTX AND ANTI-TNF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: A MULTI-MODALITY IMAGING STUDY

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Background: Magnetic resonance imaging (MRI) provides noninvasive methods to quantify joint inflammation and early cartilage degeneration in monitoring rheumatoid arthritis (RA) progression[1]. High-resolution peripheral quantitative computed tomography (HR-pQCT) provides reliable evaluation of bone erosion volumes[2].

Objectives: To investigate if changes in MR measures from baseline to 3-month (3M) can predict changes in erosion volumes, clinical and functional assessment from baseline to 12-month (12M) in RA patients receiving methotrexate (MTX) and anti-tumor necrosis factor alpha (Anti-TNFα) therapy using MRI and HR-pQCT.

Table 1. Longitudinal changes of MRI and HR-pQCT data, clinical and functional scores

	Low disease activity (N=9)			High disease activity (N=8)		
	BL	3M	12M	BL	3M	12M
SYN (cm^3)	30.6±16.4	**33.2±15.8***	38.5±18.2	66.4±22.6	**46.8±17.1***	58.6±34.4
BMEL (cm^3)	1.8±1.2	2.5±2.0	1.9±1.8	5.1±3.8	**3.2±2.4***	3.4±1.8
T1ρ (ms)	37.8±3.0	39.2±4.6	37.8±3.0	38.0±3.4	36.5±3.0	38.2±2.1
Bone Erosion (mm^3)	15.4±25.1	**17.2±27.7***	**17.3±27.3***	33.5±88.7	32.3±86.0	30.3±83.2
DAS-CRP	1.8±0.6	**2.4±0.8***	2.3±1.3	5.4±1.0	**3.4±1.5***	**3.8±0.9***
HAQ	0.5±0.7	0.6±0.8	0.5±0.8	1.4±0.8	**0.7±07***	**0.9±0.8***
MHQ	80.2±20.3	81.5±23.9	82.9±20.8	43.8±16.3	**65.5±19.7***	**66.5±21.1***

Data presented as mean ± standard deviation, *: P<0.05 (vs BL)

Abstract THU0067 –Table 1

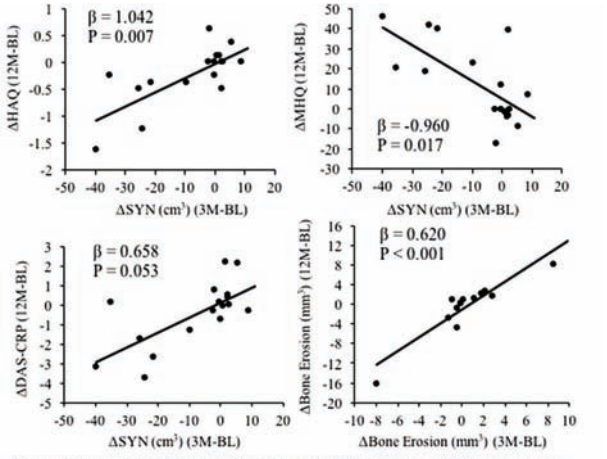


Figure 1. Associations between 3M change in SYN volume and 12M changes in DAS-CRP, HAQ, MHQ, and 3M and 12M changes in bone erosion volumes evaluated by linear regression models after adjusting for age, gender, disease duration and therapy (Anti-TNFα added or not).

Abstract THU0067– Figure 1

Methods: Seventeen RA patients with MTX treatment were recruited into either a low disease activity score (DAS) group (n=9, DAS28≤3.2) or high DAS group (n=8, DAS28>3.2). The low DAS group received MTX treatment only, while the high DAS group received additional Anti-TNFα treatment to MTX immediately after baseline visit (BL). Volumes of synovitis (SYN), bone marrow edema-like lesions (BMEL) and cartilage T1ρ values in wrist joint by MRI, bone erosion volumes in wrist joint by HR-pQCT, DAS28-CRP, Health Assessment Questionnaire (HAQ), and Michigan Hand Outcome Questionnaire (MHQ) were assessed at BL, 3M and 12M in all patients. Longitudinal changes were evaluated using paired t-test. Linear regression models were used to evaluate whether changes in imaging measure changes from BL to 3M predict changes in erosion volumes and patient outcomes (DAS28-CRP, HAQ, MHQ) from BL to 12M, after adjusting for age, gender, disease duration and therapy (Anti-TNFα added or not).

Results: Anti-TNFα therapy in the high DAS group resulted in significant decreases of SYN, BMEL at 3M and DAS28-CRP, HAQ and MHQ at 3M and 12M from BL (Table.1). The low DAS group in contrast, displayed significant increases in SYN and DAS-CRP at 3M and bone erosion volume at 3M and 12M from BL despite low disease activity (Table.1). Changes in SYN, not BMEL, T1ρ or bone erosion, from BL to 3M were significantly correlated with changes in HAQ and MHQ from BL to 12M ($P < 0.05$), and with changes in DAS-CRP from BL to12 M with marginal significance (P=0.053) (Figure 1). Changes in erosion volumes from BL to 3M were significantly correlated with changes from BL to 12M (Figure 1).

Conclusion: Despite the low disease activity, patients on MTX only showed significantly increased erosion volumes as measured by HR-pQCT at 3M and 12M; on the other hand, patients with MTX+Anti-TNFα treatment showed decreased erosion volumes at 3M and 12M, implying erosion repair. In this study, changes in erosion (but not other MR measures including synovitis and bone marrow edema) within the first 3M predicted changes in erosion at 12M. On the other hand, changes in synovitis volumes predicted patient functional outcomes at 12M. These results suggest that multimodality quantitative imaging with MRI and HR-pQCT provides powerful tools for evaluating early changes and predicting disease progression and therapy response after treatment in RA. Large scale studies with larger sample size are warrant to confirm the observations.

REFERENCES:

[1] Shimizu, et al. ACR (2017)
[2] Shimizu, et al. Arthritis Research & Therapy (2017)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.1986

THU0068

ANTI-CARBAMYLATED ANTIBODIES ARE ASSOCIATED WITH TOBACCO AND POOR OUTCOMES IN RHEUMATOID ARTHRITIS

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Background: Anti-carbamylated protein antibodies (Anti-CarP) represent a novel autoantibody family present in sera of patients with rheumatoid arthritis (RA) with high specificity.

Objectives: To analyse the prevalence of Anti-CarP in an established RA cohort and evaluate their association with the presence of other autoantibodies and disease activity and severity.

Methods: Cross-sectional study. Presence of Anti-CarP was analyzed in a cohort of patients with established RA (n: 158) by a home-made ELISA test using fetal calf serum. We investigated the demographic, radiological and current and at disease onset clinical features. Rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) status were also assessed.

Results: Anti-CarP were positive in 46.2% of the patients in our cohort and in 15.1%, 19.2% and 9.1% of the patients negative for ACPA, RF and both respectively. Demographic and clinical features are shown in table 1. The mean titer of ACPA (1361±1054 U/mL vs. 918 ± 1092 U/mL) and RF (258 ± 255 AU vs. 174 ± 205 AU) were significantly higher in Anti-CarP positive patients. No difference in symptoms at RA onset was observed. Current (24.7% vs. 11.8%) and previous (54.8% vs. 37.6%) smoking consumption were significantly associated with Anti-CarP antibodies. Anti-CarP positive patients presented a higher CRP values (1.0±1.6 mg/dL vs. 0.5 ±0.8 mg/dL), swollen joint count (1.3±2.2 vs 0.7 ±1.8) and patient global health assessment VAS (34.8 ±21.5 mm vs. 26.4 ±17.1 mm); although no between-group differences in disease activity (DAS28, CDAI, SDAI and RAPID3) or demographic features were observed. Anti-CarP positive patients presented significant higher scores in Larsen index (23.6 ± 15.7 vs. 15.7 ± 12.6) and disability (HAQ-DI >1) (23.3% vs. 8.3%).

Conclusion: Anti-CarP were present in approximately half of the RA cohort and were also detected in seronegative (RF and/or ACPA)

patients. In our cohort, patients with Anti-CarP antibodies presented higher tobacco consumption and poorer disease outcomes.

Table 1. Demographic and Clinical Features According to Anti-CarP Status

	Anti-CarP positive n: 73	Anti-CarP negative n: 85
Female	52 (71.2%)	71 (83.5%)
Mean age at diagnosis (SD)	53.6 (±11.9)	53.8 (±14.4)
Mean age at inclusion (SD)	58.7 (±11.9)	58.9 (±14.1)
Extra-articular manifestations	21 (28.8%)	15 (17.6%)
Disease duration (SD)	5.1 (±2.7)	5.0 (±2.7)
Smoking history	40 (54.8%)	32 (37.6%) *
• Previous and/or current	18 (24.7%)	10 (11.8%) *
• Current		
RA family history	12 (16.4%)	10(11.8%)
BMI	27.5 (±4.5)	27.1 (±5)
Disease presentation at initiation (%)	15 (20.5%)	14 (16.5%)
• Palindromic rheumatism	7 (9.6%)	6 (7.1%)
• Inflammatory arthralgia	4 (5.5%)	1 (1.2%)
• Pseudopolymyalgia	47 (64.4%)	64 (75.3%)
• Polyarticular arthritis		
Mean DAS28 (SD):	3.0 (±1.3)	2.8 (±1.2)
• Remission/Low	65.8%	68.2%
Mean DAS28 PCR (SD);	2.7 (±1.2)	2.4 (±1.1)
• Remission/Low	72.6%	80.0%
Mean CDAI (SD);	9.2 (±8.2)	7.2 (±6.5)
• Remission/Low	71.2%	80.0%
Mean SDAI (SD);	10.2 (±8.6)	7.8 (±6.9)
• Remission/Low	68.5%	77.6%
Mean RAPID3 (SD):	10.2 (±8.6)	7.8 (±6.9)
• Remission/Low	47.2%	48.2%
Mean HAQ (SD)	0.45 (±0.52)	0.29 (±0.39)
Poor HAQ (>1)	17 (23.3%)	7 (8.3%) **
Pain Analogue Scale mm (SD)	27.6 (±29.8)	20.6 (±22.7)
Treatment:	44 (61.1%)	49 (57.6%)
• Glucocorticoids	63 (86.3%)	71 (83.5%)
• cDMARDs	48 (65.8%)	56 (65.9%)
• MTX	7 (9.6%)	12 (14.1%)
• HCQ	14 (19.2%)	14 (16.5%)
• LEF	17 (23.3%)	32 (24.8%)
• bDMARDs		
Erosive disease	37 (50.7%)	46 (54.8%)
Modified Larsen Score	23.6 (±15.7)	15.7 (±12.6) **

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THU0069 RHEUMATOID CACHEXIA ASSESSED BY BODY COMPOSITION IS ASSOCIATED WITH WORSE DISEASE IN RHEUMATOID ARTHRITIS PATIENTS WITH NORMAL BODY MASS INDEX

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Background: Abnormal body composition (BC) has been reported in rheumatoid arthritis (RA) patients with normal body mass index (BMI). Rheumatoid cachexia (RC) was found in RA patients with a decrease in muscle mass and an increase or limited change in fat mass, resulting in no or limited changes in BMI. However, there is no consensus on the clinical criteria for its diagnosis, and the clinical significance of RC has not been well known until now.

Objectives: To investigate the characteristics of BC in RA patients with normal BMI and the association between RC and disease characteristics.

Methods: Consecutive RA patients were recruited and clinical data including disease activity, function and radiographic assessment were collected. BC was assessed by bioelectric impedance analysis. RC was defined as those with concurrent overfat (body fat percentage $\geq$25% for men and $\geq$35% for women) and myopenia (appendicular skeletal muscle mass index $\leq$7.0 kg/m^2 in men and $\leq$5.7 kg/m^2 in women) in this study. Multivariate logistic regression analysis was performed to identify the association between disease characteristics and RC in RA patients with normal BMI, following the step-forward selection rule that variables were included in the equation when the P value was <0.05 or removed when the P value was >0.10.

Results: 1. There were 516 RA patients recruited, with 13.8% RC as well as 17.4% underweight, 56.4% normal weight, 22.5% overweight and 3.7% obese respectively. Among 71 RA patients with RC, 73.2% showed normal BMI, while 2.8% underweight, 22.5% overweight and 1.4% obese. Among RA patients with normal BMI (n=291), 17.9% patients showed RC, 28.1% showed normal fat but myopenia, 1.4% showed overfat but non-myopenia, while 52.6% showed both normal fat and non-myopenia. **2.** For RA patients with normal BMI, compared with those with both normal fat and non-myopenia, RA patients with RC were older with longer disease duration, higher disease activity indicators including 28TJC, PtGA, PrGA, PainVAS, ESR, CRP, DAS28-CRP, SDAI and CDAI, higher functional indicators including HAQ-DI and rate of functional limitation, higher radiographic assessment including mTSS, JSN and JE subscores, higher rate of previous use of glucocorticosteroids (75.0% vs. 52.3%), and higher prevalence of hypertension (25.0% vs. 7.8%). Further compared with those with normal fat but myopenia, RA patients with RC showed the similar results with significantly longer disease duration, higher CRP, HAQ-DI, mTSS, JSN subscore, JE subscore, and higher rate of previous use of glucocorticosteroids (all *P*<0.0167, bonferroni correction). **3.** Multivariate logistic regression analysis showed that CRP (*OR*=1.024, 95%*CI*: 1.009-1.040), mTSS (*OR*=1.017, 95%*CI*: 1.010-1.025), previous use of glucocorticosteroids (*OR*=2.605, 95%*CI*: 1.217-5.575), and suffering from hypertension (*OR*=3.462, 95%*CI*: 1.448-8.274) were positively associated with RC in RA patients with normal BMI.

Conclusion: Our data show rheumatoid cachexia is associated with worse disease including RA disease activity, functional limitation and radiographic joint damage, which imply that RC should be emphasized especially in RA patients with normal BMI.

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THU0070 WHAT IS THE ADDITIONAL VALUE OF MRI OF THE FOOT TO THE HAND IN UNDIFFERENTIATED ARTHRITIS TO PREDICT RHEUMATOID ARTHRITIS DEVELOPMENT?

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Background: MRI-detected subclinical joint inflammation in hand-joints of patients with undifferentiated arthritis (UA) predicts progression to rheumatoid arthritis (RA). It is unknown if adding MRI of the foot increases predictive accuracy compared to the hand alone.

Objectives: To assess whether MRI-detected inflammation of the foot is predictive for RA-development, and whether combining MRI-detected inflammation of the foot to that of the hand is of additional value.

Methods: 1.5T-contrast-enhanced MRI of unilateral foot (MTP-1-5), and hand (MCP-2-5 and wrist) was performed in 123 patients presenting with UA (not fulfilling 2010 RA-criteria) and scored for bone marrow edema (BME), synovitis and tenosynovitis. Symptom-free controls (n=193) served as a reference for defining an abnormal MRI. Patients were followed for RA-development ≤1-year, defined as fulfilling classification criteria or initiation of disease modifying anti-rheumatic drugs because of the expert opinion of RA. The added predictive value of foot-MRI to hand-MRI was evaluated.

Results: 52% developed RA. Foot tenosynovitis was predictive (OR 2.55, 95%CI 1.01-6.43), independent of BME and synovitis (OR 3.29, 95%CI 1.03-10.53), but not independent of CRP and number of swollen joints (OR 2.14, 95%CI 0.77-5.95). Hand tenosynovitis was also predictive independent of BME and synovitis (OR 3.99, 95%CI 1.64-9.69) and independent of CRP and swollen joints (OR 2.36, 95%CI 1.04-5.38). Adding foot tenosynovitis to hand tenosynovitis changed sensitivity from 72% to 73%, specificity from 59% to 54% and AUC from 0.66 to 0.64, the net reclassification index was -3.5.

Conclusion: MRI-detected tenosynovitis of the foot predicts progression to RA. However adding MRI of the foot does not improve predictive accuracy compared to MRI of the hand alone. In view of cost-reduction, performance of foot-MRI for prognostic purposes in UA can be omitted.

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THU0071 THE COMBINATION OF RHEUMATOID FACTORS WITH ANTIBODY SYSTEMS TARGETING CITRULLINATED, CARBAMYLATED AND PEPTIDYL ARGININE DEIMINASE AUTOANTIGENS DISTINGUISHES RHEUMATOID ARTHRITIS

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Background: Novel antibody systems including anti-Carbamylated Protein Antibody (anti-CarP IgG) and anti-Peptidyl Arginine Deiminase Antibody (anti-PAD4 IgG) are emerging as independent diagnostic and prognostic biomarkers for Rheumatoid Arthritis (RA) (ref, 1-3). As such, these antibody systems may add value to rheumatoid factor (IgM) and anti-citrullinated peptide antibody (ACPA IgG), the hallmark antibodies in RA.
Objectives: We evaluated the diagnostic performance of Rheumatoid Factor (RF) with antibody systems targeting citrullinated, carbamylated and PAD4 autoantigens in RA.
Methods: The cohort consisted of 638 consenting subjects with RA (fulfilling the 1987 or 2010 ACR classification criteria, mean age: 59.8±0.5 years [SEM], 80% female) and a control group of 775 subjects (mean age: 44.7±0.5 years, 85% females, including Systemic Lupus Erythematosus [n=369], primary Sjogren's Syndrome [n=64], Primary Fibromyalgia [n=85], other connective tissue diseases [n=63], and a group of normal healthy donors [n=194]). Autoantibodies titers from serum were measured using fluoroenzyme immunoassays (anti-RF [IgM] and anti-CCP [IgG]; Phadia Upsala, Sweden), ELISA (anti-CarP [IgG], research use only [RUO], Inova Diagnostics, San Diego) and bead-based Aptiva™ technology (anti-PAD4 [IgG], RUO, Inova Diagnostics) in a clinical laboratory accredited by the College of American Pathologists. For each positive antibody (above each cutoff) a score of 1 was assigned and the cumulative presence of the 4 antibodies was determined [range 0-4]. The ability of the biomarkers to distinguish RA from controls was calculated using sensitivity, specificity and interval likelihood ratio (LR). Positive Predictive Value (PPV) was estimated at 10% pre-test probability. Statistics consisted of Mann-Whitney and Chi-square tests.
Results: In this cohort anti-CarP IgG (>20 Units) yielded 33.5% sensitivity and 77.9% specificity. Anti-PAD4 (>1000 Units) yielded 35.0% sensitivity and 95.0% specificity. RF IgM (>5 Units/ml) and anti-CCP (>10 Units/ml) were 67.4% and 66.5% sensitive, respectively (87.5% and 97.0% specific, respectively). RA presented 5-fold higher 4-antibody system scores (2.02 ±0.05) than controls (0.42±0.02); (p<0.01). Scores greater than 2 yielded 42% sensitivity and 98.8% specificity. A total of 82 subjects presented with the full-house 4 antibodies (score = 4) while 81 of them had RA (99.9% specific). Interval LR and PV for each of the 4-antibody score are presented in the Table. There was no difference in the 4-antibody score between RA who fulfilled the 1987 ACR or 2010 ACR criteria (1.99±0.07 vs 2.08±0.09; p=0.40). In the subset of subjects newly diagnosed (less than one year), the average 4-antibody system score for RA (n=33) was 1.72±0.22 (36.3% with score greater than 2) and 0.58±0.12 for other diseases (0% with score greater than 2, 100% specific); (p<0.01).
Conclusion: This cumulative combination of antibody systems targeting citrullinated, carbamylated, PAD4 and Fc autoantigens (RF IgM) is highly specific for RA. It may be useful in diagnosing and classifying RA even in symptomatic patients who present early in the course of disease.

REFERENCES:

[1] Shi, et al. Proc Natl Acad Sci USA. 2011 108(42):17372-7
[2] Darrah E et al. Sci Transl Med. 2013 2;5186ra65
[3] Verheul, et al. Arthritis Rheumatol. 2018 Nov;70(11):1721-1731

Table I: Combination of Rf IgM, anti-CCP (IgG), anti-CarP (IgG) and anti-PAD4 (IgG)

Score	RA (%, N)	CTL (%, N)	Likelihood Ratio [CI 95%]	Pre-test Probability	Post-test Probability	Change
0	20.5% (131/638)	65.8% (510/775)	0.31 [0.27 to 0.37]	10%	3.4%	-6.6%
1	11.6% (74/638)	27.2% (211/775)	0.43 [0.33 to 0.54]	10%	4.5%	-5.5%
2	25.5% (163/638)	5.8% (45/775)	4.40 [3.22 to 6.02]	10%	32.8%	22.8%
3	29.6% (189/638)	1.0% (8/775)	28.70 [14.26 to 57.77]	10%	76.1%	66.1%
4	12.7% (81/638)	0.1% (1/775)	98.39 [13.73 to 705.04]	10%	91.6%	81.6%

Disclosure of Interests: Thierry Dervieux Shareholder of: Exagen (a diagnostics company not a pharmaceutical company), Employee of: Exagen (a diagnostics company not a pharmaceutical company), John Conklin Employee of: Exagen (a diagnostics company not a pharmaceutical company), Tyler O'Malley Employee of: Exagen (a diagnostics company not a pharmaceutical company), Kelley Brady Employee of: Exagen (a diagnostics company not a pharmaceutical company), Roberta Alexander Employee of: Exagen (a diagnostics company not a pharmaceutical company), Jing Shi Employee of: Exagen (a diagnostics company not a pharmaceutical company), Claudia Ibarra Shareholder of: Exagen (a diagnostics company not a pharmaceutical company), Employee of: Exagen (a diagnostics company not a pharmaceutical company), Michael Mahler Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Joel Kremer Shareholder of: Corrona, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Genentech, GSK, Lilly, Pfizer, Regeneron and Sanofi, Employee of: Corrona, Michael E. Weinblatt Shareholder of: Stock option: CanFite, Lycera, Scipher, Inmedix, Grant/research support from: Crescendo Bioscience, Bristol Myers Squibb, Sanofi, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, CanFite, Corrona, Crescendo, GlaxoSmithKline, Gilead, Horizon, Lilly, Lycera, Merck, Novartis, Pfizer, Roche, Samsung, Scipher, Set Point, Arthur Weinstein Shareholder of: Exagen (a diagnostics company not a pharmaceutical company), Consultant for: Exagen (a diagnostics company not a pharmaceutical company)
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THU0072 ULTRASOUND PREDICTS IMMINENT PROGRESSION TO ARTHRITIS IN ANTI-CCP POSITIVE AT-RISK INDIVIDUALS

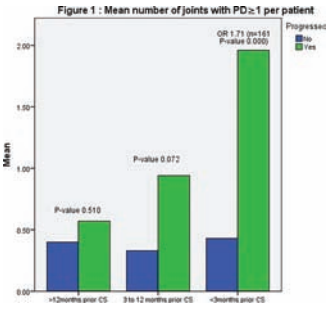
Laurence Duquenne[1,2], Kulveer Mankia[1,2], Jacqueline Nam[1,2], Peta Pentony[1,2], Leticia Garcia-Montoya[1,2], Andrea Dimatteo[1,2], Laura Hunt[1,2], Paul Emery[1,2]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*; *[2]NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*

Background: Ultrasound (US) Power Doppler (PD) signal is predictive for the development of inflammatory arthritis (IA) in anti-cyclic citrullinated protein antibodies positive (CCP+) individuals with musculoskeletal (MSK) symptoms but no clinical synovitis (CS) [1]. Our previous data showed a late increase in the overall US inflammation before arthritis development, suggesting that a sub-clinical phase of synovitis could be detected [2]. This abstract describes the prediction of PD abnormalities in the months following US scan.
Objectives: 1. Presence of PD in one joint is predictive of imminent progression to IA in the next 3months.
2. A rise in the number of joints with presence of PD increases the odds of progression to IA.
Methods: In a single-centre prospective observational cohort between June 2008 and December 2018, 307 CCP+ patients with a new MSK symptom but no synovitis were followed until CS occurred. Clinical and US findings were analysed. Following our previous study, we compared progression in the 3, 12 or >12 months after a US scan. 38 joints were included in the analysis (MTPs, hands, wrists, elbows, ankles and knees). Patients with palindromic rheumatism were excluded.
Results: Data from 96 CCP+ at-risk patients who developed CS (progressors) are compared to 211 CCP+ patients who did not (non-progressors). Age and gender are similar, the mean follow-up of the non-progressors is higher, with significantly more smokers and high titre CCP in the progressors group (Table1).
Overall, progressors have more joints with PD than non-progressors (Figure1). Patients with PD in one joint are more likely to develop CS in the following 3 months compared to those without PD (OR 7.52) and this remain significant when only the hands and wrists are included

(Table2). The highest OR is shown when PD≥2 is found in at least one wrist. Similarly, there is a significant but smaller prediction of progression between 3 to 12 months after US (Table2).

When a new joint develops PD, the likelihood of progression to IA within the next 3 months increases (Table2). This is especially predictive with wrists involvement (OR 3.10). Prediction of progression between 3 to 12 months before CS is significantly different between groups, with a higher OR for the wrists.

Conclusion: The presence of PD in one joint and every new joint with PD are both predictive of progression to IA within the next 3months. These results should lead to a logical programme for therapy and follow -up.



Abstract THU0072– Figure 1

REFERENCES:

[1] Nam J. et al., *US findings predict progression to inflammatory arthritis in anti-CCP positive patients without CS*. Ann Rheum Dis, 2016. 75(12).

[2] Pentony P, et al., *Sequential US shows a late increase in inflammatory burden in anti-ccp positive patients with non-specific MSK symptoms just before progression to IA*. Ann Rheum Dis, volume 77, year 2018

Table 1. demographics

	Progressors	Non-progressors	p-value
N	96	211	
Age*	53.4 (13)	49.8 (13.2)	0.494
CCP titre: High/Low(%)	92.7/7.3	50.2/48.8	0.000
Gender F/M(%)	74/26	74.9/25.1	0.863
Weeks follow-up*	76.44 (93.5)	189.9 (126.5)	0.000
Smoker: Ever/Never (%)	72.9/27.1	48.3/51.7	0.000

*Mean(SD)

Table 2. Probability of progression

if PD≥1 in ≥1joint									
	<3M			**3-12M**			**>12M**		
	OR (CI)	**P-value**	**n**	**OR**	**P-value**	**n**	**OR**	**P-value**	**n**
All joints	7.52 (2.9,18.9)	0.000	161	3.17	0.006	174		0.177	125
Hands	5.01 (2.1,11.9)	0.000	187	3.39	0.004	219		0.174	148
Wrists	4.47 (1.9,10.5)	0.001	188	5.21	0.000	219		0.999	148
for every new joint with PD≥1									
	<3M			**3-12M**			**>12M**		
All joints	1.71 (1.3,2.3)	0.000	161	1.38	0.020	174		0.678	125
Hands	1.83 (1.2,2.7)	0.003	187	1.72	0.013	219		0.301	148
Wrists	3.10 (1.6,5.8)	0.000	188	3.05	0.000	219		0.998	148
if PD≥2 in ≥1joint									
	<3M			**3-12M**			**>12M**		
All joints	2.63 (1.5,4.5)	0.001	161	2.29	0.012	174		0.128	125
Hands	2.89 (1.4,5.9)	0.004	187		0.137	219		0.078	148
Wrists	12.11 (3.2,46.5)	0.000	188	5.78	0.015	219		0.999	148

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THU0073 HAVE THE CLINICAL CHARACTERISTICS OF RHEUMATOID ARTHRITIS AT PRESENTATION BECOME MILDER OVER TIME? RESULTS FROM A NATIONWIDE STUDY OVER THREE DECADES IN SWEDEN

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Background: The course of rheumatoid arthritis (RA) has become milder during the last decades, which could at least partly be attributed to major advances in the pharmacological treatment of the disease and the implementation of "treat to target"-strategies (1,2). It has also been suggested that RA is already milder at presentation (3)

Objectives: To investigate whether the clinical status, markers of inflammation, functional status, and patient and evaluator reported disease activity measures in patients with newly diagnosed RA, have improved over the recent decades.

Methods: Baseline data on all DMARD-naïve patients with early RA (<6 months duration) included in the nationwide Swedish Rheumatology Quality registry (SRQ) between 1991 and 2014 were retrieved. The RA diagnosis relied on the clinical judgement of the treating physician and the information comprised swollen and tender joints count (SJC; TJC), markers of inflammation (CRP; ESR), functional status (HAQ; 0-3), patient´s and evaluator´s assessment of global disease activity (PtGA; EGA) and patient´s assessment of pain (on a visual analog scale, VAS; 0-100 mm). Baseline demographic and disease characteristics were compared between patients with disease onset 1991-2000 vs. those with onset 2011-2014, using Mann-Whitney U test and Pearson's chi-squared test.

Results: A total of 6559 early RA patients were included. Over the study period of 23 years the majority of the patients were women (68%), and the mean age at inclusion increased from 57,4 to 59,1 years. Results are summarised in Table 1. Mean CRP, ESR, TJC and SJC all decreased significantly between the two time periods compared, which was also the case for HAQ. In contrast, mean pain, PtGA and EGA increased significantly between the time periods. Furthermore, time from symptom onset to inclusion was shorter 2011-2014.

TABLE 1 (Mean (SD))	**1990s**	**2000s**	**2011-2014**	**p-value***
Number of patients	1227	4344	988	-
Age at inclusion (years)	57,4 (15,4)	58,4 (15,0)	59,1 (14,7)	0,006
Female gender	67,3%	67,6%	70,4%	0,12
Time from symptom onset (months)	3,8 (1,5)	3,6 (1,5)	3,3 (1,5)	<0,001
CRP (mg/L)	33,1 (36,3)	29,3 (36,7)	22,6 (29,9)	<0,001
ESR (mm)	36,4 (25,8)	35,4 (24,8)	32,4 (23,7)	<0,001
TJC (0-28)	8,0 (6,6)	8,0 (6,1)	7,1 (6,0)	0,005
SJC (0-28)	9,5 (5,9)	9,0 (5,8)	7,6 (5,5)	<0,001
HAQ (0-3)	1,1 (0,6)	1,1 (0,6)	1,0 (0,6)	0,028
EGA(VAS 0-100)	50,3 (19,5)	54,4 (19,4)	54,8 (20,1)	<0,001
Pain (VAS 0-100)	49,5 (26,1)	52,3 (25,5)	53,4 (26,4)	<0,001
PtGA (VAS 0-100)	48,6 (26,7)	52,4 (25,5)	51,8 (26,7)	0,006

*1990S vs 2011-2014

Conclusion: In Swedish patients with early RA, baseline joint counts and inflammatory markers improved over the last three decades. This could partly be explained by shorter symptom duration at diagnosis but also suggests that, at onset, RA might be an inherently milder disease today. However, pain and patient´s global assessment and evaluator´s global assessment of disease activity increased over the same period of time, possibly indicating changes in both patients´ and evaluators´ expectations for management of early RA today

REFERENCES:

[1] Gwinnutt, et al. Arthritis Rheumatol. 2017; 69:1566–75.

[2] Matsumoto, et al. J Rheumatol. 2017; 44:1575–82.

[3] Diffin, et al. J Rheumatol. 2014; 41:1590–9.

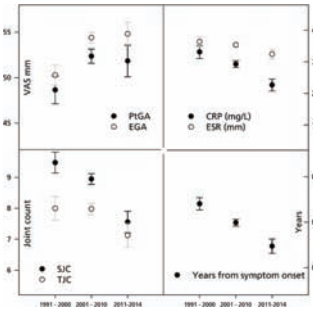


Figure 1. Mean baseline values with 95% confidence interval.

Disclosure of Interests: Jon Einarsson: None declared, Tor Olofsson: None declared, Olafur Palsson: None declared, Johan K Wallman Consultant for: Consultant for AbbVie, Celgene, Eli Lilly, Novartis, and UCB Pharma., Meliha C Kapetanovic: None declared
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THU0074 EVALUATION OF MEDICATION PERSISTENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SJÖGREN'S SYNDROME/INTERSTITIAL LUNG DISEASE TREATED WITH NON-TNFI DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

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Background: RA is a systemic disease driven by pathogenic autoantibodies and inflammatory cytokines that can involve tissues and organs as well as synovial joints. Sjögren's syndrome (SS) and interstitial lung disease (ILD) are frequently reported extra-articular manifestations of RA. However, there are currently limited data on the persistency of non-TNF inhibitor (TNFi) biologic (b)DMARDs and targeted synthetic DMARDs, such as tofacitinib (TOF), in patients (pts) with SS and ILD secondary to RA (RA-SS and RA-ILD).
Objectives: To compare medication persistence between non-TNFi DMARDs including abatacept (ABA), TOF and tocilizumab (TOC) in RA-SS and RA-ILD.
Methods: Pts (≥18 years) from the Truven MarketScan™ administrative claims database with RA (≥2 prescription claims for RA identified with International Classification of Diseases [ICD]-9 or ICD-10) being treated with a non-TNFi DMARD from Jan 2006 to Sep 2017 were included. The date of the first claim for a drug of interest on or after diagnosis of RA was considered the index date. Pts were required to have at least 6 months of continuous enrolment prior to the index date (baseline). Pts with claims for other bDMARDs on the index date were excluded from the study. Pts with a diagnosis of SS or ILD any time in the baseline or follow-up periods were included in the RA-SS or RA-ILD cohorts, respectively. Persistence was defined as the number of days from index date to first switch or discontinuation of the index date DMARD, or end of the study period, or end of enrolment, whichever came first. Pts in both cohorts were stratified by prior TNFi use (TNFi-naïve or TNFi-experienced) and by prior corticosteroid (CS) use. Pairwise comparison of persistence between the non-TNFi DMARDs was performed with ABA as the reference, using the Kruskal–Wallis test for both cohorts separately. A p value of <0.05 was considered statistically significant.
Results: A total of 2503 and 3856 pts satisfied the inclusion and exclusion criteria for the RA-SS and RA-ILD cohorts, respectively. In the RA-SS cohort, 1767, 378 and 358 pts were taking ABA, TOF and TOC, respectively; in the RA-ILD cohort, these numbers were 2937, 343 and 576. The majority (90% in RA-SS and 75% in RA-ILD) of the study population was female. In the RA-ILD cohort, the proportion of pts with prior CS use was significantly lower in pts taking ABA (vs TOF). In the RA-SS cohort, the comorbidity index between treatment cohorts was similar; however, ABA pts had significantly lower pulmonary nodules vs TOF pts (Table 1). In the RA-ILD cohort, the comorbidity index was significantly lower for ABA (vs TOF and TOC), with differences in types of comorbidities at baseline (Table 1). In the RA-SS cohort, the mean time on therapy for pts in the ABA cohort was longer compared with pts in the TOF cohort. Persistency of ABA was higher compared with TOF in the TNFi-experienced pts and in CS-experienced pts (Table 2). In the RA-ILD cohort, overall mean time on therapy for pts taking ABA was longer compared with TOC. Persistency of ABA was higher compared with TOC in the TNFi-naïve cohort.
Conclusion: Based on the analysis of a large US claims database, pts with RA-SS prescribed ABA (vs TOF) had higher persistency, and pts with RA-ILD prescribed ABA (vs TOC) had higher persistency. Further analysis of medication persistence, adjusting for pt characteristics, is warranted.

Abstract THU0074–Table 1. demographics

Table 1. Baseline characteristics by cohort

	RA-SS cohort			RA-ILD cohort		
	ABA (n=1767)	TOF (n=378)	TOC (n=358)	ABA (n=2937)	TOF (n=343)	TOC (n=576)
Mean (SD) age, years	55.1 (11.4)	54.6 (10.5)	55.6 (12.1)	61.4 (12.0)	62.4 (11.3)	60.6 (12.8)
Female, n (%)	1635 (92.5)	349 (92.3)	325 (90.8)	2247 (76.5)	262 (76.4)	449 (78.0)
TNFi-experienced, n (%)	829 (46.9)	175 (46.3)	213 (59.5)*	1338 (45.6)	132 (38.5)*	297 (51.6)*
CS use, n (%)	1114 (63.0)	257 (68.0)	221 (61.7)	1885 (64.2)	261 (76.1)*	375 (65.1)
CCI score, mean (SD)	1.4 (0.9)	1.4 (0.9)	1.5 (0.9)	1.8 (1.2)	2.0 (1.3)*	1.9 (1.4)*
Select comorbidities, n (%)						
COPD/asthma	19 (1.1)	7 (1.9)	6 (1.7)	118 (4.0)	39 (11.4)*	40 (6.9)*
Pneumonia	60 (3.4)	19 (5.0)	16 (4.5)	309 (10.5)	53 (15.5)*	68 (11.8)
Pulmonary nodule	47 (2.7)	22 (5.8)*	12 (3.4)	216 (7.4)	81 (23.6)*	89 (15.5)*
Heart failure	42 (2.4)	3 (0.8)	5 (1.4)	219 (7.5)	31 (9.0)	45 (7.8)
Dyslipidaemia	269 (15.2)	66 (17.5)	67 (18.7)	526 (17.9)	104 (30.3)*	138 (24.0)*
Ischemic heart disease	100 (5.7)	19 (5.0)	22 (6.1)	418 (14.2)	70 (20.4)*	68 (11.8)
Osteoarthritis	524 (29.7)	126 (33.3)	118 (33.0)	935 (31.8)	127 (37)	209 (36.3)*
Lupus	171 (9.7)	26 (6.9)	37 (10.3)	132 (4.5)	9 (2.6)	28 (4.9)
Infections	953 (53.9)	198 (52.4)	187 (52.2)	1613 (54.9)	192 (56.0)	330 (57.3)

*p<0.05 vs ABA
ABA=abatacept; CCI=Charlson Comorbidity Index; COPD=chronic obstructive pulmonary disease; CS=corticosteroid; RA-ILD=patients with interstitial lung disease secondary to RA; RA-SS=patients with Sjögren's syndrome secondary to RA; TNFi=TNF inhibitor; TOC=tocilizumab; TOF=tofacitinib

Abstract THU0074–Table 2. demographics

Table 2. Persistence by cohort: overall and stratified by prior TNFi and CS use

	RA-SS cohort			RA-ILD cohort		
	ABA (n=1767)	TOF (n=378)	TOC (n=358)	ABA (n=2937)	TOF (n=343)	TOC (n=576)
Overall	n=1767 367.9 (440.5) 204	n=378 281.2 (310.3)* 167	n=358 316.1 (343.6) 175	n=2937 367.4 (439.9) 211	n=343 315.3 (317.9) 186	n=576 316.0 (366.9)* 179
TNFi-naive	n=938 357.9 (447.8) 193	n=203 269.6 (281.9) 178	n=145 297.5 (374.6) 147	n=1599 358.5 (426.5) 201	n=211 307.3 (317.3) 165	n=279 269.7 (311.6)* 156
TNFi-experienced	n=829 379.1 (432) 225	n=175 294.7 (340.5)* 163	n=213 328.7 (321.1) 205	n=1338 378 (455.3) 223	n=132 328.3 (319.5) 211.5	n=297 359.6 (408) 208
CS-naive	n=653 368.4 (441.7) 197	n=121 327.2 (313.6) 235	n=137 311.2 (351.5) 175	n=1052 360.7 (443.7) 208	n=82 363.1 (322.8) 281	n=201 303.9 (357.4) 175
CS-experienced	n=1114 367.6 (440) 206	n=257 259.6 (306.9)* 138	n=221 319.1 (339.4) 190	n=1885 371.1 (437.8) 213	n=261 300.3 (315.4)* 164	n=375 322.6 (372.2)* 181

Values expressed as mean (SD) median, in days reported
*p<0.05 vs ABA
ABA=abatacept; CS=corticosteroid; RA-ILD=patients with interstitial lung disease secondary to RA; RA-SS=patients with Sjögren's syndrome secondary to RA; TNFi=TNF inhibitor; TOC=tocilizumab; TOF=tofacitinib

Disclosure of Interests: Leticia Ferri Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Evo Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Aarti Rao Consultant for: Bristol-Myers Squibb
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THU0075 EARLY VERSUS DELAYED START OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A PHASE 3 TRIAL OF PATIENTS NAÏVE TO METHOTREXATE TREATMENT

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Background: Baricitinib (bari) is an oral Janus kinase (JAK)1/JAK2 inhibitor approved to treat moderately to severely active rheumatoid arthritis (RA) in adults in over 50 countries including European countries, the US and Japan. In the 52-week (wk) Phase 3 RA-BEGIN study, bari 4-mg alone or in combination with methotrexate (MTX) showed clinical improvements compared to MTX monotherapy for MTX-naïve patients (pts) with early active RA.[1]
Objectives: To assess if pts who receive bari monotherapy early attain enhanced clinical, functional and radiographic outcomes compared to pts who initiated MTX and switched to bari at wk 52.

Methods: In RA-BEGIN, 588 pts (mean disease duration 1.4 years) were randomized 4:3:4 to MTX, bari 4-mg once-daily, or combination MTX and bari 4-mg. At Wk 52, pts could enter a long-term extension study in which all pts received open-label bari 4-mg. Pts initially randomized to bari-4 mg monotherapy were defined as early-start and MTX pts who switched to bari 4-mg at Wk 52 were defined as delayed-start for this analysis. Change from baseline using mixed model repeated measures and mean scores were assessed for the Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Disease Activity Score 28-joints–high-sensitivity C-reactive protein (DAS28-hsCRP), Disease Activity Score 28-joints–erythrocyte sedimentation rate (DAS28-ESR), Health Assessment Questionnaire-Disability Index (HAQ-DI), and modified Total Sharp Score (mTSS) to compare early- vs delayed-start groups between Wks 0 and 100 (Wks 52-100 for mTSS). Percent of pts achieving low disease activity (LDA, SDAI ≤11) and remission (SDAI ≤3.3) were also assessed.

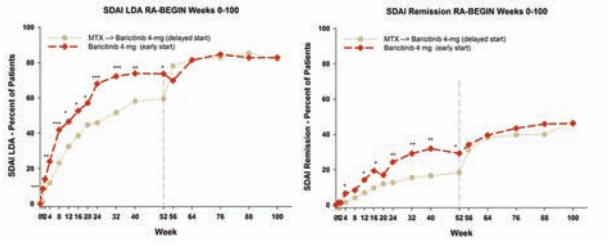
Results: LDA and remission response rates in the delayed-start group increased from 60% to 78% and 18% to 31%, respectively, within 4 wks after switching to bari 4-mg. Remission rates reached 47% within 1 year after switching, but were not different from the group that initiated bari (Figure 1). Similar results were seen for CDAI, DAS28-ESR, and DAS28-hsCRP (only up to Wk 40 for DAS28-ESR) (data not shown). Pts initially randomized to bari 4-mg had significantly greater change from baseline, observed as early as Wk 1 and up to Wk 52, for HAQ-DI than pts treated with MTX (Figure 2). After switching to bari, the delayed-start group showed a rapid improvement in HAQ-DI with similar improvement at Wk 56 – 4 wks after switching to bari. Upon initiating bari, there was a reduction in the rate of structural damage; however, delaying initiation of bari for 1 year resulted in numerically higher mTSS.

Conclusion: In early MTX-naïve pts, improved clinical, functional, and radiographic efficacy with bari 4-mg vs MTX was observed in most outcome measures up to 52 wks. Switching from MTX to bari at Wk 52 provided a rapid clinical response, allowing the majority of pts to achieve similar results 4 wks post-switch. However, if the goal of therapy is to achieve rapid and sustained control of disease activity, the differences noted here for HAQ-DI and especially structural progression support earlier switch to bari for pts who do not obtain disease control with MTX. Further analysis may be needed to explore prognostic factors, such as hsCRP and disease duration (< or >6 months), baseline erosion, or anti-citrullinated protein antibody positivity, which may help clinicians identify pts who may benefit from earlier treatment with bari.

REFERENCES:

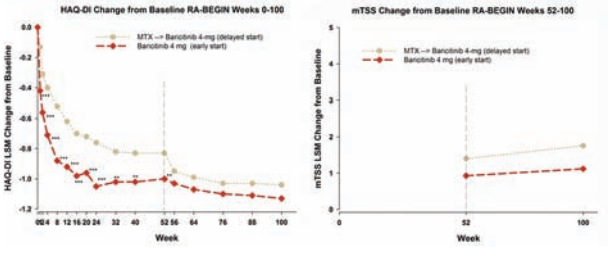
[1] Fleischmann, et al. Arthritis & Rheumatol. 2017;69:506-517

Figure 1. Percent of patients achieving low disease activity (SDAI ≤11) or remission (SDAI ≤3.3) in the early (baricitinib group) and delayed (MTX group) start patients *P-value ≤0.05, **≤0.01, ***≤0.001 vs MTX. Note: Dashed lines indicate that at Week 52 all MTX patients who entered the LTE were switched to baricitinib 4-mg. MTX=methotrexate; SDAI=Simplified Disease Activity Index.



Abstract THU0075 – Figure 1

Figure 2. Efficacy outcomes in the early (baricitinib group) and delayed (MTX group) start patients *P-value ≤0.05, **≤0.01, ***≤0.001 vs MTX. Note: Dashed lines indicate that at Week 52 all MTX patients who entered the LTE were switched to baricitinib 4-mg. HAQ-DI=Health Assessment Questionnaire-Disability Index; LSM=least squares mean; MTX=methotrexate; mTSS=modified Total Sharp Score



Abstract THU0075 – Figure 2

Disclosure of Interests: Roy Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Michael Schiff Consultant for: Abbvie, BMS, Eli Lilly and Company, JJ, UCB, Speakers bureau: Abbvie, BMS, Tore K. Kvien Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB., Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB, Cem Gabay Grant/research support from: Roche, Pfizer, AB2 Bio Ltd, Consultant for: Roche, Pfizer, Lilly, AbbVie, Sanofi, Regeneron, Bristol-Myers Squibb, Novartis, UCB, AB2 Bio Ltd, Debiopharm, Patrick Durez Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celltrion, Anabela Cardoso Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jinglin Zhong Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Yun-Fei Chen Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jennifer Workman Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Tsutomu Takeuchi Grant/research support from: Astellas Pharma Inc, Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Takeda Pharmaceutical Co., Ltd., AbbVie GK, Asahikasei Pharma Corp., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Eisai Co., Ltd., AYUMI Pharmaceutical Corporation, Nipponkayaku Co. Ltd., Novartis Pharma K.K., Grant/research support from: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Grant/research support from: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Abbivie GK, Nipponkayaku Co.Ltd, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Taiho Pharmaceutical Co. Ltd., Chugai Pharmaceutical Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., GlaxoSmithKline K.K., UCB Japan Co. Ltd., Consultant for: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Asahi Kasei Medical K.K., AbbVie GK, Daiichi Sankyo Co., Ltd., Bristol Myers Squibb, and Nipponkayaku Co. Ltd., Speakers bureau: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Speakers bureau: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Astellas Pharma Inc, Diaichi Sankyo Co. Ltd., Eisai Co. Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co. Ltd., Novartis Pharma K.K.
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THU0076 THE IMPACT OF VARYING EXCLUSION CRITERIA ON TREATMENT RESPONSE: REAL-WORLD EVIDENCE TO GUIDE THE DESIGN OF FUTURE CLINICAL TRIALS

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Background: Clinical trials of novel pharmaceuticals in Rheumatoid Arthritis routinely use strict inclusion/exclusion criteria aimed at selecting a defined homogeneous population and producing a non-confounded demonstration of the agent's clinically relevant pharmacologic effect. However, the act of strictly defining numerous individual criteria has the potential

for impacting the observed response rates, while the effect upon limiting the pool of eligible subjects is often poorly understood. Unnecessarily narrow criteria may limit the generalizability of trial results to real world patient populations. Conversely, certain patient characteristics may be associated with high or low probabilities of response to active treatment or to placebo.

Objectives: To assess the impact of applying a range of different exclusion criteria on the proportion eligible subjects, and on the observed treatment response rates, in a large real-world patient population.

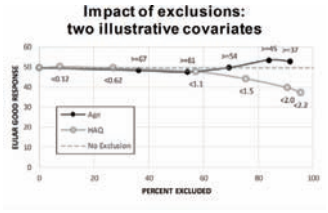
Methods: Data on RA characteristics, demographics, and co-morbidities among RA patients were identified by linking the Swedish Rheumatology register (SRQ) to the nationwide and virtually complete Swedish census and healthcare registries. Representing an early RA trial scenario, we identified patients starting methotrexate monotherapy as first ever DMARD (N=8981) between 2007 and 2016. The cohort was assessed overall and stratified by baseline DAS28. Treatment outcome was defined as the proportions reaching (1) EULAR Good Response and (2) Low Disease Activity, and the change in (3) HAQ and (4) CDAI at 3 and 6 months. Exclusions were made based on age, baseline disease activity, sex, RF, predefined comorbidities, degree of healthcare utilization history, education, and taxed income level (cut-offs for continuous variables were based on distributions from recent clinical trials of tofacitinib). In total, 165 different definitions of exclusion criteria were evaluated.

Results: Within the entire cohort, 50% of patients achieved EULAR DAS28 good response at 3 months. Exclusions based on age, sex, RF status, or duration of RA symptoms before RA diagnosis generally lead to large reductions in number of eligible subjects but did not appreciably affect (< 5% change) the proportion of EULAR good responders. Exclusions based on HAQ had a noticeable drop in the proportion of EULAR good response (-10%, see Figure), although exclusions above 80% was necessary to observe an effect. A similar pattern was observed for TJC, patient's global health and ESR but exclusions based on SJC or CRP did not impact EULAR response.

Exclusions of specific comorbidities, such as history of myocardial infarction, history of joint replacement, generally had no or modest impact on the observed response rate. Exclusions based on health care use (total number of drugs, hospitalizations), affected response rates (+/- around 5%), while exclusions based on educational level, work ability, or income did not.

The impact of exclusions was very similar on the 3 and 6 month responses.

Conclusion: Exclusions in a range of criteria commonly used in clinical trials had only a modest impact on observed treatment outcome, while impacting on the enrollment pool – sometimes dramatically. More extreme restrictions (excluding well above half the potentially eligible patients) were generally necessary to shift the proportion EULAR Good Response by more than 5 percentage points. This should not be a surprise given the lack of identified strong predictors of treatment outcome in RA, but may raise the question of whether the lowered generalizability and impacts on enrollment rates caused by strict inclusion criteria in clinical trials is warranted by the aspiration to increase chances of demonstrating clinically meaningful effects.



Abstract THU0076– Figure 1

Disclosure of Interests: Thomas Frisell: None declared, Scott Jelinsky Shareholder of: Pfizer, Employee of: Pfizer, Mark Peterson Shareholder of: Pfizer, Employee of: Pfizer, Johan Askling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer.

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THU0077 RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS CLINICAL TRIALS: HOW TO ENCOURAGE PATIENTPARTICIPATION? RESULTS FROM A REAL-WORLD STUDY CONDUCTED VIA CARENITY, A WORLDWIDE ONLINE PATIENT COMMUNITY

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Background: Involving patients affected with rheumatoid arthritis or ankylosing spondylitis in clinical trials may be highly challenging: in a worldwide context of competitive rheumatoid arthritis and ankylosing spondylitis clinical research, patient engagement is key to optimize medical research and increase participation rates.

Objectives: The aim of this study was to identify patients' motivations for and hindrances to joining a trail in order to increase participation rate by implementing tailored services and information.

Methods: An online questionnaire was submitted from August 2017 to October 2017 to Carenity's French members affected with rheumatoid arthritis or ankylosing spondylitis.

Results: 136 patients affected with rheumatoid arthritis (n = 55, 40%, mean age = 55 y/o, 71% of women) or ankylosing spondylitis (n = 81, 60%, mean age = 48 y/o, 80% of women) participated in the study. 10 patients (7%) already participated in a clinical trial.

Non-participants (n=126) exposed the incentives that may increase participation rate: reimbursing the expenses related to the clinical trial can improve their motivation (median weight on motivation to join a trial = 10/10) as well as a better medical follow-up (8.0/10) or leveraging the trial's investigator notoriety (8.0/10). Patients' healthcare practitioners could be leveraged as well: their favorable opinion turns patients on to clinical trials (7.0/10). On the contrary, a doctor's negative opinion may strongly deter patients from joining a trial (median weight on reluctance to join a trial = 8.0/10). Communication should aim at reassuring them about side effects (9.0/10), potential risks for their health (8.0/10) and more generally the risk that the new treatment would not be better than their current one (8.0/10). Logistic challenges should also be taken into account: the trip between patients' home and the site of the clinical trial is perceived as an important burden (8.0/10).

Implementing tailored services and information would be an efficient way to reassure patients and increase their willingness to participate. 81% of non-participants would be enticed to participate if they had access to a website to exchange with healthcare professionals or to follow the results of the trial. 79% would be interested in participants' testimonials and 74% in a 24-hour phone helpline. Spreading and clarifying information before the trial is also critical: 6/10 patients who participated in a clinical trial did not understand clearly if they will have out-of-pocket costs and 5/10 patients were also unclear on the terms and conditions for leaving the clinical trial.

Informing patients via convenient channels is key: 88% of participants and non-participants think that an online patient community is a relevant medium to convey information about clinical trials and 81% of non-participants would like to have access to an information brochure about the trial process.

Conclusion: This real-world study allowed to identify concrete levers to reassure patients affected with rheumatoid arthritis or ankylosing spondylitis about the benefits/constraints balance and to clarify information at each stage of the trial (before, during, after), which is essential to accelerate clinical trial recruitment.

Disclosure of Interests: None declared

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THU0078 SAFETY PROFILE OF BARICITINIB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS UP TO 7 YEARS: AN UPDATED INTEGRATED SAFETY ANALYSIS

Mark C. Genovese[1], Josef S. Smolen[2], Tsutomu Takeuchi[3], Gerd Rüdiger Burmester[4], Dennis Brinker[5], Terence Rooney[5], Jinglin Zhong[6], Daojun Mo[5], Chadi Saifan[5], Anabela Cardoso[5], Maher Issa[5], Wen-Shuo Wu[5], Kevin Winthrop[7]. *[1]Stanford University Medical Center, Palo Alto, United States of America*; *[2]Medical University of Vienna, Vienna, Austria*; *[3]Keio University, Tokyo, Japan*; *[4]Charité – University Medicine Berlin, Berlin, Germany*; *[5]Eli Lilly and Company, Indianapolis, United States of America*; *[6]IQVIA, Rockville, United States of America*; *[7]Oregon Health Sciences University, Portland, United States of America*

Background: Baricitinib (bari), is an oral, selective inhibitor of Janus kinase (JAK) 1/JAK 2, to treat moderately to severely active RA in adults.

Objectives: To update bari's safety profile with data from an additional Phase (Ph) 3 trial and on-going long-term extension (LTE) study.

Methods: Long-term safety of once-daily bari was evaluated in the All-Bari-RA dataset: all patients (pts) exposed to any bari dose from 9

randomized trials (5 Ph3, 3 Ph2, 1 Ph 1b) and 1 LTE (data to 13-Feb-2018). Placebo (PBO) comparisons were evaluated to Week 24 from 7 Ph2/3 trials: pts randomized to PBO, bari 2-mg or 4-mg, with censoring at rescue/treatment switch. Dose responses were evaluated in the 2-mg/4-mg extended dataset from 4 Ph2/3 trials: pts randomized to 2- or 4-mg, LTE data included; data censored at rescue/dose change (as-treated analysis) and, due to latent period for malignancy, analyzed without censoring (as-randomized analysis). Incidence rates (IR) per 100 patient-years (PY) were calculated.

Results: 3770 pts received bari (10127 PYs); maximum exposure was 7 yrs (Table). No significant differences were seen for bari 4-mg vs PBO in adverse events leading to permanent drug discontinuation, death, malignancy, serious infection, or major adverse cardiovascular events. Herpes zoster IR was significantly higher for bari 4-mg vs PBO (3.8 vs 0.9) and numerically higher for bari 2-mg (3.1). IRs for deep vein thrombosis/pulmonary embolism were numerically higher in bari 4-mg vs PBO; IRs were similar by dose in 2-mg/4-mg-extended dataset. Malignancy (excluding non-melanoma skin cancer) IRs were 0.8 (2-mg) and 1.0 (4-mg; as-randomized analysis). Fewer than 1% of pts discontinued due to abnormal laboratory results.

Conclusion: In this updated integrated analysis of pts with active RA exposed to bari for up to 7 yrs, across safety topics, bari maintained a safety profile similar to that previously reported[1] and acceptable in the context of demonstrated efficacy.

Abstract THU0078–Table 1. demographics

Table

	Placebo-controlled (to Week 24)			2-mg – 4-mg extended		All-Bari-RA
	Placebo (N=1215)	Bari 2-mg (N=479)	Bari 4-mg (N=1142)	Bari 2-mg (N=479)	Bari 4-mg (N=479)	All Bari RA (N=3770)
Exposure						
Total patient-years	450.8	185.8	471.8	675.6	698.6	10127
Median duration, days	166	168	169	257	342	1115
Longest exposure, days	235	197	211	1805	2520	2520
≥1 AE, n (EAIR)						
TEAE	748 (165.9)	316 (170.1)	803 (170.2)	378 (55.9)	417 (59.7)	3332 (32.9)
Serious adverse event including death	54 (12.0)	18 (9.7)	58 (12.3)	62 (9.2)	84 (12.0)	786 (7.8)
Temporary interruption due to AE	98 (21.7)	50 (26.9)	117 (24.8)	108 (16.0)	118 (16.9)	1111 (11.02)
Permanent discontinuation due to AE	37 (8.2)	20 (10.8)	50 (10.6)	39 (5.7)	59 (8.3)	426 (4.2)
Death, n (IR)	2 (0.4)	0	3 (0.6)	1 (0.2)	4 (0.6)	44 (0.4)
Malignancy, n (IR)						
Malignancy excluding NMSC						
As treated	2 (0.4)	1 (0.5)	2 (0.4)	3 (0.4)	10 (1.4)	85 (0.8)
As randomized				12 (0.8)	14 (1.0)	
Lymphoma	0	0	0	0	1 (0.1)	8 (0.1)
NMSC	1 (0.2)	0	3 (0.6)	2 (0.3)	8 (1.1)	37 (0.4)
Infections, n (IR)						
Serious infection	19 (4.1)	8 (4.2)	19 (4.0)	21 (3.1)	32 (4.6)	283 (2.8)
Herpes zoster	4 (0.9)	6 (3.1)	18 (3.8)*	18 (2.7)	27 (3.9)	323 (3.3)
Tuberculosis	0	0	1 (0.2)	0	7 (0.5)	15 (0.2)
Opportunistic infection including MD HZ[a]	2 (0.5)	0	4 (0.9)	2 (0.3)	3 (0.4)	52 (0.5)
Adverse cardiovascular events of special interest, n (IR)						
Major adverse cardiovascular events	2 (0.5)	0	3 (0.7)	2 (0.3)	2 (0.3)	51 (0.5)
DVT/PE	0	0	6 (1.3)	4 (0.6)	4 (0.6)	49 (0.5)
DVT	0	0	3 (0.6)	4 (0.6)	2 (0.3)	35 (0.4)
PE	0	0	3 (0.6)	1 (0.2)	2 (0.3)	24 (0.2)
Gastrointestinal perforations, n (EAIR)	0	0	0	0	1 (0.1)	4 (0.04)

*$P<0.05$ Bari 4-mg vs PBO
[a]No statistical comparisons were performed.
AE=adverse event; Bari=baricitinib; DVT=deep vein thrombosis; EAIR = exposure adjusted incidence rate; IR=incidence rate; NMSC=non-melanoma skin cancer; PE=pulmonary embolism; TE=treatment-emergent

REFERENCE:

[1] Smolen JS, et al. J Rheumatol. 2019;46:7-18.

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THU0079 AUTOANTIBODY-NEGATIVE PATIENTS, THE CUT-OFF OF SIX POINTS ACCORDING TO THE 2010 ACR/EULAR CRITERIA FOR RHEUMATOID ARTHRITIS MAY MISS A POPULATION OF SEVERE, PERSISTENT POLYARTHRITIS

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Background: At the group level, the classification criteria for rheumatoid arthritis (RA) developed in 2010 identify patients earlier than the 1987 criteria. However, performance of the new criteria in subjects negative for rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) is object of debate [1, 2]. In these patients, classification may be missed despite severe joint and systemic inflammation.

Objectives: To evaluate disease characteristics and arthritis persistence in autoantibody-negative patients with early polyarthritis fulfilling only 5 of the 10 points of the 2010 classification criteria for RA.

Methods: We included early arthritis patients from our Early Arthritis Cohort with at least one clinically swollen joint, symptoms for less than 12 months, no other explanation of arthritis and naïve to glucocorticoids and disease modifying anti-rheumatic drugs (DMARDs) at presentation. At baseline, fulfillment of each specific domain of the 1987 and the 2010 criteria was recorded. RF and ACPA were centrally determined on baseline sera. RF- and ACPA-negative patients achieving a total score of 5 in the 2010 criteria were compared to patients fulfilling RA criteria for baseline characteristics and for arthritis persistence (28-joints disease activity score [DAS28] >3.2) after 2 months of follow-up.

Results: Of the total population of 882 patients with new-onset inflammatory arthritis, comprehensive evaluation of the fulfillment of the 1987 and the 2010 criteria was available in 771 cases (87.4%). Of these, 476

(61.7%) were negative for both RF and ACPA. Among autoantibody-negative patients, 193 (40.5%) scored less than 6 points according to the 2010 criteria, with 82 (42.4%) scoring 5 points. 35.4% of these patients were captured by the 1987 criteria at baseline. Reasons for not fulfilling 1987 criteria in the remaining were morning stiffness <60 min in the majority of the cases (62.3%). As expected, autoantibody-negative patients scoring 5 points had lower disease activity with respect to autoantibody-negative patients fulfilling RA criteria (Table 1). Rather, disease activity, pain and loss of function were comparable to those of autoantibody-positive early RA patients (Table 1). After 2 months of follow-up, 58.1% of autoantibody-negative patients scoring 5 points remained in moderate disease activity (DAS28 >3.2).

Conclusion: In autoantibody-negative patients with new-onset arthritis scoring 5 of the 10 points of the 2010 criteria for RA classification, arthritis is equally severe and disabling compared to autoantibody-positive patients classified as RA from baseline. In the majority of these patients, arthritis persists in the short term. Prospective data are thus awaited in order to assess whether the cut point of the 2010 criteria needs to be lowered in autoantibody-negative inflammatory polyarthritis.

REFERENCES:

[1] Jung SJ, et al. Ann Rheum Dis 2012;71:1097-8
[2] Boeters DM, et al. Semin Arthritis Rheum 2017;47:170-174.

Abstract Table 1. Baseline characteristics of the study cohort

	autoantibody-negative 2010 ACR/ EULAR score=5	autoantibody-negative 2010 ACR/ EULAR score ≥6	p	autoantibody-positive 2010 ACR/ EULAR score ≥6	p
symptoms' duration, median (IQR), weeks	30.6 (10.7 to 37.1)	15.6 (9.9-26.3)	0.04	15.3 (8.5 to 28.8)	0.04
DAS28, mean (SD)	4.53 (0.83)	5.25 (1.08)	<0.001	4.72 (1.15)	0.05
VAS pain, median (IQR)	51.5 (32.5-70.5)	62 (50-80)	0.01	50 (31-77.5)	0.76
HAQ, median (IQR)	1 (0.47-1.5)	1.25 (0.75-1.88)	0.003	1 (0.5-1.5)	0.44

Disclosure of Interests: Silvia Grignaschi: None declared, Serena Bugatti Speakers bureau: Bristol-Myers Squibb, Celgene, Lilly, Novartis, Sanofi, Janssen, Francesca Benaglio: None declared, Garifallia Sakellariou: None declared, Antonio Manzo: None declared, Roberto Caporali Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Roche, Genzyme, Lilly, MSD, Pfizer, UCB, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB
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THU0080 DEVELOPMENT OF ULTRASOUND DETECTABLE ARTHRITIS AMONG ACPA POSITIVE SUBJECTS WITH MUSCULOSKELETAL SYMPTOMS: THE RISK RA PROSPECTIVE STUDY

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Background: Retrospective studies have shown that anti-citrullinated protein antibodies (ACPA) are a risk factor for the development of clinical arthritis.

Objectives: We aimed to investigate in a prospective setting if ACPA and other biomarkers could predict development of ultrasound detected arthritis.

Methods: Subjects with positive ACPA-test referred from primary care to the Rheumatology clinic that lacked arthritis in hands, feet and any other symptomatic joints by clinical and ultrasound examination (according to EULAR-OMERACT definition), were recruited into the Risk-RA research program during 2015-2016 and were followed up to the end of 2017. At inclusion a detailed clinical examination was performed and blood samples were analyzed for 13 specific ACPA reactivities (using a custom made peptide microarray) as well as 92 inflammation-associated protein biomarkers (using a multiplex immunoassay with Olink proximity extension technology). Presence of HLA-SE was analyzed using DR low-resolution kit. Univariate and multivariate analysis were used to investigate the association between clinical and laboratory parameters and development of ultrasound detected arthritis adjusting for the follow-up time.

Results: 42% (27 out of 65) of the Risk RA subjects developed ultrasound detectable arthritis during a median follow up of 8 months. The remaining 58% (38 out of 65) were followed for a median of 25 months (range 12-44) without any signs of ultrasound detectable arthritis. Subjects developing arthritis had higher prevalence of HLA-SE (89% vs 56%) and increased occurrence of ultrasound detected tenosynovitis (44% vs 5%), as compared to those not developing arthritis. ACPA reactivities to citrullinated vimentin peptides (cit vim 2-17: 22% vs 6%; and cit vim 60-75: 70% vs 43%) and citrullinated histone peptides (cit H4 31-50: 89% vs 49%; and cit H3 21-44: 48% vs 23%) were a more common occurrence in subjects developing ultrasound detectable arthritis. Backward selection in a Cox regression model showed that ultrasound detectable arthritis could be predicted in a model including HLA-SE, tenosynovitis and ACPA reactivity to cit H4 31-50. Hazard ratio (HR) for arthritis development were 3.4 (95% CI 1.0-12, p 0.06) for HLA-SE carriers, 2.9 (95% CI 1.3-6.7, p 0.01) for tenosynovitis and 4.1 (95% CI 1.2-14, p 0.02) for Anti-citrullinated H4 31-50 positivity. Only modest differences were observed for few of the tested inflammatory markers in those developing as compared to those not developing ultrasound detectable arthritis: Interleukin-6 (3.9 vs 3.3 AU/ML), Programmed death-ligand 1 (4.9 vs 5.2 AU/ML) and Chemokine (C-X-C motif) ligand 6 (9.2 vs 9.5 AU/ML).

Conclusion: Certain ACPA fine specificities, HLA-SE and tenosynovitis predict the development of ultrasound detectable arthritis in seropositive individuals with musculoskeletal symptom who are at risk for RA.

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THU0081 ELEVATED SERUM TREM-1 LEVELS ARE ASSOCIATED WITH DAS28 AND PERIODONTITIS IN RHEUMATOID ARTHRITIS

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Background: The Triggering Receptor Expressed on Myeloid cells 1 (TREM-1) along with its putative ligand peptidoglycan recognition protein 1 (PGLYRP1) are involved in the propagation of the inflammatory response to microbial exposure(1). Periodontal disease (PD) has been suggested as an environmental risk factor for rheumatoid arthritis (RA), yet further studies are required to dissect the mechanisms underlying the association between the two(2).

Objectives: The present study aimed to investigate whether serum levels of TREM–1 and PGLYRP1 in patients with RA correlate with the presence and severity of PD, as well as bacterial load in saliva.

Methods: Serum and saliva samples were collected from 65 individuals with RA (F/M: 48/17), under sDMARD treatment for more than 6 months and never used biologic treatment), with Behcet syndrome (BS, n= 45, F/M: 31/12) and with systemic health (HC, n= 59, F/M: 40/19). RA disease activity was assessed by using 28-joint disease activity score (DAS-28). Oral health was evaluated by dental and periodontal indices. TREM-1 and PGLYRP1 were measured by ELISA, while total oral bacteria in saliva was assessed by quantitative real-time polymerase chain reaction and normalized against tooth number. For statistical analysis, non-parametric Kruskal Wallis, Mann-Whitney U and Spearman correlation tests were used.

Results: Patients with RA presented with a smaller number of teeth than the BS and HC groups (18.67±8.45; 24.02±3.7; 25.36±3.83, respectively) (p<0.001). Prevalence of severe periodontitis was higher in the RA group (33,8%) compared to BS (20,9%) and HC (5,1%). Total bacterial load was significantly higher in saliva of RA than HC (p<0.05). Serum TREM-1 and PGLYRP1 levels were significantly higher in RA (167,1±95,0 pg/ml; 157,5±228,8 pg/ml) than BS (102,8±44,4 pg/ml; 52,4±26,01pg/ml) and HC

(90,7±56,5 pg/ml; 68,8±37,7 pg/ml) (p<0.05). Correlation analysis showed a significant positive correlations between TREM-1 and and DAS-28 scores (p<0.05). In the RA group, while TREM-1 levels (127,9±61,7 pg/ml vs 198,4±105,7 pg/ml) were significantly reduced by methotrexate intake, but presence of severe periodontitis resulted in higher TREM-1 and PGLYRP1 (p<0.05).

Conclusion: The present study demonstrated that there is an increased levels of TREM-1 and PGLYRP1 in serum of patients with RA which is further potentiated by periodontitis. Moreover, TREM-1 correlates with clinical disease activity. MTX therapy of patients with RA is accompanied by reduced TREM-1 levels in serum.

REFERENCES:

[1] Cheng Z, Meade J, Mankia K, Emery P, Devine DA. Periodontal disease and periodontal bacteria as triggers for rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2017 Feb;31(1):19-30

[2] Tammaro A, Derive M, Gibot S, Leemans JC, Florquin S, Dessing MC. REM-1 and its potential ligands in non-infectious diseases: from biology to clinical perspectives. Pharmacol Ther. 2017 Sep;177:81-95.

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THU0082 EFFECT OF TREAT-TO-TARGET STRATEGY ON DISEASE ACTIVITY AND RADIOLOGIC OUTCOMES IN RHEUMATOID ARTHRITIS: RESULTS FROM A 9-YEAR CHINESE COHORT

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Background: Treat-to-target (T2T) strategy has been implied in clinical practice for 9 years. However, a recent study showed that the radiologic outcome didn't associate with the adherence to protocolized treatment in clinical practice[1]. Furthermore, in clinical practice, nonadherence to a T2T protocol has been reported[2]. The reasons varied. In our previous study, there was a substantially decrease of RA activity over 8 years after tight control applied[3]. However, whether T2T strategy can improve the long term radiographic outcomes in daily practice is still unknown.

Objectives: the arm of our study was to determine the effect of treat to target (T2T) protocol on disease activity and radiographic outcomes in a 9-year Chinese RA cohort.

Methods: RA patients who were followed-up for more than 1 year in a longitudinal observational cohort were included in our study. The adherence rate of the patients was evaluated by the calculation of the percentage of whether the patients followed the time schedule to clinic. Adherence rate$\geq$0.7 was defined as adherent to T2T. The overall disease activity was evaluated by time adjusted mean (TAM) method. The radiological change was evaluated by radiographies of the hands regularly, with the interval between 1 and 3 years. We defined the primary radiological outcome as $\triangle$ modified total Sharp score (mTSS) >3 over the follow-up time.

Results: There were 209 patients enrolled in our study. The median interval of two radiographies was 31.0 (17.0, 50.0) months. 45.0% of patients got clinical remission using TAM DAS28(ESR) and 25.4% of patients got the radiological outcome. Adherence rate was significantly negatively correlated with the mean disease activity [β coefficient=-0.423 (-0.540, -0.298), p=0.000, using DAS28ESR]. Moreover, adherent to T2T and baseline high disease activity (HDA) were independent predictors of radiological outcome [adherent to T2T: HR=0.47 (0.27, 0.82), p=0.007; baseline HDA: HR= 2.04 (1.16, 3.62), p=0.014] (Figure 1). As for bone erosion aspect, besides baseline HDA and adherent to T2T, baseline bone erosion existing also independently associated with erosion progression [HR=1.90 (1.12, 3.23), p=0.018]. When divided the adherence rate into three subgroups, we can find that patient not following the T2T protocol were more easily to get radiological progression. There was statistically significant difference among three groups (p=0.004 using log rank, and p=0.001 using Tarone ware). To our surprise, increased adherence rate didn't provide more benefit when adherence rate was more than 0.9 (Figure 2). In patients who got overall clinical remission, we found none of these variables correlated with the radiological outcome.

Conclusion: The mTSS progression was associated with baseline HDA and adherence rate, independently. Adherence to T2T strategy may improve the remission probability and halt the radiological deterioration, especially in the patients who didn't get clinical remission.

REFERENCES:

[1] Wabe NT, Sorich MJ, Wechalekar MD, et al. Effect of Adherence to Protocolized Targeted Intensifications of Disease-modifying Antirheumatic Drugs on Treatment Outcomes in Rheumatoid Arthritis: Results from an Australian Early Arthritis Cohort. J Rheumatol. 2016;43(9):1643–9.

[2] Wabe N, Sorich MJ, Wechalekar MD, et al. Characterising deviation from treat-to-target strategies for early rheumatoid arthritis: the first three years. Arthritis Res Ther. 2015 Mar 8;17:48.

[3] Xie W, Li J, Zhang X, et al. Trends in the activity of rheumatoid arthritis as the consequence of treat-to-target strategy: eight-year data from 2009 to 2016. Clin Exp Rheumatol. 2018 Sep-Oct;36(5):820-8.

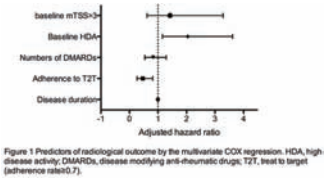


Figure 1 Predictors of radiological outcome by the multivariate COX regression. HDA, high disease activity; DMARDs, disease modifying anti-rheumatic drugs; T2T, treat to target (adherence rate≥0.7).

Abstract THU0082 – Figure 1

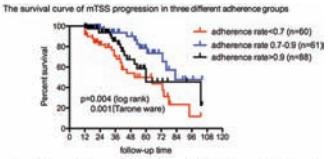


Figure 2 The survival curve of patients having radiological progression in different adherence rate groups. Patient whose adherence rate<0.7 were more easily to get △mTSS>3. There was statistically significant difference among three groups (p=0.004 using log rank, and p=0.001 using Tarone ware).

Abstract THU0082 – Figure 2

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THU0083 ROLE OF CLINICAL IMPACT, DISEASE-SPECIFIC KNOWLEDGE AND BELIEFS ABOUT MEDICATION ON THERAPEUTIC ADHERENCE IN RHEUMATOID ARTHRITIS: AN INTEGRATIVE STRUCTURAL EQUATION MODELING APPROACH

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Background: Treatment of rheumatoid arthritis (RA) to remission is the optimal way to ensure control of symptoms, prevention of structural damage, optimization of function and quality of life. Adherence to medical treatment is, therefore, an integral part of a comprehensive and successful management of RA.

Objectives: We interrogated the influence of three distinct domains of RA clinical impact (disease activity, functional limitations, mood disturbance), patient specific knowledge about RA and beliefs about medications on treatment adherence.

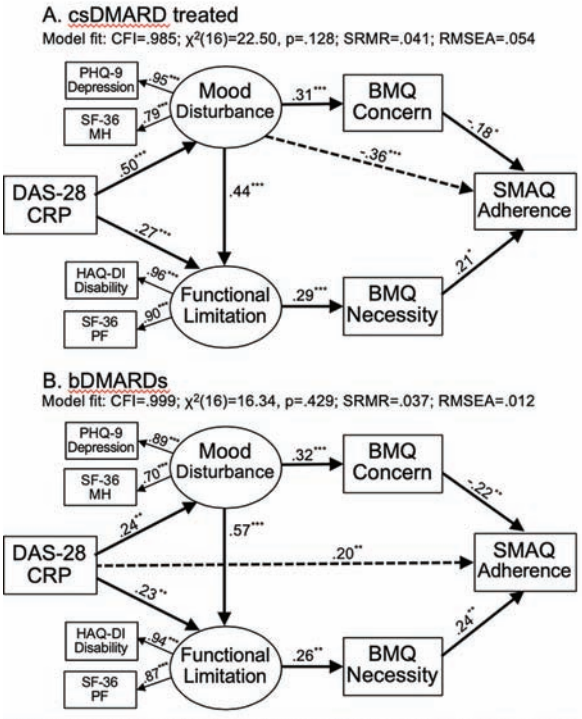
Methods: We evaluated 285 patients with established RA from a single center. In the proposed model, disease activity DAS28(CRP), mood disturbance (Patient Health Questionnaire-9 depression scale and SF-36 Mental Health domain), functional limitations (Health Assessment Questionnaire Disability Index and SF-36 Physical Function domain) and RA-specific knowledge (Patient Knowledge Questionnaire) were expected to predict beliefs about the necessity of RA medications and concerns about them (Beliefs about Medicines Questionnaire) which, in turn, would impact adherence (Simplified Medication Adherence Questionnaire). Cross-sectional multi-group structural equation modeling evaluated the model separately in patients treated with bDMARDs and those only receiving csDMARDs.

Results: RA-specific knowledge was not significantly associated with medication beliefs or adherence and therefore was dropped from the model. Modification indices suggested addition of two supplementary paths (dashed lines) that significantly improved the proposed model fit for both

treatment groups, shown in Figure 1. Disease activity, functional limitations and mood disturbance influenced adherence via multiple and often competing pathways, directly or indirectly through a necessity/concerns evaluation by the patient. Notably, RA activity directly promoted adherence in patients on bDMARDs (p<0.01). In contrast, in patients on csDMARDs, RA activity had an indirect, net negative effect on adherence (p<0.01); the main pathway was through worsening mood disturbance which in turn attenuated adherence (p<0.01). This may imply that the experience of disease activity in patients requiring bDMARDs may be sufficiently impactful to independently promote medication adherence. In contrast, disease activity may be largely experienced as depressed mood in patients on csDMARDs which may in turn overwhelm their capacity to adhere. Additionally, mood disturbance adversely influenced adherence directly in patients on csDMARDs (p<0.01) yet there was no significant direct or net indirect effect of mood disturbance on adherence to biologics. Functional limitations fostered adherence through enhanced awareness of medication necessity (p<0.05).

Conclusion: Distinct domains of the impact of clinical RA influence treatment adherence directly or indirectly through a necessity/concerns framework. Mood disturbance and concerns about medications may represent complementary yet salient intervention targets of comprehensive RA management promoting medication adherence; the former may be more relevant for patients on csDMARDs whereas the latter may be more significant with bDMARDs.

Figure 1: Contributions of clinical RA impact and beliefs about medication on therapeutic adherence.



DAS28-CRP: Disease activity score based on 28-joint count and c-reactive protein, PHQ-9: 9-item patient health questionnaire, SF-36 MH: Short Form 36 Health Survey mental health scale, HAQ-DI: health assessment questionnaire-disability index, SF-36 PF: Short Form 36 Health Survey physical function scale, BMQ: beliefs about medication questionnaire, SMAQ: Short medication adherence questionnaire.
*p<0.05, **p<0.01, ***p<0.001.

Abstract THU0083 – Figure 1

Disclosure of Interests: George Karpouzas Grant/research support from: Pfizer, Consultant for: Sanofi-Genzyme-Regeneron, Janssen, Roche-Genentech, Pfizer, Speakers bureau: BMS, Sanofi-Genzyme-Regeneron, Janssen, Roche-Genentech, Elizabeth Hernandez: None declared, Vibeke Strand Consultant for: AbbVie, Amgen, Bayer, BMS, Boehringer Ingelheim, Celgene, Celltrion, CORRONA, Crescendo, EMD Serono, Genentech/Roche, GSK, Horizon, Inmedix, Janssen, Kezar, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Servier, UCB., Sarah Ormseth: None declared

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THU0084 THE LONG-TERM OUTCOME OF INTRA-ARTICULAR GLUCOCORTICOID INJECTED JOINTS ON RADIOGRAPHIC CHANGES IN PATIENTS WITH RHEUMATOID ARTHRITIS: A REAL WORLD DATA FROM A SINGLE CENTER

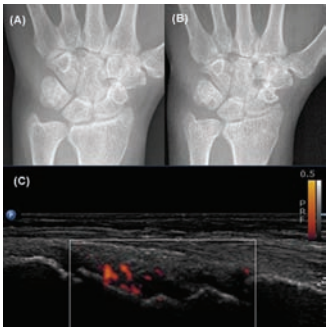
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Background: Intra-articular glucocorticoids injections (IAGI) have been an important part of a treat-to-target strategy in patients with Rheumatoid arthritis (RA). However, it is not known the long-term outcome of glucocorticoids-injected joint.

Objectives: To explore the long-term outcome of IAGI, the impact on the radiographic joint space narrowing and erosion in patients with RA.

Methods: We performed a retrospective cohort study of IAGI for patients with RA. We identified 88 RA patients who received IAGI into wrists or hand joints determined by ultrasound and had pre-injection and follow-up hand radiographs from a rheumatology department in a tertiary hospital. As a comparator, 88 RA patients who had not received IAGI although they had clinical synovitis (defined as both tender and swollen joint) in wrist or hand joint were randomly selected (Non-IAGI group). Hands radiographs scored using the van der Heijde-modified Sharp Score (HSS) method was used to assess radiographic progression ($\Delta HSS \geq 1$ in joint areas of synovitis). Multivariable Cox regression estimated the hazard ratio (HR) and 95% confidence interval (95% CI) for radiographic progression of joint with synovitis.

Results: Among 88 RA patients who received IAGI (median age, 60 years, 42 (48%) patients had radiographic progression of triamcinolone-injected joint, while 38 patients (43%) in non-IAGI group (median age, 57 years) presented radiographic progression of joint area suffered clinical synovitis (not significant) in the median 2 years follow-up. At baseline, IAGI group presented longer disease duration, lower acute phase reactant levels and less involvement of proximal interphalangeal joints than non-IAGI group did. In the IAGI group, a median number of 1 (IQR, 1–2) joint was injected. After 3 months from IAGI, 63.5% of patients reported improvement of injected joint and 16.5% of patients received a second or more IAGI. The radiographic progression of injected joint (Figure 1) waspronounced at the wrists (87.8% of radiographic progressor). The level of C-reactive protein at active arthritis, baseline HSS and power Doppler grade in ultrasound was higher in radiographic progressor than in non-radiographic progressor. A high baseline HSS of hands (HR, 1.021 [95% CI, 1.002–1.040]), wrist joint involvement (HR, 5.356 [95% CI, 1.705–16.813]) and use of NSAIDs (HR, 0.373 [95% CI, 0.179–0.776]) were associated with radiographic progression in joint areas which suffered active synovitis.



Abstract THU0084 – Figure 1

Conclusion: In patients with RA, IAGI did not have an additional effect on radiographic progression in the next 2 years. High baseline HSS and wrist joint involvement are independent risk factors of radiographic progression in joints suffered synovitis.

REFERENCES:

[1] Hetland ML, Ostergaard M, Ejbjerg B, Jacobsen S, Stengaard-Pedersen K, Junker P, Lottenburger T, Hansen I, Andersen LS, Tarp U, et al: **Short- and long-term efficacy of intra-articular injections with betamethasone**

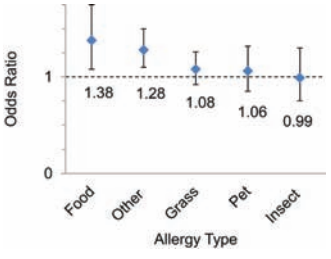
as part of a treat-to-target strategy in early rheumatoid arthritis: impact of joint area, repeated injections, MRI findings, anti-CCP, IgM-RF and CRP. Annals of the rheumatic diseases 2012, 71(6):851-856.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.951

THU0085 RHEUMATOID ARTHRITIS AND ALLERGIC DISEASES

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Background: Historically, RA was considered a T_H1 disease while asthma and allergy were considered T_H2 diseases (1). However, several studies show an association between RA and asthma (2), and more recently, allergic disease (3).
Objectives: We first aimed to determine the association between RA and asthma after controlling for important confounders including allergic disease, urban environment, and passive smoke exposure. Second, we aimed to determine the association between RA and various allergy types.
Methods: This case-control study identified 1,023 cases of RA (175 incident) within a single-center biobank population using a rules-based algorithm that combined self-report with two diagnosis codes. Exposures were self-reported on biobank questionnaires. Logistic regression models calculated the association of exposures with RA, adjusting for potential confounders.
Results: Asthma was associated with RA after adjusting for allergies, urban environment, and passive smoke exposure (OR 1.28, 95% CI 1.04 to 1.58). History of allergic disease was also associated with RA (OR 1.30, 95% CI 1.12 to 1.51), especially food allergy (OR 1.38, OR 1.08 to 1.75, see Figure 1). Results from the incident RA cohort mirrored these findings, though the association with asthma was not significant (OR 1.17, 95% CI 0.66 to 2.06).



Abstract THU0085 – Figure 1. Adjusted association between allergy types and RA.

Conclusion: Asthma and allergies may be associated with increased risk of RA. It is possible a broader problem with immune dysregulation underlies both RA and allergic diseases, and having one predisposes to the other.

REFERENCES:

[1] Singh VK, Mehrotra S, Agarwal SS. The paradigm of Th1 and Th2 cytokines: its relevance to autoimmunity and allergy. Immunol Res. 1999;20 (2):147-61.
[2] Sheen YH, Rolfes MC, Wi CI, Crowson CS, Pendegraft RS, King KS, et al. Association of Asthma with Rheumatoid Arthritis: A Population-Based Case-Control Study. J Allergy Clin Immunol Pract. 2018;6(1):219-26.
[3] Lai NS, Tsai TY, Koo M, Lu MC. Association of rheumatoid arthritis with allergic diseases: A nationwide population-based cohort study. Allergy Asthma Proc. 2015;36(5):99-103.

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Disclosure of Interests: Vanessa Kronzer: None declared, Cynthia S. Crowson: None declared, Jeffrey Sparks Grant/research support from: Bristol-Myers Squibb, Amgen, Consultant for: Optum, Robert Vassallo: None declared, John Davis Grant/research support from: Pfizer
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THU0086 PREDICTING TNFALPHA INHIBITOR TREATMENT RESPONSE USING SERUM CYTOKINES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Tumour necrosis factor-αlpha inhibitors (TNFαi) are the main biologics (b-MARDs) used to treat active rheumatoid arthritis (RA) in patients that have failed disease modifying treatment (DMARD). However, 10% of patients with rheumatoid arthritis, TNFα inhibitors do not work at all. Patients are continued on this treatment for several months risking side-effects in the hope that the treatment will work. Another 40% of patients respond partially to this treatment and have to also be treated with other drugs such as methotrexate and prednisone in addition to treatment with TNFαi. Biomarkers offer an opportunity to identify before starting or soon after starting treatment with TNFαi which patients will be responders and whether prednisone and other drugs can be reduced and optimise the risk-benefit of treatment.
Objectives: We undertook a series of experiments with the following objectives: determine whether cytokine biomarkers will predict which patients with rheumatoid arthritis are: (a) sustained DMARD early treatment responders (b) sustained TNFαi early treatment responders, (c) TNFαi early treatment failures.
Methods: We used the Millipore's MILLIPLEX MAP Human Th17 Magnetic Bead kit for the simultaneous quantification of the following cytokines: IL-1β, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL- 12p70, IL-13, IL-15, IL-17A, IL-17E/IL-25, IL-17F, IL-21, IL-22, IL-23, IL-27, IL-28A, IL-31, IL-33, GMCSF, IFNγ, MIP-3α, TNFα and TNFβ. γ, MIP-3α, TNFα and TNFβ. We evaluated 14 patients with RA starting on a DMARD and 26 patients with RA starting on a TNFαi after failing DMARDs. These cytokines were assayed monthly 2 or 3 months prior to starting a TNFαi to evaluate month-to-month cytokine variability and every month up to 5 months after initiation of treatment. RA disease activity was measured using the RA Disease Activity Score (DASCRP28) which includes joint counts, CRP and a patient-reported outcome of health status. All samples were blocked with Heteroblock to reduce rheumatoid factor and other heterophilic antibodies. Rheumatoid factor was measured before and after blocking. The same negative and positive controls were included across all plate runs. All assays were done in singlet to accommodate longitudinal samples. Mixing studies were undertaken to evaluate whether cytokine results could be analysed using quantitative statistics.
Results: We had 67 serum samples in the DMARD treated group and 202 serum samples in the TNFαi treated group because of the longitudinal study design. Using mixed effects linear regression to account for longitudinal data in a model that included all 25 cytokines, treatment-time and treatment type (DMARD or TNFαi+/-DMARD), we found that in patients on DMARDs, IL-6, IL-1β, IL-28A, and TNFβ were associated with treatment response. However, in TNFαi treated patients, TNF-a, GM-CSF and IL-6 were associated with treatment response. Only p values <0.005 are reported given that 25 cytokines were included in the model.
Conclusion: In this study of treatment response comparing DMARDs and TNFαi in a longitudinal cohort of 26 patients with a total of 202 samples measuring TNFα and GM-CSF may predict early TNFαi responders.
Disclosure of Interests: Marissa Lassere Grant/research support from: I have received research support with educational grant funding from Sanofi-Aventis, Pfizer, MSD, Abbvie, Sue Baker: None declared, Jenny Gu: None declared
DOI: 10.1136/annrheumdis-2019-eular.6445

THU0087 UTILITY OF INFRARED THERMOGRAPHY FOR THE EVALUATION OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory disease, which predominantly affects the hands. Currently in clinical practice, we explore the number of swollen and painful joints in order to evaluate the activity of the disease. Infrared thermography (IT) is a non-invasive, lacking ionizing radiation, operator-independent and low-cost technique that allows to measure the temperature of the cutaneous surface through the taking of a photograph.
Objectives: To determine the utility of IT in the evaluation of hands arthritis in patients with RA.

Methods: A cross-sectional study was performed, including patients with RA according to 2010 ACR/EULAR criteria attended in our Hospital between February and March 2018. Demographic, clinical and analytical characteristics of patients were registered. Number of painful and swollen joints were assessed for each patient, including wrist, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints. Subsequently, a standardised photograph of the dorsal aspect of both hands was taken with a thermal camera (FLIR T250 model) (Figure 1). With this technique mean temperature (MeanT) and maximum temperature (MaxT) were assessed at each joint. Also, differential temperature (DifT) was assessed (mean temperature at joint - temperature at forearm skin).

Results: We included a total of 42 patients. 76% were women, mean age at diagnosis was 56.7 years old. 29 patients were positive for rheumatoid factor and 31 for anti-citrullinated peptide antibody. At the time of the assessment, medium CRP was 9.19 mg/L and ESR was 14.77 mm/h.

MeanT for the 65 swollen joints was 1.5°C higher than the 847 non-swollen joints (p=0.000). Independent analysis for each joint level (wrist, MCP and PIP) revealed higher temperature in swollen joints (Table 1). Similar results were obtained for painful joints. ROC curves and areas under the curve (AUC) were calculated for wrist, MCP and PIP joints, obtaining the most favorable results for DifT in wrist and MCP joints, and for MaxT in PIP joints, allowing to calculate a cut-off point at each joint level (Table2).

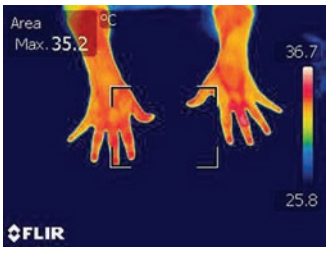


Figure 1. Selective temperature increase over third PIP of the left hand.

	Swollen	Number of joints	MeanT	P value	MaxT	P value	DifT	P value
TOTAL	NO	847	31.68°C	0.000	32.26°C	0.000	-1.26C	0.000
	YES	65	33.18°C		33.71°C		-0.28°C	
Wrist	NO	68	32.62°C	0.005	33.21°C	0.004	-0.31°C	0.000
	YES	14	33.79°C		34.40°C		+0.55°C	
MCP	NO	391	32.02°C	0.044	32.72°C	0.066	-0.95°C	0.036
	YES	23	33.02°C		33.61°C		-0.15°C	
PIP	NO	388	31.18°C	0.000	31.64°C	0.000	-1.74°C	0.013
	YES	28	33.01°C		33.47°C		-0.81°C	

Table 1. Correlation between swollen joints and MeanT, MaxT and DifT.

	AUC	Cut-off value	Sensibility	Specificity
Wrist	0.878 (DifT)	-0.0169°C	0.929	0.743
MCP	0.640 (DifT)	+ 0.10331°C	0.609	0.770
PIP	0.713 (MaxT)	34.27°C	0.679	0.770

Tabla 2. AUC, sensibility and specifity.

Conclusion: In patients with RA, there is a statistically significant relationship between joint temperature measured by thermal imaging and the presence of swollen and painful joints in the assessment by the rheumatologist. The ROC curves indicate an acceptable sensitivity and specificity and allow to determine cut-off temperatures for clinical use.

Infrared thermography could be a useful tool in the assessment and monitoring of arthritis in RA patients.

REFERENCE:

[1] Jones B, Hassan I, Tsuyuki RT, Dos Santos MF, Russell AS, Yacyshyn E. Hot joints: myth or reality? A thermographic joint assessment of inflammatory arthritis patients. Clin Rheumatol. 2018 Sep 20;37(9):2567–71

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.5601

THU0088 BASELINE ADIPONECTIN LEVELS PREDICT FUTURE DEVELOPMENT OF RHEUMATOID ARTHRITIS IN SUBJECTS WITH OBESITY

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Background: Adiponectin is a cytokine produced by the adipose tissue and is involved in both metabolic and inflammatory processes[1]. In obese subjects, serum adiponectin levels are surprisingly low[2]. On the contrary, adiponectin levels are increased in serum and synovial fluid of subjects with established rheumatoid arthritis (RA)[1,3].

Objectives: By exploiting a longitudinal study enrolling more than 4000 obese subjects, we aim to determine if serum adiponectin levels are a risk factor for the development of RA in obese subjects.

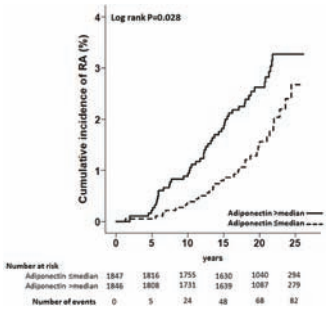
Methods: The Swedish Obese Subjects (SOS) study is a longitudinal controlled trial on the effect of bariatric surgery on the incidence of obesity-related diseases. It includes 4047 obese subjects whereof 2010 underwent bariatric surgery and 2037 constituted the matched control group[4,5]. SOS study participants who developed RA were identified by searching the Swedish National Patient Register. Eleven subjects with prevalent RA at baseline are excluded by the analyses. Patients were followed up until diagnosis of RA, death, migration or end of follow-up (December 2016). Total adiponectin was measured using the Quantikine ELISA kit from Quantikine ELISA kit from Bio-Techne (Minneapolis, MN, USA).

Results: Adiponectin measurement at baseline was available for 3691 subjects. Among those subjects, 82 subjects developed RA during a follow up for up to 29 years. High serum adiponectin levels at baseline were associated with the incidence of RA, independently of bariatric surgery, sex, age, body-mass index, smoking, and C-reactive protein and erythrocyte sedimentation rate levels (adjusted Hazard Ratio HR per 10 µg/mL adiponectin 1.70, 95% confidence interval CI 1.12-2.60, P value=0.01). When stratifying the population according to the median of baseline adiponectin, subjects with adiponectin greater than 6.8 µg/mL had a higher risk to develop RA during follow up (log-rank P 0.028, unadjusted HR 1.64, 95% CI 1.05-2.56, P=0.03, Figure 1).

Conclusion: In a large cohort of obese subjects followed up for up to 29 years, serum adiponectin levels were associated with the incidence of RA years before the onset of clinical signs. The association between adiponectin and the incidence of RA was independent of other risk factors, including C-reactive protein, smoking and bariatric surgery.

REFERENCES:

[1] Fantuzzi G. Adiponectin in inflammatory and immune-mediated diseases. Cytokine 2013;64:1-10.
[2] Hotta K, Funahashi T, Arita Y, et al. Plasma concentrations of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients. Arterioscler Thromb Vasc Biol 2000;20:1595-9.
[3] Lee YH, Bae SC. Circulating adiponectin and visfatin levels in rheumatoid arthritis and their correlation with disease activity: A meta-analysis. Int J Rheum Dis 2018;21:664-72.
[4] Sjöström L, Larsson B, Backman L, et al. Swedish obese subjects (SOS). Recruitment for an intervention study and a selected description of the obese state. Int J Obes Relat Metab Disord 1992;16:465-79.
[5] Sjöström L, Narbro K, Sjöström CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med 2007;357:741-52.



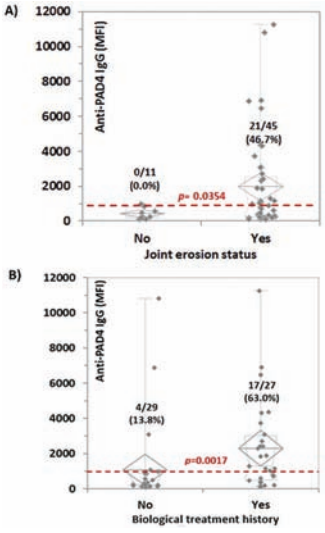
Abstract THU0088 – Figure 1. Cumulative incidence of RA in the SOS study stratified by baseline adiponectin

Disclosure of Interests: Cristina Maglio: None declared, Yuan Zhang: None declared, Christian Herder Speakers bureau: Eli Lilly, Sanofi-Aventis Deutschland, Anna Rudin Grant/research support from: I have received research grants från AstraZeneca (2017-2018), Consultant for: I was paid consultant för AstraZeneca (2015-2018), Lena Carlsson Consultant for: I have received lecture fees from AstraZeneca, MSD and Johnson&Johnson
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THU0089 ASSOCIATION OF ANTI-PAD4 ANTIBODIES WITH EROSION AND BIOLOGICAL TREATMENT USE IN RHEUMATOID ARTHRITIS

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Background: Novel biomarkers have been described in rheumatoid arthritis (RA) patients, including antibodies to carbamylated proteins (anti-CarP) and to protein-arginine deiminases (PAD). Anti-PAD4 antibodies are associated with anti-citrullinated protein antibodies (ACPA) and worse baseline radiographic joint damage [1]. A subset of anti-PAD4 antibodies that cross-react with PAD3 and are associated with erosive disease, ACPA and progress despite treatment have also been described [1].
Objectives: To evaluate several novel RA markers in a cohort of RA and controls and their association with erosive disease and biological treatment use in RA.
Methods: Sera from 116 RA patients [63 young onset RA (YORA) and 53 elderly onset RA (EORA)] and 155 controls [134 polymyalgia rheumatica (PMR) patients and 21 healthy individuals (HI) older than 60 years old] were included. Information on erosion status and biological treatment was available for 56 of the RA patients. The samples were tested for anti-PAD3 and anti-PAD4 IgG using the novel particle-based multi-analyte technology (PMAT, research use only, RUO), as well as for ACPA [CCP3 IgG ELISA and chemiluminescent immunoassay (CIA)] and anti-CarP IgG (ELISA, RUO).
Results: Significantly higher levels of anti-PAD3, anti-PAD4 and ACPA (ELISA and CIA) but not CarP were observed in YORA vs. EORA (p<0.0001 for anti-PAD3 and ACPA ELISA and CIA, p=0.0016 for anti-PAD4). In the RA patients with erosion and treatment information available, anti-PAD4 antibody levels, but not ACPA, anti-CarP or anti-PAD3, were significantly higher in patients on biologic treatment vs. patients that were not on biologics (p=0.0017). Anti-PAD4 positive patients, were 10.1 [95% CI 2.5-52.0, p=0.0002] times more likely to be on biologic treatment vs. the negative group. Similarly, anti-PAD4 antibodies, but neither ACPA nor anti-CarP or anti-PAD3, were also significantly higher in patients with joint erosions (p=0.0354). All patients that were positive for anti-PAD4 antibodies (n=21) had erosive disease. Anti-PAD4 positive patients, were 20.2 [95% CI 1.1-363.2, p=0.0041] times more likely to have erosive disease.
Conclusion: Anti-PAD3, anti-PAD4 and ACPA are associated with disease onset at an early age. Anti-PAD4 are associated with erosive disease and biological treatment use in RA and represent a useful marker for better patient stratification.



Abstract THU0089 – Figure 1. Association of anti-PAD4 antibodies with joint erosion status (A) and to biological treatment use (B). Results are in Median Fluorescence Intensity (MFI). P-values of the Mann-Whitney analysis are shown in red. Dashed line indicates the preliminary cut-off of the assay. Number of positives and% within each subgroup are shown.

REFERENCE:

[1] Darrah, E., et al., *Erosive rheumatoid arthritis is associated with antibodies that activate PAD4 by increasing calcium sensitivity*. Sci Transl Med, 2013. 5(186): p. 186ra65.

Disclosure of Interests: Laura Martinez-Prat Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Victor Martinez-Taboada: None declared, Marcos Lopez-Hoyos Consultant for: Inova Diagnostics (Not pharmaceutical, diagnostics company), Michael Mahler Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company)
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THU0090 MORTALITY OVER UP TO 14 YEARS FOLLOW-UP IN MTX-REFRACTORY PATIENTS RANDOMIZED TO A STRATEGY STARTING WITH ADDITION OF INFLIXIMAB OR ADDITION OF SULFASALAZINE AND HYDROXYCHLOROQUINE

Heather Miller[1], Johan K Wallman[2], Ingemar Petersson[3], Saedis Saevarsdottir[1,4], Jonas Söderling[1], Sofia Ernestam[1,5], Johan Askling[1], Ronald van Vollenhoven[6], Martin Neovius[1]. *[1]Karolinska Institutet, Department of Medicine, Solna, Stockholm, Sweden*; *[2]Lund University, Department of Rheumatology, Clinical Sciences Lund, Lund, Sweden*; *[3]Lund University, Department of Orthopaedics, Clinical Sciences, Lund, Sweden*; *[4]Karolinska Institutet, Stockholm, Institute of Environmental Medicine, Stockholm, Sweden*; *[5]Academic Specialist Center, Stockholm Health Services, Stockholm, Sweden*; *[6]University of Amsterdam, Amsterdam Rheumatology and immunology Center, Amsterdam, Netherlands*

Background: Longevity is the ultimate health outcome measure, incorporating treatment effectiveness as well as treatment safety. Randomized

Table 1. Prevalence of the assays in the different groups and in the entire cohort (percentage and number of individuals).

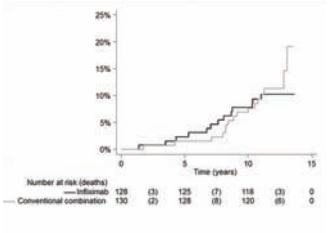
Assay/Group	PMR	HI	YORA	EORA	RA (YORA+EORA)	Total
% (N/total)	*49% (134/271)*	*8% (21/271)*	*23% (63/271)*	*20% (53/271)*	*43% (116/271)*	*100% (271/271)*
CCP3 ELISA	7% (9/134)	0% (0/21)	92% (58/63)	23% (12/53)	60% (70/116)	29% (79/271)
CCP3 CIA	7% (9/134)	0% (0/21)	95% (60/63)	25% (13/53)	63% (73/116)	30% (82/271)
CarP ELISA	41% (55/134)	14% (3/21)	49% (31/63)	62% (33/53)	55% (64/116)	45% (122/271)
PAD3 PMAT	1% (1/134)	5% (1/21)	16% (10/63)	0% (0/63)	9% (10/116)	4% (12/271)
PAD4 PMAT	10% (13/134)	14% (3/21)	38% (24/63)	13% (7/63)	27% (31/116)	17% (47/271)
PAD3+/4+ PMAT	1% (1/134)	0% (0/21)	16% (10/63)	0% (0/63)	9% (10/116)	4% (11/271)

controlled trials tend to report data only on short term effects, while extended follow-up of long-term mortality data of treatment strategies are scarce.

Objectives: To compare mortality risk over up to 14 years of follow-up in MTX-refractory patients with early RA, randomized to a strategy starting with addition of infliximab versus addition of sulfasalazine and hydroxychloroquine.

Methods: We used data from a 2-arm, parallel, randomized, active-controlled, open-label trial (Swefot), in which patients with early RA (symptom duration <1y) were recruited from 15 rheumatology clinics in Sweden from 2002-2006. Patients who did not achieve low disease activity after 3-4 months of MTX were randomized to receive additional biological treatment with infliximab (n=128) or conventional combination treatment with sulfasalazine and hydroxychloroquine (n=130). By linking the trial database to the Swedish Total Population Register and Cause of Death Register, we collected complete data on all-cause mortality and emigration until August 31, 2017. Participants were followed until death, emigration, or end of follow-up, whichever came first. Analyses were by intention to treat.

Results: Over a total 1477 and 1504 person-years of follow-up in the infliximab and the conventional combination treatment group there were 13 and 16 deaths, respectively (8.8 [95%CI 0.0-25.1] versus 10.6 [95%CI 0.0-28.4] deaths per 1000 person-years; mortality hazard ratio 1.2 [0.6-2.5]; P=0.62; **Figure**). After 5 years, approximately 50% of patients in the infliximab arm remained on biologic therapy and 50% in the conventional combination arm remained on synthetic DMARDs.



Abstract THU0090 – Figure 1. Cumulative incidence of death over up to 14 years of follow-up in the Swefot trial in patients with early RA with an insufficient response to MTX, randomized to a strategy starting with addition of either infliximab or conventional combination DMARD treatment.

Conclusion: No increased or decreased mortality risk could be observed over up to 14 years of follow-up in patients with MTX-refractory early RA, randomized to a strategy starting with addition of infliximab compared to patients randomized to a strategy starting with conventional combination treatment. At the end of the extended follow-up, a minority of patients remained on their assigned therapy, reflecting the treat to target paradigm.

Disclosure of Interests: Heather Miller: None declared, Johan K Wallman Consultant for: Consultant for AbbVie, Celgene, Eli Lilly, Novartis, and UCB Pharma., Ingemar Petersson: None declared, Saedis Saevarsdottir Employee of: Part-time employee at deCODE Genetics/Amgen Inc, working on genetic research unrelated to this project., Jonas Söderling Consultant for: Abbvie, Merck, Novartis, Pfizer and Shire (unrelated to the present work), Sofia Ernestam: None declared, Johan Askling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer., Ronald van Vollenhoven Grant/research support from: AbbVie, BMS, GSK, Pfizer, UCB, Consultant for: AbbVie, AstraZeneca, Biogen, Biotest, BMS, Celgene, Gilead, GSK, Janssen, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Lilly, Pfizer, UCB, Martin Neovius: None declared

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THU0091 DEPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS: UNDER RECOGNIZED, UNDERTREATED AND ASSOCIATED WITH POORER CLINICAL STATUS AND LOWER RATES OF REMISSION IN ROUTINE CARE

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Background: Depression in patients with rheumatoid arthritis (RA) may be pre-existent, amplified, or newly-developed after onset of RA. Together with other comorbidities, socioeconomic, or affective factors can influence perception of pain, functional disability, and health status. The prevalence of depression in RA patients is 19% and affect remission rates according to a classical composite index.[1]

Objectives: We compared patient self-reported scores included on the Multidimensional Health-Assessment Questionnaire (MDHAQ) and levels of remission according to RAPID3 in patients who self-reported depression versus no depression.

Methods: All patients complete a MDHAQ at each visit, which includes physical function (FN), three 0-10 visual analogue scales (VAS) for pain (PN), patient global estimate (PATGL), fatigue (FT), RADAI self-report joint count, a review of 60 symptoms (ROS) on a checklist, three evaluations for depression, anxiety and sleep quality (0-3.3), and demographics. RAPID3 (0-30) is the sum of FN, PN, and PATGL; being remission RAPID3 <3. Patients with RA (ICD10) were classified according to self-reported depression on the ROS. Agreement between MDHAQ-depression and by the Patient Health Questionnaire (PHQ-9) was evaluated in 57 patients. Demographic and clinical characteristics were compared by self-reported depression status using Student t-test and chi-square test.

Results: 464 RA patients were studied: 118 (25%) self-reported depression. In 57 patients, who also completed the PDQ-9, agreement with MDHAQ depression was 93% (kappa=0.80 95% IC 0.61-0.99). Only 37 (31%) of all patients reporting depression had evidence in the medical record of treatment and/or specialist evaluation for depression. No differences between depression groups were seen for mean age or sex. Patients reporting depression had lower education level (12.5 vs 14.3, p<0.001) and poorer scores for physical function, pain, and patient global leading to higher RAPID3 and lower percentage of patient in remission (12.4 vs 4%, p<0.001) (Table). Depressed patients also reported higher scores for fatigue, number of painful joints, number or symptoms, and more difficulty with sleep, and anxiety.

Table: MDHAQ patient self-report scores in patients with RA according to depression status. Data are presented as mean (SD) and percentages. *p<0.001

	No self-reported depression N= 346 (75%)	**Self-reported depression** N= 118 (25%)
Demographic variables		
Age, years	55.4 (14.9)	55.8 (15.1)
Female,%	84%	91%
Education level, years	14.3 (3.1)	12.5 (3.4)*
MDHAQ/RAPID3: Patient self-report scores		
Physical function (0-10)	2.4 (2.0)	3.4 (1.9)*
Pain (0-10)	5.3 (3.0)	6.8 (2.6)*
Patient global estimate (0-10)	4.9 (3.0)	6.6 (2.7)*
RAPID3 (0-30)	12.6 (7.2)	16.6 (6.4)*
% patients in RAPID3 remission	12.4%	4%*
Fatigue (0-10)	4.2 (3.2)	6.3 (3.0)*
Self-reported joint pain-RADAI (0-48)	12 (10)	18 (12)*
Review of Symptoms (0-60)	8 (7)	18 (9)*
Sleep problems (0-3.3)	1.1 (0.9)	1.9 (0.9)*
Dealing with depression/feeling blue (0-3.3)	1.1 (0.9)	1.9 (0.9)*
Dealing with anxiety/being nervous (0-3.3)	0.1 (0.4)	0.7 (0.4)*

Conclusion: The prevalence of self-reported depression in our RA patients was 25%, with only 31% treated for this condition. RA patients with self-reported depression exhibit higher scores for all MDHAQ scores, and a lower rate of RAPID3 remission. MDHAQ may be useful to identify patients with depression in busy clinical settings.

REFERENCE:

[1] Leblanc-Trudeau, C, et al. Rheumatology 2015;54:2205-14.

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THU0092 DEFINING A LEARNING CURVE FOR CLINICIANS PERFORMING ULTRASOUND-GUIDED DEFINING A LEARNING CURVE FOR CLINICIANS PERFORMING ULTRASOUND-GUIDED NEEDLE SYNOVIAL BIOPSIES: A RETROSPECTIVE ANALYSIS OF THE EXPERIENCE AT THE EXPERIMENTAL MEDICINE AND RHEUMATOLOGY, QUEEN MARY UNIVERSITY OF LONDON

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Background: Despite the significantly better outcome reached by patients with Rheumatoid Arthritis following the introduction of the biologics, the absence of predictors of individual response to the available agents constitutes a huge unmet clinical need. The histological analysis of the diseased synovial tissue (ST) may represent a valuable prognostic tool. The ultrasound-guided needle synovial biopsy (US-nSB) is a safe, effective and increasingly used method to retrieve ST from both large and small joints. Therefore, assessing the 'learning curve' for clinicians training in this technique is critically important.
Objectives: To retrospectively evaluate the learning curve for clinicians performing US-nSB at the Centre for Experimental Medicine and Rheumatology, Queen Mary University of London.
Methods: The performance of 5 clinicians has been evaluated from their first to >20 procedures based on the training phase (Table). The standard teaching method included: US/US-guided injections; observation of US-nSB; initial procedures occurring under the strict active supervision of an expert.

Training Phase	1st - 10th	11th - 20th	21st- 30th	31st - 40th	41st- 50th	>50th
Total n° of procedures included	50	50	43	35	30	90

Results: The total number of ST fragments retrieved during the procedure did not significantly change during the learning phase (17.3 ± 3.5 from 1st to 10th biopsy vs 17.2 ± 3.4 if expert performer). Independently of the training phase, a significantly higher number of samples were retrieved from knees/wrists in comparison with metacarpo-, metatarso-, and proximal inter-phalangeal joints. The average weight of a ST fragment at the beginning of the learning curve was comparable with the mean weight of ST samples retrieved by expert performers (3.7±2.5mg from 1st to 10th biopsy vs 2.9±2.4mg if experts). ST from knees had a significantly higher mean weight, which could be explained by the more frequent use of a 14G (rather than 16G) needle. At the beginning of the learning curve, 48.2%±29.5% of the retrieved ST-samples were considered histologically 'gradable' (visible lining and/or clear sub-lining based on H&E/CD68 IHC staining); the rate of gradable ST progressively increased and remained ≈60% when >20 procedures have been performed. The duration of the US-nSB significantly decreased during the learning time (49 ± 18 min from 1st to 10th biopsy vs 30 ± 9 min if expert performer). No serious adverse events (AEs) such as haemarthrosis or joint infection have occurred during the learning time. The overall rate of minor AEs (e.g., minor bleeding) was not the highest at the beginning of the training. During the 1st-10th procedures, 18.2% of the patients reported severe pain compared to the average 8.4%.
Conclusion: In this single-centre retrospective study we showed that, with an appropriate training and the presence of the initial strict supervision, performing US-nSB is safe and effective since the beginning of the learning curve. Further prospective and multi-centre studies are needed to confirm the optimal learning time and training method.

REFERENCES:

[1] Ultrasound-guided synovial biopsy: a safe, well-tolerated and reliable technique for obtaining high-quality synovial tissue from both large and small joints in early arthritis patients. S Kelly et al. Ann Rheum Dis. 2015 Mar;74 (3):611-7.
[2] Patient-reported outcomes and safety in patients undergoing synovial biopsy: comparison of ultrasound-guided needle biopsy, ultrasound-guided portal and forceps and arthroscopic-guided synovial biopsy techniques in five centres across Europe. SA Just, et al. RMD Open. 2018 Oct 26;4(2): e000799.

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THU0093 BASAL METABOLIC RATE AND CHARLSON COMORBIDITY INDEX ARE INDEPENDENT PREDICTORS OF METABOLIC SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Metabolic syndrome (MetS) is associated with 2-fold increase in cardiovascular disease (CVD) and 1.5-fold increase in all-cause mortality in the general population. The overall pooled prevalence of MetS in the meta-analysis of rheumatoid arthritis (RA) patients is 30.65%. Along with high prevalence of MetS in RA, several studies showed the contribution of MetS to the increased risk of CVD or cardiovascular mortality in RA patients. Although controversial, the inflammatory activity of RA was significantly associated with MetS in several cross-sectional studies. However, no prospective studies have confirmed an increased risk of MetS development during the course of RA.
Objectives: This 2-year prospective study investigated the predictors of metabolic syndrome (MetS) in patients with rheumatoid arthritis (RA).
Methods: We recruited 319 consecutive RA patients who did not have MetS at baseline. MetS was defined according to the modified NECP/ATP III 2005 for Asian populations. Predictors of MetS were assessed using univariate and multivariate logistic regression analyses.
Results: Of the 247 RA patients who finished 2-year follow-up, 37 (15.0%) developed MetS. At baseline, the patients who developed MetS were older and had higher BMI (P = 0.002), higher waist circumference (P = 0.011), higher waist-hip ratio (P = 0.035), greater skeletal muscle mass (P = 0.005), higher body fat mass (P = 0.011), higher percent body fat (P = 0.004), lower basal metabolic rate (P = 0.004) and higher Charlson comorbidity index score (P < 0.001). The percent of diabetes (P = 0.007) and hypertension (P < 0.001) were higher in patients with MetS than without MetS. And they also had elevated glucose (P = 0.004), triglyceride levels (P < 0.001), and a lower low-density lipoprotein cholesterol (LDL-C) (P < 0.001). These patients were also more likely to take less hydroxychloroquine (P = 0.044), more oral hypoglycemic agents (P < 0.001) and had a lower EQ-5D score (P = 0.025). In the multivariate analysis, when variables that belong to the composition of MetS were excluded, basal metabolic rate (OR = 0.205, 95% CI: 0.078–0.541, P = 0.001) and Charlson comorbidity index score (OR = 2.191, 95% CI: 1.280–3.751, P = 0.004) remained significant predictors of MetS.
Conclusion: The development of MetS in RA patients was associated with basal metabolic rate and Charlson comorbidity index at baseline. Physicians should pay more attention to RA patients who have these risk factors to avoid CVD and cardiovascular mortality.
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THU0094 SERONEGATIVE RHEUMATOID ARTHRITIS: MILD NO MORE

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Background: Seronegative rheumatoid arthritis (RA) patients have been historically considered to have a milder disease. This confers a potential risk for under treatment. The quality of their response to early intensive therapies has not been thoroughly studied.
Objectives: To compare the disease course in seronegative and seropositive patients from the Care in early RA (CareRA) trial treated with COBRA Slim.

Methods: The CareRA trial included 379 patients with early RA (≤1 year) fulfilling 1987 or 2010 ACR criteria and naïve to disease modifying anti-rheumatic drugs (DMARDs). Patients were randomized to one of four different intensive treatment strategies based on methotrexate (MTX) monotherapy or synthetic (cs)DMARD combinations with or without glucocorticoid (GC) bridging. Before randomization, stratification into a high- or low-risk group according to classical poor prognostic markers (presence of erosions, positivity to rheumatoid factor (RF) and/or anti-citrullinated protein antibody (ACPA), and elevated disease activity) was conducted. One of these strategies, COBRA Slim, a combination of MTX and a prednisone remission induction scheme stepping-down from 30 mg QD, was initiated in 141 patients from both risk strata, of which 38 were negative for both RF and ACPA (seronegative). Following the treat-to-target principle, using the disease activity score in 28 joints with C-reactive protein (DAS28CRP), treatment adaptations were steered at low disease activity (≤3.2), while aiming for remission (<2.6) as final outcome.

The "as observed" population was analysed for differences in disease activity and radiographic progression between seronegative and seropositive patients at several time points during the 2-year study using independent sample t-test, Man Whitney-U or adjusted X^2 (Yate's correction for small samples). Survival analysis using Kaplan Meier was employed for time to first response to treatment. First response to treatment was defined as achieving first remission (DAS28CRP<2.6) or first relevant improvement (ΔDAS28CRP>1.2) after screening. Sensitivity analyses were applied on the complete CareRA cohort.

Results: Seronegative patients starting COBRA Slim (n=38), had similar age (53 vs 51 years, p=0.52), body mass index (25.5 vs 26.7, p=0.08), symptom duration (7.9 vs 7.2 months, p=0.23), presence of erosions (24% vs 23%, p=0.99) and gender distribution (82% vs 63%, p=0.06), compared to seropositive patients (n=103). However, parameters of disease activity were higher in seronegative patients at screening: DAS28CRP (5.1 vs 4.5, p=0.01), 28 swollen joint count (8.2 vs 5.7, p=0.02) and 28 tender joint count (10.3 vs 6.9, p=0.006). These results were corroborated when analysing the entire CareRA cohort.

The mean disease activity was significantly higher in seronegative patients at the first stages (week 8 and 16), but became comparable by year 1 and 2 (Table 1). There was a significant difference in time to first treatment response between seronegative and seropositive patients, despite being treated with the same strategy, as depicted in the inverted Kaplan Meier plot (Figure 1).

Conclusion: In conclusion, CareRA participants with seronegative RA had a higher initial disease activity, longer time to experience a first treatment response, but achieve comparable remission status as seropositive patients with COBRA Slim, a combination of MTX with moderate dose GC bridging. This provides further evidence that, seronegative RA can no longer be considered a milder form of disease and requires an equally intensive initial treat-to-target therapy as seropositive RA.

Abstract THU0094 –Table 1. demographics

Table 1: Disease activity and radiographic progression throughout the 2-year trial.

DAS28CRP at		SERONEGATIVE	SEROPOSITIVE	p-value
	W8	2.9 ± 1.2 (35)	2.3 ± 1.0 (100)	**0.006**
	W16	2.6 ± 1.1 (35)	2.2 ± 0.9 (100)	**0.023**
	Y1	2.3 ± 1.0 (33)	2.3 ± 1.0 (93)	0.929
	Y2	2.0 ± 0.9 (27)	2.1 ± 0.8 (87)	0.162
SHARP VAN DER HEIJDE SCORE		**SERONEGATIVE**	**SEROPOSITIVE**	**p-value**
	W0	1.3 ± 2.2 (33)	1.1 ± 2.2 (78)	0.156
	W28	1.4 ± 2.3 (31)	1.2 ± 2.5 (77)	0.107
	Y1	1.7 ± 2.4 (29)	1.3 ± 2.8 (79)	**0.026**
	Y2	1.5 ± 2.2 (22)	1.8 ± 3.4 (70)	0.384
	Δ Y1-W0	0.3 ± 0.5 (28)	0.3 ± 0.9 (71)	0.345
	Δ Y2-W0	0.3 ± 0.8 (21)	0.8 ± 1.6 (62)	0.724

Data is presented as mean ± standard deviation, () number of patients, w=week, y=year, Δ=change/delta

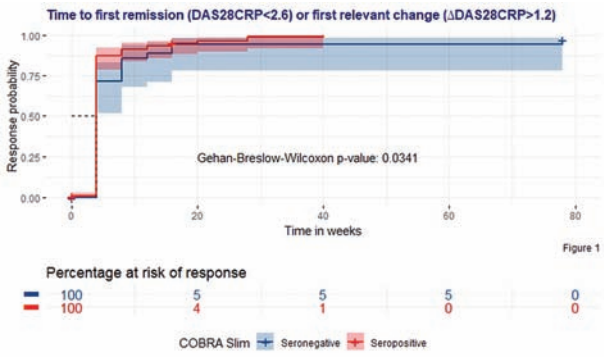


Figure 1

Abstract THU0094 – Figure 1

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THU0095 CIGARETTE SMOKING AS PREDICTOR OF INADEQUATE RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITISPATIENTS NAÏVE TO DMARDS

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Background: Methotrexate (MTX) is the gold standard as first line treatment in rheumatoid arthritis (RA). Identifying predictors of response to MTX should be crucial in the view of a personalized therapy.

Objectives: To identify prevalence and potential clinical baseline predictors of inadequate response (IR) to MTX in RA patients naïve to disease modifying anti-rheumatic drugs (DMARDs)*.

Methods: Data of 233 consecutive RA patients (according to ACR/EULAR 2010 criteria) naïve to traditional and biologic DMARDs, attending the AOU University Clinic, Rheumatology Unit, Monserrato (Cagliari), Italy, were analyzed. Table 1 shows baseline demographic, clinical and serological characteristics of the cohort. Patients failing to reach low disease activity state (DAS 28 > 3.2) at 6 months (T1) since the beginning of MTX (T0) or patients undergoing therapeutic modification for persistently high disease activity (switch or addition of other traditional or biological DMARDs) before T1 were considered as IR. By univariate analysis, demographic, clinical and serological factors recorded at T0 were evaluated as potential predictors of IR at T1. Afterwards, factors with p<0.10 were included in a logistic regression model, to identify independently associated factors to IR (p <0.05). Odd-Ratio (OR) with 95% confidence interval (CI) was calculated.

Results: At T1, 104 patients (44.6%) were classified as IR to MTX. In univariate analysis, factors significantly associated with IR were: female

gender (69.2% vs. 54.3%; p=0.02), condition of "current smoker" (22.1% vs. 10.9%; p=0.012), ESR [median (IQR): 30.0 (19.0-48.0) vs. 40.0 (25-62); p=0.035] and DAS28 (mean ± standard deviation: 5.5 ± 1.1 vs. 5.2 ± 1.3; p=0.037). High-titre positivity for RF and/or ACPA (57.3% vs. 45.9%; p=0.095) and high cumulative steroids dose [852 mg (300-1200) vs. 691 mg (0-150); p=0.071] were numerically higher in IR.

In multivariate analysis, the "current smoker" condition was confirmed as the only independent factor associated with IR to MTX after 6 months of treatment (OR: 2.333, 95% CI: 1.132-4.805; p=0.022).

No significant association between ex-smoker status and IR to MTX was demonstrated. This result was confirmed even after stratification of ex-smokers over the time since smoking stop. Finally, for both current smokers and ex-smokers, the duration of exposure to cigarette smoking did not show any significant association with IR.

Conclusion: In this RA cohort, the condition of "current smoker" was the only predictor of IR to MTX. This observation, together with the lack of association between previous smoking habit and IR to MTX, further prompt to recommend cessation of cigarette smoking in patients with RA who begin treatment with MTX.

Table 1. Baseline demographic, clinical and serological features.

Gender, n (%) Female	142 (60.9%)
Age at enrollment, mean (± SD), yrs	54.2 (±14.5)
RF/ACPA positivity, n (%)	132 (60.5%)
BMI, mean (± SD) Kg/m^2	24.9 (± 4.1)
Current smoker, n (%)	37 (15.9%)
Ex smoker, n (%)	89 (38.2%)
DAS28, mean (± SD)	5.3 (± 1.2)
TJC28, median (IQR)	9 (5-15)
SJC28, median (IQR)	5 (2-10)
ESR, mean (± SD)	39.9 (± 24.9)
X-ray Erosion, n (%)	36 (22.3%)
Rheumatoid Nodules, n (%)	8 (3.4%)

DS: standard deviation; RF: factor rheumatoid factor; ACPA: anti-citrullinated peptide antibodies; BMI: body mass index; DAS-28: disease activity score; TJC: tender joint count; SJC: swollen joint count; ESR: erythrocytes sedimentation rate.

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THU0096 PERSISTENT HIGH DISEASE ACTIVITY IN THE ANTI-CARBAMYLATED PROTEIN ANTIBODY POSITIVE EARLY ARTHRITIS PATIENTS INDEPENDENTLY OF TREATMENT

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Background: There is great interest in the identification of prognostic biomarkers informing early therapeutic decisions for the improvement of rheumatoid arthritis (RA) evolution. Promising results in early arthritis (EA) patients indicate the anti-carbamylated protein antibodies (ACarPA) may serve this function. In effect, they are associated with high baseline disease activity and, in our patients, with less improvement in the first 6-months of follow-up. This association was independent of sex, age at diagnosis, time since symptoms onset, smoking and the year of onset. However, the influence of the treatment has not been explored yet.

Objectives: We aimed to explore the influence of the initial treatment on the persistent high disease activity associated with the presence of ACarPA in EA patients.

Methods: Samples were obtained at the first visit of two EA cohorts from Hospital Universitario La Paz and Hospital Universitario La Princesa, which recruit patients within one year from the clinical onset. Information on the initial treatment and the disease activity at the baseline and at 6-months of follow-up was available from 546 patients. Treatment was categorized according to the use of corticosteroids, methotrexate (MTX) and other DMARDs, and considering changes in the first 6 months. In addition, MTX dose was considered either quantitatively or as a dichotomous variable ($\geq$ 12.5 mg and < 12.5 mg). Main effects general linear regression was used for analysis, including the treatment and the other confounders as covariates.

Results: A large fraction (83%) of the EA patients received specific treatment from the initial visit. It comprised DMARD (50.1%), corticosteroids (10.6%), or a combination of both (39.3%). The most common DMARD was MTX (82.2%), whereas less frequently used medications included sulfasalazine (5.4%), leflunomide (3.2%), hydroxychloroquine (8.1%) and other (1.0%). The 35.5% of the treated patients maintained the treatment during the 6-month follow-up. The presence of ACarPA was associated with a 0.45 higher mean baseline DAS28 and with less decrease of DAS28 (ΔDAS28) from the baseline to 6 months of follow-up (β = 0.08, p = 0.016), as already communicated. This latter association persisted without modification after accounting for the initial treatment (DMARD, corticosteroids, and changes in treatment). In addition, it was independent of the consideration of all DMARDs in a single group, or separated into two categories: MTX and the other. Similarly, the association was independent on MTX dose, defined both as a categorical or a quantitative variable.

Conclusion: The association of ACarPA with a persistently increased disease activity in EA patients is independent of the initial treatment. These results reinforce the possibility that ACarPA can be useful as prognostic biomarkers for the first 6 months of evolution and indicate the need for personalized management of the patients carrying ACarPA.

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THU0097 VALUEOF ANTIBODIES AGAINST ACETYLATED PEPTIDES FOR THE CLASSIFICATION OF PATIENTS WITH EARLY ARTHRITIS

Lorena Rodríguez-Martínez[1], Holger Bang[2], Laura Nuño[3], Diana Peiteado[3], Ana Ortiz[4], Alejandro Villalva[3], Dora Pascual-Salcedo[3], Ana Martínez-Feito[3], Alejandro Balsa[3], Isidoro González-Álvaro[4], Antonio Gonzalez[1]. *[1]Instituto de Investigación Sanitaria-Hospital Clínico Universitario de Santiago, Experimental and Observational Rheumatology, Santiago de Compostela, Spain*; *[2]Orgentec Diagnostika GmbH, Mainz, Germany*; *[3]Instituto de Investigacion del Hospital de La Paz (IDIPAZ), Madrid, Spain*; *[4]Instituto de Investigación del Hospital de La Princesa (IIS-IP), Madrid, Spain*

Background: Patients with rheumatoid arthritis (RA) achieve the best response when they receive adequate treatment as soon as possible. This fact motivated the modification of the classification criteria by the ACR and the EULAR in 2010 to enable early detection. One of the changes is the increased weight conferred to the autoantibodies: rheumatoid factor and anti-citrullinated protein antibodies. As these antibodies are not present in all patients, other antibodies could provide similar information. In this regard, the antibodies that recognize an acetylated peptide from mutated vimentin (Anti-Acetylated Peptide Antibodies or AAPA) stand out (1).

Objectives: We aimed to evaluate the AAPA predictive value at the baseline visit for the classification of early arthritis patients.

Methods: A total of 438 patients with available samples and information were randomly selected from two early arthritis clinics. The AAPA were determined in baseline sera as previously described (1). Two peptides were included, one acetylated at a lysine (anti-AcLys) and the other at an ornithine (anti-AcOrn) and considered either individually or combined. The sensitivity, specificity, predictive positive (PPV) and negative (PNV) values and the AUC of the ROC curve were assessed. Logistic regression was also applied adjusting for age, sex, the centre of origin, anti-CCP, and RF. The study was approved by the ethics committee of the Hospital Universitario La Paz, the Hospital Universitario La Princesa, and Autonómico de Galicia.

Results: The AAPA at baseline were sensitive and specific for the classification of the patients fulfilling RA criteria (46.8%) at the end of the 2-year follow-up (table 1). Specifically, the anti-AcOrn antibodies were slightly

more sensitive and specific than the anti-AcLys ones. The two and their combination showed a conserved specificity for the seronegative patients, but a lower sensitivity than for the seropositive ones. Consequently, the PPV for the seronegative patients was low, although the NPV was high. In the same vein, the AUC was insufficient for the seronegative patients. The regression analysis including the anti-CCP and RF revealed a significant contribution of the anti-AcOrn antibodies (OR = 2.1, 95% CI = 1.1 – 4.0, P = 0.02), but not of the anti-AcLys antibodies. On the other hand, the inclusion of the AAPA in the classification resulted in an increase in sensitivity of 5.4% at the cost of a 13.7% lower specificity, which is an improvement over the anti-carbamylated protein antibodies.

Abstract THU0097 – Table 1. Parameters assessing the diagnostic value of the anti-acetylated peptide antibodies taken individually and in combination for the classification of the RA patients or the indicated patient subsets subset.

	anti-AcLys	anti-AcOrn	AAPA
Sensitivity			
all	37.9	44.2	50.5
anti-CCP-	16.9	16.9	22.5
anti-CCP- & RF-	15.7	15.7	21.6
Specificity			
all	84.5	86.6	81.0
anti-CCP-	87.4	87.9	83.8
anti-CCP- & RF-	86.8	86.8	82.8
PPV			
all	68.4	74.6	70.3
anti-CCP-	32.4	33.3	33.3
anti-CCP- & RF-	25.8	25.8	26.8
NPV			
all	60.5	63.6	64.8
anti-CCP-	74.6	74.7	75.1
anti-CCP- & RF-	77.8	77.8	78.3
AUC			
all	0.61	0.65	0.66
anti-CCP-	0.52	0.52	0.53
anti-CCP- & RF-	0.51	0.51	0.52

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Conclusion: The AAPA show high specificity and sensitivity for RA in early arthritis patients. However, their contribution to RA classification is minor once RF and the anti-CCP antibodies have been considered. But nevertheless, AAPA supports the drive to close the diagnostic gap in this early disease phase and to increase the likelihood of successful therapy.

REFERENCES:

[1] Juarez, M, et al. Ann Rheum Dis. 2016; 75:1099-1107

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THU0098 WHICH FACTORS INFLUENCE ACHIEVEMENT OF TREATMENT SATISFACTION IN RHEUMATOID ARTHRITIS?

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Background: The satisfaction of RA patients with their pharmacological therapy is a relevant patient reported outcome which influences treatment adherence and continuation. However, it has not been investigated frequently, and almost never in large studies.

Objectives: To assess factors exerting a potential influence on the satisfaction with the pharmacological treatment and to quantify this influence.

Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. This analysis comprises patients who were enrolled with start of a DMARD between 01/2009 and 04/2018, who were observed for at least 12 months and had been on the therapy prescribed at enrolment for at least six months.

Abstract THU0098 –Table 1.

Table 1: Results of logistic regression to analyze potential factors influencing satisfaction with drug treatment

Parameter	Odds Ratio	95% confidence limits
Satisfied at treatment start	**3.11**	**(2.61; 3.70)**
DAS28 reduction (one unit) after one year	**1.34**	**(1.26; 1.41)**
Reduction (one unit on a scale of 1-10) of pain after one year	**1.28**	**(1.23; 1.32)**
Reduction of sleeping problems (one unit on a scale of 1-10)	1.01	(0.99; 1.04)
Reduction of fatigue (one unit on a scale of 1-10)	1.00	(0.97; 1.03)
Improvement of physical function by 10 percentage points of full capacity	**1.19**	**(1.13; 1.26)**
Prior biologic therapy	**0.80**	**(0.67; 0.96)**
Reduction of glucocorticoid dose (one log(mg)/d)*	**1.37**	**(1.18; 1.59)**
Congestive heart failure	1.08	(0.62; 1.90)
Diabetes	0.98	(0.77; 1.25)
Chronic kidney disease	0.96	(0.66; 1.38)
Prior malignancies	1.08	(0.74; 1.57)
Degenerative spine disease	0.93	(0.75; 1.14)
Degenerative joint disease	0.93	(0.75; 1.14)
Osteoporosis	0.86	(0.68; 1.07)
Fibromyalgia	0.75	(0.50; 1.13)
Depression	**0.65**	**(0.50; 0.86)**
Obesity	**0.82**	**(0.69; 0.96)**
Age at disease onset (years)	1.00	(0.996; 1.01)
Women (reference: men)	1.04	(0.87; 1.24)
Seropositivity (RF/ACPA)	1.13	(0.97; 1.32)
Ever smoked	0.89	(0.76; 1.04)
Smoking habits unknown	1.09	(0.74; 1.62)
Biologic therapy (reference: csDMARDs)	1.07	(0.90; 1.28)

**Due to a highly skewed distribution of the glucocorticoid dose, the reduction of the logarithmically transformed glucocorticoid dose was used in the model.*

Satisfaction with the applied treatment was measured in four categories from ”very satisfied” to ”very unsatisfied”. Logistic regression combined with multiple imputation of missing values was performed to calculate odds ratios (ORs) for factors which might have an influence on treatment satisfaction.

Results: At treatment onset, 55% of the 8,177 patients were ”very” or ”rather” satisfied (in the following: ”satisfied”), while the rest was ”very” or ”rather” unsatisfied (in the following: ”unsatisfied”) with their therapy. After one year of treatment, 86% of patients were satisfied with their treatment. Factors with positive impact on whether patients reached the target of treatment satisfaction were satisfaction at baseline, reduction of DAS28-BSG, pain and glucocorticoid dose as well as the increase of physical function. Depression, obesity as well as a prior treatment failure of bDMARDs had a negative influence on the outcome (see Table 1). The DAS28 component most influential on treatment satisfaction was the patient global health assessment. Regarding glucocorticoid therapy, being still treated with either 5 to 15 mg (OR: 0.66, 95% CI: 0.55; 0.79) or $\geq$ 15 mg glucocorticoids (OR: 0.25, 95% CI: 0.15; 0.41) had a negative impact on the achievement of therapy satisfaction (data not shown).

Conclusion: Reductions in disease activity, pain and glucocorticoid dosage as well as improvement of physical function increase the chance to achieve treatment satisfaction. On the other hand, depression and obesity as well as prior treatment failures with bDMARDs are obstacles to therapy satisfaction. For physicians, these results suggest that efforts to taper glucocorticoid doses are worthwhile to improve patient’s satisfaction.

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THU0099 DEVELOPMENT OF A NEW PATIENT-GENERATED OUTCOME MEASURE TO IDENTIFY DISEASE-SPECIFIC DISTRESS IN PEOPLE WITH RHEUMATOID ARTHRITIS

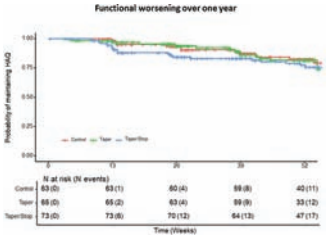
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Background: Rheumatoid Arthritis (RA) is a progressive inflammatory disease which causes pain, joint damage and disability. Patients with RA may experience psychological distress in addition to their physical symptoms. They may also experience disease-specific distress (DSD), which is related to the burden of living with their life-long illness. This phenomenon has been identified in patients with other long-term conditions, e.g. cancer, Irritable Bowel Disease, and Diabetes. In type 1 and 2 diabetes elevated DSD is associated with poorer clinical outcomes, and effective interventions can reduce diabetes distress. Patient involvement in the development of patient generated outcome measures (PGOM's) is important, as they may have different perspectives about their health condition that researchers and/or health care professionals may not have considered. Previous secondary data analysis of patient interviews has suggested that DSD does seem to exist in people with RA, as an entity distinct from other forms of psychological difficulties.
Objectives: The aim of this study was to develop a PGOM, based on previously reported domains of distress, to identify DSD in people with RA for use in clinical and research practice. The study aimed to involve patients in the development of the new outcome measure.
Methods: A three-phase qualitative study was conducted. In Phase 1 items were generated from secondary data analysis of patient interviews. In Phase 2, a focus group of people with RA were consulted with the aim to establish initial face and content validity of the measure and perform item reduction. In Phase 3, individual cognitive interviews (n=9) with people with RA were conducted to further establish face and content validity of the Scale, refine items if necessary and ensure the questionnaire _made sense' to participants. A psychometrician was consulted to consider the development of the new Scale.
Results: In Phase 1, 44 items were initially created to form the Rheumatoid Arthritis Distress Scale (RADS). After Phase 2 and 3 focus group and cognitive interviews respectively, items were reduced from 44 to 39 and three additional supplementary questions were created, to include items such as time since diagnosis and disease activity. Dimensions were classified into five domains of RA distress. Overall participants reported the content of the RADS to be clear and relevant, and that DSD is a valid concept in RA, distinct from clinical depression or anxiety
Conclusion: DSD appears to be an important concept in RA. The 39-item RADS currently demonstrates acceptable face and content validity in this patient group. It may be beneficial to establish face and content validity in a more diverse patient sample before proceeding with further psychometric testing. The RADS may be a useful tool for healthcare professionals to identify DSD in patients with RA. Direct patient involvement and their commitment have been instrumental in the development of new outcome measures.
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THU0100 PHYSICAL FUNCTION IN RA PATIENTS IN REMISSION UNDERGOING TAPERING AND/OR STOPPING OF DMARDS

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Background: Several studies including our own RETRO study have shown that tapering or stopping disease modifying anti-rheumatic drugs (DMARDs) in rheumatoid arthritis (RA) patients in sustained remission is feasible (1-3). However, tapering/stopping bears the risk of decline in physical function as some patients may relapse and face increased disease activity.
Objectives: Here we analysed the impact of tapering or stopping DMARD treatment on the physical function of RA patients, who were randomized into continuation, tapering or stopping DMARD treatment in the RETRO study.
Methods: RETRO is a multicentre, parallel-group phase 3 trial in which RA patients in stable DAS-28-ESR remission were randomized to (i) DMARD tapering, (ii) stopping DMARDs after a 24-week-taper or (iii) control strategy that continued DMARDS.[1,2,3] HAQ and DAS-28 scores were measured at 0, 3, 6, 9 and 12 months.[1,2] Functional worsening was defined as a HAQ increase of$\geq$0.25. We calculated incidences of functional worsening (per 100 person-months) in each treatment group with 95% Poisson confidence intervals and plotted event-free survival by treatment arm. The effect of treatment reduction strategy on functional worsening was assessed in a recurrent-event Cox regression model with control, taper or taper/stop group as the predictor.
Results: 201 patients were analysed. In 44 patients functional worsening was observed. Incidence (95%CI) of functional worsening was in the control 1.48 (0.77-2.59), taper 1.74 (0.95-2.92) and taper/stop arm 1.96 (1.16-3.10). The incidences suggest higher probability of functional worsening in tapering and/or stopping DMARDs, however at the end of study, functional worsening was similar among the groups (Figure). Thus, in comparison to the control group, hazard ratio (HR) (95%CI) for functional worsening was 1.21 (0.56 -2.62) in the taper arm and 1.32 (0.76-2.60) in the taper/stop arm.
Conclusion: Point estimates and survival curves show that functional decline after tapering or stopping DMARDs in RA patients with stable remission is small. Although the incidence figures suggest a trend these results do not reject with good certainty the null hypothesis of no worsening in functional status.



Abstract THU0100 – Figure 1.

REFERENCE:
[1] Haschka, J. et al. 2016; 2 Rech, J. et al. 2016; 3 Hagen, M. et al. 2018

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THU0101 TORQUE TENO VIRAL LOAD FOR MONITORING OF BIOLOGICAL THERAPIES IN RHEUMATOID ARTHRITIS

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Background: The apathogenic and highly prevalent Torque Teno Virus (TTV) is associated with the immunocompetence of its host and has been proposed for immunologic monitoring in solid organ transplantation.
Objectives: Herein we explore TTV levels in rheumatoid arthritis (RA) patients receiving biological disease-modifying anti-rheumatic drugs (bDMARDs) in the context of clinical response.
Methods: The BIOBIO study was designed to evaluate biomarkers for prediction of clinical response in patients with RA. Within this multicentre open-label trial, patients with insufficient response to MTX were randomized to TNFi (infliximab; INF), anti-IL-6 receptor (tocilizumab; TCZ), CTLA4-Ig (abatacept; ABA) or anti-CD20 (rituximab; RTX) in addition to MTX. TTV in peripheral blood samples was quantified at baseline and 3 months by RT-PCR.
Results: TTV was measured in 95 RA patients [INF (n=23), TCZ (n=22), ABA (n=27) or RTX (n=23)]. Median TTV levels at baseline were $4.2x10^4$ c/ml with no difference between the treatment groups. After 3 months of treatment patients with INF (p=0.018), ABA (p=0.071) and RTX (p≤0.001) showed an increase in TTV levels compared to baseline. There was no change in TTV in patients with TCZ, who were omitted from further analyses. TTV at 3 months after treatment was higher in patients achieving a SDAI85 response at month 6 (p=0.019). Levels of above $5.6x10^5$ c/ml at month 3 showed a 67% specificity and 81% sensitivity for a SDAI85 response at month 6, corresponding to a positive likelihood ratio of 2.6 (95% CI: 1.6-4.1). Patients in the top tertile of month 3 TTV (>$7.8x10^5$ c/ml) had lower SDAI, CDAI and DAS28 and higher SDAI85 response rates at month 6 (OR: 4.18, CI: 1.41-16.42; p=0.012). The highest non-response rates were found in patients within the lowest TTV tertile (**Table A**), and the highest remission rates were found in the highest TTV tertile (**Table B**). No patient below a TTV value of $2.7x10^4$ c/ml at month 3 showed SDAI85 treatment response at month 6.
Conclusion: Our data suggest that TTV levels in patients with RA treated with INF, ABA or RTX at month 3 are associated with clinical responses at month 6, and thus may constitute a biomarker for therapeutic monitoring.

Abstract THU0101 –Table 1.

A	No response	SDAI50	SDAI70	SDAI85	Total
LTTV	43.8%	37.5%	18.8%	0.0%	100%
MTTV	15.8%	42.1%	26.3%	15.8%	100%
HTTV	27.3%	18.2%	18.2%	36.4%	100%

B	HDA	MDA	LDA	REM	Total
LTTV	25.0%	31.3%	43.8%	0.0%	100%
MTTV	5.0%	35.0%	40.0%	20.0%	100%
HTTV	17.4%	26.1%	21.7%	34.8%	100%

Cross-tables: **A – Left:** depicting distribution of patients in different SDAI response categories at 6 months (non-overlapping) by tertiles of TTV at 3 months (LTTV: low tertile; MTTV: middle tertile; HTTV: high tertile). **B – Right:** depicting distribution of patients in different disease activity states at 6 months (HDA=high disease activity; MDA=moderate disease activity; LDA=low disease activity; REM=remission) by tertiles of TTV at 3 months

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THU0102 PATIENT DISEASE TRAJECTORIES IN BARICITINIB-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO METHOTREXATE

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Background: In RA-BEAM phase 3 study, baricitinib (bari) 4mg demonstrated clinical efficacy in patients (pts) with rheumatoid arthritis (RA) and an inadequate response to methotrexate. Bari, a selective Janus kinase 1/2 inhibitor, is approved for the treatment of moderate to severe active RA in adults in >50 countries. For improved treatment strategy, it is important to understand whether the pt population is composed of distinct pt groups with differing treatment responses and associated baseline characteristics.
Objectives: To identify different treatment trajectories, based on CDAI improvement, in bari 4mg treated pts over 52 weeks; and examine the associated clinical disease measures, structural damage score and baseline characteristics.
Methods: Growth Mixed Model (GMM), a novel latent class mixed model, was used to classify the longitudinal disease patterns instead of

predefining a clinical responder at a specific time point. GMM was applied to observed CDAI values for bari 4mg pts, continuously treated from 0-52 weeks or up to rescue, to cluster pts into subgroups based on their trajectory patterns. Following identification of the groups, baseline pt characteristics and disease measures were compared between groups.
Results: Bari 4mg treated pts (N=487) were classified into 3 groups based on their CDAI trajectory patterns: Group 1 (n=344, 71%), Group 2 (n=56, 11%), and Group 3 (n=87, 18%) (Figure). Group 1 had lower baseline CDAI (34, Table 1), achieved CDAI≤10 (low disease activity, LDA) rapidly and maintained LDA up to 52 weeks. Group 2 had higher CDAI at baseline (48, Table 1), responded quickly, and although pts took longer to attain LDA, they continued to show CDAI improvement. Group 3 had similar baseline CDAI values (48, Table 1) to Group 2 but higher baseline damage (mean total Sharp score [mTSS] of 50, versus 41 for Groups 1 and 2, Table 1). Most Group 3 pts did not achieve LDA but continued to show improvement over time. The majority of pts had no radiographic progression with the highest proportion in Group 1 (Table 2). The trajectories of average pain VAS, Health Assessment Questionnaire–Disability Index (HAQ-DI), tender joint count 28, and swollen joint count 28 were consistent in the 3 groups.

Abstract THU0102 –Table 1. Baseline characteristics:

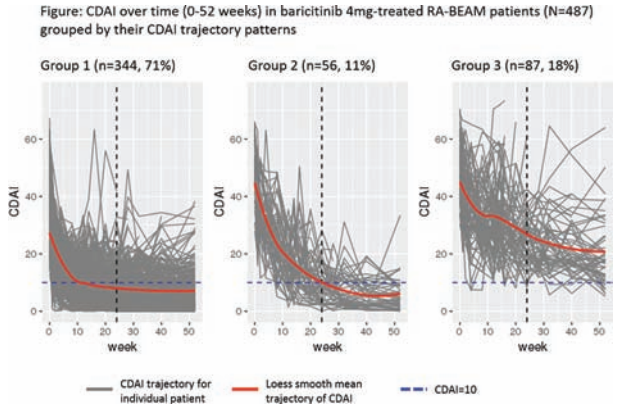
	Group 1 N=344	Group 2 N=56	Group 3 N=87
Age	53.8 (12.1)	54.0 (12.7)	52.2 (12.4)
Male, n (%)	74 (21.5)	16 (28.6)	22 (25.3)
BMI (kg/m^2)	26.8 (5.7)	25.9 (6.0)	27.0 (6.1)
CDAI	33.8 (10.0)	48.5 (10.0)	48.0 (10.4)
mTSS	41.0 (49.1)	40.6 (41.8)	49.8 (58.6)
Duration from RA diagnosis (years)	8.4 (8.0)	8.4 (9.3)	9.8 (10.2)
HAQ-DI	1.48 (0.68)	1.75 (0.64)	1.80 (0.60)

Data reported as mean (SD) unless indicated

Abstract THU0102 – Table 2. Response rates in patient groups, n (%)

		Group 1 N=344	Group 2 N=56	Group 3 N=87
CDAI ≤10	W24	214 (66.3)	28 (57.1)	2 (3.5)
W52	235 (76.8)	36 (85.7)	8 (16.0)	
mTSS change from baseline ≤0.5	W24	285 (90.8)	42 (85.7)	51 (83.6)
	W52	266 (89.3)	34 (82.9)	40 (80.0)

W=week
Conclusion: Baseline severity is associated with different treatment trajectories. With bari treatment, majority of pts achieved LDA and had no structural progression. Pts with high baseline disease activity were associated with longer time to achieve LDA. Pts with higher baseline structural damage in addition to high disease activity were less likely to achieve LDA, but consistent with the other groups, had similar low rate of joint damage progression. Long-term maintenance and continued improvement in CDAI were observed with bari treatment.



Abstract THU0102 – Figure 1

Disclosure of Interests: Peter C. Taylor Grant/research support from: Celgene, Galapagos, Eli Lilly, UCB, Consultant for: AbbVie, Galapagos, Gilead, Eli Lilly, Pfizer Inc, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead,Samsung, Sandoz and Lilly, Michael E. Weinblatt Shareholder of: Stock option: CanFite, Lycera, Scipher, Inmedix, Grant/research support from: Crescendo Bioscience, Bristol Myers Squibb, Sanofi, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, CanFite, Corrona, Crescendo, GlaxoSmithKline, Gilead, Horizon, Lilly, Lycera, Merck, Novartis, Pfizer, Roche, Samsung, Scipher, Set Point, Eduardo Mysler Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Pfizer, Novartis, Janssen, Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lily, Janssen, Medimmune, Pfizer Inc, and Roche, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lily, Janssen, Medimmune, Pfizer Inc, and Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Pfizer, Novartis, Janssen, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lily, Janssen, Medimmune, Pfizer Inc, and Roche, Andrea Rubbert-Roth Consultant for: Chugai, Eli Lilly, Roche, and Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Hexal/Novartis, Janssen, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, and Sanofi, Bochao Jia Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Luna Sun Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Yushi Liu Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Yun-Fei Chen Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Anabela Cardoso Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Yoshiya Tanaka Grant/research support from: Abbvie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Ono, Taisho-Toyama, Takeda, Speakers bureau: Abbvie, Asahi-kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Eisai, Glaxo-Smithkline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer Japan Inc, Sanofi, Takeda, UCB, YL Biologics
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THU0103 ONE IN FIVE PATIENTS WITH RAPIDLY AND PERSISTENTLY CONTROLLED EARLY RHEUMATOID ARTHRITIS REPORT POOR WELLBEING AFTER ONE YEAR OF TREATMENT

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Background: In rheumatoid arthritis (RA), good disease control without major joint damage, loss of function or disability can be achieved. Still, a substantial number of patients report poor wellbeing. A better understanding is needed on why some patients still feel unwell despite good disease control. Specific attention to this mismatch, especially early in the disease, could help to further optimize the clinical course of new patients with RA.
Objectives: To identify and characterize patients with early RA treated optimally to current standards but reporting not feeling well after 1 year of treatment.
Methods: We included participants of the Care in early RA trial with an early and persistently favorable treatment response, defined as having a disease activity score (DAS28CRP) <2.6 from 16 weeks after initiation of treatment until year 1. Feeling well was assessed with 5 patient-reported outcomes (PROs): pain, fatigue, physical functioning, RA-related quality of life and sleep quality. K-means clustering was carried out to assign patients to clusters based on these PRO scores at year 1. After clustering, Cohen's d was computed to determine the magnitude of the difference between clusters, already at treatment start (BL) and 4 months

later (w16), with respect to the 5 clustering PROs as well as for coping behavior, illness perceptions and social support.
Results: Analyses revealed 3 distinct clusters. Details are depicted in Table 1. Of 140 patients, 77.9% were assigned to the 'concordant to disease activity' cluster, 9.3% to the 'dominant fatigue' cluster and 12.9% to the 'dominant pain and fatigue' cluster. When comparing the concordant cluster with both discordant clusters, differences at BL and w16 were shown, with small effects on patients' evaluation of their disease at year 1, such as more negative beliefs about the consequences of RA at w16 in patients reporting dominant pain and fatigue at year 1. Few differences with medium effects were identified, such as a moderately higher use of avoidance as a coping style at w16 and a stronger belief that symptoms can be explained by RA at w16, in patients reporting dominant fatigue at year 1 compared to patients in the concordant cluster. Large differences between patients in concordant and discordant clusters were found for pain and fatigue levels, which were already higher after 4 months of treatment for those patients reporting persistent pain and fatigue at year 1.

Abstract THU0103 –Table 1.

Table 1. Mean scores at year 1 of the patient-reported outcomes used to assign patients to a cluster (n=140 persistent responders)

	Clusters		
	Concordant to disease activity n=109 (77.9%)	Dominant fatigue n=13 (9.3%)	Dominant pain and fatigue n=18 (12.9%)
Pain (VAS 0-100)	7	15	45
Fatigue (VAS 0-100)	10	70	42
Functionality (HAQ 0-3)	0.07	0.24	0.26
RA-related quality of life (RAQoL 0-30)	3.92	6.21	5.55
Sleep quality (PSQI 0-21)	5	6	5

Note. RA: Rheumatoid arthritis. VAS: Visual Analog Scale; HAQ: Health Assessment Questionnaire; RAQoL: Rheumatoid Arthritis Quality of Life questionnaire; PSQI: Pittsburgh Sleep Quality Index; Higher scores indicate worse pain, worse fatigue, more functional loss, worse health-related quality of life and worse sleep quality. Clinical response was defined as achieving a disease activity score (DAS28CRP) <2.6. Persistent response was defined as an early clinical response at week 16, sustained between week 16 and year 1.

Conclusion: Three distinct groups of persistent responders with early RA were identified based on their 1-year PRO profile. The majority of patients were well-synchronized, reporting very low pain and fatigue levels in concordance with their well-controlled disease activity. One in 5 persistent responders, however, seemed to have unmet needs. In view of early identification of patients at risk of poor wellbeing despite good disease control, early pain and fatigue levels and certain coping behavior and illness perceptions were recognized as potential targets for future interventions.
Disclosure of Interests: Kristien Van der Elst: None declared, Patrick Verschueren Grant/research support from: Unrestricted Pfizer Grant for Early RA research, Diederik De Cock: None declared, An De Groef: None declared, Veerle Stouten: None declared, Sofia Pazmino: None declared, Johanna Vriezekolk: None declared, Johan Joly: None declared, Philip Moons: None declared, Rene Westhovens Grant/research support from: Bristol-Myers Squibb, Consultant for: Celltrion, Galapagos-Gilead

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THU0104 HIGH-PERFORMANCE CHEMICAL ISOTOPE LABELING LIQUID CHROMATOGRAPHY MASS SPECTROMETRY FOR DISCOVERY OF METABOLITE BIOMARKERS OF RHEUMATOID ARTHRITIS

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Background: Early diagnosis of rheumatoid arthritis (RA) is hampered by suboptimal accuracy of currently available serological biomarkers. Recent advancements in metabolomic profiling include liquid chromatography mass spectrometry (LC-MS) and in-depth profiling of amine/phenol and carboxyl submetabolomes, resulting in 1000-fold increase in detection sensitivity, and universal metabolome-standard methodology to facilitate metabolome comparisons among different data sets.
Objectives: We aimed to identify a metabolite signature with consistently high accuracy for RA.
Methods: Sera from 2 RA cohorts were analyzed: Cohort A samples were from 50 RA patients, 39 female (mean age 49.9), 11 male (mean age 47.8), symptom duration <3 years, DAS >3.7, naïve to b-DMARD, and 50 age and sex-matched healthy controls. Cohort B samples were from 50 RA patients, 40 female (mean age 53.4), 10 male (mean age 57.2), symptom duration <5 years, samples from both pre- and post- (3 months) treatment with TNFi and a second set of 50 age and sex-matched healthy controls. Amine/phenol- and carboxyl-containing metabolites were labeled by ^{12}C-dansyl (Dns) chloride and ^{12}C-dimethylaminophenacyl (DmPA) bromide, respectively. A pooled sample was generated and labeled by ^{13}C-Dns and ^{13}C-DmPA, respectively. LC-UV quantification was applied for sample normalization. After mixing individual ^{12}C-labeled serum with the ^{13}C-labeled pool in equal amounts, the mixtures were analyzed by LC-QTOF-MS for relative quantification.
Results: A total of 3415 amine/phenol and 2114 carboxyl metabolites were commonly detected in more than 80% of the samples. For amine/phenol submetabolome profiling, partial least squares discriminant analysis (PLSDA) showed a clear separation of the groups for each cohort (R2=0.98;Q2=0.92 for cohort A and R2=0.93;Q2=0.79 for cohort B). Similarly, for carboxyl submetabolome profiling, a clear separation between RA and controls was demonstrable (R2=0.93;Q2=0.80 for cohort A and R2=0.84;Q2=0.55 for cohort B). 13 positively identified amine/phenol-containing metabolites, including o-phosphoethanolamine and glycyl-valine, were both significant in cohort A and cohort B, and each of these metabolites showed similar fold changes between RA and controls for both cohorts. 5 carboxyl-containing metabolites, with 1 positively identified, azelaic acid, and 4 unidentified, were both significant in 2 cohorts. The ROC AUC (95%CI) of the 13 amine/phenol-containing metabolite panel were 0.99 (0.94-1.00), 0.98 (0.92-1.00) and 0.98 (0.95-1.00) for cohort A and cohort B (pre- and post-treatment), respectively, with sensitivity/specificity of 94%/96%, 94%/95%, 94%/94%. The ROC AUC (95%CI) of the 5 carboxyl metabolite panel were 0.92 (0.86-0.97), 0.96 (0.91-0.99), 0.89 (0.82-0.95), respectively, with sensitivity/specificity of 86%/86%, 90%/91%, 80%/80%. The combined panel of 18 metabolites demonstrated ROC AUC>0.99 with sensitivity and specificity>95% for each cohort. None of these biomarker metabolites correlated with age, gender, or symptom duration.
Conclusion: Consistent discrimination in metabolite profiles between discovery and verification cohorts generated high priority candidates for further biomarker validation in RA.
Disclosure of Interests: Xiaohang Wang: None declared, Joel Paschke: None declared, Rana Dadashova: None declared, Edna Hutchings: None declared, Liang Li: None declared, Walter P Maksymowych Grant/research support from: AbbVie, Pfizer, Janssen, Novartis, Consultant for: AbbVie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis
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THU0105 DIVERSE DISEASE ACTIVITY MEASURES DEMONSTRATE THAT THE INITIATION OF TOFACITINIB LEADS TO SUSTAINED CLINICAL RESPONSES IN THE MAJORITY OF RHEUMATOID ARTHRITIS PATIENTS IN A CLINIC UTILIZING A TREAT TO TARGET STRATEGY

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Background: Treating Rheumatoid Arthritis (RA) patients to target (T2T) has been shown to result in better outcomes in patients with RA [1] and offers the opportunity to analyze clinical responses and changes in certain laboratory parameters after treatment with specific therapeutic agents.
Objectives: To determine the frequency, magnitude, and duration of clinical responses and changes in certain laboratory parameters after initiating Tofacitinib in a single community rheumatology clinic (author's) utilizing a T2T strategy.
Methods: Patients at a community based rheumatology clinic undergo disease activity measure assessments (DAMs) on a routine basis as part of the implementation of the T2T strategy. These assessments include the disease activity score in 28 joints (DAS28CRP), and the more objective

measures, the power Doppler joint count (UPDJC), which demonstrates hyper vascularization of the synovium, and the 12-multibiomarker disease activity test (MBDA), which incorporates 12 biomarkers in an algorithm leading to a single disease activity score. The UPDJC includes scoring at six dorsal wrist and six dorsal MCP sites [2]. The average duration of RA in patients at this clinic is > 10 years.

Results: Fifty two patients were found to be in inadequate control at the clinic and were started on Tofacitinib. Ten patients discontinued treatment with Tofacitinib within the first year, four because of an inadequate response, and four because of adverse effects (two deaths, one with lung cancer and one with colon cancer), and two because of noncompliance or loss to follow up.

Forty two patients remained on treatment with Tofacitinib for at least one year, and at this point in time, 21 patients have remained on the drug for two or more years. The DAM assessments and selected changes in certain laboratory parameters for two yearly time points are shown for these patients in Table 1.

Clinical significance was determined by Paired-samples T tests.

Conclusion: Patients showed sustained significant clinical responses for two or more years by all three diverse DAMs and several other common measures of clinical response. The initiation of Tofacitinib in a Rheumatology clinic utilizing a T2T strategy clearly showed sustained clinical responses for up to two years for a significant number of patients. Significant changes in some of the cytokine components of the MBDA were also noted, including increases in leptin levels.

The use of the T2T strategy offers a unique opportunity to obtain real time data on patients treated with specific therapeutic agents at a community rheumatology clinic.

Abstract THU0105 –Table 1.

Table I. Clinical Responses Following the Treatment of RA Patients with Tofacitinib

	Baseline	Year One	Year One		Year Two	Year Two	
	Data	N	Data	Prob*	N	Data	Prob*
USPDJC[1]	8.7 +/- 3.8	35	6.2 +/- 2.2	***	20	6.6 +/- 2.2	**
DAS28CRP	4.97 +/- 1.01	26	3.55 +/- 1.00	***	15	3.12 +/- 1.28	***
DAS28ESR	5.37 +/- 0.83	21	3.91 +/- 1.28	***	15	3.94+/- 1.15	***
CDAI	30.1 +/- 11.5	25	14.7 +/- 7.8	***	15	14.3 +/- 10.3	***
MBDA[2]	48.5 +/- 12.2	39	42.4 +/- 10.4	***	24	38.2 +/- 11.5	**
Dr Global	4.8 +/- 1.3	35	2.9 +/- 1.0	***	19	3.0 +/- 1.3	***
Pt Global	5.3 +/- 2.7	33	3.8 +/- 2.7	***	18	3.1 +/- 2.4	*
TJC[3]	13.1 +/- 6.6	36	7.2 +/- 6.6	***	20	6.3 +/- 6.8	***
SJC[4]	7.9 +/- 3.8	36	3.4 +/- 4.5	***	19	3.2 +/- 2.1	***
CRP	8.4 +/- 8.5	24	4.3 +/- 2.8	*	12	3.5 +/-3.5	NS
ESR	24.4 +/- 15	32	22.9 +/- 16	NS	19	20.6 +/- 15	NS
VCAM1	0.70+/- 0.22	25	0.60+/- 0.14	*	15	0.57+/- 0.11	*
TNFR_1	1.7 +/- 0.5	24	1.4 +/- 0.4	**	15	1.4 +/- 0.5	*
YKL_40	114 +/- 72	26	85 +/- 55	*	14	75 +/- 38	*
Leptin	36.5 +/- 35	23	40 +/- 32	***	17	39 +/- 26	***
	prob <0.05 *		prob <0.01 **		prob <0.001 ***		
	Ultrasound Powerdoppler Joint count[1]		Multi-biomarker Disease Activity Score[2]				
	Tender Joint Count[3]		Swollen Joint Count[4]				

REFERENCES:

[1] Smolen, J. et al. Treating Rheumatoid Arthritis to Target: Recommendations of an International Task Force. Ann. Rheum. Dis 2010;69:631-6372.

[2] Shin-ya Kawashiri et. All. The power Doppler Ultrasonography Score from 24 Synovial Sites or 6 Synovial Sites, including the MCP joints, reflects the Clinical Disease Activity and Level of Serum Biomarkers in Patients with RA. Rheumatology (2011) 50 (5): 962-965.

Disclosure of Interests: None declared

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THU0106 SYSTEMIC IMMUNE-INFLAMMATION INDEX IN RHEUMATOID ARTHRITIS PATIENTS: RELATION TO DISEASE ACTIVITY

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Background: Among the immune system elements, neutrophils, lymphocytes and platelets play a role in the regulation of inflammation while also undergoing changes secondary to inflammation. Recently, the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been used as markers of systemic inflammation including rheumatoid arthritis (RA). It was reported that systemic immune-inflammation index (SII) is positively correlated with neutrophil and platelet counts and inversely correlated with lymphocyte count.

Objectives: We investigated whether SII in RA patients and compare between active cases and those in remission.

Methods: This research is a cross-sectional study. In 734 RA patients registered in the database of our department from January to April in 2016, a total of 574 eligible RA patients were included in this study, excluding 160 patients whose neither RA disease activity or laboratory data were available. Correlations of SII with the disease activity of RA were evaluated. SII was calculated by the following calculation formula; SII = Netrophils (%)/Lymphocyte (%) * Platelets (G/L).

Results: The median age of patients was 65.0 (IQR: 53.0-73.0) years and the median of disease duration was 9.0 (6.0-14.0) years. The DAS28-ESR was median 2.65 (1.90 - 3.37). SII was 612.0 (400.6 – 951.8). There was a significant correlation between SII and DAS28-ESR ($r=0.322$, $P<0.0001$), and SII was significantly elevated as disease activity increased (median 513.6 in remission group, 605.7 in low disease activity group, 793.8 in moderate disease activity group and 1367.1 in high disease activity group, respectively; $P<0.00001$). In contrast to SII, in NLR no significant difference was observed in all groups. The cut-off of SII was 635.9, 688.6 and 912.5 for DAS28-ESR remission, low disease activity and high disease activity. In multiple regression analysis of LogSII, compared to conventional DMARDs treatment, anti-cytokine therapy such as anti-IL-6 receptor inhibitor or anti-TNF inhibitor showed a significant negative correlation, but no significant differences were observed with abatacept or JAK inhibitor.

Conclusion: In this study, for the first we demonstrated that SII was more strongly related to disease activity than NLR. SII is an emerging inflammatory biomarker which could be used to evaluate disease activity in RA patients. A larger scale longitudinal study is recommended to confirm the present results and further demonstrate the relation to medications received and disease outcome.

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THU0107 BARIATRIC SURGERY DOES NOT PREVENT THE DEVELOPMENT OF RHEUMATOID ARTHRITIS IN OBESE SUBJECTS

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Background: Obesity is among the risk factors for rheumatoid arthritis (RA)[1,2]. In subjects with RA, bariatric surgery-induced weight loss has been associated with a lower disease activity, a decrease in inflammatory markers and a lower use of disease-modifying antirheumatic drugs[3]. However, the effect of bariatric surgery on the prevention of RA is not known. We have previously shown that bariatric surgery reduces the risk of gouty arthritis and psoriasis in obese subjects[4,5].

Objectives: By exploiting a longitudinal study enrolling more than 4000 obese subjects, we aim to determine if bariatric surgery prevents the incidence of RA.

Methods: The Swedish Obese Subjects (SOS) study is a longitudinal controlled trial on the effect of bariatric surgery on the incidence of obesity-related diseases. It includes 4047 obese subjects: 2010 underwent bariatric surgery and 2037 constituted the matched control group[6]. Seven Swedish local ethics review boards approved the study protocol. SOS study participants who developed RA were identified by searching the Swedish National Patient Register. Eleven subjects with prevalent RA at baseline are excluded by the analyses. Patients were followed up until diagnosis of RA, death, migration or end of follow-up (December 2016).

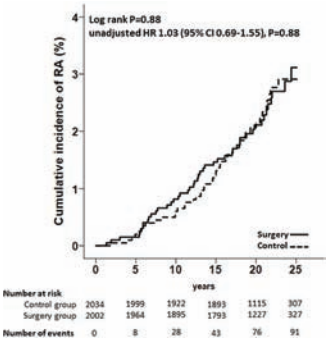
Results: During a follow-up for up to 29 years, 92 subjects developed RA. Fifty-one individuals (55%) had a seropositive RA (serostatus was unknown for 17 subjects). Forty-seven subjects (2.3%) developed RA in the surgery group compared to 45 subjects (2.2%) in the control group. Bariatric surgery was not associated with the incidence of RA during follow up (log-rank P=0.88; unadjusted Hazard Ratio-HR 1.03, 95% Confidence Interval-CI 0.69-1.55, P=0.88, Figure 1). Similar results were

obtained if only subjects with seropositive RA were included in the analysis. Adjustment for confounding factors did not affect the results (HR for bariatric surgery after adjustment for confounding factors 0.92, 95% CI 0.58-1.45, P=0.72).

Conclusion: In a large cohort of obese subjects followed up for up to 29 years, bariatric surgery did not affect the incidence of RA years.

REFERENCES:

[1] Qin B, Yang M, Fu H, et al. Body mass index and the risk of rheumatoid arthritis: a systematic review and dose-response meta-analysis. Arthritis Res Ther 2015;17:86.
[2] Lu B, Hiraki LT, Sparks JA, et al. Being overweight or obese and risk of developing rheumatoid arthritis among women: a prospective cohort study. Ann Rheum Dis 2014;73:1914-22.
[3] Sparks JA, Halperin F, Karlson JC, Karlson EW, Bermas BL. Impact of Bariatric Surgery on Patients With Rheumatoid Arthritis. Arthritis Care Res (Hoboken) 2015;67:1619-26.
[4] Maglio C, Peltonen M, Neovius M, et al. Effects of bariatric surgery on gout incidence in the Swedish Obese Subjects study: a non-randomised, prospective, controlled intervention trial. Ann Rheum Dis 2016.
[5] Maglio C, Peltonen M, Rudin A, Carlsson LMS. Bariatric Surgery and the Incidence of Psoriasis and Psoriatic Arthritis in the Swedish Obese Subjects Study. Obesity (Silver Spring) 2017;25:2068-73.
[6] Sjöström L, Narbro K, Sjöström CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med 2007;357:741-52.



Abstract THU00107 – Figure 1

Abbreviations: HR, hazard ratio; C.I., confidence interval.

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THU0108

11. RHEUMATOID ARTHRITIS – PROGNOSIS, PREDICTORS AND OUTCOME CONCORDANCE BETWEEN PHYSICIAN AND PATIENT ASSESSMENT OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS USING DISEASE ACTIVITY SCORE

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Background: Involving patients with rheumatoid arthritis (RA) in the assessment of their disease may increase adherence to treatment, improve disease outcomes and reduce consultation time.

Objectives: To evaluate the concordance between physician and patient assessment of disease activity in RA using Disease Activity Score (DAS-28).

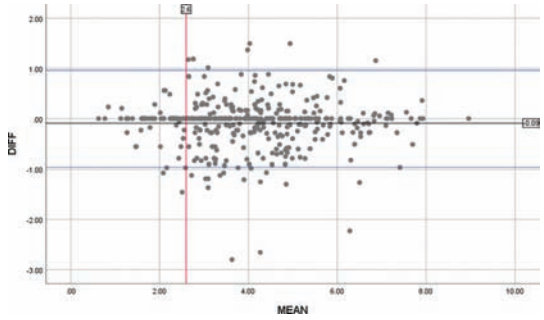
Methods: During the routine consultation, patients were briefed about DAS-28 by their rheumatologist. Using a standard DAS-28 mannequin, physicians, patients and nurses reported the number of tender and swollen joint, inflammatory markers and global health on a 0-10 Likert scale. DAS-28, Clinical Disease Activity Index (CDAI) and Simple Disease Activity Index (SDAI) were calculated blindly by each participant. Agreement between physician- and patient-DAS categories was calculated using weighted kappa (WK) for category comparison. Concordance between physician- and patient-DAS was estimated using the Bland-Altman method. Predictive factors of positive concordance between physician and patient-DAS were identified using logistic regression.

Results: Four hundred and twenty patients from 7 Middle-Eastern countries were included, with a mean age of 49 years (SD 12), 84% of females, disease duration of 11 years (SD 8). Mean physician-DAS-28 was 4.03 (SD 1.51). 65% had positive rheumatoid factor, 56% had positive ACPA, 30% had erosive disease and 34% were on biotherapy. Agreement between physician- and patient-DAS categories was 89%, WK was 0.84. WK were 0.80 for DAS physician-nurse, 0.79 for DAS patient-nurse, 0.83 for CDAI physician-patient and 0.88 for SDAI physician-patient agreements respectively. All activity measures were higher in patients compared to physicians, except for the swollen joints count. The mean difference between physician- and patient-DAS was -0.09 [95% CI -0.14; -0.04] and was smaller in patients in remission (Figure 1: Bland Altman plot). Concordance was statistically associated with CRP and patient SDAI.

Conclusion: Concordance between patient and physician assessment of disease activity in RA was excellent and was higher using SDAI followed closely by DAS-28 and CDAI. Self-assessment of disease activity should be decided according to the physician's clinical judgment.

REFERENCES:

[1] Gossec L, et al. Arthritis Rheumatol 2016; 68 (suppl 10).
[2] Smolen J, et al. Arthritis Research & Therapy (2016) 18:114.
[3] Studenic Pet al. Arthritis Rheumatol. 2012;64(9):2814–23.



Abstract THU0108 – Figure 1. Concordance between physician- and patient-DAS-28 using the Bland and Altman method.

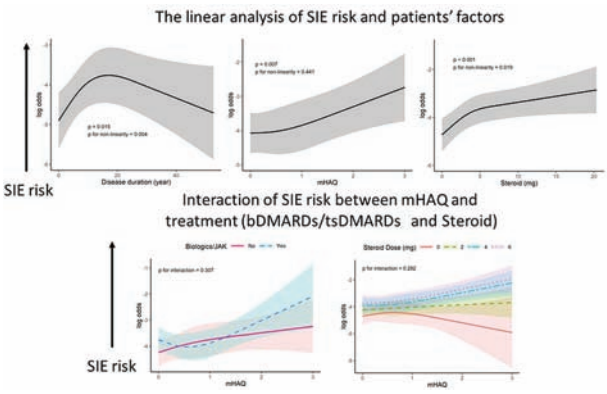
The physician-patient DAS-mean is plotted on the X-axis. The physician-patient DAS-difference is plotted on the Y-Axis. The horizontal black line corresponds to the mean DAS difference (-0.09 [95% CI -0.14; -0.04]). The horizontal blue lines correspond to +/-1.96 SD. The vertical red line corresponds to the DAS-28 cut-off for remission (2.6).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.6055

Rheumatoid arthritis – comorbidity and clinical aspects

THU0109 INCREASED MODIFIED HEALTH ASSESSMENT QUESTIONNAIRE (MHAQ) SCORE IS INDEPENDENTLY ASSOCIATED WITH HIGH RISK OF SEVERE INFECTION IN RHEUMATOID ARTHRITIS (RA) PATIENTS

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Background: Severe infections that complicate rheumatoid arthritis may cause significant morbidity and mortality. The Modified Health Assessment Questionnaire (MHAQ) is one of the scores most used for measuring the functional status of rheumatoid arthritis (RA) patients. However, the relationship between the MHAQ score and severe infection risk has not been well studied [1].
Objectives: To examine the relationship between disease-associated functional status (MHAQ) and severe infection events (SIE) in rheumatoid arthritis patients.
Methods: We used data from the "MiRAi" cohort in Japan. In total, 2174 RA outpatients were examined at the Osaka Minami Medical Center between January 2012 and October 2017. The risk factors were identified and evaluated by multivariate logistic regression, linearity analysis. Interactions of SIE risk between MHAQ and treatment were also observed.
Results: The cohort contributed to 8206 patient-years of follow-up. Overall, 251 SIEs were observed and the incidence of SIE was 3.0 infections per 100 patient-years. The mean age at first observation was 61.7 years and the mean disease duration was 10.3 years. The use of glucocorticoids (GCs), methotrexate (MTX), and biologic and targeted synthetic disease-modifying antirheumatic drugs (bDMARDs/tsDMARDs) was 59.2%, 63.8%, and 40.3%, respectively. The mean Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), Disease Activity Scores of 28 joints (DAS28), and MHAQ at first observation were 9.76±6.39, 10.1±6.87, 2.67±0.96, and 0.43 ±0.58, respectively. Disease duration, the MHAQ score, and prednisolone dose (p=0.015, 0.007, and <0.001, respectively) were significantly associated with SIE risk (Figure). Age, sex, stage, bDMARDs/tsDMARDs use, DAS28-CRP, and MTX dose (mg/week) did not predict a significant increase in SIE. The risk of SIE increased linearly with the MHAQ. The SIE risk increased rapidly from 0 to 5 mg of prednisolone, and then increased gradually over 5 mg. The SIE risk peaked at around 20 years disease duration. No significant interaction between MHAQ and bDMARDs/tsDMARDs or glucocorticoid use were observed (p=0.307, 0.282, respectively).
Conclusion: An increased MHAQ score was lineally associated with SIE, and did not show significant interactions with bDMARD/tsDMARD use or the oral glucocorticoid dose. Therefore, the MHAQ score is considered to be a strong, independent risk factor for infection in RA patients.



Abstract THU0109 – Figure 1.

REFERENCE:

[1] Yamanaka H, Askling J, Berglind N, Franzen S, Frisell T, Garwood C, Greenberg JD, Ho M, Holmqvist M, Novelli Horne L, et al: Infection rates in patients from five rheumatoid arthritis (R017, 3(2):e000498A) registries: contextualising an RA clinical trial programme. *RMD Open* 2017, 3(2): e000498.

Disclosure of Interests: Yuji Yoshida: None declared, Shiro Ohshima Grant/research support from: AbbVie, Eisai, Asahikasei, Speakers bureau: AbbVie, Eisai, Bristol-Meyers, Novartis, Astellas, Nippon-Kayaku, Pfizer, UCB, Ayumi, Daiichi-Sankyo, Takeda, Tanabe-Matsubishi, Chugai, Eri Oguro: None declared, Kentaro Kuzuya: None declared, Yasutaka Okita: None declared, Hidetoshi Matsuoka: None declared, Satoru Teshigawara: None declared, Maiko Yoshimura: None declared, Kentaro Isoda: None declared, Yoshinori Harada: None declared, Jun Hashimoto: None declared, Yukihiko Saeki: None declared
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THU0110 DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RA WITH SJÖGREN'S SYNDROME ENROLLED IN A LARGE OBSERVATIONAL US REGISTRY

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Background: Sjögren's syndrome (SS) is known to occur secondary to RA diagnosis, but its impact on RA outcomes is poorly understood. In the US-based Corrona registry, SS has a prevalence rate of 0.30 in patients (pts) with RA.[1]
Objectives: To compare disease activity and patient-reported outcomes (PROs) in pts with and without SS, in a national sample of pts with RA.
Methods: We identified adult pts with rheumatologist-diagnosed RA from a large observational US registry (Corrona RA), with at least one visit with known SS status between 22 Apr 2010 and 31 Jul 2018 and a visit 12 (±3) months after index date. SS status was captured using physician forms at enrollment and follow-up visits. The index date was the date of first capture of SS diagnosis, or first visit in which SS status was recorded for pts without a diagnosis of SS (non-SS pts). Both those with and without SS were required to have initiated a targeted synthetic (ts) or biologic (b)DMARD. Non-SS pts had to be enrolled for ≥12 months. Pts were frequency matched 1:1 based on RA duration prior to 1:1 propensity score matching (PSM) based on variables associated with treatment response. Outcomes 12 months after index visit were compared in pts with and without SS. Primary outcome was mean change in CDAI score from index visit to Month 12; secondary outcome was mean change in PROs (pain, fatigue, pt global assessment and morning stiffness).

Abstract THU0110 –Table 1.

Table 1. Baseline characteristics of the matched RA cohort

	Patients with RA + SS (n=283)	Patients with RA only (n=283)
Age, years, mean (SD)	58.4 (12.2)	58.7 (12.8)
Sex, female	235 (83.0)	235 (83.0)
Duration of RA, years, mean (SD)	10.5 (10.0)	10.3 (9.7)
Co-morbidities		
CV disease*	32 (11.3)	31 (11.0)
Malignancy†	29 (10.2)	31 (11.0)
Serious infections‡	24 (8.5)	24 (8.5)
Anti-cyclic citrullinated peptide +, n/m (%)	56/114 (49.1)	66/119 (55.5)
RF+, n/m (%)	91/137 (66.4)	80/144 (55.6)
Erosive disease, n/m (%)	74/216 (34.3)	64/197 (32.5)
Subcutaneous nodules, n/m (%)	69/283 (24.4)	73/283 (25.8)
CDAI score, mean (SD)	24.0 (14.9)	24.1 (14.7)
Number of prior b/tsDMARDs		
0	116 (41.0)	121 (42.8)
1	77 (27.2)	70 (24.7)
≥2	90 (31.8)	92 (32.5)
Number of prior csDMARDs		
0	16 (5.7)	16 (5.7)
1	116 (41.0)	110 (38.9)
≥2	151 (53.4)	157 (55.5)

Data are n (%) unless otherwise stated
*History of coronary artery disease, myocardial infarction, congestive heart failure requiring hospitalisation, acute coronary syndrome, unstable angina, cardiac revascularisation procedure, cardiac arrest, ventricular arrhythmia, stroke, transient ischemic attack or other CV event
†History of lung cancer, breast cancer, lymphoma, skin cancer (melanoma and squamous cell carcinoma) or other cancer
‡Infection required hospitalisation or IV treatment
b/tsDMARD=biologic or targeted synthetic DMARD; csDMARD=conventional synthetic DMARD; CV=cardiovascular; n/m=number of patients/total number of patients with available data; SS=Sjögren's syndrome

Abstract THU0110 –Table 2.

Table 2. Mean (SD) change in CDAI score and PROs from index visit to 12 month follow-up visit

	Patients with SS + RA (n=283)	Patients with RA only (n=283)	p value*
CDAI	8.8 (14.6)	9.3 (14.3)	0.704
Patient pain	6.5 (29.2)	14.0 (28.0)	0.002
Patient fatigue	4.3 (29.9)	13.0 (29.9)	0.001
Patient global assessment	5.5 (29.1)	13.0 (28.5)	0.002
Morning stiffness (min)	19.8 (245.2)	21.2 (250.7)	0.947

*Estimated using Student's *t*-tests
PRO=patient-reported outcome

Results: After PSM, baseline characteristics in 283 pairs of pts with and without SS were well balanced (Table 1). Mean change in CDAI score was numerically lower in SS than non-SS pts (8.8 vs 9.3; Table 2), but this did not reach statistical significance. Improvements in pain, fatigue and stiffness were 2–2.5-fold greater for non-SS than SS pts (Table 2).
Conclusion: Among those initiating b/tsDMARD treatment, improvements in RA-related PROs were lower in pts with RA with SS than non-SS pts. Physicians may want to consider SS status secondary to RA when managing pts with RA and specifically explore whether additional intervention is needed to improve the pt experience for pts with RA.

REFERENCES:

[1] Harrold LR, et al. *Arthritis Rheumatol*. 2018;70(suppl 10): abstract 541.

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Disclosure of Interests: Leslie R Harrold Shareholder of: Corrona LLC, Grant/research support from: Grant funding: Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Genentech, Employee of: Corrona LLC, Ying Shan Employee of: Corrona LLC, Sabrina Rebello Employee of: Corrona, LLC, Neil Kramer Shareholder of: Johnson & Johnson, Pfizer, Regeneron, AbbVie, Amgen, Sean Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Evo Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Sheila Kelly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Joel Kremer Grant/research support from: AbbVie, Genentech, Lilly, Novartis, Pfizer, Consultant for: AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, Elliot D Rosenstein Grant/research support from: AbbVie, Novartis, Consultant for: Amgen, Bristol-Myers Squibb, Boehringer Ingelheim, Speakers bureau: Amgen, Bristol-Myers Squibb
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THU0111 ANGIOGENIC T CELLS AS AN INDEPENDENT PREDICTOR OF VASCULAR STIFFNESS IN VERY EARLY RHEUMATOID ARTHRITIS

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Background: Angiogenic T cells (Tang) are responsible of vascular repair and homeostasis. Decreased Tang frequencies have been reported in rheumatoid arthritis (RA), in association with disease activity and previous history of cardiovascular (CV) disease. However, excess of CV risk is already present during the early stage of RA. Whether Tang cells are associated with subclinical vascular abnormalities remains unknown.
Objectives: To evaluate whether Tang cells could be associated with subclinical CV endpoints (subclinical atherosclerosis and vascular stiffness) in the very early stage of RA.
Methods: Patients were recruited upon early referral to the rheumatology department. All patients were untreated at the time of sampling. Tang (CD3+CD31+CXCR4+) frequency was assessed by flow cytometry in peripheral blood samples. Plaque occurrence, cIMT and stiffness parameters were analyzed by Doppler ultrasound in internal carotid, middle cerebral and basilar arteries.
Results: 53 patients were recruited, 47 fulfilling 2010 ACR/EULAR classification criteria for RA (36 women, 26 FR+ and 26 ACPA+) and 6 fulfilling criteria for Clinically Suspect Arthralgia (CSA) (6 women, 3 RF+ and 2 ACPA+). Tang frequency did not differ between RA and CSA (p=0.382) and it was negatively associated with DAS28 (r=-0.448, p<0.001) and SDAI (r=-0.385, p=0.006), but not with duration of the symptoms (r=0.053, p=0.713)). Tang levels were not related to individual traditional CV risk factors, body mass index, wait circumference (all p>0.050) nor with the modified SCORE (r=-0.173, p=0.244) or Framingham Risk Score (r=-0.127, p=0.399). Neither atherosclerosis plaque occurrence (r=0.631) nor the cIMT (r=0.070, p=0.652) were associated with Tang levels.
Tang frequency paralleled carotid peak systolic velocity (r=0.399, p=0.008) and end diastolic velocity (r=0.332, p=0.034) in internal carotid artery. Moreover, Tang positively correlated stiffness parameters: vascular strain (VS, r=0.428, p=0.010), vascular distensibility (VD, r=0.479, p=0.004), vascular stiffness (VSf, r=-0.519, p<0.001) and pressure-strain elastic modulus (PSEM, r=-0.531, p<0.015) in left internal carotid artery. Finally, Tang frequency was an independent predictor of stiffness parameters after adjusting for mSCORE, body mass index, DAS28, RF and ACPA positivity: VS (β=0.451, p=0.045), VD (β=0.462, p=0.026), VSf (β=-0.422, p=0.035) and PSEM (β=-0.446, p=0.026).
Conclusion: Tang cells may have a very early role on vascular stiffness in RA. These results point to the Tang subset as the missing link between disease activity and vascular abnormalities during the first stage of the disease.
Disclosure of Interests: None declared
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THU0112 SECULAR TRENDS IN THE INCIDENT RISK OF ACUTE MYOCARDIAL INFARCTION IN RHEUMATOID ARTHRITIS RELATIVE TO THE GENERAL POPULATION

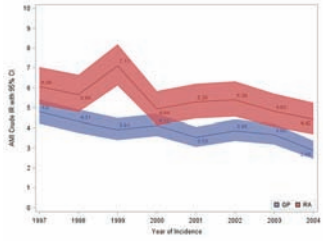
Kiana Yazdani, Hui Xie, Antonio Aviña, Yufei Zheng, Michal Abrahamowicz, Diane Lacaille. *Arthritis Research Canada, Richmond, Canada*

Background: Recent studies have demonstrated a declining trend in RA mortality relative to the general population (1). This improvement in mortality could be due to improvement in incident risk of cardiovascular events that are the leading cause of excess deaths in RA (2).
Objectives: Our objective was to assess secular trends in ten-year incident risk of acute myocardial infarction (AMI) in incident cohorts of RA versus general population controls, using administrative health data.
Methods: We conducted a retrospective study of a population-based cohort of incident RA cases who first met previously published RA criteria between 01/01/1997 and 31/12/2004 in British Columbia, followed until 12/2014, with general population controls matched 2:1 on gender, age, and index year. Individuals were excluded if they had a diagnosis of MI prior to index date. Incident AMI was defined as first AMI during follow-up using ICD codes (ICD-9 code 410/ICD-10 code I21) in Hospital Discharge data or death certificate in Vital Statistics data. RA and general population cohorts were stratified according to year of RA incidence,

defined according to first RA visit, using a 7-year wash-out period. Incident rates (IRs) of AMI for RA and general population cohorts, as well as incident rate ratios (IRRs), with 95% confidence intervals (CI) were calculated per calendar years of incidence. Multivariable Cox Proportional Hazard models with left truncation were used to estimate risk of AMI in RA relative to general population while controlling for potential confounders, with contribution of person time of follow-up starting from index date (second RA visit) to avoid immortal time bias and censoring at ten years from incident year, or last health care utilization. To examine whether secular trends differed in RA relative to general population, an interaction term was tested between the RA indicator and year of RA incidence. To account for non-linear effect of cohort year, we compared cox regression models with linear, quadratic, and flexible spline forms of the cohort-year effects and the model with the best AIC was used to interpret the data.

Results: 23,237 RA individuals (66.4% female; mean [SD] age 58[16.88] years) and 46,474 controls experienced 1,133 and 1,646 incident AMI, respectively. Cox Proportion model with the lowest AIC best fit the data. Risk of AMI was significantly higher in RA vs. general population [aHR (95% CI): 1.21(1.10, 1.32); p<0.001]. A significant decline was observed in risk of AMI over calendar year of incidence in both RA [0.94(0.92, 0.97); p<.0001] and controls [0.93(0.91, 0.95); p<.0001]. The decline in AMI risk did not differ significantly in RA vs. general population [interaction p=0.555].

Conclusion: Our finding suggests that the risk of AMI has significantly decreased over time in RA and general population cohorts. However, the declining trend was not significantly different in RA compared to the general population.



Abstract THU0112 – Figure 1

REFERENCES:

[1] Lacaille, D., et al., *Improvement in 5-year mortality in incident rheumatoid arthritis compared with the general population—closing the mortality gap*. Annals of the Rheumatic Diseases, 2016.

[2] Myasoedova, E. and S.E. Gabriel, *Overview of rheumatoid arthritis and mortality in relation to cardiovascular disease*, in *Handbook of Cardiovascular Disease Management in Rheumatoid Arthritis*, A.G. Semb, Editor. 2017, Springer International Publishing: Cham. p. 1-17.

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THU0113 RHEUMATOID ARTHRITIS ASSOCIATED INTERSTITIAL LUNG DISEASE, CLINICAL CHARACTERISTICS AND PREDICTORS OF MORTALITY

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Background: Interstitial lung disease (ILD) is a serious extraarticular manifestation of rheumatoid arthritis (RA) associated with excess mortality. No evidence-based approach to therapy for RA-ILD exists, but ongoing studies investigate the role of antifibrotic therapies for progressive fibrosing ILD, including progressive fibrosing RA-ILD.

Objectives: The aim of the present study was to investigate the frequency of progressive fibrosing ILD, the clinical characteristics and mortality of RA-ILD in a well-characterised, population-based cohort.

Methods: We identified patients with RA-ILD diagnosed and followed at the ILD referral center in Aarhus, Denmark between 2004 and 2016. Adjusted hazard rate ratios for death were estimated using Cox regression models. The presence of progressive fibrosing ILD was assessed using recently proposed definitions of relative forced vital capacity (FVC) decline ≥10%, relative diffusion capacity of the lung for carbon monoxide (DLco) decline ≥15% or worsening symptoms or a worsening radiological appearance accompanied by a ≥ 5-<10% relative decrease in FVC.

Results: We identified 102 patients with RA-ILD. Mean follow-up was 3.8 years and median survival was 7.1 years. Thirty-eight patients died during follow-up, and the majority of deaths were from respiratory causes. Predictors of mortality in a multivariate model were DLco and high titers of IgM rheumatoid factor, but not the presence of a UIP-pattern on high resolution computed tomography. Fifty-three patients (52%) had progressive fibrosing ILD.

	Progressive fibrosing RA-ILD n=53	Stable RA-ILD n=49	p-value	Typical UIP n=42	Probable UIP n=13	NSIP n=43	p-value**
Age (SD)	68.8 (9.6)	67.6 (11.7)	0.86	70.2 (9.7)	69.2 (7.3)	66.2 (12.1)	0.17
Female gender%	51	57	0.53	50	54	53	0.80
FVC (SD)	87.3 (24.7)	91.7 (24.2)	0.35	86.5 (25.1)	91.8 (30.6)	92.2 (21.7)	0.39
DLco	53.9 (17.9)	55.8 (14.6)	0.57	52.7 (15.9)	55.4 (21.7)	55.7 (14.5)	0.49
High titer of IgM RF n%*	36 (68)	28 (57)	0.16	33(79)	9 (69)	22 (51)	0.013*

*>3 x upper limit of normal

** typical and probable UIP vs NSIP

Clinical characteristics for progressive fibrosing RA-ILD and stable RA-ILD at the time of the ILD diagnosis and stratified by HRCT pattern.

Conclusion: Progressive fibrosing RA-ILD was common and the associated mortality was high. IgM rheumatoid factor and DLco were independent predictors of mortality.

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Disclosure of Interests: None declared

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THU0114 MITIGATING MEDICATION RISK AVERSION IN THE CONFIDENT TREATMENT DECISIONS FOR LIVING WITH RHEUMATOID ARTHRITIS TRIAL

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Background: Controlling disease activity in RA using a treat-to-target (T2T) strategy can optimize clinical and patient-important outcomes. Yet, many patients are not familiar with T2T and report medication risk aversion as a major barrier to changing therapy.

Objectives: To develop and evaluate an educational, direct-to-patient video intervention aimed at improving willingness of patients to appropriately escalate treatment in RA.

Methods: We conducted a controlled, randomized trial of our intervention among US patients with self-reported RA enrolled in the ArthritisPower patient registry. We recruited participants by email, and surveyed their satisfaction with disease control, values about RA medications, decisional conflict and willingness to change treatment if/when recommended by their rheumatologist. Intervention group participants were invited to view up to 6 videos (3 required) relevant to T2T; those in the control group viewed 2 vaccination-related videos unrelated to T2T as an "attention control". The primary outcome, collected using surveys, was patient-reported willingness to change RA treatment, measured by the choice predisposition scale (0-10, anchors: "Not willing at all"; "Extremely willing") that reflected preference for RA treatment change. We compared the difference in pre-post differences in willingness to change RA treatment between the two groups using t-test.

Results: We invited 1264 RA patients by email. We reached our enrollment goal in 8 weeks. Study participants (N=208) were 90% Caucasian, 90% women, with mean (SD) age 50 (11) years, in good health (51%); 52% reported familiarity with T2T. A majority (89%) reported having values that favored RA medications. We observed no differences in baseline sociodemographics, patient global assessment of disease activity, health

literacy, willingness to change treatment, or decisional conflict. We found a significant improvement in pre-post willingness to change treatment in intervention vs. control participants (0.5 vs 0.01, p=0.01). We calculated an effect size (Glass's delta) for the intervention of 0.48 (i.e. moderate). Moreover, decisional conflict about treatment change decreased; there was no significant difference in pre-post differences in decision conflict between groups.

Conclusion: This randomized trial testing a novel patient-directed intervention advocating for T2T strategy implementation in RA care increased self-reported willingness to change RA treatment. Further studies are needed to evaluate if this effect is sustained over time and if it translates into actionable behavior change.

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THU0115 IS INCIDENT RHEUMATOID ARTHRITIS INTERSTITIAL LUNG DISEASE ASSOCIATED WITH METHOTREXATE TREATMENT? RESULTS FROM A MULTIVARIATE ANALYSIS IN THE ERAS AND ERAN INCEPTION COHORTS:

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Background: Rheumatoid arthritis interstitial lung disease (RA-ILD) is a rare but significant manifestation of RA, with high mortality. Methotrexate (MTX) is known to cause hypersensitivity pneumonitis, but its effect on the onset of RA-ILD is less clear.

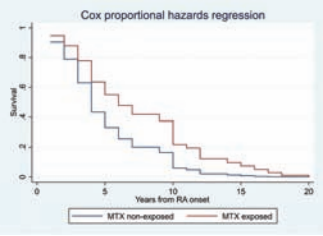
Objectives: To assess predictive factors for rheumatoid arthritis interstitial lung disease (RA-ILD) in two early RA inception cohorts with a focus on MTX exposure.

Methods: Patients with new diagnosis of RA recruited to the early RA study (ERAS) and the early RA network (ERAN). Standardised data including demographics, drug therapies and clinical outcomes including the presence of RA-ILD were collected at baseline, within 3- 6 months, at 12 months and annually for up to 25 years thereafter. Primary outcome was the association of MTX exposure with incident RA-ILD. Secondary outcomes were the association of demographic, comorbid and RA specific factors on incident RA-ILD using univariate and multivariate analyses and the association of MTX exposure on time to RA-ILD diagnosis using time to event Cox proportional hazards analysis.

Results: Of 92 eligible ILD cases, 39 occurred in 1578 (2.5%) MTX exposed and 53 in 1114 (4.8%) non-MTX exposed cases. The primary analysis of incident RA-ILD cases only developing after any csDMARD treatment (n=67) showed MTX exposure not to be associated with incident RA-ILD (O.R. 0.85 CI 0.49, 1.49 p=0.578) and a non-significant trend for delayed ILD diagnosis (O.R. 0.54 CI 0.28, 1.06 p=0.072) (see Figure). In an extended analysis including all RA-ILD cases (n=92, including those present pre csDMARD exposure), MTX exposure was associated with a significantly reduced risk of incident RA-ILD (O.R. 0.48, CI 0.3, 0.79 p=0.004) and longer time to ILD diagnosis (O.R. 0.41, CI 0.23, 0.75 p=0.004). Other independent baseline associations with incident RA-ILD were higher age of RA onset, ever smoking, male gender, rheumatoid nodules and longer time from first RA symptom to first out-patient visit (see Table).

Table Multivariate logistic analysis showing co-variates independently associated with RA-ILD development

	Primary analysis, RA-ILD onset after any csDMARD exposure, n=67	Wald test	Extended cohort, including RA-ILD onset pre any csDMARD, n=92	Wald test
	O.R. (95% C.I.)	p value	O.R. (95% C.I.)	p value
Methotrexate exposure	0.85 (0.49, 1.49)	0.578	0.48 (0.3, 0.79)	0.004
Age RA onset	1.04 (1.02, 1.06)	<0.001	1.04 (1.02, 1.06)	<0.001
Smoking, ever, baseline	2.21 (1.21, 4.03)	0.01	1.91 (1.13, 3.25)	0.016
Male gender	1.44 (0.83, 2.48)	0.193	1.74 (1.05, 2.86)	0.03
RF positive, baseline	2.02 (1.07, 3.82)	0.029		n.s.
RA nodules, baseline		n.s.	2.19 (1.08, 4.41)	0.029
Onset – 1st OPD	1.04 (1.00, 1.07)	0.027	1.03 (1.0, 1.07)	0.04
Baseline major co-morbidities	0.62 (0.40, 0.95)	0.027	0.67 (0.46, 0.98)	0.037
Baseline ESR	-	n.s.	1.01 (1.0, 1.02)	0.047



Abstract THU0115 – Figure 1. Cox proportional time to event analysis showing time of onset of RA-ILD from first joint symptoms of RA in MTX exposed and non-MTX exposed groups; primary analysis: cases with RA-ILD first recorded after any csDMARD exposure, n=67.

Conclusion: In ERAS/ERAN, incident RA-ILD is significantly associated with older age of RA onset, ever smoking, nodules, RF positivity, male gender, ESR, and a longer time from first RA symptoms to first secondary care visit. There is no association between MTX treatment and incident RA-ILD. MTX may have a protective role in delaying the onset of RA-ILD.

Acknowledgement: All recruiting ERAS and ERAN centers

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THU0116 COMPARATIVE SAFETY OF BIOLOGIC DMARDS AND ABATACEPT IN RHEUMATOID ARTHRITIS WITH COPD: A REAL-WORLD POPULATION-BASED OBSERVATIONAL STUDY

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Background: The biologic DMARD abatacept has been associated with respiratory adverse events in patients with RA who have chronic obstructive pulmonary disease (COPD) in the ASSURE trial (NCT00048932), based on only 54 patients with RA and COPD.[1] A large observational study of patients with RA and COPD, involving over 1,800 patients using abatacept did not find an increased incidence of respiratory adverse events with abatacept compared with other biologic DMARDs.[2] It remains uncertain, however, whether this potential respiratory risk affects all biologic DMARDs, including abatacept, when compared with non-biologic DMARDs.

Objectives: To assess in a real-world observational setting whether patients with RA and COPD treated with biologic DMARDs, including abatacept, have an increased risk of serious respiratory adverse events compared with similar patients treated with non-biologic DMARDs.

Methods: The Truven MarketScan® Commercial and Supplemental Medicare databases were used to identify patients diagnosed with RA and COPD, treated with a biologic or non-biologic DMARD between January 2007 and December 2015. A prevalent new-user cohort design was used to match each new user of a biologic DMARD with a new user of a non-biologic DMARD on time-conditional propensity scores.[3]Patients were followed up from new use until the end of enrolment or 31 December 2015. The Cox model was used to estimate the hazard ratios (HRs) of respiratory adverse events associated with biologic DMARDs compared

with non-biologic DMARDs, further adjusted for confounders found to be unbalanced despite matching on propensity scores.
Results: The study cohort included 7,424 new users of biologic DMARDs matched to 7,424 new users of non-biologic DMARDs, followed for up to 9 years. The adjusted HR (95% CI) of the combined respiratory endpoint, including severe COPD exacerbation, bronchitis and severe pneumonia or influenza, with biologic DMARD use relative to non-biologic DMARDs was 1.06 (0.91-1.24). For severe COPD exacerbation it was 0.88 (0.64-1.21), 1.02 (0.82-1.27) for bronchitis, while for pneumonia or influenza it was 1.18 (0.90-1.54) if hospitalized and 1.01 (0.89-1.14) as outpatient. For users of abatacept relative to non-biologic DMARDs, the HR of the combined respiratory endpoint was 1.06 (0.80-1.42). Results remained unchanged with sensitivity analyses.
Conclusion: In this large real-world study of patients with RA and COPD, the risk of pre-specified serious respiratory adverse events was not significantly increased in patients using biologic DMARDs, and specifically abatacept, compared with those using non-biologic DMARDs. This study does not support the safety signal for abatacept from the ASSURE trial.

REFERENCES:

[1] Weinblatt E, et al. Arthritis Rheum 2006;54:2807–16.
[2] Suissa S, et al. Ann Rheum Dis 2018;77:613-614.
[3] Suissa A, et al. Pharmacoepidemiol Drug Saf 2017;26:459–68.

Disclosure of Interests: Samy Suissa Grant/research support from: Advisory board meetings, or as speaker, or received research grants from AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Novartis, Speakers bureau: Advisory board meetings, or as speaker, or received research grants from AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Novartis, Marie Hudson Grant/research support from: Unrestricted research funds from Bristol-Myers Squibb, Pierre Ernst: None declared, Sophie Shen Employee of: Bristol-Myers Squibb, Teresa Simon Employee of: Bristol-Myers Squibb
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THU0117 PHARMACOKINETICS AND SHORT-TERM SAFETY OF FILGOTINIB, A SELECTIVE JANUS KINASE 1 INHIBITOR, IN SUBJECTS WITH MODERATE HEPATIC IMPAIRMENT

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Background: Filgotinib (FIL) is an oral selective Janus kinase 1 (JAK1) inhibitor being developed to treat inflammatory diseases.
Objectives: This phase 1 study evaluated the pharmacokinetics (PK) and short-term safety of FIL in subjects with hepatic impairment (HI) to guide safe and appropriate dosing in the presence of this comorbidity.
Methods: This study enrolled 20 subjects: 10 with moderate (Child-Turcotte-Pugh-B) HI and 10 healthy controls. All were matched for age, sex, and body mass index and received a single oral dose of FIL 100 mg followed by intensive plasma PK sampling over 120 hours. Plasma concentrations of FIL and its primary circulating metabolite were measured by validated LC-MS/MS methods; plasma protein binding was also evaluated. A parametric analysis of variance was applied to the natural logarithmic transformation of PK parameters (AUC and C_{max}) for FIL and its metabolite. Geometric least squares means (GLSM) ratios and 90% confidence intervals (CIs) of PK parameters were evaluated in subjects with moderate HI relative to controls, with clinically relevant exposure change defined as $\geq$2-fold for FIL or its metabolite. Safety endpoints consisted of the incidence of adverse events (AEs), laboratory abnormalities, and vital sign and electrocardiogram changes monitored through day 15.
Results: All subjects completed the protocol-specified dosing and assessments. FIL and metabolite AUCs were increased by 1.6- and 1.2-fold, respectively, in subjects with moderate HI compared to controls. Protein bindings of FIL and its metabolite (f_u: 41%–44% and 55%–61%, respectively) were unchanged in subjects with moderate HI. FIL was well tolerated, with no serious AEs reported. All treatment-emergent AEs were Grade 1 in severity. Serum and plasma markers did not show evidence of treatment-emergent hepatotoxicity or worsened liver function and were consistent with the use of FIL in a population with moderate HI.
Conclusion: In the setting of moderate HI, a single oral dose of FIL 100 mg was well tolerated. FIL can be administered without predefined dose adjustment to patients with mild to moderate HI.
Disclosure of Interests: Kacey Anderson Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Hao Zheng Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Oliver Medzihradsky Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Yizhao Li Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Ann Qin Employee of: Gilead Sciences, Inc., Brian Kearney Employee of: Gilead Sciences, Inc., Anita Mathias Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc.
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THU0118 TREATMENT OF RHEUMATOID ARTHRITIS WITH COMBINATION THERAPY USING A BIOLOGIC AGENT AND METHOTREXATE LOWERS THE RISK OF DECREASING KIDNEY FUNCTION COMPARED TO METHOTREXATE MONOTHERAPY

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Background: Rheumatoid arthritis (RA) is associated with reduced kidney function, possibly due to chronic inflammation or the use of nephrotoxic therapies. However, little is known about the effects of novel non-nephrotoxic biologic agents (biological disease-modifying antirheumatic drugs [bDMARDs]) on the risk of decreasing kidney function.
Objectives: To elucidate the effects of bDMARDs on decreasing kidney function.
Methods: We recruited a cohort of 1058 patients with RA from the All Showa University of RA database. The following background factors were analyzed: age, sex, type of bDMARD, methotrexate and prednisolone dosages, use of conventional synthetic DMARDs and nonsteroidal anti-inflammatory drugs, body mass index, smoking history, diabetes status, hypertension status, dyslipidemia status, serum creatinine (Cr) level, CRP level, and matrix metalloproteinase-3 level. Furthermore, we used the simplified disease activity index (SDAI) for the evaluation of the disease activity of RA. The estimated glomerular filtration rate (eGFR) was calculated using the serum Cr level, age, and sex. We divided the patients into two groups according to the treatment, as follows: bDMARD with methotrexate (MTX) treatment (combination) group (744 patients) and MTX monotherapy group (314 patients). The patients followed the same treatment plan for 1 year. Patients who had primary and secondary failures, adverse effects of drugs, and missing data and those who relocated or withdrew from the study were excluded. Propensity scores were calculated based on the following factors: age, sex, prednisolone dosage, MTX dosage, SDAI, Cr level, eGFR, diabetes status, hypertension status, and dyslipidemia status. Overall, 285 patients in each group were identified by propensity score matching. The primary end-points were the eGFR values before treatment and 6 months and 1 year after treatment. Significance was determined using the repeated-measures analysis of variance (ANOVA).
Results: The eGFR (mL/min/1.73 m^2) decreased from 88.5 ± 21.8 to 86.1 ± 21.5 and 83.7 ± 21.0 at 6 months and 1 year, respectively, in the combination treatment group and from 86.3 ± 37.9 to 79.5 ± 19.1 and 78.5 ± 19.5 at 6 months and 1 year, respectively, in the MTX monotherapy group. No interaction was observed between the groups. A significant difference was observed between the groups ($p = 0.0066$) and even during the treatment period ($p < 0.001$) by repeated-measures ANOVA.
Conclusion: The decrease in eGFR was smaller in the combination treatment group than in the MTX monotherapy group. bDMARD use may lower the risk of decreasing kidney function in patients with RA.
Acknowledgement: Cooperation on data collection: All Showa University in Rheumatoid Arthritis (ASHURA) group
Disclosure of Interests: YUSUKE MIWA Grant/research support from: Mitsubishi Tanabe Pharma Corporation and AbbVie CK. Astellas Pharma Inc., Mitsubishi Tanabe Pharma Corporation, AbbVie CK, Pfizer Japan Inc., Chugai Pharmaceutical Co., Ltd., Eizai Co., Ltd, Asahi Kasei Pharm Co., Ltd, YL Biologics Ltd., Japan Blood Products Organization, Ono Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., and Teijin Pharma Ltd.
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THU0119 SUCCESSFUL PSYCHOPHARMACOTHERAPY OF ANXIETY AND DEPRESSIVE DISORDERS IMPROVES RHEUMATOID ARTHRITIS REMISSION RATE AT FIVE YEARS FOLLOW-UP

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Background: Anxiety and depressive disorders (ADD) affect rheumatoid arthritis (RA) disease activity and remission rate. Psychopharmacotherapy (PPT) of ADD attempts to improve the remission rate.
Objectives: To determine factors associated with RA remission rate.
Methods: 128 RA-patients (pts) were enrolled, 86% were women with a mean age of 47,4±11,3 (M±SD) yrs. All pts met the full ACR criteria for RA. Remission was defined as DAS28<2,6. Mean RA activity by DAS28 was high (5,27±1,78) at baseline. 69,4% RA-pts were already taking prednisone (9 [5; 10] mg/day (Me (25%; 75%)), 84,4% - conventional disease-modifying antirheumatic drugs (cDMARDs), 7,8% - biologic DMARDs (bDMARDs) - anti-TNF-α – 6,3%, rituximab – 1,6%. ADD were diagnosed in 123 (96,1%) of RA-pts in accordance with ICD-10 in semi-structured interview. Severity of depression and anxiety was evaluated with Montgomery–Asberg Depression Rating Scale (MADRS) and Hamilton Anxiety Rating Scale (HAM-A). RA-pts with ADD were divided into the following treatment groups: 1 – cDMARDs (n=39), 2 – cDMARDs + PPT (sertraline or mianserine) (n=43), 3 – cDMARDs + bDMARDs (n=32), 4 – cDMARDs + bDMARDs + PPT (sertraline or mianserine) (n=9). Biologics treatment duration varied from 1 to 6 years, antidepressants – from 6 to 96 weeks. Logistic regression analysis was conducted to determine factors associated with RA remission rate.
Results: At 5-yrs endpoint in 83 RA-pts remission rate was 22,9% (8,3%, 34,5%, 19,0% and 33,3% in groups 1, 2, 3 and 4, respectively). Significantly higher proportion of patients achieved remission in cDMARDs + PPT group vs cDMARDs group (34,5% vs 8,3%, RR 1,8 (95%CI 0,35 – 9,2), p=0,024). By univariate logistic regression, male sex, younger age, shorter RA duration, RF and ACPA negativity, lower baseline DAS28 and HAQ, absence of extraarticular RA manifestations and depression at the beginning of the study, and remission of anxiety and depressive symptoms at the end of the study were significantly associated with RA remission (table 1). These variables were subjected to multivariate stepwise logistic regression. Only lower baseline DAS28 (OR 0,636 (95%CI 0,515 – 0,785), p<0,001) and remission of anxiety and depressive symptoms at 5-yrs endpoint (OR 6,89 (95%CI 1,8 – 26,29), p=0,005) were independently associated with RA remission at 5-years follow-up.

Table 1. Factors associated with RA remission at 5 years (univariate logistic regression).

Factor	p	OR	95%CI	
			low	up
Female sex	<0,001	0,310	0,166	0,577
Baseline age	<0,001	0,974	0,961	0,986
RA duration	0,001	0,913	0,866	0,964
RF +	<0,001	0,265	0,127	0,552
ACPA +	0,003	0,321	0,152	0,681
Baseline DAS28	<0,001	0,754	0,663	0,858
Baseline HAQ	<0,001	0,381	0,236	0,614
Baseline extraarticular RA manifestations	0,005	0,211	0,072	0,619
Baseline minor depression	0,011	0,278	0,103	0,748
Baseline major depression	0,028	0,353	0,139	0,895
Baseline generalized anxiety disorder	0,215	0,25	0,028	2,237
Anxiety and depressive symptoms remission at 5-yrs enpoint	0,007	5,891	1,63	21,29
Schizotypal personality disorder	0,22	0,429	0,111	1,657

Conclusion: Lower baseline DAS28 and remission of anxiety and depressive symptoms at 5-yrs endpoint are associated with higher rheumatoid arthritis remission rate at five years follow-up.
Disclosure of Interests: None declared
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THU0120 RHEUMATIC DISEASE COMORBIDITY INDEX IMPACT ON DISEASE ACTIVITY IN PATIENTS ENROLLED IN KUWAIT REGISTRY OF RHEUMATIC DISEASES (KRRD)

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Background: Its known that the presence of certain comorbidities in patients with Rheumatoid arthritis (RA) can have an impact on the chance of achieving low disease activity (LDA).
Objectives: The purpose of this study was to examine the association of different comorbidities with low disease activity index in patients enrolled in KRRD.
Methods: The database of KRRD was used to include patients with RA and multiple visits. Comorbid conditions were collected at enrollment by the treating rheumatologist and modeled using the Rheumatic Disease Comorbidity index (RDCI) score, and by individual comorbid condition. Disease activity (DAS28) was assessed at routine clinic visits. Associations of comorbidity measures with disease activity over 4 years of follow up were examined using multivariable linear models. The odds of ever achieving DAS28 low disease activity (<3.2) were examined using multivariable logistic regression.
Results: Among 1511 participants with mean age of 52 (SD 12) years, RA duration 8 (SD 6) years, 60.7% female, 77.1% RF positive, 64.6% anti-CCP positive, and 10.8% with smoking history, 1.29 had a RDCI. Hypertension (21%), diabetes mellitus (21%), hyperlipidemia (12%), cardiovascular (CV) disease (3.6%) and interstitial lung disease (ILD) (1.1%), were the most prevalent comorbidities. Select individual comorbidities, including DM, kidney disease and COPD, were more closely associated with unfavorable longitudinal disease activity, and achievement of low disease activity status. Correlation test between DAS28 and all comorbidities showed signification negative association for achieving low disease activity if the patient has history of diabetes mellitus, COPD or kidney disease.
Conclusion: DM, kidney disease and COPD but not composite comorbidity scores, are associated with higher measures of disease activity and lower odds of achieving low disease activity status in RA patients enrolled in KRRD registry.

Table (1) : *Cox Proportional Hazards Regression for LDA and comorbidities*

Variable	B	SE	95% CI	P	OR
DM	0.24	0.05	(0.14, 0.34)	**0.001**	**1.27**
CAD	0.16	0.13	(-0.09,0.40)	0.221	1.17
Hyperlipidemia	-0.12	0.06	(-0.24,0.01)	0.65	0.89
Hypertension	-0.04	0.05	(-0.14,0.05)	0.394	0.96
COPD	0.66	0.33	(0.01,1.32)	**0.047**	**1.94**
Cancer	0.86	0.45	(-0.02,1.74)	0.055	2.36
Kidney disease	0.97	0.39	(0.20,1.74)	**0.014**	**2.63**
ILD	0.09	0.21	(-0.33,0.50)	0.685	1.09

Disclosure of Interests: None declared
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THU0121 CIRCULATING FIBROBLAST GROWTH FACTOR-23 IS ASSOCIATED WITH DYSLIPIDEMIA IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) patients have an increased risk of morbidity and mortality from cardiovascular (CV) events as a result of accelerated atherosclerosis. The bone-derived fibroblast growth factor-23 (FGF23) is a novel marker of chronic kidney disease (CKD)-associated mineral bone disorder, which increases progressively with declining renal function. FGF23 is associated with left ventricular hypertrophy, impaired left ventricular function, endothelial dysfunction, heart failure and progression of renal failure in adult CKD.

Objectives: The objectives of this study were to: compare serum FGF-23 levels between *RA patients and healthy controls* and investigate possible associations between FGF23 as surrogate measures of cardiovascular disease.
Methods: This cross-sectional study was performed in Vega-Baja Hospital, Orihuela (Spain) from November 2016 to May 2018. We prospectively enrolled 63 consecutive women patients affected by RA and followed at the Vega-Baja Hospital (Orihuela, Spain) and 65 matched healthy women controls. All patients included in this study had normal serum creatinine (Cr) levels and met the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA. Total cholesterol and triglyceride levels were determined by fully enzymatic techniques. High-density lipoprotein (HDL) was determined after precipitation of apolipoprotein B (apoB)–containing lipoproteins with magnesium sulfate and dextran sulfate. Low-density lipoprotein (LDL) was calculated using the Friedewald formula. Serum FGF-23 was analyzed using ELISA.
Results: The mean serum total cholesterol, HDL-C, LDL-C, and triglycerides were 212.74±41 mg/dL, 69.92±19.45 mg/dL, 120.18±29.24 mg/dL and 112.93±55.67 mg/dL, respectively.
There was no significant differences in FGF-23 levels between the patients and controls [85.7 (5.2-275.4) vs. 81.2 (2.6-269.9), pg/ml; *P*=0.4316], but we found that FGF23 levels were positively associated with total cholesterol (p <0.05), low-density lipoprotein (LDL-c) level (p <0.05) and smoking (p = 0.008) in patients with RA.
Conclusion: We report an association between circulating FGF-23 and LDL-c in RA patients, representing a novel pathway linking high FGF23 to an increased cardiovascular risk.

REFERENCES:

[1] Castañeda S, Nurmohamed MT, González-Gay MA. Cardiovascular disease in inflammatory rheumatic diseases. Best Pract Res Clin Rheumatol. 2016; 30(5):851-869.
[2] Kendrick J, Cheung AK, Kaufman JS, Greene T, Roberts WL, Smits G, Chonchol M. FGF-23 associates with death, cardiovascular events, and initiation of chronic dialysis. J Am Soc Nephrol. 2011; 22(10):1913–1922.
[3] Scialla JJ, Xie H, Rahman M, Anderson AH, Isakova T, Ojo A, et al. Fibroblast growth factor-23 and cardiovascular events in CKD. J Am Soc Nephrol. 2014; 25(2):349–360.
[4] Mirza M, Alsiö J, Hammarstedt A, Erben RG, Michaëlsson K, Å Tivesten Å, et al. Circulating Fibroblast Growth Factor-23 Is Associated With Fat Mass and Dyslipidemia in Two Independent Cohorts of Elderly Individuals. Arterioscler Thromb Vasc Biol. 2011; 31:219-227.

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THU0122 THE LACK OF EXERCISE HABIT WAS A RISK FACTOR FOR CLINICAL FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS -TOMORROW STUDY-

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Background: Patients with rheumatoid arthritis (RA) might be considered to be at increased risk of falls and fractures. However, little is known about the exact properties of risk factors for clinical fractures in patients with RA. Recently, the disease activity of RA has been more satisfactorily controlled by the ''treat-to-target'' strategy, including the use of biologics. Given this new era, it is important to accurately estimate the incidence of clinical fracture in patients with RA and to elucidate contributing risk factors.
Objectives: The objective of this study was to evaluate the incidence of clinical fractures and associated risk factors in 208 patients with RA and in age- and sex-matched 205 controls (Cont) who participated in the TOMORROW (TOtal Management Of Risk factors in Rheumatoid arthritis patients to lOW er morbidity and mortality) study, a 10-year cohort study that started in 2010 in Japan. This research was conducted using TOMORROW study data for 7 years.
Methods: We evaluated the incidence of clinical fractures by self-administered questionnaire every year and confirmed them by medical records. We also collected information about daily walking time and weekly exercise time, general health status, body composition including bone mineral density, lean body mass, fat mass and laboratory data at baseline. We compared the frequency of the incidence of clinical fractures in RA patients and Cont for seven years and analyzed risk factors for clinical fractures in RA patients using multivariate regression analysis.
Results: A total of 208 patients with RA (mean age: 54.9 ± 10.1 years, female: 85.1%, mean disease duration 14.0 ± 11.8 years) and 205 Cont (mean age: 56.3 ± 10.4 years, female: 83.9%) were finally analyzed. The number of clinical fractures were no differences between RA and Cont group (RA: 47, Cont: 38, p=0.37). Comparing RA patients with or without the clinical fractures, age (p=0.006), disease duration (p=0.005), the average glucocorticoid dose (p<0.001), the average number of falls (p<0.001), and the average DAS28-ESR of seven years (p=0.029) were higher in patients with the incidence of clinical fractures. Multivariate logistic regression analysis revealed that RA was not a risk factor (OR: 0.655, 95%CI: 0.296 – 1.448, p=0.296), and the lack of exercise habit (OR: 2.221, 95% CI: 1.208-4.082, p=0.001) and glucocorticoid use (OR: 2.279, 95%CI: 1.036-5.015, p=0.04) were the risk factor for clinical fractures. Multivariate logistic regression analysis in RA patients, the lack of exercise habit represented an independent risk factor for the incidence of clinical fractures (OR: 4.466, 95%CI: 1.212-16.454, p=0.025).
Conclusion: Seven years of data from the TOMORROW cohort study including both RA patients and age- and sex-matched Cont showed no difference in the incidence rate of clinical fractures between RA and Cont groups. Multivariate logistic regression analysis revealed that RA was not a risk factor. However, the lack of exercise habit was significantly associated with an increased frequency of the incidence of clinical fracture among RA patients.
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THU0123 FEMALES UNDERGO MORE TREATMENT CHANGES COMPARED TO MALES: ANALYSIS OF GENDER DIFFERENCES IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Gender differences may contribute to treatment tailoring in rheumatoid arthritis (RA) patients. Observational data shows a trend toward worse disease activity and worse response to treatment in

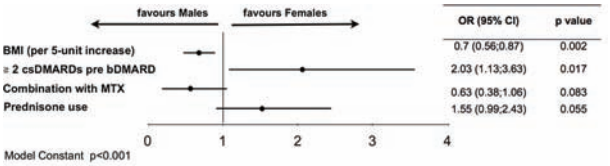
females. Only few data are available specifically focused on differences in drug use according to gender.

Objectives: To evaluate gender differences in treatment approaches in RA patients treated with bDMARDs (biological DMARDs)

Methods: We included RA patients aged ≥18 years, with disease duration ≥1 years, with a stable bDMARD treatment (≥12 months) in a monocentric cohort in the North-East of Italy. Social, demographic, and clinical features in addition to treatments were considered. To assess variables independently associated with gender, all variables achieving a p<0.20 in univariate analysis were included in a multivariate regression model.

Results: Among 721 RA patients, 514 patients were eligible for the analysis and 407 were females. Compared with males, females had a lower BMI, a higher DAS28, a higher number of conventional synthetic DMARDs (csDMARDs) used before the start of bDMARDs, a higher number of bDMARDs with different mechanism of action (MoA), a larger use of prednisone and a lower rate of combination with MTX (Table 1). After adjustment for confounding factors, females had an increased probability of taking ≥ 2 DMARDs before bDMARDs (OR 2.21, 95% CI 1.25-3.93, p=0.007) and a lower BMI (per 5-unit increase, OR 0.70, 95% CI 0.56-0.87, p=0.001) compared to males (Figure 1).

Conclusion: In a cohort of Italian RA patients, females were treated with a higher number of csDMARDs before starting a bDMARD compared to males and a trend toward the use of more bDMARDs with different MoA. Further insight is needed regarding possible differences in the accessibility to bDMARD treatment and reasons for unsatisfactory treatment control in females.



Variables included in multivariate analysis: Age, Disease duration, Positive RF and/or ACPA, BMI, ≥2 csDMARDS prior to bDMARDs, Disease activity (DAS28), Combination with MTX, PDN use, Time on bDMARDs, TNF ihnibitors use, ≥2 Mechanisms of action of biological drugs

Abstract THU0123 – Figure 1

Abstract THU0123 –Table 1.

Characteristics of the patients in the entire cohort (514 patients) and according to gender.

		Univariate Analysis			Multivariate Analysis	
	All patients	Females	Males	p value	OR (95% CI)	p value
Number	514	407	107	-		
Females, n (%)	407 (79.2)	407 (100)	0 (0)	-		
Positive RF or ACPA, n (%)	300 (58.4)	247 (60.7)	53 (49.5)	0.037		
Age, years, median (IQR)	62.5 (53,70)	63 (53;71)	62 (51.5;68.5)	0.186		
BMI, median (IQR)	23.88 (21.24;27.54)	23.38 (20.76;26.99)	25.93 (23.05;28.36)	0.001	per 5-unit increase 0.7 (0.56;0.87)	0.002
Overweight, n (%)	210 (40.9)	149 (36.6)	61 (57)	<0.001		
Disease duration, year, median (IQR)	18 (12;25)	18 (13;26)	17 (12; 22)	0.122		
Fibromyalgia*, n (%)	24 (22.4)	24 (26.7)	0 (0)	0.016		
Employed*, n (%)	39 (41.5)	31 (39.2)	8 (53.3)	0.310		
Education level*, n (%)	11 (10.7)	11 (12.8)	0 (0)	0.480		
Social status*, n (%)	5 (6.2)	4 (6)	1 (7.1)	0.325		
Smokers*, n (%)	16 (18)	13 (17.1)	3 (23.1)	0.604		
Distance from clinic, km, median (IQR)	37 (20;51.25)	35 (20;60)	40 (30;45)	0.943		
No. of assessment per year, median (IQR)	4 (3;4)	4 (3;4)	3 (2.75;4)	0.087		
High adherers to treatment*§, n (%)	50 (46.3)	39 (42.9)	11 (64.7)	0.097		
csDMARDs prior to bDMARD treatment						
Number, median (IQR)	3 (2;3)	3 (2;3)	3 (2;3)	0.072		
≥ 2 csDMARDs, n (%)	448 (87.2)	364 (89.4)	84 (78.5)	0.003	2.03 (1.13;3.63)	0.017
MTX, n (%)	496 (96.5)	399 (98)	97 (90.7)	<0.001		
LFN, n (%)	221 (43)	184 (45.2)	37 (34.6)	0.048		
SSZ, n (%)	139 (27)	105 (25.8)	34 (31.8)	0.215		
HCQ, n (%)	334 (65)	274 (67.3)	60 (56.1)	0.030		
Other csDMARDs, n (%)	184 (35.8)	145 (35.6)	39 (36.4)	0.437		
Disease assessment at the last follow-up visit						
TJC, median (IQR)	0 (0;2)	0 (0;2)	0 (0;2)	0.842		
SJC, median (IQR)	2 (2;4)	2 (2;4)	2 (2;4)	0.893		
Patient-VAS, median (IQR)	40 (30;40)	40 (30;40)	40 (30;40)	0.970		
CRP, mg/L, median (IQR)	5 (2;5)	5 (2;5)	5 (2;6.3)	0.113		
DAS28, median (IQR)	3.09 (2.68;3.49)	3.1 (2.68;3.49)	2.99 (2.73;3.46)	0.855		
DAS28				0.028		
Remission, n (%)	112 (21.8)	93 (22.9)	19 (17.8)			
LDA, n (%)	196 (38.1)	147 (36.1)	49 (45.8)			
MDA, n (%)	189 (36.8)	157 (38.6)	32 (29.9)			
HDA, n (%)	17 (3.3)	10 (2.5)	7 (6.5)			
HAQ, median (IQR)	1.5 (1;1.8)	1.5 (1.1;1.83)	1.5 (1;1.8)	0.217		
Physician-VAS, median (IQR)	35 (25;35)	35 (25;35)	35 (25;35)	0.873		
SDAI, median (IQR)	11 (8;13.8)	11 (8;13.8)	10 (8;13.95)	0.796		
CDAI, median (IQR)	10.5 (7.5;13.5)	10.5 (7.5;13.5)	9.5 (7.5;13.5)	0.802		
csDMARDs associated with the bDMARD treatment						
MTX, n (%)	99 (19.3)	70 (17.2)	29 (27.1)	0.021	0.63 (0.38;1.06)	0.083
MTX dose, mg/week, median (IQR)	10 (10;10)	10 (10;10)	10 (10;10)	0.463		
Subcutaneous/intramuscular vs oral MTX, n (%)	84 (60.4)	64 (61.5)	20 (57.1)	0.646		
LFN, n (%)	29 (5.6)	26 (6.4)	3 (2.8)	0.153		
SSZ, n (%)	3 (0.6)	2 (0.5)	1 (0.9)	0.592		
HCQ, n (%)	3 (0.6)	3 (0.7)	0 (0)	0.373		
Other csDMARD, n (%)	2 (0.4)	2 (0.5)	0 (0)	0.468		
Combination with MTX and/or LFN, n (%)	128 (24.9)	96 (23.6)	32 (29.9)	0.179		
PDN use, n (%)	319 (62.1)	261 (64.1)	58 (54.2)	0.060	1.55 (0.99;2.43)	0.055
PDN dose, mg/day, median (IQR)	2.5 (0;5)	2.5 (0;5)	2.5 (0;5)	0.176		
NSAIDs use, n (%)	43 (9.5)	33 (9.2)	10 (10.5)	0.699		
bDMARD treatment						
Time on treatment, years, median (IQR)	10.05 (5.96;13.05)	10.13 (6.43;13.21)	9.72 (3.96;12.63)	0.106		
Disease duration at the start, median (IQR)	8.1 (3.88;14.1)	8.3 (4;15)	8 (3.3;12)	0.205		
Number (ever), median (IQR)	2 (1;2)	2 (1;2)	1 (1;2.5)	0.431		
TNF-inhibitors use (ever), n (%)	482 (93.8)	378 (92.9)	104 (97.2)	0.100		
MOA number (ever), median (IQR)	1 (1;2)	1 (1;2)	1 (1;2)	0.179		
≥2 MOA, n (%)	118 (36.6)	157 (38.6)	31 (29)	0.066		
Current subcutaneous vs endovenous administration, n (%)	449 (87.4)	354 (87)	95 (88.8)	0.617		
					Model Constant	<0.001

IQR: inter-quartile range; MTX: methotrexate; LFN: leflunomide; SSZ: sulfasalazine; HCQ: hydroxicloroquine; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs: biological DMARDs; TJC: tender joint count; SJC: swollen joint count; CRP: C reactive protein; DAS28: disease activity score 28; LDA: low disease activity; MDA: moderate disease activity; HDA: high disease activity; HAQ: health assessment questionnaire; SDAI: simplified disease activity index; CDAI: clinical disease activity index; PDN: prednisone; NSAIDs: non steroidal anti-inflammatory drugs; MOA: mechanisms of action; TNF-inhibitors: tumor necrosis factor inhibitors; *data available in 107 patients; §adherence measured with the Italian validated 5-item Compliance Questionnaire for Rheumatology (I.-CQRS)[15,16];

Disclosure of Interests: None declared

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THU0124 INFLUENCE OF AUTOIMMUNE VASCULITIS ON LUNG DISEASES IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS

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Background: Complications of rheumatoid arthritis (**RA**) may modify the clinical course and symptoms of allied disorders leading to missed diagnosis or late recognition of associated diseases.

Objectives: The **aim** of this study was to determine the possible role of classic **complications** of **RA**: systemic autoimmune vasculitis (**AV**), AA amyloidosis (**AAa**), lethal cardiac insufficiency (**CI**) caused by endo-, myo- or pancarditis, with or without interstitial pneumonitis, furthermore lethal septic infection (**SI**) on **prevalence** and **mortality** of coexistent **associated diseases**: atherosclerosis (**Ath**), hypertension (**HT**), type 2 diabetes mellitus (**DM**), and tuberculosis (**Tb**) with miliary dissemination (**mTb**).

Methods: 234 non- selected autopsy patients with **RA** were studied. **RA** was confirmed clinically according to the criteria of the **ARA**.

The presence of **AV**, **AAa**, **CI** and **SI** was determined at autopsy and confirmed by a detailed review of extensive histological material. The prevalence and mortality of associated diseases **Ath**, **HT**, **DM**, **Tb** or **mTb** were determined and analyzed retrospectively, reviewing the clinical and pathological reports.

The link between **AV**, **AAa**, **CI** or **SI** and **Ath**, **HT**, **DM**, **Tb** or **mTb** was analyzed by (χ^2) test.

Results: RA was complicated by **AV** in **43** (18.4%), by **AAa** in **48** (**20.5**%), by **CI** in **15** (**6.4**%), and by lethal **SI** in **33** (**14.1**%) of **234** patients.

RA associated with severe **Ath** in **106** (**45.3**%), with **HT** in **41** (**17.5**%), with **DM** in **41** (**17.5**%), with **Tb** in **28** (**11.9**%) and with **mTb** in **9** (**3.8**%) of **234** patients.

As a basic disease **Ath** led to death in **61** (**26.1**% of 106), **HT** in **2** (**0.9**% of 41), **DM** in **none** (**0**% of 41) and **Tb** with **mTb** in **3** (**1.3**% of 28) of **234** patients. **Tb** without miliary dissemination was not lethal in our patient population.

The statistical links ("p" values of significance) between complications of **RA** and prevalence or mortality of allied disorders are summarized in Table. (*asterisk indicates a negative value of associations' coefficient with inverse relationship).

Complications of RA	**AV n=43** of 234	**AAa n=48** of 234	**CI n=15** of 234	**SI n=33** of 234
Allied disorders in RA				
Ath n=106 of 234	**χ^2=6.43*, p<0.01**	**χ^2=10.04*, p<0.001**	χ^2=0.92*, p<0.33	**χ^2=5.03*, p<0.02**
Ath lethal n=61 of 106	**χ^2=15.92*, p<0.00**	**χ^2=11.04*, p<0.00**	**χ^2=4.29*, p<0.03**	**χ^2=12.01*, p<0.00**
HT 41 of 234	χ^2=3.20*, p<0.07	χ^2=0.03*, p<0.86	χ^2=0.00*, p<0.92	χ^2=1.27*, p<0.25
HT lethal n=2 of 41	χ^2=0.05*, p<0.80	χ^2=0.02, p<0.87	χ^2=1.16*, p<0.28	χ^2=0.19*, p<0.65
DM 41 of 234	χ^2=0.05*, p<0.81	χ^2=**1.05***, p<0.30	χ^2=0.92, p<0.33	χ^2=0.01, p<0.91
Tb 28 of 234	**χ^2=4.02, p<0.04**	χ^2=2.61*, p<0.10	χ^2=0.33, p<0.56	χ^2=0.37, p<0.54
Tb lethal n=3 of 28	χ^2=0.00*, p<0.93	χ^2=0.02*, p<0.86	χ^2=0.53*, p<0.46	χ^2=0.01*, p<0.89
mTb 9 of 28	**χ^2=4.24, p<0.03**	χ^2=0.08, p<0.77	χ^2=0.01, p<0.91	χ^2=0.05, p<0.82
mTb lethal n=3 of 9	χ^2=0.00*, p<0.93	χ^2=0.02*, p<0.86	χ^2=0.53*, p<0.46	χ^2=0.01*, p<0.89

Conclusion: The inverse correlations between **AV**, **AAa**, **CI**, **SI** and **Ath**, **HT**, **DM**, **Tb** or **mTb** indicate that the prevalence and mortality of allied disorders were not influenced basically by the complications of **RA**.

The consequently inverse and (in most cases) significant correlations between prevalence of **AV**, **AAa**, **CI**, **SI** and the prevalence and mortality of **Ath** show that these are independent entities in **RA**. The **AV**, **AAa**, **CI** and **SI** are the most important complications of **RA**, and are characterize severe forms of disease, mostly involving younger patients, with an earlier onset (without pronounced atherosclerosis); while **Ath** is basically an age dependent phenomenon, characteristically present in **RA** patients with advanced age. **RA** patients with **Ath** may represent a special group of **RA**, characterized by lower incidence of **AV**, **AAa**, **CI** or **SI**, and a better prognosis.

Disclosure of Interests: None declared

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THU0125 CARDIOVASCULAR DISEASE RISK FACTORS MAY NEGATIVELY IMPACT RHEUMATOID ARTHRITIS DISEASE OUTCOMES: FINDINGS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE

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Background: Rheumatoid arthritis increases the risk of cardiovascular disease (CVD). Less is known about the direct influence of CVD and CVD risk factors (RF) on RA outcomes, but higher comorbidity burden has been suggested to adversely affect RA treatment response[1-2].
Objectives: We tested our hypothesis that CVD risk factors (RFs) alone, in the absence of CVD, are associated with higher disease activity and disability in RA.
Methods: The Ontario Best Practices Research Initiative (OBRI) is a clinical registry of RA patients followed in routine care. RA subjects with complete data to calculate disease activity according to the Disease Activity Score-28 (DAS28), Clinical Disease Activity Index (CDAI), 28 swollen joint count (SJC28) and functional status (Health Assessment Questionnaire Disability Index [HAQ-DI]) at cohort entry were selected. Patients were divided into mutually exclusive groups by baseline CVD status as: (1) no CVD/no CVD RFs; (2) CVD including coronary artery disease, myocardial infarction, cerebral vascular accidents, and peripheral arterial disease; (3) no CVD but CVD RFs including hypertension (HTN), dyslipidemia (DLD), diabetes (DM), or smoking. We performed separate linear regression analyses for each outcome, adjusted for baseline clinical and demographic variables, to determine the independent effect of CVD status on disease outcomes at baseline and one year follow-up.
Results: Of 2033 patients examined, 49.5% had no CVD, 5.4% had CVD and 45.1% had CVD RFs alone. The most common RF was HTN (33%) followed by DLD (19.7%), current smoking (17%), and DM (8.1%). At cohort entry, having a CVD RF was associated with significantly higher DAS28 (β 0.13, 95%CI 0.002-0.26, p 0.04) and HAQ-DI (β 0.16, 95%CI 0.10-0.23, p<0.0001). At one year, CVD RF was associated with worse DAS28 (β 0.17, 95%CI 0.05-0.30, p 0.01) and CDAI (β 0.96, 95%CI 0.05-1.87, p 0.04) but not HAQ-DI (β 0.03, 95%CI -0.002-0.08, p 0.17). Having higher number of CVD RF was associated with worse disease outcomes. No association between CVD status and swollen joint count was observed.
Conclusion: Even in the absence of CVD, traditional CVD RF are associated with greater RA disease severity and disability both at baseline and one year. Self-perceived impact of comorbidity (patient global assessment of health) may be driving this relationship. Moreover, patients with CVD RF maybe more treatment-resistant, suggesting that co-management of CVD RF in RA patients may be beneficial on both fronts.

REFERENCES:

[1] Avina-Zubieta, J. A., Thomas, J., Sadatsafavi, M., Lehman, A. J. & Lacaille, D. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann. Rheum. Dis. 71, 1524–1529 (2012).
[2] Crepaldi, G. et al. Cardiovascular Comorbidities Relate More than Others with Disease Activity in Rheumatoid Arthritis. PLoS One 11, (2016).

Abstract THU0125 Table 1. Multivariable linear regression of disease activity outcomes and functional status at one-year according to CVD status.

	β - coefficient (95% CI); p-value			
	DAS28-ESR	**CDAI**	**SJC-28**	**HAQ-DI**
CVD status	N=1965	N=1965	N=1965	N=1965
No CVD/No CVD RFs	Ref	Ref	Ref	Ref
CVD	0.12 (-0.14,0.38), 0.37	0.50 (-1.45,2.46), 0.61	0.44 (-0.21,1.10), 0.19	0.09 (-0.02,0.19), 0.10
CVD RFs/No CVD	**0.17 (0.05,0.30), 0.01**	**0.96 (0.05,1.87), 0.04**	0.29 (-0.01,0.60), 0.06	0.03 (-0.02,0.08), 0.17

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THU0126 FACTORS AFFECTING THE DISCREPANCY BETWEEN PATIENT AND PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS OVER TIME

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Background: Rheumatoid Arthritis (RA) is a chronic disease that requires regular follow-ups over time. Physicians make treatment adjustments based on their evaluation of disease status and patients' response to treatment while patients' perception of disease activity may change over time.
Objectives: we aimed to assess the discrepancy between patient global assessment of disease activity and physician assessment of disease activity at baseline and after one year in patients with early RA. We also evaluated factors affecting this discrepancy at these two time points.
Methods: Patients enrolled in the Ontario Best Practices Research Initiative (OBRI), a prospective observational cohort of patients with RA who had disease duration of <12 months (early RA) and had visits both at baseline and after one year were included. The discrepancy between patient global assessment of disease activity (PTGA) and physician global assessment of disease activity (MDGA) was calculated by simple subtraction (PTGA-MDGA). The value of $\geq$30 was considered discordant which could be either positive or negative in favor of PTGA or MDGA. Linear regression analysis was used to assess factors affecting PTGA, MDGA, and PTGA-MDGA discrepancy at baseline and one year.
Results: A total of 460 patients with early RA were analyzed. Majority were female (72.4%) with mean (± SD) age of 57 years (±0.6). the discordance rate was 109 (24%) and 99 (21%) at baseline and one year, respectively. In the majority of the discordant cases, PTGA was higher (98 (90%) at baseline and 85 (86%) at one year). Discordant patients had significantly higher fatigue score, health assessment questionnaire disability index (HAQ-DI), pain score, PTGA, MDGA, tender join, composite measures of disease activity and higher number of comorbidities at baseline.
Multivariable regression analysis showed that the higher PTGA is significantly associated with higher SJC, TJC and fatigue both at baseline and one year and with higher pain score only at one year. Similar associations were found for MDGA except fatigue which was not significant. Multivariable regression analysis showed that the higher discrepancy between PTGA and MDGA is associated significantly with lower SJC (β=-2.75), higher TJC (β=1.17), and higher fatigue (β=0.85) at baseline. At one-year follow-up, higher pain was the strongest factor (β=4.99) for affecting the higher PTGA-MDGA discrepancy compared with SJC (β=-1.65) and fatigue (β=1.24).
Conclusion: Significant discrepancy between PTGA and MDGA exists in about a quarter of patients with early RA at baseline and slightly less after one year. In the majority of these patients PTGA is higher over time. The number of active joints affects both assessments and this effect persists at one year. Clinicians should consider the above associations when makin
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THU0127 IMMUNOGENICITY AND SAFETY OF 23-VALENT PNEUMOCOCCAL VACCINE IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM 5-YEAR FOLLOW UP

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Background: In rheumatology, comorbid infections have significant impact on patients' morbidity, mortality and quality of life. Prevention of infections is an integral part of supervision of these patients.
Objectives: The aim of the study is to investigate immunogenicity and safety of 23-valent polysaccharide pneumococcal vaccine (PPV-23) in patients with rheumatoid arthritis (RA) in a five-years period.
Methods: The study included 79 RA patients with ≥2 recent episodes of respiratory tract infections (bronchitis, pneumonia). 52 RA pts were treated with methotrexate (MT), 14 – with leflunomide (Lef), 13– with TNF- α inhibitors + MT. One dose (0,5 ml) of PPV-23 was administered subcutaneously without discontinuing MT/Lef or 28-30 days prior to initiation of TNF- α inhibitors. Control visits were scheduled as follows: at baseline (Visit 1), and in 1, 3, and every year after immunization. 39 out of 110 pts were followed for 24 months, 23 pts – for 36 months, 23 pts – for 48 months, and 18 - for 60 months. Standard clinical examination and lab tests were performed at each visit.
Levels of serum antibodies (AB) to Pneumococcal capsular polysaccharide were measured with VaccZymeTM PCP IgG 2 panels (The Binding Site Group Ltd, Birmingham, UK). Coefficient of post-immunization response (CPR) was determined for each patient as the ratio of AB levels at Visits II, III, IV, V, VI and VII to AB level at Visit I.
Results: 53 (67%) patients did not have any reactions to the vaccine, 26 (33%) patients indicated pain, swelling and hyperemia of the skin (diameter up to 2 cm) at the injection site of the vaccine, low-grade fever. These typical reactions following vaccination are completely regressed within days without any additional treatment. They were not associated with RA therapy and did not require changes in ist schemes.
Pronounced positive immune reaction to PPV-23 was documented in all RA patients on different therapeutic regimens as significant AB incremental growth. Significantly high level of post-immunization response still persisted after 4 and 5 years of follow-up.The proportion of responders to PPV-23 after 5 years reached 73% among RA patients. (Table).
No case of clinically or radiographically confirmed pneumonia was documented during the follow up period, although one case of interstitial viral pneumonia was registered in 6 month after immunization.
Not a single vaccination-related RA exacerbation episode or new autoimmune phenomenon was documented during the follow-up.

Table. AB dynamics in RA pts during 5-year FUP, M± σ.

	Visit II (1 month)	Visit IV (12 month)	Visit V (24 month)	Visit VI (36 month)	Visit VII (48 month)	Visit VIII (60 month)
RA patients	82,20 [46,00; 133,50]	250,62* [187,70; 316,90]	298,70* [175,99;420,81]	107,8 [98,2;159,4	140,5* [107,9;208,3]	194,8* [120,1;361,4]

*p<0,05
Conclusion: Thus, all given prove the sufficient immunogenicity and safety of 23-valent pneumococcal vaccine in RA patients after 5 years of follow-up, getting different therapeutic regimens.
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THU0128 GLUCOCORTICOID TAPERING IN MONTHLY 1-MG DECREMENTS DOES NOT RESULT IN CLINICALLY MANIFEST ADRENAL INSUFFICIENCY IN PATIENTS WITH RHEUMATOID ARTHRITIS: LEARNINGS FROM THE PHASE 3/4 SEMIRA STUDY

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Background: Systemic glucocorticoids (GCs) are used to treat serious inflammatory diseases but are associated with adverse events. Guidelines recommend tapering GCs to the lowest possible dose and discontinuing them as soon as possible. Physicians have concerns that reductions, even from low doses, may increase disease symptoms or cause adrenal insufficiency (AI), especially in patients receiving GCs long-term. The expectation of AI risk may be inflated by false positives in cortisol testing of patients without relevant symptoms and by a lack of robustly designed GC taper trials. The international, multicenter SEMIRA trial evaluated a taper scheme in rheumatoid arthritis (RA) patients receiving tocilizumab (TCZ) ± conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).[1]
Objectives: To determine whether GC tapering in the SEMIRA trial resulted in any cases of AI.
Methods: Eligible patients had low disease activity or remission for ≥4 weeks and were receiving a stable prednisone regimen (5 mg/day) + TCZ ± csDMARDs for ≥4 weeks. Patients had to have received ≥6 months' total TCZ + GCs (prednisone equivalent 5-15 mg/day). Patients were randomly assigned (1:1) to double-blind continued prednisone 5 mg/day (n = 128) or prednisone taper (n = 131). TCZ ± csDMARDs remained stable during the 24-week study. The prednisone taper consisted of 1-mg decrements every 4 weeks starting at randomization and ending at GC discontinuation (week 16). RA flares were treated with prednisone 5 mg/day for 2 weeks. The primary assessment was maintenance of disease control with GC discontinuation. The protocol provided evidence-based guidance for diagnosis and management of AI. Confirmatory testing was recommended for patients with suspected AI, but routine precautionary ACTH stimulation testing was not mandated.
Results: In the taper arm, 65% of patients achieved "treatment success" by meeting all key secondary end point components (maintained low disease activity, experienced no flares, and had no confirmed AI necessitating replacement therapy) at week 24 versus 77% of continued patients (risk ratio for treatment success, 0.833 [95% CI, 0.714-0.972]; p = 0.021). None of the taper patients required ACTH stimulation testing, and no cases of AI were reported.
Conclusion: SEMIRA demonstrated the usefulness of a new standardized GC dose taper scheme. Two-thirds of patients receiving TCZ underwent successful tapering and could stop GCs entirely, which is higher than the spontaneous 35% discontinuation rate observed in real-world RA patients[2] and underscores the potential to further reduce glucocorticoid burden. Clinical AI was not observed; thus, routine laboratory testing may be unnecessary in real-world applications of this taper scheme.

REFERENCES:

[1] Burmester GR, et al. *Arthritis Rheumatol*. 2018;70(suppl 10):L18. 2. Yagız B, et al. *Arthritis Rheumatol*. 2018;70(suppl 10):627.

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THU0129 ASSESSMENT OF LONELINESS IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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Background: Rheumatic disease and psychosocial status have bi-directional impacts on each other. Loneliness, as a component of psychosocial status, may be interrelated with affect and social support and may also be influenced by the disease itself in patients with inflammatory arthritis[1].
Objectives: The aim of this study is to document loneliness and associated factors in patients with inflammatory arthritis. Effects of demographic and disease-related factors, functional status, affect, and social support on loneliness, and loneliness on functional status will be evaluated.
Methods: Consecutive patients with rheumatoid arthritis(RA), ankylosing spondylitis(AS), and psoriatic arthritis(PsA), meeting ACR, ASAS, and CASPAR criteria, respectively, were included in the study. Demographic data and general clinical parameters(Table 1) were identified for each patient. Beck depression and Beck anxiety inventory, revised multidimentional scale of percieved social support, HAQ-DI, and UCLA loneliness scale (ULS-8), all validated in Turkish population, were used for the assessments. Nonparametric comparison (Wilcoxon-Mann-Whitney and Kruskal-Wallis) and correlation(Spearman) tests were used to evaluate associations of demographic data, clinical parameters, and depression, anxiety, social support, HAQ-DI scores with ULS-8 score. Multiple regression models were generated for significant associations.
Results: Demographic data, general clinical features, functional status, and ULS-8 scores of disease groups are summarized in Table 1. Among demographic and general clinical parameters, higher number of total drugs and lower education were associated with significantly higher ULS-8 scores (data not shown). Although weak, there were significant correlations between ULS-8 and HAQ-DI, depression, anxiety, social support, and doctor global VAS scores (Table 2). Stronger correlations were observed between HAQ-DI and depression, anxiety, and patient global VAS scores (Table 2). Among demographic and general clinical parameters, only number of drugs was weakly associated with HAQ-DI score (rho=0.18, p=0.037). Two multiple regression models were generated for predicting HAQ-DI and ULS-8 scores. Depression, anxiety and patient global VAS scores remained significant for predicting HAQ-DI after multiple regression with covariates ULS-8, depression, anxiety, social support, patient and doctor global VAS scores, and number of drugs used (adjusted R^2=0.53, p<0.001). Although significant (p<0.001), only 14% of variance in ULS-8 may be jointly explainable with covariates HAQ-DI, depression, anxiety, social support, doctor global VAS scores, number of drugs used, and education status. The only independent predictor was the education status. ULS-8 score did not correlate with DAS28, CDAI, and SDAI in RA; BASDAI, BASFI, and ASDAS in AS; and number of swollen and tender joints, ESR, CRP, patient global, doctor global, pain, and fatigue VAS scores in PsA.

Abstract THU0129 –Table 1.

Table 1. Demographic data, general clinical parameters, functional status, and ULS-8 scores according to disease groups.

	RA (n=58)	AS (n=53)	PsA (n=30)	p value
Age, years	58 (IQR 12)[a,b]	42 (IQR 14)[a]	45 (IQR 20)[b]	<0.001
Female, n(%)	41 (70,7)[a]	19 (35,8)[a,b]	21 (70)[b]	<0.001
Married, n(%)	46 (79,3)	46 (86,8)	28 (93,3)	0.196
Number of children	2 (IQR 0)	2 (IQR 1)	2 (IQR 1)	0.102
Household size	3 (IQR 2)	4 (IQR 1)	4 (IQR 1)	0.057
Education status, n(%)				0.001†
Primary school or lower	33 (56,9)[a]	13 (24,5)[a]	14 (46,7)	
Secondary or high school	17 (29,3)[a]	28 (52,8)[a]	16 (53,3)	
Higher education	8 (13,8)	12 (22,6)[a]	-[a]	
Actively working, n(%)	16 (27,6)[a]	31 (58,5)[a]	10 (33,3)	0.003†
Comorbid disease present*, n(%)	36 (62,1)[a]	19 (35,8)[a]	12 (40)	0.014†
Number of drugs	5 (IQR 3)[a]	2 (IQR 1)[a,b]	5 (IQR 3)[b]	<0.001†
Disease duration, years	8 (IQR 8)	9 (IQR 9)	9,5 (IQR 14)	0.555
ESR, mm/h	25 (IQR 26)[a]	13 (IQR 15)[a]	19 (IQR 22)	0.014†
CRP, mg/L	6 (IQR 8,8)	7,6 (IQR 9,3)	5,1 (IQR 6)	0.396
bioDMARD use, n(%)	6 (10,3)[a,b]	37 (69,8)[a]	16 (53,3)[b]	<0.001
Adherent to treatment, n(%)	52 (89,7)	47 (88,7)	27 (90)	0.978
HAQ-DI groups, n(%)				0.757
Mild disability	52 (89,7)	48 (90,6)	29 (96,7)	
Moderate disability	5 (8,6)	5 (9,4)	1 (3,3)	
Severe disability	1 (1,7)	-	-	
ULS-8 score‡	15 (IQR 7)	15 (IQR 5)	14,5 (IQR 7)	0.749

Continuous variables are given as medians with interquartile ranges (IQRs). Disease group, age, sex, education and working status, presence of comorbid disese, number of drugs, and ESR were controlled for each other as appropriate. [a] and [b] denote statistically significant pairs in the same raw (post hoc adjusted p<0.05). *psoriasis was excluded. †no actual difference after control for confounders. ‡Score ranges from 8 to 32, with higher scores suggesting higher degree of loneliness.

Abstract THU0129 –Table 2.

Table 2. Correlations between ULS-8, HAQ-DI, depression, anxiety, social support, and patient and doctor global VAS scores

		Beck depression score	Beck anxiety score	Social support score	Patient global VAS score	Doctor global VAS score	HAQ-DI score
ULS-8 score	rho	0.32	0.33	-0.22	0.1	0.16	0.27
	p value	<0.001	<0.001	0.009	0.224	0.058	0.001
HAQ-DI score	rho	0.53	0.53	-0.25	0.5	0.28	-
	p value	<0.001	<0.001	0.003	<0.001	<0.001	

Significant correlations exist between Beck depression, Beck anxiety, social support, and patient and doctor global VAS scores.

Conclusion: Loneliness is associated with depression, anxiety, lack of social support, and lower education but not with disease activity in patients with inflammatory arthritis. Self -report loneliness, can be a contributing factor to the disability of the inflammatory arthritis.

REFERENCE:

[1] Kool MB, et al. Loneliness in patients with rheumatic diseases: the significance of invalidation and lack of social support. J Psychol 2012;146:229-41

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THU0130 INCIDENCE AND RISK FACTORS OF FALLING IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: People with rheumatoid arthritis (RA) may be at greater risk of falling than the non-RA population [1]. This increased falls risk may be due to RA disease-related impairments including pain, deformity and decreased muscle strength, as well as reduced functioning such as altered gait and a decline in postural stability.

Objectives: The aim of this study was to evaluate the prevalence of falls and its association with clinical data, disease-related outcomes and physical performance tests.
Methods: Cross-sectional study including patients with RA, followed in the Rheumatology Department over a period of 1 month in 2018. The following parameters were evaluated: clinical aspects; fall occurrence in the previous 12 months; pain on a visual analogue scale (VAS); RA disease Activity Score 28 (DAS28)/erythrocyte sedimentation rate (ESR); Functional capacity assessed by the Health Assessment Questionnaire (HAQ); anxiety and depression by the Hospital Anxiety and Depression Scale (HADS) and Physical performance, assessed by 3 tests, the Timed Up and Go (TUG), one leg standing balance (OST) and sternal nudge test (SNT).
Results: Forty-eight patients were enrolled, the average age was 55.8 ± 13.9 and the sex ratio was 0.14. The average disease duration was 13.49 years ± 9.12. The average DAS28 was 4.63 ± 1.19 and HAQ was 0.77 ± 0.88. Falls were reported by 44.7% of patients: 27.7% had one fall and 17% had $\geq$ 2 falls. Patients had a fractures history in 10.9% of cases and dislocations in 6.5% of cases. The HAQ (p=0.04) and c reactive protein (p=0.01) was associated with fall history; the other parameters (Gender, number of medications, age, disease activity and physical tests) showed no associations with history of falls. Physical performance was decreased to: 58.4% for TUG test, 61.7% for OST and 36.2% for SNT. The worst performance in physical tests (TUG, OST and SNT) was associated with older age, higher erythrocyte sedimentation rate, higher HAQ, and increased DAS28 (p<0.05). In addition, hips and especially knees involvement was significantly associated with TUG (p=0.03) and OST test (p=0.003). TUG test was significantly associated with depression (p=0.04). The OST test was associated with higher disease duration (p=0.004), VAS (p=0.006) and tender joints (p=0.001). There was no association between number of falls and any of the physical performance tests.
Conclusion: It was observed that the occurrence of falls is quite common in this population. The occurrence of falls in this sample of rheumatoid arthritis patients bears no relation to disease activity or physical performance tests. But, falls were associated with functional capacity.

REFERENCE:
[1] StanmoreEK,OldhamJ,SkeltonDA,O'Neill T,PillingM,CampbellAJ,etal.Risk factors forfallsinadultswithrheumatoidarthritis:aprospectivestudy. Arthritis CareRes2013;65:1251–8.

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THU0131 EFFECT OF METABOLIC SYNDROME ON THE COURSE OF RHEUMATOID ARTHRITIS AND CARDIOVASCULAR RISK

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Background: Both rheumatoid arthritis (RA) and metabolic syndrome (MS) have an inflammatory component in the pathogenesis and both aggravate cardiovascular risks.
Objectives: The aim is to study the effect of MS on the course of RA and the increase in cardiovascular risk in these patients.
Methods: 100 patients (men 7%, women 93%) aged 21 to 81 years (average age 55±12.4) with reliable RA were examined. High activity in DAS28 scale was observed in 68%, moderate - in 30%, low - in 2%, rheumatoid factor (RF) positivity - in 88%, ACCP - 81%. Disease-modifying antirheumatic drugs received 78%, glucocorticosteroids 60% of patients. Arterial hypertension (AH) was present in 45% of patients. MS according to NCEP/ATPIII criteria was identified in 59 patients, according to its presence, patients were divided into 2 groups (MS+ and MS-). Patients were examined in standard laboratory tests, all of them had echocardiogram.
Results: In the presence of MS, RA activity was significantly higher (DAS28 4.2±0.5) compared with patients without it (DAS28 3.5±0.6) most of all because of pain syndrome (p<0.01). A correlation was observed between the presence of MS and pain on a visual analogue scale and the number of painful joints (p<0.05). However, there was no significant difference according to the level of the ESR, CRP, the presence of the RF, the X-ray stage of RA. There were no differences in the range of received therapy, but the dose of prednisone was higher in the MS+ group (7.8±3.5 vs 6.4±3.69, p<0.05).
Systolic blood pressure (BP) was higher in the MS+ group (128.3±17.3) vs MS- (119.3±15.9). The level of BP correlated (p<0.05) with the severity of pain. The verified AH was present in 42 (71.2%) patients of the MS+ group (1 stage -2, 2 stage -24, 3 stage -16 patients) and in 3 (7.3%) patients of the MS- group (1 stage in 1 patient, 2 stages in 2 patients). The cholesterol level was higher in the MS+ group 5.1±1.1 compared with the MS- group 4.6±0.6 (p<0.01). There was observed a persistent tendency (p<0.01) in increasing of the mass index of the left ventricle myocardium according to echocardiogram. In patients with MS+, hypertrophy of the left ventricular myocardium was detected according to echocardiogram even with a normal level of BP.
Conclusion: The presence of MS in patients with RA is associated with a higher activity of RA most of all because of pain syndrome. At the same time, pain syndrome correlates with the level of blood pressure. The combination of MS and RA leads to an increase of cardiovascular risk factors: cholesterol level and myocardial hypertrophy, which causes the need of using the echocardiography for this group of patients.

REFERENCE:
[1] rheumatoid arthritis, metabolic syndrome.

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THU0132 EVALUATION OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICAL AGENTS: 3-MONTH FOLLOW-UP

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Background: Systemic inflammation is an additional and independent predictor of cardiovascular disease (CVD) in rheumatoid arthritis (RA). It is worth mentioning that lipid levels, blood pressure and other major risk factors of CVD constitute a wide field of investigation in case of treatment with biological disease-modifying anti-rheumatic drugs (DMARDs).
Objectives: The aim of this study is to assess the impact of biological agents on markers of CVD risk in patients with RA.
Methods: This is a prospective, observational study which included biologic-naïve RA patients treated with synthetic DMARDs, who had a negative history of CVD. Thirty-one patients and 31 healthy matched-controls (for gender, age and smoking) were compared for total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides (TGs), Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB) and Lipoprotein A (LpA). Additionally, an ultrasonographic measurement of intima-media thickness (IMT) of carotids was performed by an experienced sonographer to all patients in order to detect the presence of atherosclerosis at baseline. Furthermore, in a subgroup of 19 of these 31 RA patients, the parameters we previously reported (except for IMT) were compared between baseline and a 3-month follow up. We also compared disease activity indexes [disease activity score (DAS28), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)] at these predefined time-points.
Results: As regards the demographic characteristics of 31 RA patients, the mean (SD) age was 54.7 (14.05) years, disease duration was 4.5 (1.3) years, there were 11 (35.5%) men and 20 (64.5%) women and 6 (31.6%) smokers. As far as the immunological profile of patients is considered, 17 (54.8%) were RF(+) and 8 (25.8%) ACPA(+). The comparison of the parameters between RA patients and matched-controls revealed an increased IMT in RA patients [0.9 (0.17) vs 0.6 (0.13) mm; p<0.001], while the other parameters involving the lipid profile did not differ among the two groups.
In the subgroup of 19 patients, there was a significant increase in mean (SD) HDL-C and ApoA1 levels from baseline to 3-month follow-up [55.3 (15.44) vs 61.68(15.3) and 163.16(28.89) vs 173.11(29.65) respectively; p<0.05)]. There was also a reduction in mean systolic blood pressure [137.89(14.36) vs 130.53(12.68); p<0.05)], diastolic blood pressure [81.63 (6.8) vs 77.63(6.09); p<0.05)], ESR [25.53(18,57) vs 19.84(16.44); p<0.05)] and DAS28 score [3.41(1.14) vs 2.62(1.12); p<0.05)]. No

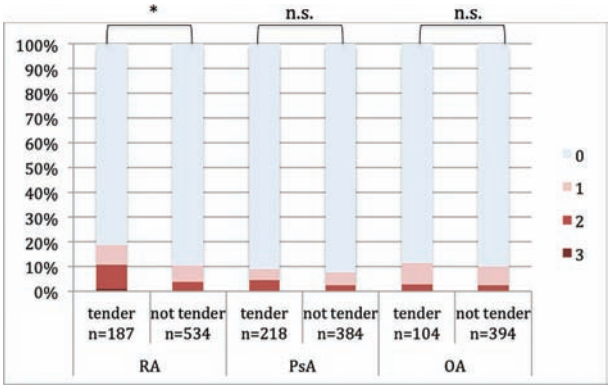
statistically significant difference was found for the rest of parameters of lipids or inflammation markers.
Conclusion: IMT measurement confirmed that patients with RA are at a higher risk of developing early atherosclerosis. The results of this study demonstrate an improvement of cardiovascular risk in RA patients treated with biological DMARDs via an increase in HDL-c and ApoA1 levels and a reduction of ESR and blood pressure measurements even from the first 3 months of treatment initiation. Long term studies are needed to determine the impact of biological agents on cardiovascular risk in RA.
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Disclosure of Interests:
None declared
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THU0133 TENDERNESS CAN BE REGARDED AS A SIGN OF INFLAMMATION IN RHEUMATOID ARTHRITIS

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Background: In inflammatory joint diseases, joint swelling is regarded as a sign of inflammation, which is associated with structural progression [1-3]. However, the significance of tenderness without swelling is unclear.
Objectives: To determine whether clinical tenderness can be considered a sign of inflammatory joint activity in patients with rheumatoid arthritis (RA), osteoarthritis (OA), or psoriatic arthritis (PsA)
Methods: 36/24/30 patients respectively with RA, OA and PsA were included in the study. Each patient underwent clinical examination, followed by an ultrasound examination of bilateral MCP 1-5 (metacarpophalangeal), PIP 1-5 (proximal interphalangeal) joint and wrists; the sonographer was blinded to clinical data. On clinical examination synovial swelling and tenderness were evaluated using a binary scoring method, and tender, non-swollen joints (TNS) were identified. Grey-scale signs of synovitis (GS) and Power Doppler signal (PD) were evaluated using a semiquantitative grading system.
Differences of PD signals between groups (RA vs. OA, RA vs. PsA, TNS vs. non-tender non-swollen joints) were calculated by Chi-Square test. Furthermore, joints of RA and PsA patients were tracked back for up to 6 years to identify the time point of the last swelling of that respective joint. Kaplan-Meier estimates for the occurrence of the last time point of swelling were compared between PD positive and PD negative TNS joints.
Results: TNS joints more often showed PD signal in RA patients as compared to those with OA and PsA (18.7% vs. 11.5% vs. 9.2%, respectively, p=0.135 for RA vs. OA; p<0.01 for RA vs. PSA). TNS joints were significantly more often PD positive as compared to non-tender non-swollen joints (18.7% vs. 10.3% respectively, p<0.01) in RA, but not in PsA (9.2% vs. 7.6%, p=0.54) or OA (11.5% vs. 10.2%, p=0.72) (fig. 1). Kaplan-Meier analysis revealed a significantly shorter time period to last observed swelling in PD positive as opposed to PD negative TNS joints in both RA (45.2 vs. 65.5 months, p=0.017) and PsA (20.6 months vs. 107.7 months, p<0.001), however we found no difference in GS positive vs. negative TNS joints.
Conclusion: The results of this study confirm the current practice of considering tenderness a sign of active inflammation in RA, but imply that this may not be the case in PsA or OA. The fact that shorter time to last swelling was associated with positive PD in TNS joints suggests that, at least in RA, tenderness might reside after prior clinical swelling has resolved.

REFERENCES:
[1] Conaghan PG, et al., Arthritis Rheum 2003; 48: 64-71.
[2] Aletaha D, et al. Ann Rheum Dis 2011; 70: 1975-1980.
[3] Aletaha D, et al. Arthritis Rheum 2011; 63: 3702-3711.



Abstract THU0133 – Figure 1. Power Doppler signals of tender non-swollen joints compared to non-tender non-swollen joints in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and osteoarthrosis (OA).

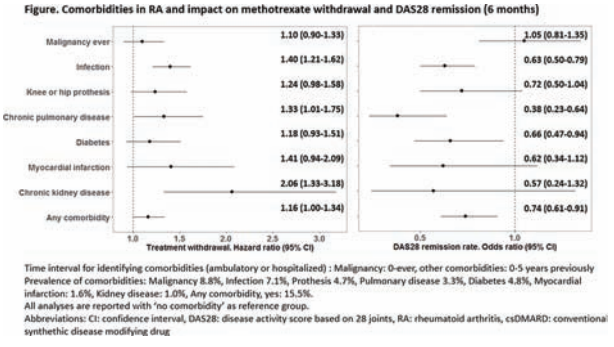
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THU0134 COMORBIDITIES IN >5000 PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING TREATMENT WITH METHOTREXATE IN ROUTINE CARE: PREVALENCE AND IMPACT ON TREATMENT OUTCOMES. AN OBSERVATIONAL COHORT STUDY FROM DANBIO

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Background: Methotrexate remains the anchoring drug for the treatment of rheumatoid arthritis (RA). Patients with RA often have comorbidities e. g. diabetes or pulmonary disease. Although methotrexate has been used for decades, little is known about the impact of various comorbidities on treatment outcomes.
Objectives: To describe the prevalence of comorbidities in csDMARD naïve RA patients initiating treatment with methotrexate in routine care and to explore the impact of common comorbidities on methotrexate treatment outcomes (achieving remission and adherence to treatment).
Methods: Observational cohort study based on the Danish nationwide quality registry, DANBIO. Adult RA patients who started treatment with methotrexate (oral or injection) as first csDMARD year 2010-2017 and who had been followed since onset of disease with regular controls were included. Concomitant treatment with other DMARDs were allowed. Treatment outcomes after ≈ 6 months of treatment were identified in DANBIO. Data were censored by April 2018. Seven different comorbidities (Figure) prior to start of methotrexate were identified in the national patient registry (NPR) through linkage by social security numbers.
Impact of each comorbidity was explored as 1) overall methotrexate treatment retention rate and 2) DAS28 remission rate (after 6 months' treatment). Analyses were by Cox- and logistic-regression analyses (adjusted for gender and age). The comorbidities were included one by one in the models. Finally, similar analyses were performed summed for all the seven comorbidities as any comorbidity yes/no.
Results: 5828 patients were included (66% female, median age 61 (IQR 51-70) years), whereof 906 (15.5%) had ≥1 of the predefined

comorbidities (63% female, median age 68 (60-74) years). Only 70 patients (1.4%) had ≥2 comorbidities.
Patients with comorbidities had increased withdrawal rate of methotrexate with hazard ratios ranging from 1.10-2.06 (Figure). Similarly, patients with comorbidities had poorer remission rate with odds ratios ranging from 0.38-0.74 except for previous cancer.
Conclusion: In this nationwide cohort of >5000 RA patients treated with methotrexate in routine care, approximately 15% of patients had comorbidities at treatment start. Patients with comorbidities had higher rate of withdrawal and poorer remission rates. This warrants specific attention when treating these patient groups in routine care.
Acknowledgement: Thank you for the Danish departments of Rheumatology for reporting to DANBIO



Abstract THU0134 – Figure 1

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THU0135 DETERMINANTS OF DISCORDANCE IN PATIENT'S AND PHYSICIAN'S GLOBAL ASSESSMENTS OF DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS IN THE "REAL" STUDY – BRAZIL

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Background: Discordance between the patient's global assessment of disease activity (PGA) and examiner's global assessment (EGA) has been described in rheumatoid arthritis (RA) (1,2). Understanding the reasons for this discrepancy is essential in the context of treat-to-target treatment strategy.
Objectives: To assess the determinants of PGA and EGA and factors associated with discordance between them.
Methods: The REAL study included RA patients from Brazilian public health centers. Clinical, laboratory and outcomes measures were collected. PGA and EGA were rated on a visual analog scale and analyzed. Three groups were defined: no discordance (a difference between PGA and EGA within 3 cm), positive discordance (PGA exceeding EGA by >3 cm), and negative discordance (PGA less than EGA by >3 cm). Multivariate regression analysis was used to identify determinants of PGA and EGA and their discordance.
Results: 1115 patients (89,4% female, mean age 56.7y and median disease duration of 12.7y) were enrolled. Two factors were associated with PGA in the final multivariate model: one point increase in the pain scale (PS) leads to an increase of 0.62 in PGA; one point increase in HAQ increases by 9,25 points the PGA. The factors associated with EGA were: PS, number of tender and swollen joints (NTJ and NSJ), RF, ESR, HAQ and use of corticosteroids. Discordance between patient and physician was found in 30.52%: positive discordance (PD) in 24.6% and negative discordance (ND) in 5.92%. An increase of one point in the NSJ was associated with a 12% increase in the chance of ND. The chance of PD increased by 90% and 2% for each unit increased in HAQ and PS respectively. Finally, the chance of PD decreased by 3% for each point increased in NTJ and by 15% for each point increased in NSJ.
Conclusion: In one-third of the assessments, there was disagreement between PGA and EGA (a PD in 80% of them). Pain and function were determinants for patients to estimate disease activity, while swollen joints were the main factor related to a worse examiner´s evaluation. These data show how different can be the perspectives of patients and assistants.

REFERENCES:

[1] Smolen JS, Strand V, Koenig AS, Szumski A, Kotak S, Jones TV. Discordance between patient and physician assessments of global disease activity in rheumatoid arthritis and association with work productivity. Arthritis Res Ther. 2016; 18:114.
[2] Desthieux C, Hermet A, Granger B, Fautrel B, Gossec L. Patient-physician discordance in global assessment in rheumatoid arthritis: a systematic literature review with meta-analysis. Arthritis Care Res (Hoboken). 2016; 68:1767.

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clinical and/or experimental studies related to this work and sponsored by AbbVie, BMS, Janssen, Pfizer and Roche; has received personal or institutional support from AbbVie, BMS, Janssen, Pfizer and Roche; has delivered speeches at events related to this work and sponsored by AbbVie, Janssen, Pfizer and Roche, Paid instructor for: Has participated in clinical and/or experimental studies related to this work and sponsored by AbbVie, BMS, Janssen, Pfizer and Roche; has received personal or institutional support from AbbVie, BMS, Janssen, Pfizer and Roche; has delivered speeches at events related to this work and sponsored by AbbVie, Janssen, Pfizer and Roche, Speakers bureau: Has delivered speeches at events sponsored by AbbVie, Janssen, Pfizer and Roche, Licia Mota Speakers bureau: Has delivered speeches at events sponsored by AbbVie, Janssen, Pfizer, Roche and UCB., Geraldo Castelar-Pinheiro Consultant for: Has received consulting fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Glaxosmithkline, Janssen, Pfizer, Sanofi Genzyme and Roche

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THU0136 TNF INHIBITORS IN PREGNANCY: STOP, REDUCE OR CONTINUE? – OBSERVATIONS FROM A PREGNANCY OUTPATIENT CLINIC

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Background: Women with active Rheumatoid Arthritis (RA) are more prone to relapses and complications during pregnancy. The potential risks of disease activation and treatment during gestation should be weighed in a shared decision prior to conception. An increasing number of women who wish to conceive are being treated with TNF inhibitors (TNFi). Some wish to discontinue or at least reduce therapy while pregnant and require information on opportunities and risks.

Objectives: To study the outcome of pregnancies in women with RA who either discontinued, reduced or maintained their TNFi treatment after conception.

Methods: Pregnancies from an outpatient pregnancy clinic were evaluated before conception, during each trimester and postpartum. Clinical characteristics, disease activity (DAS28-CRP), medication use and pregnancy outcome were analysed. A flare was defined as increase in clinical activity leading to intensified treatment (new treatment with prednisolone or increase in dosage $\geq$5 mg/day and/or treatment with intraarticular glucocorticoids and/or (re-)treatment with DMARDs/TNFi). All women received extensive counselling before pregnancy based on current knowledge and subsequently decided to continue or stop TNFi at conception. If they stayed on TNFi and were in remission, women received the suggestion to stretch the therapy intervals in a disease activity guided manner.

Results: After exclusion of one miscarriage, 56 completed pregnancies were enrolled and grouped according to their decision to stop (group 1) or continue (group 2) TNFi therapy during pregnancy. The latter were subdivided into those who could stretch the therapy intervals (group 2a) and those who could not (group 2b). Group 1 also contained seven women who received Tocilizumab or Rituximab until conception.

Despite low disease activity (DAS $\leq$ 3.2) at conception in all groups, a higher flare rate during pregnancy and postpartum was observed after discontinuation of TNFi. In addition, a higher dose of oral prednisolone and more frequent intraarticular therapy was reported in group 1 (table 1). Postpartum, 38.9% restarted TNFi therapy. About half of the women who chose to stay on therapy during gestation were able to stretch the injection interval of their TNFi, which was either Adalimumab (every 3.0 weeks), Certolizumab (median every 4.0 [min 4.0, max 5.0] weeks) or Etanercept (median every 3.0 [min 2.0, max 6.0] weeks) (Table 2). Relapse rate as well as prednisolone consumption was comparable between group 2a and group 2b.

Abstract THU0136 –Table 1.

	TNFi exposure until conception (N=37)	Pregnancies with ongoing TNFi exposure (N=19)	
		Successful reduction (N=9)	No reduction possible (N=10)
Patient characteristics at conception			
Age (years), median (IQR)	32 (29-36)	32 (30-34)	36 (34.25-36.75)
Disease duration (months), median (IQR)	80 (48-204)	96 (84-276)	70 (54-109.5)
Seropositivity, n (%)	21 (56.8%)	5 (55.6%)	8 (80.0%)
DAS28, median (IQR)	2.8 (2.5-3.1)	2.9 (2.5-3.0)	2.7 (2.6-2.9)
Prednisolone (mg/day), (median, IQR)	5.0 (5.0-7.0)	5.0 (3.5-5.0)	5.0 (3.5-5.0)
Sulfasalazine, n (%)	2 (5.4%)	3 (33.3%)	-
HCQ, n (%)	1 (2.7%)	2 (22.2%)	3 (30.0%)
Pregnancy outcomes			
DAS28-CRP ≤ 3.2, n (%)			
1st trimester	23 (62.2%)	8 (88.9%)	8 (80.0%)
2nd trimester	16 (43.2%)	8 (88.9%)	8 (80.0%)
3rd trimester	23 (62.2%)	8 (88.9%)	8 (80.0%)
3 months postpartum	18 (48.6%)	7 (77.8%)	7 (70.0%)
6 months postpartum	28 (76.5%)	7 (77.8%)	8 (80.0%)
Flare during pregnancy, n (%)	25 (67.6%)	-	2 (20.0%)
Flare postpartum, n (%)	19 (51.4%)	2 (22.2%)	2 (20.0%)
Preterm birth[1], n (%)	10 (27.0%)	1 (11.1%)	-
Low birth weight[2], n (%)	7 (19.0%)	-	-
Breastfeeding, n (%)	25 (67.6%)	9 (100.0%)	9 (90.0%)
Glucocorticoid use during pregnancy			
Prednisolone (mg/day), (median, IQR)			
1st trimester	10.0 (5.0-10.0)	5.0 (5.0-5.75)	5.0 (3.5-5.0)
2nd trimester	10.0 (10.0-15.0)	5.0 (5.0-5.75)	5.0 (3.5-7.0)
3rd trimester	10.0 (9.5-13.0)	5.0 (5.0-5.0)	5.0 (3.5-7.0)
Of those taking prednisolone – taking ≥ 10mg/d, n (%)			
1st trimester	15 (65.2%)	1 (16.7%)	2 (20.0%)
2nd trimester	23 (85.2%)	-	2 (20.0%)
3rd trimester	18 (75%)	-	1 (10.0%)
Intraarticular prednisolone therapy, n (%)	17 (45.9%)	-	1 (10.0%)

[1] delivery ≤ 36+6 weeks of gestation, [2] birth weight < 2500g, HCQ = hydroxychloroquine

Table 1

Abstract THU0136 –Table 2.

	No TNFi	Adalimumab	Certolizumab	Etanercept
Women on therapy at preconception				
All Groups, n (%)	7 (12.5%)	7 (12.5%)	18 (32.1%)	23 (41.1%)
Group 1, n (%)	7 (18.9%)	4 (10.8%)	8 (21.6%)	18 (48.6%)
Group 2a, n (%)	-	1 (11.1%)	5 (55.6%)	3 (33.3%)
Group 2b, n (%)	-	2 (20.0%)	6 (60.0%)	2 (20.0%)
Women of group 2a during pregnancy				
Therapy interval (weeks), median (min-max)	-	3.0	4.0 (4.0-5.0)	3.0 (2.0-6.0)

Conclusion: Women with RA who discontinue TNFi at conception face a higher risk of flares during pregnancy and often have an increased demand for steroids to control disease activity. When in remission under ongoing TNFi therapy during pregnancy, it seems possible and safe for women to reduce the frequency of injections in a disease activity guided manner. These real-world data will help to provide women with comprehensive advice on treatment options and risks regarding TNFi therapy at pregnancy counselling.

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THU0137 SUBCLINICAL THYROID DYSFUNCTION IS A CARDIOVASCULAR DISEASE RISK IN FEMALE RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a multisystem autoimmune disease that proved to be associated with other autoimmune diseases particularly hypothyroidism. Subclinical hypothyroidism had been reported in RA. As well, RA patients are at double the risk of cardiovascular diseases (CVD). The increased risk of CVD is not fully explained by the

traditional and non-traditional CVD risk factors. In general population, hypothyroidism had been reported as a CVD risk factor.
Objectives: This study aimed for the first time to investigating the relationship between thyroid function parameters and the CVD risk as manifested by the carotid intima media thickness (cIMT) among RA patients.
Methods: All the RA patients were recruited through a specialized rheumatology clinic at the Ministry of Health and Prevention of UAE, from April 2016 to December 2018. Fasting Free thyroxine (FT4), Free triiodothyronine (FT3), and thyroid stimulating hormone (TSH) were assessed in all the participants within the same week of the cIMT measurement. Linear regression analysis used to look for the correlation of the thyroid function test (TSH, T$, and T3) and the cIMT.
Results: A total of 154 female RA patients satisfying ACR/EULAR criteria for diagnosis of RA were recruited. None of the patients had history of thyroid, renal, or hepatic disorders. None of the patients were pregnant. The mean age for the participants was 50 ±12 years (Min16 –Max 87). The mean FT4 was 15.7 ± 3.6 (NR: 12-22 pmol/L), mean FT3 was 4.54 ± 1.0 (NR: 4-6.8 pmol/L), and mean TSH was 2.60 ± 3.3 (NR:0.27-4.2 mIU/L). The mean cIMT was 0.57±0.11 mm. correlating TFT with cIMT showed that while there was no correlation between each of the FT3 and FT4with the cIMT (P value 0.46 and 0.19, respectively), there were a significant negative linear relationship between TSH value and the cIMT (P=0.03, β=- -0.006).
Conclusion: Subclinical thyroid dysfunction might be an additional non-traditional CVD risk factors that can help in filling the gap of understanding the increased risk of CVD in RA. Further studies at a larger scale are needed to confirm the study findings. Also, there is a need to confirm if management of thyroid dysfunction in RA may help in overall improvement of this subset of population.

REFERENCES:

[1] Atzeni F, Doria A, Ghirardello A, Turiel M, Batticciotto A, Carrabba M, Sarzi-Puttini P. Anti-thyroid antibodies and thyroid dysfunction in rheumatoid arthritis: Prevalence and Clinical Value. Autoimmunity. 2008;41:111–5.
[2] Andonopoulos A, Siambi V, Makri M, Christofidou M, Markou C, Vagenakis A. Thyroid function and immune profile in rheumatoid arthritis. A controlled study Clin Rheumatol. 1996;15:599–603.
[3] Shiroky J, Cohen M, Ballachey M, Neville C. Thyroid dysfunction in rheumatoid arthritis: a controlled prospective survey. Ann Rheum Dis. 1993;52:454–6

Disclosure of Interests: None declared
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THU0138 RHEUMATOLOGISTS' ADHERENCE TO THE TREAT-TO-TARGET PRINCIPLE IN EARLY RA PATIENTS WITHIN THE PRAGMATIC CARERA TRIAL: ROOM FOR IMPROVEMENT?

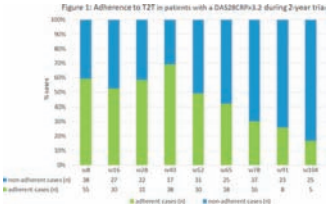
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Background: Treating to a predefined target is a principle adopted in guidelines to treat rheumatoid arthritis (RA). It is currently the most efficient strategy to control disease activity, but its implementation in daily clinical practice remains challenging.
Objectives: To evaluate rheumatologists' adherence to a treat-to-target (T2T) approach at a threshold of low disease activity (DAS28CRP≤3.2) in patients with early RA during the 2-year Care in early RA (CareRA) study.
Methods: CareRA is an investigator-initiated pragmatic multicentre trial, in which patients with early RA and naïve to conventional synthetic disease modifying anti-rheumatic drugs (csDMARD) were included (n=379). Participants were randomized to different remission induction schemes consisting of a csDMARD combination or methotrexate (MTX) monotherapy with and without a prednisone tapering down scheme. Following the T2T approach, specific treatment adaptations had to be performed in case of DAS28CRP>3.2 during the first study year, unless a predefined reason not to intensify treatment was provided. As first step, dose of MTX had to be increased from 15mg to 20mg weekly. As second step, dose of the other csDMARD was escalated in the combination arms and leflunomide was added in the MTX monotherapy arms. From week (w)52 onwards, further T2T was advised but type of treatment adaptation was left at the rheumatologists' discretion. Adherence to this T2T approach was defined as performing a dose escalation or changing/adding DMARD medication in case of DAS28CRP>3.2 and was evaluated at every study visit during 2 years. Additionally, remission (DAS28CRP<2.6) rates at w104 were compared between patients in which T2T was applied at every visit and patients not always treated to target. Only data from patients for which DAS28-CRP scores were available were taken into account to evaluate the low disease activity state.

Table 1. Lipid profile in RA patient with and without IR

Lipid parameters	1 group IR (+) (n=15)	2 group IR(-) (n=32)	p
TC, mmol/l	5,5 [4,8;6,5]	5,2 [4,3;5,8]	0,16
HDL-C, mmol/l	1,7 [1,3;1,9]	1,7 [1,6;2,1]	0,25
LDL-C, mmol/l	3,4 [2,5;4,2]	2,9 [2,1;3,5]	0,12
TG, mmol/l	1,3 [0,8;2,2]	0,9 [0,7;1,1]	0,007
Non-HDL, mmol/l	4,0 [2,9;4,9]	3,2 [2,6;3,8]	0,09
TG/HDL-C ratio	0,8 [0,5;1,3]	0,5 [0,4;0,7]	0,01

Results: The proportion of patients with DAS28CRP>3.2 was 26% (93/365) at w8, but decreased to a stable average of 16% on the following visits and further diminished to 10% (30/303) at w104. The frequency of T2T adherence in these patients varied from 59% (55/93) at w8 to 17% (5/30) at w104 (Figure 1). The most frequent reason not to intensify treatment during the first study year was that rheumatologists considered the disease already well-controlled. This reason was reported in 50% of non-adherent cases at w8, in 15% at w16, 14% at w28, and 24% at w40. The second most frequently given reason for non-adherence during the first study year was that giving glucocorticoids or NSAIDs temporarily was preferred over changing DMARDs, as reported in 3% of cases at w8, 15% at w16, 27% at w28, and 35% at w40. T2T was applied at all visits in 41 out of 110 (37%) patients needing at least 1 adaptation during the 2-year trial. Of these 41 patients, 36 (88%) were in remission at w104, while of the 69 patients not always treated to the T2T principle, 40 (58%) were in remission at the end of the 2-year trial (p=0.001).
Conclusion: This study shows the difficulty of applying T2T strictly, both with and without a fixed protocol to follow. In less than half of patients theoretically in need of a treatment adaptation, treatment was intensified at all visits during the first 2 years of treatment. In the majority of cases rheumatologists gave as reason for overruling the T2T guidance that they estimated disease activity to be sufficiently controlled. However, patients in which the T2T principle was applied strictly, showed higher remission rates after 2 years of treatment.



Abstract THU0138 – Figure 1

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THU0139 IS ADDING ANTI-CARP OR ANTI-PADI4 BENEFICIAL FOR DIAGNOSIS OF RHEUMATOID ARTHRITIS?

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Background: Post-translatory modification (PTM), such as protein citrullination or homocitrullination (carbamylation) are key issues for the development of RA. There are known more than 300 PTMs. Some of them such as homocitrullination, are of chemical origin, but most of them (over 200) are of enzymatic origin. ACPA, anti-PADI4, anti-CarP and indirectly

RF are originated as a result of such post-translational modifications [1]. From the above-mentioned RA markers only synthesis of anti-CarP is a result of chemical protein modification. The synthesis of anti-PADI4 may facilitate the production of citrullinated proteins and contribute to the formation of ACPA. All of the above markers appear before RA onset [2].
Objectives: The aim of our study is to discover the potential utility of using additional markers (anti-CarP and anti-PADI4) in RA diagnosis.
Methods: 121 RA patients, 82.4% female, aged 52.2±12.3 years (mean ±SD) and 30 healthy controls (HC), 76.7% female, aged 53.2±8.1 years, were enrolled in the study. ACPA, RF, anti-CarP and anti-PADI4 antibodies were determined in serum by enzyme-linked immunosorbent immunoassay (ELISA).
Results: The markers positivity rate was 85.95%, 67%, 55.37% and 46.28% in ACPA, RF, anti-PADI4 and anti-CarP respectively. Among ACPA negative patients we found 44.44% and 16.67% anti-CarP and anti-PADI4 positive results respectively. The data concerning ACPA are gathered in Table 1.

RA patients, n=121		
RA markers positivity	**ACPA(+), n=103 (85,95%)**	**ACPA(-), n=18 (14,88%)**
Anti-CarP(+)	48 (46,6%)	8 (44,44%)
RF(+)	77 (74,76%)	4 (22,22%)
Anti-PADI4(+)	64 (62,14%)	3 (16,67%)
Anti-CarP(+) and RF(+)	41 (39,81%)	3 (16,67%)
Anti-CarP(+) and anti-PADI4(+)	33 (32,04%)	1 (5,56%)
RF(+) and anti-PADI4(+)	54 (52,43%)	2 (11,11%)
Anti-CarP(+) and RF(+) and anti-PADi4(+)	30 (29,13%)	1 (5,56%)

Table 1. The profile of anti-CarP, RF, anti-PADI4 positivity in ACPA(+) and ACPA(-) RA patients.

In HC group we found 0%, 0%, 7.14% and 7.14% positivity in ACPA, RF, anti-PADI4 and anti-CarP respectively. We found 91.7% positivity for ACPA(+) or anti-CarP (+) vs 88.4% for ACPA(+) or RF(+).
Conclusion: The measurement of anti-CarP antibodies may be useful in RA diagnosis. The positivity for ACPA/anti-CarP is even higher than ACPA/RF. This might be caused by the similarity of the origins of ACPA and RF (enzymatic citrullination), while anti-CarP origin is different (chemical carbamylation). It is known that anti-CarP appears years before RA onset and might be used as a potential biomarker for pre-RA diagnosis. We didn't confirmed the usefulness of anti-PADI4 as RA biomarker.

REFERENCES:

[1] Tan, E.M. and J.S. Smolen, *Historical observations contributing insights on etiopathogenesis of rheumatoid arthritis and role of rheumatoid factor*. The Journal of Experimental Medicine, 2016. 213(10):1937-1950.
[2] Shi J, van de Stadt LA, Levarht E, et al. Anti Carbamylated Protein Antibodies (anti-CarP) are present in arthralgia patients and predict the development of rheumatoid arthritis. Arthritis Rheum. 2012;21:37830.

Disclosure of Interests: Bogdan Kolarz: None declared, Magdalena Dryglewska: None declared, Marek Ciesla: None declared, Maria Majdan Speakers bureau: MSD, UCB, Abbvie, Roche
DOI: 10.1136/annrheumdis-2019-eular.2117

THU0140 INSULIN RESISTANCE AND LIPID PROFILE IN RHEUMATOID ARTHRITIS PATIENTS WITHOUT DIABETES MELLITUS OR FASTING HYPERGLYCEMIA

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Background: Diabetes mellitus (DM) is known to be associated with proatherogenic lipid profile and cardiovascular complications. Insulin resistance (IR) is the major pathophysiological mechanism contributing to type II DM development. Established in general population correlation between IR and dyslipidemia sometimes even without DM, should nevertheless be confirmed in patients (pts) with rheumatoid arthritis (RA).
Objectives: To analyze IR rates and identify IR predictive lipid profile in RA patients without DM or hyperglycemia.
Methods: Totally 47 RA pts (41 women, 6 men, 56 [39; 62] years old) without established DM and with normal fasting glucose levels (<6,1 mmol/l) were enrolled in the study. Median disease duration was 6 [5;14] years. The majority of pts were IgM RF (83%) and anti-CCP (83%) seropositive, had low (40,4%) or moderate (42,6%) RA activity based on DAS28-ESR scores. RA pts were treated with glucocorticoids (51,1%), methotrexate (57,4%) or other disease-modifying antirheumatic drugs (23,4%), biological agents (17,0%) and statins (10,6%). IR was defined as Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index $\geq$2,77. Lipid profile included evaluation of the following parameters: serum levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG). Additionally, non-HDL-C = TC - HDL-C and TG/HDL-C ratio were also evaluated.
Results: Median HOMA-IR levels were 1,7 [1,1;3,2]. HOMA-IR index correlates with age (r=0,3, p=0,04), body mass index (r=0,6, p<0,001), waist circumference (r=0,6, p<0,001), TC (r=0,3, p=0,02), non-HDL (r=0,3, p=0,03), TG concentrations (r=0,5, p<0,001) and TG/HDL-C ratio (r=0,4, p=0,006). IR was detected in 15 (31,9%) RA pts. RA pts with (group 1, n=15) or without IR (group 2, n=32) were comparable in terms of age, sex, disease duration and activity, therapy, and comorbidities including arterial hypertension, myocardial infarction + coronary revascularization. Hypertriglyceridemia ($\geq$1,7mmol/l) was more often present in pts with IR compared to pts without IR (33,3% vs 6,3%, p=0,03).
Conclusion: More than 30% of RA pts without DM and with normal serum fasting glucose concentration had IR. The IR was associated with increased TG levels and elevated TG/HDL-C ratio in RA pts. This proatherogenic lipid profile could be responsible for earlier development of cardiovascular complications.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3015

THU0141 SEVERELY DESTRUCTIVE UNILATERAL WRIST ARTHRITIS AS A RARE MANIFESTATION IN PATIENTS WITH RHEUMATOID ARTHRITIS – ANALYSIS OF CLINICAL AND IMAGING FEATURES AT A SINGLE CENTER

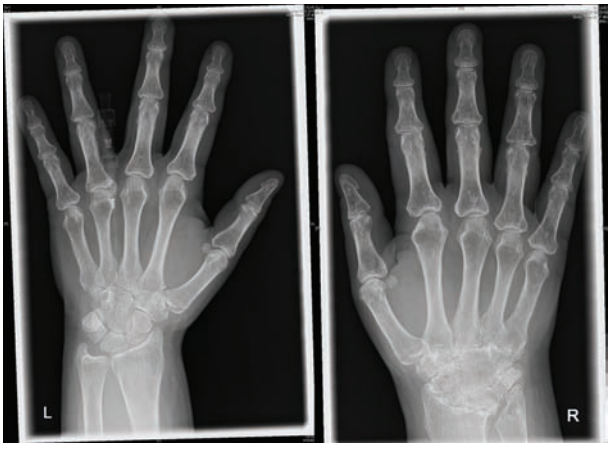
Viktor Korendovych[1,1], Radovan Vasko[1], Elena Nikiphorou[2], Jan-Gerd Rademacher[1], Gerhard A Müller[1], Peter Korsten[1]. [1]*University Medical Center Göttingen, Department of Nephrology and Rheumatology, Göttingen, Germany*; [2]*Whittington Hospital, London, United Kingdom*

Background: Rheumatoid arthritis (RA) is characterized by symmetrical involvement of small and large joints. New treatment modalities have not only allowed to achieve clinical remission or low disease activity, but also to halt the radiographic progression of joint destruction. In some patients, the disease progresses and leads to joint destruction despite treatment with disease-modifying antirheumatic drugs (DMARDs). Occasionally, wrist arthritis leads to severe destruction of carpal bones with ankyloses, so-called "os carpale". Severely destructive wrist arthritis in an asymmetrical, unilateral pattern has only rarely been reported in the literature and has not been systematically assessed (1). A severely destructive yet often symmetrical arthritis has been described in seronegative RA patients (2).
Objectives: To systematically analyze the presence of severely destructive unilateral wrist arthritis in a single-center, seropositive RA population and to identify risk factors for its development.
Methods: This is a single-center retrospective cohort study using routine clinical data. We performed a database search of our RA population for the presence of rheumatoid factor (RF) and/or anti-CCP antibodies (ACPA) from 2011 to 2017. Radiographs were assessed independently by two investigators for the presence of severely destructive unilateral wrist arthritis. Discrepancies were resolved by discussion. Epidemiological data including age, gender, disease duration, occupation, dexterity and smoking status were recorded. Patients with psoriasis, a family history of psoriasis or posttraumatic osteoarthritis were excluded. Past and current treatments were recorded. Conventional radiographs of the hands were scored using the modified Sharp score, magnetic resonance images were examined if available.
Results: We identified 1247 patients with either positive RF, ACPA, or both. After exclusion of non-RA diagnoses and radiograph review, 17 eligible patients were included in the study. Of these, 7 were excluded because of incomplete clinical data. All of the remaining ten patients were female (100%). Median age was 58.1 years (33-70), median disease duration was 15.5 years (1-22). Seven patients were right-handed, one was left-handed, in two patients, dexterity was not known. Six patients were smokers, two patients were non-smokers, in two patients, smoking status was not known. Median ACPA levels were 134,6 IU/ml (normal range <5), median RF 54.2 IU/mL (NR <16). All but two patients were positive for both antibodies; in three patients, ACPA were only mildly elevated (6, 11, and 14, respectively). 6/8 (75%) patients with severe destruction were smokers. In 5/7 (71.4%) right-handed patients, destruction occurred in the dominant wrist, whereas in 2/7 (28.5%) right-

handed patients, destruction occurred in the non-dominant wrist. Patients received a mean number of 4.7 DMARDs.
Conclusion: Severely destructive unilateral wrist arthritis represents a rare phenotype of RA. In our cohort, this type of joint involvement was only present in women, it occurred primarily in the dominant hand (75%), and in smokers (75%). The mean number of used DMARDs was very high. Further studies for assessing the prevalence of this entity, also in seronegative patients, are required.

REFERENCES:

[1] Cassone, et al. (2004), Clinical and Experimental Rheumatology
[2] Nikiphorou, et al. (2016), BMC Musculoskeletal Disorders



Abstract THU0141 – Figure 1. Illustrative sample radiograph showing severely destructive unilateral wrist arthritis. While there is generalized osteopenia, other joints are relatively spared.

Disclosure of Interests: Viktor Korendovych Consultant for: Novartis, Radovan Vasko Consultant for: Novartis, Speakers bureau: Lilly, Elena Nikiphorou: None declared, Jan-Gerd Rademacher: None declared, Gerhard A Müller Grant/research support from: Novartis
Boehringer-Ingelheim, Consultant for: Lilly, PETER KORSTEN Grant/ research support from: Novartis
Boehringer-Ingelheim, Consultant for: Novartis
Pfizer: Lilly, Paid instructor for: Chugai, Speakers bureau: Novartis
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THU0142 DIAGNOSTIC AND PREDICTIVE VALUE OF CAROTID AND TIBIAL ARTERIES ULTRASOUND MORPHOLOGY CHANGES IN FEMALE WITH RHEUMATOID ARTHRITIS

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Background: Carotid plaque (CP) is one of the surrogate markers of atherosclerosis. The association of ultrasound carotid and tibial intima-media morphology abnormalities with clinical and laboratory markers of atherosclerosis in patients with rheumatoid arthritis (RA) is uncertain.
Objectives: To determine the diagnostic and prognostic value of the carotid and tibial arteries ultrasound changes in women with RA, depending on age, menopause and laboratory parameters.
Methods: The study was performed on 105 women with RA according to the ACR/EULAR 2010 criteria in the mean age 44,2±13,3 years without history of CVD. Female patients were divided in two groups by menopause: 51.4% premenopausal (PreM) and 48.6%; postmenopausal (PM) women. Carotid and tibial arteries ultrasonography examination included the measurement of cIMT in 3 points, detection of focal plaques in the extracranial carotid tree, blood flow velocity and morphology of the intima was performed. 30 age-matched healthy women were examined by the same parameters.
Results: The cIMT > 0.9 mm was detected in 38 (36.2%) patients. Patients with cIMT > 0.9 mm had significantly higher age, RA duration, serum levels of the total cholesterol (TC), LDL, apolipoprotein apo B and CRP. CPs were observed three times more often in patient with cIMT > 0.9 mm than without thickness of carotid intima-media (cIM) ((50% vs 16,4%, p<0.05). Carotid intima-media morphology abnormalities (fragmentation and sclerosis) were observed in 73.3% RA patients, mostly with CP (100%) and cIMT > 0.9 mm (97.4%). In the most Prem RA women (58.1%) with low CV risk according to mSCORE calcinosis of the tibial artery (TA) was identified. Among the patients with CP 86.7% had calcinosis of the TA, 92% of whom were PM. No vascular abnormalities were detected in healthy control. The TC and LDL levels were significantly higher in patients with CP, cIMT > 0.9 mm, TA fibrosis and calcinosis than without (5.4 mmol/L vs 4.6 mmol/L). The significant correlations between LDL level and cIMT > 0.9 mm (r=0.32; p= 0.04); presence of CP (r=0.38; p=0.00006), cIM fragmentation (r = 0.34; p = 0.0003), RI CA (r=0.21; p=0.03), diffuse TA fibrosis (r = 0.44; p = 0.03) were identified. The DAS28, CRP level, Vps CA, anti-CCP positivity, cIMT > 0.9 mm had high predictive value for the development TA fibrosis in PreM RA women. The TA calcinosis was positively correlated with carotid intima-media morphology abnormalities (χ2=31.6; p<0.01), presence of the CP (χ2=26.2; p<0.01), cIMT > 0.9 mm (χ2=8.5; p<0.01).
Conclusion: According to the data of multiple logistic regression the risk factors for the development of moderate, high and very high CV risk in RA women were DAS28, levels of CRP and LDL, swollen joint count, menopause, cIMT > 0.9 mm and TA fibrosis. Prem RA women with low CV risk according to mSCORE, high level of TC and/or LDL, presents of cIMT > 0.9 mm and/or carotid intima-media morphology abnormalities and/or TA calcinosis can be candidate for initiation lipid-lowering therapy.
Disclosure of Interests: None declared
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THU0143 LOW-ENERGY FRACTURES IN RHEUMATOID ARTHRITIS – ASSOCIATIONS WITH GENES AND CLINICAL CHARACTERISTICS

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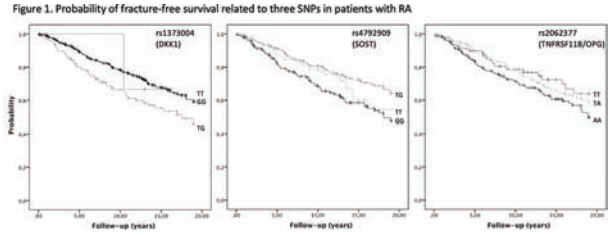
Background: Patients with rheumatoid arthritis (RA) have increased risk of osteoporosis and low-energy fractures. Several genes associated with bone mineralization, osteoporosis or risk of fracture in the general population have been identified.
Objectives: To analyse the association between nine selected SNPs and the risk of low-energy fracture, taking clinical patient characteristics into account.
Methods: We identified a cohort of patients (n=896, 70% women, age at inclusion 60.0±14.8 years) with RA according to ACR criteria from the catchment area of the register of Umeå injury database, Umeå, Sweden, which enabled identification of low-energy fractures (n=254). The follow-up (mean 8.8±6.1 years, total 7928 person-years) started two years after RA diagnosis but not earlier than January 1, 1993 and ended at the first of December 31, 2011, death or the first low-energy fracture. Nine SNPs were analysed in all patients with available DNA-samples (n=667) using KASPTM genotyping assays (LGC genomics Ltd, Hoddesdon, UK): rs3801387 (WNT16), rs6666455 (SOAT), rs3736228 (LRP5), rs4796995 (FAM210A), rs4792909 (SOST), rs2062377 (TNFRSF11B/OPG), rs884205 (TNFRSF11A/RANK), rs9533090 (TNFSF11/RANKL), and rs1373004 (DKK1). Anti-CCP was analysed and clinical patient characteristics (duration of RA, ever smoking, disease activity the first two years after RA diagnosis, and joint erosions) were extracted from patient files. Associations between the risk of fracture and risk alleles in the cohort were evaluated using Kaplan-Meier curves (K-M) and Cox proportional hazards models: crude, adjusted for age and sex, and for clinical patient characteristics.
Results: The SNPs: rs1373004, rs4792909, and rs2062377 were associated with the risk of fracture in K-M analyses (Figure 1). For the other genes no significant associations were observed. Patients carrying the risk allele of rs1373004 (22.6% of the patients), or who were homozygous for the risk allele of SNP rs4792909 (38.6%), had a >50% higher risk of low-energy fracture compare to other patients, irrespectively of disease characteristics (Table 1). The association between rs2062377 and the risk of fracture was not independent of clinical patient characteristics (Table 1).

Abstract THU0143 –Table 1. Cox proportional hazards models estimating the risk of low-energy fracture associated with SNPs in patients with RA

	Freq	HR1*	95% C.I.	HR2*	95% C.I.	HR3*	95% C.I.
rs1373004, T-carrier	22.6%	1.61	1.16;2.22	1.61	1.16;2.22	1.68	1.17;2.41
rs4792909, GG vs. TT+TG	38.6%	1.59	1.19;2.14	1.53	1.13;2.05	1.54	1.12;2.13

r2062377, AA vs. TA +TT	35.7%	1.36	1.01;1.83	1.28	0.81;1.59	1.19	0.86;1.65

*Hazard ratio (HR)1=crude model, HR2= adjusted for age at inclusion and sex, HR3=adjusted for age at inclusion, sex, duration of RA, anti-CCP positivity, ever smoking, disease activity the first two years after RA diagnosis, and erosive disease.



Abstract THU0143 – Figure 1

Conclusion: Genes related to bone metabolism may have a considerable contribution to the already high risk of low-energy fractures in RA.

REFERENCES:

[1] Estrada K, et al. Nat Genet 2012
[2] Baron R & Kneissel M. Nat Med 2013

Disclosure of Interests: Lotta Ljung: None declared, Kristina Wiberg: None declared, Lisbeth Ärlestig: None declared, Solbritt Rantapää Dahlqvist Consultant for: Member of the advisory board, Lipum AB, Umeå, Sweden.

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THU0144 ECHOCARDIOGRAPHIC ABNORMALITIES AMONG HISPANIC PATIENTS WITH RHEUMATOID ARTHRITIS: A CASE CONTROL STUDY

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Background: Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disease that mainly affects the synovial joints. Subjects with RA have an increased cardiovascular (CV) morbimortality (1). This increase in cardiovascular diseases (CVD) is not explained by traditional risk factors (2). Screening for CVD in RA patients is an essential part of CV risk management. Echocardiography is a simple, non-invasive approach that provides reliable markers for cardiac evaluation (3).
Objectives: To determine the prevalence of echocardiographic abnormalities in RA patients and compare them to matched controls.
Methods: Observational, cross-sectional study. RA patients aged 40 to 75 years that fulfilled the 2010 ACR/EULAR classification criteria and matched controls were included. Patients with a poor ultrasound window, history of previous atherosclerotic CVD (ischemic heart disease, cerebrovascular accident or peripheral arterial disease) and pregnancy were excluded. Transthoracic echocardiogram was performed and reviewed by 2 board-certified cardiologists. Differences were solved by consensus. Descriptive analysis was done with frequencies (%) and median (q25-q75), and comparisons with Chi-square and Mann U-Whitney's test.
Results: A total of 133 subjects were included. Baseline characteristics are shown in Table 1. Groups were well balanced, with no differences among them. Echocardiographic comparisons are shown in Table 2. Prevalence of abnormal left ventricle (LV) geometry was higher in RA patients (p= .038), as were mitral and tricuspid valvular dysfunction (p<0.001). The LV ejection fraction was lower in RA subjects (p= .044).

Abstract THU0144 –Table 1. Clinical characteristics.

	RA (n=85)	Control (n= 48)	*P*
Female, n (%)	81 (95.3)	46 (95.8)	1
Age, mean ± SD	54.4 ± 8.4	53.1 ± 6.9	0.169
T2DM, n (%)	10 (11.8)	2 (4.2)	0.210
Hypertension, n (%)	21 (24.7)	11 (22.9)	0.817
Active smoking, n (%)	7 (8.2)	5 (10.4)	0.341
Dis. duration, yr, mean ± SD	9.8 ± 8.4	-	-
BMI, Kg/m^2, mean ± SD	28.5 ± 4.8	27.9 ± 4.3	0.375
DAS 28-CRP, mean ± SD	3.1 ± 1.1	-	-

Abstract THU0144 –Table 2. Echocardiographic findings

	RA (n=85)	Control (n=48)	*P*
Diastolic dysfunction, n (%)	32 (37.6)	17 (35.4)	0.906
LV Geometry alterations, n (%)	27 (31.7)	6 (12.5)	**0.038**
LV mass index (g/m^2), median (q25 –q75)	70.1 (36.5 - 119.4)	72.9 (39.7 - 134.5)	NS
LV end diastolic diameter (cm), median (q25 –q75)	1.2 (.9 -1.9)	1.2 (.9 - 1.8)	NS
LV end systolic diameter (cm), mean ± SD	2.7 ± .4	2.8 ± .4	NS
Aortic valvulopathy, n (%)	16 (18.8)	3 (6.2)	0.078
Mitral valvulopathy, n (%)	47 (55.2)	8 (16.6)	**0.001**
Pulmonary valvulopathy, n (%)	9 (10.5)	-	0.066
Tricuspid valvulopathy, n (%)	71 (83.5)	25 (52.1)	**0.000**
LV Ejection Fraction (%), median (q25 –q75)	60.5 (51-76)	63.7 (54-77)	**0.044**

LV= Left ventricle.
Conclusion: Patients with rheumatoid arthritis have higher prevalence of mitral and tricuspid valves dysfunction in our population, and greater left ventricular geometry alterations, compared to controls. As the left ventricular ejection fraction is a strong prognosticator for CV disease, echocardiography might be a simple non-invasive tool for cardiac risk screening in RA.

REFERENCES:

[1] Avina-Zubieta JA, et al. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. Arthritis Rheum 2008; 59(12):1690-1697.
[2] Curtis JR, et al. Is Rheumatoid Arthritis a Cardiovascular Risk-Equivalent to Diabetes Mellitus? Arthritis Care Res. 2018 Nov; 70(11):1694-1699.
[3] Fine NM, et al. Evaluation of myocardial function in patients with rheumatoid arthritis using strain imaging by speckle-tracking echocardiography. Ann Rheum Dis. 2014; 73(10):1833-1839.

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THU0145 INCIDENCE, TREND AND FACTORS ASSOCIATED WITH OPPORTUNISTIC INFECTION (OI) IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN. (TREND-AR STUDY)

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Background: The epidemiology of hospitalizations for Opportunistic Infections (OI) in patients with rheumatoid arthritis (RA) is unknown despite an increase in RA treatments that confer risk of infection.
Objectives: To analyze the incidence, trend and factors associated with hospitalizations due to OI in patients with RA, in Spain, during the period between 1999 and 2015.
Methods: Population study based on the analysis of a national administrative database that includes a Minimum Basic Data Set (MBDS) of the income of patients with RA (ICD 9 714). Period: January 1, 1999 to December 31, 2015. The following entities were included as OI: tuberculosis (tbc), nontuberculous mycobacteria, cytomegalovirus (CMV), Epstein-Barr virus (EBV), Herpes zoster (HZ), Candidiasis, Toxoplasmosis, Pneumocystosis, Cryptococcosis, Listeriosis, Nocardiosis, Aspergillosis, Coccidioidomycosis, Histoplasmosis, Blastomycosis, Strongyloides, Leishmaniosis, Cryptoporidium, Trypanosoma cruzi, JVC and other prion viruses. These diagnoses were identified by the presence in primary and secondary diagnosis of their ICD9 codes. The population at risk was estimated

through the population census of the National Institute of Statistics, with an estimated prevalence of RA of 0.5% in both sexes (0.2% in men and 0.8% in women). Crude and adjusted rates were calculated at the national level. The trend was analyzed by Generalized Linear Models (GLM) using the year variable as the analysis variable. Clinical-demographic factors associated with these infections were analyzed, using uni and multivariate logistic regression.

Results: Of the total of 338,343 hospital admissions in patients with RA during the 17 years of the study period, there were 4,097 (1.2%) admissions with opportunistic infection, 1591 (38.8%) in men and 2506 (61.2%) in women (p <0.001). The infections found in order of frequency were: HZ 1295 (29.9%), Tbc 1227 (29.9%), Aspergillosis 357 (8.7%), systemic candidiasis 342 (8.3%), CMV 270 (6.5%), EBV 133 (3.2%), Pneumocstosis 122 (2.9%), Leishmaniosis 100 (2.4%), Listeriosis 98 (2.3%), Mycobacteria no tbc 85 (2%), Nocardiosis 86 (2.1%), Trypansoma Cruzzi 19 (<1%), JVC 19 (<1%), Cryptococcosis 15 (<1%), Toxoplasmosis 14 (< 1%), Strongyloides 11 (<1%), Cryptosporidium 6 (<1%), Histoplasmosis 1 (<10%), blastomycosis 1 (<1%). Between 20-40 years the most frequent infections were: Tbc, EBV, CMV; Between 40-60 years: Tbc, HZ, CMV; Over 60 years old: HZ, tbc, aspergillus. The mean age was 65.54 (SD16.6). 445 (10.9%) died during admission; 217 (13.6%) in men and 228 (9.1%) in women (p <0.001). The mean of the Charlson index was 1.96 (1.49), 2.21 (SD1.6) in men and 1.81 (SD1.3) in women (p <0.001). The Relative Risk male: female was 2.77. The infections with the highest male/female RR were: Leishmaniosis (4.77), Listeriosis (4.1) and Aspergillosis (3.8). The infections with the highest lethality were: Pneumocystosis (31%), Candidiasis (29.8%) and Aspergillosis (27.7%). The age-adjusted rate for all OI was 146.21/100,000 inh*year, 297.05 in men and 107.37 in women. Adjusted IO rates increased from 85.47 in 1999, to 193.48 in 2015. It is estimated that this increase is of 4,96% per year. In the multivariate analysis, the factors associated with OI were: male, COPD and liver disease.

Conclusion: In Spain, during the period 1999 to 2015, there has been an increase in the incidence rate of OI in patients with RA. We estimate an annual increase of 4,9%. Being male and having COPD or liver disease are associated with OI.

Disclosure of Interests: None declared

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THU0146 POOR COMPLIANCE BY RHEUMATOLOGISTS AND ORTHOPAEDISTS WITH GUIDELINES FOR THE PERIOPERATIVE MANAGEMENT OF RHEUMATOID ARTHRITIS PATIENTS UNDERGOING ARTHROPLASTY

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Background: Appropriate management can reduce the increased perioperative infection risk in RA patients(1). In 2017, American College of Rheumatology (ACR) and the American Association of Hip and Knee Surgeons released *Guidelines for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty*(1). Atlanto-axial subluxation at induction of general anaesthetic (GA) is another concern. Preoperative C-spine X-rays with flexion-extension views are recommended(2).

Objectives: Assess compliance with medication guidelines and C-spine imaging practices for RA patients undergoing arthroplasty under GA.

Methods: An anonymous 24 question paper-based survey was distributed at Irish Society of Rheumatology Meeting (September 2017) and Irish Institute of Trauma and Orthopaedic Surgery Curriculum Day (January 2018) examining clinician demographics, imaging and prescribing practices.

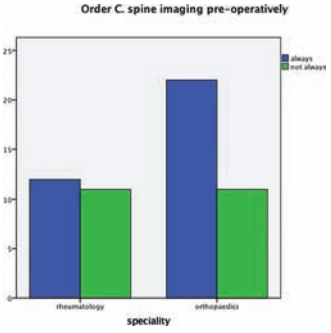
Results: 33 orthopaedists and 23 rheumatologists responded. The majority (n=46) were trainees and <40 years old (n=43). Most rheumatologists were female and orthopaedists male.

The guideline advocates cDMARD continuation perioperatively(1). Rheumatologists are more likely than orthopaedists to continue cDMARDs (Pearson Chi squared, 0.001). 8 (36%) rheumatologists continue cDMARDs, 6 (27%) stop one week preoperatively and 8 (36%) at two weeks. 1 orthopaedist never stops cDMARDs. 8 (24%) stop at one week preoperatively, 13 (39%) at 2 weeks, 5 (15%) at 4 weeks. 6 (18%) were unsure.

The guideline advocates stopping bDMARDs 1 dosing cycle preoperatively and restarting after wound healing. Depending on the agent, 2 to 4 rheumatologists never stop bDMARDs preoperatively. Responses varied by medication half-life. 18 hold etanercept for <4 weeks and 11 hold rituximab for >8 weeks. 2 orthopaedists never stop bDMARDs preoperatively. Depending on the agent, 14-15 would stop <4 weeks prior, 10-12 were unsure, 4-8 weeks was chosen 4-5 times and >8 weeks 0-1 times.

Regarding patients on glucocorticoids for RA, the guideline advocates continuing current dosing perioperatively. 6 orthopaedists always increase steroids (13 sometimes, 9 never, 5 unsure). 7 never stop (13 sometimes, 6 always, 5 unsure). 12 rheumatologists sometimes increased steroids (8 always, 1 never, 1 not sure, 1 no answer). 14 never stop steroids (8 sometimes, one not sure).

In RA patients undergoing GA, 22 orthopaedists always perform C spine imaging prior (10 sometimes, 1 never). 11 rheumatologists always do C spine imaging prior (11 sometimes, 1 never). Orthopaedists are more likely than rheumatologists to always perform spinal imaging preoperatively (P value=0.002, Fisher's exact test).



Abstract THU0146 – Figure 1. Number of clinicians who always order C spine imaging prior to arthroplasty in RA patients undergoing GA

Conclusion: There is poor compliance with guidelines and variability and uncertainty in prescribing. Orthopaedists often discontinue sDMARDs preoperatively despite guidelines to the contrary. Orthopaedists are more likely than rheumatologists to perform preoperative C spine imaging as per recommendations.

REFERENCES:

[1] Goodman SM, Springer B, Guyatt G, Abdel MP, Dasa V, George M, et al. 2017 American College of Rheumatology/American Association of Hip and Knee Surgeons guideline for the perioperative management of antirheumatic medication in patients with rheumatic diseases undergoing elective total hip or total knee arthroplasty. Arthritis care & research. 2017;69 (8):1111-24.

[2] Wasserman BR, Moskovicich R, Razi AE. Rheumatoid arthritis of the cervical spine. Bull NYU Hosp Joint Dis. 2011;69:136-48.

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THU0147 FACTORS CONTRIBUTING TO DISCREPANT ESTIMATED GLOMERULAR FILTRATION VALUES MEASURED BY CREATININE AND CYSTATIN C IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: In rheumatoid arthritis (RA) patients, it is important to evaluate renal function, because it may deteriorate due to RA itself or drug use requiring drug dose adjustment. Recently, Cystatin C (CysC) has been used as a more accurate marker of renal function than Creatinine (Cr), because it is not affected by muscle mass.[1)] Renal function of some RA patients is overestimated by Cr, and shows a discrepancy in the estimated glomerular filtration between Cr and CysC. However, what

factors contribute to this discrepancy and in what RA patients CysC should be evaluated remain to be elucidated.
Objectives: To clarify the factors contributing to the discrepancy between eGFR measured using Cr (eGFR-Cr) and CysC(eGFR-CysC).
Methods: We enrolled 236 RA patients (188 females, 48 males; mean age 65.3±14.0 years; disease duration 12.0 ± 11.0 years). We measured BUN, Cr, CysC, IgG, IgA, IgM, C3,C4, CH50, RF and aCCP in patient serum, urinary proteins, urinary blood, and urinary casts and evaluated CDAI, SDAI, disease activity score (DAS) 28-CRP and DAS28-ESR. Steinbrocker functional classification and radiological grading were evaluated. History of diabetes mellitus, hypertension and hyperlipidemia was determined from the medical records. Estimated glomerular filtration rate (eGFR) was calculated by the new Japanese coefficient-modified Modification of Diet in Renal disease (MDRD) study equation.
Results: The eGFR-Cr and eGFR-CysC of RA patients were 72.5±20.2 (12.0~142.0) and 72.3±24.9 (6.3~167.8), with no significant difference between the two. The correlation between them was significant (r=0.715, p<0.0001). However, 26 of 180 patients with eGFR-Cr greater than or equal to 60 showed eGFR-Cys of less than 60. To clarify the factors that contribute to a greater than 20% discrepancy (eGFR-Cr $\geq$20% higher than eGFR-CysC) between eGFR-Cr and eGFR-CysC, we divided our patients into group A (eGFR-Cr/eGFR-CysC $\geq$ 1.2) and group B (eGFR-Cr/eGFR-CysC < 1.2). Group A was older (73.8±12.5 vs 63.2±13.6 years), had longer disease duration (17.7±14.0 vs 10.4±9.5 years), lower BMI (20.0±2.9 vs22.4±3.6), lower CK (63.9±36.0 vs 92.5±79.6), higher disease activity, more frequent diabetes mellitus (35.6% vs 11.0%) and more frequent stage 4 of Steinbrocker radiological grading (47.7% vs 15.3%) than Group B by univariate analysis significantly (p<0.01). We then performed multifactorial analysis using logistic regression analysis by stepwise method. Diabetes mellitus (OR 63.475, 8.394-479.990), SDAI (OR 1.088, 1.006-1.177), lower RBC counts (OR 0.753, 0.645-0.880), lower CK (OR 0.724, 0.598-0.876), no NSAIDs (OR 0.024, 0.003-0.219) and stage 4 of Steinbrocker radiological grading (OR 12.009, 2.962-48.678) were found as independent risk factors for group A.
Conclusion: Renal functions of RA patients with high disease activity, diabetes mellitus, advanced stage, anemia or lower CK could be overestimated when judged using eGFR-Cr alone. Assessment of renal function in such RA patients requires particular attention.

REFERENCE:

[1] Nozawa Y, Sato H, Wakamatsu A, et al. Utility of estimated glomerular filtration rate using cystatin C and its interpretation in patients with rheumatoid arthritis under glucocorticoid therapy. Clin Chim Acta 2018; 487, 299-305.

Disclosure of Interests: None declared
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THU0148 COMPARISON OF SERUM LEVELS OF GDF-15 IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH OR WITHOUT DISEASE ACTIVITY

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Background: The increase in morbidity and mortality in Rheumatoid arthritis (RA) is due to 50% by cardiovascular risk factors associated with chronic-inflammatory processes, among these factors, GDF-15 has been associated with chronic-inflammatory processes such as RA; in addition to being related to the state of the disease of several pathologies with similar mechanisms. GDF-15 could be involved in the pathogenesis of RA and thus, show an association with the activity of a disease in RA. The most common clinimetric tool to evaluate disease activity in RA is Disease Activity Score on 28 joints (DAS28).
Objectives: To compare the serum levels of GDF-15 in patients with RA with or without disease activity.
Methods: Cross-sectional study, including 162 patients with RA, aged $\geq$18 years old who fulfilled the 1987 ACR classification criteria. RA disease activity was assessed using DAS28-PCR. Sera samples were obtained from venous blood by centrifugation at 3500 rpm for 15 min at room temperature. Serum GDF-15 was measured using an ELISA kit (BioVendor, Germany). Descriptive statistics (mean and standard deviation (SD)) were used for assessing the demographics and clinical parameters. Differences between patients with and without disease activity were assessed using T-student and Chi^2 tests. P-values $\leq$0.05 were considered statistically significant.
Results: The mean age was 57.2 ± 11.5 years and mean BMI was 27.52 ± 4.78 kg/m^2. The mean disease duration was 13.60 ± 9.50 years. The GDF-15 was 435.54 ± 310.64 ng/L. For number of swollen and tender joints, the score was 1.50 ± 3.52 and 2.81 ± 4.59 respectively. VAS-pain was 37.00 ± 27.77. DAS28-CRP score was 3.15 ± 1.18. When applying the cut-off value for disease activity (DAS28 score $\geq$2.6) or remission (DAS28 score <2.6) we obtained 65 (40.1%) and 97 (59.9%) respectively. Comparison of GDF-15 serum levels between active (455.09 ± 333.47) and remission (406.36 ± 272.94) showed no significant associations (p=0.32). When performing Pearson's correlation among GDF-15 serum levels and PCR levels (r=0.142, p=0.07) or DAS28-PCR values (r=0.081, p=0.30) no relevant correlations were obtained.
Conclusion: RA activity is not associated with values of serum levels of GDF-15. Prospective studies are necessary to explain changes in GDF-15 levels throughout RA.

REFERENCES:

[1] Wiklund FE, Bennet AM, Magnusson PK, Eriksson UK, Lindmark F, Wu L, Yaghoutyfam N, Marquis CP, Stattin P, Pedersen NL, Adami HO, Grönberg H, Breit SN, Brown DA. Macrophage inhibitory cytokine-1 (MIC-1/GDF15): a new marker of all-cause mortality. Aging Cell. 2010 Dec; 9 (6):1057-64.
[2] Brown DA, Moore J, Johnen H, Smeets TJ, Bauskin AR, Kuffner T, Weedon H, Milliken ST, Tak PP, Smith MD, Breit SN. Serum macrophage inhibitory cytokine 1 in rheumatoid arthritis: a potential marker of erosive joint destruction.Arthritis Rheum. 2007 Mar; 56(3):753-64.

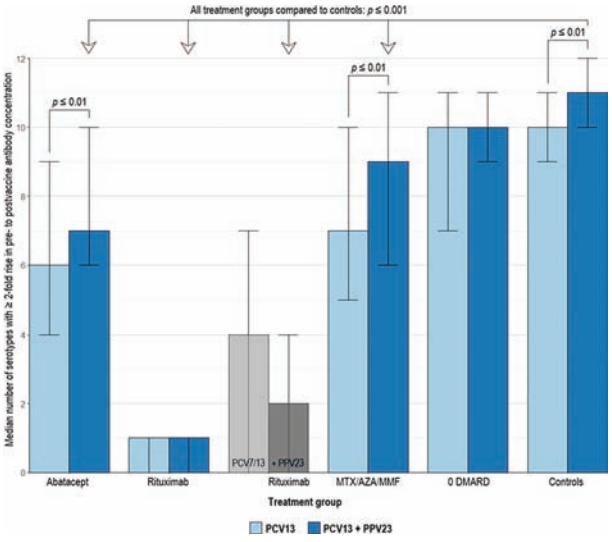
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THU0149 PRIME-BOOSTER RESPONSE TO PNEUMOCOCCAL CONJUGATE AND POLYSACCHARIDE VACCINES IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

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Background: A vaccination using a combination of a dose of 13-valent pneumococcal conjugate vaccine (PCV13) followed by a dose of 23-valent polysaccharide vaccine (PPV23) after at least 8 weeks is currently recommended for the immunosuppressed patients with rheumatic diseases.
Objectives: To explore if the prime-booster vaccination strategy using the combination of PCV13 + PPV23 improves antibody response compared to PCV alone in immunosuppressed patients with inflammatory rheumatic diseases, and to compare with the prime-booster response in patients not treated with disease modifying anti-rheumatic drugs (DMARDs) and controls.
Methods: In total, 45 patients treated with rituximab (rheumatoid arthritis (RA)/arthritis=35 and vasculitis=10), 20 RA patients on abatacept; 27 patients on methotrexate/azathioprine/mycophenolate mofetil (MTX/AZA/MMF; RA=14 and vasculitis=13); 17 patients without DMARDs (RA/arthritis=12 and vasculitis=5) and 25 healthy controls participated. Only patients on an unchanged dose of DMARDs for at least 4 weeks before vaccination were eligible for the study. All participants were vaccinated with a dose PCV followed by a dose PPV23 after at least 8 weeks. A subgroup of rituximab treated patients had been vaccinated earlier with either 7-valent pneumococcal conjugate vaccine (PCV7) or PCV13. Blood samples were taken immediately before and 4-6 weeks after each vaccine dose. Pneumococcal serotype-specific antibodies to the 12 serotypes

common to both vaccines were analyzed using a multiplex bead array assay (Luminex). Positive antibody response was defined as at least 2-fold increase in prevaccination serotype-specific antibody concentration. Number of serotypes with positive antibody response after prime-booster vaccination were compared between treatment groups and controls using Mann-Whitney U test. In addition, the difference in number of serotypes with positive antibody response between prime and prime-booster vaccination in each treatment group was compared using Wilcoxon signed-ranks test.



Abstract THU0149 – Figure 1

Results: Compared to PCV alone, the combined schedule with PCV+ PPV23 resulted in increased antibody response for patients treated with abatacept, MTX/AZA/MMF, and controls (all $p \leq 0.01$). In patients with rituximab and previous PCV7 or PCV13, booster vaccination with PPV23 did not result in increased antibody levels (Figure: bars marked grey). The numbers of serotypes with a positive antibody response to the combined vaccination with PCV + PPV23 was reduced in patients with rituximab (median 1, $p \leq 0.001$), abatacept (median 7, $p \leq 0.001$) and MTX/AZA/MMF (median 9, $p \leq 0.001$), but not in patients without DMARDs (median 10, $p=0.12$), compared to controls (median 11).
Conclusion: Prime-booster vaccination strategy using a combination of a dose of pneumococcal conjugate vaccine followed by a dose of polysaccharide vaccine improved antibody responses in patients with inflammatory rheumatic disease treated with abatacept and traditional DMARDs compared to PCV alone. The combined vaccination resulted in a markedly lower response in rituximab treated patients, and was to a lesser degree reduced in patients with abatacept or traditional DMARDs compared to healthy controls.
Disclosure of Interests: Per Nived: None declared, Göran Jönsson: None declared, Bo Settergren: None declared, Jon Einarsson: None declared, Tor Olofsson: None declared, Johan K Wallman Consultant for: Consultant for AbbVie, Celgene, Eli Lilly, Novartis, and UCB Pharma., Charlotte Sværke Jørgensen: None declared, Meliha C Kapetanovic: None declared
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THU0150 FINGER JOINT CARTILAGE EVALUATED BY ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS AND HEALTHY SUBJECTS

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Background: Joint destruction in rheumatoid arthritis (RA) includes both bone and cartilage lesions. Since joint space narrowing (JSN) is not a direct evaluation of cartilage using X-ray, we aimed to examine the validity of ultrasound (US) cartilage evaluation in patients with RA.
Objectives:
Methods: The cartilage thickness of bilateral metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of the 2nd to 5th fingers were visualized from a dorsal view with joints in approximately 90 degrees flexion and measured at the middle portion. Furthermore, one US examiner performed the semiquantitative scoring of the recorded cartilage images in a blinded manner on a scale of 0–2. In addition, the JSN of the corresponding joints was scored using the van der Heijde-modified Sharp method with a hand X-ray. Continuous variables were analysed using the Mann–Whitney U test. The relationships among the total measurement of cartilage thickness, its semi-quantitative score, and the JSN score were assessed using Spearman's rank correlation coefficients.
Results: One hundred and three patients with RA and 42 healthy subjects were enrolled in this study. The total cartilage thickness was significantly thinner in patients with RA compared to healthy subjects for both the MCP and PIP joints (both $p<0.001$). The semi-quantitative sum of 16 joints ranged from 2 to 26 (median 8) in patients with RA, which was significantly greater than the 0 to 11 (median 4) seen in healthy subjects ($p<0.001$). In patients with RA, the semi-quantitative score showed a significant negative correlation with cartilage thickness (rho=−0.64; $p<0.001$) as well as a significant positive correlation with JSN score (rho=0.66; $p<0.001$). In addition, in healthy subjects, semi-quantitative score, but not cartilage thickness was significantly correlated with age (rho=0.49; $p=0.001$ and rho=−0.25; $p=0.118$, respectively). On the other hand, in RA, these scores showed a significant correlation with RA disease duration but not correlated with age.
Conclusion: A simplified and direct evaluation of finger joint cartilage damage by semi-quantitative US score is valid and useful for patients with RA.
Disclosure of Interests: Takehisa Ogura: None declared, Ayako Hirata: None declared, Norihide Hayashi: None declared, Hideki Ito: None declared, Sayaka Takenaka: None declared, Yuki Inoue: None declared, Takaharu Kagtagiri: None declared, Chihiro Imaizumi: None declared, Yuto Takakura: None declared, Hideto Kameda Grant/research support from: AbbVie, Asahi Kasei Pharma, Astellas, Chugai, Eisai, GlaxoSmith-Klein, Mitsubishi-Tanabe, Novartis, Consultant for: AbbVie, Eli Lilly, Novartis, Speakers bureau: AbbVie, Asahi Kasei Pharma, Bristol-Myers, Chugai, Eli Lilly, Janssen, Mitsubishi-Tanabe, Novartis, Pfize
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THU0151 COMPARISON BETWEEN THREE PROPOSED DEFINTIONS OF DIFFICULT-TO-TREAT/REFRACTORY RHEUMATOID ARTHRITIS IN A COHORT OF BDMARD-TREATED PATIENTS

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Background: A definition of difficult-to-treat/refractory rheumatoid arthritis (RA) (RRA) has not been established yet, nevertheless, RRA is commonly associated with the resistance to multiple bDMARDs [1,2,3].
Objectives: The objective was to evaluate the rate of RRA according to three definitions, the agreement between the definitions and major determinants of such definitions in a large monocentric cohort of RA patients.
Methods: We included RA patients treated with any bDMARD (>=1 year), who started bDMARDs after 2001. Considered definitions of RRA were: B-RAA, according to Buch [3], failure of >=1 anti-cytokine (TNF and/or IL6 ihnibitor) and >=1 cell-targeted (B-cell and/or T-cell ihnibitor) bDMARD; KF-RAA, according to Kearsley-Fleet [2], exposed to >=3 bDMARDs classes; DH-RRA, according to de Hair [1], signs and/or symptoms suggestive of inflammatory RA activity (in the study we assumed DAS28>=3.2 or extra-articular manifestations) and failure of >=1 csDMARD and >=2 bDMARDs. Agreement was measured with Cohen's kappa. To assess variables independently associated with RRA, multivariate regression analysis was used including variables achieving $p<0.10$ in univariate analysis.
Results: Patients included in the study were 572. B-RRA was observed in 165 (28.8%), KF-RRA in 96 (16.8%) and DH-RRA in 57 (10.0%). DH-RRA was the most stringent definition. Agreement between the definition was fair: DH-RRA and B-RRA kappa=0.330, $p<0.001$; DH-RRA and KF-RRA kappa=0.260, $p<0.001$; B-RRA and KF-RRA kappa=0.275, $p<0.001$. Most common last bDMARD choice in RRA patients differed according to the definition: B-RRA mostly adalimumab (30.9%) ($p<0.001$), KF-RRA tocilizumab (78.1%) ($p<0.001$), DH-RRA tocilizumab (33.3%) or abatacept (31.6%) ($p<0.001$) (Figure). Multivariate analysis revealed that, as expected, all definitions were affected by the number of bDMARDs, and DH-RRA also by the disease activity. Mean PDN daily dose was associated with B-RRA; lower BMI with KF-RRA; the start of bDMARD treatment in earlier years with KF-RRA and DH-RRA; and radiographic progression (in the 24 months before the study) with DH-RRA (Table).

Conclusion: RRA was observed in a 20-30% of RA patients, slightly higher compared to previous evidence [1,2]. Characteristics of patients fulfilling different RRA definitions are diverse. Particularly, disease severity (disease activity and structural damage) was not associated with RRA if the definition considers only the exposure to bDMARDs. Given the large time span of the study period, RRA patients were more frequently those who started bDMARDs in earlier years.

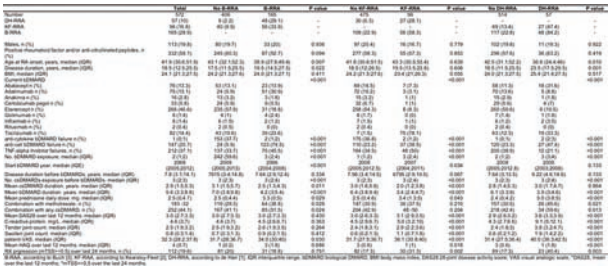
REFERENCES:

[1] de Hair MJH, et al. Rheumatology 2018;57:1135-1144.
[2]. Kearsley-Fleet L, et al. Ann Rheum Dis 2018;77:1405–1412.
[3] Buch MH. Ann Rheum Dis 2018;77:966–969.

Table. Factors associated with three definitions of difficult-to-treat/refractory rheumatoid arthritis (RRA), multivariate analysis.

		OR (95% C.I.)	p value
B-RRA			
No. bDMARDs		18.77 (11.06;31.85)	p<0.001
Current bDMARD			p<0.001
Prednisone daily dose	per 5 mg increase	2.15 (1.17;2.15)	0.014
Model Constant			p<0.001
KF-RRA			
BMI	per 5 unit increase	0.61 (0.35;1.05)	0.072
No. bDMARDs		8.69 (5.16;14.64)	p<0.001
bDMARD treatment start year	per year increase	0.92 (0.84;1.01)	0.087
Current bDMARD			p<0.001
Model Constant			0.069
DH-RRA			
No. bDMARDs		3.9 (2.67;5.71)	p<0.001
bDMARD treatment start year	per year increase	0.91 (0.83;0.99)	0.026
DAS28*	per 0.6 unit increase	5.55 (3.34;9.23)	p<0.001
Radiographic progression**		2.7 (1.21;6.03)	0.015
Model Constant			0.04

OR odds ratio, C.I. confidence interval, *DAS28, mean over the last 12 months; *mTSS>=0,5 over the last 24 months.



Abstract THU0151 – Figure 1. Characteristics of the patients according to 3 definitions of difficult-to-treat/refractory rheumatoid arthritis (RRA),

Disclosure of Interests: None declared
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THU0152 SARCOPENIA IS ASSOCIATED WITH PERSISTENT DISEASE ACTIVITY DURING FOLLOW-UP OF RHEUMATOID ARTHRITIS

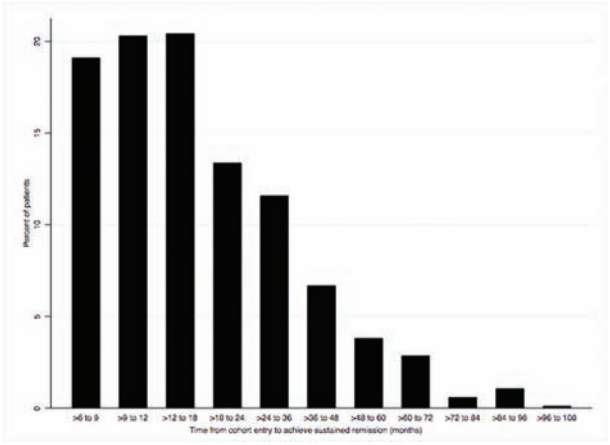
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Objectives: This study investigated the prevalence and impact of sarcopenia on clinical outcomes during follow-up in patients with rheumatoid arthritis (RA).
Methods: We enrolled 294 RA patients from a single tertiary center. Data were collected at the time of enrollment and annually thereafter for 3 consecutive years. Sarcopenia was assessed by bioelectrical impedance analysis and defined as a relative skeletal mass index (RSMI) < 5.14 kg/m^2 in women and < 7.40 kg/m^2 in men. Univariate and multivariate analyses were performed to identify the association between sarcopenia and clinical outcome.
Results: Of the 294 RA patients, 8.2% had sarcopenia at the time of enrollment. Patients with sarcopenia were more likely to be older (*P*=0.001), male (*P*=0.001), and smokers (*P*=0.001), and to have a higher body fat mass (*P*=0.034) and body fat percentage (*P*=0.039), and a lower basal metabolic rate (*P*=0.013), than non-sarcopenic patients. Biologic agents were more commonly prescribed to sarcopenic patients than to non-sarcopenic patients (*P*=0.048). The sarcopenic patients had higher Physician Global Assessment (PGA) (*P*=0.015), higher mean and delta tender joints (*P*=0.007), higher mean and delta swollen joints (*P*=0.007), and higher mean DAS28-ESR (*P*=0.014) and DAS28-CRP (*P*=0.020) scores than the non-sarcopenic patients. In the multivariate analysis, sarcopenia was significantly associated with male gender (OR = 0.112, 95% CI: 0.041–0.304, P <0.001), mean PGA score (OR = 1.680, 95% CI: 1.067–2.646, *P*=0.025), and mean DAS28-ESR score (OR = 4.477, 95% CI: 1.661–12.067, *P*=0.003).
Conclusion: Sarcopenia at baseline was an independent predictor of disease activity during follow-up in Korean patients with RA. Our results provide a rationale for lifestyle interventions designed to maintain normal weight in RA patients and thus help control disease activity.
Disclosure of Interests: None declared
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THU0153 PATTERNS OF SUSTAINED REMISSION AND SUBSEQUENT DMARD TAPERING IN EARLY RHEUMATOID ARTHRITIS: DATA FROM THE CANADIAN EARLY ARTHRITIS COHORT

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Background: Rheumatoid arthritis (RA) treatment emphasizes aggressive titration of disease-modifying antirheumatic drugs (DMARDs) with the goal of achieving disease remission. This often includes the use of multiple DMARDs in combination, which can have a significant impact on patients' lives and add costs to the healthcare system.
Objectives: To describe the patterns of sustained remission and subsequent treatment reduction in usual clinical practice for patients with early RA.
Methods: Patients (age >18) enrolled in the Canadian early ArThritis CoHort (CATCH) between January 2007 to March 2017 were analyzed. CATCH is a prospective, observational study of patients with early inflammatory arthritis (symptoms <1 year) treated in rheumatology clinics across Canada. The analysis cohort included patients with a diagnosis of RA according to the 1987 or 2010 ACR/EULAR classification criteria, active disease at enrolment (DAS28>2.6) and those treated with at least one DMARD or biologic agent within the first three months of study enrolment. We defined sustained remission as achieving a DAS28 < 2.6 at two consecutive follow-up visits at least six months apart. Reduction of therapy was defined as a minimum of a 25% dose reduction of conventional synthetic, targeted or biologic DMARDs. Descriptive statistics were used to summarize the time to remission and reductions in DMARD therapy.
Results: Eight hundred and thirty-seven (40%) of the 2,097 eligible patients achieved sustained remission during the study period. Of these, 60% did so within the first 18 months and 92% within the first four years (Figure 1). The mean (SD) baseline DAS28 was 5.1 (1.3), and HAQ-DI was 1.0 (0.7). At the time of remission, 80% were prescribed methotrexate (55% subcutaneously), 71% were prescribed combination therapy with other conventional synthetic DMARDs, and 13% were prescribed a biologic agent. In the year after attaining sustained remission, 327 (39%) patients reduced treatment in the following pattern (patients may have had more than one change): 250 patients (30%) reduced or stopped methotrexate, 196 patients (23%) reduced or stopped non-methotrexate DMARDs, and 34 patients (4%) reduced or stopped biologic agents. Of those that reduced or stopped a biologic, only one was due to side effects. For the 250 patients who reduced or stopped methotrexate, 25 were for a side effect.
Conclusion: Achieving sustained remission occurred in 40% of early RA patients in usual clinical practice. Treatment reductions following sustained remission occurred in over a third of patients over the next 12 months, and consisted mainly of adjustment in non-biologic DMARDs.



Abstract THU0153 – Figure 1. Bar graph demonstrating distribution of time (in months) to achieve first sustained remission

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Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, UCB., Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Carter Thorne Grant/research support from: Investigator-initiated studies: Amgen, Pfizer. RCTs: Abbvie, Celgene, CaREBiodam, Novartis, Pfizer, Consultant for: Advisory board: Abbvie, Amgen, Celgene, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi. Consultant: Abbvie, Centocor, Janssen, Lilly, Medexus/Medac, Pfizer, Speakers bureau: Medexus/Medac, Diane Tin: None declared, Marie-France Valois: None declared, Glen Hazlewood : None declared
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THU0154 HIGH RESOLUTION COMPUTED TOMOGRAPHY (HRCT) OF THE LUNG IN PATIENTS WITH RHEUMATOID ARTHRITIS: PREVALENCE OF INTERSTITIAL LUNG DISEASE INVOLVEMENT AND DETERMINANTS OF ABNORMALITIES

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Background: Interstitial lung disease (ILD) causes significant morbidity and mortality in patients with rheumatoid arthritis (RA). An international consensus about the identification of a subgroup of RA-patients with an high risk to develop ILD is still lacking.
Objectives: To assess: (a) the prevalence of ILD involvement in RA on high resolution computed tomography (HRCT) scan; (b) the relationships between pulmonary function tests (PTFs), patient-centred measures and ILD, (c) the potential risk factors that contribute to ILD in RA-patients.
Methods: We retrospectively evaluated the data of RA patients afferent to an italian rheumatological center from 1/1/2014 to 30/6/2018. We extrapolated clinical (age, gender, age at onset the RA), laboratoristic [rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs)], respiratory functional data [forced vital capacity (FVC) and single-breath diffusing capacity for carbon monoxide (DLco)], patient-centred measures of dyspnea (PCMD) (modified Borg Dyspnea Index and VAS for breathing), health assessment questionnaire-disability index (HAQ-DI), and HRCT. HRCT abnormalities were scored using a conventional visual reader-based score (CoVR)(1) and a computer-aided method (CaM)(2). The relationships among the two HRCT scores, PFTs and PCMD were calculated using Pearson's correlation. The AUC-ROC curve was calculated to determinate the discriminative performance of measures between patients with and without ILD. Multivariate regression model was used to assess the strength of association between ILD and RA features.
Results: 151 patients with RA were included (45 males and 106 females, mean age of 53.4 ± 7.6 years). We identified ILD in 29 of 151 patients (19.2%). Usual interstitial pneumonia was the most common pattern on HRCT. Patients with ILD were older ($p<0.01$), their age at RA-onset and HAQ-DI were higher (respectivelly with $p<0.01$ and $p<0.05$) than patients without RA-ILD. RF positivity and titer were similar in the two groups, whereas ACPA positivity and titre were higher in ILD group ($p=0.02$). Extent and severity of ILD, total CoVR and CaM score correlated closely with DLco and PCMD (both with $p<0.0001$) A reduced DLco was the most sensitive test to predict the presence of ILD on HRCT (AUC-ROC, 0.811±0.037). Multivariate analysis showed that older age ($p<0.0001$), age at RA onset, ($p=0.025$), APCA titers ($p=0.004$) and smoking habit ($p=0.008$) were independent explanatory variables of HRCT damage.
Conclusion: ILD is a frequent feature of RA. RA-ILD is associated with age, age at RA-onset, smoking habit, and ACPA titer. DLco seems the most sensitive measure to predict ILD on HRCT scan, followed by PCMD.

REFERENCES:

1 Warrick JH, Bhalla M, Schabel SI, Silver RM. High resolution computed tomography in early scleroderma lung disease. J Rheumatol. 1991; 18 (10):1520-8.
2 Shin KE, Chung MJ, Jung MP, Choe BK, Lee KS. Quantitative computed tomographic indexes in diffuse interstitial lung disease: correlation with physiologic tests and computed tomography visual scores. J Comput Assist Tomogr. 2011; 35(2):266-27.

Disclosure of Interests: Fausto Salaffi Grant/research support from: Abbvie, Roche, Novartis, Pfizer, Sanofi, Speakers bureau: Abbvie, Roche, Novartis, Pfizer, Sanofi, BMS, marina carotti Speakers bureau: abbvie pfizer novartis roche bms sanofi, Marco Di Carlo: None declared, Marika Tardella: None declared, Andrea Giovagnoni: None declared
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THU0155 PATIENT ADHERENCE WITH A SMARTPHONE APP FOR DISEASE MONITORING IN RHEUMATOID ARTHRITIS

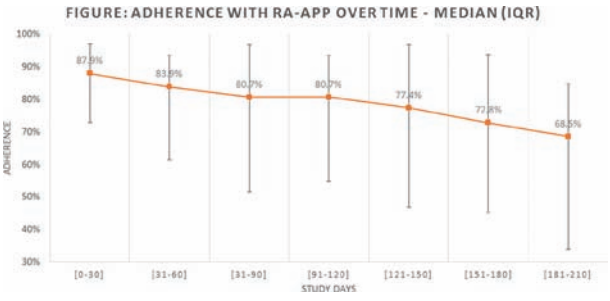
Daniel Solomon[1], Fengxin Lu[1], Chang Xu[1], Joshua Colls[1], Dong Hyun Suh[1], Meredith Murray[1], Cassandra Corrigan[1], Yvonne Lee[2]. *[1]Brigham and Women's Hospital, Rheumatology, Boston, United States of America*; *[2]Northwestern Medical Center, Rheumatology, Chicago, United States of America*

Background: Patients increasingly are asking for tools to improve self-management. Electronic patient reported outcomes (ePROs) transmitted digitally allow patients to both communicate with their clinicians between visits and help track their own disease activity. While several tools have been developed in rheumatology, few data have been reported regarding patient adherence.
Objectives: To examine patient adherence to a smartphone app for rheumatoid arthritis (RAapp).
Methods: We developed a smartphone app to deliver daily disease assessments to patients with RA (RAapp). The app was tested as part of a randomized controlled trial examining the potential clinical benefits of RAapp compared to a wait-list control. These analyses focus only on the adherence of patients who received RAapp and completed the 6-month trial. We recruited RA patients from the rheumatology practice at a large academic medical center in the US. Patients with at least 6weeks of stable DMARD use who were at least 18years of age were required to give written informed consent, be fluent in English, and have a smartphone with an iOS or android operating system. RAapp was downloaded by patients through a password protected link on to the patient's phone after consent. Patient's received daily notifications regarding disease

assessments, including disease activity (RADAI), function (MDHAQ), pain (PROMIS), fatigue (PROMIS), sleep (PROMIS), and depression (PROMIS). The current set of analyses focused on adherence to RAapp, overall, by scale, and over the 6 months of the trial. We examined adherence to RAapp over the duration of the study and examined factors related to adherence using mixed regression models. Factors tested included patient age, sex, educational attainment, and baseline CDAI.

Results: 75 patients received RAapp and have data included in these analyses (5 patients are in the last month of follow-up). 60 (80%) were female; age breakdown was 24% < 45 years, 49% 45-64 years, and 27% 65 years and over; and educational attainment was 19% high school, 59% college, and 23% beyond college. Baseline CDAI demonstrated 20% in remission, 45% low, 24% moderate, and 11% high disease activity. During the 6-month study, median adherence to the RAapp daily questionnaires was 81.6% (interquartile range 48.4% to 92.3%). Broken down by the type of questionnaire, median adherence was: disease activity 79.8%; pain 80.8%; mood 76.2%; function 79.3%; fatigue 77.0%; and sleep 77.8%. Adherence to the daily questionnaires was highest in the first month but decreased a small amount each of the following months (see **Figure**, p for trend < 0.001). The only significant predictor of higher adherence was age 65 or over (p = 0.04). High baseline CDAI was associated with a lower adherence but was not statistically significant (p = 0.07).

Conclusion: We developed and tested an ePRO app for RA (RAapp). Among a large group of patients, adherence to the app was good but declined slightly over time. There was no substantial variation in adherence with different ePRO scales. Older age was the only significant predictor of adherence.



Abstract THU0155 – Figure 1

Disclosure of Interests: Daniel Solomon Grant/research support from: Abbvie, Amgen, Genentech, Janssen, and Pfizer, Fengxin Lu Grant/research support from: Pfizer, Chang Xu Grant/research support from: Pfizer, Joshua Colls Grant/research support from: Pfizer, Dong Hyun Suh Grant/research support from: Pfizer, Meredith Murray Grant/research support from: Pfizer, Cassandra Corrigan Grant/research support from: Pfizer, Yvonne Lee Shareholder of: Express Scripts, Grant/research support from: Pfizer

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THU0156 NO CONFIRMATION OF INCREASED RISK OF IDIOPATHIC FACIAL NERVE PALSY UNDER TOCILIZUMAB

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Background: Spontaneous reports of nine facial paralyses and five facial pareses made by healthcare professionals from Europe have recently prompted EMA's Pharmacovigilance Risk Assessment Committee (PRAC) *to consider a potentially increased risk of idiopathic facial nerve palsy* for patients receiving tocilizumab.

Objectives: To assess whether this signal can be confirmed with data of a large data set with known denominators for various treatments, comparing the risk in patients receiving tocilizumab with the risk in patients receiving other DMARDs.

Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients with a new start of a DMARD after at least one csDMARD failure. For this analysis, patients were included who were enrolled with a biologic DMARD start between 01/2007 and 04/2018. DMARD specific, unadjusted incidence ratios were calculated.

Results: Between 2007 and 2018, a total of 20 facial nerve palsies (FNP) were observed in 11963 RABBIT patients, of those, three were excluded due to obvious reasons (e.g. stroke) leaving 17 idiopathic FNP. Three of them were observed in tocilizumab patients, leading to an incidence rate of 0.47 per 1000 PY (95% CI: 0.10, 1.14), which is higher than the incidence rate observed in patients receiving conventional synthetic (cs)DMARDs (0.21, 95% CI: 0.04; 0.51) but does not stand out among the incidence rates observed for other biologicals (see Table 1). The overall incidence of an idiopathic FNP among patients receiving (synthetic or biological) DMARDs was 0.37 (95% CI: 0.22, 0.57) which is higher than the incidence of idiopathic FNP in the general population (with 20-30 cases per 100,000 persons [1]). Age and gender were roughly equally distributed among patients with and without idiopathic FNP. Patients with idiopathic FNP had longer disease duration, more frequently presented with joint erosions and with prior treatment with biologics. They also had lower physical function and more comorbidities. In one patient with idiopathic FNP receiving treatment with Rituximab (original biologic) a Sjoegrens' syndrome was reported as comorbidity, which is associated with an increased risk of neuropathies.

Conclusion: The overall incidence of idiopathic FNP among rheumatoid arthritis patients receiving DMARDs was higher than the incidence in the general population. However, an increased risk for patients receiving tocilizumab compared to patients treated with other biologicals cannot be confirmed. The incidence of idiopathic FNP is higher for patients receiving biologicals compared to patients receiving csDMARDs. This might be due to the higher disease activity. However, the small number of cases with an idiopathic facial nerve palsy is a limiting factor in analysing and interpreting these results.

REFERENCE:

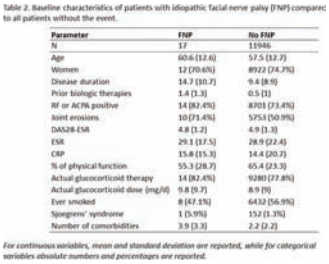
[1] Murthy, J.M.K., Saxena, A.B. (2011): Bell's palsy; treatment guidelines. Ann Indian Acad Neurol. 2011 Jul; 14(Suppl1): S70–S72.

Abstract THU0156 –Table 1. Unadjusted incidence rates for idiopathic facial nerve palsies.

Drug	Number of events	Incidence rate (per 1000 patient years under treatment)	95%	CI
csDMARDs	3	0.2	(0.0;	0.5)
Etanercept (original)	4*	0.7	(0.2;	1.6)
Etanercept (biosimilar, SB4)	1	1.9	(0.1;	6.9)
Golimumab	1	0.7	(0.0;	2.4)
Rituximab	5*	0.8	(0.3;	1.6)
Abatacept	1	0.3	(0.0;	1.2)
Tocilizumab	3	0.5	(0.1;	1.1)
All	17	0.4	(0.2;	0.6)

* One patient was exposed to both Etanercept (original) and Rituximab at the time of event.

Abstract THU0156 –Table 2.


Table 2. Baseline characteristics of patients with idiopathic facial nerve palsy (FNP) compared to all patients without the event.

Parameter	FNP	No FNP
N	17	11946
Age	60.6 (12.6)	57.5 (12.7)
Women	12 (70.6%)	8922 (74.7%)
Disease duration	14.7 (10.7)	9.4 (8.9)
Prior biologic therapies	1.4 (1.3)	0.5 (1)
RF or ACPA positive	14 (82.4%)	8701 (73.4%)
Joint erosions	10 (71.4%)	5753 (50.9%)
DAS28-ESR	4.8 (1.2)	4.9 (1.3)
ESR	29.1 (17.5)	28.9 (22.4)
CRP	15.8 (15.3)	14.4 (20.7)
% of physical function	55.3 (28.7)	65.4 (23.3)
Actual glucocorticoid therapy	14 (82.4%)	9280 (77.8%)
Actual glucocorticoid dose (mg/d)	9.8 (9.7)	8.9 (9)
Ever smoked	8 (47.1%)	6432 (56.9%)
Sjoegrens' syndrome	1 (5.9%)	152 (1.3%)
Number of comorbidities	3.9 (3.3)	2.2 (2.2)

For continuous variables, mean and standard deviation are reported, while for categorical variables absolute numbers and percentages are reported.

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Disclosure of Interests: Anja Strangfeld Speakers bureau: Speakers fees from Bristol-Myers Squibb, MSD, Pfizer, Roche, Yvette Meißner Speakers bureau: Pfizer, Martin Schaefer: None declared, Lisa Baganz: None declared, Matthias Schneider Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Speakers bureau: Chugai, Elke Wilden: None declared, Silke Zinke: None declared, Angela Zink Speakers bureau: Speakers fees from AbbVie, Janssen, Pfizer, Roche, Sanofi

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THU0157 REASONS FOR NON-PARTICIPATION IN A RANDOMIZED CONTROLLED TRIAL COMPARING TWO SEASONAL INFLUENZA VACCINES IN RHEUMATOID ARTHRITISPATIENTS

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Background: Low recruitment rates (12%) into influenza vaccine studies are reported among healthy older adults. Fear of side effects, lack of insight into personal risk status, and doubts about vaccine efficacy are the most commonly reported reasons for non-participation[1]. Rheumatoid arthritis (RA) patients are also at high risk for influenza and benefit from yearly immunization[2]. A number of influenza vaccines are currently available; however, it is unknown which vaccine(s) provides optimal protection to RA patients. Estimating participation rates is key for designing studies to address that issue.
Objectives: To define the rate of non-participation and reported reasons for refusing entry into a randomized clinical trial (RCT) comparing two influenza vaccine formulations (NCT02936180 - ClinicalTrials.gov).
Methods: Seropositive RA patients from McGill University Health Centre, on stable treatment prior to recruitment ($\geq$3 months), were invited by their treating rheumatologists to participate in the study. A vaccine nurse contacted participants from Year 1 (Y1) and those from Year 2 (Y2) encountered a recruiter immediately after their rheumatologist's appointment. Patients who agreed to participate signed the consent form and were later contacted by a vaccine nurse to schedule their appointment. Reasons for non-participation were documented.
Results: Over two influenza seasons, 692 RA patients were invited to participate in the study. The non-participation rate was 59.5% (Y1=64.6%, Y2= 53.1%, p=0.1). Non-participants and participants did not differ in age or sex (age mean±SD: 61.7±14.7 vs 60.9 ±12.9, p=0.5; female sex%: 76.8 vs 79.9, p=0.33). Inclusion and exclusion criteria resulted in the loss of 17 (4.1%) and 19 (4.6%) subjects, respectively. The three most commonly reported reasons for non-participation were vaccine misconceptions (n=49, 20.4%), reluctance to participate in a clinical trial (n=35, 14.6%), and lack of available time (n=29, 12.1%). Thirty-one patients reported more than one reason for non-participation. Reasons for non-participation were similar according to sex and patient age (> or < 65 years).
Conclusion: Only half of eligible RA patients accepted to be enrolled in this influenza vaccine study. Enhancing patient literacy on vaccines and the relevance of conducting clinical trials is essential to optimize both recruitment to such trials and immunization rates.

REFERENCES:

[1] Allsup SJ, Gosney MA. Difficulties of recruitment for a randomized controlled trial involving influenza vaccination in healthy older people. Gerontology. 2002; 48:170–173.
[2] Blumentals WA, Arreglado A, Napalkov P, Toovey S. Rheumatoid arthritis and the incidence of influenza and influenza-related complications: a retrospective cohort study. BMC Musculoskelet Disord. (2012) 13:158.

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THU0158 IMPAIRED OLFACTORY FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Recent studies indicated that rheumatic disorder can be associated with olfactory loss.
Objectives: To specifically investigate chemosensory function in patients with rheumatoid arthritis (RA) by valid and reliable psychophysical tests and compare them to healthy controls.
Methods: We investigated 212 RA patents (43 men, 169 women; mean age 59 years) and compared their results to 30 healthy controls (10 men, 20 women; mean age 40 years). All participants received standardized olfactory (odor thresholds, odor discrimination and identification for suprathreshold testing) and gustatory tests (taste sprays – suprathreshold taste function; taste strips – quasi-threshold gustatory test). In addition, blood chemistry was also assessed (e.g., for CRP, RA factors, and anti-CCP).
Results: RA patients rated their senses of smell and taste to be as good as that of controls. However, in RA patients 4% were found to be anosmic, and 36% to be hyposmic. These numbers were 0 and 20%, respectively, in controls. RA patients exhibited significantly lower scores in odor identification and discrimination. Gustatory test scores were also decreased in RA patients. No such differences were found for odor thresholds. Interestingly, the changes in olfactory and gustatory function neither correlated with disease duration nor with indicators of RA activity or severity like C-reactive protein, rheumatoid factors, anti-CCP antibodies orDAS28-Score. Moreover, there was no correlation between olfactory dysfunction and treatment with DMARDs, e.g. amount of MTX, or Tumor necrosis factor α inhibitors.
Conclusion: These results indicate that olfactory and gustatory function is significantly decreased in patients with RA. This decrease in function seems to be unnoticed by most patients which may be due to the fact that RA patients have no compete loss of function (anosmia), but still function in the range of hyposmia or even normosmia. Importantly, the changes in olfactory function are not observed at the level of odor thresholds but only for suprathreshsold tasks, which may suggest that the decrease in function is due to higher-order central-nervous processing of olfactory information. In addition, the lack of correlations between disease parameters and chemosensory dysfunction indicates that the decrease in chemosensory function may be a trait characteristic of RA patients.
Disclosure of Interests: Joerg Wendler Consultant for: Chugai, Roche, AbbVie, Novartis, Janssen-Cilag, Speakers bureau: Chugai, Roche, AbbVie, Novartis, Janssen-Cilag, Khang Tran: None declared, Martin Aringer Grant/research support from: Roche, Consultant for: AstraZeneca and Eli Lilly, Florian Schuch Consultant for: Celgene, Lilly, UCB, Roche, Sanofi-Aventis, Abbvie, Novartis, Speakers bureau: Celgene, Lilly, UCB, Roche, Sanofi-Aventis, Abbvie, Stefan Kleinert Grant/research support from: Novartis, Consultant for: Novartis, UCB, Chugai, Celgene, Medac, Roche, Abbvie, Speakers bureau: Novartis, UCB, Chugai, Celgene, Medac, Roche, Abbvie, Antje Haehner: None declared, Thomas Hummel: None declared
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THU0159 RISK FACTORS FOR DEVELOPING SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS AT 2 YEARS: FROM THE CHIKARA STUDY

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Background: Patients with rheumatoid arthritis (RA) are at higher risk of sarcopenia due to joint dysfunction and chronic inflammation. The prospective observational CHIKARA study (Correlation research of sarcopenia, skeletal muscle and disease activity in rheumatoid arthritis; registration number UMIN000023744) was started in 2016 to clarify the correlation between RA disease activity and sarcopenia. We reported that glucocorticoid use and low body fat were independent risk factors for developing sarcopenia at 1 year in RA patients last year.
Objectives: Risk factors for sarcopenia were investigated over a 2-year period this time.
Methods: 100 patients (78 female, average age 68 years) enrolled in the prospective CHIKARA study underwent examinations of body composition (body weight, muscle mass, fat mass, predicted bone mass, etc.; measured by a body composition analyzer (MC-780A; TANITA, Tokyo, Japan)), laboratory data, disease activity, Health Assessment Questionnaire (HAQ), and treatment condition at baseline and at 2 years. Sarcopenia was diagnosed using the criteria of the Asia Working Group on Sarcopenia. Of 64 patients without sarcopenia at baseline, those who developed sarcopenia at 2 years were identified, and risk factors were investigated by univariate and multivariate analyses.
Results: Six patients (9.4%) developed sarcopenia during the 2-year follow-up. Glucocorticoid use >5 mg/day was significantly higher (p=0.009), and MMP3 (p=0.018) and HAQ (p=0.045) were significantly increased in the patients who developed sarcopenia during the 2-year follow-up. Sarcopenia development was significantly associated with male sex (r=0.28, p=0.03), age (r=0.27, p=0.03), glucocorticoid use >5 mg/day (r=0.33,

p<0.01), CRP (r=0.33, p<0.01) at baseline, ΔMMP3 (r=0.30, p=0.02), and ΔHAQ (r=0.25, p=0.04) on univariate analysis. Multivariate analysis identified no independent factors (Table 1)

Table 1. Risk factors for developing sarcopenia in patients with rheumatoid arthritis

	Univariate		Multivariate		
	R value	p value	Odds ratio	95% CI	P value
Male sex	0.28	0.02	-	-	-
Age	0.27	0.03	1.05	0.92-1.20	0.47
GC use >5mg/day	0.33	<0.01	10.20	0.45-229.0	0.14
ΔMMP3	0.30	0.02	1.02	0.99-1.04	0.08
ΔHAQ	0.25	0.04	1.26	0.94-1.67	0.11

GC: glucocorticoids, CI: confidence interval, Δ: change from baseline to 2 year
Conclusion: Male sex, old age, glucocorticoid use >5 mg/day, and high elevations of MMP3 and HAQ are associated with developing sarcopenia at 2 years in RA patients.

REFERENCES:

[1] Yamada Y., Tada M., Mandai K. et al. Glucocorticoid use is an independent risk factor for sarcopenia in patients with rheumatoid arthritis – from the CHIKARA study -. EULAR 2018 THU0181.
[2] Chen LK., Liu LK., Assantachai P., et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2014; 15: 95-101.

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, Koji Mandai: None declared, Noriaki Hidaka: None declared, Kentaro Inui Speakers bureau: Takeda Pharmaceutical, Pfizer Japan, Daiichi-Sankyo Co.Ltd., Abbvie, Mitsubishi Tanabe Pharma Corporation, Janssen Pharmaceutical, Chugai Pharmaceutical, Ono Pharmaceutical, Eisai Co. Ltd., Eli-Lilly, Nippon Kayaku Co.,Ltd., Maruho Co.,Ltd, Kaken Pharmaceutical Co.,Ltd., Hiroaki Nakamura: None declared
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THU0160 FEATURES OF LIPID PROFILE INDICATORS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CONNECTION WITH ARTERIAL HYPERTENSION

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Background: Patients with rheumatoid arthritis (RA) have an early development of endothelial dysfunction, an increase of the atherogenicity index (AI), and a high risk of fatal cardiovascular events. The presence of arterial hypertension (AH) in patients with RA accelerates the process of early atherogenesis and increases the risk of fatal cardiovascular events.
Objectives: To evaluate the dynamics of lipid profile changes in patients with RA in combination with AH.
Methods: It was examined 47 patients with RA in combination with AH (by all patients was discovered IIstage/2degree of AH). The age of the patients ranged from 18 to 72 years. Among the surveyed group dominated men (41 patients). All patients were assessed for the levels of total cholesterol (TC), low density lipoprotein (LDL), very low density lipoprotein (VLDL), triglycerides (TG), high density lipoprotein (HDL), AI (AI = TC – HDL/LDL), antibodies to modified citrulline vimentin (anti-MCV), rheumatoid factor (RF), C-reactive protein (CRP) before treatment. All patients were also assessed for the risk of death for 10 years by the SCORE scale (> 15% - very high risk, 10-14% high, 5-3% - moderate, <1% - low) and RA activity by DAS28 score.
Results: Due to the obtained data, it can be asserted, that in patients with seronegative RA the moderate risk by SCORE was prevalent, and among seropositive RA patients– high risk. The high level of anti-MCV titres was directly corelated with the risk of the death by SCORE (p > 0,05, r = 0,64). We found that patients with RA and AH had relatively low levels of TC (5,82 ± 2,21 mmol/L) and LDL (2,82 ± 0,81 mmol/L), but the AI in these patients was 4,42 ± 0,68. It was measured the correlation between the levels of LDL and the activity of the inflammatory process DAS28, the level of CRP and the duration of RA (r = 0,56, p <0,05, r = 0,49, p <0,05, r = 0,53; p <0,05, respectively). There was also a reverse correlation between the duration of RA and the level of HDL (r = -0,47; p <0,05).
Conclusion: 1. Seropositivity, high activity and anamnesis of RA for more than 10 years are the factors, that are associated with high risk of fatal cardiovascular events. 2. In patients with RA in combination with AH, serum lipid levels have paradoxical ratio, resulting in lower levels of TC and LDL associated with an increased risk of cardiovascular events ("lipid paradox"). 3. The presence of high anti-MCV titres serves as a prognostically unfavorable feature of the course of RA and AH, since its association with a high risk of fatal cardiovascular events.
Disclosure of Interests: None declared
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Rheumatoid arthritis - non biologic treatment

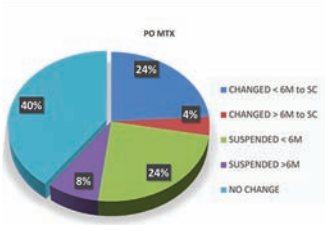
THU0161 ORAL VERSUS SUBCUTANEOUS METHOTREXATE IN RECENTLYDIAGNOSED RHEUMATOID ARTHRITIS: DO WE GET THE SAME RESULTS?

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Background: As we know, the use of disease modifying antirheumatic drugs (DMARDs) improves the overall prognosis of rheumatoid arthritis (RA) specially when treatment is started early in the course of the disease.
The most widely used DMARD is methotrexate (MTX) mainly because of its favorable efficacy-toxicity ratio. However, there is a lot of variability using MTX when it comes to dosage and route of administration; and little research on the overall response of patients to the different strategies used.
Objectives: To compare the clinical response of oral (PO) versus subcutaneous (SC) MTX in recently diagnosed RA patients with no previous use of DMARDs. We evaluated the data collected at baseline, the 3º, 6º and 12º month after the beginning of MTX treatment.
Methods: This descriptive, observational, longitudinal retrospective study was achieved using a cohort of patients with recently diagnosed RA in which treatment with MTX was started between August 1st 2015 to September 1st 2018. We collected demographic and clinical data, disease activity markers, MTX and corticoid dosage, routes of administration and treatment changes.
Results: In total, 52 patients were included of which 39 (75%) were women, with an average age of 57.56 years. There was a mean of 26 weeks between the first symptoms and the beginning of MTX.

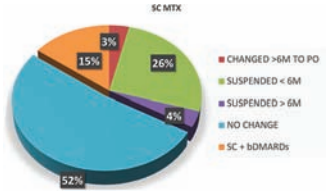
Abstract THU0161 –Table 1.

	Total	Oral	Subcutaneous	(p)
Patients n(%)	52(100)	25(48.1)	27(51.9)	
Mean Starting MTX dose (SD)	12.6(+/-2.5)	11.1(+/-2)	13.98(+/-2.2)	**<0.0001**
Mean Starting Prednisone dose (SD)	6.21(+/-6.2)	5.92(+/-4.3)	6.48(+/-7.5)	0.74
Mean Starting Painful Joint Count (SD)	9.5(+/-6.9)	8.56(+/-5.9)	10.41(+/-7.5)	0.34
Mean Starting Swollen Joint Count(SD)	5.38(+/-6.6)	5.04(+/-4.6)	7.34(+/-7.8)	0.2
Mean Staring CRP (SD)	1.67(+/-2.2)	1.51(+/-2.4)	1.76(+/-1.8)	0.69
Mean Starting ESR (SD)	27.3(+/-19.6)	30.44(+/-20)	24.22(+/-18.4)	0.25



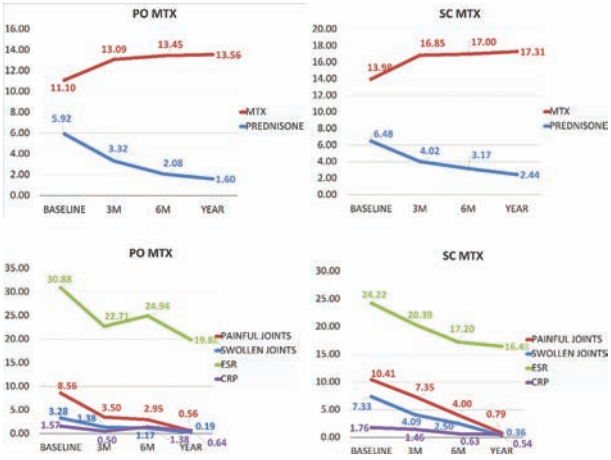
Abstract THU0161 – Figure 1

In the PO MTX group, 8 (32%) patients required a change to SC MTX; in 87.5% of cases due to treatment inefficacy and 7 (87.5%) of these patients kept the SC route until the end of the study.



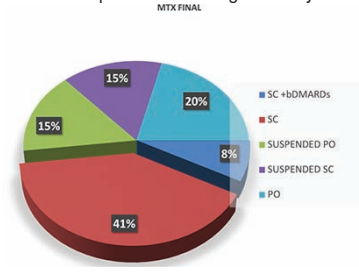
Abstract THU0161 – Figure 2

Out of the patients that began with SC MTX, the one that changed route to PO maintained a good response. All the patients with biologic DMARDs kept the SC MTX as adjuvant therapy. On the other hand, the 3 (12%) patients of the PO that used a biologic DMARD had suspended MTX several months before.



Abstract THU0161 – Figure 3

Both groups had a good response to MTX. There was a significant reduction in corticoid requirements during the first year of treatment(P



Abstract THU0161 – Figure 4

At the end of the study, 21 (41%) patients received SC MTX and the number goes up to 25 (49%) if we include those who also had biologic DMARDs.
Of those who suspended MTX, 85% were due to adverse effects, similar in both groups.
Conclusion:

- Our study suggests that patients that start with PO MTX require route administration changes more frequently than the SC group during the first year of follow-up.
- SC MTX was the route used by almost half the patients by the end of the study.
- We can also see that the inflammatory response to MTX was acceptable regardless of administration route and that corticoids could be reduced significantly in both groups.

REFERENCES

[1] Braun, J. et al. Comparison of the clinical efficacy and safety of subcutaneous versus oral administration of methotrexate in patients with active rheumatoid arthritis: Results of a six-month, multicenter, randomized, double-blind, controlled, phase IV trial. Arthritis Rheum 2008; 58: 73-81.
[2] Tornero Molina, J et al. Recommendations for the use of methotrexate in rheumatoid arthritis: Up and down scaling of the dose and administration routes. Reumatol Clin 2015;11:3-8.

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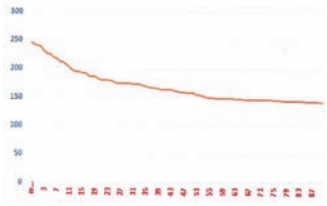
THU0162 WHICH PERSISTENCE OF METHOTREXATE AFTER INITIATION OF THE 1ST BDMARD IN RHEUMATOID ARTHRITIS? THE RETRO-RIC2 STUDY

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Background: ACR and EULAR guidelines recommend to prescribe bDMARDs and particularly TNFi in combination with methotrexate (MTX). However, the MTX observence in RA is poor, mainly due to side effect and some bDMARDs (IL6 receptor antagonist) are almost as effective in monotherapy.
Objectives: to evaluate MTX use (dosage, route of administration…) in RA after initiation of the first bDMARD.
Methods: RETRO-RIC2 is a multicentric retrospective study. Were included all patients with RA under MTX therapy at the initiation of the 1st bDMARD from October 2008 to September 2016. The main criteria is the persistence of MTX after 1 and 2 years.
Results: 409 patients were included : mean-age = 58.9 years, female 69%, RF positive 76% and ACPA positive 83%, mean RA duration = 13.14y and mean DAS28-ES=4.48. The mean duration of previous MTX therapy = 32 months (mean dose = 16.2mg/w). At the inclusion MTX was administrated by oral route in 52% and subcutaneous in 48%. The first bDMARD was a TNF inhibitor in 70%
At inclusion, 1.2% of the patients switch from oral route MTX for subcutaneous; inversely in only 0.2% the SC route was switched for oral administration.
The results are presented in table 1 and Figure 1.

	NB patients evaluable	MTX dose reduction	MTX dose increase	MTS dose unchanged	MTX stopped
V-1/ inclusion	404	4.5%	2.7%	93%	0%
M0-M4	255	14.1%	6.3%	79%	0.4%
M4-M12	173	16.8%	5.4%	77%	1.2%
M12-M24	159	14.5%	4.4%	80%	1.3%

V-1 = last previous visit before inclusion



Abstract THU0162 – Figure 1

Conclusion: In almost all patients MTX dose and route of administration are unchanged at the initiation of the first bDMARD in RA. With a 2 years follow up 49.9% of MTX dose were reduced and MTX was stopped in 2.9%. At 2 years MTX route of administration is oral for 64% of the patients and s/c for 36%.
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THU0163 **A DESCRIPTIVE ANALYSIS OF LONGITUDINAL CHANGES IN RELATIVE MARKET SHARE PROPORTIONS OF BIOLOGIC AND TARGETED SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS FOR TREATMENT OF RHEUMATOID ARTHRITIS: DATA FROM THE OBRI DATABASE**

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Background: For patients with Rheumatoid Arthritis (RA) who do not achieve adequate clinical response with combined conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), the next step in goal-directed therapy is initiation of either biologic DMARDs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs). bDMARDs include tumour-necrosis factor inhibitors (TNFi) or non-TNFi classes. Since inception of Ontario Best Practice Research Initiative (OBRI), new treatment options have become available

Objectives: We aimed to describe the evolution of relative use of non-TNFi vs. TNFi in Ontario-based practices from 2008-2017.

Methods: Adult patients with RA enrolled in the OBRI who started therapy with bDMARDs or tsDMARDs anytime during, or up to 30 days before, enrollment were included. Using descriptive analysis of data from each year between 2008 and 2017, the relative proportion of the population treated with TNFi and non-TNFi therapy was measured for (i) all patients and (ii) those initiating their first bDMARD/tsDMARD. TNFi included: Etanercept, Adalimumab, Certolizumab, Golimumab, and Infliximab. Non-TNFi included: Abatacept, Rituximab, Tocilizumab, and Tofacitinib.

Results: A total of 1,057 patients were included of whom 653 were bDMARD/tsDMARD naïve. In 2008, the relative non-TNFi use was 3/56 (5.4%) in all patients and 0/31 (0%) in treatment-naïve patients. By 2013 the proportion non-TNFi use increased to 135/562 (24%) in all patients and 11/92 (12.0%) in treatment-naïve patients. This increasing trend in relative non-TNFi utilization continued in both groups until 2016 when relative use was 224/679 (33.0%) in all patients and 17/56 (30.4%) in treatment-naïve. This was followed by 144/426 (33.8%) and 4/15 (26.7%), respectively in 2017.

Conclusion: This descriptive analysis of data from the OBRI cohort shows an increase in the use of non-TNFi therapies. The overall trend towards greater use of non-TNFi therapies as first line agents after combined csDMARDs may be partially explained by the presence of guidelines that allow clinicians to select any of the above options as first line advanced therapies. Future analyses evaluating patient-, disease- and concomitant drug use-specific determinants of physician decision-making will be conducted.

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THU0164 **THE DAS28 BASED ON THE ERYTHROCYTE SEDIMENTATION RATE MAY OVERESTIMATE DISEASE ACTIVITY IN EARLY, TREATMENT-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS WITH HIGH LEVELS OF RHEUMATOID FACTOR**

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Background: Disease activity in rheumatoid arthritis (RA) is commonly measured with the DAS28-ESR. However, ESR levels may be affected by factors not related to inflammation leading to possible disparities with the DAS28-CRP. In particular, increased levels of gammaglobulins may cause increase in ESR. In RA levels of autoantibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) may be particularly high; however, their effect on the assessment of disease activity has not been investigated.

Objectives: To evaluate whether positivity and levels of RF and ACPA determine discordance between the DAS28-ESR and the DAS28-CRP, impacting on disease activity stratification in RA.

Methods: 578 early treatment-naïve RA patients (symptoms' duration <12 months) consecutively recruited at our Early Arthritis Clinic between 2005 and 2014 were studied. Paired DAS28-ESR and DAS28-CRP were obtained at baseline and after 6 months of therapy with conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). RF and ACPA were determined centrally on baseline sera, and levels were considered high when >3 times the upper limit of normal (ULN). Agreement between the disease activity scores was compared using Bland-Altman statistics before and after stratification for autoantibody-positivity and levels.

Results: Female/male ratio was 2.5:1, with mean (SD) age of 59.7 (14.8) years and median (IQR) symptoms' duration at inclusion of 15.6 (9.4 to 27.8) weeks. Mean DAS28-ESR values at baseline were 0.39 points higher compared to DAS28-CRP in the whole cohort, with more pronounced differences in females and subjects aged ≥65 years (**Table 1**). Collectively RF-positive patients had significantly higher discrepancies compared to –negative subjects (mean [SD] difference 0.45 [0.46] vs 0.35 [0.47], p=0.03), particularly in females irrespective of age. The highest disagreement was recognized in patients with high autoantibody levels; females with RF >3 ULN had DAS28-ESR scores 0.56 points higher. Disparities in these patients impacted on disease activity stratification, as more RF-high females were in DAS28-ESR high disease activity compared with DAS28-CRP (43.1% vs 23%, p<0.001). In contrast, ACPA-positivity did not affect the agreement between the two disease activity indices (**Table 1**). After 6 months of treatment with csDMARDs discrepancies between the DAS28-ESR and DAS28-CRP in RF-positive patients was reduced but still significant in association with levels >3 ULN (mean difference [95% CI] 0.44 [0.33-0.55]).

Conclusion: In patients with early treatment-naïve RA, the DAS28-ESR and DAS28-CRP are not inter-exchangeable. In particular, the DAS28-ESR may overestimate disease activity when levels of RF are high. These findings suggest that disease assessment for treat-to-target approaches should take into account additional factors such as autoantibody-positivity.

Abstract THU0164 –Table 1. Comparative mean differences (95% CI) between DAS28-ESR and DAS28-CRP stratified for autoantibodies

	whole cohort	female	male	age ≥65 years	age <65 years
overall	0.39 (0.35-0.43)	0.44 (0.47-0.50)	0.26 (0.18-0.34)	0.42 (0.36-0.49)	0.37 (0.31-0.43)
RF-pos	0.45 (0.38 - 0.53)	0.52 (0.43-0.61)	0.26 (0.13-0.39)	0.47 (0.33-0.61)	0.46 (0.37-0.55)
RF-pos >3 ULN	0.50 (0.40-0.60)	0.56 (0.45-0.68)	0.29 (0.10-0.49)	0.51 (0.30-0.72)	0.51 (0.39-0.62)
ACPA-pos	0.41 (0.34-0.48)	0.49 (0.41-0.57)	0.20 (0.07-0.34)	0.46 (0.32-0.58)	0.40 (0.31-0.49)
ACPA-pos>3 ULN	0.41 (0.33-0.48)	0.47 (0.39-0.56)	0.25 (0.12-0.38)	0.42 (0.27-0.56)	0.41 (0.32-0.50)
ACPA-pos>100 U	0.39 (0.30-0.49)	0.44 (0.33-0.56)	0.27 (0.10-0.44)	0.42 (0.22-0.61)	0.39 (0.28-0.51)

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THU0165 A COMPARATIVE ANALYSIS OF UPADACITINIB MONOTHERAPY AND UPADACITINIB COMBINATION THERAPY FOR THE TREATMENT OF RHEUMATOID ARTHRITIS FROM TWO PHASE 3 TRIALS

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Background: Upadacitinib (UPA), a selective JAK1 inhibitor, has demonstrated efficacy and safety in patients with rheumatoid arthritis (RA) as monotherapy and in combination with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) such as methotrexate (MTX).1,2 However, UPA monotherapy has not been compared directly with UPA combination therapy in the Phase 3 program.
Objectives: To compare the efficacy of UPA monotherapy and UPA in combination with MTX using data from two Phase 3 trials of RA patients with an inadequate response (IR) to prior MTX therapy.
Methods: In SELECT-MONOTHERAPY, 648 MTX-IR patients were randomized to receive UPA 15 mg or 30 mg monotherapy once daily (QD), or continue with MTX monotherapy (cMTX; given as a blinded study drug), for 14 weeks. In SELECT-NEXT, 661 csDMARD-IR patients were randomized to receive UPA 15 mg or 30 mg QD or placebo (PBO) for 12 weeks on a background of csDMARDs. Only patients receiving concomitant MTX (with or without additional csDMARDs) at baseline in SELECT-NEXT were included in this analysis. The primary endpoints of both studies were the proportion of patients achieving ACR20 and DAS28(CRP) ≤3.2. Additional endpoints included ACR50/70, DAS28(CRP) <2.6, CDAI remission (≤2.8), CDAI low disease activity (LDA; ≤10), and change from baseline in HAQ-DI. Logistic regression or ordinary least squares analyses were used to compare outcomes with monotherapy versus combination therapy, adjusting for demographics and baseline disease characteristics.
Results: A total of 1114 patients were included in the analysis, of whom 648 received monotherapy in SELECT-MONOTHERAPY and 466 received combination therapy in SELECT-NEXT. Of the patients receiving combination therapy, 338 (72.5%) were receiving MTX background therapy only and 128 (27.5%) were receiving MTX plus other csDMARDs. Baseline characteristics were generally similar between the study cohorts; the majority of patients in both studies were female and of white ethnicity, with a mean age of approximately 55 years and a mean MTX dose of approximately 17 mg/week. Consistent with previously reported results from SELECT-MONOTHERAPY1 and SELECT-NEXT,2 both UPA monotherapy and UPA combination therapy led to significant improvements in efficacy outcomes versus cMTX/PBO+MTX (Table). No significant differences were observed between UPA monotherapy and UPA combination therapy across a range of clinical endpoints, including ACR20/50/70 responses and measures of LDA and remission. In addition, improvements in quality of life as measured by HAQ-DI were similar with UPA monotherapy and combination therapy. Efficacy was comparable between the two UPA doses in the combination therapy group, whereas in the monotherapy group numerically higher responses were observed with UPA 30 mg versus UPA 15 mg.

Table. Week 12/14 efficacy outcomes in patients receiving monotherapy and combination therapy.

Endpoint	Monotherapy (Week 14) (SELECT-MONOTHERAPY)			Combination therapy with MTX (Week 12) (SELECT-NEXT)			p-value (mono vs combo)*	
	cMTX (n=216)	UPA 15 mg QD (n=217)	UPA 30 mg QD (n=215)	PBO+MTX (n=165)	UPA 15 mg QD+MTX (n=148)	UPA 30 mg QD+MTX (n=153)	UPA 15 mg QD	UPA 30 mg QD
ACR20, %	41.2	67.7	71.2	38.2	66.2	65.4	0.962	0.561
DAS28(CRP) ≤3.2, %	19.4	44.7	53.5	18.2	48.6	49.7	0.564	0.878
ACR50, %	15.3	41.9	52.1	16.4	41.2	43.1	0.578	0.217
ACR70, %	2.8	22.6	33.0	4.8	20.9	26.1	0.172	0.134
DAS28(CRP) <2.6, %	8.3	28.1	40.9	9.7	28.4	30.7	0.594	0.142
CDAI ≤2.8, %	0.9	12.9	19.5	3.0	9.5	13.7	0.063	0.069
CDAI ≤10, %	24.5	34.6	46.5	20.6	41.2	43.8	0.164	0.661
HAQ-DI change from baseline	-0.22	-0.56	-0.63	-0.32	-0.61	-0.60	0.593	0.108

*Based on logistic regression (binary outcomes) or ordinary least squares (continuous outcome) analyses for the comparison of monotherapy versus combination therapy, with treatment group as the fixed factor and various demographic (age, sex, race, region, weight, and smoking status) and baseline characteristics (hsCRP, DAS28[CRP], HAQ-DI, RA duration, and RF and anti-CCP positivity) as covariates.

Conclusion: In MTX-IR patients with RA, the efficacy of UPA appears comparable when administered as monotherapy or when given in combination with MTX.

REFERENCES:

1 Smolen J, et al. Ann Rheum Dis 2018;77:67?8;
2 Burmester GR, et al. Lancet 2018;391:2503-12

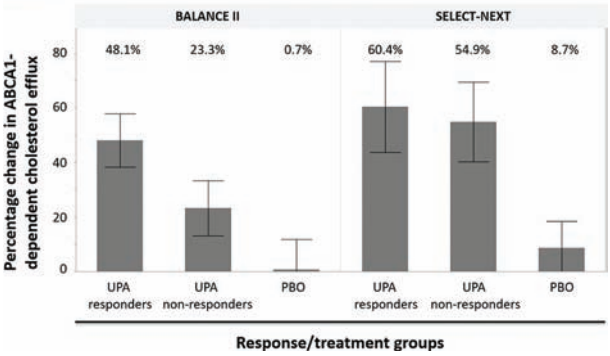
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THU0166 TREATMENT WITH UPADACITINIB IS ASSOCIATED WITH IMPROVEMENTS IN REVERSE CHOLESTEROL TRANSPORT IN PATIENTS WITH RHEUMATOID ARTHRITIS: CORRELATION WITH CHANGES IN INFLAMMATION AND HDL LEVELS

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory condition associated with increased rates of atherosclerotic morbidity and mortality. One mechanism by which inflammation may increase atherosclerotic progression is via pathogenic remodeling of high-density lipoprotein (HDL)-associated proteins with resultant reduction in HDL function.[1] Upadacitinib (UPA), a selective JAK1 inhibitor, has demonstrated efficacy in patients with moderate-to-severe RA.
Objectives: To assess the effect of UPA treatment on cholesterol efflux capacity (CEC) and evaluate the association of CEC with changes in inflammation and serum lipids.
Methods: A subset of patients from the Phase 2 BALANCE II study[2] and the Phase 3 SELECT-NEXT study[3] were selected from the pool of patients with serum samples available at baseline and Week 12. Patients were matched for age and sex, and selected based on level of response to UPA therapy (BALANCE II, UPA 6 mg BID: 39 responders [mean change in DAS28-CRP at Week 12 -3.22] and 30 non-responders [mean change in DAS28-CRP -0.33]; SELECT-NEXT, UPA 15 mg QD: 20 responders [mean change in DAS28-CRP -3.78] and 20 non-responders [mean change in DAS28-CRP -0.67]). A demographically similar placebo (PBO) group without selection based on degree of response was also included (20 patients from each study). J774 macrophages labeled with [^{3}H]-cholesterol (treated with cAMP to express ABCA1 or left untreated) were exposed to patient sera. The difference between cholesterol efflux from serum-exposed and unexposed cells provided a measurement of CEC. Results were compared between the responder, non-responder, and PBO groups using Tukey's mean comparison method; correlations were calculated using the Pearson method; and all statistical analyses were performed in JMP 13.10 (SAS Institute).
Results: In both studies, changes in global and ABCA1-dependent CEC, and to a lesser extent non-ABCA1-dependent CEC, were significantly higher in the UPA-treated group compared with the PBO group (Figure). In the BALANCE II study, there was a significant increase in CEC among UPA responders relative to PBO and a numerically apparent difference observed between UPA non-responders and PBO. Notably, in the SELECT-NEXT study, a similar and highly significant improvement in CEC was observed for both UPA-treated groups relative to PBO (without a significant difference between the responder and non-responder groups). Despite the lack of a consistent association between change in CEC and change in clinical disease activity, observed increases in CEC correlated significantly with reductions in CRP levels in all groups across all active treatment groups. Additionally, increases in CEC at Week 12 correlated well with changes in total blood cholesterol and HDL levels, but weakly with changes in blood low-density lipoprotein (LDL) levels.
Conclusion: UPA treatment is associated with significant improvement in CEC. This effect was observed even among those demonstrating minimal clinical response (but not in those treated with PBO). The effect seems to be primarily driven by ABCA1-dependent cholesterol efflux and is strongly correlated with a rise in HDL cholesterol as well as reduction in systemic inflammation as measured by change in CRP.

Figure: Changes in ABCA1-dependent cholesterol efflux are significantly elevated in UPA-treated patients at Week 12



Abstract THU0166 – Figure 1

REFERENCES:

[1] Charles-Schoeman C, et al. Arthritis Rheumatol 2017;69:46–57;
[2] Genovese MC, et al. Arthritis Rheumatol 2016;68:2857–66;
[3] Burmester GR, et al. Lancet 2018;391:2503–12

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THU0167 SAFETY PROFILE OF UPADACITINIB IN RHEUMATOID ARTHRITIS: INTEGRATED ANALYSIS FROM THE SELECT PHASE 3 CLINICAL PROGRAM

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Background: Upadacitinib (UPA), a JAK1-selective inhibitor, significantly improved clinical signs and symptoms of rheumatoid arthritis (RA) in patients (pts) naïve to methotrexate (MTX) and with an inadequate response to conventional synthetic DMARDs (csDMARD-IR) or biologic DMARDs (bDMARD-IR)[1,2,3].

Objectives: Assess the safety of UPA as monotherapy (mono) and as combination therapy with background csDMARDs in pts with moderately to severely active RA from the safety database of the Phase 3 clinical program.

Methods: Treatment-emergent adverse events (TEAEs) from 5 pivotal, randomized, double-blind, controlled Phase 3 trials of UPA 15 mg [included in all 5 trials] or 30 mg QD [included in 4 trials] in RA pts were analyzed using integrated short-term (ST, 12/14 week, placebo [PBO]–controlled; n [%]), individual studies with long-term [LT] active comparator (UPA mono vs MTX; UPA 15 mg with background MTX vs originator adalimumab, ADA, events/100 patient–years [E/100PY]) and integrated LT (all Phase 3 exposure; E/100PY) analyses sets.

Results: Across the Phase 3 trials, 3834 pts received ≥1 dose of UPA 15 mg (n=2630) or 30 mg QD (n=1204) ≈4020.1 PY of UPA exposure with no option to switch doses. The ST frequencies of overall SAEs and AEs leading to discontinuation were low, but higher on both UPA doses vs PBO. LT event rates were similar on UPA 15 mg vs ADA and slightly higher on UPA vs MTX mono. Deaths occurred in all treatment groups. Serious infection (SIEs) frequencies were higher on both UPA doses vs PBO. SIE rates on both UPA doses were higher vs MTX, but similar on UPA 15 mg vs ADA. Herpes zoster (HZ) frequencies and rates were higher on both UPA doses vs PBO, and vs MTX, ADA, respectively. The rates of SIE and HZ were higher on UPA 30 vs 15 mg. Adjudicated MACE were reported in all treatment groups including PBO. LT MACE rates were similar on UPA 15 mg and ADA and on UPA 15 mg and MTX mono, but higher on UPA 30 mg mono (low number of events, 2-4 per set). Adjudicated VTEs occurred at comparable frequencies on UPA vs PBO and at comparable rates on UPA vs active comparators. Malignancy (excluding non-melanoma skin cancer [NMSC]) rates were similar on UPA vs MTX, UPA 15 mg vs ADA, and 15 vs 30 mg. The NMSC rates on UPA 15 mg and ADA were similar; the rate on 30 mg was higher than 15 mg, but both UPA NMSC rates were in the range reported for RA patients treated with DMARDS[4]. The standardized incidence ratio (95% CI) for malignancy (15 mg: 0.98 [0.61, 1.49], 30 mg: 1.49 [0.85, 2.42]) was not elevated vs the general population.

Conclusion: Treatment with UPA increased the risk of SIE and HZ, but not those of VTE, MACE, and malignancy vs comparators. These data support that UPA has an acceptable safety profile in the treatment of moderately to severely active RA.

Abstract THU0167 –Table 1.

Table: Overall TEAEs and AESIs in pts treated with UPA compared to PBO and active control

	PBO-Controlled Short-term Exposure			Long-term MTX-controlled Analysis			Long-term Adalimumab Controlled Analysis*		All Phase 3 Long-term	
	UPA 15 mg QD (N=1035), %	PBO (N=1042), %	UPA 30 mg QD (N=384), %	UPA 15 mg QD Mono† (N=317) PY=343.1, E/100 PY	UPA 30 mg QD Mono† (N=314) PY=336.7, E/100 PY	MTX Mono† (N=314) PY=314.4, E/100 PY	Any UPA 15 mg QD (N=1417) PY=1243.3, E/100 PY	Any ADA 40 mg EOW (N=579) PY=467.8, E/100 PY	Any UPA 15 mg QD (N=2630) PY=2655.1, E/100 PY	Any UPA 30 mg QD (N=1204) PY=1365.0, E/100 PY
Any AE	56.0	48.4	59.9	345.4	358.2	303.1	266.4	294.8	295.7	368.7
Any SAE	3.4	1.8	4.9	14.3	15.4	11.8	12.9	15.6	15.0	21.3
Any AE leading to discontinuation	2.8	2.0	7.3	11.4	10.7	8.9	7.4	11.1	8.4	13.3
Deaths‡	0	0.2	0.3	1.2	1.8	0.3	0.4	0.9	0.5	1.0
AESIs										
Serious Infections	1.2	0.6	1.8	4.1	5.0	2.9	4.1	4.3	3.8	6.2
Herpes Zoster	0.7	0.3	1.6	6.4	4.8	1.3	3.1	1.3	3.7	7.9
MACE (adjudicated)	<0.1	0.3	0.3	0.9	1.2	0.6	0.4	0.4	0.6	1.0
VTE (adjudicated)	0.2	<0.1	0	0	0.3	0.6	0.3	1.1	0.6	0.3
Any non-melanoma skin cancer (NMSC)	0	<0.1	0.5	0.3	0.3	0	0.2	0.2	0.3	1.1
Any malignancy other than NMSC	<0.1	<0.1	0.8	1.2	0.6	1.0	0.4	0.8	0.9	1.4

*Patients on monotherapy; includes patients who started on original randomized treatment with data censored at time of rescue to combination therapy (either to UPA + MTX or addition of csDMARD); †This trial studied only the UPA 15 m dose and therefore contributed only to the 15 mg data in the integrated 'PBO-controlled short-term' analysis and 'all phase 3 long-term' analysis; ‡Deaths included non-treatment emergent deaths. MACE was defined as CV death, non-fatal MI, and non-fatal stroke. VTE was defined as deep vein thrombosis and pulmonary embolism.

ADA, adalimumab; AE, adverse events; CV, cardiovascular; E, events; MACE, major adverse cardiovascular events; MI, myocardial infarction; Mono, monotherapy; MTX, methotrexate; PBO, placebo; PY, patient years; QD, once-daily; RTI, respiratory tract infection; SAE, serious adverse events; TEAEs, treatment-emergent adverse events; UPA, upadacitinib; VTE, venous thromboembolic events.

REFERENCES:

[1] Burmester GR, et al. The Lancet. 2018;391,2503-12.
[2] Genovese MC, et al. The Lancet. 2018;391,2513-24.
[3] van Vollenhoven R, et al. Arthritis Rheumatol. 2018;70 (S 10) [Abs].
[4] Solomon DH, et al. Sem Arth Rheum. 2014,43:489-97.

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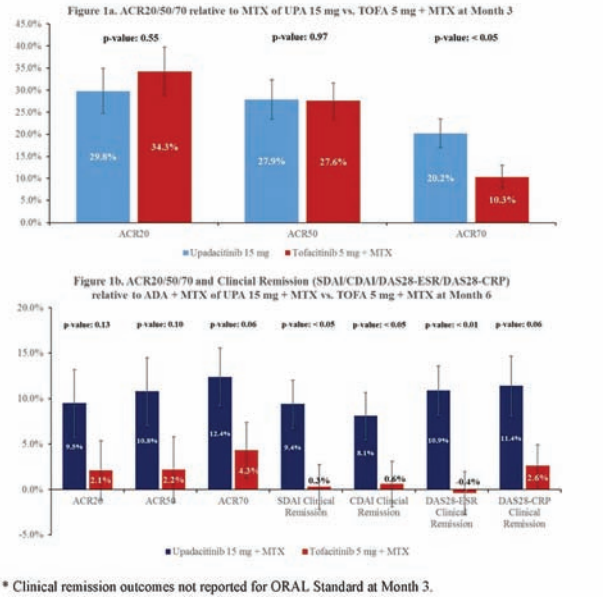
THU0168

A MATCHING-ADJUSTED INDIRECT COMPARISON (MAIC) OF UPADACITINIB VERSUS TOFACITINIB IN CSDMARD-IR PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS (RA)

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Background: Upadacitinib (UPA), a JAK1 selective inhibitor, is being investigated as monotherapy and combination therapy with DMARDs for the treatment of moderate-to-severe RA. To date, no head-to-head trials have compared the effectiveness of UPA with tofacitinib (TOFA).
Objectives: To compare the efficacy of UPA 15 mg monotherapy and combination therapy with TOFA 5 mg combination therapy using MAICs.
Methods: Two MAICs were conducted. MAIC is an indirect comparison technique that utilizes individual patient data (IPD) for one treatment and aggregate data for the other treatment to provide comparative evidence after balancing differences in patient characteristics. The first MAIC used IPD from the SELECT-MONOTHERAPY trial of UPA monotherapy vs. methotrexate (MTX) and published data from the Oral Standard trial[1] of TOFA+MTX vs. MTX. The second used IPD from the SELECT-COMPARE trial of UPA+MTX vs. adalimumab (ADA)+MTX and published data from the ORAL Strategy trial[2] of TOFA+MTX vs. ADA+MTX. UPA monotherapy was not compared to TOFA monotherapy based on feasibility analysis and trial selection criteria. Patients in the UPA trials were re-weighted based on age, gender, race, swollen joint count 66/28, tender joint count 68/28, C-reactive protein (CRP), and patient's global assessment, to match the baseline characteristics in each comparator trial. After matching, ACR20/50/70 and clinical remission (SDAI(CRP)≤3.3, CDAI≤2.8, DAS28-ESR/CRP<2.6) were compared for UPA monotherapy vs. TOFA +MTX relative to MTX at month 3 and UPA+MTX vs. TOFA+MTX relative to ADA+MTX at month 3 and 6 using a Wald test.

Figure 1: MAIC results for UPA 15 mg vs. TOFA mg + MTX at Month 3* and UPA 15 mg + MTX vs. TOFA 5 mg + MTX at Month 6



* Clinical remission outcomes not reported for ORAL Standard at Month 3.

Abstract THU0168 – Figure 1

Results: After matching, baseline characteristics were balanced across the trial populations. At month 3, UPA monotherapy patients experienced significantly greater improvement in ACR70 compared to TOFA+MTX with a mean difference in difference (DD) of 9.9% (p<0.05) (Figure 1a) while UPA+MTX was associated with a higher ACR50 compared to TOFA+MTX with a DD of 12.9% (p<0.05). At month 6, UPA+MTX patients experienced significantly larger improvement in SDAI/CDAI/DAS28-ESR clinical remission compared to TOFA+MTX with DDs of 9.1% (p<0.05), 7.5% (p<0.05), and 11.3% (p<0.01), respectively (Figure 1b).
Conclusion: The results from MAICs indicate that treatment with UPA 15 mg when used as monotherapy or in combination with MTX appears to produce improved outcomes at 3/6 months as compared to TOFA 5 mg +MTX (mono: ACR70 and combination: ACR50, SDAI, CDAI and DAS28-ESR remission).

REFERENCES:

[1] van Vollenhoven RF, et al. "Tofacitinib or adalimumab versus placebo in rheumatoid arthritis." NEJM 367.6 (2012): 508-519.
[2] Fleischmann R, et al. "Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy)." The Lancet 390.10093 (2017): 457-468.

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THU0169

JANUS KINASE INHIBITORSDEMONSTRATE EFFECTIVENESS IN A REAL-WORLD MULTI-BIOLOGIC DMARD REFRACTORY RHEUMATOID ARTHRITIS POPULATION

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Background: The Janus Kinase inhibitors (JAKi) Tofacitinib and Baricitinib are licensed for use in Rheumatoid arthritis (RA). Trials in refractory RA (inefficacy and/or toxicity) to date (1, 2) suggest targeting intracellular signalling molecules and interrupting downstream effects of multiple cytokines may confer benefit in the management of patients who have failed multiple targeted therapies.
Objectives: To evaluate safety and efficacy of JAKi in a real-world population, including response in multi-bDMARD refractory RA.
Methods: We evaluated RA patients who had failed at least 2 csDMARD +/- one or more bDMARD, who were commenced on a JAKi. Patients who commenced Tofacitinib on a compassionate use programme in 2014 have been included (with Baricitinib available since February 2018).
Results: Seventy seven RA patients (80% female; mean (SD) age 55.9 (12.52) years) have been treated with one (or more) JAKis; 38 have received Tofacitinib and 39 Baricitinib (5 both). Table 1 details treatment stage and clinical outcomes where available (majority pending assessments). Number of previous bDMARD was higher in the Tofacitinib group (reflecting compassionate access scheme).

Characteristic	Combined JAKi grp (n=77)	Tofacitinib (n=38)	Baricitinib (n=39)
Disease duration, years; mean (SD)	13.8 (5.34)	15.9 (4.52)	11.9 (6.16)
Previous number of targeted therapies (median, range)	4 (0-9)	5 (2-7)	3 (0-9)
Targeted therapy naïve	5	0	5
Baseline DAS28	5.84 (SD 1.07) (n=67)	6.23(SD 1.08) (n=31)	5.5 (SD 0.95) (n=36)
3m change in DAS28	-1.8(SD1.63) (n=29)	-2.07 (SD 1.72) (n=14)	-1.54 (SD 1.6) (n=15)
6m change inDAS28	-1.35 (SD1.8) (n=13)	-1.05 (SD 2.07) (n=7)	-1.7 (SD 1.52 (n=6)

Of the 38 patients who received Tofacitinib, 24 stopped treatment, 10 due to primary non-response, 2 secondary non-response and 12 due to

adverse effects (1 deranged LFTs, 3 infection, 1 rash, 1 headache, 2 flares of IBD, 1 dizziness, 1 malignancy). Despite the refractory nature of their RA, 14 patients responded sufficiently to remain on Tofacitinib for an average of 24.5 months to date. 1 Patient who failed 3 bDMARDs achieved remission (DAS28 1.82) with 4 confirmed as having moderate disease activity (Mean DAS 3.58, SD 0.42). Of the 39 patients to receive Baricitinib, three had primary non-response, whilst the others remain on therapy. Response is to be determined in 16, 4 have achieved remission (Mean DAS 2.2, SD 0.32) and 14 MDA (Mean DAS 4.04, SD 0.44). 5 patients received both JAKis sequentially, switching from Tofacitinib to Baricitinib, 2 due to adverse events (both flares of IBD) and 3 due to non-response. Of these 5, 1 patient to date has shown a good response at 3 months, 2 have shown no response, with results pending for others.
Conclusion: Our experience of patients treated with JAKi for RA indicates improvement in disease activity. Benefit was observed in a severely refractory subgroup that had previously failed multiple biologic therapies.

REFERENCES:

[1] Genovese, M.C. et al. Response to baricitinib based on prior biologic use in patients with refractory rheumatoid arthritis. Rheumatology (Oxford). 2018, 57(5), pp.900-908.
[2] Genovese, M.C. et al. Baricitinib in Patients with Refractory Rheumatoid Arthritis. N Engl J Med. 2016, 374(13), pp.1243-52.

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THU0170 A MULTICENTER STUDY ASSESSING THE EFFICACY AND SAFETY OF REPOSITORY CORTICOTROPIN INJECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS: INTERIM DATA FROM THE OPEN-LABEL TREATMENT PERIOD

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Background: Rheumatoid arthritis (RA) is an autoimmune disorder associated with chronic inflammation and is treated with disease-modifying antirheumatic drugs (DMARDs) for active disease. Both American College of Rheumatology (ACR) and EULAR recommend that short-term administration of corticosteroids (CSs) may be beneficial for its anti–inflammatory effects. Repository corticotropin injection (RCI) is a complex mixture containing purified porcine pituitary adrenocorticotropic hormone (ACTH)-analogue and an agonist for all 5 melanocortin receptors (MCRs). Activation of MCRs by ACTH has been shown to have direct and indirect anti–inflammatory and immunomodulatory effects. RCI is approved in the United States as adjunctive therapy for short–term administration in RA.
Objectives: To present interim data after 100% enrollment from the initial 12-week open-label phase of a multicenter, 2–part study evaluating the efficacy, safety, and appropriate duration of RCI therapy in patients with persistently active RA despite receiving 1 or 2 DMARDs and/or CSs.
Methods: In the open–label period (Part 1, Weeks 0–12), all enrolled patients received RCI 1 mL (80 U SC) twice weekly for 12 weeks. Patients who achieved low disease activity (LDA; DAS28-ESR score <3.2) at Week 12 continued in the double–blind, randomized maintenance phase of the trial (Part 2) for an additional 12 weeks. The primary endpoint was the proportion of patients who achieved LDA at Week 12. Secondary endpoints included assessment of the safety and tolerability of RCI. Disease activity was also assessed by the proportion of patients who achieved ACR 20%, 50%, and 70% (ACR20, 50, 70) responses and patient reported outcomes at Week 12. Bone turnover markers were assessed as an exploratory endpoint.
Results: 259 patients had enrolled, 235 had completed and 24 had discontinued the 12-week open-label period of the study; 88.9% were female and mean age was 51 years. RCI treatment resulted in 62.5% of patients achieving LDA at Week 12; results for this interim analysis are presented in the **Table**. Bone turnover markers were stable from baseline to Week 12, indicating no effect of RCI on bone metabolism. 98 (37.8%) patients reported adverse events (AEs) with 3 (1.2%) patients reporting serious AEs (ie, non–cardiac chest pain, pneumonia, and craniocerebral injury). The most common AEs were urinary tract infection (n=10), headache (n=9), and pharyngitis (n=7).

Abstract THU0170 –Table 1.

Table. Results for Patients Who Completed the Open-label Period (mITT; N=259)

Endpoints	Baseline	Week 4	Week 8	Week 12
LDA (DAS28-ESR <3.2; Primary Endpoint)	-	6.6%	14.3%**	62.5%**
ACR20	-	48.6%**	69.9%**	79.5%**
ACR50	-	12.0%**	35.9%**	62.2%**
ACR70	-	4.6%	8.5%	31.7%**
DAS28-ESR score, mean	6.3	4.9*	4.4*	3.6*
Tender joint count, mean	14.6	7.7*	5.7*	3.9*
Swollen joint count, mean	10.9	5.6*	4.0*	2.8*
Patient global assessment of disease activity (20% improvement)	-	56.0%**	71.8%**	80.3%**
FACIT-F, mean	22.9	17.5*	16.0*	13.9*
HAQ-DI, mean	1.7	1.2*	1.0*	0.8*

FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue Scale; HAQ-DI, Health Assessment Questionnaire – Disability Index; LDA, low disease activity.
The *modified intent to treat* (mITT) population includes all subjects who received RCI with any post-treatment efficacy assessments.
* $p < 0.001$ vs baseline. ** $p < 0.0001$ vs baseline.

Conclusion: In the 12-week open label period of this study, RCI appeared to be generally safe and effective in patients with persistently active RA who were nonresponsive to DMARDs and CSs. This was demonstrated by improvement in multiple measures of disease activity. Further results will be evaluated in Part 2 of the study.
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THU0171 TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF RHEUMATOID ARTHRITIS – THE RESULTS OF RUSSIAN NATIONAL REGISTER OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB

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Background: Tofacitinib (TF) is an oral Janus Kinase inhibitor for the treatment of rheumatoid arthritis (RA).
Objectives: To evaluate the one-year effectiveness of tofacitinib as first-line therapy in RA conventional synthetic (cs) DMARDs non-responders.
Methods: Data from 415 patients from Russian national register of patients with RA treated with TF were analyzed. 119 RA patients, who had complete clinical and laboratory data from 4 consecutive visits after baseline with an interval of 3 months between the visits and who used the TF as first-line therapy after failure of cs DMARDs, were included. Treatment with any biologics ever was an exclusion criteria.

Demographical (age, sex) and RA activity data (DAS28, SDAI, number of tender and swollen joints (NTJ, NSJ), erythrocytes sedimentation rate (ESR), C-reactive protein (CRP), and HAQ, EQ5D were collected, table 1. Statistical analysis performed in SPSS2017. p-value <0.05 considered as significant.

Results: At baseline 12 (10%) were treated with NSAIDs, 15 (12.6) with 5-10 mg/dayof prednisolone, 82 (68.9) – with methotrexate (10-25 mg/week), 8 (6.7%) – with sulfasalazine (2.0-3.0 g/day).

Abstract THU0171 – Table 1. Baseline characteristics of the patients with RA (n=119)

Parameter	Characteristics
Male, n (%)	24 (20.16)
Age of disease onset, years (mean ±SD)	41.1±11.5
Symptoms duration, month (mean ±SD)	113.7± 96.61
Positive rheumatoid factor, n (%)	68 (34.17)
Positive antibodies to cyclic citrullinated peptide (anti-CCP), n (%)	82 (68.9)
Erosions of hand joints (X-rays), n (%)	28 (23.5)
BMI, kg/m^2(mean ±SD)	21.82±5.37
Smokers (current and in the past), n (%)	42 (35.3)

Changes in the disease activity in patients with RA, treated with tofacitinib after csDMARD are presented in Table 2

Abstract THU0101 –Table 1. Efficacy outcomes in patients with RA treated with tofacitinib

	NTJ 28	NSJ 28	Patients' Global	ESR, mm/h	CRP, mg/l	DAS28	HAQ	EQ-5D
Baseline	8.48 ±6.53	3.68 ±5.02	52.48 ±19.22	29.32 ±22.69	19.10 ± 37.4	4.56 ±1.32	1.61 ±0.63	0.58 ±0.2
Month3#	6.29 ±5.64*	1.0 ±3.52*	39.29 ±20.41*	22.29 ±19.51*	8.43 ±27.5*	3.84 ±1.33*	1.08 ±0.7	0.71 ±0.17
Month 6#	4.69 ±4.6*	2.34 3.2*	37.51 ±20.22*	27.12 ±20.54	10.86 ±17.47*	3.85 ±1.3*	1.02 ±0.7	0.68 ±0.18
Month 9#	4.61 ±5.51*	2.28 ±3.56*	36.23 ±20.6*	26.85 ±19.96	10.91 ±20.96*	3.80 ±1.3*3	1.0 ±0.68	0.68 ±0.16
Month12#	3.64 ±4.21*	1.6 ±2.41*	30.92 ±18.12*	24.54 ±18.94*	9.28 ±14.11*	3.55 ±1.15*	0.82 ±0.58*	0.71 ±0.16

*difference with baseline is significant (p<0.05). #- ±1 month

At visit 3 DAS28 <3.2 achieved 80 (67.22%) of the patients: 71 patients on 20 mg of TF (59.66%) and 9 patients on 10 mg of TF 11 (9.24%) patients at visit 3 had DAS28 $\geq$5.1.

Conclusion: Treatment with TF may provide good response rates in RA patients, refractory previous cs DMARDs.

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THU0172 UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDS: RESULTS AT 60 WEEKS FROM THE SELECT-BEYOND STUDY

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Background: In patients (pts) with active rheumatoid arthritis (RA) and inadequate response or intolerance to bDMARDs, treatment with upadacitinib (UPA), a JAK1-selective inhibitor resulted in significant improvements over 24 weeks (wks).[1]

Objectives: We assessed UPA safety and efficacy through Wk60 in an ongoing extension of the phase 3 SELECT-BEYOND study.

Methods: SELECT-BEYOND enrolled a population of patients with active RA who had failed at least one prior biologic therapy.[1] Pts received UPA 15mg or 30mg once daily (QD) or placebo (PBO) on top of background csDMARD treatment for 12 wks. From Wk12, pts randomized to UPA at baseline (BL) continued their assigned doses while pts initially randomized to PBO received UPA 15mg or 30mg QD per pre-specified assignment at BL. Patients who completed Wk 24 entered the blinded long-term extension. Dose adjustments to UPA were not allowed. Adverse events (AE) per 100 pt years (PY) are summarized based on a cut-off date of 16 April 2018. Efficacy data up to the Wk60 visit are reported "As Observed".

Abstract THU0172 –Table 1.



Table 1. Treatment-Emergent Adverse Events (AE): Event Rate in E/100PYs	UPA 15 MG N=236 PYs=301.7 E/100PYs	UPA 30 MG N=240 PYs=290.7 E/100PYs
Any Adverse Event	353.3	435.8
Serious AE	17.9	29.2
AE Leading To Study Drug D/C	9.6	15.1
Serious Infection[a]	3.0	8.3
Herpes Zoster[a]	4.6	8.9
Hepatic disorder[a]	4.6	8.3
Any Malignancy (exc NMSC)[b]	1.7	1.0
MACE (adjudicated)[c]	1.0	0.3
VTE (adjudicated)[d]	2.3	0.7
Deaths[e]	0.7	1.0

E, events; PYs, patient-years; E/100PYs, events per 100 patient-years; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event (cardiovascular death, non-fatal myocardial infarction (MI), non-fatal stroke); VTE, venous thromboembolism (DVT, deep vein thrombosis; PE, pulmonary embolism).

[a]Most frequently reported serious infections were pneumonia, HZ, influenza, and respiratory tract infections.

[a]HZ: most involved 1 or 2 dermatomes. No meningoencephalopathic/ noncutaneous involvement. Two HZ events were reported as ophthalmic.

[b]Malignancy (excluding NMSC): UPA15: 1 malignant melanoma in situ, 1 bladder cancer, 1 pancreatic carcinoma Stage IV, 1 colon cancer, 1 non-small cell lung cancer metastatic; UPA30: 2 prostate cancers, 1 rectal cancer metastatic.

[c]MACE (adjudicated): UPA15: 1 CV death, 1 non-fatal MI, 1 non-fatal stroke; UPA30: 1 pt with 2 concurrent events (non-fatal MI and acute congestive heart failure) adjudicated to non-fatal MI

[d]VTE: UPA15: 3 pts with PE, 1 pt with DVT, 2 pts with PE and DVT, 1 pt with non-assessable thrombotic event; UPA30: 1 pt with PE, 1 pt with PE and DVT; no dose relationship in the rates of VTE or patterns in the time to onset of the events, were observed.

[e]Deaths: UPA15: 1 due to other CV causes, 1 due to cardiac arrest; UPA30: 1 pt with cardiac decompensation, 1 pt with presumed MI, 1 pt with rectal cancer metastasized to liver

Results: 418/498 (84%) pts were randomized, completed 24 wks and entered the extension on study drug. By the safety data cut-off date, 19% pts discontinued study drug: 5% due to AE, 4% due to lack of efficacy, 3% withdrew consent, 2% were lost to follow-up, and 5% discontinued due to other reasons. Cumulative exposures to UPA15 and UPA30 were 301.7 and 290.7 PYs, respectively. Rates (Events/100PYs) of treatment-emergent AEs are reported (Table 1), and were numerically higher in the UPA30 vs UPA15 arm for serious AEs, AEs leading to discontinuation, serious infections, herpes zoster and hepatic disorders. Based on As Observed analysis, for pts completing Wk60 on UPA15 [172/216 (80%)] and UPA30 [168/202 (83%)], clinical and functional outcomes continued to improve compared to Baseline, or were maintained from Wk24 onwards[1] in pts initially randomized to UPA15 or 30; Remission by CDAI≤2.8 at Wk60 was achieved by 20% and 32%, respectively, and DAS28-CRP<2.6 was achieved by 53% and 52%. Pts who were switched to UPA from PBO at Wk12 had comparable efficacy to pts initially randomized to UPA (Table 2).

Abstract THU0172 –Table 2.

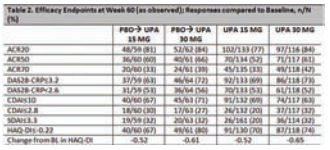


Table 2. Efficacy Endpoints at Week 60 (as observed): Responses compared to Baseline, n/N (%)	PBO→ UPA 15 MG	PBO→ UPA 30 MG	UPA 15 MG	UPA 30 MG
ACR20	48/59 (81)	52/63 (84)	102/133 (77)	97/116 (84)
ACR50	36/60 (60)	40/61 (66)	70/134 (52)	71/117 (61)
ACR70	20/60 (33)	24/61 (39)	45/135 (33)	49/118 (42)
DAS28-CRP≤3.2	37/59 (63)	46/64 (72)	92/133 (69)	86/118 (73)
DAS28-CRP<2.6	31/59 (53)	36/64 (56)	70/133 (53)	61/118 (52)
CDAI≤10	40/60 (67)	45/63 (71)	95/132 (69)	74/117 (63)
CDAI≤2.8	18/60 (30)	17/63 (27)	26/132 (20)	37/117 (32)
SDAI≤3.3	19/59 (32)	20/63 (32)	26/161 (20)	36/114 (32)
HAQ-DI≤-0.22	40/60 (67)	49/61 (80)	91/130 (70)	87/118 (74)
Change from BL in HAQ-DI	-0.52	-0.61	-0.52	-0.65

Conclusion: The benefit:risk of upadacitinib treatment in this refractory population remains favorable. No new safety signals were identified. Some AEs were numerically higher for UPA30 vs 15; however the clinical significance of this, the assessment of rare safety events in this study, and the overall benefit:risk of upadacitinib 15mg and 30mg in the treatment of RA are best evaluated in an integrated analysis across the phase 3 program. UPA15mg and 30mg continued to be effective in treating RA signs and symptoms, and in improving physical function.

REFERENCES:

[1] Genovese, et al. 2018; Lancet.18;31116-4

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THU0173

FILGOTINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDS (BDMARD-IR) BY RACE & GEOGRAPHIC REGION

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Background: Filgotinib (FIL), an oral, selective Janus kinase 1 (JAK1) inhibitor, significantly improved the signs and symptoms of rheumatoid arthritis (RA) in the phase 3 FINCH2 study in bDMARD-IR patients with active RA.[1]
Objectives: To evaluate the efficacy and safety of FIL by geography and race in FINCH2.
Methods: FINCH2 enrolled 449 bDMARD-IR patients with active RA, who were randomized in a 1:1:1 manner to receive FIL 200 mg, FIL 100 mg, or placebo (PBO) on a background of csDMARDs for 24 weeks. In this prespecified subgroup analysis, patient and disease characteristics and treatment effects were analyzed by race and geographic region (Region 1: AU, BE, FR, DE, IS, IT, NL, KR, ES, CH, UK, US; Region 2: HU, CZ, PL; Region 3: AR, PR, MX; Region 4: JP).
Results: 448 patients received $\geq$1 dose of study drug; they were 80.4% female, with a mean [SD] age of 56 [12.2] years, and 23.4% had received $\geq$3 prior bDMARDs). Baseline characteristics were similar across regions and race. The primary endpoint and all key secondary endpoints were met in the primary analysis.[1] Efficacy and safety parameters by geography and race are shown below. There were 2 MACE (white/Region 1, 1 FIL 100/1 PBO), 4 cases of uncomplicated herpes zoster (2 black/1 white/1 Asian; 3 Region 1/1 Region 4, 2 FIL 200/2 FIL 100), and 1 VTE (retinal vein occlusion, white/Region 1/FIL 200), but no cases of DVT/PE, opportunistic infection, active tuberculosis, malignancy, gastrointestinal perforation, or death.

Table 1. Week 24 key efficacy and safety measures by geographic region.

	Regimen	N[1]=	ACR20; %[2]	DAS28(CRP) <2.6; %[2]	CFB HAQ-DI	TEAE; %	SAE; %
Region 1	FIL 200	111	67‡	31†	–0.7 (0.6)‡	73	5
	FIL 100	110	48*	24	–0.6 (0.7)*	66	6
	PBO	110	32	14	–0.4 (0.6)	70	5
Region 2	FIL 200	12	75	25	–0.7 (0.7)	58	0
	FIL 100	12	75	33	–0.6 (0.5)	75	17
	PBO	11	46	9	–0.5 (0.6)	73	0
Region 3	FIL 200	12	67	17	–1.2 (0.6)	42	8
	FIL 100	16	81	38	–1.0 (0.7)	44	0
	PBO	14	64	14	–0.8 (0.6)	36	0
Region 4	FIL 200	12	92‡	50†	–0.7 (0.5)‡	75	0
	FIL 100	15	60*	27	–0.5 (0.7)†	60	0
	PBO	13	15	0	–0.1 (0.6)	77	0

[1]n's for HAQ-DI at week 24 were different. [2]Nonresponder imputation. *p<0.05,†p<0.01, ‡p<0.001 vs PBO. CFB, change from baseline as mean (SD); SAE, serious adverse events; TEAE, treatment-emergent adverse events.

Table 2. Week 24 key efficacy and safety measures by race.

	Regimen	N[1]=	ACR20; %[2]	DAS28(CRP) <2.6; %[2]	CFB HAQ-DI	TEAE; %	SAE; %
White	FIL 200	110	67‡	30*	–0.7 (0.6)†	71	5
	FIL 100	109	49*	25	–0.5 (0.6)	63	6
	PBO	97	34	16	–0.5 (0.6)	66	4
Black	FIL 200	14	57	21	–0.7 (0.6)*	57	0
	FIL 100	12	67	17	–0.6 (0.7)	67	8
	PBO	21	38	14	–0.2 (0.5)	67	0
Asian	FIL 200	15	93‡	47†	–0.8 (0.6)‡	73	0
	FIL 100	20	60†	30*	–0.6 (0.7)†	65	0
	PBO	15	13	0	–0.1 (0.5)	80	7

[1]n's for HAQ-DI at week 24 were different. [2]Nonresponder imputation. *p<0.05,†p<0.01, ‡p<0.001 vs PBO. CFB, change from baseline as mean (SD); SAE, serious adverse events; TEAE, treatment-emergent adverse events.
Conclusion: FIL demonstrated consistent safety and efficacy in bDMARD-IR patients with RA regardless of geography or race.

REFERENCES:

[1] Genovese MC, et al. ACR 2018. Abstract L06.

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THU0174 CHARACTERIZATION OF REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH UPADACITINIB OR COMPARATORS

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Background: Across all phase 3 studies, treatment with upadacitinib (UPA), a JAK1-selective inhibitor, was associated with significantly higher remission (REM) rates, compared to placebo (PBO) or active comparators, in RA patients (pts) who were methotrexate (MTX)-naive, had inadequate response to conventional synthetic (csDMARD-IR) or had inadequate response or intolerance to biologic DMARDs (bDMARD-IR)

Objectives: REM definitions are based on composite scores of various individual assessments of disease activity. To determine the response to UPA on REM and component assessments, we assessed the proportions of pts achieving REM using multiple REM definitions, and the improvement in their respective individual components, compared to PBO or active comparators, in 3 different RA pt populations spanning a range of RA pt populations.

Methods: Three phase 3 studies included pts who were MTX naïve (SELECT EARLY, n=945), MTX-IR (SELECT COMPARE, n=1629) and bDMARD-IR (SELECT BEYOND, n=498). The proportion of pts achieving REM at Week (Wk) 12 by 4 definitions (DAS28-CRP<2.6; CDAI ≤2.8; SDAI ≤3.3 and Boolean, defined as ≤1 for TJC, SJC, patient's global assessment of disease activity [PtGA], and CRP ≤1 mg/L) were determined. For each definition of REM, the mean change in each of the respective component scores was also assessed. Binary endpoints are based on Non-responder imputation (NRI), and continuous endpoints on mixed-effect model repeat measurement (MMRM). Comparisons were made between UPA-treated groups vs respective control arms (MTX, adalimumab [ADA] or PBO).

Results: Pt demographics and disease characteristics have been previously reported. [1-3] At 12 wks, in EARLY and COMPARE, a significantly greater proportion of pts receiving UPA 15 mg or 30 mg QD achieved REM by all 4 definitions vs MTX, PBO or ADA (Table). In BEYOND, (a refractory population many of whom had inadequate response to multiple bDMARDs), a significantly greater proportion of pts receiving UPA 30mg achieved all REM definitions vs PBO within the first 12 wks, with significantly greater proportions on UPA 15mg achieving DAS28-CRP<2.6 and Boolean REM (Table). Rates of REM in BEYOND further increased through Wk 24 for both dose groups.[1]Compared to respective control groups, pts receiving UPA 15 or 30 mg QD had significantly greater improvements in each REM disease component (except for PhGA vs ADA in COMPARE). Significantly more pts receiving UPA also achieved the required cutoffs on the individual components of Boolean REM compared to respective controls.

Conclusion: Significantly greater proportions of pts receiving UPA 15 or 30mg achieved REM by multiple definitions at 12 wks compared to PBO, MTX or ADA. All disease activity components of each REM definition were significantly improved in pts receiving UPA compared to MTX or PBO, and all Boolean components were significantly improved in pts receiving UPA 15mg compared to ADA.

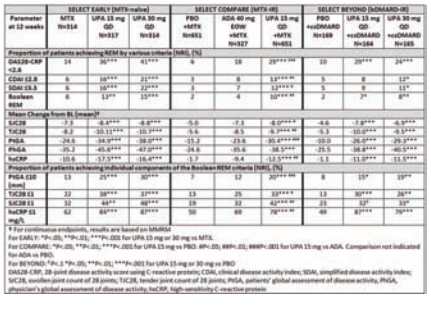
REFERENCES:

[1] Genovese, et al. 2018;Lancet.18;31116-4.
[2] van Vollenhoven R, et al. Arthritis Rheumatol. 2018;70 (supp10).
[3] Fleischmann, et al. Arthritis Rheumatol. 2018;70 (supp10).

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Abstract THU0174 –Table 1.



Parameter at 12 weeks	SELECT EARLY (MTX-naïve) MTX N=314	SELECT EARLY (MTX-naïve) UPA 15 mg QD N=317	SELECT EARLY (MTX-naïve) UPA 30 mg QD N=314	SELECT COMPARE (MTX-IR) PBO +MTX N=651	SELECT COMPARE (MTX-IR) ADA 40 mg EOW +MTX N=327	SELECT COMPARE (MTX-IR) UPA 15 mg QD +MTX N=653	SELECT BEYOND (bDMARD-IR) PBO +csDMARD N=169	SELECT BEYOND (bDMARD-IR) UPA 15 mg QD +csDMARD N=164	SELECT BEYOND (bDMARD-IR) UPA 30 mg QD +csDMARD N=165
Proportion of patients achieving REM by various criteria (NRI), (%)									
DAS28-CRP <2.6	16	36****	41****	8	18	29****,###	10	29****	34****
CDAI ≤2.8	6	16****	21****	3	8	13****,##	3	8	12*
SDAI ≤3.3	6	16****	22****	3	7	13****	5	8	11*
Boolean REM	8	13**	15****	3	4	10****,##	2	7*	8**
Mean Change from BL (mean)†									
SJC28	-7.3	-8.4****	-8.8****	-5.0	-7.3	-8.0****,#	-4.6	-7.8****	-8.9****
TJC28	-8.2	-10.1****	-10.3****	-5.6	-8.5	-9.7****,##	-5.3	-10.0****	-9.5****
PtGA	-24.6	-34.9****	-38.0****	-15.2	-23.8	-30.4****,###	-10.0	-26.0****	-29.1****
PhGA	-35.2	-45.3****	-47.0****	-24.6	-35.6	-38.5****,#	-25.5	-38.8****	-40.5****
hsCRP	-10.6	-17.5****	-16.4****	-1.7	-9.4	-12.5****,##	-1.1	-11.0****	-11.5****
Proportion of patients achieving individual components of the Boolean REM criteria (NRI), (%)									
PtGA ≤10 (mm)	13	25***	30***	7	12	20****,##	8	15*	19**
TJC28 ≤1	22	38***	37***	13	25	33****,#	13	30***	28**
SJC28 ≤1	32	48**	48***	19	32	42****,#	23	37*	33*
hsCRP ≤1 mg/L	62	84****	87****	50	69	79****,##	49	83****	79****

† For continuous endpoints, results are based on MMRM
For EARLY: *P<.05; **P<.01; ***P<.005 for UPA 15 mg or 30 mg vs MTX.
For COMPARE: *P<.05; **P<.01; ***P<.005 for UPA 15 mg vs PBO. #P<.05; ##P<.01; ###P<.001 for UPA 15 mg vs ADA. Comparison not indicated for ADA vs PBO.
For BEYOND: *P< .1 *P<.05; **P<.01; ***P<.001 for UPA 15-mg or 30 mg vs PBO
DAS28-CRP, 28-joint disease activity score using C-reactive protein; CDAI, clinical disease activity index; SDAI, simplified disease activity index; SJC28, swollen joint count of 28 joints; TJC28, tender joint count of 28 joints; PtGA, patients' global assessment of disease activity, PhGA, physician's global assessment of disease activity; hsCRP, high-sensitivity C-reactive protein

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THU0175 DOSE-DEPENDENT RISK OF METHOTREXATE FOR RENAL IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is a mainstay in the therapy of rheumatoid arthritis (RA). It is recommended that MTX should be rapidly

escalated to the maximum tolerated dose (16 - 30 mg/week) and tapering MTX can be considered after a persistent remission [1]. Renal impairment is one of the major concerns in treatment with high dose MTX for malignancy, but it is still unclear whether low dose MTX administration in RA cause the renal impairment or not.

Objectives: The purpose of this study is to elucidate the association between MTX dosage and a one-year change of estimate glomerular filtration rate (eGFR) in RA patients.

Methods: Of outpatients with RA in Okayama university hospital between 2006 and 2017, 497 patients who had continued the administration of MTX for more than one year were enrolled. All patients fulfilled the ACR/EULAR 2010 Classification Criteria for RA. Patients who had nephrotic syndrome, unilateral kidney or other rheumatic disorders other than secondary Sjögren's syndrome were excluded. The primary outcome was the change of eGFR during the most recent one year in each patient. The revised Japanese equation of Modification of Diet in Renal Disease[2] was used to calculate eGFR. MTX dosage was defined as an average dosage of MTX during the observational period. We evaluated the association between MTX dosage and the primary outcome using univariate and multivariate analysis.

Results: Median (IQR) age was 64 (54 - 72) years, 78% were female, and median disease duration was 73 (31 - 160) months. The median dosage of MTX was 8 mg/week (6 - 10.1) and biological agents were used in 28% of the patients. The eGFR (mean ± SD) decreased by 1.2 ± 8.3 ml/min/1.73m2 in one year and MTX dosage was associated with the change of eGFR significant inversely ($p<0.0001$). The eGFR in patients treated with MTX <8 mg/week (n=185), ≥8 and <10 (n=131), ≥10 and <12 (n=86), ≥12 (n=95) decreased 0.2 ± 0.6, 0.6 ± 0.7, 1.0 ± 0.9, and 4.6 ± 0.8 ml/min/1.73m2/year, respectively. After adjusting possible confounding factors such as sex, age, concomitant use of NSAIDs, hypertension, and C reactive protein (CRP) using multiple linear regression analysis, MTX dosage was still an independent risk factor for the decrease of eGFR (beta-coefficient: -0.4, 95% confidence interval -0.12 - -0.61, $p=0.003$).

Conclusion: Careful monitoring of renal function should be required in long-time treatment for RA patients with MTX.

REFERENCES:

[1] Smolen JS, et al. Ann Rheum Dis. 2017;76:960-977.
[2] Imai E, et al. Am J Kidney Dis. 2007;50:927-937.

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THU0176 COMPARISON OF ADHERENCE TO MONOTHERAPY VERSUS COMBINED THERAPY IN RHEUMATOID ARTHRITIS

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Background: Treatment adherence in Rheumatoid Arthritis (RA) patients vary from 30 to 80% (1). It is important to identify the associated factors to a low adherence, so clinicians can make interventions to obtain better therapeutic results. Adherence to treatment has been described to be affected by several factors, such as access to healthcare facilities, education, socioeconomic status, quality of communication between physician and patient, among others (2). There are no previous studies that investigate if the number of drugs received in RA patients affects this adherence. REPAIR ® is a program designed with the purpose of improve data collection and medical practice in our outpatient clinic.

Objectives: To compare the adherence to synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) among RA patients prescribed with monotherapy and combined therapy.

Methods: Cross sectional, observational, comparative study. This study was conducted in the outpatient rheumatology clinic of University Hospital in Monterrey, México. Consecutive patients with RA, were approached during their normal routine rheumatology appointments, in the March 2018 to December 2018 period. They were asked how many days of the last month they forgot or took their DMARDs (self-report). We classified the adherence rate in 2 categories based on the days of the last month they took the indicated medication; adequate: 75%-100% (> 21 days), inadequate <75% (<21 days). When adherence was inadequate we interrogated about the cause. Data was obtained from REPAIR ® (internal electronic patient record). The Kolmogorov Smirnov test was used to determine normal distribution. Categorical variables are expressed as total number and percentage (%), and numerical variables as median and the 25th-75th percentiles (q25-q75). Chi square and Mann Whitney U test were used to compare groups and considered significant if $p<0.05$. Data was analyzed with the statistical package SPSS version 24 (New York, USA).

Results: A total of 959 patients were included. When comparing adherence to treatment and gender between groups, no statistically significant difference was found. The main cause of inadequate adherence in the monotherapy group was the economic (30.3%) and own decision in the combined therapy group (29.1%).

Table 1:

	Monotherapy (n=346)	Combined therapy (n=613)	*p*
Age (years), median (q25-q75)	54 (44-63)	53 (43-59)	**0.018**
Women, n (%)	317 (91.6)	575 (93.8)	0.362
Inadequate adherence to treatment, n (%)	52 (15)	102 (16.6)	0.514
Adequate adherence to treatment, n (%)	294 (85)	511 (83.4)	

Conclusion: Patients with combined therapy had the same percentage of inadequate adherence as patients with monotherapy. These results may indicate that number of drugs prescribed not necessarily affects adherence to treatment. The principal causes for an inadequate adherence to treatment were: economic for monotherapy group and own decision for combined therapy group. However, long-term studies are needed to evaluate the persistence of treatment in these groups of patients.

REFERENCES:

[1] Van den Bemt BJF, Zwikker HE, van den Ende CHM. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Rev Clin Immunol. 2012;8(4):337–51.
[2] M.F. M. Improving treatment adherence in patients with rheumatoid arthritis: What are the options? Int J Clin Rheumtol [Internet]. 2015;10(5):345–56.

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THU0177 TREATMENT PATTERNS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH A BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUG OR JAK INHIBITOR: A NATION-WIDE STUDY IN KOREA

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Background: Limited data are available on whether patients with rheumatoid arthritis (RA) are treated with conventional disease-modifying antirheumatic drugs (cDMARDs) according to the current recommendations before they initiate biologic DMARDs (bDMARDs) or JAK inhibitors (JAKis).

Objectives: We examined the treatment patterns among Korean RA patients who received bDMARDs or JAKis in a real world setting, using the 2002-2016 Korean National Health Insurance Service database that covers the entire Korean population.

Methods: We identified RA patients who initiated bDMARDs (TNF inhibitor, abatacept, rituximab and tocilizumab) or JAKis (tofacitinib). Their treatment patterns during 1 year after RA diagnosis (defined as free of any RA diagnosis or any DMARD use for one year before the diagnosis) and prior to the initiation of index drugs (bDMARDs or JAKis) were examined regarding: initial cDMARD used, dose and parenteral use of methotrexate (MTX), use and time to combination therapy of cDMARDs, and steroid use.

Results: 10,145 RA patients were identified who used index drugs from the database (mean age 57 years, 82% female). Among them, 6,986 patients had identifiable dates for RA diagnosis (mean age 57 years, 79% female). The mean (SD) duration from RA diagnosis to index drug initiation was 1,425 (1,162) days with 1,509 (22%) patients having a duration ≤1 year. At diagnosis, the most common 1st cDMARD used was hydroxychloroquine (63%), followed by MTX (55%) and sulfasalazine (29%) with steroids used in 75%. During the 1 year from the diagnosis, 85% of patients eventually used MTX, 42% ever used MTX ≥ 15mg/week, only 3% used parenteral MTX, and 85% patients used combined cDMARDs with a mean 188 days from the RA diagnosis to combination therapy. Patients whose maximal MTX dose reached 20mg/week were rare (9%) and 62% were still on steroid after 1 year.

During the 1 year prior to the index drug use (n = 10,145), the most common cDMARD was MTX used in 89% patients with 46% who ever used ≥ 15mg/week and 4% of parenteral users, followed by hydroxychloroquine (55%), leflunomide (52%), sulfasalazine (38%), and tacrolimus (20%). All patients used combination therapy and 98% steroids.

Conclusion: These data indicate that a substantial proportion of RA patient did not try maximal dose or parenteral use of MTX during the 1 year post-diagnosis as recommended by the current treatment guideline. Instead, they often used cDMARDs combination therapy. During the 1 year before initiating bDMARDs or JAKis, they were treated with intensive cDMARD combination therapy rather than escalating their MTX dose.

REFERENCE:

[1] Smolen, Josef S., et al. "EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update." Annals of the rheumatic diseases 76.6 (2017): 960-977.

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THU0178 THE EFFECT OF TOLEROGENIC DENDRITIC CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SMALL PILOT TRIAL

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Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through thepresentation of cartilage glycoprotein, production ofproinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, utilization of tolerogenicDCs seems to be a promising immunotherapeutic toolto treat RA.

Objectives: The aim of our study is to evaluate the safety and tolerability of a single intra-articular injection(into the knee joint) of autologous monocyte-derived dendritic cells generated in the presence of IFN-α/GM-CSFand tolerized with Dexamethasone inRApatients.

Methods: DCs were generated by culturing blood monocytes for 5 days with GM-CSF and IFN-α in the presence dexamethasone, applied on third day. Azoximer bromides maturation stimuli was added on fourth day. Twelve RA patients with moderate and high disease activity and ultrasound-defined kneesynovitis were recruited in this study. All patients fullfield ACR/EULAR criteria (2010) and received methotrexate, leflunomide, sulfasalazine or their combination. The patients received intra-articular injections of$1*10^6$, $3*10^6$, $5*10^6$,$8*10^6$,10^*10^6DCs in knee joints. Safety was assessed by evaluation of adverse events (AE). Acceptability was assessed by questionnaire. DAS28 and HAQ were used for assessment of treatment efficiency. This trial registered on clinicaltrials.gov (ID:NCT03337165).

Results: DCs injections were safe and well tolerated. No one participants showed worsening of symptoms in targeting knee, fever, elevation of blood pressure or other AE within 7 days after injection. All patients, evaluated at 6 months follow-up showed a good EULAR response (improvement of DAS28-ESR >1.2). The median DAS28-ESR decreased from 5.1to 3.1 (p=0.03). The median pain VAS score decreased from 52 (41-70) mm to 42 (15-55) mm; p=0.04. In addition, we detected median HAQ improvement (from 1.45 to1.0; p=0.04).The effect of treatment had been continued for 6 month and after that we indicated escape of effect.

Conclusion: The data obtained suggest that single intra-articular injection of autologous tolerogenic dendritic cells is safe, well tolerated, and have a potential not long term efficiency and requires the repeating of procedure.

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THU0179 PATIENT AND THEIR ILLNESS – ATYPICAL SOURCES OF THERAPY RISKS. CHARACTERISTICS OF THE USE OF METHOTREXATE (MTX) AND FOLIC ACID (FA) SUPPLEMENTATION IN THERAPY LASTING MINIMUM 8 WEEKS IN ADULT PATIENTSWITH RHEUMATOID ARTHRITIS (RA)

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Background: MTX is a well-established treatment with an anchor role in RA (1). Patients being treated for RA must pay attention to the specific dosage of drugs and the different routes of administration. Additionally they suffer from the inconvenience related to the progression of the disease.

Objectives: We observed patients diagnosed with RA, who were treated with subcutaneous (SC) MTX and possible risks associated with this therapy. The attention paid to the inconvenience for the patient associated with SC form of drug administration and the principles of MTX dosing with FA supplementation.

Methods: 32 rheumatologists were invited to non-interventional, post marketing observation. They collected information from 690 patients who already received a minimum of 1 dose of MTX SC. As part of a standard medical visit, the sociographic data of the patient and information obtained during the medical interview as well as subjective and objective examination were recorded in the prepared form. Data was collected on a weekly basis over a period of 8 weeks. The protocol was compliant with the regulatory and ethical requirements in the country.

Results: Out of 682 enrolled patients, 581 (85.2%) were sero-positive and 95 (14%) were sero-negative. The average level of anti-CCP antibodies before enrollment was 85.76 Units. The mean time from the diagnosis of the underlying disease was 28.7 months. The vast majority of patients confirmed that they had previously used FA supplementation (92.2%), only 10 patients showed DAS28 at the remission level. During each visit no adverse events (AE) were reported in over 90% of patients. The most commonly reported AE are nausea or weakness. No severe, live threatening AE were recorded.

Patients evaluated the pain of the injection on a scale of 1 to 10, where 1 is the minimum and 10 the maximum pain. Most patients assessed the pain of injections as the minimum (1) (56.5% - week 1 (W1), 52.9% - W2, 56.7% - W3, 61.5% - W4, 56.7% - W5, 53.8% - W6, 65.2% - W7, 61.8% - W8). The second most frequently mentioned pain assessment by respondents was 2 (34.6% - W1, 35.3% - W2, 34.3% - W3, 29.2% - W4, 34.3% - W5, 38.5% - W6, 26.1% - W7, 32.9% - W8). No patients reported values between 6 and 10. Patients also assessed how the pain at the site of injection on a scale of 1 to 10, where 1 is the minimum and 10 the maximum pain. Each week, more than half of the patients assessed pain at the injection site as 1 (55.9% - W1, 56.7% - W2, 56.7% - W3, 57.8% - W4, 50.8% - W5, 62.5% - W6, 60.3% - W7, 61.6% - W8). Patients did not report any value of 5-10. More than seven out of ten patients reported FA administration the day 2 of their therapy (76.5%, at W1). In remaining days FA supportive therapy reported 30.3-52.3% of patients (2).

Conclusion: Neither pain related with injection nor local AE was reported as a significant issue by patients. Adherence to FA administration recommendation is low. This should be evaluated in further studies, but there is a risk that inappropriate FA administration may reduce efficacy of MTX treatment.

REFERENCE:

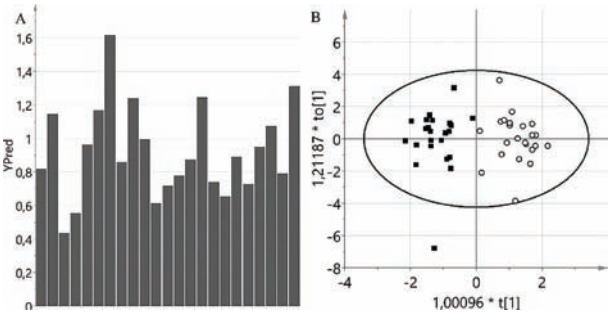
[1] Smolen JS, et al. Ann Rheum Dis 2017;0:1–18; 2. Todoerti M, et al., Reumatismo. 2013 Dec 18;65(5):207-18.

Disclosure of Interests: Piotr Ligocki Consultant for: Accord Healthcare, Grzegorz Orlik Employee of: Accord Healthcare, Vishal Vekariya Employee of: Intas Pharmaceuticals
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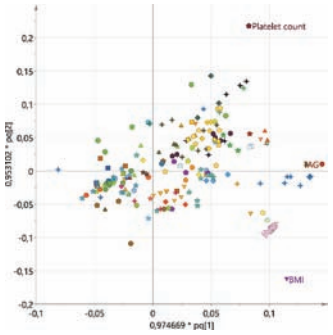
THU0180 INFLUENCE OF BLUE MUSSEL (MYTILUS EDULIS) INTAKE ON FATTY ACID COMPOSITION IN ERYTHROCYTES AND PLASMA PHOSPHOLIPIDS AND SERUM METABOLITES IN WOMEN WITH RHEUMATOID ARTHRITIS

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Background: The positive effects of omega-3 on risk of cardiovascular disease, on inflammation and immune function are well established [1]. Unfortunately fish as a source of omega-3 is not economically or environmentally sustainable. In contrast, blue mussel farming is beneficial for the environment since excessive nitrogen is removed at harvest and eutrophication of the sea is reduced [2]. Blue mussels contain not only omega-3, but are rich in nutrients such as zinc, selenium, riboflavin and carotenoids. We have previously shown, in the randomized cross-over trial Mussels, Inflammation and RA (MIRA), that disease activity (DAS28-CRP), fatigue, pain and general health in RA is improved by a dietary intervention with blue mussels compared to control [3]. It is not clear what the mechanisms of the intervention were, and if the intake of omega-3 from the blue mussels plays a role.
Objectives: The aim of this study was to investigate if the intake of blue mussels in patients with RA lead to changes in fatty acid composition in plasma phospholipids and erythrocytes and/or in metabolites (detected by NMR-metabolomics), compared to a control diet, in an attempt to understand the health beneficial effects found in the MIRA study.
Methods: Twenty-three women completed the randomized 2 × 11-week cross-over dietary intervention, exchanging one cooked meal a day, five days a week, with a meal including 75 g blue mussels or 75 g meat. Fatty acid composition in erythrocytes and plasma and ^{1}H-NMR metabolomics data were analysed and multivariate data analysis; Orthogonal Projections to Latent Structures with Discriminant Analysis (OPLS-DA) and OPLS with effect projections (OPLS-EP)) were performed to compare the two diets.
Results: Intake of the blue mussels led to a different fatty acid profile in erythrocytes, compared to control, and all samples could be correctly classified with OPLS-DA (figure 1). The changes included significant increases in omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The patterns for plasma phospholipids and ^{1}H-NMR serum metabolites were not as specific for the diets and metabolites were strongly influenced by body mass index (BMI) (figure 2).



Abstract THU0180 – Figure 1. A) Model prediction for all individuals in OPLS-EP models for erythrocyte fatty acids (%) B) OPLS-DA models showing separation for erythrocyte fatty acids (%, Black boxes = control diet, grey circles = blue mussel diet



Abstract THU0180 – Figure 2. Orthogonal Projections to Latent Structures (OPLS) for metabolites in relation to significant related factors (n=92). TAG= triacylglycerides, BMI= body mass index

Conclusion: To conclude, the change in fatty acid pattern in erythrocytes could be related to reduction in disease activity in the MIRA-study, although it cannot be excluded that other factors than omega-3 fatty acids potentiate the effect. Multivariate modelling of fatty acids in erythrocytes increased the precision for compliance, compared to evaluating EPA and DHA content alone.

REFERENCES:

[1] Calder PC. Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance. Biochim Biophys Acta. 2015;1851:469-84. doi: 10.1016/j.bbalip.2014.08.010. Epub Aug 20.
[2] Lindahl O, Hart R, Hernroth B, Kollberg S, Loo LO, Olrog L, et al. Improving marine water quality by mussel farming: a profitable solution for Swedish society. Ambio. 2005;34:131-8.
[3] Lindqvist HM, Gjertsson I, Eneljung T, Winkvist A. Influence of Blue Mussel (Mytilus edulis) Intake on Disease Activity in Female Patients with Rheumatoid Arthritis: The MIRA Randomized Cross-Over Dietary Intervention. Nutrients. 2018;10(4).nu10040481. doi: 10.3390/nu.

Disclosure of Interests: Helen Lindqvist Employee of: Yes, for Janssen-Cilag AB in 2001-2003, Before I was a phD-student and within a different field (dementia). My research field is within diet and Rheumatology., Inger Gjertsson: None declared, Philip Calder: None declared, Linnea Barebring: None declared
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THU0181 TREATMENT WITH UPADACITINIB RESULTS IN THE NORMALIZATION OF KEY PATHOBIOLOGIC PATHWAYS IN PATIENTS WITH RHEUMATOID ARTHRITIS: BIOMARKER RESULTS FROM THE PHASE 3 SELECT-NEXT AND SELECT-BEYOND STUDIES

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Background: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA) with an inadequate response (IR) to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or biologic DMARDs (bDMARDs) in the SELECT-NEXT[1] and SELECT-BEYOND[2] trials, respectively. The pivotal immune regulatory pathway targets served by JAK1 in patients have not been comprehensively explored.
Objectives: To investigate the mode of action (MoA) of UPA in patients with RA via a proteomic approach that evaluates a set of plasma proteins associated with inflammation.
Methods: Patients from the SELECT-NEXT and SELECT-BEYOND (PBO, n=167; UPA 15 mg QD, n=200) studies were randomly selected from the pool of patients with plasma samples available at baseline, Week 2, and Week 12. Samples from 24 age- and sex-matched healthy controls were included. The levels of 92 proteins were analyzed using the Olink® Inflammation Panel. Results from both studies were combined. Data were clustered using the Ward (unsupervised) method; correlations were calculated using the Pearson method; and multiple comparisons were corrected using the Benjamini–Hochberg method; all statistical analyses were performed in JMP 13.10 (SAS Institute). Pathway analysis was performed with Ingenuity® Pathway Analysis (Qiagen Inc.) version 45868156.

Results: At baseline, levels of IL-6, CXCL9, CXCL10, and CCL7 correlated significantly with baseline DAS28-ESR, consistent with effector roles for IL-6 and interferon (IFN) in intercurrent disease activity. Clustering of the differential protein fold change at Weeks 2 and 12 for UPA and PBO groups revealed four clusters enriched for proteins related to: 1) IL-6, IFN, leukocyte trafficking, and macrophage activation (↓↓↓); 2) T helper cell differentiation (↓); 3) T and B cell signaling (↓↓); and 4) hematopoiesis and myeloid cell differentiation (↑). Pathway analysis based on the differential expression of 37 significantly modulated proteins suggests that treatment with UPA results in the normalization of key pathways associated with the pathobiology of RA including: 1) pathways associated with IL-1, IL-6, IL-12, IL-15, IL-18, IFNα, IFNβ, IFNγ, CSF2, and TNF; and 2) pathways associated with behaviors of leukocytes (lymphocytes, myeloid cells, and granulocytes), including leukocyte migration, T cell response, and inflammatory response. In keeping with the latter, the changes in IL-6, CCL23, CCL7, MMP1, and S100A12 levels at Week 12 correlated significantly with the relative change in DAS28-ESR, suggesting a link between UPA MoA and macrophage activation.
Conclusion: In keeping with its selectivity for JAK1, UPA operates via inhibition of multiple JAK1-dependent upstream pathways that result in the normalization of key functional downstream effects associated with the pathobiology of RA, including T cell and myeloid cell-related pathways. Notably, non-JAK signaling pathways also normalize, suggesting functional integration of JAK1 with parallel pathogenic signaling in RA effector cells.

REFERENCES:

[1] Burmester GR, et al. Lancet 2018;391:2503–12;
[2] Genovese MC, et al. Lancet 2018;391:2513–24

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THU0182 PHARMACOKINETICS AND SAFETY OF A SINGLE ORAL DOSE OF PEFICITINIB (ASP015K) IN SUBJECTS WITH NORMAL AND IMPAIRED RENAL FUNCTION

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Background: Peficitinib (ASP015K), a novel oral Janus kinase inhibitor, was shown to be efficacious as once-daily therapy for moderate-to-severe rheumatoid arthritis (RA) in a phase 2b study (NCT01649999)[1] and in two phase 3 studies (NCT02308163[2] and NCT02305849).[3] Mean urinary excretion of peficitinib accounted for 9–15% of the oral dose.[4]
Objectives: To assess the pharmacokinetics (PK) and safety of a single, oral dose of peficitinib 150 mg in subjects with normal and impaired renal function.
Methods: This was an open-label, single-dose, parallel-group study conducted at two centres in Japan. All subjects were aged 20–75 years with a body mass index ≥17.6 to <30.0 kg/m^2. Renal function was classified according to estimated glomerular filtration rate (eGFR) using a GFR predictive equation for Japanese subjects: normal ≥90 mL/min/1.73 m^2; mild impairment ≥60 to <90 mL/min/1.73 m^2; moderate impairment ≥30 to <60 mL/min/1.73 m^2; and severe impairment ≥15 to <30 mL/min/1.73 m^2. Subjects with impaired renal function had unchanged renal impairment treatment (including diet) within 14 days prior to dosing. Subjects received a single, oral dose of peficitinib 150 mg tablet under fasting conditions in a hospital setting. The selected dose was based on the peficitinib daily dose in the phase 3 RA studies. Blood samples for peficitinib plasma PK analysis were collected before administration and up to 72 h post dose. Safety was assessed throughout the study.
Results: A total of 31 subjects (87.1% male; **Table 1**) were enrolled and received study drug according to study protocol. Subjects comprised 8 with normal renal function, and 8 with mild, 8 with moderate and 7 with severe renal impairment. The peficitinib concentration–time profiles from dosing to 72 h (**Fig. 1**), extrapolated to infinity (AUC_{inf}) and maximum concentration (C_{max}) were similar between those with normal and impaired renal function (**Table 2**). Two subjects had mild/grade 1 (CTCAE v4.0 JCOG) treatment-emergent adverse events (TEAEs): 1/8 (12.5%) with normal renal function had a headache (considered to be drug-related) and 1/8 (12.5%) with mild renal impairment had increased alanine aminotransferase (ALT) (not considered to be drug-related). There were no serious TEAEs or deaths during the study. There were no clinically significant mean changes from baseline in other clinical laboratory parameters or vital sign measurements, except for grade 1 increased ALT in a subject with mild renal impairment.

Abstract THU0182 –Table 1.

Table 1 Demographic characteristics (PKAS)

Parameter	Renal function[1]				Total
	Normal (n=8)	Mild impairment (n=8)	Moderate impairment (n=8)	Severe impairment (n=7)[2]	
Male, n (%)	6 (75.0)	7 (87.5)	7 (87.5)	7 (100.0)	27 (87.1)
Median (min, max) age, y	56.5 (23, 69)	59.5 (37, 70)	62.0 (46, 75)	67.0 (58, 71)	60.0 (23, 75)
Median (min, max) weight, kg	65.8 (55.5, 73.0)	66.8 (46.7, 72.6)	66.4 (56.5, 76.4)	69.4 (62.9, 77.5)	67.6 (46.7, 77.5)
Median (min, max) BMI, kg/m^2	23.4 (20.9, 28.3)	23.0 (18.6, 24.7)	23.6 (22.3, 28.0)	25.0 (23.2, 29.0)	23.6 (18.6, 29.0)
Median (min, max) eGFR, mL/min/1.73 m^2	94.4 (91.7, 104.4)	79.8 (66.7, 83.4)	48.2 (37.0, 58.8)	23.5 (18.0, 27.3)	66.7 (18.0, 104.4)

[1]Classification of renal impairment was based on the predictive glomerular filtration rate equation: for males, $eGFR_{crea}$ (mL/min/1.73 m^2) = 194 x (serum creatinine [mg/dL])-1.094 x (age)-0.287; and for females, (male eGFR) x 0.739. Definitions were: normal function ≥90 mL/min/1.73 m^2; mild impairment ≥60 to <90 mL/min/1.73 m^2; moderate impairment ≥30 to <60 mL/min/1.73 m^2; and severe impairment ≥15 to <30 mL/min/1.73 m^2.
BMI=body mass index (weight in kg ÷ height in m^2); eGFR=estimated glomerular filtration rate.

Conclusion: Exposure after a single 150 mg oral dose of peficitinib under fasting conditions was similar between subjects with and without renal impairment. The peficitinib dose was generally well tolerated, with no differences in TEAE incidence by renal function.

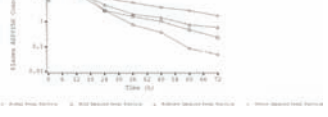
Abstract THU0182 –Table 2.

Table 2 Plasma PK parameters of peficitinib (PKAS)

Parameter	Renal function[1]			
	Normal (n=8)	Mild impairment (n=8)	Moderate impairment (n=8)	Severe impairment (n=7)[2]
Mean (SD) AUC_{inf}, ng.h/mL	1595 (360.2)	1419 (385.0)	1427 (562.7)	1933 (984.6)
GMR (90% CI) for AUC_{inf} vs normal renal function	-	0.87 (0.61, 1.25)	0.83 (0.58, 1.19)	1.09 (0.74, 1.60)
Mean (SD) C_{max}, ng/mL	426.4 (156.8)	376.7 (119.6)	342.1 (134.9)	387.2 (260.4)
GMR (90% CI) for C_{max} vs normal renal function	-	0.90 (0.60, 1.35)	0.78 (0.52, 1.18)	0.78 (0.51, 1.20)
Mean (SD) $t_{1/2}$, h	6.80 (4.34)	14.96 (8.33)	14.36 (14.33)	10.80 (5.13)

[1]Classification of renal impairment was based on the predictive glomerular filtration rate equation: for males, $eGFR_{crea}$ (mL/min/1.73 m^2) = 194 x (serum creatinine [mg/dL])-1.094 x (age)-0.287; and for females, (male eGFR) x 0.739. Definitions were: normal function ≥90 mL/min/1.73 m^2; mild impairment ≥60 to <90 mL/min/1.73 m^2; moderate impairment ≥30 to <60 mL/min/1.73 m^2; and severe impairment ≥15 to <30 mL/min/1.73 m^2.
[2]Number of subjects available for AUC_{inf} and $t_{1/2}$ was 6.
AUC_{inf}=area under the concentration–time curve from the time of dosing extrapolated to infinity; CI=confidence interval; C_{max}=maximum concentration; $eGFR_{crea}$=estimated glomerular filtration rate based on serum creatinine; GMR=geometric mean ratio; SD=standard deviation; $t_{1/2}$=terminal elimination half-life; t_{max}=time of C_{max}.

Figure 1 Mean (± standard deviation) plasma concentration–time profile of peficitinib by degree of renal impairment (semi-log scale, PKAS)



Abstract THU0182 – Figure 1

REFERENCES:

[1] Takeuchi T, et al. Ann Rheum Dis 2016; 75: 1057–64; 2. Tanaka Y, et al. ACR/ARHP Annual Meeting 2018: Abstract 887; 3. Takeuchi T, et al. ACR/ARHP Annual Meeting 2018: Abstract 888; 4. Cao YJ, et al. Clin Pharmacol Drug Dev 2016;5:435–49

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THU0183 UPADACITINIB PHARMACOKINETICS IN JAPANESE SUBJECTS WITH RHEUMATOID ARTHRITIS WITH THE EXTENDED-RELEASE FORMULATION AND COMPARABILITY TO NON-JAPANESE SUBJECTS

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Background: Upadacitinib (UPA), an oral selective JAK1 inhibitor, is being developed for treatment of patients with moderate to severely active rheumatoid arthritis (RA). UPA efficacy was demonstrated in subjects with moderate to severe RA in five global Phase 3 studies and a regional Phase 2b/3 study in Japanese subjects.
Objectives: To characterize the pharmacokinetics of UPA after administration of the extended-release formulation in Japanese subjects with RA and to compare UPA plasma exposures between Japanese and non-Japanese subjects.
Methods: Population pharmacokinetic analyses were conducted using UPA data across Phase 1 to 3 studies including Japanese and non-Japanese subjects. The population pharmacokinetic model was used to estimate UPA plasma exposures from the extended-release formulation regimens in non-Japanese and Japanese subjects with RA in Phase 3 trials. Additionally, a total of 29 Japanese subjects with RA who were enrolled in SELECT-SUNRISE Phase 2b/3 study participated in a pharmacokinetics substudy in which serial blood samples were collected from each subject over a 24 hour period after UPA dosing. UPA was administered in the study at doses of 7.5 mg, 15 mg, and 30 mg QD using the extended-release formulation. Pharmacokinetic parameters were calculated in the pharmacokinetic substudy using noncompartmental methods.
Results: UPA maximum plasma concentration was reached within 2 hours of dosing under fasting condition. UPA plasma exposures were approximately dose proportional over the evaluated dose range in Japanese subjects with RA. UPA model estimated plasma exposures (based on population pharmacokinetic analyses) were comparable (within 20%) between Japanese and non-Japanese subjects with RA (Table 1). Results from the pharmacokinetic substudy using noncompartmental methods were consistent with the population pharmacokinetic analyses.

Abstract THU0183 – Table 1. Upadacitinib Model Estimated Exposures in Japanese and Non-Japanese Subjects with RA for the Extended-Release Formulation

		Median (5th, 95th Percentiles)		
Population	**Treatment**	**C_{max} (ng/mL)**	**C_{avg} (ng/mL)**	**C_{trough} (ng/mL)**
Japanese (N = 104)	7.5 mg QD	24.0 (18.0, 31.0)	8.8 (5.0, 15.2)	2.4 (0.7, 7.7)
Non-Japanese (N = 1495)	15 mg QD	40.9 (28.2, 54.7)	15.1 (8.9, 32.4)	3.8 (1.3, 21.3)
Japanese (N = 97)		47.0 (36.7, 70.2)	16.5 (10.4, 33.6)	4.0 (1.3, 22.2)
Non-Japanese (N = 850)	30 mg QD	81.0 (57.2, 113.9)	29.1 (17.9, 63.8)	7.5 (2.4, 40.5)
Japanese (N = 99)		97.7 (72.7, 124.3)	35.1 (21.7, 59.7)	9.5 (2.9, 27.8)

Cmax: maximum plasma concentration; Cavg: average plasma concentration during a dosing interval; Ctrough: trough plasma concentration
Conclusion: No clinically relevant difference was observed in UPA plasma exposures between Japanese and non-Japanese subjects with RA.

REFERENCES:
[1] Mohamed, et al. Clin Pharmacol Drug Dev. 2018 Apr 24.
[2] Genovese et al. Lancet. 2018;391(10139):2513-2524.
[3] Burmester et al. Lancet. 2018;391(10139):2503-2512.

Disclosure of Interests: Mohamed-Eslam Mohamed Shareholder of: AbbVie, Employee of: AbbVie, Ben Kluender Shareholder of: AbbVie, Employee of: AbbVie Deutschland GmbH & Co. KG, Sebastian Meerwein Shareholder of: AbbVie, Employee of: AbbVie Deutschland GmbH & Co. KG, Ahmed Othman Shareholder of: AbbVie, Employee of: AbbVie
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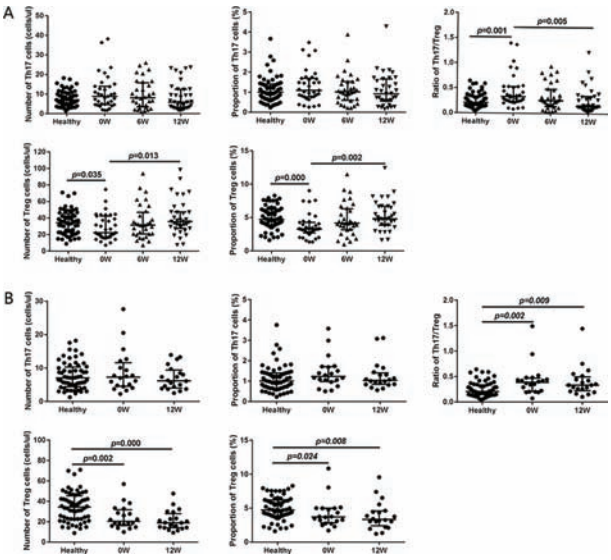
THU0184 SIROLIMUS SELECTIVELY INCREASES CIRCULATING TREG CELL NUMBERS AND RESTORES THE TH17/TREG BALANCE IN RHEUMATOID ARTHRITIS PATIENTS WITH DAS28 ≤ 3.2 WHO PREVIOUSLY RECEIVED CONVENTIONAL DMARDS

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Background: Many immunosuppressants used to treat rheumatoid arthritis (RA) were designed to broadly suppress T cell function, including that of regulatory T cells (Tregs). Patients with inactive RA also show a reduced frequency of peripheral Tregs [1]. Tregs are essential for maintaining effective immune tolerance and a homeostatic balance of Th17/Treg. Accordingly, there has been increasing interest in developing Treg-friendly regimens to minimize or eliminate the immunosuppression of conventional medications for RA. mTOR signaling negatively controls the development and function of Tregs. Rapamycin, an mTOR inhibitor, could expand Tregs ($CD4^+CD25^+FoxP3^+$) in patients with active systemic lupus erythematosus [2] and active RA [3]; however, the response of Tregs to rapamycin in RA patients with DAS28 ≤ 3.2 is still unclear.
Objectives: To investigate the effects of rapamycin, under the generic name sirolimus, on Tregs in RA patients with DAS28 ≤ 3.2 who previously received conventional DMARDs.
Methods: Fifty-five RA patients and 60 healthy controls were enrolled in this study. All patients had previously received conventional DMARDs and had a low DAS28 score (≤ 3.2). Peripheral blood samples and clinical information were obtained at baseline and following 6 and 12 weeks of sirolimus treatment, or after 12 weeks of conventional treatment. The circulating levels of lymphocyte subpopulations were assessed by flow cytometry.
Results: Thirty-five patients received sirolimus and 20 patients continued treatment with conventional DMARDs. None of the baseline clinical characteristics differed significantly between the two groups. The absolute counts and proportions of $CD4^+CD25^+FoxP3^+$ Tregs were significantly lower in all RA patients with DAS28 ≤ 3.2 as compared with those in healthy controls. By contrast, the difference in circulating Th17 cell numbers was not significant. Sirolimus administration resulted in significant elevations in circulating Treg cell numbers and significant reductions in the Th17/Treg cell ratio, whereas the circulating level of Tregs and the Th17/Treg cell ratio in patients under conventional treatment both showed a tendency of reduction (Figure 1). Furthermore, a greater proportion of patients under sirolimus treatment achieved DAS28-based remission at 12 weeks.
Conclusion: Sirolimus can favorably expand Tregs in RA patients with DAS28 ≤ 3.2, consequently restoring a healthy balance of Th17/Treg cells, which might improve the likelihood of long-term and sustained clinical remission and reduce the probability of disease flare-ups in RA. These findings provide valuable insights that might potentially lead to changes in clinical practice for the routine treatment of RA.

REFERENCES:
[1] Niu Q, Cai B, Huang ZC, Shi YY, Wang LL. Disturbed Th17/Treg balance in patients with rheumatoid arthritis. Rheumatol Int, 2012, 32(9): 2731-2736.
[2] Lai ZW, Kelly R, Winans T, et al. Sirolimus in patients with clinically active systemic lupus erythematosus resistant to, or intolerant of, conventional medications: a single-arm, open-label, phase 1/2 trial. Lancet, 2018, 391 (10126): 1186-1196.
[3] Wang J, Zhang SX, Hu FY, et al. Sirolimus treatment in patients with refractory rheumatoid arthritis: a double-arm, open-label, phase 1/2 trial.

Arthritis Rheumatol, 2018, 70 (Suppl 9): 2018 ACR/ARHP Annual Meeting Abstract Supplement.



Abstract THU0184 – Figure 1. The numbers of Th17, Tregs, and the ratio of Th17/Treg in healthy controls and RA patients. **A**: Healthy controls and RA patients before and after sirolimus treatment. **B**: Healthy controls and RA patients before and after conventional treatment.

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THU0185 THE FIRST REPORT OF SIGNIFICANTLY IMPROVEMENT OF NT-PROBNP LEVEL IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB DURING 12-MONTH FOLLOW-UP

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Background: The amino-terminal fragment of the B-type natriuretic peptide prohormone (NT-proBNP) is a marker for functional cardiac impairment and is increased in heart disease with or without symptoms of congestive heart failure (CHF)[1].
Objectives: To prospectively investigate the effect of tofacitinib (TOFA) on the levels of NT-proBNP, as a predictor of CHF in patients (pt) with active rheumatoid arthritis (RA).
Methods: Twenty six RA pt (median age 54 [40;62] years, 81% female, disease duration 44[24;63,0] month (m), moderate to high activity (DAS28-5.1[4.6;6.1], SDAI–27(22;35)), positive for ACCP (73%)/RF (77%), who were non-responders to MTX at least 15 mg/week and/or other synthetic DMARDs and bDMARDs) free of clinical overt cardiovascular disease were treated with TOFA and followed for 12 m. TOFA therapy was started in all pt in dose 5 mg BID per os with dose escalation to 10 mg BID in 8 (31%) pt. TOFA used in combination with MTX in 24 (92%) pt, leflunomide in 1 (4%). Low-dose oral corticosteroids (<10 mg/day prednisone or equivalent) were received by 9 (35%) pt. Remission was achieved in 38,5% pt (DAS28), 38,5% (SDAI). Cardiovascular risk factors (CVRF) and the NT-proBNP levels were measured at baseline and after 12m. At baseline the most of pt had multiple CVRF and subclinical organ damage. Cardioprotective therapy received 16 (57%) pt (β-AB–7, ARA/ACE inhibitors–11, statins–11, dihydropyridine CCB-7). Twenty controls matched for CVRF were included for comparison of normal NT-proBNP levels with those of RA pt.
Results: The NT-proBNP level was significantly higher in RA pt than in the control group (median 62.2(26.9-101.7) pg/mL vs 44.0 (34.0-54.3) pg/mL, p<0.05). At baseline NT-proBNP level was higher in female than in male (p=0,019). Its concentration correlated with DAS28 (r=0,41,p=0,036). Three pt (11,5%) had NT-proBNP level over 125 pg/mL. All RA pt with a NT-proBNP level over 125 pg/mL were asymptomatic and exhibited normal echocardiography. Median DAS28 and SDAI were significantly reduced following TOFA treatment (from 5.1 to 2.9, p < 0.001 and from 26.8 to 4.7, p < 0.001, respectively). During follow-up, no RA pt exhibited a cardiovascular event or CHF. NT-proBNP levels decreased by 63% over the 12-m of TOFA treatment (from 62.16 pg/mL to 14.8 pg/mL, p= 0.011). The incidence rate of arterial hypertention (58%vs65%), overweight (62%vs62%), abdominal obesity (58%vs62%), smokers (27%vs27%), menopausal status (52%vs52%), DM type 2 (7%vs7%), mSCORE≥5% (23% vs27%), subclinical carotid atherosclerosis (58%vs58%) did not change significantly. An increase in body mass index (BMI) was observed from 26.5[22.9;29.0] to 26.9[24.0;30.1],p<0.001 and in HDL level from 1.37 [1.06;1.87] to 1.90[1.29;2.16],p<0.01. The percentage change in the NT-proBNP level significantly correlated with the percentage change in the BMI (r=0,6,p=0,007), DAS 28 (r = 0.41, p = 0.038) SDAI (r = 0.51, p = 0.009). Changes in NT-proBNP levels in RA pt with remission was greater than that observed in pt who didn't achieve remission (-87% vs -26%, p=0,005). The percentage change in the NT-proBNP level was not correlated with the percentage change in other CVRF.
Conclusion: TOFA decreased the NT-proBNP level in patients with RA without clinical overt cardiovascular disease and CHF. TOFA may have a cardioprotective effect in those with active RA.

REFERENCE:

[1] Breunig M., Kleinert S., Lehmann S. et al. Simple screening tools predict death and cardiovascular events in patients with rheumatic disease. Scand J Rheumatol 2018;47(2):102-109. doi: 10.1080/03009742.2017.1337924.

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THU0186 SAFETY, TOLERABILITY AND PHARMACOKINETICS OF MBS2320, A SELECTIVE MODULATOR OF IMMUNE METABOLISM, IN HEALTHY VOLUNTEERS AND PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Despite the availability of several treatment options some patients with Rheumatoid Arthritis (RA) fail to benefit and for those who do response rates are similar across therapeutic classes. Thus there remains a need for new therapies with novel mechanisms of action. MBS2320 is a selective modulator of immune metabolism that shows anatomically appropriate osteoid layering and a broader spectrum of osteoprotective efficacy compared to TNFα inhibition in preclinical models.
Objectives: To investigate the safety, tolerability and pharmacokinetics of MBS2320 in healthy volunteers and patients with Rheumatoid Arthritis (RA) receiving a stable dose of methotrexate (MTX).
Methods: Cohorts of healthy volunteers (randomised 6:2 drug:placebo) received single or multiple oral doses of MBS2320 for 14 days. Single Ascending Dose (SAD) cohorts comprised 2, 10, 25, 50, 75, 125, 250, 375 mg (PO) and Multiple Ascending Dose (MAD) cohorts 75, 100, 160 mg/d. Patients with RA received 75 mg/d for 14 days in addition to their existing weekly MTX treatment. Safety and tolerability were assessed throughout. Plasma MBS2320 (SAD, MAD and patients with RA) and MTX (patients with RA only) were measured using LC-MS/MS. In patients with RA, C-reactive protein (CRP) and biomarkers of bone turnover were assessed on Day 14.
Results: A total of 96 healthy subjects and 9 patients with RA entered the Study and were randomised to the drug or matching placebo.
MBS2320 was well tolerated by healthy subjects at single oral doses of 2 to 375 mg. There were no serious adverse events (SAEs). Nausea was the most commonly reported adverse event (AE) and occurred most frequently at the high doses but was mild and resolved without treatment. Daily doses of 75 to 160 mg QD MBS2320 for 14 days were generally well tolerated by healthy subjects. The most common drug-related treatment emergent adverse events (TEAEs) were gastrointestinal disorders,

particularly nausea. There were no significant effects on clinical laboratory tests, vital signs, ECG or physical examination.
Multiple doses of MBS2320 (75 mg) were also generally well tolerated by subjects with RA when co-administered with MTX. There were no clinically significant findings or trends in the laboratory tests, vital signs or ECG data, and no clinically significant findings on physical examination. No SAEs were reported. The majority of TEAEs were mild in severity with diarrhoea and nausea reported most frequently.
In healthy subjects, MBS2320 was steadily absorbed following doses of 50 to 375 mg MBS2320. Systemic exposure (AUC) increased in a dose-proportional manner across all doses and was unaffected by food. In RA patients there was no indication of a PK interaction between MTX and MBS2320 in either direction.
In patients with RA, serum CTX-1, P1NP and osteocalcin increased following 14 days of treatment, while TRAP5b was decreased or unchanged. Median CRP was decreased relative to baseline in after 7 days' treatment with MBS2320, and remained low on Day 14.
Conclusion: MBS2320 was well tolerated for up to 14 days when administered to healthy volunteers and to patients with RA receiving MTX. Systemic exposure was dose-proportional with no evidence of a pharmacokinetic interaction with MTX. Evaluation of biomarkers of bone turnover and inflammation in RA patients showed changes consistent with those expected of an agent with the potential to directly protect the bone and simultaneously ameliorate inflammation.
Louise Jopling, Ian Anderson, Ian Gourley, Helen Marley and Ezi Otti
Disclosure of Interests: Lisa Patel Shareholder of: Shareholder of Istesso Ltd, Employee of: Employee of Istesso, Paul Marcus Consultant for: Istesso Ltd, Jim Bush Shareholder of: Labcorp, Employee of: Covance, Andy Gray Shareholder of: Shareholder of Istesso Ltd, Consultant for: Istesso Ltd, Employee of: Astra Zeneca, Richard Fitzgerald: None declared, Sonya Abraham Shareholder of: UCB Pharma, Grant/research support from: Pfizer, Riche, Abbvie, Consultant for: Abbvie Roche Pfizer BMS UCB pharma, Eli Lilly, Employee of: UCB Pharma, Martyn Foster Shareholder of: AstraZeneca, Consultant for: Istesso, Levicept, Employee of: AstraZeneca, Hiep Huatan Consultant for: Istesso Ltd, Employee of: Pfizer, Laurence Skillern Consultant for: Istesso, Employee of: Astellas, Anna Daroszewska Consultant for: Istesso Ltd, Rob van't Hof Shareholder of: OsteoRx Ltd, Sam Williams Shareholder of: Shareholders of Istesso Ltd, Employee of: Employees of Istesso
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THU0187 EFFICIENCY OF TREATMENT SEQUENCES CONTAINING TOFACITINIB FOR RHEUMATOID ARTHRITIS IN SPAIN

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Background: The availability of oral janus kinase inhibitors, as tofacitinib, has extended the treatment pathways for management of patients with rheumatoid arthritis (RA)
Objectives: To assess the cost-effectiveness of tofacitinib as second-line treatment compared to treatment sequences containing standard biological-therapies in patients with moderate to severe RA after failure to disease-modifying antirheumatic drugs (DMARDs) from the Spanish National Health System perspective.
Methods: A patient-level microsimulation model was used to compare the lifetime cost and quality-adjusted life-years (QALY) for treatment sequences initiating with tofacitinib (5mg BID) followed by biological therapies versus sequences of biological treatments excluding tofacitinib. The sequences were selected by a panel of experts based on clinical practice in Spain. Concomitant treatment with methotrexate (MTX) was considered along all the therapies in the treatment sequences.
Model parameters included age, weight, initial Health Assessment Questionnaire (HAQ) score and clinical response to short and long treatment. Efficacy was measured by means of HAQ score changes using mixed-treatment-comparisons (for the first 6 months) and data from long-term extension trials (for later periods).
Serious adverse event (SAE) information derived from literature.
The estimation of total cost for sequences included: drugs acquisition (public ex-factory prices with mandatory deduction or reference prices) and parenteral administration, disease progression and SAE management. Local unitary costs (€, 2018) were applied. Additional comparisons were explored testing other potential sequences.
Results: The base case results showed that sequences initiating with tofacitinib provided greater outcomes than the correspondent sequences excluding tofacitinib. In scenario 1 tofacitinib+MTX→Rituximab+MTX→sc Tocilizumab+MTX→Etanercept+MTX→Certolizumab+MTX provided 13.99 QALYs versus 13.92 QALYs for adalimumab+MTX→Rituximab+MTX→sc Tocilizumab+MTX→Etanercept+MTX→Certolizumab+MTX. In scenario 2 tofacitinib+MTX→Adalimumab+MTX→Rituximab+MTX→sc Tocilizumab +MTX→Etanercept+MTX provided 13.75 QALYs versus 13.62 QALYs for Baricitinib+MTX→Adalimumab+MTX→Rituximab+MTX→sc Tocilizumab +MTX→Etanercept+MTX.
Tofacitinib-containing sequences provided lower total costs than the alternative sequences (-€ 5,783 and -€ 13,975 for the pairwise comparisons previously described), resulting, therefore, dominant options versus sequences excluding tofacitinib.
On the probabilistic sensitivity analyses, sequences initiating with tofacitinib resulted cost-effective in 64.0% (scenario 1) and 56.9% (scenario 2) of the 1,000 iterations performed, because incremental cost-effectiveness ratio fell below a € 25,000/QALY gained willingness to pay threshold.
Conclusion: These results suggest that the inclusion of tofacitinib could be a dominant strategy for treatment of moderate to severe RA patients after DMARDs failure in Spain.
Disclosure of Interests: Carmen Peral Shareholder of: Carmen Peral is employee of and shareholder in Pfizer, Employee of: Carmen Peral is employee of and shareholder in Pfizer, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Federico Navarro Grant/research support from: Pfizer, Consultant for: Pfizer, José Luis Pablos: None declared, Jose Manuel Martinez Sesmero Consultant for: Pfizer, Susana Gómez Employee of: I am a current employee of Pfizer., Monica Valderrama Shareholder of: Have received shares from Pfizer, Employee of: employee in Pfizer, Itziar Oyagüez Consultant for: I am employee of PORIB a consultant company which has received financial support from Grünenthal for development of this project, Miguel Angel Casado Grant/research support from: Pfizer, Consultant for: Pfizer, Fernando De Andres Grant/research support from: Pfizer, Employee of: Pfizer, Maria Montoro Shareholder of: Maria Montoro is employee of and shareholder in Pfizer, Employee of: Maria Montoro is employee of and shareholder in Pfizer
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THU0188 INHIBITION OF STRUCTURAL JOINT DAMAGE WITH UPADACITINIB AS MONOTHERAPY OR IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: 1 YEAR OUTCOMES FROM THE SELECT PHASE 3 PROGRAM

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Background: Long–term prevention of structural joint damage is a key treatment goal in the management of RA[1]. Upadacitinib (UPA), a JAK1-selective inhibitor, inhibited the progression of structural joint damage at 6 months as monotherapy in methotrexate (MTX)–naïve RA patients (pts)[2] and in combination with MTX in pts with inadequate response (IR) to MTX[3].
Objectives: To evaluate the progression of structural joint damage (radiographic) through Week 48 in pts with moderately to severely active RA treated with UPA monotherapy or in combination with MTX.
Methods: Radiographic progression was assessed in 2 phase 3 randomized controlled trials (RCTs), as previously described[2,3]. MTX–naïve pts were randomized to UPA 15 or 30mg QD or MTX monotherapy [SELECT–EARLY, N=945], while MTX-IR pts were randomized to UPA 15mg QD or adalimumab (ADA) 40 mg eow or placebo (PBO), with continuous background MTX [SELECT–COMPARE, N=1629]. Both RCTs specifically enrolled pts at high risk for progression of joint damage (high disease activity including elevated hsCRP, presence of baseline erosions and ACPA and/or RF positivity[2,3]). The mean changes (Δ) from baseline

(BL) in modified Total Sharp Score (mTSS), joint space narrowing (JSN), and erosion scores (ES) as well as the proportion of pts with no radiographic progression (ΔmTSS ≤0) at Weeks 24/26 and 48 were determined in both RCTs. Data were analyzed by linear extrapolation (LE) for missing data imputation and treatment switching, and as observed (AO).

Results: BL demographics have been reported previously[2,3]. At Weeks 24/26, UPA as monotherapy and in combination with background MTX significantly inhibited radiographic progression measured by mean ΔmTSS and the proportion of pts with no radiographic progression vs MTX and PBO, respectively (LE and AO, **Table**). The significant inhibition of radiographic progression with UPA was maintained through Week 48 vs MTX (LE and AO) in EARLY and vs PBO (LE) in COMPARE. Following the switch of all PBO pts to UPA in COMPARE by Week 26, no further change in mean mTSS was observed through Week 48 (AO, **Table**). The inhibition of radiographic progression vs comparators was not only observed for the overall mTSS scores but also its components – the JSN and ES in both RCTs (LE and AO).

Abstract THU0188 –Table 1.

Table: Radiographic Progression at Weeks 24/26 and 48 in SELECT-EARLY and SELECT-COMPARE trials.

METHOD of IMPUTATION: Linear Extrapolation

	MTX-naive (SELECT-EARLY)						MTX-IR (SELECT-COMPARE)					
	Week 24			Week 48			Week 26			Week 48		
	MTX (N=264)	UPA 15 mg QD (N=280)	UPA 30 mg QD (N=273)	MTX (N=268)	UPA 15 mg QD (N=287)	UPA 30 mg QD (N=283)	PBO (N=601)	ADA 40 mg EOW (N=297)	UPA 15 mg QD (N=596)	PBO→UPA 15 mg QD (N=599)	ADA 40 mg EOW (N=298)	UPA 15 mg QD (N=604)
LSM differences in ΔmTSS (within group)	0.66	0.03	0.10	1.00	0.03	0.14	0.94	0.19	0.16	1.73	0.39	0.28
LSM differences in ΔmTSS (UPA or UPA-MTX vs Control)	—	-0.63***	-0.56***	—	-0.97***	-0.87***	—	—	-0.79*** (vs PBO)/ -0.03 (vs ADA)	—	—	-1.44*** (vs PBO)/ -0.11 (vs ADA)
Non-progressors, %	78.0	90.4***	90.8***	74.3	89.9***	90.8***	73.9	88.2	87.4***	74.1	87.9	86.4***

METHOD of IMPUTATION: None (As Observed)

	MTX-naive (SELECT-EARLY)						MTX-IR (SELECT-COMPARE)					
	Week 24			Week 48			Week 26			Week 48		
	MTX (N=268)	UPA 15 mg QD (N=281)	UPA 30 mg QD (N=275)	MTX (N=247)	UPA 15 mg QD (N=264)	UPA 30 mg QD (N=262)	PBO (N=588)	ADA 40 mg EOW (N=291)	UPA 15 mg QD (N=584)	PBO→UPA 15 mg QD (N=574)	ADA 40 mg EOW (N=276)	UPA 15 mg QD (N=569)
LSM differences in ΔmTSS (within group)	0.65	0.03	0.10	0.85	0.07	0.09	0.67	0.14	0.16	0.51	0.14	0.26
LSM differences in ΔmTSS (UPA or UPA-MTX vs Control)	—	-0.62***	-0.55***	—	-0.78***	-0.76***	—	—	-0.52*** (vs PBO)/ 0.01 (vs ADA)	—	—	-0.26 (vs PBO)/ 0.11 (vs ADA)
Non-progressors, %	78.4	90.4***	90.9***	74.9	89.8***	91.6***	74.1	88.3	86.8***	75.8	85.9	84.7***

Results are summarized by randomized group. In SELECT-EARLY, non-responders (<20% improvement in SJC 66/TJC68 counts) were rescued from MTX monotherapy and UPA monotherapy to UPA+MTX at Week 26. In SELECT-COMPARE, non-responders were rescued from PBO to UPA, UPA to ADA and ADA to UPA at Weeks 14 to 26 (and all remaining non-rescued PBO pts were switched to UPA at Week 26). In AO analysis, observed data at Week 48 are summarized under the randomized group regardless of rescue. In LE analysis, data after rescue are imputed by linear extrapolation. The above mTSS values are from a second reading session of radiographs from Weeks' 24/26 and 48 in both RCTs, previously presented data were from the first reading session and consisted of data for Weeks' 24 and 26 for EARLY and COMPARE RCTs, respectively.
Non-progressors are defined as patients in whom ΔmTSS ≤0. Comparison to control (EARLY: MTX or COMPARE: PBO/ADA) was calculated by ANCOVA; *p<0.05, **p<0.01, ***p<0.001.
ΔmTSS, change from baseline in modified total Sharp score; ADA, adalimumab; EOW, every other week; LSM, least-square means; MTX, methotrexate; PBO, placebo; QD, once-daily.

Conclusion: UPA both as monotherapy, and in combination with background MTX, was effective in inhibiting the progression of structural joint damage through Week 48 in MTX-naïve, and MTX-IR patients, respectively.

REFERENCES:

[1] Smolen JS et al. Ann Rheum Dis 2017;0: 1–18.

[2] van Vollenhoven R, et al. Arthritis Rheumatol. 2018; 70 (suppl 10) [ACR 2018 abstract].

[3] Fleischmann R, et al. Arthritis Rheumatol. 2018; 70 (suppl 10) [ACR 2018 abstract].

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THU0189 A PROSPECTIVE STUDY OF TAPERING CONVENTIONAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (C- DMARDS) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) IN STABLE REMISSION

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Background: Remission in RA is being achieved more often nowadays with effective early aggressive therapy with DMARDS. Studies ((1 2 3 4)) have shown that it is possible to taper and stop biologic DMARDS in patients with RA in stable remission. However there are no such studies or recommended protocols for c-DMARDS treated patients.

Objectives: To study the incidence and timing of flares in RA patients in sustained remission of at least 6 months duration on slow withdrawal of c-DMARDS and to identify predictors of flares.

Methods: Consenting adult(age >18 years) RA patients satisfying the ACR 2010 criteria attending our outpatient department with a disease duration of minimum 1 year and a stable remission (CDAI <2.8 on consecutive 2 visits at 3 months interval in last 6 months) on c- DMARDS were included. Patients receiving steroids or biologics were excluded.

Protocol for tapering:

On monotherapy: 50% dose reduction 3 weekly and stop eventually

On combination therapy: sequential dose reduction as monotherapy followed by stoppage of cDMARDs(in order from first to last: hydroxychloroquine, sulphasalazine, leflunomide, methotrexate)

Flare was defined as CDAI of >2.8. Number of RA flares and timing of flares were noted. Predictors of flare were analysed using univariate and multivariate regression

Results: 66 patients satisfied inclusion criteria of which 5 did not consent, 5 committed protocol violation and 2 lost to follow up.

Total 54 patients were included in the final analysis. 42 patients (77.78%) flared during the study period. Of these 42 patients, 29(69.05%) flared whilst on the tapering protocol whereas, 13 (30.95%) flared after complete withdrawal of c-DMARDs. 20 patients (47.62%) flared within first 3 months of the tapering regimen and total 31 patients (73.8%) flared within first 6 months of tapering regimen. Baseline CDAI scores were significantly higher in patients who developed flare compared to those who remained in remission (0.82±0.82 v/s 0.29 ±0.54, p=0.04).

RF positivity and age more than 60 years were predictors of flare in univariate regression analysis. With multivariate logistic regression, RF positivity was the only variable significantly associated with risk of flare (p=0.0098, SE =1.62 OR 66.31).

Conclusion: We found that on tapering of c DMARDs at 3 weekly interval in RA patients with stable remission the incidence of flare was 78%. Most flared during tapering therapy itself and not after the drugs were stopped. Rheumatoid factor positivity seemed to predict flares. Although within the definition of remission, CDAI scores at baseline were significantly higher in patients who developed flare compared to those who remained in remission.CDAI has limitation in defining remission and inclusion of imaging in defining remission may lead to better remission on tapering cDMARDs.

REFERENCES:

[1] Schett G, Emery P, Tanaka Y, Burmester G, Pisetsky DS, et al. Tapering biologic and conventional DMARD therapy in rheumatoid arthritis: current evidence and future directions. Ann Rheum Dis. 2016 Aug;75(8):1428–37.

[2] Haschka J, Englbrecht M, Hueber AJ, Manger B, Kleyer A, et al. Relapse rates in patients with rheumatoid arthritis in stable remission tapering or stopping antirheumatic therapy: interim results from the prospective randomised controlled RETRO study. Ann Rheum Dis. 2016 Jan 1;75(1):45–51.

[3] Fautrel B, Pham T, Alfaiate T, Gandjbakhch F, Foltz V, et al. Step-down strategy of spacing TNF-blocker injections for established rheumatoid

arthritis in remission: results of the multicentre non-inferiority randomised open-label controlled trial *(STRASS)*. Ann Rheum Dis. 2016 Jan;75(1):59–67.
[4] Huizinga TWJ, Conaghan PG, Martin-Mola E, Schett G, Amital H, et al. Clinical and radiographic outcomes at 2 years and the effect of tocilizumab discontinuation following sustained remission in the second and third year of the ACT-RAY study. Ann Rheum Dis. 2015 Jan 28;74(1):35–43.

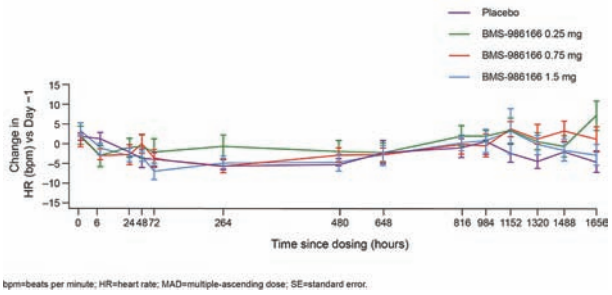
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THU0190 THE SAFETY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF BMS-986166, A NOVEL, SELECTIVE, PARTIAL AGONIST OF THE SPHINGOSINE-1-PHOSPHATE (S1P) SUBTYPE 1 RECEPTOR IN HEALTHY PARTICIPANTS

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Background: S1P mediates a number of immune processes including the egress of lymphocytes from lymphoid organs via stimulation of the S1P subtype 1 receptor (S1P1R). S1P1R inhibition has the potential to suppress abnormal immune responses and modulate autoimmune inflammatory diseases.[1] BMS-986166, a novel, selective partial agonist of S1P1R, which is phosphorylated in vivo to its pharmacologically active form, BMT-121795, may have utility for the treatment of autoimmune and/or inflammatory diseases.
Objectives: To investigate safety, pharmacokinetics (PK), and pharmacodynamics (PD) of BMS-986166 in single- and multiple-ascending dose (SAD/MAD) placebo (PBO)-controlled studies in healthy participants.
Methods: SAD study (NCT02790125): BMS-986166 was administered as a single dose of 0.75, 2.0, or 5.0 mg (n=10/group; 4:1 ratio of BMS-986166:PBO); a series of upwardly titrated single daily doses of 0.25, 0.5, 0.75, 1.0, then 1.5 mg over 14 days (n=16; 3:1 ratio); or as a single 2.0-mg dose in participants who were fed, fasted, or administered famotidine prior to dosing (n=8/group). MAD study (NCT03038711): BMS-986166 was administered as once-daily doses of 0.25 (n=12; 2:1 ratio), and 0.75 or 1.5 mg (n=10/dose; 4:1 ratio), for 28 days. Safety, PK, and PD (absolute lymphocyte count [ALC]) were assessed. Cardiac safety was assessed by continuous cardiac monitoring and at intervals by 12-lead electrocardiogram.
Results: 70 (60 BMS-986166, 10 PBO; mean [standard deviation (SD)] age: 32.8 [8.5] years) and 32 (24 BMS-986166, 8 PBO; mean [SD] age: 35.8 [8.6] years) participants were randomised to dosing in the SAD and MAD studies, respectively. Participants were predominantly male. Mean (SD) body mass index was 26.8 (2.9) and 27.2 (2.5) kg/m^2, respectively. Multiple oral doses of BMS-986166 up to 1.5 mg daily for 28 days were generally well tolerated, and all treatment-related adverse events were mild (Grade 1). In the MAD (Figure 1) and SAD studies, a clinically insignificant, dose-related decrease in mean hourly heart rate (HR) was observed following administration of BMS-986166 compared with PBO, based on a time-matched analysis of nominal hourly HR data from continuous cardiac monitoring over 72 hours post dose. Compared with participants receiving PBO, a mean decrease from baseline in hourly HR was apparent for participants in the 2 higher dose panels (2.0 mg, 5.0 mg) in the SAD study. In the SAD study, the largest decreases in PBO-corrected, time-matched, nadir hourly HR were –0.29, –6.38, and –8.37 bpm for the 0.75, 2.0, and 5.0 mg dose panels, respectively. Similarly, in the MAD study, these numbers were –0.83, –3.46, and –5.54 bpm at the 0.25, 0.75, and 1.5 mg dose levels, respectively. Increases in systemic plasma exposure (maximum concentration and area under the curve from time 0–24 hours) of BMS-986166 and its active metabolite BMT-121795 were approximately proportional to dose increases over the range of 0.75–5 mg with single doses, and of 0.25–1.5 mg on Days 1, 14, and 28 with multiple doses. Decreases in percent change from baseline in ALC with multiple doses of BMS-986166 vs PBO were dose-related over the 28-day treatment period. Between Day 0 and 35, median (range) nadir in lymphocyte reductions were 53.7% (31.7–55.9%), 75.9% (63.3–85.8%), and 81.9% (37.9–92.2%) at 0.25, 0.75, and 1.5 mg BMS-986166 dose levels, respectively. Recovery of ALC levels began 14, 14–21, and 7 days after the last dose of 0.25, 0.75, and 1.5 mg, respectively, on Day 28.

Figure 1. Mean (SE) time-matched change from Day −1 in HR (bpm) following dosing in the MAD study



bpm=beats per minute; HR=heart rate; MAD=multiple-ascending dose; SE=standard error.

Abstract THU0190 – Figure 1

Conclusion: In healthy participants, multiple daily doses of BMS-986166 in the range of 0.25–1.5 mg were well tolerated, with no clinically relevant lowering of HR. PK were linear and decreases in ALC were dose related.

REFERENCE:

[1] Urbano M, et al. Bioorg Med Chem Lett 2013;23:6377–89

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THU0191 UPADACITINIB AS MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 48 WEEKS FROM THE SELECT-MONOTHERAPY STUDY

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Background: In the SELECT-MONOTHERAPY trial, upadacitinib (UPA), an oral JAK1-selective inhibitor, showed efficacy when used as monotherapy over 14 weeks (wks) in rheumatoid arthritis (RA) patients (pts) with an inadequate response to methotrexate (MTX).[1]
Objectives: Safety and efficacy of UPA monotherapy were assessed through 48 wks in an ongoing long-term extension period of SELECT-MONOTHERAPY.
Methods: At baseline (BL), pts on stable MTX were randomized to either continue MTX (cMTX, given as a blinded study drug) or switch to once-daily (QD) UPA at 15 (UPA15) or 30 mg (UPA30) monotherapy for 14 wks. From Wk14, the start of a long-term blinded extension, pts randomized to cMTX were switched to UPA15 or 30mg per pre-specified assignment at BL, pts randomized to UPA15 or 30 continued their initial treatment. No dose adjustments for UPA were allowed. Starting at Wk26, for pts who did not achieve CDAI ≤10, background csDMARDS could be initiated. Efficacy data up to the Wk48 visit are reported “As Observed”. Adverse events (AE) per 100 pt yrs (PYs) are summarized up to May 25 2018.
Results: Of 648 pts randomized at BL, 598 (92%) completed 14 wks and continued on to the extension period. By May 25 2018, 16% discontinued study drug; 5% due to AE, 0.5% due to lack of efficacy, 4% withdrew consent, 1% were lost to follow-up, and 6% due to other reasons. Cumulative exposures to UPA15 and UPA30 were 336.0 PYs and 337.1

PYs, respectively. Starting from Wk26, background csDMARDs were initiated for approximately 18% of pts.

Based on As Observed data, for pts on UPA from BL through Wk48 on UPA15 [250/300 (83%)] and UPA30 [251/298 (84%)], clinical and functional outcomes continued to improve, or were maintained (Table 1). For pts continuing UPA15 and 30, DAS28-CRP<2.6 was 55% and 68%, and CDAI≤2.8 was 28% and 42%, respectively. Pts who were switched from cMTX to UPA15 or 30 at Wk14 had similar responses at Wk 48.

The most frequently reported treatment-emergent AEs were urinary tract infection, blood creatine phosphokinase increase, upper respiratory tract infection, nasopharyngitis, worsening of RA, herpes zoster (HZ), alanine aminotransferase increase, and bronchitis. The most frequently reported serious AE was pneumonia (8 events). Events/100PYs were numerically higher in the UPA30 vs UPA15 arm for HZ, and hepatic disorders, and were comparable for serious infections and malignancies excluding non-melanoma skin cancer (Table 2). Adjudicated venous thromboembolic events (VTE) were observed only on UPA15 (2 pts with deep vein thrombosis and 2 pts with pulmonary embolism; all patients had at least one risk factor for VTE).

Conclusion: UPA 15 or 30 monotherapy resulted in similar improvements in signs and symptoms and physical function through 48 wks. The overall benefit-risk profile of both doses of UPA was favorable based on safety and efficacy data through Wk48 but will be confirmed through an integrated safety analysis across all the ph 3 trials.

Abstract THU0191 –Table 1.

Table 1. Efficacy Endpoints at Week 48 (as observed): Percentage of patients with a response; n/N (%)

	cMTX→ UPA 15 MG	cMTX→ UPA 30 MG	UPA 15 MG	UPA 30 MG
ACR20	77/96 (80)	75/91 (82)	150/172 (87)	162/186 (87)
ACR50	63/94 (67)	55/92 (60)	121/174 (70)	133/185 (72)
ACR70	44/94 (47)	39/93 (42)	80/176 (46)	99/183 (54)
DAS28-CRP≤3.2	67/96 (70)	66/92 (72)	126/174 (72)	148/185 (80)
DAS28-CRP<2.6	56/96 (58)	50/92 (54)	96/174 (55)	126/185 (68)
CDAI≤10	69/95 (73)	65/90 (72)	123/172 (72)	142/185 (77)
CDAI≤2.8	26/95 (27)	19/90 (21)	48/172 (28)	77/185 (42)
Change from BL in HAQ-DI	-0.69	-0.73	-0.73	-0.83

Abstract THU0191 –Table 2.

Table 2. Adverse event (AE) summary; E/100PY

	UPA 15 MG N=318 PYs=336.0 E/100PYs	UPA 30 MG N=311 PYs=337.1 E/100PYs
Any Adverse Event	254.2	319.2
Serious AE	19.6	17.8
AE Leading To Discontinuation Of Study Drug	8.9	10.1
Serious Infection[§]	5.1	4.4
Herpes Zoster[¶]	3.3	7.7
Hepatic disorder[¥]	7.7	12.5
Any Malignancy (excluding NMSC)[ψ]	1.5	1.2
MACE (adjudicated)[δ]	0.9	1.5
Venous Thromboembolism (adjudicated)	1.2	0
Death[†]	0.9	0.3

E/100PY, events per 100 patient-years; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular (CV) event (CV death, non-fatal myocardial infarction [MI], non-fatal stroke)

[§]Serious Infection: Most frequently reported SI were pneumonia, bronchitis, cellulitis, HZ and UTI

[¶]Herpes zoster: mostly 1 or 2 dermatomes,1 opthalmic

[¥]Hepatic disorder: mostly transaminase elevations that were mild to moderate in severity.

[ψ]Malignancies: 5 breast cancers (UPA15: 3 pts, UPA30: 2 pts), 2 colorectal cancers (UPA15:1 pt, UPA30:1 pt), 1 non-Hodgkin's lymphoma (UPA15), 1 malignant melanoma (UPA30)

[δ]MACE : UPA15: 3 CV deaths; UPA 30: 2 non-fatal MI, 2 non-fatal stroke; 1 CV death

[†]Deaths: UPA15: 1 hemorrhagic stroke (ruptured aneurysm), 1 congestive cardiomyopathy and 1 sudden cardiac death; UPA30: 1 fatal MI.

REFERENCE:

[1] Smolen, et al. Arthritis and Rheumatol 2018 Nov 70;supp 10

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THU0192 UPADACITINIB MONOTHERAPY IMPROVES PATIENT-REPORTED OUTCOMES IN METHOTREXATE-NAÏVE PATIENTS WITH MODERATELY TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS: RESULTS FROM SELECT-EARLY

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Background: Monotherapy use of upadacitinib (UPA), a selective JAK1 inhibitor, demonstrated clinically meaningful improvement in the signs and symptoms of rheumatoid arthritis (RA) compared with methotrexate (MTX).[1] To better understand the impact of UPA treatment in RA from the patient's perspective, we examined the effect of UPA on patient-reported outcomes (PROs).

Objectives: To evaluate the effect of UPA monotherapy vs MTX at week 12 on PROs in SELECT-EARLY (NCT02706873), a randomised controlled trial in MTX-naïve patients with moderate to severe RA.

Methods: Patients were randomised 1:1:1 to receive once daily UPA (15 mg or 30 mg) or weekly MTX (titrated by Week 8). PROs assessed included Patient Global Assessment of Disease Activity (PtGA) by visual analogue scale (VAS), pain by VAS, physical function by Health Assessment Questionnaire Disability Index (HAQ-DI), fatigue by Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), duration and severity of morning (AM) stiffness, HRQoL by Short Form 36 (SF-36), and Work Productivity and Activity Impairment (WPAI) measure. Least square mean (LSM) changes from baseline (BL) to Week 12 were based on analysis of covariance. Percentages of patients reporting changes in PRO scores from BL to Week 12 $\geq$ minimum clinically important differences (MCIDs) or scores $\geq$ normative values (age- and gender-matched for SF-36 only) were determined for UPA and MTX groups; comparisons used chi-square tests. For each PRO, the incremental number needed to treat (NNT) to achieve clinically meaningful improvement from BL was calculated.

Results: Data from 945 patients (MTX: 314; UPA 15 mg: 317; UPA 30 mg: 314) were analysed. Mean age was 53 years; 76% were female; 49% had RA for <6 months. Statistically significant LSM changes from BL to Week 12 were reported for both doses of UPA vs MTX for all PROs (**Table**). At Week 2, both UPA doses had significantly higher proportions of patients reporting improvements $\geq$ MCID vs MTX in HAQ-DI, duration and severity of AM stiffness, pain, and PtGA. Compared with MTX at Week 12, a significantly greater proportion of patients receiving UPA at either dose reported improvements $\geq$ MCID in all PROs. A significantly greater proportion of patients receiving UPA also reported scores $\geq$ normative values for all PROs except SF-36 Mental Health (UPA 15 mg) and SF-36 General Health (both UPA doses) domains. For most PROs, NNTs with UPA ranged from 4 to 8 patients at Week 12.

Abstract THU0192 –Table 1.

LSM Changes From Baseline and Percentage of Responders at Week 12 After UPA Initiation							
PRO	Baseline Mean	LSM Changes From Baseline			Patients Reporting Improvements ≥MCID, n (%)		
	(n=945)	MTX (n=314)	UPA 15 mg (n=317)	UPA 30 mg (n=314)	MTX (n=314)	UPA 15 mg (n=317)	UPA 30 mg (n=314)
PtGA	65.8	−24.6	−34.9*	−38.0*	190 (60.5)	248 (78.2)*	230 (74.0)*
Pain VAS	66.5	−25.4	−36.3*	−39.7*	195 (62.1)	249 (78.5)*	241 (77.5)*
HAQ-DI	1.6	−0.5	−0.8*	−0.9*	189 (60.2)	248 (78.2)*	247 (79.4)*
FACIT-F	26.9	6.8	10.0*	9.6*	171 (54.5)	207 (65.5)*	203 (65.5)*
Duration AM stiffness[a]	144.7	−72.4	−106.0*	−111.5*	72 (23.0)[b]	120 (38.0)*[b]	115 (36.7)*[b]
Severity AM stiffness[c]	6.5	−3.0	−4.0*	−4.1*	222 (70.9)[b]	262 (82.9)*[b]	262 (83.7)*[b]
SF-36 PCS	33.2	5.8	10.1*	10.1*	182 (58.0)	250 (79.1)*	245 (78.5)*
SF-36 MCS	43.0	3.9	5.8*	5.8*	139 (44.3)	187 (59.2)*	165 (52.9)*
SF-36 PF	32.2	5.6	10.0*	10.1*	205 (65.3)	253 (80.1)*	245 (78.0)*
SF-36 RP	34.0	4.7	8.4*	8.6*	164 (52.2)	232 (73.4)*	221 (70.4)*
SF-36 BP	33.8	7.4	11.9*	11.9*	194 (61.8)	262 (82.9)*	249 (79.3)*
SF-36 GH	39.8	4.4	6.3*	6.8*	174 (55.4)	214 (67.7)*	219 (69.7)*
SF-36 VT	40.8	5.5	9.3*	8.6*	183 (58.3)	242 (76.6)*	221 (70.4)*
SF-36 SF	38.3	4.6	7.7*	8.1*	155 (49.4)	199 (63.0)*	195 (62.1)*
SF-36 RE	38.2	4.2	6.4*	6.8*	138 (43.9)	188 (59.5)*	176 (56.1)*
SF-36 MH	41.0	4.6	6.9*	6.8*	160 (51.0)	214 (67.7)*	200 (63.7)*
WPAI Work Impairment[d]	56.3	−9.8	−26.6*	−23.5*	47 (35.9)	87 (61.3)*	66 (55.0)*
WPAI Activity Impairment	62.8	−19.0	−27.6*	−31.2*	183 (58.3)	231 (73.3)*	233 (75.2)*

*$P<0.05$ for UPA vs MTX.
[a] Duration in minutes. [b] % responders reporting scores ≥minimal important difference. [c] Assessed on a numeric scale of 1–10, with 10 being the worst level. [d] Calculated only for employed patients.
AM, morning; BP, bodily pain; Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F); GH, general health; HAQ-DI, Health Assessment Questionnaire Disability Index; LSM, least squares mean; MCID, minimum clinically important difference; MCS, Mental Component Summary; MH, mental health; MTX, methotrexate; PCS, Physical Component Summary; PF, physical function; PRO, patient-reported outcome; PtGA, Patient Global Assessment of Disease Activity; RE, role emotional; RP, role physical; SF, social function; SF-36, 36-Item Short Form Health Survey; UPA, upadacitinib; VAS, visual analogue scale; VT, vitality; WPAI, Work Productivity and Activity Impairment questionnaire.

Conclusion: Among MTX-naïve patients with active RA, treatment with UPA 15 mg or 30 mg daily for 12 weeks resulted in statistically significant and clinically meaningful improvements in physical function, pain, fatigue, AM stiffness, HRQoL, and work productivity compared with MTX. The NNTs to achieve these improvements were favourable.

REFERENCE:

[1] van Vollenhoven R, et al. *Arthritis Rheumatol.* 2018;70(S9):983, abstract 891.

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THU0193

EFFICACY OF TOFACITINIB MONOTHERAPY, TOFACITINIB WITH METHOTREXATE AND ADALIMUMAB WITH METHOTREXATE IN PATIENTS WITH EARLY (≤2 YEARS) VS ESTABLISHED (>2 YEARS) RHEUMATOID ARTHRITIS: A POST HOC ANALYSIS OF DATA FROM ORAL STRATEGY

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. Greater improvements in efficacy outcomes have been reported with tofacitinib 5 mg BID ± csDMARDs in patients (pts) with early vs established RA.[1,2]

Objectives: This post hoc analysis of ORAL Strategy data evaluated the efficacy and safety of tofacitinib monotherapy, tofacitinib + methotrexate (MTX) and adalimumab (ADA) + MTX, stratified by baseline (BL) RA duration.

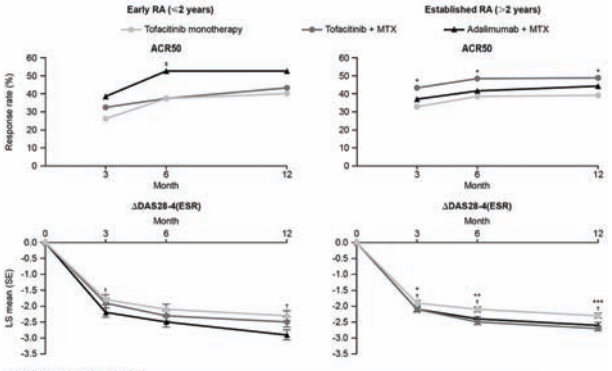
Methods: ORAL Strategy (NCT02187055) was a P3b/4, 1-yr, double–blind, triple-dummy, active comparator-controlled study. MTX inadequate-responder pts were randomised 1:1:1 to receive tofacitinib 5 mg BID (tofa mono), tofacitinib 5 mg BID + MTX (tofa+MTX), or ADA SC 40 mg Q2W + MTX (ADA+MTX); MTX was dosed at 15–25 mg/wk except in cases of intolerance/toxicity. In this analysis, pts were stratified by BL RA duration as having early (≤2 yrs) or established (>2 yrs) RA. Efficacy outcomes (Months [M]3, 6 and 12): ACR20/50/70; change from BL (Δ) in DAS28–4(ESR), SDAI and CDAI; and rates of DAS28-4(ESR)-, SDAI- and CDAI–defined LDA (≤3.2, ≤11 and ≤10, respectively) and remission (<2.6, ≤3.3 and ≤2.8, respectively). Nominal p values for treatment comparisons were calculated without multiplicity adjustment; p<0.05 was considered significant. Treatment-emergent AEs and serious AEs (SAEs) were assessed throughout the study.

Table: Demographics and disease characteristics at baseline, and safety up to Month 12

	Early RA (≤2 years) N=241			Established RA (>2 years) N=905		
	Tofacitinib monotherapy N=80	Tofacitinib + MTX N=83	Adalimumab + MTX N=78	Tofacitinib monotherapy N=304	Tofacitinib + MTX N=293	Adalimumab + MTX N=308
Baseline demographics and disease characteristics*						
Age (years), mean (SD)	47.1 (12.9)	46.2 (13.8)	49.2 (13.5)	50.4 (12.0)	51.0 (13.1)	51.0 (13.3)
Female, n (%)	66 (82.5)	69 (83.1)	60 (76.9)	253 (83.2)	242 (82.6)	260 (84.4)
RA duration (years), mean (SD)	1.0 (0.5)	1.1 (0.5)	1.0 (0.5)	10.4 (7.7)	9.4 (6.9)	10.0 (7.1)
DAS28-4(ESR), mean (SD)	6.6 (0.8)	6.4 (0.8)	6.4 (1.0)	6.5 (0.9)	6.6 (0.9)	6.5 (1.0)
SDAI, mean (SD)	41.9 (12.6)	38.9 (11.1)	39.9 (12.9)	39.8 (13.1)	42.4 (13.6)	39.8 (13.5)
CDAI, mean (SD)	40.0 (12.2)	37.2 (10.9)	38.2 (12.4)	38.2 (12.6)	40.5 (13.1)	38.2 (13.0)
HAQ-DI, mean (SD)	1.6 (0.6)	1.4 (0.7)	1.5 (0.6)	1.6 (0.6)	1.6 (0.6)	1.6 (0.6)
RF+, n (%)	45 (56.3)	42 (50.6)	47 (60.3)	214 (70.4)	203 (69.5)	212 (69.3)
Anti-CCP+, n (%)	59 (73.8)	56 (67.5)	52 (66.7)	232 (76.3)	223 (76.1)	246 (79.9)
Prior medications						
TNFi, n (%)	2 (2.5)	1 (1.2)	0	26 (8.6)	15 (5.1)	19 (6.2)
Non-TNFi, n (%)	1 (1.3)	1 (1.2)	0	18 (5.9)	13 (4.4)	20 (6.5)
MTX dose[a] (mg/wk)	16.4 (3.2)	17.1 (3.1)	16.9 (3.7)	16.6 (3.5)	16.5 (3.9)	16.3 (3.7)
GC use, n (%)	50 (62.5)	47 (56.6)	39 (50.0)	178 (58.6)	168 (57.3)	184 (59.7)
GC dose[a] (mg/day), mean (SD)	7.0 (3.1)	6.6 (2.4)	6.5 (3.5)	7.7 (15.5)	6.4 (2.6)	6.4 (2.4)
Safety						
AE	52 (65.0)	47 (56.6)	53 (67.9)	174 (57.2)	184 (62.8)	200 (64.9)
SAE	10 (12.5)	2 (2.4)	8 (10.3)	25 (8.2)	24 (8.2)	16 (5.2)

*N for each assessment may differ from N for each treatment group; [a]Average dose immediately prior to randomisation
AE, adverse event; Anti-CCP, anti-cyclic citrullinated peptide antibody; CDAI, Clinical Disease Activity Index; DAS28-4(ESR), Disease Activity Score in 28 joints based on erythrocyte sedimentation rate; GC, glucocorticoid; HAQ-DI, Health Assessment Questionnaire-Disability Index; MTX, methotrexate; RA, rheumatoid arthritis; RF, rheumatoid factor; SAE, serious adverse event;SDAI, Simplified Disease Activity Index; SD, standard deviation; TNFi, tumour necrosis factor inhibitor; wk, week

Figure: ACR50[a] response rates and ΔDAS28-4(ESR) up to Month 12 (FAS)



[a]Using non-responder imputation
*p<0.05, **p<0.001, ***p<0.0001 tofacitinib monotherapy vs tofacitinib + MTX; †p<0.05 tofacitinib monotherapy vs adalimumab + MTX; ‡p<0.05 tofacitinib + MTX vs adalimumab + MTX
Δ, change from baseline; ACR, American College of Rheumatology; DAS28-4(ESR), Disease Activity Score in 28 joints based on erythrocyte sedimentation rate; FAS, full analysis set; LS, least squares; MTX, methotrexate; RA, rheumatoid arthritis; SE, standard error

Abstract THU0193 – Figure 1

Results: 241 pts had early RA (tofa mono: N=80; tofa+MTX: N=83; ADA +MTX: N=78; mean RA duration: 1.0–1.1 yrs); 905 pts had established RA (tofa mono: N=304; tofa+MTX: N=293; ADA+MTX: N=308; mean RA duration: 9.4–10.4 yrs). BL demographics and disease characteristics were generally comparable for early vs established RA pts, with some expected differences (the latter were slightly older, and a greater proportion had received prior bDMARDs); RF+ and anti-CCP+ rates were higher for established RA pts (Table). ACR50 and ΔDAS28-4(ESR) were generally similar for tofa mono and tofa+MTX up to M12 in early RA but significantly greater with tofa+MTX in established RA ($p<0.05$); ADA+MTX was not statistically different vs tofa+MTX in early RA (Figure). Trends were similar for all outcomes. AE rates were generally similar in early vs established RA. Trends for SAEs were less clear; rates were lowest for tofa+MTX in early RA and slightly higher for both tofacitinib arms vs ADA+MTX in established RA (Table).

Conclusion: Efficacy was similar for tofa mono and tofa+MTX in early RA, and significantly higher with tofa+MTX in established RA. ADA+MTX was numerically but not always significantly more effective than tofacitinib in early RA. AE rates were generally similar regardless of BL RA duration. These findings, especially in established RA, are consistent with the conclusion of the primary analysis.[3] Limitations to this post hoc analysis include low numbers of early RA pts.

REFERENCES:

[1] Hall S, et al. Arthritis Rheum 2016; 68(S10): 1999-2001.
[2] Fleischmann RM, et al. RMD Open 2016; 2: e000262.
[3] Fleischmann RM, et al. Lancet 2017; 390: 457-468.

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Ltd., and UCB Japan, Speakers bureau: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Astellas Pharma Inc, Diaichi Sankyo Co. Ltd., Eisai Co. Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co. 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THU0194 SELECTIVE INHIBITION OF JANUS KINASE 1 (JAK1) BY FILGOTINIB MODULATES THE DISEASE-ASSOCIATED WHOLE BLOOD TRANSCRIPTIONAL PROFILE OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: Filgotinib (FIL), an oral selective JAK1 inhibitor, was safe and efficacious in FINCH2, a randomized, double-blind, placebo-controlled, phase 3 study in patients with active rheumatoid arthritis (RA) who had an inadequate response to biologic disease-modifying anti-rheumatic drugs (bDMARDs).[1] The whole blood transcriptional profile of patients was evaluated.

Objectives: Identify RA-associated gene transcripts and biological pathways that are altered in response to FIL treatment and interrogate FIL-modulated biomarkers correlated with disease activity.

Methods: RA patients enrolled in FINCH2 (n=449) were randomized 1:1:1 and received FIL (100 mg, 200 mg) or placebo (PBO) once daily plus a stable background dose of methotrexate. Whole blood samples from enrolled patients were collected at baseline (BL) and weeks 4 and 12 for RNA sequencing. Spearman's rank correlation of BL disease activity (DAS28[CRP]) was calculated to define disease-associated genes (DAGs) and pathways (DAPs). Differential expression of 5155 genes and FIL-specific changes were determined after subtracting gene expression changes in the PBO group. Biological pathways (910 total) were analyzed by Gene Set Enrichment Analysis (GSEA) or single-sample GSEA. A false-discovery rate of 5% was applied for all analyses.

Results: At weeks 4 and 12, more genes were significantly differentially expressed in the FIL 200 mg arm vs the 100 mg arm; and, consistent with increased clinical efficacy, the average magnitude of change in gene expression was larger. No single gene reached a threshold of significance for differential expression in PBO-treated patients. FIL treatment induced a stronger reversal of DAG expression (rho range: –0.35 to –0.59) compared to PBO (rho –0.3) at weeks 4 and 12. DAGs most prominently reversed by FIL included *FAM20A* and *METTL7B*. Top-ranked pathways associated positively with disease activity at BL included inflammatory response, complement activity, and cell cycle. Hallmark pathways most significantly reduced following FIL treatment included IL-6/JAK/STAT, inflammatory, and interferon response, consistent with observed effects of FIL in preclinical models and phase 2 DARWIN studies. In contrast, IL-6/JAK/STAT signaling increased at weeks 4 and 12 with PBO. DAPs showed a similar reversal of gene expression (rho range: –0.43 to –0.58) with FIL at weeks 4 and 12 compared to PBO (rho range: –0.007 to –0.024) suggesting that FIL treatment may attenuate RA-mediated IL-6/JAK/STAT signaling, inflammation, and other RA-associated pathways correlated with clinical outcome measures.

Conclusion: The whole blood transcriptional profile of patients following FIL treatment showed a dose-dependent reduction in the expression of

JAK/STAT signaling and inflammation genes. No significant changes in the expression of DAGs were observed in PBO-treated patients. FIL also broadly reversed DAGs and DAPs, and ongoing research is exploring the relationship between changes in gene and pathway modulation across a range of clinical endpoints.

REFERENCE:

[1] Genovese MC, et al. ACR 2018. Abstract L06.

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THU0195 ULTRASOUND EVALUATION FOR MONITORING RESPONSE TO BARICITINIB IN RHEUMATOID ARTHRITIS PATIENTS AT EARLY STAGE AFTER TREATMENT

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Background: Baricitinib (bari) is approved for treating moderate-severe RA in many countries including Japan. Bari, an oral Janus kinase (JAK1)/JAK2 selective inhibitor, has shown the efficacy in patients with rheumatoid arthritis (RA) and in adequate response to conventional synthetic DMARDs in some clinical trials. Thanks to technological improvement in Ultrasound (US) equipment and the use of internationally approved scanning techniques and definitions for normal findings and pathology, US monitoring are widely used to assess inflammatory and structural lesions in daily clinic.

Objectives: To monitor the short-term response to baricitinib therapy in bilateral wrist and finger joints of RA patients by US and to evaluate correlation between US findings and clinical assessments.

Methods: We included 23 Japanese patients with RA who have inadequate response to csDMARDs or bDMARDs (biologics-naïve 19 cases and biologics-experience 4 cases). Patients were scheduled to receive bari 4mg or 2mg once daily dose as monotherapy or in combination with other csDMARDs. They were allowed to be decreased predonisolone when their disease activity was improved. Clinical evaluation was performed blinded to the results of the US assessment that had been carried out on the same day. Swollen joint counts on 28 joints (SJC), tender joint counts on 28 joints (TJC) and Clinical Disease Activity index (CDAI) were registered for each patient. Each parameter was evaluated at baseline, after 1 month and 3 months. Four sonographers, experiences in musculoskeletal US, who were blinded to the clinical and laboratory data, performed the US examination. The US assessment and scanning technique included evaluation of synovial sites in 26 joints (wrist- radiocarpal, midcarpal, radiocarpal joints, 1 - 5 MCP joints and 1 - 5 PIP joints). Gray scale (GS) and power doppler (PD) were graded according to a 0 - 3 semi-quantitative score depending on their severity [1]. We calculated total scores for each patient in GS (GS score) and PD (PD score) differently. We compared the change of GS score and PD score. In addition, we evaluated the correlation between the changes in GS score or PD score and the variations in clinical evaluation items.

Results: Patient's backgrounds were provided in Table 1. All clinical parameters were significantly improved at each follow-up periods after treatment. Mean SJC, TJC and CDAI decreased from 7.52 ± 3.89, 8.26 ± 3.82 and 26.89 ± 9.48 at baseline to 1.52 ± 1.75, 1.82 ± 1.89 and 6.40 ± 5.17 at 1month and to 1.27 ± 1.39, 1.27 ± 1.38 and 3.99 ± 3.49 at 3 months respectively (Table 2). GS and PD score at each follow-up periods after treatment were also significantly improved. Mean GS and PD decreased from 8.11 ± 3.41 and 12.42 ± 4.45 at baseline to 3.63 ± 2.45 and 7.73 ± 4.70 at 1month and to 2.10 ± 1.49 and 4.21 ± 2.70 at 3 months respectively (Table 2). GS score significantly correlated with SJC (r= 0.586, p<0.01), TJC (r=0.602, p<0.01) and CDAI (r=0.656, p<0.01). PD score significantly correlated with SJC (r= 0.606, p<0.01), TJC (r=0.624, p<0.01) and CDAI (r=0.658, p<0.01).

Conclusion: Baricitinib therapy had significantly improved disease activity of RA patients at early stage after the treatment. GS and PD score were also significantly improved and correlated with clinical parameters. These data confirm that the use of US evaluation is very useful method for evaluating the monitoring the response of treatment and feasible method complementary to clinical assessment for guiding the clinician in the appropriate therapeutic decision.

Abstract THU0195 –Table 1.

Table 1. Patients' background (mean ± SD)

Age (years)	66.6 ± 9.4	RF positive (%)	73.9
Disease duration (years)	3.93 ± 5.07	ACPA positive (%)	78.2
MTX dose (mg/week)	7.65 ± 8.82	Stage (I/II/III/IV)	6 / 10 / 7 / 0
PSL dose (mg/day)	1.28 ± 1.80	Class (I/II/III/IV)	3 / 8 / 10 / 2

Table 2. Changes of clinical assessments and GS/PD scores (mean ± SD)

	baseline	1 month	3 months
SJC	7.52 ± 3.89	1.52 ± 1.75*	1.27 ± 1.39*
TJC	8.26 ± 3.82	1.82 ± 1.89*	1.27 ± 1.38*
CDAI	26.89 ± 9.48	6.40 ± 5.17*	3.99 ± 3.49*
GS score	8.11 ± 3.41	3.63 ± 2.45*	2.10 ± 1.49*
PD score	12.42 ± 4.45	7.73 ± 4.70*	4.21 ± 2.70*

*p < 0.01 vs baseline

Disclosure of Interests: None declared

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THU0196 EFFICACY AND SAFETY UP TO 24 WEEKS OF BARICITINIB FOR JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL WORLD MULTICENTER CLINICAL DATA

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Background: Baricitinib (bari) is approved for treating moderate–severe rheumatoid arthritis (RA) in many countries, including Japan. Bari is an oral Janus kinase (JAK1)/JAK2 selective inhibitor that has shown good efficacy in patients with RA and adequate response to conventional synthetic DMARDs in some clinical trials. However, there have been few reports about the efficacy and safety of bari in real-world clinical data.

Objectives: We evaluated the efficacy and safety of bari for Japanese RA patients who have an inadequate response to DMARDs in real-world multicenter clinical data.

Methods: We included 32 Japanese patients with RA who show an inadequate response to csDMARDs or bDMARDs (biologics-naïve (BN group): 19 cases and biologics-experience (BE group): 13 cases). Patients were scheduled to receive bari 4 or 2 mg once daily dose as a monotherapy or in combination with other csDMARDs. If the disease activity was not improved within 3 months in patients treated with bari 2 mg, the bari dose was increased to 4 mg. Patients were allowed to decrease their predonisolone treatment if their disease activity improved. First, we evaluated changes in the number of swollen joints and tender joints, CRP (mg/dL), visual analog scale of pain (0–100 mm), patient's global assessment (0–100 mm), Clinical Disease Activity Index, and HAQ-DI for 24 weeks. Second, we evaluated the proportion of patients with adverse events (AEs) and progress after these AEs.

Results: Patients' backgrounds are provided Table 1. Many patients felt the early effect of bari. At 1 month after treatment, ACR20/50/70 were 84.2%/63.2%/21.1% in the BN group and 53.8%/23.1%/7.7% in the BE group, respectively. All measurement items of disease activity and patient-reported outcomes were significantly improved after treatment. This tendency continued until the final evaluation (Table 2). At 24 weeks, remission and low disease activity rates were 47.4% and 78.9% in the BN group and 15.4% and 61.5% in the BE group, respectively. One case in the BE group discontinued bari treatment due to no response. These data were better than clinical trial data (Japanese subpopulation data from RA-BEAM and RA-BUILD studies[1]). We determined that we could take an aggressive treatment course according to treat to target strategies in real-world clinics. Greater early improvements in HAQ-DI were seen. HAQ-DI was improved significantly at each evaluation time point after bari treatment (Table 2).

We had two cases of mild pneumonia and one case of herpes zoster. These cases were improved after 1–2 weeks of antibiotic therapy or antiviral drug therapy. One case discontinued bari. Although the other two cases withdrew from bari treatment, we could restart it. We think that the most important reason why they did not advance in severe because we were able to diagnose and treat these cases earlier. No patient showed malignancies, cardiovascular events, or deep vein thrombosis. No patient discontinued bari treatment due to AEs. Also, increases in blood pressure and d-dimer were not observed during the follow-up period. Other mild AEs, including upper respiratory tract infection, nasopharyngitis, and laboratory data abnormalities occurred in 62.5% of patients (Table 3). A small increase in lymphocyte count and small decrease in neutrophil count

were seen at 1 month after bari treatment. These either remained flat or improved 3 months after treatment. An increase from baseline in creatinine was also seen. These tendencies continued to the final observation. Moving forward, these items should be monitored for long-term evaluation.

Abstract THU0196 –Table 1.

Table 1. Patients' background (mean ± SD)

	Bio naïve	Bio experienced
Age (years old)	66.4±9.0	69.8±11.2
Disease duration (years)	3.81±5.80	4.57±3.13
Male / Female	3 / 16	4 / 9
RF positive / ACPA positive (%)	68.4 / 73.7	84.6 / 76.9
Stage (I/II/III/IV) / Class (I/II/III/IV)	(10/5/4/0) / (4/8/4/3)	(5/4/3/1) / (2/5/4/2)
MTX dose (mg/week)	8.94±9.23	6.67±7.10
PSL dose (mg/day)	1.41±1.87	1.33±2.06

Table 3. Adverse events

Bari group + TNFi group	N (%)
Pneumonia	2 (6.3)
Herpes zoster	1 (3.1)
upper respiratory tract infection	5 (15.6)
nasopharyngitis	3 (9.3)
Laboratory data abnormality	15 (46.9)

Table 2. Change of clinical assessments (mean ± SD)

(Bio naïve)	baseline	1 month	3 months	6 months
SJC	7.06±2.54	1.68±1.70**	0.75±1.29**	0.66±0.85**
TJC	7.68±3.18	2.19±1.94**	1.13±1.50**	0.98±1.05**
CRP (mg/dl)	2.00±1.50	0.67±0.93**	0.17±0.25**	0.15±0.24**
CDAI	24.92±7.26	7.11±4.84**	3.87±4.31**	2.94±3.13**
Pain VAS	50.3±21.4	21.4±16.8**	15.3±13.8**	12.0±9.8**
PGA	49.9±18.6	21.2±17.6**	11.5±13.8**	9.8±12.5**
HAQ-DI	0.76±0.33	0.43±0.24**	0.30±0.18**	0.28±0.17**

**p < 0.01 vs baseline

(Bio experienced)	baseline	1 month	3 months	6 months
SJC	7.78±5.65	2.22±1.92*	0.78±1.09*	0.75±1.49*
TJC	8.67±4.82	2.22±1.79*	1.78±1.72*	1.62±1.84*
CRP (mg/dl)	4.40±4.51	0.82±1.45**	0.78±1.00*	0.72±1.10*
CDAI	28.77±12.30	9.06±6.82*	6.23±6.16*	6.28±6.50*
Pain VAS	59.0±28.0	29.1±27.5*	23.8±25.0*	22.3±27.9*
PGA	66.6±25.2	25.4±24.3*	20.6±26.3*	21.6±25.4*
HAQ-DI	1.04±0.56	0.68±0.57*	0.56±0.47*	0.50±0.54*

*p < 0.01 vs baseline

Conclusion: These data showed that bari has a favorable benefit–risk balance in a real-world clinic and thus may be considered as a good treatment option for Japanese RA patients who have an inadequate response to csDMARDs or bDMARDs.

REFERENCE:

[1] Tanaka Y, et al. Mod Rheumatol 2018;28:583-91

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THU0197 MONOTHERAPY WITH UPADACITINIB IN MTX-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 48 WEEKS FROM THE SELECT-EARLY STUDY

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Background: Upadacitinib (UPA), a JAK1-selective inhibitor, was efficacious as monotherapy upto 24 weeks (wks) in MTX-naive patients (pts) with active RA.[1]

Objectives: To assess safety and efficacy of UPA through 48 wks in an ongoing extension of the ph 3 SELECT-EARLY RCT.

Methods: SELECT-EARLY had a 48-wk double-blind active comparator-controlled period. Pts were initially randomized to monotherapy (mono) with UPA 15 or 30 mg or MTX (titrated up to Wk8). Rescue therapy was offered if pts met the following: (1) From Wk 12-24, pts without ≥20% improvement from BL (Δ) in both TJC and SJC at 2 consecutive visits continued blinded study drug with optimized background RA medications. (2) At Wk26, pts with CDAI ≤2.8 continued their original study drug; in pts with CDAI >2.8 and <20% Δ in TJC and SJC, for those on MTX, UPA15/30mg was added; for those on UPA15/30mg, MTX was added. For pts with CDAI>2.8 but ≥20%Δ in TJC and SJC, background medications were optimized. Background csDMARDs could be initiated after Wk26. After Wk48, pts could continue in a long-term extension. Efficacy data up to the Wk48 visit are reported based on initial randomized treatment. For binary non-radiographic endpoints, NRI was used for missing data and rescue handling; for continuous non- radiographic endpoints, LOCF was used for rescue handling. Radiographic analyses are based on linear extrapolation for missing data imputation and rescue handling. Adverse events (AE) per 100 pt yrs (PY) are summarized up to a cut-off date of Aug 16 2018.

Results: Of 945 pts randomized and treated, 747(79%) completed Wk48 treatment, 163 (17.2%) discontinued (D/C) study drug prior to Wk48, 35 pts (4%) had not completed the Wk48 treatment as of this analysis. Primary reasons for D/C were AEs for 62 pts (6.5%), and lack of efficacy in 20 pts (2.1%). At Wk26, UPA15/30 was added for 37 (12%) of pts on MTX; MTX was added for 19 (6%) and 9 (3%) of pts on UPA15 and UPA30, respectively. Cumulative exposures to MTX mono, UPA15 mono and UPA30 mono were 314.4, 343.1 and 336.7 PYs, respectively. Through Wk48, pts on UPA15 and 30 vs MTX continued to have significantly greater improvements in clinical, functional and pt-reported outcomes (except FACIT-F for UPA15, p=.058 vs MTX) (Table 1). At Wk 48, CDAI Remission (REM) was achieved by 33% and 40% of pts on UPA15 and 30 respectively vs 17% on MTX; 28% and 33% vs 13% achieved Boolean REM. At Wk48, ΔmTSS were significantly less on UPA15 and UPA30 vs MTX. The safety profile of UPA15 and UPA30 mono was generally similar to MTX, except for total AEs and herpes zoster, which were higher with UPA15 and 30 vs MTX (Table 2). There were 11 deaths (including 3 non-treatment emergent deaths) due to varied causes.

Abstract THU0197 –Table 1.

Table 1. Efficacy Endpoints at Week 48

	MTX N=314	UPA 15 MG N=317	UPA 30 MG N=314
ACR20, %	57	74***	75***
ACR50,%	43	63***	68***
ACR70,%	29	51***	53***
DAS28-CRP LDA (≤3.2), %	39	59***	66***
DAS28-CRP <2.6, %	29	49***	53***
CDAI LDA, (≤10), %	43	60***	64***
CDAI REM, (≤2.8), %	17	33***	40***
Boolean REM, %	13	28***	33***
Change in HAQ-DI	-0.74	-0.96***	-1.04***
Change in FACIT-F	8.5	10.1#	11.6***
Change in mTSS§	1.00	0.03***	0.14***

Results are based on NRI (binary endpoints), LOCF for rescue (change in HAQ-DI, FACIT-F), or linear extrapolation (change in mTSS); ***, p<.001 vs MTX; #p=.058;
Boolean REM: TJC ≤1, SJC ≤1, CRP ≤1 mg/dl, PGA ≤1 (0–10 scale)
§mTSS from 2nd reading session of radiographs at Wk48

Abstract THU0197 –Table 2.

Table 2. Treatment emergent adverse event (AE) summary; E/100PY in Patients on monotherapy (censored at time of change to combination exposure of UPA+MTX/csDMARD)

	MTX MONO N=314, PYS=314.4	UPA 15 MONO N=317 PY=343.1	UPA 30 MONO N=314 PY=336.7
Any Adverse Event	303.1	345.4	358.2
Serious AE	11.8	14.3	15.4
AE Leading To D/C Of Study Drug	8.9	11.4	10.7
Serious Infection	2.9	4.1	5.0
Herpes Zoster†	1.3	6.4	4.8
Hepatic disorder*	19.7	18.7	15.7
Any Malignancy (excluding NMSC)‡	1.0	1.2	0.6
MACE (adjudicated)‖	0.6	0.9	1.2
VTE (adjudicated)¶	0.6	0	0.3
Deaths#	0.3	1.2	1.8

†Herpes zoster: most involved a single dermatome and were non-serious. No cases of CNS involvement.
*Hepatic disorders: majority were asymptomatic transaminase elevations.
‡Malignancies excl. NMSC: MTX: 1 malignant neoplasm of ovary, 1 pt with gall bladder adenocarcinoma and hepatic cancer; UPA15: 1 malignant neoplasm progression, 1 metastatic malignant melanoma, 1 squamous cell carcinoma of lung, 1 uterine carcinoma in situ;
UPA30: 1 cervix cell carcinoma, 1 uterine cancer
‖MACE (includes cardiovascular [CV] death, non-fatal Myocardial infarction [MI], non-fatal stroke):
MTX: 1 CV death, 1 non-fatal stroke; UPA15: 1 CV death, 1 pt had 2 adjudicated events: a non-fatal MI, followed by CV death (due to hypoxic encephalopathy, not MI); UPA30: 3 CV deaths, 1 non-fatal MI
¶VTE: MTX: 1 pt with PE, 1 pt with DVT and PE; UPA30: 1 DVT
#Deaths (includes non-treatment emergent [NTE] deaths): MTX: 1 due to acute MI; UPA15: 2 due to MI (1 was NTE), 1 due to malignant melanoma and malignant neoplasm (NTE), 1 non-CV death; UPA30: 1 due to pneumonia /sepsis, 1 fatal MI, 2 CV deaths, 1 due to peritonitis, 1 CV death due to other causes (NTE); 1 death due to meningitis was reported on combination of UPA30+csDMARDs

Conclusion: UPA15 and 30 monotherapy continued to show significant improvements in RA signs and symptoms and inhibition of structural damage vs MTX through 48 wks. Only a small proportion of pts required MTX addition to UPA mono at Wk26 to achieve and maintain response. The safety profile based on all exposure remained consistent with ph 2 and 3 RCTs in RA, although an integrated safety analysis of UPA across the full ph 3 RA program will provide a more comprehensive understanding of the benefit:risk profile of UPA in RA.

REFERENCE:

[1] van Vollenhoven R, et al. Arthritis Rheum 2018;70

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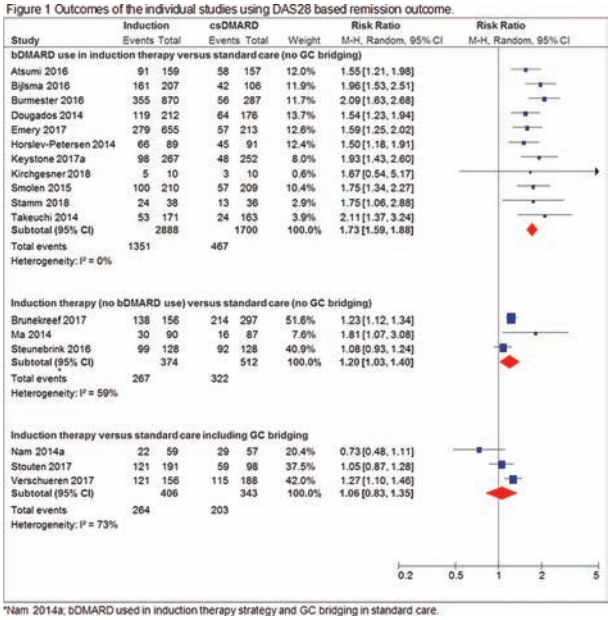
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THU0198 EFFECTIVENESS OF REMISSION-INDUCTION STRATEGIES FOR EARLY RHEUMATOID ARTHRITIS (RA): A SYSTEMATIC LITERATURE REVIEW

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Background: Several trials studied initiation of therapy in early RA patients with a more intensive strategy than the standard disease modifying anti-rheumatic drug (DMARD) strategy according to current guidelines, with the aim of rapidly inducing clinical remission (remission-induction strategies).
Objectives: To establish in early RA patients the effectiveness of remission-induction strategies compared to standard DMARD strategies according to current guidelines.
Methods: A systematic literature review was performed, searching Embase and Medline October 2018 for RCTs and other comparative studies in early RA patients, published the past 5 years. Induction therapy was defined as initiating treatment with a biological (b)DMARD or a targeted small molecule (ts)DMARD, both with or without a conventional synthetic (cs)DMARD, or initiating a csDMARD with moderately-high dosed glucocorticoids (GCs), with delayed tapering (not 'bridging therapy') or starting ≥2 csDMARDs. Standard DMARD strategy was defined as starting monotherapy with a csDMARD, with or without GCs as bridging therapy.
The outcome was remission according to a validated disease activity index or the Boolean definition.[1] Numbers of patients were extracted from all studies and relative risks (RR) for achieving remission with 95% confidence intervals (95%CI) per study were calculated. Subgroup analyses were performed for different definitions of remission, the use of a b/tsDMARD as part of the induction therapy strategy (yes/no) and the use of concomitant GC bridging therapy (yes/no) in standard DMARD strategies.
Results: Included were 22 clinical studies, involving 4435 patients in induction strategies and 3314 in standard DMARD strategies. For remission, 17 studies applied the criterion of DAS28 <2.6, 12 the Boolean remission definition, 7 CDAI ≤2.8 and 10 studies SDAI ≤3.3. Remission had to be present during 6 to 12 months in all studies. Heterogeneity in study design prohibited providing an overall pooled effect estimate, but for subgroups pooled estimates were given for descriptive purposes.
In the figure we provide results for studies applying the DAS28 remission definition. Of those studies, 13/17 (76%) showed a statistically significant effect in favour of induction therapy. The pooled RR of achieving remission for strategies initiating bDMARDs was 1.73 [95%CI 1.59 to 1.88] versus the standard DMARD strategy without GC bridging, and it was 1.20 [95%CI 1.03 to 1.40] for induction strategies without bDMARD versus standard DMARD strategies without GC bridging. No superior effect of any induction strategy was found compared to that of standard DMARD strategies with GC bridging (pooled RR 1.06, 95%CI 0.83 to 1.35).
When using other remission definitions, all induction strategy studies with Boolean/CDAI/SDAI outcomes applied a b/tsDMARD, and 63%, 100% and 78%, respectively found a statistically significantly superior effect compared to standard DMARD strategies without GC bridging; however, compared to standard DMARD strategies with GC bridging, only trends in the same direction were found.

Figure 1 Outcomes of the individual studies using DAS28 based remission outcome.



*Nam 2014a: bDMARD used in induction therapy strategy and GC bridging in standard care.

Abstract THU0198 – Figure 1

Conclusion: Induction therapy strategies initiated in early RA patients are more effective in achieving remission compared to standard DMARD strategies. However, their benefit compared to that of a standard DMARD strategy with GC bridging seems to be limited.

REFERENCES:

[1] Felson DT, et al. Arthritis Res Ther. 2011;63;573-586

Akdemir G, et al. RMD Open. 2018;4
Atsumi T, et al. Ann Rheum Dis. 2016;75:75-83
Bijlsma JWJ, et al. Lancet. 2016;388:343-355
Brunekreef T, et al. Ann Rheum Dis. 2017;76:147-148
Burmester GR, et al. Ann Rheum Dis. 2016;75:1081-1091
de Jong PH, et al. Ann Rheum Dis. 2014;73:1331-1339
Dougados MR, et al. Rheumatol. 2014;74:1233-1240
Emery P, 2017 et al. Ann Rheum Dis. 2017;76:96-104
Horslev-Petersen K, et al. Ann Rheum Dis. 2014;73:654-661
Keystone EC, 2017 et al. Arthritis Rheum. 2017;69.
Keystone EC, 2017a et al. RMD Open. 2017;3
Kirchgesner T, et al. Ann Rheum Dis. 2018;77:1764
Ma MY, et al. J Rheumatol. 2014;41:1298-1303
Nam JL, a et al. Ann Rheum Dis. 2014a;73:75-85
Nam JL, b et al. Ann Rheum Dis. 2014b;73:1027-1036
Smolen JC, 2014 et al. Lancet. 2014;383:321-332
Smolen JC, 2015 et al. Arthritis Res Ther. 2015;17:157
Stamm TA, et al. Arthritis Res Ther. 2018;20
Steunebrink LMM, et al. Arthritis Res Ther. 2016;18:60
Stouten V, et al. Ann Rheum Dis. 2017;76:147
Takeuchi T, et al. Ann Rheum Dis. 2014;73:536-543
Ter Wee MM, et al. Ann Rheum Dis. 2015;74:1233-1240
Verschueren P, et al. Ann Rheum Dis. 2017;76:511-520

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THU0199 PHARMACOKINETICS, SAFETY AND TOLERABILITY OF SINGLE- AND MULTIPLE- DOSE ONCE-DAILY BARICITINIB IN CHINESE HEALTHY VOLUNTEERS – A RANDOMIZED PLACEBO-CONTROLLED STUDY

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Background: Baricitinib, an oral selective inhibitor of JAK1 and JAK2, is efficacious in patients with moderately to severely active rheumatoid arthritis and an inadequate response to methotrexate.
Objectives: To evaluate the pharmacokinetics (PK), safety and tolerability of baricitinib when given orally as single and multiple doses in healthy Chinese subjects.
Methods: This was a single-site, subject- and investigator-blinded, randomized, and placebo-controlled study (NCT02758613) conducted from 04 May 2016 to 25 July 2016. Eligible subjects were healthy Chinese adults ($\geq$18 years) with a body mass index of 19.0 to 24.0 kg/m^2 (inclusive). Subjects received a once daily dose (QD) of baricitinib 2, 4 or 10 mg or placebo on Day 1 (single dose) and Days 4 through 10 for 7 consecutive days (multiple dose). Safety assessments were performed throughout the treatment period. Plasma PK samples were collected up to 48 hours after dosing on Days 1 and 10, with predose samples collected prior to dosing on Day 1 and Days 4 through 10. PK parameters were calculated using noncompartmental analysis.
Results: A total of 33 healthy volunteers were randomized and received at least 1 dose of study drug (placebo, n=8; baricitinib 2 mg, n=8; baricitinib 4 mg, n=9; baricitinib 10 mg, n=8). All subjects were male and the mean age was 27.8 years. After both single- and multiple-dose administration, baricitinib 2 to 10 mg was rapidly absorbed, reaching peak plasma concentrations within 0.5 to 1 hour (median). Plasma concentrations declined rapidly following attainment of peak concentrations, with a mean terminal half-life of 5.7 to 7.3 hours. Steady state plasma concentrations of baricitinib were achieved after the second day of QD dosing, with minimal accumulation of baricitinib in plasma (up to 10%) during 7 days of QD oral doses of 2 to 10 mg baricitinib. Single- and multiple-dose mean values for $AUC_{(0-\infty)}$ and C_{max} appeared to increase in an approximately dose-proportional manner across the dose range. Overall incidence of treatment-emergent AEs (TEAEs) is 33.3%. All TEAEs reported were mild in severity, with no serious AEs reported and no subjects were withdrawn due to AEs. Although there was an apparent increase in the incidence of drug-related TEAEs over the 2 to 10 mg dose range, the incidence of drug-related TEAEs at the 10 mg dose was comparable to placebo.
Conclusion: The PK of baricitinib in Chinese healthy subjects were characterized by rapid absorption and elimination following single and multiple oral doses of up to 10 mg. Systemic exposure to baricitinib increased in an approximately dose-proportional manner following single and multiple doses. Single and multiple oral doses of daily-administered baricitinib up to 10 mg were well tolerated by healthy Chinese subjects.
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THU0200 DRUG UTILISATION IN PEOPLE WITH EARLY RHEUMATOID ARTHRITIS IN THE UNITED KINGDOM

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Background: Despite a growing body of evidence in the pharmacological management of people with early rheumatoid arthritis (RA), there is still uncertainty concerning the most effective treatment regimen. Until 2018, guidance for England and Wales stated that everyone with early RA should receive combination therapy with 2 or more conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) in parallel. However, from epidemiological studies and anecdotal information, we know that this has not been the case in practice.
Objectives: (i) To determine the proportion of patients with new onset RA who start methotrexate (MTX) either alone or in combination with another csDMARD (ii) to describe which combinations are currently being prescribed and (iii) to describe the characteristics associated with the choice of initial RA treatment strategy
Methods: Consecutive patients with RA participating in the Rheumatoid Arthritis Medication Study (RAMS), a large UK study recruiting patients starting MTX for the first time, were eligible. Data on demographics, disease activity, comorbidity and all RA treatments are captured at baseline, 6 and 12 months following start of MTX. Analysis was limited to patients starting MTX within the first 2 years of symptom onset as part of their first treatment regimen for RA. Prevalent users of alternative csDMARDs, defined as use > 6 weeks prior to MTX start, were excluded. Participants were categorised as either starting MTX monotherapy or MTX in combination with another csDMARD (defined as started +/- 6 weeks of MTX start date). Baseline characteristics were compared between monotherapy and combination therapy groups using descriptive statistics.
Results: 1,374 patients with a mean (SD) age of 58 (14) years were included in this study; 64% were female. At baseline, 996 (76%) started MTX monotherapy and 316 (24%) started MTX/csDMARD combination therapy (84% with hydroxychloroquine and 16% with sulphasalazine). Patients starting combination therapy were younger (p<0.005), with higher DAS28 scores (p<0.005), higher HAQ scores (p<0.05), lower MTX starting doses (p<0.005), and shorter symptom duration (p<0.05) compared with the monotherapy group.
Conclusion: These data show that despite national guidelines recommending combination csDMARD therapy in all patients diagnosed with RA, over three quarters of patients still started MTX monotherapy. People who were prescribed combination therapy had more severe disease suggesting that prescribers do consider prognosis in their treatment decisions. A majority of patients starting combination therapy did so with hydroxychloroquine, despite a lack of evidence for the benefits of this particular combination in clinical practice.

Table 1. Baseline characteristics of the monotherapy and combination therapy groups

Characteristic	Monotherapy (n=1,034)	Combination therapy (n=340)	P value
Age (years)	61 (50, 70)	57 (46, 67)	0.001
Female sex	655 (63)	223 (66)	0.455
Symptom duration (months)	6.3 (3.7, 11.0)	5.8 (3.4, 9.0)	0.020
HAQ score	1.0 (0.4, 1.5)	1.13 (0.5, 1.6)	0.015
DAS28	4.1 (3.2, 5.1)	4.5 (3.5, 5.5)	0.002
Co-morbidities: >=1	468 (45)	130 (38)	0.023
MTX starting dose (mg/week)	15 (10, 15)	10 (10, 12.5)	0.000

Values are frequency (%) or median (IQR)
Abbreviations: HAQ, health assessment questionnaire; DAS, disease activity score; MTX, methotrexate

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THU0201 **ANALYSIS OF GUT MICROBIOTA DIVERSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND BENEFICIAL EFFECTS OF PROBIOTICS ON INTESTINAL FLORA**

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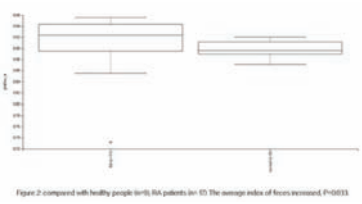
Background: Rheumatoid arthritis (RA) is a progressive, irreversible disease characterized by autoimmune imbalance. Recent studies have found that the number and type of intestinal flora in RA patients were changed (called disorders), which in turn leads to immune imbalance in RA patients. The breath test can indirectly assess the growth of bacteria in the intestine. This study aimed to investigate the intestinal flora imbalance in RA patients and the effect of probiotics on the intestinal flora of RA patients using methane and hydrogen breath test.
Objectives: To study the beneficial effects of probiotics on the intestinal flora of RA patients by detecting the concentrations of methane and hydrogen and the microbial populations in patients with rheumatoid arthritis (RA) before and after probiotic treatment.
Methods: The lactulose methane and hydrogen breath technique were used to detect and compare the concentration of methane and hydrogen in 36 patients with RA before and after probiotic treatment (mainly Bifidobacterium, Clostridium butyricum, Lactobacillus) for 3 weeks. At the same time, the 16SRNA V3 region in stool samples of 17 patients with RA was qualitatively analyzed by Roche/45 high-throughput sequencing platform and compared with 9 healthy adult stool samples.
Results: Compared with pre-intervention, after 3 weeks of probiotic treatment, the exhaled methane concentration was significantly increased in RA patients at 30 minutes, 60 minutes, and 90 minutes ($P < 0.05$). The sum of methane and hydrogen concentrations increased at 30 minutes ($P = 0.041$). There was no significant difference in hydrogen concentration before and after intervention ($P > 0.05$) (Table 1). Compared with healthy adults, the fecal diversity index (Shannon) of RA patients increased ($P < 0.05$) and the species uniformity index (flatness) also increas.



Figure 1: Compared with healthy subjects (n=9), RA patients (n=17) increased the fecal diversity index, P<0.05.

Abstract THU0201 – Figure 1

Conclusion: Patients with RA had a significant difference in the structure of intestinal flora compared with that of healthy controls, which may represent perturbations of microbial communities and contribute to the pathogenesis and condition of RA. Probiotics can restore the composition of the gut microbiome and introduce beneficial functions to gut microbial communities through diet, probiotics or fecal transplantation, providing a promising prospect for clinical treatment of RA.



Abstract THU0201 – Figure 2

REFERENCES:

[1] Schett I B M a G, *The pathogenesis of rheumatoid arthritis.* The New England Journal of Medicine, 2011. 365(23): p. Number of 2205–2219.
[2] Edwards C J, *Commensal gut bacteria and the etiopathogenesis of rheumatoid arthritis.* J Rheumatol, 2008. 35(8): p. Number of 1477-14797.
[3] Horta-Baas G, Romero-Figueroa MDS, Montiel-Jarquín AJ, Pizano-Zárate ML, García-Mena J, Ramírez-Durán N. Intestinal Dysbiosis and Rheumatoid Arthritis: A Link between Gut Microbiota and the Pathogenesis of Rheumatoid Arthritis. J Immunol Res. 2017;2017:4835189

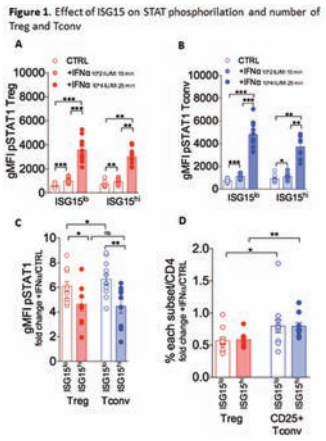
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SLE, Sjögren's and APS – etiology, pathogenesis and animal models

THU0202 **INTERFERON STIMULATED GENE 15 PROTECTS REGULATORY T CELL OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS FROM INTERFERON ALPHA-MEDIATED DEPLETION**

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Background: Data on T regulatory (T reg) cells number and functions in patients with Systemic Lupus Erythematosus (SLE) are conflicting (1). Type I interferon (IFN) decreases Treg proliferation and induces Treg apoptosis (2). IFN stimulated gene 15 (ISG15) is an IFN-induced protein with a negative effect on IFN pathway.
Objectives: Aim of the study was to evaluate the effect of IFN alpha and ISG15 on Treg number and on STAT1 phosphorilation in patients with SLE.
Methods: We recruited patients with SLE classified according to 1997 ACR criteria. We collected demographic and clinical data including disease duration, disease activity scored according to *Systemic Lupus Erythematosus Disease Activity Index* (SLEDAI) 2K. Peripheral blood mononuclear cells (PBMC) were isolated from whole blood samples. Intracellular phosphorilated STAT1 (pSTAT) levels were evaluated in Treg (CD4+FOXP3+CD127 low cells) and conventional T cell (Tconv, CD4 +FOXP3- cells) by multiparametric flow cytometry, *ex vivo* or after stimulation with recombinant IFN alpha. PBMC were cultured for 48 hours with anti-CD3 or anti-CD3 and IFN alpha; the frequency of Treg was analysed by multiparametric flow cytometry. ISG15 mRNA expression was evaluated by RT-PCR on PBMC from SLE patients. Data were expressed as mean ± standard deviation or median (interquartile range(according) to the distribution; Mann-Whitney and Spearman tests were applied. P value <0.05 were considered statistically significant.
Results: We enrolled 21 SLE patients [F:M 20:1; mean age 45.2 ± 12.9 years; mean disease duration 157.5± 103 months; median SLEDAI 2(4)] Overall, median baseline ISG15 mRNA expression was 0.06 (IQR 0.16); patients were divided into ISG15-high (n=9) and ISG15-low (n=12), according to the mean mRNA expression. *Ex vivo*, after short-term treatment with IFN alpha (15 and 25 minutes), we observed a significant increase in STAT1 phosphorilation compared to baseline both in Treg and Tconv ($p<0.00001$), in ISG15-high and ISG15-low patients (Figure 1 A and B); however, high ISG15 levels protect both Treg and Tconv from STAT1 phosphorilation (Figure 1 C). After 48 of colture with IFN alpha, we observed a decrease in Treg and Tconv number, significantly greater in ISG15-low cells (Figure 1D). Treg frequency and ISG15 expression in Treg were higher in active vs inactive SLE patients [SLEDAI > 4 vs SLEDAI <4] ($p<0.05$).
Conclusion: ISG15 protects T conventional cells from STAT1 phosphorilation and induces resistance to T regulatory cells depletion. The results of the study suggest that ISG15, a protein induced by IFN in the acute phase of the disease, exerts a negative feedback, allowing the recovery of T reg.



Abstract THU0202 – Figure 1

REFERENCES:

[1] Zhang SX, et al. J Immunol res. 2018
[2] Piconese S, et al. Cytokine Growth Factor rev. 2014

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THU0203 PROMOTER DNA METHYLATION AND HSA-MIR-424-5P REGULATE ATF6 ALPHA EXPRESSION IN SALIVARY GLANDS OF PATIENTS WITH SJÖGREN'S SYNDROME

Patricia Carvajal[1], Sergio Aguilera[2], María-José Barrera[3], Carolina Lagos[1], Isabel Castro[4], Sergio González[5], Daniela Jara[1], Claudio Molina[3], María-Julieta González[1]. *[1]ICBM, Facultad de Medicina, Universidad de Chile, Santiago, Chile*; *[2]Clínica INDISA, Santiago, Chile*; *[3]Facultad de Odontología, Universidad San Sebastián, Santiago, Chile*; *[4]Departamento Tecnología Médica, Universidad de Chile, Santiago, Chile*; *[5]Escuela de Odontología, Universidad Mayor, Santiago, Chile*

Background: Salivary glands (SG) from Sjögren's syndrome (SS)-patients show chronic inflammation and endoplasmic reticulum (ER) stress. To counteract ER stress, eukaryotic cells activate adaptive mechanisms referred to as the unfolded protein response via sensors present in the ER membrane, such as ATF6α[1,2]. In response to ER stress, ATF6α is translocated to the Golgi apparatus where is processed releasing ATF6f, which translocates into the nucleus as a transcription factor to activate ER-associated degradation and protein folding-related gene transcription[3]. The overexpression of ATF6α observed in Labial SG (LSG) from SS-patients[1] could be modulated by epigenetic mechanisms.
Objectives: To evaluate the involvement of epigenetic mechanisms such as promoter-specific DNA methylation and microRNA (miRNA) regulation on ATF6α expression in LSG from SS-patients and controls. The effect of IFN-γ on both mechanisms was also evaluated in a 3D-acini model.
Methods: SG biopsies from 12 SS-patients and 10 controls were analyzed. For in vitro assays 3D-acini incubated with 1 or 10 ng/mL IFN-γ for 24 h were employed. Specific DNA methylation of ATF6α gene promoter was evaluated by methylation sensitive-high resolution melting PCR. The profile of miRNAs differentially expressed was determined by miRNA sequencing (seq), of which hsa-miR-424-5p was selected because the *in silico* analysis showed that ATF6α mRNA is a target of this miRNA. The levels of hsa-miR-424-5p were determined by Taqman miRNA assays. Functional assays using miRNA mimic and miRNA inhibitors were also performed.
Results: LSG from SS-patients showed a significant decrease of ATF6α promoter DNA methylation percentage (p=0.04), which was inversely correlated with high ATF6α mRNA levels (p= 0.02). The hsa-miR-424-5p was found downregulated by miRNA-seq in LSG from SS-patients. Taqman miRNA assays validated the significant decrease of hsa-miR-424-5p levels found in LSG from SS-patients (p=0.02), which were inversely correlated with ATF6α mRNA levels (p=0.02). Functional assays suggest that hsa-miR-424-5p regulates the mRNA levels of ATF6α. Finally, stimulation of 3D-acini with IFN-γ induced a significant increase of ATF6α mRNA levels together with a decrease in ATF6α promoter DNA methylation percentage and hsa-miR-424-5p levels.
Conclusion: The results suggest that the ATF6α overexpression is regulated by two complementary epigenetic mechanisms: the DNA hypermethylation of its promoter and the silencing of its mRNA by hsa-miR-424-5p in LSG from SS-patients. IFN-γ affects the expression of ATF6α by modulation of epigenetic mechanisms, regulating the ability of epithelial cells to handle the chronic ER stress. Interestingly, these changes carry out under a global DNA hypomethylation condition[4].

REFERENCES:

[1] J Autoimmun 2016;75:68-81
[2] Rheumatology 2018;57:1021-1032
[3] Autoimmun Rev 2018;17:796-808
[4] Clin Immunol 2018;196:85-96

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THU0204 ASSOCIATION OF LILRA3 GENE WITH LYMPHOMAGENESIS RISK IN YOUNG SS PATIENTS

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Background: Primary Sjögren's Syndrome (SS) is a systemic autoimmune disease, characterized by increased risk of non-Hodgkin's lymphoma development. A functional polymorphism of the immunoreceptor LILRA3 (Leukocyte immunoglobulin-like receptor A3) has been recently identified as a potential etiopathogenic factor for both pSS susceptibility and lymphomagenesis in the general population.
Objectives: The aim of the current study was to explore the potential contribution of the LILRA3 functional polymorphism in primary SS susceptibility and SS related lymphomagenesis.
Methods: In this study, 346 primary SS patients (ACR/EULAR classification criteria, 2016) and 350 healthy controls were included. The presence of LILRA3 functional polymorphism was detected by polymerase chain reaction (PCR), whereas serum levels were measured by Enzyme-Linked Immunosorbent Assay (ELISA), respectively. Statistical analysis was performed by Graph Pad Prism.
Results: LILRA3 wild type gene variant was detected in 84% of healthy controls, 86.3% of pSS non-Lymphoma patients and 89.7% of patients complicated with lymphoma. Of interest, in pSS patients ≤40 years complicated by lymphoma, LILRA3 wild type variant was detected in 100% in contrast to pSS - non lymphoma patients (81.8%) and healthy controls (HC) (83.2%) [p=0.03]. In line with these results, LILRA3 protein serum levels were increased in pSS-lymphoma patients with pSS onset ≤40 years compared to healthy controls (p=0.009).
Conclusion: Increased LILRA3 protein levels, as a result of predominance of the LILRA3 wild type gene variant in the young pSS onset patients complicated by lymphoma, imply a potential role of the LILRA3 gene in pSS related lymphomagenesis.
Disclosure of Interests: Evangelia Argyriou: None declared, Petros Roussos: None declared, Adrianos Nezos: None declared, Aliki Venetsanopoulou: None declared, Kyriaki A. Boki: None declared, Athanasios Tzioufas Grant/research support from: ABBVIE, PFIZER, AMGEN, NOVARTIS, GSK, Haralampos M. Moutsopoulos: None declared, Clio Mavragani: None declared
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THU0205 THE HEMATOPOIETIC STEM CELLS (HSCS) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) REPROGRAM THEIR TRANSCRIPTOME: IMPLICATIONS FOR THE PATHOGENESIS OF THE DISEASE

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Background: In SLE, all terminally differentiated blood cells demonstrate an aberrant phenotype. HSCs the most primitive cell type of the hematopoietic lineage when exposed within the bone marrow (BM) to adjuvants and inflammatory mediators change their transcriptional landscape and this may persist in the HSCs circulating in the peripheral blood or those infiltrating peripheral tissues. Within peripheral tissues these reprogramed HSCs differentiate into myeloid cells mounting enhanced protective or aberrant immune responses[1].
Objectives: To dissect whether aberrant phenotypes of blood cells in SLE could be traced back to HSCs and explore how the inflammatory environment of SLE shapes the HSC differentiation process.
Methods: We analyzed the transcriptional alterations (genetic or epigenetic) of $CD34^+$ cells in the BM of SLE patients, compared it to healthy individuals and the NZB/W lupus mice at the onset of disease (6 months). $CD34^+$ cells were isolated from BM aspirates and peripheral blood of SLE patients (n=8) and healthy subjects (n=2) with magnetic separation (Stem Cell Technologies). mRNA was extracted and libraries were prepared. Sequencing was performed in NextSeq Illumina Platform. Alignment in human genome v.38 was done by Star package and differential expression analysis was performed by edgeR algorithm. Genes with $FC \geq 1.5/\leq -1.5$, $FDR \leq 0.05$ were considered statistically significantly up-/down-regulated, respectively. Heatmaps were constructed in R, GO/Pathway Analysis and enrichment analysis were performed in ClueGo, RNEA, GeneMania and GSEA, respectively.
Results: Overlaying the transcriptome of BM-derived $CD34^+$ of SLE patients and healthy subjects, we identified in total 598 differentially expressed genes(DEGs) (82 up-/514 down-regulated in SLE). DEGs participate in hematopoietic cell lineage fate, regulation of stem cell differentiation, cell adhesion and cell cycle regulation. We also found evidence for cell cycle checkpoints signature which drives HSCs to experience replication stress and activate ATR pathway. Comparison of $CD34^+$ profile between severe-moderate SLE reveals a prominent neutrophilic signature in severe disease. Comparative transcriptomic analysis of human vs murine SLE revealed a panel of common genes again related to cell proliferation, differentiation and platelet activation.
Conclusion: HSCs in SLE patients and murine lupus reprogram their transcriptome in response to the inflammatory milieu within the BM, thus exiting from dormancy, differentiating to myeloid cells and mounting a DNA damage response to the replication stress. This activated phenotype renders HSCs both susceptible to cell exhaustion while at the same time priming them and their progenies towards enhanced immune responses.

REFERENCES:

[1] Mitroulis, Ioannis, et al. "Modulation of myelopoiesis progenitors is an integral component of trained immunity." Cell 172.1 (2018): 147-161.
[2] Kaufmann, Eva, et al. "BCG educates hematopoietic stem cells to generate protective innate immunity against tuberculosis." Cell 172.1 (2018): 176-190.

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THU0206 ANTI-D4GDI ANTIBODIES ACTIVATE PLATELETS IN VITRO: A POSSIBLE LINK WITH THROMBOCYTOPENIA IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Background: Thrombocytopenia is a manifestation associated with Primary Antiphospholipid Syndrome (PAPS) and many studies have stressed the leading role played by platelets in the pathogenesis of Antiphospholipid Syndrome (APS) (1). Platelets are highly specialized cells and their activation involves a series of rapid rearrangements of the actin cytoskeleton (2). Recently, we described the presence of autoantibodies against D4GDI (Rho GDP Dissociation Inhibitor Beta, ARHGDIB) in the serum of a large subset of SLE patients and we observed that anti-D4GDI antibodies activated the cytoskeleton remodeling of lymphocytes by inhibiting D4GDI and allowing the upregulation of Rho GTPases, such as Rac1(3). Proteomic and transcriptomic studies indicate that D4GDI is very abundant in platelets and small GTPases of the RHO family are critical regulators of actin dynamics in platelets (4).
Objectives: The aim of the present study was to evaluate the presence of anti-D4GDI antibodies in PAPS sera and whether they can affect platelet activation, contributing to the thrombotic events and the thrombocytopenia of PAPS patients.
Methods: 38 PAPS patients diagnosed according to the 2006 Sydney classification criteria were enrolled from the Lupus Clinic of the Sapienza University of Rome. 20 normal healthy subjects (NHS) served as controls. Sera were stored at -20 °C to performed an ELISA test using commercial D4GDI protein. Anti-D4GDI antibodies were purified from PAPS sera and used for *in vitro* treatment of platelets purified from NHS. Flow cytometry analysis was performed to determination of integrin $\alpha IIb\beta 3$ activation, a well-established marker of platelet activation and adhesion.
Results: We identified anti-D4GDI antibodies in sera from 18/38 (47%) patients with PAPS, but in no sera from NHS. Dividing the patients with PAPS according to the presence or absence of thrombocytopenia, we found a significant association between this hematologic manifestation and a higher titer of anti-D4GDI antibodies. Our *in vitro* results show a significant 30% increase in the activation of integrin $\alpha IIb\beta 3$ upon stimulation of platelets from healthy donors preincubated with the antibody anti-D4GDI purified from the serum of APS patients. Interestingly the antibody does not only increase the overall integrin activation but also the rate/speed of integrin activation.
Conclusion: We demonstrated that antibodies anti-D4GDI are present in the sera of PAPS patients and can prime platelet activation. Thus, explaining, at least in part, the pro-thrombotic state and the thrombocytopenia of PAPS patients. These findings may lead to improved diagnosis and treatment of APS.

REFERENCES:

[1] Shechter Y, Tal Y, Greenberg A, Brenner B. Platelet activation in patients with antiphospholipid syndrome. Blood Coagul Fibrinolysis. 1998 Oct;9 (7):653-7.
[2] Seong-Hoon Yun, Eun-Hye Sim, Ri-Young Goh, Joo-In Park, and Jin-Yeong Han. Platelet Activation: The Mechanisms and Potential Biomarkers. BioMed Research International,Volume 2016, Article ID 9060143. Review
[3] Barbati C, Alessandri C, Vomero M, Vona R, Colasanti T, Vacirca D, Camerini S, Crescenzi M, Pendolino M, Truglia S, Conti F, Garofalo T, Sorice M, Pierdominici M, Valesini G, Malorni W, Ortona E.Autoantibodies specific to D4GDI modulate Rho GTPase mediated cytoskeleton remodeling and induce autophagy in T lymphocytes. J Autoimmun. 2015 Apr;58:78-89.
[4] Rowley JW, et al. Genome-wide RNA-seq analysis of human and mouse platelet transcriptomes. Blood. 2011;118(14).

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THU0207 HELPER AND CYTOTOXIC FOLLICULAR T-CELLS IN SJÖGREN'S SYNDROME

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Background: Follicular T-cells, characterized by the expression of CXCR5, secrete interleukin 21 (IL-21) and help B-cell differentiation in lymphoid follicles. They are also found in circulation and may play a key role in Sjögren's syndrome's (pSS) chronic autoimmune epithelitis.

Objectives: To characterize circulating follicular helper (Tfh) and cytotoxic (Tfc) T-cells in peripheral blood (PB) from pSS patients, Rheumatoid Arthritis (RA) patients and healthy controls (HC), and to investigate how they correlate with B-cell subsets. We also aimed to explore associations between the Tfh and Tfc cells and clinical and laboratory features of pSS.

Methods: PB from 57 pSS patients, 20 RA patients and 24 HC was analysed by flow cytometry to characterize T and B-cell subsets, with CXCR5 defining Tfh and Tfc within CD4 and CD8 T cells, respectively. A stimulation assay was used to assess the production of IL-21 by $CD4^+$ and $CD8^+$ T-cells.

Results: Compared to HC, pSS and RA patients presented significantly lower lymphocyte absolute counts (1615 and 1935 cells/μL respectively, compared to 2228 cells/μL in HC, p<0.001 for HC vs pSS, p=0.018 for HC vs RA), and percentages (29.9% in pSS, 24.0% in RA, and 35.4% in HC, p=0.022 for HC vs pSS, and p<0.001 for HC vs RA). B-cell and T-cell absolute counts were also lower in both groups of patients compared to HC (in HC vs pSS, p=0.011 for B-cells and p<0.001 for T-cells; in HC vs RA, p<0.001 for B-cells and p=0.018 for T-cells). B-cells absolute counts and percentages in pSS were higher than in RA (177 vs 132 cells/μL, p=0.013; 9.7 vs 6.4%, p<0.001). There were no differences in CD8 T-cells percentages between groups, but pSS had lower CD4 T-cell percentages compared to HC (p= 0.004).

pSS patients presented lower absolute counts of CXCR5+ Tfh compared to RA (134 vs 181 cells/μL, p=0.038) and HC (134 vs 241 cells/μL, p<0.001). No differences were found in Tfh percentages. RA patients had lower percentages of CXCR5+ Tfc compared to pSS (2.1 vs 2.6%, p=0.113) and HC (2.1 vs 3.0%, p=0.046).

pSS patients exhibited higher percentages of $IL21^+CD4$ and $IL21^+CD8$ T cells ($IL21^+CD4$ T cells: 12.4% in pSS vs 9.0% in RA, p=0.046; vs 9.7% in HC, p=0.028; $IL21^+CD8$ T cells: 4.1% in pSS vs 2.3% in RA, p=0.001; vs 2.8% in HC, p=0.030).

In pSS patients, CXCR5+ Tfh correlated positively with the percentages of plasmablasts (r=0.262 for $CD24^-CD38^{++}$ cells, and r=0.282 for $IgM^{-/+}CD38^{++}$ cells). $IL21^+CD8$ T cells correlated positively with the Naïve/Memory B cells ratio (r=0.323; p=0.014) and negatively with Bm1 memory B cells (r=-0.370; p=0.005). IL21+CD4 T cells behaved similarly, though without statistical significance.

Anti-SSA-positive patients (n=38) presented higher $CD4^+IL21^+$(13.3 vs 8.5%, p=0.025) and $CD8^+IL21^+$ cells percentages (4.4 vs 4.0%, p=0.198) than SSA-negative patients (n=19). Although there were no differences between pSS patients with active (n=27) and inactive disease (n=30), a tendency for positive correlations was found between $IL-21^+CD4$ and $IL21^+CD8$ T-cells and the ESSDAI score (r= 0.229, p=0.086 for CD4, r= 0.223, p=0.096 for CD8). Moreover, ESSDAI correlated positively with the Tfh1/Tfh17 ratio.

Conclusion: pSS patients present a profile of circulating Tfh and Tfc distinct from RA and HC, both phenotypically and functionally. Moreover, our data support a crucial role for these cells in B cell development, as they correlate with B cells, in pSS patients, which are known to exhibit a typical circulating B cell compartment. Both Tfc and Tfh cells can be critical for disease pathophysiology and activity, as underlined by the correlations between these cells and ESSDAI scores.

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THU0208 EBV SEROLOGICAL PROFILE AFFECTS CIRCULATING LYMPHOCYTES IN PSS

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Background: Genetic, hormonal, and environmental triggers have been related to the dysregulated autoimmune response observed in primary Sjögren Syndrome (pSS), but its aetiology is still unestablished. Epstein-Barr virus (EBV) is a strong candidate as a trigger for the autoimmune epithelitis in pSS.

Objectives: We aimed to evaluate the EBV serology in pSS patients, and to compare it with other autoimmune patients and healthy controls (HC). In parallel, we have characterized the immune profile of pSS patients, in order to assess if the viral background affects the circulating lymphocytes.

Methods: We have recruited 34 pSS patients (2002 AECG criteria), 20 Rheumatoid arthritis (RA) patients (ACR/EULAR classification criteria) and 20 HC. Immunoenzymatic assays were used to determine the serum levels of IgG, IgA and IgM antibodies against EBV Nuclear Antigen (EBNA), Early Antigen (EA) and Capside antigen (VCA). Flow cytometry was used for the characterization of T and B cells, including regulatory (Tregs) and follicular (Tfh) T cells, T helper and Bm1-Bm5 subsets. Significance was considered for p<0.05.

Results: All sera were negative for VCA-IgM. Only 2 HC and 3 RA were positive for EA-IgA. For VCA-IgG and EBNA-IgG we found no differences in positive cases between groups (all participants, except 2 pSS were positive for VCA-IgG; 26/34 pSS, 16/20 RA and 13/20 HC were positive for EBNA-IgG). However, pSS patients evidenced more positive sera for EA-IgG than HC (32% vs 5%; p=0.0215) and RA (32% vs 20%; p=0.2312), suggesting a more prevalent state of late acute/chronic active infection in pSS.

Thus, according to the serologic pattern observed, we divided pSS patients in 3 groups: G1 (n=18), past infection ($EA\text{-}IgG^-$, $EBNA\ IgG^+$); G2 (n=11), late acute/chronic active infection ($EA\ IgG^+$, $EBNA\ IgG^{+/-}$), and G3 (n=5), without serological evidence of active infection ($EA\ IgG^-$, $EBNA\ IgG^-$). Within the T cell compartment, G2 patients presented increased percentages Tregs compared to G1 pSS patients (p=0.031). G1 and G2 patients presented increased $CXCR3^+$ Th1 cells and $CXCR3^+$ Tfh1 compared to G3 (Th1: G1vsG3, p=0.120 and G2vsG3, p=0.008; Tfh1: G1vsG3, p=0.003 and G2vsG3, p=0.067).

As for B cells, pSS patients are known to have increased percentages of transitional Bm2' cells in circulation, and in fact we found that these cells were also augmented in G2 patients compared to G1 (p=0.024). Moreover, plasmablasts (Bm3+Bm4) were increased in G1 and G2 patients compared to G3 (%, G1vsG3, p=0.088 and G2vsG3, p=0.003; absolute counts, G1vsG3, p=0.020 and G2vsG3, p=0.003). Plasmablasts were also slightly augmented in G2 patients compared to G1 (p=0.099).

Conclusion: Our study shows a higher prevalence of EA-IgG in pSS patients. Moreover, the distinct EBV serological profiles observed in pSS patients seem to affect circulating B and T cells. Particularly, pSS patients with serological evidence for late acute/chronic active infection show a more proinflammatory pattern, with increased Th1 cells, and elevated transitional B cells with increased plasmablast differentiation. Despite the low number of cases and the absence of other confirmatory methodologies, our study reveals for the first time the association of EBV with distinct immune profile in pSS patients.

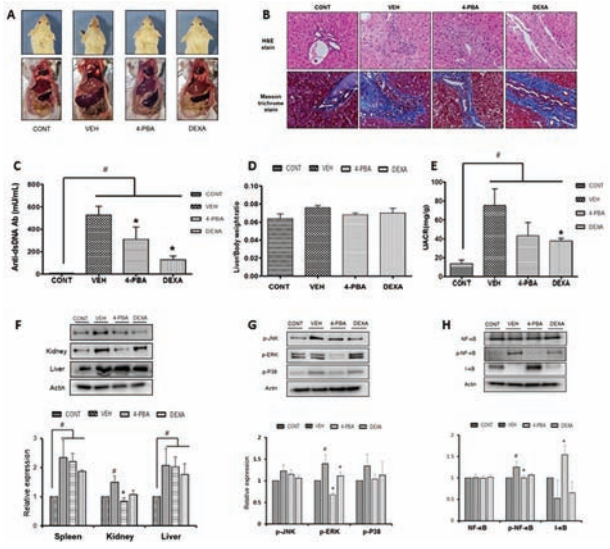
Disclosure of Interests: Filipe Barcelos Consultant for: Pfizer; Ely-Lilly, Speakers bureau: Novartis, Catarina Martins: None declared, Ricardo Monteiro: None declared, Tiziano Prussiani: None declared, Miguel Sítima: None declared, José Vaz-Patto: None declared, Jaime Branco: None declared, Luís Miguel Borrego Grant/research support from: MSD, Consultant for: MSD; Tecnifar, Paid instructor for: MSD; AstraZeneca, Speakers bureau: MSD; Tecnifar; AstraZeneca

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THU0209 4-PHENYLBUTYRIC ACID AMELIORATES LUPUS HEPATITIS AND NEPHRITIS THROUGH SUPPRESSION OF NF-KB ACTIVATION IN EXPERIMENTAL LUPUS MODEL

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease presenting diverse manifestation involving multiple organs, such as liver and kidney. Endoplasmic reticulum (ER) stress has been revealed as the one of the contributing factors of lupus pathogenesis.
Objectives: The purpose of the present study was to investigate whether ER stress inhibition suppresses organ inflammation including liver and kidney in lupus murine model and the activation of mitogen activated protein kinases (MAPK) and NF-kB.
Methods: A murine lupus model was induced through a 4-week treatment with Resiquimod, a toll-like receptor agonist 7. From the 8th week, the mice were treated with phosphate buffered saline, 4-phenylbutyric acid (4-PBA), and dexamethasone for 4 weeks. The increment of body weight, liver weight, inflammation mediator level, and the pathology of hepatitis and nephritis were analyzed at 12 weeks of age. The level of phosphorylated MAPK expression and activation of NF-kb were also evaluated.
Results: 4-PBA-treated group showed lower level of body weight increment with liver to body weight ratio compared with vehicle-treated group. 4-PBA group showed decreased inflammatory cell infiltration and fibrosis in the histologic finding of liver and kidney and lower level of inflammatory mediators, including TNF-α and IL-6, compared to vehicle-group. GRP78 and CHOP expression was decreased in the spleen of 4-PBA treated mice compared to vehicle-treated mice and 4-PBA group showed the lower expression level of phosphorylated JNK, ERK, p38 and NF-kB of the spleen.
Conclusion: Our results suggest that 4-PBA attenuates the inflammation on liver and kidney of experimental lupus model through suppression of MAPK and NF-kB activation. Thus, inhibition of ER stress could be function as anti-inflammatory therapeutics for SLE.



Abstract THU0209 – Figure 1

REFERENCES:

[1] Navid F, Colbert RA. Causes and consequences of endoplasmic reticulum stress in rheumatic disease. Nat Rev Rheumatol 2017;13:25-40
[2] Hosoi T, Ozawa K. Endoplasmic reticulum stress in disease: mechanisms and therapeutic opportunities. Clin Sci (Lond) 2009;118:19-29

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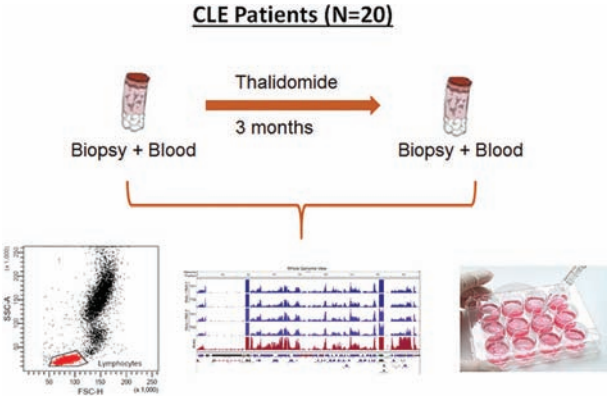
THU0210 RNA-SEQ REVEALS THE MECHANISM OF THALIDOMIDE IN LUPUS CUTANEOUS LESIONS

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Background: Cutaneous Lupus Erythematosus (CLE) is common, largely heterogeneous and characterized by a chronic relapsing course. As many as 70 to 80% of patients with SLE will develop skin lesions at some point during the course of their disease, with a significant proportion being disfiguring and debilitating [1]. Conventional therapy consists of topical steroids and antimalarial agents but 40% of patients will be refractory to this regimen [2]. Thalidomide has been the only one that has shown an effectiveness of 90% [3], however, its mechanism of action in the disease is not known at all. In addition, its use is limited due mainly to its side effects such as teratogenicity and the development of peripheral polyneuropathy.
Objectives: Identification of the possible mechanisms of thalidomide in cutaneous lupus erythematosus.
Methods: Skin biopsies before and during treatment has been performed on a cohort of CLE patients treated (N=20) and not treated with thalidomide (N=5). Through a differential study of gene expression with RNA-seq and its subsequent validation, the mechanism of thalidomide action has been identified. The cell population in the tissue and in the blood of the patients and their evolution due to the treatment has also been studied by flow cytometry. *In vitro* experiments using isolated lupus cutaneous lymphocyte and keratinocytes has been performed to see the specific biological effect of thalidomide (Figure 1).
Results: Flow cytometry of immune cells from blood obtained pre- and post-treatment revealed a significant activation of Thelper ($p<0.001$), a differentation towards Th2 subpopulation and an increase of natural killer after thalidomide effect. Not significant difference were observed in macrophages and dendritic cell. In addition, after RNA-seq analysis two fundamental molecular pathways has been identified in responder thalidomide treatment patients: 1) via IRF4-NF$\kappa\beta$ pathway modulation. 2) via AMPK-mTOR pathway modulation. *In vitro* experiments using isolated primary cells from lupus cutaneous patients demostrated that thalidomide modulate IRF4 in lymphocytes to inhibite NF$\kappa\beta$ pathway; however, AMPK-mTOR pathway is inhibited in keratinocytes by thalidomide effect.
Conclusion: Taken together, we show that mechanism of thalidomide in CLE is dual. It might inhibited NF$\kappa\beta$ pathway by modulation of IRF4 in lymphocyte but, in the same time, might inhibited MTOR pathway by modulation of AMPK in keratinocytes.

REFERENCES:

[1] Henry J. Lee, et al. Cutaneous lupus erythematosus: Understanding of clinical features, genetic basis, and pathobiology of disease guides therapeutic strategies. Autoimmunity 2006; 39(6): 433–444.
[2] Callen JP. Update on the management of cutaneous lupus erythematosus. Brit J Dermatol 2004; 151: 731-736.
[3] Cortés-Hernández J, et al. Thalidomide in the treatment of refractory cutaneous lupus erythematosus: prognostic factors of clinical outcome. Br J Dermatol. 2012; 166(3):616-23.



Abstract THU0210 – Figure 1. Scheme of the project to discover thalidomide mechanism in lupus cutaneous patients.

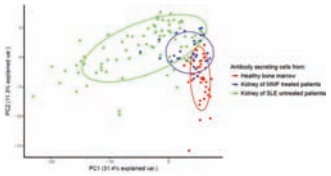
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THU0211 EVOLUTION OF KIDNEY ANTIBODY SECRETING CELLS MOLECULAR SIGNATURE IN LUPUS PATIENTS WITH ACTIVE NEPHRITIS UPON IMMUNOSUPPRESSIVE THERAPY

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Background: Pathogenic antibody secreting cells (ASC) have been identified in the kidney of SLE-prone mice, but are poorly characterized in human lupus nephritis (LN). We hypothesized that long-lived plasma cells may contribute to the failure of immunosuppressive therapy in refractory patients.
Objectives: To characterize and compare the single cell molecular signature of ASC in kidney and urine from patients with active LN, either untreated or after immunosuppressive therapy failure.
Methods: We included patients with biopsy proven active LN from 4 centers and meeting the ACR revised classification criteria for SLE diagnosis. Renal biopsies were scored according to 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification, and stained with anti-CD138 to visualize ASC. ASC were single cell sorted as CD3-/CD14-/CD16-/CD27^{high}/CD38^{high} cells. Single-cell gene expression profiling was performed by multiplex RT-PCR using Fluidigm Dynamic Arrays. We used a set of genes derived from a previous transcriptomic analysis of human splenic and bone marrow ASC to distinguish the process of ASC maturation from plasmablast (PB) to long-lived PC. We also studied ASC transcriptional program from urine of untreated LN patients at diagnosis and after 3 and 6 months of a prospective follow up during induction therapy (Plasmo-Lup study).
Results: Immunohistochemistry stainings on kidney biopsies from both untreated (N=15) and refractory patients (N=6) showed infiltrates of CD138+ ASC mainly located in the interstitium, particularly in untreated patients. Single cell molecular signature of kidney ASC from 3 untreated patients with class IV LN revealed that these cells were mostly PB expressing multiple genes linked with cell division, and PC without long-lived genes expression. This contrasted with ASC signature from 3 patients with active LN and mycophenolate mofetil (MMF) failure that expressed long-lived PC genes and no proliferative genes. Primary component analysis of 170 single-cells showed clustering of ASC from MMF treated patients with long-lived bone marrow PC from healthy donors that were distinct from PB/PC from untreated patients (Figure 1). A PB signature was observed in urine ASC at diagnosis, similar to their kidney counterpart. The concentration of ASC in urine in 22 untreated patients correlated with ISN/RPS classification, with higher concentration in class IV patients ($p<0.01$).
Conclusion: These results suggest that PB infiltrate kidney of untreated LN patients, and that kidney long-lived PC may contribute to the failure of immunosuppressive therapy.



Abstract THU0211 – Figure 1. Single cell principal component analysis of 170 individual cells analyzed for the expression of 20 genes. Each dot represents a single cell.

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THU0212 BARICITINIB-ASSOCIATED CHANGES IN GLOBAL GENE EXPRESSION DURING A 24-WEEK PHASE 2 CLINICAL SLE TRIAL DESCRIBE A MECHANISM OF ACTION THROUGH INHIBITION OF JAK/STAT AND IFN RESPONSIVE GENE EXPRESSION

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Background: Baricitinib (bari) is an oral selective Janus kinase (JAK)1 and JAK2 inhibitor. In the Phase 2 study, JAHH (NCT02708095), treatment with bari resulted in significant improvements in patients (pts) with active systemic lupus erythematosus (SLE) receiving standard background therapy, compared with placebo (PBO).[1]
Objectives: To use global gene expression to characterize baseline (BL) gene expression among SLE pts in JAHH and to describe the mechanism of action (MoA) of bari during treatment in active SLE.
Methods: A total of 314 pts were randomized 1:1:1 to PBO, bari 2-mg, or bari 4-mg once daily for 24 weeks (Wks) in JAHH. RNA isolated from whole blood at BL and Wks 2, 4, 12, and 24 was analyzed using HTA2.0 arrays, possessing over 925,000 specific individual probes. Data were summarized to transcript level and analyzed using a mixed effects model on a log2 transformed response with multiplicity correction.
Results: Baseline gene expression analysis comparing healthy controls to SLE pts revealed elevated expression of genes involved in innate and adaptive immune pathways and biologic processes thought to be key to SLE pathogenesis. Baseline findings from the ILLUMINATE trial of tabalumab (1760 SLE pts at BL)[2] were independently replicated, including individual gene-specific changes in the SLE populations versus controls. Treatment-induced changes were predominantly observed in the bari 4-mg versus PBO group at early time points (Wks 2 and 4; bari 4-mg > 2-mg). Statistically significant changes were observed for type I and II IFN responsive genes, and in the JAK/signal transducer and activator of transcription (STAT) canonical and noncanonical signaling pathways, in the bari 4-mg versus PBO group comparisons. There were biologically notable and statistically significant bari-associated decreases in gene expression from BL, compared to PBO, for interleukin (IL)-3, -5, -6, -7, and granulocyte macrophage colony-stimulating factor pathways, attributable to inhibition of JAK/STAT signaling.
Conclusion: These results build upon previous studies of gene expression in ILLUMINATE, comparing SLE at BL with healthy controls; they advance our understanding of lupus pathogenesis, and further delineate the MoA of bari in SLE. These data independently confirm the marked elevations of specific type I and II IFN genes at BL in clinical trial pts on standard of care treatment. Changes in gene expression with bari impacted IFN responsive genes as well as JAK/STAT signaling pathways. Interpretation of results is limited by sample size and statistical power, and presence of concomitant medications. Importantly, gene expression may not translate directly to protein expression; however, ongoing proteomic studies (including specific assays for type I IFN, IFN-γ, IL-12, IL-17, and IL-23) will help extend these gene expression results and further describe the MoA of bari in SLE.

REFERENCES:
[1] Wallace D, et al. Lancet. 2018;392:222-231
[2] Hoffman R, et al. Arthritis Rheumatol. 2017;69:643-654

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THU0213 TRAASVIR STUDY: THROMBOTIC MANIFESTATIONS IN ANTIPHOSPHOLIPID ANTIBODY TRANSIENT POSITIVITY RELATED TO VIRAL INFECTIONS:

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Background: The mollecular pathogenesis of antiphospholipid syndrome is complex (environmental triggers, predisposed individuals). Previous studies suggested that infection may lead to the development of transiently elevated non-thrombogenic aPL antibodies. However, there are increasing case reports of patients with viral infections who develop antiphospholipid antibodies and thromboembolic events.
Objectives: To evaluate the role of acute viral infections in the development of thrombotic events related to aPL transitory (or permanent) positivity.
Methods: We include patients with a current viral infection that was diagnosed before elevated aPL antibodies were identified. One positive laboratory test either LA, aCL, or anti β2 GPI antibodies after a prior diagnosis of infection was required (< 3 months). Infection must be followed by thromboembolic manifestations (arterial or venous). A time frame of 3 months between infection diagnosis and recognition of aPL antibodies positivity was established. Normal PT and APTT test were observed in all previous patient's blood tests.
Results: From January 2014 to date we have collected 40 cases with a demonstrated acute virosis and an aPL positive result with a thrombotic manifestation. 9 cases (22.5%) for Epstein-Barr virus, 17 cases (42.5%) were positive for CMV, 8 (20%) for Parvovirus B19, 3 cases were positive for Influenza A H1N1,3 for HIV, 1 for RSV, 1 for HCV and 1 case for Rotavirus. Lupus anticoagulant (L A) positivity was showed in 22 cases (55%), 15 cases (37.5%) tested positive for IgM anticardiolipin antibody and 13 cases (32.5%) also tested positive for IgM anti-β2GPI antibodies. Unfortunately, anti-prothrombin antibodies could not been analysed. The clinical manifestations were: leg deep venous thrombosis (17 cases) (42.5%), pulmonary embolism (5 cases) (12.5%), superior limbs (3 cases)(7.5%) livedoid vasculopathy (3 cases) (7.5%), splenic infarction (1 case), ovarian venous thrombosis (1 case). Only four arterial thromboses were observed: superior limbs (2 cases), digital ischemia (1case) and transverse myelitis (1 case). We have observed how the IgM virus related antibody became negative and the aPL became negative in parallel in 20/40 cases (50%).
Conclusion: We hypothesized that thrombotic manifestations of aPL-related acute viral infections are underdiagnosed, and probably in predisposed host, some viral infections may induce the transient apparition of aPL, mainly those with LA activity with potential pathogenic thrombotic properties.

REFERENCES:

[1] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an Update of classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost. 2006 Feb;4(2):295-306.
[2] Ascer E, Marques M, Gidlund M. M pneumoniae infection, pulmonary thromboembolism and antphospholipid antibodies. BMJ Case Rep. 2011 Apr 19;2011.
[3] Abuaf N, Laperche S, Rajoely B, et al. Autoantibodies to phospholipids and to the coagulation proteins in AIDS. Thromb Haemost 1997; 77: 856–861.

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THU0214 THE PI3KΔ SELECTIVE INHIBITOR INCB050465 ABROGATES KIDNEY PATHOLOGY IN A SPONTANEOUS MURINE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that affects multiple organs, including the skin, joints and kidneys. Though SLE typically cycles through periods of flares and remission, patients often eventually succumb to end-stage kidney or cardiovascular damage[1]. SLE is characterized by the presence of autoantibodies that form immune complexes resulting in kidney deposition that significantly contribute to lupus nephritis pathogenesis. Phosphatidylinositol 3-kinases (PI3Ks) are divided into three classes (Class I, II, and III) according to their structure, regulation and substrate specificity. The Class I PI3K delta isoform (PI3Kδ) has been implicated in autoimmune diseases associated with aberrant B cell and antibody responses. INCB050465 is an oral small molecule PI3Kδ selective inhibitor currently being evaluated in clinical trials for the inflammatory indications Sjögren's syndrome and autoimmune hemolytic anaemia (NCT03627065 & NCT03538041).
Objectives: To quantify the efficacious potential of INCB050465, a selective PI3Kδ inhibitor, in a preclinical model of systemic lupus erythematosus with kidney pathology.
Methods: The MRL/lpr mouse model spontaneously develops multiple inflammatory phenotypes that mimic human SLE pathologies, including kidney damage resulting in proteinuria, cutaneous skin lesions and anti-double stranded DNA (anti-dsDNA) antibodies. Kidney sections were stained with hematoxylin and eosin (H&E) and assigned a composite score based on glomerulus, crescents, protein casts, interstitial inflammation and vasculitis by a rater unaware of the treatment groups[2]. Flow cytometry was performed on splenocytes to characterize B cell and T cell subsets. Anti-dsDNA antibodies were determined by commercial ELISA.
Results: In vitro enzymatic selectivity screening revealed INCB050465 potently inhibited the PI3Kδ kinase enzyme (IC50 = 1.1 ± 0.5 nM), with 20,000-fold selectivity for the other PI3K family member enzymes. Proteinuria identified spontaneous kidney damage in 85%+ of vehicle treated mice by 21 weeks of age, and kidney histology revealed gross tissue enlargement associated with structural abnormalities. In contrast, therapeutic INCB050465 treatment (0.3 – 3.0 mg/kg, b.i.d.) dose-dependently reduced the incidence of proteinuria ($p < 0.01$), and kidney structural integrity was normalized ($p < 0.0001$). A feature of the MRL/lpr model is lymphocyte hyper-proliferation resulting in lymphadenopathy and splenomegaly. Therapeutic INCB050465 treatment dose-dependently reduced spleen ($p < 0.01$) and lymph node ($p < 0.01$) weight. Cutaneous skin lesions were unaffected by INCB050465 treatment. Splenocyte flow cytometry revealed no reduction in absolute lymphocyte, $CD19^+$ B cell, $CD4^+$ or $CD8^+$ T cell frequencies following INCB050465 treatment. However

INCB050465 reduced the absolute counts of germinal center ($CD19^+GL7^+$) and marginal zone ($CD19^+CD21^+$) B cell subsets. Anti-dsDNA antibodies were abrogated by INCB050465 therapy ($p < 0.0001$).
Conclusion: INCB050465, a selective PI3Kδ inhibitor, was highly efficacious against immune-mediated mechanisms associated with lupus nephritis, but not cutaneous lupus disease manifestations in this preclinical model. Treatment-induced preservation of kidney tissue integrity corresponded to specific B cell subset modulation and autoantibody reduction. Selective PI3Kδ inhibitor treatment did not induce lymphocyte depletion.

REFERENCE:

[1] Grande, et al. Experimental models of lupus nephritis. Contrib Nephrol. 2011; 169:183-97. [2] Chan, et al. The roles of B cells in MRL/lpr murine lupus. Ann N Y Acad Sci. 1997 Apr 5;815:75-87.

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THU0215 IGM ANTIBODIES AGAINST MALONDIALDEHYDE AND PHOSPHORYLCHOLINE IN DIFFERENT SYSTEMIC RHEUMATIC DISEASES

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Background: IgM antibodies against phosphorylcholine (anti-PC) and malondialdehyde (anti-MDA) may have protective properties in cardiovascular or rheumatic diseases including SLE and RA.[1-4] Little is known about their role in other systemic rheumatic conditions.
Objectives: The objective is to compare different rheumatic conditions in relation to these antibodies, and also clinical outcome, with focus on cardiovascular disease. We also aim to characterize them and compare them by use of proteomics.
Methods: IgM anti-PC and anti-MDA was measured using ELISA in patients with SLE (374), RA (354), Mixed connective tissue disease (MCTD, 77), Systemic sclerosis (SSc, 331), Sjögren's syndrome (SjS, 324), primary antiphospholipid syndrome (PAPs, 65), undifferentiated connective tissue disease (UCTD, 118) and 515 matched healthy controls (HC). Cardiovascular score (CV) was broadly defined based on clinical disease symptoms. Anti-PC and anti-MDA peptide/protein characterization were compared using a proteomics de novo sequencing approach. IgM anti-MDA and anti-PC were extracted from total IgM. The proportion of Treg cells was determined by flow cytometry.
Results: The maximal difference between cases and controls was shown for MCTD: significantly lower IgM Anti-PC but not anti-MDA among patients (median 49.3RU/ml vs 70.4 in healthy controls, p(t-test)=0.0037). Low levels (below 25th percentile) of anti-PC but not anti-MDA were significantly more prevalent in MCTD, SLE, SjS and SSc. The IgM anti-PC variable region profiles were distinctly different and also more homologous in their content than anti-MDA. Anti-PC but not anti-MDA were significantly negatively correlated with CV in the whole patient group. In contrast to IgM anti-PC, IgM anti-MDA did not promote polarization of Tregs.
Conclusion: Anti-PC could be a protection marker for MCTD and also for SLE, SjS and SSc while anti-MDA did not differ. anti-PC level is negatively correlated with CV in the patient group cohort. These findings could have both diagnostic and therapeutic implications, one possibility being active or passive immunization with PC.

REFERENCES:

[1] Frostegard J. Immunity, atherosclerosis and cardiovascular disease. BMC Med. 2013;11:117.
[2] Anania C, Gustafsson T, Hua X, Su J, Vikstrom M, de Faire U, Heimburger M, Jogestrand T and Frostegard J. Increased prevalence of vulnerable atherosclerotic plaques and low levels of natural IgM antibodies against phosphorylcholine in patients with systemic lupus erythematosus. Arthritis Res Ther. 2010;12:R214.
[3] Rahman M, Sing S, Golabkesh Z, Fiskesund R, Gustafsson T, Jogestrand T, Frostegård AG, Hafstrom I, Liu A and Frostegård J. IgM antibodies against malondialdehyde and phosphorylcholine are together strong protection markers for atherosclerosis in systemic lupus erythematosus: Regulation and underlying mechanisms. Clin Immunol. 2016;166-167:27-37.
[4] Ajeganova S, Fiskesund R, de Faire U, Hafstrom I and Frostegard J. Effect of biological therapy on levels of atheroprotective antibodies against phosphorylcholine and apolipoproteins in rheumatoid arthritis - a one year study. Clin Exp Rheumatol. 2011;29:942-50.

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THU0216 IGG1 ANTIBODIES AGAINST PHOSPHORYLCHOLINE ARE ASSOCIATED WITH PROTECTION IN SLE AND ATHEROSCLEROSIS: POTENTIAL UNDERLYING MECHANISMS

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Background: IgM antibodies against phosphorylcholine (anti-PC) may be protective in atherosclerosis, cardiovascular disease (CVD) and systemic lupus erythematosus (SLE). Less is known about other anti-PC isotypes and subclasses. In this study, we study the role of IgG1 and IgG2 anti-PC, with focus on atherosclerosis and SLE.
Objectives: To study the role of IgG1 and IgG2 anti-PC, with focus on atherosclerosis and SLE, both in a clinical setting and by experimental studies, where we use our in-house produced monoclonal IgG1 anti-PC.
Methods: We determined IgG1 and IgG2 anti-PC in our SLE cohort study (SLEVIC), among 116 SLE-patients from Karolinska University Hospital Huddinge and 110 population controls matched for age and gender. The level of antibodies was measured by ELISA. For functional studies, we used three of our in-house generated, fully human monoclonal IgG1 anti-PC (A01, D05, E01). Primary human macrophages were derived from peripheral blood. Apoptosis was induced in Jurkat T-cells and pre-incubated with A01, D05, E01 or isotype control IgG1 and effect on phagocytosis by marcophages studied. Anti-PC peptide/protein characterization was determined in anti-PC clones compared to isotype control using a proteomics de novo sequencing approach.
Results: IgG1 but not IgG2 anti-PC levels were higher among SLE patients than controls (p=0.02). IgG1 anti-PC was negatively associated with prevalence of atherosclerotic plaques, below 10^{th}percentile, (OR: 2.48, CI: 0.69-9.00). IgG1 Anti-PC was negatively associated with CVD, SLICC and SLEDAI (OR: 4.74 CI: 1.29-17.39, OR: 2,978 CI: 0.876-10.098, OR: 5.108 CI 1.3 20.067 respectively). Monoclonal D05 had maximum effect on macrophage efferocytosis efficiency, followed by A01 and E01. This is because anti-PC IgG1s bind to phosphorylcholine exposed on apoptotic cells and facilitate the uptake by macrophage. The in-house produced monoclonal antibodies showed differential binding specificity to PC and PC associated neo-epitopes. Peptide analysis showed difference in the CDR3 region of the three anti-PC IgG1 clones which are crucial for recognition of the phosphorylcholine on the apoptotic cell surface and other neo-epitopes.

Conclusion: anti-PC IgG1 is negatively associated with disease activity and atherosclerosis in SLE. One potential underlying mechanism could be increased phagocytosis and clearance of dead cells. Our findings raise the possibility of prevention and/or treatment of SLE (and atherosclerosis) to raise anti-PC levels, by passive or active immunization.

REFERENCES:

[1] Frostegard J. Immunity, atherosclerosis and cardiovascular disease. BMC Med. 2013;11:117.
[2] Anania C, Gustafsson T, Hua X, Su J, Vikstrom M, de Faire U, Heimburger M, Jogestrand T and Frostegard J. Increased prevalence of vulnerable atherosclerotic plaques and low levels of natural IgM antibodies against phosphorylcholine in patients with systemic lupus erythematosus. Arthritis Res Ther. 2010;12:R214.

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THU0217 SERUM THYMIC STROMAL LYMPHOPOIETIN (TSLP) AS A BIOMARKER OF B-CELL LYMPHOPROLIFERATION IN SJÖGREN'S SYNDROME

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Background: Thymic stromal lymphopoietin (TSLP) has been demonstrated to be expressed on salivary glands (SG) biopsies of patients with primary Sjögren's syndrome (pSS), mainly in more advanced degrees of lymphoproliferation and in B-cell MALT lymphoma tissues in pSS (1).
Objectives: To study serum TSLP in a larger number of pSS patients, to confirm its correlation with the already studied tissue expression, and then to investigate a possible role of TSLP not only as a tissue biomarker, but also as a peripheral blood biomarker.
Methods: Serum TSLP levels were assessed by ELISA in sera collected from ninety-one anti-SSA-positive pSS patients (females n=86, 94.5%; mean age 57.2 years, range 25-80), fulfilling the 2016 ACR-EULAR pSS classification criteria, 80 matched healthy blood donors (HBDs) and 21 patients with non-autoimmune sicca syndrome (nSS).
pSS patients were then stratified according to the degree of lymphoproliferation (2), well previously defined by tissue studies in the same patients, as follows: pSS fully benign (fbSS), pSS with myoepithelial sialadenitis (MESA), and pSS B-cell MALT lymphoma (NHL); the difference in serum TSLP levels was studied between these three subgroups.
In addition, prospective serum samples, collected both at the time of MESA diagnosis and later at the time of NHL development in the same patient, were studied in 3 cases.
All the pSS patients were naïve to immunosuppressants, biotechnological drugs, chemotherapies, and were not receiving steroids at the time of sample collection.
The most relevant features of pSS linked to a heavier mucosa-associated lymphoid tissue (MALT) involvement and lymphoproliferation, i.e. persistent parotid swelling and mixed cryoglobulinemia, were recorded, as well as the pathologic evidence of ectopic germinal centres (GCs) in SG biopsy. EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) was calculated for all the pSS patients.
Results: Serum TSLP was significantly higher in pSS (mean 47.19 pg/mL, range 0-324.89) compared to nSS (mean 2.74 pg/mL, range 0-15.9) ($p<0.0001$) and to HBDs controls (mean 0.59 pg/mL, range 0-11.09: very low levels being detected only in 4/80) ($p<0.0001$). The significance was the same ($p<0.0001$) also after excluding NHL pSS patients. Serum TSLP showed a progressive, significant increase from patients with fbSS (n=65; mean 26.54 pg/mL; range 0-75.11) to MESA (n=14; mean 69.72 pg/mL; range 20.62-140.8) (MESA vs fbSS $p<0.0001$) and finally to NHL (n=12; mean 151.96 pg/mL; range 58.16-324.89) (NHL vs fbSS $p<0.0001$; NHL vs MESA $p=0.009$).
In prospective sera, TSLP levels significantly increased in all the 3 pSS patients from MESA to NHL.
pSS patients showing a heavier involvement of MALT, i.e. with persistent parotid swelling, mixed cryoglobulinemia, or GCs in SG biopsy, showed significantly higher TSLP serum levels compared to pSS patients without this heavier MALT involvement.
A significant correlation between higher TSLP serum levels and increasing ESSDAI was finally found ($p<0.0001$).
Conclusion: Serum TSLP could represent a novel biomarker of pSS-related B-cell lymphoproliferation, characterized by a heavier MALT involvement. The validation of the present monocentric results is currently ongoing within the EU HarmonicSS Project.

REFERENCES:

[1] Gandolfo S. et al, Arthritis Rheumatol. 2017; 69 (suppl 10).
[2] De Vita S. et al. Blood Cells Mol Di. 2001;27:757-66.

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THU0218 IDENTIFICATION, VERIFICATION AND VALIDATION OF NEW BIOMARKER CANDIDATES FOR MONITORING ACTIVITY IN PSORIATIC ARTHRITIS AND OTHER IMMUNE-MEDIATED INFLAMMATORY DISEASES (IMIDS)

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Background: Immune-Mediated Inflammatory Diseases (IMIDs) are a group of conditions/diseases characterized by common pathways leading to inflammation, which may result from a dysregulation of the normal immune response. The activity of these diseases is usually measured by the assessment of clinical symptoms.
Objectives: To apply a three-stage proteomic strategy to find plasma biomarkers useful to monitor disease activity in patients three different IMIDs: rheumatoid arthritis (RA), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE).
Methods: A three-stage proteomic strategy was conducted: **1) Discovery stage:** a random selection of 80 plasma samples from patients with different RA activities according to the DAS28, which were classified as low activity (LA, n=40) and high activity (HA, n=40). The analysis was conducted by shotgun mass spectrometry (MS) applying an iTRAQ 8-plex strategy, by nanoLC-MS/MS using three different MS instruments. **2) Verification stage:** a targeted proteomics strategy was used to verify the candidate biomarkers from the screening, using the same 80 samples of this first stage. This analysis was performed by Multiple Reaction Monitoring (MRM) with the aid of synthetic heavy-labelled peptides, by nanoLC-MS/MS in an ESI-QTRAP 5500. **3) Validation stage:** ELISA experiments were performed to confirm the previous results on an independent set of plasma samples from patients with RA (n=170), PsA (n=80) and SLE (n=80).
Results: 1) Discovery stage: The MS analysis led to the identification of 186 proteins. A panel of 9 proteins was identified as candidate biomarkers for disease activity monitoring in RA. Most of these proteins are related with the pathogenic process and the effects caused by this type of disease (inflammation and immune disorder in joints). **2) Verification stage:** four from the 9 proteins (SAA1, AACT, HPT, A1AG1) were found to be quantitatively altered between patients with extreme disease activities ($p<0.05$). All these proteins were up-regulated in patients with HA. **3) Validation stage:** as shown in the top row of the Figure, serum amyloid 1 (SAA1), alpha-1-antichymotrypsin (AACT) and haptoglobin (HPT) are higher in the three IMIDs compared to healthy controls, being the highest in RA. Regarding their levels in patients with different disease activities, they are all increased in the plasma of HA individuals compared to LA (bottom row). Interestingly, the levels of these 3 proteins are associated with the activity of PsA: HPT ($p<0.0001$), SAA ($p=0.0209$) and AACT ($p=0.0418$), showing a potential utility for the molecular monitoring of this disease.
Conclusion: Using a three-stage proteomic strategy, we have identified HPT, SAA1 and AACT as protein biomarker candidates for monitoring PsA activity.
Disclosure of Interests: Lucia Gonzalez Rodriguez: None declared, Valentina Calamia: None declared, Rocío Paz González: None declared,

Patricia Fernández Puente: None declared, Cristina Ruiz-Romero: None declared, Juan D. Cañete: None declared, Antonio Julià: None declared, Antonio Fernández Nebro: None declared, Jesús Tornero: None declared, Sara Marsal: None declared, Francisco J. Blanco Consultant for: AbbVie, Bioiberica, BMS, GSK, Grünenthal, Janssen, Lilly, Pfizer, Regeneron, Roche, Sanofi, TRB Chemedica, and UCB

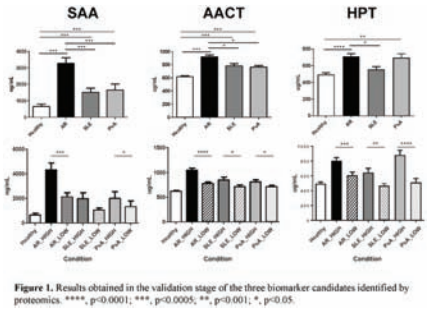


Figure 1. Results obtained in the validation stage of the three biomarker candidates identified by proteomics. ****, p<0.0001; ***, p<0.0005; **, p<0.001; *, p<0.05.

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THU0219 THE INVOLVEMENT OF MITOCHONDRIAL ACTIVATION VIA GLUTAMINOLYSIS IN HUMAN B CELL DIFFERENTIATION AND ITS RELEVANCE TO THE PATHOGENESIS OF SLE

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Background: B cells play a crucial role in Systemic Lupus Erythematosus (SLE). Recently, "Immunometabolism" attract much attention. Glucose and glutamine are important nutrition for energy production such as ATP in various cells. It has been reported that aerobic glycolysis, glutaminolysis and mitchondrial functions enhanced in cancer cells. However, the involvement of metabolic reprograming in plasmablast differentiation and its relevance to the pathogenesis of SLE remained elusive.

Objectives: We first investigated the abnormality of mitochondria in B cells from patients with SLE by flow cytometry. Next, B cells were isolated from healthy donors (HDs) and metabolic reprograming were assessed in vitro.

Methods: First, peripheral blood mononuclear cells (PBMCs) were obtained from age-matched 31 HDs and 29 patients with SLE. The mitochondrial membrane potential was measured with DiOc6 by flow cytometry. In addition, $CD19^+$ cells were isolated from HDs and stimulated with CpG (TLR9 ligand) and IFN-α. Change of aerobic glycolysis, glutaminolysis and mitochondrial functions were assessed in the absence of glucose or glutamine and in the addition of metformine, which is known as AMPK activator, in vitro.

Results: We first examined the abnormality of mitochondria in B cells from patients with SLE using DiOc6 as a marker of depolarization-activated mitochondrial membrane. Baseline characteristics of SLE were males: females=1:28, age 40.2 years, disease duration 132.2 months, SLEDAI 6.4 and BILAG 6.2 at the timing of admission due to exacerbation of SLE. The percentage of IgD^-CD27^- memory B cells were higher than those of HDs, while the percentage of IgM memory B cells were lower than that of HDs. The percentage of $CD24^-DiOc6^+$ cells in IgD^-CD27^- memory B cells from patients with SLE were higher than that of HDs. These results indicate that B cells from patients with SLE have the abnormality of differentiation and mitochondrial functions. Next, we assessed the change of aerobic glycolysis, mitochondrial functions and glutaminolysis in the process of plasmablast differentiation in vitro. Stimulation with CpG and IFN-α, 1) enhanced aerobic glycolysis, which was assessed by lactate production. 2) increased the area of cytoplasm including many expanded mitochondrial cristae with slightly wider and loosely organized intermembrane space in electric microscopy, accompanied with ROS production and DiOc6 up-regulation, 3) induced $CD27^{hi}CD38^{hi}$ plasmablasts differentiation and immunoglobulin production. Lactate production was decreased in the absence of both glucose or glutamine. ROS production and DiOc6 expression were decreased in the absence of glutamine, leading to inhibition of plasmablasts differentiation and immunoglobulin production. On the other hand, this tendency was not shown in the absence of glucose. Next, we evaluated oxygen consumption rate (OCR). OCR was also suppressed in the absence of glutamine. Metformin, abrogated glutamine uptake, resulting in suppression of ROS production, DiOc6 expression, plasmablast differentiation and immunoglobulin production.

Conclusion: These results suggest that mitochondrial activation via glutaminolysis may play an important role in the differentiation from IgD^-CD27^- double negative B cells to plasmablasts and production of immunoglobulins in patients with SLE.

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THU0220 PEPTIDYLARGININE DEIMINASE 4 DEFICIENCY AMELIORATED A MURINE MODEL OF LUPUS BY REDUCING NEUTROPHIL MIGRATION TO THE KIDNEY

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Background: Peptidylarginine deiminase 4 (PADI4) is reported to play several biological roles in neutrophils, including neutrophil extracellular trap formation, apoptosis, and epigenetic regulation. Neutrophils could play pivotal roles in the pathogenesis of SLE.

Objectives: We set to determine the pathological role of neutrophils and PADI4 in SLE using *Padi4* knock out (KO) mice.

Methods: A murine model of imiquimod (IMQ)-induced lupus was analyzed. A TLR7 agonist, IMQ, was administered topically to the ear skin of B6 wild-type (WT) and *Padi4* KO mice. Proteinuria, spleen weight, serum anti-dsDNA level, frequencies of spleen and renal immune cells, and the histopathological findings of ear skin and kidney, were assessed. Neutrophil migration and adhesion were evaluated by adoptive transfer experiments *in vivo*, and adherence assays *in vitro*.

Results: Compared with IMQ-treated WT (WT-IMQ) mice, *Padi4* KO-IMQ mice showed decreased spleen weight. Moreover, proteinuria, and dermatitis were not exacerbated in the *Padi4* KO-IMQ mice. There was a positive correlation between the frequency of kidney neutrophils and the degree of proteinuria, while significant decreases in kidney neutrophils were noted in the *Padi4* KO-IMQ mice. Notably, the elevation of serum anti-dsDNA levels, or the degree of immune complex deposition in the kidney, showed no significant difference between the WT-IMQ and *Padi4* KO-IMQ mice. In the adoptive transfer experiment, there was a significant decrease in the transferred *Padi4* KO neutrophil infiltrations in the kidney compared with those of WT neutrophils. The frequency of adhesive neutrophils toward ICAM-1 was significantly decreased in the *Padi4* KO neutrophils primed by the TLR7 agonist.

Conclusion: Nephritis was ameliorated in *Padi4* KO-IMQ mice. Our study shed light on the importance of neutrophils in the pathogenesis of SLE, and the suppression of neutrophil function by inhibition of PADI4 will be a unique therapeutic strategy for SLE.

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Chugai, Eisai, Taisho Toyama, UCB, Janssen, Eli Lilly, and NIPPON KAYAKU., Speakers bureau: Astellas, BMS, Daiichi-Sankyo, Mitsubishi Tanabe, Pfizer, Ayumi, Takeda, Chugai, Eisai, Taisho Toyama, UCB, Janssen, Eli Lilly, and NIPPON KAYAKU.
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THU0221 DRY EYE IN SJÖGREN'S SYNDROME: CHEMOKINE AND CYTOKINE TEAR SPECTRUM

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Background: Previous studies have linked the participation of multiple chemokines and cytokines in the physiopathology of primary Sjögren's syndrome (PSS), however data regarding their presence in tears is scarce
Objectives: To evaluate a panel of chemokines/cytokines in the tears of patients with PSS and correlate them with ocular symptoms as well as objective ocular tests.
Methods: We included 21 patients with PSS (EULAR/ACR criteria). A single expert ophthalmologist in dry eye evaluated the patients and assessed the tear film break-up time, Schirmer-I test, tear meniscus height, the *Van Bijsterveld* staining score and the SICCA Ocular Staining Score (OSS). We classified lacrimal dysfunction severity in two categories (1=mild, mild/moderate or moderate, and 2= moderate/severe and severe). We scored the ESSPRI, and ocular dryness VAS as well as the Ocular Surface Disease Index (OSDI), a 12-item scale for the assessment of symptoms related to dry eye disease and their effect on vision. Tear samples were collected using sterile tear flow strips, that were immediately frozen at -86°C until assayed. Once defrosted, the tears were extracted from the strips using a buffer containing 0.5 M NaCl and 0.5% Tween-20. We tested IFN-γ, IL-10, IL-12, IL-17A, IL-1β, IL-2, IL-21, IL-23, IL-5, IL-6, IL-8, TNF-α, BAFF, CXCL10 and CCL2 by Luminometry. We also included 21 healthy controls without dry eye, to test chemokines/cytokines that after our initial screening were meaningful.
Results: Most patients were females (90.4%), mean age 59.3±13 years and median disease duration 7.9 years (0.5-27). All of them had ocular and oral symptoms. The median tear film break-up time was 6 seconds (2-9), median Schirmer-I test 6 mm (1-25), median lacrimal meniscus height 1.5 mm (0.5-2), median Van Bijsterveld staining score 10 points (2-18), median OSS 7 points (2-11), median ESPPRI score 6.7 points (2-9.2) and median ocular dryness EVA score 9 points (1-10).
We did not detect most of the evaluated chemokines/cytokines with the exception of IL-8, CXCL10, and CCL2. The former was similar in both, patients and controls. PSS patients had lower levels of CXCL10 (472.8 pg/µL vs 1652 pg/µL, p=0.01) and CCL2 (1.08 pg/µL vs 9 pg/µL) than controls. Indeed, patients with worst lacrimal dysfunction severity had the lowest levels of CXCL10 (239.3 pg/µL vs. 646.2 pg/µL, p=0.02). We found correlations among CXCL10 and CCL2 (T=0.30, p=0.02) and lacrimal meniscus height (T=0.55, p=0.005), as well as with CCL2 and lacrimal meniscus height (T=0-57, p=0.01). None of the other variables were correlated.
Conclusion: We identified CXCL10 and CCL2 as the main chemokines in tears of patients with PSS. CXCL10 seems to participate in the normal eye homeostasis.
Disclosure of Interests: None declared
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THU0222 PLASMACYTOID DCS FROM PATIENTS WITH SJÖGREN'S SYNDROME ARE TRANSCRIPTIONALLY PRIMED FOR ENHANCED PRO-INFLAMMATORY CYTOKINE PRODUCTION

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Background: Type-I IFN activity is associated with pathogenesis and increased disease activity in primary Sjögren's syndrome (pSS). In addition, deficiency for the type-I IFN receptor in mice prevents experimental-Sjögren's syndrome. Plasmacytoid dendritic cells (pDC) are the premier type-I IFN producing immune cells and aberrances in their functional properties may underlie pSS immunopathology. Assessing the molecular basis of this may provide a better understanding of pSS pathogenesis and new opportunities for therapeutic intervention.
Objectives: To delineate the dysregulation of pSS pDCs using RNA-sequencing and compare their transcriptional profile to pDCs obtained from patients with non-Sjögren's sicca (nSS) and healthy controls (HC).
Methods: All pSS patients met the classification criteria. nSS patients presented with dryness complaints without a known cause, did not have any generalized autoimmune disease including pSS as evaluated by an experienced rheumatologist, and did not fulfil the classification criteria. pSS (n=25), nSS (n=20), and HC (n=17) donors were included in two independent cohorts (n=31 each). Circulating BDCA-4 expressing pDCs were isolated and RNA-sequencing was performed, after which data-driven networks and modular analysis were used to identify signatures of consistently differentially-expressed genes. pSS and HC pDCs were cultured in the presence of endosomal TLR ligands, after which gene expression and secreted cytokine levels were measured.
Results: We identified signatures of consistently co-expressed and differentially expressed genes that indicated transcriptional activation in patient pDCs, which was remarkably reproducible in two independent cohorts. These included a type-I IFN-associated signature, a ribosomal protein signature, and a transcriptional machinery signature. Corroborating the transcriptomic profile, stimulated pSS pDCs produced higher levels of type-I interferon upon *in vitro* stimulation. nSS patients formed an intermediate group in which some patients were molecularly similar to pSS patients. Finally, we developed a discriminative classifier on the basis of the identified transcriptional profiles that discriminated pSS patients from HC with 100% sensitivity and 80% specificity, and identified a group of pSS-like patients within the nSS group.
Conclusion: Circulating pSS pDCs exhibit a transcriptional signature similar to activated pDCs and are primed for enhanced production of pro-inflammatory cytokines, including type-I IFN. Our data provide in-depth characterization of the aberrant regulation of pSS pDCs and substantiate their perceived role in the immunopathology of pSS and other type-I interferon-associated autoimmune diseases.
Disclosure of Interests: None declared
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THU0223 CHRONIC ADRENERGIC STIMULATION OF MINOR SALIVARY GLANDS OF PATIENTSWITH PRIMARY SJÖGREN'S DRIVES ER STRESS AND ACTIVATION OF THE UNFOLDED PROTEIN RESPONSE

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Background: Sjögren's syndrome (SS) is a common autoimmune disease in which the main targets of immune injury are specific secretory epithelia, such as salivary and lacrimal glands. Stress appears to play a significant role in the initiation of this entity.
Objectives: The aim of the present study was to investigate whether chronic stress plays a role in triggering endoplasmic reticulum (ER) stress in salivary gland epithelial cells from SS patients.
Methods: Minor salivary gland biopsy specimens were obtained from six SS patients and six control patients with sicca symptoms not fulfilling AECG criteria [1]. The expression and cellular localization of β1-, β2- and α1-adrenoceptors and the levels of cAMP were measured by immunofluorescence. The morphology of the ER was evaluated *in situ* by Transmission Electron Microscopy (TEM). Primary salivary gland epithelial cell lines (SGEC) derived from minor salivary gland biopsies, were established by the explant out-growth technique [2] and were treated with epinephrine and norepinephrine. The protein levels of the ER stress markers GRP78/Bip and C/EBP homologous protein (CHOP) were determined by immunoblot analysis.
Results: *In situ* immunofluorescence staining revealed increased expression of β1-, β2- and α1 adrenoceptors as well as cAMP levels in tissues derived from SS patients compared to controls. TEM evaluation of salivary tissues from SS subjects revealed extensive dilation of the ER lumen compared to controls. Treatment of SGEC with epinephrine and norepinephrine did not influence cell survival (cell viability assay). To mimic chronic stress *in vitro*, epinephrine was applied for 10 days on SGEC. It was found that 20µM Epinephrine induced severe ER stress on SGEC, as attested by increased expression of GRP78/Bip and CHOP, after 3 and 6 days of treatment. The expression of ER stress markers returned to basal levels after 10 days of treatment.

Conclusion: Our data revealed that adrenergic receptors are differentially expressed by salivary epithelium of SS patients compared to control tissues. This finding was further substantiated by the increased levels of cAMP, indicating a profound sympathetic stimulation of this secretory tissue. The dilatated ER lumen of the salivary gland epithelial cells from SS patients confirmed the occurrence of ER stress. Moreover, the finding that catecholamines induce severe ER stress *in vitro* in SGEC under conditions resembling chronic stress suggests a causal relationship between sympathetic tone and ER stress. Deciphering the role of chronic stress in ER machinery will provide important insights that may lead to novel therapeutic targets for SS.

REFERENCES:

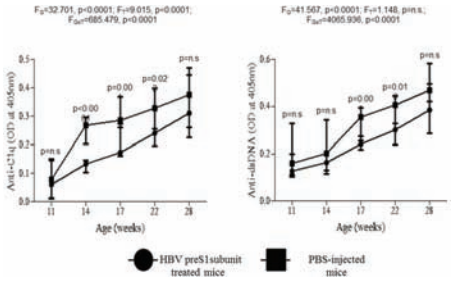
[1] Vitali C, et al. Ann Rheum Dis 2002; 61:554–8.
[2] Kapsogeorgou EK, et al. J Immunol 2001; 166:3107–13.

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Disclosure of Interests: None declared
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THU0224 THE HEPATITIS VIRUS PRES1 PROTEIN RETARDS THE ONSET OF LUPUS-LIKE GLOMERULONEPHRITIS IN NZB/W F1 MICE

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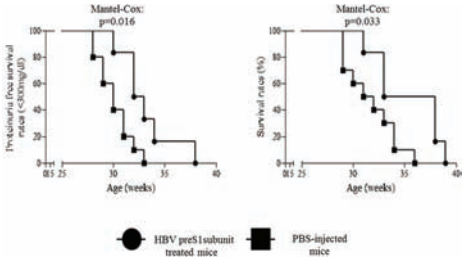
Background: Infection can trigger autoimmunity but the nature of the pathogen could enhance or inhibit the onset of the disease. In this study we tested the tolerogenic effect of the surface Hepatitis B Virus capside protein preS1 in a lupus mouse model.
Objectives: To evaluate the effect of administration of Hepatitis B virus preS1 subunit to NZB/WF1 mice
Methods: Mice (10 each group) were injected with a total volume of 200µl of 32.5 µg PreS1 in 200µl PBS (group 1), 200µl PBS (group 2), 3 times at 11th, 14th and 17th weeks of age. Urine samples were collected weekly to evaluate proteinuria by reactive strips. Blood samples were collected before every injection, at 22th and 28th weeks, and at death to evaluate levels of anti-C1q and anti-dsDNA by home-made ELISA tests. Tissues were harvested for histological analyses. Proteinuria free and survival rates were analyzed by Kaplan-Meier method using Mantel-Cox test for comparisons. Neurocognitive functions were evaluated with Staircase, Y-Maze and Forced Swim Test.



Abstract THU0224 – Figure 1

Results: Anti-dsDNA and Anti-C1q levels (OD±SD) were significantly higher in PBS than in preS1 treated mice (Figure 1). Mean proteinuria levels (mg/dl±SD) were higher in PBS than in preS1 treated mice. Proteinuria free survival rate (<300 mg/dl) was lower in group 2 than group 1 (p=0.016; Figure 2). Also survival rate was significantly lower in PBS than in preS1 injected mice (p=0.033). Memory deficits (p<0.01) and anxiety-like behavior was pronounced in PBS treated mice.
Severe segmental and focal glomerulonephritis in both groups with large proliferation of mesangial and endothelial cells and Russell bodies were found by histological analysis. Mice treated with preS1 had more chronic inflammation in the kidneys and extramedullary hematopoiesis in the spleen and liver. Notably, in salivary glands, severe acute inflammation was observed in group 1 and chronic inflammation in group 2.

Conclusion: HBV capsid protein preS1 causes a delay in the onset of lupus-like glomerulonephrits and ameliorates behavioral disorders in NZW/BF1 mice. This peptide seems to induce a tolerizing rather than a pathogenic effect in these autoimmune prone mice models.



Abstract THU0224 – Figure 2

REFERENCES:

[1] F. McKinney et al; *T-cell exhaustion, co-stimulation and clinical outcome in autoimmunity and infection*. Nature 523, 612–616 (2015).
[2] T-cell exhaustion, co-stimulation and clinical outcome in autoimmunity and infection. Nature 523, 612–616 (2015).
[3] D. R. Getts et al, *Virus infection, antiviral immunity, and autoimmunity*. Immunol. Rev. 255, 197–209 (2013)

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THU0225 THE MOLECULAR PROFILING OF MONOCYTES FROM PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME IDENTIFIES SEVERAL NETWORKS RELATED TO THEIR ATHEROTHROMBOTIC STATUS. ROLE OF ANTIPHOSPHOLIPID ANTIBODIES ON MONOCYTE MIRNA SECRETION

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Objectives: 1. To characterize the mRNAs and microRNAs transcriptomes of monocytes, key immune cells in the atherothrombotic pathology of Antiphospholipid Syndrome patients (APS). 2. To evaluate the role of antiphospholipid antibodies (aPL) in the regulation of these processes. 3. To identify and characterize circulating microRNAs secreted by activated monocytes.
Methods: Monocytes from peripheral blood of 40 APS patients and 40 healthy donors were purified by negative immunomagnetic selection. Gene expression microarray (Agilent G4112F platform) and nCounter microRNA expression array (Nanostring) were performed on purified RNA. Functional categorization of altered genes and miRNAs was made using IPA software, and miRNA-mRNA interaction networks showing inverse correlation expression were identified. Genes and miRNAs integrating the networks were validated in the whole APS cohort by RT-PCR, as well as on a set of thrombotic non-autoimmune patients. Predicted miRNA-mRNA interactions were tested by microRNA transfection experiments.
In parallel, a miRNA array in the plasma of those patients was performed, and common deregulated miRNAs between monocytes and plasma were identified. Monocytes isolated from HD were treated in vitro with purified aPLs and the altered gene/miRNA expression induced in monocytes was evaluated. Moreover, the effects of aPLs on the secretion of common deregulated microRNAs in the supernatant of cultured cells were assessed.
Results: Microarray identified 518 altered genes in APS monocytes. Relevant biofunctions on which these genes were involved included hematological and cardiovascular system development and function, inflammatory response, and embryonic development, among others. Gene alterations were validated in the whole cohort, demonstrated to be stable along the time, divergent of the gene profile in monocytes from non-autoimmune thrombotic patients, and associated to thrombotic recurrences and early atherosclerosis. Analysis of miRNA profiles showed altered expression of 22 miRNAs in APS monocytes. Fifty-four genes were inversely correlated and predicted as CVD-related target genes of 19 differentially expressed miRNAs in monocytes. Association of these genes and miRNAs with the

occurrence and type of thrombotic events, obstetric complications and presence of atheroma plaques were demonstrated. Transfection studies further confirmed the relationship between specific miRNAs and their identified target genes. In vitro studies demonstrated the specific modulation of several genes/miRNAs by aPLs. Furthermore, those autoantibodies promoted the increase in several secreted miRNAs, found simultaneously altered in plasma and monocytes, and deeply involved in the development of inflammation and cardiovascular disease.

Conclusion: 1. Gene and microRNA expression profiles allowed the identification of relevant genes and pathways altered in monocytes and plasma of APS patients, associated with the pathogenesis of the disease and modulated, at least partially, by aPLs. 2. Specific microRNA-miRNA regulatory networks control the biological processes and factors related to the CV pathology in APS. 3. aPL antibodies induce the secretion by monocytes of specific microRNAs that might act as messengers in the bloodstream to propagate their deleterious effects.

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THU0226 DOES THE PRESENCE OF CLASSIC AND NOVEL ANTIPHOSPHOLIPID ANTIBODIES INFLUENCE THE RISK OF THROMBOSIS DEVELOPMENT IN PATIENTS WITH UTERINE MALIGNANCIES?

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Background: Patients with uterine malignancies (UM) are at a higher risk of venous thromboembolism (VTE) than the general population. The malignancy itself, the treatment modalities including medication, surgery and also increased levels of leukocytes, platelets, and tissue factor-positive microvesicles contribute to the risk of developing VTE.

Objectives: Several authors have shown that the antiphospholipid antibodies (aPLs) can be detected in peripheral blood of patients (pts) with malignancies. However, whether or not the aPLs could induce thrombosis in pts with UM is not yet known.

The aim of our study was to determine whether the presence of aPLs in patients with **uterine malignancies** is associated with higher VTE risk than in pts with **non-cancer gynecological disorders (NCGD).**

Methods: The study involved 151 female pts scheduled for gynecological surgery divided into two groups:

Group I with UM (70 pts) confirmed by histopathological examination after surgery; group II with non-cancer gynecological disorders (NCGD) (81pts). The presence of aPLs was detected in patients' serum before surgery using the commercially available test aPL-immunodot assay Anti-Phospholipid 10 Dot, for the qualitative detection of IgG or IgM antibodies. The statistical data analysis was performed using Statistica v13.0.

The following aPLs were assessed in the study groups: IgM and IgG of a- cardiolipin; a-phosphatidic acid; a-phosphatidylcholine; a-phosphatidylethanolamine; a- phosphatidylglycerol; a-phosphatidylinositol; a-phosphatidylserine; a-annexin V; a-ß 2-GP I and a-prothrombin.

Results: The VTE occurred significantly more frequently in pts with UM, compared to pts with NCGD.

In UM group VTE was diagnosed before surgery in 9/70 (12.9%) pts; in NCGD group VTE was diagnosed in 3/81 (3.7%) pts, p=0.0001.

We have obtained positive test results for classic and novel aPLs significantly more frequently in group I pts with UM (mainly a-ß 2-GP I IgM and IgG; a-prothrombin IgM, a-annexin V IgM) than in group-II NCGD pts. The positive test for classic or novel aPLs was detected in 17/70 pts with UM (24,3%) and in 6/81 pts with NCGD (7.4%). The differences were statistically significant (p=0.003). All pts with thrombosis in group I (9 pts UM) were positive for at least 3 aPls (a-ß 2-GP I IgM and IgG; a-prothrombin IgM, a-annexin V IgM).

Conclusion: The classic and novel aPLs are found more frequently in pts with uterine malignancies than in pts with **non-cancer gynecological disorders**. The higher risk of thrombosis is connected with malignancy and the presence of classic and novel aPLs.

The better understanding of the relationships between thrombosis in cancer patients and its immunological determinants (presence of aPLs) may lead to reducing the morbidity and mortality associated with thrombosis in cancer and non-cancer **gynecological disorders.** We suggest that aPLs could be a novel biomarker of thrombosis risk in gynecological malignancies.

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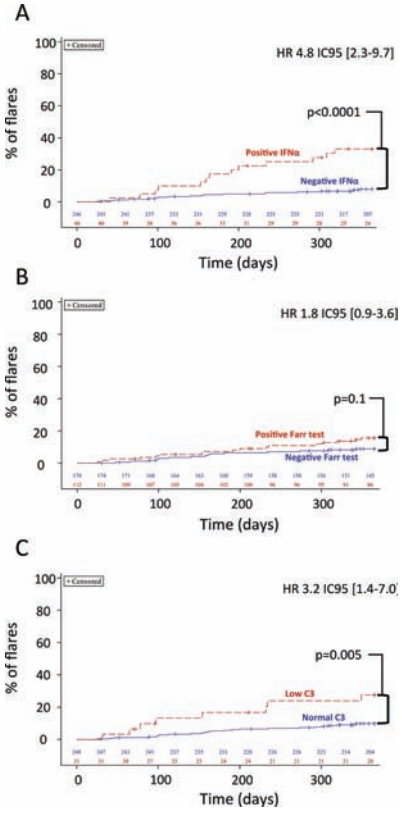
THU0227 BIOLOGICAL MONITORING OF REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS: ABNORMAL SERUM INTERFERON-ALPHA LEVELS PREDICT RELAPSE

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Background: Remission and relapses prevention are the main objectives of the treatment of Systemic Lupus Erythematosus (SLE). Interferon alpha (IFNα) is a key cytokine in SLE, but its usefulness for the definition of remission and for the prediction of flare has not been validated in clinical practice.

Objectives: To study the association between serum IFNα level, remission and risk of relapse.

Methods: 502 SLE patients were assessed for serum IFNα level using a biological functional assay(1). Remission was defined by the absence of clinical manifestation of lupus activity (clinical SELENA-SLEDAI = 0) and a prednisone intake ≤ 5 mg/day(2). Patients in remission were subsequently followed for one year. The SELENA-SLEDAI Flare Index was used to identify SLE flare. Uni- and multivariable analyses were performed to define disease parameters associated with serum IFNα positivity in patients in remission at baseline. Survival curve analysis, log-rank tests and Hazard Ratios (HR) were calculated to evaluate the risk of flare depending on IFNα, dsDNA Abs and C3 levels at baseline.



Abstract THU0227 – Figure 1

Results: 345 samples were obtained from patients in remission. 28.6% of the patients in *clinical remission on treatment* (requiring clinical SELENA-SLEDAI = 0, positive anti-dsDNA antibodies and/or C3 decrease and prednisone intake 1 – 5 mg/day) had an abnormal serum IFNα level, compared to 6.5% of the patients in *complete remission on treatment* (requiring clinical SELENA-SLEDAI = 0, no anti-dsDNA antibodies nor C3 decrease and prednisone intake 1 – 5 mg/day). In patients in remission, high serum IFNα levels at baseline were associated in multivariable analysis with the positivity of anti-dsDNA Abs (HR 3.4 [95%CI 1.6-7.2], p=0.0001) and anti-RNP Abs (HR 3.2 [95%CI 1.5-6.8], p=0.0002). In patients in remission, high serum IFNα level at baseline was a significant and independent risk factor of lupus flare (HR=4.8 [95%CI 2.3-9.7], p<0.0001). Low C3 was also associated with the risk of relapse with a HR=3.2 [95%CI 1.4-7.0], p=0.005, but positive anti-dsDNA Abs was not (HR=1.8 [95%CI 0.9-3.6], p=0.1).**Conclusion:** A large number of SLE patients in remission display abnormal levels of serum IFNα. Abnormal levels of serum IFNα in patients in remission were significantly associated with positive anti-dsDNA and anti-RNP Abs and were an independent predictive biomarker of lupus flare in the following year. Adding serum IFNα to the routine laboratory assessments perform in patient in remission could help clinicians to identify a subgroup of SLE patient clinically in remission but serologically active and at higher risk of relapse.

REFERENCES:

[1] Mathian A, et al. Monitoring disease activity in systemic lupus erythematosus with single-molecule array digital ELISA quantification of serum interferon-α. Arthritis Rheumatol Hoboken NJ. 2018 Dec 3;

[2] Vollenhoven R, et al. A framework for remission in SLE: consensus findings from a large international task force on definitions of remission in SLE (DORIS). Ann Rheum Dis. 2017 Mar 1;76(3):554–61.

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THU0228 EXPRESSION OF APOBEC FAMILY MEMBERS AS REGULATORS OF ENDOGENOUS RETROELEMENTS AND MALIGNANCY IN SYSTEMIC LUPUS ERYTHEMATOSUS AND SJÖGREN'S SYNDROME

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Background: Activation of type I and II interferon (IFN) pathways contributes to the pathogenesis of systemic autoimmune diseases. We have previously shown increased expression of the LINE-1 (L1) endogenous retrotransposon in systemic lupus erythematosus (SLE) kidneys and in minor salivary glands (MSG) from primary Sjögren's syndrome patients (SS) that strongly correlates with IFNα expression in the same tissues. Moreover, an imbalance between type I and II IFNs in SS salivary gland tissues has been related to non-Hodgkin's lymphoma (NHL) development. Members of a family of retroviral resistance factors (APOBECs) have been implicated in L1 control and are regulated by both type I and II IFNs.
Objectives: We investigated whether these mechanisms are involved in the response to inappropriate expression of L1 retroelements in primary SS and SLE, as well as in SS related lymphomagenesis.
Methods: MSG and kidney biopsy specimens were obtained from 41 patients with primary SS and 23 patients with SLE, respectively. Peripheral blood mononuclear cells (PBMC) and sera were also collected from 73 SLE patients. Relative mRNA expression was quantified by real-time polymerase chain reaction for full-length L1 transcripts, along with members of the APOBEC family [APOBEC3A, APOBEC3B, APOBEC3G, AID (activation-induced cytidine deaminase)] and IFNα and γ transcripts. Type I IFN activity was assessed in lupus plasma by a reporter cell assay. The induction of APOBEC3A and B by IFNα in healthy control PBMCs was also assessed.
Results: APOBEC3A, previously implicated in control of endogenous retroelements, was increased in SS MSG and lupus nephritis kidney tissues and in SLE PBMC and strongly correlated with L1 retroelement expression in both SS and SLE tissues. APOBEC3A was also associated with IFNα mRNA expression in SS MSG tissues and lupus kidneys and with type I IFN activity in lupus plasma. While APOBEC3A expression was induced by IFNα, such a relationship was not observed with APOBEC3B. Moreover, a strong correlation was detected between AID and APOBEC3G with IFNγ expression in SS MSG tissue, a relationship particularly relevant to development of NHL.
Conclusion: Increased expression of APOBEC3A reflects a host-intrinsic and IFNα-dependent mechanism regulating potentially harmful L1 retroelements in patients with SS and SLE. Moreover, IFNγ-related induction of APOBEC3G, together with AID, might contribute to SS-related lymphomagenesis by increasing mutational load or epigenetic alterations. These data reveal a previously unappreciated role of APOBEC family proteins in the pathogenesis of autoimmune disorders.
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THU0229 AMPHIREGULIN ATTENUATES LUPUS NEPHRITIS VIA SUPPRESSION OF PRO-INFLAMMATORY T-CELL FUNCTIONS IN AN ANIMAL MODEL OF SLE

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Background: Amphiregulin (AREG) is a member of the epidermal growth factor (EGF) family and plays a role in development, tissue homeostasis and tumorigenesis. Recently, however, AREG has also emerged as novel player in immunity. Interestingly, AREG expression was shown to be one of the most highly upregulated transcripts in peripheral blood leukocytes of patient with systemic lupus erythematosus (SLE) [1]. The functional role of AREG in SLE, and inflammation in general, remains unclear to date and both, pro- and anti-inflammatory functions have been postulated [2, 3].
Objectives: Our aim was to investigate the role of AREG in the mouse model of pristane induced lupus (PIL) with particular focus on lupus nephritis (LN). We further wanted to identify target cells and mechanisms by which AREG exerts its immunomodulatory effects.
Methods: PIL was induced in AREG knock-out (KO) mice and wild type controls. Animals were sacrificed at pre-specified time points. Renal histology, immune complex deposition, leukocyte influx and mRNA expression levels were analyzed. Furthermore, broad in vivo and in vitro analyses of renal and systemic immune responses were carried out.
Results: Renal AREG mRNA expression significantly increased during development of LN, indicating functional relevance. Indeed, lupus nephritis was significantly aggravated in AREG-KO mice both at early (9 months) and later (12 months) stages after PIL induction. In line with this, we noted an increased deposition of immune complexes and renal influx of pro-inflammatory leukocytes ($CD3^+$ T-cells, macrophages and neutrophils). In addition, we found the $CD4^+$ T-cells of AREG-KO mice to have a more pro-inflammatory phenotype with significantly increased production of pro-inflammatory cytokines (IFNγ and IL-17A) both in ex-vivo culture, as well as FACS-analyses of nephritic kidneys. Mechanistically, we found that AREG treatment of spleen cell cultures potently suppressed cytokine production. More detailed evaluation by further in-vitro studies indicated, that AREG can directly suppress cytokine production by effector $CD4^+$ T-cells as well as enhance the suppressive capacity of $FoxP3^+$ regulatory T-cells (Tregs).
Conclusion: These data show that AREG has a protective role on development of LN induced by pristane, which might be therapeutically exploited. Our results further suggest, that direct effects on $CD4^+$ T-effector cells, as well as indirect effects via Tregs, are two mechanisms by which AREG exerts its protective role.

REFERENCES:

[1] Ishii, T., et al., *Isolation and expression profiling of genes upregulated in the peripheral blood cells of systemic lupus erythematosus patients.* DNA Res, 2005. 12(6): p. 429-39.

[2] Kefaloyianni, E., et al., *ADAM17 substrate release in proximal tubule drives kidney fibrosis.* JCI Insight, 2016. 1(13).

[3] Zaiss, D.M., et al., *Amphiregulin enhances regulatory T cell-suppressive function via the epidermal growth factor receptor.* Immunity, 2013. 38(2): p. 275-84.

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THU0230 TNF-ALPHA PROMOTER POLYMORPHISMS (G-308A AND G-238A) ARE ASSOCIATED WITH SUSCEPTIBILITY TO SLE: A HOSPITAL-BASED CASE-CONTROL INVESTIGATION

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Background: Tumour necrosis factor-α (TNF-α) is a proinflammatory cytokine associated with various autoimmune disorders[1]. High levels of TNF-α has been reported in systemic lupus erythematosus (SLE)[2]. Two functional common polymorphisms (G-238A and G-308A) at promoter region of TNF-α gene have been linked to SLE susceptibility in different populations[3,4].
Objectives: To investigate association of TNF-α (G-238A and G-308A) polymorphisms with susceptibility/resistance to SLE.
Methods: A total of 102 female SLE patients and 112 age and sex matched healthy controls were enrolled in the study. Patients were examined in detail, physical findings recorded and SLEDAI 2K calculated to assess disease severity. TNF-α polymorphisms (G-238A & G-308A) were typed by polymerase chain reaction and restriction length polymorphism (PCR-RFLP). Plasma level of TNF-α was quantified by ELISA. Statistical analysis was carried out using GRAPH PAD PRISM -7.01.
Results: Mean age of SLE patients and healthy controls was 27.84±8.83 and 29.56±5.48 years, respectively. At the time of enrolment, mean disease duration of patients was 2.07±1.13 years. The mean SLEDAI 2K of patients was 16.07±7.66. The prevalence of heterozygous mutant and minor allele of TNF-α (G-238A) polymorphisms were significantly higher in SLE patients compared to healthy controls (GA: P=0.04, OR=2.16; A: P=0.02, OR: 2.09). Furthermore, heterozygous (GA) and minor allele (A) of TNF-α (G-238A) polymorphism were associated with susceptibility to lupus nephritis (GA: P=0.02, OR=2.89; A: P=0.001, OR: 2.92). SLE patients displayed higher levels of plasma TNF-α compared to healthy controls. Although the prevalence of heterozygous mutant and minor allele of TNF-α (G-308A) polymorphism was higher in SLE patients, it was not statistically significant. TNF-α (G-238A and G-308A) variants were associated with higher plasma TNF-α in both SLE patients and healthy control. However, no significant association was observed on distribution of TNF-α polymorphisms (G-238A and G-308A) with severity of disease activity of SLE patients.
Conclusion: The results of the present study demonstrate that TNF-α (G-238A) variant is associated with higher plasma TNF-α level and increased susceptibility to development of SLE and lupus nephritis.

REFERENCES:

[1] Aggarwal BB, Gupta SC, Kim JH. Historical perspectives on tumor necrosis factor and its superfamily: 25 years later, a golden journey. Blood. 2012;119(3):651–665.
[2] Studnicka-Benke A, Steiner G, Petera P, Smolen JS. Tumour necrosis factor alpha and its soluble receptors parallel clinical disease and autoimmune activity in systemic lupus erythematosus. Br J Rheumatol. 1996;35 (11):1067–1074.
[3] D'Alfonso S, Colombo G, Della Bella S, Scorza R, Momigliano-Richiardi P. Association between polymorphisms in the TNF region and systemic lupus erythematosus in the Italian population. Tissue Antigens 1996;47(6):551–555.
[4] Lee YH, Harley JB, Nath SK. Meta-analysis of TNF-alpha promoter−308 A/G polymorphism and SLE susceptibility. Eur J Hum Genet. 2006;14:364–371.

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THU0231 GELSOLIN A NEW BIOMARKER OF DISEASE ACTIVITY IN SLE PATIENTS ASSOCIATED WITH HDL-C

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Background: Recent proteomics techniques have demonstrated that high-density lipoprotein (HDL) associated proteins are involved in functions related to systemic inflammatory and immune responses in several pathological conditions, including autoimmune diseases. HDL undergoes structural and functional modifications in systemic lupus erythematous (SLE) patients.
Objectives: To identify potential biomarkers of disease activity analyzing the proteome of HDL particles from SLE patients in clinical remission and when they develop a flare compared to a healthy control group.
Methods: Quantitative proteomic analyses of purified HDL were performed using Tandem Mass Tag (TMT) isobaric tag-labeling and nanoLC-Orbitrap (nLC-MS/MS) from 9 SLE patients in clinical remission when they developed a flare and from 9 healthy controls (9-9-9). We verified the identified proteins by Western blot and ELISA in a cohort of 104 SLE women patients, 46 healthy women and 14 SLE patients when developed a flare.
Results: A total of 83 proteins associated with HDL were identified. We found 17 proteins with a significant fold-change (>1.1) compared with their levels in control patients. In lupus patients experiencing a flare compared with those in remission, we identified 4 proteins with a significant fold-change (C4, Indian Hedgehog protein, S100A8 and gelsolin). Plasma Gelsolin (pGSN) levels were decreased in the 104 SLE patients (176.02 (74.9) mcg/l) compared with the control group (217.13(86.7)mcg/l); p =0.005 and when they developed a clinical flare (104.84(41.7)mcg/l); p = 0002). pGSN levels were associated with HDL-c levels (r =0.316, p< 0.001). Antimalarial treated patients showed significant higher levels of pGSN (214.56(88.94)mcg/l respect 170.35(66.36) mcg/l); p = 0.017.
Conclusion: The proteome cargo from HDL differentiates SLE patients from healthy controls. HDL from SLE patients carries proteins that are involved in the activation of the immune system. Decreased pGSN are associated with clinical disease activity in SLE patients. Antimalarial treatment and HDL-c are associated with higher levels of pGSN in SLE patients. pGSN is a potential biomarker of disease activity in SLE patients.

Disclosure of Interests: None declared
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THU0232 DIFFERENTIAL METHYLATION OF IL8 AND TISSUE FACTOR PROMOTER IN ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid syndrome (APS) is an autoimmune thrombophillia characterized by recurrent thromboembolism and/or pregnancy morbidity in the presence of Antiphospholipid antibodies mainly anti-β2glycoprotein I (anti-β2GPI), which lead to monocyte and endothelial cell activation and subsequent tissue factor and proinflammatory cytokine expression such us IL-6 and IL-8 (1). Epigenetics describes changes in gene expression without alterations in the genomic sequence. Methylation of DNA at CpG islands by adding a methyl group to the nucleotide cytosine, is one of main epigenetic mechanisms.
Objectives: To explore the possible differential methylation of IL8 and Tissue Factor (F3)gene promoters, which are critical for the pathophysiology of APS.
Methods: Whole blood and serum were isolated from 27 APS patients and 25 healthy donors (HDs). Human umbilical vein endothelial cells (HUVECs) and peripheral blood monocytes were isolated from 3 HDs. Anti-β2GPI IgG was isolated and pooled from 8 APS patients.HUVECs and monocytes were stimulated with a mixture of IgG, β2GPI and CXCL4.Then mRNA was isolated and qPCR was performed for the assessment of IL8 and tissue factor (F3)gene expression.Whole blood DNA from APS patients and HDs,and DNA from the *in vitro* experiments was isolated and bisulphite treated. The methylation of 1CpG in the

promoter of F3 gene and 1CpG in the promoter of IL8 gene was assessed with Methylation Specific PCR

Results: DNA from APS patients had significantly lower methylation levels in the IL8 promoter compared to HDs (mean: APS 0,6715vs HD1,153, p < 0,0001). Patients with history of arterial thromboembolism had the lowest IL8 methylation levels compared to ones with history of venous thrombosis or pregnancy morbidity, p=0.0003.An inverse correlation was noted between the IL8 methylation levels and the time passed since the last clinical event. APS patients who suffered 3 or more clinical incidents had significantly lower methylation levels.

APS DNA was significantly methylated in the F3 promoter compared to HD (APS 1,902vs HD1,335, p<0,0001). Negative association of F3 methylation was noted with anti-β2GPI, auto-antibody titers and APTT elongation.

HD HUVECs and monocytes stimulated with anti-β2GPI IgG/β2GPI/CXCL4 obtained an activated and procoagulant phenotype. In HUVECs the triple mixture induced an 8fold increase for the SELE gene, 3fold for the IL8, 1.5fold for F3. At the same time 2-fold decreased F3 promoter methylation levels correlated inversely to F3 gene expression (r -0.7679, p=0.0008). No change was noted in the IL8 promoter methylation levels. Treated monocytes had a 40fold increase in the IL8 and 20 fold increase in the F3 gene levels, while methylation of IL-8 and F3 promoter regions was decreased by 2-fold.

HUVECs stimulation resulted in the differential expression of genes involved in DNA epigenetic alterations. Significant difference was observed for MeCP2 (2fold), DNMT3B (2 fold) and HDAC9 genes (3fold), which correlate with theexpression of activation markers of SELE, F3 and IL8.

Conclusion: APS patients expressed decreased relative IL8 methylation levels which associate with arterial clinical events and significantly with more recent events. The mixture of anti-β2GPI IgG-β2GPI-CXCL4 activate HD HUVECs and monocytes to a procoagulant phenotype and decrease methylation in the F3 and IL8 promoters.

REFERENCES:

[1] Allen, K.L., et al., *A novel pathway for human endothelial cell activation by antiphospholipid/anti-beta2 glycoprotein I antibodies*. Blood, 2012. 119(3): p. 884-93.

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THU0233 ASSOCIATION BETWEEN DEMYELINATING DISEASE AND AUTOINMMUNE RHEUMATIC DISEASE. A MULTIDISCIPLINARY EVALUATION

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Background: Multiple sclerosis (MS) and neuromyelitis optica (NMO) are autoimmune disease which target is the mielina of the white substance of CNS. Presents alterations of the white substance observed in MRI, like hyperintense injuries in T2, in brain and/or the spinal cord. These injuries are unspecific; they can appear as regards to arterial hypertension or diabetes, thus the MS diagnosis will be established according to criteria of location and course of these injuries. The systemic autoimmune rheumatic diseases (SARD) may be presented by demyelination areas in the white matter of the brain and spinal cord, which are difficult to differentiate from MS and other demyelinating processes; but although most of CNS pathologic of the SARD are small vessels disease. On the other hand, it has been described in the MS positividad for ANA, antiphospholiped antibodies (aPL) and Anti-Ro52 without SARD evidences that there might reflect a disrregulación of the immune system or a form fruste of associate SARD.

Objectives: 1.To describe the SARD predominance in patients whose the guide sign is the presence of injuries desmielinizantes in CNS. 2 To describe the clinical profile of these patients. 3. To describe the frequency of reumatic antibody posivity in MS.

Methods: Retrospective observational study of patients with CNS demyelinating lesions as a guide sign and clinical-analytical findings suggestive of SARD assessed jointly by the Demyelinating Diseases Unit and and by the Rheumatology Service. MS diagnosis according to McDonald 2010 criteria. Statistical analysis with SPSS 17.0. carried out in the conditions of the usual clinical practice in the Consultations of Rheumatology and Neurology. We analyzed the patients referred from Consultations of Rheumatology to Neurology by finding demyelinating lesions in imaging test or suggestive neurological symptoms. And patients referred fro Consultations of Neurology to Rheumatology by finding clinical or analytical signs of systemic autoimmune rheumatologic disease during the study of a demyelinating lesion. We included patients assessed in Consultations of both services from 1/1/2010 to 31/12/2017.

Results: Of 561 patients evaluated in Demyelinating Diseases Unit, 89 were evaluated also in Rheumatology. 82% were women, with avarage age of start the neurological symptoms at 40.6 years (SD 13.15), the average age at the time of assessment by Rheumatology 42.9 years (SD 12.8). Only 17 (19%) had previous a rheumatology diagnosis: Fibromyalgia 5 (5.6%); SARD 9 (10%). A definitive diagnosis was made in 63 patients (71%), probable 14 (16%) and nonspecific 12 (13.5%). Definitive diagnoses include: MS 32 (35.9%), NMO 4 (4.5%) and SARD 32 (35.9%): Neurosarcoidosis 3, NeuroSjögren 6, NeuroBeçhet 2, Neurolupus 3, aPLS 7 and in the context of UCTD 11. First neurological symptom in the SARD was sensitive decifit 11 (22%). SARD was ruled out in 50 patients (fibromyalgia or degenerative pathology). Patients with definitive diagnosis of MS (32) and positivity for antibodies: ANA requested in 29 patients; positive 46.6%, Anti-Ro52 requested in 28 and all negative.

Conclusion: 1.The multidisciplinary assessment allowed to establish a definitive diagnosis in 71% of the patients. It allowed the new diagnosis of SARD in 55% of patients. 2. The 22% of SARD presented a sensitive deficit as the first neurological symptom. The main symptom suggestive of SARD that manifested the patients with demyelinating lesions were the inflammatory arthralgias, second probable Raynuad phenomenon and third ocular dryness.3. The 46.6% of MS have ANA positive without another sign of SARD.

Distinguishing between an MS and SARD with neurological manifestations is a diagnostic challenge.

Disclosure of Interests: None declared

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THU0234 THE TRANSCRIPTION FACTORS IKAROS (IKZF1) AND AIOLOS (IKZF3) ARE EXPRESSED IN THE SALIVARY GLANDS OF SJÖGREN'S SYNDROME PATIENTS WITH LYMPHOID AGGREGATES AND MODULATE B CELL ACTIVATION IN VITRO

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Background: Polymorphisms of Ikaros (IKZF1) and Aiolos (IKZF3), transcription factors essential for the maturation, differentiation and survival of B cells, have been linked to systemic autoimmunity. The Cereblon modulator iberdomide, known to induce their degradation, is being explored as a therapeutic option in Systemic Lupus Erythematosus (SLE). However, the involvement of Ikaros and Aiolos in other autoimmune diseases is poorly known, and their effects on B cell activation and differentiation in the context of autoimmunity have been only partially described.

Objectives: To evaluate the expression of Ikaros and Aiolos in the salivary glands (SGs) of patients with Sjögren's syndrome (SS) and the effects of Iberdomide on the TLR7-mediated activation of B cells from patients with Sjögren's.

Methods: Immunohistochemical staining for Ikaros and Aiolos was performed on SG biopsies of patients with SS (n=23), classified into Ectopic Lymphoid Structures (ELS) positive (n=12) and negative (n=11) according to the presence of infiltrating B cells (CD20) and T cells (CD3), assessed by immunohistochemistry. SGs of patients with non specific chronic sialoadenitis (NSCS) (n=12) were used as controls. Digital image analysis and automated cell count (QuPath software) were used to calculate the density of Ikaros and Aiolos positive cells, which were correlated with histological and serological markers (SG semiquantitative scores for CD3+ T cells, CD20+ B cells, CD138+ plasmacells;Immunoglobulins; C3, C4) and disease activity (ESSDAI). $CD19^+$ B cells were isolated from the peripheral blood of patients with Sjögren's (n=7) and triggered with the TLR7 ligand Resiquimod, with or without iberdomide (100 nM). After 5 days, cells were analysed by FACS and IgG and IgM in the supernatants were measured by ELISA.

Abstract THU0234 –Table 1.

Table 1. Correlations of Ikaros and Aiolos in the SGs of Sjogren's patients with histological and clinical parameters

		IKAROS	AIOLOS	CD3	CD20	CD138	FOCI	IgA	IgG	IgM	C3	C4	ESDDAI
Spearman's rho	IKAROS	1.000	.511**	.477**	.453**	.150	.417*	.053	.337*	.012	-.137	-.293	.440*
	AIOLOS	.511**	1.000	.577**	.370*	.256	.514**	-.019	.160	.052	.110	.092	.286

**p<0.01 level *p<0.05. n=23 SG=Salivary Glands

Results: The density of Ikaros and Aiolos positive cells was significantly higher in the SGs of ELS positive SS patients compared to NSCS. As shown in Table 1, the density of Ikaros and Aiolos positive cells in the SG of SS patients significantly correlated with B and T cell semiquantitative scores and the number of lymphocytic foci. Ikaros positive cell density also correlated with IgG levels and disease activity measured by ESSDAI. Accordingly, SS patients with high expression of Ikaros (>10 Ikaros$^+$ cells/mm^2, n=11/23) had significantly higher ESSDAI (p=0.023) and higher prevalence of ANA positivity (p=0.019). *In vitro*, iberdomide significantly inhibited the TLR7-mediated production of IgG from Sjögren's B cells (p=0.03) and significantly reduced the number of CD27$^+$CD38$^+$ plasmablasts (p=0.03).

Conclusion: We here show that the transcription factors Ikaros and Aiolos are expressed in the salivary glands of patients with Sjögren's syndrome with ELS. The association of Ikaros with disease severity and autoantibody positivity and the inhibition of B cell activation by iberdomide point to the relevance of these transcription factors in Sjögren's, thus suggesting their potential use as therapeutic targets in patients with Sjögren's and other B cell-mediated autoimmune diseases.

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THU0235 INHIBITION OF EZH2 AMELIORATES LUPUS-LIKE DISEASE IN MRL/LPR MICE

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Background: We previously revealed a role for EZH2 in inducing pro-inflammatory epigenetic changes in lupus CD4+ T cells.

Objectives: In this study, we sought to determine if inhibiting EZH2 ameliorates lupus-like disease in MRL/lpr mice.

Methods: EZH2 expression levels in multiple cell types in lupus patients were evaluated using flow cytometry and mRNA expression data. Inhibition of EZH2 in MRL/lpr mice was achieved by DZNep intraperitoneal administration using a preventative and a therapeutic treatment model. Effects of DZNep on animal survival, anti-dsDNA antibody production, proteinuria, renal histopathology, cytokine production, and T and B cell numbers and percentages were assessed.

Results: EZH2 expression levels were increased in whole blood, neutrophils, monocytes, B cells, and CD4+ T cells in lupus patients. In MRL/*lpr* mice, inhibiting EZH2 with DZNep treatment before or after disease onset improved survival and significantly reduced anti-dsDNA antibody production. DZNep-treated mice displayed a significant reduction in renal involvement, splenomegaly, and lymphadenopathy. Lymphoproliferation and numbers of double-negative T cells were significantly reduced in DZNep treated mice. Concentrations of circulating cytokines and chemokines, including TNF, IFN-γ, CCL2, RANTES/CCL5, IL-10, KC/CXCL1, IL-12, IL-12p40 and MIP-1β/CCL4 were decreased in DZNep treated mice.

Conclusion: EZH2 is upregulated in multiple cell types in lupus patients. Therapeutic inhibition of EZH2 abrogates lupus-like disease in MRL/lpr mice, suggesting that EZH2 inhibitors may be repurposed as a novel therapeutic option in lupus patients.

Disclosure of Interests: None declared

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THU0236 URINARY EXOSOMAL MIR-31, MIR-107 AND MIR-135B-5P FROM TUBULAR RENAL CELLS AS RESPONDER BIOMARKER IN LUPUS NEPHRITIS

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Background: Lupus nephritis (LN), occurring in 40–75% of patients with systemic lupus erythematosus (SLE), continues to be one of the most severe forms of lupus with an unpredictable course. Conventional clinical parameters are not sensitive or specific enough for detecting ongoing disease activity, early relapse, disease progression or response to therapy [1]. Exosomal-derived urinary miRNAs can accurately reflect renal dysfunction and structural damage making them good biomarkers for diagnosis and prognosis [2]. In LN, urinary exosomal miR-29c expression levels have been identified as predictor of early fibrosis [3] and miR-146a upregulation as marker to discriminate active LN [4]. To the best of our knowledge, this is the first screening of miRNAs in urinary exosomes from LN patients to study their role as predictors of response to therapy.

Objectives: Identify a non-invasive miRNA profile predictive of clinical response in LN following standard treatment.

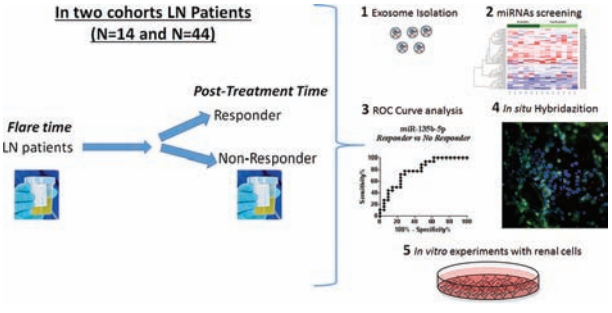
Methods: Urinary exosomes were isolated and characterized from lupus patients (N=14) during flare and post-treatment time. Patients were divided between responder and non-responder and urinary exosomal miRNA screening analysis was performed according their clinical response. To validate initial results, a new cohort of LN patients were used (N=44). *In situ hybridization* of miRNAs in kidney renal biopsies and *in vitro* experiments with human primary renal cells were performed in order to determinate cell origin of exosome production and their delivery cell target (Figure 1).

Results: In the screening, 25 miRNAs were significantly differences in comparative group analysis. High levels of miR-31, miR-107 and miR-135b-5p were confirmed to be related with responder patients. We found that miR-135b has the best profile to distinguish the two groups (AUC= 0.783 (95% confidence interval [CI], 0.640 - 0.926), cut-off <0.0884 with 77.8% sensitivity and 71.4% specificity). Renal tissue samples from responder patients showed miR-31, miR-107 and miR-135b-5p to be highly expressed compared with non-responders. All miRNAs were predominantly localized in the tubular cells. Stimulated tubular renal cells displayed the higher expression levels of exosome-derived miR-31, miR-107 and miR-135b-5p when compared with endothelial or mesangial cells (p<0.0001). Nevertheless, urinary exosomes from non-responder patient's internalization was only of 50% by mesangial cells compared to 90% from responders.

Conclusion: These results indicated that levels of urinary exosomal miRNAs produced by tubular cells might have a renal recovery role in mesangial cells and be used as new biomarkers of lupus nephritis outcome.

REFERENCES:

[1] Adler M, et al. Rheumatology. 2006;45(9):1144–7.
[2] Valadi H, et al. Nat Cell Biol. 2007;9(6):654-U672.
[3] Solé C, et al. Neprol Dial Transplant. 2015. 30(9):1488-96.
[4] Perez-Hernandez J, et al. PLoS One. 2015 10(9):e0138618.



Abstract THU0236 – Figure 1. Methodology Scheme. Urine from two cohorts of LN patients to isolate exosomes, perform miRNAs screening, ROC curve analysis, *in situ* hybridazition and *in vitro* experiments.

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design; collection, analysis, and interpretation of data; writing the report; and the decision to submit the report for publication.
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THU0237 MUSCLE ARCHITECTURE IN PATIENTS WITH SJÖGREN'S SYNDROME

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Background: Although fatigue and skeletal muscle involvement is not rare in Sjögren's Syndrome (SS) patients, there is not much data about the macroscopic structure of the skeletal muscle.
Objectives: 1) To investigate if ultrasonographic muscle architecture and muscle strength differed in SS patients 2) To investigate if these changes correlated with disease activity, fatigue, anxiety and depression.
Methods: Assuming 2.40 mm mean difference and 2.5 mm SD of thickness at vastus lateralis muscle with 80% power and 5% significance 19 SS patients and 19 healthy controls (HCs) were recruited (1). Disease activity was measured by EULAR Sjögren Disease Activity Index (ESSDAI), anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS), fatigue with Multidimensional Assessment of Fatigue scale (MAF), quality of life with Health Assessment Questionnaire (HAQ). A single rheumatologist, blind to the participants' group assignment, performed the ultrasonographic evaluation using a multi-frequency linear probe. Thickness of bilateral quadriceps femoris, gastrocnemius and soleus muscles, pennation angle and fascicle length was measured. Isokinetic knee and ankle muscle strength tests were performed at 60- 180°/s and 30- 120°/s respectively by a calibrated isokinetic testing machine.
Results: Patients with SS scored higher than HCs for depression, anxiety, quality of life and fatigue ($p<0.0001$). At dominant leg, pennation angle of vastus medialis muscle was significantly lower in SS group than HCs (10.263.63 SD deg vs 14.156.36 SD deg, $p=0.049$). At non-dominant leg, pennation angle of gastrocnemius medialis muscle was significantly higher in SS group than HCs (22.894.82 SD vs 19.154.68 SD deg, $p=0.006$). In addition, fascicle length of gastrocnemius medialis muscle was significantly shorter in SS group than HCs (42.2610.33 SD mm vs 49.258.27 SD mm, $p= 0.036$). Peak torque/body weight of knee and ankle muscles in SS group did not differ from that of HCs. However, in SS group, at dominant leg, ESSDAI was negatively correlated with knee extension strength at velocities 60°/s and 180°/s ($r=-0.572$, $p=0.010$; $r=-0.617$, $p=0.05$ respectively), knee flexion strength at 60°/s velocity ($r= -0.492$, $p=0.033$), ankle plantar flexion strength at 30°/s velocity ($r=-0.730$, $p=0.001$). Similarly at non-dominant leg, ESSDAI was negatively correlated with knee extension strength at velocities 60°/s and 180°/s ($r=-0.575$, $p=0.010$, $r=-0.508$, $p=0.026$ respectively) and ankle plantar flexion strength at 30°/s velocity ($r=-0.506$, $p=0.027$). Fatigue was negatively correlated with ankle plantar flexion strength at 120°/s velocity ($r=-0.484$, $p=0.036$) at dominant leg, knee extension strength at 180°/s velocity ($r=-0.521$, $p=0.022$) knee flexion at 60°/s velocity ($r=-0.585$, $p=0.011$) at non-dominant leg. There was no correlation between anxiety, depression and muscle strength.
Conclusion: Patients with SS have some minor structural changes on ultrasonographic evaluation. Although there was no difference in isokinetic muscle strength measurements between groups, knee strength and endurance had a moderate negative correlation with disease activity in SS patients.

REFERENCE:

[1] Kaya A, et al. *Ultrasonographic evaluation of the muscle architecture in patients with systemic lupus erythematosus*. Clin Rheumatol 2013; 32: 1155-1160.

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THU0238 CLINICAL EFFICACY OF LEFLUNOMIDE/ HYDROXYCHLOROQUINE COMBINATION THERAPY IN PRIMARY SJOGREN'S SYNDROME IS PREDICTED BY SERUM PROTEOME BIOMARKERS – RESULTS FROM REPURPSS-I

Joel van Roon, Eefje van der Heijden, Sofie Blokland, Ana Lopes, Frederique Moret, Paco Welsing, Nard Janssen, Toine Rosenberg, Aridaman Pandit, Weiyang Tao, Maarten Hillen, Aike A. Kruize, Timothy R. Radstake. *University Medical Center Utrecht, Utrecht, Netherlands*

Background: Despite major efforts to treat primary Sjogren's syndrome (pSS) advances in pSS treatment remain disappointing. Treatment strategies effective in other immunological conditions lack an effect in pSS. Hence, there is a huge unmet need in finding an effective treatment, let alone to have the ability to predict who responds to what treatment. Based on the unique immunosuppressive properties of leflunomide (LEF) and hydroxychloroquine (HCQ), we recently conducted a randomized, double–blind, placebo-controlled proof of concept study.
Objectives: To evaluate the efficacy, safety and tolerability of LEF/HCQ therapy in patients with pSS and to predict treatment response by molecular profiling using baseline serum proteomics.
Methods: Clinically active (European SS disease activity index ESSDAI score $\geq$5) pSS patients (n=29) were randomized to receive LEF 20 mg daily and HCQ 200 mg twice daily or placebo/placebo (2 verum:1 placebo) for 24 weeks. Clinical and safety outcomes were assessed at baseline, 8, 16 and 24 weeks. Clinical response was defined by a decrease in ESSDAI of $\geq$3 points at 24 weeks. In addition, at baseline 386 proteins involved in inflammation, immune response, metabolism and cardio-metabolism were measured in serum of all patients using the Olink platform (for panels, see Olink website).
Results: Overall, LEF/HCQ was safe and well-tolerated and significantly reduced ESSDAI scores, the primary endpoint ($p<0.0001$). Furthermore, LEF/HCQ treatment was associated with improvement of oral dryness, ESSPRI, Physician's and Patient's Global Assessment, serum IgG, IgM rheumatoid factor, C3 and C4 levels (all at least $p<0.05$), which was not observed in the placebo group. Clinical response was observed in 11 out of 21 patients receiving treatment, providing a unique opportunity to examine biomarkers to predict response. However, except for C3 levels, clinical markers at baseline were not significantly different between responders and non-responders, underscoring the challenges in prediction of therapy response. Olink proteomic analysis revealed 43 significantly differentially expressed proteins between responders and non-responders. Unsupervised hierarchical clustering using the most differentially-expressed analytes (p-value based) demonstrated distinct serum proteomes in responders vs. non-responders. Using multidimensional scaling, based on all measured analytes, a high degree of dissimilarity of responders and non-responders was observed. Next a random forest machine-learning model was established to identify the proteins that best predict response to treatment using the baseline serum proteome. The results were validated using 500 leave-7-out iterations. The highest mean accuracy (84%) was achieved using a set of 16 differentially expressed analytes, indicating a 96% chance to robustly predict responders and a 74% chance to correctly identify non-responders.
Conclusion: We demonstrated a clinical response in pSS patients treated with the combination of leflunomide and hydroxychloroquine1. Strikingly, a set of 16 circulating proteins predicts response to therapy with clinically meaningful accuracy. Given the exciting but preliminary nature of these observations a follow-up RCT aimed at replication of these results is warranted.

REFERENCE:

[1] Clinical Efficacy of Leflunomide/Hydroxychloroquine Combination Therapy in Patients with Primary Sjogren's Syndrome: Results of a Placebo-Controlled Double-Blind Randomized Clinical Trial. Radstake T, et al. Abstract L10 ACR 2018.

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THU0239 IDENTIFICATION OF BIOMARKERS AND IMMUNE PATHWAYS FOR PERSONALIZED DRUG TARGETING IN PATIENTS WITH NEWLY DIAGNOSED PRIMARY SJÖGREN'S SYNDROME

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Background: Patients with primary Sjögren's syndrome (pSS) present with heterogeneous clinical symptoms and immune dysregulation. How immune dysregulation in SS arises is poorly understood, which hampers development of effective therapies. Identification of key immune pathways contributing to pSS pathogenesis is essential for successful drug development. Systemic treatment of patients early in the disease process will limit irreversible damage to salivary and lacrimal glands, as well as to other affected tissues.

Objectives: To identify early systemic biomarkers and dysregulated immune pathways in newly diagnosed pSS patients by multidimensional immuno-profiling.

Methods: We included 40 newly diagnosed pSS patients (39 female; mean age 51±14) and 20 age- and sex-matched non-SS sicca patients (19 female; mean age 50±13). All pSS patients fulfilled ACR-EULAR criteria. Serum and peripheral blood mononuclear cells (PBMC) were collected and cryopreserved. PBMCs were thawed for immunophenotyping by flow cytometry and RNA isolation. RNA sequencing was performed using TruSeq Stranded Total RNA Library Prep Gold (Illumina), following manufacturer's recommendations, and RNAseq libraries were sequenced on a HiSeq2500 system. Additionally, serum proteomics and immunoassays for pro-inflammatory cytokines in serum were performed.

Results: Interferon (IFN) type I signaling pathways were at the top of enriched pathways in PBMCs from pSS patients, compared with non-SS sicca controls (adjusted p<0.05). Additionally, the gene signature of $IgD^-CD27^-CXCR5^-CD11c^+$ (double negative 2; DN2) B cells was significantly upregulated in pSS patients (adj. p<0.05). Immunophenotyping analysis showed increased frequencies of $CD40^+$ pDCs (p=0.004), intermediate monocytes (p=0.008), $ICOS^+$ memory $CD4^+$ T cells (p<0.001), cTfh cells (p=0.001), and cTfr cells (p<0.001) in pSS patients. Memory B cells were significantly decreased in pSS patients (p<0.001). Serum proteomics showed that the top proteins up-regulated in pSS patients were immunoglobulin subunits. The top of up-regulated pathways involved IFN signaling (adj. p<0.05), similar to RNAseq data. Consistently, immunoassays showed increased levels of CXCL10 in serum and MxA in whole blood of pSS patients, compared with non-SS sicca controls (p=0.009 and p=0.001, respectively). Blood MxA protein levels correlated strongly with the IFN signature score in PBMCs (Rs=0.8; $p=10^{-12}$). The T cell-related biomarkers described above, the frequency of memory B cells, and MxA levels correlated significantly with EULAR Sjögren's disease activity index (ESSDAI) scores, whereas the frequency of $CD40^+$ pDCs, intermediate monocytes, and serum CXCL10 levels did not correlate with these scores. When a correction for multiple testing was applied, only cTfr cells correlated significantly with ESSDAI scores (Rs=0.5; p=0.002).

Conclusion: Newly diagnosed patients with pSS show co-activation of the IFN type I and B cell activation pathways, compared to non-SS sicca controls. At the same time, $CD4^+$ T cell subsets critical for B cell function are activated, which can enhance B cell activation and plasma cell formation. Personalized treatment based on the activity of each pathway in individual patients potentially increases the efficacy of such treatments.

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THU0240 GENE EXPRESSION SIGNATURES ARE RELATED TO SPECIFIC SUBSETS OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous, lifelong autoimmune disease, with a more severe phenotype in children compared to adult-onset SLE [1]. To date, approved drugs are by far not effective enough and have significant side effects, especially due to the use of prednisone. Although profiling of the blood transcriptome revealed a prevalent IFN type I signature in SLE, blocking the IFN pathway only showed efficacy in a subset of adult-onset SLE patients. Recent studies revealed that other gene signatures like IFN type I+II (M5.12), B cell, plasmablast and neutrophil signatures are important in SLE as well and some could be linked to specific clinical phenotypes [2, 3]. Assessment of these novel gene signatures in SLE may help to distinguish specific disease phenotypes and guide treatment choices in the future.

Objectives: To determine and compare the expression of the IFN-, B cell-, plasmablast- and neutrophil signatures in pediatric and adult SLE patients.

Methods: The IFN-I-, M5.12-, neutrophil-, B cell- and plasmablast signatures were measured using real-time quantitative PCR expression on whole blood RNA samples. To identify correlated groups of genes and reduce data complexity, the expression of a selection of genes identified by blood transcriptional profiling was tested and subsequently added to a principle component analysis to obtain a limited set of genes (2-5 per signatures), that reliably represent a specific signature.

These signatures were analyzed in three separate pilot cohorts of healthy controls (n=12), pediatric- (n=22; average disease duration=0.9 years) and adult SLE patients (n=36; average disease duration=17.4 years).

Results: IFN-I signature was significantly higher in SLE patients compared to healthy controls (p=0.001). M5.12 (p=0.05) and the B cell (p=0.0001) signature showed a significant difference between the pediatric and adult cohort while there was no difference between the neutrophil- and plasmablast signatures in the two patient groups. Interestingly, the B cell gene signature, correlated with age (p=0.0001, r= -0.49) and disease duration (p=0.001, r= -0.42). In addition, the possible correlation between the IFN-I signature and the other signatures was investigated. While the IFN-I signature in both adults and children showed a significant positive correlation to the M5.12- (p<0.0001, r=0.97; p=0.006, r=0.61) and plasmablast (p=0.03, r=0.37; p=0.0037, r=0.62) signature expression, only adult patients had a significant positive correlation of the IFN-I signature to the neutrophil signature (p=0.001, r=0.55).

Conclusion: In this pilot study we found significant differences in gene expression signatures between pediatric and adult SLE patients. Additionally, age and disease duration were significantly correlated to the B cell gene signature. These findings indicate differences in transcriptional profiles in specific subsets of SLE patients which could have therapeutic consequences.

REFERENCES:

[1] Groot, N., et al., *Long-term clinical outcomes in a cohort of adults with childhood-onset Systemic Lupus Erythematosus*. Arthritis Rheumatol, 2018.

[2] Banchereau, R., et al., *Personalized Immunomonitoring Uncovers Molecular Networks that Stratify Lupus Patients*. Cell, 2016. 165(3): p. 551-65.

[3] Bodewes, I.L.A., et al., *Systemic interferon type I and type II signatures in primary Sjogren's syndrome reveal differences in biological disease activity*. Rheumatology (Oxford), 2018. 57(5): p. 921-930.

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THU0241 LUPUS PROGRESSION IS PREVENTED BY TREATMENT WITH VERDINEXOR, AN INHIBITOR OF THE NUCLEAR EXPORT PROTEIN EXPORTIN-1, BY LIMITING GERMINAL CENTER FORMATION AND DEVELOPMENT OF AUTOREACTIVE ANTIBODY SECRETING CELLS

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Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by simultaneous activation of the innate and adaptive arms of the immune system. Recently the nuclear export protein exportin-1 (XPO1) has surfaced as an attractive target for the treatment of SLE and other autoimmune disorders. Selective Inhibitor of Nuclear Export (SINE) compounds are potent, orally available and well-tolerated XPO1 inhibitors. SINE compounds inhibit the nuclear export of over 220 cargoes, and this pleiotropic effect on multiple signaling pathways exerts apoptotic and anti-inflammatory effects, particularly in dampening the NF-κB response. Based on previous studies with different SINE compounds, we decided to define the minimal amount and frequency of verdinexor treatment necessary to maintain disease inhibition after induction therapy.
Objectives: The primary objective of this study was to examine the ability of verdinexor to control the formation of germinal centers and limit the numbers of autoreactive antibody secreting cells (ASC) in a NZB/NZW F1 murine model of SLE.
Methods: To evaluate the minimal efficacious dose of SINE compounds in a preclinical recovery model of SLE, cohorts of lupus-prone mice with established disease (elevated anti-dsDNA antibody titer and proteinuria) were dosed with SINE compound or vehicle for eight weeks, at which time treatment groups were stratified, and escalating administration schedules (both dose and frequency) of verdinexor were examined for their ability to control recurrent disease. We used flow cytometry to enumerate dsDNA antibody-secreting cells (ASC) in the spleen and bone marrow and immunofluorescence to visualize germinal centers (GC) in spleen.
Results: We found that following induction therapy, treatment with verdinexor significantly maintained disease inhibition effectively at 7.5mg/kg administered weekly. Concomitantly, we observed significantly decreased levels of GC B cells, plasma cells and plasmablast levels in the bone marrow and the spleen 4 weeks after treatment groups were stratified. The potent effect of SINE compound monotherapy on GC and auto-reactive ASC showed that a pronounced elimination of GC and auto-reactive ASC is achieved after 4 weeks of maintenance therapy administered once weekly. When combined with a proteasome inhibitor (PI), short-term verdinexor plus PI treatment resulted in a synergistic effect, resulting in a significant reduction in the number of auto-reactive antibody secreting cells (ASC).
Conclusion: Verdinexor has demonstrated efficacy in a murine induction/disease inhibition model of SLE by reducing generation, survival and function of auto-reactive immune cells. It is likely that inhibition of the canonical NF-κB pathway underlies verdinexor's inhibitory effect. The reversible impact of SINE compounds on SLE (symptoms return when therapy is removed) provides a potential window of time for immunization of lupus patients. Together, our findings suggest the potential of SINE compounds to have a significant impact on disease progression in SLE.
Disclosure of Interests: Javier Rangel-Moreno: None declared, Nida Meednu: None declared, Douglas Widman Shareholder of: Karyopharm Therapeutics, Employee of: Karyopharm Therapeutics, Savanna Gornisiewicz Shareholder of: Karyopharm Therapeutics, Employee of: Karyopharm Therapeutics, Sharon Tamir Shareholder of: Karyopharm Therapeutics, Employee of: Karyopharm Therapeutics, Jennifer H. Anolik: None declared
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THU0242 MIR-326 OVEREXPRESSION IN T CELLS BREAKS TH17/TREG BALANCE IN MRL/LPR MICE

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease involving multiple organs leading to tissue damage[1]. T lymphocytes have been recognized as key contributors to disease pathogenesis[2]. Inflammatory Th17 subsets promote inflammation, while defects in regulatory T cells (Tregs) lead to unchecked immune responses[3]. Emerging data suggest that single miR species can profoundly alter the phenotype and outcome of immune responses in SLE[4].
Objectives: we describe a role for miR-326 in driving deregulation of Th17/Treg balance in lupus mouse and highlight therapeutic advances of miR-326.
Methods: 3 groups of female MRL/lpr mice were injected with lentivirus-miR-326 (LV-326) or lentivirus-miR-326 specific inhibitor (LV-sponge) to increase or inhibit miR-326 expression, respectively, and lentivirus-no-encoding (LV-ctrl) as control, 10 mice per group. The percentage of Th17 cells and Tregs in spleen $CD4^+$ T cells and kidney were detected by flow cytometry. The levels of serum cytokine (IL-17A, IFN-γ, TGF-β) were detected by CBA. Urinary collections (24 h) were collected and assessed for albumin using ELISA. Immunohistochemistry labeled kidney IL-17A and TGF-β expression. Differences between groups were analyzed by SPSS software.
Results: Day 7 analysis of differentiation of Th17 cells and Tregs in spleen after injection of lentivirus showed an increased percentage of Th17 in LV-326 mice, while reduction of percentage of Tregs in these mice. Testing the serum cytokines revealed that the significantly increased levels of IL-17A and IFN-γ in LV-326 mice, and decreased in LV-sponge mice, no different has been found in TGF-β between the groups. Moreover, LV-326 mice showed higher levels of 24h urinary albumin than LV-sponge and LV-ctrl mice in day 7 after injection of lentivirus. The lentivirus-miR-326 injection promoted the infiltration of Th17 cells and simultaneously increased the expression of IL-17A in kidney, no different has been found of TGF-β.
Conclusion: Our data reveal that miR-326 overexpression increased the differentiation of Th17 cells and decreased the differentiation of Tregs, and accelerated the renal injury in MRL/lpr mice. These suggest that miR-326 may play a catalytic role in the development of lupus-like changes in lupus model mouse by breaks Th17/Treg balance.

REFERENCES:

[1] Tsokos, G.C. Systemic lupus erythematosus. N Engl J Med 365, 2110-2121 (2011).
[2] Moulton, V.R. et al. Pathogenesis of Human Systemic Lupus Erythematosus: A
[3] Cellular Perspective. Trends Mol Med 23, 615-635 (2017).
[4] Suarez-Fueyo, A., Bradley, S.J. & Tsokos, G.C. T cells in Systemic Lupus Erythematosus. Curr Opin Immunol 43, 32-38 (2016).
[5] Lam, I.K.Y., Chow, J.X., Lau, C.S. & Chan, V.S.F. MicroRNA-mediated immune regulation in rheumatic diseases. Cancer Lett 431, 201-212 (2018).

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THU0243 ROLE OF METHIONINE AND ITS TRANSPORTER CD98 IN HUMAN B CELL DIFFERENTIATION AND THE RELEVANCE TO PATHOLOGICAL PROCESSES OF SLE

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Background: B cells play an important role in systemic lupus erythematosus (SLE). Several research protocols have focused in recent years on the topic of immunometabolism. Activation of immunocompetent cells depends on rapid synthesis of cell structure components and biomolecules, which requires enormous amounts of energy, nucleic acids and lipids. Amino acids are important ingredients of many metabolic processes. However, the role of amino acids in plasmablast differentiation and their relevance to the pathogenesis of SLE remain elusive.
Objectives: To determine the role of essential amino acids in human B cell differentiation and relevance to the pathogenesis of SLE.
Methods: In the *in vitro* arm of the study, purified $CD19^+$ B cells from healthy donors were cultured with TLR7/9 ligand (LOX or CpG), IFN-α and B cell receptor (BCR) cross-linking, in the presence or absence of amino acids. We determined 1) the types of amino acids that are important for PB differentiation, 2) the amino acid transporters that are important for PB differentiation, 3) the main signaling pathway(s) involved in the presence of amino acids, 4) the transcriptional factors used in the presence of amino acids. In the clinical arm of the study, peripheral blood mononuclear cells (PBMCs) were obtained from 24 patients with RA, 35 patients with SLE, and 28 age-matched healthy controls, and

subjected to flow cytometric analysis to determine the expression of amino acids-related markers.
Results: 1) Stimulation with the combination of BCR, IFN-α and TLR7/9 ligand induced PB differentiation accompanied by uptake of amino acids. PB differentiation was abrogated in the absence of essential amino acid methionine, and to a lesser extent leucine, but not in non-essential amino acid cystine. 2) LAT1 and CD98 are known amino acid transporters. Stimulation with BCR, IFN-α and TLR7/9 ligand induced CD98 expression but suppressed LAT1 expression. CD98 expression was higher in $CD27^{hi}CD38^{hi}$ PB than in $CD27^{-}CD38^{-}$ non-PB. 3) Previous studies reported that amino acids were perceived by the sensor, leading to mTORC1 phosphorylation. However, the mechanism by which amino acids activate other intracellular signaling pathways in B cells remains elusive. We found that methionine facilitated both the BCR and mTORC1 signals. In addition, the two signals synergistically induced EZH2 expression, which is well known as a transcriptional factor for histone modification via induction of H3K27me3, in the presence of methionine. 4) Methionine induced EZH2 expression, leading to suppression of BACH2, induction of BLIMP1, XBP1 and PB differentiation. These results indicate that EZH2 is a critical factor for PB differentiation in the presence of methionine. Assessment of the expression of amino acid transporters CD98, LAT1 and EZH2 in B cells in RA and SLE patients showed overexpression of CD98 and EZH2, but not LAT1, in SLE, compared with RA and control. In SLE patients, EZH2 expression level correlated with that of CD98 in B cells. EZH2 expression also correlated with ESR and disease activity scores, such as of SLEDAI and BILAG, in SLE patients.
Conclusion: The results indicate that essential amino acid methionine plays an important role in PB differentiation through the CD98-EZH2-axis. The pathological process of SLE seems to involve essential amino acids and their metabolic/activation pathways throughout the process of PB differentiation.
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SLE, Sjögren's and APS – clinical aspects (other than treatment)

THU0244 PULMONARY MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by inflammation and tissue damage mediated by the immune system. Respiratory manifestations are common in SLE, appearing in up to 50% of patients throughout their lives. Furthermore, it is associated with higher mortality.
Objectives: To describe the prevalence and characteristics of pulmonary involvement in patients with SLE
Methods: Observational, descriptive, cross-sectional, retrospective study performed in patients with SLE in follow-up by the Rheumatology Department of Valme Hospital. The following information is collected from medical records; age, sex, mean age at diagnosis, characteristics of pleuropulmonary involvement and ANA and antiDNA positivity.
Results: We studied 165 patients with SLE, with mean age of 37.01 +/- 14.65 years, predominance of the female patients 153 (92.72%). Thirty eight of them had pulmonary involvement (23.03%), with a total of 47 episodes related to lung manifestations. Mean age at diagnosis was 39.70 +/- 15.50 years. Below is shown information about lung involvement:

Variable	*Prevalence*	*ANA +*	*antiDNA +*	*Hospitalization required*
Pleuritis	19	18	5	17
Lupus pneumonitis	1	1	0	1
ILD	2	2	0	1
Shrinking lung	4	4	1	2
Pulmonary embolism	5	4	1	3
Other	16	15	9	10

Eleven patients (28.94%) presented pulmonary involvement at the time of diagnosis; pleuritis (10.63%) and only one case of interstitial lung disease, varicella pneumonia, shrinking lung syndrome, pulmonary embolism (PE) and bronchiolitis obliterans with organizing pneumonia. Two patients (4.24%) died due to severe respiratory failure secondary to bilateral pneumonia. Three of the 5 patients with PE were diagnosed with antiphospholipid syndrome secondary to SLE. Regarding treatment, most of patients who required hospitalization were in basic treatment with synthetic DMARDs (78.57% in monotherapy and 21.43% with double therapy) and only 2 patients with biologic DMARDs (Rituximab and etanercept). Six patients had no treatment because the pulmonary event was at time of diagnosis, 2 patients were with antiaggregating therapy and there was no information registered in two patients (episode before 1997). 91.10% of the patients presented positive for ANA, of which 37.14% (13 patients) also presented positive antiDNA. No information was collected about autoimmunity in one patient (2.12%).
Conclusion: Pulmonary involvement in SLE is prevalent, although a significant proportion may remain asymptomatic. The little prevalence of pulmonary manifestations in our series might be due to low mean age, according to the result of a recent systematic review where analysed more than 10000 patients and concluded pulmonary manifestations are more frequent in late-onset SLE. The differential diagnosis is broad and the infectious cause, the main cause of mortality in patients with SLE, must always be ruled out.

REFERENCES:
[1] 10.1016/j.semarthrit.2018.01.010
[2] 10.1016/j.reuma.2018.03.012
[3] 10.1186/s13075-018-1776-8
[4] 10.1097/BOR.0000000000000531

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THU0245 LOW SPECIFICITY OF THE PROPOSED 2017 ACR-EULAR CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COMPARED TO PREVIOUS CRITERIA IN SLE PATIENTS WITH NEUROPSYCHIATRIC SYMPTOMS

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Background: New ACR-EULAR SLE criteria have been proposed in order to attempt to improve classification for clinical and translational research (1, 2).
Objectives: We evaluated the performance of the proposed 2017 ACR-EULAR classification criteria in a cohort of SLE patients with neuropsychiatric (NP) symptoms and compared to previous classification criteria.
Methods: Medical records of patients visiting the NPSLE clinic of the Leiden University Medical Center (LUMC) between 2007-2017 were retrospectively evaluated. The performance of the proposed 2017 ACR-EULAR criteria, the 2012 SLICC criteria and the 1997 ACR criteria was evaluated by calculating sensitivity and specificity.
Results: 360 patients were included, of which 294 were clinically diagnosed with SLE. The newly proposed 2017 ACR-EULAR showed a sensitivity of 87% (95% CI: 83-91%) and a specificity of 74% (95% CI: 62-84%), as shown in *Table 1.* The 2012 SLICC criteria had a sensitivity of 85% (95% CI: 80-89%) and a specificity of 76% (95% CI: 64-85%). The 1997 ACR criteria had a sensitivity of 89% (95% CI: 85-92%) and a specificity of 89% (95% CI: 80-96%).
Sixty out of 294 patients fulfilled the proposed NP domain (delirium/psychosis/epilepsy). Using more specific criteria for NP symptoms related to SLE, as previously proposed by Bortoluzzi *et al.* (3), only 37 patients fulfilled this domain. However, this did not improve specificity, which remained 74% (95% CI: 62-84%).

In addition, the performance of the newly proposed criteria was evaluated including patients with more than 10 points, but negative ANA. This led to an increase of sensitivity to 90% (95% CI 86-94%), but also did not influence specificity.

Proposed 2017 ACR-EULAR classification criteria in SLE patients with NP symptoms			
		With adjusted NP domain	Including ANA negative patients
Sensitivity (95% CI)	87% (83-91%)	87% (83-91%)	90% (86-94%)
Specificity (95% CI)	74% (62-84%)	74% (62-84%)	74% (62-84%)

Table 1. Performance of the proposed 2017 ACR-EULAR classification criteria for SLE

Conclusion: In a cohort of SLE patients with NP symptoms, the proposed 2017 ACR-EULAR classification criteria showed similar sensitivity as the 1997 ACR and the SLICC 2012 criteria, but lower specificity. Including ANA negative patients improved sensitivity.

REFERENCES:

[1] 2018 ACR/ARHP Annual Meeting Abstract Supplement. Arthritis Rheumatol, 2018. 70 Suppl 9: p. 1-355.
[2] Tedeschi SK, et al., Developing and Refining New Candidate Criteria for Systemic Lupus Erythematosus Classification: An International Collaboration. Arthritis Care Res (Hoboken), 2018. 70(4): p. 571-581.
[3] Bortoluzzi A, et al., Development and validation of a new algorithm for attribution of neuropsychiatric events in systemic lupus erythematosus. Rheumatology (Oxford), 2015. 54(5): p. 891-8.

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THU0246 ASYMPTOMATIC MYOCARDIAL DYSFUNCTION DETECTED BY SPECKLED TRACKING ECHOCARDIOGRAPHY (STE) IN ACTIVE SLE PATIENTS

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Background: Clinical myocarditis is seen in 10% of SLE patients, but autopsy studies have shown myocardial involvement in up to 50% of patients. Lupus myocarditis may be silent and can be detected by newer echocardiographic technique like STE especially when SLE is active.(1)
Objectives: To study asymptomatic myocardial dysfunction by STE in active SLE patients.
Methods: All consecutive active SLE patients having a SLEDAI score ≥ 6 without any cardiac symptoms with disease duration ≤ 5 years aging between 18- 45 years, who attended the Rheumatology and Clinical Immunology department (Outpatient and Inpatient) of Medanta, The Medicity, Gurgaon, from May 2016 to March 2018, were enrolled. They were evaluated for myocardial dysfunction by using a novel ultrasound technique - STE, which was reviewed by one observer cardiologist. Global longitudinal systolic strain (GLSS) was calculated by STE in all patients. GLSS<-19.7 was considered as an indicator of myocardial dysfunction.(2) Age and sex matched controls in the form of thirty healthy volunteer subjects were enrolled and their echocardiography findings were compared with active lupus patients. Atherosclerotic risk factors like hypertension, Diabetes Mellitus and age >45 years were excluded to avoid confounding effects.
Results: Fifty eight active lupus patients were analysed. In the cohort female: male ratio was 8.6:1, median duration of disease was 22 months (0.5 - 60) and mean SLEDAI was 11.02 ± 2.30.GLSS was significantly low in active lupus patients compared to healthy controls (p=0.0001) suggestive of myocardial dysfunction.
In active lupus patients, abnormal echocardiographic findings (myocarditis, non-bacterial thromboendocarditis, pulmonary arterial hypertension and pericarditis) were seen in 62.1%. Myocardial dysfunction was found in 27 (46.6%), 20 (34.5%) patients had low GLSS with normal left ventricular ejection fraction (LVEF) and these were significantly associated with APLA and anti Sm/RNP antibodies. Multivariate Logistic Regression analysis of myocardial dysfunction with SLEDAI and other system parameters showed that musculoskeletal, CNS, haematological and nephritis were associated with increased risk for developing higher disease activity and myocardial dysfunction, although it was not statistically significant.

Table 1. Comparison of GLSS and LVEF between active SLE patients and healthy control group patients

Table No.1 Comparison of GLSS and LVEF between active SLE patients and healthy control group patients

Echocardiographic parameters	Active SLE (n-58)	Healthy control (n-30)	P value
Mean LVEF, (Mean ± SD)	58 ± 7.5	61.7 ± 5	0.016*
Mean GLSS, (Mean ± SD)	-19.6 ± 3.0	-23.5 ± 3.2	0.0001*
PAH (>30mmhg), n (%)	10(17.2 %)	0	-
NBTE, n (%)	10(18.2 %)	0	-
Pericarditis, n (%)	11(19.6 %)	0	-

Table No.2 Myocardial dysfunction in active SLE based GLSS <-19.7 %.

Parameters	No. of patients (n- 58)	%
GLSS < -19.7	27	46.6
< LVEF 52%	7	12.1
Both low	7	12.1
GLSS < - 19.7 with normal LVEF	20	34.5

Table 2. Myocardial dysfunction in active SLE based GLSS <-19.7 %.

Conclusion: Almost half of active lupus patients have silent myocarditis. GLSS is more sensitive in detecting asymptomatic myocardial dysfunction than LVEF.Regular Echocardiography with Speckled tracking should be performed in Lupus patients especially when disease is active.

REFERENCES:

1 Løgstrup BB, Nielsen JM, Kim WY, Poulsen SH. Myocardial oedema in acutemyocarditis detected by echocardiographic 2Dmyocardial deformation analysis. Eur Heart J Cardiovasc Imaging. 2016;17(9):1018-26.
2 Yingchoncharoen T, Agarwal S, Popovi? ZB, Marwick TH. Normal ranges of left ventricular strain: A meta-analysis. J Am Soc Echocardiogr. 2013;26 (2):185-91.

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THU0247 LRRN4: A NOVEL PROGNOSTIC BIOMARKER OF RENAL OUTCOME IN LUPUS NEPHRITIS PATIENTS

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Background: Lupus nephritis (LN) is the most common organ-threatening manifestation of systemic lupus erythematosus (SLE) and can result in kidney deterioration and end-stage renal disease (ESRD). Newly discovered biomarkers exhibit qualities of disease activity and damage, predict long term preservation of renal function.
Objectives: Combine the transcriptomics profile of kidney with long-term renal outcome in LN patients, to explore the novel non-invasive predictive biomarker for renal outcome.
Methods: The transcriptomics profile of kidney in 24 LN patients was obtained by using Affymetrix human HTA 2.0 gene expression chip. Random Forest method was used to screen the candidate mRNA biomarkers by correlate the gene expression profile with eGFR slope during the follow-up (Mean time 5.2±1.2 years). In addition, in an independent LN cohort enrolled 45 patients, qRT-PCR and immunochemistry staining was performed to validate the correlation of mRNA level and protein level of candidate gene with renal outcome.

Results: (1) There were 3212 gene was regulated in LN kidney (Fold change>1.5, FDA<0.05, compared with healthy control. DCBLD2, NPNT, CPVL, RGS5, LRRN4 were found to have the leading correlation with eGFR slope of LN patients by using random forest method. (2) In the independent cohort, we validate that the mRNA and protein level of DCBLD2, NPNT, CPVL, RGS5, LRRN4 was significantly evaluated in tubulointerstitial component in LN kidney, compared with healthy controls ($p<0.05$), and also significantly correlated with eGFR slope [LRRN4(r=-0.715, P<0.0001, DCBLD2(r=-0.620, P<0.0001, CPVL(r=-0.517, P=0.004, RGS5(r=-0.489, P=0.008, NPNT(r=-0.412, P=0.016]. In addition, the mRNA level of LRRN4 and DCBLD2 in kidney was correlated with SLEDAI score(r=0.611and r=0.512, respectively, P<0.001 and serum C3 level (r=0.501, r=0.435, P<0.05). LRRN4 mRNA level also significantly associated with tubulointerstitial fibrosis scoring(r=0.432, P<0.05;(3 he protein of LRRN4 was expressed both in glomeruli and tubulointerstitial tissue. And IHC level of LRRN4 protien was significantly associated with eGFR slope (r=0.534, P<0.05 in LN patients.

Conclusion: LRRN4 in kidney may be used as a novel predictive biomarker of renal outcome in LN patients.

REFERENCES:

[1] Dall'Era M, Cisternas MG, Smilek DE, et al. Predictors of long-term renal outcome in lupus nephritis trials: lessons learned from the Euro-Lupus Nephritis cohort. Arthritis Rheumatol. 2015 May; 67(5):1305-13.

[2] Misra R, Gupta R. Biomarkers in lupus nephritis. Int J Rheum Dis. 2015 Feb; 18(2):219-32.

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THU0248 UTILITY OF A MOBILE PHONE BASED APPLICATION TO COLLECT PATIENT REPORTED OUTCOME INFORMATION FROM SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patient Reported Outcomes (PROs) can provide important data about the impact of a disease on an individual subject and/or the quality of the response to medication. However, in most circumstances, PRO information is collected only intermittently and usually at the point of care or treatment. The development of mobile technology to collect PRO data provided the opportunity to acquire this information more frequently, in real time, and in the subject's normal environment.

Objectives: To test the utility of a smart phone application (app) to collect PRO information in subjects with systemic lupus erythematosus (SLE).

Methods: A smart phone app was developed that collects data from a number of PRO instruments, including FACIT-F(fatigue), SF-36 (health-related quality of life) and patient global assessment (PtGA). Subjects with SLE were involved in the initial development and evaluation of the acceptability of the app. To test the utility of this app, a multi-center clinical study (VALUE, NCT03142711) was carried out in collaboration with subjects with SLE, in whom PRO information was collected with the app daily (PtGA) or weekly (FACIT-F and SF-36) in the subject's environment and also with the app and a standard paper form monthly at each clinical site. Demographic information, compliance and intra-class correlation coefficients between information collected with the app and using a paper form at the clinical site were assessed.

Results: Of the 80 subjects enrolled in this study, 91.3% were women; 57.5%, 16.3% and 17.5% identified themselves as of European, African or Asian ancestry, respectively. The mean age of the subjects was 42.6 years and the mean duration of education was 15.6 years. Overall compliance with completing the PRO instruments with the app at the scheduled time was 88%. To determine the consistency of information collected with the app, PRO instruments were completed on three occasions: a) in standard fashion using a paper form and b) using the app, separated by an interruption at the clinical site. The mean (SD) PtGA scores at baseline, month 1 and month 2 were 3.3(2.4), 3.5(2.4) and 3.5(2.5) using the app and 3.2(2.4), 3.5(2.3) and 3.3(2.4) using the paper form. The Intra-class Correlation Coefficient (ICC) and 90%CI were 0.97 (0.96-0.98), 0.96 (0.94-0.97) and 0.95(0.93-0.97) at the three time points, respectively. For the FACIT-F instrument, the mean (SD) score with the app was 33.2 (11.7), 31.0(12.6) and 32.3(12.7) and with the paper form was 34.1(11.6), 32.0(12.2) and 32.0(12.5) at the 3 time points with ICCs of 0.94(0.91-0.96), 0.96(0.95-0.98) and 0.96(0.94-0.97), respectively. For the SF-36 Physical Functioning score, the mean (SD) with the app was 66.3(26.1), 65.5(26.9) and 67.4(25.8) and with the paper form was 68.4(25.1), 66.1 (26.6) and 67.6(25.8) for the 3 time points, respectively. The ICCs were 0.96(0.94-0.97), 0.94(0.91-0.96) and 0.96 (0.94-0.97) for the 3 time points, respectively.

Conclusion: Compliance with completion of PRO instruments using a mobile app was excellent and the content collected with the app conformed with that collected using a standard paper form. Since patient compliance with the use of a mobile app to collect PRO information and the consistency of the information obtained compared to that obtained in standard fashion using a paper form were high, the app affords the potential opportunity to acquire frequent and highly reliable information about the impact of disease and response to medication in individual subjects with SLE.

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THU0249 URINARY NEUTROPHIL GELATINASE ASSOCIATED LIPOCALCIN AND PROSTAGLANDIN D-SYNTHETASE PREDICT DISEASE FLARES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease commonly characterized by periods of flares and quiescence. Conventional markers of disease activity (serum complement and anti-dsDNA antibodies) have a limited predictive value of disease flares. Recent evidence suggests that urine biomarkers are able to discriminate between SLE patients with ongoing renal activity and those without nephritis (1-2).

Objectives: To investigate if urinary Neutrophil Gelatinase Associated Lipocalcin (NGAL) and Lipocalin-type Prostaglandin D-Synthetase (L-PGDS) are early biomarkers that could be used as flare predictors in SLE.

Methods: Patients prospectively followed at our clinic from March 2017 to September 2018, who fulfilled classification criteria for SLE (3), were considered for the study. Flares were identified by SELENA-SLEDAI Flare Index (SFI) after 3 months of urine collection (4). NGAL and L-PGDS levels were measured in the second void urinary sample by ELISA. Data were compared by the unpaired student's t test or the Mann–Whitney U test as appropriate. Logistic regression analysis was used to assess the independent baseline predictors of flares. Receiver operating characteristic (ROC) analysis was used to calculate the area under the curve (AUC) with associated 95% confidence interval (CI) to find the best cut-off values.

Results: Urine specimen was collected from 66 patients, including 64 females and 2 males with a median age at diagnosis of 27 years (IQR 21,5-38). During 3 months-follow-up, 18 (27%) out of the 66 patients experienced a single disease flare. Urinary levels of L-PGDS (Fig. 1) and NGAL (Fig. 2) significantly increased 12 weeks before a disease flare (p=0.0001 and p=0.002, respectively). Urinary NGAL levels correlated with anti-DNA antibody titre (r=0.254, p=0.042) and not with serum complement prior to the disease flare (P>0.05). Moreover, urinary L-PGDS slightly correlated with anti-DNA antibody titre (p=0.08), and was not associated with serum complement levels. Based on ROC analysis, urinary NGAL (AUC: 0.752) and L-PGDS (AUC: 0.811), outperformed conventional biomarkers (Table1). ROC analysis revealed that NGAL levels above 10.95ng/ml had a sensitivity of 84% and a specificity of 63% for flare prediction, while urine L-PGDS cut-off value in the ROC curve, 1500 ng/ml, predicted a flare with 78% sensitivity and 86% specificity. At multivariate analysis, NGAL and L-PGDS were independent predictors of flare with OR=10.34 (95% CI 1.46 – 73.05) and 24.85 (95% CI 4.32-

142.68), respectively. Increase in anti-dsDNA antibodies levels also predicted flares with an OR of 6.70 (p=0.040), while hypocomplementemia was not a significant risk factor.

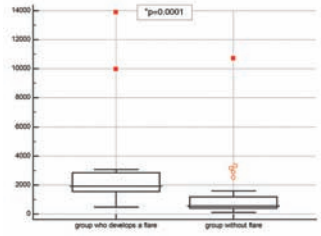
Conclusion: Urine NGAL and L-PGDS perform better than conventional markers in predicting a lupus flare in its incipient phase, in particular preceding the corresponding change in serum complement. Urinary NGAL and L-PGDS levels seem to be potential tools for monitoring patients with SLE. Further studies are needed to determine their clinical utility in everyday practice.

REFERENCES:

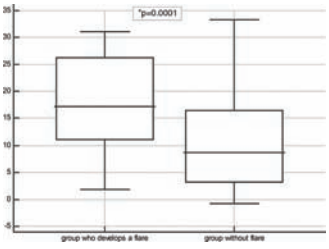
[1] Rubinstein T, et al. Rheumatol Oxf Engl. 2010;49:960–71.
[2] Gupta R, et al. Clin Exp Rheumatol. 2015;33:694-8.
[3] Tan EM, et al. Arthritis Rheum. 1982;25:1271–7.
[4] Petri M, et al. NEJM 2005;353: 2550-58.

Table 1. Area under the curve (AUC), cut off values, sensitivity and specificity for L-PGDS, NGAL and standard biomarkers for disease flares.

Variables	AUC	95% CI	Cut off values	sensitivity	specificity
C3	0.683	0.555 - 0.793	107 mg/dl	94%	40%
Anti dsDNA antibodies	0.705	0.579 - 0.812	30 UI	55%	89%
PGDS	0.811	0.694 - 0.897	1500 ng/ml	78%	86%
NGAL	0.752	0.630 - 0.851	10.95 ng/ml	84%	63%



Abstract THU0249 – Figure 1



Abstract THU0249 – Figure 2

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THU0250 EARLY IMPROVEMENT IN SLEDAI-2K RESPONDER INDEX-50 PREDICTS SRI-4 RESPONSE IN A RANDOMIZED PLACEBO-CONTROLLED TRIAL OF USTEKINUMAB (UST) IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: While traditional Systemic Lupus Erythematosus (SLE) Disease Activity Index 2000 (SLEDAI-2K) scoring assesses complete SLE response for individual disease manifestations, the SLEDAI-2K Responder Index-50 (S2K RI-50) evaluates responses using partial improvement (≥50%) in each of the 9 organ systems of SLEDAI-2K. Ustekinumab (UST), a monoclonal antibody that targets the shared p40 subunit of the cytokines IL-12 & IL-23, is being investigated in patients with active SLE. We have previously shown in a Phase 2 placebo (PBO)-controlled trial of UST in SLE[1] that not only SLEDAI-2K and the SLE Responder Index 4 (SRI-4), but also S2K RI-50 can discriminate a treatment effect of UST vs PBO at week 24.[2,3]

Objectives: Here, we aimed to ascertain whether a minimal threshold of partial improvement in S2K RI-50 could be used as an early predictor of SRI-4 response.

Methods: This phase 2, PBO-controlled study enrolled adults with seropositive, active disease (SLEDAI score ≥6 with ≥1 BILAG A &/or ≥2 BILAG B scores) despite standard therapy. Patients (n=102) were randomized (3:2) to receive UST IV 6 mg/kg or PBO at week 0, followed by SC injections of UST 90mg or PBO q8w beginning at week8, both added to standard of care. We calculated S2K RI-50 response through week 24 in all patients, including 60 patients receiving UST and 42 patients receiving PBO, using increasing cut-offs of S2K RI-50 reductions from baseline. To help determining a minimal cut-off that discriminated a treatment effect reflecting partial improvement, nominal p values are reported for this post hoc analysis. Logistic regression models were used to evaluate the relationship between reduction in S2K RI-50 at week 12 or week 16 and SRI-4 response at week 24, followed by correlation of binary response data between the two instruments.

Abstract THU0250 –Table 1.

Treatment Group	Visit	Correlation	Odds Ratio[a] [95% CI]	Predictive p-value[a]
Total Population	Week 12	0.62	7.6 [2.4-24.3]	0.0007
UST	Week 12	0.49	4.4 [1.1-16.9]	0.0311
PBO	Week 12	NE[b]	NE[b]	NE[b]
Total Population	Week 16	0.76	15.4 [4.2-55.8]	<0.0001
UST	Week 16	0.74	13.5 [2.6-69.8]	0.0020
PBO	Week 16	0.74	15.0 [1.7-130.7]	0.0142

[a] Predictive p-values and odds ratios are based upon logistic regression models. Predictive p-values are nominal and represent measures of the likeliness of association between a 2-point response in S2K RI-50 at week 12/16 and SRI-4 response at week 24 in the model.
[b] Not estimable (NE) due to no values present in one cell in the 2x2 table.
UST = Ustekinumab, PBO = Placebo

Results: A 2-point reduction from baseline (improvement) in S2K RI-50 appeared to be the lowest threshold of response to demonstrate a treatment difference in the proportion of responders at week 24 with UST (93.5%) vs PBO (79.3%) (Δ14.2%, p=0.03). The relationship between 2-point improvement in S2K RI-50 at week 12 or week 16 and SRI-4 response at week 24 is presented in the total study population and by treatment group (Table). In the total population, 78/102 (76.6%) patients at week 12 and 74/102 (72.5%) of patients at week 16 had at least a 2-point improvement in S2K RI-50. Of those, 47/78 (60.3%, r=0.62) at week 12 and 48/74 (64.9%, r=0.76) at week 16 achieved an SRI-4 response at week 24. Odds ratios for the association between SRI-4 response at week 24 and 2-point or greater improvement in S2K RI-50 were 7.6 (CI 2.4-24.3, p=0.0007) at week 12 and 15.4 (CI 4.2-55.8, p<0.0001) at week 16. Similar analyses performed by treatment group demonstrated that these relationships were consistent in the UST and PBO groups (Table).

Conclusion: 2K RI-50 captures partial improvement of ≥50% in SLE disease activity and could be a useful outcome in clinical trials to predict early clinical response. These findings will be confirmed in an ongoing Phase 3 study.

REFERENCES:
[1] van Vollenhoven, et al. Lancet. 2018:392:1330.
[2] Touma Z, et al. EULAR June 2018, Amsterdam, NL.
[3] Touma Z, et al. APLAR. April 2019, Brisbane, Australia.

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THU0251 ASSOCIATION OF SMOKING STATUS AND TOTAL AND INDIVIDUAL DAMAGE INDEX IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Smoking is a risk factor for systemic lupus erythematosus (SLE). It has been associated with increased disease activity and decreased effectiveness of hydroxychloroquine in cutaneous lupus.
Objectives: The objective of the study was to determine the association between smoking status and total and individual damage items in SLE.
Methods: We analyzed data from the Hopkins Lupus Cohort. Damage was recorded using the Systemic Lupus Erythematosus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index. Fisher's exact test and Wilcoxon test were used in exploratory analysis. Logistic regression was used to estimate the association between damage and smoking status (ever/never). Odds ratios and 95% confidence intervals were reported. Stratification by ethnicity was done for individual damage items that were found to be significantly associated with smoking.
Results: The prevalence of ever smokers in our cohort was 36%. SLE patients who ever smoked had higher odds of total damage with higher mean total damage index scores (p <0.0001). Data for individual damage items significantly associated with smoking are presented in Table 1.
The association between cataract and smoking was still present after adjusting for ethnicity, diabetes, and prednisone use in a multivariate regression model (OR= 1.4, p= 0.0083).
Stratification by ethnicity showed that African- American SLE patients who ever smoked were more likely to have cataract, scarring chronic alopecia, extensive scarring, skin ulceration, pulmonary hypertension, cerebrovascular events, cardiomyopathy, and diabetes compared to non-smokers. Caucasian SLE patients who ever smoked were more likely to have extensive scarring, gastrointestinal infarction and resection, and muscle atrophy (Table 1).

Abstract THU0251 – Table 1. Relationship between SLICC/ACR Damage Index Items and Smoking (ever/never)

ALL			Caucasian		African American	
Damage Item	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Total damage	1.73 (1.44, 2.07)	< 0.0001	1.55 (1.22, 1.97)	0.0003	1.96 (1.44, 2.66)	<0.0001
Cataract	1.50 (1.17, 1.92)	0.00122	0.96 (0.68, 1.36)	0.8176	2.26 (1.56, 3.28)	<0.0001
Scarring alopecia	2.08 (1.42, 3.06)	0.00019	1.63 (0.60, 4.45)	0.3320	2.24 (1.46, 3.47)	0.0003
Extensive scarring or panniculum other than scalp	3.37 (1.95, 5.85)	0.0001	2.57 (1.01, 7.03)	0.0522	3.68 (1.90, 7.47)	0.00017
Skin ulceration	2.76 (1.37, 5.57)	0.00465	2.03 (0.8, 5.36)	0.1370	4.45 (1.48, 16.32)	0.0121
Pulmonary hypertension	1.79 (1.21, 2.63)	0.00367	1.11 (0.70, 1.75)	0.6430	1.53 (1.15, 2.03)	0.00334
Infarction or resection of bowels	1.42 (1.12, 1.79)	0.0032	1.37 (1.03, 1.84)	0.0338	1.36 (0.90, 2.04)	0.1461
Pancreatitis	3.57 (1.07, 11.88)	0.0382	2.44 (0.68, 8.67)	0.1694	N/C	N/C
Muscle atrophy	1.80 (1.11, 2.94)	0.0183	2.62 (1.26, 5.44)	0.0099	1.09 (0.54, 2.19)	0.8210
Coronary artery disease	2.26 (1.50, 3.41)	0.0001	2.33 (1.39, 3.91)	0.0013	2.35 (1.13, 4.89)	0.0226
Myocardial Infarction	2.30 (1.29, 3.32)	<0.0001	2.17 (1.30, 3.62)	0.0032	2.22 (1.27, 3.87)	0.0051
Cardiomyopathy	1.94 (1.29, 2.93)	0.0016	1.64 (0.81, 3.30)	0.1687	2.18 (1.27, 3.74)	0.0045
Claudication	4.53 (2.17, 9.48)	<0.0001	3.86 (1.47, 1.10)	0.0060	4.91 (1.55, 15.52)	0.0068
Cerebrovascular accident	1.41 (1.08, 1.84)	0.0127	1.16 (0.80, 1.69)	0.4279	1.69 (1.13, 2.54)	0.0115
Diabetes	1.72 (1.29, 2.28)	0.0002	1.33 (0.88, 2.03)	0.1764	2.08 (1.39, 3.12)	0.0004

N/C: data are not sufficient for calculating odds ratio

Conclusion: Smoking is a modifiable factor for organ damage in SLE. It is already known that it interferes with the efficacy of hydroxychloroquine. Now we are able to prove that smokers have more cutaneous damage (scarring) even after stratification for ethnicity. As expected, smokers had more cardiovascular damage. New findings include associations with gastrointestinal damage, cataracts, pulmonary hypertension, pancreatitis and diabetes.

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THU0252 HORMONE DEPENDENCE AND CANCER IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Objectives: To estimate the incidence of cancer in systemic lupus erythematosus (SLE) patients and to analyze factors associated with cancer differentiating between hormone-sensitive (HS) and non-HS cancers.

Methods: Multicenter retrospective study of a cohort of patients included in Spanish Society of Rheumatology Lupus Registry (RELESSER). The first cancer after the diagnosis of SLE, sociodemographic, clinical, activity, cumulative damage, severity, comorbidity, treatments, and refractory disease data were collected. Cancers were classified into HS (prostate, breast, endometrial and ovarian) and non-HS (the rest). Standardized incidence ratio (SIR) was calculated and logistics regression models were constructed to identify factors associated with cancer.

Results: We included 3539 patients (90.4% women) with SLE (ACR-97 criteria), of whom 154 had cancer (91% women), and 44 were HS (100% women). The SIR for cancer was 1.37 (95% CI: 1.15-1.59), reaching higher values in women under 65 years [2.38 (95% CI: 1.84-2.91)]. The SIR in women with cancer HS vs. non-HS was 1.02 (95% CI: 0.13-1.91) and 1.93 (95% CI: 0.98-2.89)], respectively. In HS vs. non-HS cancers, age at diagnosis of SLE [Odds ratio (OR) 1.04 (p = 0.002) vs. 1.04 (p = 0.019), respectively] and the evolution time [OR 1.01 (p <0.001) vs. OR 1.00 (p = 0.029), respectively] were factors associated with cancer. SLICC/ACR damage index [OR 1.27 (p = 0.022)] and Angiotensin-Converting Enzyme (ACE) inhibitors prescription [OR 2.87 (p = 0.048)] were associated with non-HS cancers.

Conclusion: The incidence of cancer in patients with SLE is increased compared to the Spanish population, specially in younger women. This increase might be due to non-HS cancers. SLE with more cumulative damage and more prescription of ACE inhibitors might associate with non-HS cancers.

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THU0253 EFFECT OF GLUCOCORTICOIDS ON DAMAGE ACCRUAL IN SLE PATIENTS WITH NO CLINICAL OR SEROLOGICAL DISEASE ACTIVITY

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Background: : Observational studies have previously found associations between glucocorticoid therapy and irreversible organ damage in SLE. As glucocorticoid use and lupus disease activity are highly concordant, disease activity potentially confounds analysis of the contribution of glucocorticoid use to organ damage. This could be obviated through the study of damage accrual in patients without detectable disease activity.

Objectives: We studied whether glucocorticoids contribute to damage accrual in SLE in the absence of disease activity, by analysing the effect of glucocorticoids on SLE damage accrual in patients with no clinical or serological lupus disease activity (SLEDAI-2K=0).

Methods: 1707 SLE patients were recruited from 13 centres in 8 countries and followed longitudinally between 2013-2016. As per a standardised protocol, disease activity (SLEDAI-2K) and treatment details were recorded at each visit, and organ damage measured annually (SDI). Cox-proportional hazards analyses were used to examine time-dependent associations of glucocorticoid use with damage accrual.

Results: 196/1707 (11.4%) patients had no clinical or serological disease for the entire study period (time adjusted mean (TAM) SLEDAI2K=0). Of these, 95% were female; median (IQR) age at diagnosis 36.5yrs (26.0-46.5) years, median (IQR) baseline SDI 0 (0-1). 68% were exposed to prednisolone, with a median (IQR) TAM-prednisolone dose 2mg/day (0-5). Despite SLEDAI2K=0 throughout, irreversible damage accrual occurred in 13% of the cohort, with 26 damage events captured over median (range) 1.9 years (1.0-2.2) followup. Prednisolone exposure at doses in the upper two quartiles was associated with damage accrual (HR 1.11 (1.02, 1.22), p=0.02).

Conclusion: Irreversible damage accrual occurs in patients with no clinical or serological disease activity as captured by SLEDAI-2K, and glucocorticoid use contributes to the risk of organ damage in these patients.

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THU0254 TRENDS OF SEVERITY, PROGRESSION AND BURDEN OF DISEASE IN THE ''ATTIKON'' SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COHORT: EVIDENCE FOR THE RULE OF ''ONE THIRD'' IN DISEASE SEVERITY

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Background: SLE phenotype, severity and prognosis varies widely, while its course, prognosis and pattern of severity cannot be predicted with confidence.
Objectives: We analyzed the phenotype and severity patterns of a SLE cohort in the Attica area of Greece, based in "Attikon" University Hospital, and assessed whether these patterns change over the course of the disease.
Methods: Retrospective cohort study of 512 Caucasian SLE patients fulfilling the ACR 1997 and/or SLICC 2012 criteria. Data on clinical course, pattern of severity and SLICC damage index (SDI) were recorded for each patient at the time of diagnosis and at last evaluation. Severity of disease was stratified based on BILAG manifestations and patients were assessed for progression to a more severe phenotype over their disease course. Patients with disease duration < 12 months were excluded. Binary logistic regression was performed to identify independent predictors of such progression.
Results: More than half patients (53.7%, 275/512) presented with mild disease, while in approximately 20% (20.8%, n=106) lupus presented with severe manifestations at diagnosis. Median (IQR) follow-up was 96.5 (144) months. Of 246 patients with initially mild disease, 126 (56.4%) retained their mild phenotype, 73 (29.7%) progressed to a moderate phenotype, while the remaining 47 (19.1%) eventually developed severe lupus. Also, 30 patients (29.4%, 30/102) who initially manifested moderately severe manifestations progressed to severe disease over time. At last evaluation, a nearly equal distribution in severity patterns was evident (mild 30%, moderate 34% and severe 36%). Independent factors for disease progression were older age at diagnosis (OR: 0.97 per 1-year, 95% CI 0.95-0.98), disease duration (OR: 1.10 per 1-year, 95% CI 1.06-1.13), positive anti-dsDNA (OR: 2.20, 95% CI 1.38-3.49) and presence of fever at diagnosis (OR: 1.67, 95% CI 1.00-2.77). By multivariate regression, only disease duration (OR: 1.09, 95% CI 1.05-1.12) and anti-dsDNA (OR: 1.73, 95% CI 1.05-2.85) were independently associated with disease progression.
Ninety-two subjects (18%) had organ damage at the time of diagnosis, mainly due to neuropsychiatric and thrombotic events. At last visit, mean (SE) SDI was 0.67 (0.57). Two-hundred eight patients (59.8%) had no damage (SDI=0), while high damage (SDI $\geq$ 3) was measured in 25 subjects (7.2%).
Conclusion: In this SLE cohort of Caucasian patients, almost half of cases have mild disease at presentation, yet with significant damage accrual. Of patients with disease duration $\geq$1 year, 43.1% progressed to more severe phenotypes, with patients distributed evenly in the mild, moderate and severe categories. These data reiterate the rule of one third for severity observed in other autoimmune diseases.
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THU0255 IMPACT OF IL34, IFNA AND IFN-λ1 ON DISEASE ACTIVITY OF SLE PATIENTS IN EGYPT

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Background: SLE is a systemic inflammatory and autoimmune disease. IL-34 plays pivotal roles in the proliferation and differentiation of mononuclear phagocyte cells, osteoclastogenesis and inflammation [1]. IFN-α play an important role in SLE pathogenesis [2] and proportion of patients displays increased serum IFN-α and IFN-λ1 [3]. Interestingly, the gene signatures of IFN-λ1 and IFN-α overlap [4].
Objectives: Assessment of IL34, IFN-λ1 and IFN-α in SLE with relationship to clinical, laboratory parameters, treatment response and disease progression. We hypothesized a subgroup of patient with a concordance of high level of these cytokines that could have a different disease behavior.
Methods: 82 newly diagnosed SLE Egyptian patients. History, examination and laboratory investigation with assessment of disease activity. Pretreatment assessment of IL34, IFN-α and IFN-λ1 level by ILIZA. Patients started treatment (antimalarial ±Steroid ±immunosuppressive drugs) with response evaluation after six months.
Results: 14 male (17.1%) and 68 female (82.9%), age mean±SD (48.6 ±8.2). Mean±SD of IL34, INFα and INF-λ1were 175.9±125.9 pg/mL, 109.3±32.5 pg/mL and 227.9±144.8 pg/mL respectively. 21 patients (25.6%) had lupus nephritis, 32 patients (39%) with SLAM >6 and 22 patients (26.8%) with SLEDAI >6.
IL34 was positively correlated with anti-dsDNA (P= 0.002) but inversely correlated with C3 level (P = 0.009). IL34 was highly presented with lupus nephritis (P 0.005), SLAM>6 (P 0.03), SLEDAI>6 (P 0.007) and poor responder to treatment (P 0.02).
IFNα was inversely correlated with C3 (P 0.001). IFNα was highly presented with lupus nephritis (P 0.02) and poor responders (P 0.01) however no relation with SLAM>6 nor SLEDAI>6.
INF-λ1 was positively correlated with anti-dsDNA (P= 0.02) but inversely correlated with C3 (P = 0.01). INF-λ1 was highly presented with lupus nephritis (P 0.001), with SLAM>6 (P 0.04), with SLEDAI>6 (P 0.02).
Accumulation of $\geq$3 clinical features during follow up was associated with high IL34 (P 0.001), high IFNα (P 0.001) and high INF-λ1 (P 0.001).
We assigned high levels (i.e., $\geq$ 75% or third quartile) of each cytokine. Triple high ($IL34^{high}$, $IFN\alpha^{high}$ and $IFN\text{-}\lambda1^{high}$) found in 17 patients (20.7%) and were positively correlated with anti-dsDNA (P= 0.001) but inversely correlated with C3 (P = 0.001). Triple cytokines level was highly presented with lupus nephritis (P 0.001), SLAM>6 (P 0.02), SLEDAI>6 (P 0.03) and poor response to treatment (P 0.01) indicating these patients have aggressive disease. 28 patients developed (3 – 8) accumulated clinical features during the disease course, out of them 15 patients (53.5%) have high level of the triple cytokines indicating a poor prognosis of these subgroup.
Conclusion: High pretreatment IL-34 or IFN-λ1 has a prognostic significance in SLE. Patients with high IL-34 or IFNα or IFN-λ1 had more kidney affection and poor response to treatment. Triple cytokines elevation significantly associated with lupus activity, more kidney affection and poor response to treatment so, this aggressive phenotype may need combination of targets or multicytokines targeted therapy.

REFERENCES:

[1] Zhou, R.P., et al., *Functions of interleukin-34 and its emerging association with rheumatoid arthritis.* Immunology, 2016. 149(4): p. 362-373.
[2] Munroe, M.E., et al., *Altered type II interferon precedes autoantibody accrual and elevated type I interferon activity prior to systemic lupus erythematosus classification.* Annals of the rheumatic diseases, 2016: p. annrheumdis-2015-208140.
[3] Ronnblom, L. and M.L. Eloranta, *The interferon signature in autoimmune diseases.* Curr Opin Rheumatol, 2013. 25(2): p. 248-53.
[4] Rusinova, I., et al., *Interferome v2. 0: an updated database of annotated interferon-regulated genes.* Nucleic acids research, 2012. **41**(D1): p. D1040-D1046.

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THU0256 RISK OF LONG-TERM INCIDENT CARDIOVASCULAR EVENT AND MORTALITY IN PATIENTS WITH SLE AND POPULATION CONTROLS IS ASSOCIATED WITH A HIGHER CAROTID INTIMA-MEDIA THICKNESS

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Background: Measurement of carotid intima-media thickness (cIMT) is promoted as one of the tools for cardiovascular (CV) risk assessment in primary prevention in general population. The diagnosis of systemic lupus erythematosus (SLE) is a strong risk factor for premature CV events and mortality. Whether assessment of cIMT has a value for prediction of CV morbidity and mortality in patients with SLE compared with population controls of similar age and sex is not established.

Objectives: To examine association of cIMT with risk of incident CV events and mortality in SLE and controls.

Methods: We used the cross-sectional SLEVIC (SLE vascular impact cohort study) cohort of consecutive patients with SLE aged <70 years who were regularly treated in a tertiary referral rheumatology center. Carotid ultrasound was performed at inclusion to the cohort (from September 2006 to January 2008) in 118 patients and in 122 population controls matched by age and sex. Incident CV events were defined as hospitalization for angina pectoris, myocardial infarction, bypass grafting, percutaneous coronary or peripheral artery intervention, ischemic stroke and TIA. Combined outcome of incident CV event and all-cause mortality was evaluated for a mean (SD) follow-up of 9.6 (1.5) years. Participants with prevalent CV before inclusion, n=18, and those who were lost to follow-up, n=14, were excluded from this analysis.

Event-free survival rates in patients and controls were compared using Kaplan-Meier curves. Relative hazard ratios from Cox proportional-hazards regression models were used to estimate the effect of cIMT measurement on the outcome.

Results: At inclusion, mean age (SD) of the included 99 patients was 47 (13) years, 87% females, mean disease duration 12 (9) years, SLEDAI 4.0, and SLICC/ACR 1.0. Mean age of included 109 controls was 49 (12) years, 91% females.

Baseline mean (SD) cIMT did not differ between the groups (p=0.345) and was 607 (127) μm in patients and 623 (118) μm in controls.

During follow-up, 12 patients and 4 controls were defined with the outcome. The outcome was reached more often in patients than in controls, p=0.022. The mean time to outcome (SD) was 9.9 (0.2) years for patients and 10.3 (0.1) years for controls.

The hazard rate (HR) for the combined outcome of CV event and mortality was 3.7-fold (95% CI, 1.2–11.5) higher in patients than in controls, adjusted for age, sex and smoking history, p=0.025. A higher baseline mean cIMT was significantly associated with the outcome, HR 1.0 (95% CI, 1.0-1.01) per 1.0 μm increase in cIMT, p=0.040, irrespective of the group. Additional adjustment for traditional risk factors, disease duration, treatments, presence of anti-phospholipid antibodies and defining with carotid plaque yielded similar risk estimates.

Conclusion: In this analysis we confirm an elevated long-term risk of important adverse clinical events in patients with SLE compared with controls. A measure of cIMT is associated with incident CV event and mortality. This suggests that assessment with carotid ultrasound may have a value for CV risk stratification and would encourage validation in large-cohort prospective populations.

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THU0257 DIAGNOSTIC PERFORMANCE OF 2002 AECG, 2012 ACR AND 2016ACR/EULAR CLASSIFICATION CRITERIA FOR SJÖGREN'S SYNDROME IN A HISPANIC POPULATION

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Background: Primary Sjögren's syndrome (pSS) has several classification criteria, whose diagnostic performances vary depending on the studied population[1]. Concordance and differences among these criterias should be evaluated for independent populations to determine the diagnostic performance.

Objectives: To compare the performance among 3 classification criteria for pSS and determine the level of concordance among them.

Methods: Descriptive, retrospective, and cross-sectional study including 172 patients from the Rheumatology Service of the Hospital Universitario "Dr. José Eleuterio González", who were studied for dry syndrome. The clinical criterion of the attending physician was considered as the gold standard for diagnosis. Different parameters were collected: presence of xerostomia, xerophthalmia, Schirmer's test, sialometry, ocular staining, ANA, anti-Ro/SSA and anti-La/SSB antibodies, RF isotypes (IgA, IgM, IgG), and focal lymphocytic infiltrate in minor salivary gland biopsy. The criteria proposed by the American European Consensus Group (AECG), ACR and, ACR/EULAR were used to evaluate the classification. Compliance was determined for each set of criteria.

Results: Sociodemographic characteristics and clinical manifestations are shown in Table 1. For the AECG, ACR, and ACR/EULAR criteria, the sensitivity was 89.1%, 98.9% and 88% and the specificity was 93.8%, 71.3%, and 96.3%, respectively (Table 2). The ACR/EULAR criteria have an adequate level of agreement (k=0.663, *P*<0.001) with those of the AECG and with respect to the ACR criteria a moderate level of agreement (k=0.561, *P*<0.001).

Abstract THU0257 – Table 1. Clinical characteristics.

	pSS* n=92	Dry Syndrome n=80	*P*
Age, Median (IQR)	53[47-64]	51[43-59]	0.214
Female, n (%)	89(97%)	74(93%)	0.213
Xerostomia, n (%)	77/90 (86%)	52/71(73.2%)	0.052
xerophthalmia, n (%)	79/89 (89%)	58/69 (84%)	0.307
Schirmer test, n (%)	63 (68%)	36 (45%)	0.002
OSS ≥ 3, n (%)	60 (65%)	18 (22%)	<0.001
OSS ≥ 5, n (%)	59/91 (64%)	11/56 (19%)	<0.001
USF <1.5 ml/15 min, n (%)	74 (80%)	35 (43.8%)	<0.001
USF ≤0.1 ml/min, n (%)	76 (83%)	35 (43.8%)	<0.001
Minor Salivary Gland, n (%)	73/85 (86%)	23/67(34.5%)	<0.001
Anti-Ro/SSA, n (%)	70/90(78%)	5/69(7%)	<0.001
Anti-La/SSB, n (%)	27/86(31%)	1/65(2%)	<0.001
ANA, n (%)	62/88 (65%)	23/66 (35%)	<0.001
Rheumatoid Factor, n (%)	51/88 (58%)	24/66 (36%)	0.008
IgG, n (%)	17/86 (20%)	7/67 (10%)	0.116
IgM, n (%)	50/85 (59%)	23/63 (36%)	0.017
IgA, n (%)	34/83 (41%)	8/63 (13%)	0.001

OSS: Ocular Staining Score; USF: unstimulated salivary flow.

* The diagnosis of primary Sjögren's Syndrome was made based on clinical criteria ^P< 0.001

Abstract THU0257 – Table 2. Diagnostic criteria performance.

		Kappa Cohen	
Sensitivity		2012	2016
2002 AECG	89.10%	0.545^	0.663^

2012 ACR	98.90%	0.561^
2016 ACR/ EULAR	88.00%	
Specificity		
2002 AECG	93.80%	
2012 ACR	71.30%	
2016 ACR/ EULAR	96.30%	

AECG: American European Consensus Group criteria;

Conclusion: In our population, the ACR criteria showed the highest sensitivity, while the ACR/EULAR criteria showed the highest specificity, showing a moderate level of agreement. Despite the validation of these criteria, its application in real life tests its performance according to the population studied.

REFERENCES:

[1] Tsuboi, H., et al. (2017). Comparison of performance of the 2016 ACR-EULAR classification criteria for primary Sjögren's syndrome with other sets of criteria in Japanese patients. Annals of the Rheumatic Diseases, 76(12), 1980?1985. https://doi.org/10.1136/annrheumdis-2016-210758.

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THU0258 NERVOUS SYSTEM INVOLVEMENT IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by the involvement of the exocrine glands, mainly salivary and lacrimal glands. Approximately half of patients will experience extraglandular complications throughout their evolution.

Objectives: To characterize the involvement of the nervous system (NS) in patients with pSS.

Methods: Multicenter cross-sectional study of a cohort of patients with pSS, constructed by random selection of pSS patients fulfilling the 2002 American-European Consensus Criteria for pSS[1] from 33 rheumatology units. Through review of clinical records and interview with patients, demographic, clinical, analytical, therapeutic data and disease activity indexes were collected. Univariate analysis was done by Chi square test, Mann-Whitney U test and Student's t test. Multivariate analysis was done by linear logistic regression. A p <0.05 was considered significant. Patients signed an informed consent. The study was authorized by the ethics committees.

Results: 437 patients were included (95% women, median age of 58 years). 65 patients developed NS involvement: 26 patients central NS, 31 peripheral NS and 8 both. Multivariate analysis showed association between NS involvement and atherosclerotic stroke (OR 10.4, 95% CI 2.8-38.5), ear disease (OR 2.1, 95% CI 1.1-4.2) and myopathy (OR 6.5, 95% CI 1.3-31,6). Patients with NS involvement had higher probability of being treated with glucocorticoids (OR 3.3, 95%CI 1.5-7.2) and cyclophosphamide (OR 6.8, 95% CI 1.5-31).

Conclusion: 15% of patients with pSS develope NS involvement that is associated with atherosclerotic stroke, ear disease and myopathy.

REFERENCE:

[1] Vitali C. et al. Ann Rheum Dis 2002; 61:554

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THU0259 ULTRASOUND OF MAJOR SALIVARY GLANDS IDENTIFIES PATIENTS WITH MORE COMPLEX SALIVARY GLAND HISTOPATHOLOGY BUT NOT MILDER LESIONS

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Background: Ultrasonography of major salivary glands (SGUS) has been proposed as a feasible and reliable tool for the assessment of parotid and submandibular glands inflammation and damage in Sjögren's syndrome (pSS). However, the relationship between major SGUS and labial salivary gland (LSG) histopathology is still unclear.

Objectives: to investigate the correlation between SGUS abnormalities and LSG histopathology in patients newly diagnosed patients with pSS

Methods: Consecutive patients suspected of having pSS were enrolled in this study. All the patients underwent a complete diagnostic work up. The echostructure of each gland on B-mode images was graded on a 5-point scale (0–4), and a SGUS score $\geq$2 was defined as pathological. Hypo-anechoic areas in the glands were defined as isolated (<25% of the surface), localized (25-50%) and diffuse-scattered (>50%). Hyperechoic bands present in more than 50% of the parenchyma were also recorded. An expert pathologist analyzed all the LGS samples assessing focus score (FS), number of foci and presence of ectopic germinal centers (GCs).

Results: We included 115 pts (105 F: 10 M, mean age (SD) 54.8 (12.5) years). Out of them 51 were diagnosed with pSS and 64 represented the no-SS sicca controls. A SGUS score $\geq$2 identified pSS patients with a sensitivity of 62.7% and a specificity of 96.7%. SGUS score significantly correlated with FS (r=0.457**, p=0.000), number of foci (r=0.359**, p=0.000) and number of ectopic GCs (r=0.505**, p=0.000). However, the overall concordance between SGUS and LSG histopathology was moderate (Cohen's kappa =0.574). Thus, we specifically focused on 19/51 pSS "discordant" cases who presented normal SGUS findings but focal lymphocytic sialadenitis in their LSG biopsy. These "discordant" patients tended to present a lower FS (1.7±0.5 vs 2.6±1.5, p=0.04) and a significantly lower number of foci in their biopsies (2.7±1.6 vs 4.6 ±2.9,

p=0.01) when compared to patients with both abnormal SGUS findings and LGS focal lymphocytic sialadenitis.
Conclusion: SGUS and LSG histopathology showed only a moderate correlation in patients with pSS. SGUS may be useful to identify pSS patients with a more severe inflammatory LSG infiltrates, ultimately contributing to promote non-invasive phenotyping of multiple subsets in pSS.
Disclosure of Interests: Chiara Baldini: None declared, Francesco Ferro: None declared, Nicoletta Luciano: None declared, Gianmaria Governato: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB, Stefano Bombardieri: None declared, Valentina Donati: None declared
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THU0260 SYSTEMIC LUPUS ERYTHEMATOSUS AND CYTOPENIAS: THE KEY FINDINGS IN BONE MARROW

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Background: Cytopenias are common in systemic lupus erythematosus (SLE), and it is fundamental to determine their etiology in order to establish an adequate therapeutic strategy.
Objectives: To describe the findings in the bone marrow aspirations (BMA) and biopsies of patients with SLE and cytopenias, as well as clinical and laboratory features associated with the etiology of the hematological abnormalities.
Methods: We performed a retrospective study in a third-level hospital in Mexico City. We included patients who fulfilled ACR criteria for SLE, presented with cytopenias and had a BMA and biopsy performed between 2000 and 2016. We described the main aspirate and biopsy findings, and also analyzed the final diagnosis and its association with clinical, laboratory and serological features.
Results: We included 101 patients; median age was 32 years and 81.2% were women. Leukopenia (<3000 cells/μl) was found in 47.5% of patients, with 29.7% having moderate or severe neutropenia (<1000 cells/μl). Lymphopenia (<1000 cells/μl) was a common finding (71.3% of patients). Moderate-to-severe thrombocytopenia (<50 K/μl) was present in 28.7% of patients. Finally, 25.8% of patients presented with pancytopenia. Regarding bone marrow findings, there was erythroid dysplasia in 50.5% of patients, granulocytic dysplasia in 28.7% and megakaryocytic dysplasia in 16%. Myelofibrosis was found in 2.6%. An increase in plasma cells (≥5%) was found in 21.8%.
In 72.3% of patients, bone marrow interpretation was conclusive. The most common diagnoses were disease activity (24.8%) and drug-associated myelotoxicity (28.7%). When compared to other etiologies, in patients with cytopenias secondary to disease activity, it was more frequent for the bone marrow be hypercellular (56 vs 23%, p=0.006) and to have increased megakaryocytes (40 vs 17.4%, p=0.048). Conversely, granulocytic dysplasia was less common in this group of patients (17.4% vs 54.3%, p=0.036)
We analyzed factors associated with both activity and toxicity as final diagnoses (Table 1). After multivariate analysis, a neutrophil count <1000 cells/μl was a protective factor for disease activity (OR 0.021; 95% CI 0.001-0.428, p 0.012). On the other hand, a history of renal activity (OR 4.3; 95% CI 1.3-14.2, p=0.024) and neutrophils less than 1000 cells/μl (OR 4.05; 95% CI 1.15-14.19, p=0.029) were found to be independent risk factors for myelotoxicity.

Table 1.

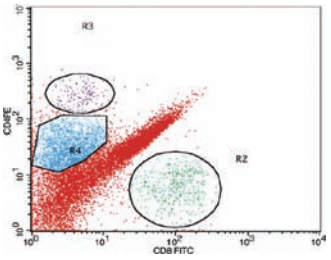
Characteristic	Disease activity (N=25)	Drug-associated toxicity (N=28)	p
History of disease activity	80%	86%	0.719
- Mucocutaneous	100%	96.4%	1
- Hematologic	**44%**	**78.6%**	**0.012**
- **Renal**			
Neutrophils (cells/μl)	**16%**	**17.9%**	**0.004**
- **Mild neutropenia (1000-1499)**	**4%**	**7.1%**	
- **Moderate neutropenia (500-999)**	**4%**	**39.3%**	
- **Severe neutropenia (<500)**			
Lymphopenia (<1000 cells/μl)	68%	70%	1
Platelets (K/μl)	16%	10.7%	0.859
- MIld thrombocytopenia (50-99)	28%	32.1%	
- Severe thrombocytopenia (<50)			
SLEDAI score	6 (0-23)	6 (1-14)	0.370
SLICC damage index	0 (0-5)	0 (0-6)	0.791
Treatment	**24%**	**53.6%**	**0.048**
- **Azathioprine**	0%	14.3%	0.113
- Mofetil mycophenolate	**4%** 56%	**35.7%** 46.2%	**0.006**
- **Hydroxychloroquine**	16%	28.6%	0.553
- Prednisone	28%	25%	
o ≤7.5 mg			
o 7.6-30 mg			
o >30 mg			

Conclusion: The main causes of cytopenias in our SLE patients were disease activity and bone marrow toxicity. Our findings suggest that when patients present with less than 1000 neutrophils/μl, it is unlikely for the cytopenias to be secondary to disease activity. Our study reinforces the diagnostic utility of BMA and biopsy, and the associations we described may assist clinicians to determine the etiology of cytopenias in SLE patients, in order to make appropriate therapeutic decisions.
Disclosure of Interests: Ana Barrera-Vargas: None declared, Jonathan Campos-Guzmán: None declared, Samuel Govea-Peláez: None declared, Aldo García-Ramos: None declared, Roberta Demichelis-Gómez: None declared, Christianne Bourlon: None declared, Javier Merayo-Chalico Speakers bureau: Pfizer, Jorge Alcocer-Varela: None declared
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THU0261 THE URINARY CELLULAR PROFILE AS A BIOMARKER FOR LUPUS NEPHRITIS

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Background: Proliferative lupus nephritis is one of the most common and serious manifestation of SLE and is a major cause of morbidity. A search for the ideal biomarker for LN is still underway, one that can be used for early detection, and correlate with the class & activity of LN. Urine is normally devoid of leucocytes, however it has been observed that macrophages and T-lymphocytes are routinely present in the urine of LN patients and those with other proliferative renal diseases.(1) This provided the idea for their potential use as biomarkers for proliferative LN.
Objectives: To study the urinary CD4+, CD8+ T Lymphocytes, and CD14 + monocytes in patients with proliferative lupus nephritis, and explore their use as a biomarker for LN.
Methods: Our subjects included 30 patients with biopsy proven proliferative LN and 30 SLE patients without clinical or lab evidence of LN as controls. Lab investigations included serum creatinine, urine analysis, protein creatinine ratio, anti-ds DNA Ab, C3 and C4. For the flowcytometric analysis 100 ml of freshly voided urine in a sterile container were obtained from patients and controls. All samples were processed within 2-4 hours of collection to ensure viability of the cells. Urine mononuclear cell count was done using a hemocytometer. The urine samples were centrifuged then washed twice by phosphate-buffered saline/bovine serum albumin (PBS/BSA) and resuspended in about 300 μls PBS. The cells were stained with anti CD8- FITC, anti CD4- PE, anti CD14-PERCP and anti- CD3-APC monoclonal antibodies. The flow cytometric analysis was done using Becton Dickinson, FACS Calibur multi-parameter flow cytometer equipped with BD CellQuest Pro software for data analysis.



Abstract THU0261 – Figure 1

Results: CD14 + cells were the most abundant cells in the urine of LN patients. The mean numbers of urinary CD8+, CD4+ and CD14+ cells/ml were significantly higher in patients with LN (405.6 ± 200.0, 281.1 ± 195.3, and 1554.7 ± 606.8 respectively) than in those without (39.30 ± 17.56, 34.33 ± 16.41, and 161.17 ± 90.91 respectively). AUC for ROC = 1.0 for all 3 markers with CD8+ >85 cells/ml, CD4+ >80 cells/ml, and CD14+ >400cells/ml being observed exclusively in LN. The cell counts correlated significantly with the protein:creatinine ratio, but not with other markers of disease activity.The CD4:CD8 ratio was significantly lower in LN patients (0.69 ± 0.21) than in those without (0.91 ± 0.31). Urinary CD14+ cells seem to occur in much higher counts in Class IV (1736.7 ± 522.0) than Class III LN (898.5 ± 17.68) p=0.084. Figure 1 shows a dot plot of flow cytometric analysis of urinary T cells and monocytes in a patient with lupus nephritis showing increased both CD4+ and CD8+ T cells and monocytes(dim CD4 expression and CD14 positive(not shown))
Conclusion: Urinary CD8+, CD4+ and CD14+ cells are highly sensitive and specific markers for detecting proliferative LN. A low CD4:CD8 ratio provides a further clue. The cell counts correlate with proteinuria. CD14 cell counts may be a potential biomarker to differentiate between the different classes of proliferative LN.

REFERENCE:

[1] Kopetschke K, Klocke J, Grießbach A-S, Humrich JY, Biesen R, Dragun D, et al. The cellular signature of urinary immune cells in Lupus nephritis: new insights into potential biomarkers. Arthritis research & therapy. 2015;17(1):94.

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THU0262 FATIGUE IN PRIMARY SJÖGREN'S SYNDROME AS A DISEASE MANIFESTATION REFLECTING THE DEGREE OF MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) INVOLVEMENT

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Background: fatigue in primary Sjögren's syndrome (pSS) is a very common and complex symptom, heavily impairing a wide range of patient functions, quality of life and health policies. To date, measures of fatigue and other patient-reported symptoms/outcomes (PROs) poorly correlate with pSS disease activity assessed by ESSDAI. On the other hand, therapeutic interventions reducing pSS disease activity proved useful to improve fatigue burden in pSS.
Objectives: to evaluate if fatigue correlates to other pSS disease manifestations which may also reflect disease activity, by investigating if: a) higher levels of fatigue shows a higher frequency of a heavier involvement of mucosa-associated lymphoid tissue (MALT) documented by histopathology, persistent glandular swelling, or cryoglobulinemia (1); and b) if fatigue correlates to other pSS-related somatic symptoms, such as dryness and arthralgias.
Methods: among pSS patients undergoing clinical evaluation in our Sjögren's Clinic in a six-months period, 86 consecutive unselected patients, fulfilling the latest ACR/EULAR pSS classification criteria, accepted to report their degree of fatigue, general dryness, ocular dryness, oral dryness and pain on 10-cm VAS (range 0-100), and to complete the ESSPRI (range 0-10), the PROFAD-SSI-SF (range 0-28) and the EQ-5D-scale (0-100) questionnaires. Four subgroups of fatigue severity were preliminary defined (2), presenting, as previously described (3): no fatigue (VAS=0): 12.8% (n=11); low fatigue (VAS=1-24): 25.3% (n=19); moderate fatigue (VAS=25-74): 58.7% (n=44); high fatigue (VAS=75-100): 16% (n=12). As previously reported (3) no significant age or sex difference was present between subgroups, and potential contributors to fatigue, such as autoimmune thyroiditis, anemia and fibromylagia did not play a role.
The frequencies of peculiar manifestations related to an increased activity in MALT involvement in pSS, such as persistent salivary gland swelling, cryoglobulinemia and biopsy-proven diagnosis of myoepithelial sialadenitis (MESA) or of pSS-related MALT lymphoma, at any time in the clinical history of patients, were evaluated for each subgroup.
Secondly, the correlations between fatigue VAS and PROs reflecting somatic symptoms were performed.
Results: pSS patients reporting moderate or high fatigue VAS showed significantly higher frequencies of salivary gland swelling (p=0.0274), of MESA or lymphoma proven by histological diagnosis (p=0.0397), if compared to pSS patients with no or low levels of fatigue. Cryoglobulinemia was not significantly increased, although more frequent, in patients with moderate or high fatigue (10.7%) compared to patients with no or low fatigue (6.6%).
Fatigue VAS score did not correlate with ESSDAI.
Patients with higher levels of fatigue showed significant (p<0.0001) higher scores in total ESSPRI, dryness-ESSPRI, pain-ESSPRI, ocular dryness VAS, oral dryness VAS, pain VAS, somatic fatigue domain of PROFAD, arthralgia domain of PROFAD, total SSI and PROFAD-SSI-SF.
Finally, patients with higher levels of fatigue reported worst scores in quality of life EQ-5D-scale.
Conclusion: The severity of fatigue appears to mirror the degree of MALT involvement, and this involvement is the biological substrate of pSS itself. This represents a demonstration that fatigue is biologically related to pSS, and supports the notion that fatigue should be treated by disease-modifying drugs rather than only with symptomatic therapies in pSS. In addition, dedicated scores of pSS activity can be developed for pSS patients where fatigue is one of the dominant symptoms. Since fatigue may also correlate with pSS somatic symptoms, such as dryness and arthralgia, they could also be included.

REFERENCES:

[1] De Vita S et al, Clin Exp Rheumatol 2018
[2] James K et al, PLoS one 2015
[3] Gandolfo S et al, Ann Rheum Dis 2018

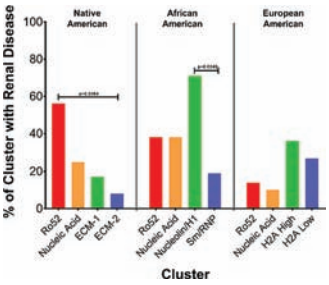
Disclosure of Interests: Saviana Gandolfo: None declared, Marco Binutti: None declared, Elena Doriguzzi Breatta: None declared, Cinzia Fabro: None declared, Salvatore De Vita Grant/research support from: Roche, Pfizer, Abbvie, Novartis, BMS, MSD, Celgene, Janssen, Consultant for: Roche
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THU0263 NOVEL SUBSETS OF SLE PATIENTS ENRICHED FOR RENAL MANIFESTATIONS IDENTIFIED BY CLUSTERING WITH EXPANDED AUTOANTIBODY PROFILES OF NATIVE AMERICAN (NA), AFRICAN AMERICAN (AA), AND EUROPEAN AMERICAN (EA) SLE PATIENTS

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Background: Autoantibodies (AAbs) are a hallmark of systemic lupus erythematosus (SLE). Common SLE AAbs show differences in specificities, levels and associations with clinical characteristics of disease which may be influenced by ethnicity.(1-2) NA SLE patients do not always exhibit classical AAb profiles.(2) Understanding how AAb profiles associate with clinical disease, including in NA patients, is important to better inform disease management.
Objectives: To identify patient subsets enriched for renal disease by clustering NA, AA and EA SLE patients into more homogeneous disease subsets based on expanded AAb profiles.
Methods: Serum samples from 49 NA, 49 AA, and 49 EA age, sex and ANA titer-matched SLE patients who met ACR classification and 10 sex and age matched controls from each ethnicity were tested for AAb reactivity by autoantigen microarray. Normalized fluorescence intensity (NFI) for AAb binding was determined for each individual for all autoantigens. Ratios of NFIs to total IgG were calculated and converted to Z-scores. Kruskal-Wallis analysis of Z-score transformed AAb ratios were used to identify AAbs that differed significantly between patients and controls for each ethnicity; these AAbs were used for hierarchal clustering of SLE subjects within each ethnicity. The enrichment of SLE clinical criteria within each cluster was determined by Fisher's exact test.
Results: AAbs to nucleic acids and Ro52 were present in SLE patients of all three ethnicities. On average, NA SLE patients, but not EA or AA SLE patients, had lower levels of AAbs against extracellular matrix (ECM) antigens compared to controls. AA and EA, but not NA, SLE patients had significantly higher levels of AAbs to Sm, RNP and histones compared to matched controls. In each ethnicity four clusters of SLE subjects were identified by ethnicity-specific AAbs. All three groups had a cluster of subjects enriched in nucleic acid-specific AAbs and a cluster of subjects enriched in Ro52 AAbs. The NA group also had two clusters enriched in ECM AAbs. The AA group had an Sm/RNP AAb enriched cluster and a nucleolin/histone AAb enriched cluster. Two additional EA

SLE clusters had similar levels of nucleic acid-specific AAbs and Ro52 AAbs, but were distinguished by significant differences in histone 2A (H2A) AAb levels. Renal manifestations were significantly enriched in the NA Ro52 cluster and the AA nucleolin/histone cluster compared to other SLE patient clusters of the same ethnicity.



Abstract THU0263 – Figure 1

Conclusion: Expanded AAb profiles can be used to identify SLE subsets that are more likely to have renal manifestations of disease.

REFERENCES:

[1] Sánchez E, et al. Impact of genetic ancestry and sociodemographic status on the clinical expression of systemic lupus erythematosus in American Indian-European populations. Arthritis Rheum. 2012;64(11):3687-94.

[2] Kheir JM, et al. Unique clinical characteristics, autoantibodies and medication use in Native American patients with systemic lupus erythematosus. *Lupus Sci. & Med.* 2018;5:e000247.

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THU0264 ANALYSIS OF SURVIVAL ASSOCIATED WITH PULMONARY ARTERIAL HYPERTENSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Identifying clinical variables that predict outcome of Systemic lupus erythematosus (SLE)-pulmonary arterial hypertension (PAH) is important.[1] Data focusing on SLE-PAH is lacking as previous studies were based on connective tissue disease (CTD)-PAH patients.
Objectives: To examine clinical, serological and echocardiographic features that are 1) associated with SLE-PAH at baseline and 2) predictors of mortality in SLE-PAH.
Methods: Data on SLE-PAH patients (SLE-PAH group, n=67) attending the Prince of Wales Hospital, from 2008 to 2018 was retrieved. Diagnosis of PAH was based on echocardiogram showing pulmonary artery systolic pressure (PASP) > 30mmHg. Age-, sex- and disease duration-matched SLE patients with PASP < 30mm Hg were selected from the same database as control (SLE-non PAH group, n=154). Clinical, serological, echocardiographic features and medication at baseline (PAH diagnosis) were collected. Censor date was death or last visit on or before 31st December 2018. PAH targeted therapy and immunosuppressant used for PAH were recorded after diagnosis of PAH. Hazard ratio were analysed by cox regression model, and adjusted by age-, sex-, disease-duration, comorbidities and baseline medication.
Results: The cohort (n=221) mean age was 42.7 +/- 12.6 with 96.3% female, and a disease duration of 8.26 +/- 7.61 years. At baseline, the SLE-PAH group had higher anti-ds DNA titre; lower haemoglobin level; higher prevalence of renal impairment; but a lower prevalence of arthritis and thrombocytopenia/neutropenia and anti-phospholipid antibodies compared to the control (Table 1). SLE-PAH group's echocardiogram had a higher prevalence of reduced left ventricular ejection fractions, moderate-severe tricuspid regurgitation and pericardial effusion compared to the control (Table 1). Amongst the SLE-PAH group, 11/67 had a right heart catherization done and all were confirmed to have PAH. 8/11 patients received PAH specific treatment and 23/67 received escalated immunosuppressive therapy for presumed PAH, within 1 years of PAH diagnosis. The mortality rate of the SLE-PAH group was 3.82 (95% confident interval 1.50-9.83; p=0.005) compared to the control after adjusting for baseline parameters and medication used after the diagnosis of PAH. Poor prognostic factors at baseline are summarized in table 2.

Table 1. Comparison between SLE-PAH and control at baseline

	SLE non-PAH (N=154)	SLE-PAH (N=67)	p-value
Female	149 (96.8%)	64 (95.5%)	0.701
Age, Mean (SD)	41.84 (11.76)	44.78 (14.18)	0.111
Follow up time (year) [Median (IQR)]	9.78 (4.39-12.42)	8.24 (4.54-12.07)	0.835
Disease duration (year), Median (IQR)	6.85 (1.29-11.77)	7.33 (0.94-15.06)	0.681
Death at end of follow up (%)	8/154 (0.05%)	14/67 (20.1%)	0.001
Renal impairment	25/154 [16.3%]	19/67 [29.7%]	0.026
Arthritis	91/154 [59.9%]	29/67 [43.3%]	0.023
Thrombocytopenia/neutropenia	78/154 [51.3%]	24/67 [35.8%]	0.047
Anti-ds DNA titre (median [IQR])	52 IU/ml [IQR 0-292.5]	160 IU/ml [IQR 0-789.5]	0.036
Haemoglobin (median [IQR])	11.7 g/dL [IQR 10.5-12.9]	10.8 g/dL [IQR 10-10.2]	0.009
Anti-phospholipid antibodies	38/154 [25.5%]	8/67 [12.1%]	0.027
Reduced left ventricular ejection fractions	1/154 [0.6%]	6/67 [9%]	0.003
Moderate-severe tricuspid regurgitation	2/154 [1.3%]	20/67[29.9%]	<0.001
Pericardial effusion	22/154 [14.3%]	17/67 [25.4%]	0.047

Table 2. Predictors of mortality in SLE-PAH at baseline

	Alive (N=53)	Death (N=14)	p-value
Hyponatremia	7/49 [14%]	4/12 [30.8%]	p=0.011*
Renal impairment	11/51 [21.6%]	8/13 [61.5%]	p=0.007*
Severe tricuspid regurgitation	2/53 [3.8%]	2/14 [14.3%]	p=0.071

Conclusion: SLE-PAH had 3.8-fold increase in mortality despite treatment with PAH specific therapy and immunosuppressants. Hyponatremia and renal disease were associated with poor survival outcome in SLE-PAH patients.

REFERENCE:

[1] Raina, A, et al. European Respiratory Review, 2016

Disclosure of Interests: None declared
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THU0265 IDENTIFYING COMORBID FIBROMYALGIA IN SYSTEMIC LUPUS ERYTHEMATOSUS USING PATIENT-REPORTED OUTCOMES

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Background: Fibromyalgia (FM) is disproportionately common in patients with systemic lupus erythematosus (SLE) and difficult to diagnose on a background of classical SLE symptoms [1]. The Multi-Dimensional Health Assessment Questionnaire (MDHAQ) has been shown to be useful to recognise improvement over 2 months in a variety of rheumatic conditions including SLE [2] but has not previously been shown to be useful to alert the clinician to comorbid FM in the latter condition. Conversely, the 2011 FM self-report questionnaire is disease-specific and available for use in clinical and epidemiological studies. Administration of multiple forms may be difficult in a busy clinical setting.
Objectives: To identify comorbid FM in patients with SLE using patient-reported outcomes (PROs) from the routinely distributed MDHAQ, in comparison to the 2016 revision of the 2010/2011 FM criteria.
Methods: Patients with SLE completed an MDHAQ and the 2011 FM Criteria questionnaire. FM status was assigned using the 2016 revision of the 2010/2011 FM criteria as the gold standard. The MDHAQ features

six main PROs: body pain, patient global and fatigue score on a 0-10 visual analogue scale, as well as a functional impact score, self-report joint count and symptom checklist which have a range of 0-10, 0-48 and 0-60 respectively. Composite indices consisting of either two or three of patient pain score 6, self-report joint count 16 and symptom checklist 16 or three of four of the same measures plus a fatigue score 6 have been described previously to provide clues to comorbid FM in other rheumatic diseases [3,4]. Individual PROs and these composite indices were compared between patients with and without FM by student's unpaired t-test and Area Under the Curve (AUC) analysis. The physician's diagnosis of FM was analysed against the FM criteria using Cohen's kappa. Physicians were blinded to the results of the 2016 FM criteria.

Results: 88 patients with SLE were studied, of whom 23 (26%) satisfied FM criteria. Those with FM reported higher scores in all PROs. A patient global of 6 could correctly classify 90% of patients and provided the highest AUC of 0.95, followed by the symptom checklist and body pain. An index of three measures (pain score, self-report joint count and symptom checklist) gave an AUC of 0.90. An index of four measures (additional fatigue criterion) gave an AUC of 0.93. Both indices correctly classified 89% of patients with a cut-off of 2 and 3 respectively. The physician's diagnoses had moderate agreement with the FM criteria (kappa = 0.43).

	AUC	Sensitivity	Specificity	Correctly classified
3 PROs (≥2)	0.90	78%	92%	89%
4 PROs (≥3)	0.93	74%	94%	89%
Patient global (≥6)	0.95	91%	89%	90%

Conclusion: Comorbid FM is prevalent in SLE yet often missed by physicians. In busy clinical settings, composite indices provide useful clues to coexisting FM in SLE, although a simple MDHAQ patient global is quick and potentially just as valuable in this patient group. These findings require further validation in a larger cohort.

REFERENCES:

[1] Wolfe F, Petri M, Alarcon GS, Goldman J, Chakravarty EF, Katz RS, et al. Fibromyalgia, systemic lupus erythematosus (SLE), and evaluation of SLE activity. J Rheumatol. 2009;36(1):82-8.

[2] Castrejon, I., M.J. Bergman, and T. Pincus, MDHAQ/RAPID3 to recognise improvement over 2 months in usual care of patients with osteoarthritis, systemic lupus erythematosus, spondyloarthropathy, and gout, as well as rheumatoid arthritis. J Clin Rheumatol, 2013. 19(4):p.169-74

[3] Gibson K et al. 2016 MDHAQ as a useful screening tool for fibromyalgia in busy clinical settings Ann Rheum Dis, volume 75, supplement 2, page 88

[4] Schmuckler J, et al. 2018 A simple index based on scores on a multidimensional health assessment questionnaire (MDHAQ) provides information quite similar to ACR criteria for fibromyalgia in routine care Ann Rheum Dis, volume 77, Suppl, page A465

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THU0266 ULTRASONOGRAPHY IN THE DIAGNOSIS OF LOWER LIMB ENTHESOPATHY IN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: RELATION TO THE DISEASE ACTIVITY

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease characterized by variable clinical manifestations due to different organ involvement[1]. Musculoskeletal involvement is extremely common in patients with SLE. Musculoskeletal ultrasound (MSUS) is an important tool for evaluation of patients with inflammatory arthritis and early detection of subclinical inflammation at the joint, tendon and entheseal level[2].

Objectives: To investigate the presence of entheseal abnormalities in SLE patients and correlating it with parameters of disease activity.

Methods: In this cross-sectional study we evaluated 50 patients with SLE who fulfilled the 2012 ACR/SLICC criteria[3]. Patients underwent clinical, laboratory and ultrasonographic examination of both lower limbs at the sites of entheses. Disease activity was assessed by using the SLE disease activity index (SLEDAI)[4]. The scanned entheses were those included in the Glasgow Ultrasound Enthesitis Scoring System (GUESS)[5]. The anatomical sites were scanned bilaterally, both in longitudinal and transverse planes, in grey-scale (GS) and power Doppler (PD) mode. Ultrasonography was performed using (esaote) MyLab^{TM}Six ultrasound machine, equipped with a 6-18 MHz linear probe.

Results: In our cohort of 50 SLE patients we found 29 patients had clearly evident MSUS features of enthesopathy (58%) and 16 patients with minimal and isolated entheseal abnormalities (32%). Five patients had normal MSUS findings with no evidence of entheseal affection (10%). The mean of total GUESS score of all patients was 3.54 ± 2.6. MSUS examination of the quadriceps tendon insertion at the patella revealed mean thickness of 5.89 ± 0.7 mm, the patellar tendon attachment at the patella (proximal) was 4.26 ± 0.84 mm and the mean thickness of the patellar tendon at the tibial insertion (distal) was 4.08 ± 0.7 mm. The Achilles tendon insertion at the superior pole of calcaneus and the plantar fascia insertion at inferior pole of calcaneus were 4.2 ± 0.7 and 3.7 ± 0.7 mm respectively. Age, body mass index (BMI), SLEDAI score, and ESR; had a highly significant positive correlation with GUESS score. The increase in BMI, SLEDAI score and creatinine; had an independent effect on increasing GUESS score.

Conclusion: Lower limb enthesopathy is common in SLE patients and considered one of the important causes of knee and ankle joints pain. Entheseal involvement in SLE patients is affected by variable parameters, mainly disease activity. Entheseal abnormalities can be early detected by ultrasonography even in clinically asymptomatic SLE patients without evidence of clinical symptoms and/or signs of entheseal affection.

REFERENCES:

[1] Alyoussef A, Alassar B, Mohammed O, et al. Patterns of systemic lupus erythomatosis in Tabouk, Saudi Arabia. Indian Journal of Applied Medical Research. 2016; 5(2): 23-28.

[2] Gutierrez M, Filippucci E and De Angelis R. Subclinical entheseal involvement in patients with psoriasis: An ultrasound study. Semin Arthritis Rheum 2011; 40: 407–412.

[3] Petri M., Orbai AM., Alarcón GS, et al. Derivation and Validation of the Systemic Lupus International Collaborating Clinics Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheum. 2012; 64: 2677-86.

[4] Bombardier C, Gladman D, Urowitz M, et al. Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. Arthritis Rheum 1992; 35: 630–640.

[5] Balint PV, Kane D, Wilson H, McInnes IB, Sturrock RD. Ultrasonography of entheseal insertions in the lower limb in spondyloarthropathy. Ann Rheum Dis 2002; 61: 905–910.

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THU0267 THE SLE DISEASE ACTIVITY SCORE (SLE-DAS) ENABLES ACCURATE DEFINITIONS OF SLE REMISSION AND LDA AS ACHIEVABLE TARGETS IN DISEASE MANAGEMENT

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Background: The treat-to-target strategy in Systemic Lupus Erythematosus (SLE) aims to achieve remission. However, to define a target based on the SLE Disease Activity Index (SLEDAI) is questionable, due to its limitations (especially its dichotomous nature). The SLE Disease Activity Score (SLE-DAS) is a recently validated continuous disease activity score which has a higher accuracy in measuring SLE activity and a higher sensitivity-to-change compared to SLEDAI.[1]

Objectives: To assess the ability of SLE-DAS to define SLE remission and other disease activity states.

Methods: Cross-sectional study of SLE patients fulfilling the ACR'97 and/or SLICC'12 classification criteria and followed at the Padua Lupus Clinic from March to June 2018. At each outpatient visit, the attending clinician scored SLE disease activity (in the last 30 days) using Physician Global

Assessment (PGA) (0-3 points, 10 cm scale), SLEDAI-2K and SLE-DAS. A senior rheumatologist expert in SLE, blinded to the disease activity scores, classified each patient in 1 of 4 categories: (i) remission, (ii) low disease activity (LDA), (iii) mild disease activity and (iv) moderate/severe disease activity. The best cut-off values of SLE-DAS to define these categories were estimated using Receiver Operating Characteristic (ROC) curve analysis. Accuracy, precision, sensitivity and specificity values for these cut-off values were then calculated. The agreement between the SLE-DAS and physician's classification was measured using Kappa coefficient. Statistical significance was set at 0.05.

Results: We included 221 patients (84.2% female, mean age of 45.4 ±13.5 years, mean disease duration of 15.4±9.5 years). In this preliminary study, the proposed cut-off values of SLE-DAS to define each disease activity category were: remission SLE-DAS≤2.08, LDA 2.08<SLE-DAS≤3.77, mild disease activity 3.77<SLE-DAS≤7.64, and moderate/severe disease activity SLE-DAS>7.64 for (Table 1). The overall accuracy of these SLE-DAS cut-off values to identify each disease activity state was 96.4%. The agreement between SLE-DAS and physician's classification was very high (k=0.925, p<0.001). Distribution of SLE-DAS and SLEDAI-2K scores in each disease activity state is presented in Figure 1.

According to the SLE-DAS cut-offs, 68.8% of the patients were in remission, 2.3% in LDA, 10.9% in mild disease activity and 18.1% in moderate/severe disease activity.

Abstract THU0267 – Table 1. Performance of SLE-DAS to assess each disease activity state.

Disease activity state	Sensitivity (%)	Specificity (%)	Precision (%)
Remission (SLE-DAS≤2.08)	99.3	97.1	98.7
Low Disease Activity (2.08<SLE-DAS≤3.77)	66.7	99.5	80
Mild Disease Activity (3.77<SLE-DAS≤7.64)	88.0	99.0	91.7
Moderate/Severe Disease Activity (SLE-DAS>7.64)	94.9	98.4	92.5

Conclusion: The SLE-DAS has a high precision in identifying remission, LDA, and other disease activity states in SLE. These results suggest that the SLE-DAS is an accurate tool in defining achievable targets in SLE management.

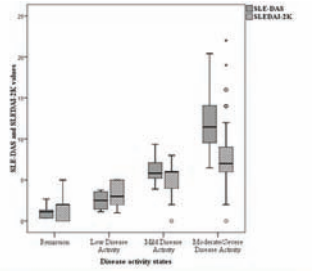


Figure 1. SLE-DAS and SLEDAI-2K boxplots for each disease activity state according to the physician's classification. The superiority of SLE-DAS to separate the disease activity levels is indicated by the clear separation of its boxplots, in contrast to the overlap of the SLEDAI-2K boxplots.

Abstract THU0267 – Figure 1

REFERENCES:

[1] Jesus D, Matos A, Henriques C, et al. Derivation and validation of the SLE Disease Activity Score (SLE-DAS): a new SLE continuous measure with high sensitivity for changes in disease activity. Ann Rheum Dis 2019, Epub ahead of print 9 January 2019. DOI: 10.1136/annrheumdis-2018-214502.

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THU0268 CLINICAL AND LABORATORY FEATURES OF PRIMARY SJOGREN'S SYNDROME ASSOCIATED WITH ANTICENTROMERE ANTIBODIES

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Background: The prevalence of ACA among patients with pSS varies from 2% to 27%. Among experts, there is a lot of controversy about whether primary Sjögren's syndrome with ACA is a separate disease subtype or overlap-syndrome with systemic sclerosis.

Objectives: To evaluate clinical and laboratory features of anticentromere antibody-positive (ACA) primary Sjögren's syndrome (pSS); to evaluate the spectrum of autoantibodies in patients of this group; to evaluate conformity of the patients to the pSS and systemic sclerosis (SSc) classification criteria; to evaluate prevalence of salivary MALT-lymphoma in this group of patients; to evaluate prevalence of primary biliary cirrhosis (PBC)/biliary lesions in this group of patients.

Methods: From 2012 to 2018, we examined 83 patients with pSS and ACA. Inclusion criteria were conformity to the 2001 Russian Sjögren's syndrome criteria and high ACA titer. We used ACR 2012 and ACR/EULAR 2016 criteria to evaluate conformity to the pSS, and ACR 2013 criteria to evaluate conformity to the SSc. Diagnosis of salivary MALT lymphoma was established on the basis of histological, immunohistochemical and PCR studies of biopsy specimens of parotid salivary glands. Diagnosis of PBC/biliary lesions was made on the basis of histological and immunohistochemical studies of liver biopsy specimens.

Results: We found a low detection rate of anti-Ro antibodies (32.5%), anti-La antibodies (7.2%), RF (21.7%), increased ESR (14%), leukopenia (7%), hypergammaglobulinemia (17.6%), increased IgG (9.5%), increased IgA (18.7%) hypocomplementemia (16.1%) in the group of patients with pSS and ACA. Despite the low frequency of detection of the RF, some patients of this group had MALT-lymphoma: 14 patients had salivary MALT-lymphoma (16.8%), one patient had tonsil MALT-lymphoma with nodal involvement (1.2%). In addition, patients of this group are characterized by a high frequency of detection of AMA antibodies 17/52(32.7%), increased IgM (29.7%) and increased risk of biliary lesions (14.4%). Acccording to our data increased risk of developing biliary lesions (28.5%), primary biliary cirrhosis (28.5%), autoimmune hepatitis (AIH) (28.5%), overlap-syndrome between PBC and AIH (14,5%) was observed in patients with functional signs of liver damage (ALT/AST, GGT, ALP >2N), AMA-positivity, high levels of IgM. Only two patients, who were diagnosed with liver disease according to studies of biopsy specimens, lacked AMA-antibodies. Damage to the nervous system, kidneys, antiphospholipid syndrome, rheumatoid arthritis, hypergammaglobulinemic purpura and cryoglobulinemic vasculitis were much less common and were single. Also patients with pSS and ACA often have Raynaud's phenomenon (54.9%) with capillaroscopic changes of the scleroderma type (68%) and an increased risk of developing limited form of systemic scleroderma (24%).

Conclusion: pSS associated with ACA is a subtype of the disease, significantly different from the "classic" in a number of clinical and laboratory signs and characterized by an increased risk of SSc and PBC/biliary lesions which in some cases leads to the underdiagnosis of pSS. ACA should be considered as pathogenetically related to pSS antibodies and all ACA-positive patients should be examined for pSS and PBC/biliary lesions regardless of whether they have SSc or not. Patients with a significant enlargement of salivary glands should be biopsied to confirm the presence of MALT-lymphoma before initiating hormonal, antilymphoproliferative and anti-B-cell therapy.

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THU0269 SERUM IL-6 AND CIRCULATING IMMUNE COMPLEXES AS BIOMARKERS OF DISEASE ACTIVITY IN MULTI-ETHNIC ASIAN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: IL-6 plays an important role in B cell hyperactivity and immunopathology of systemic lupus erythematosus (SLE), and may have a direct role in mediating tissue damage [1]. Elevated levels of serum

circulating immune complexes (CICs) have been described in SLE but the relationship with disease activity in our multi-ethnic Asian patients remains unclear.

Objectives: To determine the correlation between disease activity and the levels of CICs, serum and urine IL-6 in a Singapore cohort of multi-ethnic Asian SLE patients.

Methods: Serum levels of CICs, IL-6 and urine IL-6 were measured in 88 SLE patients using CIC-C1q and high sensitivity IL-6 ELISAs. All patients fulfilled the 1997 revised American College of Rheumatology (ACR) classification criteria. Clinical and laboratory manifestations, therapy, disease activity and damage at the time of sample collection was collated. Disease activity was scored with the SLE Activity Measure-revised (SLAM-R) and damage with the ACR/Systemic Lupus International Collaborating Clinic SLE damage index (SDI). The correlation between disease activity score and CICs, serum and urine IL-6 were assessed using Spearman's correlation. Receiver operator characteristic (ROC) curve analysis was performed to assess the performance of the individual biomarkers in discriminating SLE disease activity.

Results: The cohort of 88 patients were predominantly female (n = 78, 89.6%), with a mean age of 40 years±13.1. The majority were of Chinese ethnicity (n = 73, 83%), 13% were Malay (n = 11) and 4 individuals were of other races. The mean disease duration was 98.4 months ± 86.4. The mean scores of SLAM-R and SDI were 2.9 ± 2.2 and 0.9 ± 0.9 respectively. SLE disease manifestations at the time of sample collection included mucocutaneous involvement (5.7%) and active urine sediment (28.7%). 77% had hypocomplementaemia and 70.1% had elevated titres of anti-dsDNA antibody. The majority were on corticosteroids (75.9%) and hydroxycholoroquine (65.5%). Immunosuppressive drugs included azathioprine in 37.9%, mycophenolate in 6.9%, intravenous pulse cyclophosphamide in 6.9% and cyclosporin in 1 patient. There was significant positive correlation between SLAM-R and serum CICs ($R = 0.4121$, $p < 0.01$), serum IL-6 ($R = 0.4227$, $p < 0.01$) and urine IL-6 ($R = 0.3142$, $p = 0.01$). Based on the area under the curve(AUC), CICs and urine IL-6 were better in discriminating active SLE (AUC 0.8002, $p < 0.01$ and AUC 0.7397, $p < 0.01$ respectively) compared to serum IL-6 (AUC 0.5554, $p = 0.1718$).

Conclusion: Our study observed significant correlation between levels of serum circulating immune complexes, serum and urine IL-6 with SLE disease activity in our multi-ethnic Asian patient cohort. ROC curve analysis suggests that serum CICs and urine IL-6 may serve as sensitive biomarkers to identify SLE patients at risk of flares.

REFERENCE:

[1] Tackey E, et al. Rationale for interleukin-6 blockade in systemic lupus erythematosus. Lupus. 2004;13(5):339-43.

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THU0270 THE BURDEN OF CHRONIC KIDNEY DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS: A NATIONWIDE EPIDEMIOLOGIC STUDY

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Background: Clinical-epidemiological research has advanced our knowledge on the negative impact of lupus nephritis (LN) on systemic lupus erythematosus (SLE) outcomes. Impaired renal function at LN diagnosis and failure to normalize renal function upon aggressive immunosuppressive therapy are associated with a very poor long-term renal outcome. Most reports on that field are however based on tertiary care data of limited sample size that impede the ability to generalize the findings. In order to measure the impact of renal function impairment on clinical outcome such as death or cardiovascular events effectively, updated comprehensive information at national level is needed.

Objectives: We conducted an analysis of a French nationwide database to assess the characteristics associated with the presence of CKD (i.e. eGFR <60mL/min/1.73m^2) and the prognosis associated with CKD in SLE patients

Methods: Characteristics of all admitted SLE patients experiencing CKD in France from 2009 to 2015 were analyzed through the French medico-administrative database. Factors associated with CKD and major clinical outcomes such as end-stage renal disease (ESRD), cardiovascular event (CVE), septic shock and death were assessed. We used a multivariate Cox proportional hazard model and subdistribution hazard models to analyze survival without major clinical events according to the presence of CKD.

Results: From 2009 to 2015, 26 320 SLE patients were hospitalized in France. Among them, 6 439 (86.5% women; mean age 45.7 [16.5] years old) had a baseline stay in 2009 during which CKD was reported in 428 (6.7%) cases. Multivariate analysis showed that lupus nephritis (OR 6.6 [5.2-8.4]), high blood pressure (OR 3.5 [2.8-4.5]), septic shock (OR 3.2 [1.7-6.0]) and past cardiovascular history (OR 1.4 [1.0-2.0]) were associated with CKD status.

From 2009 to 2015, ESRD, CVE, septic shock, and death occurred in 4.0%, 14.4%, 6.3% and 9.6% of the 6 439 SLE patients. CKD at baseline was independently and strongly associated with the occurrence of ESRD (sdHR 15.9 [11.6-21.9]), CVE (sdHR 1.7 [1.4-2.2]), septic shock (sdHR 2.1 [1.5-2.8]) and death (HR 1.7 [1.3-2.2]) during the follow up

Conclusion: CKD is a major risk factor for overall morbidity and mortality in SLE patients, highlighting the need for early pre-CKD lupus nephritis diagnosis and treatment

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THU0271 SERUM LEVELS OF TRANSFORMING GROWTH FACTOR B (TGF-B) IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjogren's syndrome (pSS) is an autoimmune disease affecting primarily exocrine, especially salivary, glands. The epithelial damage, autoantigens release, activation of innate and acquired immunity form the underlaying of the pSS pathogenesis. The main role in pSS is played by B-lymphocytes and production of autoantibodies. One of the cytokines which may play a role in autoimmune processes is tumor growth factor beta (TGF-β), pleiotropic cytokine, which is involved in the control of autoimmune reactions, cell proliferation and the organ accumulation of lymphocytes. Numerous studies focused on the expression of TGF-β in salivary glands, as an organ targeted in pSS.

Objectives: The aim of this study was to evaluate the activity of TGF- β in serum of patients with pSS and to show its significant relationships with other cytokines active in the pathogenesis of this syndrome.

Methods: 33 patients with pSS (according to current EULAR/ACR criteria) were included into the study, female 28 (85%), men 5 (15%), mean age 47± SD=16. Routine laboratory tests (blood morphology, ESR, CRP, rheumatoid factor) were performed along with ophthalmological assessment (Schirmer's test, ocular staining score) with confirmation of dry eye. Patients had routine chest X-ray and, in case of clinical indications, high resolution computed tomography to assess interstitial changes. Serum concentrations of TGF-β were determined using an Quantikine ELISA Kit. Serum cytokines levels of BAFF, APRIL, FLT-3L, LT-α, IL-21, TNF-α were evaluated using standard ELISA assays. Level of antinuclear antibodies (IF;HEp-2000) was measured; presence of anti-SS-A and anti-SS-B antibodies was determined by semi-quantitative immunoblotting evaluation. Biopsy of minor salivary gland with the histopathological evaluation (focus score-FS) and the immunochemistry (CD3 +, CD4 +, CD19 +, CD21 +, CD35 + cells) was performed. Statistics: differences between groups were analyzed using U Mann-Whitney test (continuous variables). Correlations between quantative variables were assessed with the Spearman correlation coefficient. Statistical significance $p<0.05$. The study was approved by the ethics committee.

Results: The negative correlation (rho = -0.472) between TGF-β and TNF-α was demonstrated. There was no correlation between TGF-β and other tested cytokines or autoantibodies (ANA, anti -SS-A, anti-SS-B). There was no correlation between TGF-β and results of ocular examinations, FS and immunochemistry. There was no correlation between TGF-β and lung involvement, especially fibrosis, in this group.

Conclusion: i) results may indicate that TGF-β, influences the serum TNF-α activity in pSS patients, ii) our findings suggest, that TGF-β may

be the strongest inhibitor of TNF-α among cytokines involved in pSS pathogenesis, iii) results may explain the ineffectiveness of anti-TNF drugs in the treatment of pSS

REFERENCES:

[1] Fechtner S, et al. Transforming growth factor β activated kinase 1: a potential therapeutic target for rheumatic diseases. Rheumatology (Oxford). 2016;56(7):1060-1068.
[2] Zhou J, et al. Pathogenic role of endogenous TNF-α in the development of Sjögren's-like sialadenitis and secretory dysfunction in non-obese diabetic mice. Lab Invest. 2017;97(4):458-467.
[3] Keystone EC. The utility of tumour necrosis factor blockade in orphan diseases. Ann Rheum Dis. 2004;63 Suppl 2(Suppl 2):ii79-ii83.

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THU0272 FUNCTIONAL GASTROINTESTINAL DISORDERS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multisystemic involvement. Gastrointestinal (GI) manifestations are frequent in patients with SLE, but functional gastrointestinal disorders (FGIDs), a heterogeneous group of GI diseases have hardly been evaluated in SLE patients.
Objectives: We evaluated the prevalence of FGIDs in SLE patients compared with age-matched controls and the role of potential risk factors for FGIDs.
Methods: SLE patients who met the ACR classification criteria for SLE and age-matched controls completed the Rome III questionnaire to assess the prevalence of FGIDs. Exclusion criteria were organic gastrointestinal disorders. Patients completed a structured interview to assess sociodemographic, clinical and treatment variables. Logistic multivariate analysis was performed to determine potential clinical factors (alcohol ingestion and medications) for FGIDS.
Results: The study responders included 116 SLE patients and 122 controls. The prevalence of FGIDs was higher in SLE patients than in controls (74.1% vs. 54.1%; p= 0.01). The most frequent FGIDs were nausea and vomiting disorders, belching disorders and globus pharyngeus. Anorectal disorders, mainly anorectal pain, were more frequent in SLE patients than controls (14.7% vs. 5.7%). After adjusting for confounding variables, SLE was associated with globus pharyngeus (OR: 3.5, 95%CI: 1.3-9.3), functional heartburn (OR: 2.5, 95% CI: 1.5-4.4), nausea and vomiting disorders (OR 7.1, 95% CI 2.7-19.1) and anorectal disorders (OR: 3.4, 95% CI 1.4-8.4). Overlap symptoms were present in 69.8% of patients vs. 31.8% of controls. When only SLE patients were evaluated, glucocorticoid therapy and non-steroidal anti-inflammatory drugs (NSAIDs) were associated with any FGID and functional bowel disorders, while alcohol ingestion was associated with gallbladder and sphincter of Oddi disorders.
Conclusion: There is a higher prevalence of FGIDs in patients with SLE and a wider distribution of various GI tract symptoms compared with controls. Medication that may alter gastrointestinal homeostasis, such as NSAIDs and protein pump inhibitors, were associated with FGIDs in SLE patients.
Disclosure of Interests: None declared
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THU0273 EVALUATION OF RELAPSE RATE AND LIFE PROGNOSIS AFTER INDUCTION THERAPY IN PROLIFERATIVE AND MEMBRANOUS LUPUS NEPHRITIS

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Background: The most common cause of morbidity and mortality in systemic lupus erythematosus (SLE) is lupus nephritis (LN). Renal flares are disadvantageous to the renal function of patients with severe LN, and the flares contribute to morbidity in patients with SLE. The reported incidence of renal flares has varied with the populations studied, the distribution of histological classes of LN, the treatment administered and the definitions of renal flare.
Objectives: Here we evaluated the relapse rate and life prognosis after induction therapy in proliferative and membranous LN.
Methods: We retrospectively analyzed the cases of 151 patients who underwent renal biopsy at our hospital and community hospitals from 1993 to 2016. We determined the complete response (CR) rate at 6 and 12 months after induction therapy and evaluated the predictive factors for CR, relapse rate, and life prognosis in proliferative and membranous LN.
Results: We were able to examine the therapeutic response, relapse rate and life prognosis at 6 and 12 months after therapy was introduced in 140 cases. Most of the patients were female (84.3%). The median age at LN onset was 34.0 years (interquartile range [IQR] 25.3–45.0 years), and the disease duration of SLE was 42 months (IQR 2.0–121.0 months). The median follow-up duration after renal biopsy was 96 months (IQR 44.0–168.0 months). The renal pathology of 99 (70.7%) patients was classified as ISN/RPS Class III or IV, and 41 (29.3%) patients were ISN/RPS Class V. Thirty-five patients (35.4%) were Class III or IV, and 17 patients (41.5%) in Class V achieved a CR at 6 months. Fifty patients (50.5%) in Class III/IV and 22 patients (53.7%) in Class V achieved a CR at 12 months. A multivariate analysis showed that a lower index of chronicity as assessed by the NIH histological scoring system in Class III/IV, and neutrophil infiltration and CH50 in Class V were predictive factors for achieving a CR at 12 months. A Kaplan-Meier analysis showed that the relapse rate and life prognosis were not different between proliferative and membranous LN.
Conclusion: Our results suggest that the predictive factors for a CR at 12 months after induction therapy are a lower index of chronicity in class III/IV and neutrophil infiltration and CH50 in Class V. In general, proliferative LN is more immunologically active than membranous LN, but we observed no significant differences in the achievement of a CR at 6 or 12 months after induction therapy, the relapse-free period, of life prognosis between proliferative and membranous LN. The therapeutic response and life prognosis of membranous LN as well as proliferative LN should be monitored closely.

REFERENCES:

[1] Ichinose K, et al. Factors predictive of long-term mortality in lupus nephritis: A multicenter retrospective study of a Japanese cohort. Lupus. 2019 *in press*
[2] Ichinose K, Okamoto M, et al. Complete renal response at 12 months after induction therapy is associated with the renal relapse-free rate in lupus nephritis a single center retrospective cohort study. Lupus. 2019 *in press*

Disclosure of Interests: Momoko Okamoto: None declared, Kunihiro Ichinose: None declared, Mineaki Kitamura: None declared, Shuntaro Sato: None declared, Keita Fujikawa: None declared, Yoshiro Horai: None declared, Naoki Matsuoka: None declared, Masahiko Tsuboi: None declared, Fumiaki Nonaka: None declared, Yukitaka Ueki: None declared, Toshimasa Shimizu: None declared, Tomohiro Koga: None declared, Shin-ya Kawashiri: None declared, Naoki Iwamoto: None declared, Mami Tamai: None declared, Hideki Nakamura: None declared, Tomoki Origuchi:

None declared, Tomoya Nishino: None declared, Atsushi Kawakami Grant/ research support from: Astellas Pharma, Consultant for: Astellas Pharma, Speakers bureau: Astellas Pharma
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THU0274 QUALITATIVE AND QUANTITATIVE ANALYSIS OF THE INMUNOLOGIC CHARACTERISTICS OF THE MINOR SALIVARY GLAND BIOPSY IN SJÖGREN'S SYNDROME

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Background: Minor salivary gland biopsy (MSGB) is the most important diagnostic test of Sjögren's Syndrome (SS). It demonstrates the presence of the inflammatory infiltration in the most affected site. It's possible role as a biomarker in the disease is still unknown. The Inmunology Department of our center conducts a detailed analysis of the MSGB about the leukocyte infiltration and quantifies number of each cell.
Objectives: To describe the inmunologic features of the MSGB and carry out an association analysis with clinical variables
Methods: Clinical variables, ESSDAI index at the moment of diagnosis and laboratory parameters were recorded. As from the MSGB, number of infiltration focus (1, 2 or several), big infiltrations (>100 cells), number of B and T cells, CD4/CD8 ratio and presence of isolated lymphocyte were collected. Categorical variables were described as frequencies and analysed using Fisher exact test. T student and Wilcoxon Rank Sum Test were used for comparison of means (μ).
Results: In 2017, a total of 104 MSGB were carried out in our center. Among them 58 were diagnosed as SS by medical and ACR/EULAR 2016 criteria. Finally 41 patients with SS and abnormal MSGB result were included for this study.

Basal characteristics of patients	Frequency (number/percentage)
Men	8/19,5%
Extraglandular disease	18/43,9%
ESSDAI≥2	17/41,46%
Other autoinmune diseases	2/4,87%
Ac. Ro/La	0/0
CRP	13/31,71% (μ 9,79mg/dL)
ANA pattern	8/19,51%
Negative	1/2,44%
Homogenous	16/39,02%
Speckled	10/24,39%
Speckled and Homogeneous	6/14,64%
Other	

Biopsy: Patients with active disease (ESSDAI≥2) had greater amount of cells (μ 159 cells vs 509 cells; p=0,055) as well as those with extraglandular disease (μ 160 vs 488; p=0.08). Patients with active disease also had larger number of infiltration focus (p= 0.062). The presence of isolated CD8+ T cells was observed in 13 patients and they had lesser cells (μ 136 vs 381; p=0.35). In those samples with predominance of T cells over B cells had larger number of infiltrate focus (7/20; 35% vs 12/21; 57.14%; p=0.155). No association with disease activity or extraglandular manifestation was found.
Extraglandular manifestation and disease activity: 18 patients had extraglandular disease. Moderate or severe ESSDAI activity was found in 14 of these patients (34.2%, p=0.00). The biopsy of patients with extraglandular disease had larger amount of cells (μ 200 vs 145; p=0.01). Patients with active disease had more infiltratre focus (6/22 vs 11/19; p=0.047). Disease evolution time was similar with a mean duration of 8-9 years in both groups.
Corticosteroids: There were 3 patients with active steroid treatment (≥prednisone 10mg/d) at the moment of the biopsy. All 3 of them had >1 focus in the sample and 2 of them had large infiltrate with >150 cells. Eight of them had received steroids in the last 5 years, 6 of them had large infiltate with >150 cells and 4 had >1 infiltrate focus in the biopsy. A study with more sample should be carried out to study the influence of steroids in the biopsy results.
Conclusion:

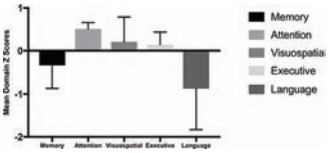
- Patients with extraglandular disease have larger amount of cells in the composition of infiltration. Those with more disease activity had more number of infiltration focus.
- In 14 patients specific antibodies and antinuclear antibodies were negative. In these patients the biopsy is the most useful diagnostic test.
- Possible association of those variables that were statistically not signifcant should not be ruled out due to the small sample size of the study.

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THU0275 NEW PROSPECTIVE OF COGNITIVE IMPAIRMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A PRAGMATIC LANGUAGE EVALUATION

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Background: Cognitive impairment (CI) in Systemic Lupus Erythematosus (SLE) is a frequent neuropsychiatric manifestation affecting several domains, even in apparently asymptomatic patients. Current research revealed that the typical CI pattern affects frontal-subcortical circuit and thus executive functions. The impairment of non-literal language or Pragmatic Language (PL), including metaphors, idioms, inferences or irony has been well described in several conditions such as autism disorders, Parkinson's disease, brain injury and even in earlier phases of neurodegenerative processes. Even if PL neuro-anatomy remains controversial, correlation between executive dysfunctions and non-literal language involvement has been reported both in traumatic injury and mild cognitive impairment patients. Nonetheless, no specific study has been performed to evaluate PL impairment in SLE patients so far.
Objectives: We aimed at assessing the PL domain in a monocentric SLE cohort in comparison to healthy controls, matched to age and education, through a specific battery, BLED [1]. Secondly, we focused attention on possible correlations between CI and clinical and laboratory SLE-related features.
Methods: Forty adult patients affected by SLE, according to the ACR criteria, and thirty healthy subjects were enrolled consecutively in this cross-sectional study. The protocol included complete physical examination, extensive clinical and laboratory data collection (comprehensive of demographics, past medical history, co-morbidities, disease activity, chronic damage evaluation, previous and concomitant treatments) and cognitive assessment for five different domains: memory, attention, pragmatic language, executive and visuospatial functions. Self-reported scale for anxiety and depression were performed to exclude the influence of mood disorders on cognitive dysfunction.
Results: We enrolled forty Caucasian SLE patients (M/F 3/37; mean±SD age 45.9±10.1 years, mean±SD disease duration 120.8±81.2 months) and thirty healthy subjects (M/F 9/21; mean±SD age 41.3±13 years). According to the low level of disease activity and damage (mean±SD SLEDAI-2K of 1.3±2.3, mean±SD SDI of 0.2±0.5), only 30% of patients was on glucocorticoid treatment at the study entry. PL was the most compromised domain in terms of Mean Domain Z scores (Fig. 1). As regards the Domain Cognitive Dysfunction score, a deficit of PL was observed in 45% of patients and resulted significantly more prevalent than memory, executive and visuospatial functions impairment (P=0.0002, P=0.0002 and P<0.000001, respectively). According to Global Cognitive Dysfunction score 25% of patients experienced a mild impairment and 7.5% a moderate one. Anti-phospholipid antibodies positivity was significantly associated with memory impairment (P<0.0005), whereas the presence of other neuropsychiatric events was associated with executive dysfunctions (P<0.05); neither further significant association nor correlation were identified.



Abstract THU0275 – Figure 1. Distribution of neurocognitive impairment expressed in Mean Domain Z score.

Conclusion: We evaluated for the first time PL in a single center SLE cohort finding a dysfunction in almost half of patients enrolled, significantly more frequent than the other assessed domains.

REFERENCE:

[1] Rinaldi C, Marangolo P, Lauriola M. "BLED Santa Lucia: Batteria sul Linguaggio dell'Emisfero Destro Santa Lucia" Giunti O.S., 2006.

Disclosure of Interests: Carmelo Pirone: None declared, Fulvia Ceccarelli: None declared, Concetta Mina: None declared, Alfredo Mascolo: None declared, Carlo Perricone Speakers bureau: BMS; Lilly, Celgene, Sanofi, Barbara Mazzotta: None declared, Laura Massaro: None declared, francesca spinelli: None declared, cristiano alessandri: None declared, Guido Valesini: None declared, fabrizio conti: None declared

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THU0276 CHARACTERISTICS OF NEUROLOGIC INVOLVEMENT AND ITS RELATED FACTORS IN PRIMARY SJÖGREN SYNDROME

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Background: Neurological manifestations seem common in primary Sjögren's syndrome (pSS) but their reported prevalences vary in Chinese. And few studies reveal if the disease activity is associated with neurological involvement.

Objectives: To analyze the clinical neurological manifestations of primary Sjögren syndrome(pSS), and to evaluate the relationship with disease activity.

Methods: 112 patients(7 male, 105 female) who fulfilled the 2002 American-European Consensus Group criteria for pSS were enrolled in the study. For each patient, the clinical features were evaluated by medical data including clinical, laboratory and immunologic data, and neurological examinations including electromyography, magnetic resonance imaging, cerebrospinal fluid, and electroencephalogram. Statistical methods used were t-test, chi-square test and Logistic regression.

Results: Data at inclusion were available for 112 patients, whose mean age was 55±10 years. Neurological involvement was noted in 19.6(22/112) patients, including 17(15.2%) with peripheral nervous system(PNS) manifestations, 3(2.8%) with central nervous system (CNS) manifestations and 2(1.8%) with both PNS and CNS involvements. Optic neuritis and trigeminal neuralgia were revealed frequently in cranial neuropathy. Anti-aquaporin 4 antibody was detected in two patients with optic neuritis. The clinical spectrum of peripheral neuropathies encountered in Sjögren's syndrome patients was wide with sensory neuropathies being the most common. Tibial nerve, peroneal nerve and sural nerve were the most likely involved and lower limb involvement accounted for 68.4%(13/19). The frequency of Raynaud's phenomenon was significantly higher[31.8%(7/22) vs 4.4%(4/90), P<0.01] as well as acroanesthesia(72.7% vs 8.9%, P<0.01) in pSS with neurological involvement than in pSS without neuropathy. The median values of EULAR Sjögren's syndrome disease activity index(ESSDAI) were 5.6(range 2.6-7.6) and 3.2(range 1.4-5.2) in the NS and non-NS groups respectively(P<0.01). We found a significant rise of neuropathy risk associated with Raynaud's phenomenon(relative risk 9.365, 95%CI 3.191 40.093,P=0.003) and ESSDAI(relative risk 1.628, 95%CI 1.169 1.969, P=0.001). Elevated liters of rheumatoid factor(P<0.05) and ANA(P<0.01) were common in patients with neuropathy.

Conclusion: Neuropathy is not a rare manifestation of pSS. Prevalence of neurological involvement in pSS is 19.6%. Raynauds phenomenon and high disease activity may be the risk factors for neuropathy. Autoantibodies might contribute to the injury of the nervous system.

REFERENCES:

[1] Jamilloux Y, Magy L, Hurtevent JF, et al. Immunological profiles determine neurological involvement in Sjögren's syndrome. Eur J Intern Med 2014;25:177–81.
[2] Ramos-Casals M, Brito-Zeron P, Solans R, et al. Systemic involvement in primary Sjögren's syndrome evaluated by the EULAR-SS disease activity index. Rheumatology (Oxford) 2014;53:321–31.
[3] Teixeira F, Moreira I, Silva AM, et al. Neurological involvement in Primary Sjögren Syndrome. Acta Reumatol Port. 2013 Jan-Mar;38(1):29-36.

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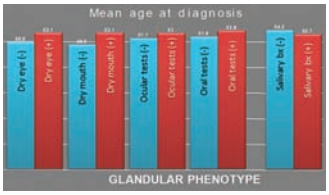
THU0277 HOW THE AGE AT DIAGNOSIS MODIFIES THE PHENOTYPE OF PRIMARY SJÖGREN SYNDROME: ANALYSIS IN 11,420 PATIENTS (BIG DATA SJÖGREN PROJECT)

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Objectives: To analyse how the age at diagnosis modifies the phenotype of primary Sjögren syndrome (SS)

Methods: The Big Data Sjögren Project was formed in 2014 to take a "high-definition" picture of the main features of primary SS at diagnosis by merging international SS databases. By January 2019, the database included 11,420 patients from 24 countries of the 5 continents.

Results: Women (52.7 vs 54.6 yrs in men, p<0.001) and non-White patients (49.6 vs 53.5 yrs in Whites, p<0.001) were diagnosed at a younger age. Patients without sicca symptoms, with normal oral/ocular diagnostic tests and with positive biopsy were also diagnosed at younger ages (p<0.001 all comparisons).

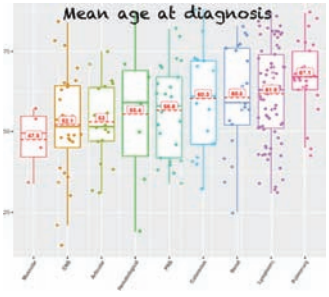


Abstract THU0277 – Figure 1



Abstract THU0277 – Figure 2

Patients with positive immunological markers had a younger diagnostic age, except for cryoglobulins (p<0.001 all comparisons).
Patients without systemic activity (ESSDAI score = 0) were diagnosed at an older age (55.5 vs 52.1 yrs in those with systemic activity, p<0.001). There was a wide variation in the age at diagnosis of patients presenting with systemic activity according to the organ involved.
Conclusion: Age at diagnosis plays a key role in the glandular and systemic phenotype expressed by primary SjS patients at the time of diagnosis.



Abstract THU0277 – Figure 3

Disclosure of Interests: Soledad Retamozo: None declared, Nihan Acar-Denizli: None declared, Wan Fai Ng: None declared, Ildiko Fanny Horváth: None declared, Astrid Rasmussen: None declared, Raphaèle Seror Grant/research support from: Pfizer, Consultant for: Bristol-Myers Squibb, Pfizer, Amgen, Eli Lilly, Roche, Celgene, GlaxoSmithKline, MedImmune, Xiaomei Li: None declared, Chiara Baldini: None declared, Jacques-Eric Gottenberg Grant/research support from: Bristol-Myers Squibb, Grant/research support from: Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Lilly, Pfizer, Sanofi-Genzyme, UCB Pharma, Consultant for: Bristol-Myers Squibb, Eli Lilly, UCB, Sanofi-Genzyme, Pfizer, Pulukool Sandhya: None declared, Luca Quartuccio: None declared, Roberta Priori: None declared, Gabriela Hernandez-Molina: None declared, Berkan Armagan: None declared, Aike A. Kruize: None declared, Seung-Ki Kwok: None declared, Marika Kvarnstrom: None declared, Sonja Praprotnik: None declared, Damien Sene: None declared, Elena Bartoloni Bocci: None declared, Roser Solans-Laqué: None declared, Maureen Rischmueller Consultant for: Abbvie, Bristol-Meyer-Squibb, Celgene, Glaxo Smith Kline, Hospira, Janssen Cilag, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Thomas Mandl: None declared, Yasunori Suzuki: None declared, David Isenberg: None declared, Valeria Valim: None declared, Agata Sebastian: None declared, Gunnel Nordmark: None declared, Hendrika Bootsma: None declared, Hideki Nakamura: None declared, Roberto Giacomelli Grant/research support from: Pfizer, Actelion, Speakers bureau: Actelion, Bristol-Myers Squibb, Merck Sharp & Dohme, Abbvie, Pfizer, Sobi, Roche, Valerie Devauchelle-Pensec Grant/research support from: Roche-Chugai, Speakers bureau: MSD, BMS, UCB, Roche, Benedikt Hofauer Consultant for: Consultant for Galvani Bioelectronics for the area of sleep disorders., Michele Bombardieri Grant/research support from: Celgene, Consultant for: Medimmune, Virginia Fernandes Moça Trevisani: None declared, Daniel Hammenfors: None declared, Sandra Pasoto: None declared, Tamer A Gheita: None declared, Fabiola Atzeni: None declared, Jacques Morel: None declared, Cristina Vollenveider: None declared, Sandra Consani-Fernández: None declared, Xavier Mariette Grant/research support from: Servier, Consultant for: AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Pfizer, UCB Pharma, Manuel Ramos-Casals: None declared, Pilar Brito-Zerón: None declared
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THU0278 ADVERSE PREGNANCY OUTCOMES (APOS) AFTER MULTI-PROFESSIONAL FOLLOW-UP IN WOMEN AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS (SLE). REPORT FROM A SINGLE CENTER IN SOUTHERN SWEDEN.

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Background: Systemic lupus erythematosus (SLE) often affects women in childbearing age. Modern management of SLE patients has improved the pregnancy outcomes over the last years. However, there is still an increased risk of maternal, fetal and neonatal complications (1).
Objectives: We report our experience in the multi-professional follow-up of pregnant women affected by SLE. Our aim was to investigate the association of potential risk factors with the occurrence of adverse pregnancy outcomes (APOs).
Methods: We selected the patients who have had one or more pregnancies, between January 2002 and January 2018, among all the SLE patients at the Department of Rheumatology, University Hospital in Lund, Sweden. Longitudinal clinical and laboratory data from rheumatology and obstetrics units, as well as from neonatal units, were collected and analyzed. We assessed the association between APOs and putative SLE-related risk factors as well as known risk factors in the selected population.
Results: We investigated the outcome of 59 pregnancies in 28 SLE patients. Eighteen (64.3%) patients had one or more APOs. Forty-four (74.6%) pregnancies terminated with a delivery, whereof 36 (61%) term pregnancies and 8 (13.6%) before 36 gestational weeks. Caesarean section terminated 13 (29.5%) pregnancies. Thirteen (22%) miscarriages and two (3.4%) intentional abortions were recorded. HELLP syndrome occurred in 1 (1.7%) and pre-eclampsia in 11 (18.6%) gestations. Among 16 cases of fetal growth restriction, 5 (8.5%) gestations resulted in intrauterine growth restriction, 1 (1.7%) in a small for gestational age baby and 10 (24.4%) in low birth weight. No cases of eclampsia, stillbirths or congenital heart disease were recorded. Neonatal lupus erythematosus occurred in 1 (1.7%) baby. APOs were associated with anti-phospholipid syndrome and/or presence of anti-phospholipid antibodies (OR 4.5 - p= 0.009). Previous renal involvement was associated with APOs (OR 5.9 - p= 0.005) and with fetal growth restriction (OR 11 - p=0.03). Active disease (SLEDAI >3) six months before or during pregnancies was associated with miscarriage (OR 13 - p=0.02). Pre-eclampsia and pre-term deliveries were not significantly associated with any of the investigated risk factors.
Conclusion: One or more APOs occurred in the majority of patients in our study and a few severe outcomes were recorded. Our experience suggests that the presumptive risk factors for APOs in SLE patients are disease related, such as high disease activity six months before or during pregnancies, previous renal involvement and anti-phospholipid syndrome/antibodies.

REFERENCE:

1 IM Jakobsen, RB Helmig & K Stengaard-Pedersen (2015) Maternal and foetal outcomes in pregnant systemic lupus erythematosus patients: an incident cohort from a stable referral population followed during 1990-2010,Scandinavian Journal of Rheumatology, 44:5, 377-384, DOI: 10.3109/03009742.2015.1013982

Disclosure of Interests: None declared
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THU0279 POLYUNSATURATED FATTY ACIDS (PUFAS) AND SPECIALIZED PRO-RESOLVING MEDIATORS (SPMS) ARE DECREASED IN PLASMA AND SERUM FROM SLE PATIENTS COMPARED TO HEALTHY CONTROLS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with persistent, inflammatory mediated organ damage. It has been suggested that omega-3-polyunsaturated fatty acids (PUFAs) are low in SLE patients and that

supplementation with omega-3 PUFAs might be beneficial. Omega-3 PUFAs can be metabolized to specialized pro-resolving mediators (SPM) in inflamed tissues. PUFAs, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), give rise to protectins and E-series and D-series resolvins, respectively. These SPMs help promote tissue repair and healing in addition to reducing neutrophil infiltration.
Objectives: To investigate (1) if SMPs can be measured in lupus patient blood and (2) whether EHA and DHA and SPMs were dysregulated in lupus patients compared to controls.
Methods: Blood samples were collected from 12 patients enrolled in the Autoimmune Disease Registry and Repository, a single center registry (1996-present) of patients meeting ACR SLE classification criteria. Samples were collected from 12 non-SLE-controls who were age (± 5 years) and race/ethnicity matched. Metabolomic profiling via tandem mass spectrometry (LC-MS-MS) was performed on serum and plasma to assess the PUFA and SPM levels.
Results: Levels of EPA and DHA were highly correlated in serum and plasma. Both EPA and DHA were significantly decreased in SLE patients compared to controls (Table 1). Neither plasma nor serum DHA or EPA levels was correlated with disease activity assessed by SLEDAI score. SPMs including PD1 and RvE1 as well as their precursors, 17-HDHA and 18-HEPE, were identified in plasma and serum samples from SLE patients. Plasma levels of 17-HDHA, as well as serum levels of PD1, 17-HDHA, and 18-HEPE tended to be reduced in SLE (Table 1). The SLE patients with a history of nephritis had significantly lower levels of DHA (p=0.03), EPA (p=0.05), 18-HEPE (p=0.03), and 17-HDHA (p=0.04) than SLE patients without nephritis.
Conclusion: SLE patients have lower levels of circulating EPA and DHA, the substrates for SPMs, relative to individuals without SLE. Lower levels of these PUFAs and some SPMs are associated with history of nephritis. Additionally, the levels of PD1, 17-HDHA, and 18-HEPE were measurable in SLE serum and plasma and tended to be reduced, especially in subjects with lupus nephritis. SPMs suppress the production of inflammatory mediators and promote resolution of inflammation. The lower levels of PUFAs and SPMs could contribute to the likelihood of developing lupus nephritis. Further evaluation of this relationship is warranted.

Abstract THU0279 – Table 1. Metabolipidomics of SLE and Control Serum

Metabolite (in serum) mean, (SD)	Control (n=12)	SLE (n=12)	P Value
EPA	6779.7 (3985.2)	2822.9 (3082.9)	0.013
DHA	19584.0 (15785.1)	7664.0 (5613.3)	0.003
PD1	55.0 (128.6)	23.3 (57.1)	0.489
17-HDHA	47.4 (25.3)	15.7 (14.9)	<0.001
18-HEPE	20.8 (7.1)	17.3 (9.8)	0.195

Metabolite (in serum) mean, (SD) Control (n=12) SLE (n=12) P Value
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THU0280 SEXUAL FUNCTION IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-CONTROL STUDY

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Background: Normal sexual function consists in the transition, during sexual activity, through the phases of excitement to relaxation without problems, and with a feeling of pleasure, satisfaction and fulfillment (1). The effect of systemic lupus erythematosus (SLE) in sexual function has been one of the least studied areas, but it is thought that some disease-related characteristics could have a negative effect. There are few previous studies that investigate sexual function in SLE, general results indicate a negative impact (2).
Objectives: The main aim of this study is to determine if there is an altered sexual function in Mexican women with SLE and compare if it occurs in a greater proportion than in healthy women.
Methods: A case-control study with 102 Mexican women between 18 and 60 years, with SLE diagnosis (according to SLICC 2012 criteria) and a control group of healthy women (n=156) matched by age. Patients were excluded if they couldn't answer the questionnaires reliably and pregnant women. They were asked about the presence of active sexual life in the last month and the Female Sexual Function Index (FSFI) self-questionnaire was applied. Variables between groups were compared with Chi-square and Mann U Whitney test.
Results: Baseline demographic characteristics between groups are shown in table 1. Women with SLE had less sexual activity, during the last month, than controls (63.7% vs 77.5%, p = 0.01). Out of the total women included, the FSFI was applied only to those that had an active sexual life, 65 with SLE and 121 healthy women. Sexual disfunction (<26.5 points) was found in 28% women with SLE and in 22% of controls, with no significant differences (p=0.4). In the SLE group, a worse total score was found, as well as alteration in the desire and excitation domains when compared to healthy women (Table 2). In the multivariate linear regression analysis (using FSFI as the variable), no relationship was found with any demographic or disease-related variables.

Abstract THU0280 – Table 1. Comparison of demographic variables between the SLE and control group.

	Control group (n=156)	SLE group (n=102)	*p**
Age, years (±SD)	33.2 (±10.8)	36.3 (±11.6)	**0.030**
Civil Status			0.977
Single, n (%)	56 (35.9)	38 (37.3)	
Married, n (%)	76 (48.7)	47 (46.1)	
Divorced, n (%)	8 (5.1)	6 (5.9)	
Domestic partnership, n (%)	16 (10.3)	11 (10.8)	
Widowed, n (%)	0 (0)	0 (0)	
Education			
< 10 Years, n (%)	91 (58.3)	58 (56.9)	0.815
Menopause, n (%)	21 (13.5)	23 (22.5)	0.058
Has children, n (%)	82 (52.6)	69 (67.6)	**0.016**

*-Mann U Whitney or Chi-Square test according to type of variable. SD – Standard Deviation.

Abstract THU0280 – Table 2. Female Sexual Function Index according to group.

Female Sexual Function Index	Control group (n=121)	SLE group (n=65)	*p**
Sexual disfunction, n (%)	27 (22)	18 (28)	0.414
Total, 2–36 points	30.5 (34.8)	29.3 (25.7)	**0.017**
Desire (1.2-6)	5.1 (6)	4.5 (4.8)	**<0.001**
Excitation (0-6)	5.2 (6)	4.8 (4.8)	**0.046**
Lubrication (0-6)	5.6 (6)	5.2 (4.8)	0.181
Orgasm (0-6)	4.2 (4.8)	4.2 (4.2)	0.254
Satisfaction (0.8-6)	5.4 (6)	5.4 (4.8)	0.409
Pain (0-6)	5.6 (6)	5.2 (4.8)	0.590

*-Mann U Whitney or Chi-square test according to type of variable.
Conclusion: Women with SLE, in this study, have less sexual activity than healthy women, but no greater sexual disfunction. However, they have a worse performance in the desire and excitation areas. This alteration did not show a relation with demographic nor disease-related variables. The abnormality found could be explained by a psychosocial factor not evaluated in this study.

REFERENCES:

[1] Tristano AG. The impact of rheumatic diseases on sexual function. Rheumatol Int. 2009. doi:10.1007/s00296-009-0850-6
[2] Daleboudt GMN, et al. The impact of illness perceptions on sexual functioning in patients with systemic lupus erythematosus. J Psychosom Res. 2013.

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THU0281 SALIVARY GLAND ULTRASOUND FINDINGS ARE ASSOCIATED WITH CLINICAL AND SEROLOGIC FEATURES IN PRIMARY SJÖGREN'S SYNDROME PATIENTS

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Background: Primary Sjögren's syndrome (pSS) is a multisystem immune-mediated disease characterized by hypofunction of salivary and lacrimal glands and possible multi-organ systemic manifestations. Over the past years, three sets of diagnostic criteria have been proposed, but none included salivary gland ultrasound (SGUS). However, SGUS has been recently applied for diagnosis and there are some reports regarding the correlation of SGUS findings with immunological and serological features in pSS patients (1, 2).
Objectives: To investigate the association of SGUS fndings with clinical and analytical features of pSS patients.
Methods: A total of 54 patients diagnosed with pSS, fulfilling both the 2016 ACR/EULAR and 2002 AECG criteria for the disease, followed-up at our Rheumatology department, underwent SGUS evaluation. The parenchymal homogeneity of bilateral parotid and submandibular glands was graded using a score of 0 (normal) to 4 (gross inhomogeneity). Patients were classified into two groups according to the highest US score obtained. The grades 1 and 2 were considered to be normal and grades 3 and 4 to represent pathological SGUS findings. Demographics (age, sex and disease duration), European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI) and laboratorial data (erythrocyte sedimentation rate, autoantibodies, rheumatoid factor, hypergammaglobulinemia, β2-microglobulin and complement levels) were collected and compared between the two SGUS groups. The association between SGUS and these data was explored by multivariable analysis. Statistical significance was defined as $p < 0.05$.
Results: The mean age of patients was 57.5±13.3 years and median disease duration was 5.0 [IQR (2.75-11.25)]. The majority of the study population were women (96%) and 35% (19/54) had pathological SGUS findings.
Differences between the group with pathological SGUS *versus* the group with normal SGUS are depicted in table 1.
Multivariate logistic regression revealed that anti-SSB ([OR] = 6.6, 95% [CI] 1.7 to 25.8, p = 0.006) was independently associated with the presence of pathological features in SGUS.

Table 1. Comparison of demographics, clinical and serologic features of pSS according to SGUS.

	Pathological SGUS (n=19)	Normal SGUS (n=35)	P value
Mean age, years	54.3±12.6	59.2±13.5	0.497
Mean disease duration, years	6.6±6.1	7.7±5.2	0.976
ESSDAI (IQR)	2.2 (0-5)	0.9 (0-1)	**0.044**
Mean Sedimentation rate, mm	36.3±22.1	22.7±15.8	0.160
Antinuclear antibody, n (%)	19 (100)	32 (91.4)	0.544
Anti-SSA, n (%)	18 (94.7)	27 (77.1)	0.137
Anti-SSB, n (%)	14 (73.7)	9 (25.7)	**0.001**
Rheumatoid factor, n (%)	14 (73.7)	14 (40.0)	**0.018**
Hypergammaglobulinemia, n (%)	12 (63.2)	14 (40)	0.104
Mean β2-microglobulin, mg/L	2.9±0.9	2.2±0.7	0.378
Mean Complement 3, mg/dL	115.1±28.9	120.7±24.5	0.938
Mean Complement 4, mg/dL	21.6±6.0	21.9±8.1	0.165
Hydroxychloroquine treatment, n (%)	15 (78.9)	21 (60.0)	0.229

Conclusion: In our study, pathological US findings were associated with higher disease activity and positivity for rheumatoid factor and anti-SSB. Additionally, anti-SSB antibody was strongly and independently associated with pathological US findings in the salivary gland of pSS patients.
Further and larger studies are necessary to support these findings and include SGUS as part of the diagnostic criteria for Sjögren's syndrome.

REFERENCES:

[1] J-W Kim, et al. Salivary gland ultrasonography findings are associated with clinical, histological, and serologic features of Sjögren's syndrome. Scand J Rheumatol 2018;00:1–8.
[2] J. Nieto-González *et al.* Salivary gland ultrasound is linked to the autoimmunity profile in patients with primary Sjögren's syndrome. Journal of International Medical Research 2018; 0(0) 1–11.

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THU0282 ULTRASOUND FINDINGS IN THE SALIVARY GLANDS IN A COHORT OF PATIENTS WITH SUSPECTED SJÖGREN'S SYNDROME

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Background: Ultrasound has been shown to be a promising tool in the evaluation of salivary glands for parenchyma changes with the potential to improve diagnosis. The changes range from mild inhomogeneity of the glandular tissue to large vesicular changes almost eliminating all normal glandular tissue. American-European Consensus Group (AECG) classification criteria for SS are often used diagnostically (1).
Objectives: To describe ultrasound findings in salivary glands (SGUS) in a cohort of patients with suspected Sjögren's syndrome (SS) and assess their positive and negative predictive value for the diagnosis.
Methods: 191 consecutive patients with suspected SS (ocular and/or oral dryness) referred to the department of Rheumatology between March 2017 and March 2018 were evaluated by SGUS as part of the initial evaluation. All had unstimulated sialometry, Schirmer's test and laboratory test done (including autoantibodies (ANA screening, Rheumatoid factor and anti-cyclic citrullinated peptide, anti-Ro/SSA and anti-La/SSB), and screenings test for hepatitis B+C). In doubtful cases, a minor salivary gland (MSG) biopsy was performed. SGUS was performed with a GE Logiq E9 equipped with a linear ML6-15 probe and included grey-scale evaluation of the submandibular and parotid gland bilaterally. SGUS was considered abnormal when moderate to severe inhomogeneity with anechoic or hypoechoic areas was present in at least one gland.
Results: 63 patients were diagnosed with SS according to the AECG classification criteria - 57 patients with primary SS, 6 with secondary SS. 128 patients with sicca symptoms did not fulfill AECG criteria for SS and none were diagnosed with SS based on other parameters. Demographic data for the cohort is shown in table 1. 55 patients had MSG biopsy performed. The SGUS examination and evaluation was performed in less than 15 min per patient. The sensitivity of SGUS is 0.51 and the specificity 0.88; the PPV of SGUS for the SS diagnosis was 0.68 and the NPV was 0.78
The sensitivity of SGUS for positive MSG biopsy was 0.29 and the specificity 0.82 – the PPV was 0.50 and the NPV was 0.65; for abnormal sialometry the sensitivity of SGUS was 0.32 and the specificity 0.82 - the PPV for SGUS was 0.64 and NPV was 0.55.
Table 2 shows the association between SGUS and final diagnosis, MSG biopsy and sialometry, respectively.

Abstract THU0282 –Table 1.

Table 1	Primary SS	Secondary SS	Not fulfilling SS classification criteria
Female/male, n	55/5	6/0	101/27
Mean age, years (range)	56 (27-83)	56 (42-68)	56 (17-86)
Positive Shirmers test, n(%)	26(46%)	2(33%)	6 (5%)
Positive Sialometry, n(%)	44(77%)	6 (100%)	45(35%)
Anti-RO/SSA, n(%)	48(84%)	1 (17%)	37(29%)
Anti-La/SSB, n(%)	18(32%)	0 (0%)	6(5%)

n= number, SS= Sjögren's Syndrome

Table 2	Fulfilling SS classification criteria n (%)	Not fulfilling SS classification criteria n (%)	Positive MSG biopsy	Negative MSG biopsy	Positive sialometry for SS	Negative sialometry for SS
Positive SGUS for SS n (%)	32 (51%)	15 (12%)	6 (29%)	6 (18%)	30 (32%)	17(18%)
Negative SGUS for SS n (%)	31 (49%)	113 (88%)	15 (71%)	28 (82%)	64 (68%)	80 (82%)

n= number, SS= Sjögren's Syndrome, MSG=minor salivary gland

Conclusion: SGUS has a high specificity but poor sensitivity for the SS diagnosis with a good NPV and a high specificity for positive MSG

biopsy and positive sialometry. SGUS is a feasible method for the evaluation of structural changes in the salivary gland and may aid in the diagnosis and classification of SS.

REFERENCE:

[1] Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, et al. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis. 2002;61:554–8.

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THU0283 PATIENT ACCEPTABLE SYMPTOMS STATE (PASS) QUESTIONNAIRE APPLICATION IN THE COHORT OF SLE PATIENTS FROM THE SPANISH SOCIETY OF RHEUMATOLOGY (RELESSER): ASSOCIATION WITH ACTIVITY INDEX

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Background: Little is known about the patient related outcomes and disease activity in systemic lupus erythematosus. Damage and impact are issues that have not been associated with activity in lupus previously.

Objectives: In a large cohort of systemic lupus erythematosus (SLE) patients, to evaluate the association between a Patient Acceptable Symptom State (PASS) and three different domains of the disease: activity, damage and impact of SLE on patients' lives

Methods: Cross-sectional study of 1,364 SLE (ACR 97 Criteria) patients from the Spanish Society of Rheumatology Lupus Registry (RELESSER). Patients were clinically assessed by the physicians, who collected data about demographics, clinical manifestations, laboratory features and therapies. SLE activity was assessed by using the SLEDAI (SLE Disease Activity Index). The Systemic Lupus International Collaborating Clinics/ American College of Rheumatology Damage Index (SLICC/ACR DI) was used to measure damage accrual. The impact of SLE on patients' lives was evaluated by using the Lupus Impact Tracker (LIT). The PASS question "Considering all the different ways your disease is affecting you, if you would stay in this state for the next months, do you consider that your current state is satisfactory?" was answered in a dichotomized way: yes/no. Measures of central tendency and spread were used to describe responses and T-test was used to evaluate the independence between PASS and the other questionnaires and indices.

Results: Mean age (years) ± S.D. of the 1,364 patients included in the study was 49.9 ± 13.3; 90.3% were female and 94.9% were Caucasian. In the total of patients, 979 (71.8%) were in PASS. Patients in PASS had significantly lower activity (SLEDAI Score) than those not in PASS (2.4 ± 3.2 *vs.* 3.0 ± 3.9, respectively; p=0.007). The SLICC/ACR DI was significantly lower in the group of patients in PASS compared to those without PASS (0.64 ± 1.1 *vs.* 0.81 ± 0.21, respectively; p=0.022). SLE had a significantly lower impact on patients in PASS in comparison to those without PASS (LIT Score: 8.47 ± 7.5 *vs.* 19.8 ± 8.34, respectively; p=0.001).

Conclusion: In the largest observational European Registry of SLE patients, PASS was associated with other domains of the disease: activity, damage and impact on patients' life. PASS is a simple and reliable patient-reported outcome that can be a useful tool to evaluate patients' well-being.

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THU0284 WHAT DO HEMATOLOGICAL ABNORMALITIES TELL US IN SLE? RESULTS FROM TWO INDEPENDENT MULTICENTER EUROPEAN SLE COHORTS

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Background: Detailed analysis of hematological manifestations are limited and their clinical impact on disease remain obscure.

Objectives: To scrutinize factors associated with different hematological abnormalities (HA) in SLE patients and their impact on infections, bleeding and damage accrual.

Methods: A dataset (GIPTSLE) originated from SLE patients in Europe was studied. The dataset consisted of six monthly visits of each patients for at least 2 years. Results were compared with another well-established SLE cohort from Sweden (Swedish SLE network). Patients in both cohorts fulfilled the ACR1982 SLE criteria. Variables collected at each visit included CBC, presence or absence of haemolytic anemia, all domains of SLEDAI-2K, medications, infection or bleeding episodes, Systemic Lupus International Collaborating Clinics/ACR damage index (SDI). HA occurred at the beginning or during follow-up were defined according to the ACR criteria. HA was only considered in patients with no prior use of immunsuppressives or biologic agents at least 3 months before the first HA events. The Swedish confirmation cohort included all the variables of interest. We excluded all haematological domains from SLEDAI-2K (aSLEDAI) for the analysis. Based on six monthly change in SDI, each visit was labelled either "damage transition"or "non-damage transition". Generalized estimating equations (GEE), multiple logistic regression, Chi-square test and independent samples t test were used where it was appropriate.

Results: Of the 1430 visits of 286 patients analysed from the first cohort (89.5% female, 95.8% Caucasian, 64.7% dsDNA positive) 60% had at least one HA. At the enrolment, the median (range) disease duration was 8 yrs (0-38), aSLEDAI-2K was 6 (0-25) and SDI was 0(0-6). Upon GEE analysis, lymphopenia was significant for SDI (OR=2.5, 1.0-5.9).Upon GEE analysis after further adjusting prednisolone exposure, HA found be significant for SDI was thrombocytopenia (OR=3.6, 1.04-12.1) but no significant evidence for the dependence of this relationship on time. The effect of lymphopenia was attenuated. HR for bleeding was significant when platelets were below 50K (HR=2.6, 1.15-6.1) Of the 1395 patients analysed from the second set (86.8%female, 93.0% Caucasian, 61.6 dsDNA positive), 63.4% had HA. At the last visit, the median (range) disease duration was 14yrs (1-65) and SDI was 1(0-14). Upon multiple regression analysis after adjusting age, sex and prednisolone exposure both thrombocytopenia (OR=2.2, 1.3-3.6) and lymphopenia (OR=1.8, 1.2-

2.6) had significant effect on SDI. HA at the time of diagnosis or occurring at any time during disease course did not contribute to mortality.
Conclusion: Lymhopenia contributes independently damage accrual in European background. Lymphopenia and thrombocytopenia at early disease appear to be independent risk factors for subsequent damage.

REFERENCES:
[1] Seminar in Arthritis and Rheumatism 45(2016):675-83

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THU0285 UMBILICAL ARTERIAL DOPPLER ULTRASONOGRAPHY PREDICTS LATE PREGNANCY OUTCOMES IN PATIENTS WITH LUPUS NEPHRITIS: A MULTICENTER STUDY FROM SOUTHERN CHINA

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Background: Compared with the general population, patients with lupus nephritis (LN) are still at high risk of adverse pregnancy outcomes (APOs). Umbilical artery is the last vessel upstream of the placenta and is particularly important for placental perfusion and foetal development. Increased umbilical artery resistance could be traced by Doppler velocimetry, which is frequently related to pre-eclampsia, intrauterine growth restriction (IUGR), and foetal distress. Umbilical artery Doppler is used as a screening tool for placenta-related diseases in the general population. However, the predictive value in complications of LN pregnancies has not been widely assessed.
Objectives: To investigate the fetal adverse pregnancy outcomes (APOs) and the predictive value of umbilical arterial Doppler ultrasonography in the third trimester in pregnant women with LN.
Methods: A retrospective cohort study enrolling 203 LN patients with pregnancies from 2007 to 2017 from three centers was performed. These patients received umbilical arterial Doppler ultrasound examination during 28-34 gestational weeks. Doppler velocity waveforms of the umbilical arteries were assessed with resistance index (RI), systolic/diastolic ratio (S/D) and pulsatility index (PI).
Results: Fetal APOs occurred in over half of the patients (103/203, 50.7%). Sixty-six pregnancies (66/203, 32.5%) ended with preterm births. The incidence rate of IUGR was 18.2% (37/203). Fetal distress was noted in 23 pregnancies (23/203, 11.3%). All the Doppler parameters were higher in patients with IUGR, fetal distress and composite APOs than in patients without any APOs. Patients with IUGR and fetal distress had significantly higher values of PI, RI, and S/D. It was noted that PI, RI and S/D was higher in patients with premature delivery than those with full-term delivery. However, only the difference of RI and S/D reached statistical significance. RI indicated the highest risk of IUGR and composite APOs. The cut-off values were 0.66 and 0.67, respectively. Sensitivities were 51.4% and 33.7%, and specificities were 87.4% and 92.1%. S/D was also a best predictor for IUGR, with the optimal cut-off value of 2.88. Sensitivity and specificity were comparable with RI. PI over 0.84 was an ideal indicator for fetal distress with an optimal combination of sensitivity (89.5%) and specificity (51.6%).
Conclusion: Fetal complications were frequent in patients with LN. Umbilical arterial Doppler ultrasonography was a useful measure to predict late IUGR, fetal distress, and the composite APOs.
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17. Vasculitis

THU0286 MANAGEMENT OF TAKAYASU ARTERITIS: A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2018 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF LARGE VESSEL VASCULITIS

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Background: European League Against Rheumatism (EULAR) recommendations on large vessel vasculitis (LVV) management were published in 2009.[1] However, given recent advances, especially in therapeutics, an update was needed.
Objectives: To collect available evidence on management of LVV to inform the 2018 update of the EULAR management recommendations.
Methods: Two independent systematic literature reviews (SLRs) were performed, one focused on diagnosis and monitoring and the other on drugs and surgical treatments. Using a predefined PICO strategy, Medline, Embase and Cochrane databases were accessed, and eligible papers reviewed. This abstract reports the main results for Takayasu arteritis (TAK). Results on giant cell arteritis (GCA) are presented elsewhere.
Results: A total of 283 articles were selected from the SLRs. Relevant heterogeneity precluded a meta-analysis.
The clinical pattern of TAK disease may differ according to age and gender. Males appear to have more complications than females. The presence of major complications (e.g. aneurysm formation), a progressive disease course and a weaker inflammatory response appear to relate to a more unfavorable prognosis, with survival rates as low as 43% at 15 years after diagnosis. Thus, follow up is essential, but there is no good quality evidence regarding the best timing and methods for disease monitoring.
High-quality evidence to guide the treatment of TAK was not found. Glucocorticoids (GC) are widely accepted as first line treatment. However, many patients require doses above 10 mg prednisolone per day for disease control. Conventional immunosuppressive drugs and TNF-inhibitors appeared to be beneficial in case series and open-label studies, but high-quality evidence for their use is lacking. Tocilizumab showed modest signs of efficacy in a randomized controlled clinical trial, although the primary endpoint was not achieved. Revascularization procedures (aneurysm/stenosis) may be required and should be performed during stages of inactive disease.
Conclusion: Evidence to guide monitoring and treatment of TAK patients is predominantly derived from observational studies with low level of evidence. Therefore, higher-quality studies are needed in the future.

REFERENCES:
[1] Mukhtyar C, Guillevin L, Cid MC, et al. EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis. 2009;68(3):318-323.

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THU0287 ANEURYSM IN BEHÇET'S DISEASE: MANAGEMENT, PROGNOSIS AND MORTALITY

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Background: Arterial aneurysms are one of the unique features of Behçet's disease (BD). Although arterial aneurysms are relatively rare, they carry risk of rupture and have poor prognosis.
Objectives: To evaluate the medical and interventional therapies and long-term outcomes of BD patients with extracranial arterial aneurysms.
Methods: We retrospectively reviewed the medical records of 441 BD patients according to ISG criteria between 2013 and 2018 at the Hacettepe University Vasculitis Center (HUVAC). We determined 45 BD patients with an arterial aneurysm. Six patients with isolated carotid and/or cranial arterial aneurysms who were followed by other clinics excluded from the analysis. Overall, 39 BD patients with an extracranial and extra carotidal aneurysm included in the study. Data regarding demographic characteristics, clinical, laboratory and vascular imaging findings, history of medical treatments and outcomes were collected. Vascular intervention of patients were grouped as surgery or endovascular intervention. Radiological response after vascular intervention divided into 3 groups as regression, stable and progression according to radiological evaluation. Regression was defined as a decrease or disappearance of the aneurysm. Stable was defined as no change in the aneurysm diameter. Progression was defined as an increase in diameter of a previous aneurysm or occurrence of a new vascular event. We colligated the stable and regression groups and compared with the progression group. Relapse was defined the progression of the aneurysm which underwent an intervention.
Results: A total of 39 BD patients (Male, 80%) with an arterial aneurysm were analyzed in this study. Mean age and mean age of diagnosis patients were 40.9±11.0 and 29.7±7.7 years, respectively. The clinical features of BD was as follows; oral ulcer 100%, genital ulcer 80.6%, acneiform lesion 47.2%, erythema nodosum 33.3%, pathergy positivity 34.5%, arthritis 27.8%, fever 24.3%, uveitis 34.5%, neurological involvement 30.6% and, gastrointestinal involvement 7.7%. Distribution of arterial aneurysms were 5.1% subclavian, 5.1% coronary artery & cardiac, 38.8% pulmonary, 10.3% thoracic aorta, 33.3% abdominal aorta, 5.1% renal, 25.6% iliac and 12.8% femoral. Induction and maintenance treatments are shown in figure 1. In our cohort, 25 (64%) patients needed a vascular intervention, including 9 (23%) open operations and 16 (41%) endovascular interventions. Of 7 (18%) patients had to perform an urgent open operation or endovascular intervention but we didn't find any relation between the progression of an aneurysm and urgent intervention. First induction treatment options and prognosis of arterial aneurysms shown in figure 2. At median 71.8 months follow up, 7 (18%) patient died in the BD aneurysm group. The rate of progression of the aneurysm was 20% in BD patients with pulmonary artery involvement and 64% in BD patients with aortic and its branch involvement (p=0.038). In the absence of medical induction treatment, 5 patients had progression, 1 had regression and 1 had no follow-up.

Abstract THU0287 – Table 1.

	Induction treatment, n=39 (%)	Maintenance treatment*, n=39 (%)
No treatment, n (%)	7** (17,9)	3 (7.6)
Colchicine	32 (82)	15 (38.4)
Medium-high dose steroid, n (%)	31 (79.4)	11 (28.2)
Cyclophospamide, n (%)	18 (46.1)	9 (23.0)
Interferon-α, n (%)	21 (53.8)	18 (46.1)
Azatiopurine, n (%)	5 (12.8)	11 (28.2)
TNFi, n (%)	1 (2.5)	5 (12.8)
Anticoagulant n (%)	12*** (30.7)	7 (17.9)

*Some patients have received more than one type of immunosuppressive in maintenance therapy
** These patients were followed by rheumatology department after the surgical or endovascular intervention.
*** Patients already using anticoagulants due to venous thrombosis

Abstract THU0287 – Table 2.

Figure 2. Evaluation of response according to vascular intervention and induction treatments *

	Stabile/Regression, n=18	Progression, n=18	p
Vascular intervention			
Done, n=23 (%)	10 (43.5)	13 (56.5)	0.298
Not done, n=13 (%)	8 (61.5)	5 (38.5)	
Induction treatment			
Cyc	2	1	
Cyc+IFN-α	10	5	
IFN	3	2	
Anti-TNF	0	1	0.315
Azatiopurine	2	3	
No treatment	1	5	
Only steroid	0	1	

*3 patients have no follow-up data
Cyc: Cyclophospamide, IFN: Interferon-α

Conclusion: Arterial aneurysms in BD have poor prognosis and high mortality. Glucocorticoids, cyclophosphamide and interferon-α are the most preferred treatments for induction and maintenance therapy for aneurysm of the BD. Approximately 2/3 of the patients required a vascular intervention. Clinical and radiological progression was more prominent in the aorta and its branches. As expected, there is more progression in interventional procedures without medical treatment.
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THU0288 LONG-TERM FOLLOW-UP OF ANTI-IL6-RECEPTOR TOCILIZUMAB IN REFRACTORY UVEITIS IN PATIENTS WITH BEHÇET'S DISEASE. MULTICENTER STUDY OF 14 PATIENTS IN CLINICAL PRACTICE

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Background: Ocular involvement in Behçet's disease (BD) is a potential severe and disabling complication. Anti-TNF-α agents have shown an improvement of visual outcome in BD-related uveitis refractory to conventional immunosuppressive (IS) drugs. However, these drugs do not achieve control of intraocular inflammation in all patients or are not well tolerated. Tocilizumab (TCZ) has shown efficacy in different refractory ocular inflammatory diseases.
Objectives: To assess the efficacy of long-term therapy with TCZ in refractory uveitis associated to extraocular manifestations (EOM) due to BD.
Methods: Multicenter study of patients with BD refractory to standard systemic treatment.
Results: We followed up 14 patients (9 men/5 women) (26 affected eyes); mean age 40.8±19.5 years. Pattern of ocular involvement: panuveitis (10; 4 with retinal vasculitis), anterior (3) and posterior (1) uveitis; 8 recurrent and 6 chronic; 9 with cystoid macular edema. At TCZ onset the following EOM were present: oral and/or genital ulcers (10), arthritis (6), folliculitis/pseudofolliculitis (6), erythema nodosum (3), livedo reticularis (1), intestinal affection (1) and neurological involvement (3).
Before TCZ, they had received corticosteroids (13 intraocular, 12 oral and 12 iv), conventional IS drugs and biologic agents: methotrexate (11), cyclosporine (8), azathioprine (10), colchicine (1), cyclophosphamide (2), mycophenolate mofetil (1), adalimumab (10), infliximab (6), golimumab (3), canakinumab (1), or etanercept (1). TCZ was used in monotherapy (7) or

combined with conventional IS drugs (7) at 8 mg/kg/iv/4 w (11) or 162 mg/sc/w (3).

Abstract THU0288 – Table 2.

TABLE. Evolution of ocular parameters with TCZ therapy in a long-term follow-up.

	BASAL n=26	1 WEEK n=20	2 WEEKS n=24	1 MONTH n=24	3 MONTHS n=24	6 MONTHS n=20	1 YEAR n=17	2 YEARS n=11	3 YEARS n=7	4 YEARS n=4
BCVA	0.38±0.35	0.46±0.34*	0.56±0.36*	0.58±0.38*	0.61±0.37*	0.65±0.37*	0.61±0.38*	0.61±0.33	0.63±0.29*	0.93±0.12
AC CELLS	1 [0-3]	1 [0-2]*	0 [0-1]*	0 [0-0.75]*	0 [0-0.25]*	0 [0-0]*	0 [0-1]*	0 [0-0]	0 [0-0]	0 [0-0]
VITRITIS	1 [0-2]	1 [0-2]	0 [0-1]*	0 [0-1]*	0 [0-0]*	0 [0-0]*	0 [0-0]*	0 [0-0]*	0 [0-0]	0 [0-0]
OCT	339.9±110.1	329.3±109.1*	324.6±108.5	298.7±83.5	263.4±88.4*	251.8±87.4*	232.8±45.8*	245.8±29.9	247.25±6.2	247.25±6.2

*p< 0.05

Abbreviations: AC= anterior chamber; BCVA= best corrected visual acuity; n= number of available eyes; OCT= optical coherence tomography.

After a mean follow-up of 21.7±14.5 months using TCZ, all patients experienced ocular improvement, with complete remission in 10. However, TCZ was only effective in 5 of the patients with EOM. TABLE shows the evolution of ocular parameters.

TCZ had to be withdrawn temporally in 1 case, due to an episode of cellulitis with sepsis, and definitely in 4 cases, due to a severe infusion reaction, arthritis impairment, persistence of oral ulcers or a new episode of uveitis (1 each). Prednisone dose was significantly reduced until suspension in all patients.

Conclusion: TCZ seams a useful and secure therapy in highly refractory BD-related uveitis.

REFERENCES:

[1] Atienza-Mateo B, Calvo-Río V, Beltrán E, et al. Anti-interleukin 6 receptor tocilizumab in refractory uveitis associated with Behçet's disease: multicentre retrospective study. Rheumatology (Oxford). 2018 May 1;57(5):856-864.

[2] Calvo-Río V, de la Hera D, Beltrán-Catalán E, et al. Tocilizumab in uveitis refractory to other biologic drugs: a study of 3 cases and a literature review. Clin Exp Rheumatol.2014; 32(4 Suppl 84): S54-7.

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THU0289 PERSISTENCE OF CIRCULATING CRYOGLOBULINS AND RELATED SYMPTOMS AFTER HEPATITIS C VIRUS ERADICATION IN PATIENTS WITH MIXED CRYOGLOBULIN SYNDROME

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Background: The powerful drugs with direct antiviral action (DAA) against hepatitis C virus (HCV) has made it possible to eliminate the trigger factor of Mixed Cryoglobulin Syndrome (MCS) and to extend the treatment to patients who could not tolerate IFN-based antiviral regimens. However, the persistence of cryoglobulin production and MCS-related symptoms despite SVR achievement is frequently reported.

Objectives: The aim of this study was to assess the persistency rate of MCS-related clinical and laboratory indexes after successful treatment with DAA.

Methods: CRESO (CRyoglobulinaemia Eradication Study Observational) is a multicentre observational study promoted by the Italian Society of Infectious and Tropical Diseases (SIMIT) and the Italian Group for the Study of Cryoglobulinaemias (GISC), aimed to assess the impact of DAA therapy on MCS symptoms and cryoglobulin production. Patients could be enrolled if they presented, during the 12 months before the enrolment, a cryocrit ≥0.5% and, at least, one episode of palpable purpura or, alternatively, arthralgia and fatigue with at least one symptom among peripheral neuropathy, Raynaud's phenomenon, lower limb ulcers or nephropathy, and a C_4 level ≤8 mg/dL.

Results: The present analysis was based on clinical and laboratory data of 94 patients (75.5% female with a median age of 67.5 years) that have been followed up for a median time of 24 weeks (IQR 12-24) after SVR_{12} achievement. At baseline the cryocrit was frankly positive in 85 (90.43%), detectable (>0.5%) in 4 and negative in 4 cases; patients with type II cryoglobulins and C_4levels ≤8 mg/dL were prevalent, respectively with 81.5% and 75.9%. Low eGFR values (≤45 mL/min/1.73m^2) were present in 12 cases (12.8%), 10 patients (10.6%) had a history of B-cell non-Hodgkin's lymphoma (NHL), and 1 of hepatocellular carcinoma, while liver cirrhosis was diagnosed in 22 cases (23.4%) and glomerulonephritis in 17 cases (18.1%). Patients were treated for 12 (72 cases) or 24 (21 cases) weeks with a total of ten different IFN-free DAA regimens. SVR_{12} was achieved in all 94 cases. Both prevalence and median cryocrit values decreased significantly after DAA treatment (p<0.0001), however, at the time of the last observation 56.4% of patients were still positive for MCs. The prevalence of purpura and fatigue significantly decreased (p<0.0001) as well sicca syndrome prevalence (p<0.015), while arthralgia and lower limb ulcers decrease did not reach statistical significance. In multivariate analysis, eGFR≤45 mL/min/1.73m^2 was an independent predictor of persistence of cryoglobulin production (AOR 7.7, CI 95% 1.6-37.2; p<0.011).

Conclusion: CRESO study data confirm the persistence of cryoglobulin production and MCS symptoms in some patients, despite the eradication of HCV. This finding rises questions about the possible further evolution of the disease over time regardless the persistence of its original trigger.

Disclosure of Interests: None declared

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THU0290 DISEASE AND TREATMENT-RELATED MORBIDITY IN YOUNG AND ELDERLY PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: Advancing age may be a risk factor for morbidity in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

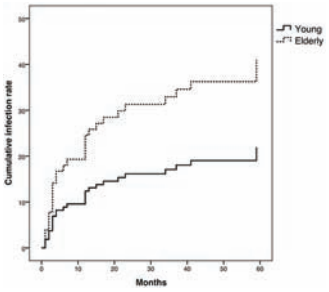
Objectives: We aimed to compare the rates and better characterize the type of disease- and treatment-related complications affecting young and elderly patients with AAV.

Methods: All new cases of granulomatosis with polyangiits or microscopic polyangiitis diagnosed between 2000 and 2016 in three referral centers in Northern Italy were included. Patients were stratified by age into young or elderly (</≥65 years old). Data were collected from time of diagnosis until end of follow-up, with scheduled annual visits or additional visits in case of relapse or complication requiring hospitalization.

Results: Of 141 patients included, 99 were young and 42 elderly at the time of AAV diagnosis. Median follow-up was 58.0 months (25-75% IQR, 31.0-60.0) in young and 48.0 months (25-75% IQR, 23.25-60.0) in elderly patients (p>0.05).

Overall, total chronic damage assessed by Vasculitis Damage Index (VDI) significantly increased in elderly patients compared to young ones during follow-up (=0.28, p<0.05). Although rates of the most common complications scored in the VDI (i.e. arterial hypertension, heart failure, ischemic cardiovascular complications, diabetes, and malignancy) accumulated over time when analyzed singularly, no difference between the two age groups was observed (p>0.05). Sixty-three (44.7%) patients had acute kidney injury due to AAV-glomerulonephritis at diagnosis, 37 were young and 26 were elderly. In these patients, renal function recovery in the first 6 months was significantly lower for elderly (median ΔeGFR (25-75%IQR), 5.3 (0.4-14) ml/min/1.73m2) compared to young patients (22.8 (5.9-52.1) ml/min/1.73m2, p=0.008) while on induction treatment. Stratification for

ANCA status (MPO-ANCA+ versus PR3-ANCA+), did not change these results. Despite similar immunosuppressive therapy approaches and relapse rates, elderly patients had a higher rate of severe infections compared to younger patients (OR 2.1, 95% CIs: 1.1-4.4, p=0.043; Figure below).



Abstract THU0290 – Figure 1

Conclusion: Our findings indicate that elderly patients had higher susceptibility to morbidity related to vasculitis or its treatment than younger patients, particularly to worst renal function recovery and higher infection rate.

REFERENCES:

[1] Harper L, et al. ANCA-associated renal vasculitis at the end of the twentieth century-a disease of older patients. Rheumatology (Oxford, England). 2005;44(4):495-501.
[2] Pagnoux C, et al. Treatment of systemic necrotizing vasculitides in patients aged sixty-five years or older: results of a multicenter, open-label, randomized controlled trial of corticosteroid and cyclophosphamide-based induction therapy. Arthritis & rheumatology (Hoboken, NJ). 2015;67(4):1117-27.
[3] Yates M, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Annals of the rheumatic diseases. 2016;75 (9):1583-94.

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THU0291 THE CHARACTERISTICS OF PEDIATRIC BEHÇET'S DISEASE IN TURKEY VERSUS ISRAEL

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Background: Behçet's disease (BD) is a variable vessel vasculitis affecting all sizes of vasculature in both the arterial and venous systems. Children with BD comprises 3-24% of all BD patients.
Objectives: To compare the demographics, presentation, clinical manifestations, disease activity, and treatment in pediatric Behçet's disease in Turkey versus Israel.
Methods: Three centers from Turkey and two centers from Israel participated in this study. The diagnosis of BD was before 16 years of age and based on expert opinion at each center. BD current activity form (BDCAF) was used for assessing disease activity.
Results: A total of 205 patients were included (165 from Turkey; 40 from Israel). HLA-B51 positivity (68.3% vs 46.2%, p=0.028), male gender (52.1% vs 30%, p=0.012), and skin involvement (especially necrotic folliculitis) (55.2% vs 22.5%, p<0.001) were more frequent among patients from Turkey compared to the ones from Israel. The first disease-related symptom was oral aphthosis in both groups followed by genital aphthosis and arthralgia/arthritis in patients from Turkey and Israel, respectively. The median BDCAF values were worse at the first visit for patients from Turkey than those from Israel (4 vs 2, p<0.001). The most commonly prescribed drug was colchicine in the whole group (96.6%). Significantly more patients were treated with corticosteroids (50% vs 28.5%, p=0.006), methotrexate (17.5% vs 3%, p=0.002), infliximab (10% vs 1.8%, p=0.026), and nonsteroidal anti-inflammatory drugs (12.5% vs 1.8%, p=0.007) in Israel than Turkey. For the classification of BD in the whole group, ICBD criteria had the highest sensitivity (73.2%) followed by PED-BD (pediatric BD) (47.8%) and ISG (The International Study Group) (42%) criteria sets.

Abstract THU291 – Table 1. The characteristics of children with Behçet's disease

Characteristics, n (%)	All patients (n=205)	Patients from Turkey (n=165)	Patients from Israel (n=40)	P value
Male	98 (47.8)	86 (52.1)	12 (30)	0.012
Age at symptom onset, months, median (min-max)	133 (12-191)	132 (12-191)	134 (12-190)	1
Age at diagnosis, months, median (min-max)	156 (48-191)	156 (48-191)	153 (55-191)	0.96
Oral aphthosis	204 (99.5)	165 (100)	39 (97.5)	0.195
Genital aphthosis	134 (65.4)	107 (64.8)	27 (67.5)	0.75
Skin involvement	100 (48.8)	91 (55.2)	9 (22.5)	<0.001
Eye involvement	29 (14.1)	22 (13.3)	7 (17.5)	0.49
Neurologic involvement	30 (14.6)	26 (15.8)	4 (10)	0.35
Vascular involvement	22 (10.7)	19 (11.5)	3 (7.5)	0.77
Pathergy positivity	45/167 (26.9)	42/154 (27.3)	3/13 (23.1)	1
HLA-B51 positivity	122/187 (65.2)	110/161 (68.3)	12/26 (46.2)	0.028
BDCAF at first visit	3 (0-15)	4 (1-15)	2 (0-5)	<0.001
BDCAF at last visit	1 (0-13)	1 (0-13)	1 (0-4)	0.15

Conclusion: This is the largest cohort of pediatric BD reported to date. The disease manifestations and disease activity significantly differ among pediatric BD patients from Turkey and Israel which emphasizes the effect of the ethnicity on disease phenotype.

REFERENCE:

[1] Kone-Paut I, et al. Consensus classification criteria for paediatric Behcet's disease from a prospective observational cohort: PEDBD. Ann Rheum Dis 2016;75:958-64.

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THU0292 EXTRACRANIAL VESSEL INVOLVEMENT IN PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a large vessel vasculitis with a predisposition for the cranial branches of the external carotid artery. However, aorta and/or its main branches may also be involved.

Objectives: In a series of patients with GCA who presented extracranial vessel involvement, our aim was to assess **a)** the vascular territories most frequently affected and **b)** correlation of a major extension of extracranial vascular involvement with a more severe clinical and analytical features.
Methods: Multicenter study of 68 patients with GCA who presented a compromise of extracranial vessels confirmed by PET/CT. Visual analysis of vascular uptake was performed on supra-aortic trunks (SAT), aortic arch (AA), thoracic aorta (TA), abdominal aorta (AbA), iliac arteries (IA), lower limb arteries (LLA), and upper limb arteries (ULA).
Results: We evaluated 68 patients with GCA (51w/17m) with a mean age of 68.0±8.3 years. The vascular territories affected were: TA (n=58, 85.29%), SAT (n=38, 55.88%), AbA (n=28, 41.18%), AA (n=18, 26.47%), LLA (n=17, 25%), IA (n=13, 19.12%) and ULA (n=6, 8.82%). We considered 3 groups according to the number of vascular territories affected: a) 1 or 2 territories, b) 3 or 4 territories and c) 5 or more territories and made a comparative study between this groups. In patients with ≥5 vascular territories affected, we observed a higher baseline ESR, and the most frequent systemic manifestations were polymyalgia rheumatica and constitutional symptoms with statistical significance (**TABLE**). Distribution of categorical variables was compared by the Pearson Chi-squared test. Quantitative variables were analyzed using the ANOVA test.
Conclusion: In patients with GCA the involvement of TA is very frequent, followed by the SAT and the AbA. Regarding the laboratory findings, patients with higher levels of ESR presented a major extension of extracranial vascular involvement, as well as presenting PMR and/or constitutional symptoms was also related to more affection of extracranial territories.

Abstract THU0292 – Table 2.

TABLE

	NUMBER OF VASCULAR TERRITORIES AFFECTED			p
ACUTE PHASE REACTANTS	**1-2**	**3-4**	**≥5**	
CRP, mg/dL, mean (SD)	3.1 ± 1.0	5.4 ± 1.8	7.3 ± 3.2	0.315
ESR, mm/1st hour, mean (SD)	36.8 ± 5.3	44.4 ± 6.2	74.5 ± 13.0	0.031
Hemoglobin, g/dL, mean (SD)	12.4 ± 0.2	12.0 ± 0.4	11.6 ± 0.5	0.439
SYSTEMIC MANIFESTATIONS				
Constitutional syndrome, n (%)	6 (17.1)	5 (22.2)	5 (83.3)	0.002
PMR, n (%)	28 (52.9)	23 (85.2)	4 (66.7)	0.03
ISCHEMIC MANIFESTATIONS				
Headache, n (%)	11 (31.4)	10 (37)	2 (33.3)	0.898
Jaw claudication, n (%)	1 (2.9)	3 (11.1)	1 (16.7)	0.307
Visual involvement, n (%)	2 (5.7)	2 (7.4)	-	0.783

REFERENCES:

[1] Loricera J, Blanco R, Hernández JL, et al. Use of positron emission tomography (PET) for the diagnosis of large-vessel vasculitis. Rev Esp Med Nucl Imagen Mol. 2015; 34: 372-377.
[2] Loricera J, Blanco R, Hernández JL, et al. Non-infectious aortitis: a report of 32 cases from a single tertiary centre in a 4-year period and literature review. Clin Exp Rheumatol. 2015; 33: S19-31.

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THU0293 DRUG RETENTION AND DISCONTINUATION REASONS BETWEEN SEVEN BIOLOGICS IN PATIENTS WITH TAKAYASU'S ARTERITIS: A SINGLE-CENTER EXPERIENCE

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Background: Biologic disease-modifying anti-rheumatic drugs(bDMARDs) have been showed to be effective in refractory Takayasu arteritis(TA) [1]. Data about bDMARDs drug retention rate(DRR) in TA are scarce.
Objectives: To investigate DRR and reasons for discontinuation of 7 bDMARDs in a real-world setting
Methods: TA patients fulfilling the 1990 ACR criteria and treated with ≥1 bDMARD were selected. Data about disease duration, number of bDMARDs, reasons for bDMARDs discontinuation (classified as inefficacy, toxic reactions, non-toxic reasons), concomitant conventional synthetic (cs) DMARDs were collected. Survival curves were examined by the Kaplan-Meier method and compared using a stratified log-rank test. DRR was evaluated at 24 months. Hazard ratio(HR) for concomitant csDMARDs therapy and for previous bDMARDs was performed. A comparative sub-analysis between antiTNFα drugs and tocilizumab(TCZ) was performed
Results: We identified 50 patients and 86 bDMARD-courses. At baseline, mean age was 39.1±12.1 years, mean disease duration was 119.5±110.1 months. No significant differences were observed in age and disease duration between the 7 groups. 31 patients were treated with 1 bDMARD, 11 with 2, 4 with 3, 2 with 5, 1 with 6, 1 with 7. Infliximab was the most frequent first-line bDMARD(78.6%). At bDMARDs initiation all patients were on prednisone(mean dose 13.5±10.3 mg), 85.2% on csDMARD(53 methotrexate, 13 azathioprine, 6 sirolimus, 3 mycophenolate-mofetil, 1 sulfasalazine). 43% of treatment courses were stopped by 24 months. Table1 summarizes DRR and reasons for treatment discontinuation for each bDMARD. Golimumab had the highest DRR(71.4%), followed by infliximab (69%), adalimumab (56.3%), abatacept (50%), tocilizumab (41.1.%), anakinra (0%) and rituximab (0%), p=0.016. Only concomitant csDMARDs therapy (HR=2.87,95%CI=1.19-6.92,p=0.019) showed positive effects on DRR. AntiTNFα drugs had significantly higher DRR compared to TCZ (67.2% vs 41.1%,p=0.028). Even in these subgroups csDMARDs (HR=3.79,95% CI=1.49-9.6,p=0.005) showed positive effects on DRR

bDMARDs (n° of treatment courses)	N° of previous bDMARDs	csDMARD associated	24-month DRR	Reasons for bDMARDs discontinuation			24-month DRR
				Inefficacy	Toxicity	Non-toxic events	
IFX (42)	0 (0-2)	38 (90%)	69%	5 (12%)	6 (14%)	2 (5%)	67%
ADA (12)	0 (0-5)	11 (92%)	56%	4 (33%)	1 (8%)	0	
GOL (7)	2 (0-6)	5 (71%)	71.4%	1 (14%)	1 (14%)	0	
TCZ (17)	1 (0-4)	15 (88%)	41%	7 (41%)	2 (12%)	1 (6%)	41%
ANK (4)	2.5 (1-3)	2 (50%)	0%	2 (50%)	1 (25%)	1 (25%)	
ABT (2)	4.5 (4-5)	1 (50%)	50%	1 (50%)	0	0	
RTX (2)	2.5 (2-3)	1 (50%)	0%	2 (100%)	0	0	
Overall (86)	0.5 (0-6)	75 (86%)	60%	22 (26%)	11 (13%)	4 (5%)	

Conclusion: In our TA cohort, antiTNFα agents had the highest DRR and, notably, they had a higher DRR in a head-to-head comparison with TCZ. Concomitant use of csDMARDs had a significant positive effect on bDMARDs DRR

REFERENCES:

[1] Management of large-vessel vasculitis. Salvarani C, Hatemi G. Curr Opin Rheumatol. 2019 Jan;31

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THU0294 TREATMENT PATTERNS, DISEASE BURDEN AND OUTCOMES IN PATIENTS WITH GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA

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Background: For patients with giant cell arteritis (GCA) and/or polymyalgia rheumatica (PMR), glucocorticoids are the mainstay of treatment. However, due to the chronic nature of these diseases, patients may require continued glucocorticoid treatment to achieve treatment targets or prevent disease relapse, over time resulting in high cumulative doses and associated adverse events.
Objectives: To assess patterns of glucocorticoid use and outcomes in patients with GCA, PMR or both.
Methods: This retrospective cohort study used electronic medical records from a single US community-based rheumatology clinic utilizing the JointMan rheumatology software application. Patients age $\geq$ 50 years with a diagnosis of either GCA or PMR and $\geq$ 1 entry for glucocorticoid following the diagnosis were included and followed until lost to follow-up or the end of the study period (30 Nov 2017). The index date was defined as the date of first glucocorticoid prescription received at or after the earliest GCA or PMR diagnosis date. Outcomes at 2 years included the proportion of patients achieving remission (defined as not receiving steroids for $\geq$ 6 months), time to remission, persistence of remission (defined as not receiving steroids for $\geq$ 6 months and still not receiving steroids at 2 years) and prednisone dose at follow-up, and were compared between patients with GCA only, PMR only or both GCA and PMR. *P* values are reported using F-test (ANOVA) for continuous variables and Chi-squared test for categorical variables.
Results: We identified 81 patients with GCA only, 779 with PMR only and 97 with GCA and PMR. Mean (SD) age was 70.0 (9.1) years; 64.2% were women. Mean (SD) daily prednisone dose at the index date was 46.7 (30.9) mg for patients with GCA only, 20.1 (14.2) for PMR only and 29.0 (23.4) for patients with both GCA and PMR. Two years after the index date, 32% of patients with GCA only, 32% with PMR only and 27% with GCA and PMR had achieved remission; 17%, 23% and 18% were in persistent remission, respectively (**Table 1**), with no significant differences between groups. Among patients who achieved remission, overall median time to first remission was 202.5 (0-635) days and was shorter for patients with both GCA and PMR (157 [0-619] days) vs GCA (213 [0-577] days) or PMR (203.5 [0-635] days) only. Kaplan-Meier estimates of time to remission for each group are shown (**Figure 1**.). Most patients required a daily prednisone dose at 2 years, with similar doses observed between groups (**Table 2**).
Conclusion: Patients with either GCA and/or PMR are exposed to significant doses of prednisone. In this study, fewer than one-third of patients with GCA and/or PMR achieved remission; the majority of patients continued to require prednisone therapy for at least 2 years after its initiation. These data highlight the need for the use of more efficacious and steroid-sparing therapies in patients with GCA and/or PMR.

Abstract THU294 – Table 1. Outcomes at 2 Years Post-Index Date

Total patients	GCA Only (N = 81)	PMR Only (N = 779)	GCA and PMR (N = 97)	Total (N = 957)	*P* Value
Achieved remission, n (%)	26 (32.1)	248 (31.8)	26 (26.8)	300 (31.3)	0.7921
Persistent remission, n (%)	14 (17.3)	176 (22.6)	17 (17.5)	207 (21.6)	0.5139
Time to remission, days*					
Mean (SD)	224.3 (171.7)	226.5 (198.6)	208.4 (186.6)	224.7 (194.9)	0.0361
Median (range)	213 (0-577)	203.5 (0-635)	157 (0-619)	202.5 (0-635)	

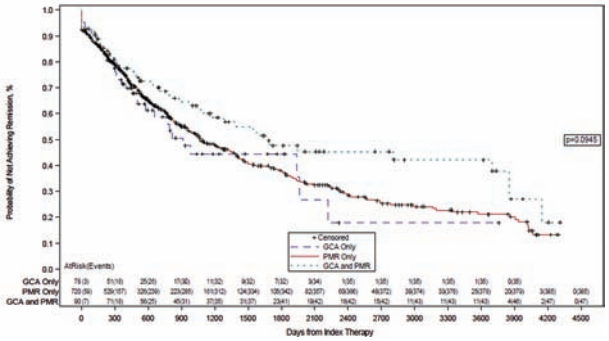
* Among patients who achieved remission.

Abstract THU294 – Table 2. Prednisone Dose at 2 Years Post-Index Date

	GCA Only (N = 26)	PMR Only (N = 341)	GCA and PMR (N = 60)	Total (N = 427)	*P* Value
Prednisone dose, mg/day*					
Mean (SD)	9.5 (10.6)	8.8 (9.2)	12.6 (15.9)	9.4 (10.5)	0.0819
Median (range)	5 (0-40)	5 (0-66)	7.5 (0-80)	5 (0-80)	

* Among patients who had prednisone dose information available at 2 years.

Figure 1. Time to Remission Following Initiation of Glucocorticoids



Abstract THU0294 – Figure 1

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THU0295 POLYMYALGIA RHEUMATICA ASSOCIATED WITH GIANT CELL ARTERITIS CONFIGURES A SUBTYPE WITH LOWER MORTALITY WITHIN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is the most frequent systemic vasculitis in older than 50 years old, with marked general state involvement or ischemic phenomena that can cause blindness to the patient's death. Its form of presentation is heterogeneous however the therapeutic approach tends to be homogeneous. In recent years, the possible existence of subtypes of the disease has been pointed out and this can have important repercussions in the prognosis and approach of the disease. Two studies have suggested that the coexistence of GCA and Polymyalgia rheumatica (PMR) identifies a subgroup of patients at low risk for developing cranial ischemic symptoms. However, this was refuted by three other studies that did not find that effect.
Objectives: To study if, excluding the articular manifestations, the GCA against the association of PMR with ACG presents a phenotype with clinical differences relevant in clinical practice.
Methods: Retrospective observational study based on data from the Database of Hospital from the Spanish National Health Service with primary or secondary diagnostic of GCA between January 1st, 2005 and December 31th, 2015. In this substudy the data demographics and comorbidities and mortality, presenting patients with GCA were collected and compared with patients with GCA and PMR.
Results: The study cohort included 29.576 patients with GCA, of whom 4,189 had PMR as an associated diagnosis. The comorbidities associated with ACG and ACG/PMR and the statistical significance of the differences can be seen in the table. As a relevant fact, a lower risk of mortality was observed in patients presenting GCA along with PMR (OR 0.682 IC95% 0,581-0,801) and a lower frequency of cerebrovascular events and ischemic optic neuropathy.

Table 1. Differences between GCA associated with PMR vs ACG without PMR

		WTIHOUT PMR		WITH PMR	
		N	%	N	%
Sex*	Men	9533	37,6%	1474	35,2%
	Woman	15853	62,4%	2715	64,8%
Age group*	≤ 74	5646	22,2%	997	23,8%
	75-79	5779	22,8%	954	22,8%
	80-84	6789	26,7%	1210	28,9%
	≥ 85	7173	28,3%	1028	24,5%
DM2*		6486	25,5%	1131	27,0%

RENAL		3393	13,4%	576	13,8%
ICC*		3651	14,4%	501	12,0%
IHM		1035	4,1%	156	3,7%
Cancer*		1177	4,6%	131	3,1%
ECV*		1030	4,1%	123	2,9%
EPOC		736	2,9%	112	2,7%
ION*		431	1,7%	41	1%
CCI*	Without Comorbidities	11943	47,0%	2065	49,3%
	≤ 2 Comorbidities	12355	48,7%	1977	47,2%
	> 2 Comorbidities	1089	4,3%	147	3,5%
Mortality*		1618	6,4%	177	4,2%

*Statistically significant differences (P < 0.05) DM2: Diabetes mellitus Type 2 **PMR**: Polymyalgia rheumatica **ICC:** Congestive heart failure **IHM:** Ischemic Heart Disease **ECV:** Cerebrovascular disease **ION:** ischemic optic neuropathy CCI: Charlson Index of Comorbidities

Conclusion: The patients with GCA with PMR represent a subtype of GCA with lower risk of stroke, ischemic optic neuropathy and mortality than patients with ACG without associated PMR.

Disclosure of Interests: : None declared

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THU0296 CORRELATIONS AMONG VASCULAR ULTRASOUND ABNORMALITIES OF THE TEMPORAL AND LARGE ARTERIES IN GIANT CELL ARTERITIS

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Background: Vascular ultrasound (VUS) is a sensitive and specific method for evaluating giant cell arteritis (GCA). Understanding patterns of temporal artery (TA) and large artery involvement may be important for aiding in diagnosis.

Objectives: To determine correlations among VUS abnormalities in patients with GCA.

Methods: We performed a retrospective study among 503 patients that underwent VUS to evaluate suspected or known GCA at an academic medical center, 2013-2017. Demographics, clinical features, VUS reports, and pathology data were extracted through electronic medical record review. Trained cardiovascular ultrasonographers imaged the right and left temporal, common carotid (CCA), subclavian (SCA), and axillary (AXA) arteries. The superficial temporal arteries (STA) and their frontal (TA-F) and parietal (TA-P) branches were abnormal if halo sign or hyperechoic wall thickening was present; the CCA, SCA and AXA were abnormal if those findings and/or stenosis or occlusion were present. Cardiovascular medicine physicians trained in VUS interpreted studies as acute arteritis, no arteritis, or hyperechoic wall thickening without acute arteritis. Among patients diagnosed with GCA by the treating physician (n=139), we determined correlations between abnormal vessels using phi coefficients (ϕ). We created composite variables representing each TA and its branches, and the left and right CCA, SCA, and AXA to test correlations between temporal and large arteries. Significance was determined using Fisher's exact test with Bonferroni correction.

Results: Among 139 patients, 50% were diagnosed before VUS (median disease duration 17 months). Median age at VUS was 73 years; 75% were female and 93% White. Forty patients (29%) had TA biopsy-proven GCA; an additional 14 (10%) had biopsy-proven giant cell aortitis. Prevalence of abnormalities of TAs and large arteries were similar (20% of right and 27% of left TAs; 20% of right and 24% of left large arteries). VUS was consistent with acute arteritis in 32%, no arteritis in 53%, and hyperechoic without acute arteritis in 15%. Abnormalities in the STA, TA-F, and TA-P were moderately correlated ipsilaterally (ϕ = 0.46-0.62, p<0.0001) and contralaterally (ϕ = 0.51-0.58, p<0.0001) (Table). Abnormalities in the AXA and SCA were strongly correlated with the ipsilateral and contralateral AXA and SCA (ϕ = 0.64-0.82, p<0.0001). Correlation between right and left TAs was moderate (ϕ = 0.59, p<0.0001), while a stronger relationship was found between right and left large arteries (ϕ = 0.77, p<0.0001). Abnormalities in TAs were not correlated with large arteries ($\phi \approx 0$ for all comparisons; not significant).

Conclusion: We observed moderate correlations of TA branches and strong correlations of large artery branches on VUS among GCA patients. Abnormalities in the TAs and large arteries were not correlated, underscoring the importance of scanning both groups of vessels with VUS.

Table. Notable correlations between abnormal arteries on VUS among 139 GCA patients

Artery	Correlated Artery	ϕ	p
R STA	R TA-F	0.60	†
	R TA-P	0.62	†
	L STA	0.58	†
	L TA-F	0.51	†
R TA-F	R TA-P	0.58	†
	L STA	0.48	†
R TA-P	L TA-P	0.51	†
L STA	L TA-F	0.55	†
L TA-F	L TA-P	0.46	†
R CCA	L CCA	0.66	†
R AXA	R SCA	0.81	†
	L AXA	0.82	†
	L SCA	0.81	†
L AXA	L SCA	0.69	†
R SCA	L AXA	0.64	†
	L SCA	0.73	†
R temporal composite	L temporal composite	0.59	†
	R large composite	-0.07	NS
	L large composite	-0.07	NS
L temporal composite	R large composite	0.06	NS
	L large composite	0.05	NS
R large composite	L large composite	0.77	†

Temporal composite: abnormal superficial TA, TA-frontal branch, and/or TA-parietal branch. Large composite: abnormal common carotid, subclavian, and/or axillary artery. NS: not significant

† p<0.0001

Disclosure of Interests: None declared

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THU0297 STEROID TREATMENT MAY IMPROVE ARTERIAL STIFFNESS IN PATIENTSWITH POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS: A PROSPECTIVE COHORT STUDY

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Background: Polymyalgia rheumatica (PMR)/Giant cell arteritis (GCA), common inflammatory diseases, are associated with increased risk of aortic stiffness, possibly due to an inflammatory process.[1,2]

Objectives: To evaluate the effect of steroid treatment on aortic stiffness in patients with PMR/GCA.

Methods: This is an ongoing 1-year prospective cohort study. 37 consecutive patients with newly diagnosed PMR/GCA were included. Aortic pulse wave velocity (PWV) and aortic augmentation index normalized to heart rate of 75 beats per minute (AIx@75) were measured at baseline and subsequently at 1st and 4th months of treatment initiation with oral prednisolone.

Results: Of 37 patients, 3 pts. were excluded from the study because of lack of interest or a change in the initial diagnosis. Of all included pts. 61.8% were female and mean age was 71 (69-74) years. At diagnosis, 24 pts. presented with pure PMR symptoms, 2 pts. with pure cranial GCA, 8 pts.with concurrent PMR and GCA. The mean of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) at baseline were 62.3±22.9 and 46.4±43.7, respectively. AIx@75 was significantly decreased after 4 months of treatment initiation (from 26.1±11.6 to 19.5 ±11.5, p=0.016). Though aortic PWV was decreased after 4 months of treatment initiation (from 12.3±2.4 to 11.6±2.4), the results was not statistically significant (p=0.070). We did not find any significant changes at 1st month, nor in aortic PWV neither in AIx@75.

Conclusion: Steroid treatment may improve arterial stiffness in PMR/GCA patients due to suppression of the inflammatory process. However this is a time consuming effect and may not be seen as early as the first month.

REFERENCES:

[1] Emamifar A, et al. Polymyalgia rheumatica and giant cell arteritis-three challenges-consequences of the vasculitis process, osteoporosis, and

malignancy: A prospective cohort study protocol. Medicine (Baltimore). 2017;96(26):e7297.
[2] Schillaci G, et al. Aortic stiffness is increased in polymyalgia rheumatica and improves after steroid treatment. Ann Rheum Dis 2012;71:1151-6.

Disclosure of Interests: None declared
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THU0298 INITIAL MANIFESTATIONS AND OUTCOME OF PATIENTS WITH INCOMPLETE BEHÇET'S SYNDROME

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Background: Behçet's syndrome (BS) has a heterogeneous expression involving many organ systems and is diagnosed by recognizing the coexisting manifestations. Several patients initially have few of these manifestations and do not fulfill the International Study Group (ISG) criteria. When these are major organ manifestations, failure to recognize BS and treat promptly may lead to permanent damage in these organs.
Objectives: The aim of this study is to highlight the magnitude of this problem by surveying the frequency, presentation patterns and outcome of patients who did not fulfill ISG criteria when they presented to our clinic, but were followed and treated for manifestations strongly suggesting BS.
Methods: We conducted a retrospective chart review of all BS patients who were registered between 2003 and 2008. Among these 2385 patients, 199 (8%) BS patients who did not fulfill ISG criteria at their initial visit were included in this study. Patients were called and a standard form was used for collecting demographic characteristics, BS manifestations at initial visit and during follow-up and treatment.
Results: Among the 199 patients (M/W: 90/109, mean age: 34 ± 11 years) who did not fulfill ISG criteria when they presented to our clinic, 70 (35%) had major organ involvement. The types of major organ involvement that led to a diagnosis of BS at initial visit despite not fulfilling ISG criteria were eye involvement in 37, vascular involvement in 29 (venous thrombosis in 22, arterial aneurysms in 7), nervous system involvement in 3 and gastrointestinal (GI) involvement in 1 patient. Thirty-five patients (18%) had a family history of BS.
Of 199 patients, 167 had at least one more visit with a median follow-up of 11 years (IQR: 7-12). We were able to contact 116 of these patients and saw that 53 had fulfilled ISG criteria in the meantime. Among the 51 patients that we were not able to contact, 17 had fulfilled criteria while they were being followed in our clinic. Thus, a total of 70 (42%) patients fulfilled ISG criteria after a median follow-up of 1.5 years (IQR: 1-4.25). All but 2 patients who developed eye involvement during the follow-up had fulfilled ISG criteria with a new mucocutaneous manifestation. After a median follow-up of 4 years (IQR: 1-7), 23 (14%) patients had developed at least one non-criteria BS manifestation, including vascular involvement in 10, arthritis in 13, neurologic involvement in 2 patients and GI involvement in 1 patient.
Among the 81 patients who developed at least one new manifestation, 16 (20%) were under immunosuppressive or interferon-alpha treatment at the time they developed their new manifestation. The remaining 65 patients had only received colchicine.
Among the 29 patients who had vascular involvement at initial visit, 7 (24%) had a vascular relapse at different vascular site.
Three patients had another rheumatologic diagnosis (ankylosing spondylitis, seropositive rheumatoid arthritis and sarcoidosis) at the end of the follow-up.
Conclusion: In our 10-year follow-up cohort study, 42% of the 167 incomplete BS patients had fulfilled ISG criteria within a median duration of 1.5 years. Sixty-two (37%) of these had major organ involvement that could have caused severe morbidity and mortality if the diagnosis of BS was missed and patients were untreated.
Disclosure of Interests: : Sinem Nihal Esatoglu: None declared, Seyda Bilgin: None declared, Cem Sulu: None declared, Vedat Hamuryudan Consultant for: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Zekayi Kutlubay: None declared, Serdal Ugurlu: None declared, Emire Seyahi: None declared, Melike Melikoglu: None declared, Izzet Fresko: None declared, Sebahattin Yurdakul: None declared, Hasan Yazici: None declared, Gulen Hatemi Consultant for: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB,
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THU0299 PATIENT GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN BEHÇET'S SYNDROME: A MULTICENTER STUDY

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Background: Disease activity evaluation is mandatory according to the OMERACT Core Set of Domains for Behçet's Syndrome (BS). Poor data are available on Patient (PtGA) and physician (PGA) global assessment of disease activity in BS.
Objectives: To assess PtGA performance in patients with BS and how different disease manifestations influence the patient and physician's perception of disease activity.
Methods: A multicenter cross-sectional cohort of consecutive BS patients was enrolled. Disease activity was evaluated by PtGA, PGA and the Behçet's disease current activity form (BDCAF). PtGA and PGA were assessed trough a single question ("How active was BS during the last week?") in a 10-cm visual analogic scale. Health related quality of life (HRQoL) perception was evaluated by the Physical Component Summary (PCS) and the Mental Component summary (MCS) of the SF36v2 questionnaire.
Correlation between PtGA, PGA, BDCAF and between them and SF36v2 component summaries was assessed trough the Spearman's correlation coefficient (rho). Two separated multiple regression models were built to measure the independent effect (β regression) of each active clinical manifestation on PtGA and PGA.
Results: Overall, 226 BS patients from 5 Mediterranean Countries were enrolled. Out of them, 111 (49.1%) were males and the median (IQR) age and disease duration were 46.9 (35.6-55.2) and 11.7 (5.9-20.8) years, respectively.
The median (IQR) value of PtGA, PGA and BDCAF were 2.0 (0.3-5.0), 1.0 (0.0-3.0) and 3.0 (0.0-5.0), respectively. PtGA significantly correlated (Figure) with both PGA (rho 0.759. $p < 0.001$) and BDCAF (rho 0.523. $p < 0.001$), in support of its construct validity. PtGA scores were significantly higher than PGA with a mean (SD) difference of 0.8 (1.8), suggesting a different weighing of disease activity between patients and physicians. Indeed, PtGA and PGA were differently influenced by active clinical manifestations (Table). PtGA was mainly dependent on active mucocutaneous (β 0.243), gastrointestinal (β 0.216) and ocular (β 0.209) involvement whereas a major effect of ocular manifestations was observed in PGA (β 0.378). PtGA was correlated with worse HRQoL perception measured by PCS (rho -0.476. $p > 0.001$) and MCS (rho -451. $p > 0.001$).
Conclusion: PtGA seems to be a valid outcome measure in BS and should be considered as a separate outcome measure or better be included in composite index for overall disease activity evaluation.

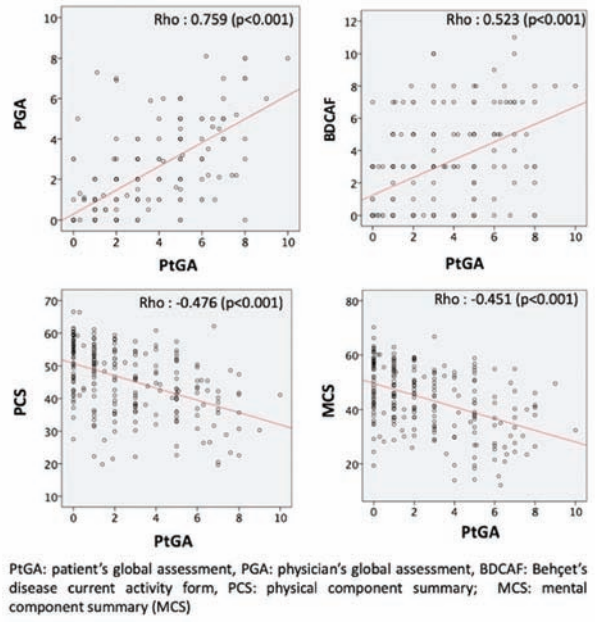
Abstract THU299 – Table 1.

PtGA	PGA

Active involvement	β	p	Active involvement	β	p
Mucocutaneous	0.243	<0.001	Ocular	0.378	<0.001
Gastrointestinal	0.216	0.001	Mucocutaneous	0.284	<0.001
Ocular	0.209	0.001	Gastrointestinal	0.192	<0.002
Vascular	0.108	0.086	Vascular	0.129	<0.027
Arthritis	0.088	0.185	Arthritis	0.121	0.048
Neurologic	0.003	0.962	Neurologic	0.047	0.420

Disclosure of Interests: Alberto Floris: None declared, Matteo Piga: None declared, Gerard Espinosa: None declared, Nikolaos Kougkas: None declared, Andrea Lo Monaco: None declared, Giuseppe Lopalco Speakers bureau: SOBI, BMS, Ida Orlando: None declared, Vittorio Pirani: None declared, Ernestina Santos: None declared, Luísa Serpa Pinto: None declared, George Bertsias: None declared, Luca Cantarini: None declared, Alberto Cauli: None declared, Ricard Cervera: None declared, João Correia: None declared, Marcello Govoni: None declared, Florenzo Iannone Consultant for: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Ana Martins da Silva: None declared, Piergiorgio Neri: None declared, Carlos Vasconcelos: None declared, Alessandro Mathieu: None declared

Figure. Correlation between PtGA and other outcomes measures



PtGA: patient's global assessment, PGA: physician's global assessment, BDCAF: Behçet's disease current activity form, PCS: physical component summary; MCS: mental component summary (MCS)

Abstract THU0299 – Figure 1

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THU0300 IMPACT OF VASCULAR ULTRASOUND ON EVALUATION OF GIANT CELL ARTERITIS AMONG 503 PATIENTS IN AN ACADEMIC MEDICAL CENTER

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Background: As vascular ultrasound (VUS) is increasingly used in evaluation of giant cell arteritis (GCA), its impact on clinical care is of great interest.

Objectives: To describe utilization of VUS in GCA evaluation at a large academic medical center and investigate impact of VUS on clinical impression.

Methods: We performed a retrospective cohort study of patients who underwent VUS at a single center in Boston, 2013-2017, to evaluate suspected or known GCA. Trained cardiovascular ultrasound technicians used a standardized protocol to image the temporal, carotid, subclavian, and axillary arteries for presence of hypoechoic circumferential wall thickening (halo sign), hyperechoic wall thickening, stenosis, and occlusion. VUS images were interpreted by trained cardiovascular medicine physicians as consistent with acute arteritis ("acute"), no evidence of arteritis ("none"), or hyperechoic wall thickening without halo sign ("hyperechoic"). Demographic, laboratory, medication, pathology and clinical data including the treating physician's clinical suspicion for GCA pre- and post-VUS were obtained by electronic medical record review. Fisher's exact test and Wilcoxon rank-sum tests compared baseline characteristics among patients with VUS positive for acute arteritis ("acute") vs. negative for acute arteritis ("none" or "hyperechoic"). We compared the treating physician's pre- and post-VUS clinical suspicion for GCA among patients with no history of GCA or aortitis.

Results: We identified 503 patients with median age 70.4 years; 69.0% were female and 87.5% White. VUS interpretation was acute in 48 patients (9.5%), none in 427 (84.9%), and hyperechoic in 28 (5.6%). Baseline characteristics are presented in Table 1. Weight loss, cranial symptoms, higher ESR, and steroid use were more common in patients with VUS positive for acute arteritis. Change in the treating physician's clinical suspicion for GCA is shown in Figure 1. VUS positive for acute arteritis increased suspicion for GCA in 26/35 (74%) cases, and VUS negative for acute arteritis lowered suspicion for GCA in 303/396 (77%). Of 110 patients with a temporal artery biopsy after VUS, 16 (14.6%) biopsies showed active arteritis; 11 of these were in patients with VUS negative for acute arteritis.

Conclusion: VUS result changed the clinical suspicion for GCA in approximately 75% of patients in this large cohort.

Abstract THU300 – Table 1. Characteristics at the time of VUS

Age, years	70.4 (62.7, 77.5)	73.2 (65.8, 79.7)	69.9 (62.6, 77.3)	NS
History of GCA or aortitis	14.3	27.1	13.0	0.02
History of PMR	31.2	22.9	32.1	NS
New headache	51.3	60.4	50.3	NS
Weight loss	13.3	22.9	12.3	0.05**
Fatigue	36.2	45.8	35.2	NS
Jaw claudication	10.9	33.3	8.6	<0.01
Scalp tenderness	17.1	37.5	15.0	<0.01
TA tenderness/decreased TA pulse	14.5	29.2	13.0	<0.01
Transient vision loss	7.8	10.4	7.5	NS
Permanent vision loss	3.0	6.3	2.6	NS
CRP*, mg/L	15.7 (3.1, 76.0)	36.3 (8.1, 81.9)	13.7 (2.9, 75.3)	NS
ESR*, mm/h	40 (18, 83)	67 (30, 95)	40 (17, 81)	<0.01
Steroids at time of VUS	57.5	75.0	55.6	0.01 0.02
>0 to <15mg/day	34.3	30.6	34.8	NS
≥15 to <40mg/day	23.5	8.3	25.7	
≥40mg/day	42.2	61.1	39.5	
Steroids ≥3 weeks	56.8	41.7	59.3	

Presented as% or median (interquartile range).
CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GCA: giant cell arteritis; PMR: polymyalgia rheumatica; TA: temporal artery; VUS: vascular ultrasound. NS: not significant.
*Among 418 patients with CRP and 370 with ESR checked within 3 weeks before VUS
**p=0.046

Figure 1. Treating physician's clinical suspicion for GCA before and after VUS among 431 patients without a history of GCA/aortitis

VUS positive for acute arteritis (n=35)

Pre-test impression	Post-test impression: Definite GCA	Very likely GCA	Possible GCA	Unlikely GCA	Not GCA
Definite GCA	3	-	-	-	-
Very likely GCA	13	3	-	-	-
Possible GCA	8	3	3	-	-
Unlikely GCA	1	1	-	-	-
Not GCA	-	-	-	-	-

VUS negative for acute arteritis (n=396)

Pre-test impression	Post-test impression: Definite GCA	Very likely GCA	Possible GCA	Unlikely GCA	Not GCA
Definite GCA	1	-	-	1	-
Very likely GCA	4	9	7	9	5
Possible GCA	3	2	35	41	141
Unlikely GCA	-	-	2	20	99
Not GCA	-	1	-	2	14

Increased suspicion | No change | Decreased suspicion

Abstract THU0300 – Figure 1

Disclosure of Interests: None declared
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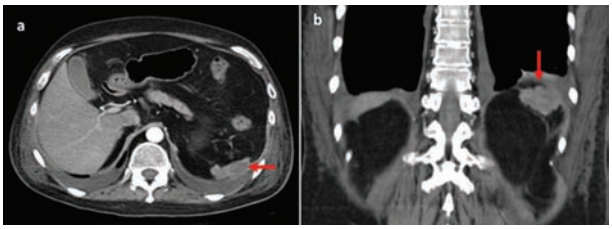
THU0301 SPLENIC INVOLVEMENT IS NOT RARE IN ANCA-ASSOCIATED VASCULITIS HOWEVER SPLENIC INFARCT MIGHT ONLY BE ASSOCIATED WITH GRANULOMATOSIS WITH POLYANGIITIS

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Background: Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) is a systemic necrotizing vasculitis of small and medium-sized arteries. Although, upper and lower respiratory tracts and kidneys are predominantly affected; other organs/systems can also be involved in the course of the disease and in some cases, it might be difficult to differentiate subgroups based on the clinical presentation. Splenic involvement has been rarely reported, mainly in patients with granulomatosis with polyangiitis (GPA), in fact, it was thought to be underestimated, as it is often asymptomatic.
Objectives: In this study, we aimed to investigate systematically the frequency of splenic infarct and related factors in our AAV patients. We also evaluated the role of splenic involvement in the differentiation of AAV subgroups.
Methods: Patients with a diagnosis of AAV in whom abdomen/thorax computed tomography (CT) was performed were included in the study. An experienced radiologist examined CT images for the presence of splenic involvement. The clinical and demographic data were retrospectively collected.
Results: In total 70 (30 [43%] female and mean age 56.1 ± 15.7 years) AAV patients (38 [54%] had granulomatosis with polyangiitis (GPA); 20 [29%] microscopic polyangiitis; 11 [16%] renal-limited disease and 1 [1%] eosinophilic granulomatosis with polyangiitis) were included in the analysis. Splenic pathologies including splenomegaly, hypodense lesion/s, lobulation, and infarction were seen in 21 (30%) patients with AAV. Splenic infarct was observed in seven (10%) patients and all had GPA with renal involvement and PR3ANCA positive. Three of them had total splenic infarct or auto-splenectomy. None of these patients had a history of endocarditis, shock or malignancy before CT. Splenic infarction was found to be negatively correlated with age at diagnosis (p=0.017; rho=-0.285), and positively associated with ENT (ear-nose-throat) (p= 0.002; rho=0,370) and eye involvements (p=0.013; rho=0,324).
Conclusion: Our results show that splenic pathologies might not be rare in AAV however, infarction can help to separate GPA from other AAVs. In young GPA patients, in particular, those with ENT and eye involvement, physicians should remember splenic infarction. Since almost half of our cases had severe infarction or autosplenectomy, clinicians might consider immunization in GPA patients for vaccine-preventable infections.

REFERENCES:

[1] Fishman D, Isenberg DA. Splenic involvement in rheumatic diseases. Semin Arthritis Rheum. 1997;27(3):141-55
[2] Ghinoi A, Pipitone N, Cavazza A, Boiardi L, Salvarani C. Wegener granulomatosis with spleen infarction: case report and review of the literature. Semin Arthritis Rheum. 2008;37(5):328-33



Abstract THU301 – Figure 1. Computed abdominal tomography scan of one the patients with splenic infarction; transverse (a) and coronal images (b) show an irregular contoured shrunken spleen (arrows).

Disclosure of Interests: Önay Gerçik: None declared, Şebnem Karasu: None declared, Dilek Solmaz: None declared, Zeki Soypaçacı: None declared, Fulya Çakalağaoğlu: None declared, Servet Akar Grant/research support from: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Speakers bureau: Pfizer
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THU0302 OUTCOMES OF PREGNANCY IN BEHCET'S DISEASE

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Background: Behcet's disease (BD) is multisystemic disease of unknown cause. The relationship between BD and pregnancy is reported in limited number of studies.
Objectives: To evaluate outcomes of pregnancies in BD patients (pts).
Methods: We retrospectively collected data of 22 women with BD diagnosis (according to ISGBD 1990 and ICBD 2014) and their 68 pregnancies. Pts' mean age was 30 [26;35] yrs, disease duration 7 [2;10] yrs. Ten (45,5%) pts had severe BD according to Ch.Zouboulis classification (due to generalized uveitis, retinal vasculitis and parenchymatous CNS lesions), while other 10 (45,5%) pts had mild disease with mainly dermal-mucous manifestations, and remaining two (9%) pts had moderate disease. These patients did not receive cytotoxic therapy.
Results: Sixty-eight pregnancies in 22 pts resulted in 45 live birth (4 cesarean section in 2 pts). Four patients had 11 medical abortions on request before 12 weeks of gestation, one patient - due to medical reasons (rubella on the 7th week of gestation). Seven (32%) out of 22 pts had adverse pregnancy outcomes. Five (23%) pts had 8 intrauterine deaths: one patient – 3 intrauterine deaths (4-10 weeks), two pts – 2 (10-12 weeks) and one -1 intrauterine deaths (10 weeks). Two (9%) pts had 3 miscarriages 5–10 weeks. Antiphospholipid syndrome was never detected in pts from this cohort.
BD Severity and pathology of pregnancy

BD Severity	N=22 (%)	Intrauterine deaths/Miscarriage
Mild	10 (45,5)	3/2
Moderate	2 (9)	5/0
Severe	10 (45,5)	0/1

Out of 45 babies children born by BD patients only two had relapsing aphthous stomatitis and one – congenital glaucoma ("Neurobehcet" inherited from mother).
Conclusion: BD pts demonstrated high rates of adverse pregnancy outcomes. Unfavorable outcomes of pregnancy were documented in pts regardless (with all grades of) BD severity.

REFERENCE:
[1] Zouboulis C., Vaiopoulos G., Macromichelakis N. et al. Onset signs, clinical course, prognosis, treatment and outcome of adult patients with Adamantiades – Behcet's disease in Greece. Clin.Exp.Rheum.2003, 21, (suppl.30) S19-S26.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.6657

THU0303 THE OMERACT CORE DOMAIN SET FOR CLINICAL TRIALS IN BEHÇET'S SYNDROME

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Background: There is an unmet need for reliable, validated, and widely-accepted outcome measures for clinical trials in Behçet's syndrome (BS).
Objectives: The Outcome Measures in Rheumatology Clinical Trials (OMERACT) Behçet's Syndrome Working Group has worked to advance the creation of a data-driven Core Domain Set for use in all clinical trials.
Methods: The Core Domain Set was developed through a comprehensive, iterative, multi-stage, multi-year project that followed the methodologically rigorous processes and standards set forth by OMERACT: i) a systematic review; ii) a survey among experts in BS; iii) an outcome measures interest group meeting during the International Conference on Behçet's Disease; iv) qualitative patient interviews; v) a three-round modified Delphi exercise involving both patients with BS and a multidisciplinary set of physicians expert in BS, focused on obtaining consensus on the domains of illness necessary in the study of BS; and vi) utilization of the data, insight, and feedback generated by the outlined processes to develop a final Core Domain Set. The final Core Set was presented and put up for a vote of endorsement at the 2018 OMERACT meeting.
Results: All steps in the processes outlined were completed. The systematic review clearly demonstrated the substantial variability in the domains studied in clinical trials of BS and a lack availability of validated outcome measures in BS. The survey of physicians, the in-person meeting of experts, and the qualitative research with patients all helped generate an extensive list of candidate domains and sub-domains to consider for use in clinical trials. It also become clear that there was a need and strong interest in delineating domains across the several major organ systems involved in this disease and in recognizing that clinical trials in BS often focus on specific manifestations and not the disease in its entirety. The Delphi involved 74 physicians expert in BS from 21 countries and from a wide range of specialties, and 64 patients from 10 countries. The Delphi utilized both ratings and rankings to prioritize the 56 domains and sub-domains originally under consideration.
The final proposed Core Set included 5 sub-domains mandatory for study in all trials in BS, with additional sub-domains mandatory for study of specific organ-systems when that system is the focus of a trial: mucocutaneous (2 additional sub-domains), ocular (4), central nervous system (3), musculoskeletal (2), vascular (4), and gastrointestinal (2). The final Core Set was strongly endorsed at the 2018 OMERACT meeting.
Conclusion: Multiple disease-related domains in BS have been identified by physicians and patients as important to address in clinical trials, leading to the development and endorsement of a final Core Set of Domains for use in clinical trials in BS. The Core Set provides the foundation through which the international research community, including clinical investigators, patients, the biopharmaceutical industry, and government regulatory bodies can harmonize the study of this complex disease, compare findings across studies, and advance development of effective agents.
Disclosure of Interests: : Gulen Hatemi Consultant for: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Alexa Meara: None declared, Yesim Ozguler: None declared, Haner Direskeneli: None declared, Alfred Mahr: None declared, Beverley Shea: None declared, Esen Cam: None declared, Ahmet Gül: None declared, Yusuf Yazici Shareholder of: Samumed, LLC, Consultant for: Celgene Corporation, BMS, Genentech, Sanofi, Employee of: Samumed, LLC, Peter Tugwell: None declared, Hasan Yazici: None declared, Peter Merkel: None declared
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THU0304 PREVALENCE AND MANAGEMENT OF CARDIOVASCULAR RISK FACTORS IN ANCA-ASSOCIATED VASCULITIS: A CROSS-SECTIONAL STUDY IN THE NETHERLANDS AND CANADA

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Background: Patients with ANCA-associated vasculitis (AAV) are at increased risk of cardiovascular (CV) disease.(1)
Objectives: The aim of the present study was to determine the prevalence of CV risk factors in patients with AAV and to evaluate the management of CV risk factors according to current guidelines.
Methods: A cross-sectional study was performed in patients with AAV in the Netherlands and Canada. Information on traditional CV risk factors, as well as markers of inflammation and kidney function, were collected. Their prevalence and treatment were studied and compared with recommendations in current guidelines.
Results: A total of 144 consecutive patients with AAV were included (71 from the Netherlands; 73 from Canada). Mean age was 62 ± 15 years, and 56% were male. The mean disease duration was 7.0 ± 6.6 years; 69% had granulomatosis with polyangiitis, 17% microscopic polyangiitis and 14% eosinophilic granulomatosis with polyangiitis. Mean body mass index was 28 ± 6 kg/m^2 and 65 patients (45%) had an estimated glomerular filtration rate <60 ml/min. The mean C-reactive protein was 6.5 ± 12.3 mg/l. Dyslipidemia was present in 69% and hypertension in 72%. In 36% and 25% of the included patients, blood pressure and dyslipidemia, respectively, were not managed in accordance with national guidelines.
Conclusion: Patients with AAV have a high prevalence of traditional CV risk factors. Whether past or persistent inflammation and chronic kidney disease further increases the CV risk remains to be studied. Strict adherence to CV risk management guidelines should be encouraged.

REFERENCE:
[1] Houben E, Penne EL, Voskuyl AE, van der Heijden JW, Otten RHJ, Boers M, et al. Cardiovascular events in anti-neutrophil cytoplasmic antibody-associated vasculitis: a meta-analysis of observational studies. Rheumatology (Oxford) 2018; 57: 555-62.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.704

THU0305 ABSTRACT WITHDRAWN

THU0306 NEUTROPHIL ADHESION MOLECULES AND INFLAMMATORY CYTOKINES AS BIOMARKERS FOR MONITORING DISEASE PROGRESSION IN GIANT CELL ARTERITIS

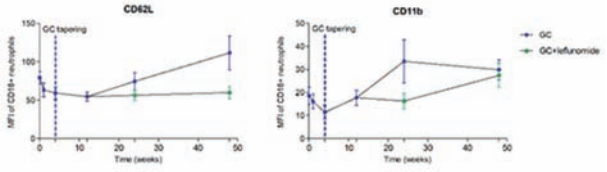
Tadeja Kuret[1,2], Katja Lakota[1,3], Gerhard Thallinger[4,5], Polona Zigon[1], Sasa Cucnik[1,2], Matija Tomsic[1,6], Snežna Sodin-Šemrl[1,3], Alojzija Hocevar[1]. [1]*University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia*; [2]*University of Ljubljana, Faculty of Pharmacy, Ljubljana, Slovenia*; [3]*University of Primorska, FAMNIT, Koper, Slovenia*; [4]*Graz University of Technology, Institute of Computational Biotechnology, Graz, Austria*; [5]*BioTechMed Graz, OMICS Center Graz, Graz, Austria*; [6]*University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia*

Background: Monitoring giant cell arteritis (GCA) activity with appropriate biomarkers is important, as current evaluation, based mainly on clinical symptoms/signs and traditional markers of inflammation, is not always sufficient and reliable.
Objectives: Our goal was to identify cellular and molecular biomarkers that could help clinicians to closely monitor GCA progression and/or treatment response.
Methods: Peripheral blood was obtained from 27 GCA patients at time of diagnosis (before glucocorticoid (GC) treatment), and subsequently at

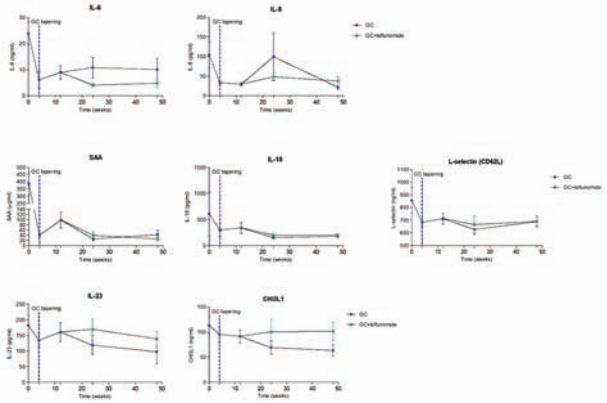
weeks 1, 4, 12, 24 and 48 of follow-up (FU). At diagnosis, all patients received GC in line with EULAR recommendations with a slow GC tapering starting after week 4. At week 12, some of the patients (16/27) received additionally leflunomide (10 mg). Whole blood samples were stained, lysed, fixed and analyzed by flow cytometry. The expression of adhesion molecules (CD62L, CD11b) was determined on neutrophils. Sera levels of serum amyloid A (SAA) and IL-6 were measured by nephelometry and ELISA, respectively. Levels of IL-8, IL-18, IL–23, L-selectin and CHI3L1 were determined by MagPix using human pre-mixed multi-analyte kits.

Results: At weeks 1 and 4 of FU we detected a decrease in neutrophil expression of CD62L and CD11b, as well as in sera levels of SAA, IL-6, IL-8, IL-18, L-selectin and CHI3L1 in all GCA patients. At week 12 (8 weeks after GC tapering) an elevation of CD11b, SAA, IL-6 and IL-23 as compared to week 4 was observed (Figures 1 and 2). At weeks 24 and 48 of FU we identified four different groups of biomarkers. The first group consisted of neutrophil CD62L ($p<0.05$) and serum IL-6, that showed a marked increase in patients receiving GC therapy only, while decreasing in patients receiving GC in combination with leflunomide. The second group is represented by neutrophil CD11b and serum IL-8 that were higher at week 24 in the GC-treated group (the first FU after receiving leflunomide), however their levels were equal at week 48 in both groups of GCA patients (Figures 1 and 2). In the third group, the serum levels of SAA, IL-18 and L-selectin decreased at week 24 and remained stable through week 48, regardless of therapy used. The fourth group of biomarkers included serum IL-23 and CHI3L1, levels of which declined at weeks 24 and 48 in patients receiving GC only and substantially increased in patients receiving leflunomide and GC (Figure 2).

Conclusion: Neutrophil surface markers CD62L and CD11b together with inflammatory parameters (SAA, IL-6, IL-8 and IL-23) could represent informative biomarkers for monitoring disease progression in GCA patients. Important biomarker differences were observed between GC-treated GCA patients, in the presence and absence of leflunomide, serving as a good basis for predicting relapses.



Abstract THU306 – Figure 1. Longitudinal L-selectin (CD62L) and integrin αM (CD11b) surface expression on neutrophils from GCA patients at T0 (prior to therapy) and 1, 4, 12, 24 and 48 weeks after therapy. Shown is mean±SEM. At week 12, 16/27 GCA patients received leflunomide, in addition to GC therapy.



Abstract THU306 – Figure 2. Serum levels of IL-6, IL-8, SAA, IL-18, L-selectin, IL-23 and CHI3L1 in longitudinally followed GCA patients at T0 (prior to therapy) and 4, 12, 24 and 48 weeks after therapy. Shown is mean±SEM. At week 12, 16/27 GCA patients received leflunomide, in addition to GC therapy.

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THU0307 THE HALO SIGN IN THE EMERGENCY DEPARTMENT: COMPLEMENTARY VALUE TO THE APPLICATION OF THE CRITERIA FOR THE CLASSIFICATION OF GIANT CELL ARTERITIS IN AN ACUTE ENVIRONMENT

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Background: In a previous study (Acta Reum 2018; Vol.4.No.1:5), we identified the low diagnostic value of the criteria for classification of giant cell arteritis (GCA) in patients with such suspicion in an emergency setting of a third level hospital. In some emergency units, linear probe ultrasound equipment is available for immediate use. It would be of interest to determine whether the training of healthcare personnel in halo sign recognition could be useful in addition to the CGA criteria in situations of suspicion.

Objectives: We present a sub-study in which we incorporate the ultrasound study of temporal atheria (TA) as an added criterion to determine its contribution in terms of diagnostic validation.

Methods: We reviewed the casuistry of patients who consulted the emergency department with different combinations of the rest of the ACG classification criteria, included in the aforementioned study. The entry requirements were: Age > 40 years and headache as a reason for consultation. We identified those patients who underwent temporal artery ultrasound during assessment before receiving corticoid therapy. The pattern of comparison was the definitive diagnosis of ACG (biopsy).

Results: Thirty cases of ACG were identified by compatible biopsy that had an ultrasound study of AT in the emergency department. On the other hand, 47 ultrasound AT studies were identified in patients who were not finally diagnosed with ACG. All included records were distributed between 2012 and 2016. Ultrasound exploration of positive AT was understood as that with 2 or more branches with positive halo sign (Sifuentes, Ann Rheum Dis 2013-eular- OP0208). Tables 2x2 were elaborated to establish the results of the validation test with three and four ACG classification criteria. One patient was identified with the combination of criteria: cephalea + VSG > 50mm/h + Alt. of the exploration of the AT and 4 with cephalea + Age > 50 years + Alt. of the exploration of the AT. Of these patients, only one had ultrasound study of AT so they were excluded from the study. With 4 criteria + halo sign (+), an S of 93.3% and NPV of 93.3% was achieved; with 3 criteria + halo sign (+) an S of 83.3% and NPV of 93.7% was achieved. The attached table shows all the results of the validation test.

Abstract THU0307 –Table 1.

CRITERIA COMBINATION	SENSITIVITY	SPECIFICITY	PPV	NPV
HEADACHE + AGE > 50 YEARS + ESR > 50 + TEMPORAL ARTERY ANORMALITY	94.1%	35.4%	56.2%	93.6%
4 CRITERIA + HALO (+)	82.3%	93.3%	93.3%	82.3%
HEADACHE + AGE > 50 YEARS + ESR > 50MM/H	96.9%	25.7%	38.3%	94.5%
3 CRITERIA + HALO (+)	76.9%	93.7%	83.3%	90.9%

Conclusion: Although the application of the GCA classification criteria has insufficient specificity and low positive predictive value, when adding the ultrasound study of TA, specificity exceeds 93% and PPV exceeds 93% when combined with 4 criteria and 83% when combined with 3 criteria. Although our results should be supported by a larger sample size, our findings assume that the routine use of this technique would contribute to improving the diagnostic accuracy of this disease and our ability to initiate treatment in a more timely manner.

Disclosure of Interests: None declared
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THU0308 ASSESSMENT OF SEXUAL AND PSYCHOLOGICAL STATES OF BEHÇET'S DISEASE MALE PATIENTS

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Background: Behçet's disease (BD) is a chronic multisystem autoimmune disease characterized by orogenital ulceration, uveitis, skin lesions and vascular involvement of different organs in the body. The sexual and psychological aspects of the disease are still not fully recognized.

Objectives: We aimed to evaluate the sexual and psychological status of BD male patients and to assess the relationship between the sexual function and depression in this cohort.

Methods: The patients, fulfilling the International Criteria for Behçet's disease (ICBD), and healthy controls, of a comparable age, were evaluated in the Rheumatology and Urology Clinics. The demographic and clinical data was collected. Disease activity of the patients was assessed using Behçet's Syndrome Activity Score (BSAS). For both groups, the sexual function and the psychological status were evaluated using the International Index of Erectile Functions (IIEF- 5) and the Beck Depression Inventory (BDI), respectively. Spearman's rho, Chi-Square and Mann-Whitney U tests were used as appropriated.
Results: The number of BD patients was 26 and that of the controls was 27. The mean age of the patients was 36±7.4 and that of controls was 40.9±5.2. Though BD patients were younger in age they exhibited significantly lower scores in sexual function, and scored higher in depression as illustrated in **Table 1**.

Abstract THU308 – Table 1. Demographic and clinical data of the participants

	Patients (n=26)	Controls (n=27)	P value
Smoking, n (%)	8 (30.8%)	4 (14.8%)	0.4
Disease duration (years), mean ± SD	4.2±1.9	NA	NA
Erectile dysfunction (IIEF-5 score), median (Interquartile range)	15 (9-20)	20 (20-25)	<0.001*
Depression score (Beck questionnaire), median (Interquartile range)	13 (9-18)	9 (7-14)	0.039*

There were no associations between the disease duration, smoking status or different clinical phenotypes and the sexual or psychological functions. However, there was an inverse relationship between BSAS and the sexual function (rho= -.443, p=.024). The duration of corticosteroids intake was negatively correlating with the sexual function (rho= -.604, p= .001) as well. The depression scores correlated significantly with the presence of inflammatory back pain (rho= .413, p=.036).
There was no association between the severity of sexual dysfunction and that of depression. The patients showed different degrees of depression, and there was a tendency towards increased rates of erectile dysfunction in all groups as shown in **Table 2**.

Abstract THU308 – Table 2. Correlation of IIEF-5 and BDI

Sexual function (IIEF-5 score)	Beck Depression Inventory (BDI)			Total	P value
	Minimal (n=14)	Mild (n=7)	Moderate (n=5)		
No ED or Mild ED ≥ 17, n (%)	4 (28.6%)	3 (42.9%)	2 (40%)	9	0.78
ED ≤ 16, n (%)	10 (71.4%)	4 (57.1%)	3 (60%)	17	

ED; erectile dysfunction.
Conclusion: BD has a negative impact on men's psychological state and sexual function. Severe disease states, evident in the long duration of corticosteroids use and the high activity scores, are linked to sexual dysfunction.
Disclosure of Interests: None declared
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THU0309 NONLINEAR PHARMACOKINETICS OF RITUXIMAB IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS

Denis Mulleman[1,2], Amina Bensalem[1], David Ternant[1,3], Gilles Paintaud[1,3], Divi Cornec[4,5], Ulrich Specks[6], The rituximab vs cyclophosphamide for ANCA-associated vasculitis (RAVE) trial. *[1]University of Tours, EA 7501 GICC, Tours, France*; *[2]CHRU de Tours, Service de Rhumatologie, Tours, France*; *[3]CHRU de Tours, Laboratoire de Pharmacologie-Toxicologie, Tours, France*; *[4]University of Brest, Inserm UMR1227 LBAI, Brest, France*; *[5]CHRU de Brest, Service de Rhumatologie, Brest, France*; *[6]Mayo Clinic, Division of Pulmonary and Critical Care Medicine, Rochester, United States of America*

Background: Rituximab (RTX) was approved in patients with anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV).
Objectives: To describe the pharmacokinetics of rituximab in AAV patients and to explore its sources of variability
Methods: Rituximab pharmacokinetics was described in 92 AAV patients from the RAVE trial (rituximab for ANCA- associated vasculitis) using a population modeling approach. A semi-mechanistic model including a latent target antigen turnover allowed the estimation of specific target-mediated elimination of rituximab in addition to its non-specific elimination. Sex, body surface area (BSA), BVAS/WG score, and status newly diagnosed on pharmacokinetic parameters were investigated as covariates.
Results: A two compartments model including target mediated elimination best described rituximab pharmacokinetics. The mean (interindividual standard deviation) estimated central volume of distribution was 3.06 L (2.61%), systemic clearance was 0.135 L $days^{-1}$ (6.43%), and target-mediated elimination rate constant was 19.13 x 10^{-6} $nmol^{-1}$ $days^{-1}$(fixed to 0). The initial activity of the disease was higher in male than in female (p=4.09 x 10^{-14}), and in patients newly diagnosed at inclusion (p=7.91 x 10^{-5}). Moreover, systemic clearance was slightly lower in granulomatosis with polyangiitis group than in other AAV groups (p=3.6 x 10^{-3}). Neither BVAS/WG score nor BSA were significant covariates in a multivariate analysis.
Conclusion: We report a nonlinear target-mediated elimination of rituximab in AAV patients. Granulomatosis with polyangiitis patients have a lower global clearance of rituximab than other AAV groups. Our study not support the utility of BSA based individualized dosing protocols, as previously reported (1).

REFERENCE:

[1] Cornec D, *et al.* Pharmacokinetics of rituximab and clinical outcomes in patients with anti-neutrophil cytoplasmic antibody associated vasculitis. Rheumatology. 2018;57:639-50.

Disclosure of Interests: Denis Mulleman Speakers bureau: Pfizer, Novartis, Grifols, Amina Bensalem: None declared, David Ternant Speakers bureau: Sanofi, Amgen, Gilles Paintaud Grant/research support from: Novartis, Roche Pharma, Sanofi-Genzyme, Chugai, Pfizer and Shire, Divi Cornec: None declared, Ulrich Specks: None declared
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THU0310 OPTIMAL INITIAL DOSE OF GLUCOCORTICOID FOR ELDERLY-ONSET ANCA ASSOCIATED VASCULITIS: SAFTY OUTCOME ANALYSIS OF TWO NATIONWIDE, PROSPECTIVE, INCEPTION COHORT STUDIES

Keiji Ohashi[1], Kenei Sada[1], Yosuke Asano[1], Keigo Hayashi[1], Sumie Hiramatsu Asano[1], Yuriko Yamamura[1], Michiko Morishita[1], Haruki Watanabe[1], Mariko Narazaki[1], Yoshinori Matsumoto[1], Tomoko Kawabata[1], Jun Wada[1], Masayoshi Harigai[2], Hirofumi Makino[3], On behalf of Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis Syndrome (JPVAS). *[1]Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama, Japan*; *[2]School of Medicine, Tokyo Women's Medical University, Department of Rheumatology, Tokyo, Japan*; *[3]Okayama University, Okayama, Japan*

Background: Glucocorticoid (GC) is still the mainstay of treatment for antineutrophil cytoplasmic antibody (ANCA) -associated vasculitis (AAV) while GC use, disease severity, and older age are risk factors for accrual of damage and infection in AAV[1)2)].
Objectives: To explore optimal initial dose of GC for patients with elderly-onset AAV based on safety outcome analysis using data from two nationwide prospective inception cohort studies (RemIT-JAV and RemIT-JAV-RPGN).
Methods: RemIT-JAV and RemIT-JAV-RPGN enrolled consecutive patients with newly diagnosed AAV fulfilling the criteria for primary systemic vasculitis as proposed by the European Medicines Agency algorithm and requiring immunosuppressive treatment. From the cohort studies, elderly-onset (≥65 years) patients with microscopic polyangiitis and granulomatosis with polyangiitis, classified as generalized or severe disease type according to the European Vasculitis Study Group-defined disease severity, were enrolled in this analysis. The primary outcome measures were Vasculitis Damage Index (VDI) at 24th month and serious infections during 2 years after starting treatment for AAV. The patients were divided into three groups based on initial dose of GC: high-dose (HD) group, prednisolone (PSL) ≥0.8 mg/kg/day; medium-dose group (MD), 0.6≤ PSL <0.8 mg/kg/day; low-dose (LD) group, PSL <0.6 mg/kg/day. The VDI were classified into treatment-related VDI[1)] and disease-related VDI

(excluding treatment-related VDI from total VDI). We evaluated associations between initial GC dose and the primary outcomes.
Results: Of 477 patients registered in the original cohort studies, 161 patients were enrolled in the present study. Mean age (± SD) were 74 (± 5) in HD group, 74 (± 5) in MD group, and 78 (± 6) years in LD group, respectively. There was no significant difference in sex, disease severity, type of ANCA, C-reactive protein levels at baseline, Birmingham Vasculitis Activity Score at baseline, remission rates, and relapse rates. HD group exhibited significantly lower creatinine levels at baseline than MD and LD groups (216 ± 207 in HD, 339 ± 263 in MD, 331 ± 301 μmol/L in LD, respectively; p = 0.0012). Proportion of concomitant cyclophosphamide use during 90 days after starting treatment for AAV decreased (58% in HD, 36% in MD, and 15% in LD, respectively; p <0.0001) while disease activity-related VDI at 24th month increased (2.09 ± 1.39 in HD, 2.54 ± 1.16 in MD, and 2.83 ± 1.60 in LD, respectively; p = 0.018) as the initial GC dose went down. HD group developed serious infections more frequently than MD and LD groups (25/65 [38%] in HD, 10/50 [20%] in MD, 9/46 [20%], respectively; p = 0.033).
Conclusion: Based on safety outcome analysis, 0.6 ≤ PSL <0.8 mg/kg/day might be optimal initial dose of GC for treatment of elderly-onset patients with AAV.

REFERENCES:

[1] Robson J, et al. Rheumatology (Oxford). 2015 Mar;54(3):471-81.
[2] Watanabe-Imai K, et al. Mod Rheumatol. 2017 Jul;27(4):646-651.

Disclosure of Interests: Keiji Ohashi: None declared, KENEI SADA Speakers bureau: Ken-Ei Sada received speaker honoraria from Chugai., Yosuke ASANO: None declared, Keigo Hayashi: None declared, Sumie Hiramatsu Asano: None declared, Yuriko Yamamura: None declared, Michiko Morishita: None declared, Haruki Watanabe: None declared, Mariko Narazaki: None declared, Yoshinori Matsumoto: None declared, Tomoko Kawabata: None declared, Jun Wada Grant/research support from: Jun Wada received grant support from Astellas, Bayer, Chugai, Daiichi Sankyo, Kissei, Kyowa Hakko Kirin, MSD, Otsuka, Teijin, Torii, Pfizer, Takeda, and Taisho Toyama., Speakers bureau: Jun Wada received speaker honoraria from Astellas, Boehringer Ingelheim, Novartis, and Tanabe Mitsubishi., masayoshi harigai Grant/research support from: Tokyo Women's Medical University (TWMU) has received unrestricted research grants for
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THU0311 PERSISTENT LOW-GRADE VASCULAR INFLAMMATION IN LARGE VESSEL VASCULITIS: A LONGITUDINAL STUDY USING FULLY INTEGRATED 18F-FDG PET/MR

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Background: Persistent low-grade vascular inflammation in large vessel vasculitis (LVV) treated patients could represent the expression of persistent subclinical disease activity or post-inflammatory vascular remodelling. Whether these findings have any impact on future vascular outcomes is still an unmet need[1].
Objectives: To evaluate the frequency and evolution of the low-grade vascular inflammation using a fully integrated 18F-FDG PET/MR in a longitudinally followed cohort of LVV patients.
Methods: All consecutive patients with LVV who underwent at least 2 PET/MR scans (median time 9[6] months) between January 2015 and January 2019 were included. For each scan vessel's metabolic activity was assessed using the Meller's grading and the standard uptake value[2]. Low-grade inflammation was defined as Meller 1 and 2 (inferior or equal to liver), as previously reported. Demographic and clinical data, as well as disease remission or flares, were recorded and compared to vascular metabolic activity.
Results: In total, 107 PET scans were performed (from min. 2 scans to max. 5 scans per patient), mainly during follow-up (78.8%) in 33 LVV patients (72.7% GCA, 27.3% TAK), predominantly female (84.8%), with a regular BMI (24.1[5.3]) and with a long-standing disease (30[29] months).
At PET examination, low-grade metabolic activity was reported in 60% of the cases (86.4% GCA and 13.6% TAK), while complete remission in 15% and highly pathological in 25%. Comparing patients with low-grade vascular inflammation to those with complete remission (Meller 0), they resulted significantly older (64[12] vs 57[33] years, p=0.005), with a lower disease duration (26.5[21.4] vs 52.5[34.8] months, p=0.001) and with higher daily prednisone dosage, but without significance (5[7.5] vs 2.5 [8.75], p=0.096). No significant differences were noted in acute phase reactants and type of treatment. Moreover, when compared to those with high metabolic activity (Meller 3), patients with low-grade inflammation resulted significantly older (64[12] vs 62[25] years, p=0.025), with a lower disease duration (26.5[21.4] vs 33[46] months, p=0.041), lower CRP level, but without significance (3.05[5.92] vs 10.35[13.75], p=0.069). Clinical remission, before PET examination, was registered in 55.6% of patients with Meller 3 activity, significantly lower compared to those with Meller 1 +2 (87.5%, p=0.002). Steroids and immunosuppressants tapering rate did not differ between patients with low-grade metabolic activity and those without activity.
Among all patients with low-grade vascular inflammation, 60% underwent to steroids or immunosuppressants tapering. At the subsequent PET examination, a persistence/worsening of metabolic activity was found in 88.9% of them. Change or increase of the treatment regimen led to an improvement (complete remission) in 58.9% of the cases. Low-grade metabolic activity was associated with a significant increased risk of worsening/flare at the subsequent PET examination (RR 5.29[1.87-16.11], p=0.002).
Conclusion: Low-grade vascular inflammation at PET examination is a common feature in LVV treated patients, especially GCA. It is significantly associated with an older age, lower disease duration and clinical remission. However, steroids or immunosuppressants tapering is these patients is associated with an increased risk of worsening/flare. Further research is urgently needed to address this issue.

REFERENCES:

[1] Dejaco C, et al. Ann Rheum Dis 2018.
[2] Meller J, et al. Eur. J. Nucl. Med. Mol. Imaging, 2003.

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THU0312 ADVENTITIAL FIBROBLAST, AN IMPORTANT PLAYER IN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a systemic vasculitis affecting large vessels. The diagnosis is based on the temporal artery biopsy (TAB) which shows a segmental and focal arterial infiltration composed of CD4 T cells and macrophages. It is accompanied by a destruction of the internal elastic layer of the media and a hyperplasia of the intima by proliferation of myofibroblasts (Weyand). The origin of these myofibroblasts is controversial (Ly). Evidences suggest the activation of adventitial fibroblasts into myofibroblasts and their migration into the intima (Stenmark).
Objectives: The objective of this study was to determine whether adventitial fibroblasts migrate to the intima and thereby contribute to intimal hyperplasia during CGA.
Methods: Arterial sections from TAB of patients with GCA (n=24) and control subjects (n=24) were analyzed. Immunohistochemical analysis was

performed using antibodies directed against fibroblasts (CD90, vimentin), myofibroblasts (alpha smooth muscle actin {ASMA}) and vascular smooth muscle cells (desmin). Staining of prolyl-4-hydroxylase (P4H) and myosin were also performed. Stainings were quantified using the ODPviewer® software (Kamax Innovative System, France) by two double-blind observers. Moreover, co-expression of CD90 with different stainings (ASMA, myosin and P4H) was also performed. Cells in culture were identified by immunocytochemistry using anti-CD90 and markers of activity such as myosin and P4H. Functional assays were performed using culture cells obtained from GCA patients' BATs (n=4) and controls (n=4). The BATs were dissected to separate the adventitia from the other two layers. Each dissected fragment was seeded separately. The proliferation was studied using a bromodeoxyuridine incorporation test under different conditions: DMEM, fetal calf serum (FCS), PDGF and supernatants of cells in culture. The study of migration was performed using a scratch test under the same conditions.

Results: CD90 was significantly higher in GCA than controls in adventitia and intima. Vimentin and ASMA were significantly higher in the 3 tunics of patients with GCA. Expression of desmin was only present in the media for both groups with no significant difference. P4H was present in adventice significant differences between both groups. The adventitial and intimal CD90+ cells co-expressed P4H, ASMA and myosin more importantly during GCA. Cultured cells from BATs' adventices expressed CD90 and did not express desmin. These cells had a greater myosin staining during GCA and had an increased proliferation ability during GCA in the presence of FCS, PDGF and fibroblast supernatants of control or GCA patients. The migration rates of these cells were also significantly increased during GCA in the presence of FCS or PDGF.

Conclusion: Vascular remodeling during GCA would start in the adventitial layer with a key role of fibroblasts. Adventitial fibroblasts could be activated into myofibroblasts and acquire proliferative and migratory abilities. They would participate in the intimal hyperplasia, responsible for ischemic complications. Their inhibition could be a therapeutic way to limit these complications. The activating signal of adventitial fibroblasts into myofibroblasts is not yet known during GCA and requires further studies.

REFERENCES:

[1] Weyand, C.M., Goronzy, J.J., (2014). Clinical practice. Giant-cell arteritis and polymyalgia rheumatica. N Engl J Med. 371, 50-7.
[2] Ly, K.H., Liozon, E., Fauchais, A.L., Vidal, E., (2013). Pathophysiology of giant cell arteritis. Rev Med Interne. 34, 392-402.
[3] Stenmark, K.R., Yeager, M.E., El Kasmi, K.C., Nozik-Grayck, E., Gerasimovskaya, E.V., Li, M., Riddle, S.R., Frid, M.G., (2013). The adventitia: essential regulator of vascular wall structure and function. Annu Rev Physiol. 75, 23-47.

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THU0313 COMPARATIVE STUDY OF CLINICAL, ANALYTICAL AND VASCULAR 18F-FDG UPTAKE EVOLUTION IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH METHOTREXATE VS TOCILIZUMAB

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Background: Glucocorticoids remain to be the cornerstone therapy in giant cell arteritis (GCA). However, relapses are common when the prednisone dose is tapered. Thus, additional therapies are required in relapsing GCA. The most widely used conventional immunosuppressive drug is methotrexate (MTX) which efficacy is modest. Consequently, in some cases biological therapy in needed. Among them, the most frequently used is the recombinant humanized anti-IL6 receptor antibody tocilizumab (TCZ).[1]

Objectives: To compare clinical evolution, normalization of acute phase reactants and normalization of vascular ^{18}F-FDG uptake assessed by PET/CT in patients with GCA treated with MTX vs TCZ.

Methods: Comparative multicentric study of 23 patients with GCA treated with MTX vs 36 patients with GCA treated with TCZ who had a baseline and follow-up PET/CT scan. We assessed clinical improvement (no improvement/partial/complete), normalization of acute phase reactants (CRP ≤ 0.5mg/dL and/or ESR ≤ 20 mm/1st hour) and reduction of ^{18}F-FDG uptake in PET/CT (no reduction/partial/complete normalization). Images were evaluated qualitatively by experienced nuclear medicine physicians. Prednisone tapering was also assessed. Statistical analysis was performed with SPSS. Student´s t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher´s exact test for categorical variables as appropriate.

Results: We included 23 patients with GCA treated with MTX (20 women/3 men); mean age 65.6 ± 7.9 years; and 36 patients treated with TCZ (27 women/9 men); mean age 67.5 ± 8.3 years. Clinical, analytical and vascular ^{18}F-FDG uptake evolution is shown in the TABLE. After one year of treatment, the percentage of patients who experienced complete clinical improvement was higher in those who received TCZ (88.9% vs 44.4%; p=0.003). Normalization of acute phase reactants was also more frequent in patients who received TCZ (92.6% vs 47.6%; p=0.001). In regard with reduction of vascular ^{18}F-FDG uptake, complete normalization was only achieved in 25% of patients who received TCZ and 14.3% of those who received MTX.

Conclusion: Patients with GCA who received TCZ experienced a more rapid and effective clinical and analytical improvement than patients who received MTX. Besides, prednisone tapering was quicker in patients with TCZ. However, no significant differences were found in complete normalization of ^{18}F-FDG vascular uptake between both treatments.

Abstract THU0313 –Table 1.

TABLE

	MTX (n=23)	TCZ (n=36)	P
Age, *mean ± DS*	65.6 ± 7.9	67.5 ± 8.3	0.39
Sex (woman), *n (%)*	20 (87.0)	27 (77.1)	0.50
Complete clinical improvement, *n/N (%)*			
- 6 months	9/23 (39.1)	28/35 (80.0)	0.002
- 12 months	8/18 (44.4)	24/27 (88.9)	0.003
- 18 months	7/11 (63.6)	21/22 (95.4)	0.03
- 24 months	7/9 (77.8)	17/18 (94.4)	0.25
Normalization of ESR and/or CRP, *n/N (%)*			
- 6 months	6/23 (26.1)	30/35 (85.7)	< 0.01
- 12 months	10/21 (47.6)	25/27 (92.6)	< 0.01
- 18 months	10/11 (90.9)	23/23 (100.0)	0.32
- 24 months	9/9 (100.0)	19/19 (100.0)	0.99
Normalization of ^{18}F-FDG PET/CT, *n/N (%)*			
- 6 months	0/11 (0.0)	0/8 (0.0)	0.99
- 12 months	0/14 (0.0)	3/13 (23.0)	0.10
- 18 months	0/5 (0.0)	3/11 (27.3)	0.51
- 24 months	1/7 (14.3)	1/4 (25.0)	0.99
Dose of Prednisone (mg/day), *median [IQR]*			
- 6 months	7.5 [5.0-15.0]	5.0 [0.3-5.0]	< 0.01
- 12 months	5.0 [5.0-10.0]	0.0 [0.0-5.0]	< 0.01
- 18 months	5.0 [3.0-6.0]	0.0 [0.0-3.3]	0.03
- 24 months	2.5 [0.0-3.0]	0.0 [0.0-0.0]	0.07

REFERENCE:

[1] M. Calderón-Goercke et al. Tocilizumab in giant cell arteritis. Observational, open-label multicenter study of 134 patients in clinical practice. Semin Arthritis Rheum. (2019). doi: 10.1016/j.semarthrit.2019.01.003. [Epub ahead of print])

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THU0314 OUTCOMES OF PATIENTS TREATED WITH TOCILIZUMAB OR ABATACEPT AS STEROID-SPARING AGENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a common form of systemic vasculitis. The current mainstay of GCA management is glucocorticoid (GC) therapy. Recently, at least 2 biological therapies [tocilizumab (TCZ) and abatacept (ABA)] have been proven to be effective in the management of CGA in randomized controlled trials. Nevertheless, their use as steroid sparing agents might need further investigation.

Abstract THU0314 –Table 1.

Table 1. Characteristics of the patients included in the study

	Total number of patients (33)	%
Demographic characteristics		
Female/Male	21/12	
Age (years) (mean, SD)	73.6 ±8.7	
Clinical characteristics at the onset of GCA		
Fever (n)	12	36.4
Fatigue (n)	18	54.5
Headache (n)	28	84.8
Scalp tenderness (n)	8	24.2
Jaw claudication (n)	15	45.4
Vision loss (n)	16	48.5
PMR (n)	11	33.3
Diagnosis		
Biopsy proven	27/32	84.4
PET positivity	12/29	41.4
Eco-color-doppler positivity	30/31	97
GC therapy		
Previous methylprednisolone pulses (n)	7	21.2
Oral prednisone (n)	33	100
Dose of oral prednisone (mg/day) (mean, SD)	49.7 ±15.1	
Previous immunosuppressive therapies		
Methotrexate (n)	11	33.3
Mean dose (mg/week) (mean, SD)	15.6 ±1.7	
Mycophenolate (n)	6	18.1
Mean dose (g/day) (mean, SD)	2.2 ±0.4	

Objectives: We aimed to investigate the steroid-sparing effect of biological therapies, namely TCZ and ABA, in a cohort of GCA patients when compared to standard GC treatment.

Methods: We retrospectively collected data from GCA patients who attended the S.G. Bosco Hospital, Turin, Italy, who were treated with TCZ, both intravenous (IV) and subcutaneous (SC), and/or ABA SC (8 mg/kg/month, 162 mg/week, and 125 mg/week respectively). These therapies were prescribed as first line agents or as second line when patients were refractory/intolerant/contraindicated to standard immunosuppressive therapies. Complete response to the treatment was define as a clinical and serological remission after 12 months of therapy; partial response was defined as clinical or serological remission after 12 months of therapy.

Results: This retrospective study included 33 GCA patients [mean age 74 (range 85-57), females 63%, mean follow-up from GCA diagnosis 44.4 ±33.5 months). Table 1 resumes the characteristics of the GCA patients included in the study.

Twenty-eight patients out of 33 (85%) received one biologic agent. Five patients (15%) needed a therapeutic switch (one patient from TCZ to ABA, and 4 patients from ABA to TCZ). Patients were treated as follow: 9 with TCZ IV, 11 with TCZ SC, and 18 with ABA. Among the TCZ IV group, all patients experienced a response (57% complete response, and 43% partial response). Among the TCZ SC group, 83% experienced a response (67% complete response, and 16% partial response). Among the ABA group, 86% experienced a response (36% complete response and 50% partial response). After 12 months of therapy, 100% of patients in TCZ groups, both IV and SC, and 64.2% of ABA group were treated with low doses of oral prednisone (≤ 7.5 mg/day) as maintenance. We noticed a significant reduction of inflammatory parameters [C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)] after 12 months of therapy with TCZ [TCZ IV group: mean baseline CRP (mg/dl) 1.9±2.3, mean CRP after 12 months of therapy 0,3±0.2; mean baseline ESR (mm/h) 58.1±25.6, mean ESR after 12 months 9.5±4.2; TCZ SC group: mean baseline CRP 4.5±3.8, mean CRP after 12 months 0.2±0.2; mean baseline ESR 51.9±27, mean ESR after 12 months 6.5±6]. When compared to standard GC regimen [1], in patients treated with TCZ, both IV and SC, we estimated a median steroid-sparing effect quantifiable in 30 mg/daily in the first month and an overall steroid-sparing effect of 15 mg/daily when assessed in 12 months.

Conclusion: This retrospective study confirms the efficacy of biological therapies in the management of CGA. Besides, in our experience TCZ allowed a significant reduction of GCs use, especially in the first month of therapy, when compared to standard GCs based regimens.

REFERENCE:

[1] Dasgupta B, et al. BSR and BHPR Standards, Guidelines and Audit Working Group. BSR and BHPR guidelines for the management of giant cell arteritis. Rheumatology. 2010 Aug;49(8):1594-7.

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THU0315 SEVERITY AND RESPONSE TO INDUCTION THERAPY IN NEW AND RELAPSING ANCA ASSOCIATED VASCULITIS PATIENTS – REAL WORLD PRACTICE DATA

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Background: ANCA-associated vasculitis (AAV) presents clinically with variable severity of disease and current clinical guidelines give varying advice on initial treatment to induce remission. Achieving remission quickly is important to gain disease control and avoid cumulative organ damage from treatment related adverse events.

Objectives: This study examined real world practice of AAV treatment in Europe to understand the AAV severity spectrum and the response to therapy over 12 months.

Methods: 929 incident and 268 relapsing EU AAV patients receiving care from 399 physicians were studied. Patients were referred between 2014-17 and data collected retrospectively at baseline and 1, 3, 6 and 12 months following induction therapy. Birmingham Vasculitis Activity Score (BVAS) was collected in only 12% of patients and severity was defined as mild (localized disease with no systemic symptoms), moderate (Mod, systemic disease with lung and/or kidney involvement) or systemic (rapidly progressive systemic disease with lung and/or kidney involvement).

Results: AAV disease severity varied in both incident (mild 12.2%, moderate 54.3%, severe 33.6%) and relapsing (corresponding values 9.7, 64.6 and 25.7) patients at start of treatment. Comorbidity at time of

Abstract THU0315 –Table 1

	1 month			3 months			6 months			12 months		
	Mild	Mod	Severe	Mild	Mod	Severe	Mild	Mod	Severe	Mild	Mod	Severe
Full	55.3	21.0	13.5	59.4	47.2	28.7	82.6	64.7	45.0	82.8	70.7	53.5
Partial	42.2	74.1	67.9	38.4	48.8	56.8	14.5	32.0	40.6	17.2	26.0	35.7
No	2.5	4.9	18.6	2.2	4.0	14.5	2.9	3.3	14.4	0	3.3	10.8

induction therapy was more common in severe patients (71.8% of patients having at least one comorbidity) compared to mild patients (55.1%). Since BVAS was not measured routinely, clinical response was categorized as full (no vasculitis activity and GC taper on track), partial (reduction in vasculitis activity and major organ damage arrested) and no response (no improvement in vasculitis). Clinical response is presented below (% patients) for combination of incident and relapsing patients demonstrating that response varied with many patients having slow and/or incomplete response. Response varied by severity of the disease when induction therapy commenced.

Conclusion: Incident and relapsing AAV patients have variable disease severity at the time of induction therapy. Response to induction therapy is with few exceptions better in patients with milder AAV but overall many patients are slow to respond or have only a partial response to current induction therapy.

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THU0316 PROTEINASE-3 REGULATING MICRO-RNA IN GRANULOMATOSIS WITH POLYANGIITIS

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Background: Dysregulated miRNA expression profiles have been described in diverse chronic inflammatory diseases. We previously did a microarray screening of 847 miRNAs in nasal tissue from GPA patients and we found a disease associated alteration of miRNA expression compared to healthy controls (HC) and chronic rhinosinusitis (CRS).

Objectives: In order to identify new miRNA targets of potential pathophysiological relevance in GPA, we validated dysregulated miRNAs by qPCR in GPA nasal tissue biopsies and sera. Moreover, we screened GPA associated miRNAs for their potential to regulate proteinase-3 (PRTN3).

Methods: In an independent validation cohort (tissue and sera from 14 GPA-patients, 10 disease controls: CRS and Crohn's/CD) 12 miRNAs were examined by qPCR. Validated and computational miRNA targets were identified by mirDIP algorithms. The inhibitory capacity of miRNAs on Proteinase-3 (PRTN3) was estimated by a dual-luciferase reporter system (Promega®). The 3'UTR-PRTN3 sequence was cloned and inserted into the pmirGlo vector and co-transfected with the hsa-mirna mimics (Dharmacon®) into HeLa cells. As a second method, the effect of miR-184 transfection on the endogenous PRTN3 expression in the human myeloid leukemia cell line HL-60 was estimated by western blot.

Results: Microarray screening revealed alterations of 24 miRNAs in GPA nasal tissue compared to HC and CRS. qPCR confirmed dysregulation of 6 tissue related miRNAs also in GPA sera. Compared to CD 4 miRNAs (miR-10b, -99a/100, -125b, -532–3p) were down regulated in GPA tissue. The miRNA with the highest expression level in nasal tissue from GPA was miR-184. miR-184 along with miR-708 and mir-214-5p were also predicted to target PRTN3 by the mirDIP algorithm. The dual-luciferase reporter assay revealed a significant reduction of PRTN3 expression by miR-184, while these effects could not be observed for miR-708 or miR-214-5p. The transfection of miR-184 into HL-60 cells resulted in a dose-dependent knockdown of PRTN3 expression as detected by Western blot.

Conclusion: Characteristic miRNA signatures in GPA, CRS and CD suggest distinct pathophysiological mechanisms. It indicates at a local miRNA dysregulation in inflamed GPA tissue with a corresponding serum signature that might serve as novel biomarkers. To our knowledge this is the first analysis that attempts to correlate GPA-associated miRNA expression patterns in tissue with serum. Moreover, this is the first description of a miRNA (miR-184) that potentially regulates the expression of the GPA autoantigen PRTN3.

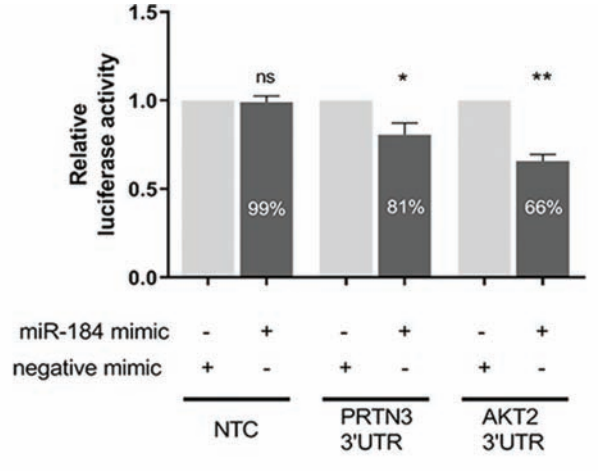


Fig. 1: Dual-luciferase reporter assays showing a decrease in luciferase activity when fused to the 3'UTR of PRTN3 and co-transfected with microRNA-184 mimic. No reduction can be observed for the pmirGLO reporter without inserted 3'UTR (NTC). The 3'UTR of AKT2 was used as a positive control, since it is a validated target of miR-184[1]. Effects of miR-184 targeting the reporter was compared to co-transfection of reporter with cel-miR-67 (negative mimic). Data represent 3 independent experiments with triplicate measurements. P values were calculated by one sample t-test. *P<0.05; **P<0.005; ns = not significant; error bars display standard deviation.

Abstract THU0316 – Figure 1.

REFERENCES:

[1] O'Connell R et.al. Physiological and pathological roles for microRNAs in the immune system. Nat Rev Immunol. 2010;10(2):111-122.
[2] Fasseu M et al. Identification of restricted subsets of mature microRNA abnormally expressed in inactive colonic mucosa of patients with inflammatory bowel disease. PLoS One. 2010 Oct 5;5(10).
[3] Neudecker, V. MicroRNAs in mucosal inflammation. J Mol Med (Berl). 2017 September; 95(9): 935–949
[4] Coit P et al. An update on the role of epigenetics in systemic vasculitis. Curr Opin Rheumatol. 2018; 30(1): 4–15.

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THU0317 IDENTIFICATION OF ENDOTHELIAL PROTEIN C RECEPTOR AND SCAVENGER RECEPTOR CLASS B TYPE 1 AS MAJOR AUTOANTIGENS IN TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) affects the aorta and its major branches. It has been recognized that high numbers of patients with TAK possessed antiendothelial cell antibodies (AECA), which have potential to induce vascular lesion. However, their major target antigens remain unclear. The target antigens of AECA are plasma membrane proteins, and traditional methods to identify autoantigens do not differentiate between cell-surface molecules and intracellular molecules. To overcome this problem, we have developed an expression cloning system to identify cell-surface antigens: serological identification system for autoantigens using a retroviral vector and flow cytometry (SARF)[1-3]. Because there

exists no disease-specific testing for TAK, identification of autoantigens would be extremely important.
Objectives: To identify major autoantigens in TAK using SARF and analyze clinical significance of autoantibodies
Methods: Two hundred and seventy-eight patients with collagen diseases were enrolled: 80, TAK; 10, giant cell arteritis (GCA); and 188, other collagen diseases. A cDNA library of human umbilical vein endothelial cells (HUVECs) was retrovirally transfected into a rat myeloma cell line. Cells expressing the cDNA library were stained with prototype AECAs and fluorescent-conjugated secondary anti-human IgG, and cells with fluorescence were sorted with flow cytometry. Autoantigen identification was performed by analyzing the cDNA inserted into the sorted cells. Cells expressing the identified autoantigens were generated, and the presence of autoantibodies was confirmed. The autoantibodies against identified autoantigens were measured in TAK and other collagen diseases, and the prevalence and clinical characteristics of each autoantibody were evaluated.
Results: AECA activity against HUVECs were measured in patients with TAK and nine AECA serum samples were selected for subsequent SARF. Four distinct AECA-positive clones were successfully isolated using serum IgG from TAK patients. Two clones were identical to the cDNA of *PROCR* encoding protein C receptor (EPCR), and others, to *SCARB1* encoding scavenger receptor class B type 1 (SR-BI). A validation experiment involving 52 patients with TAK confirmed disease specificity in TAK; autoantibodies against EPCR or SR-BI accounted for 34.6% or 36.5% cases, respectively, with minimal overlap (3.8%). Measurement of these autoantibodies in other collagen diseases was performed, and the sensitivity and specificity of these two autoantibodies were 67.3% and 96.5%, respectively. Importantly, these autoantibodies were not detected in patients with GCA who were positive for temporal artery biopsy. TAK was classified into three subtypes based on the profile of these autoantibodies. Anti-EPCR positive group showed high prevalence of stroke, ulcerative colitis, and type II artery lesion. Anti-SR-BI positive group presented higher levels of inflammatory markers, type V artery lesion, and older age at onset. Aortic regurgitation was rare in anti-SR-BI positive group. Double-negative group presented higher rates of vascular surgery.
Conclusion: We identified EPCR and SR-BI as novel autoantigens in TAK. Autoantibodies against EPCR or SR-BI were observed in 66.7% of patients, and different types of autoantibodies showed distinct clinical characteristics. These autoantibodies would aid in clinical application and elucidating pathomechanisms.

REFERENCES:
[1] Shirai T et al. Arthritis Res Ther 2012;14:R157.
[2] Shirai T et al. Clin Dev Immunol 2013;2013:453058.
[3] Shirai T et al. J Neuroinflammation. 2013;10:128.

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THU0318 ANCA-ASSOCIATED GLOMERULONEPHRITIS WITHOUT CRESCENT FORMATION HAS ATYPICAL CLINICOPATHOLOGICAL FEATURES; A MULTICENTER RETROSPECTIVE STUDY

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Background: The most typical histopathological feature of ANCA-associated glomerulonephritis (ANCA-GN) is crescentic GN. However, ANCA-GN is also complicated by other renal lesions, including vascular ones (arteritis and arteriolitis) and tubulointerstitial ones (tubulitis and peritubular capillaritis) [Reference 1], and tubulointerstitial or vascular-dominant inflammation without glomerulopathy sometimes exists. Few reports have focused on ANCA-GN without crescent formation in a large multicenter study.
Objectives: To identify the clinicopathological features of ANCA-GN without crescent formation.
Methods: We enrolled 122 Japanese ANCA-GN patients who were subjected to renal biopsy in 16 hospitals from 2001 to 2018. We measured various clinical parameters at the time of renal biopsy, including creatinine (Cr), estimated glomerular filtration rate (eGFR), C-reactive protein (CRP), MPO-ANCA, PR3-ANCA in the sera, urinalysis findings, and presence of comorbidities (hypertension, hyperlipidemia, diabetes mellitus, and hyperuricemia). Renal biopsy findings were evaluated by light microscopy. We also measured serum Cr and eGFR at the last patient visit, and recorded medications prescribed for ANCA-GN. We retrospectively compared these clinical and histological findings between those with crescent (C+ group) and without crescent (C- group). The primary endpoint was the cumulative percentage of patients who died from any cause.
Results: Of 122 patients (63 females; mean age 69.5 years; observational period 37.1±41.8 years), C- group included 20 (16.4%). Although C- group had higher CRP levels (11.2±8.5 vs 6.6±6.2 mg/dl, p=0.01), they had less proteinuria (0.8±0.9 vs 1.6±1.7 g/gCr, p=0.04) and better renal function (eGFR; 52.1±29.5 vs 32.0±25.4 ml/min/1.73m2, p<0.01) than C+ group. There were no significant differences in any other clinical findings including ANCA serology. In histological findings, C- group had a higher frequency of arteritis (40.0% vs 16.8%, p=0.03), while other histological findings such as arteriolitis, tubulitis and peritubular capillaritis did not differ. There were no significant differences in medications or observational period. C- group had better latest renal function (eGFR; 57.3±27.8 vs 39.0±23.6 ml/min/1.73m2, p=0.02) than C+ group. However, overall survival rate did not differ (68.4% vs 78.7%, p=0.37).
Conclusion: ANCA-GN without crescent formation had specific clinicopathological features including higher systemic inflammation and frequency of renal arteritis than ANCA-GN with crescent formation. Though renal function throughout the clinical course was better in ANCA-GN without crescent formation, overall survival rate was similar with ANCA-GN with crescent formation.

REFERENCE:
[1] J. C. Jennette and H. K. Singh. Pauci-Immune and Antineutrophil Cytoplasmic Autoantibody-Mediated Crescentic Glomerulonephritis and Vasculitis. In: J. C. Jennette, J. L. Olson, F. G. Silvia, V. D. D'Agati editors. The Heptinstall's Pathology of the Kidney. SEVENTH EDITION. Wolters Kluwer; 2015. p. 685-713.

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THU0319 TAKAYASU'S ARTERITIS: BEYOND THE VESSELS

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Background: Takayasu arteritis (TAK) is an inflammatory disease which primarily affects large vessels[1]. However, as a systemic disease, the spectrum of its manifestations is not limited to the arterial wall[2].
Objectives: To describe characteristics of extravascular manifestations of TAK patients from a single Italian Centre.
Methods: Data records of TAK patients diagnosed according to the 1990 ACR criteria and followed-up at our Large Vessel Vasculitis Clinic were reviewed. Any significant inflammatory/autoimmune comorbidity and family history for inflammatory/autoimmune diseases were considered. For each comorbidity, temporal correlation with TAK diagnosis was assessed. Need for biological therapy for TAK control, as an indirect measure of TAK aggressiveness, was evaluated. Non-parametric statistic tests were used.
Results: In our cohort of 129 TAK patients, 46 patients (35.7%) were identified as having an inflammatory/autoimmune comorbidity, for a total of 64 comorbidities (14 patients experienced >1 comorbidity). Comorbidities were classified into 6 categories: systemic inflammatory diseases (17.2%); gastro-intestinal (9.4%), articular (10.9%), ocular (20.3%) and muco-cutaneous (39.1%) involvement; miscellaneous (autoimmune hepatitis (1.6%), retroperitoneal fibrosis (1.6%)). In 33 cases (51.6%) the comorbidity onset preceded, in 25 (39%) followed and in 6 (9.4%) was synchronous with TAK diagnosis (Table 1). In 25 patients (54.3%) use of a biological therapy to control TAK activity was needed (versus 35.4% in patients without comorbidities, p=0.042). Having a comorbidity increased the risk for the introduction of a biologic therapy, odds ratio=2.176 (1.042-4.541). Of the 129 TAK patients, 17 (13.2%) had a positive family

Abstract THU0319 –Table 1. Prevalence and characteristics of inflammatory/autoimmune extravascular comorbidities in a cohort of 129 TAK patients, temporal correlation with TAK diagnosis, and need for biological therapy.

	DISEASE	N° OF CASES	ANTECEDENT TO TAK DIAGNOSIS	SUBSEQUENT TO TAK DIAGNOSIS	SYNCHRONOUS WITH TAK DIAGNOSIS	NEED FOR BIOLOGICAL THERAPY
AUTO-INFLAMMATORY	**Pericarditis**	4	3	0	1	3
	Relapsing Polychondritis	4	4	0	0	3
	Sarcoidosis	3	0	1	2	1
	TOT.	**11**	**7**	**1**	**3**	**7 (63.7%)**
GUT	**Ulcerative Rectocolitis**	3	2	1	0	2
	Crohn Disease	1	1	0	0	1
	Undifferentiated Colitis	1	1	0	0	1
	Celiac Disease	1	0	1	0	0
	TOT.	**6**	**4**	**2**	**0**	**4 (66.7%)**
ARTICULAR	**Psoriatic Arthritis**	4	0	4	0	3
	Enteropathic Arthritis	2	0	2	0	2
	Seronegative Rheumatoid Arthritis	1	1	0	0	1
	TOT.	**7**	**1**	**6**	**0**	**6 (85.7%)**
EYE	**Scleritis**	6	3	3	0	4
	Anterior Uveitis	3	2	1	0	1
	Posterior Uveitis	1	0	1	0	0
	Optic Neuritis	2	2	0	0	1
	Serpiginous Choroiditis	1	1	0	0	0
	TOT.	**13**	**8**	**5**	**0**	**6 (46.2%)**
SKIN/MUCOSA	**Erythema Nodosum**	18	8	8	2	10
	Chronic Urticaria	4	3	1	0	3
	Chronic Recurrent Oral Aphthous Ulcers	2	1	1	0	2
	Skin Psoriasis	1	1	0	0	0
	TOT.	**25**	**13**	**10**	**2**	**15 (60%)**
MISCELLANEOUS	**Retroperitoneal fibrosis**	1	0	0	1	0
	Autoimmune Hepatitis	1	0	1	0	0
		64 (46 patients)	**33 (51.6%)**	**25 (39%)**	**6 (9.4%)**	**38 (25 patients)**

history for inflammatory/autoimmune diseases (8 psoriasis, 5 rheumatoid arthritis, 3 inflammatory bowel disease, 1 sarcoidosis).

Conclusion: In TAK patients, extravascular involvement is a common finding and usually precedes the vascular involvement (the only significant exception is represented by inflammatory arthritis). Inflammatory and autoimmune extravascular comorbidities seem to be associated with a significant higher burden of vascular inflammation, as inferred by the higher rate of biological therapies use in these TAK patients.

REFERENCES:

[1] Numano, et al. Takayasu arteritis. Lancet (2000).
[2] Kwon, et al. Extravascular manifestations of Takayasu arteritis: focusing on the features shared with spondyloarthritis. Arthritis Res Ther (2018)

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THU0320 RISK FACTORS OF INTRAVENOUS IMMUNOGLOBULIN RESISTANCE AND CORONARY ARTERIAL LESIONS IN TURKISH CHILDREN WITH KAWASAKI DISEASE

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Background: Kawasaki Disease (KD) is an acute, systemic, febrile vasculitis that occurs during infancy and is the most common cause of childhood coronary artery disease. The incidence of coronary artery lesions (CALs) has declined with the routine use of intravenous immunoglobulin (IVIG) treatment, but there is still considerable risk for resistance to IVIG treatment and development of CALs (1).

Objectives: Previously defined risk scoring systems have limited predictive capacity for IVIG resistance of KD in Turkish children. The present study was aimed to determine the risk factors in Turkish children with IVIG resistant KD and coronary artery involvement.

Methods: Clinical, laboratory and echocardiographic data were retrospectively analyzed in 94 Kawasaki patients. IVIG resistant and responsive groups were compared.

Results: Of the 94 patients included in the study, 55 (58.5%) were male and 39 (41.5%) were female and the ratio was 1.41. The median (25-75 percentage) age at the time of diagnosis was 35 (19-52) months. CALs were observed at echocardiographic evaluation in 31 patients (33%) and 17 patients (18.1%) were IVIG resistant. IVIG resistant group had a higher rate of CALs compared to the IVIG responsive group ($p<0.05$). When two groups were compared prior to IVIG, neutrophil/lymphocyte ratio (NLR) and C-reactive protein (CRP) parameters were statistically higher in IVIG resistant group. NLR values still remained as statistically higher in the IVIG-resistant group after initial IVIG.

Regarding IVIG resistance, duration of fever $\geq$ 9.5 days, CRP $\geq$ 88 mg/L and NLR $\geq$1.69 were the best cutoff values. The criteria for at least two of these three predictors were considered to be statistically significant risk factors for detecting IVIG resistance in KD before treatment (76.47% sensitivity, 71.05% specificity and 95% confidence intervals were 50.1-93.19% and 59.51-80.89%, respectively).

Regarding risk for CALs, duration of fever $\geq$ 9.5 days before IVIG, (OR: 3.4) and Plt count after IVIG $\geq$ 670x10^3/uL, (OR: 5.5), were the best cutoff values.

Abstract THU0320 –Table 1. ROC analyses and Odds ratios for best cut-off values of variables for predicting IVIG resistance before IVIG treatment.

Variable	*Value*	*Sensitivity*	*Specificity*	*Discriminative ability*	*Odds ratio*
Duration of fever before IVIG	9.5 days	58.8%	72.7%	0.667±0.080 (95% CI: 0.510-0.824, p=0.032)	3.809 (95% CI: 1.28-11.31, p=0.016)
CRP before IVIG	88.0 mg/L	70.0%	64.7%	0.669±0.076 (95% CI: 0.520–0.817, p=0.032)	4.40 (95% CI: 1.38-13.97 p=0.012)
NLR before IVIG	1.69	93.3%	43.4%	0.679±0.070 (95% CI: 0.541–0.817, p=0.031)	4.40 (95% CI: 1.38-13.97 p=0.012)

p<0.05

Conclusion: This study defined three criteria for IVIG resistance in KD prior to treatment: Duration of fever before IVIG ≥ 9.5 days, CRP ≥ 88 mg/L and NLR value ≥ 1.69. Presence of two of these three criteria were found as a significant risk factor for IVIG resistance. Following initial therapy with IVIG, if NLR value is ≥ 1.25, it also predicted ongoing inflammation and IVIG resistance, possibly a need for steroid therapy instead of second IVIG.
Based on the clinical and laboratory features, we established a new risk-scoring system for predicting IVIG resistance in Turkish children with KD. This may be useful for choosing optimal treatment for KD before coronary artery involvement.

REFERENCE:

[1] Newburger JW, Takahashi M, Burns JC, Beiser AS, Chung KJ, Duffy CE, Glode MP, Mason WH, Reddy V, Sanders SP, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. N Engl J Med. 1986 Aug 7 ve 315(6):341-7.

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THU0321 CLINICAL OUTCOMES OF PATIENTS WITH GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA SYMPTOMS TREATED WITH TOCILIZUMAB IN ROUTINE CLINICAL PRACTICE

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Background: Approximately 50% of patients with giant cell arteritis (GCA) also have polymyalgia rheumatica (PMR) symptoms.[1]
Objectives: To determine whether the presence of PMR symptoms upon GCA diagnosis impacts GCA clinical outcomes and to evaluate the effectiveness of tocilizumab (TCZ) for controlling PMR symptoms in patients with GCA.
Methods: Retrospective analysis of patients with GCA treated with TCZ at a single center (2010-2018). Disease flares, defined as re-appearance of clinical manifestations (eg, cranial or PMR signs or symptoms), were assessed among patients with or without PMR at the time of GCA diagnosis. PMR symptoms during disease flares were assessed before and after TCZ initiation.
Results: A total of 60 patients with GCA (71.7% female; mean age, 69.3 years) were followed for a mean (SD) of 2.3 (2.17) years. At diagnosis, 32 had PMR symptoms (2 patients with PMR symptoms only). **Table 1** shows baseline patient characteristics. Among patients with PMR at diagnosis, 75% (n = 24) had a total of 60 flares before TCZ initiation and 34.3% (n = 11) had a total of 23 flares after TCZ initiation (**Table 2**). Among 28 patients without PMR at diagnosis, 67.9% (n = 19) had a total of 42 flares before TCZ initiation and 25% (n = 7) had a total of 14 flares after TCZ initiation (**Table 2**). TCZ was associated with a significant reduction in the annual flare rate both in patients with PMR symptoms (P = 0.003) and without PMR symptoms (P = 0.03) at diagnosis (**Table 2**). Median time to flare was significantly longer after initiation of TCZ in patients with PMR symptoms (hazard ratio [HR] [95% CI]: 0.18 [0.06 to 0.53]; P = 0.002) and without PMR symptoms (HR [95% CI]: 0.21 [0.05 to 0.87]; P = 0.032) at diagnosis. Before TCZ initiation, PMR symptoms were observed in 55.9% of flares (57/102) occurring in 43 patients (71.1%). After TCZ initiation, PMR symptoms were observed in 56.8% of flares (21/37) occurring in 18 patients (30%).
Conclusion: TCZ improved clinical outcomes in patients with GCA regardless of the presence or absence of PMR symptoms at diagnosis. These real-world findings suggest that TCZ is also effective in patients with GCA who have symptoms of PMR.

REFERENCE:

[1] Buttgereit F, et al. JAMA. 2016;315(22):2442-2458.

Abstract THU0321 –Table 1.

Table 1. Patient characteristics at GCA diagnosis and treatment received

	With PMR Symptoms (n = 32)	Without PMR Symptoms (n = 28)
Age, mean (SD)	67.0 (9.27)	71.8 (9.05)
Female, n (%)	23 (71.9)	20 (71.4)
White, n (%)	27 (84.4)	26 (92.9)
Clinical manifestations at disease onset, n (%)		
Localized headache	28 (87.5)	19 (67.9)
Scalp tenderness	15 (46.9)	11 (39.3)
Jaw claudication	16 (50.0)	15 (53.6)
Amaurosis fugax	5 (15.6)	6 (21.4)
Blurry vision	9 (28.1)	9 (32.1)
Permanent vision loss	2 (6.3)	6 (21.4)
Diplopia	1 (3.1)	1 (3.6)
Weight loss	6 (18.8)	14 (50.0)
PMR symptom(s) only, n (%)	2 (6.3)	0
ESR (mm/hr), mean (SD)	67.9 (36.52)	78.3 (29.41)
CRP (mg/L), mean (SD)	63.1 (59.69)	92.4 (84.85)
Positive TA biopsy, n (%)*	14/27 (43.8)	11/24 (39.3)
Disease duration before TCZ initiation, median (IQR), years	0.7 (0.2-1.9)	0.6 (0.2-1.4)
Duration of TCZ treatment (years), median (IQR)	0.6 (0.3-1.3)	0.5 (0.2-1.5)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PMR, polymyalgia rheumatica; TA, temporal artery; TCZ, tocilizumab.
* Of patients with TA biopsies performed.

Abstract THU0221 –Table 2. Clinical outcomes before and after TCZ initiation

	With PMR at Diagnosis (n = 32)		Without PMR at Diagnosis (n = 28)	
	Before TCZ Initiation	After TCZ Initiation	Before TCZ Initiation	After TCZ Initiation
Patients with ≥ 1 flare, n (%)	24 (75.0)	11 (34.3)	19 (67.9)	7 (25.0)
With PMR symptom(s)*	21 (65.6)	8 (25.0)	4 (14.3)	2 (7.1)
Without PMR symptom (s)*	3 (9.4)	3 (9.4)	15 (53.6)	5 (17.9)
No. of flares	60	23	42	14
With PMR symptom(s), n (%)*	50 (83.3)	18 (78.3)	7 (16.7)	3 (21.4)
Without PMR symptom (s), n (%)*	10 (16.7)	5 (21.7)	35 (83.3)	11 (78.6)
Annual flare rate (95% CI)†	1.34 (0.84 to 2.13)	0.54 (0.28 to 1.05)	1.59 (0.78 to 3.23)	0.71 (0.29 to 1.74)
Time to flare (years), median (IQR)	0.3 (0.2-0.7)	2.1 (0.6-2.6)	0.5 (0.3-0.8)	2.6 (0.9-2.6)

GC, glucocorticoids; GCA, giant cell arteritis; IQR, interquartile range; PMR, polymyalgia rheumatica; TCZ, tocilizumab.
* Symptoms are after GCA diagnosis.
† Rates are estimated from a Poisson regression model with treatment, age, smoking history and new and relapsing GCA as covariates and random patient effect.

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THU0322 CLINICAL CHARACTERISTICS OF BIOPSY-PROVEN IGA VASCULITIS IN CHILDREN AND ADULTS: A RETROSPECTIVE COHORT STUDY

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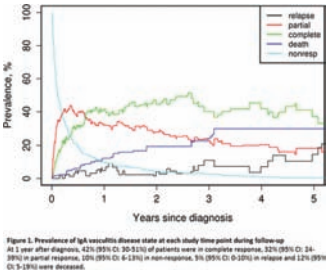
Background: Differences in both presentation and outcome based on age of diagnosis have been described in patients with IgA vasculitis (IgAV) but data are limited due to cohort size and follow-up duration.
Objectives: To describe the differences in clinical characteristics and outcome between adult- and child-onset biopsy-proven IgA vasculitis (IgAV) in North America.

Methods: Patients with IgAV from January 1, 1997, through December 31, 2016 were retrospectively identified. Clinical characteristics, laboratory parameters and outcomes were abstracted from direct medical chart review. Proteinuria was classified as non-nephrotic (≥0.2 g/d, ≤3.5 g/d) or nephrotic (>3.5 g/d). Microscopic hematuria was defined as ≥5 RBCs/hpf or ≥2+ on dipstick. Disease activity at each follow-up visit was categorized as complete response (normalization of all baseline abnormalities due to IgAV), partial response, non-response (lack of improvement of any abnormalities) or relapse (development of clinical signs of IgAV after a symptom-free period of at least one month). Prevalence of disease activity and competing risks were estimated using multi-state models.

Results: A total of 243 IgAV patients were identified (97% Caucasian, 58% male). 174 patients were adults (>21 years) and 69 were <21 years. Compared to patients <21 years, adults at baseline had more frequent ulcerative skin lesions (11% vs. 1%; p=0.02) and nephrotic-range proteinuria (22% vs. 3%; p=0.007) but less commonly had abdominal pain (34% vs. 61%; p<0.001), ischemic gastrointestinal involvement (10% vs. 20%; p=0.04) and arthralgias (38% vs. 61%; p<0.001). Frequency of microscopic hematuria was similar between groups (47%). Oral corticosteroids were the most common initial treatment used (80%).

Dialysis was required in 13 patients (8 adults) and renal transplant was performed in 4 cases (1 adult). Of 137 patients with hematuria during the study, 72% had complete resolution by 1 year after onset, compared to 50% of 179 patients with proteinuria. The prevalence of disease activity state at each follow-up time point is shown in figure 1. During 389 person-years of follow-up, 29 deaths were observed. The main causes of death were cancer, cardiovascular disease, infection and vasculitis. Five year survival rates (95% CI) for patients aged <21, 21-50, and 51+ years were 100%, 94% (87, 100) and 40% (26, 63), respectively (p<0.001). Standardized mortality ratio for patients aged 21-50 years at diagnosis was 5.62 (0.68, 20.3) and 7.60 (5.0, 11.1) for those 51 or older.

Conclusion: IgAV in adults is associated with more severe skin/kidney involvement and poorer renal outcome. Among adults with IgAV, patients aged 51 years or older at diagnosis have significantly higher mortality.



Abstract THU0322 – Figure 1

REFERENCES:

[1] Audemard-Verger A, Terrier B, Dechartres A, et al. Characteristics and Management of IgA Vasculitis (Henoch-Schonlein) in Adults: Data From 260 Patients Included in a French Multicenter Retrospective Survey. Arthritis & rheumatology (Hoboken, N.J.). 2017;69:1862-1870.

[2] Pillebout E, Thervet E, Hill G, Alberti C, Vanhille P, Nochy D. Henoch-Schonlein Purpura in adults: outcome and prognostic factors. Journal of the American Society of Nephrology : JASN. 2002;13:1271-1278.

[3] Westman K, Flossmann O, Gregorini G. The long-term outcomes of systemic vasculitis. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2015;30 Suppl 1:i60-66.

[4] Shrestha S, Sumingan N, Tan J, Alhous H, McWilliam L, Ballardie F. Henoch Schonlein purpura with nephritis in adults: adverse prognostic indicators in a UK population. QJM : monthly journal of the Association of Physicians. 2006;99:253-265.

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THU0323 **THE MANAGEMENT OF BIOPSY NEGATIVE GIANT CELL ARTERITIS BY AUSTRALIAN RHEUMATOLOGISTS**

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Background: The diagnosis of Giant Cell Arteritis (GCA) by Rheumatologists is based on a typical history of headache, jaw claudication and visual disturbance, examination findings such as scalp tenderness and abnormal temporal arteries, and confirmed by temporal artery biopsy (TAB) (1). Temporal artery biopsy is the gold standard for GCA diagnosis (2, 3). However clinicians may diagnose biopsy-negative GCA if there is a high enough pre-test probability for this condition, even if the biopsy is negative. There are few guidelines to assist clinicians with management of biopsy-negative GCA.

Objectives: The primary aim of this research project was to determine if there were differences in the management of patients with biopsy-positive versus biopsy-negative GCA with respect to duration of corticosteroid (CS) use, relapse rates, and use of steroid-sparing agents over a 12-month follow-up period in an Australian cohort. We also sought to determine if there were differences in patient characteristics, examination findings and investigation results between the two groups.

Methods: All patients who underwent a temporal artery biopsy during 2013-2016 for suspected GCA at three geographic sites (Prince of Wales Hospital, Royal Prince Alfred Hospital and Mid-North Coast Arthritis Clinic, Coffs Harbour) had their files reviewed for clinical presentation, examination findings, investigation results, and management over the 12-months following presentation. Comparison was made between biopsy-positive and biopsy-negative patients.

Results: One hundred and forty-two patient files were reviewed. One hundred and one patients were excluded. Of those remaining, 23 were biopsy-positive and 18 were biopsy-negative GCA. Biopsy-negative patients were younger at presentation compared to biopsy-positive GCA patients (69.3 years vs 76.1 years, p = 0.01). There was no difference in the frequency of headache, jaw claudication, polymyalgia rheumatica symptoms or visual disturbance between the two groups of patients. There was also no difference in ESR, CRP, platelet count, total WCC, ALP or Hb level. However, there was a trend towards higher ALP levels in biopsy-positive patients (p = 0.058). The length of temporal artery biopsy was similar between biopsy-positive and biopsy-negative patients (19.4mm vs 19.7mm, p = 0.902). Fewer biopsy-negative patients remained on corticosteroids at 12 months following presentation (65% vs 100%) and of those that did remain on corticosteroids, their dosage tended to be lower than for those with positive biopsies (3.4mg/d vs 7.5mg/d, p = 0.002). Fewer biopsy-negative patients were commenced on methotrexate (5.6% vs 34% p = 0.02). There was no difference in the frequency of relapse between biopsy-positive vs biopsy-negative patients (p = 0.40). Biopsy-positive patients were more likely to present in December or January compared to biopsy-negative patients (p = 0.07). There was no difference in corticosteroid duration prior to biopsy (p = 0.42).

Conclusion: Biopsy-positive patients were treated with corticosteroids for longer and at higher doses than those with a negative biopsy. They were also more likely to present in summer and be treated with methotrexate compared to biopsy-negative patients. The seasonal difference in presentation may suggest a different trigger compared to biopsy-negative patients.

REFERENCES:

[1] Grossman C, et al. Baseline clinical predictors of an ultimate giant cell arteritis diagnosis in patients referred to temporal artery biopsy. Clin Rheumatol 2016; 35: 1817-1822.

[2] Hall S, et al. The therapeutic impact of temporal artery biopsy. The Lancet 1983; 322 (8361): 1217-1220.

[3] Dasgupta B, et al. Concise guidance: diagnosis and management of giant cell arteritis. Clin Med (Lond) 2010; 10 (4): 381-6.

Disclosure of Interests: None declared
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9. Systemic sclerosis, myositis and related syndromes – etiology, pathogenesis and animal models

THU0324 AXONAL DYSFUNCTION IN CEREBRAL WHITE MATTER IN SYSTEMIC SCLEROSIS: A PROTON MAGNETIC RESONANCE SPECTROSCOPIC IMAGING (^{1}H-MRSI) STUDY

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Background: Systemic sclerosis (SSc) is a diffuse connective tissue disease characterized by varying degrees of cutaneous and visceral fibrosis, presence of autoantibodies and vasculopathy. In addition, central nervous system (CNS) involvements are often observed [1].
Objectives: The aim of the present study was to investigate the presence of axonal dysfunction in systemic sclerosis (SSc) and to determine if clinical, laboratory and treatment features are associated with its occurrence.
Methods: In this longitudinal study we included 38 SSc patients (32 woman, mean age of 50.86, SD±11.66 years; range 31- 74) and 38 healthy volunteers (32 woman, mean age of 49.23, SD±12.03 years; range 26 - 77). All individuals were evaluated (neuropsychiatric evaluation and MRI) at study entry and after 12 months. Cognitive evaluation was performed using the Montreal Cognitive Assessment (MoCA), mood disorders were determined through Beck´s Depression (BDI) and Beck´s Anxiety Inventories (BAI). Individual with scores: MoCA ≤26, BDI ≥11 and BAI ≥7 were considered impaired. SSc patients were further assessed for clinical and laboratory SSc manifestations, disease activity (Valentini Activity Index), severity activity (Medsger Severity Index). We performed multi-voxel ^{1}H-MRSI over the superior-posterior region of the corpus callosum. Our MRI/MRSI protocol consisted of: T1-weighted images; 2D pulse sequence (PRESS); excitation angle of 90˚; Long TE: 144ms and TR: 2000ms; VOI (MRSI) size (mm) ≈ (116 x 79 x 16) grid with 208 spectra. Scans were performed with a Philips 3.0T MRI scanner. We measured signals from *N*-acetyl-compounds (NAA), creatine (Cr), choline (Cho), glutamate (Glu), glutamine (Gln) and Glx (the sum of Glu and Gln) using TARQUIN software.
Statistics was performed according nature of the variable.
Results: We observed a significant reduction in NAA/Cr (mean value=1.72; SD=2.4) and Cho/Cr (mean value=2.4; SD=2.04) ratio in SSc when compared to controls (NAA/Cr mean value=1.85; SD=2.7; p = 0.36; Cho/Cr mean value=0.377; SD=0.169; p<0.001). Reduction in NAA/Cr ratio was associated with cognitive impairment (p = 0.017), presence of migraine (p = 0.001), current use of prednisone (p=0.010) and current use of methotrexate (p < 0.001). NAA/Cr ratio correlated with MOCA scores (r=0.4; p=0,015).
Follow up study showed a reduction in NAA/Cr values when compared to patients´ baseline values (p = 0.0341).
Conclusion: Our results showed a significant reduction in NAA/Cr ratio in SSc patients associated with cognitive impairment and the use of some drugs (MTX and prednisone) during the treatment. Therefore, NAA/Cr ratios may be a useful biomarker in follow-up studies of SSc.

REFERENCES:

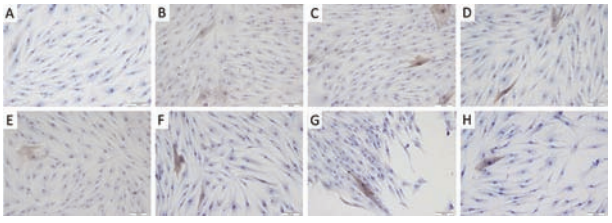
[1] Hietaharju A, Jaaskelainen S, Hietarinta M, Frey H. Central nervous system involvement and psychiatric manifestations in systemic sclerosis (scleroderma): clinical and neurophysiological evaluation. Acta neurologica Scandinavica. 1993
[2] Mountford, C. E., Stanwell, P., Lin, A., Ramadan, S., and Ross, B., Neurospectroscopy: the past, presente and future," Chemical reviews, 2010
[3] Wilson, M., Reynolds, G., Kauppinen, R. A., Arvanitis, T. N., and Peet, A. C., A constrained least-squares approach to the automated quantitation of in vivo 1h magnetic resonance spectroscopy data," Magnetic resonance in medicine, 2011.

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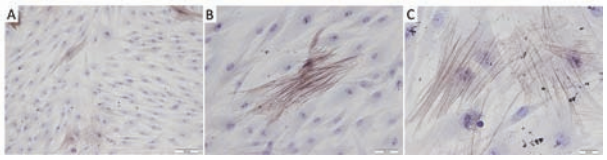
THU0325 THE HMGB1/AGE-RAGE AXIS IN SYSTEMIC SCLEROSIS PATIENTS: A POTENTIAL ROLE IN ITS VASCULOPATHY?

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Background: Systemic sclerosis (SSc) is a progressive fibro-inflammatory autoimmune disease of which the pathogenetic pathways are incompletely understood. Advanced glycation endproducts (AGEs) are oxidative stress derived compounds with potential proinflammatory effects. Their exact role in fibrosis remains unknown. The receptor for AGEs is RAGE, which is also the receptor for high mobility group box 1 (HMGB1), a nuclear protein, which is proinflammatory when released from activated or apoptotic cells. We hypothesize that AGEs and HMGB1 may promote inflammation and profibrotic processes, presumably mediated by RAGE.
Objectives: To study the role of the HMGB1/AGE-RAGE axis in the pathogenesis of SSc.
Methods: Distribution of N-(carboxymethyl)lysine (CML) and N^{δ}-(5-hydro-5-methyl-4-imidazolon-2-yl)-ornithine (MG-H1) was assessed by immunohistochemistry in skin biopsies of 12 SSc patients [median age 56 years (IQR 52-61); 6 of affected, 6 of unaffected skin]. The intensity was assessed semi-quantitatively on endothelium and fibroblasts. In vitro experiments were performed on healthy human dermal fibroblasts, which were stimulated by HMGB1, AGE-BSA or TGF-β1 as control. Inflammatory and profibrotic markers were measured by ELISA and rt-PCR. Differentiation to myofibroblasts was assessed by staining of α-smooth muscle actin (α-SMA). In an additional clinical study, we included 20 SSc patients [51 years (44-58)] and 20 age- and sex-matched healthy controls [(HC) 52 years (45-62)]. Sera were obtained to determine CRP, ESR, HMGB1 and soluble RAGE (sRAGE) levels. AGE accumulation in skin was assessed as skin autofluorescence (SAF) by the AGE Reader.
Results: MG-H1 staining was more intense on all skin structures in SSc patients, compared to HC, while CML staining showed no differences. MG-H1 was more pronouncedly detected on endothelium and fibroblasts in affected compared to unaffected skin. In vitro stimulation of fibroblasts with AGE-BSA resulted in increased expression of IL-6, collagen-1α and connective tissue growth factor. Finally, HMGB1 and AGE-BSA induced myofibroblast differentiation and formation of SMA fibers (Fig. 1, 2). In regards to the clinical study CRP (SSc: median 1.8 mg/l (IQR 0.8-3.5), HC: 0.7 (0.4-1.8), p=0.04), ESR (SSc: 8.5 mm/h (5.3-15.5), HC: 5.0 (3.0-7.0), p=0.02), HMGB1 (SSc: 3.4 ng/ml (1.6-6.1), HC: 1.6 (0.8-2.8), p=0.03), sRAGE (SSc: 956.3 pg/ml (717.9-1670.0), HC: 684.9 (517.0-890.5), p=0.02) and SAF (SSc: 2.2 AU (1.8-2.5), HC: 1.8 (1.4-2.1), p=0.02) were significantly increased in SSc patients, compared to HC.
Conclusion: This is the first translational study that might indicate a prominent role of the HMGB1/AGE-RAGE axis in systemic sclerosis by promoting inflammation and fibrosis. Further studies investigating this pathway are ongoing.



Abstract THU0325 – Figure 1. Smooth muscle actin (α-SMA) expression by immunohistochemistry in stimulated and unstimulated human skin fibroblasts. Fibroblasts were treated with 0 **(A)**, 1 **(B)**, 10 **(C)** or 50 **(D)** ng/ml TGF-β1, 10 **(E)** or 100 **(F)** μg/ml AGE-BSA or 1 **(G)** or 10 **(H)** μg/ml HMGB1. All cells were treated for 24 hours. Detection was performed with 2 μg/ml anti α-SMA. Bar 100 μm.



Abstract THU0325 – Figure 2. Smooth muscle actin (α-SMA) expression by immunohistochemistry in TGF-β1 treated fibroblasts. Fibroblasts were treated with 1 ng/ml TGF-β1. Detection was performed with 2 μg/ml anti α-SMA. **A)** α-SMA expression observed with a 10x manifestation. Bar 100 μm. **B)** 20x manifestation. Bar 50 μm. **C)** 40x manifestation. Bar 20 μm.

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Disclosure of Interests: Isabella Atzeni: None declared, Amaal Eman Abdulle : None declared, Anniek van Roon: None declared, Gilles Diercks: None declared, Harry van Goor: None declared, Andries Smit Shareholder of: Has been co-founder, and is still shareholder of Diagnoptics Technologies, the company which developed the AGE reader., Johanna Westra: None declared, Douwe J Mulder Grant/research support from: My University has received research grants for my research from: Boehringer Ingelheim and Actelion, Speakers bureau: My University has received speakers fee from: Sanofi
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THU0326 ANALYSIS OF PHOSPHATIDYLINOSITOL 3-KINASE PATHWAY IN B CELL ACTIVATION OF SYSTEMIC SCLEROSIS PATIENTS

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Background: B cell activation is an early event in the development of systemic sclerosis (SSc) as transcriptome profiling identified local B-cell activation in early diffuse cutaneous (dc) SSc skin biopsies. Autoantibody production is a widely investigated function of B cells in SSc but less attention has been devoted to the role of innate immune molecules and their receptors, like Toll-like receptors (TLRs). The classical B cell activation downstream of BcR and CD19 co-receptor engagement involves phosphatidylinositol-3 kinases (PI3K) signaling pathway that integrates the effects of multiple co-stimulatory receptors.
Objectives: Our goal was to examine PI3K signaling by investigating the mRNA expression of 92 pathway related genes in B cells from early dcSSc patients. Akt is a central element of PI3K pathway, but it can also converge into innate receptor mediated pathways such as mTOR and MAPK. Thus for functional relevance we also analyzed the phosphorylation of Akt, S6 and NF-κB in B cells from early dcSSc patients.
Methods: Twenty-one patients with early dcSSc were enrolled with disease duration of 2.0 (±1.2) years based on the date of the first non-Raynaud's symptom. 30% of patients received immunosuppressive therapy. Peripheral blood CD19+ B cells were purified from dcSSc patients and age- and sex-matched healthy controls (HC, n=15). mRNA expression of 92 B cell specific PI3K pathway related genes was measured using a Taqman qPCR array and was validated by individual qPCR. Isolated B cells were activated through BcR using anti-IgG/M antibody or anti-CD180 antibody, and their combination followed by flow cytometric analysis of phospho-Akt (S473), phospho-S6 (S235/S236) and phospho-NF-κB p65 (S529) positive cells.
Results: Analyzing the expression of 92 PI3K pathway associated genes we found altered expression of molecules playing a role in alternate B cell activation and innate signaling. The expression of both IL-4 receptor and osteopontin (SPP1) was upregulated in B cells of untreated dcSSc patients, but became downregulated upon immunosuppressive therapy. Innate molecules like TLR4 and complement component 3 remained highly upregulated and the downregulation of CD180 was not inhibited by immunosuppressive treatment, thus may preserve the activated state of B cells in dcSSc. We aimed to model B cell activation via TLR4 and CD180 but LPS and endogenous ligands of TLR4 failed to activate isolated B cells. Since there are not known ligands of CD180, we investigated the effects of anti-CD180 itself and also its combination with BcR mediated stimulation of B cells. Analyzing the phosphorylation of the PI3K pathway-associated molecules revealed an impaired responsiveness of dcSSc B cells to anti-CD180 alone, and the combination of anti-CD180 and anti-Ig induced different phosphorylation patterns of Akt, S6 and NF-kB molecules in dcSSc and healthy controls (HC).
Conclusion: Analysis of B cells from early dcSSc patients revealed that B cells possess molecular changes in PI3K pathway that involves innate immune components. Gaining new insight into innate B-cell activation in SSc could be helpful for finding new therapeutic targets.

REFERENCES:
[1] Bhattacharyya S, et al. Adv wound care (2017) 6:356–369.
[2] Chaplin JW, et al. J Immunol (2011) 187:4199–209.

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Disclosure of Interests: None declared
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THU0327 ANTIBODIES AGAINST EXTRACTABLE NUCLEAR ANTIGENS (ENA) IN SCLERODERMA ARE NOT ONLY DIAGNOSTIC AND PROGNOSTIC TOOLS, BUT PATHOGENETIC REGULATORS INDUCING A PROFIBROTIC PHENOTYPE IN CULTURED SKIN FIBROBLASTS

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Background: The importance of systemic sclerosis (SSc) autoantibodies for diagnosis has become increasingly recognized, as evidence by incorporation into the 2013 ACR/EULAR clinical classification criteria (1). Clear prognostic and phenotypic associations with cutaneous subtype and internal organ involvement have been extensively described (2). However, little is known about the potential of those autoantibodies to exert a direct pathogenetic role in the disease (3).
Objectives: The aim of the study is to assess the potential pathogenetic role of anti-topo isomerase I (Topo-I) and anti-centromeric protein B (Cenp B) autoantibodies to induce pro-fibrotic markers in dermal fibroblasts.
Methods: Dermal fibroblasts were isolated from unaffected and affected skin samples of (n=10) limited cutaneous SSc (LcSSc) patients, from affected skin samples of (n=10) diffuse cutaneous (DcSSc) patients and from (n=20) healthy subjects. Fibroblasts were stimulated with serum-isolated fractions of Topo-I, Cenp B and control IgGs in ratios 1:100 and 1:200 for 24 and 48 hours. Cells were also incubated with 10% SSc Topo-I$^+$, Cenp B$^+$ whole serum and with 10% control serum for 24 and 48 hours. Viability was assessed by MTT test, while apoptosis was assessed by flow cytometry. Activation of pro-fibrotic genes ACTA2, COL1A1 and TAGLN was evaluated by quantitative-real-time-PCR (qPCR), while protein levels alpha-smooth-muscle actin (α-SMA), type-I-collagen (Col-I) and SM22 were assessed by immunocitochemistry (ICC).
Results: MTT test showed that Cenp B ($p<0.05$) and with more extent Topo-I ($p<0.01$) IgGs reduced unaffected LcSSc and control fibroblast viability in a time- and dilution-dependent manner compared to control IgGs. Similar results were obtained with Cenp B$^+$ ($p<0.05$) and Topo-I$^+$ ($p<0.01$) sera compared to control sera. Flow cytometry analysis revealed that both Cenp B/Topo-I IgGs and Cenp B$^+$/Topo-I$^+$ sera induce apoptosis in unaffected LcSSc and control fibroblasts only, while affected LcSSc/DcSSc fibroblasts showed apoptosis resistance. qPCR showed that basal levels of pro-fibrotic markers ACTA2, COL1A1 and TAGLN were upregulated in affected LcSSc/DcSSc fibroblasts compared to LcSSc unaffected and to control ones. Stimulation with Cenp B and Topo-I IgGs and with Cenp B$^+$ and Topo-I$^+$ sera statistically increased all the profibrotic markers compared to control IgGs ($p<0.05$) and to control sera ($p<0.05$). ICC proved that α-SMA, Col-1 and SM22 levels were upregulated in a time- and dilution-dependent manner in unaffected LcSSc and control fibroblasts upon stimulation with Cenp B and Topo-I IgGs and with Cenp B$^+$ and Topo-I$^+$ sera, while they remained stably high in affected LcSSc/DcSSc fibroblasts.
Conclusion: This study demonstrates the pathogenetic role of antibodies targeting Topo-I and Cenp B to directly induce pro-fibrotic activation of fibroblasts. Therefore, besides the diagnostic and prognostic use of those autoantibodies in SSc, these data justify the importance of therapeutic use of immunosuppressive drugs in the early stages of the disease.

REFERENCES:
[1] Denton CP. *Advances in pathogenesis and treatment of systemic sclerosis*. Clin Med (Lond) 2016;16:55-60.
[2] Asano Y. *Systemic Sclerosis*. J Dermatol 2017; doi: 10.1111/1346-8138.14153.
[3] Yayla ME, İlgen U, Düzgün N. *An analysis of the relationship between autoantibodies and clinical findings in patients with systemic sclerosis*. Turk J Med Sci 2018;48(1):10-15.

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THU0328 DO PATIENTS WITH SYSTEMIC SCLEROSIS HAVE ULTRASONOGRAPHIC MODIFICATIONS OF SALIVARY GLANDS SUGGESTIVE OF SJOGREN SYNDROM?

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Background: Modifications in ultrasonographic aspect of major salivary glands have been reported in patients with primary Sjogren Syndrom (pSS) with good diagnostic accuracy. Sicca symptoms are frequently observed in Systemic sclerosis (SSc).
Objectives: To assess the ultrasonographic echostructure of major salivary glands in patients with SSc and compare the modifications with those of patients with pSS or controls with sicca symptoms.
Methods: We performed a monocentre case-control study between 2014 and 2017 in the universitary hospital of Clermont-Ferrand (France). Patients with SSc and pSS were fullfilling the American College of Rheumatology/European League against Rheumatism (ACR/EULAR) 2013 and the ACR 2012 classification criteria respectively. Controls patients were complaining of sicca symtoms but did not meet the ACR 2012 criteria. Bilateral parotid and submandibular glands ultrasound (US) were performed in all patients by the same operator blinded to the diagnosis. Inhomogeneity of each of the 4 major salivary glands in B-Mode was graded using the Jousse-Joulin scoring system (scale of 0 to 4) as previously described.[1] The highest grade among the 4 glands was retained as suggestive of Sjogren Syndrom if $\geq$ 2.
Results: A total of 108 patients were included: SSc (n=25), pSS (n=48) and controls (n=35). Among the 48 patients with pSS, 12 were receiving hydroxychloroquine, 4 an immunosuppressor, 77% had antinuclear antibodies at a significant level ($\geq$1/640), 26 (54%) anti-SSA antibodies, 14 (29%) anti-SSB antibodies, 40/45 (89%) had a labial salivary biopsy suggestive of pSS (Chisholm and Mason score $\geq$3). Comparing the pSS and the control groups, performance of a US echostructure grade $\geq$ 2 for the diagnosis of pSS was good: Se=75%, Sp=91.4%, positive predictive value= 92.3%, negative predictive value= 72.7%.
Among the 25 SSc patients, 7 had immunosuppressor therapy, 8 had a localized SSc. Shirmer's test $\leq$ 5 mm in 5 minutes was present in 9/18 (53%), unstimulated salvary flow $\leq$ 0.1 mL/minute in 8/14 (57.1%).
In the SSc group, 12 patients had an US echostructure grade 0, 6 grade 1, and 7 patients (28%) had an US echostructure grade of $\geq$ 2: US score=3 (n=5), US score=4 (n=2). Anti-SSA antibodies were found in 1/7 patients with an US echostructure grade $\geq$ 2 and 2/18 patients with US echostructure grade 0 or 1.

	SSc group (n=25)	pSS group (n=48)	Control group (n=35)
Age, mean ± SD, years	64.8 ± 9.3	62.1 ± 12.3	55 ± 15
Female sex,%	88	96	97.2
Disease duration, mean ± SD, years,	16.7 ± 11.1	10.5 ± 7.7	Not applicable
US Score ≥ 2, n (%)	7 (28)	36 (75)	3 (8.6)

Conclusion: Nearly one third of patients with SSc have US echostructure changes suggestive of Sjogren Syndrom regardless of the presence of anti-SSA antibodies.

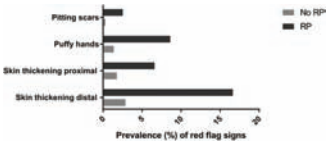
REFERENCES:
[1] - Cornec D, Jousse-Joulin S, Pers JO, et al. Contribution of salivary gland ultrasonography to the diagnosis of Sjögren's syndrome: toward new diagnostic criteria? Arthritis Rheum. 2013;65:216-25.

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THU0329 RED FLAG SIGNS OF SYSTEMIC SCLEROSIS ARE PREVALENT IN SUBJECTS WITH RAYNAUD'S PHENOMENONIN THE GENERAL POPULATION AND MAY BE A PROXY FOR LUNG INVOLVEMENT

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Background: Pulmonary involvement in systemic sclerosis (SSc) is very difficult to treat when diagnosed too late. Therefore, in order to optimally use "the window of opportunity" more attention should be given to the early identification of SSc. To the best of our knowledge, no studies exist that have structurally assessed the epidemiology of red flag signs and potential signs of pulmonary involvement in patients with Raynaud's phenomenon (RP).
Objectives: To assess the prevalence of red flag signs in participants with RP. Moreover, we aim to investigate the occurrence of pulmonary signs and symptoms in participants with red flag signs.
Methods: We retrospectively analyzed data from the LifeLines Cohort Study, which is a large population-based cohort study in the Northern parts of the Netherlands. A total of 74011 participants completed the connective tissue disease questionnaire. The presence of RP and red flag signs for SSc (i.e., puffy fingers, skin thickening distal, skin thickening proximal, and pitting scars) were obtained. Patients were classified as having red flag signs by the presence of at least one red flag sign in addition to RP. In addition, patient characteristics, self-reported pulmonary complaints, spirometry (screening for interstitial lung disease (ILD)), and uric acid (global screening for pulmonary arterial hypertension (PAH)) were also obtained. Three groups of participants were formed, namely: participants with RP and red flag signs (n=981), participants with RP without red flag signs (n=2946), and participants without RP and without red flag signs (n=70037).
Results: The prevalence of red flag signs was 5 fold higher in participants with RP, as compared to the non-RP group (RP 25% [23.7-26.4], non-RP 5% [4.9-5.2], p<0.001). A total of 413(42.1%) of the participants with RP and red flag signs reported dyspnea, which was 1.5 fold higher than in those with RP but without red flag signs, and two-fold higher compared to participants without RP and without red flag signs (p<0.001). Moreover, dyspnea in rest and after exertion was more prevalent in participants with RP and red flag signs (p<0.001). In addition, participants with RP and red flag signs more frequently reported to suffer from pulmonary fibrosis (p<0.001, table 1), and had the lowest forced vital capacity, as compared to the other groups (p<0.001). Conversely, uric acid was not found to be elevated in participants with RP and red flag signs.
Conclusion: This unselected cohort study from the general population demonstrates that the prevalence of red flag signs in subjects with RP may be as high as 25%. Potential signs and symptoms of pulmonary complaints are more prevalent in participants with RP who also reported red flag signs. This could indicate an increased risk of pulmonary involvement (i.e., ILD and PAH) in RP patients with red flag signs, although additional specific tests are mandatory to substantiate definite disease.



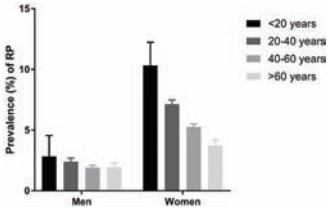
Abstract THU0329 – Figure 1. Prevalence of red flag signs in participants with and without Raynaud's phenomenon.

Disclosure of Interests: Amaal Eman Abdulle : None declared, Elisabeth Brouwer Speakers bureau: Dr. Brouwer as an employee of the UMCG received speaker fees and consulting fees from Roche which were paid to the UMCG, Harry van Goor: None declared, Johanna Westra: None declared, Karina de Leeuw: None declared, Douwe J Mulder Grant/ research support from: My University has received research grants for my research from: Boehringer Ingelheim and Actelion, Speakers bureau: My University has received speakers fee from: Sanofi
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THU0330 PREVALENCE OF RAYNAUD'S PHENOMENONIN THE NORTHERN PARTS OF THE NETHERLANDS: AN EPIDEMIOLOGICAL STUDY OF THE LIFELINES COHORT

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Background: Although several previously conducted studies reported on the prevalence of Raynaud's phenomenon (RP) in different regions of the world, these studies often included a limited number of selected individuals. Moreover, no studies exist that have systematically assessed the relative contribution of known etiological factors of RP in the general population of the Netherlands.
Objectives: To assess the prevalence of RP, and gender-specific etiological factors associated with RP in the Northern parts of the Netherlands.
Methods: Data from the Lifelines cohort were analyzed, in which all participants completed the self-administered validated connective tissue disease questionnaire. Subjects who reported cold-sensitive fingers and bi- or triphasic colour changes in response to cold were considered to suffer from RP. Known etiological factors such as hormonal status, body mass index (BMI), smoking behaviour, and comorbidities were all assessed in a standardised way.
Results: In total 93935 participants completed the questionnaire (mean age 45.6 ±12.9). The prevalence of RP was 4.2% [95% CI 4.1-4.4] which was approximately three-fold higher in females (5.7%, 95% CI [5.5-5.9]), as compared to males (2.1%, 95% CI [1.9-2.2], p-value <0.001, figure 1). Regarding gender-specific risk factors associated with RP, we observed that BMI <18.5 (OR 4.6 [2.4-8.7], p<0.001), cardiovascular disease (OR 1.53 [95% CI 1.31-1.78], p<0.001), history of cancer (OR 1.40 [1.00-1.95], p=0.049), use of beta-blockers (OR 1.39 [1.06-1.83], p=0.01), and smoking (OR 1.28 [1.09-1.51], p=0.003) were associated with an increased odds of RP in men. Conversely, alcohol consumption, diabetes and age were not associated with RP in men. In females, BMI<18.5 (OR 2.9 [2.27-3.64], p<0.001), cardiovascular disease (OR 1.42 [1.32-1.54], p<0.001), receiving hormonal contraception (OR 1.17 [1.08-1.26], p<0.001), and hormonal replacement therapy (OR 1.14 [1.04-1.25], p=0.007) were associated with increased odds of RP. Moreover, smoking behavior, use of beta-blockers, alcohol consumption, and diabetes were not associated with RP in women. A BMI>30 was associated with a strongly decreased odds of RP in both men (OR 0.22 [0.11-0.42], p<0.001) and women (OR 0.35 [0.28-0.44], p<0.001).
Conclusion: This large cohort study found a prevalence of 4.2% of RP in the Northern part of the Netherlands, with an expected predominance in young female subjects. Moreover, the etiologic risk factors of RP are multifactorial and clearly gender-specific (e.g., hormonal status in women, smoking behavior and use of beta-blockers in men), with underweight strongly increasing and obesity strongly decreasing the likelihood of RP in both sexes. This might suggest that different mechanisms influence the expression of RP in men and women.



Abstract THU0330 – Figure 1. Prevalence of RP depicted for men and women.

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THU0331 SKELETAL TROPONIN I A POSSIBLE NOVEL BIOMARKER FOR MANAGEMENT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: The current biomarkers for the diagnosis and monitoring of diseased and injured skeletal muscles, such as creatine kinase (CK), have limited tissue specificity and incapability to differentiate between pathological and physiological changes. Thus, new biomarkers with improved diagnostic certainty are needed. Skeletal troponin I (skTnI) is a promising new biomarker for injured and diseased skeletal muscle tissue. Although studies have reported that circulating skTnI levels are elevated in response to trauma, exercise and various muscular diseases (1), its clinical utility to serve as a diagnostic indicator has largely been unexplored.
Objectives: Our aim was to develop and validate a novel assay for skTnI, and to assess its clinical performance with idiopathic inflammatory myopathy (IIM) patients.
Methods: A two-step fluoroimmunoassay was used to analyze the levels of skTnI in samples from healthy reference individuals (n=125), trauma patients (n=151), and patients with IIM (n=94). Later, skTnI and CK levels in patients with IIM were compared according to their disease activity status (active, pre-active or stable).
Results: The limit of detection was 1.2 ng/ml, and the upper reference limit (90th percentile) was 5.4 ng/ml. The median skTnI concentrations were <LoD, 2.7 ng/ml, and 9.8 ng/ml in reference, trauma, and IIM cohorts, respectively. Differences in measured skTnI levels were statistically significant between all three study cohorts (Mann-Whitney p<0.001 for all). skTnI and CK had a strong positive correlation (Spearman´s r=0.848, p<0.001). With skTnI, patients in both pre-active and active IIM were differentiated from stable phase patients (33.9 and 34.5 ng/ml vs 5.1 ng/ml, p<0.001 for both). This was not possible with CK as significantly elevated CK levels were mainly present in active IIM (median 16.5 µkat/L) and the medians of pre-active and stable phase patients (4.8 µkat/L vs 1.7 µkat/L, p=0.060) remained close to normal reference ranges. The area under the receiver operator characteristic curve was 0.87, 0.84, and 0.87 for skTnI and CK individually and combined, respectively.
Conclusion: With the developed skTnI assay, IIM patients were identified from healthy individuals and from patients with traumatic muscular injuries. Also, skTnI was shown to outperform CK in detecting IIM patients in different disease activity statuses.

REFERENCE:

[1] Kiely PDW, Bruckner FE. Serum skeletal troponin I in inflammatory muscle disease: Relation to creatine kinase, CKMB and cardiac troponin I. Ann Rheum Dis 2000;59:750–1.

Disclosure of Interests: Katriina Bamberg: None declared, Laura Mehtälä: None declared, Olli Arola: None declared, Seppo Laitinen: None declared, Pauliina Nordling: None declared, Marjatta Strandberg: None declared, Niko Strandberg: None declared, Johanna Paltta: None declared, Markku Mali: None declared, Fabricio Espinosa-Ortega: None declared, Laura Pirilä Consultant for: Abbvie, Novartis, Eli Lilly, MSD Finland, Pfizer, UCB, Roche, Jansen- Cilag, Sandoz, Speakers bureau: Pfizer, Ingrid E. Lundberg Grant/research support from: Dr. Lundberg has received honoraria from Bristol Myers Squibb and MedImmune and is currently receiving a research grant from Bristol Myers Squibb and from Astra Zeneca., Consultant for: She is a scientific advisor for Bristol Myers Squibb, and aTyr, Tanja Savukoski: None declared, Kim Pettersson: None declared
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THU0332

ABSOLUTE REDUCTION OF REGULATORY T CELLS AND EFFICACY OF SHORT-TERM AND LOW-DOSE IL-2 IN PATIENTS WITH DERMATOMYOSITIS OR POLYMYOSITIS

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Background: Dermatomyositis (DM) and polymyositis (PM) are heterogeneous, chronic and progressive autoimmune disorders characterized by symmetrical, proximal muscle weakness[1,2]. Although the pathogenesis of PM/DM remains unclear, immune intolerance caused by the deficiency of regulatory T (Treg) cells may be an important cause of PM/DM, and quantitative status of peripheral Treg cells is unclear in this disease. Low-dose interleukin-2 (ld-IL2) has been found to enhance proliferation, function and survival of Treg cells to regulate immune tolerance[3]. However, the therapeutic effect of ld-IL2 on PM/DM has not been reported.

Objectives: To investigate whether peripheral Treg cells are reduced and whether ld-IL2 has therapeutic efficacy in PM/DM.

Methods: Total 71 PM/DM inpatients (10 PM and 61 DM) were retrospectively studied. Five PM and 35 DM patients were treated with ld-IL2 (5.0*105 international units (IU) per day for 5 days) accompanied by conventional therapy, while the rest PM/DM patients only with conventional therapy. Thirty of age- and gender-matched healthy adults were regarded as healthy controls (HCs). CD3+T, CD4+T, CD8+T, B, NK, Th1, Th2, Th17 and Treg cells, as well as cytokines [interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-10 (IL-10), tumor necrosis factor-α (TNF-α), interferon-γ (IFN-γ) and interleukin-17 (IL-17)] were measured by flow cytometry. The correlation coefficients between various indicators and Myositis Disease Activity Assessment Visual Analogue Scale (MYOACT) were calculated by Spearman correlation test.

Abstract THU0332 –Table 1.

Table1. The demographic baseline data of PM/DM patients and HCs

	PM(n=10)	DM (n=61)	HCs(n=30)	*P*
Age (years)	47.40±13.59	54.39±13.77	53.77±6.77	0.225
Female/male	5/5	42/19	20/10	0.521
disease duration (month)	36.00 (20.50, 102.00)	6.00 (2.00, 36.00)	-	-
WBC (*10^9/L)	7.25 (5.42, 8.20)	7.49 (5.50, 9.34)	5.83 (4.73, 6.72)	0.005
NEUT (*10^9/L)	5.48 (3.58, 6.74)	5.58 (3.49, 7.04)	3.28 (2.57, 3.96)	<0.001
LYMP (*10^9/L)	0.85 (0.45, 1.93)	1.15 (0.83, 1.76)	1.91 (1.70, 2.27)	<0.001
PLT (*10^9/L)	282.00 (182.25, 314.75)	240.00 (174.00, 306.00)	245.50 (218.25, 270.25)	0.791
RDW (fL)	46.20 (43.15, 52.10)	44.70 (41.88, 48.43)	41.30 (40.48, 43.38)	<0.001
ESR (mm/h)	73.00 (26.25, 120.00)	40.00 (23.25, 71.50)	12.50 (6.00, 15.00)	<0.001
CRP (mg/L)	18.95 (9.31, 74.63)	12.85 (5.08, 49.55)	-	0.391
ALT (U/L)	50.10 (25.70, 63.50)	34.75 (16.35, 65.95)	-	0.412
AST (U/L)	35.25 (26.35, 62.58)	36.30 (25.78, 72.50)	-	0.880
CK (U/L)	536.50 (38.00, 2291.50)	54.00 (32.77, 283.00)	-	0.090
LDH (U/L)	406.50 (324.00, 632.63)	338.00 (262.00, 476.00)	-	0.168
HBDH (U/L)	286.50 (223.00, 527.48)	247.00 (195.50, 328.50)	-	0.116
anti-u1-SRP	1	4	-	1.000
anti-Jo-1	0	3	-	1.000
anti-PM-Scl	1	2	-	0.895
anti-Mi-2	0	1	-	1.000
anti-Ku	1	3	-	1.000
MYOACT	4.00 (3.00, 5.25)	6.00 (4.00, 7.00)	-	-

•Continuous data were expressed as Mean±standard deviation (M±SD) or Median (Q_{25}, Q_{75}) and analyzed by one-way analysis of variance (ANOVA) or the Independent-samples Kruskal-Wallis test one-way ANOVA or Mann-Whitney U test. Categorical data were reported as numbers and compared with Chi-square test.

•Abbreviation: WBC: white blood cell; NEUT: neutrophile granulocyte; LYMP: lymphocyte; PLT: platelet; RDW: red cell distribution width; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; LDH: lactate dehydrogenase; HBDH: hydroxybutyrate dehydrogenase.

Results: Both PM and DM patients had significantly lower number of CD3+T (*P*=0.018, *P*=0.003) and CD4+T cells (*P*=0.035, *P*=0.016) than HCs, as well as the number and percentage of Treg cells (*P*≤0.001) in PM/DM and these of NK, Th1 cells in DM, while Th2 and Th17 cells didn' t exhibit any significant difference. In addition, the ratio of Th1/Th2 in DM (*P*<0.001) and that of Th17/Treg was obviously decreased in PM/DM (*P*=0.015, *P*=0.001). Meanwhile, the production of serum IL-2 was reduced in PM/DM (*P*≤0.001), while, in contrast, IL-4, IL-6, IL-10, TNF-α, IFN-γ and IL-17 increased. ld-IL2 could significantly increase the number of Treg cells but have little effect on Th17 cells in DM. In addition, MYOACT was correlated with the number of CD3+T, CD4+T, CD8+T, Th1, Th2, Treg cells, PLT and lymphocyte (r=-0.388, *P*=0.002; r=-0.360, *P*=0.004; r=-0.364, *P*=0.004; r=-0.386, *P*=0.002; r=-0.282, *P*=0.028; r=-0.262, *P*=0.041; r=-0.311, *P*=0.015; r=-0.388, *P*=0.002; respectively) negatively, as well as the percentage of CD3+T and CD8+T cells (r=-0.277, *P*=0.030; r=-0.291, *P*=0.023), opposite to aspartate transaminase (AST) (r=0.289, *P*=0.025) in DM.

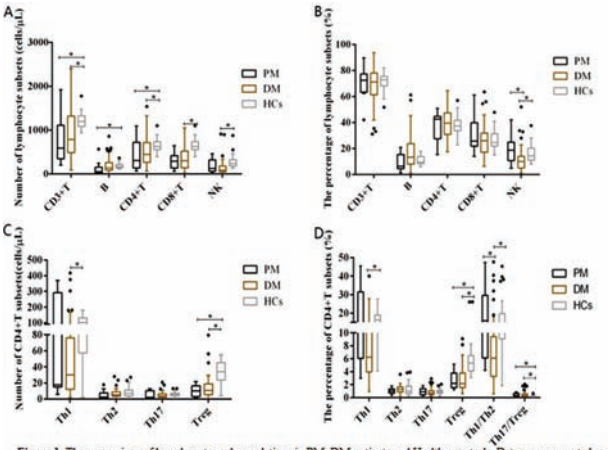
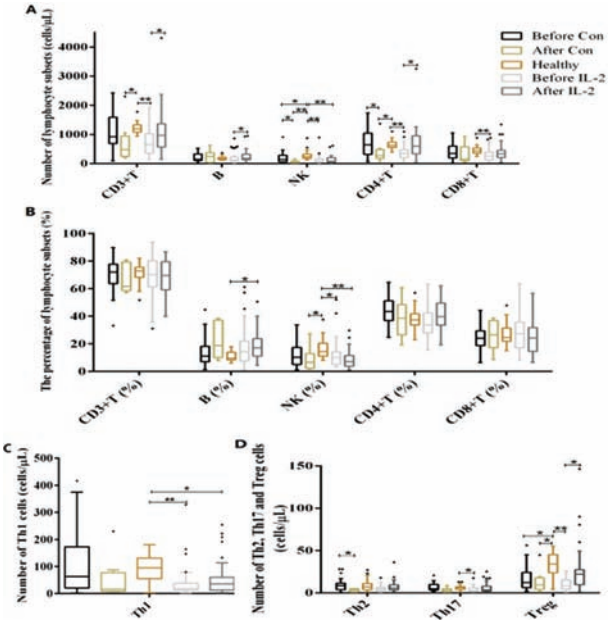


Figure 1. The comparison of lymphocytes subpopulations in PM, DM patients and Healthy controls. Data were presented as Median (Q25, Q75). Statistical analysis was performed by the Independent-Samples Kruskal-Wallis test one-way ANOVA. *P <0.05.

Abstract THU0332 – Figure 1



Abstract THU0332 – Figure 2

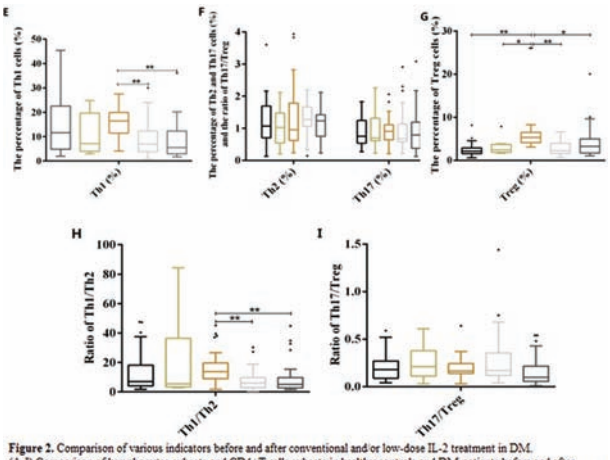


Figure 2. Comparison of various indicators before and after conventional and/or low-dose IL-2 treatment in DM. (A-I) Comparison of lymphocytes subsets and CD4+T cells subsets in healthy controls and DM patients before and after conventional and low-dose IL-2 treatment. Data were expressed as Median (Q25, Q75). Data were analyzed by the Independent-Samples Kruskal-Wallis test one-way ANOVA. *P<0.05;**P<0.001

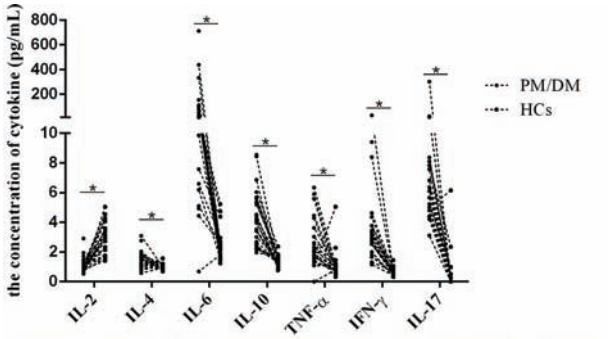


Figure 3. Comparison of serum concentrations of cytokines (including IL-2, IL-4, IL-6, IL-10, TNF-α, IFN-g and IL-17) between PM/DM and Healthy Controls by Mann-Whitney U test. *P<0.05.

Abstract THU0332 – Figure 3

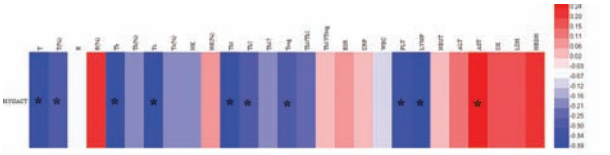


Figure 4. The correlation between multiple indicators and MYOACT. Heatmap representation of correlation of MYOACT with lymphocyte subpopulation (including the number and percentage of CD3+T, B, Th, Ts and NK cells), CD4+T subsets (including the number of Th1, Th2, Th17, Treg cells and the ratio of Th1/Th2 and Th17/Treg), Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), White Blood Cell (WBC), Platelet (PLT), Lymphocyte (LYMP), Neutrophile Granulocyte (NEUT), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Creatine Kinase (CK), Lactate Dehydrogenase (LDH) and Hydroxybutyrate Dehydrogenase (HBDH) in DM patients (n=61). *P<0.05 by Spearman correlation test.

Abstract THU0332 – Figure 4

Conclusion: The decrease of Treg cells was found in PM/DM accompanied with lower serum IL-2, which should be associated with the pathogenesis of PM/DM. Meanwhile, various pro-inflammatory T cells also showed a downward trend with or without significant difference, indicating PM/DM is caused by immunodeficiency rather than hyperimmunism. ld-IL2 combined with conventional therapy could restore the reduction of CD4Treg cells and help to alleviate disease activity.

REFERENCES:

[1] Yang WM, Chen JJ. Advances in biomarkers for dermatomyositis. Clin Chim Acta 2018; 482: 172-177.
[2] Yuan L, Yao L, Zhao L, Xia L, Shen H, Lu J. Serum levels of soluble ST2 and interleukin-33 in patients with dermatomyositis and polymyositis. Clin Exp Rheumatol 2013; 31:428-432.
[3] Mizui M, Tsokos GC. Low-Dose IL-2 in the Treatment of Lupus. Curr Rheumatol Rep 2016; 18:68.

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THU0333

2-CARBA CYCLIC PHOSPHATIDIC ACID (2CCPA) SUPPRESSES PROFIBROTIC ACTIVITY IN SYSTEMIC SCLEROSIS SKIN FIBROBLASTS AND BLEOMYCIN-INDUCED SKIN FIBROSIS IN MICE

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Background: Systemic sclerosis (SSc) is a connective tissue disorder with progressive fibrosis in multiple organs including skin, lung and the gastrointestinal tract. Fibrosis is thought to be driven by activated fibroblasts. Therefore, inhibition of the profibrotic activity of activated fibroblasts may be a promising therapeutic approach in skin fibrosis in SSc. The autotaxin (ATX)/lysophosphatidic acid (LPA) axis is reportedly involved in fibrotic pathogenesis in SSc[1]. 2-carba cyclic phosphatidic acid (2ccPA) is a naturally occurring lipid mediator and one of its pleiotropic properties is to inhibit the ATX/LPA axis.
Objectives: We investigated the anti-fibrotic effect of 2ccPA on human SSc skin fibroblasts and bleomycin-induced skin fibrosis in mice. Furthermore, we searched signaling pathways related to the anti-fibrotic effects of 2ccPA.
Methods: This study was approved by the ethics committee and the ethical review committee of animal experiments of Tokyo Women's Medical University. We informed all participants of the content of this study, and written consent was obtained. Skin fibroblasts were taken from SSc patients and adult healthy individuals were purchased. The cells were incubated with 1-10 μM 2ccPA in the presence or absence of 10 ng/ml transforming growth factor-β1 (TGF-β1). Messenger RNA (mRNA) and protein expression for type I collagen, connective tissue growth factor (CTGF), α smooth muscle actin (αSMA), fibronectin (FN) and TGF-β1 were assessed by qRT-PCR or Western blotting. Procollagen type I C-peptide, prostaglandin E_2 (PGE_2) and hepatocyte growth factor (HGF) levels in the supernatant were assessed by ELISA. Intracellular cyclic adenosine monophosphate (cAMP) levels were calculated using a commercially available EIA kit. Forskolin was used to increase intracellular cAMP levels in cultured SSc skin fibroblasts. An inhibitor of adenylate cyclase (AC), 2'-deoxyadenosine, was used to investigate whether the anti-fibrotic effect of 2ccPA was mediated via the AC/cAMP pathway. Furthermore, we used a mouse model of bleomycin-induced skin fibrosis to investigate the safety and anti-fibrotic effects of 2ccPA.
Results: Ten μM 2ccPA significantly reduced mRNA and protein expression for type I collagen, CTGF and αSMA in SSc skin fibroblasts and adult healthy skin fibroblasts treated with TGF-β1. PGE2 and HGF levels in the supernatant of SSc skin fibroblasts were also reduced by 2ccPA treatment. 2ccPA increased intracellular cAMP levels as well as the AC stimulator, forskolin. In addition, forskolin decreased the mRNA expression of profibrotic markers. Reduction of *COL1A1* mRNA expression by 2ccPA was blocked by treatment with 2'-deoxyadenosine in cultured SSc skin fibroblasts, suggesting that the anti-fibrotic activity of 2ccPA was partially mediated via AC stimulation. In mouse experiments, intraperitoneal injection of 10 mg/kg 2ccPA significantly reduced the development of skin thickness, collagen content and αSMA-positive cell counts.
Conclusion: 2ccPA suppressed the profibrotic activity of SSc skin fibroblasts and the development of bleomycin-induced skin fibrosis. Our experiments suggested that the anti-fibrotic property of 2ccPA was at least in part due to increased intracellular cAMP levels in skin fibroblasts. 2ccPA has been reported to be well tolerated in clinical trials of other diseases and may be expected for the treatment of fibrotic lesions in SSc.

REFERENCE:

[1] Castelino FV et al. Arthritis Rheumatol. 2016;68:2964-2974.

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THU0334 EFFECT OF THE DELAY FROM INITIAL SYMPTOMS TO DIAGNOSIS OR THERAPY INITIATION, ON DISEASE CONTROL AND MORTALITY, IN INFLAMMATORY MIOSITIS PATIENTS FROM THE INFLAMMATORY MIOSITIS REGISTRY FROM THE MADRID COMMUNITY (REMICAM)

Beatriz Joven-Ibáñez[1], Laura Nuño[2], Francisco J López-Longo[3], Julia Martinez-Barrio[3], Carmen Larena[4], Valentina Maldonado[4], Carmen Barbadillo[5], Paloma García de la Peña[6], Irene Llorente[7], Eva Tomero Muriel[7], Ana Pérez Gómez[8], Henry Moruno[8], Tatiana Cobo-Ibáñez[9], Raquel Almodovar[10], Leticia Lojo[11], María Jesús García de Yébenes[12], Patricia Carreira[1]. *[1]University Hospital 12 de Octubre, Madrid, Spain*; *[2]Hospital La Paz-madrid, Madrid, Spain*; *[3]Gregorio Marañón Hospital, Madrid, Spain*; *[4]Hospital Ramón YCajal, Madrid, Spain*; *[5]Hospital Puerta de Hierro-Majadahonda, Majadahonda, Spain*; *[6]HM University Sanchinarro Hospital, Madrid, Spain*; *[7]Hospital de La Princesa, Madrid, Spain*; *[8]Hospital Príncipe de Asturias, Alcalá de Henares, Spain*; *[9]Hospital Infanta Sofía, San Sebastián de los Reyes, Spain*; *[10]Fundación Hospital Alcorcón, Alcorcón, Spain*; *[11]Hospital Infanta Leonor, Madrid, Spain*; *[12]Instituto de salud musculoesquelética, Madrid, Spain*

Background: In inflammatory diseases, such as rheumatoid arthritis, early treatment has demonstrated to improve disease control and decrease mortality. It is not known if an early treatment could have similar effects on inflammatory myositis (IM) patients.
Objectives: To analyze if the delay between initial symptoms and diagnosis or therapy initiation influences disease control or mortality in IM patients.
Methods: All patients from REMICAM were included (1). The influence of time elapsed between initial symptoms and diagnosis or start of therapy, and the year of diagnosis (before or after 2000), on mortality and disease control (defined as the possibility of glucocorticoid (GC) withdrawal due to IM improvement), was studied by means of survival analysis and regression proportional hazard bi and multivariate Cox models. All factors with p<0,2 in bivariate were included in multivariate models. The mortality analysis was controlled for age, sex, and other known mortality factors: cardiovascular risk factors, interstitial lung diseases (ILD), cardiac involvement and cancer. The disease control analysis was controlled for age, sex and other known severity factors such as ILD, cardiac involvement and IM subtypes.
Results: From 479 patients (74% females, 52% polimiositis, 44±22 years at diagnosis, 10±8 years follow up), 208 (43%) were diagnosed before 2000, and 473 (99%) received any treatment: 473 (99%) oral GC, 50/344 (15%) GC pulses, 78 (16%) HCL, 355 (74%) immunosuppressants (IS) (MTX 228, LF 10, AZA 190, CYP 44, MP 38, CyS 32), 55 (12%) biologics (RTX 45, abatacept 2, aTNF 16) and 79 (17%) IVIG. Disease control was more frequent in younger patients, diagnosed after year 2000, and was independently associated with less ILD presence, lower n° of therapies and a shorter time between the initial symptoms and the start of IS therapy (Table 1). Risk factors for mortality were age, male sex and cancer, but not the delay in diagnosis or in the start of therapy (Table 2)

Abstract THU0334 –Table 1.

	Bivariate		Multivariate	
	HR (IC95%)	**p**	**HR (IC95%)**	**p**
Age at diagnosis	**0.97 (0.96-0.98)**	**<0.0001**	**0.97 (0.96-0.98)**	**<0.0001**
ILD	**0.3 (0.2-0.5)**	**<0.0001**	**0.4 (0.3-0.8)**	**0.006**
Diagnosis < 2000		0.07	**1.9 (1.2-3.1)**	**0.006**
N therapies	**0.8 (0.7-0.9)**	**<0.0001**	**0.7 (0.6-0.8)**	**<0.0001**
Any IS	**0.6 (0.4-0.8)**	**0.004**	**0.08 (0.01-0.6)**	**0.02**
Initial symptoms to IS	**0.987 (0.981-0.993)**	**<0.0001**	**0.98 (0.97-0.99)**	**<0.0001**

Abstract THU0334 –Table 2.

	Bivariate		Multivariate	
	HR (IC95%)	**p**	**HR (IC95%)**	**p**
Sex	**0.5 (0.3-0.8)**	**0.003**	**0.56 (0.36-0.87)**	**0.01**
Age at diagnosis	**1.05 (1.04-1.07)**	**<0.0001**	**1.05 (1.04-1.06)**	**<0.0001**
Cancer	**3.4 (2.2-5.2)**	**<0.0001**	**1.9 (1.2-2.9)**	**0.003**

Conclusion: In the REMICAM cohort, disease control is more frequent in younger patients, diagnosed after 2000, with early initiation of IS therapy. Mortality was not associated with the delay in diagnosis or therapy in our study. Our data support the hypothesis that, in IM, as in other inflammatory diseases, an early treatment is essential to decrease inflammation and achieve disease control.

REFERENCE:

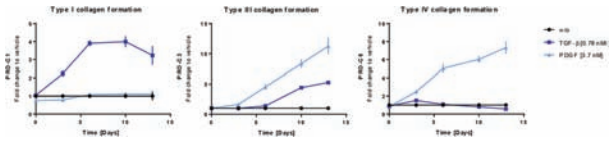
[1] Nuño L, Rheumatol Clin 2017; 13:331-337

Disclosure of Interests: Beatriz Joven-Ibáñez Speakers bureau: Celgene, Novartis, MSD, Pfizer, AbbVie, and Janssen, Laura Nuño: None declared, Francisco J López-Longo: None declared, Julia Martinez-Barrio: None declared, Carmen Larena: None declared, Valentina Maldonado : None declared, Carmen Barbadillo: None declared, Paloma García de la Peña: None declared, Irene Llorente : None declared, Eva Tomero Muriel: None declared, Ana Pérez Gómez: None declared, Henry Moruno : None declared, Tatiana Cobo-Ibáñez: None declared, RAQUEL ALMODOVAR: None declared, LETICIA LOJO : None declared, María Jesús García de Yébenes: None declared, Patricia Carreira: None declared
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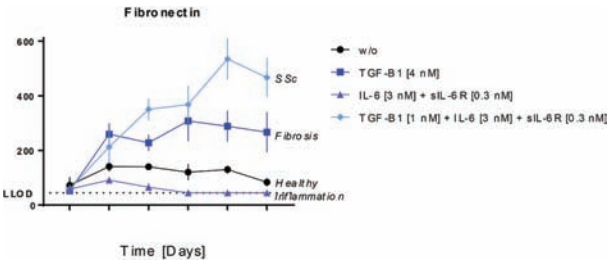
THU0335 FIBROSIS IS NOT JUST FIBROSIS – TGF-B AND PDGF INDUCE DIFFERENT EXTRACELLULAR MATRIX PROFILE: A MODEL OF DERMAL FIBROBLASTS WHICH MIMICS SYSTEMIC SCLEROSIS POTENTIAL FOR EVALUATION OF ANTI-FIBROTIC COMPOUNDS WITH TRANSLATIONAL BIOMARKERS

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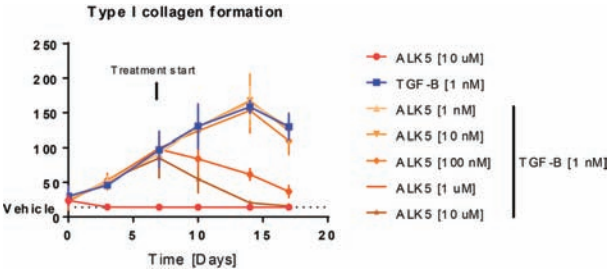
Background: Fibroblasts are responsible for the excessive extracellular matrix formation (ECM) observed in systemic sclerosis (SSc). These cells are activated by stimulants from both the vascular and immune systems, including platelet derived growth factor (PDGF) and transforming growth factor beta (TGF-β). While both TGF-β and PDGF induces extracellular matrix (ECM) formation, there is a need to understand the quantitative differences to allow for more optimal drug development and patient targeted therapies. This may be accomplished by using translational tools in cell culture systems for the evaluation of potential anti-fibrotic compounds in SSc.
Objectives: This study investigated the ability of dermal fibroblast to produce ECM that mimics SSc though the use of clinical validated biomarkers.
Methods: Primary human dermal fibroblasts were grown in DMEM media containing 0.4% fetal calf serum, FICOLL (to produce a crowded environment) and ascorbic acid for 14 days. The cells were stimulated with PDGF [0.04-4 nM], TGF-β [0.01-4 nM], a combination of interleukin 6 (IL-6) [3 nM] and the soluble IL-6 Receptor (sIL-6R) [0.3 nM], or a combination of TGF-β [1 nM], IL-6 [3 nM], and sIL-6R [0.3 nM]. An ALK-5 (TGF-β receptor) inhibitor (iALK-5, [1 nM-10 μM]) was added together with 1 nM TGF-β with or without 7 days pretreatment and stimulated for 17 days in total. Media were changed twice a week. Unstimulated cells (w/o) were used as controls. Type I, III and VI collagen formation (PRO-C1, PRO-C3, PRO-C6) and fibronectin (FBN-C) were evaluated by ELISAs in the supernatant collected at each media change. Staining with hematoxylin and eosin (H&E) together with immunohistochemical staining were performed.
Kruskal-Wallis tests were used examine the difference between treatments at different days.
Results: Stimulation with TGF-β induced type I collagen formation from day 3, with a 4-fold change (FC) detected on day 10 compared to w/o (P<0.0001, Figure 1), and type III collagen formation in a dose dependent manner from day 10 (4.4-FC, P<0.0001). TGF-β did not induce type VI collagen formation. PDGF induced type III collagen formation from day 6, with an 8.3-FC by day 10 (P<0.0001) and type VI collagen formation from day 3 with a 6.0-FC by 10 (P=0.0006). PDGF did not induce type I collagen formation. Media alone did not induce any collagen formation.
H&E staining showed that fibroblasts treated with PDGF and TGF-β were more confluent and disorganized compared to untreated cells. Visual examination showed type I collagen attachment to the bottom of the wells and this increased in response to stimulants.



Abstract THU0335 – Figure 1



Abstract THU0335 – Figure 2



Abstract THU0335 – Figure 3

Stimulation with IL-6 decreased fibronectin levels compared to w/o, whereas TGF-β increased this. A combination of both cytokines resulted in a further increase in fibronectin levels (IL-6: 44 ng/ml, TGF-β: 308 ng/ml, IL-6+TGF-β: 368 ng/ml, P<0.0001) (Figure 2). Treatment with iALK-5 (≥1 μM) decreased type I collagen formation levels to those of the vehicle, while 100 nM showed a tendency to be lower (TGF-β: 129 ng/ml, TGF-β+100 nM iALK-5: 94 ng/ml, not significant). IALK-5 at 1 μM or above, could rescue cells after 7 days pretreatment with 1 nM TGF-β (TGF-β: 129 ng/ml, TGF-β+1 μM iALK-5: 37 ng/ml, TGF-β+10 μM iALK-5: 14 ng/ml). Levels were decreased from day 10 (Figure 3).

Conclusion: TGF-β and PDGF induced very different ECM compositions, with PDGF inducing much more type VI collagen formation as compared to TGF-β. In contract, TGF-β induce a highly type I collage dependent ECM. This model system and biomarkers may be used to test novel anti-fibrotic compounds, and allow for identification of patient with the endotype of fibrosis that may responds the best to treatment.

Disclosure of Interests: Pernille Juhl: None declared, Sandie Bomdesen: None declared, Anne-Christine Bay-Jensen Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Morten Karsdal Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Michael Jonathan Davies: None declared, Anne Sofie Siebuhr Employee of: I am a full-time employee in Nordic Bioscience

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THU0336 DEVELOPING A NOVEL RAPID EX VIVO MODEL OF SKIN FIBROSIS FOR SYSTEMIC SCLEROSIS RESEARCH

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Background: Systemic Sclerosis (SSc) is an autoimmune disease that causes tissue fibrosis in multiple systems. Immune dysfunction and dysregulation are known to play a role in the disease, but the pathophysiology of SSc is not clearly understood.(1) Adipose-derived stromal cells (ADSCs) reside in the dermal white adipose tissue (DWAT) and have reparative and regenerative functions.(2) We have previously shown that ADSCs are lost in SSc and that injecting these along with a survival signal can partially reverse fibrosis.(3) To better understand how ADSCs reverse fibrosis, we wanted to develop an ex vivo skin fibrosis model. As the commonly used in vivo bleomycin-injected fibrosis model takes three to four weeks to prepare, a more rapid ex vivo model would further facilitate mechanistic dissection.

Objectives: This pilot study aims to establish a novel ex vivo experimental model that can demonstrate fibrotic change in mouse skin and represent ADSC loss within days rather than within weeks needed for current models.

Methods: Six B6 mice were sacrificed at between 12-16 weeks of age and skin tissues were obtained from the back by 8mm punch biopsies. Skin samples were immersed in Dulbecco's Modified Eagle's Medium containing either bleomycin (5 or 10mU/ml) or PBS as control for one or three days. After harvesting, H&E staining was performed on skin samples to assess phenotypic fibrotic changes. Flow cytometry (FACS Canto) was used to measure the viability, total cell number and ADSC change. A total collagen assay quantified collagen production in samples.

Results: On H&E staining, compared to controls, samples cultured with 5mU/ml bleomycin for a day showed increased density of dermis and deposition of amorphous pink material, likely representing increased collagen. With 10mU/ml bleomycin, these changes were greater and especially affected the upper dermis. On day 3, samples in 5mU/ml and 10mU/ml bleomycin appeared to have denser fibrosis, broader dermis band, and narrower DWAT layer. The histopathological change was most prominent on day 3 sample in 10mU/ml bleomycin, with the dermis layer 40% thicker and the DWAT layer 37% narrower than the control. However, all the samples on day 3 showed stress, such as epidermis detachment and apoptosis in the epidermis. On the Total Collagen Assay, collagen deposition on day 1 in control sample was 7.7ug/mm, compared to 33.9ug/mm from sample in 10mU/ml bleomycin. On day 3, collagen deposition in 10mU/ml bleomycin was 37ug/mm which was 2.5 to 5 times higher than control. On FACS, the decrease in ADSC level correlated to the increase in concentration of bleomycin and the number of days treated, with the greatest drop in samples in 10mU/ml bleomycin on day 3.

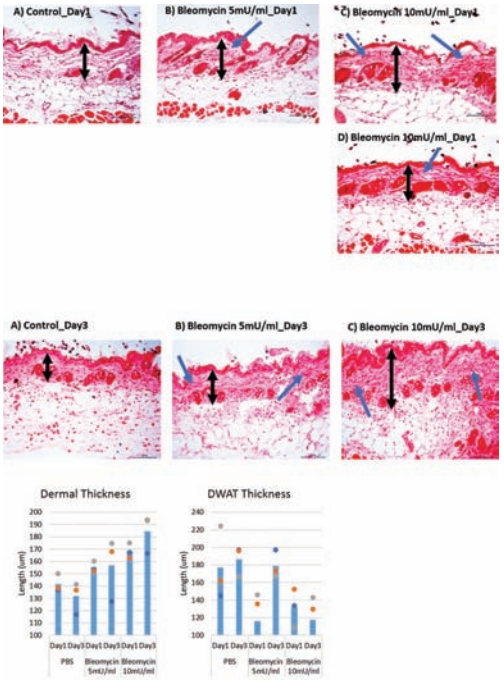
Conclusion: Our results thus far suggest that we are creating a novel ex vivo model of skin fibrosis that can help better understand how ADSCs can be of therapeutic benefit in SSc. This rapid ex vivo model will complement the existing in vivo model. Our next step will be to investigate the changes of profibrotic cytokines before and after applying ADSCs purified from healthy mice to understand how skin fibrosis can be reversed.

REFERENCES:

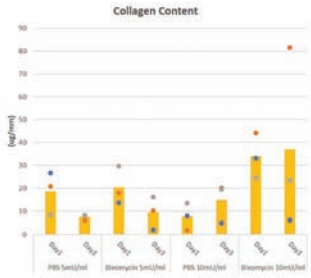
[1] Gilbane, Adrian J et al. "Scleroderma pathogenesis: a pivotal role for fibroblasts as effector cells" Arthritis research & therapy vol. 15,3 (2013): 215

[2] Marangoni, Roberta G.; Lu, Theresa T. "The roles of dermal white adipose tissue loss in scleroderma skin fibrosis" Current Opinion in Rheumatology vol 29(6), (2017): 585–590

[3] Chia, Jennifer J et al. "Dendritic cells maintain dermal adipose-derived stromal cells in skin fibrosis" Journal of clinical investigation vol. 126,11 (2016): 4331-4345

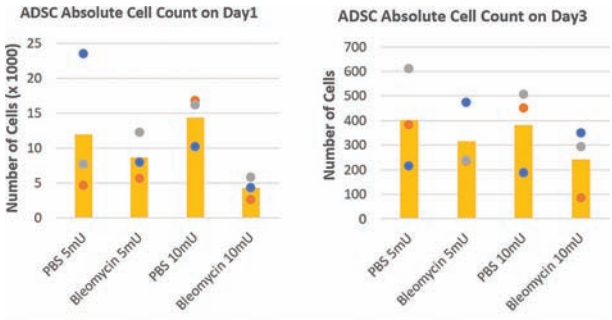


Abstract THU0356 – Figure 1. H&E. Blue arrows showed the areas where there are increased collagen deposition and density.



Total Collagen/Length	PBS 5mU/ml		Bleomycin 5mU/ml		PBS 10mU/ml		Bleomycin 10mU/ml	
	Day1	Day3	Day1	Day3	Day1	Day3	Day1	Day3
M1	26.62221	8.075801	13.65193	2.020586	7.889791	4.814997	33.09294	6.023478
M2	20.72036	6.119037	17.93023	10.1741	1.852593	20.07658	44.17843	81.4925
M3	8.364862	8.10193	29.75995	16.07763	13.43434	19.56702	24.42635	23.34717
Average	18.56914	7.432256	20.44737	9.424107	7.725576	14.81953	33.89924	36.95438

Abstract THU0356 – Figure 2. Total collagen content



	Value	Sample1	Sample2	Sample3	Average
ADSC Absolute Cell Count on Day1	PBS 5mU	23446.8	4709.1	7657.2	11937.7
	Bleomycin 5mU	7985.04	5680.08	12243.6	8636.24
	PBS 10mU	10209.06	16826.4	16199.16	14411.54
	Bleomycin 10mU	4349.34	2640.96	5853.12	4281.14
	Value	Sample1	Sample2	Sample3	Average
ADSC Absolute Cell Count On Day 3	PBS 5mU	214.272	381.264	609.96	401.832
	Bleomycin 5mU	474.24	234.396	236.232	314.956
	PBS 10mU	185.328	449.064	506.88	380.424
	Bleomycin 10mU	349.272	85.86	292.032	242.388

Abstract THU0356 – Figure 3. ADSC cell count measured by flow cytometry

Disclosure of Interests: None declared
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THU0337 COMPARISON OF THE EFFICACY OF TWO RITUXIMAB REGIMENS IN THE PATIENTS WITH SYSTEMIC SCLEROSIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE

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Background: Rituximab (RTM) is considered as a promising therapeutic agent for treatment of insterstitial lung disease (ILD) in the patients with systemic sclerosis (SSc). However, the limited number of RTM-treated patients, heterogeneity of the studies in relation to main parameters, considerably different dose regimens, cumulative doses, and observation periods does not allow univocal conclusions on RTM efficacy or definitive recommendations on RTM use in the patients with SSc. The question whether to combine RTM with immunosupressants (IS) or it is possible to use it as a single-agent therapy in the patients with SSc associated with ILD is still relevant.
Objectives: To compare the time courses of pulmonary function parameters and dermal fibrosis parameters during the use of RTM in combination with IS and as a single-agent therapy in the patients with SSc associated with ILD in the open-label prospective non-randomized study.
Methods: 90 patients with the confirmed SSc diagnosis and ILD evidence based on HRCT findings were enrolled into the study. All patients received low-dose and moderate-dose prednisolone regimens. **Group A** (n=45) **received a total RTM dose** 3.1±1.2 g **in combination with IS** (27/60% mycophenolate mofetyl, 16/35.6% cyclophosphamide, 2/4.4% methotrexate; the patient's average age was 47.4±11.6 years, with female proportion 82%; SSc duration 4.6±3.5 years; diffused/localized forms 1.3/1). **Group B (n=45) received RTM as a single therapy agent** in a total dose 2.7±1 g (average age 45.0±15 years, female proportion 82%, SSc duration 6.7±5.6 years, diffused/localized forms 1.5/1). The age, gender proportion, SSc form, FVC and DLCO, and RTM cumulative doses were similar in the both groups. The follow-up period was 42 months. The time courses of FVC, DLCO, modified skin count (mRss, points), activity index (EScSG, points) were assessed in the study.
Results: In Groups A and B during the therapy significant decrease in mRss (p=0.00034 and 0.000002 respectively) and EScSG (p=0.00011 and 0.000000 respectively), FVC increase (p;=0.00017 and 0.00001, respectively), and stabilization of the DLCO were observed.
The treatment groups did not differ significantly in the median FVC increment, clinically meaningful FVC and DLCO increments of decrements, and EScSG and mRss time courses.

Parameters	Group A	Group B
EScSG 1 *M ± SD*	3.2±1.9*	2.7±1.6*
EScSG 2 *M ± SD*	1.6±1.3*	1.2±0.98*
mRss 1 *M ± SD*	11.0±9.3 *	11.5±9.3*
mRss 2 *M ± SD*	7.2±5.6 *	5.6±4.2*
FVC 1 *M ± SD*	76±20.3*	77.8±19.7 *
FVC 2 *M ± SD*	82.7±22.5*	86.8±19.7*
Δ FVC%	5.7	8.3
	[0; 11.2]	[1.1; 15.4]
FVC increment by ≥10%, n/%	14/31	17/37.8
FVC decrement by ≥10% n/%	2/4.4	2/4.4
DLCO 1 *M ± SD*	44.5±19	47.8±17.1
DLCO 2 *M ± SD*	45.4±16.8	50.4±16.9
Δ DLCO%	1.3	2.1
	[-1.6; 6.9]	[-1.41; 7.1]
DLCO increment by ≥10%, n/%	3/6.7	5/11
DLCO decrement by ≥10% n/%	5/11	4/8.9

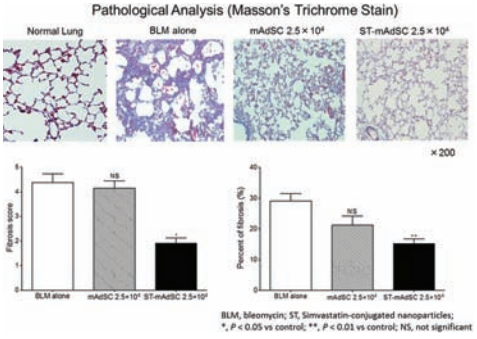
Notes: *in Parameters column 1 = before treatment, 2 = after treatment; M ± SD = mean value and standard deviation; * = significant difference between the vales measured before and after the treatment*
Conclusion: RTM administration both in combination with IS and as a single agent therapy in the patients with SSc associated with ILD effectively alleviated skin induration and EScSG, improved or stabilized the pulmonary function parameters. The absence of statistically significant difference in the time course of evaluated parameters between the groups substantiate potential RTM use as a single-agent therapy that, this is most important for the patients with poor tolerability or contraindications to IS administration.
Disclosure of Interests: None declared
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THU0338 SIMVASTATIN-CONJUGATED NANOPARTICLE ENHANCES THE THERAPEUTIC EFFECT OF ADIPOSE-DERIVED STEM CELLS ON INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) associated with connective tissue disease is a life-threatening pathological condition that causes respiratory failure when it progresses. Lung inflammation is treated with corticosteroids and immunosuppressants, and pulmonary fibrosis is treated with anti-fibrosis agents such as pirfenidone and nintedanib. However, many cases are treatment-resistant and the outcome is poor. Moreover, adverse effects such as infections resulting from immunosuppressive therapy are problematic. The development of new treatments is thus required for ILD from the viewpoint of the poor effect and adverse effects of the currently available treatments. Research and development with adipose-derived stem cells (AdSCs) in immunosuppressive therapy have progressed for autoimmune diseases, and favorable outcomes have been reported. In recent years, the effectiveness of AdSCs in ILD model mice has been demonstrated (ref). The statin preparation has not only an angiogenesis promoting action, an immunosuppressive action, an anti-fibrotic action but also an action of promoting a cellular function including a migratory ability.

Objectives: We have investigated the hypothesis that statin, an agent with pleiotropic effects, could augment the therapeutic potential of AdSCs.
Methods: ILD was induced by bleomycin (BLM) in C57BL/6 mouse, and the mice were assigned in the following groups: 1) Control, 2) NP-AdSCs (2.5×10^4 cells), and 3) STNP-AdSCs (2.5×10^4 cells).
Results: Simvastatin-conjugated nanoparticles (STNP) significantly promoted the migration activity and cell survival without changing the proliferation activity, and up-regulated transforming growth factor (TGF) -β1 in vitro assays. Lung inflammation and fibrosis assessed were significantly supressed at 4 weeks after starting BLM administration in STNP-AdSCs group (Figure). The levels of IL-4, IFN-gamma, TNF-alpha, COL1A1, and TIMP1 mRNA expression at 28 days after BLM administration were significantly lower in STNP-AdSCs group compared with that in other groups.
Conclusion: Simvastatin-conjugated nanoparticles enhanced the therapeutic effect of a small number of AdSCs transplantation.



Abstract THU0338 – Figure 1

REFERENCE:
[1] Sci Rep 6; 7 (1): 14608, 2017.

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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.6636

THU0339 PULMONARY INVOLVEMENT AND OUTCOME IN SYSTEMIC SCLEROSIS (SSC) – ILD-PH AS AN IMPORTANT SUBSET

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Background: Pulmonary involvement is the leading cause of death in SSc and can manifest as interstitial lung disease (ILD), pulmonary hypertension (PAH) or a combination (ILD-PH). Aim of this analysis was to determine prevalence, clinical characteristics and outcomes of different forms within the German SSc Network.
Objectives:
Methods: SSc patients were analyzed for pulmonary involvement, clinical characteristics and outcome.
Results: There were 3699 pts in 42 centers with a mean follow up time of 34.4±12.6 months. At baseline, ILD was frequent (29.5%), while ILD-PH and PAH had lower prevalences (7.5%, 6.1%). At the end of follow up, 32% of SSc pts had ILD, 13% ILD-PH and 7% PAH. ILD and ILD-PH were more frequent in the diffuse form (47%, 12%), while PAH did not differ between subforms. Significant differences in baseline characteristics between PAH vs. ILD-PH vs. ILD were found for age (62, 59, 54 years), sex (males: 15%, 22%, 24%) and smoking prevalence (non-smokers 49%, 63%, 57%). Mean DLCO and FVC were 56%/93% for PAH, 49%/78% for ILD-PH and 56%/81% for ILD. Significant decreases for DLCO (≥15%) and FVC (≥10%) were found in 45%/26% in PAH, 45%/26% for ILD-PH and 36%/16% in ILD. All-cause mortality was 8.1% for the total cohort and differed significantly between patients without pulmonary involvement (4%), ILD (7.8%), PAH (14.2%), and ILD-PH (21%, p<0.001).
Conclusion: ILD is the most prevalent pulmonary involvement in SSc, while PH-ILD is associated with the most detrimental survival. Significant differences in baseline characteristics of types of pulmonary SSc involvement may help to identify patients at risk in the future.
Disclosure of Interests: : Michael Kreuter Grant/research support from: Boehringer Ingelheim, Roche Pharma, Consultant for: Boehringer Ingelheim, Roche Pharma, Speakers bureau: Boehringer Ingelheim, Roche Pharma, Francesco Bonella Consultant for: Boehringer Ingelheim, Roche Pharma, Speakers bureau: Boehringer Ingelheim, Roche Pharma, Ulf Müller-Ladner Grant/research support from: Projekt supported by an unrestricted educational grant from Celgene GmbH., Elise Siegert Shareholder of: Astra Zeneca, Grant/research support from: Actelion, Consultant for: AEC Partners, Speakers bureau: Actelion, Norsk, Jörg Henes: None declared, Gabriela Riemekasten Consultant for: Chugai, F. Hoffmann-La Roche, Speakers bureau: Chugai, F. Hoffmann-La Roche, Norbert Blank Grant/research support from: SOBI and Novartis, Speakers bureau: Novartis and SOBI, Marc Schmalzing Grant/research support from: Pfizer, Chugai, MSD, Janssen-Cilag, BMS, Celgene, UCB, Consultant for: Abbvie, Chugai, Genzyme, Hexal/Sandoz, MSD, Novartis, Roche, Sanofi Pasteur, Speakers bureau: Actelion, Baxalta/Shire, BMS, Celgene, Chugai, Janssen-Cilag, MSD, Novartis, Pfizer, Roche, UCB, Ina Koetter: None declared, Claudia Guenther Grant/research support from: Pfizer, Novartis, Employee of: 20 years ago, Novartis, Speakers bureau: Celtis, Tim Schmeiser Speakers bureau: Actelion, UCB, Pfizer, Gabriele Zeidler Grant/research support from:

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THU0340 IMPACT OF LANIFIBRANOR, A PAN-PPAR AGONIST, ON THE PULMONARY VASCULAR TONE

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Background: Pulmonary hypertension (PH) is common in patients with fibrosing interstitial lung diseases (ILDs) such as systemic sclerosis (scleroderma) and has a significant impact on survival. The pan-peroxisome proliferator-activated receptor (PPAR) agonist lanifibranor is currently being tested in a phase II clinical trial in scleroderma patients. Although, the antifibrotic effects of lanifibranor have been previously shown in preclinical mouse models of scleroderma and related PH (1), its effects in modulating the pulmonary vascular tone are largely unknown.
Objectives: To evaluate the acute effect of lanifibranor (pan-PPAR agonist) and selective PPAR agonists on the pulmonary vascular tone.
Methods: Freshly isolated intra-pulmonary arteries from explanted human and rat lungs were used in wire myography experiments to assess the acute effect on pulmonary vascular tone of pan-PPAR agonist -lanifibranor and the selective PPAR agonists PPARα -fenofibrate, PPARβ/δ -GW50156 and PPARγ –troglitazone (0.01μM-30μM) versus vehicle (DMSO). The intra-pulmonary arteries were pre-constricted with 300nM of the thromboxane A2 receptor agonist U46619. The contribution of endothelium and nitric oxide was investigated using both native and endothelium-denuded vessels, with and without the nitric oxide synthase inhibitor L-NAME.
Results: Isometric tension measurements in rat pulmonary arteries showed that lanifibranor and the selective PPAR agonists PPARβ/δ -GW50156 and PPARγ –troglitazone, induced a significant relaxation compared to their vehicle controls, whereas the PPARα agonist fenofibrate did not show any vasoactive effect on the pre-constricted arteries. Lanifibranor showed a significant vasodilatory effect already at 1μM whereas GW50156 and troglitazone showed significant vasodilatory effects starting from 10μM as compared to their vehicle controls. At the maximum concentration used (30μM), lanifibranor caused a relaxation response of -85% whereas GW50156 and troglitazone caused just -45% and -50% vasorelaxation (n=6), respectively. The vasodilation induced by pan-PPAR and selective PPAR agonists remained unaffected by pre-treatment of L-NAME or denuded endothelium. Lanifibranor had vasodilatory effects that were strongly superior to any of the selective PPAR agonists in the isolated pulmonary artery from the explanted human lungs (n=3).
Conclusion: The current study revealed that the pan-PPAR agonist lanifibranor caused a rapid dose-dependent relaxation in both rat and human intra pulmonary arteries which were superior to any other PPAR agonists suggesting additive effects of the pan-PPAR agonism. The observed vasoactive effects of pan-PPAR are independent of nitric oxide and endothelium, delineating the specific effect of PPAR agonism on the pulmonary artery smooth muscle cells. These results suggest that lanifibranor could be a promising therapy for vasculopathies such as PH observed in scleroderma patients.

REFERENCE:

[1] Avouac J et al. Pan-PPAR agonist IVA337 is effective in experimental lung fibrosis and pulmonary hypertension. Ann Rheum Dis. 2017 Nov;76 (11):1931-1940.

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THU0341 MICRORNA27A3P REGULATES WNT SIGNALLING BY TARGETING SFRP-1 IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune idiopathic connective tissue disease that results in fibrosis of the skin and lungs. Wnt signaling is a highly conserved signaling pathways that is involved in organogenesis and tissue homeostasis. In recent years it has emerged that aberrant Wnt signaling is key in SSc and animal models of the disease. The Wnt pathway comprises of secreted glycoproteins that bind to specific receptors that initiate the pathway and result in beta catenin stabilization. However, secreted antagonists are secreted to block and negatively regulate Wnt signaling. We and others have found reduced sFRP-1 in SSc, a key Wnt antagonist. Although lower in SSc skin and isolated fibroblast from patients the mechanism governing this is unknown. This work seeks to identify epigenetic mechanisms.
Objectives: Determine the epigenetic regulation of sFRP-1 in SSc.
Methods: Serum sFRP-1 was measured in healthy and diffuse SSc patients to ascertain the levels of sFRP-1. Mir27a was identified as a possible microRNA that targets sFRP1 using in silico modeling. miR27a was transfected into healthy dermal fibroblasts using transfection methods and sFRP-1 was measured. Collagen was also measured by western blotting after transfection. MiR27a was also measured in SSc dermal fibroblasts using specific Taqman probes and normalized to RNU44 miR. Cloning of the 3'UTR of sFRP1 into a luciferase reporter vector was performed and then transfected into HEK293 cells with miR27a mimics or with concentration matched scramble and after 24 hours luciferase was monitored.
Results: Significantly reduced expression of sFRP-1 was found in SSc serum compared to controls (n=10). SSc dermal fibroblasts had 3 fold higher levels of miR27a compared to healthy fibroblasts. Increased miR27a in healthy dermal fibroblasts resulted in significantly less sFRP-1 secreted into conditioned media and this was co-incident with an increase of collagen1 levels. Finally cloning of the 3'UTR binding site in a luciferase plasmid and overexpression of miR27a led to reduced levels of luciferase in HEK293 cells in vitro.
Conclusion: Reduced sFRP-1 in systemic sclerosis is mediated by miR27a and this leads to fibrosis via enhanced Wnt signaling. Targeting the epigenetic changes that mediate this may be a therapy in SSc.
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THU0342 SYSTEMIC SCLEROSIS IS A DISEASE OF A PREMATURELY SENESCENT, INFLAMMATORY AND ACTIVATED IMMUNOME

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterised by excessive fibrosis of skin and internal organs, and vascular dysfunction (1). Association of T and B cell subsets have been reported in SSc, however there is lack of systematic studies of functional relations between immune cell subsets in this disease (2,3,4). This lack of mechanistic knowledge hampers targeted intervention.
Objectives: In the current study we ought to determine differential immune cell composition and their interactions in peripheral blood of SSc patients and its impact on disease severity and progression.
Methods: Mononuclear cells from blood of SSc patients (n=20) and healthy controls (n=10) were analysed by mass cytometry using a 36 marker (cell-surface and intracellular) panel to aid in identification of major PBMC lineages including T cells, B cells, monocytes and NK cells and their subsets. Transcriptome analysis (m-RNA sequencing) was performed on sorted T and B cell subsets. Unsupervised clustering of mass cytometry data was performed using in-house developed analysis software MARVIS. This software combines dimension reduction and clustering steps to identify all possible cellular subsets. Further, custom R scripts helped in identifying nodes that were differentially expressed between the study groups and also phenotype of these nodes.
Results: Unsupervised clustering analysis revealed significant differences in the frequencies of T and B cell subsets in patients. Correlation network analysis highlighted an overall dysregulated immune architecture coupled with domination of inflammatory senescent T cell modules in SSc patients. Transcriptome analysis of sorted immune cells revealed an activated phenotype of CD4 and MAIT cells in patients, accompanied with increased expression of inhibitory molecules, reminiscent of

phenotype exhibited by functionally adapted, exhausted T cells in response to chronic stimulation.
Conclusion: Overall this study provides an in depth analysis of systemic immunome in SSc, highlighting role of inflammation and chronic stimulation mediated "premature senescence" of immune cells, with implications to delineate mechanism of pathogenesis and identify diagnostic/therapeutic targets.

REFERENCES:
[1] Denton, C. P. and D. Khanna (2017). "Systemic sclerosis." Lancet 390 (10103): 1685-1699.
[2] Fuschiotti, P. (2017). "Current perspectives on the role of CD8+ T cells in systemic sclerosis." Immunol Lett. In Press
[3] Liu, M., et al. (2016). "New insights into CD4(+) T cell abnormalities in systemic sclerosis." Cytokine Growth Factor Rev 28: 31-36.
[4] Sanges, S., et al. (2017). "Role of B cells in the pathogenesis of systemic sclerosis." Rev Med Interne 38(2): 113-124.

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THU0343 PU.1 INHIBITOR DB1976 CONTROLS FIBROBLAST POLARIZATION IN SYSTEMIC SCLEROSISAND LEADS TO REGRESSION OF FIBROSIS IN DIFFERENT MODELS OF ORGAN FIBROSIS

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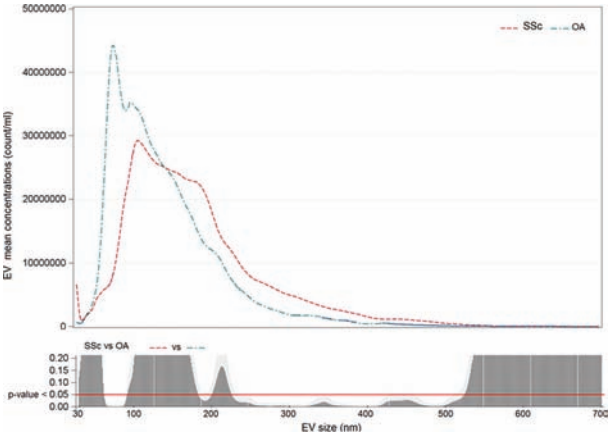
Background: Persistent activation of fibroblast with excessive release of extracellular matrix is a hallmark of systemic sclerosis (SSc). Fibroblasts can either acquire a "pro-fibrotic" phenotype with excessive matrix production or a "pro-inflammatory" phenotype with releasing of matrix-degrading enzymes and subsequent tissue destruction. Despite these well-characterized phenotypic differences, the molecular mechanisms that drive polarization of fibroblasts into these two functionally opposing phenotypes remain enigmatic.
Objectives: We aimed to evaluate the transcriptional network that promotes the extracellular matrix-producing fibrotic fibroblast fate.
Methods: We investigated the transcriptional network that induces the profibrotic phenotype of fibroblasts by in silico and immunofluorescence analyses of human fibrotic skin, lung, liver and kidney, and performed functional assays to address the fibrogenic potential of fibroblasts in vitro and in several mouse models of systemic sclerosis. The heterocyclic diamidine DB1976 was used as new therapeutic compound to induce regression of fibrosis.
Results: We identified the ETS transcription factor PU.1 as molecular checkpoint for acquisition of a "pro-fibrotic" phenotype of fibroblasts. Our data demonstrate that expression of PU.1 is effectively silenced in fibroblasts during tissue homeostasis. When the epigenetic control of PU.1 is lost and PU.1 expression is induced, fibroblasts differentiate into a fibrotic phenotype that includes the transcription of numerous pro-fibrotic mediators. PU.1 polarized resting fibroblasts and even repolarized extracellular matrix-degrading inflammatory fibroblasts to an extracellular matrix-producing fibrotic phenotype. PU.1 is associated with a network of pro-fibrotic factors including members of the TEAD–HIPPO, canonical TGF-β–SMAD and AP1 signaling pathways. Other transcription factors with fibrotic abilities, such as SNAI2 and myocyte enhancer factor (MEF) 2, bind in close vicinity to PU.1-binding sites within the genome and contribute to the recruitment of the transcription machinery that drives the switch towards the fibrotic phenotype. PU.1 has a major coordinating role within this complex network of transcription factors in fibroblasts, as the inactivation of PU.1 alone is sufficient to prevent fibrotic polarization in vitro and in vivo. Finally, we investigated pharmacological targeting of PU.1 as a potential strategy to prevent uncontrolled fibrotic tissue remodelling. DB1976 showed anti-fibrotic effects in vivo in various fibrosis models and across several organs. Treatment with DB1976 not only prevented bleomycin-mediated skin fibrosis, but also induced regression of pre-established fibrosis, and was well tolerated.
Conclusion: These findings suggest that PU.1 inhibition may represent a novel and effective therapeutic approach to treat a wide range of fibrotic diseases. Inactivation of PU.1 effectively reverted the fibrotic phenotype of fibroblasts to a resting state and induced the regression of tissue fibrosis:
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THU0344 A PILOT STUDY ASSESSING THE EFFECT OF AIR POLLUTION ON EXTRACELLULAR VESICLES IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a severe autoimmune disease characterized by a progressive multi-organ fibrosis. The identification of specific diagnostic and prognostic biomarkers remains an unmet need. Over the past few years, it has been suggested that extracellular vescicles (EVs) and environmental toxicants, such as particulate matter (PM), may have an important role in the pathogenesis of autoimmune diseases. At present, no data are available on the impact of PM exposure on EVs from patients with SSc.
Objectives: Our aim was to evaluate the effects of PM with aerodynamic diameter ≤ 10 μm (PM_{10}) and ≤ 2.5 μm ($PM_{2.5}$) on EVs in SSc and osteoarthritis (OA) as control.
Methods: Plasma EVs were analyzed by Nanosight and flow cytometry after labeling with the following markers: CD14 (monocyte), CD61 (platelet), CD25 (T-reg), human endogenous retrovirus w (HERV-w), human leukocyte antigen G (HLA-G). Demographic and clinical data were collected for each patient. Plasma EV concentrations were measured in SSc and OA patients and were analyzed by generalized linear regression models. Daily PM concentrations, estimated by Regional Environmental Protection Agency at municipality resolution, were used to assign short-term exposure (mean of the 7 days preceding the evaluation) to each study subjects.
Results: 12 consecutive patients with limited cutaneous SSc (11 female, median age 66.8, median disease duration 12.3, 7 anti-centromere positive, median mRSS 3.5) and 12 patients with OA (median age 67.1, median disease duration 9.3, 8 female) were enrolled. The increase of $PM_{2.5}$ led to a decrease of HERV-w+ microvesicles (MV) in both SSc (β=-0. 10; p=0. 01) and OA (β=-0. 09; p=0. 01) and of HLA-G+ (β=-0.11; p<0. 01) only in SSc. Similar results were observed analyzing PM_{10} exposure. Analysis of EVs concentration according to their dimensions showed a negative association in the size range of exosomes (63-

92nm) in SSc compared to OA (p<0. 05) and in the range of MV (230-510 nm) (figure below). Finally, we observed a positive association between HLA-G+ with Erythrocyte Sedimentation Rate (ESR) (β=0.34; p<0.01).



Abstract THU0344 – Figure 1

Conclusion: In our study, limited cutaneous SSc showed different EVs concentrations from controls: SSc tends to have less exosomes and more MV than OA. Moreover, environmental stimuli (*e.g.* PM exposure) are confirmed to be able to influence HERV-w+ MV release both in SSc and controls. Finally, in SSc patients PM exposure could significantly alter the release of HLA-G+ MV that has been correlated to the process of self-tolerance maintenance. Further studies are required to fully unlock the role of PM and EVs in SSc.

Disclosure of Interests: None declared

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THU0345 TEXTURE-BASED RADIOMICS FEATURES DISCRIMINATE DIFFERENT STAGES OF EXPERIMENTAL INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a life-threating complication of systemic sclerosis (SSc). There is an unmet need for validated, routinely available biomarkers for disease staging and individualized patient stratification. In that respect, high-resolution computed tomography (HRCT), routinely performed in the work-up of SSc-ILD patients, has great potential as a source for non-invasive imaging biomarkers. Recently, radiomics, the quantitative extraction of hundreds of radiologic image features, has emerged as a powerful tool for biomarker research and precision medicine approaches; however, so far, it has been applied predominantly in oncology.

Objectives: To evaluate the performance of CT-based radiomics for disease detection, staging and as surrogate marker for tissue pathophysiology in the model of bleomycin (BLM)-induced lung fibrosis.

Methods: To mimic different stages of SSc-ILD, small-animal CT imaging was performed at days 3, 7, and 14 after instillation of BLM or saline solution, respectively (n=5-6 mice/group). Trained observers manually segmented the left and right mouse lungs in the CT images, and 154 radiomics features were extracted including 17 histogram- and 137 texture-based features using the in-house developed software Z-Rad (Python 2.7). To link the radiomics features with the underlying pathophysiology, Pearson correlation analysis between radiomics and histological features (Ashcroft score, Sirius red and CD45 staining positivity) was performed.

Results: CT imaging visualized morphological changes of the lung architecture in BLM-treated mice, as evidenced by a time-dependent increase of grey areas on chest CT images and a gradual increase in tissue density on density-masked lungs. Accordingly, 6 out of 17 classical histogram features (e.g. mean CT density, skewness and kurtosis) precisely distinguished diseased from healthy mice with area under the curve values (AUCs) of >0.87 (p<0.05) and thus detected lung remodelling. However, histogram-based features failed to differentiate between the different time points and thus stages of experimental lung fibrosis as investigated by receiver operating characteristic curve analysis and by hierarchical clustering. In contrast, 59 out of 137 texture-based radiomics features, including features describing image homogeneity or contrast detected ILD and distinguished the different stages with excellent accuracy (AUCs>0.84; p<0.05) thus outperforming the classical histogram features.

In addition, texture-based, but not histogram-based features were associated (R^2>0.5, p<0.05) with histological parameters, thereby possibly reflecting changes in lung (micro-)architecture, which may result from both inflammatory and/or fibrotic changes.

Conclusion: If confirmed in human SSc-ILD, texture-based radiomics features have great potential to provide biological and stage-specific quantitative information on lung (micro-)architecture and thus could serve as quantitative imaging biomarkers for guided decision making in SSc-ILD.

Disclosure of Interests: : Janine Schniering: None declared, Matthias Brunner: None declared, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Matthias Guckenberger Grant/research support from: Grant/research support by Varian Medical Systems and Siemens Healthcare, Marta Bogowicz: None declared, Diem Vuong: None declared, Cristina Müller: None declared, Thomas Frauenfelder: None declared, Stephanie Tanadini-Lang Grant/research support from: Grant/research support by Varian Medical Systems and Siemens Healthcare, Britta Maurer Grant/research support from: Grant/research support from AbbVie, Protagen, Novartis; congress support from MSD, Pfizer, Roche, and Actelion

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THU0346 EVALUATION OF A NOVEL PARTICLE-BASED ASSAY FOR DETECTION OF MYOSITIS SPECIFIC ANTIBODIES

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Background: Myositis specific antibodies (MSA) represent important diagnostic tools and also help stratify idiopathic inflammatory myositis (IIM) patients with particular clinical features, treatment responses, and disease outcomes. Standardization of MSA detection is of high importance because these antibodies also have the potential to be used in classification criteria.

Objectives: The objective of this study was to evaluate the clinical performance of a novel particle based multi-analyte technology (PMAT) for the detection of MSA as an aid in the diagnosis and also in the differentiation of IIM subtypes.

Methods: The study included 464 patient samples collected at Hospital Vall d'Hebron, Autonomous University of Barcelona, most of whom had a diagnosis of IIM (n=264). As controls, samples from patients with myositis like conditions (ML, n=20), rheumatoid arthritis (RA, n=33), systemic lupus erythematosus (SLE, n=40), Sjögren's syndrome (SjS, n=25), infectious diseases (ID, n=40) and healthy individuals (HI, n=42) were included. All samples were tested using a novel fully automated particle-based multi-analyte technology (PMAT, Inova Diagnostics, research use only; Jo-1, PL-7, PL-12, EJ, Mi-2b, NXP2, SAE, TIF1y, MDA5, HMGCR, SRP) which utilizes paramagnetic particles with unique signatures and a digital interpretation system.

Abstract THU0346 –Table 1.

Analyte	IIM Subtype	Sensitivity (95% CI)	Specificity (95% CI)	Odds Ratio (95% CI)
Jo-1	ASS (n=67)	71.6% (59.9-81.0%)	98.0% (94.9-99.2%)	121.9 (40.8-360.0)
PL-7	ASS	10.4% (5.2-20.0%)	100.0% (98.1-100.0%)	+∞ (5.8-+∞)
PL-12	ASS	7.5% (3.2-16.3%)	100.0% (98.1-100.0%)	+∞ (4.0-+∞)
EJ	ASS	3.0% (0.8-10.2%)	99.5% (97.2-99.9%)	6.0 (0.7-46.8)
Mi-2	DM (n=70)	21.4% (13.4-32.4%)	97.9% (94.8-99.2%)	13.0 (4.3-38.7)
NXP2	DM	7.1% (3.1-15.7%)	98.5% (95.6-99.5%)	4.9 (1.3-19.1)
SAE	DM	11.4% (5.9-21.0%)	99.0% (96.3-99.7%)	12.4 (2.9-52.9)
TiF1y	DM	15.7% (9.0-26.0%)	96.2% (92.0-98.3%)	4.8 (1.7-13.0)
TiF1y	cDM (n=35)	62.9% (46.3-76.8%)	96.2% (92.0-98.3%)	43.2 (15.1-122.8)
MDA5	CADM (n=21)	71.4% (50.0-86.2%)	97.1% (94.2-98.6%)	84.3 (25.7-277.5)
HMGCR	IMNM (n=16)	50.0% (28.0-72.0%)	96.8% (93.8-98.4%)	30.0 (9.2-98.2)

ASS = Anti-Synthetase Syndrome, DM = Dermatomyositis, cDM = Cancer Associated Dermatomyositis, CADM = Amyopathic Dermatomyositis

Results: The sensitivity/specificity of the individual MSA were: 19.7%/100% (Jo-1), 7.2%/100.0% (Mi-2), 3.0%/99.0% (NXP2), 3.8%/100.0% (SAE), 2.7%/100.0% (PL-7), 1.9%/99.5 (PL-12), 1.1%/100.0% (EJ), 15.5%/99.5% (TIF1y), 8.3%/98.5% (MDA5), 6.1%/99.0% (HMGCR) and 1.9%/98.5% (SRP). The overall clinical performance was: sensitivity 68.2% (95% confidence interval 62.3-73.5%), specificity 94.0% (95% CI 89.8-96.5%) and odds ratio 33.8. In the table below, the sensitivity and specificity of each analyte for IIM subtypes was calculated along with odds ratio.

Conclusion: The novel PMAT used to detect a spectrum of MSA in IIM on a fully automated system showed good sensitivity and specificity in line with the known associations of MSA. Sensitivities and specificities of the individual MSA are within expected ranges. Lastly, the individual markers help to stratify patients into IIM subtype which is important for management of the patients.

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THU0347 TESTING THE IN VITRO EFFECTS OF NINTEDANIB ON CIRCULATING FIBROCYTES AND RESIDENT SKIN FIBROBLASTS FROM THE SAME SYSTEMIC SCLEROSIS PATIENTS: PRELIMINARY RESULTS

Maurizio Cutolo[1], Paola Contini[2], Giulia Martinelli[1], Paola Montagna[1], Samuele Tardito[1], Sabrina Paolino[1], Massimo Patanè[1], Carmen Pizzorni[1], Elisa Alessandri[1], Veronica Tomatis[1], Vanessa Smith[3,4,5], Stefano Soldano[1]. *[1]University of Genova, IRCCS Polyclinic San Martino Hospital, Research Laboratory and Academic Division of Clinical Rheumatology, Dept. of Internal Medicine, Genoa, Italy; [2]University of Genova, IRCCS Polyclinic San Martino Hospital, 2Clinical Immunology, Dept. of Internal Medicine, Genoa, Italy; [3]Ghent University Hospital, Dept. of Rheumatology, Ghent University Hospital, Ghent, Belgium; Dept. of Internal Medicine, Ghent, Belgium; [4]Ghent University, Dept. of Internal Medicine, Ghent, Belgium; [5]VIB Inflammation Research Center (IRC), Unit for Molecular Immunology and Inflammation, Ghent, Belgium*

Background: The fibrosis in systemic sclerosis (SSc) progresses from microvascular alterations, immune system activation, and increased extracellular matrix protein synthesis into the skin and internal organs, primarily mediated by myofibroblasts.[1] Myofibroblasts are characterized by a higher expression of α-smooth muscle actin (αSMA) and by the overproduction of type I collagen (COL1) and fibronectin (FN).[2] Although myofibroblasts primarily derive from fibroblasts differentiation and transition, circulating fibrocytes represent a further important source.[3] Nintedanib is a tyrosine kinase inhibitor that interacts with several inflammatory and profibrotic pathways implicated in the pathogenesis of fibrosis, including those of platelet derived growth factor receptors, vascular endothelial growth factor receptors and fibroblast growth factor receptors.[4]

Objectives: To investigate, in primary cultures, the effects of nintedanib on the differentiation of circulating fibrocytes and on the profibrotic activity of skin fibroblasts isolated from the same SSc patients.

Methods: Circulating fibrocytes and fibroblasts were obtained from peripheral blood and skin biopsies, respectively, from three untreated SSc patients with diffuse skin involvement (mean age 55±6 yrs). To investigate the complete differentiation, fibrocytes were maintained in DMEM at 20% of foetal bovine serum, either with or without treatment with nintedanib at the concentrations of 0.1μM and 1μM for 8 days.[5] Fibrocytes were characterized as $CD45^+CXCR4^+COL1^+$cells, and their percentage was detected by Flow Cytometry analysis.[6] Fibroblasts were grown until the 3[dr] culture passage and then maintained in normal growth medium with or without nintedanib treatment for 4, 24 and 48 hours. The gene expressions of αSMA, COL1 and FN were evaluated by qRT-PCR.

Results: Nintedanib reduced the percentage of differentiated SSc fibrocytes ($CD45^+CXCR4^+COL1^+$cells), already at the concentration of 0.1μM compared with untreated fibrocytes. In cultured SSc skin fibroblasts, nintedanib 1μM downregulated αSMA, COL1 and FN expressions already after 4 hours of treatment, and this effect was also maintained after 24- and 48-hours' treatment. Nintedanib 0.1μM downregulated the αSMA expression at all timepoints, whereas the downregulation of COL1 and FN expressions was observed at 4 and 24 hours, with no more effect at 48 hours of treatment compared with untreated cells.

Conclusion: Initial experiments seem to indicate an evident *in vitro* concentration-dependent antifibrotic activity of nintedanib on SSc fibrocytes and skin fibroblasts from the same SSc patients; in particular by reducing the fibrocyte differentiation as potential source of myofibroblasts and contrasting the profibrotic activity of already activated fibroblasts/myofibroblasts. These results have translational implications in clinical trials using nintedanib in SSc patients.

REFERENCES:

[1] Furue M, et al. Immunol Res 2017;65:790−7.
[2] Kendall RT, et al. Front Pharmacol 2014;5:123.
[3] Strieter RB, et al. *J Leukocyte Biol* 2009;88:111−8.
[4] Huang J, et al. Ann Rheum Dis 2017;76:1941–8.
[5] Cutolo M, et al. Arthritis Res Ther 2018;20:157.

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THU0348 IDENTIFICATION OF CIRCULATING CELLS WITH AN HYBRID M1/M2 MACROPHAGE PHENOTYPE IN SYSTEMIC SCLEROSIS PATIENTS AND CORRELATIONS WITH SELECTED CLINICAL ASPECTS

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Background: Systemic sclerosis (SSc) is characterized by immune system alterations, vascular damage and fibrosis (1). Macrophages seem to have an emerging role in SSc, and the characterization of their polarized phenotype, starting from the dichotomic definition of classically activated (M1) or alternatively activated (M2) macrophages, is a recent research topic of interest (2).

Objectives: The study investigated a possible imbalance in the distribution of circulating cells expressing M1 and M2 markers in SSc patients (pts) compared to healthy subjects (HSs), and the presence of circulating cells co-expressing M1 and M2 surface markers. Possible correlations between their percentage and selected SSc clinical aspects were investigated.

Methods: In the study 55 SSc pts (50 females/5 males, mean age 64 ±13 yrs), fulfilling the new EULAR/ACR criteria for SSc diagnosis, and 27 age-matched HSs (25 females/2 males, mean age 57±7 yrs) were enrolled after written informed consent. Nailfold videocapillaroscopy (NVC), evaluation of SSc-related antibodies and pulmonary functional tests were performed. In particular, circulating cells belonging to the leukocyte and monocyte populations ($CD45^+$and $CD14^+$cells) were investigated by flow cytometry (FC) using the surface markers characterizing M1 (CD80, CD86, TLR2, TLR4) and M2 phenotypes (CD204, CD206, CD163). Statistical analysis was performed using Mann-Whitney and Kruskal-Wallis tests, and correlations were explored by bivariate Pearson's analysis.

Results: Increased circulating cells showing an M2 phenotype and characterized as $CD204^+CD206^+CD163^+$cells was observed in SSc pts compared to HSs ($p<0.0001$), whereas no difference in $CD80^+CD86^+TLR2^+TLR4^+$(M1) cell percentage was observed. A significant higher percentage of circulating cells showing a hybrid M1/M2 phenotype ($CD204^+CD206^+CD163^+TLR4^+CD80^+CD86^+$cells) was observed in SSc pts compared to HSs. These hybrid M1/M2 cells were significantly increased in SSc pts either treated with steroids or under no immunosuppressive treatment ($p<0.01$; $p<0.05$), as well as in $Scl70^+$pts ($p<0.05$ vs. $Scl70^-$pts)

and SSc pts with interstitial lung disease (ILD) and high systolic pulmonary artery pressure (PAP). A linear negative correlation between the high hybrid M1/M2 cell percentage and diffusing capacity of the lungs for carbon monoxide (DLCO)% and the forced vital capacity (FVC)/DLCO ratio higher than 1.5 was observed. No significant correlations were reported with SSc duration, other treatments, NVC patterns, renal artery resistive index, heart and kidney involvements, digital ulcers, telangiectasias, calcinosis.
Conclusion: The study identified a circulating cell population expressing both M1 and M2 surface markers, which is increased together with circulating M2 cells in SSc pts, in particular affected by ILD and high PAP, suggesting their possible involvement in the pathogenesis of those disease complications. Further evaluations are in progress.

REFERENCES:
[1] Cutolo M, et al. Nat Rev Rheumatol. 2015;11:569-71. 2. Stifano G, et al. Curr Rheumatol Rep. 2016;18:2.

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THU0349 AUTOLOGOUS FAT GRAFTING IN THE TREATMENT OF PATIENTS WITH SYSTEMIC SCLEROSIS: CURRENT EXPERIENCE AND FUTURE PROSPECTS

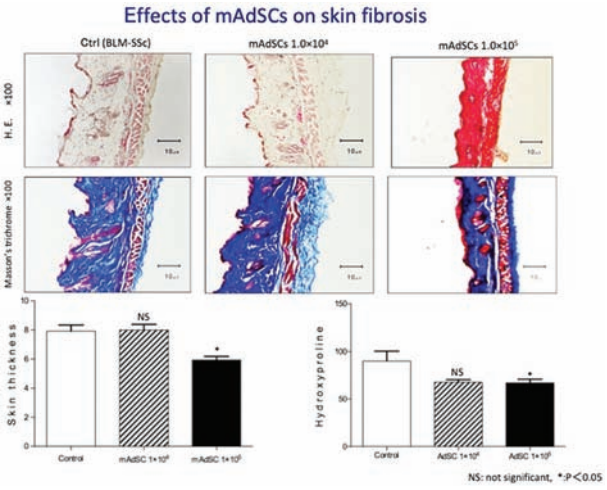
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Background: Systemic Sclerosis (SSc) is a connective tissue disease, characterized by endothelial dysfunction and fibrosis, potentially affecting internal organs and reducing life expectancy. Digital ulcers (DUs), as well as hand and face skin thickening, are the hallmarks of the disease. These alterations lead to pain, functional impairment, aesthetic damages, and psychological distress. Autologous fat grafting (AFG) is a surgical technique used also to promote tissue regeneration. In the last decade, AFG has been successfully developed to treat clinical conditions characterized by skin atrophy or fibrosis. AFG composition of multipotent cells, carrying angiogenic, and immunogenic properties, may be able to restore the damaged tissues.
Objectives: Evaluate our experience with AFG to treat and prevent damage and disability due to DUs and SSc skin complications.
Methods: We analyzed 25 SSc patients, extrapolated from a larger series of 45 subjects, complaining about mouth and/or hand impairment, due to skin involvement, and, in some cases, long-lasting DUs (M/F 6/19, mean age 55.69±9.25-SD-years, mean disease duration 184.68±121.09-SD-months, L/D cutaneous subsets 21/4). Surgical procedures consisted in the injection of centrifuged and purified autologous fat, harvested from hips or abdomen. 2ml of fat were grafted in each of the 8 sites around the mouth, while 0.5 or 1 ml around the neurovascular bundle at the base of each finger. The study included: preoperative data collection; 2 or 3 surgical sessions at a distance of 6 months one from the other; data collection at 3 months after each surgical session; data collection at 3 and 6 months of follow up-FU after the last surgical procedure. Data collection consisted of clinic-serological SSc features and clinimetric measures about hand and mouth, if present DUs were assessed as well. Furthermore, patients were asked to fill in questionnaires in order to express their level of satisfaction with hand and mouth functionality.
Results: Overall 63 surgical procedures were performed. After 1 to 3 procedures, patients reported an improvement of perioral skin tension (p=0.0238) and a reduced dry mouth feeling (p=0.0269). Similarly, patients stated an improvement of hands tension (p=0.0037). Furthermore, we observed a complete healing of DUs in 8/9 patients (p=0.0297). These positive clinical changes were mirrored by a subjective amelioration. In particular, pain decreased, evaluated by short-form McGill Pain Questionnaire (SF-MPQ), scrutinizing sensory (p=0.3340) and affective (p=0.2234) descriptors. The perception of disability improved too, showing an amelioration trend in Health Assessment Questionnaire-HAQ (p=0.4301) and Mouth Handicap in Systemic Sclerosis scale-MHISS-(p=0.9775).
Conclusion: Our results confirm the potential efficacy of AFG to treat SSc skin complications and DUs. We reported an almost complete healing of DUs and a promising improvement of skin thickness and hardness both at hands and mouth, with good safety profiles. These clinical results were reflected by the subjective improvement of patients' well-being. Population enlargement and extended FU is ongoing to identify more responsive SSc subsets. Long term results with soft tissue biopsies will give us further data to finally evaluate the efficacy of this approach that aims to improve the care and quality of life of our SSc patients.
Disclosure of Interests: None declared
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THU0350 ANTI-INFLAMMATORY AND ANTI-FIBROTIC EFFECTS OF INTRAVENOUS ADIPOSE-DERIVED STEM CELL TRANSPLANTATION IN A MOUSE MODEL OF BLEOMYCIN-INDUCED SCLERODERMA

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by microvascular damages and fibrosis. The main lesions of SSc are peripheral circulation insufficiency, sclerodermia, and interstitial pneumonia. Skin lesions are related to patient's ADL and QOL, however there is no effective treatment for normalizing the disease state. Adipose-derived stem cells (AdSCs) have recently been considered a useful treatment tool for autoimmune disease because of their anti-inflammatory and immunosuppressive effects (ref).
Objectives: We investigated the therapeutic effect of intravenous mouse AdSCs (mAdSCs) transplantation in a SSc mouse model.
Methods: SSc was induced by bleomycin (BLM) in Balb/c mice, and the mice were assigned in the following groups: 1. Control (BLM-SSc), 2. mAdSCs (1.0×10^4 cells), 3. mAdSCs (1.0×10^5 cells). After the administration of BLM, mAdSCs were injected via a tail vein on day 7. The mice were sacrificed at 14 days after mAdSCs injection, and the skins were harvested for histological analysis.
Results: In mAdSCs (1.0×10^5 cells) group, thickening of skin, hydroxyproline content, infiltration of inflammatory cells, gene expression of inflammatory cytokines, and fibrotic factors were significantly reduced compared with control group (Figure). But in mAdSCs (1.0×10^4 cells) group, there were no reduction of them. mAdSCs did not accumulate in skin. The levels of MMP-2, MMP-9, and COL1A1 mRNA expression at 21 days after BLM administration were significantly lower in mAdSCs (1.0×10^5 cells) group compared with those in control group.



Abstract THU0350 – Figure 1

Conclusion: Intravenous mAdSCs inhibited both skin inflammation and fibrosis of BLM-SSc mice in a dose-dependent manner.

REFERENCES:
[1] Cell Transplant 2015.24: 2297-2305.
[2] Journal of Autoimmunity, 2016. 70: 31-39.

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THU0351 LOW ERA EXPRESSION MIGHT BE IMPLICATED IN THE DEVELOPMENT OF PULMONARY HYPERTENSION IN FEMALE MICE LACKING PSGL-1

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Background: Pulmonary arterial hypertension (PAH) is a rare disease with unknown etiopathogenesis and no curative treatment [1]. PAH is one of the major complications of connective tissue diseases, and 7-15% of patients with systemic sclerosis (SSc) develop PAH [2]. Mice deficient for the leukocytic receptor P-selectin glycoprotein ligand-1 (*PSGL-1*$^{-/-}$) spontaneously develop a SSc-like autoimmune syndrome with ageing [3].
Objectives: To check whether *PSGL1*$^{-/-}$ mice may develop PAH and the molecular mechanisms that might be implicated in the initiation and establishment of the disease.
Methods: Doppler pulse echochardiography was used to evaluate pulmonary artery flow acceleration time/ejection time (PAAT/ET) ratio in WT and *PSGL-1*$^{-/-}$ C57BL/6 mice. Isolated pulmonary artery rings were incubated with acetylcholine and responses were registered with a wire myograph coupled to an isometric force transducer. Expression levels of the NO-sensing probe DAR-4M AM by fluorescence microscopy and flow cytometry. Angiotensin II lung concentration was quantified by ELISA. eNOS, p-ENOS, AT1R and AT2R expression was evaluated by western blot. In all cases, data are expressed as the mean±SD.
Results: Aged *PSGL-1*$^{-/-}$ females showed reduced flow PAAT/ET ratio indicating PAH. Moreover, pulmonary arterial rings from aged *PSGL-1*$^{-/-}$ females presented ROS-independent reduced vasodilation response to acetylcholine. Importantly, eNOS phosphorylation was impaired and NO production by lung EC was reduced in aged *PSGL-1*$^{-/-}$ females. Vascular remodeling and reduced expression of AT2R were observed in lungs of *PSGL-1*$^{-/-}$ females from a younger age. With ageing, the levels of angiotensin II and the percentages of IFNγ-producing interstitial macrophages, T and B lymphocytes were increased in *PSGL-1*$^{-/-}$ females. The differences in the gender-biased genotype could be explained by the reduced expression of ERα in the lungs of aged *PSGL-1*$^{-/-}$ females while WT and *PSGL-1*$^{-/-}$ males showed similar expression.
Conclusion: PSGL-1 deficiency leads to pulmonary hypertension in >18-months-old female mice, involving various mechanisms:

1. Lung vessel wall remodeling and reduced AT2R expression.
2. Reduced eNOS phosphorylation and reduced NO production with the subsequent specific lung endothelial dysfunction in PSGL-1$^{-/-}$ females. Importantly, ROS production is not increased nor help to NO reduction.
3. Increased pulmonary AngII levels with ageing in PSGL-1$^{-/-}$ females.
4. Increased Th1 polarization, reduced Treg population and increased IFN-γ production by interstitial macrophages.

Impaired ageing up-regulation of ERα expression in the lungs of PSGL-1$^{-/-}$ females.

REFERENCES

[1] Montani et al. Orphanet Journal of Rare Diseases. 2013, 8 (97).
[2] Tedford et al. Circ Heart Fail. 2013, 6 (5): 953-63.
[3] Pérez-Frías et al. Arthritis Rheumatol. 2014, 66 (11): 3178-89.

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THU0352 THE ROLE OF PRURITOGENIC MEDIATORS IN DERMATOMYOSITIS RELATED ITCH

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Background: Pruritus is a common symptom in systemic autoimmune diseases like dermatomyositis (DM). Recent researches have indicated that interleukin-31 (IL-31), IL-33, IL-6, or inflammatory cytokines, such as tumor necrosis factor (TNFα), peroxisome proliferator-activated receptor γ (PPARγ) and ion channels belonging to the transient receptor potential (TRP) family are involved in pruriception.
Objectives: We examined targeted gene expression analysis of lesional versus non-lesional skin samples of patients affected with active DM. We looked for correlations between the examined pruriceptive signaling molecules, disease activity and itching sensation of DM patients.
Methods: Gene expression of TNFα, PPARγ, IL-33, IL-6 and TRPV channels in lesional DM skin was evaluated by RT-qPCR and was compared with non-lesional DM skin samples. Pruritus and disease activity of DM was evaluated by the 5-d itch scale and Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), respectively. Statistical analysis was performed with IBM SPSS 20.0 software.
Results: Skin samples of 17 active DM patients were analyzed. We could show, that itching index in DM was positively correlated with CDASI score with a correlation coefficient of 0.82 ($p<0.001$). TNFα gene expression was significantly higher (34.87%) in lesional DM skin than non-lesional DM skin ($p=0.03$). The normalized TNFα mRNA expression was positively correlated with itch scale ($R= 0.605$, $p=0.022$) and its level was significantly higher in skin samples of patients with severe itch (itching score: 15-20) versus mild itch (itching score: 5-10) (2.02±0.38 vs. 1.12±0.20; $p<0.01$). The level of PPARγ was decreased in lesional DM skin, but this was statistically not significant. The mRNA expression of normalized PPARγ was negatively correlated with itch scale ($R= -0.618$, $p=0.019$), and its level was significantly lower in skin samples of patients with severe itch versus mild itch (0.28±0.36 vs. 1.53±0.98; $p=0.038$). Lesional IL-6 mRNA levels were associated with CDASI activity score ($R=0.619$, $p=0.018$). The mRNA levels of TRPV1-4 channels were not associated with 5-D itch score, but normalized TRPV1 and TRPV4 mRNA expressions were positively correlated with CDASI damage score ($R=0.699$, $p=0.008$; $R=0.789$, $p=0.001$). Interestingly, itching sensation of DM patients was not correlated with IL-33 mRNA levels measured in skin samples.
Conclusion: Our results argue for that higher cutaneous disease activity generate pruritus. TNFα and PPARγ might play a determining, but opposite role in DM-associated itch. Furthermore IL-6, TRPV1 and TRPV4 channels might participate in pathomechanism of cutaneous manifestation of the disease.

DISCLOSURE OF INTERESTS: :
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THU0353 AN ORALLY AVAILABLE HIGHLY SELECTIVE 5-HYDROXYTRYPTAMINE 2B (5-HT2B) RECEPTOR ANTAGONIST AMELIORATING PULMONARY AND DERMAL FIBROSIS IN PRECLINICAL MODELS OF SYSTEMIC SCLEROSIS

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Background: Serotonin or 5-hydroxytryptamine (5-HT) is well known as a stimulator of tissue fibrosis and a significant role of peripheral 5-HT$_{2B}$ receptors in fibrosis has been suggested with the receptor being upregulated in fibrotic tissues. In addition, agonism of the 5-HT$_{2B}$ receptor has been implicated in human tissue fibrosis caused by drugs known to activate the receptor. Pharmacologic inhibition of 5-HT$_{2B}$ receptor signalling consequently represents a promising treatment strategy for fibrotic disorders including systemic sclerosis. 5-HT is released from platelets activated upon vascular damage, one of the first pathological events in systemic sclerosis. The local 5-HT concentration is increased and leads to activation of 5-HT$_{2B}$ receptors on *e.g.* fibroblasts. The pro-fibrotic effects of 5-HT and the 5-HT$_{2B}$ receptor are believed to be mediated through activation of the TGF-β/Smad signaling pathway.
Objectives: The objective of the present study was to evaluate a novel highly selective orally available 5-HT$_{2B}$ receptor antagonist, AM1476, for its ability to reduce pulmonary and dermal fibrosis in the sclerodermatous

chronic graft-versus-host disease model and dermal fibrosis in the tight-skin-1 model of systemic sclerosis. Effects on the TGF-β/Smad signaling pathway were investigated *in vivo*. Exposure of AM1476 was measured to ensure proper target engagement.

Methods: The murine sclerodermatous chronic graft-versus-host disease (cGvHD) model was used to evaluate anti-fibrotic effects after therapeutic dosing of the 5-HT_{2B} receptor antagonist, AM1476. The compound was orally administered at 1, 10 and 30 mg/kg b.i.d. from day 21, several days after the first clinical signs of cGvHD, to day 49. Dermal thickness, myofibroblast counts and collagen production were used to evaluate dermal fibrosis. Effects on pulmonary fibrosis were measured using hydroxyproline content, Sirius Red staining and Ashcroft score. Plasma was collected for PK analysis at different timepoints in each treatment group using sparse sampling, on the last day of the experiment. The tight-skin-1 model was used to evaluate anti-fibrotic effects after therapeutic treatment. AM1476 was orally administered at 10 mg/kg, b.i.d. from week 5 to week 10. Hypodermal thickening, myofibroblast counts and hydroxyproline content in skin biopsies were evaluated at the end of the treatment period. The number of phosphorylated Smad3 (pSmad3) positive cells was used to evaluate inhibition of TGF-β signaling.

Results: The 5-HT_{2B} receptor antagonist AM1476, significantly reduced all measured dermal and pulmonary fibrosis readouts in the cGvHD model using an oral therapeutic treatment approach. Pharmacokinetic analysis of plasma samples supported 5-HT_{2B} receptor engagement. Therapeutic treatment of dermal fibrosis in the tight-skin model effectively and significantly reduced hypodermal thickening, number of myofibroblast and hydroxyproline content. The number of pSmad3 positive cells was significantly reduced in skin samples isolated from treated animals.

Conclusion: Inhibition of 5-HT_{2B} receptor activity resulted in pronounced anti-fibrotic effects in pulmonary and dermal fibrotic tissues. AM1476 was well tolerated without obvious signs of toxicity. Effects on pSmad3, reflecting TGF-β-inhibition, will be evaluated as a potential biomarker in upcoming clinical trials. The highly selective 5-HT_{2B} receptor antagonist AM1476 represents a promising drug candidate for treatment of fibrotic conditions and is currently in development for systemic sclerosis.

Disclosure of Interests: Christina Wenglén Employee of: Employed by AnaMar AB, Lund, Sweden, Helena Arozenius Employee of: AnaMar AB, Lund, Sweden, Lars Pettersson Employee of: AnaMar AB, Lund, Sweden, Gunilla Ekstrom Employee of: AnaMar AB, Lund, Sweden DOI: 10.1136/annrheumdis-2019-eular.6808

THU0354 MACHINE LEARNING CLASSIFICATION OF SKIN GENE EXPRESSION IDENTIFIES A SUBSET OF SYSTEMIC SCLEROSIS PATIENTS MOST LIKELY TO SHOW CLINICAL IMPROVEMENT IN RESPONSE TO ABATACEPT

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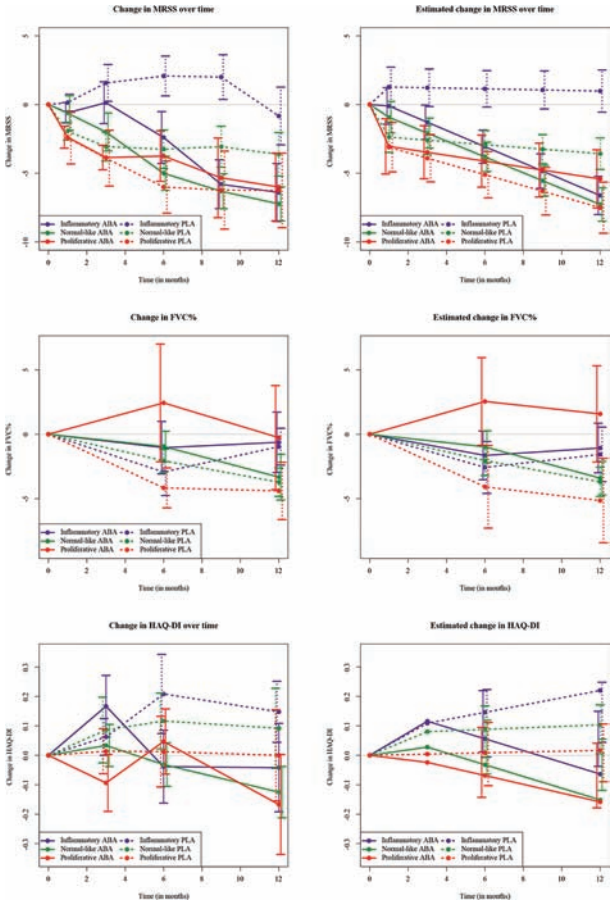
Background: A prior pilot study of abatacept in SSc with molecular gene expression data in skin (*1*) found that four of five patients who improved on abatacept, as determined by change in mRSS, were in the inflammatory intrinsic gene expression subset. Improvement was accompanied by a decrease in gene expression for immune pathways, including the CD28 and CTLA4 receptors—the target of abatacept. Here we tested our *a priori* hypothesis that the inflammatory subset shows a significant decline in mRSS during abatacept therapy.

Objectives: ASSET (Abatacept Systemic SclErosis Trial) is a Phase 2 study designed to assess the efficacy of subcutaneous abatacept to treat diffuse cutaneous systemic sclerosis. We performed RNA-sequencing (RNA-seq) analysis of skin biopsies and analyzed associations between intrinsic molecular subsets and clinical outcomes in the ASSET trial.

Methods: RNA-seq was performed on skin biopsies from 84 participants in the ASSET trial. A machine learning classifier was trained on independent cohorts and used to objectively classify patients into intrinsic gene expression subsets prior to study unblinding (*2*). Treatment differences in longitudinal outcomes were assessed using linear mixed effect models.

Results: 84 participants were assigned to intrinsic subset at baseline resulting in 33 inflammatory, 18 fibroproliferative, and 33 normal-like samples. Change in mRSS over 12 months was significantly different between the abatacept and placebo treatment arms for the inflammatory (p<0.001) and normal-like (p=0.03) subsets, but there was no difference in the fibroproliferative subset of patients (p=0.47) (Figure 1). For FVC% predicted, the fibroproliferative subset showed a numerical increase in FVC% in the abatacept arm (p=0.19) while all other groups showed decreases in FVC%. All gene expression subsets showed decreases in HAQ-DI in the abatacept arm not observed in the placebo arm, with the most robust changes occurring in the inflammatory (p=0.09) and normal-like (p=0.06) subsets.

Conclusion: There was a marked divergence of the trajectory for mRSS change for the inflammatory subset and no apparent impact for the fibroproliferative subset. In contrast, only the fibroproliferative subset showed a clinically meaningful FVC change for abatacept. For the broader functional measure of HAQ-DI, there were similar impacts of abatacept on all three intrinsic skin gene expression subsets but is numerically greatest for the normal-like and fibroproliferative subsets. Together these data show for the first time in a placebo-controlled trial that intrinsic skin gene expression subsets may predict differential response to a targeted biological therapy, and also that this may reflect impact on different facets of SSc pathogenesis in skin or lung. This suggests that stratification of cases according to intrinsic gene expression subsets may maximize the number of informative SSc cases in clinical trials, and potentially improve future clinical practice.



Abstract THU0354 – Figure 1

REFERENCES:

[1] E. F. Chakravarty, et al., Gene expression changes reflect clinical response in a placebo-controlled randomized trial of abatacept in patients with diffuse cutaneous systemic sclerosis. Arthritis Res Ther 17, 159 (2015).

[2] J. M. Franks, et al., A Machine Learning Classifier for Assigning Patients with Systemic Sclerosis to Intrinsic Molecular Subsets., Arthritis Rheum. (2019) *In Press*.

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THU0355 IGURATIMOD MIGHT TREAT SCLERODERMA WITH INTERRUPTED EGR1/TGF-B LOOP

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized with multiple organ fibrosis. Previous studies showed transcription factor early growth response 1 (Egr1) overexpressed in the lesional skin of SSc patients, as well as Egr1 inducible genes[1]. Egr1 forms a positive feedback loop with master pro-fibrotic cytokine TGFβ and thus promotes fibrosis.
Objectives: To investigate the anti-fibrotic effect of a novel DMARD iguratimod in scleroderma models and patient skin grafts.
Methods: We used iguratimod to treat TGFβ-stimulated human skin fibroblast, bleomycin induced mice, tight skin 1 (TSK-1) mice and SSc skin grafts. The bleomycin model contained pre-establish fibrosis and late onset treatment. The skin grafts came from three SSc patients and was planted into irradiated nude mice.
Results: Iguratimod down-regulated egr1 expression in human skin fibroblast, with decreased collagen production and α-SMA expression. Knocking down Egr1 in fibroblast could mimic these effects. Both oral and topical iguratimod could reduce dermal thickening and collagen deposition in bleomycin induced skin fibrosis. α-SMA (+) myofibroblast counts, as well as Egr1 (+) and/or TGFβ (+) fibroblast counts in iguratimod treated groups were significantly less than the controls. Similarly, topical iguratimod ameliorated fibrosis with deduced dermal thickening in TSK-1 mice. Of note, 5-week iguratimod local injection remarkably reduced collagen content in skin grafts from three SSc patients. Staining of Egr1 and TGFβ in skin tissue were inhibited after iguratimod treatment simultaneously.
Conclusion: We found the potential of iguratimod to treat SSc, which was characterized as an Egr1 inhibitor. Further clinical investigation is needed to establish its safety and efficacy.

REFERENCES

[1] Bhattacharyya S, Sargent JL, Du P, et al. Egr-1 induces a profibrotic injury/repair gene program associated with systemic sclerosis. PloS one 2011;6(9):e23082 doi: 10.1371/journal.pone.0023082
[2] Chen SJ, Ning H, Ishida W, et al. The early-immediate gene EGR-1 is induced by transforming growth factor-beta and mediates stimulation of collagen gene expression. The Journal of biological chemistry 2006;281 (30):21183-97 doi: 10.1074/jbc.M603270200
[2] Wu M, Melichian DS, de la Garza M, et al. Essential roles for early growth response transcription factor Egr-1 in tissue fibrosis and wound healing. The American journal of pathology 2009;175(3):1041-55 doi: 10.2353/ajpath.2009.

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THU0356 STAPHYLOCOCCUS AUREUS REGULATES FIBROBLAST FUNCTIONS – IMPLICATIONS FOR TISSUE REPAIR IN CHRONIC DIGITAL ULCERS IN SYSTEMIC SCLEROSIS

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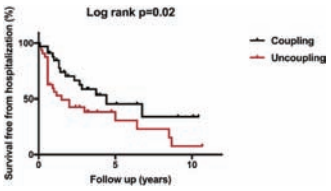
Background: Chronic digital ulcers (DU) are a major complication in systemic sclerosis (SSc). Non-healing wounds are characterized by persistent inflammation, defective re-epithelialization and impaired matrix remodeling, and are often accompanied by bacterial colonization. In DU, the breach of the basement membrane exposes tissue and cell layers to commensal skin bacteria.
Objectives: To investigate whether interactions between commensal skin bacteria and dermal fibroblasts affect tissue repair mechanisms.
Methods: Dermal fibroblasts isolated from healthy controls (HC) and patients with diffuse cutaneous SSc (dcSSc) (n=3, each) were co-cultured with *Staphylococcus aureus* (SA) for 3 h at using a lower inoculum rather representing colonization (1 x 10^5 CFU/ml) and a higher inoculum reflecting infection (1 x 10^7 CFU/ml). Thereafter, fibroblasts were cultured with flucloxacillin-containing medium to kill extracellular and adherent bacteria. For mechanistic studies, a fibroblast cell line (BJ-5ta) was used. IL-6, IL-8, pro-collagen Iα, and interferon (IFN)-β proteins in culture supernatants were measured by ELISA. Gene expression was assessed by quantitative PCR. Contractility was analyzed by collagen gel contraction assay. Wound closure assay was performed on a confluent cell layer with a uniform cell-free gap, generated by a cell culture insert. Expression of alpha-smooth muscle actin (α-SMA) was evaluated by Western blotting, cell proliferation with a colorimetric assay. Cell death was analyzed by live cell real time assay. Bacterial invasion was assessed by immunofluorescence staining using confocal microscopy and CFU recovery. Gene knockdown was performed using siRNA.
Results: Exposure to 1 x 10^7 CFU/ml of SA influenced fibroblast function. In brief, exposure to SA increased the secretion of IL-6 and IL-8 in dermal fibroblasts by 1571/455-fold (HC/dcSSc; p=0.08/<0.05) and by 325/1402-fold (HC/dcSSc; p<0.05 each) respectively. In addition we observed upregulation of the expression of MMP1 by 8.2/5.7-fold (HC/dcSSc; p<0.05 each) and MMP3 by 5.1/5.7-fold (HC/dcSSc; p=0.06/<0.05). There was a trend towards decreased secretion of pro-collagen Iα. TGF-β-induced α-SMA expression was completely inhibited. Cell contraction was impaired by 22.0/31.6% (HC/dcSSc; p=0.08/<0.05), wound closure by 18.8/14.9% (HC/dcSSc; p<0.05 each), and proliferation by 30.5/44.3% (HC/dcSSc; p=0.24/<0.05). SA induced apoptosis and necrosis. SA invaded fibroblasts via endocytosis (25-50% of inoculated live SA). IFN-β secretion was induced 8.4/31.7-fold (HC/dcSSc; p<0.05 each). The genes of cytosolic dsDNA sensor molecules such as cyclic GMP-AMP synthase (cGAS) were upregulated 11.9/8.6-fold (HC/dcSSc; p<0.05 each). TLR9, an endosomal DNA sensor, was constitutively expressed. Knockdown of STING or MyD88, downstream mediators of cGAS and TLR9 respectively, reduced the induction of IFN-β (down to 68.2/66.2%; p=0.20/0.16), IL-6 (down to 57.2/55.2%; p<0.05 each), and IL-8 (down to 45.3/36.0%; p<0.05 each). Furthermore, inhibition of endocytosis with cytochalasin D decreased the expression of IFN-β (down to 24.6%; p<0.05), IL-6 (down to 34.9%; p<0.05), and IL-8 (down to 27.6%; p<0.05). In contrast, inhibition of endocytosis did not affect induction of apoptosis. This suggests that the invasion of fibroblasts by SA and the subsequent intracellular DNA sensing are crucial for the induction of these genes independently of apoptosis.
Conclusion: Invasion of dermal fibroblasts by SA with activation of the STING and TLR9-MyD88 pathways is a key element in the impairment of tissue repair responses.

THU0357 VENTRICULAR-ARTERIAL COUPLING AS A PREDICTOR OF CARDIOVASCULAR EVENTS IN SYSTEMIC SCLEROSIS

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Background: Standard Transthoracic Echocardiography (TTE) parameters have shown a low sensitivity in the detection of primary miocardial involvement (PMI) in systemic sclerosis (SSc). Arterial-ventricular coupling (VAC) is calculated by TTE as the ratio between arterial elastance (Ea) and ventricular end-systolic elastance (Ees), which reflects left ventricle stifness. VAC is a central determinant of cardiovascular performance.
Objectives: We aimed to assess TTE-derived measures of cardiac mechanics and the prognostic role of VAC in SSc.
Methods: 75 patients affected by SSc without symptoms of cardiac involvement and 10 controls matched for sex and age were retrospectively evaluated. We considered the first TTE available after SSc diagnosis. Determinants of cardiac mechanics were calculated by TTE[1]: end systolic elastance (Ees), arterial elastance (Ea), ventricular arterial coupling (VAC=Ees/Ea), end diastolic elastance (Eed). A value of VAC > 0.62 was considered indicative of altered VAC (i.e. uncoupling), whereas a lower value as normal (i.e. coupling). Finally, we considered the hospitalization for cardiovascular event during a mean follow-up of 10.8±1.8 years.

Results: Among the 75 patients 42 (59.2%) had a diffuse cutaneous form of SSc (dSSc) and 64 (85.3%) were female; in SSc patients the mean age was 53±12.1 yrs and the mean disease duration 10.1± 2.3 yrs. 36 (52.2%) patients had positive SCl70, 31 (44.9%) ACA, and 2 (2.9%) anti-RNA pol III. Compared to controls, SSc patients had higher Ea (2.28 vs 0.95 mmHg/ml, p=0.003) and Ees (3.95 vs 2.98 mmHg/ml, p=0.05), and increased diastolic stiffness (Eed) (0.210 vs 0.146 mmHg/ml, p=0.01). VAC was consequently comparable to controls. SSc patients affected with dcSSc had a lower Ees (2.90 vs 4.367, p<0.001) and Eed (0.24 vs 0.17, p=0.032) and a higher VAC (0.52 vs 0.70, p=0.01) compared to lSSc. No differences were found between patients with anti-Scl70 and ACA. At 10 years, 23% of patients was hospitalized for at least one cardiovascular event. The analysis of survival free hospitalization or death in all SSc patients demonstrated a worse outcome and poor prognosis in patients with an altered VAC (31, 47.7%) compared to those with a normal VAC (34, 52.3%) (Figure 1).



Abstract THU0357 – Figure 1

Conclusion: Our study suggests that both ventricular and arterial stifness may be increased in SSc patients without signs and symptoms of heart disease. Since VAC seems to have a prognostic role in the prediction of cardiovascular events in SSc, it could be helpful to define an early therapeutic strategy to prevent or delay cardiac manifestations in these patients.

REFERENCE:

1. Sagawa K et al, Am J Cardiol 1977;40:748-753.

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20. Spondyloarthritis – clinical aspects (other than treatment)

THU0358 DEVELOPMENT OF A SET OF ASAS QUALITY STANDARDS FOR ADULTS WITH AXIAL SPONDYLOARTHRITIS

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Background: There is wide variation in the management of patients with axial spondyloarthritis (axSpA) worldwide with significant unmet needs such as delayed diagnosis. A major goal of the international organization Assessment of SpondyloArthritis international Society (ASAS) is to improve quality of care and health outcomes in axSpA. One way to achieve this is to define quality standards (QS) in order to identify resources and processes which may need to be optimized. Such standards must be specific, measurable, aspirational and achievable in daily care.

Objectives: To develop ASAS QS to ultimately improve the quality of care for adults with axSpA.

Methods: The ASAS QS group, established in 2015, developed a stepwise approach starting with (I) an overview and open discussions resulting in a proposal for possible key areas for quality improvement. Thereafter, (II) ASAS members and invited patients discussed and commented on a provisional list via a web-based survey with the possibility to propose additional key areas for quality improvement. (III) The complete list was then evaluated by ASAS members and invited patients. (IV) Then, the ASAS QS group prioritized key areas for which quality statements and measures are to be developed, and (V) phrased QS for the most important key areas. Finally (VI), a draft version was commented on, discussed and finally agreed by the ASAS members at the Annual ASAS Meeting 2019.

Results: The ASAS QS group, consisting of 20 rheumatologists, 2 physiotherapists and 2 patients, provided 34 potentially key areas for quality improvement which were commented by 140 participants (86 physicians, 42 patients). Within that process 3 new key areas were proposed and all 37 key areas for improvement were again evaluated by 120 participants (86 physicians, 29 patients). Five key areas were identified to be most important to phrase QS: referral, rheumatologic assessment, treatment, education/self-management and comorbidities. Altogether, 9 QS, each accompanied by a rationale and a measure (figure), were endorsed by ASAS.

Conclusion: ASAS successfully developed the first QS set for improvement of health care provided for adults with axSpA. All QS are achievable in daily care in an optimized situation and intend to minimize variation in quality of care. It is emphasized that ASAS is well aware that all QS are ideal visions of an optimal care which may currently not be realistic in many countries.

No	Domain	Quality statement
1	Referral	People with suspicion of axial SpA are referred to a rheumatologist for diagnostic assessment within 3 working days.
2	Time to specialist	People with suspicion of axial SpA are assessed by a rheumatologist within 3 weeks after referral.
3	Assessment	People with suspected axial SpA have their diagnostic work-up completed within 2 months.
4	Monitoring	Disease activity of people with axial SpA is monitored under the supervision of a rheumatologist with validated composite scores at least twice a year.
5	Disease control	In people with axial SpA and active disease despite conventional therapy, treatment escalation with biologics is discussed.
6	Non-pharmacological treatment	People with axial SpA are informed about the benefits of regular exercise.
7	Education and self-management	People with axial SpA are offered education on the disease including self-management within two months of diagnosis.
8	Rapid access	Patients with axial SpA and disease flare or possibly drug-related side effects receive advice within 2 working days of contacting the rheumatologist.
9	Annual review	People with axial SpA have a comprehensive annual review by the rheumatologist.

Abstract THU0358 – Figure 1. ASAS quality standards for patients with axial spondyloarthritis

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THU0359

WHAT IS THE LEVEL OF AGREEMENT BETWEEN LOCAL AND CENTRAL READERS IN THE DETECTION OF ACTIVE AND STRUCTURAL LESIONS ON MRI TYPICAL OF AXIAL SPONDYLOARTHRITIS? DATA FROM THE ASAS CLASSIFICATION COHORT STUDY

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Background: There has been no central reader evaluation of MRI scans from the ASAS Classification Cohort (ASAS-CC)[1] to compare detection of lesions in the sacroiliac joints (SIJ) between central and ASAS-CC local site readers. Active MRI lesions typical of axSpA were reported in 61.6% and 2.2% of patients from this cohort diagnosed with axSpA and non-axSpA back pain, respectively[1]. Structural lesions were recorded but not reported in the literature.

Objectives: We aimed to compare detection of active and structural lesions on MRI images of the SIJ from the ASAS-CC between ASAS-CC local site readers and central readers from the ASAS-MRI group.

Methods: MRI images were available from 258 of the 495 cases who had MRI performed in the ASAS-CC and also had a local rheumatologist diagnosis. Seven central readers recorded MRI lesions in an eCRF that included wording of lesions defining active and structural lesions typical of axSpA that was exactly the same as in the original ASAS-CC eCRF permitting comparisons between central and local site readers. In addition, lesions that met the criteria for an ASAS positive MRI were recorded by central readers. Active and structural lesion frequencies were assessed descriptively according to majority agreement (≥4/7) of central reader data and also any 2 central readers. Reliability of detection of MRI lesions was compared between central and local readers using the kappa coefficient.

Results: Significant differences in lesion frequencies were observed according to diagnostic category (Table 1). The frequency of active lesions reported by local readers (61%)was greater than for central readers that agreed on the presence of an active lesion (49.7%). Structural lesions were reported less frequently by local readers (44.0%) compared to central readers that agreed on the presence of a structural lesion (54.9%). Reliability of local readers for detection of active lesions was good but only fair for structural lesions (Table 2).

Reader	MRI Lesion Type	Local Rheumatologist Diagnosis		P value
		AxSpA (n=187)	Not AxSpA (n=71)	
Local	Active	114 (61.0%)	3 (4.2%)	<0.0001
Central (≥4 in agreement)	Active	83 (44.4%)	3 (4.2%)	<0.0001
Central (≥4 in agreement)	ASAS positive	76 (40.6%)	2 (2.8%)	<0.0001
Central (≥2 in agreement)	Active	93 (49.7%)	6 (8.5%)	<0.0001
Central (≥2 in agreement)	ASAS positive	89 (47.6%)	5 (7.0%)	<0.0001
Local	Structural	72 (44.0%)[#]	3 (5.2%)[#]	<0.0001
Central (≥4 in agreement)	Structural	51 (31.5%)[#]	6 (10.3%)[#]	<0.0001
Central (≥2 in agreement)	Structural	89 (54.9%)[#]	10 (17.2%)[#]	<0.0001

Local Readers		Central Readers			
		Active lesion (2 reader agreement)		Active Lesion (≥4 reader agreement)	
		Yes	No	Yes	No
Active lesion	Yes	85	32	78	39
	No	14	127	8	133
Kappa (95% CI)		0.64 (0.54-0.73)		0.62 (0.53-0.72)	
		Structural lesion (2 reader agreement)		Structural Lesion (≥4 reader agreement)	
Structural lesion	Yes	58	17	43	32
	No	41	104	27	118
Kappa (95% CI)		0.46 (0.34 to 0.57)		0.39 (0.27 to 0.52)	

Conclusion: Local readers may have overestimated the presence of active lesions and underestimated the presence of structural lesions in the ASAS-CC. Their reliability for detection of structural lesions was limited which could reflect lack of awareness of structural lesions related to axSpA.

REFERENCES

[1] Rudwaleit et al. Ann Rheum Dis 2009;68: 777-83

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THU0360

INCREASING IMPACT ON STRUCTURAL DAMAGE WITH INCREASING CUMULATIVE INFLAMMATION AT THE SI-JOINT QUADRANT LEVEL IN AXIAL SPONDYLOARTHRITIS – 5-YEAR DATA FROM THE DESIR COHORT

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Background: Axial inflammation is a key feature in axial SpA (axSpA). There is lack of data relative to the persistence of BME in the same anatomical quadrant (Q, 8 in total for both SIJ together), regardless of the overall presence of BME.
Objectives: This study aims to investigate particular patterns of distribution of SIJ-BME across quadrants over time, their persistence over time, and their impact on clinical and structural outcomes.
Methods: Patients from the DESIR cohort (early axSpA according to the rheumatologist) with MRI-SIJ available at baseline, 2 and 5 years were included. Each image was scored by 3 trained central readers blinded to chronological order. BME was considered positive if detected in ≥1/6 slices in each of the 8 quadrants, according to each individual reader. Four different patterns of BME over time were defined (no BME, sporadic pattern, fluctuating BME and persistent BME) considering all 8 quadrants (Figure). The effect of BME patterns on 5-year structural (mNY, mSASSS, ≥5 erosions and/or fatty lesions in MRI-SIJ) and clinical outcomes (BASFI, BASMI and ASQoL) was evaluated using multilevel generalised estimating equations (GEE) models (taking the individual reader data into account) and linear regression (using the agreement of ≥ 2 out of 3), as appropriate. All models were adjusted for relevant confounders including treatment (Table).
Results: In total, 136 patients were included (age 34 (SD 9) years, 50% male, and 63% HLA-B27 positive). 'No BME' was seen in 63 patients (46%), the 'sporadic pattern' in 34 patients (25%), the 'fluctuating pattern' was seen in 21 patients (15%) and the 'persistent BME pattern' was seen in 18 patients (13%). Compared to the 'no BME' pattern (reference), the 'sporadic' [OR (95% CI): 2.1 (1.0;4.5)], 'fluctuating' [OR: 5.6 (2.2;14.4)] and 'persistent' [OR: 7.5 (2.8;19.6)] patterns were associated with higher likelihood to be mNY positive at 5-years, suggesting a gradient between cumulative inflammation and damage. Similar findings were observed for mNY as a continuous outcome variable and for ≥5 erosions and/or fatty lesions on spinal MRI as outcomes, but not for mSASSS (Table). There was no association between the BME patterns and the clinical outcomes.
Conclusion: Only 13% of the patients showed persistent inflammation in the same Q over a 5-year period and in 15% inflammation was fluctuating across different Qs. More structural damage was found in patients with increasing cumulative levels of local inflammation in the quadrant. Even when BME (temporarily) disappears there is an important effect on structural outcomes, and that effect t is independent of treatment.
Disclosure of Interests: Santiago Rodrigues-Manica Grant/research support from: Novartis, MSD, Speakers bureau: Novartis, Alexandre Sepriano: None declared, Sofia Ramiro Grant/research support from: MSD, Consultant for: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Speakers bureau: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Robert B.M. Landewé: None declared, Pascal Claudepierre Consultant for: Honoraria from Novartis as steering committe of this survey, Anna Moltó: None declared, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Miranda van Lunteren: None declared, Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge

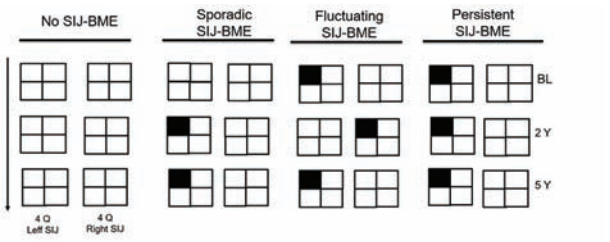


Figure. Graphical representation of examples of presentation of BME throughout time (baseline, 2 and 5 years) across 8 SIJ quadrants combined into four patterns. **No BME:** No BME in all observations; **Sporadic BME:** Other pattern of BME (not included in the previous; **Fluctuating BME:** Fluctuating BME at any of the 8 quadrants (e.g. 1-0-1 or 0-1-0), without simultaneous persistent BME in the remaining quadrants; **Persistent BME:** Constant BME, in at least one quadrant, regardless of the pattern of BME in the remaining quadrants).

Table – Association between SIJ-BME patterns and structural and clinical outcomes

Outcome at 5 years	N	No BME	Sporadic BME	Fluctuating BME	Persistent BME
mNY (0-8)[a]	124	(reference)	0.4 (0.1;0.8)	**1.7 (1.1;2.3)**	**2.3 (1.6;3.0)**
mNY (yes/no)[b]	124	(reference)	2.1 (1.0;4.5)	**5.6 (2.2;14.4)**	**7.5 (2.8;19.6)**
mSASSS (0-72)[a]	117	(reference)	-0.2 (-0.9;0.6)	-0.3 (-1.3;0.3)	-0.5 (-1.3;0.3)
≥5 erosions or/and fatty lesions on MRI (yes/no)[b]	127	(reference)	**2.9 (1.4;5.9)**	**4.2 (1.6;10.8)**	**8.1 (4.1;16.6)**
BASFI (0-10)[c]	124	(reference)	-2.1(-8.8;4.7)	-5.9(-14.5;2.7)	0.2(-8.5;8.9)
BASMI (0-10)[c]	117	(reference)	-0.03(-0.44;0.38)	-0.43(-0.99;0.13)	0.03(-0.49;0.56)
ASQoL (0-18)[c]	123	(reference)	-1.3(-2.9;0.3)	**-2.2(-4.2;-0.2)**	-0.7(-2.7;1.3)

[a] Estimated by linear GEE, [b] Estimated by binomial GEE, [c] Estimated by linear regression
All analyses are adjusted for symptom duration, sex, smoking status, HLA-B27, medication (NSAID, csDMARD, bDMARD) and ASDAS.
csDMARD, bDMARD) and ASDAS.

Abstract THU0360 – Figure 1

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THU0361

DIAGNOSTIC PERFORMANCE OF MRI LESIONS IN THE SACROILIAC JOINTS ACCORDING TO UPDATED ASAS LESION DEFINITIONS: A CENTRAL READER ASSESSMENT OF MRI SCANS FROM THE ASSESSMENTS IN SPONDYLOARTHRITIS CLASSIFICATION COHORT

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Background: The ASAS MRI group has generated updated lesion definitions for MRI lesions in the SIJ. While the ASAS definition of a positive MRI for classification purposes remains unchanged, these additional ASAS definitions for active and structural lesions may also be of diagnostic value. It is important to understand their relative contribution and complementarity as diagnostic indicators.
Objectives: To determine optimal cut-offs for the number of SIJ quadrants with MRI lesions reflecting diagnosis of axSpA in patients with undiagnosed back pain.
Methods: MRI lesions on baseline scans from the ASAS Classification Cohort were recorded by 7 experienced readers from the ASAS-MRI group. Detailed scoring of lesions per SIJ quadrant (SPARCC SIJ quadrantic method) was available for assessment of bone marrow edema (BME) and structural lesions in 158 and 146 cases, respectively, who were diagnosed by the local rheumatologist at baseline. Of these, 86 and 79 cases with BME and structural lesion data, respectively, were also diagnosed by the local rheumatologist at follow up (mean 4.4 years). We calculated sensitivity and specificity for varying numbers of SIJ quadrants with MRI lesions with rheumatologist diagnosis of axSpA at baseline and follow up as gold standard.
Results: Lesion cut-offs based on BME were most sensitive for diagnosis at baseline and follow up but erosion- and fatty-lesion cut-offs were more specific (Table). At least 2 SIJ quadrants with erosion or fat metaplasia were associated with >90% specificity for the diagnosis of axSpA. There was also a consistent improvement in the sensitivity and specificity performance of cut-offs based on erosions and fatty lesions according to diagnosis at baseline and at follow up after 4.4 years but not for cut-offs based on BME. Lesion cut-offs that combined BME and/or erosion enhanced sensitivity without compromising specificity.

Abstract THU0361 –Table 1.

MRI lesion SIJ quadrant cut-offs, Agreement by ≥2 central reader data	axSpA Diagnosed at Baseline		axSpA Diagnosed at Follow up	
	Sensitivity (95%CI)	Specificity (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)
BME Score ≥2	50.0 (40.6-59.4)	82.5 (70.1-91.3)	46.5 (34.5-58.7)	86.4 (65.1-97.1)
BME Score ≥3	40.5 (31.5-50.0)	94.7 (85.4-98.9)	33.8 (23.0-46.0)	90.9 (70.8-98.9)
Erosion Score ≥2	35.3 (26.7-44.8)	93.0 (83.0-98.1)	33.8 (23.0-46.0)	95.5 (77.2-99.9)
Erosion Score ≥3	31.0 (22.8-40.3)	93.0 (83.0-98.1)	33.8 (23.0-46.0)	95.5 (77.2-99.9)
Fatty lesion ≥2	34.5 (25.9-43.9)	93.0 (83.0-98.1)	38.0 (26.8-50.3)	95.5 (77.2-99.9)
Fatty lesion ≥3	31.9 (23.6-41.2)	94.7 (85.4-98.9)	35.2 (24.2-47.5)	95.5 (77.2-99.9)
Sclerosis ≥2	32.8 (24.3-42.1)	82.5 (70.1-91.3)	29.6 (19.3-41.6)	90.9 (70.8-98.9)
Sclerosis ≥3	28.5 (20.5-37.6)	82.5 (70.1-91.3)	26.8 (16.9-38.6)	90.9 (70.8-98.9)
BME score ≥1 and Erosion score ≥1	36.1 (26.6-46.5)	92.1 (78.6-98.3)	32.8 (21.3-46.0)	84.6 (54.6-98.1)
BME score ≥2 and/or Erosion score ≥1	58.8 (48.3-68.7)	81.6 (65.7-92.3)	49.2 (36.1-62.3)	84.6 (54.6-98.1)
BME score ≥2 and/or Erosion score ≥2	58.8 (48.3-68.7)	81.6 (65.7-92.3)	49.2 (36.1-62.3)	84.6 (54.6-98.1)
BME score ≥3 and/or Erosion score ≥1	51.6 (41.2-61.8)	86.8 (69.9-93.4)	39.3 (27.1-52.7)	84.6 (54.6-98.1)

Conclusion: The updated ASAS definitions based on the presence of MRI lesions in 2-3 SIJ quadrants have comparable diagnostic performance. This performance improves for erosion and fatty lesion cut-offs after follow up.

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THU0362 THE IMPACT OF A REFERRAL ALGORITHM FOR AXIAL SPONDYLOARTHRITIS: A FOUR MONTH FOLLOW-UP OF PATIENT REPORTED OUTCOMES

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Background: A substantial amount of patients with chronic low back pain (CLBP) have axial spondyloarthritis (axSpA), but early recognition of these patients is difficult for general practitioners (GPs).[1] As a result, several referral strategies have been developed to help physicians identify patients at risk for axSpA within the large group of CLBP patients.[2] Most referral strategies were developed in secondary care patients. The only referral strategy that was developed and validated in primary low back patients is the CaFaSpA strategy.[3] An essential step before implementing referral strategies in daily clinical practice is the execution of an impact analysis.[4]

Objectives: The purpose of this study is to assess the impact of using a referral strategy on patient outcomes in young primary care patients with CLBP at risk for axSPA.

Methods: A clustered randomized controlled trial was performed in a primary care setting (ClinicalTrials.gov Identifier: NCT01944163). Each cluster contained the general practices from a single primary care practice and their included patients. Clusters were randomized to either the intervention (use of CaFaSpA referral strategy) or the control group (usual care). Primary outcome was disability caused by CLBP, measured with the Roland Morris Disability Questionnaire (RMDQ) at baseline and 4 months. Secondary outcome was axSpA diagnosis made by a rheumatologist. A linear mixed-effects model was used to analyze mean change in RMDQ score.

Results: In total 679 patients were included within 93 GP clusters. Sixty-four percent of our study population were female and mean age was 36 years. Median RMDQ score at baseline was 8 (IQR 4-12) in both groups. Compared to baseline, mean RMDQ score decreased by 0.74 points at 4 months (intervention) and by 0.46 points (control) (Fig. 1). This decrease did not significantly differ between groups (p=0.50). Eight percent of the finally referred patients in the intervention group, received an axSPA diagnosis (8%) from the rheumatologist. The median RMDQ among patients who visited the rheumatologist decreased from 8 to 5 after 4 month. This was not statistically significant (p-value=0.17).

Conclusion: Although the CaFaSpA referral strategy did not have an early impact on disability caused by CLBP, it can be used as a screening strategy for GPs to identify axSpA patients.

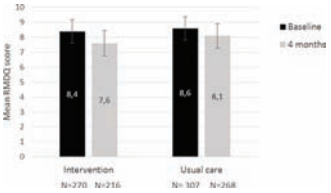
REFERENCES:

[1] Jois RN, Macgregor AJ, Gaffney K. Recognition of inflammatory back pain and ankylosing spondylitis in PC. Rheumatology (Oxford) 2008;47:1364-1366.

[2] Abawi O, van den Berg R, van der Heijde D, van Gaalen FA. Evaluation of multiple referral strategies for axial spondyloarthritis in the SPondyloArthritis Caught Early (SPACE) cohort. RMD Open 2017 Apr 7;3(1):e000389-2016-000389. eCollection 2017.

[3] van Hoeven L, Vergouwe Y, de Buck PD, Luime JJ, Hazes JM, Weel AE. External Validation of a Referral Rule for Axial Spondyloarthritis in Primary Care Patients with Chronic Low Back Pain. PLoS One 2015 Jul 22;10(7): e0131963.

[4] Moons KG. Kengne AP, Grobbee DE, Risk prediction models: II. External validation, model updating, and impact assessment. Heart. 2012;98 (9):691-8.



Abstract THU0362 – Figure 1. Estimated mean RMDQ scores over time for the overall intervention and usual care group.

Bars indicate 95% confidence intervals for the mean estimates.

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THU0363 DO ILLNESS PERCEPTIONS AND COPING CHANGE OVER TIME IN PATIENTS RECENTLY DIAGNOSED WITH AXIAL SPONDYLOARTHRITIS? A 2-YEAR FOLLOW-UP STUDY IN THE SPACE COHORT

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Background: In recently diagnosed axial spondyloarthritis (axSpA), illness perceptions are important in the relationship between back pain and Health-Related Quality of Life (HRQoL) or work productivity loss (WPL). [1] Coping did not have an additional impact on this relationship, but was associated with HRQoL. Therefore, health outcomes might be improved by influencing illness perceptions and possibly coping. With respect to disease management, it is important to know if illness perceptions and coping remain stable over time. However hardly any information is available, especially for early axSpA, as the few studies that have been conducted mostly had a cross-sectional design and investigated patients with long-standing radiographic axSpA.

Objectives: To investigate if illness perceptions and coping strategies change in the first 2 years after diagnosis of axSpA.

Methods: Patients diagnosed with axSpA and ≥1 follow-up visit (1 year and/or 2 years) in the SPACE cohort were included in the analysis. Mixed linear models were used to test if illness perceptions (measured by the Revised Illness Perception Questionnaire (IPQ-R, scale 1-5)), coping (Coping with Rheumatic Stressors (CORS, scale 1-4)), back pain (scale 0-10), HRQoL (physical (PCS) and mental component summary (MCS), scale 0-100, of the 36-item Short-Form Health Survey (SF-36)), WPL and activity impairment (Work Productivity and Activity Impairment (WPAI, range 0-100%)) changed over time. Results were stratified for gender and age when the interaction term was statistically significant ($p<0.05$).

Results: In total, 150 axSpA patients (mean age 30.4 years, 51% female, 65% HLA-B27+) were analysed. Baseline mean back pain (SD) was 4.0 (2.5), PCS was 28.8 (14.0), MCS was 47.8 (12.4), WPL was 34.1% (29.8) and activity impairment was 38.7% (27.9). Illness perceptions and coping strategies showed minimal changes over time (**Table 1, 2**). Over two years patients remained having negative illness perceptions (which were important in the association between back pain and health outcomes in the previous study). For example, over 2 years patients had strong beliefs in severe consequences ('*consequences*'), had still negative emotions towards their disease ('*emotional representation*') and had strong beliefs in chance ('*chance*') as a cause for axSpA.

Over two years, back pain (mean change ± SD is -1.5 ± 2.2) and activity impairment (-14.4% ± 27.2) decreased, PCS (11.1 ± 13.3) and WPL (-15.3% ± 28.7) improved statistically significantly, but MCS did not change (0.7 ± 13.9).

Abstract THU0363 –Table 1.

Table 1 Illness perceptions in early axSpA patients at baseline and 1-2 years after diagnosis in the SPACE cohort

	Range	Baseline n=150	Year 1 n=130	Year 2 n=114
Identity	0-15	4.7 (2.4)	5.0 (2.7)	4.6 (2.4)
Consequences	1-5	2.9 (0.7)	2.8 (0.8)	2.8 (0.9)
Timeline (acute/chronic)	1-5	3.6 (0.8)	3.8 (0.8)	3.8 (0.8)
Personal control	1-5	3.3 (0.6)	3.3 (0.6)	3.4 (0.6)
Treatment control	1-5	3.5 (0.5)	3.4 (0.6)	3.5 (0.6)
Illness coherence*	**1-5**	**3.3 (0.8)**	**3.5 (0.8)**	**3.6 (0.7)**
Timeline (cyclical)	1-5	3.6 (0.8)	3.6 (0.8)	3.6 (0.8)
Emotional representation*	**1-5**	**2.7 (0.8)**	**2.6 (0.8)**	**2.5 (0.8)**
Psychological attributions	1-5	2.1 (0.9)	2.1 (0.9)	2.1 (0.9)
Risk factors	1-5	2.2 (0.6)	2.2 (0.6)	2.1 (0.6)
Immunity	1-5	2.3 (0.8)	2.4 (0.9)	2.3 (0.9)
Accident				
Male	1-5	2.3 (1.2)	2.1 (1.1)	2.0 (1.1)
Female	1-5	1.8 (1.0)	2.1 (1.2)	1.9 (1.1)
Chance	1-5	3.3 (1.2)	3.2 (1.2)	3.3 (1.2)

Results are presented as mean (SD) unless stated otherwise. *Results of the mixed linear models with p=0.002 (p=0.05/21, correction for multiple testing) were considered to be statistically significant and are printed in bold.

Abstract THU0363 –Table 2.

Table 2 Coping strategies in early axSpA patients at baseline and 1-2 years after diagnosis in the SPACE cohort

	Range	Baseline n=150	Year 1 n=130	Year 2 n=114
Pain				
Comforting cognitions	1-4	2.8 (0.6)	2.9 (0.6)	2.8 (0.6)
Decreasing activities	1-4	2.1 (0.6)	2.1 (0.6)	2.0 (0.6)
Diverting attention	1-4	2.3 (0.6)	2.4 (0.6)	2.4 (0.6)
Coping with limitations				
Optimism	1-4	2.8 (0.7)	2.9 (0.7)	2.9 (0.7)
Pacing				
Male	1-4	2.1 (0.6)	2.1 (0.6)	2.0 (0.6)
Female	1-4	2.2 (0.6)	2.3 (0.6)	2.4 (0.6)
Creative solution seeking				
Male	1-4	2.3 (0.6)	2.4 (0.6)	2.3 (0.07)
Female*	**1-4**	**2.3 (0.6)**	**2.4 (0.6)**	**2.6 (0.06)**
Dependency				
Accepting	1-4	1.8 (0.6)	1.8 (0.6)	1.7 (0.6)
Consideration	1-4	2.7 (0.6)	2.7 (0.6)	2.7 (0.6)

Results are presented as mean (SD) unless stated otherwise. *Results of the linear mixed models with p<0.002 (p<0.05/21, correction for multiple testing) were considered to be statistically significant and are printed in bold.

Conclusion: Despite clear improvements in back pain and health outcomes over 2 years, illness perceptions experienced and coping strategies applied by the patients showed little change in recently diagnosed axSpA patients. Further research is recommended why despite improved outcomes illness perceptions do not change, to investigate the impact of these unchanged illness perceptions and coping strategies on health outcomes and how these negative perceptions can be improved.

REFERENCES:

[1] van Lunteren, et al. AC&R 2018.

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THU0364 THE DIAGNOSTIC UTILITY OF THE RELATION BETWEEN MRI BONE MARROW EDEMA AND OTHER TYPES OF MRI LESIONS IN THE SACROILIAC JOINTS IN AXIAL SPONDYLOARTHRITIS

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Background: MRI detected bone marrow edema (BME) plays a central role in the ASAS (Assessment of Spondyloarthritis International Society) classification criteria for axial spondyloarthritis (axSpA)[1, 2]. However, BME in the sacroiliac joints (SIJs) is also present in other conditions[3-7].

Objectives: The aim was to investigate the diagnostic utility of MRI BME and its relation to different types of MRI SIJ lesions to separate patients with axSpA from persons with other conditions.

Methods: The MASH study is a prospective cross-sectional study of 204 participants, aged ≤45 yrs. The study included patients with axSpA (n=41), women with (n=46) and without (n=14) postpartum pain, patients with lumbar disc herniation (n=25), persons with hard physical labor (cleaning assistants) (n=25), long-distance runners (≥30 km/week) (n=23) and healthy men (n=29). Participants with pain should all have VAS pain >2 (on a scale 0-10) for ≥2 months. Participants in the non-axSpA groups were not allowed to have any clinical SpA features or rheumatological conditions. Participants underwent clinical, laboratory and MRI examination (semi-coronal STIR and T1W sequences) of the SIJs. MRIs were evaluated for BME, erosion, fat, ankylosis, and sclerosis according to the SPARCC MRI definitions of lesions[8, 9] by two independent readers. In nine slices of the cartilaginous compartment each SIJ was separately assessed for the presence of BME in relation to joint space and each of the above-mentioned structural lesions (range of total score per patient: 0-18).

Results: The table shows the clinical characteristics of each group, the mean MRI scores and MRI cut-off levels for the concordant reads. BME located adjacent to joint space, adjacent to erosions and adjacent to fat were more frequent in patients with axSpA, but these lesions were also seen in the other study groups, mainly women with postpartum pain. When increasing amounts of lesions were required (higher cut-offs),

almost only AxSpA patients fulfilled the requirements. BME adjacent to sclerosis was most frequent in women with postpartum pain, whereas BME adjacent to ankylosis was only seen in patients with axSpA.

Conclusion: BME located adjacent to joint space, adjacent to erosion and adjacent to fat was most frequently, but not exclusively, occurring in patients with axSpA, whilst BME adjacent to sclerosis was most frequent in women with postpartum pain. Detailed analysis of lesions and their anatomical location may help differentiate axSpA from other conditions.

Abstract THU0364 –Table 1.

Clinical characteristics and relations between MRI BME and other MRI lesions

		AxSpA (N=41)	Post-partum with pain (N=46)	Post-partum without pain (N=14)	Disc herniation (N=25)	Cleaning staff (N=26)	Long distance runners (N=23)	Healthy men (N=29)
Age (years)		31 31 (19; 44)	33 33 (26; 41) *	33 33 (27; 41)	35 37 (21; 43) **	39 39 (28; 45) ***	33 32 (22; 43)	31 30 (20; 45)
Male sex		26 (63)	0 (0) ***	0 (0) ***	11 (44)	0 (0) ***	18 (78)	29 (100) ***
HLA-B27 positive		33 (81)	5 (11) ***	1 (7) ***	0 (0) ***	0 (0) ***	1 (4) ***	4 (14) ***
CRP (mg/L)		11 6 (0.3; 58)	2 1 (0.3; 7) ***	2 1 (0.3; 13) **	2 1 (0.3; 14) ***	3 1 (0.3; 20) ***	1 0.4 (0.3; 8) ***	1 0.3 (0.3; 5) ***
Body mass index (kg/m²)		23 23 (18; 32)	25 24 (17; 37)	23 21 (19; 32)	26 25 (20; 35) **	26 25 (21; 36) **	23 23 (19; 26)	25 25 (20; 31) **
Symptom duration (years)		8 (6) 8 (1; 24)	1 (1) (0.3; 6)	NA	1 (1) 1 (0.2; 4)	NA	NA	NA
Childbirths		1.7 2.0 (0; 2)	1.5 1.0 (1; 4)	1.9 2.0 (1; 3)	1.6 2.0 (0; 3)	2.5 3.0 (0; 5)	0.5 0 (0; 2)	NA
Low back pain (VAS, 0-10)		4 4 (0; 10)	6 6 (0; 10) **	0.4 0 (0; 2) ***	6 6 (0.3; 10) *	0.8 0 (0; 7) ***	0.2 0 (0; 2) ***	0.1 0 (0; 1) ***
BME adjacent to joint space		5 4 (0; 16)	2 1 (0; 13) **	1 0 (0; 6) **	0.3 0 (0; 2) ***	0.2 0 (0; 3) ***	0.2 0 (0; 2) ***	0.2 0 (0; 2) ***
BME adjacent to fat		1 0 (0; 10)	0.1 0 (0; 4) ***	0 0 (0; 1) *	0 0 (0; 0) ***	0 0 (0; 0) ***	0 0 (0; 0) ***	0 0 (0; 0) ***
BME adjacent to sclerosis		1 0 (0;10)	2 0 (0; 13)	1 0 (0; 4)	0 0 (0; 1) **	0.2 0 (0; 4) *	0 0 (0; 1) *	0 0 (0; 1) **
BME adjacent to erosion		2 1 (0; 14)	0.2 0 (0; 7) ***	0 0 (0; 0) **	0 0 (0; 0) ***	0 0 (0; 0) ***	0.1 0 (0; 2) ***	0 0 (0; 0) ***
BME adjacent to ankylosis		0.1 0 (0; 1)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)	0 0 (0; 0)
BME adjacent to joint space	≥ 1	26 (63)	20 (44)	3 (21)	2 (8)	2 (8)	0	1 (3)
	≥ 3	23 (56)	13 (28)	1 (7)	0	0	0	0
	≥ 5	19 (46)	4 (9)	1 (7)	0	0	0	0
	≥ 10	7 (17)	1 (2)	0	0	0	0	0
BME adjacent to fat	≥ 1	7 (17)	1 (2)	0	0	0	0	0
	≥ 3	2 (5)	0	0	0	0	0	0
	≥ 5	2 (5)	0	0	0	0	0	0
BME adjacent to sclerosis	≥ 1	7 (17)	13 (28)	2 (14)	0	1 (4)	0	0
	≥ 3	2 (5)	6 (13)	1 (7)	0	1 (4)	0	0
	≥5	1 (2)	6 (13)	0	0	0	0	0
BME adjacent to erosion	≥ 1	11 (27)	2 (4)	0	0	0	0	0
	≥ 3	7 (17)	1 (2)	0	0	0	0	0
	≥ 5	4 (10)	0	0	0	0	0	0
	≥ 10	1 (2)	0	0	0	0	0	0
BME adjacent to ankylosis	≥ 1	1 (2)	0	0	0	0	0	0

In cells with 1 row, values are N (%). In cells with 2 rows, values are mean (upper row) and median (min; max) (lower row).
Mann-Whitney test, compared with patients with axSpA. p<0.05*; p<0.01**; p<0.001***.
MRI SIJ scores are equal to the number of SIJs with a lesion per slice in '9 slices' (0-18).
CRP: C-Reactive Protein; HLA-B27: Human Leucocyte Antigen B27; VAS: Visual Analogue Scale; BME: Bone marrow edema.

REFERENCES:

[1] Rudwaleit, et al. Ann Rheum 2009.
[2] Lambert, et al. Ann Rheum 2016.
[3] Weber, et al. Arthritis Rheum 2010.
[4] Varkas, et al. Rheumatology (Oxford) 2018.
[5] de Winter, et al. Arthritis Rheumatol 2018.
[6] Arnbak, et al. Eur Radiol 2016.
[7] Seven, et al. Ann Rheum 2018.
[8] Maksymowych, et al. Arthritis Rheum 2005.
[9] Maksymowych, et al. J Rheumatol 2015.

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THU0365 THE IMPACT OF UVEITIS, PSORIASIS AND INFLAMMATORY BOWEL DISEASE ON MUSCULOSKELETAL DISEASE ACTIVITY AND FUNCTION IN AXIAL SPONDYLOARTHRITIS: A POPULATION-BASED ANALYSIS OF INSURANCE CLAIMS LINKED TO PATIENT SURVEY DATA

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Background: Uveitis, psoriasis and inflammatory bowel disease (IBD) are common in axial spondyloarthritis (axSpA) but data on their impact on activity of musculoskeletal manifestations and functional status in general are contradictory.

Objectives: The aim of this study was to assess the impact of uveitis, psoriasis and IBD on disease activity and functional status in a population-based cohort of patients with axSpA.

Methods: A stratified random sample of subjects with a diagnosis of axSpA (ICD-10 M45) was drawn from health insurance data in Germany. These patients received a questionnaire on disease-related, demographic and socioeconomic parameters. Age, sex, drug prescriptions and non-pharmacological treatment were retrieved from claims data and linked to the questionnaire data. Information on recent/current occurrence of uveitis, psoriasis and IBD (within one year) was obtained from claims data; in addition, information on history of uveitis, psoriasis and IBD was obtained from survey data. Patients with uveitis, psoriasis or IBD were compared to those without uveitis, psoriasis or IBD. Separate multivariable linear regression models were calculated to determine the effect of uveitis, psoriasis and IBD on disease activity and functional status after adjustment for other relevant parameters including treatment.

Abstract THU0365 –Table 1.

Table Results from multivariable linear regression models showing the association of psoriasis, inflammatory bowel disease and uveitis with disease activity (BASDAI) and functional impairment (BASFI) in patients with axial spondyloarthritis (N=1,729).

Recent psoriasis, inflammatory bowel disease, and uveitis (based on claims data)				
		Reference	**BASDAI* β (95% CI)**	**BASFI** β (95% CI)**
Model 1a	Psoriasis, recently present	not present	0.07 (-0.27, 0.40)	0.30 (-0.09, 0.70)
Model 1b	Inflammatory bowel disease, recently present	not present	0.30 (-0.10, 0.71)	0.33 (-0.14, 0.80)
Model 1c	Uveitis, recently present	not present	**-0.44 (-0.77, -0.10)**	-0.38 (-0.77, 0.02)
History of psoriasis, inflammatory bowel disease, and uveitis (based on survey data)				
		Reference	**BASDAI* β (95% CI)**	**BASFI** β (95% CI)**
Model 2a	Psoriasis, ever present	not present	**0.31 (0.05, 0.58)**	**0.37 (0.05, 0.68)**
Model 2b	Inflammatory bowel disease, ever present	not present	**0.37 (0.01, 0.73)**	0.35 (-0.07, 0.77)
Model 2c	Uveitis, ever present	not present	-0.10 (-0.31, 0.11)	-0.01 (-0.26, 0.24)

*Model adjusted for age, sex, body mass index, rheumatological care, smoking, suffering from stress, NSAIDs, bDMARDs, non-opioid analgesics, opioids, systemic steroids, physical therapy; **Model adjusted for age, sex, body mass index, rheumatological care, lack of exercise, smoking, suffering from stress, non-opioid analgesics, opioids, systemic steroids, physical therapy.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; bDMARDs, biological disease-modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs.

Results: A total of 1,729 patients with axSpA were included in the analyses; mean age was 55.9 years and 46.1% were female. The prevalence was 9% (27%) for recent (ever) uveitis, 10% (15%) for recent (ever) psoriasis, and 6% (9%) for recent (ever) IBD. In 1.6% (6.9%) of the patients two of these conditions were recently (ever) present, and in 0% (0.5%) of the patients, all three conditions were recently (ever) present.

The multivariable linear regression analyses revealed that history of psoriasis was significantly associated with both higher level of disease activity and higher level of functional impairment. History of IBD was also associated with higher disease activity, whereas recent psoriasis or IBD showed no strong association with disease activity and functional status (Table). In contrast, history of uveitis showed no strong association with disease activity and functional status while recent uveitis was significantly associated with lower disease activity according to the BASDAI even after adjustment for treatment.

Conclusion: Disease activity and functional impairment are higher in axSpA patients with a history of psoriasis or IBD, whereas history of

uveitis does not have a major impact on activity of musculoskeletal manifestations and functional status in axSpA. However, recent uveitis showed a somewhat unexpected association with lower disease activity. The latter might be related to a higher likelihood of being treated with TNF inhibitors in the presence of uveitis.

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THU0366 MAGNETIC RESONANCE IMAGING IN COMPARISON WITH CONVENTIONAL RADIOGRAPHY FOR DETECTION OF STRUCTURAL CHANGES TYPICAL FOR SPA – DATA FROM THE ASSESSMENT OF SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS) COHORT

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Background: In axial spondyloarthritis, magnetic resonance imaging (MRI) is useful for depicting active inflammatory lesions. The utility of MRI to display structural changes is not that well established.

Objectives: Comparison of MRI and conventional radiography of the sacroiliac joints (SIJs) for detection of structural lesions typical for axial spondyloarthritis (axSpA) in an international multireader exercise.

Methods: Patients from the ASAS Cohort with symptoms suggestive of axSpA and both radiographs and T1-weighted MRIs of SIJs available for central reading were included. SIJs radiographs were scored by 3 central readers according to the modified New York (mNY) criteria grading system. Structural damage on radiographs was defined as fulfillment of the radiographic mNY criterion (patient level) or presence of grade 2 sacroiliitis (single joint level) (majority decision). MRI scans were assessed for structural changes compatible with axSpA (global statement) and separate changes (erosion, sclerosis, periarticular fat metaplasia and ankylosis) by 7 central readers (majority decision). Absolute agreement between MRI and radiography and Kappa coefficient were determined.

Results: Overall, 199 patients (398 joints) were included, 149 (74.9%) had a diagnosis of axSpA. 102 (51.3%) had definite radiographic sacroiliitis, 65 (32.7%) had structural changes suggestive of SpA on MRI (global assessment). The absolute agreement between MRI and radiography was 69.3%, kappa - 0.39 (Table 1). Structural damage on radiographs often (48.1% of cases) could not be confirmed by MRI. Among structural lesions, erosions on MRI showed the best discriminative capacity regarding the structural damage on radiographs (Table 1).

Conclusion: Only modest agreement between MRI and conventional radiography in detection of structural changes typical for SpA in the SIJs was revealed; erosions on MRI showed the best agreement with the presence of definite structural damage on radiographs.

Abstract THU0366 –Table 1.

Table 1. Comparison of MRI with conventional radiographs for the detection of structural damage in the sacroiliac joints at the patient level (n=199)

		Radiographic sacroiliitis fulfilling the mNY criteria		Absolute agreement	Kappa value
		No (n=97)	Yes (n=102)		
Presence of structural lesions typical for SpA on MRI according to the global assessment	No (n=134)	**85 (42.7%)**	49 (24.6%)	69.3%	κ=0.39
	Yes (n=65)	12 (6.0%)	**53 (26.6%)**		
Presence of any structural changes (erosions, sclerosis, ankylosis or fat metaplasia) on MRI	No (n=120)	**77 (38.7%)**	43 (21.6%)	69.3%	κ=0.37
	Yes (n=79)	20 (10.1%)	**59 (29.6%)**		
Presence of erosions or sclerosis or ankylosis on MRI	No (n=124)	**79 (39.7%)**	45 (22.6%)	68.3%	κ=0.37
	Yes (n=75)	18 (9.0%)	**57 (28.6%)**		
Presence of erosions on MRI	No (n=141)	**85 (42.7%)**	56 (28.1%)	65.8%	κ=0.32
	Yes (n=58)	12 (6.0%)	**46 (24.1%)**		
Presence of sclerosis on MRI	No (n=163)	**90 (45.2%)**	73 (36.7%)	59.8%	κ=0.21
	Yes (n=36)	7 (3.5%)	**29 (14.6%)**		
Presence of ankylosis on MRI	No (n=195)	**97 (48.7%)**	98 (49.2%)	50.8%	κ=0.04
	Yes (n=4)	0 (0.0%)	**4 (2.0%)**		
Presence of fat metaplasia on MRI	No (n=157)	**90 (45.2%)**	67 (33.7%)	62.8%	κ=0.27
	Yes (n=42)	7 (3.5%)	**35 (17.6%)**		

mNY criteria – modified New York Criteria for ankylosing spondylitis; SpA – spondyloarthritis; MRI – magnetic resonance imaging

Abstract THU0366 –Table 2.

Table 2. Comparison of MRI with conventional radiographs for the detection of structural damage in the sacroiliac joints at the single joint level (n=398)

		Definite radiographic sacroiliitis (grade >=2)		Absolute agreement	Kappa value
		No (n=209)	Yes (n=199)		
Presence of any structural changes (erosions, sclerosis, ankylosis or fat metaplasia) on MRI	No (n=272)	**184 (46.2%)**	88 (22.1%)	71.6%	κ=0.42
	Yes (n=126)	25 (6.3%)	**101 (25.4%)**		
Presence of erosions or sclerosis or ankylosis on MRI	No (n=283)	**187 (47.0%)**	96 (24.1%)	70.4%	κ=0.39
	Yes (n=115)	22 (5.5%)	**93 (23.4%)**		
Presence of erosions on MRI	No (n=312)	**192 (48.2%)**	120 (30.2%)	65.6%	κ=0.29
	Yes (n=86)	17 (4.3%)	**69 (17.3%)**		
Presence of sclerosis on MRI	No (n=345)	**201 (50.5%)**	144 (36.2%)	61.8%	κ=0.21
	Yes (n=53)	8 (2.0%)	**45 (11.3%)**		
Presence of ankylosis on MRI	No (n=393)	**209 (52.5%)**	184 (46.2%)	53.8%	κ=0.03
	Yes (n=5)	0 (0.0%)	**5 (1.3%)**		
Presence of fat metaplasia on MRI	No (n=330)	**195 (49.0%)**	135 (33.9%)	62.6%	κ=0.23
	Yes (n=68)	14 (3.5%)	**54 (13.6%)**		

MRI – magnetic resonance imaging

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THU0367 ANALYSING IMPAIRMENTS IN PHYSICAL PERFORMANCE (AS ASSESSED BY THE AS PERFORMANCE INDEX (ASPI)) IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: In patients with axial spondyloarthritis (axSpA) physical functioning is often impaired. The current gold standard to assess physical functioning is self-reported questionnaires (i.e. BASFI), which can be influenced by patients' subjective feelings. Therefore, a performance-based test-battery was designed to measure physical functioning more objectively: the ankylosing spondylitis (AS) Performance Index (ASPI)) [1]. Based on domains taken from BASFI tasks were designed to imitate activities of daily living (ADL). Although the ASPI has been evaluated a thorough analysis of the deficits of physical functioning and factors which influence the performance of patients with axSpA has not been performed to date.

Objectives: The aim of the present study assesses the relation between self-reported assessments of physical functioning and actual performance of patients, and to detect influencing factors.

Methods: Consecutive axSpA patients underwent standardized assessments concentrating on the following variables: patient and disease characteristics, patient-reported outcomes (ASDAS, BASFI, BASMI, ASAS Health Index (ASAS HI), PHQ-9, IPAQ), mSASSS and ASPI (ASPI 1: Bending, 2. Putting on socks, 3. Getting up from the floor) [1]. The performance was measured in seconds as time to complete a task based on published instructions. Impairment in physical performance was defined as inability of patients to perform $\geq$ 1 ASPI test. Spearman Rho correlation was used to compare self-reported functioning and performed physical functioning. Logistic regression analysis was used to identify factors associated with impaired physical performance.

Results: A total of 200 patients (AS 66%, nr-axSpA 34%) was included: 69% males, 44.3±12.5 years old, mean symptom duration 17.9 ±12.6 years, BMI 27.2±5.5, mean ASDAS 2.5±1.1, BASFI 4.0±2.7, BASMI 3.5 ±1.8), ASAS HI 7.0±4.1, PHQ-9 8.8±6.2, and mSASSS (n=157) 10.2 ±18.8). 133 patients were treated with bDMARDs (66.5%). In total 44 patients (22%) were not able to perform one or more ASPI tests. The mean time for bending was 18.6±9.5 sec (n=179/90%), for putting on socks 12.8±6.4 sec (n=156/78%), and for getting up from floor 6.5±5.0 sec (n=187/94%). A significant correlation was found for all three ASPI-tests with BASFI (0.5-0,7), ASAS HI (0.4-0.6) and spinal mobility as assessed by BASMI (0.4-0.7). Self-reported physical activity (IPAQ) correlated weakly with ASPI (all 0.2) and structural damage correlated only with the task putting on socks (r=0.3), whereas the other tests did not correlate. Logistic regression showed influence of obesity, spinal mobility and global functioning on actual performance but not of disease activity and self-reported physical function, (Figure 1).

Conclusion: This study confirms a good correlation of the ASPI with standard questionnaires but it showed a substantial floor effect strongly suggesting that additional information on actual performance is needed. Thus, to obtain a complete picture of function and impairments of patients with axSpA the actual performance needs also to be assessed. Moreover, obesity should be addressed as a potential modifying factor contributing to limitation in actual performance.

	Univariable		Multivariable	
	OR (CI)	p	OR (CI)	p
Age	1.08 (1.04-1.11)	<0.001		
Male sex	1.46 (0.68-3.11)	0.332		
BMI	1.17 (1.01-1.25)	<0.001	1.20 (1.09-1.32)	<0.001
ASDAS	2.35 (1.67-3.41)	<0.001		
BASFI, 0-10	1.95 (1.58-2.40)	<0.001		
ASAS HI 0-17	1.41 (1.26-1.60)	<0.001	1.40 (1.06-1.86)	0.019
BASMI, 0-10	2.44 (1.87-3.19)	<0.001	2.78 (1.77-4.36)	<0.001
PHQ-9 0-27	1.15 (1.08-1.21)	<0.001		

Abstract THU0367 – Figure 1. Association between clinical characteristics of patients with SpA and physical performance

REFERENCE:

[1] Van Weely SFE, Dekker J, Steultjens MPM, van Denderen JC, Nurmohamed MT, Dijkmans BAC, van der Horst-Bruinsma IE. Objective evaluation of physical functioning after tumor necrosis factor inhibitory therapy in patients with ankylosing spondylitis: a selection of 3 feasible performance-based tests. J Rheumatol. 2015 Apr;42(4):623-9.

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THU0368 THE IMPACT OF PROFESSIONAL ACTIVITY IN ANKYLOSING SPONDYLITIS

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Background: The mechanical stress due to strenuous professional activity cannot be easily quantified, yet it may lead to a wide range of musculoskeletal complaints. In ankylosing spondylitis (AS) patients mechanic stress may lead to the occurrence and the aggravation of enthesitis (1) and a profession involving an intense physical strain is correlated with the radiologic progression (2). While studies regarding the professional activities in ankylosing spondylitis patients are focused on the disease's impact on the work capacity, the type of labor may also influence the disease progression (3).
Objectives: To assess the relationship between the professional activity in AS patients, disease activity and radiological changes.
Methods: We enrolled 193 patients with AS admitted in the Rheumatology Department of the "Sf. Apostol Andrei" Emergency Clinical County Hospital. Patient evaluation was performed by a rheumatologist. All the data obtained from the medical history, clinical examination, laboratory tests and imaging studies was recorded at the same date. Data regarding the professional history, type of labor involved was also recorded. The physical strain due to professional activity was done using the methodology established by the National Institute for Medical Expertise and Recovery of Work Capacity which takes into account the amount of energy used in order to perform certain tasks.
Results: We included 193 patients, mostly men, 171 men (81.9%), with a mean age of 47.94±12,04 years and a mean disease duration of 20.07 ±11.18 years. At the moment of the evaluation 49.7% were still employed and 50.3% were retired due to work disability. Most patients had a professional qualification (89.2%), and manual labor was identified in 132 (6.,4%) of the patients. In the study cohort the professional physical strain was mostly low (39.4%) and medium (50.8%). Manual laborers (77.3%) had an active disease, with a mean BASDAI of 5.67(p=0.006) and a mean ASDAS-PCR of 3.2±1.23, the high and very high disease activity (ASDAS-PCR>2.1) being registered in 86.1% of them (p<0.001). Manual workers had an important functional deficit (BASFI=6.32±2.41) (p=0,001). Regarding radiological features, manual laborers had stage IV sacroiliitis in 68.9%of the cases, 82.6% had syndesmophytes, which were generalised in 59.8% of the cases (p=0.005).
A high professional physical strain correlates with active disease (BASDAI=6.22), with the presence of bridging syndesmophytes (81.8%, p=0.009), and generalized syndesmophytes (68.8%, p=0.007).
Conclusion: Manual labor, with strenuous physical activities correlates with high disease activity, severe functional impairment and radiological changes in AS patients.

REFERENCES:

[1] .
Jacques, Peggy, et al. "Proof of concept: enthesitis and new bone formation in spondyloarthritis are driven by mechanical strain and stromal cells." Annals of the rheumatic diseases73.2 (2014): 437-445.
[2] Ramiro, Sofia, et al. "Lifestyle factors may modify the effect of disease activity on radiographic progression in patients with ankylosing spondylitis: a longitudinal analysis." *RMD open* 1.1 (2015): e000153.
[3] 3. Sirjita N. Elemente de expertiză medicală şi recuperarea capacităţii de muncă. Editura TipArg, 2004 pp 112-118

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THU0369 INCREASED PREVALENCE OF CARDIAC DISORDERS IN DUTCH ANKYLOSING SPONDYLITIS PATIENTS: THE CARDAS STUDY

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Background: The overall mortality rate in ankylosing spondylitis (AS) patients is increased by 60–90% compared with the general population. This higher mortality rate is predominately caused by cardiovascular disease (CVD) comprising both by increased prevalence of cardiac diseases such as valvular heart disease, conduction disturbances and cardiomyopathies as well as atherosclerotic diseases such as myocardial infarctions. However, there is some diversity in the literature and there is a lack of contemporary studies. Therefore, we investigated current prevalences of cardiac disorders in a well characterized cohorts of Dutch patients with AS.
Objectives: The CARDAS study aims to describe the prevalence of CVD in AS patients in a Dutch cohort.
Methods: We performed a cross-sectional study in consecutive AS patients between 50-75 years. Subjects were recruited from a large rheumatology outpatient clinic (Reade) in Amsterdam, the Netherlands. Patients underwent echocardiography with 2D, spectral and Color Doppler imaging. Diastolic dysfunction was evaluated by an experienced cardiologist based on the 2008 ASE guideline. Furthermore, an ECG, blood sample, surveys and physical examination were performed. Disease activity and function were measured with the BASFI, BASDAI and the ASDAS-CRP.
Results: 191 Consecutive AS patients were included with a median age of 58 years (54-65) of which mostly men (136/191, 71%) (Table 1). The mean disease duration was 34.9 years (± 11.9) The disease activity measures, BASDAI, ASDAS-CRP and BASFI, indicated moderate disease activity and were, respectively 3.1 (±2,3), 2.1 (±1.0) and 3.5 (1.6-5.7). The use of bDMARD's was present in 42% of the AS patients. As cardiac manifestations are age related, AS patients were divided in 3 age categories, respectively, 50-59 years, 60-69 years and 70-75 years. Hypertension was diagnosed in respectively 45.3%, 64.1% and 85.7%. History of CVD described as angina pectoris, myocardial infarction, stroke and/or peripheral ischemia were present in respectively 7.5%, 9.4% and 19%. Diastolic dysfunction was present in respectively 40.4%, 61.9% and 89.5% of the AS patients. The diastolic dysfunction present in this population was mainly mild with 60.2% of patients presenting with grade 1 and 39.8% with grade 2 diastolic dysfunction. Moderate to severe aortic regurgitation was present in, respectively 10.4%, 12.5% and 33.4% and moderate to severe mitral valve regurgitation in 33%, 31.3% and 42.9% of the AS patients. These prevalences are substantially increased in comparison to the general Dutch population.
Conclusion: We demonstrated increased prevalences of diastolic dysfunction, aortic valve regurgitation, mitral valve regurgitation and hypertension in Dutch AS patients compared to age matched general population. Although our results suggest mandatory echocardiography screening, this first needs to be established in prospective follow-up studies.

Abstract THU0369 – Table 1. Patient characteristics

	All	50-59 years	60-69 years	70-75 years
N	191			
Men	131 (71%)			
Age (years)	58 (54-65)			
Disease activity				
BASDAI	3.1 (±2,3)			
ASDAS-CRP	2.1 (±1.0)			
BASFI	3.5 (1.6-5.7)			
CVD				
History of CVD*		7.5%	9.4%	19%
Hypertension		45.3%	64.1%	85.7%
Aortic valve regurgitation**		10.4%	12.5%	33.4%
Mitral valve regurgitation**		33%	31.1%	42.9%
Diastolic dysfunction		40.4%	61.9%	89.5%

* Described as angina pectoris, myocardial infarction, stroke and/or peripheral ischemia
** moderate – severe regurgitation.

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THU0370 PERFORMANCE OF THE ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE (ASDAS) IN PATIENTS WITH PERIPHERAL AND AXIAL SPONDYLOARTHRITIS IN CLINICAL PRACTICE

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Background: The Ankylosing Spondylitis Disease Activity Score (ASDAS) is a widely used composite measure of disease activity in axial spondyloarthritis (axSpA). Such a tool is lacking for peripheral SpA (pSpA). However, the ASDAS also assesses peripheral joint symptoms. Previously, trial data have shown that the ASDAS has high sensitivity to change and high discriminatory ability between disease states in pSpA (1). We hypothesized that the ASDAS can be used to measure disease activity in all patients with pSpA in clinical practice.

Objectives: To investigate the construct validity of the ASDAS in pSpA in comparison with axSpA in clinical practice.

Methods: Data from a registry for SpA in the Netherlands (SpA-Net) were used. Construct validity of the ASDAS was assessed by testing hypotheses about Spearman correlations with other outcomes measures including individual components of disease activity, physical functioning and health-related quality of life (HRQoL). Construct validity was also assessed by stratifying patients according to ASDAS cut-offs to compare means of different health outcomes across ASDAS states by one-way ANOVA analyses. All analyses were repeated after stratification for the presence/absence of psoriasis in pSpA. Results were compared to the performance of the ASDAS in axSpA.

Results: In total, 194 patients with pSpA and 222 patients with axSpA were included. Poor to high correlation was found between ASDAS and measures of disease activity (r_s0.20 to 0.78), a moderate correlation was found between ASDAS and measures of physical functioning (r_s0.61 to 0.64) and a poor to moderate correlation was found between ASDAS and measures of HRQoL in pSpA (r_s-0.27 to -0.66) (table 1). With increasing ASDAS states, significantly worse scores were found on (other) measures of disease activity, physical functioning and HRQoL in pSpA (table 2). Stratification for the presence/absence of psoriasis showed similar results (data not shown). All results for pSpA were comparable to axSpA (see for example Table 1).

Abstract THU0370 – Table 1. Construct validity of ASDAS with health outcomes in pSpA and axSpA

	pSpA n=194	axSpA n=222
Disease activity		
BASDAI	0.78	0.81
Patient global	0.77	0.75
CRP	0.41	0.51
VAS pain	0.73	0.67
Physician global	0.55	0.46
TJC68	0.38	0.28
SJC66	0.20	0.24
Physical functioning		
BASFI	0.61	0.59
HAQ-S	0.62	0.58
ASAS-HI	0.64	0.46
Quality of life		
EQ5D	-0.56	-0.40
SF36 MCS	-0.27	-0.26
SF36 PCS	-0.66	-0.54

All correlations were statistically significant (p<0.05)

Criteria for correlations: $r_s < 0.29$ poor, $0.30 \leq r_s < 0.49$ low, $0.50 \leq r_s < 0.69$ moderate, $0.70 \leq r_s < 0.89$ high and $r_s \geq 0.90$ very high

Abstract THU0370 – Table 2. Health outcomes according to ASDAS states in pSpA

ASDAS cut-off Disease activity	< 1.3 n = 40	1.3 to < 2.1 n = 59	2.1 to ≤ 3.5 n = 81	> 3.5 n = 14	p-value
BASDAI	1.6 (1.0)	2.9 (1.4)	5.1 (1.8)	7.1 (1.3)	<0.01
Patient global	1.2 (1.1)	2.7 (1.7)	5.0 (2.1)	7.4 (1.9)	<0.01
CRP	1.7 (1.3)	3.4 (3.6)	5.4 (7.3)	9.0 (7.2)	<0.01
VAS pain	1.1 (1.6)	2.6 (2.3)	5.3 (2.2)	6.5 (1.3)	<0.01
Physician global	0.9 (0.9)	1.2 (0.1)	2.4 (1.8)	4.4 (1.6)	<0.01
TJC68	0.2 (0.4)	1.2 (3.8)	2.1 (4.0)	2.6 (2.5)	<0.05
SJC66	0.1 (0.4)	0.4 (1.0)	0.5 (1.2)	0.6 (0.9)	0.29
Physical functioning					
BASFI	1.1 (1.4)	2.1 (2.0)	4.0 (2.2)	5.4 (2.4)	<0.01
HAQ-S	0.3 (0.3)	0.7 (0.6)	1.0 (0.6)	1.5 (0.8)	<0.01
ASAS-HI	2.8 (2.7)	4.6 (3.1)	7.0 (3.2)	9.4 (1.8)	<0.01
HRQoL					
EQ5D	0.9 (0.1)	0.8 (0.1)	0.7 (0.2)	0.6 (0.3)	<0.01
SF36 MCS	52.8 (8.1)	52.7 (9.7)	47.1 (10.7)	41.5 (14.1)	<0.01
SF36 PCS	48.9 (8.3)	40.6 (10.7)	35.1 (7.6)	29.5 (5.6)	<0.01

Values are expressed as mean (SD)

Conclusion: The ASDAS demonstrated similar construct validity in all patients with pSpA and axSpA in clinical practice. Therefore, the ASDAS can also be used to measure disease activity in pSpA in daily practice.

REFERENCE:

[1] Turina MC, et al. A psychometric analysis of outcome measures in peripheral spondyloarthritis. ARD 2016;75:1302-7.

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THU0371 PREVALENCE OF WORK DISABILITY AND PREDICTORS OF WORK PRODUCTIVITY AMONG EMPLOYABLE PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS IN A CANADIAN REAL WORLD OBSERVATIONAL COHORT: INTERIM RESULTS FROM THE COMPLETE STUDIES

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Background: Work disability is an important functional outcome among patients with chronic inflammatory diseases such as ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Maintenance of patients in the work force and return to employment are important treatment outcomes with implications for both patients and the healthcare system.

Objectives: The aim of this analysis is to describe the prevalence of unemployment due to disability at baseline and to identify factors associated with work productivity loss in patients with AS and PsA followed in Canadian routine clinical care.

Methods: Patients eligible for the COMPLETE studies were anti-TNFα naïve adults, with active AS or PsA per the judgment of the treating physician, who required change in their treatment regimen. This interim analysis included patients that were treated with adalimumab or non-biologic DMARDs and, were either employed or on disability at baseline. Work productivity was measured by the Work Limitations Questionnaire (WLQ). Depression was defined as a Beck's Depression Inventory (BDI) score $\geq$20 and/or treatment with an antidepressant/anxiolytic at baseline. Multivariate generalized linear models were used to identify determinants of% WLQ productivity loss (WLQ-PL) scores at 6 and 12 months of treatment, along with the respective changes from baseline. Least Square Means (LSM) for the WLQ-PL improvement were reported from the multivariate model.

Results: A total of 486 AS patients and 292 PsA patients were included in the analysis. The mean (SD) disease duration was 5.2 (8.6) and 12.8 (12.1) years, mean (SD) age was 41.7 (11.6) and 48.3 (10.5) years, and male predominance was 58.4% and 54.5%, in the AS and PsA groups, respectively. At baseline, 13.4% of AS patients and 17.8% of PsA patients were unemployed due to disability.

Among employed patients, the mean (SD) WLQ-PL score at baseline was 9.2% (5.7) in the AS patient group and 8.3% (6.0) in the PsA patient group. After 6 months of treatment significant improvement was observed in both patient populations (Δ_{AS} [95% CI]: -2.7% [-3.4,-2.0]; Δ_{PsA} [95% CI]: -2.1% [-2.9,-1.3]) which was maintained until 12 months.

Among AS patients, after adjusting for baseline parameters including age, sex, tobacco use, HLA B27 status, treatment group, depression, and baseline scores for BASFI and WLQ-PL using multivariate analysis, presence of depression (LSM: -0.2% vs. -2.5%; p=0.016) and female sex (LSM: -0.7% vs. -2.0%; p=0.047) were identified as significant negative

predictors of improvement in work productivity at 6 months, while increased baseline work productivity was a positive predictor of improvement. In the PsA group, other than higher baseline work productivity (positive predictor of improvement), no significant predictors were identified at 6 months. However, a negative trend was observed for the presence of depression (LSM: -0.4% vs. -2.5%; p=0.068).

Conclusion: We observed a significant proportion of AS and PsA patients unemployed in this real-world Canadian cohort. Treatment with adalimumab or non-biologic DMARDs was associated with significant improvement in work productivity irrespective of potential risk factors. Presence of depression was identified as an independent negative predictor of improvement in work performance/productivity.

REFERENCES:

N/A.

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THU0372 NEUROPATHICPAIN IN THE PATIENTS WITH SPONDYLOARTHRITIS: RELATINSHIP WITH FATIGUE, SLEEP QUALITY AND QUALITY OF LIFE

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Background: Neuropathic pain is defined as the pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory system. Low back pain has nociceptive, neuropathic or mixed components. Inflammatory back pain is one of the key clinical criteria for the classification of spondyloarthritis (SpA). There are no accurate data for the overall prevalence of neuropathic pain in the inflammatory disorders.

Objectives: In the present study we aimed to determine whether there is a neuropathic component in SpA and also to determine the relationship with disease activity, clinical findings, fatigue, sleep quality and quality of life.

Methods: Eighty SpA patients fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for SpA (M/F=42/38) (37.3±11 years), 53 patients with chronic low back pain (CLBP) (M/F=22/31) (45.5±13.6 years) and 50 healthy controls (M/F =28/22) (38.1 ±12.7years) were enrolled in the study. Pain was assessed with visual analogue scale (VAS rest and activity), disease activity with Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), functional capacity with Bath Ankylosing Spondylitis Functional Index (BASFI), fatigue with multidimensional assessment of fatigue (MAF), sleep quality with Pittsburgh Sleep Quality Index (PSQI) and quality of life was assessed with Short Form 36 (SF-36). Neuropathic pain was determined by using painDETECT questionnaire, a simple and reliable screening questionnaire. Scores ≤12 indicate that a neuropathic pain component is unlikely, and scores ≥19 indicate that neuropathic component is very likely to be present. Scores between 12 and 19 suggest that the result is unclear.

Results: The PainDETECT score of the SpA patients, CLBP patients and healthy controls were 12.06±5.9, 13.8±7.5, 2.6±4.2, respectively. While there was no significant difference between the patients with SpA and CLBP ($p>0.05$), the SpA patients had significantly higher scores than the healthy controls ($p<0.0001$). 14 (17.5%) of the SpA patients, 14 (26.4%) of the CLBP patients and none of the healthy controls had PainDETECT score ≥19 ($p<0.05$). The MAF score and all subscales of SF 36 all components were significantly different in the three groups ($p<0.05$). There were also statistically significant differences between three groups for all subscales of PSQI except duration of sleep and need medications to sleep ($p<0.05$). PainDETECT score was positively correlated with VAS rest, BASDAI, and BASFI in the patients with SpA. While PainDETECT score was positively correlated with MAF and total PSQI, sleep quality, sleep disturbance, daytime dysfunction scores, it was negatively correlated with SF-36 subscales of social functioning, mental health, general health, bodily pain ($p<0.05$).

Conclusion: We found that SpA and CLBP patients had higher painDETECT scores than the healthy controls. 17% of the SpA patients had neuropathic pain. We also found that neuropathic pain was correlated with fatigue, sleep quality and quality of life. Since pain in SpA consists of inflammatory and neuropathic components, a better understanding of neuropathic pain mechanisms in SpA will provide a more targeted approach to the assessment and treatment of patients.

REFERENCES:

[1] Bidad K, Gracey E, Hemington KS, et al. Pain in ankylosing spondylitis: a neuro-immune collaboration. Nat Rev Rheumatol. 2017;13(7):410-420

[2] Bennett MI, Attal N, Backonja MM, et al. Using screening tools to identify neuropathic pain. Pain 2007;127(3):199-203

[3] Wu Q, Inman RD, Davis KD. Neuropathic pain in ankylosing spondylitis: a psychophysics and brain imaging study. Arthritis Rheum. 2013;65(6):1494-503

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THU0373 ACTIVE SACROILIITIS ON MAGNETIC RESONANCE IMAGING IN PATIENTS WITH ANTERIOR UVEITIS

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Background: Anterior uveitis (AU) is a common extraarticular manifestation in spondyloarthritis (SpA). The disease can precede the typical axial and peripheral features. Additionally, some studies had described positive bone marrow edema in patients with AU lacking chronic back pain.

Objectives: The aim of this study was to examine patients with AU, to determine whether the patients already fulfil criteria for axial and/or peripheral SpA and compare the findings to healthy controls (HC).

Methods: We recruited 65 patients without prior rheumatologic diagnosis who developed at least one episode of AU and 33 age and sex matched HC. The clinical data were collected and rheumatology examinations were performed by trained rheumatologists. Magnetic resonance imaging (MRI) of sacroiliac joints (SIJ) was read by trained rheumatologist who was blinded to the patient´s data. Patients were divided into SpA subsets (axial: imaging and clinical arm and peripheral SpA) fulfilling The Assessment of SpondyloArthritis international Society (ASAS) classification criteria and non-SpA subset. The ASAS modified Berlin algorithm for diagnosis of axial SpA (axSpA) was also applied.

Results: Altogether, 72% (n=47) patients referred back pain including 22.0% (n=14) patients referring inflammatory back pain, 28% (n=18) did not refer back pain. Similar results were found in HC subset. Bone marrow edema (BME) was found in 51% (n=33) of all patients with AU, however 35% (n=23) had highly suggestive BME (hsBME) corresponding to typical findings in sacroiliitis compared to HC where 30% (n=10) had BME, however none had hsBME ($p=0.08$, $p< 0.0001$, respectively). Furthermore, patients with AU had higher serum CRP levels compared to HC ($p=0.001$), no other significant differences were observed. The diagnosis of SpA was confirmed in 46% (n=30) of all patients with AU, 34% (n=22) patients fulfilled the imaging arm and 12% (n=7) fulfilled the clinical arm of ASAS classification criteria for axSpA, 3% (n=2) patients fulfilled ASAS classification criteria for peripheral SpA. Two patients lacking back pain developed hsBME on SIJ. The diagnosis of axSpA according to the ASAS modified Berlin algorithm was confirmed in 42% (n=27) patients. Analysis of clinical characteristics showed significant difference between BASDAI in SpA vs. non-SpA (1.6±1.5 vs 0.8±1.0, $p=0.007$, respectively), and remained significant in those fulfilling imaging arm of axial SpA ($p=0.04$). The levels of CRP were significantly higher in SpA compared to non-SpA subsets (8.6±9.7 vs 2.6±2.7 mg/L, $p=0.003$). Presence of back pain and inflammatory back pain were more often in SpA compared to non-SpA subsets (97% and 43% vs. 51% and 3%, $p=0.001$ and $p=0.001$ respectively). Patients with hsBME had significantly higher serum CRP levels compared to patients lacking hsBME (9.0±10.4 vs 3.3 ±4.2 mg/L, $p=0.005$), no other significant differences were observed.

Conclusion: More than one third of patients with AU fulfilled the criteria for axial or peripheral SpA. Furthermore, the prevalence of back pain, increased BASDAI and serum CRP levels was significantly higher in AU patients with SpA compared to non-SpA subjects and HC. Inflammatory back pain was significantly more often in patients with AU classified as axSpA. Patients with hsBME had significantly higher serum CRP levels compared to the rest of the patients.

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THU0374 GENDER DIFFERENCE IN ASAS HEALTH INDEX IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: The Assessment of Spondyloarthritis international Society Health Index (ASAS HI) has been develop and validated to assess health and function in patients with spondyloarthritis. However, whether ASAS HI differs between men and women is unknown. The aim of this study was to compare ASAS HI between men ans women in patients with ankylosing spondylitis (AS).

Objectives: The aim of this study was to compare ASAS HI between men ans women in patients with ankylosing spondylitis (AS).

Methods: Since November 2016, we measured and recorded data of demography, comorbidity, family history, medication use, the Ankylosing Spondylitis Disease Activity Score (ASDAS), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) and the ASAS HI for AS patients in clinical practice using an electronic patient reported data system linked to an electronic medical record system in Taichung Veterans General hospital (TCVGH). We retrieved the last recorded data of AS patients in TCVGH during 2017/11–2018/10. We assessed the association between gender and the ASAS HI using a multivariable linear regression model. Variables from the univariable linear regression analysis with $p < 0.2$ were included in then multivariable analysis. We used a forward selection method to build the models.

Results: A total of 307 AS patients [62 (20.2%) females, mean age 46.4 years (S.D. 13.3), mean symptom duration 20.6 years (S.D. 12.1)] were included. Female patients had an older age at onset (29.2 ± 12.6 vs 24.9 ± 9.6 years, $p = 0.015$), a shorter symptom duration (15.7 ± 11.6 vs 21.8 ± 12.0 years, $p < 0.001$), a lower proportion of smoking (6.5% vs 48.2%, $p < 0.001$), higher ASAS HI (5.9 ± 3.8 vs 4.3 ± 3.4, $p = 0.001$), higher ASDAS-ESR (1.9 ± 0.8 vs 1.5 ± 0.8, $p < 0.001$) and lower mSASSS (6.0 ± 11.4 vs 21.8 ± 23.1, $p < 0.001$) than male patients. There were no significant differences in BASFI (1.1 ± 1.6 vs. 1.2 ± 1.7, $p = 0.765$), ASDAS-CRP (1.5 ± 0.9 vs. 1.5 ± 0.9, $p = 0.972$) and BASDAI (2.4 ± 1.8 vs. 2.0 ± 1.4, $p = 0.115$) between females and males. In multivariable analysis, male gender was significantly associated with a better ASAS HI (B = -1.73, 95% CI: -2.55, -0.91, $p < 0.001$). Other significant predictors of ASAS HI included BASDAI (B = 1.29, 95% CI: 1.07, 1.50, $p < 0.001$), disease duration (B = 0.04, 95% CI: 0.01, 0.06, $p = 0.015$), mSASSS (B = 0.02, 95% CI: 0.01, 0.04, $p = 0.003$) and hepatitis B (B = 0.99, 95% CI: 0.03, 1.96, $p = 0.044$).

Conclusion: This single center, cross-sectional study revealed that male gender was significantly associated with lower ASAS HI in AS patients.

REFERENCE:

[1] Kiltz U, van der Heijde D, Boonen A, Akkoc N, Bautista-Molano W, et al. 2018. Measurement properties of the ASAS Health Index: results of a global study in patients with axial and peripheral spondyloarthritis. Annals of the rheumatic diseases 77:1311-7.

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THU0375 CLINICAL FEATURES OF AXIAL SPONDYLOARTHRITIS PATIENTS DIAGNOSED IN PERIPHERAL VERSUS AN ACADEMIC HOSPITAL

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Background: Diagnosis of axial spondyloarthritis (axSpA) often relies on a positive magnetic resonance image of the sacroiliac joints (MRI-SIJ). However, pitfalls in interpretation of MRI-SIJ were recently acknowledged (1). Thus reader's expertise might be a source of heterogeneity in patient populations diagnosed with non-radiographic axSpA.

Objectives: We compared clinical characteristics of axSpA patients diagnosed in peripheral hospitals (MRI evaluation by local experts) versus an academic hospital (MRI central reading by trained radiologists and rheumatologists).

Methods: Patients originate from the Be-Giant cohort, a Belgian nationwide observational registry of axSpA patients diagnosed by expert opinion. Included patients fulfill the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA and are anti-TNF-α naïve prior to inclusion. Patient enrollment started in 2010 and 2012 at the outpatient clinic of 1 academic and 7 peripheral hospitals respectively. Patients were free to visit a rheumatologist of their choice without necessity for referral by a general practitioner.

Results: By January 2019, 291 axSpA patients were included. Table 1 presents demographic and clinical characteristics according to the diagnostic echelon. The patient fraction fulfilling the imaging arm of the ASAS classification criteria was similar in both settings (75,4% vs. 88,7%, $p = 0,21$). However, because of a higher HLA B27 positivity rate in patients diagnosed in an academic versus peripheral hospitals (73,5% vs. 57,4%, $p = 0,01$), a significantly higher fraction of patients fulfilled both the clinical and imaging arm in the former diagnostic setting (63,0% vs. 37,7%, $p = 0,01$).

Conclusion: Patients diagnosed with axSpA in peripheral versus an academic hospital generally show similar demographic and clinical characteristics. In an academic center, patients diagnosed with axSpA are more likely to be HLA B27 positive and to fulfill both ASAS classification arms, indicating that rheumatologists in peripheral hospitals seem to assign more value to MRI findings compared to HLA B27 status in the diagnostic process.

REFERENCES:

[1] Varkas G, de Hooge M, Renson T, De Mits S, Carron P, Jacques P, et al. Effect of mechanical stress on magnetic resonance imaging of the sacroiliac joints: assessment of military recruits by magnetic resonance imaging study. Rheumatology (Oxford). 2018;57(3):508-13.

Abstract THU0375 – Table 1

	Peripheral center (n = 61)	Academic center (n = 230)	p-value
Age at diagnosis (years)	33,6 (9,23)	31,3 (9,01)	0,08
Male gender	20 (32,8)	118 (51,3)	**0,01**
HLA B27 positivity	35 (57,4)	169 (73,5)	**0,01**
Symptom duration at diagnosis (years)	4,8 (5,45)	4,2 (5,60)	0,51
ASAS classification criteria imaging arm	46 (75,4)	204 (88,7)	0,21
ASAS classification criteria clinical arm	35 (57,4)	169 (73,5)	**0,01**
ASAS classification criteria both arms	23 (37,7)	145 (63,0)	**0,01**
Arthritis	11 (18,0)	39 (17,0)	0,99
Dactylitis	1 (1,6)	7 (3,1)	0,88
Enthesitis	11 (18,0)	28 (12,2)	0,33
Psoriasis	7 (11,5)	20 (8,7)	0,68
Inflammatory bowel disease	3 (4,9)	14 (6,1)	0,87
Acute anterior uveitis	6 (9,8)	32 (13,9)	0,53
BMI (kg/m²)	23,8 (3,86)	24,4 (4,02)	0,26
BASMI	1,1 (1,13)	1,3 (1,17)	0,33
MASES + fascia plantaris (/15)	1,4 (2,50)	0,9 (1,54)	0,69
BASDAI (/100)	46 (19,3)	43 (20,2)	0,31
BASFI (/100)	30 (22,5)	28 (21,8)	0,77
ASDAS – CRP	2,43 (0,89)	2,47 (0,93)	0,80

Continuous variables: mean (SD); other: counts(%).

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THU0376 THE VALUE OF SACROILIAC JOINT RADIOGRAPHS IN THE EARLY SPONDYLOARTHRITIS ESPERANZA COHORT

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Background: X-Ray sacroiliitis is the cornerstone in the diagnosis of the ankylosing spondylitis (AS). It is clear that the presence of sacroiliitis is a specific lesion in long standing AS, but little evidence exists on the reliability of this image technique in early axial spondyloarthritis (axSpA), which associates with reduced structural damage. This is relevant because some rheumatologists and pharmacological authorities feel more confident with the diagnosis of AS rather than with non radiographic axial spondyloarthritis (nr-axSpA) forms. On the other hand, according to various research studies, clinicians are subject to potential bias when interpreting radiographs, influenced by their pretest clinical judgment.

Objectives: The aim of this study is to determine the value of X-Ray sacroiliitis in the early diagnosis of axSpA.

Methods: This study included 290 radiographs of the SI joints from patients of the Esperanza early spondyloarthritis cohort. Nine readers, blinded for the diagnosis, participated in the reliability exercise, all of them experienced rheumatologists and members of the Spanish spondiloarthritis working group (GRESSER). Patients with axSpa were classified as having AS if the radiographic criteria of the modified NY criteria (presence of radiographic changes in the SIJ of at least grade II bilaterally or at least grade III unilaterally) were fulfilled. The gold standard was the categorical opinion of at least five of the expert readers. For the statistical analysis, the Chi-square and Kappa tests were performed.

Results: The radiographic diagnosis, sensitivity, specificity, likelihood ratio, grade of agreement and mean K values compared to gold standard are showed in table 1. The concordance Kappa test was highly variable among the readers, ranging from fair to excellent. The agreement with the gold standard varied from 68 to 94% and the sensitivity and specifity, from 50-100% and 64-96%, respectively. Additionally, the number of AS was 61, with an inter-reader variability rate of 31 to 138. Larger discrepancies were observed when assessing sacroiliitis grade 2.

Abstract THU0376 –Table 1.

	Gold standard	Reader 1	Reader 2	Reader 3	Reader 4	Reader 5	Reader 6	Reader 7	Reader 8	Reader 9
Kappa		.716	.345	.468	.606	.599	.459	.612	.513	.809
Agreement		90.97	68.06	85.52	84.48	85.12	73.79	87.59	78.47	94.14
SIJ mNY+	61	54	138	31	92	80	137	55	115	48
SIJ mNY TP	61	44	53	25	54	49	61	40	57	46
SIJ mNY FP	229	10	85	6	38	31	76	15	58	2
Sensitivity		73.33%	88.33	59.02	88.52	80.33	100	65.57	93.44	75.41
Specificity		95.61%	62.72	97.38	83.41	86.40	66.81	93.45	74.45	91.13
LR +		16.70	2.369	22.53	5.336	5.907	3.013	10.01	3.657	8.502

SIJ = (SI) joint; mNY+ = number of patients that meet diagnosis of ankilosing spondylitis; TP = true positives; FP = false positives; LR+ = Likelihood ratio +

Conclusion: The diagnosis of AS in early axSpa is characterized by a marked variability. At least in doubtful cases, a second central evaluation performed by highly qualified experts should be advisable.

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THU0377 THE CARDIOVASCULAR ASSOCIATIONS WITH ENTHESITIS AND DACTYLITIS IN PATIENTS WITH SPONDYLOARTHRITIS: RESULTS FROM THE ASAS-COMOSPA STUDY

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Background: Enthesitis and dactylitis are considered characteristic inflammatory musculoskeletal manifestations of spondyloarthritis (SpA). These manifestations are usually assessed in the context of their assumed underlying specific condition rather than as distinct entities. Data from the ASAS-COMOSPA cohort have recently been shown that duration of SpA disease is associated with higher odds of hypertension particularly in axial SpA (1).

Objectives: To evaluate the possible associations of dactylitis and enthesitis phenotypes with cardiovascular comorbidities in a heterogeneous cohort of patients with SpA.

Methods: ASAS-COMOSPA is a global cross-sectional study assessing comorbidities in 3984 patients with SpA. History of enthesitis or dactylitis was based on self-report with confirmation using the medical records. Associations between dactylitis or enthesitis with hypertension, dyslipidaemia, diabetes, ischemic heart diseases (IHD) and stroke were analysed by separate logistic regression models unadjusted, adjusted for age and sex (models 1), and adjusted for age, sex and BMI (model 2).

Results: The data of 3905 participants were available for analysis. There were 1480 (37.9%) with history of enthesitis and 611 (15.6%) with dactylitis, while 1814 (46.5%) had neither.

Presence of dactylitis was associated with hypertension in the univariable analysis [OR=1.68; 95%CI: 1.39– 2.03]. The association remained significant when adjusted for age and sex, but not following further adjustment for BMI (Table). Similarly, enthesitis was associated with hypertension in the univariable analysis [OR=1.36; 95%CI: 1.17-1.59], which remained after adjusted for age and sex, as well as after further adjustment for BMI (Table). Similar associations were seen for dyslipidaemia and dactylitis [OR=1.60; 95%CI: 1.29– 1.98] or enthesitis [OR=1.50; 95%CI: 1.26-1.77], with the association with dactylitis lost after further adjustment for BMI while the association with enthesitis remained significant (Table).

While there were significant associations between dactylitis and diabetes [OR: 1.50 (95% CI: 1.07–2.11)], and between enthesitis and diabetes [OR=1.35; 95%CI: 1.02-1.78] in unadjusted models, no associations were

seen after adjustments. There were no significant associations between dactylitis or enthesitis and either IHD or stroke (Table).

Abstract THU0377 – Table 1

		Model 1 adjusted for age and sex		Model 2 adjusted for age, sex and BMI	
	Comorbidity	***p***	**OR (95%CI)**	***p***	**OR (95%CI)**
Dactylitis	Hypertension	**0.009**	**1.34 (1.08- 1.67)**	0.067	1.24 (0.99- 1.55)
	Dyslipidaemia	**0.015**	**1.33 (1.06- 1.66)**	0.064	1.25 (0.99- 1.57)
	Diabetes	0.234	1.24 (0.87- 1.75)	0.494	1.14 (0.79- 1.63)
	IHD	0.211	1.37 (0.84- 2.25)	0.176	1.41 (0.86- 2.33)
	Stroke	0.458	0.74 (0.33- 1.66)	0.462	0.74 (0.33- 1.66)
Enthesitis	Hypertension	**<0.001**	**1.38 (1.16- 1.65)**	**0.003**	**1.32 (1.10- 1.58)**
	Dyslipidaemia	**<0.001**	**1.48 (1.23- 1.78)**	**<0.001**	**1.43 (1.18- 1.72)**
	Diabetes	0.052	1.33 (1.06- 1.08)	0.121	1.27 (0.40- 1.71)
	IHD	0.565	1.13(0.74- 1.73)	0.492	1.16 (0.76- 1.79)
	Stroke	0.361	0.75 (0.41- 1.38)	0.359	0.75 (0.41- 1.38)

Conclusion: In patients with SpA, both dactylitis and enthesitis are associated with higher risk of hypertension and dyslipidaemia. The loss of associations with dactylitis with adjustment for BMI could suggest a potential shared underlying metabolic mechanism.

REFERENCE:

[1] Derakhshan MH, et al. J Rheumatol 2019;180538

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THU0378 COEXISTENCE OF ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS (ANALYSIS OF 73 CASES)

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Background: The coexistence of rheumatoid arthritis (RA) and ankylosing spondylitis (AS) in the same patient is a rarely described phenomenon. Both ankylosing spondylitis and rheumatoid arthritis are common entities in the field of rheumatic diseases with a high impact on the patient's quality of life and morbidity and mortality. The possibility of the coexistence of both diseases in the same person is not known exactly, however, with the data published to date, it is estimated that it ranges from 1 in 500,000 to 1 in 2,000, 000.
Objectives: The epidemiological, clinical and study characteristics (radiographic/laboratory) of 73 patients with concomitant diagnosis of RA and AS are described. It includes 71 patients detected in the literature (32 articles) and 2 own cases
Methods: The platforms used for the search using the terms AR and AS (coexistence/concomitance/concurrence) were Pubmed, Medline, Embase, Scopus, hospital virtual libraries, non-indexed journals and a secondary manual search. All the articles were taken into account, regardless of the language in which they were written, making the relevant translations (1 article in French, 1 article in Portuguese, 1 article in Spanish and the rest in English), and only those well documented cases were included.
Results: Of the total of registered cases, 55 patients were men (75.3%), with a mean age of 54 years, and a mean age of onset of the disease at 33.7 years (SD 14.0). Ankylosing spondylitis was the first of the two diseases diagnosed in 52.2% of cases (35/67). The mean duration of the disease (RA or AS) up to the time of diagnosis of both was 19 years. The first symptom of onset was low back pain in 50% of cases (34/68), followed by arthritis in 46% of cases (32/68), 56% of patients (36/64) had nodules rheumatoid and 85% of patients had presented low back pain at some point of their assessment. In 15% of the patients (11/73) the presence of uveitis was documented (in some old articles the term of iritis was limited), in 22% of cases there was extra-articular involvement (16/73), being the most frequent was the presence of Felty syndrome with 4 cases. **(table 1)**
Regarding the findings in the imaging studies, up to 78% of the patients had syndesmophytes in the spine (either in plain radiography). 88% (62/70) presented erosions in the X-rays of the hands and/or feet, the Radiological sacroiliitis was present in almost all patients 72/73, RF was positive in 90%, in 9 of the 11 patients in whom anti-CCP was performed were positive, and, in addition, almost 90% of the cases were HLA B-27 positive
Conclusion: The coexistence of AR and SpA is highly uncommon. With the data obtained, there seems to be a greater aggressiveness in the evolution, since most of them present an erosive radiological pattern, positivity for RF, involvement of the axial skeleton and presence of rheumatoid nodules in a frequency higher than that which occurs in patients with diagnosis isolated from either of the two entities.

REFERENCE:

[1] Simon TA, Kawabata H, RayN, Baheti A, Suissa S, Esadile JM. Prevalence of co-existing autoinmune disease in rheumatoid arthritis: A cross-sectional study. Adv Ther 2017; 34: 2481-2490.E

Abstract THU0378 – Table 1. Clinical and epidemiological characteristics

	n=73 (percentaje)	Observations
Sex		
Male	55 (75.3%)	
Mean age (years)	53.5	DT(15.0)
Mean age of onset disease (years)	33.7	DT(14)
First disease		6 cases unspecified
Rheumatoid arthritis	32/67 (47.8%)	
Ankylosing spondylitis	35/67 (52.2%)	
Mean duration of the disease (years)	19.0	DT (13.3)
First symptom		4 cases unspecified
Back pain	34/68 (50.0%)	
Arthritis	32/68 (46.6%)	
Uveítis	2/68 (2.98%)	
Rheumatoid nodules	37/65 (56.9%)	8 cases unspecified
Back pain (Inflammatory)	59/69 (85.5%)	4 cases unspecified
Uveitis	11/73 (15.1%)	
Extra-articular involvement (except uveitis)	16/73 (21.2%)	

Abbreviations: DT= Typical deviation

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THU0379 DEPRESSIVE SYMPTOMS AND FUNCTIONAL IMPAIRMENT ARE FREQUENT AND AFFECT QUALITY OF LIFE IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS: A QUESTIONNAIRE-BASED ASSESSMENT OF 300 PATIENTS COMPARED WITH 150 PATIENTS WITH PSORIASIS AND 150 PATIENTS WITH MECHANICAL BACK PAIN

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Background: Axial ankylosing spondylitis (axSpA) and psoriatic arthritis (PsA) constitute chronic inflammatory conditions affecting the axial skeleton as well as peripheral joints. Insufficient treatment may lead to joint destruction associated with a high rate of disability. Extra-articular manifestations contribute to morbidity and a reduced quality of life.

Furthermore, both, axSpA and PsA have been associated with an increased risk of depression.
Objectives: The aim of this project was to assess quality of life, functional impairment in everyday life as well as the prevalence of depression in axSpA and PsA and determine associated factors.
Methods: A questionnaire-based screening tool (FFbH, WHOQOL-BREF, Phq9, GHQ-12) was used to assess 150 patients with PsA and 150 patients with axSpA as well as 300 controls (150 with skin psoriasis only and 150 mechanical back pain patients) for quality of life, functional impairment as well as signs of depression.
Results: Both, SpA and PsA patients had a significantly reduced health-related quality of life compared to published normal values as well as psoriasis only patients (p=0.0003). Pain and functional impairment in everyday life correlated highly with perceived overall quality of life (p<0.01). Both, physical health as well as psychological health in turn highly correlated with the presence of depressive symptoms. In total, 35.4% of SpA and 41.2% of PsA patients had mild signs of depression, whereas 25% respectively 28.4% of SpA and PsA patients had moderate to severe signs of depression. Patients with active disease (BASDAI>4) at the time of evaluation showed significantly more frequent depressive symptoms compared to patients with no or low disease activity (p<0.0001). Female patients had a significantly reduced physical and psychological health-related quality of life compared to male patients (p=0.0003, respectively 0.0009). Female SpA and PsA patients also had significantly more depressive symptoms (p=0.0190). In our cohort, also age correlated with perceived quality of life. SpA and PsA patients <45 years of age reported a significantly higher perceived overall quality of life compared to patients >45 years (p<0.0001). Quality of life regarding physical health, mental health as well as social relationships was significantly better in younger patients (p=0.0014, p=0.0109, p=0.0196 respectively). However, this did not translate into a reduced rate of depressive symptoms in young patients. Body mass index (BMI) was associated with reduced health-related quality of life and psychological wellbeing, but did not correlate with depression. Smoking was neither associated with quality of life nor depression.
Conclusion: Despite treatment many SpA and PsA patients suffer from a reduced quality of life. Depression constitutes an important comorbidity, which needs to be addressed. Adequate therapy is not only important to reduce irreversible joint damage and disability but may also have a role in avoiding comorbidities such as depression.
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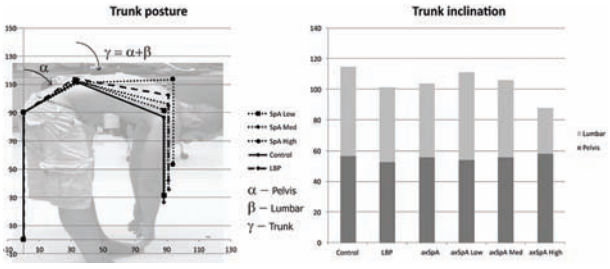
THU0380 LUMBOPELVIC RHYTHM IN PATIENTSWITH AXIAL SPONDYLOARTHRITIS COMPARED WITH LOW BACK PAIN AND HEALTHY SUBJECTS

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Background: Lumbar back pain reduces spinal mobility in patients. Although there are some symptoms that characterise 'inflammatory back pain', these are non-specific and the diagnosis is often delayed. It is not clear if there are kinematic differences between axial Spondyloarthritis (axSpA) and other types of back pain. Inertial motion sensors are now available that can accurately and reliably measure spinal mobility. The ViMove system uses two inertial sensors located at L1 and S1 allowing spinal flexion to be separated into its lumbar and pelvic components. The relation between different parts of the spine during a full flexion movement is known as lumbopelvic rhythm. The trunk sensor measures the total flexion, whilst the contribution of hip is measured by the pelvis sensor leaving lumbar flexion as the difference between the two angles.
Objectives: To analyse relation of lumbopelvic angles in axSpA patients, LBP patients and healthy controls.
Methods: 92 subjects were included in our study: 56 axSpA (from the COSPAR cohort of the Reina Sofia University Hospital), 14 LBP and 22 healthy controls. Inertial based system, the ViMove, was used to measure mobility. axSpA patients were stratified in three groups according their overall mobility using the BASMI: axSpA Low (< 2), Med (2-4) and High (>4)
Results: Table shows the results of spinal mobility tests in each group. The trunk, pelvis and lumbar angles are expressed in degrees (Mean and SD). cPelvis is the contribution of pelvis to the overall movement as percentage. Three of the five measurements in BASMI are outside the lower back so unlikely to be affected in LBP patients.

	n	Trunk	Pelvis	Lumbar	cPelvis	BASMI
Control	22	114.8 (13.6)	56.7 (15.1)	58.0 (9.6)	48.7% (9.5%)	1.7 (0.6)
axSpA	56	103.7 (19.1)	56.0 (14.6)	47.7 (17.5)	54.8% (15.0%)	3.1 (1.8)
LBP	14	101.3 (29.5)	52.8 (20.0)	48.5 (16.4)	52.0% (11.4%)	1.8 (1.0)
axSpA Low	21	111.3 (13.3)	54.2 (10.5)	57.0 (9.2)	48.5% (6.6%)	1.5 (0.5)
axSpA Med	22	105.9 (18.8)	56.2 (17.1)	49.6 (13.1)	52.6% (12.3%)	2.9 (0.5)
axSpA High	13	87.8 (19.4)	58.3 (16.4)	29.4 (21.3)	68.5% (20.4%)	6.0 (1.2)

There were significantly differences in the trunk, lumbar and pelvis angles between control and axSpA groups (p<0.01). The only significant difference between LBP and axSpA was in the lumbar angles (p<0.05).
The left part of the figure shows a reconstruction of the mean flexion angles for each group: these are also represented in the bar graph on the right. The trunk angle is higher in the healthy control group, is similar to the less affected axSpA patients (No significant differences between two groups). The most severely affected axSpA patients show reduced lumbar movement, and the pelvic contribution of the pelvis is also higher than the other two axSpA groups (p<0.001) controls (p<0.001) and LBP (p<0.01).



Abstract THU0380 – Figure 1

Conclusion: A reduction in spinal flexion was found in all patient groups, but there are interesting differences in the pattern of movement. LBP patients were characterised by a greater reduction in pelvis movement compared to the axSpA patients, although the final trunk flexion angle is actually lower in axSpA. When we compared more and less affected axSpA patients (according to BASMI), the most severely affected had severe restriction in lumbar movement whilst pelvic movement was increased. Lumbo-pelvic rhythm can also be analysed throughout early, middle and the end of the movement. Investigating spinal kinematics could help us to understand better axSpA and how it affects spinal mobility.
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THU0381 PATIENT-REPORTED IMPACT OF AXIAL SPONDYLOARTHRITIS ON WORKING LIFE: RESULTS FROM THE EMAS SURVEY

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Background: Axial spondyloarthritis (axSpA) impacts multiple dimensions of patients' lives, including working life.
Objectives: To evaluate work-related issues, their associations and determinants among European axSpA patients.
Methods: The European Map of Axial Spondyloarthritis (EMAS), conducted from July 2017 to February 2018, was a cross-sectional on-line survey of unselected patients with self-reported axSpA from Austria, Belgium, France, Germany, Italy, Netherlands, Norway, Russia, Slovenia, Spain, Sweden, Switzerland, and the UK. Participants were recruited through an on-line panel and patient organizations. Participants were classified as active (employed, unemployed between 15-64 years) or inactive (retirees, on sick leave, students and homemakers). Those employed were asked to report work-related issues (sick-leave, difficulty fulfilling work hours, missing work for doctors' appointments, reducing working hours or taking days off) in the past 12 months. Disease activity (BASDAI), self-reported spinal stiffness, diagnostic delay and psychological distress (General Health Questionnaire, GHQ-12) were compared between employed patients with or without work-related issues using a Mann-Whitney and Kruskal-Wallis test. Two-stage regression analysis was conducted to determine explicative sociodemographic (using stepwise method for income, age, gender, education) and disease-related factors (enter method for BASDAI, self-reported spinal stiffness, functional limitation) over work-related issues.
Results: 2846 axSpA patients participated in EMAS: mean age was 44 ±12 years, 61.3% were female and 48.1% were university educated. Mean disease duration and diagnostic delay were 17.2±12.4 and 7.4±8.4 years, respectively, and mean BASDAI was 5.5±2.0. 61.3% (n=1653) were considered active, of which 87.7% (n=1450) were employed. Of those employed, 67.7% reported a work-related issue, specifically 56.3% took sick leave, 44.6% had difficulties in fulfilling the working hours, 34.6% missed work due to doctor's appointments, 31.6% requested days off, and 25.7% reduced their number of working hours (Table 1). Among all patients, 74.1% faced or believed they would face difficulties finding a job due to axSpA. Experiencing work-related issues due to axSpA was significantly associated with higher disease activity, self-reported spinal stiffness, longer diagnostic delay, and higher level of psychological distress (p<0.001). First regression step showed gender and educational level as explanatory sociodemographic control factors, while educational level and BASDAI were the only statistically significant explanatory factors in the second step (p≤0.001) (Table 2).

Abstract THU0381 –Table 1.

Table 1. Statistical correlations between the work-related issues of employed and sociodemographic and clinical characteristics, (n:1422, unless other specified)

	Work-related issues (mean ± SD or %)	No work-related issues (mean ± SD or %)	p-value
Age (years)	41.4 ± 9.7	42.3 ± 10.4	0.09
Gender (Male)	37.9%	47.9%	<0.001*
Education level (University)	60.7%	56.6%	0.002*
Marital status (Married)	67.5%	69.3%	0.06
BASDAI (0-10), n:1310	5.4 ± 1.8	4.0 ± 2.0	<0.001*
BASDAI (≥ 4), n:1,310	79.0%	50.2%	<0.001*
Stiffness index (3-12)	7.5 ± 2.4	6.3 ± 2.5	<0.001*
GHQ-12 (0-12), n:1,344	5.1 ± 4.0	2.6± 3.2	<0.001*
GHQ-12 (≥ 3), n:1,344	64.6%	34.1%	<0.001*
Depression, n:1,371	26.1%	11.1%	<0.001*
Anxiety, n:1,368	32.2%	16.1%	<0.001*

*Test χ^2 and Mann-Whitney to indicate if there is an association between the variables.

Abstract THU0381 –Table 2.

Table 2. Regression analysis on the determinants of the presence of work-related issues of patients with axSpA and their demographic, socioeconomic and disease-related parameters. n=1162.

	Sig. of change in first stage (those above 0.05 are not considered sociodemographic control factors)	Second stage Coefficients	Sig. of coefficients	Goodness of fit statistics	
Income	0.568	NA		Cox-Snell R^2	,234
Age	0.443	NA			
Gender	0.009	,052	,691	Nagelkerke R^2	,312
Education level	0.033	,160	,016		
Stiffness Index	NA	-,032	,271	Percentage of correct predictions	72%
Limitation Index	NA	,001	,891		
BASDAI	NA	-,284	,000		

Conclusion: Nearly two-thirds of employed patients experienced work-related issues due to axSpA. The strongest factor associated with work-related issues was high disease activity. Understanding the determinants of work-related issues is needed to ensure that patients have adequate workplace and holistic medical support to lead productive work-lives
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THU0382 FACTORS ASSOCIATED WITH POOR WORK OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN SINGAPORE

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Background: Axial spondyloarthritis (axSpA) can lead to significant limitation of mobility and function, resulting in poor work outcomes.[1] Factors associated with poor work outcomes have not been studied in an Asian population. Singapore is an urban Asian city with a low unemployment rate and a healthcare model with heavy emphasis on self-reliance.[2] This socio-cultural context may influence risk factors for poor work outcomes.
Objectives: To identify factors associated with poor work outcomes in patients with axSpA in Singapore.
Methods: A cross-sectional study was performed in two tertiary centres in Singapore. Patients ≥21 years fulfilling Assessment in Spondyloarthritis International Society (ASAS) 2009 criteria for axSpA were included. We collected social demographics, clinical data, treatment modalities and patient reported outcomes, including the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), EQ-5D index, and Work Productivity and Activity Impairment scale (WPAI:SpA). WPAI:SpA was used to derive scores for presenteeism (reduced productivity while at work), absenteeism (time absent from work), work impairment (combining presenteeism and absenteeism scores) and activity impairment (impairment in activities performed outside of work). Univariable and multivariable linear regressions were used to

examine factors associated with presenteeism, absenteeism, work impairment and activity impairment.

Results: A total of 156 patients with axSpA were included: 72.4% employed, 80.1% male, 86.5% Chinese, mean age 39.2 (13.0) years, mean disease duration 8.5 (8.9) years. The mean BASDAI was 3.2 (2.0), mean BASFI was 2.1 (2.1), mean EQ-5D was 0.8 (0.1) and mean activity impairment was 28.2%. Among employed patients, mean absenteeism was 4.5%, mean presenteeism was 24.9% and mean work impairment was 27.6%. In multivariable analysis, absenteeism was associated with disease duration (ß: -0.44;95% CI: -0.80, -0.07;p=0.02)and EQ-5D (ß: -46.28; 95% CI: -89.63, -2.92; p=0.04). Presenteeism was associated with BASDAI≥4 (ß: 8.23;95% CI: 0.24, 16.22; p=0.04), BASFI (ß: 3.59; 95% CI: 1.25, 5.92; p<0.01) and EQ-5D (ß: -64.40; 95% CI: -115.79, -13.02; p=0.02). Work impairment was associated with BASFI (ß: 3.57; 95% CI: 0.71, 6.43; p=0.02) and EQ-5D (ß: -88.00, 95% CI: -150.87, -25.13; p<0.01). Activity impairment was associated with age (ß: -0.21; 95% CI: -0.41, -0.01; p=0.04), BASDAI≥4 (ß: 19.94; 95% CI: 13.79, 26.09; p<0.01), BASFI (ß: 3.29; 95% CI: 1.63, 4.95; p<0.01), EQ-5D (ß: -82.28; 95% CI: -125.15, -39.41; p<0.01).

Conclusion: Factors such as active disease, reduced physical function and poorer quality of life are associated with reduced work outcomes in patients with axSpA in Singapore. These factors need to be addressed to improve work outcomes.

REFERENCES:

[1] Martindale, J., et al. (2015). "The impact of ankylosing spondylitis/axial spondyloarthritis on work productivity." Best Pract Res Clin Rheumatol 29 (3): 512-523.

[2] Ng, I. Y., et al. (2012). "Designing and implementing an evaluation of a national work support program." Eval Program Plann 35(1): 78-87

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THU0383 PREVALENCE OF SPONDYLOARTHRITIS IN FIRST DEGREE RELATIVES OF PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a common rheumatic disease with higher prevalence in relatives of patients already diagnosed with the disease. Heritability of AS in twins is estimated to 90%.

Objectives: The aim of this study was to examine first degree relatives (FDR) of AS patients, to determine whether the patients already fulfil criteria for axial and/or peripheral spondyloarthritis (SpA) and compare the findings to healthy controls (HC).

Methods: We recruited 32 patients without prior rheumatologic diagnosis with first degree relative treated for AS and 20 age and sex matched HC. The clinical data were collected and rheumatology examinations were performed by trained rheumatologists. Magnetic resonance imaging (MRI) of sacroiliac joints (SIJ) was read by trained rheumatologist who was blinded to the patient´s data. Patients were further divided into the subsets of axial SpA (imaging and clinical arm) and peripheral SpA fulfilling The Assessment of SpondyloArthritis international Society (ASAS) classification criteria[1] and subset of non-SpA. The ASAS modified Berlin algorithm for diagnosis of axial SpA[2] (axSpA) was also applied.

Results: Altogether, 78% (n=25) FDR referred back pain, 34% (n=11) referred inflammatory back pain (IBP), and 22% (n=7) did not refer back pain, which was significantly different from that in HC (65% referred back pain, 0% referred IBP, 35% referred no back pain, p=0.0038 and p=0.03, respectively). Bone marrow edema (BME) was found in 50% (n=16) of FDR, and 22% (n=7) had highly suggestive BME[3] (hsBME) corresponding to typical findings of active sacroiliitis compared to HC where 10% (n=2) had BME, and none had hsBME (p=0.063, p=0.035, respectively). Furthermore, FDR had higher BASDAI and higher prevalence of HLA-B27 positivity compared to HC (2.0 (±1.5) and 75% vs. 0.4 (±0.6) and 5%, p= 0.001 and p= 0.001, respectively), no other significant differences were observed. The diagnosis of SpA was confirmed in 37% (n=12) of all FDR, 25% (n=8) patients fulfilled the imaging arm and 6% (n=2) fulfilled the clinical arm of ASAS classification criteria for axSpA, 6% (n=2) patients fulfilled ASAS classification criteria for peripheral SpA. The diagnosis of axSpA according to the ASAS modified Berlin algorithm was confirmed in 41% (n=13) patients. Analysis of clinical characteristics showed significant difference between serum CRP levels in SpA vs. non-SpA (8.2 (±12.5) vs. 2.3 (±4.4), p=0.02, respectively) and HLA-B27 positivity (100% vs. 60%, p=0.01, respectively). Presence of back pain and inflammatory back pain were more often in SpA compared to non-SpA subsets (100% and 67% vs. 65% and 15%, p=0.03 and p=0.006, respectively).

Conclusion: More than one third of first degree relatives of patients with AS fulfilled the criteria for axial or peripheral SpA, and had significantly higher prevalence of inflammatory back pain and increased BASDAI compered to HC. Based on these data, screening of family members of patients with AS should be recommended.

REFERENCES:

[1] Rudwaleit M, van der Heijde D, Landewé R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validization and final selection. Ann Rheum Dis 2009; 68: 777-83.

[2] van der Berg R, de Hooge M, Rudwaleit M, et al. ASAS modification of the Berlin algorithm for diagnosing axial spondyloarthritis: results from the SPondyloArthritis Caught Early (SPACE)-cohort and from the Assessment of SpondyloArthritis international Society (ASAS)-cohort. Ann Rheum Dis 2013; 72: 1646-53.

[3] Lambert RG, Bakker PA, van der Heijde D, et al. Defining active sacroiliitis on MRI for classification of axial spondyloarthritis: update by the ASAS MRI working group. Ann Rheum Dis 2016; 75: 1958-68.

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THU0384 IMAGING OF SACROILIAC JOINTS IN EARLY SPONDYLOARTHRITIS: SHOULD WE CHOOSE COMPUTED TOMOGRAPHY OR MAGNETIC RESONANCE IMAGING?

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Background: In view of the limited utility of pelvic radiography to recognize sacroiliitis in its earliest stages, magnetic resonance imaging (MRI) has been considered as a reliable imaging modality to detect acute subchondral inflammation at disease onset. However, several recent studies reported a high proportion of false-positive of sacroiliac joints (SIJ) MRI. Other studies demonstrated that computed tomography (CT), by its ability to detect early structural damage, may be helpful. Consequently, strengths and limitations of each imaging technique need to be considered when choosing the most appropriate first-line modality in clinical practice.

Objectives: We aimed to assess the performance of CT scanning and MRI for detecting sacroiliitis in early SpA by estimating the sensitivity and the specificity of each imaging technique.

Methods: Consecutive patients, aged 16 years and over, referred for symptoms suggestive of SpA from February 2014 to February 2017 were enrolled in this cohort. After excluding patients whose conventional radiography showed a confirmed sacroiliitis, eligible patients underwent SIJ CT and/or MRI. The CT and MR images were reviewed by 2 musculoskeletal radiologists blinded to clinical findings. Then, 2 rheumatologists recorded from the clinical files if patients fulfilled the ASAS (Assessment of Spondyloarthritis international Society) classification criteria for SpA. This classification was considered as the gold standard of this study.

Results: Fifty-three patients were included: 14 men and 39 women. The mean age was 36 years. The prevalences of HLA–B27 and elevated CRP were 27.6% and 16%, respectively. Fifty-eight percent of the patients (n=31) fulfilled the ASAS criteria for axial SpA. Among these patients, 30 patients underwent SIJ CT and 27 underwent SIJ MRI. Sacroiliitis was visualized by CT in 28 out of 30 patients (93.3%) and by MRI in 17 out of 27 patients (63%). Among the 22 patients who did not

fulfill the ASAS criteria for SpA, 21 patients underwent SIJ CT and 20 underwent SIJ MRI. Sacroiliitis was not visualized by CT in any patients and was visualized by MRI in 2 out of 20 patients (10%). Sensitivity, specificity, positive and negative likelihood ratio of CT calculated with ASAS classification as golden standard were respectively estimated at 93.3%, 100%, 100% and 91.3%. Youden index was estimated at 0.93 and Q Yule coefficient at 1. Sensitivity, specificity, positive and negative likelihood ratio of MRI calculated with ASAS classification as golden standard were respectively estimated at 62.9%, 90%, 89.5% and 64.3%. Youden index was estimated at 0.53 and Q Yule coefficient at 0.88.

Conclusion: In our study, the evaluation of sacroiliitis by CT, in comparison with MRI, has shown to be more sensitive and more specific. However, other factors should also be taken into account while comparing CT and MRI such as the high radiation exposure of CT scanning in the one hand and the cost and the restricted accessibility of MRI in the other hand.

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THU0385 COMPARISON OF CLINICAL AND DEMOGRAPHIC FEATURES OF JUVENILE SPONDYLOARTHRITIS BETWEEN ISRAELI AND US CHILDREN

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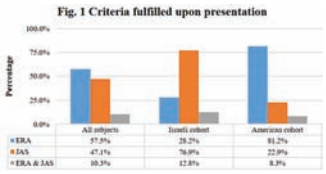
Background: Clinical observations among Israeli pediatric rheumatologists reveal that some of the clinical and demographic features of Israeli children diagnosed with Juvenile Spondyloarthritis (JSpA) are different as compared to the typical characteristics described in US studies.

Objectives: In this study, we compared clinical, laboratory and radiographic features to determine whether differences occur between the two populations of JSpA.

Methods: We performed a retrospective, cross-sectional, multicenter comparison of JSpA patients from 3 large Israeli pediatric rheumatology centers and a large US pediatric rheumatology center. Patients with a diagnosis of Juvenile Ankylosing Spondylitis (JAS) and/or Enthesitis-related Arthritis (ERA) were included. The demographic, clinical and imaging features of the subjects upon presentation were compared, including MRI of the sacroiliac joints. Inter Center Comparison (ICC) between the Israeli and US musculoskeletal radiologists was conducted.

Results: Overall 87 patients met the inclusion criteria (39 Israeli, 48 US). As compared to the US population, the Israeli population was less likely to be male (56% vs. 75%, p=0.11), and more likely to be older at time of diagnosis (14.3 vs. 11.9 years, p<0.001). Upon presentation, axial symptoms (inflammatory back pain) and physical examination findings consistent with sacroilitis (SIJ tenderness, modified Schober test), were significantly more prevalent among Israeli patients (59% vs. 35.4%, 48.7% vs. 16.7%, and 41.2% vs. 21.5%, respectively, all p<0.05), whereas peripheral arthritis and enthesitis were significantly more prevalent among the US patients (43.6% vs. 91.7% and 7.7% vs. 39.6% in Israeli patients vs. US patients, p<0.05). For HLA-B27, 32% of the Israeli patients vs. 66.7% of the US patients were positive (p=0.007). In addition, of those who had imaging (N= 30 and N=37 for Israeli and US cohorts) 96.7% of the Israeli patients versus 29.7% of the US patients demonstrated positive MRI findings that were consistent with sacroiliitis (p<0.001, overall N=67). An excellent level of agreement was observed between the Israeli and US musculoskeletal radiologists (kappa=0.9).

Conclusion: We found important distinctions between two populations with JSpA. Israeli children were more likely to present with axial disease, less likely to demonstrate HLA B27 carrier positivity, and more likely to demonstrate sacroiliitis on MRI than US children, who more commonly presented with peripheral arthritis and enthesitis, HLA-B27 positivity and negative MRI findings. These unique findings of the Israeli JSpA population, also as compared to descriptions of JSpA patients in the medical literature, point to environmental and/or population specific factors that merit additional studies in order to unravel the differences in disease presentation between the two countries.



Abstract THU0385 – Figure 1

REFERENCE:

[1] Shirley M. L. Tse; Ronald M. Laxer. New advances in juvenile spondyloarthritis. Nature Reviews Rheumatology, 2012, Vol.8(5), p.269–279.

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THU0386 CHILEAN AXIAL SPONDYLOARTHRITIS PATIENTSREPORT HIGH DISEASE BURDEN AND IMPAIRED WORK ACTIVITY – AN INTERNET SURVEY IN 472 PATIENTS

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Background: Axial spondyloarthritis (axSpA) can be associated with significant burden and impaired work activity. In Chile, several barriers impede adequate treatment, such as insufficient access to specialists and biological treatment. Furthermore, there is an important lack of insight into the local situation. This hampers the development of adequate national treatment standards and financial support.

Objectives: 1. To evaluate the disease burden, quality of life and work participation in Chilean axSpA patients. 2. To assess gender differences in disease burden and 3) compare patients with and without biologics.

Methods: A cross sectional online survey among Chilean SpA patients, recruiting via the internet website and associated social media of the Chilean SpA Patient Foundation ("Espondilitis Chile"). The survey was written in Spanish and requested information, mostly via multiple choice options, on gender, age, disease characteristics (diagnosis, disease duration, treatment), disease burden (BASDAI and BASFI), quality of life (ASAS Health Index) and work participation (WPAI). Only axSpA patients were included for further analyses. The association between BASDAI, quality of life or work participation (presenteeism, absenteeism) and subgroups (gender, biologics) was assessed through univariable regression and subsequently multivariable regression analyses, correcting for age, disease duration and concomitant treatment (NSAIDs, DMARDs, opiates).

Results: Between July and October 2018, 625 patients completed the website survey, of whom 472 reported a diagnosis with axSpA (91% radiographic axSpA, 37% male, mean age 42 years, 83% BASDAI$\geq$4, table 1). Twenty percent used a biological and patients with biologics were more likely to have a paid job (p=0.01) and had significantly lower BASDAI, BASFI, ASAS HI and risk of absenteeism. In multivariable analyses, biologics remained significantly associated with a lower BASDAI. Interestingly, biologics were used significantly more often in male patients compared to females (26% versus 16%, p<0.01), while BASDAI, ASAS HI and chance of absenteeism and presenteeism were significantly higher in female patients (table 1). After correction for treatment, the gender difference in BASDAI, absenteeism and presenteeism was not significant anymore.

Conclusion: The results of the web survey demonstrate a high level of disease burden and work impairment in Chilean axSpA patients. The use of biologics is low, although its use is independently associated with having a lower disease activity. Women used significantly less biologics despite reporting a worse disease state (BASDAI, ASAS HI) and greater work disability, suggesting inequality in access to treatment.

Abstract THU0386 – Table 1. Patient characteristics of Chilean axSpA patients (n=472).

	Overall (n = 472)	Men (n = 173)	Women (n = 299)	p=	Biologics (n= 92)	No Biologics (n=372)	p=
Gender, men	173 (37)				45 (49)	124 (33)	<.01
Age, yrs	42 ±10	43 ±11	41 ±9	.02	41 ±9	41 ±10	ns
Disease duration, yrs	13 ±10	13 ±9	15 ±12	.02			
HLA-B27 positive *	232 (49)	110 (77)	121 (52	<.01	47 (57)	180 (61)	ns
Current treatment							
DMARD	261 (55)	88 (51)	173 (59)	ns	41 (46)	217 (59)	.02
NSAIDs	370 (78)	126 (73)	244 (82)	.02	59 (65)	305 (82)	<.01
BASDAI	6.1 ±2.1	5.8 ±2.3	6.3 ±2.0)	.03	5.2 ±2.2	6.3 ±2.1	<.01
BASFI	5 ±3	5.1 ±2.8	5.4 ±2.4)	ns	4.7 ±2.4	5.5 ±2.6	<.01
ASAS Health Index	10 ±4	9 ±4	10 ±3	<.01	9 ±3	10 ±4	ns
Currently paid job	304 (64)	69 (75)	228 (61)	.01	131 (76)	172 (58)	<.01
Absenteeism, patients	125 (41)	21 (30)	101 (44)	.04	28 (31)	66 (48)	<.01
Presenteeism, patients	202 (81)	46 (79)	151 (83)	ns	81 (75)	120 (88)	<.01

Legend: Values are reported as numbers (%) or mean (±standard deviation, SD).

Acknowledgement: This study was conducted with help of the Chilean spondyloarthritis patient foundation "Espondilitis Chile".

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THU0387 ENTEROPATHIC ARTHRITIS PATIENTS UNDER BDMARD TREATMENTS HAD FREQUENTLY RADIOGRAPHIC SACROILIITIS: HUR-BIO REAL LIFE RESULTS

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Background: Enteropathic spondyloarthritis (eSpA) is one of the diseases in the Spondyloarthritis (SpA) spectrum and occurs in patients with inflammatory bowel disease (IBD). Sacroiliitis is frequently found in patients with IBD and can be overlooked because of focusing on IBD.

Objectives: Aim of this study is to evaluate the general features of eSpA and compare with psoriatic spondylitis (PsA), and ankylosing spondylitis (AS).

Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a prospective, single center database of biological treatments since 2005. eSpA patients were enrolled from HUR-BIO registry. Sacroiliitis was defined as modified New York criteria or based on ASAS magnetic resonance imaging criteria. Age and disease duration matched 128 ankylosing spondylitis and 96 psoriatic spondylitis patients were selected as a control group from HUR-BIO database. Demographic, clinical, laboratory, therapeutic data and imaging features were collected from this database: age, gender, age at disease onset, disease duration, type of IBD. Baseline disease activity before the first biologic therapy use was assessed with BASDAI, BASFI, VAS-patient global assessment, ESR and CRP.

Results: HUR-BIO SpA registry included 2576 SpA patients, and 90 (3.5%) patients had enteropathic arthritis (EA). Sixty four of 90 (71.1%) patients had sacroiliitis according to modified NY criteria, and these patients were included in the study. Of the 64 patients with eSpA, IBD type was ulcerative colitis (UC) in 34 (53%) patients, Crohn's disease (CD) in 30 (47%) patients. For eSpA patients, initial biological DMARDs were infliximab in 26 (40.6%), adalimumab in 23 (35.9%), etanercept in 10 (15.6%), golimumab in 4 (6.3%), and certolizumab in 1 patient (1.6%). The proportion of bDMARDs were similar with control group. Baseline disease activity were similar between eSpA and control group. However, baseline ESR levels were higher in eSpA than AS (p=0.037) and psoriatic spondylitis (p=0.001), as well. Baseline demographic and clinical features were summarized in Table 1.

Conclusion: Enteropathic spondyloarthrtis was present only a small part of all SpA patients. Sex, SpA family history, and uveitis were different from other SpA subgroups. Disease activities were similar with other spondyloarthritis, but particularly ESR level was higher in eSpA probably due to bowel disease activity. Sacroiliac and spine involvement seems to be the main reason for starting bDMARD in IBD patients, rather than peripheral arthritis.

Abstract THU0387 – Table 1. Baseline demographic features and disease activity in enteropathic spondylitis, ankylosing spondylitis and psoriatic spondylitis

	Enteropathic spondylitis (n=64)	Ankylosing spondylitis (n=128)	Psoriatic spondylitis (n=92)	P value
Female, n (%)	30 (46.9)	50 (39)	57 (62)	0.004*
Age, years	45.0 ± 12	45.3 ± 10.6	41.8 ± 12.2	0.163
Age at diagnosis, years	35.6 ± 11	34.8 ± 10.5	34.1 ± 11.6	0.763
Disease duration, years	9.17 ± 6.9	10.5 ± 5.4	7.7 ± 6.9	0.021*
SpA family history, n (%)	15 (23.4)	15 (11.7)	31 (33)	0.000*
Uveitis, n (%)	4 (6.3)	28 (21)	2 (2.1)	0.000*
HLA-B27 n (%)	11 (40.7)	31 (59.6)	13 (39.4)	0.117
Syndesmophyte	21 (43.8)	45 (35.2)	15 (30)	0.355
Switching between biological drugs, n(%)	31 (48.4)	46 (35.9)	36 (39.1)	0.246
Baseline BASDAI	5.7 ± 2.1	5.4 ± 1.7	5.8 ± 1.8	0.271
Baseline BASFI	4.6 (0-8.6)	3.5 (0-9.8)	4.1 (0-8.7)	0.577
Baseline ESR mm/hr (min-max)	33.5 (2-140)	22 (2-140)	18 (2-95)	0.007*
Baseline CRP mg/dL (min-max)	1.6 (0.12-19)	1.3 (0.1-10.6)	1.05 (0.1-13.9)	0.021*
Baseline patient global assessment VAS (min-max)	60 (20-100)	50 (10-90)	60 (0-100)	

Data were given as mean (standard deviation) or median (min-max)
HLAB27 were assessed in 27 eSpA, 52 AS and 33 PSA patients.

Disclosure of Interests: Gözde Kübra Yardımcı: None declared, Bayram Farisoğulları: None declared, Alper Sarı: None declared, Levent Kılıç: None declared, Berkan Armagan: None declared, Emre Bilgin: None declared, Ertuğrul Çağrı Bölek: None declared, Omer Karadag: None declared, Ali Akdoğan: None declared, Şule Apraş Bilgen: None declared, Sedat Kiraz: None declared, Ali İhsan Ertenli: None declared, Umut Kalyoncu Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim

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THU0388 CLINICALLY RELEVANT DEFICITS IN PERFORMANCE TESTS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS (AXSPA) - MORE THAN COLLECTING QUESTIONNAIRES NEEDS TO BE DONE

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Background: Physical function in axial spondyloarthritis (axSpA) usually assessed by the BASFI questionnaire is an established core domain of that disease. There is evidence that self-reported physical function is not equivalent with the actual performance of patients. Physical performance can be assessed as a single task such as grip strength or single stance, or as a generic compound measure such as the short physical performance battery test (SPPB). SPPB comprises a chair rising test, a balance test and gait speed.

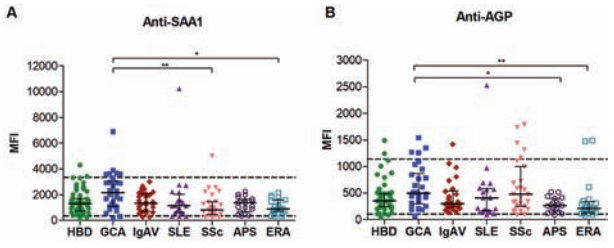
Objectives: To investigate which performance tests are most frequently impaired in patients with axSpA.

Methods: Consecutive axSpA patients presenting to our tertiary hospital underwent a standardized assessment including patient and disease characteristics, patient-reported outcomes (ASDAS, BASFI, BASMI, ASAS Health Index (ASAS HI), PHQ-9) and performance tests (SPPB, grip strength and single stance). Structural damage was assessed by mSASSS. Validated cut-offs were used for SPPB, chair rise test, grip strength and gait speed. Impairment of performance tests as well as discrimination between subgroups was analysed.

Results: A total of 200 patients (r-axSpA 65.5%, nr-axSpA 34.5%) were included: 69% males, 44.3±12.5 years of age, mean symptom duration

17.9 years, mean ASDAS 2.5±1.1, BASFI 4.0±2.7, BASMI 3.5±1.8, ASAS HI 7.0±4.1, PHQ-9 8.8±6.2, mSASSS (n=157) 10.2± 18.8. A total of 132 patients were treated with bDMARDs (66.5%). The two most impaired performance tests were repeated chair rising and single stance (Figure 1). An impairment in $\geq$ 1 performance test was seen in 87 patients (43.5%). Patients with impairments, in comparison to those without, were older (48.9 vs. 40.8 years), more often obese (28.7 vs. 26.1%), more often depressed (PHQ 12.1 vs. 6.3%), had lower BASFI values (5.7 vs. 2.8), a decreased ASAS HI (9.6 vs. 5.0), and higher disease activity (ASDAS 3.0 vs. 2.1), all p<0.01. The documented impairment in performance was irrespective of medication and structural damage on the group and the individual patient level. The correlation between BASFI and the performance test was moderate for SPPB (0.6), gait speed (0.5), chair rise (0.5) and single stance (0.4), while the correlation between BASFI and grip strength (0.2) and mSASSS (0.2) was rather limited.

Conclusion: In this consecutively recruited relatively young axSpA patients with limitations in physical function and health as assessed by established measures, we found a high prevalence of patients who didn't perform well in tests originally developed for older people. Importantly, a lot of impairment was seen when patients were asked to perform complex tasks requiring coordination and muscle strength. Impairment was present even though most patients received bDMARDs. Since such impairment is potentially influenced by physiotherapeutic interventions, we propose to perform studies to address these deficits. Our data strongly suggest to not only collect questionnaires but also do performance tests to better assess the 'real' physical capacity of patients.



Abstract THU0388 – Figure 1. Performance tests in patients with axSpA *14 patients were not able to perform the test ** 4 patients were not able to do a single stance.

Disclosure of Interests:
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THU0389 A SYSTEMATIC REVIEW OF PREGNANCY OUTCOME IN ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic, systemic inflammatory arthritis predominantly affecting spine and sacroiliac joints. AS affects young individuals in their third and fourth decades of life. Pregnancy poses challenges in AS patients. Unlike other chronic autoimmune diseases, not much is known regarding pregnancy outcome in AS and a systematic review would help treating clinicians and health professionals.
Objectives: Our main objective was to evaluate the pregnancy outcomes in ankylosing spondylitis. We reviewed the management and care related to preconception counselling, antenatal,intrapartum and postpartum period, particularly disease activity,medications and birth outcomes.
Methods: A systematic search of PUBMED and EMBASE was performed. Relevant peer reviewed papers were identified using inclusion criteria which included articles on pregnancy outcomes in AS patients above 16 years. We included only English articles covering systematic reviews, randomized control trials, case reports, observational studies published in medical literature between 1970 and March 2017.We excluded papers discussing general management of AS and articles on other autoimmune diseases and pregnancy. Each author screened the title and abstracts individually based on our criteria. A standardized data collection form was used for assessment of study quality and evidence synthesis. Systematic review was registered in PROSPERO and we followed the PRISMA flow chart.
Results: Our search yielded 544 papers. After initial screening of the titles and abstracts 443 papers were identified of which 42 potentially relevant papers were selected for full text review. 18 papers were finally included. Our initial results are based on individual papers. Zhou et al studied 12 AS patients retrospectively with no adverse outcomes, all had term pregnancies with 5 normal vaginal delivery, 7 caesarean,delivery was based on obstetric reasons. Nai Lee Lui et al observed a reduction in pain in the first trimester, first month postpartum with increase in the second and third trimester and in up to 6 months postpartum. Monika Ostensen et al observed unaltered or aggravated disease symptoms during pregnancy in 80%. Delivery was mainly uncomplicated and was normal in most cases. A postpartum flare during the first 3 months occurred in 90% of AS pregnancies. Hakan Timur et al did not notice any adverse pregnancy outcomes. Worsening of symptoms was seen in 60-90%of patients up to 6 months after delivery. Jakobsson et al noticed women with AS had a higher prevalence for several adverse birth outcomes with an influence by both disease severity and comorbidities. Case reports highlighted anaesthetic difficulties during delivery. There was paucity of articles studying the treatment aspects and complications only in pregnant AS patients.
Conclusion: To the best of our knowledge, this systematic review is the first one reviewing the outcome of pregnancy in ankylosing spondylitis. As the studies were heterogeneous, the pregnancy outcome was not consistent. There is paucity of data about pregnancy management for women with AS and further research is needed in this area to guide evidence based management of these pregnancies.

REFERENCE:
[1] Management of pregnancy with ankylosing spondylitis: Zhou, Qian, et al. : Chinese medical sciences journal = Chung-kuo i hsueh k'o hsueh tsa chih; Mar 2012; vol. 27 (no. 1); p. 46-49.The effect of pregnancy on ankylosing spondylitis, psoriatic arthritis, and juvenile rheumatoid arthritis: Ostensen, M: American journal of reproductive immunology (New York, N.Y. : 1989); 1992; vol. 28 (no. 3-4); p. 235-237. Pregnancy outcomes in patients with ankylosing spondylitis: a nationwide register study:Jakobsson, Gustav L, et al: Annals of the rheumatic diseases; Oct 2016; vol. 75 (no. 10); p. 1838-1842. Effect of pregnancy on ankylosing spondylitis: a case-control study: Lui, Nai Lee, et al. : The Journal of rheumatology; Nov 2011; vol. 38 (no. 11); p. 2442-2444

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THU0390 GENETIC STUDY OF MEDICAL IMAGE PROGRESSION IN A CHINESE AS POPULATION FOR SIX MONTHS' FOLLOW-UP

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Background: Genetic factors accounts for about 90% pathogenesis of ankylosing spondylitis (AS), and may predict the disease progression. MRI is an important tool for evaluating disease progression and assessing treatment response in patients with AS.
Objectives: This study aims to define correlation between AS-associated genetic variations and MRI scores of AS patients in Chinese population.
Methods: A total of 62 AS patients treated with TNF blockers from Guanghua medical center (Shanghai, China) were recruited in this study. All of AS patients were evaluated for disease progression with MRI (SPARCC) [1-3]. Measures of inflammation (bone marrow edema (BME) of sacroiliac joints (SIJ) and spine) and structural damage (fat metaplasia, erosion, backfill and ankylosis of SIJ) were recorded at baseline and six months' follow-up. The changes of MRI scores were defined as the score of six months' follow-up minus that of baseline. All of patients were examined with whole exon sequencing for genetic polymorphisms. Logistic regression analysis was performed and genetic variants with $p < 1E-4$ were considered as significant.
Results: The results showed that seven genetic variants significantly enriched in extracellular matrix pathways were associated with the changes of BME score of SIJ and spine. Four genetic variants regulating bone homeostasis, such as *ABCA4*, were significantly associated with the changes of fat metaplasia. Twelve variants were associated with the changes of erosion, one of which regulated expression of *FBF1* according to GTEx database (β/p-value = -5.0/1.1E-5). Mouse with *Fbf1* knockout showed abnormality in insulin metabolism and skeleton (MGI database). Genetic variants of the adipose related gene (*CTBP2*) and bone related genes (*RGMA, BMP8A*) were associated with the changes of backfill. In addition, genetic variants of *FAT4* was associated with the changes of ankylosis (β/p-value = 6.8/1.4E-8). Mutation of *FAT4* caused two bone related diseases and mouse with *Fat4* knockout showed severe abnormality of skeleton (MGI database).
Conclusion: Overall, the results suggested that the polymorphisms of genes involved in extracellular matrix were associated with BME, and genetic variants involved in adipose and bone metabolism were associated with structural damage in AS patients.

REFERENCES:

[1] Maksymowych WP, Inman RD, Salonen D, Dhillon SS, Krishnananthan R, Stone M, et al. Spondyloarthritis Research Consortium of Canada magnetic resonance imaging index for assessment of spinal inflammation in ankylosing spondylitis. Arthritis and rheumatism. 2005 Aug 15; 53(4):502-509.
[2] Maksymowych WP, Inman RD, Salonen D, Dhillon SS, Williams M, Stone M, et al. Spondyloarthritis research Consortium of Canada magnetic resonance imaging index for assessment of sacroiliac joint inflammation in ankylosing spondylitis. Arthritis and rheumatism. 2005 Oct 15; 53(5):703-709.
[3] Maksymowych WP, Wichuk S, Chiowchanwisawakit P, Lambert RG, Pedersen SJ. Development and preliminary validation of the spondyloarthritis research consortium of Canada magnetic resonance imaging sacroiliac joint structural score. The Journal of rheumatology. 2015 Jan; 42(1):79-86.

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THU0391 COMPARISON OF CHARACTERISTICS AND BURDEN OF DISEASE IN PATIENTS WITH RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Background: In 2009, the ASAS criteria allowed to classify patients with radiographic (r-axSpA) and non-radiographic (nr-axSpA) axial Spondyloarthritis (axSpA), and enhanced the concept of axSpA as a whole disease with different phenotypic presentations. However, some have claimed that the burden of r-axSpA and nr-axSpA is so different that they should be considered as different forms of the same disease.
Objectives: To compare the characteristics, burden of disease and treatment effect in patients with r-axSpA and nr-axSpA.
Methods: A systematic literature review until October 2018 was performed using PubMed, EMBASE and Cochrane databases. The PICO approach was used to formulate the research questions: P (r-axSpA patients), I (no intervention/drugs (only for the treatment effect evaluation), C (nr-axSpA patients), O (clinical presentation, disease activity, structural damage, function, quality of life, mobility, treatment modalities and treatment effect). Only observational studies and Randomized Controlled Trials (RCT) published after 2009 (year of publication of the ASAS criteria) were included. For the evaluation of the treatment effect, only RCT were considered. Risk of bias was evaluated on each manuscript with the Cochrane Risk of Bias tool for RCT and Hayden tool for observational studies. Pooled analysis was performed (Standardized Means Differences (SMD) and Relative Risk (RR) for continuous and binary variables, respectively) with a random effects model after evaluation of the heterogeneity of the studies.
Results: A total of 60 studies out of 787 references were included. Clinical presentation, disease activity, burden of disease (function, quality of life and mobility), treatment and treatment effect were evaluated in 54 (90.0%), 40 (67.7%), 37 (61.7%), 18 (30.0%) and in 9 (15.0%) manuscripts, respectively. Only 3 cross-sectional studies were classified as high risk of bias. Pooled results concerning continuous and binary variables are represented in tables 1 and 2. Only two RCTs (Etanercept vs. Sulfasalzine and Certolizumab vs. Placebo) directly compared the treatment effect between both groups, and none of them showed differences regarding ASAS partial remission, ASDAS major improvement and ASAS 40.
Conclusion: Published data suggest that r-axSpA and nr-axSpA patients share a similar clinical presentation except for peripheral manifestations (which are more prevalent among nr-axSpA), males and smokers (which are more frequent among r-axSpa). Disease activity and burden of disease are identical in both groups, except mobility, which is poorer among r-axSpA. The treatment effect was similar in both groups.

Abstract THU0391 –Table 1.

Table 1. Pooled results for clinical presentation, disease activity, burden of disease and treatment for continuous variables in r-axSpA vs. nr-axSpA patients.

	r-axSpA Pooled mean (95%CI)	nr-axSpA Pooled mean (95%CI)	SMD (95%CI)*
Clinical presentation			
Age at symptom onset	26.3 (24.8 to 27.9)	27.8 (26.2 to 29.4)	-0.11 (-0.2 to 0.01)
Time to diagnosis	6.1 (5.5 to 6.6)	4.2 (2.2 to 6.2)	0.31 (0.1 to 0.5)
MRI inflammation			
SPARCC total SIJ	7.7 (5.4 to 10.1)	7.2 (5.9 to 8.6)	0.31 (-0.3 to 0.9)
Berlin activity score spine	5.5 (1.6 to 9.4)	2.9 (-0.2 to 5.9)	1.87 (-0.5 to 0.6)
Structural damage			
mSASSS	8.1 (5.3 to 10.9)	2.7 (1.7 to 3.6)	**0.52 (0.4 to 0.6)**
Disease activity			
BASDAI	4.6 (4.3 to 4.9)	4.6 (4.3 to 5.0)	-0.03 (-0.1 to 0.0)
CRP	9.3 (7.9-10.6)	6.2 (5.2 to 7.3)	0.29 (0.2 to 0.4)
ASDAS-CRP	2.7 (2.4-3.0)	2.6 (2.3 to 2.8)	0.11 (0.0 to 0.2)
Function			
BASFI	3.4 (3.1 to 3.7)	3.0 (2.7 to 3.3)	0.19 (0.1 to 0.3)
HAQ-S	0.6 (0.5 to 0.8)	0.6 (0.5 to 0.7)	0.06 (-0.1 to 0.2)
Quality of life			
SF36-MCS	48.5 (46.5 to 50.6)	48.2 (44.1 to 52.3)	0.02 (-0.1 to 0.1)
SF36-PCS	40.6 (37.0 to 44.3)	41.9 (37.2 to 46.7)	-0.04 (-0.2 to 0.1)
Mobility			
BASMI	2.8 (2.3 to 3.3)	1.6 (1.3 to 1.9)	**0.69 (0.5 to 0.9)**

*SMD < 0.2 = irrelevant difference / 0.2<SMD<0.5 = doubtful / **SMD >0.5 = meaningful difference**

Abstract THU0391 –Table 2.

Table 2. Pooled results for clinical presentation and treatment for binary variables in r-axSpA vs. nr-axSpA patients.

	r-axSpA Pooled percentage (95%CI)	nr-axSpA Pooled percentage (95%CI)	RR (95%CI)
Clinical presentation			
Sex (male)	69.8 (66.2 – 72.8)	53.6 (49.0 – 58.1)	**1.30 (1.2 – 1.4)**
Smoker	37.7 (26.9 – 50.0)	31.1 (21.6 – 42.6)	**1.18 (1.1 – 1.3)**
HLAB27 positive	76.7 (71.6 - 81.1)	71.9 (66.7 - 76.6)	1.04 (0.9 - 1.1)
Good NSAIDs response	68.5 (56.0 - 78.8)	61.7 (53.3 - 69.4)	1.09 (0.9 - 1.1)
Peripheral arthritis	32.8 (27.6 - 38.5)	35.2 (28.9 - 41.9)	**0.87 (0.8 - 0.9)**
Dactylitis	5.6 (3.9 - 7.9)	7.6 (5.5 - 10.5)	**0.64 (0.5 - 0.8)**
Any enthesitis	23.0 (14.0 - 35.4)	30.1 (22.0 - 39.7)	**0.84 (0.7 - 0.9)**
Uveitis	18.0 (13.4 - 23.8)	14.3 (12.0 - 16.9)	**1.31 (1.1 - 1.6)**
Psoriasis	8.5 (5.6 - 12.8)	9.3 (7.4 - 11.7)	0.98 (0.8 - 1.1)
IBD	6.5 (5.2 - 8.2)	5.6 (4.0 - 7.9)	1.04 (0.9 - 1.3)
MRI inflammation			
Patients with positive MRI-SIJ ASAS definition	45.8 (18.7 – 75.7)	71.5 (66.9 – 75.8)	0.57 (0.3 – 1.1)
Structural damage			
Patients with erosion MRI-SIJ	70.8 (41.8 – 89.1)	41.0 (19.0 – 67.3)	**1.8 (1.1 – 3.0)**
Patients with fatty lesions MRI-SIJ	79.4 (56.1 – 92.1)	51.5 (28.4 – 74.0)	**1.4 (1.2 – 1.7)**
Treatment			
NSAIDs	73.5 (63.1 – 81.8)	69.1 (55.5 – 80.0)	1.04 (0.9 – 1.1)
csDMARDs	29.3 (20.5 – 39.9)	28.5 (21.9 – 36.1)	1.04 (0.8 – 1.3)
bDMARDs	28.7 (19.7 – 39.7)	26.2 (26.1 – 39.6)	1.08 (0.9 – 1.3)

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THU0392 DESCRIPTIONAND PREVALENCE: OF SPONDYLOARTHRITIS IN UNSELECTED PATIENTS WITH PSORIASIS, ACUTE ANTERIOR UVEITIS, AND INFLAMMATORY BOWEL DISEASE PRESENTING WITH UNDIAGNOSED BACK PAIN

Walter P Maksymowych[1,2], Raj Carmona[3], James Yeung[4], Jon Chan[5], Liam Martin[6], Sibel Aydin[7], Dianne Mosher[6], Ariel Masetto[8], Stephanie Keeling[1], Olga Ziouzina[6], Sherry Rohekar[9], Joel Paschke[2], Amanda Carapellucci[2], Robert G Lambert[1]. *[1]University of Alberta, Edmonton, Canada*; *[2]CaRE Arthritis, Edmonton, Canada*; *[3]McMaster University, Hamilton, Canada*; *[4]James Yeung Rheumatology, Vancouver, Canada*; *[5]Artus Health Center, Vancouver, Canada*; *[6]University of Calgary, Calgary, Canada*; *[7]University of Ottawa, Ottawa, Canada*; *[8]University of Sherbrooke, Sherbrooke, Canada*; *[9]Lawson Health Research Institute, London, Canada*

Background: There is limited prospective data as to the frequency of axial spondyloarthritis (axSpA) in unselected patients referred to rheumatologists with undiagnosed back pain. It is also unclear which clinical features discriminate between axSpA and non-specific causes of back pain that might inform the development of a screening strategy.

Objectives: To determine the prevalence of axSpA in unselected patients referred with undiagnosed back pain presenting with AAU, psoriasis, or colitis and determine which clinical characteristics define patients with axSpA.

Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at facilitating early detection of axial SpA. First and last patients were recruited on February 2013 and March 2018, respectively. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, AAU, or colitis had routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation ordered per rheumatologist decision. Differences in clinical characteristics between those who were diagnosed as axSpA or non-specific back pain were analyzed using chi-squared and t-tests.

Results: A total of 246 patients were recruited, 47.6% were diagnosed with axSpA, and these included 68.5% of B27 positive patients (Table 1). Diagnosis of axSpA was established in 45.7%, 61.6%, and 40.2% of patients, while ASAS classification criteria were met by 26.1%, 71.2%, and 27.6% of patients with psoriasis, AAU, and IBD, respectively. Features of inflammatory back pain, male gender, and B27 positivity, but not physical measures discriminated axSpA from other causes of back pain (Table 2).

Abstract THU0392 –Table 1.

	Psoriasis	AAU	IBD
Total number (%)	46 (18.7%)	73 (29.7%)	127 (51.6%)
Age, mean (SD) years	36.7 (6.0)	34.0 (5.8)	34.0 (7.3)
Males, N (%)	24 (52.2%)	41 (56.2%)	64 (50.4%)
Symptom Duration, mean (SD) years	7.7 (7.7)	8.7 (6.7)	6.3 (5.9)
B27+, N (%)	10 (21.7%)	51 (69.9%)	28 (22.0%)
Family history of SpA, N (%)	15 (32.6%)	15 (20.5%)	20 (15.7%)
Enthesitis, N (%)	15 (32.6%)	13 (17.8%)	39 (30.7%)
Peripheral arthritis, N (%)	13 (28.3%)	2 (2.7%)	5 (3.9%)
Dactylitis, N (%)	4 (8.7%)	2 (2.7%)	3 (2.4%)
Radiographic sacroiliitis,%	6.5%	23.3%	10.2%
Axial SpA rheumatologist diagnosis,%	45.7%	61.6%	40.2%
Axial SpA diagnosis and B27+,%	15.2%	52.1%	12.6%
Meets ASAS criteria,%	26.1%	71.2%	27.6%

Abstract THU0392 –Table 2.

Demographics	axSpA YES (n=117, 47.6%)	Not axSpA (n=129, 52.4%)	P value
Male, N (%)	72 (61.5%)	57 (44.2%)	0.006
Mean (SD) age, years	33.7 (6.7)	35.2 (6.7)	ns
Inflammatory Back Pain Yes, N (%)	102 (87.2%)	72 (55.8%)	<0.00001
Duration stiffness > 60 mins, N (%)	57 (48.7%)	30 (23.3%)	0.001
Nocturnal awakening 2nd half of night, N (%)	72 (61.5%)	51 (39.5%)	0.001
Alternating buttock pain, N (%)	53 (45.3%)	21 (16.3%)	<0.00001
Improvement with exercise but not rest, N (%)	77 (65.8%)	48 (37.2%)	<0.00001
Respond to NSAID within 48 hrs, N (%)	58 (49.6%)	59 (45.7%)	ns
Family history of SpA, N (%)	22 (18.8%)	28 (21.7%)	ns
B27 positive	61 (52.1%)	28 (21.7%)	<0.00001
Elevated CRP (> 6.0mg/L)	43 (36.8%)	32 (24.8%)	0.042
Radiographic sacroiliitis, N (%), local readers	54 (46.2%)	7 (5.4%)	<0.00001

Conclusion: Patients with extra-articular manifestations and undiagnosed back pain have a high prevalence of axSpA and referral to a rheumatologist should constitute standard of care, especially if B27 positive.

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THU0393 PERFORMANCE OF THE ASAS CLASSIFICATION CRITERIA PRESENTING WITH UNDIAGNOSED BACK PAIN? DATA FROM THE SCREENING IN AXIAL SPONDYLOARTHRITIS IN PSORIASIS, IRITIS, AND COLITIS (SASPIC) COHORT

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Background: Classification criteria for axial spondyloarthritis (axSpA) that capture the spectrum of disease present challenges due to the frequency of back pain, the relative infrequency of axSpA, and limited physical and laboratory findings in early disease. Several cohorts have reported the performance of the ASAS classification criteria in settings where patients have been selected for certain features such as the presence of inflammatory back pain and/or short symptom duration.

Objectives: We aimed to test the performance of the ASAS classification criteria in unselected patients referred with undiagnosed back pain who have presented with acute anterior uveitis (AAU), psoriasis, or colitis to their respective specialists and whether performance varied according to demographic factors and symptom severity.

Methods: he multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at early detection of axial SpA. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation is ordered per rheumatologist decision. The rheumatologist determines the presence or absence of axial SpA and the degree of confidence in the diagnosis (-10 (definitely not SpA) to +10 (definite SpA)) at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. Assessment of imaging was conducted by local and central readers. We calculated the sensitivity and specificity of the ASAS criteria and the component imaging and clinical arms using the stage 3 diagnostic assessment by the local rheumatologist as gold standard.

Results: A total of 246 patients were recruited, 47.6% being diagnosed with axSpA (61.5% male, age 33.7 years, symptom duration 7.6 years, B27 positive 52.1%), after stage 3 evaluation. Sensitivity/specificity of the ASAS criteria, imaging arm, clinical arm were 74.4/79.8%, 55.6/93.8%, 50.4/82.2%, respectively (Table). For patients diagnosed with a high degree of confidence sensitivity/specificity was 87.5/82.7%, 68.8/94.5%, 56.3/84.5%, respectively. Specificity, especially for the clinical arm, was notably higher in patients with a higher degree of back pain (≥5/10), and in those with longer symptom duration (≥5 years).

Abstract THU0393 –Table 1.

Patient Category	Number	ASAS criteria		Imaging arm		Clinical arm	
		Sen	Spec	Sen	Spec	Sens	Spec
All patients	246	74.4	79.8	55.6	93.8	50.4	82.2
Patients diagnosed with confidence >7 for axSpA yes and <-4 for not axSpA (-10 to +10 scale)	190	87.5	82.7	68.8	94.5	56.3	84.5
Patients with back pain ≥5 (0-10 scale)	165	74.7	83.7	54.4	94.2	51.9	84.9
Patients with back pain <5 (0-10 scale)	81	73.7	72.1	57.9	93.0	47.4	76.7
Patients with symptom duration ≥5 years	143	78.1	85.7	53.4	95.7	56.2	85.7
Patients with symptom duration <5 years	103	68.2	72.9	59.1	91.5	40.9	78.0
Males	129	73.6	78.9	61.1	89.5	48.6	84.2
Females	117	75.6	80.6	46.7	97.2	53.3	80.6

Conclusion: The performance of the ASAS criteria in the SASPIC cohort is comparable to the findings in the original ASAS classification study. Performance may vary according to symptom duration and severity of symptoms which likely impacts diagnostic ascertainment.

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THU0394 THE PREVALENCE OF EXTRA-ARTICULAR MANIFESTATIONS IN AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS IS ASSOCIATED TO DISEASE DURATION: RESULTS FROM THE LEEDS SPECIALIST SPONDYLOARTHRITIS SERVICE

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Background: Psoriasis, uveitis and inflammatory bowel disease (IBD) are extra-articular manifestations (EAMs) that can occur in both axial Spondyloarthritis (axSpA) and psoriatic arthritis (PsA). Their prevalence has been outlined independently in a recent meta-analysis[1] for axSpA and in several series in PsA with variable results. Although the diagnostic delay of inflammatory arthritis has been reduced in the last years, it remains a significant unmet need, particularly in axSpA. There are limited data on the relationship between diagnostic delay and the appearance of EAMs.

Objectives: To explore the prevalence of EAMs in a cohort of axSpA and PsA patients, and its relationship to disease duration and possible diagnostic delay in both groups.

Methods: Cross-sectional, single centre, observational cohort study of consecutive patients attending a large tertiary specialist clinic. All subjects provided written consent (2005-2018). Only patients fulfilling the modified New York (mNY) criteria for ankylosing spondylitis and CASPAR criteria for PsA were considered for this analysis. Demographic and clinical data were retrieved during enrolment and cross-referenced with the clinical notes. To explore the relationship between presence of EAMs, disease duration and delay to diagnosis, only uveitis and IBD were considered because of psoriasis being common in the PsA group. Univariate (Mann Whitney U-test) and multivariate analysis (binary logistic regression) with variables of sex, age, disease duration and diagnostic delay were performed.

Results: Data from 988 patients were available for analysis (n= 418 axSpA, n=570 PsA). Demographic and clinical characteristics are summarised in Table 1.

In the axSpA group, 187 cases (44.7%) presented with EAMs (including psoriasis) and 67 (16.02%) of these had more than 1 EAM. In the PsA group, 32 cases (5.6%) presented with EAM (excluding psoriasis) and only 3 cases (0.5%) had more than one EAM.

In the PsA group, a median delay of 4 years (IQR 2-9) was observed between psoriasis onset and PsA. In 42 cases the psoriasis appeared after the PsA onset. The predominant PsA phenotype was polyarticular (n=298; 52.3%) of which n=118, 20.7% had erosive disease. 101 (17.7%) had a predominantly axial phenotype.

Disease duration and delay to diagnosis were longer in the axSpA group (p<0.0001). Further univariate analysis showed an association between disease duration and the presence of EAMs when analysing the whole cohort (p<0.001) and the axSpA group (p<0.001), but not in the PsA group (p=0.832). The diagnostic delay was associated to the presence of EAMs in the whole cohort (p<0.001), but not in the individual disease groups. In the multivariate analysis only disease duration was related to presence of EAMs in the whole cohort (OR 1.064 95%IC 1.044-1.086) and axSpA group (OR 1.043 95%IC 1.016-1.070).

Abstract THU0394 – Table 1. Demographics of the study population.

Variable	PsA n=570	axSpA n=418
Females, n (%)	292 (51.2)	117 (28.5)
Age, years, mean (SD)	52,68 (13.09)	50,14 (14.55)
Disease duration, years, median (IQR)	12 (8-19)	20 (13-31)
Delay to diagnosis, years, median (IQR)	1 (0-2)	4 (1-10)
Psoriasis, n (%)	528 (92,6)	58 (13,9)
Uveitis, n (%)	21 (3,7)	118 (28,2)
IBD, n (%)	14 (2,6)	52 (12,4)
Crohn, n (%)	7 (1,3)	23 (5,5)
Ulcerative colitis, n (%)	4 (0,7)	21 (5,0)
Undifferentiated colitis, n (%)	3 (0,5)	8 (1,9)

Conclusion: The prevalence of EAMs (uveitis and IBD) in this cohort appears higher in axSpA than PsA and is related to disease duration. Diagnostic delay occurs in both groups being more significant in axSpA, and should be highlighted as a priority research area in order to improve the outcome of people affected by SpA.

REFERENCES:

[1] De Winter JJ, et al. Arthritis Res Ther (2016); 18:196.

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THU0395 MUSCLE STRENGTH COMPROMISE IN YOUNG AXIAL SPA PATIENTS: PRELIMINARY RESULTS FROM MYOSPA STUDY

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Background: Pain and stiffness are characteristic clinical features of axial Spondyloarthritis (axSpA), leading to functional impairment. Patients describe beneficial effects of physical activity, suggesting a possible involvement of muscle tissue. Body composition data in young axSpA patients with short disease duration are scarce and its implications in muscle strength are not yet clarified.
Objectives: The purpose of this study is to assess the muscle strength and body composition of different body segments (trunk, upper and lower limbs), in patients with axSpA and to compare them with healthy controls.
Methods: Patients with clinical diagnosis of axSpA meeting the ASAS classification criteria, aged 18 to 50 years, with symptoms duration ≤ 10 years, were included in this study. Healthy individuals matched by gender and age (1:1) were used as control group (HC). Muscle strength was measured by resisted hand-held dynamometer performed by a single reader, in three different body segments: trunk, upper and lower limbs (on both sides). The mean strength of right and left, upper and lower limbs, was calculated and used in the analysis. Strength of each body segment was also normalized to the total lean mass (LM) of the respective segment. Body composition was measured by octapolar multifrequency bioelectrical impedance analysis (InBody770). Physical activity was assessed by the International Physical Activity Questionnaire (IPAQ). Fisher's exact test or chi-square test and Mann-Whitney U test were used to compare differences between groups.
Results: A total of 27 axSpA patients and 27 HC were included. Mean age was 36.5 ± 1.0 years, 67% were males. There was no significant difference between both groups in terms of age, gender, body mass index and physical activity. AxSpA patients had a mean symptoms duration of 7.0 ± 0.9 years.
AxSpA patients had lower muscle strength in the upper limbs (50.55 ± 31.60 vs 71.70±31.41 p=0.023) and lower limbs (52.25±18.45 vs 59.83 ±9.75, p=0.001), compared to HC. Trunk muscle strength did not show any difference between groups (59.10±26.1 vs 56.45±11.2, p=0.856).
There were no significant differences in LM and body water, between both groups, for each segment (upper limbs, lower limbs and trunk). Fat mass was significantly higher in the trunk (10.90±8.80 vs 8.10±5.83, p=0.035) and upper limbs (1.40±1.35 vs 0.88±1.0, p=0.05) of axSpA patients, but not in the lower limbs (3.10±1.90 vs 2.45±1.68, p=0.157).
Normalized appendicular muscle strength was lower in axSpA patients (upper limbs: 18.63±8.25 vs 21.21±5.92, p=0.018) (Table).
Conclusion: Young patients with short duration have reduced appendicular muscle strength, compared to HC, with no differences in LM, suggesting a possible muscle dysfunction. Further studies are needed to confirm these findings and understand the underlying pathophysiological mechanisms.

Abstract THU0395 –Table 1.

Table. Comparison of subjects' characteristics between axSpA patients and healthy controls.

Variable	Patients n=27	Controls n=27	p-value
Age*	36.25±7.82	36.81±7.36	0.808
Gender (male), *n* (%)	18 (66.7%)	18 (66.7%)	1.000
Body height (cm)	169.80±10.7	172.40±13.3	0.522
Body mass (Kg)	73.00±19.2	70.050±16.5	0.347
BMI (Kg/m2)	25.10±7.00	23.80±3.00	0.303
IPAQ (%)			0.871
Low	10.4	14.6	
Moderate	20.8	18.8	
High	18.8	16.7	
BASDAI	3.0±2.11	-	-
BASFI	0.90±4	-	-
Strength (Nm/s)			
Trunk	59.10±26.1	56.45±11.2	0.856
Upper Limb	50.55±31.60	71.70±31.41	**0.023**
Lower Limb	52.25±18.45	59.82±9.75	**0.001**
Lean Mass (Kg)			
Trunk	24.90±4.40	25.25±8.35	0.831
Upper Limb	3.00±0.76	3.12±1.40	0.782
Lower Limb	7.96±2.38	9.17±3.07	0.128
Fat Mass (Kg)			
Trunk	10.90±8.80	8.10±5.83	**0.035**
Upper Limb	1.40±1.35	0.88±1.05	**0.050**
Lower Limb	3.10±1.90	2.45±1.68	0.157
Body water (L)			
Trunk	10.40±3.40	19.30±5.98	0.837
Upper Limb	2.34±0.59	2.40±0.96	0.885
Lower Limb	6.13±1.84	6.93±2.33	0.274
Strength/LM (Nm/s/Kg)			
Trunk	2.40±0.60	2.34±0.58	0.628
Upper Limb	18.63±8.25	21.21±5.92	**0.018**
Lower Limb	6.47±1.71	6.80±2.03	0.233

Values are median ± IQR, unless otherwise indicated.
* Mean ± SD.
BMI: Body Mass Index. IPAQ: International Physical Activity Questionnaire. BASDAI: Bath AS Activity Index. BASFI: Bath AS Functional Index. LM: Lean Mass.

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THU0396 SMALL INTESTINAL BACTERIA OVERGROWTH IN SPONDYLOARTHRITIS

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Background: It has shown different alterations in the intestinal microbiota in patient with SpA. Tests for the detection of intestinal dysbiosis have focused on the identification of dysbiosis at the terminal ileum and colon

and little has been explored in the alterations at the level of the jejunum. The tests for its detection are expensive, unavailable and invasive. The breath test is used to detect small intestine bacterial overgrowth (SIBO), being a non-invasive, simple and inexpensive test.

Objectives: To determine the frequency of SIBO and the relation to the clinical activity of SpA.

Methods: An analytical cross-sectional study was conducted in the period March 2018-October 2018. Patients older than 18 years, who signed informed consent, who met modified New York criteria and Caspar criteria were included. Patients were excluded who were diagnosed with active lung infection, active oral infections, interstitial lung disease, chronic obstructive pulmonary disease, acute diarrheal disease, short bowel syndrome, abdominal surgery in less than 6 months, and oral or IV antibiotics used one month before the test.

Patients who fulfilled the inclusion criteria were collected demographic and clinical data, gastrointestinal manifestations were interrogated and ASDAS pcr, BASMI, BASDAI, BASFI activity scales were measured. The breath test was performed by a gastroenterologist. The concentrations of hydrogen produced by bacteria were measured by GASTROLYZER® according to the recommendations of the consensus of the American Gastroenterology Association. It was considered a positive test to change the concentrations of more than 20 ppm with respect to the basal test. To compare the frequency of SIBO, a historical cohort of patients without rheumatic diseases matched by age was taken. The data were presented in means and percentages. Student's T and Mann-Whitney U were performed for numerical variables. Groups with chi square were compared.

Results: We studied 20 patients with ankylosing spondylitis (M/F 9/11) and 11 psoriatic arthritis (M/F 1/12), mean age 54.45 ±13.52, 33 healthy controls matched by age. Positive test was found in 11 (33%) patients (8/3 EA/APs) vs 1 (3%) in controls. When comparing groups with positive test versus negative test groups, patients with SIBO consumed less SSZ (72.7 vs 90.9, p 0.008), had higher frequency of irritable bowel (54 vs 5 vs 9.1, p 0.004), antecedent of cholecystectomy (27.3 vs 9.1 p 0.01), steatorrhea (18.2 vs 0, p 0.001), and higher activity: ASDAS> 2.1 (100% vs 86.4%, p 0.199), BASMI> 4 (36.4% vs 31.8% p 0.79), BASFI> 4 (72.7% vs 50%, p 0.21), enthesitis> 1 (45.5% vs 13.6%, p 0.61).

Conclusion: We found a higher frequency of SIBO in patients with SpA compared to healthy controls, but not related to disease activity. This is the first study to investigate SIBO by breath test in patients with SpA

REFERENCES:

[1] Rezaie A, Pimentel M, Rao SS. How to Test and Treat Small Intestinal Bacterial Overgrowth: Evidence-Based Approach. Curr Gastroenterol Rep. 2016;18(2):8.

[2] Rezaie A, Buresi M, Lembo A, Lin H, McCallum R, Rao S, etal.Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus. Am J Gastroenterol. 2017;112(5):775–84.

[3] Machado PM, LandewéR, Heijde Dvander, Assessment of Spondylo Arthritis international Society (ASAS). Ankylosing Spondylitis Disease Activity Score (ASDAS): 2018 update of the nomenclature for disease activity states. Ann Rheum Dis. 2018;77(10):1539–40.

[4] Levy M, Kolodziejczyk AA, Thaiss CA, Elinav E. Dysbiosis and the immune system. Nat Rev Immunol. abril de 2017;17(4):219–32.

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THU0397

CLINICAL CHARACTERISTICS AND TREATMENT PROFILES OF PATIENTS WITH ANKYLOSING SPONDYLITIS WHO INITIATED SECUKINUMAB AND OTHER BIOLOGICS: RESULTS FROM THE CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

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Background: Secukinumab is the first non–tumor necrosis factor inhibitor biologic therapy approved for the treatment of ankylosing spondylitis (AS) in the United States. Patients with AS in clinical trials who receive biologics, including secukinumab, may not be representative of those treated in real-world clinical practice due to differences in patient characteristics, practice patterns, physician experience, and insurance coverage (ie, access). Few real-world studies have characterized patients with AS who initiate secukinumab. The Corrona PsA/SpA Registry collects data on a robust list of outcome measures, many of which overlap with those used in clinical trials.

Objectives: To describe the characteristics of patients who initiated secukinumab and other biologics for the treatment of AS in the Corrona PsA/SpA Registry.

Methods: This study included patients aged $\geq$ 18 years with AS (and without concurrent PsA diagnosis) enrolled in the Corrona PsA/SpA Registry who initiated secukinumab or other biologics (adalimumab, etanercept, certolizumab pegol, infliximab, and golimumab) between April 2017 and December 2018. Patient demographics, clinical characteristics, treatment profiles, disease activity, quality of life, and work productivity were assessed at the time of biologic initiation (baseline) and compared between patients who initiated secukinumab and other biologics using *t* tests or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher's exact tests for categorical variables.

Results: Of the 106 patients with AS who initiated a biologic 26 (24.5%) initiated secukinumab and 80 (75.5%) initiated other biologics. Secukinumab initiators were similar to patients who initiated other biologics in terms of demographics and clinical characteristics except that a higher proportion of secukinumab initiators had a history of prior biologic use (69.2% vs 45.0%; P = 0.03) and were more likely to have used a higher number of prior biologics compared with other biologic initiators (P < 0.01; **Table 1**). No significant differences were observed between patients who initiated secukinumab and other biologics in terms of measures of disease activity, quality of life, and work productivity (**Table 2**).

Abstract THU0397 –Table 1.

Table 1. Demographic and Clinical Characteristics and Treatment Profiles Among Patients With AS Who Initiated Secukinumab or Other Biologics*

Characteristic	Secukinumab Initiators (n = 26)	Other Biologic Initiators (n = 80)	*P* Value
Age, mean (SD), years	47.7 (12.5)	47.3 (14.7)	0.88
Female, n (%)	14 (53.8)	40 (50.0)	0.73
White, n (%)	26 (100.0)	72 (90.0)	0.37
Work status, n (%)			
Full time	18 (69.2)	36 (45.0)	0.26
Part time	0	6 (7.5)	
Disabled	3 (11.5)	14 (17.5)	
Retired	2 (7.7)	14 (17.5)	
Other	3 (11.5)	10 (12.5)	
BMI, mean (SD), kg/m²	28.7 (7.9)	31.3 (7.7)	0.06
Symptom duration, mean (SD), years	14.8 (8.9)	13.9 (12.1)	0.35
Disease duration, mean (SD), years	6.8 (6.5)	5.5 (8.8)	0.06
HLA-B27 positive test result, n (%)	16 (61.5)	43 (53.8)	0.49
Comorbidities, n (%)			
Hypertension	10 (38.5)	28 (35.0)	0.75
Depression	3 (11.5)	18 (22.5)	0.22
Hyperlipidemia	4 (15.4)	13 (16.3)	1.00
Anxiety	1 (3.8)	15 (18.8)	0.11
Cardiovascular disease	3 (11.5)	11 (13.8)	1.00
Serious infections	5 (19.2)	6 (7.5)	0.13
Uveitis	1 (3.8)	9 (11.3)	0.45
Diabetes mellitus	2 (7.7)	6 (7.5)	1.00
Fibromyalgia	2 (7.7)	5 (6.3)	1.00
Metabolic syndrome	2 (7.7)	5 (6.3)	1.00
Psoriasis	2 (7.7)	4 (5.0)	0.63
Nail psoriasis	1 (3.8)	2 (2.5)	1.00
Crohn disease	0	3 (3.8)	1.00
Ulcerative colitis	1 (3.8)	1 (1.3)	0.43
Any cancer (excluding NMSC)	1 (3.8)	1 (1.3)	0.43
Prior csDMARD use, n (%)	7 (26.9)	16 (20.0)	0.46
Prior biologic use, n (%)	18 (69.2)	36 (45.0)	0.03
Number of prior biologics, n (%)			< 0.01
0	8 (30.8)	44 (55.0)	
1	6 (23.1)	25 (31.3)	
≥ 2	12 (46.2)	11 (13.8)	
Current csDMARD use, n (%)	2 (7.7)	11 (13.8)	0.51

BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HLA-B27, human leukocyte antigen B27; NMSC, nonmelanoma skin cancer.
* Other biologics included adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab.

Abstract THU0397 –Table 2.

Table 2. Disease Activity, Quality of Life, and Work Productivity Among Patients With AS Who Initiated Secukinumab or Other Biologics*

Characteristic	Secukinumab Initiators (n = 26)	Other Biologic Initiators (n = 80)	*P* Value
ASDAS, mean (SD) [n]	3.1 (0.9) [23]	3.2 (0.9) [67]	0.84
BASDAI (0-10), mean (SD) [n]	5.7 (1.7) [26]	5.4 (2.1) [80]	0.52
BASFI (0-10), mean (SD) [n]	4.7 (2.5) [26]	4.2 (2.4) [75]	0.30
Lateral lumbar flexion (average of left and right), mean (SD) [n], cm	30.2 (20.1) [23]	28.4 (21.3) [70]	0.69
Enthesitis, n/m (%)	12/26 (46.2)	31/80 (38.8)	0.50
SPARCC Enthesitis Index (1-16), mean (SD) [n]	5.6 (3.1) [12]	4.6 (2.9) [31]	0.24
Dactylitis, n/m (%)	2/26 (7.7)	2/80 (2.5)	0.25
Dactylitis count (1-20), mean (SD) [n]	1.5 (0.7) [2]	1.5 (0.7) [2]	1.00
Tender joint count (0-68), mean (SD) [n]	3.3 (5.0) [26]	3.7 (7.0) [80]	0.39
Swollen joint count (0-66), mean (SD) [n]	0.4 (1.0) [26]	0.9 (2.0) [80]	0.61
Physician global assessment (VAS 0-100), mean (SD) [n]	40.7 (20.3) [26]	41.2 (20.9) [80]	0.92
Physician global assessment of psoriasis (VAS 0-100), mean (SD) [n]	36.2 (19.3) [6]	29.1 (22.6) [18]	0.61
Patient pain (VAS 0-100), mean (SD) [n]	66.6 (22.5) [26]	58.9 (25.5) [79]	0.21
Patient fatigue (VAS 0-100), mean (SD) [n]	54.3 (26.3) [26]	53.1 (25.9) [80]	0.81
Morning stiffness, n/m (%)			0.77
< 30 minutes	5/26 (19.2)	13/80 (16.3)	
≥ 30 minutes	21/26 (80.8)	67/80 (83.8)	
HAQ-S (0-3), mean (SD) [n]	0.78 (0.63) [4]	0.99 (0.73) [18]	0.61
EQ VAS (0-100), mean (SD) [n]	55.8 (21.3) [26]	55.2 (21.6) [80]	0.82
WPAI domains, mean (SD) [n]			
Current employment, n/m (%)	19/26 (73.1)	42/80 (52.5)	0.07
% Work time missed	10.7 (14.3) [17]	11.9 (25.3) [42]	0.32
% Impairment while working	43.3 (24.4) [19]	36.1 (23.8) [42]	0.28
% Overall work impairment	46.9 (26.4) [17]	41.7 (28.8) [42]	0.52
% Activity impairment	51.0 (28.7) [26]	48.5 (28.1) [79]	0.69

ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; EQ, Euroqol questionnaire; HAQ-S, Health Assessment Questionnaire for the Spondyloarthropathies; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment Questionnaire.
* Other biologics included adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab.

Conclusion: In this real-world study of US patients with AS, secukinumab initiators had similar demographics, clinical outcomes, disease burden and patient reported outcomes compared with other biologic initiators, with the exception of higher prior biologic use.

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THU0398 GAIT 3D KINEMATICS UNVEILS A SPECIFIC PATTERN IN PATIENTSIN EARLY YEARS OF AXIAL SPONDYLOARTHRITIS INDEPENDENT OF THEIR BODY COMPOSITION AND MUSCLE PERFORMANCE VARIABLES

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease characterized by a progressive mobility reduction of the rachis. The postural changes may cause balance problems with gait repercussions. However, we lack information during the early years of the disease regarding gait pattern and the possible variables that may influence gait parameters.

Objectives: In order to gain insight into the gait patterns in patients at early stages of axSpA and the potential influence of some patient-specific features, the aim of this study was therefore to evaluate: (i) the 3D gait signature in patients at early years of axSpA; and (ii) the relation between gait parameters, and body composition and muscle performance variables.

Methods: A cross-sectional study was conducted on 46 participants (18-50 years old), 23 patients with axSpA (according to ASAS criteria, with less than 10 years since symptoms onset) and 23 healthy controls, matched by gender and age, with a mean age of 37±7.5 years, predominantly males (60%). The patients with axSpA had 5±3.2 years of disease duration, with BASDAI and BASFI of 3±2.2 and 2±2.9, respectively. Subjects' movement was reconstructed using a 3D full-body kinematic model (Kinetikos, Coimbra, Portugal) fed by 15 inertial sensors placed in the head, arms, trunk, pelvis, thighs, shanks and feet. The primary outcomes comprise the general gait parameters such as gait deviation index, speed, cadence, stance duration, body vertical regularity (sample entropy), step length, range of movement and peak velocity of the different joints. Body composition was assessed by performing octapolar multifrequency bioelectrical impedance analysis (BIA; InBody 770). Muscle performance was assessed with a 60 second sit-to-stand test (STS60), while physical activity was controlled by the international physical activity questionnaire (IPAQ).

Variables (except age, disease duration, BASDAI, BASFI) are presented as median. Non-parametric tests were used to compare groups. Correlations between gait, body composition and skeletal muscle function parameters, were performed.

Results: Gait analysis showed statistically significant differences between axSpA and healthy control groups on gait deviation index (median 83 vs 87%, p=0.022, with higher score values representing similar performance to normal movement), speed (median 0.79 vs 0.85m/s, p=0.015), stance duration at the left side (median 68 vs 67s, p=0.027), left step length (median 0.47 vs 0.49m, p=0.008), and vertical regularity (median 0.39 vs 0.33, p=0.029, with higher values representing a less regular and predictable movement pattern). At the sagittal plane, patients showed higher values of left arm maximum flexion (median 14 vs 10°, p=0.011), lower lumbar extension peak velocity (median 45 vs 60°/s, p=0.016) and higher ankle angular peak velocity on right side (median 330 vs 299°/s, p=0.020). However, no statistically significant differences between groups were found for physical activity. In addition, no statistically significant correlation was found between the gait parameters and weight, body fat, torso fat, visceral fat, body mass index, total body water, extracellular water, fat free mass, lean mass, bone mineral content and STS60.

Conclusion: These results provide evidence that although young axSpA patients at early years of the disease display a particular gait pattern

and this behavior does not seem to be influenced by the body composition and muscle performance. The main determinant for this gait pattern remains an open question.

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THU0399 DEVELOPMENT OF AN OPTIMIZED ONLINE SELF-REFERRAL TOOL FOR EARLY RECOGNITION OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS (AXSPA) – DATA FROM THE ´OPTIREF´-STUDY

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Background: One of the major reasons for a long diagnostic delay in axial spondyloarthritis (axSpA) is the late referral of patients by primary care physicians dealing with patients with chronic back pain. We developed and implemented an online self-referral tool (www.bechterew-check.de), which gave access to a rheumatological consultation if patients declared suffering from chronic back pain (≥ 3 months) with a symptom onset ≤ 45 years of age, and at least one feature indicative of SpA. In the prospective "Identification of the Optimal Referral Strategy for Early Diagnosis of Axial Spondyloarthritis (OptiRef) Study" we could diagnose axSpA in 19% of the self-referred patients [1].

Objectives: To optimize the online-self-referral tool for recognition of patients with high suspicion of axSpA in order to increase the specificity by keeping the high level of sensitivity.

Methods: 181 patients who had fulfilled the online self-referral strategy were included and underwent a standardized rheumatology examination. The final diagnosis of axial SpA/no axial SpA by the rheumatologist served as the gold standard. The performance of all possible combinations of the referral parameters (13 parameters in total including 5 features of inflammatory back pain (IBP) and 8 other SpA features) added to both stem parameters (chronic back pain starting at age of ≤45 years) was tested. In addition, the following pre-specified combinations were evaluated: 1) ≥1 IBP parameter AND ≥1 other SpA parameter, 2) ≥1 IBP parameter OR ≥1 other SpA parameter. For all combinations, a sensitivity, a specificity, positive and negative predictive values (PPV and NPV), as well as a positive and negative likelihood ratio (LR+ and LR-) were calculated. We targeted the maximal specificity by acceptable sensitivity (defined as ≥90% of the original strategy).

Results: For 163 of the included patients, full data of the online questionnaire as well as of rheumatology examination including the final diagnosis was available. 31 (19%) of them were diagnosed with axial SpA. Raising the threshold of the number of positive parameters (table 1) resulted in a quick drop of the sensitivity. According to the pre-defined selection criterion, only a strategy with any four positive parameters would be acceptable. An analysis of combined strategies (IBP parameters and/or other SpA parameters) resulted into identification of a strategy with an improved performance: a combination of ≥2 IBP parameters with ≥1 other SpA parameters (in addition to both stem parameters) showed a sensitivity of 90% (28/31), a specificity of 27% (35/132), a PPV of 22% (28/125), a NPV of 92% (35/38), LR+ of 1.23 and LR- of 0.36. Thus, identifying 28 of 31 patients with axSpA would have been possible after the assessment of 125 patients instead of 163.

Conclusion: The data-driven optimized online self-referral tool (figure 1) requires the following parameters to be positive: chronic back pain (≥3 months) plus back pain onset before 45 years of age plus ≥2 IBP parameters plus ≥1 other SpA feature. The performance of this tool should be confirmed in a prospective study.

Abstract THU0399 –Table 1.

Table 1: Performance of self-referral strategies based on combinations of SpA parameters in addition to the stem parameters (chronic back pain starting at age of ≤45 years).

Number of fulfilled criteria* (≥)	Number of patients	PPV	NPV	Sensitivity	Specificity	LR+	LR-
1**	163	0.19 (31/163)		1.00 (31/31)			
2	158	0.20 (31/158)	1.00 (5/5)	1.00 (31/31)	0.04 (5/132)	1.04	0.00
3	147	0.21 (31/147)	1.00 (16/16)	1.00 (31/31)	0.12 (16/132)	1.14	0.00
4	128	0.22 (28/128)	0.91 (32/35)	0.90 (28/31)	0.24 (32/132)	1.19	0.40
5	114	0.23 (26/114)	0.90 (44/49)	0.84 (26/31)	0.33 (44/132)	1.26	0.48
6	74	0.31 (23/74)	0.91 (81/89)	0.74 (23/31)	0.61 (81/132)	1.92	0.42
7	48	0.38 (18/48)	0.89 (102/115)	0.58 (18/31)	0.77 (102/132)	2.55	0.54
8	27	0.48 (13/27)	0.87 (118/136)	0.42 (13/31)	0.89 (118/132)	3.95	0.65
9	17	0.59 (10/17)	0.86 (125/146)	0.32 (10/31)	0.95 (125/132)	6.08	0.72
10	7	0.43 (3/7)	0.82 (128/156)	0.10 (3/31)	0.97 (128/132)	3.19	0.93
11	1	1.00 (1/1)	0.81 (132/162)	0.03 (1/31)	1.00 (132/132)	-	0.97
12	1	1.00 (1/1)	0.81 (132/162)	0.03 (1/31)	1.00 (132/132)	-	0.97
13	1	1.00 (1/1)	0.81 (132/162)	0.03 (1/31)	1.00 (132/132)	-	0.97

*Criteria: insidious onset; improving with exercise, no improvement with rest; waking up in the second half of the night; morning stiffness ≥ 30 minutes; alternating buttock pain; good response to NSAIDs; arthritis/enthesitis ever; HLA-B27 positive; uveitis; psoriasis; inflammatory bowel disease; SpA family history; elevated acute phase reactants.

**The original strategy, reference for the calculation of the performance of all other strategies

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REFERENCES:

1. Proft F, et al. EULAR 2018, Abstract THU0230.

1	**Does your back pain last 3 months or longer?**	No □ Yes □
2	**Did your back pain start prior to 45 years of age?**	No □ Yes □
3	**What are the characteristics of your back pain?**	
	• The back pain onset was rather slow and was not related to a trauma	No □ Yes □
	• I suffer from stiffness in my back of 30 minutes or longer upon getting up in the morning	No □ Yes □
	• Movement or exercises (but not rest) improve my back pain	No □ Yes □
	• I wake up sometimes in the night (especially 2nd half) because of back pain	No □ Yes □
	• I have or I had alternating (flipping from side to side) pain in my buttocks	No □ Yes □
4	**Other signs and symptoms which might indicate an inflammatory nature of the back pain:**	
	• I took a nonsteroidal anti-inflammatory drug (such as Diclofenac or Ibuprofen) because of back pain, and pain was completely relieved or was much better after the drug intake	No □ Yes □
	• I have / had joint pain with swelling and/or inflammation in the areas of tendons insertion to the bone (e.g., heels).	No □ Yes □
	• The genetic marker HLA-B27 has been tested in my blood already and the result was „positive"	No □ Yes □
	• I have / had elevated markers of inflammation in the blood (C-reactive protein or erythrocyte sedimentation rate), which are unlikely to be explained by other reasons (such as infections)	No □ Yes □
	• I suffer from psoriasis	No □ Yes □
	• I suffer from inflammatory bowel disease (Crohn's disease or ulcerative colitis)	No □ Yes □
	• I suffer / suffered from (iritis)	No □ Yes □
	• One or several of my direct relatives suffer / suffered from ankylosing spondylitis, psoriasis or inflammatory bowel disease (Crohn's disease or ulcerative colitis)	No □ Yes □
	The strategy is fulfilled if 1 + 2 + ≥ 2 questions in the 3 + ≥ 1 question in the 4 are answered with yes.	

Abstract THU0399 – Figure 1. The data-driven optimized self-referral strategy.

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THU0400 COMPLICATIONS OF ANTERIOR UVEITIS ASSOCIATED WITH HLA-B27 ANTIGEN IN PATIENTS WITH AND WITHOUT SPONDYLOARTHRITIS

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Background: HLA-B27- associated anterior uveitis (AU) can be an isolated disease or part of a systemic inflammatory process, such as spondyloarthritis. Differences in the outcome of uveitis with and without spondyloarthritisare still under researh.

Objectives: To compare the incidence of complications in HLA-B27- associated anterior uveitis patients with and without spondyloarthritis (SpA).
Methods: 189 patients with HLA-B27- associated anterior uveitis were observed in Research Institute of Eye Disease for 10 years. The pts were underwent standard ophthalmological examination, and, if necessary, computer perimetry, ultrasound examination (B-scan.), optical coherence tomography of the retina and optic nerve (OCT), fluorescence fundus angiography (FAGD) and electrophysiological studies (EFI). All pts were examined for clinical and imaging signs of SpA: inflammatory back pain, arthritis, enthesitis, sacroiliitis.
Different variants of SpA were diagnosed in 108 pts: ankylosing spondylitis – in 48 (44,4%), reactive arthritis – in 9 (8,3%), psoriatic arthritis - in 9 (8,3%), inflammatory bowel disease – in 2(1,9%), juvenile SpA – in 4 (3,7%), undifferented SpA - in 36 (33,3%). In 81 pts SpA was not confirmed: 11 had a viral infection (13,5%), 7- bacterial infection (8,6%), 1 (1,2%)-multiple sclerosis, 3 (3,7%) -psoriasis, 59 (72,8%)- idiopathic AU.
Results: Complications were identified in 74 of 108 (68,5%) pts – 147 eyes in SpA-group and in 39of 81(48,1%) – 110 eyes in group without SpA. Cataract was identified in 89 (60,5%) of 147 eyes in SpA-group and in 35(1,8%) of 110 eyes in group without SpA, p=0,0001;glaucoma – in 28 of 147 eyes (19,0%) in SpA-group and 8 of 110 eyes (7,3%) in group without SpA, p=0,005; synechia - in 24(16,3%) and in 8 (7,3%) respectively, p=0,021;vitreous destruction - in 59(40,1%) and in 26 (23,6%), p=0,005. Maculopathy, optic atrophy, corneal degeneration, panuveitis were observed more often in SpA-group, but the differences were not significant. Combinations of several complications were detected in 59 (40,1%) in SpA-group and in 31 (28,2%) in group without SpA, p=0,03.
Conclusion: Complications of HLA-B27- associated AU were identified more often in pts with SpA than without SpA (the majority of which was idiopathic AU). It confirms the effect of systemic inflammatory disease on the severity of uveitis.

REFERENCE:

[1] Yang P, Wan W, Du L, et al. Clinical features of HLA-B27-positive acute anterior uveitis with or without ankylosing spondylitis in a Chinese cohort. Br J Ophthalmol. 2018 Feb;102(2):215-219. doi: 10.1136/bjophthalmol-2016-309499. Epub 2017 Jun 12

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THU0401 WOMEN WITH SPONDYLOARTHROPATHIES HAVE HIGHER DISEASE BURDEN ACCORDING TO RAPID3 COMPARED TO MEN, BUT THERE IS NO GENDER DIFFERENCES ACCORDING TO A MODIFIED ASDAS-CRP

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Background: Women with Spondyloarthropathies (SpA) may be late or under-diagnoses due to a less typical presentation than in men, with a more peripheral clinical manifestation. Although some studies have suggested a higher burden of disease in women[1, 2], others did not confirm these differences[3, 4]. In addition, women present higher scores for pain and fatigue, which may influence the BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) score [5].
Objectives: To evaluate possible gender differences in clinical presentation and disease severity in men and women with SpA in routine care at one academic center.
Methods: All patients complete a Multidimensional Health-Assessment Questionnaire (MDHAQ) as part of their routine care. It includes physical function (FN) (0-10), three 0-10 visual analogue scales (VAS) for pain (PN), patient global estimate (PATGL), and fatigue (FT), RADAI self-reported painful joints, and morning stiffness (MS). Patients with SpA (ICD10 codes) were included: ankylosing spondylitis (AS), psoriatic arthritis (PsA), undifferentiated, and inflammatory bowel disease associated (IBD). Data extracted were clinical presentation, treatment and laboratory tests including C-reactive protein (CRP), HLA-B27 (Human leukocyte antigen), and erythrocyte sedimentation rate (ESR). Composite indices, RAPID3 (0-30) previously validated in SpA, as the sum of 0-10 scores for FN, PN, and PATGL, and a modified ASDAS-crp using a *"back pain"* score derived from RADAI neck, back and hips; a "peripheral pain" score derived from the remaining RADAI joints; and MS in minutes were also included. Demographic and clinical characteristics were compared according to gender.
Results: 190 patients were included, 60% males and 40% females, with no differences in age, disease duration, and treatment. Men had significantly more frequent inflammatory back pain. Patient global assessment and pain scores were significantly higher in women versus men resulting in a higher RAPID3 (moderate disease severity in both groups). Axial, peripheral pain, morning stiffness and laboratory data did not show differences by gender, and as a result ASDAS-CRP was similar between men and women, with a value corresponding to moderate disease activity (Table).

Abstract THU0401 – Table 1. Demographic and clinical characteristics of patients with SpA by gender. Data as median (IQR) unless otherwise specified (*p<0.05)

	Men N=113	Women N=77
Age (yrs), mean (SD)	45.2 (14.4)	47.0 (15.3)
Self-reported race/ethnicity,% White/Black/Hispanic/Others	61/15/13/11	50/20/13/17
Disease duration, (yrs)	6.1 (1.4-11)	5.2 (2.1-9.3)
SpA subgroup,%: AS/PsA/Undifferentiated/IBD	57/24/16/3	36/29/31/4*
Peripheral arthritis,%	67%	69%
Inflammatory back pain%	78%	63%*
PROs-MDHAQ		
PATGL	2.5 (1.0-5.0)	5.0 (2.0-7.0)*
Axial pain-RADAI (neck, back and hips)	4 (0.8-5.0)	3.3 (1.7-5.8)
Peripheral pain-RADAI	0.9 (0.2-1.9)	0.9 (0-2.6)
Total PN	3.0 (1.0-6.0)	6.0 (2.0-7.5)*
MS (min)	30 (15-60)	37.5 (15-120)
Fatigue	2.0 (0-6.0)	5 (2.0-8.0)*
Laboratory Data		
HLA-B27 positive,%	66.7%	67.4%
CRP (mg/L)	5 (5-15.6)	5 (5-15.6)
ESR (mm/h)	12 (4-29)	19.5 (9-33)
Composite index, mean (SD)		
RAPID3	7.7 (6.9)	10.9 (7.5)*
Modified ASDAS-CRP	1.8 (0.9)	1.9 (0.9)

Conclusion: Women with SpA have higher RAPID3 scores than men, in contrast to a modified ASDAS-CRP based on scores from the MDHAQ which did not show gender differences. These data suggest that RAPID3 scores in women may be attributable in part to a gender bias rather than clinical severity and a careful interpretation in the context of gender is necessary.

REFERENCES:

[1] Ann Rheum Dis. 2013; 72(7):1221-4.
[2] Reumatol Clin. 2013; 9(4):221-5.
[3] Rheumatology (Oxford). 2014; 53(5):875-81.
[4] Clin. Rheumatol. 2015; 34(2):285-93.2015.
[5] Ann Rheum Dis. 2017; 76: Suppl.2. 657-658.

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THU0402 CONTRIBUTION OF THE EOS IMAGING SYSTEM IN ASSESSING PELVIC AND SPINAL DEFORMITIES IN SPONDYLOARTHRITIS

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Background: The severity of Spondyloarthritis (SA) lies mainly in the progressive ankylosis of the axial skeleton and the deformations generated. The means of assessing the spinal static disorders in SA are currently subjective and difficult to reproduce. Multidisciplinary collaboration has led to the development of a new biplane low dose radiology technology named EOS. It allows a simultaneous acquisition of the axial skeleton and the lower limbs in a standard standing position.
Objectives: We aimed to assess pelvic and spinal parameters and spinal stature in patients with SA using the EOS system.
Methods: This is a prospective cross-sectional study conducted over a 10-month period (January-October 2018) involving 50 patients with SA meeting the criteria of Assessment of SpondyloArthritis International Society. An entire body EOS examination of the vertebral column in a standardized standing position was performed in all patients. Pelvic parameters measured by the EOS system were pelvic incidence (PI: normal value:

48-55°), sacral slope (SS: normal value: 36-42°) and lateral pelvic tilt (LPT: normal value: 12-18°). Spinal stature parameters were thoracic kyphosis (normal value: 41-48°), lumbar lordosis (normal value: 43-61°), sagittal vertical axis (SVA: normal value: <30mm) and spinosacred angle (SSA: normal value: <132).

Results: We enrolled 29 men (58%) and 21 women (42%) with an average age of 42.6 ± 11.09 years [20 -79]. The mean duration of SA was 12.4 ± 9.71 years [2-46]. SA was axial in 17 patients (34%), and axial and peripheral in 29 patients (58%). The median PI was 50.7 ± 11.81°. The median SS was 35.8 ± 11.64°. The median LPT was 14.9 ± 8.97°. The average value of thoracic kyphosis was 52.1± 12.1°. The average value of lumbar lordosis was 37.4 ± 16. The median SVA was 25.2 ± 55.88 mm and the median of SSA was 123.9 ± 16.64°. Thus, deformity of the thoracic spine was found in 40 patients (80%) with thoracic hypercyphosis type and thoracic rectitude in 12% and 68% of cases respectively. The deformity of the lumbar spine was found in 40 patients (80%) with lumbar hyperlordosis type and lumbar rectitude in 74% and 6% of cases respectively. From this construction and segmenting the SS values, we were able to classify the type of back according to Roussouly : the type 2 back was the most frequently found (40%), followed by type 3 back (34%), type 4 back (24%), and type 1 back (2%). Spinal deformities were more frequent in women (p=0.004) and associated with a longer duration of the disease (p<0.0001) and a longer duration before initiation of treatment (p<0.0001) (Table 1).

Conclusion: Our study showed that the EOS system was a useful technique in assessing pelvic and spinal stature in patients with SA.

Abstract THU0402 –Table 1. Association of the spinal deformities with clinical parameters

Parameter	Spinal deformities
Female sex	p=0.004
Age	p=0.126
Duration of the disease	p<0.0001
Active disease	p=0.233
Axial spondyloarthritis	p=0.146
Duration before treatment	p<0.0001

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THU0403 AXIAL SPONDYLOARTHRITIS INDUCES MUSCLE DISFUNCTION, THE ROLE OF BODY COMPOSITION PARAMETERS: MYOSPA STUDY

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Background: Sarcopenia as well as abnormalities in body composition are common features in several chronic diseases and have been shown to lead to increased morbidity and mortality. However, their assessment in young patients with axial spondyloarthritis (axSpA) has not been performed thus far.

Objectives: To assess the skeletal muscle mass, strength and performance as well as body composition in patients with axSpA compared to healthy controls.

Methods: Patients between 18 and 50 years of age with the diagnosis of axSpA and short disease duration (under 10 years) and classified according to the ASAS criteria were included. Healthy individuals matched by gender and age (1:1) were used as control group. Muscle strength (MS) was assessed by resisted flexion of the dominant forearm using a hand dynamometer. Muscle performance was assessed with the 60 second sit-to-stand test (STS60) and with 5 times sit-to-stand test (STS5). Body composition was assessed with octapolar multifrequency bioelectrical impedance analysis (InBody 770). The level of physical activity was measured by the IPAQ questionnaire. BASDAI and BASFI were used to evaluated disease activity and function, respectively. All measures (except age and disease duration) are reported as median and 25th and 75th percentiles. Non-parametric tests were used to compare groups.

Results: A total of 27 patients and 27 controls were included [mean age (36.5 ± SD 1.0), 66% males]. AxSpA patients had symptom duration of 7.0 ± SD 0.9 years, BASDAI 2.7 (1.4-3.6) and BASFI 0.9 (0.3-3.2). Compared to controls, axSpA patients had less MS in the dominant upper limb (DUL) (46.0 (37.5-70.6) vs 71.2 (54.1-83.4) kg, p=0.006) and worse performance on the STS60 test (48.0 (27.5-64.3) vs 63.0 (53.0-68.0) repetitions, p=0.010). These differences were maintained after normalization for lean mass (LM) (MS_DUL/LM_DUL and STS60/Total_LM). In addition, compared to controls, axSpA patients had higher body fat (BF) (19.8 (12.1-29.1) vs 15.7 (10.1-22.2) kg, p=0.041), torso fat (TF) (10.3 (6.3-15.9) vs 8.1 (5.1-11.1) kg, p=0.450) and visceral fat (VF) (87.3 (52.7-145.1) vs 65.4 (41.8-96.4) cm^2, p=0.034). No differences were registered for weight, body mass index, total body water, extracellular water, fat free mass, LM and bone mineral content between groups. The level of physical activity, measured by the IPAQ questionnaire, was identical between patients and healthy controls (p=0.500).

Conclusion: Compared to healthy controls, young axSpA patients have a reduction in muscle strength and muscle performance with maintenance of muscle mass and levels of physical activity. These preliminary results underline the relevance of further investigations.

Abstract THU0403 – Table 1. Subject characteristics

Variable	Patients N=27	Controls N=27	p-value
Age (years)	37 (32-43)	36(30-44)	0.808
Gender (♂% : ♀%)	66.7:33.3	66.7:33.3	0.922§
Symptom duration (years)	7.0 (4.0-10.0)	———	———
IPAQ (low% : moderate-high%)	29.2:70.8	20.8:79.2	0.505§
LM (Kg)	50.1 (44.5-57.8)	54.1 (43.2-60.2)	0.592
BF (Kg)	19.8 (12.1-29.1)	15.7 (10.1-22.2)	0.041
TF (Kg)	10.3 (6.3-15.9)	8.1 (5.1-11.1)	0.045
VF Area (cm2)	87.3 (52.7-145.1)	65.4 (41.8-96.4)	0.034
MS_DUL (Kg)	46.0 (37.5-70.6)	71.2 (54.1-83.4)	0.006
STS60 test (repetitions)	48.0 (27.5-64.3)	63.0 (53.0-68.0)	0.010

*Values are median (IQR) unless otherwise indicated. Comparison between patients and controls tested by paired samples *t*-test unless otherwise indicated. §Comparison between patients and controls tested by Chi-Square test in Gender and Physical Activity variables.

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THU0404 DICKKOPF-1 SERUM LEVELS AND THEIR CORRELATION WITH ACTIVE AND CHRONIC MRI-CHANGES OF SACROILIAC JOINTS AND CLINICAL INDICES IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: The lack of valid biochemical markers for spondyloarthritis (SpA) patients requires searching the additional options to increase sensitivity of clinical and radiological methods in validation of changes in sacroiliac joints (SIJ). The molecular basis for the link between inflammation and new bone formation in SpA is still not clear. It has recently been shown that low serum levels of the Dickkopf-1 (Dkk-1), the natural inhibitor of Wnt protein, is associated with the formation of new syndesmophytes in patients with SpA [1]. Dkk-1 may be a main factor in blocking new bone formation [2], and might play a role of potential biomarker in SpA patients.

Objectives: To determine the serum levels of Dkk-1 and their relationship with active and chronic changes in SIJ on MRI, indices and laboratory parameters of disease activity and functional status in SpA patients.
Methods: This study includes 105 SpA patients (89.5% HLA B27 positive) and 15 healthy age- and gender- matched controls. Dkk-1 serum levels (pmol/l) were conducted by ELISA. Active inflammatory lesions in SIJ were evaluated by Spondyloarthritis Research Consortium of Canada (SPARCC) MRI SIJ score (0-72, n=69) and chronic changes by Danish scoring method (0-48). Bath Ankylosing Spondylitis Disease Activity Index (BASDAI, mm), Bath Ankylosing Spondylitis Functional Index (BASFI, mm), C-reactive protein (CRP, mg/l) and erythrocyte sedimentation rate (ESR, mm/hr) were recorded. Statistical analysis was performed using Spearman correlation coefficient, Student t-test and receiver operating characteristic (ROC) curves.
Results: Mean value (M±σ) of Dkk-1 was 45.1±36.3. The mean value of indices and laboratory parameters were: BASDAI – 44.5±19.3, BASFI – 31.1±23.1, CRP – 20.6±31.3, ESR – 26.8±22.0. SPARCC score was 22.2±12.0, Danish score – 19.5±9.83. Dkk-1 serum levels were lower ($P < 0.01$) in SpA patients compare with the controls. ROC analysis indicated that the AUC for Dkk-1 is 0.88±0.05 ($p<0.001$), which indicates strong capacity to differentiate groups of SpA patients with healthy controls (sensitivity - 87%, specificity - 79%).
There was significant negative correlation between Dkk-1 with chronic lesions in SIJ by Danish score ($r=-0.250$, $p=0.046$). Dkk-1 showed positive correlation with CRP ($r=0.216$, $p=0.028$).
There was no significant correlation of serum Dkk-1 levels with SPARCC, BASDAI, BASFI and ESR.
Conclusion: Dkk-1 levels are significantly lower in SpA patients compare with healthy controls and has a strong association with SpA. Dkk-1 significantly negatively correlates with chronic changes in SIJ on MRI, that may confirm that deficiency of Dkk-1 could increase progression of pathological changes in SIJ. Dkk-1 correlates only with CRP level, but none of the other indices and laboratory parameters of disease activity and functional status.

REFERENCES:
[1] Song I-H. Ann Rheum Dis. 2011; 70: 1257-1263.
[2] Zhao Z. Clin Rheumatol. 2018. doi: 10.1007/s10067-018-4284-y.

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THU0405 PREVALENCE OF FIBROMYALGIA IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS: A SINGLE CENTRE OBSERVATIONAL PROSPECTIVE STUDY

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Background: Joint pain is frequently reported by IBD patients and can be associated to extra-intestinal manifestations of diseases or adverse events associated to anti-TNF or vedolizumab therapy and also associated with other non-SpA-disease related factors including mechanical/degenerative problems. An appropriate rheumatological referral pathway is crucial to drive therapeutic strategy in case of concomitant spondyloarthritis (SpA). Fibromyalgia is a frequent cause of chronic pain that needs to be identified in order to not overestimate the prevalence of SpA in IBD patients
Objectives: The aim of the study was to assess the prevalence of FM in a cohort of IBD outpatients
Methods: Consecutive patients of the IBD Unit coming for a routine visit were screened by a rheumatologist in order to identify cases presenting the 2010 ACR criteria for FM or ASAS criteria for SpA (1,2). Patients affected by other rheumatic conditions such as rheumatoid arthritis and crystal arthritis were excluded from the study. The rheumatological assessment included a 66 swollen joint count (SJC) and 68 TJC, MASEI, LEI and the fibromyalgia tender points examination. The patient completed BASDAI and BASFI on the day of clinical evaluation. Imaging exams (MSK ultrasound, MRI) and HLA-B27 determination were requested if needed for diagnostic confirmation
Results: Between January to May 2018, 210 patients were enrolled in the study and 181 completed the clinical and imaging/laboratory assessment if requested for diagnostic purpose. examination. A total of 44 patients (24.3%) in the IBD cohort met the ACR 2010 criteria for FM. 34 patients (18.8%) presented the criteria for primary FM, and 10 patients (5.5%) presented FM and SpA. Of note FM patients presented LEI; BASDAI and BASFI scores higher than SpA patients
Conclusion: FM is a common comorbidity in IBD patients and can be associated to SpA. An appropriate rheumatological referral is crucial exclude a concomitant SpA and to manage FM

REFERENCES:
[1] Wolfe, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care and Research. 2010;62(5):600–610.
[2] Rudwaleit M, et al. The Assessment of SpondyloArthritis international Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis 2011;70:25–31

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THU0406 ULTRASONOGRAPHIC INVOLVEMENT OF THE ANTERIOR CHEST WALL IN SPONDYLOARTHRITIS, A FIVE YEARS FOLLOW UP STUDY

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Background: Spondyloarthrits is characterized by inflammatory back pain. Anterior chest wall pain is common and a previous study reported a prevalence à 37% of ultrasonographic lesions of this anatomical region [1].
Objectives: The objective of this study is to evaluate, in patient with Spondyloarthritis, the prevalence of ACW ultrasonographic lesions after a follow up of 5 years and to identify factors associated with the development of new lesions.
Methods: This a monocentric and prospective study including patients with Spondyloarthritis meeting the ASAS 2009 criteria. Patients were followed during five years. ultrasound B mode and power Doppler examination of the two sternoclavicular joint and the manubrio-sternal joint were performed by the same two examinators at baseline and five years later. The presence of erosion, synovitis, ankylosis, power Doppler signal, joint effusion and bone margin narrowing were assessed. Clinical characteristics and disease activity were evaluated at 5 years.
Results: In the 136 patients at baseline, 58 patients were evaluated 5 years later. The mean age was 48.2 +/- 11.9 years old, with 86% male and 89% HLA B27. 60.3% of these patients had a history of pain of the ACW. The prevalence of ultrasonographic involvement of the ACW was 34% at baseline and 67.2% five years later. The most frequent lesions were ankylosis of the manubriosternal joint (38%) and erosions of the sternoclavicular joint (29%). At 5 years, patients with lesions of the ACW are significantly older (51.4 +/- 11.5 VS 41.5 +/- 9.98, $p<0,01$). There were no differences concerning the presence of HLA B27 and the presence of a radiographic sacroilitis or syndesmophytes. Among these 58 patients, 31 (53%) developed a new lesion of the ACW. There is a statistically significant association between a higher ASDAS CRP and new lesions of the ACW (1,86 +/- 1,07 VS 3,0 +/- 2,17 $p < 0,01$) and with the level of CRP (5,34 +/- 7,85 VS 16,2 +/- 35, $p = 0,035$). Baseline ASDAS CRP is not a predictor of new chest wall lesions prior to 5 years of age. Nevertheless, poor control of disease activity is associated with the development of new lesions. Patients with new lesions have an ASDAS CRP score that increase (0,882 +/- 2,48) between 2013 and 2018, while patients with no new lesions have an ASDAS CRP score that decrease (-0,641 +/- 1,50) between 2013 and 2018.
Conclusion: The prevalence of ultrasonographic lesions of the ACW increased after 5 years of follow up. The development of new lesions is associated with a higher disease activity, a higher CRP and an increased disease activity over 5 years.

REFERENCES:
[1]]Verhoeven f. et al. Ultrasonographic evaluation of the anterior chest wall in spondyloarthritis: a prospective and controlled study.J Rheumatol. 2015;42:87-92.

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THU0408 ACHIEVING DISEASE REMISSION IN AXIAL SPONDYLOARTHRITIS: A TWO-CENTRE RETROSPECTIVE ANALYSIS OF RELEVANT BASELINE PATIENT CHARACTERISTICS

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Background: ASAS-EULAR Axial Spondyloarthritis (AxSpA) guidelines recommend that AxSpA treatment should be guided according to a predefined target[1], following increasing evidence that persistent, uncontrolled inflammatory disease activity results in long-term damage and poor outcomes[2,3]. Despite this, there remains no single definition for "remission" in AxSpA.
Objectives: To identify baseline characteristics of individuals achieving AxSpA disease "remission" 6 months after initiation of biologic disease-modifying therapy (bDMARD).
Methods: A two-centre retrospective cross-sectional analysis was performed, of AxSpA patients receiving their first bDMARD at the Royal National Hospital for Rheumatic Diseases, Bath, and Norfolk and Norwich Univeristy Hospital, Norwich. AxSpA "remission" was defined as Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) <1; Bath Ankylosing Spondylitis Functional Index (BASFI) <3.8 or serum C-reactive protein (CRP) <5. A non-parametric (2-tailed Chi-Square) test was applied to identify differences in baseline characteristics which distinguished those patients achieving "remission" after 6 months bDMARD treatment from others.
Results: 538 patients were included. Sufficient BASDAI data was available for 440, CRP data for 448 and BASFI data for 354. Overall, 42 (9.5%) patients achieved BASDAI <1; 275 (61.4%) achieved CRP <5 and 206 (58.2%) achieved BASFI <3.8. The differences in baseline characteristics of individuals achieving these AxSpA "remission" outcomes compared with others are summarised in Table 1, with statistically significant results at the 95% level highlighted.

Abstract THU0408 – Table 1. p-values of 2-tailed non-parametric test comparing baseline characteristics of individuals achieving AxSpA "remission" outcomes after 6 months versus others.

Baseline characteristics	p-values		
	BASDAI <1 N=42/440	**CRP <5** N=275/448	**BASFI <3.8** N=206/354
Lower mean age at axSpA diagnosis	**0.04**	0.78	0.09
Less mean time from diagnosis to bDMARD initiation	0.56	**0.00**	0.66
Lower median baseline BASDAI	0.35	0.39	**0.00**
Lower median baseline CRP	**0.01**	**0.00**	0.67
Lower median baseline BASFI	0.08	**0.04**	**0.00**
Lower median baseline BASMI	0.73	0.44	**0.00**
HLA B27+	0.21	0.06	0.10
Male sex	0.87	0.52	0.62

Conclusion: Our self-defined measures of BASDAI and CRP remission were most achievable in our cohort for patients with lower CRP and less functional limitation before bDMARD initiation. This may reflect remission being more achievable when treating milder disease. Functional "remission" was influenced by baseline BASMI and BASDAI in our cohort, highlighting the importance of both disease activity and pre-existing structural damage on functional outcomes. Further work could include longitudinal follow-up of outcomes in these patients to establish the relevance of targeting AxSpA remission. "BASDAI remission" was very narrowly defined in this study, and this analysis could be repeated with a more achievable target eg BASDAI <3.

REFERENCES:

[1] Van der Heijde D, et al. 2016 *update of the ASAS-EULAR management recommendations for axial spondyloarthritis*. Ann Rheum Ds *2017;* 76 (6): 978-91.
[2] Ramiro S, van der Heijde D, van Tubergen A, et al. Higher disease activity leads to more structural damage in the spine in ankylosing spondylitis: 12-year longitudinal data from the OASIS cohort. Ann Rheum Dis 2014;73:1455–61.
[3] Poddubnyy D, Protopopov M, Haibel H, et al. High disease activity according tothe Ankylosing Spondylitis Disease Activity Score is associated with accelerated radiographic spinal progression in patients with early axial spondyloarthritis: results from the GErman SPondyloarthritis Inception Cohort. Ann Rheum Dis 2016;75:2114–18.

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THU0409 PATTERN AND INFLUENTIAL FACTORS IN PROMOTING TREAT-TO-TARGET (T2T) FOR FOLLOW-UP ANKYLOSING SPONDYLITIS (AS) PATIENTS WITH A RHEUMATOLOGIST-PATIENT INTERACTIVE SMART SYSTEM OF DISEASE MANAGEMENT (SSDM): A COHORT STUDY FROM CHINA

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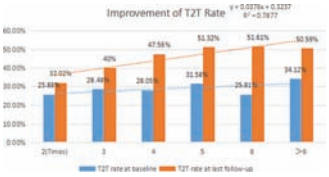
Background: Ankylosing Spondylitis Disease Activity Score (ASDAS) is adopted to evaluate the degree of disease activity and the inflammatory response in AS patients. ASDAS score ≤ 1.3 represents inactive disease status and achievement of T2T.
Objectives: To evaluate the patterns of T2T and related influential factors among AS patients after applying SSDM in the real world.
Methods: SSDM is a mobile application for disease management. Patients were trained to master SSDM by healthcare professionals and to conduct ASDAS self-assessments. Patients were also required for repeating self-evaluation after leaving the hospital. After entry by patients, data can synchronized to the SSDM terminal of authorized rheumatologists.
Results: From Jan 2015 to Jan 2019, 667 AS patients across China were followed up for more than 6 months through SSDM. The results at baseline and in final follow up were summarized in Table 1. The rate of T2T achievers were 28.49% (190/667) at baseline, and improved significantly to 41.38% (276/667) after 6 months follow up, $p<0.01$. Among T2T achievers at baseline, 64.21% (122/190) maintained T2T, 35.79% (68/190) relapsed. Of patients who didn' t achieve T2T at baseline, only 32.29% (154/477) of the other AS patients achieved T2T after 6 months follow up. We further analyzed the impact of the times of self-assessment for ASDAS on T2T. The patients were stratified according to their frequency of self-assessment: more than 3 times, less than or equal to 3 times self-assessments within 6 months follow-up. Results show that the more frequent of the self-assessment, the higher improvement of T2T rate (19.34% vs. 8.40%, Table 2). A linear regression analysis of variables in statistics and parameter estimation was conducted by least square method. The improvement of T2T rate(y) was positively correlated with times of self-assessment for ASDAS(x) independently (Figure 1).
Conclusion: Significant improvement was observed under applying SSDM through empowering AS patients. After proactive disease management via SSDM for more than 6 months, Patients with ASDAS≤1.3 score at baseline had a significantly higher retention rate of disease activity. The patients who performed more self-assessments through SSDM had lower probability of relapse and higher rate of T2T. SSDM is a valuable tool for long term follow-up through empowering patients.

Abstract THU0409 – Table 1.

Baseline\Last follow-up	Number	%	ASDAS≤1.3	%	ASDAS≥1.3	%
ASDAS≤1.3	190	28.49%	122	64.21%	68	35.79%
ASDAS≥1.3	477	71.51%	154	32.29%	323	67.71%
Total	667	100%	276	41.38%	391	58.62

Abstract THU0409 – Table 2.

Self-Assessments	Number	Baseline (T2T rate)	Last follow-up (T2T rate)	Improvement
≤3 times	393	26.97%	35.37%	8.40%
>3 times	274	30.66%	50.00%	19.34%



Abstract THU0409 – Figure 1.

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THU0410 UVEITIS RELATED FACTORS IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Uveitis is the most common extra-articular feature of spondyloarthritis (SpA). Sometimes uveitis may be the only clinical finding of SpA leading to diagnosis. In the current literature, there is information about frequency and characteristics of uveitis in SpA patients; however, factors associated with uveitis are not clear(1,2).
Objectives: Our aim in this study was to analyze uveitis-related factors in a large cohort of SpA patients.
Methods: This multicenter, prospective observational cohort study used the TReasure database in which web-based registration of rheumatoid arthritis and SpA patients are being performed in 15 centers across different regions of Turkey. Age, gender, duration of illness, delayed onset, SpA clinical findings, HLA B27 and acute phase responses (erythrocyte sedimentation rate and C-reactive protein, BASDAI and BASFI values, clinical findings and direct X-ray findings of SpA patients with and without uveitis were retrospectively evaluated.
Results: As of January 2019, there were 4557 registered SpA patients. Overall, 491 (10.8%) patients had experienced one or more episodes of uveitis. The median (Q1-Q3) uveitis onset age was 46 years (38-53 years) and the median (Q1-Q3) uveitis attack number was 2 (1-4). Uveitis was usually unilateral (74.2%). Records of eye damage was available in 373 patients, of whom 45 (12.1%) had permanent damage in the eye. Patients with permanent eye damage had more frequent uveitis attack (3 (2-6) vs. 2 (1-3), p=0.003) and had tendency of bilateral uveitis attack (41.5% vs 24%, p=0.017).
Duration between the first uveitis attack and onset of SpA symptoms was 68 months (7-141). On the other hand, the mean duration between the first uveitis attack and SpA diagnosis is 7 months (17-68 months). In 320 patients (70%), uveitis was diagnosed before the onset of SpA symptoms and 52% (n=240) of the patients had uveitis before SpA diagnosis.
Demographic and clinical features of the patients are given in Table 1.
Conclusion: In our cohort, genetic background, radiographic severity, and disease duration may be related with uveitis. HLA B27 positivity and family history may be risk factors for development of uveitis. First attack of uveitis is nearly always before the onset of symptoms and diagnosis of SpA. Although uveitis is usually self-limited; however, almost 10% of SpA patients may have permanent eye damage. Thus, patients with uveitis should be carefully investigated because it may be the diagnostic feature of SpA.

Abstract THU0410 –Table 1.

Table 1. Comparison of demographic, clinical, and laboratory findings of the patients with and without uveitis

	Uveitis (-) n=4066	Uveitis (+) n=491	p
Sex (Male/Female, %)	55.6/44.4	59.7/40.3	0.083*
Age, year, median (Q1-Q3)	42 (35-50)	48(38-53)	<0.001*
Delay time of diagnosis, months, median (Q1-Q3)	24 (5-71)	37 (5-97)	0.002*
Duration of disease, months, median (Q1-Q3)	82 (43-140)	129 (73-202)	<0.001*
Enthesitis, n (%)	615 (28.1)	83 (33.5)	0.075**
Dactylitis, n (%)	178 (6.6)	17 (5)	0.252**
Psoriasis, n (%)	640 (15.9)	21 (4.3)	<0.001**
HLA B27 (+), n (%)	1156 (49.3)	218 (70.6)	<0.001**
Family history for SpA, n (%)	1091 (29)	180 (40)	<0.001**
Sacroiliitis, n (%)	2098 (88.7)	317 (94.3)	0.002
Syndesmophytes, n (%)	460 (24.5)	119 (45.2)	<0.001**
Bamboo spine, n (%)	241 (11.2)	70 (23.1)	<0.001**
BASDAI, median (Q1-Q3)	5.8 (4.1-7)	5.5 (3.7-6.8)	0.007*
BASFI, median (Q1-Q3)	4.4 (2.4-6.1)	3.7 (1.9-5.2)	0.007*
ESH, mm/h, median (Q1-Q3)	22(10-38)	26 (11-46)	0.008*
CRP, mg/L, median (Q1-Q3)	12.1 (4.6-27.6)	13.5 (6.1-34)	0.016*

*Mann Whitney U test, **Chi-Square test

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THU0411 **CLINICAL, ECONOMIC, AND HUMANISTIC BURDEN ASSOCIATED WITH DELAYED DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW**

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Background: Delayed diagnosis in patients with axial spondyloarthritis (AxSpA) has been shown to negatively impact disease prognosis and contributes to worse economic and quality of life outcomes; however, there is limited evidence available regarding the association of delayed diagnosis of AxSpA with the comprehensive burden of disease.
Objectives: To identify and summarize current published literature evaluating the clinical, economic, and humanistic burden associated with delayed diagnosis in patients with AxSpA.
Methods: This systematic literature review was conducted and reported according to the PRISMA guidelines (**Figure 1**.).[1] Publications were retrieved from the MEDLINE® (including MEDLINE® In-Process) and Embase® databases. English-language publications of original research articles (up to July 12, 2018) and conference abstracts (2014 to 2018) reporting studies of delayed diagnosis of adult patients with AxSpA associated with clinical, economic, or humanistic burden were eligible for inclusion. Abstracts from all records retrieved from the literature search were screened for eligibility by two independent reviewers (first-level screening); discrepancies between reviewers were resolved by a third independent reviewer. Citations that did not match the eligibility criteria and duplicates of citations were excluded at the abstract screening stage. Full-text publications underwent second-level screening as described for first-level screening. Data were extracted from all records that met the eligibility criteria after second-level screening.
Results: Of the 1391 publications retrieved, 21 studies from 13 countries (Argentina, Australia, China, Egypt, Korea, India, Iran, Ireland, Israel, Italy, Morocco, Turkey, and the United Kingdom) were included (**Figure 1**.); 15 reported clinical burden, 7 reported economic burden, and 4 reported humanistic burden (6 studies reported data on a combination of clinical, economic, and/or humanistic burden [**Table 1**]). Patients with delayed diagnosis of AxSpA generally had worse clinical outcomes, including higher disease activity (Bath Ankylosing Spondylitis Disease Activity Index), poorer mobility and physical function (Bath Ankylosing Spondylitis Functional Index), and more structural damage, compared with patients who had an earlier diagnosis (**Table 1**). Patients with delayed diagnosis also had higher healthcare costs, including costs of unnecessary treatments, and greater likelihood of work disability compared with those who had an earlier diagnosis (**Table 1**). Delayed diagnosis was associated with worse quality of life, including greater likelihood for depression and negative psychological impact (**Table 1**).

Abstract THU0411 –Table 1.

Table 1. Study Characteristics and Outcomes Related to Delayed Diagnosis of AxSpA

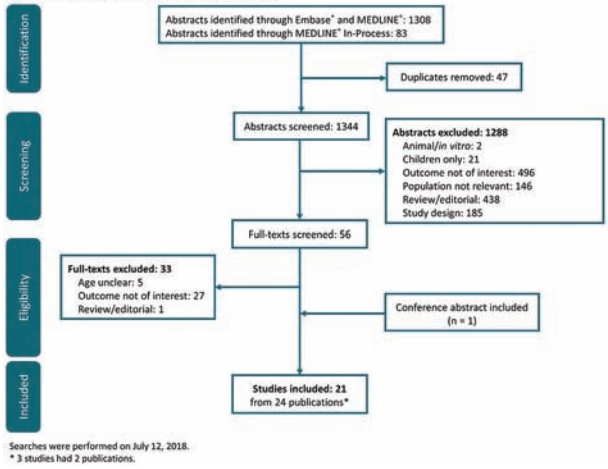
Ref	Patient Pop.	N	Study Type*	Impact of Diagnostic Delay
1	AS	281	C	Poorer sleep quality
2	AxSpA	1084	E	Delay of 3 years result in ≈ €153,000 in patient costs related to specialist visits and unnecessary drugs
3	AS	190	E	Greater likelihood of work disability
4	AxSpA	564	C	Longer delays were associated with higher prevalence of depression; patients with depression had worse QoL outcomes than those without depression
5	AS	163	C, H	Poorer QoL and function, more severe disease activity, and greater limitation of spinal and hip mobility
6	SpA	105	C	Worse clinical outcomes and poorer treatment responses in patients with SpA
7	AS	85	C	Worse outcomes in BASFI score and more radiographic damage
8	AS	256	C	Associated with severe hip disease in patients with AS; the severity of hip involvement was associated with functional status
9	AS/AxSpA	10	H	Negative psychological impacts including desperation, distress, depression, and feeling disheartened; employed patients felt stigmatized by the perception of a "bad back"
10	AS	106	C, E	Significantly worse mobility and work disability, both of which were highly dependent on age at diagnosis; however, no significant impact on BASDAI, BASFI or current TNFi use in this cohort
11	AS	60	C	Patients with a delay > 3 years had worse BASFI scores than those with a delay < 3 years
12	AS	92	C	No association with employment status or likelihood of biologic treatment
13	AS	147	C, H	No substantial impact on functional capacity, QoL, or radiographic damage in this cohort
14	AS	100	C	Significantly greater structural damage (BASRI) and severely limited spinal mobility in patients with a delay > 5 vs < 5 years; however, there was no correlation between diagnostic delay and disease activity
15	AS	127	C, E	Associated with significant economic burden with respect to treatment cost and employability
16	AxSpA	148	C	Patients with a delay > 1 year had a greater occiput-to-wall difference, indicating less spinal flexibility, than those diagnosed within 1 year
17	AS	59	E	The overall mean delay in diagnosis of AS was 7 years; longer delay in diagnosis was correlated with a greater likelihood of work disability
18	AS	121	C, E, H	Longer delay was associated with greater work disability
19	AS	70	C	Significantly worse BASDAI, BASFI, and BASMI scores
20	AS	111	C	No significant differences in BASDAI or BASFI scores between patients with a delay < 3 vs > 3 years
21	AxSpA	126	C, E	More doctor visits, more unnecessary spinal surgeries, higher direct healthcare costs, worse BASDAI, BASFI, and BASMI scores

* C, clinical; E, economic; H, humanistic.
AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis international Society; AxSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; BASRI, Bath Ankylosing Spondylitis Radiology Index; HLA B27, human leukocyte antigen B27; QoL, quality of life; SpA, spondyloarthritis; TNFi, tumor necrosis factor inhibitor.

References
1. Nio A, et al. *Clin Rheumatol.* 2018;37:2161-8.
2. Mennini FS, et al. *Clinicoecon Outcomes Res.* 2018;10:45-51.
3. Abdul-Sattar A, About El Magd S. *Int J Rheum Dis.* 2017;20:2028-34.
4. Fitzgerald G, et al. *Rheumatology (Oxford).* 2017;56:i93-4.
5. Fallahi S, Jamshidi AR. *Arch Rheumatol.* 2016;31:24-30.
6. Seo MR, et al. *Clin Rheumatol.* 2015;34:1397-405.
7. Akyol G, et al. *Osteoporos Int.* 2015;26:3335.
8. Zhao J, et al. *J Rheumatol.* 2015;42:106-10.
9. Martindale J, Goodacre L. *Musculoskelet Care.* 2014;12:221-31.
10. Gunasekera W, et al. *Ann Rheum Dis.* 2014;73:1046.
11. Hajialilo M, et al. *Iran Red Crescent Med J.* 2014;16:e11798.
12. Sullivan C, et al. *Ir J Med Sci.* 2014;183:579-84.
13. Cayetti LA, et al. *Arthritis Rheumatol.* 2013;65:S657.
14. Ibn YY, et al. *Rheumatol Int.* 2012;32:357-60.
15. Grigg SE, et al. *Arthritis Rheumatol.* 2011;63:A1308.
16. Slobodin G, et al. *Clin Rheumatol.* 2011;30:1075-80.
17. Sullivan C, FitzGerald O. *Ir J Med Sci.* 2011;180:S183.
18. Cakar E, et al. *Clin Rheumatol.* 2009;28:1309-14.
19. Aggarwal R, Malaviya AN. *Clin Rheumatol.* 2009;28:327-32.
20. Dincer U, et al. *Clin Rheumatol.* 2008;27:457-62.
21. Abdelrahman FI, Mortada M. *Ann Rheum Dis.* 2018;77:1556-7.

Conclusion: Delayed diagnosis in patients with AxSpA demonstrated a decrease in physical function, higher direct and indirect costs, and poorer quality of life. This study highlights the importance of early recognition and diagnosis of AxSpA in order to improve outcomes and mitigate extensive burden on patients and society. Therefore, further efforts by the healthcare community are warranted to increase awareness of early signs of disease and reduce the delay in diagnosis of AxSpA.

Figure 1. PRISMA Diagram for Study Selection



Abstract THU0411 – Figure 1

REFERENCE:
[1] Hutton B, et al. Ann Intern Med. 2015;163(7):566-7.

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22. Osteoarthritis

THU0412 **LONGITUDINAL ASSOCIATIONS BETWEEN MRI-DEFINED INFLAMMATION AND PAIN IN THUMB BASE OSTEOARTHRITIS**

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Background: : Hand osteoarthritis (OA) typically affects the interphalangeal (IP) joints and the thumb base (TB), including the first carpometacarpal (CMC-1) and scaphotrapeziotrapezoid (STT) joints. Based on previous studies, TB OA can be considered a distinct hand OA subset with a high burden of disease. In a cross-sectional study it was shown that TB pain is more strongly associated with radiographic damage than with MRI-defined inflammation, yet it is unknown if and how TB pain changes over time, and whether this is related to changes seen on imaging.
Objectives: Our aim was to investigate the course of TB OA pain and its association with changes in MRI-defined inflammation and structural damage.
Methods: Longitudinal data of the Hand OSTeoArthritis in Secondary care (HOSTAS) study, which included patients diagnosed with primary hand OA by their treating rheumatologist, were used. Patients who underwent hand radiography, MR imaging and clinical examination of the right TB at baseline and two-year follow-up were studied. Pain on palpation of the TB was assessed by trained research nurses (0-3). Baseline and follow-up MR images were scored paired in known time-order by two readers following the OMERACT TB OA MRI scoring system (TOMS). The CMC-

1 and STT joints were assessed for synovitis (0-3) and bone marrow lesions (BMLs; 0-6 and 0-9, respectively). Radiographs were assessed for the presence of osteophytes in CMC-1 and STT joints following the OARSI atlas by two readers. Since pain was assessed for the TB as a whole, imaging scores of CMC-1 and STT joints were combined, comparing no change in both joints (i.e. 'stable') versus change in at least one joint. In TBs without maximum baseline pain, associations between increase in MRI features and increase in TB pain were investigated using logistic regression, presented as odds ratios (ORs) with 95% confidence intervals (CIs). Similarly, in TBs with pain and MRI features present at baseline, associations between decrease in imaging features and decrease in TB pain were investigated.

Results: Out of 161 patients (82.6% women, mean age 60.8 years, 91.3% fulfilling ACR hand OA criteria) 64 had TB pain at baseline (of whom 11 with maximal score). At the two-year follow-up visit, pain had decreased in 31 patients and increased in 33 patients. The majority had stable synovitis (n=106) and BML (n=96) scores over two years, although decreased (n=22, n=26, resp.) and increased (n=29, n=36, resp.) scores were common. Increase in radiographic osteophytes was rarely (n=10) observed. Increase in synovitis or BML was associated with increased pain, also after adjusting for baseline osteophyte status (Table). A decrease in BML was associated with a decrease in pain, although it did not reach statistical significance. Presence of osteophytes on baseline radiographs was weakly associated with change in pain in univariate analyses and attenuated when adjusting for the change in MRI features. Decrease of synovitis in patients with baseline pain was scarce (n=7), therefore ORs were not computed.

Abstract THU0412 –Table 1.

Table 1 Longitudinal associations between change in MRI-defined synovitis or BMLs and change in thumb base pain in 161 patients with hand OA after two-year follow-up

	Change in pain yes/no, n	Crude OR (95% CI)	Adjusted* OR (95% CI)
Associations with increased pain			
(in joints without maximum pain, n=150)			
Delta synovitis†			
Stable/decrease	20/99	1	1
Increase	12/15	3.89 (1.54 – 9.8)	3.54 (1.31 – 9.6)
Delta bone marrow lesions‡			
Stable/decrease	16/98	1	1
Increase	15/18	4.9 (2.08 – 11.8)	5.0 (2.05 – 12.3)
Baseline osteophytes§			
Absent	13/69	1	1
Present	20/47	2.02 (0.90 – 4.5)	1.68 (0.70 – 4.0)
Associations with decreased pain			
(in joints with baseline pain, n=64)			
Delta synovitis†‖			
Stable/Increase	18/19	-	-
Decrease	4/3	-	-
Delta bone marrow lesions‡¶			
Stable/Increase	10/17	1	1
Decrease	12/7	2.91 (0.86 – 9.8)	3.10 (0.90 – 10.7)
Baseline osteophytes			
Absent	10/9	1	1
Present	21/24	0.79 (0.27 – 2.31)	0.84 (0.28 – 2.52)

BMLs, bone marrow lesions; CI, confidence interval; OR, odds ratio. *Adjustments were made for the other imaging scores of features in this table. †Four/ ‡three missing change scores due to unreadable MR images and §one missing baseline radiograph. ‖Synovitis or ¶BMLs had to be present at baseline to study decrease resulting in n<64.

Conclusion: In this cohort of hand OA patients, thumb base pain levels varied over the course of two years in approximately forty percent of patients. Changes in MRI-defined synovitis and BMLs of the TB joints were positively associated with change in pain on palpation. Baseline osteophytes were not significantly associated with change in pain. While cross-sectionally MRI-defined inflammation may be a less important determinant of pain than radiographic damage, this study shows that a change in inflammatory features may indeed be relevant.

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THU0413 MAJOR SUB-HAPLOGROUP H1 IS A RISK FACTOR FOR RAPIDLY PROGRESSIVE OSTEOARTHRITIS OF THE KNEE. DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Background: There is a pressing need to identify individuals with accelerated osteoarthritis to include them in clinical trials and to implement prevention strategies. During the last years, the mtDNA haplogroups have been consistently associated with OA in terms of genetic factors influencing both the incidence and progression of the disease (1,2)

Objectives: To analyze the influence of mtDNA haplogroups on the risk of rapid knee OA progression in patients from the Osteoarthritis Initiative (OAI).

Methods: We selected Caucasian patients from the OAI that were assigned into three different groups based on previously described criteria: i) rapid progressors, with baseline KL grade 0-I in at least one knee and increase up to KL≥III during 48 month follow-up; ii) non-rapid progressors, with baseline KL grade 0-I in at least one knee and increase up to KL=II during 48 month follow-up; and iii) non-progressors, with KL grade 0-I at baseline in at least one knee and bilaterally stable during the 48-month follow-up period. We performed different regression models adjusting for the confounder clinical variables of gender, age, body mass index, contralateral OA, previous injury in target knee and total WOMAC. mtDNA haplogroups and major H sub-haplogroups (H1,H3,H5 and H*) were previously assigned using sequencing techniques. The analyses were performed using IBM SPSS Statistics v24

Results: We could assign the progression status to 2092 subjects, of which 181 were rapid progressors (8,7%), 321 non-rapid progressors (15,3%) and 1590 non-progressors (76%).

All the classical risk factors for disease progression showed significant differences between rapid progressors and non-progressors, including gender (female) (OR=1,934; 95%CI:1,377–2,717;p<0,001), age (OR=1,040;95% CI:1,021–1,060;p<0,001), BMI (OR=1,113;95%CI:1,073–1,154;p<0,001), contralateral OA (OR=2,710;95%CI:1,938–3,773;p<0,001), previous injury of target knee (OR=2,849;95%CI:2,032–4,000;p<0,001) and total WOMAC (OR=1,016;95%CI:1,008–1,023;p<0,001). In terms of haplogroups, compared with the most common haplogroup H, the haplogroup J showed a lower frequency in the rapid progressors group in relation to non-progressors, although this difference did not reach the statistical significance (OR=0,526;95%CI:0,251–1,101;p=0,088). When the analysis included the major H subtypes, the most frequent sub-haplogroup H1 appeared over-represented in the rapid progressors group in relation to both non-progressors (OR=1,832;95%CI:1,102–3,044) and non-rapid progressors (OR=1,587;95%CI:0,876–2,877), being this difference statistically significant in the case of non-progressors (p=0,020).

After re-categorizing the dependent variable into rapid-progressors and non-rapid progressors, in addition to the significant association of the classical risk factors such as gender (female), age, BMI, contralateral OA, previous injury of target knee and total WOMAC at baseline, the sub-haplogroup H1 appeared significantly associated as a risk factor for rapid progression too (OR=1,781;95%CI:1,08 –2,919;p=0,022)

Conclusion: The mtDNA haplogroups, more specifically the major sub-haplogroup H1, increase the risk of rapidly progressive OA of the knee. The assignment of this mitochondrial genetic sub-haplogroup could be useful as complementary genetic biomarker for the early identification of this OA phenotype

REFERENCES:

[1] Fernández-Moreno, et al. Ann Rheum Dis 2017;76(6):1114-1122
[2] Fernández-Moreno, et al. Rheumatology (Oxford) 2017;56(2):263-270

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THU0414 COMPARISON OF INTRA-ARTICULAR SHAM AND VEHICLE INJECTIONS FROM A PHASE 2B TRIAL OF SM04690, A SMALL-MOLECULE WNT PATHWAY INHIBITOR FOR KNEE OSTEOARTHRITIS

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Background: Intra-articular (IA) saline, commonly used as a placebo (PBO) comparator in knee osteoarthritis (OA) trials, has consistently shown improvements from baseline in patient-reported outcomes (PROs).[1] These effects have been attributed to contextual and/or physiological benefits of saline, thus causing interpretation of potential IA therapeutics trial results to be questioned.[2,3]

Objectives: A prospective, randomized, controlled, 24-week phase 2b study compared effects of vehicle PBO to sham and SM04690 (an IA Wnt pathway inhibitor in development as a potential disease-modifying knee OA drug (DMOAD)) injections. Potential unblinding impact of PBO or sham was also tested. Primary study results are presented separately.

Methods: Knee OA subjects with Kellgren-Lawrence (KL) grades 2-3 and Pain Numeric Rating Scale (NRS) $\geq$4 and $\leq$8 in the target knee and <4 in the contralateral knee were randomized to receive a single blinded IA injection of 2 mL vehicle (PBO, 0.5% carboxymethylcellulose sodium, 0.05% polysorbate 80 in pH 7.4 saline), sham (dry needle), or SM04690 in the target knee on Day 0. PROs included change from baseline in weekly average of daily pain in the target knee by NRS, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Physical Function, and Patient Global Assessment (PtGA). Subjects were asked which treatment assignment they thought they received; their accuracy was compared using Bang's Blinding Index (BBI), a method used to evaluate blinding across clinical trial treatment arms. The index scale is -1< 0 <+1, with values toward -1 indicating more subjects incorrectly guessing treatment allocations, toward 0 indicating perfect blinding, and toward +1 indicating more subjects correctly identifying treatment allocations.

Results: In the full analysis set of PBO and sham subjects (N=233; 207 [89%] completed), both groups showed clinically relevant improvements (>10% of full scale[4]) from baseline at first measurement that persisted through Week 24. However, no clinically meaningful or statistically significant differences were evident between the two groups at any timepoints **(Figure)**. BBI did not indicate unblinding.

Conclusion: Subjects with knee OA receiving a single IA injection of PBO reported no differences in changes from baseline in knee OA PROs compared to subjects who received sham injections. These data suggested the effects were "contextual," meaning they resulted from the injection procedure, rather than from direct therapeutic effects of PBO or saline in the joint.

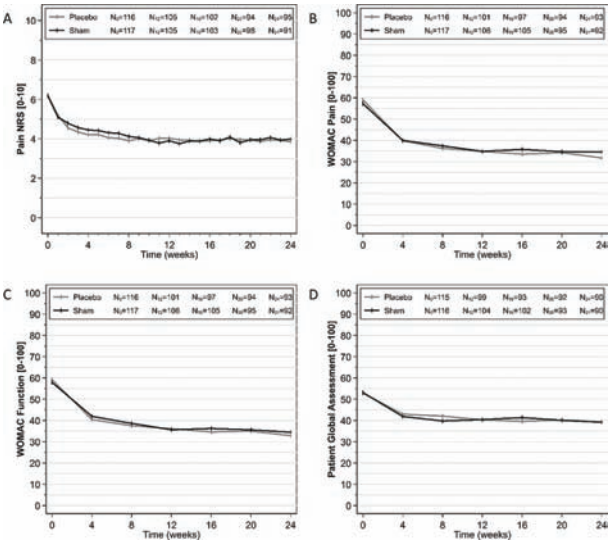


Figure: Observations over time depicting mean improvements (± 95% CI) of PBO compared to sham injection adjusted for baseline. A. Pain NRS, B. WOMAC Pain, C. WOMAC Function, and D. Patient Global; in all subjects.

Disclosure of Interests: Yusuf Yazici Shareholder of: Samumed, LLC, Consultant for: Celgene Corporation, BMS, Genentech, Sanofi, Employee of: Samumed, LLC, Jeyanesh Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Christopher Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Sarah Kennedy Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Vibeke Strand Consultant for: Samumed, LLC, AbbVie, Amgen, EMD Serono, Eupraxia, Flexion, Iroko, Novartis, Pfizer, Regeneron, Sanofi, SKK, Brian Cole Shareholder of: Ossio, Regentis, Grant/research support from: Aesculap/B. Braun, Arthrex, Inc, Regentis, Consultant for: Arthrex, Inc, Regentis, Samumed LLC, Marc Hochberg Shareholder of: BriOri Biotech, Theralogix LLC., Consultant for: Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis Pharma AG, Pfizer Inc., Samumed LLC, Symic Bio Inc., Theralogix LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., Zynerba, Galapagos, IQVIA, Hoffman LaRoche., Raveendhara Bannuru Consultant for: Samumed, LLC, Bioventus, Timothy McAlindon Grant/research support from: Samumed, LLC, Consultant for: Samumed, LLC, Astellas, Flexion, Pfizer, Regeneron,
Seikugaku

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REFERENCES:

[1] Altman RD, et al. Semin Arthritis Rheum. 2016;46:151-9
[2] Zou K, et al. Ann Rheum Dis. 2016;75:1964–197
[3] Bannuru R, et al. Ann Intern Med. 2015;163(5):365-72
[4] Devji, Tahira, et al. BMJ open 7.5 (2017): e015587.

THU0415 EXPLORATORY PROTEIN PROFILING OF HUMAN SYNOVIAL FLUID FROM KNEE OSTEOARTHRITIS

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Background: There is a lack of valid and robust biomarkers in the field of OA diagnosis, prognosis, and treatment evaluation [1]. Synovial fluid is in direct contact with articular cartilage, ligament, meniscus and joint capsule it is therefore an excellent sample to explore the protein profile in which could provide pathogenesis information from several surrounding parts.

Objectives: The aim with this project was to perform mass spectrometry (MS) of human synovial fluid using a global discovery approach, to identify biomarker candidates associated with meniscus degradation and/or knee OA.

Methods: Synovial fluid was sampled from 3 different subject groups: i) end-stage medial compartment knee OA patients undergoing arthroplasty (n=11, age range 55-80 years), ii) knee arthroscopy patients who typically had a degenerative meniscal tear (n=7, age range 50-64 years), and iii) deceased human donors without known chronic knee disease (n=13, age range 19-79 years). All synovial fluids were centrifuged and freshly frozen and stored at -80°C. For the analysis, 50 µL of synovial fluid was mixed with MS-safe proteinase inhibitor cocktail, hyaluronidase, depleted, reduced, alkylated, precipitated, digested with sequencing grade trypsin (Promega), filtered and desalted. The samples were further analyzed with an EASY-nLC 1000 coupled to an Orbitrap Fusion mass spectrometer

Abstract THU0422 – Table 2. WOMAC and VAS mean scores at baseline, 2, 6 and 12 months after injection.

	WOMAC index									
	Pain		Stiffness		Function		Total		VAS	
	PRGF	HA	PRGF	HA	PRGF	HA	PRGF	HA	PRGF	HA
Baseline	8.25±2.7	8.14±2.6	2.86±1.8	2.57±.1.4	30.75 ±8.5	29±8.1	41.96±11.71	39.71 ±10.4	7.8±1.5	7.8±1.1
At 2 mo	4.98±2.6	5.31±2.3	1.53±1.4	1.2±1.1	19.75 ±8.2	20.78 ±6.6	26.25±11.17	27.37 ±9.09	4.2±2.01	4.4±1.6
At 6 mo	5.22 ±3.05	5.9±2.3	1.43±1.5	1.2±1.2	18.22 ±9.9	21.12 ±6.6	24.86±14	28.35±9.4	4.3±2.3	4.7±1.9
At 12 mo	5.47±2.6	6.3±2.6	1.8±1.34	1.6±1.2	19.82 ±8.9	24.43 ±8.4	[b]27.10±12.3	32.41 ±11.8	4.5±1.7	6.1±1.8
P-value Within groups	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
P-value Between groups	0.339		0.856		[a]0.009		[b]0.02		[c] 0.0001	

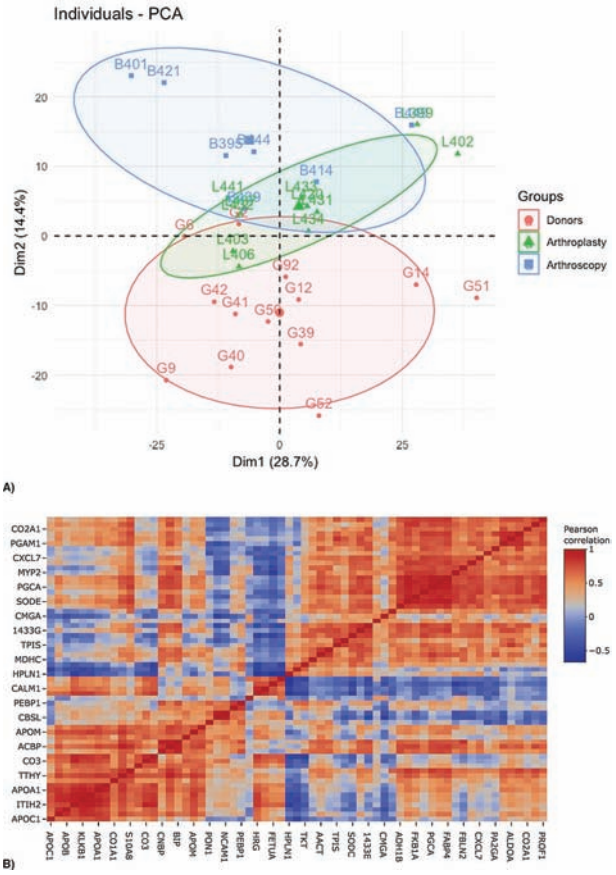
using data-independent acquisition. The raw MS data were further analysed with Spectronaut™ for protein identification and quant data extraction. Differences in protein levels were analyzed in two steps: 1) Donors vs arthroplasty 2) Between all 3 different groups. Analyses were adjusted for age, gender and weight. Differentially expressed proteins between the groups were clustered using Pearson correlation coefficient as the distance metric.

Results: In total, 529 proteins were identified in the 31 different synovial fluid samples analyzed. Principal component analysis suggested a profound difference between the protein profiles of synovial fluid from donors vs arthroplasty patients, while the arthroscopy group had a protein profile that was in-between donors and the arthroplasty group (Figure 1A). Statistical differential analysis yielded significant differences in the levels of 43 proteins comparing donors vs arthroplasty patients. 36 proteins differed between the 3 groups when comparing all groups in the same statistical model. Extracellular matrix proteins like collagens and aggrecan showed higher expression in donors than in arthroplasty patients. Collagen on the other hand was higher in arthroscopy patients compared to donors. Decorin was significantly higher in donors compared to both arthroscopy and arthroplasty patients. The differentially expressed proteins associated with the inflammatory response were higher in the arthroscopy group compared to both donors and arthroplasty patients. Generally, extracellular matrix proteins like collagen1/2 were positively correlated with lipoproteins like APOB and APOA but negatively correlated with acute phase proteins like PON1(Figure 1B).

Conclusion: There is a profound difference in the protein profile of synovial fluid in donors vs knee OA patients (Figure 1). The inflammatory response seems to be higher in the early stages of OA than in later stage. Our findings emphasize the importance of OA staging in the development and use of biomarkers.

REFERENCE:

[1] Mobasheri A. Osteoarthritis year 2012 in review: biomarkers. Osteoarthritis and Cartilage. 2012 Dec 1;20(12):1451-64.



Abstract THU0415 – Figure 1. Data analysis of the protein results. A) Principal component analysis plot of the protein profile from the different groups. B) Pearson correlation matrix of 63 significant differentially expressed proteins presented as gene names on the y- and x-axes.

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THU0416

PREDICTORS OF RADIOGRAPHIC PROGRESSION IN HAND OSTEOARTHRITIS: A TEN-YEARS PROSPECTIVE COHORT STUDY

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Background: Osteoarthritis (OA) is the most common musculoskeletal disease in the general population and is inherent to ageing.[1] Limited evidence is available on risk factors for radiographic progression in hand OA (HOA) and in erosive HOA.[2] A previous evaluation of the Ghent

HOA cohort showed a positive association between soft tissue swelling, tenderness upon pressure and pain with radiographic progression.[3]
Objectives: To identify new prognostic factors and to confirm existing evidence on already identified prognostic factors for radiographic progression in HOA.
Methods: All 270 patients from this cohort were contacted to participate in a second follow-up visit after ten years at the Ghent University Hospital. A total of 106 patients consented to this follow-up visit. Presence of tender and swollen joints was assessed. Grip strength was measured. Functional Index for HOA (FIHOA) and Australian/Canadian OA Index questionnaires (AUSCAN) were completed by the patients. Pain was scored on a visual analogue scale from 0-100mm (VAS pain). Radiographs of hands were taken and scored using the anatomical phase scoring system for HOA by Verbruggen and Veys[4]. Patients were defined as radiographic progressor when two or more joints progressed to another phase within the scoring system, except for N-phase to S-phase. Logistic regression was performed on the clinical data and outcomes such as presence of tenderness (yes or no), soft tissue swelling (yes or no), VAS pain, disease duration, FIHOA and AUSCAN. VAS pain was dichotomized into two groups: VAS ≤33mm and VAS >33mm. Disease duration was dichotomized in ≤5 years and >5 years: p-values and odds ratios (OR) with 95% confidence intervals (95% CI) were calculated.
Results: After a mean follow-up of 9.7 years, 73.3% of the patients showed radiographic progression. The following clinical factors were associated with radiographic progression on patient level (OR [95%CI]): presence of tenderness (4.19 [1.52-11.61]), presence of soft tissue swelling (2.73 [1.08-6.92]) and disease duration > five years (4.00 [1.50-10.66]). Other outcomes were retained as prognostic factors for radiographic progression (OR [95%CI]): VAS pain (1.02 [1.00-1.04]), total FIHOA (1.12 [1.03-1.23]), total AUSCAN (1.02 [1.01-1.04], AUSCAN pain (1.07 [1.02-1.12], AUSCAN function (1.03 [1.01-1.06]) and VAS pain > 33mm (2.87 [1.14-7.24]). The mean number of E and R joints was 1.2 and 1.4 at baseline, and 0.2 and 5.2 after 10 years (p<0.001). The total number of joints that progressed to the E-phase and R-phase over a period of ten years was respectively 20 (1.05%) and 399 (21%).
Conclusion: Clinical presence of pain and soft tissue swelling at baseline remain strong predictors of radiographic progression in HOA after ten years. Tenderness upon pressure, moderate VAS pain and moderate impaired function at baseline are identified as new predictors. After ten years, more remodeling and less erosive joints are seen.

REFERENCES:

[1] Haugen IK, Englund M, Aliabadi P, et al. Ann Rheum Dis. 2011;70 (9):1581-6.
[2] Bijsterbosch J, Watt I, Meulenbelt I, et al. Ann Rheum Dis. 2011;70(1):68-73.
[3] Meersseman P, Van de Vyver C, Verbruggen G, et al. Osteoarthritis Cartilage. 2015;23(12):2129-33.
[4] Verbruggen G, Veys EM. Arthritis Rheum. 1996;39(2):308-20.

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THU0417 THE SEVERITY OF STRUCTURAL AND INFLAMMATORY FEATURES OF HAND OSTEOARTHRITIS ASSOCIATE WITH PERIPHERAL PAIN SENSITIZATION

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Background: Increased sensitivity to pain in the area around joints with osteoarthritis (OA), i.e., peripheral sensitization, is associated with higher pain severity. The mechanisms underlying peripheral sensitization in hand OA have not been substantially explored in previous studies.
Objectives: We aimed to explore whether the severity of structural or inflammatory OA features in the distal and proximal interphalangeal (DIP/PIP) joints were associated with lower pressure pain thresholds (PPT) at the same joint in a large study sample of persons with hand OA.
Methods: In these cross-sectional analyses we included 277 persons with hand OA from the Nor-Hand cohort. All participants underwent radiography and ultrasound examination (GE S8, ML 6-15MHz probe) of both hands. Pressure pain threshold (PPT) was tested with a hand-held algometer (FPIX25, 1cm^2 flat rubber probe) in perpendicular position at the dorsal side of the DIP/PIP joint reported to be the most painful. Information about demographics and psychosocial factors was collected with questionnaires. We examined whether increasing radiographic severity (Kellgren-Lawrence 0-4 score) and ultrasound-detected inflammation (grey-scale synovitis 0-3 score and presence of power-Doppler activity) were associated with PPT at the same joint. We conducted separate analyses of linear regression with adjustments for age, sex, BMI, education level, use of analgesics, sleep disturbance, the Pain Catastrophizing Scale and the Hospital Anxiety and Depression Scale.
Results: The majority of the study population were women (89%), median age was 61 (IQR 57-66) years, mean BMI was 26.3 (SD 4.6) kg/m^2 and median duration of hand OA symptoms was 6 (IQR 3-13) years. The DIP/PIP joints demonstrated a wide range of PPT (mean (SD) 3.9 (1.9), range 0.6-11.4 kg/cm^2) and OA severity (Table). We found that both increasing radiographic severity and inflammation were associated with lower PPTs (Table). When including grey-scale synovitis and power Doppler as confounders in analysis of radiographic severity, the results became weaker but remained significant (Table).

Abstract THU0417 –Table 1. Associations of structural and inflammatory OA features of DIP/PIP joints to pressure pain thresholds at the same joint, n=277.

	PPT (SD), kg/cm^2	Adjusted beta (95% CI)	
Radiographic severity (Kellgren-Lawrence)			
Grade 0 (n=63)	4.5 (1.9)	0.0 (ref.)	0.0 (ref.)
Grade 1 (n=39)	4.3 (1.8)	-0.4 (-1.1, 0.3)	-0.4 (-1.1, 0.4)*
Grade 2 (n=61)	4.6 (2.2)	-0.1 (-0.7, 0.6)	0.1 (-0.6, 0.7)*
Grade 3 (n=54)	3.2 (1.6)	-1.5 (-2.2, -0.8)	-1.3 (-2.0, -0.6)*
Grade 4 (n=60)	2.9 (1.2)	-2.0 (-2.6, -1.3)	-1.6 (-2.3, -0.8)*
p for trend		<0.001	<0.001*
Grey-scale synovitis			
Grade 0 (n=155)	4.3 (2.0)	0.0 (ref.)	
Grade 1 (n=56)	3.8 (2.0)	-0.6 (-1.2, -0.1)	
Grade 2 (n=42)	3.3 (1.2)	-1.1 (-1.8, -0.4)	
Grade 3 (n=24)	2.6 (1.5)	-1.7 (-2.5, -0.9)	
p for trend		<0.001	
Power Doppler			
Grade 0 (n=266)	4.3 (2.1)	0.0 (ref.)	
Grade 1-3 (n=14)	3.0 (1.3)	-1.3 (-1.8, -0.9)	

Adjusted for age, sex, BMI, analgesics, education, sleep disturbance, the Pain Catastrophizing Scale and the Hospital Anxiety and Depression Scale. *Additional adjustments for grey-scale synovitis and power Doppler.
Conclusion: Both structural and inflammatory hand OA features in DIP/PIP joints were associated with lower pressure pain thresholds, i.e. pain sensitization, at the same joint. Our results suggest that peripheral sensitization might be driven by structural and inflammatory features, and that targeting the disease early might prevent peripheral sensitization and reduce pain.
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THU0418 NEUROPATHIC-LIKE PAIN IN PERSONS WITH HAND OSTEOARTHRITIS AND ASSOCIATIONS WITH PERIPHERAL AND CENTRAL SENSITIZATION

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Background: Despite no current knowledge of lesions or disease of the sensory nervous system in osteoarthritis (OA), subgroups of knee OA patients report neuropathic-like pain. The neuropathic-like pain component has been suggested to reflect central sensitization.
Objectives: To describe the prevalence of neuropathic-like pain in persons with hand OA and explore whether neuropathic-like pain associate with peripheral and/or central sensitization.
Methods: These cross-sectional analyses included 280 participants with hand OA from the Nor-Hand study. A modified PainDETECT questionnaire was used to characterize neuropathic-like hand pain (mPD-hand, 0-36 scale). We conducted quantitative sensory testing (QST) of pressure pain thresholds (PPT) and temporal summation (TS). Low PPTs at local sites (painful finger joint and non-painful finger joint) indicate peripheral and/or central sensitization, while low PPTs at extra-segmental sites (radioulnar joint, musculus trapezius and tibialis anterior) indicate central sensitization. TS, defined as an increase in pain $\geq$2 on a numeric rating scale (NRS, 0-10) during a repetition of ten punctate stimuli at the wrist, indicate central sensitization. Participants with painful hand OA (NRS of hand pain above the patient acceptable symptom score of $\geq$4), were categorized as having either nociceptive pain (mPD-hand $\leq$12) or neuropathic-like pain (mPD-hand score >12). We examined whether reporting nociceptive or neuropathic-like pain, as compared to no/mild pain (NRS hand pain below 4) was associated with QST results using regression analyses.
Results: In this study sample, 88% were female, median age was 61 (IQR 57-66) years and 94% fulfilled the ACR criteria for hand OA. Median mPD-hand score was 8 (IQR 3, 13). Half of the participants (n=144, 51%) reported NRS pain $\geq$4, of whom 58 (40%) had neuropathic-like pain. Those with neuropathic-like pain reported higher mean (SD) NRS pain severity than persons with nociceptive pain (5.9 (1.6) vs 5.3 (1.5), p=0.01). We found that neuropathic-like pain was associated to higher pain sensitization reflected by lower PPT at the painful finger joint (Table), non-painful finger joint (beta -1.6, 95% CI -2.3, -0.9), radioulnar joint (beta -1.1, 95% CI -1.8, -0.4), trapezius (Table) and tibialis anterior (-1.0, 95% CI -1.8, -0.2) and presence of TS (Table). The associations between nociceptive pain and sensitization were weaker than the associations observed for neuropathic-like pain (Table).

Abstract THU0418 –Table 1. Associations between neuropathic-like pain and quantitative sensory testing

	PPT painful finger joint[1]		PPT trapezius muscle[1]		Temporal summation[2]	
	Mean (SD)	beta(95% CI)	Mean (SD)	beta(95% CI)	N(%)	OR(95% CI)
No/Mild pain (n=136)	4.3 (2.1)	0.0 (ref.)	4.9 (2.1)	0.0 (ref.)	43 (32%)	0.0 (ref.)
Nociceptive pain (n=86)	3.9 (1.7)	-0.5 (-1.0, 0.1)	4.1 (1.9)	-0.6 (-1.1, 0.0)	35 (41%)	1.3 (0.7, 2.4)
Neuropathic-like pain (n=58)	2.9 (1.4)	-1.6 (-2.2, -0.9)	3.6 (1.9)	-0.9(-1.5, -0.2)	39 (67%)	3.8 (1.8, 8.2)

[1]Linear regression, [2]logistic regression. Adjusted for age, sex, BMI, use of analgesics, level of education, sleep disturbance, Pain Catastrophizing Scale, the Hospital Anxiety and Depression Scale and radiographic hand OA severity (Kellgren-Lawrence sum score).

Conclusion: Of persons with painful hand OA, 40% have a neuropathic-like pain component. Reporting neuropathic-like pain is associated with peripheral and central sensitization, indicated by low PPTs and presence of TS. Our results suggest that patients who report neuropathic-like symptoms are more likely to have sensitization-associated pain.

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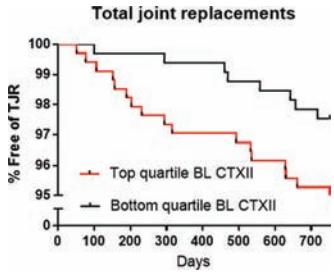
THU0419 BIOMARKERS OF BONE AND CARTILAGE TURNOVER CTX-I AND CTX-II PREDICT TOTAL JOINT REPLACEMENTS IN OA

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Background: Osteoarthritis (OA) can lead to joint failure and ultimately total joint replacement (TJR). Identifying risk-factors of developing joint failure is of interest for clinicians and researchers. Currently late-stage clinical trial design for evaluating new treatments in OA is evolving with the possible utilization of accelerated approval pathways. This may require outcome studies with longer duration, in which joint failures may qualify as an endpoint. However, TJRs are relatively rare events and are known to be biased by doctor/patient interactions as well as local practice guidelines, and consequently, there is a need for objective non-invasive measures, such as soluble biomarkers (BM), to enrich the population for this outcome. BM may act as important tools in investigating the association between biochemical/pathological processes and risk of joint failure. Degradation of collagens type I and II are known to be involved in OA disease progression, and the biomarkers CTX-I (C-telopeptide of crosslinked collagen type I), a marker of bone degradation, and CTX-II (C-telopeptide of crosslinked collagen type II), a marker of cartilage degradation, may reflect disease progression with clinical relevance for the risk of joint failure.
Objectives: To evaluate baseline (BL) BM sCTX-I and uCTX-II as predictors of TJR.
Methods: Data from two clinical trials investigating oral salmon calcitonin (SMC) in OA, NCT00486434 and NCT00704847, was analyzed post-hoc. Data was dichotomized by the bottom and top quartile of the respective BM concentration at BL to compare the number TJRs of the knee or hip in groups with high vs. low sCTX-I or uCTX-II, respectively. For means of visualization, plotted in Kaplan-Meier curves.
Cox Proportional Hazard Regression was performed to determine the association of BL sCTX-I and uCTX-II to the incidence of TJR while adjusting for co-variates; age, BMI, and gender. Data from both treatment groups were analyzed. Only the first reported incident was included in the analysis for each subject.
Results: A total of 68 TJRs of knee or hip were reported, of which 49 were knees and 18 were hips. One patient underwent two TJRs, resulting in 67 subjects with events.
Results from the Cox Proportional Hazard Regression adjusted for covariates of age, BMI, and sex (table 1), indicate that high BL sCTX-I compared to low was associated with a 3.4 times higher risk of undergoing an arthroplasty of the knee or hip within a two-year period (p=0.04). High BL uCTX-II compared to low was associated with a 3.1 times higher risk of undergoing a TJR of the knee or hip during the study period (p=0.04), and an 8.9-fold increased risk of undergoing a knee replacement during the study period (p=0.02).
TJR events over time in groups of high or low uCTX-II through the study are illustrated in figure 1.

Abstract THU0419 –Table 1. Cox Proportional Hazards Regression analysis

Group	Low CTX-I *N = 336*, high CTX-I *N = 340*			Low CTX-II *N = 318*, high CTX-II *N = 322*		
	HR top vs. bottom quartile	95% CI	P-value	HR top vs. bottom quartile	95% CI	P-value
Knee or hip replacement (Cases: CTX-I = 23, CTX-II = 27)	3.40	1.05-11.06	0.042	3.08	1.04-9.10	0.043
Knee replacement (Cases: CTX-I = 16, CTX-II = 19)	2.72	0.70-10.57	0.15	8.94	1.50-53.48	0.017



Abstract THU0419 – Figure 1. TJR events during the entire study, CTX-II.

Conclusion: High levels of sCTX-I and uCTX-II at BL were associated with increased risk of undergoing TJR of the knee or hip during the two year study. Our findings support the role of sCTX-I and uCTX-II as important biomarkers in clinical OA trials evaluating incidence of TJRs.
Disclosure of Interests: : Jonathan Bjerre-Bastos Employee of: I am a full-time employee in Nordic Bioscience, Anne-Christine Bay-Jensen Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Morten Karsdal Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Inger Byrjalsen Employee of: I am a full-time employee in Nordic Bioscience, Jeppe Ragnar Andersen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Bente Juel Riis Shareholder of: Yes, I own shares in Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Claus Christiansen Shareholder of: Yes, I own shares in Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Asger Reinstrup Bihlet Shareholder of: Yes, I own shares in Nordic Bioscience., Employee of: I am a full-time employee in Nordic Bioscience
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THU0420 METABOLIC SYNDROME AND TRAJECTORIES OF LOCALISED PAIN AND GENERALISED PAIN

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Background: Metabolic syndrome (MetS) has been suggested as having a link to the pathophysiology of pain; however, no study has assessed whether MetS and its components are associated with localised pain and generalised pain and their courses over time.
Objectives: To describe the associations of MetS and its components with trajectories of localised knee pain (pain severity) and generalised pain ((number of painful sites (NPS)) in a general older population.
Methods: 1,099 participants from a population-based older adult cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Data were collected on demographic, psychological, lifestyle and comorbidities, blood pressure, glucose, triglycerides, and high-density lipoprotein (HDL) cholesterol. MetS was defined based on the National Cholesterol Education Program-Adult Treatment Panel III criteria. Radiographic knee osteoarthritis (ROA) was assessed by X-ray. Knee pain was measured by Western Ontario and McMaster Universities Osteoarthritis Index pain questionnaire at each time-point. Presence/absence of pain at the neck, back, hands, shoulders, hips, knees and feet was collected by questionnaire at each time-point. Group-based trajectory modelling was applied to identify pain trajectories. Multi-nominal logistic regression was used for the analyses.
Results: Of 985 participants included in this study, 32% of participants had MetS and 60% had ROA at baseline. Three localised knee pain severity trajectories were identified: 'Minimal pain' (52%), 'Mild pain' (33%) and 'Moderate pain' (15%). Three NPS trajectories were identified: 'Low NPS' (12%), 'Medium NPS' (38%), and 'High NPS' (49%). In multivariable analysis without adjusting for central obesity, central obesity increased risk of belonging to both 'Mild pain' and 'Moderate pain' trajectories as compared to the 'Minimal pain' trajectory group, but MetS, hypertriglyceridemia and low HDL were only associated with 'Moderate pain' trajectory [relative risk (RR): 1.67-2.26, all P<0.05]. Similarly, central obesity was also associated with both 'Medium NPS' (RR 2.35, 95%CI 1.40−3.92) and 'High NPS' trajectories (RR 3.07, 95%CI 1.85−5.08) compared to 'Low NPS' trajectory group, whereas MetS was only associated with 'High NPS' trajectory (RR 2.60, 95%CI 1.54−4.41). These associations became weak and non-significant after further adjustment for central obesity.
Conclusion: MetS is predominantly associated with trajectories of localised and generalised pain through central obesity, suggesting that weight management is important in the prevention and therapy of pain over time.
Disclosure of Interests: None declared
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THU0421 EFFECT OF GAME BASED EXERCISE PROGRAMS ON PAIN, FUNCTIONAL MOBILITY AND BALANCE IN PATIENTS WITH KNEE OSTEOARTHRITIS: RANDOMIZED CONTROLLED STUDY

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Background: Osteoarthritis is a chronic joint disease affecting the knee, hip and hand joints. Exercise is an integral component of conservative treatment for osteoarthritis. However, virtual reality applications using interactive games for rehabilitation have become a focus of interest in recent years.
Objectives: The aim of this study was to evaluate the effects of virtual reality games on knee pain, functional mobility and balance in patients with knee osteoarthritis.
Methods: Fifty patients who were complaining of knee pain, aged 40-70 years, and were diagnosed with Kellgren-Lawrence stage 2, 3, 4 idiopathic knee osteoarthritis was included. Patients were randomly assigned to two equal groups (n = 25) as the control and the study group. Age, sex, weight, height, duration of illness was recorded for all patients. In the bilateral two-way knee radiography; Kellgren-Lawrence score of the knee with the higher visual analog scale (VAS) pain score was recorded. Conventional physical therapy program, associated with knee osteoarthritis exercises, was applied routinely to all patients with knee osteoarthritis for three weeks. In the study group, all patients received virtual reality game-based exercise program by using a game console. In both groups, baseline and final values of VAS score, osteoarthritis index total score (WOMAC), and intra-community balance and mobility scale (CB&M) score of each patient were recorded. Mann-Whitney U and Independent Samples T tests were used for statistical analysis, and *p* value less than 0.05 was considered significant.
Results: In both groups, significant change in VAS, WOMAC osteoarthritis index, and CB&M score was observed ($p<0.05$). In the study group, VAS, WOMAC osteoarthritis index, and CB&M scores were significantly different than control group ($p<0.05$). The differences between baseline

Abstract THU0429 – Table 1. Results of four separate multiple linear regression models with the WOMAC as the dependent variable. Regression coefficients with 95% confidence intervals are shown.

			WOMAC			
	Parameter	Reference	**Polyarthrosis**	**Hip OA**	**Knee and Hip OA**	**Knee OA**
Model 1	Age	per 10 years	0,7 (-0,6 ; 2,0)	0,7 (-1,2 ; 2,6)	2,0 (-0,5 ; 4,4)	-0,1 (-3,5 ; 3,3)
	Gender: Male	Female	**-3,8 (-6,7 ; -1,0)**	0,8 (-3,5 ; 5,0)	-3,7 (-8,1 ; 0,6)	-0,5 (-7,6 ; 6,6)
Model 2*	BMI, kg/m²	per 5 units	**4,4 (3,2 ; 5,5)**	**3,1 (1,1 ; 5,2)**	**4,2 (1,8 ; 6,6)**	**4,1 (0,6 ; 7,6)**
Model 3*	Symptom duration	per year	**0,3 (0,2 ; 0,5)**	**0,4 (0,2 ; 0,6)**	0,2 (-0,0 ; 0,4)	0,4 (0,0 ; 0,8)
Model 4*	WHO-5 (0-100)	per 10% worsening	4.4 (3.8; 5.0)	3.2 (2.2; 4.1)	4.1 (3.3; 5.1)	3.9 (2.1; 5.9)

*Model adjusted for age, gender. BMI: Body Mass Index, OA: Osteoarthritis, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Score.

and final scores of VAS and WOMAC were significantly higher (p<0.05) in study group.
Conclusion: The results of the present study showed that virtual reality game-based exercise programs performed better results than conventional treatment program in patients with knee osteoarthritis.

REFERENCES:
[1] Bennell KL, Dobson F, Hinman RS. Exercise in osteoarthritis: moving from prescription to adherence. Best Pract Res Clin Rheumatol. 2014; 28(1): 93-117.
[2] Ju SB, Park GD, Kim SS. Effects of proprioceptive circuit exercise on knee joint pain and muscle function in patients with knee osteoarthritis. J Phys Ther Sci. 2015; 27(8): 2439-41.
[3] Molina KI, Ricci NA, de Moraes SA, Perracini MR. Virtual reality using games for improving physical functioning in older adults: a systematic review. J Neuroeng Rehabil. 2014; 11: 156.

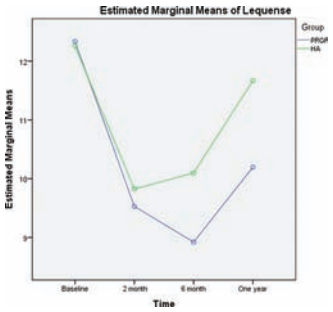
Disclosure of Interests: None declared
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THU0422 COMPARISON OF PRP DERIVED GROWTH FACTOR (PRGF) VERSUS HYALURONIC ACID (HA) IN MILD TO MODERATE KNEE OSTEOARTHRITIS; A SINGLE BLIND ONE YEAR RANDOMIZED CLINICAL TRIAL STUDY

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Background: Osteoarthritis (OA) is the most common joint disease with characteristics of progressive loss of joint cartilage.
Objectives: Aim of this study was to evaluate clinical outcomes of intra-articular injection of PRP derived growth factor (PRGF) versus hyaluronic acid (HA) in patients with knee osteoarthritis.
Methods: 102 patients with grade П or grade Ш knee OA were randomly assigned to 2 intra-articular injections of PRGF 3 weeks apart or 3 weekly injections of HA. Primary outcome was the mean change from baseline until 2, 6 and 12 months post intervention in scores of visual analog scale (VAS), WOMAC and Lequesne index.
Results: The mean age of patients was 57.08±7.3 in PRGF compared to 58.63±7.09 in HA group. In PRGF group, VAS decreased from 7.8±1.5 to 4.5±1.7, and from 7.8±1.1 to 6.1±1.8 in the HA group after 12 months (P<0.0001). Total WOMAC score decreased from 41.96±11.71 to 27.10 ±12.3 (P = 0.02), and from 39.71±10.4 to 32.41±11.8 after 12 months, respectively (P > 0.05). In Lequesne index, all scores were significantly decreased after 12 months in PRGF group in comparison to HA group (P<0.001).
Conclusion: Although PRGF and HA were both effective, but PRGF injection resulted in significantly higher satisfaction, lower VAS and Lequesne pain score and improvement in function of patients with symptomatic mild to moderate knee osteoarthritis.

REFERENCES:
[1] Raeissadat SA, Rayegani SM, Tabibian E, Rahimi Dehgolan S. Intra-articular ozone injection efficacy in knee osteoarthritis: A systematic review with meta-analysis. Annals of Physical and Rehabilitation Medicine. 2018;61:e132-e3.
[2] Raeissadat SA, Rayegani SM, Hassanabadi H, Fathi M, Ghorbani E, Babaee M, et al. Knee Osteoarthritis Injection Choices: Platelet- Rich Plasma (PRP) versus Hyaluronic Acid (A one-year randomized clinical trial). Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders. 2015;8:CMAMD.S17894.
[3] Raeissadat SA, Rayegani SM, Ahangar AG, Abadi PH, Mojgani P, Ahangar OG. Efficacy of Intra-articular Injection of a Newly Developed Plasma Rich in Growth Factor (PRGF) Versus Hyaluronic Acid on Pain and Function of Patients with Knee Osteoarthritis: A Single-Blinded Randomized Clinical Trial. Clinical medicine insights Arthritis and musculoskeletal disorders. 2017;10:1179544117733452.



Abstract THU0422 – Figure 1. Mean values of Lequesne total at baseline, 2, 6 and 12 months after injection. PRGF indicates plasma rich in growth factor

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THU0423 ANTERIOR TIBIOTALAR FAT PAD MORPHOLOGY AND SIGNAL INTENSITY ON MAGNETIC RESONANCE IMAGING ARE CORRELATED WITH PATIENT CHARACTERISTICS AND JOINT PATHOLOGY

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Background: Ankle sprains are the most frequent form of trauma in the ankle and up to 33% of patients experience ongoing pain 1 year after the initial trauma.[1] In the ankle, trauma is the primary etiology of osteoarthritis with an overwhelming proportion of 70-78%.[2] Recently, our group completed a small pilot study that suggested that the anterior tibiotalar fat pad (ATFP) should be investigated as a source of inflammation and pain.[3]
Objectives: In this study, we tried to investigate the innovative concept of the ATFP as missing link in the pathogenesis of persistent complaints and potential source driving inflammation in the development of osteoarthritis.
Methods: The present study is a secondary analysis of an observational case control study by Van Ochten et al.[4] We included 106 patients with a Kellgren & Lawrence score of 0 in the tibiotalar joint on x-ray. T1 MRI scans were assessed for the signal intensity and area of the ATFP by mapping the fat pad in 'Mimics 18.0'. After importing those mapped scans in the program 'MATHLAB', quantitative values of intensity and area were generated. Those values were statistically tested for correlations with patient characteristics and structural abnormalities by univariate and multivariate linear regression.
Results: MRI signal intensity of the ATFP is associated with BMI (p= 0.03), sex (p<0.01) and age (p= 0.01). ATFP area is correlated with sex (p<0.01) and presence of pre-OA signs in the subtalar joint (p= 0.01). After multivariate analysis, correcting for sex, subtalar pre-OA signs and BMI, persistent complaints were associated with ATFP area (p= 0.04).
Conclusion: This study demonstrates the involvement of the ATFP in hindfoot joint pathology. ATFP MRI characteristics were also influenced by patient characteristics. Further research should confirm these findings in a more elaborate population including OA patients, focus on histological validation and determine underlying pathogenic processes that may explain the observed correlations.

REFERENCES:
[1] van Rijn, R. M. et al. What Is the Clinical Course of Acute Ankle Sprains? A Systematic Literature Review. American Journal of Medicine 121, (2008).
[2] Valderrabano, V., Horisberger, M., Russell, I., Dougall, H. & Hintermann, B. Etiology of ankle osteoarthritis. Clinical Orthopaedics and Related Research 467, 1800–1806 (2009).
[3] Clockaerts, S. et al. The anterior tibiotalar fat pad as a source of pain and inflammation in osteoarthritis of the ankle: anatomy, histology and imaging. Osteoarthr. Cartil. 26, S120 (2018).

[4] Van Ochten, J. M. et al. Structural abnormalities and persistent complaints after an ankle sprain are not associated: An observational case control study in primary care. Br. J. Gen. Pract. 64, e545–e553 (2014).

Disclosure of Interests: Stijn Arnaert: None declared, Paul Byttebier: None declared, Sam Van Rossom: None declared, Evie Vereecke: None declared, Ilse Jonkers: None declared, Edwin Oei: None declared, S.M.A. Bierma-Zeinstra: None declared, Rik Lories Consultant for: Abbvie, Celgene, Eli-Lilly, Janssen, Merck, Novartis, Pfizer, UCB, Marienke Van Middelkoop: None declared, Stefan Clockaerts: None declared
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THU0424 THE NEW TREATMENT APPROACH IN KNEE OSTEOARTHRITIS: EFFICACY OF CELLULAR MATRIX COMBINATION OF PLATELET RICH PLASMA WITH HYALURONIC ACID VERSUS TWO DIFFERENT TYPES OF HYALURONIC ACID (HA) (PROSPECTIVE, RANDOMIZED, DOUBLE BLIND CONTROL STUDY)

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Background: Osteoarthritis pathogenesis is a complex process associated with decreased ability to regenerate cartilage mainly due to lack of physiological vascularization. One of the most commonly affected joints is the knee.
Objectives: The aim of this study was to compare the efficacy of intra-articular (IA) injections of platelet rich plasma (PRP) combined with hyaluronic acid (HA) prepared with the Cellular Matrix device *versus* IA injections with two different types of hyaluronic acid for treatment of knee osteoarthritis.
Methods: This is a prospective, randomized, double-blind, controlled study on 53 patients (90 knees) suffering from knee osteoarthritis, divided in 3 groups. The first group comprised 19 patients (30 knees) treated with 3 IA injections, one every second week, of Cellular Matrix (CM) PRP-HA combination. The second group of 19 patients (30 knees) was treated with 3 weekly IA injections of 2% non-cross-linked sodium hyaluronate and the third group of 15 patients (30 knees) treated with 3 weekly IA injections of 2% non-cross-linked sodium hyaluronate with mannitol. All groups were homogeneous concerning gender, age and Kellgren Lawrence scale (I to III). For all patients visual analog pain scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee Injury and Osteoarthritis Outcome Score (KOOS), The International Knee Documentation Committee (IKDC) score ("well-being" scale for all 4 scores between 0 and 100) and ultrasound (US) cartilage thickness on lateral, trochlear, and medial compartments, with normal range values from 2 to 2.5 mm, were measured at the beginning of the treatment (baseline) and at each follow up visit, that is at 2, 6 and 12 months after the last injection.
Results: A statistically significant difference ($p < 0.05$) in the CM group was found compared to AV and OP group in the values of VAS, WOMAC, KOOS and IKDC after two months, although an improvement, compared to baseline values, was observed for the indicated parameters in all groups. A high statistically significant difference ($p < 0.01$) was obtained in the CM group compared to the AV and OP group for VAS, WOMAC, KOOS and IKDC after 6 and 12 months. In both groups of patients treated with hyaluronic acid, a deterioration of values for VAS, WOMAC, KOOS and IKDC score was seen at 12 months in relation to values at 6 months. The CM treated group showed statistically significant improvement ($p < 0.05$) of the cartilage thickness after 2, 6 and 12 months in the medial and highly statistically significant improvement ($p<0.01$) in the lateral segments of knee cartilage in comparison to baseline values.
Conclusion: The Cellular Matrix PRP-HA combination might be one of the most potent, safe, fast and novel therapeutic option for osteoarthritis of the knee, as well as a useful tool for postponing arthroplasty surgery when it is necessary.

REFERENCES:

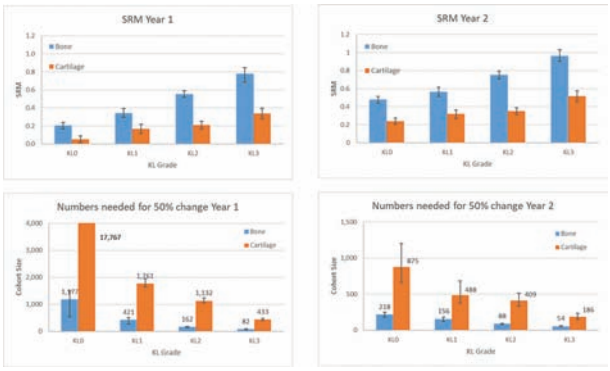
[1] Saturveithan C, Premganesh G, Fakhrizzaki S, et al. Intra-articular Hyaluronic Acid (HA) and platelet rich plasma (PRP) injections versus Hyaluronic acid (HA) injections in grade III and IV knee osteoarthritis (OA) patients: A retrospective study on functional outcome. 45th Malasyan Orthopedeic Association(2015).
[2] Chen SH, Khuan TS, Kao MJ, et al. Clinical effectiveness in severe knee osteoarthritis after intra-articular platelet rich plasma therapy in association with hyaluronic acid injection: three case reports. Clin. Interv.Aging. 11, 1213-1219 (2016).
3. Renevier JL, Marc JF, Adam P, et al. "Cellular Matrix TM PRP-HA": A new treatment option with platelet-rich plasma and hyaluronic acid for patients with osteoarthritis having had an unsatisfactory clinical response to hyaluronic acid alone: Results of a pilot multicenter French study with long-term follow-up. Int J Clin Rheumatology 2018; 13(4), 226-229

Disclosure of Interests: Branko Barac: None declared, Nemanja Damjanov Grant/research support from: AbbVie, Pfizer and Roche, Consultant for: Abbvie, Gedeon Richter, Merck, Novartis, Pfizer and Roche., Speakers bureau: Abbvie, Gedeon Richter, Merck, Novartis, Pfizer and Roche., Ana Zekovic: None declared
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THU0425 COST-EFFECTIVE OA TRIALS REQUIRE ENROLMENT OF KNEES WITH DEFINITE JOINT SPACE NARROWING (KELLGREN LAWRENCE 3); DATA FROM 6,939 KNEES FROM THE OSTEOARTHRITIS INITIATIVE

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Background: The design of clinical trials for osteoarthritis is challenging; structural changes in tissues are quantitatively small and proceed very slowly. No clear guidance exists on how to optimise recruitment. We have previously shown that the use of radiographic joint space width of 2 to 4.5 mm is of major importance for improving responsiveness in clinical trials using MRI bone and cartilage outcomes. However, it can be technically challenging to screen for joint space width this carefully, so we considered whether Kellgren-Lawrence (KL) grade could be used as an enrichment strategy. As no other commonly used covariates have been shown to reliably increase responsiveness, it would be useful to know the numbers needed using ONLY an expert-read KL grade structural inclusion criterion.
Objectives: To determine responsiveness of change in femur bone shape and cartilage thickness using a large observational dataset and calculate likely trial cohort sizes per arm for each KL grade.
Methods: We used all knees from the Osteoarthritis Initiative which had MR images at baseline, 1 and 2 years, and a baseline KL grade (centrally read and adjudicated by 2 experienced radiologists). Quantitative 3D femur bone shape, and cartilage thickness in the central medial femoral region were used as outcome measures. Responsiveness was assessed using standardised response means "SRM" (CIs were assessed using the bootstrap method of Efron) and derived the number of patients per arm in a putative trial to demonstrate 50% change, at 80% probability, α=0.05.
Results: 6,945 knees (3,667 subjects, 2,085 female) were included (KL 0: 2,798; KL1: 1,338 knees; KL2: 1,879 knees; KL3: 924 knees). Table 1 provides summary results and Figure 1 shows SRM and putative trial cohort numbers by KL grade for bone shape and cartilage thickness. Femur bone shape had higher SRM values at all timepoints, typically twice that of SRM for cartilage thickness in all KL groups. Cohort size when using cartilage thickness increased significantly between KL2 and KL3.
Conclusion: Expert-read KL3 inclusion, using 2 independent radiologists, with strict attention to standards provides increased responsiveness for common MRI OA outcomes. It is worth noting that 80% of KL3 knees have OARSI JSN grade 3, and 78% of KL3 knees have radiographic JSW of 2 to 4.5 mm, and similar enrichment can be expected using these alternatives. Few clinical studies can afford cohort sizes of greater than 200 knees, and for these studies, using a large proportion of KL3 knees is critical, especially if cartilage thickness is to be used as the outcome.



Abstract THU0425 – Figure 1. SRM and cohort numbers by KL grade for bone shape and cartilage thickness in 6,939 knees. Top row shows SRM values at 1 year (left) and 2 years for femur bone shape and central medial femur cartilage thickness, with 95% confidence limits calculated using a bootstrap method. Bottom row shows numbers needed per cohort arm, assuming 50% change, 80% probability, alpha 0.05. Units are in vector units for bone shape, and mm for cartilage thickness.

Abstract THU0425 – Table 1. Responsiveness of bone shape and cartilage thickness by KL Grade

B score Change (femur)								
	1 year				2 year			
	SRM (±95% CL)	Cohort Size	Mean Change	SD	SRM (±95% CL)	Cohort Size	Mean Change	SD
KL 0	0.21 (0.17 , 0.24)	1177 (851 , 1808)	0.030	0.147	0.48 (0.44 , 0.51)	218 (188 , 258)	0.090	0.189
KL 2	0.34 (0.29 , 0.39)	421 (324 , 578)	0.064	0.186	0.56 (0.51 , 0.61)	156 (132 , 188)	0.158	0.281
KL 2	0.55 (0.52 , 0.59)	162 (141 , 185)	0.125	0.225	0.75 (0.71 , 0.79)	88 (79 , 98)	0.259	0.344
KL 3	0.78 (0.68 , 0.85)	82 (69 , 106)	0.251	0.322	0.96 (0.9 , 1.03)	54 (47 , 62)	0.459	0.477
Cartilage Thickness Change (cMF region)								
	1 year				2 year			
	SRM (±95% CL)	Cohort Size	Mean Change	SD	SRM (±95% CL)	Cohort Size	Mean Change	SD
KL 0	-0.05 (-0.09 , -0.01)	17857 (310065 , 6130)	-0.004	0.068	-0.24 (-0.27 , -0.2)	875 (1202 , 663)	-0.019	0.079
KL 1	-0.17 (-0.22 , -0.12)	1761 (3689 , 1063)	-0.016	0.093	-0.32 (-0.36 , -0.27)	488 (683 , 376)	-0.037	0.117
KL 2	-0.21 (-0.17 , -0.25)	1132 (1798 , 787)	-0.023	0.110	-0.35 (-0.31 , -0.39)	409 (514 , 328)	-0.049	0.140
KL 3	-0.34 (-0.4 , -0.28)	433 (636 , 314)	-0.054	0.161	-0.52 (-0.58 , -0.46)	186 (235 , 148)	-0.107	0.207

Detailed breakdown of SRM values, cohort size, mean change, and SD of that change for Figure 1. Units are in vector units for bone shape, and mm for cartilage thickness.

Disclosure of Interests: Michael Bowes Shareholder of: Stryker Corporation, Employee of: Stryker Corporation, Alan Brett Shareholder of: Stryker Corp, Employee of: Stryker Corp, Philip G Conaghan Consultant for: Flexion Therapeutics, AbbVie, Medivir, Merck Serono, Novartis, GlaxoSmithKline

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THU0426 EFFECTS OF SODIUM SUCCINATE AND HYALURONIC ACID IN KNEE OSTEOARTHRITIS TREATMENT

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Background: At present hyaluronic acid (HA) is rather widely used in treatment of patients with osteoarthritis (OA). HA normalizes the properties of the synovial fluid; has a protective effects; promotes the cartilage nutrition and so improves the signs of OA and function of the joints. Sodium succinate (the salt of the succinic acid) helps to normalize intracellular metabolism and tissue respiration in hypoxic conditions via mitochondrial mechanism of action; normalizes acidic – alkaline balance; takes part in K^+ and Ca^{2+} transportation and provides antioxidant defense, - so is a promising compound for cartilage treatment

Objectives: To investigate the clinical efficacy of combination of hyaluronate and sodium succinate in treatment of early OA stages

Methods: The study included 126 patients with knee OA (stages I-II, Kelgren and Lawrence), mean age (54.3 ± 2.7) years, among them - 75 women (60%) and 51 men - (40%). All enrolled patients had OA exacerbation (without clinically evident synovitis) and received standard OA treatment (NSAIDs, exercises, orthopedic devices) for 15 days; Gr.1 patients (58) also got 5 intra-articular injections of 1.1% hyaluronic acid, stabilized with sodium succinate (2 ml, once a week); patients of Gr.2 (68) in addition to standard treatment received 5 intra-articular injections of 1,1% solution of non-stabilized HA (2 ml, once a week). Clinical observation and evaluation of the results were performed at the beginning of the treatment, at 6th, 12th and 24th week after the study beginning

Results: During the treatment period, patients in both groups showed the positive changes in clinical signs and symptoms of OA which led to the lowering of the general WOMAC index (from (78.3 ± 4.1) in Gr. 1 and (75.4 ± 3.8) in Gr. 2 at the beginning of the study to (27.9 ± 2.6) and (29 8 ± 1.9) accordingly at week 12 (p<0,05 for both groups). The VAS score in both groups indicated a significant pain reduction, but the stability and duration of the clinical effect in the groups was different. In patients of Gr.1, the pain syndrome continued to decrease after 12 weeks till 24th week, whereas in Gr.2 after the treatment course there was no significant changes in further pain regression after 6th week point. The changes in Lisholm score were also significantly better in Gr.1 than in Gr. 2 (before treatment (21.7 ± 4.6) and (22.6 ± 5.3), at week 6 - (86.4 ± 5.7) and (71.3 ± 4.8), at week 12 – (87.6 ± 6.2) and (63.8 ± 5.3), respectively, p<0,05 between groups at week 12th

Conclusion: Combination of the hyaluronic acid and sodium succinate biochemical and physiologic properties in early stages of knee OA (as intra-articular injections) allows to increase the treatment efficacy, achieve better pain control, and more stable remission comparing to use of the hyaluronic acid alone

Disclosure of Interests: None declared

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THU0427 THE LIFETIME RISK OF KNEE AND HIP REPLACEMENT FOLLOWING A GP DIAGNOSIS OF OSTEOARTHRITIS: REAL WORLD COHORT DATA FROM CATALONIA INCLUDING 48,311 PARTICIPANTS WITH UP TO 9 YEARS OF FOLLOW-UP

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Background: The lifetime risk of knee and hip replacement following a primary care diagnosis of knee or hip osteoarthritis is unknown and overly negative beliefs about prognosis act as a barrier to implementing recommended management strategies.

Objectives: To estimate lifetime risk of knee and hip replacement following a GP diagnosis of osteoarthritis and assess how this risk varies with patient characteristics.

Methods: Primary care and linked hospital data from Catalonia, covering 2006 to 2015, were used. Study participants had a newly recorded GP diagnosis of knee or hip osteoarthritis. Parametric survival models were specified for risk of knee/hip replacement and death following diagnosis. Survival models were combined and extrapolated using a Markov model and lifetime risk estimated for the average patient profile. The effects of age at diagnosis, sex, comorbidities, socioeconomic status, body mass index (BMI), and smoking on risk were assessed.

Results: 48,311 individuals diagnosed with knee osteoarthritis were included with a median follow-up of 4.3 years (IQR: 2.1 to 6.5) and of whom 2,561 underwent knee replacement. Respective figures for hip osteoarthritis were 15,105 individuals diagnosed with a median follow-up of 3.8 years (IQR: 1.8 to 6.1) and 1,247 hip replacements. The average participant's lifetime risk for knee replacement was 30% (95% CI: 25% to 36%) and for hip replacement was 14% (10% to 19%). Notable patient characteristics influencing lifetime risk were age at diagnosis for knee and hip replacement, sex for hip replacement, and BMI for knee replacement. BMI increasing from 25 to 35 was associated with lifetime risk of knee replacement increasing from 24% (20% to 28%) to 32% (26% to 37%) for otherwise average patients.

Conclusion: Knee and hip replacement are not bound to happen for most after a GP diagnosis of osteoarthritis, with average lifetime risks of less than a third and a sixth, respectively. Patient characteristics influence lifetime risks with, most notably higher BMI associated with a meaningfully increased risk of knee replacement.

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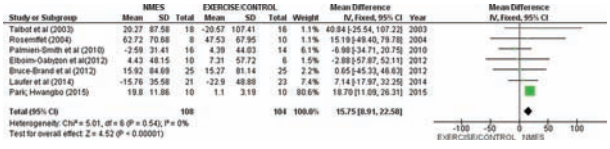
DOI: 10.1136/annrheumdis-2019-eular.5401

THU0428

THE EFFECTS OF NEUROMUSCULAR ELECTRICAL STIMULATION ON STRENGHT, PAIN, AND FUNCTION IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

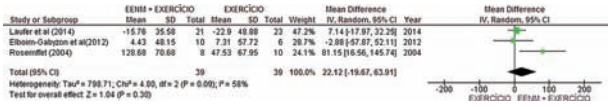
Camila Cadena[1,2], Vinícius Bispo[3], Karenina Modesto[1], Gerson Cipriano[4], João Luiz Durigan[4]. [1]*Universidade de Brasília, Faculdade de Educação Física, Brasília, Brazil*; [2]*Tribunal Superior Eleitoral, Fisioterapia, Brasília, Brazil*; [3]*CEFITE, Brasília, Brazil*; [4]*Universidade de Brasília, Fisioterapia, Brasília, Brazil*

Background: Even thought Neuromuscular electrical stimulation (NMES) has been widely used as a non-pharmacological intervention in patients with knee osteoarthritis (OA) to improve muscle strength and function, prior research has shown conflicting results regarding NMES effectiveness in knee OA treatment.
Objectives: The aim of this systematic review and meta-analysis was to investigate the effectiveness of NMES in muscle strengthen, pain, and function in individuals with knee OA.
Methods: Only randomized controlled trials (RCTs) were included in this study. Two authors independently performed the study selection. We use Pubmed, Embase, LILACS, PEDro and Cochrane Central Register of Controlled Trials as data sources. The main outcome evaluated was muscle strength. Function and pain were assessed as secondary outcomes using the Western Ontario Macmaster (WOMAC) questionnaire and Timed get up and go (TUG) test. The methodological quality was assessed using PEDro scale.
Results: A total of 23,215 were initially identified. After selection of titles and abstracts, studies were selected for the full-text analysis, ten studies were included with a total sample size of 622 patients. The methodological quality of the selected studies was moderate, with a mean score of 5.5 on a 0-10 scale (PEDro). The following analysis were performed:



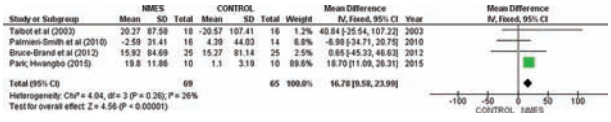
Abstract THU0428 – Figure 1. Meta-analysis of the effect of NMES on the increase of isometric muscle strength.

Legend: All measurements were standardized in N/m. A homogeneity in the data (Chi² = 5.01; I² = 0%) was identified, with a significant difference in favor of NMES (Z = 4.52, p = 0.01). NMES - Neuromuscular electro stimulation.



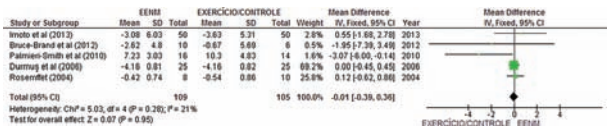
Abstract THU0428 – Figure 2. Meta-analysis of the effect of NMES associated with exercise vs conventional exercise in increasing isometric muscle strength.

Legend: A heterogeneity in the data was identified (Chi² = 4.80, I² = 58%), with no significant difference in favor of NMES (Z = 1.04, p = 0.30).



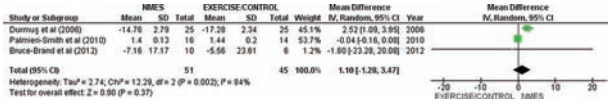
Abstract THU0428 – Figure 3. Meta-analysis of the effect of NMES vs control (No intervention) on isometric muscle strength

Legend: A homogeneity in the data (Chi² = 4.04; I² = 26%) was identified, with a significant difference in favor of NMES (Z = 4.56, p = 0.01). N



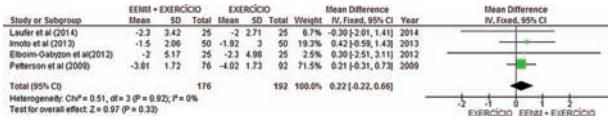
Abstract THU0428 – Figure 4. Meta-analysis of the effect of NMES on WOMAC pain

Legend: Data homogeneity (Chi² = 5.03; I² = 21%) was identified, with no significant difference in favor of NMES (Z = 0.07, p = 0.95). NMES - Neuromuscular electro stimulation.



Abstract THU0428 – Figure 5. Meta-analysis of the effect of NMES on WOMAC function

Legend: Data homogeneity (Chi² = 12.29; I² = 84%) was identified, with no significant difference in favor of NMES (Z = 0.90, p = 0.37).



Abstract THU0428 – Figure 6. Meta-analysis of the effect of neuromuscular electrical stimulation on a secondary outcome: Timed Up and Go (TUG)

Legend: A homogeneity in the data (Chi² = 0.51; I² = 0%) was identified, with no significant difference in favor of NMES associated with exercise (Z = 0.97, p = 0.33).
Conclusion: NMES increased muscle strength in patients with OA compared to the active control group. However, the evidence to date did not demonstrate effects for pain control nor improvement in physical function.

REFERENCES:

[1] Elboim-Gabyzon M, Rozen N, Laufer Y. 2013 Does neuromuscular electrical stimulation enhance the effectiveness of an exercise programme in subjects with knee osteoarthritis? A randomized controlled trial. Clinical Rehabilitation.27(3):246-257.
[2] De Oliveira Melo M, Aragão FA, Vaz MA. 2013 Neuromuscular electrical stimulation for muscle strengthening in elderly with knee osteoarthritis - A systematic review. Complementary Therapies in Clinical Practice.19(1):27-31.

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Disclosure of Interests: None declared
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THU0429

DISEASE BURDEN OF PERSONS WITH OSTEOARTHRITIS: RESULTS OF A CROSS-SECTIONAL ANALYSIS FROM A SURVEY LINKED TO CLAIMS DATA IN THE PROCLAIR PROJECT

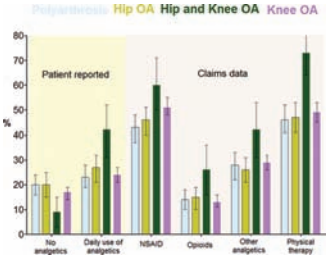
Johanna Callhoff[1], Katinka Albrecht[1], Imke Redeker[2], Toni Lange[3], Jens Goronzy[3], Klaus-Peter Günther[3], Angela Zink[1,2], Jochen Schmitt[4], Anne Postler[3]. [1]*German Rheumatism Research Centre, Epidemiology, Berlin, Germany*; [2]*Charité University Medicine, Berlin, Germany*; [3]*University Medicine Carl Gustav Carus Dresden, University Center of Orthopedics and Traumatology, Dresden, Germany*; [4]*University Medicine Carl Gustav Carus Dresden, Dresden University Center for Evidence-Based Healthcare, Dresden, Germany*

Background: Osteoarthritis (OA) is a major reason for chronic pain, stiffness and functional limitation. While disease burden is frequently examined prior to surgery in knee and hip OA, burden in patients with unknown indication of joint surgery and the impact of polyarticular involvement are less often studied.
Objectives: The aim was to analyze factors associated with the burden of OA, taking the pattern of joint involvement into account.
Methods: From a random sample of 8,995 persons with OA (ICD-10 codes M15 [polyarticular], M16 [hip] or M17 [knee]) from a large German statutory health insurance, 3,564 persons completed a questionnaire including the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Persons with knee, hip, concomitant knee and hip or polyarticular manifestation were compared concerning pain, stiffness, function, and impact on work/personal life, excluding asympomatic OA. Data were linked to dispensation records. The association of age, gender, BMI, symptom duration and WHO-5 with the WOMAC was assessed in multiple linear regression models.
Results: Persons with symptomatic knee (1,130), hip (538), knee and hip (131) and polyarthritic (653) OA were included. Concomitant knee and hip OA was accompanied with the highest WOMAC values (mean 51),

frequent impairment on work (66%) and personal life (87%) and the highest use of analgesics (60% NSAIDs, 25% opioids and 40% others). In the regression analyses, BMI per 5 units and WHO-5 per 10% worsening were associated with an increase in WOMAC values of 3-4 points, irrespective of the joint manifestations.

			WOMAC			
	Parameter	Reference	Polyarthrosis	Hip OA	Knee and Hip OA	Knee OA
Model 1	Age	per 10 years	0,7 (-0,6 ; 2,0)	0,7 (-1,2 ; 2,6)	2,0 (-0,5 ; 4,4)	-0,1 (-3,5 ; 3,3)
	Gender: Male	Female	**-3,8 (-6,7 ; -1,0)**	0,8 (-3,5 ; 5,0)	-3,7 (-8,1 ; 0,6)	-0,5 (-7,6 ; 6,6)
Model 2*	BMI, kg/m²	per 5 units	**4,4 (3,2 ; 5,5)**	**3,1 (1,1 ; 5,2)**	**4,2 (1,8 ; 6,6)**	**4,1 (0,6 ; 7,6)**
Model 3*	Symptom duration	per year	**0,3 (0,2 ; 0,5)**	**0,4 (0,2 ; 0,6)**	0,2 (-0,0 ; 0,4)	0,4 (0,0 ; 0,8)
Model 4*	WHO-5 (0-100)	per 10% worsening	4.4 (3.8; 5.0)	3.2 (2.2; 4.1)	4.1 (3.3; 5.1)	3.9 (2.1; 5.9)

Table: Results of four separate multiple linear regression models with the WOMAC as the dependent variable. Regression coefficients with 95% confidence intervals are shown.
*Model adjusted for age, gender. BMI: Body Mass Index, OA: Osteoarthritis, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Score.



Abstract THU0429 – Figure 1. Patient reported use and claims data prescriptions of analgesics and physical therapy. NSAID: Non-steroidal anti-rheumatic drugs, OA: Osteoarthritis.

Conclusion: Disease burden is high in persons with concomitant knee and hip OA, going along with frequent prescription of analgesics. The pattern of joint affection, BMI and depressive symptoms need to be considered when using the WOMAC as an outcome instrument.
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Disclosure of Interests: Johanna Callhoff: None declared, Katinka Albrecht: None declared, Imke Redeker: None declared, Toni Lange: None declared, Jens Goronzy: None declared, Klaus-Peter Günther: None declared, Angela Zink Speakers bureau: Speakers fees from AbbVie, Janssen, Pfizer, Roche, Sanofi, Jochen Schmitt: None declared, Anne Postler: None declared
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THU0430 PREPARING AN ORTHOPAEDIC CONSULTATION USING AN EHEALTH TOOL: A RANDOMIZED CONTROLLED TRIAL IN PATIENTS WITH HIP AND KNEE OSTEOARTHRITIS

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Background: Hip and knee OA patients who are referred to an orthopaedic surgeon often expect action to be taken.[1] However, the majority who of those patients is not (yet) eligible for a joint replacement.[2,3] We hypothesized that a solid preparation using the eHealth tool is likely to streamline patients' expectations and increase satisfaction, irrespective of the outcome of the consultation.
Objectives: To evaluate the effect of a stand-alone mobile and web-based educational intervention (eHealth tool) compared to usual preparation of a first orthopaedic consultation of patients with hip or knee osteoarthritis (OA) on patients' satisfaction.
Methods: A two-armed unblinded randomized controlled trial involving 286 patients with (suspicion of) hip or knee OA, randomly allocated to either receiving an educational eHealth tool to prepare their upcoming consultation (n=144) or usual care (n=142). Satisfaction with the consultation on three subscales (range 1-4) of the Consumer Quality Index (CQI - primary outcome) and knowledge (assessed using 22 statements on OA, range 0-22), treatment beliefs (assessed by the Treatment beliefs in OsteoArthritis questionnaire, range 1-5), pain medication use (yes/no), assessment of patient's involvement in consultation by the surgeon (assessed on a 5-point Likert scale) and patient satisfaction with the outcome of the consultation (numeric rating scale), were assessed.
Results: No differences between groups were observed on the 3 subscales of the CQI (group difference (95% CI): communication 0.009 (-0.10, 0.12), conduct -0.02 (-0.12, 0.07) and information provision 0.02 (-0.18, 0.21)). Between group differences (95% CI) were in favour of the intervention group for knowledge (1.4 (0.6, 2.2)), negative beliefs regarding physical activities (-0.19 (-0.37, -0.002) and pain medication (-0.30 (-0.49, -0.01)). We found no differences on other secondary outcomes.
Conclusion: An educational eHealth tool to prepare a first orthopaedic consultation for hip or knee OA does not result in higher patient satisfaction with the consultation, but it does influence cognitions about osteoarthritis.

REFERENCES:

[1] Samsson KS, Bernhardsson S, Larsson ME. "Take me seriously and do something!" - a qualitative study exploring patients' perceptions and expectations of an upcoming orthopaedic consultation. BMC Musculoskelet Disord 2017 Aug 24;18(1):367
[2] Barten DJ, Smink A, Swinkels IC, Veenhof C, Schers HJ, Vliet Vlieland TP, et al. Factors Associated With Referral to Secondary Care in Patients With Osteoarthritis of the Hip or Knee After Implementation of a Stepped-Care Strategy. Arthritis Care Res (Hoboken) 2017 Feb;69(2):216-25
[3] McHugh GA, Campbell M, Luker KA. GP referral of patients with osteoarthritis for consideration of total joint replacement: a longitudinal study. Br J Gen Pract 2011 Aug;61(589):e459-e468

Disclosure of Interests: None declared
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THU0431 FREQUENCY OF TENDON INVOLVEMENT AND ITS EFFECT ON HAND FUNCTION IN HAND OSTEOARTHRITIS

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Background: Tenosynovitis and consequent tendon damage are common findings in inflammatory arthritides. In contrast to rheumatoid arthritis (RA) and psoriatic arthritis, little is known about the frequency of tendon involvement in hand osteoarthritis (HOA) and the influence thereof on hand function. Ultrasound has been reported to have a high specificity in diagnosing tenosynovitis and tendon damage.
Objectives: We aimed to appraise the frequency of tendon involvement in HOA and to assess the agreement between ultrasound (US) and clinical diagnosis of tenosynovitis and tendon damage in HOA. In addition, we wanted to assess the influence of tendon involvement on hand function.
Methods: We included 73 patients with HOA in the study. Each patient underwent a clinical as well as a US examination of the 6 extensor tendon compartments and 6 flexor tendons of the hand (fig. 1). They were assessed for US signs of tenosynovitis and tendon damage as well as osteophytes (presence/absence) by a sonographer blinded to clinical information, as well as for clinical tendon involvement (presence/absence) by a biometrician blinded to the US results. Difference in frequency of sonographically detected tendon involvement between flexor and extensor tendons and between right and left hand were calculated by Chi-Square test. Osteophytes were also evaluated on standard radiographs. Agreement between US and clinical examination was calculated by Cohen's kappa. Hand function was quantified using the Score for the Assessment and Quantification of Chronic Rheumatoid Affections of the Hands (SACRAH) questionnaire as well as the Moberg pick-up test (MPUT). Correlation between MSACRAH and tendon involvement was calculated by Spearman's correlation.
Results: In 41 patients (56.2%), at least one tenosynovitis was observed and in 8 (11%) patients, at least one tendon damage was detected by US. Tendon damage was found more often in flexor tendons (0.2% vs. 2.2%, p<0001), while tenosynovitis was found more often in extensor

tendons (6.9% vs. 0.7%, p<0001). The right hand was affected more often by tendon damage than the left hand (2.5% vs. 1.1%, p<0.05), but not by tenosynovitis (3.5% vs. 4%, p=0.7). Among all tendons, tenosynovitis affected most often the sixth extensor compartment (in 28.1%), while tendon damage most frequently involved Flexor digitorum II and II (each 4.8%) detected by US (fig. 1).

Clinically, any tendon involvement was observed in 57 (78.1%) patients. There was no agreement between the US and the clinical examination on the level of individual tendons (kappa -0.0007) and only slight agreement on the level of individual patients (any affected tendon yes/no) (kappa 0.16). We also found no association between osteophytes (radiographic or US) and tendon involvement regardless of assessment. Neither total MSACRAH nor the MPUT correlated with the number of affected tendons detected by US. However, there was a slightly significant correlation between the number of clinically affected tendons and the MSACRAH subtest for hand function and stiffness.

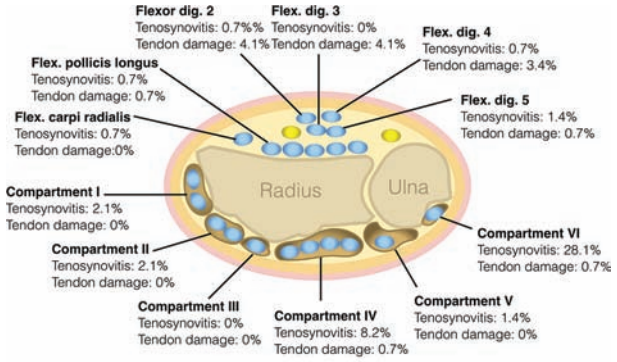


Fig.1 Distribution of tenosynovitis and tendon damage in the sonographic examination

Abstract THU0431 – Figure 1.

Conclusion: This study revealed a high frequency of tendon involvement in HOA. The prevalence of tenosynovitis was similar as reported for RA and other inflammatory arthritides. The fact that we could demonstrate marked differences in the distribution of tenosynovitis and tendon damage between and among flexor and extensor tendons as assessed on US, coupled with the overall homogeneous clinical involvement, suggests that clinical examination may be less specific for tendon involvement as compared to US. Tendon involvement on US does not seem to have an impact on hand function in HOA.

Disclosure of Interests: Irina Gessl Grant/research support from: Travel Grant, Anna Vinatzer: None declared, Gabriela Supp: None declared, Michael Zauner: None declared, Michaela Loiskandl: None declared, Martina Durechova: None declared, Valentin Ritschl: None declared, Josef S. Smolen Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer, Roche, Consultant for: AbbVie, Amgen, Astra-Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, MedImmune, MSD, Novartis, Pfizer, Roche, Samsun, Sanofi, UDB, Speakers bureau: AbbVie, Amgen, Astra-Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, MedImmune, MSD, Novartis, Pfizer, Roche, Samsun, Sanofi, UDB, Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Peter Mandl: None declared

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THU0432 LUMBAR FACET JOINT OSTEOARTHRITIS IS A RISK FACTOR OF SACROILIAC JOINTS DEGENERATION

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Background: Degeneration of sacroiliac joints (SIJ) is common in the general population, which associates with age, gender and body mass index (BMI). This degenerative disease relates to various lumbar disorders. Lumbar facet joint osteoarthritis (LFJOA) is highly prevalent, but relationship between this disease and SIJ degeneration remains poorly evaluated.

Objectives: This study aimed to investigate the relation between LFJOA and SIJ degeneration. We hypothesized that LFJOA patients might suffer more serious SIJ degeneration, thus multiple linear regression was employed to compare the effect of LFJOA and demographic characteristics on degeneration of SIJ.

Methods: We reviewed pelvic and lumbar computed tomography (CT) examinations of LFJOA patient with low back pain (LBP) through a picture archiving and communication system. The controls were age, gender and BMI-matched individuals who were free of LFJOA and LBP, and underwent pelvic and whole abdomen CT scans due to the non-musculoskeletal symptoms. Severity of SIJ degeneration was scored using a quantitative method which has been described by Bäcklund et al [1]. LFJOA was graded using a method which has been mentioned by Weishaupt et al [2]. Briefly, this method concerns facet joint space, osteophytes, hypertrophy of the articular processes, and subarticular bone erosions, which ranges from 0 to 3 for a joint. If there is a discrepancy between 2 joints in the same level, the greater one was used. LFJOA was defined at least one level $\geq$2 from L1-2 to L5-S1. Scores of SIJ degeneration were compared between LFJOA patients and the controls. Correlation analysis between SIJ degeneration score and number of LFJOA levels, number of LFJOA joints, sum of LFJOA grades were performed. Stepwise multiple linear regression model was used to find the most important contributor of SIJ degeneration among LFJOA, gender, age and BMI.

Results: (1) CT examinations of 992 LFJOA patients and 399 controls were reviewed. (2) Score of SIJ degeneration in LFJOA patients were higher than that of the controls (8.85±2.94 vs. 4.31±2.52, P<0.05). (3) SIJ degeneration score positively correlated with number of LFJOA levels (r=0.11, P<0.05), number of LFJOA joints (r=0.09, P<0.05) and sum of grades (r=0.10, P<0.05). (4) Results of multiple linear regression were shown in Table 1. LFJOA had the greatest standardized coefficient in the regression model.

Conclusion: LFJOA patients suffers more significant SIJ degeneration, and more severe LFJOA leads to more serious SIJ degeneration. Influence of LFJOA on SIJ degeneration is stronger than demographic characteristics.

REFERENCES:

[1] Bäcklund J, Clewett Dahl E, Skorpil M. Is CT indicated in diagnosing sacroiliac joint degeneration? Clin Radiol 2017;72(8):693.e9-693.e13.

[2] Weishaupt D, Zanetti M, Boos N, et al. MR imaging and CT in osteoarthritis of the lumbar facet joints. Skeletal Radiol 1999; 28: 215-219.

Abstract THU0432 – Table 1. Stepwise multiple linear regression model for sacroiliac joints degeneration score

Independent variables	Unstandardized coefficient		Standardized coefficient	*P* value	95% confidence interval for B		Variance inflation factor
	B	SE			Lower bound	Upper bound	
LFJOA	-4.49	0.12	-0.58	<0.001	-4.73	-4.25	1.00
Age	0.124	0.00	0.55	<0.001	0.12	0.13	1.01
BMI	0.05	0.01	0.06	<0.001	0.02	0.07	1.00
Gender	0.30	0.11	0.04	0.009	0.08	0.53	1.01

SE standard error, *LFJOA* lumbar facet joint osteoarthritis, *BMI* body mass index R^2=0.65, adjusted R^2=0.65

Acknowledgement: None.

Disclosure of Interests: None declared

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THU0433 THE BURDEN OF OSTEOARTHRITIS PAIN FROM THE PATIENT'S PERSPECTIVE IN EUROPE

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Background: Pain, the primary symptom of osteoarthritis (OA), affects multiple aspects of a patient's life.

Objectives: To evaluate the burden of OA pain from the patient's perspective in 5 European countries (France, Germany, Italy, Spain, the United Kingdom; EU5).

Methods: This real-world cross-sectional study used data from the 2017 EU5 Adelphi OA Disease Specific Programme, a survey of physicians and their OA patients. Physicians completed a Patient Record Form on need for treatment, opioid use, and comorbidities. The patient-completed questionnaire included assessment of pain and physical function (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC]), health-related quality of life (HRQoL; EuroQol 5-dimension 5-level [EQ-5D-5L]), activity/productivity impairment (OA-specific Work Productivity and Activity Impairment questionnaire), and other functional limitations (e.g., need for walking aid, suffered a fall). Patients with hip/knee OA diagnosed by physicians were stratified by their current OA pain intensity (no/mild pain [WOMAC score 0–3] or moderate/severe pain [WOMAC score ≥4]) and opioid use. Multivariate testing was used to compare outcomes for patients with no/mild pain & no opioid use vs those with no/mild pain & opioid use; moderate/severe pain & no opioid use; and moderate/severe pain & opioid use.

Results: The study included 1,547 patients with hip/knee OA (55.0% knee only, 26.8% hip only, 18.2% both hip and knee; mean [SD] age 66.8 [11.1] years; 57.0% female). Among this sample, 34.4% of patients (n=532) had no/mild pain & no opioid use; 11.2% (n=173) had no/mild pain & opioid use; 32.8% (n=508) had moderate/severe pain & no opioid use; and 21.6% (n=334) had moderate/severe pain & opioid use. Patients with moderate/severe pain with or without opioid use had higher comorbidity burden compared with patients with no/mild pain & no opioid use (Charlson Comorbidity Index: 0.7 and 0.4, respectively, vs 0.3, *P*<.05) and were more likely to report physical mobility impacted by OA (87.2% and 77.0%, respectively, vs 51.2%; *P*<.0001), need for a walking aid (68.6% and 46.6%, respectively, vs 36.4%; *P*<.05), ever suffering a fall due to OA (45.8% and 30.8%, respectively, vs 24.1%; *P*<.05), dissatisfaction with current OA treatment (39.1% and 25.7%, respectively, vs 6.6%; *P*<.0001), poorer HRQoL (EQ-5D-5L utility score 0.5 and 0.6, respectively, vs 0.8; *P*<.0001), higher overall activity impairment (66.8% and 59.7%, respectively, vs 31.1%, *P*<.0001) and work impairment due to OA (employed patients only: 60.9% and 45.3%, respectively, vs 29.1%, *P*<.0001). Patients with no/mild pain & opioid use had poorer outcomes (*P*<.05) vs no/mild pain & no opioid use except for falls, treatment dissatisfaction, and work impairment due to OA.

Conclusion: In this EU cohort, patients with moderate/severe OA pain reported significant burdens that comprised greater treatment needs; more comorbidities; and reductions in physical functioning, HRQoL, and work productivity and daily activities. Patients with moderate/severe OA pain and opioid use experienced the highest burdens. These results demonstrate the multidimensional impact of OA pain on a patient's life and underscore an unmet need for more effective treatment options for OA pain.

References: N/A

Disclosure of Interests: James Jackson Consultant for: Regeneron Pharmaceuticals, Inc., and Teva Pharmaceutical Industries, Wenhui Wen Employee of: Regeneron Pharmaceuticals, Inc., Pavlina Hubanova Consultant for: Regeneron Pharmaceuticals, Inc., and Teva Pharmaceutical Industries, Nathan Williams Consultant for: Regeneron Pharmaceuticals, Inc., and Teva Pharmaceutical Industries, Jennifer Mellor Consultant for: Regeneron Pharmaceuticals, Inc., and Teva Pharmaceutical Industries, Ravi Iyer Employee of: Teva Pharmaceutical Industries Ltd.

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THU0434 KNEE JOINT DISTRACTION AS STANDARD OF CARE TREATMENT FOR KNEE OSTEOARTHRITIS: A COMPARISON WITH CLINICAL TRIAL PATIENTS

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Background: Knee joint distraction (KJD) has been evaluated as joint-preserving treatment for patients with knee osteoarthritis (OA) in 3 clinical trials since 2004. KJD aims to delay a total knee arthroplasty (TKA) in young knee OA patients, to decrease the risk for revision surgery. KJD temporarily separates the tibia and femur, unloading the knee joint. In an open prospective study (OPS) and 2 randomized controlled trials (RCTs), KJD showed cartilage regeneration and clinical improvement[1,2]. Since 2014, KJD is a standard of care treatment option in several Dutch hospitals for younger (≤65 yrs) knee OA patients.

Objectives: Compare baseline characteristics and clinical outcome at 1 year post-treatment between KJD patients treated in regular care *vs* study conditions.

Methods: In the OPS, patients (n=20; age <60 years) with end-stage OA indicated for TKA were treated with KJD for 8 weeks between 2004 and 2006. In an RCT comparing KJD with TKA, end-stage knee OA patients considered for TKA were treated with KJD (n=19; age <65 years) and completed 1-year follow-up. In an RCT comparing KJD with HTO, medial knee OA patients considered for HTO were treated with KJD (n=22; age <65 years). In both RCTs, patients were treated with KJD for 6 weeks between 2011 and 2014. From 2014-2017, 84 patients were treated with 6-week KJD in regular care and available for 1-year follow-up.

All distraction surgery was performed using two external fixators with built-in springs. The knee was distracted 5 mm and weight-bearing was supported. WOMAC questionnaires were assessed at baseline (0) and 12 months. Only regular care patients who completed both questionnaires were included in analyses.

Abstract THU0434 –Table 1.

Table I: Baseline characteristics of patients treated with knee joint distraction.

	Study patients (n = 61)	Regular care patients (n = 41)	P-value
Age, years (mean ±SD)	51,7 (6,8)	54,0 (6,9)	0,102
Male gender, n (%)	35 (57)	23 (56)	0,898
BMI, kg/m² (mean±SD)	28,1 (3,7)	27,8 (3,9)	0,744
Left index knee, n (%)	26 (43)	19 (46)	0,711
Range of motion, degrees (mean±SD)	122,7 (14,9)	125,4 (14,1)	0,362
Leg axis, degrees (mean±SD)	4,8 (4,4)	4,6 (4,7)	0,876
Kellgren&Lawrence grade, n (%)			0,084
- Grade 0	0 (0)	0 (0)	
- Grade 1	9 (15)	0 (0)	
- Grade 2	9 (15)	7 (17)	
- Grade 3	30 (49)	24 (59)	
- Grade 4	13 (21)	10 (24)	
Distraction duration, days (mean±SD)	48,2 (8,2)	45,5 (4,2)	**0,032**
- without OPS	42,8 (2,3)	45,5 (4,2)	**0,001**
WOMAC Baseline, points (mean±SD)			
- Total	49,8 (15,7)	47,5 (14,9)	0,464
- Pain	49,8 (15,7)	46,3 (16,9)	0,293
- Stiffness	45,4 (18,3)	39,3 (23,1)	0,141
- Function	51,0 (16,2)	48,9 (15,2)	0,498

Baseline patient characteristics were compared between 'study' (OPS/RCT) and 'regular care' patients. For each group, the total WOMAC scores and subscales at follow-up were compared to baseline. The influence of different characteristics on the 1-year change in WOMAC scores was analyzed. Characteristics predicting being a responder to KJD treatment were analyzed according to the OMERACT-OARSI responder criteria, defined as an increase of ≥50% and ≥20 points in WOMAC pain or function scales, or a ≥20% and ≥10-point improvement in both scales.

Results: In regular care, 41 patients completed both questionnaires. Baseline characteristics for both groups are shown in table I, showing a significant, but small difference in distraction duration, which was longer for study patients, but shorter when excluding the OPS patients who received distraction 2 weeks longer. The total WOMAC score and subscales for both groups increased significantly at 1 year compared to baseline (figure 1). The increase in total WOMAC and all subscales was over 15 points and thus clinically significant for both groups. The increase in the WOMAC function subscale was statistically, but not clinically, significantly higher for study patients (6.7 points) than regular care patients, while the total WOMAC, pain and stiffness were not different between groups (figure 1). After 1 year, 69% of patients were responders (60% regular care, 75% study patients, p=0.120). None of the baseline characteristics could significantly predict being a responder or had a significant influence on the increase in total WOMAC.

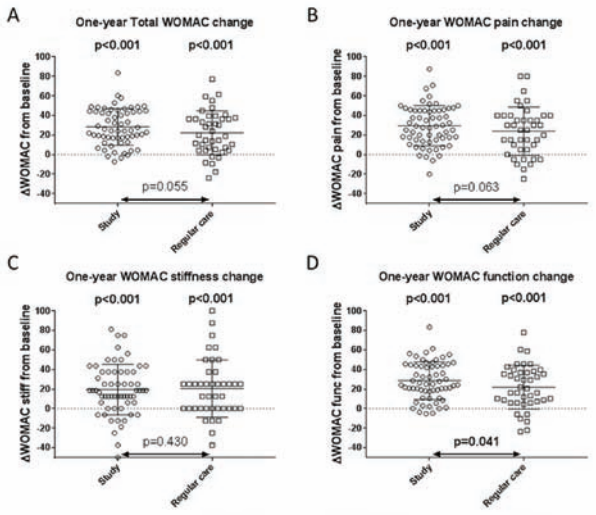


Figure 1: One-year change in total WOMAC score (A) and the WOMAC subscales pain (B), stiffness (C) and function (D) for patients treated with knee joint distraction in clinical studies and in regular care. In all graphs, the p-values above patient groups indicate significant one-year changes while the p-values between patient groups indicate the differences between the groups, corrected for baseline values.

Abstract THU0434 – Figure 1

Conclusion: KJD results in a statistically and clinically significant 1-year improvement in total WOMAC and subscales for most patients. There were no clinically relevant differences between study and regular care patients. Longer follow-up will show whether this is maintained. As such, KJD not only shows good efficacy in study conditions, but also in regular care and can be a joint-preserving treatment of choice for young knee OA patients.

REFERENCES:

[1] Van der Woude et al, Cartilage 2017;8(3):263-271.
[2] Jansen et al, *Cartilage* (accepted)

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THU0435 ASSESING THE EFFECTS OF PULSED ULTRASOUND TREATMENT ON PAIN, FUNCTIONALITY, SYNOVIAL FLUID AND CARTILAGE THICKNESS, IN KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a progressive rheumatic disease which is the most common cause of musculoskeletal pain and functional impairment, particularly in the elderly group. Ultrasound therapy is one of the most commonly used physical modalities in the OA treatment. It has deep heating effect and increases tissue regeneration, blood flow and metabolic effects while reducing the inflammation. In addition, it increases the cartilage regeneration according to certain in vivo and in vitro studies (1).
Objectives: To research the effect of pulsed ultrasound treatment on pain, functionality, synovial fluid and cartilage thickness in knee osteoarthritis.
Methods: This study was a randomised-controlled and parallel group study. 96 patients (79 females and 17 males) were included to study who had knee pain, aged between 45-75 years. They also have diagnosed as knee osteoarthritis according to ACR diagnostic criteria and their Kellgren-Lawrence grades were ≤3. These patients were divided in two groups randomly: Treatment group (exercise + US), (9 male, 39 female), control group (exercise + Sham US), (8 male, 40 female). The patients in the treatment group were treated with a 1 MHz probe and a density of 1w/cm², 1: 4 for 10 minutes, and 3 sessions a week for 8 weeks. Sham US treatment was applied to each group at the same time. Both groups received a home exercise program including knee range of motion and isometric strengthening exercises. All patients were evaluated by ultrasonographic measurements and quality of life tests; VAS (Visuel Analog Scale) rest, VAS walking, Timed Up and Go Test, WOMAC Questionnaire scores (before treatment, after treatment, 3 months after treatment).
Results: 9 out of 48 patients in the treatment group and 12 out of 48 patients in the control group were excluded from the study because they did not continue treatment or come to the control. The distribution of groups was similar (Table-1). VAS rest, VAS walking, Timed up and go test, WOMAC questionnaire scores, were improved statistically significant in both groups (P<0.05), but group effect could not be demonstrated (P>0.05) There were no statistically significant results in terms of both synovial fluid and femoral cartilage thickness measurements (P>0.05) (Table 2).

Abstract THU0435 –Table 1.

Table-1	Treatment group (exercise + US) n=48	Control group (exercise +Sham US) n=48	P
Age	58.52 ±7.28	60.02 ± 7.43	0,320
Gender	39 female 9 male	40 female 8 male	0.789
BMI (kg/m²)	28.59±4.97	29.29±9.23	0,700
VAS Rest	4.75 ± 2.23	4.37 ± 1.90	0,507
VAS Walking	7.10 ± 2.15	6.75± 2.03	0,360
Timed up and go test (sec)	12.52 ± 3.00	12.53 ± 2.20	0,990
WOMAC questionnaire scores	42.98 ± 18.32	39.85 ± 15.59	0,370
Synovial Fluid Amount (Right Knee)	0.39 ± 0.18	0.32 ± 0.15	0.081
Synovial Fluid Amount (Left Knee)	0.35 ± 0.16	0.39 ± 0.19	0.422
Femoral Cartilage Thickness (cm) (Right Knee)	0.17 ± 0,03	0.17 ± 0.02	0,722
Femoral Cartilage Thickness (cm) (Left Knee)	0.17 ± 0.02	0.17 ± 0.03	0,730

Table-2		Treatment group (exercise + US) n=39	Control group (exercise +Sham US) n=36	P**
VAS Rest	Before treatment	4.79±2.22	4.11±1.86	
	After treatment	2.49±1.87	2.89±2.21	
	3 months later	2.41±2.61	2.44±2.14	
	P*	P*<0,001	P*<0,001	0.140
VAS Walking	Before treatment	7.26±2.17	6.75±2.04	
	After treatment	4.08±2.45	4.39±2.49	
	3 months later	3.62±2.99	4.31±2.44	
	P*	P*<0,001	P*<0,001	0.144
WOMAC questionnaire scores	Before treatment	43.84± 19.01	41.05±13.73	
	After treatment	27.61±18.81	29.61±15.98	
	3 months later	25.56±18.72	28.67±13.42	
	P*	P*<0,001	P*<0,001	0.281
Timed up and go test (sec)	Before treatment	12.85±3.10	12.56±2.25	
	After treatment	11.44±1.92	11.97±2.10	
	3 months later	11.60±2.49	12.08±2.87	
	P*	P*<0,001	P*<0,001	0.166
Synovial Fluid Amount (Right Knee)	Before treatment	0.39±0.19	0.32±0.15	
	After treatment	0.37±0.16	0.34±0.15	
	3 months later	0.35±0.17	0.32±0.16	
	P*	P*=0.648	P*=0.670	0.370
Synovial Fluid Amount (Left Knee)	Before treatment	0.36±0.16	0.37±0.18	
	After treatment	0.37±0.14	0.39±0.13	
	3 months later	0.35±0.14	0.35±0.14	
	P*	P*=0.263	P*=0.864	0.888
Femoral Cartilage Thickness (cm) (Right Knee)	Before treatment	0.17±0.03	0.17±0.02	
	After treatment	0.17±0.02	0.17±0.02	
	3 months later	0.17±0.03	0.17±0.03	
	P*	P*=0.868	P*=0.879	0.864
Femoral Cartilage Thickness (cm) (Left Knee)	Before treatment	0.17±0.02	0.16±0.02	
	After treatment	0.17±0.02	0.16±0.02	
	3 months later	0.17±0.02	0.16±0.02	
	P*	P*=0.486	P*=0.599	0.611

P *: In-group evaluation P **: Intergroup evaluation (In-group comparison and group effect comparison was performed by ANOVA variance analysis)

Conclusion: Therapeutic ultrasound treatment in addition to home exercise program has not been shown to be effective rest and walking pain, functionality, synovial fluid and femoral cartilage thickness in the treatment of knee osteoarthritis. This is the first study to evaluate the effect of therapeutic intermittent ultrasound on synovial fluid and cartilage thickness by

ultrasonography. International collaborative studies and randomized clinical trials will help in clarifying these areas of uncertainty.

REFERENCES:

[1] -Loyola-Sánchez, A. 2012.'' Effect of low-intensity pulsed ultrasound on the cartilage repair in people with mild to moderate knee osteoarthritis: a double blinded, randomized, placebo-controlled pilot study'', Archives of Physical Medicine and Rehabilitation, 93(1), 35-42

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THU0436 THE RELATIONSHIP OF BONE MINERAL DENSITYOF THE AXIAL SKELETON ON THE RISK OF PROGRESSION OF OSTEOARTHRITIS OF THE KNEE

Natalia Kashevarova, Elena Taskina, Ludmila Alekseeva, Nikolay Demin, Aleksandr Lila. *VA Nasonova Research Institute of Rheumatology, Moscow, Russian Federation* **Objectives:** To find the relationship between bone mineral density (BMD) and risk of knee OA progression in a 5-year prospective study.
Methods: 110 females with knee OA were examined twice with 5-year interval. Examination included filling questionnaires, VAS pain assessment, plain knee radiography and axial skeleton densitometry. I stage knee OA was established in 33 (30%) patients, II stage - in 46 (41,8%, III stage – in 26 (23,6%), and IV - in 5 (4,5%). Normal lumbar vertebrae densitometry BMD values were found in 45 patients (40,9%), osteopenia-corresponding BMD values – in 33 (30,0%), and osteoporosis – in 32 (29,1%). Normal femoral neck BMD values were identified in 60 (54,5%) patients, osteopenia-level BMD – in 48 (43,7%), osteoporosis – in 2 (1,8%). In all premenopausal patients (n = 15) axial skeleton BMD values were normal.
Results: In 5-year interval radiographic progression was established in 40 patients (Group 2), while in 70 (Group 1) patients no progression occurred. Both groups were comparable in terms of age and disease duration, although, more patients from Group 2 tended to have normal baseline densitometry BMD values - both in lumbar vertebrae and femoral neck: 47,5% vs 37,1%, and 62,5% vs 44,3% as compared to Group 1 patients. Patients from Group 1 more often had BMD values corresponding to osteoporosis and osteopenia: 32,9 vs 22,5%, and 55,7 vs 37,5%, respectively, as compared to Group 2 patients, although not achieving statistical significance. These differences were still identifiable after 5-year interval. Absolute BMD values at the second examination in 5 years were indicative of statistically significant increase in femoral neck and total hip BMD in Group 2 patients with knee OA progression: 0,79 ± 0,11 vs 0,73 ± 0,16, p<0,01, and 0,93 ± 0,14 vs 0,84 ± 0,25, p<0,05; respectively.

Abstract THU0436 –Table 1.

Femoral BMD differences correlating with OA stage
(Scheffe's method, p < 0,05000)

	I stage	II stage	III stage	IV stage
I stage		0,651186	0,996946	**0,039177**
II stage	0,651186		0,747927	0,213481
III stage	0,996946	0,747927		**0,046981**
IV stage	**0,039177**	0,213481	**0,046981**	

Abstract THU0436 –Table 2.

Lumbar vertebrae BMD differences correlating with OA stage
(Scheffe's method, p < 0,05000)

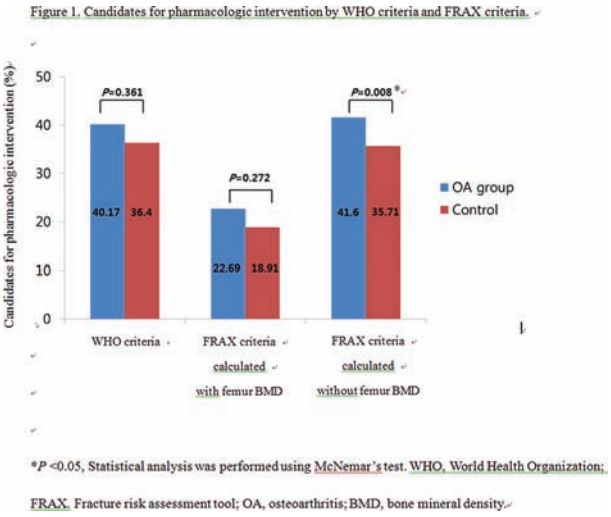
	I stage	II stage	III stage	IV stage
I stage		0,726047	0,998565	**0,004315**
II stage	0,726047		0,790777	**0,021175**
III stage	0,998565	0,790777		**0,004115**
IV stage	**0,004315**	**0,021175**	**0,004115**	

Thorough analysis of lumbar vertebrae BMD (g/cm^2) relationship with OA stages revealed that in patients with stage IV OA lumbar BMD values were significantly higher than in patients with stages I-III OA (stage I OA - BMD 0,87±0,12 g/cm^2; stage II OA - 0,92±0,21 g/cm^2; stage III OA - 0,88±0,13 g/cm^2, stage IV OA – BMD 1,07± 0,17 g/cm^2) (Table1). Femoral BMD values didn't show evident correlation with knee OA stage, although there was a trend towards higher BMD values in patients with stage IV OA compared to stage III OA (p = 0,06). Total hip BMD values were quite similar to lumbar BMD values (p = 0,01) (Table 2). BMD values were statistically significantly higher in patients with stage IV OA, than in patients with stages I and III (respectively, IV – 0,98 ± 0,13 g/cm^2, I - 0,85 ± 0,10 g/cm^2 and III - 0,86 ± 0,16 g/cm^2). Correlation analysis also confirmed direct correlation between knee OA stage and BMD values in all evaluated compartments (p<0,05).
Conclusion: Increasing during the 5-eyar follow up period femoral neck and total hip BMD values can be interpreted as the predictor of knee PA progression. More advanced OA stages are associated with higher BMD values. Future multicenter prospective studies are deemed to better establish the correlation between BMD and knee OA progression.
Disclosure of Interests:
Natalia Kashevarova: None declared, Elena Taskina Speakers bureau: Bayer, Sandoz, Boeringer-ingelheim, Ludmila Alekseeva Speakers bureau: Bayer, Boeringer-ingelheim, Gedeon-Richter, Servier, Nikolay Demin: None declared, Aleksandr Lila Speakers bureau: Sandoz, Pfizer, Abbvie, Novartis, Bayer
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THU0437 INCIDENCE OF OSTEOPOROTIC FRACTURE IN PATIENTS WITH KNEE OSTEOARTHRITIS: CLINICAL IMPACT OF FRAX-BASED OSTEOPOROSIS TREATMENT

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Background: The relationship between osteoporosis and osteoarthritis is complex and controversial. Several previous studies have indicated inverse relationship between osteoporosis and osteoarthritis [1-2]. However, the increased bone mineral density in osteoarthritis does not confer a reduce risk for fractures in other studies [3-4]. From the Rotterdam study, although patients with knee osteoarthritis had a higher bone mineral density, their incident fracture risk was increased as compared with those without knee osteoarthritis [5]. Therefore, fracture risk assessment in patients with knee osteoarthritis should not be overlooked.
Objectives: We aimed to evaluate the incidence of high risk group of osteoporotic fracture in patients with knee osteoarthritis comparing the FRAX and WHO criteria. We also examined whether patients with knee OA differ from age, sex, and BMI matched community-based control group without knee OA in terms of the incidence of high risk group of osteoporotic fracture.
Methods: We retrospectively assessed 282 Korean patients with knee OA who visited 5 medical centers between November 2012 and November 2015. For control group, 991 subjects aged of $\geq$ 50 years-old were enrolled in database of health chekup centers. After matching for age, sex and body mass index, 552 subjects (276 subjects in knee OA group and 276 subjects in control group) included for this study.
Results: Osteoporosis according to WHO criteria was detected 110 (39.86%) subjects in OA group, and 101 (36.59%) subjects in control group; these difference were not significant. However, mean FRAX major osteoporotic fracture probabilities calculated with femur neck T-score were significant different between OA group and control group (7.72% vs 6.10%, p<0.001). Mean FRAX major osteoporotic fracture probabilities calculated without femur neck T-score were also significant different between OA group and control group (8.85% vs 6.86%, p<0.001). Mean FRAX hip fracture probabilities calculated with femur neck T-score were significant different between OA group and control group (2.48% vs 1.73%, p<0.001). Mean FRAX hip fracture probabilities calculated without femur neck T-score were also different significant between OA group and control group (3.50% vs 2.37%, p<0.001). When FRAX calculations without the use of femur neck BMD was adjusted for knee OA group rather than control group, 5.9% more patients would be recommend for osteoporosis treatment. Among the clinical risk factors of FRAX, previous fracture was significant different between knee OA group and control group (15.9% vs 0%, p<0.001).



Abstract THU0437 – Figure 1

Conclusion: We demonstrated that knee OA patients have an increased risk of osteoporotic fracture according to FRAX criteria, but not WHO criteria. Our study suggests that FRAX supports clinical decision to reduce osteoporotic facture in patients with knee OA.
Disclosure: All authors agree that there are no conflicts of interest (both personal and institutional) regarding scientific financial interests that are relevant to the work conducted or reported in this manuscript.

REFERENCES:

[1] Stewart A, Black AJ. Bone mineral density in osteoarthritis. Curr Opin Rheumatol 2000;12:464-7.
[2] Dequeker J, Aerssens J, Luyten FP. Osteoarthritis and osteoporosis: clinical and research evidence of inverse relationship. Aging Clin Exp Res 2003;15:426-39.
[3] Jones G, N guren T, Sambrook PN, Lord SR, Kelly PJ, Eisman JA. Osteoarthritis, bone density, postural stability, and osteoporotic fracture: a population based study. J Rheumatol 1995;22:921-5.
[4] Arden NK, Nevitt MC, Lane NE, Gore LR, Hochberg MC, Scott JC, et al. Osteoarthritis and risk of falls, rates of bone loss, and osteoporotic fractures. Study of osteoporotic fracture research group. Arthritis Rheum 1999;42:1378-85.
[5] Bergink AP, van der Klift M, Hofman A, Verhaar JA, van Leeuwen JP, Uitterlinden AG, et al.

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THU0438 DO CORTICOSTEROIDS OR HYALURONIC ACID INTRA-ARTICULAR INJECTIONS IMPACT THE RISK OF TOTAL KNEE REPLACEMENT? REAL-LIFE DATA FROM THE KHOALA COHORT

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Background: Long-term structural outcomes of corticosteroids (CS) or hyaluronic acid (HA) intra-articular injections in knee osteoarthritis (KOA) are unclear. Whether HA injections delay the need for total knee replacement (TKR) remains controversial, and an increased risk of cartilage damage has been reported with repeated CS injections.
Objectives: We conducted this study to compare, in real-life setting, the risk of TKR in patients receiving CS or HA vs. in those who did not receive intra-articular injections.
Methods: Khoala cohort is a French nationwide population-based cohort of 878 patients with symptomatic hip or knee OA (ACR criteria), aged 40-75 years. This study included patients with baseline KOA only. Patients were followed annually by self-reported questionnaires and by clinical examination and radiography at baseline (year 0), years 3 and 5. The risk of incident TKR was compared between patients who had never received intra-articular injections vs. patients who received at least 1 CS or HA injection during follow-up.
We used a marginal structural model with inverse probability of treatment weighting to determine the causal relationship between treatment and the risk of incident TKR in the treated knee during the 5-year follow-up. This model allows the adjustment for time-varying confounding factors (i.e. pain, function and mental health scores) in addition to constant confounders (i.e. baseline age, sex, BMI, Kellgren-Lawrence grade).
Results: This study involved 656 patients (mean age 62.2 ± 8.5 years; 70.3% females) of which 91 (13.9%) underwent TKR during follow-up. CS or HA injections were performed in 143 (21.8%) and 191 (29.1%) patients, respectively, and 92 (14.0%) received both treatments. The 5-year relative risk of incident TKR in treated vs. untreated knee was 0.96 (95%CI 0.35 to 2.66; p=0.94) CS-treated knees and 0.38 (95%CI 0.15 to 1.03; p=0.06) in HA-treated knees.
Conclusion: In this study, CS injections for symptomatic KOA did not increase the 5-year risk of incident TKR. There was a non-significant trend for a reduced risk of TKR in HA-treated knees.
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THU0439 MEASUREMENT PROPERTIES OF PAIN CATASTROPHIZING SCALE IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Up to 20% of patients with knee osteoarthritis (OA) do not respond well to knee replacement surgery (KR) despite surgical success. We hypothesize that pain catastrophizing among these patients may affect KR outcomes.
Objectives: To assess the validity and reliability of the Pain Catastrophizing Scale (PCS) in patients with knee osteoarthritis (OA) in Singapore.
Methods: We used cross-sectional data from 675 knee OA patients enlisted for knee replacement surgery (KR) in a Singapore tertiary referral hospital from May to September 2018. Data was collected 2 weeks prior to KR. Analyses were guided by the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) framework. Internal consistency was assessed using Cronbach's alpha. Construct validity was assessed through seven *a priori* hypotheses by correlation of overall PCS score with other patient-reported outcomes. Structural validity was evaluated via confirmatory factor analysis using maximum likelihood method. Measurement invariance across gender subgroups was assessed using multi-group confirmatory factor analysis.
Results: There were 675 patients (mean±SD age = 65.52±6.84 years, 70.37% female) with knee OA enlisted for KR (91.7% total, 8.3% unicompartmental). The mean±SD PCS score was 12.65±10.55, 0.14% and 8.63% ceiling and floor effects. PCS demonstrated high internal consistency (Cronbach's alpha=0.94). Construct validity was demonstrated by fulfilment of six out of seven (85%) a priori hypotheses. The PCS model showed good fit for a two-factor structure after accounting for appropriate modification indices (CFI=0.957, TLI=0.950, RMSEA=0.073, SRMR=0.043), demonstrating good structural validity. Measurement invariance across gender groups was demonstrated.
Conclusion: This study supports internal consistency, construct validity and structure validity of PCS as a measure of pain catastrophizing in knee OA patients in Singapore.

Abstract THU0448 –Table 1. Mean MDHAQ scores in patients with primary OA or RA at 1st visit, and 1 or 2 years later

Mean scores at…	1st visit			1-year later			2-years later			P Change in OAvsRA	
Variable:	0A	RA	P	OA	RA	P	0A	RA	P	1 year	2 years
# patients	101	175		101	175		45	113			
RAPID3 (0-30)	11.9	13.7	0.03	11.5	10.9	0.50	11.9	9.0	0.02	0.004	0.0004
Function (0-10)	0.63	0.78	0.03	0.61	0.66	0.43	0.72	0.53	0.046	0.119	0.009
Pain (0-10)	5.0	5.5	0.16	4.9	4.3	0.43	4.7	3.6	0.03	0.004	0.004
PATGL (0-10)	4.8	5.6	0.01	4.6	4.4	0.54	4.9	3.7	0.009	0.005	0.0001
Fatigue (0-10)	3.9	4.9	0.008	3.7	4.0	0.43	3.6	4.0	0.41	0.073	0.359
Self-report painful JC 48 (0-48)	12.0	15.4	0.014	9.5	11.7	0.10	11.9	10.2	0.35	0.415	0.035

Abstract THU0439 – Table 1. Hypothesized and actual correlations for hypothesis testing

PCS total score	Hypothesized Correlations		Actual Correlation	Hypothesis met
	Magnitude	Direction	R (p-value)	
Internal resource				
Pain self-efficacy questionnaire	Moderate	-	-0.4186 **	Yes
Mental well-being				
HADS	Strong	+	0.5823 **	Yes
SF-36 mental health	Moderate	-	-0.3323 **	Yes
Physical well-being				
WOMAC physical function	Moderate	+	0.4767 **	Yes
WOMAC pain	Moderate	+	0.4671 **	Yes
SF-36 physical functioning	Moderate	-	-0.2632 **	No
Social well-being				
Lubben's social network score	Weak	+/-	-0.0486	Yes

** $p < 0.001$; HADS: Hospital Anxiety and Depression Scale

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THU0440 THE ASSOCIATION OF PLASMA FATTY ACIDS LEVELS WITH HAND AND KNEE OSTEOARTHRITIS

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Background: Obesity is one of the most important risk factors for osteoarthritis (OA). For long the association between obesity and OA was thought to be explained by increased mechanical loading. However, the role of systemic factors is increasingly recognized, especially in non-weightbearing joints. Obesity is strongly associated with increased levels of circulating fatty acids, which may result in lipotoxicity. However, our knowledge about the effect of different fatty acids on OA is sparse.

Objectives: To investigate the association of plasma saturated fatty acids (SFAs), monounsaturated fatty acid (MUFAs), polyunsaturated fatty acids (PUFAs), omega (n-)3 and n-6 PUFAs with clinically defined hand and knee OA.

Methods: In the population-based Netherlands Epidemiology of Obesity (NEO) study, a total of 6,671 middle-aged participants were recruited from the greater area of Leiden. Clinical hand and knee OA were defined by the ACR clinical classification criteria. Blood samples were obtained after an overnight fast and 150 minutes after consumption of a standardized liquid mixed meal containing 600kCal, with 16% of energy (En%) derived from protein, 50 En% from carbohydrates and 34 En% from fat. EDTA-plasma samples were used for a high-throughput proton nuclear magnetic resonance (NMR) metabolomics platform (Nightingale Health Ltd., Helsinki, Finland) to quantify 159 lipid and metabolite measures. For the present analyses the concentrations of fasting and postprandial total fatty acids, SFAs, MUFAs, PUFAs, n-6 PUFAs and n-3 PUFAs in mmol/l were used. Since we are in a postprandial state most of the day, these samples were used for the primary analyses. All fatty acid concentrations were standardized (mean 0, SD 1), to ensure a similar interpretation of the estimated effect. We excluded participants who reported to have inflammatory rheumatic disease or fibromyalgia, with missing physical examination, who were non-fasting at baseline, or reported using lipid-lowering medication. Logistic regression analyses were used to investigate the association between fatty acids and clinical OA phenotypes. All analyses were stratified by sex and corrected for age, education, ethnicity and total body fat percentage. Data are presented as odds ratios (OR) with 95% confidence intervals (CI).

Results: In the current analysis 5,328 NEO participants were included, with a mean age of 56 years and 58% were women. Hand OA, knee OA and concurrent hand and knee OA were defined in 8%, 10% and 4% of participants, respectively. After correction for possible confounders, total fatty acids, SFA, total PUFA and omega–3 PUFA levels were positively associated with clinical hand OA in men, with OR (95% CI) of 1.24 (1.01; 1.53), 1.23 (1.00 – 1.50), 1.26 (1.00 – 1.58) and 1.24 (1.01 – 1.52), respectively. Although not significant, similar effect estimates were observed for men with concurrent hand and knee OA, but not for clinical knee OA alone. In women no associations were seen of any of the fatty acids with clinical hand or knee OA. Analyses of the association between fasting fatty acid levels and clinical hand and knee OA showed rather similar results, with slightly lowered ORs and wider confidence intervals.

Abstract THU0440 –Table 2.

Table 2. Association between postprandial plasma fatty acids and clinical OA phenotypes

		Hand OA OR (95% CI)	Knee OA OR (95% CI)	Hand and knee OA OR (95% CI)
Total FA				
	Men	1.24 (1.01; 1.53)	0.93 (0.78; 1.12)	1.21 (0.76; 1.90)
	Women	1.05 (0.85; 1.30)	0.88 (0.74; 1.05)	0.93 (0.61; 1.13)
SFA				
	Men	1.23 (1.00; 1.50)	0.99 (0.83; 1.19)	1.19 (0.80; 1.75)
	Women	1.05 (0.84; 1.31)	0.86 (0.72; 1.03)	0.76 (0.56; 1.04)
MUFA				
	Men	1.20 (0.96; 1.50)	0.92 (0.76; 1.12)	1.12 (0.64; 1.98)
	Women	0.98 (0.80; 1.20)	0.92 (0.78; 1.08)	0.81 (0.60; 1.10)
PUFA				
	Men	1.26 (1.00; 1.58)	0.90 (0.74; 1.09)	1.31 (0.84; 2.04)
	Women	1.13 (0.91; 1.41)	0.88 (0.73; 1.06)	0.86 (0.64; 1.14)
n-3 PUFA				
	Men	1.24 (1.01; 1.52)	1.06 (0.86; 1.29)	1.24 (0.83; 1.85)
	Women	1.13 (0.90; 1.40)	0.85 (0.70; 1.04)	0.96 (0.74; 1.26)
n-6 PUFA				
	Men	1.24 (0.98; 1.56)	0.87 (0.72; 1.06)	1.29 (0.85; 1.97)
	Women	1.12 (0.91; 1.39)	0.89 (0.74; 1.08)	0.85 (0.64; 1.13)

Fatty acid levels have been standardized (mean = 0, SD = 1), OR represents increased odds for every increase in SD. Analyses have been adjusted for age, fat percentage, education and ethnicity. Abbreviations: SFA= saturated fatty acid, MUFA= monounsaturated fatty acid, PUFA= polyunsaturated fatty acid, n= omega

Conclusion: Quantitively measured plasma postprandial SFA and PUFA levels were significantly associated with hand OA in men. In women no associations were found. Intriguingly, although SFA and omega-3 PUFAs are deemed to have opposing effects on inflammation, both were positively associated with hand OA. Future research is warranted to replicate the association and determine whether there is a causal role for plasma fatty acid levels in hand OA.

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THU0441 IMPROVED KNEE PHYSICAL FUNCTION CORRELATES SIGNIFICANTLY WITH TIBIOFEMORAL CARTILAGE THICKNESS INCREASE AFTER IA TPX-100: RESULTS OF A POST HOC ANALYSIS

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Background: In new draft guidance for OA drugs, the U.S. FDA notes the "well-recognized discordance" in clinical trials between structural imaging and patient benefit. In a randomized, double-blind, placebo-controlled trial, IA TPX-100 was associated with statistically significant and clinically meaningful improvement in knee functions among subjects (n=93) recruited for mild-moderate (ICRS grades 2-3) bilateral patellofemoral OA. No treatment differences in PF cartilage were detected, consistent with FDA concerns. However, only 14% of knees had measurable PF cartilage change on follow-up MRIs, limiting power for analysis of treatment differences in PF cartilage (ACR/ACHP 2017).
Objectives: To conduct a subset analysis of knee function and cartilage thickness correlations among the 73% of subjects (n=68) who had, in addition to PFOA, bilateral tibiofemoral OA (TFOA).
Methods: Subjects received 4 weekly injections of IA TPX-100 in one knee and identical saline placebo in the contralateral knee, as randomly assigned. MRIs were obtained at baseline, 6 and 12 months; and patient-reported outcomes (KOOS/WOMAC) were obtained at baseline, 3, 6 and 12 months. Subjects, sites, sponsor and central readers were blind to treatment assignment. All subjects receiving 4 weekly injections of 200 mg TPX-100 with at least one follow-up MRI were included for efficacy. The database was locked prior to all analyses, and clinically meaningful differences in outcome measures were selected *a priori*, based on the literature (Roos 2003).
Results: Of 68 subjects with bilateral TFOA, 47% had ICRS grade 4 (severe) TFOA at baseline, and 43% had ICRS grade 3 (moderate) disease. Demographics for this cohort were consistent with the U.S. knee OA population in mean age (60.8 years), BMI (30.6), and gender distribution (60% females). IA TPX-100 was safe and well tolerated, with no drug-related serious adverse events or safety concerns. The mean functional improvement of TPX-100-treated knees was significantly higher than that of placebo-exposed knees at 6 and 12 months ($p<0.04$ and $p<0.02$, respectively). Responder knees, defined *a priori* with $\geq$ 8 points increase in KOOS physical function, had mean improvements in function of 20.5 and 22.4 at 6 and 12 months, respectively. Pearson analysis revealed a significant positive 12-month correlation ($p<0.05$) between degree of functional improvement and cartilage thickness increase/stabilization in TF cartilage in TPX-100-treated knees (Table 1).

Abstract THU0441 –Table 1.

Cartilage Thickness vs, Knee Function (KOOS ADL)			
Month	Cartilage Thickness	Pearson Correlation	
12	Correlation	p-value	
	Lateral TF	0.359	0.003
	Medial TF	0.242	0.048
	Entire TF	0.332	0.007

Conclusion: In subjects with bilateral TFOA, statistically significant and clinically meaningful, robust functional improvements in TPX-100-treated knees were seen at 6 and 12 months compared with placebo-exposed knees. Formal analysis revealed statistically significant correlations between functional improvement and increase or stabilization of lateral, medial and total TF cartilage thickness. To our knowledge, TPX-100 is the first candidate DMOAD to show improvement in critical knee function concordant with increase/stabilization of cartilage structure compared with placebo-exposed knees.

REFERENCE:

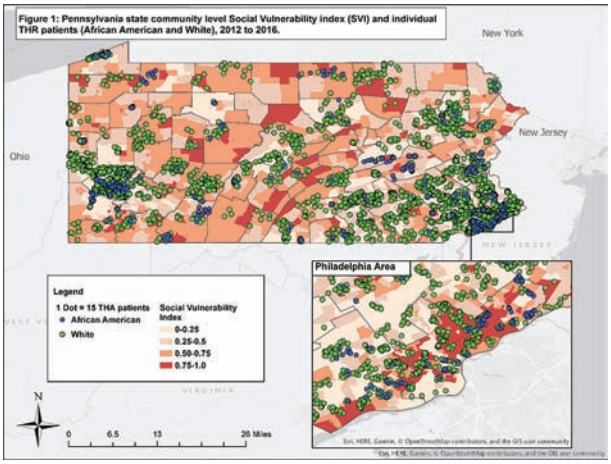
[1] Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. Health Qual Life Outcomes. 2003;1:64.

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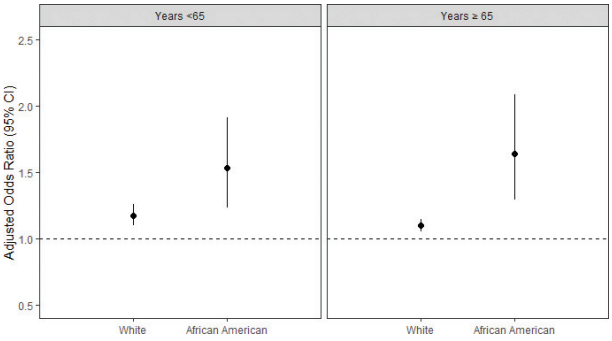
THU0442 SOCIAL VULNERABILITY AND DISCHARGE DISPOSITION AFTER ELECTIVE TOTAL HIP REPLACEMENT? RISK-ADJUSTED ANALYSIS OF LARGE REGIONAL DATASET

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Background: With the aging of the world population and the rising prevalence of Osteoarthritis (OA), elective joint replacement (JR) has become one of the fastest growing procedures in the management of end-stage OA. There is also increasing evidence that social determinants of health such as where one lives impact healthcare utilization and decision-making. Furthermore, elective JR of the hip and knee is one of the most important cost-centers for Medicare, the largest payer in the US, and has therefore been the subject of ongoing payment reform models that shape discharge destination and risk of readmission.
Objectives: In a large regional dataset, we sought to examine how social vulnerability impacts discharge destination after elective THR, and what is the role in this relationship of patient race, another key social determinant of health which has been previously associated with disposition after surgery.
Methods: We used the Pennsylvania Health Care Cost Containment Council (PHC4) database to identify all patients who underwent elective THR between 2012 and 2016. Community level Social Vulnerability Index (SVI) was derived from the American Census Survey, which draws 15 different measures of vulnerability including socioeconomic, housing, and disability among others. SVI ranges from 0 (least vulnerable) to 1 (most vulnerable). SVI was dichotomized into low (below median) and high (above median). We used binary logistic regression to test the association between community SVI and discharge disposition: Institution (Nursing home or inpatient rehabilitation vs Home with/out home health). We adjusted for important clinical, demographic, and facility level covariates. To examine the role race (African American (AA) vs White) in this relationship, we included in the model an interaction term for SVI and race.
Results: There were a total 86,215 THR done between Jan 2012 and Dec 2016 that met our inclusion criteria. About 40,881 were <65 years of age; and 45,334 were $\geq$ 65 years of age. Patients from low SVI community went to high volume hospitals as compared to high SVI in all age groups. Figure 1 shows the geospatial localization and relationship of THR patients in the State of Pennsylvania by community SVI level. Compared to white patients, AA patients were more likely to live in higher SVI communities (median SVI_{AA} 0.66; IQR 0.48-0.83 vs median SVI_{W} 0.42; IQR 0.28-0.55, respectively). Compared to low SVI communities, patients from high SVI communities were more likely to be discharged to an institution (vs home) (for age <65; aOR= 1.22, 95% CI: 1.14,1.30, $p<0.001$; for ages $\geq$ 65; aOR= 1.11,95% CI: 1.07,1.16, $p<0.001$). The odds of discharge to an institution (vs Home) for patients living in high SVI communities (vs low SVI) was higher in AA compared to whites in all age groups. [Figure 2].
Conclusion: In this large regional dataset of patients who underwent THR, social vulnerability index of the community is associated with discharge disposition after surgery. Moreover, this association was stronger in African-Americans compared to Whites. This association when coupled with ongoing payment reform models may have implications for access to care for socially vulnerable populations.



Abstract THU0442 – Figure 1. Pennsylvania state community level Social Vulnerability index (SVI) and individual Total Hip Replacement patients (African American and White), 2012 to 2016



Abstract THU0442 – Figure 2. Adjusted odds of discharge to an Institution (vs Home) for patients living in High SVI compared to Low SVI stratified by race

[a]Adjusted covariates for all models include patient sex, age, insurance, facility metro status, volume of cases, surgical complications, and Elixhauser Index.

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THU0443 ASSESSING PAIN CHARACTERISTICS IN PERSONS WITH HAND OSTEOARTHRITIS USING THE MCGILL PAIN QUESTIONNAIRE

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Background: Pain in osteoarthritis (OA) causes significant physical, psychological and social limitations. Increased understanding of the pain experience is important for improved patient care.

Objectives: We aimed to assess the pain characteristics of hand OA using the McGill Pain Questionnaire, a multidimensional self-reporting questionnaire that assesses the quality and intensity of the pain. Secondly, the external validity was examined.

Methods: Three-hundred persons with hand OA from the Nor-Hand study completed questionnaires, including a modified McGill questionnaire. The participants are presented with a list of 106 pain descriptors in 18 sections. The questionnaire consists of three subscales: sensory (12 sections, 0-71.3 scale), affective (5 sections, 0-32.9 scale) and evaluative (one section, 0-8.6 scale), and an intensity score (no pain – severe pain). The total scale is rated from 0-112.8. The subscales and total scale were normalized to 0-100 scales. The participants also completed the Numeric Rating Scale (NRS, 0-10 scale) about hand pain, the Australian/Canadian (AUSCAN) hand pain subscale (0-20 scale) and questionnaires about psychological factors; Hospital Depression and Anxiety Scale (HADS, 0-42 scale), Pain Catastrophizing Scale (PCS, 0-52 scale) and the pain subscale of the Arthritis Self Efficacy Scale (ASES, 10-100 scale). For all scales except ASES, high scores indicate poor health. We identified the adjectives in the McGill questionnaire with most frequent responses. To determine the external validity, the McGill questionnaire was correlated to other questionnaires (AUSCAN, NRS, HADS, PCS and ASES) using Spearman correlation coefficients.

Results: The participants (89% women) with median (IQR) age of 61 (57-66) years demonstrated a wide range in pain characteristics and intensity, with a median (IQR) of 34.5 (0-62.3), 14.9 (0-39.2) and 44.2 (34.9-48.8) for the sensory, affective and evaluate subscales, respectively. The median for the total pain sum score was 29.7 (7.0-53.2). A floor effect was detected for the sensory (23.7% with score 0) and affective (40.3% with score 0) subscales. The reported adjectives with highest frequency were "sore" (n=208, 69.3%), "inhibiting" (n=124, 41.3%) and "annoying" (n=97, 32.3%). The participants frequently reported neuropathic-like characteristics such as sticking/stabbing/pricking (n=137, 45.7%), speeding/radiant (n=110, 36,6%), smarting/burning (n=89, 29.6%) and creeping (n=43, 14.3%).

The McGill total scale showed moderate correlations with AUSCAN and NRS pain (Table). Similar strength of correlations was found for all the subscales, and stronger for the intensity score (0.63-0.64). The correlation with HADS was similar for the McGill questionnaire, AUSCAN and NRS pain. The correlations with PCS and ASES were weaker for McGill than for the other pain questionnaires.

Abstract THU0443 –Table 1. Correlations between the McGill questionnaire and questionnaires assessing pain and psychological health.

	McGill total	AUSCAN	NRS pain	HADS	PCS	ASES
McGill total	1.0					
AUSCAN	0.41	1.0				
NRS pain	0.45	0.73	1.0			
HADS	0.31	0.24	0.29	1.0		
PCS	0.26	0.40	0.41	0.47	1.0	
ASES	-0.20	-0.35	-0.40	-0.30	-0.42	1.0

Conclusion: The McGill Pain questionnaire may be a useful tool in research settings for a broad evaluation of pain characteristics in hand OA. Moderate correlations with other pain questionnaires suggest that the McGill questionnaire measures other constructs. For the first time, we have shown that neuropathic-like pain characteristics are frequently reported by persons with hand OA.

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THU0444 CROSS-CULTURAL TRANSLATION, ADAPTATION AND VALIDATION OF A JAPANESE VERSION OF THE FUNCTIONAL INDEX FOR HAND OSTEOARTHRITIS (J-FIHOA)

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Background: Hand osteoarthritis (HOA) is a highly prevalent and heterogeneous musculoskeletal disorder. Although well-designed clinical trials and guidelines have been published, there are comparatively few HOA

studies concerning Asian countries. To both pursue appropriate clinical courses for patients and to engage in future research, physicians need to discriminate symptomatic HOA. The Functional Index for Hand Osteo-Arthritis (FIHOA) assesses hand OA-related functional impairment and is accepted as a gold standard with excellent reliability and responsiveness [1,2].

Objectives: Our objective was to make a Japanese version of the FIHOA (J-FIHOA) and to validate it among Japanese HOA patients.

Methods: J-FIHOA was created following forward/backward translation processes distilled from the established guidelines. A prospective, multi-center study was undertaken for its validation. Seventeen collaborating hospitals recruited hand OA patients from September 2017 to September 2018. Patients who met the ACR classification criteria were included. A medical record review and the following patient-rated questionnaires were collected: J-FIHOA, Japanese Health Assessment Questionnaire (J-HAQ), numerical rating scale for pain (NRS pain) and Japanese Short Form 36 Health Survey (J-SF-36). As item 7 is a gender-role question, an item total correlation needed to be calculated independently for women and men.The J-FIHOA scores at enrollment were used to assess Cronbach's alpha coefficient/item-total correlation and compared with the J-HAQ, NRS pain and J-SF-36 yielding respective Spearman's rank correlation coefficients. To assess reliability, we used test-retest methods for patients with unchanged symptoms/treatments. The interval was 1-2 weeks and data sets were assessed with the intraclass correlation coefficient (ICC). To evaluate responsiveness, those who started new pharmacological treatments were required to answer the questionnaires and to have a 1-month follow-up visit. Differences between pre- and post- pharmacological treatments were used to calculate the effect size (ES).

Results: Twenty-nine male and 145 female HOA patients participated (mean age 65 years). Cronbach's alpha was 0.91, showing high internal consistency. Each item was well correlated with the total score (all values >0.30; range 0.46 to 0.89). Construct validity between J-FIHOA and other scales was: 0.73 (J-HAQ), 0.56 (NRS pain), -0.31 (J-SF-36 physical component) and -0.21 (J-SF-36 mental component). Although the FIHOA has no pain-related question, previous reports showed moderate correlations between the FIHOA and pain. Our results were concordant with these reports. It was expected that J-SF-36 mental component had the weakest correlation. One hundred fifty-seven longitudinal data sets were pooled and used to evaluate reliability (137 for test-retest) and responsiveness (20 for ES). ICC for test-retest was 0.83 (95% CI, 0.77 to 0.88). The ES were 0.56 for J-FIHOA and 0.44 for J-HAQ. We assumed that this higher ES related on the HOA specificity of J-FIHOA.

Conclusion: We created a cross-culturally adapted J-FIHOA. Our results showed its good metric qualities to assess dysfunction in HOA and equivalence with the original FIHOA.

REFERENCES:

[1] Dreiser RL, Maheu E, et al. Validation of an algofunctional index for osteoarthritis of the hand. Revue du rhumatisme (English ed). 1995; 62(6 Suppl 1):43s-53s.

[2] Dreiser RL, Maheu E, et al. Sensitivity to change of the functional index for hand osteoarthritis. Osteoarthritis Cartilage. 2000; 8:S25-S28.

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THU0445 ASSOCIATION BETWEEN PATIENT'S EXPECTATION AND SATISFACTION FOLLOWING TOTAL KNEE REPLACEMENT FOR OSTEOARTHRITIS

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Background: Up to 20% of patients are dissatisfied with the outcome of total knee replacement (TKR). Pre-operative expectations may affect patient's outcomes, including satisfaction after surgery. Better understanding of patient's expectation could aid the development and improvements of pre-operative education. Pre-operative expectations and post-operative satisfaction may vary across cultures and have not been described in an Asian context.

Objectives: We aimed to evaluate the association between patient's pre-operative expectation and post-operative satisfaction following TKR for osteoarthritis.

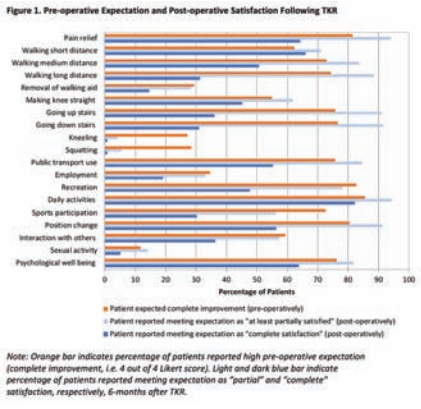
Methods: Patients listed for TKR because of OA in a tertiary referral centre were recruited. Pre-operatively, participants completed sociodemographic questions, Western Ontario and McMaster Universities Index (WOMAC) pain and function, and the Hospital for Special Surgery (HSS) KR expectation survey. At 6 months after TKR, patients rated their satisfaction with each expectation on the HSS as completely satisfied, partially satisfied or dissatisfied. Overall satisfaction with TKR was assessed with a 4-point Likert scale and dichotomized to satisfied or dissatisfied. Association between overall satisfaction at 6 months and pre-operative expectation was analysed using logistic regression after adjustment for demographic data.

Results: Between June 2017 and December 2017, 215 patients were recruited and completed follow up at 6 months after TKR (71% female, 82% Chinese, mean age 65±7 years). The overall satisfaction rate was 92%. The most prevalent pre-operative expectations were improved ability to perform daily activities (85%), participation in recreation (83%), pain relief (81%) and ability to change position (81%) (Figure 1). At 6 month after TKR, the top five fulfilled expectations (defined as 'completely satisfied') were improvement in the ability to perform daily activities (82%), walking short distance (66%), improvement in psychological well-being (64%), pain relief (64%) and position change (56%) (Figure 1). For most items on the questionnaire, expectations were high and not fully met; however most patient's expectations were at least partially met. In the logistic regression model, post-operative HSS total score, but not pre-operative HSS score, was associated with overall satisfaction (P<0.01) after adjusting for demographic data (Table 1).

Abstract THU0445 – Table 1. Variables Associated with Overall Satisfaction at 6 Months after TKR by Logistic Regression Analysis

	Exp(B), (95% Confidence Interval)	P
Age	0.985 (0.869, 1.115)	0.809
Gender	0.589 (0.128, 2.700)	0.496
Ethnic group	0.729 (0.093, 5.741)	0.764
Education level	0.142 (0.010, 2.065)	0.153
BMI	0.992 (0.872, 1.128)	0.901
Radiographic index of knee	0.917 (0.228, 3.689)	0.902
WOMAC pain, baseline	0.988 (0.926, 1.053)	0.710
WOMAC function, baseline	0.978 (0.903, 1.060)	0.589
HSS total score at baseline	1.024 (0.967, 1.084)	0.421
HSS total score at 6 months	1.172 (1.092, 1.259)	**<0.001**

Conclusion: Although most patient's expectations were at least partially met, they were not fully met. This suggests that many patients have unrealistic expectations of TKR outcome. Fulfilment of expectations, rather than expectation per se, was the most important variable associated with patient's overall satisfaction.



Abstract THU0445 – Figure 1

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Nee Pang: None declared, Darren Tay: None declared, Ying Ying Leung Grant/research support from: Abbvie, Novartis, Speakers bureau: Abbvie and Novartis, Speakers bureau: Novartis
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THU0446 DIACEREIN PROVEN AS EFFECTIVE AS CELECOXIB IN REDUCING PAIN AND SYMPTOMS IN KNEE OSTEOARTHRITIS PATIENTS IN A MULTICENTRE DOUBLE-BLIND RANDOMISED STUDY (DISSCO)

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Background: There was a need to ascertain in a clinical trial the comparative efficacy of diacerein, an IL-1 inhibitor, vis-à-vis celecoxib, a COX-2 inhibitor, in relieving knee osteoarthritis (OA) symptoms.
Objectives: The primary outcome of this study was to show that diacerein is non-inferior to celecoxib in terms of pain reduction (WOMAC A pain subscale) after 6 months of treatment in moderate-to-severe symptomatic knee OA patients.
Methods: A randomised double-blind multicentre trial was conducted in four European countries (Spain, Belgium, Austria, Czech Republic) and in Canada evaluating treatment with diacerein versus celecoxib in patients with OA diagnosed according to ACR criteria, with KL grade 2-3 knee OA and moderate-to-severe pain (VAS pain score [0-100 mm] while walking on a flat surface $\geq$ 40 mm). Eligible patients were randomised to treatment for 6 months with either diacerein 50 mg once daily for the first month and twice daily thereafter, or celecoxib 200 mg once daily. The primary outcome was the change from baseline in WOMAC pain subscale (0-50 scale) after 6 months of treatment. Secondary outcomes included WOMAC function and stiffness, VAS pain, presence of joint swelling/effusion, rescue medication consumption, percentage of OMERACT-OARSI responders, and SF-36. A total of 380 patients were randomised in the study. The primary outcome assessment on the per protocol set (PPS) (n=288) was followed by sensitivity analysis on the ITT population (n=370). Exploratory statistical analysis on other efficacy criteria and safety were performed.
Results: The analysis of the PPS population showed that the adjusted mean change in WOMAC pain was -11.14 (SEM, 0.91) with diacerein (n=140) and -11.82 (0.89) with celecoxib (n=148). Diacerein met the non-inferiority criterion, as the upper bound of the 95% CI is inferior to the pre-specified non-inferiority margin of 5 (inter-group difference 0.67; 95% CI -1.83 to 3.18; p=0.597). The sensitivity analysis using the ITT population was supportive of those results. All other exploratory outcomes demonstrated no difference between the two treatment groups. The OMERACT-OARSI responder rate (PPS) at 6 months was similar in the diacerein (62.1%) and celecoxib (60.1%) groups. The incidence of adverse events related to drug treatment was in general low and balanced between groups. The only exception was a greater incidence of gastrointestinal side effects (diarrhoea) in the diacerein vs. the celecoxib group (10.2% vs. 3.7%, respectively), but accounted for 4.8% of permanent discontinuation in the diacerein group compared to 1.6% in the celecoxib group. In all but one patient, this diarrhoea was considered to be of a mild-to-moderate grade with complete resolution in all cases.
Conclusion: This clinical trial showed that in patients with moderate-to-severe knee OA pain, diacerein has comparable efficacy to celecoxib with respect to reducing pain and stiffness and improving function after 6 months in a clinically relevant manner. The drug also demonstrated a good safety profile with positive benefit to risk ratio.
Disclosure of Interests: : Jean-Pierre Pelletier Shareholder of: Shareholder in ArthroLab Inc., Grant/research support from: Study funded by TRB Chemedica SA, Consultant for: TRB Chemedica SA, Jean-Pierre Raynauld Consultant for: ArthroLab Inc., Patrice Paiement Employee of: ArthroLab Inc., Johanne Martel-Pelletier Shareholder of: ArthroLab Inc., Consultant for: TRB Chemedica SA
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THU0447 THE RELATIVE EFFICACY OF TOPICAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND CAPSAICIN IN OSTEOARTHRITIS: MOVING FROM AVERAGE TREATMENT EFFECTS TO INDIVIDUAL TREATMENT PREFERENCES

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Background: Pain is an important issue for people with osteoarthritis (OA). Topical non-steroidal anti-inflammatory drugs (tNSAIDs) and capsaicin are recommended treatments, but reduce OA pain by different mechanisms.
Objectives: To [1] determine the relative efficacy of tNSAIDs and capsaicin in OA and [2] identify predictors of response that may allow tailoring of topical therapy to the individual.
Methods: Systematic literature searches were conducted up to 16/11/2015 for randomised controlled trials (RCTs) of tNSAIDs or capsaicin in OA. Placebo-controlled RCTs were pooled in conventional meta-analyses (CMA) for specific (difference between treatment and placebo) and overall (pain reduction in treatment arm) treatment effects. Bayesian network meta-analysis (NMA) compared treatments via placebo. RCT data custodians were contacted and an individual patient data meta-analysis (IPDMA) examined for predictors of response.
A pilot n-of-1 trial series (PNTS) examined treatment effects, patient preferences, and predictors of response. Participants with painful radiographic knee OA were allocated to three treatment cycles, each comprising four weeks treatment with 5% ibuprofen gel and 0.025% capsaicin cream in a random order.
Effect sizes (ES) are Hedges' g and 95% confidence interval (CI) or credible interval (CrI). Predictors of response were identified in regression modelling for treatment-by-covariate interactions (specific effect) or covariate associations (overall effect). 9 and 25 predictors were examined in IPDMA and PNTS, respectively.
Results: Of 63 tNSAID and 10 capsaicin RCTs identified, CMA and NMA analysed 21 tNSAID (n=6191) and five capsaicin (n=415) RCTs. The quality of evidence was moderate for tNSAIDs and very low for capsaicin. Overall treatment effects were large and likely clinically significant (tNSAIDs ES 1.23, 95%CI 1.06-1.41; capsaicin ES 1.05, 95%CI 0.52-1.57). tNSAIDs (all drugs/doses grouped) were superior to placebo (ES 0.31, 95%CI 0.20-0.41), but capsaicin was only effective at 0.025% concentration (ES 0.41, 95%CI 0.17-0.64; ES of all capsaicin RCTs 0.28, 95%CI -0.04-0.60). On average, tNSAIDs and capsaicin were equally effective (ES 0.04, 95%CrI -0.29-0.37).
IPD were provided for 15 (n=3889) tNSAID RCTs, including 11 (n=3140) placebo-controlled RCTs. No IPD were obtained for capsaicin. A significant but small interaction was observed between sex and tNSAID use for pain relief, with women reporting greater effect (11 RCTs, n=2939, p=0.023).
22 participants enrolled in the PNTS and completed 104 treatment periods. Clinically important pain relief ($\geq$1 on 0-10 numeric rating scale) was achieved in 64% of periods, with no difference in efficacy between treatments overall (p=0.271). Individual responses to treatment varied, with c.60% of people preferring one treatment over the other, but without clear predictors for the preference.
Conclusion: tNSAIDs and capsaicin may relieve OA pain, but treatment effects from group comparisons do not directly translate to treatment outcomes at an individual level. No baseline characteristics robustly determine which treatment is more likely to benefit an individual. Patients may benefit from trying both treatments to determine which is better for them.
Acknowledgement: M Underwood (Warwick University), A Suter (Bioforce AG/A.Vogel Produkte), GR Mautone (IBSA Institut Biochimique SA), and GSK for sharing IPD; D Burke for statistical advice; and D McWilliams for trial randomisation
Disclosure of Interests: Monica Persson: None declared, Joanne Stocks Grant/research support from: Co-I on research grant from Pfizer/Eli Lilly, Aliya Sarmanova: None declared, Gwen Fernandes: None declared, Gyula Varadi Employee of: Inpellis, Inc. (previous); BioPhysics Pharma, Inc (current), Mohammad Hashem Hashempur: None declared, Robbert van Haselen Consultant for: Consultancy services for homeopathic pharmaceutical companies, David Walsh Consultant for: Pfizer, GlaxoSmithKline. Consultancies on arthritis pain, Speakers bureau: Pfizer Ltd for a talk at OARSI 2018, Michael Doherty Grant/research support from: AstraZeneca funded the Nottingham Sons of Gout study, Consultant for: Advisory Boards on Grunenthal and Mallinckrodt, Weiya Zhang Consultant for:

Grunenthal for advice on gout management, Speakers bureau: Bioiberica as an invited speaker for EULAR 2016 satellite symposium

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THU0448 DISEASE BURDEN IN OSTEOARTHRITIS (OA) IS SIMILAR TO RHEUMATOID ARTHRITIS (RA) FROM THE PATIENT'S PERSPECTIVE, SLIGHTLY HIGHER IN RA AT PRESENTATION, SIMILAR ONE YEAR LATER, AND SLIGHTLY HIGHER IN OA TWO YEARS LATER AT ONE PRIVATE PRACTICE SETTING

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Background: Disease burden traditionally has been regarded as considerably greater in rheumatoid arthritis (RA) versus osteoarthritis (OA). However, recent reports of cross-sectional data indicate similar disease burden in OA vs RA according to MDHAQ/RAPID3 (multidimensional health assessment questionnaire/routine assessment of patient index data). One concern is that these findings may reflect only better treatment for RA, and initial disease burden may be considerably higher in RA vs OA.
Objectives: To analyze disease burden in patients with OA vs RA at baseline and 1- and 2-year follow-up according to MDHAQ/RAPID3 scores in routine care at a single rheumatologist private practice site.
Methods: All patients seen in routine care at this site complete an MDHAQ at each visit in the waiting area prior to seeing the rheumatologist. The MDHAQ includes three 0-10 scores for physical function, pain visual analogue scale (VAS), and patient global VAS, compiled into a 0–30 RAPID3, as well as 0-10 fatigue VAS, and 0-48 self-report painful joint count scores. Mean MDHAQ scores were compared in OA versus RA patients at 1st visit and visits 1 and 2 years later, using t tests, adjusted for age and body mass index (BMI) using analysis of variance (ANOVA).
Results: Among 101 OA and 175 patients with RA, at first visit, all MDHAQ scores except pain VAS were statistically significantly higher in RA vs OA, e.g., mean 0-30 RAPID3 was 11.9 in OA and 13.7 in RA. However, none of these differences appear clinically significant (Table). After 1-year, all scores were improved, but more in RA vs OA patients (Table), e. g., mean RAPID3 of 11.5 in OA and 10.9 in RA; no differences between OA and RA were statistically or clinically significant. After 2-years, mean RAPID3 was 11.9 in OA vs 9.0 in RA, indicating continued improvement in RA but little change in OA. All scores other than fatigue VAS were higher in OA, including the self-report painful joint count. Differences between OA and RA were explained only minimally by age and BMI.

Table. Mean MDHAQ scores in patients with primary OA or RA at 1st visit, and 1 or 2 years later

Mean scores at...	1st visit			1-year later			2-years later			P Change in OAvsRA	
Variable:	OA	RA	P	OA	RA	P	OA	RA	P	1 year	2 years
# patients	101	175		101	175		45	113			
RAPID3 (0-30)	11.9	13.7	0.03	11.5	10.9	0.50	11.9	9.0	0.02	0.004	0.0004
Function (0-10)	0.63	0.78	0.03	0.61	0.66	0.43	0.72	0.53	0.046	0.119	0.009
Pain (0-10)	5.0	5.5	0.16	4.9	4.3	0.43	4.7	3.6	0.03	0.004	0.004
PATGL (0-10)	4.8	5.6	0.01	4.6	4.4	0.54	4.9	3.7	0.009	0.005	0.0001
Fatigue (0-10)	3.9	4.9	0.008	3.7	4.0	0.43	3.6	4.0	0.41	0.073	0.359
Self-report painful JC 48 (0-48)	12.0	15.4	0.014	9.5	11.7	0.10	11.9	10.2	0.35	0.415	0.035

Abbreviations: MDHAQ=multidimensional health assessment questionnaire, OA=osteoarthritis, RA=rheumatoid arthritis, RAPID3=routine assessment of patient index data, PATGL= patient global assessment, JC=joint count

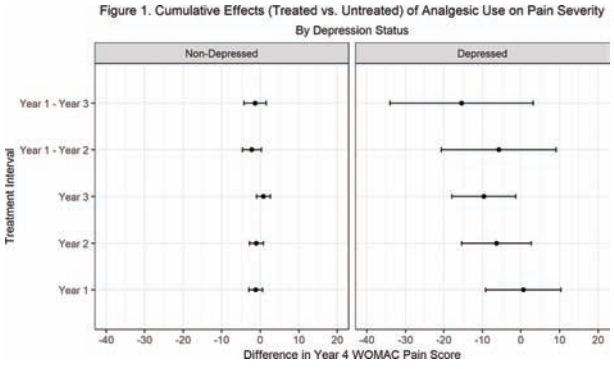
Conclusion: Most MDHAQ/RAPID3 scores were higher in RA than in OA at the first visit, indicating greater severity of RA, although OA was almost as severe. One year later, scores were similar with no statistically significant differences. Two years later, most scores were higher in OA. These findings likely reflect superior treatments for RA vs OA. At an individual level, patients with primary OA may have better or poorer status than other patients with primary RA. Nonetheless, at a group level, the severity of disease burden in OA appears almost as great as in RA, and becomes greater over the next 2 years, likely as a result of better treatment. The severity of OA is underrated, suggesting a need for increasing resources for research toward better treatment for OA.
Disclosure of Interests: Martin Bergman Shareholder of: Johnson and Johnson (parent company of Janssen), Consultant for: AbbVie, Amgen, BMS, Celgene, Genentech/Roche, Janssen, Merck, Novartis, Pfizer, and Sanofi/Regeneron, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Genentech/Roche, Janssen, Merck, Novartis, Pfizer, and Sanofi/Regeneron, Mariam Riad: None declared, Theodore Pincus: None declared

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THU0449 EFFECT MODERATION OF ANALGESIC TREATMENT OUTCOMES BY DEPRESSION IN PERSONS WITH OR AT-RISK FOR SYMPTOMATIC KNEE OSTEOARTHRITIS

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Background: Depression often accompanies knee osteoarthritis (OA), exacerbates pain severity, and may negatively affect analgesic treatment outcomes.
Objectives: To determine whether depression moderates the effect of analgesics on pain severity in persons with or at-risk for symptomatic knee OA.
Methods: Participants (n=2059) were from the Osteoarthritis Initiative, with or at-risk for symptomatic knee OA, and had complete data on selected measures at baseline and four annual follow-up visits. Analgesic initiation (acetaminophen, non-steroidal anti-inflammatory drugs, opioids) was assessed at three annual follow-up visits in those who were not analgesic users at baseline. Depression was evaluated concurrent to assessment of analgesic use with the Center for Epidemiological Studies Depression (CES-D) scale using the corresponding CES-D screening threshold (CES-D score $\geq$ 16). Pain severity at the fourth annual follow-up visit was the outcome and measured with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scale (rescaled range = 0-100). Time-invariant confounders measured at baseline were: age, gender, race, education, marital status, employment, health insurance, smoking, alcohol consumption, Charlson comorbidity index, and symptomatic knee OA status. Time-varying confounders measured at three annual follow-up visits were: WOMAC pain score, Kellgren-Lawrence grade, body mass index, physical performance, knee injuries, and knee injections. Structural nested mean models appropriate for evaluating time-varying effect moderation of dynamic treatments by evolving effect modifiers were implemented using an inverse-probability-of-treatment-weighting regression-with-residuals approach.
Results: In non-depressed participants, analgesic treatment effect at years one, two, and three on pain severity at year four was minimal (Figure 1). Time-specific associations in the non-depressed ranged from -1.18 (95% CI: -2.94, 0.59) to 0.81 (95% CI: -0.99, 2.61) and were not statistically significant. The persistent use of analgesics at years one and two (β = -2.17; 95% CI: -4.62, 0.27) or years one, two, and three (β = -1.36; 95% CI: -4.22, 1.50) did not increase the magnitude of the treatment effect in non-depressed participants. In contrast, time-specific associations in depressed participants increased during follow-up from 0.61 (95% CI: -9.17, 10.38) to -9.64 (95% CI: -17.96, -1.33), and the treatment effect of year three analgesic use on year four pain severity was statistically significant. The magnitude of the treatment effect increased from year one with persistent analgesic use at years one and two (β = -5.75; 95% CI: -20.65, 9.15) and years one, two, and three (β = -15.39; 95% CI: -33.99, 3.21). However, effect moderation was only significant concerning year three analgesic use, where the subsequent difference in treatment effect between depressed and non-depressed participants was -10.46 (95% CI: -18.97, -1.94).



Abstract THU0449 – Figure 1

Conclusion: Findings indicate a significantly greater one-year treatment effect of analgesic use that lowered pain severity in persons with or at-risk for symptomatic knee OA who also had depression. Thus, knee OA patients with depression may derive more benefit from analgesic treatment for chronic pain than non-depressed patients, perhaps because their pain is undertreated in routine clinical practice.

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Disclosure of Interests: Alan Rathbun: None declared, Michelle Shardell: None declared, Joseph Gallo: None declared, Alice Ryan: None declared, Elizabeth Stuart: None declared, Megan Schuler: None declared, Michelle Yau: None declared, Marc Hochberg Shareholder of: BriOri Biotech, Theralogix LLC., Consultant for: Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis Pharma AG, Pfizer Inc., Samumed LLC, Symic Bio Inc., Theralogix LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., Zynerba, Galapagos, IQVIA, Hoffman LaRoche.

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THU0450 QUALITY OF LIFE OF PATIENTS WITH A COMBINATION OF SARCOPENIA AND OSTEOARTHRITIS OF LOWER EXTREMITY

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Background: In accordance with the updated recommendations of the EWGSOP (2018), sarcopenia is a muscle disease (muscle failure) rooted in adverse muscle changes that accrue across a lifetime [1]. Sarcopenia and osteoarthritis significantly affect the self-esteem quality of life which is associated with a decrease in muscle strength and muscle performance, falls, joint pain [2]. In 2015, the SarQoL® questionnaire (Sarcopenia and Quality of Life, www.sarqol.org) was developed, specific to patients with sarcopenia. Improvement of quality of life should be the priority of any interventions to prevent and treat osteoarthritis and sarcopenia in the ageing population [3].

Objectives: Perform quality of life analysis in patients with osteoarthritis and sarcopenia.

Methods: Prospective study of 159 women, mean age 74 ± 13.3. Sarcopenia was diagnosed according to the algorithm proposed by the European Working Group on Sarcopenia in Older People (EWGSOP, 2010). Life quality assessment was performed using EQ-5D questionnaires and a specific questionnaire in patients with sarcopenia SarQoL.

Results: 31.45% of people with OA older than 65 years had sarcopenia. The results of the study showed a statistically significant decrease in overall health on the questionnaire EQ-5D in patients with sarcopenia compared with patients without sarcopenia (0.48 ± 0.22 points and 0.74 ± 0.27 points, respectively, p <0.01) and no differences according to the EQ-VAS scale in the studied groups (p> 0.05). The decrease in the general health status of EQ-5D in patients with OA sarcopenic compared with non-sarcopenic is associated with a restriction of the usual daily activities: in 70% (95% CI: 55.4-82.1) and 52.3% (95% CI: 42.5-61.9) respectively, (p <0.01). In patients with OA, reduced global SarQoL in sarcopenic subjects compared to non-sarcopenic ones: 50,65±14,23 vs. 75,10±14,46, p<0,001. Significantly lower scores for all domains were found in patients with OA sarcopenic compared with non-sarcopenic patients (p<0.001).

Conclusion: In patients with OA sarcopenic, the quality of life is worse than that of non-sarcopenic due to a decrease in habitual daily activities, probably associated with low muscle strength.

REFERENCES:

[1] Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Guidelines. Sarcopenia: revised European consensus on definition and diagnosis on definition and diagnosis. Age and Ageing 2018; 0: 1–16. doi: 10.1093/ageing/afy169Milte R, Crotty M. Musculoskeletal health, frailty and functional decline. Best Pract Res Clin Rheumatol. 2014;28(3):395–410

[2] Beaudart C., Biver E., Bruyère O. et al. Assessment of Quality of Life in Musculo-Skeletal Health. Aging Clin Exp Res. 2018 May; 30(5): 413–418Hoops ML, Rosenblatt NJ, Hurt CP, Crenshaw J, Grabiner MD. Does lower extremity osteoarthritis exacerbate risk factors for falls in older adults? Womens Health (Lond Engl). 2012;8(6):685–96

[3] Beaudart C, Biver E, Reginster J-Y, et al. Development of a self-administrated quality of life questionnaire for sarcopenia in elderly subjects: the SarQoL. Age Ageing. 2015; 44 (6):960–6

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THU0451 CHONDROITIN SULFATE USE AND INCIDENCE OF CANCER: A LONGITUDINAL ANALYSIS OF THE OSTEOARTHRITIS INITIATIVE DATA

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Background: Chondroitin sulfate (CS) is widely used nutritional supplement for the treatment of osteoarthritis. There is growing *in vitro* evidence that CS may play a role in oncogenesis and metastasis of several solid tumors including melanoma [1] and breast cancer [2]. The data evaluating pro-oncogenic effects of CS in humans are lacking.

Objectives: To assess influence of CS use on incidence of cancer.

Methods: For the current study we used 6-year longitudinal data obtained from the Osteoarthritis Initiative (OAI) progression (n= 1390) and incidence (n = 3284) subcohorts, which are publically available at https://oai.nih.gov. To reduce the risk of bias, only participants who did not take CS at baseline were included in the analysis (a "new-user" design). Incident cancer was defined as an occurrence of self-reported cancer, other than skin cancer, leukemia or lymphoma. The information on self-reported cancer was collected from the Charlson Comorbidity Index. CS users with cancer were defined using the following criteria (1) a person who used CS for at least 6 months (2) chondroitin use was at least 1 year before the incident self-reported cancer. For CS users without a cancer, the duration of CS use had to be at least 6 months. All other participants were classified as non-users. To examine the cancer risk for CS users compared with non-users, we calculated the incidence rate ratios (IRRs), adjusting for age (2-year age groups), using the Mantel-Haenszel test.

Results: A total of 3167 participants neither having cancer nor taking CS at baseline were included in the analysis. There were 570 (21.95%) new users of CS. We identified 160 (6.2%) and 37 (6.5%) cases of incident self-reported cancer in the non-users and users groups, respectively. The adjusted IRR for the association between CS use and cancer was 0.22 (95% CI 0.77-1.62) which was not statistically significant (p = 0.64).

Conclusion: CS use was not associated with excess overall incidence of self-reported cancers. Nonetheless, given the strong *in vitro* evidence of CS pro-oncogenic effects on several types of tumors there is a need for further epidemiological data evaluating CS effects on specific kinds of cancer.

REFERENCES:

[1] Lin R, Xia S, Shan C, Chen D, Liu Y, Gao X, Wang M, Kang HB, Pan Y, Liu S, et al: The Dietary Supplement Chondroitin-4-Sulfate Exhibits Oncogene-Specific Pro-tumor Effects on BRAF V600E Melanoma Cells. Mol Cell 2018, 69(6):923-937 e928.

[2] Cooney CA, Jousheghany F, Yao-Borengasser A, Phanavanh B, Gomes T, Kieber-Emmons AM, Siegel ER, Suva LJ, Ferrone S, Kieber-Emmons T, et al: Chondroitin sulfates play a major role in breast cancer metastasis: a role for CSPG4 and CHST11 gene expression in forming surface P-selectin ligands in aggressive breast cancer cells. Breast Cancer Res 2011, 13(3):R58.

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THU0452 PREVALENCE OF AXIAL OSTEOARTHRITIS IN SPAIN: EPISER-2016

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Background: Osteoarthritis (OA) is a heterogeneous group of diseases with common clinical and radiographic manifestations involving the peripheral and axial skeletal. OA is the most prevalent rheumatic disease however, there are very few publications focused in axial OA. In 2016, the Spanish Society of Rheumatology (SER) started a population descriptive study (EPISER 2016) to analyze the prevalence of 13 rheumatic diseases

in Spain, including peripherical (hip, knee and hand) and axial (cervical and lumbar spine) OA.

Objectives: To estimate in adult population the prevalence in Spain of symptomatic axial OA (cervical and lumbar spine) and associated factors.

Methods: EPISER 2016 study is a cross-sectional, population-based descriptive study. To estimate the OA prevalence, adult population aged 40 or older was selected. The initial recruitment was made through by a call center. Participants who met the premises of an initial screening based on symptoms were also identified. In a second phase rheumatologists confirmed the diagnosis. The axial OA diagnostic criteria to confirm new diagnosis were both clinical and radiographic criteria. Clinical criteria: mechanical pain longer than 3 months of evolution and stiffness of less than 30 minutes or absence of it; and radiographic criteria: vertebral osteophytes or reduction of intervertebral space with sclerosis of vertebral plate and sclerosis in interapofisary joints. To confirm the diagnosis, it was necessary that both clinical criteria and at least one radiographic criteria were met.

Figure 1: Prevalence of OA in Spain

	GLOBAL	PERIPHERICAL	AXIAL
40-49	125 (12,8)	53 (8,2)	91 (13,7)
50-59	242 (24,7)	131 (20,2)	167 (25,2)
60-69	257 (26,3)	181 (27,9)	189 (28,5)
70-79	201 (20,6)	158 (24,3)	127 (19,1)
≥ 80	153 (15,6)	126 (19,4)	90 (13,6)
Women	730 (74,6)	487 (75)	515 (77,6)
Northern	259 (26,5)	172 (26,5)	177 (26,7)
Mediterranean	378 (38,7)	268 (41,3)	247 (37,2)
Centre	341 (34,9)	209 (32,2)	240 (36,1)
Rural	212 (21,7)	145 (22,3)	135 (20,3)
Urban	766 (78,3)	504 (77,7)	529 (79,7)
Basic studies	611 (62,6)	431 (66,4)	425 (64)
Medium	207 (21,2)	122 (18,8)	138 (20,8)
Higher	158 (16,2)	94 (14,5)	101 (15,2)
Normal weight	266 (27,2)	149 (23)	192 (28,9)
Under weight	4 (0,4)	2 (0,3)	2 (0,3)
Overweight	405 (41,4)	260 (40,1)	267 (40,2)
Obesity	229 (23,4)	175 (27)	157 (23,6)
Non smoker	561 (57,4)	387 (59,6)	383 (57,7)
Former smoker	259 (26,5)	177 (27,3)	165 (24,8)
Smoker	158 (16,2)	85 (13,1)	116 (17,5)

Abstract THU0452 – Figure 1

Results: The sample of the EPISER study was 3,336 subjects ≥ 40, of whom 978 had peripherical or axial OA. The mean age was 64.72 years, 730 were women, 62.6% had basic education, 64,8% were overweight or obese and 83,9% were ex-smokers or non-smokers (Figure 1). The prevalence of global OA (peripheral+axial) was 29.35%. Prevalence of peripherical and axial OA was 19,62% and 19,17% respectively. The characteristics of patients with peripheral and axial OA follow similar patterns. Both types of OA are more frequent in women with basic education levels. Regarding age, there are more patients with axial osteoarthritis between 40-49 years than with peripheral OA. Obesity or overweight are more strongly associated with peripheral OA.

Figure 2: Multivariate analysis of axial OA

	CERVICAL OA		LUMBAR OA	
	p value	OR (TI 95%)	p value	OR (TI 95%)
40-49				
50-59	<0,001	2,047 (1,387-3,022)	<0,001	2,000 (1,438-2,781)
60-69	<0,001	3,347 (2,270-4,934)	<0,001	3,228 (2,319-4,494)
70-79	<0,001	2,337 (1,495-3,654)	<0,001	3,200 (2,223-4,4607)
≥ 80	<0,001	2,916 (1,751-4,854)	<0,001	4,049 (2,667-6,148)
Women	<0,001	2,241 (1,660-3,025)	<0,001	2,324 (1,816-2,973)
Northern				
Mediterranean	0,013	1,489 (1,089-2,029)	0,161	0,832 (0,643-1,076)
Centre	0,007	1,565 (1,132-2,163)	0,036	1,322 (1,019-1,716)
Basic studies				
Medium	0,009	0,659 (0,481-0,902)	0,071	0,788 (0,609-1,020)
Higher	<0,001	0,431 (0,304-0,613)	<0,001	0,433 (0,322-0,583)
Normal weight				
Under weight	0,84	0,857 (0,192-3,821)	0,998	<0,001
Overweight	0,208	1,197 (0,905-1,584)	0,001	1,528 (1,201-1,945)
Obesity	0,002	1,679 (1,209-2,332)	<0,001	2,490 (1,881-3,295)

Abstract THU0452 – Figure 2

Prevalence of cervical OA was 10.10%. In the multivariate analysis, it was observed that cervical OA is more frequent in women and older subjects, with the prevalence peak between 60-69 years. It is also more frequent in subjects with obesity and in subjects with a basic education level (Figure 2). OA cervical prevalence is lower in subjects from northern Spain than in population from the Mediterranean area (including the Canary Islands) and central Spain. Smoking, living in a rural or urban environment or having been born abroad were not associated with cervical OA.

Prevalence of lumbar OA was 15.52%. Multivariate analysis also showed that lumbar OA is more frequent in women and it increases with age (prevalence peak in ≥80 years). Greater association was observed with obesity or overweight and with basic study levels. Lumbar OA prevalence was higher in population from centre of Spain compared with other areas. Tobacco consumption, living in a rural or urban environment or having been born abroad were not associated with lumbar OA.

Conclusion: EPISER2016 study shows similar prevalence of peripherical and axial OA. Lumbar OA is more prevalent than cervical OA. Axial OA in Spain is more frequent in women, increases with age with a peak between 60-69 years for cervical OA and ≥ 80 years for lumbar OA. Both cervical and lumbar OA are more frequent in patients with obesity or overweight and with basic studies.

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THU0453 PROGRESSION OF PAIN, NUMBER OF PAINFUL AND SWOLLEN JOINTS AND ULTRASOUND DETECTED CHANGES IN THE GROUP OF 133 PATIENTS WITH HAND OSTEOARTHRITIS OVER THREE YEARS

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Background: Hand osteoarthritis (HOA) is a common and frequent cause of pain. HOA is a heterogeneous group of disorders with two main subsets including non-erosive and erosive disease. Few studies demonstrated inflammatory ultrasound changes and more severe clinical symptoms in patients with erosive compared with non-erosive disease, however the results are inconsistent.

Objectives: The aim of this study was to evaluate progression of pain, stiffness, physical impairment and ultrasound features in patients with erosive and non-erosive HOA in a three years longitudinal study.

Methods: Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. Joint pain and swelling were assessed. Patients reported joint pain on 100 mm visual analogue scale (VAS). Pain, joint stiffness and disability were assessed by the Australian/Canadian OA hand index (AUSCAN). Radiographs of both hands were examined, and erosive disease was defined by at least one erosive interphalangeal joint. Synovial hypertrophy and power Doppler signal (PDS) were scored with ultrasound. Synovitis was graded on a scale of 0–3 and osteophytes were defined as cortical protrusions seen in two planes. Patients were examined at baseline and at the first, second and third year of follow-up.

Results: Altogether, 133 patients (14 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2019. Out of these patients, 72 (6 male) had erosive disease. The disease duration ($p<0.01$) was significantly higher in patients with erosive compared with non-erosive disease.

Pain reported on VAS was significantly higher ($p<0.01$) in patients with erosive compared with non-erosive disease at baseline. Progression of pain after the third year of follow up was significantly higher in patients with erosive disease ($p<0.05$). The number of painful and clinically swollen joints ($p<0.05$) was significantly higher in patients with erosive compared with non-erosive disease at baseline. The number of painful and clinically swollen joints remained statistically higher ($p<0.01$) at the third year of follow up in patients with erosive disease.

According to the AUSCAN, patients with erosive compared with non-erosive disease had more pain ($p<0.05$) and stiffness ($p<0.01$) at baseline. Pain ($p<0.05$) and function ($p<0.01$), but not stiffness, worsened in patients with erosive compared with non-erosive disease at the third year of follow up.

US-detected pathologies such as gray-scale synovitis ($p<0.001$), intensity of PDS ($p<0.01$) and number of osteophytes ($p<0.01$) were significantly higher in patients with erosive compared with non-erosive disease at

baseline. There were improvements in gray-scale synovitis total score and intensity of PDS in patients with non-erosive disease while patients with erosive disease worsened after the lso third year of follow up. On the other hand, the progression of US-determined osteophyte formation was observed in both groups but were significantly higher in patients with erosive compared with non-erosive disease after the third year of follow up.
Conclusion: The findings of this study show that pain and number of painful and clinically swollen joints associated with US-detected synovial changes and osteophyte formation is more severe in patients with erosive HOA than in patients with non-erosive disease. In addition, osteophyte formation is more likely to progress independent of synovial inflammation.

REFERENCE:

[1] Meersseman P, Van de Vyver C, Verbruggen G, et al. Clinical and radiological factors associated with erosive radiographic progression in hand osteoarthritis. Osteoarthritis and Cartilage 2015;23:2129-2133.

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THU0454 CONDITIONED PAIN MODULATION AND TEMPORAL SUMMATION IN PERSONS WITH HAND OSTEOARTHRITIS AND ASSOCIATIONS WITH PAIN SEVERITY

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Background: Conditioned pain modulation (CPM) assesses adequacy of descending modulatory pathways. Temporal summation (TS) reflects ascending facilitation of nociceptive signals in the central nervous system (central sensitization). Inadequate CPM and enhanced TS of pain are both known to contribute to pain in chronic pain conditions. Different pain phenotypes may respond to different treatments strategies and may therefore be important to assess in clinical practice. CPM has not previously been explored in persons with hand OA and its relation to pain severity is unknown.
Objectives: To examine the prevalence of CPM and central sensitization alone or in combination in persons with hand OA, and to explore their associations with pain severity.
Methods: These cross-sectional analyses included 248 participants with hand OA from the Nor-Hand study. Participants reported hand pain severity during the last 24 hours on a numeric rating scale (NRS, 0-10). CPM was tested with pressure pain threshold (PPT) at the left wrist before (PPT1) and during (PPT2) a painful ischemic cuff conditioning stimulus at the opposite upper arm. Adequacy of CPM was calculated as CPM-ratio (PPT1/PPT2). CPM-ratio < 1 (increased PPT) indicates adequate CPM, while CPM-ratio $\geq$ 1 (unchanged/decreased PPT) indicate inadequate CPM. TS, increase in perceived pain to repetitive noxious stimuli as a marker of central sensitization, was assessed using mechanical punctate probes. We defined presence of TS as an increase in pain of $\geq$2 points on an NRS (0-10) during a repetition of ten punctate stimuli. We analyzed whether groups having adequate CPM and no TS, inadequate CPM only, TS only, or having both inadequate CPM and TS were associated with hand pain severity. We used linear regression analysis adjusted for age, sex, BMI, use of analgesics, education level, sleep disturbance, the Pain Catastrophizing Scale, the Hospital Anxiety and Depression Scale and radiographic hand OA severity (Kellgren Lawrence sum score).
Results: Of the 248 participants included, 90% were women, median age was 61 (IQR 57, 66) years and mean BMI was 26.3 (SD 4.7) kg/m^2. CPM-ratio ranged from 0.4 to 1.6 (mean 0.9, SD 0.2), and 32% showed inadequate CPM. Presence of TS was found in 46% of the study population. Overall, 38% had no TS and adequate CPM, 29% had inadequate CPM only, 16% TS only and 16% had both (Table). We found that persons with inadequate CPM only and TS only reported higher pain severity than persons with adequate CPM and no TS (Table). Those with both inadequate CPM and TS reported similar levels of pain as persons with inadequate CPM only and TS only.

Abstract THU0454 – Table 1. Associations of conditioned pain modulation (CPM) and temporal summation (TS) with pain severity in persons with hand OA, (n=248)

	Mean (SD) NRS hand pain	Adjusted beta (95%CI)
No TS and adequate CPM (n=96)	3.2 (1.8)	0.0 (ref.)
Inadequate CPM-only (n=39)	3.9 (2.3)	1.1 (0.4, 1.8)
TS-only (n=73)	4.2 (2.5)	0.8 (0.3, 1.4)
TS and inadequate CPM (n=40)	4.6 (2.3)	1.1 (0.4, 1.8)

Adjusted for age, sex, BMI, analgesics, education, sleep disturbance, Pain Catastrophizing Scale, the Hospital Anxiety and Depression Scale and Kellgren Lawrence sum score.
Conclusion: One third of persons with hand OA had inadequate CPM. Those with inadequate CPM, central sensitization or both reported higher pain severity than persons without any signs of altered central pain processing. Having both inadequate CPM and central sensitization was not associated with higher pain severity than having only one of the features. Our results are the first to demonstrate such a heterogenous variety of clinically relevant pain phenotypes in persons with hand OA.
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THU0455 PHARMACOKINETICS (PK) OF A SINGLE INTRA-ARTICULAR (IA) INJECTION OF CNTX-4975 (TRANS-CAPSAICIN) VS TOPICAL 8% CAPSAICIN PATCH

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Background: CNTX-4975 is in phase 3 trials for treatment of moderate to severe pain associated with knee osteoarthritis (OA). PK data from prior studies of CNTX-4975 in subjects with moderate to severe knee OA pain suggest low systemic and short-term exposure, similar to the FDA-approved topical capsaicin 8% patch.
Objectives: We compared single-dose systemic exposure to *trans*- and *cis*-capsaicin following IA injection of CNTX-4975 (>99.5% *trans*-capsaicin, <0.5% total impurities) with 8% capsaicin patch in subjects with moderate to severe knee OA pain.
Methods: This open-label, crossover study enrolled adults aged 50–75 y with moderate to severe knee OA pain in $\geq$1 knee (most painful knee, index knee; nonindex knee, no to mild pain [0–1; NPRS 0–4 scale]). Subjects were randomized 1:1 to 2 sequences: A (CNTX-4975 1 mg IA, index knee) followed by B (topical capsaicin 8% patch, posterior rib cage for 60 min) or BA sequence, with $\geq$7-day washout between treatments. Plasma samples for *trans*- and *cis*-capsaicin concentration assays were taken before and at specified times after study treatment. PK parameters, including maximum observed plasma concentration (C_{max}), area under the plasma concentration-time curve from time 0 to last quantifiable plasma concentration (AUC_{0-t}) and to infinity ($AUC_{0-\infty}$), time to C_{max} (T_{max}), and half-life ($t_{1/2}$), were determined. PK parameters were reported using descriptive statistics. Geometric means ratios of ln-transformed AUC_{0-t}, $AUC_{0-\infty}$, and C_{max} were evaluated using ANOVA.
Results: Sixteen subjects (median age, 62 y; female, 62.5%) were randomized to treatment (PK analysis population). T_{max} showed more rapid absorption of *trans*-capsaicin from IA CNTX-4975 vs the topical patch (**Table**). AUC_{0-t} and C_{max} indicated greater *trans*-capsaicin exposure

with CNTX-4975 vs the patch; however, exposure was short term, with mean $t_{1/2}$0.5 h. *Cis*-capsaicin concentrations were insufficient for calculating PK.

Conclusion: *Trans*-capsaicin from CNTX-4975 injection was rapidly absorbed and eliminated. The extent of systemic exposure to *trans*-capsaicin was significantly higher after CNTX-4975 vs the 8% capsaicin patch.

Abstract THU0455 –Table 1.

***Trans*-Capsaicin PK**

Parameter	IA CNTX-4975 1 mg N=14[a]	Topical 8% Capsaicin N=16[a]
AUC_{0-t}, h•pg/mL	n=14	n=15
Mean (SD)	3477.72 (1935.045)	257.57 (353.759)
GM (% CV)	3035.61 (55.6)	85.10 (137.3)
Geometric LS mean	2930.10	81.72
GM ratio[b] (90% CI)	35.85 (15.00–85.71)	
$AUC_{0-\infty}$, h•pg/mL	n=13	n=0
Mean (SD)	3668.85 (1888.667)	
GM (% CV)	3287.05 (51.5)	
Geometric LS mean	3113.42	
GM ratio[b] (90% CI)	NE	
C_{max}, pg/mL	n=14	n=16
Mean (SD)	3875.79 (2101.535)	123.28 (134.076)
GM (% CV)	3371.88 (54.2)	0 (108.8)
Geometric LS mean	3305.31	72.05[c]
GM ratio[b] (90% CI)	45.88 (23.87–88.18)	
T_{max},[d] h	n=14	n=16
Median (range)	0.2 (0–1)	1.0 (0–8)
$t_{1/2}$, h	n=13	n=0
Mean (SD)	0.54 (0.201)	

BLQ, below limit of quantification; CV, coefficient of variation; GM, geometric mean; LS, least squares; NE, not estimable.
[a]N=no. of subjects in PK population; [b]CNTX-4975/8% capsaicin patch; [c]n=15; 1 subject had C_{max}=0 and could not be included in log-transformed data analysis; [d]BLQ plasma concentrations before T_{max} were set to 0, except for BLQ value occurring between 2 measurable concentrations, which was set to missing. BLQ concentrations after T_{max} were set to missing.

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THU0456 EVALUATION OF THE USE OF ORLISTAT IN THE COMPLEX TREATMENT OF OBESITY IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Currently in the world there is a pandemic of obesity, which leads to an increase in diseases associated with overweight. Obesity is an important factor in the development and progression of osteoarthritis (OA). The metabolic phenotype of OA, which is directly associated with obesity, is highlighted. Due to the growing number of patients with obesity and OA, a high level of comorbidity and the lack of effectiveness of non-drug therapy, the problem of the effectiveness and safety of the therapy of obesity is very relevant.

Objectives: To evaluate the efficacy and safety of drug therapy for obesity in patients with OA of the knee.

Methods: 50 female patients (45-65 y.o.) with Kellgren-Lawrence stage II-III KOA and obesity (BMI>30kg/m²). Patients in Group 1 (n = 25) took 120 mg of orlistat 3 times a day in combination with a low-calorie diet and exercise for 6 months. Patients in Group 2 (n = 25) were on a low-calorie diet combined with exercise for 6 months. All patients initially received various non-steroidal anti-inflammatory drugs (NSAIDs) in tablet form. All patients were assessed for body mass, parameters of the WOMAC index, EQ-5D quality of life index, NSAID consumption, and orlistat therapy safety assessment.

Results: After 6 months of drug therapy for obesity, patients from Group 1 achieved a significant weight loss by 10.07% ($p < 0.05$). Patients from Group 2 the use of non-medical methods of treating obesity reduced body weight by 0.84% ($p > 0.05$). Patients from Group 1 improved the WOMAC index: pain decreased by 52.5% ($p < 0.05$), stiffness by 47.98% ($p < 0.05$), and functional insufficiency by 51.55% ($p < 0.05$). Patients from Group 2 also showed a decrease in the WOMAC index, but these changes were worse than in patients with greater weight loss. Patients from Group 1 showed a significant improvement in the quality of life for the EQ-5D index by 52.27% ($p < 0.05$). Patients from Group 2 against the background of insignificant changes in body weight, the quality of life index EQ-5D did not change. The need to take NSAIDs on the background of drug therapy for obesity and weight loss decreased by 4.6 times. On the contrary, in Group 2 of patients on the background of non-pharmacological treatment of obesity after 3 months of observation, the need for NSAIDs was maintained in 76%. The need for NSAIDs in patients of Group 2 decreased 1.3 times. In general, the tolerability of orlistat in patients of Group 1 was good. Adverse reactions were observed in two patients in the form of steatorrhea. The appearance of an undesirable reaction was associated with errors in nutrition (eating food saturated with animal fats), which did not require discontinuation of the drug. After correcting the diet, no adverse reactions were noted in patients.

Conclusion: The results of our study showed a significant decrease in body weight by more than 10% in the group of patients with OA while receiving orlistat. Significant weight loss helps reduce pain intensity, improve joint function, improves the quality of life of patients with OA, reduces the need for NSAIDs, which can help stabilize other comorbid diseases in patients with OA and obesity. The study noted good safety of therapy with orlistat; no serious adverse reactions were reported. Thus, drug therapy for obesity using orlistat can be included in the management of patients with OA and obesity, who cannot achieve weight loss using non-drug methods.

Disclosure of Interests: : Ekaterina Strebkova: None declared, Ludmila Alekseeva Speakers bureau: Bayer, Boeringer-ingelheim, Gedeon-Richter, Servier

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THU0457 EVALUATION OF THE EFFECTIVENESS OF COMPLEX TREATMENT OF OBESITY ON THE CLINICAL MANIFESTATIONS OF KNEE OSTEOARTHRITIS AND THE DYNAMICS OF CYTOKINES, DEPENDING ON THE DEGREE OF WEIGHT LOSS

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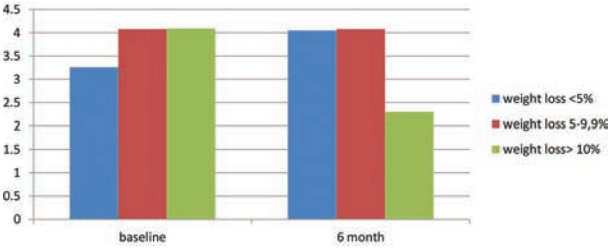
Background: Obesity is a risk factor and progression of the metabolic phenotype of osteoarthritis (OA). The decrease in body weight is important in the treatment of OA. Non-drug therapy aimed at altering the eating behavior, allows you to achieve a decrease in body weight of only 5%, which does not always contribute to the achievement of the clinical effect in patients with diseases of the joints.

Objectives: Assess the effectiveness of complex treatment of obesity with the use of orlistat (intestinal lipase inhibitor) on the clinical manifestations of the knee OA and the dynamics of cytokines (CRP, IL-6, TNF-α) depending on the degree of weight loss.

Methods: 50 female patients (45-65 y.o.) with Kellgren-Lawrence stage II-III KOA and obesity (BMI>30kg/m²). Patients in Group 1 (n = 25) took 120 mg of orlistat 3 times a day in combination with a low-calorie diet and exercise for 6 months. Patients in Group 2 (n = 25) were recommended non-drug therapy for obesity for 6 months. At baseline and after 6 months, the clinical parameters of the knee OA (WOMAC) were evaluated, the quality of life was assessed (EQ-5D). A laboratory study of peripheral blood was conducted at baseline and after 6 months: CRP, IL-6, TNF-α.

Results: After 6 months of complex treatment of obesity with the use of orlistat, patients in Group 1 achieved a significant weight loss of 10.07% ($p < 0.05$). Depending on the degree of weight loss in Group 1, 15 patients lost> 10% and 10 patients lost 5–9.9% of the initial body weight. In the 2nd group, an insignificant weight loss of 0.84% ($p > 0.05$) was achieved, all patients in Group 2 lost less than 5%. Depending on the degree of weight loss, it is noted that in patients with weight loss more than 5% better than WOMAC (pain, stiffness, functional state) ($p < 0.05$), EQ-5D ($p < 0.05$) compared with less weight loss. In patients with weight loss> 10%, a significant decrease in CRP level was observed ($p = 0.03$) (Fig. 1) compared with baseline and patients with a 5–9.9% weight loss ($p = 0.03$) and <5% ($p = 0.02$). Data for statistically significant changes

from TNF-α and IL-6, depending on the degree of weight loss was not detected.



Abstract THU0457 – Figure 1. Dynamics of CRP depending on the degree of weight loss (p <0.05)

Conclusion: The results of the study demonstrated a significant effectiveness of the complex treatment of obesity in patients with knee OA, compared with the use of only non-pharmacological methods of weight loss. A decrease in body mass of more than 5% helps to improve the clinical manifestations of knee OA and the quality of life of patients. A decrease in body weight of more than 10% demonstrates a decrease in the level of CRP, which suggests an effect on meta-inflammation in OA.
Disclosure of Interests: Ekaterina Strebkova: None declared, Ludmila Alekseeva Speakers bureau: Bayer, Boeringer-ingelheim, Gedeon-Richter, Servier
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THU0458 EFFICACY AND SAFETY FROM A PHASE 2B TRIAL OF SM04690, A NOVEL INTRA-ARTICULAR WNT PATHWAY INHIBITOR FOR THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE

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Background: A phase 2a study of SM04690, a small-molecule, intra-articular (IA) Wnt pathway inhibitor reduced knee pain and improved physical function and medial joint space width (mJSW) at 52 weeks in subgroups of subjects with unilateral symptomatic knee osteoarthritis (OA) compared to placebo (PBO).[1]
Objectives: A 24-week phase 2b study was conducted to refine patient-reported outcome (PRO) measures, target population, medication dose, and to evaluate safety. PRO results for Weeks 12 and 24 are presented here.
Methods: Study subject inclusion criteria required ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2-3, and Pain Numeric Rating Scale (NRS) ≥4 and ≤8 in the target knee and <4 in the contralateral knee. A single IA injection of 2 mL SM04690 (0.03, 0.07, 0.15, or 0.23 mg), vehicle PBO, or sham (dry needle only) was given in the target knee at baseline. PRO endpoints included change from baseline in weekly average of daily pain in the target knee by NRS diary (NRS) [0-10], Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain [0-100], WOMAC Physical Function [0-100], and Patient Global Assessment (PtGA) [0-100]. Differences between active treatment groups and vehicle PBO were analyzed with baseline-adjusted analysis of covariance (ANCOVA).
Results: 695 subjects (mean age 59.0 [±8.5] years, BMI 29.0 [±4.0] kg/m^2, female 58.4%, KL3 57.3%) were enrolled and dosed; 635 subjects (91.4%) completed the study. No meaningful differences in the incidence of adverse events were observed between treatment and control groups.
In the Full Analysis Set, significant improvements from baseline compared to vehicle PBO were observed in pain NRS for 0.07 mg (Week 12 [*P*=0.001], Week 24 [*P*=0.031]) and 0.23 mg (Week 12 [*P*=0.012], Week 24 [*P*=0.022]) SM04690 dose groups (**Figure**). Similar improvements were observed in WOMAC Pain for 0.07 mg (Week 12 [*P*=0.04]) and 0.23 mg (Week 12 [*P*=0.003], Week 24 [*P*=0.031]) dose groups. For WOMAC Physical Function, improvements were observed for 0.07 mg (Week 12 [p=0.021]) and 0.23 mg (Week 12 [p=0.006], Week 24 [P=0.017]) dose groups. PtGA improvements were observed for 0.07 mg (Week 12 [*P*=0.031]) and 0.23 mg (Week 12 [*P*=0.010], Week 24 [*P*=0.033]) dose groups.
Conclusion: SM04690, in development as a potential disease-modifying OA drug, showed in this phase 2b study statistically significant improvements from baseline in both the 0.07 mg and 0.23 mg dose groups compared to vehicle PBO for Pain NRS, WOMAC Pain, WOMAC Physical Function, and PtGA. These data support the continued development of SM04690 as a treatment for knee OA. Phase 3 studies are being planned.

REFERENCE:
[1] Yazici Y, et al. *Arthritis Rheumatol.* 2017; 69 (suppl 10).

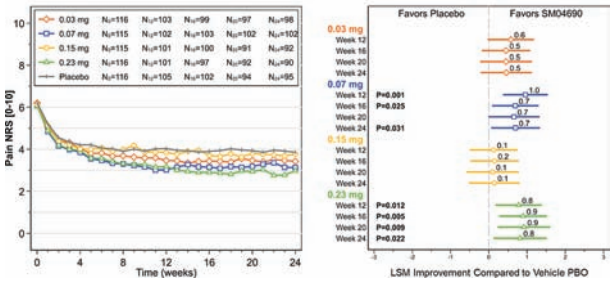


Figure. Actual observations over time and ladder plots depicting least squares mean (LSM) improvement of Pain NRS (± 95% CI) in SM04690 compared to vehicle PBO, adjusted for baseline.

Disclosure of Interests: Yusuf Yazici Shareholder of: Samumed, LLC, Consultant for: Celgene Corporation, BMS, Genentech, Sanofi, Employee of: Samumed, LLC, Timothy McAlindon Grant/research support from: Samumed, LLC, Consultant for: Samumed, LLC, Astellas, Flexion, Pfizer, Regeneron,
Seikugaku, Allan Gibofsky Shareholder of: AbbVie, Amgen, Johnson&Johnson, Regeneron, Consultant for: AbbVie, Pfizer, Horizon, Celgene, Novartis/Sandoz, Samumed, LLC, Merck, Flexion, Lilly, Speakers bureau: AbbVie, Celgene, Pfizer, Flexion, Lilly, Merck, Nancy Lane Consultant for: Samumed, LLC, Christian Lattermann Shareholder of: Cocoon, Consultant for: Samumed, LLC, Vericel, Cariheal, Joint Restoration Foundation, Nebojsa Skrepnik Grant/research support from: Samumed, LLC, Consultant for: Orthofix, Sanofi, Regeneron, Christopher Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Anita DiFrancesco Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Jeyanesh Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Marc Hochberg Shareholder of: BriOri Biotech, Theralogix LLC., Consultant for: Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis Pharma AG, Pfizer Inc., Samumed LLC, Symic Bio Inc., Theralogix LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., Zynerba, Galapagos, IQVIA, Hoffman LaRoche.
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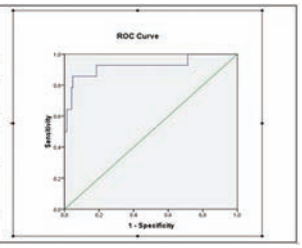
THU0459 PREDICTORS ASSOCIATED WITH RAPID PROGRESSION OF KNEE OSTEOARTHRITIS

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Objectives: To identify knee OA rapid progression factors in a multicenter prospective study
Methods: 185 female patients from 5 RF constituent territories aged 40-75 with confirmed Kellgren-Lawrence score grade I-III knee OA were included into prospective study after signing the informed consent form. Mean age was 59,2±7,4 years (42-75), mean BMI–27,7±4,4 kg/m^2, mean disease duration–12±8,1 years. Individual patient's medical record included relevant anthropometric data, records from case history and clinical examination, VAS articular pain assessment, WOMAC scores, comorbidities. Instrumental diagnostic methods included plain radiography of knee joints, DEXA of the lumbar spine and femoral neck, MRI examination of knee joints. Stage II knee OA was established in 135 (73%) out of 185 patients, stage III – in 50 (27%).

Results: Knee OA progression (form radiographic stage II to stage III) within 1 year follow up was documented in 15 patients (Group 2 – with progressed OA), while 170 patients did not show any progression (Group 1 - no progression). Both groups were comparable in terms of age, age at RA onset, and duration of the disease. Although patients who progressed had higher body weight (97,1±14,0 vs 74,2±10,8 kg, p<0,0001) and BMI (31,9±5,8 vs 27,3±4,1 kg/m^2, p<0,0001). Patients from Group II had more intense knee pain during walking (VAS - 65,8±11,8 vs 47,5 ±18,7 mm (p<0,0003), and higher WOMAC: pain- 330,5±66,0 vs 237,8 ±85,4 mm, p<0,0001; function - 1044±190,4 vs 859,8±243,8 mm, p<0,007. Patients from Group II showed higher rates of varus knee alignment (66,7% vs 35,3%, RR=1,89, 95% CI 1,25-2,85, p=0,02) and H.valgus (86,7% vs 61,8%, RR=1,4, 95% CI 1,11-1,77, p=0,04), as well as higher rates of arterial hypertension (93,3% vs 71,8%, respectively, RR=1,3, 95% CI 1,1-1,53, p=0,05) and type 2 diabetes mellitus (DM) (33,3% vs 12,9%, RR=2,57, 95% CI 1,14-5,82, p=0,04). MRI showed higher percentage of medial and lateral tibia cartilage defects in Group 2 patients (57,2% vs 18,6%, respectively; RR=3,06, 95% CI 1,74-5,38, p<0,003; 57,2% vs 14%, RR=4,08, 95% CI 2,23-7,46 p<0,0006); bone marrow edema (BME) in medial (71,4% vs 12,2%, RR=5,83, 95% CI 3,38-10,1, p<0,000004) and lateral tibial compartments (21,4% vs 4,1%, RR=5,25, 95% CI 1,47-18,7, p=0,03); subchondral cysts, occupying more than 25% of the area in medial and lateral tibial compartments (respectively, 28,6% vs 7,4%, RR=3,84, 95% CI 1,4-10,5, p<0,03; and 35,7% vs 8,8%, RR=4,06, 95% CI 1,7-9,7, p=0,01). Synovitis (MRI findings) was documented in 100% patients from Group 2 and in 58,4% patients without OA progression (RR=1,71, 95% CI 1,5-2,0, p=0,002). A multivariate (discriminant) analysis showed that the most important risk factors for knee OA progression were: higher body weight, high WOMAC pain score, presence of type 2 DM, BME in medial tibial compartment, and cartilage damage in medial tibial compartment (MRI findings). A model capable of predicting rapid progression of knee OA in an individual patient with high accuracy (area under the ROC-curve 0,925 (95% CI 0,828–1,022)) has been developed based on identified RF and their coefficients.

Factors	Discriminant function coefficients
Body weight, kg	0,1698
Pain WOMAC, mm	0,0068
DM type 2	1,8387
BME in medial tibia	1,1848
Cartilage destruction in the medial tibial compartment	0,4724
Constant	21,6615



Abstract THU0459 – Figure 1

Conclusion: In a prospective multicenter study, using comprehensive instrumental examination the following key predictors of rapid knee OA progression were identified: excessive body weight, high WOMAC pain score, presence of type 2 DM, BME in medial tibial compartment, and cartilage damage in medial tibial compartment (MRI findings).

Disclosure of Interests: Elena Taskina Speakers bureau: Bayer, Sandoz, Boeringer-ingelheim, Ludmila Alekseeva Speakers bureau: Bayer, Boeringer-ingelheim, Gedeon-Richter, Servier, Natalia Kashevarova: None declared, Sergey Anikin: None declared, Evgenia Sharapova: None declared, Ekaterina Strebkova: None declared, Lena Zonova Speakers bureau: Sandoz, Pfizer, Abbvie, Novartis, Bayer, Tatiana Raskina: None declared, Elvira Otteva Speakers bureau: Pfizer, Abbvie, Novartis, Irina Vinogradova Speakers bureau: Pfizer, MSD, Aleksandr Lila Speakers bureau: Sandoz, Pfizer, Abbvie, Novartis, Bayer

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THU0460 IDENTIFICATION OF POSTOPERATIVE PAIN BIOMARKERS USING GENE EXPRESSION ANALYSES IN THE PERIPHERAL BLOOD OF OSTEOARTHRITIC PATIENTS PRIOR TO JOINT REPLACEMENT

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Background: Osteoarthritis (OA) is a chronic rheumatic disease, which involves pain, limited inflammation and local destruction of the knee joint. OA pain is a major clinical symptom, which limits working capacity and denotes an important indication for joint replacement in the end-stage OA. In spite of significant number of positive outcomes, chronic postoperative pain represents a major adverse consequence of surgery, which is observed in 10-40% of OA patients. Therefore, identification of patients potentially capable of developing chronic postoperative pain prior to surgery could significantly improve therapy outcome. Central sensitization is in charge of pain symptoms in about 30% of end-stage OA patients. Several recently identified molecular markers such as cytokines, chemokines, calcium and glutamate transporters, caspases, and proteases has been shown to be responsible for central sensitization. Therefore, we hypothesized that genes related to pain sensitization whose expression is upregulated in about 30% of the examined end-stage OA patient cohort might be responsible for postoperative pain.

Objectives: To outline an approach for search of biomarkers related to chronic postoperative pain development before joint replacement in the peripheral blood of end-stage OA patients.

Methods: We examined peripheral blood of 26 healthy volunteers (average age 55±8.3 years old) and 53 end-stage OA patients (average age 56.5±8.9 years old) undergoing joint replacement surgery. MMP-9, TIMP1, TGFβ1, and caspase 3 protein levels were quantified by ELISA. Total RNA isolated from whole blood was used in expression studies for the genes related to central sensitization such as mechanistic target of rapamycin, mTOR; caspase 3; metalloproteinase (MMP)-9; tissue inhibitor of metalloproteinase TIMP1; cathepsins K and S; interleukin (IL)-1β; cyclooxygenase (COX)2; tumor necrosis factor (TNF)α, and transforming growth (TGF)β1. These were performed with quantitative real-time RT-PCR.

Results: Retrospective analysis of gene expression in the peripheral blood of end-stage OA patients before joint replacement surgery revealed that gene expression data for TNFα, IL-1β, COX2, TGFβ1, and mTOR were not applicable as these gene expressions were significantly higher compared to healthy controls in all the examined OA patients. High expression of pain associated cathepsin S in 17% of the examined OA patients and cathepsin K, in 21% might indicate the possibility of postoperative pain development in these OA patients. In contrast, low expression of caspase 3 in 43% of the examined OA patients and MMP-9, in 23%, might point toward the absence of postoperative pain in these subjects.

Conclusion: Gene expression analysis in the peripheral blood of the end-stage OA patients measured before joint replacement surgery might represent an approach for prediction of postoperative pain development.

Disclosure of Interests: : None declared

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THU0461 IDENTIFICATION OF DEFINITIONS OF POOR OUTCOME AFTER TREATMENT OF KNEE OSTEOARTHRITIS: A LITERATURE REVIEW

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Background: Total knee replacement (TKR) is considered an effective intervention of the treatment of advanced knee osteoarthritis (OA) (Kellgren & Lawrence >2). However, a significant proportion of patients could be considered as a poor-responder to TKR (i.e. no or little improvement) in terms of chronic knee pain, functional disability, poor quality of life (QoL), and dissatisfaction after TKR. Both in research and in clinical practice it is challenging to identify those patients with an unfavourable course after TKR. It is difficult though to quantify the proportion of patients with poor response to TKR, as different definitions of, and perspectives (clinician's and patient's) on failure are being used.

Objectives: The aim of this study was to review the literature and summarize definitions of poor response to TKR.

Methods: A systematic search up to 2016 was performed to identify and review previously used definitions of poor response to primary TKR in the literature. Studies were included if dichotomous definitions of outcome after primary TKR were used, if a prospective design was used and in English full text available. The type, amount and combination of domains (i.e. pain and physical function), outcome measures, type of responses (absolute/relative, change/cut-off), values and moments of follow-up used in definitions were summarized.

Results: A total of 44 different dichotomous definitions of poor response to TKR, were extracted from 1849 initially identified studies. 34 definitions incorporated one domain, six definitions comprised two domains and four definitions comprised three domains. Eight different domains were used in identified definitions: pain, physical function (mobility), physical functioning

(body), QoL, satisfaction, anxiety, depression and patient global assessment. Patient satisfaction was most commonly used (n=10) as single domain with a wide variation in wording of questions and answering categories. The absolute cut-off value was the most common type of response, with large variety in value and timing of follow-up. Table 1 shows one definition for each combination of domains.

Conclusion: Our review shows that definitions for poor response to TKR are ambiguous. Our findings stress the need for an unambiguous definition of poor response to draw conclusions about the prevalence of poor-responders to TKR across hospitals and countries, and to identify patients at risk.

Abstract THU0461 –Table 1. The table shows one definition for each combination of domains

Domain	Outcome measures used	Absolute/relative cut-off value/ change	Value	Time points used
Unidimensional (single domain used)				
Pain	WOMAC, pain	*absolute change*	MCID ≤4	6M
Function (impairment)	Knee flexion	*absolute cut-off*	<90°	1Y
Physical functioning	WOMAC, function	*relative change*	<50% improvement from baseline to 6M FU	6M
HRQoL	SF-12, mental & physical component	*absolute change*	Deterioration of ≥1 compared to preoperative	6W + 12W + 6M
Satisfaction	Single item question	*absolute cut-off*	Dissatisfied *(=somewhat dissatisfied and dissatisfied)*	12M
Multidimensional (two domains used)				
Anxiety + Depression	HADS, anxiety & depression	*absolute cut-off*	≥8	6M
Pain + Physical functioning	OKS, pain & functioning	*absolute change*	MCID ≤5	12M
Multidimensional (three domains used)				
Pain + Function (impairment) + Global assessment	OMERACT-OARSI responder criteria	*absolute & relative change*	Non-responder: <50% improvement and less than an absolute improvement of 20 points in either pain or function	12M
Pain + Function (impairment) + Physical functioning	WOMAC, pain, stiffness & function	*absolute cut-off*	>40.4	6M

Disclosure of Interests: : None declared
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THU0462 OUTCOME PREDICTION FOR TREATMENT OF KNEE OSTEOARTHRITIS WITH A TOTAL KNEE ARTHROPLASTY. DEVELOPMENT AND VALIDATION OF A PREDICTION MODEL FOR PAIN AND FUNCTIONAL OUTCOME USING THE DUTCH ARTHROPLASTY REGISTER (LROI) DATA

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Background: One of the main determinants of treatment satisfaction after total knee arthroplasty (TKA) is the fulfilment of preoperative expectations. For optimal expectation management it is useful to be able accurately predict the treatment result. Multiple patient factors that are obtained for registration in the Dutch Arthroplasty Registry (LROI) are associated with the treatment result. Therefore, these factors can potentially be utilised to estimate the most likely outcome on pain and functional outcome for an individual patient

Objectives: The aim of the present study was to create and validate models that predict residual symptoms on 10 specific outcome parameters at 12-month follow-up for patients undergoing primary TKA for knee osteoarthritis.

Methods: Data was extracted from the LROI on TKA patients who had pre- and postoperative PROMs registered in the LROI registry. Multiple logistic regression analyses were performed to construct predictive algorithms for satisfaction, treatment success, and residual symptoms concerning pain in rest and during activity, sit-to-stand movement, stair negotiation, walking, performance of activities of daily living, kneeling and squatting. Models were developed for men and women separately. We assessed predictive performance by examining measures of calibration and discrimination.

Results: Data of 7071 patients could be included for data analysis. Residual complaints on kneeling (♀72%/ ♂59%) and squatting (♀71%/ ♂56%) were reported most frequently, and least residual complaints were scored for walking (♀16%/ ♂12%) and pain in rest (♀18%/ ♂14%). The predictive algorithms for residual symptoms concerning sit-to-stand movement, stair negotiation, walking, activities of daily living and treatment success showed acceptable discriminative values (AUC 0.68 – 0.74). The prediction models for residual complaints regarding kneeling, squatting, pain and satisfaction showed the least favourable results (AUC 0.58 – 0.64). The calibration curves showed adequate calibration for most of the models.

Conclusion: A considerable proportion of patients has residual complaints after TKA. The present study showed that demographic and PROMs data collected for the LROI registry, can be used to predict the chance for residual symptoms after TKA. The predictive models that have been developed can be useful for individual expectation management in patients planned for TKA for knee osteoarthritis.

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Disclosure of Interests: None declared
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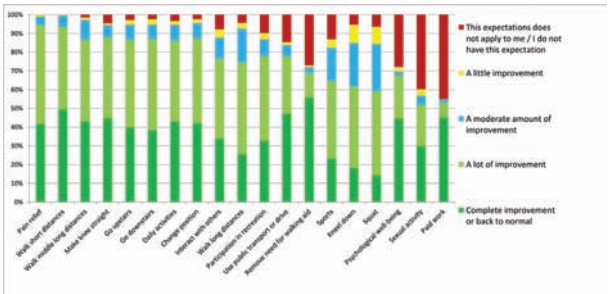
THU0463 EXPECTATIONS OF TREATMENT RESULT OF KNEE OSTEOARTHRITIS PATIENTS TREATED WITH A TOTAL KNEE ARTHROPLASTY. THE INFLUENCE OF DEMOGRAPHIC FACTORS, PAIN, PERSONALITY TRAITS, PHYSICAL AND PSYCHOLOGICAL STATUS

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Background: Unrealistic preoperative expectations have a strong influence on the outcome after total knee arthroplasty (TKA). More insight into determinants of the level of expectations is useful in identifying patients at risk for unrealistic expectations. This information can be used in optimizing pre-operative expectation management.

Objectives: The aim of the current study was to analyze to what extent pre-operative outcome expectations of TKA patients are determined by psychological factors, demographic factors, pain, physical function and general health status.

Methods: A cross-sectional analysis of 204 patients with symptomatic and radiographic knee OA, scheduled for primary TKA was conducted. Outcome expectations were measured using the Hospital for Special Surgery knee replacement expectations survey. Independent variables included were age, sex, body mass index and patient reported outcome measures for pain, physical function, quality of life, anxiety, depression, catastrophizing, optimism and pessimism. Multiple linear regression analyses were used to evaluate associations between these variables and pre-operative outcome expectations



Abstract THU0463 – Figure 1

Results: The mean overall survey score on the HSS-KRES was 70.9 (SD 17.9). Distribution of expectation scores is shown in Figure 1.

Highest expectations were scored for pain relief and improvement of the ability to walk of short and medium distances. Patients had the lowest expectations for improvement in kneeling, squatting, psychological well-being sexual activity and the ability to have paid work.
Female sex, higher age, higher depression score and duration of complaints > 50 months showed to be significant predictors of lower expectations for the treatment outcome after TKA. Baseline pain and function scores were not related to the level of pre-operative expectations.
Conclusion: In conclusion young, male patients with a short duration of complaints might be at risk of having too high expectations of the treatment result. On the contrary patients with depressive symptoms are more likely to have low expectations, with a potential negative influence on their treatment result. The present study aids in identifying patients at risk for having either too high or too low expectations. This knowledge can be utilized in individualized expectation management interventions.
Acknowledgement: We would like to thank C. van Doesburg and H. Kox for their support in data collection and study procedures.
Disclosure of Interests: None declared
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THU0464 PHASE 2 CLINICAL TRIAL OF THE GI SAFETY OF A HYDROGEN SULFIDE-RELEASING ANTI-INFLAMMATORY DRUG (ATB-346)

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Background: Hydrogen sulfide (H_2S) is a naturally occurring gaseous mediator produced by intestinal bacteria and various eukaryotic cells. H_2S exerts anti-inflammatory, pro-resolution and cytoprotective effects *in vivo*. ATB-346 is an H_2S-releasing derivative of naproxen, which in animals was shown to produce negligible gastrointestinal (GI) damage and bleeding. In human studies, ATB-346 was found to be much more potent and long-lasting than naproxen. A phase 2 open-label efficacy study demonstrated that ATB-346 (250 mg daily) significantly reduced pain in patients with osteoarthritis of the knee, and markedly suppressed cyclooxygenase (COX) activity. The aim of the present study was to determine if ATB-346 would induce less gastroduodenal ulceration than standard dose naproxen.
Objectives: To determine if healthy subjects taking ATB-346 for 14 days would develop significantly less gastroduodenal ulcers ($\geq$3 mm diameter with depth) than subjects taking an equi-effective dose of naproxen.
Methods: This was a double-blind, active control, endoscopic study. 244 healthy volunteers completed the study. Upper GI endoscopy was performed prior to and on day 14 after commencing treatment with naproxen (550 mg twice daily) or ATB-346 (250 mg) once daily in the morning and placebo once daily in the evening. Whole blood thromboxane synthesis was measured on days 0, 7 and 14. Plasma H_2S levels were also measured.
Results: 53 subjects taking naproxen (42.2%) developed at least one ulcer, while only 3 subjects (2.5%) treated with ATB-346 developed at least one ulcer ($p<0.0001$). The two drugs suppressed COX activity to the same extent (>95%). Affected subjects in the naproxen group developed more ulcers (an average of 4 per subject) than in the ATB-346 group (an average of 1.3), and there was a much greater incidence of larger ulcers ($\geq$5 mm diameter) in the naproxen group than in the ATB-346 group (125 vs 0, respectively). The incidence of gastro-esophageal reflux, abdominal pain and nausea was lower with ATB-346 than with naproxen. Plasma H_2S levels were significantly elevated (by 50%; $p<0.001$) in the ATB-346 group.
Conclusion: Consistent with the pre-clinical studies, this phase 2 clinical trial demonstrated a dramatic reduction of upper GI ulcer formation in subjects treated with equi-effective doses of ATB-346 versus naproxen. The COX inhibition observed in this trial was consistent with a previous phase 2A trial that demonstrated significant pain relief with ATB-346 in patients with osteoarthritis of the knee. ATB-346 appears to be an effective and much safer alternative to existing NSAIDs.
Disclosure of Interests: : John Wallace: None declared, Andre Buret Shareholder of: Antibe Therapeutics, Peter Nagy: None declared, Marcelo Muscara Grant/research support from: Antibe Therapeutics, Gilberto de Nucci Shareholder of: Antibe Therapeutics, Employee of: BioLab Brasil
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THU0464B IS THERE AN ASSOCIATION BETWEEN METABOLIC SYNDROME AND SEVERITY OF HAND OSTEOARTHRITIS? RESULTS FROM A NATIONWIDE STUDY

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Background: Hand osteoarthritis (HOA) is a highly prevalent rheumatic disease that predominates in females and causes pain, joint deformities and loss of functional capacity. Overweight and metabolic syndrome have been previously suggested to associate with the severity of HOA, but clarity on these associations is yet to be achieved.
Objectives: To test the possible association between body mass index (BMI) and other individual components of metabolic syndrome with severity of HOA in females from a nationwide epidemiological study.
Methods: EpiReumaPt was a three-stage national health survey where, in the first phase, 10,661 adult participants were randomly selected and interviewed using a structured face-to-face questionnaire that included screening for rheumatic diseases, such as HOA. In the second phase, positive screenings for $\geq$1 rheumatic complaint plus 20% of the negative screenings were invited for an assessment by rheumatologists. Finally, 3 rheumatologists revised all the information and defined the final diagnosis by consensus. Female patients with a final clinical diagnosis of primary HOA were included in this analysis. Hand functional status as assed by the Cochin questionnaire was the outcome of interest. The explanatory variables of interest were: BMI evaluated as a categorical variable (Normal: 18-24.99; overweight: 25-29.99; obesity: $\geq$ 30), diabetes mellitus, hypertension and hypercholesterolemia (all self-reported and as binary variables: yes/no). The possible associations between BMI and the individual components of the metabolic syndrome with the Cochin score were tested in a multivariable linear regression model. Only significant variables ($p<0,05$) were kept in the final model. Potential confounders of the associations of interest and the outcome were defined a priori on clinical grounds and included age and symptoms of depression (HADS score).
Results: Out of the 3,877 participants evaluated by Rheumatologists, 473 women had primary HOA (national prevalence: 6.6%). In this population, 40% were overweight and 29% were obese. Ninety-three (20%) participants had diabetes, 261 (56%) had hypertension and 261 (56%) had hypercholesterolemia. In the multiple regression model, BMI and diabetes were found to significantly associate with HOA severity, whereas hypertension and hypercholesterolemia did not, thus not being selected in the final model (table).

Abstract THU0464 –Table 1. Association between individual components of the metabolic syndrome and HOA severity (Cochin score). Multivariable linear regression model

	HOA severity (Cochin score) β coefficient (95% CI) N= 408
BMI (categorical)	0.31 (0.05; 0.57)
Diabetes (yes vs no)	3.63 (0.13; 7.13)
Age (years)	0.13 (-0.01; 0.27)
HADS score (continuous)	0.90 (0.59; 1.22)

Conclusion: In this study, higher BMI and the presence of diabetes mellitus associated with a worse functional capacity in women with primary HOA. These data add to the body of evidence suggesting a possible role of metabolic factors in the severity of HOA.

REFERENCES:

[1] Yusuf E, Nelissen RG, Ioan-Facsinay A et al. Association between weight or body mass index and hand osteoarthritis: a systematic review. Ann Rheum Dis 2010. 69: 761-765
[2] Schett G, Kleyer A, Perricone C et al. Diabetes is an independent predictor for severe osteoarthritis: results from a longitudinal cohort study. Diabetes Care 2013; 36: 403-409

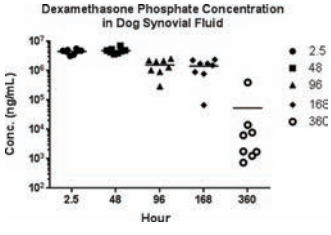
Acknowledgement: The authors thank all the participants of EpiReumaPt survey, the interviewers and staff and the Rheumatologists that worked in the field
Disclosure of Interests: Margarida Cruz: None declared, Alexandre Sepriano: None declared, Sara Dias: None declared, Ana Maria

Rodrigues: None declared, Helena Canhão: None declared, Nélia Gouveia: None declared, Mónica Eusébio: None declared, Sofia Ramiro Grant/research support from: MSD, Consultant for: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Speakers bureau: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Jaime Branco: None declared
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THU0465 PHARMACOKINETICS AND TOXICOKINETICS STUDIES OF A SUSTAINED RELEASE LIPOSOMAL FORMULATION OF DEXAMETHASONE SODIUM PHOSPHATE (TLC599) FOLLOWING INTRA-ARTICULAR INJECTION IN DOGS

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Background: Osteoarthritis (OA) is a degenerative joint disorder with limited long-lasting treatment options. Various steroid formulations on the market are effective but required frequent intra-articular (IA) injections due to short-term symptomatic relief. IA steroids have been shown to increase cartilage loss in knee and the rapid absorption into systemic circulation could cause adverse side effects, limiting their effectiveness [1]. To circumvent these issues, TLC599, a novel sustained-release liposome formulation of dexamethasone sodium phosphate (DSP) was developed to provide a sustained OA pain management over an extended period with reduced side effects and toxicity. TLC599 resulted in sustained presence in the synovial fluid without significant local and systemic side effects from OA treatments following IA injection.
Objectives: To evaluate pharmacokinetics (PK) and toxicokinetics (TK) of TLC599 following IA injection in dogs.
Methods: In two studies, the dexamethasone phosphate (DP) and dexamethasone (DEX) concentration was quantified and the PK/TK profile of TLC599 was evaluated in dogs following IA injection. DSP is the sodium salt form of DP and DEX is the active form of DSP. Study#8351851: TLC599 was administered as a single- or multiple-dose injection (once every 13 weeks for total of four times) at 18 mg/knee (36 mg/animal). Synovial fluid was collected at 2.5, 48, 96, 168 and 360 hours post-dose from 4 animals/time point, and plasma was collected at 0.25, 0.75, 1.25, 2, 4, 6, 24, 48, 96 and 168 hours post-dose from 8 animals/time point. Study#8388198: TLC599 was administered as a single-dose injection at 18 mg/knee. The synovial fluid was collected at 15, 30, 45, 90, and 120 days post-dose from 4 animals/time point.
Results: Study#8351851: Following a single-dose IA injection of TLC599, DP concentration declined gradually after 2.5 hr but remained detectable through 360 hr, demonstrating the prolonged local exposure in the joint (Figure 1). The PK parameters of DP and DEX in dog plasma were assessed in the multiple-dose group. The mean C_{max} and AUC_{0-t} values of DP and DEX were comparable between the first dose (Day 1) and the fourth dose (Day 274) (Table 1), indicating there was no accumulation of systemic exposure of DP and DEX following four repeated IA injections of TLC599. By evaluating the effect on cartilage, it was also shown that the local safety profiles were similar between multiple-dose and single-dose TLC599 injections.

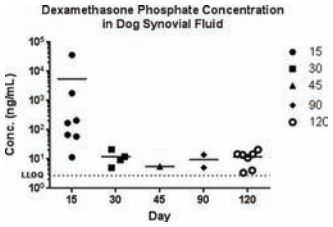


Abstract THU465 – Figure 1. Mean Concentration of DP in Dog Synovial Fluid.

Abstract THU465 – Table 1. Summary of Mean C_{max} and AUC_{0-t} of DP and DEX in Dog Plasma.

Analyte	Dose #	Dose Level (mg/animal)	C_{max} (ng/mL)	AUC_{0-t} (hour*ng/mL)
Dexamethasone Phosphate	First Dose (Day 1)	36	450	419
	Fourth Dose (Day 274)	36	522	505
Dexamethasone	First Dose (Day 1)	36	498	6385
	Fourth Dose (Day 274)	36	427	5955

Study#8388198: Following a single-dose IA injection of TLC599, DP concentration declined after 15 days but remained at similar level from 30 days to 120 days post-dose. Overall, the prolonged 120-day residence time of TLC599 in synovial joint was observed (Figure 2).



Abstract THU465 – Figure 2. Mean Concentration of DP in Dog Synovial Fluid.

Conclusion: TLC599, a novel extended-release liposome formulation of DSP, showed a long-lasting profile up to 120 days in synovial joint after a single IA injection in a preclinical dog study. In addition, no significant systemic exposure and accumulation of DP and DEX in dog plasma was observed following multiple-dose administration of TLC599. Animal studies indicate that TLC599 may be an effective and superior chronic treatment for OA.

REFERENCE:

[1] Zhang W, *et al*., OARSI recommendations for the management of hip and knee osteoarthritis, part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage 2008;16(2): 137-62

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Disclosure of Interests: Tzung-Ju Wu Employee of: Current employee of Taiwan Liposome Company, Wan-Ni Yu Employee of: Current employee of Taiwan Liposome Company, Ming-Ju Wu Employee of: Current employee of Taiwan Liposome Company, Po-Chun Chang Employee of: Current employee of Taiwan Liposome Company, Sheue-Fang Shih Employee of: Current employee of Taiwan Liposome Company
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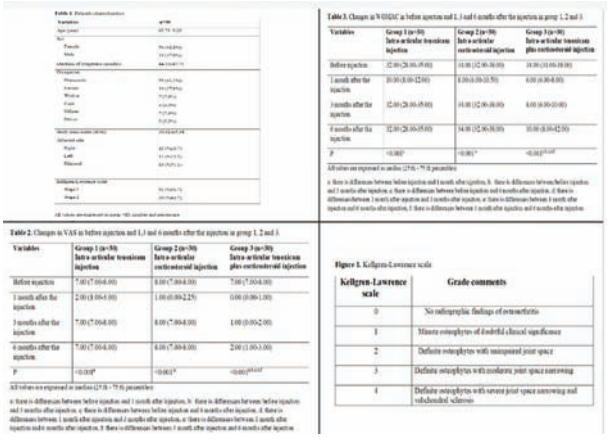
THU0466 THE EVALUATION OF THE EFFECTIVENESS OF INTRA-ARTICULAR STEROID, TENOXICAM AND COMBINED STEROID-TENOXICAM INJECTIONS IN THE TREATMENT OF PATIENTS WITH KNEE OSTEOARTHRITIS

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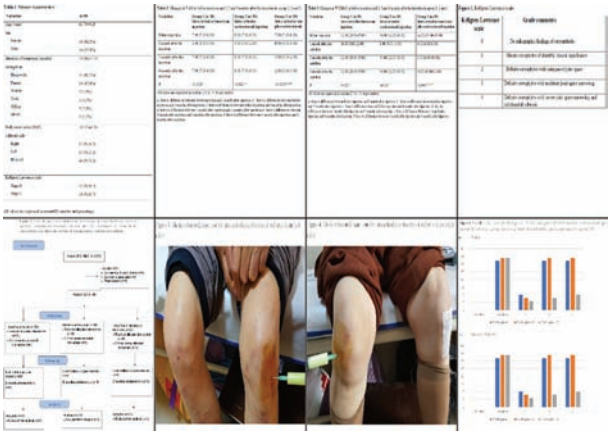
Background: Intra-articular corticosteroid injections are widely applied in the treatment of symptomatic knee osteoarthritis (OA). There is an evidence of short-term effects of intra-articular corticosteroid injection (up to 3-4 weeks), however there is no consensus for the long-term benefit of this treatment yet (1). Tenoxicam is an effective analgesic and anti-inflammatory drug for symptomatic treatment of OA. Additionally, apart from oral use, tenoxicam is also applied as an intra-articular treatment option to minimize gastrointestinal side effects of NSAIDs (2). Clinical evidence suggests that the combined use of NSAIDs and corticosteroids is synergistic (especially macular edema after cataract surgery in ophthalmology) (3).
Objectives: The aim of this study is to compare the effectiveness of intra-articular administration of these treatments and their combination and determine whether the combination of intraarticular steroid and tenoxicam was more effective for a long period rather than only tenoxicam and steroid injection alone in OA treatment.
Methods: 90 patients (56 female, 34 male) with diagnosis of knee osteoarthritis were randomly divided into three groups (30 patients per group): Group 1 were treated by intra-articular injection of tenoxicam. Group 2 were treated by intra-articular injection of triamcinolone hexacetonide. Group 3 were treated by intra-articular injection of triamcinolone hexacetonide combined with tenoxicam. The estimation of the severity of pain by the visual analog scale (VAS) were enrolled at baseline and 1, 3, 6 months post-injection. Additionally, the Western Ontario and McMaster Universities Index (WOMAC) was used to determine the outcome measures of pain, stiffness and physical functioning at baseline and 1, 3, 6 months post-injection.

Results: The mean age of patients was 65.97±9.29 years. In tenoxicam group, median pre- and post-treatment (at 1, 3 and 6 months) VAS/WOMAC scores were 7.00/32.00, 2.00/10.00, 7.00/32.00 and 7.00/32.00, respectively. In steroid group, median pre- and post-treatment (at 1, 3 and 6 months) VAS/WOMAC scores were 8.00/34.00, 1.00/8.00, 8.00/34.00 and 8.00/34.00, respectively. In steroid plus tenoxicam group, median pre- and post-treatment (at 1, 3 and 6 months) VAS/WOMAC scores were 7.00/34.00, 0.00/6.00, 1.00/8.00 and 2.00/10.00, respectively. VAS and WOMAC scores in 1 month after the injection significantly decreased in both groups compared to baseline ($p<0.01$). However, there was a pronounced improvement in only steroid plus tenoxicam group at 3 and 6 months post-injection ($p<0.01$). Steroid plus tenoxicam group showed significantly improved VAS and WOMAC scores when compared to only steroid and tenoxicam group at follow-up 3 and 6 months ($p<0.01$).

Abstract THU0466 –Table 1.



Abstract THU0466 –Table 2.



Conclusion: The combination of corticosteroids and tenoxicam seems to produce a more effective result than alone therapy in reducing pain and improving functional recovery.

REFERENCES:

1) Maricar N, Callaghan MJ, Felson DT, O'Neill TW. Predictors of response to intra-articular steroid injections in knee osteoarthritis- a systematic review. Rheumatology. 2013;52:1022-1032.
[2] Evcik D, Kızılay B, Maralcan G. The efficacy of intraarticular tenoxicam in the treatment of knee osteoarthritis. The Pain Clinic. 2003;15:405-408.
[3] Malik A, Sadafale A, Gupta YK, Gupta A. A comparative study of various topical nonsteroidal anti-inflammatory drugs to steroid drops for control of post cataract surgery inflammation. Oman J Ophthalmol. 2016;9:150-156.

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THU0467 **DOES GENERALISED PAIN AND LOCALISED PAIN SEVERITY INCREASE RISK OF PREVALENT AND INCIDENT FRACTURES IN OLDER ADULTS?**

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Background: Musculoskeletal pain is common particularly in the elderly and typically occurs in multiple sites. Pain has been linked to falls risk; however, whether increased risk of falls related to pain can subsequently increase fracture risks remains unclear.
Objectives: To describe the associations of localised pain severity and generalised pain (number of painful sites) with incident fractures, and to explore whether their associations are independent of falls risk, bone mineral density (BMD) and potential confounders.
Methods: Data from a longitudinal population-based study of older adults (mean age 63 years, 51% female) were utilised. A mean follow-up was performed at 2.6, 5.1 and 10.7 years later, respectively. Pain severity in the knee was measured by the Western Ontario and McMaster Universities Osteoarthritis Index pain questionnaire. Presence/absence of pain at the neck, back, hands, shoulders, hips, knees and feet was assessed by questionnaire at baseline. Fractures were self-reported at each time-point. BMD was measured by Dual-energy X-ray absorptiometry (DXA). Falls risk was calculated based on the short form Physiological Profile Assessment.
Results: A total of 455 fractures at baseline and 154 new fractures were reported during follow-up. In multivariable analyses, both pain severity and number of painful sites were associated with prevalent fractures at any site. Pain severity was associated with prevalent vertebral fractures, while number of painful sites was associated with prevalent fractures at non-vertebral and hip sites. Furthermore, pain severity was associated with an increased risk of incident fractures at any site [relative risk (RR) 1.04, 95%CI 1.02-1.06], major (including the femur, radius, ulnar, vertebral, rib and humerus) (RR 1.10, 95%CI 1.05-1.15) and vertebral (RR 1.04, 95%CI 1.01-1.08). Similarly, number of painful sites was also associated with increased risk of incident fractures at any site [RR 1.69, 95% CI 1.13-2.53], major (RR 2.17, 95%CI 1.12-4.22) and vertebral (RR 6.44, 95%CI 1.64-25.33). There was a dose-response relationship between number of painful sites and risk of incident fractures. These associations remained significant after further adjustment for falls risk and BMD. No significant associations were found for fractures occurring at non-vertebral and hip sites.
Conclusion: Both pain severity and generalised pain are associated with increased risk of prevalent and incident fractures, which is independent of falls risk, BMD and potential confounders, suggesting that pain may be an independent marker of fracture risk. Improved pain management may have the potential to prevent fractures in older adults.
Disclosure of Interests: : None declared
DOI: 10.1136/annrheumdis-2019-eular.4040

Fibromyalgia

THU0468 **THE INTERACTIONS OF PHYSICAL ACTIVITY LEVELS WITH THE SODIUM CHANNEL PROTEIN TYPE 9 SUBUNIT ALPHA AND METHYLENE TETRAHYDROFOLATE REDUCTASE GENES ARE ASSOCIATED WITH FATIGUE IN WOMEN WITH FIBROMYALGIA**

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Background: People with fibromyalgia identify fatigue as one of the main symptoms of the disease [1]. It is hypothesised that the pathogenesis of fibromyalgia involves a genetic susceptibility that is modulated by environmental factors [2]

Objectives: To examine the possible role of genetic susceptibility for fatigue in southern Spanish women with fibromyalgia, by looking at the possible associations of fatigue and single nucleotide polymorphisms in 34 fibromyalgia candidate-genes, at the interactions between genes, and at the associations between gene-physical activity.
Methods: In this cross-sectional study participated 276 women with fibromyalgia. We extracted DNA from saliva in order to analyse gene-polymorphisms related to fibromyalgia susceptibility, symptoms, or potential mechanisms. Accelerometers registered the participants' physical activity and sedentary time. Five dimensions of fatigue were assessed with the Multidimensional Fatigue Inventory. Age, body fat (%), and analgesics and antidepressants consumption were considered as confounders in all analyses. Based on the Bonferroni's and False Discovery Rate (FDR) values, the statistical significance was interpreted.
Results: AT carriers of the rs4453709 polymorphism (sodium channel protein type 9 subunit alpha, SCN9A, gene) showed the highest scores on fatigue. Carriers of the heterozygous genotype of the rs1801133 (methylene tetrahydrofolate reductase, MTHFR, gene) or rs4597545 (SCN9A gene) polymorphisms who were physically active reported lower fatigue compared to their inactive counterparts. Highly sedentary carriers of the homozygous genotype of the rs7607967 polymorphism (AA/GG genotype; SCN9A gene) presented higher fatigue than those with lower levels of sedentary time.
Conclusion: Physical (in)activity behaviours and the SCN9A and MTHFR genes were jointly related to fatigue. Thereby, the potential benefits of following an active lifestyle might be observed more clearly in women with fibromyalgia genetically predispose to higher levels of fatigue.

REFERENCES:

[1] Bennett RM, *et al. BMC Musculoskelet Disord* 2010;**11**:134. doi:10.1186/1471-2474-11-134
[2] McBeth J, Mulvey MR. *Nat Rev Rheumatol* 2012;**8**:108–16. doi:10.1038/nrrheum.2011.216

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Disclosure of Interests: None declared
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THU0469 CLUES TO RECOGNIZE SECONDARY FIBROMYALGIA IN PATIENTS WITH OSTEOARTHRITIS ACCORDING TO A FIBROMYALGIA ASSESSMENT SCREENING TOOL OF SCALES ON A MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE (MDHAQ/FAST3-F)

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Background: A multidimensional health assessment questionnaire (MDHAQ) includes scales for a self-report painful joint count, symptom checklist, and fatigue visual analog scale (VAS), which may be compiled into a fibromyalgia assessment screening tool (FAST3-F), in addition to physical function, pain VAS, and patient global VAS, compiled into routine assessment of patient index data (RAPID3). FAST3-F agrees >80% with 2011 formal fibromyalgia (FM) criteria in rheumatoid arthritis (RA) patients who have secondary FM.
Objectives: To recognize clues to secondary FM in osteoarthritis (OA) patients seen in routine care, according to FAST3-F, and to analyze MDHAQ demographic and other clinical data in OA patients who did or did not meet MDHAQ/FAST3-F criteria for secondary FM.
Methods: All patients complete an MDHAQ at all visits prior to seeing the rheumatologist at an academic rheumatology site. The 2-page MDHAQ includes RAPID3 to analyze clinical status, and a cumulative 0–3 FAST3-F scale to recognize FM, FAST3-F is scored 0-3, with 1 point each for 0-10 fatigue VAS $\geq$6, 0-54 self-report joint count $\geq$16, and 0-60 symptom checklist $\geq$16. FAST3-F scores of $\geq$2/3 agree >80% with formal 2011 FM revised diagnostic criteria, based on data for area under the curve (AUC) on receiver operator characteristic (ROC) curves. A two-sample t test was used to compare the two groups; p values were considered significant if $\leq$0.05.
Results: Among 173 OA patients, 55 (32%) met FAST3–F criteria of $\geq$2/3 for secondary FM. Patients who met criteria had lower formal educational level (p=0.01-Table), but did not differ significantly from those who did not meet criteria according to age, sex, or body mass index (BMI) (Table). MDHAQ scores for physical function, pain, patient global assessment, RAPID3, poor sleep quality, anxiety, and depression were significantly higher in the FAST3-F positive than negative patients (p<0.001-Table).

Abstract THU0469 – Table 1. Mean values for demographics and clinical variables at baseline of 173 patients with OA

Mean (standard deviation=SD) or% of variable:	All patients	Fibromyalgia according to FAST3-F		P
		Yes	No	
N (%)	173	42 (24%)	131 (76%)	
Demographics				
Age (years), mean (SD)	66.1 (10.7)	64.5 (11.7)	66.6 (10.5)	0.27
Female,%	84%	88%	82%	0.38
BMI, mean (SD)	32.9 (7.8)	33.8 (6.8)	32.7 (8.0)	0.58
Educational level (years), mean (SD)	13.7 (3.8)	12.0 (3.9)	14.2 (3.6)	0.01
Clinical Variables				
Physical function (0-10), mean (SD)	3.1 (1.9)	4.6 (1.8)	2.6 (1.6)	<0.001
Pain (0-10), mean (SD)	6.9 (2.3)	8.2 (1.5)	6.5 (2.4)	<0.001
Patient global assessment (0-10), mean (SD)	5.9 (2.7)	7.8 (1.9)	5.3 (2.6)	<0.001
RAPID3 (0-30), mean (SD)	15.8 (6.0)	20.4 (4.6)	14.4 (5.7)	<0.001
Sleep quality (0-3.3), mean (SD)	1.4 (1.0)	1.9 (0.9)	1.2 (0.9)	<0.001
Anxiety (0-3.3), mean (SD)	0.7 (0.8)	1.2 (0.8)	0.5 (0.8)	0.001
Depression/feeling blue (0-3.3), mean (SD)	0.6 (0.8)	1.2 (0.8)	0.5 (0.7)	0.001
Clinical diagnosis of depression,%	13%	32%	7%	0.01

Abbreviations: FAST3-F= fibromyalgia assessment screening tool, BMI=body mass index
Conclusion: MDHAQ/FAST3-F provides clues to identify OA patients with secondary FM in routine care. Nonetheless a definitive diagnosis requires a physician. The findings may be useful to recognize a basis for poor responses in clinical care, clinical trials, and other clinical research, and enhance understanding of pain mechanisms in OA versus FM versus OA with FM.
Disclosure of Interests: : None declared
DOI: 10.1136/annrheumdis-2019-eular.5858

THU0470 ASSOCIATION OF SEDENTARY TIME AND PHYSICAL ACTIVITY WITH PHYSICAL FITNESS IN WOMEN WITH FIBROMIALGIA: AN ISOTEMPORAL SUBSTITUTION APPROACH

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Background: Behaviours of people with fibromyalgia may impact their levels of physical fitness, which is a marker of physical and psychological health[1,2,3]. However, scarce research has studied the association of sedentary time (ST) and physical activity (PA) with physical fitness. Interestingly, increasing time in one behaviour requires decreasing time in another. Thus, it is also of interest to understand what is the theoretical impact of replacing sedentary time (ST, e.g., sitting) by light or moderate PA (LPA and MPA, respectively) as well as replacing LPA by MPA on physical fitness in fibromyalgia.
Objectives: To assess the association of replacing ST for different physical activity levels (i.e., ST by LPA or MPA) as well as of LPA by MPA with physical fitness in women with fibromyalgia.
Methods: A total of 407 women with fibromyalgia (51.87 ± 8.01 years old) participated in this cross-sectional study. ST, LPA and MPA were objectively measured with triaxial accelerometer for 7 consecutive days. Vigorous physical activity was not analysed as this is a very uncommon behaviour in the population. Physical fitness was assessed through the Senior Fitness Test Battery plus the handgrip strength test. The associations between the replacement of 30 min/day of ST with an equivalent time of LPA or MPA were tested by isotemporal substitution analyses. Body mass index and age were included as covariates.

Results: Replacing 30 minutes of ST with LPA was associated with better strength in upper limb (*B*=0.19), handgrip strength (*B*=0.02) and aerobic fitness (*B*=2.29); all p<0.03 Replacing 30 minutes of ST with MPA was related to better strength and flexibility in lower and upper limb (*B* ranging from 0.43 to 1.97; all p<0.02). Finally, replacing 30 minutes of LPA with MPA was associated with better strength and flexibility in lower and upper limb, aerobic fitness and balance (*B* ranging from 0.15 to 8.54; all p<0.04).
Conclusion: Replacing short time periods (30 min) of ST by PA (especially of moderate intensity) was related to better physical fitness. Moreover, to replace 30 min of LPA by MPA was related to better physical fitness. Our findings support the implementation of experimental research to better understand the extent to which replacing sedentary time (by LPA or MPA) or replacing LPA (by MPA) might enhance increase different components of physical fitness in fibromyalgia. Such findings would have direct clinical implications.

REFERENCES:

[1] Estévez-López, et al. Disabil Rehabil. 2018 Feb;40(3):329-337. DOI: 10.1080/09638288.2016
[2] Gavilán-Carrera B., et al. Arthritis Care Res. 2018 Jul. DOI: 10.1002/acr.23717
[3] Estévez-López, et al. Rheumatology (Oxford). 2017 Nov 1;56(11):2015-2024. DOI: 10.1093/rheumatology/kex302

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Disclosure of Interests: None declared
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THU0471 THE EFFECT OF VIRTUAL REALITY EXERCISES ON PAIN, FUNCTIONALITY, CARDIOPULMONARY CAPACITY AND QUALITY OF LIFE IN FIBROMYALGIA SYNDROME: A RANDOMIZED, SINGLE-BLIND, CONTROLLED STUDY

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Background: Fibromyalgia Syndrome (FMS) is a clinical condition with many symptoms such as chronic generalized pain, fatigue, sleep disorder, cognitive dysfunction and depressive mood. Management of FMS is difficult and the most important component is regular exercise.[1] In this syndrome, patients generally have compliance and motivation problems in maintenance of exercises. In recent years, exercises, with fun and game components, have been prescribed to increase patient compliance.[2] Motion-controlled video games targeting virtual reality are examples of these exercises.[3]
Objectives: To investigate the effect of motion controlled video games on pain, functionality, cardiopulmonary capacity and quality of life in fibromyalgic women.
Methods: Forty women (> 18 years) who have FMS were included in study. Patients were randomized into study and control groups. Control group performed aerobic exercise (cycling, 3 days/week, 20 minutes/day) for 4 weeks. Study group performed virtual reality exercise (Volleyball, Microsoft Xbox Kinect®, 3 days/week, 15 minutes/day) together with cycling exercise. After the four week supervised exercise program, both groups received the same home exercise program for four weeks. All patients were evaluated at baseline, 4th and 8th weeks. Primary outcome measure was Fibromyalgia Impact Questionnaire. Visual Analog Scale (VAS), Hospital Anxiety and Depression Scale, Fatigue Severity Scale (FSS), Symptom Severity Scale, EuroQol-Quality of Life/Visual Analogue Scale (EQ5D-QoL/VAS) and 6 Minute Walk Test (6MWT) were used as secondary outcome measures. Positive and Negative Affect Schedule (PANAS) was used for patient satisfaction. T-test was used to compare demographic data between two groups. Repeated measures ANOVA was used in evaluation of intra-group efficiency of treatment. Treatment group and time interaction was evaluated by two-way analysis of variance. We calculated 20 patients per group, in order to find 14% minimal clinical difference in Fibromyalgia Impact Questionnaire with 80% power and 0.05 error rate (Tip 1 error).[4]
Results: All patients completed supervised exercise program (4 weeks). 34 patients (17 study group, 17 control group) were evaluated at the 8th week. Age, body mass index, education status, comorbidities and drug use were similar in both groups (p> 0.05). After four weeks, all outcome measures improved significantly in both groups (p<0.05). However, there was no statistically significant difference in all outcome measures between 4th and 8th weeks. Group and time interactions for 6MWT (F (1.21, 46.33) = 4.04, p = 0.043), FSS (F (1.61, 61.24) = 4.21, p = 0.026), EQ5D-QoL Scale (F (2, 76) = 4.55, p = 0.014) and EQ5D-VAS Scale (F (1.4, 53.55) = 3.59, p = 0.049) were significant only for the study group. In addition, PANAS score was significantly higher in study group (p <0.001).
Conclusion: Virtual reality exercises along with aerobic exercise increase cardiopulmonary capacity and quality of life in FMS. In addition, they increase patient satisfaction and may improve patient compliance to exercise.

REFERENCES:

[1] Bidonde J et al. Aerobic exercise training for adults with fibromyalgia. The Cochrane Library, 2017.
[2] Botella C et al. Virtual reality in the treatment of pain. JCR 2008;1:93.
[3] Garcia-Palacios A et al. Integrating Virtual Reality With Activity Management for the Treatment of Fibromyalgia. The Clinical Journal of Pain, 2015, 31.6: 564-572.
[4] Bennett RM et al. Minimal clinically important difference in the fibromyalgia impact questionnaire. The Journal of Rheumatology, 2009, jrheum. 081090.

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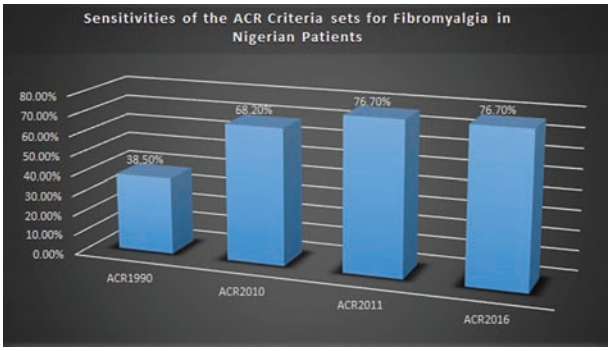
THU0472 FIBROMYALGIA SYNDROME IN WEST AFRICA: ACR 1990 IS NOT SENSITIVE FOR THE UNDER-DIAGNOSED AND WIDELY MISUNDERSTOOD DISORDER

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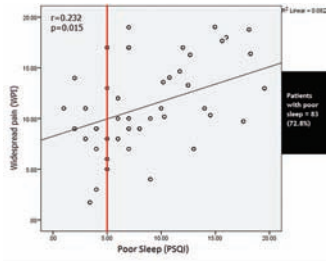
Background: Like most poorly understood rheumatic conditions, Fibromyalgia is thought to be rare in West Africa. Many clinicians rely on the various ACR classification criteria to make a diagnosis of Fibromyalgia despite the unknown performance of these criteria among patients of sub-Saharan African origin.
Objectives: To describe the characteristics of fibromyalgia in Nigerian patients and determine the sensitivities of four ACR criteria sets.
Methods: Consecutive patients diagnosed with fibromyalgia for the first time by a rheumatologist were evaluated using ACR 1990, ACR 2010, 2011 modification of ACR 2010 (ACR 2011) and ACR 2016 classification criteria for fibromyalgia. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI), fatigue with the Fatigue Severity Scale (FSS) and severity of fibromyalgia with the Revised Fibromyalgia Impact Questionnaire (FIQR). The overall characteristics and the beliefs of these patients regarding their disease were analysed.
Results: Of the one hundred and fourteen (114) patients, ninety six (96) were females; male-to-female ratio is 1:5.3. The median duration of symptoms before diagnosis is 54 months (3 to 273 months) and the mean age is 44.6±15.6 years. Mild, moderate, and severe fibromyalgia were found in 32(28.1%), 53(46.5%) and 29(25.4%) patients respectively. Sensitivities of ACR 1990, ACR 2010, ACR 2011, and ACR 2016 were 38.5%, 68.2%, 76.7% and 76.7%, respectively. Poor sleep was found in 83 (72.8%) patients. Patients in functional classes I, II, and III were 71 (62.3%), 19 (16.7%) and 24 (21.1%), respectively. There was none in class IV. There was positive history of widespread pain in at least one first degree relative of 56 (49.1%) patients. Twenty-one (18.4%) patients had changed or quit their job due to the disease and there was

significant association between job loss and number of tender points as well as disease severity. The Mean FFS score is 4.48±1.3 and 73 (64.0%) patients believed their problem is a spiritual attack while 43 (37.7%) had done one form of ritual or the other in search of cure.

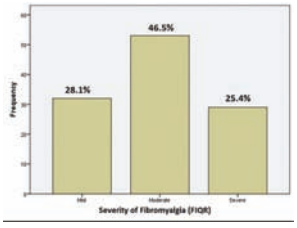
Conclusion: Fibromyalgia syndrome exists in West Africa. It is poorly understood among the sufferers and ACR 1990 is not sensitive as a diagnostic tool for the condition.



Abstract THU0472 – Figure 1



Abstract THU0472 – Figure 2



Abstract THU0473 – Figure 3

REFERENCES:

[1] Bidari A, Ghavidel Parsa B, Ghalehbaghi B. Challenges in fibromyalgia diagnosis: from meaning of symptoms to fibromyalgia labeling. The Korean journal of pain. 2018 Jul;31(3):147-54.

	Quit/Changed job	Not quit/changed job	P
Fibromyalgianess (ACR 2011)	17.5 ± 6.1	20.3 ± 6.5	0.120
Fatigue (FSS)	40.9 ± 12.9	42.7 ± 12.9	0.565
Sleep (PSQI)	6.2 ± 3.4	6.5 ± 3.5	0.715
Widespread pain (WPI)	9.8 ± 4.3	10.7 ± 4.2	0.405
ACR Tender Points	14.8 ± 4.1	9.5 ± 4.7	0.001
Severity (FIQR)	57.1 ± 17.0	49.5 ± 14.4	0.038
Duration Of Symptoms	24 (12 - 120)	24 (3 - 276)	0.662

Disclosure of Interests: None declared
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THU0473 MINDFULNESS IN FIBROMYALGIA: MEAN LEVELS AND CORRELATION WITH DISEASE BURDEN

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Background: Limited evidence suggests that mindfulness-based interventions can have a role in the management of fibromyalgia (FMS) [1], with positive effects on quality of life, pain perception [2] and sleep problems [3]. However, there is little data on the levels of mindfulness in FMS and its relationship with the impact of disease.

Objectives: To evaluate the levels of mindfulness and its correlation with disease burden in FMS.

Methods: Mindfulness was assessed in 112 FMS patients (mean age 45.34±11.36 yrs, 86.5% females) and in 128 (43.60±14.35 yrs, 75% females) healthy control subjects by the Mindful Attention Awareness Scale (MAAS) questionnaire [4]. The MAAS, a 15-item scale developed to assess individual differences in the frequency of mindful states over time, is the most popular scale measuring mindfulness. Each item can be scored on a Likert scale from 1 to 6, lower scores indicating a greater tendency towards mindfulness. FMS patients were further evaluated by Widespread Pain Index (WPI) and Symptom Severity Scale Score as per 2016 criteria, by the revised FIQ score, and by the Facit-Fatigue scale. Data analysis, including ANOVA and Pearson correlations, was performed with the SPSS software.

Results: In the whole population, mean MAAS score was 4.17±0.72, a value comparable to literature data in different populations, and was correlated to age (r=0.175, p= 0.008) but not significantly different in males vs females (4.28±0.67 vs 4.16± 0.72). FMS patients and control subjects showed similar values (4.12±0.80 and 4.22±0.63, p=0.291). In FMS patients, the MAAS score showed a significant direct correlation with FACIT-fatigue scores, and a significant inverse correlation with overall impact of disease, as assessed by the burden of somatic symptoms and FIQR score. MAAS score showed no significant correlations with variables directly related to pain domain (WPI, tender points), nor with disease duration (Table 1).

Conclusion: Mindfulness levels, as assessed by MAAS questionnaire, are not significantly different in FMS patients as compared to unselected healthy control subjects. However, levels of mindfulness are higher in patients reporting a higher disease burden, but lower in patients reporting lower levels of fatigue, and are not significantly correlated to pain.

Mindfulness in FMS shows complex interactions with the different domains of the disease, and needs to be further investigated, in order to clarify its relationship with disease features, and eventually to establish guidelines for mindfulness-based interventions.

REFERENCES:

[1] Lauche R, et al. A systematic review and meta-analysis of mindfulness-based stress reduction for the fibromyalgia syndrome. J Psychosom Res. 2013;75:500-10.
[2] Van Gordon W, et al. Meditation awareness training for the treatment of fibromyalgia syndrome: A randomized controlled trial. Br J Health Psychol. 2017 Feb;22:186-206.
[3] Amutio A, et al. Effects of Mindfulness Training on Sleep Problems in Patients With Fibromyalgia. Front Psychol. 2018 Aug 3;9:1365. doi: 10.3389/fpsyg.2018.01365. eCollection 2018.
[4] Brown KW1, Ryan RM. The benefits of being present: mindfulness and its role in psychological well-being. J Pers Soc Psychol. 2003 Apr;84:822-48.

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Abstract THU0473 – Table 1. Correlation between MAAS score and selected variables in FMS patients

	Symptom Severity Scale	N of Somatic Symptoms	WPI Score	Tender Points (N)	Disease Duration	FIQR Score	FIQR Function	FIQR Overall Impact	FIQR Symptoms	FACIT-fatigue score
r	-.384	-.406	.047	-.002	.050	-.255	-.191	-.002	-.320	.214
p	.000	.000	.625	.986	.622	.019	.068	.986	.001	.028

THU0474 PREVALENCE OF TIREOIDIAN DISORDERS IN A POPULATION WITH FIBROMYALGIA

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Background: Fibromyalgia (FM) is a clinical syndrome characterized by diffuse pain associated with other symptoms such as fatigue, sleep disturbance and mood. It presents a series of differential diagnoses such as thyroid disorders, hypoparathyroidism, systemic inflammatory diseases and myopathies. Hypothyroidism is a disease with a prevalence of 4-6% of the population, having many symptoms in common with FM, such as fatigue, mood changes, constipation, and diffuse pain in some cases.
Objectives: The purpose is to evaluate the association between FM and thyroid disorders.
Methods: A retrospective monocentric case-control study in a tertiary hospital, with patients and controls having regular follow-up. The cases were composed of women over 40 years old, diagnosed with FM by the criteria ACR 1990 and ACR 2010, without autoimmune disease or other confounding diseases for pain. The control consisted of women over 40 years old, without autoimmune diseases. Laboratory tests included TSH and free T4 in all patients. Evaluation by ANA, anti-TPO and anti-thyroglobulin antibodies, only when appropriate. The sample was classified into euthyroid, clinical and subclinical hyperthyroid, clinical and subclinical hypothyroid. Statistical analysis included Fischer's T-tests and others where appropriate. The p value was significant when ≤ 0.05.
Results: The sample consisted of 142 patients (median age of 58 years) and controls with 136 patients (median age of 67 years). Patients with FM had a greater number of thyroid disorders (31.7%) than controls (14.7%) (p = 0,001). FM patients had a TSH higher than the controls (mean 9.06 *vs* 2.96; p = 0,0026), with a lower free T4 (mean 1.06 *vs* 1.31; p = 0,0001). ANA, anti-TPO and anti-thyroglobulin antibodies analysis showed no differences between both groups (p = 1; p = 0,08, p = 1; respectively), when performed. Because of the small difference in median age between the two groups, a sub analysis was performed separating patients between the ages of 40 to 60 years and over 60 years. The same results previously seen were found.
Conclusion: Patients with FM had a greater association with clinical hypothyroidism. However, we did not find any association with autoantibodies in our casuistic.

REFERENCES:

[1] Claw, DJ, JAMA, volume 311, página 1547, 2014.
[2] Hollowell JG, J Clin Endocrinol Metab, 87:489, 2002.
[3] Suk, JH, Experimental and Clinical Endocrinology and Diabetes, 120: 401, 2012.
[4] J.Rodríguez-Espinosa, Reumatologia Clinica, 2:70, 2006.
[5] J. Ahmad, Rheumatology International, 35:1415, 2015.

Disclosure of Interests: Marco Antonio G Pontes Filho Speakers bureau: Novartis and Janssen, DIOGO SOUZA DOMICIANO: None declared, Rafael Pontes Andreussi: None declared, Leonardo Rodrigues da Silva: None declared
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THU0475 THE EFFECT OF SUPERVISED DYNAMIC EXERCISE PROGRAM ON SOMATOSENSORY TEMPORAL DISCRIMINATION IN PATIENTS WITH FIBROMYALGIA SYNDROME

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Background: Somatosensory temporal discrimination (STD) is the detection of two separate stimuli applied to the body over a short period of time (1). It is thought that STD provides information about the central processing of sensory stimuli. It has recently been reported that STD is impaired in fibromyalgia syndrome (FMS), which is considered to be the prototype of central sensitization syndromes (2).
Objectives: To evaluate the effect of dynamic exercise program on STD in patients with FMS.
Methods: The study included 48 female FMS patients diagnosed according to the ACR 2010 classification criteria who applied to outpatient clinics of Physical Medicine and Rehabilitation Department. Patients with inflammatory rheumatic disease, peripheral and central neurological disease, history of malignancy and cardiac problems, and those who started a new medical therapy or exercise program related to FMS in the last 3 months were excluded. Before the study, local ethics committee approval was obtained. The study was designed as a prospective, randomized, single blind and controlled study. The patients were divided into two groups. Those included in the supervised exercise group (SEG) were given an exercise program that consisted of submaximal aerobic exercise (treadmill) and low-medium resistant isotonic exercises under the supervision of a physiotherapist, 1-hour per day, 3 days in a week for 4-weeks. Those included in the home exercise group (HEG) were given a home exercise program that consisted of low-to-medium resistance isotonic exercises and aerobic exercises 1-hour per day, 3 days in a week for 4-weeks. All patients were evaluated at baseline and after 4 weeks of treatment. Visual analogue scale (VAS) for pain, hospital anxiety and depression scales (anxiety: HADA, depression: HADD), fibromyalgia effect questionnaire (FIQ), symptom severity scale (SSS) were used for clinical assessment. Additionally somatosensory temporal discrimination threshold (STDT) was measured by a blinded investigator. In order to achieve a difference of 25ms in STDTs between two groups, we calculated 20 FMS patients per group (power: 80%, alpha: 0.05 two sided) (2). However, 24 patients were included in the study because of the 20% chance of discontinuation. For the demographic, basal clinical and neurophysiological comparisons between the two groups, the independent sample-T test was used for the normally distributed data, and the Mann Whitney U test was used for the non-normally distributed data. In order to assess the effect of treatment on outcome measures, 2-way repeated measures of variance analysis (Treatment group x time) was used. Intention to treat analysis was performed.
Results: There were statistically significant changes in the VAS, HADA, HADD, FIQ and SSS scores and STDTs in both groups after treatment programs ($p < 0.001$). In the 2-way repeated measures of variance analysis, the treatment group x time interactions for VAS, HADA, HADD, FIQ and SSS scores were found to be significant in favor of the supervised exercise group ($p < 0.05$). However, no statistically significant interaction (treatment group x time) was found for STDT (p: 0.18).
Conclusion: We demonstrated that STD improves with exercise in patients with fibromyalgia for the first time. However, this change was similar in both groups. Additionally, we showed that dynamic exercise program ameliorates pain, psychological status, function and other symptoms related to fibromyalgia syndrome.

REFERENCES:

[1] Lacruz F, Artieda J, Pastor M A, Obeso J A. The anatomical basis of somaesthetic temporal discrimination in humans. J Neurol Neurosurg Psychiatry. 1991;54:1077-1081
[2] Gunendi Z, Polat M, Vuralli D, Cengiz B. Somatosensory temporal discrimination is impaired in fibromyalgia. J Clin Neurosci. 2019; 60:44-48

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THU0476 NEW PARADIGMS IN FIBROMYALGIA RESEARCH: INFLAMMATORY CELLS-TO-LIPOPROTEINS RATIOS AS PREDICTIVE AND DISCRIMINATOR MARKERS

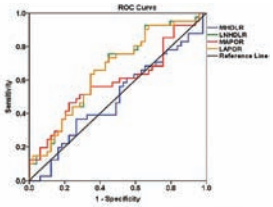
Marwan Alnimer[1], Talar Merza[1], Avin Maroof[2]. [1]*Hawler Medical University, College of Pharmacy, Erbil, Iraq*; [2]*Rizgary Teaching Hospital, Rheumatology, Erbil, Iraq*

Background: Fibromyalgia (FM) is a chronic idiopathic disease characterized by diffuse pain, fatigue, sleep disturbances, stiffness, anxiety and depression. Compared to healthy subjects. FM patients have significant high ratios of mean platelet volume, Neutrophil-to-lymphocyte, and platelet to lymphocyte. Fibromyalgia showed a significant abnormal lipid profile characterized by higher levels of fasting serum triglyceride and cholesterol.
Objectives: This study aimed to derive ratios from the circulating inflammatory cells and serum lipoprotein levels as markers of disease-severity in newly diagnosed fibromyalgia.
Methods: We carried out a cross-sectional study with 90 newly-diagnosed fibromyalgia patients and 25 aged-matched healthy subjects to determine the haematological indices and serum lipoprotein profile. Revised

fibromyalgia impact questionnaire (FIQR), Tender points (TPs), fatigue severity scale, insomnia severity index, and the Hamilton's scale for depression were used to assess the disease severity.

Results: Monocyte- to- high density lipoprotein ratio (MHDR) correlated significantly and inversely with tender points and FIQR scores while lymphocyte- to- high density lipoprotein ratio(LNHDLR) and lymphocyte-to-apolipoprotein-B100 (LAPOR)ratio correlated significantly and directly with FIQR. None of the circulating inflammatory cells-to-lipoprotein ratios correlated with fatigue, insomnia, and depression-related symptoms.

Multi-variable regression analysis revealed a significant mean score of FIQR-symptoms equal to 63.2 with prediction of 11.9% (R=0.346, F=5.903, p=0.004, β-coefficients for MHDLR=-0.257, and for LNHDLR=3.789). The area under the curve and 95% confidence intervals of LNHDL is 0.658 (0.545-0.771) at the cut-off score of the FIQ3-related symptoms at 63.2.



Test Result Variable(s)	AUC	p-value	95% confidence interval	
			Lower bound	Upper bound
MHDL	0.490	0.868	0.369	0.611
LNHDL	0.658	0.010	0.545	0.771
MAPO	0.589	0.148	0.468	0.710
LAPOR	0.658	0.010	0.545	0.770

Figure 1: The area under the curve and 95% confidence intervals of the circulating inflammatory cells-to-lipoproteins ratios taking the cutoff score of symptoms-related disease at 63.2 as a discriminator. AUC: Area under the curve, MHDLR: monocyte-to high density lipoprotein ratio, LNHDLR: lymphocyte-to non-high density lipoprotein ratio.

Abstract THU0476 – Figure 1

Conclusion: Circulating inflammatory cell-to-lipoprotein ratios can serve as prognostic markers in the assessment of disease-severity in fibromyalgia patients.

REFERENCES:

[1] Al-Nimer MSM, Mohammad TAM. Correlation of haematological indices and ratios derived from them with FIQR scores in fibromyalgia. Pak J Med Sci. 2018;34(5):1219-1224.

[2] Aktürk S, Büyükavcı R Evaluation of blood neutrophil-lymphocyte ratio and platelet distribution width as inflammatory markers in patients with fibromyalgia. Clin Rheumatol. 2017;36(8):1885-1889.

[3] Cordero MD, Alcocer-Gómez E, Cano-García FJ, Sánchez-Domínguez B, Fernández-Riejo P, Moreno Fernández AM, Fernández-Rodríguez A, De Miguel M. Clinical symptoms in fibromyalgia are associated to overweight and lipid profile. Rheumatol Int. 2014;34(3):419-422.

[4] Wolfe F, Clauw DJ, Fitzcharles M, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res. 2010;62(5):600-610.

[5] Abu-Dahab S, AbuRuz SM, Mustafa K, Sarhan Y. Validation of the Arabic version of the revised Fibromyalgia Impact Questionnaire (FIQR_A) on Jordanian females with fibromyalgia. Clin Rheumatol. 2014;33(3):391-396.

Abstract THU0476 – Table 1. Correlations between disease-related symptoms with the ratios of circulating inflammatory cells-to-lipoproteins.

Disease-related symptoms scoring	MHDLR	LNHDLR	MAPOR	LAPOR
FIQR-Function	-0.352	0.170	0.016	0.167
	<0.001	0.110	0.879	0.116
FIQR-Global	-0.071	-0.018	-0.016	-0.015
	0.504	0.865	0.884	0.881
FIQR-Symptoms	-0.022	0.290	0.162	0.292
	0.839	0.006	0.126	0.005
FIQR-Overall total	-0.207	0.261	0.111	0.261
	0.050	0.013	0.298	0.013
Tender points	-0.254	0.078	0.018	0.076
	0.016	0.467	0.868	0.477
Fatigue severity scale	-0.102	-0.071	-0.104	-0.067
	0.340	0.506	0.329	0.528
Insomnia severity index	-0.086	0.031	-0.072	0.034
	0.424	0.776	0.500	0.749
The Hamilton's scale for depression	0.103	0.014	0.085	0.012
	0.334	0.896	0.425	0.912

Disclosure of Interests: None declared
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THU0477 A FIBROMYALGIA ASSESSMENT SCREENING TOOL ON A MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE (MDHAQ) WHICH DOES NOT INCLUDE A SELF-REPORT PAINFUL JOINT COUNT (PAINFUL JC), FAST3NJC, RECOGNIZES FIBROMYALGIA SIMILARLY TO OTHER FAST3 INDICES WHICH INCLUDE A PAINFUL JC

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Background: Fibromyalgia (FM) generally is easily recognized, but a diagnosis may be difficult, particularly in patients with secondary FM who have other primary diagnoses. Criteria for FM initially were reported in 2000, and revised in 2011 and 2016, based entirely on a patient self-report questionnaire. However, FM criteria are not collected in most routine clinical care, as it is not feasible to use multiple patient questionnaires in busy clinical settings. MDHAQ/RAPID3 (multi-dimensional health assessment questionnaire/routine assessment of patient index data) has been found informative in all diseases in which it has been studied. Cumulative indices based on MDHAQ scales known as FAST3 (fibromyalgia assessment screening tool3) recognize FM at levels of agreement with revised FM criteria of >80% and correlations of >0.80, p<0.001). Pragmatic recognition of FM in non-rheumatic diseases based on MDHAQ may be possible, as most components of the MDHAQ (as well as the HAQ) appear generic rather than disease-specific. One component of MDHAQ/FAST indices, a self-report painful joint count (painful JC), is rheumatology-specific. Therefore, a FAST3-nJC (no painful JC) index was analyzed vs revised FM criteria as gold standards for possible use in non-rheumatology patients to recognize FM.

Objectives: To analyze FAST3-nJC versus 2011 and 2016 FM criteria, and compared to other FAST3 indices which include a painful JC, to recognize FM.

Methods: All patients with all diagnoses complete an MDHAQ at all visits in routine care at one setting. The self-report questionnaire to recognize the 2011 and 2016 FM Criteria was added over a 6-month period to be completed by consecutive patients. The MDHAQ includes 0-10 scores for physical function, pain and patient global visual analog scales (VAS), compiled into 0-30 RAPID3, as well as a 0–10 fatigue VAS, 0–54 self-report painful joint count, and 0–60 symptom checklist. All MDHAQ scales were analyzed for agreement with FM Criteria according to receiver-operator-characteristic (ROC) curves for area under the curve (AUC). Optimal cut points for each measure were identified, based on specificity and sensitivity, to develop optimal cumulative indices for clues to FM versus the 2011 and 2016 Criteria as gold standards.

Results: Among 502 patients with complete data, primary ICD-10 diagnoses were FM in 49, OA in 74, RA in 78, SLE 88 and other rheumatic diseases in 213. Primary or secondary FM was identified in 131 (26%) who met 2011 FM criteria, and 112 (22%) who met 2016 FM criteria. The 4 MDHAQ scales with the highest AUC vs FM Criteria (0.829-0.889) were symptom checklist, painful JC, fatigue, and pain. Three cumulative FAST3 measures were: FAST3-P with symptom checklist, painful JC and pain VAS; FAST3-F with symptom checklist, painful JC and fatigue VAS; FAST3nJC with symptom checklist, pain and fatigue VAS, but no painful JC. All FAST3 indices agreed with FM Criteria >79% and kappas were >0.52, indicating good agreement (Table). As expected, lowest agreement was seen for FAST3nJC, since the FM criteria include a self-report painful joint count, but differences are quite small.

Abstract THU0477 –Table 1. Percent agreement and kappa of 3 FAST3 (fibromyalgia assessment screening tool) indices vs 2011 and 2016 FM Criteria

FAST Index:	FAST3-P (pain)	FAST3-F (fatigue)	FAST3-nJC (no painful JC)
vs 2011 FM Criteria			
% Agreement	84.3%	86.6%	81.5%
Kappa	0.63 (0.56–0.70)	0.68 (0.60–0.75)	0.58 (0.50–0.66)
vs 2016 FM Criteria			
% Agreement	81.7%	83.8%	79.1%
Kappa	0.56 (0.48–0.53)	0.60 (0.51–0.68)	0.52 (0.44-0.60)

Conclusion: FAST3nJC had slightly lesser agreement with 2011 and 2016 FM criteria than FAST3-P and FAST3-F but would appear

satisfactory as a candidate for clues to recognize FM in patients with non-rheumatic diseases, as a diagnosis of FM ultimately is made by a physician.

Disclosure of Interests: : None declared

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THU0478 IS FIBROMYALGIA ASSOCIATED WITH STRUCTURAL OR FUNCTIONAL ABNORMALITIES IN SKELETAL MUSCLE?

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Background: Fibromyalgia (FM) is a chronic nonarticular pain syndrome of unknown etiology characterized by diffuse muscular pain, fatigue and mood disturbances. Previous studies have shown absence of skeletal muscle degeneration, regeneration or inflammation. Altered muscle fiber size distribution and decreased capillary density were the only abnormalities reported.

From the clinical point of view some FM symptoms (fatigue, pain, myalgias, trigger points, stiffness) suggest skeletal muscle involvement.

Objectives: The objective of this study is to determine if there are structural and functional abnormalities in the skeletal muscle in patients with primary FM assessed by means of a non-invasive, low-cost multimodality approach.

Methods: Female patients > 18 years, with FM diagnosis (ACR 2010 criteria) and healthy controls matched by age. Skeletal muscle morpho-structure and function were assessed by: body mass index (BMI), total fat mass and total muscle mass calculated by direct segmental multi-frequency bioelectrical impedance analysis. Cross-sectional measurements of rectus femoris muscle area and tissue echogenicity were evaluated by ultrasound and pixel analysis. Maximum handgrip strength by digital dynamometry, gait speed (6-meter time walk test), and FM Health Assessment Questionnaire (FHAQ).

Results: A total of 94 FM patients and 140 healthy controls were included, mean age was 51.8 years +/- 10.8 vs 50.2 +/- 11.3, respectively (p = 0.27). FM patients compared with controls had similar BMI (27.9 kg/m^2 +/- 4.9 vs 26.8 +/- 4.5, p = 0.14), higher total body fat mass (27.8 kg +/- 9.2 vs 25.1 +/- 7.6, p = 0.04); rectus femoris muscle area was also higher for FM patients (44.6 cm^2 +/- 11.4 vs 41.7 +/- 13.9, p = 0.05); regarding ultrasound tissue echogenicity, FM patients demonstrated higher mean brightness in rectus femoris (157.2 pixels +/- 19.4 vs 149.9 +/- 22.4, p = 0.01); lesser handgrip strength (22.0 kg +/- 6.6 vs 26.2 +/- 5.4 p = 0.0001); slower gait speed (1.14 m/s +/- 0.2 vs 1.3 +/- 0.2 p = 0.0001); and major impairment in daily activities by FHAQ (47% vs 2.90% p = 0.0001).

Conclusion: This non-invasive multimodal evaluation of the skeletal muscle showed the presence of structural and functional abnormalities in women with FM. These changes can be attributed to sedentary and hypoactive lifestyle with consequent higher total body fat mass, skeletal muscle fat infiltration, and functional impairment of activities of daily living. Alternatively, these abnormalities may also be an expression of a small-fiber polyneuropathy (myoneurovascular dysregulation). Further studies are required to elucidate its underlying pathological process.

REFERENCES:

[1] Lodahl M, Treister R, Oaklander AL. Specific symptoms may discriminate between fibromyalgia patients with vs without objective test evidence of small-fiber polyneuropathy. *Pain Rep* 2018; 3(1): e633.

[2] Martínez-Lavín, M. Fibromyalgia and small fiber neuropathy: the plot thickens. *Clin Rheumatol* 2018;37: 3167.

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THU0479 SAFETY AND EFFICACY OF MEDICAL CANNABIS IN FIBROMYALGIA

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Background: Although chronic pain is a well established indication for medical cannabis therapy, there is scarce evidence to support the role of medical cannabis in the treatment of fibromyalgia.

Objectives: The aim of the study was to investigate the characteristics, safety and effectiveness of medical cannabis therapy for fibromyalgia.

Methods: A prospective study with 6 months follow-up period based on fibromyalgia patients who were willing to answer questionnaire in a specialized medical cannabis clinic between 2015 and 2017.

Results: Among the 367 fibromyalgia patients the mean age was 52.9 ±15.1, of whom 301 (82.0%) were women. 28 patients (7.6%) stopped the treatment prior to the six months follow-up. The six months response rate was 70.8%. Pain intensity (scale 0-10) reduced from a median of 9.0 at baseline to 5.0 (p<0.001), and 194 patients (81.1%) achieved treatment response. In a multivariate analysis age above 60 years (Odds ratio [OR] 0.34, 95% C.I 0.16-0.72), concerns about cannabis treatment (OR 0.36, 95% C.I 0.16-0.80), spasticity (OR 2.26, 95% C.I 1.08-4.72) and previous use of cannabis (OR 2.46 95% C.I 1.06-5.74) were associated with treatment outcome. The most common adverse effects were mild and included dizziness (7.9%), dry mouth (6.7%) and gastrointestinal symptoms (5.4%).

Conclusion: Medical cannabis appears to be safe and effective alternative for the treatment of fibromyalgia symptoms. Standardization of treatment compounds and regimens are required.

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THU0480 IS PROLONGED SEDENTARY TIMEASSOCIATED WITH THE IMPACT OF THE DISEASE IN WOMEN WITH FIBROMYALGIA? THE AL-ÁNDALUS PROJECT

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Background: Spending time seated has previously shown to be associated with worse symptomatology in fibromyalgia[1]. In addition, to accumulate sedentary time (ST) in prolonged, unbroken periods (bouts) has shown to be particularly harmful in the general population[2].

Objectives: To examine the association of prolonged ST with the impact of the disease in women with fibromyalgia.

Methods: Four-hundred-and-seven (51.4±7.6 years old) fibromyalgia women participated in this cross-sectional study. Sedentary time accumulated in bouts of ≥10, ≥20, ≥30 and ≥60 minutes, and moderate-to-vigorous physical activity (MVPA) were measured with triaxial accelerometry (GT3X+). To control for total ST, the percentage of ST spent in different bout categories were calculated (e.g., (time spent in bouts ≥30 min/ total ST) ×100). We assessed different domains of fibromyalgia impact (function, overall, symptoms) and the global impact of fibromyalgia (total score) with the Revised Fibromyalgia Impact Questionnaire (FIQR). Separate linear regression models were built to assess the association of percentage of ST spent in different bout categories (independent variables) with the domains of fibromyalgia impact and the global impact of the disease (dependent variable) while controlling for age, fat percentage, medication for pain and depression, and total accelerometer wear time. Model 2 additionally included time spent in MVPA.

Results: Greater percentage of ST spent in bouts ≥10 min (β=0.171, p<0.001), ≥20 min (β=0.163, p=0.001), ≥30 min (β=0.169, p<0.001), and ≥60 min (β=0.161, p=0.001) was associated with greater global impact of the disease. In model 2, greater percentage of ST spent in bouts ≥10 min (β=0.145, p=0.003), ≥20 min (β=0.138, p<0.004), ≥30 min (β=0.146,

p<0.002), and ≥60 min (β=0.144, p<0.002) was associated with greater global impact of the disease. Similar results were observed for the association of percentage of sedentary time spent in different bout categories with the domains of fibromyalgia impact (function, overall, and symptoms). **Conclusion:** The results seem to indicate that ST accumulated in bouts is negatively associated with the impact of the disease in women with fibromyalgia. Overall, these associations were independent of time spent in MVPA. It might be advisable to promote reducing prolonged ST in this population.

REFERENCES:
[1] Segura-Jiménez V, Borges-Cosic M, Soriano-Maldonado A, et al. Scand. J. Med. Sci. Sports. 2017;27:83–92.
[2] Benatti FB, Ried-Larsen M. Med. Sci. Sports Exerc. 2015;47:2053–61.

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THU0481 SLEEP DISTURBANCES IN FIBROMYALGIA – AN AUSTRALIAN TERTIARY HOSPITAL EXPERIENCE

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Background: Fibromyalgia (FM) is a central pain disorder with an estimated population prevalence of 2-7% and six times as common in women than men.[1]Obstructive sleep apnoea (OSA) is a structural sleep disorder, with an estimated incidence of 14% of males and 5% females. Incidence of OSA in FM has been variably reported but estimated at 25-81%.[2] Despite its frequency, the underlying nature of sleep disturbances haven't been consistently replicated. A 2017 meta-analysis found significant differences in sleep efficiency (SE), a measure of total time spent in REM (Rapid Eye movement) sleep, number of arousals and sleep quality.[3] Prados et al in 2013 showed women with FM have less severe sleep disturbance than males, suggesting a gender difference.[4]
Objectives: To identify the incidence of FM in a cohort referred to the respiratory department for diagnostic polysomnography (dPSG) at the Gold Coast University Hospital (GCUH), a tertiary referral centre in Australia. We aim to identify epidemiological, gender differences and sleep abnormalities in patients with FM and OSA.
Methods: dPSG reports of 998 patients with 1053 studies at the GCUH from 2015 - 18 was audited. We included FM diagnosed by a rheumatologist from the general Rheumatology clinics of the same facility. Two control groups were formed, one with a random number generator. The second from manual matching of major OSA risk factors such as age, gender and Body mass index (BMI), with a two to one ratio for statistical power. All were subsequently subdivided into gender. Statistical analysis was performed with calculation of mean, standard deviation and T tests for significance as calculated by the computer software Stata.
Results: **Abstract THU0481 – Table 1**. Demographics Data

	Age (Yrs)	Gender	BMI (kg/m²)
Control (Random)	51.38 (15.92)	15F/22M	34.51 (10.43)
Control (Matched)	5625 (9.87)	64F/10M	33.66 (8.71)
FM group	55.83 (10.1)	32F/5M	32.93 (9.14)

Abstract THU0481 – Table 2. Sleep Study Data

A. One to One Random Group

Mean (Standard Deviation)	FM –	FM +	P value
Epworth Sleep Scale (ESS)	8.57 (5.58)	9.86 (5.27)	0.8898
Total Sleep time (min)	325.43 (66.44)	330.59 (83.67)	0.6648
Sleep Efficiency (%)	78.97 (10.21)	77.58 (11.89)	0.376
Sleep Onset Latency (min)	14.96 (15.79)	24.05 (20.86)	0.9723
Stage NREM (%)	85.81 (6.12)	83.71 (9.47)	0.2629
Stage REM (%)	13.98 (6.09)	16.47 (9.60)	0.8893
Arousals per hour	29.69 (17.71)	28.03 (21.78)	0.3389
Oxygen Desaturation Index (ODI)	**23.59 (25.25)**	**12.26 (18.99)**	**0.0176**
Periodic Limb Movement Index (PLM)	5.79 (19.67)	6.73 (12.15)	0.5348
Total Apnoea Hypopnoea Index (AHI)	**29.22 (25.65)**	**19.79 (20.06)**	**0.0423**

B. Two to One Matched Group

FM –	FM +	P Value
10.07 (6.43)	9.86 (5.27)	0.4867
326.61 (85.93)	330.59 (83.67)	0.662
75.31 (17.24)	77.58 (11.89)	0.8015
26.88 (38.80)	24.05 (20.86)	0.315
80.39 (21.90)	83.74 (9.47)	0.3874
13.83 (8.00)	16.47 (9.60)	0.9117
30.19 (28.94)	28.03 (21.78)	0.3407
17.45 (24.3)	12.26 (18.99)	0.1522
7.40 (16.64)	6.73 (12.15)	0.352
24.32 (25.53)	19.79 (20.06)	0.1984

C. Matched Male Group

Mean (Standard Deviation)	FM -	FM +	P value
Epworth Sleep Scale (ESS)	9.2 (6.03)	12 (4.74)	0.8083
Total Sleep time (min)	**359.45 (32.46)**	**255.5 (54.72)**	**0.0002**
Sleep Efficiency (%)	**78.83 (8.20)**	**65.82 (14.02)**	**0.0194**
Sleep Onset Latency (min)	11.55 (7.06)	20.5 (11.36)	0.9598
Stage NREM (%)	85.05 (3.83)	89.14 (8.14)	0.2006
Stage REM (%)	14.96 (3.84)	10.8 (8.144)	0.0965
Arousals per hour	24.15 (9.39)	31.2 (10.19)	0.8975
Oxygen Desaturation Index (ODI)	16.28 (22.18)	19.72 (22.77)	0.6084
Periodic Limb Movement Index (PLM)	4.98 (9.66)	5.72 (8.62)	0.5563
Total Apnoea Hypopnoea Index (AHI)	24.4 (25.27)	37.7 (23.86)	0.8262

D. Random Male Group

FM -	FM +	P value
7.63 (1.07)	12 (2.12)	0.955
606.63 (13.98)	255.5 (24.47)	0.0596
77.14 (2.21)	**65.82 (6.26)**	**0.0247**
12.81 (2.94)	20.5 (5.07)	0.8702
86.63 (5.67)	89.14 (8.14)	0.4161
13.25 (1.2)	10.8 (3.64)	0.2119
34.66 (4.42)	31.2 (4.55)	0.3611
30.44 (6.38)	19.72 (10.18)	0.2305
9.15 (5.35)	5.72 (3.85)	0.3843
37.6 (6.25)	37.7 (10.66)	0.5025

N.B. Statistically significant data is highlighted in bold

Abstract THU0481 – Table 3. Female Study Data

E. Matched Female Group

Mean (Standard Deviation)	FM -	FM +	P Value
Epworth Sleep Scale (ESS)	10.34 (6.54)	9.53 (5.35)	0.4061
Total Sleep time (min)	319.9 (90.63)	342.33 (81.81)	0.9015
Sleep Efficiency (%)	74.83 (18.22)	79.42 (10.63)	0.9283
Sleep Onset Latency (min)	130.39 (93.75)	29.26 (41.14)	0.244
Stage NREM (%)	17.12 (9.49)	13.72 (8.49)	0.0841
Stage REM (%)	13.72 (8.49)	17.35 (9.62)	0.958
Arousals per hour	31.00 (30.85)	27.54 (23.15)	0.2737
Oxygen Desaturation Index (ODI)	17.36 (24.73)	11.1 (18.48)	0.1151
Periodic Limb Movement Index (PLM)	7.69 (17.49)	6.89 (12.71)	0.3335
Total Apnoea Hypopnoea Index (AHI)	23.91 (25.74)	16.99 (18.28)	0.094

F. Random Female Group

FM -	FM +	P value
9.93 (1.6)	9.87 (0.96)	0.48
353 (15.33)	345.15 (14.78)	0.37
81.64 (2.48)	80.05 (1.96)	0.3182
18.1 (4.74)	23.79 (3.91)	0.8042
84.6 (6.73)	82.86 (9.49)	0.5288
15.06 (1.74)	17.12 (1.67)	0.7735
22.39 (2.05)	27.22 (4.11)	0.7798
13.54 (2.75)	11.32 (3.25)	0.3338
0.87 (0.6)	6.18 (2.16)	0.9479
16.91 (2.9)	17.07 (3.22)	0.5127

Conclusion: Female predominance and 3% population incidence of FM was congruent with literature. We note the mean age was nearing expected upper limits for FM. Increased age as a risk factor for OSA may have led this selection bias. Unexpectedly, overall severity of OSA as per AHI and number of desaturating events as per ODI3 was less in FM. We hypothesise that this is due to a higher proportion of females in the FM group compared to males, confirmation would require a larger study cohort, a limitation of this study. It was beyond the scope of this study to explore concomitant medication use and comorbidities and its effect on sleep. Another significant finding was in males, where sleep efficiency (SE) was lower in both matched and random groups. Furthermore, when matched for age, gender and BMI, males FM have reduced total sleep time. Suggesting that males with FM may have additional impediments to good sleep efficiency which may not be readily recognised during clinical evaluation. Similarly to Prados et al, we found females with FM (fig. 3) had a trend for better sleep quality and less sleep disturbance. However, no domain reached statistical significance, which again reflects low study power. This study emphasises the contribution of OSA as a comorbidity for patients with FM and its effect on sleep quality. Importantly, also the differences in gender.

REFERENCES:
[1] Neumann L, Buskila D. Epidemiology of fibromyalgia. Curr Pain Headache Rep. 2003 Oct;7(5):362-8.
[2] Ferré A. Chronic fatigue syndrome and sleep disorders: clinical associations and diagnostic difficulties. Neurologia. 2016 Feb 11. pii: S0213-4853(16)00010-4.
[3] Wu YL, Chang LY, Lee HC, Fang SC, Tsai PS. Sleep disturbances in fibromyalgia: A meta-analysis of case-control studies. J Psychosom Res. 2017 May;96:89-97.
[4] Prados G, Miró E, Martínez MP, Sánchez AI, López S, Sáez G. Fibromyalgia: gender differences and sleep-disordered breathing. Clin Exp Rheumatol. 2013 Nov-Dec;31(6 Suppl 79):S102-10.

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Back pain, mechanical musculoskeletal problems, local soft tissue disorders

THU0482 HUMAN LUMBAR SPINE FACET JOINT OSTEOARTHRITIS DISPLAYS PREDOMINANT NGF EXPRESSION AND SIGNALING IN CAPSULAR SYNOVIUM AND SUBCHONDRAL BONE MARROW TISSUES INDEPENDENT OF OSTEOARTHRITIS GRADE

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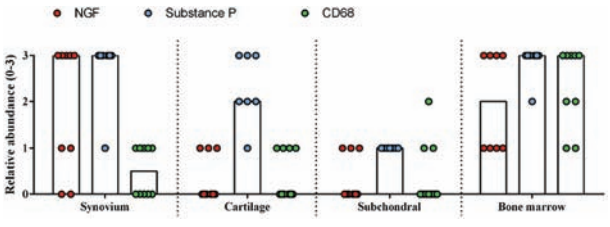
Background: Increased nerve growth factor (NGF) levels are associated with chronic pain conditions, including low back pain and osteoarthritis (OA). NGF signalling through its receptor TrkA regulates pro-inflammatory neurotransmitters such as substance P (SP). Inhibition of NGF has shown therapeutic efficacy in knee OA [1] and chronic back pain [2], but trials have revealed rare cases of rapidly progressive OA of peripheral joints.

Objectives: To describe the tissue distribution of NGF, TrkA, SP and macrophages in facet joint osteoarthritis (FJOA) of the lumbar spine and their association with FJOA grade.

Methods: FJOA specimens were obtained by facetectomy from patients undergoing intervertebral fusion *(n*=10, average age 69 years, 5 males). FJOA severity and presence of synovial hypertrophy was graded using preoperative magnetic resonance imaging (MRI). Relative abundance of NGF, CD68 (macrophages), TrkA and SP in capsular synovium (SY), cartilage (CL), subchondral bone (SB) and subchondral bone marrow (BM) was evaluated semi-quantitatively on a scale ranging from 0-3 using immunohistochemistry. Association between imaging parameters and tissue expression was determined using Pearson correlation analysis.

Results: Synovial hypertrophy as determined by MRI was present in six cases (60%) and median Weishaupt grade of FJOA was 2 (1.5-3) corresponding with moderate to severe OA. NGF was abundantly expressed in SY (3 [0.5-3]) and to a lesser extent in BM tissues (2 [1-3]), whereas TrkA expression was detected in BM exclusively. NGF abundance in SY and BM showed a strong correlation (*r*=0.94), but did not associate with synovial hypertrophy or FJOA severity. CD68+ macrophages were highly abundant in BM (3 [1.5-3]) and sparse in SY tissues (0.5 [0-1]). The relative abundance of macrophages and NGF was strongly correlated in SY tissue only (*r* = 0.78). SP as a downstream mediator of NGF signalling was also abundantly expressed in SY, CL and BM tissues. Tissue distributions of CD68, NGF and SP are summarized in the figure.

Conclusion: NGF expression and signalling is evident in lumbar spine FJOA specimens, but not strongly associated with synovial hypertrophy or disease severity. These results are in agreement with recent studies of human knee OA, which have shown osteochondral NGF expression as a hallmark of symptomatic OA independently of chondropathy or synovitis [3].



Abstract THU0482 – Figure 1.

REFERENCES:

[1] Lane NE, Schnitzer TJ, Birbara CA, Mokhtarani M, Shelton DL, Smith MD, Brown MT.(2010) Tanezumab for the treatment of pain from osteoarthritis of the knee. N Engl J Med. 363:1521.

[2] Katz N, Borenstein DG, Birbara CA, Bramson C, Nemeth MA, Smith MD, Brown MT. (2011) Efficacy and safety of tanezumab in the treatment of chronic low back pain. Pain. 152(10):2248

[3] Aso K, Shahtaheri SM, Hill R, Wilson D, McWilliams DF, Walsh DA. (2019) Associations of symptomatic knee OA with histopathologic features in subchondral bone. Arthritis Rheumatol. ePub

Disclosure of Interests: Matthias Seidel Grant/research support from: Pfizer, Actelion, Consultant for: Pfizer, Lilly, Nathalie Busso: None declared, Veronique Chobaz: None declared, Cordula Netzer: None declared, Thomas Huegle Grant/research support from: AbbVie, Lilly, Novartis and Pfizer, Speakers bureau: AbbVie, Lilly, Novartis and Pfizer, Jeroen Geurts: None declared

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THU0483 DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF A NATIONAL COHORT OF 280 PATIENTS WITH JOINT HYPERMOBILITY SYNDROME, THEIR SOCIOECONOMIC BURDEN AND THE PERFORMANCE OF THE 2017 INTERNATIONAL CLASSIFICATION CRITERIA OF THE EHLERS DANLOS SYNDROMES

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Background: Joint hypermobility syndromes (JHS) encompass a spectrum ranging from asymptomatic joint hypermobility through to Ehlers Danlos syndromes (EDS) including hypermobile EDS (equivalent to the former diagnosis of EDS type 3). Many EDS patients have significant musculoskeletal pain and other systemic comorbidities including autonomic, bowel and bladder dysfunction. We present data from a cohort of patients with JHS referred to our tertiary centre from December 2015 to May 2017.

Objectives: To increase the awareness of the hypermobility syndrome among general rheumatologists and other health professionals

To assess the impact of this condition on the patient general health and their work disability

To reflect on the 2017 Ehlers Danlos International Criteria

Methods: We undertook a retrospective analysis of medical records. Statistical analysis utilised non parametric Chi squared analysis for between group comparisons

Results: There were 280 patients: 253 patients (90%) were female and 27 were male (10%) with a female to male ratio of 9:1. The age distribution was from 18 to 66 (mean age 42 years). The age at which they were first diagnosed ranged from 4 to 55 (mean age 29 years); 279 (96%) had Ehlers Danlos Syndrome type 3, one patient had Marfan's, one Kyphoscoliotic EDS, and two patients had Tenascin X deficiency. Family history of hypermobility was reported among 185 patients (66%). In relation to the autonomic dysfunction, 185 patients (66%) had orthostatic intolerance, 126 (45%) had gastrointestinal problems; 109 (39%) had bladder dysfunction with 2.5% of them requiring catheterisation. Chronic joint and muscle pain was reported in 91%; 49.6% of these used opioid analgesia long term. One hundred and twenty patients (43%) had work disability.

Patients taking opioids were more likely to have work disability: 54% vs. 34% *(p*<0.001). Bladder problems were more common in the group taking opioids (46% vs 32%; *p*<0.02). A significant association between orthostatic intolerance and bowel problems was observed. Almost half (47%) of those with orthostatic intolerance had bowel problems, compared to only 19% without (p<0.001). Patients with bowel problems were more likely to have bladder problems compared to those without bowel problems (*P* <0.001).

Conclusion: The 2017 EDS International Classification defined thirteen subtypes of EDS. The molecular basis for the hypermobile Ehlers Danlos Syndrome (previously Ehlers Danlos Syndrome type 3) remains to be identified and diagnosis is clinical, preferentially characterised by joint hypermobility, skin hyper extensibility and tissue fragility. However, this study shows that systemic manifestations are frequently observed and they tend to appear in clusters.

As important is the diagnosis of joint hypermobility, the same is the recognition of every aspect of hypermobility syndrome. A tailored multidisciplinary approach can potently improve the quality of life and lessen the socioeconomic and NHS burden of these patients. In addition we would strongly discourage use of opioids in patients with hypermobility.

REFERENCE:

[1] Fransiska Malfait at al : The 2017 international classification of Ehlers – Danlos syndromes. American Journal of medical Genetics Part C: Seminars in medical Genetics, Vol 175, Issue 1, March 2017, pages 8-26

Disclosure of Interests: None declared

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THU0484 ESTIMATION OF PATIENT ACCEPTABLE SYMPTOM STATE FOR PATIENT-REPORTED OUTCOMES BETWEEN 2 POPULATIONS OF PATIENTS WITH NON-SPECIFIC CHRONIC LOW BACK PAIN

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Background: Clinical relevance of commonly used patient-reported outcomes (PROs) is unclear in people with non-specific chronic low back pain (cLBP) (1).
Objectives: To estimate and compare patient acceptable symptom state (PASS) at 1 month post-intervention for 4 PROs between 2 populations of patients with non-specific cLBP and to determine which baseline variables contribute to having an acceptable symptom state at 1 month.
Methods: Overall, we included 256 patients: 135 patients with cLBP and active discopathy participated in a randomized controlled trial assessing the efficacy on pain at 1 month of a single glucocorticoid intradiscal injection compared to contrast alone (2), and 121 patients with cLBP and without active discopathy participated in a randomized controlled trial assessing the efficacy on pain at 4 months of 12 sessions of immersive virtual reality (VR) compared to usual care (3). Using an anchor-based method, PASS estimates for PROs were obtained using the 75th percentile method (4). Logistic regression was used to determine baseline variables contributing to achieving PASS at 1 month.
Results: At 1 month, 137/256 (53.52%) participants self-rated their health as acceptable. In the whole population, PASS (95% IC) were 47.50 (40.00 to 50.00) for the lumbar-pain VAS, 30.50 (30.00 to 40.00) for the radicular-pain VAS, 39.27 (33.60 to 45.26) for the QUEBEC score, 9.95 (9.16 to 10.00) for the HAD anxiety subscale and 6.70 (6.00 to 8.00) for the HAD depression subscale. The PASS estimates did not differ between the 2 populations of cLBP patients for any of the PRO. The only baseline variable contributing to having an acceptable symptom state at 1 month was symptom intensity.
Conclusion: PASS estimates at 1 month did not vary across 2 independent samples of people with cLBP and 2 distinct nociceptive sources of cLBP. The main contributor of the PASS was symptom intensity at baseline. Our findings can be useful in interpreting the clinical relevance of PROs values.

REFERENCES:

[1] Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, et al. Evaluation of clinically relevant states in patient reported outcomes in knee and hip osteoarthritis: the patient acceptable symptom state. Ann Rheum Dis. 2005;64(1):34-7.
[2] Nguyen C, Boutron I, Baron G, Sanchez K, Palazzo C, Benchimol R, et al. Intradiscal Glucocorticoid Injection for Patients With Chronic Low Back Pain Associated With Active Discopathy: A Randomized Trial. Ann Intern Med. 2017;166(8):547-56.
[3] Nguyen C, Boutron I, Perrodeau É, Sanchez K, Borderie D, Palazzo C et al. 3D immersive virtual reality in patients with chronic low back pain: a randomized controlled trial. PlosOne (under review). 2017.

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THU0485 EFFICACY OF EXTRACORPOREAL SHOCK-WAVE THERAPY IN THE TREATMENT OF SHOULDER CALCIFIC TENDINITIS IN INSUFFICIENT RESPONDERS TO LOCAL STEROID INJECTION THERAPY: A RETROSPECTIVE ANALYSIS

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Background: Calcific tendinitis (CT) results from the deposition of calcium hydroxyapatite crystals in periarticular muscular attachments, and most commonly affects the tendons of the shoulder (1). Extracorporeal shock wave therapy (ESWT) is based on the use of shock waves, and used for pain reduction and tissue healing (2).
Objectives: The aim of this analysis is to demonstrate the effects of ESWT in patients with shoulder CT with inefficient response to local steroid injection.
Methods: 2-year data of shoulder outpatient clinic were scanned. 10 patients with shoulder calcific tendinitis without satisfying response to local steroid injection (less than 50% decrease in pain-visual analogue scale (VAS) score) who were treated with ESWT were reviewed.
Results: 10 patients (9 women, 1 man) fulfilled the inclusion criteria. The mean patient age was 51.3 years (range, 32-70 years) and body mass index was 26.2 kg/m2. The affected shoulder was left in 6 (60%) patients and right in 4 (40%). The calcific tendinitis involved the dominant side in 5 (50%) patients and non-dominant side in other 5 (50%). All patients had one peritendinous local steroid injection-2 ml 2% prilocain and 1 ml steroid (5 mg of betamethasone dipropionate + 2 mg betamethasone sodium phosphate). Mean time from symptom onset to the ESWT treatment was 3.5 weeks (range, 2-6 weeks). Mean VAS score was 9 and Shoulder Disability Index (SDI) score was 84.4 before ESWT treatment. ESWT system Elmed-Vibrolith ver.3.0 was used in the treatments, each treatment consisted 2000 shocks with a frequency of 150 shocks a minute with maximum tolerable energy density (range, 3.2-3.4 bar). Mean ESWT session was 3.3 (8 patients had 3, 1 patient had 4 and 1 patient had 5 sessions of treatment). Mean post-treatment VAS score was 4.2 (53.3% decrease) and SDI score was 43.8 (48.1% decrease) which were evaluated after the last ESWT session.
Conclusion: With its good tolerance and safety, ESWT might be an alternative treatment method for calcific tendinitis of the shoulder. Although limited number of patients, we hope that this study might give rise to future randomized-controlled studies about the efficacy of ESWT in acute-subacute shoulder calcific tendinitis.

REFERENCES:

[1] Holt, P. D., & Keats, T. E. (1993). Calcific tendinitis: a review of the usual and unusual. Skeletal radiology, 22(1), 1-9.
[2] Cosentino, R., Selvi, E., De Stefano, R., Frati, E., Manca, S., Hammoud, M., & Marcolongo, R. (2004). Extracorporeal shock wave therapy for chronic calcific tendinitis of the shoulder. Clinical rheumatology, 23(5), 475-477.

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DOI: 10.1136/annrheumdis-2019-eular.4330

THU0486 PREGABALIN EFFICACY IN THE TREATMENT OF CHRONIC PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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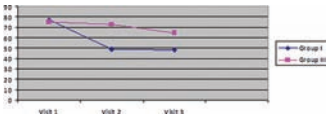
Background:
Objectives: To study the efficacy of Pregabalin in the treatment of chronic pain in patients with rheumatoid arthritis.
Methods: We enrolled 80 patients with rheumatoid arthritis. Screening with the DN4 neuropathic pain questionnaire showed that 31% of patients (n=25) had a neuropathic pain component (NPC+), DN4>4 points. Mean age was 57,0 ±7,49 years, disease duration - 9.87 ± 9.5 years, DAS28 disease activity - 5.5 ± 1.3, VAS pain intensity - 73.1 ± 17.4. All patients were randomized into two groups: group I received pregabalin in combination with DMARDs; group II received DMARDs only. All patients underwent a clinical and neurological examination, disease activity was assessed with the DAS28 index, the effect of treatment on neuropathic pain was assessed with the DN4 and Pain DETECT questionnaires, pain intensity at rest – with the VAS scale.
Results: There were no significant differences between groups before the start of the study (Table 1)

Abstract THU0486 –Table 1.

	Group I	Group II	P<0.05
Mean age (years)	58.2±9.15	56.2 ±6.69	0.6
Disease duration (years)	13.6 ±11.45	7.07 ±8.42	0.3
DAS28	5.3±0.6	4.8±1.6	0.4
DN4 (points)	5.,2±1.1	5.0±0.6	0.7
Pain Detect (points)	17.0±3.2	18.2±2.9	0.4
HADS-Anxiety	6.8±3.2	12.0±4.8	0.7
HADS-Depression	8.4±2.2	8.0±2.6	0.7
VAS, mm	77.0±13.5	75.2 ±14.7	0.5

Positive dynamics of VAS pain intensity was observed in both groups [Fig. 1] (77.0 ± 13.5 vs 75.2 ± 14.7, at week 2 48.8 ± 14.2 vs 72.9 ±

16.9, at week 5 48.3 ± 34.2 vs 64.5 ± 20.2 p = 0.004). Neuropathic pain indices improved significantly according to the DN4 (5.2 ± 1.1 vs 5.0 ± 0.6, at week 5 2.3 ± 0.6 vs 4.5 ± 0.6) and Pain DETECT questionnaires (17.0 ± 3.2 vs 18.4 ± 2.2, at week 5 7.3 ± 3.06 vs 16.8 ± 3.8).



Abstract THU0486 – Figure 1. Dynamics of VAS pain intensity with different treatments

However, disease activity did not differ significantly in either group (group I 5.6 ± 0.6 vs 4.8 ± 1.6 p = 0.4; group II 4.9 ± 0.3 vs 5.2 ± 1.2 p = 0.8).

Conclusion: This preliminary data shows greater effectiveness of Pregabalin in comparison with NSAID and DMARD treatment, both in terms of pain intensity and the neuropathic pain component, which is of practical importance.

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THU0487 PERINEURAL INJECTION THERAPY; A NEW MODALITY IN MANAGEMENT OF MECHANICAL LOW BACK PAIN; A COMPARATIVE STUDY

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Background: Chronic mechanical low back pain represents the second leading cause of disability worldwide being a major welfare and economic problem[1].

Subcutaneous prolotherapy treats prolonged pathological peripheral neurogenic inflammation for several painful conditions. As it induces apoptosis of proliferating peptidergic noceffectors and neovessels by reducing vascular endothelial growth factor [2]

Objectives: To assess the effectiveness of subcutaneous perineural injection therapy in management of pain, physical function, disability and psychological status in mechanical low back pain

Methods: Ninety patients with non-radiating non-specific chronic mechanical low back pain (LBP) that persisted for 12 weeks or more were selected in this study. (Patients with inflammatory LBP, radiating, or LBP due to specific cause, pregnant women or Patients with implanted pacemaker or spinal cord stimulator were excluded from this study). After giving written consent; the patients were randomly divided into 3 groups 30 patients in each. Group I recieved 8 weekly subcutaneous injections of 1 ml of buffered dextrose 5% in each chronic constriction injury points and tender points in back and buttock. Group II treated by using pulsed electromagnetic field stimulation (PEMFs) for 30 minutes over the lower lumbar region with frequency of 10 Hz and intensity of 2 millitesla every other day for 8 weeks. Group III received sham PEMFs. All patients will be instructed to follow an exercise program in the form of stretching for hamstring, calf, and back muscles, and strengthening exercises for back and abdominal muscles. Assessments were performed at baseline, at the end of the treatment and after four months, using the following measurements: visual analog scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, Lequesne index, Hospital Anxiety and Depression Scale (HADS).

Results: The mean age of patients in the 3 groups was 40.2±10.5, 38.3 ±9.9, and 43.1±10.8 respectively. The mean VAS was 7.9+1.4, 8.2+0.6, and 7.6+1.1 respectively. No baseline differences existed between all groups in all parameters. There was significant improvement in VAS, WOMAC and HDAS in group I & II ($p<0.05$) after treatment, and 4 months later (figure 1). While the improvement in group III was non-significant ($p>0.05$). The improvement in group I was better than in group II with significant difference between the two groups ($p<0.05$) after treatment and 4 months follow up.

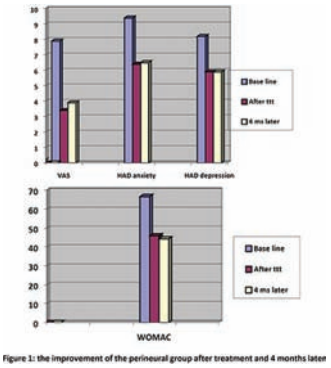


Figure 1: the improvement of the perineural group after treatment and 4 months later

Abstract THU0487 – Figure 1

Conclusion: Perineural Injection Therapy is an effective new modality in management of pain, physical function, psychological status and disability in mechanical low back pain.

REFERENCES:

[1] Massimo Allegri, Silvana Montella, Fabiana Salici et al., Mechanisms of low back pain: a guide for diagnosis and therapy. F1000Research 2016, 5 (F1000 Faculty Rev):1530 Last updated: 11 OCT 2016 doi: [10.12688/f1000research.8105.2]

[2] Lyftogt, J. Prolotherapy for Recalcitrant Lumbago. Australasian Musculoskeletal Medicine, 2008; 13(1): 18-20.

Disclosure of Interests: None declared

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THU0488 ACHILLES TENDON RUPTURE ASSOCIATED WITH THE USE OF FLUOROQUINOLONES IN PATIENTS OLDER THAN 60 YEARS

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Background: Fluoroquinolones (FQ) are a class of broad-spectrum antibiotics whose use has spread as they are considered safe and well tolerated drugs. Among its musculoskeletal side effects, Achilles tendon rupture (ATR) is a well-known complication that can be disabling, arising recent interest from the pharmacovigilance system after evaluating the reported side effects.

Objectives: To describe the epidemiological and clinical features of patients diagnosed with FQ-associated ATR in a Spanish tertiary hospital.

Methods: A retrospective observational study was performed, which included all patients older than 60 years who were diagnosed of ATR in our center during the period 2000-2017, identifying patients who had been previously treated with FQ. The demographic, clinical and outcome data were obtained from their medical records.

Results: During the study period, 44 patients with ATR were identified, 8 (14.6%) of them previously treated with FQ. In this group of patients, the mean age at diagnosis of ATR was 77.37 ± 9.54 years, being male 6 (75%). Four of them (50%) received concomitant treatment with corticosteroids (CS) and one patient had undergone kidney transplantation due to nephroangiosclerosis. Seven patients (87.5%) were treated with Levofloxacin and one case received Ciprofloxacin, all of them orally. The indication for FQ treatment in half of the cases was acute bronchitis and in the other half exacerbations of underlying respiratory pathology (chronic obstructive pulmonary disease and diffuse interstitial lung disease). The mean duration of treatment with FQ was 6.16 ± 2.4 days, while the mean time from the start of treatment to the diagnosis of ATR was 19.25 ± 14.83 days. In seven patients (87.5%) the rupture was spontaneous, while one patient presented traumatic rupture (low impact traumatism). 87.5% of the ruptures were total ruptures and all cases required surgical treatment, without recurrence reported. The comparison of the characteristics of patients with ATR who had or not received treatment with FQ is shown in the table, identifying significant differences in favor of a higher percentage of patients who were smokers, received concomitant treatment with CS and had spontaneous rupture in the group of patients who had received FQ.

	Fluoroquinolones	Non-Fluoroquinolones	p-value
Age (years)	77,37 ± 9,54	70,13 ± 8,3	0,48
Sex			
Male	6 (75%)	25 (69,4%)	0,75
Female	2 (25%)	11 (30,6%)	
Smoking	5 (62,5%)	1 (2,8%)	0,00
Treatment with CS	4 (50%)	2 (5,6%)	0,01
Treatment with statins	0 (0%)	5 (13,9%)	0,26
Type of rupture			
Spontaneous	7 (87,5%)	8 (25,8%)	0,01
Traumatic	1 (12,5%)	23 (74,2%)	

Conclusion: The Achilles tendon is the most frequent location of tendinopathy associated with FQ, being affected in 95% of cases. The risk factors associated to an increased risk to develop FQ-associated ATR includes age over 60 years, male gender, chronic treatment with CS and organ transplantation, all these being present in our cases. Despite being a relatively frequent adverse event, it is underdiagnosed and the risk of ATR is not usually assessed when indicating FQ treatment. It is important to perform a risk/benefit assessment, specially in patients with associated risk factors, because most ruptures are complete and require surgical treatment, and may be a potential cause of disability.

REFERENCES:

[1] Bidell M, Lodise T. Fluoroquinolone-Associated Tendinopathy: Does Levofloxacin Pose the Greatest Risk?. Pharmacotherapy. 2016;36(6):679-93.
[2] Godoy-Santos A, Bruschini H, Cury J, Srougi M, De Cesar N, Fonseca L, Maffulli N. Fluoroquinolones and the Risk of Achilles Tendon Disorders: Update on a Neglected Complication. Urology. 2018;113:20-25.

Disclosure of Interests: None declared
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THU0489 REAL-WORD EFFECTIVENESS OF FIXED-SITE HIGH-FREQUENCY TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN CHRONIC LOW BACK PAIN

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Background: Fixed-site high-frequency transcutaneous electrical nerve stimulation (FS-TENS) is a form of TENS in which the stimulator is designed for a predetermined location rather than for co-localization with the patient's pain. A small wearable device for localized application while active and sleeping facilitates adequate dosing.
Objectives: To evaluate the effectiveness of regular FS-TENS use in a large, real-world chronic low back pain (CLBP) population.
Methods: This retrospective, observational study evaluated use of FS-TENS (worn on upper calf; providing semi-continuous stimulation of sensory nerves) to treat CLBP across a 10-week period using previously collected therapy utilization, demographic, and clinical (pain characteristics/ratings) data. Data collected by the device and companion smartphone app are stored in a cloud database. Device users were eligible for inclusion if they consented to allow their anonymized data to be used for research, had demographic data and pain characteristics indicative of CLBP (daily/weekly pain for >3 months, low back pain, and self-reported herniated disc, spinal stenosis, and/or previous back injury) and had baseline and 10-week pain ratings. Participants were assigned retrospectively to the treatment group or reference group based on device use (% of days with $\geq$30 min of FS-TENS use) of $\geq$50% or <50%, respectively. The primary study outcome was the baseline to 10-week change in composite pain, defined as the average of pain intensity and pain interference with activity, sleep, and mood, measured on an 11-point numeric rating scale. Treatment effect was estimated by comparing outcomes in the treatment group to a matched reference group constructed from the original reference group by propensity score (PS) matching estimated by logistic regression. Differences between groups were tested by Wilcoxon rank-sum test for continuous variables and by Pearson chi-square test for proportions.
Results: A total of 834 device users met the inclusion criteria and were assigned to the treatment (671, 80%) or reference (163, 20%) groups. With few exceptions, the two groups had similar demographic and pain characteristics at baseline: the treatment group was older (58±13 vs 56 ±14, P=0.035), had lower body mass index (30.5±6.8 vs 31.9±7.9 kg/m^2, P=0.043), was more likely to have hip pain (P=0.037), and less likely to have diabetes (P=0.002) or prior neck injury (P=0.006). There was no difference in baseline composite pain (6.3±2.1, treatment; 6.5±1.9, reference; P=0.364). Device usage was significantly different between groups (86±15%, treatment; 31±13%, reference; P<0.001), as was duration of therapy per week (46±22 hrs/week, treatment; 11±7 hrs/week, reference; P<0.001), median stimulation intensity (ratio of stimulation to sensation level expressed in decibels) (5.3 dB, treatment; 6.0 dB, reference; P=0.045). Of the 163 participants in the original reference group, 143 (88%) served as matches for the treatment group. The baseline to 10-week follow-up change in composite pain was −0.89±2.30 for the treatment group and −0.01±2.3 for the matched reference group, with a standardized mean difference between the groups of 0.38 (95% confidence interval, 0.27–0.49; P<0.001).
Conclusion: This study demonstrated that 10 weeks of regular FS-TENS use improved pain outcomes in a real-world sample of CLBP patients compared with a reference group with low FS-TENS use. This study suggests that regular FS-TENS use may be effective in improving pain outcomes in CLBP patients.
Disclosure of Interests: : Xuan Kong Employee of: Xuan Kong is an employee of NeuroMetrix, Inc., Dawn Chesher Employee of: Dawn Chesher is an employee of GlaxoSmithKline Consumer Healthcare.
DOI: 10.1136/annrheumdis-2019-eular.6106

THU0490 PREDICTORS OF CHRONIC PAIN RELIEF BY FIXED-SITE HIGH-FREQUENCY TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

Xuan Kong[1], Dawn Chesher[2]. [1]*NeuroMetrix, Inc., Waltham, United States of America*; [2]*GlaxoSmithKline Consumer Healthcare, Weybridge, Surrey, United Kingdom*

Background: Fixed-site high-frequency transcutaneous electrical nerve stimulation (FS-TENS) is a form of TENS in which the stimulator is designed for a predetermined location rather than for co-localization with the patient's pain. Previous studies in individuals with chronic pain have demonstrated the efficacy and real-world effectiveness[1,2] of a small wearable FS-TENS device designed for localized application to a single placement site to ensure comfort while both active and sleeping. Results demonstrated that 50–80% of FS-TENS users with chronic lower extremity or low back pain experience clinically meaningful pain relief,[1,2] and daily use of the device was associated with greater pain relief relative to intermittent use.[2]
Objectives: To determine predictors of a positive FS-TENS response.
Methods: This retrospective, observational study evaluated users of a FS-TENS device to treat chronic pain over a 10-week period. The device and companion smartphone app collected dosage data, demographics, pain characteristics, and pain ratings and all data were stored in a cloud database. The primary study outcome was the baseline to week 10 change in composite pain (average of pain intensity and pain interference with sleep, activity, and mood). Device users were included if they provided demographic data, pain characteristics indicative of chronic pain, and baseline and week 10 pain ratings. Participants were defined as a responder or comparator based on their change in composite pain (responder: $\geq$15% decrease; comparator: $\geq$15% increase). Stepwise forward probit regression was used to determine independent predictors.
Results: There were 451 responders and 263 comparators. Independent predictors (Table) that were associated with greater response to FS-TENS included age, baseline composite pain, adherence/utilization rate (defined as the percentage of days with at least 30 minutes of stimulation), and stimulation intensity (defined as the ratio of therapeutic stimulation to sensation threshold, expressed in decibels). Negative predictors (associated with lower response) included history of headache/migraine and diabetes. The area under the receiver operating characteristic curve was 0.76 (95% confidence interval, 0.72–0.79).
Conclusion: FS-TENS effectiveness is predicted from baseline pain characteristics and dosage variables, such as frequency/regularity of use and stimulation intensity, with moderate accuracy.

REFERENCE:

[1] Gozani SN. *J Pain Res*. 2016;9:469-79. 2. Kong X, Gozani SN. *J Pain Res*. 2018;11:703-14.

Abstract THU0490 – Table 1. Independent predictors of responders from probit regression.

Variable	Coefficient
Age (years)	0.01
Baseline composite pain (0–10)	0.27
Headache or migraine	−0.37

Diabetes	−0.33
Weather sensitivity	−0.22
Adherence (%)[a]	0.01
Stimulation intensity (dB)[b]	0.02
Constant	−2.36

[a]Adherence, percentage of days with at least 30 minutes of stimulation.
[b]Stimulation intensity, ratio of therapeutic stimulation to sensation threshold expressed in decibels (20log[therapy/sensation]).
All coefficients $P<0.05$.

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THU0491 RELIABILITY AND VALIDITY OF THE İSTANBUL LOW BACK PAIN DISABILITY INDEX IN LUMBAR RADICULOPATHY

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Background: The Istanbul Low Back Pain Disability Index (ILBPDI) was developed to assess the disability in patients with mechanical low back pain with 18 daily activities questions (1).
Objectives: The aim of this study is to investigate the validity and reliability of the İstanbul Low Back Pain Disability Index in lumbar radiculopathy.
Methods: Patients who were diagnosed with radiculopathy due to lumbar spinal stenosis and/or disc herniation by physical examination and imaging methods were included in the study. Data about age, sex, body mass index (BMI), disease duration (month) were noted. Short Form 36 (SF-36) was used to assess the quality of life. Disability due to low back pain was assessed with Oswestry Low Back Disability Questionnaire. The severity of low back pain and extremity pain due to radiculopathy were assessed on the Visual Analogue Scale (VAS).
The reliability of ILBPDI was determined by internal consistency (Cronbach's alpha coefficient). The construct validity (convergent and divergent validities) was evaluated. The correlations of the ILBPDI with SF-36, Oswestry Low Back Disability Questionnaire, and the VAS scores of the low back pain and radiculopathy were assessed for convergent validity. The relations of the ILBPDI with age, BMI, and disease duration were assessed for divergent validity. The construct validity of the ILBPDI scale was determined by Spearman's correlation coefficient. The descriptive analysis was done for demographic data. P<0.05 accepted as significant. SPSS 20.0 (Statistical package for social sciences for Windows 20.0) program was used for the statistical analysis.
Results: The mean age of 82 patients (44 female, 38 male) with lumbar radiculopathy was 45.45 (SD: 11.96) years. The median (min-max) duration of disease was 5 (1-120) months. The mean BMI of patients was 29.09 (SD: 5.04). The mean score of ILBPDI was 30.73 (SD: 17.04) ant the mean score of Oswestry Low Back Disability Questionnaire was 52.73 (SD: 16.98).
The Cronbach's alpha coefficient of the ILBPDI for internal consistency was 0.764. The ILBPDI score had moderate and significant positive correlations with Oswestry Low Back Disability Questionnaire (rho: 0.610, p<0.005). Statistically significant but low correlation was detected between ILBPDI and the VAS score of radiculopathy (rho: 0.285, p: 0.010), but there was no correlation with the VAS score of low back pain (p>0.05). As for the correlations between the ILBPDI total score and SF-36 subgroups, significant negative correlations were detected with physical functioning (rho: -0.672, p<0.005), physical role limitation (rho: -0.230, p: 0.038), bodily pain (rho: -0.546, p<0.005), general health (rho: -0.262, p: 0.017), and social function (rho: -0.337, p<0.005) subgroups of the SF-36. There were no significant correlations between ILBPDI and age, disease duration, and BMI (p>0.05).
Conclusion: The Istanbul Low Back Pain Disability Index is a valid and reliable instrument in patients with lumbar radiculopathy. This is a preliminary study. The study will continue for the factor analysis.

REFERENCE:

[1] Duruoz MT et al. Development and validation of a functional disability index for chronic low back pain. J Back Musculoskelet Rehabil. 2013; 26: 45-54.

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THU0492 EFFICACY OF US-GUIDED HYALURONIC ACID INJECTIONS IN ACHILLES AND PATELLAR MID-PORTION TENDINOPATHIES: A PROSPECTIVE MULTICENTRIC CLINICAL TRIAL

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Background: Achilles and patellar tendinopathies are common clinical conditions that determine chronic pain and functional impairment. Conservative treatment can be effective, but it is time-consuming and it requires intensive patient compliance.
Hyaluronic acid (HA) is a key component of the extracellular matrix, and its anti-inflammatory, lubricant and analgesic properties are well established in osteoarthritis. Growing pre-clinical evidence point toward a possible role of HA in the management tendon pathology, while clinical evidences are still lacking.
Objectives: The primary objective was to assess the efficacy of a new formulation of HA (20 mg/2 ml; 500-730 kDa), obtained from biofermentation, in function improvement on VISA-A and VISA-P scores at 90 days of follow-up in patients with Achilles or patellar tendinopathy.
Secondary objectives were to evaluate improvement in pain (NRS-11), US parameters (tendon composition and neovascularization), and quality of life (EQ-5D). Safety of this new HA formulation was also evaluated.
Methods: This was a prospective, open-label, multicenter clinical trial. Thirty-five patients (25in AT group; 9 patients in PT group), who satisfied strict inclusion and exclusion criteria, were recruited over a 4-month period. Each patient received 1 injection weekly for 3 weeks under US-guidance at the painful site of tendinopathy, and was evaluated at 14, 45 and 90 days after the procedure. Subjects were instructed to record on a diary any intake of the permitted rescue medication for pain relief (i.e. paracetamol up to 3 g per day) throughout the study period and to interrupt treatment at least 24 hours prior to each visit.
Results: Significant improvement on VISA-A (23.22±23.17; 95% CI: 13.20; 33.24; p<.0001) occurred, and improvement on VISA-P was also revealed (19.25±11.61; 95% CI: 9.54; 28.96; p=0.0022). NRS-11 score significantly decreased in the AT group (4.52±3.25; 95% CI: -5.93; -3.12; p<0.0001) and in the PT group(-4.75±3.20; 95% CI: -7.42; -2.08; p=0.0040).
Significant improvement of US parameters in the AT group was evidenced (McNemar's test; p=0.0016 and p=0.0114, respectively), while in the PT group the presence of these clinical symptoms showed only a tendency to decrease (p=0.3173 for both). EQ-5D-5L total score tended to increase in both the AT and PT groups (mean change vs. baseline at day 90 equal to 15.96±18.95 (range: -50; 45) and 15.50±32.42 (range: -40; 71), respectively).
Conclusion: Three US-guided HA injections may improve pain and function in patients with Achilles and patellar tendinopathy for up to 90 days of follow-up. Amelioration in tendon structure, neovscolarization and clinical parameters may also be achieved. The hyaluronic acid injection was also safe and well tolerated.

REFERENCES:

[1] Frizziero A, Salamanna F, Giavaresi G, Ferrari A, Martini L, Marini M, Veicsteinas A, Maffulli N, Masiero S, Fini M. Hyaluronic acid injections protect patellar tendon from detraining-associated damage. Histol Histopathol. 2015 Sep;30(9):1079-88
[2] Lynen N, De Vroey T, Spiegel I, Van Ongeval F, Hendrickx NJ, Stassijns G. Comparison of Peritendinous Hyaluronan Injections Versus Extracorporeal Shock Wave Therapy in the Treatment of Painful Achilles' Tendinopathy: A Randomized Clinical Efficacy and Safety Study. Arch Phys Med Rehabil. 2017 Jan;98(1):64-71

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THU0493 A MULTICENTRE RANDOMISED CONTROLLED FOLLOW-UP STUDY OF EFFECTS OF THE UNDERWATER TRACTION THERAPY IN CHRONIC LOW BACK PAIN

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Background: Chronic low back pain established for more than 3 months is one of the most common problems in the world. The prevalence could reach the 33%.
Objectives: To investigate the effects of underwater traction therapy on chronic low back pain.
The primary objective was to prove the hypothesis that underwater traction therapy has favourable effect of LBP using the change in the clinical parameters. Our secondary objective was to evaluate whether it also leads to the improvement in the quality of life.
Methods: A prospective, multicenter, comparative (intervention arm vs. control arm), randomized follow-up study.
Participants aged between 18 and 85 years with more than 3 months low back pain and selected from outpatient clinics.
The participants were randomized to three groups: underwater weight bath traction therapy, weight bath and non-steroidal anti-inflammatory drugs (NSAIDs) medication and only non-steroidal anti-inflammatory drugs (NSAIDs) medication.
During the traction therapy ankle weights were used.
The following parameters were measured before, right after, and nine weeks after the three-week therapy: level of low back pain in rest, level during activity tested using the Visual Analog Scale (VAS); specific questionnaire on back pain (Oswerty); questionnaire on quality of life (EuroQual-5D) and clinical parameters.
Results: 141 participants aged 57.67 (±13.04) years. All of the investigated parameters improved significantly ($p<0.001$) in the underwater weight bath traction therapy groups by the end of the treatment compared to the base period, and this improvement was persistent during the follow-up period. There were no significant changes in the measured parameters in the control group except for the Oswestry Disability Index, which may also be the result of that group receiving pain-relieving drug therapy.
Conclusion: Based on our results, underwater weight bath traction therapy, might have favourable impact on the clinical parameters and quality of life of patients suffering from chronic low back pain.

REFERENCES:

[1] Alrwaily M, Almutiri M, Schneider M. Assessment of variability in traction interventions for patients with low back pain: a systematic review. Chiropr Man Therap. 2018 Sep 17;26:35. doi: 10.1186/s12998-018-0205-z. eCollection 2018. Review. PubMed PMID: 30237870; PubMed Central PMCID: PMC6139896.
[2] Kurutz M, Oroszváry L. Finite element analysis of weightbath hydrotraction treatment of degenerated lumbar spine segments in elastic phase. J Biomech. 2010 Feb 10;43(3):433-41. doi: 10.1016/j.jbiomech.2009.10.004. Epub 2009 Nov 1. PubMed PMID: 19883918.
[3] Oláh M, Molnár L, Dobai J, Oláh C, Fehér J, Bender T. The effects of weightbath traction hydrotherapy as a component of complex physical therapy in disorders of the cervical and lumbar spine: a controlled pilot study with follow-up. Rheumatol Int. 2008 Jun;28(8):749-56. doi: 10.1007/s00296-008-0522-y. Epub 2008 Jan 12. PubMed PMID: 18193231.

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THU0494 RELATIONSHIP BETWEEN THE AREA OF THE MEDIAN NERVE CROSS SECTION AND THE CIRCUMFERENCE OF THE CARPUS AS A DIAGNOSTIC TOOL FOR CARPAL TUNNEL SYNDROME

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Background: The diagnosis of carpal tunnel syndrome (CTS) is fundamentally electrophysiological, however, on diagnostic suspicion ultrasonography has been shown to correlate satisfactorily with the electromyogram. The limitations of the ultrasound study of the median nerve in patients with STC are due to the fact that the intervals of normality of the area of the median nerve cross section (ACTNM) are variable according to the sources consulted, the sex and the anthropometry of the individual.
Objectives: The purpose of this study is to determine whether NMTA can be correlated with a simple measurement such as wrist circumference length (MCL) in patients with electrophysiological diagnosis of TCEs and healthy subjects and used to discriminate them better than with the simple measurement of NMTA.
Methods: We included 50 patients with electrophysiological diagnosis of CTS and 43 healthy subjects of white ethnicity, older and with different anthropometric characteristics. The patients came from the Rheumatology consultations of three different centres. Healthy volunteers were subjects without CTS clinic, thyroid alterations, diabetes or known autoimmune rheumatological diseases whose data were obtained from a previous study. Circumference was measured with a flexible tape measure around the carpus immediately distal to the interstylloid line. The ultrasound measurements were made at the height of the escofoid and pisciforme bones using three different ultrasound scanners according to the headquarters: Toshiba Nemio XG, 13Mhz linear probe, Samsung HM70a 14 MHz and Logiq e GE 12 MHz. All the measured images were captured for analysis and correction of circumference lengths by an observer not linked to the identity of the subjects nor to their character of patient or control. An association study between wrist circumference and ACTNM was performed for both groups and a correlation index was submitted to a validation test for the determination of sensitivity and specificity.
Results: ACTNM was 11.11 SD 1.18mm2 in the control group and 12.73 SD 1.50mm2 in the patient group ($p<0.05$). The LCM was 18.81 DE 1.50cm and 18.72 DE 1.85 ($p=0,803$). In healthy subjects, the correlation between ACTNM and carpal circumference showed a satisfactory correlation (Coef Pearson 0.809, $p<0.01$, bilateral) as well as in patients (Coef Pearson 0.878, $p<0.01$, bilateral). The ACTNM/LCM index in the control group was 0.590 and for the patient group 0.679 ($p<0.01$). The area under the ACTNM curve was 0.808 EE 0.049 while in the case of the ACTNM/LCM index was 0.954 EE 0.019. The area under the ACTNM curve was 0.808 EE 0.049 while in the case of the ACTNM/LCM index was 0.954 EE 0.019. With an index of 0.62 or a sensitivity of 93% and specificity of 78% are obtained for the diagnosis of CTS.
Conclusion: LCM correlates well with ACTNM in healthy patients. It could be considered a good anthropometric marker for further studies of normal ultrasound ranges of the median nerve. The LCM/ACTNM index is a useful measure to discriminate controls of patients with electrophysiological diagnosis of JTS. In our series, this index exceeds the discriminatory capacity of the ACTNM as an individual measure.

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THU0495 ROLE OF PLATELET RICH PLASMA IN TREATMENT OF ROTATOR CUFF TENDINOPATHY AND PARTIAL THICKNESS TEAR: FOLLOW UP BY ULTRASOUND

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Background: Shoulder pain is the third most common musculoskeletal reason for seeking medical care. The diagnosis of Rotator Cuff Tendinopathy (RCT), with supraspinatus partial thickness tendon tears and tendonosis, constitutes more than 50% of adult cases presenting with shoulder pains at any time. Platelet rich plasma (PRP) injections are nowadays being used as an alternative for treating the tendinopathies, who have failed to be managed by conservative management.
Objectives: This work aimed to asses the effect of PRP injection under musculoskeletal ultrasound (MSUS) guidance in patients with rotator cuff tendinopathy, and partial thickness tear in comparison with those who received a rehabilitation program only. Baseline assessment and after three months was done using clinical, functional and ultrasonographic evaluation.
Methods: Our study included 60 patients with RCT diagnosed both clinically and by MSUS. Patients were divided into two groups (gI, gII); group I included 30 patients who received a Supervised Rehabilitation Program and group II included 30 patients who received PRP injection. Patients in both groups were assessed clinically, functionally [(VAS), (WORC) and (SPADI)] and sonographically at baseline and after 3 months. Rehabilitation Program included: hot packs, (TENS), and (therapeutic ultrasound). The Exercise Programs (supervised and home-based) were applied, including: (ROM, stretching and strengthening exercises of the rotator cuff and scapular muscles). PRP injection was prepared under complete sterile conditions by whole blood centrifugation with specific

protocol; blood was centrifuged firstly at 1000 rpm for 10 minutes. The plasma was then transferred to a new glass tube and centrifuged at 3000 rpm for 15 minutes. Platelets will form a pellet at the bottom of the tube. Finally, a pure platelet rich plasma was obtained with a concentration 4 times greater than baseline. Ca gluconate was mixed with PRP (in a ratio of 0.3 ml ca gluconate/ml PRP) immediately before the injection. Under ultrasound guidance, 3ml PRP was injected slowly into the bursa without usage of local anesthetics prior to injection. Post injection, patients were advised to rest, use cold packs and were allowed to do light range of motion exercises 2–5 days post injection. Acetaminophen was allowed for intolerable post injection pain.

Results: Statistical analysis was made to 60 patients. Intragroup analysis showed statistical significant difference in both groups at follow up compared to baseline regarding clinical, functional and radiological data. Intergroup analysis showed more significant results in PRP group regarding clinical assessment (p <0.0001), functional assessment (SPADI (PS, DS and total) and WORC scores (p <0.0001) and sonographic assessment in (subscapularis tendinopathy, supraspinatus tendinopathy, supraspinatus fibrillar tendon disruption and supraspinatus tendon thickness) (p <0.0001) and sonographic subacromial subdeltoid bursitis (p= 0.001).

Conclusion: Single PRP injection is an effective mean of treatment of RCT as it improves patients' quality of life clinically, functionally and structurally, better than traditional physical therapy program.

REFERENCES:

[1] Jacobson JA (2011). Shoulder US: anatomy, technique, and scanning pitfalls. Radiology; 260 (1):6–16.

[2] Lansdown DA and Fortier LA (2017). Platelet-Rich Plasma: Formulations, Preparations, Constituents, and Their Effects. Operative Techniques in Sports Medicine; 25(1):7-12.

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THU0496 RESULTS OF AN EARLY INTERVENTION PROGRAM ON THE VARIATIONS IN THE LENGTH OF MUSCULOSKELETAL TEMPORARY WORK DISABILITIES

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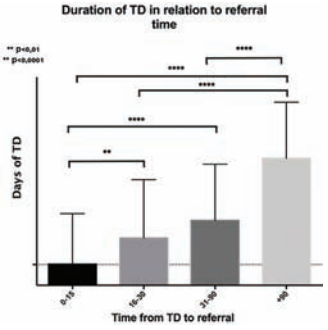
Background: Musculoskeletal disorders cause in Spain 23% of temporary work disability (TD). They are the first cause of permanent work disability (PD). A study of early intervention by a rheumatologist reduced TD days reduced PD. Using the "Fit for Work" European coalition led by AbbVie, the program was implemented nationwide.

Objectives: To analyze the variation in the duration of sick leaves in patients referred to an early intervention program in relation to the delay on the referral from primary care and from the Occupational Health service of our hospital.

Methods: Cross-sectional observational study of a hospital cohort of patients referred for 34 consecutive months to the Rheumatology Early Intervention program due to TDdue to musculoskeletal pathologies. Patients whoseTD had a traumatic or surgical origin, or with incomplete information were excluded from the analysis. We created 4 groups of patients according to the time elapsed from the start of the TD until the referral to our office: 0 to 15 days, 15 to 30 days, 30-60 days or> 90 days. We compared the patients referred from primary care with those referred from occupational health.

Results: For the analysis we included 394 patients, 63.3% women, with a mean age (±D.E.) of 48.5 (±9.8) years. We analyzed the most frequent pathologies: back pain (33.5%), shoulder pain (19.8%) and neck pain (8.4%). 85.8% came from primary care, 10.2% from occupational health and 4.1% from other units. The median time between referral and 1st consultation was 6 days. We found statistically significant differences in the total duration of TD among the patients referred to consultation in the first 30 days compared to those sent later in the 3 pathologies (decreasing the duration of TD between 50 and 100 days in low back pain, between 44 and 54 days in shoulder pain and between 13 and 20 days in neck pain). In back pain we found statistically significant differences in the duration of the TD after the 1st consultation, obtaining an average decrease in the duration of the TD between 42 and 52 days. In shoulder pain and neck pain an important decrease is observed without reaching statistical significance, probably related to the sample size.

Regarding the patients referred from occupational health, the median time between TD and referral was 2.5 days. The pathology most frequently evaluated was low back pain (60% of cases), finding statistically significant differences in the total duration of TD, with a mean decrease in the duration of TD of 59 days compared to the general population.



Abstract THU0496 – Figure 1

Conclusion: Early intervention by rheumatologists in patients with TD due to musculoskeletal disorders reduces the duration of the processes, saving costs to the health system.

Disclosure of Interests: None declared
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THU0497 THE EFFECT OF ADDITION OF BUFFERED DEXTROSE SOLUTION ON PAIN OCCURRING DURING LOCAL STEROID INJECTION FOR PLANTAR FASCIITIS

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Background: 5%dextrose water (D5W) has been previously reported to decrease pain when co-administered with noxious agents as chemotherapeutics and microspheres[(1,2)]. It has also been reported to have an immediate analgesic effect on low back pain and radiculopathy when injected epidurally[3].

Objectives: To evaluate the potential immediate analgesic effect of D5W when added to the injectate during local steroid injection for treatment of plantar fasciitis.

Methods: In this single blind study**,** a total of 122 patients with plantar fasciitis were randomly assigned to receive either 40 mg triamcinolone acetonide/1ml + 0.5ml. lidocaine 2% (group A: 61 patients; 73 heels) or 40mg triamcinolone acetonide/1ml+0.5ml. lidocaine2%+ 0.5ml. buffered D5W (group B: 61 patients; 69 heels) as a local injection using the medial approach. Clinical assessment including disease duration, BMI, history of previous injection and post-injection complications and 2week recurrence rate was performed. Plain X-ray lateral view on the painful heel was obtained for diagnosis of associating calcaneal spur. Visual analogue scale (VAS 0-10) was used to assess the degree of pain intensity during injection.

Results: There were no significant difference between both groups regarding age, sex or BMI where the mean for age was 42.56 years in group A and 43.39 years in group B (P = 0.86), the male to female ratio was 16:45 in both groups and the mean for BMI was 31.49 in group A and 30.86 in group B (P=0.51). The mean disease duration was 6.02 months in group A and 10.77 months in group B (P=0.005). Calcaneal spur was diagnosed in 60 patients (82%) in group A and in 47 patients (68%) in group B. **A highly significant difference in VAS was observed as the mean was 8.26±2.00 in group A and 4.25±2.05 in group B (P <0.0001)** with a confidence interval (95% CI)of 7.78 -8.74 for group A and 3.76 - 4.72 for group B. On 2 week follow up, only 4 patients in each group reported a recurrent heel pain. No injection related side effects or complications have been reported.

Conclusion: The addition of 0.5 ml. D5W can significantly decrease the pain associated with local steroid injection for treatment of plantar fasciitis.

REFERENCES:

[1] T. Nakashima, Y. Ogawa, A. Kimura et al., "Coadministration of 5% glucose solution has a decrease in bendamustine-related vascular pain grade," Journal of Oncolog y Phar mac y Prac tice, vol. 18, no. 4, pp. 445–447, 2012.

[2] K. J. Paprottka, S. Lehner, W. P. Fendler et al., "Reduced periprocedural analgesia aftr replacement of water for injection with glucose 5% solution as the infusion medium for 90Y-Resin microspheres," Jour nal of Nuclear Medic ine, vol. 57, no. 11, pp. 1679–1684, 2016.
[3] Maniquis-Smigel L., Reeves K. D., Rosen H. J. et al., "Short term analgesic effects of 5% dextrose epidural injections for chronic low back pain: a randomized controlled trial," Anesthesiology and Pain Medicine, vol. 7, no. 1, Article ID e42550, 2017.

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THU0498 PAIN RELIEF AND GAIN OF FUNCTION FROM LOW DOSE RADIOTHERAPY FOR EPICONDYLITIS, FINGER OSTEOARTHRITIS AND PLANTAR FASCIITIS – RESULTS OF A PROSPECTIVE CLINICAL TRIAL

Brigitte Eberle[1], Susanne Rogers[1], Debroah Vogt[2], Elisabeth Meier[1], Lorenz Moser[1], Silvia Gomez[1], Susanne Desborough[1], Istvan Takacs[3], Hasler paul[1], Stephan Bodis[1,4]. [1]*Kantonsspital Aarau, Aarau, Switzerland*; [2]*University of Basel and University Hospital of Basel, Basel, Switzerland*; [3]*Kantonsspital Baden, Baden, Switzerland*; [4]*University Hospital Zurich, Zurich, Switzerland*

Background: Low dose radiotherapy (LDRT) is an effective treatment for therapy-resistant musculoskeletal disorders that is associated with only minimal toxicities and low costs [1]. As the population in many countries ages and such disorders result in significant impairment in quality of life and costs, there is now a wider international interest in LDRT for these conditions [2]. Numerous retrospective series describe the benefits of LDRT for non-malignant joint disorders, with response rates between 63-89% [3], but randomized and prospective data are scarce, [4, 5, 6].
Objectives: To prospectively evaluate pain, function and quality of life after low dose radiotherapy (LDRT) in patients with lateral and medial epicondylitis (LE and ME), finger osteoarthritis (OA) and plantar fasciitis (PIF).
Methods: Patients over 40 years old were recruited to this single center trial. LDRT (8 x 0.5 Gy, 200 kV X-rays) was repeated once up to a total dose of 8.0 Gy. Pain scores (visual analogue scale=VAS), function tests and quality of life questionnaires were documented at 0, 2, 6, and 12 months.
Results: 204 sites were treated. At 12 months after last LDRT (first or second course) compared with baseline prior to first LDRT: 39 LE sites reported pain reduction (median change in VAS) at rest (-2.5, p<0.001), during activity (-6.0, p<0.001) and increase in handgrip strength (median change: extension 16 kg, p<0.001, flexion 5.2 kg, p=0.002). 10 ME sites showed pain relief at rest (-3.0, p=0.041), during activity (-0.4, p=0.041) and an increase in handgrip strength (6.5 kg, p=0.022). 99 finger OA sites reported significant pain relief during activity (-3.0, p<0.001) with a trend at rest (0.0, p=0.056) and gain in handgrip strength (2.5 kg, p=0.004) with a trend to stronger pinch grip (0.5 kg, p=0.099). 56 PIF sites reported reduction in pain scores at rest (-4.0, p<0.001), during activity (-6.0, p<0.001) and an improvement in the walking test (-5.0 seconds, p<0.001). A trend towards improved quality of life was seen in patients with ME and PIF.
Conclusion: Patients with LE and ME, finger OA and PIF achieved sustained analgesia and an objective improvement in musculoskeletal function 12 months after completion of LDRT with 4-8 Gy.

REFERENCES:

[1] Keilholz L et al. Radiotherapy for painful degenerative joint disorders. Indications, technique and clinical results. Strahlenther Onkol 1998;174:243-250.
[2] Taylor RE et al.Radiotherapy for benign disease: Current evidence, benefits and risks. Clin Oncol 2015;27:433-435.
[3] Seegenschmiedt MH et al. Radiotherapy for non-malignant disorders: State of the art and update of the evidence-based practice guidelines. Br J Radiol 2015;88:20150080.
[4] Ott OJ et al. Radiotherapy for calcaneodynia. Results of a single center prospective randomized dose optimization trial. Strahlenther Onkol 2013;189:329-334.
[5] Prokein B et al. Radiotherapy of painful heel spur with two fractionation regimens : Results of a randomized multicenter trial after 48 weeks' follow-up. Strahlenther Onkol 2017;193:483-490.
[6] Niewald M et al. German Cooperative Group on Radiotherapy for Benign Diseases of the German Society for Radiation O. Randomized, multicenter trial on the effect of radiation therapy on plantar fasciitis (painful heel spur) comparing a standard dose with a very low dose: Mature results after 12 months' follow-up. Int J Radiat Oncol Biol Phys 2012;84:e455-462.

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THU0499 RISK FACTORS FOR SHOULDER PAIN PERSISTENCE IN ROTATOR CUFF DISORDERS

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Background: A large proportion of patients with atraumatic painful shoulder have an unfavorable outcome with long-term disability (1). Predictors of no recovery in patients with shoulder disorders were identified previously: repetitive overhead activity in sport and work (2) duration of complaints, somatization, low social support, older age, unemployment, musculoskeletal comorbidity, recurrent complaint (3,4).
Objectives: To identify the risk factors for over 6 mounth pain persistence in patients with rotator cuff disorders
Methods: Our prospective study included 51 hospitalized patients with atraumatic shoulder pain. The assessment was clinical and shoulder MRI for confirmation of rotator cuff disorders. We have studied the influence of the patient's characteristics and the influence of the condition's characteristics for pain persistence. Statistical analysis was performed in SPSS-18, p<0.05 was significant.
Results: No significant correlations were found between pain persistence and age, gender, smoking status, occupational overuse, physical demands before the onset of pain, marital status, continuous pain, lesions on shoulder MRI. The association with the following elements is statistically significant for pain persistence: opposite shoulder previously affected (p=0.01), diabetes mellitus(p=0.04), insidious onset(p=0.004), the high educational level(p=0.02), physical therapy(p=0.03), local injection (p=0.08). Using multinominal regression we observed only acute onset of the pain shoulder (RR=7.1) and physiotherapy treatment (RR=0.1) with p=0.026.
Conclusion: The factors that determine the shoulder pain persistence are non-specific and can be sometimes psyhosocial, local, physical or other comorbidities like diabetes.

REFERENCES:

[1] Herin F et al. Predictors of chronic shoulder pain after 5 years in a working population. *Pain.* Volume 153, Issue 11, Pages 2253-2259, November 2012
[2] Coggon D., Ntani G., Vargas-Prada S., et al. International variation in absence from work attributed to musculoskeletal illness: findings from the CUPID study. *Occup Environ Med.* 2013 Aug;70(8):575-84.
[3] Keijsers E et al. *Psychosocial factors predicted nonrecovery in both specific and nonspecific diagnoses at arm, neck, and shoulder.* J Clin Epidemiol. 2010 Dec;63(12):1370-9;
[4] Feleus A et al. Prognostic indicators for non-recovery of non-traumatic complaints at arm, neck and shoulder in general practice—6 months follow-up. *Rheumatology 2007*;46:169–176

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THU0500 PELVIC CONGESTION SYNDROME, UNCOMMON CAUSE OF LOW BACK PAIN

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Background: The pelvic congestion syndrome (PCS) is an under and often misdiagnosed entity that appears more frequently in premenopausal age and multiparous women. The pathophysiology consists of a sum of phenomena including venous stasis and inversion of the pelvic venous flow that cause varicose veins and congestion. The left ovarian vein is usually the most affected. Typically it presents as a dull, chronic abdominal-pelvic (AP) pain, which worsens with menstruation and prolonged

standing, and lasts longer than six months. Pain is associated with dyspareunia and varicosities in lower limbs (LL) and genitals. It is challenging and important to consider atypical clinical presentations that simulate osteoarticular (OA) pathologies. It is usually diagnosed by Angio-CT, and a safe, definitive and successful treatment is the embolization of the affected vein.

Objectives: The objective of this study was to evaluate the characteristics of those patients diagnosed with PCS in our University hospital from January 2014 to May 2018, paying close attention to the atypical forms of presentation that simulate OA pathology.

Methods: We included all patients from our center who were operated by embolization due to a PCS from January 2014 to May 2018. Socio-demographic variables, forms of presentation, pain characteristics, associated symptoms, patient management and outcome data were collected.

Results: Sixty women were included with a mean age of 43 years at diagnosis, 87% (n=52) were multiparous, with a mean of 2 previous pregnancies. In 95% (57) of all cases the duration of symptoms until the diagnosis exceeded 6 months. Patients were classified according to presence and location of pain in 4 groups: 1. Women with AP pain, 23% (14); 2. Women with OA pain 5% (3); 3. Women with mixed AP and OA pain, 59% (35); and 4. Women with other symptoms 13% (8). Regarding patients from groups 2 and 3 (only OA pain or mixed pain) (38), 90% (34) of them presented low back pain, 53% (20) hip pain and 40% (15) sciatic pain. Only 5% (3) of all patients were evaluated by a rheumatologist.

As for the pain characteristics from groups 1, 2 and 3 (52), in 72% (37) of patients it was diurnal, in 48% (25) it worsened with menstruation, in 62% (32) it worsened with prolonged standing and in 35% (18) it worsened at rest. Among the associated manifestations, stand out the presence of LL varicose veins in 74% (38) of patients, genital varicosities in 58% (30), dyspareunia in 42% (22), dysmenorrhea in 40% (21), hemorrhoids in 37% (19) and dysuria in 18% (9). All patients underwent embolization of the affected vein, with an initial Visual Analogue Scale (VAS) mean of 7.38 over 10, and final VAS mean of 2.63. The mean recovery time was 36 days. The evolution was good or very good in 84% (32) of patients with mixed (AP and OA) pain and in 57% (8) of those who only had AP pain. Less than 2% (1) had a recurrence without the need for reoperation.

Conclusion: PCS is a rare entity, typically associated with long lasting AP pain, but, in more than half the cases, is accompanied with OA symptoms, mainly low back pain. It is important and challenging for the rheumatologist to identify these patients, since treatment is usually safe and effective, and diagnostic delay worsens their quality of life.

Disclosure of Interests: None declared

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27. BACK PAIN, MECHANICAL MUSCULOSKELETAL PROBLEMS, LOCAL SOFT TISSUE DISORDERS

THU0501 MUSCULOSKELETAL DISORDERS IN TYPE 1 AND 2 DIABETIC PATIENTS: PREVALENCE AND ASSOCIATION WITH MICROVASCULAR COMPLICATIONS OF DIABETE

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Background: Diabetes mellitus (DM), a worldwide high prevalence disease, is associated with a large variety of musculoskeletal (MS) disorders. They are poorly treated, as compared to microvascular complications. However, they are a common source of disability.

Objectives: We designed this study to assess the prevalence of MS disorders among diabetic patients and their relation to microvascular complications of diabetes.

Methods: A cross-sectional study enrolled consecutive subjects with diabetes seen in the Endocrinology department. We recorded age of patients, sex, body mass index, type and duration of diabetes, Long-term glycemic control assessed by hemoglobin A1c levels, and lipid profile. Musculoskeletal and microvascular disorders assessment was done by detailed history with clinical examinations and investigations if needed.

Results: A total of 376 subjects were studied, (84.6% had type 2 diabetes). The mean age was 52.5±13.9 years, 41% had one or more microvascular complications, among which retinopathy was present in 28.2%, nephropathy in 16.1% and neuropathy in 12.8%. Moreover, 23.4% of the patients had one or more musculoskeletal disorders. Shoulder capsulitis was present in 12.5%; carpal tunnel syndrome in 8.8%; trigger finger in 5.9%; and 2.9% had diabetic cheiroarthropathy. Dupuytren's contracture and Charcot foot, were found in 0.5% and 0.3% of the cases respectively. Symptomatic osteoarthritis was found in 19.4%. Musculoskeletal disorders prevalence increased with age, diabetes duration, presence of dyslipidemia and various microvascular complications.

Abstract THU0460 –Table 1. Distribution of cases according to MS disorders in relation to type of diabetes

MS disorders	Type of diabetes					Total N =376	
	Type 1 N = 58		Type 2 N = 318		P		
	No.	%	No.	%	%	No.	%
Osteoarthritis	2	3.4	71	22.3	**0.001***	73	14.9
Shoulder capsulitis	2	3.4	45	14.2	**0.023***	47	12.5
Carpel Tunnel Syndrome	5	8.6	28	8.8	0.969	33	8.8
Limited joint mobility	0	0	11	3.5	0.151	11	2.9
Trigger Finger	2	3.4	20	6.3	0.397	22	5.9
Dupuytren's contracture	0	0	2	0.6	0.545	2	0.5
Charcot's Foot	1	1.7	0	0	0.154	1	0.3
Total MS disorders	10	17.2	78	24.5	0.149	88	23.4

Conclusion: this study shows a high prevalence of musculoskeletal disorders in diabetic's patients which were significantly associated with advanced age, longer duration of diabetes, presence of dyslipidemia and microvascular complications.

Disclosure of Interests: : None declared

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THU0502 DIFFERENTIAL DIAGNOSIS OF MONOARTHRITIS: THREE CASES WITH PIGMENTED VILLONODULAR SYNOVITIS

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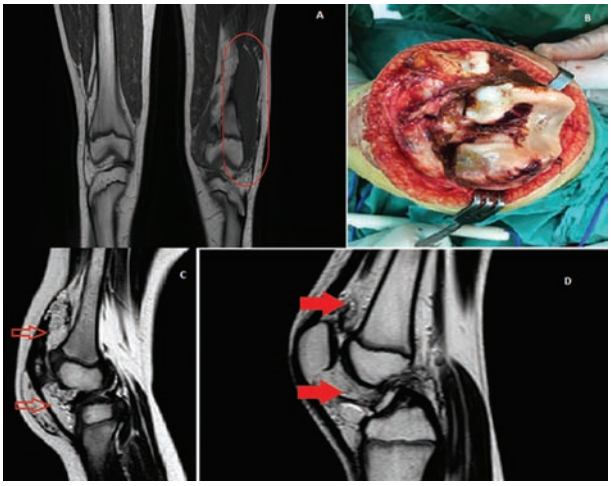
Background: Pigmented Villonodular Synovitis (PVNS) is a proliferative disorder of synovium that affects synovial joints, tendon sheaths and bursas. The estimated incidence is around 1.8 cases per million people in a population. PVNS is usually found in adults aged 20-50 years, but it may occur also in children. As it is a rare pathology in children, diagnosis is often delayed, and it is difficult to distinguish from Juvenile Idiopathic Arthritis (JIA), hemophilic arthropathy, tuberculosis, and other neoplastic processes.

Objectives: The aim of this case series is to emphasize PVNS in the differential diagnosis of monoarthritis, and the importance of interpretation of imaging, i.e. MRI.

Methods: Three pediatric PVNS cases who were misdiagnosed as monoarticular JIA and familial Mediterranean fever (FMF) are presented as case series.

Results: Case-1. A 14 year-old male had swelling and pain on his left knee for one year. An MRI of knee was reported as joint effusion in suprapatellar bursa, and he was referred to our clinic as monoarticular JIA. He was on methotrexate (MTX) 15 mg/m^2/wk. SC, and despite effective treatment there was no improvement. MRI was performed by a pediatric radiologist who was an expert on musculoskeletal diseases. Joint effusion and a lesion compatible with PVNS were observed in left suprapatellar recess (Figure-A). Arthroscopic synovectomy was performed and histopathological result was PVNS.

Case-2: A one year-old female had swelling on her right knee for three months after a minor trauma. On physical examination, she had effusion of the right knee which was confirmed on USG. She was diagnosed as monoarticular JIA and intraarticular triamcinolone hexacethonide injection was performed. She was unresponsive to adequate non-steroid drug therapy, and MTX was started. Despite intensive therapy, there was no change. MRI showed focal lesions with high signal in T2 weighted images in suprapatellar and intraarticular areas, and findings were evaluated as compatible with PVNS (Figure-B). Total synovectomy was performed and PVNS was confirmed in pathological evaluation (Figure-C). she is in complete remission without treatment.



Abstract THU0502 – Figure 1. **A.** Hypo intense mass lesion in the left knee of the first case and on the in the suprapatellar and intraarticular areas (T-1-weighted MRI image). **B.** Intraoperative image of open approach total synovectomy (second case). **C.** Suprapatellar and intraarticular lesions compatible with PVNS right knee of second case (T-2 weighed image). **D.** Suprapatellar and intraarticular focal hyper intense lesions (T-2-weighted MRI image).

Case-3: An eleven-year-old female was referred to our clinic with recurrent swelling and pain on her right knee. Attacks lasted for 2-3 days and resolved spontaneously, accompanied by abdominal pain and vomiting. FMF attack was suspected, for she had signs of peritonitis with knee arthritis, and elevated acute phase reactants. A744S/R202Q compound heterozygote mutations were detected in the MEFV analysis. Colchicine was started 1 mg/kg/ per day. Abdominal pain attacks were resolved with colchicine, but articular symptoms persisted. MRI of the right knee detected focal hyper intense lesions in T2 weighted images compatible with PVNS. Total synovectomy was performed and confirmed PVNS.

Conclusion: PVNS is a rare but serious reason for joint effusion, presented as chronic arthritis. It should be considered in the differential diagnosis of mono-arthritis, especially when the patient is unresponsive to specific treatment for JIA. MRI is the best diagnostic tool in imaging, and histopathological evaluation should be performed to confirm the diagnosis.

REFERENCE:

[1] Karami M, Soleimani M, Shiari R. Pigmented villonodular synovitis in pediatric population: review of literature and a case report. Pediatr Rheumatol Online J.2018 Jan 17;16(1):6.

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THU0503 ICONOGRAPHIC STUDY OF ACUTE MECHANICAL HIP PAIN IN YOUNG PATIENTS: CLINICAL-ULTRASONOGRAPHIC CORRELATE AND PROPOSAL OF DIAGNOSTIC-THERAPEUTIC ALGORITHM

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Background: Coxarthrosis is the first cause of mechanical pain and functional limitation of the hip joint, however its prevalence in subjects over 65 years is much higher than the incidence of these symptoms so its causal link is not complete. In a young population, mechanical groin pain of acute origin is usually linked to periarticular processes mainly related to adductor muscles, psoas and tendons with pertrocanteric entheses. In the routine approaches of these patients, when they consult, the simple radiological study is included and it is usually treated with NSAIDs, assuming tendinopathy as a diagnostic process.
Objectives: The purpose of this study is to determine the ultrasound characteristics of the coxofemoral joint of patients who consult for acute inguinal pain, correlate it with its clinical presentation and propose a reasoned strategy for its management.
Methods: We reviewed the clinical records of patients under the age of 50 who consulted for direct non-traumatic hip joint pain. Only cases with less than one week of evolution were included. Patients who consulted on weekends or in the afternoon were not included in this register because of the lack of immediate ultrasound study during these periods of time. We excluded those patients who, during the consultation, acknowledged having used anti-inflammatory drugs in the last 24 hours and those whose records are incomplete. The ultrasounds were performed with a portable Logiq e ultrasound machine, equipped with a linear probe of up to 12MHz.
Results: Between 2014 and 2017, 211 patients under 50 years of age consulted for non-traumatic mechanical groin pain. Excluding patients who consulted outside of the immediate ultrasound study access hours, who had recently taken NSAIDs and whose clinical records were incomplete, we reviewed 116 clinical and image records. The mean age of the patients whose records were included was 37.8 SD 8.5. The mean time, in days, between the consultation and the onset of symptoms according to history constancy was 4 SD 2. 59 subjects were male (50.9%). In the physical examinations described in the reports, 29 patients (25%) presented painful passive manoeuvres, 38 (32.8%) presented painful active manoeuvres, and 22 (19%) could not maintain standing due to the impossibility of loading due to coxofemoral pain. Regarding the ultrasound findings, 5 patients presented unequivocal capsular distension at the level of the upper anterior labrum (4.3%) and 32 (27.6%) presented distension of the anterior recess. One patient with capsular distension was finally diagnosed with ONA and another with APso.

Abstract THU0503 – Table 1. summarizes the prevalence of clinical findings depending on the existence or not of distension of the anterosuperior labrum or of the previous recess in the ultrasound scan performed.

Physical examination results		Joint capsule				Joint recess			
		Normal		Distended		Normal		Distended	
		N	% of row	N	% of row	N	% of row	N	% of row
Inability to stand	NO	94	100,0%	0	0,0%	79	84,0%	15	16,0%
	YES	17	77,3%	5	22,7%	5	22,7%	17	77,3%
Painful passive maneuvers	NO	87	100,0%	0	0,0%	72	82,8%	15	17,2%
	YES	24	82,8%	5	17,2%	12	41,4%	17	58,6%
Pain to mobility against resistance	NO	78	100,0%	0	0,0%	65	83,3%	13	16,7%
	YES	33	86,8%	5	13,2%	19	50,0%	19	50,0%

Conclusion: Our results show that in the studied population (<50 years old, non-traumatic coxofemoral pain of sufficient intensity to be consulted in the emergency department in less than 7 days of evolution) synovitis is a finding present in a quarter of patients and that it is severe in approximately 4%. Its strong association with incapacity for load and passive joint dysfunction would condition the incorporation of these findings in therapeutic decision making, including -in these cases- rest in unloading. On the other hand, the absence of synovitis in $^{3}/_{4}$ parts of the patients strongly suggests a muscular etiology that with high probability will respond positively only to NSAIDs. The incorporation of ultrasound, in our opinion, plays a role of diagnostic clearance when the semiological exploration is doubtful.

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THU0504 ROTATOR CUFF CALCIFICATION AND SHOULDER PAIN: A CLINICAL AND ECHOGRAPHIC STUDY OF 465 PATIENTS

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Background: Shoulder pain is a common cause for medical consultation and is commonly linked to lesions of the rotator cuff. Rotator cuff calcification (due to BCP crystal deposition) is also a common finding and can give rise to chronic pain as well as acute inflammatory episodes
Objectives: The goal of the study was to compare the clinical and the echographic characteristics of patients with BCP calcification in the rotator cuff and shoulder pain to those with no signs of calcification
Methods: A retrospective case-control study of 465 patients whose primary complaint was shoulder pain presenting between 1997 and 2011 and seen by one rheumatologist. 125 patients who had rotator cuff calcification (RCC) were identified and constituted the study group. We compared the patients with RCC with 125 patients without calcification who were randomly extracted from the same registry which constituted the control group. All had detailed demographic and clinical documentation as well as a precise description of the echographic findings. Subgroups

were defined according to the type and the duration of symptoms (Hyperacute painful shoulder, subacute inflammatory symptoms and chronic mechanical pain). Short-term response (up to 6 weeks) to treatment was also analyzed for the two first subgroups

Results: 25% of the patients consulting for shoulder pain had evidence of RCC as demonstrated by ultrasound. Hyperacute and subacute inflammatory symptoms were not linked to calcification (Hyperacute: 16 pts with 13pts without (p value : ns), subacute: 32 pts in both groups). The mean age (54 years) and female predominance (60%) were also similar in patients with or without calcification. However, patients with hyperacute painful shoulder with RCC were younger (mean years: 49 against 58 years; p: 0.007). None were <35 or > 60 years old and 75% of them were females. In 60% of cases of hyperacute painful shoulder linked to calcification, the acute flare was the first shoulder complaint compared to <30% in the overall sample (p: <0.0001).

More than a 1/3 of the patients with RCC (35% in chronic and 43% in acute symptom groups) had no other echographic lesion compared to < 5% of patients without RCC. Calcifications were rarely associated with partial or total rotator cuff rupture (<10% against 25% without, p: 0.007).

Steroid infiltrations were mostly performed with rapid short-term response in the acute and subacute groups linked to calcification: 15/16, 24/34 against 4/13 p:0.001, 10/34 p:0.001 without calcification. Surgery was necessary in 7/101 pts with chronic symptoms without calcification against only 1/95 when calcifications were present (p:0.03).

Conclusion: Clinical and demographic data cannot clearly predict the presence of RCC in patients presenting with shoulder pain. However, acutely symptomatic RCC is found preferentially in middle aged women, often with no degenerative or traumatic echographic lesions. Steroid infiltration appears to be the treatment of choice when acute inflammatory symptoms linked to RCC are present

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Basic science in paediatric rheumatology

THU0505 INTRINSIC AND EXTRINSIC B CELL DEFECT IN DADA2 PATIENTS

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Background: ADA2 Deficiency is an autoinflammatory disease characterized by systemic vasculopathy, strokes and mild immunodeficiency. The defect is due to a mutation in ADA2 gene. It regulates the catabolism of extracellular adenosine, which is an important regulator of Class Switch Recombination in B lymphocytes.

Objectives: We addressed if ADA2 mutation affects directly B-cell function and the capacity of helper T cells to support B cells.

Methods: 14 patients carrying LOF mutations in ADA2 were examined. We analyzed immunophenotype by flow cytometry. B cells isolated from DADA patients or HD have been cultured alone or in co-culture with CD4+ T cells and *in vitro* B cell proliferation has been evaluated by CFSE dilution, whereas B cell differentiation to Immunoglobulins secreting cells in response to TLR9 agonist and T cell help has been evaluated by ELISA assay.

Results: Flow-cytometric analysis showed a significant reduction of switched memory B cells and of CD4+/CD8+ T cells. We identified an significant expansion of circulating Tfh cells in DADA2. Then we investigated a role of ADA2 in B cells: we found that it is expressed, secreted but the activity is strongly impaired in DADA2. We also addressed the interaction between B and T cells; we found that proliferation and differentiation of patients' B cells were not sustained from patient's T cells. Moreover DADA2 T cells showed an impairment in the IL21 production and a downregulation of CD40L.

Conclusion: Our findings suggest that ADA2 mutation could affects directly B cell function and T cell help functions.

REFERENCES:

[1] Zhou Q, et al. Early-onset stroke and vasculopathy associated with mutations in ADA2. N Engl J Med 2014 Mar 6;370(10):911-20.

[2] Navon EP, et al. Mutant adenosine deaminase 2 in a polyarteritis nodosa vasculopathy. N Engl J Med 2014 Mar 6;370(10):921-31.

[3] Schepp J, et al.Screening of 181 Patients with Antibody Deficiency for Deficiency of Adenosine Deaminase 2 sheds new lights on the disease in Adulthood. Arthritis and Rheum 2017 August; Vol. 69, 8:1689–1700.

[4] Caorsi R, Monogenic polyarteritis: the lesson of ADA2 deficiency. Pediatr Rheumatol Online J 2016;14(1):51.

[5] Caorsi R. et al.ADA2 deficiency (DADA2) as an unrecognised cause of early onset polyarteritis nodosa and stroke: a multicentre national study. Ann Rheum Dis 2017; 0:1-9.

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I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:

AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.

The money received for these activities are directly transferred to the Gaslini Institute's bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Elisabetta Traggiai Employee of: Novartis, Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis

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THU0506 MAST CELL DEFICIENCY AMPLIFIES INFLAMMATORY RESPONSE IN A MOUSE MODEL OF KAWASAKI'S DISEASE

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Background: Kawasaki's disease is a pediatric medium vessel vasculitis causing coronary arteritis and potentially coronary artery aneurysms. Higher systemic levels of Interleukin-6 (IL-6) in the first week of disease has been shown to be associated with a higher risk of coronary artery aneurysms (1, 2). Mice injected with *Candida albicans* water-soluble fraction (CAWS) develop coronary and aortic arteritis like that seen in Kawasaki's disease. Our prior work has demonstrated that mast cell degranulation can inhibit lipopolysaccharide (LPS)-induced IL-6 gene expression in the aorta and systemic IL-6 production (3).

Objectives: The objective of this study was to determine if mast cells play a role in the IL-6 homeostasis in an established mouse model of Kawasaki's disease (CAWS model).

Methods: 8-10-week-old male wild type controls (WT) and kitW-sh/W-sh mice (mast cell deficient, MCD) of C57Bl/6 background were randomly distributed into four groups (WT-PBS, WT-CAWS, MCD-PBS, MCD-CAWS). They were either injected intraperitoneally with PBS or CAWS (2 mg/mouse) daily for a period of 5 days. Eight animals from each group

were sacrificed at either 7, 14 or 30 days after the last injection and blood, aorta and heart specimens were harvested. A pathologist (OT), blinded to treatment groups, examined aortic root and adjacent myocardium specimens and assigned a score for the degree of inflammation (0-6).

Results: Seven MCD-CAWS mice died unexpectedly within 24 hours of the first CAWS injection. Autopsies reviewed marked liver sinusoidal dilation in all and patchy necrosis of the liver in 4. Similar, liver findings were seen in 75% of MCD-CAWS after 7 days, but not in other groups. MCD-CAWS mice had higher systemic IL-6 compared to WT-CAWS at both 7 days (208± 21 vs 152 ± 12 pg/ml; p<0.001) and 14 days (226 ± 49 vs 169 ± 19 pg/ml; p=0.04), but not at 30 days. By 14 days mice in MCD-CAWS had significantly higher serum INFγ compared to WT-CAWS mice (97 ± 4 vs 87 ± 7 pg/ml, p=0.0086) which remained persistently elevated even at 30 days (103±8 vs 91±4 pg/ml; p=0.002). TNFα was higher in MCD-CAWS compared to WT-CAWS at 7 days (258 ± 8 vs 243 ± 6.5 pg/ml, p=0.0016), 14 days (266± 14vs 239 ± 6pg/ml, p<0.001) and 30 days (326±52 vs 256±8 pg/ml, p=0.002). The average aortic root inflammatory score was non-significantly higher in the MCD-CAWS group compared to WT-CAWS at both 7 days (1.5 vs 1.3) and 14 days (3.7 vs 2.4).

Conclusion: Mast cell deficiency resulted in higher systemic levels of IL-6, TNFα and INFγ in the CAWS mouse model of Kawasaki's disease. Similarly, mast cell deficiency resulted in more intense inflammation at the root of the aorta in this model. These results support the novel concept that mast cells play a protective role in reducing the initial systemic inflammatory response in Kawasaki's disease.

REFERENCES:

[1] Ueno Y, Takano N, Kanegane H, Yokoi T, Yachie A, Miyawaki T, et al. The acute phase nature of interleukin 6: studies in Kawasaki disease and other febrile illnesses. Clinical and experimental immunology. 1989;76 (3):337-42.

[2] Chow YM, Lin CY, Hwang B. Serum and urinary interleukin-6 (IL-6) levels as predicting factors of Kawasaki disease activity. Zhonghua Minguo xiao er ke yi xue hui za zhi [Journal] Zhonghua Minguo xiao er ke yi xue hui. 1993;34(2):77-83.

[3] Springer J, Raveendran V, Smith D, Maz M, Dileepan K. OP0138 Novel Role of Mast Cells in the Regulation of Large Vessel Vasculitis. EULAR Paris, France: *Ann Rheum Dis*; 2014. p. 112-3.

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THU0507 TYPE I INTERFERON SCORE AND INTERFERON INDUCED MEDIATORS CXCL10 AND NEOPTERIN ARE CORRELATED WITH DISEASE ACTIVITY IN JUVENILE DERMATOMYOSITIS

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Background: Interferons (IFNs) seem to play an important role in the pathogenesis of juvenile dermatomyositis (JDM). Our group previously reported that expression of both type I and type II IFN related genes is increased in muscle biopsies of JDM patients and correlates with histological and clinical features of the disease.

Objectives: The aim of this study was to investigate expression of interferon regulated genes (IRGs), as well as serum levels of two type I and type II IFN induced chemokines (CXCL9, CXCL10) and neopterin in peripheral blood of JDM patients and to assess their correlations with clinical and laboratory findings.

Methods: We collected 189 blood samples from 39 JDM patients at different time points during follow-up. In 11 patients we obtained the first blood sample at time of muscle biopsy. We measured expression of type I IRGs (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1), IFNg and type II IRGs (CXCL9, CIITA, IDO1) by quantitative PCR (qPCR) and calculated a type I and type II IFN score for muscle and blood samples; serum levels of CXCL9, CXCL10 and neopterin were analyzed by ELISA. Ten healthy subjects were used as controls (HC). At each visit, the following clinical data were recorded: physician's global assessment (PGA) of disease activity VAS (Visual Analogue Scale), cutaneous VAS, Cutaneous Assessment Tool (CAT) activity score, Childhood Myositis Assessment Score (CMAS), serum levels of creatine phosphokinase (CK, IU/l), presence of myositis specific or myositis associated antibodies (MSA/MAA), prednisone (or equivalent) dose (mg/kg/daily), ongoing immunosuppressive medications.

Results: Serum levels of CXCL9 where significantly correlated with muscle expression of IFNg and type II IFN score. The correlation of CXCL10 levels with muscle type I and type II IFN score was weaker. Muscle expression of CXCL9 and CXCL10 correlated with serum levels of these chemokines. Type I IFN score in blood of JDM patients was increased compared to HC and significantly correlated with PGA, cutaneous VAS, CAT activity score. Serum levels of CXCL9 and CXCL10 were significantly higher in JDM patients compared to HC. MSA positive JDM patients showed higher levels of CXCL9 and CXCL10 compared to MSA negative patients. CXCL10 levels correlated with PGA and CMAS, but not with cutaneous disease activity. CXCL9 showed no significant association with the evaluated clinical features. Neopterin levels significantly correlated with PGA, cutaneous VAS, CAT activity score and CMAS.

Conclusion: Our findings indicate that expression of IRGs, measured as type I IFN score, and serum levels of CXCL10 and neopterin reflect specific features of disease activity in JDM, supporting their role as valuable disease biomarkers.

REFERENCES:

[1] Moneta GM, Pires Marafon D, Marasco E, Rosina S, Verardo M, Fiorillo C, Minetti C, Bracci-Laudiero L, Ravelli A, De Benedetti F, Nicolai R. Muscle Expression of Type I and Type II Interferons Is Increased in Juvenile Dermatomyositis and Related to Clinical and Histological Features. Arthritis Rheumatol. 2018 Dec 15. doi: 10.1002/art.40800.

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THU0508 CHANGES IN MIR-17–92 CLUSTER EXPRESSION LINK SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS, MONOCYTE-TO-MACROPHAGE DIFFERENTIATION, AND INTERFERON REGULATION

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Background: MicroRNAs (miRNAs) are small noncoding RNAs which post-transcriptionally regulate gene expression. The miR-17-92 cluster is well studied in cancer biology and cellular differentiation; its overexpression has been found to serve a major oncogenic role in the targeting and downregulation of tumor-suppressive pathways, such as PTEN or TGFß. Our previous work identified several members of the cluster – miR-18, miR-19a/b, miR-20a, and miR-92a – with significantly higher levels in monocytes from patients with active Systemic Juvenile Idiopathic Arthritis (SJIA). SJIA is a chronic inflammatory disease of childhood with features of autoinflammation, and innate immune cells including monocytes have important roles in disease pathogenesis. Children with SJIA are at risk for life-threatening complications including Macrophage Activation Syndrome (MAS), an episode of overwhelming inflammation characterized by macrophage proliferation and driven by IFNγ.

Objectives: Characterize the regulation of the miR-17-92 cluster, define key targets, and determine the cluster's role in inflammation and SJIA.

Methods: MiRNA levels were examined in THP-1 cells, as well as primary human monocytes isolated from healthy donors over the course of the monocyte to monocyte-derived macrophage (MDM) transition. MiR-17, miR-19a, and miR-20a were overexpressed via transfection in CD14+ monocytes for 2 days. Transcriptional profiles were performed using Ampliseq Transcriptome and the Ion Torrent S5 system and analyzed using AltAnalyze. Potential targets of the miR-17-92 cluster determined from sequencing analysis were then validated via dual-luciferase reporter assay.
Results: Neither blood monocytes nor fully differentiated THP-1 cells showed significant changes in miR-17-92 levels under standard polarization conditions, including M1, M2a, and M2b conditions, or IL-6 and IL-10 stimulation. The most sizable changes in miR-17-92 levels were found during monocyte to macrophage transition. Interestingly, primary monocytes showed increases in miR-17-92 levels within the first 48 hours of differentiation towards MDM, variable by miRNA and experiment, similar to that seen in SJIA monocytes. In contrast, both PMA-differentiated THP1 cells and fully differentiated MDMs showed decreased miR-17-92 compared to undifferentiated monocytic cells. MiR-17-92 was overexpressed in vitro in primary monocytes to model these early transition changes. Genome-wide transcriptional profiling showed an upregulation of genes involved in Type I and II Interferon pathways, including response to interferon-alpha (adjusted $p=2.71x10^{-12}$) and interferon-gamma (adjusted $p=7.81x10^{-9}$). Analysis of genes significantly downregulated by miR-17, miR-19a, or miR-20a identified several putative and previously validated miR-17-92 cluster targets, including ATG5, IFRD2, JAK1, PPARG, and PTPN2 which have interferon-regulatory functions. Dual-luciferase reporter assay experiments support that these genes are direct targets of miR-17, miR-19a, and/or miR-20a.
Conclusion: MiR-17-92 cluster members demonstrate initial increase followed by subsequent decrease in expression during 2-week human monocyte to macrophage differentiation. Overexpression of miR-17-92 miRNAs upregulates Type I and II interferon pathway genes, and these miRNAs target multiple genes involved in regulating interferon signaling and/or inflammatory response. Taken together, miR-17-92 cluster overexpression in SJIA monocytes may suggest a more differentiated phenotype, and contribute to IFNγ sensitivity and risk for MAS.
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THU0509 MONOCYTES PROTEOMIC PROFILE OF PATIENTS WITH DIFFERENT AUTOINFLAMMATORY DISEASES: A NEW APPROACH TO CHARACTERIZE THESE DISEASES

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Background: Autoinflammatory diseases are a group of inherited diseases characterized by early onset and systemic inflammation. These pathologies are caused by mutations in genes involved in the regulation of innate immune response with a consequent inflammatory phenotype. The most common genetically defined periodic fevers are Familial Mediterranean Fever (FMF), Cryopyrin-associated periodic syndromes (CAPS), TNF receptor-associated periodic syndrome (TRAPS) and mevalonate kinase deficiency (MKD/HIDS).
Some patients show clinical features similar to autoinflammatory diseases but no genetic mutation has been found.
Objectives: Our aim is to evaluate the differences in the expression of proteins or pathway in monocytes, and plasma metabolites in patients with autoinflammatory diseases compared with healthy subjects to clusterize and better understand the mechanisms underlying different genetically defined disorders and try to characterize the genetically undefined pathologies.
Methods: Monocytes, purified from peripheral blood and incubated with or without LPS, were collected from patients and healthy donors; samples have been processed by iST protocol. Each digested sample was analyzed by high-resolution liquid chromatography and tandem mass spectrometry (LC-MS/MS) based on Orbitrap technology. The quantification strategy is a label-free approach (LFQ) available in MaxQuant suite.
Results: Here we identified a median of about 5000 proteins from the monocyte samples of each 4000 are quantified by LFQ approach. PCA analysis and Person's correlation show good reproducibility of data and a good separation between the different groups. The data were then submitted to an appropriate statistic. T-Tests highlighted differentially expressed proteins and through Cytoscape with the ClueGo app we obtained the differently regulated pathways in the different conditions. It has also been constructed, starting from significative proteins, a network, related to disease using the information of String Disease db. We observed that the expression of proteins is differently enriched according to the different conditions. For each autoinflammatory disease, a list of significantly modulated proteins was obtained: some of which are already known to be related to the disorders, while others have not yet been described. In FMF, MEFV, RhoA and some related proteins were significantly up-regulated together with genes linked to the interferon pathway. In TRAPS relevant proteins turn up related to the maintenance of Golgi and cellular trafficking. The bioinformatics analysis allows us to better understand the functional interaction between these monocytes proteins and map which are involved in the diseases.
Conclusion: Here, we addressed how a high-resolution proteomics approach could be used to better understand the biology of autoinflammatory diseases. The characterization of a broad spectrum of proteins and their interaction network will allow us to identify new biomarkers for the different pathologies and better comprehend and recognize the genetically undefined disorders.

REFERENCES:

[1] Lucherini O M, Rigante D, Sota J, et al. Update overview of molecular pathways involved in the most common monogenic autoinflammatory diseases. *Clin Exp Rheumatol* 2018.
[2] Rieckmann JC, Geiger R, Hornburg D, et al. Social network architecture of human immune cells unveiled by quantitative proteomics. *Nat Immunol* 2017.

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THU0510 NEUTROPHIL FUNCTION IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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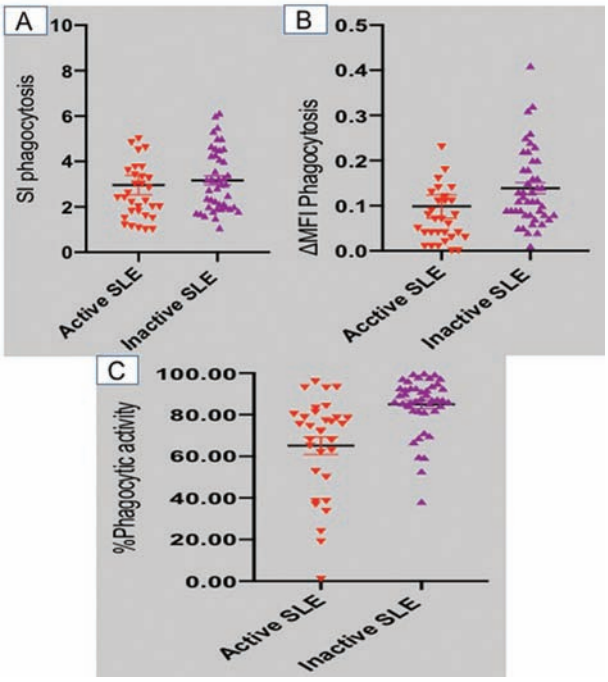
Background: While the role of adaptive immune system in pathogenesis of systemic lupus erythematosus (SLE) has been well characterized, there is paucity of literature on innate immunity in these patients. There are limited data on neutrophil function in pediatric lupus. In this study we analyzed neutrophilic functions in a cohort of pediatric lupus from North India.
Objectives: To evaluate phagocytic and oxidative burst activity of neutrophils in patients with pediatric-onset SLE
Methods: This prospective study was carried out at a tertiary care center in North India in patients with SLE during the period July 2017 to December 2018. Diagnosis of lupus was based on SLICC 2012 criteria and patients who had disease onset below 18 years were included. Controls were age matched children attending the outpatient clinic of department. Disease activity was measured by SELENA-SLEDAI score. Phagocytic activity was estimating using the pH Rhodo *Escherichia coli (E coli)* BioParticles kit by flow cytometry. Phagocytic function was measured as% phagocytic activity of neutrophils, delta mean fluorescent intensity (ΔMFI), and stimulation index (SI). Oxidative burst activity was performed by Dihydrorhodamine (DHR) flow cytometry assay and% positivity neutrophils, ΔMFI, and SI were calculated.
Results: Eighty-seven children with lupus (63 girls; 24 boys) comprised the study group. 44 healthy controls were also enrolled. Disease onset was 8.52±2.95 years whereas age at enrolment was 12.34±5.67 years. Phagocytic activity in neutrophils SLE and controls were 76.59 ± 20.70%; 91.30 ± 4.47%; $p<0.001$ respectively. ΔMFI phagocytosis in patients with SLE and control were 0.09 (005-0.16), 0.18 (0.15, 0.22); (p.= 0.002) respectively. SI of phagocytosis in patients with SLE and controls were 2.79 (1.92, 3.93); 5.00 (4.50, 6.12); $p<0.001$. SLEDAI score was negatively correlated with phagocytic function in neutrophils in patients with SLE. Oxidative burst activity of neutrophils in patients with SLE and controls in form of%positivity on neutrophils were 84.03±17.36%, 92.26±

5.49; p<0.001 respectively. ΔMFI and SI on DHR between patients and healthy controls were comparable. There was no difference in oxidative burst activity between active and inactive SLE patients. Two patients showed a double peak in DHR flow cytometry consistent with mosaic pattern associated with a probable carrier state for X-linked chronic granulomatous disease. Both oxidative burst activity and phagocytic activity did not show significant correlation with the dose of prednisolone.

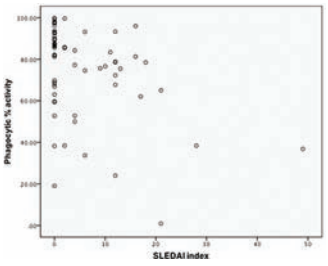
Conclusion: This study suggests that there is impaired neutrophil function in childhood SLE and also there may be a correlation between neutrophil dysfunction and disease activity. The *E.coli* based phagocytic functions of neutrophils were significantly reduced in pediatric SLE patients compared to healthy controls. Phagocytic activity of neutrophil was significantly lower in patients with disease activity and coexistent infection in patients with pediatric SLE. Oxidative burst activity was reduced in patients with pediatric SLE compared to healthy controls. However, there was no significant correlation of oxidative burst activity to the age, disease activity and coexistent infections.

REFERENCES:

[1] Wu S-A, Yeh K-W, Lee W-I et al. Impaired phagocytosis and susceptibility to infection in pediatric-onset systemic lupus erythematosus. Lupus.2013;22(3):279–88.
[2] Marini R, Condino-Neto A, Appenzeller S et al. Superoxide release in juvenile systemic lupus erythematosus. Rheumatol Int.2012;32(7):1977–83.



Abstract THU0510 – Figure 1. Phagocytic functions in patients with active SLE versus inactive disease



Abstract THU0510 – Figure 2. Correlation of SLEDAI and phagocytic activity

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THU0511

COMPARISON OF PAXGENE AND TEMPUS WHOLE BLOOD RNA COLLECTION AND ISOLATION SYSTEMS FOR THE QUANTIFICATION OF TYPE I INTERFERON-STIMULATED GENE EXPRESSION

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Background: Type I interferons (IFN) have important roles in many pediatric and adult rheumatic diseases and are a new therapeutic target for which several "anti-interferon (anti-IFN)" treatments are currently in use or in development. Since the direct detection of these proteins in biological samples has proved challenging, indirect methods are often used to infer the presence of type I IFN. Most commonly this involves quantification of the relative expression of interferon-stimulated genes (ISGs) that are used to calculate an interferon score (IS) (1). This score has been used for example to asses type I IFN activity in pediatric patients with type I interferonopathies, systemic lupus erythematosus, dermatomyositis and systemic juvenile idiopathic arthritis (2). Both qPCR and Nanostring technology have similar sensitivity and reproducibility for IS determination (3). The use of different whole blood RNA collection systems on the IS have not been evaluated however despite evidence of method-dependent changes in gene expression (4).

Objectives: The aim of the study was to compare expression of six common ISGs (*IFI27, IFI44L, IFIT1, ISIG15, RSAD2, SIGLEC1*) and the corresponding IS in RNA derived from two commonly used whole blood RNA collection systems (PAXgene and Tempus).

Methods: Whole blood was collected from ten healthy individuals (median age 25.5 years) in sodium heparin tubes and incubated without or with recombinant human interferon alpha 2b (rhIFNα, 2 IU/ml, 4 hrs, 37C°, 5% CO_2). Next, samples were divided between PAXgene (PreAnalytiX, Becton Dickinson) and Tempus (Applied Biosystems) tubes and RNA was isolated according to the manufacturer's protocols. cDNA was synthesized (500ng input RNA; qScript cDNA synthesis kit) and ISG expression measured on a QuantStudio 6 Real-Time PCR instrument using a TaqMan Fast Advanced Assay. For each ISG, expression was normalized against the geometric mean of two housekeeping genes (18s rRNA and HPRT1) and calculated using the formula $2^{-\Delta Ct}$. Relative gene expression is reported as the normalized expression of each ISG divided by the median of normalized expression of the same ISG in unstimulated samples. The median relative expression of all six ISGs was used to calculate the IFN score for each sample.

Results: There was no statistically significant difference in the normalized expression of any of the six ISGs in either the rhIFNα-stimulated or unstimulated samples derived from PAXgene or Tempus tubes. The greatest difference in mean normalized expression in both unstimulated and stimulated samples was observed for *ISG15* (difference in mean normalized expression was 0.0034 and 0.11, respectively). Overall there was a strong correlation of the IFN score between PAXgene and Tempus tubes for both the unstimulated (R^2 = 0.9117, p<0.0001) and and rhIFNα-stimulated samples (R^2 = 0.8529, p=0.0001).

Conclusion: Despite reported differences in gene expression patterns associated with samples collected in PAXgene versus Tempus tubes, our results demonstrate that 6-gene interferon scores do not differ significantly between RNA samples obtained with these two systems. These results suggest that health care and research centres can use either tubes for IFN score determination using these 6 ISGs and results can be directly compared irrelevant of the RNA collection system employed.

REFERENCES:

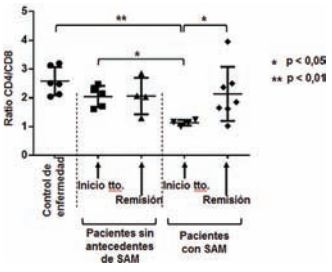
[1] Rice GI *et al*, Lancet Neurol 2013; 12: 1159-69;
[2] Rice GI *et al,* J Clin Immunol 2017; 37: 123-32
[3] Pescarmona R *et al*, Cytokine. 2019;113:446-452.;
[4] Skogholt AH *et al*, BMC Research Notes 2017; 10:136.

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THU0512 **WHAT IS HIDDEN BEHIND SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS, ADULT ONSET STILL'S DISEASE AND SECONDARY MACROPHAGIC ACTIVATION SYNDROME. THE UTILITY OF THE BIOMARKERS**

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Background: Systemic Juvenile Idiopathic Arthritis (SJIA) and adult onset Still's disease are rare diseases of unknown etiology that share several clinical and laboratory features. The pathogenesis of these two diseases is complex and multifactorial, with an important role of innate immunity: activation of neutrophils and macrophages and increased levels of cytokines dependent on the activation of the inflammosome. A proportion of these patients will develop a Macrophage activation syndrome (MAS), a serious and life-threatening complication.
Objectives: To identify immunological markers that allow a differential diagnosis between patients with inactive SJIA, active SJIA or MAS. To evaluate if there are differences between biomarkers in SJIA and adult onset Still's disease
Methods: Observational, prospective and multicenter study. Inclusion criteria: patients with SJIA or adult onset Still's disease, followed in Paediatric or Adult Rheumatology Department from 5 Madrid hospitals. Group 1: Patients with active SJIA or adult onset Still's disease +/- diagnosis of secondary MAS at the first visit, have been followed-up performing a second clinical and analytical visit at 3 months. Group 2: Patients with inactive SJIA or adult onset Still's. Clinical and analytical data were collected, PBMCs were obtained before and after treatment, and several leukocyte subtypes were evaluated by flow cytometry (FACS). The intracytoplasmic expression of TNF-α, IL-1b and IL-6 in monocytes was determined by flow cytometry before and after stimulation with lipopolysaccharides (LPS) in the presence of monensin (Golgi inhibitor). In addition, IL-18 levels were determined by ELISA in all visits.
Results: A total of 25 patients were included (18 SJIA and 7 adult onset Still's diseases), 2 of them being excluded from the analysis because exclusions criteria. 30,4% patients presented MAS at the first visit (5 SJIA and 2 adult onset Still's disease) and other 2 at some time during the disease. The median of IL-18 was 296.1 (CI 108.3-346.0) in patients who have never had MAS and 899.85 (CI: 397.32-1095.6) in the other group. Patients with active MAS had a CD4/CD8 ratio close to the lower limit (1.1 +/- 0.1 SD) reflecting a decrease in the CD4 + population and an increase in CD8 +. On the other hand, the rest of the groups presented a CD4/CD8 ratio of 2.6 +/- 0.5 SD in patients without disease activity and 2.0 +/- 0.7 SD in patients with active SJIA or adult onset Still's disease but without MAS. No significant differences were found between patients with SJIA or adult onset Still's disease.



Abstract THU0512 – Figure 1

Conclusion: The results of this study show that the analysis of three determinations:%CD4,%CD8 and the CD4/CD8 ratio can help in the early detection of patients with MAS secondary to SJIA or adult onset Still's disease. The determination of IL-18 has been in our study a marker of MAS, similar to several published studies. No significant differences were found in the immunological tests between patients with SJIA and adult onset Still's disease with active or inactive disease.

REFERENCE:

[1] Weiss ES et all **Interleukin-18 diagnostically distinguishes and pathogenically promotes human and murine macrophage activation syndrome.** Blood. 2018 Mar 29;131(13):1442-1455

Disclosure of Interests: None declared
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THU0513 **WHOLE BLOOD CELLS FROM PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA) IN CLINICAL INACTIVE DISEASE DISPLAY A DYSREGULATED RESPONSE TO TLR-4 STIMULATION**

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Background: Systemic juvenile idiopathic arthritis (sJIA) is a polygenic autoinflammatory disease. Innate immune mechanisms appear to play a central role in the pathogenesis of the disease. Nevertheless, a better understanding of the pathophysiology of sJIA is still needed to identify patients responsive to IL-1 or IL-6 targeted therapies.
Objectives: In this study, we evaluated the production of IL-1β, IL-6 and TNF-α by fresh whole blood cells isolated from sJIA patients in disease remission, after stimulation with the TLR-4 ligand lipopolysaccharide (LPS), and we investigated whether sJIA patients that respond or not-respond to treatment with the IL-1 receptor antagonist anakinra show a different response.
Methods: We collected fresh whole blood samples from sJIA patients during clinical inactive disease (inactive sJIA, n=19) and sJIA patients during active disease (active sJIA n=4). Active and inactive disease was defined at time of sampling. As controls, fresh whole blood samples from healthy subjects (HS, n=10) were used. Whole blood cells were left unstimulated or stimulated with 10ug/mL of LPS for 24 hours. Cytokine levels (IL-1β, IL-6 and TNF-α) released in the supernatants were measured by ELISA. Response to anakinra was defined as achievement of clinical inactive disease off glucocorticoids at 6 months after initiation of anakinra treatment.
Results: We found that LPS-stimulated cells from inactive sJIA patients released significantly higher amounts of all the inflammatory cytokines tested, compared to HS ($p<0.01$). In addition, cells from inactive sJIA patients produced significantly higher levels of IL-1β also compared to active sJIA patients ($p<0.05$). When we divided inactive sJIA patients in two groups (responders and non-responders), depending on the clinical response to anakinra treatment, we observed that in both groups of patients IL-1β, IL-6 and TNF-α levels were significantly higher than those observed in HS. In addition, we found that LPS-stimulated whole blood cells from non-responder inactive sJIA patients released significantly higher levels of IL-1β and TNF-α compared to responder inactive sJIA patients.
Conclusion: Our preliminary results show a dysregulated production of inflammatory cytokines by whole blood cells from sJIA patients in remission disease, when stimulated with a TLR-4 agonist.
Disclosure of Interests: : Antonia Pascarella: None declared, Manuela Pardeo: None declared, Ivan Caiello: None declared, Claudia Bracaglia: None declared, Marianna Rossi: None declared, Giulia Marucci: None declared, Emanuela Sacco: None declared, Fabrizio De Benedetti Grant/ research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer, Giusi Prencipe: None declared
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THU0514 **ROLE OF THE ORAL MICROBIOME IN CHRONIC NON-BACTERIAL OSTEOMYELITIS IN CHILDREN**

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Background: Chronic non-bacterial osteomyelitis (CNO) is a rare autoinflammatory disease of the bone and bone marrow. The presentation of the disease is broad, but pain and osteoedema on MRI are the hallmarks of CNO. While the activation of inflammasomes and the subsequent release of IL-1ß seems to play a central role, the exact molecular pathophysiology of CNO is largely unexplained. In respect of the potential role of the microbiome to date only experimental data on mice are available, indicating that the manipulation of the microbiome through dietary modulation might alter the course of the disease and also plays a role in the release of IL-1ß from innate immune cells[1].

Objectives: To identify the impact of the oral microbiome on CNO in children and adolescents. Dysbiosis as a state of pathological alteration of the microbiome has been discussed as an environmental factor in rheumatic diseases in adults and in children[2]. Human data in CNO are lacking.
Methods: 20 patients (12 male and 8 female, aged 3 to 13 years) with a median of 10.3 years were examined. Two different sites of the oral cavity (center and left part of the tongue) were swabbed. In total, 143 individual samples were retrieved and subjected to 16s r-RNA amplicon sequencing: DNA was extracted using the QIAamp® DNA Microbiome Kit. The V4 region of the 16S ribosomal RNA gene was amplified by PCR with V4 specific primers. A limited cycle amplification step was performed. Libraries were normalized and pooled, and sequenced on a MiSeq system (Illumina). Raw sequence reads were demultiplexed and clustered into sub-OTUs (operational taxonomic units) via Deblur in Qiita. Qiime2 was used to calculate alpha- and beta- diversity for multiple alternative metrics. Statistical significance was calculated with non-parametric tests (Mann-Whitney and Permanova).
Results: The administration of medication in general (mostly NSAIDs) had a significant impact on the microbiome (p-value < 0.02).
With limited statistical power of the small cohort, gender, age and disease activity do not significantly influence the microbiome.
There is a significant difference between the variable swab sites at the 1% level (p<0.01). Whereas swabs from the center of the tongue exhibit more Streptococci salivarius, the left outer part of the tongue shows more Haemophilus parainfluenza.
Conclusion: To the best of our knowledge, this is the first study of the oral microbiome in children and adolescents in CNO. Our data suggests that administration of medication to CNO patients alters the microbiome. It is also influenced by a change of the swab site. Limited patient numbers did not allow to show an effect on disease activity, but enrollment will continue.

REFERENCES:

[1] Lukens JR, Gurung P, Vogel P, Johnson GR, Carter RA, McGoldrick DJ et al. Dietary modulation of the microbiome affects autoinflammatory disease. Nature 2014; 516: 246-249.
[2] Verwoerd A, Ter Haar NM, de Roock S, Vastert SH, Bogartt D. The human microbiome and juvenile idiopathic arthritis. Pediatric Rheumatology 2016 Sep 20; 14(1):55

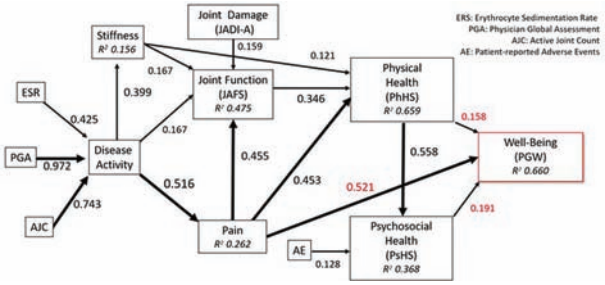
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Paediatric rheumatology

THU0515 **PAIN IS THE MAIN DETERMINANT OF WELL-BEING IN OLIGO- AND POLYARTICULAR JIA: EVIDENCE FROM THE PHARMACHILD REGISTRY**

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Background: Juvenile idiopathic arthritis (JIA) affects patients' well-being as the result of a complex interplay of multiple factors, including disease activity, symptoms, physical and emotional quality of life, and treatment burden. Little evidence exists about the relative contribution of these elements to disease impact.
Objectives: 1) To identify direct and indirect determinants of well-being, expressed by VAS-measured patient/parent global assessment of well-being (PGW), in children with oligo- and polyarthritis. 2) To assess whether the impact of the major determinants varies with level of disease activity.
Methods: We analyzed data of 1873 patients evaluated in 4464 prospective visits from the international JIA pharmacovigilance registry Pharmachild. Patient-reported outcomes were collected through the Juvenile Arthritis Multidimensional Assessment Report (JAMAR). Evaluated predictors of PGW included VAS-measured physician global assessment, inflammatory markers, active joint count, VAS-measured pain, morning stiffness duration, Juvenile Arthritis Functional Score (JAFS), Physical (PhHS) and Psychosocial (PsHS) subscales of the Pediatric Rheumatology Quality of Life (PRQL) scale, disease damage measured through the Juvenile Arthritis Damage Index (JADI) and adverse events (AE). We used path analysis to assess direct and indirect effects of variables on PWG. We repeated the analysis on subsets of visits stratified by disease activity, measured with JADAS10, to test differences across activity states.
Results: Pain severity proved the strongest direct determinant of PGW (b 0.521, p<0.001), followed by Psychosocial (b 0.191, p<0.001) and Physical Health (b 0.158, p<0.001). Stiffness (f2 0.047, p<0.001) and joint damage by the JADI (f2 0.025, p<0.001) were also indirectly associated with PGW, through their effects on function and PhHS. Patient-reported adverse events (AE) had a small effect on PGW (f2 0.025, p<0.001) through their impact on PsHS. Relations among variables and relative coefficients are depicted in the graph. Multi-group comparison between Remission, Low (LDA), Moderate (MDA) and High Disease Activity (HDA) groups revealed that for subjects in Remission, pain had a lower impact on function and physical health compared to those with LDA, while remaining the strongest predictor of PGW. Among the HDA group, the direct effect of pain on well-being and the impact of physical health on psychosocial health was greater than in other activity states (table). The effect of AE remained significant across all activity categories.



Abstract THU0515 – Figure 1.

	Path Coefficients (b)				Comparison			
	REM n=2262	LDA n=665	MDA n=1351	HDA n=186	REM/ LDA	HDA/ REM	HDA/ LDA	HDA/ MDA
Pain -> JAFS	0.312	0.401	0.400	0.402	p 0.042	p 0.131	p 0.488	p 0.001
Pain -> PhHS	0.292	0.377	0.391	0.409	p 0.032	p 0.041	p 0.324	p 0.018
Pain -> PGW	0.367	0.420	0.467	0.614	p 0.208	p 0.003	p 0.016	p 0.033
PhH -> PsHS	0.400	0.429	0.409	0.557	p 0.652	p 0.002	p 0.018	p 0.003

Conclusion: : Pain was the main determinant of PGW in all disease activity states. The level of PGW also reflected other aspects of disease impact, particularly physical and psychosocial distress, and, to a lesser extent, treatment adverse events. The impact of pain and physical functioning on psychosocial health and well-being varies with disease activity, being greater in patients with higher disease activity.

REFERENCE:

[1] Moorthy et al, Pediatric Rheumatology 2010; 8:20

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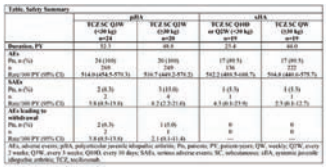
for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda.
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THU0516 **LONG-TERM SAFETY OF SUBCUTANEOUS TOCILIZUMAB ADMINISTRATION IN SYSTEMIC AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS**

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Background: Tocilizumab (TCZ) administered intravenously (IV) was effective for the treatment of polyarticular (p)JIA and systemic (s)JIA.[1,2]
Objectives: To evaluate the long-term safety and efficacy of subcutaneous (SC) TCZ in patients (pts) with pJIA or sJIA enrolled in a long-term extension (LTE) phase of two 52-week, open-label studies.
Methods: Pts aged 1-17 years received body weight (BW)–based TCZ SC: pJIA pts who failed/could not tolerate MTX received TCZ 162 mg every 3 weeks for BW <30 kg or every 2 weeks (Q2W) for BW ≥30 kg; sJIA pts with inadequate response to NSAIDs and glucocorticoids received TCZ 162 mg Q2W for BW <30 kg or weekly for BW ≥30 kg. All pts discontinued biologic DMARDs (approximately 50% switched from TCZ IV to TCZ SC). After 52 weeks, pts continued BW-based TCZ in a separate LTE study; safety data (adverse events [AEs], serious AEs [SAEs]) in the LTE study to clinical cutoffs December 1, 2017 (pJIA), and February 28, 2018 (sJIA), are reported for all pts who received ≥1 dose of TCZ SC and had ≥1 postdose safety assessment.
Results: Most pJIA (n=44) and sJIA (n=38) pts were female (72.7% and 55.3%) and white (88.6% and 84.2%); median (range) age was 9.0 (2-18) years. AE rates (Table) were similar regardless of BW. Most AEs were grade 1 or 2; grade ≥3 AEs were reported by 10/44 (20.8%) pJIA pts and 4/38 (10.5%) sJIA pts, most commonly nasopharyngitis (pJIA, 17/44 [38.6%]; sJIA, 11/38 [28.9%]). Other AEs reported in ≥15% of pts included arthralgia, gastroenteritis, cough, vomiting, diarrhea, pyrexia, headache, and oropharyngeal pain (pJIA) and upper respiratory tract infection, cough, pyrexia, arthralgia, and rash (sJIA). No opportunistic infections developed. Neutropenia AEs were reported by 6/44 (13.6%) pJIA pts and 7/38 (18.4%) sJIA pts. SAEs occurred in 5/44 (11.4%) pJIA pts (furuncle, appendicitis, pneumonia, eye pain/headache, infectious mononucleosis) and 2/38 (5.3%) sJIA pts (pneumonia, craniocerebral injury from a fall); only pneumonia (pJIA) was considered treatment related. Neutralizing anti-TCZ antibodies developed in 2 (4.7%) pJIA pts and no sJIA patients. No deaths were reported in the LTE study.
Conclusion: In this LTE study in children with pJIA or sJIA, SC TCZ continues to have an acceptable tolerability profile with no new safety concerns.

Abstract THU0516 –Table 1.



REFERENCES:
[1] Brunner HI et al. *Ann Rheum Dis*. 2015;74:1110-1117.
[2] 2. De Benedetti F et al. *N Engl J Med.* 2012;367:2385-2395.

Disclosure of Interests: Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer, Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Athimalaipet Ramanan Consultant for: AbbVie, UCB, Sobi, Eli Lilly, Speakers bureau: Speaker fees/honoraria from Abbvie, SOBI, Eli Lilly and UCB, Speakers bureau: AbbVie, UCB, Sobi, Eli Lilly, Ruben Cuttica Grant/research support from: Roche, Pfizer, Lilly, Bristol Myers Squibb, Novartis, Sanofi Aventis, UCB, Janssen., Consultant for: Roche, Pfizer, Lilly, Bristol Myers Squibb, Novartis, Sanofi Aventis, UCB, Janssen., Speakers bureau: Roche, Pfizer, Lilly, Bristol Myers Squibb, Novartis, Sanofi Aventis, UCB, Janssen., Jennifer E. Weiss: None declared, Michael Henrickson: None declared, Heinrike Schmeling Grant/research support from: F. Hoffmann-La Roche Ltd, Jordi Anton Grant/research support from: Grant/research support, consultant or speakers bureau from AbbVie, Alexion, Bristol-Myers Squibb, ChemoCentryx, Gebro, GlaxoSmithKline, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Consultant for: Grant/research support, consultant or speakers bureau from AbbVie, Alexion, Bristol-Myers Squibb, ChemoCentryx, Gebro, GlaxoSmithKline, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Speakers bureau: Grant/research support, consultant or speakers bureau from AbbVie, Alexion, Bristol-Myers Squibb, ChemoCentryx, Gebro, GlaxoSmithKline, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Kirsten Minden Consultant for: AbbVie, Gerd Horneff: None declared, Maria Luz Gámir Gámir: None declared, Markus Hufnagel: None declared, Wendy Douglass Shareholder of: Roche, Employee of: Roche, Chris Wells Employee of: Roche Products Ltd, Navita L. Mallalieu Shareholder of: Roche, Employee of: Roche, Alberto Martini: None declared, Daniel J Lovell Consultant for: Consulting fees and/or honoraria from Astra Zeneca, Wyeth Pharma, Amgen, Abbott, Pfizer, F. Hoffmann-La Roche, Novartis, UBC, Takeda, GSK, Boehringer, and Celgene, Hermine Brunner Grant/research support from: Bristol-Myers Squibb, Pfizer, Consultant for: Pfizer, Bristol-Myers Squibb, Janssen, Novartis, Lilly, Roche, GlaxoSmithKline, Sanofi, Speakers bureau: Novartis, Roche
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THU0517 THE LONGITUDINAL EUROFEVER PROJECT: AN UPDATE ON ENROLLMENT

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Background: In 2008 the Paediatric Rheumatology European Society (PReS) promoted an International Project for the study of Autoinflammatory Diseases (AIDs) named Eurofever, whose main purpose is to create a web-based registry for the collection of information in AIDs patients.
Objectives: To implement the Registry with the new recently described AIDs and to increase the collection of longitudinal data.
Methods: The data were extracted from the Eurofever registry, which is hosted in the PRINTO website (http://www. printo.it). From February 2015 we started the longitudinal collection of follow-up data with particular focus on treatment, modification of the clinical picture, onset of complication/adverse events. We have enrolled patients included in the registry up to 28 September 2018.
Results: Up to date 4175 patients have been enrolled (3843 of them with complete demographic information, 1903 M e 1940 F) from 62 countries. For 3356 (87%) patients also clinical data from onset to diagnosis, collected during the first visit performed at referred pediatric or adult center, are available. For each disease the number of enrolled patients is: FMF 1086 pts (951 with complete clinical data); TRAPS 273 pts (256 complete); CAPS 298 pts (279 complete); MKD 205 pts (190 complete); Blau's disease 49 pts (26 complete); PAPA 42 pts (41 complete); NLRP12 mediated periodic fever 13 pts (11 complete); DADA2 14 pts (9 complete); DIRA 3 pts (all complete); SAVI 3 pts (all complete); CANDLE 1 pt (complete) and Majeed 4 pts (all complete). Among multifactorial autoinflammatory diseases: PFAPA 676 pts (551 complete); CNO 581 pts (540 complete); Behcet 214 pts (186 complete), undefined periodic fever 368 pts (292 complete) and Schnitzler 13 pts (all complete). The median onset age is 4 years (range 1 month – 75 years), the median diagnosis age is 8 years (range 1 month – 78 years). Most of patients (3509, 91%) presented disease onset during pediatric age (<16 years), 334 (9%) during adult age (81 FMF, 31 CAPS, 53 TRAPS, 40 CRMO, 12 Schnitzler syndrome e 90 unknown fever). 405 of 3509 (12%) patients with pediatric onset received diagnosis during adult age. The median diagnostic delay is 5 years; diseases with longer diagnostic delay are: NLRP12 (24 years, range 4-76), CAPS (15 years, range 0-77), PAPA (14 years, range 2-57), TRAPS (12 years, range 0-77). 396 patients have been treated with at least one biologic drug, 1031 with DMARDs, 427 with systemic steroid and 686 with others drugs. The most frequent diseases treated with biologic drugs are: CAPS (38%), multifactorial diseases (22%), TRAPS (14%), MKD (11%), rare monogenic (8%: 1 CANDLE, 2 DIRA, 2 NALP12, 3 Majeed, 8 DADA2 and 14 PAPA), and FMF (7%). Since February 2015, longitudinal visits have been inserted for 477 (12%) patients, with detailed data on treatment and safety.
Conclusion: The enrollment in Eurofever Registry is still ongoing. The analysis of data will improve our knowledge both on the natural history of the single disease and on the efficacy/safety of treatment commonly used in the clinical practice.
Disclosure of Interests: : Ilaria Gueli: None declared, Martina Finetti: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer, Jordi Anton Grant/research support from: JA has received grant/research support, consulting fees and/or honoraria from AbbVie, Alexion, BMS, ChemoCentryx, Gebro, GSK, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Consultant for: JA has received grant/research support, consulting fees and/or honoraria from AbbVie, Alexion, BMS, ChemoCentryx, Gebro, GSK, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Maria Alessio: None declared, Joost Frenkel: None declared, Luca Cantarini: None declared, Romina Gallizzi: None declared, Judith Sanchez Manubens: None declared, Marco Cattalini: None declared, Efimia Papadopoulou-Alataki: None declared, Rolando Cimaz: None declared, Donato Rigante: None declared, Alma Nunzia Olivieri: None declared, Pavla Dolezalova: None declared, Alberto Martini Consultant for: I do not have any conflict of interest to declare since starting from 1 March 2016 I became the Scientific Director of the G. Gaslini Hospital; therefore, my role does not allow me to render private consultancies resulting in personal income.
I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:
AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.
The money received for these activities are directly transferred to the Gaslini Institute's bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis
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THU0518 EFFICACY AND SAFETY OF ETANERCEPT IN JUVENILE IDIOPATHIC ARTHRITIS – 18 YEAR EXPERIENCE USING DATA OF THE BIKER REGISTRY

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Background: Since 2000, Etanercept is approved for polyarticular juvenile idiopathic arthritis (JIA). Subsequently, approval has been extended to additional JIA categories.
Objectives: To describe efficacy and safety of Etanercept in clinical practice in JIA patients in comparison to a biologic-naïve JIA cohort using the German Biologics registry (BiKeR).
Methods: Baseline demographics and disease activity parameters were documented. Efficacy was determined using the JADAS10. Safety assessments were based on adverse events reports (AE) processed according to MedDRA.
Results: Until October 1, 2018, 2645 JIA patients treated with Etanercept were registered, representing 5820 patient-years (PY) of exposure. The total observation time (from date of first dose until last follow-up, censored, if another biologic was started) was calculated as 8080 PY.
In general, the cohort treated with Etanercept had experienced disease duration of 4.2+/-3.7 years (mean+/-SD). 2303 patients (87%) were pretreated with methotrexate, 100 with alternative biologics. Concomitantly, 1822 patients (69%) received methotrexate, 2098 (79%) NSAIDs, 949 (36%) systemic corticosteroids as well as further drugs in lower numbers. In the control cohort, 1517 biologic naive JIA patients started methotrexate.
At last follow-up, 68%/62%/50%/34% of patients reached JIAACR30/50/70/90 criteria. The median (IQR1-3) JADAS10 score decreased from 15.0 (10-20.4) at baseline to 3.5 (0.7-10.1). 60% of patients achieved a JADAS defined minimal disease activity, 40% reached a JADAS remission.
1924 AE were observed (33.1/100PY [95% CI 31.6-34.6]). 221qualified as SAE (3.8/100PY [3.3-4.3]). These figures were compared to 1292 AE reported during 3714PY in the control cohort (34.8/year [32.9-36.8]) and 52 SAE (1.4/100PY [1.1-1.8]).
The most frequent SAE in the Etanercept cohort were grouped in the MedDRA SOC infections and infestations (n=54) followed by musculoskeletal and connective tissue disorders (n=27), eye disorders (n=21), gastrointestinal disorders (n=17) and nervous system disorders (n=15). There were 5 deaths. Serious infections were of bacterial and viral origin and mostly occurred once only.

Adverse events of special interest were uveitis (n=109), H. zoster (n=24), chronic inflammatory bowel disease (n=19), pregnancies (n=4), depression (n= 11), malignancies (n=8), demyelination (n=2). Adverse Events of Special Interest (AESI) were in the MTX–cohort uveitis (n=52), H. zoster (n=4), chronic inflammatory bowel disease (n=1), depression (n= 2), malignancies (n=4).

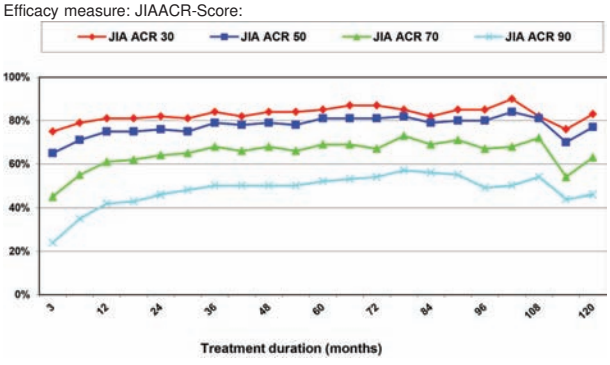
A total of 1606 patients (60.7%) discontinued treatment. Of these 638 (39.7%) discontinued due to remission, 565 (35.2%) due to lack of efficacy and 188 (11.7%) because of intolerance.

Conclusion: The current analysis adds to the established safety profile of Etanercept and demonstrates that the rate of SAEs is comparable and consistent with the overall AE profile in paediatric patients. As expected, infections are the most frequent SAE. Uveitis is likely associated with JIA. Of notice, few patients developed a chronic inflammatory bowel disease and some a malignancy. No new safety signals specific to the paediatric population were identified in this large cohort of JIA patients.

REFERENCES:

[1] Geikowski T, Becker I, Horneff G; German BIKER Registry Collaborative Study Group. Predictors of response to etanercept in polyarticular-course juvenile idiopathic arthritis. Rheumatology (Oxford). 2014 Jul;53(7):1245-9

Efficacy measure: JIAACR-Score:



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THU0519 DISEASE COURSE AND OUTCOMES OF PREGNANCY IN JUVENIL IDIOPHATIC ARTHRITIS: ANY DIFFERENCE AMONG DISEASE SUBSETS?

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Background: Data on the disease activity and pregnancy outcomes taking into account the different types of Juvenile idiopathic arthritis (JIA) patients are limited.

Objectives: To analyze the course of disease during pregnancy and pregnancy outcomes in patients with JIA according to disease subtype, with focus on the medication use.

Methods: A retrospective observational study was conducted on pregnant JIA patients followed in our pregnancy clinic between 2010 and 2018. Disease activity (DAS28-PCR3) was analyzed before conception, at each trimester and postpartum. Flare was defined as an increase in clinical activity leading to intensified therapy with at least one of: new prednisone, increase in dosage $\geq$5 mg/day, treatment with intraarticular glucocorticoids, (re-)treatment with DMARDS/TNFi. Pregnancy outcome were also recorded.

Results: Sixteen patients and 22 pregnancies were included. Two pregnancies were voluntary interrupted (1 for Methotrexate exposure and 1 for fetal encephalocele). Table 1 summarizes disease features and pregnancy outcomes according to disease subsets.

10/22 (45,5%) were pregnancies observed in Oligoarticular Extended (OLA-E), 6 (27,3%) Polyarticular (PLA), 4 (18,2%) Systemic (SYS), 1 (4,5%) Oligoarticular (OLA) and 1 (4,5%) Enthesitis related Arthritis (ERA) JIA patients.

Abstract THU0519 –Table 1.

Table 1	Polyarticular	Oligoarticular	Oligoarticular extended	Systemic	Enthesitis related arthritis
Patients, n(%)	5(31.2)	1(6.25)	6 (37.5)	3 (18.8)	1 (6.25)
Pregnancies, n(%)	6 (27.3)	1 (4.5)	10 (45.5)*	4 (18.2)	1 (4.5)
Age at pregnancy (years) mean+SD, yrs	33 (5.51)	28 (0)	27.8 (5.63)*	24.5 (6.25)	26 (0)
Disease duration, months, mean+SD,	20.5 (2.6)	22 (0)	19.5 (6.2)*	19.5(6.5)	19 (0)
CCS before conception, n (%), daily dose, mg/day, mean+DS	4 (66.7) 6.6 (5.82)	0 (0) 0 (0)	3(33.3)* 4.5 (0.86)*	0 (0) 0 (0)	0 (0) 0 (0)
cDMARDs before conception None (%) Ciclosporin (%) Hydroxycloroquine (%) Methotrexate (%)	5 (83.3) 1 (16.7) 0 0	0 (100) 0 0 0	6 (60)* 0 (0) 3 (30)* 1 (10)*	0 (100) 0 0 0	0 (100) 0 0 0
bDMARDs before conception None (%) ETANERCEPT (%) GOLIMUMAB (%) ABATACEPT (%)	1 (16.7) 3 (50) 1 (16.7) 1 (16.7)	0 (100) 0 0 0	5 (50) 5 (50)* 0 0	0 (100) 0 0 0	0 (100) 0 0 0
Stop bDMARDS at positive pregnancy test, n (%)	4 (80)	0 (0)	4 (80)*	0 (0)	0 (0)
DAS28PCR, mean+DS PC 1T 2T 3T PP	 1.69 (0.42) 2.47 (1.36) 3.11 (1.05) 2.84 (1.61) 2.66 (1.13)	 1.15 (0) 1.64 (0) 1.64 (0) 1.64 (0) Not available	 1.73 (0.45) 1.82 (0.47) 2.29 (0.53) 1.94 (0.29) 2.85 (0.71)	 1.27 (0.25) 1.53 (0.31) 1.56 (0.30) 1.71 (0.10) 1.59 (0.14)	 1.15 (0) 1.64 (0) 2.09 (0) 1.99 (0) 1.60 (0)
Flare, n (%) 1T 2T 3T PP	 1/7 (14.3) 3/7 (43) 1/7 (14.3) 2/8 (25)*	 0/7 (0) 0/7 (0) 0/7 (0) Not available	 1/7 (14.3) 1/7 (14.3) 1/7 (0) 6/8 (75)*	 0/7 (0) 0/7 (0) 0/7 (0) 0/8 (0)	 0/7 (0) 0/7 (0) 0/7 (0) 0/8 (0)
Pregnancy outcome Live-births, n (%) Ongoing pregnancies, n (%) Spontaneus pregnancy loss n (%) VPI, n (%) P-PROM(%) Delivery week, median min-max Premature delivery, n (%)	 5 (83.3) 1(16.7) 0 (0) 0 (0) 1 (16.7) 36 (33-41) 2 (33.3)	 No available 	 7 (77.8)* 0 (0) 0 (0) 2 (22.2)* 0 (0) 38 (35-39) 3 (37.5)	 1 (100) 0 (0) 0 (0) 0 (0) 0 (0) 41 (38-41) 0 (0)	 1 (100) 0 (0) 0 (0) 0 (0) 0 (0) 41 (0) 0 (0)

cDMARDS conventional disease-modifying antirheumatic drug, bDMARDs biological disease-modifying antirheumatic drug, 1T, First trimester, 2T Second trimester, 3T Third trimester, PC preconception, PP postpartum, CCS corticosteroids, VPI voluntary pregnancy interruption, PROM premature rupture of membranes.
* Methotrexate exposure during 1^T at 8W and fetus malformation at 17W.
* Taking into account voluntary pregnancy interruption.

At conception 19(95%) pregnancies were on remission, 1(5%) OLA-E patient in low disease activity. Among the 20 pregnancies ended with a live birth, 1 OLA, 4 SYS and 1 ERA patients mantained sustained remission, without cDMARDs or bDMARDs, throughout pregnancy.

There were 7 flares in 6 (31,8%) pregnancies, 5 (71,4%) of them among PLA patients and 2 (28,6%) among OLA-E patients. No extrarticular flare was recorded. There was no flare among SYS, OLA and ERA patients. One pregnancy in a patient with PLA JIA (4,5%) was characterized by more that one flare, but none had more than two flares. Most of flares (2/29% 1^trimester, 4/57% 2^trimester, 1/14% 3^trimester) occurred during 2^trimester. Eigth flares occurred in postpartum, also in 2 pregnancies after voluntary pregnancy interruption.

Regarding treatment at conception; 8 (40%) pregnancies were on bDMARDs, treatment was stopped at positive pregnancy test in 6 pregnancies, 2 (33,3%) required restart of treatment due to a flare in 1^Trimester (1 CTZ) and 3^Trimester (1 ETA), and 3 flared in puerperium with restart of bDMARDs. Two (25%) pregnancies continued bDMARDs at positive pregnancy test throughout the pregnancy to prevent a flare, that had been already experienced in previous pregnancies (not followed in our centre).

Regarding pregnancy complications and outcomes, no cases of Pre-clampsia, eclampsia, small for gestational age babies, intrauterine death, were observed. One pregnancy was complicated with pre-term premature rupture of membranes at 35 gestational week, in a patient not taking prednisone. There were 5 (25%) pre-term deliveries.

Conclusion: Nearly one third of pregnant patients with JIA had a disease flare during pregnancy. Flares were observed only in 2 disease subsets (PLA; OLA-E) and associated with discontinuation of bDMARDs at positive pregnancy index. The preconception counseling of patients with JIA should include the disease subset in the risk stratification and consequently the continuation of bDMARDs during pregnancy. Maternal disease control is necessary to minimize the risk of adverse pregnancy outcomes (especially pre-term birth).

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THU0520 EARLY IDENTIFICATION OF VENTRICULAR DYSFUNCTION IN JUVENILE SYSTEMIC SCLEROSIS BY SPECKLE TRACKING ECHOCARDIOGRAPHY

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Background: Juvenile Systemic Sclerosis (JSSc) is a rare multisystemic connective tissue disease, with onset before the age of 16. Cardiac involvement, recognized in 8-24% of the patients [1], begins in early stages of JSSc and has a poor prognosis. The traditional cardiac US imaging, including the left ventricular ejection fraction (EF), evaluates the global function of the heart, thus being inappropriate to assess the subclinical course of the disease. A new echocardiographic technique, the speckle tracking echocardiography (STE), has been shown to be able to identify regional ventricular dysfunctions also in early stages of adult-onset SSc[2,3].

Objectives: Aim of our study was to assess the longitudinal strain of right and left ventricle in JSSc patients, in order to identify ventricular dysfunctions earlier and more effectively than with traditional echocardiography. Furthermore, we investigated the evolution of cardiac involvement during the follow-up and possible correlations with the overall disease severity, measured by the Juvenile Systemic Sclerosis Severity Score (J4S)[4].

Methods: Consecutive patients with JSSc underwent clinical and cardiologic evaluation. This included traditional echocardiography (such as M-Mode, EF, Pulsed- and Tissue-Doppler), 3D-Echocardiography and STE, measuring the global longitudinal strain of left ventricle (GLS) and the longitudinal strain of right ventricle free-wall (RVLS). Each patient was assessed several times by pediatric rheumatologists for J4S and by cardiologists with STE and standard echo.

Results: 18 JSSc patients (12 F, 6 M), mean age 12.3 years, disease duration 4.5 years, entered the study. At baseline evaluation, EF was abnormal in 1 patient, whereas GLS and RVLS were abnormal in 5. The diagnostic sensitivity of cardiac involvement of STE increased, with a prevalence rising from 22.2% to 38.8%. During the follow-up, lasted mean 30 months (range 17–43), the mean GLS values gradually worsened (-21.2; -20.1; -19.4%) while there was no significant variations of EF. The strong correlation between GLS and J4S, found at baseline, vanished during the follow-up.

Conclusion: Speckle tracking echocardiography is a useful technique to evaluate the cardiac involvement in patients with JSSc. In comparison with traditional EKG or echocardiography, it allows to increase the diagnostic sensitivity of cardiac involvement. Over time, we observed a gradual worsening of GLS, sign of a progressive left ventricular dysfunction, that was not identified by EF. It is possible that the coronary microvascular damage compromises the subendocardial fibers function which are more sensitive to ischemia and whose contractility is well assessed by GLS [5]. Finally, the initial correlation between strain and J4S disappeared during the follow-up, maybe because of the pharmacological therapy, which was effective on several aspects of the disease but had low impact on the ventricular function.

REFERENCES:

[1] Martini G et al. Arthritis Rheum 2006; 54:3971–3978.
[2] Spethmann S et al. Eur. Heart J Cardiovascular Imaging 2012; 13:863–870.
[3] Dedeoglu R et al. Pediatric Cardiol 2017; 38:1686–1695.
[4] La Torre F et al. Arthritis Rheum 2012; 64:4143–4150.
[5] Geyer H et al. J Am Soc Echocardiog 2010; 23:351– 369.

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THU0521 JUVENILE DERMATOMYOSITIS IN GERMANY – DATA OF THE NATIONAL PEDIATRIC RHEUMATOLOGY DATABASE WITH SPECIAL REGARD TO MYOSITIS-SPECIFIC ANTIBODIES AND ASSOCIATED CLINICAL PHENOTYPES

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Background: Next to weakness of the proximal muscles and typical skin lesions as leading symptoms in juvenile dermatomyositis (JDM) there can be involvement of other organ systems and tissues. Myositis-specific antibodies (MSA) may help to distinguish clinically distinct phenotypes

Objectives: 1) to analyse the clinical presentation of JDM and how diagnosis was verified and 2) to determine the spectrum of MSA and the associated clinical phenotypes in a German cohort of JDM patients.

Methods: We analyzed data of the national pediatric rheumatology database (NPRD), where children and adolescents with chronic rheumatic diseases are documented yearly by means of disease-specific questionnaires. Cross-sectional data of patients with JDM documented between 2014 and 2016 were analyzed. MSA were determined by a commercial multiplex array. To further specify the phenotype and patient`s outcome, an additional retrospective chart review was conducted.

Results: We identified 186 patients with a diagnosis of JDM (69% female). Mean age at disease onset was 6.8 ± 3.5 years, mean time between first symptoms and first contact to a pediatric rheumatologist was 6.1 ± 8.9 months, mean age at documentation was 11.5 ± 4.4 years. The following diagnostic procedures were pathologic/positive for JDM: Histology 44/147 (30%), electromyography 28/144 (19%), magnetic resonance imaging 103/148 (70%), Creatine kinase (CK) elevation at diagnosis 126/148 patients (85%). At last consultation (mean disease duration 5.0 ± 3.9 years), the mean physician`s global assessment of disease activity (PGA, NRS 0 – 10) was 1.6 ± SD 2.3, the mean manual muscle test (MMT, range 0 – 80, best 80) was 69.7 ± SD 19, the mean disease activity score (DAS, range 0 – 20, best 0) was 4.4 ± D 4.7, the mean CHAQ was 0.5 ± SD 0.8. MSA testing was performed on 88 patients (73% female); 42% tested positive: anti-NXP2 16%, anti-TIF1γ 14%, anti-MDA5 6%, anti-Mi2 3%, anti-synthetase-antibodies 3%. The most common clinical feature was dysphagia in patients with anti-NXP2, calcinosis in patients with anti-TIF1γ, lung involvement in patients with anti-synthetase antibodies, and pronounced muscle weakness in patients with anti-Mi2. Patients with anti-MDA5 were characterized by frequent lung involvement, mucosal ulcers, fever and polyarticular arthritis of small joints. Muscle weakness tested by Childhood Myositis Assessment Score (CMAS) was significantly associated with an increased CK level. At last consultation, 32% and 14% received oral glucocorticoids (GC) < 0.2 mg/kg or ≥ 0.2 mg/kg body weight, respectively, 52% were treated with methotrexate (MTX) and 27% with intravenous immunoglobulins (last 12 months). PGA was ≤ 1 in 65% of patients at last consultation, 22% of those were off therapy.

Conclusion: Demographic and clinical parameters of patients with JDM in Germany are comparable to JDM-cohorts in other countries. MRI has gained diagnostic importance and is used more than twice as often as biopsy. MSA could be found in almost half of the patients. Clinical

phenotypes were associated with specific MSA. After 5 years, 2/3 of patients had an inactive disease, but about half of all patients still received MTX and GC therapy.

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THU0522 CLINICAL MANIFESTATIONS AND COMPARISON OF SUBTYPES OF JUVENILE IDIOPATHIC INFLAMMATORY MYOPATHIES: DATA FROM THE REMICAM REGISTRY

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Background: Juvenile idiopathic inflammatory myopathies (JIIM) are a heterogeneous group of autoimmune diseases affecting children, characterized by symmetric muscular weakness, cutaneous rash and systemic organ involvement. Given its low incidence, there are few studies describing the characteristics of this disease and its subtypes in Spanish patients[1].

Objectives: To describe the demographic, clinical and analytical characteristics of patients with JIIM from the registry of inflammatory myopathies in Madrid community (REMICAM), and to compare those measures between polymyositis (PM) and juvenile dermatomyositis (JDM) subgroups.

Methods: A multicentre retrospective study from the REMICAM registry was performed. Patients were selected if they were 18 years or younger at onset of JIIM and met definite or probable criteria for IIM by the modified Bohan and Peter criteria. We included patients with JDM or PM subgroups, overlap myositis patients were excluded.

Results: 86 patients were included, 12 classified as PM and 74 as JDM. 70% were women and 96% were Caucasian. Mean age at diagnosis was 11.8 years in PM group vs 7.2 years in JDM group. 44% presented arthritis and 93% presented muscular weakness. Gottron sign was present in 76% of the patients, and calcinosis was present in 31.4%. Cardiac and pulmonary manifestations were rare (<5%). There were no cases of neoplastic disease. Clinical features and complementary analysis are shown in table 1 and table 2.

Abstract THU0522 –Table 1. Clinical features

	Total (n=86)	PM (n=12)	JDM (n=74)	p-value
Fever	23 (29,1%)	6 (50,0%)	17 (25,4%)	0,084
Weight loss	12 (15,2%)	1 (8,3%)	11 (16,4%)	0,680
Arthralgia	38 (44,2%)	7 (58,3%)	31 (41,9%)	0,287
Arthritis	24 (28,4%)	6 (50%)	18 (24,7%)	0,071
Gottron sign	66 (76,7%)		65 (87,8%)	
Heliotrope erythema	46 (53,5%)		46 (62,2%)	
Mechanic hands	10 (12,3%)		10 (14,5%)	
Skin ulcers	3 (3,7%)		3 (4,3%)	
Raynaud	12 (13,9%)	3 (25,0%)	9 (12,2%)	0,362
Calcinosis	27 (31,4%)	2 (16,7%	25 (33,8%)	0,325
Muscular weakness	80 (93,0%)	11 (91,7%)	69 (93,2%)	1,000
Myalgia	68 (83,9%)	8 (66,7%)	60 (87,0%)	0,095
Myocarditis	2 (2,3%)		2 (2,7%)	
Arrythmia	3 (3,5%)	1 (8,3%)	2 (2,7%)	0,370
Heart failure	1 (1,2%)		1 (1,4%)	1,000
Interstitial lung disease	1 (1,2%)	1 (8,3%)		0,140
Dysphagia	19 (22,1%)	2 (16,7%)	17 (23,0%)	1,000
GI reflux	7 (8,1%)	1 (8,3%)	6 (8,1%)	1,000
GI hemorrhage	1 (1,2%)		1 (1,3%)	1,000

Abstract THU052 –Table 2. Complementary test.

	Total (n=86)	PM (n=12)	JDM (n=74)	p-value
Anemia	13 (15,1%)	4 (33,3%)	9 (12,2%)	0,079
Leukopenia	4 (4,6%)	1 (8,3%)	3 (4,0%)	0,458
Thrombocytopenia	3 (3,5%)	2 (16,7%)	1 (1,3%)	0,050
ANA+	34 (40,5%)	7 (58,3%)	27 (37,5%)	0,173
Anti-Jo1	2 (2,6%)		2 (3,0%)	1,000
CPK	431 (97-3131)	206 (36-7428)	659 (104-3110)	0,730
Aldolase	12 (9-18)	9 (5-12)	12 (9-19)	0,230
CRP	0,35 (0-1,3)	0,12 (0-2,8)	0,42 (0-1,3)	0,817
ESR	19 (11-29)	25 (13-42)	19 (11-29)	0,450
Myopathic pattern	72 (92,3%)	12 (100%)	60 (90,1%)	0,508

Conclusion: JDM was the most frequent form of MIIJ in our study (86%). The most frequent manifestations were the muscular and dermatological ones, but an important group also presented arthritis and fever. There was no statistical difference between both groups, regardless, myalgias and dysphagia were more common in JDM group, and they had higher CPK and aldolase values. PM patients were older, had more fever and arthritis, also, cytopenia and ANA positivity were more common.

REFERENCE:

[1] Shah M, Mamyrova G, Targoff IN, Huber AM, Malley JD, Rice MM, et al. The Clinical Phenotypes of the Juvenile Idiopathic Inflammatory Myopathies. Medicine (Baltimore). 2013 Jan;92(1):25–41.

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THU0523 OBESITY IS ASSOCIATED WITH SEVERE RENAL INVOLVEMENT, PERSISTENT PURPURA AND LONGER JOINT SYMPTOMS IN CHILDREN WITH HENOCH SHÖNLEIN PURPURA

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Background: Over the last 20 years, the prevalence of obesity is increased in the developed and developing countries. Adipose tissue has an effect on inflammatory processes and immune system besides metabolic and appetite regulating mechanisms. On this basis, it is now of major interest to clarify the relationship between obesity and autoimmune/inflammatory diseases (1,2).

Objectives: We aimed to evaluate the role of obesity on the clinical course and response to treatment in patients with Henoch Shönlein Purpura (HSP).

Methods: Data charts of children with HSP followed in Dokuz Eylül University Childrens' Hospital were reviewed retrospectively. Obesity was defined as BMI $\geq$95 percentile in conformity with Centers for Disease Control and Prevention (CDC) (3). Persistant purpura was defined as skin involvement persisting for $\geq$30 days. Mild nephropathy was defined by the presence of microscopical hematuria and/or nonnephrotic proteinuria, and severe nephropathy by nephrotic syndrome and/or acute nephritic syndrome and/or renal insufficiency (4). Patients were grouped as obese and non-obese depending on BMI. Two groups were compared for demographic, clinical and laboratory parameters.

Results: There were 199 patients [M/F:104/95; presenting age 7.1 years (range 5.0-9.2); follow-up period 17.5 months (range 3-50)]. Obesity was

present in 35 (17.5%) of children. These patients were determined to have significantly higher rate of persistent purpura (45.7% vs 20.7%), severe renal involvement (57.7% vs 30.8%), hypertension (28.6% vs 9.1%) and increased erythrocyte sedimentation rate (79.2% vs 55.9%). Obese patients also showed delayed improvement of skin (25 vs 14 days), joint (12.5 vs 10.0 days) and renal (280 vs 57 days) symptoms. While the rate of children requiring steroid treatment was not different between the two groups, obese children used steroids for significantly longer time (236 vs 40 days). Furthermore, need for immunosuppressive medications (azathioprine and cyclophosphamide) were higher in obese patients (40.0% vs 8.6%).

Conclusion: Obese children with HSP seem to have higher ESR, hypertension and severe renal involvement; show delayed improvement of skin, joint and renal findings; need more immunosuppressive medications and longer period of immunosuppressive treatment. These findings may be associated with the effect of adipose tissue on inflammation.

REFERENCES:

[1] Versini M, Jeandel P-Y, Rosenthal E, Shoenfeld Y. Obesity in autoimmune diseases: not a passive bystander. Autoimmun Rev. 2014;13:981–1000.
[2] Zhao Y, Liu Z, Bai X et all. Obesity increases the risk of renal involvement in children with Henoch–Schönlein purpura. Eur J Pediatr (2015) 174:1357–1363
[3] Styne DM, Arslanian SA, Connor EL et all. Pediatric Obesity—Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline. *The Journal of Clinical Endocrinology & Metabolism*, Volume 102, Issue 3, 1 March 2017, Pages 709–757
[4] Trapani S, Micheli A, Grisolia F et all. Henoch Schonlein Purpura in childhood: epidemiological and clinical analysis of 150 cases over a 5-year period and review of literature. Seminars in arthritis and rheumatism. doi:10.1016/j.semarthrit.2005.08.007

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THU0524 ARE CHILDREN AND ADULTS HAVING DIFFERENT PHENOTYPE AND GENOTYPE OF FMF?

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Background: Familial Mediterranean fever (FMF) is an autosomal recessively inherited autoinflammatory disease and begins in childhood. In nearly 60% of patients, the first attack occurs before the age of 10, and in 90% of them before the age of 20 years. There isn't a prospective study designed for comparing childhood onset and adult onset FMF.

Objectives: To compare the demographic data, clinical features, genetic analysis, laboratory values and severity scores of both childhood and adult onset FMF. Compliance and resistance to colchicine, presence of accompanying diseases and complications due to FMF were also analyzed and reviewed.

Methods: The patients were divided into two groups; group I: children with FMF (symptoms begin before 18 years of age) and group II: adults with FMF (symptoms begin after 18 years of age). A questionnaire for collecting age at disease onset, sex, age at diagnosis, delay at diagnosis and duration of the disease, family history of FMF, consanguinity and accompanying diseases were filled. The questions were asked by an adult and pediatric rheumatologist to both groups by face to face interviews. Genetic analysis results and treatment protocols were taken from patient's charts. Laboratory data concerning complete blood count, ratio of urine protein to creatinine, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum amyloid A (SAA) levels were obtained during their routine follow-up at attack-free period.

Results: There were 178 (60.3%) children with the diagnosis of FMF; 73 female and 104 male and 117 (39.7%) adults diagnosed as FMF after 18 years of age; 69 female and 48 male. The mean±SD age at symptom onset, at the diagnosis and current age was 4.92±3.03, 6.45±3.61, 11.59±4.38 for group I and was 18.35±10.34, 32.23±11.62, 38±11.64 for group II, respectively. Consanguinity was significantly more frequent among children with FMF (36.1%). A positive family history of FMF was similarly present in 102 (57.6%) of group I and 66 (56.4%) of group II. Twelve (10.2%) adult patient have FMF at their children. Family history of amyloidosis was equally distributed between groups; 6.2% in group I and 6.8% in group II. The median number of FMF attacks per year was 18 in children and 15 in adults. While children were having significantly more frequent attacks, the duration of attacks were longer in adults compared to children ($p<0.001$). The most frequent symptom was fever (91.5%) in children and abdominal pain (96.5%) in adults. Arthritis, chest pain and erysipelas like rash were seen similarly in both cohorts. Sacroileitis (10.2%), amyloidosis (5.1%) and chronic renal insufficiency (5.1%) were significantly more common in patients with FMF diagnosed after 18 years of age. Colchicine resistance and compliance were evenly distributed among groups. In genotypic evaluation, groups were compared for homozygotes, compound heterozygotes and heterozygotes and had put forth similar results. Attack free acute phase reactants like CRP; median 2.8 mg/dl and SAA; median 3.86 mg/dl were significantly higher in group I.

Conclusion: Both clinical features and acute phase response in FMF were less pronounced in patients diagnosed at adulthood. Children were having more frequent attacks,but accompanying diseases were more common in adults. While following patients taking age of the patient in to account will help to better understand the disease course.

REFERENCE:

[1] Yasar Bilge NS, Sari I, Solmaz D, et al. Comparison of early versus late onset familial Mediterranean fever. Int J Rheum Dis. 2018 Apr;21(4):880-884. doi: 10.1111/1756-185X.13259. Epub 2018 Jan 5.

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THU0524B EXTRA-OCULAR MANIFESTATIONS OF CHILDREN WITH SARCOID-LIKE UVEITIS

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Background: Paediatric sarcoidosis may represent a spectrum of disease. Early onset sarcoidosis & its genetically defined counterpart Blau syndrome associated with NOD2 mutations are characterized by fever, rash, arthritis and organomegaly. Later onset sarcoidosis has wider organ involvement including lungs, kidneys, lachrymal and extra-ocular glands. Both presentations may lead to long term complications due to end-stage organ damage. Although similar disease manifestations can be seen in adults and children, some entities are essentially pediatric at onset, namely Blau syndrome and most forms of immunodeficiency associated granulomatous diseases. Ocular sarcoidosis has a well described uveitis phenotype (1). We created a retrospective cohort of patients currently followed at GOSH with likely ocular manifestation of sarcoidosis (1)

Objectives: To describe a retrospective cohort of children with sarcoid-like uveitis, To describe their extra-ocular manifestations at the time of the study,To describe their management

Methods: retrospective case review of children currently followed at GOSH with a phenotype of ocular sarcoidosis with uveitis (ophthalmologist defn (5, 6)), or a diagnosis of idiopathic uveitis (anterior, posterior, intermediate or panuveitis) with raised ACE level at least once. We collected demographics and all extra-ocular involvement described in sarcoidosis

Results: 52 patients. 27/52 males. Median age onset of uveitis 4.20 yrs (1.41-15.16). 30/52had onset <8 yrs. Median ACE 73 and mean ACE 77 at presentation (0-90U/L normal). Median max ACE79& mean max ACE 88.2 (14-420).NOD2 done in 12 patients: 6+, 6-. Only 4/6 patients Blau phenotype.

Ethnicity: black 13, asian 10, caucasian 13, unknown 16/52. 49/52 patients had bilateral uveitis. Uveitis anterior 17/52, intermediate 5/52, posterior 2/52, panuveitis 25/52, unknown 1/52. ANA+15/47(32%).

Extra-ocular (n=52): Lymphadenopathy: 15 (29%) clinically Liver: 16 (31%) - transaminitis 9, ultrasound(USS) abnormality (hepatomegaly, calcification, increased echogenicity) 5 & both abnormal USS & blood 2 Arthritis: 15 (29%) large joints of lower limbs & joints hands. Tenosynovitis 4 (7.7%) Renal: 15 (29%) (USS or Blood/urine tests – raised serum creatinine,

raised urinary ca creat ratio, raised urinary NAG/RBP) — 4/15 on USS and 9/15 in blood/urine tests, 2/15 on both USS and blood/urine tests. Lungs: 7 (13.5%): 6 abnormal lung function test, 1abnormal CXR, lung function& CT chest - severe interstitial lung disease & presented- progressive shortness of breath. Skin: 10(19.2%), eczema-like/non-specific skin Parotid/glandular: 1 (1.9%) on USS Splenomegaly: 4 (7.7%) on USS Sensorineural hearing loss: 2 (3.8%)

Medications to treat uveitis and/or extra-ocular manifestations were: Methotrexate 13 (25%), Methotrexate + Adalimumab 11 (21.2%), MMF 6 (11.5%), topical steroids 8 (15.4%), systemic steroids 2 (3.8%). 10 patients no medication

Conclusion: Most of the sarcoid-like *uveitis* patients had at least one extra-ocular involvement. ACE does not appear to be a sensitive biomarker. Some patients (19.2%) have a mild phenotype and require no treatment. Our data demonstrate the importance of close monitoring for extra-ocular manifestations and highlight good clinical response to steroids, MTX, MMF and anti-TNF.

REFERENCE:

[1] Acharya NR et al International Ocular Sarcoidosis Working Group. Distinguishing Features of Ocular Sarcoidosis in an International Cohort of Uveitis Patients. Ophthalmology. 2018 Jan;125(1):119-126.

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THU0525 DEVELOPMENT OF A PREDICTIVE TOOL FOR RESPONSE TO ANTI-TNF-ALPHA THERAPY IN JIA USING GENE EXPRESSION PROFILES IN PERIPHERAL DERIVED MONONUCLEAR CELLS

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Background: Heterogeneity in response to biological medication is a major challenge in the management of Juvenile Idiopathic Arthritis (JIA) (1). Biomarkers such as cytokines or whole blood RNA expression profiles that predict therapy efficacy prior to treatment pose a solution and could enable precision medicine. It was previously demonstrated that whole blood gene expression profiles can predict response to anti-TNF-α therapy in patients with JIA (2). These findings currently await validation in a multicenter prospective cohort study. Harmonization of data from different cohorts, however, is often hampered by site-dependent differences in biological sample collection and processing (3). For instance, the biological material that is retrospectively available from biobanks depends on what is stored exactly, e.g. whole blood versus peripheral blood mononuclear cells (PBMC). Furthermore, different blood collection tubes containing different additives can affect sample quality at an early stage and make interchangeability or comparability of data impossible.

Objectives: We evaluated the comparability of gene expression profiles when whole blood from patients with JIA is collected in different RNA collection tubes and processed accordingly. Next, we will investigate the predictive capacity for therapy response of RNA expression profiles from frozen PBMC of 63 JIA patients.

Methods: Peripheral blood from 11 children with non-systemic JIA with active disease was collected in PAXgene (PreAnalytiX) and Tempus (Applied Biosystems) tubes. All tubes were subsequently stored in the freezer at -80 °C. After thawing, RNA from the PAXgene tubes was extracted with use of the PAXgene Blood RNA Kit and RNA from the Tempus tubes was isolated by using the Tempus Preserved Blood RNA Purification Kit I. Gene expression of *CSNK1D*, *C1D*, *ASAP2*, *SRRD*, *PPP1R3B*, *HLA-DQA1*, *PDZK1IP1* and *MZB1* was determined with qPCR. For our next experiment, frozen PBMC derived from patients with non-systemic JIA who are included in our longitudinal Pharmachild registry biobank will be used. Of the 63 patients, 28 (44.4%) children were diagnosed with oligo articular JIA, 19 (30.2%) with poly articular JIA, 9 (14.3%) with enthesitis-related JIA, 4 (6.3%) with psoriatic JIA and 3 (4.8%) with undifferentiated JIA. The average age at sampling was 11.5 years ± 4.0 and 65% of the patients was female. These samples will be run on a 96-analyte NanoString panel and associated with clinical response at time points 3 and 6 months after start of TNF-α blockade.

Results: Both RNA blood collection systems yielded high-quality RNA, with overall higher RNA concentrations for blood collected in Tempus tubes in comparison to PAXgene tubes. qPCR data showed that gene expression of all measured genes is affected by the method of blood collection and processing. However, the inter-individual variation was similar between both collection tubes, indicating that similar RNA profiles were observed.

Conclusion: Gene expression profiles derived from whole blood collected in PAXgene or Tempus tubes are comparable, but are not interchangeable.

REFERENCES:

[1] Swart JF, de Roock S, & Prakken BJ. Understanding inflammation in juvenile idiopathic arthritis: How immune biomarkers guide clinical strategies in the systemic onset subtype. *Eur J Immunol* 2016;46(9):2068-2077.

[2] Cui A, Quon G, Rosenberg AM et al. Gene Expression Deconvolution for Uncovering Molecular Signatures in Response to Therapy in Juvenile Idiopathic Arthritis. *PloS one* 2016;11(5):1-17.

[3] Yeung RS, Albani S, Feldman BM et al. Enhancing translational research in paediatric rheumatology through standardization. *Nature Reviews Rheumatology* 2016;12(11):684.

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THU0526 LONG-TERM OUTCOME IN JUVENILE IDIOPATHIC ARTHRITIS – A POPULATION-BASED STUDY FROM SWEDEN

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children. The incidence rate among Caucasians is reported to be 8-15/100 000/year (1, 2). The long-term prognosis is insufficiently studied in JIA, although it is known that the disease often proceeds into adulthood and may cause joint damage leading to significant morbidity and physical disability. There are many challenges in elucidating the long-term prognosis. Amongst others, frequent occurrence of disease misclassification in diagnostic registers and the heterogeneity of JIA have made it difficult to interpret results (3, 4).

Objectives: To study the epidemiology, incidence and long-term outcome of JIA in southern Sweden using a population-based cohort of children with a validated diagnosis of JIA collected over nine years.

Methods: Potential cases of JIA, diagnosed between 2002 and 2010 were collected from a local search at the Department of Rheumatology in Lund and at the National Board for Health and Welfare, using the ICD-codes M08-M09. The study area is Skåne, the southernmost county of Sweden (population 1.24 million; 19.1% aged < 16 years) and the median follow-up time was eight years. The JIA-diagnosis was validated and subcategorised through medical record review based on criteria defined by The International League of Associations for Rheumatism. Parameters on disease activity and pharmacologic treatment were recorded annually until the end of the study period.

Results: 251 cases of JIA were confirmed. The mean annual incidence rate for JIA was estimated to be 12.8/100 000/year. The highest age specific annual incidence is at the age of two years (36/100 000/year). This peak is consistent in the female group, but the incidence peak among males is at twelve years of age.

Almost all patients are at some point during their disease course prescribed non-steroidal anti-inflammatory drugs (98%). Intra-articular steroid injections are also frequently used (78.9% in the total cohort). Methotrexate is the most common disease modifying anti-rheumatic drug prescribed (60.6%). Tumor necrosis factor alpha-inhibitors are used as treatment in 23.9% of the children.

Oligoarthritis was the largest subgroup (44.7%), followed by undifferentiated JIA (16.3%), polyarticular rheumatoid factor negative JIA (13.9%), enthesitis-related arthritis (8.8%), polyarticular rheumatoid factor positive JIA (6.8%), juvenile psoriatic arthritis (6.8%) and systemic JIA as the smallest subgroup (2.8%).

Uveitis, both acute and chronic, was seen in 10.8% of the children. Permanent joint affection was seen in 20.7% of the children and 8.8% have been treated with joint corrective orthopedic surgery.
At five-year follow-up, 57% of the children had disease activity, defined as arthritis and/or uveitis (2.1% with uveitis as active disease).
Conclusion: This is a well-defined, population-based and validated cohort of children diagnosed with JIA investigating long-term outcome in the era of biologics. We found that a considerable part of the children still develop uveitis, permanent joint affection and need joint corrective surgery. Surprisingly, more than 50% of the cohort has active disease five years after diagnosis. In conclusion, we still have long-term challenges in children with JIA, in spite of state-of-the-art treatment.

REFERENCES:
[1] Thierry S, et al. Joint, bone, spine. 2014;81(2):112-7.
[2] Berntson L, et al. J Rheumatol. 2003;30:2275-2282.
[3] Harrold LR, et al. J Rheumatol. 2013;40(7):1218-25.
[4] Ravelli A, et al. Lancet. 2007;369(9563):767-78.

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THU0527 RISK SCORE OF MACROPHAGE ACTIVATION SYNDROME IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Macrophage Activation Syndrome (MAS) is a severe, life-threatening, complication of rheumatic diseases in childhood, particularly of systemic Juvenile Idiopathic Arthritis (sJIA), occurring in approximately 25% of the patients with sJIA. A score that identifies sJIA patients who are at high risk to develop MAS would be useful in clinical practice.
Objectives: To evaluate whether routine laboratory parameters at disease onset may predict the development of MAS in patients with active sJIA. To define a risk score of MAS for sJIA patients using these parameters.
Methods: Laboratory parameters of disease activity and severity (WBC, N, PLT, Hb, ferritin, AST, ALT, gGT, LDH, TGL, fibrinogen, D-dimer and CRP), were retrospectively evaluated in 86 sJIA patients referred to our Division of Rheumatology from 1998 to 2017 with at least one year of follow-up. Laboratory parameters were evaluated during active sJIA, without MAS, at time of hospitalization (T1) and before treatment for sJIA was started (T2). Patients were divided in two groups: group 1 (patients without history of MAS), group 2 (patients with at least one MAS episode during disease course). To calculate a MAS risk score, laboratory parameters, collected at T2, with a statistical significant difference between the two groups of patients were selected.
Results: Thirty-three patients, who fulfilled the 2016 classification criteria for MAS [1] at time of sampling, were excluded from the analysis. Therefore, we analysed laboratory parameters of 53 patients with sJIA, 33 of whom without history of MAS (group 1) and 20 who developed at least one episode of MAS during disease course (group 2). Levels of ferritin, AST, LDH, gGT and TGL, collected at T2, were statistically significant higher in patients with a history of MAS compared to those without a history of MAS. For each of these parameters an arbitrary cut-off was defined. In order to define the final score an arbitrary rate was attributed to each parameter. Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were calculated to define the best scoring system. The scoring system with the best sensitivity was chosen (Table 1). A MAS risk score >3 identified 19 out of 20 sJIA patients with a history of MAS and 4 out of 33 sJIA patients without history of MAS.

Abstract THU0527 –Table 1.

Table 1. Laboratory parameters and cut-off used to create the MAS risk score in sJIA patients.

Laboratory parameters	Cut-off	Rate
Ferritin (ng/ml)	>900	1
AST (UI/L)	>35	1
LDH (UI/l)	>550	1
gammaGT (UI/L)	>30	2
Triglycerides (mg/dl)	>150	2
Sensitivity (Se)	0.950	CI95% 0.842-0.988
Specificity (Sp)	0.879	CI95% 0.753-0.948
Positive predictive value (PPV)	0.826	CI95% 0.692-0.912
Negative predictive value (NPV)	0.967	CI95% 0.865-0.995

In order to validate the MAS risk score on a different population, we applied it on 53 patients from other paediatric Rheumatologic centres. Thirty-seven of these patients without history of MAS while 16 with at least one episode of MAS. Sensitivity and specificity were 0.750 and 0.784 respectively.
Conclusion: In conclusion we developed a MAS risk score based on routine laboratory parameters that are available worldwide, that can help clinicians to identify patients at higher risk to develop MAS. A validation on a larger population is necessary.

REFERENCES:
[1] Ravelli A et al. Ann Rheum Dis. 2016 Mar;75(3):481-9.

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THU0528 DISCONTINUATION OF COLCHICINE THERAPY IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Clinical phenotype of FMF exists in some carriers of MEFV mutation. These patients tend to have a mild disease. Prolonged colchicine free remission was reported in a small group of FMF patients.
Objectives: To describe and characterize a group of children with FMF in whom colchicine was discontinued.
Methods: The study cohort consisted of all children with FMF followed at 2 referral centers in Israel in whom colchicine was discontinued following prolonged attack free period.
Clinical presentation, mutations in MEFV gene and disease outcome of patients who successfully ceased colchicine therapy were compared with patients with relapse of FMF attacks.
We performed a retrospective study in two referral centers in Israel of 43 patients with FMF with 1 or non-mutated MEFV allele who ceased colchicine therapy following prolonged attack free period. The phenotype of the patients was investigated in detail, and the MEFV mutations, laboratory findings, clinical picture and outcome of 30 (70%) patients that successfully ceased colchicine therapy were compared to 13 (30%) patients who failed.
Results: 47 patients (55% males), mean age 6±3.2 years at the diagnosis, were enrolled in the study, of them 4 patients were excluded due to poor follow up. Fever (93%), abdominal pain (79%), arthralgia (19%) and arthritis (12%) were the most common symptom at attack. The average period free of attacks before enrolment was 11.3±9.2 months. The average follow-up after ceasing colchicine was 5.1± 2.9 years. Thirteen patients (30.2%) had an attack during follow up with most common symptoms of fever (92%) and abdominal pain (77%) and colchicine therapy was restarted within 10.1 months (1.1-36.4months). There were no differences between the groups of patients that were able to stop

colchicine and the group that needed to renew therapy in demographic, genetic and most clinical parameters, including the age (13.4±3.9 vs 11.9 ±3.7p-0.26), level of SAA at enrolment (4±3.6 vs 3.3±2.4p-0.7) and time of last attack prior to enrolment (12.6±9.6 vs 8.6±8.2 months p-0.08). Myalgia and arthritis were more common among children that required to renew therapy compared to the group that didn't (31% vs 6.7% p-0.058 and 31% vs 3% p-0.024 respectively).
Conclusion: Cessation of colchicine therapy following prolonged remission in selected group of patients who are not homozygous for MEFV mutation could be considered. Patients with arthritis or arthralgia are more likely to have an attack after ceasing colchicine therapy.

REFERENCES:
[1] Discontinuing **colchicine** in symptomatic carriers for MEFV (Mediterranean FeVer) variants.
[2] Sönmez HE, Batu ED, Bilginer Y, Özen S.
[3] Clin Rheumatol. 2017 Feb;36(2):421-425. d

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THU0529 WHOLE BODY MAGNETIC RESONANCE IMAGINGIN JUVENILE DERMATOMYOSITIS. A LONGITUDINAL STUDY

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Background: Juvenile dermatomyositis (JDM) is a rare multisystem connective tissues disorder of unknown aetiology. Assessment of disease activity is a chalange in clinical practice.
Objectives: To compare whole-body MRI (WB-MRI) with clinical examination in the assessment of disease activity in JDM.
Methods: We included consecutive JDM patients followed in the rheumatology unit. All patients were submitted to clinical and laboratory evaluation. WB-MRI images were obtained using a 1.5 T MRI scanner and short T inversion recovery sequences (STIR). Muscle, peripheral inflammation and subcutaneous inflammations signal abnormalities were scored in 42 muscular groups. Muscle inflammation was classified as: 0 = absent; 1 = Mild to moderate/involvement less than 50% of muscle extension and 2 = Accentuated/greater than 50%. Peripheral and subcutaneous inflammations were classified as: 0 = absent; 1 = present; and on proximal and distal extremities. WB-MRI and clinical assessments were performed concurrently and results compared. Evaluation was repeated after 12 months. Statistics was performed according to the nature of the variable.
Results: WB-MRI revealed muscle inflammation in 6 (31.6%) at study entry. We observed grade 2 muscle inflammation of the right and left scapular girdle (1/19 patients), right and left pelvic girdle (2/19 patients) and right and left tight (1/19 patients). Grade 1 inflammation was observed in peripheral right and left arm (2/19 patients), peripheral right and left thigh (1/19 patients). Grade 1 subcutaneous inflammation was observed in right and left thigh (1/19 patients) and left leg (1/19 patients). Additionally we observed sacroiilitis (1/19 patients), spinal cord infarction (21%) and osteonecrosis (5.2%). All patients were treated with standardized treatment. After 12 months 13/19 (68.4%) patients repeated the WB-MRI. Five (38.4%) patients had new/worsening of muscle and subcutaneous inflammation, one (7.7%) patient had tibial medullary infarction. Correlations between WB-MRI muscle score and disease activity measures were excellent (Manual Muscle Test: r=−0.88, Childhood Myositis Assessment Scale: rs=−0.81). Patients with subcutaneous inflammation developed clinically evident subcutaneous calcifications during follow-up.
Conclusion: WB-MRI provides additional information to clinical evaluation and represents a promising tool to determine the grade of muscle inflammation to additional peripheral and subcutaneous tissue inflammation.

REFERENCES:
[1] Malattia C, Damasio MB, Madeo A, et al. Ann Rheum Dis 2014;73:1083–1090

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THU0530 IDIOPATHIC RECURRENT PERICARDITIS: CLINICAL FINDINGS AND TREATMENT APPROACH

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Background: Recurrent pericarditis affects 15-30% of patients with acute pericarditis. The etiology is poorly understood, with about 80% being idiopathic. Several treatment options are available for recurrences, including NSAIDs, colchicine, glucocorticoids and IL-1 inhibitors (i.e. Anakinra). Standardized guidelines for the management of these patients are still lacking
Objectives: To analyze clinical findings and treatment approach in a cohort of pediatric patients with recurrent pericarditis
Methods: Patients with at least two episodes of idiopathic pericarditis, followed at two Pediatric Rheumatology centers between 2006 and 2018, were included
Results: A total of 42 patients (18 males) were included. Mean age at disease onset was 11.8 years (range 4-17). Chest pain and fever were the presenting symptoms in all patients. In 47% pleural effusion was detected. Laboratory tests showed increased white blood cell count (mean 14.509/mm3), C-reactive protein (mean 18.01 mg/dl) and erythrocyte sedimentation rate (mean 39 mm/h) in all patients. The first episode was variably treated: 18/42 (43%) received NSAIDs alone, 5/42 (11.9%), colchicine alone or associated to NSAIDs and 3/42 patients (7%) received antibiotics alone. 16/42 (38%), not responsive to NSAIDs or colchicine, received glucocorticoides. Patients who received glucocorticoids at the first episode relapsed earlier (median time of 2.1 months range 10 days-5 months), than patients treated with NSAIDs (6.6 months range 10 days -24 months) or with colchicine (5 months range 10 days-5 months) ($p<0.05$). In our study, initial treatment of the first episode did not affect the number of subsequent flares. To evaluate treatment strategy at relapses, we divided our study population in two groups: Group 1 (20 pts) in which recurrence was treated with NSAIDs, colchicine or glucocorticoid (alone or combined); group 2 (22 patients) in which anakinra was started. Among patients belonging group 2, 9 received anakinra at first relapse, 7 at the second, 2 at the third and 2 at the fourth. Anakinra treatment was followed by a prompt resolution of symptoms and inflammatory signs within 2 days. During daily treatment with full dose anakinra, no relapses were reported over a median of 13.3 months (range 5-24 months). In 13 out of 22 patients, anakinra was gradually tapered reducing the days of administration during the week. Four of these patients relapsed. The mean time from the start of anakinra to tapering was 17±4 months (range 14-23 months) in the 4 patients who experienced a relapse versus 14±4 months (range 7-21 months) in patients who did not flare, with no statistical difference. Among the 22 patients belonging to group 2 anakinra was finally discontinued in 11 after a mean time of 23.4 months (range 12-36). Among these, 8 relapsed after anakinra withdrawal including 2 of the 4 patients already relapsed during tapering). Only 3 patients didn't present any relapse (up to 20.3 months of follow-up). All patients who relapsed responded quickly to the reintroduction of anakinra
Conclusion: Our study confirms the lack of a standardized treatment approach in patients with recurrent pericarditis. Patients treated with glucocorticoid at first episode relapse before than those treated with other drugs. Anakinra is an effective treatment; however, tapering/discontinuation of the drug lead to relapses in several cases. Further experience on larger population is needed to define the best treatment duration and approach to withdrawal of IL-1 inhibitor
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THU0531 "BOTHERING TO LISTEN": ENABLING PATIENT AND FAMILY INVOLVEMENT IN CHILDHOOD UVEITIS HEALTHCARE

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Background: Childhood uveitis is a group of heterogenous, potentially blinding inflammatory disorders. Management is complex. There is growing recognition of the importance of actively involving affected children and their families in their own care. Co-designed interventions, developed through active involvement of staff and patients, can provide effective solutions to problems identified by those affected.
Objectives: To use findings from a patient and family discussion group to inform the co-designed development of health care processes and interventions.
Methods: Five children/young people with uveitis (age ranges 8 to 17), seven parent/carers of children with uveitis and four health care professionals attended a 90 minute discussion group. Main discussion topic was the identification of areas in need of interventions or support structures. Sub-topics were determined a priori using previous PPI and existent research (REFS). They comprised: Direct health care; Impact on families; School, education and peers. Responses were collated. Consent was taken for use of direct quotes from participants.
Results: We outline the areas identified by children and families:
Direct health care: Four interconnected areas were identified: (1) Transitioning to adult services, (2) peer support (health care services being a valuable site for identifying peers), (3) communication between care structures, and (4) education for families. With regards to family education, there was identification of the need for specific services or interventions around the communication of (4a) diagnosis, (4b) treatment, (4c) likely long term outcomes/prognosis, (4d) and the child's progress. There was also discussion on (4e) the formats used to communicate with families.
Impact on families: Participants discussed support around (1) family relationships, (2) the impact of systemic medication. They also discussed (3) a need for recognition of the changing nature of their lived experience as affected families over the disease course and the need for on-going psychologic support especially at presentation to help with acceptance.
School, education and peers
Participants discussed the need for support around: (1) the impact of treatment on school life, (2) communication with school professionals and peers, (3) impact of visual impairments, (4) managing the visibility/invisibility paradox (ie being made to feel different but also having a disorder which was not externally apparent), and (5) managing adolescence.
Conclusion: Through the above approach, we have identified a range of issues affecting our patients and their families. Our findings are similar to those of other groups (1, 2) These lived experiences will be used to inform the co-design of supportive services (patient leaflets, videos, website, psychology intervention) and research on the effectiveness of these interventions in improving the management of affected children and their families.

REFERENCES:

[1] Parker DM, Angeles-Han ST, Stanton AL, Holland GN. Chronic Anterior Uveitis in Children: Psychosocial Challenges for Patients and Their Families. Am J Ophthalmol. 2018 Jul; 191:xvi-xxiv
[2] Silva LMP, Arantes TE, Casaroli-Marano R, Vaz T, Belfort R Jr, Muccioli C. Quality of Life and Psychological Aspects in Patients with Visual Impairment Secondary to Uveitis: A Clinical Study in a Tertiary Care Hospital in Brazil. Ocul Immunol Inflamm. 2017 Oct 11:1-9.

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THU0532 RITUXIMAB FOR RAPIDLY PROGRESSIVE JUVENILE SYSTEMIC SCLEROSIS

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Background: Juvenile Systemic Sclerosis (JSSc) is a rare multi-systemic disease characterized by fibrous changes of the skin and internal organs [1]. Patients with "rapidly progressive SSc" usually present rapid development of skin induration and important organ damage [3], leading to poor prognosis [2, 3]. Recently Rituximab (RTX), a monoclonal antibody against the CD20 antigen on B cells, has demonstrated to be a promising therapy for adult patients with SSc [4, 5].
Objectives: We describe four pediatric patients with rapidly progressive JSSc treated with RTX.
Methods: Data on clinical, laboratory and instrumental parameters were collected from four patients with rapidly progressive JSSc treated with RTX for at least one year. Data were recorded at baseline and every 6 months after initiation of therapy. All patients underwent i.v. RTX therapy with four cycles (375 mg/m^2 every 2 weeks), at 3 months intervals. Oral prednisone (PDN, 0.5 mg/Kg/day) and oral mycophenolate mofetil (MMF, 500 mg/m^2/day) were administered between RTX pulses. Skin changes were assessed by MRSS, changes on muscles involvement by CMAS. Variations on BMI, pulmonary function tests (FVC, FEV1, DLCO) and cardiac involvement (LVEF, LVEDV, GLS) were expressed as% change from baseline. J4S was used to assess the overall disease severity [6].
Results: Four JSSc patients (3M, 1F), aged 8-17 years, entered the study. Three patients presented with prevalent cardiological involvement. One patient (Case 3) presented with severe pulmonary involvement. After one year RTX treatment, all patients showed significant decreased of number/duration of Raynaud Phenomenon attacks and 3 patients of cutaneous involvement. Two patients needed an implantable cardioverter defibrillator (ICD) because of episodes of severe ventricular tachycardia (VT). After 12 months of therapy one patient presented improvement LVEF (+19%) and J4S, the other showed a global cardiac improvement (LVEF +37%, LVEDV -18%) and J4S. Both underwent a second year-long treatment with RTX with no worsening of internal organs' involvement. Case 3 showed a significant improvement of the respiratory function (FVC +46%, FEV1 +33%, DLCO +30%) with decrease of J4S. Case 4 improved her arrhythmia and muscle strength (CMAS +17%). No major RTX-related side effects were reported.
Conclusion: Rapidly progressive JSSc still carries a high mortality rate. To the best of our knowledge this is the first case series of patients with JSSc successfully treated with RTX. Our experience, although in a small cohort, confirms the beneficial effect of this therapy on the life-threatening internal organ involvement, particularly on cardiac function.

REFERENCES:

[1] Martini G, et al. *Arthritis Rheum* 2006; 54(12): 3971.
[2] Martini G, et al. *Rheumatology (Oxford)* 2009;48(2):119.
[3] Joven BE, et al. Semin Arthritis Rheum. 2010; 39:285.
[4] Daoussis D, et al. *Semin Arthritis Rheum* 2017; 46 (5): 625-31.
[5] Jordan S, et al. *Ann Rheum Dis*, 2015; 74: 1188-94.
[6] La Torre F, et al. *Arthritis Rheum.* 2012;64(12):4143-50

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THU0533 IMPAIRED PLATELET FUNCTIONS IN PATIENTS TREATED WITH COLCHICINE

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Background: Colchicine has been used in the treatment of Familial Mediterranean Fever (FMF) since 1972. Apart from the inhibiting mitosis in all cells, colchicine has an anti-inflammatory effect by inhibiting activation and migration of neutrophils. Colchicine is a safe drug at recommended

doses, but it can cause rare side effects including hematological findings such as lymphopenia, thrombocytopenia and neutropenia.
Objectives: In this study we aimed to define the adverse effect of colchicine on platelet function and its clinical relevance.
Methods: A total of 220 FMF patients between June 2016-2017, followed at Hacettepe University Pediatric Rheumatology Department and were on colchicine treatment for at least one year, were included to the study.
Results: Among the selected 220 FMF patients, 100 of them (54% female) described hematological symptoms when questioned in detail. The mean age of these patients was 11.74 ± 4.86 years. The mean cumulative colchicine exposure was 5.7±3.8 years. The most common referral symptom was frequent epistaxis (79%) followed by easy bruising (69%), and menstrual disorder including prolonged or heavy menstrual bleeding (21.8% among female patients). Among these 100 patients, 36 of them had prolonged bleeding time and impaired platelet aggregation test. Patients who had abnormal platelet function tests (the group with abnormal bleeding time) were receiving higher colchicine doses (median 0.05 vs 0.03 mg/kg/day; p:0.001) compared to the patients who had normal platelet function tests (bleeding time normal group) However there were no significant difference in terms of cumulative colchicine exposure (median 6.5 vs 4.5 years; p:0.07) and total platelet counts (median 288500 vs 279000/mm3; p:0.61). Patients with abnormal platelet function tests also had more epistaxis (47% vs 7%; p<0.001) bruising (51% vs 3%; p<0.001) and dysmenorrhea (among female patients 100% vs 26%; p<0.001). Colchicine was not reduced in these patients and no life-threatening event was observed.
Conclusion: In our study, we have shown prolonged bleeding time for the first time in the literature. Colchicine may cause microtubule inhibition in platelets as well as in other cells and impair platelet function. Further prospective studies are needed to clarify the significance of this side effect.

REFERENCE:

[1] Padeh S, Gerstein M, Berkun Y. Colchicine is a safe drug in children with familial Mediterranean fever. J Pediatr 2012;161(6):1142-1146.

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THU0534 NEW CLASSIFICATION CRITERIA FOR RECURRENT AUTOINFLAMMATORY DISEASES APPLIED TO AN INDEPENDENT COHORT: EXPERIENCE FROM THE JIR COHORT DATABASE

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Background: New classification criteria for the inherited periodic fever syndromes (TRAPS, FMF, MKD and CAPS) have recently been developed during a Consensus Conference held in Genoa in March 2017.
Objectives: The aim of our study was to compare these new classification criteria for monogenic recurrent fever syndromes with the diagnoses of clinicians. For this purpose we used the JIRcohort database, an international platform gathering data of patients with pediatric inflammatory disease.
Methods: The Genoa classification criteria were applied to all the patients, then compared to the clinical diagnosis of the treating physician. As patient diagnosis could be confirmed or suspected, the patients could have up to two diagnoses. Classification criteria relied on genetical HRF pathogenicity classification. Finally, criteria performance were assessed by firstly determining sensitivity and specificity and secondly analyzing true positive, false positive and false negative patients.
Results: 455 patients included to the JIRcohort database with a recurrent fever syndrome were enrolled to the study.
CAPS: The analysis of the performance of the CAPS criteria showed sensitivity of 60% and specificity of 98%. 14 patients fulfilled Genoa CAPS classification criteria, with 6 true positive and 8 false positive patients. Patients with confirmatory genotype always fulfilled classification criteria. 4 patients, who carried heterozygous mutations, were false negative.
TRAPS: The analysis of the performance of the TRAPS criteria showed sensitivity of 100% and specificity of 98%. 22 patients fulfilled Genoa TRAPS classification criteria, all true positive patients with confirmatory and non-confirmatory genotype. 5 were false negative with 4 patients with non-confirmatory genotype.
FMF: The analysis of the performance of the FMF criteria showed sensitivity of 96% and specificity of 89%. 118 patients were true positive while 35 were false positive patients. True positive patients were all patients with confirmatory genotype, patients with non-confirmatory genotype and no mutation. 37 were false positive patients. 5 patients were false negative with 3 patients with non-confirmatory genotype.
MKD: The analysis of the performance of the CAPS criteria showed sensitivity of 64% and specificity of 66%. 7 patients with confirmatory genotype were true positive patients. 148 were false positive patients with 44 patients diagnosed TRAPS, FMF, CAPS while the rest were SURF. 4 were false negative including 3 patients with non-confirmatory genotype.
Conclusion: This study is the first Genoa criteria evaluation among a cohort of patients seen with recurrent fever. This descriptive study shows tremendous performance Genoa criteria for patients with confirmatory genotype and help classifying patients with non-confirmatory genotype. On the other hand, those classification criteria were less performant when patients did not display at least one gene mutation. Therefore, Genoa classification criteria for TRAPS outperformed the others, because mandatory genetical screening. This study also highlights permissive criteria for clinical CAPS, FMF and MKD. The implementation of biological criteria in MKD would improve MKD criteria.
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THU0535 NATURE AND IMPACT OF THE FRENCH NETWORK RESRIP ON SCHOOLING, FOR CHILDREN WITH CHRONIC INFLAMMATORY RHEUMATISM

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Background: Pediatric chronic inflammatory rheumatism (CIR) has a significant impact on daily life, especially on schooling, that can lead to child's drop-out. In this context, a French paediatric health network, RESRIP (Réseau pour les Rhumatismes Inflammatoires Pédiatriques), has been created in 2014 for children with CIR and living in the Ile-de-France region. Patients are included in this network if they meet certain criteria such as the need to find trained health professionals close to their home or for support because of adverse social conditions or difficulties with their schooling. If the criteria are fulfilled, the patient and his family participate in an intake interview which allows RESRIP to understand the patient's need and to set up targeted actions.
Objectives: In our study, we aim to describe and evaluate RESRIP's role on improving school attendance and tackling absenteeism
Methods: A descriptive retrospective study was performed regarding the support provided by RESRIP with respect to patients' schooling and education professionals. Rates of non-attendance were collected at inclusion

and every 6 months from 2014 to 2017, through a standardized auto-questionnaire.
Results: 278 patients (M/F: 0.29) aged 12.7 years on average (± 4.9, range 2-21) were taken care of between 2014 and 2017 by RESRIP. Juvenile idiopathic arthritis (JIA) (n = 142), connective tissue disease (n = 49) and auto-inflammatory disease (AID) (n = 32) are the 3 main pathologies covered. Among the 278 patients, twenty-one percent of patients needed academic support when entering the network, including: 37% in the JIA group, 34% in the connective tissue group and 18% in the AID group. Educational assistance was set up for all patients with school difficulties at inclusion but also for all the patients during their follow-up.
Patient Support: 178 Individual Action Plan (IAP) were implemented by RESRIP. Twelve patients benefited from additional time for their school exams and 10 were allowed to pass the baccalaureat (French final college exam) over two years instead of a year. In thirty patients, sports education has been adapted. Forty-one MDPH files (Departmental Houses for the Disabled) were produced to enable the establishment of a school life assistant (AVS), teaching materials and/or technical aids. Finally, 8 patients received home schooling assistance through Home Learning Assistance Services (SAPAD).
Education professional support: RERSIP established partnerships with the French National Education (FNE) and the SAPAD (home tuition service for ill children). For the FNE, RESRIP provided school doctors or nurses with: 8 continuing medical training and 25 personal interviews to explain the pathologies. In addition, 5 multidisciplinary meetings, within the institutions were organized, for 5 patients with social integration difficulties and stigmatization. RESRIP actions, has allowed a significant decrease in school absenteeism between 2014 and 2017: 3.2 days per year on average at day 1 to 0.5 days per year on average ($p < 0.05$) at 42 months.
Conclusion: Over time, a better understanding of the impact of chronic illness over school and education professionals, has allowed RERSIP to improve its support. The result is a notable decline in school absenteeism and in unjustified physical education exemptions. Several projects are underway: The development of a standard IAP available for doctors, the set-up of a partnership with hospital school, willing to help for the implementation of home school support courses in addition to SAPAD.
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THU0536 LONG TERM IMMUNITY IN A PAEDIATRIC COHORT OF PATIENTS WITH RHEUMATIC DISEASES FROM A TERTIARY HOSPITAL IN SPAIN

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Background: Pediatric patients with rheumatic diseases (RD) are at increased risk of infections. Vaccines have been proved to be very effective to prevent them. Nevertheless the long-term immunity after vaccination remains quite unknown in this group.
Objectives: To comapre the long term seroprotecction in pediatric patients with rheumatic diseases who recieved measles, rubella, mumps, tetanus, diphteria, hepatitis B, hib and meningoccocus C vaccination acording to the routine immunization schedule in Spain, and healthy children.
Methods: We designed a cross-sectional study including consecutive pediatric patients with RD who attended the rheumatology clinic and healthy children older than 10 y.o. The administered vaccines, treatment and pathology of each patient will be recorded. Their antibodies titters against each antigen were quantified and compared to healthy children.
Results: 60 patients (median age 13 y.o IQR 10.2-12-7) and 15 healthy children (mean age 11.3 y.o. IQR 11.3-12.7) were included. In the patients group 62% were female, and 35% in healthy. Diagnosis: 85% Idiopathic juvenile arthritis, 18% Lupus or juvenile dermatomiositis. 46% had received biologic treatment sometime. Seroprotection rate was (patient vs control): measles 85%% vs 81%%, rubeola 78.8% vs 73.3%, parotiditis 84.7% vs 66.7%; VHB 27.% vs 10.5%, diphteria 89.5% vs 81%, tetanos 64.9% vs 61.1%. Hib 42% vs 53%, pneumococo 92.4% vs 100%, meningococcus C 12% vs 11%. $p>0.05$
Conclusion: No statistical differences were detected, althought the scarce number of control subjects might have infuenced this result. There is a tendence towards a lower antibody persistence anti-Hib in patients compared to healthy children. The response to life virus vaccine and tetanus seem to be as good as in healthy chidren.
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THU0537 ANGIOMATOID FIBROUS HISTIOCYTOMA MIMICKING SYSTEMIC JIA VIA MUTATION-DRIVEN IL-6 PRODUCTION

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Background: Angiomatoid Fibrous Histiocytoma mimicking Systemic JIA via mutation-driven IL-6 production: Angiomatoid Fibrous Histiocytoma (AFH) is a rare tumour associated with mutation-driven production of Interleukin-6 (IL-6) which causes a systemic inflammatory picture similar to Systemic Juvenile Idiopathic Arthritis (sJIA).
Objectives: A previously well 6-year old girl was referred with 6 weeks of abdominal pain, nausea, weight loss, night sweats, & lethargy.
Examination was unremarkable apart from a 2cm lump in the right popliteal fossa. This had been reported on USS 2 months earlier, at an external hospital, to be a Sebaceous cyst. There was no rash, organomegaly, lymphadenopathy, or synovitis.
She had persistent recurrent fevers of >39C, but not in the classical quotidian pattern of sJIA.
Methods: Bloods showed persistent Hb <70, platelets >600, ESR >100, & CRP >200.
Autoantibody & full infection screens were negative.
Urine HMMA:creatinine ratio was minimally raised at 7.2 (normal 1.8 - 5)
Faecal calprotectin, upper & lower GI endoscopy were normal.
Bone-Marrow Aspiration was reported as being highly reactive but with no malignancy seen.
Whole-body STIR MRI was reported as normal, but repeat localised USS &MRI of the knee showed a 27x18x21mm well circumscribed, mixed cystic/solid lesion with marked vascularity. The lesion was then biopsied, and subsequently excised
Plasma IL-6 levels were significantly elevated at 46.7pg/ml (normal range: 0-2), but normalised after excision. TNF and IL1b levels were normal
Results: Initial biopsy and FISH analysis confirmed the diagnosis of AFH with an abnormal EWSR1 signal pattern and classical EWSR1-CREB1 fusion. She went on to have a full excision, and staging investigations were negative.
AFH is rare (<0.3% of all soft-tissue tumours) and arises in the deep dermis/subcutis of the extremities of children & young adults. It has been regularly described in the axilla & popliteal fossa. It has a high (15%) local recurrence rate but rarely metastasises.
In >90% of cases AFH is associated with a characteristic translocation: t (2:22) (q33:q12). This forms the fusion gene EWSR1-CREB1 which in turn leads to continuous activation of CREB1. The promoter region of IL-6 has a CREB1 binding site thus causing IL-6 over-production and leading to the paraneoplastic syndrome.
Conclusion: Paraneoplastic immune dysregulation is a rare, but important cause of symptoms often otherwise associated with rheumatic diseases. Careful physical examination, and liaison with oncology teams, is needed, particularly before treatment with steroids or IL-6 inhibitors such as Tocilizumab are considered
Disclosure of Interests: : Mark Friswell: None declared, Stephen Owens Consultant for: paid a consultancy fee by Chimerix to act as an advisor on a study of adenovirus in transplant patients, Gail Halliday: None declared
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THU0538 **ABSTRACT WITHDRAWN**

THU0539 **SERUM SOLUBLE CD25: AN USEFUL BIOMARKER OF MACROPHAGE ACTIVATION SYNDROME IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS**

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Background: Systemic juvenile idiopathic arthritis (SJIA) is an auto-inflammatory disorder secondary to innate immune dysfunction with a propensity to develop macrophage activation syndrome (MAS), a life-threatening condition (1). sCD25 has been used as a sensitive biomarker for the diagnosis of Hemophagocytic lymphohistiocytosis which has similarities in clinical features and pathogenesis to MAS (2).
Objectives: To assay serum soluble CD25 in children with systemic juvenile idiopathic arthritis (SJIA) and to compare levels of sCD25 in children with inactive disease, active disease and those with macrophage activation syndrome (MAS).
Methods: This prospective study was conducted in a tertiary care referral centre in North India from January 2017 to June 2018. All patients fulfilling the International League of Associations for Rheumatology (ILAR) 2001 criteria for SJIA were eligible for enrolment. At enrolment, all patients were examined clinically for signs of disease activity. Appropriate investigations were carried out and sCD25 was analyzed by using commercially available sCD25/IL-2R ELISA kit.
Results: A total of 35 children (1-18 years) with 43 events were included in the study. Mean age at enrolment in the study was 7.3±3.59 years with male to female ratio of 2.5. Based on clinical features and investigations, events were categorized into 3 groups; SJIA with inactive disease (15; 34.9%), SJIA with active disease (15; 34.9%) and SJIA with MAS (13; 30.2%). Mean sCD25 levels in the study population were 10,966.02 ± 10,854.93 pg/ml. Children with inactive disease, active disease and disease with MAS had mean ± SD serum sCD25 levels of 4710.6 ± 1817.04 pg/ml, 7604 ± 2376.24 pg/ml, and 22062.9 ± 14335.97 pg/ml respectively. Although, Mean level of sCD25 in children with active disease was higher than those with inactive disease, but no significant difference could be found. sCD25 levels significantly (p value 0.0001) varied between MAS and other 2 groups. sCD25 cut off level of 10,385 pg/ml was found to have sensitivity of 100% and specificity of 96.7% in differentiating MAS in SJIA from disease flare and inactive disease. There was no significant correlation of sCD25 with demographic parameters, Total leucocyte count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), platelet counts, urea, creatinine, prothrombin time, activated partial prothrombin time and fibrinogen levels. A correlation of sCD25 was found with levels of haemoglobin (p-value .01), ferritin (p-value .001), aspartate aminotransferase (AST) (p-value .000), alanine aminotransferase (ALT) (p-value .000), alkaline phosphatase (ALP) (p-value .005) and triglycerides (p-value .001). Higher sCD25 levels were found in patients who had low Hb, elevated ferritin, elevated AST, ALT, ALP and serum triglyceride levels.
Conclusion: sCD25 is a useful biomarker in differentiating MAS in SJIA from disease flare and inactive disease with sensitivity and specificity of 100% and 96.7% respectively at a cut off level of 10,385 pg/ml. Coupling sCD25 with other laboratory parameters may be useful for early diagnosis of MAS in SJIA.

REFERENCES:

[1] Kelly A, Ramanan AV. Recognition and management of macrophage activation syndrome in juvenile arthritis. Curr Opin Rheumatol. 2007;19:477–81.
[2] Henter J-I, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007;48:124–31.

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THU0540 **SYSTEMATIC REVIEW OF BIOLOGICAL TREATMENT OF DEFICIENCY OF INTERLEUKIN-36 RECEPTOR ANTAGONIST (DITRA) IN CHILDREN AND ADOLESCENTS**

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Background: Deficiency of interleukin-36 receptor antagonist (DITRA) is a life threatening autoinflammatory disease caused by autosomal recessive mutations of the *IL36RN* gene leading to recurrent episodes of generalized pustular psoriasis with systemic inflammation and fever. The disease is rare and no standardized treatment guidelines exist
Objectives: To systematically review and analyze the literature on biologically treated pediatric DITRA patients
Methods: A NCBI pubmed database research was performed to identify all relevant articles on pediatric DITRA patients treated with biologicals. According to defined response criteria therapeutic efficacy was analyzed.
Results: Our literature research revealed 13 pediatric patients with DITRA and biolocial treatment. Ten patients were homozygous including six with the p.Leu27Pro, three with the p.Arg10 Argfs* and one with the p. Thr123Met mutation and three were compound heterozygous. We add an unreported DITRA patient with a compound heterozygous *IL36RN* p. Pro76Leu/pSer113Leu mutation. In total 29 flares in 14 patients were treated with biological agents- targeting IL-1/R, IL-17, IL-12/23 and TNF-α. Complete response was achieved in 15 (52%), partial in 4 (14%), and no response in 10 (34%) of the flares. Response rates were heterogeneous among the different agents. While complete/partial/no response with inhibition of TNF-alpha could be achieved in 6 (46%)/3 (23%)/4 (31%), the inhibition of IL-17 and of IL-12/23 led in each 4 flares to a 100% complete response. IL-1/R inhibition led to complete/partial response in each 1 (13%) and was not effective in 6 (75%) flares. Of note, the unreported patient was successfully treated with weekly dosed adalimumab.
Conclusion: DITRA is a rare disease that has to be considered in patients with generalized pustular psoriasis with systemic inflammation and fever. It can be effectively treated with specific biological inhibition of TNF-alpha, IL-12/23 and IL- 17, while anti-IL-1/R treatment seems less effective. Weekly dosed adalimumab appears to be a novel treatment option for pediatric patients. Further reports and studies of biological treated pediatric DITRA patients are warranted for evaluation of optimal treatment.

REFERENCE:

[1] Marrakchi, S., P. Guigue, et al. (2011). "Interleukin-36-receptor antagonist deficiency and generalized pustular psoriasis." N Engl J Med **365**(7): 620-628.

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THU0541 **ANTI-VACCINE ANTIBODY LEVELS IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS: PRELIMINARY DATA IN 90 PATIENTS**

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Background: Patients with juvenile idiopathic arthritis (JIA) may have lower protective levels of anti-vaccine antibodies (AVA) due to high inflammatory activity, interrupted or incomplete vaccination schedule, using of immune-modulating drugs, e.g. systemic corticosteroids (CS), methotrexate (MTX) and biologics [1].
Objectives: The aim of our study was to evaluate levels of AVA in the patients with JIA.

Methods: We included data about 90 JIA (26 M and 64 F) aged from 2 to 17 years, who received scheduled vaccination before the age of 2 years and before JIA onset. In all patients the Ig G anti-measles (AM), anti-parotitis (AP), anti-hepatitis B (AHB), anti-diphtheria (AD) and anti-rubella (AR) AVA levels were detected with ELISA. In each patient we evaluate the type of the JIA (oligoarthritis – OA (n=38), polyarthritis – PA (n=36), systemic-SA (n=7) and enthesitis-related arthritis – ERA (n=10), routine disease activity and treatment. In healthy controls were measured anti-measles (n=40) and anti-parotitis (n=30) antibodies (AB) for comparison with JIA.

Results: The main demographic characteristics: age of inclusion in the study 11 (8-15) years, disease onset–6 (4-8) years, JIA duration–4 (2-7) years. The AM AB in JIA patients were 0.2 (0.0-0.5) IU/ml and in HC 0.3 (0.2-1.1) IU/ml (p=0.00002), despite the higher age of JIA patients than HC (p=0.0000001); AP AB were 2.6 (1.0-5.1) IU/ml vs 1.1 (0.0-4.9) IU/ml in JIA and HC, respectively (p=0.08). Protective levels of AM AB was detected in 50% of all JIA population, vs. HC – 87.5% (p=0.00005), AP–67.7% vs. 60% in HC (p=0.076), AHB – 54.4%, AD–50%, AR–97.8%. The main data related to vaccination status in the table. We have found correlation between JIA duration and levels AM AB (r=-0.27, p=0.015), AP AB (r=-0.22, p=0.039), AD AB (r=-0.27, p=0.015); MTX treatment with AM AB (r=-0.37, p=0.001), and AD AB (r=-0.29, p=0.007); treatment with biologics and AM AB (r=-0.25, p=0.018), and using more than one biologics with AR AB (r=-0.27, p=0.047). In the regression model only MTX had a negative impact on AM (r=-0.001) and AD AB level (p=0.01).

Parameter	OA	PA	SA	ERA	P
Onset age, y	5 (4-7)	6 (4-8)	8 (4-11)	9 (7-12)	0.01
JIA duration, y	3 (2-5)	5.4 (2-9)	4 (1-6)	6 (5-10)	0.006
# AM vaccinations	2 (1-2)	2 (1-2)	1 (1-2)	2 (2-2)	0.005
# of patients with AM revaccination,%	51	60	43	100	0.06
AM IgG, IU/ml	0.2 (0-0.6)	0 (0-0.4)	0.2 (0; 1.6)	0.2 (0.1-0.3)	0.2
Protective AM IgG level,%	58	39	57	50	0.42
# of patients with AP revaccination,%	50	61	43	100	0.05
# AP vaccinations	1.5 (1-2)	2 (1-2)	1 (1-2)	2 (2-2)	0.004
AP IgG, IU/ml	3 (1.5-5)	2.3 (0-5)	1.3 (0; 5)	2.6 (1.1-3.3)	0.67
Protective AP IgG level,%	82	72	71	75	0.8
# AD vaccinations	4 (4-5)	5 (4-5)	4 (4-5)	5 (4-6)	0.09
AD IgG, IU/ml	0.1 (0.03-0.3)	0.1 (0.03-0.2)	0.04 (0.0; 0.2)	0.16 (0.05-0.4)	0.64
Protective AD IgG level,%	53	50	29	50	0.71
# AHB vaccinations	3 (3-3)	3 (3-3)	3 (3-3)	3 (3-3)	0.87
AHB IgG, IU/ml	5 (0-20)	17 (2-45)	1 (0; 10)	19 (4-228)	0.09
Protective AHB IgG level,%	45	67	29)	63	0.13
# AR vaccinations	1 (1-2)	1 (1-2)	1 (1-1)	2 (2-2)	0.57
AR IgG, IU/ml	72 (35-145)	54 (27-96)	200 (18; 200)	67 (42-2000)	0.52
Protective AR IgG level,%	100	97	100	100	0.69

Conclusion: Children with JIA are in the risk of decreased level of AVA, especially in measles, diphtheria and parotitis. The measurements of AVA in the individual JIA vaccination schedule required.

REFERENCES:

[1] Toplak N, Avčin T. Long-term safety and efficacy of varicella vaccination in children with juvenile idiopathic arthritis treated with biologic therapy. Vaccine. 2015; 33(33):4056-9.

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THU0542 THE PSYCHIATRIC DISORDERS IN CHILDHOOD, ADOLESCENCE AND YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS PATIENTS IN FINLAND

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Background: Reported psychiatric morbidity among juvenile idiopathic arthritis (JIA) patients has varied between 9.3-51% (1-3). The variation between studies can be explained by differences in the study populations (age, disease duration and disease state) and differences in the study methods (1-3). Depression and anxiety are the most common disorders, but most studies were based on questionnaires to investigate incidence of only these two diseases (1,3).

Objectives: To explore mental and behavioral disorders in JIA patients compared to the control population.

Methods: All incidents patients with JIA during 2000-2014 were collected from the nationwide register, maintained by the Social Insurance Institution of Finland (4). The National Population Registry identified three controls (similar regarding age, sex and residence) for each case. They were followed up together until 31stDec 2015. ICD-10 codes of psychiatric diagnosis (F10-F99) were picked up from the Care Register for Health Care of the National Institute for Health and Welfare.

Results: During 28,941 follow-up years, 974 (23%) JIA patients were diagnosed with mental or behavioral disorders, whereas the number in the control group was 1,807 (15%), (p<0.001). Neurotic, stress-related and somatoform disorders (F40-48) and mood (affective) disorders (F30-39) were the most common psychiatric diagnoses in the JIA (10.41% and 8.18%) and in the control group (5.44% and 5.13%). The odds ratio for neurotic disorders (F40-48) was 2.02 (95% CI 1.78-2.29) and for mood disorders (F30-39) 1.65 (95% CI 1.44-1.89). Additionally, JIA was statistically significantly associated with behavioral and emotional disorders and disorders of psychological development (Table). Female patients with JIA had higher odds ratios than males for all mental and behavioral disorders except behavioral syndromes (F50-59), for which males with JIA had higher odds ratio.

Conclusion: The risk of psychiatric disorders in JIA patients is increased.

REFERENCES:

[1] Raab A, Sengler C, Niewerth M, Klotsche J, Horneff G, Zink A, et al. Comorbidity profiles among adult patients with juvenile idiopathic arthritis: results of a biologic register. Clin Exp Rheumatol 2013;31(5): 796-802.
[2] Vandvik I. Mental Health and psychosocial functioning in children with recent onset of rheumatic disease. J. Child Psychol. Psychiat. 1990; 3:961-971.
[3] Packham JC, Hall MA & Pimm TJ. Long-term follow-up of 246 adults with juvenile idiopathic arthritis: predictive factors for mood and pain. Rheumatology (Oxford) 2002;41(12): 1444-1449.
[4] Kyllönen MS, Kautiainen H, Puolakka K, Vähäsalo P. The mortality rate and causes of death among juvenile idiopathic arthritis patients in Finland. Clin exp Rheumatol. 2019; in press.

Abstract THU0542 –Table 1. Percentages and odds ratios (OR) for psychiatric disorders in JIA compared to controls

Psychiatric disorders (ICD-10)	JIA n/%	Controls n/%	OR (95% CI)
Mental and behavioral disorders due to psychoactive substance use (F10-19)	70/1.67	212/1.69	0.99 (95% CI 0.75-1.30)
Schizophrenia, schizotypal and delusional disorders (F20-29)	31/0.74	68/0.54	1.37 (95% CI 0.89-2.09)
Mood (affective) disorders (F30-39)	342/8.18	642/5.13	**1.65 (95% CI 1.44-1.89)**
Neurotic, stress-related and somatoform disorders (F40-49)	435/10.41	681/5.44	**2.02 (95% CI 1.78-2.29)**
Behavioral syndromes (F50-59)	134/3.21	204/1.63	**2.00 (95% CI 1.60-2.49)**
Disorders of adult personality and behavior (F60-69)	34/0.81	80/0.64	1.27 (95% CI 0.85-1.91)
Disorders of psychological development (F80-89)	192/4.59	414/3.31	**1.41 (95% CI 1.18-1.68)**
Behavioral and emotional disorders and unspecified mental disorder (F90-99)	192/4.59	414/3.31	**1.41 (95% CI 1.18-1.68)**

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THU0543 LATENT TUBERCULOSIS INFECTION IN CHILDREN WITH PEDIATRIC RHEUMATOLOGIC DISEASES TREATED WITH CANAKINUMAB

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Background: Little is known about the long-term safety of canakinumab about tuberculosis (TB) risk in paediatric rheumatologic diseases.

Objectives: To determine the incidence of latent tuberculosis infection and evaluate the follow-up protocol of the patients treated with canakinumab in a single pediatric rheumatology center from a TB-medium burden country.
Methods: The hospital charts of patients treated with canakinumab between 2012 and 2019 were retrospectively reviewed. The patients were screened for TB using tuberculin skin test (TST) and/or QuantiFERON-TB Gold (QFT-G) test. They had no history of active TB prior to screening and no signs or symptoms of active TB. None of the patients had recent close contact with a person diagnosed as active TB. At initial evaluation, in patients who had never been given immunosuppressive therapy, TST $\geq$15 mm (if BCG vaccinated) and TST $\geq$10 mm (if BCG unvaccinated) were considered as positive. In the case of prior immunosuppressive drug use TST cut-off limit was accepted as 5 mm. Patients with either a positive TST or QFT-G result, in whom active TB ruled out, were to receive appropriate treatment for latent TB one month prior to the first dose of canakinumab and continue throughout 9 months. Chest radiographs were performed prior to therapy and every 6 months. In case TST was anergic, both chest X-ray and TST were repeated after 3 months. Patients were evaluated for signs and symptoms of active TB by an infectious disease specialist every 3 months while on canakinumab therapy according to the "guidelines of Ministry of Health for use of biologic agents". The TST conversion was considered as a variation $\geq$5 mm between the two TSTs performed within an interval at least 3 months. If TB was suspected during the study, repeat TB testing (TST, QFT-G, and chest radiograph) was recommended.
Results: 29 Familial Mediterranean fever, 6 systemic juvenile idiopathic arthritis, 1 TRAPS and 1 hyper Ig D syndrome patients were evaluated. The mean age at canakinumab onset was 12.4 ± 4.3 years (min: 2, max: 17 years). The average duration of canakinumab use was 2.3 ± 1.4 years (min: 1 max: 6.5 years). Among 37 patients, 5 patients had positive TST and one had positive QFT-G with normal chest X-ray prior to therapy. They were given isoniasid prophylaxis for latent TB. QFT-G was checked in 6 patients prior to canakinumab, 5 were negative. Seven patients had TST conversion during follow-up. Their chest X-rays were normal. None of them had active TB symptoms, such as; cough, fever, night sweats and weight loss. The mycobacterial cultures, mycobacterium tuberculosis PCR of induced sputum (via hypertonic saline nebulization) or morning gastric aspirates were negative in these patients. QFT-G was checked in 10 patients during follow-up and all were negative. None of the patients experienced active TB during follow-up.
Conclusion: To the best of our knowledge, this is the first study investigating the frequency of latent tuberculosis infection among patients treated with canakinumab. The results of this study suggest that although frequency of latent TB infection in children treated with canakinumab may not be low in a TB-medium burden country, canakinumab seems to be a safe treatment option in terms of active tuberculosis risk. Close follow-up of children on canakinumab treatment with respect to TB by the pediatric infectious disease department is important to prevent possible complications.

REFERENCE:

[1] T.C Sağlık Bakanlığı Türkiye Halk Sağlığı Kurumu AntiTNF Kullanan Hastalarda Tüberküloz Rehberi. Available at: http://www.mhsm.gov.tr/images/diger_haberler/anti_tnf_kullanan_hasta_tb_rehber.pdf.

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THU0544 ULTRASOUND EVALUATION OF UPPER LIMBS ENTHESES AND JOINTS IN HEALTHY CHILDREN

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Background: Enthesitis in children can result from mechanical or inflammatory processes. Enthesitis is a common finding in several JIA categories, particularly in ERA. Most of the available data on the potential application of ultrasound (US) for paediatric enthesitis is currently focused on lower extremity with limited data in upper extremity entheses. To know how normal US findings of extremities by age are lead to early diagnosis and might avoid misinterpretations.
Objectives: To describe the age-related sonographic features of tendon insertions in the elbows and shoulders in healthy children.
Methods: This is a prospective cross-sectional study of 43 healthy volunteer children. Selection criteria: free of musculoskeletal symptoms, medical conditions or medication affecting the MSK system assessed by a paediatric rheumatologist. Exclusion criteria: history of trauma/surgery, family history of spondyloarthritis and more than three hours of physical activity the previous week of the evaluation. Children were grouped according to age: group 1 (3–9 years, n=22), group 2 (10–13 years, n=12) and group 3 (14–18 years, n=9).
The supraspinatus, common extensor, common flexor, and triceps tendon insertions were bilaterally examined in Power Doppler (PD) as well as grey-scale US using a GE Logic e machine with a linear transducer [8–13 MHz]. All entheses were evaluated in the longitudinal and transverse planes. Additionally, the corresponding joint was examined. Since there was no examination protocol available for scanning upper limbs entheses, a preferred US protocol for scanning children was used (1). Detailed description of entheses in grey-scale and Doppler modes was collected: echogenicity, thickness, presence of power Doppler signal (intra-entheseal at the bone/cartilage interface, peri-entheseal and within the unossified cartilage), as well as potential lesions (enthesophytes, erosions and calcifications). Measurement of tendon thickness was taken using US calipers at the site just where the tendon first contacts bone. All images were acquired by a single examiner (VM) and read by two readers. The inter-observer reliability for the tendon thickness measurements and Doppler signal was estimated between the two readers.
Results: A total of 344 entheses were evaluated in 43 healthy children. Children had a median age of 9 years (IQR 6-13) and 55% were males. All the entheses appeared normal (homogenous fibrillar pattern) on grey-scale imaging. Mean tendon measurements are reported in Table 1.
In group 1, Doppler signal was seen in: supraspinatus (intracartilage) in one patient; common extensor (intra-entheseal) in 2 patients and triceps (intracartilage) in 1 patient. In group 2, common extensor (intracartilage) in 2 patients and common flexor in 2 patients (intracartilage) showed PD. None of the patients in group 3 exhibit PD signal. Children did not show either potential lesions on entheses or joint synovitis at shoulders or elbows. The ICC for entheseal measurement demonstrated high concordance 0.92 (0.84-0.93).

Abstract THU0544 – Table 1. Entheses measurement

Entheses	Group 1	Group 2	Group 3
Supraspinatus m (SD)	2.3 (0.56)	2.9 (0.35)	3.4 (0.75)
Common flexor m (SD)	2.2 (0.83)	2.44 (0.86)	2.57 (0.54)
Common extensor m (SD)	1.96 (0.6)	2.3 (0.66)	2.72 (0.48)
Triceps m (SD)	2.7 (0.89)	3.1 (0.56)	3.5 (1.2)

Abbreviations: m: mean SD: standard deviation
Conclusion: Tendon echogenicity was similar in all ages. Entheses thickness has a linear relationship with age. Detection of entheses Doppler signals at the bone/cartilage interface is rare, but its detection in the insertion to unossified cartilage may be taking account as a physiological finding in upper healthy limbs in younger children.

REFERENCES:

[1] Collado P, Naredo E. Sonographic images of children's joints. Badalona (Spain): EUROMEDICE, Ediciones Medicas SL; 2007.

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THU0545 A PROSPECTIVE OUTCOME OF ALL 17 CONSECUTIVE PEDIATRIC PATIENTS WITH CHRONIC NONBACTERIAL OSTEOMYELITIS TREATED WITH INTRAVENOUS PAMIDRONATE AND FOLLOWED AT A SINGLE CENTER OVER 15 YEARS

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Background: Intravenous pamidronate (IV-PAM) has been reported to be effective in pediatric patients with severe chronic nonbacterial osteomyelitis

(CNO) in short term. Little is known about longterm outcome in CNO after IV-PAM.

Objectives: To describe a consecutive series of pediatric CNO (pCNO) patients who were prospectively followed after treatment with IV-PAM between 2003-2018 at a single center regarding: 1) The effect of IV-PAM on pain and Whole Body Magnetic Resonance Imaging (WBMRI) documented inflammation initially and after flare; 2) Relapse rate and; 3) Spinal CNO and 4) Urine N-telopeptide/creatinine ratio (UNtx/Cr) (a product of collagen 1 breakdown).

Methods:

Patients: All consecutive pCNO patients <18 years at diagnosis, with WBMRI confirmed active disease who required IV-PAM between 2003-2018.**IV-PAM:** First dose 0.5 mg/kg; subsequent doses 1 mg/kg (maximum annual dose 11.5 mg/kg). IV-PAM was administered once monthly x 9. With confirmed flare IV-PAM was repeated (max 9 doses/year).**Pain response:** Visual analogue scale for pain (VAS) with "0" indicating no pain and "10" maximum pain was administered at baseline, at each IV-PAM treatment, and at suspected flare. **Imaging:** WBMRI before 1st IV-PAM, at 6 and 12 months, at suspected flare and after retreatment. CNO resolution was documented as complete (CR) if there was 95% improvement in the WBMRI signal. Spinal x-rays were performed at baseline and annually.**UNtx/Cr** was measured at baseline, after each IV-PAM and with suspected flare.

Results: 17 patients (9F, 8M) were included. The median [range] age at CNO diagnosis was 10.3[4-15] years, and at first IV-PAM 11.6[4-20] years. The median [range] follow-up was 9.2[1-15] years. Six patients had unifocal CNO, 4 had spinal CNO (2 with baseline vertebral fractures) and 6 had multifocal non-spinal CNO. VAS was uniformly 10/10 at baseline and decreased to 0-1/10 first month after IV-PAM. CR was achieved by all at 6 months, which persisted at 12 months. Four patients, 3 unifocal and one multifocal, had no further flares. Twelve patients had WBMRI confirmed flare at previously active sites at 9-36 months and 11 received 1-9 further doses of IV-PAM. With flare, VAS ranged from 4-9/10 and decreased to 0-3/10 within first month after re-initiation of IV-PAM. On final WBMRI, 12/17 (70%) had CR and 5/17 (30%) stable mild increased signal but no clinical symptoms. No further spinal compression fractures occurred. One patient required a third course of IV-PAM. Regarding UNtx/Cr, each patient had appropriate reduction after first IV-PAM. No patients flared while UNtx/Cr remained suppressed. Three patients developed arthritis and one acne. At last follow-up, 10/17 (59%) patients were on no medications, 4/17 (24%) required prn Naproxen for CNO and 3/17 (18%) were on Naproxen and/or disease modifying medications for arthritis.

Conclusion: Long-term follow-up of pCNO patients treated with IV-PAM confirms that while several patients eventually flare, the flares are less painful and have an excellent response to IV-PAM retreatment. No further spinal fractures occurred. No flares occurred while UNtx/Cr remained suppressed, suggesting a role of osteoclasts in CNO. Further prospective multicenter studies are now required to define the long-term clinical and imaging response to IV-PAM.

Disclosure of Interests: None declared

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THU0546 RETROSPECTIVE STUDY ON ANKLE INVOLVEMENT IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) WITH A FOCUS ON HOW TREATMENT IS LINKED TO OUTCOMES

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Background: Ankle and midfoot joints have poorer long-term outcomes in JIA compared to other joints. Esbjornsson et al found that children with ankle involvement in the first year of disease have higher CHAQ scores and are less likely to have achieved remission by eight years [1].

Adherence to treatment has been shown to improve short term outcomes in children with JIA but there is a lack of studies which look at the long-term outcome of children who experience barriers to treatment [2].

Objectives: The aim of this study was to identify risk factors for severe ankle involvement in children with JIA. This abstract focuses on barriers to treatment; one of the main identified risk factors for adverse ankle outcomes.

Methods: This was a retrospective study which looked at JIA patients who had been treated at the Children's Hospital in Glasgow and had tibiotalar, subtalar or midfoot involvement (TT, ST and MF respectively).

680 patients with JIA were identified from clinic lists from 2002 until 2018, inclusive. The clinic lists from 2008-2010 were inaccessible meaning that anyone who was seen exclusively within those two years has not been identified. Children with systemic arthritis were excluded. Of the 680 who were identified to have JIA; 123 have been found to have TT, ST or MF involvement. Of these; 104 were included in this study and the results of 19 patients were not avaliable for analysis. For each of the 104 patients with ankle involvement their notes were reviewed and information about their JIA disease course was noted; specifically looking at any ankle involvement or potential risk factors for a adverse outcome.

Poor ankle outcomes was defined as ankle arthritis having a significant impact on the child's quality of life, persistently limited joint movemet for more than 12 months or damage on imaging.

Results: Barriers to treatment was defined as anything which prevented a child from getting their medication as prescribed.

Figure 1 shows the outcomes of children who had barriers to treatment compared to the children who did not. The difference between the two groups is stark with 67% of children who faced barriers to treatment having poor ankle outcomes compared to only 25% in the group which did not experience barriers to treatment. Furthermore, children with poor ankle outcomes are almost three times more likely to need surgery if they have experienced barriers to treatment compared to those who have not. This shows that children who experience barriers to treatment are more likely to have severe long-term damage to their ankle resulting in pain and limited functionality.

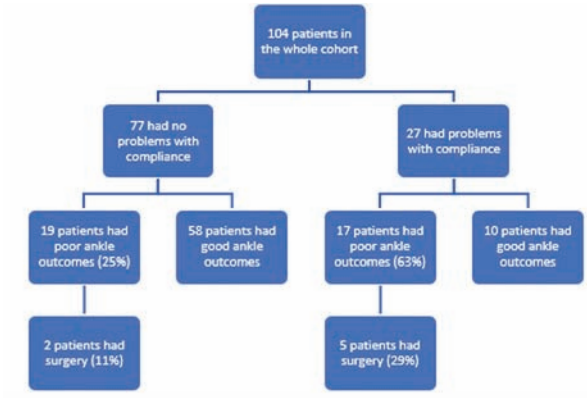


Figure 1: Outcomes in Children who experienced Barriers to Treatment

Abstract THU0546 – Figure 1

Five children declined any treatment at one point in their care against the advice of their healthcare team and of these five; four (80%) had severe ankle involvement with one requiring surgery and another's ankle auto-fused.

Conclusion: Experiencing barriers to treatment has been shown to increase the risk of poor ankle outcomes. Identified barriers to treatment ranged from concerns about adherence to needle phobias in addition to side effects and medication being with-held or taken incorrectly. This study demonstrates the need for further work to explore how these barriers can be effectively minimised.

REFERENCES:

[1] Esbjörnsson A-C, Aalto K, Broström EW, et al. Ankle arthritis predicts polyarticular disease course and unfavourable outcome in children with juvenile idiopathic arthritis. Clin Exp Rheumatol;33:751–7.

[2] Feldman DE, De Civita M, Dobkin PL, et al. Effects of adherence to treatment on short-term outcomes in children with juvenile idiopathic arthritis. Arthritis Care Res 2007;57:905–12. doi:10.1002/art.22907

Disclosure of Interests: None declared

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THU0547 FIBRODYSPLASIA OSSIFICANS PROGRESSIVA IN PEDIATRIC RHEUMATOLOGY PRACTICE: LARGE SERIES EXPERIENCE OF THE SINGLE CENTER

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Background: Fibrodysplasia Ossificans Progressiva (FOP), also known as a ''second skeleton disease'' is extremely rare (1: 2000000) and disabling genetic disorder, caused by mutation of ACVR1 gene, a bone morphogenetic protein receptor. Among medical specialties there are no certain, capable to provide not only diagnostics, but also all medical maintenance (assessment and monitoring of extent of damages, the differentiated drug treatment, rehabilitation, contact with adjacent experts). It would be reasonable if the rheumatologist carried out a role of the main attending physician for the patient with FOP. It seems to be a lot of similarities between rheumatic diseases, especially spondyloarthritis (SpA) and FOP in the pathophysiology, clinical manifestation and the therapy approach.
Objectives: to present the single-center experience of the FOP patients and to identify similar symptoms in FOP and rheumatic disease.
Methods: The analysis of the large series of patients with FOP, who observed in the rheumatologic clinic.
Results: Our single center experience includes 26 patients with FOP. All 26 patients (13 male and 13 female) had 3 basic FOP clinical manifestations. In 23 patients molecular-genetic tests were performed and typical mutation (Arginine 206) occurred in 22 cases and one had an extremely rare mutation (Glicine 328). 22 (85%) patients had common for FOP massive heterotopic ossifications. 3 of them had formed heterotopic ossification through the X-ray negative stage to visible changes. Among typical phenotypic stigmas were: great toe malformation; thumbs malformation; peripheral osteochondromas; cervical spine abnormalities. Majority of the cases presented some similarities to SpA manifestations: ankylosis of the apophysial joints and vertebral bodies mostly in cervical spine; X-ray/CT evidence of the sacroiliitis in all patients, who were examined (n=8). Because of severe body deformity or metal details after previous surgery intervention there were no possibility to perform MRI in most patients, but we confirm typical sacroiliitis with extended bone edema on MRI in 3 patients. Recurrent episodes of the large joints synoviitis were present in 5 patients. 4 patients demonstrated gradually formation of great toe ankylosis during the follow-up observation. The involution and decreasing of new FOP nodes associated with non-steroidal anti-inflammatory drug intake and/or glucocorticoids therapy were occurred in all patients.

Clinical features		Male	female	Total N of patients
Sex ratio		13	13	26 (1:1)
Age of initial manifestations	<1	8	1	9 (35%)
(years)	1-9	6	8	14 (54%)
	≥10	0	3	3 (11%)
Great toe malformation		13	12	25 (96%)
Thumbs malformation		2	3	5 (19%)
Cervical spine abnormalities		12	9	21 (81%)
Peripheral osteochondromas		8	7	15 (58%)
Massive heterotopic ossifications		12	10	22 (85%)
CT/X-Ray/MRI picture of sacroiliitis		2 (of 2)	6 (of 6)	8 of 8 (100%)

Conclusion: Appearance of the similarities in FOP and SpA manifestation and the therapy approach could identify FOP as a potential rheumatic disease. Clinical observation of FOP patients could provide the important information for rheumatologist about insufficiently explored process of new bone formation.
Disclosure of Interests: None declared
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THU0548 ASSOCIATIONS BETWEEN: MARKERS OF BONE TURNOVER AND RADIOLOGICAL FINDINGS IN CHILDREN DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Although many children attending pediatric rheumatology departments are diagnosed with low bone mineral density on the basis of clinical imaging, it is difficult to determine which patients have the higher risk of developing osteoporosis as the secondary disease. Recently performed studies involving rheumatological patients have proposed numerous serological indicators for better evaluation of the disease activity. These include markers of bone turnover, among others: bone alkaline phosphatase and osteoprotegerin (which are more specific for bone formation) and also beta isomerized carboxy terminal telopeptide of type I collagen, also known as Beta-Crosslaps (which is considered as an indicator of bone resorption).
Objectives: The main objective of the study was to evaluate the clinical usefulness of measuring serum concentrations of the selected markers of bone turnover in juvenile idiopathic arthritis (JIA) patients and assess their potential significance in prevention of osteoporosis in these children.
Methods: Study involved 59 children previously diagnosed with JIA (mean age at diagnosis: 9.0±4.3 years, mean age at study baseline: 12.7±3.9 years). All patients underwent Dual X-Ray Absorptiometry (DXA) examinations in order to assess bone mineral density. Wrist radiographs were also taken for evaluation according to the Steinbrocker classification. The presence of abnormalities in these tests was chosen as the criterion to divide patients into subgroups to perform group comparisons for the serum levels of markers of bone turnover: bone alkaline phosphatase, osteoprotegerin and Beta-Crosslaps.
Results: According to the Steinbrocker classification, 10 (16.9%) patients were staged as class I or higher. These children had significantly lower serum levels of bone alkaline phosphatase (p=0.0333) than patients with no radiological changes on wrist radiographs. The non-zero Steinbrocker subgroup had also lower Total Body Less Head Z-Score results (p=0.010) than the remaining patients.
The DXA results, expressed as Total Body Less Head and Lumbar Spine Z-Score, disclosed low bone mineral density in 10 (16.9%) and 12 (20.3%) patients, respectively. There were no significant correlations between serum levels of markers of bone turnover and bone mineral density measurements. However, bone alkaline phosphatase and osteoprotegerin were negatively correlated with DXA muscle mass (r=-0.359 p=0.040 for bone alkaline phosphatase, r=-0.372 p=0.0392 for osteoprotegerin). Similar correlation was found for bone alkaline phosphatase and DXA fat mass (r=-0.418 p<0.01).
Although Beta-Crosslaps appeared to be the only marker of bone turnover significantly (p=0.0410) associated with Juvenile Arthritis Disease Activity Score 27-Joint Count (JADAS27), it was independent from radiological findings involved in the analysis. However, serum levels of Beta-Crosslaps were higher in patients evaluated in summer than in those assessed in winter (p=0.0464). Radiological findings were not season-variable.
Conclusion: Low serum concentration of bone alkaline phosphatase seems to be a risk factor for low bone mineral density and, by extension, for osteoporosis. Therefore it should be considered as an important laboratory test in JIA patients suspected of secondary osteoporosis. Clinical significance of osteoprotegerin and Beta-Crosslaps needs to be further investigated.
Disclosure of Interests: None declared
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THU0549 SURGICAL MANAGEMENT IN JUVENILE IDIOPATHIC ARTHRITIS: A MONOCENTRIC EXPERIENCE OF 257 PROSTHESIS

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Background: Juvenile idiopathic arthritis (JIA) includes all forms of inflammatory arthritis, with onset before the 16th birthday, lasting more than 6 weeks. Although conservative management with nonsteroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs can be effective, a significant number of young adults affected by JIA requires a major surgical procedure, including different types of prosthetic devices.
Objectives: This article presents a monocentric experience of an interdisciplinary team of rheumatologists and orthopedic surgeons for JIA and the outcome of patients subjected to prosthesis implantation.
Methods: Data were collected through a retrospective analysis of 583 patients attending to our transitional care center for JIA between 1999 and 2018, in the context of a once-week rheumatologic counseling with the orthopedic surgeons. Descriptive statistics were used to evaluate the baseline and follow-up data.
Results: On a total of 257 prosthesis implantations, 137 were total hip prosthesis, 101 total knee prosthesis and 19 total ankle prosthesis. The 10-year implant survival rate was 97%, with good results in term of function and comfort for the patients. Complications were observed in 9% of

patients, including intraoperative fractures, periprosthetic joint infections and wound dehiscence. The majority of patients were treated with biologic therapy before surgery.
Conclusion: Prosthesis implantation in JIA patients is a complicated and difficult procedure, related to the management of the biologic therapy, the low quality of bone, the remarkable stiffness and deformity of the joints. Long-term results were good, even in patients with severe arthritis, showing drastic reduction of joint pain and an improvement of functionality. The risk of complications results to be modest compared to a great survival rate and a valid recovery of joint range of motion. The interdisciplinary team composed by rheumatologists and orthopedic surgeons for the all follow-up of these patients is a cornerstone to obtain the perfect schedule for prosthetic implantation.

REFERENCES:

[1] C. Mertelsmann-Voss et al. US Trends in Rates of Arthroplasty for Inflammatory Arthritis Including Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, and Spondyloarthritis. Arthritis & Rheumatology, June 2014.
[2] M. P. Abdel et al. Surgical Management of the Juvenile Idiopathic Arthritis Patient with Multiple Joint Involvement. Orthopedic Clinics of North America, 2014-10-01.

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THU0550 MYCOPHENOLATE MOFETIL (MMF) IN DEFINED AND UNDEFINED INTERFERONOPATHIES

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Background: Type I interferonopathies are genetic disorders characterized by an up-regulation of type I interferon (IFN) activity. An increased expression of type I IFN regulated genes, IFN signature (IS), is described in these conditions. They are characterized by autoinflammation and varying degrees of autoimmunity or immunodeficiency. Some patients with a phenotype strongly suggestive for type I interferonopathy with a high IS, do not show any mutations in known type I interpheronopaties related genes, being classified as undefined
Objectives: To evaluate the effect of mycophenolate mofetil (MMF) in patients with defined and undefined type I interferonopathy
Methods: 7 patients with type I interferonopathy followed at a Pediatric Rheumatology center, were included. Leucocyte (WBC) and platelet count, hemoglobin (Hb), CRP, ESR, serum amyloid A (SAA), autoantibodies, complement levels and IS, were assessed before and after 5-7 months of MMF treatment (600 mg/m2 BID). IS was determined by qPCR (high scores >1.42)
Results: Patient 1 and 2 presented respectively with SAVI and Aicardi-Goutieres syndrome. The others were classified as undefined. In patient 1(table), treated with JAK1/2 inhibitor, MMF was followed by decrease of inflammatory markers and resolution of lung involvement; in patient 2 to an increase in Hb and normalization of inflammatory markers. Among patients with an undefined phenotype the addition of MMF to low dose prednisone led to complete resolution of inflammation. A reduction of the antinuclear antibodies titre was observed in patients 2, 3 and 7 and a normalization of complement level in patients 3, 4 and 7. Patient 5 had normal inflammatory markers already before the beginning of MMF possibly due to previously administered immunosuppressive treatment. Despite all patients presented a significant improvement of clinical picture after 5 months of MMF treatment, the IS decreased only in 4/7 patients while it remain stable or increased in the others

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7
Disease	SAVI (lung and skin involvement, systemic inflammation)	Aicardi Goutieres (neurological involvement, rash, fever)	Undefined (epilepsy, arthritis,skin involvement)	Undefined (recurrent fever, hypertransaminasemia, hemophagocytic lymphohistiocytosis)	Undefined (hemiplegia)	Undefined (epilepsy, arthritis,skin involvement)	Undefined (recurrent fever, lymphadenopathy, hypogammaglobulinemia
Clinical improvment after MMF	Resolution of lung involvement	Resolution of fever and rash	Resolution of rash, arthritis, improvement of seizures	Resolution of fever, inflammation and hypertransaminasemia	Improvement of motility	Resolution of arthritis and skin involvement	Resolution of fever and limphadenopathy
Gender	F	F	M	M	M	F	M
Age at onset (yrs)	3 (days)	2	4	7	4	6	16
WBC/ mmc³	16 /7,4	8,0/8,4	9,8/8,5	1,7/8,4	4,4/8,2	4,4/5,2	6,6/5,9
Hb g/dl	7,7/8,9	8,5/12,3	12,9/12,8	9,7/13	12,1/10,7	12/12,9	11,5/15,1
PLT/mmc³	950 /766	680/320	194/181	56/161	358/421	381/390	218/323
ESR (mm)	44/40	49/9	38/10	7/6	2/5	24/6	3/3
CRP (mg/dl)	1,22/0,73	3,13/0,06	5,55/0,32	<0,05/<0,05	<0,05/<0,05	1,15/<0,05	8,34/0,98
SAA (mg/dl)	95,8/3,62	5,37/2,82	188/8,11	-/1,89	<0,84/-	4,19-0,78	/
C3	154/134	122/108	81/92	83/118	203/170	127/108	53/133

Abstract THU0550 – Figure 1

Conclusion: Our data suggest that mycophenolate mofetil might be an effective therapy in patients with type I interferonopathy leading to improvement of clinical and laboratory features thus allowing a glucocorticoid sparing
Disclosure of Interests: Carmela Gerarda Luana Raffaele: None declared, Gian Marco Moneta: None declared, Silvia Federici: None declared, Manuela Pardeo: None declared, Claudia Bracaglia: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer, Antonella Insalaco: None declared
DOI: 10.1136/annrheumdis-2019-eular.6305

THU0551 VACCINATION COVERAGE IN FRENCH CHILDREN WITH AUTO-INFLAMMATORY DISEASES : PRELIMINARY DATA FROM THE JIRCOHORTE

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Background: Autoinflammatory diseases (AID) comprise a large number of rare diseases that manifest as recurrent sterile inflammation or disproportionate infection-induced inflammatory symptoms. Vaccine relation to AID is complex: on one hand the susceptibility to infections vary with the treatment options of the patient, on the other hand the disease activity may be triggered by vaccination. Nevertheless, effective immunization is crucial in this population. Up to know very little is known about vaccination coverage in AID children.
Objectives: To determine vaccination coverage in French children with an autoinflammatory disease.
Methods: Patients between 2 and 18 years with autoinflammatory diseases followed at the French Reference Center for Auto-Inflammatory Diseases-Versailles Hospital and included to the Juvenile Inflammatory Rheumatism cohort (JIRcohorte) network - an international multicenter prospective cohort for children with inflammatory and rheumatological diseases - were included in this retrospective monocentric observational study. Vaccination coverage of each disease and complete status of vaccination was assessed at the last out-patient visit, according to the national immunization program.
Detail of every vaccine received (number of doses and date of administration) were collected by a pediatrician from written immunization record (vaccination card). Demographic data, disease and medications used since diagnosis were also assessed. Patients with no available immunization record were excluded.
Results: 128 patients met the inclusion criteria. Sex ratio was 1.2 (70/58). Median age at the last out-patient visit was 8.4 years (2.5-17.9 years). 53 children (41%) presented periodic fever with aphtous stomatitis, pharyngitis and adenitis (PFAPA) syndrome, 30 familial mediterranean

fever, 29 unexplained autoinflammatory recurrent fevers, 8 TNF receptor associated periodic syndrome (TRAPS), 8 other autoinflammatory diseases. 68 patients (53%) were treated by on-demand corticosteroids, nine patients (0.7%) by biological agents, the other patients did not receive any immunosuppressive treatment.

At the last clinic visit, only 49% (n=63) of our entire cohort had a complete vaccination status (human papilloma virus and tuberculosis excluded). Coverage rates was superior to 85% for diphtheria/tetanus/poliomyelitis (89%), pertussis (95%), *haemophilus influenza* type B (94%) and measles/mumps/rubella (89%). 84% of the children were well-vaccinated against pneumococcus. Lowest individual vaccination coverage rates were observed for hepatitis B at 77% and for meningococcus C at 77%. Only one girl received complete vaccination against human papilloma virus.

Conclusion: Vaccination coverage in children with autoinflammatory diseases appears suboptimal. Measures to optimize vaccination coverage in these children should be implemented.

REFERENCES:

[1] Jaeger VK, et al. Safety of vaccinations in patients with cryopyrin-associated periodic syndromes: a prospective registry based study. Rheumatology (Oxford). 2017 Sep 1;56(9):1484-1491

[2] Jeyaratnam J. et al. The safety of live-attenuated vaccines in patients using IL-1 or IL-6 blockade: an international survey. Pediatr Rheumatol Online J. 2018 Mar 21;16(1):19

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THU0552 SCORING ULTRASOUND SYNOVITIS IN JUVENILE IDIOPATHIC ARTHRITIS: RESULTS OF A RELIABILITY EXERCISE USING OMERACT US PAEDIATRIC DEFINITIONS

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Background: Despite the increasing use of musculoskeletal ultrasound (MSKUS) in assessing joints in juvenile idiopathic arthritis (JIA) in daily practice, there is still a lack of data on its reliability in the evaluation of synovitis in children. Lately, the OMERACT ultrasound paediatric task force has developed preliminary definitions and scoring system for US synovitis in children (1).

Objectives: To evaluate the reliability of the OMERACT paediatric definitions and scoring system of synovitis through a web reading images exercise.

Methods: Thirteen sonographers with at least 2 years' experience in paediatric MSKUS JIA were invited to participate in the reliability exercise. After a training session, participants were asked to analyze 75 images for the presence/absence of elementary lesions and for the grading of synovitis (2), synovial hypertrophy, effusion and Doppler signal. US images of elbow, wrist, second MCP, knee and ankle were collected using standardized scanning by 2 sonographers experienced (LR and SB), from JIA patients with different age in different disease stages. The intra-reader reliability (evaluated 4 weeks after the first assessment) was calculated by the Cohen's kappa coefficient and by the quadratic weighted kappa and the inter-reader reliability by the Light's kappa.

Results: The intra-reader reliability was good for the detection of the presence/absence of any elementary lesion (median Cohen's kappa 0.62, range 0.47-0.75), and for scoring synovitis and synovial hypertrophy and almost perfect for the scoring of Doppler signal (median quadratic weighted kappa 0.77, 0.66-0.86, 0.76, 0.61-0.84 and 0.87, 0.77-0.94 respectively), while it was moderate and rather variable for scoring effusion (0.55, 0.24-0.76). The inter-reader reliability was good for scoring synovitis and synovial hypertrophy (Light's kappa 0.68, CI 95% 0.61-0.75 and 0.63, CI 95% 0.54-0.71 respectively), almost perfect for scoring Doppler signal (0.85, CI 95% 0.77-0.90) and moderate for the detection of any elementary lesion and for scoring effusion (0.48, CI 95% 0.36-0.64 and 0.49, CI 95% 0.40-0.60 respectively). We found a trend for better results in the evaluation of all parameters in older children (9-16 vs 0-8 years : light's kappa 0.53 vs 0.44 for any lesion, 0.71 vs 0.64 for synovitis, 0.53 vs 0.43 for effusion, 0.71 vs 0.64 for synovial hypertrophy and 0.78 vs 0.90 for Doppler). Concerning the five joints evaluated the best results were obtained for the knee for all parameters (median Lights kappa 0.71, range 0.54-0.85) excepted for Doppler whose reliability was higher for second MCP (Lights' kappa 0.87).

Conclusion: Excepted for effusion, whose evaluation is limited on static images, the reliability of the OMERACT paediatric US definitions and scoring system for synovitis in JIA was good among a large group of sonographers. These results suggest their potential applicability in clinical practice and in multicenter studies.

REFERENCE:

[1] Preliminary definitions for the sonographic features of synovitis in children. Roth J, Ravagnani V, Backhaus M, et al. Arthritis Care Res (Hoboken). 2017 Aug;69(8):1217-1223.

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THU0553 THE IMPACT OF BACKGROUND BIOLOGICAL THERAPY ON SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED MACROPHAGE ACTIVATION SYNDROME: A SINGLE CENTER STUDY

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Background: Macrophage activation syndrome (MAS) is a severe complication of Systemic juvenile idiopathic arthritis (SJIA). Biological therapy of SJIA may modify the clinical expression of MAS (1).

Objectives: to assess and compare the clinical, biochemical. and haematological features of SJIA-associated MAS in patients treated with biologic (B) or non-biologic (NB) agents.

Methods: retrospective analysis of data from dedicated medical records and databases. Inclusion criteria included: diagnosis of SJIA according to the ILAR criteria, diagnosis of MAS according to the expert´s opinion, and prescription of corresponding therapy. Patients were followed and treated at a tertiary center from 2006 to 2018. Demographical, clinical, haematological, biochemical and treatment-related features were recorded. The worst recorded values (e.g. highest ferritin levels) during each MAS episode were included for analysis. Outcomes (complete or partial recovery, death) and fulfillment of current classification criteria (2) were also recorded. Comparisons between groups (patients developing MAS during B therapy vs. NB therapy) were performed by chi square or Wilcoxon rank sum tests.

Results: Twenty-four (14 F, 10 M) patients who developed 31 MAS episodes were included. Age at SJIA onset 4 years, age at MAS onset 6 years; 10 episodes occurred during the initial (0-3 months) stage of SJIA course. Patients were receiving biological agents (canakinumab 4, tocilizumab 4, anakinra 1, etanercept 1) in 10 (32%) MAS episodes. Frequency of cardinal clinical features was similar in both groups. During MAS course, ferritin (1,408 vs 26,574 ng/ml, $p < 0.001$), LDH (922 vs 3308 IU/L, $p = 0.04$), SGOT (66.5 vs 389 IU/L, $p = 0.02$), and triglycerides levels (259 vs 352 IU/L, $p = 0.03$) were lower in B than in NB treated patients, while platelet count (215 vs 66 n/µl, $p < 0.01$), and hemoglobin (104 vs 79 g/dL, $p < 0.01$) were higher in the B than in the NB treated patients. No significant differences were found in GGT, fibrinogen, SGPT levels or neutrophil count. Duration of admission during MAS tended to be longer in the NB treated group (31 days) than in the B group (16 days). Treatment of MAS included high dose steroids, cyclosprin, and/or biological agents. Five patients, all belonging to the B group ($p < 0.001$), did not fulfill current SJIA-MAS classification criteria. There were 4 deaths recorded, all belonging to the NB group.

Conclusion: SJIA patients treated with biological agents exhibit similar clinical features than those treated with non-biologic therapy. However,

different haematological and biochemical variables are significantly milder in patients on biological therapy, which may limit the utility of classification criteria in this group. Assessment of these findings in larger cohorts is needed.

REFERENCES:

[1] Schulert GS, et al. Effect of Biologic Therapy on Clinical and Laboratory Features of Macrophage Activation Syndrome Associated With Systemic Juvenile Idiopathic Arthritis. Arthritis Care Res 2018;70:409-19. 2. Ravelli A, et al. 2016 Classification Criteria for Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis: A European League Against Rheumatism/American College of Rheumatology/Paediatric Rheumatology International Trials Organisation Collaborative Initiative. Ann Rheum Dis 2016;75:481-9.

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Other orphan diseases

THU0554 THE CLINICAL UTILITY OF TWO VASCULITIS ACTIVITY SCORES(BVAS AND BDCAF) IN BEHÇET'S SYNDROME: A PROSPECTIVE COHORT STUDY

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Background: Behçet's Disease(BD) is a rare chronic autoinflammatory condition that can lead to irreversible organ damage. The potential for multi-organ involvement and fluctuating activity highlights the need to perform a careful and systematic assessment of disease activity that is sensitive to change. Several disease activity tools have been used in both daily practice and clinical trials, yet there is no published data comparing the clinical utility of different tools in informing changes to therapy.
Objectives: To compare the utility of two major activity scores:BD Current Activity Form (BDCAF2006)[1] and Birmingham Vasculitis Activity Score (BVAS)[2] in predicting physician's decision to adjust treatment (step-up/step-down) in patients with BD.
Methods: A 6-month prospective observational study was performed in a cohort of patients meeting the International Criteria for Behcet's Disease (ICBD),at the National Centre for BD in Liverpool,UK. Participants were described for their demographics, clinical manifestations and treatment plan.BVAS and BDCAF2006 activity scores were completed for each patient at evaluation.The outcome of interest was treatment change which was classified as 'step-up' or 'step-down', reflecting escalation or de-escalation in treatment (dosage adjustment or adding new immunosuppressant), respectively. We assessed the association between BVAS and BDCAF scores and step-up/step-down treatment using Spearman rank correlation and multivariate logistic regressions, adjusting for gender, age and patient's perception of disease activity on visual analogue scale (VAS).Odds ratios(OR) and 95% confidence intervals were calculated. Data analysis was conducted in Microsoft Excel,SPSS 2.0 and STATA.
Results: Ninety-five patients met inclusion criteria: 25 males(26.3%) and 70females(73.7%) with a mean age at diagnosis of 32.7years(±11.3 SD). HLAB51 was positive in 11/51 cases(11.6%).The most frequent clinical manifestations were oral ulcerations(100%), genital ulcerations(94.7%) followed by papulo-pustular skin lesions(37.8%) arthralgia(31.6%)and headache(30.5%).
Mean BVAS score(range 0-6) was 2.14(±1.8 SD) and mean BDCAF score (range 0-8) was 3.04(±1.72 SD). Both BVAS and BDCAF correlated with decision to step-up treatment (r=0.752; r=0.370, respectively). Furthermore, BVAS was more strongly associated with decision to step-up treatment than BDCAF(OR 4.25 95%CI 2.37 to 7.61; 1.51 95%CI 1.15 to 2.00, respectively). Adjusting for gender, a stronger association was observed in male participants across BVAS and BDCAF scores(OR 5.89 95%CI 1.17 to 29.63; 3.48 95%CI 1.20 to10.09,respectively). Following adjustment for patient's perception of their disease (VAS), BVAS remained significantly associated with treatment step-up(OR 3.87 95%CI 2.08 to7.19) but not BDCAF(OR 1.30 95%CI 0.91 to1.84).
Regarding different clinical manifestations,the BVAS mucocutaneous and ocular activity showed a significant odds ratio for step-up therapy (OR=5.78, CI:1.49-22.15; and OR=4.2,CI: 2.26-7.83).
Conclusion: BVAS can be a useful tool to asses BD activity. In this study, BVAS correlated better with clinical treatment decisions than BDCAF, particularly in male participants. It also appears to be less influenced by patient's subjective perception of disease activity, and therefore may be a more objective measure of BD activity.

REFERENCES:

[1] International Society for Behçet's Disease, Behçet's Disease Current Activity Form 2006
[2] Mukhtyar C,et al(2008). "Modification and validation of the Birmingham Vasculitis Activity Score (version 3) AnnRheumDis.2008Dec 3.

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THU0555 10 YEAR PROGNOSIS OF PATIENTS DIAGNOSED WITH FAMILIAL MEDITERRANEAN FEVER

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Background: In Familial Mediterranean Fever (FMF), other than amyloidosis factors affecting mortality are being debated. In our previous study, we did not observe any atherosclerotic plaque formation in carotid or femoral artery. We thought that the risk of atherosclerosis did not increase in patients diagnosed with FMF.
Objectives: The aim of this study was to assess the 10 year prognosis and comorbidity of patients diagnosed with FMF who have been treated in our rheumatology clinic.
Methods: The sample group is a subset of 2009 study. In 2009, the patients who already had myocardial infarction or cancer diagnosis were excluded. The patients were interviewed with polar questions of whether they were diagnosed with acute myocardial infarction (AMI), cerebrovascular events, cancer, diabetes, and hypertension.
Results: We studied 71 patients (37 males, 34 females; mean age: 49.66±6.91) with FMF, and 59 patients (24 males, 35 females) in healthy control (HC) group. The gender and age difference between two groups was not found significant.
During 10 year follow-up, 8% of FMF patients had either a cardiovascular or cerebrovascular event comparing to 5% in HC (p>0.05). 3% of FMF patients had a cancer diagnosis comparing to 3% in HC (p>0.05). Even though diabetes mellitus diagnosis rate was higher in FMF patients (15% to 10%), results were still not significant (p>0.05). Hypertension diagnosis was 5% higher in FMF group (p<0.05)

Table. Prognostic Factors of FMF patients compared with Healthy Controls

	FMF 2018, n (%)	HC 2018, n (%)	p value
Female	34 (47.89)	35 (59)	0,193
Age	49±6.91	51±5.59	0,076
AMI/Stroke	6 (8.45)	3 (5.08)	0,45
Cancer	2 (2.82)	2 (3.39)	0,85
DM	9 (14.86)	6 (10.17)	0,198
Hypertension	25 (33.78)	10 (16.95)	0,019*
Total	71	59	

Conclusion: Even though there was a significant increase in hypertension, increased diabetes, cancer, and AMI/Stroke ratio was not found significant when compared to the HCs. Therefore, any cardiovascular and malignancy related comorbidities are not associated with FMF.

REFERENCES:

[1] Ugurlu S, Seyahi E, Cetinkaya F, Ozbakir F, Balci H, Ozdogan H. Intima media thickening in patients with familial Mediterranean fever. Rheumatology (Oxford). 2009 Aug;48(8):911-5.

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THU0556 ARTERIAL AND VENOUS THROMBOTIC EVENTS IN IGG4-RELATED DISEASE: A NATIONAL OBSERVATIONAL RETROSPECTIVE STUDY

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Background: IgG4-related disease (IgG4-RD) is a fibro-inflammatory disorder that can affect virtually every organ. Although arterial involvements have been reported, no studies have examined the occurrence of arterial or venous thrombotic events in these patients.
Objectives: To explore the frequency, the characteristics, and risk factors of arterial and venous thrombotic events in IgG4-related disease patients.
Methods: An observational, descriptive, retrospective study was conducted from a multicentric national case registry for IgG4-RD. Patients fulfilled the Comprehensive Diagnostic Criteria (CDC) for IgG4-RD, and all patients with arterial or venous thrombotic events confirmed by imaging during follow-up were analyzed. Clinical, radiological, biological, histological and therapeutic characteristics were retrospectively collected using a standardized online data sheet. Results obtained in patients with thrombosis were compared to those without thrombosis.
Results: One hundred eighty-nine patients with IgG4-RD (135 men/54 women, median age 61 years) were included. During a 12-months median follow-up, one or more arterial thrombotic events occurred in 10 patients and venous thrombotic events in 16 (5.3 and 8.5 events/100 patient-years, respectively).
Arterial complications (coronary artery disease n=5, lower limb peripheral arterial disease n=2, mesenteric ischemia, transient ischemic attack, and carotid thrombosis: n=1) occurred on average 30 months [0-140] after the first symptoms of IgG4-RD. They were inaugural in 2 patients without any cardiovascular risk factor, and associated with IgG4-RD arterial involvement in 3 (coronary aneurysms n=2, leg arteritis n=1). Among patients with arterial thrombosis, 60% had systemic involvement (≥3 organs involved), 89% elevated serum IgG4 (> 3N in 56%), and 57% CRP >10 mg/l. Only 5/10 were treated with steroids at the time of arterial complication, and 4 had never been exposed to steroid therapy. Renal involvement was associated with the occurrence of an arterial thrombotic event ($p = 0.03$).
Venous thromboembolic complications (deep venous thrombosis (DVT) n=12, pulmonary embolism n=4) occurred on average 24 months [0-164] after the first symptoms of IgG4-RD, but were inaugural in 6 patients. Usual venous thrombosis risk factors were found in only 3/16. Seven patients had retroperitoneal fibrosis (RPF), 2 had mediastinal fibrosis, 60% had localized IgG4-RD (≤2 organs involved), serum IgG4 level was normal in 67% and CRP <10 mg/l in 79%. Nine patients were on steroids at the time of venous thrombosis. RPF was more frequent in the group of IgG4-RD patients with a venous thrombotic event ($p = 0.05$), and largely associated with DVT in a multivariate analysis (OR=8.36 [2.25-35.93], $p = 0.002$).
Conclusion: Arterial and venous thrombotic complications are common in IgG4-RD patients. While arterial events are associated with mulitorgan involvement and elevated serum IgG4, venous thrombotic complications appear to affect more likely patients with compressive localized forms of the disease, such as RPF. Mechanisms responsible for this over-risk and clinical benefit of a preventive platelet antiaggregant or anticoagulant treatment in high risk of thrombosis subgroups remain to be evaluated.
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THU0557 NERVE GROWTH FACTOR, SCLEROSTIN AND DKK-1 SERUM LEVELS IN COMPLEX REGIONAL PAIN SYNDROME1 (CRPS-1): A PILOT STUDY ON 41 PATIENTS

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Background: Pain is the hallmark of Complex Regional Pain Syndrome (CRPS). Nerve growth factor (NGF), widely known as pain mediator, is increased in the affected skin[1] and in tibia bone of rat models of CRPS, while is lowered by administration of anti-NGF antibodies[2]. CRPS usually develops after limb trauma, most frequently a fracture[3]. Some reports considered bone as a main player in CRPS pathogenesis, hypnotizing that sclerostin (SOST)[4] and Dickkopf-related protein-1 (DKK-1) may be involved in CRPS pathogenesis.
Objectives: To evaluate NGF, SOST, and DKK-1 serum levels from affected arm of CRPS patients and compare them with unaffected one and healthy controls (HCs).
Methods: Adults patients affected by CRPS diagnosed according to IASP criteria at upper limb were consecutively enrolled from April 2017 to August 2018. Patients with prior treatment with bisphosphonates, and history of disorders of mineral metabolism were excluded. Sera from the basilica vein of affected and unaffected arm of CRPS patients were collected, as well as sera from HCs paired for age and sex. NGF, SOST, and DKK-1 concentrations were determined by ELISA kit. Comparisons between patients and HCs were performed by Student test, while comparison between affected and unaffected arms were performed with Wilcoxon test for paired data. Pearson correlation was used to correlate NGF, SOST, and DKK-1 levels with demographic and clinical variables.
Results: The overall population included 41 patients: males (M) 21.9%, mean age at diagnosis [± standard deviation, SD] 61.9±8.4 yrs, median disease duration 67 days (inter quartile range (IQR) 14.0; 22.5), 39 (95.2%) experienced a fracture as inciting event, mean VAS pain score (0-100) 54.8±18.6 mm. Mean NGF levels (pg/mL) were 12.0±28.8 and 11.4±35.5 in the affected and unaffected side, respectively, and 13.5±55.0 in HCs. NGF was undetectable in most patients; no statistical significant differences of NGF levels were found between patients and HCs. Mean SOST levels (pmol/L) were 32.6±16.1, 29.8±17.7, and 34.0±13.3 in affected, unaffected arm, and in HCs, respectively. No statistical significantly differences of SOST levels were found between patients and HCs, while a significant difference was found between affected and unaffected arms (p=0.03). Mean DKK-1 levels (pmol/L) were higher in affected arm (31.2±29.5) than in unaffected one (29.3±28.6) or in HCs (27.5±18.2) without reaching statistical significance. NGF was significantly correlated with VAS pain score (p=0.04).
Conclusion: To our best knowledge, this is the first study to evaluate NGF, SOST, and DKK-1 levels in adults affected by CRPS-1. SOST levels were significantly higher in affected arms compared to unaffected ones, suggesting a possible role of this bone mediator in CRPS pathogenesis. NGF was consistent with the expression of pain, trough VAS pain score. Further studies need to clarify these preliminary findings.

REFERENCES:
[1] Li WW, et al. Pain 2010; 151:843–52.
[2] Sabsovitch I, et al. Pain 2008; 138: 47–60.
[3] de Mos M, et al. Pain 2007; 129:12-20.
[4] Robling AG, et al. J Biol Chem 2008;283:5866-75.

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THU0558 ADULT-ONSET STILL'S DISEASE PROGNOSIS SCORE. CLINICAL PATTERNS, COMPLICATIONS AND BIOLOGIC TREATMENT

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Background: Adult-onset Still's disease (AOSD) is an uncommon disease with an unpredictable clinical course and variable prognosis. Sometimes, it requires biologic treatment in early phases. A prognosis score has been described, which has never been applied in a Spanish case series.
Objectives: To apply the prognosis score described by *Pouchot et al* (Systemic Score System (SSS)) on a 64 cases series diagnosed with AOSD in Spanish population and to determine if SSS high values registered at the onset of the pathology are related to AOSD clinical patterns (monocyclic, polycyclic and chronic course), requirement of biologic treatment along the disease`s course and development of AOSD clinical

complications. To establish the relationship between its value and the AOSD-related mortality.

Methods: Retrospective study realized in two University Hospitals. Clinical, laboratory, AOSD-related complications data, administered biologic treatments and number of deaths (AOSD related or not) were recorded. Each patient was characterized for the presence of AOSD-related complications such as macrophage activation syndrome (MAS), myocarditis, lung involvement (pulmonary hypertension, interstitial infiltrate), renal involvement (tubulointerstitial nephritis, acute renal failure), secondary amyloidosis and AOSD-related death. SSS was applied at the onset of the disease development, assigning a point to each of the next 12 variables: fever, exanthema, pleuritis, pneumonitis, pericarditis, alteration of liver tests or hepatomegaly, splenomegaly, lymphadenopathy, odynophagia, leukocytosis >15,000/mm^3, myalgia and abdominal pain. A $\geq$7 score has been validated on other populations as the one which identifies the patients with high risk of complications. The relationship between SSS value and the next parameters was determined: clinical course, complications, biologic treatments administered and AOSD-related mortality.

Results: Data from 64 patients was analyzed (40,6% men, mean age 37 years). SSS values of <7 were obtained in 50 patients (78,3%) and of $\geq$7 in 14 patients (21,7%). MAS and renal involvement were significantly related with a score of $\geq$7 (Table 1). Lung involvement, myocarditis and secondary amyloidosis were not significantly associated with a high SSS value. Even so, analyzing each case, it was found that individually they had a score of $\geq$7 (except for lung involvement). Biologic treatment requirement along the disease course was related to SSS $\geq$7. Moreover, SSS value was not related to the different clinical patterns or the not-related-AOSD deaths. It was not possible to determine the relationship between the score and the AOSD complications-related deaths due to having only two registered cases. Despite this, it was found that individually both had a SSS of $\geq$7.

TABLE 1. AOSD RELATED COMPLICATIONS

COMPLICATIONS	*SSS <7 N= 50*	*SSS ≥7 N= 14*	*P-Value*
MAS	2	3	<0.05
Myocarditis	0	1	0,500
Lung involvement	1	1	0,920
Renal involvement	0	3	<0.05
Secondary amyloidosis	0	2	0.06
Biologic treatment	14	10	<0.05
All-cause deaths	3	2	0,970

Conclusion: The prognosis score described by *Pouchot et al* could be useful to identify those patients with high risk of developing clinical complications and those who will need biologic treatment along the course of their disease. It is necessary a higher number of patients to determine if the score could be useful to estimate the death risk related to AOSD complications.

REFERENCES:

[1] Ruscitti, et al. Adult-onset Still's disease: evaluation of prognostic tools and validation of the systemic score by analysis of 100 cases from three centers. BMC Medicine (2016)14:194

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THU0559

PSYCHOLOGICAL EFFECTS OF A BEHÇET'S DIAGNOSIS ON DISEASE ACTIVITY PERCEPTION- A PROSPECTIVE OBSERVATIONAL STUDY

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Background: There is a pressing need to understand more about the psychological experience in patients with Behçet's Disease (BD). The presence of poor wellbeing, low mood and anxiety may affect the ability to both manage and cope with this complex disorder and also impact upon the perception and experience of disease activity[1,2,3].

Objectives: Our aim was to investigate the relationship between patient rating of disease activity and their psychological experience (anxiety, low mood, illness perception and coping style) in a UK Centre of Excellence for BD.

Methods: This study had full UK research ethics approval.

A 12-month prospective observational study of a cohort of patients diagnosed with BD according to the International Criteria for BD(ICBD) under surveillance in the BD Centre of Excellence Liverpool, UK. All patients that agreed to a psychological evaluation were included. Participants were described for demographics and clinical presentation. BD Current Activity Form 2006 and a clinician's and patient's visual analogue scale (VAS) were recorded. Participants completed validated self-reported measures: Brief COPE, IPQ-R, PHQ-9, GAD-7 and WEMWBS. Spearman Rank correlations, multivariate regression analysis and mediation analysis were used to investigate the relationship between patient perception of disease activity, coping mechanisms and mood. For data analysis Excel and SPSS were used.

Results: 86 patients were selected (24 males, 68 females; mean age at time of evaluation 43.58 years ±11.8 SD; mean disease duration 9.76years ±10.01). The correlation between Clinician's VAS and Patient's VAS was strong 0.754 ($p<0.005$). Strong correlations were also observed between Patient's VAS and low mood (PHQ-9) $r=0.533$ ($p<0.005$), anxiety (GAD-7) $r=0.433$($p<0.05$), illness perception- emotional representation (IPQ-R) $r=0.377$ ($p<0.05$) and emotion-focused coping (COPE) $r=0.320$ ($p<0.05$).

The results of the mediation analysis indicated that patient's perception of disease activity was a significant predictor for Dysfunctional Coping Strategies ($b=1.5$,se=0.57, $p<0.05$). Dysfunctional Coping Strategies had a mediating impact on the relationship between patient perception of disease activity (VAS) and mood 0.645(CE: 0.68-1.389).

Conclusion: Psychological experience plays an important part in the patient evaluation and experience of disease activity. Patient coping strategies and psychological representation of illness experience influence their perception of disease activity and their mood. This highlights the need of patients for psychological support and for improving coping mechanisms in order to obtain a better disease control and a higher quality of life.

REFERENCES:

[1] RJ Moots, S Campbell, **Is Psychological Status Related to Symptom Experience in Behçet's Syndrome?** 2014 ACR/ARHP Annual Meeting

[2] IM Atay,I Erturan, A Demirdas, GB Yaman, VA Yürekli The impact of personality on quality of life and disease activity in patients with Behcet's disease: a pilot study Compr Psychiatry. 2014 Apr;55(3):511-7

[3] **MA Melikoglu,M Melikoglu The relationship between disease activity and depression in patients with Behcet disease and rheumatoid arthritis**. Rheumatol Int. 2010 May;30(7):941-6

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THU0560 **DISTINCTIVE IMAGING FEATURES BETWEEN IGG4-RELATED OPHTHALMIC DISEASE AND GRAVES' ORBITOPATHY: A COMPARATIVE STUDY**

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Background: IgG4-related ophthalmic disease (IgG4-ROD) may present as a cause of orbital myositis leading to proptosis and diplopia. This clinical scenario can be mistakenly diagnosed as Graves' orbitopathy (GO), preventing a timely and adequately treatment.
Objectives: To elucidate if there are specific radiological features that might differentiate between IgG4-ROD and GO by imaging.
Methods: We included 19 patients with diagnosis of IgG4-related disease (IgG4-RD) according to the Comprehensive Diagnostic Criteria for IgG4-RD, who regularly attended a tertiary referral center in Mexico City. All the patients had ophthalmic involvement and available computed tomography (CT) and/or magnetic resonance imaging (MRI) of the orbits. We also included 32 patients with GO with available CT and/or MRI of the orbits. Imaging studies were evaluated by a blinded head and neck radiologist for the following features: exophthalmos, extraocular muscles (EOM) size and morphology, lacrimal gland enlargement, orbital fat involvement, stretching of the optic nerve (ON), ON sheath thickening and orbital bone changes.
Results: Both groups were similar in age (49.1±15.8 vs. 51.6±14.7, p=0.58) and gender (men 58.9% vs. 40.6%, p=0.23). In addition to ophthalmic involvement, 18 (94.7%) IgG4-RD patients had extra-ophthalmic involvement with a median number of organs involved of 7 (1-12), mainly submandibular glands (73.7%), lymph nodes (68.4%), parotid glands (63.2%) and pancreas (47.4%). Three patients were misdiagnosed as GO before IgG4-RD diagnosis. Graves' disease was the underlying thyroid disorder in 28 (87.5%) GO patients, Hashimoto's thyroiditis in 2 (6.3%), papillary thyroid carcinoma in one (3.1%) and one patient was euthyroid with positive thyroid stimulating immunoglobulin. The prevalence of exophaltmos (78.9% vs. 93.8%), bilateral involvement (78.9% vs. 87.8%) and overall EOM involvement (47.4% vs. 68.8%) was similar between IgG4-ROD and GO groups. However, IgG4-ROD patients had a higher frequency of lacrimal gland involvement (73.7% vs. 10.7%, p=0.001) and a tendency for the lateral rectus to be the most frequently involved EOM (22.2% vs. 0%, p=0.07); conversely they had a lower prevalence for the inferior rectus to be the most frequently involved EOM, (33.3% vs. 72.7%, p=0.04), orbital fat involvement (47.4% vs. 81.3%, p=0.01), ON stretching (57.9% vs. 87.5%, p=0.02) and orbital bone changes (0% vs. 25%, p=0.02). EOM bellies were involved in all the IgG4-ROD and GO cases, whereas EOM tendon involvement was present in 9% of GO and in none of the IgG4-ROD group. Patients with IgG4-ROD had more frequently the combination of lacrimal gland and lateral rectus (31.6% vs. 3.1%, p=0.008) and less frequently the combination EOM and orbital fat involvement (21.2% vs. 59.4%, p=0.008).
At the logistic regression analysis we found an association of lacrimal gland involvement (OR 64.4.0, 95% CI 6.8-609.5, p=0.001) with IgG4-ROD. In a second model including combined variables, the combination of lacrimal gland and lateral rectus involvement was associated with IgG4-ROD (OR 62.5, 95% CI 3.31-1000), P=0.006), whereas the presence of EOM and orbital fat involvement was protective (OR 0.05, 95% CI 0.006-0.48, p=0.009).
Conclusion: Imaging features may reliably differentiate between IgG4-ROD and GO. The presence of both lacrimal gland and lateral rectus enlargement must alert clinicians to consider IgG4-ROD diagnosis.

REFERENCES:

[1] Tiegs-Heiden CA, Eckel LJ, Hunt CH, et al. Immunoglobulin G4-related disease of the orbit: imaging features in 27 patients. AJNR Am J Neuroradiol. 2014 Jul;35(7):1393-7.

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THU0561 **CANAKINUMAB FOR THE TREATMENT OF ADULT ONSET STILL'S DISEASE TO ACHIEVE REDUCTION OF ARTHRITIC MANIFESTATION AT WEEK 12: AN INVESTIGATOR-INITIATED MULTI-CENTRE, PLACEBO-CONTROLLED STUDY (CONSIDER)**

Claudia Kedor[1], Joachim Listing[2], Jan Zernicke[1], Anja Weiß[2], Frank Behrens[3], Norbert Blank[4], Jörg Henes[5], Jörn Kekow[6], Andrea Rubbert-Roth[7], Hendrik Schulze-Koops[8], Eva Seipelt[9], Christof Specker[10], Eugen Feist[1], The Study was supported by Novartis Germany. *[1]Charité – Universitätsmedizin Berlin, Rheumatology and clinical Immunology, Berlin, Germany*; *[2]Deutsches Rheuma-Forschungszentrum (DRFZ), Epidemiology, Berlin, Germany*; *[3]Goethe University Frankfurt, Fraunhofer Institut für Molekularbiologie und Angewandte Onkologie IME, Frankfurt a.M., Germany*; *[4]University Hospital Heidelberg, Internal Medicine 5, Rheumatology, Heidelberg, Germany*; *[5]University Hospital Tuebingen, Centre for Interdisciplinary Clinical Immunology, Rheumatology and Auto-inflammatory Diseases (INDIRA) and Internal Medicine II, Tübingen, Germany*; *[6]Helios Fachklinik Vogelsang-Gommern, Klinik für Rheumatologie, 39245 Vogelsang-Gommern, Germany*; *[7]Kantonsspital St Gallen, Klinik für Rheumatologie, St Gallen, Switzerland*; *[8]University of Munich, Department of Internal Medicine IV, Divison of Rheumatology, München, Germany*; *[9]Immanuel Krankenhaus Berlin, Rheumatologie und Klinische Immunologie, Berlin, Germany*; *[10]Evangelisches Krankenhaus • Kliniken Essen-Mitte, Klinik für Rheumatologie and Klinische Immunologie, Essen, Germany*

Background: Inhibition of interleukin-1 (IL-1) represents a promising treatment option in adult-onset Still's disease (AOSD). Canakinumab (CAN) is approved for treatment of systemic juvenile idiopathic arthritis (sJIA) since 2013 and recently for AOSD in Europe. In sJIA, CAN has a proven marked impact on systemic and articular disease activity, but for AOSD RCT data is limited.
Objectives: Investigation of efficacy and safety of CAN in AOSD patients with joint involvement by means of a multi-centre, double-blinded, randomized, placebo controlled trial.
Methods: AOSD patients with joint involvement (tender and swollen joint count $\geq$4 each) were stratified by pre-treatment status with biologics and randomized in a ratio of 1:1 to CAN (4 mg/kg up to a maximum of 300 mg) or placebo (PBO) s.c. every 4wks. The primary endpoint was defined as the proportion of patients with a clinical-relevant reduction ($\geq$1.2) in disease activity as measured by change in disease activity score (DAS28) at week 12. There were two major protocol violations: two PBO patients received blinded CAN at week 4. Therefore, a per-protocol (PP) analysis, which excluded data of these two patients, was performed.
Results: The study was prematurely stopped with 35 out of 68 planned patients enrolled due to approval of CAN for AOSD by EMA. At enrollment, mean DAS28 represented high disease activity for both: 5.4 in CAN (n=18) and 5.3 in PBO (n=17). In the intention-to-treat analysis, 12 (67%) CAN and 7 (41%) PBO patients met the primary endpoint. The 25.5% [95%CI: -10.3%; 55.9%] difference in the response rate did not achieve statistical significance (p=0.18). Using the PP analysis, the treatment difference for primary endpoint was 33.4% [95%CI: -10.3%; 55.9%, p=0.08]. We observed higher ACR50 (50% CAN vs. 6.7% PBO, p= 0.009), ACR70 (28% CAN vs. 0% PBO, p=0.049) response rates, (PP analysis). Higher mean improvements in the CAN vs PBO group for DAS28(ESR and CRP), ESR, CRP, 66 swollen and 68 tender joint counts at week 12 were observed (PP analysis). There were 47 and 21 non-serious adverse events (AE) reported in CAN and PBO groups, respectively. Two CAN patients experienced an SAE (hepatotoxicity and patellofemoral pain syndrome).
Conclusion: Although the study was terminated prematurely and the primary endpoint did not achieve statistical significance, treatment of patients with active AOSD with CAN led to improvement of several outcome measures. In addition, safety profile was similar to that reported in sJIA and no unexpected safety issues were observed. This data support the treatment of AOSD patients with CAN.

REFERENCES:

[1] Ruperto. NEJM (2012): 2396-2406

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Table 1. Characteristics of 9 patients from 1 center

Patient	Age/ Sex	Tumor type	Checkpoint Inhibitor	Fulfilled EULAR/ACR Classification Criteria*	Unfulfilled Criteria	Atypical Features	Treatment
1	63 M	RCC	Nivolumab	No; 5 points	Acute phase reactants		Prednisone 40 mg; tocilizumab 162 mg q2 weeks
2	69 M	Melanoma	Ipilimumab/ nivolumab	Yes; 6 points		Sicca symptoms; ANA 1:1280, anti-SSA >8 IU	Prednisone 30 mg
3	79 M	Melanoma	Ipilimumab/ nivolumab	Yes; 7 points**		Sicca symptoms	Prednisone 20 mg
4	57 M	Melanoma	Pembrolizumab	No; 3 points	Acute phase reactants; RF 35 IU/ml; knee involvement		Prednisone 60 mg
5	60 M	Melanoma	Pembrolizumab	No; 3 points	RF 45 IU/ml; knee involvement		Prednisone 60 mg
6	66 M	Melanoma	Nivolumab	Yes; 5 points	Hand involvement		Prednisone 20 mg; MTX
7	69 F	RCC	Nivolumab	Yes; 5 points	Hand involvement		Prednisone 10 mg; tocilizumab 162 mg q2 weeks
8	66 M	RCC	Durvalumab; tremilimumab	Yes; 5 points	Hand involvement		Prednisone 20 mg
9	72 F	RCC	Avelumab	Yes; 4 points	Acute phase reactants; hand and knee involvement		Prednisone 20 mg

from: SOBI and Novartis, Speakers bureau: Novartis and SOBI, Jörg Henes: None declared, Jörn Kekow: None declared, Andrea Rubbert-Roth Consultant for: Chugai, Eli Lilly, Roche, and Sanofi
, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Hexal/Novartis, Janssen, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, and Sanofi
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THU0562 PREVALENCE, UNDERLYING FACTORS AND DAMAGE ASSOCIATED WITH CHRONIC PERSISTENT INFLAMMATION IN PATIENTS WITH FMF

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Background: Familial Mediterranean Fever (FMF) is the most frequent auto-inflammatory disease characterized by recurrent, self-limiting attacks of fever, peritonitis, pleuritis, synovitis, myalgia, and erysipelas-like erythema (ELE). Attacks has a robust inflammatory response which completely normalize when attacks subside. However, substantial number of FMF patients possess chronic persistent inflammation even in between attacks. Clinical significance of persistent inflammation and its contribution to damage accrual are yet to be determined.

Objectives: We aimed to determine the prevalence and underlying factors of chronic persistent inflammation and its association with the domains of Auto-inflammatory disease damage index (ADDI) in a large cross-sectional multicenter cohort.

Methods: All patients recruited from FMF in Central Anatolia (FiCA) cohort, which is a duplication disabled, internal and externally controlled, cross-sectional, multicenter accessible web-based cohort. Demographic data, disease characteristic, attack features (ever presented) were meticulously questioned. Genotype data (if available) and laboratory features including inflammatory markers were recorded. FMF related damage scores was assessed by auto-inflammatory disease damage index (ADDI) which is recently validated. Patients were stratified according to their antecedent acute phase responses as having persistent inflammation (PI group) or not, both groups compared in terms of disease characteristics, attack features, inflammatory comorbidities and damage domains.

Results: Study is comprised 970 adult patients (mean age 35.3±12.1, 61% female). 54 of them were excluded for their first inclusion. 15% of patients had persistent inflammation. PI group had significantly younger age of diagnosis, male dominance, homozygous M694V, more frequent attacks it the last year, more pleuritis, arthritis, myalgia and ELE and more severe disease according to ISSF than other patients (Table-1). Moreover, colchicine resistance and ADDI damage scores were remarkably higher in PI group.

In multi-variate analyzes colchicine resistance OR=2.71 [95%CI 1.38-5.35], ISSF OR=11.06 [95%CI 5.23-23.39], male gender OR= 2.38 [95%CI 1.51-3.76], homozygous M694V mutation OR= 2.31 [95%CI 1.41-3.78] and ELE OR= 1.72 [95%CI 1.04-2.857] found as independent predictors of persistent inflammation. PI group had more damage in multiple domains like joint restriction, musculoskeletal pain, proteinuria, amyloidosis, renal insufficiency and developmental delay. Same variables and persistent inflammation further analyzed in in terms of predicting the damage. Persistent inflammation found to be an independent predictor of proteinuria OR=2.02 [95%CI 1.05-3.90], amyloidosis OR=2.71 [95%CI, 1.34-5.48]), and renal insufficiency OR=4.36 [95%CI 1.84-10.32].

Conclusion: Persistent inflammation is relatively common in FMF patients particularly in those harboring M694V homozygous mutation and is associated with major complications of disease indicating poor prognosis.

Acknowledgement: None

Table 1 Patients demographics and disease characteristics |

		Persistent inflammation (n=142)	Others (-) (n=784)	p
Age, years		35(12.1)	35 (12.1)	0.09
Female		74 (52.1%)	492 (62.8%)	0.017
Disease onset <20 years		128 (90.1%)	585 (74.6%)	<0.001
Age at FMF diagnosis, years		22.6 (14.2)	25.1 (13.0)	0.041
M694V/M694V*		91 (71.1%)	240 (36.8)	<0.001
Fever		116 (81.7%)	655 (83.5%)	0.708
Peritonitis		125 (88%)	723 (92.2%)	0.158
Pleuritis		84 (59.2%)	351 (44.8%)	0.001
Arthritis		93 (65.5%)	301 (38.4%)	<0.001
Myalgia		57 (40.1%)	138 (17.6%)	<0.001
Erysipelas like erythema		68 (47.9%)	170 (21.7%)	<0.001
Attack frequency in the last year		8.37 (9.9)	3.78 (5.3)	<0.001
ISSF	Mild Disease	9 (6.3%)	440 (56.1%)	<0.001
	Intermediate Disease	91 (64.1%)	325 (%41.5)	
	Severe disease	42 (29.6%)	19 (%2.4)	
Colchicine resistance		38 (26.8%)	38 (4.8%)	<0.001
ADDI		2.2 (2.5)	0.9 (1.2)	<0.001
Joint restriction		13 (9.2%)	14 (1.8%)	<0.001
Musculoskeletal pain		84 (59.2%)	364 (46.4%)	0.006
Proteinurea		27 (19%)	37 (4.7%)	<0.001
Amyloidosis		28 (19.7%)	27 (%3.4)	<0.001
Renal insufficiency		20 (14.1)	15 (1.9%)	<0.001
Developmental delay		5 (3.5%)	9 (1.1%)	0.049
Splenomegaly		21 (14.8%)	34 (4.3%)	<0.001

ISSF: international severity scoring system for FMF. ADDI: autoinflammatory disease damage index
*n=14 missing in PI, n=132 missing in others

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Gözde Kübra Yardımcı: None declared, reyhan bilici salman: None declared, Levent Kılıç: None declared, mehmet akif ozturk: None declared, Berna Goker: None declared, seminur haznedaroglu: None declared, Umut Kalyoncu Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, abdurrahman tufan: None declared

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THU0563 COMPARISON BETWEEN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSISAND INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES: A PROSPECTIVE COHORT

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Background: The term "Interstitial Pneumonia with Autoimmune Features (IPAF)" is used to describe patients with Interstitial Lung Disease in combination to clinical, serological and/or pulmonary features that are suggestive, but insufficient to satisfy classification criteria of a specific Connective Tissue Disease (CTD). Some retrospective studies available in literature described patient cohorts with IPAF heterogenous in terms of clinical, serological, and radiographic manifestations

Objectives: To prospectively recruit a cohort of consecutive ILD patients classified as IPAF or as affected by Idiopathic Pulmonary Fibrosis (IPF); to describe their clinical, serological, and radiological features by a multidisciplinar team composed by Pulmonologists, Radiologists, and Rheumatologists, comparing IPAF and IPF patients.

Methods: In the lasts 2 years, they were enrolled 45 patients with IPAF and 143 with IPF among a total of 506 patients with Interstitial Lung Disease (ILD). All patients were evaluated clinically by both rheumatologists and pulmonologists, also by means of chest high resolution computed tomography (hrCT), pulmonary function tests (PFT), and nailfold videocapillaroscopy.

Results: In IPAF cohort the most common characteristics from the clinical, serological and morphological domain were Raynaud's phenomenon (RP) (31.1%) antinuclear antibodies positivity with titre $\geq$1/320 or any titre for centromeric or nucleolar pattern (17.7%) and nonspecific interstitial pneumonia (68.8%) respectively. The majority of patient (88.9%) had the minimum of 2 criteria at the recruitment. Female gender was more common in IPAF compared to IPF (62.2% vs 23%, p<0.0001) and the mean age of onset was lower in patient with IPAF (66 vs 73, p <0.0001). NVC resulted positive in 2 patients, both without RP. Patients with IPAF showed better performances in PFT than patients with IPF than those with IPF (mean forced vital capacity 83% vs 74%, p =0.01; mean diffusing lung capacity for carbon monoxide 64% vs. 52%, p=0.01). Patients with IPAF less commonly than patients with IPF needed oxygen therapy (44.4% vs 77.6%, p <0.0001) and more commonly showed at hrCT NSIP (68.8% vs 6.9%, p <0.0001) than UIP pattern (0% vs 86%, p <0.0001).

Conclusion: IPAF criteria recruit a rare cohort of patients with a disease probably less severe than IPF, even though clinically relevant. Further prospective studies may better define the long-term prognosis of ILD in IPAF. The follow-up of these patients by a multi-disciplinary team may be useful in order to early recognize and treat the new cases of CTDs. Some IPAF criteria probably are useless due to their high specificity for definite CTD and the classification need a revision in the light of the prospective experiences. Nevertheless, IPAF classification can recruit incomplete form or early onset of CTD that can allow a timely treatment in patients without a structured damage.

REFERENCES:

[1] Sambataro G, Sambataro D, Torrisi SE, Vancheri A, Pavone M, Rosso R, Schisano M, Crimi C, Pignataro F, Fischer A, Del Papa N, Vancheri C. State of the art in interstitial pneumonia with autoimmune features: a systematic review on retrospective studies and suggestions for further advances. Eur Respir Rev 2018:27(148)

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THU0564 COULD A PROBABILISTIC REASONING AI ACCELERATE RARE DISEASE DIAGNOSIS? EVALUATING THE POTENTIAL IMPACT OF A DIAGNOSTIC DECISION SUPPORT SYSTEM IN A RETROSPECTIVE STUDY

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Background: The diagnosis of rare diseases is often delayed by years [1]. The main factor for this delay is believed to be the lack of knowledge and awareness regarding rare diseases [2]. Probabilistic diagnostic decision support systems (DDSS) have the potential to accelerate rare disease diagnosis by highlighting differential diagnoses for physicians [3, 4]. DDSS's are based on case input and incorporated medical knowledge.

Objectives: We examine a probabilistic DDSS prototype and assess its potential to provide accurate rare disease suggestions early in the course of rare disease cases.

Methods: Retrospectively, information from the medical records of 93 patients was transferred to the DDSS. Each of these patients had a confirmed rare inflammatory systemic disease. The accuracy of the DDSS disease suggestions was assessed for all documented visits over time. Time to correct top fit (TF) and top five fit (T5F) disease suggestion was assessed, as was the original time to clinical diagnosis (TD). TF/TD as well as T5F/TD were calculated to allow for comparison of TF respective T5F normalized to TD. Wilcoxon signed-rank test was conducted for TD-TF and TD-T5F.

Results: The DDSS suggested the correct disease at a time *earlier* than the time of clinical diagnosis among the top five fit disease suggestions in 53.8% of cases (50 of 93), and as the top fit disease suggestion in 37.6% of cases (35 of 93). Median advantage of correct disease suggestions compared to the time point of clinical diagnosis was 3 months or 50% for top five fit respective 1 month or 21% for top fit. The correct diagnosis was suggested at the *first* documented patient visit among the top five fit disease suggestions in 33.3% (top five fit), respective 16.1% of cases (top fit). Wilcoxon signed-rank test shows a significant difference between the time to clinical diagnosis and the time to correct disease suggestion for both top five fit and top fit (z-score -6.68, respective -5.71, α=0.05, p-value <0.001). The DDSS suggested the correct rare disease at the time of diagnosis in 89% of cases (83 of 93)

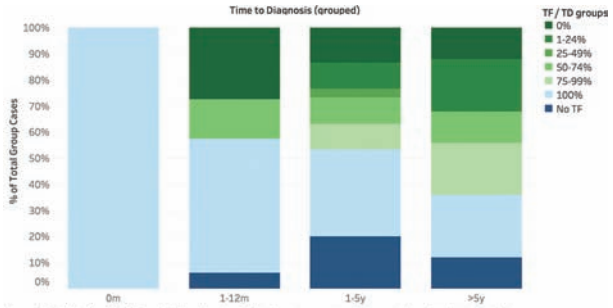


Figure 1. Distribution of TF/TD by TD. Visualisation of the time to correct top fit suggestion relative to the time to diagnosis, grouped by time to diagnosis. Number of cases per group: 0m: 5; 1-12m: 33; 1-5y: 30; >5y: 25

Conclusion: The DDSS was capable of providing accurate rare disease suggestions in most of the rare disease cases. In many cases it provided correct rare disease suggestions early in the course of the disease, sometimes in the very beginning of a patient's journey. The interpretation of these results suggests that DDSS's have the potential to highlight the possibility of a rare disease to physicians early in the course of a case. Limitations of this study derive from its retrospective and unblinded design, data input by a single user, and the optimization of the knowledge base during the course of the study. Whether the use of this DDSS leads to a reduced time to rare disease diagnosis in a clinical setting should be validated in prospective studies.

REFERENCES:

[1] Blöß S, et al. Diagnostic needs for rare diseases and shared prediagnostic phenomena: Results of a German-wide expert Delphi survey. PLOS ONE. 2017 feb;12(2):e0172532. Available from: http://dx.plos.org/10.1371/journal.pone.0172532.

[2] Nationales Aktionsbündnis für Menschen mit Seltenen Erkrankungen (NAMSE). Nationaler Aktionsplan für Menschen mit Seltenen Erkrankungen. 2013. Available from: http://www.namse.de/images/stories/Dokumente/nationaler_aktionsplan.pdf.

[3] Kostopoulou O, et al. Early diagnostic suggestions improve accuracy of family physicians: a randomized controlled trial in Greece. Family Practice. 2015 jun;32(3):323–328.

[4] Riches N, et al. The effectiveness of electronic differential diagnoses (DDX) generators: A systematic review and meta-analysis. PLoS ONE. 2016 mar;11(3):e0148991. Available from: http://dx.plos.org/10.1371/journal.pone.0148991.

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THU0565 COMPARISON OF SURVIVAL RATES AMONG SUBGROUPS OF PATIENTS EVALUATED FOR FEVER OF UNKNOWN ORIGIN

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Background: Fever of unknown origin (FUO) is one of the most challenging clinical situations. Although several studies showed a relatively benign course of patients remained undiagnosed, long-term outcome of patients with a certain diagnosis remain non-established (1).

Objectives: To describe the follow-up results of patients investigated for FUO and had a certain diagnosis.

Methods: Data from patients who admitted to Hacettepe University Hospitals, inpatients sections of department of the internal medicine with the complaint of FUO collected prospectively from January 2015 to October 2017. Patients with an uncertain diagnosis after all diagnostic procedures excluded. Patients were divided into 3 main subgroups: rheumatologic, infectious and malignant groups. We compared Kaplan-Meier curves for all diagnosis-to-death time frames with the standart log-rank test. $p<0.05$ was considered as statistically significant.

Results: Total 106 patients were included, 58(55%) of them were female. Median age was 48 (18-81) years. Patients were also divided into three subgroups: rheumatologic (RHE) (n=49, 46.2%), infectious (INF) (n=28, 26.4%) and malignant (MLG) (n=29, 27.4%) causes; adult-onset Still's disease (n=20; 41% of), tuberculosis (n=9; 32%) and lymphoma (n=19; 66%) were the most common diagnosis among groups, respectively. Mortality rates in decreasing order were RHE, INF and MLG groups, respectively. As an interaction was found between gender and survival, results of survival analysis were given as stratified according to gender. While there was no survival difference between RHE and INF groups among men, both of these groups had better survival than MLG group (ROM-INF p=0.13; ROM-MLG p=0,001; INF-MLG p=0,022). Among women, only there was a significant survival difference between RHE and MLG groups (ROM-INF p=0.15; ROM-MLG p=0,007; INF-MLG p=0,42).

Conclusion: Among patients evaluated for FUO, survival rate was higher in patients who had a rheumatological diagnosis. Further diagnostic algorithms are needed to identify these subgroups, because of the higher mortality among INF and MLG groups.

REFERENCES:

[1] Knockaert DC, Dujardin KS, Bobbaers HJ. Long-term follow-up of patients with undiagnosed fever of unknown origin. Arch Intern Med. 1996;156 (6):618.

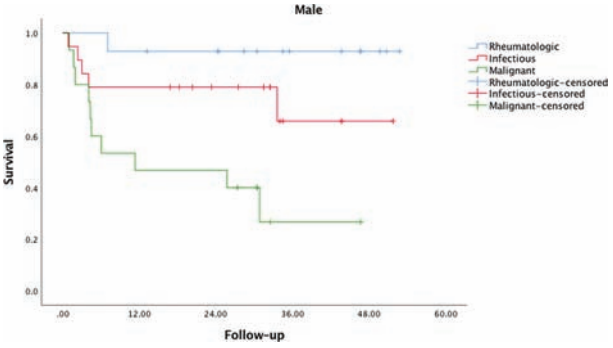


Figure 1. Kaplan-Meier curves of male patients (RHE vs. INF p=0.13; RHE vs. MLG p=0.001; INF vs. MLG p=0.022)

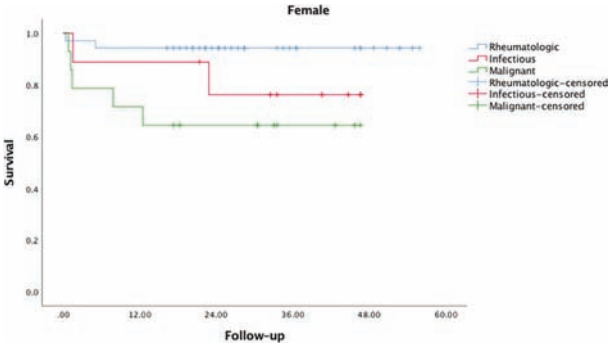


Figure 2. Kaplan-Meier curves of female patients (RHE vs. INF p=0.15; ROM vs. MLG p=0.007; INF vs. MLG p=0.42)

Disclosure of Interests: Emre Bilgin: None declared, Berkan Armagan: None declared, Alper Sarı: None declared, Ertuğrul Çağrı Bölek: None declared, Bayram Farisoğulları: None declared, Gözde Kübra Yardımcı: None declared, Levent Kılıç: None declared, Ali Akdoğan: None declared, Omer Karadag: None declared, Şule Apraş Bilgen: None declared, Ali İhsan Ertenli: None declared, Sedat Kiraz: None declared, Umut Kalyoncu Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim

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THU0566 OCULAR FEATURES IN 381 PATIENTS WITH SYSTEMIC SARCOIDOSIS AND ITS CORRELATION WITH THE IWOS CRITERIA. STUDY IN A UNIVERSITY HOSPITAL

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Background: Sarcoidosis is a multisystemic inflammatory disease characterized by non-caseating epitheliod granulomas that can affect any organ system. The three most frequency affected organs are lung, skin and eyes. Ocular involvement is the presenting symptom in approximately 20-30% and can involve any part of the eye and its anexal tissues. Sarcoidosis may cause uveitis, conjunctivitis, episcleritis/scleritis, optical nerve disease and orbital inflammation.

Objectives: To analyze the prevalence of ocular involvement is systemic sarcoidosis, the clinical patterns and their correlation with the International Workshop on Ocular Sarcoidosis (IWOS) criteria. These criteria classify ocular sarcoidosis as definite, presumed, probable and possible, according to some ophthalmological and analytical findings. They are especially useful if a biopsy is not obtained or it is negative.

Methods: Retrospective study of patients admitted to a single reference University Hospital between 1999 and 2019 with diagnosis of sarcoidosis. Clinical findings, demographics features, anatomic location and IWOS intraocular signs were recorded. We also collected serum angiotensin

converting enzyme (ACE), liver enzyme test, chest radiography, chest computed tomography scan, treatment and biopsy if performed.

TABLE. Demographic and clinical features of the 50 patients with ocular sarcoidosis.

	Patients (n=50)
Age, mean (SD) years	45.5 (16.7)
Sex, men/women, n/n	23/27
Affected organs, n (%)	
Lung	30 (60)
Skin	14 (28)
Liver	4 (8)
Kidney	3 (6)
Musculoskeletal system	3 (6)
Central nervous system	3 (6)
Hearth	2 (4)
Ocular signs, n (%)	
Bilaterality	22 (44)
Snowballs/strings of pearls	19 (38)
Mutton-fat KPs	12 (24)
Multiple chorioretinal peripheral lesions	7 (14)
Periphlebitis	5 (10)
Anterior synechiae	1 (2)
Optic disc granulomas	1 (2)
IWOS criteria, n (%)	
Definite	22 (44)
Presumed	13 (26)
Possible	4 (8)
Treatment, %	
Prednisone (oral)	44 (88)
Methylprednisolone (bolus)	5 (10)
Conventional IS	
.....MTX	21 (42)
.....AZA	9 (18)
.....CsA	2 (4)
.....MMF	2 (4)
Biologic therapy	
.....IFX	5 (10)
.....ADA	4 (8)
.....GLM	2 (4)

Abbreviations: ADA, adalimumab; AZA, azathioprine; CsA, cyclosporine A; GLM, golimumab; IFX, infliximab; IS, immunosuppressor; KPs, keratic precipitates; MMF, mycophenolate mofetil; MTX, methotrexate; SD: standard deviation.

Results: We selected patients with ocular inflammation from a cohort of 381 patients with sarcoidosis (n=50, 13%). Most of the cases were women (54%) and median age was 45.5±16.7 years. In these 50 cases, the most affected organ was lung (60%), followed by skin (28%). Forty patients had uveitis, 32 of them with ocular symptoms. Thirty-nine out of 50 patients (78%) met one of the 4 IWOS diagnostic categories: 22 with definite (44%), 13 presumed (26%) and 4 with possible (8%) sarcoidosis. Eleven patients did not meet IWOS criteria. The most common ocular signs were bilaterality (44%), snowballs or strings of pearls (38%), mutton-fat KPs (24%), multiple chorioretinal peripheral lesions (14%) and periphlebitis (10%). The median value of ACE was 69 U/l. Forty-four patients (88%) received oral corticosteroids, 21 (42%) received methotrexate, 11 (21%) received another conventional immunosuppressor and 11 (21%) a biological treatment. TABLE shows demographic and clinical features.

Conclusion: In our population the IWOS Criteria had a sensitivity of 78%. Even though there is no gold standard for diagnosing ocular sarcoidosis yet, IWOS signs can help clinicians suspect it.

REFERENCES:

[1] Herbort CP, Rao NA, Mochizuki M; members of Scientific Committee of First International Workshop on Ocular Sarcoidosis. International criteria for the diagnosis of ocular sarcoidosis: results of the first International Workshop On Ocular Sarcoidosis (IWOS). Ocul Immunol Inflamm. 2009 May-Jun;17(3):160-9.

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THU0567 POLYMYALGIA RHEUMATICA-LIKE SYNDROME FROM CHECKPOINT INHIBITOR THERAPY: CASE SERIES AND SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Checkpoint inhibitor therapy has caused a paradigm shift in the field of oncology, producing significant survival benefits in patients with an ever-growing list of malignancies, but their use is attended by a spectrum of immune related adverse events (irAEs). Many rheumatic irAEs have been described. A critical and presently unanswered question is what proportion of these rheumatic irAEs represent new appearances of classic rheumatic diseases or, alternatively, represent new clinical variants with potentially different pathogenesis, clinical course and treatment responsiveness. Little is known about the PMR-like entity that has been described in the setting of ICI therapy.

Objectives: To assess whether the polymyalgia rheumatica (PMR)-like syndrome reported as an irAE from checkpoint inhibitor therapy is consistent with the 2012 EULAR/ACR provisional criteria for PMR[1].

Methods: The cases were derived from two sources. Group 1 represents reported cases from three contributing centers. Group 2 was derived from a systematic review of the literature searching for all cases reported as PMR or PMR-like illness associated with checkpoint inhibitor therapy. Cases were assessed for the quality of reporting and then analyzed to determine whether they fulfilled the 2012 EULAR/ACR provisional criteria for PMR.

Results: A total of 49 patients were included for analysis, including 9 cases from Cleveland Clinic (Table 1), 4 cases from Johns Hopkins University, and 7 cases from University Hospital of Bordeaux, in addition to the 29 separate cases found by systematic review. Among the entire group, 37 (75%) were designated "complete" indicating that they had sufficient data to reliably apply the 2012 EULAR/ACR criteria of which 28 (75%) cases fulfilled complete criteria for PMR. A number of cases also demonstrated some clinical features unusual for idiopathic PMR.

Conclusion: This study suggests a high proportion of reported cases of checkpoint inhibitor-related PMR fulfill preliminary criteria for PMR yet in one quarter clinical details were incomplete making verification problematic. Furthermore, in the absence of a gold standard for the diagnosis of PMR, the relationship of checkpoint inhibitor-related PMR to the idiopathic form remains unclear.

REFERENCES:

[1] Dasgupta B, Cimmino MA, Maradit-Kremers H, et al. 2012 provisional classification criteria for polymyalgia rheumatic: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Ann Rheum Dis 2012;71:484-492.

Disclosure of Interests: cassandra calabrese Speakers bureau: Regeneron/Sanofi, Laura Cappelli Grant/research support from: Bristol-Myers Squibb, Consultant for: Regeneron/Sanofi Genzyme, Marie Kostine: None declared, Elizabeth Kirchner Consultant for: Celgene, Horizon, Novartis, Regeneron, Speakers bureau: Merck and Sanofi, Tawnie Braaten Grant/research support from: supported by T32 grant and "research reported in this publication was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under Award Number T32AR048522. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.", Leonard Calabrese Consultant for: Bristol-Myers-Squibb, Genentech and Astra-Zeneca.

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THU0568 CLINICAL CHARACTERISTICS OF SEVEN RELAPSING POLYCHONDRITIS CASES MISDIAGNOSED AS ARTHRITIS

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Background: Relapsing polychondritis (RPC) is a rare autoimmune disease. It mainly affects the tissue abundant of cartilage, such as ear, nose, and tracheoles. The multiple systems including eye, joint, mucocutaneous, and kidney could be involved[1]. As the presentation of arthritis was nonspecific and could appear in several connective tissue diseases,

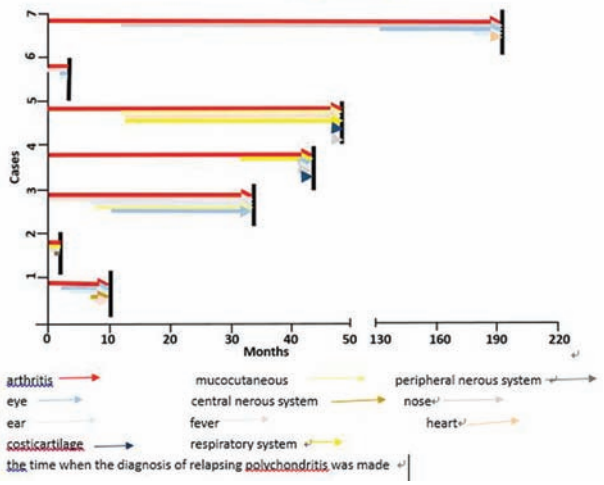
it was easily misdiagnosed. The delay in establishing the diagnosis of RPC was common. A survey from the United Kingdom found a median length of 1.9 years from the first disease attack to diagnosis[2]. One recent research reported 64% of RPC patients had a diagnostic delay with more than five years[3].

Objectives: We made a retrospective study to explore distinct characteristics of relapsing polychondritis with arthritis as the first attack. By comprehending the nature of disease fully, misdiagnosis at the early phase of illness could be avoided.

Methods: The clinical features and prognosis of 7 RPC patients in Peking Union Medical College Hospital between October 2012 and October 2018, presenting as arthritis at onset, were retrospectively analyzed.

Results: There were five female patients. The female to male ratio of the case series was 5:2. The age of 7 patients was 43.43±9.86 years. The number of affected joints was 20.14±10.92. The joint involvement was most common in the bilateral proximal interphalangeal joints (PIPs) and interphalangeal joints of the thumb. Recurrent arthritis occurred in 5 patients. There was no accompanying enthesitis. The specific serum indexes of RA, such as rheumatoid factor (RF), anti-cyclic citrullinated peptide (CCP) antibody, were negative. There were three patients administered with conventional synthetic disease modifying anti-rheumatic drugs firstly, and they did not respond well. The median delay time from onset to diagnosis of RPC was ten month (Figure 1). The deformity and destruction of the joint were not observed in all patients, by clinical and radiological assessment. The average duration from arthritis to the occurrence of other involved system was 8.3 months. Four patients were misdiagnosed as rheumatoid arthritis at first. One patient was considered as ankylosing spondylitis at first. Two patients were diagnosed as arthritis at the beginning. As regards to treatment, glucocorticoids (GCs), cyclophosphamide and mycophenolate mofetil were used. Two patient was complicated with palmoplantar pustulosis and Kikuchi-Fujimoto disease. During follow up, myelodysplastic syndrome occurred in one patient. After following up for 35.43±30.92 months, all patients survived and were not with the recurrence of arthritis.

Figure 1. The demonstration of multiple system involvement and the interval from onset to diagnosis in seven patients with relapsing polychondritis



Conclusion: RPC patients with arthritis onset were characteristic of middle-aged women and symmetric multiple joint involvements. The RF and anti-CCP antibody were negative. The arthritis was recurrent and not erosive. The interphalangeal joints of the thumb and PIPs were the most frequently involved joints. In clinical practice, physicians should be alert to the possibility of RPC, when encountered the patients with abovementioned arthritis. The inquiry about manifestations of other system involvement in RPC and a regular follow-up was warranted. After the combined therapy of GCs and immunosuppressants, all patients had a favorable prognosis.

REFERENCES:

[1] Chopra R, Chaudhary N, Kay J. Relapsing polychondritis. Rheumatic diseases clinics of North America 2013; 39(2): 263-76.

[2] Hazra N, Dregan A, Charlton J, Gulliford MC, D'Cruz DP. Incidence and mortality of relapsing polychondritis in the UK: a population-based cohort study. Rheumatology 2015; 54(12): 2181-7.

[3] Ferrada MA, Grayson PC, Banerjee S, et al. Patient Perception of Disease-Related Symptoms and Complications in Relapsing Polychondritis. Arthritis care & research 2018; 70(8): 1124-31.

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THU0569 MANAGEMENT OF ADULT-ONSET STILL'S DISEASE (AOSD) WITH IL-1 INHIBITORS: EVIDENCE- AND CONSENSUS-BASED STATEMENTS BY A PANEL OF ITALIAN EXPERTS

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Background: Still's disease is a rare autoinflammatory disease, presenting in both pediatric [systemic juvenile idiopathic arthritis (SJIA)] and adult patients [adult-onset Still's disease (AOSD). Due to the rarity of the disease, clinical trials are limited and treatment guidelines are not available. In patients refractory to the classical therapy with NSAIDs, corticosteroids and DMARDs, the introduction of drugs targeting IL-1 has greatly expanded treatment options. Among these, canakinumab, a human monoclonal anti-IL-1β antibody, and anakinra, a human recombinant IL-1RA, have been recently approved for the treatment of refractory patients.

Objectives: To produce recommendations, based on evidence and expert consensus, that can help clinicians in choosing the most appropriate treatment of AOSD, with particular attention to anti-IL-1 therapies, in order to achieve disease remission before the development of complications.

Methods: The recommendations development process took place from April to October 2018 and consisted of three steps. The first step was dedicated to a comprehensive literature review and development of statements. Two separate literature searches were performed: a) similarities and differences between SJIA and AOSD; b) efficacy and safety of IL-1 blockade in AOSD. The issue related to the treatment of AOSD with anti-IL1 therapies was specified into 4 questions: 1) efficacy and safety; 2) comparison among IL-1 inhibitors; 3) early versus late treatment; 4) systemic versus chronic articular pattern of the disease. In the second step, the statements were submitted in a Delphi process to a panel of 67 rheumatologists. Consensus threshold was set at 66%: positive, > 66% of voters selected scores 3 to 5; negative, > 66% of voters selected scores 1 or 2. At the third step of the consensus process, the voting results were analyzed, and the statements were finalized.

Results: In the two literature searches, 332 and 358 publications were identified; 30 and 25 publications, respectively, were selected according to the inclusion criteria. Based on the review of the literature and personal clinical experience, 11 statements were developed. 48/67 rheumatologists (72%) participated to the Delphi process. Positive consensus was reached after the first round of voting and was full (> 95%) on the majority of statements. A large consensus was achieved in considering AOSD and SJIA as the same disease. The use of anti-IL-1 therapies in refractory patients was considered quite safe and effective both as first and as subsequent line of biologic treatment, especially in systemic patients. Because of the lack of head-to-head comparisons, a different profile of efficacy among IL-1 inhibitors could not be established. There was a large consensus that failure of the first IL-1 inhibitor does not preclude a therapeutic response with another one. The lack of studies comparing early versus late treatment in AOSD patients did not allow to draw conclusions, however data from SJIA suggest a better response in early treated patients.

Conclusion: The Delphi method was used to develop recommendations that we hope will help clinicians in the management of patients with AOSD refractory to conventional therapies.

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THU0570 EFFICACY AND SAFETY OF ANAKINRA IN THE TREATMENT OF AUTOIMMUNE MYOCARDITIS

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Background: Virus-negative or "autoimmune" myocarditis(VNM) is a severe, inflammatory heart disease with a poor prognosis, and is a leading cause of inflammatory dilated cardiomyopathy(i-DCM). Therapies are limited. Preliminary data indicate that interleukin-1(IL-1) plays a key role in the initiation and maintainance of the inflammatory heart response, sustaining an auto-inflammatory cycle[1,2].

Objectives: to evaluate the efficacy and safety of anakinra(ANK) in improving Left Ventricular Ejection Fraction(LVEF) on transthoracic echocardiography(TTE) in patients with VNM.

Methods: Biopsy-proven VNM patients were enrolled and treated with ANK 100 mg daily subcutaneously. All patients received treatment with the maximum tolerated dose of any beta blockers and ACE-inhibitors, according to current guidelines. At baseline and 8±4 weeks after ANK therapy, all patients underwent a full evaluation with assessment of functional status(New York Heart Association[NYHA]), measurement of high-sensitive troponin T(hs-TnT) and NT-proBNP serum levels, electrocardiography(ECG), 24h-ECG-Holter, TTE and cardiac magnetic resonance(CMR). Any myocarditis-related complication, cardiovascular deaths and adverse events(AEs) was recorded during follow-up. Continuous variables were assessed with the Wilcoxon signed-rank test for non-parametric tests and a p value<0.05 was considered statistically significant.

Results: Eleven patients(F/M=5/6, mean age 46,2±12,2 years) diagnosed with EBM-proven VNM were enrolled. Nine patients received ANK as first line therapy, and in 5 cases ANK was used as monotherapy; ANK was combined with prednisone(mean dose 31,7±16,7 mg daily) in 6 patients, 5 of them were concomitantly treated with azathioprine. On EMB, 6 patients were classified as i-DCM, 3 with acute VNM e 1 with active and chronic VNM[3-4]. Clinical onset was characterized by congestive heart failure in the most cases(72.7%). The majority of patients(72.7%) was in NYHA class III-IV. Mean LV-EF on TTE at baseline was 38,7% ±19,6, with comparable findings on CMR(36,45%±18,0), and 8 patients (72.7%) had a depressed LV-EF(<55%). At baseline, mean levels of hs-TnT and NT-proBNP were 150,0±153,9 ng/L and 6968,8±10788,4 pg/ml, respectively. Hs-TnT and NT-proBNP levels were elevated in 10(90.9%) and 9 patients(81.8%) respectively. At 8 weeks, LV-EF improved in 10 patients(90.9%). The LV-EF increase was>10% in 5 patients(45.5%) and between 5-10% in 5 cases(45.5%); only 1 patient showed a <10% LV-EF decrease. Mean LV-EF at the end of follow-up improved to 49,4% ±10,8(p=0.059). When evaluating the 8 patients with baseline reduced LV-EF, the LV-EF improvement was statistically significant (baseline 29,2%±12,9; after ANK 45.2%±9.2,p=0.025). The LV-EF amelioration was paralleled by clinical improvements in all patients, since the majority of them(90.9%) were in NYHA class I-II at the end of follow-up. Consistently, hs-TnT declined after 8 weeks(64,6±100,7 ng/L,p=0,028), and a similar trend was observed for NT-proBNP, even though not statistical significant(2582,6±5048,1 pg/ml,p=0,06). We did not observe any myocarditis-related death or complications, nor any ANK-related AEs.

Conclusion: Our pilot study supports the efficacy and safety of ANK in the treatment of inflammatory heart failure in VNM and provides the first clinical evidence to support the therapeutic blockade of IL-1 in myocarditis.

REFERENCES:

[1] De LucaG,et al.Ann Intern Med.2018;169:819-820.
[2] De LucaG,et al. Front Immunol.2018;9:1335.
[3] RichardsonP,et al. Circulation.1996;93:841-2.
[4] AretzHT,et al. Am J Cardiovasc Pathol.1987;1:3-14.

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THU0571 THE IMPACT OF AGING ON FAMILIAL MEDITERRANEAN FEVER PATIENTS

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Background: Familial Mediterranean Fever (FMF) is a monogenic autoinflammatory disorder with innate immune activation with an onset before age 20 in approximately 90% of the patients. There is scarce data on the effect of aging on FMF patients over 40 years of age

Objectives: This study aims to collect data on FMF patients who have survived over 40 years of age. Here we report our preliminary data on disease course and treatment status and comorbidities of our patients with FMF.

Methods: Among the FMF patients who have been followed in our FMF outpatient clinic with a pool of approximately 5000 patients, those who have aged 40 and over are being included to the study. As by today 180 patients are considered for evaluation. The files of patients were reviewed and a standard questionnaire was used to interview the patients. Here we report the results of 100 of these patients (56%) who were contacted for this purpose. These patients were questioned on their demographic characteristics, comorbid conditions, colchicine treatment details, and attack information. In order to see the trend of the change in the parameters assessed, the patients were divided into two groups based on their present age (Group 1: 40-50 years, Group 2: $\geq$50 years).

Results: A total of 100 (78 F, 22M) patients were evaluated. There were 61(46F, 15M) patients aged between 40-50 years and 39 (32F, 7M) over 50. The demographic characteristics and clinical features of these patients are given in Table 1. Besides 3, all patients were still on colchicine regularly. Ninety-six percent of the patients declared overall benefit from colchicine therapy; however 38% experienced a side effect related to this treatment. Over 88% of the patients reported decrease in severity and frequency of FMF attacks. The mean daily colchicine dose was lower in the age 50 and over group (1.7±0,77 mg versus 1,35 ±0,38 mg). There were no patients with AA amyloidosis in neither age group. The mean duration from the last attack increased from 15.3 ±19.7 months to 35.6± 52 months in the older patients. One or more additional disease was present in 75% of this patient group. Among the comorbidities hypertension was the most frequent, diagnosed in 25% of the patients, followed by hypothyroidism (16%), diabetes mellitus (10%) and cardiac disease (5%). Sixty-five of the patients were receiving other medications in addition to colchicine.

Table 1. Clinical course and co-morbidities in two age groups over 40 years

n	Group 1* (n=61)	Group 2** (n=39)	p
Sex (F:M); current age (mean±SD) (yr)	(46 :15);45.5 ± 2.29	(32:7); 57.05 ± 6.81	0,43; <0.001
Mean duration since the last episode, (mean±SD, mo)	**15.3 ± 19.7 (1-60)**	**35.67 ± 52.05 (1-276)**	**0,012**
Number of patients on colchicine therapy, n (%)	59 (96.7)	38 (97.4)	NS
Mean colchicine dose, mg/day (current)	**1.7±0.76**	**1.41±0.45**	**0.03**
Number of patients with decrease in attack severity, n (%)	54(88,5)	35 (89,7)	NS
Number of patients with decrease in attack frequency, n (%)	57(93,4)	37 (94,8)	NS

Co-morbidities, n (%)			
Hypertension, n (%)	12(19.6)	13 (33.33)	NS
Hypothyroidism, n (%)	12(19,6)	4(10,2)	NS
Type 2 Diabetes Mellitus, n (%)	5(8.2)	5(12.82)	NS
Rheumatological diseases, n (%)	5(8,2)	3(7,7)	NS
Cardiac disease, n (%)	3(4,9)	2(5,1)	NS
Malignancies, n (%)	2(3,2)	2(5.13)	NS
Additional medications (number of patients, %)	36 (61)	29 (74.3)	NS

Conclusion: According to our preliminary data the majority of the patients continue to take colchicine after age of 40. However the frequency of FMF attacks as well as daily colchicine dose decrease as the patients get older. With well designed trials stopping colchicine treatment may be considered in a subgroup of patients after 50 years of age. Approximately ¾ of the FMF population over 40 years of age has a comorbidity that necessitates additional medications which underlines the need for special attention.

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THU0572 RHEUMATOLOGICAL ASPECTS OF FORMS AND VARIANTS OF PANNICULITIS

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Background: Panniculitis (Pn) is a set of heterogeneous inflammatory diseases characterized by lesions of subcutaneous fat (SCF) and often accompanied with the defeat of the musculoskeletal system and internal organs. Depending on the etiology and histomorphological picture, Pn is divided into two forms: septal (SPn) and lobular panniculitis (LPn) with and without signs of vasculitis, which is reflected in the clinical picture of the disease. Often Pn is one of the symptoms of rheumatic diseases (Rd), it can lead to late diagnosis of the underlying disease.

Objectives: to study the frequency of occurrence of forms and variants of Pn in rheumatological practice on the basis of long-term prospective observation

Methods: We examined 687 patients with Pn (613 women and 74 men, mean age 39.7±11.31 and 41.2±12.57 years, respectively) with the referral diagnosis of "Erythema Nodosum" (EN) or "Panniculitis", who were observed in the rheumatologic clinic in 2007-2017. In addition to general clinical examination, we determined serum concentrations of α-1 antitrypsin, amylase, lipase, ferritin, creatine phosphokinase, conducted a CT scan of the chest organs, immunological, TB tests and pathological study of skin biopsy from the node.

Results: As a result of application of the developed diagnostic algorithm, 430 patients (62.6%) were diagnosed with Spn and 249 patients (36.2%) - with LPn. In 9 cases (1%) (3 patients with SPn and 6 — with LPn), it was not possible to confirm the variant of Pn, despite the comprehensive examination. In 8 patients (1.1%) no Pn data were revealed, the following diagnoses were verified: 2 patients (25%) — discoid lupus and lipodystrophy, 1 (12.5%) — erysipelas, lichen, fixed erythema and keratoacanthoma. SPn in 94% of cases (400 patients) was presented by EN, in 4% (18) — by superficial migrating thrombophlebitis, in single cases (1-0%) — by eosinophilic fasciitis, skin nodular polyarteritis and scleroderma-Pn (2, 6 and 1 patients, respectively). In 28% of cases LPn was associated with systemic connective tissue lesions, in 27% with idiopathic lobular Pn (Weber — Christian panniculitis) (p<0.002), in 32.92% with lipodermatosclerosis and in 14.28% with subcutaneous sarcoid. In a few cases Lpn was caused by lymphoproliferative (2,88%) and cancer (2,49%) diseases, calciphylaxis (2,05%), erythema Bazin (1.64%), cold Pn (0.82%) and alpha 1-antitrypsine failure (0.41%)

Conclusion: the results confirm that patients with SPn were found twice as often as with LPn. Prenosological Pn was mainly associated with sarcoidosis, EN and Rd, which confirms the relevance of further research of Pn.

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THU0573 COMPLICATIONS AND ACTIVITY OF UVEITIS IN A MULTIDISCIPLINARY REFERENCE UNIT IN THE NORTH OF SPAIN

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Background: Uveitis, an intraocular inflammatory disease, is a significant cause of visual impairment. It is not known how many patients with uveitis will retain visual acuity and how many develop visual impairment or even blindness. The activity of uveitis, the use of topic and oral steroids could produce ocular complications.

Objectives: To describe the complications and the activity of the uveitis in a cohort of 500 patients diagnosed in one unit of reference in the North of Spain.

Methods: A prospective study of complications and the activity of the 500 adults with uveitis were evaluated in the multidisciplinary Uveitis Unit of Complejo Hospitalario de Navarra from January of 2010 to March of 2015. Uveitis activity and the type of complication to the year of follow-up were analysed. The variables were collected according to the terminology of the activity of the SUN (inactive, worsening, improvement and remission). To facilitate statistical analysis variables inactive and remission were grouped in a same term. A study of characterization of the evolution and worsening of the activity to the year of follow-up with age, sex, foreign, type of uveitis, etiology, laterality, treatments and complications. The characterization was carried out through the SPAD 8 program and was carried out by contrast Chi square.

Results: We collected a total of 500 patients, 54.4% of patients remained inactive or in remission after 1 year of follow-up, 13.2% presented worsening of their activity and 32.45% had improved. A bivariate analysis was performed between the variable evolution per year and other variables. We díd´nt observe relationship between the evolution per year and age, sex, foreign, type of uveitis, etiology, laterality, topical etreatment, intravitreal treatment, biological treatment or surgical treatment. Relationship was found statistically significant between the evolution with the existence of complications (p = 0, 0) and oral immunosuppressive treatment (p = 0, 008). There was statistically significant relationship between the variable worsening with the existence of complications(p = 0, 0), topical eye treatment (p = 0, 035), oral immunosuppressive treatment (p = 0, 011), and not relationship with age was found (p = 0, 8), sex (p=0,35), foreign (p = 0, 27), type of uveitis (p = 0, 85), laterality (p = 0, 6) etiology (p = 0, 1), periocular treatment (p = 0, 50), intravitreal (0.56) and biologic treatment (p=0,182). 65% of the patients did not show any complication a year of follow-up and the most frequent complications were cataract (10%), synechiae (8%), macular edema (5%), glaucoma (3%), detachment of retina (3%), epiretinal membrane (2%) and other (5%).

Conclusion: 87% of the patients were in remission or improvement to the year of follow-up. The worsening of the uveitis is related with the existence of complications and oral immunosuppressive treatment.

REFERENCES:

[1] - D.A. Jabs, R.B. Nussenblatt, J.T. Rosenbaum, Standarization of uveitis nomenclature (SUN) Working Group Standarization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol. 2005; 140: 509-516

[2] - A. Rothova, M.S. Suttorp-van Schulten, W. Frits Tretters, A. Kijlstra. Causes and frequency of blindness in patients with intraocular inflammatory disease.Br J Ophthalmol.1996; 80: 332-336

[3] - Prieto-del-Cura M, González-Guijarro J. Complications of uveitis: prevalence and risk factors in a series of 398 cases.Arch Soc Esp Oftalmol. 2009;84:523-8.

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THU0574 DOES THE USE OF CHOLCHICINE EFFECT COGNITIVE FUNCTIONS IN FAMILIAL MEDITERRANEAN FEVER? PRELIMINARY STUDY

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Background: In Familial Mediterranean Fever (FMF), although cognitive functions have been shown to be impaired in children and adolescents, it has been shown that colchicine can be preservative on the cognitive functions in patients who are on long term colchicine treatment.
Objectives: This study aimed to evaluate cognitive functions in adult patients with FMF and cognitive effects of colchicine use.
Methods: The study included patients who were diagnosed with FMF according to Tel-Hashomer criteria. The control group included patients with no other inflamatory or systemic disease. Clinical features such as disease duration, comorbid diseases, colchicine treatment duration and dosage, amyloidosis and chronic renal failure (CRF), FMF gene mutation and PRAS scoring for evaluation of disease activity were recorded. Pittsburg Sleep Quality Index (PSQI), Fatigue Severity Scale, FMF Quality of Life Scale and Beck Depression Scale were used to assess patents clinical situations. Cognitive measurements were evaluated under executive-propellent functions. KAS test was used for information processing and fluency skills; fruit-name test was used for the evaluation of focusing, concentration, and attention skills; animal counting test and The Montreal Cognitive Rating Scale (MOCA) which can evaluate different subunits (visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation) were used for the fluency and maintenance of attention. Different attention parameters were evaluated for patients and healthy individuals. These attention parameters were; focusing, eloborate, sustainability, ability to pay attention to two information at the same time.
Descriptive analysis was performed for all parameters. Mann-Whitney U-test and Spearman correlation coefficient were used to compare parameters. P <0.05 was accepted as statistically significant.
Results: The study included 24 (21 women, 3 men) patients with FMF and 10 (7 female, 3 male) age, sex and BMI matched healthy controls. The mean age of the patients and controls were 36.83 (SD:10.9) and 39.3(SD:8.6), respectively. No significant difference was found between FMF and healthy control groups regarding animal counting, KAS test, MOCA test, and subgroups. Only fruit-name counting test was decreased in the FMF group compared to the healthy controls ($p < 0.05$). As the duration of colchicine treatment was prolonged, a moderate positive correlation was found in KAS scores ($r=0.511$) and MOCA naming scores ($r=0.445$). In the FMF group, the number of attacks in the last three months and the sleep scores of Pittsburgh and depression scores had a moderate positively correlation ($r = 0.496$). Depression scores and quality of life scores were highly correlated ($r = 0.631$).
Conclusion: FMF patients attention parameters are impaired compared to the healthy controls. Information processing and fluency performance is increased in FMF patients with the duration of colchicine treatment that demonstrate the ability to categorize and fluent use of the information. Number of attacks are correlated with poor sleep quality and depression.

REFERENCES:

[1] Keskindemirci, G., et al., Does familial Mediterranean fever affect cognitive function in children? Electrophysiological preliminary study. Int J Neurosci, 2018. 128(1): p. 10-14.
[2] Leibovitz, A., et al., Colchicine therapy and the cognitive status of elderly patients with familial Mediterranean fever. Isr Med Assoc J, 2006. 8(7): p. 469-72.

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THU0575 HYPERCOAGULABILITY AS A CAUSE OF THROMBOSIS IN BEHÇET'S SYNDROME: A SYSTEMATIC REVIEW AND META ANALYSIS

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Background: While thrombosis in Behçet's Syndrome (BS) is considered to be mainly caused by inflammation in the vessel wall, several prothrombotic factors have been studied with inconsistent results.
Objectives: We aimed to perform a systematic review of clinical studies investigating the thrombophilic factors in BS.
Methods: The online database of PubMed was searched with the keyword "Behcet*" in four languages (English, German, French and Turkish) from inception up to May 2018. Titles and/or abstracts of all studies were screened independently by two reviewers (GG and BY) for studies reporting on thrombosis, fibrinolysis, endothelial factors and comparing BS patients with and without thrombosis. Conflicts were solved by a third reviewer (GH). The pooled odds ratios (OR) with 95%CI were calculated for binary outcomes and standardized mean differences (MD) were calculated for continuous outcomes by using RevMan 5.3.
Results: Of 9937 articles, 9373 were excluded due to repetition and inappropriate study design after reviewing titles and abstracts. Full text review of the remaining 564 articles yielded 86 papers meeting our predetermined inclusion criteria.
Several factors such as protein C, protein S, active protein C resistance, anti-thrombin III, plasminogen, plasminogen activator inhibitor, fibrinogen, factor 7, factor 12, thrombin activatable fibrinolysis inhibitor, anticardiolipin antibodies, antiß2 Glycoprotein1 antibodies and methylenetetrahydrofolate reductase gene C677T mutation were not different in BS patients with thrombosis compared to those without thrombosis. On the other hand, vascular endothelial growth factor levels, P-selectin glycoprotein ligand-1, platelet-activating factor seemed to be more frequent in BS patients with thrombosis in the few studies reporting on these, including a small number of patients.
Among the 11 parameters with controversial results across studies, meta-analysis showed significantly higher homocysteine levels, higher factor 8 levels, more frequent Factor V Leiden mutations and higher von Willebrand factor levels in BS patients with thrombosis, whereas the pooled difference was not significant for mean platelet volume, tissue plasminogen activator, prothrombin gene mutations, lupus anticoagulant, P-selectin level, erythrocyte aggregation and thrombomodulin level (Table).
Conclusion: Among the several prothrombotic factors that were studied in BS patients, factor V Leiden mutation, high homocysteine levels, factor 8 levels and von Willebrand factor levels may be associated with thrombosis in BS. Studies investigating these factors together in a large number of patients together with appropriate controls are needed to confirm these results.

Table. Meta-analysis of studies with controversial results

Prothrombotic Factor	Number of studies	Number of Behçet's patients		MD/OR (95% CI)
		With thrombosis	Without thrombosis	
vWF (U/dl)	3	37	93	MD: 10.09 (2.70, 17.47)
Factor V Leiden	9	204	446	OR: 2.17 (1.32, 3.57)
Homocysteine	12	285	436	MD: 1.26 (0.86, 1.66)
FVIII level	3	53	128	MD: 14.68 (2.87, 26.49)
tPA	5	103	200	MD: 0.09 (-0.47, 0.66)
Prothrombin mutation	7	189	398	OR: 1.63 (0.85, 3.13)
Mean platelet volume	5	73	327	MD: 0.13 (-0.13, 0.39)

Lupus anticoagulant	3	37	85	OR: 3.66 (0.98, 13.72)
P-selectin	2	33	75	MD: 0.85 (-0.08, 1.77)
Thrombomodulin	5	92	264	MD: -0.22 (-0.86, 0.41)
Erythrocyte aggregation	3	47	112	MD: -0.24 (-0.62, 0.15)

MD: mean difference, OR: odds ratio, tPA: tissue plasminogen activator
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THU0576 PROGNOSTIC FACTORS PREDICTING THE SURVIVAL OF PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME

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Background: Macrophage activation syndrome (MAS) is a hyperinflammatory condition, which can lead to death in patients with rheumatologic disease. However, the prognosis of adult patients with MAS is largely unknown.
Objectives: We aimed to investigate the mortality in patients with MAS accompanied Adult-onset Still's disease (AOSD) or systemic lupus erythematosus (SLE) and to evaluate the prognostic factors predicting the mortality in patients with MAS.
Methods: We retrospectively reviewed febrile patients with AOSD or SLE admitted to Severance Hospital between 2005 and 2018. Patients who satisfied the classification criteria of MAS was included in the analysis. Cox-regression analysis was performed to evaluate the clinical factors associated with the overall mortality in patients with MAS.
Results: Of the total 123 patients, 48 (39%) patients and 75 (61%) patients were diagnosed with AOSD and SLE, respectively. Forty-three patients (35%) were died from MAS during hospitalization. There was no significant difference in mortality between AOSD and SLE (P = 0.675). In multivariate analysis, cytopenia, and insufficient reduction of ferritin and rebound of inflammation after initial treatment with glucocorticoid were independently associated with death in patients with MAS (P = 0.019, < 0.001, and 0.011, respectively).
Conclusion: The presence of cytopenia, and treatment response after glucocorticoid treatment was closely related with death in patients with MAS. More intensive treatment should be considered in high-risk patients with poor prognostic factors.

REFERENCES:

[1] Carter, S.J., R.S. Tattersall, and A.V. Ramanan, *Macrophage activation syndrome in adults: recent advances in pathophysiology, diagnosis and treatment*. Rheumatology (Oxford), 2018.
[2] Grom, A.A., A. Horne, and F. De Benedetti, *Macrophage activation syndrome in the era of biologic therapy*. Nat Rev Rheumatol, 2016. 12(5): p. 259-68.
[3] Ahn, S.S., et al., *Application of the 2016 EULAR/ACR/PRINTO Classification Criteria for Macrophage Activation Syndrome in Patients with Adult-onset Still Disease*. J Rheumatol, 2017. 44(7): p. 996-1003.
[4] Ahn, S.S., et al., *In-hospital mortality in febrile lupus patients based on 2016 EULAR/ACR/PRINTO classification criteria for macrophage activation syndrome*. Semin Arthritis Rheum, 2017. 47(2): p. 216-221.

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THU0577 EFFICACY OF RADIOSYNOVIORTHESIS IN PIGMENTED VILLONODULAR SYNOVITIS OF THE KNEE

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Background: Pigmented villonodular synovitis (PVNS) is a rare disorder with the benign tumoral proliferation of the synovium. The surgical treatment of PVNS alone in most cases is unsatisfactory, because if a few cells have not been removed, the disease will recur.[1] Post-synovectomy adjuvant treatment with intra-articular injection of Yttrium-90 (^{90}Y) or Holmium-166 (^{166}Ho) yielded better results. The radiosynoviorthesis (RSO) is an effective way of treating the chronic synovitis, with this method we are eliminate the inflammation in 75 percent of the cases.[2]
Objectives: To study efficacy of radiosynoviorthesis after the surgical synovectomy in pigmented villonodular synovitis of the knee.
Methods: Between May 1986 and August 2018, 17 patients (seven men and ten women aged 14–68 years) with diffuse PVNS were treated. All patients had monoarticular arthritis of the knee with histologically proved PVNS. The patients underwent 33 operations, two patients had four surgical procedures, one patient underwent three surgeries, eight patients had two surgeries and six patients had one surgical procedure (Table 1.). The radiosynoviorthesis was performed according to the method accepted in the national protocol.Yttrium-citrate injectable suspension marked by 185 MBq 90Y-citrate injectable suspension, and 40 mg of 1 ml triamcinolone acetonide and 1 ml of lidocaine 1%.[3] Holmium-phytate injectable suspension marked by 600 MBq 166Ho-phytate injectable suspension, and 40 mg of 1 ml triamcinolone acetonide and 1 ml of lidocaine 1%.[3]
Evaulation was based on the criteria as described by Müller, Rau and Schütte the score system was developed by the authors.[4] The circumference of joint-swelling, the joint function, the measure of flexio-contracture, pain in state of rest and load on a pain analogue scale 1-10, joint warmth, walking capacity, the numbers of joint-punctions after the treatment, whether operation was necessary or not after the treatment were examined.

Number of patients	age	surgery before RSO				number of RSO		
7 men and 10 women total: 17	14-68 years	1	2	3	4	1	2	3
6 patients	8 patients	1 patient	2 patients	10 patients	6 patients	1 patient		

Table 1. Patients with pigmented villonodular synovitis

Results: Mean follow-up time was 56 months (range from 4 to 144 months). All patients were followed up using clinical assesment. After the first injection excellent and good results were recorded in 41%. After the second radiosynoviorthesis thirteen patients (76%) showed excellent and good response (Table 2.). The mean functional evaluation score of 17 patients was 28 (range 16-34). Most of the ratings were excellent or good, in four cases moderate (24%). No complications were noticed after surgery or after the radiosynoviorthesis.

functional evaluation score	response	patients	%
29-35	excellent	10	59%
22-28	good	3	18%
15-21	moderate	4	23%
8-14	mild	0	
0-7	worsening	0	

Table 2. Functional evaluation score after the RSO

Conclusion: A combination of debulking surgery with radiosynoviorthesis of Yttrium or Holmium for diffuse PVNS of the knee joint is a reliable treatment method, with good results.

REFERENCES:

[1] Jaffe HL, Lichtenstein L, Sutro CJ (1941) Pigmented villonodular synovitis: bursitis and tenosynovitis. Arch Pathol. 31:731–765.
[2] Jahangier ZN, Moolenburgh JD, Jacobs JWG, et al. The effect of radiation synovectomy in patients with persistent arthritis: A prospective study. Clin. and Exp. Rheumatol. 2001; 19:417-424.
[3] EANM Procedure Guidelines for Radiosynovectomy, Eur J Nucl Med (2003) 30:BP12–BP16, Vol. 30, No. 3, March 2003.

[4] Rau R, Schütte H. Results of radiosynoviorthesis with yttrium 90 in chronic synovitis: a long-term prospective study. I. Total results and effect of local factors. Z Rheumatol. 1983; 42: 265-70.

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THU0578 COMMON VARIABLE INMUNODEFICIENCY IN PATIENTS WITH SARCOIDOSIS

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Background: Common variable immunodeficiency (CVID) is a primary immunodeficiency characterized by hypogammaglobulinemia and a deficient production of specific antibodies. Almost 30% of patients with CVID develop an autoinmmune and granulomatous disease, similar to clinical and histological sarcoidosis (S), it affects the lung fundamentally. This can lead to a misdiagnosis of S in a patient with CVID, this leads to inadequate treatment and increases the morbidity and mortality of the disease.
Objectives: Describe the clinical and radiological characteristics of a cohort of patients diagnosed with S with predominant pulmonary involvent. Make a study of immunoglobulin (IG) levels to see the frequency of CVID in these patients.
Methods: Retrospective descriptive study of patients treated in our Hospital (2008-2018), with diagnosis of S. The data was obtained by reviewing medical records. The delay in the diagnosis of S was defined as the difference in months between the initial diagnostic suspicion and the final diagnosis of S.
In patients with low levels IG, we have done and expanded ID study.
Results: 55 patients (31 women) were included, with a mean age of 52 ±12 years. The initial diagnosis was: 85% S, 10% lymphoma and 4% tuberculosis. The median of months from the start of the clinic to the diagnosis of S was 5.5 months.
Regarding the clinic, 21% patients present fever at the beginning of the disease, and 65% extrathoracic localization (cutaneous was the most frequent in 27%, and renal was the least frequent 5%). Simple x-ray and high resolution tomography of chest were done in all patients. Pulmonary stage 2 was the most frequent (51%), followed by stage 3 (16%), stage 0 (14%) and stage 4 (9%).
In 90% of the patients, histological confirmation was obtained by transbronchial (47%), cutaneous (11%) or lymph node biopsy (29%).
Igs were normal in 87% of patients, only 4 patients had low IG levels (Ig G in 3 patients and Ig M in 1). An extended ID study was performed in these 4 patients, being diagnosed with CVID 3 patients.
Results of the 4 patients and the differential characteristics between CVID and S in table 1.

Differential diagnosis	CVID	Sarcoidosis	Patient 1	Patient 2	Patient 3	Patient 4
Recurrent infections	+++	+/-	Yes	Yes	Yes	Yes
Autoimmunity	+++	+	Yes	Yes	No	No
Splenomegaly	+++	+/-	Yes	Yes	Yes	Yes
Hepatomegaly	+++	+/-	Yes	Yes	Yes	Yes
Low levels IG	+++	+/-	Yes	Yes	Yes	Low levels IgM
Clinic Radiological stage			Pulmonary Stage 2	Pulmonary Stage 2	Pulmonary Stage 2	Pulmonary Stage 2
Histological granuloma	+++	+++	Yes	Yes	Yes	Yes
Increase of CD4/CD8 in BAL	+	+++	Low levels	Low levels	Low levels	Not done
Treatment			Corticoids	Corticoids	Corticoids	Corticoids

Conclusion: Although their clinical presentation and histological appearance may be identical, the management of these two conditions is very different. The difficulties in the differential diagnosis between S and CVID, shows the importance of a history of screening for recurrent infections and the measurement of IG levels before the diagnosis of possible S.
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THU0579 CHEMOKINE AND CYTOKINE TEARS PROFILE OF PATIENTS WITH IGG4-RELATED DISEASE

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Background: The lacrimal gland is frequently involved in both IgG4-related disease (IgG4-RD) and Sjögren's syndrome (SS) and presents with swelling and/or dry eye symptoms. Although a distinct chemokine and cytokine tear profile might distinguish SS from idiopathic dry eye, as of today no study has assessed this issue in IgG4-RD.
Objectives: To evaluate and compare a set of chemokine/cytokine in the tears of patients with IgG4-RD and primary SS.
Methods: We included 11 patients with IgG4-RD according to the Comprehensive Diagnostic Criteria for IgG4-RD and 17 with primary SS according the AECG criteria, who attended a tertiary referral center in Mexico City. Schirmer-I test were performed using two standardized sterile tear strips, and then immediately frozen at -86°C until assayed. Once defrosted, the tears were extracted from the strips using a buffer containing 0.5 M NaCl and 0.5% Tween-20. Then, the amount (pg/mL) of the following selected chemokines and cytokines were measured by Luminometry: CCL11, G-CSF, IFN-γ, IL-12p40, IL-12p70, IL-13, IL-17A, IL-1α, IL-1β, IL-4, IL-7, CXCL10, CCL2, CCL3, CCL4 and TNF-α.
Results: Patients with IgG4-RD were younger (51.3±14.7 vs. 55.7±10.6) and more frequently men (45.5% vs. 5.9%) than SS patients. Regarding the IgG4-RD group, 7 (63.6%) had lacrimal gland involvement, 5 (45.5%) dry eye symptoms and 6 (54.5%) positive Schirmer-I test. We observed multi-organic involvement in 9 patients (81.8%), median number of involved organs of 5, 9 (81.8%) patients had active disease, median IgG4-RD responder index of 6 points, 8 (72.7%) patients had high IgG4 serum levels, and 9 (81.8%) biopsy proven diagnosis. We found higher levels of IL-7 and CCL2, and a trend for G-CSF in the IgG4-RD group. Conversely, primary SS patients had higher levels of IL-12p40, IL-1α, IL-1β, CCL3 and CCL4. At the logistic regression analysis, the variables that remained associated with IgG4-RD were IL-7 (OR 1.43 95% CI 1.06-1.93, p=0.01) and IL12p40 (OR 0.92, 95% CI 0.84-0.99, p=0.01).
In a sensitivity analysis, including only 7 IgG4-RD patients with dacryoadenitis, we also observed higher levels of IL-7 and G-CSF in the IgG4-RD group vs primary SS.
Conclusion: The chemokine and cytokine profile of tears of patients with IgG4-RD is characterized by a mixed immune response (Th1/Th2/Th17) compare with a predominantly Th1 response in primary SS. Our results also suggest a possible role of IL-7 in the pathogenesis of IgG4-RD.

REFERENCES:

[1] Hernández-Ruiz M, Zlotnik A, Llorente L, Hernandez-Molina G. Markedly high salivary and lacrimal CXCL17 levels in primary Sjögren's syndrome. Joint Bone Spine. 2018 May;85(3):379-380.

Table 1:

Chemokine/cytokine pg/mL, median (range)	IgG4-RD n=11	pSS n=17	*p*
CCL11	11.9 (3.7-34.4)	15.4 (3.7-33.0)	0.06
G-CSF	118.7 (14.5-325.9)	88.5 (14.5-226.5)	0.08
IFN-γ	1.3 (0.3-2.1)	1.7 (0.01-7.2)	0.19
IL-12p40	8.7 (1.3-35.5)	24.1 (1.3-69.3)	0.02
IL-12p70	0.5 (0.09-3.1)	1.6 (0.09-28.1)	0.05
IL-13	19.2 (4.6-84.9)	18.1 (2.4-75.0)	0.30
IL-17A	0.9 (0.2-1.7)	0.9 (0.08-4.9)	0.89
IL-1α	25.8 (10.5-166.8)	54.3 (21.6-119.1)	0.003
IL-1β	0.1 (0.1-1.5)	1.5 (0.1-7.2)	0.001
IL-4	11.0 (1.8-17.6)	8.2 (1.8-19.8)	0.45
IL-7	13.8 (6.6-65.1)	6.4 (1.27-15.0)	0.001
CXCL10	5399.5 (296.9-11394)	5368.1 (1205-11553.6)	0.51
CCL2	11.4 (1.1-104.4)	1.1 (1.1-166.3)	0.03
CCL3	2.4 (0.3-4.0)	3.4 (1.1-40.7)	0.01
CCL4	1.2 (1.2-27.6)	11.1 (1.2-164.3)	0.02
TNF-α	0.8 (0.1-5.4)	2.03(0.1-7.6)	0.06

Disclosure of Interests: None declared
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THU0580 JOINT MANIFESTATIONS SECONDARY TO IMMUNOTHERAPY: CLINICAL CHARACTERISTICS AND EVOLUTION

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Background: Inhibitors of CTLA-4 and PD-1 have shown improvements in survival in multiple advanced cancers. Immune-mediated effects such as arthralgias and arthritis have been described, but their prevalence and characteristics have not been well defined.
Objectives: The objective of the study is to describe the prevalence of immunomediated joint manifestations (IJM), its characteristics and evolution in patients who received immunotherapy (nivolumab (NV), pembrolizumab (PB)) from January 1, 2016 to December 31, 2018 in our center.
Methods: Data collection was performed at through the RPT (Registre Pacients Tractats) database of the CatSalut, and the patients referred to the monographic medical office of inflammatory joint diseases of our center. In all cases, the variables: age, sex, neoplasia, drug, number of doses, were recorded. In patients with joint involvement: other autoimmune manifestations, joint affectation prior to treatment, delay rheumatology derivation, joint affectation type, swollen and tender joint counts, ESR, CRP, RF, ACPA, ANA, HLA B 27, Hb, leukocytes, neutrophils, lymphocytes, treatment and evolution, were recorded. The statistical analysis was carried out with the SPSS 15.0 computer package
Results: 106 patients received treatment (TTO) with immunotherapy (71 NV, 35 BP) for neoplasia (81 lung, 10 renal, 8 melanoma, 2 oropharynx). The mean age was 67.93 ± 10.7 years (21.7% women, 78.3% men). There were 11 events cataloged as IJM. The overall prevalence was 10.3% (5.6% NV, 14.3% PB). Patients with IJM received a greater number of doses (17.67 ± 9.3 vs9.24 ± 10.1 p = 0.018). No patient with melanoma presented IJM. All IJM suspicions cases were assessed by a rheumatology. When studying their characteristics (Table 1), 3 patients were added from the database of the rheumatology service (14 cases). They received in a clinical trial BP29541 (rectal cancer), Atezolizumab (lung cancer) and Durvalumab (lung cancer). 42.9% of the patients presented inflammatory arthralgias (IAT) and 57.1% arthritis (AT). In reference to their previous history, 2 patients had a history of hyperuricemia and arthritis. One patient concomitantly presented lymphocytic colitis confirmed by biopsy. The delay time for assessment by rheumatology was 18.1 ± 22.1 days. Patients with AT were older (p = 0.014), had higher ESR (p = 0.047) than those with IAT. No differences were found in other variables (table1). With reference to the analytical study, 1 patient was RF +, 2 ANA + at mean titers (1/160-1/320), none ACPA or HLA B 27 +. After assessment by rheumatology, two patients with IAT were diagnosed with bone M1 and two AT were categorized as gouty arthritis. The rest of the IAT responded to NSAIDs, did not require corticosteroids and were resolved. 6 cases of AT received prednisone, 3 required treatment dose 1 mg/kg weight and subsequently MTX in 2 of them, with evolution to low disease activity at present. Only one patient met RA classification criteria.
Conclusion: The prevalence of IJM was higher than 10%, depending on the number of doses. Patients with arthritis had higher age and higher ESR. No patient presented ACPA and HLA B 27 +, so to include them in the initial analytical could be not necessary. In these patients, it is important the assessment by a rheumatologist to make a correct differential diagnosis, as well as establish referral circuits to avoid delay of care

	ARTRHITIS (AT)	ARTHRALGIA (IAT)	P value
Age	71 ± 6,0	59,3 ± 9,7	**0,014**
Swollen joints	3,63 ±3,4	0	**0,026**
Painful joints	10,75 ± 15,7	10,0 ± 8,7	0,919
ESR	39,5 ± 25,3	9,0 ± 4,3	**0,047**
CRP (mg/dl)	15,6 ±11,6	5,0 ± 8,8	0,156
Leukocytes (cel x 10^3)	11.026,2 ± 3264,2	8.156± 3.357,6	0,134
Lymphocytes (cel x10^3)	1.696,2 ± 1042,8	1.836,6± 1.188,4	0,818
Neutrofilos (cel x10^3)	8263, 7± 2.668	5.523,6 ± 3.531	0,123
Hb(mg/dl)	10,8 ± 2,1	12,1 ± 2,64	0,325

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THU0581 BIOLOGICAL THERAPY IN NON ISCHAEMIC OPTIC NEURITIS ASSOCIATED TO IMMUNE-MEDIATED INFLAMMATORY DISEASES. MULTICENTER STUDY

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Background: Non ischaemic optic neuritis (NION) is a severe inflammation of the optic nerve that may lead to blindness. It can be primary or associated to immune mediated inflammatory diseases (IMIDs). The treatment of the NION is based on systemic corticosteroids and conventional immunosuppressive drugs.
Objectives: To assess the efficacy of the biological treatment in refractory NION to conventional treatment.
Methods: Multicenter study of 12 patients diagnosed with NION refractory to systemic corticosteroids and at least one conventional immunosuppressive drug. The main outcomes were visual acuity (VA) and optical coherence tomography (OCT) of the optic nerve and the ganglionar cells. Comparisons were made between baseline and the 1st week, 1st and 6th month and 1st year. (STATISTICA, StatSoft Inc. Tulsa, Oklahoma, USA).
Results: We studied 12 patients (19 affected eyes) (5 men/7 women); mean age of 29.8 ±12.9 years. The underlying diseases were systemic lupus erythematosus (n=1), neuromyelitis optica (n=1), neuroretinitis (n=1), relapsing polychondritis (n=1), pars planitis (n=1), Behçet´s disease (n=2) and idiopathic (n=5). Before biological treatment and besides oral corticosteroids, patients had received intravenous (IV) methylprednisolone boluses (n=9), cyclosporine A (n=1), cyclophosphamide (n=2), mycophenolate (n=2), hydroxychloroquine (n=1), methotrexate (n=8) and azathioprine (n=5). Biological treatment was bases on rituximab (n=2) (2 IV, doses of 1 g/every 2 weeks and every 6 moths), adalimumab (n=5) (40 mg/1-2 week), tocilizumab (n=4) (8 mg/kg/2-4 weeks) and infliximab (n=3) (5 mg/kg at 0, 2 and 6 week and then every 8 weeks). The characteristics of the 12 patients are shown in the TABLE.
After biological treatment we observed an improvement in the ocular parameters: VA [0.66±0.32 to 0.84±0.29; p= 0.03], OCT of the optic nerve [123.20±58.28 to 190.54±175.38; p= 0.11], and OCT of the ganglionar cells [369.55±137.37 to 270.67±23.21; p= 0.03] at one year. After a mean follow-up of 29.09 ±19.23 months, there were no severe adverse effects.
Conclusion: Biologic therapy in NION idiopathic or associated to IMIDs, refractory to conventional treatment, seems to be effective.

Case	Sex/Age (years)	Underlying disease	Laterality	Immunosuppressive drugs before biological therapy	Biological therapy
1	Man/29	Idiopathic	Right	AZA	TCZ
2	Man/26	Idiopathic	Bilateral	AZA	TCZ
3	Man/21	Idiopathic	Bilateral	MTX, AZA	ADA
4	Woman/25	Behçet´s disease	Right	MTX, CyA	ADA
5	Woman/39	Behçet´s disease	Right	MTX, MMF	IFX
6	Woman/14	Neuroretinitis	Bilateral	MTX	ADA
7	Man/56	SLE	-	Hydroxychloroquine, MMF, CFM	RTX
8	Woman/43	Neuromyelitis optica	Bilateral	AZA	RTX
9	Man/43	Relapsing polychondritis	Bilateral	MTX, CFM	IFX, TCZ
10	Woman/24	Pars planitis	Bilateral	MTX, AZA	ADA
11	Woman/13	Idiopathic	Bilateral	MTX	ADA
12	Woman/25	Idiopathic	Bilateral	MTX	IFX, TCZ

ADA: adalimumab, AZA: azathioprine, CFM: cyclophosphamide, CyA: cyclosporine A, HCQ: hydroxychloroquine, IFX: infliximab, MMF: mycophenolate, MTX: methotrexate, RTX: rituximab, SLE: systemic lupus erythematosus, TCZ: tocilizumab

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THU0582 THE TNF RECEPTOR-ASSOCIATED PERIODIC SYNDROME (TRAPS): CLINICAL AND GENETIC CHARACTERIZATION OF A COHORT OF ADULTS DIAGNOSED OF TRAPS SYNDROME

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Background: Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is a disease that is included within of hereditary syndromes of periodic fever. It presents an autosomal dominant pattern of inheritance. It´s due to mutations of TNFRSF1A gene. It is usually present in childhood although it can also appear in adulthood and it tends to cause high levels of acute phase reactants, fever, musculoskeletal symptoms (myalgias, arthralgias, arthritis), rash, abdominal pain, etc

Objectives: To describe the clinical characteristics and genetic variants of patients diagnosed with TRAPS syndrome in a cohort of patients with autoinflammatory syndromes with follow-up in a tertiary hospital from 2013 to the present

Methods: Retrospective descriptive study of adult patients diagnosed with autoinflammatory syndrome since 2013 (year of introduction of genetic tests in the hospital laboratory) until now. The data was obtained from the review of medical records. All patients with mutations in TNRFSF1A gene and clinically compatible with this diagnosis were reviewed

Results: Of a total of 44 adult patients diagnosed with hereditary syndromes of periodic fever (FMF, TRAPS, cryopyrinopathies, HIDS) and compatible genetic mutations (excluding polymorphisms), 13 (29.5%) presented mutations in the TNFRSF1A gene. Of those 13 patients, 9 (69.2%) were women. The most frequent mutations were the mutation in heterozygosis in exon 4 (p.R92Q) with 12 cases (92.3%) and one case (7.6%) with mutation in heterozygosis in exon 3 (p.P46L). The mean age at diagnosis was 27.92 years (IR 12-55 years). 5 patients showed simultaneous genetic variants in other genes related to autoinflammatory syndromes. Signs and/or symptoms were myalgia and elevation of acute-phase reactants with 12 patients (86%) followed by fever and joint symptoms (arthralgias and/or arthritis) with 11 patients (79%) were the most frequent. 2 patients (14%) had conjunctivitis. 9 patients (64%) presented cutaneous involvement. 2 cases (14%) presented lymphadenopathy. Regarding treatment, 5 patients (36%) had received treatment with biological therapy (anti-IL-1 or anti-TNF) and another 5 patients (36%) had used colchicine. The corticoids were used in 6 patients (43%)

Conclusion: The TRAPS syndrome is a clinical entity to consider when making a differential diagnosis in patients with suspected autoinflammatory syndrome, that present fever, acute phase reactants elevation, arthromyalgia and its confirmation diagnosis is with genetic test

Disclosure of Interests: None declared

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THU0583 EXPERIENCE OF ANAKINRA AND CANAKINUMAB IN PATIENTS WITH COLCHICINE-RESISTANT FAMILIAL MEDITERRANEAN FEVER AND COMPLICATED WITH AMYLOIDOSIS

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Background: Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disease characterized by recurrent fever and serosal inflammation (1). The goal of FMF treatment is to prevent the attacks and to minimize subclinical inflammation between attacks, and in attacks-free period. Colchicine is a major drug that sine qua non in the treatment of FMF. However, anti-interleukin-1 agents are recommended in colchicine resistant and/or intolerant FMF patients (2).

Objectives: The aim of this study is to evaluate the efficacy of anti-interleukin-1 (anti-IL-1) agents in 54 FMF patients with resistant/intolareted to colchicine or complicated with amyloidosis.

Methods: Between January 2014 and December 2018, fifty four patients who were diagnosed as FMF according to the criteria of Tel-Hashomer that following-up at Sivas Cumhuriyet University Medical Faculty, Rheumatology-Internal Medicine Department were included in to the study.

Results: 25 (46.3%) male and 29 (53.7%) female were included in the study. The median age of the patients was 29 (min:17-max: 60) years and the median age at diagnosis was 18 (min: 3-max: 46) years. Anakinra was used in 34 (63%) FMF patients (100 mg/day), and canakinumab was used in 20 (37%) patients (150mg/8weeks). 37 cases were resistant to colchicine, 8 were intolerant to colchicine, 9 (20%) cases were comlicated with amyloidosis. 8 patients had renal transplantation. MEFV gene mutations are shown in Table 1. Median duration of anti-IL-1 agent use was 12 months (min:2-max40). 5 patients were resistant to anakinra, 4 patients had side effects which anakinra related. After a median follow up 12 months overall clinical response was%95 (frequency of attacks <1/6months). Median proteinuria decreased from 3850 mg/day to median 1600 mg/day (p= 0.04) (Table 2). IL-6 treatment was started in 3 patients because of ineffectiveness of canakinumab. One pregnant patient was followed up with anakinra during pregnancy and there were no problems.

Conclusion: Anti-interleukin-1 agents can be used effectively and safely in the treatment of FMF patients. These agents are especially effective in the treatment of proteinuria due to amyloidosis. Large and long-lasting follow-up studies are needed to evaluate long-term effects of these drugs.

REFERENCES:

[1] Ozdogan H, Ugurlu S. Familial Mediterranean Fever. Presse Med. 2019 Jan 24. pii: S0755-4982(18)30486-X. doi: 10.1016/j.lpm.2018.08.014. [Epub ahead of print].

[2] Seza Özen ve ark. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis. 2016 Apr;75(4):644-51.

Table 1. MEFV mutations in FMF patients

MEFV Mutations	n
M694V homozygus	20 (37%)
M694V heterozygous	8 (15%)
Compound mutation	14 (26%)
Other mutation	8 (15%)
No mutation	4 (8%)

Table 2. Laboratory Findings of the FMF patients treated with anti-IL-1 agents

	Pre-treatment (median)	Post-Treatment (median)	p
Number of attacks	>2/6month	<1/6month	p<0.05
ESR mm/h	33	8	p<0.05
CRP mg/dl	43	4.3	p<0.05
Proteinuria mg/day	3856	1600	p<0.05

Disclosure of Interests: None declared

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THU0584 RHEUMATOLOGICAL IMMUNE-RELATED ADVERSE EVENTS ASSOCIADTED WITH IMMUNOTHERAPY IN SOLID ORGAN TUMOR. STUDY OF 102 CASES FROM A REFERRAL SINGLE CENTER FOR LAST 4 YEARS

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Background: Immune checkpoint blockade therapy (ICBT) currently is one of the most used therapies against cancer. The activation of the immune system can lead to different immune-related adverse events (irAEs), being the rheumatological side effects among the most common.

Objectives: Our aim was to assess the rheumatological irAEs in patients who received immunotherapy.

Methods: We set up an observational study of patients treated with Nivolumab and Pembrolizumab (anti-PD1), Atezolizumab (anti-PD-L1) and Ipilimumab (antiCTLA-4) for solid organ tumors. All these patients were followed in a single reference University Hospital from March-2015 up to December-2018. The main outcome was to determinate the incidence of rheumatological irAEs.

Results: We studied 102 patients (63♂/39♀) with a mean age of 60.6 ±9.7 with different solid organ tumors. Only 7 patients (6.8%) had a previous diagnosis of an immune-mediated disease: psoriasis (n=2), psoriatic arthritis (1), systemic lupus erythematosus (1), spondyloarthitis (1), rheumatoid arthritis (1) and skin lupus (1).

Rheumatological side effects were observed in 15 patients (14.7%): inflammatory arthralgia (8), arthritis (6), myositis (2) and aortitis (1). The time of appearance of the rheumatological irAEs was of 6.36 months (±5.81). From the 7 patients with previous diagnosis of an immune-mediated disease, only 1 patient with psoriasis suffered a worsening of skin symptoms and another one with psoriatic arthritis had a monoarthritis episode.

Among the 14 patients who suffered from arthralgia/arthritis, the most frequent pattern was oligoarticular (40%), followed by poly (30%) and monoarticular (30%). The most affected joint was the knee (n=4), followed by wrist (3), hands (3), ankle (2), shoulder (2) and foot (1).

Apart from the articular disease, 2 patients suffered from myositis in lower limbs, with weakness of legs and arthralgia in their knees. A patient was diagnosed of aortitis through a PET, although the patient did not have any symptom.

Immunology tests with RF, ACCP and ANA were done in 8 out of the 15 patients with musculoskeletal irAEs, being negative in all cases.

Interviewing 40 of the patients who received ICBT, 7 of them (17.5%) referred xerophthalmia. 6 of them (15%) had a positive Schrimer test, and 3 (7.5%) had a reduced tear break-up time. None patient met Sjögren criteria.

In 6 out of the 15 patients with rheumatological irAEs (all of them with arthralgia/arthritis) the ICBT was removed, temporary in all cases, and could be reintroduced after a mean of 33 ± 18.9 days. 6 patients were treated with NSAIDs and 5 with oral prednisone (2 of them also required intra-articular corticoids).

Conclusion: Rheumatological irAEs are common in clinical practice. Arthralgia-Arthritis and dry-syndrome are the most frequent adverse events.

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THU0585 LYMPHADENOPATHY IN IGG4-RELATED DISEASE IS ASSOCIATED WITH DISEASE ACTIVITY AND EOSINOPHILIA

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Background: IgG4-related disease (IgG4-RD) is an immune-mediated systemic disease characterized by the enlargement of multiple organs. IgG4-RD frequently involves the pancreas, lacrimal glands, salivary glands, bile duct, kidneys, lungs, and retroperitoneum, but can potentially affect any organs. Lymphadenopathy is often seen in patients with IgG4-RD along with other organ involvements, but the significance of the exist of lymphadenopathy in IgG4-RD is unclear.

Objectives: The aim of this study is to clarify the characteristics of patients with IgG4-RD who have lymphadenopathy.

Methods: We conducted cluster analysis with clinical data in consecutive 85 patients with untreated active IgG4-RD in our institute. We divided the patients into two groups who had lymphadenopathy or not (lymph group and non-lymph group), and compared clinical characteristics between the two groups. We counted the areas of swollen lymph nodes and performed correlation analysis with clinical characteristics. We also comprehensively screened serum protein concentrations in IgG4-RD patients (n=15) and healthy controls (n=5) by using high-throughput proteomic analysis, and differentially expressed proteins were extracted. We compared the concentrations of serum proteins which were extracted between lymph group and non-lymph group.

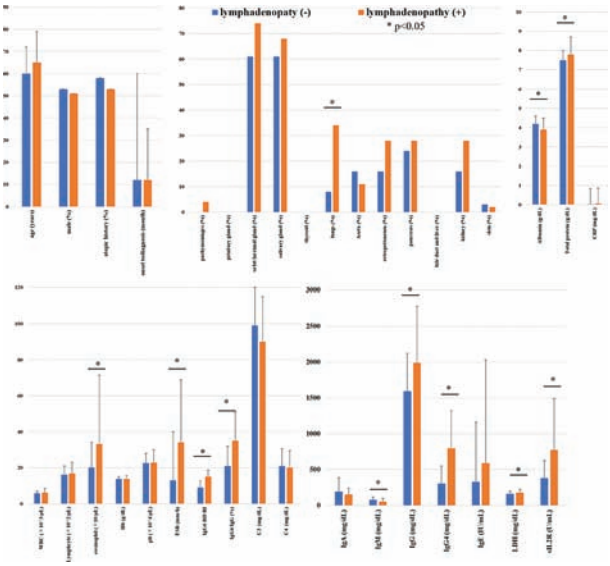
Results: Among 85 patients with IgG4-RD, 44 (52%) were male. Median age was 63 years old. Forty-seven (55%) patients were lymph group. Cluster analysis revealed that lymphadenopathy was in a cluster with serum IgG4, IgG4/IgG, IgG4-RD responder index (IgG4-RD RI), soluble interleukin-2 receptor (sIL-2R), eosinophilia, erythrocyte sedimentation rate (ESR), lung involvement, hemoglobin, albumin, C3 and C4. In lymph group, serum IgG4, IgG4/IgG, IgG4-RD RI, eosinophilia, sIL-2R and ESR were significantly higher than non-lymph group (Figure). Spearman's correlation analysis revealed that areas of the swollen lymph nodes were positively correlated with serum IgG4, IgG4/IgG, sIL-2R, eosinophilia. Proteomics analysis revealed that 68 proteins were significantly higher in IgG4-RD ($p<0.05$). Among them, proteins related to adhesion of immune cells, fibrosis, formation of lymph node and eosinophil activation such as integrin$\alpha1\beta1$, CCL18, CCL19 and eotaxin3 were higher in lymph group ($p=0.03$, $p=0.03$, $p=0.06$ and $p=0.06$, respectively)

Conclusion: Lymphadenopathy in IgG4-RD is associated with disease activity and eosinophilia. Proteomics analysis can provide some clues for elucidating the significance of lymphadenopathy in IgG4-RD.

REFERENCES:

[1] Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med 2012;366:539–51.

[2] Bookhout CE, Rollins-Raval MA. Immunoglobulin G4-Related Lymphadenopathy. Surg Pathol Clin. 2016;9:117-29.



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Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Asahi Kasei Medical K.K., AbbVie GK, Daiichi Sankyo Co., Ltd., Bristol Myers Squibb, and Nipponkayaku Co. Ltd., Speakers bureau: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Speakers bureau: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Astellas Pharma Inc, Diaichi Sankyo Co. Ltd., Eisai Co. Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co. Ltd., Novartis Pharma K.K.

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THU0586 CLINICAL CHARACTERISTICS AND RISK FACTORS OF POLYMYOSITIS AND DERMATOMYOSITIS COMBINED WITH INTERSTITIAL LUNG DISEASE IN PATIENTS RESIDING IN THE NORTHEAST SICHUAN PROVINCE IN CHINA

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Background: Idiopathic inflammatory myositis (IIM) is a systemic autoimmune disease characterized by nonsuppurative inflammation of striated muscle, myalgia, and proximal and symmetric muscle weakness. IIM can affect numerous organ systems, such as the skin, lungs, heart, and gastrointestinal tract. Polymyositis (PM) and dermatomyositis (DM) are the most common forms of IIM. Interstitial lung disease (ILD) is a common and severe complication of PM/DM, and concurrent ILD in patients with PM/DM is a major cause of death, with a fatality rate that exceeds 50% [1]. To explore the clinical features and risk factors of PM/DM combined with ILD (PM/DM-ILD)can improve the early diagnosis rate, put early interventions and improve the therapeutic effect.

Objectives: We explored the clinical features and risk factors of PM and DM, combined with ILD to increase early diagnosis and improve treatment outcomes.

Methods: Data were collected from 130 patients with PM/DM, treated at a single center from January 1, 2014 to September 30, 2018. General medical status, clinical symptoms, laboratory indicators, high-resolution computed tomography, therapeutic outcomes, and prognoses were retrospectively reviewed in patients with PM/DM with (ILD group) and without (NILD) ILD.

Results: There was statistically significant difference in age between the ILD group (n=65) and the NILD group (n=65) ($p<0.05$), but no significant between-group differences in PM/DM ratio, sex, or disease duration ($p>0.05$ for all). In the ILD group, initial symptoms were arthritis and respiratory symptoms, and myasthenia for the NILD group. Incidences of Raynaud's phenomenon, dry cough, expectoration, dyspnea on exertion, arthritis, fever, globulin (GLOB), erythrocyte sedimentation rate (ESR), and anti-Jo-1 antibody rate were higher for ILD ($p>0.05$ for all); however, albumin (ALB), creatine kinase aspartate aminotransferase activity ratio (CK/AST) and CK were significantly lower in the ILD group ($p>0.05$ for all). Bivariate logistic regression analysis showed that age, dry cough, arthritis, dyspnea on exertion, anti-Jo-1 antibody, and elevated GLOB were independent risk factors for ILD among patients with PM/DM.

Table 1. Bivariate logistic regression analysis on risk factors associated with ILD in patients with PM/DM

Variables	*B*	SE	*p* value	OR	95% CI for OR	
					Lower limit	Upper limit
Age	.053	.018	.003	1.054	1.018	1.092
Dry cough	.997	.449	.026	2.71	1.125	6.592
Arthritis	1.089	.481	.024	2.971	1.157	7.63
Dyspnea on exertion	1.192	.483	.014	3.295	1.279	8.493
Anti-Jo-1 (+)	1.517	.706	.032	4.558	1.141	18.201
GLOB	.093	.029	.001	1.097	1.036	1.162

Conclusion: The morbidity associated with PM/DM-ILD is high. Older age, dry cough, arthritis, dyspnea on exertion, anti-Jo-1 antibody positivity, and increased GLOB increase the risk of developing ILD. This information could be used to carefully monitor changing lung function in these patients.

REFERENCES:

[1] Lega JC, Reynaud Q, Belot A, et al. (2015) Idiopathic inflammatory myopathies and the lung. Eur Respir Rev 24(136):216-238.

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THU0587 COMPARING OF TWO DISTINCT SEVERITY SCORES FOR EVALUATING DISEASE SEVERITY IN FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is a chronic hereditary disease which is characterized by recurrent attacks of fever accompanied by serositis. Severity of disease is related with morbidities such as amyloidosis and chronic renal failure.

Objectives: The aim of this study was to evaluate disease severity with two disease severity scores in FMF patients, and compare them.

Methods: The study included 160 patients with FMF. Demographic and clinical data were recorded in the patients' form. The patients' disease severity were evaluated with International Severity Scoring System for FMF (ISSF) and The Second Set of FMF severity score (F-SS-2).

Results: A total of 160 patients, comprising of 106 males (66.3%) and 54 (33.8%) females with a mean age of 33.5 ± 12.2 years were evaluated. Mean disease duration was 16.6 ± 10.3 years. Other demographic and clinical characteristics of the patients were shown in Table 1. According to ISSF, 67 (41.9%) patients were classified as having mild disease, 80 (50.0%) patients as intermediate disease and 13 (8.1%) patients as severe disease. On the other hand, 59 (36.9%) patients were classified as having mild disease, 41 (25.6%) patients as intermediate disease and 60 (37.5%) patients as severe disease according to F-SS-2 score. Higher rates of patients were found having severe disease according to F-SS-2 compared with ISSF ($p<0.001$). Also, lower rates of patients were scored as having intermediate disease with F-SS-2 compared with ISSF ($p<0.001$) (Table 2).

Table 1. Sociodemographic and clinical characteristics of patients (n=160)

Characteristics	
Gender, n (%)	
Male	106 (66.3)
Female	54 (33.8)
Age (years), mean ± SD	33.5 ± 12.2
Disease duration (years), mean ± SD	16.6 ± 10.3
Age of diagnosis (years), mean ± SD	23.1 ± 12.7
Delay of diagnosis (years), mean ± SD	6.2 ± 7.9
Age of symptom onset (years), mean ± SD	16.9 ± 11.8
Dose of colchicine, (mg/day), mean ± SD	
ISSF Score (n, %)	
Mild	67 (41.9)
Intermediate	80 (50.0)
Severe	13 (8.1)
F-SS-2 Score (n, %)	
Mild	59 (36.9)
Intermediate	41 (25.6)
Severe	60 (37.5)

Table 2. Comparison between F-SS-2 and ISSF Score

		ISSF Score (n=160)				
		Mild	**Intermediate**	**Severe**	**Total**	p[a]
F-SS-2 Score (n=160)	**Mild**	37 (62.7)	20 (33.9)	2 (3.4)	59 (100.0)	**<0.001**
	Intermediate	22 (53.7)	17 (41.5)	2 (4.9)	41 (100.0)	
	Severe	8 (13.3)	43 (71.7)	9 (15.0)	60 (100.0)	
	Total	67 (100.0)	80 (100.0)	13 (100.0)	160 (100.0)	

F-SS-2: The second set of Familial Mediterranean Fever severity score, ISSF: International Severity Scoring System for Familial Mediterranean Fever, [a]Pearson Chi-Square test

Conclusion: Disease severity scores should be used for treatment choice, evaluation of disease prognosis and classify patients according to disease severity in clinical trials. In the current study, we found a difference between the classifications of disease severity, which could be a result of each scoring system uses different parameters of the disease.

Disclosure of Interests: None declared

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THU0588 CLINICAL PHENOTYPES OF IGG4-RELATED DISEASE IN SPAIN

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Background: Recently, several clinical phenotypes in IgG4-related disease have been described in a multinational and ethnically variate cohort[1].

Objectives: To assess the clinical presentation of IgG4-related disease (IgG4-RD) in Spanish patients and assess the distribution among different clinical phenotypes.

Methods: Clinical data were obtained from the Spanish IgG4-RD registry (REERIGG4) from October 2013 to December 2018, including 9 centers. We reviewed demographic data and organ involvement. The assignation of clinical phenotypes was done by 2 experts, based on organ involvement and clinical manifestations, following Wallace et al.[1] subsets. The phenotypes were: pancreato-hepato-biliary (HBP), retroperitoneum and aorta (RA), head and neck limited (HNL) and Mikulicz and systemic (MS). A fifth group designated not defined (ND), included the patients that did not fit in the previous phenotypes.

Results: One-hundred patients were included. Thirty-four (34%) were females, median age at diagnosis was 54.8 years (IQR 20.7). The ethnicity of the participants was: Caucasian 83%, Hispanic 12% and North-African/Middle-East 5%. Ninety-two percent were diagnosed with a biopsy. Regarding the diagnostic criteria, 85% met consensus pathology criteria and 94% comprehensive criteria.

Fifty-one patients (51%) had systemic IgG4-RD involving >1 tissue. The most commonly involved tissues were: retroperitoneum (35%), lymph nodes (19%), orbit pseudotumor (18%), salivary glands (16%) and pancreas (14%). Forty-two patients (42%) had elevated serum IgG4.

The representation of each clinical phenotype was: HBP 14%, RA 25%, HNL 26%, MS 20%, ND 15%. Patients were equally distributed from the perspective of ethnicity. Men were predominant in all groups (71, 84, 70, 73%) except in HNL (61% for women). Systemic disease was present in all the MS patients, but in 1/3 of the other groups. Serum IgG4 was elevated in 86% of the cases in HBP, 28% in RA, 19% in HNL, 60% in MS and 40% in ND.

Conclusion: The Spanish IgG4-RD population was mainly ethnically Caucasian. Few patients had serum IgG4 elevation. The most frequent phenotype was HNL, followed by RA. The HBP phenotype was less frequent than in previous reports. The influence of race could modify the clinical expression of IgG4-RD. Knowing the regional phenotypes of IgG4-RD may help clinicians improve disease management.

REFERENCES:

[1] Wallace ZS, Zhang Y, Perugino CA, et al. Clinical phenotypes of IgG4-related disease: an analysis of two international cross-sectional cohorts. Ann Rheum Dis. doi: 10.1136/annrheumdis-2018-214603

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THU0589 FREQUENCY, CHARACTERISTICS AND CLINICAL DETERMINANTS OF "PRODROME" IN FAMILIAL MEDITERRANEAN FEVER PATIENTS

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Background: Prodrome was defined by the presence of manifestations that precede an FMF attack and predict its emergence. This period might be turned to a window of the opportunity for the prompt treatment of impending attacks with fast-acting IL-1 inhibitors.

Objectives: We aimed to determine the frequency, characteristics and clinical determinants of prodrome in patients with FMF

Methods: 401 FMF patients were enrolled in this cross-sectional study. We applied a questionnaire to the FMF patients about attack types, pre-attack manifestations and latent time. Four hours was accepted as the cutoff point for prodrome as based on the literature, which is compatible with the pharmacokinetics of anakinra.

Results: The mean age was 37.7 (±11.0) years, and the disease duration was 20 years (3-58). 248 of the patients (61.8%) were female. MEFV gene mutations were achieved in 364 (90.8%) patients, of these 121 (30.2%) patients harbored homozygous exon 10 mutations. Patients with a latent time over four hours considered as prodrome positive (PP) patients (n=141). Male gender, homozygous MEFV mutations, peritonitis, pleuritis, arthritis and ELE were more pronounced in PP group. 25.9% of patients with peritonitis, 14.7% of patients with pleuritis, 13.2% with arthritis and 5.5% with ELE had prodrome with variable latent time durations (median, 6.7(4-72), 6 (4-48), 6 (4-72), and 7.7 (4-30) hours, respectively). Prodrome was found to be more common in those with peritonitis. Male gender, having peritonitis or arthritis were found to be the independent clinical determinants of having prodrome (RR 1.72 (1.07-2.76), P=0.02, 4.27 (1.80-10.1), P=0.001, 1.77 (1.04-3.04), P=0.04, respectively). Age, MEFV mutations, pleuritis and ELE were not found as clinical determinants of prodrome.

Conclusion: Especially male patients with peritonitis or arthritis tend to have prodrome more than other patients, and should be questioned. Prodrome positive patients are candidates for prevention of the impending attacks with on-demand treatments.

Table 1. Patients demographics and disease characteristics

	Prodrome (+) (n=141)	**Prodrome (-) (n=260)**	**p**
Age, years	37.7 (10.5)	37.8 (12.8)	0.92
Female	78 (55.3%)	170 (65%)	*0.05*
Age at FMF diagnosis, years	24(3-62)	25(2-59)	0.52
Disease duration, years	21 (4-58)	19 (3-58)	0.08
Fever	0	9 (3.5%)	*0.03*
Peritonitis	133 (94.3%)	197 (75.8%)	*<0.001*
Pleuritis	92 (65.2%)	123 (47.3%)	*0.01*
Arthritis	103 (72.9%)	129 (49.8%)	*<0.001*
Myalgia	0	6 (2.3%)	0.09
Erysipelas like erythema	46 (32.6%)	58 (22.3%)	*0.02*
Homozygous*	57 (43.2%)	64 (27.6%)	*0.02*
M694V/M694V	50(35.5%)	51(19.6%)	*0.01*
M694V/-	19 (13.5%)	46(17.7%)	0.19
M694V/M680I	13 (9.2%)	23 (8.8%)	0.98
M694V/V726A	12 (8.5%)	20 (7.7%)	0.88
M694V/E148Q	6 (4.3%)	15 (5.8%)	0.45
M680I/M680I	6 (4.3%)	9(3.5%)	0.76

* 364 patients MEFV mutations were achieved. 9.2% of patients MEFV mutations is not known, 7.7% of patients is gen negative FMF.

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THU0590 COMPARISON OF FMF PATIENTS WITH AGE OF ONSET BEFORE 20 VERSUS 40 YEARS AND OVER

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Background: Familial Mediterranean fever (FMF) is a disease with an onset before 20 years of age in 90% of the patients. However late onset FMF defined as age of onset over 40 years is being recognised more frequently.

Objectives: To better define patients with FMF who had their first attack before age 40 and compare them with early onset patient group in Turkish population

Methods: The files of 2180 FMF patients followed in a single center between 2008-2017 who have fulfilled Tel-Hashomer criteria, were reviewed with regard to age of onset 40 years and over (index patients, Group 1). For control purposes files before and after the index patients were browsed and first patients with an onset before age 20 years (Group 2) were included. The demographic, clinical and genetic characteristics are compared between these 2 subgroups.

Results: Patients with an onset after 40 years consisted 2.7% of our FMF population. 50 of the 59 patients with an onset 40 years or over were re-evaluated and compared with early onset group consisting of 100 patients (Table 1). The delay in diagnosis, and disease duration were significantly longer and number of patients with M694V homozygosity and M694V allele frequency were significantly more frequent among group 2. In general, phenotypes of both onset groups were similar, the only significant differences being the frequency of fever and myositis which were less common among group 1. Also response to colchicine was more pronounced in group 1. One other interesting observation was the low incidence of amyloidosis in a group with such a significant delay in diagnosis and thus treatment.

Table 1. Demographic, clinical and genetic features of the study groups

	≥40 years n=50	**≤20 years n= 100**	p
Sex (F:M); present age (mean±SD) (yr)	32:18; **57.2±7.9**	62:38; **31.8±9.1**	NS; **<0.001**
Mean age at onset,(mean±sd) (yr)	**45.6±5.2**	**8.7±4.8**	**<0.001**
Mean age at diagnosis (mean ±sd) (yr)	**50.4±7.3**	**19.1±11.2**	**<0.001**
Delay in diagnosis (mean ±sd) (yr)	**4.8±5.5**	**10.4±11.8**	**<0.001**
Mean disease duration (mean ±sd) (yr)	**11.5±6.4**	**23.1±10.8**	**<0.001**
Abdominal pain, n (%)	44(88)	89(89.0)	NS
Chest pain, n (%)	7(14.0)	27 (27.0)	NS
Fever, n (%)	**30(60.0)**	**81(81.0)**	**0.005**
Arthritis, n (%)	12(24.0)	33(33.0)	0.25
Myalgia, n (%)	**1(2.0)**	**12(12.0)**	**0.04**
Amyloidosis, n (%)	1(2.0)	3(3.0)	NS
Positive family history, n (%)	33(68.7)	62 (65.2)	NS
Response to colchicine, n (%)	**37(82.2)**	**93 (94.8)**	**0.014**
M694VHomozygous, n (%)	**2(4.5)**	**23(25.8)**	**0.003**
N of M694Vallelles	**24(48)**	**82 (82)**	**0.014**
No mutation, n (%)	3(6.8)	2(2.2)	NS

Conclusion: FMF should be included among the differential diagnosis of patients over 40 years of age with recurrent autoinflammatory manifestations. Less than 3% of FMF patients experience their first attacks after 40 years of age. The frequency of M694V is significantly less in the late onset group, pointing out a milder disease.

Disclosure of Interests: None declared

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THU0591 SALIVARY GLAND INVOLVEMENT DISPARITIES IN CLINICAL AND LABORATORY CHARACTERISTICS OF IGG4-RELATED DISEASE: A RETROSPECTIVE STUDY OF 428 PATIENTS

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Background: IgG4 related disease (IgG4-RD) is recently recognized as a fibro-inflammatory condition featured by tumefactive lesions in multiple organs, among which salivary gland is one of the most commonly involved sites. Some previous studies have suggested that salivary gland involved IgG4-RD (IgG4-RD SG+) patients may present different features compared to IgG4-RD patients without salivary gland lesions (IgG4-RD SG-), however, only dozens of patients were examined and the comparison has not been studied in detail.

Objectives: We undertook this study to compare detailed demographic, clinical and laboratory characteristics of IgG4-RD patients with salivary gland lesion (IgG4-RD SG+) and salivary gland free IgG4-RD (IgG4-RD SG-) in a large cohort.

Methods: We carried out a retrospective review of the medical records of 428 cases of IgG4-RD diagnosed at Peking University People's hospital between March 2006 and May 2018.

Results: Among 428 patients, 249 had salivary gland affected. IgG4-RD SG+ patients showed younger age at disease onset and diagnosis, and a longer interval between symptom onset and diagnosis. IgG4-RD SG+ group involved more female patients, and allergic diseases were more common in this group. In terms of organ involvement, IgG4-RD SG+ group were more frequently presented with lacrimal gland involvement, while lymph node, retroperitoneal fibrosis, pancreas, biliary system, kidney, and aorta were more prominent in IgG4-RD SG- group. In addition, the serum IgG4 levels, IgG4/IgG ratio and IgE level were significantly higher in IgG4-RD SG+ patients. Patients with eosinophilia were more common in IgG4-RD SG+ group, while elevated ESR, CRP, and positive ANA were more common in IgG4-RD SG- group.

Conclusion: We have revealed demographic, clinical and laboratory differences between IgG4-RD SG+ and SG- patients, which indicated potential differences in pathogenesis and important implications for the diagnosis and management of these two phenotypes.

REFERENCES:

[1] Kamisawa T, Zen Y, Pillai S, Stone JH. IgG4-related disease. Lancet. 2015;385(9976):1460-71.

[2] Moriyama M, Ohta M, Furukawa S, Mikami Y, Tanaka A, Maehara T, et al. The diagnostic utility of labial salivary gland biopsy in IgG4-related disease. Mod Rheumatol. 2016;26(5):725-9.

[3] Higgs BW, Liu Y, Guo J, Sebastian Y, Morehouse C, Zhu W, et al. High-throughput RNA sequencing reveals distinct gene signatures in active IgG4-related disease. Sci Rep. 2017;7(1):17567.

[4] Inoue D, Yoshida K, Yoneda N, Ozaki K, Matsubara T, Nagai K, et al. IgG4-related disease: dataset of 235 consecutive patients. Medicine (Baltimore). 2015;94(15):e680.

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THU0592 PREDICTORS OF RELAPSE OF IGG4-RELATED DISEASE AFTER INDUCTION THERAPY: A RETROSPECTIVE STUDY

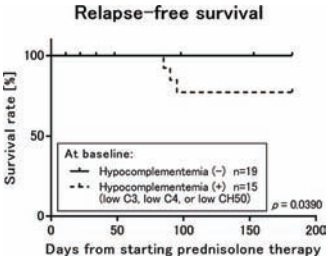
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Background: IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory condition characterized by tumefactive lesions and, often but not always, elevated serum IgG4 levels [1]. Glucocorticoids (GC) are usually used as induction therapy for IgG4-RD. However, relapse often occurs following GC tapering, and predictors of relapse remain unclear.

Objectives: To identify predictors of relapse of IgG4-RD after induction therapy.

Methods: We retrospectively reviewed 57 patients diagnosed with IgG4-RD and treated with GC in our hospital between January 2004 and November 2018. Clinical features at baseline, including organ involvement and blood markers (total hemolytic complement [CH50], its fractions [C3 and C4], IgG4, IgG, IgE, anti-nuclear antibody, rheumatoid factor, C-reactive protein, soluble interleukin-2 receptor, eosinophils), were collected. We divided patients into 2 groups on the basis of clinical features and examined whether they relapsed. In this study, hypocomplementemia was defined as decreased serum C3, C4, or CH50 less than the lower limit of normal. A relapse was defined as any new or worsened state of disease activity that required an escalation in treatment (immunosuppressants and/or GC). The follow-up period was defined as 182 days.

Results: Forty-three men and 14 women (mean age 68.1 ± 10.9 years) were included. Both serum IgG4 and IgG were measured at baseline in all patients (mean IgG4 798.8 ± 873.1 mg/dL and mean IgG 2874.0 ± 1934.1 mg/dL, respectively). All of the serum C3, C4, and CH50 were measured at baseline in 34/57 patients (mean C3 75.7 ± 33.3 mg/dL; mean C4 14.8 ± 11.5 mg/dL; and mean CH50 37.0 ± 23.1 U/mL). Fifteen patients had at least one episode of hypocomplementemia, and 19 patients did not. Most patients had multiple organ lesions. The details of dominant lesions were as follows: Dacryoadenitis and/or sialadenitis (Mikulicz disease), 36/57 patients (63.2%); biliary or pancreatic lesion, 29/57 (50.1%); retroperitoneal fibrosis, 22/57 (38.6%); and renal lesion 16/57 (28.1%). All patients were given prednisolone and gradually reduced (mean induction dose 31.7 ± 9.8 mg/day). No patients received immunosuppressant as induction therapy. During the follow-up period, 6 patients relapsed, and the dose of prednisolone was increased immediately. Relapsed lesions were as follows: Mikulicz disease, 3/6 patients (50.0%); biliary or pancreatic lesion, 1/6 (16.7%); retroperitoneal fibrosis 1/6 (16.7%); and pulmonary lesion 1/6 (16.7%). Patients with hypocomplementemia had significantly shorter relapse-free survival than those without (p=0.039, Figure 1). Patients with decreased serum C4 or CH50 (less than the lower limit of normal) also had significantly shorter relapse-free survival than those without, but those with decreased serum C3 did not. Such a tendency was not seen in other blood markers (IgG4, IgG, IgE, anti-nuclear antibody, rheumatoid factor, C-reactive protein, soluble interleukin-2 receptor, eosinophils).



Conclusion: Hypocomplementemia at baseline in patients with decreased serum C4 or CH50 may predict relapse of IgG4-RD after prednisolone therapy.

REFERENCES:

[1] Stone JH, et al. N Engl J Med 2012; 366: 539-51.

Disclosure of Interests: None declared

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THU0593 CLINICAL AND GENETIC FEATURES OF CHINESE ADULT PATIENTS WITH TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME

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Background: Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) is an autosomal dominant autoinflammatory disase, associated with the mutation of tumor necrosis receptor superfamily member 1A (*TNFRSF1A*) gene, located on chromosome12p13. TRAPS is usually diagnosed during pediatric age. However, adult-onset disease or diagnosis during adulthood has been occasionally described. Moreover, TRAPS has been hardly reported in the Chinese population. Herein, we aimed to characterize the clinical and genetic features of Chinese adult patients with TRAPS.

Objectives: Adult patients (≥16 years) suspected monogenic autoinflammatory diseases during the period April 2015 to October 2018, at the adult autoinflammatory disease center, Department of Rheumatology, Peking Union Medical College Hospital (PUMCH).

Methods: Clinical data were evaluated. Gene sequencing was performed in each patient to support the diagnosis and exclude other monogenic autoinflammatory diseases. Finally we compared the data with those from Japan and Europe.

Results: During the study period, 8 patients with TRAPS were diagnosed and follow-up. The ratio of male to female was 3: 1. The median age of disease onset was 4 (0.5–38.5), and adult-onset was observed in 2 (25%) patients. The median time of diagnosis delay was 17.8 (1.5-50.5) years. There were seven Chinese Han and one Manchu patients. One patient had a family history of TRAPS. The most frequent symptom was fever (8, 100%). The attacks of 5 (62.5%) patients lasted more than 1 week, and the intervals of 7 (87.5%) patients were longer than 2 weeks. Skin involvement occurred in 6 (75%) patients, with maculopapular mentioned in 6 and erythema annulare presented in 3. Four (50%) patients had arthralgia, while one had polyarthritis. 4 (50%) patients complained respectively of myalgia or headache. 4 (50%) patients experienced abdominal pain and one (12.5%) had vomiting. One (12.5%) patient had periorbital edema, while 3 (37.5%) had conjunctivitis. Up to 5 (62.5%) patients got nonspecific pharyngitis. No patient suffered from chest pain or amyloidosis. Eight gene variants were detected in *TNFRSF1A* gene. Heterozygous gene variants were found in 7 Chinese Han patients, and homozygous (c.769-23, T>C) happened to the Manchu patient. The variants included C58 (exon 2), G65E (exon 3), F89L (exon 3), C99G (exon 3), V202G (exon 6), c.769-23T>C (IVS8), S290I (exon 9) and m.1735A>G (non-coding region). NSAIDs were given to 2 patients, glucocorticoid or immunosuppressive agents given to 3 patients respectively, and etanercept to 5 patients. A complete response was found in all the 5 patients received etanercept. The effectiveness of other drugs were 50% in NSAIDs, 66.7% in glucocorticoid and immunosuppressive agents.

Conclusion: This is the first and largest case series of TRAPS in Chinese adult patients. It highlights the importance of screening *TNFRSF1A* gene in patients with unexplained periodic fever syndrome. Four novel *TNFRSF1A* variants, S290I, F89L, V202G and m.1735A G in non-coding region, have been identified. The atypical clinical manifestations of our patients compared to those from Europe might be related to their low-penetrance *TNFRSF1A* variants. Further studies are needed to explore the more accurate phenotypes and genotypes of the Chinese patients with TRAPS.

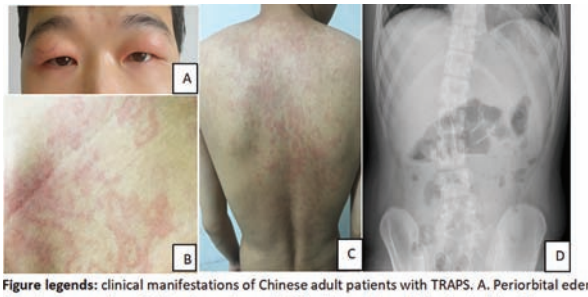


Figure legends: clinical manifestations of Chinese adult patients with TRAPS. A. Periorbital edema; B.erythema annulare; C. Maculopapular rash; D.Radiology showed intestinal obstruction.

Table 1 Summary of the main clinical and genetic features of the 8 Chinese adult patients with TRAPS

Patient	1	2	3	4	5	6	7	8
Sexuality	M	F	M	F	M	M	M	M
Nationality	Han	Han	Han	Han	Han	Han	Manchu	Han
Age at onset (years)	0.5	17	5	5	2.5	2	38.5	3
Age at diagnosis (years)	17	24	24	25	16	52	40	27
Diagnosis delay (years)	16.5	7	19	20	13.5	50	1.5	24
Family History	-	-	-	+	-	-	-	-
TNFRSF1A Variant	m.1735A >G	G65 E	S29 0I	C58 R	F89L	V202 G	c.769-23(IVS8)T>C	C99 G
Variant in other genes	-	-	-	-	R202Q in *MEFV*	-	D424E in *MEFV*, G39V in *NLRP12*	-
Fever	+	+	+	+	+	+	+	+
Duration	>3w	1w	2-3 d	1-2 w	1-2w	2-3d	2-3w	1w
Interval	<1w	3m	1-2 m	≥1 m	≥1m	< 1m	>1w	1m
Rash	+	-	-	+	+	+	+	+
Periorbital edema	-	-	-	-	-	-	-	+
Conjunctivitis	-	-	+	-	-	+	+	-
Arthralgia/Arthritis	+	-	+	-	-	+	-	+
Myalgia	+	-	-	+	+	+	+	-
Abdominal pain	-	+	-	+	-	+	-	+
Angina	-	+	-	+	-	+	+	+
Headache	+	-	-	-	-	+	+	+

Table 2 Comparison of phenotypic and genotypic features among reported cohorts

Cohorts	PUMCH (n=8)	Japan (n=51)	Europe (n=158)
M : F	6:2	22:29	78:80
Young onset (<18 years old, %)	87.5	68.1*	78
Age at onset (years)	4 (0.5-38.5)	ND#	4.3 (0 - 63)
Age at diagnosis (years)	24.5 (14- 52)	ND	25.9 (0-77)
Diagnosis delay (years)	17.8 (1.5 - 50.5)	ND	10.3 (0-77)
Family history (%)	12.5	45.1	ND
Fever (>38℃, %)	100	100	84
Rash (%)	75	55	63
Periorbital edema (%)	12.5	9.1	20
Conjunctivitis (%)	37.5	18.2	22
Arthralgia/Arthritis (%)	50	59	64
Myalgia (%)	54	43	70
Abdominal Pain (%)	50	36	70
Pharyngitis (%)	62.5	ND	21
Headache (%)	50	23	23
Diarrhea (%)	12.5	ND	18
Chest pain (%)	0	13.6	25
Amyloidosis (%)	0	0	10

*Age onset<20 years old; #ND: No Data

REFERENCES:

[1] Lachmann HJ, et al. The phenotype of TNF receptor-associated autoinflammatory syndrome (TRAPS) at presentation: a series of 158 cases from the Eurofever/EUROTRAPS international registry. Ann Rheum Dis 2014, 73: 2160-2167.

[2] Ueda N, et al. Clinical and Genetic Features of Patients With TNFRSF1A Variants in Japan: Findings of a Nationwide Survey. Arthritis Rheumatol 2016, 68: 2760-2771.

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Diagnostics and imaging procedures

THU0594

CLINICAL VERSUS IMAGING REMISSION IN JUVENILE IDIOPATHIC ARTHRITIS (JIA): PRELIMINARY RESULTS OF THE REMECO STUDY

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Background: remission is becoming a realistic target in JIA, but clinical remission (CR) may not accurately reflect real absence of synovitis. It would be desirable to have instruments to predict the risk of relapse in patients in CR in order to establish the most appropriate therapeutic strategy. Despite in RA the role of imaging to predict disease flare is established, this field has remained almost unexplored in JIA.
Objectives: 1) to investigate the prevalence of musculoskeletal ultrasound (MSUS)-detected subclinical synovitis in JIA patients in CR; 2) to establish which and how many joints should be scanned to reliably assess remission; 3) to evaluate the persistence of subclinical synovitis over the time; 4) to investigate whether subclinical synovitis entails a risk of disease flare; 5) MSUS data will be integrated with serum levels of inflammatory biomarkers to develop a multidimensional measure of remission.
Methods: it is a longitudinal prospective 4 years study started on November 2017. So far we have enrolled 99 consecutive JIA patients who met the Wallace criteria for CR. For each patient 46 joints were scanned for synovial hyperplasia/joint effusion and PD signal, all graded semiquantitatively on a 0–3 scale independently by 2 expert ultrasonographers. Subclinical synovitis was defined when total synovitis score for each joint was ≥2. MSUS was performed at baseline and at 6 month follow up visit. At inclusion serum assays have been stored to determine levels of inflammatory biomarkers (S100A8/9-A12, bFGF, IL-6, IL-10, CXCL9-10, VEGF, YKL40). A flare of synovitis was defined as a recurrence of clinically active arthritis.
Results: 99 patients (79.8% F; median age 11.3 y; median disease duration 5.3 y; median CR duration 1.6 y) were included. Thirty-eight/99 (38.4%) patients had persistent oligoarthiritis; 34/99 (34.3%) extended oligoarthiritis; 22/99 (22.2%) polyarthiritis; 5/99 (5.1%) systemic arthritis. Fifty-nine/99 (59.6%) patients were in CR on medication. Subclinical synovitis was detected in 54/99 (54.5%; 95% CI: 45.2 – 65.5%) patients, PD in 18/99 (18.2%; 95% CI: 11.1 – 27.2%) patients; subclinical tenosynovitis in 7/99 (7.1%; 95% CI: 2.9 – 14%) patients. Subclinical synovitis was found more frequently in the ankle [31/54 (57.4%) patients] and wrist joints [17/54 (31.5%) patients]. No patients had subclinical synovitis in the hip. A 14-joint reduced count including bilateral knee, ankle (tibiotalar, subtalar and talonavicular joints), wrist (radiocarpal and intercarpal joints) and elbow joints, detected 92.6% of children with subclinical synovitis. Twenty-five/99 (25.2%) patients in persistent CR were reassessed with MSUS at a follow up visit (median follow up duration 7 months): 82.3% of patients showed persistent subclinical synovitis. Sixty-four/99 (64.6%) patients had a clinically follow up of at least 6 months and 9/64 (14%) patients experienced a disease flare (median time to flare 6.6 months). Six/9 (66.7%) patients who experienced a relapse had subclinical synovitis at baseline.
Conclusion: our preliminary results confirm the discrepancy between clinical and imaging remission and that clinical evaluation may not sensitive to detect an inflammation-free state. Bilateral US assessment of the elbow, wrist, knee and ankle joints is reliable to detect subclinical synovitis. So far, patients who have relapsed are a small percentage, but to extend follow up is crucial to test predictive value of MSUS. Imaging findings will be combined with serum biomarkers leading to the construction of a predictive model.

REFERENCES:

[1] De Lucia O, et al. Baseline ultrasound examination as possible predictor of relapse in patients affected by juvenile idiopathic arthritis (JIA). Ann Rheum Dis. 2018 Oct;77(10):1426-1431.

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THU0595 DEVELOPMENT OF AN AUTOMATED SEGMENTATION ALGORITHM TO IDENTIFY BONES OF THE HAND

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Background: The evaluation of structural damage with plain radiography is important to clinicians and patients. Standard scoring methods include the Sharp-van der Heijde (SVdH) and Ratingen methods [1] however these systems are time-consuming. Therefore, it is difficult to perform large cohort studies. We set out to develop an automated algorithm to identify bones on plain radiographs as a step towards developing automated quantification of structural damage for use on large datasets.
Objectives: To develop a novel algorithm to segment outlines of finger bones in hand radiographs.
Methods: 101 hand radiographs were gathered from the Bath longitudinal cohort (UK). All patients fulfilled the CASPAR criteria for Psoriatic Arthiritis (PSA). None of the patients had damage on SVdH and Ratingen scoring (blinded). The metacarpal (MC), proximal phalanx (PP), middle phalanx (MP), and distal phalanx (DP) in the right index finger were delineated by a rheumatologist. These outlines were used to build a statistical model of the shape using a Gaussian Process Latent Variable Model (GPLVM) [2]. Bones are segmented by matching the shape on a radiograph to the statistical model.
Results: The performance of the matching algorithm was compared with a traditional algorithm (snakes) using the Adjusted Rand Score (ARND). The ARND score measures the similarity of the segmentation with the ground truth. A perfect segmentation has a score close to 1. We tested the algorithm on 9 PP, 9 MP and 8 DP and 6 MC bones in the right index finger. The results are reported in table 1. We report a mean improvement in ARAND of 0.19, 0.87, 0.43 and 0.30 for the PP, MP, DP and MC respectively.
Conclusion: We report a reliable algorithm for the identification of metacarpal, proximal, middle and distal phalanx bones of the hand. Future work will focus on using the output of the segmentation algorithm to track damage progression over time.

REFERENCES:

[1] Van der Heijde, D., PAULUS, H., and SHEKELLE, P. (2000). How to read radiographs according to the Sharp/vander Heijde method. Discussion: Heterogeneity in rheumatoid arthritis radiographic trials. Issues to consider in a metaanalysis. Journal of rheumatology, 27(1):261–263.
[2] Titsias, M. K. and Lawrence, N. D. (2010). Bayesian Gaussian process latent variable model. In International Conference on Artificial Intelligence and Statistics, pages 844–851.

Table 1. Adjusted RAND scores for comparing our algorithm to a traditional one (snakes)

	Bone	Snakes ARAND	Shape matching ARAND
Case 1	PP	0.70	0.95
Case 2	PP	0.89	0.96
Case 3	PP	0.82	0.96
Case 4	PP	0.72	0.94
Case 5	PP	0.53	0.96
Case 6	PP	0.87	0.97
Case 7	PP	0.79	0.96
Case 8	PP	0.74	0.96
Case 9	PP	0.88	0.97
Case 1	MP	0.79	0.95
Case 2	MP	0.75	0.95
Case 3	MP	0.75	0.94
Case 4	MP	0.72	0.95
Case 5	MP	0.77	0.96
Case 6	MP	0.51	0.96
Case 7	MP	0.76	0.96
Case 8	MP	0.77	0.96
Case 9	MP	0.83	0.97
Case 10	MP	0.77	0.93

Key: Adjusted Rand Score (ARND) score measures the similarity of the segmentation with the ground truth. A perfect segmentation has a score close to 1. Metacarpal (MC), proximal phalanx (PP), middle phalanx (MP), and distal phalanx (DP)



Figure 1. Shape matching algorithm output demonstrating segmented outlines of the DP, MP, PP and MC in red, green, orange, and blue respectively.

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THU0596 DIAGNOSTIC VALUE OF ULTRASOUND AND DUAL ENERGY COMPUTED TOMOGRAPHYTO ACHIEVE ACR-EULAR GOUT CLASSIFICATION CRITERIA IN REAL LIFE CLINICAL PRACTICE

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Background: 2015 ACR/EULAR gout classification criteria (1) include ultrasound with double contour (DC) sign as key ultrasound features and dual energy computed tomography (DECT) with evidence of urate deposition. The positivity of either DECT or ultrasound allows 4 points in addition to others clinical and biological criteria to classify as gout is $\geq$8/23. However, in routine care, the imaging modality that should be promoted remains unclear between ultrasound or DECT.
Objectives: To validate a possible diagnostic algorithm for the clinical use of DECT and ultrasound in suspected gouty arthritis.
Methods: We conducted a single-center prospective study in the Rheumatology Department of Dijon University Hospital from july 2016 to december 2018, including all patients hospitalized for suspected gouty arthritis. Each patient received joint aspiration if possible, an ultrasound assessment (DC sign and/or tophus) and DECT scanning of symptomatic joints. All these examinations were performed blind of the clinical data and results of joint aspiration. The gold standard used for this study was the 2015 ACR/EULAR gout classification criteria. We have established two

scenarios derived from the algorithm proposed by Nötzel et al (2): in scenario A, the DECT was performed first followed by ultrasound; in scenario B, ultrasound was performed first followed by DECT. Test performance such as sensitivity, specificity, positive and negative predictive value (PPV, NPV)) were calculated for each imaging techniques. Statistical analysis was performed by SAS/STAT software and Macnemar test was used to compare the two scenarios.

Results: 40 consecutive patients were included. 3 patients had a score ≥8 from clinical data alone and classified as gout. The remaining 37 patients were included according to the two scenarios. In scenario A, 9/37 patients had a DECT positive with urate deposition leading to the diagnostic of gout with an ACR/EULAR score ≥ 8. 7/37 patients had a positive DECT without reaching ACR/EULAR treshold (< 8). 21/37 patients had a negative DECT. The ultrasound study of these 28 patients did not find any sign of gout (DC sign). In scenario B, 6/37 patients had a DC sign and an ACR/EULAR score ≥ 8. 1/37 patient had a DC sign but an ACR/EULAR score < 8. 30/37 patients had no ultrasound DC sign. DECT in these 31 patients revealed sodium urate deposits in 3/31 patients, leading to a score ≥8. DECT was positive in 7/31 patients with an ACR/EULAR score < 8. The comparison between the 2 scenarios did not find a significant difference (p = 0.250). For the DC sign, sensitivity = 66%, specificity = 96%, PPV = 89% and NPV = 87%. For the presence of DC sign and/or tophus, the values were 91%, 96%, 91%, 96% respectively. For DECT, sensitivity =100%, specificity = 75%, PPV = 63%, NPV = 100%.

Conclusion: Our results confirm that ultrasound (DC sign alone) and DECT have similar diagnostic performance in gouty arthritis in routine care. It seems clinically relevant to propose the ultrasound as first imaging modality considering both the presence of the DC sign and/or ultrasound tophus (not included in ACR-EULAR criteria). It significantly improves the sensitivity of ultrasound while maintaining its PPV, with less false positive patients compared to DECT.

REFERENCES:

[1] Neogi T, Jansen TLTA, Dalbeth N, et al. 2015 Gout Classification Criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis & Rheumatology. 2015; 67:2557–68.

[2] Nötzel A, Hermann K-G, Feist E, et al. Diagnostic accuracy of dual-energy computed tomography and joint aspiration: a prospective study in patients with suspected gouty arthritis. Clin Exp Rheumatol. 2018; 36 :1061–7.

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THU0597 ULTRASOUND REVEALS SUB-CLINICAL ATHEROSCLEROSIS IN PATIENTS WITH GOUT AND ASYMPTOMATIC HYPERURICEMIA

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Background: Accelerated atherosclerosis and the higher risk of developing premature cardiovascular disease are well known in chronic inflammatory rheumatic diseases. Moreover, strong evidence supporting both proatherogenic and protrombotic characteristics of high levels of uric acid have been published.

Ultrasound (US) measurement of the carotid intima-media thickness (cIMT) is a non-invasive outcome measure of premature sub-clinical atherosclerosis with a predictive value in terms of vascular events.

Objectives: To determine the prevalence of increased cIMT, as sign of pre-clinical atherosclerosis, in patients with gout and asymptomatic hyperuricemia by an automated ultrasound (US) method.

Methods: 342 subjects (138 with gout, 105 with asymptomatic hyperuricemia and 99 healthy control subjects) were enrolled. Before the US assessment, all patients underwent a clinical examination aimed to record age, gender, disease duration, smoking, ischemic cardiopathy, comorbidities (including diabetes mellitus, high blood pressure, dyslipidemia, renal insufficiency, obesity), and current therapy. Moreover, ESR, CRP, total cholesterol, HDL-high-density lipoprotein, triglycerides, fasting serum glucose, serum creatinine and uricemia were recorded. Patients with history of myocardial infarction, cerebrovascular events or autoimmune diseases were excluded.

US examinations of the IMT at both common carotids were performed by a rheumatologist expert in US, using a linear probe and an automatic method (QIMT) based on the radio-frequency technology. For the IMT, a cut-off point of 0.8 mm was adopted, according Mannheim cIMT Consensus.

Results: A total of 684 common carotids were assessed. In 65 (47.10%) out of the 138 patients with gout and 50 (47.62%) out of the 105 patients with asymptomatic hyperuricemia, US detected an increased cIMT and only 9 (0.09%) of the control group patients had an increased cIMT (p=0.0001). The regression analysis found a significant positive correlation between increased cIMT and disease duration in gout group (p=0.001) and between the level of uric acid and increased cIMT in asymptomatic hyperuricemic patients (p=0.009). No significant correlation was found with the other clinical and laboratory parameters. There was a significant difference in cIMT between in gout and control groups (p=0.0001) and between asymptomatic hyperuricemia and control group (p=0.0001).

Conclusion: Our results demonstrate that patients with gout and hyperuricemia without clinically evident cardiovascular disease have a high prevalence of atherosclerosis represented by the increased cIMT.

Disclosure of Interests: None declared
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THU0598 ROLE OF DUAL-ENERGY CT AS A SCREENING TOOL FOR CORONARY GOUT

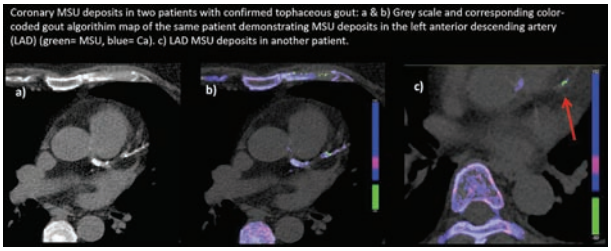
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Background: Gout is prevalent in older men and has been demonstrated as independent cardiovascular risk factor. Presence of clinical gout rather than isolated hyperuricemia is related to the increased cardiovascular risk. Dual-Energy CT (DECT) has proven to be of high sensitivity and specificity in detection of monosodium urate (MSU) deposits in joints and soft tissues.

Objectives:

1. Evaluate DECT as a potential screening tool for monosodium urate deposits within the coronary arteries.
2. Calculate prevalence of coronary gout in patients with confirmed tophaceous gout in comparison to asymptomatic control group.

Methods: Cases were retrospectively assigned into two groups. The first (tophaceous gout) group included patients who were referred for DECT gout screening. The inclusion criteria were: males > 50 years of age and clinical diagnosis of tophaceous gout confirmed by DECT. The second (control) group included patients who underwent non-contrast DE Cardiac CT for calcium scoring during the same duration as part of cardiovascular risk workup. Inclusion criteria were males > 50 years of age, no clinical diagnosis of gout and Agatston calcium score less than 400. All DECT scans were done on the same scanner, which was validated and adequately titrated before the start of and during the study. All scans were reviewed by two radiologists with expertise in DECT gout deposits.



Coronary MSU deposits in two patients with confirmed tophaceous gout: a & b) Grey scale and corresponding color-coded gout algorithim map of the same patient demonstrating MSU deposits in the left anterior descending artery (LAD) (green= MSU, blue= Ca). c) LAD MSU deposits in another patient.

Results: Among the 13 cases that met the inclusion criteria for the tophaceous gout group, 11 were positive (84.62%) for coronary MSU deposits. Among the 48 cases that met the inclusion criteria for the control group: 47 were negative and one was positive (2.08%). DECT sensitivity was 84.62% (95% CI: 54.55-98.08%), specificity was 97.92% (95% CI: 88.93- 99.95%), positive predictive ratio was 91.67% (95% CI: 60.94-98.73%), negative predictive value was 95.92% (95% CI: 86.78- 98.83%) and accuracy was 95.08% (95% CI: 86.29- 98.97%).

Conclusion: Coronary MSU deposits are seen in 84.62% of tophaceous gout patients and in 2.08% of gout-asymptomatic individuals (of the same

age and sex group). DECT has high sensitivity, specificity and diagnostic accuracy in detection of MSU coronary deposits and can be used as a feasible, quick, low dose and low risk screening tool to detect coronary gout. DECT cardiac scans should be included in the routine CT gout protocol. Performing CT Calcium score using dual-energy has the added value of coronary gout detection as part of cardiovascular risk assessment and workup.

REFERENCES:

[1] - He, J., Yang, Y., & Peng, D. Q. (2012). Monosodium urate (MSU) crystals increase gout associated coronary heart disease (CHD) risk through the activation of NLRP3 inflammasome. International journal of cardiology, 160(1), 72-73.

[2] - Andrés, M., Quintanilla, M. A., Sivera, F., Sánchez Payá, J., Pascual, E., Vela, P., & Ruiz Nodar, J. M. (2016). Silent monosodium urate crystal deposits are associated with severe coronary calcification in asymptomatic hyperuricemia: an exploratory study. *Arthritis & Rheumatology*, 68(6), 1531-1539.

[3] - Yu, Z., Mao, T., Xu, Y., Li, T., Wang, Y., Gao, F., & Sun, W. (2018). Diagnostic accuracy of dual-energy CT in gout: a systematic review and meta-analysis. Skeletal radiology, 1-7.

[4] - Nicolaou, S., Yong-Hing, C. J., Galea-Soler, S., Hou, D. J., Louis, L., & Munk, P. (2010). Dual-energy CT as a potential new diagnostic tool in the management of gout in the acute setting. American Journal of Roentgenology, 194(4), 1072-1078.

[5] - Rai, S. K., Aviña-Zubieta, J. A., McCormick, N., De Vera, M. A., Shojania, K., Sayre, E. C., & Choi, H. K. (2017, February). The rising prevalence and incidence of gout in British Columbia, Canada: population-based trends from 2000 to 2012. In *Seminars in arthritis and rheumatism* (Vol. 46, No. 4, pp. 451-456). WB Saunders.

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THU0599 RESOLUTION OF VASCULAR INFLAMMATION IN PATIENTS WITH GIANT CELL ARTERITIS RECEIVING GLUCOCORTICOIDS, METHOTREXATE OR TOCILIZUMAB TREATMENT-DATA FROM THE ITALIAN/GERMAN RIGA STUDY

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Background: ^{18}F-FDG-PET/CT is a sensitive and comprehensive technique to diagnose giant cell arteritis (GCA) (1). This technique may be also very useful to test whether vascular inflammation in GCA has disappeared or not, judging effectiveness of anti-inflammatory treatment. However, the role of ^{18}F-FDG-PET/CT in monitoring disease activity and judging disease remission is less well-established to date

Objectives: RIGA is an observational 2-center study that addresses the resolution of vascular inflammation in patients with new-onset GCA that are treated with either glucocorticoid monotherapy (GLC), GLC/methotrexate (MTX) or GLC/tocilizumab (TOC).

Methods: Patients with newly diagnosed GCA with large vessel involvement were clinically documented, subjected to sequential ^{18}F-FDG-PET/CT scanning and received treatment with GLC, MTX or TOC upon physicians' decision. Images were graded as active, questionable active and inactive according to nuclear medicine physician opinion and additionally graded by PETVAS score proposed by Grayson et al. (0-27) (2). We performed a mixed effects linear regression analysis to estimate the change in the PETVAS score adjusted by baseline CRP level and tested for treatment group interactions. We compared the proportion of radiologic activity states according to the activity tracer uptake in the follow up ^{18}F-FDG-PET/CT scan in three treatment groups with a chi-squared test.

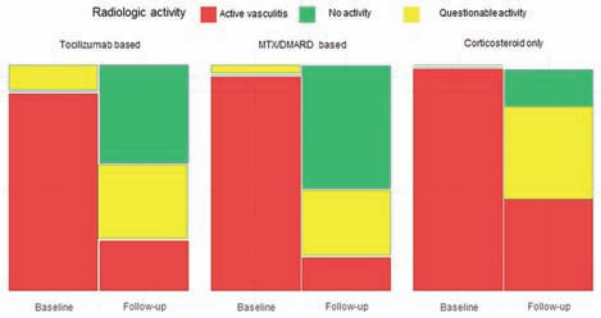
Results: We included 48 patients (n=20 from Germany, n=28 from Italy) with a mean age of 66 years. At baseline ^{18}F-FDG-PET/CT scan was graded active in 46 patients while it was graded as questionable active in the remaining 2 patients. The mean CRP level was 66,8 mg/L (min 1,2; max 233,2 mg/l) and the mean PETVAS score was 21,1 (min=10 max=27). 12 patients received GLC, 27 MTX and 9 TOC as primary treatment. Follow-up PET/CT scans were graded as active in 11, questionable in 16 and inactive in 21 patients. The mean CRP level at follow up was 12,4 mg/l (min 0,2; max 76,0) and the mean PETVAS score was 9,1 (min 0, max 27) with significant decreases in all 3 groups. The mean adjusted improvement in the PETVAS score (95%CI) was 13.0 (8.7 – 17.3) in GLC, 11.7 (8.9 – 14.6) in MTX and 11.8 (6.8 – 16.7) in TOC groups and interaction terms for treatment effect were not significant. However, only 17% of patients who received GLC showed no vasculitis activity in their follow up PET-CT compared to 53% of patients who received MTX or TOC (figure 1).

Conclusion: GLC, MTX and TOC significantly reduced vascular inflammation in GCA, but no significant differences between the three treatment strategies was found in this yet small population. However, when looking at complete resolution of vascular inflammation, MTX and TOC appear as being superior to GLC monotherapy, suggesting that addition of these agents right from the beginning of treatment of GCA may be beneficial to achieve complete control of vascular inflammation

REFERENCES:

[1] Schönau V, et al. The value of ^{18}F-FDG-PET/CT in identifying the cause of fever of unknown origin (FUO) and inflammation of unknown origin (IUO): data from a prospective study. Ann Rheum Dis. 2018 Jan;77(1):70-77 doi: 10.1136/annrheumdis-2017-211687

[2] Grayson, P. C. et al, 18F Fluorodeoxyglucose–Positron Emission Tomography As an Imaging Biomarker in a Prospective, Longitudinal Cohort of Patients With Large Vessel Vasculitis. Arthritis Rheumatol, 70: 439-449 doi:10.1002/art.40379



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THU0600 QUANTITATIVE INDEXES TO ASSESS THE INTERSTITIAL LUNG DISEASE, AND ITS EXTENSION, IN SJÖGREN'S SYNDROME

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Background: Interstitial lung disease (ILD) is the most frequent pulmonary impairment in Sjögren's syndrome (SS). The diagnosis is challenging, as there are not specific tests (i.e. autoantibodies or pulmonary function tests) or symptoms. Chest CT is the gold standard. Semiquantitative visual scores (SQCT) estimate ILD extent, though burdened by relevant intra-, inter-rater variability. Quantitative chest CT (QCT) is a promising method to assess ILD severity

Objectives: to verify if QCT assessment could identify SS subjects affected by ILD and to identify those SS patients with an extensive lung disease.

Methods: in this multi-center, cross-sectional, and retrospective study, subjects affected by SS and with a chest CT were enrolled. A blind and centralized SQCT assessment was carried out in order to calculate both Goh and Taouli scores. An operator-independent analysis of all CTs with an open-source software (i.e. Horos), provided the QCT indexes. Patients were clustered in cohorts according to ILD extent. Differences in QCT indexes distribution were analyzed using non-parametric tests.

Results: 102 consecutive SS patients were enrolled. ILD prevalence was 36% (36/102). There was a difference in QCT indexes' distribution in SS-ILD versus SS without ILD ($p < 0.001$). Moreover, SS-ILD patients with an ILD >20% (according to Goh score) had QCT indexes statistically different from those with a limited ILD extension ($p<0.001$). QCT indexes have a moderate to good correlation with Goh and Taouli scores (from 0.44 to 0.65; absolute numbers, +/-; $p < 0.001$). To value its potential of diagnosis, ROC curves were calculated, achieving several of them values of AUC > 0.7; the best QTC index was: tSkew AUC 0.87 (95CI 0.78-0.95), $p< 0.001$; cut-off ≤ 2.72 - sensitivity 0.81 (95CI 0.65-0.9), specificity 0.82 (95CI 0.7-0.89).

Conclusion: QCT indexes are a serious alternative to visual scorings in ILD related to autoimmune diseases. This innovative tool will open up a potential research area in SS as it appears able to select ILD patients with an extensive lung impairment and likewise a worse prognosis. We are confident that in the next future, QCT will have a pivotal role in the diagnosis, monitoring and treatment pathway of ILD associated to SS.

REFERENCES:

[1] Silva M, Milanese G, Seletti V, Ariani A, Sverzellati N. Pulmonary quantitative CT imaging in focal and diffuse disease: current research and clinical applications. Br J Radiol 2018; 91: 20170644.

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THU0601 SALIVARY GLAND ULTRASONOGRAPHY FOR SJÖGREN SYNDROME AND SICCA SYMPTOMS WITH EVALUATION THE DIFFERENT IMAGE PARAMETERS AND BIOPSY RESULT

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Background: Sjögren's syndrome involves multiple organs, especially the lacrimal and salivary glands. Salivary gland ultrasonography (SGUS) is quick and easily accessible, which provides visibility of salivary glands. Currently, there were several scoring systems for SGUS. Acuity for different image parameters remained unclear, and these parameters including heterogeneity of glands, clearance of posterior border, size of glands, fibrosis bands and size of vacuoles in the glands. Each gland would be scored through these parameters which may rank from 0 to 3 or 0 to 4. The weight of different parameters have not been clarified.

Objectives: To evaluate the effectiveness of different image parameters of SGUS in evaluation Sjögren's syndrome.

Methods: Total SGUS with 56 patients were retrospectively evaluated, who also underwent minor salivary gland biopsy. SGUS was conducted by a 10MHz-13MHz linear probe at both parotid and submandibular glands. Each gland was scored from 0 to 4 according to the scoring scale proposed previously. The total maximum score was 16. Heterogeneous structure, fibrosis band and size of vacuoles were evaluated for each gland. Minor salivary gland biopsy was evaluated with Chisholm-Mason grade, ranging from 1-4.

Results: The distribution of minor salivary gland biopsy was grade 1 (28.6%), grade 2 (14.3%), grade 3 (19.6%), and grade 4 (37.5%). The average SGUS score was 6.00 for grade 1, 6.38 for grade 2, 7.00 for grade 3 and 10.00 for grade 4 ($p=0.019$). Evaluation different image parameters for each gland, heterogeneous structure and fibrosis bands revealed significant in linear regression of parotid gland score (heterogeneous structure $p=0.043$ for left side, $p=0.025$ for right side; fibrosis bands $p<0.001$ for both sides) but size of vacuoles did not reveal significant. Fibrosis bands and size of vacuoles revealed significant in the linear regression model of submandibular glands (both <0.001 in both sides). Final pathology grade correlated with fibrosis bands of left side parotid gland ($p=0.006$), fibrosis bands of both sides of submandibular glands ($p=0.006$ for left side, $p=0.001$ for right side), and size of vacuoles among submandibular glands ($p=0.003$ for left side, $p=0.012$ for right side). In regarding to the different image parameters, the biopsy result correlated well with total summation of SGUS ($p=0.004$).

Conclusion: Different image parameters had different significance for representing the gland conditions. For parotid glands, fibrosis bands and heterogeneous structure were main parameters. For submandibular glands, fibrosis bands and size of vacuoles accounted for the change of glands. SGUS correlated with final pathology result.

REFERENCES:

[1] Jousse-Joulin S, et al. Rheumatology (Oxford). 2016;55:789-800.
[2] Takagi Y, et al. Ann Rheum Dis 2010;69:1321-4.
[3] Seror R, et al. Ann Rheum Dis 2011;70:968-72.

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THU0602 THE ROLE OF INFRARED THERMOGRAPHY IN THE ASSESSMENT OF PERIPHERAL VASCULOPATHY AND IN THE THERAPEUTIC MANAGEMENT OF SYSTEMIC SCLEROSIS PATIENTS TREATED WITH SYNTHETIC PROSTANOIDS

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Background: Skin lesions represent the leading feature of systemic sclerosis (SSc), with Raynaud's phenomenon (RP) the most frequent and early clinical manifestation of the disease. Digital vasculopathy severely affects SSc patients, lowering their quality of life and negatively impacting on their daily functions. Digital ulcers is associated with poor cardiovascular prognosis and decreased survival rate [1]. Nevertheless, standardized treatment strategies and non-invasive tools for the management of RP and SSc skin manifestations are badly needed.

Objectives: The aim of this study was a) to evaluate the efficacy of infrared thermography in the assessment of peripheral vasculopathy in a cohort of SSc patients treated with cyclic intravenous infusions with synthetic prostanoids b) to identify those patients who might benefit from an intensified infusional treatment protocol with prostanoids.

Methods: Twenty-six SSc patients [2], attending our Department for their routinely 28-days apart intravenous therapy with prostanoids (Iloprost) based on the presence of severe secondary RP and/or digital ulcers, were enrolled in this study. Thermographic evaluation of both hands was made at baseline (T0), and at days 14 and 28 after the first prostanoid infusion (named T1 and T2, respectively). Statistical analyses have been performed and a p-value <0.05 was considered statistically significant.

Results: A total of 26 SSc patients, 24 (92.3%) female, mean age 65.3 ±12.6 yrs, mean disease duration at time of data collection 12.4±6.6 years, were prospectively enrolled in the study. Among them, 15 patients (57.7%) presented with limited cutaneous SSc, while 11 patients (42.3%) showed an extra-cutaneous form of the disease. Demographic, clinical, and laboratory characteristics of the patients included in the study are detailed in Table 1.

	Total of patients (n=26)	Skin-limited forms of SSc (n=15)	SSc with systemic involvement (n=11)
Age, years (mean, SD)	65.3 ±12.6	69.6	61
Female (n,%)	24 (92.3)	13	11
Disease-duration, years (mean, SD)	12.4 ±6.6	12	13
Interstitial lung disease (n,%)	7 (27)	0	7
Pulmonary hypertension (n,%)	2 (8)	0	2
Cutaneous telangiectasia (n,%)	14 (54)	8	6
Skin thickening (n,%)	25 (96)	15	10
Digital ulcers (n,%)	11 (42.3)	4	7
Raynaud's phenomenon (n,%)	26 (100)	15	11
Articular involvement (n,%)	14 (54)	7	7
Cardiac involvement (n,%)	2 (8)	0	2
Gastrointestinal involvement (n,%)	1 (4)	0	1
Abnormal nailfold capillaroscopy (n,%)	26 (100)	15	11
ANA positivity (n,%)	26 (100)	15	11
ENA positivity (Scl70) (n,%)	11 (42)	6	5

Table 1. Characteristics of the patients included in the study.
SSc means Systemic Sclerosis; ANA, antinuclear antibodies; ENA, extractable nuclear antigen.

The thermographic assessment showed a substantial stability of the temperature values when comparing T0 and T1 (mean differences of the right hands 0.4 ±5.6; mean differences of the left hands 1.2 ±4.5), while they are significantly reduced when comparing T1 and T2 (mean differences of the right hands -3.1 ± 9.3, p=0.049; mean differences of the left hands -3.4 ±8.5, p=0.012 respectively) (Figure 1A). When stratifying according to clinical manifestation, a higher differences in temperature variations were observed between T1 and T2 in SSc patients with systemic involvement, when compared to those with limited cutaneous SSc (mean of the differences of the right hands -5.0 ±11; mean of left-hands differences -4.9 ±11.5 Vs. mean right-hands differences -2.5 ±11; mean left-hands differences -3±8.6; p=0..035 respectively) (Figure 1B).

Conclusion: Thermography could represent a reliable, non-invasive, manageable and cost-effective method for the assessment and monitoring of peripheral vasculopathy in patients with SSc. These data also show that SSc patients with systemic involvement could benefit more from an intensified infusion protocol with prostanoids compared to SSc patients with a limited skin form of the disease. Thermography has shown excellent potential to be a reliable and objective outcome measures to facilitate clinical trials of novel treatments SSc-related RP.

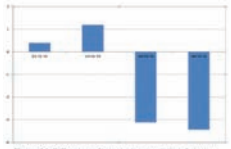


Figure 1A. Differences of temperatures variations between T0 and T1 (left) and between T1 and T2 (right).

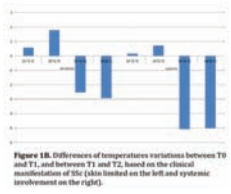


Figure 1B. Differences of temperatures variations between T0 and T1, and between T1 and T2, based on the clinical manifestation of SSc (skin limited on the left and systemic involvement on the right).

REFERENCES:
[1] Mihai C, et al. Digital ulcers predict a worse disease course in patients with systemic sclerosis. Ann Rheum Dis 2016;75:681–6.
[2] van den Hoogen F, et al. 2013 classification criteria for systemic sclerosis: an ACR/EULAR collaborative initiative.Arthritis Rheum. 2013 Nov;65 (11):2737-47.

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THU0603 SUITABILITY OF PET-CT IN REFRACTORY POLYMYALGIA RHEUMATICA

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Background: Polymyalgia rheumatica (PMR) is characterized by pain in the shoulders and hips, elevation of acute phase reactants and a rapid response to treatment with corticosteroids. Currently, there is no specific test for its diagnosis, and it presents a wide differential diagnosis. Positron Emission Tomography - Computed tomography (PET-CT) is a non-invasive technique, capable of measuring metabolic activity by locating and quantifying glucose consumption. The use of PET-CT in the study of neoplastic, infectious or inflammatory processes suggests that it may be a suitable technique for the study of the differential diagnosis of patients with PMR. It is unknown if there are differences in the result of the technique in patients with debut PMR vs. patients with cortico-resistant PMR.

Objectives: To describe the findings of PET-CT in patients with PMR.
To analyze if there are significant differences between the results of patients with onset PMR and those of cortico-resistant PMR patients.

Methods: This is a cross-sectional prospective study performed in a cohort of patients with PMR. Out of all patients with PMR who do follow up treatment in our centre, the patients selected for this study included those who underwent a PET scan at the time of diagnosis and those who presented corticosteroid resistance (patients who did not respond to conventional therapy with corticosteroids or with a relapse with doses <7.5mg/day of prednisone or equivalent). Demographic, epidemiological data of the disease, treatment, as well as analytical parameters (CRP, ESR, Hematological and Biochemical) were collected from all the patients at the time the PET-CT was performed.
For the categorical variables, the chi-square test or Fisher's exact test were used, as appropriate. In the case of quantitative variables, we used the comparison of the mean values, by means of a "t" test. The level of statistical significance was established for those values of p <0.05.

Results: 103 patients with a PMR diagnosis who had undergone a PET-TC were included, out of the total number of patients that we visited in our service. 52 (50.4%) patients had an onset PMR and 51 (49.9%) had PMR refractory to treatment. The demographic, clinical and serological characteristics of the patients at the time of PET-CT are shown in Table 1.
The PET-CT showed a distribution of uptake compatible with the diagnosis of PMR in 73 (70.9%) patients, vasculitis of large vessels in 16

Table 1 ANA positive rate and main karyotype distribution in AID group and health controls

Gr;o;up;	n;	ANA karyotypes;								ANA negativity
		H;o;mo;g;e;n;e;o;us;	p;ar;t;icl;e;	ce;n;t;r;o;me;r;e;	n;ucl;e;o;l;ar;	cytoplasmic granular	nuclear membrane	mixe;d;	o;t;h;e;r;	
SLE	2034	337(16.6)*	1328 (65.3)	23(1.1)	28(1.4)	86(4.2)	9(0.4)	23(1.1)	10(0.5)	190(9.3)
RA	973	186(19.1)	255(26.2)	16(1.6)	10(1.0)	49(5.0)	1(0.1)	0(0.0)	8(0.8)	448(46.0)
SS	309	34(11.0)	181(58.6)	13(4.2)	8(2.6)	15(4.9)	3(1.0)	10(3.2)	3(1.0)	42(13.6)
PSS	155	22(14.2)	27(17.4)	28(18.1)	42(27.1)	8(5.2)	2(1.3)	9(5.8)	2(1.3)	15(9.7)
MCTD;	39	3(7.7)	30(76.9)	1(2.6)	0(0.0)	2(5.1)	0(0.0)	0(0.0)	0(0.0)	3(7.7)
PBC	137	1(0.7)	6(4.4)	17(12.4)	2(1.5)	36(26.3)	15(10.9)	46 (33.6)	5(3.6)	9(6.6)
AIH;	57	3(5.3)	13(22.8)	7(12.3)	0(0.0)	0(0.0)	0(0.0)	3(5.3)	2(3.5)	29(50.9)
AID;	3704	586(15.8)	1840 (49.7)	105(2.8)	90(2.4)	196(5.3)	30(0.8)	91(2.5)	30(0.8)	736(19.9)
H;e;al;t;h;Y;s;ubje;ct; s;	1073	14(1.3)	75(7.0)	3(0.3)	10(0.9)	23(2.2)	1(0.1)	2(0.2)	3(0.3)	942(88.5)

Note: The mixed type contains more than two karyotypes, and other types include spindle, centrosome, Golgi, cytoplasmic fiber, etc.* refers to number (percentage).

(15%) and contributed in the diagnosis of neoplastic processes in 5 (4.8%). Table 2 shows the final diagnoses.
When analyzing the results of PET in patients with onset PMR vs. those who are corticosteroids resistant, no significant differences were observed in the final diagnoses (p = 0.078).

Table 1. Patient's features

Women, n (%)	73 (70.9%)
Disease duration (months), mean ± SD	24 ± 41.92
Shoulder pain, n (%)	100 (97.1%)
Hip pain, n (%)	89 (86.4%)
Amaurosis, n (%)	5 (4.9%)
Temporal artery tenderness, n (%)	2 (1.9%)
ESR (mm/s), mean ± SD	55.92 ± 31.09

Table 2. Diagnoses

	TOTAL	Onset PMR	Cortico- resistant PMR
PMR, n (%)	73 (70.9)	37 (50.7%)	36 (49.3)
Large vessel vasculitis, n (%)	16 (15.5)	6 (37.5)	10 (62.5)
Neoplasia, n (%)	5 (4.8)	5 (100)	0 (0)
EORA associated PMR, n (%)	6 (5.8)	2 (33.3)	4 (66.7)

Conclusion: PET-CT confirms the diagnosis of PMR in the significant majority of patients included in the study. In this cohort, PET-CT allowed to diagnose vasculitis of large vessels and neoplasms in 16% and 5% of the patients respectively. We did not observe differences in the PET findings in those patients who underwent a PET at the time of diagnosis vs. those who are corticosteroid resistant.

REFERENCES:

[1] Ann Nucl Med. 2018 Oct;32(8):573-577;
[2] Semin Nucl Med. 2017 Jul;47(4):408-424;
[3] Br J Radiol. 2017 Aug;90(1076):20170198

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THU0604 CARPAL TUNNEL SYNDROME: CAN ULTRASOUND PREDICT RESPONSE TO STEROID INJECTION?

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Background: Carpal tunnel syndrome (CTS) is the commonest nerve entrapment disorder of the upper limb. Diagnosis is often clinical, based on a suggestive history and physical examination. Neurophysiological studies correlate closely with clinical evaluation. The use of ultrasound has been evaluated, and a feature which consistently supports a clinical diagnosis of CTS is increased cross sectional area (CSA) of the median nerve within the carpal tunnel. Local injection with corticosteroid is generally accepted as the next step in those who remain symptomatic after conservative treatment with splinting and nonsteroidal anti-inflammatory drugs. If this is unsuccessful referral for consideration of surgery should be considered.
Objectives: To evaluate the utility of ultrasound in the assessment of CTS and identify predictors of response to injection.
Methods: Patients were recruited via primary care referrals to the rheumatology department. Inclusion criteria were age over 18 years, appropriate symptoms in the distribution of the median nerve for at least 3 months, and positive nerve conduction studies (NCS). Patients with evidence of thenar atrophy were excluded. At initial review a full symptom and medical history was taken. A Boston Carpal Tunnel Questionnaire was completed, along with visual analog scale (VAS). Ultrasound assessment was carried out by a rheumatology physician who was blinded to the above information. CSA of the median nerve was measured at the level of the proximal third of the pronator quadratus muscle and the largest CSA within the carpal tunnel. The presence or absence of tenosynovitis, Doppler signal and a bifid median nerve were noted. Steroid injection was carried out under indirect ultrasound guidance with 20mg depomedrone. Follow-up assessment was carried out 12 weeks post-injection. Repeat ultrasound scan was performed to measure the CSA of the median nerve, as before. Repeat Boston Questionnaire and VAS were recorded. After the second assessment those who had not responded adequately were referred on for consideration of surgical release.
Results: 52 patients attended for initial assessment, with 47 patients reattending for follow up. 53% of patients were discharged at follow up; the remainder were referred for consideration of surgery. 78.9% of patients met the criteria for defining CTS with a median nerve CSA 0.1cm^2, with 77% meeting this at the entrance to the carpal tunnel, and 55.8% at the level of the pronator quadratus muscle. A bifid nerve was noted in 12 patients.
There was no statistically significant relationship between the initial size of the median nerve on ultrasound and the change in Boston score. There was a statistically significant correlation between a decrease in the size of the median nerve at the entrance to the carpal tunnel and an improvement in the Boston score (r=0.42, p-value 0.003). There was no correlation between change in median nerve measurement and final outcome (discharged or referred to surgery). There was no relationship between the degree of entrapment on NCS and pre-test Boston score. There was a significant change in the Boston score of 0.944 post-injection (95% CI 0.41-1.48, p-value 0.001). There was a statistically significant change in the VAS score of 9.87 post-injection (95% CI 0.78-18.95, p-value 0.03). No patients demonstrated evidence of surrounding tenosynovitis or positive power doppler signal.
Conclusion: There is an overall improvement in symptoms of CTS, based on the Boston questionnaire, following corticosteroid injection. There is a clear role for the use of ultrasound to confirm diagnosis of CTS in symptomatic patients by measuring the CSA of the median nerve at the entrance to the carpal tunnel. There are no definite ultrasound or clinical prognostic indicators of response to injection. References:
Disclosure of Interests: : Cathy Donaghy: None declared, Ashley Elliott Speakers bureau: Novartis, Adrian Pendleton: None declared, Claire Benson: None declared, Kerry Aston: None declared, Aidan O'Neill: None declared, Roger Stewart: None declared, Mark Leith: None declared, Colette Beattie: None declared
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THU0605 SHEAR WAVE ELASTOGRAPHY MUSCLE STIFFNESS MAY DIMINISH AFTER CORTICOSTEROID TREATMENT

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Background: The use of corticosteroids is associated with several adverse effects including corticosteroid-induced myopathy (CIM). CIM may cause structural alterations to the myofibres, which support the hypothesis of altered muscle stiffness as seen in histological and preclinical studies [1,2]. Shear wave elastography is an ultrasound technology that can quantify tissue stiffness non-invasively.
Objectives: To investigate the changes in muscle stiffness as measured by SWE and muscle strength tests in giant cell arteritis (GCA) patients exposed to high doses (40–60 mg/day) of corticosteroid treatment.
Methods: Fourteen GCA patients (4 males, mean age 68.2±4.3 years) were recruited and evaluated at baseline, after 3 months and 6 months on prednisolone. Shear wave velocity (SWV), as a surrogate for tissue stiffness, and muscle strength were evaluated at each visit. Baseline data were compared to frequency-matched healthy controls. Linear mixed models were used to analyse the longitudinal data.
Results: The patients did not have a significantly different muscle SWV to healthy controls (all p >0.05) at baseline. However, after 3 months, the quadriceps and hamstrings SWV decreased on average by 14% (range 8.3%–17.3%; p=0.001) and after 6 months decreased by 18% (range 10.2%–25.3% p<0.001). The biceps brachii SWV did not change with time (p=0.92) (Fig 1). The baseline, 3-months and 6-months mean SWV for the vastus lateralis were 1.62 m/s, 1.40 m/s and 1.31 m/s

respectively (p<0.001). Muscle strength was generally preserved at follow-up. However, there were moderate to strong correlations (r= 0.54–0.96) between weaker muscle strength at follow-up and greater reduction in SWV.

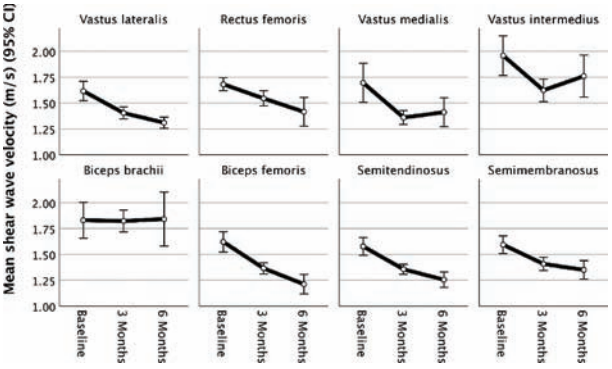


Figure 1. Muscle stiffness changes in the quadriceps, hamstrings and biceps brachii.

Conclusion: The GCA patients showed a significant loss of muscle stiffness after 3 and 6 months of corticosteroid treatment. With further validation in larger samples, shear wave elastography may be useful for detecting subclinical CIM.

REFERENCES:

[1] -Alev, K., et al., Glucocorticoid-Induced Changes in Rat Skeletal Muscle Biomechanical and Viscoelastic Properties: Aspects of Aging. J Manipulative Physiol Ther, 2018. 41(1): p. 19-24.
[2] - Schakman, O., et al., Glucocorticoid-induced skeletal muscle atrophy. The International Journal of Biochemistry & Cell Biology, 2013. 45(10): p. 2163-2172.

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THU0606 PROLIFERATIVE GLOBULAR SYNOVITIS, A CHARACTERISTIC ULTRASONOGRAPHIC PATTERN OF SEROPOSITIVE RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) have a different ultrasound (US) patterns. Synovial changes are characteristic of RA patients and soft tissue changes are more frequently found in PsA. However, no previous studies have analysed if US findings differ between seropositive and seronegative RA patients.
Objectives: To analyse differences in the ultrasound pattern among patients with seropositive and seronegative RA. To assess if proliferative globular synovitis is characteristic of seropositive RA.
Methods: Retrospective Analysis. We collected clinical, epidemiological and ultrasound images of patients with RA who met American College of Rheumatology/European League Against Rheumatism 2010 criteria[1] with bilateral carpal and hand ultrasonography carried out during the last five years. Synovial hypertrophy (SH) and Power Doppler signal (PD) in wrist and hand (1-5 metacarpophalangeal [MCP]) were evaluated. We calculated the SH score (sum of the SH degrees of each joint), PD (sum of the PD degrees of each joint) and the total score (sum of the score of SH and PD) for each patient. We also evaluated the presence of proliferative globular synovitis, defined as big synovial hypertrophy with exophytic growth and a convex upper limit.
Results: 145 RA patients were collected. 80% were women. Mean age was 59.06 (14.8) years and the mean time of disease evolution was 114.6 (112.8) months. 68.3% were RF positive and 74.5% ACPA positive. Overall, 115 of the 145 (79.3%) patients were seropositive for RF/ACPA. 53.1% had radiographic erosions, 73.1% used conventional synthetic Disease-modifying drugs (DMARDs), 29.7% biological therapy, and 57.2% low doses of corticosteroids (<5 mg prednisone). The mean DAS28 was 2.81 (1.14), the number of swollen joints was 3 (3.4), and the C reactive protein (CRP) was 0.99 mg/dl (1.6).
No significant differences between seropositive and seronegative patients in terms of disease activity (swollen joints count [SJC], tender joint count [TJC], CRP, DAS28), treatment (use of corticosteroids, DMARDs, biological), time of evolution or US scores (SH, PD and total scores) were found. Globular synovitis was present in 62% and 13.7% of seropositive and seronegative RA patients, respectively (p<0.0001).
Globally, 75 (51.7%) out of 145 patients had "globular" synovitis by US (Figure 1). 71 out of 75 patients were FR/ACPA positive (94.6%). Only four patients with seronegative RA had this US pattern (p <0001). Furthermore, patients with "globular" synovitis had more erosions (72% vs 33%, p <0.0001), higher SJC (3.3 vs 2.5, p = 0.013) and higher SH and PD scores (p=0.0001).
Conclusion: The presence of proliferative globular synovitis was significantly associated with the presence of RF/ACPA in patients with RA. This US pattern identified a subgroup of RA patients with poor prognosis: more erosions and greater inflammatory activity both at clinical and ultrasound level.

REFERENCES:

[1] Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Hawker G, et al. 2010 *rheumatoid arthritis classification criteria: an American College of Rheumatology/European League against rheumatism collaborative initiative*. Arthritis Rheum. 2010; 62(9):2569-81.

Disclosure of Interests: Ana Belén Azuaga-Piñango: None declared, Beatriz Frade-Sosa: None declared, Roberto Gumucio: None declared, Katherine Cajiao: None declared, Stanislava Mandelikova: None declared, Raul Castellanos-Moreira Speakers bureau: MSD, Lilly, Virginia Ruiz: None declared, Raimón Sanmartí Speakers bureau: PFIZER, SANOFI, LILLY, MSD, UCB, NOVARTIS, JANSSEN, Juan D. Cañete: None declared, Julio Ramirez: None declared
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THU0607 CORRELATION BETWEEN ULTRASOUND AND STANDARD RADIOGRAPHY AND BETWEEN ULTRASOUND AND CLINICAL DATA IN RHEUMATOID ARTHRITIS

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Background: Early diagnosis in Rheumatoid Arthritis (RA) is essential in order to quickly introduce a background treatment to prevent joint destruction. In recent years, ultrasound has become an essential part of the initial assessment of polyarthritis because of its superior sensitivity to clinical examination and standard imaging for the investigation of synovitis, tenosynovitis and erosions.
Objectives: To evaluate concordance between clinical examination, standard radiography and joint ultrasonography in a heterogeneous group of patients with RA.
Methods: 40 patients were included in a prospective, transverse and monocentric study conducted in the radiology department of Farhat Hached University Hospital in Sousse over a period of 03 months whatever the level of activity of the disease, the duration of evolution or the treatment received. For each patient, 24 joints were evaluated for a total of 960 joints. Synovitis was scored using clinical examination, B-mode ultrasound, and pulsed Doppler. Concordance between joint swelling assessed by clinical examination, synovial thickening assessed by E-B and inflammation assessed by PD was evaluated by calculating the Kappa coefficient (k). A comparison between the reliability of ultrasound versus standard imaging was evaluated for the detection of bone erosions. The onset of RA, stage, and ultrasound score were assessed by Spearman coefficient.
Results: 960 joints were studied. The mean age was 54.6 years. The sex ratio was 0.29. The mean duration of illness was 3.4 months. Clinical examination revealed 207 active synovitis versus Ultrasonography: 474 active synovitis. The concordance between clinical examination and ultrasound was very low at the metacarpophalangeal (MCP) (<0.1), low at

the proximal interphalangeal (PIP) (0.26) and moderate at wrist (0, 56), ultrasound detected more erosions than standard radiography (56% versus 17%), and a statistically significant correlation was observed between the onset of RA, its stage, and the ultrasound score.
Conclusion: Evaluation of a heterogeneous group demonstrated that ultrasound completes clinical examination information, particularly at the PIP and MCP levels, and detects erosions earlier than standard imaging.
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THU0608 CAPILLAROSCOPIC DIFFERENCES IN PRIMARY BILIARY CHOLANGITIS WITH OR WITHOUT SCLERODERMA AND RAYNAUD'S PHENOMENON, A PRELIMINARY STUDY

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Background: A high proportion of capillaroscopic alterations have been reported in patients with Primary Biliary Cholangitis (PBC) (1). Association with an abnormal capillaroscopic pattern has been described in patients with PBC and Raynaud's phenomenon (RP), possibility for anticentromere antibodies (ACA) and overlap with another systemic autoimmune disease, the most frequent being Systemic Sclerosis (SSc) (association with a prevalence up to 17% of PBC patients called Reynolds Syndrome) (2). However, studies are scarce and not very detailed in terms of the differential capillaroscopic findings between patients with PBC with/without SSc and with/without RP.
Objectives: To analyze the differences between clinical, serologycal and capillary morphological alterations observed in three different groups of patients with PBC: patients with PBC alone (PBC-A), patients with PBC and RP (PBC-RP) and patients with Reynolds Syndrome (PBC-RS).
Methods: Periungual capillaroscopy was performed on 12 patients with PBC-A, 10 with CBP-RP and 13 with PBC-RS, who received follow-up in our systemic diseases and hepatology monographic outpatients. Capillaroscopy was made with USB Digital Microscope Dino-Lite ® epiluminiscence video. The capillaroscopic alterations were according to a semiquantitative method. All patients were given a detailed clinical evaluation. Variables related to clinical, serological and capillaroscopic parameters were collected. A comparative study was done.
Results: Of the 36 patients analyzed, 32 (88.9%) were women, with no sex differences between the three groups. The median age at PBC diagnosis was 50 + -12.8 years in PBC-A group, 60.5 + -15 years in PBC-RP and 62 years in PBC-RS, showing significant difference between the first group and the other two (p 0.039). 14 patients had other systemic diseases: 1 hemolytic anemia, 1 SLE, 2 Psoriasis, 1 PTI and 9 Sicca. The only clinical parameter with significant difference between the three groups was association with Sicca: 3 (25%) PBC-A, 5 (50%) PBC-RP and 12 (85.7%) PBC-RS, p 0.002. Twenty five (73.5%) patients had positive AMA, with no differences between groups. All 11 patients who had ACA were from the PBC-RS group. Statistically significant differences observed between the capillaroscopy parameters were the presence of capillary dilatations [5 (41.7%) PBC-A, 5 (50%) PBC-RP, 11 (84.6%) PBC-RS, p 0.03] and pathological hemorrhages [1 (8.3%) in PBC-A, 2 (22.2%) PBC-RP, 11 (78.6%) PBC-RS, p <0.001] as well as the presence of a different capillaroscopic pattern (p <0.001): normal or nonspecific in 9 (75%) of PBC-A, 4 (44.4%) PBC-RP and 2 (15.4%) PBC-RS; connective tissue disease suggestive pattern in 3 (25%) of PBC-A, 5 (55.6%) of PBC-RP and 1 (7.7%) of PBC-RS; sclerodermiform pattern in 10 (76.9%) PBC-RS, and none of the other two groups. We did not find significant differences in the presence of simple tortuosities, complex tortuosities, branched capillaries or capillary loss. No capillaroscopic parameters correlated with other systemic diseases.
Conclusion: This preliminary study shows an evolutionary trend in some clinical (age at PBC diagnosis, sicca asocciation) and capillaroscopic parameters (capillary dilatation, hemorrhages, general capillaroscopic pattern) in patients with PBC-A, PBC-RP and PBC-RS, which may suggest three different phenotypic expressions of the same pathogenic process.

REFERENCES:

[1] Fonollosa V, et al. Morphologic capillary changes and manifestations of connective tissue diseases in patients with primary biliary cirrhosis. Lupus. 2001;10(9):628-31.
2. Zheng B, et al. Prevalence of Systemic Sclerosis in Primary Biliary Cholangitis Using the New ACR/EULAR Classification Criteria.

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THU0609 ULTRASOUND AS A USEFUL TOOL IN THE DIAGNOSIS OF RHEUMATOID ARTHRITIS IN PATIENTS WITH UNDIFFERENTIATED ARTHRITIS

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Background: Nowadays, rheumatologists face challenges in finding an effective method to classify and treat patients with undifferentiated arthritis (UA). There is a need for new tools that could ensure accurate characterization of inflammatory processes in these patients.
Objectives: To investigate if a characterization of UA patients using US may help to fulfill the 2010 ACR/EULAR RA classification criteria in a real-life cohort.
Methods: We conducted a cross sectional study in two rheumatology care clinics. Patients not fulfilling the 2010 ACR/EULAR RA criteria were included. On the examination day, all patients underwent a physical examination, radiographs and US. The 7-joint US score (US 7) was adopted to scan all patients. US was performed according to EULAR criteria and interpreted by OMERACT definitions. Greyscale and power Doppler synovitis and tenosynovitis were scored. Bone erosions were also evaluated during the US examination.
Results: A total of 204 patients were included. The diagnosis was modified from UA to RA in 86 (42.1%) patients. The greater proportion of synovitis detected by US was the main parameter that allowed changing the diagnosis from UA to RA, and modified the final score of the 2010 ACR/EULAR classification criteria, from a mean (±SD) of 4.6 (0.5), by clinical examination, to 6.5 (0.6) by US. The changes in the score of the 2010 ACR/EULAR classification criteria were from score 4 to score 6 in 6 (7%) patients; from 4 to 7 in 24 (27.9%) patients; from 5 to 6 in 42 (48.8%) patients; from 5 to 7 in 5 (5.8%) patients and from 5 to 8 in 5 (5.8%) patients.
In addition to synovitis, a wide range of tenosynovitis and bone erosions were detected by US. Synovitis was more frequently detected in 2ndMCPj followed by 2ndMTPj and 5thMTPj. The tendons of the wrist, 2nd and 3th finger were the most affected. In relation to bone erosions, 2ndMCPj and 5thMTPj where the joints with more proportion of anatomical damage.
Conclusion: US demonstrated to be useful to help accurately classify as RA, patients previously diagnosed with UA.
Disclosure of Interests: Marwin Gutierrez: None declared, Chiara Bertolazzi: None declared, Edwin Castillo: None declared, Denise Clavijo Cornejo: None declared, Luis Carlos Rodriguez Delgado: None declared, Jaime Mendoza Torres: None declared, Carlos Pineda: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB
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THU0610 ANALYSIS OF ANTINUCLEAR ANTIBODY ANTIBODIES POSITIVITY AND THEIR MAJOR KARYOTYPES IN PATIENTS WITH AUTOIMMUNE DISEASES AND HEALTHY SUBJECTS

Qiujing Wei, Yutong Jiang, Jiewen Xie, Jun Qi, Jieruo Gu. *the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

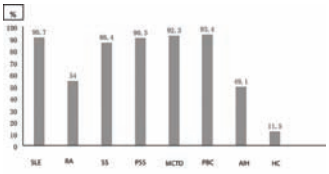
Background: Autoantibodies, especially antinuclear antibodies (ANA), play an important role in the diagnosis and differential diagnosis of autoimmune disease (AID), disease monitoring, efficacy observation and pathogenesis research.
Objectives: Our aim was to investigate the rate of ANA positivity and their major karyotypes in different AIDs and healthy controls.
Methods: The distribution and positive rate of Antinuclear antibody (ANA) karyotypes detected by indirect immunofluorescence in 3704 patients with AID and 1073 healthy subjects were retrospectively analyzed.
Results: The positive rate of ANA in different AID groups was 90.7% (1845/2034) in SLE, 54% (525/973) in RA, 86.4% (267/309) in SS,

90.3% (140/155) in pSS, 92.3% (36/39) in MCTD, 93.4% (128/137) in PBC and 49.1% (28/57) in the AIH group. The positive rate of ANA in the health subjects was 11.5% (123/1073), see Figure 1.
Totally, the positive rate of ANA in the AID group was 80.1% (2967/3704). The karyotypes were detected as homogeneous type (15.8% (586/3704)), nuclear particle type (49.7% (1840/3704)), cytoplasmic particle type (5.3% (196/3704)), mixed type (2.8% (91/3704)) which was mainly composed of nuclear membrane/cytoplasmic granules, more common in PBC. See Table 1. The karyotype of ANA in the health group was mainly homozygous (7.0% (75/1073)).

Group	n	ANA karyotypes								ANA negativity
		Homogeneous	particle	centromere	nucleolar	cytoplasmic granular	nuclear membrane	mixed	other	
SLE	2034	337(16.6)*	1328(65.3)	23(1.1)	28(1.4)	86(4.2)	9(0.4)	23(1.1)	10(0.5)	190(9.3)
RA	973	186(19.1)	255(26.2)	16(1.6)	10(1.0)	49(5.0)	1(0.1)	0(0.0)	8(0.8)	448(46.0)
SS	309	34(11.0)	181(58.6)	13(4.2)	8(2.6)	15(4.9)	3(1.0)	10(3.2)	3(1.0)	42(13.6)
PSS	155	22(14.2)	27(17.4)	28(18.1)	42(27.1)	8(5.2)	2(1.3)	9(5.8)	2(1.3)	15(9.7)
MCTD	39	3(7.7)	30(76.9)	1(2.6)	0(0.0)	2(5.1)	0(0.0)	0(0.0)	0(0.0)	3(7.7)
PBC	137	1(0.7)	6(4.4)	17(12.4)	2(1.5)	36(26.3)	15(10.9)	46(33.6)	5(3.6)	9(6.6)
AIH	57	3(5.3)	13(22.8)	7(12.3)	0(0.0)	0(0.0)	0(0.0)	3(5.3)	2(3.5)	29(50.9)
AID	3704	586(15.8)	1840(49.7)	105(2.8)	90(2.4)	196(5.3)	30(0.8)	91(2.5)	30(0.8)	736(19.9)
Healthy subjects	1073	14(1.3)	75(7.0)	3(0.3)	10(0.9)	23(2.2)	1(0.1)	2(0.2)	3(0.3)	942(88.5)

Note: The mixed type contains more than two karyotypes, and other types include spindle, centrosome, Golgi, cytoplasmic fiber, etc.* refers to number (percentage).

Figure 1 ANA positive rate in difference AID patients and healthy subjects

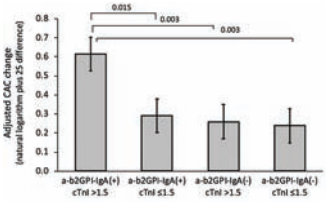


Conclusion: There are differences in ANA positive rates among patients with different AIDs. Some mixed karyotype analyses may provide important evidence for the diagnosis of PBC and AIH. Healthy subjects can have partial ANA positivity which is predominantly homogenous.
Disclosure of Interests: None declared
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THU0611 SERUM HIGHLY-SENSITIVE CARDIAC TROPONIN-I AND ANTI-BETA2-GLYCOPROTEIN-1 IGA ANTIBODIES AT BASELINE PREDICT CORONARY PLAQUE PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: We recently reported that serum levels of highly-sensitive cardiac troponin-I (hs-cTnI)- a specific structural myocardial biomarker-associated with occult coronary plaque presence, burden and long-term cardiovascular events in patients with rheumatoid arthritis (RA). We further demonstrated that presence of IgA antibodies against beta2-glycoprotein-1 (a-b2GPI-IgA, an apolipoprotein readily expressed in human atherosclerotic plaque) associated with baseline coronary artery calcium (CAC) scores and independently predicted CAC progression in patients with RA.
Objectives: We here explored whether baseline evaluation of both hs-cTnI and a-b2GPI-IgA better predicts CAC progression than either of them in isolation.
Methods: Ninety five participants with a baseline plaque evaluation by coronary computed tomography angiography (CCTA) underwent follow-up assessment within 6.9±0.3 years. Coronary artery calcium (CAC) was quantified by the Agatston method. Hs-cTnI and a-b2GPI IgA Ab were assessed on the day of baseline CCTA; the latter were reconfirmed 12 weeks later, if positive. CAC change was evaluated with the MESA method as the natural logarithm plus 25 difference [(ln $CAC_{(follow-up)}$+ 25) – (ln $CAC_{(baseline)}$ + 25)]. Generalized linear models evaluated the effect of hs-cTnI, a-b2GPI-IgA and their interaction on CAC change. Models were adjusted for age, hypertension, waist-to height ratio (obesity indicator), cumulative inflammatory burden (time-averaged C-Reactive protein), total prednisone dose and duration of statin exposure from baseline to follow-up scan.
Results: Baseline hs-cTnI was higher in a-b2GPI-IgA positive compared to negative patients [median (IQR) of 1.9 (1.6-2.6) vs. 1.4 (1.3-1.7) respectively, p=0.043]. Hs-cTnI alone did not independently predict CAC change (β=0.214, p=0.132) in the multivariable model whereas a-b2GPI-IgA presence did (β=0.454, p=0.003). There was a significant interaction between hs-cTnI and a-b2GPI-IgA on CAC progression (Wald Chi-square=4.19, p=0.041); high hs-cTnI (>1.5pg/ml) predicted significantly greater CAC change in a-b2GPI-IgA positive patients but not in negative ones [estimated marginal mean difference (IQR)=0.36 (0.12-0.59), p=0.003) and figure 1].
Conclusion: Baseline hs-cTnI in isolation is not predictive of CAC progression in patients with RA; however, in the context of a-b2GPI-IgA presence, high hs-cTnI independently predicts significant increase in coronary atherosclerosis burden.



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THU0612 KNEE JOINT PAIN IN AN ELDERLY, HEALTHY POPULATION IS ASSOCIATED WITH INFLAMMATORY ARTICULAR AND ENTHESEAL CHANGES DETECTED BY ULTRASOUND

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Background: Knee pain is highly prevalent in elderly and influences quality of life. Pathogenesis of knee pain in such population is commonly related to osteoarthritis (OA). It is yet unclear however, which pathological lesions in the knee contribute most to symptomatic disease.
Objectives: To define the articular and enthesal inflammatory and structural lesions that contribute to knee pain in an elderly healthy population using Power Doppler ultrasound (PDUS).
Methods: All subjects (≥65 years) were part of the prospective long-term population-based Bruneck Study (1) and received a clinical and ultrasound investigation of both knees. Ultrasound was performed by an independent investigator unaware of clinical symptoms. Knee entheses (quadriceps insertion, proximal and distal patella insertion) and joint cavity were assessed. Demographic variables were recorded in all individuals. Pain sensation during knee palpation was collected and participants were asked to complete a standardized pain questionnaire for knee joints (Knee injury and osteoarthritis outcome score [KOOS], question P1-P9) (2). Joint changes (synovial hypertrophy, power doppler (PD) signal, joint effusion, baker cysts, osteophytes) were assessed using a GE Logic E

device. Enthesial changes such as positive PD, calcification, enthesiophytes as well as hypoechogenecity were also recorded. All ultrasound abnormalities were scored using validated OMERACT scores. The prevalence of observed changes was compared between subjects without palpation pain and participants with pain. By summing up the articular and entheseal changes a total score was calculated and correlated with the KOOS pain values.

Results: A total of 303 (Male 154; Female 149) aged participants (age: 75.3±6.9 years) underwent ultrasound examination of both knees. Knee tenderness was found by 30/149 (20.1%) women and 15/154 (9.7%) men. Ultrasound effusion (p=0.010), synovial hypertrophy (p=0.001), PD synovial activity (p=0.003) and osteophytes (p=0.001) were more prevalent in women with knee tenderness than without. In men, knee tenderness was associated PD synovial activity (p=0.0014), and entheseal calcification (p=0.020). Presence of more than 1 ultrasound pathology was associated with lower KOOS pain values, indicating higher impact on symptoms. This was observed in both women (r=-0.285, p=0.021) and men (r=-0.298, p=0.008).

Conclusion: In an elderly healthy population, knee pain is associated with the presence of joint and entheseal inflammatory lesions.

REFERENCES:

[1] D'Agostino MA, Iagnocco A, Aegerter P, Kleyer A, Zwerina J, Perricone C, Lorenzini R, Aschenbrenner F, Willeit J, Kiechl S, Schett G. Does subclinical inflammation contribute to impairment of function of knee joints in aged individuals? High prevalence of ultrasound inflammatory findings. Rheumatology (Oxford). 2015 Sep;54(9):1622-9.

[2] Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)–development of a self-administered outcome measure. J Orthop Sports Phys Ther 1998;28:88-96.

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THU0613 MRI AND ULTRASOUND (US) ASSESSMENT OF TEMPORO-MANDIBULAR JOINT (TMJ) INVOLVEMENT IN ADULT PATIENTS WITH DIAGNOSIS OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) AND NON-JIA CHRONIC INFLAMMATORY ARTHROPATIES

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Background: TMJ is involved in about 50% of JIA cases, often bilateral and asymptomatic in up to 71% of cases[1], leading to higher rate of dysfunction and anatomical abnormalities (as retrognathia, facial asymmetry, limited mouth opening, pain)[2]. To date MRI is the gold standard to study both TMJ inflammation and damage[3] but US is a widely used diagnostic imaging tool in rheumatic patients and may be a cheaper and more accessible alternative.

Objectives: To investigate the prevalence of TMJ involvement in young adults with JIA and young adults with non-JIA inflammatory rheumatisms, comparing MRI with US.

Methods: Patients were recruited prospectively in 2 clinical centers. Inclusion criteria were: patients <35 years diagnosed with JIA who had undergone transition from the pediatric to the adult rheumatologist, and patients diagnosed with non-JIA inflammatory arthropathies. All patients underwent clinical examination for TMJs (tenderness to palpation, swelling, signs of damage such as joint crepitations, lateral deviation, retrognathia and decreased mouth opening) and MRI of the TMJs to detect inflammation (bone marrow edema, effusion, synovial thickening) or damage (condylar flattening, erosions, disk abnormalities). Blindly to MRI, US was performed to evaluate presence of inflammation (effusion and/or joint capsule abnormalities) or damage (erosion). MRIs and US with either inflammation or damage were considered pathological. Demographic and clinical characteristics were described using frequency or median and interquartile range (IQR), depending on the distribution of the variable. Differences between groups were analyzed using the Mann-Whitney U test, the χ^2 test and Cohen's correlation index when appropriate. US sensibility (Se) and specificity (Sp) were also calculated.

Results: 11 patients were included in the JIA group and 7 patients in the non-JIA group. Patients' and TMJs involvement characteristics were reported in Table 1.

	JIA n 11	**Non-JIA** n 7
Sex F, n (%)	8 (72.7%)	4 (57.1%)
Age (ys) at diagnosis, median (IQR)	10 (5-12)	23 (22-26)
Current age (ys), median (IQR)	22.3 (20.3 – 25.1)	30.1 (28.8-32.5)
Disease duration (ys), median (IQR)	13.2 (11.9-16.1)	5.6 (5.3-7.8)
TMJs tenderness, n (%)	1 (9.1%)	2 (28.6%)
TMJs swelling, n (%)	0 (0%)	0 (0%)
TMJ damage, n (%)	7 (63.6%)	3 (42.9%)

Table 1. MRI and US results are collected in Table 2.

	JIA TMJs n 22	**Non-JIA** TMJs n 14
Inflammation on MRI, n (%)	11 (50.0%)	5 (35.7%)
Joint damage on MRI, n (%)	16 (72.7%)	9 (64.2%)
Pathological MRI, n (%)	16 (72.7%)	9 (64.2%)
Inflammation on US, n (%)	2 (9.1%)	0 (0%)
Joint damage on US, n (%)	10 (45.4%)	4 (28.6%)
Pathological US, n (%)	11 (50.0%)	4 (28.6%)

Table 2. Twelve out of 36 TMJs presented with damage on both MRI and US, 2 TMJs had damage on US but not on MRI and 13 TMJs had damage on MRI only; the concordance was discrete (k = 0.23 (0-0.48). Only 2 TMJs had inflammation on US, of which only one was confirmed by MRI. 12 TMJs were pathological on both MRI and US, 3 TMJs were pathological on US only and 13 TMJs on MRI only; the concordance was poor (k = 0.17 (0-0.43)), Se=48% (95%CI 0.28,0.68), Sp=73% (95%CI 0.47,0.99).

Conclusion: The concordance between MRI and ultrasound is not optimal, and existing TMJ US protocols are based on children. Further studies are needed to develop a suitable US protocol to detect TMJ involvement in adult patients as a screening tool.

REFERENCES:

[1] Billiau AD, et al. J Rheumatol. 2007 Sep;34(9):1925–33.

[2] Arvidsson LZ, et al. Radiology 2010 Jul;256(1):191–200.

[3] Hemke R, et al. Eur Radiol. 2014 Feb;24(2):327–34.

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THU0614 FINGER EXTENSOR TENDON INVOLVEMENT IS FREQUENT IN EARLY RHEUMATOID ARTHRITIS

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Background: Finger extensor tendon (FET) involvement at ultrasound examination (US) was previously described in patients suffering from early and established psoriatic arthritis[1]. The reliability of the US measure of FET was as least as good as for synovitis[2]. The involvement of the FET in patients suffering from rheumatoid arthritis remains controversial.

Objectives: To assess the involvement of FET in early rheumatoid arthritis (ERA) patients and in asymptomatic subjects (CTR).

Methods: Inclusion criteria for ERA patients were: less than 6 months since the ERA diagnosis; age >18 years; without DMARD treatment or oral glucorticoid treatment. Inclusion criteria for CTRL subjects were : age >18 years; no pain in hands and fingers (VAS pain =0/100); no known rheumatic disease such a systemic diseases, rheumatoid, psoriatic arthritis, spondyloarthritis, hand osteoarthritis, gout, chondrocalcinosis; no psoriasis, no inflammatory bowel diseases. US assessments were performed blindly to the clinical and laboratory data. FET were assessed in longitudinal and in transverse view at the metacarpo phalangeal joint (MCP) and proximal phalangeal joint (PIP) level both in grey-scale (GS), power Doppler (PD) and in color Doppler (CD) mode. In addition the following joints were assessed for the presence and grade (0-3 according to OMERACT definitions) for both GS and PD synovitis: wrists, ankles, metatarsophalangeal (MTP) (2-5) and MCP (1-5) joints.

Results: Sixty-two consecutive ERA patients and 34 CTR were included in this study. Mean age and gender distribution were comparable between ERA and CTR (47,3±14,5 vs. 43,4±12,5). ACPA were present in 61%, rheumatoid factor in 54%, and bone erosions in 27% of ERA patients. 57% of ERA patients presented with FET and 0% of CTR (p<0.001). The delay between the first symptom and diagnosis, the DAS28CRP, SDAI, CDAI, CRP level, 44TJC, 44SJC, HAQ did not differ significantly between patients with FET involvement and those without. In univariate analysis, the presence of FET involvement was significantly associated with the presence of bone erosions (p=0.02), ACPA (p=0.002), rheumatoid factor (p=0.02) and tobacco use (p=0.02). In multivariate analysis, the presence of FET involvement was significantly associated with the presence of bone erosions (p=0.01), ACPA (p=0.001), RF (p<0.01).
Conclusion: FET is relatively frequent in ERA patients and it is not present in asymptomatic subjects. Our results show that FET involvement is associated with the presence of ACPA, rheumatoid factor and bone erosions, thus identifying patients with possibly more aggressive or severe disease at baseline.

REFERENCES:

[1] Wiell C, Szkudlarek M, Hasselquist M, Møller JM, Vestergaard A, Nørregaard J, Terslev L, Østergaard. Ultrasonography, magnetic resonance imaging, radiography, and clinical assessment of inflammatory and destructive changes in fingers and toes of patients with psoriatic arthritis Arthritis Res Ther. 2007;9(6):R119.
[2] Macía-Villa C, Falcao S, Gutierrez M, Medina J, Hammer HB, De Miguel E. What is metacarpophalangeal joint swelling in psoriatic arthritis? Ultrasound findings and reliability assessment. Clin Exp Rheumatol. 2018;36 (5):896-899.

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THU0615 POSITIVE MRI OF THE SPINE AS IMAGING CRITERION IN THE ASAS CLASSIFICATION CRITERIA FOR AXIAL SPONDYLOARTHRITIS

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Background: MRI is a useful tool for the evaluation of patients with chronic back pain suspected of axial spondyloarthritis. As defined by ASAS classification criteria, MRI suggestive of axial spondyloarthritis is based on the presence of inflammatory lesions in the sacroiliac joints. However inflammatory lesions in the spine may also occur. A consensus definition for a positive MRI-spine was developed by OMERACT MRI working group. In this consensus a positive MRI-spine is described as the presence of $\geq$ 3 inflammatory lesions in the corner of the vertebrae (bone marrow edema lesions), whereas each lesion needs to be present on $\geq$2 consecutive slices.
Objectives: The purpose of this study was to evaluate the presence of spinal inflammatory lesions on MRI performed between January, 2015 and December, 2015 in the Universidad de Chile Clinical Hospital.
Methods: Data from MRI performed between January, 2015 and December, 2015 in the Universidad de Chile Clinical Hospital was collected. The patients were derived by a physician as part of the study of chronic back pain.
Results: A total of 118 MRI were performed in this period, from which 8 showed evidence of spinal involvement without sacroileitis. The finding in MRI were: 3 patients with enthesitis of spinal ligaments, 2 patients with spondylodiscitis and 3 patients with bone marrow edema in the corner of the vertebrae. However, no patients fulfilled the OMERACT criteria for a positive MRI-spine ($\geq$ 3 corner based inflammatory lesions). Patients with inflammatory lesions in the corner of vertebrae only showed 1 or 2 bone marrow edema sites. When we hypothetically added this criteria (assuming 2 bone marrow edema sites as a positive MRI-spine) to the ASAS-criteria for axial spondyloarthritis, only one patient could be classified via the imaging arm.
Conclusion: Adding a positive MRI-spine as an imaging criterion to the ASAS-criteria for axial spondyloarthritis did not resulted in newly classified patients in this cohort. A combination of MRI-spine and MRI-SI had no incremental value compared with MRI-SI alone.

REFERENCES:

[1] Zaitouni Z. El al. The yield of a positive MRI of the spine as imaging criterion in the ASAS classification criteria for axial spondyloarthritis: results from the SPACE and DESIR cohorts Ann Rheum Dis 2017, 76: 1731.

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THU0616 WHOLE-BODY MRI OF PSORIATIC ARTHRITIS AND RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY CONTROLS – INTERSCAN, INTRAREADER AND INTERREADER AGREEMENT AND DISTRIBUTION OF FINDINGS

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Background: Whole-body MRI (WBMRI) is a promising tool for monitoring disease activity in inflammatory joint diseases. Earlier studies have shown good correlation with conventional MRI and scoring systems for WBMRI have been developed [1,2]. However, the validation of WBMRI is limited; no studies have evaluated the agreement between repeated scans (interscan agreement) and only few studies have evaluated the intra- and interreader agreement.
Objectives: To validate WBMRI by evaluating the interscan agreement in patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA) and healthy controls (HC) and to evaluate the intra- and interreader agreement and determine the distribution of pathologies in the subjects.
Methods: WBMRI was performed twice with a one-week interval in 14 patients with PsA, 10 with RA and 16 HC. Coronal images of shoulders, hips, hands and ankles/feet, and sagittal images of knees, ankles, feet and spine were obtained (STIR and pre- and post-contrast T1 weighted spin echo images). Images were anonymized and read in pairs with unknown chronological order by experienced readers (peripheral: IE; spine: SK). WBMRI was scored for 83 peripheral joints and for 33 peripheral entheses according to the OMERACT WBMRI scoring system [1], and according to the CanDen MRI spine scoring system [2]. Ten image sets were re-anonymized for assessment of intra- and interreader agreement (peripheral and spine: MO). Agreement was calculated on lesion level by percentage exact agreement (PEA) and Cohen's kappa with squared weights, and for sum scores by absolute agreement single-measure intraclass correlation coefficient (ICC).
Results: The age in the PsA/RA/HC was median (range) 48(31-68)/49(26-58)/35(23-54) years and the symptom duration 10(0-24)/7(3-24)/NA years. WBMRI of the spine and peripheral joints and entheses generally showed moderate to almost perfect interscan agreement with a PEA ranging from 95-100%, kappa ranging from 0.71-1.00 and ICC ranging from 0.95-1.00 (Table 1). Intra- and interreader agreement showed moderate to almost perfect agreement with few exceptions (Table 2).
More lesions were found in patients than HC. PsA patients had more lesions in acromioclavicular and sternoclavicular joints, whereas RA patients had more hand lesions (Figure 1). PsA patients had more lesions in the spine (Figure 2).
Conclusion: WBMRI of the spine and peripheral joints and entheses showed very good interscan agreement, implying that repositioning between examinations does not markedly affect scoring of lesions. Intra- and interreader agreement showed moderate to almost perfect agreement. The distribution of findings in PsA, RA and HC was determined.

REFERENCES:

[1] Krabbe, et al., J Rheumatol, 2019 (in press)
[2] Krabbe, et al., RMD Open, 2018;4;e000624.

Table 1. Interscan agreement between two WBMRI examinations performed with a one-week interval for all participants

			%-agreement	Kappa	ICC
WBMRI; Peripheral	Synovitis	Feet	96	0.83	0.93
		Hands	96	0.84	0.95
		Shoulders	92	0.54	0.60
		Pelvis	97	0.94	0.93
		Knees	87	0.64	0.79
		All	95	0.82	0.96
	Joint BME	Feet	98	0.84	0.98
		Hands	99	0.87	0.91
		Shoulders	95	0.87	0.91
		Pelvis	99	0.95	1.00
		Knees	100	0.97	1.00
		All	98	0.88	0.99
	Entheseal STI	Feet	98	0.96	0.98
		Hands	*NA*	*NA*	*NA*
		Shoulders	95	0.27	0.40
		Pelvis	96	0.82	0.93
		Knees	97	0.75	0.95
		All	97	0.79	0.96
	Entheseal BME	Feet	96	0.59	0.71
		Hands	*NA*	*NA*	*NA*
		Shoulders	96	0.70	0.60
		Pelvis	99	0.40	-0.04
		Knees	100	0.87	1.00
		All	98	0.71	0.93
WBMRI; Spine	BME	All	100	0.99	0.99
	Fat	All	100	0.99	1.00
	Erosion	All	100	1.00	1.00
	New bone formation	All	100	1.00	1.00

BME: bone marrow edema, STI: soft tissue inflammation, ICC: intraclass correlation coefficient

Figure 1: Percentage of participants with pathologies in the examined joints and entheses

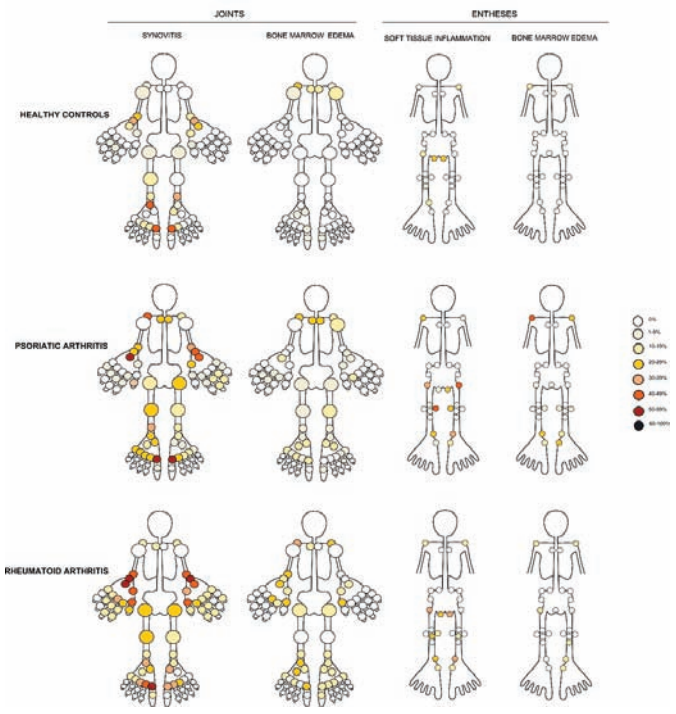
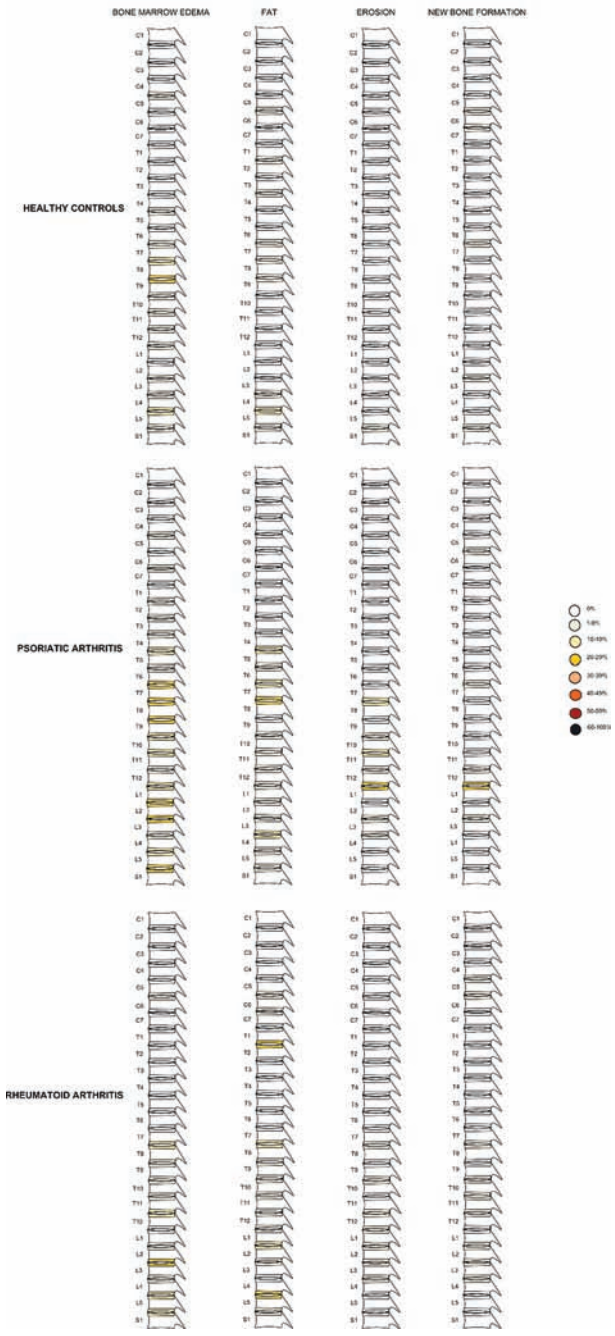


Table 2. Intra- and interreader agreement for ten participants (4 PsA, 3 RA, 3 HC)

INTRAREADER				
		%-agreement	Kappa	ICC
WBMRI; Peripheral	Synovitis	90	0.58	0.87
	Joint BME	97	0.52	0.45
	Entheseal STI	92	0.67	0.85
	Entheseal BME	97	0.08	0.14
WBMRI; Spine	BME	100	0.93	0.99
	Fat	99	0.91	0.99
	Erosion	100	1.00	1.00
	New bone formation	100	1.00	1.00
INTERREADER				
		%-agreement	Kappa	ICC
WBMRI; Peripheral	Synovitis	84	0.41	0.85
	Joint BME	97	0.72	0.91
	Entheseal STI	93	0.41	0.74
	Entheseal BME	97	0.34	0.35
WBMRI; Spine	BME	100	0.93	0.67
	Fat	99	0.82	0.97
	Erosion	100	0.83	0.91
	New bone formation	98	0.17	0.23

BME: bone marrow edema, STI: soft tissue inflammation, ICC: intraclass correlation coefficient

Figure 2: Percentage of participants with pathologies in the spine



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THU0617 WRIST ULTRASOUND (US) PATHOLOGY IN EARLY RHEUMATOID ARTHRITIS (RA); OBSERVATIONS FROM AN EARLY INFLAMMATORY ARTHRITIS (EIA) DIAGNOSTIC SERVICE

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Background: To ensure a timely diagnosis of RA, diagnostic US is increasingly being utilized to detect subclinical pathology in order to implement treatment plans rapidly. There are several 'optimal' synovitis scoring protocols in the literature but a consensus regarding a definitive system still eludes us. There are few studies that have focussed specifically on wrist US pathology in early RA. Hence, we assessed what the common wrist US pathologies are in patients diagnosed with early RA.
Objectives: To identify the patterns of wrist US abnormalities seen in patients diagnosed with early RA from our EIA service in a large urban London hospital.
Methods: Retrospective service review of patients seen in the EIA US diagnostic service at Croydon Health Services in South London. Patients diagnosed with RA (EULAR/ACR 2010 criteria) with wrist US synovitis/tenosynovitis (EULAR-OMERACT definitions) between Jan2017-Dec2018 were included. The US protocol in the EIA diagnostic service includes lateral and dorsal (long axis & short axis views) of the ulnarcarpal(UCJ) & radiocarpal(RCJ) joints with views covering the radioulnar joints & ulnar-styloids and views of the extensor & flexor tendons. Images and reports were reviewed and correlations with rheumatoid factor(RhF), anti-CCP antibodies(CCP), CRP & ESR were also assessed.
Results: 86 patients with RA (meeting EULAR-ACR criteria) were found to have wrist pathologies on US. The commonest finding (36%) was moderate (grade 2) greyscale(GSUS) synovitis in the UCJ with almost all having moderate (grade 2) power Doppler(PDUS) synovitis (32%). Only a few (5/86) had more severe pathology with GSUS/PDUS (grade 3). 22% (19/86) had milder changes GSUS grade 1 with three quarters of these patients having concomitant PDUS signal. Just under 10% had RCJ US synovitis and 3 cases had radioulnar joint synovitis. Only 6% of the cohort had whole wrist joint involvement. Erosions were very uncommon (2/86). In total just under 25%(21/86) had tendon disease with roughly 70% affecting 1 tendon compartment and the others affecting 2 or more. Of those with tendon pathology, the two most commonly affected tendons were the 2nd [48%(10/21)] and 4th [38%(8/21)] extensor compartments. Extensor tenosynovitis was more common than flexor(26 v 4 cases). US synovitis 'only' was seen in 76%, US tendon disease 'only' in 7% and concomitant pathology in 17%. Correlation with inflammatory markers was not seen with only 3 patients presenting with significantly elevated CRP (>15) and ESR (>20). Though CCP was more commonly seen compared to RhF(32% vs 17%), just over half did not have positive antibodies.
Conclusion: Our observational study found that in early RA, mild-to-moderate GSUS and PDUS in the UCJ is the commonest wrist US pathology with tenosynovitis of the 2nd and 4th extensor compartments. Severe disease and erosions were very uncommon. The pattern of these US wrist pathologies are likely to reflect the initial disease course of these patients that present to our EIA service (i.e. early RA patients). Furthermore, biochemical markers do not seem to be useful in these patients and serology may not be present in over 50%. Therefore, clinicians who are running EIA diagnostic services with US should be expectant of milder-to-moderate US findings when diagnosing early RA and not be misled by the absence of more severe findings. Our understanding of US pathologies in the RA disease course therefore needs to be more nuanced and further work in other specific joint areas may help to elaborate what US pathology is most common in early RA.
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THU0618 CLINICAL COMPARISON BETWEEN MAGNETIC RESONANCE TOMOGRAPHY AND X-RAY IN DIAGNOSIS OF EARLY RHEUMATOID ARTHRITIS

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Background: For decades, X-ray images have been used to help detect rheumatoid arthritis (RA) and to monitor for the progression of bone damage. In early RA, however, X-rays may appear normal although the

disease is active – making the films useful as a baseline but not much help in getting a timely diagnosis and treatment. Modern imaging techniques, including ultrasound and magnetic resonance imaging (MRI), which can reveal early, non-bony signs of RA that are invisible on X-ray

Objectives: To conduct a comparative analysis of the possibility of MRI in RA patients in the early diagnosis of the disease with the data X-ray of hands and feet

Methods: The study included 56 patients with a reliable diagnosis of RA aged from 17 to 66 years, with disease duration from 4 months to 1 year. Verification of the diagnosis of RA was carried out in accordance with the diagnostic APA criteria (1987). The criteria for the selection of patients was the presence of disease activity. Patients were mainly with the II degree of disease activity. All patients underwent radiography of the small joints of the hands and feet, and 28 patients underwent MRI with dominant hands

Results: The study showed certain changes in the structures of the joint based on MRI in the early stages of RA. So, according to MRI of the brushes, it was revealed: thickening of the synovial membrane - in 23 (86%) patients; marginal erosion and subchondral cysts - in 21 (75%) patients; bone erosions - in 25 (90%) patients; phenomena of destruction of the articular cartilage (thinning, ulceration and destruction) - in 16 (57%) patients; effusion to the joints - in 19 (68%) patients and tenosynovitis - in 18 (64%) patients. In turn, the radiological data of the hands and feet showed that erosive arthritis was found in 23 (41%) patients and marginal erosions - in 22 (39%) patients

Conclusion: Thus, MRI of the hands plays an important role in the early diagnosis of RA, since it allows visualizing the characteristic changes in all joint structures in RA. MRI is a highly effective diagnostic method in diagnosis of RA, which in combination with other methods of research helps to establish the diagnosis at an early stage diseases and timely appointment of adequate basic treatment unlike radiography

REFERENCES:

[1] Klarlund M, Ostergaard M, Jensen KE, Madsen JL, Skjodt H, Lorenzen I. Magnetic resonance imaging, radiography, and scintigraphy of the finger joints: one year follow up of patients with early arthritis—the TIRA group. Ann Rheum Dis 2000; 59:521 –528

[2] McQueen FM, Stewart N, Crabbe J, et al. Magnetic resonance imaging of the wrist in early rheumatoid arthritis reveals a high prevalence of erosions at four months after symptom onset. Ann Rheum Dis 1998; 57:350 –356

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THU0619 THE VALUE OF MORPHOLOGICAL AND BIOCHEMICAL MAGNETIC RESONANCE IMAGING (MRI) OF RADIOCARPAL CARTILAGE FOR THE DIFFERENTIATION OF RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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Background: Using high-field MRI to differ morphologically between OA and RA.

Objectives: To evaluate the value of morphological and biochemical, contrast-agent free high-field (3 Tesla) MRI of the radiocarpal cartilage to differ between osteoarthritis (OA) and rheumatoid arthritis (RA).

Methods: The group consisted of 47 subjects, who were examined during the period from October 2016 to December 2017. The clinical dominant hand of 11 patients suffering from early rheumatoid arthritis (RA) (German ArthroMark cohort, Ø 52.8years; min: 32; max 74), seropositive (ACPA and/or RF), disease duration < 6 months (range 2 –23 weeks)), 10 with osteoarthritis (OA) (Ø 48.55 ± 15.23 years, min: 34 years, max: 68 years, disease duration Ø 6 years ± 8.29) and 26 healthy volunteers (Ø 46.55 ± 17.55 years, min: 20 years, max: 79 years) were examined with a 3T MRI scanner, prospectively. Morphological and biochemical assessment of radiocarpal cartilage was performed using DESS, TrueFISP and T2* images.

Results: Morphological sequences demonstrated significantly higher cartilage damage in RA and OA compared to healthy controls (DESS: $p = 0.01$, $p = 0.0004$; TrueFISP: $p = 0.02$, $p = 0.0001$), while there was no significant difference between RA and OA patients. With biochemical MRI using T2* imaging, patients with OA showed higher cartilage integrity compared to patients with RA ($p = 0.01$).

Conclusion: Morphological and biochemical MRI of radiocarpal cartilage could be helpful to differentiate between RA and OA patients. Both, RA and OA, are associated with cartilage damage measured by morphological MRI of the hand. Hence, OA was associated with more loss of cartilage integrity compared to RA using biochemical MRI, whereby only early RA patients were analyzed in this first evaluation. Non-contrast-agent morphological and biochemical MRI could be a non-invasive tool to investigate cartilage integrity in RA and OA patients and could help to differ disease pattern in the future.

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THU0620 THE PHYSIOLOGICAL FINGER JOINT ARCHITECTURE – AGE-RELATED INCREASE OF EROSIONS AND OSTEOPHYTES IN THE JOINTS OF HEALTHY INDIVIDUALS

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Background: The "normal" finger joint architecture has not yet been defined and could change in the course of life. Therefore the objective was to assess the physiological finger joint architecture of healthy individuals and the relation of structural changes to age and sex.

Objectives: Therefore the objective was to assess the physiological finger joint architecture of healthy individuals and the relation of structural changes to age and sex using high-resolution quantitative computed tomography (HR-pQCT) of the hands.

Methods: Healthy individuals without rheumatic diseases and other comorbidities were recruited through a field campaign and received HR-pQCT examination of the Metacarpophalangeal 2/3 and Proximal Interphalangeal 2/3 joints of one hand. The number of erosions and osteophytes was quantified across different sexes and age decades (6 decades within the age range of 21-80 years).[1,2,3]

Results: 120 healthy individuals (10 women and 10 men in each decade) were recruited. Bone erosions [median (Q1-Q3), 1 (0-2)] and osteophytes [2 (1-4)] were found in both sexes without significant differences. However, structural changes increased with age: the overall incidence rate ratio (IRR) for the number of erosions and osteophytes per age were 1.04 (95% CI 1.03-1.06; 95% CI 1.03-1.05), which indicates a 4% increase in the number of erosions and osteophytes per year. The use of the 3rd decade as the reference demonstrated that healthy individuals in the age decades from 50 years had higher IRR for erosion number (6th, 7th, 8th decade: 4.87 (2.20-11.75), 6.81 (3.08-16.46) and 6.92 (3.11-16.79)) compared to younger subjects (4th, 5th decade: 1.80 (0.69-4.87), 1.53 (0.59-4.10)). The IRRs of osteophytes also indicate a progressive increase after the fifth decade, with IRRs of 2.32 (1.32-4.17), 4.17 (2.38-7.49) and 6.86 (3.97-12.20) for the 6th, 7th and 8th decades, respectively.

Conclusion: Structural changes in the finger joints of healthy individuals are age-related. While being rare under 50 years of age, erosions and osteophytes accumulate above the age of 50, suggesting that the threshold between "normal" and "pathological" shifts with increasing age.

REFERENCES:

[1] Simon D, Kleyer A, Stemmler, et al. Age- and Sex-Dependent Changes of Intra-articular Cortical and Trabecular Bone Structure and the Effects of Rheumatoid Arthritis. J Bone Miner Res. 2017 Apr

[2] Figueiredo CP, Simon D, Englbrecht M, et al. Quantification and Impact of Secondary Osteoarthritis in Patients With Anti-Citrullinated Protein Antibody-Positive Rheumatoid Arthritis. Arthritis Rheumatol. 2016 Sep

[3] Figueiredo CP, Kleyer A, Simon D, et al. Methods for segmentation of rheumatoid arthritis bone erosions in high-resolution peripheral quantitative computed tomography (HR-pQCT). Semin Arthritis Rheum. 2018 Apr;

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THU0621 VERY LOW PREVALENCE OF ULTRASOUND DETERMINED TENDON ABNORMALITIES IN HEALTHY SUBJECTS THROUGHOUT THE AGE RANGE: OMERACT ULTRASOUND MINIMAL DISEASE STUDY

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Background: Tenosynovitis (TS) is a common, often clinically undetectable finding in Rheumatoid Arthritis (RA). Recent data showed TS on ultrasound (US) has a role in predicting outcome in early disease and flare in clinical remission. However data is limited on US measured TS in healthy subjects (HS), none specifically encompassing the older age range when RA commonly presents.

Objectives: This OMERACT study aimed to determine prevalence of US measured tendon abnormalities in HS throughout the age range.

Methods: Adult HS without: joint pain (VAS <10/100), hand osteoarthritis (ACR criteria), or inflammatory arthritis were recruited in 23 international centres from Aug 2017-Dec 2018. MCP, PIP and wrist joints were clinically examined. Bilateral digit flexor (DF) 1-5 and extensor carpi ulnaris (ECU) tendons were scanned for tenosynovial hypertrophy (TSH) and power Doppler (PD) signal and graded (OMERACT US scoring system[1]). A comparison cohort of DMARD-naive patients with RA (ACR-EULAR 2010 and/or 1987 criteria) at presentation was taken from the Birmingham Early Arthritis (BEACON) inception cohort, who underwent identical tendon US assessment. They were grouped into ≤12 and > 12 weeks from symptom onset.

Results: Data from 899 HS and 144 RA patients were included.

	HS 18-39 y	HS 40-59 y	HS ≥60 y	RA ≤12	RA > 12	5 groups p value	RA ≤12 vs >12 p value
n	408	311	180	30	114		
Age, y (IQR)	29 (25-33)	49 (44-55)	68 (62-72)	58 (52-69)	53 (42-65)	<0.001	0.03
Female (%)	270 (66)	270 (83)	114 (62)	20 (67)	86 (75)	<0.001	0.2
DAS 28 CRP (IQR)	-	-	-	5.4 (4.2-6.1)	4.8 (4.1-5.7)	-	0.1
Tender joint* (IQR)	0	0	0	18 (10-23)	17 (11-29)	<0.001	0.9
Swollen joint* (IQR)	0	0	0	8 (3-18)	6 (3-9)	<0.001	0.1
DF 1-5 TSH gd ≥1 (%)	8 (0.2)	9 (0.3)	2 (0.1)	54 (18)	125 (11)	<0.001	0.06
DF 1-5 PD gd ≥1 (%)	3 (0.05)	2 (0.06)	0	49 (16)	85 (8)	<0.001	0.02
ECU TSH gd ≥1 (%)	1 (0.1)	11 (1.8)	5 (1.4)	13 (22)	52 (23)	<0.001	0.8
ECU PD gd ≥1 (%)	0	0	0	12 (20)	50 (22)	<0.001	0.7

*RA had 66/68 joint count

Prevalence of TSH and particularly PD abnormalities in HS was very low at all ages, and was all grade 1 except in one individual ECU tendon. ECU TSH grade≥1 was more common than DF grade≥1 in the older HS groups, and less common in the 18-39 age group (p=0.011). TSH and PD of grade ≥1 were common in RA patients, with DF PD abnormalities more common in early disease (p=0.02).

Conclusion: Low prevalence of TSH or PD abnormalities in tendons of HS even in old age suggests US determined TS will be a robust tool in clinically managing RA.

REFERENCES:

[1] Naredo E, D'Agostino MA, et al. Reliability consensus-based US score TS RA. ARD.2013;72(8):1328-34

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THU0622 MRI OF THE CRANIO-CERVICAL JUNCTION IN RHEUMATOID ARTHRITIS – DEFINITION OF NORMAL AND PATHOLOGICAL FINDINGS

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Background: In rheumatoid arthritis (RA), disease involvement at the cervical spine is common and may lead to malposition of the dens axis, resulting in severe neurological impairment. To date, malalignment is mostly described by X-rays.

Objectives: The aim of this investigation was to systematically define osseous and ligamentous MRI-findings in cranio-cervical RA in comparison to a control group without the disease.

Methods: MRI datasets of patients with cranio-cervical RA were identified retrospectively from the institutional image database and matched regarding age and gender with control patients. All image datasets were systematically reviewed for: position and morphology of dens axis (including erosions and osteitis); width and angle of the cranio-cervical joints; length, angle and visibility of peridental ligaments; vascularization of peridental

soft tissue. Prior to image analysis, an atlas of normal findings and measurements was comprised. Group differences were investigated using students T-test for continuous data and Fisher's exact test for nominal and ordinal data.
Results: A total of 40 patients were included in this retrospective case-control study, 20 in each group (RA and control). Position of dens was significantly more cranial in the RA group (dens to McGregor line: -1.62 mm for RA vs. 2.15 mm for controls, p=0.002; dens to McRae line: 3.20 for RA vs. 5.36 for controls, p<0.001). Visibility of alar ligaments was significantly lower in RA patients (fully visible in 10% of RA and 35% of control patients, p=0.012). Similarly, signal of transverse ligaments was normal in 5% of RA vs. 35% of control patients (p<0.001). There was no difference in length of the aforementioned ligaments ($p \geq 0.056$).
Conclusion: With this case control study, MRI data on the position of the osseous and ligamentous structures of the cranio-cervical junction in patients with rheumatoid arthritis are available for the first time. Cranialization of the dens axis and signal changes of the transverse ligament and the alar ligaments are the most obvious findings. In a next step, the diagnostic value of MRI of the cervical spine in RA should be prospectively investigated and the available scoring system developed into an internationally established outcome measure.
Disclosure of Interests: [2] Katharina Ziegeler: None declared, Christoph Korsing: None declared, Mattias Bollow: None declared, Kay Geert A. Hermann Speakers bureau: AbbVie, MSD, Pfizer, UCB, Samsung
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THU0622B **PREVENTION OF ACTIVE TUBERCULOSIS INFECTION USING INTERFERON GAMMA RELEASING ASSAY (IGRA) IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING TUMOR NECROSIS FACTOR-ALPHA INHIBITORS TREATMENT**

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Background: Data on effectiveness reducing incidence of active tuberculosis (TB) by use of interferon gamma releasing assay (IGRA) have not yet been available.
Objectives: To evaluate whether diagnosis of latent tuberculosis infection (LTBI) using IGRA is effective in reducing occurrence of active-TB among patients with RA who will use Tumor Necrosis Factor alpha inhibitors (TNFi).
Methods: A retrospective cohort study was conducted using the National Health Information Database of Korea between 2008 and 2017. The enrollees had at least two claims with the RA diagnosis code, and has at least one prescription of TNFi since 2009 when national insurance of Korea started to cover the expense of IGRA. Exclusion criteria were organ transplantation, HIV infection, or active TB infection within 1 year prior to enrollment. The follow up was initiated on the day of the first prescription for TNFi, and ended on the date of the first claim on active TB, the date of death or December 31, 2017 whichever came first. The utilization of the diagnostic test method was confirmed by the codes for tuberculin skin test (TST) and IGRA claimed within 2 months prior to the initiation of the TNFi. Patients were categorized into 3 groups; no-test, TST only, IGRA (IGRA only or IGRA and TST). The incidence of active TB was defined as the presence of claims with diagnosis code for TB and the start of standard 3-drug or 4-drug first line anti-TB medication combination therapy.
Descriptive statistics on baseline characteristics of participants in each group were presented before and after application of weighting method using standardized mortality rate weight (SMRW). The incidence of active TB in each group was presented as event per 1000 person-year (PY). We treated death as competing event to the occurrence of TB. Therefore a sub-distributional hazard model was used to calculate weighted hazard ratio (wHR) and 95% confidence intervals (CI).
Results: Among the 27,021 patients who started TNFi, 15,538 RA patients were included in the analysis through inclusion and exclusion criteria. There were 6,287 patients in the no-test group, 4,677 patients in the TST group, and 4,574 patients in the IGRA group. Diabetes mellitus, chronic kidney disease, and congestive heart failure were more prevalent in IGRA group, while stroke was observed less frequently in IGRA group. After weighting using SMRW, all confounders were well balanced. During the follow up period, 4.24, 4.93, and 4.01 active TB events per 1,000 PY were observed for no-test, TST, and IGRA group, respectively. The death rate was 8.63, 9.75 and 7.96 per 1,000 PY for no-test, TST, and IGRA group, respectively. Considering death as competing event, IGRA significantly reduced the risk of active TB than no-test group (wHR 0.628, 95% CI: 0.459-0.859) and TST group (wHR 0.416, 95% CI: 0.311-0.556).
Conclusion: The incidence of active TB in RA patients using TNFi could be reduced by use of IGRA.

REFERENCES:
[1] Internal Clinical Guidelines Team (UK). Tuberculosis: Prevention, Diagnosis, Management and Service Organisation. London: National Institute for Health and Care Excellence (UK); 2016 Jan. (NICE Guideline, No. 33.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK338750/
[2] Joint Committee for the Development of Korean Guideline for Tuberculosis, Korean Centers for Disease Control and Prevention. Korean guidelines for tuberculosis. 2nd ed. Seoul: Medrang Inforang Ltd;2014
[3] Jeong DH, Kang J, Jung YJ, Yoo B, Lee CK, Kim YG, Hong S, Shim TS, Jo KW. Comparison of latent tuberculosis infection screening strategies before tumor necrosis factor inhibitor treatment in inflammatory arthritis: IGRA-alone versus combination of TST and IGRA. PLoS One. 2018 Jul 5;13(7):e0198756. doi:10.1371/journal.pone.0198756.

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Public health, health services research, and health economics

THU0623 **FACTORS RELATED TO NON-ADHERENCE BEHAVIORS OF PATIENTS WITH RHEUMATIC DISEASES**

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Background: Non-adherence to medication may lead to poorer clinical outcomes and should be prevented.
Objectives: We describe the frequency of non-adherence behaviors in patients with rheumatic diseases and its relationship to potentially modifiable variables.
Methods: Data were obtained through an anonymous survey handed to patients by physicians or nurses from 25 rheumatology clinics from Spain. Patients completed the survey anonymously at home and returned it by pre-paid post mail. Five different non-adherence behaviors were defined. Co-variables analyzed were patients' demographics, medication characteristics, experience with healthcare (assessed with IEXPAC "*Instrument to Evaluate the EXperience of PAtients with Chronic diseases*" scoring 0 [worst] to 10 [best experience]), and beliefs in medicines (Beliefs About Medicines Questionnaire [BMQ], composed of a necessity and a concerns subscales and scoring -20 [weaker] to +20 [stronger beliefs]). Variables associated to non-adherence were studied with a multivariate logistic regression model.
Results: The survey was handed to 625 patients with rheumatic diseases, of which 336 (53.8%) returned it with the necessary data completed (mean age 55 [14] years, 64% women). Of them, 188 (56.0%) described at least one non-adherence behavior. The frequencies of the specific non-adherence behaviors were: 1) Forgetfulness in taking medication: 28.6%; 2) Taking medication at unscheduled hours: 5.6%; 3) Stopping medication when feeling well: 10.1%; 4) Stopping medication when feeling sick: 33.0% and 5) Stopping medication after reading the patients' information leaflet: 11.5%. The frequency of at least one non-adherence behavior was similar by age, gender, educational level, working status or by number of medicines. It was slightly higher in patients needing to take their medication 3-4 times a day (63.2%) versus 1-2 times a day (52.4%, p= 0.089). IEXPAC scores were similar in patients with or without non-adherence behaviors (5.5 [2.0] in both groups, p= 0.960). BMQ overall score was lower in patients with non-adherence behaviors (4.3 versus 6.5 in those without non-adherence behaviors, p= 0.001). The frequency of non-adherence behaviors did not differ by quartiles of IEXPAC score, but it was higher in patients with lower BMQ score (Q1: 59.5%, Q2: 65.9%, Q3: 54.3%, Q4: 52.0%, p-trend = 0.014). The multivariate model (table) confirmed a relationship of non-adherence behaviors with lower BMQ beliefs scores.
Conclusion: Non-adherence behaviors are frequent in patients with rheumatic diseases and are mainly associated to patients' beliefs in their medications (assessed with BMQ). This is an important aspect that can

be addressed by clinical teams to improve adherence and clinical outcomes.

Table 1. Multivariate analysis. Factors associated to non-adherence behaviors of patients with rheumatic diseases.

	OR (95% CI)	p-value
Age (1-year increment)	1.00 (0.98 – 1.02)	0.984
Gender (female versus male)	1.04 (0.57 – 1.90)	0.892
Need of taking medication 3-4 times per day (versus 1-2 times per day)	1.40 (0.74 – 2.66)	0.306
Number of different medicines (1-unit increment)	1.00 (0.89 – 1.14)	0.967
IEXPAC overall score (1-unit increment)	1.04 (0.90 – 1.21)	0.581
BMQ overall score (1-unit increment)	0.95 (0.91 – 1.00)	0.052

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THU0624 UNDERSTANDING ETHNIC DIFFERENCES IN THE UTILIZATION OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS FOR OSTEOARTHRITIS

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Background: The prevalence of arthritis-attributable activity limitation, work limitation and severe pain are significantly higher among Hispanics than among non-Hispanic Whites (NHWs) in the US. While Hispanics are less likely to report regular use of nonsteroidal anti-inflammatory drugs (NSAIDs), reasons for this decreased NSAID use are unknown. It is also unclear whether there are ethnic differences in the use of both over-the-counter (OTC) and prescription NSAIDs.
Objectives: To determine: 1) if there are ethnic differences in the use of OTC and prescription oral NSAIDs for knee/hip osteoarthritis (OA); 2) if there are differences in familiarity with and perceptions of efficacy and risk of NSAIDs between Hispanics and NHWs; and 3) if patient attitudes/beliefs about NSAIDs mediate observed ethnic differences in the use of NSAIDS for OA.
Methods: Participants ≥50 years of age with chronic frequent pain due to knee/hip OA completed structured interviews. Data on sociodemographic characteristics, clinical information, actual use of oral NSAIDs for OA treatment (last 6 months), and familiarity with NSAIDs (3 items, yes/no response) were collected. Perceptions of efficacy (4 items) and risk (3 items) of NSAIDs were evaluated using five-category ordinal response scale questions. Responses were averaged, with higher values indicating higher perception of efficacy/risk. Fisher's exact or Wilcoxon-Mann-Whitney tests were conducted to determine if knowledge and perceptions about NSAIDs differed by ethnicity. Multivariable logistic regression models were built to determine if ethnic differences in NSAID use were mediated by knowledge and perceptions about the medication.
Results: Among knee/hip OA patients, Hispanics (n=130), in comparison to NHWs (n=204), were younger (mean age 61.8 vs. 65.7) and less likely to have an annual income of ≥$40K (21.6% vs. 56.5%). Hispanics, compared to NHWs, had lower odds of using an OTC NSAID (OR 0.57, 95% CI 0.36-0.90) but greater odds of using a prescription NSAID (OR 1.66, 95% CI 1.04-2.64) for OA. Hispanics, compared to NHWs, were also less likely to ever hear about OTC and prescription oral NSAID to treat OA or have a good understanding of either oral NSAID type as a treatment for OA (Table 1). Mean [SD] perceived efficacy of OTC and prescription oral NSAIDs were slightly lower among Hispanics than NHWs (2.91 [0.98] vs. 3.12 [0.88], p=0.0565; 3.03 [1.02] vs. 3.34 [0.87], p=0.0047; respectively). Mean [SD] perceived risk of prescription NSAIDs was lower among Hispanics than NHWs (2.44 [1.03] vs. 2.82 [1.01], p=0.0012). After adjustment for all familiarity with OTC NSAIDs questions, and perceived efficacy and risk of OTC oral NSAIDs scores, the association between OTC NSAID use and ethnicity was attenuated and no longer significant (OR 1.01, 95%CI 0.54-1.89). After adjustment for familiarity with and perceptions of efficacy and risk of prescription NSAIDs, the association between prescription NSAID use and ethnicity remained significant (OR 2.62, 95%CI 1.51-4.54).
Conclusion: Among patients with knee or hip OA, Hispanics were less likely than NHWs to utilize an OTC oral NSAID as treatment for arthritis. They were also less familiar with the use of NSAIDs for OA treatment and less likely to believe in their efficacy. Patient familiarity and perceptions of OTC oral NSAIDs may mediate ethnic differences in the use of NSAIDs for knee/hip OA.

Table 1. Familiarity with NSAIDs

	Hispanics (n = 130)	NHWs (n = 204)	p-value*
OTC NSAIDs, n (%)			
Heard About It	100 (78.13)	192 (95.05)	< .0001
Family/Friends Received It	67 (52.76)	127 (62.25)	0.1080
Have Good Understanding	79 (63.20)	168 (83.58)	< .0001
Prescription NSAIDs, n (%)			
Heard About It	92 (74.80%)	173 (85.22)	0.0274
Family/Friends Received It	56 (45.16%)	107 (52.45)	0.2120
Have Good Understanding	78 (62.90%)	148 (74.00)	0.0462

*Fisher's exact

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THU0625 CAN WE IMPROVE INPATIENT REFERRALS TO RHEUMATOLOGY IN A TEACHING HOSPITAL IN THE UK?

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Background: Inpatient referrals to rheumatology vary nationally from paper/electronic methods to phone conversations with the rheumatology registrar. In our Trust, which includes two large teaching hospitals in the UK, rheumatology referrals were hand written, faxed to secretaries and then given to the rheumatology registrar. This method was time consuming and referrals often lacked vital information. The referrer would also not know when the registrar had received the referral. A quality improvement project (QIP) in another UK hospital has shown an electronic referral system to be more efficient and safer for patients [1].
Objectives: This QIP aimed to evaluate the current system for inpatient referrals to two rheumatology departments within one large UK NHS trust and to identify aspects for improvement.
Methods: Two hundred and ten inpatient rheumatology referrals received between January 2018 - January 2019 were analysed retrospectively for inclusion of important information such as, patient location and referrer's contact details.
Results: The review of current referrals identified several areas for improvement. The results are summarised in Table 1. The reasons for referrals ranged from swollen, painful joints to new rashes and medication reviews.

Table 1. Inclusion of important items in inpatient rheumatology referrals

Item	Inclusion of item in referral n (%)		
	Wythenshawe Hospital (n=105)	Manchester Royal Infirmary (n=105)	Combined (n=210)
Date of referral	78 (74)	95 (90)	173 (82)
Time of referral	26 (25)	7 (7)	33 (16)
Name of referrer	102 (97)	92 (88)	194 (92)
Referrer's contact details	38 (36)	13 (12)	51 (24)
Patient's name, hospital number	104(99)	102 (97)	206 (98)
Patient location	95 (90)	101 (96)	196 (93)
Past medical history	62 (59)	75 (75)	137 (65)

A process mapping session was undertaken to identify how the referral system could be improved. An electronic referral system, via the local electronic patient record (EPR), was created. As well as ensuring that there is an audit trail and referrals are received in a timely manner, referrers are provided with a proforma to direct them to supply the

relevant information. There is also functionality for the rheumatology team to reply to the referral with advice, which creates a new permanent document in the patient's EPR.The Orthopaedic team, who are the first point of call for hot joints in our Trust, were consulted to ensure that there were not any unintended consequences as a result of this change. The form included the following sentence to avoid delays in patient care for septic arthritis: 'patients with suspected septic arthritis should be referred to Orthopaedics by ringing the on-call registrar'.
Conclusion: The current method of paper rheumatology referrals was inefficient and referrals often lacked vital information. The new electronic system will ensure relevant items are included in the referral and that there is a clear audit trail of the referral process. Referrals will be re-evaluated again in three months to assess the impact of this change on outcomes including time to rheumatology review and inpatient bed stay. In the second round of this project we plan to include an education component onto the rheumatology referral form. For example, if gout is suspected, the referrer will be linked to guidelines and patient information sheets to assist best management whilst awaiting review. We would encourage others to consider their referral systems- could you improve yours?

REFERENCES:

[1] Shephard E, Stockdale C, May F, et al. E-referrals: improving the routine interspecialty inpatient referral system. *BMJ Open Quality* 2018;7:e000249. doi:10.1136/bmjoq-2017-000249

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THU0626 SOCIAL NETWORKS AS A SOURCE OF INFORMATION FOR PATIENTS WITH RHEUMATIC DISEASES

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Background: Internet is an informative source for patients with different diseases. False information in social networks about health issues is a growing problem. Rheumatology is no stranger to this problem and there is a lot of false information regarding rheumatic diseases.
Objectives: To show objective data on misinformation published in social networks available to spanish-speaking rheumatic patients
Methods: We create accounts on Facebook (FB) and Google unique for this work. Multimedia was included in Spanish, with a convenience sampling according to the deployment of the platform (FB) or in descending order for reproductions on YouTube (YT). Two independent reviewers extracted information on online time, number of reproductions and characteristics of the most popular videos. Videos consulted on 10-11-18.
Results: With the search term "rheumatoid arthritis" (RA), the most reproduced video is titled "celery green juice for arthritis" (6.4 million reproductions). Of the first 50 videos with more reproductions, 39 are of natural or home remedies such as vinegar, "moringa", etc., and 35 videos indicate in their content, that they can cure RA. With the term "lupus", the most reproduced video is titled "God's tea, cure chronic tiredness, thyroid, arthritis, lupus and vertigo" (1.4 million reproductions). Of the first 50 videos with more reproductions, 31 correspond to natural or home remedies such as celery, thyme, diets among others and 29 videos indicate that they can cure lupus. With the term "fibromyalgia", the most reproduced video is entitled "I am 61 years old and this cured my arthritis, vertigo, fibromyalgia, lupus, chronic fatigue and the thyroid" (1.1 million reproductions). Of the 50 first videos with more reproductions, 40 are of natural or home remedies such as thyme, tea, among others and 33 videos indicate that they can cure the disease. With the data of the videos uploaded online in October 2018, 50 videos were chosen in YT and FB. There was no correlation between online time and the number of views on any platform. In FB, 56% of the videos contained false information, with no difference in online time in both groups (16 [12-22] vs 18 [13-25], p = 0.3).). In YT, only 38% was considered false information, without differences between groups in online time (19 [11-26] vs 22 [12-24]).

Youtube				
	Total	Trustwhorty	False	P valor [c]
n (%)	50	31 (62)	19 (38)	-
Time on line[a, b]	21 (11-25)	19 (11-26)	22 (12-24)	0,76
# Reproductions [b]	40,5 (15,2-295,5)	25 (11-180)	239 (38-1082)	0,018
Most played video	*"Rheumatoid arthritis: biological treatment changed my life"*		*"Green celery juice for arthritis"*	-
Time on line	7 years		5 years	
# Reproductions	1 million		6.4 millions	

[a] Days; [b]median with interquartile range; [c] Mann-Whitney

Facebook				
	Total	Trustwhorty	False	P valor [c]
n (%)	50	22 (44)	28 (56)	-
Time on line[a, b]	17,5 (13-24)	16 (12 – 22,2)	18 (13 -24,7)	0,3
# Reproductions[b]	444 (47,5-18 89)	1050 (308- 2077)	89,5 (4,7- 1204)	0,012
Most played video	*"This woman lives with Rheumatoid Arthritis"*		"Why remove gluten and dairy products in cases of rheumatoid arthritis?"	-
Time on line	19 days		11 days	
# Reproductions	295 679		22 874	

[a] Days; [b]median with interquartile range; [c] Mann-Whitney

Conclusion: YT and FB are social networks with a high content of false information. The majority of available videos promise to cure different rheumatic diseases (even several simultaneously). This is the first work of a line of research that seeks to highlight the high degree of misinformation. We will continue to analyze other diseases and social networks, to make publications and communications in different media and to alert local regulatory entities.
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THU0627 VACCINATIONS IN PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES: STILL ROOM FOR IMPROVEMENT

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Background: Patients with autoimmune inflammatory rheumatic diseases (AIIRD) have an increased risk for acquiring infections. Vaccines were developed to diminish the prevalence of vaccine-preventable infections. The EULAR recommendations for vaccination in adult patients with AIIRD emphasise the importance of assessing the vaccination status of patients with AIIRD.
Objectives: To determine the vaccination status of patients with AIIRD, the reason for non-vaccination and the proportion of patients that are vaccinated according to the EULAR recommendations.
Methods: The single-centre cross-sectional COLOSSeUM study was conducted in a tertiary referral centre. Between August and December 2018, all consecutive patients with AIIRD including Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Ankylosing Spondylitis (AS) and Juvenile Idiopathic Arthritis (JIA) who visited the outpatient clinic were included. The vaccination status (influenza winter season 2017-2018, pneumococcal, tetanus toxoid and hepatitis B vaccine) and history of varicella zoster virus infection was determined using a one-page questionnaire which was completed by the treating rheumatologist after discussion with the patient.

The patients' reason for non-vaccination was registered if applicable. Patients were classified as vaccinated according to the EULAR recommendations if they had a yearly influenza, an every-five-year pneumococcal and a decennial tetanus toxoid vaccine, the latter as recommended in the general population.

Table 1: The vaccination status of AIIRD patients

		All AIIRD patients (n=633)	RA (n=489)	PsA (n=73)	AS (n=58)	JIA (n=13)
Influenza vaccine n(%)	Yes	438 (69.2)	360 (73.6)	45 (61.6)	28 (48.3)	5 (38.5)
	No	195 (30.8)	129 (26.4)	28 (38.4)	30 (51.7)	8 (61.5)
	Unk	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pneumococcal vaccine n(%)	Yes	203 (32.1)	174 (35.6)	19 (26.0)	10 (17.2)	0 (0)
	No	352 (55.6)	259 (53.0)	45 (61.6)	39 (67.2)	9 (69.2)
	Unk	78 (12.3)	56 (11.5)	9 (12.3)	9 (15.5)	4 (30.8)
Tetanus toxoid vaccine n(%)	Yes	348 (55.0)	265 (54.2)	41 (56.2)	33 (56.9)	9 (69.2)
	No	174 (27.5)	139 (28.4)	21 (28.8)	12 (20.7)	2 (15.4)
	Unk	111 (17.5)	85 (17.4)	11 (15.1)	13 (22.4)	2 (15.4)
Compliant with EULAR recommendations n(%)	Yes	117 (18.5)	100 (20.4)	9 (12.3)	8 (13.8)	0 (0)
	No	429 (67.8)	318 (65.0)	55 (75.3)	45 (77.6)	11 (84.6)
	Unk	87 (13.7)	71 (14.5)	9 (12.3)	5 (8.6)	2 (15.4)
Hepatitis B vaccine n(%)	Yes	193 (30.5)	138 (28.2)	20 (27.4)	28 (48.3)	7 (53.8)
	No	339 (53.6)	289 (59.1)	31 (42.5)	15 (25.9)	4 (30.8)
	Unk	101 (16.0)	62 (12.7)	22 (30.1)	15 (25.9)	2 (15.4)
History of Varicella zoster virus n(%)	Yes	447 (70.6)	355 (72.6)	47 (64.4)	34 (58.6)	11 (84.6)
	No	58 (9.2)	46 (9.4)	3 (4.1)	8 (13.8)	1 (7.7)
	Unk	128 (20.2)	88 (18.0)	23 (31.5)	16 (27.6)	1 (7.7)

AIIRD autoimmune inflammatory rheumatic diseases, RA Rheumatoid Arthritis, PsA Psoriatic Arthritis, AS Ankylosing Spondylitis, JIA Juvenile idiopathic arthritis, Unk unknown by patient

Results: The vaccination status of 633 consecutive patients was obtained. The group consisted of 489 (77.2%) patients with RA, 73 (11.5%) patients with PsA, 58 (9.2%) patients with AS and 13 (2.1%) patients with JIA with a mean ± standard deviation age of 59.8 ± 13.6, 55.8 ± 13.5, 45.2 ± 14.0 and 35.0 ± 13.9 respectively. Of all included patients with AIIRD, 69.2% were vaccinated for influenza, followed by vaccination rates of 55.0%, 32.1% and 30.5% for tetanus toxoid, pneumococcal and hepatitis B vaccination, respectively (Table 1). In addition, 70.6% of patients with AIIRD had a history of varicella zoster virus infection. Various reasons for non-vaccination were reported, of which 'No specific reason' was the most common, closely followed by non-awareness of the need for pneumococcal vaccination. The compliance with EULAR recommendations was 18.5%. Of the 429 patients with AIIRD not vaccinated according to the EULAR recommendations, 68 (15.9%) patients were not compliant with all three of the vaccines, 136 (31.7%) were not compliant with 2 vaccines (1: pneumococcal and 2: influenza or tetanus toxoid vaccine), 148 (34.5%) were not compliant with 1 vaccine (103 pneumococcal, 41 tetanus toxoid and 4 influenza vaccine) and 77 (17.9%) patients were unaware of their vaccination status for at least 1 vaccine.

Conclusion: In our patients with AIIRD, the highest vaccination rate for recommended vaccines was observed for influenza (nearly 70%). Not being vaccinated for pneumococcus was the main reason why patients did not comply with the EULAR recommendations. More attention is needed to determine and optimise the vaccination status of AIIRD patients and to increase the awareness regarding the pneumococcal vaccine.

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THU0628

IMMUNE-RELATED ADVERSE EVENTS INDUCED BY CANCER IMMUNOTHERAPIES. BIG DATA ANALYSIS OF 13,051 CASES (IMMUNOCANCER INTERNATIONAL REGISTRY)

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Background: The ImmunoCancer International Registry (ICIR) is a Big Data-Sharing multidisciplinary network composed by 39 specialists in Rheumatology, Internal Medicine, Immunology and Oncology from 18 countries focused on immune-related adverse events (irAEs) related to cancer immunotherapies (CIs).

Objectives: To analyse the worldwide scenario of irAEs associated with the use of CIs in this Century.

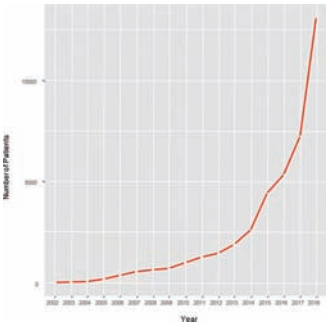
Methods: The first objective of the ICIR has been the development of a systematic literature review crossing CIs terms with immune diseases defined according to MedDRAVR 15.0.

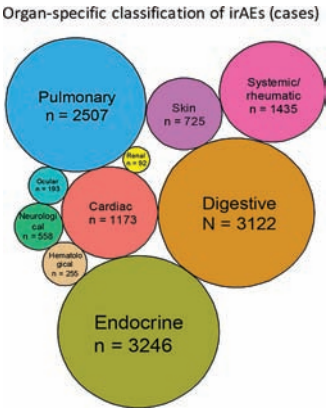
Results: The cumulated number of cases per year of irAEs has increased exponentially, with 12,648 patients who developed 13,051 irAEs reported until Dec 31, 2018:

: Combined CIs were used in 1962 (16%) patients, checkpoint inhibitors in 7099 (66%, overwhelmingly CTLA4 and PD1 inhibitors) and Tyrosine Kinase inhibitors in 3327 (31%); ipilimumab, nivolumab and pembrolizumab were associated with nearly 60% of reported cases. Organ-specific classification of irAEs is summarized in the figure:

The Top10 irAEs included enterocolitis (18%), pneumonitis (12%), thyroiditis (11%), myocarditis (6%), myositis (5%), hypophysitis (5%), hepatitis (5%), neuropathy (4%), adrenal (3%) and joint involvement (3%). Most irAEs are organ-specific symptoms not fulfilled criteria of systemic/rheumatic diseases.

Conclusion: More than 13,000 cases of irAEs triggered by CIs have been reported, with the organ-specific autoimmune damage of the endocrine, digestive and pulmonary systems accounting for 70% of the total reported irAEs.





Disclosure of Interests: Manuel Ramos-Casals: None declared, Oliver Lambotte: None declared, Marie Kostine: None declared, Leonard Calabrese Consultant for: Bristol-Myers-Squibb, Genentech and Astra-Zeneca., Maria Suarez-Almazor : None declared, Clifton Bingham Grant/research support from: BMS, Consultant for: AbbVie, BMS, Eli Lilly, Genentech/ Roche, Janssen, Pfizer, Sanofi/Regeneron, Timothy R. Radstake: None declared, Chiara Baldini: None declared, Thierry Schaeverbeke: None declared, Jacques-Eric Gottenberg Grant/research support from: Bristol-Myers Squibb, Grant/research support from: Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Lilly, Pfizer, Sanofi-Genzyme, UCB Pharma, Consultant for: Bristol-Myers Squibb, Eli Lilly, UCB, Sanofi-Genzyme, Pfizer, Hendrik Schulze-Koops Grant/research support from: Novartis, Pfizer, Roche, Consultant for: Abbvie, Actelion, Amgen, AstraZeneca, Biogen International, BMS, Celgene, Chugai, GSK, Hospira, Janssen-Cilag, Leo Pharmaceuticals, Lilly, MSD, Medac, Merck, Novartis, Pfizer, Hexal Sandoz, Sanofi, Roche, UCB, Paid instructor for: Abbvie, Actelion, Amgen, AstraZeneca, Biogen International, BMS, Celgene, Chugai, GSK, Hospira, Janssen-Cilag, Leo Pharmaceuticals, Lilly, MSD, Medac, Merck, Novartis, Pfizer, Hexal Sandoz, Sanofi, Roche, UCB, Speakers bureau: Abbvie, Actelion, Amgen, AstraZeneca, Biogen International, BMS, Celgene, Chugai, GSK, Hospira, Janssen-Cilag, Leo Pharmaceuticals, Lilly, MSD, Medac, Merck, Novartis, Pfizer, Hexal Sandoz, Sanofi, Roche, UCB, Jan Leipe Grant/research support from: Novartis, Pfizer; Scientific Support: Novartis, Pfizer, Consultant for: AbbVie, AstraZeneca, Bristol-Myers Squibb, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, Novartis, Roche, Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Janssen-Cilag, Lilly, Novartis, MSD, Pfizer, Roche, Sanofi, UCB, cassandra calabrese Speakers bureau: Regeneron/Sanofi, Pilar Brito-Zerón: None declared, Alejandra Flores-Chávez: None declared, Belchin Kostov: None declared, Soledad Retamozo: None declared, Gustavo Citera: None declared, Eva Aguilar: None declared, Michael Richter: None declared, Merav Lidar: None declared, Benjamin Fisher Consultant for: Novartis, Roche, MedImmune, Bristol-Myers Squibb, Jean-Marie Michot: None declared, David Liew: None declared, Russell Buchanan: None declared, Marte Schrumpf-Heiberg: None declared, Philippe Guilpain: None declared, Debashish Danda: None declared, Peter Olsson: None declared, Yasunori Suzuki: None declared, Saadettin Kılıçkap: None declared, Gabriela Hernandez-Molina: None declared, Virginia Fernandes Moça Trevisani: None declared, Sonja Praprotnik: None declared, Ildiko Fanny Horváth: None declared, Naoto Azuma: None declared, Berkan Armagan: None declared, Munther Khamashta: None declared, Xavier Mariette Grant/research support from: Servier, Consultant for: AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Pfizer, UCB Pharma

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THU0629 TREATMENT PATTERNS WITH DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN UNITED STATES VETERANS WITH NEWLY DIAGNOSED RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, OR ANKYLOSING SPONDYLITIS

Jessica A. Walsh[1], Shaobo Pei[1], Gopi Penmetsa[1], Brian Sauer[1], Vikas Patil[1], Jodi Walker[2], Jerry Clewell[2], Kevin Douglas[2], Daniel Clegg[1], Grant Cannon[1], Ahmad Halwani[1]. *[1]Salt Lake City Veteran Affairs and University of Utah Medical Centers, Salt Lake City, United States of America*; *[2]AbbVie, Inc, North Chicago, United States of America*

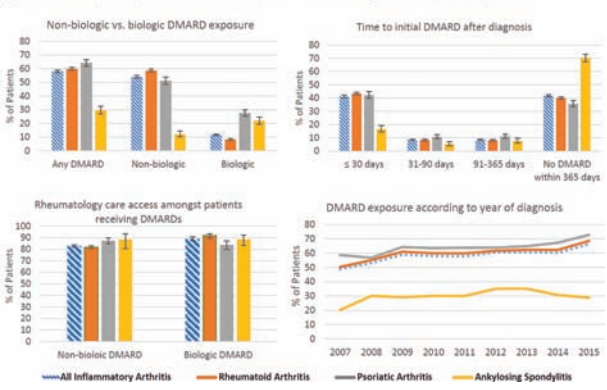
Background: Delays in treatment for inflammatory arthritis (IA) are associated with unfavorable outcomes, including impaired quality of life, irreversible joint damage, and disability.

Objectives: To characterize treatment initiation patterns in patients with newly diagnosed rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS).

Methods: Incident IA cases were identified between January 1, 2007 and December 31, 2015, in patients enrolled in the Veteran Health Administration, using International Classification of Diseases codes and natural language processing. Patterns of treatment initiation and non-treatment with disease modifying anti-rheumatic drugs (DMARDs) were assessed in the 12-month follow-up period after the incident diagnosis.

Results: The population consisted of 12, 118 IA patients (9,711 RA, 1,472 PsA, 935 AS), with 91.3% males and a mean age of 63.7. In total, 58.2% of patients initiated a DMARD within 12 months after diagnosis (RA 60.0%, PsA 64.3%, AS 29.6%) (Figure). A DMARD was dispensed ≤30 days after IA diagnosis in 41.2% of patients and ≤90 days in 50.0% of patients. Rheumatology specialty care was accessed during the study period, prior to DMARD dispensation, by 82.7% of patients exposed to a non-biologic DMARD and 90.0% of patients exposed to a biologic DMARD. The percentage of IA patients with DMARD exposure during the 12-month follow-up period increased from 48.8% in 2008 to 66.4% in 2015.

Figure. DMARD exposure patterns within 12 months after the initial diagnosis of inflammatory arthritis



Conclusion: Approximately one-half of patients received treatment with a DMARD within 90 days after their initial IA diagnosis. DMARD treatment rates during the initial 12 months after diagnosis increased between 2007 and 2015, but non-treatment remained common, particularly in patients with AS. Timely access to a rheumatology provider is likely important for early DMARD treatment.

REFERENCES:

[1] Ng, et al. BMJ Open. 3:e002468.

Disclosure of Interests: Jessica A. Walsh Grant/research support from: Abbvie, Pfizer
, Consultant for: Abbvie, Celgene, Lilly, Novartis
, Shaobo Pei: None declared, Gopi Penmetsa: None declared, Brian Sauer Grant/research support from: Amgen, Vikas Patil: None declared, Jodi Walker Shareholder of: Abbvie, Employee of: Abbvie, Jerry Clewell Shareholder of: Abbvie, Employee of: Abbvie, Kevin Douglas Shareholder of: Abbvie, Employee of: Abbvie, Daniel Clegg Grant/research support from: Amgen grant, Grant Cannon Grant/research support from: Amgen

Inc., Ahmad Halwani Grant/research support from: Bristol-Myers Squibb, Kyowa Hakko Kirin, Roche, Abbvie, Genentech, Immune Design, miRagen, Amgen, Seattle Genetics, Takeda, Pharmacyclics
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THU0630 THE ACR'S RHEUMATOLOGY INFORMATICS SYSTEM FOR EFFECTIVENESS (RISE) DEMONSTRATES IMPROVEMENTS IN MANY MEASURES OF QUALITY OF CARE BETWEEN 2016 AND 2017

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Background: The ACR's Rheumatology Informatics System for Effectiveness (RISE) is a national, EHR-enabled registry that passively collects data on all patients seen by participating practices, thus reducing the selection bias present in single-insurer claims databases. Launched in 2014, RISE is designed to help practices improve their quality of care.
Objectives: The objectives of our study were to a) examine changes in practice-level performance on selected quality measures for patients with rheumatoid arthritis (RA) in 2016 and 2017 and b) assess variations in performance over time between practices.
Methods: We analyzed data collected on all patients with a diagnosis of RA who had at least one clinic visit between January 1, 2016 and December 31, 2017. Six quality measures in the areas of RA management (disease activity measurement and tuberculosis (TB) screening), and cardiovascular risk reduction (body mass index (BMI) screening in 18-64 years, BMI screening in >64 years, tobacco use screening and cessation, and blood pressure (BP) control) were examined. Performance on quality measures, defined as the percentage of eligible patients receiving recommended care, was examined at the practice level. We used a hierarchical linear model to predict change in practice-level measure performance per quarter, accounting for clustering by practice. We also assessed variations in within-practice performance changes over time by calculating the range for each measure.
Results: Data from 150,099 patients from 135 practices was examined. Mean age was 63±14 years, 77% were female, 72% were Caucasian. The most common practice structure was a single-specialty group practice (65%), followed by solo (20%) and multi-specialty group practice (10%). From January 2016 to December 2017 there was an improvement in quarterly performance on disease activity measurement (+2.9%, p<0.001), TB screening (+1.9%, p<0.001), BMI screening in 18-64 years (+2.4%, p<0.001), and tobacco use screening and cessation (+1.2%, p<0.001), and a decline in quarterly performance on BMI screening in >64 years (-0.4%, p<0.001) and BP control (-0.6%, p<0.001). Improvements in performance on RA management measures were steady from Q1 2016 to Q4 2017 (Figure). Within-practice change in performance varied significantly across practices (Table). For example, from 2016 to 2017 within-practice change in performance on blood pressure control varied from a decrease by 66.7% to an increase by 100%.
Conclusion: Among practices participating in RISE, from 2016 to 2017 average performance on most measures for individuals with RA improved. We found significant variations in performance over time between practices, suggesting that future work to identify workflow patterns leading to high performance or to dramatic improvements in quality are warranted.
Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

Figure. Performance on Rheumatoid Arthritis Management Quality Measures in the RISE Registry, by quarter.

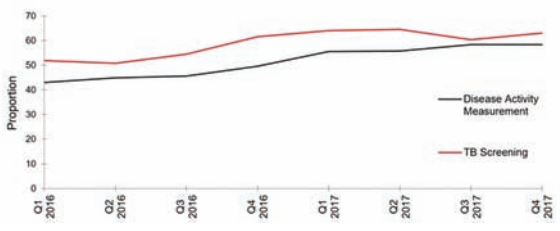


Table. Performance on Quality Measures in the RISE Registry in 2016 and 2017.

Quality Measure	2016		2017		
	Measure denominator (N)	Average practice-level performance (%) Percentile (50th, 99th)	Measure denominator (N)	Average practice-level performance (%) Percentile (50th, 99th)	Change in average practice-level performance from 2016 to 2017 (%) Range
Disease Activity Measurement	327,964	24.0, 100	323,263	55.0, 100	-67.2 - +86.5
Tuberculosis Screening	37,237	60.0, 98.6	28,505	67.9, 96.6	-35.7 - +53.6
BMI Screening, 18-64 years	183,407	35.7, 98.8	291,387	48.1, 98.7	-32.3 - +72.1
BMI Screening, >64 years	146,637	56.7, 96.8	285,691	46.4, 97.1	-55.3 - +72.4
Tobacco Use Screening and Cessation	332,771	88.2, 100	326,151	90.3, 100	-44.1 - +88.3
Blood Pressure Control	55,087	64.1, 100	63,922	60.3, 100	-66.7 - +100

Table. Performance on Quality Measures in the RISE Registry in 2016 and 2017.

Quality Measure 2016 2017 Measure denominator (N) Average practice-level performance (%) Measure denominator (N) Average practice-level performance (%) Change in average practice-level performance from 2016 to 2017 (%) Percentile (50th, 99th) Percentile (50th, 99th) Range

Disclosure of Interests: Zara Izadi Consultant for: I worked as a paid consultant for Celgene from 2014 to 2017., Gabriela Schmajuk Grant/research support from: Investigator initiated award from Pfizer from 2015-2018, unrelated to this work, Julia Kay: None declared, Rachel Myslinski: None declared, Jinoos Yazdany Grant/research support from: Pfizer, Consultant for: AstraZeneca
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THU0631 IMPACT OF DAY OF ADMISSION AND TIME TO DIAGNOSTIC ARTHROCENTESIS ON MORTALITY AND OTHER OUTCOMES IN SEPTIC ARTHRITIS: A NATIONWIDE ANALYSIS

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Background: Multiple studies have been done assessing the "weekend effect" and outcomes for hospitalized patients[1,2,3,4], however, there is no data evaluating the outcome of patients with septic arthritis of a native joint (SANJ) who are admitted on the weekend compared to the rest of the week.
Objectives: To evaluate whether important outcomes in SANJ, including in-hospital mortality, differ between patients admitted on weekends versus weekdays and the time to diagnostic arthrocentesis.
Methods: The National Inpatient Sample (NIS) database of the year 2016 was utilized for patients admitted to the hospital with a principal discharge diagnosis of SANJ. This was a retrospective cohort study of patients hospitalized in 2016 with SANJ in hospitals across the US. Patients were included if they were adults with a principal diagnosis of SANJ based on ICD-10 codes. Admissions between midnight Friday and midnight Sunday were classified as weekend admissions. Early arthrocentesis was defined as percutaneous arthrocentesis performed within 24 hours of admission. The proportion of patients with SANJ admitted over weekends versus weekdays was determined. Odds ratios (OR) were calculated for primary and secondary outcomes including in-hospital mortality rate, rates of diagnostic arthrocentesis and early arthrocentesis, length of stay and total hospital charges, These results were compared after multivariable logistic regression adjusted for age, gender, race, day of admission, Charlson comorbidity index and median household yearly income in the patient's zip code. We used STATA-15 for statistical analysis.
Results: The study included 12819 patients with SANJ. Compared with patients admitted on weekdays, patients with SANJ admitted on weekends had increased in-hospital mortality rates (adjusted odds ratio[aOR] 3.67; 95% [CI] 1.52 – 8.86, p<.005), but similar early arthrocentesis rates ([aOR] 1.14; 95%, [CI] 0.90 – 1.45 p>0.05), length of stay (p>0.05) and hospital charges ($ 2751.11; 95% [CI] -4449.6 – 9951.8; P>0.05). However, regardless of the day of admission those who received an early arthrocentesis had lower length of stay (-1.46, p<0.05), and lower total hospital charges ($ -6527 $; p<0.05).

Conclusion: This study showed that compared with patients admitted on weekdays, patients with SANJ admitted on weekends had increased mortality rates but similar length of stays and total hospital charges. However, patients who received an early arthrocentesis had significantly lower length of stay and hospital charges regardless of the day of admission. This results add weight to the hypothesis of negative outcomes in weekend admissions. Moreover, we believe that our findings require further investigation to establish the role of early arthrocentesis in the management of septic arthritis.

REFERENCES:

[1] Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. N Engl J Med 2001;345:663-8.
[2] Pauls LA, et al. The Weekend Effect in Hospitalized Patients: A Meta-Analysis. J Hosp Med. 2017 Sep;12(9):760-766.
[3] Honeyford K, et al. The weekend effect: does hospital mortality differ by day of the week? A systematic review and meta-analysis. BMC Health Serv Res. 2018 Nov 20;18(1):870
[4] Kostis WJ, Moreyra AE. Severity of illness and the weekend effect. Lancet. 2017 Oct 14;390(10104):1734-1735.

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DOI: 10.1136/annrheumdis-2019-eular.5197

THU0632 A POPULATION-BASED STUDY OF TUBERCULOSIS INCIDENCE AMONG RHEUMATIC DISEASE PATIENTS UNDER ANTI-TNF TREATMENT

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Background: Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, with a high incidence in the general population of Brazil. The advent of immunobiologic therapy with anti-TNF agents for rheumatic diseases, despite achieving substantial efficacy in controlling disease activity, has been associated with a significant increase in incident cases of tuberculosis in this population due to blockade of TNF, which is responsible for maintenance of granuloma structure.
Objectives: Estimate the incidence of tuberculosis in Public Health System patients receiving anti-TNF therapy for rheumatic diseases. As secondary objectives, we sought to evaluate mortality and the influence of screening for latent tuberculosis infection on clinical outcomes in this population.
Methods: This retrospective cohort study included all Public Health System patients from the Brazilian state of Rio Grande do Sul (RS) who received prescriptions of anti-TNF agents for treatment of rheumatic diseases between 2006 and 2016. All data were obtained from official government records (drug dispensing, tuberculosis reporting, and mortality) where notification was mandatory. For a subset of patients, latent tuberculosis screening data were obtained through a review of medical records.
Results: A total of 5853 patients were included from 2006 to 2016, out of which 3653 (62.4%) had rheumatoid arthritis, 1150 (19.7%) had ankylosing spondylitis, 872 (14.9%) had psoriatic arthritis, and 123 (2.1%) had juvenile idiopathic arthritis. Overall, 43 cases of TB were found, with an incidence of 734.7 cases per 100,000 exposed, which corresponds to 2.86 per 1000 person-years exposed. Two hundred and fifty deaths occurred in this cohort. In a subgroup of patients recruited from the outpatient rheumatology clinic of Hospital de Clínicas de Porto Alegre (n = 268), screening for latent tuberculosis infection (LTBI) was performed in 86% of patients before initiation of anti-TNF therapy; 30.1% had a positive tuberculin skin test. LTBI treatment was administered to 74 patients. In this subgroup of patients, 5 cases of TB were diagnosed, 2 in patients who had previously completed LTBI treatment.
Conclusion: In this population-based study, a high incidence of tuberculosis among patients with rheumatic diseases exposed to anti-TNF agents was found, reinforcing the need for screening and treatment of LTBI to reduce the risk of reactivation of granulomatous disease. No significant impact on mortality was demonstrated.

REFERENCES:

[1] Gómez-Reino JJ, Carmona L, Rodríguez Valverde V, Mola EM, Montero MD. Treatment of rheumatoid arthritis with tumor necrosis factor inhibitors may predispose to significant increase in tuberculosis risk: A multicenter active-surveillance report. Arthritis Rheum. 2003;
[2] Arkema E V, Jonsson J, Baecklund E, Bruchfeld J, Feltelius N, Askling J. Are patients with rheumatoid arthritis still at an increased risk of tuberculosis and what is the role of biological treatments? Ann Rheum Dis. 2014;
[3] Gomez-Reino JJ, Carmona L, Angel Descalzo M. Risk of tuberculosis in patients treated with tumor necrosis factor antagonists due to incomplete prevention of reactivation of latent infection. Arthritis Rheum. 2007;
[4] Yonekura CL, Oliveira RDR, Titton DC, et al. Incidência de tuberculose em pacientes com artrite reumatoide em uso de bloqueadores do TNF no Brasil: dados do Registro Brasileiro de Monitoração de Terapias Biológicas BiobadaBrasil. Rev Bras Reumatol. 2017.

Disclosure of Interests: None declared
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THU0633 ECONOMIC IMPACT OF HEALTHCARE RESOURCE UTILIZATION AND WORK DISABILITY IN PORTUGUESE PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS FROM THE ASSESSMENT OF RESULTS IN ANKYLOSING SPONDYLITIS(AREA) STUDY

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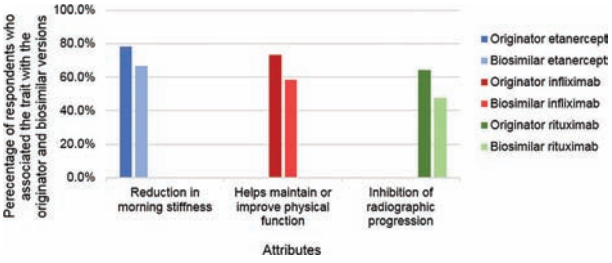
Background: Ankylosing spondylitis (AS) has a significant burden upon the individual, family and society. Understanding the economic impact of AS is crucial to substantiate policies that promote early referral, diagnosis and treatment.
Objectives: To assess the economic impact of AS in Portugal concerning healthcare utilization and work disability.
Methods: The Assessment of REsults in Ankylosing spondylitis (arEA) study was developed by the NOVA-Information Management School (Lisbon) in collaboration with the Portuguese Society of Rheumatology, the Portuguese Association of Family Physicians, the National Association of Primary Care Units, the National Association of AS Patients and the Portuguese League Against Rheumatic Diseases. The arEA aimed at assessing reasons for delayed diagnosis of AS, as well as disease impact in patients' lives, global health and work. A comprehensive online survey was developed and sent to AS patients. Data on demographics, lifestyle habits, daily life activities, working habits, disease indexes and healthcare utilization was retrieved. Costs of the disease for patients resulting from the use of health systems was obtained thorough patient's declaration, the cost for the national health service (SNS) was obtained combining primary data and secondary data related with the average costs of service use. Finally, the impact over the economy was also estimated through the participation of patients in labor market and using as mediator variables the absenteeism and presenteeism. A set of generalized linear models were used to identify the factors with significant effect over health status, SNS costs and impact over economy.
Results: 354 patients responded the survey, 42.1% female, more frequently from the 35-44 year-old age group. In the previous 12 months, 76% reported using the National Healthcare System (SNS) for AS-related reasons (85% outpatient visits; 74% diagnostic exams; 48% ER visits; 8% inpatient admissions). During that period, estimated SNS expenditure with AS patients reached € 47 million, excluding costs with medication (ongoing analysis), distributed as: outpatient visits € 25 million, diagnostic exams € 7 million, ER visits € 3 million and inpatient admissions € 12 million. Adding to this, patients spent on average € 84 million out of their own pocket on AS-related expenses (€ 1.786 per patient: outpatient visits € 245, diagnostic exams € 151, ER visits € 48, inpatient admissions € 415, medication € 593, travelling expenses € 334). Regarding work disability, working AS patients reported an average of 12 days on leave of absence and 25 days on sick leave per year, with an estimated cost of € 28 and € 57 million, respectively. Presenteeism led to a loss of 73 working days with a cost of € 165 million. Taking also into account patients with prolonged leaves of absence (€ 72 million), permanent leaves (€ 18 million), unemployed (€ 50 million) and family medical leaves (€ 47 million), the overall costs with work disability in AS reached € 437 million in one year.

Conclusion: AS-related work disability and healthcare resource utilization have an enormous economic impact in Portugal. Investment in strategies that encourage early referral, diagnosis and treatment is fundamental to mitigate such burden.
Disclosure of Interests: None declared
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THU0634 PHYSICIAN PERCEPTIONS OF BIOLOGICS VERSUS THEIR BIOSIMILAR COUNTERPARTS IN RHEUMATOLOGY: A MULTICOUNTRY STUDY IN EUROPE

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Background: Following LOE for the originator brand of etanercept in 2016 and the subsequent launch of its first biosimilar version, several other biosimilars have arrived in the rheumatoid arthritis treatment space. Due to their potential for reducing healthcare spend and their supposed equivalence, biosimilars are expected to be of rising relevance and impact in the following years. 12 biosimilar brands of biologic originator treatments are now available in Europe to treat rheumatoid arthritis; it will be crucial to understand physician perceptions of biosimilars relative to branded products and the impact such views have on potential prescribing decisions.
Objectives: The objective of the study was to assess perceptions of efficacy and safety for biosimilars relative to branded biologic originator products among treating Rheumatologists in the EU5 countries (United Kingdom (UK), France (FR), Italy (IT), Spain (SP) and Germany (DE)).
Methods: A cross-sectional survey was conducted in Q3 2018 in the EU5 among national, regional and hospital physicians who had been practicing between 3-30 years. Respondents completed a Physician Perceptual Questionnaire online, which assessed the overall perception of biologic brands and anti-TNF biosimilars, important attributes for treatments, and specific barriers to prescribing them. Data were analyzed using descriptive statistics.



Results: A total of 261 rheumatologists in the EU5 were recruited as part of the study (with almost equal numbers of rheumatologists representing each EU5 country). Treating rheumatologists were practicing for an average of 17.4 years, mainly in teaching hospitals (50.2%) and urban hospitals (20.7%)[1]. Physicians consistently expressed greater satisfaction for branded products, with 73.9% (range: 63.5% DE to 90.6% FR) of physicians having rated satisfaction with the originator brand of etanercept as a 6 or 7 (on a 7-point scale where 7 corresponded to highest satisfaction), compared to only 37.5% for biosimilar etanercept (range: 28.6% IT to 51.9% DE)[1]. When asked about specific attributes related to RA treatments, 64.4% of our sampled rheumatologists associated the originator brand of rituximab with 'Inhibition of radiographic progression' (range: 55.1% IT to 81.1% FR) – versus 47.5% association for biosimilar rituximab (range: 32.7% IT to 62.3% FR)[1]. 73.2% of physicians associated the originator brand of infliximab with 'helps maintain or improve physical function' (range: 55.8% DE to 87.0% ES) compared to 58.6% of biosimilar infliximab (range: 44.9% IT to 67.9% FR)[1]. For 'reduction in morning stiffness', 78.5% of our rheumatologists associated it with originator etanercept (range: 65.4% DE to 88.7% FR) versus only 66.7% for biosimilar etanercept (range: 55.1% IT to 81.1% FR)[1].

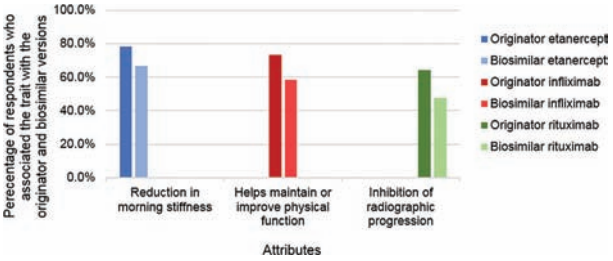


Figure: EU5 Physician Perceptions: Attribute associations for branded versus biosimilar products

Conclusion: Biosimilars score lower on overall satisfaction and are less frequently associated with specific efficacy attributes relative to branded products. This is possibly due to their relatively short time in clinical practice, and the resulting lack of experience and supporting data compared to the older branded equivalents. Proof of concept may be essential to close the perceptual gap that still exists between branded products and biosimilars.

REFERENCES:

[1] Ipsos RA Therapy Monitor (261 sampled rheumatologists reporting on RA patients in EU5 in Q3 2018)

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THU0635 REAL WORLD PHYSICIAN SATISFACTION WITH SECUKINUMAB IN PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS IN EUROPE

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Background: Psoriatic arthritis (PsA) and ankylosing spondylitis (AS) can lead to reduced physical functioning and quality of life. Secukinumab has demonstrated clinical benefits in PsA and AS, however little is known about physician satisfaction with its ability to control disease in the real world.
Objectives: Assess physician satisfaction with secukinumab's ability to control disease in a real-world setting.
Methods: This was a cross-sectional survey of rheumatologists and dermatologists (PsA only) in France, Germany, Italy, Spain, and UK. Data were collected from Jun-Aug 2018 via physician-completed patient record forms. Patients receiving any treatment were included in the survey. Patients receiving secukinumab >1 month were included in this analysis. Physicians rated satisfaction on a 5-point scale (Very satisfied to very dissatisfied), a binary variable of satisfied/not satisfied was created by grouping "Very satisfied" and "Satisfied" responses as satisfied and "Neutral", "Dissatisfied", and "Very dissatisfied" as not satisfied. Data were reported by disease, then stratified by overall physician-rated disease severity (mild/moderate/severe) at initiation of secukinumab, prior biologic use, treatment duration, and concomitant medication.
Results: 438 PsA and 277 AS patients were receiving secukinumab >1month at time of data collection. Patient mean age was 46.9 years (48.2 PsA, 44.8 AS) with 35.2% female (41.8% PsA; 24.9% AS). On average, patients had received secukinumab for 8.8 months (9.2 PsA; 8.2 AS). At secukinumab initiation, 44.2% of patients were rated by their physician as severe vs. 3.5% at the current consultation (39.3% vs. 2.7% PsA; 52.0% vs. 4.7% AS).
Overall, 87.6% of physicians were satisfied with the ability of secukinumab to control disease (87.9% PsA; 86.3% AS). Physicians report high satisfaction across each stratification (Table 1).

Table 1. Population characteristics, and physician reported satisfaction with secukinumab

	Population characteristics		Satisfaction level	
	N (%) PsA patients in each category (n=438)	N (%) AS patients in each category (n=277)	N (%) PsA physicians satisfied (n=438)	N (%) AS physicians satisfied (n=277)
Overall satisfaction	-	-	385 (87.9)	239 (86.3)
*Severity at initiation**	28 (6.4)	5 (1.8)	18 (64.3)	4 (80.0)
Mild	236 (54.3)	128 (46.2)	210 (89.0)	109 (85.2)
Moderate	171 (39.3)	144 (52.0)	155 (90.6)	126 (87.5)
Severe				
Prior biologic use	191 (43.6)	147 (53.1)	155 (81.2)	118 (80.3)
Bio-experienced patients	247 (56.4)	130 (47.9)	230 (93.1)	121 (93.1)
Bio-naive patients				
Secukinumab duration	82 (18.7)	72 (26.0)	56 (68.3)	48 (66.7)
1-4 months	120 (27.4)	68 (24.5)	108 (90.0)	61 (89.7)
>4-6 months	236 (53.9)	137 (49.5)	221 (93.6)	130 (94.9)
>6 months				
Concomitant medication	236 (53.9)	117 (42.2)	214 (90.7)	103 (88.0)
Monotherapy	104 (23.7)	113 (40.8)	89 (85.6)	95 (84.1)
Combination with a non-csDMARD	98 (22.4)	47 (17.0)	82 (83.7)	41 (87.2)
Combination with a csDMARD				

*PsA base size=435

Conclusion: This study provides insight into physician satisfaction with secukinumab in a real-world clinical setting. Physicians reported being highly satisfied with the ability of secukinumab to control PsA and AS disease, regardless of patient population subgroups.

Disclosure of Interests: Elizabeth Holdsworth Employee of: Adelphi Real World, Nicola Booth Employee of: Adelphi Real World, Steve Lobosco Employee of: Adelphi Real World, Olivia Massey Employee of: Adelphi Real World, Amie Scott Consultant for: Novartis Pharmaceuticals Corporation, Haijun Tian Shareholder of: Novartis Pharmaceutical Corporations, Employee of: Novartis Pharmaceutical Corporations, Dorothy Keininger Shareholder of: Novartis, Employee of: Novartis

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THU0636 HIGHER SOCIAL MEDIA USER STICKINESS ON SELF-MANAGEMENT SYSTEM MAY IMPROVE THE REMISSION RATE OF PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: With the advence of mobile health technologies, it is possible to set up economic management systems to improve health care. By using a Smart-phone Spondyloarthritis Management System (SpAMS), the Chinese Ankylosing Spondylitis (AS)/Spondyloarthritis Prospective Imaging Cohort (CASPIC) was launched.

Objectives: To explore the improvement of disease management and cost effectiveness of SpAMS for Chinese patients with AS.

Methods: Patients enrolled in the CASPIC cohort who fulfilled the 1984 modified New York criteria and with at least 2 evaluations of Ankylosing Spondylitis Disease Activity Score (ASDAS) were included in this analysis. All physician-reported assessments were collected at the Chinese People's Liberation Army General Hospital using SpAMS in Beijing. The disease activity states were defined according to ASDAS1, which separated inactive disease (ID) from low disease activity (LDA) by 1.3, LDA from high disease activity (HDA) by 2.1, and HDA from very high disease activity (VHDA) by 3.5. According to ASDAS at the baseline visits and final visits, patients were divided into four groups (Figure 1): maintainer of ID/LDA, patients with relapse, maintainer of active disease, and new achiever of ID/LDA.

Results: From April 2016 to April 2018, 1201 patients with AS were enrolled in CASPIC. 4659 patient self-assessments were completed, including 3304 pre-visit assessments and 1355 assessments during the follow-up interval. After online consultation, 29.1% of clinic visits to a tertiary hospital were considered unnecessary and could be solved in the primary care hospital. The time and cost of each patient's journey to Beijing were calculated based on the location of each patient. For the 1037 (86.3%) patients who lived outside the vicinity of Beijing, at least an average of 5.3 hours and 327.4 RMB for each person (USD: RMB =1:6.418) for traffic time and expenses were saved, which equaled to 16% of the Chinese monthly disposable personal income (data in 2016).

Table 1. Characteristics of disease activity

Characteristics	ID/LDA at baseline (n=445, 57.2%)			Active at baseline (n=332, 42.7%)		
	Maintainers of ID/LDA (n=410, 92.1%)	Patients with relapse (n=35, 7.9%)	*P* value	Maintainers of active disease (n=127, 38.2%)	New achievers of ID/LDA (n=205, 61.7%)	*P* value
Age, mean (S.D.), years	30.2 (9.1)	29.8 (7.6)	0.785	30.8 (8.6)	30.6 (8.3)	0.816
Disease duration, mean (S.D.), years	7.6 (6.2)	7.3 (5.6)	0.787	9.0(6.1)	9.3(6.1)	0.714
Number of self-assessments, mean (S.D.)	5.0 (2.7)	3.3 (1.8)	<0.001*	4.5(2.5)	5.6(3.1)	<0.001*
Male sex,%	79.8	88.6	0.207	89.8	83.9	0.133
ASDAS at baseline, mean (S.D.)	1.4 (0.5)	1.5 (0.4)	0.031*	3.2 (0.8)	3.0 (0.8)	0.134
Smoker,%	24.7	40.0	0.047*	44.0	32.8	0.042*
NSAIDs at baseline,%	98.1	99.8	0.448	97.9	99.4	0.263
TNFi at baseline,%	19.2	13.8	0.479	24.5	29.8	0.359
DMARDs at baseline,%	64.0	72.4	0.363	66.0	68.5	0.679
TNFi during follow-up period[a],%	29.9	27.3	0.755	32.3	45.6	0.016*

*$P < 0.05$.

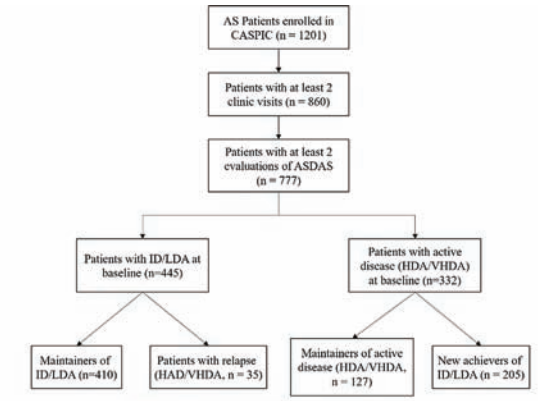


Figure 1. Flow chart of participants in the study

Abbreviation: ID: inactive disease; LDA: low disease activity; HDA: high disease activity; VHDA: very high disease activity

Of these patients enrolled in CASPIC, 777 patients had at least 2 evaluations of ASDAS. The rate of patients with ID/LDA was 57.2% at baseline and increased significantly to 79.2% with a mean (SD) follow-up of 13.3 (5.9) months (Table 1). Compared with patients who relapsed, those that maintained the ID/LDA had more patient assessments [5.0 (2.7) vs 3.3 (1.8), P < 0.001]. The new achievers of ID/LDA also completed online patient assessments more frequent [5.6 (3.1) vs 4.5 (2.5), P < 0.001] compared to patients who maintained active disease.

Conclusion: Higher social media user stickiness on self-management system may improve the remission rate of AS patients. SpAMS could serve as a cost- and time-saving specialty care online platform for patients with AS.

REFERENCES:

[1] Machado PM, Landewé R, Heijde Dvd. Ankylosing Spondylitis Disease Activity Score (ASDAS): 2018 update of the nomenclature for disease activity states. Ann Rheum Dis 2018:annrheumdis-2018-213184

Disclosure of Interests: None declared
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THU0637 ACADEMIC ACHIEVEMENT, EMPLOYMENT STATUS, WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA): DETERMINANTS AND CONSEQUENCES

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Background: Changes occurring in childhood due to JIA leads to activity and work impairment during their transition to adulthood. The factors impairing work and overall activity among adults with JIA need to be explored to formulate policy decisions and rehabilitation measures.
Objectives: • To assess the level of academic achievement, employment, work productivity and activity impairment among adults suffering from JIA
• To identify factors determining activity impairment among adults with JIA
Methods: Consecutive adults classified as JIA (1) were included. Consenting patients filled a questionnaire comprising of demographic details, occupational/educational status, Indian health associated questionnaire (iHAQ), Work Productivity and Activity Impairment score (WPAI) (2)in the language of their choice. Clinical evaluation for disease activity and damage was done and remission was assessed by Wallace criteria. Remission was defined as ever remission: ≥3 months and sustained remission: ≥ 6 months of disease control. Appropriate statistical tests to assess association and correlation of various factors with WPAI were used.
Results: Demography (n=51) is depicted in table 1. Never attaining remission resulted in significantly higher college dropouts (8 vs 17, p<0.05), functional impairment (mean iHAQ 1.08 vs 0.5, p<0.05) and articular damage (mean JADI A 3 vs 8, p<0.01). Disease duration, JADI A and iHAQ correlated well (r^2 >.400, p<0.05) with measures of WPAI (table 2). Assessment of patient variables like gender, occupation, disease activity and remission status (figure 1) showed that women, especially the homemakers and individuals with moderate to high disease activity had significant activity impairment (P<0.05).
Conclusion: Early effective treatment directly impacts employment levels and activity in adults with JIA. Homemakers in middle- and low-income countries have the most impairment in activity as they cannot alter their work. Replacement costs for homemakers would be an added financial burden to the family and is seldom captured by studies. Our study highlights the need to look further into the indirect and intangible costs involving women that will help policy makers formulate effective economic policies for individuals with JIA.

REFERENCES:

[1] Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004 Feb;31(2):390–2.
[2] Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics. 1993 Nov;4(5):353–65.

Table 1. Demographic, educational, occupational, health profile and WPAI measures of adults with JIA

S.No	Parameter (N=51)	Median	IQR
1	**Age**	22	8
2	**Disease duration (years)**	9	10
3	**Duration of treatment (years)**	5	5
4	**WPAI Measures (in percentage)**	40	50
	Overall Activity Impairment	64.06	61.66
	Overall Work Impairment (N=14)	40	72.05
	Presentism (N=12)	33.03	51.14
	Absenteeism (N=14)		
		Frequency (n)	**Percentage (%)**
1	**Gender**	**24/27**	**47.1/52.9**
	Male/Female		
2	**Residential type**	10/41	19.6/80.4
	Urban/Rural		
3	**Educational Status**	1	2
	Illiterate	10	19.6
	Less than high school	14	27.5
	High School	8	15.7
	Intermediate/Diploma	18	35.3
	Graduate/Postgraduate or above		
4	**Occupation status**	18	35.3
	Student	14	27.5
	Employed/Professional/Business	12	13.7
	Housewife	7	11.8
	Unemployed/Quit job due to illness		
5	**JIA Subtype**	6	11.8
	Systemic Arthritis	4	7.8
	Oligo Arthritis	2	3.9
	Polyarthritis (RF-Negative)	15	29.4
	Polyarthritis (RF-Positive)	23	45.1
	Enthesitis-Related JIA	1	2.0
	Undifferentiated Arthritis		
6	**Deformity**	27/24	52.9/47.1
	Absent/Present		
7	**Remission**	16/35	31.4/68.4
	Never/Ever Remission	10/14	19.6/27.5
	Sustained remission before/after 18 yrs		

Figure 1: Correlation between various disease associated factors and WPAI measures.

Variables	Current Age	Disease duration (Years)	Damage Index (JADIA)	Functional disability score (IHAQ)	Patient VAS (%)	Physician VAS (%)	Overall work Impairment	Overall Activity Impairment	Absenteeism
Current Age	1								
Disease duration (Years)	.763**	1							
Damage Index (JADIA)	.378**	.301*	1						
Functional disability score (IHAQ)	.572**	.476**	.715**	1					
Patient VAS (%)	.228	.259	.723**	.638**	1				
Physician VAS (%)	.338*	.374**	.679**	.588**	.931**	1			
Overall work Impairment	.606*	.398	.691**	.636*	.549*	.541*	1		
Overall Activity Impairment	.481**	.410**	.414**	.519**	.373**	.381**	.844**	1	
Absenteeism	.661*	.600*	.480	.644*	.360	.398	.822**	.546*	1
Presentism	.358	.187	.634*	.368	.354	.295	.911**	.826**	.388

WPAI- Work productivity and activity impairment, JADI A- Juvenile arthritis damage index- articular, VAS- Visual analogue scale, IHAQ- Indian Health associated questionnaire. * P value<0.05, ** P value<0.001.

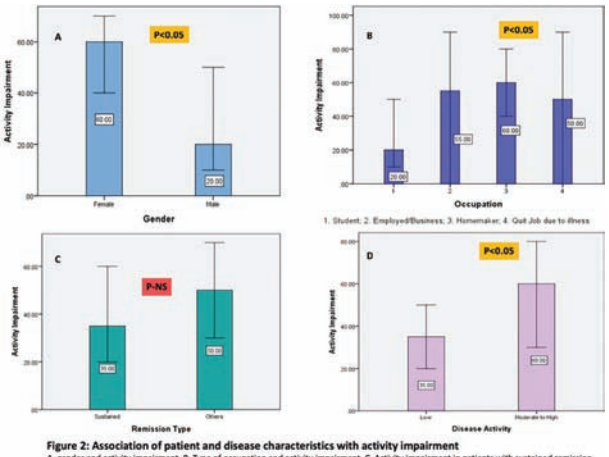


Figure 2: Association of patient and disease characteristics with activity impairment
A. gender and activity impairment, B. Type of occupation and activity impairment, C. Activity impairment in patients with sustained remission and others, D. current disease activity by cJADAS/ JSpADA and activity impairment

Disclosure of Interests: None declared
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THU0638 CONSIDERATIONS FOR IMPROVING QUALITY OF CARE IN RHEUMATOID ARTHRITIS AND ASSOCIATED COMORBIDITIES

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Background: The presence of comorbidities in patients with rheumatoid arthritis (RA) contributes to increased morbidity and mortality(1). Patients

with RA have an increased risk of comorbidities e.g. interstitial lung (IL) disease (7.7% incidence[2]; up to 60% IL abnormalities in early RA[3]), depression (up to 200%[4]; 16.8%[5]), cardiovascular disease (40-70%[6]; 5-12.9%[7]) and diabetes (IR of 8.6 per 1000 person-years[8]; 20%[9]). Yet, there are few comprehensive recommendations on the management of RA-related comorbidities.

Objectives: This study aimed to identify models of good quality care for patients with RA and their associated comorbidities in Europe and understand how these practices can be widely implemented.

Methods: Existing published recommendations across Europe on good practice in RA care including screening/managing selected comorbidities were reviewed. Team members of 12 specialist centres across Europe were interviewed. The interventions identified were reviewed and prioritised to form a selection of considerations by a consensus process involving 18 experts including rheumatologists, a patient rep., a nurse and also RA comorbidity specialists: cardiologist, psychologist, pulmonologist and diabetologist.

Results: The interventions were prioritised for each patient profile:

a. suspected RA:
1. rapid access to care (online referral, triage, ultrasound–guided diagnosis)
2. enhanced communication with primary care (hotline, education sessions)
3. early arthritis clinic (timely clinical assessment and diagnosis)

b. recently diagnosed:
1. enabling self–management (self–monitoring and disease activity management support)
2. early arthritis clinic
3. comprehensive comorbidity assessment (standalone or in conjunction with RA appointment)

c. established disease:
1. dedicated comorbidity specialist
2. integrating patient registries into daily clinical practice
3. enabling self–management

Eleven other interventions were identified including task-shifting to non-physician healthcare professionals, tailored education to patients and family members, and developing care networks.

Conclusion: Despite limited European recommendations on management of RA comorbidities, a range of good practice care model interventions across Europe were identified which are non-complex, high-impact and meaningful. Next step will be to assess how these care models can be implemented in different healthcare systems for the benefit of patients with RA.

REFERENCES:

[1] Dougados, et al. Ann Rheum Dis 2014; 73:62
[2] Bongartz, et al. Arthritis Rheum 2010; 62(6):1583
[3] Reynisdottir, et al. Arthritis Rheum 2014; 66:31
[4] Sheehy, et al. Rheum 2006; 45(11):1325-1327
[5] Matcham, et al. Rheumatology 2013; 52:2136
[6] Holmquist, et al. Ann Rheum Dis 2017; 76:1642
[7] Van Halm, et al. Ann Rheum Dis 2009; 68(9):1395
[8] Solomon D, et al. Ann Rheum Dis 2010; 69(12):2114
[9] Albrecht K, et al. Rheum 2018; 57(2):329-336

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THU0639 AUTOMATED CAPTURE AND HIGH UPTAKE RATES OF PATIENT REPORTED OUTCOME MEASURES IN ROUTINE RHEUMATOLOGY PRACTICE

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Background: Patient reported Outcome Measures (PROMs) are an integral part of value based healthcare and outcomes that matter to patients; however resource and time constraints are often barriers for routine collection in clinic.

Objectives: We piloted an automated, electronic collection of PROMs for patients attending an outpatient specialist rheumatology clinic.

Methods: All patients with a clinic appointment were sent an automated text message, one day before their scheduled doctor's appointment, with a hyperlink to fill in the Routine Assessment of Patient Index Data (RAPID3) [0-30, 30 being worst, calculated as the sum of physical function measured using the 10-item multidimensional health assessment questionnaire (mdHAQ), pain visual analogue scale (VAS), and patient global VAS questionnaire]. The text message was personalised with the attending physician's name and thumbnail photograph and the questionnaire was presented in the patient's preferred language (English or simplified Chinese) by detecting their phone configuration. RAPID3 responses flowed back to the electronic medical record and were available for the attending clinician to view during the clinic consult the next day. Patients who did not fill in the questionnaire within 6 hours were sent a reminder, and those still remaining were encouraged to fill it in the clinic waiting room. Hardcopy flyers were distributed to inform patients of the initiative and clinicians were encouraged to discuss the responses at the clinic visit. Patients were sent the survey only once during the study period. Weekly usdage reports were sent to the clinicians (Figure 1).

Results: 4078 patients [mean (SD) age 55.8 (16.3) years, 67.9% female, 70.6% Chinese] were sent the text message invitation over 6 months, of which 64.4% responded. Diagnosis data from SNOMED codes were available for 2262 patients. The most common primary diagnoses were rheumatoid arthritis (653, 29,5%), Spondyloarthritides (SpA), including psoriatic arthritis (318, 14.4%) and lupus (310, 14%). Data on disease duration, clinical features and medications were not available for this study. The mean (SD) mdHAQ score (range 0-3, 3 being the worst) was 0.3 (0.5), mean (SD) pain-VAS (0-10, 10 being worst) was 2.4 (2.3), patient global was 2.6 (2.2) and RAPID3 was 6.1 (5.2). On multivariable logistic regression, age (OR = 0.38, 95% CI 0.32, 0.44 for the top tertile), gender (OR 1.22, 95% CI 1.06, 1.4 for females), race (OR = 0.79, 95% CI 0.64, 0.98 for Indian vs. Chinese race) and treating physician (OR 0.7, 95% CI 0.61, 0.8 for junior vs. senior doctor) were independent predictors of survey response, while primary rheumatic disease was not (Figure 2). Ten of 11 clinicians (from 13 surveyed) found the information from PROMs useful, and 8/11 supported expansion of the pilot project to include more PROMs. Lack of time was cited as the biggest challenge to implementing PROMs routinely.

Conclusion: Automated collection of PROMs in routine clinical care is feasible with high uptake rates and minimal clinician burden.

[1] Figure 1: Weekly usage reports

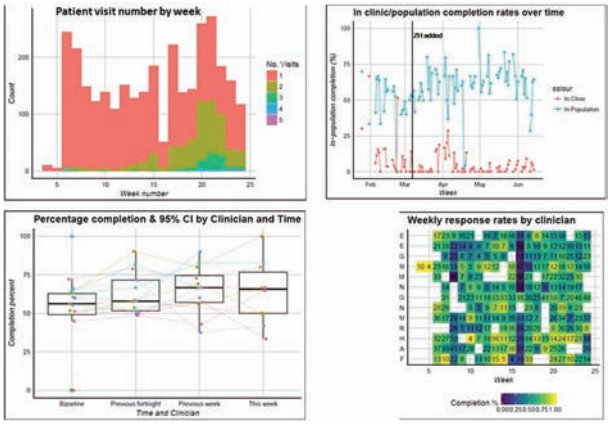
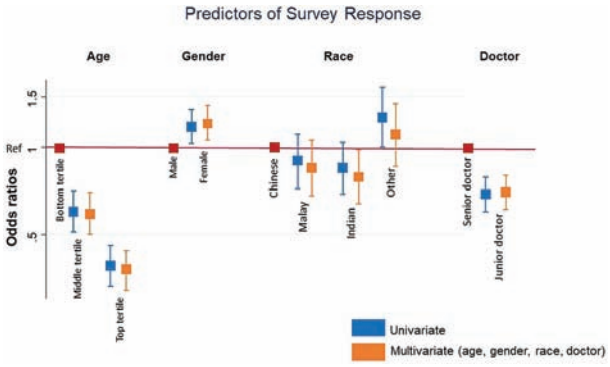


Figure 2. Predictors of Survey Response



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THU0640 EARLY RETIREMENT ATTRIBUTED TO RHEUMATOID ARTHRITIS AND ITS PREDICTORS IN PORTUGAL

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Background: Work disability is a common consequence of Rheumatoid Arthritis (RA) with economic implications for both the patient and society. Scarce information is available on work and disease-related factors associated with early retirement in Portugal.
Objectives: To evaluate the rate of early retirement due to RA. Secondary aim consists in the identification of its main predictors, both work and disease-related.
Methods: Retrospective cohort study involving two national rheumatology centers, including patients with RA according the ACR/EULAR 2010 or the 1987 ACR Classification Criteria for RA. Patients retired prior to RA diagnosis, never-employed or with missing information on current work status were excluded. Type of work was independently classified as non-manual/manual/heavy manual by two authors based on patient's occupation with excellent inter-agreement (Cohen's kappa coefficient 0.91). Retirement due to RA versus retirement for other reasons were compared using T-test and Chi-2 test as adequate. Variables with p<0.05 in univariate analysis and other potential predictors selected on clinical and epidemiological grounds were included in multivariable binary logistic regresssion.
Results: 492 patients were included (80.3% female, aged 60.9 ±13.1 years-old, mean disease duration 15.9 ±10.5 years). Until the present time, 45.1% (n=222) of the patients retired, this being due to RA in 59.5% of the cases. Early retirement due to RA translated into 6.5 years of active work lost, compared to retirement due to other causes. Patients who retired due to RA are more likely to be younger at diagnosis (49.6 ± 9.0 vs. 56.1 ± 8.6 years-old; p<0.01), female (82.6% vs. 68.9%, p<0.01), have longer disease duration (23.2 ± 10.7 vs. 18.3 ± 9.9 years, p<0.01) and lower educational level (4.5 ± 2.3 vs. 6.0 ± 4.1 school years, p<0.01). In the multivariate analysis, disease-related predictors for early retirement were: disease duration (OR: 1.11; 95% CI 1.08-1.13/year), erosive disease (OR: 4.45 95% CI 2.37-8.35) and the need for biologic therapy switching (OR:1.37; 95%CI 1.02-1.83). Work-related predictors were: educational level (OR: 0.75; 95%CI 0.68-0.81/year) and heavy manual type of work (OR: 1.62; 95%CI 1.16-2.26).
Conclusion: Early retirement is still common among patients with RA: 60% in this cohort. The main reasons for early retirement are associated with the disease itself, but work-related factors also play a relevant role.

REFERENCES:
[1] P. A. Laires, M. Gouveia. Association of rheumatic diseases with early exit from paid employment in Portugal. Rheumatol Int (2014) 34:491–502.
[2] K. Puolakka, H. Kautiainen, T. Mottonen, P. Hannonen, et al. Predictors of productivity loss in early rheumatoid arthritis: a 5 year follow up study. Ann Rheum Dis 2005;64:130–133.
[3] D. Lacaille, S. Sheps, J. J. Spinelli, A. Chalmers, J. M. Escaile. Identification of modifiable work-related factors that influence the risk of work disability in rheumatoid arthritis. Arthritis Rheum. 2004 Oct 15;51(5):843-52.

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THU0641 USE OF A WEB-BASED RHEUMATOLOGY PATIENT MANAGEMENT PORTAL

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Background: The benefit of incorporating tele-rheumatology into standard care is increasingly recognised. In January 2017, we introduced a web-based Rheumatology Patient Management Portal (RPMP), developed by MedMet, to our rheumatology patients at the North Devon District Hospital. In 2018 the portal service was fully operational. Suitable patients included undifferentiated inflammatory arthritis, rheumatoid arthritis, psoriatic arthritis and spondyloarthritides. Patients were consented to collected data such as diagnosis, treatment and disease activity onto the RPMP. For a selected group of patients who agreed to their email use, we set up schedules in the form of email reminders for them to complete PROMs (patient reported outcome measures) such as Health Assessment Questionnaire, Spinal Pain, Bath Ankylosing Spondylitis Disease Activity Index and Work Productivity and Activity Impairment. Patients can also report disease flares electronically, which is acknowledged by a health care professional who will contact them with advice as necessary.
Objectives: To understand patient participation in the use of the RPMP, between 01.01.18 and 31.12.18.
To develop a cohort of clinically stable patients who can self-manage via RPMP use and scheduled PROMs. The potential to remotely manage these patients has the advantage of reducing the number of face-to-face clinic appointments and eventually will lead to setting up a virtual clinic.
To examine patient perception on the RPMP use.
To examine whether tele-rheumatology is a useful adjunct to standard care.
Methods: The data was collected from interrogating the web-based RPMP database. Specific data was reviewed including; total number of patients on the portal, number of patients consenting to use their email, number of PROMs completed on the RPMP, number of flares reported and time to acknowledgment. In order to gain further understanding of user experience, a survey questionnaire (figure 1) was sent on 14.01.19.
Results: In total we have 883 patients recruited to the RPMP.
During the study period of one year, 289 patients have consented to share their emails and set up schedules. Therefore 33% of patients on the RPMP are using their emails through 2018. 310 patients responded to their portal request to complete a schedule. 758 PROMs were completed as part of the schedule response. 1744 PROMs were completed face to face whilst in standard clinic review. Therefore, 30% of PROMs were completed through a scheduled response. 55 patients contacted us through the RPMP to report a flare. The average time to acknowledging a flare is 37 hours. 78% of flare reports were acknowledged within 3 days. Results from the survey of patient experience as follow: number of patients responded to the survey was 99 and respond rate was 34%.

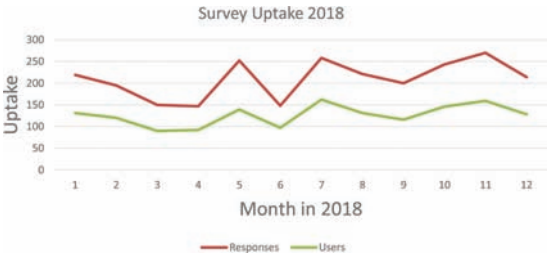
Among them, 94% reported the RPMP as easy to use, 54% found that RPMP helped them in understanding their rheumatology condition and 25% reported a flare through the RPMP.

Q1	Do you find the rheumatology portal easy to use?
Q2	Has the portal helped your understanding of your rheumatology condition?
Q3	Have you used the portal to report a flare?
Q4	If you have reported a flare using the portal, was your issue/concern answered quickly?
Q5	If you have reported a flare using the portal, was your issue/concern answered satisfactorily?
Q6	Would the portal service be more useful as an app?
Q7	Would you be happy to consider a one off payment of no more than Â£1 to use an app version?
Q8	Any further comments?

Conclusion: A large number of our rheumatology patients have consented to use the RPMP and their email. Uptake of the RPMP use is increasing (figure 2).

We have identified a significant proportion of 289 patients using the portal and email that could be targeted for virtual clinic use. Our data showed that use of tele-rheumatology in conjunction with standard care has potential to reduce number of standard clinic appointments however further work is required to investigate this.

Feedback from clinical staff is that having PROMs completed prior to consultation gives more time to discuss key issues whilst facilitating appropriate monitoring. The survey showed that majority of patients found the RPMP easy to use and helpful in understanding their rheumatology condition. The RPMP is an effective monitoring system for selected patients and has improved patient understanding in monitoring their disease activity.



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THU0642

EULAR POINTS TO CONSIDER FOR THE DEVELOPMENT, EVALUATION AND IMPLEMENTATION OF MOBILE HEALTH APPLICATIONS FOR SELF-MANAGEMENT IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: In the expanding era of e-health, a wide range of mobile health applications (apps) have become available to enable people with rheumatic and musculoskeletal diseases (RMDs) to better self-manage their health. However, guidance on the development and evaluation of such apps is lacking.

Objectives: The objective of this EULAR task force was to establish points to consider (PtC) for the development, evaluation and implementation of apps for self-management of RMDs.

Methods: A systematic literature review of app content and development strategies was conducted, followed by a qualitative study with six patients and an online survey of people living with RMDs (n=394). Based on these data and expert opinion, the PtC were formulated in a face-to-face meeting in November 2018 by a multidisciplinary TF panel of experts, including patients, from 10 countries. The level of agreement among the panel in regard to each PtC was established by anonymous online voting.

Results: Three overarching principles and 10 PtC were formulated (Table). Out of the 10 PtC, three were related to patient safety (1,5,6), considered as a critical issue by the panel, along with accuracy of information provided by apps. Three were related to relevance of the content and functionalities (2,7,9) and the importance of apps being tailored to the individual needs of people with RMDs. The requirement for transparency around app developers and funding sources (3,4), along with involvement of relevant health professionals were also raised. Ease of app access across ages and abilities was highlighted (8), in addition to considering the cost-benefit of apps from the outset (10). The level of agreement was high (Table).

Conclusion: These PtC provide guidance on important aspects that should be considered for the development of new apps, the quality assessment of existing apps, as well as for further development of existing apps. As part of the dissemination phase, these PtC will be shared with a larger group of health professionals, patients and app developers and for wider consensus.

	Points to consider	Level of agreement mean (SD)
1.	The information content in self-management Apps should be up to date, scientifically justifiable, user-acceptable and evidence-based where applicable.	9.8 (0.4)
2.	Apps should be relevant and tailored to the individual needs of people with RMDs.	9.7 (0.5)
3.	The design, development and validation of a self-management App should involve people with RMDs and relevant health care providers.	9.8 (0.6)
4.	There should be transparency on an Apps' developer, funding source, content validation process, version updates and data ownership.	9.9 (0.3)
5.	Data collection as part of an App must adhere to all applicable regulatory frameworks, particularly data protection.	9.9 (0.3)
6.	Apps must not result in physical or emotional harm to people with RMDs.	9.3 (1)
7.	Apps could facilitate patient-health care provider communication and contribute to electronic health records or research.	9.4 (0.9)
8.	App design should consider accessibility of people with RMDs across ages and abilities.	9.4 (0.9)
9.	If a social network is an important component of an App, structures should be in place to ensure appropriate content moderation.	9.5 (0.6)
10.	The rheumatology community should consider the cost-benefit balance of Apps before its endorsement and/or its promotion.	8.9 (1.3)

Table 1. The 10 Points to Consider.

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THU0643 ARE PSORIATIC ARTHRITIS OUTCOMES BETTER IN EARLY ARTHRITIS SERVICE? STUDY FROM A NATIONAL AWARD WINNING CENTRE

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Background: There is good evidence that dedicated early arthritis clinics (EACs) improve referral lag time and reduce delay in establishing disease-modifying therapy. However it remains arguable whether such clinics improve outcomes especially for arthritides other than RA. In the UK, only 57% of units have dedicated EACs. Our early arthritis service won national best practice commendation award for achieving high standards.

Objectives: We analysed our psoriatic arthritis (PsA) population data to ascertain whether this cohort benefits from EACs.

Methods: The department set up an early arthritis service with introduction of six clinics (EACs) every week. An agreed treatment protocol incorporating ultrasound was developed to ensure standardised approach to early initiation of treatment, drug education and timely review. This is a retrospective study of all patients with PsA presenting to the service in the first year

Results: Our catchment area covers a population of 350,000 with 40% ethnic minorities. Of 1884 patients referred, 482 (25.5%) were triaged into EACs based on set criteria. All were reviewed within 3 weeks. 247 (51%) were confirmed to have early inflammatory arthritis (EIA). Mean age was 52.4 years (17-86y). 157 (63.5%) were women. 177 (71.6%) were White, 58 (23.5%) of Asian and twelve of other background. 159 (64.3%) had RA, 55 (22%) with PsA and 33 had other inflammatory arthritides. There was median 26 weeks delay (0.4-1043 weeks) from symptom onset to GP presentation. Median time for GP referral to the department was 4.0 days (0-84 days).

All PsA patients had regular PsARC assessment. Mean tender (TJ) and swollen joint (SJ) counts at first visit were 8.2 (1-35) and 3.5 (0-14) respectively [n=55]. The patient (PtGA) and physician (PhGA) global assessments mean were 3.0 and 2.9 (1-5).

95% commenced their DMARDs within 3 week of initial review. Other 5% who missed the target was owing to patient factors. Target [TJ & SJ ≤2] was achieved for 38 patients (69%) and good PsARC response for a further four (7%). Median time to achieve the target or good response was 22 weeks (0-48 weeks). Of 55, only four (7%) patients required escalation to biologic therapy. Final TJ and SJ mean was significantly better at 1.2 (0-4) and 0.3 (0-2) [p <.0001] with similar improvement in PtGA [mean 1.8 (1-4)] and PhGA [mean 1.6 (1-3)]. Only six (11%) patients were true non-responders as the remaining seven declined therapy.

Conclusion: Dedicated EACs help achieve good clinical outcomes in majority of PsA patients. Nearly 76% of our cohort attained the target or good PsARC response in less than six months. This was despite a significant delay in patients presenting to their GPs and moderately-high disease activity. 100% of our patients were treated to target facilitated by protocol driven escalation of therapy in these clinics. This is in contrast to the national audit findings whereby only 68% of patients were treated with disease modifying drugs within 6 weeks of referral and 89% had treatment to target.

This study shows that the establishment of dedicated EACs improve the prognosis of psoriatic arthritis in terms of primary clinical outcomes compared to patients managed outside of EACs.

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THU0644 PATIENTS' PERCEPTION AND USE OF MEDICAL MARIJUANA

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Background: Though the introduction of biologics has resulted in significant improvements in their quality of life, people living with rheumatic and musculoskeletal disease (RMD) often seek alternative treatments, such as marijuana (THC) and cannabidiol (CBD). As these substances become more widely available, and legal in some jurisdictions, health care providers (HCP) need to understand patients' THC/CBD perceptions, use and information needs.

Objectives: To examine patient behavior and information needs regarding THC/CBD medical use.

Methods: A 77-item survey was developed in partnership with RMD patient partners and administered online via CreakyJoints and the ArthritisPower research registry. Participants (pts) were eligible if they were ≥19 years of age, resided in the US and reported physician-diagnosed RMD. Pts reported current health status (NIH PROMIS Global Health), use and perceptions of THC/CBD, and related information needs.

Results: To date, 189 pts completed the survey. A majority of pts were female (87%) and white (93%), with mean age of 55(11). More than half of all pts (62%) reported a diagnosis of rheumatoid arthritis. Most pts (78%) reported fair/poor health (PROMIS Global Physical Health <43). Only 30% of all pts were satisfied with their current treatment, and more than half (63%) had been on their current treatment for >1 year. Of those surveyed, a majority of pts (n=168, 89%) reported trying THC and/or CBD for a purpose they perceived as medical and offered various reasons for initiating its use (Table). Half of all pts (n=98, 52%) reported ever using CBD and a third (n=70, 37%) ever using THC "for medical reasons," fifty-one (73%) of whom currently use THC. More than half (53%) of those currently using THC reported using it at least once daily. Top reasons for stopping among the 19 who previously used THC were cost (26%) and illegality (26%). Most pts who had ever used THC reported that THC improved their symptoms (83%) and/or their condition (71%). Pain (100%) and sleep disturbance (73%) were the main symptoms pts sought to relieve with THC. Many pts had used THC in lieu of prescribed (56%) or OTC (73%) medications. Two thirds (67%) reported telling their HCP about their THC use, most of whom (64%) reported that their HCP did not consider it when making treatment changes nor offer advice about mode of administration or dosage. When acquiring THC, 39% of pts used a medical marijuana card issued by the state; the main reason given for not using a card was that THC was not legal for medical use where the pt lived (44%). Whether they had used THC for medical reasons or not, nearly all pts wanted information about THC, including its effectiveness (37%) and its interaction with other medications (34%); a majority preferred to receive information from HCPs (55%) or online educational resources (34%). Two thirds (60%) of all pts expressed interest in THC/CBD trial participation.

Table: Participants' Reasons for Initiating THC/CBD Use (N=168)

Reasons (not mutually exclusive)	**n (%)**
To address symptoms (e.g. pain) experienced despite taking medication	74 (44)
To address symptoms with less or no medication	50 (30)
Nothing else worked to treat condition or symptoms	33 (20)
Friend suggested it	30 (18)
Saw information online	28 (17)
Had used marijuana recreationally and wanted to try it for medical reasons	25 (15)
Medical marijuana became legal in state	24 (14)
To address side effect(s) from medication	19 (11)
Physician suggested it	17 (10)
Relative suggested it	17 (10)

Conclusion: Though many pts have used or currently use THC/CBD to substitute for or augment their prescribed treatment, pts lack adequate information to guide its use for medical reasons.

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THU0645 VIRTUAL VISITS IS THE FUTURE COMING? TELEREUMATOLOGY. PILOT PROJECT: REVIR PROGRAM, RHEUMATOLOGY SERVICE. BARCELONA, SPAIN

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Background: The prevalence of rheumatic diseases in the Spanish population is estimated at 22.6% according to the EPISER 2000 study. A new epidemiological study is currently underway, EPISER 2016 and its preliminary results point towards a higher prevalence. Within the national health system, primary care is the first level of access to the health system and is provided at primary care centers (CAP). The rheumatology at primary care centers at Spain has been a pioneer in the application from the team at Parc de Salut Mar (Hospital del Mar), with the physical presence of rheumatologists in the 14 centers belonging to the CAP network of the SAP Litoral. The high prevalence of the medical pathology of the musculoskeletal syste and the aging of the population, can condition an increase in visit requests in rheumatology, and with it, the increase in the waiting lists of patients.

Objectives: The main objective of this study is to know the resolutive possibility of virtualization, measured in the number of visits resolved telematically, as well as its impact on the resolution capacity of the primary care physician and the reduction of the waiting list of first face-to-face visits.

Methods: Prospective experimental study, started on December 1, 2017 and ended on May 31, 2018. Four primary care centers were selected according to population and waiting list: Sant Martí Nord, Sant Martí Sud, Ramón Turró and Villa Olímpica. The REVIR program proposes the creation of a circuit for the assessment of referrals to rheumatology from primary care physicians (MAP).

Results: 726 first visit requests were received during the REVIR program. The most common categorized pathology was mechanical pathology, representing about 70% of the first visits requested. Metabolic bone disease ranked second with 16%, and inflammatory pathology ranked third (SLE, RA, SA, SPA, PsA). Chronic musculoskeletal pain ranked fourth (including fibromyalgia) and lastly soft tissue pathology. The number of first visit requests was multiplied by two in all the participating primary care centers of the project. Despite this increase, the telematic resolution of the visits created was stable, with a value greater than 40%.

Conclusion: The implementation of a system of assessment of the first visits in rheumatology requested from Primary Care is effective in decreasing the waiting list to make face-to-face visits, as well as to detect early serious pathology that requires hospital control. It has been achieved, therefore, that the patient is treated at the level of attention that corresponds to him. Guaranteeing the adequate use of hospital resources and reducing the waiting list for a first in-person visit in rheumatology in primary care is one of the most important goals fulfilled, given that it is directly related to maintaining the accessibility and equity of the public health system.

REFERENCES:

[1] Kataria, S., & Ravindran, V. (2018). Digital health: a new dimension in rheumatology patient care. Rheumatology International. https://doi.org/10.1007/s00296-018-4037-

Tabla 1: Resolution of the first virtual visits to 6 months of REVIR project

CAP	Total	First CAP	First Hospital	Virtual resolution
Ramón Turró	193 (26,4%)	94 (49%)	22 (11,3%)	77(40%)
Villa Olímpica	96 (13,2%)	36 (37,5%)	13(13,5%)	47(49%)
Sant Martí (1 y 2)	437 (60,2)	216 (49,5%)	53(12,1%)	168(38,4%)
Total	726 (100%)	346 (47,6%)	88(12,1%)	292(40,2%)

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THU0646 HIGH LEVELS OF DAMAGE IN INFLAMMATORY RHEUMATIC DISEASES: A CLUE TO LOW RATES OF REMISSION AND LOW DISEASE ACTIVITY

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Background: Despite introduction of powerful biologic medications over the last 2 decades, rates of remission and low disease activity rates in RA remain less than 50%. One possible basis is that measures and indices such as disease activity score 28 (DAS28) and clinical disease activity index (CDAI), while sensitive primarily to disease activity in clinical trial patients selected for high inflammatory activity, may also reflect clinically important joint damage and patient distress in unselected patients in routine care. Similar considerations may pertain to systemic lupus erythematosus disease activity index (SLEDAI), Bath ankylosing spondylitis disease activity index (BASDAI), and other measures and indices initially designed to assess disease activity. Levels of organ damage and patient distress, as well as inflammation, may be quantitated according to 3 physician (0-10) visual analog scales (VAS), in addition to physician global assessment VAS (DOCGL), scored in fewer than 10 seconds in routine care.

Objectives: To test a hypothesis that damage and distress may be prominent in patients with inflammatory conditions, according to mean VAS for inflammation or reversible findings (DOCINF), damage or irreversible findings (DOCDAM), and distress (DOCSTR), e.g., fibromyalgia.

Methods: All patients at one site complete a multidimensional health assessment questionnaire (MDHAQ), which includes patient global VAS (PATGL), at each visit in routine care. Physicians complete four 0–10 (none-highest) VAS for DOCGL, DOCINF, DOCDAM, and DOCSTR, and a query to estimate the proportion of clinical decisions (total=100%) attributed to each of the 3 findings. Patients were classified into various diagnostic groups, in which scores were analyzed according to mean and standard deviation.

Results: Analyses included 563 patients (Table). Mean levels of DOCGL ranged from 3.2 to 5.2, and PATGL from 3.6 to 6.5, which might be interpreted to indicate high disease activity. Highest mean DOCINF scores were seen in patients with RA, SLE, vasculitis, polymyalgia rheumatica (PMR), spondyloarthropathy (SpA), and gout (2.2-2.8), while highest mean DOCDAM was seen in OA (4.9) and DOCSTR in FM (6.2) (Table). However, in RA, mean DOCDAM was 3.7 vs 2.4 for DOCINF. DOCDAM also was almost as high or higher than DOCINF in SLE, SpA, vasculitis, and gout. Mean estimates of distress were also $\geq$1.5 in patients with all inflammatory diagnoses.

Diagnosis (per ICD code)	N (%)	Global Estimates (0-10)		Physician subscales (0-10)		
		PATGL	DOCGL	DOCINF	DOCDAM	DOCSTR
RA	64	4.9 (2.9)	4.5 (2.4)	2.4 (2.2)	3.7 (2.8)	1.9 (2.7)
SLE	47	4.1 (3.1)	3.7 (2.8)	2.2 (2.4)	1.5 (1.7)	1.8 (2.5)
SpA and psoriatic arthritis	34	4.1 (2.9)	3.9 (2.4)	2.4 (2.5)	2.7 (2.3)	1.9 (2.8)
Vasculitis and PMR	23	3.6 (2.6)	3.4 (3.0)	2.6 (1.8)	2.3 (2.2)	1.7 (2.6)
Gout	21	4.4 (2.9)	4.2 (2.7)	2.8 (2.5)	3.2 (2.8)	1.5 (1.9)
Osteoarthritis	135	5.8 (2.9)	4.9 (2.2)	1.2 (1.9)	4.9 (2.5)	2.2 (2.7)
Fibromyalgia	84	6.5 (2.6)	5.2 (2.2)	0.9 (1.2)	1.7 (2.0)	6.2 (2.6)
Other diagnosis	155	4.0 (3.0)	3.2 (2.2)	1.6 (2.0)	2.4 (2.3)	1.6 (2.1)
TOTAL	563	4.8 (3.0)	3.9 (2.4)	1.6 (2.0)	2.9 (2.5)	2.4 (2.9)

Conclusion: Rheumatologists estimated high levels of damage in patients with RA and other inflammatory rheumatic diseases, similar or higher than inflammation, as well as recognizable distress which may elevate measures such as tender joint count and PATGL. These findings may explain in part low rates of remission and low disease activity noted in RA and other inflammatory diseases, as index scores used to document improvement are not affected by anti-inflammatory therapy. Most rheumatology clinical quantitative measurement is directed to inflammatory activity. However, an estimate of damage and distress may clarify why many patients may appear to have suboptimal control of inflammatory activity despite aggressive treatment, including treat to target in RA.

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THU0647 CHARACTERIZING PERSISTENCE OF IV ABATACEPT AMONG ELDERLY PATIENTS WITH RA IN THE US MEDICARE POPULATION

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Background: Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease characterized by inflammation of the joints, which can ultimately lead to cartilage damage and bone destruction.[1] While early and aggressive intervention with biological treatment may alter the course of the disease and improve physical functioning, persistence to these medications varies, ranging from just 30 to 80%.[2] It is important to understand the factors associated with persistence to RA treatment, as non-adherence may incur greater healthcare costs and utilization, disease progression, and the potential requirement for even more aggressive therapy in the future.

Objectives: To describe patient characteristics and baseline healthcare costs that affect persistence to intravenous (IV) abatacept, which may be supportive in evaluating the risk-benefit ratio of abatacept for treatment of RA.

Methods: Patients (aged ≥65 years) with at least one inpatient or two outpatient medical claims for RA and subsequent treatment of IV abatacept from 01JUL2006 to 31DEC2016 were identified in the Truven MarketScan Medicare Supplemental database. The date of first prescription of IV abatacept was considered the index date; patients with another biologic DMARD claim on the index date were excluded. Patients were required to have 6 months continuous enrollment before and 12 months continuous enrollment following index date. Persistence was defined as the number of days from treatment initiation (index date) to first switch to another biologic DMARD, discontinuation of abatacept, or end of follow-up. Patients with >6 months of treatment were categorized as high persistence and ≤6 months of treatment as low persistence. Patient characteristics were summarized by level of persistency and compared using Wilcoxon's rank sum test for continuous variables and chi-square test for categorical variables.

Results: Among 1,963 patients meeting inclusion criteria, 1,167 patients (59.4%) were categorized as having high persistence to IV abatacept. Patient characteristics were similar at baseline between cohorts; the mean age was 74 years, 79% were female, and the mean Charlson Comorbidity Index (CCI) score was 2.02. Compared to low persistence cohort, patients with high persistence to IV abatacept had significantly greater prior exposure to methotrexate (44% vs 51%, p=0.001) and infliximab (18% vs 24%, p<0.001). Patients with high persistence to abatacept also had higher, albeit non-significant, prior use of TNFi (39% vs 41%, p=0.304). In addition, higher persistence to abatacept was significantly associated with higher all-cause baseline medical per patient per month (PPPM) costs ($450 vs $475, p=0.005) and higher RA-related baseline medical PPPM costs ($177 vs $231, p<0.0001). Patients with lower all-cause baseline pharmacy PPPM costs ($709 vs $596, p=0.174) and RA-related baseline pharmacy PPPM costs ($375 vs $272, p=0.773) had higher persistence to abatacept, although these associations were not statistically significant.

Conclusion: Among US Medicare patients with RA, surrogate markers of high disease severity, including prior methotrexate and infliximab use and higher baseline medical costs, were significantly associated with higher IV abatacept persistence. These results may assist both physicians and payers in identifying Medicare patients who benefit from abatacept and tailoring their approach accordingly to minimize the risk of non-persistence.[3]

REFERENCES:

[1] Pruijn GJ, et al. Arthritis Res Ther 2010;12:203.
[2] de Vries-Bouwstra JK, et al. Rheum Dis Clin North Am 2005;31:745-762.
[3]van den Bemt BJ, et al. *Nat Clin Pract Rheumatol* 2007;**3**:681.

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THU0648 WORK DISABILITY IN A PERUVIAN COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Work disability in patients with systemic lupus erythematosus (SLE) is common but the factors associated with it in Low and Middle Income Countries have been scarcely evaluated(1).

Objectives: To determine the prevalence of and the factors associated with work disability in SLE patients.

Methods: We studied 239 consecutive (1997 American College of Rheumatology (ACR) criteria) patients from a Peruvian SLE cohort from October 2017 to December 2018. Work disability was measured from a single self-report questionnaire. Data were collected and included sociodemographic information, clinical lupus features including disease activity [Systemic Lupus Erythematosus Disease Activity Index 2000 update (SLEDAI-2K)], damage [Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)], as well as Health-Related Quality of Life (LupusQoL), and medication use. Work disability was defined by patients' self-report of not being able to work because of SLE. Univariable analysis comparing those patients with work disability and those who remained working were performed with the Mann Whitney U test for continuous variables and the Chi-square test for dichotomous variables. For the multivariable analyses, binary logistic regression with backward elimination was used to determine which factors remained associated with work disability.

Results: Of 239 patients, 194 patients were working at least for at least some time since diagnosis, 181 (93.0%) were female, they had a mean age at diagnosis of 34.5 (12.3) years, and a mean disease duration of 11.5 (7.4) years, their mean SLEDAI was 2.53 (3.7) and their mean SDI was 1.2 (1.5). Twenty-eight patients changed their activities at work due to SLE and 51 (26.6%) stopped working after their diagnosis; 21 of them (41.1%) stopped working because of SLE. One hundred and forty-three were working at the time of the evaluation. In the multivariate analyses, those work- disabled due to SLE were more likely to have higher SDI: OR=1.650 (CI95%: 1.134-2.403) p=0.009, and lower HRQoL in two domains, planning: OR=0.975 (CI 95%: 0.954-0.996) p=0.020 and body image OR=0.977 (CI95%: 0.956, 0.998), p=0.032.

Conclusion: Work disability due to SLE is associated with higher damage accrual and a poorer HRQoL.

REFERENCES:

[1] Mak A. The economic burden of systemic lupus erythematosus in Asia: the current state. Sing Lau C, editor. Lupus. 2010 Oct 14;19(12):1442–6.

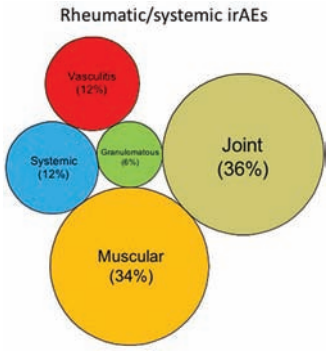
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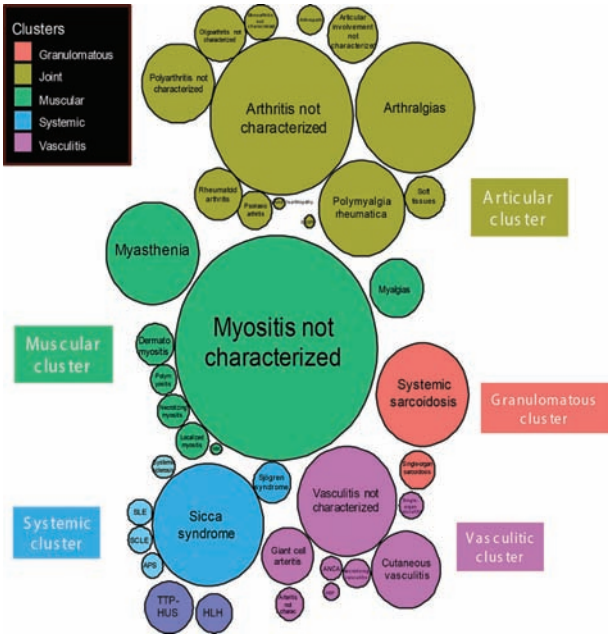
THU0649

PHENOTYPIC CLUSTERS OF RHEUMATIC/SYSTEMIC IMMUNE-RELATED ADVERSE EVENTS INDUCED BY CANCER IMMUNOTHERAPIES (IMMUNOCANCER INTERNATIONAL REGISTRY)

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Background: The ImmunoCancer International Registry is a Big Data-Sharing multidisciplinary network focused on the research of the immune-related adverse events (irAEs) related to cancer immunotherapies (CIs).
Objectives: To analyse the worldwide scenario of rheumatic/systemic autoimmune diseases (RSirAEs) associated with the use of CIs during the last 20 years.
Methods: The first objective was to develop a systematic literature review crossing the CIs terms with rheumatic and systemic autoimmune diseases using MedDRAVR 15.0 terms.
Results: RSirAEs were identified in 11% of 12648 patients with irAEs, including 1435 cases (30% fulfilled criteria for a systemic disease) that were classified in 5 phenotypic clusters:





: Non-characterized cases included myositis (25%), arthritis (12%), arthralgias (8%), sicca syndrome (7%) and vasculitis (6%); sarcoidosis (6%), myasthenia gravis (5%), polymyalgia rheumatica (4%), leukocytoclastic vasculitis (3%) and giant cell arteritis (2%) were the most frequent systemic diseases identified:
: In comparison with patients with organ-specific irAEs, RSirAEs were more frequently associated with combined therapies (OR 2.46, CI 2.16-2.81), checkpoint inhibitors -ICis- (OR 4.01 vs TKis, CI 3.26-4.92), and PD-1is (OR 2.46 vs CTLA4is, CI95% 2.16-2.81)
Conclusion: Rheumatic/systemic irAEs can be divided into 5 phenotypic clusters: articular, muscular, granulomatous, vasculitic and systemic. These findings must be confirmed in real-life patients, and an international data-sharing ICIR registry is planned to be launched.

REFERENCES: :

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THU0650 COMPLEMENTARY AND ALTERNATIVE MEDICINE IN RHEUMATOLOGY: A SURVEY OF ITS USE FOR COMMON RHEUMATOLOGICAL CONDITIONS AMONG MULTI-ETHNIC PATIENTS IN LEICESTERSHIRE

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Background: The use of complementary and alternative medicine (CAM) is common in patients with chronic disease.[1] However, the usage of CAMs among patients with rheumatological conditions has been understudied. A significant proportion of primary care trusts are now providing therapies such as acupuncture and osteopathy to some of the 9 million users of CAMs in the United Kingdom (UK).[2] As the NHS serves a varied patient populace, it is important to appreciate the perceptions and utilisation of CAM amongst multi-ethnic groups.

Objectives:

1. To identify the different types CAMs utilised by Rheumatology patients.
2. To identify Rheumatology patients' views towards the role and use of CAMs in managing their condition(s).
3. To identify locations where patients receive CAM and to determine patient's spending practices.

Methods: A cross-sectional survey on CAMs, and its use for common rheumatological conditions was conducted among multi-ethnic patients in Leicestershire, UK, through convenience sampling. The initial questionnaire was created by a multi-disciplinary input, with a patient-centred focus. Thereafter 10 questionnaires were piloted and revised accordingly. The data subsequently underwent statistical analyses.

Results: A total of 107 patients completed the survey over a 3-month period with a response rate of 90%. Most of the respondents (91.8%) were over the age of 35 (age range 19 to 78 years, mean age 50.512.8SD). Among the respondents, 66% were women and 34% were men. 72.9% were of white British or European ethnicity and 20.6% of South Asian ethnicity (17.8% Indian and 2.8% Pakistani). Majority of the patients (66.4%) had rheumatoid arthritis (RA), followed by psoriatic arthritis (11.2%) and ankylosing spondylitis (4.7%). The respondent demographics were consistent with known epidemiology of common rheumatological conditions, with a higher prevalence among women than in men (female-to-male ratio of 3:1 in RA).

31.8% used CAM for managing symptoms related to their condition(s). Almost half of these respondents (41.2%) used CAM products and/or practices daily, with up to 64.7% spending between £10- £100. The majority of respondents (82.4%) received CAM therapy within the UK, followed by India (17.6%). Commonly used CAM products include: ginger (35.3%), fish oil supplements (32.4%), turmeric (32.4%) and cannabidiol (CBD) oil (23.5%). The most common CAM therapies were acupuncture (44.1%), yoga (14.7%), chiropractice (14.7%), meditation (2.9%) and stretch-fit (2.9%). Many respondents (64.7%) used more than one product and/or practice. 60% of the respondents that used CAMs had RA. 9 out of 34 (26.5%) respondents found CAM therapies to be beneficial for their condition(s), with seven (20.6%) finding it to be useful for pain control/relief. Up to 17.8% of all respondents, including those with no prior experience of CAM, perceived potential benefits. However, 65.4% reported neutral views towards CAM.

Conclusion: In our local multi-ethnic population, it is evident that a notable proportion of patients have utilised CAM to supplement the management of their condition. Healthcare professionals need to be aware of the CAMs available, particularly when informing and treating their patients. Effective communication is required in this area to maintain patient's confidence and safety. Further qualitative research should consider the reasons for the use of CAMs.

REFERENCES:

1. Metcalfe A, Williams J, McChesney J, Patten S, Jetté N. Use of complementary and alternative medicine by those with a chronic disease and the general population - results of a national population-based survey. BMC Complementary and Alternative Medicine. 2010;10(1)
[2] Verkek R. The Alliance for Natural Health International e-alert number 333. 2017.

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THU0651 AN INDIVIDUALIZED DECISION-AID FOR DIVERSE WOMEN WITH LUPUS NEPHRITIS (IDEA-WON): A RANDOMIZED CONTROLLED TRIAL

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Background: Medication decision-making is challenging in lupus. No validated, effective decision-aids are available to assist patients with medication decision-making.

Objectives: Our objective was to assess the effectiveness of an individualized, culturally-tailored, computerized decision-aid for immunosuppressive medications for lupus nephritis.

Methods: In a multicenter, randomized controlled trial, diverse adult women with lupus nephritis, largely racial/ethnic minorities with low socioeconomic status, were randomized to decision-aid vs. American College of Rheumatology lupus pamphlet (1:1 ratio). Co-primary outcomes were change in decisional conflict and informed choice regarding immunosuppressive medications.

Results: Of 301 randomized women, 47% were African-American, 26% were Hispanic, and 15% White. Mean age (standard deviation [SD]) was 37 (12) years, 57% had annual income of <$40,000, and 36% had a high-school education or less. Compared to the pamphlet (n=147), participants randomized to the decision-aid (n=151) had: (1) a clinically meaningful and statistically significant larger decrease in decisional conflict, 21.8 (standard error [SE], 2.5) vs. 12.7 (SE, 2.0; p=0.005); and (2) a clinically meaningful difference in informed choice, statistically non-significant in the main analysis, 41% vs. 31% (p=0.08), but significant in sensitivity analysis (net values for immunosuppressives positive [in favor] vs. negative [against]), 50% vs 35% (p = 0.006). Respectively, unresolved decisional conflict post-intervention was significantly lower, 22% vs. 44% (p<0.001). Significantly more patients in decision-aid vs. pamphlet group rated information to be excellent for understanding lupus nephritis (49% vs. 33%), risk factors (43% vs. 27%), medication options (50% vs. 33%; p≤0.003 for all); and the ease of use of materials higher (51% vs. 38%; p=0.006).

Conclusion: An individualized decision-aid was effective in reducing decisional conflict for immunosuppressive medications in diverse women with lupus nephritis.

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THU0652 THE ECONOMIC BURDEN OF ANCA-ASSOCIATED VASCULITIS IN GERMANY – A CLAIMS DATA STUDY

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Background: ANCA-associated vasculitis AAV is a rare systemic disease, characterized by recurrent episodes of systemic inflammation. It is a severe disease associated with hospitalization, risk of renal failure and a therapy inducing serious side effects. The economic impact of AAV to the German health care system is currently not well understood.

Objectives: The aim of this study was to better understand and quantify the economic burden of AAV in Germany. Therefore, selected aspects, such as prevalence and incidence, frequency of hospitalization, frequency of intensive care unit (ICU) stays and treatments costs, were systematically assessed in a claims data study.

Methods: Longitudinal data from years 2013 to 2016, provided by German statutory health insurance (SHI) companies from the InGef database have been analyzed representing an age- and gender stratified cohort of approx. 4 million insured persons representative for the German population.

Results: Prevalence and incidence data show that, in accordance with the previously published literature (1, 2), Granulomatosis with Polyangiitis (GPA) was more frequent than Microscopic Polyangiitis (MPA). On average, a combined prevalence of 256 : 1 000 000 (210 : 1 000 000 for GPA and 46 : 1 000 000 for MPA) was identified within the data set over the observed time period of 4 years (2013-2016). Incidence rates were found to be 46 : 1 000 000 (34 : 1 000 000 for GPA and 13 : 1 000 000 for MPA) within the same time period. Over the observed time period, prevalence and incidence rates remained stable.

The majority of AAV (GPA and MPA) diagnoses were made in hospitals (61%), another 24% were diagnosed in the outpatient sector and 15% were diagnosed in both within one quarter. In total, 97% of newly diagnosed patients (GPA and MPA) were hospitalized within 4 years post diagnosis. Especially during the induction period (quarter of diagnosis and the following 2 quarters) 91% (GPA) to 95% (MPA) of the patients were hospitalized. Of these patients, approx. 60% were hospitalized due to GPA and MPA disease, showing the high rate of severe co-morbidities. Patients diagnosed with GPA and MPA were frequently treated at ICUs (in average 1 stay per quarter); in particular severe infections and renal involvements increased the likelihood of ICU stays.

Treatment costs were highest during the induction period; within this period hospitalization represented the largest cost factor. Severe kidney disease, which occurred in 11,6% of GPA and 24,3% of MPA patients, induced total costs ranging between 131.521€ (GPA) to 145.472 € (MPA) over four years post diagnosis, with the induction period being most expensive (approx. 58.826 € to 50.339 € for GPA and MPA during the induction period). In the following years total treatment and hospital costs decreased, however remained high.

Conclusion: AAV represents an underestimated financial burden to the German healthcare system, especially during induction therapy. The high level of hospitalizations amongst AAV patients also represents a high usage of healthcare resources. Thus, AAV represents an underestimated cost factor for the German health care system, and better treatment options are desperately needed.

REFERENCES:

1. Herlyn K, Hellmich B, Gross WL, Reinhold-Keller E. Stable incidence of systemic vasculitides in schleswig-holstein, Germany. Dtsch Arztebl Int. 2008;105(19):355-61.
2. Reinhold-Keller E, Herlyn K, Wagner-Bastmeyer R, Gross WL. Stable incidence of primary systemic vasculitides over five years: results from the German vasculitis register. Arthritis Rheum. 2005;53(1):93-9.

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THU0653 SOCIOECONOMIC ANALYSIS OF GOLIMUMAB TREATMENT IN PATIENTS WITH RA, PSA, AND AS – NON-INTERVENTIONAL STUDY GO-NICE

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Background: Rheumatic diseases are associated with pain, loss of functionality, fatigue, hospitalization, sick leave, and work disability. This results in high economic burden for patients and society.

Objectives: Golimumab (GLM) is an effective but costly treatment option for patients (pts.) with moderate to severe, active rheumatic diseases. The aim of this analysis of the GO-NICE study was to investigate the direct and indirect costs of healthcare utilization and sick leave after starting a treatment with GLM.

Methods: Data of outpatients collected in the non-observational study GO-NICE in 1,483 pts. with RA (n = 474), PsA (n=501), and AS (n=483) in 158 sites (2010-2015) in Germany were analysed. Details on the study design, pts. characteristics, the clinical and patient-reported outcomes, and safety data have been reported earlier [1,2].

Direct medical and indirect costs per patient and year were calculated for consultations, physiotherapy, massages, hospitalisations and inpatient rehabilitation, medication (DMARDs, Glucocorticoids, NSAIDs, and biologics) as well as sick leave days. Findings were shown for RA-, PsA- and AS-pts. and categorised by biological-naïve pts. and pts. with a pre-treatment with a biologic. The 6-month periods prior baseline (BL)/start of a GLM therapy vs. month 24 (M24) were compared.

For this calculation the standardized evaluation rates were used (Bock et al. (2015), AG MEG of the DGSMP (2005). Costs for prescribed and documented medication were calculated by the mean cost per defined daily dose (based 2010-2015). Indirect costs were estimated through the human capital approach (HCA).

Results: Data of 758 biologic-naïve pts. (n = 265 RA, 247 PsA and 246 AS) and 694 pts. with biologics as pre-therapy (n = 208 RA, 252 PsA and 234 AS) were included in the analysis.

Direct medical costs (excl. medication) decreased in all 6 groups, min. 765€ (PsA pre-treatment group) and max. 2,426€ (AS pre-treatment) as well as the costs due to work disability/absenteeism, min. 855€ (PsA pre-treatment) and max. 2.564€ (RA pre-treatment, table).

Total costs in biological-naïve pts. increased due to the additional expense of the biologic agent.

Absolute changes in costs totalled 15,665€ (RA-, table), 15,799€ (PsA-) and 14,764€ (AS-patients) per patient and year when comparing the BL vs. M24 periods.

Total savings of 6,289€ (RA-, table), 2,617€ (PsA-), and 5,555€ (AS-patients) per patient and year were generated in the group of biologic-pre-treated patients.

	RA pts. biologic-naïve (n=265)			RA pts. with biologics as pre-treatment (n=208)		
	Baseline	Month 24	Changes	Baseline	Month 24	Changes
Consultation fees/€	354	168	- 186	369	178	- 191
Physiotherapy, massages etc./€	162	59	- 103	144	91	- 53
Hospitalisation/€	939	99	- 840	1,163	423	- 740
Rehabilitation measures/€	163	55	- 109	148	0	- 148

(in- and outpatients)

Direct med. costs/€ (excl. medication)	1,618	381	- 1,237	1,823	692	- 1,131
Comedication/€	498	417	- 81	417	414	- 3
Biologicals/€	0	19,082	+ 19,082	21,673	19,082	- 2,591
Medication/€	498	19,498	+ 19,000	22,091	19,496	- 2,595
Absenteeism/€	2,991	892	- 2,099	3,028	464	- 2,564
Total/€	5,107	20,771	+ 15,664	26,942	20,653	- 6,289

Table 1. Costs per patient and year (Subgroup patients with RA)

Conclusion: Costs of healthcare utilization, as well as work disability decreased after starting GLM within an observation period of 24 months, for pts. with RA, PsA, and AS, respectively. Due to the high costs of TNFi therapy, drug costs in the group of biologic-naive pts. rose markedly. Savings were generated in the group of pts. pre-treated with biologics.

REFERENCES:

[1] K. Krüger, et al. BMJ Open 2018
[2] K. Krüger, et al. Rheumatology International 39 (1) 2019

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THU0654 INFLUENCE OF THE NEW PHARMACOLOGICAL AND NON-PHARMACOLOGICAL APPROACHES IN RHEUMATOID ARTHRITIS ON WORK PARTICIPATION: A SYSTEMATIC LITERATURE REVIEW

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Background: Rheumatoid arthritis (RA) is a chronic and progressive autoimmune disease that frequently has a negative impact on work participation among patients. Even more, patients with RA are at greater risk to become work disabled, have a reduced work productivity (presenteeism) or increased sick leave (absenteeism) compared to the general population. This outcome can be related to the World Health Organization International Classification of Functioning, Disability and Health (the WHO ICF framework), that is useful in understanding the impact of RA regarding functioning. Since 2000, the management of RA has made significant progress. With the establishment of the new ACR/EULAR criteria and the treat-to-target (T2T) strategies, patients are nowadays diagnosed and treated earlier. Furthermore, the improvement of the management of RA has led to much better results regarding disease activity and joint destruction. However, many of these patients are confronted with additional fees when contracting private insurances, since the risk assessment by insurances is mainly based on historical data.
Objectives: This systematic literature review was performed to study the influence of new pharmacological and non-pharmacological approaches on work participation among patients with RA with the objective to improve the risk assessment of RA patients when contracting private insurances.
Methods: A systematic literature review from January 1990 until January 2018 was performed using Pubmed, Embase and Web of Science. Different search terms were used in each database: employment, workplace, sick leave, absenteeism, work capacity and international classification of functioning, disability and health. All studies assessing one of the search terms were analysed.
Results: Finally, 49 relevant articles were selected. The selected studies were subdivided according to study design (RCT versus cohort study) and disease duration of the studied patients. Studies that examined the value of an adequate early intervention were grouped separately. Overall, studies on the impact of the non-pharmacological approach were limited and very heterogeneous. Positive results of pharmacological agents (combination of DMARDs or biologic therapy) on work participation could be demonstrated in patients with recent-onset RA. Long-term observational studies showed an association between initiation of new therapeutic strategies and a reduction in work disability among patients with RA. However a causal relation was difficult to confirm because of the study design. Moreover, some studies pointed out other contextual factors that also influence work disability such as political policy, demographic changes in age distribution or educational level.
Conclusion: The large heterogeneity in terms of patient population, study design and outcome measures limits interpretation of the data. However, this systematic literature review could demonstrate that the effect of a treatment is of utmost importance and not the treatment itself. This emphasizes also the importance of early intervention with pharmacological agents regarding work productivity outcomes in RA. In addition, the impact of personal and environmental factors on work participation may not be neglected.

REFERENCES: :
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Epidemiology, risk factors for disease or disease progression

THU0655 LONG-TERM OUTCOME OF JUVENILE IDIOPATHIC ARTHRITIS: COMPARISON OF BIOLOGIC AND METHOTREXATE ERAS

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Background: After nearly two decades from the start of the Biologic era, systematic analyses of patient with juvenile idiopathic arthritis (JIA) have shown a high frequency of attainment of inactive disease (ID) and satisfactory levels of physical function and quality of life. However, whether and to what extent the disease prognosis has improved in comparison with the methotrexate (MTX) era is still uncertain.
Objectives: To compare the long-term disease state, in terms of activity and damage, of children with JIA who had their disease onset in MTX or Biologic eras.
Methods: Patients were included in MTX or Biologic era cohort depending on whether their disease presentation occurred before or after January 2000. Patients in the MTX era cohort and part of the patients in the Biologic era cohort were taken from a previous cross-sectional study published by our group,[1] which enrolled 310 patients with disease onset between December 1986 and December 2002. An additional sample of patients with onset in the Biologic era was enrolled in a subsequent prospective cross-sectional study, which included all consecutive patients meeting the ILAR criteria for JIA, who were seen consecutively at the Istituto Gaslini of Genoa, Italy, between January 2015 and June 2017. All patients had disease duration $\geq$ 5 years and underwent a prospective cross-sectional assessment, which included measurement of disease activity and damage. ID and low disease activity (LDA) states were defined according to Wallace, JADAS10 and cJADAS10 criteria. Articular and extra-articular damage was assessed with the Juvenile Arthritis Damage Index (JADI).
Results: MTX and Biologic era cohorts included 239 and 269 patients, respectively. Patients were divided in the "functional phenotypes" of oligoarthritis and polyarthritis. At cross-sectional visit, patients in the Biologic era cohort with either oligoarthritis or polyarthritis had consistently higher frequencies of ID and LDA than patients in the MTX era cohort. The measurement of disease damage at cross-sectional visit revealed that the frequency of impairment of > 1 JADI-Articular items was higher in MTX than in Biologic era cohort (17.6% versus 11% in oligoarthritis and 52.6% versus 21.8% in polyarthritis). Likewise, frequency of involvement of > 1 JADI-Extraarticular item was higher in MTX than in Biologic era cohort (26.5% versus 16.2% in oligoarthritis and 31.4% versus 13.5% in polyarthritis). The sole JADI items that were detected in more than 5% of patients in the Biologic era cohort were temporomandibular damage in oligoarthritis and polyarthritis, ankle damage in polyarthritis and leg-length inequality in oligoarthritis. The analysis of the temporal trend of damage development over the 25 years of our analysis (1986-2011) highlighted

the marked decrease in damage over time and the more pronounced decline in the Biologic era (Figure 1).
Conclusion: Our study provides evidence of the remarkable prognostic improvement obtained with the recent therapeutic advance in JIA.

REFERENCES:
[1] Solari et al. Arthritis Care Res. 2008;59:1571–9.

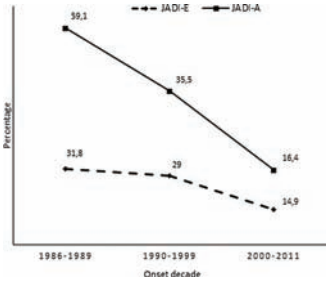


Figure 1. Trend in disease damage throughout methotrexate and biologic era.

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THU0656 IMMUNE CHECKPOINT INHIBITORS IN PATIENTS WITH CANCER AND RHEUMATOLOGIC DISEASES: A SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Immune checkpoint inhibitors (ICI) have resulted in unprecedented advances in the treatment of cancer, with remarkable survival benefits, unseen with traditional treatment. While the benefits of ICI have been clearly documented, a myriad of immune-related-adverse events (irAEs) have been recognized in multiple organs and systems, secondary to persistent activation of the immune system.
Objectives: To systematically review the literature and provide an updated summary on adverse events associated with the use of ICI therapy in patients with cancer and rheumatologic diseases.
Methods: Five electronic databases were searched through 2018 with no restrictions. Articles were screened and selected by two independent investigators using a 2-step approach. Case reports, series, and observational studies describing patients diagnosed with rheumatologic disease prior to initiation of ICI for treatment of concomitant cancer were included.
Results: A total of 69 patients in 27 publications were identified. Median age was 65 (38-87) years; 50% were female; 90% had metastatic melanoma; and 64% were receiving anti-cytotoxic T-lymphocyte-associated protein 4 (anti-CTLA-4) antibody. Rheumatoid arthritis was the most common in 64% (n=32). Other rheumatologic diseases included 16 spondyloarthropathy (7 psoriatic arthritis, 4 ankylosing spondylitis, 1 reactive arthritis, and 4 unspecified), 8 sarcoidosis, 6 vasculitis (3 eosinophilic granulomatosis with polyangiitis, and 1 each with granulomatosis with polyangiitis, Behcet's diseases, and polymyalgia rheumatica), 2 each with systemic lupus erythematosus and scleroderma, and 1 each with rheumatic fever, Sjögren's syndrome, and myositis. Overall, 73% (n=50) had an adverse event after initiation of ICI; 33% (n=32) had an exacerbation of the underlying disease, and 55% (n=38) had *de novo* irAEs. Patients with active diseases at ICI initiation seemed to have more disease flare than those with inactive disease (61% vs. 29%; p = 0.03), while no differences were observed in de novo irAEs (36% vs. 39%). Patients with rheumatoid arthritis were reported to have more flares with anti-CTLA-4 antibody (63% vs. 33%), while those with spondyloarthropathy reported more flares with anti-programmed cell death 1 agents (63% vs. 29%); however numbers were small. Patients receiving immunosuppressive therapy at ICI initiation had fewer adverse events than those not receiving treatment (26% vs. 44%). Most flares and irAEs were managed with corticosteroids, and 13% required additional disease modifying anti-rheumatic drugs. Adverse events improved in 64% and did not require discontinuation of ICI therapy. In melanoma patients, disease control rate was 44%. In all patients, no treatment related mortality was reported.
Conclusion: About one third of patients with pre-existing rheumatologic autoimmune disease flared after receiving ICI therapy for treatment of cancer. However, flares and irAEs can often be managed and may not require discontinuation of cancer therapy. Prospective longitudinal studies are needed to evaluate potential differences among diseases and to determine optimal toxicity therapy while conserving antitumor immunity.
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THU0657 ASSOCIATION OF DIET AND SPICES WITH TREATMENT OUTCOME IN ASIAN INDIAN PATIENTS WITH RHEUMATOID ARTHRITIS – A CROSS SECTIONAL STUDY

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Background: Influence of diet on inflammation, specially foods like fish oil, spices like turmeric, capsaicin, garlic etc. are reported in published literature. However, a well-designed study on this subject amongst Asian Indian patients is lacking.
Objectives: To analyze whether the type and quantity of intake of various food constituents, with particular reference to Indian spices, makes an impact on the control of disease activity in patients with Rheumatoid arthritis(RA)
Methods: Patients diagnosed as RA by the ACR 2010 criteria and receiving standard triple drug therapy in our clinic between June 2017 and June 2018, for at least one year were enrolled. Disease activity was assessed during the routine OPD visit. They were administered a food frequency questionnaire [1] pertaining to the quality as well as quantity of food and spice intake. Analysis was done using multivariate logistic regression
Results: A total of 400 patients were included with 86.75% females. 67.75% patients were in disease remission, 10% had mild disease activity and 22.25% moderate to high disease activity; only 18.09% were vegetarians and the rest consumed non-vegetarian food. Median age was 47.99years(SD 10.67),median duration of illness prior to presentation to our clinic was 7years(IQR 4,10), median ESR was 37mm/hr(IQR 23,52), median CRP was5.34mg/L(IQR 2.04,12.4), and median DAS28CRP was 2.07(IQR 1.64,2.97). Patients with DAS28CRP of <2.6 were compared with those >3.2. Statistically higher consumption of ginger, garlic, turmeric and coriander were noted amongst patients in remission. Similar results were obtained when patients with DAS28CRP of <1.4 were compared with DAS28CRP >5.1. Nonsignificant numerical differences were noted for intake of food constituents like wheat, total pulse, vegetables, fruit, milk and fish

	DAS28CRP <2.6		DAS28CRP > 3.2		
Dietary items	n	Quantity in grams Median (IQR)	n	Quantity in grams Median(IQR)	P value
ginger	244	4.17 (2.67, 6.67)	80	2.08 (1.39, 3.33)	0.0001
garlic	253	4.17 (2,78, 6.67)	78	2.08 (1.67, 3.33)	0.0001
turmeric	267	1.11 (0.71, 1.67)	88	0.83 (0.51, 1.11)	0.0003
jeera	215	0.55 (0.37, 0.83)	64	0.42 (0.28, 0.75)	0.0138
cinnamon	64	0.42 (0.28, 0.55)	24	0.35 (0.25, 0.52)	0.7212
cloves	85	0.42 (0.28, 0.55)	28	0.33 (0.2, 0.45)	0.6754
coriander	230	1.11 (0.67, 1.67)	78	0.67 (0.48, 1.11)	0.0001
pepper	179	0.42 (0.33, 0.67)	57	0.37 (0.28, 0.55)	0.0351
chilli	259	2.08 (1.67, 3.33)	88	1.67 (1.02, 2.82)	0.0023

Table 1. Comparison between patients in remission with those having moderate/high disease activity

Variables	OR (95% CI)	P - Value
Ginger	0.62 (0.47, 0.81)	<0.001
Garlic	0.61 (0.46, 0.79)	<0.001
Turmeric	0.63 (0.46, 0.87)	0.01
Jeera	0.75 (0.51, 1.09)	0.13
Coriander	0.59 (0.41, 0.83)	0.01
Pepper	0.82 (0.55, 1.21)	0.3
Chilli	0.69 (0.53, 0.90)	0.01

. Multivariate logistic regression for the statistically significant variables

Conclusion: Higher consumption of Indian spices like ginger, garlic, turmeric and coriander were found to be associated with better control of disease activity and hence the inflammation, as evidenced by DAS28CRP in patients with Rheumatoid arthritis, receiving standard triple therapy

REFERENCES:

[1] Shim JS, Oh K, Kim HC. Dietary assessment methods in epidemiologic studies. Epidemiol Health. 2014

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THU0658

WHO IS AT RISK FOR PERSISTENT FATIGUE IN THE FIRST YEAR OF RA? CHARACTERISTICS OF PATIENTS WITH PERSISTENT FATIGUE IN THE FIRST YEAR BY SEX IN THE CANADIAN EARLY ARTHRITIS COHORT (CATCH)

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Background: While treat-to-target strategies can dramatically reduce RA inflammation, persistent fatigue is present in up to half of RA patients, and is an important unmet need. Proposed underlying causes include RA disease, cognitive/emotional/behavioral (CEB), and personal (health) factors.

Objectives: To identify risk factors for persistent fatigue at 12-months in men and women with ERA on immunomodulatory therapies.

Methods: Data were from patients enrolled in the Canadian Early Arthritis Cohort (CATCH) between 01-2007 and 03-2017 who met 1987 or 2010 ACR/EULAR RA criteria, had active disease treated with DMARDS, and had complete data on DAS28, BMI, and fatigue severity (0-10) over 12-months. Persistent fatigue, was defined as fatigue >4 at baseline with <20% improvement at 12 months. Multivariable logistic regression was used to identify RA disease, CEB, and personal/health factors associated with persistent fatigue.

Results: Patients were mostly white (81%), female (71%), with a mean (SD) age of 54 (15), symptom duration of 6 (3) months, and BMI of 28.0 (6.1); 32% were obese (BMI≥30). Women were generally younger, better educated, seropositive, and had greater disability, fatigue, depressive symptoms, and major stress in the past year (p<.05). 21% of women and 19% of men reported persistent fatigue.

Mean (SD) or N (%)	Women N=579	Men N=208	P value
Age	**52 (15)**	**59 (13)**	**<0.0001**
> High School education	**405 (57%)**	**134 (47%)**	**<0.01**
RA Disease			
Symptom duration (mnth)	5.7 (3.0)	5.6 (2.9)	0.65
RF+ or ACPA +	**526 (84%)**	**177 (75%)**	**<0.01**
DAS28 (MDA/HDA v. LDA/REM)	688 (96%)	272 (94%)	0.17
Pain (0-10)	5.8 (2.8)	5.7 (2.8)	0.55
HAQ-DI	**1.1 (0.7)**	**1.0 (0.7)**	**0.02**
Cognitive/Emotional/Behavioral (CEB)			
Baseline fatigue (0-10)	**5.6 (3.0)**	**4.9 (2.9)**	**<0.01**
Obese (BMI≥30)	223 (31%)	93 (32%)	0.74
Current Smoking	110 (15%)	54 (19%)	0.19
Depressive Symptoms (SF12 MCS <45.6)	**356 (53%)**	**92 (35%)**	**<0.0001**
Major stress past year	**401 (56%)**	**123 (43%)**	**0.0001**
Personal/Health			
Work (full/part time)	401 (56%)	149 (52%)	0.20
Rheumatoid Disease Comorbidity Index	1.1 (1.3)	1.3 (1.3)	0.06
OA or backpain	164 (23%)	57 (20%)	0.27
Fibromyalgia	20 (3%)	3 (1%)	0.09
Poor sleep	5.2 (3.2)	5.0 (3.3)	0.41

In multivariable regression that included all Table 1 variables, predictors of persistent fatigue in women were obesity (OR 1.7; 95% CI 1.1, 2.6), initial steroid use (OR 1.7; 95% CI 1.1, 2.7), seronegativity (OR 0.6; 95% CI 0.4, 1.0) and poor sleep (OR 1.1; 95% CI 1.0, 1.2). Obesity was the only significant predictor in men and was assoicated with a 2.4 times higher odds (95% CI 1.1, 5.1) of persistent fatigue at 1 yr. Other sociodemographic, RA characteristic, CEB and personal/health factors were not associated with persistent fatigue in either sex in multivariable models.

Conclusion: Obesity is common in ERA and a major determinant of persistent fatigue in women and men. In obese RA patients on guideline-based treatment, lifestyle interventions targeting weight loss may play an important role in reducing persistent fatigue that does not improve with RA treatment.

REFERENCES: :

Disclosure of Interests: : Susan J. Bartlett Consultant for: Pfizer, UCB, Lilly, Novartis, Merck, Jansen, Abbvie, Orit Schieir: None declared, Marie-France Valois: None declared, Janet Pope Consultant for: Eli Lilly and Company, Louis Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant for: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Speakers bureau: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, CArol Hitchon Grant/research support from: Pfizer, UCB (unrelated studies), Carter Thorne Grant/research support from: Investigator-initiated studies: Amgen, Pfizer. RCTs: Abbvie, Celgene, CaREBiodam, Novartis, Pfizer, Consultant for: Advisory board: Abbvie, Amgen, Celgene, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi. Consultant: Abbvie, Centocor, Janssen, Lilly, Medexus/Medac, Pfizer, Speakers bureau: Medexus/Medac, Diane Tin: None declared, Glen Hazlewood: None declared, Gilles Boire Grant/research support from: Investigator-initiated studies: Amgen, Abbvie, BMS, Eli Lilly, Merck, Novartis, Pfizer, Consultant for: Advisory boards: Amgen, BMS, Celgene, Eli Lilly, Pfizer, Speakers bureau: Merck, BMS, Pfizer, Edward Keystone Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, Consultant for: AbbVie, Amgen, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Celltrion, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, UCB., Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Vivian Bykerk Grant/research support from: Mallinckrodt, BMS, Crescendo Biosciences, Sanofi/Regeneron., Consultant for: Amgen, Pfizer, UCB, Scipher, Sanofi/Genzyme/Regeneron
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THU0659 CATASTROPHIZING IN RHEUMATOLOGY

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Background: Rheumatic disorders (RD) provide chronic pain. Catastrophizing is a negative cognitive and affective response resulting in inadequate expression of pain. Catastrophizing in RD patients is suspected to be involved in persistence and amplification of chronic pain.
Objectives: To assess catastrophizing level in RD and to evaluate the association between catastrophizing and physical pain intensity, disease activity, disability, depression and quality of life.
Methods: We performed a systematic review of literature and search in the following databases: MEDLINE, COCHRANE and EMBASE until April 2018. All observational, cross-sectional and randomized control studies investigating catastrophizing in patients with RD (rheumatoid arthritis (RA), low back pain (LBP), osteoarthritis) were included. Statistical analysis defined pooled mean catastrophizing level by using the Pain Catastrophizing Scale (PCS), the latter ranging from 0 to 52. To assess the association between catastrophizing and disease activity (DAS28), pain (Numerical Rating Scale NRS), disability (ODI) and quality of life (SF36, WOMAC) we collected correlation coefficients and pooled them in meta-analysis using the Fisher's z transformation with MedCalc v18.11.3.
Results: From 1494 articles concerning catastrophizing and RD, 51 were selected for a meta-analysis :
- 601 RA patients (mean age 57.4 years, 67.7% female, mean pooled DAS 28 = 3.4 and mean pooled NRS = 3.8) included in 7 studies. The mean pooled catastrophizing level at baseline was 14.7 (SD = 11.4) in RA patients vs 2.7 (SD = 3.0) in control group patients (n= 82 in 2 studies). In one study, a RA sample identified 22% of high catastrophizers (defined by PCS > or = 30).
- 2521 LBP patients (mean age 43.6 years, 57% female, mean pooled NRS = 4.5 and mean pooled ODI = 30.3) included in 27 studies. The mean pooled catastrophizing level at baseline was 19.9 (SD = 11.3).
- 3388 osteoarthritis patients (knee and hip, mean age 67.7 years, 65% female, mean pooled NRS = 5.0) included in 17 studies. The mean pooled catastrophizing level at baseline was 11.2 (SD = 10).
In RA, a significant positive correlation between catastrophizing and DAS 28 was observed**: pooled r=0.278 p<0.001 (3 studies) (Figure 1).** Pain level was strongly associated with catastrophizing (r=0.71 (p<0.01). Higher PCS scores were significantly associated with higher levels of distress i. e. lower SF-36 Mental Health score (r= -0.52 (p<0.01)) and significantly associated with reduced physical function (r=-0.35 (p<0.01) for SF36 Physical Function).
In LBP, higher PCS scores were significantly associated with higher levels of pain and disability : pooled **r=0.486 p<0.001** (NRS) and **r=0.465 p<0.001 (**ODI), respectively. The association between catastrophizing and depression was significant (r=0.538 p<0.01).
Catastrophizing in osteoarthritis was strongly associated with an increase in functional limitations and pain (i.e. higher WOMAC total score, correlation coefficient: **r= 0.641 p<0.001)**.
Conclusion: Catastrophizing is a common psychological trait clearly associated with disease activity, pain, mental health and physical function. Nevertheless catastrophizing is rarely measured. It might be relevant to detect it earlier in order to adapt pharmacologic and non-pharmacologic treatment in at-risk patients.

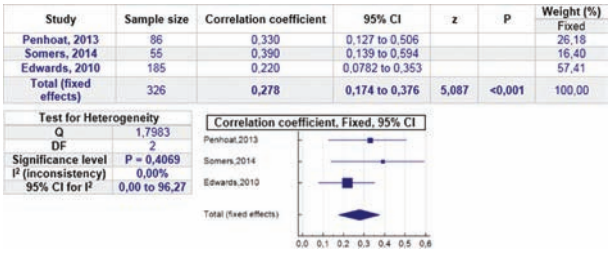


Figure 1. Forest plot for correlation coefficient between catastrophizing (PCS) and disease activity (DAS 28) in rheumatoid arthritis

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THU0660 CHARACTERIZATION OF SCLERODERMA PATIENTS ACCORDING TO RO52 AND KU ANTIBODIES

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Background: Systemic Sclerosis (SSc) is an autoimmune desease that is characterized by progressive and severe fibrosis with cutaneous and visceral involvement, fibroproliferative vasculopathy and alterations of cellular and humoral immunity, very heterogenous from the clinical and immunological point of view. There are many types of antibodies related to the disease that are used in the diagnosis and characterization. Antibodies anti-Ku and anti-Ro52 have been found, although they are not specific to the disease, that could play an important role in the prognosis and clinical expression.
Objectives: To evaluate the clinical pattern and prognosis of SSc patients who carry antibodies Anti-Ku and Anti-Ro52.
Methods: A retrospective, multicentric study of SSc patients included in the Spanish Registry of Scleroderma (RESCLE). Clinical, demographic, prevalence, serological, and survival data were analyzed
Results: A total of 401 samples were analyzed for anti-Ku with 12 positive results (3%). For anti-R052, 1724 sampled were analyzed with 246 positive results (14%). It is observed, from the multivariant analysis, that patients with anti-Ro52 presented, in higher frequency, an association with Sicca syndrome (p<0.001) and its coexistence with the antibody anti-La (OR 44.8 with 95% CI and p<0.001). Regarding patients with anti-Ku, no clinical association was found with statistical significance.
Conclusion: As opposed to finding SSc specific antinbodies such as anti-centromere (ACA), anti-topoisomerase I (ATA), and anti-RNA polymerase III (ARA), the presence of anti-Ku or anti-Ro52 is not conclusive of any distinctive clinical profile.

REFERENCES:

[1] Mehra S., et al. Autoantibodies in systemic sclerosis. Autoinmunity Reviews 2013; 12:340-354.
[2] Stern E., Denton C. The Pathogenesis of systemic Sclerosis. Rheum Dis Clin North Am 2015; 41(3):367-82.
[3] Cavazzana I., et al. A subset of systemic sclerosis but not of systemic lupus erythematosus is defined by isolated anti-Ku autoantibodies. Clin Exp Rheumatology 2013; 31:118-21.
[4] Iniesta N.; et al. Influence of antibody profile in clinical features and prognosis in a cohort of Spanish patients with systemic sclerosis. Clin Exp Rheumatology 2017; 35(suppl. 106)S00-S00.

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THU0661 RISK OF PSORIASIS, CROHN'S DISEASE, ULCERATIVE COLITIS AND ANKYLOSING SPONDYLITIS IN PATIENTS WITH UVEITIS: A NATIONWIDE, POPULATION-BASED COHORT STUDY

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Background: A recent study showed that the risk of ankylosing spondylitis (AS) was increased in patients with uveitis.(1)
Objectives: The study aimed to test the risk of psoriasis (PsO), Crohn's disease (CD), ulcerative colitis (UC) and AS in uveitis patients.
Methods: The data source of this study was the 2003–2012 claims data from the Taiwanese National Health Insurance Research Database. We identified 4,943 incident patients with uveitis defined as having $\geq$ 2 ambulatory or $\geq$1 inpatient visits with a diagnosis of ICD-9-CM 360.12, 364.00–364.02, 364.04–364.05 or 364.3 made by an ophthalmologist from 2006 to 2012 after excluding those having prior PsO (ICD-9-CM 696.1), PsA (ICD-9-CM 696.0), CD (ICD-9-CM 555), UC (ICD-9-CM 556) or AS (ICD-9-CM 720) and randomly selected 49,430 non-uveitis individuals matching (1:10) uveitis cases for age, sex and the year of the index date from a one million representative population. We estimated the incidence rates of PsO (diagnosed by dermatologists), CD, UC and AS for the uveitis and non-uveitis cohorts, and the incidence rate ratios (IRR) and hazard ratios (HRs) after adjusting for sex, age, Charlson comorbidity index and concomitant medications.
Results: No incident case of CD was identified in uveitis patients and non-uveitis individuals. Compared with non-uveitis individuals, patients with uveitis had significantly higher incidence rates of PsO (IRR, 8.82; 95% CI, 6.80–11.43), CD (IRR, 7.23; 95% CI, 1.21–43.27) and AS (IRR, 171.69; 95% CI, 143.15–205.93). However, after adjusting for potential confounders, uveitis patients had a significantly higher risk of developing PsO and AS, but not CD.
Conclusion: This nationwide, population-based cohort study revealed that uveitis patients had an increased risk of PsO and AS, but not CD.

REFERENCES:

[1] Varkas G, Vastesaeger N, Cypers H, Colman R, Renson T, Praet LV, et al. Association of Inflammatory Bowel Disease and Acute Anterior Uveitis, but Not Psoriasis, With Disease Duration in Patients With Axial Spondyloarthritis: Results From Two Belgian Nationwide Axial Spondyloarthritis Cohorts. Arthritis Rheumatol. 2018;70(10):1588-96.

Table 1. The associations between covariates with psoriasis, ankylosing spondylitis, Crohn's disease and traffic accident shown as adjusted hazard ratios with 95% confidence intervals estimated by Cox regression analyses

Covariate	Psoriasis	Ankylosing spondylitis	Crohn's disease
Uveitis	13.73 (10.30–18.31)	232.22 (192.29–280.44)	4.06 (0.46–36.13)
Age	1.02 (1.01–1.03)	0.96 (0.96–0.96)	0.99 (0.94–1.05)
Male	2.37 (1.82–3.09)	1.83 (1.66–2.03)	1.01 (0.17–6.18)
Charlson comorbidity index	0.97 (0.85–1.11)	0.56 (0.51–0.62)	1.45 (0.96–2.18)
Concomitant medication			
DMARD	0.39 (0.24–0.63)	1.32 (1.19–1.47)	0.65 (0.04–10.37)
Immunosuppressant	0.55 (0.17–1.76)	0.29 (0.21–0.40)	5.76 (0.43–77.61)
Corticosteroid	0.57 (0.43–0.74)	0.55 (0.49–0.60)	2.45 (0.24–24.55)

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Disclosure of Interests: Hsin-Hua Chen Speakers bureau: Johnson & Johnson, Novartis, Pfizer, Abbvie, Roche, UCB, Bristol-Myers Squibb, Chugai, Tsu-Yi Hsieh: None declared, Ching-Heng Lin: None declared, Yi-Ming Chen Grant/research support from: GSK, Pfizer, BMS, Astra & Zeneca, Consultant for: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Sanofi, MSD, Guigai, Astellas Inova Diagnostics, UCB Agnitio Science Technology, United Biopharma, Thermo Fisher, Paid instructor for: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Astra& Zeneca, Sanofi, MSD, Guigai, Astellas UCB Thermo Fisher, Speakers bureau: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Lilly, GSK, Astra& Zeneca, Sanofi, MSD, Guigai, Astellas UCB Thermo Fisher, Kuo-Lung Lai: None declared, Der-Yuan Chen: None declared
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THU0662 THE FREQUENCY OF MULTIPLE MYELOMA IN PATIENTS WITH ELEVATED ACUTE PHASE RESPONSE AND LOW BACK PAIN IN A RHEUMATOLOGY OUTPATIENT CLINIC

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Background: Multiple myeloma (MM), is a malignant hematological monoclonal neoplasm of plasma cells. Main clinical findings of MM are anemia, bone pain, elevated erythrocyte sedimentation rate and CRP levels, M-spike on protein electrophoresis, monoclonal protein in serum or urine. Anemia, low back pain and elevated acute phase reactants are frequently seen symptoms of patients who admit to a rheumatology outpatient.
Objectives: We aimed in this study to evaluate the frequency of plasma cell malignancies in patient with elevated acute phase reactants and low back pain.
Methods: 4100 rheumatology patients from rheumatology outpatient clinic are screened retrospective for >50 age, elevated ESR, anemia and back pain or hip pain. 548 patients (312 female and 236 male, mean age: 61 ±6) fulfilled these criteria and these patients are screened with protein electrophoresis for monoclonal gammopathies. If M-spike is seen in protein electrophoresis, patients are evaluated for lambda and kappa chains in serum and urine.
Results: 3 patients were diagnosed for multiple myeloma. All three patients had moderate to severe anemia (Hgb<8 g/dl) and ESR>70 mm/h. Two patients are classified as rheumatoid arthritis and one patient had no inflammatory rheumatological diseases. 7 patients were diagnosed as MGUS and 5 patients from this group is diagnosed as rheumatoid arthritis and 2 patient polymyalgia rheumatica. In MGUS patient group mean ESR level was 44±9 mm/h and mean Hgb level was 10,8±6 g/dl.
Conclusion: We found no increased frequency for MM in rheumatology outpatient clinic. Patients >50 years with high ESR and moderate to severe anemia should be screened with protein electrophoresis for monoclonal gammopathies.

REFERENCES:

[1] A population study to define the incidence and survival of multiple myeloma in a National Health Service Region in UK. Phekoo KJ et al. Br J Haematol. (2004)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7878

THU0663 DO ANTIBODIES DIRECTED AGAINST HUMAN CILIARY BODY TISSUE PREDICT THE DEVELOPMENT OF UVEITIS IN JIA- A PRELIMINARY STUDY

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Background: Eleven -30% of Juvenile Idiopathic arthritis (JIA) children develop uveitis. JIA associated uveitis is completely asymptomatic and thus all children with oligo/extended oligo and polyarticular JIA require regular slit lamp examination by an ophthalmologist– a time consuming and distressing procedure particularly for small children. If not diagnosed early, or inadequately treated, it may lead to glaucoma, cataracts, persistent cystoid macular oedema and ultimately results in visual impairment and blindness. Whilst Anti- nuclear antibody positivity is found more commonly in those with uveitis, it is not sufficiently sensitive or specific as a screening tool. However the presence of these antibodies and the detection of B cells in the inflammatory infiltrate around the ciliary body in JIA Uveitis suggests a significant role for humeral mediated immune dysregulation in the pathogenesis of JIA
Objectives:
1. Does the serum from Children with JIA associated uveitis contain antibodies directed against the ciliary body tissue of the human eye?
2. Could these be used to identify JIA patients at risk of developing uveitis?

Methods: Whole human globe were formalin fixed paraffin embedded and 4um sections were obtained. Following blocking with Goat sera blocking,

sections were incubated with JIA sera from children with and without uveitis (1:50 in PBT) for 1h.
Secondary antibody (goat anti-human IgG-488).DAPI counterstaining was used
Sections analysed by EE, using a Leica SP8 confocal microscope using LAS software. The operator was blinded to the status of the patient
Results: Sera from 13 patients were analysed: 5 with uveitis and 8 with no uveitis. Six had oligo JIA; 3 extended Oligo; 4 Poly JIA. Four were ANA –ve; 8 ANA+ve Max titre1/80 (using HEp2 cells); 1 unknown. Treatment: Seven NSAID; 1 MTX; 2 MTX and Pred; 3 Biologics. 5 Topical steroids
All tissue sections were analyzed blindly. Of the 5 patients with Uveitis 3 had antibodies against ciliary antigens and 2 did not. Of the 8 patients without uveitis 2 had antibodies against ciliary antigens and 6 did not. Fig 1 demonstrates immune histochemical findings from 2 typical patient's sera. No patient had high titres of antinuclear antibodies and there was no association between ANA positivity and ciliary body positivity. Fluorescent intensity was also higher in the Uveitis +ve patients Fig 2.

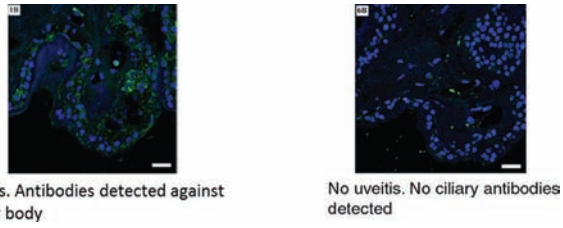


Fig 1 Ciliary body antibody detection in serum of patients with and without uveitis

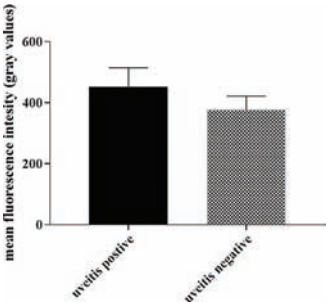


Fig 2 Mean fluorescent intensity between Uveitis and Non Uveitis labelling

Conclusion: This preliminary work suggests that antibodies to ciliary body proteins may be valuable in identifying patients with JIA at risk of developing uveitis with 60% of those with uveitis being antibody positive compared with only 25% of those without uveitis. Concurrent treatment may alter the presence of antibodies in the serum and may also have suppressed the development of uveitis in those patients who were antibody positive yet had not developed uveitis. Antibody patterning within the ciliary body may also provide further useful information. We are currently studying a further group of patients who have not received immunosuppressive drugs
Disclosure of Interests: None declared
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THU0664 THE ABSOLUTE RISK OF CLINICALLY DIAGNOSED GOUT BY CLUSTERS OF GOUT ASSOCIATED COMORBIDITIES AND LIFESTYLE FACTORS – RESULTS FROM 30 YEARS FOLLOW-UP OF THE MALMÖ PREVENTIVE PROJECT COHORT IN SOUTHERN SWEDEN

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Background: Clinical gout is predicted by a number of factors. Several of these (comorbidities and lifestyle) have been shown to cluster in gout patients[1,2] indicating several different pathophysiological pathways, but it is not known if and to what extent such clusters predict gout.
Objectives: To examine; 1) the prevalence of comorbidity clusters in the population and 2) the long-term absolute and relative risks for developing gout in these clusters defined at baseline in subjects of Malmö Preventive Project (MPP).
Methods: The MPP is a screening program for cardiovascular risk factors, alcohol abuse and breast cancer in Malmö, Sweden. A total of 33,346 individuals (67% male, age=45.7 years, mean follow-up=28.2 years), screened between 1974 and 1992, participated. Date of gout diagnosis was defined as the first visit with gout (using ICD-codes) to physicians within primary or specialized care, through linkage of the MPP cohort with regional and national health care registers. End of follow-up was defined as the date of first gout diagnosis, death, moving from the area or December 31st, 2014. Hierarchical clustering was performed in a subset of 22,057 individuals (screening period: 1975-1992) to group observations. Variables clustered included obesity, renal dysfunction, diabetes mellitus (DM), hypertension, cardiovascular disease (CVD), dyslipidemia, pulmonary dysfunction (PD), smoking and use of diuretics. For the five identified clusters, their population prevalence as well as the incidence and hazard ratio (HR) for gout were computed using cox-proportional hazard analysis in Rv3.5.2.
Results: Cluster-1 (C1) with "few comorbidities" was by far the most common in the population (73%), followed by cluster-4 (C4) characterized by "obesity and hyperlipidaemia" (17%). These two pathways included 86% of incident gout cases during the follow-up. The four clusters (C2-5) identified by different comorbidity patterns all resulted in a 2-3-fold increased risk for incident gout. The highest incidence for gout was seen for cluster-2 (C2) characterized by "renal dysfunction" and cluster-3 (C3) characterized by "cardiovascular disease" (Table).

Table Incidence and hazard ratios for gout in observation-clusters of MPP cohort

Cluster name	Main characteristics	Occurence, n (%)	Incident gout (n)	Incidence*	HR (95% CI)°
C1 Few comorbidities	No history of diabetes, CVD or renal disease.	16063 (72.8)	551	119	1
C2 Renal dysfunction	Renal dysfunction (100%), higher age at inclusion	750 (3.4)	53	269	2.31 (1.73-3.07)
C3 Cardiovascular disease and lifestyle	High frequency of CVD (100%), smoking (74%), alcohol risk behaviour (40%) &PD (22%)	528 (2.4)	26	224	2.41 (1.63-3.58)
C4 Obesity and hyperlipidaemia	High frequency of obesity (34%) & hyperlipidemia (74%)	3673 (16.7)	235	235	2.02 (1.73-2.35)
C5 Diabetes mellitus and hypertension	High frequency of DM (51%), hypertension (53%) & diuretics use (52%)	1043 (4.7)	45	184	1.98 (1.46-2.68)

*Incidence per 100,000 person-years at risk, °Adjusted for age, sex

Conclusion: In a population-based study, we identified five clusters based on gout-related comorbidities. Most gout cases occurred in the cluster characterized by few comorbidities. Such cases may have predisposing factors not captured by comorbidity patterns, e.g. genetics related to serum urate. In addition, we identified four pathways each defined by different comorbidity patterns and contributing to increased risk for gout, pathways that may require partly individual interventional strategies.

REFERENCES:
[1] Richette P, et al. Ann Rheum Dis 2015; 74(1):142-47.
[2] Megan B, et al. Rheumatol 2018; 57(8):1358-63.

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THU0665 PREVALENCE OF RHEUMATIC DISEASES IN COLOMBIA: AN APPROACH FROM MINISTRY OF HEALTH AND SOCIAL PROTECTION DATA (SISPRO)

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Background: The ministry of health and social protection of Colombia uses a system named SISPRO as a tool to establish the basic information of the health system. This information is public and available for anyone to search. We analyze the prevalence and specific characteristics of patients with rheumatic diseases registered in colombian health system between 2012 to 2016.
Objectives: To establish the prevalence and basic epidemiological characteristics of the main rheumatic diseases in Colombia
Methods: This is a descriptive epidemiological study using the International Statistical Classification of Diseases and Related Health Problem (CDI), as keywords for each rheumatic disease during the analysis of SISPRO data and National Statistical System (DANE) populations projections, as from the last census in Colombia to estimated prevalence of each disease.
Results: Colombia is a middle-income country with an estimated population of 49.834.240 habitants to 2018 according to 2005 census projections. Despite some limitations of SISPRO data, actually is the only official database of the government. We calculate the estimated prevalence and number of patients with some rheumatic diseases (table 1), confirming that autoimmune diseases are more frequent in woman, and surprisingly, spondyloarthritis (ankylosing, psoriasis and inflammatory bowel disease) are also discreetly more frequent in woman population.

	Total cases	Prevalence (%)	Ratio woman: man
Rheumatoid arthritis	248.995	0,520	4,71 : 1
Ankylosing spondylitis	84.356	0,177	2,71 : 1
Gout	70.881	0,149	0,25 : 1
Sjögren syndrome	58.680	0,123	4,63 :1
Systemic lupus erythematosus	41.804	0,088	4,17 : 1
Polymyalgia rheumatic	35.331	0,070	6,69 : 1
Sjögren syndrome	10.473	0,022	3,22 : 1
Inflammatory miopathy	8.498	0,018	1,76 : 1
Psoriatic arthritis	1.670	0,004	1,32 : 1
Granulomatosis with polyangiitis	750	0,002	7,44 : 1
Beçhet Disease	523	0,001	2,15 : 1
Churg Strauss disease (EGPA)	186	0,0001	2,24 :1

Table 1. Prevalence of rheumatic diseases in Colombia

Conclusion: Epidemiological and prevalence information of rheumatic diseases in Colombia is presented. The data found in the present study are concordant with epidemiological studies in other countries.
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THU0666 SERIOUS/AT LEAST MODERATE INFECTIONS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ON SYNTHETIC AND BIOLOGIC DRUGS FROM THE PHARMACHILD REGISTRY

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Background: Infections are a major concern for patients affected by juvenile idiopathic arthritis (JIA) treated with immunosuppressive therapy. Evidence is inconsistent as to whether the start of synthetic or biological disease modifying anti-rheumatic drugs (DMARDs) is associated with an increased risk of serious and at least moderate infection.
Objectives: To determine whether the addition of a TNF inhibitor (TNFi) to methotrexate (MTX) may increase the risk of serious and at least moderate infections in JIA patients included in the Pharmachild registry. (1)
Methods: Serious and at least moderate infections were analysed in JIA patients, enrolled in the Pharmachild registry at September 30th, 2018, who started as first drug with MTX. We divided patients in 3 treatment groups: "MTX alone", in which patients had received MTX as the only drug all over their history; "MTX Start", in which patients had received MTX as first drug; "MTX+TNFi" for those patients who received a TNFi in addition to MTX after a period of "MTX Start". All the 3 groups were pure, since they received only these drugs. We considered initial infections as related to the treatment if the infection occurred in the drug period or within 90 days after treatment stop.(2) For the group "MTX Start", infection was related to treatment if occurring in the drug period stopped as soon as the second drug was introduced. For the group "MTX+TNFi", we considered all the possible correlations between start and end dates of the two drugs, including the time lag of 90 days after any treatment stop. If the interval between two drugs was shorter than 90 days, treatment was considered continuous. Crude rates (number of infections divided by drug exposure, excluding off-drug periods) and true incidence rates (number of first infections divided by the time lag between first drug administration and the date of the infection if the patient experienced the infection, the last Pharmachild visit if the patient didn't experience the event) were calculated.
Results: We enrolled in Pharmachild a total of 8061 patients who experienced 1686 infections. We excluded 41 patients who had infections before any treatment start. Of the final number of 8020 patients, we considered: 1226 patients in the group "MTX alone", 3128 in the group "MTX start" and 1026 in the group "MTX+TNFi". 7.7% of the patients in the "MTX alone" group, 2.7% of the patients in the "MTX Start" group and 7.0% of the patients in the "MTX+TNFi" group experienced at least one infection. Crude rates of infections per 1000 person-years resulted: 48.0 for the group "MTX alone", 22.0 for "MTX Start", 74.0 for "MTX +TNFi". Incidence rates per 1000 person-years were: 32.0 for the group "MTX alone", 17.0 for "MTX Start", 59.5 for "MTX+TNFi". The percentage of drug exposure on the patient follow-up was variable among the 3 treatment groups (from 15.6% for the "MTX+TNFi" group to 51.5% for the "MTX alone" group).
Conclusion: Pharmachild showed, through the analysis of pure treatment groups, that the addition of the anti-TNF biologic to MTX even triples the incidence rate of infections.

REFERENCES:

[1] Swart, et al. Arthritis Res Ther. 2018;20:285; (2) Dixon WG, et al. Arthritis&Rheumatism 56:2896–2904.

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THU0667 OVERALL INFECTION RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING ABATACEPT, RITUXIMAB AND TOCILIZUMAB. AN OBSERVATIONAL COHORT STUDY

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Background: Most infections in patients with rheumatoid arthritis (RA) are treated in primary care with a prescription of antibiotics. Only a small fraction requires hospitalization. Existing studies of infection risk in patients with RA, who receive non-tumor-necrosis-factor-inhibitor biologic (non-TNFi) therapy, however, have focused primarily on hospitalized infections.(1)
Objectives: In Danish RA patients treated in routine care with the three non-TNFi abatacept, rituximab and tocilizumab 1) to compare adjusted incidence rates (IR) of infections overall, and 2) to estimate the relative risk (RR) of infections across the drugs during the first year of non-TNFi treatment.
Methods: We conducted an observational cohort study including all RA patients in DANBIO who started a non-TNFi treatment between January 2010 and December 2017. Clinical characteristics at baseline were described. We defined infections as either a prescription of antibiotics or a hospitalization due to infection. Baseline comorbidities, antibiotic prescriptions and hospitalized infections were identified through linkage to national registries. We calculated IRs of infections per 100 person-years (age and gender adjusted) and rate ratios (as estimates of RRs, adjusted for additional covariates) during the first year of treatment (Poisson regression).
Results: We identified 3,696 treatment series of non-TNFi (abatacept 1,115/rituximab 1,017/tocilizumab 1,564). Patients receiving rituximab tended to be older, had longer disease duration and more previous malignancies. During the first year of treatment, 1,747 infections were identified. Age and gender adjusted IRs per 100 person years were (abatacept/rituximab/tocilizumab): 76.1(69.3; 83.6)/87.3(79.3; 96.1)/77.4(71.4; 83.9). Adjusted RRs (Table) were 0.88(0.76; 1.02) for abatacept and 0.87 (0.75; 1.00) for tocilizumab compared to rituximab. For abatacept vs. tocilizumab it was 1.02 (0.89; 1.16).

Table. Baseline characteristics, one-year IRs and RRs of infections in RA patients starting non-TNFi treatment stratified by drug.

Variable	Abatacept, N=1115	Rituximab, N=1017	Tocilizumab, N=1564
Female gender, %	78 %	78 %	78 %
Age, years	59 (50-68)	62 (53-70)	59 (50-67)
Disease duration, years	8 (3-16)	11 (5-19)	9 (3-16)
DAS28	4.7 (3.9-5.4)	4.8 (4.0-5.9)	4.9 (4.1-5.7)
CRP, mg/L	8 (3-20)	10 (4-22)	12 (4-30)
HAQ	1.4 (0.9-1.9)	1.5 (1.0-2.0)	1.4 (1.0-2.0)
Previous cancer, %	1 %	9 %	2 %
Previous infection*, %	24 %	28 %	24 %
Incidence rates (IR) of infections, 0-12 months			
Person years	631	520	888
Infections, n	512	500	735
IR/100 PY (95%CI)*	76.1 (69.3; 83.6)	87.3 (79.3; 96.1)	77.4 (71.4; 83.9)
Risk ratios (RR) for infections, 0-12 months			
	ABA vs TCZ (ref)	ABA vs RTX (ref)	TCZ vs RTX (ref)
Adjusted RR (95%CI)**	1.02 (0.89; 1.16)	0.88 (0.76; 1.02)	0.87 (0.75; 1.00)

Numbers are medians (IQR) unless otherwise stated. *previous hospitalized infection *adjusted for age and sex, ** Adjusted for age, sex, DAS28, smoking, disease duration, HAQ, glucocorticoids use at baseline, previous hospitalized infection, previous cancer, previous chronic obstructive pulmonary disease. Abbreviations: CI: confidence interval; DAS28: disease activity score of 28 joints, HAQ: health assessment questionnaire, PY: person years

Conclusion: In patients with RA receiving treatment with abatacept, rituximab or tocilizumab in routine care, rituximab had the highest risk of infection during first year of treatment. However, this finding should be interpreted with caution due to differences in baseline characteristics across drugs and potential residual confounding.

REFERENCES:

[1] Gron KL, Arkema EV, Glintborg B, Mehnert F, et al. Risk of serious infections in patients with rheumatoid arthritis treated in routine care with abatacept, rituximab and tocilizumab in Denmark and Sweden. Annals of the rheumatic diseases. 2019.

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THU0668 THE ASSOCIATION BETWEEN ANTI-CCP TITRE LEVEL AND DISEASEACTIVITY AND DISABILITY OVER ONE YEAR FOLLOWING THE INITIATION OF METHOTREXATE OR BIOLOGIC THERAPY FOR ANTI-CCP+ RHEUMATOID ARTHRITIS

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Background: Whilst anti-cyclic citrullinated peptide antibody (anti-CCP) positivity in associated with poor outcomes in patients with rheumatoid arthritis (RA), it is unclear whether titre level over time is associated with outcome.
Objectives: Whilst anti-cyclic citrullinated peptide antibody (anti-CCP) positivity in associated with poor outcomes in patients with rheumatoid arthritis (RA), it is unclear whether titre level over time is associated with outcome.
Methods: Patients were recruited to one of two, UK-based, multi-centre prospective cohort studies: MTX-starters = Rheumatoid Arthritis Medication Study (RAMS); biologic-starters = Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS). Anti-CCP titre (Axis-Shield Anti-CCP test; U/ml; anti-CCP titre >5 U/ml = anti-CCP+) was measured at the co-ordinating centre from blood samples taken at baseline, 6 months and 12 months. Patients who were anti-CCP+ at baseline and had titre measured at one other assessment were included in the analysis. Patients completed the Health Assessment Questionnaire (HAQ) and the Disease Activity Score (DAS28) was calculated at each assessment. The association between anti-CCP titre and DAS28 and HAQ was assessed using linear random effects models, controlling for age, gender and disease duration (months). Anti-CCP titre was natural log-transformed. Missing data resulting from anti-CCP assay failure were imputed using multiple imputation.
Results: In total, 686 MTX-starters and 346 biologic-starters were included. Biologic-starters had worse disease at baseline compared to MTX-starter (Table). Median [IQR] titre decreased slightly over follow-up for MTX-starters (baseline = 147 [48, 416]; 6 months = 133 [47, 454]; 12 months = 124 [44, 421]; p=0.63) and biologic-starters (baseline = 138 [37, 492]; 6 months = 112 [30, 468]; 12 months = 103 [30, 451]; p=0.36) but this was non-significant. For MTX-starters, anti-CCP titre was statistically significantly associated with DAS28 and HAQ, but the effect sizes were small (mean difference [95% CI] per unit increase in log anti-CCP: DAS28 = 0.07 [0.02, 0.11]; HAQ = 0.06 [0.03, 0.08]). There was no significant association between anti-CCP titre and DAS28 and HAQ for biologic-starters (mean difference [95% CI] per unit increase in log anti-CCP: DAS28 = 0.03 [-0.05, 0.10]; HAQ = 0.02 [-0.01, 0.05]).
Conclusion: Time-varying anti-CCP titre level was not strongly associated with disease activity or disability over one year in either MTX-starters or biologic-starters who were anti-CCP+ at baseline, indicating repeat testing of anti-CCP level may not be necessary.

Baseline characteristics

Baseline characteristics	MTX-Starters	Biologic-starters
N	686	346
Age, years	59 (49, 67)	59 (51, 67)
Female, N (%)	441 (64.3)	269 (77.8)
Disease duration, months	9 (4, 27)	72 (24, 180)
Smoking:		
Never	240 (35.5)	106 (30.6)
Former	265 (39.1)	163 (47.1)
Current	172 (25.4)	77 (22.3)
Swollen joint count (28)	5 (2, 10)	8 (5, 11)
Tender joint count (28)	5 (2, 11)	13 (9, 18)
CRP, mg/l	7 (3, 19)	10 (5, 26)
DAS28-CRP	4.2 (3.3, 5.2)	5.6 (5.2, 6.2)
HAQ	1.13 (0.50, 1.63	1.63 (1.13, 2.00)
Pain VAS, mm	50 (26, 73)	69 (52, 78)
Fatigue VAS, mm	51 (24, 72)	71 (52, 85)
Anti-CCP+, N (%)	686 (100)	346 (100)
Anti-CCP titre	147 (48, 416)	138 (37, 492)

Anti-CCP = anti-cyclic citrullinated peptide antibody, CRP = C-reactive protein, DAS28 = Disease Activity Score (28), HAQ = Health Assessment Questionnaire, MTX = methotrexate, N = number, VAS = visual analogue scale

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THU0669 GESTATIONAL AGE AT BIRTH AND THE RISK OF AUTOIMMUNE DISEASE

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Background: A preterm newborn has an immature immune system. Although preterm birth is associated with autoimmune hypothyreosis, it is unclear, whether it also could lead to an overall increased risk of autoimmune disease.

Objective: We assessed whether a shorter gestation increases the risk of special reimbursement for medication for hypothyreosis, rheumatic disease, or ulcerative colitis/Crohn's disease

Design/Methods: A total of 235 622 children were born in Finland from Jan 1987 to Sep 1990, according to the Medical birth register, which provided also gestational age (GA) at birth. Data were linked by help of the personal identity number. A register held by the Social Insurance Institution provided the data on special reimbursements. We calculated cumulative incidences within gestational age groups until December 2014 and tested statistical significance by the chi-squared –test.

Results: At the end of the follow-up, 1354 men and 2200 women had at least one of the specified autoimmune diseases.

The cumulative incidences differed by gestational age only regarding a 50% higher incidence for hypothyreosis among all subgroups of preterm wome (P=0.05). No other clear patterns were seen regarding autoimmune diseases among preterm born or early term born subgroups.

Conclusion(s): Those born preterm develop hypothyreosis more often. However, the two other composite categories of autoimmune diseases were unrelated to gestational age pointing against an overall tendency toward autoimmune disease in preterm born young adults.

Cumulative incidence (1/100,000) of four groups of autoimmune diseases

		Hypoth[104]	Rheuma[202]	UC&CD[208]	n
Men	0 <31	0	597	398	1005
	1 32 or 33	263	658	395	760
	2 34 to 36	206	494	762	4856
	3 37	149	512	776	6057
	4 38	140	504	625	15687
	5 39 to 41	122	550	692	85753
	6 >41	120	519	798	5010
	99 missing	0	512	448	1563
	Total	128	539	687	120690
	P-value (Chi^2)	0.40	0.99	0.49	
Women	0 <31	649	519	389	771
	1 32 or 33	651	163	814	614
	2 34 to 36	771	795	675	4149
	3 37	502	929	799	5380
	4 38	537	975	692	14152
	5 39 to 41	460	1056	704	83712
	6 >41	278	1069	684	4678
	99 missing	474	880	609	1477
	Total	478	1021	702	114932
	P-value (Chi^2)	0.05	0.16	0.95	

202 Disseminated connective tissue disorders, rheumatoid arthritis and other rheumatic diseases (A04.6, A39.8, A50.5, D76.0, D76.3, H20.1, H30, I33.0, I40.8, J84, K50.9, K51.9, K73.2, K74.3, K83.0, L40.5, M02, M05, M06, M08, M13.9, M30–M35, M45, M46.1, M46.9, M94.1, N03, N04, Q44.2).

104 Hypothyreosis

208 Ulcerative colitis or Crohn's disease

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THU0670 PATERNAL USE OF METHOTREXATE AND CONGENITAL MALFORMATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Maternal exposure to methotrexate (MTX) during pregnancy is known to be teratogenic, but less is known about the risk due to paternal MTX exposure. Because of a theoretical teratogenic risk from paternal exposure, treatment recommendations advocate that men should discontinue MTX three months before conception and continue discontinuation during the partners' pregnancy. This may lead to suboptimal adherence to treatment, fear among the future parents and pregnancy termination.

Objectives: The aim was to systematically review and meta-analyze the collective data on paternal MTX exposure and the risk of congenital malformations.

Methods: We performed a systematic search in the databases – PubMed, Embase, Cochrane Central, and Cinahl – on March 1, 2018. We included studies with an English abstract that assessed major or all (both major and minor) malformations following any paternal exposure to MTX. Studies that included a control group were included in the meta-analysis. No time restriction was applied. Review Manager Version 5.3 was used for the meta-analysis.

Results: We identified 36 studies assessing the risk of congenital malformations following paternal exposure to MTX of which 20 contained original data. Five studies met the inclusion criteria for the meta-analysis: Three studies from Denmark had a major overlap in study populations, one study from Norway, and one German study. All studies were cohort studies using national registries except the German that used structured interviews and phone interviews. Because of the overlapping Danish studies, only the largest Danish study for each of the outcomes were included. We included a total of 265 fathers exposed to MTX and 1,004,834 controls in the meta-analysis investigating risk of major congenital malformations. Among the offspring of the MTX-exposed 7 (2.64%) had a major malformation compared to 33,816 (3.37%) among the unexposed. Pooled odds ratios were 1.02 (95% confidence interval [CI] 0.48-2.20) for major malformations and 1.02 (CI 0.62-1.66) for all malformations.

Conclusion(s): In this systematic review and meta-analysis, we found no association between preconceptional paternal MTX use and major or all congenital malformations. The current recommendations to avoid paternal MTX use before conception do not appear to be supported by evidence and paternal treatment with MTX could be continued when planning a pregnancy.

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THU0671 PULMONARY INVOLVEMENT IN RHEUMATOID ARTHRITIS: PATTERNS AND EPIDEMIOLOGICAL CHARACTERISTICS FROM A MONOCENTRIC COHORT STUDY

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Background: Extra-articular manifestations (EAM) are not an uncommon finding in patients with Rheumatoid Arthritis (RA). Pulmonary involvement is a potential life-threatening EAM with deleterious effects on the quality of life and is reported in different occurrence among studies.
Objectives: To evaluate the frequency of pulmonary involvement in RA patients followed-up in a 15-years period.
Methods: 549 RA patients were diagnosed according to the ACR/EULAR classification criteria since 2003. A full clinical examination as well as a detailed laboratory and immunological evaluation has been carried-out at baseline. Furthermore, chest, hand and wrist but also feet radiographs had been obtained. All patients were followed-up at predefined times and were treated appropriately with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and/or biologic (b)DMARDs. Any laboratory abnormalities or comorbidities were recorded and investigated appropriately at every visit. In addition, the disease activity score (DAS) using the 28-joints count (DAS-28) was recorded.
Results: Initial evaluation revealed 15 patients as having pulmonary abnormalities. Thus, these patients were excluded. From the rest, 37 (6.7%) patients manifested lung involvement. There were 26 males and 11 females, with mean age of 62.9 ±3.4 years and disease duration of 8.5 ±2.2 years. 14 were smokers and 10 ex-smokers. Dry cough and dyspnea on exertion were the main pulmonary symptoms. High resolution computed tomography (HRCT) scan of the chest revealed interstitial lung disease (ILD). More specifically, 23 patients showed usual interstitial pneumonia (UIP), 10 patients had nonspecific interstitial pneumonia (NSIP), while 4 had a mixed pattern. Six patients died 4 years after ILD development. ILD was associated with high DAS-28, seropositivity and male gender.
Conclusion: ILD is not a frequent EAM in patients with RA, but it carries a poor prognosis with high morbidity and mortality and it is associated with RA disease activity and male gender. UIP is the most prevalent pattern of ILD in RA patients.
Disclosure of Interests: None declared
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THU0672 PREVALENCE OF OSTEOPOROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A MULTICENTER COMPARATIVE STUDY OF THE FRAX AND WHO CRITERIA

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Background: Reduced bone mass or osteoporotic fracture are one of major complications in chronic inflammatory diseases including systemic lupus erythematosus (SLE). Fracture risk was found to be determined not only by conventional factors such as age and a lack of physical activity, but also by systemic inflammation, musculoskeletal symptoms, and administration of glucocorticoids.
Objectives: We evaluated the prevalence of osteoporosis and fracture risk in patients with systemic lupus erythematosus (SLE), and compared the fracture risk assessment tool (FRAX) criteria and bone mineral density (BMD) criteria established by the World Health Organization (WHO).
Methods: Data of 182 female patients with SLE were collected retrospectively in 5 hospitals between January 2012 and December 2016. The FRAX criteria for high-risk osteoporotic fractures were calculated including and excluding the scores in BMD, respectively. The high risk for fracture by FRAX criteria and BMD criteria by WHO was defined as 10-year probability of $\geq$ 20% for major osteoporotic fracture or $\geq$ 3% for hip fracture, and T score ≤ -2.5 or Z score ≤ -2.0, respectively.
Results: The mean age was 51.1 ± 11.23 years, 114 (62.3%) were postmenopausal. Osteoporotic fractures were detected in 9 (4.9%) among the 127 patients taking T-L spine X-ray. The numbers of candidates for pharmacological intervention using the FRAX criteria with and without BMD and the WHO criteria were 26 (14.2%), 23 (12.6%), and 51 (27.9%), respectively. Only 50–69.6% of the patients in the high-risk group using the FRAX criteria and the WHO criteria were receiving osteoporosis treatments. The following were associated with candidates for pharmacological intervention for fracture using the FRAX criteria without BMD and WHO criteria: Age (OR 1.422, 95% CI 1.22–1.659 and OR 1.157, 95% CI 1.083–1.236), and weight (OR 0.87, 95% CI 0.798–0.949 and OR 0.943, 95% CI 0.901–0.986), respectively. In addition, cumulative glucocorticoids dose (OR 1.073, 95% CI 1.024–1.123) was associated with candidates for pharmacological intervention for fracture using the FRAX criteria with BMD.
Conclusion: The proportion of SLE patients with a high risk of osteoporotic fractures by the FRAX criteria with and without BMD and the WHO criteria was 12.6%–27.9%. Among the candidate patients, only 50%–69.6% were taking osteoporotic medications. Independent risk factors for osteoporotic fractures in SLE patients were older age, lower weight and cumulative glucocorticoids dose.

REFERENCES:
[1] Cramarossa G, Urowitz MB, Su J, Gladman D, Touma Z. Prevalence and associated factors of low bone mass in adults with systemic lupus erythematosus. Lupus. 2017;26:365-372.
[2] Barbulescu A, Vreju FA, Criveanu C, Rosu A, Ciurea P. Osteoporosis in Systemic Lupus Erythematosus - Correlations with Disease Activity and Organ Damage. *Curr Health Sci J.* 2015;41:109-114

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THU0673 CARDIOVASCULAR DISEASE AS A RISK FACTOR FOR DEVELOPMENT OF RHEUMATOID ARTHRITIS – A DANISH FOLLOW-UP STUDY

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Background: It is well-established that patients with rheumatoid arthritis (RA) have higher risk for development of atherosclerotic cardiovascular diseases (CVD) than the general population (1). The evidence shows that a CVD burden is already notable at the onset of RA (2). It is well-known, that atherosclerosis is an inflammatory condition (3). Therefore, we hypothesize that atherosclerotic CVD is positively associated with subsequent development of RA.
Objectives: To examine the risk of developing RA in persons who have had CVD, defined as acute myocardial infarction (AMI) or ischaemic stroke while controlling for established shared risk factors.
Methods: We conducted a population-based cohort study within the Danish Diet, Cancer and Health (DCH) cohort. The cohort was recruited 1993-97 and included individuals aged 50 to 64 years, born in Denmark and living in geographically defined parts of Denmark. Data on lifestyle factors and anthropometric measurements were collected at enrolment into the DCH. Information on incident AMI (ICD-10 code: I21), ischemic stroke (ICD-10 code: I63) and RA (ICD-10 codes: M05, M06 combined with ATC codes for DMARDs) was obtained from nationwide administrative registers. Participants were followed until development of RA, death, loss to follow-up or October 2016, whichever came first. Data were analyzed using Cox´s proportional hazards regression models with delayed entry and age as the underlying time scale and cardiovascular disease (CVD) as a time-varying exposure variable, stratifying by gender. Established shared risk factors - smoking, body mass index and waist circumference - were included in the multivariable analyses.
Results: Complete data were available on 53287 subjects (52% female) without a AMI, stroke or RA diagnosis prior to their enrolment into the DCH. Median age at entry into DCH was 56 years. During follow-up (median 21 years), 4,627 participants developed CVD (37% female) and 516 participants developed RA (69% female). The risk for developing RA was 30% higher in women with CVD than in women without CVD (adjusted hazard ratio (HR) 1.30 (95% CI 0.70-2.38)) (Table 1). In men, there was no clear association between CVD and development of RA (adjusted HR 0.73 (95% CI 0.34-1.58)).

Table 1. The relationship between cardiovascular disease and the development of rheumatoid arthritis, stratified by gender.

	Adjusted* Hazard Ratio (95% confidence interval)	
	Men (number of RA cases=158)	Women (number of RA cases=358)
CVD non-exposed, n=48,660	1 (ref.)	1 (ref.)
CVD exposed, overall, n=4,627	(number of RA cases=151)	(number of RA cases=347)
	0.73 (0.34-1.58)	1.30 (0.70-2.38)
	(number of RA cases=7)	(number of RA cases=11)

Conclusion: The investigation showed tendency towards a higher risk of developing RA in women with previous CVD than women without CVD. Male gender was not associated with subsequent development of RA, possibly related to low sample size.

REFERENCES:

[1] Avina-Zubieta et al. Ann Rheum Dis. 2012;71(9):1524–9.
[2] Hannawi et al. Arthritis Res Ther. 2007;9(6):R116.
[3] Ross R. N Engl J Med. 1999 Jan 14;340(2):115–26

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THU0674 CLINICAL PRESENTATION AND MANAGEMENT OF MONO- AND BILATERAL KNEE ARTHRITIS: RESULTS FROM THE LEIDEN EARLY ARTHRITIS CLINIC COHORT

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Background: Patients presenting with arthritis in one or both knees propose a challenge regarding diagnosis, prognosis and treatment decisions.
Objectives: To characterize the patients with knee arthritis who presented to the Leiden Early Arthritis Clinic (EAC) and to evaluate the disease course and initial treatment decisions.
Methods: All patients with arthritis confined to the knee(s) were selected from all patients included in the EAC between 1993 and 2015. The EAC captures patients with arthritis and symptom duration < 2 years, excluding arthritis diagnosed at presentation as definite infectious, gouty or osteoarthritic. EAC follow up is at 2 weeks, 3 months and thereafter yearly. Medical files were revised for information on treatment and clinical outcomes. Baseline characteristics were summarized, treatment and outcome was evaluated over time up to 12 months. Patients were stratified over 3 groups: 1. Early remission (at 3 months no clinical synovitis and no flare in the first year); 2. Persistent gonarthritis at 3 months (improving or stable up to 12 months, without progression); 3. Progression to oligo-/polyarthritis ≤ 12 months. Between-group differences were analysed using χ^2, Fischer exact tests, two-way ANOVA or Kruskal Wallis tests.
Results: Of the 206 patients identified, 174 (85%) had mono- and 32 (15%) bilateral gonarthritis. Early remission was observed in 67/206 patients (32.5%, group 1), gonarthritis persisted in 109/206 patients (52.9%, group 2) and progression to oligo-/polyarthritis occurred in 30/206 patients (14.6%, group 3) within the first 12 months. At 12 months, 32/109 (29.4%) patients in group 2 still had gonarthritis, 40/109 (36.7%) were in remission, and 37/109 (33.9%) patients had been lost to follow-up (11 patients were in remission and 26 patients still had (residual) gonarthritis at the last available visit). RF and ACPA positivity and high ESR at baseline were predictive for progression (group 3), but did not differ between patients in groups 1 and 2. There was a trend for longer symptom duration at presentation in group 3 (76.5 days, IQR 25.5-175.5, p=0.040 vs. group 1) (table 1).
The initial treatment consisted of NSAIDs (in 125/206 patients, 60.7%), an intra-articular corticosteroid injection (IAC) (39/206, 18.9%) or other (29/206, 14.1%) including prednisone, csDMARDs, anti-gout medication and antibiotics (AB). In 13/206 (6.3%) patients symptoms remitted without any treatment. No differences in initial treatment were observed between groups 1, 2 and 3.

Table 1. Baseline characteristics – stratified analysis.

	Early remission	n	Persistent gonarthritis	n	Progression to oligo-polyarthritis	n	p
Age at presentation, yrs.	47.7 (31.6-57.6)	67	47.0 (31.6-57.1)	109	45.4 (30.8-56.1)	30	0.92
Female, %	50.8	67	51.4	109	46.7	30	0.90
Caucasian, %	89.6	67	82.6	109	96.7	30	0.09
Mono-arthritis, %	91.0	67	81.7	109	80.0	30	0.19
RF-positive, %	3.08	65	9.35	107	20.7	29	0.02
ACPA-positive, %	3.77	53	4.71	85	23.1	26	0.01
ANF-positive, %	19.7	61	23.4	94	11.5	26	0.41
Weight, kg	78.0 (16.0)	41	73.4 (15.0)	70	76.4 (13.4)	13	0.30
BMI, kg/m2	24.8 (23.4-28.2)	39	24.0 (21.7-27.0)	68	25.5 (21.6-26.9)	13	0.50
Length, cm *	174.5 (12.3)	39	173.3 (11.5)	68	175.6 (12.1)	13	0.75
Smoking, % never	55.7	61	56.7	97	60.7	28	0.96
Symptom duration, days	29 (9-709)	63	52 (16-143)	101	76.5 (25.5-175-5)	28	0.07
ESR, mm/h	23 (10-42)	67	18 (8-34)	109	33 (12-75)	30	0.01
HAQ	0.5 (0.13-1.0)	50	0.38 (0-0.75)	83	0.62 (0.25-1.12)	25	0.10
DAS	1.74 (0.39)	17	1.87 (0.59)	47	2.35 (0.67)	5	0.11
VAS patient global	25 (16-37)	18	30 (10-41)	47	47 (20-52)	5	0.49

Values are median, (IQR), unless indicated otherwise. *Mean, (standard deviation). RF: rheumatoid factor; ACPA: anticitrullinated protein antibodies; ANF: anti-nuclear factor; BMI: body mass index; ESR: erythrocyte sedimentation rate; HAQ: health assessment questionnaire; DAS: disease activity score; VAS: visual analogue scale; SJC: swollen joint count; TJC: tender joint count. p comparing the three stratification groups using two-way ANOVA, Kruskal Wallis, Chi-square or Fischer exact test.

Table 2. Cumulative treatment prescriptions within first year of follow-up – stratified analysis.

Treatment (group)	Total n=206 n,(%)	Early remission n=67 n,(%)	Persistent gonarthritis n=109 n,(%)	Progression to oligo-/poly n=30 n,(%)	p
NSAID only	62 (30.1)	30 (44.8)	29 (26.6)	3 (10.0)	<0.01
Intra-articular corticosteroid injection(s)	93 (45.1)	18 (26.9)	58 (53.2)	17 (56.7)	<0.01
Prednisone (oral)	11 (5.4)	-	6 (5.5)	5 (16.7)	<0.01
Antibiotics	23 (11.2)	9 (13.4)	10 (9.2)	4 (13.3)	0.61
csDMARD(s)	28 (11.7)	-	15 (13.8)	13 (43.3)	<0.01
bDMARD(s)	2 (<1)	-	1 (<1)	1 (3.3)	0.38
Yttrium	3 (1.5)	-	3 (2.8)	-	0.40
Colchicine/Allopurinol	6 (3.0)	2 (3.0)	4 (3.7)	-	0.85

Values are the number (and % within this stratum) of patients ever using drugs from this class within the first year of follow-up. p comparing the three stratification groups using Chi square test or Fischer exact test.

During the first year, in 62/206 patients (30.1%) treatment remained limited to NSAIDs, most often in group 1 (p <0.01). IACs were (also) administered to 93/206 (45.1%), mainly in group 2 and 3 (p <0.01). Three patients (1.5%) underwent Yttrium radiosynovectomy, all in group 2. CsDMARDs were (also) prescribed in 28/206 patients (13.6%) and 2/206 patients (<1%) subsequently received a bDMARD. Prednisone was prescribed in 11/206 patients (5.4%). DMARD therapy was prescribed most frequently in group 3 (p<0.01) as was prednisone (p=0.20). ABs were prescribed in 23/206 patients (11.2%), when a diagnosis of Borreliosis or other bacterial arthritis was made or suspected, and 6/206 patients (3.0%) received with colchicine and/or allopurinol (NS between the groups) (table 2).
Conclusion: Of 206 consecutive patients with undifferentiated arthritis limited to the knee(s) the majority was in remission after 12 months. Progression to arthritis in other joints was relatively rare. Routinely acquired baseline characteristics could not completely predict the disease course at presentation and initial treatment choices suggest that physicians could not either. To timely start appropriate treatment, apart from effective treatment options, more research is needed to identify disease characteristics that predict chronicity or progression and identify patients that could profit from early more effective therapy.
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THU0675 ASSOCIATION OF GLUCOSE HOMEOSTASIS MEASURES AND METABOLIC SYNDROME WITH KNEE CARTILAGE DEFECTS AND CARTILAGE VOLUME IN YOUNG ADULTS

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Background: Diabetes mellitus and knee osteoarthritis (OA) were commonly coexisting, and metabolic syndrome (MetS) shared many pathways with knee OA. However, the effects of glucose homeostasis and MetS on knee cartilage in young adults were unknown.
Objectives: To describe the associations of glucose homeostasis measures and MetS measures with knee cartilage defects and cartilage volume in young adults.
Methods: Australian young adults from the Childhood Determinants of Adult Health Study were selected to undergo knee magnetic resonance imaging (MRI) scans during 2008-2010 (aged 31-41 years). Fasting blood sample, waist circumference and blood pressure measures were collected during 2004-2006 (aged 26-36 years). Glucose, insulin, triglyceride and high-density lipoprotein cholesterol (HDL-C) were measured using serum samples. Homeostatic model assessment 2-insulin resistance (HOMA2-IR), HOMA2-beta cell function (HOMA2-β), HOMA2-insulin sensitivity (HOMA-S) were calculated using HOMA2 calculator (version 2.2.3 available from http://www.dtu.ox.ac.uk/homacalculator) according to fasting glucose and fasting insulin. MetS was defined when at least three of the following five components were present: high waist circumference (male ≥102 cm, female ≥88 cm), high fasting glucose (≥5.6 mmol/L), high serum triglycerides (≥1.7 mmol/L), low HDL-C (male <1.03 mmol/L, female <1.3 mmol/L), and high blood pressure (≥130/85 mmHg). Cartilage defects and cartilage volume were measured from MRI scans. Data were analysed using log binomial or linear regressions and were adjusted for age, gender, body mass index and physical activity.
Results: Among 328 participants (47.3% were females), 40 (12.7%) had hyperglycaemia and 21 (6.7%) had MetS. Glucose homeostasis measures (except fasting glucose) were associated with tibiofemoral cartilage defects (Fasting insulin: relative risk (RR) 1.05/mU/L, 95% confidence interval (CI) 1.01 to 1.08; HOMA2-IR: 1.44, 1.08 to 1.92; HOMA2-β: 2.59, 1.33 to 5.07; HOMA2-S: 0.36, 0.18 to 0.72), but not patellar cartilage defects. There were no associations between glucose homeostasis measures and knee cartilage volume. MetS measures were not associated with either cartilage defects or cartilage volume, except the associations between high waist circumference and tibiofemoral cartilage defects (RR 2.32, 95% CI 1.18 to 4.54) and between low HDL-C and tibiofemoral cartilage defects (RR 1.99, 95% CI 1.08 to 3.69).
Conclusion: Insulin resistance was associated with higher risk of tibiofemoral cartilage defects amongst young adults. MetS was not associated with neither cartilage defects nor cartilage volume. These suggest that glucose homeostasis, but not MetS, may play a role in cartilage damage in young adults and may lead to knee OA in later life.
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THU0676 HEPATITIS B VIRUS REACTIVATION IN A COHORT OF PATIENTS TREATED WITH BIOLOGICS – DATA FROM THE ROMANIAN REGISTRY OF RHEUMATIC DISEASES

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Background: Accompanying the increased use of biological and non-biological antirheumatic drugs, a greater number of cases of hepatitis B virus (HBV) reactivation have been reported in inactive hepatitis B surface antigen (HBsAg) carriers and also in HBsAg-negative patients (pts) who have resolved HBV infection (1). Romania has a high prevalence for HBV infection. According to a national epidemiological study conducted in 2013, 27,9% from the Romanian population has serological markers of resolved HBV infection, while 4.2% of inactive carriers of HBsAg (2).
Objectives: To estimate the rate of HBV reactivation in a cohort of patients treated with biologics, in Romania.
Methods: Data were gathered from the Romanian Registry of Rheumatic Diseases (RRBR) for rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA). The cohort included patients previously exposed to HBV: HBsAg inactive carriers or resolved HBV infection. HBV reactivation was considered as the presence of DNA-HBV or positivity of HBsAg in a previously negative patient. The collected data included exposure to biologics in person-years (PY) and serological markers of HBV.
Results: The cohort included 1744pts (5505.95 PY): 936 RA pts (2762.97 PY), 640 AS pts (2037.64 PY) and 168 PsA pts (705.34 PY). The mean age was 58.72yrs (65yrs for RA, 49.58yrs for AS, 61.58yrs for PsA); 1058 (60.6%) women: 786 (74.2%) RA pts, 175 (16.5%) AS pts and 97 (9.1%) PsA pts. Mean disease duration was 14.5yrs for RA, 10.7yrs for AS and 10.5yrs for PsA.The prevalence of HBsAg inactive carriers were 44 (4.7%) in RA group, 53 (8.28%) in AS group and 6 (3.57%) in PsA. The frequency of resolved HBV infection was 892 (95.3%) in RA group, 587 (91.7%) in AS and 162 (96.4%) in PsA. The total number of observed HBV reactivation cases was 16 (0.9%). In RA, 9 (0.9%) cases of HBV reactivation (0.31/100 PY) were observed, all cases on resolved HBV infection state; 7 pts were treated with rituximab (RTX), 2 pts with TNFa blockers. 8 cases (0.28/100PY) of HBV reactivation were observed in those without antiviral prophylaxis, compared to a single reactivation case (0.03/100PY) when antiviral prophylaxis was used. In AS cohort occurred 6 (0.9%) cases of HBV reactivation (0.29/100 PY), all patients being treated with TNFa blockers (3 etanercept, 1 adalimumab, 1 infliximab, 1 golimumab): 4 cases of HBV reactivation developed in inactive carriers of HBsAg and 2 in resolved HBV infection. 5 cases (0.24/100PY) of HBV reactivation were observed in those without antiviral prophylaxis, compared to a single reactivation case (0.04/100PY) when antiviral prophylaxis was used. In PsA group, only 1 case of HBV reactivation (0.14/100PY), on inactive carrier of HBsAg state, during TNFa blocking agent (golimumab).
Conclusion: HBV reactivation appeared more often on a resolved infection state, especially without antiviral prophylaxis. No cases of fulminant hepatitis were noted. Most cases developed in RTX exposed RA patients, while in AS group all HBV reactivation appeared with TNFa blockers exposure.

REFERENCES:

[1] Shunsuke M, Shigetoshi F. World J Gastroenterol 2015 September 28; 21 (36): 10274-10289
[2] https://www.cnscbt.ro/index.php

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THU0677 IDENTIFICATION OF PREVALENCE, PROGNOSTIC FACTORS, AND OUTCOMES OF PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES: A SINGLE CENTER LARGE-SCALE OBSERVATIONAL COHORT STUDY

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Background: Patients with idiopathic interstitial pneumonia (IIP) may have features of connective tissue diseases (CTDs). The term interstitial pneumonia with autoimmune features (IPAF) has been recently proposed for such patients. A few studies have been reported in prevalence of IPAF which was varied from 7.3% to 34.1% [1, 2]. Factors reported to indicate a poor prognosis in IPAF include age, smoking history, organizing pneumonia pattern in HRCT, anti-RNP antibody positivity, decline in%DLCO and presence of a multi-compartment feature within the morphological domain [2, 3]. To date, however, no study has comprehensively described prevalence of IPAF and factors of exacerbation.
Objectives: The aim of study was to identify of prevalence of IPAF in patients with interstitial lung disease, prognostic factors for exacerbation in patients with IPAF, and compared outcomes among patients with IPAF, IIP, and CTD-ILD.
Methods: Six hundreds- and seventy-two patients who visited our department between April 2009 and March 2018 and were evaluated by chest

HRCT scan. Then, they were clinically and radiologically diagnosed as having interstitial lung disease (ILD), IIP or connective tissue diseases associated ILD were enrolled. We applied IPAF criteria to these patients. Then, we purified 68 patients. The prognostic factors for exacerbation were prospectively calculated and statistically analyzed using clinical, laboratory and imaging data collected from medical records.

Results: Prevalence of IPAF was 10.1%. Of 68 patients with IPAF, 60% were women and mean age at diagnosis was 64.2 ± 13.8 years old. Mean observation period was 27.1 ± 29.6 months. Smoking history was 42.6% (n=29). Treatment including oral glucocorticoid or/and immunosuppressant use were 44.1% (n=30). Exacerbation rate was 25% (n=17). Overall death rate was 5.9% (n=4) and respiratory death rate was 2.9% (n=2). Comparison of characteristics at diagnosis between the exacerbation group and non-exacerbation group showed that the exacerbation group had a significantly elevated rate of smoking history, KL-6, and SP-D (P=0.01, 0.006, and 0.03, respectively). We then analyzed transition of KL-6 in patients with IPAF, IIP, or CTD-ILD. KL-6 at baseline in patients with IPAF (1212 ± 1626 U/mL) was higher than those with IIP and significantly higher than those with CTD-ILD (1030 ± 1027 U/mL(P=0.69) and 829.5 ± 1002 U/mL(P=0.024)), while exacerbation rate in patients with IPAF (25%) was significantly lower than those in IIP patients (40%) and CTD-ILD patients (41%) (P=0.03). Furthermore, KL-6 in IPAF patients gradually decreased during course and was lower than IIP or CTD-ILD patients at 84 months from diagnosis.

Conclusion: Our large-scale observational cohort study revealed prevalence of IPAF in patients with ILD and identified three baseline factors associated with exacerbation in the patients with IPAF and suggested that IPAF might have a better prognosis than IIP or CTD-ILD.

REFERENCES:

[1] Respir Med. 2017; 123:56–62,
[2] Eur Respir J. 2016; 47:1622–1624,
[3] Clin Rheumatol. 2018 Apr 18

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THU0678 MALIGNANCY RISK IN MALE PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: In recent studies, the association between autoimmune disease and malignancy has been reported. However in Ankylosing spondylitis (AS), a chronic inflammatory rheumatic disease with marked male predominance, the evidence of this relationship is scarce and inconsistent.

Objectives: To determine the overall cancer and site-specific cancer risk in male patients with AS.

Methods: Using the claims database of Health Insurance and Review Assessment (HIRA), male patients with AS without prior cancer history between 2012 and 2014 were enrolled (n=21,780). For the control group, male general population, stratified random samples of claims data were used (n=342,361). All individual was observed up to the development of any cancer, or end of the study period (December 31, 2015). Incidence rates (IR) of overall and site-specific cancer were presented as the number of event per 10,000 person-years. To make fairer comparison between AS patients and general population, we calculated age adjusted incidence ratio by dividing cancer event of general population with corresponding age. The standardized incidence ratio (SIR) was used to represent the association between AS and cancer, accounting for person-years at risk.

Results: During 71,046 person-year, total 552 cases of cancer occurred in male AS group. Prostate cancer was the leading type of cancer in male AS patients (101 cases, IR 14.22, 95% CI 11.44-16.99). And it was followed by liver cancer (70 cases, IR 9.9, 95% CI 7.5-12.2), lung cancer (48 cases, IR 6.8, 95% CI 4.9-8.7), colorectal cancer (45 cases, IR 6.3, 95% CI 4.5-8.2) and stomach cancer (43 cases, IR 6.1, 95% CI 4.2-7.9). Compared to general population, the overall incidence of cancer was increased in male patients with AS (SIR 1.25, 95% CI 1.14-1.36). At a specific malignancy type, the risk of pancreas cancer (SIR 1.75, 95% CI 1.12-2.37) and malignancy of male reproductive system were increased (SIR 1.97, 95% CI 1.59-2.35).

Table 1. The standardized incidence ratio of overall malignancy.

Type of Malignancy	Male general population	Male AS patients		SIR (95% CI)
	IR (95% CI)	Age-adjusted expected IR (95% CI)	IR (95% CI)	
All malignancy	102.5 (100.7-104.3)	65.0 (63.7-66.2)	77.7 (71.2-84.2)	1.25 (1.14-1.36)
Hematologic malignancy	3.4 (3.0-3.7)	2.3 (2.1-2.6)	3.8 (2.4-5.2)	1.69 (1.06-2.34)
Solid malignancy	99.1 (97.4-100.9)	62.6 (61.4-63.9)	73.9 (67.6-80.2)	1.24 (1.13-1.34)

Incidence rate was presented as the number of events per 10,000 person-year with 95% CI
AS, ankylosing spondylitis; IR, incidence ratio; SIR, standardized incidence ratio; CI, confidence interval

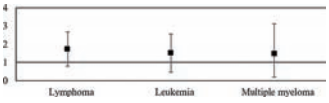


Figure 1. The standardized incidence ratio of hematologic malignancy.

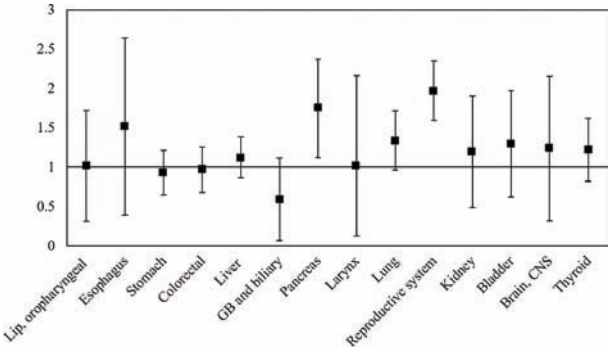


Figure 2. The standardized incidence ratio of solid cancer.

Conclusion: Male patients with AS have a increased overall cancer risk, especially in pancreas cancer and malignancy of male reproductive system.

REFERENCES:

[1] Deng, C. et al., Risk of malignancy in ankylosing spondylitis: a systematic review and meta-analysis. Sci Rep, 2016. **6**: p. 32063.
[2] Egiziano, G. et al., Cancer and autoimmunity: Harnessing longitudinal cohorts to probe the link. Best Pract Res Clin Rheumatol, 2016. **30**(1): p. 53-62.

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THU0679 ADHERENCE TO THE MEDITERRANEAN DIET AND RISK OF RHEUMATOID ARTHRITIS IN THE FRENCH PROSPECTIVE E3N COHORT STUDY

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Background: The Mediterranean diet (MD), widespread in Southern European countries, mainly consists of olive oil, cereal products, fresh or dried fruit and vegetables, nuts, a moderate amount of dairy and meat, and many condiments and spices. It has been associated with significant reduction of overall mortality, cardiovascular diseases, and neoplastic diseases. It has been suggested to have a beneficial effect on rheumatoid arthritis (RA) activity due to its richness in antioxidants and unsaturated fatty acids. However, data on MD as a prevention of RA are limited.
Objectives: To assess the association between adherence to MD and risk of RA in a general population cohort.
Methods: The E3N cohort study (*Etude Epidémiologique auprès des femmes de la Mutuelle générale de l'Education Nationale*) is a French prospective cohort of 98,995 healthy women included in 1990-91 and followed since then (median follow-up of 28 years). Among women who completed a food-frequency questionnaire, we calculated the modified MD score (from 0 to 9) according to the consumption status of nine food components. Incident RA cases were detected using a validation process using a specific validation questionnaire and a drug reimbursement database. Hazard ratios (HRs) and 95% confidence intervals (CIs) for incident RA were estimated using Cox proportional hazards regression models with age as the time scale, and adjusting for known risk factors of RA and potential confounders. Because of the known importance of smoking on RA risk, we performed analyses adjusted and stratified on the smoking status.
Results: Among 62,630 women, 480 validated incident RA cases were diagnosed after a mean (± standard deviation) of 11.7 (± 5.9) years after the food-frequency questionnaire. In the whole population, high adherence to MD was not associated with a decreased risk of RA (HR for a 6-9 vs. 0-3 score = 0.86, 95% CI: 0.68−1.09, $P_{\text{linear trend}}$ = 0.11). However, among ever-smoking women (current or past smokers), high adherence to MD was associated with a decreased risk of RA (HR for a 6-9 vs. 0-3 score = 0.77, 95% CI: 0.53−1.05; $P_{\text{linear trend}}$ = 0.025), while there was no association in non-smokers (HR for a 6-9 vs. 0-3 score = 0.98, 95% CI: 0.70−1.38, $P_{\text{linear trend}}$ = 0.90).

HR (95% IC) for RA according to the MD score

MD score	[0-3]	[4-5]	[6-9]	*P* for trend
All population (N = 62,630)				
Cases no./person-years, no.	152/372,306	211/575,893	118/325,196	
Age adjusted	1	0.89 (0.72-1.10)	0.86 (0.68-1.09)	0,11
Multivariate*	1	0.89 (0.72-1.10)	0.86 (0.67-1.10)	0,1098
Ever smokers (N = 29,072)				
Cases no./person-years, no.	73/165,745	101/270,722	57/154,709	
Age adjusted	1	0.78 (0.58-1.04)	0.74 (0.53-1.05)	**0,0247**
Multivariate*	1	0.79 (0.58-1.06)	0.77 (0.54-1.09)	**0,0444**
Non smokers (N = 33,558)				
Cases no./person-years, no.	73/206,562	110/305,171	61/170,488	
Age adjusted	1	1.01 (0.75-1.36)	0.98 (0.70-1.38)	0,9011
Multivariate*	1	0.99 (0.74-1.34)	0.96 (0.68-1.35)	0,7725

* HRs were adjusted for age, educational level, body mass index, smoking status, passive smoking during childhood, energy intake, physical activity, gastrointestinal transit.

Conclusion: High adherence to a MD could reduce RA risk in ever-smoking women. Further studies are needed to confirm our findings.
Acknowledgement: We would like to thank the Foundation for Research in Rheumatology (FOREUM) and the French Rheumatology Society (SFR) for their financial support.
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THU0680 ANTI-PEPTIDYL-ARGININE DEIMINASE 3 AND 4 AUTOANTIBODIES IN A COHORT OF RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) affects up to 30% of patients with rheumatoid arthritis (RA). Peptidyl-arginine deiminases (PAD) are key enzymes in RA pathogenesis as they are involved in the citrullination of proteins, targets of anti-citrullinated protein antibodies (ACPA). Although RA-ILD significantly contributes to disease burden including mortality, diagnostic and prognostic biomarkers are still lacking.
Objectives: To measure anti-PAD3 and anti-PAD4 antibodies in a cohort of RA and compare their prevalence in patients with and without ILD. To assess the associations of anti-PAD3, anti-PAD4 and ACPA with disease activity, joint erosions, lung involvement and smoking history.
Methods: A total of 71 patients fulfilling the 2010 ACR/EULAR RA Classification Criteria were recruited; the mean age was 63.3±12.4 and 87% of them were females, 11 (15.5%) of them had been diagnosed with ILD. Demographic, clinical as well as radiological data were retrospectively collected. ILD was defined as usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP) or indeterminate patterns on chest high-resolution computed tomography, according to ATS/ERS guidelines. Particle-based Multi-Analyte Technology (PMAT) (Inova Diagnostics, USA, research use only) was used to measure anti-PAD3 and anti-PAD4 autoantibodies. ACPA IgG were measured by chemiluminescence (QUANTA Flash CCP3, Inova Diagnostics, USA).
Results: Anti-PAD4 levels were correlated with erosive disease (p=0.043) and morning stiffness (p=0.031). Anti-PAD3 and anti-PAD4 levels were associated to DAS28-ESR at the time of sampling (anti-PAD3, r=0.34, p=0.004; anti-PAD4, r=0.34, p=0.004). Anti-PAD4 antibodies were significantly lower in patients with ILD (p=0.043). There was no association between anti-PAD4 and smoking, while anti-PAD3 antibodies were higher in non-smokers (p=0.004). A strong correlation was found between anti-PAD4 and anti-PAD3 levels (r=0.73, p<0.0001).
Conclusion: In our cohort, anti-PAD4 antibodies were correlated with joint erosions and RA disease activity, whereas a negative association with ILD was found. Smoking history was not associated with the presence and levels of anti-PAD antibodies. Our data validate the usefulness of anti-PAD4 antibodies as a biomarker for erosive disease. Further studies that take into account relevant confounders like therapy and larger RA-ILD cohorts are needed.

REFERENCES:

[1] Darrah E, Martinez-Prat L, Mahler M (2019) Clinical Utility of Antipeptidyl Arginine Deiminase Type 4 Antibodies. J Rheumatol jrheum.180905

Disclosure of Interests: Boaz Palterer: None declared, Gianfranco Vitiello: None declared, Bernardo D'Onofrio: None declared, Emanuele Vivarelli: None declared, Daniele Cammelli: None declared, Maria Grazia Giudizi: None declared, Laura Martinez-Prat Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Silvia Casas Employee of: Inova Diagnostics, Chelsea Bentow Employee of: INOVA Diagnostics, Michael Mahler Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Paola Parronchi: None declared
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THU0681 SEXUAL FUNCTION AND REPRODUCTION CAN BE IMPAIRED IN MEN WITH RHEUMATIC DISEASES: A SYSTEMATIC REVIEW

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Background: Sexual function and reproduction are important aspects of quality of life for the majority of men (1,2). In the last decade inflammation has been associated with male factor infertility and sexual dysfunction (3,4). Because many patients with rheumatic diseases have a

chronic state of inflammation, it is reasonable to believe that this can result in impaired sexual function and reproduction. Previous research on this topic in Rheumatology mainly focused on the effect of drugs on fertility parameters.

Objectives: Our objective is to summarize the information on the influence of rheumatic diseases on male sexual function and reproduction.

Methods: A systematic search of Embase, Medline, Web of science and Cochrane Central was carried out in May 2018 to find relevant papers. The search strategy was extensive and included a complete list of immune mediated diseases from Rheumatology, Dermatology and Gastroenterology and several keywords for our outcomes (sexual function, fertility and pregnancy outcome). This review was registered in PROSPERO (5). The search yielded 6568 articles. Titles and abstracts were screened independently by LP and JC, resulting in 177 papers selected for full text review. Methodological quality of the studies was assessed with the Newcastle Ottawa Scale (6).

Results: Regarding rheumatic diseases a total of 104 papers were included in the final analysis. 4 diseases (Spondyloarthropathies (SpA), Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE) and Systemic Sclerosis (SSc)) represented 60% of the articles. The overall quality of the studies was low to moderate.

Sexual dysfunction (SD) is a common problem for patients with rheumatic diseases and it is usually undiagnosed. It was reported in approximately half of men with RA, SLE and SpA and in almost all the men diagnosed with SSc. It should be noted that, although in several studies increasing age was correlated with a higher prevalence and severity of SD, young patients with SpA or SLE can also be affected.

Regarding fertility and reproduction, different results per disease were found. Hypogonadism might be a common problem in men with RA and SLE. Many men with SLE and RA have endocrine axis abnormalities. Interestingly, these disturbances were not detected in SpA patients (See Table 1). Semen quality abnormalities are frequent in SLE patients and this was found to be associated not only with medication toxicities but also with disease activity. The number of children of male patients diagnosed with SLE and SSc was lower than healthy controls.

A brief summary of our findings per disease are presented in Figure 1.

Conclusion: Our findings suggest that not only medication can have detrimental effects on sexual function and reproduction of men with rheumatic diseases but also the disease itself. Therefore, clinicians should be aware of a high prevalence of sexual and reproduction problems in this population and take this into account when counseling them. More research focusing on this association is needed.

Disease	Outcome	
RA	**Sexual dysfunction**	**Prevalence: 33-62% [range]** in 282 patients compared to **11-40% [range]** 140 controls. **Main correlations:** Age, pain, fatigue. Almost 30% of patients want advice on this topic.
	Hormones	Lower serum testosterone levels. Lower LH levels. Testosterone levels increased in a group of patients that responded to treatment.
	Pregnancy outcomes	Paternal RA was not associated with preterm birth or fetal growth abnormalities compared to the general population. No higher risk of serious congenital malformations.
SLE	**Sexual dysfunction**	**Prevalence: 12-69% [range]** in 245 patients compared to **0-22% [range]** 197 controls. **Main correlations:** Arterial events, SLICC damage score, persistent lymphopenia, lower median penis circumference. In one study: 81% of patients considered it would be appropriate to be asked about their sexual function
	Hormones	Median of FSH and LH were significantly higher in SLE patients versus controls.
	External genitalia	Reduction of testicular volume correlates with semen quality abnormalities.
	Semen quality	Sperm concentration and motility was abnormal in a significant proportion of patients. High FSH levels correlated with sperm abnormalities.
	Pregnancy outcomes	Percentage of partner with gestation was statistically lower in SLE patients compared to controls: • 20% vs 60%
SpA	**Sexual dysfunction**	**Prevalence: 32-63.6% [range]** in 856 patients compared to **14.6-51.9% [range]** in 580 controls. **Main correlations:** Disease activity and duration, depression, fatigue. In one study: 95.9% had never been asked by any doctors about sexual activity.
	Hormones	No differences in FSH, LH and testosterone among patients and controls.
	External	No differences in testicular volume among patients and

Figure 1:

REFERENCES:

[1] Flynn KE, et al. The journal of sexual medicine. 2016;13(11):1642-50.
[2] Ilacqua A, et al. Reprod Biol Endocrinol. 2018;16(1):115.
[3] Haervig KK, et al.Hum Fertil (Camb). 2018;21(2):146-54.
[4] Fijak M, et al. Hum Reprod Update. 2018 Jul 1;24(4):416-441
[5] Perez LF, et al. Retrived from: www.crd.york.ac.uk/prospero/display_record.php?RecordID=99845)
[6] Wells GA, et al. Retrieved from: www.ohri.ca/programs/clinical_epidemiology/oxford.asp

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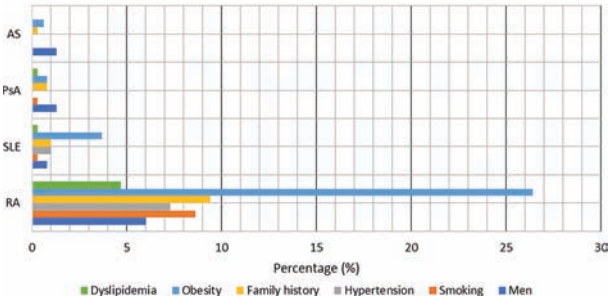
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THU0682 UNDERDIAGNOSIS OF TRADITIONAL CARDIOVASCULAR RISK FACTORS IN RHEUMATIC DISEASES

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Background: Patients with rheumatic diseases (RD) have a higher cardiovascular risk (CVR), compared to the general population (1). The increased risk, in this population, tends to be associated with the chronic inflammation generated by RD. Another contributor is the coexistence of traditional CVR factors, such as diabetes, hypertension, obesity, smoking, and dyslipidemia (2). It is known that adequate control of this factors can reduce the overall CVR. Due to the increased CVR burden, there's a growing awareness of cardiovascular assessment in rheumatic patients. Therefore, the 2016 EULAR guidelines recommend making this assessment every 5 years, in order to decrease their morbidity and mortality by early treatment.

Figure 1. Traditional cardiovascular risk factors.



Objectives: To determine the prevalence of underdiagnosis and inefficient treatment of traditional cardiovascular risk factors in RD patients.

Methods: A cross-sectional, observational study of patients between 30 and 75 years with rheumatoid arthritis (RA), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE) and ankylosing spondylitis (AS) recruited at the rheumatology clinic at a University Hospital in northeastern Mexico. Exclusion criteria: previous cardiovascular disease, overlap syndromes, diabetes, or pregnancy. Evaluation included history of lifestyle, comorbidities, medications, blood pressure, anthropometry and fasting glucose measures. Framingham-BMI (FRS-BMI) was used to calculate their predicted CVR to 10 years.

Results: A total of 382 patients were recruited, 90.6% were women (n=346), with a median age of 53 years (45-59). In this population, 87.4% of the patients (n=334) had at least one CVR factor; the presence of traditional CVR factors according to RD is shown in Figure 1. Other population characteristics are in Table 1. Around half of the patients were not in their ideal weight, 32% being diagnosed as overweight and 31.4% with obesity. Out of the patients with no previous diagnosis of hypertension (n=350, 91.5%), 36.1% had elevated or high blood pressure levels. The patients that did have previous diagnosis, 68.7% didn't have an adequate control of their blood pressure, even though they're on pharmacological treatment. History of dyslipidemia was found in 5.2% of patients. Half of them arrived at consultation with a recent lipid profile, having a median LDL of 133.5 (109-158) mg/dL, not meeting target levels. Even though no diabetic patients were included, 20.8% of the patients had hyperglycemia. According to FRS-BMI, 80.4% of the patients had a low CVR, 14.9% moderate risk, and 4.7% had a high CVR.

Table 1. RD patients' characteristics.

	(n=382)
RA, n (%)	313 (81.9)
PsA, n (%)	12 (3.1)
SLE, n (%)	49 (12.8)
AS, n (%)	8 (2.1)
Corticosteroid use, n (%)	110 (28.8)
Fasting glucose, mg/dL, median (q25-q75)	91 (83-98)
FRS BMI score, median (q25-q75)	5.15 (2.9-8.82)

Conclusion: In this study, an underdiagnosis and insufficient treatment of traditional CVR factors in rheumatic patients was found. Besides having a RD and at least one traditional CVR factor, 19.6% of the patients had a moderate or high CVR according to FRS-BMI. The observed burden of CVR factors in RD is significant. Therefore, rheumatologists must improve the CV assessment made to each of their patients.

REFERENCES:

[1] Eder, L et al (2018). Gaps in Diagnosis and Treatment of Cardiovascular Risk Factors in Patients with Psoriatic Disease: An International Multicenter Study. The Journal of Rheumatology, 45(3), 378–384. http://doi.org/10.3899/jrheum.170379

[2] Nurmohamed MT, et al (2015). Cardiovascular comorbidity in rheumatic diseases. Nature Reviews Rheumatology, 11(12), 693–704. http://doi.org/10.1038/nrrheum.2015.112

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THU0683 COVERAGE, PREDICTORS OF VACCINATION AND FREQUENCY OF SEVERE INFECTIONS DUE TO STREPTOCOCCUS PNEUMONIAE IN A COHORT OF PATIENTS WITH CHRONIC INFLAMMATORY ARTHRITIS WITHIN AN EIGHTEEN-YEAR PERIOD

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Background: Community-acquired pneumonia (CAP), the most common pneumococcal infection, is a leading cause of morbidity and mortality among immunocompromised hosts. Although vaccination against *Streptococcus Pneumoniae* is recommended by international guidelines, most studies report a sub-optimal coverage.
Objectives: To describe the pneumococcal vaccination coverage, predictors for vaccination uptake and frequency of severe CAP and invasive pneumococcal disease during the study period.
Methods: We performed a cross-sectional study using electronic medical record data from October 2000 to October 2018, including patients diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and Ankylosing Spondylitis (AS), treated with biologic (bDMARD) and conventional synthetic DMARD (csDMARD) with or without glucocorticoids (GC), followed-up at a referral centre.
Since pneumococcal vaccination guidelines have changed during the study period, patients who received at least one dose of any of the available vaccines were defined as being "ever-vaccinated" whereas those who received a complete scheme defined as one dose of conjugated vaccine and one of polysaccharide vaccine 8 weeks apart were defined as having "optimal vaccination".
Predictors of vaccination were analyzed using logistic regression modelling using a set of covariates selected according to the literature. Model assessment was done using Akaike information criterion.
To analyze the frequency of severe infections we defined two outcomes:

1. Severe CAP: An episode requiring hospitalization or intravenous antibiotic treatment
2. Invasive pneumococcal disease (IPD): an infection confirmed by the isolation of the micro–organism from a normally sterile site (i.e. blood).

Results: A total of 279 patients were included, their main clinical features are shown in Table 1.
The vaccination coverage was 38.7% and 13.3% overall when analyzing as "ever-vaccinated" and having "optimal vaccination" respectively. A 66% of patients were vaccinated in primary care with a 7% of optimal vaccination whereas the remaining ones received vaccination in referral centres with an 85.3% of optimal vaccination.
After adjustment in a multivariate model, age, presence of bronchiectasis, history of severe CAP, current use of csDMARD or GC were predictors of being ever-vaccinated against *Streptococcus Pneumoniae*. (Table 2)
During the study period, 27 (10%) episodes of severe CAP and 4 of IPD were identified, 8 of the former with evidence of pneumococcal infection (either positive urine antigens or isolation in sputum).
Conclusion: Pneumococcal vaccination coverage remains lower than expected with most patients vaccinated in primary care and not receiving the current recommended scheme. Age, bronchiectasis, history of severe CAP and current use of csDMARD or GC were independent predictors of receiving vaccination.
The frequency of severe CAP and IPD was 10% and 1,43% within this cohort.

Age (mean ± SD)	60.7 ± 13.4
Female	210 (75%)
Diagnosis	237 (85%)
RA	42 (15%)
SpA (PsA and AS)	
Disease duration (mean ± SD, years)	13 ± 10.4
Ever–smoker	91 (33%)
Charlson score $\geq$ 2	142 (51%)
Chronic Respiratory Disease	65 (23%)
ILD	35 (13%)
Bronchiectasis	26 (9%)
History of severe CAP	28 (10%)
Current treatment bDMARD csDMARD	153 (55%)
GC	84 (30%)
	139 (50%)

Table 1. Clinical features of the cohort. ILD: Interstitial lung disease

Variable	aOR [CI95]	p
Age at time of analysis (years)	1.08 [1.05 – 1.1]	0.00
Bronchiectasis	4 [1.09 – 14.7]	0.03
History of severe CAP	4.7 [1.3-17.3]	0.02
Current csDMARD	2.3 [1.4 - 3.9]	0.00
Current GC	2.2 [1.04 – 4.4]	0.03

Table 2. Predictors of vaccination after adjustment

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THU0684 HOW MANY OF YOUR PATIENTS HAVE DEPRESSIVE SYMPTOMS? HOW TO ASSESS DURING ROUTINE CLINICAL PRACTICE?

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Background: Patients with rheumatic diseases have a high prevalence of depressive symptoms that affect the patients' self-assessment, adherence to medication [1], and mortality [2].
Objectives: To evaluate patients with rheumatic diseases regarding depressive symptoms by using the PHQ-2 (Patient Health Questionnaire with 2 items) and assess its feasibility during routine clinical practice.
Methods: 485 consecutive patients with rheumatic diseases attending a rheumatology practice that is part of the public health care system in Erlangen, Germany underwent a routine clinical assessment by different rheumatologists. In addition to disease-specific assessments and questionnaires, every patient answered two questions regarding depressive symptoms which form the PHQ-2 (range of 0[best] to 6[worst]). All questionnaires were answered digitally by touchscreen and Software RheumaDok and RheumaDokM (Nils Körber und Joachim Elgas G.b.R).

A PHQ-2 score $\geq$ 3 points has a sensitivity of 87% and a specificity of 78% for detecting a major depressive disorder compared to a structured clinical interview. [3] A positive screening result was either addressed during subsequent medical consultation or by notifying the patient's general practitioner. The PHQ-2 is a short form of the PHQ-9 which previously had been validated in rheumatoid arthritis. [4].

Results: Overall, 26% of patients stated depressive symptoms (PHQ score $\geq$ 3). Table 1 shows the prevalence of depressive symptoms by disease entity which was not significantly different among the subgroups ($\chi^2(5)=6$, p=0.3). However, given our results indicating depressiveness to be common across subgroups, all of these patients merit further evaluation. The PHQ-2 was widely accepted by patients, and seemed very feasible due to its concise form.

	Age				PHQ-2				PHQ-2 ≥ 3	
	Mean	Median	N	SD	Mean	Median	N	SD	N	%
Rheumatoid Arthritis, RF+	62.1	61.0	169	11.9	1.7	2.0	169	1.4	37	22
Rheumatoid Arthritis, RF-	63.1	64.0	51	13.7	1.9	2.0	51	1.7	16	31
Psoriatic Arthritis	54.6	55.0	59	11.4	1.5	1.0	59	1.4	11	19
Ankylosing Spondylitis	47.7	48.0	47	13.0	1.7	2.0	47	1.6	13	28
Various rheumatic diseases *	60.0	63.0	82	14.8	2.0	2.0	82	1.6	25	30
Not diagnosed yet/initial assessment	55.8	55.0	77	17.8	1.9	2.0	77	1.7	24	31

* Polymyalgia, Connective tissue diseases, and other.

Conclusion: The PHQ-2 questionnaire is a highly feasible and well accepted tool in routine clinical practice, helping to screen for depressive symptoms as a highly prevalent condition across rheumatic diseases. Real world evidence of depressive symptoms may improve healthcare by shedding light on the patients' mental well-being and comorbidity.

REFERENCES:

[1] Brandstetter S, Riedelbeck G, Steinmann M, Loss J, Ehrenstein B, Apfelbacher C. Depression moderates the associations between beliefs about medicines and medication adherence in patients with rheumatoid arthritis: Cross-sectional study. J Health Psychol. 2016 May 04.

[2] Kleinert S, Marx A, Faller H, M F, C K, Lehmann S, et al. Prevalence and Relevance of Depressive Symptoms in Patients with Rheumatic Diseases [abstract]. Arthritis Rheumatol 2015; 67 (suppl 10). 2015.

[3] Lowe B, Kroenke K, Grafe K. Detecting and monitoring depression with a two-item questionnaire (PHQ-2). J Psychosom Res. 2005 Feb; 58(2):163-171.

[4] Englbrecht M, Alten R, Aringer M, Baerwald CG, Burkhardt H, Eby N, et al. Validation of Standardized Questionnaires Evaluating Symptoms of Depression in Rheumatoid Arthritis Patients: Approaches to Screening for a Frequent Yet Underrated Challenge. Arthritis Care Res (Hoboken). 2017 Jan; 69(1):58-66.

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THU0685 THE IMPACT OF ACHIEVEMENT OF RESPONSE AT ONE YEAR AFTER STARTING THERAPY ON THE LONG-TERM OUTCOME OF LUPUS NEPHRITIS

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Background: A variable percentage of lupus nephritis (LN) patients (pts) achieve response after the start of induction therapy. The impact of response on long-term renal outcome of LN is still unclear.
Objectives: To establish the response rate at one year after starting induction therapy and its impact on long-term development of chronic kidney disease (CKD) in LN.
Methods: 381 biopsy proven LN pts (86% females, mean age 31.3 ±12.1years), (18 pts:class II; 88 pts:class III; 199 pts:class IV; 76 pts: class V ISN/RPS) with estimated glomerular filtration rate (eGFR) 89.8 ±40.4 and proteinuria 4.3±3.9g/24h entered this study. As induction therapy, pts received methylprednisolone pulses (72%), oral prednisone (28%), cyclophosphamide (55%), mycophenolate mofetil (24%), azathioprine (5,5%), other immunosuppressants (15.5%). During a follow-up of 13.5 years after LN diagnosis, 53 pts (13.9%) developed CKD and 22 (5.8%) died.
Definitions: Complete response (CR) at one year: eGFR>60ml/min and proteinuria$\leq$0.5/die, partial response (PR): eGFR>60ml/min, 50% reduction of proteinuria to sub-nephrotic range, no response (NoR): all the other cases. Survival curves were drawn using the Kaplan-Meier estimate and compared using the log-rank test. Cox regression model was used to test variables at univariate and at multivariate analysis.
Results: One year after the start of therapy, 220 pts (58%) achieved CR, 100 pts (26%) PR and 61 pts NoR. CKD developed in 11 out of 220 CR pts (5%), 18 out of 100 PR pts and 24 out of 61 NoR (39%). CKD free survival at 5, 10, 15 and 20 years were 99.5%, 96.5% 95.2% and 92.5 in CR pts, 99%, 90%, 87,6% and 83% in PR pts, and 81%, 65%, 54% and 44% in NoR pts (p<0.0001). In detail: CR vs RP p=0.067, RP vs NoR p<0.0001, and CR vs NoR p<0.0001. We have searched for the predictors of NoR among the clinical/therapeutic characteristics at diagnosis of LN. At univariate analysis, chronicity index at renal biopsy (p=0.0001), serum creatinine (p=0.001), eGFR (p=0.036), presentation with nephritic syndrome or rapid progressive renal failure (p=0.02), serum albumin (p=0.02) and arterial hypertension (p=0.001), were the predictors of NoR at one year. At multivariate analysis chronicity index (p=0.013) and arterial hypertension (p=0.017) were the independent predictors.
Conclusion: The achievement of CR or PR at one year is associated with preservation of renal function in the long-term. For this reason, any effort should be made to achieve response. Patients with impaired renal function, with high chronicity index at renal biopsy and arterial hypertension should be more tightly monitored as they have the highest risk of NoR.

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THU0686 EARLY MENOPAUSE AND/OR DURATION OF MENOPAUSAL HORMONAL TREATMENT MAY INCREASE THE RISK OF RHEUMATOID ARTHRITIS IN TOBACCO EXPOSED WOMEN: RESULTS OF THE E3N COHORT

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Background: Smoking has been reproducibly reported as associated with an increased risk of ACPA-positive Rheumatoid Arthritis (RA) [1]. The involvement of female hormones in the pathogenesis of RA is supported by numerous observations: a 2-4 female to male ratio before age 50, but below 2 after the age of 60, an increased incidence in the first year post-partum, and a peak of RA incidence around the age of menopause. To date, many studies have evaluated the association between hormonal

treatments and other reproductive factors, and RA risk with conflicting results [2, 3].

Objectives: To assess the relationships between endogenous and exogenous female hormonal exposures and the risk of RA in women involved in the E3N cohort.

Methods: E3N is an ongoing French prospective cohort that included 98,995 women aged 40-65 years in 1990. Women completed mailed questionnaires every 2-3 years on lifestyle, reproductive factors, and health-related information. Female endogenous hormonal exposures were assessed using age at menarche, age at menopause, and the duration of reproductive life. Exogenous hormonal exposures included oral contraception and menopausal hormonal treatment (MHT). Hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of incident RA were estimated using Cox proportional hazards regression models with age as the time scale, first applied to the overall population, then stratified for smoking exposure.

Results: A total of 698 incident RA cases were validated among and 78,452 women over 1,865,213 women-years. Multivariate models for age at menopause and cumulative duration of MHT appear in Table. After stratification for smoking exposure, early age at menopause was associated with a somewhat stronger RA risk in women exposed to smoking (HR=1.6, 95% CI: 1.1-2.4; $p_{linear\ trend}$=0.0270) than in those with no smoking exposure (HR=1.3, 95% CI: 0.8-2.2; $p_{linear\ trend}$ =0.1811). However when adjusting for cumulative duration of MHT, early age at menopause was no longer associated with incident RA, even in women exposed to smoking (HR=1.3, 95% CI: 0.8-2.2; $p_{linear\ trend}$ =0.7973), while a cumulative duration of MHT > 4 years was borderline associated with RA in women exposed to smoking [HR=1.3, 95%CI: 1.0-1.7; $p_{linear\ trend}$=0.09] in comparison with women who did not received MHT. Age at menopause and duration of THM were strongly correlated: in women with early menopause duration of MHT was significantly longer: 7.01 (7.3) years *versus* 4.8 (5.0) years (p<0.001). There was no evidence of an association between oral contraception use, age at menarche and duration of reproductive life with the risk of RA.

	RA	HR (95% CI) for RA	P for trend
Age at menopause (N=78,452)			
≤45 years	68	1.50 (1.1-2.1)	
[45-53[years	482	1.22 (0.9-1.5)	
≥53 years	148	1	0.0096
Cumulative duration of MHT in menopausal women (N=71,616)			
0	178	1	0.2417
[0-4[years	307	1.15 (0.9-1.4)	
> 4 years	208	1.14 (0.9-1.4)	

Multivariate models adjusted for age, smoking status, passive smoking during childhood, educational level, BMI, type of menopause (surgical or natural).

Conclusion: Early age at menopause and/or duration of MHT > 4 years use may increase the risk of RA. Further studies are requested to disentangle the effect of early menopause to that of long-term MHT.

REFERENCES:

1. Raphaèle Seror, Julien Henry, Gaelle Gusto, Henri-Jean Aubin, Marie-Christine Boutron-Ruault, Xavier Mariette. Passive Smoking In Childhood Increases The Risk Of Developing Rheumatoid Arthritis. Rheumatology 2018.
2. Merlino LA, Cerhan JR, Criswell LA, et al. Estrogen and other female reproductive risk factors are not strongly associated with the development of rheumatoid arthritis in elderly women. Semin Arthritis Rheum 2003;33:72–82.
[3] Bengtsson C, Malspeis S, Orellana C, Sparks JA, Costenbader KH, Karlson EW.Association Between Menopausal Factors and the Risk of Seronegative and Seropositive Rheumatoid Arthritis: Results From the Nurses' Health Studies. Arthritis Care Res (Hoboken). 2017;69:1676-1684.

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THU0687

THE RISK OF SCHIZOPHRENIA AND EPILEPSY AMONG FAMILIAL MEDITERRANEAN FEVER PATIENTS: A BIG DATABASE ANALYSIS

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Background: Several autoimmune diseases have been associated with schizophrenia and epilepsy, however little is known about putative links with the auto-inflammatory conditions.

Objectives: We investigated the association between familial Mediterranean fever (FMF), a paradigmatic auto-inflammatory disease, schizophrenia and epilepsy, and assessed the impact of the latter disorders on the survival of FMF patients utilizing a large sample database.

Methods: A case-control study was performed by utilizing the database of Clalit Health Services. FMF patients were compared to age- and sex-matched counterparts in terms of prevalence of schizophrenia and epilepsy. The chi-squared test was used to assess the distribution of categorical variables, while the t-test were applied for continuous variables. Analysis regarding survival were performed using Kaplan-Meier curves, log rank test and multivariate Cox proportional-hazards method.

Results: The study included 7,747 FMF patients, and 10,080 age- and sex- matched controls. At the univariate analysis, schizophrenia and epilepsy as co-morbidities, 50 FMF patients (0.6%) and 89 controls (0.9%) had schizophrenia, respectively. On multiple logistic regression model, FMF was inversely associated with schizophrenia (OR 0.64 [95%CI 0.43-0.90], p=0.0173), while there was no association between FMF and epilepsy. Subjects having either FMF (HR 1.43 [95%CI 1.23-1.66]), schizophrenia (HR 3.97 [95%CI 1.47- 10.70]) or epilepsy (HR 2.54 [95%CI 1.72-3.75]) were independently associated with all-cause mortality. However, schizophrenia as co-morbidity in FMF subjects did not worsen their prognosis (HR 2.17 [95%CI 0.60-7.86]).

Conclusion: FMF patients have a significantly lower proportion of schizophrenia than controls. Patients with either FMF, schizophrenia or epilepsy are at higher risk of all-cause mortality**,** a finding that calls for assessment of better medical management on mortality outcome.

Table 1. Overall population basic characteristics.

Characteristic	All population (n=17,827)	Controls without FMF (n=10,080)	FMF patients (n=7,747)	Statistical significance (p-value)
Age (mean±SD)	38.43±19.62	37.69±19.55	39.38±19.68	NS
Age at diagnosis (mean±SD)	26.41±18.41	25.67±18.35	27.37±18.45	NS
Gender (female; %)	9,000 (50.5%)	5,121 (50.8%)	3,879 (50.1%)	NS
BMI (mean±SD)	24.81±63.91	24.42±50.61	25.30±77.41	NS
SES (n;%)[a]				p=0.0054 (p=0.0200 for trend)
Low	8,370 (50.6%)	4,729 (50.3%)	3,641 (51.1%)	
Medium	5,609 (33.9%)	3,153 (33.5%)	2,455 (34.5%)	
High	2,548 (15.4%)	1,524 (16.2%)	1,024 (14.4%)	
Smoking (n;%)	5,000 (28.0%)	2,588 (25.7%)	2,412 (31.1%)	<0.001
Schizophrenia (n;%)	139 (0.8%)	89 (0.9%)	50 (0.6%)	NS
Epilepsy (n;%)	267 (1.5%)	146 (1.4%)	121 (1.6%)	NS
All-cause mortality (n;%)	707 (4.0%)	341 (3.4%)	366 (4.7%)	<0.001

Table 2. Multivariate logistic regression assessing covariates associated with schizophrenia and epilepsy.

Variable	Coefficient	Std. Error	Wald	P	OR	95% CI
Schizophrenia						
Age	0.02	0.00	10.75	0.0010	1.02	1.01 to 1.03
Sex (female)	-0.28	0.19	2.16	0.1421	0.76	0.52 to 1.10
FMF	-0.45	0.19	5.67	0.0173	0.64	0.44 to 0.92
SES (medium)	0.26	0.20	1.66	0.1974	1.29	0.87 to 1.91

SES (high)	0.13	0.27	0.22	0.6374	1.13	0.67 to 1.91
Smoking	0.91	0.19	21.83	<0.0001	2.48	1.69 to 3.63
BMI (kg/m^2)	0.00	0.00	0.01	0.9136	1.00	1.00 to 1.00
Constant	-5.71	0.28	428.26	<0.0001		
Epilepsy						
Age	0.01	0.00	10.50	0.0012	1.01	1.01 to 1.02
Sex (female)	-0.16	0.14	1.43	0.2321	0.85	0.66 to 1.11
FMF	-0.09	0.14	0.41	0.5216	0.92	0.70 to 1.19
SES (medium)	-0.04	0.15	0.08	0.7769	0.96	0.72 to 1.28
SES (high)	-0.34	0.21	2.49	0.1148	0.72	0.47 to 1.09
Smoking	-0.03	0.15	0.03	0.8638	2.48	1.69 to 3.63
BMI (kg/m^2)	-0.01	0.01	0.24	0.6272	0.99	0.97 to 1.02
Constant	-4.28	0.26	267.26	<0.0001		

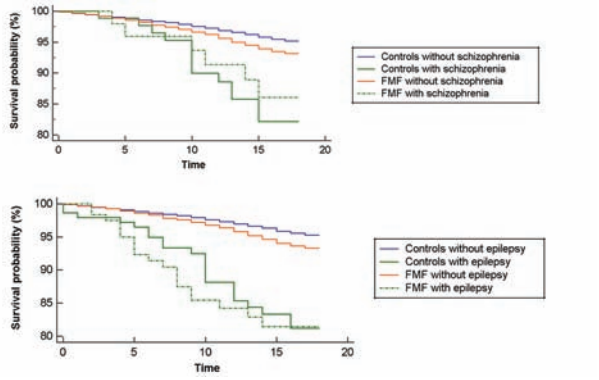


Figure 1. a+b. Kaplan-Meier survival plot of study cohorts

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THU0688

ASSESSMENT OF THE QRISK2, QRISK3, SLE CARDIOVASCULAR RISK EQUATION, FRAMINGHAM AND MODIFIED FRAMINGHAM RISK CALCULATORS AS PREDICTORS OF CARDIOVASCULAR DISEASE EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is recognized as an independent risk factor for cardiovascular disease (CVD), and patients with SLE are at an elevated risk of CVD compared to the general population[1]. The complex interplay between conventional CVD risk factors, the inflammation caused by SLE and the pharmacological treatment of SLE contributes toward CVD risk[1]. Despite knowledge of this increased risk, there is no agreement on the use of risk assessment tools in the prediction of CVD in SLE. The Modified Framingham Risk Score (mFRS), QRISK3 and SLE Cardiovascular Risk Equation (SLECRE) have been introduced as promising CVD risk assessment tools considering SLE in prognosticating patients.
Objectives: To determine which cardiovascular risk assessment tool amongst the QRISK2, QRISK3, SLECRE, Framingham (FRS) and mFRS best predicts CVD events in SLE.
Methods: Single-centre analyses on prospectively collected data of 1887 SLE patients were performed to compute 10-year CVD risk scores for each tool. Tools' scores were evaluated against CVD events at or within ten years for cases (CVD events) and controls (no CVD events). For cases, the index date for risk score calculation was chosen 10 years, or as close to 10 years as possible prior to the CVD event. For controls, risk scores were calculated as close to 10 years as possible prior to the most recent clinic appointment. Proportions of patients classified as low (<10%), median (10-20%) and high risk (>20%) of developing CVD according to each tool were determined. Sensitivity, specificity, positive/negative predictive values and c-statistics of these tools were analysed.
Results: 232 total CVD events were identified in the cohort including myocardial infarction, stroke, transient ischemic attack, heart failure and CVD death. QRISK2 and FRS risk-stratification was similar, while QRISK3 and mFRS risk-stratification was similar (Figure 1). The SLECRE classified the highest number of patients as median-high risk (Figure 1). The sensitivities and specificities are as follows for each tool: QRISK2 (19%, 93%), FRS (22%, 93%), mFRS (46%, 83%), QRISK3 (47%, 78%), SLECRE (61%, 63%). The tools were similar in negative predictive value, ranging from 89% (QRISK2) to 92% (SLECRE). The FRS and mFRS had the greatest c-statistics, both equalling 0.73, demonstrating the greatest predictive accuracy amongst the tools, while the QRISK3 had the lowest (0.67).

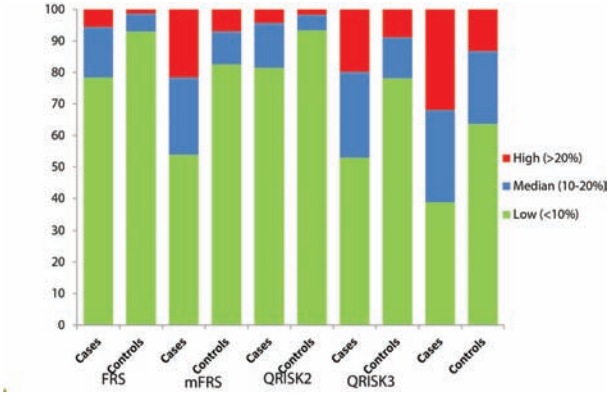


Figure 1. Percentage of patients considered low (<10%), median (10-20%) and high risk (>20%) between cases (CVD, n=232) and controls (no-CVD, n=1655) according to the FRS, mFRS, QRISK2, QRISK3 and SLE CRE.

Conclusion: While the mFRS performance was superior to the FRS, the QRISK3 did not outperform the mFRS. Although the SLECRE had the highest sensitivity, it had the lowest specificity, demonstrated by grouping the most cases and controls in the median-high risk category. Several factors are important to consider when deciding which risk assessment tools to utilize: ease of use/computation, sensitivity/specificity, and laboratory data accessibility. Of the tools currently available, the mFRS is a practical tool with a simple, intuitive scoring system appropriate for the ambulatory clinic setting based on the initial weighting of the FRS while adjusting for SLE. However, much room for improvement exists in predicting CVD in SLE.

REFERENCES:

1. Hippisley-Cox, J., Coupland, C., & Brindle, P. (2017). Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. *BMJ*, *357*, j2099.

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THU0689 ASTHMA AND ELEVATION OF ANTI-CITRULLINATED PROTEIN ANTIBODIES PRIOR TO THE ONSET OF RHEUMATOID ARTHRITIS

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Background: Anti-citrullinated protein antibodies (ACPA) are central to RA pathogenesis, with serum ACPA titers elevated years prior to clinical RA onset. Aberrant protein citrullination may occur in inflamed airway mucosa, forming neoantigens producing ACPA before articular involvement. Thus, individuals with inflammatory airway diseases, such as asthma, may be susceptible to RA-related autoimmunity.
Objectives: To investigate asthma as a risk factor for ACPA+ in serum prior to clinical RA onset.
Methods: We performed a cross-sectional analysis among women in the Nurses' Health Studies to examine whether asthma was associated with pre-RA ACPA+. Incident RA cases occurring after blood draw met research criteria and were each matched to 3 controls by age and menopausal status. Presence of self-reported asthma and potential confounders, including smoking pack-years, were assessed using questionnaires. The sensitive (primary) definition for ACPA+ was: >3 units on CCP2 or elevation (>99th percentile of the control distribution) on a research assay composed of autoantibodies targeting specific citrullinated protein epitopes. The specific (secondary) definition for ACPA+ was: >5 units on CCP2 or elevation of $\geq$2 different antibodies to citrullinated proteins on the research assay. Logistic regression was used to obtain ORs for ACPA+ independent of confounders. We performed secondary analyses using the specific definition for ACPA+ and in subgroups restricted to never smokers and pre-RA cases.
Results: We measured ACPA on 1,135 women, including 286 pre-RA cases. Serum was banked a mean of 9.7 years (SD 5.8) prior to RA diagnosis, mean age of 51.9 years (SD 7.9). Overall, 12% of pre-RA cases reported asthma compared to 7% of controls; pre-RA cases were heavier smokers than controls. Of pre-RA cases, 96 (34%) were ACPA+ by the sensitive definition and 60 (21%) by the specific definition. Among the entire sample, women with asthma were more likely to have ACPA+ (unadjusted OR 2.51, 95%CI 1.42-4.44) compared to those without asthma. After adjusting for age, smoking, BMI, and time to RA/matched date, asthma remained significantly associated with ACPA+ (OR 2.32, 95%CI 1.29-4.16). In the secondary analyses, we found similar associations of asthma with ACPA+ when using the specific definition for ACPA + (multivariable OR 2.28, 95%CI 1.11-4.69) and when restricted to never smokers (OR 3.11, 95%CI 1.29-7.47) and only pre-RA cases (OR 2.22, 95%CI 1.01-4.88).
Table: Odds ratios for elevated ACPA* by asthma status at time of blood draw.

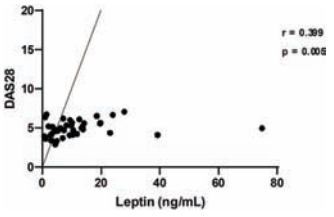
	Unadjusted OR (95%CI)	Multivariable** OR (95%CI)
Entire sample (n=1,135)		
No asthma	1.00 (Ref)	1.00 (Ref)
Asthma	2.51 (1.42-4.44)	2.32 (1.29-4.16)
Never smoker subset (n=573)		
No asthma	1.00 (Ref)	1.00 (Ref)
Asthma	3.19 (1.37-7.39)	3.11 (1.29-7.47)
Pre-RA case-only subset (n=286)		
No asthma	1.00 (Ref)	1.00 (Ref)
Asthma	2.34 (1.13-4.87)	2.22 (1.01-4.88)

*ACPA positivity (sensitive version) was defined as >3 units on the commercial CCP2 assay or >99th percentile of control distribution on the research ACPA assay.
**Adjusted for age at blood draw, time to RA diagnosis/matched date for controls, BMI, smoking pack-years (continuous, pack-years).
Conclusion: Asthma may be a novel risk factor for elevation of ACPA prior to RA onset, independent of smoking. These findings encourage further research on the contribution of airway inflammation to RA pathogenesis.
Disclosure of Interests: : Alessandra Zaccardelli: None declared, Xinyi Liu: None declared, Julia Ford: None declared, Sara Tedeschi: None declared, Jing Cui: None declared, Bing Lu: None declared, Su Chu: None declared, Peter Schur: None declared, Cameron Speyer: None declared, Karen Costenbader: None declared, William Robinson: None declared, Jeremy Sokolove Shareholder of: AbbVie, Employee of: AbbVie, Carlos Camargo, Jr.: None declared, Jeffrey Sparks Grant/research support from: Bristol-Myers Squibb, Amgen, Consultant for: Optum
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THU0690 DISEASE ACTIVITY CORRELATES WITH INSULIN RESISTANCE AND ADIPOCYTOKINES IN PATIENTS WITH DMARD-NAÏVE RHEUMATOID ARTHRITIS

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Background: Cardiovascular events such as myocardial infarction and stroke are frequent comorbidities in rheumatic diseases [1]. In relation, components of the metabolic syndrome (MS) including insulin resistance (IR), central obesity, high blood pressure, high triglycerides, and low high-density lipoprotein (HDL) are related to a high rate of endothelial dysfunction and atherosclerosis in patients with RA [2].
Objectives: We aimed to investigate the relationship between disease activity and insulin resistance (IR) and the levels of adipocytokines in non-diabetic patients with newly diagnosed rheumatoid arthritis (RA) who are naïve to disease modifying anti-rheumatic drugs (DMARDs).
Methods: Forty-seven DMARD-naïve patients with RA and 25 age-, gender-, and BMI-matched controls were included. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), 28-joint-count disease activity score (DAS28), serum lipids, glucose, HbA1c, insulin, leptin, resistin, visfatin, and RBP4 levels were measured. Homeostasis model assessment for insulin resistance (HOMA-IR) was calculated. Patients were studied before and 3 months after treatment with DMARDs.
Results: Levels of adipokines were similar in patients with RA and controls ($p > 0.05$ for all). However, RA patients with active disease (DAS28 > 3.2) had numerically higher levels of leptin (9.3 (3.7-17.4) vs. 7.6 (3.7-11.0), p = 0.289), insulin (8.0 (5.2-12.7) vs. 5.9 (4.2-8.7), p = 0.285), and HOMA-IR (1.9 (1.1-3.0) vs. 1.3 (1.0-1.9), p = 0.209). DAS28 was correlated with HOMA-IR (r = 0.356, p = 0.016), insulin (r = 0.323, p = 0.02), and leptin (r = 0.399, p = 0.005) in the study group (Figure-1). Regardless of the type of treatment modality, leptin levels (7.4 (4.4-13.4) vs. 6.4 (3.3-11.6, p = 0.047) decreased significantly after treatment, as did insulin levels (6.9 (4.9-12.5) vs. 5.9 (4.1- 8.8), p =0.01) and HOMA-IR score (1.7 (1.1-2.7) vs. 1.3 (1.0-2.0), p= 0.012). The reduction in leptin was more prominent in patients with active disease (9.3 (3.7-17.4) vs. 6.9 (3.1-11.4), p = 0.028). The reduction in ESR was correlated with ΔHOMA-IR (r = 0.308, p = 0.039), and CRP reduction was correlated with Δresistin (r = 0.288, p = 0.049) and ΔRBP4 (r = 0.456, p = 0.001).
Conclusion: Disease activity is associated with IR and correlates with circulating levels of adipokines in patients with RA. Treatment with DMARDs reduces leptin and improves IR.



REFERENCES:

[1] Maradit-Kremers H, Crowson CS, Nicola PJ, Ballman KV, Roger VL, Jacobsen SJ et al. Increased unrecognized coronary heart disease and sudden deaths in rheumatoid arthritis: a population-based cohort study. Arthritis Rheum.2005; 52:402–11.

[2] Burggraaf B, van Breukelen-van der Stoep DF, de Vries MA, Klop B, van Zeben J, van de Geijn GM et al. Progression of subclinical atherosclerosis in subjects with rheumatoid arthritis and the metabolic syndrome Atherosclerosis. 2018; 271:84-91.

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THU0691 CLINICAL, RADIOLOGICAL, THERAPEUTIC ASPECT AND PROGNOSTIC OF INFECTIOUS SPONDYLODISCITIS WITHOUT BACTERIOLOGICAL EVIDENCE

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Background: Early microbiological diagnosis and multidisciplinary management are the main predictive factor for successful treatment in septic spondylitis. However, the therapeutic management of spondylodiscitis without bacteriological diagnosis is not well codified.
Objectives: To evaluate whether there is clinical, biological or significant imaging between patients with infectious sondylodiscitis as they had or not a microbiological diagnosis.
Methods: Retrospective study including 107 patients hospitalized in our department between 1999 and 2018. The diagnosis was based on clinical, biological, radiological and bacteriological data.
Results: This study involved 107 patients, including 58 men (54.2%) and 49 women (45.8%) with a mean age of 55 years [16–86]. Spinal pain was observed in all cases and the lumbar spine was most affected (54.2%). A neurological deficit was noted in 16.82% of cases. The inflammatory syndrome was present in 90.6% of cases. Radiographs of the spine were abnormal in 83.1% of cases. CT and Spinal MRI were performed respectively in 60% and 78.8% of cases. Disco vertebral biopsy was performed in 73 patients and was contributory in 46.5% of cases.
We divided patients into two groups: patients with a confirmed biological diagnosis (group 1: 45.3%) versus patients in whom the diagnosis had been held on presumptive criteria (group2: 54.2%). There was no statically significant difference in the age (p=0.5), sex (p=0.3), risk factors such as diabetes (p=0.8), the start mode (p= 0.4), the presence of an impaired general condition (p=0.3), night sweats (p=0.1) and a neurological deficit (p=0.8), biological parameters (p=0.3) and the occurrence of complications (p=0.09) between the two groups. Vertebral condensation in radiographs of the spine was higher in group 2 and this was statically significant (p=0.03). In addition, the consumption of unpasteurized milk and positivity of wright serology was higher in the first group (p= 0.001 and p<0.001; respectively). Similarly, contributive histological result of vertebral biopsy was more frequent in group 1 (p=0.007).
Conclusion: Diagnosing infectious spondylodiscitis is facilitated by improved access to MRI testing. However, microbiological diagnosis is the main key to a successful management of this life threatening infection.
Disclosure of Interests: : None declared
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THU0692 OCULAR MANIFESTATIONS IN BEHCET'S DISEASE MAY BE MORE COMMON IN CHILDREN THAN ADULTS: RESULTS OF A SYSTEMATIC REVIEW

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Background: Behcet's disease (BD) can develop in both children and adults, but they may have different clinical features. Ocular involvement is common in BD and causes substantial impairment. The frequency of ocular involvement in BD has a wide range (5 to 89%).
Objectives: This study determined the frequency and type of ocular manifestations in childhood and adult BD and compared prevalence of ocular manifestations by geographic location in those with BD.
Methods: The protocol of ocular conditions in rheumatic conditions was registered at clintrials.gov (NCT03753893). Search terms were: conjunctivitis, keratoconjunctivitis sicca, xeropthalmia, uveitis, eye hemorrhage, optic neuritis, papilledema, orbital disease, retinal artery/vein occlusion, macular edema, retinitis, chorioretinitis, scleritis, iridocyclitits, choroid hemorrhage, blindness and amaurosis fugax in patients with BD. The search was performed with the assistance of an information specialist. Medline, Cochrane and Web of Science were used searching papers that spanned from their inception (1966, 1991 and 1990 respectively) to October 5, 2018. Studies were included if they had a minimum of twenty patients and reported the frequency of ocular manifestations within BD. Random effects models were used to combine the prevalence of ocular manifestations using Revman 5.3. Heterogeneity was evaluated using I^2 and funnel plots.
Results: The search resulted in 3129 articles, of which 33 were included for meta-analysis. Eye manifestations were more frequent in childhood onset BD with the mean [95% Confidence Interval] frequency of 50 [38-63]% compared to 34 [25-43]% in adults. In both children and adults, posterior uveitis (children 27% vs. adults 25%) was the most common ocular manifestation, followed by anterior uveitis (children 18% vs. adults 23%). When comparing the distribution of ocular manifestations in Behcet's in adults, there was geographic variation higher along the ancient Silk Road with ocular manifestations occurring in 40% of patients from Turkey and the Middle East. Ocular manifestations were similar in Europe (36%) and North America (36%), but less frequent in North Africa (26%) and East Asia (20%).
Conclusion: The frequency of ocular involvement is higher in children when compared to adults with BD. The most common manifestation in the eyes is posterior and then anterior uveitis. Ocular involvement also presents regional differences.

REFERENCES:

[1] Arevalo JF, Lasave AF, Al Jindan MY, Al Sabaani NA, Al-Mahmood AM, Al-Zahrani YA, et al. Uveitis in Behçet Disease in a Tertiary Center Over 25 Years: The KKESH Uveitis Survey Study Group. American Journal of Ophthalmology 2015;159:177-184.e2.

[2] Frigui M, Kechaou M, Jemal M, Ben Zina Z, Feki J, Bahloul Z. Optic neuropathy in Behçet's disease: a series of 18 patients. Rev Med Interne 2009;30:486-91.

[3] Keino H, Okada AA. Behçet's disease: global epidemiology of an Old Silk Road disease. Br J Ophthalmol 2007;91:1573-4.

[4] Leonardo NM, McNeil J. Behcet's Disease: Is There Geographical Variation? A Review Far from the Silk Road. International Journal of Rheumatology 2015;2015:1-7.

[5] Uva L, Miguel D, Pinheiro C, Filipe P, Freitas JP. Mucocutaneous manifestations of Behçet's disease. Acta Reumatol Port 2013;38:77-90.

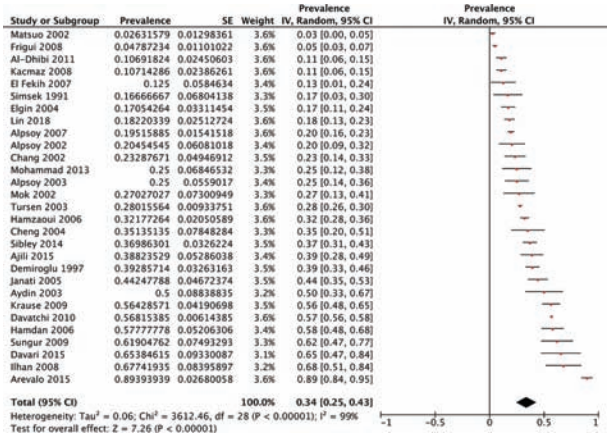
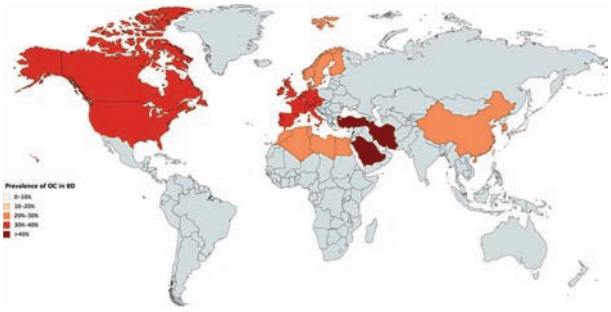


Figure: The prevalence (A) and geographic distribution (B) of ocular manifestations in adults with Behcet's disease.



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THU0693 INPATIENT PREVALENCE, EXPENDITURES AND COMORBIDITIES OF TAKAYASU'S ARTERITIS: A PROPENSITY-MATCHED COHORT STUDY

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Background: Takayasu's arteritis (TAK) was first described in Japan. Since then, the disease has been extensively studied in Japan and other Asian countries [1]. However, little is known about the characteristics, inpatient burden, expenditures and comorbidities of TAK in the United States (US).
Objectives: To investigate the inpatient prevalence, expenditures and comorbidities of patients with TAK in the US.
Methods: Patients with TAK were identified within the Nationwide Inpatient Sample (NIS) database of the years 2013-2014 using ICD-9 diagnostic code. NIS is a publicly available inpatient database that contained data of over 7 million hospital stays, which are a 20% stratified sample of over 4,000 non-federal acute care hospitals from more than 40 states of the US. Data on patient characteristics, comorbidities, resource utilization and expenditures was collected. A propensity-matched cohort of patients without TAK was also created from the same database to serve as comparators for the analysis of comorbidities. Inpateint prevalence of TAK was calculated using all admissions in the NIS database as denominator. Odds ratios (OR) comapring the prevalence of comorbities between cases with TAK and propensity-matched controls without TAK were calculated.
Results: A total of 2,840 patients with TAK were identified from the database, corresponding to an inpatient prevalence of 4.6 cases per 100,000 admissions. The 5 main reasons for admission in patients with TAK were as follows; chest pain (17%), acute myocardial infarction (16%), stroke (14%), sepsis (14%) and pneumonia (11%). Compared to the propensity-matched cohort of patients without TAK, patients with TAK were found to have significantly increased odds of stroke, aortic aneurysm, aortic valvulopathy and peripheral vascular disease. TAK was also associated with increased use of some procedures (Table 1). However, the mortality was not significantly different (adjusted OR: 1.44, 95% CI: 0.58 – 3.61, p=0.43). After adjusting for confounders, patients with TAK displayed a mean additional $11,275 (95% CI, $4,946 - $17,603) for total hospital costs (the amount of money invested by each institution in providing patient care) and a mean additional $45,305 (95% CI, $23,063 – $67,546) for total hospitalization charges (the amount of money that each hospital billed for providing its service on each case) when compared to patients without TAK.
Conclusion: The inpatient prevalence of TAK was higher than what would be expected from the overall incidence. The mean total hospital costs and total hospitalization charges for patients with TAK were higher than patients without TAK. Analysis of comorbidities found significantly higher odds of several vascular comorbidities compared to a propensity-matched cohort of patients without TAK.

REFERENCES:

[1] Onen F, Akkoc N. Epidemiology of Takayasu arteritis. Presse Med 2017;46:e197-e203

Table 1. Adjusted ORs comparing the prevalence of comorbidities and use of procedures between patients with TAK versus patients without TAK

	Adjusted odds ratio	95% CI	*p*-value
Comorbidities			
Stroke	4.66	2.10-10.31	<0.01
Aortic aneurysm	40.76	9.13-181.7	<0.01
Peripheral vascular disease	2.01	1.22-3.32	<0.01
Acute myocardial infarction	2.13	0.56-8.13	0.27
Aortic valvulopathy	4.92	2.09-11.55	<0.01
Chronic kidney disease	1.22	0.63-2.63	0.57
Procedures			
Aortic valve replacement	1.39	0.42-4.60	0.59
Peripheral vascular intervention	4.41	1.61-12.10	<0.01
Arteriography	6.82	2.79-16.68	<0.01
MRI use	2.60	0.42-16.28	0.31

Disclosure of Interests: None declared
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THU0694 BRAZILIAN SJÖGREN'S SYNDROME REGISTRY (BRASS): A LARGE BRAZILIAN MULTICENTRIC COHORT OF PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is an orphan systemic autoimmune disease with no treatment based on evidence[1]. There is an international effort for multicentric registries for getting information about phenotypes, complication, response of treatment, and biobank consortium.
Objectives: To describe the creation of the Brazilian Sjögren's Syndrome Registry (BRASS) and present the preliminary data.
Methods: BRASS is supported by Brazilian Society of Rheumatology (SBR) and is including patients from all regions of the country. Recruitment started in 2018 and is due to be completed in 2024. We are including patients with pSS according to AECG 2002 or ACR-EULAR 2016 classification criteria. All patients are being assessed for disease activity (ESSDAI), disease damage (SSDDI), symptoms assessment (ESSPRI), fatigue (FACIT-Fatigue), anxiety and depression (HADS), sleepiness (Epworth Sleepiness Scale), physical activity (IPAQ-SF) and quality of life (EQ-5D). In addition, demographics, immunological tests, unstimulated whole salivary flow (UWSF), salivary gland biopsy (SGB), comorbidities, treatment and complications such as cancer and cardiovascular risk assessment are being collected.
Results: There are currently 10 centers across the Brazil and 248 patients were evaluated until now. Most patients were female, white (45%) or mixed (38.3%), with the mean of the disease duration of 8 years. ESSDAI at baseline was 6.62±6.37 and currently is 4.21±5.16 ($p<0.05$). The mean of the SSDDI was 2.16±1.60 and ESSPRI 8.38 ±6.88. SGB was positive in 81.5% and focus score mean was 1.58 ±1.30. Schirmer test I was positive in 72.6%, van Bijsterveld in 70.9% and UWSF in 84.8%. About classification criteria, 91.9% fulfilled AECG 2002 and 94% ACR/EULAR 2016. Anti-Ro and anti-La were positive in 70.8% and 35.5%, respectively. Forty three percent had positive RF, 88.5% ANA, 6.9% low C3, 10.2% low C4, 34.9% high IgG. Nineteen percent were using prednisone, 40.4% immunosuppressant, 53.6% antimalarial and 17.6% biological therapy. Prevalence of cardiovascular event was 7.5%, hypertension 43.3%, diabetes 13.3%, dyslipidemia 31.5%, smoking 5.8% and cancer 7.5%.
Conclusion: ESSDAI has decreased over time and more than half of patients are on hydroxychloroquine, immunosuppressant or biological therapy. Further analysis is needed to understand whether the reduction in ESSDAI reflects the natural course of the disease or greater access to

treatment. BRASS Registry will be important to enhance research and to develop public health planning.

REFERENCES:
[1] Valim V et al. Recommendations for the treatment of Sjögren's syndrome. Rev Bras Reumatol 55:446–57, 2015.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3800

THU0695 DIFFERENCES OF LIFESTYLE HABITS OF SMOKING, DRINKING ALCOHOL AND CAFFEINATED COFFEE CONSUMPTION BETWEEN RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY CONTROL – TOMORROW STUDY-

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Background: Previous reports indicated the strong association between smoking and onset of rheumatoid arthritis (RA), and relation between some of lifestyle habit and disease activity of RA.
Objectives: In this study, we compared differences in habits of smoking, alcohol consumption, coffee and Japanese tea intake between RA patients and healthy volunteers (Vo) in the same study population.
Methods: This study was conducted based on baseline data from ongoing 10-years prospective cohort project TOMORROW study (UMIN000003876), which includes age and sex matched RA patients (n=208) and Vo (n=205). Data on smoking history and alcohol (Alc), coffee and Japanese tea intake were collected by self-reported questionnaires. Alc intake was categorized into 3 groups by calculating the amount per day using Alc unit (pure Alc 20 mg/Alc unit). We also categorized frequency of Alc intake per week into 3 groups, number of cups of coffee and Japanese tea intake per day into 4 groups each. The data of RA patients included anthropometric, blood test data, disease activity score28-ESR (DAS28-ESR), together with baseline characteristics. Using logistic multivariate regression lifestyle habits were compared between RA and Vo.
Results: We analyzed 191 Vo and 198 RA with complete data about lifestyle habits. Demographic data and lifestyle habits of RA and Vo were shown in the Table 1 and 2. In RA patients, the average disease activity score 28-ESR (DAS28-ESR) was 3.49±1.34 and disease duration was 13.9±11.8 years. In multivariate analysis, smoking history (OR 5.03, 95% CI 1.42-17.9; p=0.04), 2 - 6 unit of Alc intake per day (OR 0.20, 95%CI 0.04-0.96; p=0.04) and 0 - 1 cup of caffeinated coffee intake per day (OR 0.26, 95%CI 0.07-0.91; p=0.04) were significantly different between RA and Vo. However, there were no significant difference in Alc frequency, decaffeinated coffee and Japanese tea intake.
Conclusion: As shown in previous reports, the smoking history was significantly higher in RA patients with an odds ratio of 5.03. And moderate intake of Alc and caffeinated coffee seems to be low in RA patients.

Table 1. Demographic data of rheumatoid arthritis patients (RA) and healthy volunteer (Vo).

	RA (N=198)	Vo (N=191)	p.value*
Age	58.4±12.6	57.0±13.2	0.28
Sex female	167 (84.3)	158 (82.7)	0.68
BMI	22.7±3.64	22.6±3.20	0.72
Disease duration (year	13.9±11.8		
ACPA positivity	166 (83.8)		
RF positivity	136 (68.7)		
DAS28-ESR	3.49±1.34		
mHAQ	0.47±0.59		
Methotrexate dose (mg/week	6.54±3.76		
bDMARDs use	104 (54.5)		

Values are mean±SD, or n (%). *Student-T-test and Fisher's exact test for RA and Vo.
BMI, body mass index; Alc, alcohol; mHAQ, modified Health Assessment Questionnaire; bDMARDs, biologic disease modified anti-rheumatic-drugs.

Table 2. Lifestyle habits of rheumatoid arthritis patients (RA) and healthy volunteer (Vo).

		RA (N=198)	Vo (N=191)	p.value*
Smoking history		59 (29.8)	29 (15.2)	<0.01
Alc frequency (/week	0	94 (47.5)	76 (39.8)	0.17
	1-5	77 (38.9)	77 (40.3)	
	6-	27 (13.6)	38 (19.9)	
Alc (unit/day	-2	147 (74.2)	125 (65.4)	0.09
	2-6	21 (10.6)	34 (17.8)	
	6-	30 (15.2)	32 (16.8)	
Caffeinated coffee (cup/day	0	45 (22.7)	27 (14.1)	0.19
	0-1	67 (33.8)	71 (37.2)	
	1-4	69 (34.8)	75 (39.3)	
	4-	17 (8.6)	18 (9.4)	
Decaffeinated coffee(cup/day	0	188 (94.9)	188 (98.4)	0.14
	0-1	8 (4.0)	3 (1.6)	
	1-4	2 (1.0)	0 (0.0)	
	4-	0 (0.0)	0 (0.0)	
Japanese tea (cup/day	0	18 (9.1)	17 (8.9)	0.43
	0-1	42 (21.2)	53 (27.7)	
	1-4	66 (33.3)	63 (33.0)	
	4-	72 (36.4)	58 (30.4)	

Values are n (%). *Fisher's exact test for RA and Vo.
Alc, alcohol.

Disclosure of Interests: Hitoshi Yoshimura: None declared, Kentaro Inui Speakers bureau: Takeda Pharmaceutical, Pfizer Japan, Daiichi-Sankyo Co.Ltd., Abbvie, Mitsubishi Tanabe Pharma Corporation, Janssen Pharmaceutical, Chugai Pharmaceutical, Ono Pharmaceutical, Eisai Co.Ltd., Eli-Lilly, Nippon Kayaku Co.,Ltd., Maruho Co.,Ltd, Kaken Pharmaceutical Co., Ltd., Tatsuya Koike Speakers bureau: AbbVie, Astellas Pharma Inc., Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB, Yuko Sugioka: None declared, Tadashi Okano Speakers bureau: AbbVie, Koji Mandai: None declared, Yutaro Yamada Speakers bureau: Abbvie, Chugai, Mitsubishi Tanabe, Kenji Mamoto: None declared, Masahiro Tada Speakers bureau: Abbvie, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Ono Pharmaceutical, Pfizer Japan, Takeda Pharmaceutical
, Hiroaki Nakamura: None declared
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HPR Service developments, innovation and economics in healthcare

THU0696-HPR TRANSITION READINESS ASSESSMENT TOOLS (TRAT): A PRELIMINARY SINGLE-CENTRE PAEDIATRIC RHEUMATOLOGY TRANSITION PROGRAMME (PRTP) EXPERIENCE AND OUTCOMES IN SINGAPORE

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Background: Majority of childhood onset rheumatic diseases often continue into adulthood. Care for these youth especially during their transition from child centred to adult oriented healthcare system is crucial and challenging. The Paediatric Rheumatology Transition Programme at KK Women's and Children Hospital (KKH) in Singapore was developed in 2016. In 2017, we have adopted the American College of Rheumatology Transition Readiness assessment tools (TRAT) with modification to assess the readiness of our paediatric rheumatology patient cohort.
Objectives: To assess factors contributing to the outcomes of Paediatric Rheumatology Transition Programme at our institute using the Transition Readiness Assessment Tools (TRAT)
Methods: The TRAT composed of 4 components – transition-importance, transition-confidence, medical knowledge/healthcare usage (MKHU-23 questions), transition-readiness assessment questionnaires (TRAQ, 5 domains – medicine management (MM), appointment management (AM), health issue tracking (HT), communications with providers (CP) and daily activity management (DAM)). Each component score was computed into 0-10 (scores >7 defined acceptable responses). Nonparametric statistics were used to describe and analyse the data.
Results: 106 patients (52.8% female) with SLE(42.5%) and JIA(50.0%)) with median age of 20.0 (18.8-20.6) years were recruited. Median

duration of disease at 1st assessment was 7.0 years (IQR 5.5-8.8). 24 patients were transited successfully. Only 60% of our youths felt that transition preparation is important and had confidence to be prepared for/change to adult healthcare system (AHCS). Among the less confident group (scores <7), MKHU, MM, AM and HT domains scored significantly less than those from confident youths (p<0.001-0.021), but only transition importance MKHU scores were <7. Disease duration at first TRAT assessment and diagnoses did not predict confidence level. With further targeted education and counselling (median 8.3 months (IQR 5.7-9.6)), confidence and MKHU was significantly improved (p=0.001).

Conclusion: TRAT enables our PRTP team to learn and understand our local youths' perception and readiness of adult transition process. More than one-half of them did not aware of the importance of the transition process and had less confidence to do so. With further targeted counselling and preparation, all improved their perception and MKHU significantly. TRAT was able to guide individualize counselling to our cohort youths who are ready to be transited.

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THU0697-HPR CONTENT OF AND RHEUMATOLOGISTS' AND NURSES' OPINIONS ON A NURSE-LED TELEPHONE HELPLINE

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Background: To improve timely response to patients' questions and to support that care is provided by the appropriate professional, a nurse-led rheumatology telephone helpline was introduced in May 2015. Different organisational approaches have been tried out to ensure an effective as well as efficient service. Currently a voicemail system is used. A selection menu allows patients to select whether he/she needs 1) advice regarding disease complaints, 2) drug prescriptions, 3) (change in) appointment at the clinic, 4) laboratory forms.

Although the menu differentiates between requests, organising timely responses by the appropriate professional remains a challenge. Clear and joint definitions by the rheumatologists and nurses on what questions to what extent should be addressed by whom, are necessary.

Objectives: To facilitate further improvement of the helpline we explored 1) number and content of questions that were registered; 2) experiences of rheumatologists and nurses with the helpline; 3) opinions of rheumatologists and nurses on which questions should be answered via the helpline.

Methods: A file research explored the number of questions and reasons for contacting the helpline. Data were analysed descriptively. In semi-structured interviews among all rheumatologists (n=8) and nurses involved in manning the helpline service (n=6), experiences and opinions were explored. System Engineering Initiative Patient Safety (SEIPS) model, that focuses on system design and it's interaction with processes, and outcomes for patients, employees and organisation [1], was used to structure thematic coding of the transcripts.

Results: In 37 months, the helpline registered 3389 calls (see Table 1). A majority of the questions was about disease complaints (28.6%) or other related problems such as pain management, and exercise (27.8%). The proportion of requests for prescriptions was 21.8%.

The interviews revealed that both rheumatologists and nurses considered the helpline valuable in providing easy access to care for patients with disease related questions. This should be the primary aim. The rheumatologists also valued their reduced workload, which occurred most if the knowledge of the nurse was sufficient to take care of the responses independently. Moreover, they valued if requests, such as prescriptions, were clustered by the nurses. The nurses experienced an increased workload. Sufficient knowledge on and training in rheumatology, and being familiar with the patient wee considered pivotal in providing appropriate and for the patient acceptable care. As nurses cannot precribe medication, the requests for prescriptions were considered inappropriate. Availability of protocols and guidelines were considered prerequisites by all for responding to patients' requests appropriately.

Conclusion: The helpline is used frequently and the selection menu has helped to gain insight in why the helpline is used by patients. There is consensus on the primary aim of the helpline and on prerequisites for nurse-led responses to patients' disease related questions. Rheumatologists and nurses have different opinions on some issues, such as the organisation of prescriptions. Our study findings can help in jointly improving consensus on the content of nursing care within the helpline.

REFERENCES:

[1] Carayon, P., et al. (2006). Work system design for patient safety: The SEIPS model. Qual Saf Health Care, 15(SUPPL. 1), 50–58

Abstract THU0697HPR Table 1. Reasons for contacting the helpline

	Calls May 2015-July 2018
Reasons	**N (%)**
Disease complaints	970 (28.6)
Medication prescriptions	739 (21.8)
Medication side-effects	353 (10.4)
Appointments	184 (5.4)
Lab forms	126 (3.7)
*Other**	943 (27.8)
Total	**3389**

*Other: a variety of requests e.g. advice for pain management, exercise, work participation, referrals for devices.

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THU0698-HPR MORE EFFICIENT DMOAD TRIALS THROUGH INNOVATIVE SCREENING STRATEGIES

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Background: In randomized Clinical Trials (RCT), the number of patients to recruit for assessing effectiveness of disease-modifying OA drug (DMOAD) depends on the proportion of progressors in the population. The higher this proportion, the smaller the cohort to be recruited. In the general OA population, this proportion is quite low (10-30%) [1] requiring large cohorts, hence long and expensive trials.

Objectives: We study how predictive modeling based on early cartilage degradation biomarkers can be used to screen patients, make individual predictions about the likelihood of future progression, and recruit on this basis a progressor-enriched cohort. By doing so, DMOAD RCTs could achieve same or better success rates based on smaller cohorts and lower budgets, even taking into account the extra cost of this innovative screening.

Methods: Two biomarkers (Coll2-1 & Coll2-1-NO2, Artialis, Belgium) have been measured at baseline on 182 OA patients from the placebo arm of a previous RCT. For this cohort, progression at 30M is defined as in [2]. We developed two predictive models of the progression of the patients over 30 months through regularized logistic regressions: one based on Coll2-1 only, the other on Coll2-1 and Coll2-1-NO2. Based on these models, we design a strategy to produce cohorts of patients with a higher rate of progressors than the natural proportion. To do so, we make hypotheses on the expected drug effect (from 30% to 50%), on the costs generated by a trial designed according to a regular strategy (i.e. not using baseline markers for patients inclusion/exclusion), and on the costs generated by this innovative screening strategy (a.o. nb patients screened, enrolled, costs of visits, imaging, biomarkers when applicable). Based on these hypotheses, we optimize sensitivity/specificity trade-offs of each model, so as to reduce the sample size required to prove the expected effect.

Results: When we apply this strategy to realistic scenarios, both models produce substantial cost reductions (up to 30%) even considering the extra cost of the biomarker-based screening of a higher number of candidate participants. They also lead to cohort size reductions: almost 40% less patients needed. As an example, we considered a natural progressor rate of 20%, an actual effect of 50% for the DMOAD to be tested, and a study consistsµing in a screening visit, 4 follow-up visits, 2 x-rays, 2 MRI, and a final visit. Hypotheses have been made about costs of each of these items, according to Belgian practice. In the standard case, all screened patients satisfying inclusion criteria are recruited. In the modified version, only patients for which inclusion criteria are met and the tuned biomarker-based model turns positive are enrolled. In the standard version of such a study, 554 patients have to be recruited, with a cost of 1,767,260€. Through the optimized strategy, 1190 patients are screened,

but among them only 344 are recruited in the study, showing a progression rate of about 35% instead of 20%, for a total cost of 1,229,280€.
Conclusion: This work demonstrates the interest for biomarker-based OA-progressors cohort enrichment in DMOAD RCTs. It simulates the gains it could represent for the conduct of these RCTs. The cohorts used in this work (for biomarker measurement and predictive modeling) have a high proportion of women with very large BMI, with K&L grade II-III. The results might thus be replicated on other cohorts. In order to achieve yet stronger cohort enrichment and cost reductions, additional markers and/or clinical factors could be considered for the models.

REFERENCES:

[1] One-year follow-up of Coll2-1, Coll2-1NO2 and myeloperoxydase serum levels in osteoarthritis patients after hip or knee replacement. Deberg M, Dubuc JE, Labasse A, Sanchez C, Quettier E, Bosseloir A, Crielaard JM, Henrotin Y. Ann Rheum Dis. 2008 Feb;67(2):168-74.
[2] Ornetti, et al., 2009; OARSI-OMERACT

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HPR Interventions (educational, physical, social and psychological)

THU0699-HPR IS A SMARTPHONE APPLICATION USEFUL FOR SELF-MANAGEMENT SUPPORT IN PATIENTS WITH A RHEUMATIC DISEASE?

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Background: For patients with a rheumatic disease (RD), self-management is the effort to find a balance between the demands of the disease and the activities of daily life. Self-management is an important aspect in the care for patients with a RD, in which they are expected to take an active role. Over the past decade, new technologies have been developed to support self-management, including smartphone apps. These apps perfectly fit the idea that patients prefer an active role in self-management. Therefore, a smartphone application (app) was developed.
Objectives: This study 1) investigates whether the use of an app improved patients' self-management, 2) explores patients' experiences with this RD-app, 3) investigates which factors are associated with the use of the RD-app.
Methods: We performed a prospective before-after study among patients with a RD. The primary outcome was patients' self-management behavior measured with the Partners in Health scale (PIH), a generic validated 12 item self-rated scale, which indicates higher scores for better self-management behavior (1). A paired t-test was used to evaluate changes in the PIH-scale score after three months. To measure the user-experience with the app, survey questions addressed whether the RD-app had contributed to get more grip (or not) on the disease and how (why not). Logistic regression analyses served to investigate variables that are important for using the RD-app.
Results: Of the 1511 eligible patients, 397 completed both the baseline and the follow-up surveys. Participants who completed both questionnaires were most frequently diagnosed with RA, 65% was female and the mean age was 52.0 (SD 15.6) years. Hundred-fourteen participants used the RD-app. Self-management behavior did not improve according to the PIH score in the app-users group after 3 months. However, 42% of the app-users perceived that use of the RD-App had contributed to get more grip on the disease. Receiving tips, information on exercises and gaining insight on self-reported disease activity contributed to get more grip on the disease. However, the other app-users whom did not get more grip on the disease indicated the following reasons: information was not useful, no need for information or additional help, technical issues and too little usage of the app itself. Almost all users would recommend the app to others. To investigate who did use the RD-app, univariate analysis revealed a role for female patients, positive expectations of the RD-app, help needed to get more grip on the disease and a higher VAS global as associated factors with actually using the RD-app. In the multivariate analysis only positive expectations of the RD-app remained significantly associated with actually using the RD-app (p=<0.001).
Conclusion: Almost one third used the RD-app. Although the PIH-score did not change, 42 percent of the participants thought the app helped them to get more grip on the disease. Therefore, the RD-app may be useful for additional self-management support in a clinical practice. Participants seemed to be satisfied with the app, almost all participants would recommend this app to others. More research is needed for additions within the app that could improve the app as a self-management tool.

REFERENCES:

[1] Battersby, M., Ask, A., Reece, M., and M. Markwick, Collins, J. The Partners in Health scale: The development and psychometric properties of a generic assessment scale for chronic condition self-management. 2003

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THU0700 PHYSIOTHERAPISTS COULD REPLACE PHYSICIANS AS PRIMARY ASSESSORS FOR PATIENTS WITH KNEE OSTEOARTHRITIS IN PRIMARY CARE—A RANDOMISED CONTROLLED STUDY

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Background: It has been estimated that consultations to healthcare will increase with 30-50% among patients with osteoarthritis (OA) over the next 20 years [1]. Patients with knee OA (KOA) report among the lowest health-related quality of life (HrQoL) compared with other chronic diseases [2]. Most patients are assessed by a physician which claims unnecessary healthcare resources since physiotherapists also are primary assessors for patients with KOA and provide recommended treatments. However, it is unclear if physiotherapists could be the first option as primary assessor for this patient group. We hypothesise that all patients with suspected KOA in primary care could be assessed by a physiotherapist first and be referred to physician only when it is required, without having a negative impact on HrQoL.
Objectives: The aim of this study was to explore differences in HrQoL, pain and physical function in patients with suspected KOA after being assessed, diagnosed and treated by physiotherapist first compared with being assessed by a physician in primary care first.
Methods: Patients seeking primary care with suspected KOA were randomised to either a physiotherapist or a physician for assessment, diagnose and treatment. Inclusion criteria were knee pain and > 38 years old. Exclusion criteria: knee pain due to traumatic cause, other systemic, somatic, mental or rheumatic diseases, pregnancy, or already been diagnosed or assessed by another healthcare giver due to current knee pain. HrQoL (Euroqol - EQ5D-3L index, EQ5D-3L VAS), pain intensity (visual analogue scale) and physical function (30 seconds chair stand test) were measured before randomisation, and at 3-, 6- and 12 months. Mann-Whitney's U test and Chi2 test for independence were used with a significance level of p<0.05.
Results: 69 patients with suspected KOA were randomised to either a physiotherapist (n=35) or a physician (n=34). Both groups improved their HrQol, pain and physical function at all follow ups. Patients rated significantly better HrQoL (EQ5D-3L VAS) one year after physiotherapy assessment (84 (SD 11); vs 74 (SD 15), p=0.018). No other significant differences were found between the groups.
Conclusion: Physiotherapy assessment could replace physician assessment without having negative impact on patient reported outcomes after treatment for patients with suspected KOA. This may play a role in managing the expected increase in OA consultation in primary care. However, more research is needed to clarify if this management is more cost effective, and how patients with KOA experience other primary assessors than physicians.

REFERENCES

[1] Turkiewicz A, Petersson IF, Björk J, Dahlberg LE, Englund M: The consultation prevalence of osteoarthritis 2030 may increase by 50%: prognosis for Sweden. Osteoarthritis and Cartilage 2013, 21(Supplement):S160-S161.
[2] Picavet HS, Hoeymans N: Health related quality of life in multiple musculoskeletal diseases: SF-36 and EQ-5D in the DMC3 study. Ann Rheum Dis 2004, 63(6):723-729.

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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

THU0701-HPR "TO REGAIN ONE´S HEALTH" – PATIENTS' PREFERENCES OF TREATMENT OUTCOMES IN EARLY RHEUMATOID ARTHRITIS – A QUALITATIVE STUDY

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Background: Rheumatology care strives to identify and meet the needs of the patients, and to understand disease and treatment impact from the patients' perspective. A better understanding of patients' expectations from the treatment is needed to enable a patient centered approach in clinical practice and a shared-decision making as recommended in the EULAR treatment recommendations for rheumatoid arthritis (RA). Understanding of patients' expectations in the early stage of the RA disease may facilitate adherence to treatment, patient independence and prevent unmet needs in the future.
Objectives: To explore patients' preferred treatment outcomes in early rheumatoid arthritis (eRA).
Methods: A qualitative, explorative study. Individual interviews were conducted with 31 patients with eRA, defined as disease duration of ≤ 1 year and disease-modifying antirheumatic drugs (DMARDs) treatment for 3-6 months[1]. Interviews were analyzed using a constant comparison method according to the Qualitative Analysis Guide of Leuven (QUAGOL) and lasted in a core category and four related concepts.
Results: The patient-preferred treatment outcomes in eRA were described in the core category "to regain one´s health" and the four related concepts: to experience external control of the disease, to experience independence, to regain identity and to experience joy in everyday life. The patients expected to experience external control of the disease by the given treatment to regain one's health. It was perceived as controlling the symptoms and as absence of disease. Independence was perceived as regaining former activity levels, experiencing autonomy and using active coping strategies. Patients wanted to regain identity through participation, empowerment and their self-image. Joy in everyday life was perceived as vitality and believing in the future.
Conclusion: Patients' preferred treatment outcomes in eRA were to regain one's health including both external and internal control. External control as disease control and independence as well as internal control as identity and joy in everyday life. The results from this study can assist healthcare professionals to better understand patients' preferred treatment outcomes early in the disease process and to tailor the interventions accordingly to improve long term treatment outcome.

REFERENCES:

[1] Van der Elst K, Bremander A, De Groef A, Larsson I, Mathijssen E, Vriezekolk J, Westhovens R, van Eijk-Hustings Y. (2019). European Qualitative research project on Patient-preferred outcomes in Early Rheumatoid Arthritis (EQPERA): rationale, design and methods of a multinational, multicenter, multilingual, longitudinal qualitative study. BMJ Open, accepted 181220

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THU0702-HPR PATIENT UNDERSTANDING OF RISKS OF METHOTREXATE AND ANTI-TNF THERAPY: A CROSS-SECTIONAL STUDY

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Background: Disease-modifying anti-rheumatic drugs (DMARDs) have revolutionised the management and long-term prognosis of rheumatoid arthritis (RA).[1] Side-effects of DMARDs include, but are not limited to: immunosuppression, gastro-intestinal upset, skin reactions and headaches. Despite the significant potential side-effects of DMARDs, there have been limited attempts to evaluate patient understanding of the side-effects of methotrexate (MTX)[2,3] and to our knowledge no studies with regards to anti-tumour necrosis factor (anti-TNF) therapy.
Objectives: To evaluate the extent to which each of the known side-effects of MTX and anti-TNF therapy can be identified by patients receiving single or combination therapy for RA.
Methods: This was a cross-sectional study conducted in a rheumatology centre in the West of England. Patients with RA, seen in the outpatient clinic within the previous 18 months were invited to participate. Participants had to belong to one of the following treatment groups: (i) MTX only (ii) anti-TNF only or (ii) combined treatment with MTX and an anti-TNF. A postal questionnaire designed by the research team was used to obtain the data. Each participant was asked to (a) select side-effects they considered to be possible from their treatment, (b) tick if they had experienced this side-effect, and (c) select whether they believed this side-effect to be common or not. Descriptive analyses were used to determine the proportion (percentage) of patients who correctly identified the possible side-effects, correctly identified them as common, and had experienced them. Summary results are presented as ranges (minimum to maximum) and their corresponding percentages.
Results: Of the 300 patients invited, 119 returned a completed questionnaire; 48 (40%) on MTX only, 25 (21%) on anti-TNF only and 46 (39%) on combined MTX and anti-TNF. Their mean (SD) age was 62.5 (12.8) years, disease duration 13.5 (12.4) years, 111 (93%) had completed compulsory education and 94 (79%) were female. Most participants (115, 97%) spoke English as their first language.
Correct identification of each possible side-effect ranged from 29% to 63% of participants in the MTX only group, 15% to 41% of participants in the anti-TNF only group and 18% to 62% of participants in the combined MTX and anti-TNF group. Correctly recognising these as common ranged from 13% to 52% of participants in the MTX only group, 4% to 35% of participants in the anti-TNF only group and 8% to 64% of participants in the combined MTX and anti-TNF group. Of those correctly identifying possible side effects, 22% to 55% of participants in the MTX only group, 1% to 25% of participants in the anti-TNF only group and 8% to 56% of participants in the combined MTX and anti-TNF group reported experiencing them.
Conclusion: Our data suggests that a considerable number of patients are unable to correctly identify the most common side-effects of DMARDs used in RA management. Effective patient education and involvement in treatment decision-making will allow patients to be more aware of potentially serious side-effects of DMARDs.

REFERENCES:

[1] Cicirello, S, et al. Improving treatment with methotrexate in rheumatoid arthritis - development of a multimedia patient education program and the MiRAK, a new instrument to evaluate methotrexate related knowledge. Semin Arthritis Rheum. 2014; 43:437-46.
[2] Fayet, F, et al. The development of a questionnaire to evaluate rheumatoid arthritis patient's knowledge about methotrexate. J Clin Nurs. 2015; 25:682-689.
[3] Barton, J, et al. Poor knowledge of methotrexate associated with older age and limited English language proficiency in a diverse rheumatoid arthritis cohort. Arthritis Res Ther. 2013; 15:157.

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THU0703-HPR A SANCTUARY FROM EVERYDAY LIFE: A QUALITATIVE STUDY OF THE EXPERIENCE OF IN-PATIENT MULTIDISCIPLINARY REHABILITATION, FOR PATIENTS WITH RHEUMATIC DISEASES

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Background: In Denmark, patients with rheumatic diseases can receive inpatient multidisciplinary rehabilitation at a hospital for rheumatic diseases or at rehabilitation centers.
Quantitative studies indicate that it is difficult to detect a general and lasting effect of 1-4 weeks of inpatient multidisciplinary rehabilitation, but few studies have explored patients' experience of in-patient multidisciplinary rheumatology rehabilitation.
Objectives: To explore how patients, experience the process and personal impact of an inpatient rehabilitation stay.
Methods: An exploratory qualitative phenomenological-hermeneutic study was planned. Adult rheumatic patients admitted for a two-week inpatient rehabilitation stay were invited to participate. Individual semi-structured interviews were conducted in the patients' home shortly after discharge or at the ward one of the last days of admission. The interviews were audio recorded and transcribed verbatim. The analysis was inspired by Paul Ricour's interpretative philosophy (1).
Results: Fifteen interviews were conducted, 11(73%) female, age 28-89. The analysis derived a core theme,"*A sanctuary*", reflecting that the patients experienced to have sufficient time and mental resources to provide self-care. In addition, the analysis derived five subthemes: 1) "*Being seen, heard and acknowledged as an equal and whole person".* To feel acknowledged was vital for the patients' experience of quality and benefit. 2) "*Professional care and compassion"*, which were considered by the patients as the most fundamental contextual factors to facilitate their self-care. 3) "*Social relations and interactions between patients", r*eflecting the patients experience of feeling recognized by other patients and to experience common understanding. 4) "*An individually planned rehabilitation stay, but challenges regarding shared decision making*". The patients felt the rehabilitation was individually planned, but with room for improvement in relation to awareness of shared decision-making. 5) "*Rehabilitation as a personal process but problems with transferability to everyday life*". The patients experienced the rehabilitation stay as a part of a personal rehabilitation process, but expressed concerns about whether they were able to transfer new learning and habits to everyday life.
Conclusion: Patients with rheumatic diseases experience in-patient rehabilitation as a sanctuary, with rehabilitation at three levels; through multidisciplinary rehabilitation interventions at the hospital; through recognition from the multidisciplinary staff and through recognition, social relationships and interactions with fellow patients. There is a need for improved coordination of rehabilitation across primary and secondary health care, in order to ease transferal to the patients' everyday life.

REFERENCES:

[1] Dreyer PS, Pedersen BD. Distanciation in Ricoeur's theory of interpretation: narrations in a study of life experiences of living with chronic illness and home mechanical ventilation. Nurs Inq. 2009;16(1):64-73.

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THU0704-HPR PATIENT ACTIVATION AND ADHERENCE TO BIOLOGICAL THERAPY AND TARGETED SYNTHETIC DMARD: PRELIMINARY RESULTS:

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Background: Medication non-adherence has been associated with treatment failure in chronic inflammatory conditions. A positive relationship between patient activation and adherence to treatment and between activation and improved clinical outcomes has been shown for chronic conditions.
Objectives: To measure adherence to biological therapies and targeted synthetic DMARD (tsDMARD), and their relationship with the Patient Activation Measure (PAM) and with patient and therapy related factors, for chronic inflammatory arthropathies.
Methods: Cross-sectional observational descriptive study in a general tertiary university hospital.
Patients on treatment with the same biological drug (subcutaneous; phase 1) or tsDMARD (oral; phase 2) for ≥6 months were included in order of arrival and those with mental disability, which prevented understanding of the study, were excluded.
Demographic variables (sex, age, living environment, educational level), diagnosis and treatment were collected. Adherence was measured using the Simplified Medication Adherence Questionnaire (SMAQ) for biological therapies, the Compliance Questionnaire Rheumatology (CQR-19) for tsDMARD, and the medication possession ratio (MPR). Patients were considered adherent if MPR≥80% and CQR-19≥80% or adherent SMAQ. To measure activation, PAM questionnaire, was used. Patients were classified as activated or not activated.
Statistical analysis: relationship between adherence to treatment and PAM was analyzed using chi-square, considering significance level p <0,05. Statistical analysis was performed with spss v17.0.
Results: A total of 58 patients (57% women) were included. Mean age was 54 years (95% CI: 50 to 57), 86% lived in urban areas, 40% had completed elementary education, 31% high-school and 24% university studies.
Distribution by diagnosis: rheumatoid arthritis (81%), ankylosing spondylitis (14%) and psoriatic arthritis (5%). Distribution by treatment was: baricitinib (31%), tofacitinib (18%), adalimumab (16%), tocilizumab (14%), etanercept (12%), secukinumab (7%) and golimumab (3%). Median time of disease duration was 9 years (IQR 13) and time on treatment with the drug was 8 months (IQR 20), with significant differences between groups (27 (biological therapy) vs 7 months (tsDMARD)).
The proportion of adherent patients was 43%, being higher among tsDMARD (57%) vs biological treated ones (30%), with significant differences.
72% of patients were activated, being more activated biological (80%) than tsDMARD (67%) treated patients.
A higher adherent proportion of patients was found among the activated patients (48%) compared to the non-activated ones (27%) in all measures, even though the differences were not statistically significant.
Conclusion: Patients treated with biological therapies and tsDMARD have a high degree of activation for the self-management of their disease and its treatment. Adherence to treatment may be influenced by route of administration, type of drug (oral/tsDMARD 57% vs. subcutaneous/biological 30%) and time on treatment (longer time on treatment, lesser adherence).
The greater proportion of adherence found among patients with a higher degree of activation could indicate a positive relationship between activation and adherence, so analyzing and promoting patient activation seems important in order to improve adherence to drugs.
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THU0705-HPR PELVIC FLOOR AND SEXUAL DYSFUNCTION IN WOMEN WITH SJOGREN SYNDROME

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Background: Sjogren syndrome (SS) is a systemic autoimmune disease causing secretory gland dysfunction. This leads to dryness of the mainly salivary and lacrimal glands such as the mouth, eyes, nose, larynx, and vagina. The disease overwhelmingly affects middle aged women. These women have symptoms of decreased lacrimal and salivary gland function which usually precede involvement of other exocrine glands such as the upper airway, the gastrointestinal tract and the external genitalia (dyspareunia). Although genital tract symptoms are common in patients with sjogren, such as vulvar and vaginal dryness, dyspareunia, and pruritus, their pelvic floor health and functions have been rarely evaluated.
Objectives: The aim of study was investigation of pelvic floor and sexual dysfunction in patients with SS.
Methods: 23 patients with SS with an average age of 49.00±8.71 were included in the study. Pelvic floor dysfunction of patients with SS were evaluated by the Pelvic Floor Impact Questtionare-7 (PFIQ-7) and Pelvic

Floor Distress Inventory-20 (PFDI-20) and sexual dysfunction were evaluated by Pelvic Organ Prolapsed/Urinary Incontinence Sexual Questionnaire (PISQ-12).

Results: PFIQ-7 total score was 27.14±27.73 (UIQ-7: 17.07±17.88, CRAIQ-7: 7.43±10.14, POPIQ-7: 2.32±5.00);, PFDI-20 total score was 116.36±34.00 (POPDI-6:31.48±8.29, CRADI-8: 35.59±15.73, UDI-6:49.00 ±16.56) and PISQ-12 total score was 16.78±5.71.

Conclusion: According to the results of the study, patients with SS had pelvic floor dysfunction and sexual dysfunction. This study showed that pelvic floor and sexual functions of patients with SS have been negatively affected. Therefore these functions need to be routinely assessed by health professionals. Further studies need to recommend pelvic health physiotherapy and educational programme about pelvic floor dysfunction.

REFERENCES:

[1] Both, T., Dalm, V. A., van Hagen, P. M., & van Daele, P. L. (2017). Reviewing primary Sjögren's syndrome: beyond the dryness-From pathophysiology to diagnosis and treatment. International journal of medical sciences, 14(3), 191.

[2] Mavragani, C. P., & Moutsopoulos, H. M. (2010). The geoepidemiology of Sjögren's syndrome. Autoimmunity reviews, 9(5), A305-A310.

[3] Maddali Bongi S, Del Rosso A, Orlandi M, et al. Gynaecological symptoms and sexual disability in women with primary Sjogren's syndrome and sicca syndrome. Clin Exp Rheumatol 2013;31:683–90

[4] Priori, R., Minniti, A., Derme, M., Antonazzo, B., Brancatisano, F., Ghirini, S.,. .. & Framarino-dei-Malatesta, M. (2015). Quality of sexual life in women with primary Sjögren syndrome. The Journal of rheumatology, jrheum-141475.

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THU0706-HPR THERE IS ASSOCIATION BETWEEN THE LEVEL OF PHYSICAL ACTIVITY AND QUALITY OF LIFE OF WOMEN WITH FIBROMYALGIA?

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Background: Patients with fibromyalgia frequently present physical and mental symptoms associated with typical pain such as generalized fatigue, sleep disturbances, anxiety, depression and cognitive impairment. Moderate physical exercise is an alternative to promote health benefits of fibromyalgia patients, through the obstacles imposed by the symptomatology of this pathology.

Objectives: This study aimed to verify the association between the level of physical activity and quality of life of women with fibromyalgia.

Methods: It is a cross-sectional study with 177 women (42.1 ± 8.6 years) diagnosed with fibromyalgia registered in the Unified Health System (SUS) in the city of Maringá, PR, Brazil. The instruments used were: International Physical Activity Questionnaire (IPAQ) to assess the level of physical activity; Fibromyalgia Impact Questionnaire (FIQ) to assess the impact of fibromyalgia on quality of life; WHOQOL-Bref to assess overall quality of life in four domains. Data analysis was conducted through Mann-Whitney test, Spearman correlation and Structural Equation Analysis ($p<0.05$).

Results: The sample consisted of a greater proportion of women aged between 40 and 49 years (37.9%). There was a higher proportion of women with active/very active level of activity (62.1%), 20.4% with sedentary status and 17.5% with irregular activity. Fibromyalgia had a moderate impact on the quality of life of women with fibromyalgia (76.5) evaluated by FIQ. The results showed positive associations between the level of physical activity and the quality of life domain in WHOQOL-Bref, with a significant difference in all domains of quality of life: physical (p=0.007), psychological (p=0.007), social relations (p=0.012) and environment (p=0.012), with higher scores among the very active/active.

Conclusion: This study shows that the level of active/active activity is a positive factor in all areas of quality of life in women with fibromyalgia and the impact of this disease on the quality of life is moderate. There is evidence of the need to maintain an active lifestyle independent of symptomatology and incapacitating conditions in these cases. Above all, this information can help professionals who care for fibromyalgic patients about measures of maintenance of health and well-being.

REFERENCES:

[1] Matsudo S, Araújo T, Matsudo V, Andrade D, Andrade E, Oliveira LC, et al. International Questionnaire on Physical Activity (Ipaq): Study of Validity and Reproducibility in Brazil. Revista Brasileira de Atividade Física & Saúde, 2001;6(2):5-18.

[2] Marques AP, Santos AMB, Assumpção A, Matsutani LA, Lage LV, Pereira CAB. Validation of the Brazilian version of the Fibromyalgia Impact Questionnaire (FIQ). Revista Brasileira de Reumatologia, 2006; 46(1):24-31.

[3] Almeida Fleck MP. The World Health Organization quality of life assessment tool (WHOQOL-100): characteristics and perspectives. Ciência & Saúde Coletiva, 2000;5(1):33-38.

[4] Fleck MP, Louzada S, Xavier M, Chachamovich E, Vieira G, Santos L, et al. Application of the Portuguese version of the abbreviated quality-of-life assessment instrument "WHOQOL-bref". Revista de Saúde Pública. 2000;34(2):178-183.

[5] Chachamovich E, Fleck MP, Trentini C, Power M. Brazilian WHOQOL-OLD Module version: a Rasch analysis of a new instrument. Revista de Saúde Pública, 2008;42(2):308-316.

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THU0707-HPR FOLLOW-UP CARE FOR PATIENTS WITH ESTABLISHED INFLAMMATORY JOINT DISEASES – A FOCUS GROUP STUDY ON PATIENTS' EXPERIENCES FROM REFRAIMING THE ORGANIZATIONAL SUPPORT FOR INCREASED PATIENT INVOLVEMENT

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Background: Internationally, a Treat-to-Target strategy for proactive management of inflammatory joint diseases (IJD) is recommended.[1,2] This includes continuous monitoring of the arthritis, which covers symptoms and the significance of the disease for everyday life.[2,3] Control of disease activity has traditionally been ensured with fixed outpatient visits to rheumatologists. [4] However, in general there is a growing interest to involve patients in the control and treatment of their own disease.

Open Assess in our outpatient clinic was implemented during October 2016 to respond to fluctuating needs among the patients with established IJD. Patient participation in Open Assess were primarily patient-initiated. They were expected to respond to symptoms and other disease-, and treatment-related needs. In addition, two half-yearly planned visits were offered patients: 1) An a*nnual traditional medical consultation with a rheumatologist*, and 2) A new *Annual* c*onsultation with an experienced registered rheumatology nurse (RRN).*

Objectives: To explore how people with established IJD in stable phase, experience Open-Access as a way to involve patients in their own disease and treatment.

Methods: We conducted a qualitative study based on four semi-structured focus group interviews among patients with established inflammatory joint disease (Rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriasis arthritis (PsA)) participating in the Open Access set-up. The analysis of the transcribed interviews was based on content analysis. A patient research partner was involved in all phases of the study.

Results: In total 25 patients with IJD participated (20 female (80%), mean age 61.8 (range 28-79)) with RA (n=20), PsA (n=3), axSpA (n=1) and polyarthritis (n=1) participated. We identified three themes. ***Changes in follow-up care do not affect patients' perceived support in disease control,*** referring to patient's perception of more time available to both themselves and health professionals, as well as trust in access to professional support whenever needed. ***Adequate information to act within a new patient role,*** reflecting patients' uncertainty in the transition to Open Access combined with confusion about distribution of responsibilities in the new set-up. ***Arthritis in a broader perspective,*** expanding patients understanding of their illness by interaction over time with both a rheumatologist and a rheumatology nurse in a focused dialogue to involve the patient in managing their own health.

Conclusion: Patients following Open-Access welcome the flexibility and involvement in disease control. However, patients need relevant information to be able to act adequately to the new patient role. Interacting with both rheumatologists and nurses, combined with sufficient time for dialogue, broaden patients' perspective, make opportunities for action visible, and contribute to patient's ability to participate in the managing of their own condition.

REFERENCES:

[1] Smolen JS, et al. Treating spondyloarthritis, including ankylosing spondylitis and psoriatic arthritis, to target: recommendations of an international task force. Ann Rheum Dis 2014
[2] Smolen JS, et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. Ann Rheum Dis 2016
[3] Bykerk VP, et al. Flares in rheumatoid arthritis: frequency and management. A report from the BRASS registry. J Rheumatol 2014
[4] Combe B, et al. 2016 update of the EULAR recommendations for the management of early arthritis. Ann Rheum Dis 2017

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THU0708-HPR CORRELATIONS BETWEEN FATIGUE AND PATIENT REPORTED OUTCOME IN PEOPLE WITH INFLAMATORY ARTHRITIS

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Background: Fatigue is one of the most common symptoms of people with inflammatory arthritis (IA) and often rated as high as or higher than pain. However, it remains unexplored how fatigue is associated with patient related outcomes (PRO) such as work impairment, quality of life, sleep, depression, physical functioning and pain.
Objectives: To explore fatigue and to analyze possible correlations between fatigue and PROs in people with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA).
Methods: A cross-sectional study. People ≥18 years with a confirmed diagnosis of RA, PsA or axSpA were consecutively recruited for the study over a 6-month period via routine visits to outpatient rheumatology clinics in two hospitals departments. Trained study nurses collected information on informed consent, diagnosis, medical treatment and disease activity status. Fatigue was evaluated by a self-completed questionnaire using the FACIT-Fatigue sub-scale. The questionnaire also included the following PRO scales: Work Productivity and Activity Impairment scale (WPAI), EuroQol (EQ-5D), Medical Outcomes Study Sleep Scale (MOS), Major Depression Inventory (MDI), and Health Assessment Questionnaire (HAQ) on quality of life and pain. Data was analyzed in SAS. Correlations were assessed by a) Pearson correlation coefficients and b) raw and adjusted linear regressions.
Results: In total 633 persons were invited and 487 (77%) (mean age=53.5, SD 14.5) were included (62% women). The mean fatigue score (range 0-52; lower = more fatigued) was 34.3 (SD 11.1) and there was no statistically significant difference between mean fatigue in the three diagnostic groups (p=0.08). Altogether 61% expressed that they were suffering from fatigue (i.e. had a FACIT-Fatigue sub-scale ≤39). Women generally had a lower overall fatigue score (mean=33.3, SD 11.1) than men (mean=36.0, SD 11.0). Fatigue did not differ between age groups (p=0.33). Those who had changed medical treatment within 0-12 months (21.1%) suffered more from fatigue than those with unchanged treatment (mean=30.1, SD 11.7 vs. mean=35.4, SD 10.7, p<0.0001). The average disease activity as indicated by DAS28, BASDAI and BASFI showed low disease activity in the cohort. Current medical treatment (csDMARDs and/or bDMARDs or none) was not associated with severity of fatigue (p=0.85). Fatigue correlated with all PROs (Pearson correlation coefficients, all p-values <0.0001) (Table 1). Increased work impairment, sleep problems, depression, and pain were all associated with increased fatigue, whereas decreased quality of life and physical functioning were associated with increased fatigue (raw and adjusted linear regressions). The associations did not change significantly after additional adjustment for socioeconomic factors. Analyses stratified on type of disease did not differ significantly from the primary non-stratified analysis.

Table 1. Pearson correlations between fatigue (measured by FACIT-F) and PROs

	Pearson correlation coefficient	p-value	N
Work impairment (WPAI)	-0.6359	<0.0001	280
QoL (EQ-5D)	0.7010	<0.0001	487
Sleep (MOS sleep scale)	0.7009	<0.0001	481
Depression (MDI)	-0.7502	<0.0001	483
Physical Functioning (HAQ)	-0.3789	<0.0001	483
Pain (VA)	-0.6118	<0.0001	482

Note: Pearson correlation coefficients range from -1 to 1. A Pearson correlation coefficient of more than 0.80 or less than -0.80 indicates a strong correlation, a coefficient of 0.40 to 0.80 or -0.40 to -0.80 indicates a moderate correlation, and a coefficient below 0.40 or more than -0.40 indicates a weak correlation

Conclusion: Despite the study cohort represents a stable group with low disease activity, fatigue was a frequently expressed symptom across diagnoses. There was a significant correlation between fatigue and the other PROs why fatigue cannot be seen as a single problem, but rather a symptom that broadly affects people living with inflammatory arthritis.
Disclosure of Interests: Bente Appel Esbensen Speakers bureau: For Pfizer, Sandra Elkjær Stallknecht Consultant for: Paid by Pfizer to work on this and other studies, Maria Madsen Consultant for: Paid by Pfizer to work on this and other studies, Lise Hagelund Shareholder of: Pfizer, Employee of: Pfizer, Trine Pilgaard Shareholder of: Pfizer, Employee of: Pfizer

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THU0709-HPR PERSONS WITH POLYMYOSITIS AND DERMATOMYOSITIS EXPERIENCE REDUCED WORK ABILITY AND QUALITY OF LIFE

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Background: A recent study have described that persons with Polymyositis (PM) and Dermatomyositis (DM) experience reduced work ability (1). Information about whether the reduced work ability affect quality of life is lacking.
Objectives: To describe self-rated work ability with two different assessment and quality of life in persons with PM and DM. To investigate correlations between self-rated work ability and quality of life
Methods: Participants were identified through the Swedish Myositis Network registry (SweMyoNet). Of 78 possible participants, 48 agreed to participate in this study. The median (IQR) age were 57 (45-61) years with a median disease duration of 6 (2-14) years. Fifty-three percent of the participants were women. Seventy-seven percent were working, and the remaining were on sick-leave.
Self-rated work ability was measured by the questionnaire Work Ability Index (WAI) and the Work Ability Score (WAS) which is a single item question. Quality of life by the SF-36.
Results: Self-rated work ability measured by WAI in persons with PM and DM varied between poor work ability and good work ability. The median value of the group was 34 which indicates less good work ability.
Self-rated work ability measured by WAS varied between poor work ability and good work ability. The median of the total group indicates less good work ability.
There was a strong correlation between self-rated work ability measured by WAI and WAS
(rs 0,879 p=0,01).
Quality of life measured by SF-36 were rated lower in persons with PM and DM when compared to the general population in dimensions; Physical Function, Role-Physical, General Health, Vitality and Social function (p≤0.02).
There were moderate to high correlations between self-rated work ability measured by both WAI and WAS, and all dimensions of SF-36 (p<0.01)
Conclusion: Persons with PM and DM self-rated their work ability as poor and the quality of life were significantly reduced when compared to the general population. The measures WAI and WAS correlates highly with each other and revealed comparable results indicating that WAS may work as well as WAI as a screening tool to identify reduced work ability. The WAS may also be more feasible with just one single question to use in clinical practice. Our results indicate the importance to measure self-rated work ability in persons with PM and DM in clinical practice.

REFERENCES:
[1] M. Regardt, I. E. Lundberg, et al. Work ability in patients with polymyositis and dermatomyositis: an explorative and descriptive study. Accepted for publication Work 2015;53:265-77.

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THU0710-HPR IMPACT OF SPONDYLOARTHRITIS ON FAMILY AND SOCIAL LIFE IN TUNISIAN PATIENTS

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Background: Spondyloarthritis (SA) is a chronic inflammatory disease that could significantly affects the patient's quality of life and alter the social activities and relationship.
Objectives: Here, we aimed to investigate the impact of spondyloarthritis on quality of the social and family life in Tunisian patients.
Methods: This is a cross sectional study including patients with SA (ASAS criteria). A survey comprising questions about family and social relations and the impact of flare on it, were applied between November 2018 and January 2019. Demographic data, marital status, the disease activity (BASDAI and ASDAS) and the function index (BASFI) were obtained. For statistical analysis, we used Khi^2-test for qualitative variables and Student-test for quantitative variables. A p value ≤0.05 was considered significant.
Results: We included forty patients. The average age was 41 years-old (±12.9) and the sex ratio was 12.3. 60% of patients were married. The SA was axial in 25%, peripheral in 20% and both in 55%. 17.5% had psoriatic arthritis, 55% had ankylosing spondylitis and 27.5% had inflammatory bowel disease spondyloarthritis. coxitis was found in 47.4% of patients. Most of patients had a moderat activity (29.4%) and the mean activity scores were :(BASDAI =2.75±2.3, ASDAScrp=2.24±1.07), and the mean function index (BASFI) was 2.57±2.5. 57.5% of patients were on biologics (25% Adalimumab, 22.5% infliximab, 10% Etanercept).
67.5% of patients declared having difficulty in accepting their illnesses. Social relationship were deteriorated after the diagnosis of SA in: 27.5% with partners and 20% family members, 15% with friends and 20% with colleagues in work. Moreover, SA reduced the frequency of social activities like sport in 62.5%, traveling in 62.5%, cultural activities in 77.5% and sex practice in 37.5%.
The impact of flares was also evaluated, the patients declared having difficulties in: crossing the street (57.5%), corporal hygiene (30%), sleeping (70%), private life (32.5%) and doing daily tasks (77.5%) and professional activity (81.8%).
No significant relationship was found between social relationship and activities regarding biologic treatment (p=0.74, p=0.68). However presence of coxitis was significantly associated with a lack of friends (p=0.05), and a bad impact in the professional activities (absenteeism and drop job performance) (p=0.05) and the self-esteem (p=0.06).
Conclusion: Our results suggest that family and social relations are deteriorated in Tunisian SA patients due to their illness. Moreover, coxitis has substantial impact on the self-esteem and the social life.
Disclosure of Interests: None declared
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THU0711-HPR COMPARISON OF FEMALE SEXUAL FUNCTION INDEX IN PATIENTS WITH RHEUMATOID AND PSORIATIC ARTHRITIS AND HEALTHY CONTROLS

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Background: Alteration in sexual functioning is not well understood in rheumatoid arthritis (RA) and psoriatic arthritis (PsA). A review of the limited current literature suggests that decreased sexual function in female RA patients is common (Zhang et al., 2018). Although RA and PsA differ in presentation and patient experience, literature regarding sexual health of female PsA patients is lacking. The Female Sexual Function Index (FSFI) is a validated and reliable self-reporting tool to assess sexual function in women within six domains: desire, subjective arousal, lubrication, orgasm, satisfaction, and pain (Rosen, et al., 2000).
Objectives: The purpose of this study was to identify and compare the FSFI of three female populations: RA, PsA, and healthy individuals.
Methods: Convenience sampling was used for this descriptive correlational study to recruit 50 female RA patients, 33 female PsA patients, and 25 healthy females for the control group between June to September 2018. Data collection was obtained using questionnaires and a review of the medical record including demographic characteristics, the validated FSFI, medication history, pain score, patient global, Health Assessment Questionnaire (HAQ), and laboratory data. Data was analyzed using ANOVA test with Tukey's post-hoc to determine if any differences exist for FSFI scores based on diagnosis. Analysis was run twice, initially for all participants, and secondly removing the participants who reported not having had sex within the last month.
Results: The mean age of the RA patients was 53.1 ±11.8, PsA patients was 51.6 ± 13.7, and healthy controls was 37.4 ± 10.4. Controls were significantly younger than RA (p <.001) and PsA patients (p =.002).
Data including all participants: Based on the total sexual functioning cutoff score of 26.55, 68% of RA female patients (34/50), 67% of PsA females patients (22/33), and 44% of healthy controls (11/25) met the criteria for sexual dysfunction.
Data excluding participants who reported not having had sex in the past month: Controls had significantly higher FSFI scores than the RA patients across all six domains (p≤0.001) and the overall score (p<0.001). Controls had significantly higher FSFI scores than the PsA patients across four of the six domains (p≤0.026) and the overall score (p=0.008). There were no statistically significant differences between the RA and PsA group.
Conclusion: These findings demonstrate that decreased sexual functioning is more common in patients with RA and PsA when compared to a control group. All female patients with RA and PsA should be screened for sexual dysfunction.

REFERENCES:
[1] Rosen, R,. Brown, C., Heiman, J., Leiblum, S., Meston, C., Shabsigh, R., Ferguson, D., & D'Agostino, R. (2000). The Female Sexual Function Index (FSFI): A multidimensional self-report instrument for the assessment of female sexual function. *Journal of Sex &Marital Therapy,* 26(2), 191-208. doi: 10.1080/009262300278597
[2] Zhang, Q., Zhou, C., Chen, H., Zhao, Q., Li, L., Cui, Y., & Shen, B. (2018). Rheumatoid arthritis is associated with negatively variable impacts on domains of female sexual function: Evidence from a systematic review and meta-analysis. *Psychology*, Health & Medicine, 23(1), 114-125. doi: 10.1080/13548506.2017.1338738

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THU0712-HPR QUALITY OF LIFE OF PATIENTS WITH MULTIPLE SCLEROSIS AND SYSTEMIC SCLEROSIS SUBMITTED TO HSCT: A COMPARATIVE AND LONGITUDINAL STUDY

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Background: Multiple Sclerosis (MS) and Systemic Sclerosis (SSc) are chronic autoimmune diseases that comprise physical and psychological aspects. Disease progression is usually associated with a continuous decline in quality of life. In this devastating scenario, hematopoietic stem cell transplantation (HSCT) has emerged as an alternative treatment, improving physical outcomes and, at the same time, restoring a more normal life. Quality of life evaluations may be used to measure the effects of therapeutic interventions, considering their impact on patient life in the medium and long term.
Objectives: To evaluate the impact of HSCT on the Quality of Life (QoL) of SSc (G1) and MS (G2).
Methods: In this comparative, longitudinal, cross-sectional study, 56 patients (22 SSc and 34 MS) were included. The Medical Outcomes Study Short-Form 36 (MOS SF-36) scale, used for data collection, mainly assesses the physical health component (PHC) and the mental health component (MHC). The PHC encompasses the following domains: physical functioning (PF), role limitations due to physical problems (RPF), bodily pain (P) and general health perceptions (GHP). The MHC comprises: vitality (VIT), social functioning (SRF), role limitations due to emotional role functioning (ERF) and general mental health (MH). The results of each domain range from 0 to 100, where zero represents the worst and

100 the best state of health. Data were collected at admission and at 2-years after transplantation. Results underwent statistical analysis. Significance levels were established at p<0.05.
Results: The study included intragroup comparisons (Pre *vs* post-HSCT; Table 1) and intergroup comparisons (G1 *vs* G2; Table 2)

Abstract THU0712HPR Table 1. - Mean and median scores of SF-36 domains, before and after HSCT in G1 (n = 22) and G2 (n = 34)

Domain	G1 Pre-HSCT			G1 Post-HSCT			p-value
	Mean	SD	Median	Mean	SD	Median	
PF	41.3	33.9	35	67.2	28.4	85	0.008
RPF	23.8	40.4	0	42.3	30.0	50	0.008
P	46.8	32.9	46.5	71.1	25.9	67.3	0.013
GHP	52.2	27.0	55	66.6	14.3	67	0.03
VIT	55.2	30.1	60	67.2	20.3	75	0.27
SRF	20.3	23.2	62.5	68.5	27.6	68.7	0.60
ERF	54.5	45.4	50	54.5	41.8	33.8	0.96
MH	59.4	24.5	64	64.6	23.8	68	0.47
Domain	**G2 Pre-HSCT**			**G2 Post-HSCT**			**p-value**
	Mean	SD	Median	Mean	SD	Median	
PF	29,71	28,44	20	50,15	29,81	60	0.0003
RPF	19,85	30,01	0	39,71	33,78	25	0.0003
P	69,68	28,89	74	83,97	24,13	100	0.0007
GHP	68,88	18,3	67	85,97	16,78	97	0.0006
VIT	57,94	18,14	55	71,91	17,97	75	0.0004
SRF	48,97	32,57	50	71,69	24,1	75	0.0003
ERF	45,09	44,85	33,3	65,67	40,61	83,3	0.0187
MH	72,18	15,89	75	79,65	19,07	84	0.0006

Abstract THU0712HPR Table 2. – Comparison of the mean scores of SF-36 domains, in G1 (n = 22) and G2 (n = 34), before and at 2 years after HSCT

Domain	Pre-HSCT			Post-HSCT		
	Mean G1	Mean G2	p-value	Mean G1	Mean G2	p-value
PF	41.3	29,71	0.030	67.2	50,15	0.403
RPF	23.8	19,85	0.904	42.3	39,71	0.155
P	46.8	69,68	0.056	71.1	83,97	0.043
GHP	52.2	68,88	0.081	66.6	85,97	0.0001
VIT	55.2	57,94	0.912	67.2	71,91	0.337
SRF	20.3	48,97	0.779	68.5	71,69	0.156
ERF	54.5	45,09	0.412	54.5	65,67	0.357
MH	59.4	72,18	0.258	64.6	79,65	0.004

In the intragroup analyses, comparing pre and post-HSCT scores, there was general improvement in both disease groups, especially in G2. The intergroup comparisons indicate that before HSCT patients in G1 had better FP than those in G2 (p = 0.03). The other aspects were not significantly different between groups. After HSCT, patients in G2 had a better QoL scores in P (p = 0.4338), GHP (p = 0.0001) and MH (p = 0.0049).
Conclusion: These results may be interpreted as positive outcomes of HSCT for MS and SSc. However, our data indicate that HSCT may benefit patients with MS (G2) more than those with SSc (G1).

REFERENCES:

[1] Guimarães FAB, et al. Impact of autologous HSCT on the quality of life of patients with multiple sclerosis. Arquivos de Neuro-Psiquiatria, v. 68, p. 522-527, 2010.

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THU0713-HPR LINKING THE PATIENT EXPERIENCE OF FOOT INVOLVEMENT RELATED TO PSORIATIC ARTHRITIS TO THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH

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Background: Previous research has shown merit in linking domains of impact in psoriatic arthritis (PsA) to the International Classification of Functioning, Disability and Health (ICF) to categorise the effect of global disease [1, 2]. Localised disease predominance and persistence in the foot in PsA is well recognised [3], but limited foot-specific research exists and there are no outcome measures to comprehensively assess foot involvement and its impact in PsA. To date little is known about the patient experience of foot involvement and how this may link to the ICF to capture disease impact.
Objectives: To categorise the patient experience of PsA-related foot problems by linking it to the ICF.
Methods: Participants were recruited from rheumatology outpatient clinics in Sydney, Australia and Auckland, New Zealand. People with PsA were interviewed about their foot problems and the impact they have on daily living until qualitative data saturation. Three multi-disciplinary focus groups were undertaken with clinicians to explore their understanding of the patient experience. All interviews were audio-recorded and transcribed. Codes, representing concepts obtained from the interviews, were linked to the most appropriate ICF category according to established linking rules. All codes were independently linked to the ICF by 2 investigators and a third investigator for adjudication. Investigator professional backgrounds included occupational therapy and podiatry.
Results: Twenty-one people with PsA-related foot problems and 17 experienced clinicians participated. Over 100 distinct ICF categories were linked to the interview and focus group codes. The most represented ICF category was environmental factors (33%) followed by body functions (26%), activities and participation (25%) and body structure (16%). Environmental factors relevant to patients were shoes and assistive devices, healthcare access and climate. Clinicians identified a greater proportion of body functions and fewer activity and participation categories compared with patients, indicating a possible mismatch of key concerns. Concepts that could not be precisely linked to the ICF were related to coping, aspects of time and knowledge, consistent with previous work. Difficulties in linking highly specific information to categories such as sensations of pain, sensations of skin and emotional functions revealed a limitation in the ICFs ability to discriminate between various effects of the disease, a shortfall previously noted. Toenail changes were frequently cited by patients and linked to domains of body image and social relationships. Interdisciplinary group analysis demonstrated merit as differences between the predominantly medical approach by podiatry and psychosocial approach by occupational therapist in clinical practice led to additional ICF categories being identified between clinicians, which mostly related to cognitive functions.
Conclusion: Despite the localised anatomical focus of this study, the effect of foot problems in PsA was linked to all components of the ICF, confirming the profound impact on functioning and daily life. Difficulties with linking psychological concepts reflect deficiencies in the ICF and is a major limitation in defining foot disease burden. These findings offer new knowledge using patient and clinician perspectives that could inform the development of an instrument to measure the impact of foot involvement in PsA.

REFERENCES:

[1] Gudu T, et al. J Rheumatol. 2017;44(2):193-200.
[2] Taylor WJ, et al. J Rheumatol. 2010;37(9):1885-91.
[3] Hyslop E, et al. Ann Rheum Dis. 2010;69:928.

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THU0714-HPR RELATIONSHIP BETWEEN TRUNK POSITION SENSE, TRUNK MUSCLE ENDURANCE AND BALANCE IN WOMEN WITH FIBROMYALGIA SYNDROME

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Background: Position sense plays a fundamental role in human movement which is crucial for daily activities, exercise and sports [1]. Trunk endurance and balance were also integrated part of normal functional movements. Decreased balance and trunk muscle endurance were reported in women with fibromyalgia syndrome (FMS) [2]. However, to our knowledge, the relationship between trunk position sense, trunk muscle endurance and balance has not been studied in women with FMS.
Objectives: This study aimed to determine the relationship between trunk position sense, trunk muscle endurance and balance in women with FMS.
Methods: Women with FMS (n: 25, age: 42.88±11,66 years, body mass index: 25.69±3.48 kg/m²) were recruited. Trunk position sense was assessed with digital inclinometer by trunk reposition errors in which higher scores indicates poor trunk position sense [3]. Trunk flexor, extensor, dominant and non-dominant lateral side muscle endurance with McGill's trunk muscle endurance tests [4] in seconds and balance with the Mini-Balance Evaluation Systems Test (Mini BEStest) [5] were assessed. Spearman's rank correlation test was used for analysis.
Results: There were significant negative correlations between trunk position sense and trunk flexor, extensor, dominant and non-dominant lateral side muscle endurance (r=-0.61, p=0.001; r=-049, p=0.011; r=-0.048, p=0.014; r=-0,048, p=0.014, respectively). There were also high significant negative correlations between trunk position sense and Mini BEStest score (r=-0.73, p<0.001).

Conclusion: It was found that there were moderate to high correlations between trunk position sense, trunk muscle endurance and balance. Therefore, addition of trunk position sense training to the rehabilitation programs might be effective in improving trunk muscle endurance and balance in women with FMS.

REFERENCES:

[1] Han J, Waddington G, Adams R, Anson J, Liu Y (2016) Assessing proprioception: a critical review of methods. Journal of Sport and Health Science 5 (1):80-90
[2] ÇELENAY ŞT, KÜLÜNKOĞLU BA, KÜÇÜKŞAHİN O Fibromiyalji Sendromu Olan Kadınlarda Denge, Endurans ve Esnekliğin Değerlendirilmesi. Türk Fizyoterapi ve Rehabilitasyon Dergisi 28 (3):125-131
[3] Goldberg A, Hernandez ME, Alexander NB (2005) Trunk repositioning errors are increased in balance-impaired older adults. The journals of gerontology Series A, Biological sciences and medical sciences 60 (10):1310-1314
[4] McGill SM, Childs A, Liebenson C (1999) Endurance times for low back stabilization exercises: clinical targets for testing and training from a normal database. Arch Phys Med Rehabil 80 (8):941-944
[5] Horak FB, Wrisley DM, Frank J (2009) The Balance Evaluation Systems Test (BESTest) to differentiate balance deficits. Physical therapy 89 (5):484-498. doi:10.2522/ptj.20080071

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THU0715-HPR ASSESSMENT OF SELF-CARE AGENCY AND ITS ASSOCIATION WITH SYMPTOMS AND QUALITY OF LIFE IN INDIVIDUALS WITH FIBROMYALGIA: A CROSS-SECTIONAL STUDY

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Background: Fibromyalgia is a condition of high prevalence, which causes physical discomfort, mental distress and impairment of social relationships. Self-care may be a relevant factor to improve the quality of life in individuals with fibromyalgia, since it is related to the act of empowerment, leading individuals to have dominion over their own life.
Objectives: To assess self-care agency of individuals with fibromyalgia and verify its association with symptoms, quality of life and sociodemographic variables.
Methods: The study included 40 women, aged between 19 and 59 years, with fibromyalgia according to the 2010 American College of Rheumatology diagnostic criteria, and elementary education. This study was approved by the Research Ethics Committee of the School of Medicine of the University of Sao Paulo. Informed consent was obtained from all study participants. Sociodemographic and clinical data (age, civil status, educational level, social status and disease duration) were collected. Self-care was measured with the Appraisal Self-Care Agency Scale-Revised, pain with the Visual Analog Scale (VAS) and the Widespread Pain Index (WPI), severity of symptoms with the Symptom Severity (SS) Scale, and quality of life with the Revised Fibromyalgia Impact Questionnaire (FIQR). In data analysis, Pearson correlation coefficient was used for parametric data, and the Spearman correlation coefficient was used for non-parametric data. The level of significance adopted was 5%.
Results: Moderate values were found for self-care agency (52,75 ± 10,25), VAS pain (5,84 ± 2,16), WPI (13,32 ± 3,78) and SS (9,30± 1,68). Severe impact on quality of life was found with the FIQR (63,98 ± 17,26). Additionally, significant correlations of self-care agency with social status (r=0,391), function (r=-0,338), overall impact (r=-0,315), symptoms domains (r=-0,332) and total score (r=-0,375) of the FIQR were observed.
Conclusion: The study suggests that individuals with fibromyalgia have a moderate level of self-care agency, and there is a weak association of self-care with quality of life and social status.

REFERENCES:

[1] Bennett RM, Friend R, Jones KD, Ward R, Han BK, Ross RL. The Revised Fibromyalgia Impact Questionnaire (FIQR): validation and psychometric properties. Arthritis Res Ther. 2009;11(4):R120.
[2] Bennett RM, Bushmakin AG, Cappelleri JC, Zlateva G, Sadosky AB. Minimal clinically important difference in the fibromyalgia impact questionnaire. J Rheumatol. 2009;36(6):1304-11.
[3] Boonstra AM, Schiphorst Preuper HR, Balk GA, Stewart RE. Cut-off points for mild, moderate, and severe pain on the visual analogue scale for pain in patients with chronic musculoskeletal pain. Pain. 2014;155(12):2545-50.
[4] Damasio BF, Koller SH. The Appraisal of Self-Care Agency Scale - Revised (ASAS-R): adaptation and construct validity in the Brazilian context. Cadernos de Saúde Pública. 2013;29(10):2071-82.
[5] Fleiss JL. The design and analysis of clinical experiments. 1st ed. New York Wiley; 1986.
[6] Marques AP, Assumpcao A, Matsutani LA, Pereira CAB, Lage L. Pain in Fibromyalgia and Discriminative Power of the Instruments: Visual Analog Scale, Dolorimetry and the Mcgill Pain Questionnaire. Acta Reumatol Port. 2008;33(3):345-51.
[7] Marques AP, Santo A, Berssaneti AA, Matsutani LA, Yuan SLK. Prevalence of fibromyalgia: literature review update. Revista Brasileira de Reumatologia. 2017;57(4):356-63.
[8] Paiva ES, Heymann RE, Rezende MC, Helfenstein M, Jr., Martinez JE, Provenza JR, et al. A Brazilian Portuguese version of the Revised Fibromyalgia Impact Questionnaire (FIQR): a validation study. Clin Rheumatol. 2013;32(8):1199-206.
[9] Sousa VD, Zauszniewski JA, Bergquist-Beringer S, Musil CM, Neese JB, Jaber AF. Reliability, validity and factor structure of the Appraisal of Self-Care Agency Scale-Revised (ASAS-R). J Eval Clin Pract. 2010;16 (6):1031-40.

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THU0716-HPR MAJOR BARRIERS AND FACILITATORS TO PHYSICAL ACTIVITY IN RHEUMATOID ARTHRITIS ARE RELATED TO PHYSICAL AND PSYCHOLOGICAL HEALTH, SETTING AND SOCIAL ENVIRONMENTAL FACTORS: A SYSTEMATIC LITERATURE REVIEW

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Background: physical activity (PA), including engagement in structured exercise, is a key element in the management of chronic inflammatory rheumatic diseases, in particular rheumatoid arthritis (RA) (ref). However, maintaining a physically active lifestyle is a challenge for people with RA. PA determinants in this population need to be understood better to be optimised through public health or healthcare interventions and social policy changes.
Objectives: to collect qualitative evidence on barriers and facilitators of PA for patients with RA through a systematic literature review (SLR).
Methods: A SLR of Medline, Web of Science and grey literature was performed from inception to January 2019; key search terms were exercise [MeSH], barriers [Title/Abstract]), facilitators [Title/Abstract] and Arthritis, Rheumatoid [MeSH]. All qualitative reports of barriers and facilitators in RA, published in english were collected. A thematic synthesis was applied.
Results: Of 89 references, 10 (11.2%) studies were qualitative reports in RA and were analyzed: 3 (49 patients) were focus group and 7 (99 patients) were interviews. In all, 148 patients participated: mean age 57.4 years (standard deviation, SD 3.9, range of means 50.0-63.5), mean disease duration 14.3 years (SD 5.2, range 6.9-21.0). Barriers and facilitators were reported for general physical activity in 6 studies and for supervised exercises (e.g. exercise program leads by physiotherapist) in 4 studies. Overall, 7 categories of barriers (mean 3.4 (SD 1.9) per study) and 8 categories of facilitators (mean 3.7 (SD 2.1) per study) were reported. These could be grouped in 4 majors themes (physical health, psychological aspects, setting and social environment) (Table). The 3 most reported categories of barriers were symptoms of RA (8/10 studies), beliefs, fears and loss of motivation (7/10) and lack of support, exercise knowledge, confidence and conflict in advice from healthcare (4/10). The 3 most reported categories of facilitators were group socialization, influence of others, social support (8/10), positive beliefs, knowledge about benefits of PA (5/10) and positive emotions and experiences of PA (5/10).
Conclusion: Our findings emphasize the complex interplay of physical and psychological health, setting and social environmental factors, corresponding to the facilitation and hindrance of PA engagement.

REFERENCES:

[1] Osthoff A-KR, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Annals of the Rheumatic Diseases 2018;77:1251–1260.

Table major barriers to physical activity in RA qualitative studies

Major themes	Barriers	N° of studies	Facilitators	N° of studies
Physical health	Symptoms of RA	8	stable symptoms and Effective medication	3
Psychological	Belief and fear (increasing symptoms), loss of motivation	7	Positive beliefs, knowledge about benefits of PA	5
			Positive emotion and experience of PA	5
Setting	Bad weather	3	heat, warm climate, warm water	2
	Inaccessible facilities	2	convenient setting: community or gym setting, outside hospital	4
	Lack of time	2		
Social environment	Contact with other	2	external monitoring, support adherence (reminder)	3
	Lack of support, of exercise knowledge, of confidence, conflict in advice from healthcare	4	group, socialization, influence of other, social support	8
			Support form healthcare (advise, psychological issues addressed, emphatic specialist)	3

Tables for the authors, not the abstract

Characteristics	
Year of publication, mean (SD) [range]	2012 (5.8) [1999-2018]
Published in UK/other Europe/Europe	6 / 3 / 1
Number of patients, N [range]	148 [6-19]
Methods: group / individual	4 / 6
General exercise / supervised program	6 / 4
Age, mean, SD, [range]	56.7 (4.3) [50.0-63.5]
% female	78%
RA duration, mean, SD, [range]	14.7 (5.6) [6.9-21.0]

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THU0717-HPR CLINICIANS' AND PATIENTS' UNMET NEEDS IN EHLERS DANLOS SYNDROMES, THE EXPERIENCE OF ERN RECONNET

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Background: The European Reference Network for rare and complex connective tissue and musculoskeletal diseases (ERN ReCONNET) is a European network of 26 healthcare providers (HCPs), that aims at developing a comprehensive and harmonized approach to 10 rare and complex connective and musculoskeletal diseases (rCTDs). The network gathers the community of health care professionals and patients' representatives. The involvement of patients is structured thanks to the creation of the European Patient Advocacy Groups (ePAG). 3 ePAGs representing each disease pillar are members of the steering committee. The Ehlers-Danlos Syndromes (EDS) are represented in the ERN ReCONNET with the exception of vascular EDS represented in the VASCERN ERN.

Objectives: To raise awareness on the unmet needs related to EDS in the EU through attracting and engaging more experts, specialists and HCPs in order to address those needs.

Methods: At present, the EDS is represented by 2 HCPs and 2 official ePAGs, senior and junior disease coordinators have been identified both among HCPs and ePAG, in particular the EDS ePAGs intensively sought for unmet needs of EDS into their wider European Community. All needs identified by ePAGs were discussed with the senior and junior coordinators and their contribution was added in a dedicated paragraph of the article, acknowledging them as co-authors. Among other activities, a state of the art on clinical practice guidelines (CPGs) has been performed also for EDS[1], in which patients and clinicians highlighted the most important unmet needs.

Results: As the new 2017 International EDS nosology[2] was only published in March 2017, EDS still lack Clinical Practice Guidelines and recommendations. The main EDS unmet needs identified concern the need to develop data on prevalence and clinical features, the identification of reliable biomarkers and the implementation of advanced instrumental imaging techniques. The management of pain, fatigue and psychological support have also been identified as a major topic to be addressed. More efforts should be put also on the education of healthcare professionals in order to provide faster diagnosis and better care to EDS patients. A stronger representation of EDS centres of expertise in the ERNs is needed, especially considering the crucial added value represented by the possibility of discussing clinical cases in the Clinical Patient Management System provided by the European Commission.

Conclusion: The ERN offers a real opportunity to develop better standards of care taking into account patients unmet needs. It is critical to increase EDS awareness and to attract HCPs for the follow-up and care of patients to be able to meet the unmet needs of the EDS patient population and healthcare professionals.

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THU0718-HPR OVERVIEW OF THE MOST EFFECTIVE PHYSIOTHERAPY MANAGEMENT METHODS IN PEDIATRIC RHEUMATOLOGY

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Background: The majority of patients with pediatric rheumatologic conditions present with joint pain, morning stiffness and a high degree of fatigue which in turn affect their functional status, psychological wellbeing and activities of daily living (ADLs). Juvenile idiopathic arthritis - with a prevalence of 0.1-0.2/100 children- is the most common chronic pediatric rheumatic disease. When compared to healthy children, patients with juvenile idiopathic arthritis show decreased physical fitness, which necessitates systematic physiotherapy management.

Objectives: The current research was carried out to investigate the most reported physiotherapy methods for the management of common pediatric rheumatology conditions.

Methods: Pubmed and Google scholar databases were searched. Keywords were categorized into three groups. The first group included the most common pediatric rheumatologic conditions (juvenile chronic arthritis, juvenile spondyloarthropathy, juvenile psoriatic arthritis, dermatomyositis, systemic lupus erythematosus, vasculitis, scleroderma); the second group included physiotherapy management methods (physiotherapy, physical therapy, hydrotherapy, aquatic therapy); and the third group included outcomes (pain, pediatric pain, range of movement, quality of life, activities of daily living). Only primary research studies regarding patients with the aforementioned pediatric rheumatologic conditions were included.

Results: Notable variability was observed between studies as regards to applied methods and recorded outcomes. Additionally, results were not separately reported for the different diseases. Nevertheless, findings indicate that physiotherapy and hydrotherapy rehabilitation methods, focusing on reducing joint pain, joint protection, conservation of energy, and conservation of joint range of motion, achieved the treatment goals of

maintaining and/or improving joint mobility and strength, improving pain and function, as well as improving the psychological wellbeing, without increasing fatigue or joint symptoms.
Conclusion: Despite heterogeneity in study design and methodology, current evidence shows that various physiotherapy methods contribute to the achievement of treatment goals and improve the quality of life in pediatric rheumatology.

REFERENCES:
[1] American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 Update. Arthritis & Rheumatism 2002;46:328–46. doi:10.1002/art.10148.
[2] Klepper SE. Exercise in pediatric rheumatic diseases. Current Opinion in Rheumatology 2008;20:619–624.
[3] Long AR, Rouster-Stevens KA. The role of exercise therapy in the management of juvenile idiopathic arthritis: Current Opinion in Rheumatology 2010;22:213–7. doi:10.1097/BOR.0b013e328335d1a2.
[4] Takken T, Van Brussel M, Engelbert RHH, van der Net JJ, Kuis W, Helders PP. Exercise therapy in juvenile idiopathic arthritis. Cochrane Database of Systematic Reviews 2008. doi:10.1002/14651858.CD005954.pub2.

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THU0719-HPR THE PATIENT ACTIVATION MEASURE (PAM): WHAT DO PATIENTS WITH RHEUMATIC CONDITIONS THINK ABOUT IT?

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Background: Patient activation describes the skills, abilities and confidence someone has to actively manage their health. The most common way of capturing patient activation is by using the Patient Activation Measure (PAM), and the NHS has begun to integrate use of the measure into services as an outcome measure or as a tool to tailor care. The PAM has been widely adopted and used in a variety of populations both within the NHS and internationally, but case studies have reported that some patients found that the PAM was too broad to capture the skills they used to manage their health. There has been limited research gathering patients' perceptions of the suitability and acceptability of the PAM, particularly within a rheumatology context.
Objectives: To gather participants' opinions on the PAM as a method of capturing patient activation.
Methods: Seventeen participants living with a rheumatic condition in the South West of England participated in semi-structured interviews as part of a wider qualitative study investigating perceptions of patient activation. Participants completed the PAM at the beginning of the interview. In the last phase of the interview, they were asked to review and reflect on the PAM, including individual survey items and how closely they matched their experiences. Relevant sections of the interviews were analysed iteratively and participants' perspectives were grouped into themes.
Results: Participants' feedback on the PAM ranged, and some participants reported that the PAM entirely captured how they perceived patient activation and the way that they managed their conditions. However, this was not the case for all participants. Aspects of the PAM that participants felt were not sufficiently recognised included how they managed the psychological impact of their condition, and how they discussed their condition with loved ones. Participants commonly reported that they thought the phrasing of certain PAM items did not match the lived experience of their conditions. For example, PAM items capturing how well patients could prevent further problems was identified as a challenge for participants living with a fluctuating condition, and participants commented that the PAM does not check from where participants received or sought this information. The distinction between whether patients independently researched information about diagnoses and medications or received this passively from healthcare professionals also appeared important to some participants, as well as whether this information was accurate.
Conclusion: The PAM survey is generally considered a reliable and valid measure of patient activation, but there may be aspects of it that do not capture the realities of living with a long-term fluctuating condition. Rather than a stand-alone measure, the PAM would be best used in conjunction with healthcare professionals' clinical judgement to capture peoples' understanding of their conditions and how well they are able to recognise and respond to flare-ups and fluctuations.
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THU0720-HPR FACTORS ASSOCIATED WITH PAIN CATASTROPHIZING IN INDIVIDUALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with a wide spectrum of clinical manifestations such as organ damage, pain, fatigue, sleep disorders, depression and cognitive deficits. It is known that pain catastrophising may have serious impact in individuals with SLE. Furthermore, catastrophising and maladaptive coping strategies are linked to higher levels of functional impairment and depression in SLE.
Objectives: The aim of this study was to identify factors associated with pain catastrophising to detect possible susceptible targets in individuals with systemic lupus erythematosus.
Methods: A total of 104 individuals (mean age: 55.54±12.09 years; BMI: 27.17±4.01 kg/m^2) with SLE participated to the study. The Pain Catastrophizing Scale (PCS) was used to measure the extent to which people catastrophize in response to pain. The Tampa Scale for Kinesiophobia (TSK) was used to assess pain-related fear of movement. The Beck's Depression Inventory (BDI) was used to measure characteristic attitudes and symptoms of depression. The Body Awareness Rating Questionnaire (BARQ) was used to reflect on their self-reported body awareness. The multiple stepwise linear regression models with R-square (R^2) were used to compare across the models and explain the total variance.
Results: Mean PCS was 22.12±12.09; mean TSK was 42.94±7.76; mean BDI was 15.63±11.18 and mean BARS was 88.94±19.85. Linear regression analysis revealed that TSK, BDI, BARS and BMI were independently associated with PCS in predicting pain catastrophising in individuals with SLE ($p \leq 0.001$; $R^2=0.52$). There were no correlations between PCS and disease activity (mean SLAM-R:5.39±3.68; r=0.105) and organ damage (mean SLICC-DI:0.58±0.87; r=0.153) ($p>0.05$).
Conclusion: This study increases the understanding of the modifiable predictors to enhance pain coping behavior in accordance with the pharmacological treatment in SLE population. Results demonstrate major importance to explore the main stressors of pain catastrophising such as kinesiophobia, depression level, body awareness and BMI that affect coping behavior. Thus, pain catastrophising may limit the patients' ability to perform from simple to complex activities. In addition, body image concerns SLE patients as they experience weight gain which negatively impact their self-esteem. The patient reported outcomes could guide health professionals to identify unmet needs of patients at risk to facilitate incorporation of the biopsychosocial model into SLE management.

REFERENCES:
[1] Somers, T. J., Kurakula, P. C., Criscione Schreiber, L., Keefe, F. J., & Clowse, M. E. (2012). Self efficacy and pain catastrophizing in systemic lupus erythematosus: Relationship to pain, stiffness, fatigue, and psychological distress. Arthritis care & research, 64(9), 1334-1340.
[2] Fischin, J., Chehab, G., Richter, J. G., Fischer-Betz, R., Winkler-Rohlfing, B., Willers, R., & Schneider, M. (2015). Factors associated with pain coping and catastrophising in patients with systemic lupus erythematosus: a cross-sectional study of the LuLa-cohort. *Lupus science & medicine*, 2(1), e000113.

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THU0721-HPR WOMEN'S EXPERIENCE OF THE JOURNEY TO CHRONIC WIDESPREAD PAIN – A QUALITATIVE STUDY

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Background: Chronic widespread pain (CWP) is a major burden to both the person and the community. Non-tumor chronic pain is one of the most common causes for long-term sickness absence in Sweden. The prevalence of CWP in the general population is approximately 10%, and the condition is almost twice as prevalent in women, than in men. Increased understanding of how women with CWP describe triggering factors of pain and pain progress would be of importance when preventing poor pain prognosis, and when customizing the treatment strategy in a setting with person-centered care.
Objectives: To explore experiences of factors influencing the progress and severity of pain among women who have developed CWP within the last 21 years.
Methods: This is a descriptive study, using a qualitative content analysis with an abductive approach[1]. Nineteen women reporting CWP in a survey 2016, between 45-67 (median 57) years of age, who had not reported CWP in a survey 1995, participated in the study. Data were collected through individual interviews with open-ended questions: "Can you describe how your CWP has developed the last 20 years?", "How did your CWP change over time?" and "Have you experienced any important events that have influenced the development of your CWP?" Data were analyzed through a manifest qualitative content analysis and six categories emerged.
Results: The women described their journey to CWP in terms of triggering, aggravating and consolidating factors. Six different categories emerged; physical strain, emotional strain, social strain, work-related strain, biological strain and environmental strain. *Physical strain* included strenuous physical activities in leisure time, having muscle tension, inactivity or sleeping problems. *Emotional strain* included being depressed, worried and stressed, as well as neglecting the pain. *Social strain* included to prioritize other people before oneself and to meet distrust from the social surroundings. *Work-related strain* included heavy, monotonous and stressful work but also sedentary work. *Biological strain* referred to heredity, age and infections. *Environmental strain* meant that the climate or weather aggravated the pain.
Conclusion: The women in the study described how their journey to CWP was influenced by both external and internal strains. The six categories representing different types of strains were recurrent in a context describing triggering, aggravating and consolidating factors. This highlights the complexity of individual pain progress and argues for the importance of person-centred care approaches and rehabilitation programs. The fact that women with CWP feel mistrust from healthcare professionals indicates that the current care approach needs to be changed.

REFERENCES:

[1] Graneheim UH, Lindgren BM and Lundman B. Methodological challenges in qualitative content analysis: A discussion paper. Nurse education today. 2017; 56: 29-34.

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THU0722-HPR DESIGNING A DIET INTERVENTIONAL STUDY FOR AUTOIMMUNE RHEUMATIC DISEASE: ASKING PATIENTS WHAT THEY THINK

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Background: Using diet to help alleviate disease symptoms or control drug side effects in patients with autoimmune rheumatic disease is gaining renewed interest but little is known about what patients think about using diet to control their disease or what dietary interventions they would prefer.
Objectives: Our aim is to obtain patient input in the design of a potential diet interventional study in autoimmune diseases and compare the experiences and ideas of patients relating to diet from various ages and disease groups during a patient and public involvement and engagement (PPIE) event.
Methods: 35 Adult and young adult patients with Sjögren's syndrome and/or systemic lupus erythematosus were approached to participate when attending outpatient clinics at UCLH. 10 female patients with age range from 18 – 80 agreed to take part in a face-to-face PPIE event held at UCL.
During group discussions, patients were split between three groups, each facilitated by 3-4 members of the research team with different backgrounds and skills (clinical, basic science and PPIE expertise). The main themes discussed were:
1) Barriers to taking part in a research study investigating the role of diet in autoimmune disease
2) The ideal clinical trial design
3) The most appropriate patient information leaflet design for this study
Results: The majority of patients (80%) would agree to participate in a diet-related study for up to 12 months including completing questionnaires, conducting interviews and providing blood samples. The qualitative analysis of the group discussions identified the following themes: recording the daily food intake either using an app or a diary was acceptable to patients, there were concerns about drug interactions and diet; however, patients did not think that their disease would affect their ability to take part in a diet interventional study. As a means of communicating study updates, the patients preferred to be contacted by e-mail, letter, text or phone call.
In terms of intervention allocation, patients found it acceptable to be on the placebo arm of a study, to go on a diet for up to 6 months or to be administered a combination of interventions (diet, food supplements in tablet). Patients preferred to be assessed monthly or when attending outpatient clinics, and would complete questionnaires, even if lengthy. We asked patients to assess leaflets commonly available from charities and the NHS providing diet advice. Most patients had not seen such leaflets previously and suggested including recipes and a section for vegetarian food.
Conclusion: This PPIE event provided valuable ideas to improve potential study design ensuring a diet intervention would be patient centred. The unexpected findings were the high acceptability of questionnaires and patients' acceptance of a placebo intervention. Further PPIE follow-up events are planned aiming to discuss trial protocols in detail.
Acknowledgement: British Sjögren's syndrome Association and Versus Arthritis
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THU0723-HPR WHAT DO SJÖGREN'S SYNDROME PATIENTS THINK ABOUT RESEARCH?

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Background: Despite recent progress investigating the pathogenesis of Sjögren's syndrome (SS), there are currently no therapies able to influence disease progression. Patients with SS are usually treated symptomatically with variable success, therefore refining the research agenda according to patients' priorities could provide a valuable insight into the most appropriate research questions.
Objectives: The aim of this study was to explore patients' ideas and suggestions related to research in SS.
Methods: A questionnaire to investigate SS patient experience of diagnosis and ideas about research priorities in SS was designed. Over a 5 month period, patients attending outpatient clinics were invited to fill in the questionnaire. 27 patients completed our anonymous survey.
Results: The most important issue for patients with SS after they had been diagnosed was the lack of knowledge about this disease (25%), the diagnosis delay they had experienced (26%) and the persistence of symptoms of dryness (26%). Patients were interested in finding out what causes this disease (81%) and felt that our research should find a cure (92%) and better treatments (75%).
The main two research priorities selected by patients were improved understanding of the disease (89%) and attracting funding for supporting research in to SS (89%). In addition, patients wanted to have a voice

and contribute to raising awareness of SS and to participate in patient and public involvement and engagement (PPIE) events.
The majority of patients interviewed were willing to take part in research by donating blood samples and/or filling in questionnaires (96%).
58% of patients who completed the survey would either definitely or probably take part in discussion groups helping researchers to design future studies in SS.
Conclusion: This survey highlighted patients' perception of the need for more meaningful research into the causes of SS, as their priorities were centred around finding a cure or better treatments for Sjögren's Syndrome. The survey also identified patients' lack of knowledge about their condition as well as their desire to help with shaping future research ideas and support funding for research. The results of this survey will be incorporated in our future PPIE events aiming at shaping our research strategy in SS.
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THU0724-HPR RELIABILITY AND VALIDITY OF AN ACTIVITY LIMITATION MEASURE IN PERSONS WITH INCLUSION BODY MYOSITIS (IBM)

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Background: Persons with Inclusion Body Myositis (IBM) are affected in their activities of daily living (1,2).
Objectives: The aim of this study was to test validity and reliability of the questionnaire Disability in the Arm Shoulder and Hand (DASH) for patients with IBM. A second aim was to describe activity limitation measured by the Canadian occupational Performance measure (COPM).
Methods: Persons diagnosed with IBM were identified through the Swedish Myositis Network (SweMyoNet) quality registry in Stockholm Sweden. A total of 36 persons with IBM were included in the registry and were invited to participate. A total of 17 men and 9 women agreed to participate. Median (Q1-Q3) age was 74 (70-79) years and the median (Q1-Q3) disease duration was 7 (3-8) years.
Activity limitation were assessed by the questionnaire Disability of the Arm, Shoulder and Hand (DASH) and the The Canadian occupational performance measure (COPM) which investigate patient derived areas of daily activities.
The data collection was performed at the Karolinska university hospital in Stockholm Sweden. At baseline both DASH and COPM were performed. The participants received a second DASH questionnaire to be answered within two weeks (Follow-up) and send back to the researcher.
Results: There were good correlations between baseline measure and follow-up on DASH (rs 0.997; p=0.01) Indicating that the DASH is consistent over a short period of time.
The results from COPM showed a variety of activities persons with IBM experienced problem with. Area with most activity limitations were basic self-care area such as dressing and grooming, fall, feeding, managing communication.
Instrumental activities such as managing instruments, shopping and meal preparation. Leisure activities such as playing an instrument, run, paint and social activities such as visit friends, social engagements.
Some of these activities were found in the DASH but not all. E.g. missing socializing with friends and family, problems swallowing or were environment dependent.
Conclusion: The results indicate that DASH have a good test re-test reliability DASH includes some of the activities that persons with IBM experience difficulties with but not all. The participants experienced difficulties in all areas of life.

REFERENCES:

[1] Eriksson M, Lindberg C. Hand function in 45 patients with sporadic inclusion body myositis. Occup Ther Int. 2012;19(2):108-16.
[2] Cox FM, Titulaer MJ, Sont JK, Wintzen AR, Verschuuren JJ, Badrising UA. A 12-year follow-up in sporadic inclusion body myositis: an end stage with major disabilities. Brain. 2011;134(Pt 11):3167-75.

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THU0725-HPR SCREENING OF SILENT MYOCARDIAL ISCHEMIA USING A STRESS TEST IN RHEUMATOID ARTHRITIS PATIENTS: ASSOCIATION WITH TRADITIONAL RISK FACTORS AND DISEASE ACTIVITY

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Background: The rheumatoid arthritis is responsible of an increased risk of cardiovascular (CV) morbidity and mortality.
Objectives: The aim of the study is to determine, in established RA patients, the presence of silent myocardial ischemia using a stress test and its association with the disease activity and the CV risk factors and scores.
Methods: It is a transversal and prospective study in a rheumatologic center in Charles Nicolle hospital in Tunisia. 103 RA patients, asymptomatic for CV disease were submitted to a stress test. Demographic data, cardiovascular risk factors and the disease characteristics were assessed for all patients and risk factors of silent myocardial ischemia in RA patients were identified.
The comparison of qualitative variables was performed with the Chi square test and the comparison of qualitative variable and quantitative ones was performed with the Student's test. The significance level was set at 0.05.
Results: There were 103 patients (sex-ratio=0.3) with a mean age of 53 ±10 years. The evaluation of the disease activity showed that the mean DAS28 CRP, CDAI and SDAI were 3.9±1.38, 17.17±11.4 and 33.39±26, respectively. A screening for CV risk factors revealed: 13% of patients had a cardiovascular inheritance, 25% of patients were either smokers or hypertensives, 18% had diabetes, 70% were obese or overweighted and 14 patients had dyslipidemia. The ischemic ratio (CT/HDL) revealed that 42% of patients had a moderate to high myocardial ischemic risk. Heart-SCORE was high in 35% of cases. A silent myocardial ischemia in the stress test was found in 11 patients (10.6%) and was associated with male sex (p=0.03), advanced age (p=0.04), erosive character (p=0.05), the advanced age of the rheumatoid arthritis diagnosis (p=0.01) and the ischemic ratio (p=0.06). No relationship was found with the majority of traditional CV factors nor with disease activity variables.
Conclusion: Our results corroborated the hypothesis that the stress test could reveal subclinical CV dysfunction, supported the utility of the Heart-score as a screening tool, and put in perspective the potential usefulness of complementary approaches in CV risk assessment in RA patients.
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THU0726-HPR THE COMPARISON OF ARTERIAL STIFFNESS, FUNCTIONAL EXERCISE CAPACITY AND PHYSICAL ACTIVITY IN SYSTEMIC SCLEROSIS AND HEALTHY INDIVIDUALS

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Background: Systemic sclerosis (SSc) is characterized by abnormal production of fibrotic tissue in the skin and internal organs. SSc has a effect on large and conduit arteries damage as well as microvascular damage (1). It is known that sedentary lifestyle may contribute to vascular dysfunction (2). Therefore, it is important to evaluate arterial stiffness, exercise capacity and physical activity in people with SSc.
Objectives: The aim of this study is to compare arterial stiffness, functional exercise capacity and physical activity in SSc and healthy individuals.
Methods: Fifteen SSc (53 years) and 15 healthy (48 years) women were included in this study. Arterial stiffness was evaluated with pulse wave velocity that was obtained by measuring the carotid-to-radial pulse wave transit time. Functional exercise capacity was assessed by 6-minute walk test (6MWT). Physical activity was questioned International Physical Activity Questionnaire (IPAQ)-short form. The differences between the groups were analyzed with Mann-Whitney U test.
Results: Age, weight, height and body mass index were similar in the groups (p>0.05). There was significant difference in pulse wave velocity and pulse wave transit time between the two groups (p<0.05). The

6MWT distance and IPAQ score of the group with SSc were significantly lower than the healthy group ($p<0.05$).
Conclusion: This study demonstrates that women with SSc have increased arterial stiffness, decreased functional exercise capacity and physical activity. Exercise training is an important part of the comprehensive care of people with SSc. People with SSc should be included in an exercise training program to reduce arterial stiffness, increase exercise capacity and physical activity.

REFERENCES:

[1] Cypiene A, Laucevicius A, Venalis A, Dadoniene J, Ryliskyte L, Petrulioniene Z, Kovaite M, Gintautas J. The impact of systemic sclerosis on arterial wall stiffness parameters and endothelial function. Clin Rheumatol. 2008 Dec;27(12):1517-22.
[2] Laufs U, Wassmann S, Czech T, Münzel T, Eisenhauer M, Böhm M, Nickenig G. Physical inactivity increases oxidative stress, endothelial dysfunction, and atherosclerosis. Arterioscler Thromb Vasc Biol. 2005 Apr;25 (4):809-14.

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THU0726B-HPR THE FACTORS AFFECTING HANDWRITING SPEED IN PATIENTS WHO HAVE AN AFFECTED WRIST JOINT WITH OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) encompasses a complex group of disorders with arthritis. Patients with JIA may experience significantly decreased life skills owing to muscular weakness, joint pain, contracture, and reduced mobility (1). Poor handwriting speed is an example of an affected life skill that has been observed by educators and clinicians for patients with chronic disease (2).
Objectives: The aim of this study was to investigate the factors affecting handwriting speed in patients who have an affected wrist joint with oligoarticular JIA.
Methods: 42 patients (aged 6–18 years) who have an affected wrist joint with oligoarticular JIA were included in this study. Muscular strength was estimated at maximal isometric force for the muscles of the upper extremities by using a portable handheld dynamometer. Grip and pinch strengths were evaluated by a dynamometer. Handwriting speed was evaluated with a sentence writing duration of 24 letters. All tests were performed thrice and the mean values of all were recorded. The correlation between all parameters was analyzed by the Pearson Correlation Test. Also, relations between the factors affecting handwriting speed in JIA were assessed by multiple linear regression analysis.
Results: The mean age was 12.71±3.35 and the mean disease duration was 6.52±3.81 years. The mean of handwriting speed was 20.53±10.39 seconds. Significant relationships were found between handwriting speed and muscular strengths of shoulder and elbow ($p<0.05$). Also, significant relationships were found between handwriting speed and lateral ($r=-0.352$, $p=0.022$), tip ($r=-0.309$, $p=0.047$) and triple ($r=-0.375$, $p=0.015$) pinch strengths. According to linear regression analysis, handwriting speed was affected by only muscle strength of elbow pronation ($\beta=-0.515$, $p=0.037$).
Conclusion: Handwriting is a complex functional activity simultaneously involving motor skills, cognitive and visual perceptual processing in all chronic disease. In the current study, it was found that handwriting speed was related with shoulder and elbow muscle strengths and pinch strengths in patients with JIA. Although patients with JIA had only affected wrist joint, only muscle strength of elbow pronation was the only primary predictor of handwriting speed. We suggested that handwriting speed should be considered in patients with juvenile idiopathic arthritis. So, accurate assessment of handwriting speed is essential for developing appropriate intervention programs and evaluating performance and outcomes in patients with JIA Besides, not only affected joint, but also all upper extremity joints should be assessed multidimensionally.
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REFERENCES:

[1] Gowdie, P. J., & Tse, S. M. (2012). Juvenile idiopathic arthritis. Pediatric Clinics of North America, 59(2), 301-327.
[2] Van Drempt, N., McCluskey, A., & Lannin, N. A. (2011). A review of factors that influence adult handwriting performance. Australian occupational therapy journal, 58(5), 321-328.

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THU0727-HPR FOLLOW-UP CARE AND SELF-MANAGEMENT ACTIVITIES AFTER SPECIALIZED REHABILITATION FOR PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Patients with rheumatic and musculoskeletal diseases (RMDs) benefit from rehabilitation in specialized care, but the effect seems to decline over time. Implementation of healthy self-management strategies and support over an extended period may prolong the effect. Rehabilitation trajectories with planned follow-up interventions and support in primary health care are therefore recommended. Still, evidence is not clear concerning what constitutes an optimal design of supportive follow-up interventions, and to which degree such follow-up care are planned and delivered.
Objectives: To describe current follow-up care practice and self-management after specialized rehabilitation for patients with RMDs.
Methods: This is a multicentre cohort study, including 523 participants with RMDs who received rehabilitation in specialized care in Norway. Participants completed a core set of outcome measures for rehabilitation in musculoskeletal diseases covering nine aspects of health and function in a web based data collection system [1]. At rehabilitation discharge, they additionally reported needed and planned follow-up care (FU-care) from listed professions and services in primary health care and plans for self-management activities (SMA). Received FU-care and adherence to SMA were reported at 4, 8 and 12 months follow-up. A multiple logistic regression analysis was performed to explore predictors for acceptable adherence to SMA.
Results: A total of 436 participants completed all assessments at discharge, of which 429 (98%) reported a need for FU-care. A need for FU-care by primary physician was most frequently registered, followed by physiotherapist and the Norwegian Labour and Welfare Service. However, only 239 (56%) reported that FU-care was planned at discharge. Of those reporting a need for FU-care, 201 (47%) participants reported receiving such care during the follow-up year, and these participants more often had a specific follow-up plan at discharge compared to those who did not receive the FU-care they reported needing ($p=0.06$).
Hundred and sixty-four (38%) participants were adhering to their SMA throughout the follow-up year. Higher age (OR=1.04, [CI 95% 1.02, 1.06], $p<0.001$), lower degree of depression and anxiety (OR=0.73, [CI 95% 0.58, 0.94], $p=0.01$), and performing physical activity on a regular basis (OR=3.35, [CI 95% 2.08, 5.39], $p<0.001$) at baseline were predictors for acceptable adherence. Participants with acceptable adherence reported more often a need for FU-care ($p<0.001$), and had more frequently received the FU-care they needed ($p<0.001$) than those without acceptable adherence.
Conclusion: Participants with plans were more likely to receive the FU-care they reported needing, indicating that discussing and planning follow-up should be an integral part of rehabilitation in specialized health care.
The results further indicate that having structure and routines in one's daily life enhance adherence to SMA, and that patients with anxiety and depression and a sedentary life style may need more support over a longer period to be able to implement behavioural changes for healthy self-management.

REFERENCES:

[1] Klokkerud, M., et al., *Developing and testing a consensus-based core set of outcome measures for rehabilitation in musculoskeletal diseases*. Scandinavian Journal of Rheumatology, 2017: p. 1-10.

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THU0728-HPR **"I AM GOOD ENOUGH AS I AM EVEN IF I AM NOT PERFECT" –A QUALITATIVE STUDY OF FIBROMYALGIA PATIENTS' EXPERIENCES FROM PARTICIPATION IN A MINDFULNESS-BASED GROUP-PROGRAMME**

Heidi A. Zangi[1], Gyda Singstad[2]Ingrid Ruud Knutsen[2], Improved management of patients with fibromyalgia: Evaluation of an integrated care model. *[1]Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway*; *[2]Oslo Metropolitan University, Oslo, Norway*

Background: People with fibromyalgia (FM) suffer from widespread pain, non-refreshing sleep, fatigue and reduced mental wellbeing. No curative pharmacological treatment exists. Vitality Training (VTP) is a mindfulness- and acceptance-based group-programme that aims at enhancing participants' health promoting resources, strengthening their inner authority and ability to act according to own values. It combines mindfulness with creative methods and group counselling. Two RCTs have shown significant improvements in mental wellbeing, pain coping and fatigue in patients with chronic musculoskeletal pain and inflammatory arthritis. The VTP is currently being evaluated in an ongoing study for patients with newly diagnosed FM [1].
Objectives: The aim of this qualitative study was to explore FM patients' experiences from participating in the VTP, and if they perceived that it had any impact on their health and functioning.
Methods: Six qualitative in-depth interviews with participants from three VTP-courses were conducted following a semi-structured interview guide. Interviews were audio-recorded and transcribed. All three authors analysed the data by use of systematic text condensation.
Results: Three main themes were identified.

1. Understanding oneself in light of the group: Mutual understanding and acknowledgement had altered participants' self-understanding – from a feeling that "something was wrong with me" towards perceiving themselves as "a normal person with similar challenges as others".
2. Learning to accept oneself: Participants had obtained a greater understanding and acceptance for their emotions and reactions and had become kinder towards themselves. "I have realised how strict I have been towards myself… I am indeed good enough as I am even if I am not perfect".
3. Coping with everyday challenges: Becoming aware of what had provoked stress and learn how to face it had helped participants take more control. "I can do small changesthat really makes it better… the illness does not decide everything. Indeed I can decide something myself".

Conclusion: Participation in the VTP had contributed to new ways of relating to oneself and the illness. The support and acknowledgement participants experienced from the group had helped them alter their self-understanding from only being ill towards also being healthy and normal. They had learnt ways to better cope with stress and everyday challenges. Although this was a small study, the findings correspond with findings in previous studies.

REFERENCES

[1] Haugmark T. et al. Effects of a community-based multicomponent rehabilitation programme for patients with fibromyalgia: protocol for a randomised controlled trial. BMJ open. 2018 Jun 4; 8(6):e021004.

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HPR Professional education, training and competencies

THU0729-HPR **BENEFITS OF EMPOWERING THE PATIENTS TO SELF-ADMINISTER SUBCUTANEOUS LOW DOSE METHOTREXATE (LD-MTX) INJECTIONS IN PATIENTS WITH SYSTEMIC IMMUNO-INFLAMMATORY RHEUMATIC DISEASES (SIRDS): A STUDY BY RHEUMATOLOGY NURSES COUNSELLOR**

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Background: In recent years, early aggressive targeted treatment for SIRDs is recommended. LD-MTX is the "anchor drug" for these diseases. The administration of LD-MTX using subcutaneous route increases its therapeutic efficacy that ensures the maximum bioavailability and reduces gastrointestinal adverse effects. Therefore, it is preferred over the oral route. Increased use of subcutaneous self injection of medication has benefits for the patients and healthcare system. Increased use of subcutaneous self injection could alleviate pressure on medical services by reducing hospital/clinic visits. Therefore, explaining the benefits of self administration of subcutaneous injection such as early disease control, increased drug adherence, positive attitudes towards life, decreased financial burden of administration cost, decreased dependency to the others, should be an imperative part of patient's education.
Objectives: Benefits of self-administered subcutaneous LD-MTX injection in patients with SIRDs.
Methods: This retrospective study included patients who were prescribed injectable LD-MTX for their treatment. Besides the demographic information (age, gender) and disease characteristics (diagnosis, duration, prior treatment), the patients were interviewed and counselled regarding the virtues to take subcutaneous LD-MTX self-injection. The technique for self-injection of LD-MTX subcutaneously was explained and demonstrated to the patients. All the information including the follow-up details, were recorded in a pre-designed form.
Results: Three hundred (n=300) consecutive patients who were advised weekly LD-MTX injections and taught the self-injection technique were enrolled in this study. On follow-up visit it was found that among them, 177 patients (59%) learned and started to administer their own subcutaneous injection of LD-MTX and they adhered to the injection schedule, in 50 (16.7%) patients the injections was being given by the attendant (who had learnt the injection technique because the patients had deformities), while the other 73 (24.3%) were not very compliant to injections due to psychological barriers towards self-injection, worried about pain and incorrect technique, adverse effects of the incorrect injections social stigma related to self-injections, and frustration or lack of acceptance of the illness.
Conclusion: By empowering the patients to self-administer LD-MTX injections subcutaneously, a majority (59%) of them successfully continued to take the medicine appropriately. Thus this study shows the important role the nurses' play in educating patients and helping them to overcome psychological barriers to self injection. Empowering the patients to take self-administer injections would result in better long term treatment adherence, improving treatment flexibility and overall quality of life.

REFERENCES:

[1] Hazlewood, et al. The comparative effectiveness of oral versus subcutaneous methotrexate for the treatment of early rheumatoid arthritis. Ann Rheum Dis. May 2015
[2] Malaviya AN, Sharma A, Agarwal D, Kapoor S, Garg S, Sawhney S. Low-dose and high-dose methotrexate are two different drugs in practical terms. Int J Rheum Dis. 2010 Oct

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THU0730-HPR **THE MAP OF THE RHEUMATOLOGY NURSE CLINICAL AND RESEARCH INTERVENTIONS IN THE VALENCIAN REGION (SPAIN)**

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Background: There is none defined competences framework for Rheumatology Nursing at the moment in Spain. This fact leads to an heterogeneous roles and interventions in each Rheumatology department which has not ever been described nor quantified.
Objectives: To describe and quantify the rheumatology Nursing interventions in the Valencian Region (Spain).
Methods: A descriptive study was performed by the completion of an online questionnaire with a list of clinical and research intervention. The questionnaire was sent to the Head of Rheumatology Department of 33 public hospitals from the Valencian Region.
Results: 32 hospitals of the Valencian Region fulfilled the questionnaire: 15 from Valencia, 13 from Alicante and 4 from Castellón. 50% of the hospitals had a Rheumatology nurse. In those hospitals, 50% had only 1 Rheumatology nurse working at the moment. The maximum Rheumatology nurses working in the same hospitals were 4; 2 hospitals used to have a Rheumatology nurse but do not have it anymore at this moment. 11 hospitals have an auxiliary nurse (3 of them without nurses and 8 with nurses). The year of incorporation of the Rheumatology nurse in the Department was quite heterogeneous, being the earlier in 1992 and the last incorporation in 2017.
The nurses worked mainly in a Rheumatology department full time (68.75%).
The 81% of the hospitals had an specific nursing agenda but only 7 hospitals had a monographic nurse-led clinic (osteoporosis nurse-led clinic -25%-, intravenous treatments nurse-led clinic -12.5%- or cardiovascular risk nurse-led clinic -6.25%)
Nurses clinical interventions are very heterogeneous covering the patient clinical management and practice nurses intervention activities. Nurses organized patient education workshops in 25% hospitals. In 11 hospitals, nurse undertook teaching activities. 56% participating in scientific workshops/congress, 44% teaching undergraduated nurses/registered nurses and 37.5% teaching other healthcare professionals.
In 11 hospitals, nurses undertook research activities. In 2 hospitals an specific research nurse was available. 56% of nurses participated in clinical trials, 50% participated in research projects and 50% participated in scientific congress. 25% of nurses lead research projects.
In 12 hospitals, nurses belong to a scientific society; in 11 hospitals, nurses participated in regional, national and/or international nurses working groups.
Conclusion: In at least 50% of the hospitals from the Valencian Region, nurse activity was registered. There are heterogeneous clinical activities performed by nurses. This fact raised the issue of the importance of having unified criteria for nurse's intervention and competences framework comparable in each and every hospital. Teaching and research were also a common interventions mentioned. These activities are necessary for a constant recycling and updating of the nurses and will help to gain the necessary visibility for the rheumatology nurses.
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THU0731-HPR **"OSER ABORDER" SURVEY ON THE CROSSED NEEDS OF A BETTER UNDERSTANDING OF SEXUAL HEALTH ISSUES BETWEEN PATIENTS SUFFERING FROM CHRONIC INFLAMMATORY RHEUMATISMS AND HEALTHCARE PROFESSIONALS INVOLVED IN PATIENT THERAPEUTIC EDUCATION**

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Background: Chronic inflammatory rheumatisms (RIC) may negatively impact patients' sexual health and quality of life.
Overall, 31 to 76% patients suffering from rheumatoid arthritis (RA) report to suffer from sexual difficulties. Patients affected by spondyloarthritis (SA) report a negative disease impact on sexual activity in 38 to 50% of cases. On the other hand, while healthcare professionals (HP) are well aware of the utility to approach this issue, most do not carry on with it for they feel insufficiently trained in this domain.
According to the 2015 EULAR recommendations, therapeutic patient education (TPE) is an essential part of patient management in the RIC domain. TPE actually does take into account the overall patient experience including sexuality.
A survey primarily focused on needs and conducted among patients and healthcare experts involved in TPE was thus deemed necessary to better define both the content and format of TPE to be delivered to HP in order to help them dialogue with their patients, while overcoming certain obstacles on this path.
Objectives: To define the educational needs of HP involved in TPE of patients suffering from CIR concerning sexual health issues.
Methods: Using an interdisciplinary team approach, we have elaborated two different questionnaires focused on assessing specific needs and designed for patients and healthcare professionals. These questionnaires were filled in online from May 2017 to November 2017 via a secured server implemented in each of the 14 French rheumatology centers by CIR patients, TPE-involved HP, and members of three patient associations.
Results: 239 patients answered the questionnaire (60.7% suffering from SA, 6.7% from psoriasis rheumatism, and 32.6% from RA), as did 57 HP. Overall, 72% patients reported having suffered or being still suffering from sexual difficulties, whereas 80% of them had never approached the topic with their respective HP.
In 82% of cases, the patient claimed having addressed the issue, whereas 30% HPs reported having taken the initiative. Half of both the patients and HP reported they had not dared to approach the topic. To ease communication, HP would appreciate to "have a team specifically dedicated to particular sexual healthcare issues", "have specific tools available" and "undergo specific training sessions".
In line with HP answers, patients' primary expectations were to be heard and become well-informed. The people who were judged the most competent (63%) and with whom patients would feel the most secure (58%) were the psychologists. The topics thought to be the most useful by the patients were similar to those considered most useful for HP training, namely undesirable treatment effects on sexuality (95%), impact of rheumatism on sexual activity (92%), body image and chronic illness (81%), partner communication (77%), sexual dysfunctions (77%), as well as physiology of aging and sexual function (75%). About 70% HP expressed the need for complementary education, with 95% of them stressing the necessity to acquire further communications skills within this domain. Of these, 88% preferred short training sessions, and 80% group training sessions.
Conclusion: This survey clearly demonstrates the usefulness of implementing educational training, along with its appropriate content, among HP, designed to enable them to approach sexual health issues and provide their patients with appropriate advices in this domain.
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FRIDAY, 14 JUNE 2019

Genomics, genetic basis of disease and antigen presentation

FRI0001 NEXT GENERATION SEQUENCING ANALYSIS OF AN NLRP3 MUTATION NEGATIVE CAPS COHORT

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Background: Cryopyrin Associated Periodic Syndromes (CAPS) are caused by autosomal dominant gain of function mutations in the *NLRP3* gene. However, a subset of these patients with typical clinical features and good response to anti-IL-1 treatment, have no mutation in *NLRP3* detected by conventional Sanger DNA sequencing. Somatic mosaicism may account for between 19 to 69% of these, from previous reports. Genetic heterogeneity has also been implicated in patients with CAPS-like phenotypes, with the identification of pathogenic mutations in the *NLRP12*, *PLCG2* and *NLRC4* genes (Familial Cold Autoinflammatory Syndrome subsets 2, 3 and 4, respectively).
Objectives: To explore the genetic cause(s) in a paediatric cohort of mutation negative CAPS patients using Next Generation Sequencing (NGS) techniques, by assessing:

1. the rate of somatic *NLRP3* mosaicism, and
2. possible contribution of other/novel genes

Methods: Patients from a single paediatric centre who met the CAPS diagnostic criteria and had no *NLRP3* mutations identified by partial (exons 3, 4 and 6) or total Sanger sequencing, were identified. The NGS approach used in this study was Amplicon-based Deep Sequencing (ADS) for identification of *NLRP3* mosaicism; and Whole Exome Sequencing (WES) for exploration genetic heterogeneity (i.e. other causative mutations). ADS was performed on an Ion Torrent platform using the Ion Torrent PGM HiQ sequencing kit. Resulting sequences were analysed using Torrent Server and in reporter softwares.WES was performed using the Nextera Exome Capture sequencing kit and Hiseq sequencing platforms. Exome data was analysed in the Galaxy web-based suit. The wANNOVER web-based software was used for variant annotation.
Results: We identified a total of 8 patients who met the CAPS clinical diagnostic criteria and had no mutation identified by conventional Sanger sequencing. ASD identified the presence of a somatic mutation in 3 of these patients (37.5%), with an allelic frequency varying from 3.1 to 14.5%. The remaining patients were studied by WES. In Patient 4 a novel *NLRP3* mutation was identified in exon 5, which had been previously missed due to a restricted Sanger approach. Patient 5 had a novel *NOD2* mutation, thus redefining the diagnosis as Blau syndrome. WES findings in the other patients are summarized in the Table.

Patient (gender, age at testing)	CAPS phenotype	NGS	Gene	aa change	Type
1-M, 8y	CINCA	ADS	*NLRP3*	p.F566L	Mosaic 14.5%
2-M, 8y	MWS	ADS	*NLRP3*	p.E567K	Mosaic 3.1%
3-M, 1y	MWS	ADS	*NLRP3*	p.G564D	Mosaic 12.5%
4 -M, 2y	CINCA	WES	*NLRP3*	p.G779V	Heterozygous
5-F, 16y	CINCA-like	WES	*NOD2*	p.D512Y	Heterozygous
6- M, 14y	MWS-like	WES	*IL36RN*	p.S113L	Heterozygous (AR)
7- M, 8y	MWS	WES	*AP1S3*	p.F4C	Heterozygous
8- F, 2y	MWS	WES	-	-	-

Conclusion: In this study, somatic *NLRP3* mutations were identified in 3/8 (37.5%) of our cohort, and 3/8 had variants in 3 other genes, potentially of relevance to the phenotype. In particular, the identification of a *NOD2* mutation and subsequent reclassification of that patient as Blau syndrome, illustrates the limitations of current CAPS diagnostic criteria as well as potential clinical overlap between different autoinflammatory syndromes, reiterating the use of a wider NGS approach. At present it is unclear how the variants found in patients 6 and 7 could modulate the phenotype, therefore in 3 patients a clear genetic cause is yet to be found. **In conclusion**, this study suggests that NGS approaches are superior to conventional sequencing for the molecular diagnosis of CAPS and CAPS like phenotypes since they can detect somatic mosaicism or alternative molecular diagnoses mimicking CAPS.
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FRI0002 THE JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED IL2RA HAPLOTYPE CONTAINS AN INTRONIC ENHANCER WHOSE FUNCTION IS DIMINISHED BY JIA-ASSOCIATED GENETIC VARIANTS

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Background: *IL2RA* has been identified as a JIA-associated risk locus using both candidate gene and genetic fine mapping approaches. However, numerous gene expression studies comparing children with active JIA to healthy control children have failed to identify *IL2RA* as a differentially expressed gene. Furthermore, the SNPs used to identify *IL2RA* lie within the first intron of the *IL2RA* gene, not its promoter or coding regions. The risk haplotype is marked by prominent H3K4me1/H3K27ac histone marks, suggesting that genetic risk may be mediated through enhancer function.
Objectives: To confirm whether the *IL2RA* region is a functional enhancer and whether the enhancer operates in lymphoid cells, myeloid cells, or both. We also examined the effects of genetic variants on enhancer function at the *IL2RA* locus.
Methods: We used the pGL3 reporter system to query enhancer effects across a 1,000 bp region within the first intron of the *IL2RA* gene marked by H3K4me1 and H3K27ac histone marks in both CD4+ T cells and neutrophils. This region is within the linkage disequilbrium block that includes the SNPs used on both candidate gene and genetic fine mapping studies that identified *IL2RA* as a JIA risk locus. The pGL3 vector contains a minimal SV40 promoter that is, by itself, inefficient at driving luciferase function. We tiled three 500 bp constructs across the region of interest and cloned these constructs into pGL3 vectors, which were then transfected into Jurkat T cells and myeloid HL60. Cells were incubated for 24 hr, after which luciferase production was assessed using standard methods. We repeated these same experiments using constructs containing genetic variants (rs117119468 C->T and rs12722502 C->T) that we identified in children with JIA using WGS and are not annotated in the 1000 Genomes Project SNP database.
Results: Within the H3K4me1/H3K27ac-marked region within the first intron of *IL2RA*, we observed enhancer activity across a 657 bp region from chr10:6092661 to chr10:6093317 in both Jurkat T cells and HL60 myeloid cells. The reporter constructs enhanced luciferase activity by 5-8 fold in Jurkat T cells (compared with a control vector that contained only the minimal SV40 promoter and the luciferase gene) and 4-6 fold in HL60 cells. A construct carrying a sequence within the first intron of the *IL2RA* gene that was not marked by the H3K4me1/H23K27ac histone signature showed no enhancement of luciferase expression compared to background. Constructs containing the JIA-associated rs117119468 C->T allele abolished the enhancer activity within the *IL2RA* locus, while the construct containing the rs12722502 C->T allele reduced luciferase activity by 30%.
Conclusion: The JIA-associated risk locus, *IL2RA*, contains an intronic enhancer that is active in both lymphoid and myeloid cells. JIA-associated genetic variants identified by WGS attenuate or abolish enhancer activity at this locus. These findings demonstrate the importance of assessing the non-coding functions of JIA risk loci, even where the coding function a specific gene might be plausibly implicated. Our findings also underline the potential importance of rare genetic variants, which may have stronger biological effects than GWAS SNPs, in complex traits like JIA.
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FRI0003 THE FUNCTION OF IRF7 SNP ON THE PRODUCTION OF TYPE I INTERFERON

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Background: Type I IFN plays a significant role in the pathogenesis of Systemic Lupus Erythmatosus (SLE). IRF7 is a critical transcriptional factor for the production of type I interferons (IFN).

Objectives: To explore potential mechanisms for the SLE related IRF7 SNP on type I IFN production, which might indicate new theoretical basis for genetic therapeutic strategy.
Methods: We constructed different genotypes of SLE relevant SNP cell lines by Crispr/Cas9 technology, and confirmed them by sequencing. After TLR-ligand stimulation,the mRNA expression of IFNα was detected by real-time qPCR. The levels of IFNα, TNFα and IL-6 were detected by ELISA kit. The protein expression of IRF7/p-IRF7 was detected by western blot.The binding ability of endogenous IRF7 with typeIIFN promoter was studied by chromatin immunoprecipitation.
Results: We got IRF7 SNP rs1131665 GG/AA cell lines by gene editing technique. After TLR-ligand stimulation, IRF7 SNP rs1131665 AA cell line showed higher IFNα expression than GG, which indicated statistical significance. IRF7 SNP rs1131665 AA cell line showed higher p-IRF7 expression than GG detected with western blot. Endogenous IRF7 in IRF7 SNP rs1131665 AA cell line showed stronger binding ability with IFNα promoter than GG, which indicated statistical significance.
Conclusion: The missense variant of G to A in IRF7 SNP rs1131665, increased the production of typeIIFN, which indicated that IRF7 G to A missense variant increased the susceptibility of type I IFN associated diseases.

REFERENCES:

[1] Lin LH, Ling P, Liu MF.The potential role of interferon-regulatory factor 7 among Taiwanese patients with systemic lupus erythematosus.J Rheumatol. 2011,38(9):1914-1919.
[2] Xu WD, Zhang YJ, Xu K, et al. IRF7, a functional factor associates with systemic lupus erythematosus. Cytokine. 2012,58(3):317-320.
[3] Miyagawa F, Tagaya Y, Ozato K, et al.Essential Requirement for IFN Regulatory Factor 7 in Autoantibody Production but Not Development of Nephritis in Murine Lupus.J Immunol. 2016,197(6):2167-2176.

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DOI: 10.1136/annrheumdis-2019-eular.2540

FRI0004 CHROMATIN INTERACTIONS IN NOVEL CELL TYPES REVEAL PARK7 AND ERRFI1 AS PUTATIVE CAUSAL GENES IN THE SUSCEPTIBILITY TO PSORIATIC ARTHRITIS

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Background: One of the major tasks post-GWAS is to link disease associated single nucleotide polymorphisms (SNPs) to their causal genes. Unexpectedly the vast majority of disease associated SNPs lay outside protein coding regions of the genome, often in gene regulatory regions, known as enhancers. These enhancers operate by physically interacting with their target genes, often over long distance, and often skipping genes. We, and others, have demonstrated how these enhancer interactions can change with different cell type and stimulatory conditions. In psoriatic arthritis, as with all complex diseases, there are a large number of genetic loci implicated in susceptibility to disease, but relatively few of these regions have confirmed causal genes.
Objectives: Map disease associated enhancers to potential causal genes through physical chromatin interactions in relevant, novel cell types.
Methods: We used Capture HiC (CHi-C) technology to map enhancer to promoter interactions in both a keratinocyte cell line (HaCaT) and a T cell line (MyLa) in biological duplicate. We generated Hi-C libraries and enriched them for autoimmune-associated GWAS loci using RNA baits. The resultant CHi-C libraries underwent high-throughput sequencing generating 75 bp paired-ends. Significant interactions were detected using CHiCAGO.
Results: A region on chromosome 1p36 demonstrated markedly differential interactions between the T cell line (MyLa) and the skin cell line (HaCat). Here the enhancer region containing SNPs associated with PsA demonstrated a strong interaction with both the PARK7 and ERRFI1 genes in HaCaT cells, absent in the MyLa cell line (fig 1). These interactions were contained within a functionally relevant topological activation domain (TAD) boundary, enriched for enhancer to promoter links. Bioinformatic analysis demonstrated how a SNP highly correlated with the PsA lead variant is found within an open, active region of chromatin in the HaCaT cell line, shifting the priority from the (statistical) lead variant (rs11121129) to rs11121131 – demonstrating the value of this type of analysis (fig 2).
Conclusion: A region associated with PsA on chromosome 1p36, previously annotated with the TNFSF9/ERRFI1/SLC45A1 gene, makes robust interactions with the PARK7 and ERRFI1 genes, both strong candidates for causality in disease. An associated variant, within a cell type relevant enhancer, is currently being targeted with genome editing technology (CRISPR) to assess its potential for causality and possible mechanism.

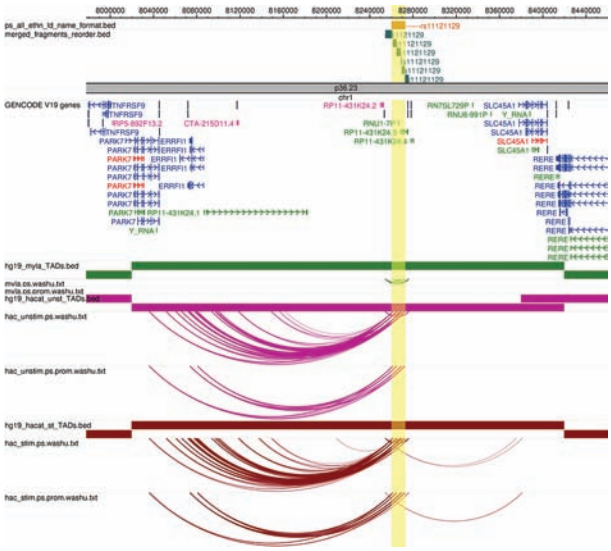


Fig1

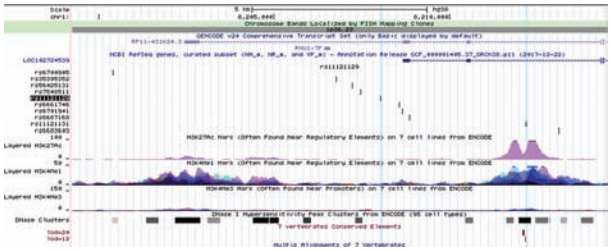


Fig2

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FRI0005 CHROMATIN CONTACTS AND TRANSCRIPTOMICS IN CD4+ T-CELLS REVEAL GENES IMPLICATED IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation of synovial joints. RA is a clinically heterogeneous disease and treatment response varies between individuals. The pathogenesis of RA is not completely understood yet, but it has been

shown that the largest factor influencing disease susceptibility is genetics. Genome-wide association studies have successfully characterized genetic variants that are associated with RA, with the vast majority of them mapping to non-coding regulatory elements. Understanding the mechanisms by which this phenomenon leads to disease is essential to translate results from genetic association studies to the clinic.
Objectives: There is evidence showing that autoimmune diseases are the consequence of erroneous wiring of the regulatory circuitry between enhancers and their target genes. The aim of this study is to characterize non-coding regions containing RA-associated variants, in order to determine the genes and pathways by which these regions act to increase the risk of disease.
Methods: We isolated CD4+ T-cells from blood obtained from RA patients. We stratified patients in two subgroups, high disease activity (DAS28>5.1, n=18) and low disease activity (DAS28<3.2, n=33). All samples were genotyped using Illumina Infinium Exome-24 v1.0 BeadChip arrays. RNA-Seq Libraries were generated for matching RNA samples using the Lexogen QuantSeq Library Prep kit and sequenced on an Illumina NextSeq500. For a subset of 6 samples (3 high disease activity and 3 low disease activity patients), capture Hi-C was performed to characterize chromatin interactions between all RA associated loci and their potential target genes.
Results: We observed numerous chromatin interactions between RA variants and potential causal genes. Preliminary results show that a number of disease-associated SNPs interact with compelling candidate genes situated several megabases away. Whilst some of these chromatin interactions are common to both patients groups, subsets of them are specific to each disease subgroup, which are correlated with differential gene expression.
Conclusion: These results suggests that there might be different biological pathways contributing to disease in RA patients with inactive disease compared to patients with high disease activity.
Disclosure of Interests: None declared
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FRI0006 PROTECTIVE ROLE OF THE PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) RS2495477 POLYMORPHISM IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SUBCLINICAL ATHEROSCLEROSIS

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Background: RA is associated with the development of cardiovascular (CV) disease and subclinical atherosclerosis[1]. The presence of carotid plaques assessed by ultrasonography studies is a surrogate marker for subclinical atherosclerosis[2]. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is involved in homeostasis of cholesterol, a traditional CV risk factor related to RA and atherosclerosis[1,3]. *PCSK9* polymorphisms can both increase and decrease the risk of CV disease in patients with atherosclerosis[3]. Moreover, PCSK9 levels have been also related with CV risk[4]. However, there is little information on PCSK9 in RA.
Objectives: To assess the role of several *PCSK9* polymorphisms in RA and subclinical atherosclerosis in RA as well as to determine if these ones may influence on *PCSK9* mRNA and protein levels.
Methods: *PCSK9* rs2479409, rs11583680, rs2483205, rs2495477 and rs562556 polymorphisms were genotyped in 1,169 Spanish RA patients, who met the 1987 ACR and the 2010 ACR/EULAR criteria for RA[5-6], and 528 healthy controls. Associations were estimated using odds ratios (OR) and 95% confidence intervals (CI). The potential association between *PCSK9* polymorphisms in both RA and controls and the presence/absence of carotid plaques in RA was evaluated by logistic regression. *PCSK9* mRNA expression and PCSK9 serum levels were determined by qPCR and ELISA, respectively. All results were adjusted by sex, age and traditional CV risk factors.
Results: Significant differences in the allele frequencies of *PCSK9* rs2495477 between RA patients and controls were found (minor allele: OR=0.55, 95% CI=0.34-0.89, p=0.01). A significant association between minor allele of rs2495477 and carotid plaques was also disclosed in RA patients (OR=0.72, 95% CI=0.56-0.92, p=0.01). PCSK9 levels were significantly decreased in RA patients carrying rs2495477 minor allele compared to controls (97.8 ± 104.9 vs 235.8 ± 93.5 ng/mL, p=0.001). None of the five *PCSK9* polymorphisms influenced on its expression.
Conclusion: Our study showed for the first time that *PCSK9* rs2495477 confers protection against RA susceptibility and the development of subclinical atherosclerosis in RA patients. Furthermore, rs2495477 decreased PCSK9 serum levels in RA that may be crucial to control the disease.

REFERENCES:
[1] Autoimmun Rev. 2016; 15: 1013–30.
[2] Ann Rheum Dis. 2014; 73: 722–7.
[3] J Am Coll Cardiol. 2005; 45: 1611–9.
[4] Atherosclerosis. 2016; 252: 50–60.
[5] Arthritis Rheum. 1988; 31: 315–24.
[6] Arthritis Rheum. 2010; 62: 2569–81.

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FRI0007 IDENTIFICATION AND VALIDATION OF PLASMA MICRO-RNA 425–5P AND -451A AS MICRO-RNAS ASSOCIATED WITH CARDIOVASCULAR DISEASE RISK OBSERVED IN RHEUMATOID ARTHRITISPATIENTS

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Background: Cardiovascular disease (CVD) risk is increased in Rheumatoid arthritis (RA) patients, and therefore, improved approaches for its early detection are needed. An accelerated atherosclerosis is considered the cause of the increase CVD risk. As microRNAs (miRNAs) are increasingly recognized as critical regulators in atherosclerosis and possess excellent stability in plasma, this study focused on using miRNAs as noninvasive CVD risk biomarkers in RA patients.
Objectives: To identify plasmatic miRNAs in RA patients that can facilitate earlier diagnosis of CVD and provide insight regarding the increase risk for CVD observed in these patients.
Methods: A discovery and validation studies were performed. To discover miRNAs candidates, we first compared plasmatic profiles of 754 miRNAs in 7 RA patients without CVD, in 7 patients with acute myocardial infarction (AMI) but without RA, and in 7 healthy controls matched for age and for classical CV risk factors. miRNAs commonly expressed in the two group of patients but differentially expressed from the controls were selected as miRNA candidates for validation. Selected miRNAs were validated in independent serum samples from 214 RA patients (validation cohort) by studying its association with subclinical atherosclerosis measured by carotid intima-media thickness (cIMT). Plasma profile of miRNAs in the discovery study was analyzed using validated TaqMan Open Array miRNA panels which enables the quantification of 754 human miRNAs.

Differential expression analysis was performed with Expression Suite software and selected miRNAs candidates were validated in the validation study by real-time PCR with LNA™ microRNA qPCR assays and analyzed with 2^{-DCt} method. KrusKal-Wallis test, Dunns post-test and linear regression were used for statistical analyses.

Results: In the discovery study we were able to measure 379 (50%) of the miRNAs represented in the array. We observed than 10 miRNAs (miRNA-Let-7a, miRNA-96, miRNA-381, miRNA-451a, miRNA-518d, miRNA-425-5p, miRNA-572, miRNA-190b, miRNA-708, and miRNA-1180) were expressed at the same level in RA and AMI patients but were significantly downregulated compared with controls. These 10 miRNAs were selected as potentially miRNAs associated with the increase risk of CVD in RA patients. Four of those miRNAs were expressed at very low level and were discarded for the validation study. In the validation study with 214 plasma samples from RA patients, we observed that two of the six candidate miRNAs (miRNA-425-5p and miRNA-451a) were significantly associated with cIMT. Thus, adjusted multivariable linear regression analysis showed that miRNA-425-5p and miRNA-451a independently explained 1.4% of the cIMT variability. Furthermore, adjusted regression estimates of the effect of miRNA-425-5p and miRNA-451a on cIMT were β = 0.029mm; p = 0.037 and β = -0.035 mm; p = 0.039, respectively. No other miRNA candidate exhibited association with cIMT values. Furthermore we observed that miRNA-425-5p was significantly correlated with ESR (r=-0.136; p=0.024) and miRNA-451a with DAS28 (r=0.19; p=0.003), ESR (r=0.23; p=0.0001), CRP (r=0.15; p=0.016) and fibrinogen (r=0.28; p=0.0001). miRNAs concentrations were not affected by any of the AR treatments. No association was observed between the presence of carotid plaque and the expression level of the microRNAs tested.

Conclusion: In the present study, we have identified miRNA-425-5p and miRNA-451 as potentially miRNAs involved in the CVD risk observed in RA patients.

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FRI0008 ADDRESSING THE DIAGNOSTIC GAP IN RHEUMATOID ARTHRITIS BY COMPLEMENTING THE SEROLOGY WITH GENETIC INFORMATION

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Background: Rheumatoid arthritis (RA) is caused by an interaction of inherited and environmental factors. The genetic component was revealed in different twin studies and the shared epitope was identified as main contributor. During several genome-wide association studies (GWAS) different genes have been highlighted as relevant for developing RA but so far, none of these have been used for a diagnostic approach to address the diagnostic gap for RA.

Objectives: The aim of this study was to identify genes within pathways relevant for developing RA and to combine these genetic risk factors with serologic data to improve the diagnosis of RA, especially in regards to CCP negative RA patients.

Methods: The cohort consists of 804 RA patients, 159 Disease controls and 495 Healthy individuals. Serology data were obtained using the EliA™ CCP IgG, EliA RF IgM and EliA RF IgA (Phadia AB, Uppsala, Sweden) tests. The genetic measurements were performed using the Next-Generation-Sequencing technology AmpliSeq™ on the Ion GeneStudio™ instruments (Thermo Fisher Scientific, Carlsbad, USA). The combined dataset was analysed by machine learning focusing on multivariate supervised models and discrete models.

Results: The Disease Research Area database (Thermo Fisher Scientific, Carlsbad, USA) uses a proprietary algorithm to create connections between genes and a specific disease highlighting relevant genes and pathways using the available datasets from NCBI, DisGeNet, ClinVar and further databases. Based on this information we were able to identify genes and variants within relevant pathways for RA and designed a sequencing panel specific for diagnosis of RA. The results from the targeted sequencing approach and the serologic data of the patients were analysed by an algorithm resulting in an improved diagnosis.

Each variant within the algorithm has a specific weighting score resulting in a combination of protective and destructive variants, which are used together with the serology to calculate a RA risk score.

In this study the combination of genetic and serology leads to an improved sensitivity of over 10% compared to CCP alone, with a comparable specificity. This increase in sensitivity results in the identification of >20% CCP-negative RA patients. Additionally, a genetic pattern was identified distinguishing between CCP-negative and CCP-positive RA patients.

Conclusion: Usage of genetic variants in combination with serologic data improves the diagnosis of RA within the measured cohort of Caucasian RA patients. Furthermore, a genetic pattern specific for CCP negative RA patients was accentuated and could be used to improve the diagnosis of CCP negative RA patients in the future. The combination of serology and genetic information for the diagnosis of RA patients could lead to an earlier diagnosis, especially for CCP negative RA patients.

REFERENCES:

[1] Svendsen AJ, Kyvik KO, Houen G, Junker P, Christensen K, Christiansen L, et al. (2013) On the Origin of Rheumatoid Arthritis: The Impact of Environment and Genes—A Population Based Twin Study. PLoS ONE 8(2): e57304.

[2] Jawaheer D, Gregersen PK. Rheumatoid arthritis: the genetic components. Rheum Dis Clin North Am 2002; 28: 1-15.

[3] Okada, Y. et al. Genetics of rheumatoid arthritis contributes to biology and drug discovery. Nature 506, 376–381 (2014).

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FRI0009 MOLECULAR PROFILING OF CIRCULATING B-LYMPHOCYTES REVEALS THE SUPERIOR PERFORMANCE OF METHYLOME OVER TRANSCRIPTOME DATA FOR DISCRIMINATING RHEUMATOID ARTHRITIS PATIENTS IN AN EARLY ARTHRITIS CLINIC: IMPLICATIONS FOR TRANSLATING "BIG DATA" INTO CLINICALLY USEFUL TOOLS

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Background: Defining optimal strategies for translating "big datasets" of transcriptome and methylome data into clinically valuable tools in RA will benefit from comparisons where potential confounders – including therapeutic background, disease phase and cell substrate heterogeneity – are controlled as far as possible.

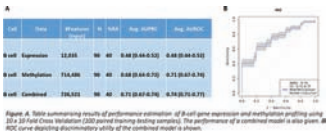
Objectives: We have obtained paired B- and CD4+ T-lymphocyte whole genome expression and methylation data from drug-naïve early arthritis clinic patients at a single centre. Focussing on B-lymphocyte data we here ask which of these datasets has most value in discriminating early RA – and the additive value of combining them.

Methods: CD19+ B-lymphocytes were isolated by positive selection from fresh peripheral blood of 90 drug-naïve patients attending the Newcastle Early Arthritis Clinic (NEAC), comprising 36 RA patients and 54 disease controls matched, so far as possible, for age, sex and acute phase response. Paired RNA and DNA extracted. Gene expression was profiled using the Human HT12 v4 BeadChip, and DNA methylation at >850,000 CpG sites quantified with the MethylationEPIC array (both Illumina). Gene expression and/or DNA methylation classifiers for RA prediction were developed based on a combined approach of classification algorithm

selection and hyperparameter optimisation. The Sequential Model-Based Optimization procedure was used to automatically select the best model configuration amongst 10 feature selection filters, 2 class imbalance correction techniques, 3 data cleaning methods and 4 classification algorithms along with their respective hyperparameters. Model optimisation was performed using a 10-fold Cross Validation (CV) while a 10 times repeated 10-fold CV was used for the predictive performance evaluation. Receiver operating characteristic (ROC) and precision recall (PR) curves were used to directly compare the classification potential of molecular approaches.

Results: 12,035 gene expression features and 714,486 methylation features were available for classifier building after quality control in our early arthritis B-lymphocyte dataset. Performance estimation showed the expression profile of B-lymphocytes alone to have no significant discriminatory utility for RA in this setting (average area under [AU] ROC 0.48). Methylation profiles were significantly superior for discriminating RA (average AU ROC 0.71). Interestingly, when a combined trancriptome/methylome model was generated, further enhancement of discriminatory function was observed, although this was modest (AU ROC 0.74).

Conclusion: Methylation profiling of B-lymphocytes affords better discrimination for RA than does transcriptional profiling. This may differ in other cell types. Combining data from molecular platforms may be an optimal approach. Functional analyses of the resultant B-lymphocyte signatures may yield insight into molecular pathobiology.



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FRI0010 TCR-CD3Z GENE EXPRESSION PROFILE IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Advances in understanding the pathogenesis of RA support the contribution of T cells in the disease process through the recognition of the arthritogenic antigen (Ag) and maintenance of chronic inflammatory response [1].

Previous gene association studies have demonstrated that CD247 gene expressions are associated with a variety of autoimmune disease. As regard Rheumatoid Arthritis (RA), this relationship has not been fully clarified yet.

Objectives: We aimed to evaluate the T-cell receptor-CD3 zeta chain (*TCR-CD3 ζ*) gene expression profile in a cohort of patients with RA.

Methods: A case-control study on 150 consecutive RA patients diagnosed according to 2010 ACR/EULAR criteria and 150 matched healthy controls without family history of RA or other autoimmune diseases. RA patients with other autoimmune diseases, viral hepatitis B or C, malignancy or hematological disorders were excluded from the study.

All participants were subjected to history taking, clinical examination, assessment of disease activity (in RA patients) using DAS-28 and HAQ, routine laboratory investigations, inflammatory markers level, serological tests, as well as molecular analysis for *TCR-CD3ζ* mRNA expression by quantitative real-time polymerase chain reaction.

Results: *TCR-CD3ζ* gene expression was significantly lower in RA cases than in healthy controls (p<0.05) *(Table 1).* Expression of *TCR-CD3ζ* **revealed** a significant negative correlation with RA disease duration, RF, and ESR (p<0.05) in RA cases. The level of ***TCR-CD3ζ* also showed a significant lower expression in +ve RF patients than in –ve RF patients (p<0.05). The AUC of *TCR-CD3ζ* level showed a moderate level of accuracy (AUC = 0.840, p=0.025) (*Figure 1),* and the calculated cutoff value (≤ 0.077) can precisely discriminate subjects with RA from those without RA with 93.5% sensitivity and 75% specificity(*Table 2*).**

Table 1. Comparison between RA cases and control group as regard CD247 (mRNA levels for TCR-CD3ζ gene expression)

TCR-CD3ζ	RA cases (n=150)	Healthy Controls (n=150)	Test of sig.	P
Min. – Max.	0.037– 12.467	0.034- 11.314	Z=-3.047*	0.002*
Mean ± SD.	0.663 ± 1.90	0.816 ± 1.64		
Median (Q1-Q3)	0.178 (0.109-0.314)	0.315 (0.198-0.922)		

Z: Z-score of Mann-Whitney test

*: Statistically significant at p≤0.05

Table 2. Analysis of ROC curve for TCR-CD3ζ level as a predictor of RA (high RF)

Variable	Cutoff point (ng/ml)	AUC	P	Sensitivity (%)	Specificity (%)	PPV	NPV	Accuracy (%)
TCR-CD3ζ	≤ 0.077	0.840*	0.025**	93.5	75.0	78.9	92.0	84.3

AUC: Area under the curve

*AUC ≥ 0.5

** Statistically significant at p ≤ 0.05

PPV: Positive Predictive Value

NPV: Negative Predictive Value

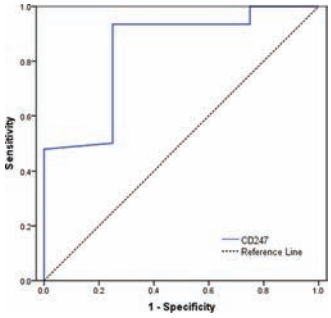


Figure 1. ROC curve for CD247 (TCR-CD3ζ) level as a predictor of Rheumatoid arthritis

Conclusion: Our results demonstrated a lower expression of TCR-CD3ζ in RA patients than in healthy controls. We suggested that CD247 gene down-regulation might contribute in the susceptibility to RA and help understanding the mechanisms responsible for deficient T-cell responses in RA patients.

REFERENCE:

[1] Wfeyand CM, Gaoronzy JJ. Pathogenesis of rheumatoid arthritis. Med Clin North Am 1997; 81:29–55.

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FRI0011 **A TRANSCRIPTIONAL REGULATOR CONTROLLING SEVERITY OF EXPERIMENTAL ARTHRITIS**

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Background: Susceptibility to Rheumatoid Arthritis (RA) is dependent on complex interactions among genetic and environmental factors. Protein candidates and their role in pathways leading to chronic inflammation of the joints, in addition to their potential as drug targets, can be revealed with the help of experimental models for disease (1). From the results of functional genetic studies, we have recently shown that the T-box gene, *TBX3*, is a candidate gene in Collagen Induced Arthritis (CIA), an experimental model for RA (2). *TBX3* encodes a transcriptional regulator involved in differentiation of several organs, including bone, during embryonic development. It has, in addition, been demonstrated important in oncogenesis (3). Our studies suggest that TBX3 has a role in B-cell activation and is important for the severity of disease in the CIA model (2).
Objectives: The objective of this project is to understand the role for the transcriptional regulator TBX3 in development of RA.
Methods: Bioinformatics based comparative studies of mouse and human alleles in the regulatory region of TBX3. CRISPR/Cas9-introduced deletions and base modifications in human B-cell lines. Activation of genetically modified B-cells in vitro, followed by analyses of proliferative response and antibody production.
Results: Studies of CIA development in mice with single nucleotide polymorphisms (SNPs) in the regulatory region of *Tbx3* revealed a significant difference in severity of arthritis. In line with this, the anti-collagen type II antibody titers were shown substantially higher in mice with more severe arthritis, even before onset of disease. In addition, preliminary data shows that the proliferative response to Type II collagen upon re-challenge of lymph node cells in vitro is higher in these mice, suggesting a more active response to the disease-inducing antigen. Because the *TBX3* gene is conserved between mouse and human, we are investigating whether similar genetic variations are found in the regulatory region of the human *TBX3* gene and whether the putative genetic variation would lead to a distinct B-cell phenotype upon activation in vitro.
Conclusion: We suggest that the oncoprotein TBX3 is a novel candidate contributing to disease severity in experimental arthritis. Investigations of genetic variation in the TBX3 gene and its role in the activation of human B-cells will reveal whether this protein is a candidate for influencing also development of RA.

REFERENCES:

[1] Sardar, S and Andersson, Å. Old and new therapeutics for Rheumatoid Arthritis: in vivo models and drug development. Immunopharmacology and Immunotoxicology. 2016, 38:1.
[2] Sardar, S, et al. The oncoprotein TBX3 is controlling severity in experimental arthritis. Arthritis Research and Therapy. 2019, 21:16.
[3] Wilmer, T, et al. The T-Box transcription factor 3 in development and cancer. 2017, BioScience Trends. 24;11(3).

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FRI0012 **THE CLINICAL SPECTRUM AND PEDIGREE ANALYSIS OF TRAPS IN GREECE, INCLUDING A NOVEL MUTATION-RESULTS FORM A NATIONAL REFERRAL CENTRE**

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Background: Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) stems from autosomal dominantly inherited mutations in the *TNFRSF1A* (accession number: NM_001065) gene, encoding for the receptor of tumor necrosis factor α (TNFR1).
Objectives: The aim of the study was to report a novel *TNFRSF1A* mutation and to describe the clinical phenotypes in families carrying different *TNFRSF1A* mutations.
Methods: Four Greek patients with TRAPS-like clinical features were evaluated for *TNFRSF1A* gene mutations. Direct sequencing of exons 2, 3 and 4 of the gene was performed. Following positive testing of the index cases, samples from other family members were collected and screened.
Results: A total of eighteen members deriving from four unrelated Greek families were investigated. In the first family, a novel (heterozygous) mutation in cysteine residue in exon 3 of the *TNFRSF1A* gene C73Y (c.305G>A) was identified in three members. Interestingly, in the same family a patient carrying the low penetrance *TNFRSF1A* R92Q mutation, as well as a patient with concomitant R92Q and C73Y mutations were identified. In the second family, the *TNFRSF1A* C73W (c.306C>G) heterozygous mutation was identified in seven members. In the third family, the *TNFRSF1A* T50M mutation was detected in two members while in the fourth family six members carried the *TNFRSF1A* R92Q mutation in heterozygous state.
Clinical manifestations amongst members of the affected families were diverse with the most serious being present in patients carrying the *TNFRSF1A* C73Y, C73W and T50M mutations. Cardinal features included disease onset in childhood (66.7% for C73Y, 85.7% for C73W and 100% for T50M), arthritis (67% for C73Y, 100% for C73W and 100% for T50M), persistent pyrexia (67% for C73Y, 100% for C73W and 100% for T50M), abdominal pain (66.7% for C73Y, 100% for C73W and 100% for T50M), recurrent adhesive ileus (33.3% for C73Y, 14.3% for C73W and 100% for T50M) anterior uveitis (33.3% for C73Y), and diffuse maculopapular rash (14.3% for C73W and 50% for T50M). The clinical presentation was more severe in the patient with concomitant R92Q and C73Y, suggesting an additive effect. On the contrary, (as expected) the disease spectrum associated with R92Q mutation found in six members encompassed a mild phenotype, extending from asymptomatic state (four members) to adult-onset disease associated with intermittent low-grade fever, arthritis and elevated inflammation markers (two members).
Conclusion: This was the first pedigree analysis of TRAPS in Greece, depicting four families with unique mutations, along with analysis of the clinical manifestation. The site of mutation might explain the diversity of clinical phenotypes in TRAPS patients that extends from mild to severe disease. In our patients, it appeared that mutations in the cysteine residues as well as in T50M were associated with more severe clinical manifestations. Among these was a novel mutation described for the first time in the literature.
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FRI0013 **ABSTRACT WITHDRAWN**

FRI0014 **GENETIC VARIABILITY IN MOLECULES REGULATING BONE REMODELING. DO THEY INFLUENCE SEVERITY OF DISEASE AND BONE MASS IN PATIENTS WITH EARLY-ONSET ARTHRITIS?**

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Background: In the last few years, an association has been described between lower bone mass at the onset of disease and higher severity of rheumatoid arthritis (RA).
Objectives: To identify single nucleotide polymorphisms (SNPs) in genes related to bone remodeling associated with severity of disease and bone mineral density (BMD) in patients with early-onset arthritis.
Methods: We included 268 PEARL (Princess Early Arthritis Register Longitudinal) patients genotyped with Illumina Inc. Immunochip. This array includes 556 SNPs with different density levels in semaphorins 4b, 4d and 4f, DKK1, 2 and 3, sclerostin, osteoprotegerin (OPG), RANK and

RANKL. All SNPs with genotyping rate <98%, with frequency of the minor allele <1% and those that were not in Hardy-Weinberg equilibrium, were excluded. In addition, among the SNPs in linkage disequilibrium, a representative one was chosen, so that only 159 were finally studied. The intensity of treatment, the activity of the disease measured by the DAS28 and HUPI indices, as well as having achieved at least low activity after 2 years of follow-up were chosen as surrogate severity variables. The association of each of the SNPs with these variables was analyzed by linear regression, and ordered logistic regression according to the variable, and adjusted for potentially confusing variables, such as age, sex and presence of anti-cyclic citrullinated peptide antibodies. We selected those SNPs that were consistently associated with $\geq$3 surrogate severity variables, and then, the relationship of the selected SNPs with BMD of the forearm, lumbar spine and hip (Hologic-4500 QDR) was analyzed by means of linear regression adjusted for age and sex.

Results: As shown in the attached table, 11 SNPs were associated with the severity of the disease; 7 of them were also associated with BMD, although only 3 confirmed the previously described relationship between severity of disease and BMD.

SNP	GENE	MOLECULE	DISEASE ACTIVITY	BMD
rs4355801	*LOC441377/ TNFRSF11B*	OPG	Decrease	No relationship
rs3134058	*TNFRSF11B*	OPG	Increase	No relationship
rs10505346	*TNFRSF11B*	OPG	Increase	No relationship
rs6469804	*TNFRS11B/ COLLECT10*	OPG	Decrease	No relationship
rs1805034	*TNFRS11A*	RANK	Decrease	Decrease
rs599323	*TNFRSF11A/ZCCHC2*	RANK	Increase	Increase
rs386283	*AKAP11/TNFSF11*	RANK-L	Increase	Increase
rs1324004	*AKAP11/TNFSF11*	RANK-L	Decrease	Increase
rs111900837	*AKAP11/TNFSF11*	RANK-L	Increase	Decrease
rs7142875	*AKAP11/TNFSF11*	RANK-L	Increase	Increase
rs7557277	*AKAP11/TNFSF11*	RANK-L	Increase	Decrease

Conclusion: This preliminary study highlights the relationship between gene variants of molecules involved in bone remodeling and the severity of early-onset arthritis. However, more studies are needed to confirm this relationship and validate it in other populations. This would confirm the involvement of these gene variants in disease activity and bone mass variation.

REFERENCES:

[1] Llorente. I, et al. Anti-citrullinated protein antibodies are associated with decreased bone mineral density: baseline data from a register of early arthritis patients. Rheumatol Int. 2017;37(5):799-806

[2] Forslind K. et al. Hand bone loss measured by digital X-ray radiogrammetry is a predictor of joint damage in early rheumatoid arthritis. Scand J Rheumatol. 2009;38(6):431-8.

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FRI0015

EXON 5 DUPLICATION IN ALPL GENE AS THE GENETIC CAUSE OF HYPOPHOSPATASIA IN A 3 YEAR OLD GIRL

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Background: Hypophosphatasia (HPP) (OMIM 146300, 241510, 241500) is an inborn error of metabolism caused by pathogenic variants in the gene *ALPL* that codifies for the tissue non-specific alkaline phosphastase ([1]). The disease presents with different degrees of severity, from perinatal forms to mild adult phenotypes, including odontohypophosphatasia where only dental complications are described. Until now, more than 380 variants are described to cause HPP, and only 2,9% are large deletions or duplications (http://www.sesep.uvsq.fr/03_hypo_mutations.php).

Objectives: Identify the genetic cause of the disease in the girl with an infantile HPP.

Methods: The patient is a female child born by cesarean at week 37 of gestation. The child required reanimation. Weight, length and cranial perimeter were bellow percentile 10th (1735g, 42 cm, 31,5 cm respectively). She presented and obstetric femur fracture and normal to low alkaline phosphatase (AF) activity (158 UI/L (reference 142-335 UI/L). After fracture, a second determination of AF (127UI/L) and pyridoxal-5′-phosphate (PLP) concentration (240,41 mgc/L, reference 6,4-23) were measured. Skeletal interrogation revealed low bone mineralization, tongues of radiofluency in long bones and narrow ribs. A clinical diagnose of hypophospatasia was done. At the three year-old revision she still presents weight and length below percentile 15th, a mild cardiac problem but had no fractures since birth. She presents lung malformation, and cannot eat solid food. She still has low AF activity (154 U/L) and high PLP (69,13 µg/L; refences 150-350 U/L and 3,6-18 µg/L respectively). She is on school but has language delay. Genetic analysis: DNA was extracted from peripheral blood of patient and her mother. From patient's sample we perfomed Sanger sequencing of exons 1 to 12, CGH analysis using a customized whole genome CGH 4x44k Agilent array enriched in probes for *ALPL* gene (130 probes) and qPCR of exons 2 to 12.

Results: The study of copy number variants of *ALPL* gene by qPCR revealed a duplication in exon 5 in the patient and her mother.

Conclusion: Although gross deletions and duplications are a rare phenomenon in HPP, here we present a case of a 3 year old child and her mother that present a single exon duplication as a probable cause of the disease. Actually, the mother is under clinical evaluation. Part of the active site is codified in exon 5, suggesting that a duplication might alter the correct structure and/or function of the protein. So, including the screening of copy number variants during the genetic screening is important to reach the correct diagnosis of HPP.

REFERENCES:

[1] Whyte, M.P. (2017). Hypophosphatasia: An overview For 2017. Bone 102, 15–25.

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FRI0016

MUTATIONAL LANDSCAPE OF MYELODYSPLASTIC SYNDROME IN PATIENTS WITH AUTOIMMUNE RHEUMATOLOGICAL DISORDERS

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Background: Autoimmune rheumatological disorders (AIRD) have been described in myelodysplastic syndrome (MDS) and related-myeloid disorders but its association remains unclear. Immunosuppressive treatment of AIRD could cause therapy-related myeloid neoplasm (t-MN) or confound the secondary diagnosis of MDS. The prevalence of cytopenia in patients with AIRD is unknown and the mutation profile of patients with AIRD and concomitant MDS have not been well characterised.

Objectives: This study aims to evaluate the prevalence of cytopenia in AIRD and analyse the mutation profile of patients with concomitant diagnosis of AIRD and MDS by interrogating the databases of 2 large institutions - Royal Adelaide Hospital Rheumatology Department (RAH-RD) and South Australia-Myelodysplastic Syndrome (SA-MDS).

Methods: Demographic, clinical, laboratory and treatment data of 2663 patients from RAH-RD and 1157 patients from SA-MDS were analysed according to the idiopathic cytopenia of undetermined significance (ICUS) criteria. Patients with persistent cytopenia (>6 months) were defined as follows: haemoglobin <100g/L, absolute neutrophil count $<1.8x10^9$/L and platelet $<100x10^9$/L. Within the SA-MDS registry, 237 bone marrow samples were analysed for 43 myeloid neoplasms associated genes and 20 Fanconi (FA) DNA repair pathway genes with targeted massively parallel sequencing. An in-house filtering pipeline was used to identify somatic mutations.

Results: Within RAH-RD database, 79 patients (3%) fulfilled the criteria for at least 1 cytopenia. 21 patients underwent bone marrow biopsy, with 9 bone marrow samples being diagnostic of MDS. Neutropenia was most common (27/79 patients, 34%), followed by anaemia (20/79 patients, 25%) and thrombocytopenia (6/79 patients, 8%). Within SA-MDS database, 62 patients (5%) had concomitant AIRD. Rheumatoid arthritis is the most common AIRD diagnosis (21/62 patients, 34%) in the SA-MDS database. Combined analysis of both databases revealed that 71/3820 patients (1.9%) had a concomitant diagnosis of both AIRD and MDS.

The cytogenetic and mutational profile of patients with concomitant diagnosis of AIRD and MDS within the SA-MDS database were analysed and 56 mutations were discovered in this group. Mutation in ASXL1 was the most common (6/20 patients, 30%), followed by TET2 (5/20 patients, 25%) and lastly TP53 (4/20 patients, 20%). There is significantly higher frequency of IDH1 mutation in the AIRD-MDS cohort compared to patients with MDS only. Three patients with TP53 mutation developed MDS following treatment for AIRD (therapy-related MDS).

Conclusion: In a large cohort of patients with AIRD, 3% of patients developed ongoing cytopenia and 0.3% were diagnosed with MDS. This finding is higher than the incidence of MDS in the general population (0.03-0.05%). Within the SA-MDS registry, 5% of patients had concomitant diagnosis of AIRD. Our findings warrant further study and have potential implications for selection of disease-modifying drugs for patients with AIRD.

REFERENCES:

[1] Mekinian, A, et al. (2015). Systemic inflammatory and autoimmune manifestations associated with myelodysplastic syndromes and chronic myelomonocytic leukaemia: a French multicentre retrospective study. Rheumatology, 55(2), 291-300.

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FRI0017

DIFFERENTIAL METHYLATION AS A PREDICTOR OF TOCILIZUMAB RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Tocilizumab (TCZ) is a biological disease-modifying antirheumatic drug that blocks IL-6 signalling and is effective in ameliorating disease activity in rheumatoid arthritis (RA). Despite this, approximately 50% of patients do not respond adequately to TCZ and some patients report adverse events. Considering there is growing evidence that DNA methylation is implicated in RA susceptibility and response to some biologics (1, 2), we investigated methylation patterns as a candidate biomarker for response to TCZ in RA.

Objectives: To identify differential DNA methylation signatures in whole blood associated with TCZ response in patients with RA.

Methods: Epigenome-wide DNA methylation patterns were measured using the Infinium EPIC BeadChip (Illumina) in whole blood-derived DNA samples from patients with RA. DNA was extracted from blood samples taken pre-treatment and following 3 months on therapy, and response was determined at 6 months using the Clinical Disease Activity Index (CDAI). Patients who had good response (n=10) or poor response (n=10) to TCZ by 6 months were selected. Samples from secondary poor responders (n=10) (patients who had an improvement of CDAI and were in remission at 3 months, followed by a worsening of CDAI at 6 months) were also analysed. Differentially methylated positions (DMPs) were identified using linear regression, adjusting for gender, age, cell composition, smoking status, and steroids use.

Results: There were 20 DMPs significantly associated with response status at 6 months in the pre-treatment samples, and 21 DMPs associated with response in the 3 months samples (unadjusted P-value < 1.00E-06). Furthermore, there were 10 DMPs significantly associated with change in methylation between pre-treatment and 3 months samples in good responders, but there were no significant findings when comparing methylation between time points in poor responders or in secondary poor responders. One DMP, cg03121467, was significantly less methylated in good responders compared to poor responders in the pre-treatment samples (p=1.06E-06). Furthermore, methylation was lower in good compared with poor responders at 3 months (p=1.03E-07). This DMP is close to *EPB41L4A*, which is thought to have a role in β–catenin signalling.

Conclusion: Whilst further analyses comparing sub-components of the CDAI with changes in methylation is ongoing, these preliminary results provide evidence that DNA methylation patterns may predict response to TCZ. Validation of these findings in other larger data sets is required.

REFERENCES:

[1] Liu,Y., Aryee,M.J., Padyukov,L., Fallin,M.D., Hesselberg,E., Runarsson,A., Reinius,L., Acevedo,N., Taub,M., Ronninger,M., et al. (2013) Epigenome-wide association data implicate DNA methylation as an intermediary of genetic risk in rheumatoid arthritis. Nat. Biotechnol., 31, 142–147.

[2] Plant,D., Webster,A., Nair,N., Oliver,J., Smith,S.L., Eyre,S., Hyrich,K.L., Wilson,A.G., Morgan,A.W., Isaacs,J.D., et al. (2016) Differential Methylation as a Biomarker of Response to Etanercept in Patients With Rheumatoid Arthritis. *Arthritis Rheumatol. (Hoboken, N.J.)*, 68, 1353–60.

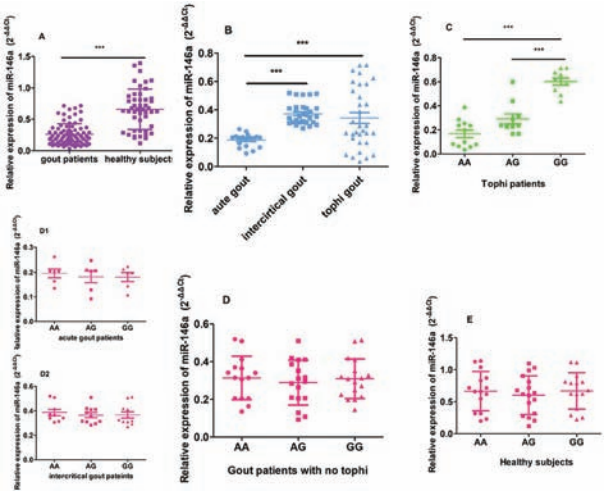
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FRI0018 **ASSOCIATION OF MICRORNA-146A RS57095329 POLYMORPHISM WITH SUSCEPTIBILITY TO GOUT TOPHI IN A CHINESE HAN POPULATION**

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Background: MicroRNA-146a (miR-146a) plays an important role in regulation of autoinflammatory diseases including gout[1]. Growing evidences have demonstrated that association of miR-146a gene single nucleotide polymorphisms (SNPs) with risk of several diseases[2], but no genetic relevance studies of miR-146a gene polymorphisms to gout have been reported by now.
Objectives: To investigate the potential association of gout and the functional rs57095329 SNP of miR-146a in the Chinese Han population.
Methods: The rs57095329 SNP was detected in 448 primary gout patients (containing 76 tophi patients) and 418 healthy control subjects. Peripheral blood mononuclear cells (PBMCs) miR-146a expression was measured in 81 gout patients (including 32 tophi patients and 49 non-tophi patients) and 47 healthy subjects.
Results: No significant difference was detected in the distribution of miR-146a rs57095329 between 448 gout patients and 418 healthy subjects (P>0.05). However, significant differences were observed between 76 gout with tophi patients and 418 healthy subjects, between gout with tophi (76) and with no tophi patients (372) both in genotypes and allele distributions (P<0.01, respectively). Gout patients carrying AG/GG genotypes had a 0.323-fold reduced risk for tophi than those carrying AA genotype, and the G allele carrier of gout patients had a 0.362-fold reduced risk for tophi. Additionally, GG genotype was significantly associated with increased expression of miR-146a in 32 tophi patients (Figure).



Conclusion: Our study shows a novel, significant association between the miR-146a rs57095329 polymorphism and a lower risk of tophi in gout patients. Furthermore, our findings suggest that this gene polymorphism might affect the genetic predisposition to tophi development and modulate the expression of miR-146a level in tophi patients. This new knowledge about miR-146a may be clinically important and confirms a role for miR-146a in the pathophysiology of tophi, with potentially important therapeutic implications.

REFERENCES:

[1] Zhang QB, Qing YF, Yin CC, Zhou L, Liu XS, Mi QS, et al. Mice with miR-146a deficiency develop severe gouty arthritis via dysregulation of TRAF 6, IRAK 1 and NALP3 inflammasome. Arthritis Res Ther. 2018;20:45.
[2] Luo X, Yang W, Ye DQ, Cui H, Zhang Y, Hirankarn N, et al. A functional variant in microRNA-146a promoter modulates its expression and confers disease risk for systemic lupus erythematosus. PloS Genet. 2011;7: e1002128.

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FRI0019 **URINARY TRANSCRIPTS AS BIOMARKERS OF LUPUS NEPHRITIS**

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Background: Children with systemic lupus erythematosus (cSLE) with kidney involvement face considerable morbidity and mortality. Commonly used methods for assessing kidney involvement in cSLE, such as renal function tests, are non-specific and provide a limited picture of disease activity. Kidney biopsy, the mainstay to assess disease class and chronicity as well as response to treatment, is an invasive procedure. The field of transcriptomics has identified markers that have helped our understanding of cSLE pathogenesis.
Objectives: Transcriptional profiling of urinary cells has the potential to provide us with non-invasive biomarkers and has not been studied thus far. Our aim is to evaluate intracellular urinary transcripts in cSLE.
Methods: Using the Human Inflammation v2 panel on the nanoString nCounter platform, expression of 255 genes was profiled from 82 urinary pellets (all from 43 cSLE with differing classes of lupus nephritis).
Results: Healthy control samples yielded low quantities of RNA and were excluded from further analysis. The patient's raw transcript counts were normalized and the use of unsupervised learning analysis revealed robustness among classes with higher disease activity (higher SLE Disease Activity Index (SLEDAI) scoring). Statistical analysis (ANOVA) showed that Classes III or IV + V (mixed nephritis; highest average SLEDAI) display robust interferon and inflammasome-related signatures in comparison to other classes. Interestingly, samples from cSLE with no known nephritis also displayed an interferon signature, although less intense than the mixed class. Some transcripts such as C3 (complement 3) were uniquely dysregulated in the mesangial class. Therapeutically targetable pathways were identified in a number of patients (specifically in the mixed class).
Conclusion: These studies are currently being extended in order to confirm the value of urinary transcriptional profiling as a source of biomarkers and to identify potential therapeutic targets in cSLE.

REFERENCES:

[1] Pascual, et al., "Understanding Human Autoimmunity and Autoinflammation Through Transcriptomics," Annu Rev Immunol, 2017 Apr 26;35:337-370. doi: 10.1146/annurev-immunol-051116-052225
[2] Bennett L, Palucka AK, Arce E, et al. Interferon and Granulopoiesis Signatures in Systemic Lupus Erythematosus Blood. The Journal of Experimental Medicine. 2003;197(6):711-723. doi:10.1084/jem.20021553.
[3] Banchereau R, Hong S, Cantarel B, Baldwin N, Baisch J, et al. 2016. Personalized immunomonitoring uncovers molecular networks that stratify lupus patients. Cell 165:551–65
[4] Chiche L, Jourde-Chiche N, Whalen E, Presnell S, Gersuk V, et al. 2014. Modular transcriptional repertoire analyses of adults with systemic lupus erythematosus reveal distinct type I and type II interferon signatures. Arthritis Rheumatol. 66:1583–95
[5] Brunner H.I., Bennett M.R., Gulati G., Abulaban K., Klein-Gitelman M.S., Ardoin S.P., Tucker L.B., Devarajan P. Urine biomarkers to predict response to lupus nephritis therapy in children and young adults (2017) Journal of Rheumatology, 44 (8), pp. 1239-1248.

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FRI0020 **CORRELATION BETWEEN EXPRESSION LEVELS OF MIR-146A AND MIR-223 IN SYNOVIAL FLUID AND ULTRASOUND SCORES FOR ACTIVE SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS**

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Background: MicroRNAs (miRNAs) are a class of small, non-coding RNAs that negatively regulate gene expression at posttranscriptional level. In the recent years studies have shown that in rheumatoid arthritis (RA) the systemic and local expression of certain miRNAs is altered [1-2]. The correlation between their expression levels and scores for disease activity and progression in RA make them possible candidate for biomarkers in the clinical practice.
Objectives: To analyze the expression levels of miR-146a and miR-223 in synovial fluid (SF) from RA patients in regard to the ultrasound scores for disease activity.
Methods: A total number of 48 RA patients according to the 1987 ACR criteria were included in the study. Expression levels of miR-146a and miR-223 SF were determined by qPCR (SybrGreen technology) and compared to healthy controls (HCs). Relative changes of gene expression levels of the studied miRNAs were calculated by $2^{-\Delta\Delta Ct}$ method. Musculoskeletal ultrasound (MSUS) examination was performed by two independent examiners on ESAOTE, MyLab60 using both grey scale and power Doppler technic. A semi quantitative assessment of the peripheral joints was performed for detecting joint inflammation and determining the grade of synovial thickening and the degree of vascularization. Ultrasound features for active disease were correlated to the local expression of the studies miRNAs. SPSS was used for statistical analysis.
Results: RA SF showed overexpression of miR-146a (in 70.83%, p=0.007) and of miR-223 (in 79.17%, p=1.64x10-3) when compared to HCs. There was a statistically significant correlation between the presence of synovitis and the degree of the power Doppler signal on MSUS and the local expression of miR-146a (p=0.030 and p=0.049, respectively) and miR-223 (p=6.19 x 10^{-4} and p=0.003, respectively). SF levels of miR-223 correlated also with the degree of synovial hypertrophy on MSUS (p = 0.013).
Conclusion: We found correlation between the SF expression of miR-146a and miR-223 and the ultrasound features of active joint inflammation. Further analysis with larger sets is needed to confirm if altered local miRNA expression could be used in the clinical practice as biomarker for disease activity especially in cases with subclinical synovitis.

REFERENCES:

[1] Li J, Wan Y, Guo Q, Zou L, Zhang J, Fang Y, et al. Altered microRNA expression profile with miR-146a upregulation in CD4+ T cells from patients with rheumatoid arthritis. Arthritis Res Ther. 2010; 12(3):R81.
[2] Lu MC, Yu CL, Chen HC, Yu HC, Huang HB, Lai NS. Increased miR-223 expression in T cells from patients with rheumatoid arthritis leads to decreased insulin-like growth factor-1-mediated interleukin-10 production. Clin Exp Immunol. 2014; 177(3):641-51.

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Rheumatoid arthritis – comorbidity and clinical aspects

FRI0021 **ORAL HYGIENE STATUS IN RA PATIENTS AND PLACE OF RHEUMATOLOGIST IN THERAPEUTIC EDUCATION ON ORAL DENTAL HEALTH**

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Background: The relationship between oral hygiene and rheumatoid arthritis has been demonstrated by several studies.
Objectives: To evaluate oral hygiene status in rheumatoid arthritis (RA) patients.
To inform about the therapeutic education given by the rheumatologist on the importance of adequate oral hygiene in the management of RA
Methods: This is a cross-sectional study that included 100 consecutive RA patients (89% female, mean age 46.7 years, median disease duration of 8 years, mean specialized care duration of 3 years). A questionnaire evaluating oral hygiene status was administered. It focused on following items: the daily frequency of brushing, the modalities of brushing, the use of other means of oral hygiene, the regular follow-up at a dentist's doctor and the place of the rheumatologist in therapeutic education on the oral dental hygiene status.
Results: Table I illustrates the results of oral hygiene evaluation in RA patients.

Table I : Evaluation of Oral Hygiene in RA patients

Items	N=100
Daily Brushing Frequency (%):	18
- 0 times/day	37
- once a day	34
- 2 times/day	8
- 3 times/day	3
- After each meal	
adequate brushing time (≥3min) (%)	31
Correct brushing method (%)	14
Use of other means of oral hygiene (%)	36
Regular dentist visit (%)	2
Never visit a dentist (%)	27

Table II illustrates the results of the place of oral hygiene information in rheumatologic management.

Table II : Place of information on oral hygiene in rheumatologic care.

Questions	Yes (%)
1. does your rheumatologist ever examined your oral cavity?	6,0
2. have you ever been informed by your rheumatologist that poor oral hygiene has a negative impact on your rheumatoid arthritis?	11,0
3. Does your rheumatologist ever recommended regular brushing of your teeth?	8,0
4. Does your rheumatologist already recommended to you to consult a dentist?	10,0

Conclusion: This study illustrates the high prevalence of oral hygiene insufficiency in patients followed for RA. It also highlights poor therapeutic education given by the rheumatologist on the importance of adequate oral hygiene in the management of RA.
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Rheumatoid arthritis - comorbidity and clinical aspects

FRI0022 EVALUATION OF DYSFUNCTIONAL HIGH-DENSITY LIPOPROTEIN LEVELS WITH MYELOPEROXIDASE/ PARAOXONASE1 RATIO IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic, systemic and autoimmune disease with inflammatory arthritis. Atherosclerosis and cardiovascular diseases are common in RA patients. Although chronic systemic inflammation in RA patients is considered to be the main cause of this condition, the relationship between systemic inflammation and vascular pathophysiology is not clear [1]. While high-density lipoprotein (HDL) is known to be a negative risk factor for atherosclerosis by reverse cholesterol transport, recent studies show that HDL can be pro-atherogen (dysfunctional, inflammatory) by losing this characteristic in cases of inflammation and oxidative stress. Myeloperoxidase (MPO)/paraoxonase 1 (PON1) ratio is a valuable marker that can be routinely used as an indicator of dysfunctional HDL. PON1 is a lipoprotein-derived enzyme which provides antioxidant properties of HDL. Although MPO is a bactericidal enzyme derived from granular leukocytes, it causes oxidative modification of circulating lipoproteins [2].
Objectives: The aim of this study is to evaluate the levels of dysfunctional HDL in RA patients and to explore the relationship between dysfunctional HDL and coronary artery disease (CAD) in RA patients.
Methods: Sixty seven healthy individuals and 130 RA patients without diabetes mellitus, hypertension and hyperlipidemia were included to study. Blood samples taken from patients and healthy volunteers were centrifuged to separate serum and these serum samples were stored at -80 °C until the study day. Total cholesterol (TC), triglyceride (TG), HDL, Low-density lipoprotein cholesterol (LDL), MPO and PON1 levels were measured. The MPO/PON1 ratio was calculated as a dysfunctional HDL marker. Cardiology notes of the patients were examined to detect patients who also have CAD.
Results: The mean age of the patient and control groups were 54.6 ± 11.3 and 52.0 ± 10.0, respectively (p:0.107). The mean DAS28 score of the patients was 2.77 ± 0.96. There were no significant differences between two groups in TC, TG, HDL and LDL (p> 0.05). MPO, PON1 and dysfunctional HDL levels were significantly higher in the RA group compared to control group (p <0.001, p <0.023, and p <0.001; respectively).
Dysfunctional HDL levels were higher in 44 RA patients with CAD compared to 86 RA patients without CAD (p = 0.002). 58 patients with active RA had higher dysfunctional HDL levels compared to 72 patients with remission (p = 0.002). There was a positive correlation between DAS28 scores and dysfunctional HDL levels (rho: 0.357, p < 0.001).
Conclusion: Our study shows that, although there is no abnormality in lipid profile parameters, dysfunctional HDL levels were higher in patients with active disease than patients with RA in remission and RA patient with CAD than without CADs. This condition could be associated with CAD in RA patients. Disturbance as a result of inflammation on HDL functions such as inhibition of LDL oxidation and reverse cholesterol transport, could be the cause of CAD in RA patients. As a result screening of conventional cardiovascular risk factors in RA patients with normal lipid panel might be inadequate. Therefore as an additional parameter, dysfunctional HDL are promising to evaluate cardiovascular risk of RA patients.

REFERENCES:

[1] Bag-Ozbek, A. and J.T. Giles, Inflammation, adiposity, and atherogenic dyslipidemia in rheumatoid arthritis: is there a paradoxical relationship? Curr Allergy Asthma Rep, 2015. 15(2): p. 497.
[2] Haraguchi, Y., et al., Serum myeloperoxidase/paraoxonase 1 ratio as potential indicator of dysfunctional high-density lipoprotein and risk stratification in coronary artery disease. Atherosclerosis, 2014. 234(2): p. 288-294.

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FRI0023 CARDIOVASCULAR RISK AND VITAMIN D DEFICIENCY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THERAPY WITH TNF-ALPHA INHIBITORS

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Background: Cardiovascular disease is the main cause of mortality and morbidity in patients with rheumatoid arthritis (RA). Correlation between vitamin D deficiency and atherosclerosis in patients with rheumatoid arthritis is a subject of medical interest.
Objectives: We studied the correlation between vitamin D deficiency, body mass index (BMI) and carotid intima-media thickness (CIMT) in patients with rheumatoid arthritis with anti tumor necrosis factor-alpha (TNF-α) therapy.
Methods: Our study included 75 RA patients with anti-TNF-alpha therapy (Adalimumab, Influximab, Etanercept) and 30 RA patients with DMARDs (Methotrexate/Leflunomide). The patients were diagnosed with RA according to ACR/EULAR (2010) classification **criteria.**
CIMT was measured using high-resolution Doppler ultrasonography. CIMT ≥ 0.9 mm is considered as a marker of atherosclerosis. Vitamin D deficiency was defined as serum 25-OH-vitamin D level <20 ng/mL. Other parameters included are age, body mass index (BMI=18,5-24,9**kg**/m^2- normal weight; BMI≥25**kg**/m^2- overweight) and disease activity (DAS28<2.6: remission; DAS28=2.6-3.2: low disease activity, **DAS28=**3.2-**5.1**: moderate **disease activity; DAS28**>**5.1:** high **disease activity).**
Patients with current use of vitamin D supplements were excluded.
Results: The anti-TNF group included 29 patients with Adalimumab (38.7%), 25 with Etanercept (33.3%) and 21 patients in treatment with Infliximab (28%). Their mean age was 52.0 years.
We evaluated patients at baseline and after 12 months with treatment.
In anti-TNF group we found 9 patients (12%) with normal BMI and normal vitamin D level correlated with high CIMT (p=0.001), 21 patients (28%) with overweight and normal vitamin D level correlated with high CIMT (p=0.003), and 31 patients (41.3%) with overweight and low vitamin D level correlated with high CIMT (p=0.001). 14 patients (18.7%) with normal vitamin D level and normal weight (9) or overweight (5) were correlated with normal CIMT (p=0.01).
In DMARDs group we followed the same correlation. Patients with normal BMI and normal vitamin D level had a low correlation with CIMT increase (p=0.01). Patients with overweight and low vitamin D level had a significant correlation with CIMT increase (p=0.003) than group with anti-TNF-alpha therapy.
After 12 months of therapy, patients treated with Adalimumab had lower CIMT levels than patients treated with Etanercept.
Conclusion: Rheumatoid arthritis patients treated with TNF inhibitors and with vitamin D deficiency but with normal BMI have been correlated with lower increase of CIMT than patients with DMARDs therapy. Normal vitamin D level was associated with low increase of CIMT in these patients. Deficiency of Vitamin D associated with overweight are risk factors for carotid atherosclerosis in patients with RA.
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FRI0024 AA AMYLOIDOSIS AND LUNG DISEASES IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 147 PATIENTS

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Background: Systemic AA amyloidosis (**AAa**) is one of the most important complications of rheumatoid arthritis (**RA**) [1].
A wide spectrum of lung diseases may complicate **RA** or associate with **RA** [2-4].
Objectives: The **aim** of this study was to determine the influence of **AAa** on lung diseases related or not related to **RA**.
Methods: We studied **161** random autopsy patients with **RA** [1]. **RA** was confirmed clinically according to the criteria of the **ARA** [5]. Tissue samples of the lungs were available for histological evaluation of **147** patients.

The prevalence of **AAa** and of distinctly different forms of multifocal inflammation, such as purulent bronchitis and bronchiolitis (**purBr**) or bronchopneumonia (**BrPn**), infarct with pneumonia (**InfPn**), occlusive pneumonia (**OcclPn** – focal pneumonia caused by compressive peribronchial nodular lymphoid hyperplasia or bronchial blockage by a necrotic nodule) were examined. In addition, rheumatoid pneumonia (**RhPn**), furthermore interstitial pneumonia (**IPn**) [1-4] were determined at autopsy and confirmed in a detailed review of extensive histological material.

The possible role of **AAa** on the prevalence of **purBr** or **BrPn**, **InfPn**, **OcclPn**, **RhPn** and **IPn** was analyzed with Pearson's chi-squared (χ^2) test.

Results: AAa complicated **RA** in **34** (**23.13**%) of 147 patients. Pulmonary blood vessels of different caliber and various tissue structures of the lungs were involved in **25** (**73.53**% of 34) cases; the lungs were not involved by **AAa** in **9** (**26.47**% of 34) cases.

purBr or **BrPn** were associated with **RA** in **19** (**21.1**%), **InfPn** in **5** (**3.4**%), **OcclPn** in **2** (**1.4**%), **RhPn** in **3** (**2.1**%) of **147** patients (only the fatal cases were considered). **IPn** – characterized by interstitial cellular infiltration with or without edema, fibrinoid deposition, with or without fibrosis, and with or without corresponding pleuritis was present in **35** (**23.8**%) of 147 patients; **IPn** alone was not fatal in our cohort and contributed to the death only in association with cardiac, circulatory or cardio-respiratory insufficiency.

Pulmonary amyloid A deposition (**n=25**) was associated with **purBr** or **BrPn** in **1** (**5.26**%) of 19, **InfPn** in **1** (**20.0**%) of 5, **OcclPn** in **2** (**100.0**%) of 2, **RhPn** in **none** (**0.0**%) of 3, **IPn** in **12** (**34.29**%) of 35 patients.

The relationship between pulmonary **AAa** and **purBr** or **BrPn** (χ^2=1.2836, p<0.25), **InPn** (χ^2=0.1800, p<0.67) or **RhPn** (χ^2=0.00025, p<0.98) was not significant. There was a **significant** and **positive correlation** between pulmonary **AAa** and **OcclPn** (χ^2=4.8313, p<0.02) or between **AAa** and **IPn** (χ^2=9.7106, p<0.0018).

Conclusion: The main complications of **RA,** such as **AAa**, may influence the prevalence, clinical course and symptoms of associated diseases and vice versa. Knowledge of these relationships is important to estimate the relative danger they potentially represent.

The **significant correlation** between **AAa** and **OcclPn** or **IPn** suggests a positive influence of pulmonary amyloid A deposition on **OcclPn** or **IPn**. The statistically not significant correlations suggest that **purBr** or **BrPn**, **InPn** and **RhPn** are independent entities which are not influenced by **AAa**.

REFERENCES:

[1] Bély M, **Apáthy Ágnes**: Clinical pathology of rheumatoid arthritis. pp 1-440, Akadémiai Kiadó, Budapest 2012 http://www.akkrt.hu
[2] Wright GP, **Heard BE**: The lungs in rheumatoid arthritis. In Symmers *Systemic pathology*, ch. 7, pp 370-371, Churcill Livingstone, Edinburgh, London, New York 1976
[3] Bély M, **Apáthy Á**: *Acta Morphologica Hungarica*, 1991, 39: 117-156.
[4] **Bély M**: *Zentralblatt für allgemeine Pathologie und pathologische Anatomie*, 1988, 134: 647-664.
[5] Arnett FC, et al: Arthritis Rheum. 1988; 3:315-24, DOI: 10.1002/art.1780310302

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FRI0025 DOES COMORBIDITY IMPACT ON THE ACTIVITY AND MANAGEMENT OF RHEUMATOID ARTHRITIS?

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Background: Patients with rheumatoid arthritis (RA) are in increased risk of developing comorbid conditions. Recent data suggest the relationship between severity of RA and concomitant diseases [1, 2]. Drug therapy is considered as impotent risk factor for numerous comorbidities. On the other hand comorbidity can impact negatively on the RA course and on the pts management [3].

Objectives: The aim of our study was to evaluate the prevalence of concomitant conditions in RA pts, to compare the RA activity and management in relation with comorbidities.

Methods: 168 pts with established and longstanding RA were observed at in-patient clinic for RA clinical assessment and revealing concomitant diseases (cardiovascular, gastrointestinal, liver, pulmonary, endocrine, blood). The activity of disease according to DAS28-ESR index in RA subgroups with different comorbidities was compared. The spectrum and used doses of anti-rheumatic medications (DMARD, biologics, GC) in these subgroups was analyzed in term to assess the RA rational treatment.

Results: The majority (88.1%) of observed RA pts had concomitant condition. The most frequent associated diseases were: cardiovascular (AH, IHD, HF, AF) in 86.9% and gastrointestinal (gastritis, duodenitis, gastroduodenal ulcer, colitis) in 64.3% less common comorbidities were anemia (30.9%), liver and kidney abnormalities (hepatomegaly, steatohepatitis, CKD, pyelonephritis) in 25% and 12.5% respectively, endocrine (type 2 diabetes mellitus, thyroid disorders) in 16.7%. Multimorbidity determined as combination of different system disorders in the setting of RA was detected in 54.8% of RA pts. We found out significant difference in RA activity on the basis of DAS28 between RA subgroup without concomitant conditions (the 1st) on the one hand and RA subgroups with comorbidities (the 2nd) (t1=2.76, p<0.01) or multimorbidities (t2=3.73, p<0.01) on the other hand (tab.1).

Index	RA without comorbidities (1st group)	RA with comorbidities (2nd group)	RA with multimorbidities (3d group)
DAS 28	4.20 ±0.31	5.09±0.09	5.44±0.12

In RA with comorbidities/multimorbidities the mean doses of MTX and SSZ were lower than in RA without comorbidities, while the dose of GC and frequency of GC use was significantly higher in the 2nd and 3d groups (χ^2=4.25, 4.41 respectively). 55% of pts from the 1st group and only 19.6% of total amount of pts from the 2nd and 3d groups were treated with biologics (χ^2=5.67).

Conclusion: Obtained data suggest that comorbidities have a negative impact on the severity of RA and can interfere in the implementation of T2T strategy in daily clinical practice.

REFERENCES:

[1] Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis (2014) 73(1):62–8. doi:10.1136/annrheumdis-2013-204223
[2] Radner H. Multimorbidity in rheumatic conditions. Wien Klin Wochenschr (2016) 128(21–22):786–90. doi:10.1007/s00508-016-1090-x
[3] Radner H, Yoshida K, Frits M, Iannaccone C, Shadick NA, Weinblatt M, et al. The impact of multimorbidity status on treatment response in rheumatoid arthritis patients initiating disease-modifying anti-rheumatic drugs. Rheumatology (Oxford) (2015) 54(11):2076–84. doi:10.1093/rheumatology/kev239

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FRI0026 SYSTEMIC, RENAL AND CARDIAC AA AMYLOIDOSIS IN RHEUMATOID ARTHRITIS – A COMPARATIVE POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS

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Objectives: The **aim** of our study was to determine the incidence of **s**ystemic **AA** **a**myloidosis (**sAAa**) in **RA**, to appraise the prevalence and severity of amyloid A deposits in different tissue structures of the kidneys and heart, to outline the development of **r**enal and **c**ardiac **AA** **a**myloidosis (**rAAa** and **cAAa**), and to estimate the role of **rAAa** and **cAAa** in mortality.

Methods: One hundred sixty one (**161**) non- selected autopsy patients with rheumatoid arthritis (**RA**) were studied. **RA** was confirmed clinically according to the criteria of the **ACR** [1]. **sAAa** was specified histologically, based on evaluation of **5** organs (heart, lung, liver, kidney and pancreas). Amyloid A deposition was diagnosed histologically according to Romhányi by a modified (more sensitive) Congo red staining [2]. Amyloid

A deposits were confirmed in serial sections by immunohistochemical and histochemical methods.
Results: **sAAa** complicated **RA** in **34** (**21.12**%) of 161 patients; in **127** (**78.88**%) of 161 patients amyloid A deposits were not found.
Amyloid A deposits were found in **29** (**87.88**%) **kidneys** of 33 patients **with sAAa**; kidneys were negative for amyloid in **4** (**12.12**%) of 33 cases (in 1 of 34 patients with **sAAa** tissue blocks of kidneys were not available).
Amyloid A deposits were found in **29** (**87.88**%) **hearts** of 33 **with sAAa**; the heart was negative for amyloid in **4** (**12.12**%) of 33 cases (the heart of one patient with **sAAa** was not available).
Renal amyloid A deposition led to death in **17** (50.0% of 34) patients **with sAAa** due to massive amyloid A deposition in the kidneys, leading to renal insufficiency and uremia. Cardiac amyloid A deposition led to death in **3** (8.82% of 34) patients **with sAAa** (and contributed to the lethal outcome in further 5). **Forteen** (41.18% of 34) patients with **sAAa** died of other causes such as peritonitis, lethal septic infection, etc.
sAAa was clinically diagnosed in **9** (26.47%) and missed in **25** (73.52%) of 34 patients, and only cases with massive renal amyloid A deposits were recognized. Cardiac **AAa** or its pathogenic role in mortality was not diagnosed.
Conclusion: **sAAa** is one of the main and the most insidious complications of **RA** affecting the kidneys and heart with high prevalence and severity. **sAAa** is related to the cardiovascular system, and **rAAa** or **cAAa** are associated with it. **sAAa**, **rAAa** and **cAAa** may developed in both sexes, and at any time in the course of the disease.
Systemic, renal and cardiac amyloid A deposition is a progressive and cumulative process, involving in its early stage only a few structures in some organs, and increasingly more in the later stages of the disease.
In **sAAa** the renal and cardiac amyloid A deposition starts after a latent stage. This latency may be caused by a not specified local protective mechanism, e.g. great excretion capacity of the kidneys, due to motility of the heart or oxygenisation etc.
Amyloid A deposition starts in the most frequently involved structures of the kidneys or heart with more massive deposits. The chronology of amyloid A deposition allows an indirect assessment of the stage of renal or cardiac amyloidosis, which may have a prognostic value in everyday surgical pathology.
Half of the patients with **sAAa** died of uremia caused by massive **rAAa** and only 9 of these were clinically recognized. Renal and cardiac amyloid A deposition should be considered a very serious, life-threatening complication of **RA**.

REFERENCES:

[1] Arnett FC, et al: Arthritis Rheum, 1988; 31: 315-324. DOI: 10.1002/art.1780310302
[2] Bély M, **Makovitzky J**: Acta Histochemica 108, 175-180 (2006). DOI: 10.1016/j.acthis.2006.03.017

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FRI0027 PROGNOSTIC MARKERS FOR PRECLINICAL CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS AND CORRELATION WITH DISEASE ACTIVITY

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Background: Patients with rheumatoid arthritis (RA) have an elevated cardiovascular (CV) disease risk, explained both by an increased prevalence of traditional CV risk factors and the presence of chronic systemic inflammation that impairs vascular function, leads to thickening of the arterial wall and increased arterial stiffness.
Objectives: In this study we investigated the effect of anti-inflammatory treatment on prognostic markers for preclinical cardiovascular disease (arterial wall thickening and arterial stiffness) and the correlation of these markers with RA disease parameters.
Methods: Carotid ultrasound (using Artlab echotracking system) was used to determine carotid intima media thickness (IMT) and pulse wave analysis was done with SphygmoCor tonometry to calculate pulse wave velocity (PWV) and augmentation index (AIx). Paired t-test was used to compare PWV, AIx and IMT prior and after 6 months of therapy. Pearson correlation was calculated to investigated the correlation of PWV, AIx and IMT with (natural logarithm of) C-reactive protein (CRP), (natural logarithm of) erythrocyte sedimentation rate (ESR) and disease activity score-28 (DAS28). For correlations, data from both time points were pooled.
Results: In total 61 consecutive RA patients (50% early arthritis starting with csDMARD and 50% established RA starting with adalimumab) were asked to undergo arterial analysis just prior to start of therapy and after 6 months. PWV was performed in 45 patients at baseline and 39 at follow-up, IMT in 56 and 45 patients respectively and AIx in 51 and 44 patients respectively. Both signs of arterial stiffness (PWV and AIx) decreased after 6 months of therapy (mean difference 0.7 and 0.8 respectively; table 1), although this did not reach statistical significance. IMT remained stable during 6 months of therapy.

Table 1. Prognostic markers of atherosclerosis prior and after 6 months of anti-inflammatory therapy

	n	Baseline	6 months	Mean difference (95% CI)
PWV (m/s)	35	8.0	7.3	0.7 (-0.2;1.5)
AIx (%)	39	27.4	26.6	0.8 (-6.4;7.9)
IMT (mm)	43	0.68	0.68	-0.007 (-0.03;0.02)

PWV (n=84) showed a significant correlation with ESR (0.262, p<0.02) and DAS28 (0.269, p<0.02). Both AIx (n=95) and IMT (n=101) showed a significant correlation with CRP (-0.223, p<0.05 and 0.244, p<0.02, respectively). Other correlation coefficients were not statistically significant (data not shown, p>0.05).

Conclusion: Arterial stiffness as measured with PWV tended to decrease after 6 months of anti-inflammatory treatment. Arterial stiffness and arterial intima media thickness correlated with clinical disease parameters. Altogether, these changes might suggest that effective antirheumatic therapy has favorable cardiovascular effects. Whether or not this ultimately leads to a significant reduction of “hard” cardiovascular endpoints remains to be established in prospective studies.
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FRI0028 LOW SERUM IGF1 IS ASSOCIATED WITH AN INCREASED RISK AND HIGH PREVALENCE OF CARDIOVASCULAR EVENTS IN MIDDLE-AGED FEMALE PATIENTS WITH RA – A 5-YEAR FOLLOW-UP

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Background: Recent meta-analysis reported that rheumatoid arthritis (RA) is associated with high frequency of hypertension and stroke (1). IGF1 is an important angioprotector and its deficiency predisposes to development of ischemic stroke (2).
Objectives: Since levels of active IGF1 are affected by systemic inflammation, we analyze if low IGF1 is associated with increased cardiovascular disease (CVD) in women with RA.
Methods: The CVD risk was estimated (eCVR) in 184 female RA patients (median age 53 years, range 21-71) using the Framingham

algorithm. A 5-year prospective follow-up for new CVD events, type II diabetes and medication for hypertension and hyperlipidemia was completed in all the patients. The event-free survival curves were built and the Mantel-Cox analysis was performed with respect to serum IGF1, where IGF1 levels below or equal to the median 139 ng/ml were considered low.

Results: Low IGF1 was clinically significant. These patients were recognized by high prevalence of hypertension (26% vs. 7.9%, p=0.001), overweight (19% vs 6.8%, p=0.016) and hypercholesterolemia (71% vs 48%, p=0.0025), which resulted in a higher eCVR in these RA patients (7.2% and 3.3%, p<0.001). When adjusted by age, low IGF1 group had higher serum IL6 (pg/ml: 2.1[0.2-3.0] vs 0.7[0.1-4.2], p=0.038) and ESR (mm/h: 12[7-15.5] vs 5.5[4-9], p=0.02), and higher prevalence of MTX monotherapy (56% vs. 39%, p=0.024). At prospective follow-up, 12 CVD events were registered. The median age at CVD event was 67 years and disease duration 14 years. Among the new CVD events were 4 ischemic strokes, 3 chronic atrial fibrillations and 2 incidental aorta aneurysms, which all could be viewed as directly related to hypertension. Low IGF1 showed high probability for new CVD events (OR 4.96, [95%CI:1.17-34.2], p=0.029). Additionally, low IGF1 group had a significant increase in medication for hypertension (+19.5% vs +4.8%, p=0.00011), but not type II diabetes and statins. In a prediction model, a combination of low IGF1 and RA duration>10 years indicated 80.5% specificity for development of new CV events.

Conclusion: We identified low normal levels of IGF1 to be associated with higher prevalence of CVD events in RA patients. Importantly, low IGF1 appeared to be an independent predictor of hypertension in middle-aged female patients.

REFERENCES:

[1] Wiseman SJ, Ralston SH, Wardlaw JM. Cerebrovascular Disease in Rheumatic Diseases: A Systematic Review and Meta-Analysis. Stroke. 2016;47 (4):943-50.

[2] Laughlin GA, Barrett-Connor E, Criqui MH, Kritz-Silverstein D. The prospective association of serum insulin-like growth factor I (IGF-I) and IGF-binding protein-1 levels with all cause and cardiovascular disease mortality in older adults: the Rancho Bernardo Study. J Clin Endocrinol Metab. 2004;89(1):114-20.

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FRI0029 DEVELOPMENT OF AN ALGORITHM FOR THE CLASSIFICATION OF CARDIOVASCULAR COMORBIDITY IN RHEUMATOID ARTHRITIS: DATA FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE

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Background: Cardiovascular disease (CVD) is increased in rheumatoid arthritis (RA). The ability to accurately identify CVD and its risk factors is important for primary and secondary prevention strategies. RA registries collect comorbidity data, but discordance between physician-reported and patient-reported comorbidities often exists.

Objectives: We aimed to develop an algorithm for the classification of CVD and CVD RF in a representative RA registry.

Methods: Data were collected from the Ontario Best-practices Research Initiative (OBRI), a clinical registry of RA patients followed in routine care in Ontario, Canada. Clinical information, including patient medication profile, was obtained at registry entry, through physician visits and patient telephone interviews. Cardiovascular disease (CVD) was defined as having $\geq$ 1 of myocardial infarction (MI), coronary artery disease (CAD), cerebral vascular accident (CVA, including transient ischemic attack and stroke), or peripheral arterial disease (PAD). CVD risk factors included hypertension (HTN), dyslipidemia (DLD), diabetes mellites (DM), and current smoking.

Results: An algorithm for classifying CVD and CVD risk factors was developed including the 2033 subjects with baseline data. At cohort entry, the prevalence of CVD was 5.4% (n=110), HTN 670 (32.9%), DLD 401 (19.7%), DM 165 (8.1%), and current smoking 346 (17%). Seventeen (15.7%) subjects were not identified as having CVD by physician-report but were classified as having CVD upon medication review. Discrepancy between physician and patient-reported CVD RF were: 207 for HTN (31%), 291 for DLD (73%), and 22 for DM (13%). Chart review of 55 patients showed sensitivity of 100% for CVD, 78% for HTN, and 42% for DLD classification.

Conclusion: An algorithm for classification of CVD has been successfully developed in a representative RA registry. The discrepancy between physician and patient-reported CVD highlights the importance of utilizing information from multiple sources when classifying comorbidities.

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FRI0030 FEELINGS OF GUILT AND SHAME IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease which causes functional disability, pain, and joint destruction. The disease has a major impact on patient's independence, social activities and self-image.

Objectives: The aims of this study were to assess whether RA is associated with increased feelings of shame and guilt, and to examine possible correlates with socio demographic characteristics and disease activity.

Methods: To measure feelings of shame and guilt, in patients with RA (ACR/EULAR 2010), we used the Experience of Shame Scale (ESS) [1] and the Test of Self Conscious Affect- Version 3 (TOSCA-3S) [2].

The ESS is a 25-item questionnaire that assesses the frequency of characterological, behavioral and bodily shame experiences over the past year. Respondents rate each item on a scale ranging from 1 (not at all) to 4 (very much), with higher scores indicating greater shame.

The TOSCA-3S is presented with 11 brief hypothetical scenarios followed by 3 common reactions, which reflect shame, guilt and externalization of blame. Each possible response is rated on a five-point scale from 1(not likely) to 5 (very likely). For the purpose of this study, only the shame and guilt response items were analyzed. Total scores for Shame Self-Talk and Guilt Self-Talk were calculated and compared to the scoring interpretation. A p<0.05 was considered significant.

Results: A total of 40 patients with RA were included, 36 women and 4 men, with a mean age of 54.2 years old [25-75]. Nine patients (22%) were illiterate, 42.5% were professionally active and 82.5% were married. The mean disease duration was 12.8 years [3-33], 80% of patients were on prednisone at a daily posology of 7 mg [2.5-12.5], 82.5% were on csDMARDs and 27.5% on bDMARDs. The mean DAS 28 ESR and CRP were respectively 4.3 [1.6-6.9] and 3.6 [1-6.2].

The mean total score of the ESS was 45.3 [27-81] with subscale means of: 19 [12-37] for characterological shame, 19 [10-30] for behavioral shame and 7.4 [4-16] for bodily shame.

For the TOSCA-3S, the mean "shame self-talk Total" score was 33.8 [17-44], and the mean "guilt self-talk Total" score was 48 [37-55], which corresponds to "you often use" for men and "you use an average amount" for women, a shame and guilt self-talk.

A significant correlation was found between disease activity (DAS 28 ESR) and total score of ESS, shame self-talk total score and guilt shame self-talk score (p=0.000). A significant correlation was also found between these scores and gender, age, level of education, professional activity and marital status.

Conclusion: Our RA patients experienced general feelings of shame and guilt, which correlate with demographic items and disease activity.

However, a case-control study with a larger population is necessary to determine whether patients with RA express more shame and guilt than their peers without RA.

REFERENCES:
[1] Andrews B, Qian M, Valentine JD. Predicting depressive symptoms with a new measure of shame: the Experience of Shame Scale. Br J Clin Psychol 2002;41:29-42.
[2] Tangney JP, Dearing RL, Wagner PE, Gramzow R (2000) The Test of Self-Conscious Affect-3 (TOSCA-3). George Mason University, Fairfax.

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FRI0031 ASSESSMENT OF EFFICACY, SAFETY AND IMMUNOGENICITY OF A TRIVALENT SPLIT-VIRUS INFLUENZA VACCINE IN PATIENTS WITH RHEUMATIC DISEASES

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Background: In current rheumatology practice concurrent infections produce significant negative impact on patients' morbidity, mortality and quality of life. Based on WHO estimations the annual incidence of influenza in adult population amounts to 5-10% worldwide. Influenza can lead to hospitalization (3 to 5 million cases per year) and even death (250-500 thousand cases per year). Flu and its complications rates are higher in patients with rheumatic diseases (RD) as compared to general population. Therefore, prevention of influenza should be viewed as integral part of RD population management.
Objectives: To study the safety, efficacy and immunogenicity of inactivated split-virus influenza vaccine in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS).
Methods: 126 subjects (90 females and 36 males, aged 22 - 82 y) with recent acute respiratory viral infections (ARVI) and flu episodes in medical records were enrolled, including 52 RA patients, 34 AS patients and 40 healthy volunteers as the control group. 39 RA pts received methotrexate (MTX), 12 - TNFα inhibitors +MTX, 8 – Leflunomide, 2 – abatacept, 2 – sulfasalazine, 1 – tofacitinib + MTX. 19 AS patients were treated with nonsteroidal anti-inflammatory drugs (NSAIDs), 15 –with TNFα inhibitors. The RD duration ranged from 2 months to 46 years. All participants were injected subcutaneously with one dose (0.5 ml) of the trivalent inactivated influenza vaccine containing the actual influenza virus strains, with ongoing therapy. The control visits were scheduled at baseline, and in 1, 3 and 6 months after vaccination (Visits 0, 1, 2 and 3, respectively). Standard clinical and laboratory tests were performed during each visit. Immunogeniity of vaccine was measured with ELISA test kits.
Results: Vaccine tolerability was good in 103 participants (77,4%). Post-vaccination pain, swelling and redness of the skin up to 2 cm in diameter were registered in 20 cases (15%), low-grade fever, myalgia and malaise were documented in 10 cases (7,5%). There was no casual relationship between these reactions and principal therapy, therefore, no modifications of therapeutic regimens were required, and complete resolution occurred within 24 hours without additional interventions. No RD exacerbations or new autoimmune disorders were observed during the FUP. At baseline mean pts' DAS28 and BASDAI scores were 3.56 and 3.85, improving up to 1.99 and 3,09, respectively, 6mo post-vaccination. For the entire FUP there were no cases of influenza or influenza-like illness registered.
The proportion of respondents to the vaccine is 70% in the group of patients with RD and 75% in the main group. The level of humoral immune response was not significantly different in the group of patients with RD and in the control. It is noteworthy that there were no significant differences in the level of post-vaccination response after a month ($p = 0.6$) or after 3 or 6 months of observation. In patients with AS, there were significantly more responses to vaccines in patients with a long duration of the disease and low activity according to the BASDAI index ($p < 0.05$). There was no significant effect of the treatment of RH on the level of post-vaccination response; there were also no differences in the level of post-vaccination response between patients with different RD.
Conclusion: Therefore, our results show good tolerability, efficacy and immunogenicity of inactivated split-virus influenza vaccine in RA and AS patients. Future studies on larger patients' populations are warranted for more complete evaluation of vaccine safety and efficacy.
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FRI0032 HIGH INDEX OF SEDENTARY BEHAVIOR IN PATIENTS WITH INITIAL RHEUMATOID ARTHRITIS: DATA FROM A LONG COHORT OF INITIAL RA

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Background: The abandonment of a healthy lifestyle can have great impact on the quality of life, the response to the treatment and the control of the symptoms, like pain and fatigue on RA patients. Smoking is a proven trigger in the pathophysiology of RA, but studies show that it also participates in inflammatory activity throughout the course of the disease. RA patients are more likely to develop various comorbidities and increased cardiovascular risk when compared to the general population.
Objectives: To access physical activity engagement along with alcohol and cigarette consumption.
Methods: A cross-sectional study was carried out with patients with rheumatoid arthritis who received treatment on the initial stage of RA and followed up during 15 years in an initial RA cohort of a University Hospital. Participants underwent standardized clinical evaluation and analysis of complementary exams. The study was approved by the Ethics Committee.
Results: A total of 107 RA patients were evaluated. In the sample, 98% of the women were found, with a median age of 52 years. The mean duration of illness was 12.8 years and 11.3% had erosive disease. In relation to the habits of life, the physical activity level, prevalence of alcoholism and smoking were investigated. In general, our population was characterized by non- alcohol users (93.5%), non- smokers (75.7%) and not engaged into regular physical activities (56.1%). In relation to frequency, 21.5% of the patients exercised a minimum of three times a week, 16.8% once or twice a week and 5.6% once or twice a month. The practice of physical activity may be difficult for the patient with RA, who often has functional limitations, but is still of great importance, since it improves the response to treatment, prevents the onset of other comorbidities, or worsening of previous diseases, complications and promotes the improvement of the quality of life.
Conclusion: Even with a multidisciplinary approach and health care professionals qualified to instruct and emphasize the importance of engaging on an active lifestyle, RA patients remain mostly sedentary after 15 years of follow up. Perhaps other strategies of intervention should be investigated to improve such habits.

REFERENCES:
[1] Løppenthin, K. et al. Physical activity and the association with fatigue and sleep in Danish patients with rheumatoid arthritis. Rheumatol. Int. 35, 1655–1664 (2015).
[2] Demmelmaier, I., Pettersson, S., Nordgren, B., Dufour, A. B. & Opava, C. H. Associations between fatigue and physical capacity in people moderately affected by rheumatoid arthritis. Rheumatol. Int. 38, 2147–2155 (2018).
[3] Manfredsdottir, V. F. et al. The effects of tobacco smoking and rheumatoid factor seropositivity on disease activity and joint damage in early rheumatoid arthritis. Rheumatology 45, 734–740 (2006)
[4] Waldschmidt, T. J., Cook, R. T. & Kovacs, E. J. Alcohol and inflammation and immune responses: summary of the 2005 Alcohol and Immunology Research Interest Group (AIRIG) meeting. *Alcohol Fayettev. N* 38, 121–125 (2006).
[5] Rajakulendran, S., Gadsby, K. & Deighton, C. Rheumatoid arthritis, alcohol, leflunomide and methotrexate. Can changes to the BSR guidelines for leflunomide and methotrexate on alcohol consumption be justified? Musculoskeletal Care 6, 233–246 (2008).

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FRI0033 QUANTIFERON GOLD-PLUS AND TUBERCULIN SKIN TEST REACTIVITY PREDICTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: RA patients have high latent tuberculosis(LTBI)prevalence(20-37%)[1]. In Mexico,ranges from 21.7% to 31.3% using tuberculin skin test (TST)[2]. The methods to detect LTBI are TST and IGRAs. QuantiFERON Gold-Plus (QTF-Plus)uses an antigen tube (TB1) that stimulates CD4+T cells and an additional tube (TB2) that also stimulates CD8+T cells[3].

Objectives: Determine the LTBI prevalence,variables that predict QTF-Plus and TST results and the concordance between TST and QTF-Plus in RA patients.

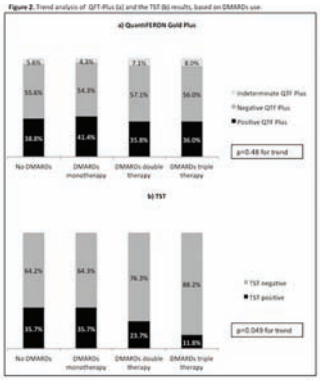
Methods: A cross-sectional study in RA patients from the rheumatology department of the University Hospital "José E. González" in Mexico between October 2017 and June 2018. RA patients with ACR/EULAR 2010 classification criteria without a history of tuberculosis (TB) were included.QFT-Plus was performed according to manufacturer instructions. TST was applied with the Mantoux technique; a ≥5mm cutoff was used. The square chi and Fisher test were used for proportions, Mann-Whitney to compare means,trend analysis using linear trend test and a binary logistic regression model for variables related to positivity to both tests.

Results: We included 111 patients (table 1), the mean age was 51.9 years, 92.3% were women,disease duration 8.7±8.8 years. QTF-Plus was positive in 46 (44.6%) patients. TST was positive in 31(27.9%) patients. Agreement between tests was 73.7% (kappa=0.45, p<0.001).The majority of patients were using conventional DMARDs (86.7%), none of the patients were using biologic DMARDs. In the linear-to-linear association analysis,there was a trend towards TST negative result with the use of ≥2DMARDs (p=0.049 for trend) (figure 1).In the logistic regression model we found a significant relationship between a positive TST active TB exposure(OR 8.5,CI 95% 1.4-51.7; p=0.01)and an inverse relationship between the positive TST and antimalarials (OR 0.11, CI 95% 0.001-0.8), none of the variables interfered with QTF-Plus results.

Table 1. Demographic characteristics of RA patients and TST and QTF-Plus comparative analysis.

	N=111	TST positive n=31/103*	QFT-Plus Positive n=46/103*
Age, median	51.9(18-87)	50.4(29-76)	54.4(18-87)
Female,%	105(94.6)	26(83.9)	43(93.5)†
BCG vaccine, %	97(87.6)	28(90.3)	40(87)
Active TB exposure, %	10(9)	5(16.1)	5(10.9)†
Seropositive, %	92(82.9)	25(80.6)	40(87)
Mean duration, years, SD	8.7(±8.8)	8.4(±9.2)	8.7(±8.5)
DAS28-PCR, SD	2.46(±1.26)	2.30(±1.21)	2.47(±1.30)
Prednisone use, %	60(54.1)	14(45.2)	22(47.8)
Prednisone, mean dosis, SD	6.8(±6.9)	4.6(±2.2)	5.3(±3.1)
DMARDs monotherapy, %	42(37.8)	15(48.4)	19(41.3)
DMARDs double therapy, %	38(34.2)	9(29.9)	12(26.1)
DMARDs triple therapy, %	17(15.3)	2(6.5)	8(17.4)†
Methotrexate, %	85(76.6)	14(45)	18(39.1)
Leflunomide, %	32(28.8)	6(19.4)	9(19.6)
Sulfasalazine, %	24(21.6)	7(22.4)	12(26.1)
Antimalarials, %	28(25.2)	6(2.5)	9(19.6)†

*8 subjects with indeterminate QTF-Plus were excluded from this analysis † p<0.05.These variables were included in the logistic regression.



Conclusion: The LTBI prevalence in RA patients in our study is similar to countries with a high TB burden.We recommend considering RA patients as a high-risk population for LTBI.An intermediate agreement between TST and QTF-Plus was found.The use of antimalarials and ≥2DMARDs influence the TST reactivity,none of the variables altered the QTF-Plus results.Based on the results, we recommend the QuantiFERON Gold Plus over TST for the LTBI screening in RA patients.

REFERENCES:

[1] Sester M,et al.Am J Respir Crit Care Med.2014;190(10):1168–76.
[2] Pérez-Barbosa L,et al.Rheumatol Int.2015;35(9):1555–9.
[3] Takasaki J,et al.J Infect Chemother.2018;24(3):188–92.

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FRI0034 A LATIN-AMERICAN PREVENTIVE CARDIO-RHEUMA CLINIC: A CASE-CONTROL STUDY

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Background: It has been described an increased prevalence of cardiovascular diseases (CVD) in rheumatoid arthritis (RA) patients. When compared with the general population, CVD mortality is 50% higher in RA (1). It is reported a 35.3% prevalence of CVD in Latin-American population with RA (2). Cardio-rheuma (CR) clinics were designed to enhance detection, prevention and treatment of CVD in patients with rheumatic conditions. Our clinic located in the University Hospital in Monterrey Mexico, is the first and only established in Latin-America since 2014.

Objectives: To describe the characteristics of patients with RA attending to a Latin-American CR clinic and compare the findings by carotid ultrasound (US) and echocardiography to controls.

Methods: Cross-sectional, observational, comparative study. RA patients aged 40 to 75 years that fulfilled the 2010 EULAR criteria and matched controls were included. Patients with prior atherosclerotic CVD and overlap syndromes were excluded. Clinical history, blood samples, physical exam, carotid US and echocardiography were performed. Carotid plaque (CP) was defined as a focal narrowing ≥0.5 mm of the surrounding lumen or a carotid intima media thickness (cIMT) ≥1.2 mm, and increased cIMT was defined as ≥0.9 mm. Transthoracic echocardiogram was performed and reviewed by 2 board-certified cardiologists. Differences were solved by consensus. Categorical variables are expressed as total number (%), and numerical variables as median (q25-q75). Chi square and Mann-Whitney U-test were used to compare groups and considered significant if p<0.05.

Results: A total of 336 RA patients and 144 controls were included (Table 1). Table 2 summarizes echocardiographic and carotid US findings; ejection fraction was higher in controls than RA patients, prevalence of bilateral CP and increased cIMT was significantly higher in RA patients.

Table 1. Patient characteristics

Variable	RA (n=336)	Controls (n=144)	*p*
Age (years), median (q25-q75)	55.5 (48-61)	53 (48-58)	0.017
Women, n (%)	311 (92.6)	134 (93.1)	NS
Disease duration (years), median (q25-q75)	7.8 (3.2-15)	-	-
BMI (kg/m²), median (q25-q75)	27.6 (25.1-31.2)	27.8 (24.9-31.5)	NS
Diabetes Mellitus, n (%)	47 (14)	14 (9.7)	NS
Dyslipidemia, n (%)	93 (27.7)	31 (21.5)	NS
Hypertension, n (%)	93 (27.7)	31 (21.5)	NS
DAS28-CRP, median (q25-q75)	3.2 (2.1-4.3)	-	-
Past or current smoker, n (%)	65 (19.3)	36 (25)	NS
Nonsteroidal anti-inflammatory drugs, n (%)	90 (26.8)	-	-
Prednisone, n (%)	195 (58)	-	-
Methotrexate, n (%)	283 (84.2)	-	-
Leflunomide, n (%)	69 (20.5)	-	-
Chloroquine, n (%)	54 (16.1)	-	-
Sulfasalazine, n (%)	59 (17.6)	-	-
Hydroxychloroquine, n (%)	34 (10.1)	-	-
Biologic DMARDs, n (%)	21 (6.3)	-	-

Table 2. Echocardiographic and carotid US findings

Echocardiography	RA (n=60)	Controls (n=28)	*p*
Ejection fraction, median (q25-q75)	60 (56.2-65.0)	63 (60-69)	**0.008**
Abnormal LV geometry, n (%)	21 (35)	7 (25)	NS
Abnormal LA geometry, n (%)	6 (10)	3 (10.7)	NS
Carotid US, n (%)	**RA (n=128)**	**Controls (n=110)**	
CP	38 (29.7)	25 (22.7)	*NS*
Increased cIMT	64 (50)	32 (29.1)	***0.001***
Unilateral CP	18 (14.1)	17 (15.5)	*NS*
Bilateral CP	20 (15.6)	8 (7.3)	***0.046***

Conclusion: RA patients from this clinic had lower ejection fraction, more prevalence of cIMT and bilateral CP when compared to controls. It is important that rheumatologists perform a complete evaluation of their patients, in which cardiovascular assessment should be included.

REFERENCES:

[1] Aviña-Zubieta JA, et al. 2008. Arthritis & Rheumatism.
[2] Sarmiento-Monroy JC, et al. 2012. Hindawi Publishing Corporation.

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FRI0035 **INFLAMMATORY ARTHRITIS INDUCED BY IMMUNE-CHECKPOINT INHIBITORS: RESULTS FROM A COMBINED RHEUMATOLOGY/ONCOLOGY OUTPATIENT CLINIC**

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Background: Immune checkpoint inhibitors (ICIs) has radically changed the oncology field: the blockade of co-stimulatory molecules on T cells, antigen presenting cells and tumor cells induces unchecked T cell activation with subsequent immune response targeting malignant cells. In the last years, different ICIs have been approved for the treatment of several malignancies. The stimulation of the immune response could be associated with the development of immune-related adverse events (irAEs), potentially involving every organ/system (1). Musculo-skeletal manifestations represent one of the most common irAEs developing during ICIs treatment: up to 40% of treated patients could experience arthralgia or arthritis. Moving from these evidences, the role of the rheumatologist became very important in the management of ICIs treated patients (2).
Objectives: To determine the frequency of musculo-skeletal manifestations in patients treated with ICIs in a combined rheumatology/oncology outpatient clinic.
Methods: From January 2015 we organised a rheumatology/oncology combined outpatient clinic: all patients starting an ICIs treatment were referred from oncologist to rheumatologist. Data from patients, including demographic features, date of diagnosis, comorbidities and previous and concomitant medications, smoke habit, were collected and registered into a standardized, computerized, electronically filled-in form. All the patients underwent to a physical and laboratory evaluation in order to assess the presence of tender and swollen joints. In case of joint involvement, we assessed disease activity by clinimetric evaluation (DAS28) and ultrasonographic assessment of involved joints (presence of active synovitis as for presence of power Doppler). Moreover, a laboratory evaluation including, ESR, CRP, and autoantibodies (ANA, ACPA, RF) was performed.
Results: Seventy-two patients were evaluated (M/F 48/24, median age 66.0 years, IQR 13.0; median disease duration 7 months, IQR 13.0). Concerning malignant disease, 75.1% were affected by non-small cell lung cancer, 15.3% by renal cell carcinoma, 6.9% by melanoma, 2.7% by other malignancies; all patients were treated with anti-PD-1, 67 (93.1%) with nivolumab and 5 (6.9%) with pembrolizumab. During ICIs treatment, 7 patients (9.7%) developed clinically evident synovitis (absolute risk: 0.1; incidence rate 0.01 patients/month): table 1 reports the main features of these 7 patients. According with ACR/EULAR 2010 criteria, two patients could be classified as affected by rheumatoid arthritis (RA). Six patients (85.7%) were treated by prednisone (dosage range 10-12.5mg/daily) or NSAIDs, experiencing a rapid, complete and persistent response. Patient 2, due to resistance to prednisone, was treated by methotrexate 10mg/weekly achieving remission after 6 weeks.
Conclusion: The present study represents the first attempt to apply a multidisciplinary approach involving rheumatologists and oncologists in the evaluation of patients treated with ICIs. We found a high absolute risk (10%) to develop synovitis in patients treated by ICIs. Interestingly, the majority of these patients experienced a clinically evident synovitis promptly responding to glucocorticoids and not requiring further DMARDs treatment. This could suggest a peculiar pathogenesis of such ICIs-induced arthritis.

REFERENCES:

[1] Calabrese L & Velcheti V, Ann Rheum Diseases 2016; 2. Mooradian MJ et al, Semin Arthritis Rheum 2018

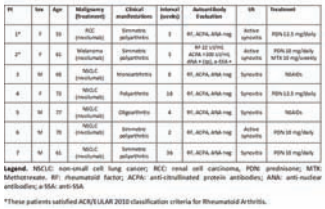


Table 1. Main features of seven patients experiencing synovitis.

Pt	Sex	Age	Malignancy (Treatment)	Clinical manifestations	Interval (weeks)	Autoantibody Evaluation	Ult.	Treatment
1*	F	59	RCC (nivolumab)	Simmetric polyarthritis	3	RF, ACPA, ANA neg	Active synovitis	PDN 12.5 mg/daily
2*	F	61	Melanoma (nivolumab)	Simmetric polyarthritis	3	RF 22 UI/ml, ACPA <100 UI/ml, ANA 1:160, n-SSA +	Active synovitis	PDN 10 mg/daily MTX 10 mg/weekly
3	M	68	NSCLC (nivolumab)	Monoarthritis	8	RF, ACPA, ANA neg	Synovitis	NSAIDs
4	F	73	NSCLC (nivolumab)	Polyarthritis	10	RF, ACPA, ANA neg	Synovitis	PDN 12.5 mg/daily
5	M	77	NSCLC (nivolumab)	Oligoarthritis	4	RF, ACPA, ANA neg	Synovitis	NSAIDs
6	M	70	NSCLC (nivolumab)	Simmetric polyarthritis	2	RF, ACPA, ANA neg	Active synovitis	PDN 10 mg/daily
7	M	61	NSCLC (nivolumab)	Simmetric polyarthritis	16	RF, ACPA, ANA neg	Synovitis	PDN 10 mg/daily

Legend. NSCLC: non-small cell lung cancer; RCC: renal cell carcinoma, PDN: prednisone; MTX: Methotrexate. RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; ANA: anti-nuclear antibodies; n-SSA: anti-SSA.

*These patients satisfied ACR/EULAR 2010 classification criteria for Rheumatoid Arthritis.

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FRI0036 **EFFECTS OF DISEASE ACTIVITY, ILLNESS PERCEPTION, SOCIAL SUPPORT AND COPING METHODS ON QUALITY OF LIFE IN THE PATIENTS WITH RHEUMATOID ARTHRITIS AND FIBROMYALGIA SYNDROME**

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Background: In chronic diseases, social support, illness perception and coping methods have important effect on quality of life.
Objectives: In the present study, we aimed to compare the quality of life (QOL) of the patients with rheumatoid arthritis (RA) with fibromyalgia (FMS) patients and healthy controls and to assess the relationship between QOL and illness perception, social support, disease coping methods in the patients with RA and FMS.
Methods: Fifty-eight patients with RA, 50 patients with FMS and 50 healthy controls were enrolled in the study. Pain (Visual Analogue Scale, VAS), QOL (Short Form SF-36), illness perception (Revised Illness Perception Scale, IPQ-R), social support (Multidimensional Perceived Social Support Scale, MSPSS) were assessed in the patients. In RA patients, disease activity was evaluated with DAS 28 and Clinical Disease Activity (CDAI), and functional status was evaluated with Health Assessment Questionnaire (HAQ). Fibromyalgia Impact Questionnaire (FIQ) scale was used in the clinical assessment of FMS patients.
Results: While RA and FMS patients had higher COPE-emotional and COPE–problem scores than the healthy controls ($p<0.05$), there was no significant difference between the patients with RA and FMS ($p>0.05$). Regarding the all MSPSS scores, there was no significant difference between the three groups ($p>0.05$). FMS patients had lower scores than the RA patients and healthy controls regarding the physical function, pain, social functioning and mental health subscales of SF-36 ($p<0.05$).
In RA patients, MSPSS-friend and MSPSS-special one scores were positively correlated with all subscales of SF-36. IPQ-R consecuences scores were negatively associated with all subscales of SF-36 ($p<0.01$). There were positive correlations between IPQ-R treatment control and SF-36 physical function and social function subscales ($p<0.05$).
In FMS patients, IPQ-R-timeline acute\chronic score was negatively correlated with physical function, pain and social function subscales ($p <0.05$). While IPQ-R timeline cyclical was negative correlated with SF-36 mental health subscale, COPE-emotional was negatively correlated with SF-36 general health
Conclusion: In RA and FMS patients, QOL and physical functions were found to be related with illness perception, social support and coping methods as much as disease activity.
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FRI0037 **DIAGNOSTIC PERFORMANCE OF CURRENT CVR SCORES FOR THE DIAGNOSIS OF CAROTID PLAQUE IN MEXICAN-MESTIZO RA SUBJECTS**

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Background: Rheumatoid arthritis (RA) is an inflammatory disease with an increased mortality compared to the general population. The measurement of carotid intima media thickness (CIMT) is used as an independent marker of subclinical atherosclerosis.
Objectives: To determine the prevalence of carotid plaque (CP) in a cohort of Mexican RA subjects and diagnostic performance of cardiovascular risk (CVR) calculators for the prediction of augmented CIMT and CP.
Methods: A cross-sectional study of subjects aged from 40-75 years that fulfilled the 2010 ACR/EULAR RA criteria. Exclusion criteria: previous CV disease and overlap syndromes. CVR was calculated by 6 scales: ACC/AHA 2013, Framingham-lipids (FRS-lipids), Framingham-Body Mass Index (FRS-BMI), Reynolds Risk Score (RRS), QRISK2 and SCORE. Carotid ultrasound (US) was performed by a board-certified radiologist and reviewed by other two. We defined an augmented CIMT as $\geq$0.9 mm and CP as CIMT $\geq$1.2 mm. We categorized subjects in 3 groups: 1) normal carotid US, 2) augmented CIMT, and 3) CP. We used Kruskal-Wallis test to compare the groups.
Results: 130 patients were included, 124 (95.4%) were females with median age of 57 years old and disease duration of 9.7 years. Almost 50% of the subjects with CP were in the low-risk strata of every CVR calculator. The presence of CP was higher in subjects categorized as moderate/high risk using ACC/AHA 2013 CVR score ($p=0.013$), moderate/high risk strata of QRISK2 ($p=0.004$), and high-risk strata of ACC/AHA 2013 CVR score ($p=0.02$). Of these 3, the highest sensitivity was obtained by the moderate risk stratum of QRISK2 with 51%; the highest specificity was obtained by the high-risk stratum of the ACC/AHA 2013 CVR score with 84%.

Table 1. Comparison groups

	CP presence N=39	**CIMT ≥0.9mm N= 29**	**Normal CIMT N= 62**	***p***
Age years	59 (55-66)	60 (53-70)	51 (44-58)	**0.00**
BMI kg/m^2	27.3 (25.3-29.9)	27.8 (24.7-31.3)	29.9 (26.6-34.5)	**0.022**
ACC/AHA 2013	4.6 (2.3-10.2)	5.6 (2.2-11.8)	1.7 (0.7-3.5)	**0.00**
FRS-LIPIDS	7.1 (5.3-10.3)	9.25 (6.1-13.4)	3.8 (2.1-6.1)	**0.00**
FRS-BMI	10.4 (7.7-15.4)	12.2 (8.7-21.6)	4.8 (2.7-9.3)	**0.00**
SCORE	1 (0.5-2)	1 (0-2)	0 (0-1)	**0.00**
QRISK2	10.5 (5.2-16.7)	11.6 (5.6-17.1)	3.1 (1.9-6.3)	**0.00**
RRS	2 (1.3-4)	3 (1-5.7)	1 (1-2)	**0.00**

Variables reported as median, (q25 - q75)

Table 2. Diagnostic test performance

CVR score moderate and high risk	**CP (n=39)**	**No CP (n=91)**	***p***	**HR (95% CI)**	**Sens (%)**	**Spec (%)**	**PPV (%)**	**NPV (%)**
ACC/AHA 2013, n (%)	19 (48.7)	24 (26.4)	**0.01**	**2.6 (1.2-5.7)**	0.48	0.73	0.44	0.77
FRS-Lipids, n (%)	11 (28.2)	17 (18.7)	0.22	1.71 (0.7-4)	0.28	0.81	0.39	0.72
FRS-BMI, n (%)	20 (51.3)	31 (34.1)	0.06	2.03 (0.9-4.3)	0.51	0.65	0.39	0.75
QRISK2, n (%)	20 (51.3)	23 (25.3)	**0.00**	**3.1 (1.4-6.8)**	0.51	0.74	0.46	0.78
RRS, n (%)	2 (5.1)	2 (2.2)	0.37	2.4 (0.3-17.7)	0.05	0.97	0.50	0.70

Conclusion: Increased CIMT or CP might be unidentified if the risk is exclusively determined by CVR calculators. Patients with a CIMT $\geq$0.9 mm had an average score that placed them in the low risk strata, leading to an underestimation of their real CVR. Calculators can be helpful to estimate the CVR, however, they don't seem to be an adequate screening tool for an increased CIMT or CP. Meanwhile, to assess CVR precisely, a carotid US should be performed in all RA patients.

REFERENCES:

[1] Peters M, et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. ARD 2010.
[2] Meune C, et al. Cardiovascular mortality in patients with rheumatoid arthritis over 50 years: a systematic review and meta-analysis of cohort studies. Rheumatology 2009.

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FRI0038 **HERPES ZOSTER IN RHEUMATOID ARTHRITIS. PROSPECTIVE SINGLE CENTER STUDY OF 390 RA PATIENTS FOR 5YEARS**

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Background: Immunosuppressed patients such as Rheumatoid Arthritis (RA) patients have a greater risk (1.5-2 times) of presenting herpes zoster (HZ). Both, the disease itself and the use of immunosuppressive

Case	Sex	Age (years)	Duration of RA (months)	RF +/-	APCA +/-	Erosive RA	HZ Localization	Previous Herpes Viral serology	HZ Treatment	Concomitant treatment for RA
1	♀	74	339	+	+	Yes	Left arm	IgG+ IgM NR	Famciclovir	Corticoids/MTX/TCZ
2	♀	86	142	+	-	Yes	-	IgG+ IgM -	None (topic)	ETN
3	♀	80	90	-	-	Yes	Gluteus (right)	IgG + IgM NR	Brivudina	HCQ
4	♀	83	313	+	-	Yes	D9-D10 metamer	IgG + IgM -	Brivudina	Corticoids/MTX/RTX
5	♀	52	222	+	-	Yes	Generalizated	IgG + IgM NR	Aciclovir	Corticoids
6	♀	70	171	+	-	No	Left arm	IgG+ IgM NR	Aciclovir	Corticoids/MTX/ADA
7	♀	68	1	+	-	Yes	Intercostal (left)	IgG + IgM -	Brivudina	Corticoids/HCQ
8	♀	61	40	-	-	No	-	IgG + IgM NR	-	Corticoids/LFN/TCZ
9	♂	58	34	+	+	No	Intercostal (left)	IgG + IgM NR	Famciclovir	None
10	♀	62	67	+	+	Yes	Intercostal (left)	IgG + IgM NR	Aciclovir	LFN/ETN
11	♀	50	5	-	-	No	Intercostal (left)	IgG + IgM NR	Aciclovir	Corticoids/MTX/ADA
12	♀	66	2	+	+	No	Gluteus (left)	IgG + IgM -	Aciclovir	None

TABLE General features of 12 RA patients at HZ infection

drugs, are involve in this increased risk. Furthermore, in these patients is more frequent a disseminated presentation of zoster involving several dermatomes.

Objectives: In a series of RA patients our aim was analyzed HZ infections and to assess **a)** HZ prevalence and **b)** HZ general features

Methods: Prospective Single center study of 390 RA patients included in the vaccination program of the Preventive and Rheumatology department of our hospital between october 2011 and october 2016. The follow-up was made until December 2017. HZ vaccination is not included in our program.

RA was diagnosed according to the ACR/EULAR 2010 proposed criteria (Arthritis Rheum 2010; 62: 2569–2581)

The diagnose of HZ was made according to the clinical manifestations and was confirmed by a dermatologist. These manifestations were characteristic skin rash and blisters, paresthesia and local pain, in one (localized) or more dermatomes (generalized)

Results: We studied 390 patients (307♀/83♂), average age 61.28±12.9 years that were included in the vaccination program and followed-up.

HZ infection was observed in 12 of 390 (3.07%) in the follow-up **(TABLE).**

The 12 RA patients (11 women/1 man) with a mean±SD age of 67.5 ±11.67. More than half of patients, 7 (58.33%) were taking corticosteroids. 8 patients (66.66%) were receiving conventional disease modifying drugs (DMARDs) methotrexate (33.33%), leflunomide (16.66%) and hydroxychloroquine (16.66%). Besides corticosteroids and conventional DMARDs, 7 patients (58.33%) were in treatment with biologic drugs, tocilizumab (n=2), etanercept (n=2), adalimumab (n=2), and rituximab (n=1).

Conclusion: Herpes zoster is a relative frequent viral infection in RA patients non-vaccine for HZ. The female sex, older age, more aggressive RA and treatment with corticosteroids were more frequent. Probably in this group of patients HZ vaccination may be useful.

Abbreviatures: MTX: methotrexate, LFN: leflunomide, HCQ: hydroxicloroquine, TCZ: tocilizumbas, ADA: adalimumab, ETN: etanercept

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FRI0039 **THE LUNG IN AN ENGLISH COHORT OF RHEUMATOID ARTHRITIS PATIENTS – AN OVERVIEW OF DIFFERENT TYPES OF INVOLVEMENT AND TREATMENT**

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Background: Lung disease is described in 5–20% of patients (pts) with Rheumatoid arthritis (RA) and affects parenchyma, pleura, airways and vasculature; drug-induced pulmonary disease also occurs. It is associated with a higher mortality and identification of safe and effective drugs is essential.

Objectives: Characterize lung involvement in a RA cohort; evaluate rituximab (RTX) effectiveness and safety in RA associated interstitial lung disease (ILD).

Methods: Retrospective analysis of the electronic records from RA cohort followed at University College Hospital. Lung involvement was based on high resolution computed tomography. Demographic data, smoking status, complementary exams at baseline/follow-up and therapies used were analysed. A sub-analysis of pts treated with rituximab (RTX) evaluated response at 12, 24 and 36 months. Declines of 15% in gas transfer from baseline and/or 10% in forced vital capacity were recognized.

Results: From 1129 RA pts, 87 (7.7%) had documented lung involvement. Mean age at last follow-up was 68.3±12 years, 74.7% were female and 85.1% Caucasian. Median disease duration was 14 (IQR 8-29) years. 54% of pts had erosive disease. Rheumatoid factor was positive in 88.1% and anti-citrullinated protein antibodies in 87.8%. 23 pts had positive antinuclear antibodies (25 missing data) and 4 anti-Ro, 2 anti-Scl70 and 2 anti-PL12. Secondary Sjögren's syndrome occurred in 6.9%, cutaneous rheumatoid nodules in 5.7% and cutaneous vasculitis in 1.1%. 11.5% and 43.7% were current and previous smokers, respectively.

Mean interval between onset of articular and pulmonary symptoms was 12.3 years; 2 pts had lung disease as a prior manifestation. Types of lung involvement are shown in table 1.

TABLE 1 - Characterisation of different types of lung involvement

	Female	Age at lung disease diagnosis (years, mean±SD)	Interval between RA and lung disease diagnosis (years, median [IQR])	Smoking habits	Positive RF	Positive ACPA
NSIP (n=18)	11 (61.1%)	66.3±12.5	1 [0-15]	13 (76.5%; 1 missing)	16 (88.9%)	15 (88.2%; 1 missing)
UIP (n=18)	11 (61.1%)	66.8±13	1 [0-13.5]	9 (52.9%; 1 missing)	14 (87.5%; 2 missing)	16 (94.1%; 1 missing)
OP (n=4)	4 (100%)	57±7.1	10 [4.25-21]	1 (25%)	4 (100%)	4 (100%)
Unclassifiable ILD pattern (n=5)	4 (80%)	65.2±12.4	4 [2.5-8.5]	4 (80%)	5 (100%)	5 (100%)
Isolated bronchiectasis (n=31)	27 (87.1%)	63.7±9.3	17 [5.5-24.5]	14 (56%; 6 missing)	25 (83.3%; 1 missing)	23 (79.3%; 2 missing)
Obliterative bronchiolitis (n=2)	1 (50%)	74.5±3.5	30.5	1 (50%)	1 (50%)	2 (100%)
Panbronchiolitis (n=2)	2 (100%)	48.5±15.5	8.5	1 (50%)	2 (100%)	2 (100%)
Small airways disease without any specific pattern (n=1)	1 (100%)	57	4	0 (0%)	1 (100%)	1 (100%)
Rheumatoid nodules (n=4)*	4 (100%)	45.8±11.4	6.5 [2.5-15.75]	3 (75%)	4 (100%)	3 (75%)
Pleural effusion (n=3)*	2 (66.7%)	41±9.3	13	2 (66.7%)	3 (100%)	3 (100%)

*1 patient had concomitant pleural effusion and rheumatoid nodules

Legend: RF – Rheumatoid factor; ACPA – anti-citrullinated protein antibodies; NSIP - non-specific interstitial pneumonia; UIP - usual interstitial pneumonia; OP – organising pneumonia;

At last follow-up appointment 22 pts were still on methotrexate (MTX) and 27 had previously received it. MTX-acute pneumonitis occurred in 2 pts, both in the 1st year of treatment.

RTX was used in 26 pts (57.8%) with ILD (14 nonspecific interstitial pneumonia-NSIP, 8 usual interstitial pneumonia-UIP, 2 organising pneumonia-OP). The mean number of cycles was 4 (range 1-12). Two pts were concomitantly receiving mycophenolate mofetil and 1 azathioprine. RTX treatment outcomes are shown in table 2.

TABLE 2. – Disease outcomes after treatment with rituximab

Time of revaluation	6 months			12 months			24 months			36 months		
ILD pattern	OP	NSIP	UIP	OP	NSIP	UIP	OP	NSIP	UIP	OP	NSIP	UIP
TLCO stable/	2/2	3/4		2/2	5/5	1/3	1/1	5/5	1/1		3/3	2/2
improvement	100%	75%		100%	100%	33.3%	100%	100%	100%		100%	100%
TLCO decline		1/4	1/1			2/3						
		25%	100%			66.7%						
FVC stable/	2/2	3/4		2/2	5/5	1/3	1/1	5/5	1/1		4/4	1/2
improvement	100%	75%		100%	100%	33.3%	100%	100%	100%		100%	50%
FVC decline		1/4	2/2			2/3						1/2
		25%	100%			66.7%						50%
HRCT stable/		2/2			1/1	1/1		3/3			2/2	
improvement		100%			100%	100%		100%			100%	
HRCT									1/1			
worsening									100%			

Legend: ILD – interstitial lung disease; TLCO – gas transfer; FVC – forced vital capacity; HRCT – high resolution computed tomography; NSIP - non-specific interstitial pneumonia; UIP - usual interstitial pneumonia; OP – organising pneumonia

There were 18 (20.7%) deaths, 7 of them related to ILD (4 UIP, 3 NSIP) and occurred 8.8 years after ILD diagnosis. Two were due to infection, but none was felt to be directly related to immunosuppressive therapy.

Conclusion: Lung disease occurred in 7.7% of our cohort, with ILD being the commonest presentation (51.7%). MTX was widely used in pts with lung disease with only 2 cases of acute pneumonitis. Although the number of ILD pts treated with RTX was small, the drug improved/stabilized the disease in most NSIP and OP pts. UIP is usually progressive, but our data suggest that disease progression might be put on hold with RTX, at least in a subset of pts.

REFERENCE:

[1] Shaw M, Collins BF, Ho LA, Raghu G. Rheumatoid arthritis-associated lung disease. Eur Respir Rev. 2015 Mar 1;24(135):1–16.

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FRI0040 **GENDER DISCREPANCY IN RHEUMATOID ARTHRITIS: PATIENTS' AND PHYSICIANS' PERSPECTIVE**

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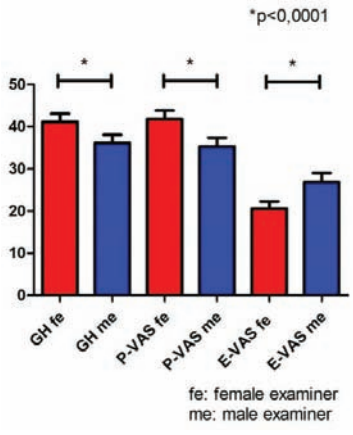
Background: Rheumatoid Arthritis (RA) is more prevalent among female individuals. Sex and gender differences may influence disease's progression and prognosis. To date, the influence of physicians' gender in the evaluation of RA activity is still largely unknown.

Objectives: aim of the study was to investigate a possible discrepancy in the assessment of disease activity in RA patients evaluated by male and female physicians. Further aim was to compare patient and evaluator perceptions about disease activity and global health status.

Methods: we enrolled consecutive RA patients. Each patient was separately visited by a female and a male rheumatologist of the same age and training level. Tender (TJ) and swollen joints (SJ) count was performed. Global Health (GH), physician's (E-VAS) and patient's (P-VAS) disease activity were reported using a visual analogue scale (VAS 0-100). Both examiners were blinded on ESR and CRP. A third rheumatologist assessed disease activity by DAS28-ESR, CDAI and SDAI.

Results: we enrolled 154 patients (122 F, 32 M). GH and P-VAS were significantly higher when collected by the female examiner compared to the male one (respectively, 41,1 ± 24,4 vs 36,1 ± 24,3, p<0,0001 and 41,7 ± 26,2 vs 35,3 ± 25,4; p<0,0001; figure 1), as well as DAS28-ESR values (3,19 ± 1,5 vs 2,97 ± 1,5; p<0,0001; figure 2) but not CDAI and SDAI. On the contrary, male E-VAS was significantly higher compared to female one (26,8 ± 27 vs 20,5 ± 20,8; p<0,0001; figure 1). GH, P-VAS and DAS28 significantly differ when the analysis was restricted to female patients (p<0,0001); among male patients, only P-VAS was significantly higher when collected by the female examiner (36,5 ± 24,7 vs 30,4 ± 25,4; p<0,0001). According to the DAS28-ESR cut off, 39,6% of patients were in remission when evaluated by the female examiner compared to 42,9% when examined by the male physician; the probability of being judged as having an active disease was not different between the female and the male examiner (p=ns). Overall, the agreement between the female and male evaluation of disease activity was high [Intraclass correlation coefficient (ICC-K) 0,92 for GH; 0,81 for E-VAS; 0,89 for P-VAS; 0,95 for DAS28-ESR; p<0,0001]. When comparing patient and examiner perception of the disease activity, P-VAS values were significantly higher than E-VAS in both female and male examiners (41,7 ± 26,2 vs 20,5 ± 20,8; 35,3 ± 25,4 vs 26,8 ± 27,1; p<0,0001; figure 3).The general agreement between male and female examiner and the whole patient population was moderate (K 0,65 and 0,62, respectively; p<0,0001), with the lowest agreement between female patients and male examiner (K 0,58; p<0,0001). Female physician had an higher agreement with both male and female patients (K 0,78, K 0,62 respectively; p<0,0001).

Conclusion: subjective measure of global health status and disease activity (GH, P-VAS) are generally higher when collected by a female examiner compared to a male one, especially among female patients. This gender discrepancy in subjective measures could influence the evaluation of disease activity indices; however, this does not affect the probability of being defined in remission. Overall, patients have a higher perception of disease activity compared to the health care providers, and the agreement between physician and patients is only moderate, with female patients having the worst perception. Female physician tend to be more in agreement with the patients' judgement of disease activity maybe because of a more emphatic setting established by the female health care provider.



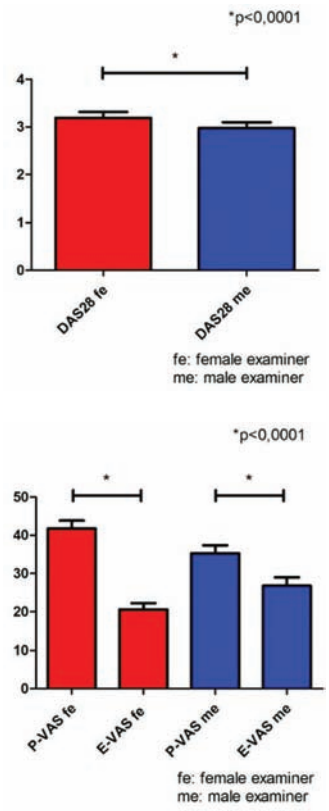


Figure 1

Disclosure of Interests: None declared
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FRI0041 **INCIDENCE AND TREND OF PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML) IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN. (TREND-AR STUDY)**

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Background: Treatment with biological agents is recognized as a potential risk factor for the development of Progressive Multifocal Leukoencephalopathy (PML), a rare and often fatal demyelinating disease of the CNS caused by John Cunningham Virus infection.
Objectives: Analyze the incidence and trend of hospital admissions for PML in patients with RA, in Spain, during the period between 1999 and 2015.
Methods: Population study based on the analysis of a national administrative database that includes a Minimum Basic Data Set (MBDS) of the income of patients with RA (ICD 9 714). Period: January 1, 1999, to December 31, 2015. The cases of PML were identified due to the presence in the primary and secondary diagnosis of the codes ICD 9 046.0 to 046.9. The population at risk was estimated through the population census of the National Institute of Statistics, with an estimated prevalence of RA of 0.5% in both sexes (0.2% in men and 0.8% in women). Crude and adjusted rates were calculated at national level. The trend was analyzed using Generalized Linear Models (MLG) using the variable year as the analysis variable.
Results: Of the total of 338,343 hospital admissions in patients with RA during the 17 years of the study period, only 14 cases (0.004%) of PML were recorded, nine (64.3%) were women and 5 (35.7%) men. The mean age was 69.5 years (SD 16.8); 74.56 (SD14.8) in women and 60 (SD18.1) in men (p = 0.145). Five patients (35.7%) died during admission (2 women and 3 men) (p = 0.266). The average of the Charlson index was 2.21 (SD 1.7); 3 (SD 2.5) in women and 1.78 (SD 1.1) in men (p = 0.227).
The crude incidence rate of PML was 0.54/100,000 inhabitants * year, 0.85/100,000 inhabitants * year in men and 0.37/100,000 inhabitants * year in women. The Relative Risk male: female was 2.34. The gross rate of PML increased from 0.32/105 * year in the period 1999-2002, to 0.74 between 2011 and 2015, both in women (from 0.19 in the period 1999-2002 to 0.52 from 2011 to 2015) as well as men (from 0.82 in the period 1999-2002 to 1.64 during 2011-2015). It is estimated that this increase is of 19.7% per year.
Conclusion: In Spain, between 1999 and 2015, there has been an increase in the incidence rate of PML in patients with RA. We estimate an annual increase of 19,7%.
Disclosure of Interests: None declared
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FRI0042 **CERTOLIZUMAB PEGOL EFFECTIVENESS IN WOMEN OF CHILDBEARING AGE WITH RHEUMATOID ARTHRITIS: RETROSPECTIVE ANALYSIS OF AN INTERNATIONAL MULTICENTRE COHORT**

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Background: Even though certolizumab pegol (CZP) has been licensed for the treatment of rheumatoid arthritis (RA) a long time ago, observational data in real-life settings are still lacking. Moreover, recent data on the lack of transplacental passage (1) make CZP particularly appealing for the treatment of RA women with a desire of pregnancy.
Objectives: To evaluate in a real-life international cohort the frequency of use, the clinical response, and the retention rate of CZP in RA women of childbearing age.
Methods: Data were retrospectively extracted from the Italian LORHEN and the Romanian Registry of Rheumatic Diseases (RRBR) registries, which include all RA patients treated with CZP between December 2010 and October 2018. The analysis was limited to women who received CZP as first-line biologic agent. The study population was stratified according to childbearing age (18-49 versus >49 years). The 6-, 12- and 24-month clinical response was evaluated as the proportion of patients achieving Disease Activity Score 28 (DAS28) remission and compared between the subgroups by a chi-squared test. The 5-year retention rate was calculated by the Kaplan-Meier method and compared between the subgroups by log-rank test.
Results: The whole cohort included 630 RA patients treated with CZP. According to the inclusion criteria, the study population consisted of 308 female RA patients (mean [± standard deviation, SD] age 54.2±12.1 years; mean disease duration 8.7±8.4 years; baseline DAS28 5.25±1.72, positive anti-citrullinated peptide antibody 161/254 [63.4%], positive rheumatoid factor 213/297 [71.7%]). Apart from mean age (39.6±6.6 vs 60.8 ±7.2, respectively; p<0.001), no other significant differences in baseline characteristics between the childbearing (n=97, 31.5%) and non-childbearing age (n=211, 68.5%) groups were observed. In the overall population, DAS28 remission was achieved by 29.9%, 42.1%, and 39.7% of patients at 6, 12, and 24 months, respectively. This proportion was significantly higher in childbearing compared with non-childbearing women at each timepoint (39.4% vs 25.4, p=0.02 at 6 months; 52.8% vs 37%, p=0.014 at 12 months; 52% vs 34.2%, p=0.014 at 24 months). The overall 5-year retention rate was 37.1%, with a higher (but not statistically significant) persistence in the childbearing versus non-childbearing subgroup (55.1%

vs 33.4%, p=0.177). In the whole cohort the most frequent reason for withdrawal was inefficacy (60.9%), whereas only 10.9% of patients discontinued the drug because of adverse events.

Conclusion: In our real-life data, CZP showed a high remission rate with a good safety profile and high persistence on treatment over 5 years. These findings were even more favorable during the childbearing age, supporting the use of CZP in RA women with a desire for pregnancy.

REFERENCE:

[1] Mariette X, Förger F, Abraham B, et al. Lack of placental transfer of certolizumab pegol during pregnancy: results from CRIB, a prospective, postmarketing, pharmacokinetic study. Ann Rheum Dis. 2018;77:228-33.

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FRI0043 CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS ADMITTED TO AN INTENSIVE CARE UNITIN SPAIN SINCE 2005–2015. TREND-AR STUDY

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Objectives: To analyse the clinical features of patients with Rheumatoid Arthritis (RA) that were admitted to an Intensive Care Unit (ICU) from January 2005 to December 2015.

Methods: A retrospective observational populational study was conducted analysing the national database that includes the Minimum Basic Data Sets (MBDSs) of admissions of RA patients to an ICU during the 2005-2015 period. Demographic characteristics, length of stay, clinical course, outcome and the MBDS codes for the main reason of admission were recorded. The cases were detected by the presence of their CIE-9 codes in the primary or secondary diagnoses. Statistical analysis was performed with Stata 15.0 software.

Results: During the 11 years of the study, a total of 2719 RA patients required 2806 admissions to an ICU. Average age was 69.7 ± 10.8 years and women constituted 58.5% of the cases. 30% of the patients admitted to an ICU had required $\geq$ 3 previous admissions and 11% required readmission within the next 30 days. Average Charlson index was 2.33 ± 1.4. Average length of stay was 9.3 ± 14 days and 64.2% died in the ICU during hospitalization. The main causes of hospitalization were cardiovascular events (45.7%), lung diseases (16%) and infections (10%). In the univariant analysis mortality was significantly increased in patients presenting infections (90%), lung disease (89%), severe hepatopathy defined by ascites and/or encephalopathy and/or gastrointestinal bleeding (88%), nephropathy/kidney disease (73%) and a higher Charlson index (2.4 vs 2.2). Multivariant analysis showed that mortality was increased among patients presenting respiratory complications and infections.

Conclusion: The most frequent hospitalization causes for patients with Rheumatoid Arthritis in Spain between 2005 and 2015 were cardiovascular, pulmonary and infectious diseases. RA patients that were admitted to the ICU showed an increased mortality. This increased mortality was mainly found in patients presenting respiratory or infectious conditions.

Disclosure of Interests: None declared

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FRI0044 RISK FACTORS FOR CORONARY ARTERY ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory disease leading to significant increase in cardiovascular morbidity and mortality. Development of coronary artery diseases (CAD) in RA patients (pts) is associated with the accumulation of traditional risk factors and immunological disorders. Coronary angiography (CAG) is the gold standard to identify coronary artery atherosclerosis (CAA).

Objectives: To identify CAA predictors and determine CAA detection rates in RA pts with suspected CAD.

Methods: Examination of 77 RA pts with suspected CAD, male/female 28/48, mean age 59 [53;64] years, with a long history of the disease (10[6;20] years), who were seropositive for IgM rheumatoid factor (RF) (82%) and anti-cyclic citrullinated peptide (ACCP) (58%), with moderate to high clinical disease activity DAS 28 4,2[3,2;5,3]). CAG was performed in all pts. CAA risk factors in RA pts were identified by the multiple linear stepwise regression analysis.

Results: Out of 77 RA pts CAA was detected in 52 (68%) (male/female 25/27 (group I)), while intact coronary arteries (CA) were found in 25 (32%) (male/female 3/22 (group II)) pts. Both groups were comparable in terms of age, disease duration and RA activity (DAS 28 score). Males prevailed in Group I: 48% vs 3% in Group II (p<0,05). Group I pts included more smokers than Group II (44% vs 8%, p<0,05). Other traditional risk factors were equally represented in both groups: arterial hypertension - 87% and 84%, dyslipidemia - 75% and 64%, diabetes mellitus - 15% and 8%, physical inactivity - 58% and 42%, obesity - 29% and 28% pts in Groups I and II, respectively. Serum HDL cholesterol (HDL-C) concentrations were lower (1,3[1,0;1,4] mmol/l) and triglyceride (1,5[1,1;2,0]mmol/l) levels were higher in Group I vs Group II (1,6[1,2;1,9] and (1,2[0,9;1,5]mmol/l), p<0,01). Concentration of total cholesterol and LDL-C were similar in pts from both Groups. Both Groups showed similar atherosclerotic plaques detection rates in carotid arteries (19/12%). Variety of administered drugs (disease-modifying antirheumatic drugs, biological drags and oral glucocorticoids) and therapeutic regimens were also comparable in Groups I and II. Multiple linear regression analysis indicates close association of CAA with pts' age (unstandardized coefficient B=0,017, 95% confidence interval (95% CI) [0,004-0,030], p=0,011), smoking (B=0,246, 95% CI [0,055-0,437], p=0,013), HDL-C (B=-0,325, 95% CI [-0,557-(-0,095], p=0,0073), atherosclerotic plaques in carotid arteries (B=0,549, 95% CI [0,120-0,901], p=0,003) and ACCP (B=0,309, 95% CI [0,028-0,589], p=0,03), coefficient of multiple determination (R^2) = 0,6. Subsequent ROC analysis confirmed the diagnostic value of HDL-C and CAA in RA pts. HDL-C levels below 1,32 mmol/l can be considered as a prognostic factor of CAA presence in RA pts with 68% sensitivity and 65%specificity (area under the curve is 0,711; 95% CI 0,580-0,842; p = 0,04).

Table 1. Values of analyzed parameters predictive of CAA according to the multiple linear stepwise regression analysis.

Variable	Unstandardized coefficient			P
	B	- 95% CI	- 95% CI	
Age	0,017	0,004	0,030	0,011
Smoking	0,246	0,055	0,437	0,013
HDL-C	-0,325	-0,557	-0,095	0,007
Carotid artery plaques	0,549	0,120	0,901	0,003
ACCP-positivity	0,309	0,028	0,589	0,03

CI – confidence interval

Conclusion: Male gender, low HDL-C levels, plaques in carotid arteries, and ACCP-positivity are associated with increased CAA risk in RA pts. Low HDL-C level can be considered as CAA predictor in RA pts.

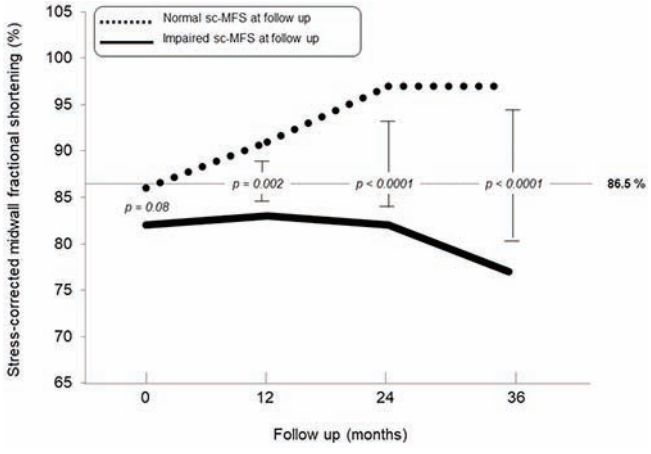
Disclosure of Interests: None declared

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FRI0045 **CHANGES IN LEFT VENTRICULAR SYSTOLIC FUNCTION ARE PREDICTED BY DISEASE SEVERITY IN PATIENTS WITH RHEUMATOID ARTHRITISWITHOUT PRIOR CARDIOVASCULAR DISEASE**

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Background: Occult left ventricular (LV) systolic dysfunction (LVSD) is associated with worse cardiovascular outcomes in asymptomatic patients with arterial hypertension and/or diabetes mellitus. In these patients, LV systolic function may worsen or improve overtime. However, little is known about the changes in LV function during follow up of patients with rheumatoid arthritis (RA).
Objectives: This prospective study analyzed incidence and factors associated with changes in LV systolic function in patients with RA without known cardiovascular disease.
Methods: One-hundred-forty outpatients with RA without overt cardiac disease were recruited between March and December 2014. Patients underwent clinical and echocardiographic evaluation at baseline and after a median period [min-max] of 35 [23-47] months of follow up. Stress-corrected midwall fractional shortening (sc-MFS) was used as measure of LVSD and considered impaired if <86.5%. Disease activity was assessed with the clinical disease activity index (CDAI).
Results: Impaired sc-MFS at follow up (sc-MFS-FU) was detected in 60/140 (43%) patients who were compared with 80 patients with normal sc-MFS-FU. Baseline sc-MFS did not differ significantly between the two groups, which appeared to diverge significantly soon after 1-year of follow up (figure). Baseline anti-citrullinated protein antibodies (ACPA) positivity, high disease activity (CDAI>10) and duration of RA were independently associated with impaired sc-MFS-FU at multiple logistic regression analysis. Among these parameters, ACPA had the highest sensitivity (80%) whereas high disease activity had the highest specificity (89%) for sc-MFS-FU. A predictive score including all three predictors (ACPA status, CDAI>10 and duration of RA) detected impaired sc-MFS-FU with a sensitivity of 78% and specificity of 82% (AUC 0.80 [IC 0.72-0.88], p<0.0001).
Conclusion: This study supports the hypothesis that changes overtime in LVSF in patients with RA are associated with ACPA, high disease activity and duration of disease.



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FRI0046 **POLYPHARMACY: A RARELY-DISCUSSED PROBLEM IN RHEUMATOID ARTHRITIS. DATA FROM A LARGE REAL-LIFE STUDY**

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Background: Polypharmacy is concomitant use of five or more drugs and is usually associated with various comorbidities and advanced age. The already demonstrated consequences of polypharmacy are increased side effects, drug interactions, increased hospitalizations, drug handling difficulties, reduced adherence, and even increased mortality. Rheumatoid arthritis (RA) is a chronic systemic disease with preferential involvement between the third and fifth decades. Owing to treatment of underlying disease and comorbidities, patients with RA frequently require combined use of several drugs. Despite the possible negative consequences of polypharmacy in RA, there is a shortage of studies in literature.
Objectives: Evaluate prevalence and factors associated with polypharmacy in patients with RA in a real-life setting.
Methods: This is a cross-sectional part of the Rheumatoid Arthritis in Real Life (REAL) study that analyzed RA patients in a real-life context from August to October 2015 in 11 public health services in Brazil. Statistical analysis involved obtaining frequencies of the variables of interest and multiple Poisson regression analyses.
Results: We evaluated 792 patients, of whom 89% were women, with median age of 56.6 years. 78.73% had a positive rheumatoid factor and 55.2% had an erosive disease. The median Disease Activity Score was 3.52, the median CDAI score was 9. Of the patients, 67.9% used 5 or more drugs as follows: mean of 2.8 and maximum of 5 drugs for RA, mean of 2.7 and maximum of 9 different types of medications for comorbidities, and mean of 5.5 and maximum of 11 drugs in total. The most commonly used drugs, besides specific drugs for underlying diseases, were vitamin D (63.8%), folic acid (61.1%), calcium (57%), and antihypertensive drugs (47%). In the multivariate analysis, the use of corticosteroids, methotrexate, and biological DMARDs and number of comorbidities (all with P <0.001) were statistically significant. Age, schooling, rheumatoid factor positivity, and measures of activity by compound disease activity indexes were not associated with polypharmacy.
Conclusion: The prevalence of polypharmacy was high (67.9%) in this population with RA, much higher than that described for elderly populations and other chronic diseases. This data can serve as an alert for this important and rarely-discussed aspect of RA.

REFERENCES:

[1] Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMC Geriatrics 2017;17:230.
[2] da Rocha Castelar-Pinheiro G, Vargas-Santos AB, de Albuquerque CP, Bértolo MB, Júnior PL, Giorgi RDN, et al. The REAL study: a nationwide prospective study of rheumatoid arthritis in Brazil. Adv Rheumatol 2018;58:9.
[3] Kim J, Parish AL. Polypharmacy and medication management in older adults. Nurs Clin North Am. 2017;52(3):457-468.
[4] Abolbashari M, Macaulay TE, Whayne TF, Mukherjee D, Saha S. Polypharmacy in cardiovascular medicine: problems and promises! Cardiovasc Hematol Agents Med Chem. 2017;15(1):31-39.

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FRI0047 SPECIFICS OF THERAPY FOR RHEUMATOID ARTHRITIS PATIENTS UPON THYROID INVOLVEMENT IN THE AUTOIMMUNE DISEASE

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Background: Apart from joints, the inflammation often involves other organs and tissues including lesions of the thyroid gland at which the disturbance of the gland affects considerably the functioning of cells of the immune system, and the activity of rheumatoid arthritis. Production of autoantibodies to thyroid hormones is assumed to be one of possible mechanisms of thyroid dysfunction.
Objectives: Studying various types of thyroid lesion in rheumatoid arthritis, searching for links between clinical manifestations of rheumatoid arthritis and specifics of thyroid lesion, and the level of antibodies to thyroid hormones.
Methods: The study included patients diagnosed with rheumatoid arthritis verified by ACR/EULAR criteria of 2010, and without any exclusion criteria. Rheumatoid arthritis activity was assessed utilizing DAS 28 Calculator. The presence of thyroid lesion was evaluated by means of clinical workup, ultrasound examination, and laboratory tests, including measuring the concentration of TTH, free T3, T4, as well as anti-TPO. Antibodies to T3 and T4 (anti-T3 and anti-T4) were measured by enzyme immunoassay, and the findings were shown in absorbance units. The cut-off values of positive and negative findings for anti-T3 (0.098 absorbance units) and anti-T4 (0.093 absorbance units) were calculated by ROC curve analysis utilizing sera from relatively healthy donors (n = 39). The results were shown as an arithmetic mean value ± standard error (M ± m).
Results: 72 patients with rheumatoid arthritis participated in the study. The mean activity of rheumatoid arthritis assessed by DAS 28 Calculator was 3.2 ± 1.4 points. Extra-articular presentations were detected in 20 patients, 5 of whom showed clinical manifestations of thyroid lesion. All five patients were marked by low TTH and a high activity of rheumatoid arthritis (4.8 ± 1.9 points of DAS28). In 73 patients antibodies to T3 were detected (0.128 ± 0.047 absorbance units). Apart from the thyroid gland, no clear association between these antibodies and lesions of other organs or systems were noted. A statistically significant tendency for an increase in X-ray stage linked to increased antibodies to T4 was noted ($p = 0.034$; ANOVA); an inverse relation was noted for antibodies to T3 ($p = 0.034$; ANOVA). The association with DAS 28 for antibodies to T4 ($r=0,525$; $p=0,031$) and for antibodies to T3 ($r=-0,391$ $p=0,040$) was also inverse and statistically significant. Besides, another statistically significant correlation was revealed between the value of DAS 28 and TTH concentration ($r=-0,330$ $p=0,046$).
Conclusion: The available findings demonstrate that a high activity of rheumatoid arthritis is associated with hypothyroidism development, despite the tendency for increased count of antibodies to T4 which is typical of rheumatoid arthritis. The possibility to modify the activity of rheumatoid arthritis by correcting thyroid dysfunction is very important both for developing a strategy of managing drug–resistant cases of rheumatoid arthritis, and for the management of this condition in general.

REFERENCES:

[1] Paramonova O.V., Alimsultanova L.R., Rusanova O.A. Are there any particularities in the clinical picture of rheumatoid arthritis with concomitant thyroid gland pathology?/Health is the basis of human cooperation: problems and their solutions. 2012. V. 7. No. 1. P. 450-452.
[2] Starova OV, Gontar I.P.INTERRELATION OF RHEUMATOID ARTHRITIS AND THYROID PATHOLOGY/In the collection: Actual problems of experimental and clinical medicine. Materials of the 64th open final scientific conference of young scientists and students of VSMU. Edited by V.I. Petrova;2006. p. 101.

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FRI0048 SARCOPENIA AND SARCOPENIC OBESITY ARE ASSOCIATED TO GLUCOCORTICOID USE AND CLINICAL AND SEROLOGICAL MARKERS IN RHEUMATOID ARTHRITIS

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Background: Sarcopenia play an important role in the quality of life, morbidity and mortality of the patients, especially in who suffer chronic disease. In rheumatoid arthritis (RA) sarcopenia risk is higher due to joint dysfunction, pharmacological therapy and chronic inflammation[1]; these conditions may induce changes in body composition such as an increase in visceral fat associated to reduced muscle mass. Recently emerge the concept of sarcopenic obesity, however the association to clinic characteristics and pharmacotherapy in RA has not been established.
Objectives: We investigated the prevalence of sarcopenia and sarcopenic obesity, as well as the relationship with glucocorticoids (GCs) use and clinic characteristic of RA patients from southern Mexico.
Methods: We carried out a cross-sectional study in 223 RA patients (89% women, mean age 44 years), all diagnosed according to ACR/EULAR 2010 criteria. The body composition was examined using a bioimpedance method (body weight, muscle mass, body fat, etc.). Abdominal

obesity was defined by WHO criteria and the hand grip strength was evaluated by dynamometry. Sarcopenia was defined according to The European Working Group on Sarcopenia in Older People, as Skeletal Muscle Mass Index less than 5.45 kg/m^2 in women and less than 7.26 kg/m^2 in men, while sarcopenic obesity was defined by the presence of sarcopenia more abdominal obesity. The GCs use and dosage (prednisone and methylprednisolone) were analyzed reviewing the clinical records. Anti-cyclic citrullinated peptides (anti-CCP) antibodies, rheumatoid factor (RF) levels, high sensitivity C reactive protein (hsCRP), erythrocyte sedimentation rate (ESR) were determinate. The morning stiffness, clinic activity of disease (DAS28-ESR score) and disability index functional (HAQ-DI) were measurement.

Results: In this study 86% of the population had sarcopenia and 44% sarcopenic obesity. The 62.8% under GCs therapy. The prednisone dosage was positively associated to sarcopenia (>5 mg/day; OR=4.3, p=0.003) and sarcopenic obesity (OR=3.2, p=0.06). The intramuscular pulse of methylprednisolone (40 mg/kg) was associated to sarcopenic obesity phenotype (OR=2.61, p=0.09). Regarding the clinical and serological markers in RA, high disease activity (DAS28-ESR score) was associated to sarcopenia (OR=6.6, p=0.01) and sarcopenic obesity (OR=6.3, p=0.02). The morning stiffness (p=0.03), RF (p=0.05), anti-CCP positive (p=0.03) and HAQ-DI score (p=0.04) were too associated, mainly to sarcopenic obesity.

Conclusion: Sarcopenia and sarcopenic obesity are associated to GCs dosage and with serological and disease activity markers in RA patients from southern Mexico. So that is needed promote monitoring and management of sarcopenia and sarcopenic obesity in RA patients.

REFERENCE:

[1] Torii M, Hashimoto M, Hanai A, et al. Prevalence and factors associated with sarcopenia in patients with rheumatoid arthritis. Mod Rheumatol. 2018;1-7. doi: 10.1080/14397595.2018.1510565

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FRI0049 COGNITIVE IMPAIRMENT AND RHEUMATOID ARTHRITIS IN MOROCCAN PATIENTS

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Background: Cognition in rheumatoid arthritis is regaining interest in publications lately. A recent experimental study(1), have shown that low grade chronic periodontal infection by Porphyromonas gingivalis result in the development of neuropathology that is consistent with that of Alzheimer dementia in adult mice. This same pathogen has been linked previously in many studies to the development of RA. These findings are raising existing doubt about an association between cognitive impairment and RA.

Objectives: Our study aims to assess cognitive impairment in RA patients in remission state.

Methods: It is a cross-sectional study realized at the rheumatology department of our University hospital. Our established RA patients regularly followed were asked to fulfill the Arabic version of the mini mental state examination (A-MMSE)(2) twice (initially and 15 days later) and the Patient Health Questionnaire (PHQ-9)(3) test for depression. Patients with neurological history (stroke, chronic infection and hematoma) have been excluded. Data about demographic, clinical (body mass index, Disease Activity Score of 28 joints, Health Assessment Questionnaire, modified total sharp score), biological (C-Reactive Protein, blood cell count, Anti-Citrullinated Peptide Antibodies, thyreotropin, vitamin B12, folic acid) characteristics was recorded. A-MMSE under 24 after adjustment for the level of education as recommended was considered abnormal. A cut-off of 10 of the PHQ-9 was considered as suggestive of depression. A descriptive study and regressions were done by SPSS.20 software and p<0.05 was taken as significant.

Results: A total of 80 patients were recruited, with an average age of 55.9 ± 8.5 years. Women were predominant (86.3%) in this population with an illiteracy rate of 66.3%. Our patients were ACPA positive in 93.8% of the cases, with mean disease duration of 11.4±8.65 years. They were receiving cDMARDs in 96.3%. Their average DAS28CRP was 2.19 ± 0.92, and their mean HAQ was 1.14±0.89. Five patients had thyroid disease and were receiving treatment, 20% of the population had anemia but with correct vitamin B dosage (essentially iron deficiency). The A-MMSE was abnormal in 57% at the first time, and in 38.8% of the cases at the second try fifteen days later, while 27.5% of the patients had a PHQ9>10. The fields of altered A-MMSE were: attention and calculation (46.3%), copying (53.8%), orientation (38.8%), recall (25%) and language (41.3%).The immediate recall part was little concerned. No association was found for low MMSE in regressions with age, gender, menopause, BMI, disease parameters (HAQ, DAS, CRP, ACPA, mTSS) or other possible influencing factors (uric acid, creatinine clearance). An elevated PHQ was not correlated to A-MMSE in our patients (P=0.22). Only their level of education was significantly related to A-MMSE (p<0.0001).

Conclusion: It is certainly true that the interpretation and evaluation of cognitive functions is a difficult task, especially in an illiterate and disabled patient. However, in our study A-MMSE results were low even after test repetition, and in a state of disease remission. Although these results underscore the high frequency of cognitive impairment in RA patients, we estimate that further studies are eligible to confirm causality.

REFERENCES:

[1] Ilievski V, Zuchowska PK, Green SJ, Toth PT, Ragozzino ME, Le K, et al. Chronic oral application of a periodontal pathogen results in brain inflammation, neurodegeneration and amyloid beta production in wild type mice. PLoS ONE. 2018;13(10):e0204941.
[2] Bellaj T, Ben Jemaa S, Attia-Romdhane N, Dhiffallah M, Ben Ali N, Bouaziz M, Mrabet A. Version arabe du Mini Mental State Examination (A-MMSE): fidélité, validité et données normatives. Tunis Med. 2008;86:768–776.
[3] Belhadj H, Jomli R, Ouali U, Zgueb Y, Nacef F. Validation of the Tunisian version of the patient health questionnaire (PHQ-9). European Psychiatry. 2017 Apr 1;41:S523.

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FRI0050 CARDIOVASCULAR RISK IN THE RHEUMATOID ARTHRITIS PATIENTS OF THE GULF CORPORATION COUNCIL-GCC: WHAT CONTRIBUTE TO THE CAROTID INTIMA MEDIA THICKNESS

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Background: Rheumatoid arthritis (RA) is a common inflammatory joints disease that occurs in 1-3% of population. RA patients are at higher risk of cardiovascular disease (CVD). This accelerated atherosclerosis can't be fully explained by the traditional CVD risk factors. The CVD risk factors had never been investigated in the RA patients of Gulf Corporation Council (GCC).

Objectives: For the first time, this study assesses the CVD as manifested by carotid intima media thickness (cIMT) and the CVD risk factors (traditional and non-traditional) in RA GCC-population.

Methods: 216 RA (179 (83%) F and 37 (17%) M) GCC patients, who were free of atherosclerosis (CVD & Cerebrovascular diseases) included over 5 years (2013-2018). Diabetic, hypertensive, gout, renal and thyroid patients, pregnant, current smokers and those with history of smoking, and patients on diuretics medications were excluded. cMIT ultrasound (US) measurements were obtained using a real-time US scanner equipped with a 7.5-MHz linear probe. Blood tests (full blood counts, liver function, renal profile, and inflammatory markers), demography details, and body mass index (BMI) had been obtained within the same week of the cIMT scan. The correlation between cIMT and other variables were calculated using simple linear and multivariate regression analysis.

Results: The mean cIMT was 0.58 ± 0.11 mm (Min 0.28, Max 0.98). The mean age was 48 ± 13 years (48 ±12 yrs for females, 50±16 yrs for males, p= 0.279).

univariate regression analysis showed a positive linear relationship between cIMT and age of the participants (p=0.001, CI: 0.00, 0.01), hemoglobin (Hb) (p=0.006, CI: 0.004, 0.023), hematocrit (p=0.006, CI: 0.001, 0.008), mean cell volume (MCV) (p=0.027, 0.000, 0.004), mean cell hemoglobin (p=0.04, CI: 0.000, 0.009), platelet (p= 0.000, CI: -0.001, -0.000), monocytes (p= 0.02, CI: 0.001, 0.018), eosinophils (p= 0.011, CI: 0.002, 0.018), erythrocyte sedimentation rate (ESR) (p=0.04, CI: 0.000, 0.001), creatinine (p=0.002, CI: .000, 0.002), uric acid (p=0.002, CI: 0.0001, 0.0004), triglycerides (p=0.033, CI: 0.002, 0.044), low density lipoprotein (LDL) (p=0.002, CI: 0.010, 0.045), C-reactive protein (p= 0.000, CI: 0.001, 0.002), ferritin (p=0.000, CI: 0.000, 0.001), body weight (Kg) (p=0.018, CI: 0.000, 0.002), body mass index (Kg/Ht^2) (p=0.026, 0.000,

0.006), systolic blood pressure; Sbp (p= 0.000, CI: 0.001, 0.003), and diastolic blood pressure; dbp (p=0.001, CI: 0.001, 0.003).
Negative linear relationship between cIMT and transferrin (p=0.001, CI: -0.001, 0.000), high density lipoprotein (p=0.000, CI: -0.103, -0.036), and glomerular filtration rate (GFR, ml/min) (p=0.024, CI: -0.0009, -0.00007).
Multiple linear regression analysis showed a positive linear relation between cIMT and age of the participants (p= 0.000, CI: 0.002, 0.005), LDL (p= 0.003, CI: 0.012, 0.053), eosinophils (p= 0.025, CI: 0.001, 0.023), Sbp (0.004, CI: 0.001, 0.003), and the ESR (p= 0.016, CI: 0.002, 0.003). And, negative linear relationship with the GFR (p= 0.022, CI: 0.000, 0.002), and transferrin (p=0.000, CI: -0.001, -0.000). The R^2 of the model was 0.65.
Conclusion: For the first time we show that high hemoglobin, transferrin level and eosinophils count seem to have a role as a CVD risk factors in RA. The glucose fasting level is important CVD risk factor even in non-diabetic RA patients. The rest of the CVD risk factors in RA GCC population are like what had been demonstrated in other population (older age, high Sbp, ESR, LDL, and GFR level).

REFERENCE:

[1] Gabriel S. Cardiovascular morbidity and mortality in rheumatoid arthritis. Am J Medi. 2008;121:S9–S14.

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FRI0051 DURATION OF EXPOSURE TO BIOLOGICS AND STATINS MODERATES THE EFFECTS OF CUMULATIVE INFLAMMATION ON CORONARY ATHEROSCLEROSIS PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: Higher inflammatory load associates with increased risk of cardiovascular events in patients with rheumatoid arthritis (RA). We recently reported that occult atherosclerosis burden on coronary computed tomography angiography (CCTA) predicted long-term cardiovascular events (CVE) in RA above and beyond cardiac risk factors or scores. We further showed that higher cumulative inflammatory burden independently predicted coronary plaque progression.
Objectives: To explore whether the duration of exposure to biologic DMARDs and/or statins during the study period mitigates the effect of cumulative inflammatory load on coronary plaque progression.
Methods: One hundred-one participants with a baseline CCTA underwent a follow-up evaluation in 83±3.6 months. Plaque burden was reported as segment involvement score (SIS, describing the number of coronary artery segments with plaque per patient) and coronary artery calcium (CAC), quantified by the Agatston method. Robust logistic and linear regression models evaluated effects of predictors on plaque (SIS) progression and CAC change, respectively. Predictors of interest were time-averaged c-reactive protein (CRP), duration of bDMARD exposure (years), duration of statin exposure (years), and their 2- and 3-way interactions. Models were controlled for age and baseline hypertension. Significant interactions were subsequently decomposed and examined based on a median split for the duration of biologic and statin exposure.
Results: A significant interaction between inflammation and statin exposure duration was observed for plaque progression p=0.019 (figure 1A); in patients with shorter statin exposure (<1 year), higher inflammation predicted a greater likelihood of plaque progression [odds ratio (OR)=1.90, 95% confidence interval (CI)=1.15 to 3.14], p=0.012. By contrast, longer statin exposure (>1 year) attenuated that effect [OR=1.37, 95% CI=0.67 to 2.82, p=0.391). Notably, significant three-way interactions were observed between time-averaged CRP, duration of bDMARD exposure and duration of statin exposure on plaque progression [p=0.050] and CAC change [p=0.006]. In patients with shorter biologic exposure (<5.5 years), statin exposure moderated the effect of cumulative inflammation on plaque and CAC change. Specifically, cumulative inflammation positively associated with plaque progression [OR=3.25, 95% CI=1.02 to 10.38, p=0.047] and CAC change [β=0.57, 95% CI=0.35 to 0.80, p<0.001] in patients with shorter treatment with statins (<1 year) [figure 1B and 1C respectively]. By contrast, in patients with longer exposure to statins (>1 year), inflammation was not related to plaque progression [OR=1.25, 95% CI=0.48 to 3.31, p=0.65] or CAC change [β=-0.16, 95% CI=-0.43 to 0.21, p=0.52]. In patients with longer biologic exposure (<5.5 years) the length of treatment with statin did not moderate the effect of cumulative inflammation on plaque progression [p=0.229, figure 1].
Conclusion: The relationship between cumulative inflammation, length of treatment with bDMARDs, statins and their ultimate impact on coronary plaque progression in RA are highly nuanced. The effect of the duration of statin exposure on coronary plaque burden progression seems relevant only in the context of insufficient biologic exposure; shorter treatment with statins in that setting allows for significant coronary plaque progression in response to higher cumulative inflammatory load. In contrast, longer statin exposure attenuates that risk.

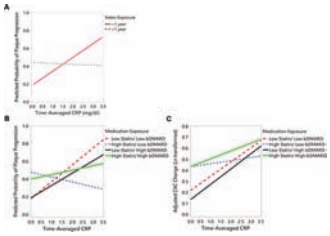


Figure 1. Interaction between cumulative inflammation, length of treatment with bDMARDs and statins on coronary plaque progression in RA.

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FRI0052 BODY COMPOSITION IN MEN WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic immune inflammation of the joints, leading to early disability of patients at high risk of cardiovascular events and osteoporotic fractures. This problem is important today in men with RA, because, due to more frequent severe disease and increased mortality in the year after the fracture. Reduction of bone mineral density (BMD) and muscle mass are significant predictors of fractures, which leads to the high importance of studying the state of BMD and body composition.
Objectives: Improving the diagnosis of osteoporosis in patients with RA of the male gender with the regard of BMD and body composition.
Methods: The study involved 110 male patients with a documented diagnosis of RA at the age of 59 [53; 65] years. Depending on the taking of glucocorticosteroids (GCS) all patients was allocated two groups: I subgroup - 60 patients who are not taking GCS and subgroup II - 50 patients who are taking GCS. The control group consisted of 30 healthy men comparable by the age and body mass index.
The study of BMD at the lumbar spine (L1-L4) and femoral bone was measured by dual-energy x-ray absorptiometry using a bone mineral density «STRATOS dR» (DMS, France). Assessment of body composition was carried out, using the «Whole body» («The whole body»). Sarcopenia was diagnosided as a decrease in lean mass index of less than 7,26 kg/m^2.
Results: 63,6% of patients with RA showed a reduction of BMD corresponding osteopenia/OP. OP was diagnosed in 28 (25,5%) patients with RA, and osteopenia - in 42 (38,2%). The detection rate of OP in the second subgroup was significantly higher (p<0,05), than in the first subgroup (48% and 5% respectively). The most significant decrease in BMD was observed in the neck of the femur in the main group as a whole and in individual subgroups. There was a negative correlation degree of activity of RA and indicators of BMD of the lumbar spine (r=-0,4, p<0,05) and proximal femur (r=-0,38, p<0,05). Assessment of body composition showed that patients of the main group were significant decrease in the total lean mass (LM) of the body, and the trunk and limbs of LM compared with patients of the control group (p<0,05). Sarcopenia detected in 66 (60%) of RA patients, whereas in the control group it was absent. In 44 (66,7%) male patients with RA with sarcopenia decreased BMD to the level of osteopenia (34,9%) and OP (31,8%). Obtained a negative

correlation parameters LM and absolute 10 years risk of osteoporotic fractures (r=-0,302, p<0,05) on FRAX.
Conclusion: 63,6% of men suffering from RA, there was a decrease in BMD, the corresponding OP/osteopenia with a primary reduction of BMD at the femoral neck. Decrease BMD in patients with RA was significantly associated with a high degree of disease activity (r=-0,4, p< 0,05). Taking GCS had no significant effect on BMD at the femoral neck. Analysis of body composition in 55% of patients with RA showed a reduction in the level of LM limbs sarcopenia. Obtained correlation lower BMD and LM limbs (p<0,05; r=0,28).
Thus, in patients with RA male along with OP/osteopenia showed a significant decrease in LM that given the biomechanics of movement can be an additional risk factor for falls and fractures.

REFERENCES:

[1] Roux, C. (2011). Osteoporosis in inflammatory joint diseases.Osteoporosis International, 22(2), 421-433.
[2] Giles, J. T., Bartlett, S. J., Andersen, et al. (2008). Association of body composition with disability in rheumatoid arthritis: impact of appendicular fat and lean tissue mass. Arthritis Care & Research: Official Journal of the American College of Rheumatology, 59(10), 1407-1415.
[3] Giusti, A., & Bianchi, G. (2014). Male osteoporosis. Reumatismo,66(2), 136-143.
[4] Thomas, D. R. (2007). Loss of skeletal muscle mass in aging: examining the relationship of starvation, sarcopenia and cachexia.Clinical nutrition, 26 (4), 389-399.

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FRI0053 ACCELERATED ATHEROSCLEROSIS IN PREMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS (15 YEARS PROSPECTIVE STUDY)

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Background: Rheumatoid arthritis (RA) is chronic inflammatory disease, associated with increased mortality and morbidity due to higher cardiovascular risk in these patients.
Objectives: Traditional risk factors are not the only answer for accelerated atherosclerosis. In long term prospective study, we investigated the relationship between asymptomatic atherosclerosis and traditional risk factors as well inflammatory markers in patients with RA and matched healthy controls.
Methods: In 60 RA premenopausal women and 34 matched controls values of laboratory test results, concentrations of inflammatory mediators, matrix metalloproteases (MMP) and markers of inflammation were measured. Using B-mode ultrasonography carotid intima-media thickness (cIMT) and plaques occurrence (markers of asymptomatic atherosclerosis) at baseline and after 15 years of observation were defined in both groups. The differences in concentrations of inflammatory mediators, MMPs and markers of inflammation were compared. The relationship of inflammatory mediators and markers, MMPs and markers of asymptomatic atherosclerosis was examined using regression models.
Results: After the follow up statistically significant higher values of inflammatory markers like selective adhesion molecules ICAM & VCAM, interleukin 6 (IL-6), tumour necrosis factor alpha (TN alpha) and MMP-3 in patient`s group was found. Among traditional risk factors only sedimentation rate and CRP levels were statistically higher in patient`s group. More plaques were found in patients' group (12.9% vs. 42.4%; p=0.005), patients had also higher values of cIMT (p<0.0001). Using multiple linear regression analysis only VCAM was found as independent prognostic factor for plaques occurrence (p=0.016), but not for cIMT (p=0.314) in RA patients after the follow up.
Conclusion: Asymptomatic atherosclerosis is accelerated in premenopausal women with RA patients. The results of our study showed the association between the inflammation and accelerated atherosclerosis, VCAM was found as independent risk factor for plaques occurrence in these patients.

REFERENCES:

[1] Dalbeni A, et al. Traditional cardiovascular risk factors or inflammation: Which factors accelerate atherosclerosis in arthritis patients?. International J Cardial 2017; 236: 488-492.
[2] Mahmoudi M, Aslani S and Jamshidi AR. New insights to the mechanisms underlying atherosclerosis in rheumatoid arthritis. International Journal of Rheumatic diseases 2017; 20: 287-297.
[3] Johnson JL. Metalloproteinases in atherosclerosis. Eur J Pharmacol. 2017;816:93-106.
[4] Agca R, Heslinga SC, Rollefstad S e tal. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Ann rheum Dis 2017; 76: 17-28.

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FRI0054 CHARACTERISTICS OF PATIENTS WITH ELDERLY-ONSET RHEUMATOID ARTHRITIS AND INVESTIGATION OF DRUG THERAPY

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Background: It is expected that the increase in average life expectancy in recent years would also be observed even in patients with rheumatoid arthritis (RA)
Objectives: We compared data for RA patients obtained between 1991 and 2018 to clarify the current clinical picture of RA in elderly patients.
Methods: We evaluated 429 and 368 RA cases seen at our department in 1991 and 2018, respectively. The patient ages and sex ratios in the two groups were first compared, and then the clinical features of 260 patients with younger-onset RA (YORA; onset age <65 years) and 108 patients with elderly-onset RA (EORA; onset age >65 years) in the 2018 group were evaluated. All patients satisfied the 1987 and 2010 Rheumatoid arthritis classification criteria for RA, and their data were obtained from the medical records. Patient data at the onset of RA were used. The study protocol was approved by the Institutional Review Board of Niigata University. All statistical analyses were performed with SPSS ver. 13 for Windows, and differences at p<0.05 were considered to be statistically significant.
Results: The peak age at RA onset was 50s-60s in 1991 and 60s-70s in 2018. In 1991, the male-female ratios in the <65-yr and >65-yr age groups were 0.14 and 0.19, respectively, whereas the corresponding ratios in 2018 were 0.25 and 0.38, respectively. Although the proportion of elderly patients increased, homogeneity testing of the odds ratio revealed no significant difference. Among the 368 RA patients in the 2018 group, initial involvement of large joints was more frequent in those with EORA, whereas initial involvement of small joints was more frequent in those with YORA (p<0.05). Statistical analysis demonstrated no significant inter-group differences in hemoglobin, WBC, BUN, uric acid, CRP, ESR or serum creatinine, but the estimated glomerular filtration rate was significantly higher in the YORA group (P=0.00). The frequencies of hematuria and proteinuria (>1.0 g/Cr) showed no inter-group differences. The frequency of RF positivity also did not differ between the groups, but the RF titer was higher in the YORA group (p<0.01). ACPA showed no inter-group difference in terms of either the frequency of positivity or titer. Among other features after diagnosis, AA amyloidosis was observed in only 7 (2.7%) of the YORA patients. RA proceeded PMR in 7 patients in each group, and the frequency of PMR was significantly (P<0.01) higher in patients aged >60 years. For therapy, MTX was used in about 70% of YORA patients, its use being more frequent than EORA patients (p<0.01), although the dose employed did not differ significantly between the two. About half of all patients received steroid, and neither the frequency nor the dose differed significantly between the YORA and EORA groups. Biological agents were used in 61% of YORA patients and 29% of EORA patients, the difference being significant (p<0.01). Abatacept was used significantly (p<0.05) more often in the EORA group because of the low frequency of severe infections, but the frequency of use of other biological agents and Jak inhibitors did not differ significantly between the groups.
Conclusion: The characteristics of EORA patients differ from those of YORA patients. Diagnosis requires attention to PMR. In YORA, attention to amyloid is also required in view of the fact that treatment was insufficient in the past. Pharmacotherapy should be based on the characteristics of aging in elderly patients with RA. The diagnosis and treatment of RA in elderly patients is an issue of future concern.

REFERENCE:
[1] Sugihara T, et, al. Structural and functional outcomes of a therapeutic strategy targeting low disease activity in patients with elderly-onset rheumatoid arthritis: a prospective cohort study (CRANE). Rheumatology (Oxford). 2015;54:798-807.

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FRI0055 AN EQUATION FOR ESTIMATED CARDIORESPIRATORY FITNESS IN RHEUMATOID ARTHRITIS PATIENTS IS NEEDED

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Background: RA patients are deconditioned and on average have decreased cardiorespiratory fitness (CRF, peak oxygen uptake) compared to the general population (1). This may contribute to an increased risk of cardiovascular disease (CVD). Because CRF is associated with cardiovascular health, it is important to assess. For the general population, various equations exist for estimation of CRF (eCRF) without the need of a resource-intensive cardiopulmonary exercise test.
Objectives: Compare eCRF of people without RA to eCRF of RA patients, using recognized equations for eCRF (2,3) based on gender, age, resting heart rate, waist circumference and self-reported physical activity.
Methods: Among participants with self-reported RA in the second and third surveys of the Norwegian population-based Nord-Trøndelag Health Study (HUNT2 and 3)(4), RA patients were identified from hospital case files using standardized diagnostic criteria (5). The mean eCRF of participants with and without RA were calculated and the 95% confidence intervals (CI) compared.

HUNT2	Men (no RA)	Men (RA)	Women (no RA)	Women (RA)
	Mean eCRF (CI), n	Mean eCRF (CI), n	Mean eCRF (CI), n	Mean eCRF (CI), n
30-39 years	50.3(50.2-50.5), 5,134	49.5(45.6-53.4), 8	40.3(40.2-40.4), 5,623	38.7(37.2-40.1), 25
40-49 years	46.2(46.1-46.3), 6,104	46.7(44.8-48.6), 22	36.6(36.5-36.7), 6,496	36.2(35.2-37.2), 72
50-59 years	42.2(42.0-42.3), 4,910	40.9(39.6-42.3), 50	32.9(32.8-33.1), 4,994	31.5(30.7-32.4), 75
60-69 years	38.3(38.2-38.5), 3,600	39.2(37.7-40.6), 40	29.0(28.9-29.1), 3,441	28.6(27.7-29.5), 71
70-79 years	34.7(34.5-34.9), 2,678	34.3(31.9-36.6), 20	25.3(25.2-25.5), 2,608	25.3(23.9-26.7), 32
80-89 years	30.4(30.0-30.8), 677	n=0	22.1(21.9-22.4), 871	24.0(18.1-29.9), 4
HUNT3	**Men (no RA)**	**Men (RA)**	**Women (no RA)**	**Women (RA)**
	Mean eCRF (CI), n	Mean eCRF (CI), n	Mean eCRF (CI), n	Mean eCRF (CI), n
30-39 years	46.6(46.4-46.9), 2,069	47.3(-24.5-119.0), 2	37.1(36.9-37.2), 3,189	34.7(30.8-38.5), 9
40-49 years	43.3(43.1-43.5), 3,406	46.5(10.2-82.9), 2	34.8(34.7-34.9), 4,668	34.9(32.9-36.8), 21
50-59 years	39.5(39.4-39.7), 4,153	39.5(37.4-41.5), 19	31.5(31.4-31.7), 4,994	30.2(29.1-31.4), 56
60-69 years	36.2(36.0-36.3), 3,764	33.1(31.3-34.8), 41	28.2(28.1-28.4), 4,222	27.5(26.5-28.6), 58
70-79 years	33.0(32.8-33.2), 2,149	34.3(32.4-36.1), 35	24.9(24.8-25.1), 2,284	24.4(23.2-25.5), 41
80-89 years	29.7(29.4-30.1), 708	28.3(24.5-32.0), 8	22.6(22.3-22.8), 812	22.8(21.2-24.3), 14

Table 1. Mean eCRF (mL/(kg x min)) and 95% CIs of RA patients and participants without RA attending HUNT2 and 3. Age categories with n<8 RA patients in grey.

Conclusion: The eCRF CIs of RA patients and participants without RA were overlapping in all age categories except for men aged 60-69 years in HUNT 3 (Table1). This is contradictory to previous findings where RA patients were deconditioned compared to healthy controls (1). A probable explanation is that equations for eCRF were developed from healthy populations, and therefore overestimate eCRF in RA patients. For better CVD risk management including CRF as an important risk factor, an equation for eCRF developed specifically for RA patients is needed.

REFERENCES:
[1] Munsterman T, et al. BMC Musculoskelet Disord. 2012;13:202.
[2] Nes BM, et al. Med Sci Sports Exerc. 2014;46(6):1159-65.
[3] Nauman J, et al. Mayo Clin Proc. 2017;92(2):218-27.
[4] Krokstad S, et al. Int J Epidemiol. 2013;42(4):968-77.
[5] Videm V, et al. J Rheumatol. 2017;44(8):1134-41

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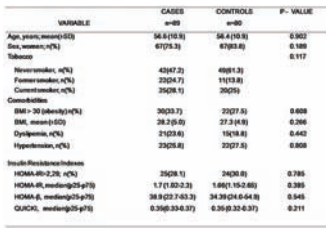
FRI0056 NESTED CASE-CONTROL STUDY : ASSOCIATED FACTORS WITH INSULIN RESISTANCE IN A RHEUMATOID ARTHRITISINCEPTION COHORT

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Objectives: To asses insulin resistance (IR) in patients with rheumatoid arthritis (RA) and compare it with healthy controls and to analyze the association between the accumulated inflammatory burden in patients with RA and IR.
Methods: Design: Nested case-control study. Population: consecutive RA-patients (ACR/EULAR 2010 criteria), >16 years, selected from a prospective inception cohort (diagnosis of RA between 2007 and 2011). Patients with Diabetes Mellitus (according to ADA 2010 criteria) were excluded. Controls: sex- age and BMI -matched controls were collected from a health center in our hospital area. Protocol: Cases and controls were evaluated by a rheumatologist. Clinical data of disease activity (RA patients), analytical values and oral glucose tolerance test (OGTT) were determined. Main outcome: IR measured by the homeostasis model for insulin resistance (HOMA-IR) (IR> 2.29 μU*mmol/ml). Secondary outcome: IR measured by quantitative insulin sensitivity check index (QUICKI) (<0.337μU*mmol/ml) and by the homeostatic model assessment of β-cell function (HOMA ß).Variables: Demographic, clinical-analytical variables, Disease Activity Score of 28 joints (DAS28-ESR), Health Assessment Questionnaire (HAQ), BMI (according to OMS classification) and glucose and insulin before and after OGTT values. Statistical analysis: Descriptive and paired T-test or Chi-square test followed by Multivariate Linear Regression in RA patients (Dependent variable: HOMA-IR).
Results: Two hundred subjects were studied, 31 of them were excluded after OGTT. Finally 169 subjects were included; 89 RA and 80 controls. The mean age of patients with RA was 56.6(±10.9) years. Most of them were women (75.3%), with seropositive (FR 82.0% y ACPA 75.3%) and erosive (61.1%) RA. The average duration of the disease was 98 months (8.1 years). The delay in the diagnosis of RA was 10.9 months (5.4 - 25.6) with a mean DAS28 index since the beginning of the disease of 3.11 (0.8). Differences between clinical characteristics and in relation to IR between cases and controls are shown in Table 1. No significant differences in the proportion of subject with IR in cases and controls were observed and 28.1% of patients with RA had IR. Of the 25 patients with IR, the majority, 68%, presented a DAS28 score> 3.2 (moderate-high activity index). In multivariate analysis, the independent variables associated with IR in patients with RA were: Obesity [OR=6.01; β=1.795 (p=0.002), disease activity (OR=2.77; β=1.021 [p=0.009]) Il-1β (OR=1.59; β=0.464 (p=0.024)). This model would explain 37.5% of the variability of the IR (R^2=0.375).
Conclusion: We did not find an increased IR in patients with RA compared with healthy controls, which may be due to adequate treatment and good control of inflammatory activity in the most of patients with RA. Obesity, inflammatory activity (measured by mean DAS28 index) and IL-1 β were the predictors of IR in patients with RA in our study.

REFERENCES:
[1] Insulin resistance and levels of adipokines in patients with untreated early rheumatoid arthritis. Manrique-Arija S, et al. Clin Rheumatol. 2016;35 (1):43-53.
[2] Abnormal Glucose Metabolism in Rheumatoid Arthritis. Pi H1, Zhou H1, Jin H1, et al. Biomed Res Int. 2017;2017:9670434.
[3] Obesity is the main determinant of insulin resistance more than the circulating pro-inflammatory cytokines levels in rheumatoid arthritis patients. Castillo-Hernandez J. Rev Bras Reumatol Engl Ed. 2017;57(4):320-329.

Table 1



VARIABLE	CASES n=59	CONTROLS n=60	P- VALUE
Age, years; mean(±SD)	56.6 (10.9)	56.4 (10.9)	0.902
Sex, women;n(%)	67(76.3)	67(83.8)	0.189
Tobacco			0.117
Never smoker, n(%)	42(47.2)	49(61.3)	
Former smoker,n(%)	23(24.7)	11(13.8)	
Current smoker,n(%)	25(28.1)	20(25)	
Comorbidities			
BMI > 30 (obesity)n(%)	30(33.7)	22(27.5)	0.608
BMI, mean(±SD)	28.2 (5.0)	27.3 (4.9)	0.266
Dyslipemia, n(%)	21(23.6)	15(18.8)	0.442
Hypertension, n(%)	23(25.8)	22(27.5)	0.808
Insulin Resistance Indexes			
HOMA-IR>2.29, n(%)	25(28.1)	24(30.0)	0.795
HOMA-IR, median(p25-p75)	1.7 (1.02-2.3)	1.66(1.15-2.65)	0.385
HOMA-β, median(p25-p75)	38.9 (22.7-63.3)	34.39 (24.6-54.9)	0.545
QUICKI, median(p25-p75)	0.35(0.33-0.37)	0.35 (0.32-0.37)	0.211

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FRI0057 INSULIN RESISTANCE IN ELDERLY ONSET RHEUMATOID ARTHRITIS AND POLYMYALGIA RHEUMATICA

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Background: Rheumatoid arthritis (RA) patients have a higher insulin resistance (IR) and some studies report that it is present at diagnosis. Systemic inflammation has been pointed out as the reason. However, data on polymyalgia rheumatica (PMR) are controversial.

Objectives: To analyse IR in a group of untreated patients with a recent diagnosis of RA and PMR, and to establish predictive factors related with IR.

Methods: Longitudinal observational study of patients older than 60 years, newly diagnosed with elderly-onset AR (ACR/EULAR 2010) and PMR (ACR/EULAR 2012). Comparison with healthy control group of the same age. Inclusion: consecutive and voluntary. Exclusion: patients with insulin-dependent diabetes. Follow-up time: 12 months. The clinical-epidemiological, anthropometric and analytical characteristics were collected. IR was calculated by HOMA-IR [(homeostatic model assessment of insulin resistance) = glucose (mg/dL) * insulin (mUI/L)/405] baseline and at 12 months. HOMA-IR>2.75 was considered IR (according to Spanish data). The statistical study was performed with Stata 15.1.

Results: We recruited 42 patients with RA, 18 with PMR and 18 healthy controls. None of them had received treatment with corticosteroids or with DMARD at the baseline visit. Baseline characteristics are summarized in the table.

	RA (N=42)	PMR (N=18)	P value
Epidemiological data			
Women n (%)	18 (42.9)	15 (83.3)	**0.001**
Age (mean ± σ)	74.4 ± 7.6	76.4 ± 5.2	0.594
Diabetes mellitus	15 (35.7)	3 (16.7)	0.140
BMI (kg/m^2)	27.7 [25.1-30.5]	26.5 [24.0-29.1]	0.393
Abdominal perimeter (cm)	100 [95-106]	94 [90-104]	0.076
Analytical data			
Glycohemoglobin%	6.1 [5.9-6.4]	5.8 [5.6-6.5]	0.107
ESR (mm/1^{a}hora)	49 [36-75]	52 [42-69]	0.508
CPR (mg/L)	24.4 [7.1-44.1]	22.1 [12.4-45.9]	0.670
RF positive n (%)	14 (33.3)	1 (5.6)	**0.023**
ACPA positive n (%)	13 (30.9)	2 (11.1)	0.104
RF and ACPA positive n (%)	17 (40.5)	3 (16.7)	0.073
Insulin resistance test			
HOMA-IR median[RIQ]	3.6 [2.1-5]	2.1 [1.6-3.4]	**0.004**

At baseline visit, 66.7% of patients with elderly-onset RA had IR, compared with 33.3% of controls (p=0.024) and 27.8% of PMR (p=0.006). Therefore, the prevalence of IR in patients with RA doubled that of controls and patients with PMR before starting treatment.

After 12 months of evolution and treatment, patients with RA and IR decreased from 66.7% to 51.2%, not being statistically significant (p=0.179). On the other hand, the percentage of patients with PMR and IR remained the same (27.8%). The differences in IR between RA and PMR at 12 months remained statistically significant (p=0.048).

Given the results we decided to analyze the predictive factors related with IR only in the 42 patients with RA. In the univariate logistic regression analysis, the predictors of presenting IR were the BMI, the abdominal perimeter and the scapular girdle involvement. Specifically for BMI, for each of 2 kg/m2 the probability of having IR was 1.24 times higher (OR=1.24, IC95%: 1.12-1.37). Patients with scapular girdle involvement had a 6-fold increased risk of developing IR (OR = 6.0, 95% CI: 1.3-26.6). And for every 5 centimetres of abdominal perimeter the risk increased almost 4 times more (OR=3.9, 95% CI: 2.9-5.1). In the multivariate analysis, the only independent factor to increase the IR was the abdominal perimeter (aOR = 1.23, IC95%: 1.07-1.41).

Conclusion: Patients with elderly-onset RA have a higher IR than the general population. High IR in RA is present at diagnosis. IR in AR is not exclusively mediated by systemic inflammation, since patients with PMR do not have this increase. The predictors of presenting IR in late onset AR were BMI, scapular girdle involvement and abdominal perimeter. Only the abdominal perimeter was shown as an independent factor.

Disclosure of Interests: None declared

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FRI0058 RHEUMATOID ARTHRITIS IS AN INDEPENDENT RISK FACTOR FOR DEVELOPING INFLUENZA REQUIRING HOSPITAL INPATIENT ADMISSION, COMPARABLE TO OLDER AGE AND GREATER THAN SMOKING, IN A LARGE, SINGLE-CENTRE COHORT

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Background: RA patients are known to be at increased risk of serious infection(1), particularly for respiratory infections such as influenza which are known to be associated with increased morbidity and mortality(2). Currently RA patients do not have enhanced access to high-dose influenza vaccination in our jurisdiction, despite the reported benefit in RA(3) and enhanced access for patients older than 65 years old. The magnitude of the risk from RA compared to smoking or age greater than 65 years old remains incompletely understood.

Objectives: To examine the association of RA, smoking, and age greater than 65 years old with hospital inpatient admissions for influenza.

Methods: We examined general medical inpatient admissions in a large tertiary hospital between January 2012 and December 2018. Major confounders (smoking status, age and gender) were selected based on causal inference analysis using a directed acyclic graph. Natural language processing and ICD-10 codes were used to determine the diagnosis of rheumatoid arthritis, smoking status and influenza diagnosis. These variables were used in a multivariable logistic regression analysis. The strength of association was assessed using adjusted odds ratios and associated 95% confidence intervals.

Results: We assessed 19,010 patients with at least one general medical inpatient admission during the study period, of which 495 had at least one admission primarily for influenza (Table 1). Within this cohort, there were 3791 patients identified as active smokers and 731 with a history of RA. In the multivariable model, patients with a history of RA were more likely to have at least one admission for influenza (OR 1.65 [1.12 - 2.36]). This risk was comparable to that experienced by patients older than 65 years old in an unadjusted analysis (OR 1.62 [1.29 – 2.04]) and stronger than that experienced by smokers in an unadjusted analysis (OR 1.38 [1.12 - 1.69]).

Conclusion: RA patients are at independent risk of influenza leading to a hospital inpatient admission, with a magnitude comparable to that of patients aged over 65 years old and greater than that of smokers. Funding authorities should consider making influenza vaccination available for RA patients in a comparable way to that available to patients aged over 65 years old.

REFERENCES:

[1] Listing, J., K. Gerhold, and A. Zink, *The risk of infections associated with rheumatoid arthritis, with its comorbidity and treatment*. Rheumatology (Oxford), 2013. 52(1): p. 53-61.

[2] Blumentals, W.A., et al., *Rheumatoid arthritis and the incidence of influenza and influenza-related complications: a retrospective cohort study*. BMC Musculoskelet Disord, 2012. 13: p. 158.

[3] Colmegna I, Useche M, Rodriguez K, Hudson M, Bernatsky S, Nedjar H, Rahme E, Ward B. Efficacy of High-Dose Versus Standard-Dose Influenza

Vaccine in Seropositive Rheumatoid Arthritis Patients [abstract]. Arthritis Rheumatol. 2018; 70 (suppl 10).

Table 1. Characteristics of patients admitted for influenza compared to those admitted for other reasons

Variable	Not admission for influenza (n = 18,515)	Admission for influenza (n = 495)
Age (years)	71.3 ± 17.2	74.1 ± 13.7
% Male	46.3%	46.1%
Smoker	3665 (19.8%)	126 (25.4%)
RA	700 (3.8%)	31 (6.3%)

Disclosure of Interests: None declared
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FRI0059 SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS (SRAGE) AND RISK FOR CARDIOVASCULAR DISEASES IN FEMALES WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is strongly associated with increased frequency of cardiovascular disease (CVD), which remains the major cause of mortality in these patients. Current CVD risk assessment algorithms have limited predictive value for RA patients. Soluble receptor for advanced glycation end products (sRAGE) has recently emerged as a biomarker of inflammation with an inverse correlation with traditional CVD risk factors as age, hypertension and hypercholesterolemia.[1]
Objectives: In a cohort of female RA patients with no previous history of CVD, we assessed whether sRAGE levels were associated with increased risk of CVD during a prospective 5 years follow up.
Methods: Serum sRAGE levels were measured in 171 female RA patients (median age 53; range 21-71) at the inclusion to the study. The CVD risk was estimated using the Framingham algorithm and both traditional and RA associated risk factors for CVD were measured. All the patients were prospectively followed up to 5 years for new CV events, type II diabetes and medication for hypertension and hyperlipidemia. Statistical analysis was performed to compare CVD risk and actual events in the patients with low sRAGE (<1700 pg/ml).
Results: The comparison of patients with low sRAGE (n=125) and normal-high sRAGE (n=46) found no significant differences in frequency of the traditional CVD risk factors including age>60 years (30% vs 41%), overweight (50% vs 41%), smoking (14% vs 11%), incidental hypertension (16% vs 16%) and hypercholesterolemia (56% vs 67%) at baseline and led to similar estimated CVD risk (7.65% vs 8,45%). The RA-related CVD risk factors including disease duration >10years (37% vs 39%), presence of autoantibodies (89% vs 95%), disease activity (DAS28, 46% vs 60%) were also similar in the low-and high sRAGE groups. At 5 years follow up, 11 new CVD events were registered. The events occurred with similar frequency in the low sRAGE and high sRAGE groups (5.6% vs 8.7%). Despite a lack of difference in CVD events, we did observe a significant increase in frequency of new medication for hypertension in the low sRAGE group (21.5% vs. 63%, p=0.01), but not in medication for type II diabetes or statins.
Conclusion: In this study, we found no association between serum levels of sRAGE and the estimated CVD risk or actually occurred CVD events in female RA patients.

REFERENCE:

[1] Santilli, F., et al. (2009). "Soluble forms of RAGE in human diseases: clinical and therapeutical implications." Curr Med Chem 16(8): 940-952.

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FRI0060 NEUROCOGNITIVE PROFILE IN CHILDREN BORN TO MOTHERS WITH CHRONIC ARTHRITIS: WHICH RELATIONSHIP WITH MATERNAL FEELING OF DISEASE?

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Background: Chronic Arthritis could begin in women in childbearing age with several consequent complications in family planning. There are few data on long term outcome of children born from these mothers.
Objectives: Evaluate the neurocognitive profile of children born to mothers with Rheumatoid Arthritis (RA), Psoriasic Arthritis (PsA), Ankylosing Spondylitis (SpA) and studied the psychological outcome of these patients in relationship to their pregnancies.
Methods: We evaluated 16 women (11 RA, 3 PsA, 2 SpA) with diagnosis before pregnancy and school-age children. Information about maternal disease and treatment during pregnancy were collected from medical records. The work was performed by a multidisciplinary team (rheumatologists and pediatric neurologists). The Child Behavior Check List (CBCL 6-18), a home-made questionnaire and others validate questionnaires (STATE-TRAIT ANXIETY INVENTORY - STAI, EDIMBURGH POSTNATAL DEPRESSION SCALE - EPDS, PAYKEL scale of stressful life events) were submitted to all mothers. A neurological physical exam was performed by a pediatric neurologist in all children. Intellectual functioning were assessed by Wechsler scale for corrected age. We also applied standardized batteries to evaluate academic learning. The study was approved by the local ethical committee.
Results: We evaluated 18 children (F/M=1/1, median age 7,4 years, range 6.4-14). All children were born at term and with normal weight. The neurological physical exam and the intelligence level were normal in all children. One child displayed a specific learning disability in reading activities (10% vs 2,5-3,5% of general pediatric population). We found in 6 children (33%) behavior aspects of somatization and anxiety/depression (internalizing problem), in 2 (11%) externalizing problems (oppositional-provocative behavior) and in 5 (28%) an "adult profile". From maternal evaluations we found significant correlations between activity of disease during pregnancy and difficult caregiving and breast-feeding (p=0,005 and p=0,0128 respectively). Finally, a relationship also exists between maternal depression/anxiety and need of psychological support.
Conclusion: This preliminary study on children born to mothers with chronic arthritis showed in children a prevalent pattern of anxiety/depression and an adult, mature profile, expression of insecurity. Therefore, data from CBCL showed that these children were less involved in sports or playful activities than peers and were more involved in school activities. It seemed they would invest more energies in intellectual functioning, as noted in children affected by chronic diseases such as asthma or juvenile idiopathic arthritis. On the maternal side clearly emerged a diffuse state of anxiety, accentuated by having an active disease during pregnancy and puerperium. Postpartum depression was detected in these mothers with higher levels than general population (39% vs 10-15%): it could be desiderable to give these mothers a psychological support during this period. The practical message of our study is also that children born to women with chronic arthritis may need a long-term followup in order to detect and correct any neurological, behavioral or cognitive alteration as early as possible.

REFERENCE:

[1] Bomba M, Galli J, Nacinovich R, et al. Neuropsychiatric aid in children born to patients with rheumatic diseases. Clin Exp Rheumatol. 2010 Sep-Oct;28(5):767-73.

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FRI0061

THE CONTRIBUTION OF TENOSYNOVITIS OF SMALL JOINTS TO THE SYMPTOM MORNING STIFFNESS IN PATIENTS PRESENTING WITH UNDIFFERENTIATED AND RHEUMATOID ARTHRITIS

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Background: Morning stiffness (MS) is characteristic of Rheumatoid Arthritis (RA) that is associated with functional disability. Despite the known parallel in the circadian rhythm of MS and that of several hormones and pro-inflammatory cytokines in the systemic circulation, it is insufficiently known to what extent local inflammatory processes contribute to this symptom. The correlation between MS and the number of swollen joints is relatively weak but may be underestimated by insufficient sensitivity in measuring local inflammation. MRI is more sensitive in detecting local inflammation. Furthermore, MRI-detected tenosynovitis of small joints is increasingly recognized as early feature of RA which is also associated with functional impairments. Recently it was proposed that this may contribute to MS.
Objectives: We assessed the relationship between MS and MRI-detected inflammation and tenosynovitis in particular.
Methods: 286 consecutive patients newly presenting with undifferentiated and rheumatoid arthritis underwent contrast-enhanced 1.5T-MRI of (2-5) MCP-, (1-5)MTP-, and wrist-joints. Scans were scored for tenosynovitis according to Haavardsholm and for synovitis, osteitis conform the RAMRIS-method. MS was dichotomized as>60 minutes. Associations between MS and tenosynovitis/synovitis were tested with logistic regression and the presence of a biologic interaction was assessed categorically (solitary or simultaneous presence of synovitis/tenosynovitis).
Results: MS was present in 40% of patients. Tenosynovitis was more often present in patients with MS than without MS (80% versus 65%), OR 2.11 (95%CI 1.21;3.69). Also synovitis was more often present in patients with MS (58% versus 44%), OR 1.83 (1.12;2.96). In categorized analyses the largest association was found for concurrent synovitis and tenosynovitis OR 2.43 (1.30;4.54); whereas single presence of synovitis was not associated (OR 0.85 (0.21;3.47)). The variance explained in all analyses on morning stiffness was small, ranging 3-6%.
Conclusion: Tenosynovitis, and simultaneous presence of tenosynovitis and synovitis in particular, was associated with MS. However, effect sizes suggested that the contribution of local inflammation to this symptom is rather limited.
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FRI0062

INFECTIONS AMONG RHEUMATOID ARTHRITIS PATIENTS STARTING OR SWITCHING BIOLOGICAL AGENTS. A SYSTEMATIC LITERATURE REVIEW

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Background: The increased rate of infections is one of the most relevant issues regarding biologic therapies in Rheumatoid Arthritis (RA). There is a large number of studies comparing different biologic agents and biologic vs synthetic DMARDs in order to assess their safety profile. Nevertheless, the main question is whether biologics really increase the infection risk by themselves. Up to date, different studies tried to clarify the actual role that these drugs have in this potentially serious adverse effect, searching for other predisposing conditions related to patient clinical characteristics.
Objectives: To compare the risk of infections between patients starting biologic for the first time (naïve) and patients with an inadequate response to a previous biologic agent (switchers)
Methods: A search strategy was performed by the Spanish Society of Rheumatology documentalist over Pubmed, Embase and Cochrane Library databases (from January 2008 to February 2018). All the references retrieved were managed using Endnote X7®. Screening of studies, data collection and data analysis was performed by 2 reviewers. Meta-analysis, systematic reviews of Randomized Controlled Trials (RCT), Clinical Trials or Cohort studies, comparing data from adult RA patients starting biologics and switching biologics, were selected. After the first screening, a critical review was performed using electronic FLC platform for critical appraisal tools (Osteba®) and The Scottish Intercollegiate Guidelines Network (SIGN) was considered to classify the scientific evidence of the selected studies. Studies including patients with chronic infections, tuberculosis reactivations or surgical infections were excluded.
Results: 8 studies were included: 1RCT, 2 Open label study, 1 Open label extension from RCT, 2 subgroups analysis from RCTs and 2 prospective cohort studies.
Overall infection rate was higher in switchers than in naïve patients, with a mean variation between 0-9 and 1.8 100 PY, serious infections were also higher in switchers patients, 2.2 100PY. In both groups, (naïve and switchers), patients treated with more cumulative dose of glucocorticoids (GC) had an increased risk of infections, and it was higher in patients with an inadequate response to previous biologic agents. Mean disease duration was longer in switchers, but this fact was not related to increase of infections.
Conclusion: This systematic review show that overall rate of infections is slightly higher in switchers than in naïve patients, but the fact of having received several biologic agents does not present itself as a risk factor for infection. However, the most important risk factor in the development infections was the higher cumulative doses of GC.
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FRI0063

EFFECTS OF MALALIGNMENT AND DISEASE ACTIVITY ON SECONDARY OSTEOARTHRITIS PROGRESSION IN KNEES OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Recent advancements in treatment of rheumatoid arthritis (RA) with disease-modifying anti-rheumatic drugs (DMARDs) have been remarkable, with disease symptoms nearly disappearing due to their strong anti-inflammatory action and many patients achieving remission. As a result, the need for RA-related surgery has shown a yearly decreasing trend, especially knee surgery and synovectomy procedures [1]. On the other hand, cases of secondary osteoarthritis (OA) in knee joints as a symptom associated with RA following a total knee arthroplasty (TKA) are increasing.
Objectives: We investigated the morphology of osteophytes by quantitatively evaluating their size using images obtained prior to performing a TKA. Additionally, the relationships of osteophyte size with patient background, disease activity, and degree of inflammation were examined.
Methods: Radiographs of 35 consecutive knees in 30 RA patients (26 females, 4 males; mean age 63.0 years; median disease duration 15 years) who underwent TKA, including preoperative standing AP view radiographs of the knee joint, were retrospectively analyzed. Using the Image-J software package, osteophyte size in the medial femur (MF), medial tibia (MT), lateral femur (LF), and lateral tibia (LT) regions was determined. Written informed consent for data collection was obtained from all patients in accordance with the Declaration of Helsinki.
Results: Preoperative Larsen grade was 2, 3, 4, and 5 in 1, 12, 18, and 2 patients, respectively, while the mean range of motion of the knee joint was 118° for flexion and -10° for extension. The mean femorotibial angle (FTA) was 178±13.6°, with varus (FTA >180°, n=14) more frequently observed as compared to valgus (FTA <170°, n=7) cases. Mean osteophyte size in the MF, MT, LF, and LT regions was 37.2, 17.0, 27.2, and 4.57 mm^2, respectively, and significantly greater in the medial compartment (MF+MT) than the lateral compartment (LF+LT) ($p<0.001$). In the varus cases, osteophyte size in the medial compartment was significantly larger as compared to the normal and valgus cases ($p=0.0016$). Furthermore, osteophyte size in the medial compartment was negatively correlated with the inflammatory markers CRP ($r=-0.492$, $p=0.0027$) and ESR ($r=-0.529$, $p=0.0016$), whereas that in the lateral compartment was negatively correlated with disease activity ($r=-0.589$, $p=0.0023$).
Conclusion: Our results suggest that secondary OA is a more prominent symptom in RA patients in whom inflammation is controlled, while disease activity has effects on osteophyte size.

REFERENCE:
[1] Momohara S, Ikari K, Mochizuki T, et al: Declining use of synovectomy surgery for patients with rheumatoid arthritis in Japan. Ann Rheum Dis 2009;68:291-2.

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FRI0064 INCREASE OF RHEUMATOID ARTHRITIS AS A CONTRIBUTORY CAUSE OF DEATH IN THE ELDERLY. A NATIONWIDE STUDY IN ITALY, 2003–2015

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Background: Metanalyses failed to show a decrease of the mortality risk in cohorts of patients with rheumatoid arthritis (RA) between 1950 and 1995. Mortality rates obtained with the analysis of multiple causes of death (MCD) can provide a more complete estimate of the burden of mortality related to RA compared to analysis considering only the underlying cause of death (UCD). Such analyses are available from a limited number of countries, and trends for RA mortality based on MCD were divergent.
Objectives: The objective of the study was to evaluate trends of rheumatoid arthritis (RA) mortality reported as the underlying cause of death (UCD) and as multiple cause of death (MCD) in Italy between 2003 and 2015.
Methods: Analyses were carried out on the Italian National Cause of Death Register, managed by the Italian National Institute of Statistics (ISTAT). Diseases mentioned in the death certificate are coded according to the International Classification of Diseases, 10th Edition (ICD-10, 2009 version). Deaths from January 1, 2003 to December 31, 2015 with mention of RA were included. Time trends of age-standardized rates were analyzed for RA both as UCD and MCD; and the annual percent change (APC) was estimated.
Results: Overall 26,564 deaths with mention of RA were retrieved out of 7,595,214 deaths (0.35% of all certificates). The yearly number of RA-related deaths increased through the study period, meanwhile the probability of selection as the UCD decreased: MCD/UCD ratio was 3.7 in 2003-2006 and 4.8 in 2012-2015 in males; 3.0 and 4.1 in females (Tab.). Mortality rates based on the UCD decreased (males APC -3.1%, CI -3.9, -2.3; females APC -3.3%, CI -4.1, -2.4); while MCD rates for RA-related mortality were stable. Specifically, rates were stable or declined among younger subjects, whereas an increase was registered for the elderly: RA-related deaths in subjects aged ≥80 years raised from 48% in 2003-2006 to 59% in 2012-2015 (Fig.).
Conclusion: RA is increasingly mentioned among diseases contributing to death in Italy. Rheumatoid arthritis declined as underlying cause of death in the last decades. We observed a shift of RA-related mortality towards the elderly, possibly because of the progress in therapeutic strategies allowing increased survival of RA patients.

Table. Rheumatoid arthritis-related number of deaths and mortality rates, based on underlying and multiple causes of death.

	2003-2006	2007-2011	2012-2015
Males			
Average annual number of RA-related deaths	441	502	535
Share of all deaths	0.16%	0.18%	0.18%
UCD, average age-standardized rate (x100,000)	0.54	0.47	0.41
MCD, average age-standardized rate (x100,000)	2.01	2.04	1.95
RA selected as the UCD	26%	23%	22%
Females			
Average annual number of RA-related deaths	1392	1557	1699
Share of all deaths	0.49%	0.52%	0.54%
UCD, average age-standardized rate (x100,000)	1.34	1.20	0.98
MCD, average age-standardized rate (x100,000)	4.00	4.04	3.98
RA selected as the UCD	33%	29%	25%

RA, rheumatoid arthritis; *UCD,* underlying cause of death; *MCD,* multiple causes of death.

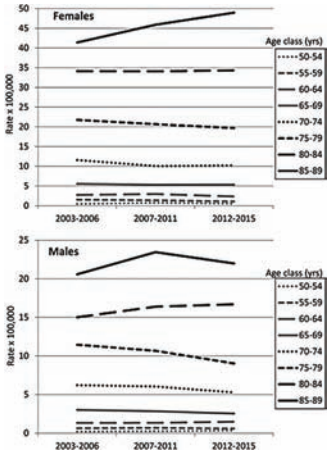


Figure. Multiple causes of death: rheumatoid arthritis-related mortality rates (x100,000) by calendar period and age class.

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FRI0065 PATIENT-REPORTED PALINDROMIC SYMPTOMS IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT

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Background: The frequency and characteristics of patients with Palindromic Rheumatism (PR) (transient acute attacks of articular inflammation) prior to early rheumatoid arthritis (ERA) are unknown.
Objectives: To compare ERA patients who did versus did not report a history of transient episodes of joint inflammation preceding RA diagnosis.
Methods: Study participants were patients with ERA or suspected RA (symptoms <1 year; 83% met 2010 ACR/EULAR criteria) enrolled in the Canadian Early ArThritis CoHort (CATCH) between April 2017 to March 2018 who completed a questionnaire on prior inflammatory joint symptoms that “come and go”. Chi-square and t-tests were used to compare characteristics in patients with versus without a reported history of prior palindromic symptoms. Simple, and multivariable logistic regression with backward selection (p<0.2) were used to determine crude and adjusted predictors of palindromic symptoms.
Results: 154 ERA patients were included; 66% were female and mean (sd) age was 54 (15) years. 54% had previous joint pain and swelling prior to their current episode; 42% endorsed prior episodic joint pain and swelling, approximately half of whom (20% of total, N=31) reported transient joint symptoms for over six months. Patients reporting previous palindromic symptoms were more often female, seropositive, had more comorbidities, and lower swollen joints and baseline CDAI (p<0.05). In multivariable regression, female sex, higher income, seropositivity, back or spine issues, and lower CDAI were associated with history of palindromic symptoms (Table 1).
Conclusion: Half of ERA patients self-reported transient episodes of inflammatory arthritis prior to being diagnosed with RA. They are more likely female, seropositive, with higher income and lower disease activity.
Acknowledgement: The CATCH study was designed and implemented by the investigators and financially supported through unrestricted research grants from: Amgen and Pfizer Canada - Founding sponsors since January 2007; AbbVie Corporation since 2011; Medexus Inc. since 2013; Eli Lilly Canada since 2016 and Merck Canada since 2017. Previously funded by Hoffmann-LaRoche and Janssen Biotech from 2011-2016,UCB Canada and Bristol-Myers Squibb Canada from 2011-2018, and Sanofi Genzyme from 2016-2017.

Table 1: Multivariable Logistic Regression Examining Associations between RA Baseline Characteristics and History of Transient Joint Episodes Prior to RA diagnosis*

Variable	N=133	
	OR	95% CI
Age (years)	0.997	0.966, 1.029
Female	3.303	1.165, 9.366
Household annual income (>$50,000 CAD)	2.539	1.063, 6.063
Rheumatic disease comorbidity index	1.347	0.994, 1.825
Osteoarthritis	3.102	0.996, 9.658
Back/spine symptoms	2.974	1.145, 7.723
Seropositivity (RF or ACPA positive)	3.641	1.343, 9.873
CDAI	0.949	0.912. 0.988

*Non-significant variables: current smoker, MD global assessment. 21 patients excluded from multivariable analysis due to missing data.
MD medical doctor, RF rheumatoid factor, ACPA anti-citrullinated protein antibodies, CDAI Clinical Disease Activity Index

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FRI0066 ASSESSMENT OF LUNG INVOLVEMENT IN RHEUMATOID ARTHRITIS IN A NORTH AFRICAN COUNTRY

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Background: Rheumatoid arthritis (RA) is a common inflammatory disease developing within joints but extra-articular organs such as the lung could be involved.
Objectives: To determine the frequency and the characteristics of lung involvement in RA Tunisian patients.
Methods: A retrospective study including patients with RA fulfilling ACR/EULAR 2010 criteria was conducted in a department of rheumatology in the north of Tunisia between 2014 and 2017. Pulmonary involvement was evaluated based on chest clinical symptoms, combined results from chest-X-ray, computed tomography of the chest and pulmonary functional tests. Patients with pulmonary involvement not directly related to RA were excluded from this study (emphysema, neoplasm, infection…)
Results: Sixty five patients with RA were collected. The mean age was 56 years ± 12.8 years. The mean age of disease onset was 46.4 ± 13.8 years ranging from 17 to 75 years. The mean disease duration was a 9.6 ±10.1 year.A total of 13 patients (20%) were noted to have clinical chest symptoms. It was dyspnea (9 cases (13.8%)), chest pain (2 cases (3%)), dry cough (5 cases (7.7%)) and expectoration (3 cases (4.4%)). Eight patients (12.3%) had crackles in pulmonary auscultation. Mean time to pulmonary involvement onset was 2.5 years [1-4 years]. Chest-X-ray was available in all patients and showed abnormalities in 24 cases (37%). Chest computed tomography was practiced in 24 patients (36.9%). It revealed pulmonary abnormalities in 18 patients (75% of those scanned). Chest computed tomography revealed abnormalities in 3 patients (4.6%) who hadn't respiratory complaints. Pulmonary functional tests was performed in 26 patients (40%) and revealed abnormalities in 3 cases(obstructive signs in 2 cases and association of obstructive and restrictive signs in 1 case).
The overall frequency of lung involvement based on different lung investigations was 27.6% (18 patients). Parenchyma was the most frequent site of pulmonary involvement: interstitial lung disease was found in 7 cases (38.8%); it was a usual interstitial pneumonia in 5 patients (27.7%) and nonspecific interstitial pneumonia in 2 cases (11.1%). Bronchiectasis was found in 5 cases (27.7%), rheumatoid nodule in 4 cases (22.2%) and pleural disease in 2 cases (11.1%).
Conclusion: Lung involvement is frequent in RA Tunisian patients and the interstitial lung disease represented the most encountered pulmonary manifestation.

REFERENCES:
[1] Megan S, Bridget FC, Lawrence AH, Ganesh R. Rheumatoid arthritis-associated lung disease. Eur Respir Rev. 2015;24:1-16.
[2] Kawassaki AM, Pereira DAS, Kay FU, Laurindo IMM, Carvalho CRR, Kairalla RA. Pulmonary involvement in rheumatoid arthritis: evaluation by radiography and spirometry. J Bras Pneumol. 2015;41(4):331-42.

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FRI0067 ANXIETY AND DEPRESSION IN A PREGNANCY AND RHEUMATIC DISEASES CLINIC

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Background: Preconceptional psychologic evaluation allows the identification of risks factors for perinatal disorders. Anxiety (13.4%) and depression (41.5%) has been reported in rheumatic diseases[1]. Hospital Anxiety and Depression Scale (HADS) is used to evaluate anxiety and depression in patients with chronic diseases[2].
Objectives: To describe the frequency of anxiety and depression disorders among preconceptional patients in a Pregnancy and Rheumatic Diseases Clinic.
Methods: An observational, cross-sectional, and descriptive study was conducted in the Rheumatology Consultation of Hospital Universitario "Dr. José Eleuterio González" in Monterrey, Mexico. We included 100 women aged between 18 and 39 years in the preconceptional stage of the Pregnancy and Rheumatic Diseases Clinic. HADS, which is divided in two subscales, one for anxiety and one for depression, indicating a disorder when a score $\geq$11 was applied. To evaluate Rheumatoid Arthritis (RA) a Disease Activity Score (DAS28) was used, for Systemic Lupus Erythematous (SLE) a Systemic Lupus Erythematous Disease Activity index (SLEDAI) was performed, and others (Sjögren's syndrome, dermatomyositis and fibromyalgia) were evaluated with the Global Quality of Life (GQL). To analyze differences among groups, Gamma coefficient was used. It was considered a statistically significant $p<0.05$.
Results: One hundred women in childbearing age were included, with a mean age of 34.48 (SD 18.33) years. RA was diagnosed in 48%, SLE in 37%, and others in 15%. We found a mean HADS total score of 11.73 (7.29), in the anxiety subscale 6.94 (4.027), and depression subscale 4.79 (4.026). A significant correlation between SLE and a high HADS score was observed (Table 1).
Conclusion: In order to have a safe pregnancy, an early intervention to assess the psychiatric status is required in patients with rheumatic diseases.

REFERENCES:
[1] Quintana, J.M., Padierna, A., Esteban, C., Arostegui, I., Bilbao, A., & Ruiz, !. (2003). Evaluation of the psuchometric characteristics of the Spanish versión of the Hospital Anxiety and Depression Scale. *Acta Scandinavica*, 107(3), 216-221.
[2] Zigmond, A. S., & Snaith, R. P. (1983). The hospital Anxiety and depresión scale. Acta psychiatrica scandinavica, 67(6), 361-370.

Table 2. Disease activity: DAS28 score, GQL score and anxiety and depression

	Anxiety			Depression			HADS total score (P)
	Without	With	P	Without	With	P	
	n (%)	n (%)		n (%)	n (%)		
DAS-28 index (N=48)	31 (64.4)	17 (35.4)	0.36	34 (70.8)	14 (29.2)	0.20	0.06
SLEDAI index (N=37)	22 (59.5)	15 (40.5)	0.79	29 (78.4)	2 (21.6)	0.42	0.05
GQL index (N=15)	7 (46.7)	8 (53.3)	0.50	13 (86.7)	2 (13.3)	0.25	0.74

Disease Activity Score 28-joint counts (DAS-28) >5.1 High activity; Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) >8 High activity; Global Quality Index (GQL) >8 high activity. HADS total score ≥11.

Disclosure of Interests: None declared
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FRI0068 SAFETY OF THE ZOSTER RECOMBINANT ADJUVANTED VACCINE IN RHEUMATOID ARTHRITIS PATIENTS: A SINGLE CENTER'S EXPERIENCE WITH 300 PATIENTS

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Background: Patients with rheumatoid arthritis (RA) and other systemic rheumatic diseases (SRD) are at increased risk of developing Herpes Zoster (HZ) due to the diseases/or medications used to treat them such as corticosteroids methotrexate, biologic disease modifying agents, and JAK inhibitors. Released in 2018, the Zoster Recombinant Adjuvanted (ZRA) is a new vaccine with >90% efficacy and can be used in patients taking immunosuppressive therapy as compared to the live Zoster vaccine[1]. There has been a concern about whether the potency of the adjuvant could trigger flares of the underlying SRD, and whether there will be more side effects in this population.
Objectives: Our goal was to study the impact of the new ZRA vaccine in RA and other SRD patients and to measure the risk of flare and incidence of side effects.
Methods: We performed a retrospective chart review from 2/1/2018 to 1/20/2019, on patients with RA and SRD seen at the BWH who had received the ZRA vaccine. Co-variates of interest were collected. A flare was defined as occurring within 12 weeks of the vaccine administration by either: 1) documentation of RA flare in the rheumatologist office notes, telephone encounter or patient portal communication, or 2) new prednisone prescription or an increase in dose of existing prednisone prescription. Vaccine side effects were defined as muscle soreness at the injection site, redness, mild swelling, fatigue, fevers, myalgias, headaches, nausea, and abdominal pain.
Results: 300 patients who received the new ZRA vaccine between 2/1/2018 to 1/20/2019 were identified. Mean follow up was 12.5 weeks ranging from 1-40 weeks following administration. Patient characteristics are identified in **Table 1**.
We identified a 3.00% (n=9) incidence of flare following the first dose and 2.86% (n=4) incidence following the second dose. One patient flared after both the first and second dose. All the flares were mild, self-limited, responded to treatment with low dose glucocorticoids, and did not warrant a change in immunosuppressive therapy. 15.3% (n=46) patients experienced side effects such as soreness at the injection site, fever, stomach ache, and flu like symptoms. Of the patients who experienced side effects, 15.4% (n=40) occurred after the first dose and 8.59% (n=11) occurred following the second dose. Five patients experienced side effects from both. All side effects were regarded as mild and did not necessitate an emergency room visit. No cases of Zoster were reported.

Total N	300
Mean Age	67.5 (±11.1)
Females	232 (77.3%)
Seropositive	111 (53.6%)
Received 2nd Vaccine	140 (46.7%)
Medications	
MTX (mean dose=17.1mg/week)	118 (39.3%)
Prednisone (mean dose=4.69 mg/day)	81(27.0%)
Tofacitinib	44 (14.7%)
TNF inhibitors *	91 (30.3%)
Other biologic therapy **	47 (15.7%)
Other immunosuppressants***	37 (12.3%)
Diagnosis	
RA	207 (69.0%)
Psoriatic Arthritis	21 (7.00%)
Vasculitis	12 (4.00%)
SLE	11 (3.67%)
CTD/MCTD	7 (2.33%)
Other ****	42 (14.0%)

* Adalimumab, Certolizumab pegol, Etanercept, Golimumab, Infliximab
** Abatacept, Tocilizumab, Rituximab, Sarilumab
***Azathioprine, Cyclophosphamide, Mycophenolic acid, Leflunomide
****Other includes: Gout, Scleroderma, Sjogren's, Ankylosing spondylitis, Dermatomyositis

Conclusion: In our experience with 300 patients who received the new ZRA (207 RA and 93 SRD) in 2018-2019, the incidence of disease flares was ≤ 3% and of side effects was 15% which is reassuring. Both flares and side effects were mild, self-limited, and did not require a change in DMARD therapy. No cases of Zoster were reported. Larger formal studies with longer term follow up are required to confirm our findings.

REFERENCE:

[1] Shingrix Recommendations.cdc.gov. https://www.cdc.gov/vaccines/vpd/shingles/hcp/shingrix/recommendations.html

Disclosure of Interests: Emma Stevens: None declared, Michael E. Weinblatt Shareholder of: Stock option: CanFite, Lycera, Scipher, Inmedix, Grant/research support from: Crescendo Bioscience, Bristol Myers Squibb, Sanofi, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, CanFite, Corrona, Crescendo, GlaxoSmithKline, Gilead, Horizon, Lilly, Lycera, Merck, Novartis, Pfizer, Roche, Samsung, Scipher, Set Point, Elena Massarotti : None declared, Frances Griffin: None declared, Sonali Desai : None declared
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FRI0069 FREQUENCY OF EYE INVOLVEMENT IN INFLAMMATORY ARTHRITIS AND CONNECTIVE TISSUE DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Rheumatoid arthritis commonly presents with extraarticular manifestations. Along with other connective tissue diseases, these manifestations may include eye involvement.
Objectives: The purpose of our work was to determine the prevalence and type of eye involvement in rheumatoid arthritis and other connective tissue diseases through a meta-analysis and literature review.
Methods: A systematic review of the literature was performed using Medline, Web of Science, and the Cochrane library from their inceptions until January 7, 2019. Conjunctivitis, keratoconjunctivitis sicca, xeropthalmia, uveitis, eye hemorrhage, optic neuritis, papilledema, orbital disease, retinal artery/vein occlusion, macular edema, retinitis, chorioretinitis, scleritis, iridocyclitits, choroid hemorrhage, blindness and amaurosis fugax were searched for prevalence in patients with rheumatoid arthritis, systemic lupus erythematosus, antiphospholipid syndrome, dermatomyositis, polymyositis, systemic sclerosis, Sjogren's syndrome, undifferentiated connective tissue disease, giant cell arteritis, granulomatosis polyangiitis (GPA; formerly Wegener's granulomatosis, systemic vasculitis, and sarcoidosis.
Results: 3394 studies were identified and 65 included. The prevalence of eye involvement was 18% in rheumatoid arthritis, 31% in systemic lupus erythematosus, 35% in antiphospholipid syndrome, 27% in giant cell arteritis, 26% in GPA and 27% in sarcoidosis. The most common manifestations was dry eyes (keratoconjunctivitis sicca) in most diseases analyzed with a frequency approaching 90% in Sjogren's syndrome. Anterior and posterior uveitis were the most common OC in sarcoidosis occurring in 16 [3-28]% and 6 [3-9]% of patients respectively.
Conclusion: Eye involvement is present in approximately one fifth of rheumatoid arthritis patients, and one quarter to one third of patients with other rheumatic diseases.

REFERENCES:
[1] Grassi W, De Angelis R, Lamanna G, Cervini C. The clinical features of rheumatoid arthritis. Eur J Radiol 1998;27 Suppl 1:S18-24.
[2] Brito-Zerón P, Acar-Denizli N, Zeher M, Rasmussen A, Seror R, Theander E, et al. Influence of geolocation and ethnicity on the phenotypic expression of primary Sjögren's syndrome at diagnosis in 8310 patients: a cross-sectional study from the Big Data Sjögren Project Consortium. Ann Rheum Dis 2017;76:1042-50.
[3] Zhang C, Zha Q-L, He Y-T, Jiang M, Lü C, Lü A-P. The extraarticular symptoms influence ACR response in the treatment of rheumatoid arthritis with biomedicine: a single-blind, randomized, controlled, multicenter trial in 194 patients. J Tradit Chin Med 2011;31:50-5.
[4] Kermani TA, Cuthbertson D, Carette S, Hoffman GS, Khalidi NA, Koening CL, et al. The Birmingham Vasculitis Activity Score as a Measure of Disease Activity in Patients with Giant Cell Arteritis. The Journal of Rheumatology 2016;43:1078-84.
[5] Seror R, Theander E, Brun JG, Ramos-Casals M, Valim V, Dörner T, et al. Validation of EULAR primary Sjögren's syndrome disease activity (ESSDAI) and patient indexes (ESSPRI). Ann Rheum Dis 2015;74:859-66.
[6] Valeyre D, Prasse A, Nunes H, Uzunhan Y, Brillet P-Y, Müller-Quernheim J. Sarcoidosis. Lancet 2014;383:1155-67.

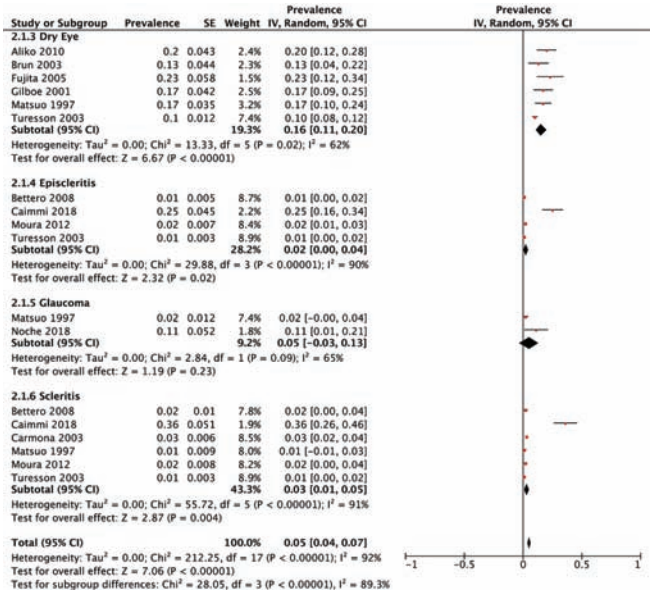


Figure 4. the frequency of different ocular manifestations in RA. A) Dry Eye, B) Episcleritis, C) Glaucoma, D) scleritis

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FRI0070

SHORT-TERM INFLAMMATORY AND LIPIDS CHANGES IN RHEUMATOID ARTHRITIS PATIENTSINFLUENCE CARDIOVASCULAR RISK ALGORITHMS: A MONOCENTRIC RETROSPECTIVE STUDY

vincenzo venerito, Marco Fornaro, Giuseppe Lopalco, Anna Abbruzzese, Sergio Colella, Maria Grazia Anelli, Giovanni Lapadula, Florenzo Iannone, Fabio Cacciapaglia. *Policlinico of Bari, Rheumatology Unit, Department of Emergency and Organ Transplantations, Bari, Italy*

Background: Chronic inflammation may change lipid profile, thus current EULAR recommendations for cardiovascular (CV) management in polyarthritis suggest to assess cholesterol status when disease activity is stable or in remission[1]. To date it is still unclear whether inflammation mediated changes in lipids profile could impact on CV risk algorithms and what score should be considered the reference one for any disease activity status.

Objectives: The aim of this study was to evaluate the influence of lipid profile, disease activity and inflammation modifications on four CV risk calculators during Treat to Target strategy with biologic agents.

Methods: In this monocentric study we retrospectively evaluated all data recorded from Rheumatoid Arthritis (RA) patients with moderate/high CDAI disease activity, who had started for the first time and maintained a bDMARD agent for at least 6 months, in our Outpatient Clinic from the 1st January 2010 to 31st December 2017. Patients with a prior CV event have been excluded from the analysis. For each patient, we assessed the CV risk in a short time period (within 6 months) to estimate the specific weight of lipids and disease activity related variables, using the Italian CV "Progetto Cuore" score[2], the QRISK3-2018 score[3], the Reynolds Risk Score (RRS)[4] and the Expanded Risk Score in RA (ERS-RA)[5]. The results of the "Progetto CUORE" and RRS algorithms were multiplied by 1.5, in accordance to the EULAR recommendations for algorithms that do not include specifically RA among variables. Wilcoxon signed-rank test was used to compare CV risk scores during follow-up.

Results: One-hundred thirteen RA patients (female n. 86 (76.8%), mean age (SD) 52.8 (12.9) years, median disease duration (IQR) 26 (13-72) months) were eligible for the analysis. CDAI and C-reactive protein levels decreased significantly either at 3 and 6 months follow-up (p<0.001). At 3 months, we observed a statistically significant increase in mean total cholesterol (TC) from 197.3±38.2 mg/dl to 205.8±37.3 mg/dl (p<0.01), which returned close to baseline levels at 6 months (201.1±34.5 mg/dl - p=0.22 vs baseline). High density lipoprotein (HDL), TC/HDL ratio and triglycerides changes did not reach the statistically significance. The estimated CV risk assessed by the "Progetto Cuore" and QRisk3-2018 did not change during the 6 months' follow-up. RRS showed a decrease either at 3 and 6 months (p=0.04). Similarly, ESR-RA highlighted a decrease of CV risk either at 3 and 6 months (p<0.01) (see Table I).

Conclusion: All evaluated "Scores" are not influenced by short term lipid changes observed during bDMARDs treatment, being applicable at any status of disease activity. Interestingly, the RRS and ESR-RA scores, evaluating RA inflammatory items, are susceptible to disease activity changes. These results should be taken into account by rheumatologists choosing a CV risk algorithm in daily clinical practice.

	Baseline	3-month follow up	6-month follow up
CRP	7.2 (3-14)	3 (1.6-7.4)**	3.9 (2.4-6.5)**
CDAI	15 (8.1-25)	6 (1-12)**	4 (1-9)**
TC (SD)	197.3 (38.2)	205.8 (37.3)**	201.1 (34.5)
HDL (SD)	60.9 (16.9)	62.9 (15.9)	61.8 (15.5)
TC/HDL ratio (SD)	3.4 (1.1)	3.4 (0.9)	3.4 (0.9)
Triglycerides (SD)	112.3 (78.2)	110.1 (60.9)	108.3 (53.1)
"Progetto Cuore"	2.8 (0.7-7.5)	2.8 (0.7-8.1)	2.6 (0.7-7.8)
QRisk3-2018	7.8 (2.4-14.9)	7.6 (2.3-14.2)	7.4 (2.2-14.4)
ERS-RA	6.3 (3.2-15.2)	6.4 (2.8-13.7)**	5.10 (1.2-13.7)**
RRS	3.0 (1.5-8.25)	3.0 (1.5-7.5)*	3.0 (1.5-7.5)*

Values expressed as median (IQR). SD: standard deviation. CRP: C-reactive protein. CDAI: Clinical Disease Activity Index. TC: Total-cholesterol. HDL: high density lipoprotein. ERS-RA: Expanded Risk Score in Rheumatoid Arthritis. RRS: Reynolds Risk Score.

*p<0.05; **p<0.01 vs baseline

REFERENCES:
[1] Agca R, et al. Ann Rheum Dis 2017;76:17–28.
[2] Palmieri L, et al. Ann Ist Super Sanita. 2004;40(4):393-9.
[3] Hippisley-Cox J, et al. BMJ. 2017 May 23;357:j2099.
[4] Ridker PM, et al. JAMA. 2007;297(6):611–9.
[5] Solomon DH, et al. Arthritis Rheumatol. 2015;67(8):1995–2003.

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FRI0071

ANTI-CITRULLINATED PROTEIN ANTIBODY SPECIFICITIES, RHEUMATOID FACTOR ISOTYPES AND RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS

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Background: The association and role of antibodies to citrullinated proteins (ACPA) on the risk of cardiovascular (CV) co-morbidity in patients with rheumatoid arthritis (RA) is incompletely understood. We have previously reported an association between high levels of CCP2 and risk of acute coronary syndrome (ACS) in RA[1].

Objectives: To further investigate any association between specific ACPA or rheumatoid factor (RF) isotypes, and CV events (ACS, stroke, CV death, and major adverse CV event (MACE)).

Methods: 2533 patients with RA from the Swedish EIRA study were tested for ACPA specificities on a custom-made microarray chip. All antibodies (Ab) detected with a prevalence >= 10% were included in the analysis. "Ab load" was defined as the number of specificities expressed in an individual, and categorized into four groups. ACPA was also measured by a commercial anti-CCP2 assay and anti-CCP2 levels divided into <25, 25- < 75, 75 - < 1500 and >1500 arbitrary units/mL, where <25 defines negativity. IgA, IgG and IgM RF positivity was assessed using EliA immunoassay. For each RF isotype, cutoff level was determined as above the 98th percentile among controls.

The data was linked to the National Patient Register and the Cause of Death register, and events of ACS (ICD10=I20.0, I21, or cause of death listed as "I21"), stroke (ICD10=I60-I64), CV death (cause of death listed as "I"), or MACE (any of the above) identified.

We used Cox proportional hazard model, adjusted for sex, age and calendar period of RA diagnosis, to assess associations between ACPA/RF status and each CV outcome.

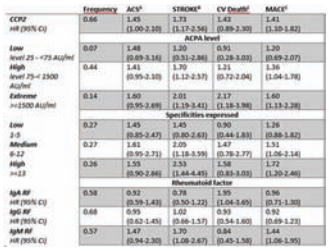
Results: Median age at diagnosis was 52 years, and median follow-up was 12 years. The incidences per 1000 person-years were 4.3 for ACS, 4.0 for stroke, 2.4 for CV deaths, and 9.4 for MACE.

66% were anti-CCP2 positive. This was associated with ACS, stroke and MACE. There was a trend with increasing CV risk with increasing anti-CCP2 levels (Table).

For RF, the pattern was markedly different across isotypes; IgM RF associated with ACS, stroke and MACE whereas IgA RF associated to CV death (Table).

18 different ACPA specificities (Fil 307-324 (CPP-1), Vim 60-75, Vim 2-17, Fib β36-52, Fib alpha 580-600, Eno 5-21 (CEP-1), Fib α621-635, Fib α36-50, Fib β60-74, Ptm13, Ptm36, Pept Z1, Pept Z2, Pept 1, Pept 5, Bla26) had a frequency >10% and included in the analyses. Median Ab load was 6 (IQR:2). There was a significant p-value for trend between Ab load and CV risk for stroke and MACE. Fib β36-52 was the only Ab associated with all 4 outcomes, and, together with CPP3 and ptm13, the only ACPAs associated to ACS. No association to ACS remained when all Abs were jointly included in the model. For stroke, 13 of the 18 Abs associated with risk, but only Fib β60-74 remained (HR 1.91 (95% CI 1.07-3.42)) in the full model. For CV death and MACE, 14 Abs were associated, but no associations remained in the full model.

Conclusion: In patients with RA, RF and ACPA are linked to CV risk. For RF, CV risks differ with isotype. For ACPAs, very high levels, and the number of individual ACPAs, are linked to CV risk, suggesting that Ab load may be more important than individual ACPAs.



	Frequency	ACS[1]	STROKE[1]	CV Death[1]	MACE[1]
CCP2 HR (95% CI)	0.66	1.45 (1.00-2.10)	1.73 (1.17-2.56)	1.43 (0.89-2.30)	1.41 (1.10-1.82)
			ACPA level		
Low level 25 - <75 AU/ml	0.07	1.48 (0.69-3.16)	1.20 (0.51-2.86)	0.91 (0.28-3.03)	1.20 (0.69-2.07)
High level 75-< 1500 AU/ml	0.44	1.41 (0.95-2.10)	1.70 (1.12-2.57)	1.21 (0.72-2.04)	1.36 (1.04-1.78)
Extreme >=1500 AU/ml	0.14	1.60 (0.95-2.69)	2.01 (1.19-3.41)	2.17 (1.18-3.98)	1.60 (1.13-2.28)
			Specificities expressed		
Low 1-3	0.27	1.45 (0.85-2.47)	1.45 (0.80-2.63)	0.90 (0.44-1.83)	1.26 (0.88-1.82)
Medium 4-12	0.27	1.61 (0.95-2.71)	2.05 (1.18-3.59)	1.47 (0.78-2.77)	1.51 (1.06-2.14)
High >=13	0.26	1.55 (0.90-2.66)	2.51 (1.44-4.45)	1.58 (0.83-3.03)	1.72 (1.20-2.46)
			Rheumatoid factor		
IgA RF HR (95% CI)	0.58	0.92 (0.59-1.43)	0.78 (0.50-1.22)	1.95 (1.04-3.69)	0.96 (0.71-1.30)
IgG RF HR (95% CI)	0.68	0.95 (0.62-1.45)	1.02 (0.66-1.57)	0.93 (0.54-1.60)	0.92 (0.69-1.23)
IgM RF HR (95% CI)	0.57	1.47 (0.94-2.30)	1.70 (1.08-2.67)	0.84 (0.45-1.58)	1.44 (1.06-1.95)

REFERENCE:

[1] Mantel A, et al, 2015. PMID 26138387

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FRI0072

PREDICTING SARCOPENIA AND OBESITY BY MEASURING THIGH MUSCLE AND FAT THICKNESS BY ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS: FROM THE CHIKARA STUDY

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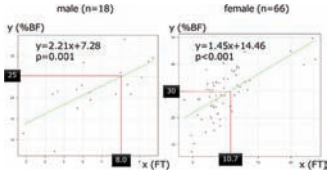
Background: Rheumatoid arthritis (RA) patients often have sarcopenia. The thickness of the quadriceps muscle, easily measurable by ultrasound (US), is known to be related to skeletal muscle mass, and its decreased thickness may suggest sarcopenia.

Objectives: To investigate the utility of US for predicting sarcopenia by examining the anterior thigh in RA patients.

Methods: Ninety-four patients (66 female) enrolled in the prospective CHIKARA study (UMIN000023744) underwent US muscle (MT) and fat thickness (FT) examinations of the anterior thigh. Muscle and body fat mass were also examined by a body composition analyzer (MC-780A; TANITA, Tokyo, Japan). Whether MT and FT can predict sarcopenia and obesity was also examined. Sarcopenia was diagnosed based on the Asian Working Group on Sarcopenia definition, and obesity was diagnosed by% body fat (%BF).

Results: MT was significantly lower in RA patients with sarcopenia than in those without (24.8 ± 3.5 mm vs. 29.6 ± 3.8 mm, p=0.01). MT was related to sarcopenia (males r=0.56, p=0.02; females r=0.32, p=0.01). The MT cut-off value for sarcopenia was 24.7 mm in males and 19.7 mm in females on receiver operating curve (ROC) analysis. FT was correlated with%BF (males r=0.66, p<0.01; females r=0.62, p<0.001).%BF was estimated by 2.21FT+7.28 in males and 1.45FT+14.46 in females by a simple linear regression model. This means that FT>8.0 mm in males and FT>10.7 mm in females indicate obesity (Table 1). When assessing the accuracy of these cut-off values, the kappa values were 0.541 and 0.469, respectively

Table 1. Relationship between%BF and FT. FT>8.0 in males and FT>10.7 in females indicate obesity.



FT: the fat thickness (FT) at anterior thigh measured by ultrasound,%BF:% body fat measured by body composition analyzer.

Conclusion: Sarcopenia and obesity can be predicted by US examination of the anterior thigh in RA patients.

REFERENCE:

[1] Kawai H., Kera T., Obuchi S., et al. Morphological and qualitative characteristics of the quadriceps muscle of community-dwelling older adults based on ultrasound imaging: classification using latent class analysis. Aging Clin Exp Res. 2018; 30:283–29.

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FRI0073 **SWELLING OR TENDERNESS, WHICH ONE CORRESPONDS BETTER WITH ULTRASOUND-DETECTED SYNOVITIS?**

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Background: Ultrasound (US) is a sensitive method for detecting joint inflammation in patients with rheumatoid arthritis (RA). The relationship between tender or swollen joints and ultrasound-detected synovitis has not been well explored in patients with RA.
Objectives: The purpose of the present study was to compare the correlation between ultrasound-detected synovitis and joint tenderness or swelling at the wrists and hands in RA patients.
Methods: Twenty-two joints, including bilateral wrists, proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints, were respectively evaluated by physical examination (PE) and ultrasound scan in 258 RA patients. All patients had at least 1 tender or swollen joint out of 22 joints. Synovitis was detected by using semi-quantitative scoring systems (0-3) for grey scale(GS) and power Doppler(PD). Positive synovitis was defined as GS$\geq$2 and/or PD$\geq$1. All correlations among US variables and clinical variables were assessed using Spearman's rank correlation test. Cohen's kappa (κ) between clinical and sonographic findings was calculated.
Results: Their median age was 51.2 years, median disease duration was 57 months, with 83.33% females. The mean (SD) Disease Activity Score based on 28 joints (DAS28)-ESR and DS28-CRP were 4.47±1.62 and 3.99±1.51, respectively. In a total of 5676 joints assessed, 968 swollen joints (17.05%) and 1296 tender joints (22.83%) were found, while on ultrasonography GS synovial hyperplasia was present in 801 (14.11%) joints, positive PD in 476 (8.38%) joints. There were more tender joints without swelling (n=574) than those swollen joints without tenderness (n=246). In all joints, higher κ coefficient was observed in joint swelling (κ=0.367, p<0.01) with ultrasound-detected synovitis compared with tenderness (κ=0.281, p<0.01).Similarly, swollen joint counts of 22 joints showed higher Spearman's correlation coefficient with either total GS scores (r=0.499, p<0.01) or total PD scores of 22 joints (r=0.430, p<0.01) than tender joint counts of 22 joints (r=0.354/0.308, p<0.01). GS and PD synovitis were more frequently detected in swollen joints without tenderness compared with tender joints without swelling. This discrepancy tend to be more significant in MCP2, MCP3, and MCP4 joints (p<0.05).
Conclusion: In RA patients with at least 1 tender or swollen joint of wrists and hands, a higher frequency of joint tenderness was observed than swelling. However, swelling had better agreement with ultrasound detected synovitis compared with tenderness. Joint swelling is more associated with ultrasound-detected synovitis than tenderness. Without swelling, joint tenderness tends to be less associated with ultrasound-detected synovitis.

REFERENCE:

[1] Tan YK, Moorakonda RB, Allen JC Jr, Chew LC, Thumboo J. Back to the basics: Understanding joint swelling and tenderness at the wrist in rheumatoid arthritis through the use of ultrasonography. Int J Rheum Dis. 2018 Oct 21.

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Rheumatoid arthritis – biological DMARDs

FRI0074 **UPDATE FOR THE CLINICAL PRACTICE: INTEGRATED, EVIDENCE-BASED APPROACH FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS**

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Background: The management of rheumatoid arthritis has evolved in the last few years with greater emphasis on a treat-to-target strategy rather than specific drug regimens.Technologies such as ultrasound have been increasingly used for diagnosis and monitoring of synovitis where it is unclear from clinical examination.These aspects of management were investigated by the Guideline Committee, and recommendations have been updated using new evidence [1, 2].
Objectives: To develop an updated evidence-based, interdisciplinary recommendations for the management of rheumatoid arthritis (RA).
Methods: The task force comprised rheumatologists, epidemiologists, health economists, and patients. A systematic literature analysis was conducted using the Cochrane Database of Systematic Reviews and MEDLINE. Data regarding the drugs prices and product information were collected to evaluate drug cost and safety. Evidence and recommendations were graded, and an algorithm for treatment and final statements were discussed in a consensus meeting (Nominal Group Technique). Recommendations were developed using a Delphi method by a multidisciplinary panel including patients.
Results: Consensus was reached on recommendations, including a standardized treatment strategy according to the RA severity, activity and prognostic factors in the individual patient. In this updated interdisciplinary guideline for RA the treat to target strategy was considered the cornerstone in these recommendations (figure 1). RA patients should reach clinical, ultrasonographic and functional remission. Treatment decisions should incorporate the disease activity status, structural damage progression (radiologic/sonographic), comorbidities, quality of life and patient motivation. Physiatrist, psychologist and ocupational therapist should be included in interdiscibilnary treatment team for RA.
Conclusion: The treatment strategy included a total of twenty-one evidence based interdisciplinary recommendations for management of RA (figure 1), and is accompanied by a more in-depth discussion of key management principles. These recommendations provide a step-wise approach to treatment, to enable practitioners to develop and support the most effective method of achieving and maintaining remission in RA patients. These recommendations are not to remove the physician's autonomy, and physicians must select the most appropriate therapeutic option, taking into consideration the patient's preferences.

1. Treat-to-target strategies of RA aiming to reach sustained clinical remission (as defined by the American College of Rheumatology-(ACR)-EULAR Boolean or index criteria) or low disease activity.
2. Implement communication, shared decision, self-management and education are very critical in treatment strategy.
3. Regular close monitoring of RA patients every 1-3 months then every 3-6 months after achieving treatment target to (assess disease activity and damage, functional ability, comorbidities and complications) is very important.
4. Ultrasonography has an important role in RA diagnosis, monitoring activity, damage and response to treatment.
5. Start the first line of treatment strategy with monotherapy using methotrexate. Shared decision making is advisable to agree which methotrexate administration form is preferable (oral Vs Subcutaneous Vs Intramuscular).
6. In patients with a contraindication to MTX or show intolerance to it, start leflunomide or sulfasalazine as first line of treatment strategy
7. When the treatment target (remission or low disease activity) has not been achieved despite dose escalation by 3 months; adding another cDMARD or use combination cDMARD therapy
8. Short-term glucocorticoids should be considered when initiating or changing csDMARDs
9. Consider oral NSAIDs when control of pain or stiffness is inadequate, offer the lowest effective dose for the shortest possible time considering the comorbidities.
10. If the treatment target not achieved after 6 months of cDMARD combination therapy; addition of a bDMARD should be considered with or without MTX.
11. The cutoff point of starting biologic therapy is High Disease Activity: DAS-28 > 5.1, or if DAS-28 > 4.2 and associated with 3 or more poor prognostic factors.
12. First line biologic therapy: Use TNF-inhibitors or IL-6 inhibitor. TNF-inhibitors had been given a slight preference over other biologics due to availability of long-term registry data worldwide.
13. Significant improvement using bDMARDAs should be achieved by 3 months and the target should be achieved by 6 months.
14. An alternative TNF α inhibitor may be considered for patients in whom treatment is withdrawn due to an adverse event.
15. If the patient has a primary failure to TNF α inhibitor, prescription of an alternative TNF α inhibitor is not advised. Switch out of therapeutic class considering a drug with other working mechanism
16. In case of secondary failure to anti-TNF agent; adding a csDMARD or alternatively switch to another anti-TNF or switch to bDMARD with other therapeutic class of bDMARD.
17. A bio-similar (bsDMARD) of any of the reference boDMARDs should not be used if the respective boDMARD (or another bsDMARD of the same molecule) has failed to induce sufficient efficacy or vice versa
18. If target not achieved after 6 months; treatment, change to a non-TNFi bDMARD (IL-6 inhibitors, rituximab or abatacept) with/without cDMARD.
19. If improvement still not achieved; try another bDMARD or use Targeted synthetic DMARDs tsDMARDs as JAK inhibitors (tofacitinib, baricitinib) or another non-TNFi bDMARD as third line bDMARDs till reach remission.
20. Non-pharmacological management (physiotherapy, occupational therapy, psychotherapy and nutritional therapy are important to improve functional, psychological and health status of RA patient.
21. Referral of RA patient for surgical opinion has certain time and indications for getting maximum benefits.

Figure 1: treat to target interdisciplinary guidelines for management of RA

REFERENCES:

[1] Qiang Guo, et al. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. Bone Res 2018; 6: 15-21.

[2] Smolen JS, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017; 76(6):960-977.

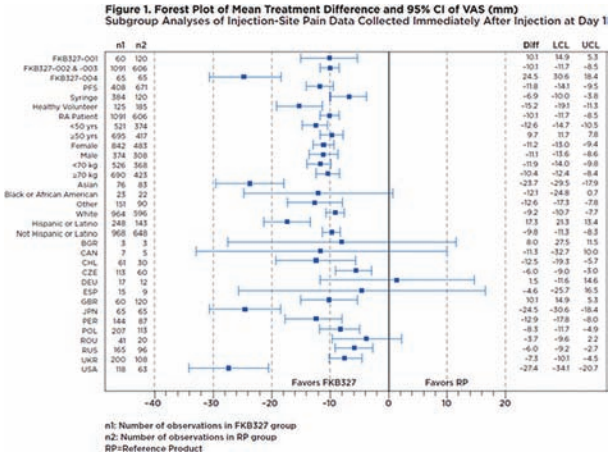
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FRI0075

SYSTEMATIC ANALYSIS OF INJECTION-SITE PAIN CAUSED BY SUBCUTANEOUS ADMINISTRATION OF THE ADALIMUMAB BIOSIMILAR FKB327 VERSUS ADMINISTRATION OF THE ADALIMUMAB REFERENCE PRODUCT VIA DIFFERENT DELIVERY METHODS

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Background: FKB327 is a proposed biosimilar of the adalimumab reference product (RP). Several studies in both healthy volunteers and patients with active rheumatoid arthritis (RA) were undertaken, the results of which have been reported elsewhere. The formulation excipients of the biosimilar product differ from those of the RP, and different injection-site pain intensity with subcutaneous injection has been reported.
Objectives: The current meta-analysis examines pooled data from these studies in relation to the amount of injection-site pain resulting from using a prefilled syringe (PFS) versus an auto-injector (AI) versus a regular syringe (RS), and the proposed biosimilar, FKB327, versus the RP.
Methods: Data from 4 studies, FKB327-001, -002, -003, and -004, were pooled in an effort to compare injection-site pain upon subcutaneous administration of FKB327 versus the RP (citrate-containing formulation of the RP [40 mg/0.8 mL]). Study FKB327-001, in healthy volunteers (n = 180), involved a single subcutaneous dose of either FKB327 or the RP. Study FKB327-004 was a similar study in healthy Japanese volunteers (n = 130). Study FKB327-002 was a randomized (FKB327 with RS or the RP), double-blind, multiple-dose study in patients with active RA. This was followed by Study FKB327-003, in which patients were rerandomized to receive either FKB327 with PFS or the RP in the randomization phase, followed by an open-label extension phase of the study, in which AI was introduced. As patients continued receiving treatment or switched treatments during the course of the FKB327-002 and -003 studies, injection-site pain was assessed at the first dosing occasion of FKB327 or the RP (n = 691). Data from all 4 studies were examined by meta-analysis of the visual analog scale (VAS) using a 100-mm horizontal scale for FKB327 versus the RP and for comparison of AI, PFS, and RS.
Results: Data were analyzed from a total of 2007 assessments in 1001 subjects. A linear mixed model of the VAS in mm for the RP versus FKB327 across all 4 studies showed a 12.6-point lower pain score for FKB327 versus the RP (95% confidence interval [CI], –14.3 to –10.8; *P* <.001). For the AI and PFS used for FKB327 administration, AI showed a 1.7-point lower pain score in the VAS compared with PFS (95% CI, –3.3 to –0.1; *P* = .035). Gender, age, body weight, and population (healthy subject or patient) were not identified for differences in injection-site pain intensity.
Conclusion: FKB327 showed a significant advantage in terms of injection-site pain intensity compared with the RP, as well as lack of inferiority for both AI and PFS versus RS.
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FRI0076

THE RISK OF TUBERCULOSIS IN PATIENTS WITH IMMUNE-MEDIATED RHEUMATIC DISORDERS RECEIVING BIOLOGICAL THERAPY: A 15-YEAR EXPERIENCE IN A ROMANIAN COHORT

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Background: The risk of tuberculosis (TB), either reactivation of latent TB or *de novo* infection, remains a point of interest in patients with immune-mediated rheumatic pathology on biological therapy, particularly TNFα inhibitors.
Objectives: We aimed to evaluate the risk and to identify predictors for TB in biologics users among patients with rheumatoid arthritis (RA),

psoriatic arthritis (PsA) and ankylosing spondylitis (AS) in North East Romania from 2003 to 2018.

Methods: We performed a hospital-based retrospective cohort study in consecutive adult patients receiving their first biologic agent (TNF or non-TNF drugs) according to local recommendations in two academic centers. Patients were classified based on the initial TB/latent TB screening test: the tuberculin skin test (positive if > 5mm, TST group) or interferon gamma release assays (positive if >0.35 IU/mL QuantiFERON-TB gold, QFT group); retesting was done regularly if negative initial.

Data about drug efficacy was recorded every 24-weeks based on standard scores (DAS28-ESR for RA, DAPSA for PsA, ASDAS-CRP for AS), while TB risks at the end of the study or prior to switching were determined as hazard ratio (HR) with 95% confidence interval (CI) using cox regression.

Statistical analysis was performed in SPSS-19, $p<0.05$, on subgroups of patients depending on whether positive TST or QFT at baseline.

Results: 673 patients (360 RA, 116 PsA, 195 AS) were recruited; 55 of them (33 RA, 13 AS, 9 PsA) had latent TB at baseline and received chemoprophylaxis with isoniazid before starting biologics according to local policy. Fourteen active TB were identified, the majority of them occurred within one year of biologics (ranging 6 to 52 months), as follows: three pulmonary TB in AS (two in etanercept, one adalimumab), one case of pulmonary TB in PsA (infliximab) and ten cases of RA (six pulmonary TB in abatacept, two adalimumab, etanercept and two infliximab; one ganglionar infection with infliximab; one peritoneal under certolizumab; one pulmonary and pleural under infliximab biosimilar; one pulmonary and peritoneal TB under adalimumab). The rate of active TB was 5/321.32 patient-years for infliximab, 4/594.64 for adalimumab, 1/38.39 patient-years for certolizumab, 3/721.51 for etanercept and 1/21.12 patient-years for abatacept, respectively. We reported an increased risk of TB disease in anti-TNF monoclonal antibodies users vs. soluble receptor, with an incidence ratio of 2.66 ($p<0.05$). Interestingly, no significant TB risk factors were demonstrated in our cohort; baseline latent TB, previous active TB, chronic glucocorticoid use, high disease activity at baseline, comorbidities, concurrent synthetic drugs were not associated with increased risk ($p>0.05$). In addition, we described 18 new patients with positive QFT when TB retesting as per protocol, classified as latent TB and requiring chemoprophylaxis.

Conclusion: The risk of tuberculosis remains a reality in biologics, despite extensive screening and prevention methods. The risk is variable with different drugs, higher with TNF inhibitors and relatively low in newer biologics, emphasizing a risk-stratification when selecting biologics in such patients.

Disclosure of Interests: CODRINA ANCUTA Speakers bureau: Abbvie, Pfizer, Novartis, MSD, Roche, Biogen, UCB, Lilly, Cristina Pomirleanu Speakers bureau: Abbvie, Pfizer, UCB, Georgiana Strugariu Speakers bureau: Abbvie, Pfizer, UCB, Luiza Petrariu Speakers bureau: Abbvie, Pfizer, Novartis, Raluca Paiu: None declared, Eugen Ancuta: None declared, Codruta Bran Speakers bureau: Abbvie, Pfizer, Novartis, Lilly, Roche, Rodica Chirieac: None declared

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FRI0077 SHORT DURATION OF CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (CSDMARDS) BEFORE AND AFTER BECOMING A CSDMARD INADEQUATE RESPONDER IN RHEUMATOID ARTHRITIS PATIENTS

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Background: ACR guidelines recommend starting rheumatoid arthritis (RA) treatment with conventional-synthetic (cs)DMARD monotherapy[1]. If disease activity remains moderate or high, the guidelines recommend adding or switching to another csDMARD, biologic (b)DMARD, or janus kinase inhibitors (JAKi) for established RA. In early (<6 months) RA, the guidelines recommend tumor necrosis factor inhibitors TNFi over JAKi and TNFi+methotrexate (MTX) over JAKi+MTX.

Objectives: This study aimed to investigate treatment patterns and duration in csDMARD IR patients.

Methods: In fully-adjudicated commercial medical and pharmacy health insurance claims database with 40 million lives annually, adult RA patients (≥2 RA diagnoses ≥30 days apart) who started csDMARD (1/1/2012—3/31/2017) and then switched to or added another DMARD (index date, ID) were selected. Real world treatment patterns of patients with ≥1-year continuous enrollment before (baseline) and after ID (index treatment) were assessed.

Results: Among 25,104 csDMARD initiators, 10,091 (40%) demonstrated IR, and 7,816 met all the inclusion and exclusion criteria (median age 54 years, 26% male). The baseline csDMARD treatment lasted for a median of 4.3 months and mostly comprised of monotherapy (96%). Upon treatment regimen change, 62% (n=4,869) initiated combination therapy (32% csDMARD+csDMARD, 28% csDMARD+TNFi, 1.4% csDMARD+other bDMARD, 0.5% csDMARD+JAKi) and 38% initiated monotherapy (27% on csDMARD, 10% TNFi, 0.7% other bDMARD, 0.5% JAKi). Post-switch, the median treatment duration was longer for combination therapy than monotherapy: 13.7 vs. 5.2 months ($p<0.001$). Among next therapies, csDMARD showed the trend towards shortest durability and JAKi – toward longest durability. Among monotherapies the median treatment duration varied: 4.9 (csDMARD), 5.9 (TNFi), and 8.1 (JAKi) months ($p=0.2$, comparing all). The median duration of combination therapies lasted: 12.5 (csDMARD +csDMARD), 14.9 (TNFi+csDMARD), and 17.2 (JAKi+csDMARD) months ($p= 0.04$, comparing all).

Characteristics	csDMARD IRs (n=7,816)	
Index therapy allocation after csDMARD IR, (n,%)	**N**	**%**
cDMARD Monotherapy	2,095	27
TNFi Monotherapy	757	10
Other bDMARD Monotherapy	55	0.7
JAKi Monotherapy	40	0.5
cDMARD + cDMARD Combination	2,539	32
TNFi + cDMARD Combination	2,178	28
Other bDMARD + cDMARD Combination	112	1.4
JAKi + cDMARD Combination	40	0.5
Index treatment duration after csDMARD IR, months, median (IQR)	**Months**	**(IQR)**
Monotherapy	5.2	9.8
csDMARD	4.9	10.1
TNFi	5.9	10.1
JAKi	8.1	11.9
Combination therapy	13.7	15.6
csDMARD+csDMARD	12.5	14.8
TNFi+csDMARD	14.9	15.9
JAKi+csDMARD	17.2	11.3

Conclusion: The real-world evidence suggests that treatment durability may be better for JAKi than TNFi (both monotherapy and combination). The majority of csDMARD patients switched to another csDMARD, which showed short durability of treatment, suggesting that switching MOA may benefit these patients.

REFERENCE:

[1] Singh JA, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2016 Jan;68(1):1-26

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FRI0078 IMPACT OF THE IMPLEMENTATION OF FLUSH SERUM ON TROUGH LEVELS OF INFLIXIMAB IN PATIENTS WITH INFLAMMATORY JOINT DISEASE

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Background: The administration of intravenous biological therapies is based on the manufacturer's instructions and the administration guidelines of Spanish Medicine Agency. We observed that a considerable amount of the solution remains in the tubing of the equipment after the administration of the drug. This amount depends on the drug and the solution used for the infusion. In the particular case of Infliximab is around 7% of the total solution to infuse, so it could potentially have a relevant therapeutic impact.

Objectives: To assess the variation in serum trough levels of Infliximab after the systematic application of flush physiological serum after drug administration.
Methods: The study was divided into two phases: a first phase in which the clinical and analytical variables (including the serum trough levels of infliximab) were measured before the application of the flush serum and a second stage in which the same variables were measured after the systematic implementation of an infusion of 50ml of 0.9% sodium chloride following the administration of infliximab.
Results: A total of 35 patients were collected, including 6 rheumatoid arthritis (13.3%), 9 psoriatic arthritis (20%) and 20 ankylosing spondylitis (AS) (44.4%). Overall, 18 patients were women (40%), the mean age was 57.6 years (12.6) and the BMI was 30.5 (13.1). The mean dose of infliximab was 4.3 mg/kg (1.1) and the mean number of years of treatment was 10 (5).
23 patients were taking infliximab on monotherapy (51.1%). The mean serum trough levels of infliximab pre-intervention with the dragging serum was 3.13 mg/dl (3.1), while postintervention levels were 3.66 mg/dl (3.9) ($p = 0.071$). In the subgroup of patients with AS there was a significant decrease in BASDAI between the pre and post intervention visit (3.4 vs 2.6, $p < 0.05$).
Conclusion: The use of flush serum after infliximab infusion increased serum drug levels. In the subgroup of patients with AS there was a clinically significant improvement measured by BASDAI.

REFERENCES:

[1] Ficha técnica de Inflectra®. Disponible en: https://cima.aemps.es/cima/pdfs/es/ft/98067002/FT_98067002.pdf
[2] Ficha técnica de Remicade®. Disponible en: https://cima.aemps.es/cima/dochtml/ft/99116001/FT_99116001.html
[3] Grupo de Trabajo de Enfermeria de la Sociedad Española de Reumatología (GTESER). Manual de terapias parenterales y procedimientos en el paciente reumatológico 2018. Madrid, 2018.
[4] Herrero Massari F, Lozano Serrano V, Rodruiguez Arteaga E. Guía de Manejo de Fármacos Biológicos para Enfermería en los Hospitales de Día. 2010
[5] Moots RJ1, Xavier RM2, Mok CC3, Rahman MU4, Tsai WC5, Al-Maini MH6, Pavelka K7, Mahgoub E4, Kotak S4, Korth-Bradley J4, Pedersen R4, Mele L4, Shen Q4, Vlahos B4. The impact of anti-drug antibodies on drug concentrations and clinical outcomes in rheumatoid arthritis patients treated with adalimumab, etanercept, or infliximab: Results from a multinational, real-world clinical practice, non-interventional study. PLoS One. 2017 Apr 27;12(4):e0175207. doi: 10.1371/journal.pone.0175207. eCollection 2017.
[6] Pascual-Salcedo D1, Plasencia C, Ramiro S, Nuño L, Bonilla G, Nagore D, Ruiz Del Agua A, Martínez A, Aarden L, Martín-Mola E, Balsa A. Influence of immunogenicity on the efficacy of long-term treatment with infliximab in rheumatoid arthritis. Rheumatology (Oxford). 2011 Aug;50(8):1445-52. doi: 10.1093/rheumatology/ker124. Epub 2011 Mar 22.
[7] Sociedad Española de Reumatología. Inforeuma. *Tratamientos: Infliximab*. 2017. Disponible en: https://inforeuma.com/wp-content/uploads/2017/03/95_Infliximab_TRATAMIENTOS-A4-v03.pdf
[8] Van Schouwenburg PA1, Rispens T, Wolbink GJ. Immunogenicity of anti-TNF biologic therapies for rheumatoid arthritis. Nat Rev Rheumatol. 2013 Mar;9(3):164-72. doi: 10.1038/nrrheum.2013.4. Epub 2013 Feb 12.

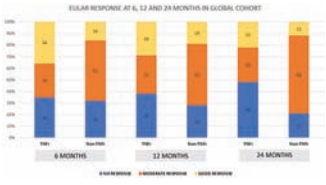
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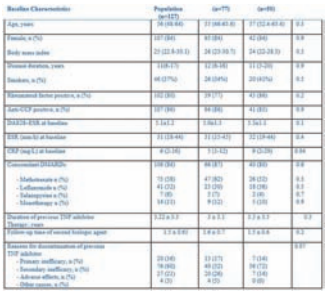
FRI0079

LONG-TERM CLINICAL EFFICACY OF CYCLING VS SWITCHING TO A NON-TNF INHIBITOR IN RA PATIENTS WHO FAILED TO A FIRST TNF INHIBITOR

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Background: In rheumatoid arthritis (RA) patients (pts) after discontinuation of tumour necrosis factor α inhibitors (TNFi) physicians can choose an alternative TNFi or a biological agent with another mode of action (non-TNFi), however little guidance on choosing one or another exists.
Objectives: To compare the long-term clinical response, survival and safety of TNFi versus non-TNFi after discontinuing a previous TNFi in pts with RA, both in the global cohort and in the subpopulations stratified by reason of discontinuation of 1st TNFi.
Methods: Observational study including 127 pts from La Paz University Hospital biological RA registry, who discontinued a first TNFi between 1999 and 2016 and subsequently were treated with a second biologic. Disease activity was assessed by DAS28 at the beginning of the second biologic and at 6 (m-6), 12 (m-12) and 24 months (m-24) follow-up. Primary outcome was the proportion of pts with good or moderate EULAR response (E-Resp). Sensitivity analysis to evaluate clinical response according to the reasons for discontinuation of the first TNFi was performed too. Pts were classified into primary and secondary failure based on the characteristics of the non-response and if possible on the measure of drug and anti-drug antibodies, which were measured by ELISA after 6 months of the first biologic treatment and before switching. Mann–Whitney U test and Fisher's exact test were used to test statistical differences. Factors associated with clinical response were assessed using univariable and multivariable logistic regression analysis. Drug retention was compared using Cox proportional hazards models.
Results: Seventy-seven (61%) pts received a TNFi and 50 (39%) a non-TNFi as second biologic therapy. Mean age was 56 years, 84% were women and 58% were also treated with methotrexate. At baseline, no significant differences between groups were found, except for significantly higher CRP levels in non-TNFi group (Table 1). No statistical differences were observed in E-resp between groups at m-6 and m-12. Nevertheless, at m-24 more pts achieved E-resp in non-TNFi group (80% vs 52%; p=0.001, Figure 1). Likewise, 100% (n=6) of the pts who achieve remission with the second biologic were treated with a non-TNFi. In the univariable analysis, higher baseline DAS28 (OR=1.65, p=0.06), being ACPA positive (OR=3.6, p=0.02) and treatment with a non-TNFi (OR=3.53, p=0.01) were associated with E-resp at m-24. In the multivariable analysis, baseline DAS28 (OR=1.65, p=0.01) and non-TNFi treatment (OR=3.7, p=0.02) remained associated. Drug survival was similar in both groups (1.6±0.7 in TNFi vs 1.6±0.6 years in non-TNFi, p=0.5). In the subgroup of pts who dropped out due to secondary inefficacy (n=76) no differences in response to the second biologic were found, however, pts who stopped the first TNFi for other reasons (primary inefficacy and adverse events) achieved more frequently E-resp after switching to non-TNFi since the beginning of treatment (m-6: 54% in TNFi vs 86% in non-TNFi, p=0.04; m-12: 56% in TNFi vs 70% in non-TNFi, p=0.4; m-24: 47% in TNFi vs 86% in non-TNFi, p=0.04). The overall incidence of AEs was similar between TNFi and non-TNFi groups (21% in TNFi vs 14% in non-TNFi (p=0.9).
Conclusion: In our cohort of patients with RA and failure to a first TNFi, and mainly after primary failure and adverse events, treatment with a non-TNFi was more effective than a second TNFi at 24 months after switch, without significant differences in the survival of the two treatments. In the subgroup of patients who failed the first TNFi due to secondary inefficacy, both treatment options were equally effective. These data reflect how the reason for discontinuation of a first biological can guide the response to a second treatment.
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FRI0080 SURVIVAL ON SECOND-LINE BIOLOGIC THERAPY AFTER THE WITHDRAWAL OF AN ANTI-TNF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: EXPERIENCE IN A SPANISH TERTIARY HOSPITAL

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Background: Patients with Rheumatoid Arthritis (RA) have been traditionally treated with other TNF inhibitors (TNFis) after the withdrawal of a first TNFi (cycling). However, due to the increase in the biological therapy options, changing to a biologic agent with different mechanism of action (switching) is an alternative choice. More studies are needed to clarify the role of both strategies in order to guide treatment decisions.
Objectives: To analyze the survival of the second biological drug, TNFi or biologic with a different mechanism of action, in patients with RA non-responders to the first TNFi. To evaluate factors associated with the survival of the second-line therapy.
Methods: A retrospective, longitudinal, observational study was performed, which included patients diagnosed of RA and treated with biological therapies between 2008 and 2017, who discontinue a first-line TNFi and started a second-line biological therapy. The demographic and clinical data were obtained from their medical records. Kaplan Meier and Log-rank survival analysis were performed, as well as Cox regression to identify related factors.
Results: 69 patients were identified, 14 men (20.3%) with a mean age at the beginning of the treatment of 52.68 ± 19.79 years. Demographic and clinical data are shown in the table. The main cause of withdrawal of the first TNFi was secondary failure (47.8%), followed by side effects (34.8%) and primary failure (13%). Cycling was performed in 34 patients (49.3%) and switching in 35 (50.7%). During the follow-up, the main causes of withdrawal of the second-line treatment were primary and secondary failure (10.1% in both cases). The survival analysis of the 42 patients who presented a primary or secondary failure to the first TNFi was stratified according to the cause of withdrawal of the second biological therapy. When cycling was chosen, the average treatment survival was 8.8 months (CI95%:4.8-12.8) whereas for the switching option it was 23 months (CI95%:5.4-40.5), being the differences statistically significant (p=0.049). Age was shown as a protective factor (HR=0.86, CI95%:0.76-98) and the positivity of Rheumatoid Factor (RF) as a risk factor (HR=4.76, CI95%:1.39-16.30) for the withdrawal of the second biological therapy. No differences were found in the withdrawal rate due to adverse effects among patients who performed switching or cycling (11.42% vs 5.88%, p=0.41).

	n= 69 (mean ± SD or%)	Switching (n=35)	Cycling (n=34)	p-value
Age (years)	52.68 ± 12.79	54.37 ± 12.48	50.91 ± 13.07	0.354
Gender				
Male	14 (20.3%)	8 (22.9%)	6 (17.6%)	0.591
Female	55 (79.7%)	27 (77.1%)	28 (82.4%)	
BMI (kg/m2)	25.42 ± 4.62	24.99 ± 4.03	25.98 ± 5.40	0.362
First treatment duration (months)	23.85 ± 22.70	23.1 ± 20.5	24.7 ± 25.1	0.856
Smokers	18 (26.1%)	9 (25.7%)	9 (25.5%)	0.943
RF (+)	56 (81.2%)	31 (88.6%)	25 (73.5%)	0.227
ACPA (+)	61 (88.4%)	32 (91.4%)	29 (85.3%)	0.189
Erosions	38 (55.1%)	20 (57.1%)	18 (52.9%)	0.198
Joint space narrowing	44 (63.8%)	22 (62.9%)	22 (64.7%)	0.569
Rheumatoid nodules	10 (14.5%)	5 (14.3%)	5 (14.7%)	0.823
Ocular manifestations	7 (10.1%)	4 (11.4%)	3 (88%)	0.938
Sjögren's syndrome	9 (13%)	6 (17.1%)	3 (8.8%)	0.305

SD: Standard Deviation; BMI: Body Mass Index; RF: Rheumatoid Factor; ACPA: Anti-Citrullinated Peptide Antibodies

Conclusion: Switching strategy showed a greater drug survival time and was considered as a better option after the failure of a first TNFi. RF positivity was associated with an increased risk for the withdrawal of the second-line biological therapy.

REFERENCE:

[1] Todoerti M, Favalli E, Iannone F, Olivieri I, Benucci M, Cauli A, Mathieu A, Santo L, Minisola G, Lapadula G, Bucci R, Gremese E, Caporali R. Switch or swap strategy in rheumatoid arthritis patients failing TNF inhibitors? Results of a modified Italian Expert Consensus. Rheumatology. 2018; 57: vii42–vii53

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FRI0081 WITHDRAWAL OF CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN THE SARILUMAB OPEN-LABEL EXTEND STUDY: EFFICACY AND SAFETY ANALYSIS

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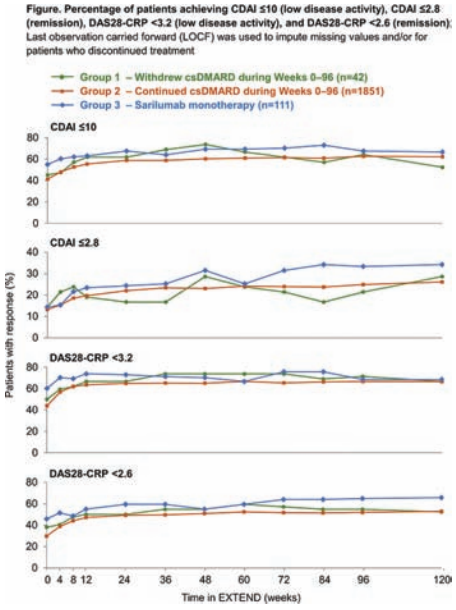
Background: The EXTEND open-label extension study (NCT01146652) is collecting data on long-term treatment of RA with sarilumab as monotherapy and in combination with conventional synthetic (cs)DMARDs, predominantly methotrexate.
Objectives: Post hoc analysis to compare outcomes between patients (pts) who received sarilumab monotherapy, received sarilumab +csDMARDs, or who discontinued csDMARDs during sarilumab treatment.
Methods: Pts enrolled in four trials of sarilumab SC 150 or 200 mg q2w +csDMARDs (MOBILITY, NCT01061736; TARGET, NCT01709578; ASCERTAIN, NCT01768572; and NCT01217814) and an open-label sarilumab monotherapy study (ONE, NCT02121210) were eligible to receive open-label sarilumab SC 200 mg q2w in EXTEND, +csDMARDs if given in the parent trial. In EXTEND, csDMARDs could be stopped at investigator discretion (reasons for csDMARD withdrawal were not recorded). Post hoc analyses were conducted on three pt groups: Group 1 permanently discontinued csDMARDs at any time during Wks 0–96 of EXTEND and subsequently received sarilumab monotherapy; Group 2 continued csDMARDs; and Group 3 enrolled from the monotherapy study and never received csDMARDs. A subgroup of Group 1, comprising pts who received csDMARDs during Wks 0–12 and discontinued csDMARDs during Wks >12–96, was used for sensitivity analysis.
Results: There were 42 pts in Group 1, 1851 in Group 2, and 111 in Group 3 with minor differences between groups in demographics and disease characteristics at entry into EXTEND. The proportion of pts remaining on study at 96 wks was 69%, 80% and 83% in Groups 1, 2 and 3, respectively. Similar substantial and durable response rates (CDAI ≤2.8, CDAI ≤10, DAS28-CRP <2.6, and DAS28-CRP <3.2) were observed between pts who discontinued csDMARDs, pts who continued csDMARDs, and pts who never received csDMARDs (Fig). Results for the sensitivity analysis subgroup (n=27) were consistent with Group 1. The adverse event (AE) profile was as expected for these groups. Incidence of AEs was greater in Group 1 than Groups 2 and 3 (Table), including hepatic disorders (21, 7 and 3 per 100 pt-years [PYs], respectively) and leucopenia (43, 13 and 20 per 100 PYs, respectively). Rates of infection and serious infection were lowest in pts receiving monotherapy.
Conclusion: Over the 120-wk study period, pts initially on sarilumab +csDMARDs who subsequently discontinued csDMARDs maintained similar clinical responses as pts who continued sarilumab +csDMARDs or received sarilumab monotherapy throughout. The AE profile was as expected, with no new safety signals.

Table. Summary of treatment-emergent AEs

n (%) [number of events per 100 PYs]	Group 1 Withdrew csDMARD during Wks 0–96 (N=42) [PYs=104]	Group 2 Continued csDMARD during Wks 0–96 (N=1851) [PYs=5870]	Group 3 Sarilumab monotherapy (N=111) [PYs=230]
Any AE	41 (97.6) [225]	1626 (87.8) [184]	83 (74.8) [138]
Serious AE	17 (40.5) [17]	475 (25.7) [13]	16 (14.4) [10]
AEs leading to sarilumab discontinuation	15 (35.7) [16]	382 (20.6) [7]	8 (7.2) [3]

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FRI0082

EFFECTIVENESS OF TNF INHIBITORS VS. NON-TNF INHIBITORS (ABATACEPT, TOCILIZUMAB AND RITUXIMAB) AFTER FAILURE OF NON-TNFI BIOLOGIC DMARD IN RHEUMATOID ARTHRITIS – COLLABORATION BETWEEN FIVE NATIONAL REGISTERS

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Table 1. Baseline (=start of 2nd bDMARD) characteristics of RA patients who switched to a 2nd bDMARD after a non-TNFi and clinical effectiveness. Results are not shown when N<20.

1st→ 2nd bDMARD	N. patients	Age,years (mean, SD)	Sex (% female)	Disease duration, years (median, IQR)	RF (% pos)	Anti-CCP (%pos)	Concomitant csDMARDs (%)	Concomitant GCs (%)	DAS28 baseline (mean, SD)	DAS28 6 months (mean, SD)	DeltaDAS28 0-6m	N (%) of patients still on drug at month 6 from start of 2nd bDMARD
ABA→TNFi	185	56.1 (13.1)	77.8	4 (2-10)	73.5	64.1	74.1	21.1	4.4 (1.3)	3.5 (1.3)	-0.9 (1.5) N=126	109 (59%)
ABA→RTX	22	57.7 (17.9)	72.7	4.3 (2-7.6)	71.4	100	40.9	31.8	4.5 (1.0)	N<20		19 (86%)
ABA→TCZ	37	59.4 (11.1)	86.5	6.3 (2.6-11.9)	73.5	54.5	29.7	32.4	4.9 (1.3)	3.3 (1.3)	N<20	21 (57%)
RTX→ABA	56	64.3 (12.6)	83.9	12.3 (4.9-21.4)	83.6	57.1	50.0	39.3	4.4 (1.3)	3.8 (1.4)	-0.7 (0.9) N=22	35 (63%)
RTX→TNFi	99	60.1 (12.9)	76.8	8.1 (3-14.2)	76.8	82.4	53.5	42.4	5.2 (1.3)	3.6 (1.4)	-1.5 (1.4) N=44	64 (65%)
RTX→TCZ	31	60.2 (11.6)	87.1	6.7 (3-21.5)	75	66.7	41.9	58.1	5.6 (1.1)	3.3 (1.1)	N<20	21 (68%)
TCZ→ABA	29	55.9 (14.6)	86.2	5.0 (2.3-14.8)	65.5	80	31.0	20.7	4.5 (1.4)	3.9 (1.3)	N<20	18 (62%)
TCZ→TNFi	131	57.6 (12.8)	84	4.0 (2-8.1)	77	71.4	36.6	24.4	3.9 (1.4)	3.5 (1.4)	-0.5 (1.6) N=80	83 (64%)
TCZ→RTX	15	60.8 (14.6)	73.3	4.0 (1.9-13.8)	92.9	100	40.0	26.7	4.4 (2.3)	N<20	N<20	11 (73%)

Background: The optimal sequencing of biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDs) in Rheumatoid Arthritis (RA) is unknown. Evidence regarding the effectiveness of a 2nd non-TNFi bDMARD, as well as of TNFi, in patients whose 1st bDMARD has been a non-TNFi is limited.
Objectives: To characterize patients switching for medical reasons after failure of a non-TNFi used as 1st bDMARD, and to assess the effectiveness of rituximab (RTX), abatacept (ABA) or tocilizumab (TCZ) vs. a TNFi.
Methods: Patients from 5 national registers (Sweden, Norway, Denmark, Iceland and Finland) with RA who started treatment with a non-TNFi as a 1st bDMARD after 2010 and switched to a 2nd bDMARD within 3 months after the discontinuation of the 1st (with the exception of RTX for which a 6-month window was used), were identified. Clinical effectiveness was assessed by DAS28 change at 6 months.
Results: 611 patients were included in the analyses. 80% were female, the majority were positive for RF (76%) and anti-CCP (69%). The mean (±SD) age, DAS28 and HAQ at baseline was 58 (13), 4.5 (1.4) and 1.3 (0.7), respectively, while the median (IQR) disease duration was 5.0 (2.2-12.0) years. Baseline characteristics of patients and the clinical response for each switching strategy are shown in table 1. Moderate responses were observed for most switching strategies. 63% of patients were still on treatment with their 2nd bDMARD at 6 months after switch.
Conclusion: The six-month drug retention for a 2nd bDMARD in patients with RA switching due to failure of a non-TNFi bDMARD as 1st ever bDMARD was lower than two thirds (63%). More detailed analyses are exploring potential subgroups of patients for whom specific switching strategies are more effective.
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FRI0083 **IS A HIGH LEVEL OF IGA PREDICTIVE OF THE EFFICACY AND TOLERANCE OF RITUXIMAB DURING RHEUMATOID ARTHRITIS NAIVE OF PRIOR BIOLOGICAL TREATMENTS?**

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Background: The elevation of immunoglobulin A levels during rheumatoid arthritis is not an exceptional situation although not as commonly found in spondyloarthritis. Hypothetically, this elevation should translate into multiple clinical as well as biological significance.
Objectives: The objective of the study is to identify whether or not a high level of IgA would have an effect on the tolerance and response of rheumatoid arthritis treated with Rituximab.
Methods: This is a retrospective study within which a total number of 33 patients with rheumatoid arthritis treated with Rituximab has been collected, whose peculiarity is the naivety to biological treatment (anti-TNF as it happens). We used regression models of Cox with univariate and multivariate analysis. The main criteria of judgment for efficiency were the EULAR response at 6 months treatment and the recourse to another cycle of rituximab. As regards tolerance, the existence of at least one adverse effect of an infectious, paradoxical or other nature constituted the eligibility argument
Results: 33 patients were included, the average age was 47.46 years. 87.9% of patients were of female gender to 12.1% of male gender. All the patients had structural articular damage. The average initial DAS28 was 6.08. The average DAS28 at 6 months of treatment was 2.98.
13 patients had to go under the use of another cycle of rituximab and an average period of 16.8 months was observed between the 1st and 2nd courses of treatment. 75.8% of the patients achieved a good EULAR response at 6 months. The average serum levels of IgA were 3.86 g/L (1.20-7.29). 33.3% of the patients showed at least one adverse effect. High IgA levels were significantly correlated with recourse to Rituximab retreatment ($p < 0.005$), to prior tuberculosis infection and also to the increase of Alpha 2 globulins on the electrophoresis of blood proteins. We could not prove a relationship between high levels of IgA and the occurrence of side effects.
Conclusion: Polyclonal elevation of IgA during rheumatoid arthritis is possible, although rare. Theoretically, several clinical eventualities should be sought in similar situations. Such as, the existence of a positive rheumatoid factor IgA Isotype, a chronic infection, Spondyloarthropathy, or associated celiac disease. More rarely, a lupus or a Sjogren syndrom. In our series, the existence of high levels of IgA was significantly correlated with recourse to rituximab retreatment, suggesting that there is an underlying entity or a particular etiopathogenic leading to incomplete anti CD20 response. At the same time, a history of tuberculosis and high levels of alpha-2-globulin also correlated with high IgA levels suggesting the existence of an infection with inflammatory reaction of chronic type.

REFERENCES:

[1] Sellam J, Rouanet S, Hendel-Chavez H, et al. CCL19, a B cell chemokine, is related to the decrease of blood memory B cells and predicts the clinical response to rituximab in patients with rheumatoid arthritis. Arthritis Rheum 2013;65:2253–61.
[2] -de Jong TD, Sellam J, Agca R, et al. A multi-parameter response prediction model for rituximab in rheumatoid arthritis. Joint Bone Spine 2018;85:219–26.
[3] Stradner MH, Dejaco C, Brickmann K, Graninger WB, et al. A combination of cellular biomarkers predicts failure to respond to rituximab in rheumatoid arthritis: a 24-week observational study. Arthritis Res Ther 2016;18:190.
[4] Vital EM, Dass S, Rawstron AC, et al. Management of nonresponse to rituximab in rheumatoid arthritis: predictors and outcome of re-treatment. Arthritis Rheum 2010;62:1273–9
[5] Jorgensen C, Anaya JM, Cognot C, Sany J. Rheumatoid arthritis associated with high levels of immunoglobulin A: clinical and biological characteristics. Clin Exp Rheumatol 199 I; 10:571-5
[6] Cowling E Ebringer P, Ebringer A. Association of inflammation with raised serum IgA in ankylosing spondylitis. Ann Rheum Dis 1980; 39:545-9

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FRI0084

THE IMPACT OF IL-6 AND TNF INHIBITORS ON HEMOGLOBIN LEVELS: AN ANALYSIS FROM RHUMADATA® CLINICAL DATABASE AND REGISTRY

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Background: Anemia is a common feature of RA. Prior to the appearance of biologic treatments, improvement of hemoglobin (Hb) levels was unusual and inconsistent. With better control of the inflammatory process with cytokine inhibitors, it has been shown that Hb levels can improve substantially. Recently in the development of IL-6 receptor antagonists (sarilumab (SARI) and tocilizumab (TOCI)) data have shown improvement in Hb levels related to the down-regulation of hepcidin. No direct comparison of Hb levels between TNF and IL-6 inhibition has been explored in observational data (1).
Objectives: This analysis compares the impact of TNF and IL-6 inhibitors on Hb levels over time.
Methods: Data collected since January 1, 2015 (when TOCI and SARI were available in Canada) at the *Institut de Recherche en Rhumatologie de Montréal* (IRRM) and the *Centre de l'Ostéoporose et de Rhumatologie de Québec* (CORQ) was extracted from the Rhumadata® clinical database and registry on January 7, 2019. Selected patients were those initiated on an IL-6 antagonist or a TNFi (adalimumab, certolizumab, etanercept, golimumab or infliximab) and had been treated for at least one year. Furthermore, patients were cancer free and had no diagnosis of Crohn's disease or ulcerative colitis and had creatinine (Cr) and ALT levels within the normal sex-specific range. IL-6 patients were matched (ratio 1:2) to TNFi patients based on age at treatment initiation, gender and baseline Hb. The collected data include baseline characteristics (socio-demographic variables, concomitant and past medication, comorbidities and the Charlson comorbidity index (CCI)), variables measured over time (Hb and other laboratory test results, patient and physician-reported outcomes, and disease activity measures such as CDAI and DAS28(4)-ESR. The groups were compared to identify potential confounder.
Results: A total of 145 patients initiating an IL-6 antagonist since January 1, 2015 were matched with 286 patients prescribed a TNF inhibitor during the same time-period. Most patients were women (86%), the mean age at treatment initiation was 54.1 (standard deviation=11.7) years, and 16% were smokers. Baseline patient global, pain and fatigue assessments, made on a visual analogue scale ranging from 1 to 10, were 5.4 (2.5), 6.1 (2.5) and 5.5 (3.0) in the IL6 group and 5.1 (2.7), 5.5 (3.0) and 5.0 (3.2) in the TNFi group. Baseline disease activity was assessed as moderate or high/severe in 85.5% (IL6) and 85.9% (TNFi) of patients (DAS28(4)-ESR criteria). At treatment initiation, mean Hb level was 126.6 (12.4) g/L, and Cr and ALT levels were 66.2 (11.5) umol/L and 18.7 (6.5) U/L in the IL6 group and 67.0 (12.0) umol/L and 19.3 (6.8) U/L in the TNFi group. At three months, Hb had increased by 5.4 (10.2) g/L in the IL6 group and by 1.8 (13.9) g/L in the TNFi group (p-value=0.024). These respective changes at 12 months were 8.7 (11.4) g/L and 5.4 (9.2) g/L (p-value=0.042).
Conclusion: This analysis confirms that IL-6 inhibition provides a numerically and statistically superior increase in Hb over TNFi.

REFERENCE:

[1] Song, et al. Arthritis Research & Therapy 2013, 15:R141

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FRI0085

TAPERING OF BIOLOGICAL ANTIRHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS PATIENTSIS ACHIEVABLE AND COST EFFECTIVE IN DAILY CLINICAL PRACTICE: DATA FROM THE BRUSSELS UCL RA COHORT

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Background: Several studies have demonstrated that Rheumatoid Arthritis (RA) patients achieving low disease activity or remission are able to taper biological disease-modifying antirheumatic drugs (bDMARDs).
Objectives: The aim of this study is to evaluate the proportion of patients in whom the bDMARD can be tapered in daily practice and to analyse the characteristics of these patients e. Another objective is to determine which bDMARDs are more adapted to dose reduction and the cost saving.
Methods: Inclusion criteria were RA patients from our Brussels UCL cohort treated with a bDMARD for at least one year. A dose reduction was proposed by the senior physician when sustained low disease activity or remission was achieved. Patient characteristics and baseline features before the introduction of the current bDMARD were collected as well as flares if happened. We also calculated, for each bDMARD, the proportion of patients who received a decreased dose and the annual cost.
Results: Data from 332 eligible RA patients were collected, 140 patients (42,1%) had a tapered regimen and 192 received a full dose of bDMARD. In the decreased dose group, age at diagnosis (43.1 vs 38.7 years, p=0.004), HAQ (1.3 vs 1.5, p=0.048), RF (83.3 vs 72.9%, p=0.026) and disease duration at the bDMARDs introduction (9.7 vs 12.1 years, p=0.034) were statistically different. As expected, the current DAS28-CRP was lower (2.26 vs 2.64, p=0.001) in the decreased dose group and interestingly, more patients receiving a decreased dose were treated with a combination of methotrexate when the bDMARD was introduced (86.7% vs 73.8%, p=0.005). No difference between groups was observed for gender, ACPA, erosion, number of previous bDMARDs, time to first conventional synthetic DMARD and biological DMARD, baseline DAS28-CRP and use of glucocorticoids. In our cohort, anti-TNF agents were the most commonly prescribed medications (anti-TNF 68%, tocilizumab 15%, rituximab 10%, abatacept 7%). Only 15 patients experienced a flare during the follow-up. Adalimumab, etanercept and rituximab were the most frequent decreased bDMARD and were associated with the most important reduction of annual cost.

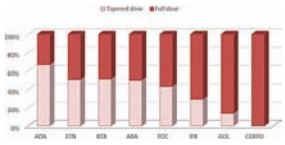


Figure 1. Proportion of patients with decreased dose for each bDMARD

ABA : abatacept, ADA : adalimumab, CZP : certolizumab, ETN : étanercept, GOL : golimumab, IFX : infliximab, RTX : rituximab, TOC : tocilizumab
Conclusion: In daily practice, tapering of bDMARDs in RA patients with low disease activity or remission is an achievable goal in a large proportion of patients, thereby reducing annual drug cost. The combination with methotrexate could be a positive predictive factor for the success of bDMARD tapering but further prospective research in daily practice are needed to confirm this result.
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FRI0086 **CHINA-MANUFACTURED ADALIMUMAB BIOSIMILAR, HLX03, DEMONSTRATED PHARMACOKINETIC EQUIVALENCE AND COMPARABLE SAFETY TO REFERENCE ADALIMUMAB**

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Background: Adalimumab first launched in China in August 2010 with now more than 10 million people have its indications.[1, 2] However, the relative high cost of the biologic drug limits the treatment accessibility and reduces the quality of life in patients living with the chronic inflammatory disease like rheumatoid arthritis and psoriasis. In accordance with the China National Medical Product Administration (NMPA) biosimilar regulatory development pathway, biosimilar products require to demonstrate similarity in pharmacokinetics (PK) and safety profile compared to its reference drug, which could further address the unmet medical needs of adalimumab. HLX03 was developed as a proposed biosimilar to adalimumab with the potential to increase affordable treatment options for access.

Objectives: The study was aiming to compare the pharmacokinetics (PK), safety and immunogenicity of the proposed adalimumab biosimilar HLX03 with reference product.

Methods: We conducted a randomised, double-blind, parallel-controlled clinical trial (NCT03357939) in China to compare the PK, safety and immunogenicity of HLX03 and China sourced adalimumab (CN-adalimumab). In this study, 211 healthy volunteers were randomised 1:1 to receive a single (40 mg) subcutaneous injection of HLX03 or CN-adalimumab. The primary PK endpoints were area under the curve (AUC) from time zero to the last quantifiable concentration (AUC_{0-t}) and maximum observed concentration (C_{max}), secondary endpoint was AUC from time zero to infinity (AUC_{0-inf}). PK equivalence was established if the 90% confidence interval (CI) for the test-to-reference ratio fall within the 80-125% equivalence margin.

Results: Based on the analysis of 210 subjects in the per protocol population (PPS) and 211 subjects in the full analysis set (FAS), HLX03 demonstrated PK equivalence to CN-adalimumab for all primary endpoints (Table 1). The incidents of adverse events (AEs) between two treatment groups were similar, with treatment-emergent AEs (TEAEs) noted by a total of 149 (70.0%), 79 (73.8%) in HLX03 and 70 (66.0%) in CN-adalimumab group, respectively. One subject suffered non-drug-related severe AE (tuberculosis) in the HLX03 arm, and one subject occurred grade 4 AE (elevated creatine phosphokinase) in the CN-adalimumab arm. In the group of CN-adalimumab, 6 more incidents of positive anti-drug antibodies (ADA) recorded at day 7 and no further significant difference observed. Based on the established clinical PK equivalence and safety similarities, 262 patients with moderate-to-severe chronic plaque psoriasis were randomized in 21 centers at 1:1 ratio to conduct a double-blind, parallel-controlled phase 3 study (NCT03316781) to further evaluate the efficacy and safety profiles of HLX03 and reference adalimumab. The primary efficacy endpoint was the improvement rate of Psoriasis Area and Severity Index (PASI) over the baseline at week 16.

	Analysis group	Parameter	Ratio-A/B	CI 90%
HLX03 vs CN-Adalimumab	PK-PPS	C_{max}	102.22	96.20, 108.61
		AUC_{0-t}	105.72	97.07, 115.15
		AUC_{0-inf}	105.31	96.12, 115.38
	PK-FAS	C_{max}	101.95	95.96, 108.31
		AUC_{0-t}	105.54	96.92, 114.92
		AUC_{0-inf}	108.48	98.73, 119.18

Conclusion: PK equivalence and safety similarities between HLX03 and CN-adalimumab were demonstrated which leads to a multi-center, randomised, double-blind, parallel-controlled phase 3 study to further evaluate the efficacy and safety of HLX03 as the proposed biosimilar of adalimumab in patients with moderate-to-severe plaque psoriasis.

REFERENCES:

[1] Chinese Rheumatology Association. 2018 Chinese guideline for the diagnosis and treatment of rheumatoid arthritis[J]. Zhonghua nei ke za zhi, 2018, 57(4): 242.

[2] Markets, R. (2018). Investigation Report on China Adalimumab Market, 2010-2018. Retrieved from https://www.prnewswire.com/news-releases/investigation-report-on-china-adalimumab-market-2010-2018-252895801.html

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FRI0087 **EFFICACY, SAFETY, AND IMMUNOGENICITY RESULTS OF THE SWITCH FROM REFERENCE ADALIMUMAB (REFADL) TO SANDOZ BIOSIMILAR ADALIMUMAB (GP2017, SDZ-ADL) FROM ADMYRA PHASE 3 STUDY IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS (RA)**

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Background: SDZ-ADL is approved by EMA in all indications of refADL based on preclinical and clinical study results. EMA submission data included results of a Phase 3 study in patients with plaque psoriasis. ADMYRA was a Phase 3 study comparing efficacy and safety of SDZ-ADL and refADL in patients with moderate-to-severe RA with inadequate response to disease modifying anti-rheumatic drugs, including methotrexate (NCT02744755).

Objectives: The ADMYRA study was designed to compare the efficacy of SDZ-ADL and refADL over 24 weeks of treatment, and to evaluate long-term efficacy, safety, and immunogenicity of SDZ-ADL up to Week (Wk) 48. The study also investigated the effect of the switch from refADL to SDZ-ADL at Wk 24 on efficacy, safety, and immunogenicity up to Wk 48. This abstract focuses on the data after switch from refADL to SDZ-ADL.

Methods: Eligible patients were randomized 1:1 to receive 40 mg subcutaneous SDZ-ADL or refADL every other week from Wk 0–22. At Wk 24, patients in the refADL arm were switched to receive SDZ-ADL; treatment continued until Wk 46. The primary endpoint was change in Disease Activity Score-28 including high-sensitivity C-reactive protein (DAS28-CRP) from baseline at Wk 12. Secondary endpoints included mean changes in DAS28-CRP scores, the proportion of patients fulfilling EULAR responses, EULAR and Boolean remission criteria, safety, and immunogenicity. EULAR remission was defined as DAS28-CRP <2.6. Boolean remission was defined as tender joint count 28 ≤1, swollen joint count 28 ≤1, CRP ≤1 mg/dL, and patient global assessment ≤10 on a 100 mm scale.

Results: As reported previously, mean change in DAS28-CRP from baseline at Wk 12 was -2.16 for SDZ-ADL (N=140) and -2.18 for refADL (N=144).[1] Efficacy in both treatment arms was maintained throughout the study, also after the switch from refADL to SDZ-ADL at Wk 24. Mean change in DAS28-CRP from baseline at Wk 48 was -2.90 and -2.92 for refADL/switched and SDZ-ADL groups, respectively. At Wk 48, the proportion of patients with moderate/good EULAR response was 29.6/68.0% in refADL/switched group and 29.0/69.2% in SDZ-ADL group. At Wk 48, the proportion of patients in EULAR remission was 54.4 and 51.4% and in Boolean remission was 21.6 and 16.8% for refADL/switched and SDZ-ADL groups, respectively. As previously reported, safety and immunogenicity were similar in both arms before switch.[1] No new safety concerns were identified after switch. After switch, 32.5% of patients in the refADL/switched group and 36.5% of patients in the SDZ-ADL group experienced adverse events (AEs); serious AEs were reported by 3.6 and 2.5%, respectively. The proportion of patients reporting injection site reactions after switch was 1.2% in the refADL/switched group and 0.6% in the SDZ-ADL group, respectively. After switch, 26.3 and 24.0% of patients

were positive for antidrug antibodies (ADAs) in refADL/switched and SDZ-ADL groups, respectively. Of these, 81.0 vs 72.2% were neutralizing. ADA positivity had no clinically meaningful impact on safety.
Conclusion: After the switch from reference to biosimilar, the rates of EULAR remission/response and Boolean remission were high and maintained until Week 48. Treatment switch from refADL to SDZ-ADL at Wk 24 did not impact efficacy, safety, or immunogenicity.

REFERENCE:
[1] Wiland P, et al. Arthritis Rheumatol 2018;70(suppl 10).

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FRI0088 SAFETY, IMMUNOGENICITY AND EFFICACY OF THE PROPOSED BIOSIMILAR MSB11022 (MODIFIED FORMULATION) COMPARED WITH ADALIMUMAB REFERENCE PRODUCT IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS: AURIEL-RA, A RANDOMISED, DOUBLE-BLIND, PHASE III STUDY

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Background: Adalimumab is a fully human anti-TNF monoclonal antibody indicated for the treatment of multiple inflammatory disorders, including rheumatoid arthritis (RA). MSB11022 is a proposed adalimumab biosimilar that has been shown to be structurally and functionally similar to the adalimumab reference product[1]. MSB11022 has been developed in two formulations, in a citrate-based buffer, and in a modified buffer and stabiliser. MSB11022 demonstrated bioequivalence and comparable safety, tolerability and immunogenicity profiles to reference adalimumab (both in citrate formulations) in a study in healthy volunteers[2]. Subsequently MSB11022 was shown to be therapeutically equivalent to reference adalimumab (both citrate formulations) in terms of efficacy, safety and immunogenicity in psoriasis patients in the 52-week, Phase III, pivotal AURIEL-PsO study[3]. MSB11022 (modified formulation) demonstrated bioequivalence and a comparable safety and immunogenicity profile to MSB11022 (citrate formulation) in an additional healthy volunteer study (EMR200588-003)[4].
Objectives: To evaluate safety, immunogenicity and efficacy of MSB11022 (modified formulation) in patients with moderately to severe active rheumatoid arthritis compared to reference adalimumab up to 52 weeks.
Methods: RA patients receiving methotrexate were randomised 1:1 to MSB11022 (modified formulation) or reference adalimumab (citrate formulation) in the double-blind, multicentre, phase III AURIEL-RA study (NCT03052322). Safety, efficacy and immunogenicity endpoints were assessed at scheduled visits up to week 52 using descriptive statistical methods only. Safety was the primary objective and the study was not powered to demonstrate equivalent efficacy.
Results: 288 RA patients were randomised (MSB11022, n = 143; reference adalimumab, n = 145). Patient baseline characteristics were comparable between treatment groups. Few adverse events of special interest (AESIs) of hypersensitivity (primary endpoint) were reported during the study and the proportions were similar across treatment arms. Efficacy endpoints, including the key secondary endpoint of American College of Rheumatology criteria 20% (ACR20) response rate at week 12, were similar between the treatment arms. The safety profiles of patients receiving MSB11022 and reference adalimumab were also similar through to week 52. There were no clinically meaningful differences in the incidence of anti-drug antibodies (ADAs) and neutralising antibodies (NAbs) between treatment arms up to week 52. Key results are presented in Table 1.
Conclusion: MSB11022 (modified formulation) and reference adalimumab had similar safety, immunogenicity and efficacy profiles over 52 weeks in patients with RA, supplementing the clinical data collected with MSB11022 (citrate formulation) in healthy volunteers and psoriasis patients

Table 1

Endpoint (analysis set)	Timepoint (Week)	MSB11022	Reference adalimumab
Incidence of AESIs of hypersensitivity (SAF)	52	6 (4.2)	8 (5.5)
Incidence of TEAEs (SAF)	52	83 (58.0)	93 (64.1)
ACR20 response (ITT)	12	113 (79.6)	114 (80.9)
DAS28-ESR (ITT)	12	3.3 ± 1.2	3.4 ± 1.2
Overall incidence of ADAs (SAF)	52	115 (80.4)	104 (71.7)
Overall incidence of NAbs (SAF)	52	57 (39.9)	57 (39.3)

Numbers are n (%) or mean±standard deviation. DAS28, Disease Activity Score-28; ESR, erythrocyte sedimentation rate; ITT, intention-to-treat set; SAF, safety analysis set; TEAE, treatment-emergent adverse event

REFERENCES:
[1] Magnenat L, et al. MAbs 2017;9(1):127-39.
[2] Hyland E, et al. Br J Clin Pharmacol 2016;82(4):983-93.
[3] Hercogova J, et al. J Am Acad Dermatol 2018;79(3):AB21.
[4] Fresenius Kabi. Data on File 2019

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, Joëlle Monnet Employee of: Employee of Fresenius Kabi SwissBioSim, Martin Ullmann Shareholder of: Amgen, BMS, Employee of: Employee of Fresenius Kabi SwissBioSim, Pantelis Vlachos: None declared
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FRI0089 SAFETY AND EFFICACY OF RADIONUCLIDE SYNOVECTOMY IN PATIENTS WITH PERSISTENT INFLAMMATORY OF SINGLE JOINT IN THE COURSE OF BIOLOGICAL THERAPY

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Background: Radionuclide synovectomy (RSV) is a form of minimally invasive treatment of persistent joint inflammation. Primary indication for RSV is hypertrophic synovitis refractory to disease-modifying anti-rheumatic drugs (DMARDs), whether synthetic or biological, and intraarticular steroid injections. This procedure has a high rate of success with a low rate of adverse events and complications in properly selected patients. Moreover, due to bactericidal properties of the radiocolloids, the risk of infection after RSV is insignificant, and incidence of post-injection septic arthritis is extremely low.
Objectives: To assess safety and efficacy of RSV in patients with inflammatory rheumatic diseases treated with biological disease-modifying anti-rheumatic drugs (bDMARDs).
Methods: We analyzed outcomes of 76 radionuclide synovectomy interventions in 47 patients (37 female and 10 male) ongoing biological therapy. The patients were diagnosed as follows: rheumatoid arthritis (RA) – 37, ankylosing spondylitis (AS) – 7, psoriatic arthritis (PsA) – 2 and juvenile idiopathic arthritis (JIA) – 1 patient. The majority of the patients were treated with TNF-alpha inhibitors (79%), which included: adalimumab (31.6%), etanercept (25%), golimumab (14.5%) and certolizumab (7.9%). The other patients were treated with interleukin-6 receptor antagonist tocilizumab (19,7%) and anti-CD20 monoclonal antibody rituximab (1.3%). Patients with overall good response to biologics and persistent inflammation of single joint confirmed by ultrasound PD examination, in case of no contraindications were qualified for RSV procedure. For the RSV following radiopharmaceuticals were used: rhenium-186 sulphide in 41 cases for shoulder (2), elbow (13), wrist (22), hip (2) and ankle (2) joints; yttrium-90 citrate in 27 cases for knee joints; erbium-169 citrate in 8 cases for small joints of hand and feet. All patients had a follow-up visit 3 and 6 months after RSV, during which a clinical and ultrasound examination of the treated joints were performed. Continuous adverse events collection was conducted.
Results: The most common indication for RSV was RA – 60 procedures (78.9%), followed by AS – 10 (13.2%), PsA – 4 (5.3%) and JIA – 1 procedure (2.6%). 27 patients had RSV intervention in one joint. 17

patients with satisfactory response to RSV in one joint required radioisotope treatment in another joint (between 2 and 4 different joints were treated in each patient – 13 patients in 2 joints, 5/3 and 2/4). Median patient age was 50 years (21 – 72). Duration of continuous bDMARD treatment preceding RSV was between 1 and 72 months. The intervals between bDMARD administration and RSV ranged from below 24 hours to 4 weeks. Satisfactory effects of RSV, defined as absence of clinical and ultrasound symptoms of inflammation, were observed after 55 (72.4%) interventions. In 11 (14.4%) cases after initial improvement, the inflammation symptoms recurred less than 6 months after RSV. In 10 (13.2%) cases RSV had no effect.

No side effects or adverse events occurred after RSV and, most importantly, there were no local or systemic infections observed up to 6 months after the procedure.

Conclusion: RSV seems to be an effective single joint treatment method in patients with active synovitis refractory to bDMARDs. Despite increased susceptibility to infection in patients partially immunocompromised and biological treatment, no septic complications were observed after RSV. RSV does not require discontinuation of biological treatment, unlike surgical synovectomy.

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FRI0090 SINGLE CENTRE COHORT OF REFRACTORY RHEUMATOID ARTHRITIS ALSO IDENTIFIES A RARE SUBGROUP OF MULTIPLE TARGETED THERAPY CLASS NON-RESPONSE

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Background: Refractory Rheumatoid Arthritis (RefRA) has emerged as an area of unmet need in the biologic era (1). Failure of 3 or more classes of targeted therapy or failure of both an anti-cytokine and a cell-targeted treatment have been proposed as possible definitions (1, 2). The BSRBR-RA reported 6% fulfil RefRA criteria (due to lack of efficacy and/or toxicity; but only including a first line TNF inhibitor bDMARD cohort) (2).

Objectives: To evaluate the extent of multi-targeted therapy RefRA in our tertiary RA single-centre experience, and identify any patterns of drug sequencing associated with development of RefRA.

Methods: We used a prospective database of RA patients established on targeted therapy, supplemented with information from individual funding requests and a review of our specialised biologic clinic patient notes to identify those who have been prescribed 2 or more classes of targeted therapies. Data on number and type of targeted therapy, and where available, reason for failure has been recorded. Disease activity state and functional outcomes are currently being evaluated

Results: Of a cohort of over 1500 RA patients that have received at least 1 targeted therapy, 172 patients have received 3 classes of targeted therapies (reasons for each drug discontinuation has been identified in 166 cases). An additional 50 patients have received multiple (2 or more) TNFi and at least 1 other class of targeted therapy. Table 1 details numbers in each category of RefRA.

	2 class bDMARD	3 or all 4 classes bDMARD	Multi bDMARD (min. 2 class) + JAKi
Number of patients (n=166)	64*	76	26
RF and/or CCP+ (n= 134)	48 (75%)	66 (87%)	20 (77%)
1st Targeted Therapy			
TNFi	54	61	24
Rituximab	5	9	1
Tocilizumab	3	1	0
Abatacept	2	5	1
Reason for drug discontinuation			
Primary NR only	5	3	2
Secondary NR only	7	6	0
Mixed primary/secondary NR	31	28	6
Mixed NR and toxicity	19	36	17
Multiple toxicity	2	3	1

*49 patients received one anti-cytokine and one cell-targeted bDMARD, 12 received two anti-cytokine bDMARD (TNFi and tocilizumab) and 3 received two cell targeted treatments (rituximab and abatacept).

In those who had failed multiple anti-TNF drugs 39 were switched to a cell-targeted therapy (31 Rituximab, 7 Abatacept), the rest were switched from a TNFi to tocilizumab. 36 out of 39 patients have maintained a response to their cell-targeted therapy after failing multiple anti-cytokines. 5 Patients demonstrate at least 3 primary non-responses with a further 4 further patients with multiple primary non-response and only 1 adverse event.

Conclusion: Over 10% of our single-centre targeted therapy exposed cohort demonstrate multi-targeted therapy RefRA. The majority comprise mixed non-response, loss of response and drug toxicity. A rare subgroup of 6% of RefRA demonstrate lack of efficacy to multiple therapies. On-going investigations aim to identify the clinical phenotype, predictors and underlying biology.

REFERENCES:

[1] Buch, M.H. Defining refractory rheumatoid arthritis. Ann Rheum Dis. 2018, 77(7), pp.966-969.

[2] Kearsley-Fleet, L. et al. Biologic refractory disease in rheumatoid arthritis: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. Ann Rheum Dis. 2018, 77(10), pp.1405-1412.

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FRI0091 UNEMPLOYED FEMALE RHEUMATOID ARTHRITIS PATIENTS ARE LESS ADHERENT TO THE BIOLOGIC DMARD TREATMENT

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Background: The 5-item Compliance Questionnaire for Rheumatology (CQR5) allows the identification of patients likely to be high adherers (HAs) to anti-rheumatic treatment (i.e. taking $\geq$80% of their medications correctly), or "low" adherers (LAs). An Italian version of the questionnaire was validated (I-CQR5) [1].

Objectives: The objective was to investigate what factors are associated with high treatment adherence according to I-CQR5 in RA patients treated with biologic DMARDs (bDMARDs).

Methods: RA patients (with disease duration >1 year, undergoing treatment with $\geq$1 self-administered biological disease-modifying anti-rheumatic drug (bDMARD), willing and capable of completing the questionnaire unaided) were enrolled in the study. I-CQR5 were anonymous and clinical data were collected from the local database. Factors included were demographic, social characteristics of the patients, clinical and treatment variables. Factors achieving a $p<0.10$ in univariate analysis were included in a multivariate regression analysis.

Results: Among 604 RA patients, 193 patients were included in the validation analysis. Median age of the patients was 57 years (46-65), 142 (73.4%) were females, median disease duration was 15 years (9-21); 82 (42.7%) patients were treated with low dose bDMARDs; 174 (91.1%) patients were in low disease activity or remission (Fig.1). HAs were 40.9% (79/193) of patients: 100% (193/193) of patients treated with bDMARDs and 22.4% (57/193) of those treated with bDMARDs in combination with conventional synthetic DMARDs. Female gender, no employment, lower education level, positive Rheumatoid Factor and/or Anti-Citrullinated Peptides Antibodies, low bDMARD dose, higher patient-VAS were significantly more frequent in LAs compared with HAs. In the multivariate analysis, employment was also positively and significantly associated with high adherence: OR 2.89 (1.3-6.44), p=0.009 (Tab.1).

Conclusion: As previously reported only one third of RA patients treated with bDMARDs were found to be HAs to treatment according to the I-CQR5. Employment status was the major determinant, increasing by almost 3-fold the likelihood of being adherent. Education level and female gender might be also taken into account as factors influencing treatment adherence.

REFERENCE:
[1] Ometto F., et al. Treatment adherence in rheumatoid arthritis italian patients using a validated version of the 5-item compliance questionnaire for rheumatology (I-CQR5). EULAR18-4294.

Univariate analysis. Demographics and clinical variables according to high and low adherence to treatment defined by I-CQR5.

	Total	HA	LA	p value
No.	193	79 (40.9)	114 (59.1)	
HA, n (%)	79 (40.9)	-	-	-
Females (%)	142 (73.4)	52 (65.8)	90 (80.4)	0.024¶
Age, years, median (IQR)	57 (46-65)	54.5 (39.8-28)	57.5 (47-66.3)	0.491
BMI, median (IQR)	24 (22-28)	25 (23-28)	24 (21-27.8)	0.545
Smokers, n (%)	28 (17.6)	12 (21.1)	16 (15.7)	0.394
Employed, n (%)	81 (47.1)	41 (64.1)	40 (37)	0.001¶
Education level				0.147
Primary school, n (%)	20 (11)	8 (10.3)	12 (11.5)	
Median school, n (%)	65 (35.7)	21 (26.9)	44 (42.3)	
Secondary school, n (%)	68 (37.4)	34 (43.6)	34 (32.7)	
University, n (%)	29 (15.9)	15 (19.2)	14 (13.5)	
Primary/middle school education, n (%)	85 (46.7)	29 (37.2)	56 (53.8)	0.026¶
Social status				0.567
Living with parents and family, n (%)	13 (8.7)	5 (9.3)	8 (8.3)	
Living alone, n (%)	16 (10.7)	6 (11.1)	10 (10.4)	
Living with partner and family, n (%)	113 (75.3)	38 (70.4)	75 (78.1)	
Other, n (%)	6 (4)	4 (7.4)	2 (2.1)	
Positive RF and/or ACPA, n (%)	79 (42.2)	27 (34.6)	52 (47.7)	0.074¶
Disease duration, years, median (IQR)	15 (9-21)	14 (10-21)	15 (9-21.5)	0.762
Fibromyalgia, n (%)	38 (20.8)	12 (15.6)	26 (24.5)	0.141
csDMARD treatment, n (%)	57 (30.5)	19 (24.4)	38 (34.9)	0.124
Methotrexate, n (%)	41 (21.9)	16 (20.5)	25 (22.9)	0.693
Leflunomide, n (%)	12 (6.4)	3 (3.8)	9 (8.3)	0.225
Other DMARD, n (%)	7 (3.7)	0 (0)	7 (6.4)	0.023
bDMARD treatment, n (%)	193 (100)	79 (100)	114 (100)	-
bDMARD				0.541
Abatacept, n (%)	13 (6.7)	8 (7)	5 (6.3)	
Adalimumab, n (%)	35 (18.1)	19 (16.7)	16 (20.3)	
Anakinra, n (%)	11 (5.7)	7 (6.1)	4 (5.1)	
Certolizumab pegol, n (%)	15 (7.8)	9 (7.9)	6 (7.6)	
Etanercept, n (%)	101 (52.3)	62 (54.4)	39 (49.4)	
Golimumab, n (%)	8 (4.1)	6 (5.3)	2 (2.5)	
Tocilizumab, n (%)	10 (5.2)	3 (2.6)	7 (8.9)	
bDMARD treatment administered ≤ 1 week, n (%)	110 (57)	43 (54.4)	67 (58.8)	0.549
Low dose bDMARD, n (%)	82 (42.7)	29 (49.4)	43 (37.7)	0.091¶
Previous bDMARD failure treatment, n (%)	62 (38.5)	29 (38.7)	33 (38.4)	0.969
Duration bDMARD treatment, months, median (IQR)	88 (45-61.8)	88 (47-130)	86 (41.5-120)	0.992
Associated treatment, n (%)	57 (30.5)	19 (24.4)	38 (34.9)	0.124
Disease duration >24 months, n (%)	149 (83.7)	63 (82.9)	86 (84.3)	0.8
PDN daily dose, median (IQR)	1.5 (0-5)	0 (0-5)	2.5 (0-5)	0.13
NSAIDs, n (%)	111 (66.1)	47 (67.1)	64 (65.3)	0.804
Painkillers, n (%)	50 (31.4)	22 (31.9)	28 (31.1)	0.917
Concomitant chronic treatment, n (%)	91 (49.7)	38 (50.7)	53 (49.1)	0.832
DAS28, median (IQR)	2.3 (1.8-2.8)	2.3 (1.7-2.8)	2.4 (1.8-3.0)	0.441
Remission†, n (%)	101 (52.9)	39 (49.4)	62 (55.4)	0.414
Low disease activity¥, n (%)	174 (91.1)	73 (92.4)	101 (90.2)	0.595
Patient-VAS, median (IQR)	38 (20-66)	30 (10-50)	45 (28-69)	0.03¶
Physician-VAS, median (IQR)	10 (5-15)	10 (0-15)	10 (5-20)	0.988
HAQ, median (IQR)	0.6 (0.1-1.1)	0.5 (0-1.1)	0.8 (0.3-1.1)	0.14
Disease flares, median (IQR)	11 (26.2)	5 (33.3)	6 (22.2)	0.433
No. of assesments per year, median (IQR)	4 (3-4)	4 (3-4)	4 (3-4)	0.98
Distance from clinic, km, median (IQR)	32 (18-50)	30 (20-50)	35 (18-50)	0.948

Defined as DAS28<2.6; defined as DAS28<3.2; ¶variables included in the analysis in patients treated with bDMARDs as achieving a p value <0.10.
bDMARD biologic DMARD, *IQR* interquartile range, *BMI* body mass index, *ACPA* anti-citrullinated peptides, *RF* rheumatoid factor, *PDN* prednisone, *NSAIDs* non-steroideal antinflammatory drugs, *HAQ* Health Assessment Questionnaire, *DAS28* disease activity score in 28 joints, *VAS* visual analogic scale.

Table. Multivariate regression analysis. Factors associated with HA to anti-rheumatic treatment according to I-CQR5.

	OR (95% C.I.)	p
Male gender	2.05 (0.9-4.66)	0.086
Employment	2.89 (1.3-6.44)	0.009
Patient-VAS (per 10-unite increase)	0.95 (0.83-1.09)	0.453
Model constant		0.035

OR odds ratio, *C.I.* confidence interval, *VAS* visual analogic scale.

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FRI0092

SAFETY AND EFFICACY OF FILGOTINIB IN ACTIVE RHEUMATOID ARTHRITIS BY PRIOR BIOLOGICAL DMARD EXPOSURE IN PATIENTS WITH PRIOR INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDS (BDMARD-IR)

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Background: Filgotinib (FIL), an oral selective Janus kinase 1 (JAK1) inhibitor, significantly improved the signs and symptoms of rheumatoid arthritis (RA) with a favorable safety profile in a global phase 3 study in bDMARD-IR patients with active RA (FINCH2).[1]
Objectives: To assess the safety and efficacy of FIL in the FINCH2 study by the number and type of prior bDMARDs.
Methods: FINCH2 enrolled 449 bDMARD-IR patients with moderate-to-severe active RA. Patients were randomized 1:1:1 to FIL 200 mg, FIL 100 mg or placebo (PBO) on a background of csDMARDs for 24 weeks. In this prespecified subgroup analysis, efficacy and safety were analyzed according to the number (<3 vs ≥3) of previous bDMARDs used.
Results: 448 patients received ≥1 dose of study drugs. Of these, 343 were previously exposed to <3 bDMARDs, while 105 were previously exposed to ≥3 bDMARDs. Table 1 shows demographics and baseline (BL) characteristics of patients in these 2 groups; efficacy and safety parameters (Table 2) were similar for both groups. There were no cases of opportunistic infection, active tuberculosis, malignancy, gastrointestinal perforation, or death.

Table 1. BL Demographics and characteristics

	<3 bDMARDs (n=343)			≥3 bDMARDs (n=105)		
	FIL 200 (n=110)	FIL 100 (n=119)	PBO (n=114)	FIL 200 (n=37)	FIL 100 (n=34)	PBO (n=34)
Female, n (%)	90 (82)	92 (77)	93 (82)	30 (81)	27 (79)	28 (82)
Mean (SD) age, yrs	54 (13)	55 (13)	56 (12)	59 (9)	54 (9)	56 (12)
Concurrent steroids, n (%)	46 (42)	49 (41)	54 (47)	22 (60)	19 (56)	17 (50)
Concurrent MTX, n (%)	98 (89)	101 (85)	96 (84)	26 (70)	26 (77)	20 (59)
Mean (SD) DAS28 (CRP)	6.0 (1.0)	5.8 (1.0)	5.9 (0.9)	5.8 (1.0)	6.1 (1.0)	5.9 (0.9)
Mean (SD) HAQ-DI	1.66 (0.65)	1.62 (0.70)	1.63 (0.65)	1.84 (0.66)	1.72 (0.61)	1.74 (0.57)
Mean (SD) hsCRP (mg/L)	17.04 (16.80)	21.82 (28.49)	16.08 (19.16)	17.70 (22.36)	20.31 (27.58)	17.56 (15.37)

Table 2. Key week 24 efficacy and safety outcomes

	<3 bDMARDs (n=343)			≥3 bDMARDs (n=105)		
	FIL 200 (n=110)	FIL 100 (n=119)	PBO (n=114)	FIL 200 (n=37)	FIL 100 (n=34)	PBO (n=34)
ACR20 n (%)[a]	Δ34.9%	Δ21.2%		Δ35.2%	Δ17.6%	
DAS28(CRP)≤3.2 n (%)[a]	Δ27.3%	Δ15.8%		Δ29.0%	Δ20.6%	
DAS28(CRP)<2.6 n (%)[a]	Δ19.6%	Δ12.9%		Δ15.7%	Δ17.6%	
HAQ-DI mean CFB (SD)	–0.74 (0.631)‡	–0.61 (0.668)*	–0.42 (0.618)	–0.77 (0.596)†	–0.54 (0.635)	–0.44 (0.525)
SF-36 PCS mean CFB (SD)	9.4 (8.45)†	8.9 (8.72)*	6.4 (8.44)	9.4 (7.65)	9.1 (7.36)	7.2 (5.44)
FACIT-Fatigue mean CFB (SD)	11.3 (11.99)†	9.7 (10.44)*	6.7 (10.68)	12.6 (10.78)‡	10.2 (10.42)†	8.4 (8.12)
TEAE	75 (68.2%)	73 (61.3)	76 (66.7%)	27 (73.0%)	24 (70.6%)	24 (70.6%)
TEAE leading to study drug discontinuation	4 (3.6%)	3 (2.5%)	2 (1.8%)	1 (2.7%)	3 (8.8)	1 (2.9%)

CFB, change from BL. *p<0.05, †p<0.01, ‡p<0,001; Δ, difference vs PBO.
[a]FIL values are PBO-corrected.

Conclusion: In bDMARD-IR patients with active RA, FIL treatment for 24 weeks significantly improved the signs and symptoms of RA with a favorable safety profile; notably, efficacy and safety results were similar for patients with <3 or ≥3 prior bDMARDs.

REFERENCE:
[1] Genovese MC, et al. ACR 2018. Abstract L06.

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FRI0093

IMPACT OF INTERLEUKIN 6 RECEPTOR INHIBITOR ON N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background:

Objectives: To investigate the impact of interleukin 6 receptor inhibitor - tocilizumab (TCZ) on NT-proBNP level changes in patients with rheumatoid arthritis (RA) during a 12- month (m) follow-up period.

Methods: The investigation enrolled 31 patients (pts) (26women/5men) with the lack of efficacy/resistance and/or intolerance of basic anti-inflammatory drugs (DMARDs); median age was 54[45; 61] years, median disease duration 10 [62;168]m; DAS28 6,2[5,1;7,1]; SDAI 35,0[23,9;51,0], CDAI 30,0[21,0;42,0], serum positivity for rheumatoid factor (RF)(100%)/anti-cyclic citrullinated peptide antibodies (ACCP)(84%). The study did not include RA pts with congestive heart failure. High incidence of traditional risk factors was found in RA pts: arterial hypertension - in 75%, dyslipidemia - 61%, smoking - 17%, overweight - 61%, family history of cardiovascular diseases - 36%, hypodynamia - 68%. Coronary artery disease was diagnosed in 11% RA pts. Lack of efficacy of 3 or more DMARDs was found in 46% of pts, intolerance to previous therapy with DMARDs - in 54% pts. These patients were administered TCZ(8mg/kg) every 4 weeks: 39% were receiving TCZ monotherapy, and 61% - TCZ in combination with methotrexate (20 [18;25]mg/week). Serum levels of of NT-proBNP were measured using electrochemiluminescence method Elecsys proBNP II (Roche Diagnostics, Switzerland).

Results: Significant positive changes in major disease activity clinical and laboratory parameters were found in RA pts after 12 m of TCZ infusion: 54% of pts achieved remission (DAS28<2,6) and 46% of pts managed to decrease activity to low level (DAS28<3,2) with accompanying improvement in DAS28, levels of ESR, C-reactive protein (CRP), and RF (table 1).

	Baseline	12 m	P
DAS 28	6,2 [5,1; 7,1]	2,7 [1,5; 3,3]	<0,001
ESR, mm/hr	38 [24; 54]	8 [4; 16]	<0,001
CRB, mg/l	27 [10; 49]	0,5 [0,2; 0,7]	<0,001
RF, IU/ml	130 [30; 564]	38 [23; 332]	нд
ACCP, IU/ml	284 [34; 300]	112 [32; 300]	нд
NT-proBNP, pg/ml	75,8 [43,0; 100,7]	37,8 [25,1; 78,5]	0,001

TCZ therapy resulted in decrease of median NT-proBNP levels from 75,8 [43,0;100,7] to 37,8[25,1;78,5] pg/ml (p=0,01), while rate of elevated (≥100pg/ml) NT-proBNP levels did not change (13%). ΔNT-proBNP correlations of with ΔESR (R=0,43; p<0,05] and with ΔCRB (R=0,46; p<0,05] were documented after 12m of TCZ therapy. No direct correlation between ΔNT-proBNP and changes in disease activity, or RF, or ACCP has been established. There was no noticeable differences in NT-proBNP levels in RA pts receiving TCZ monotherapy and TCZ in combination with methotrexate.

Conclusion: Obtained preliminary results show that 12m of TCZ therapy resulted in decreased RA activity and lower levels of NT-proBNP on both regimens – mono - or combination (TCZ+ MT) therapy.

Lowering NT-proBNP concentrations are associated with positive dynamics of inflammatory markers (CRP, ESR), therefore allowing to suggest increased NT-proBNP levels should be considered as a component of disease activity.

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FRI0094

LONG TERM DRUG SURVIVAL FOR BIOSIMILAR SB4 ETANERCEPT IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS PATIENTS WITH A NON-MEDICAL SWITCH FROM ETANERCEPT REFERENCE DRUG

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Background: In the new millennium biologic therapies e.g. tumor necrosis factor inhibitors (TNFi) have played a major role improving clinical outcomes in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (ax-SpA). A major limitation in many countries for prescribing these drugs has been the high drug costs. The patent period for several of these TNFis e.g. infliximab, etanercept and adalimumab has ended and as a consequence biosimilar TNFis are now reaching the market. This has a cost saving potential for payers. In Norway, encouraged by the health authorities, non-medical switch from originator to biosimilar has been performed in most patients on biologic originator drugs with biosimilar drugs available, including etanercept. To the best of our knowledge no longer than one year real life experienced real life evidence data for non-medical switch from originator etanercept to biosimilar etanercept SB4 exist (ref.1).

Objectives: To explore three-year drug survival for biosimilar SB4-etanercept in RA, PsA and ax-SpA patients with a non-medical switch from etanercept originator to SB4.

Methods: At the participating outpatient clinics patients with RA, PsA and ax-SpA are monitored using a clinical computer system, as standard clinical care. Demographic, clinical and treatment data were retrieved from the computer system for patients who started treatment with biosimilar etanercept SB4 between January 2016 and January 2019.

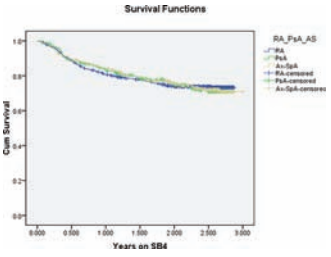
Kaplan-Meier survival curves were used to explore drug survival. Survival differences between groups were tested using Breslow statistics.

Results: At the participating outpatient clinics since 2016 a total of 474 RA, 249 PsA and 320 ax-SpA patients had a non-medical switch from etanercept originator to biosimilar etanercept SB4. In RA, PsA and ax-SpA patients the percentage of women was 68.2%, 42.6% and 30.3%, the percentage of current smokers 17.0%, 12.8% and 19.6%, mean (SD) age was 63.0 (13.1), 58.2 (11.3), 53.1 (12.1) years and disease duration 16.8 (9.8), 16.1 (9.7), 17.7 (11.0) years, respectively. In RA 80.0% were anti-CCP positive and in PsA and ax-SpA 34.4% and 90.8% were

HLAB27 positive. In the table selected disease measures at baseline are shown.

	RA	PsA	Ax-SpA
DAS28	2.6 (1.2)	2.2 (1.1)	-
ESR mm/hr	15.9 (15.1)	12.2 (13.9)	12.0 (15.1)
CRP mg/l	4.9 (8.6)	4.3 (7.6)	5.5 (10.3)
Fatigue (VAS 0-100)	34.7 (30.7)	35.8 (29.3)	40.9 (30.0)
Pain (VAS 0-100)	31.3 (23.8)	31.2 (24.1)	33.7 (24.6)
MHAQ	0.42 (0.47)	0.37 (0.40)	0.40 (0.40)
BASDAI	-	-	3.1 (2.3)
BASFI	-	-	2.6 (2.3)

No significant difference (p=0.97) in drug survival for SB4 was seen between RA, PsA and ax-SpA patients. Mean (95% CI) SB4 drug survival time (years) was for RA 2.3 (2.2-2.4), for PsA 2.3 (2.2-2.4) and for ax-SpA 2.4 (2.3-2.5). In the figure below Kaplan-Meier drug survival curves are shown. Men had a statistically significant longer mean drug survival than women (2.5 (2.4-2.6) vs 2.2 (2.1-2.3), p=0.001).



Conclusion: Our long term real life data show that the majority of patients with a non-medical switch from originator etanercept to biosimilar etanercept SB4 remained on the drug. No significant difference in drug survival was seen between RA, PsA and ax-Spa patients. Men however had a significantly longer drug survival than women. Further analyses are needed to explore reasons for cessation across gender and patient groups.

REFERENCE:

[1] Glintborg B et al. Ann Rheum Dis 2018;0:1-9

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FRI0095 CHANGES IN B CELL PROFILE AS INDICATOR OF CLINICAL REMISSION TO TNF INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease with the typical characteristic of synovitis of small-sized and medium-sized joints that leads to cartilage and bone damage. TNF inhibitors (TNFi) are widely used for the treatment of rheumatoid arthritis (RA) however, there are still no objective indicators of clinical response to TNFi therapy.

Objectives: To analyse the change of peripheral blood mononuclear cells (PBMC) profile after 6 months (m) of treatment with TNFi in order to find cellular indicators of response.

Methods: Prospective bi-center pilot study including 100 RA patients receiving TNFi therapy. PBMC were isolated from patients at baseline and 6m of treatment, and were analysed by flow-cytometry. Clinical activity at baseline and 6m of TNFi treatment was assessed by DAS28. Clinical remission (DAS28≤2.6) after 6m of treatment was considered as optimal response. The association between clinical remission and the percentage of change (Δ, 6m-0m) within each PBMC subset was analysed through univariate logistic regression model (odds ratio; 95% CI; β; p-value). All the analyses were adjusted by sex, age, disease duration, concomitant-methotrexate, seropositivity (ACPA and/or Rheumatoid factor) and baseline-DAS28.

Results: Demographic characteristics before starting TNFi therapy are shown in Table 1. After 6m of TNFi treatment, 40% patients achieved clinical remission. Decreased percentage of B cells (ΔCD19+) was found after 6m of TNFi treatment in optimal responders, while suboptimal responders did not show differences with the baseline (OR: 0.78; 95% CI: 0.63-0.97; β: -0.25; p: 0.027) (Figure 1). This effect was essentially owing to a reduction of naïve B cells (OR: 0.76; 95% IC: 0.62-0.94; β: -0.27; p: 0.011) (Figure 1). No significant association was found between the other PBMC subsets (monocytes, NK cells, CD4+ T cells and CD8+ T cells) and clinical remission (Figure 1).

Table 1

Baseline patients' characteristics	**Total patients (n=100)**
Age (years); *mean±SD*	*53±13*
Female; n (%)	*84 (84)*
Disease duration (years); *median (IQR)*	*8 (4-12)*
Rheumatoid factor positive; n (%)	*77 (77)*
ACPA positive; n (%)	*83 (83)*
Smoking habit; n (%)	
non-smoker	*46 (46)*
smoker	*20 (20)*
ex-smoker	*34 (34)*
Body mass index (kg/m^2); *median (IQR)*	*24.8 (22.9-29.6)*
DAS28; *mean±SD*	*4.8±1.2*
Previous TNFi treatment; n (%)	*13 (13)*
TNFi type; n (%)	*13 (13)*
Monoclonal antibodies	*55 (55)*
Etanercept	*45 (45)*
Concomitant csDMARD; n (%)	*96 (96)*
Only Methotrexate (MTX)	*51 (51)*
*Only other csDMARDs (OD)**	*18 (18)*
MTX + OD	*27 (27)*

* Other csDMARDs: leflunomide, sulphasalazine, hydroxychloroquine

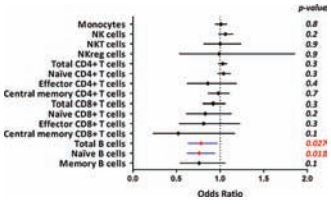


Figure 1. Association between the percentage of change (ΔPBMC, 6m-0m) within each PBMC subset and the clinical remission. Univariate logistic regression analysis was performed for each PBMC subset. The analyses were adjusted by sex, age, disease duration, concomitant-methotrexate, seropositivity and baseline-DAS28.The percentage of changes (Δ, 6m-0m) in total B cells and in naïve B cells were independently associated with the clinical response. No association was found in other PBMC subsets.

Conclusion: Our results suggest that B cells may be useful as a cellular indicator of response to TNFi in RA patients.

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FRI0096 TNF CONCENTRATIONS DURING TREATMENT OF INFLAMMATORY DISEASES WITH GOLIMUMAB

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Background: Golimumab is a monoclonal antibody that binds TNF, counteracting its pro-inflammatory effects. Berkhout et al. (2019) described the development of a novel drug-tolerant assay to quantify TNF during TNF-inhibitor treatment. Using this assay, they analyzed the dynamics of TNF during treatment of rheumatoid arthritis (RA) patients with adalimumab and found that TNF levels shortly after treatment initiation predict nonresponse (1). Our study is the first to measure TNF levels during golimumab treatment, using the same drug-tolerant assay.
Objectives: To describe the dynamics of TNF in patients with RA, ankylosing spondylitis (AS) or psoriatic arthritis (PsA) during golimumab treatment.
Methods: Consecutive patients with RA, AS, or PsA starting golimumab treatment were included in this prospective observational cohort study, named the Reade Rheumatology Registry. Serum samples drawn during the study visits were analyzed for drug levels, anti-drug antibody (ADA) formation, and TNF concentrations using a regular enzyme-linked immunosorbent assay (ELISA), a radioimmunoassay, and a drug-tolerant competition ELISA, respectively. Regression analyses were used to analyze the data. Missing data was imputed using last observation carried forward.
Results: In total, 304 serum samples from 69 patients were included in this study. The median follow-up period was 52 (interquartile range (IQR) 16-130) weeks. Median TNF concentration at baseline was 4 (IQR 3-105) pg/ml and this increased to 68 (37-127) pg/ml four weeks after treatment initiation. During follow-up, TNF concentrations remained stable for the majority of patients (Figure 1). TNF levels at baseline were already high (≥30 pg/ml) in 25% of the patients. These patients used a previous TNF-inhibitor with a median of 19 (IQR 11-32) days before start of golimumab. In contrast, patients with low baseline TNF concentrations were TNF-inhibitor naive, used a TNF-inhibitor longer before the start of golimumab treatment (median 489 (IQR 56-816) days), or used a biologic with a different target. A trend was found for the association between drug level and TNF concentration during follow-up; patients with low TNF concentrations (<30 pg/ml) had median drug levels of 0.32 (IQR 0.03-1.00) µg/ml, while patients with high TNF concentrations (≥30 pg/ml) reached a median drug level of 1.45 (0.80-2.47) µg/ml (odds ratio (OR) 1.51, CI: 0.97-2.37, p=0.071). No association was found between TNF concentrations at week 4 and low disease activity at week 52, defined as DAS28 ≤3.2 or ASDAS <2.1 (OR 1.00, CI: 1.00-1.00, p=309). Four patients (6%) developed detectable ADAs.

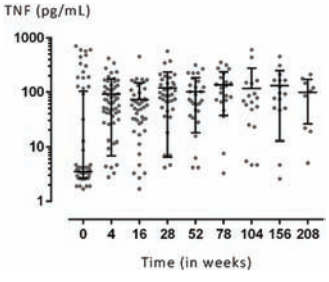


Figure 1

Conclusion: Golimumab therapy was found to induce an increase in TNF concentrations, independent of disease activity. This is in line with what has been found for adalimumab treatment. However, TNF concentrations measured in this study were at least twice as low as TNF concentrations during adalimumab treatment (1). The high baseline TNF concentrations in 25% of the patients were also surprising, as it indicates that patients switch to golimumab while their TNF is still in complex with a previous TNF-inhibitor.

REFERENCE:

[1] L.C. Berkhout, M.J. l'Ami, J. Ruwaard, M.H. Hart, P.O.-d. Heer, K. Bloem, M.T. Nurmohamed, R.F. Vollenhoven, M. Boers, D.F. Alvarez, C.H. Smith, G.J. Wolbink, T. Rispens, Dynamics of circulating TNF during adalimumab treatment using a drug-tolerant TNF assay. Sci. Transl. Med. 11, eaat3356 (2019).

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FRI0097 RA PATIENTS' PERSPECTIVES ON BIOLOGICAL DMARD-INDUCED ADVERSE DRUG REACTIONS AND THEIR BURDEN

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Background: Numerous biological DMARDs (bDMARDs) are used in RA treatment, however detailed knowledge of patients' perceptions on drug use and the impact of adverse drug reactions (ADRs) is sparse.
Objectives: To gain insight into bDMARD-induced ADRs and their burden from the RA patients' perspective.
Methods: The Dutch Biologic Monitor is an ADR-patient web-based questionnaire used for a prospective, multicentre, event monitoring cohort study including patients using a bDMARD for an immune-mediated inflammatory disease between January 1, 2017 and December 31, 2018. Patients were asked to complete questionnaires bi-monthly about used bDMARDs, indication and bDMARD-induced ADRs. ADRs were coded according to MedDRA terminology and their impact was measured on a 5-point scale, ranging from 1 (no burden) to 5 (very high burden). Per patient, every recurrent unique ADR was included as one ADR. ADRs regarding infections (INF), skin (SK), gastrointestinal (GI) and injection site (INJ) were clustered and analysed for the reported prevalence and burden. Fatigue and headache were separately analysed for prevalence and burden. The prevalence of clustered ADRs between the various bDMARDs was compared using a χ^2-test and the average burden was compared using a Mann-Whitney U test.
Results: In the Dutch Biologic Monitor 583 consecutive (44.8%) RA patients were included (71.2% female, average age 59 years, SD±12.4) using the originator or a biosimilar of etanercept (ETN, 265), adalimumab (ADA, 196), tocilizumab (41), abatacept (35), certolizumab pegol (23), rituximab (19), infliximab (18), golimumab (15), sarilumab (2), secukinumab (1), anakinra (1). Almost half of the patients (276; 47.3%) reported at least one bDMARD-induced ADR with a total of 703 ADRs in 2,559 completed questionnaires. Patients reported 129 INJ reactions (129 ADRs/583 pts, prevalence of 22.1%, reported by 86 pts) with an average

burden of 1.7 (SD±0.8), 57 GI reactions (9.8%, 41 pts) with an average burden of 2.9 (SD±1.1), 102 SK reactions (17.5%, 64 pts) with an average burden of 2.9 (SD±1.1) and 109 INFs (18.7%, 79 pts) with an average burden of 3.3 (SD±1.0). Prevalence of INJ and GI reactions was significantly higher among ETN users than among ADA users (INJ: 76 ADRs/265 ETN users (28.7%) vs 30 ADRs/196 ADA users (15.3%), P=0.007; GI: 30/265 (11.3%) vs 9/196 (4.6%), P=0.01). The prevalence of INFs and SK reactions did not differ. The perceived burden of GI reactions was higher for ETN than for ADA users (3.1 ±1.0 vs 2.0 ±0.7, p=0.006) but did not differ for other clustered ADRs. The number of patients using other bDMARDs was too low for further analysis. Prevalence of bDMARD-induced headache was 1.9% (12 ADRs/583 pts) with an average burden of 3.4 (SD±0.9). Prevalence of bDMARD-induced fatigue was 4.3% (25 ADRs) with an average burden of 2.7 (SD±1.0).

Conclusion: Almost half of the RA patients reported bDMARD-induced ADRs. From the patients' perspective INJ reactions have the highest prevalence with a relatively low burden, whereas INFs and headache are less prevalent but give the highest burden of the analysed ADRs. Further studies are required to obtain more insight into the perceived differences in ADRs between bDMARDs.

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FRI0098 SWITCHING RATE OF BIOLOGICAL DMARDS IN RHEUMATOID ARTHRITIS PATIENTS: TREASURE – REAL LIFE DATA

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Background: In rheumatoid arthritis (RA), biologic DMARDs are important treatment options in resistant patients. Inefficacy or side effects may cause switching between these drugs.

Objectives: This study aimed to determine features of patients switching from one biologic DMARD to another in RA treatment and to investigate associated reasons for switching.

Methods: This multicenter, prospective observational cohort study used the TReasure database in which web-based registration of RA and spondyloarthritis patients are being performed in 15 centers across different regions of Turkey. In this study, data of RA patients switching from one biologic agent to another were analyzed. Demographic and clinical data, follow-up duration, time to switch, and reasons for switching were retrieved from the database.

Results: Of the included 2115 RA patients, 829 (39.2%) switched between biologic agents (switched group) and 1286 (60.8%) continued to receive their current therapies (continued group). The median follow-up duration of all patients was 3.7 years and the median time to switch was 1.1 years. In the switched group, the proportion of females and the median HAQ-DI score were higher as well as disease duration was longer (Table 1). Among the biologic agents used at first, 60.9% of the patients were receiving an anti-TNF agent and 39.1% of the patients were receiving other biologic agents (Table 2, figure 1). In the switched group (n=829), the main reasons for switching were secondary inefficacy (n=269), primary inefficacy (n=238), and side effects (n=178) followed by primary or secondary unknown inefficacy (n=30), patient's demand (n=21), physician's request (n=16), willing to be pregnant (n=7), other (n=31), and unknown (n=54).

Table 1. Demographic and clinical features of the study groups

	N	Switched Group	N	Continued Group	p
Age, year, median (min-max)	829	54 (19-84)	1286	55 (18-91)	0.121
Sex, n (%) Female		688 (83.0)		1000 (77.8)	**0.003**
Sex, n (%) Male		141 (17.0)		286 (22.2)	
Body mass index, median (min-max)	823	27.74 (14.33-66.1)	1256	28.05 (15.59-58)	0.640
Disease duration, year, median (min-max)	806	12 (0-43)	1245	8 (0-41)	**<0.001**
ESR, mm/h, median (min-max)	538	34 (2-120)	1029	33 (2-174)	0.311
CRP, mg/dL, median (min-max)	533	15.7 (0.04-335)	1019	14.7 (0-11062)	0.859
RF positivity, n (%)	776	508 (65.5)	1193	785 (65.8)	0.878
Anti-CCP positivity, n (%)	585	345 (59.0)	945	582 (61.6)	0.309
Swollen joint count, median (min-max)	250	3 (0-24)	612	3 (0-32)	0.994
Tender joint count, median (min-max)	253	6 (0-30)	609	7 (0-44)	0.217
PtGA-VAS, median (min-max)	432	70 (0-100)	954	70 (0-100)	0.347
Pain-VAS, median (min-max)	345	70 (0-100)	879	70 (0-100)	0.142
Fatigue-VAS, median (min-max)	337	70 (0-100)	873	70 (0-100)	0.066
HAQ-DI score, median (min-max)	300	1 (0-3)	832	0.9 (0-2.95)	**0.040**
CDAI score, median (min-max)	115	15.5 (0-72)	293	21.5 (0-89)	0.117
SDAI score, median (min-max)	113	37.5 (1.72-137)	290	43 (2-389)	0.057

Table 2. Distribution of the biologic agents used at first and second and the rate of patients switching to another biologic agent

Biologic agents used at first	n (%)	Biologic agents used after switch	n (%)
Etanercept	482 (22.8)	Adalimumab	152 (18.3)
Adalimumab	404 (19.1)	Etanercept	135 (16.3)
Abatacept	265 (12.5)	Rituximab	140 (16.9)
Rituximab	234 (11.1)	Tocilizumab	103 (12.4)
Tofacitinib	209 (9.9)	Abatacept	101 (12.2)
Infliximab	152 (7.2)	Tofacitinib	61 (7.4)
Golimumab	136 (6.4)	Certolizumab	51 (6.2)
Certolizumab	115 (5.4)	Infliximab	44 (5.3)
Tocilizumab	114 (5.4)	Golimumab	38 (4.6)
Anakinra	4 (0.2)	Anakinra	4 (0.5)

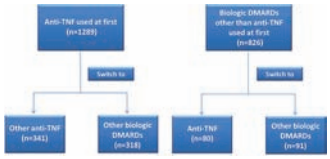


Figure 1. Switching pattern of the switched group

Conclusion: The patients in the Treasure database were followed-up approximately 4 years and about one-third of the patients had to switch from one biologic DMARD to another. The main reasons for this switching were primary (29.2%) and secondary (33.0%) inefficacy and 20% of the patients had to switch due to side effects. According to the switching pattern, about half of the patients using an anti-TNF agent at first switched to another anti-TNF agent and the other half switched to other biologic agents.

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FRI0099

PREDICTIVE FACTORS FOR REMISSION ACHIEVEMENT BY TOCILIZUMAB MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER INADEQUATE RESPONSE TO METHOTREXATE: A POST HOC ANALYSIS OF THE SURPRISE STUDY

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Background: Interleukin (IL)-6 pathway inhibitors are suggested by European League Against Rheumatism recommendations to have some advantages in rheumatoid arthritis (RA) patients who are not suitable to use methotrexate as comedication compared with other biological disease-modifying antirheumatic drugs. However, it remains to be elucidated what predicts remission achievement by IL-6 pathway inhibitor monotherapy.
Objectives: To identify predictive factors for clinical and structural remission by tocilizumab without methotrexate in patients with RA.
Methods: This is a post hoc analysis of the SURPRISE study, a 2-year randomized, controlled study comparing the efficacy of tocilizumab with (ADD-ON) and without methotrexate (SWITCH) in active RA patients despite methotrexate therapy. The primary endpoint was the DAS28-ESR remission (< 2.6) at week 24. The change in modified total Sharp score from baseline to week 52 (ΔmTSS/year) was also assessed as an endpoint. The effect of clinical parameters, including serum levels of CRP, IL-6, serum amyloid A (SAA), MMP-3, RF and IgG at baseline, on the achievement of DAS28 remission at week 24 was estimated by logistic regression analysis. Multivariate analysis was performed after adjusting for age, gender, height, body weight, body mass index, disease duration, the dose of glucocorticoids, and that of methotrexate.
Results: In SWITCH (n = 96), CRP, SAA, RF and DAS28 at baseline showed predictive value for DAS28 remission at week 24 in univariate analysis. Multivariate analysis confirmed SAA, RF and DAS28 at baseline, but not CRP, as predictive factors, with SAA having the highest value (OR [95%CI] by decrease of 5.0 μg/mL = 1.011 [1.002-1.020], p = 0.01, ROC-AUC = 0.731). SAA of < 50.0 μg/mL showed extremely high predictive value for DAS28 remission (OR [95%CI] = 6.012 [1.997-18.096], p = 0.0008, ROC-AUC = 0.761). Furthermore, structural remission (ΔmTSS/year ≤ 0.5) rate at week 52 was significantly higher in patients with SAA of < 50.0 μg/mL than those with SAA of ≥ 50.0 μg/mL (71% vs 51%, p = 0.048). In contrast, in ADD-ON (n = 98), only DAS28 at baseline showed predictive value for DAS28 remission at week 24 in both univariate and multivariate analysis. In patients with SAA < 50.0 μg/mL, both DAS28 remission (75% vs 77%, p = 0.79) and structural remission (71% vs 68%, p = 0.71) rate were comparable between SWITCH and ADD-ON.
Conclusion: SAA levels at baseline can predict the necessity of concomitant methotrexate in tocilizumab initiation in patients with RA. Patients with low levels of SAA at baseline may benefit similarly from tocilizumab therapy with and without methotrexate in terms of achieving clinical and structural remission.

REFERENCE:

[1] Kaneko Y, et al. Ann Rheum Dis. 2016 Nov;75(11):1917-1923. Kaneko Y, et al. Ann Rheum Dis. 2018 Sep;77(9):1268-1275.

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FRI0100

TOWARDS THE LOWEST EFFICACIOUS DOSE (TOLEDO): RESULTS OF A MULTICENTER NON-INFERIORITY RANDOMIZED OPEN-LABEL CONTROLLED TRIAL ASSESSING TOCILIZUMAB OR ABATACEPT INJECTION SPACING IN RHEUMATOID ARTHRITIS PATIENTS IN REMISSION

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Background: Biologic Disease Modifying Anti-Rheumatic Drugs (bDMARD) tapering is possible in rheumatoid arthritis (RA) patients in sustained remission. However, only minimal data are available on progressive tapering of non-TNF bDMARD such as tocilizumab (TCZ) or abatacept (ABA).
Objectives: The TOLEDO (Towards the Lowest Efficacious Dose) trial aimed to assess the impact on disease activity of progressive spacing of TCZ or ABA in RA patients in sustained remission compared to their maintenance at full dose.
Methods: In this multicenter open-label non-inferiority randomized controlled trial, patients fulfilling ACR-EULAR 2010 criteria for RA were included if they were 1) treated with ABA or TCZ for $\geq$ 1 year (monotherapy or in combination with csDMARD, corticosteroid allowed at a dose $\leq$ 5 mg/day), 2) in DAS28VS remission (DAS28 <2.6) for $\geq$ 6 months and 3) with no X-ray damage progression in the year before inclusion. They were randomized into 2 arms: TCZ or ABA maintenance at full dose or DAS28-driven progressive injection spacing arm adapted in which bDMARD IV or SC injections were progressively spaced out every 3 months according to a predetermined 4-step algorithm up to bDMARD discontinuation at step 4. Spacing was reversed to the previous interval in case of relapse. The primary outcome was the evolution of disease activity according to DAS44 during the 2-year follow-up, which was analyzed with a linear mixed-effect model. Relapse and durable relapse rates (respectively defined as DAS28 > 3.2, and DAS28 >3.2 not recovered at the following visit despite bDMARD escalation at previous step) were also compared between the 2 arms. Analysis were done per protocol (PP) according to a non-inferiority hypothesis (non-inferiority margin at 0.25 for DAS44 and 0.07 for relapse rates).
Results: 117 patients were randomized in Spacing arm and 116 in Maintenance arm (90 and 112 respectively for PP analysis). 165 (72.4%) patients were treated with TCZ and 63 (27.6%) with ABA. At the end of the follow-up in the Spacing arm, 12.4% of patients were able to discontinue their bDMARD (step 4), 38.9% had tapered them (step 1 to 3) and 23.9% needed to go back to initial step (step 0). In terms of disease activity, the non-inferiority of the Spacing strategy in terms of disease activity (DAS44) was not demonstrated for the whole population and the ABA subgroups: slope difference of 11% (95% CI: -9%, 32%) and 37% (95% CI: -4%, 77%) respectively. However, it was satisfied for the TCZ subgroup: slope difference 3% (95% CI: -21%, 27%) (Figure 1). Relapses (Figure 2) were more frequent in the Spacing arm: +45% (95% CI: 32%, 57%), +48% (95% CI: 24%, 71%) and +43% (95%CI: 29%, 58%) in the whole population, ABA and TCZ subgroups respectively. Durable relapses were more frequent in the Spacing arm: +10% (95%CI: 0%, 19%), 16% (95%CI: -5%, 37%) and 7% (95%CI: -3%, 16%) in the whole population, ABA and TCZ subgroups respectively, compared with Maintenance arm.
Conclusion: The TOLEDO trial generally failed to demonstrate the non-inferiority of the proposed tapering strategy in comparison to maintenance at full dose. However, the non-inferiority was satisfied in terms of disease activity for the TCZ subgroup.
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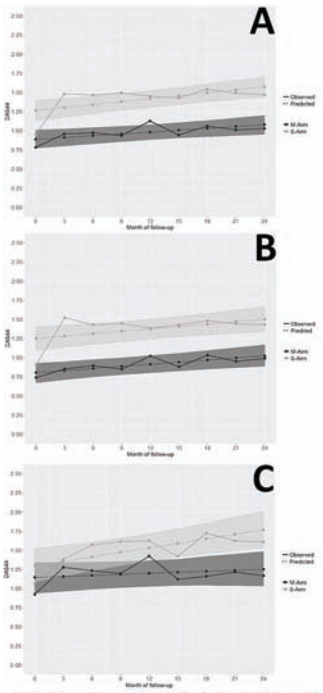


Figure 1: evolution of DAS44 in overall groups (A), TCZ patients (B) and ABA patients (C), and between Maintenance arm (M-arm) and Spacing arm (S-arm)

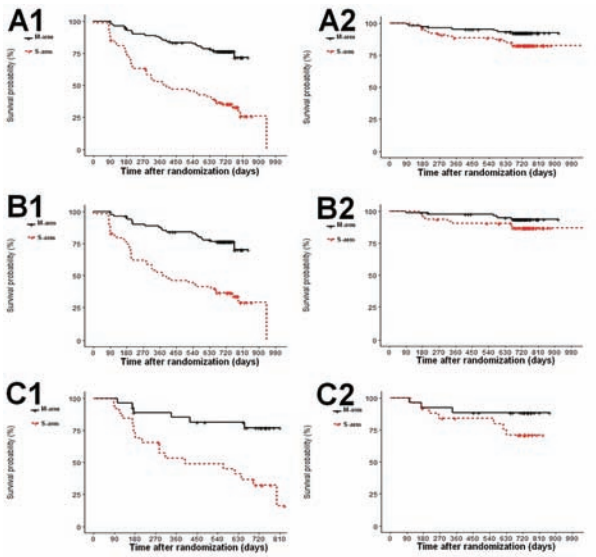


Figure 2: relapse-free (1) and durable relapse-free (2) survival in overall (A), TCZ (B), and ABA (C) populations and between Maintenance arm (M-arm) and Spacing arm (S-arm)

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FRI0101

NON-MEDICAL SWITCHING FROM ORIGINATOR TO BIOSIMILAR ETANERCEPT – NO EVIDENCE FOR A RELEVANT NOCEBO EFFECT – A RETROSPECTIVE ANALYSIS OF REAL-LIFE DATA

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Background: Real-world data about switching patients from originator product to a biosimilars are important to assess and to document the outcome of switches in clinical practice in order to confirm the low risk of major problems. It has been hypothesized that lack of efficacy and adverse drug events (ADEs) upon switching from reference biologics to biosimilar products are related to the nocebo effect [1].

Objectives: To evaluate the effectiveness and safety of systematic non-medical switching from innovator etanercept to biosimilar etanercept SB4 in adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) in a real-life setting based on different information strategies before switching.

Methods: Data of all adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) who had received innovator etanercept and were switched in our specialized center from innovator to biosimilar etanercept for economic reasons were retrospectively analysed. Whether or not patients were informed about the switch was left to the discretion of the treating physician. Disease activity and function were regularly assessed, and any changes were recorded in two consecutive visits at week 12 and 24. The scores documented at week 12 week after switching were taken as primary outcome. AEs were documented.

Results: A total of 84 patients were included (44 RA, 25 axSpA and 15 PsA patients), 24 of which had received information about switching (28.5%). The scores at week 12 of both, disease activity and function, remained rather unchanged (Table 1). Whether patients had been informed about switching or not did not influence outcomes or AE. The retention rate of the biosimilar was 96.4% (n=81) at week 12 and 87.6% (n=71) at week 24 (Figure 1). While 7 patients were lost to follow-up, 6 patients discontinued due to inefficacy or AE, including one malignant melanoma. Overall, 18 AEs were reported in 10 patients (12%). In 3 patients (3.6%) who had 5 AEs in the first 12 weeks the innovator was successfully re-administered.

Conclusion: Systematic switch from innovator to biosimilar etanercept was not associated with changes in disease activity or function in all three indications within 12 weeks. This was independent of information on the switch transmitted to the patients.

Table 1. Patient characteristics

	Assessment	Baseline (n=84)	Follow-up 12 weeks (n=81)	Follow-up 24 weeks (n=74)
RA	DAS28	3,1 (1,4)	2,8 (1,0)	3,1 (1,3)
	HAQ	1,2 (0,7)	1,3 (0,7)	1,3 (0,7)
	CRP (mg/dl)	0,5 (0,6)	0,6 (0,8)	0,7 (0,9)
PsA	DAS28	2,9 (1,4)	1,9 (1,4)	2,8 (1,5)
	HAQ	0,8 (0,5))	0,9 (0,9)	0,9 (0,9)
	CRP (mg/dl)	0,4 (0,5)	0,6 (0,6)	0,6 (0,5)
axSpA	BASDAI	4,8 (2,5)	5,0 (2,5)	4,7 (2,4)
	ASDAS	2,6 (1,3)	2,7 (0,9)	2,7 (0,8)
	BASFI	5,3 (2,7)	5,5 (2,7)	4,9 (2,8

*Values are mean ± standard deviation

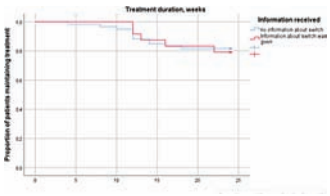


Figure 1. Retention of biosimilar stratified for patients with and without information.

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REFERENCE:

[1] Kristensen, L.E., et al., *Non-pharmacological Effects in Switching Medication: The Nocebo Effect in Switching from Originator to Biosimilar Agent*. BioDrugs, 2018. 32(5): p. 397-404.

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Braun Shareholder of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: Abbott, Bristol Myers Squibb, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: Abbvie (Abbott), Amgen, Baxter, Biogen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Hexal, Janssen, Lilly, Medac, MSD (Schering-Plough), Mylan, Mundipharma, Novartis, Pfizer (Wyeth, Hospira), Roche, Sanofi-Aventis and UCB, Consultant for: Abbvie (Abbott), Amgen, Baxter, Biogen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Hexal, Janssen, Lilly, Medac, MSD (Schering-Plough), Mylan, Mundipharma, Novartis, Pfizer (Wyeth, Hospira), Roche, Sanofi-Aventis and UCB, Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Consultant for: Abbott, Bristol Myers Squibb, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Speakers bureau: Abbvie (Abbott), Amgen, Baxter, Biogen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Hexal, Janssen, Lilly, Medac, MSD (Schering-Plough), Mylan, Mundipharma, Novartis, Pfizer (Wyeth, Hospira), Roche, Sanofi-Aventis and UCB, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB

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FRI0102

GOLIMUMAB IMPROVES WORK PRODUCTIVITY AND ACTIVITY AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA), ANKYLOSING SPONDYLITIS (AS) AND PSORIATIC ARTHRITIS (PSA): FINAL RESULTS FROM A NON-INTERVENTIONAL STUDY IN GERMANY (GO-ART)

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Background: Golimumab (GLM) has shown its efficacy and tolerability in various randomized clinical trials. Systemic data for GLM regarding health-economic parameters in daily clinical practice are essential not only for pharmaceutical companies but also for cost-benefit analyses in Germany.

Objectives: This prospective NIS was designed to evaluate the impact of GLM therapy on work productivity and activity as well as Quality of Life (QoL) in patients with RA, AS or PsA in Germany under routine settings over an observation period of 12 months, plus an additional voluntary extension period of 12 months (total 24 months) to collect long-term data on health economic parameters.

Methods: GO-ART was an observational prospective study on patients with RA, AS or PsA (biologic-naïve and biologic-experienced) who started treatment with GLM at 63 sites of Germany.

The primary endpoint was the change in work productivity/activity impairment as measured by Work Productivity and Activity Impairment (WPAI) questionnaire from baseline, measured primarily at month 3 and secondarily at months 6, 12 and 24.

As secondary endpoint the change in quality of life (RAQoL for RA patients, ASQoL for AS patients and NAPPA-QoL for PsA patients) was assessed.

Results: 748 patients (RA=250, PsA=249, AS=249) started GLM therapy.

The primary efficacy endpoint was analyzed in the modified intention-to-treat (mITT) subset of 493 patients (RA=158, PsA=157, AS=178) with full-time or part-time employment at baseline (mITTe).

A total of 348 patients entered the additional 12-month observation period, of which 303 completed the 24-month assessment.

By 3 months after initiation of Golimumab treatment, a marked improvement was seen in all 4 WPAI domain scores ("absenteeism" (time off work), "presenteeism" (on-the-job productivity), "total work productivity impairment" (TWPI), and "activity impairment") in daily living because of patient's health problems related to RA, PsA or AS, as shown in Table 1 (all p-values <0.05).

The statistically significant improvements in the mean WPAI domain scores were maintained over the 24-month observation period in all 3 indications with a higher treatment effect regarding "activity impairment" and "presenteeism" compared to "absenteeism" (Table 1).

Quality of life improved significantly (p<0.0001) from baseline at month 3, 6, 12 and 24 in patients with RA (RAQoL), AS (ASQoL) and PsA (NAPPA-QoL) based on questionnaire data of 237 RA patients (RA-mITT), 228 AS patients (AS-mITT) and 235 PsA patients (PsA-mITT) indicating a clinically relevant improvement.

Conclusion: Treatment with GLM provided sustained improvement in WPAI and QoL in patients with RA, PsA and AS over the observational period of 24 months.

All scores of the WPAI showed a significant (p< 0.05) reduction in mean score values in each indication.

GLM leads to an improvement of work productivity and daily activities in patients already within the first 3 months of treatment.

Table 1:

WPAI - Changes in the 4 domain scores from baseline to Months 3, 12 and 24 (mITTe)

Timepoint	Statistics	Total work productivity impairment	Absenteeism	Presenteeism	Activity impairment
RA patients (mITTe: N=158)					
V0 (baseline)	N	108	135	113	154
	Mean	46.8	11.9	46.0	50.9
	SD	27.60	30.80	27.76	28.36
Change in scores:					
	N	78	110	83	133
V0 - V1 (Month 3)	Mean	-11.3	-5.8	-12.5	-13.9
[primary endpoint]	SD	23.77	29.37	23.00	26.77
	p-value	<0.0001[a]	0.0429[b]	<0.0001[b]	<0.0001[b]
V0 – V3 (Month 12)	N	67	89	75	114
	Mean	-13.2	-8.8	-12.7	-15.2
	SD	23.40	35.51	22.08	24.23
	p-value	<0.0001[a]	0.0128[b]	<0.0001[b]	<0.0001[b]
V0 – V6 (Month 24)	N	43	55	45	67
	Mean	-13.7	-7.8	-12.2	-18.4
	SD	25.84	30.73	26.10	26.32
	p-value	0.0012[b]	0.0647[b]	0.0030[b]	<0.0001[a]
PsA patients (mITTe: N=157)					
V0 (baseline)	N	114	137	115	153
	Mean	35.0	12.9	33.4	43.2
	SD	27.77	30.87	26.42	28.45
Change in scores:					
V0 - V1 (Month 3)	N	81	109	85	128
[primary endpoint]	Mean	-13.8	-4.9	-15.4	-17.4
	SD	25.02	28.33	25.98	30.44
	p-value	<0.0001[a]	0.0449[b]	<0.0001[b]	<0.0001[b]
V0 – V3 (Month 12)	N	77	99	80	118
	Mean	-10.6	-4.6	-12.7	-18.3
	SD	30.40	30.62	27.82	30.28
	p-value	0.0046[b]	0.2028[b]	0.0001[b]	<0.0001[a]
V0 – V6 (Month 24)	N	39	48	41	63
	Mean	-9.5	-1.9	-16.5	-23.4
	SD	28.99	31.56	26.84	31.36
	p-value	0.0472[b]	0.6084[b]	0.0003[a]	<0.0001[a]
AS patients (mITTe: N=178)					
V0 (baseline)	N	136	160	142	177
	Mean	48.2	14.0	45.9	52.1
	SD	28.08	29.55	26.74	25.87
Change in scores:					
V0 - V1 (Month 3)	N	104	135	111	162
[primary endpoint]	Mean	-16.9	-8.9	-15.8	-18.3
	SD	26.62	30.73	24.66	26.43
	p-value	<0.0001[a]	0.0001[b]	<0.0001[b]	<0.0001[b]
V0 – V3 (Month 12)	N	93	120	100	130
	Mean	-16.8	-6.1	-16.1	-22.8
	SD	31.92	31.46	30.45	28.77
	p-value	<0.0001[a]	0.0141[b]	<0.0001[a]	<0.0001[a]
V0 – V6 (Month 24)	N	46	64	50	72
	Mean	-24.7	-14.1	-22.0	-28.3
	SD	32.71	33.29	28.64	29.79
	p-value	<0.0001[a]	0.0002[b]	<0.0001[a]	<0.0001[b]

AS = Ankylosing Spondylitis; PsA = Psoriatic Arthritis; RA = Rheumatoid Arthritis
WPAI = Work Productivity and Activity Impairment
Total work productivity impairment = Overall impairment estimate calculated by an algorithm of absenteeism and presenteeism.
Absenteeism = Percentage of work time missed because of patient's health problem in the past 7 days.
Presenteeism = Percentage of impairment experienced while at work in the past 7 days because of patient's health problem.
Activity impairment = Percentage of impairment in daily activities because of patient's health problem in the past 7 days

[a] *t-test*; [b] *Wilcoxon Signed rank test*

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FRI0103

BENEFIT STUDY: A PAN-EUROPEAN OBSERVATIONAL STUDY TO EVALUATE REAL-WORLD EFFECTIVENESS OF SB4 FOLLOWING TRANSITION FROM ORIGINATOR ETANERCEPT (ETN) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) OR AXIAL SPONDYLOARTHRITIS (AXSPA)

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Background: Having demonstrated bioequivalence and similar efficacy, safety and immunogenicity as the originator, SB4 is approved in the EU

as an ETN biosimilar. There is limited evidence on outcomes of transition from originator to biosimilar in a multi-country real-world setting.

Objectives: To provide real-world evidence on outcomes of transition from ETN to SB4 in routine clinical practice at EU sites.

Methods: Eligible patients had RA or axSpA and had initiated SB4 in routine clinical practice following a minimum of 6 months treatment with a stable dose of originator ETN, at clinics in France, Germany, Italy, and Spain. Data were captured from patient records prospectively and/or retrospectively for 6 months following transition. Outcome measures include clinical characteristics, disease scores (DAS-28 for RA, BASDAI for axSpA) and clinical management.

Results: Analysis of 533 eligible patients (347 RA, 186 axSpA) demonstrated no clinically significant difference in disease score from baseline to 6 months post-transition; mean individual change was 0.0 (95% CI -0.1, 0.1) and 0.0 (95% CI -0.3, 0.2) at 6 months post-transition in RA and axSpA subjects respectively. Regarding dose regimen, 73.5% and 63.4% of RA and axSpA subjects transitioned from ETN 50mg QW to SB4 50mg QW; by 6 months post-transition, 73.5% and 63.4% of subjects were receiving SB4 50mg QW.

Table 1. Patient baseline characteristics and disease scores at 6 months post-transition

	RA (N=347)		AxSpA (N=186)	
	Mean (SD)	**Q1, Q3**	**Mean (SD)**	**Q1, Q3**
Age in years	60.8 (11.87)	53.0, 69.0	50.2 (13.41)	40.0, 61.0
Women n (%)	255 (73.5)	–	48 (25.8)	–
Duration of disease, years	14.7 (9.41)	7.3, 21.0	12.9 (10.51)	5.1, 17.4
BMI	27.5 (5.64)	23.3, 30.4	27.5 (3.78)	24.1, 30.5
csDMARD* concomitant to SB4 n%	186 (53.6)	–	28 (15.1)	–
NSAID concomitant to SB4 n%**	48 (13.8)	–	39 (21.0)	–
	Mean (SD)	**95% CI**	**Mean (SD)**	**95% CI**
DAS-28 at transition to SB4 (n=329)	2.0 (0.83)	1.9, 2.1	–	–
DAS-28 at 6 months post-transition to SB4 (n=242)	2.1 (0.85)	2.0, 2.2	–	–
DAS-28 Individual change from baseline to 6 months post-transition to SB4 (n=237)	0.0 (0.81)	-0.1, 0.1	–	–
BASDAI at transition to SB4 (n=173)	–	–	2.5 (1.94)	2.2, 2.8
BASDAI at 6 months post-transition to SB4 (n=124)	–	–	2.3 (1.82)	2.0, 2.7
BASDAI Individual change from baseline to 6 months post-transition to SB4 (n=121)	–	–	0.0 (1.19)	-0.3, 0.2

DAS-28 Disease Activity Score 28; BASDAI Bath Ankylosing Spondylitis Disease Activity Index; BMI body mass index; SD standard deviation; Q1 1st quartile, Q3 3rd quartile; CI Confidence Interval; *conventional synthetic disease-modifying antirheumatic drug; **non-steroidal anti-inflammatory drug

Conclusion: Patients with stable RA or axSpA who transitioned from originator ETN to SB4 maintained clinical response at 6 months post-transition. Most patients transitioned to the same dose regimen of biosimilar as they had received for the originator, remaining largely unchanged at 6 months, supporting ease and effectiveness of transition.

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FRI0104

A LARGE REAL WORLD, LONG TERM SAFETY STUDY OF PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES TREATED WITH INFLIXIMAB BIOSIMILAR (CT-P13): POOLED ANALYSIS OF FOUR GLOBAL POST-MARKETING STUDIES

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Background: CT-P13 was the first approved biosimilar monoclonal antibody globally and is currently marketed in 88 countries, including the European Union (EU) and the United States (US). Since approval, 4 observational prospective cohort studies have been conducted in the EU, Canada and Korea to assess long term safety of CT-P13 in patients with Rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and psoriasis (PSO). Safety data from the 4 studies were pooled and analysed.

Objectives: To evaluate the long-term safety of CT-P13 in patients with RA, AS, PsA and PSO in global real world, post-marketing studies

Methods: Safety data from patients registered in the 4 observational studies (KOREA PMS, CT-P13 4.2, CT-P13 4.4, and PERSIST) have been collected after marketing authorisation was granted. The incidence of Adverse Events of Special Interests (AESIs) from subjects with RA, AS, PsA and PsO who were treated at least 1 dose of CT-P13 with the data cut point of Dec27, 2017 were analysed.

Results: A total of 1579 patients were treated with at least 1 dose of CT-P13 across the 4 studies (RA = 670; AS = 819; PsA/PsO = 90). Mean age (years) of patients per RA, AS and PsA/PSO indication was 54.5, 40.3 and 52.9, respectively. Average exposure duration (days) to CT-P13 in patients with RA, AS and PsA/PSO was 280.3, 254.0 and 322.1, respectively, and the mean maximum dose of CT-P13 (mg/kg) with RA, AS and PsA/PSO patients was 3.77, 4.51 and 4.31, respectively. Treatment emergent adverse events (TEAEs) were reported in 50.15%, 37.73% and 26.67% for RA, AS and PsA/PSO, respectively. Incidence of TEAEs in RA indication is consistent with the historical rate in this population. Treatment emergent serious adverse events (TESAEs) were reported for 12.39%, 4.52% and 3.33% for RA, AS and PsA/PSO patients, respectively. Incidence of TEAEs leading to discontinuation were 8.81%, 3.42% and 7.78% for RA, AS and PsA/PSO. Two deaths and 1 death were reported among RA and AS patients, respectively. The causes of death in RA patients were acute respiratory distress syndrome (ARDS) and bronchopneumonia; the cause of death in the AS patient was unknown. AESIs of CT-P13 were analysed in safety population who were treated with CT-P13 at least once by the data cut point. No events of serum sickness, haematologic malignancy, demyelinating disorder, sarcoidosis/sarcoidosis-like reaction were reported.

Table 1. Incidence of AESIs

AESIs/ Number of patients (%)	RA N=670	AS N=819	PsA/PSO N=90[1]
Serious infection including Tuberculosis (TB)	27(4.03%)	17(2.08%)	1(1.11%)
Active Tuberculosis	3(0.45%)	5(0.61%)	0
Acute hypersensitivity	1(0.15%)	1(0.12%)	0
Haematologic reaction	8(1.19%)	5(0.61%)	2(2.22%)
Systemic Lupus erythematosus/ Lupus-like syndrome	0	0	1(1.11%)
Non-Haematologic Malignancy	6(0.90%)	0	0
Hepatobiliary Event	22 (3.28%)	34(4.15%)	0
HBV reactivation	0	1(0.12%)	0
Congestive Heart Failure	0	1(0.12%)	0

[1]6 patients of PSO were analysed with PsA patients

Conclusion: The results of this analysis show that treatment with CT-P13 is well tolerated in patients with RA, AS, PsA and PSO in the real world setting. Incidence of all AESIs including serious infection and TB are comparable to historical data in literatures[1][2] and originator Infliximab EU product information.

REFERENCES:

[1] Vander Cruyssen, et al. (2010), Seven-year follow-up of infliximab therapy in rheumatoid arthritis patients with severe long-standing refractory disease: attrition rate and evolution of disease activity.

[2] Delabaye, et al. (2010), 74-week follow-up of safety of infliximab in patients with refractory rheumatoid arthritis.

Originator Infliximab EU product information https://www.ema.europa.eu/documents/product-information/remicade-epar-product-information_en.pdf
Disclosure of Interests: Kyungmin Baek Shareholder of: Celltrion, Inc., Employee of: Celltrion, Inc., Yoon Jee Lee Employee of: Celltrion, Inc., Sujin LEE Employee of: CELLTRION, INC, HoUng Kim Shareholder of: Celltrion Healthcare.Co.,Ltd, Employee of: Celltrion Healthcare.Co.,Ltd, SeulGi Lee Employee of: Celltrion, Inc., Jeong Eun Park Employee of: Celltrion, Inc., SangJoon Lee Shareholder of: Celltrion, Inc., Employee of: Celltrion, Inc.
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FRI0105 EXPRESSION OF UNCOUPLING PROTEIN-1 IN SUBCUTANEOUS FAT IS INCREASED BY TOCILIZUMAB

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Background: Adipose tissue is an important player in cardiovascular (CV) morbidity. Thermogenic brown adipocytes, rich with uncoupling protein 1 (UCP1), increase metabolic and CV health. (1)
Objectives: Study the impact of anti-rheumatic treatment on production of UCP1 in subcutaneous fat of RA patients.
Methods: Samples of subcutaneous fat were collected from 125 female RA patients by aspiration from periumbilical region. Expression of UCP1 and a reverse cholesterol transport protein ABCA1 were measured by qPCR and analysied with respect to anti-rheumatic treatment and clinical disease activity. Bt treatment, the patient comprised 4 major groups including tocilizumab (Toci, n=14), anti-TNF (n=29), methotrexate monotherapy (n=47) and methotrexate-sulfasalazine-hyroxychloroquine (tripple therapy, n=15). CV risk was estimated with the Framingham risk algorithm.
Results: Measurable expression of UCP1 was found in 54.6% of the studied fat tissue samples. Patients on Toci had measurable expression of UCP1 in 79%, which was significantly more often than among TNFi-treated (45%, p=0.04) and MTX-treated patients (42%, p=0.02). Patients on triple therapy had also often measurable UCP1 levels compared to other groups (69% vs 43%, p=0.035). Toci patients have more lean body mass than patients treated with TNFi. This was based on lower BMI in Toci and TNFi treated patients compared to triple therapy (24.1 vs 27.1, p=0.041; 23.6 vs 27.1, p=0.017; respectively). Additionally, the estimated mucle mass by creatinin/height ratio was significantly lower in TNFi than in triple therapy (p=0.034) and Toci (p=0.008). Clinically, the treatment groups were similar in age, disease activity DAS28 and disease duration with the except for Toci. Toci patients were older (65 vs 57, p=0.04) and had numerically longer disease duration (17y vs 7y) and lower DAS28 (1.98 vs 3.11).
Notably, Toci patients had significantly higher TC compared to TNFi (p=0.027), and triple therapy (p=0.041). Triple therapy had the lowest TC levels (p=0.017). The differences were due to LDL, here patients on Toci had higher LDL than TNFi (p=0.09) and triple therapy (p=0.015). Serum HDL was similar. These differences in serum lipids were not related to expression of ABCA1 or UCP1. Despite the difference in the serum lipid profile, the estimated CV risk was significantly lower in Toci compared to MTX patients (4.1[0.87-5.75] vs 6.6[3.9-9], p=0.041).
Conclusion: In this study is Toci treatment is associated with persistent UCP1 production by adipose tissue. This was followed by lower estimated CV risk and favourable body composition in female RA patients.

REFERENCE:
[1] Carpentier, A. C., Blondin, D. P., Virtanen, K. A., Richard, D., Haman, F., & Turcotte, É. E. (2018). Brown Adipose Tissue Energy Metabolism in Humans. Frontiers in endocrinology, 9, 447. doi:10.3389/fendo.2018.00447

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FRI0106 SARILUMAB AND TOCILIZUMAB RECEPTOR OCCUPANCY (RO), AND EFFECTS ON C-REACTIVE PROTEIN (CRP) LEVELS, IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

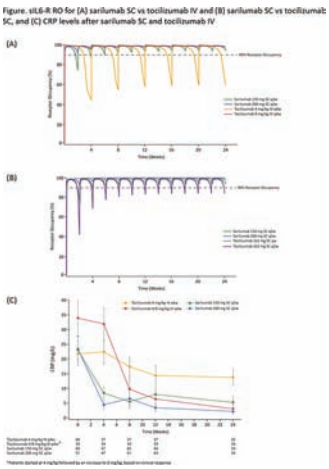
Christine Xu[1], Patrick Nolain[2], Qiang Lu[1], Anne Paccaly[3], Melitza Iglesias-Rodriguez[4], Gregory St John[3], Chad Nivens[3], Rafael Maldonado[5], Tomonori Ishii[6], Ernest Choy[7], Vanaja Kanamaluru[1]. *[1]Sanofi, Bridgewater, NJ, United States of America*; *[2]Sanofi Aventis, Montpellier, France*; *[3]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, United States of America*; *[4]Sanofi Genzyme, Cambridge, MA, United States of America*; *[5]Pompeu Fabra University, Barcelona, Spain*; *[6]Tohoku University Hospital, Sendai, Japan*; *[7]Cardiff University School of Medicine, Cardiff, United Kingdom*

Background:
Objectives: The in vitro binding affinity of sarilumab (K_D 61.9 pM) for the human interleukin-6 receptor (IL-6R) is 15- to 22-fold higher than tocilizumab.[1] We explored the relationship between IL-6R RO, relevant pharmacodynamic (PD) variables (eg CRP), and potential clinical relevance of the differences between sarilumab and tocilizumab.
Methods: Binding to total soluble IL-6R (sIL-6R) in vivo translates into the quasi-steady-state target-mediated drug disposition pharmacokinetics (PK) and indirect-response PD model with inhibition of elimination of sIL–6R and unbound sIL-6R concentration for both sarilumab and tocilizumab.[2–5] PK/PD models were used to simulate sIL-6R RO dynamic profiles (% RO over time) for: sarilumab after subcutaneous (SC) doses of 200 and 150 mg once every 2 wks (q2w); tocilizumab after SC doses of 162 mg q2w and once every wk (qw); and tocilizumab after intravenous (IV) doses of 4 and 8 mg/kg once every 4 wks (q4w). In addition, RO profiles were compared with changes in observed CRP levels in patients with RA following administration of sarilumab SC and tocilizumab IV (ASCERTAIN study; NCT01768572). In this study, 60.8% of patients required an increase in tocilizumab dose from 4 to 8 mg/kg IV during the study period, based on clinical response.
Results: Sarilumab SC 200 mg q2w achieved >90% RO after the first dose, which was maintained over the dosing interval throughout the 24-wk treatment course; at the lower dose of 150 mg q2w, RO was >90% from the second dose onwards. RO for tocilizumab SC, at 162 mg q2w, was >90% immediately after the first dose but dropped below 50% prior to the second dose. Similarly, for tocilizumab IV at 4 mg/kg q4w, the RO was high immediately after the first dose (>99% at Wk 1) but decreased over the dosing interval. At trough steady-state (Wk 24), RO was greater with sarilumab SC 200 mg q2w (98%) and 150 mg q2w (94%) compared with tocilizumab SC 162 mg q2w (84%) and IV 4 mg/kg q4w (60%). The higher doses of tocilizumab SC 162 mg qw and tocilizumab IV 8 mg/kg q4w were able to maintain RO $\geq$99% at steady state, similar to sarilumab SC 200 mg at steady state. CRP levels in patients with RA were inversely associated with RO at trough; the greatest suppression in CRP was seen in patients who received sarilumab SC (at either dose) or the higher IV tocilizumab dose (Fig). However, proportionally smaller reductions in CRP levels were observed with the lower IV tocilizumab dose (4 mg/kg q4w), consistent with the lower RO of tocilizumab.
Conclusion: The higher binding affinity of sarilumab to IL-6R compared with tocilizumab translated into higher RO and greater reduction in CRP levels for sarilumab than tocilizumab, confirming the expected association between RO and PD effect. Sarilumab SC 200 mg q2w led to a rapid and sustained suppression of CRP over the 24-wk interval investigated; however, a higher dose (IV) or frequency of administration (SC) of tocilizumab was required to maintain the same degree of RO and CRP suppression. CRP may be a useful tool in clinical practice for patients treated with an IL-6R blocker.

REFERENCES:
[1] Rafique A, et al. Ann Rheum Dis 2013;72: Abstr 797.
[2] Xu C, et al. PAGE Meeting 2017; Abstr 7283.
[3] Huizinga T, et al. Ann Rheum Dis 2014;73:1626–34.
[4] Gibiansky L, et al. J Pharmacokinet Pharmacodyn 2012;39:5–16.
[5] FDA Clinical Pharmacology Review for tocilizumab, 2013.

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FRI0107

THE EFFECT OF CO-MEDICATION WITH METHOTREXATE OR OTHER CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS ON FIRST TUMOR NECROSIS INHIBITOR DRUG SURVIVAL IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE CZECH ATTRA REGISTRY

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Background: Tumor necrosis factor inhibitors (TNFi) should be used for the treatment of rheumatoid arthritis (RA) in combination with conventional synthetic disease modifying anti-rheumatic drugs (csDMARD), preferably methotrexate (MTX). However a significant proportion of RA patients receive TNFi in combination with other csDMARD or in monotherapy.

Objectives: To assess the effect of co-medication with MTX or other csDMARDs on drug survival of TNFi treated RA patients.

Methods: All adult patients with RA followed in the Czech national registry ATTRA who started TNFi therapy after January 1st 2012 were considered. Six-year drug survival for patients on TNFi in combination with MTX, with other csDMARD or in monotherapy was analyzed using Kaplan-Meier method, log rank test was used to compare differences between groups. Reasons for TNFi discontinuation were analyzed. ATTRA is a centralized prospective computerized registry of patients receiving biologic disease modifying anti-rheumatic drugs (bDMARD) therapy for rheumatic diseases collecting data on efficacy, safety and quality of life of all patients treated with bDMARDs in the Czech Republic. TNFi therapy is indicated for patients with RA who have failed treatment with at least one csDMARD.

Results: A total of 1841 RA patients initiated first bDMARD treatment during the studied period, with 1724 patients receiving TNFi. 1307 patients (76%) started TNFi therapy in combination with MTX, 267 patients (15%) with other csDMARD and 150 patients (9%) as monotherapy. Overall unadjusted TNFi drug survival was better in patients receiving MTX co-medication (median survival 53 months) compared to those receiving other csDMARD (median survival 36 months) or those being on monotherapy (median survival 21 months; p<0.001 for monotherapy vs MTX co-medication) (Figure). The most common reason for TNFi discontinuation was loss of efficacy (33%, 37% and 28% for MTX, csDMARD combination and monotherapy respectively) followed by primary inefficacy (20%, 19% and 27%) and adverse events (19%, 15%, 23%).

Conclusion: In this registry study of patients with RA, use of MTX co-medication was associated with significantly better first TNFi drug survival compared to other csDMARD co-medication and to monotherapy.

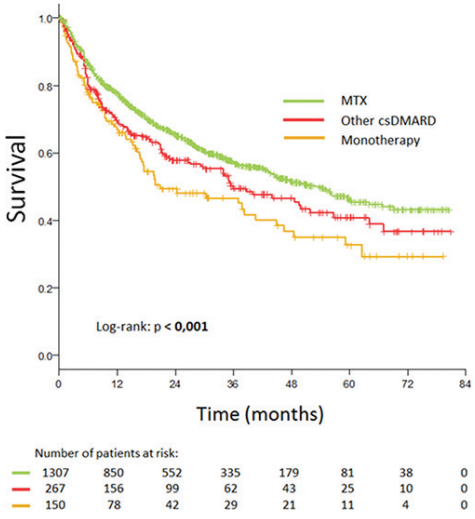


Figure. Kaplan–Meier curves of 6-year drug survival of the first TNFi based on co-medication

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, Zlatuse Kristkova: None declared, Jiří Vencovský Consultant for: Samsung, Speakers bureau: AbbVie, Novartis, Pfizer, Sanofi, Eli Lilly, Biogen, UCB, MSD, Werfen, Roche, Karel Pavelka: None declared
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FRI0108 SHORT-TERM EFFICACY OF BCD-089, NOVEL MONOCLONAL ANTI-IL-6 RECEPTOR ANTIBODY, IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: 12-WEEK RESULTS OF PHASE 2 AURORA STUDY

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Background: In the previous phase 1 study BCD-089 (INN: levilimab) was well-tolerated, had favorable safety profile and low immunogenicity[1]. Here we report 12-week efficacy and safety results of ongoing phase 2 clinical study of BCD-089 in patients with active RA.
Objectives: This study is aimed to assess efficacy and safety of 2 dosing regimens of BCD-089 in patients with MTX-IR active RA.
Methods: During this multicenter double-blind placebo-controlled randomized clinical study (NCT03455842) 105 MTX-IR patients with active RA (ACR2010) were assigned (1:1:1) to receive 162 mg of BCD-089 s.c. (QW arm and Q2W arm) or PBO. MTX (10-25 mg/week) was used in all groups. After completion of 12-week blinded period patients from QW/Q2W arms continued the treatment, patients from PBO arm were switched to BCD-089 Q2W until Wk56. The primary efficacy endpoint was the rate of ACR20 at Wk12. Secondary endpoints included ACR50/70 and DAS28-CRP(4). The safety was routinely evaluated.
Results: The efficacy analysis showed that 95% confidence interval for BCD-089 treatment effect relative to PBO was [38.45 – 81.55] for QW arm and [16.53 – 63.4] for Q2W arm, which confirms the superiority to PBO of either dosing regimens. Summary of efficacy results is presented in table 1.
The majority of adverse events (AE) were laboratory abnormalities. The spectrum of AEs is similar to other IL6R inhibitors (Table 2). Three serious AE (SAEs) were reported: community-acquired pneumonia (QW arm, treatment-related), acute cholecystitis (PBO arm, not related, did not lead to treatment discontinuation), and acute heart failure leading to death (Q2W arm, not related). One case of moderate local reaction (erythema) was reported in QW arm.
Conclusion: BCD-089 in combination with MTX had superior efficacy compared with MTX plus PBO in MTX-IR patients with active RA. BCD-089 showed safety profile consistent with other IL6R inhibitors. Further clinical studies are needed.

REFERENCE:

[1] Khlyabova P, et al. doi: 10.1136/annrheumdis-2018-eular.2410

Table 1. Safety results (full analysis set), n (%)

Efficacy parameter	BCD-089 QW+MTX (n=35)	BCD-089 Q2W+MTX (n=35)	PBO +MTX (n=35)	p-value (Fisher's exact test)
ACR20	27 (77.1%)	20 (57.1%)	6 (17.1%)	<0.0001
ACR50	18 (51.4%)	11 (31.4%)	2 (5.7%)	0.0001
ACR70	10 (28.6%)	7 (20.0%)	1 (2.9%)	0.0106
DAS28-CRP(4) < 3.2	20 (57.1%)	10 (28.6%)	1 (2.9%)	<0.0001

Table 2. Safety results (full analysis set), n (%)

Safety parameter	BCD-089 QW+MTX (n=35)	BCD-089 Q2W+MTX (n=35)	PBO+MTX (n=35)
Any AE	26 (74.29%)	23 (65.71%)	14 (40.0%)
Any SAE	1 (2.86%)	1 (2.86%)	1 (2.86%)
Any grade 3-4 AE	10 (28.57%)	6 (17.14%)	2 (5.71%)
Grade 3-4 Neutropenia	3 (8.57%)	3 (8.57%)	0 (0.00%)
AE of special interest			
ALT/AST increased	4 (11.43%)	5 (14.29%)	1 (2.86%)
Leucopenia/Neutropenia	5 (14.29%)	6 (17.14%)	1 (2.86%)
Infections and infestations	2 (5.71%)	1 (2.86%)	2 (5.71%)
Total cholesterol increased	8 (22.86%)	8 (22.86%)	2 (5.71%)
AEs leading to treatment discontinuation	0 (0.00%)	1 (2.86%)	0 (0.00%)
Deaths	0(0.00%)	1(2.86%)	0(0.00%)

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FRI0109 EFFECTIVENESS AND SAFETY OF INFLIXIMAB, GOLIMUMAB AND GOLIMUMAB-IV IN RHEUMATOID ARTHRITIS PATIENTS FROM A PROSPECTIVE OBSERVATIONAL REGISTRY

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Background: Long-term registries are essential to evaluate new therapies in a patient population that differs from clinical trials and usually varies over time.
Objectives: To describe the profile of rheumatoid arthritis (RA) patients treated with infliximab (IFX), golimumab subcutaneous (GLM) or intravenous (GLM-IV) in Canadian routine care, along with its effectiveness and safety.
Methods: 1577 RA patients treated with IFX, GLM or GLM-IV were enrolled into the Biologic Treatment Registry Across Canada (BioTRAC) between 2006-2015, 2010-2017 and 2014-2017, respectively. Study visits occurred at baseline and every 6 months thereafter. Effectiveness was assessed with changes in TJC28, SJC28, MDGA, PtGA, pain, HAQ, and acute phase reactants. Safety was evaluated with the incidence of adverse events (AEs) and drug survival.
Results: Of the 890 IFX-, 530 GLM- and 157 GLM-IV-treated patients, the proportion of females were 75.7%- 77.1%, the mean age were 55.8-57.7 and the mean disease duration were 6.5-8.6 years. Most patients were bio-naive (> 80%).
A significant decrease in disease duration and disease activity scores (DAS, TJC, SJC, HAQ, AM stiffness, MDGA, PtGA, CRP, ESR) were observed in the IFX cohort over time (p<0.001). Interestingly, baseline disease duration and disease activity scores for the GLM cohort (DAS, TJC, SJC, PtGA, Pain, CRP, ESR) were higher than in the IFX cohort from 2010-2012 when GLM was first introduced while the mean MDGA remained the same between the two groups.
Treatment with IFX, GLM and GLM-IV significantly improved all disease parameters over time (P<0.001) from baseline to 6 months and up to 120, 78 and 42 months, respectively. The proportion of patients in SDAI remission at 12, 24 and 36 months reached 16.2%, 20.8% and 22.8% in IFX-patients; 34.7%, 47.5% and 52.7% in GLM-patients and 33.8%, 47.5% and 61.9% in GLM-IV-patients (p=0.1978 and p=0.0081 vs IFX).
AEs were reported for 61.5%, 67.4% and 59.2% (105, 113 and 82.6 events/100 PYs) and SAEs for 21.2%, 15.5% and 3.8% (11.7, 34.4 and 9.0 events/100 PYs) covering 2714, 1077 and 257 years of exposure for IFX, GLM and GLM-IV-treated patients, respectively. The most frequently occurring AEs were arthralgia and upper respiratory tract infection (>5%). Eighteen, 7 and 1 deaths occurred among IFX-, GLM- and GLM-IV-treated patients, respectively. The proportion of patients who discontinued treatment were 74.0% over a mean 3.0 years of exposure to IFX-,

52.8% over 2.0 years of exposure to GLM and 45.2% over 1.6 year of exposure to GLM-IV.

Conclusion: In this real-world study of Canadian patients with RA, differences in baseline characteristics between patients treated with an anti-TNF over time and between agents shows potential selection biases when selecting a given therapy and may impact the proportion of patients achieving a target-specific outcome. Treatment significantly reduced disease activity and improved functionality in a similar fashion and were also safe and well tolerated.

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FRI0110 RITUXIMAB BIOSIMILAR NON-MEDICAL SWITCH – DOES IT WORK?

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Background: Since the introduction of anti-TNF biosimilars in routine clinical practice, there has been a drive to implement the switch program for all biosimilars at the point of availability. Rituximab biosimilar was granted marketing authorisation by the EMA in February 2017. Our Trust was one of the first centres to embrace a CQUIN which required adoption of biosimilar within three months for new patients and one year for switchers. This could help deliver significant savings to the NHS whilst achieving similar clinical outcomes.

Objectives: We report our early experience of introducing rituximab biosimilar in people with RA.

Methods: A list of all patients prescribed rituximab was extracted through our database. A 'switch' letter was drafted and sent to all patients including Truxima information sheet. Patients were given the opportunity to contact nurse helpline for information or if disease control worsened/adverse effects developed. We reviewed all relevant records and collected data on any adverse events and disease outcome on either side of the switch. Patients were reviewed as originally planned by their respective clinicians.

Results: 44 patients with RA on 2 g dose six-monthly were identified established on rituximab. Four had stopped treatment prior to switching. All 40 agreed to switch to Truxima that was completed by February 2018. Mean age of switchers was 58.6 (range 26-80 years). Eight were men and remaining 32 (80%) were women. Fourteen (35%) were Asian, one Afro-Caribbean and the rest (62%) were White Caucasian.

DAS28 scores were available for all participants. Prior to the switch median DAS28 was 3.0 (range 0.6-5.1). Following the switch it was 2.95 (range 1.5-5.7). Amongst these, eight (20%) reported adverse effects. Four had serum sickness reaction within the first week of the second dose with loss of efficacy. One required admission to ED (<24 hrs) for further management. All decided against further biosimilar and three were swapped back to the originator with no further concerns. In one case the clinician decided to change the class of drug to a TNF inhibitor. Three patients had mild intolerance and agreed to continue Truxima with no further issues. One patient developed miliary tuberculosis and was taken off biologic therapy.

Adverse events related to Rituximab biosimilar switch

Age	Gender	Previous Mabthera Cycles	Prior DAS28	Post switch DAS28	Adverse effects	Final drug choice
39	F	1	3.5	5.1	Gen unwell, achy, flu like symptoms	Humira
70	M	3	2.1	1.8	Itchy scalp, brain fog	Truxima
49	F	2	4.4	2.8	Vomiting, diarrhoea	Mabthera
48	F	2	3.1	5.5	Palpitations, dizziness	Mabthera
48	F	4	1.8	2.8	Headache, flushing	Truxima
58	F	4	4.5	5.1	Nausea, flushing, headache	Truxima
37	F	5	3.5	4.5	Body pains, headache, distaste, lethargy (hospitalised)	Mabthera
76	F	1	2.2	2.5	Miliary TB	Biologic withdrawn

Conclusion: Our experience of switching rituximab patients is certainly not as smooth as it was for infliximab and etanercept. All were happy to switch after receiving a letter and having the opportunity to contact if necessary. Substantial annual cost savings of nearly £140,000 were achieved once the switch process completed. At group level there were no major differences in disease outcomes. However, 10% had severe serum sickness reaction with loss of efficacy and loss of confidence in the drug. One patient developed military TB despite having one previous originator cycle with no issues. We support the routine switching from originator to biosimilar rituximab however close monitoring is required certainly in the first few weeks of dose administration.

Disclosure of Interests: Muhammad Khurram Nisar Grant/research support from: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Novartis, Celgene, Mallinckrodt, UCB and Lilly, Consultant for: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Novartis, Celgene, Mallinckrodt, UCB and Lilly, Speakers bureau: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Novartis, Celgene, Mallinckrodt, UCB and Lilly

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FRI0111 ASSOCIATION BETWEEN RHEUMATOID FACTOR STATUS AND DISCONTINUATION OF TUMOR NECROSIS FACTOR INHIBITORS DUE TO INEFFECTIVENESS IN RHEUMATOID ARTHRITIS

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Background: As for the treatment of rheumatoid arthritis (RA), the influence of rheumatoid factor (RF) positivity on the long-term efficacy of tumor necrosis factor inhibitors (TNFi) is controversial.

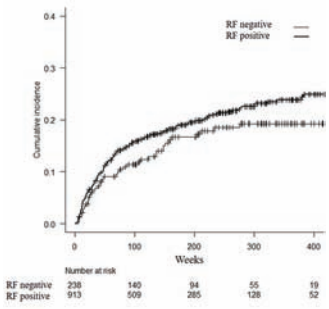
Objectives: We conducted an exploratory study in a large cohort of RA patients to evaluate the relationship between RF status and the discontinuation of TNFi treatment due to ineffectiveness in a clinical setting.

Methods: This study included bio-naïve RA patients enrolled in the Tsurumai Biologic Communication Registry in Japan. The crude comparison of TNFi discontinuation due to ineffectiveness between seropositive and seronegative patients was analyzed using the cumulative incidence function of competing events and Gray test. We assessed the associations between baseline patient characteristics and discontinuation of TNFi therapy due to insufficient response using Fine-Gray proportional hazard regression. Fine-Gray proportional hazard analysis considered competing events of interest, including insufficient response, adverse event, palliation, and personal reasons.

Results: Demographic and clinical characteristics of each group are described in Table 1. There was a higher discontinuation rate due to insufficient response in RF positive patients than in RF negative patients using Gray test (Figure). RF positivity was significantly predictive of the discontinuation of TNFi therapy due to ineffectiveness using Fine-Gray proportional hazard regression analysis after adjusting for baseline characteristics, including age, sex, stage, class, disease activity at baseline, methotrexate use, and prednisolone use (Table 2).

Conclusion: Using Fine-Gray proportional hazard regression, we demonstrated that RF positivity was related to a higher discontinuation rate of TNFi therapy due to ineffectiveness in bio-naïve RA patients.

Figure. Cumulative incidence of competing events and Gray test.



Discontinuation of tumor necrosis factor inhibitors therapy due to ineffectiveness, stratified by rheumatoid factor (RF) status ($P = 0.14$ by Gray test).

Table 1. Characteristics of RA patients at baseline by RF status.

	RF (n = 1151; 3407 patient-years)		
	RF positive (n = 913)	RF negative (n = 238)	*P*†
Age, years (SD)	56.6 (13.5)	53.1 (14.7)	<0.001
Female, no. (%)	737 (80.8)	195 (82.3)	0.64
DAS28ESR (SD)	5.28 (1.33)	4.87 (1.38)	<0.001
Stage I+II/III+IV, no. (%)	312/569 (35.4/64.6)	103/120 (46.2/53.8)	0.0032
Class I+II/III+IV, no. (%)	543/338 (61.6/38.4)	174/49 (78/22)	<0.001
Current MTX treatment, no. (%)	584 (82.7)	191 (90.1)	0.009
Current PSL treatment, no. (%)	383 (58.1)	98 (51.0)	0.083

Data are presented as mean, unless otherwise stated. SD: standard deviation; RA: rheumatoid arthritis; RF: rheumatoid factor; MTX: methotrexate; PSL: prednisolone; DAS28ESR: Disease Activity Score in 28 joints calculated with erythrocyte sedimentation rate. † Chi-square test for categorical variables and t-test for continuous variables.

Table 2. Fine-Gray proportional hazard regression.

Model including RF status (n = 643)		
Variable	HR (95% CI)	*P*
RF positive	1.73 (1.07-2.80)	0.023
Age at baseline	0.98 (0.97-0.99)	0.035
Sex (referent: male)	0.89 (0.58-1.38)	0.63
Methotrexate use	1.68 (0.96-2.96)	0.069
Prednisolone use	1.20 (0.83-1.75)	0.31
Stage III + IV (referent: I + II)	0.99 (0.98-1.01)	0.97
Class III + IV (referent: I + II)	1.00 (0.98-1.02)	0.67
DAS28ESR at baseline	1.31 (1.14-1.51)	<0.001

Disclosure of Interests: Yoshikazu Ogawa: None declared, Nobunori Takahashi Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Eisai, Mitsubishi Tanabe, and Pfizer. YS has received speakers' fees from Astellas, Bristol-Myers Squibb, and Ono, Toshihisa Kojima Grant/research support from: Chugai Pharmaceutical (Investigator Initiated Study), Novartis, Nippon Kayaku, Eli Lilly, Eisai, Speakers bureau: Chugai Pharmaceutical, Takeda Pharmaceutical, Pfizer, Eli Lilly Japan, Bristol Myers Squibb, Ono Pharmaceutical, Daiichi Sankyo, Astelas, UCB, Janssen Pharmaceutical, Tanabe Mitsubishi, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant for: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama

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FRI0112

INCREASED RISK OF SEVERE INFECTION RECURRENCE IN PATIENTS WHO DEVELOPED SEVERE INFECTIONS DURING BDMARDS THERAPY: A STUDY OF THE MIRAI COHORT

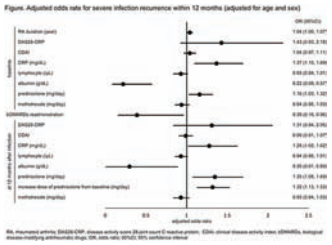
Eri Oguro[1], Yuji Yoshida[1], Kentaro Kuzuya[1], Yasutaka Okita[1], Hidetoshi Matsuoka[1], Satoru Teshigawara[1], Maiko Yoshimura[1], Kentaro Isoda[1], Yoshinori Harada[1], Shiro Ohshima[1], Jun Hashimoto[1], Yukihiko Saeki[2]. *[1]Osaka Minami Medical Center, Department of Rheumatology and Allergology, Kawachinagano, Osaka, Japan*; *[2]Osaka Minami Medical Center, Department of Clinical Research, Kawachinagano, Osaka, Japan*

Background: One of the most important complications of biological disease-modifying antirheumatic drugs (bDMARDs) is severe infection, and management of patients who develop severe infection during treatment with bDMARDs is a great concern. However, no consensus exists regarding bDMARDs readministration following treatment for bDMARDs-associated infection.

Objectives: We elucidated risk factors associated with severe infection recurrence in patients who developed severe infections during bDMARDs therapy. Severe infection was defined as an infection requiring hospitalization. Moreover, we analyzed whether bDMARDs readministration after severe infection in patients with rheumatoid arthritis (RA) was a risk for severe infection recurrence.

Methods: The study sample comprised patients with RA who were examined and prescribed bDMARDs at Osaka Minami Medical Center between January 2010 and December 2017, as part of the MiRAi cohort. The patients who developed severe infections during bDMARDs treatment were followed-up for 12 months. Logistic regression analysis was performed using baseline disease activity, baseline treatment, and disease activity and treatment during the 12-month period.

Results: Severe infections developed in 164 of a total of 1192 patients who were treated with bDMARDs during the study period, and the severe infection rate was 5.73/100 patients-years. Among the 164 patients, bDMARDs were readministered in 130 (79.3%), whereas treatment with bDMARDs was discontinued in 34 patients (20.7%). We observed 31 cases of patients with severe infections during the follow-up period (18.9/100 patients-years), of which 20 patients (15.4/100 patients-years) belonged to the bDMARDs readministration group and 11 (32.4/100 patients-years) belonged to the bDMARDs discontinuation group. The adjusted odds ratio (OR) for severe infection recurrence within 12 months in the bDMARDs readministration group was 0.39 [95% confidence interval (CI) 0.16–0.96]. At 12 months after infection, high-dose prednisolone treatment (adjusted OR 1.35, 95%CI 1.08–1.69), high C-reactive protein level (adjusted OR 1.28, 95%CI 1.02–1.62), and low serum albumin levels (adjusted OR 0.30, 95%CI 0.01–0.89) were associated with high risk of severe infection recurrence (Figure).



Conclusion: Patients who developed severe infection during bDMARDs treatment were at an extremely high risk for severe infection irrespective of the readministration or discontinuation of bDMARDs after infection. Discontinuation of bDMARDs, high dose of prednisolone 12 months after infection, high levels of C-reactive protein 12 months after infection, and low levels of albumin 12 months after infection were identified as risk factors for severe infection recurrence in these patients. However, bDMARDs readministration did not increase the risk of severe infection recurrence.

REFERENCE:

[1] Ramiro et al, Ann Rheum Dis 2017;76:1093-1101.

Disclosure of Interests: Eri Oguro: None declared, Yuji Yoshida: None declared, Kentaro Kuzuya: None declared, Yasutaka Okita: None declared, Hidetoshi Matsuoka: None declared, Satoru Teshigawara: None declared, Maiko Yoshimura: None declared, Kentaro Isoda: None declared, Yoshinori Harada: None declared, Shiro Ohshima Grant/research support from: AbbVie, Eisai, Asahikasei, Speakers bureau: AbbVie, Eisai, Bristol-Meyers, Novartis, Astellas, Nippon-Kayaku, Pfizer, UCB, Ayumi, Daiichi-Sankyo, Takeda, Tanabe-Matsubishi, Chugai, Jun Hashimoto: None declared, Yukihiko Saeki: None declared
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FRI0113 COMPARISON OF INFECTION-RELATED HOSPITALIZATION COSTS IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) TREATED WITH ABATACEPT OR OTHER TARGETED DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (TDMARDS)

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Background: Costs due to differences in risk of hospitalized infection associated with targeted disease-modifying anti-rheumatic drugs (tDMARDs) in patients with RA have not been evaluated.
Objectives: Compare the risk and cost of infection-related hospitalizations in tumor necrosis factor inhibitor (TNFi)-experienced RA patients subsequently receiving tDMARDs in the US.
Methods: A retrospective, observational study was conducted with 2 insurance claims databases (MarketScan and PharMetrics; January 1, 2009- June 30, 2017). Analyses were conducted in both datasets individually and in aggregate. The study population was adult TNFi-experienced RA patients initiating a subsequent tDMARD (date of tDMARD therapy=index date). Patients had 12 months of continuous enrollment prior to the index date (baseline period), and were required to have $\geq$1 inpatient claim or $\geq$2 outpatient medical claims on 2 different dates with a diagnosis code for RA. Patients with other autoimmune conditions were excluded. Follow-up began with the index date and included $\geq$12 months ending with the earliest of (1) end of insurance enrollment; (2) end of study period; (3) end of index treatment. Cohorts included (1) abatacept; (2) TNFi: adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab; and (3) other non-TNFi: tocilizumab, rituximab, and tofacitinib. Hospitalized infection costs were measured on a per-patient-per-month (PPPM) basis (2016 USD). Two-part multivariable generalized linear models (GLMs) examined differences in costs. Baseline comorbidities, infection incidence, healthcare costs, payer type, age, gender, and geographic region were used as regression covariates. Log transformation and gamma distribution were applied in GLMs.
Results: Overall, most patients were female (79%) with an average age of 52 years. Although a higher percentage (4.5%) of patients in the abatacept cohort had a hospital visit for infection in the baseline period compared to TNFi (2.0%, P<0.0001) and other non-TNFi (3.6%, P=0.2619), the trend reversed in the follow-up period (2.8% for abatacept vs 3.7% for TNFi and 5.2% for other non-TNFi; P<0.05). Regression results indicated a significantly higher risk for hospitalized infection for patients receiving a TNFi [HR: 1.6 (95% CI: 1.1, 2.2)] or other non-TNFi [HR: 1.9 (95%: 1.3, 2.8)] vs abatacept. Mean PPPM (95% CI) inpatient costs in the follow-up were $73 ($17-$158) for abatacept, $115 ($27-$224) for TNFi, and $125 ($29-$264) for other non-TNFi. Difference from baseline to follow-up PPPM inpatient costs was significantly lower for abatacept (difference of $42 for TNFi and $52 for other non-TNFi, P<0.05).
Conclusion: There were significantly lower infection-related hospitalizations and associated costs for TNFi-experienced RA patients who were switched to abatacept compared to patients switched to other therapies.
Disclosure of Interests: Damemarie Paul Shareholder of: Bristol-Myers Squibb, Employee of: Damemarie Paul is an employee of Bristol-Myers Squibb., Francis Lobo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Vardhaman PATEL Employee of: Bristol-Myers Squibb, Dhaval Patil Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb
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FRI0114 ABATACEPT IN EARLY RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS

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Background: Rheumatoid arthritis (RA) is a wide-spread and debilitating disorder that is becoming increasingly relevant in an aging global population. Identifying and treating RA early in disease course is critical for preventing disability and joint damage.
Objectives: The goal of this systematic literature review (SLR) and meta-analysis was to compare the relative efficacy of abatacept (ABA) to other currently recommended therapies for patients with early RA.
Methods: We followed Cochrane guidelines for conducting intervention reviews. Population of interest was adult patients with active RA for ≤2 years treated with recommended therapies per the 2015 ACR guidelines as well as targeted synthetic therapies. Studies of interest were randomized controlled trials (RCTs) and observational studies. Outcomes included ACR50, DAS28, radiographic change, and adverse events where available. A search from January 1998 to June 2018 was performed on MEDLINE®, Embase, and the Cochrane CENTRAL databases. Additionally, a hand-search was performed on US and European clinical trials registries from January 2005 to June 2018 and conference proceedings from ACR and EULAR from 2014 to 2018. A Bayesian network meta-analysis (NMA) was performed on the DOC Data™ platform for the RCTs with reported results on ACR50, DAS28 remission, total withdrawal, and withdrawal due to adverse events.
Results: We identified 90 publications on 69 unique trials reporting efficacy and safety outcomes in patients with early RA, including 43 RCTs and 26 observational studies. The included studies were low risk as assessed by the Cochrane Collaboration's tool for assessing risk of bias. The studies were predominantly double-blind phase III or IV trials. Twenty-eight trials were included in the NMA evaluating ABA (n=1 trial), ABA+MTX (n=2), ADA+MTX (n=6), CTZ+MTX (n=2), ETN (n=1), ETN +MTX (n=1), HCQ+SSZ+MTX (n=1), HCQ+SSZ+Pred+MTX (n=1), IFX +MTX (n=4), MTX (n=21), MPred+MTX (n=2), MPred+Pred+MTX (n=1), Pred+SSZ+MTX (n=2), Pred+MTX (n=4), Pred (n=1), SSZ (n=4), SSZ +MTX (n=2), TCZ (n=2), TCZ+MTX (n=2), TOF (n=2), and TOF+MTX (n=2). Abatacept as monotherapy was similar to the combination of ABA and methotrexate for efficacy outcomes, ACR 50 (ABA vs ABA+MTX RR 0.82 [95% CI 0.51-1.35]), and DAS28 Remission (RR 0.76 [95% CI 0.39-1.49]), as well as for all-cause withdrawal (RR 1.8 [95% CI 0.91-3.2]) and withdrawal due to adverse events (RR 2.35 [95% CI 0.69-7.38]). Both ABA as monotherapy and ABA+MTX were similar to all other comparators (as monotherapy or combination therapy) with respect to main efficacy and safety outcomes. Data reported in observational studies was in concert with the RCT analysis.
Conclusion: The results of this NMA demonstrate similar efficacy between ABA and other biologics both as monotherapy and in combination with traditional DMARDS in early RA. Further investigation and comparison of different treatment options for early RA is warranted as the growing evidence base evolves in favor of using more novel therapies for RA. ABA=abatacept; ADA=adalimumab; CTZ=certolizumab; ETN= etanercept; HCQ=hydroxychloroquine, IFX= infliximab, MPred= methylprednisolone, MTX=methotrexate; Pred=prednisone, SSZ=sulfasalazine, TCZ= tocilizumab, TOF=tofacitinib
Disclosure of Interests: Damemarie Paul Shareholder of: Bristol-Myers Squibb, Employee of: Damemarie Paul is an employee of Bristol-Myers Squibb., Leticia Ferri Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Grace Crocket Consultant for: Grace Crocket is a consultant for Bristol-Myers Squibb., Lauren Mintzer Grant/research support from: Lauren Mintzer is an employee of Doctor Evidence LLC, and the study was funded by Bristol-Myers Squibb., Mir Sohail Fazeli Grant/research support from: Mir Sohail Fazeli is an employee of Doctor Evidence LLC, and the study was funded by Bristol-Myers Squibb.
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FRI0115 TRAJECTORIES OF THE EQ-5D SCORE AMONG A LARGE COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BIOLOGICAL DMARDS USING THE IORRA COHORT

Kumiko Saka[1], Eiichi Tanaka[1], Eisuke Inoue[2], Mai Abe[1], Mika Kawano[1], Eri Sugano[1], Naohiro Sugitani[1,3], Moeko Ochiai[1], Yoko Shimizu[1], Rei Yamaguchi[1], Naoki Sugimoto[1], Katsunori Ikari[1], Ayako Nakajima[3], Atsuo Taniguchi[1], Hisashi Yamanaka[1]. [1]*Tokyo Women's Medical University, Tokyo, Japan*; [2]*St. Mrianna University School of Medicine, Kanagawa, Japan*; [3]*Mie University Hospital, Mie, Japan*

Background: Patient-reported outcomes are important for evaluating the disease status of patients with rheumatoid arthritis (RA). The EuroQol five-dimensional descriptive system (EQ-5D) has been used to assess health-related quality of life (QOL) in clinical research and pharmacoeconomic studies. RA is a chronic disease associated with pain, fatigue, disability, and functional loss, which can markedly decrease patient QOL.

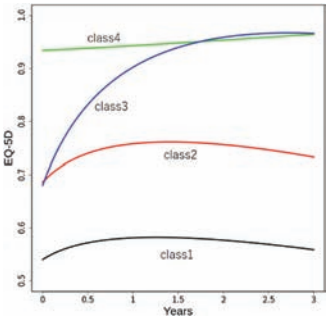
The treatment strategies for RA and the QOL of RA patients, which is evaluated in daily practice using the EQ-5D, have changed significantly since the introduction of biological disease-modifying anti-rheumatic drugs (bDMARDs).

Objectives: To identify patient subsets with distinct EQ-5D trajectories among RA patients taking bDMARDs, and to examine the clinical features of patients whose QOL improved since bDMARD use in daily practice.

Methods: Since October 2000, we have established a large observational cohort of RA patients at our institute Institute Of Rheumatology, Rheumatoid Arthritis (IORRA). Essentially, all RA patients who attend our clinic are given questionnaires, including the EQ-5D, Disease Activity Score 28 (DAS28), and the Japanese version of the Health Assessment Questionnaire (J-HAQ), every 6 months. More than 5,000 RA patients are included in this cohort, of whom 785 patients who received bDMARDs for at least 3 years were enrolled in this study. The EQ-5D scores of these 785 patients were recorded biannually for 3 years, and latent class analysis of the temporal trends in the EQ-5D score based on posterior probabilities was performed after initiation of bDMARDs. The clinical characteristics of each latent class were then compared.

Results: The 785 patients (107 taking infliximab, 341 etanercept, 100 tocilizumab, 131 abatacept, 90 golimumab, and 16 certolizumab pegol) were classified into four classes based on time-related changes in their EQ-5D scores: Class 1 (n = 160), patients with a consistently low score < 0.6 despite use of bDMARDs; Class 2 (n = 314), patients with a consistently moderate score of 0.7); Class 3 (n = 229), patients whose score improved from 0.7 to 0.9 after use of bDMARDs; and Class 4 (n = 82), patients with a consistently high score of 0.9. When comparing the patients in Classes 2 and 3, whose EQ-5D scores before bDMARD use were similar, the patients in Class 3 had a younger age (p<0.001), shorter disease duration (p<0.001), higher DAS28 score (p<0.001), lower J-HAQ score (p=0.038), and more frequent use of non-steroidal agents (p=0.002) than those of Class 2 patients.

Conclusion: The results of this study suggest that QOL is less likely to improve in patients with RA whose disabilities and QOL deterioration have already become established despite use of bDMARDs. We also determined the clinical features of RA patients whose QOL improved after initiation of bDMARDs.



Disclosure of Interests: Kumiko Saka: None declared, Eiichi Tanaka Speakers bureau: Abbvie, Asahi Kasei pharma co., Bristol Myers Squibb, Chugai Pharmaceutical, Daiichi Sankyo Co., Eisai Pharmaceutical, Janssen Pharmaceutical K.K., Nippon Kayaku, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical Co., and UCB Pharma., Eisuke Inoue: None declared, Mai Abe: None declared, Mika Kawano: None declared, Eri Sugano: None declared, Naohiro Sugitani: None declared, Moeko Ochiai: None declared, Yoko Shimizu: None declared, Rei Yamaguchi: None declared, Naoki Sugimoto: None declared, Katsunori Ikari: None declared, Ayako Nakajima Grant/research support from: Asahi Kasei pharma co., Chugai Pharmaceutical, Daiichi Sankyo Co., Pfizer, Kissei Pharmaceutical Co., and Mitsubishi Tanabe Pharma Corporation., Atsuo Taniguchi: None declared, Hisashi Yamanaka Grant/research support from: AbbVie, Eisai, Bristol-Meyers, Novartis, Behringer, Astellas, Kaken, Nippon-Shinyaku, Pfizer, UCB, Ayumi, Ono, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, YLbio, Speakers bureau: Bristol-Meyers, Astellas, Pfizer, Daiichi-Sankyo, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, YLbio

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FRI0116

SUBCUTANEOUS TOCILIZUMAB IN MONOTHERAPY OR IN COMBINATION WITH CSDMARD IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS: OBSERVATIONAL STUDY TO DESCRIBE REAL-WORLD DRUG RETENTION RATE AT 12 MONTHS

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Background: Rate of discontinuation and drug survival of biologic therapies in rheumatoid arthritis (RA) is about 60-70% in real life at one year[1]. In France, all biologics 1st prescription and yearly renewal are reimbursed, restricted to hospital rheumatologists, with renewal and monitoring done by both office-based or hospital rheumatologists.

Objectives: To evaluate the 12-month drug retention rate, efficacy and tolerance of tocilizumab (TCZ) subcutaneous (sc) in RA patients (pts).

Study design: prospective, multicentre, observational 18-month study. *Pts*: moderate to severe active RA requiring TCZ sc as prescribed in real life. *Primary endpoint*: drug retention rate of TCZ sc at 12 months in pts followed by hospital- and office-based rheumatologists, estimated using Kaplan-Meier method. *Secondary endpoints*: pts' characteristics, concomitant treatments, adherence to TCZ sc using the Compliance Questionnaire for Rheumatology (CQR5), efficacy, safety of TCZ sc and QoL using EQ-5D. *Statistical analysis*: pts with ≥1 TCZ injection were analyzed for safety. Pts fulfilling inclusion and non-inclusion criteria were analyzed for efficacy.

Results: 291 pts were recruited, 286 were analyzed for safety and 285 for efficacy.

Baseline: mean age 56.2±12.5 years, females: 74.7%, at least 1 co-morbidity: 71.9%, mean RA duration 9.4±9.0 years, RF and/or ACPA: 83.4%, erosive RA: 60.8%, mean DAS28-ESR 4.77±1.21. Past RA treatments were csDMARDs in 94.4%, biologics in 62.8%. EQ-5D Health state was 0.53±0.19. TCZ Mono (i.e. without csDMARD) was initiated in 124 (43.5%), TCZ Combo in 158 (55.4%) pts, 84.8% of whom received MTX (17.3±4.4mg/w). Glucocorticoids (GCs) were used in 48.9% of the pts (9.99±9.36mg/day).

Follow up: 161 and 148 pts completed M12 and M18 visits. 138 pts withdrew including AE 61, lack of efficacy 37, pts/doctor wish 24. At M12, drug retention rate was 63.6%: 62.6% in Mono, 64.3% in Combo (Fig.1); with similar results for pts ≤/> 65 years old and for pts ≤/> 30Kg/m^2. 5 Mono pts had ongoing csDMARD and 9 Combo pts had no csDMARD. 15.3% and 19.0% used GCs, 16.19±11.95mg/d in the Mono and 17.36±16.65mg/d in the Combo groups. Total number of TCZ injections was 36.74±25.84 done by pt in 54.0%. Mean time between 2 TCZ injections was 8.48±10.70 days. Adherence to TCZ was high in 86.5% of the 89 pts who completed CQR5 at month 12. It was 52.9% for the 121 pts who completed pts diary over the month 12-month 18 period. Mean DAS28 in all, Mono and Combo were 1.91±1.11, 1.66±1.02, 2.12±1.14 respectively. EULAR good and moderate responses were respectively 61.3 and 7.7% in all: 67.2 and 4.9% in Mono; 56.8 and 9.9% in Combo pts. EQ-5D improved in all domains with a change from baseline of 0.11 ±0.29. 234 (81.8%) pts had at least 1 adverse event (AE), 46 (16.1%) had at least 1 serious AE including 11 infections, 2 GI perforations and 2 deaths (pneumopathy and bronchial carcinoma).

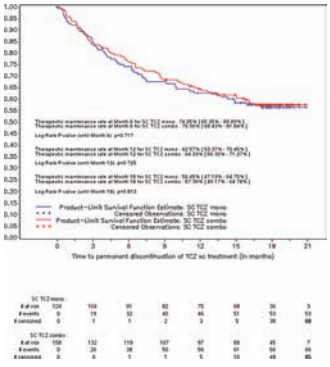


Figure 1. Kaplan-Meier curve of the drug retention rate by SC TCZ in mono vs combo - Efficacy population

Conclusion: At 12 months, drug retention rate was 63.6% in patients receiving TCZ sc in real life, with no difference between Mono and Combo groups. EULAR good/moderate response was 69.0%. QoL improved in all EQ-5D domains. No new safety signal occurred.

REFERENCE:

[1] Souto A, et al. Rate of discontinuation and drug survival of biologic therapies in rheumatoid arthritis. Rheumatology (Oxford) 2016 Mar;55(3):523-34.

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FRI0117 THE COMPARATIVE RISK OF OSTEOPOROTIC FRACTURES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TNF INHIBITORS VERSUS OTHER BIOLOGICS: A NATION-WIDE COHORT STUDY IN KOREA

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Background: Rheumatoid arthritis (RA) is associated with an increased risk of osteoporosis and osteoporotic fracture, but little is known about comparative risk of osteoporotic fractures between biologic agents.

Objectives: To investigate the comparative risk of osteoporotic fractures among RA patients who initiated TNF inhibitors, abatacept, and tocilizumab.

Methods: We identified patients aged $\geq$ 40 years with at least two ICD-10 diagnosis codes for RA who initiated TNF inhibitor, abatacept, or tocilizumab from the 2005-2015 Korean National Health Insurance Service datasets. The primary outcome was a composite osteoporotic fracture endpoint of spine, hip, forearm or humerus fractures requiring hospitalization. Secondary outcomes were spinal and non-spinal fractures. Follow-up period started from the day after the first dispensing date of the study drug to the earliest date among the following events: discontinuation of the study drugs, outcome occurrence, disenrollment, end of study dataset, or death. Propensity score (PS) matching with a variable ratio of 10:1 was conducted for TNF inhibitor versus abatacept initiators and for TNF inhibitor versus tocilizumab initiators to adjust for baseline confounding. We estimated hazard ratio (HR) and 95% confidence interval (CI) of osteoporotic fracture risks comparing TNF inhibitors to abatacept or tocilizumab by Cox proportional hazard models stratified by a matching ratio.

Results: We included 2,339 TNF inhibitor initiators and 594 abatacept initiators, and 2,486 TNF inhibitor initiators and 647 tocilizumab initiators in each PS-matched cohort. The incidence rates per 100 person-years for the primary outcome were 1.57 and 1.65 for TNF inhibitor and abatacept initiators, and 1.69 and 2.05 for TNF inhibitor and tocilizumab initiators, respectively. The HR (95% CI) for the primary outcome was 1.10 (1.54-2.23) comparing TNF inhibitors versus abatacept and it was 1.00 (0.53-1.92) comparing TNF inhibitor versus tocilizumab initiators. We also did not find any significant difference for secondary outcomes (Table1).

Table 1. Risk of osteoporotic fractures in TNF inhibitor initiators vs. abatacept initiators and tocilizumab initiators

	TNF inhibitor (n=2,339)			Abatacept (n=594)			HR (95% CI)
	Events	PYs	IR per 100 PY	Events	PYs	IR per 100 PY	
Primary outcome							
Osteoporotic fracture	47	2,998	1.57	12	727	1.65	1.10 (1.54-2.23)
Secondary outcomes							
Spinal fracture	25	3,018	0.83	8	731	1.10	0.95 (0.41-2.20)
Non-spinal fracture	22	3,022	0.73	4	737	0.54	1.52 (0.41-5.65)
	TNF inhibitor (n=2,468)			Tocilizumab (n=647)			HR (95% CI)
	Events	PYs	IR per 100 PY	Events	PYs	IR per 100 PY	
Primary outcome							
Osteoporotic fracture	54	3,196	1.69	16	781	2.05	1.00 (0.53-1.92)
Secondary outcomes							
Spinal fracture	29	3,221	0.90	10	788	1.27	0.98 (0.43-2.24)
No-spinal fracture	25	3,225	0.78	6	793	0.76	1.03 (0.36-2.90)

Conclusion: We did not find a significant difference in the risk of osteoporotic fractures between TNF inhibitor and abatacept initiators, or between TNF inhibitor and tocilizumab initiators in this Korean population-based cohort study.

Disclosure of Interests: None declared

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FRI0118 INFECTION OUTCOMES IN PATIENTS WITH RA TREATED WITH ABATACEPT AND OTHER DMARDS: RESULTS FROM A 10-YEAR INTERNATIONAL POST-APPROVAL STUDY

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Background: The abatacept global post-marketing epidemiology programme consists of observational studies based on biologic disease registries and healthcare claims databases to assess infection and malignancy risks associated with abatacept treatment, as used in routine clinical practice.

Objectives: To evaluate the risk of infection in patients with RA treated with abatacept versus conventional synthetic (cs)DMARDs and other biologic (b) or targeted synthetic (ts)DMARDs.

Methods: Data were analysed from five cohorts: two biologic registries (the Anti-Rheumatic Therapy in Sweden register and the Rheumatoid Arthritis Observation of Biologic Therapy German registry), a disease registry (FORWARD, The National Databank for Rheumatic Diseases in the USA) and two healthcare claims databases (the population-based British Columbia Canadian RA Cohort and the US Optum Research Database). Crude incidence rates (per 1000 patient-years of exposure) with 95% CIs were calculated for hospitalised infections and opportunistic infections. Adjusted risk ratios (RRs) with 95% CIs were estimated using multivariate models adjusting for demographics, co-morbidities and other potential cofounders within each database and were subsequently pooled using a random effects model for meta-analyses.[1]

Results: From all cohorts, patients treated with abatacept (6400), csDMARDs (137K) and other b/tsDMARDs (54K) were followed up for a mean of 2.3–3.7, 2.2–6.2 and 2.3–4.7 years, respectively. Patients were mainly female (71–86%), with a mean age ranging from 49–63 years, and 3–18% had a history of prior severe infections across treatment groups/cohorts. A greater number of abatacept-treated patients had a history of $\geq$2 prior biologics (44–85% vs csDMARDs, 11% [FORWARD] and other b/tsDMARDs, 0–19%). In abatacept-treated patients, incidence rates for hospitalised infections ranged from 16–56 and opportunistic infections from 0.4–7.8 (Table). Adjusted RRs (95% CIs) for abatacept vs csDMARDs (range: 0.3 [0.2, 0.7] to 2.2 [1.3, 3.7]; pooled estimate: 1.2 [0.6, 2.2]) and abatacept vs other b/tsDMARDs (range: 0.5 [0.3, 0.8] to 1.3 [0.8, 2.1]; pooled estimate: 0.9 [0.6, 1.3]) showed no increased risk in hospitalised infections.

Conclusion: In this large, international post-marketing epidemiology programme, pre-specified infection risks were more frequent with abatacept than csDMARDs and b/tsDMARDs in some, but not all, cohorts. Increased risks for individual outcomes/cohorts may be attributed to prior biologic exposure, study design and practice pattern differences. These data are consistent with the current safety profile of abatacept.

REFERENCES:

[1] DerSimonian R, Laird N. Control Clin Trials 1986;7:177–188.

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Table. IRs per 1000 PY (95% CI) for infections

	Hospitalised infections			Opportunistic infections		
	Abatacept	csDMARDs	Other bnsDMARDs	Abatacept	csDMARDs	Other bnsDMARDs
ARTIS	47 (41, 54)	40* (46, 47)	37 (36, 39)	0.97 (0.1, 1.8)	1.1 (1.0, 1.2)	1.5 (1.2, 1.8)
BC	56 (42, 72)	31 (27, 37)	43 (37, 49)#	NR	NR	NR
FORWARD	16 (12, 22)	19 (15, 24)	18 (15, 21)	0.5 (0.1, 3.1)	0.7 (0.2, 2.1)	0.6 (0.3, 1.7)
Optum	42 (36, 49)	37 (35, 39)	39 (36, 43)	7.8 (5.3, 11.1)	4.3 (3.9, 4.7)	3.6 (3.3, 4.4)
RABBIT	36 (31, 45)	24 (21, 28)	25 (20, 34)	0.4 (0.01, 2.2)	0.3 (0.0, 1.0)	0.5 (0.2, 0.9)

*Biologic-naive patients (most of whom had been receiving csDMARDs)
#3 cases
‡Other biologic group in BC only included anti-TNF inhibitors
ARTIS=Arts Rheumatic Therapy in Sweden; bnsDMARD=biologic/targeted synthetic DMARD; BC=British Columbia Canadian RA Cohort; csDMARD=conventional synthetic DMARD; FORWARD=FORWARD, The National Databank for Rheumatic Diseases in the USA; IR=incidence rate; NR=not reported; Optum=Optum Research Database; PY=patient-years; RABBIT=Rheumatoid Arthritis Observation of Biologic Therapy German registry

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FRI0119

PREDICTING REMISSION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS STARTING TOCILIZUMAB MONOTHERAPY: MODEL DERIVATION AND VALIDATION USING CONVENTIONAL REGRESSION AND MACHINE LEARNING

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Background: Most rheumatoid arthritis (RA) patients strive to consolidate their treatment from methotrexate combinations to monotherapy with the goal of the most effective and simplified therapy. Tocilizumab (TCZ) appears to have similar efficacy when used with or without concomitant csDMARDs in RA. Thus, it is clinically useful to predict treatment benefit among patients with RA starting TCZ monotherapy.

Objectives: To identify RA patients most likely to achieve remission with TCZ monotherapy by developing and validating a prediction model through conventional regression and machine learning.

Methods: We followed the TRIPOD recommendations for derivation and validation of clinical risk prediction models. Four TCZ monotherapy randomized controlled trials (RCT) in RA were identified (ACT-RAY, ADACTA, AMBITION, and FUNCTION) – two were chosen for derivation of the prediction models and two for validation. Relevant data for individual subjects from the trials were obtained, including demographics, RA characteristics, prior treatments, comorbid conditions, and baseline disease activity. In the two derivation trials, we examined each potential predictor of remission one at a time in logistic regression models, adjusted for age, sex, and baseline CDAI. The dependent variable in all models was CDAI ≤ 2.8 (remission) at 24 weeks. Three methods were used for variable selection: odds ratio (OR) based (forwarding variables to multivariable models if OR > 1.5 or < 0.66); AIC based (lowest AIC); and a machine learning approach that fit a logistic regression model to covariates selected by a LASSO-regularized logistic regression. Based on these different variable selection approaches, variables were advanced to the final multivariable model in the derivation cohort (DC). Age, sex, and baseline CDAI were forced into all models. We assessed discrimination with the area under the curve (AUC), model fit with the AIC and BIC, and calibration graphically using loess smoothing and with calibration slopes. We assessed model performance in the DC and in the validation cohort (VC), using variables selected in the DC.

Results: Baseline characteristics in the derivation (n=473) and validation (n=380) cohorts were generally similar: mean age 51.6 years in DC and 52.1 in VC; 77% female in DC and 83% in VC; mean baseline CDAI 39.8 in DC and 42.1 in VC; disease duration was longer in VC 3.6 years compared to 0.9 in DC. Seventy-eight patients (17%) reached remission in the DC; 49 (13%) in the VC. After testing possible variables in the derivation models, the variables selected as predictors of remission included younger age, male sex, lower baseline CDAI, shorter RA disease duration, region of world (Europe and South America increased odds of remission vs. Asia and North America), no previous exposure to DMARD/MTX, lower baseline HAQ-DI, and baseline hematocrit (see **Table**). In the DC, model fit and calibration were adequate in all three models, though discrimination was notably reduced under 10 fold cross-validation. The VC modeling suggested that all three models were similar in discrimination and were well calibrated (see **Table**).

Conclusion: Different modeling strategies selected similar variables to predict remission using TCZ monotherapy: shorter disease duration, lower HAQ-DI, and no prior DMARD/methotrexate use. While these results should be interpreted with caution, as the analysis combined different studies that may represent different populations, they may provide guidance to clinicians tailoring treatment options based on baseline characteristics.

Table: Factors that predict remission in patients treated with tocilizumab monotherapy: results from three modeling strategies to derive and validate a remission prediction model

Variables*		Model A (OR)	Model B (AIC)	Model C (ML)
Age		✓	✓	✓
Sex		✓	✓	✓
Baseline CDAI		✓	✓	✓
RA disease duration		✓		✓
Region of world		✓	✓	✓
Past DMARD/MTX Use		✓	✓	✓
ESR		✓		
Baseline HAQ-DI		✓	✓	✓
Baseline Hematocrit		✓		
History of CV disease		✓		
History of diabetes		✓		
(1) Model fit in derivation	AUC	0.74 (0.68-0.80)	0.728 (0.67-0.79)	0.73 (0.66- 0.80)
	AUC 10-fold cross-validation	0.66 (0.59-0.72)	0.67 (0.60-0.74)	0.67 (0.60-0.74)
	AIC	407.05	401.74	402.63
	BIC	473.59	447.49	452.54
	Calibration slope	0.99	1.00	1.00
(2) Model fit in validation*	AUC	0.76 (0.69-0.82)	0.73 (0.66-0.81)	0.73 (0.67-0.80)
	AIC	288.29	283.44	285.278
	BIC	351.33	326.78	332.560
	Calibration slope	0.97	1.02	1.014

Notes: ✓ signifies that variable was included in a specific model. *Age, sex, and baseline CDAI forced into all models. The model fit was tested in the validation cohort using all variables identified in the derivation cohort. Abbreviations: OR, odds ratio; AIC, Akaike information criterion; ML, machine learning; CDAI, clinical disease activity index; MTX, methotrexate; HAQ, health assessment questionnaire; CV, cardiovascular; AUC, area under the receiver operating characteristic curve; BIC, Bayesian information criterion; DMARD, disease modifying anti-rheumatic drug. In the ML model, tuning parameters for the selection model were chosen based on 10-fold cross-validation on the derivation set. Some of the variables included appear only as coarsened variables, i.e. not all categories were included.

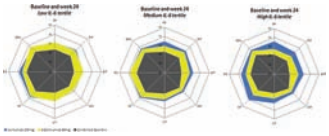
Disclosure of Interests: Jamie Collins Grant/research support from: genentech, Fredrik Johansson Grant/research support from: Genentech, Sara Gale Shareholder of: Roche, Employee of: Genentech/Roche, Seoyoung Kim Grant/research support from: Pfizer, Bristol-Myers Squibb, Roche/Genentech and AbbVie., Swastina Shrestha Grant/research support from: Genentech, David Sontag Grant/research support from: Genentech, Jacklyn Stratton Grant/research support from: Genentech, Trinh Huong Shareholder of: Roche, Employee of: Genentech/Roche, Chang Xu Grant/research support from: Pfizer, Elena Losina Grant/research support from: Genentech, Pfizer, Samumed and Flexion, Consultant for: Regeneron, Daniel Solomon Grant/research support from: Abbvie, Amgen, Genentech, Janssen, and Pfizer

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FRI0120 **HIGH LEVELS OF INTERLEUKIN-6 (IL-6) IN RA PATIENTS ARE ASSOCIATED WITH GREATER IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES (PROS) FOR SARILUMAB COMPARED WITH ADALIMUMAB**

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Background: Increased levels of cytokines, including interleukin-6 (IL-6), reflect inflammation and are predictive of therapeutic responses in patients with RA. IL-6 has been implicated in fatigue, pain and depression in RA but a formal association with PROs has not been performed. Sarilumab, a fully human monoclonal antibody directed against IL-6Ra, is approved for treatment of moderate-to-severely active RA. The phase 3 MONARCH randomized controlled trial (NCT01061736) compared the efficacy and safety of sarilumab monotherapy vs adalimumab in RA patients who should not continue methotrexate treatment due to intolerance or inadequate responses. Greater reductions in disease activity and improvements in the clinical signs of RA and physical function were demonstrated with sarilumab vs adalimumab. A better understanding of the association between IL-6 levels and PROs is warranted to evaluate as a biomarker for guiding RA clinical decision-making.
Objectives: To evaluate, by post-hoc analysis, the potential of baseline IL-6 levels to differentially predict the improvement in PRO with sarilumab vs adalimumab in MONARCH.
Methods: Serum IL-6 levels were measured at baseline in 300/369 patients in the ITT population. Patients were categorized into high, medium, or low IL-6 tertiles levels. Between-group comparisons of differences at Week 24 in Short Form-36 (SF-36) physical and mental component summaries (PCS, MCS) and domain scores, Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue, and morning stiffness visual analog scale (VAS) measures were performed within each tertile using a linear fixed effect model. In order to evaluate the differential effect of sarilumab vs adalimumab in the baseline high vs low IL-6 groups, an interaction test of treatment-by-baseline IL-6 group analysis was performed using low IL-6 group as the reference.
Results: At baseline, patients in the high IL-6 tertile presented a significantly worse MCS and morning stiffness scores ($P < 0.05$). The model interaction comparing high vs low IL-6 tertiles was significant for SF-36 PCS and physical functioning domains, and for morning stiffness. In patients with high IL-6, sarilumab treatment resulted in significant ($P < 0.05$) improvements vs adalimumab in SF-36 PCS (LS mean [LSM] of the difference: 5.57, 95%CI (2.85, 8.28)) and physical functioning (PF, 16.59 (8.15, 25.03)), role physical (9.44 (0.78, 18.10)), bodily pain (BP, 10.87 (3.92, 17.81)), vitality (8.93 (1.11, 16.74)), and social functioning (12.82 (3.07, 22.58)) domains (all raw values in **Figure**). Sarilumab also showed significant ($P < 0.05$) effects vs adalimumab in FACIT-Fatigue (4.86 (1.06, 8.65)) and morning stiffness VAS (-19.93 (-30.30, -9.56)), with LSM changes exceeding minimum clinically important differences (MCID).
Conclusion: Evaluation of IL-6 biomarker associations with PROs indicate that patients with high IL-6 levels report better improvements with sarilumab vs adalimumab with safety profile consistent with IL-6R blockade. The effects of adalimumab treatment are stable based on IL-6 tertiles but higher with sarilumab, particularly in the high IL-6 tertile group. Effects on PCS scores are mainly driven by the PF domain, consistent with previous reports of marked improvements in pain with high IL-6 levels.



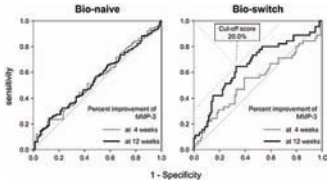
Figure

* Significant between-group difference in change from baseline ($P < 0.05$)
SF-36 domains: BP, bodily pain; GH, general health; RP, role-physical, MH, mental health; PF, physical functioning; RE, role emotional; SF, social functioning; VT, vitality.
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FRI0121 **IMPROVEMENT OF MATRIX METALLOPROTEINASE-3 AT 12 WEEKS IS AN INDEPENDENT PREDICTIVE FACTOR FOR ACHIEVEMENT OF LOW DISEASE ACTIVITY AT 52 WEEKS IN BIO-SWITCH RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT**

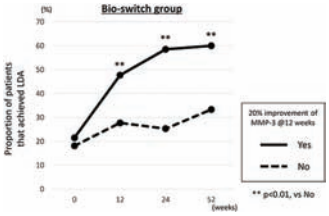
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Background: Japanese post-marketing surveillance (PMS) data demonstrated that effectiveness of abatacept in rheumatoid arthritis (RA) patients with previous biologics treatment (bio-switch) was significantly lower than that in bio-naïve patients [1]. Useful predictive factors for good clinical response of abatacept is necessary especially in the bio-switch patients. Serum matrix metalloproteinase-3 (MMP-3) is an enzyme produced by synoviocytes which can be used to predict clinical effectiveness and joint destruction in RA patients [2]. However, little is known about the relationship between MMP-3 and effectiveness of abatacept.
Objectives: This study aimed to study whether serum MMP-3 levels can predict good clinical effectiveness of abatacept in the bio-switch RA patients using data from a multicenter cohort.
Methods: Participants were consecutive 423 RA patients treated with abatacept, observed for longer than 52 weeks, and registered in the TBCR, a Japanese multicenter registry system for RA patients treated with biologics. Multivariate logistic regression analysis was used to study predictive factors for achievement of low disease activity at 52 weeks separately in bio-naïve and bio-switch group.
Results: A total of 189 bio-switch and 234 bio-naïve patients were included in this study. ROC analysis revealed that MMP-3 improvement rate at 12 weeks, compared to 4 and 24 weeks, had highest AUC and the best cut-off value was 20.0% at 12 weeks for predicting achievement of low disease activity (LDA) at 52 weeks in the bio-switch group (Figure 1, right panel). We performed multivariate logistic regression analysis to study independent predictive factors for LDA at 52 weeks using patients' background factors as well as 20% improvement of MMP-3 at 12 weeks. In the bio-naïve group, DAS28-CRP score at baseline was the only predictive factor, while the achievement of 20% improvement of MMP-3 at 12 weeks was an independent predictive factor (adjusted OR: 3.550, p=0.005) in addition to DAS28-CRP in the bio-switch group (Table). In the bio-switch group, patients that achieved 20% improvement of MMP-3 at 12 weeks demonstrated significantly higher achievement rate of LDA at 52 weeks compared to those that did not achieved 20% improvement (60.0 vs 33.3%, p=0.001) (Figure 2).



	Multivariate analysis	
Bio-naive	adjusted OR (95% CI)	p-value
Age	0.988 (0.955-1.022)	0.479
Male	0.693 (0.305-1.577)	0.382
RF positive	2.172 (0.945-4.990)	0.068
Concomitant MTX	1.769 (0.843-3.709)	0.131
Concomitant PSL	0.609 (0.294-1.262)	0.182
DAS28-CRP	0.544 (0.395-0.748)	***<0.001***
20% improvement of MMP-3 @12 weeks	1.918 (0.918-4.007)	0.083

Bio-switch	adjusted OR (95% CI)	p-value
Age	0.990 (0.952-1.029)	0.608
Male	1.010 (0.294-3.475)	0.987
RF positive	0.481 (0.151-1.532)	0.216
Concomitant MTX	1.120 (0.459-2.731)	0.803
Concomitant PSL	0.496 (0.202-1.221)	0.127
DAS28-CRP	0.603 (0.432-0.843)	***0.003***
20% improvement of MMP-3 @12weeks	3.550 (1.454-8.666)	***0.005***



Conclusion: In the bio-switch patients, we sometimes have difficulty to obtain good clinical response of abatacept and it would be even more important to judge whether to continue abatacept or whether to add other anti-rheumatic drugs as early as possible [3]. Our results suggested that the improvement of MMP-3 at 12 weeks would be a key to predict good clinical effectiveness of abatacept at 1 year. We would be better to note not only the major clinical indices such as DAS28 but also the change of MMP-3 to obtain the best clinical results in the bio-switch patients treated with abatacept.

REFERENCES:

[1] Harigai M, et al. Mod Rheumatol 2016;26(4):491.
[2] Hattori Y, et al. Mod Rheumatol 2018;28:119.
[3] Takahashi N, et al. Mod Rheumatol 2013;23:904.

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FRI0122

REAL-WORLD SAFETY DATA FROM PATIENTS WITH RHEUMATIC DISEASES TREATED WITH CT-P13, AN INFLIXIMAB BIOSIMILAR: AN INTERIM ANALYSIS FROM AN OBSERVATIONAL STUDY

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Background: CT-P13, an infliximab biosimilar, has been available in Europe and Canada since 2015, and real-world experience with CT-P13 is important to support the safety of this medication. PERSIST is an ongoing, observational cohort study evaluating CT-P13 as treatment for rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) in a real-world setting.

Objectives: This interim analysis reports safety outcomes for patients who received CT-P13 as their first biologic (Biologic-naïve) or who switched from infliximab reference product (IFX-RP) to CT-P13 (Switched) based on data collected from September 2015 to December 2017.

Methods: Patients were recruited during usual care at 38 academic and community sites in 6 European countries and Canada. Adult RA, AS or PsA patients prescribed CT-P13 or locally-sourced IFX-RP at the investigator's discretion and according to the approved label were eligible. Data were analysed descriptively.

Results: This analysis included 329 patients (RA, n=134; AS, n=110; PsA, n=85). Of these, 6 (1.8%) were not treated, 3 (0.9%) completed study treatment, 244 (74.2%) were ongoing and 76 (23.1%) discontinued study treatment, most commonly due to lack of response (30 [9.1%]). Demographics and baseline characteristics were generally similar between groups (Table 1). Most treatment-emergent adverse events (TEAEs; Table 2) were of mild or moderate intensity; 7/129 events were severe. Most commonly reported adverse events were related to infection (n=33; 10.2%); most frequently reported infection-related TEAEs were nasopharyngitis (n=6; 1.9%), respiratory tract infection (n=5; 1.5%) and pneumonia (n=4; 1.2%). No case of tuberculosis was reported. Eight (2.5%) patients reported infusion related reactions.

Table 1. Disposition, population characteristics and drug utilisation patterns for patients receiving CT-P13

	Biologic-naïve (n=216)	**Switched (n=107)**	**Total (N=323)**
Age, median (range), years	54 (19–84)	53 (23–76)	54 (19–84)
Male, n (%)	97 (44.9)	59 (55.1)	156 (48.3)
Disease duration, median (range), months	45.34 (0.03–563.91)	159.51 (12.65–464.07)	86.77 (0.03–563.91)
Baseline dose			
Patients with data for baseline dose, n	202	102	304
Mean (SD), mg/kg	3.68 (1.05)	3.96 (0.94)	3.78 (1.02)
Baseline infusion frequency, n (%)			
Once every 6 or fewer weeks	72 (33.3)	43 (40.2)	115 (35.6)
Once every 8 weeks	76 (35.2)	44 (41.1)	120 (37.2)
Other	54 (25.0)	15 (14.0)	69 (21.4)
Missing	14 (6.5)	5 (4.7)	19 (5.9)

Table 2. All-causality TEAEs for patients receiving CT-P13

	Biologic-naïve (n=216)	**Switched (n=107)**	**Total (N=323)**
Number of TEAEs	87	42	129
Patients with ≥1 event, n (%)			
TEAEs	59 (27.3)	22 (20.6)	81 (25.1)
Serious TEAEs[a]	12 (5.6)	9 (8.4)	21 (6.5)
TEAEs of special interest[b]	18 (8.3)	7 (6.5)	25 (7.7)
Discontinued from study due to adverse events	3 (1.4)[c]	0	3 (0.9)
Deaths	0	0	0

[a] Difference between groups due to higher incidence of infections in switched (3.7%) vs biologic-naïve (1.4%).
[b] Difference between groups due to higher incidence of infusion related reaction in biologic-naïve (6.0%) vs switched (1.9%).
[c] Included hepatobiliary disease, uterine cancer, and psoriasis.
TEAE=treatment-emergent adverse event.

Conclusion: Incidences of TEAEs were similar and there was no discernible pattern across the most common TEAEs between groups. These interim analysis results from the PERSIST study conducted in a real-world setting are consistent with the known safety profile of infliximab and do not demonstrate new safety information to change the benefit−risk profile of CT-P13.

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FRI0123 **BIOLOGICAL THERAPIES SURVIVAL IN RHEUMATOID ARTHRITIS PATIENTSIN CLINICAL PRACTICE: RESULTS FROM THE METEOR REGISTRY**

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Background: Several biologic disease modifying anti-rheumatic drugs (bDMARDs) are currently available, but comparisons among these different drugs in clinical trials are rare and follow-up duration in trials is often limited. A comparison of these bDMARDs in daily practice can provide clinically relevant knowledge on treatment survival of all currently available bDMARDs.
Objectives: To assess the survival of each and every one of the biological therapies available in patients with rheumatoid arthritis (RA).
Methods: The METEOR registry is a multinational project that includes data on> 40,000 patients with RA from its diagnosis and prospectively, with proven reliability, in clinical practice. Inclusion criteria: patients> 18 years in biological treatment (bDMARD). Variables under study: disease onset date, bDMARD initiation and discontinuation date, bDMARD type (infliximab, certolizumab, adalimumab, golimumab, etanercept, rituximab, tocilizumab and abatacept), concomitant treatment, line of treatment. Clinical variables: TJC, SJC, ESR, CRP, BMI, patient's VAS, and RF and ACPA levels; smoking status. Cox regression analysis that was adjusted for several potential confounders.
Results: From the 47,263 patients registered in the total METEOR database, 11,132 were eligible for inclusion of the current study. Of these, 9,516 had sufficient data available and were included in the analyses. Included patients (n=9,516) less often smoked than non-included patients (n=1,616), but other baseline characteristics were very similar between groups (data not shonw).
Baseline features of all patients were similar.
Median time on bDMARD as 1st line treatment for each drug is shown in Table 1, infliximab showed the longest median time on treatment. Using infliximab as 'reference' treatment, Table 2 shows abatacept, certolizumab, rituximab and tocilizumab showed higher hazard risk to finish the treatment prematurely, while adalimumab, golimumab or etanercept had similar results than infliximab.
Conclusion: after adjusting by several confounders, analysed data showed that most anti-TNF (infliximab, adalimumab, etanercept and golimumab) had a similar hazard to stop treatment in clinical practice. Other than anti-TNF bDMARD showed higher hazard to switch treatment than infliximab.
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FRI0124 **FACTORS ASSOCIATED WITH PERSISTENT DRUG-FREE REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: Persistent drug-free remission of RA is a condition that is close to "cure" of the disease. However, long-term drug-free remission is considered to be rare and very challenging to reach. Also, little data are available that report how often persistent drug-free remission can be achieved and what kind of clinical characteristics are associated with such state.
Objectives: To evaluate factors associated with persistent drug-free remission in patients with rheumatoid arthritis
Methods: We analyzed the long-term observational follow-up phase of the randomized controlled RETRO (REduction of Therapy in RA Patients in Ongoing Remission) study on tapering and stopping of DMARDS in RA patients in stable remission (DAS28-ESR <2.6) (1,2). We included patients having completed the 1-year randomized controlled phase of RETRO, in which DMARD treatments were either continued, tapered or stopped. In the long-term extension, (i) patients who successfully stopped, continued DMARD stop, (ii) patients who relapsed in any of the 3 groups continued DMARD treatment, (iii) patients in the continuation arm remaining in remission underwent 50% DMARD tapering followed by stopping after 6 months if still being in remission and (iv) patients in the tapering arm remaining in remission underwent DMARD stop. We assessed the percentage of patients in persistent drug-free remission in the overall population and the three randomization groups, the probability of persistent drug-free remission in the intervention groups compared to controls adjusted by baseline aCCP, erosive changes and use of biologic DMARDs in a logistic regression model and the baseline characteristics associated with reaching persistent drug-free remission.
Results: All 141 patients being in the long-term observational follow-up phase of the RETRO study for at least 1 year were analyzed. Among them DMARDs were initially continued (Control, n=38), tapered (Taper, n=50) or stopped (Taper/Stop n=53). 19/141 patients were lost to follow-up and the worst case scenario was assumed that all of them did not reach persistent drug-free remission. Median time after study entry (Q1-Q3) was 69 (37-96) months as by December 2018. Overall number of patients in drug-free remission was 34/141 (24.1%), 10/38 (26%) in the control group, 6/50 (12%) in the taper group and 18/53 (34%) in the taper/stop group. After adjustment for baseline risk factors in the likelihood to reach persistent drug-free remission between the groups (OR:0.76, 95%CI: 0.29-1.99) was highly uncertain. Positive ACPA (OR: 3.38, 1.01 – 11.31) and erosive-state (3.05, 1.32 – 7.06) at baseline were associated with a lower likelihood to reach persistent drug-free remission.
Conclusion: These data show that persistent drug-free remission can be reached in a subset of RA patients following a structured DMARD tapering approach after being in stable long-term DMARD control.

REFERENCES:

[1] Haschka J, et al. Relapse rates in patients with rheumatoid arthritis in stable remission tapering or stopping antirheumatic therapy: interim results from the prospective randomised controlled RETRO study. Ann Rheum Dis. 2016 Jan;75(1):45-51.
[2] Rech J, et al. Prediction of disease relapses by multibiomarker disease activity and autoantibody status in patients with rheumatoid arthritis on tapering DMARD treatment. Ann Rheum Dis 2016;75:1637-44.

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FRI0125 **INDIVIDUAL PATIENT DATA META-ANALYSIS OF THE EFFECTIVENESS OF TOCILIZUMAB ON INHIBITING RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS**

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Background: Several studies have shown that treatment with tocilizumab (TCZ) may reduce radiograph progression compared to treatment with methotrexate (MTX) in rheumatoid arthritis (RA). However, individual studies were not powered to detect differences in the incidence of progression. By combining several studies, a more precise estimate can be

obtained. Furthermore, by using individual patient data (IPD), outcome definitions and methods can be harmonized for a valid combined analysis.

Objectives: To determine the effectiveness of treatment with TCZ on radiographic progression compared to MTX in RA patients over two years.

Methods: Randomized controlled trials in RA patients using TCZ as one of the treatment arms with radiographic damage assessed on radiographs at baseline and after two years were identified and IPD obtained.

The primary endpoint was defined as any radiographic progression over two years. Secondary endpoint was the amount of joint damage progression (points per time unit, expressed as incidence rate). Analyses were performed on total scores and for erosions and joint space narrowing (JSN) separately. TCZ strategies were compared with the control strategies. Within the TCZ strategies, a comparison between monotherapy and the combination with MTX was made.

A two-step IPD meta-analysis was performed. In the first step, data of the individual trials were analysed using logistic regression and zero-inflated Poisson models. In the second step association measures (odds ratio's (OR) and incidence rate ratio's (IRR)) of individual trials were pooled using random effect models in Review Manager[1]. A subgroup analysis was performed on early versus established RA. All analyses were adjusted for baseline DAS28 and Sharp van der Heijde (SvdH) score to provide a more precise treatment effect estimate.

Results: Five trials were identified, one trial[2] using a tight-control treat-to-target approach, and the four other RCTs[3-6] allowed the control group to start TCZ after 6 months or 1 year when the treatment target was not reached. Two trials were performed in early RA[1–2]. The dose of TCZ was tapered down in two studies[2,6]. IPD of 4 trials could be obtained and were included (n=2439 randomized to TCZ arm and n=791 to control arm, MTX in all cases)[2–5].

The radiographs, performed at baseline and after two years, were all assessed with the SvdH method. Due to missing radiographic data, 1766 patients were evaluated in the TCZ arms and 543 patients in MTX arms. Patient characteristics are shown in Table 1. The occurrence of any radiographic progression was statically significantly less in the TCZ arms compared to MTX arms (pooled OR 0.76 [95%CI 0.67 to 0.86]). The effect for erosions (OR 0.77 [95%CI 0.67 to 0.88]) was stronger than for JSN (OR 0.88 [95%CI 0.78 to 0.98]) with both being in favour of TCZ. No clear differences between early and established RA were observed for any progression. Any radiographic progression did not occur statistically significantly more often in the TCZ monotherapy group compared to the combination group. No statistically significant difference were observed for the amount of radiographic progression.

Conclusion: Based on this individual patient data meta-analysis, radiographic progression was less common in TCZ-treated patients compared to MTX-treated patients in RCTs, possibly more for progression of erosions. No difference was observed between TCZ used as monotherapy or in combination with MTX.

REFERENCE:

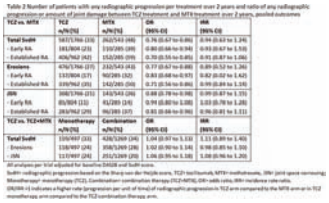
[1] Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

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Table 1 Patient characteristics per individual trial

Trial	Act-Ray[5] n= 417	Function[3] n= 857	Lithe[4] n= 803	U-Act-Early[2] n= 232
Female, n (%)	345 (83)	677 (79)	667 (83)	161 (69)
Age (years), mean (SD)	52.8 (12.1)	50.0 (13.0)	52.0 (11.9)	53.9 (12.4)
BMI (kg/m²), mean (SD)	26.2 (5.1)	27.5 (6.2)	27.4 (5.9)	26.0 (4.4)
Duration RA (months), mean (SD)	96 (93)	6 (6)	116 (97)	1 (1)
Baseline DAS28, mean (SD)	6.3 (1.0)	6.7 (1.1)	6.3 (1.3)	5.1 (1.1)
RF positive, n (%)	-	776 (91)	658 (82)	166 (72)
Baseline SvdH score, median (IQR)	29 (17.5-50.5)	1.5 (0.5-5.5)	19.5 (8-44)	0 (0-1)
Baseline Erosion SvdH score, median (IQR)	15.5 (10-24)	1 (0-3.5)	14 (6-26.5)	0 (0-0)
Baseline JSN SvdH score, median (IQR)	13.5 (7-27)	0 (0-1.5)	5.5 (1–16.5)	0 (0-0)
Initial treatment strategies, n (%)				
- MTX monotherapy	-	211 (25)	258 (32)	74 (32)
- TCZ+MTX 8mg/kg	215 (52)	220 (25)	272 (34)	78 (34)
- TCZ+MTX 4mg/kg	-	211 (25)	273 (34)	-
- TCZ monotherapy 8mg/kg	202 (48)	215 (25)	-	80 (34)

n=number of patients, SD= standard deviation, BMI= body mass index, RA= rheumatoid arthritis, DAS28= disease activity score assessing 28 joints, RF= rheumatoid factor, SvdH= Sharp van der Heijde, JSN= joint space narrowing, MTX= methotrexate, TCZ= tocilizumab.



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FRI0126

THE INFUSION-RELATED REACTIONS OF RITUXIMAB IN RHEUMATIC DISEASES: SINGLE-CENTER EXPERIENCE OF 1893 INFUSIONS OVER 5 YEARS

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Background: Rituximab has been used for treating autoimmune disease. To date, the infusion-related reaction has been mainly studied in patients with hematological malignancy, and there is limited data for rheumatic diseases.

Objectives: We accessed the incidence rate of infusion-related reactions (IRR) of rituximab (RTX) including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjogren's syndrome (SjS), dermatomyositis and polymyositis (PDM), as well as systemic sclerosis (SSc).

Methods: We included all patients with diagnosis of RA, SLE, SjS, PDM or SSc, whose first cycle of RTX therapy during January 2013 to December 2017. Each cycle of RTX consisted of 2 infusions of RTX (500-1000 mg), with combination of methylprednisolone (80-100 mg) with or without antihistamines. The infusion-related reaction was defined as the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Frequency and severity of IRR in each infusion were compared between different diseases and cycles. Logistic regression was applied for cross-sectional data analysis, and generalized estimating equations were used for longitudinal data analysis.

Table 1. Characteristics and IRRs in the patients with different diseases.

Patients features	RA (n=68)	SLE (n=137)	SjS (n=89)	PDM (n=23)	SSc (n=19)
Female sex,%	77.9	93.4	92.1	69.6	73.7
Age, median (quartile), years	60.4 (50.7-65.6)	39.6 (32.7-49.2)	52.7 (40.3-62.7)	50.6 (40-60)	49.9 (41.4-61.5)
Disease duration, median (quartile), months	33.3 (9.2-63.6)	28.3 (1.3-78.3)	7.5 (0.2-31.9)	5.7 (0.3-18.5)	0.4 (0.2-13.6)
Serum IgG level, median (quartile), mg/dL	1505 (548.4-1905)	1420 (1052.5-1667.5)	1420 (1157.5-1802.5)	1370 (877.5-1647.5)	1620 (1270-1800)
IRR per patient					
Any IRR	11/68 (16.2%)	19/137 (13.9%)	23/89 (25.8%)	2/23 (8.7%)	3/19 (15.8%)
Recurrent IRR	5/68 (7.4%)	6/137 (4.4%)	8/89 (9%)	1/23 (4.3%)	3/19 (15.8%)
IRR ≥Grade 2	2/68 (2.9%)	5/137 (3.6%)	12/89 (13.5%)	0/23 (0%)	0/19 (0%)
Any IRR per infusion					
First infusion (C1D1)	7/68 (10.29%)	9/137 (6.57%)	17/89 (19.1%)	1/23 (4.35%)	3/19 (15.79%)
Any infusion	17/461 (3.7%)	27/722 (3.7%)	46/443 (10.4%)	5/134 (3.7%)	5/133 (3.8%)
IRR ≥Grade 2 per infusion					
First infusion (C1D1)	1/68 (1.47%)	2/137 (1.46%)	7/89 (7.87%)	0/23 (0%)	0/19 (0%)
Any infusion	3/461 (0.7%)	7/722 (1%)	25/443 (5.6%)	0/134 (0%)	0/133 (0%)

Results: Totally, 336 patients were included as shown in table 1. There were 100 IRRs out of 1893 infusions, among which 37 were at the first time of RTX infusion. Patients with SjS had showed higher rate of IRR in the first infusion compared with other disease (19.1% vs 8.1%, p=0.008). Considering grade 2 or more severe IRRs, patients with SjS still has higher IRR (p=0.004). SjS was an independent risk for

developing IRR (OR 2.5, 95% CI 1.3-4.7, p=0.006). Seventy (78.7%) of the patients with SjS had positive anti-SSA antibody, but the presence of anti-SSA antibody was not a significant risk for IRR after controlling for the diagnosis of SjS. The IRR per infusion was not related to the RTX dose. The IRR in an infusion did not led to stopping of the therapy, although infusion rate and premedication can be adjusted in the following therapies. Only 39.6% of the patients with an IRR had suffer from more IRR in the following infusions. Besides, male gender and the increasing cycles were associated with less IRR (p=0.029 and 0.007, respectively). In the 100 patients received more than 4 cycles, the rate of IRR decreased along with the cycles. No life-threatening IRR happened in the 1893 infusions.

Conclusion: Our study had found that patients with SjS had higher IRR compared to other diseases. Female had more frequent IRR might due to the sexual distribution of these diseases.

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Disclosure of Interests: None declared

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FRI0127

IMPACT OF JANUS KINASE INHIBITORS ON RISK OF CARDIOVASCULAR EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Janus kinase inhibitors (JAKis) are emerging as novel therapies for patients with rheumatoid arthritis (RA). Two JAK inhibitors have been approved and more pipeline products are ongoing to be launched, but their safety profiles of cardiovascular events (CVEs) have not been fully-established yet.

Objectives: To identify the association betweenCVEs and JAKis therapies in adult patients with RA via a meta-analysis of randomized controlled trials (RCTs).

Methods: RCTs reporting safety issues in RA patients treated with JAKis were reviewed in PubMed, Embase, and Cochrane Library (from inception to October 2018). CINAHL and the major relevant congress (2016-2018) were searched for additional reports. Mantel-Haenszel fixed-effects method with odds ratios (ORs) and 95% confidence intervals (CIs) were performed on extracted data.

Results: Out of 405 references screened, 26 RCTs involving 11 800 patients were included. No statistically significant difference was observed in risk of CVEs associated with the use of JAKis in general (OR 1.04, 95% CI 0.61–1.76, p=0.89), tofacitinib (OR 0.63, 95% CI 0.26-1.54, p=0.31), baricitinib (OR 1.21, 95% CI 0.51-2.83, p=0.66), upadacitinib (OR 3.29, 95% CI 0.59-18.44, p=0.18), peficitinib (OR 0.43, 95% CI 0.07–2.54, p=0.35), decernotinib (OR 1.12, 95% CI 0.13-10.11, p=0.92) (Figure 1). Regarding frequently-used dosage, dose-ranging impact of JAKis on the risk of CVEs was not observed in tofacitinib (5mg vs. 10mg, twice daily), upadacitinib (15mg vs. 30mg, once daily), while baricitinib at 2mg once daily was found to be safer than 4mg (OR 0.19, 95% CI 0.04-0.88, p=0.03) (Figure 2).

Conclusion: The existing evidence from RCTs indicated that JAKis-based therapies are not related to statistically significant risk of CVEs in RA patients during the limited randomized controlled periods. However, a special focus on baricitinib 4mg once daily is needed concerning the cardiovascular safety in the future.

Disclosure of Interests: None declared

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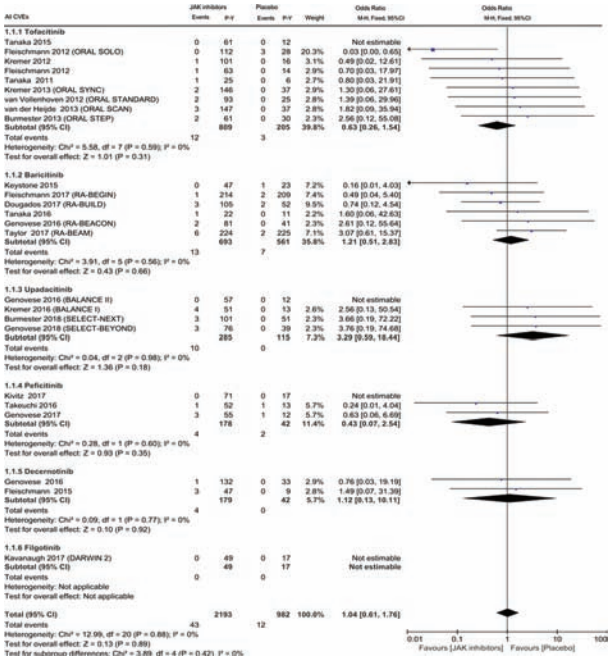


Figure 1. Odds ratio (OR) of cardiovascular events (CVEs) in patients treated with JAKis compared with placebo in randomized controlled trials using Mantel-Haenszel fixed-effects method. JAKis, janus kinase inhibitors; P-Y: person-year; CI: confidence interval; df, degrees of freedom

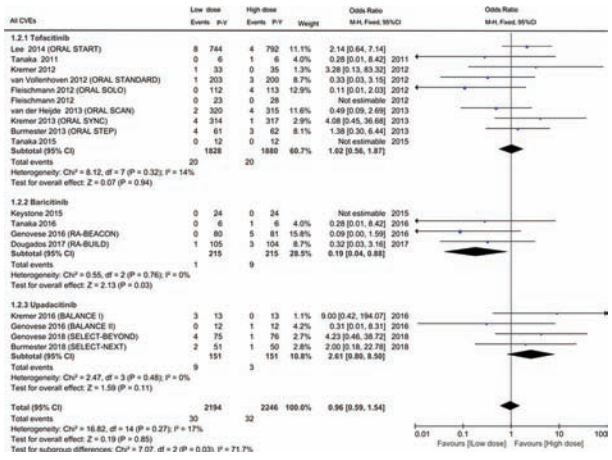


Figure 2. Odds ratio (OR) of cardiovascular events (CVEs) in patients treated with different dosages of JAKis in randomized controlled trials using Mantel-Haenszel fixed-effects method. JAKis, janus kinase inhibitors; P-Y: person-year; CI: confidence interval; df, degrees of freedom.

FRI0128

A NOVEL FORMULATION OF CT-P13 (INFLIXIMAB BIOSIMILAR) FOR SUBCUTANEOUS ADMINISTRATION: 1-YEAR RESULTS FROM A PART 1 OF PHASE I/III RANDOMIZED CONTROLLED TRIAL IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: Efficacy and safety of a new subcutaneous (SC) formulation (CT-P13 SC) up to Week 30 were comparable with intravenous (IV) formulation (CT-P13 IV) in both patients with rheumatoid arthritis (RA) [1] and Crohn's disease [2].
Objectives: This report is to further investigate pharmacokinetics, efficacy and overall safety of CT-P13 SC in patients with RA throughout the 1-year treatment period.
Methods: Patients with active RA (presence of 6 or more swollen and tender joints [of 28 assessed], and serum C-reactive protein [CRP] concentration >0.6 mg/dL) were treated with CT-P13 IV at Weeks 0 and 2, and were randomized for continuation with CT-P13 IV or SC administration at Week 6. The IV cohort received CT-P13 IV 3 mg/kg every 8 weeks and the SC cohorts received CT-P13 SC 90 mg, 120 mg or 180 mg, respectively, every 2 weeks up to Week 54. Pharmacokinetics blood samples were collected before study drug administration at each visit and drug levels were determined by electrochemiluminescent assay. Efficacy parameters including DAS28 and ACR criteria and overall safety were evaluated.

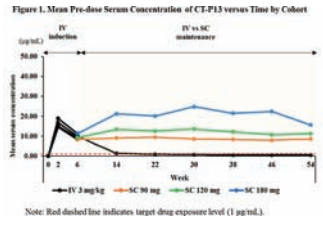


Table 1. Summary of Efficacy and Safety Results up to Week 54

		Cohort 1 IV 3 mg/kg (N=13)	Cohort 2 SC 90 mg (N=11)	Cohort 3 SC 120 mg (N=12)	Cohort 4 SC 180 mg (N=12)
DAS28 (CRP), mean±SD	Week 0	5.4±0.8	6.1±0.8	5.7±0.9	5.5±0.8
	Week 6	3.9±1.5	4.6±1.1	3.9±1.2	3.4±1.2
	Week 22	3.9±1.6	3.7±1.0	3.3±1.4	2.8±1.3
	Week 30	3.7±1.5	3.8±1.1	3.1±1.0	2.7±1.0
	Week 54	3.7±1.2	3.9±1.0	3.2±1.0	2.9±1.0
ACR20, n (%)	Week 6	8 (61.5)	8 (72.7)	7 (58.3)	7 (58.3)
	Week 22	8 (61.5)	8 (72.7)	9 (75.0)	11 (91.7)
	Week 30	11 (84.6)	10 (90.9)	10 (83.3)	12 (100.0)
	Week 54	9 (69.2)	9 (81.8)	8 (66.7)	10 (83.3)
Safety, n (%)	Treatment-emergent AEs	9 (69.2)	7 (63.6)	8 (66.7)	9 (75.0)
	Administration-related reaction	1 (7.7)	1 (9.1)	2 (16.7)	0
	Injection site reactions	0	2 (18.2)	1 (8.3)	2 (16.7)
	Infections	5 (38.5)	4 (36.4)	3 (25.0)	6 (50.0)

Results: A total of 50 patients were enrolled, of whom 48 patients were randomly assigned at Week 6 into 4 cohorts (1:1:1:1 ratio). The mean Ctrough (pre-dose serum concentration of CT-P13 before next dose injection) of SC cohorts throughout the study visits were higher than those of IV cohort after randomization at Week 6. Ctrough levels increased with SC dose and were sufficiently higher than the target therapeutic concentration (1 μg/mL) throughout the study period (Figure 1). Overall, the efficacy results of CT-P13 SC up to Week 54 were comparable to those of CT-P13 IV. Disease improvement by DAS28 (CRP) and ACR20 were comparable across all 4 cohorts, regardless of the route of administration or dosage of CT-P13 (Table 1). The safety profiles which occurred after study drug administration at Week 6 in SC cohorts were generally comparable to those of IV cohort and appeared similar to those previously reported for IV infliximab [3]. All injection site reactions were grade 1 or 2. No malignancy or death was reported (Table 1).
Conclusion: The results from 1-year treatment suggest similar efficacy and safety of CT-P13 SC to CT-P13 IV in RA. The mean serum concentration in all SC cohorts consistently exceeded the threshold of target therapeutic concentration. These results show that the novel SC formulation of CT-P13 may enhance treatment options for use of infliximab biosimilar by providing high consistency in drug exposure.

REFERENCE:
1 Westhovens et al., Annals of the Rheumatic Disease 2018;77:315.
2 Schreiber et al., Gastroenterology 2018;154(6):S-1371.
3 Yoo et al., Arthritis Research 18:82.

Disclosure of Interests: DaeHyun Yoo Grant/research support from: Celltrion, Inc., Consultant for: Celltrion, Inc., Janusz Jaworski Grant/research support from: Celltrion, Inc., Ewa Matyska-Piekarska Grant/research support from: Celltrion, Inc., Svitlana Smiyan Grant/research support from: Celltrion, Inc., Delina Ivanova Grant/research support from: Celltrion, Inc, PPD, Quintiles, Egis Pharmaceuticals, and Pfizer., Agnieszka Zielinska Grant/research support from: Celltrion, Inc., Eve-Kai Raussi Grant/research support from: Celltrion, Inc. and Board of Estonian Society of Rheumatology, Anastas Batalov: None declared, SangJoon Lee Shareholder of: Celltrion, Inc., Employee of: Celltrion, Inc., JeeHye Suh Employee of: Celltrion, Inc., Noori Han Employee of: Celltrion, Inc., Rene Westhovens Grant/research support from: Bristol-Myers Squibb, Consultant for: Celltrion, Galapagos-Gilead
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Rheumatoid arthritis – non biologic treatment

FRI0129

THE BTK INHIBITOR, FENEBRUTINIB, EFFECTIVELY MODULATES B AND MYELOID CELL BIOLOGY IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Bruton's tyrosine kinase (BTK) plays an essential role in B cell development. BTK acts downstream of the B cell receptor in B cells, and Fc receptor signaling in myeloid cells, pathways thought to be involved in the pathogenesis of RA. Fenebrutinib (FEN) is a non-covalent small molecule inhibitor of BTK with greater than 100-fold selectivity relative to other kinases[1].
Objectives: To characterize the mechanistic effects of FEN on B and myeloid cell biology and determine the potential of biomarkers to predict response to FEN treatment in patients with RA.
Methods: The ANDES study included RA patients (pts) on background methotrexate (MTX) with inadequate response to prior MTX (n=480, Cohort 1, MTX-IR) or anti-TNFs (n=98, Cohort 2, TNF-IR). Cohort 1 pts were randomized to receive PBO, adalimumab (ADA) 40 mg Q2W, or FEN 50 mg QD, 150 mg QD or 200 mg BID. Cohort 2 pts were randomized to receive PBO or FEN 200 mg BID. Clinical efficacy was assessed based on the proportion of pts achieving ACR50 at week 12. Pts for whom samples were available were assessed for levels of rheumatoid factor (RF), total IgM and IgG, CCL4, CXCL13, CRP and IL6.
Results: Primary study results are reported separately. Overall, treatment with FEN caused significant reductions in RF (by week 12) and total IgM and IgG (at weeks 4-12) relative to PBO (**Table 1**). Early and sustained reductions of the B cell chemokine CXCL13 and the myeloid-enriched biomarker CCL4 were observed with FEN or ADA relative to PBO by week 1. CRP levels were significantly reduced with 200 mg BID FEN by week 8, and with ADA by week 2 relative to PBO. By week 12, there was a trend toward lower IL6 levels with FEN treatment relative to PBO, whereas ADA significantly reduced IL6 levels by week 1 relative to PBO in MTX-IR pts. In TNF-IR patients, IL6 was significantly reduced by FEN treatment by week 12 relative to PBO. PK-PD relationships were observed for multiple B and myeloid cell biomarkers. No single biomarker at baseline was associated with clinical response (at 12 weeks) in MTX-IR and TNF-IR pts. However, greater baseline RF titers were associated with increased FEN clinical response in TNF-IR pts.
Conclusion: FEN treatment resulted in strong pharmacodynamic effects on multiple biomarkers of B and myeloid cell biology in RA. This included reductions in total IgM and IgG that were not observed with ADA. Conversely, ADA reduced IL6 and CRP faster than FEN, highlighting key mechanistic differences between FEN and ADA. Baseline RF titer was associated with FEN clinical response in the more refractory TNF-IR

pts. These data provide mechanistic insights into the efficacy of FEN in RA patients.

REFERENCE:

[1] Crawford, et al., J Med Chem 2018 61(6) 2227-2245.

Table 1. FEN Treatment Causes Changes in B and Myeloid Cell Biomarkers (median% of baseline at week 12)

	Cohort 1					Cohort 2	
	FEN 50 mg qD (n=37)	FEN 150 mg qD (n=99)	FEN 200 mg BID (n=99)	PBO (n=100)	ADA 40 mg q2w (n=103)	FEN 200 mg BID (n=45)	PBO (n=41)
RF	71	63*	58*	87	66*	56*	120
IgM	88*	86*	84*	100	103	78*	96
IgG	100	96*	91*	100	100	89*	99
CCL4	83*	88*	77*	96	64*	79*	112
IL6	63	63	60	76	43*	60*	83
CRP	66	64	59*	81	37*	42*	98

*significant versus PBO (p-value ≤ 0.05 FDR adjusted); Kruskal-Wallis test

Disclosure of Interests: Alyssa Morimoto Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, Julie Rae Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, Leslie Chinn Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, Nandhini Ramamoorthi Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, Olivia Hwang Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, Alexandra Ward Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, D. James Haddon Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, Caroline Looney Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, Rupal Desai Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, Balazs Toth Shareholder of: Stockholder of Genentech/Roche, Employee of: Employee of Genentech/Roche, Katie Tuckwell Shareholder of: Genentech/Roche, Employee of: Genentech/Roche, Michael J. Townsend Shareholder of: Stockholder of Genentech/Roche, Employee of: Genentech/Roche

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FRI0130 RELATIONSHIP BETWEEN DEPRESSION AND DISEASE ACTIVITY IN US VETERANS WITH EARLY RHEUMATOID ARTHRITIS RECEIVING METHOTREXATE

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Background: Depression is common in rheumatoid arthritis (RA) patients and exacerbates disease activity and may reduce response to first-line disease-modifying antirheumatic drugs.

Objectives: To determine whether depression affects disease activity in patients with early RA treated with methotrexate (MTX).

Methods: Patients in the Veterans Affairs Rheumatoid Arthritis registry with early RA (onset <2 years) receiving MTX were selected (n=268). Depression was assessed at baseline using International Classification of Diseases codes (296.2-296.39, 300.4, 311). Disease activity was measured using the 28 joint count disease activity score (DAS-28), tender and swollen joint counts (TJC and SJC), patient and provider global assessment (PTGA and PRGA), patient-reported pain, multidimensional health assessment questionnaire (MDHAQ), and erythrocyte sedimentation rate (ESR). Baseline confounders included sociodemographics, anthropometrics, concomitant treatments, and other clinical characteristics. Propensity score weights were used to equate the depressed and non-depressed participants on baseline confounders. Generalized linear survey models were used to compare disease activity trajectories between depressed (n=48) and non-depressed (n=220) patients over two years. Standardized causal mean outcome differences were estimated at 6 months and 1- and 2-years follow-up.

Results: Depression was associated with significantly greater DAS-28 at 6 months (β=0.36; 95% CI: 0.03, 0.69) but not at 1- or 2-years follow-up (Table 1). Associations for DAS-28 component measures were smaller in magnitude, decreased over time, and not statistically significant. Depression was also associated with significantly greater pain at both 6 months (β=0.47; 95% CI: 0.11, 0.82) and 1-year (β=0.42; 95% CI: 0.03, 0.82) follow-up but not the PRGA or MDHAQ at any assessed time interval.

Table 1. Causal mean differences in standardized disease activity at 6 months and 1- and 2-years follow-up comparing those with depression to those without at baseline.

Measure	6 Months(β, 95% CI)	1 Year(β, 95% CI)	2 Years(β, 95% CI)
DAS-28	**0.36 (0.03, 0.69)**	0.11 (-0.29, 0.51)	-0.20 (-0.75, 0.35)
SJC	0.24 (-0.01, 0.50)	0.03 (-0.28, 0.34)	0.03 (-0.49, 0.54)
TJC	0.29 (-0.02, 0.61)	0.12 (-0.22, 0.47)	-0.16 (-0.75, 0.43)
PTGA	0.30 (-0.06, 0.66)	0.27 (-0.08, 0.61)	0.00 (-0.65, 0.65)
ESR	0.17 (-0.23, 0.57)	-0.07 (-0.47, 0.33)	-0.15 (-0.72, 0.41)
PRGA	0.14 (-0.16, 0.43)	0.15 (-0.20, 0.50)	-0.33 (-1.00, 0.34)
Pain	**0.47 (0.11, 0.82)**	**0.42 (0.03, 0.82)**	0.20 (-0.35, 0.75)
MDHAQ	0.18 (-0.15, 0.51)	0.11 (-0.27, 0.48)	0.06 (-0.46, 0.58)

DAS-28: 28 joint count disease activity score; SJC: Swollen joint count; TJC: Tender joint count; PTGA: Patient global assessment; ESR: erythrocyte sedimentation rate; PRGA: Provider global assessment; MDHAQ: Multidimensional health assessment questionnaire.

Conclusion: Findings demonstrate that depression is associated with less robust short-term response to MTX, and despite clinical RA treatment, more persistent and severe pain. Depression in RA patients may be a risk factor for primary non-response to MTX treatment, and interventions targeted at treating depression could result in better initial RA disease control and DMARD persistence.

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FRI0131 ELUCIDATING THE MECHANISM UNDERLYING CREATINE PHOSPHOKINASE UPREGULATION WITH UPADACITINIB

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Background: JAK inhibitors, including Upadacitinib (UPA), have been associated with increased serum levels of creatine phosphokinase (CPK) in patients with inflammatory disorders, but not in patients with myeloproliferative disease or in healthy subjects treated for a limited duration (1). While CPK increases can be indicative of muscle damage, there are no other indicators of muscle pathology observed with JAK inhibitors, suggesting that there may be another mechanism behind the increased CPK levels. Inflammatory diseases including rheumatoid arthritis are often associated with reduced muscle mass (sarcopenia), a process reversed with disease control (2).

Objectives: We hypothesized that one or more cytokines present in the inflammatory milieu may block differentiation of myoblasts into mature myocytes and that JAK inhibition restores differentiation and associated CPK expression. We focused on the gp130-mediated cytokines IL6, Oncostatin M (OSM), CNTF, and LIF as these have been shown to impact myoblast differentiation.

Methods: Human skeletal muscle myoblast (HSMM) cells were cultured in 10% fetal bovine serum, or were serum starved (2% horse serum) to induce differentiation into myocytes, with and without stimulation with OSM (1—100 ng/ml) and/or UPA (0.0007—1 μM) for up to 5 days. RNA was purified and expression of CPK (M-type) was determined by QPCR using GAPDH as a reference. CPK expression was also measured following stimulation of HSMM cells with other JAK inhibitors (Baricitinib and Tofacitinib).

Results: We have demonstrated that the gp130-mediated cytokine oncostatin M blocks myoblast differentiation into myotubules resulting in a decrease in CPK expression. Jak inhibition restores muscle differentiation and increased CPK expression (Figure 1A). Oncostatin M is highly expressed in RA synovium and other inflammatory milieu and may be one mechanism driving sarcopenia in RA. In addition to Upadacitinib, both Baricitinib and Tofacitinib restore myoblast differentiation suggesting that this is a class effect for JAK inhibitors (Figure 1B).
Conclusion: Our studies suggest that the increase in serum CPK upon treatment with JAK inhibitors may represent recovery of muscle development via reversal of inflammation-associated inhibition of myoblast differentiation

REFERENCES:

[1] J. D. Isaacs, et al., Arthritis Res Ther 16, R158 (2014).
[2] J. T. Giles, et al.,. Arthritis Rheum 59, 807-815 (2008).

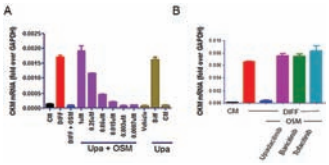


Figure 1. JAK inhibitors result in increased CPK expression in the presence of OSM. (A) M-type CPK mRNA expression in HSMM cells stimulated with OSM (100 ng/mL) and/or UPA (0.0007—1 μM) for 24 hours. (B) M-type CPK mRNA expression in HSMM cells stimulated with OSM (100 ng/mL) and UPA, Baricitinib, or Tofacitinib for 24 hours. Data is represented as a mean +/- Standard deviation. One representative is shown of 3 from two donors.CM, 10% FBS media; Diff, 2% Horse serum differentiation media; OSM, oncostatin M;UPA, Upadacitinib; CKM, creatine kinase M-type. HSMM, human skeletal muscle myoblasts.

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FRI0132

LONG-TERM SAFETY AND EFFICACY OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO CSDMARDS: RESULTS AT 60 WEEKS FROM THE SELECT-NEXT STUDY

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Background: Upadacitinib (UPA), an oral, JAK1-selective inhibitor showed efficacy over 12 weeks (wks) in patients (pts) with moderately to severely active rheumatoid arthritis (RA) and inadequate response to csDMARDs (SELECT-NEXT).[1]
Objectives: We assessed safety and efficacy of UPA through Wk60 in an ongoing extension of the phase 3 SELECT-NEXT study.
Methods: Pts received once-daily (QD) UPA at 15 mg (UPA15), 30 mg (UPA30) or placebo (PBO) for 12 wks on stable background csDMARDs. From Wk12, the start of a long-term blinded extension, pts initially randomized to PBO at BL were switched to UPA15mg or 30mg per prespecified assignment at BL. Pts randomized to UPA continued their assigned dose. No dose adjustments of UPA were allowed; however, starting at Wk24, adjustments to background RA medications were permitted. Sites/subjects remain blinded to UPA dose throughout the extension period. Efficacy data up to Wk60 are reported "As Observed". Adverse events (AE) per 100 pt yrs (PY) are summarized based on a cut-off date of Mar 22 2018.
Results: 611/661 (92%) pts completed Wk12 and continued on to the extension. By the safety data cut-off date, 125/611 (20%) had discontinued study drug, 50 (8.2%) discontinued due to an AE, and 10 (1.6%) due to lack of efficacy. Cumulative exposure was 393.3 PYs and 372.4 PYs for UPA15 and UPA30 respectively. Based on As Observed analysis, for pts who continued on UPA15 (262/310 [85%]) and UPA30 (243/301 [81%]), clinical and functional outcomes continued to improve or were maintained through Wk60, with 59% and 56% of pts achieving DAS28-CRP <2.6 and 35% and 32% achieving CDAI remission (≤2.8) with UPA 15 and 30 mg, respectively. Pts who switched from PBO to UPA15 or UPA30 showed comparable efficacy to those initially randomized to UPA (Table 1). The most frequently reported AEs were nasopharyngitis, urinary tract infection, upper respiratory tract infection, bronchitis, blood creatine phosphokinase increased, alanine aminotransferase increased, herpes zoster (HZ) and nausea. Most frequent AEs (≥0.8/100PYs) leading to premature study drug discontinuation were pneumonia, transaminase elevations, HZ and pyrexia. Event rates (E/100PYs) were numerically higher in UPA30 vs UPA15 for serious AE, AE leading to discontinuation, serious infections, HZ and malignancies, and were similar in UPA15 and UPA30 for adjudicated major adverse cardiovascular events and venous thromboembolic events (Table 2).
Conclusion: UPA15mg and 30mg on background csDMARD therapy demonstrated consistent efficacy and safety over 60 weeks in RA patients with inadequate response to csDMARDs. Both doses of UPA showed a similar efficacy profile at Wk 60, with numerically higher rates for certain safety events noted in the UPA30 group. An integrated safety analysis of upadacitinib across the phase 3 program is required to fully characterize the benefit:risk of UPA in RA.

REFERENCE:

[1] Burmester, et al. Lancet. 2018 Jun 23;391(10139):2503-2512

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Table 1. Efficacy Endpoints at Week 60 (as observed); n/N (%)

	PBO→UPA 15 MG	PBO→UPA 30 MG	UPA 15 MG	UPA 30 MG
ACR20	84/93 (90)	71/82 (87)	147/173 (85)	148/170 (87)
ACR50	64/92 (70)	55/84 (65)	122/168 (73)	120/169 (71)
ACR70	46/95 (48)	43/84 (51)	88/171 (51)	77/168 (46)
DAS28-CRP LDA (≤3.2)	74/95 (78)	56/82 (68)	129/173 (75)	125/167 (75)
DAS28-CRP<2.6	60/95 (63)	46/82 (56)	102/173 (59)	93/167 (56)
CDAI LDA (≤10)	72/93 (77)	56/83 (67)	129/171 (75)	123/169 (73)
CDAI REM (≤2.8)	28/93 (30)	29/83 (35)	59/171 (35)	54/169 (32)
Change from BL in HAQ-DI	-0.79	-0.68	-0.83	-0.73

Table 2. Treatment- emergent Adverse events; E/100PYs

	UPA 15 mg. N=324 PYs=393.3 E/100PYs	UPA 30 mg. N=321 PYs=372.4 E/100PYs
Any Adverse Event (AE)	334.6	371.9
Serious AE	16.3	24.2
AE Leading To D/C of Study Drug	8.4	17.2
Serious Infection[1]	2.3	7.5
Herpes Zoster[2]	3.1	7.5
Hepatic disorder[3]	14.2	13.7
Malignancy (excl. NMSC)	1.0	2.7
MACE (adjudicated)[4]	0.8	0.8
VTE[5] (adjudicated)	0.3	0.3
Deaths[6]	0	0.8

E, events; PYs, patient-years; E/100PY, events per 100 patient-years; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event (cardiovascular death, non-fatal myocardial infarction (MI), non-fatal stroke); VTE, venous thromboembolism (DVT, deep vein thrombosis; PE, pulmonary embolism)
[1]Most frequently reported serious infection were pneumonia, sepsis, staphylococcal wound infection and bronchitis.
[2]Herpes zoster: most involved 1 or 2 dermatomes. No meningoencephalopathic/noncutaneous involvement, except one primary varicella zoster pneumonia (chicken pox). Two HZ events were reported as ophthalmic.
[3]Hepatic disorders: Most were asymptomatic lab abnormalities.
[4]MACE: UPA15: 1 pt with non-fatal MI, 2 pts with non-fatal stroke; UPA30: 1 cardiovascular death, 1 non-fatal MI, 1 non-fatal stroke
[5]VTE: UPA15: 1 pt with DVT and PE; UPA30:1 pt with DVT
[6]Deaths: UPA30: 1 CV death in pt prior history of diabetes, hypertension, hyperlipidemia, non-fatal MI with coronary bypasses; 1 due to colon adenocarcinoma; 1 due to lymphangiosis carcinomatosa

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FRI0133 FILGOTINIB, A SELECTIVE JANUS KINASE 1 (JAK1) INHIBITOR, MODULATES DISEASE-ASSOCIATED CYTOKINES IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: Filgotinib (FIL), an oral selective JAK1 inhibitor, was safe and effective in FINCH2, a randomized, double-blind, placebo-controlled, phase 3 study in patients with active rheumatoid arthritis (RA) who had an inadequate response to biologic disease-modifying anti-rheumatic drugs (bDMARDs).[1]
Objectives: A longitudinal study of cytokines from patients in FINCH2 was conducted to identify RA-associated biomarkers related to bone biology, immune cell migration, and inflammation that are altered by FIL therapy; and FIL-associated biomarkers that correlated with clinical response (DAS28 [CRP], swollen and tender joint counts, pain, and fatigue).
Methods: Plasma, serum, and urine samples from RA patients (n=449) who received FIL (100 mg, 200 mg) or placebo (PBO) once daily plus methotrexate were analyzed at baseline (BL) and week 12 for 42 disease-relevant cytokines using validated, commercially available single or multiplex assays. PBO-corrected on-treatment changes in cytokine levels from BL to week 12 were compared between treatment arms (Wilcoxon rank sum test). Spearman rank correlation was used to compare changes in cytokine level from BL to week 12 and clinical response. P-values <0.05 were considered significant.
Results: At week 12, 18 of 42 cytokines significantly decreased with FIL 100 mg treatment relative to PBO; FIL 200 mg decreased these cytokines to a similar or greater degree. An additional 6 cytokines were significantly decreased by FIL 200 mg. Conversely, 2 cytokines increased relative to PBO with FIL 100 mg, and 5 cytokines increased with FIL 200 mg (sIL-6R, IL-10, IL-2, leptin, and IL-17A). Biomarkers most significantly modulated by FIL 200 mg (p<0.0001) included markers related to bone biology (MMP1 [–22.8%], MMP3 [–24.7%], CTX1 [–27.4%], and NTX [–16.4%]), immune cell migration (VCAM1 [–20.0%], ICAM1 [–14.2%], CXCL13 [–45.0%], and CXCL10 [–32.3%]), and inflammation (TNFRI [–20.7%], CRP [–77.4%], SAA [–61.8%], IL-6 [-13.6%], and resistin [–20.2%]).
Hierarchical clustering of BL biomarker levels revealed distinct groups of cytokines that were strongly correlated with each other. Among them, SAA, IL-6, and CXCL10 were significantly positively correlated with each other (rho >0.6) and with RA disease activity (DAS28[CRP]) at BL (rho > 0.3). Biomarkers, including CRP (IL-6, SAA), PainVAS (CRP, SAA), and SJC28 (CRP, IL-6, CXCL10), were also significantly correlated with individual components of DAS28[CRP]. Several biomarkers associated with RA disease activity at BL were decreased with FIL at week 12 relative to PBO (FIL 100 mg: CRP [–48.7%], SAA [–36.9%], and IL-6 [–2.6%]; and FIL 200 mg: CRP [–77.4%], SAA [–61.8%], IL-6 [–13.6%], and CXCL10 [–32.3%]), suggesting FIL impacts these disease activities at a molecular level.
Conclusion: Twelve weeks of FIL treatment significantly reduced 24 disease-relevant cytokines associated with bone biology, immune cell migration, and inflammation in patients with active RA. These effects were dose-dependent and suggest a shift toward a restored immune homeostasis. These findings are consistent with the clinical efficacy of FIL in FINCH2.

REFERENCES:
[1] Genovese MC, et al. ACR 2018. Abstract L06.

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FRI0134 A PHASE 3 STUDY OF THE EFFICACY AND SAFETY OF PEFICITINIB (ASP015K) IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAD AN INADEQUATE RESPONSE TO DMARDS

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Background: Peficitinib (ASP015K), a novel oral JAK inhibitor, demonstrated efficacy as once-daily monotherapy in patients with moderate to severe rheumatoid arthritis (RA) in a phase 2b study (NCT01649999).
Objectives: To evaluate the efficacy and safety of peficitinib alone or in combination with disease-modifying antirheumatic drugs (DMARDs) in patients with RA who had an inadequate response to DMARDs.

Table 1 Primary and selected secondary efficacy endpoints at week 12/ET

Result at week 12/ET	PBO	Peficitinib 100 mg/day	Peficitinib 150 mg/day	Etanercept 50 mg/week (open-label arm)
ACR20[a], n/N (%)	31/101 (30.7)	60/104 (57.7)***	76/102 (74.5)***	167/200 (83.5)
ACR50[a], n/N (%)	9/101 (8.9)	32/104 (30.8)***	43/102 (42.2)***	105/200 (52.5)
ACR70[a], n/N (%)	1/101 (1.0)	14/104 (13.5)[b,c]	28/102 (27.5)***	61/200 (30.5)
Mean (SD) CRP change from baseline, mg/dL	0.022 (1.498)	-1.056 (1.908)***	-1.734 (1.906)***	-1.207 (2.694)
Mean (SD) ESR change from baseline, mm/h	-1.96 (17.82)	-12.96 (21.51)***	-23.92 (21.26)***	-20.92 (21.66)
DAS28-CRP <2.6[a], n/N (%)	5/100 (5.0)	25/102 (24.5)***	35/101 (34.7)***	91/200 (45.5)
Mean (SD) DAS28-CRP change from baseline	-0.64 (1.20)	-1.62 (1.41)***	-2.17 (1.14)***	-2.42 (1.11)
Mean (SD) change from baseline in patient's assessment of pain, 100 mm VAS	-6.64 (24.61)	-23.78 (30.75)***	-30.65 (27.91)***	-30.82 (27.68)
SDAI remission (SDAI score ≤3.3)[a], n/N (%)	0/100 (0.0)	9/102 (8.8)[b]	9/101 (8.9)[b]	37/200 (18.5)

Last Observation Carried Forward imputation method was used. Statistical testing was performed for ASP015K 100 mg and 150 mg, compared with PBO. ***p<0.001 vs PBO according to Wald's Chi-square test for ACR20, ACR50, ACR70, DAS28-CRP <2.6, and SDAI remission, and analysis of covariance for CRP, ESR, DAS28-CRP and patient's assessment of pain. Closed testing procedure was used for multiplicity adjustment in the primary analysis.
[a]Based on logistic regression model: Response (responder, non-responder) = treatment + the prior biologic-DMARD-IR (no, yes) + concomitant DMARD use (no, yes) + study region (Japan, Korea, and Taiwan).
[b]Not estimable owing to the small number of responders.
[c]In a *post-hoc* analysis, based on the logistic regression model in which the only independent variable was treatment, the odds ratio between PBO and peficitinib 100 mg for ACR70 was estimated and p=0.009.
SD=standard deviation; SDAI=simplified disease activity index; VAS=visual analog scale.

Table 2 Treatment-emergent adverse events

	PBO (N=101)	Peficitinib 100 mg/day (N=104)	Peficitinib 150 mg/day (N=102)	Peficitinib 100 mg/day + 150 mg/day (N=206)	Etanercept 50 mg/week (open-label arm) (N=200)
Event, n (%), week 0–12					
Any AE	54 (53.5)	59 (56.7)	55 (53.9)	114 (55.3)	119 (59.5)
Drug-related AE[a]	29 (28.7)	33 (31.7)	38 (37.3)	71 (34.5)	75 (37.5)
Death	0	0	0	0	0
SAE	4 (4.0)	3 (2.9)	2 (2.0)	5 (2.4)	4 (2.0)
Drug-related SAE[a]	3 (3.0)	2 (1.9)	1 (1.0)	3 (1.5)	4 (2.0)
Grade ≥3 AE[b]	8 (7.9)	6 (5.8)	3 (2.9)	9 (4.4)	6 (3.0)
AE leading to permanent discontinuation of study drug or reference drug	4 (4.0)	6 (5.8)	3 (2.9)	9 (4.4)	5 (2.5)
Serious infection	0	0	1 (1.0)	1 (0.5)	1 (0.5)
Herpes zoster-related disease	0	1 (1.0)	0	1 (0.5)	2 (1.0)
Malignancy	0	0	0	0	0
Incidence rate per 100 patient-years (95% confidence interval), overall study period[c]	**PBO (N=101)**	**Peficitinib 100 mg/day (N=104)**	**Peficitinib 150 mg/day (N=102)**	**Peficitinib total (N=296)[d]**	**Etanercept 50 mg/week (open-label arm) (N=200)**
Serious infection[e]	0.0	1.1 (0.2, 8.1)	2.2 (0.5, 8.7)	2.0 (0.8, 4.9)	2.0 (0.8, 5.5)
Herpes zoster-related disease	0.0	5.8 (2.4, 13.8)	4.4 (1.7, 11.7)	5.8 (3.4, 9.8)	2.6 (1.1, 6.2)
Malignancy	0.0	2.3 (0.6, 9.1)	0.0	1.2 (0.4, 3.8)	0.5 (0.1, 3.6)

[a]Possibly or probably related to study drug, as assessed by the investigator, or records where relationship is missing.
[b]Based on NCI-CTCAE grade: grade 3=severe or medically significant, grade 4=life threatening, grade 5=death related to AE.
[c]Patient-years covers from initial dose up to first incidence of AE for patients who had at least one event, otherwise, the duration of the patients are summed as from initial dose through follow-up. Incidence rate was calculated as (100 x number of patients who had at least one incidence / total patient-year).
[d]Includes AEs that occurred after initial peficitinib dosing, and after switching from PBO to peficitinib 100 mg/day or 150 mg/day.
[e]Defined as an AE belonging to the system organ class of 'Infections and infestations' and regarded as serious.
AE=adverse event; SAE=serious adverse event.

Methods: This multicentre, randomised, double-blind, parallel-group, placebo (PBO)-controlled phase 3 study (NCT02308163) was conducted in Japan, Korea and Taiwan. All patients had RA diagnosed according to 1987 ACR or 2010 ACR/EULAR criteria. Patients with active RA (defined as ≥6 tender and painful joints and ≥6 swollen joints, using 68 and 66-joint assessment respectively, and CRP >0.50 mg/dL) and inadequate response to DMARDs (administered for ≥90 days) were randomised in a 1:1:1:2 ratio to 52 weeks' treatment with PBO, peficitinib 100 mg/day, peficitinib 150 mg/day or etanercept 50 mg/week (open-label reference arm). At week 12, patients initially assigned to PBO were switched (under blinded conditions) to either peficitinib 100 mg/day or peficitinib 150 mg/day until end of treatment. Concomitant stable dose of DMARDs was permitted. The primary efficacy variable was ACR20 response rate at week 12/early termination (ET).

Results: In total, 507 patients were randomised and treated: PBO (n=101), peficitinib 100 mg/day (n=104), peficitinib 150 mg/day (n=102) and etanercept (n=200). Regarding efficacy at week 12/ET, significant differences were observed with peficitinib 100 mg/150 mg vs PBO ($p<0.001$) in the proportion of patients achieving ACR20, ACR50, ACR70 (150 mg/day dose only) and DAS28-CRP <2.6, and for change from baseline to week 12/ET in DAS28-CRP (**Table 1**). Week 0–12 safety results were similar between treatment groups and serious adverse events were more common with PBO than other study treatments (**Table 2**). For the overall study period, the incidence rate of serious infections per 100 patient-years was higher with peficitinib 100 mg/150 mg than PBO (**Table 2**). There were no deaths during the study.

Conclusion: In patients with RA who had an inadequate response to DMARDs, 100 mg/day and 150 mg/day peficitinib doses significantly reduced RA symptoms according to clinical and patient assessment scores. The proportion of patients achieving the primary efficacy variable (ACR20 at week 12/ET) was significantly greater for both peficitinib doses versus PBO. Peficitinib 100 mg/day and 150 mg/day showed acceptable safety and tolerability, with no new safety signals detected compared with other JAK inhibitors.

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FRI0135

INTRAVENOUS PEGYLATED LIPOSOMAL PREDNISOLONE SODIUM PHOSPHATE MORE EFFECTIVE THAN INTRAMUSCULAR INJECTION OF METHYLPREDNISOLONE ACETATE IN TREATING RA PATIENTS WHO ARE EXPERIENCING A FLARE: A PHASE III, RANDOMIZED, DOUBLE-BLIND, DOUBLE DUMMY, ACTIVE CONTROLLED, MULTI-CENTER STUDY

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Background: Intravenous pegylated liposomal prednisolone sodium phosphate is developed to deliver liposomal entrapped prednisolone in the bloodstream; the lipid vesicles allow selective accumulation of glucocorticoids in inflamed tissues by locally increased permeability of blood vessel walls, while limiting systemic exposure.

Objectives: To assess efficacy and safety of liposomes with prednisolone in patients with active rheumatoid arthritis (RA) who are experiencing a flare in comparison to a standard of care medication (methylprednisolone injections).

Methods: The study enrolled active RA patients (≥ 18 years) who were experiencing a flare of their disease, defined as a recent switch from a period with well documented remission or low disease activity to an active disease phase, as determined by a change in the Disease Activity Score in 28 Joints (DAS28 ≥ 3.2). Patients were randomized 1:1:1 into liposomal prednisolone 75 mg, liposomal prednisolone 150 mg and methylprednisolone 120 mg groups. Treatment was administered on Day 1 and Day 15. Patients treated with liposomal prednisone IV received IM placebo injections; patients treated with methylprednisolone IM received IV placebo infusions. Evaluations were performed weekly for the first 4 weeks, and every second week thereafter. The primary endpoint was EULAR response rate (good and moderate combined) at Day 8. The primary analysis involved two comparisons: 1) liposomal prednisone 150 mg vs. methylprednisolone 120 mg, 2) liposomal prednisone 75 mg vs. methylprednisolone 120 mg. Safety results (AEs, vital signs, physical examinations, laboratory, ECG) were also evaluated. A total of 172 patients were screened and 150 were randomized to liposomal prednisone 75 mg (N=49), liposomal prednisone 150 mg (N=52) and methylprednisolone 120 mg (N=49). 144 (96%) patients completed the study; mean study duration was 82.9 days; adverse events or intercurrent illness were primary reasons for discontinuation.

Results: EULAR response rate at Week 1 (Day 8) was 90.0% for liposomal prednisone 150 mg and 85.7% for liposomal prednisone 75 mg vs. 66.7% for methylprednisolone 120 mg treated patients (p-values of 0.007 and 0.018, resp.). Other secondary endpoints supported the primary endpoint results showing significant or clinically meaningful improvements in other EULAR response evaluations, as well as DAS28, VAS, ACR20/50/70, SF-36, HAQ and FACIT-F assessments. Similar numbers of patients reported at least one adverse event (AE) in each treatment group; 42 (86 %), 46 (89 %) and 39 (80 %), resp., for the liposomal prednisone 75 mg, liposomal prednisone 150 mg and methylprednisolone 120 mg groups. Most commonly reported AEs were nausea in the liposomal prednisone groups and headache in all 3 treatment arms. Approximately 8%

of patients in the liposomal prednisone groups reported AEs related to study drug administration, versus 6% in the methylprednisolone group. Serious adverse events (SAEs) were reported by 4 (8.2%), 1 (1.9%) and 2 patients (4.1%) resp for the liposomal prednisone 75 mg, liposomal prednisone 150 mg and methylprednisolone 120 mg groups. Five of the 7 SAEs were treatment related; these included 4 events of hypersensitivity in the liposomal prednisone arms and one event of viral upper respiratory tract infection in the methylprednisolone group.

Conclusion: In this phase III trial, liposomal prednisone 75 mg and 150 mg were significantly more effective than 120 mg -methylprednisolone in treating patients with a flare of their RA. The overall incidence of AEs was similar across treatment groups, although hypersensitivity appeared to be more common with liposomal prednisone.

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FRI0136 THE EFFICACY AND SAFETY OF SIROLIMUS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A RANDOMIZED AND PARALLEL-CONTROLLED CLINICAL TRIAL

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Background: We have reported previously that the insufficient absolute number or functional defects of regulatory T cells (Tregs) in patients with rheumatoid arthritis (RA)[1-3], challenging conventional unspecific immunosuppressive therapy. Sirolimus, a mTOR inhibitor, is reported to allow growth of functional Tregs, which would be able to provide new strategy and target for the treatment of RA[4].

Objectives: To investigate efficacy and safety of sirolimus combined with conventional immunosuppressants for RA treatment.

Methods: In this non-blinded and parallel-group trial, we randomly assigned 62 patients to receive conventional glucocorticoids and immunosuppressants with or without sirolimus at a dosage of 0.5 mg on alternate days for 24 weeks in a 2:1 ratio. The demographic features, clinical manifestations and laboratory indicators including peripheral blood lymphocyte subgroups and $CD4^+$T subsets were compared before and after the treatment.

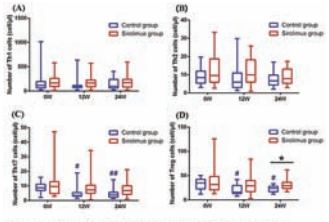


Figure 1: Changes of levels of $CD4^+T$ cells subsets after different treatments. Effects of treatments were assessed by repeated measures analysis using a mixed-effects model. Two-tailed unpaired t-test was used to compare the disease activity measures between sirolimus and conventional groups. #p< 0.05, ##p< 0.01 relative to baseline (week 0) in conventional group (blue); §p< 0.05 relative to baseline in sirolimus group (red).; * p< 0.05 compared between groups.

Results: Finally, 37 patients in sirolimus group and 18 in conventional treated group completed 6-month study. By 24 weeks, the patients with sirolimus experienced the significant reduction in disease activity indicators including DAS28, ESR, the number of tender joints and swollen joints (p<0.001). Notably, they had a higher level of Tregs as compared those with conventional therapy alone (p<0.05), indicating that sirolimus could partly restore the reduced Tregs. Concomitantly, their usages of immunosuppressants for controlling disease activity were decreased as compared with conventional group with no difference in blood routine, liver and renal functions both before and after the treatment of sirolimus and between two groups (p>0.05).

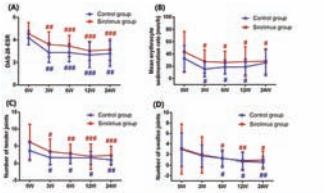


Figure 2: Efficacy of sirolimus in reducing disease activity. Mean DAS-28-ESR score (A), ESR (B), mean number of tender joints (C) and swollen joints(D). Overall changes during treatment were assessed by repeated measures analysis using a mixed-effects model. Two-tailed unpaired t-test was used to compare the disease activity measures between sirolimus and conventional groups. Error bars show SD. DAS28: 28-joint disease activity score; ESR: erythrocyte sedimentation rate. #p< 0.05, ##p< 0.01, ###p< 0.001 relative to baseline (week 0) in conventional group (blue); §p< 0.05, §§p< 0.01, §§§p< 0.001 relative to baseline in sirolimus group (red).

Conclusion: Low-dose sirolimus immunoregulatory therapy selectively upregulated Tregs and partly replaced the usage of immunosuppressants to control disease activity without over-treatment and evaluable side effect. The further study is required using a large sample of RA patients treated with sirolimus for longer period.

REFERENCES:

[1] Komatsu N, Takayanagi H. Arthritogenic T cells in autoimmune arthritis[J]. The international journal of biochemistry & cell biology, 2015, 58:92-96. doi:10.1016/j.biocel.2014.11.008.
[2] Morita T, Shima Y, Wing JB, *et al.* The Proportion of Regulatory T Cells in Patients with Rheumatoid Arthritis: A Meta-Analysis[J]. PloS one, 2016, 11 (9):e0162306.doi:10.1371/journal.pone.0162306.
[3] Spence A, Klementowicz JE, Bluestone JA, *et al.* Targeting Treg signaling for the treatment of autoimmune diseases[J]. Current opinion in immunology, 2015, 37:11-20.doi:10.1016/j.coi.2015.09.002.
[4] Perl A. Activation of mTOR (mechanistic target of rapamycin) in rheumatic diseases[J]. Nature reviews Rheumatology, 2016, 12(3):169-182. doi:10.1038/nrrheum.2015.172.

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FRI0137 UPADACITINIB IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO METHOTREXATE: RESULTS FROM SELECT-COMPARE

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Background: Upadacitinib (UPA), a selective JAK1 inhibitor, has demonstrated superior improvement in the clinical signs and symptoms of rheumatoid arthritis (RA) compared with placebo (PBO) and adalimumab (ADA).[1]

Objectives: To evaluate the effect of UPA vs PBO and vs ADA on patient-reported outcomes (PROs) at Week 12 in SELECT-COMPARE (NCT02629159), a randomised controlled trial (RCT) in an active RA population with inadequate responses to methotrexate (MTX).

Methods: Patients in SELECT-COMPARE, a phase 3 RCT, received UPA (15 mg once daily), PBO, or ADA (40 mg every other week) while on background MTX therapy. The following PROs were collected prospectively: Patient Global Assessment of Disease Activity (PtGA) by visual analogue scale (VAS), pain by VAS, Health Assessment Questionnaire Disability Index (HAQ-DI), duration and severity of morning (AM) stiffness, health-related quality of life by Short Form-36 (SF-36), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), and Work Instability Scale for RA (RA-WIS). Least squares mean (LSM) changes from baseline (BL) to Week 12 were based on mixed-effects repeated measures

models. The proportions of patients reporting improvements ≥ minimum clinically important differences (MCID) from BL to Week 12 or scores ≥ normative values were determined with UPA, PBO, and ADA treatment; comparisons used chi-square tests.

Results: Data from 1629 patients (UPA: 651; PBO: 651; ADA: 327) were analysed. Mean age was 54 years; 79% were female; 54% had RA for ≥5 years. Baseline mean PRO scores were similar across treatment groups. At Week 12, UPA treatment resulted in statistically significant LSM changes from BL vs PBO across all PROs and statistically significant LSM changes from BL vs ADA in PtGA, pain, HAQ-DI, AM stiffness severity, FACIT-F, and SF-36 physical component summary (PCS) and 6/8 domain scores (**Table**). ADA treatment resulted in statistically significant LSM changes from baseline vs PBO in PtGA, pain, HAQ-DI, AM stiffness severity and duration, FACIT-F, and SF-36 PCS and 5/8 domain scores. Compared with PBO at Week 12, significantly more UPA-treated patients reported improvements ≥ MCID and scores ≥ normative values across all PROs with numbers needed to treat (NNTs) <10. The proportions of UPA-treated patients reporting improvements ≥ MCID were similar or numerically higher than ADA-treated patients. Importantly, the proportion of UPA vs ADA treated patients reporting improvements ≥ normative values were significantly greater (all $p<0.05$) in PtGA (36% vs 26%), HAQ-DI (21% vs 14%), SF-36 PCS (16% vs 11%), and SF-36 bodily pain (29% vs 21%) and vitality (42% vs 35%) domains.

LSM Changes from Baseline and Percentage of Responders at Week 12 After UPA Initiation

PRO	Baseline Mean	LSM Changes from Baseline			Patients Reporting Improvements ≥MCID, n (%)		
	(n=1629)	UPA 15 mg (n=651)	PBO (n=651)	ADA 40 mg (n=327)	UPA 15 mg (n=651)	PBO (n=651)	ADA 40 mg (n=327)
PtGA	64.4	−30.4*§	−15.2	−23.6‡	474 (73.4)*	332 (51.1)	219 (67.6)
Pain VAS	65.5	−31.8*§	−15.5	−25.3‡	483 (74.8)*	347 (53.4)	227 (69.8)
HAQ-DI	1.6	−0.6*§	-0.3	-0.5‡	465 (72.1)*	330 (50.8)	231 (71.1)
FACIT-F	26.8	9.0*§	4.8	7.4‡	413 (64.0)*	299 (46.4)	202 (62.2)
Duration AM Stiffness[a]	142.8	−92.6*	−48.6	−82.7‡	194 (29.9)[b]*	144 (22.1)	93 (28.7)[b]
Severity AM Stiffness[c]	6.3	−3.4*§	−1.8	−2.9‡	526 (81.3)[b]*	424 (65.0)	260 (80.2)[b]
RA-WIS	14.7	−5.2*	−2.0	−4.5‡	120 (41.7)*	64 (24.4)	42 (32.1)
SF-36 PCS	32.5	7.9*§	3.6	6.3‡	469 (72.5)*	345 (53.2)	226 (69.1)
SF-36 MCS	42.9	6.4*	3.7	5.4	386 (59.7)*	309 (47.7)	192 (58.7)
SF-36 PF	31.5	7.3*§	3.6	6.2‡	479 (73.7)*	379 (58.2)	237 (72.5)
SF-36 RP	33.3	6.9*§	3.6	5.2	470 (72.3)*§	374 (57.5)	213 (65.1)
SF-36 BP	34.1	9.9*§	4.6	8.0‡	501 (77.1)*	390 (59.9)	239 (73.1)
SF-36 GH	37.8	7.3*§	3.1	5.7‡	458 (70.5)*	362 (55.6)	212 (64.8)
SF-36 VT	40.9	8.2*§	4.3	6.8‡	479 (73.7)*	372 (57.1)	225 (68.8)
SF-36 SF	38.1	7.2*§	3.4	5.8‡	418 (64.3)*	323 (49.6)	195 (59.6)
SF-36 RE	37.9	6.2*	3.6	5.2	368 (56.6)*	301 (46.2)	175 (53.5)
SF-36 MH	40.7	7.0*	4.0	5.9	449 (69.1)*	349 (53.6)	213 (65.1)

*$P<0.05$ for UPA vs PBO. LSM change from baseline P values represent statistical significance between groups.
§$P<0.05$ for UPA vs ADA. LSM change from baseline P values represent statistical significance between groups.
‡LSM change from baseline differences statistically significant between groups based on non-overlapping 95% confidence intervals.
[a] Duration in minutes. [b] % responders reporting scores ≥ minimal important difference. [c] Assessed on a numeric scale of 1–10, with 10 being the worst level.
ADA, adalimumab; AM, morning; BP, bodily pain; FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue; GH, general health; HAQ-DI, Health Assessment Questionnaire Disability Index; LSM, least squares mean; MCID, minimum clinically important difference; MCS, Mental Component Summary; MH, mental health; PBO, placebo; PCS, Physical Component Summary; PF, physical function; PRO, patient-reported outcome; PtGA, Patient Global Assessment of Disease Activity; RA-WIS, Work Instability Scale for Rheumatoid Arthritis (among employed patients); RE, role emotional; RP, role physical; SF, social function; SF-36, 36-Item Short Form Health Survey; UPA, upadacitinib; VAS, visual analogue scale; VT, vitality.

Conclusion: Among patients with active RA, treatment with UPA 15 mg QD on background MTX therapy for 12 weeks resulted in statistically significant and clinically meaningful improvements in PROs compared with PBO. Overall, PRO improvements with UPA treatment met or were superior to treatment with ADA, especially in key domains of pain, function and vitality.

REFERENCES:

[1] Fleischmann R, et al. *Arthritis Rheumatol.* 2018;70(S9), abstract 890.

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FRI0138 EXPOSURE-RESPONSE ANALYSES OF UPADACITINIB EFFICACY AND SAFETY IN RHEUMATOID ARTHRITIS – ANALYSES OF PHASE 2 AND 3 STUDIES

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Background: Upadacitinib (UPA), an oral selective JAK1 inhibitor, demonstrated favorable efficacy and acceptable safety in two Phase 2 and five Phase 3 global studies in subjects with moderately to severely active rheumatoid arthritis (RA).

Objectives: To characterize relationships between UPA plasma exposures and different efficacy and safety endpoints using data from Phase 2 and Phase 3 RA studies.

Methods: Analyses were conducted using data from 3685 (for efficacy) and 4577 (for safety) subjects with RA enrolled in the Phase 2 and 3 studies. Relationships between UPA plasma concentrations and efficacy and selected clinically relevant safety endpoints were analyzed using Markov Chain models and logistic regression analyses, respectively.

Results: Percentage of subjects achieving ACR20, ACR50, AC70, DAS28 (CRP) ≤ 3.2, and DAS28(CRP) < 2.6 increased with increasing UPA exposures, with maximum efficacy reached at exposures of 15 mg to 30 mg QD. Model-estimated efficacy responses are presented in Table 1. No relationships were observed between UPA exposure and pneumonia, herpes zoster infection, changes in platelet count (platelets $\geq 600\times10^9$/L, platelets $>400\times10^9$/L), lymphopenia (Grade 4 or higher), and neutropenia (Grade 3 or higher) at Week 12/14 or Week 24/26. Shallow trends for exposure-response relationships were observed for > 2 g/dL decrease in hemoglobin from baseline at Week 12/14 and Week 24/26, lymphopenia Grade 3 or higher at Week 12/14, and serious infections at Week 24/26. No relationship with UPA exposure was observed for Grade 3 or higher lymphopenia at Week 24/26 (Figure 1).

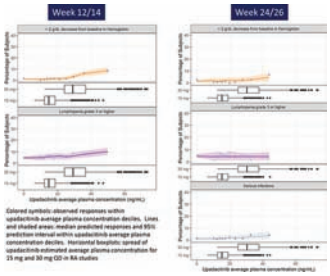


Figure 1. Observed and Model Predicted Percentage of Subjects Experiencing Laboratory Changes/Safety Events of Interest with Increasing UPA Plasma Exposures

Table 1. Model-Estimated Efficacy Responses Following Placebo and UPA 15 mg and 30 mg QD Dosing Regimens Based on Exposure-Response Analyses of Phase 2 and 3 Studies

Population	Clinical Efficacy Response Variable[a]	Upadacitinib Dose		
		Placebo	15 mg QD	30 mg QD
csDMARD-IR on Background csDMARDs	ACR20	40 (34, 47)	66 (59, 71)	68 (63, 74)
	ACR50	17 (12, 22)	41 (35, 47)	45 (39, 51)
	ACR70	6 (3, 11)	23 (17, 29)	26 (21, 33)
	DAS28(CRP) ≤ 3.2	19 (13, 24)	45 (40, 52)	50 (44, 57)
	DAS28(CRP) < 2.6	11 (8, 16)	31 (25, 36)	34 (29, 41)
bDMARD-IR on Background csDMARDs	ACR20	36 (30, 43)	58 (52, 65)	61 (54, 67)
	ACR50	14 (8, 19)	34 (27, 41)	37 (31, 45)
	ACR70	5 (2, 9)	18 (12, 24)	21 (16, 26)
	DAS28(CRP) ≤ 3.2	18 (14, 24)	40 (34, 47)	45 (39, 51)
	DAS28(CRP) < 2.6	11 (7, 15)	27 (21, 33)	31 (25, 36)
csDMARDs-IR on Upadacitinib Monotherapy	ACR20	36 (29, 44)	66 (58, 71)	68 (61, 75)
	ACR50	12 (8, 16)	42 (36, 49)	45 (37, 51)
	ACR70	3 (1, 7)	24 (18, 31)	27 (20, 34)
	DAS28(CRP) ≤ 3.2	17 (12, 23)	50 (44, 58)	55 (48, 62)
	DAS28(CRP) < 2.6	11 (7, 16)	36 (31, 44)	40 (34, 47)

MTX-IR = Methotrexate inadequate responder; csDMARDs-IR = conventional synthetic disease-modifying anti-rheumatic drug inadequate responders; bDMARD-IR = Biologic disease-modifying anti-rheumatic drug inadequate responder

a. Data are presented as median (5^{th}, 95^{th} percentiles)

Conclusion: Exposure-efficacy analyses demonstrate that UPA 15 mg QD dose maximizes efficacy in RA while 30 mg QD dose provides only a small (≤ 5%) additional incremental efficacy benefit. This was consistent across RA populations and whether UPA is used as monotherapy or on background treatment of csDMARDs. UPA plasma exposures associated with 15 mg and 30 mg QD dosing are predicted to have limited effects on the evaluated safety endpoints after 24 to 26 weeks of treatment.

REFERENCES:

[1] Genovese, et al. Lancet. 2018; 391(10139): 2513-2524.
[2] Burmester, et al. Lancet. 2018; 391(10139): 2503-2512.
[3] Mohamed et al. Clin Pharmacol Drug Dev. 2018 Apr 24.

Disclosure of Interests: Mohamed-Eslam Mohamed Shareholder of: AbbVie, Employee of: AbbVie, Ahmed Nader Shareholder of: AbbVie, Employee of: AbbVie, Insa Winzenborg Shareholder of: AbbVie, Employee of: AbbVie, Eva Doelger Shareholder of: AbbVie, Employee of: AbbVie, Peter Noertersheuser Shareholder of: AbbVie, Employee of: AbbVie, Aileen Pangan Shareholder of: AbbVie, Employee of: AbbVie, Ahmed Othman Shareholder of: AbbVie, Employee of: AbbVie

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FRI0139 IMPROVEMENT SOLUBILITY OF AMPHIPHILIC NAPROXEN-NIOSOME FOR INFLAMMATORY ARTHRITIS TREATMENT

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Background: Naproxen (S-6-methoxy-a-methyl-2-naphthaleneacetic acid) is a nonsteroidal anti-inflammatory drug (NSAID), which is used to treat rheumatoid arthritis, osteoarthritis, chronic juvenile arthritis, ankylosing spondylitis. Niosomes or nonionic surfactant vesicles (NSV's) are known as biocompatible, non-immunogenic systems and present potential applications in the delivery of hydrophilic and hydrophobic drugs in order to higher chemical stability and less production cost characteristics. Niosomes are now broadly investigated as other drug vehicles to the encapsulation and controlled release of the different drug molecules. Many studies showed micronized NSAIDs, at low dosages using nanotechnology, can increase the drug level and increase absorption and can have the best effect at the lowest dose and reduce the risk of side effects. Because insufficiently soluble and insoluble drugs exhibit low absorption and poor bioavailability, improvements in solubility and solubility are important for developing various drug preparation methods.
Objectives: The purpose of the present study was to investigate the formulations of micellar/niosomal vesicles prepared from the biocompatible surfactant tween 80 (polysorbate 80) and the squalene as an excipient, through film hydration method and their potential as a drug delivery system for NPX.
Methods: We prepared niosomal Naproxen from the biocompatible surfactant tween 80 (polysorbate 80) and the squalene as an excipient, through thin-film hydration method and their potential as a drug delivery system for NPX. The prepared system was characterized for by Fourier transform infrared spectroscopy (FT-IR), UV-visible, photoluminescence (PL), field emission scanning electron microscopy (FE-SEM), and transmission electron microscopy (TEM).
Results: By using this method, the percent drug loading that resulted by the encapsulation of niosomes was found to be 99.5 ± 0.2% for 5% of NPX weight in total ingredients weight of niosomal vesicles (w/w). It was also seen that a slower rate of release of the NPX from the drug encapsulated noisome over 7 days, suggesting stable complexation of NPX. Cell toxicity assay was carried out by A549 and HeLa cancer cell lines and showed the half maximal inhibitory concentration (IC_{50}) of NPX increased about 8.25 folds for A549 (from 3300 μM to 400 μM) and it decreases about 5.5 folds for HeLa (from 1920 μM to 350 μM by nanoformulation.
Conclusion: Niosomal formulation has been evaluated as a safe drug delivery system. In this study, we showed that niosomal naproxen has more stability and more efficiently affect the cells. It can be explained by increasing the bioavailability of naproxen by niosomal nanocarriers which probably is based on more water solubility and more efficient cell entrance of drug. It seems that niosomal naproxen is a great candidate for future in vitro and in vivo researches for evaluating potential clinical applications.

REFERENCES:

[1] M.R. Rodrigues, C.M. Lanzarini, E. Ricci-Junior, Preparation, in vitro characterization and in vivo release of naproxen loaded in poly-caprolactone nanoparticles, Pharm. Dev. Technol. 16 (2009) 12-21.
[2] K.D. Tripathi, Essentials of Medical Pharmacology. Jaypee Brothers Medical Publishers Pvt. Ltd., New Delhi, 5, (2004) 176.
[3] M. Seleci, D. Ag Seleci, R. Joncyzk, F. Stahl, C. Blume, T. Scheper, Smart multifunctional nanoparticles in nanomedicine, Bio NanoMaterials, 17 (2016) 33-41.
[4] J. Du, D. Li, J. Lu, Chemiluminescence determination of naproxen based on europium(III)-sensitized KIO4–H2O2 reaction, Luminescence 25 (2010) 76-80.
[5] A.H. Alomrani, M.H. Al-Agamy, M.M. Badran, In vitro skin penetration and antimycotic activity of itraconazole loaded niosomes: Various non-ionic surfactants, Journal of Drug Delivery Science and Technology 28 (2015) 8-15.

Disclosure of Interests: None declared

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FRI0140 EVALUATION OF EFFECTIVENESS AND USAGE PATTERNS OF TOFACITINIB IN TREATMENT OF RHEUMATOID ARTHRITIS IN AUSTRALIA: AN ANALYSIS FROM THE OPAL-QUMI REAL WORLD DATASET

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Limited data from large real-world patient populations exist to describe treatment outcomes of patients who receive tofacitinib for the management of RA in Australia.
Objectives: To evaluate effectiveness and treatment patterns of tofacitinib in a large real-world cohort of Australian adult patients with RA.
Methods: Routinely collected, de-identified clinical data were sourced from the OPAL-QUMI dataset. Data from adult patients with a diagnosis of RA, who initiated treatment with tofacitinib or a bDMARD and had at least 12 months of follow–up between March 2015 and September 2018, were included. Descriptive analyses were performed on overall and propensity score matched populations. Treatment effectiveness was evaluated from baseline to month 18 by DAS28-ESR, SDAI and CDAI measures. Treatment persistence, in part a surrogate for efficacy, was estimated by Kaplan-Meier methods. Treatment pattern evaluation included percentage

of patients receiving monotherapy or combination therapy at treatment initiation.

Results: 1950 patients were included in the matched population (1300 bDMARD initiators; 650 tofacitinib initiators). Patients were predominantly aged 55 to 74 years (57.8%), and female (81.2%). At baseline, median disease duration was 107 and 120 months, with 16.1% and 17.3% of patients in DAS28-ESR defined disease remission for the bDMARD and tofacitinib groups respectively. After three months of treatment, 49.1% and 49.7% had achieved DAS remission and after 18 months of treatment, 52.4% and 57.8% of patients had achieved DAS remission in the bDMARD and tofacitinib groups respectively. At 18 months the percentage of patients achieving CDAI/SDAI remission was similar with 29.2%/29.0% bDMARD patients and 30.9%/30.5% tofacitinib patients reporting CDAI/SDAI remission respectively. The median persistence of treatment was similar for bDMARD and tofacitinib groups: 33.8 (95% CI 28.8 to 40.4) and 34.2 (95% CI 32.2 to not reached) months respectively. In the overall population, more patients were prescribed tofacitinib as monotherapy (43.4%) compared to bDMARD monotherapy (33.4%).

Conclusion: In this analysis of a large real world dataset, tofacitinib demonstrated treatment effectiveness and persistence that was similar to bDMARDs. Overall, there was a trend for more use of tofacitinib as monotherapy than bDMARDs.

Acknowledgement: We wish to acknowledge the Australian rheumatologists who contribute data to OPAL for research.

Disclosure of Interests: Paul Bird Consultant for: Advisory boards for Eli Lily, Pfizer, Roche, AbbVie, Geoff Littlejohn Consultant for: Sat on Advisory Boards for AbbVie, Janssen, Roche, Pfizer, BMS, and Sanofi Genzyme, Belinda Butcher Consultant for: Consultant biostatistician and medical writer providing services to AbbVie, BMS, Janssen, MSD, Pfizer, UCB., Employee of: Janssen, Tegan Smith Grant/research support from: AbbVie, Consultant for: Provided medical writing services to Genentech, BioMarin, MSD, AbbVie, Roche, Actelion, Gilead, Kazia, Menarini, Candida da Fonseca Pereira Employee of: Pfizer, David Witcombe Shareholder of: Pfizer, Employee of: Pfizer, Hedley Griffiths Grant/research support from: Research funded by AbbVie, Janssen, BMS, Consultant for: Advisory boards for Sanofi, Pfizer, Novartis, Janssen

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FRI0141 EFFICACY OF JAK-INHIBITORS VERSUS BIOLOGIC DMARDS ON QUALITY OF LIFE IN RHEUMATOID ARTHRITIS :A META ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Recent studies comparing JAK-inhibitors (Jak-i) and adalimumab seem to show a better efficacy of JAK-i on patient-reported outcomes in rheumatoid arthritis (RA.)

Objectives: As there is no study comparing directly the JAK-i with other biologic DMARDs (bDMARDs), we performed a meta-analysis and compared the effect size of JAK-iand bDMARD versus synthetic DMARDs (sDMARDs) on quality of life.

Methods: We performed a systematic review of the literature until May 2018 using database including : MEDLINE (via PUBMED), EMBASE and abstracts from the ACR and EULAR congresses 2015-2017. We selected all randomized controlled trials (RCT) comparing quality of life (evaluated by SF36) in patient with rheumatoid arthritis treated with bDMARD or JAK-i versussDMARDs. We performed meta-analysis comparing the effect size of JAK-i (versus sDMARDs) and bDMARD (versus sDMARDs) on PCS SF36 and MCS SF36 at 12 weeks.

Statistical analysis determined in each study effect size.

Pooled ES were computed by meta-analysis. Data were analyzed using the inverse variance approach.

Results: The literature search identified 240 articles plus one found by manuel search and no congress abstract. Finally, 44 articles met the inclusion criteria.

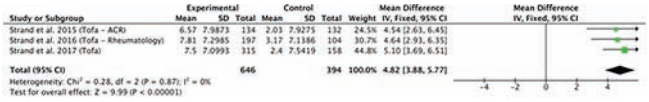
JAK-i and bDMARD showed higherlevel of quality of life than conventional therapies:

- For the SF36 PCS at 12 weeks:JAK–i:+4,82 IC95% [3,88, 5.77] and bDMARDs : +3,99 IC95% [2,81, 5,18]
- For the SF36 MCS a 12 weeks: JAK–i: +3,42 IC95% [2.24, 4,60] and bDMARD: 2,99 IC95% [2.02, 3.96]

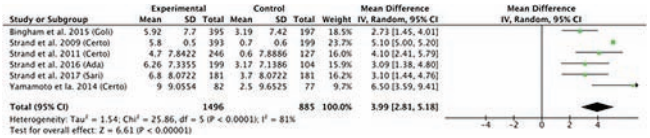
The range of the confidence intervals seems similar between JAK-I and bDMARDs.

SF36 PCS at 12 weeks:

Results for JAK-i:

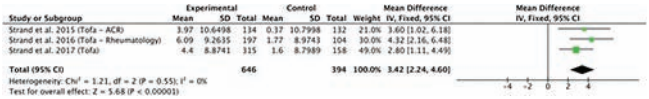


Results. for bDMARDs:

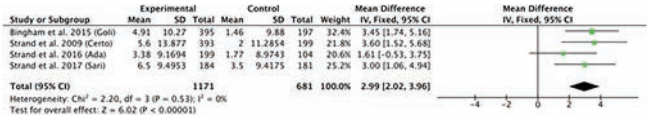


SF36 MCS at 12 weeks:

-Results for JAK-i:



-Results for bDMARDs:



Conclusion: In this meta-analysis, JAK-i and bDMARD showed better SF36 PCS and MCS at 12 weeks in comparison with sDMARDs. Although there is no significant difference, there seems to be a trend toward a better efficacy of JAK-I compared to bDMARD on quality of life.

The range of the confidence intervals seems similar between JAK-I and bDMARDs, suggesting a similar efficiency on the components of the SF36. More head-to-head studies are needed to draw definitive conclusions on potential efficacy differences between JAK-inhibitor and bDMARDs in RA.

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FRI0142 SAFETY OF THE METHOTREXATE-LEFLUNOMIDE COMBINATION IN THE BRAZILIAN REGISTRY OF BIOLOGICAL THERAPIES IN RHEUMATIC DISEASES (BIOBADABRASIL)

Markus Bredemeier, M Pinheiro, C Macieira, A Duarte, B Stadler, R Ranza, Ana Medeiros, V Valim, M Bertolo, J Miranda, C Brenol, G Castro, V Fernandes, D Titton, F Sauma, I Pereira, R Botelho, H Carvalho, A Hayata, P Louzada, A Ranzolin, I Silveira, S Schowalski, D Feldman, I Laurindo, J Provenza, Brazilian Society of Rheumatology. *BiobadaBrasil, São Paulo, Brazil*

Background: The combination of methotrexate (MTX) with leflunomide (LEF), despite being effective in the therapy of rheumatoid arthritis (RA) [1], has not been widely accepted[2,3]. In spite of evidence that the MTX-LEF combination is generally safe [1,4,5], the relatively small number of patients and treatment courses have not permitted firm conclusions.

Objectives: To evaluate the safety of the combination MTX-LEF in Brazilian patients with RA included in BiobadaBrasil.

Methods: BiobadaBrasil is a multicentric prospective cohort study involving patients with rheumatic diseases who started the first biologic or a synthetic disease modifying anti-rheumatic drug (DMARD)[6]. This analysis includes RA (2010 criteria) patients recruited from Jan 2009 to Aug 2018,followed-up for one or multiple courses of treatment until censoring (latest date, September 03, 2018) or occurrence of the outcome of interest. The primary outcome was the incidence of any serious AE (SAE). Secondary outcomes were infectious, non-mycobacterial pulmonary infectious, hepatic, hematologic and cardiovascular SAE. Multivariate Cox proportional hazards models (with DMARDs included as time-varying covariates) were used to estimate hazard ratios (HR) and 95% confidence intervals (CI); analyses were performed with the Survival package of R.

Results: Sample: 2055 RA patients, female=85.1%, median disease duration=6.02 yrs; mean (SD) age=50.3 (12.1) yrs; mean (SD) DAS28=5.3 (3.1); seronegative RA=14.1%; median follow-up duration=3.9 yrs. In total, 565 patients received 664 courses of the MTX-LEF combination (median duration, 2.5 years/course; 2209 person-years). The incidence of SAE was 4.75/100 patient-years in the entire sample. There was no significant increase in the risk of any of the outcomes with the use of combined therapy (table 1) comparing with methotrexate (without leflunomide). The use of antimalarials was associated with reduced risk of SAE (adjusted HR=0.62, 95% CI 0.48 to 0.79, P<0.001), while sulfasalazine (adj. HR= 1.78, 1.18 to 2.68, P=0.006) and biologic DMARDs/tofacitinib (adj. HR= 1.67, 1.31 to 2.12, P<0.001) increased the risk of SAE.

Table 1

Outcome(number of SAE)	HR (95% CI), p Value	HR (95% CI), p Value
SAE (457)	1.00(0.78-1.26), p=0.970	1.06(0.83-1.35), p=0.629
SAE infections (228)	1.1(0.79-1.55),p=0.538	1.24(0.89-1.75), p=0.207
SAE non-mycobacterial lung infections (78)	0.90(0.50-1.62), p=0.733	0.97(0.53-1.74), p=0.908
SAE hepatic AE(14)	1.12(0.28-4.48), p=0.873	NA
SAE hematologic (10)	2.09(0.52-8.36), p=0.299	NA
SAE CV (61)	1.22(0.65-2.30), p=0.529	1.11(0.58-2.12), p=0.755

*Comparing with MTX (without leflunomide) and adjusted for the use of LEF (without MTX) and a category representing absence of MTX and LEF. †Adjusted also for time-fixed covariates (age, gender, smoking, history of malignancy, diabetes, hypertension, renal failure, ischemic cardiomyopathy, bronchopulmonary obstructive disease) and time-varying covariates (use of sulfasalazine, antimalarials, biologic DMARDs/tofacitinib, and corticosteroids). SAE: serious adverse events, MTX: methotrexate, LEF: leflunomide, NA: not applicabledue to reduced number of events, CV: cardiovascular.

Conclusion: BIOBADABRASIL results suggest that the combination of methotrexate and leflunomide is safe in thetreatment of RA.

REFERENCES:

[1] Ann Intern Med 2002; 137: 726.
[2] Ann Rheum Dis 2010; 69: 43.
[3] Ann Pharma cother 2004; 38: 1206.
[4] J Rheumatol 2013; 40: 228.
[5] Rev Bras Reumatol 2011; 51: 141/51:152.

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Disclosure of Interests: Markus Bredemeier: None declared, M Pinheiro Consultant for: Janssen, Pfizer, Speakers bureau: Abbot,Janssen,Novartis, C Macieira: None declared, A Duarte: None declared, B Stadler: None declared, R Ranza: None declared, Ana Medeiros: None declared, V Valim: None declared, M Bertolo: None declared, J Miranda Speakers bureau: Pfizer, C Brenol Speakers bureau: Pfizer, Roche, Janssen, Bristol., G Castro: None declared, V Fernandes Speakers bureau: Janssen, D Titton: None declared, F Sauma: None declared, I Pereira: None declared, R Botelho: None declared, H Carvalho: None declared, A Hayata: None declared, P Louzada: None declared, A Ranzolin: None declared, I Silveira: None declared, S Schowalski: None declared, D Feldman: None declared, I Laurindo Consultant for: Abbvie, UCB, GSK, JANSSEN, LILLY, NOVARTIS, PFIZER, Paid instructor for: Abbvie, JANSSEN, Speakers bureau: Abbvie, UCB, GSK, JANSSEN, LILLY, NOVARTIS, PFIZER, ROCHE, J Provenza: None declared
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FRI0143 IS PATIENT – PHYSICIAN DISCORDANCE IN ASSESSMENTS OF BURDEN OF RHEUMATOID ARTHRITIS A DETERMINANT OF METHOTREXATE ADHERENCE?

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Background: Accurate assessments of disease activity in rheumatoid arthritis (RA) have a crucial role in establishing disease severity and monitoring response to treatment. There is no objective, numerical measures to estimate RA severity and treatment response. A frequently used means of quantifying the overall perception of disease activity is through an subjective assessment of global disease activity on a visual analogue scale (VAS), both by the patient, and by the physician, as well. The common direction of the discrepancy usually points toward better rating by the physicians than by the patients themselves, leading to potential medication adherence.
Objectives: The aims of the study were to explore the presence of disagreement between patients' and physicians' assessment of global disease severity, as well as to investigate the possible correlation between patient – physician discordance in assessments of RA burden and methotrexate adherence.
Methods: In the period between May 1 and September 15, 2019, 98 consecutive RA patients who were treated in Clinical center of Montenegro and private clinic "Merkur Nera" randomly chosen Montenegrin clinics were enrolled in this multi-centric cross-sectional study. The inclusion criteria were as follows: age $\geq$ 18 years, diagnosis of RA of at least 6 months, current methotrexate (MTX) use for at least 1 month (with or without concomitant usage of another RA drugs), and written informed consent. Non-adherence to MTX was defined as $\geq$1 dose missed against medical advice. The global disease activity is estimated by VAS (using a 0–10 ordinal scale), both by the patient, and by the physician. The differences between groups are assessed using the Mann-Whitney U-test. The correlation between the patient – physician discordance and MTX adherence is evaluated using the Spearman rank correlation.
Results: The most of the participants (87.8%) were female with median current age of 57.5 years (range 21-83 years). The median duration of RA was 8 years (range 0-34 years), while the median duration of MTX treatment was 6 years (range 0-26 years). The median value of VAS score estimated both, by the patients and their physician was 5, with no statistically significant difference between these two groups (Z =1.447; p =0.748). The analysis of patient – physician discordance in VAS assessment showed that full agreement is achieved in 76 (77.6%) cases, while in 21 (21,4%) RA patients their doctors underestimated their self-perception of disease burden. In only one participant, the physician overestimated patient's perception of RA severity. In total sample the self-estimated prevalence of MTX non-adherence was 32.7%. However, the analyses of the frequency of MTX non-adherence in sub-cohorts stratified by the presence of patient – physician discordance in VAS assessment showed that in "concordance group" the prevalence was 26.3% (20 out of 76 RA patients), while in "disconcordance group" the prevalence was 54.5% (12 out of 22 RA patients), with statistically significant difference between these two groups (Z =-5.745; p <0.001). Statistically significant correlation has been observed between presence of patient – physician discordance in VAS assessment and MTX non-adherence (ρ=0,427; p <0.001).
Conclusion: The results of our study have shown that the presence of patient – physician discordance in assessment of global RA activity could deeply influence the MTX adherence in a Montenegrin sample of patients with RA. This finding emphasizes the need to focus on patients' preferences and values to deliver individualized patient-centered care that could potentially enhance adherence and consequently achieved optimally control of disease activity.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8002

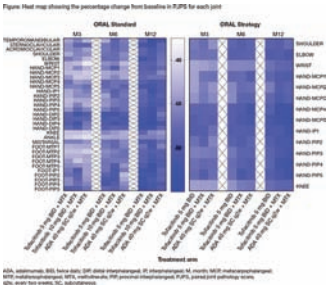
FRI0144 JOINT-SPECIFIC RESPONSES TO TOFACITINIB AND ADALIMUMAB IN RHEUMATOID ARTHRITIS: A POST HOC ANALYSIS OF DATA FROM ORAL STANDARD AND ORAL STRATEGY

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Background: Inflammatory arthritides affect joints variably despite systemic inflammatory cues. Anatomical site-specific differences have been seen in the transcriptome and function of synovial fibroblasts from different joints,[1] including evidence that some joints in rheumatoid arthritis (RA) show differential methylation of genes encoding biological pathways, such as interleukin 6 signalling via the JAK-STAT pathway.[2] Whether such site-specific JAK-STAT sensitivity translates into joint-specific responses to therapeutic JAK inhibition is unknown. Tofacitinib is an oral JAK inhibitor for the treatment of RA.
Objectives: To explore joint-specific responses to tofacitinib and adalimumab (ADA) in RA clinical trials.

Methods: This was a post hoc analysis of 3-, 6- and 12-month data from the active treatment arms of Phase (P)3 study, ORAL Standard (NCT00853385; n=609) and P3b/4 study, ORAL Strategy (NCT02187055; n=1152) in patients with active RA refractory to methotrexate (MTX). Both studies included tofacitinib 5 mg BID + MTX and ADA (40 mg SC q2w) + MTX treatment arms. ORAL Standard also included a tofacitinib 10 mg BID + MTX treatment arm and ORAL Strategy, a tofacitinib 5 mg BID treatment arm. A paired joint pathology score (PJPS), a combination of bilateral tender/swollen joint counts ranging from 0 (neither side swollen/tender) to 4 (both sides swollen/tender) was calculated. Data for 33 (ORAL Standard) and 14 (ORAL Strategy) joint pairs were available. The percentage change from baseline (%Δ) in PJPS for each joint was presented in a heat map to visualise responses. To show tofacitinib-specific effects at each joint, difference in mean PJPS for each tofacitinib regimen at 3 months minus the respective ADA + MTX group was calculated.

Results: Across all treatment arms of both studies, baseline joint involvement ranged from 15.7% (5th distal interphalangeal joint of the hand) to 93.3% (wrist). All joints showed a treatment response, with%ΔPJPS ranging from –36 to –94% (Figure). The heat map showed lower response rates in the wrist and knee vs most other joints in both studies persisting to 12 months, regardless of treatment arm. Similarly, in ORAL Standard, the ankle (not assessed in ORAL Strategy) showed a lower response vs most other joints. Tofacitinib-specific responses vs ADA + MTX (not shown) were seen (mean differences in PJPS ranged from –0.4 to 0.2) with no clear pattern in the combination therapy groups. In the tofacitinib 5 mg BID arm of ORAL Strategy, a pattern was observed in the metacarpophalangeal (MCP) joints, with tofacitinib responsiveness vs ADA + MTX increasing progressively (mean difference in PJPS increased from 0.16 in MCP1 to –0.08 in MCP5).



Conclusion: There is variation in the responsiveness of RA joints to tofacitinib ± MTX and ADA + MTX, with the wrist, knee and ankle responding less well vs other joints, irrespective of treatment mode of action. Concomitant MTX use in most treatment arms may mask joint-specific actions of tofacitinib and ADA. Observed responsiveness to tofacitinib monotherapy vs ADA + MTX increased from MCP1–5, which may be tentative evidence of differential sensitivity to JAK inhibition across embryologically imprinted functional genetic gradients. Further analyses of the monotherapy arms of randomised trials may yield additional evidence of joint-specific responsiveness, and provide a basis for personalised RA treatment.

REFERENCES:

[1] Frank-Bertoncelj M, et al. Nat Commun 2017; 8: 14852.
[2] Ai R, et al. Nat Commun 2016; 7: 11849.

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FRI0145 FACTORS ASSOCIATED WITH NEAR REMISSION DIFFER BETWEEN AUTOANTIBODY-POSITIVE AND -NEGATIVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS TREATED WITH CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

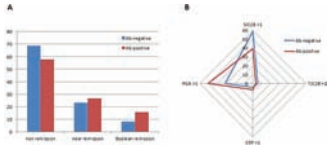
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Background: Disease remission is recommended as the treatment target in patients with early rheumatoid arthritis (RA). According to the criterion, the proportion of patients classified as in remission considerably varies, with the Boolean-based definition being the most restrictive [1]. A considerable proportion of patients with established RA misses Boolean remission solely because of one of the 4 criteria (near remission) [2]. The frequency and the limiting variables to Boolean remission in real-life cohorts of patients with early RA are however unknown.

Objectives: To assess the frequency and the limiting factors for fulfilling Boolean remission in early RA patients treated with csDMARDs according to a treat-to-target strategy.

Methods: The study population consisted of 578 early RA patients (<12 months of symptoms) consecutively recruited at our Early Arthritis Clinic, treatment-naïve at inclusion and prospectively followed-up upon initiation of therapy with methotrexate (MTX) aimed at the achievement of low disease activity (28-joints disease activity score [DAS28] ≤3.2). After 6 months of treatment, patients were classified as in remission or near remission according to the Boolean criterion as follows: (i) remission – swollen joint count (SJC28), tender joint count (TJC28), C-reactive protein (CRP) and patient global assessment of disease activity (PGA) all ≤1; (ii) near remission – just 3 of the 4 core items. Patients characteristics between remission and near remission were compared, and reasons for missing Boolean remission were analysed in relation to disease variables.

Results: Complete follow-up data after 6 months of treatment were available for 89.3% of the patients. Disease remission was achieved in 25.6% of the cases according to the DAS28, 16.7% according to the simplified disease activity index (SDAI) and 11.6% according to the Boolean criterion. One-hundred and thirty-three patients (25.8%) failed to reach Boolean remission solely because of one of the 4 criteria. Of these, 45.9% were in DAS28 remission and 22.6% in SDAI remission. No differences in baseline demographic and clinical characteristics were found between patients in Boolean remission and patients in near remission. Use of prednisone co-medication and MTX starting dose were also comparable. Patients negative for both rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) were more frequently in near remission rather than in Boolean remission compared to autoantibody-positive patients (**Fig. 1A**). The missing criterion in near remission was SJC28 >1 in 49% of the cases, PGA >1 in 41%, and TJC28 >1 or CRP >1 mg/dl in the remaining 10%. Collectively, failure to achieve Boolean remission because of SJC28 >1 was more common in RF and/or ACPA positive patients. Rather, autoantibody-negative patients more frequently missed remission due to PGA (**Fig. 1B**).



Conclusion: In patients with early RA treated with csDMARDs, near remission is up to two times more frequent than Boolean remission. Collectively, autoantibody-negative patients more commonly miss complete remission solely because of one criterion compared to autoantibody-

positive patients. Furthermore, in these patients, failure to achieve remission is mostly related to high PGA rather than to the persistence of joint inflammation. Altogether, these findings implicate that autoantibody-negative RA patients failing to achieve remission would require adjunctive tailored interventions rather than reinforcement of DMARD therapy.

REFERENCES:

[1] Mack ME, et al. Arthritis Rheumatol 2017;69:518-28.
[2] Studenic P, et al. Ann Rheum Dis 2012;71:1702-5.

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FRI0146 SURVIVAL OF JAK INHIBITORS: REAL-WORLD DATA FROM THE BIOBADASER III REGISTRY

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Background: JAK inhibitors (JAKi) have been recently authorized in the European Union. JAKi long-term performance in the clinical practice setting still needs to be assessed. Drug survival reflects a drug's effectiveness, safety, and tolerability; thus, it is an important measurement for real-world studies.
Objectives: To describe the pattern of use of JAKi in real-world dataset, and to analyze the drug survival as a group (tofacitinib+baricitinib).
Methods: Information was obtained from BIOBADASER III, an ongoing observational longitudinal multicenter cohort of patients with rheumatic diseases treated with biologic or targeted synthetic (b/ts) DMARDs in Spain. All subjects with current or previous JAKi use were included and followed until September 2018. Clinical characteristics of the patients were analyzed. Drug survival (overall, and for biologic-naive and biologic-experienced patients) was determined using Kaplan-Meier analysis.

Table 1. Diagnoses of patients with JAKi treatment

Diagnosis (patients)	n (%)
Rheumatoid arthritis	138 (92.6)
Idiopathic juvenile arthritis*	3 (2.0)
Psoriatic arthritis	2 (1.3)
Undifferentiated spondyloarthritis*	2 (1.3)
Seronegative polyarthritis*	2 (1.3)
Ankylosing spondylitis*	1 (0.7)
Enteropathic arthritis*	1 (0.7)
Total	149 (100)

*off-label use.

Results: 149 patients, 75.2% women, were treated with JAKi, receiving a total of 152 cycles of treatment (50.7% tofacitinib, 49.3% baricitinib; 3 patients had both). The most frequent diagnosis was rheumatoid arthritis (RA, 92.6%), and there is a small number of off-label uses (6%), depicted at Table 1. Use on psoriatic arthritis is scarce (1.3%). Concomitant use of methotrexate (MTX) was registered in 68 patients (45.6%). Previous use of bDMARDs was high (n=124, 81.6%); drug survival rate for biologic-experienced patients was 81.7% and 78.7% at 6 and 12 months. None of the JAKi treatments in biologic-naive patients (n=18, 18.4%) were discontinued during follow-up. Pooled survival rate of JAKi was 85.0% and 82.5% at 6 and 12 months (Figure 1). Discontinuation was seen in 19 treatments (12.5%); the reasons were inefficacy (n=15, 9.9%) or adverse events (n=4, 2.6%).

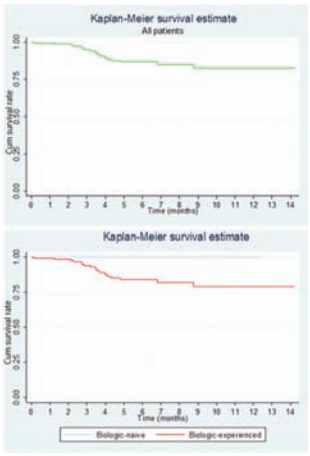


Figure 1. Overall survival of JAKi and for biologic-naive and biologic-experienced patients

Conclusion: The current use of JAKi in Spain is mainly in RA and as 2nd line after bDMARDs. The use of JAKi in psoriatic arthritis is still scarce and a small group of patients are treated off-label. Less than half use combination therapy with MTX. Overall survival of JAKi is superior to 80% at 12 months. A longer follow-up is needed to continue analyzing the survival of JAKi in a real-world context.
Acknowledgement: We thank all researchers from the BIOBADASER III group.
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FRI0147 SAFETY AND EFFECTIVENESS OF UPADACITINIB OR ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 48 WEEKS FROM THE SELECT-COMPARE STUDY

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Background: In the SELECT-COMPARE study in rheumatoid arthritis (RA) patients (pts) with inadequate response to methotrexate (MTX), upadacitinib (UPA), a JAK1- selective inhibitor, was superior to placebo (PBO) or adalimumab (ADA) for treatment of signs & symptoms and for inhibition of radiographic progression vs PBO up to 26 weeks (wks). All pts were on stable background MTX. [1]
Objectives: To report safety and efficacy of UPA plus stable background MTX up to 48 wks in this phase 3 study.
Methods: Pts were randomized to once-daily (QD) UPA 15mg, PBO, or ADA 40mg every other wk, with all patients continuing background MTX. The study was double-blind for 48 wks. Between Wks14-26, pts were rescued (from PBO to UPA, UPA to ADA, or ADA to UPA) if there was <20% improvement in tender/swollen joint count (Wks 14/18/22) or if Clinical Disease Activity Index (CDAI) was >10 (Wk26); all PBO pts who were not rescued were switched to UPA at Wk 26. Efficacy was analyzed by randomized group. Non-responder imputation (NRI) was used for binary endpoints for rescue prior to Wk26. Last observation carried

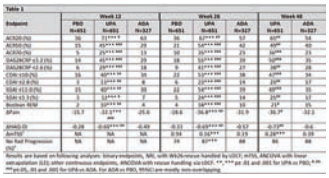
forward (LOCF) was used for continuous endpoints and binary endpoints after Wk26. Treatment-emergent adverse events (AE) per 100 pt yrs (PY) were summarized up to July 6 2018 for pts with any exposure to ADA or UPA.

Results: In SELECT-COMPARE, 1629 pts were randomized at BL. Among 651 pts randomized to UPA, 38.7% were rescued between Wks 14-26; of those who remained on UPA, 86% completed Wk 48, while 5.8% and 0.3% discontinued study drug between BL and Wk 48 due to AE and lack of efficacy (LoE), respectively. Among 327 pts randomized to ADA, 48.6% were rescued between Wks 14-26; of those who remained on ADA, 76% completed Wk48, while 13.1% and 0 discontinued study drug between BL and Wk48 due to AE and LoE, respectively. The cumulative exposures were 1243.3 and 467.8 PYs for UPA and ADA, respectively. At Wk26, and Wk48, significantly more pts in the UPA vs ADA group achieved ACR20/50/70, low disease activity and remission (Table 1); this was also true for visits between Wks 26 and 48. Similarly, improvements in pain and function were significantly greater in the UPA vs ADA group through Wk48. At Wk26, there was significantly less radiographic progression for UPA vs PBO, which was maintained through Wk48 (based on linear extrapolation). Adverse events are reported in Table 2 (in events per 100 PY). The rate of AE leading to discontinuation was higher with "any ADA" vs "any UPA", while the rate of Herpes zoster was higher with "any UPA" exposure.

Conclusion: UPA continued to demonstrate superior clinical and functional responses vs ADA through Wk48. Inhibition of structural joint damage with UPA was also maintained through 48 wks vs PBO. Safety was consistent with observations in the first 26 wks.[1]

REFERENCES:

[1] Fleischmann R, et al. Arthritis Rheumatol. 2018;70 (supp10)



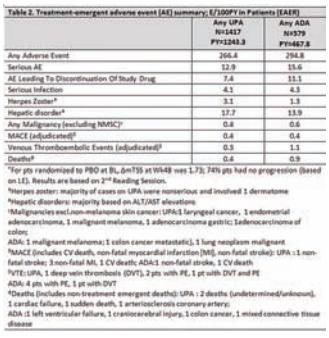


Table 2. Treatment-emergent adverse event (AE) summary; E/100PY in Patients (EAER)	Any UPA N=1417 PY=1243.3	Any ADA N=979 PY=467.8
Any Adverse Event	266.4	294.8
Serious AE	12.9	15.6
AE Leading To Discontinuation Of Study Drug	7.4	11.1
Serious Infection	4.1	4.3
Herpes Zoster[1]	3.1	1.3
Hepatic disorder[2]	17.7	13.9
Any Malignancy (excluding NMSC)[3]	0.8	0.6
MACE (adjudicated)[4]	0.4	0.4
Venous Thromboembolic Events (adjudicated)[5]	0.3	1.3
Death[6]	0.4	0.9

[1]For pts randomized to PBO at BL,@mTS at Wk48 was 1.73; 74% pts had no progression (based on LE). Results are based on 2nd Reading Session.
[2]Herpes zoster: majority of cases on UPA were nonserious and involved 1 dermatome
[3]Hepatic disorders: majority based on ALT/AST elevations
[4]Malignancies excl.non-melanoma skin cancer: UPA:1 laryngeal cancer, 1 endometrial adenocarcinoma, 1 malignant melanoma, 1 adenocarcinoma gastric; 1adenocarcinoma of colon;
ADA: 1 malignant melanoma; 1 colon cancer metastatic), 1 lung neoplasm malignant
[5]MACE (includes CV death, non-fatal myocardial infarction [MI], non-fatal stroke): UPA : 1 non-fatal stroke; 3 non-fatal MI, 1 CV death; ADA:1 non-fatal stroke, 1 CV death
[6]VTE: UPA, 1 deep vein thrombosis (DVT), 2 pts with PE, 1 pt with DVT and PE
ADA: 4 pts with PE, 1 pt with DVT
[6]Deaths (includes non-treatment emergent death): UPA : 2 deaths (undetermined/unknown), 1 cardiac failure, 1 sudden death, 1 arteriosclerosis coronary artery;
ADA :1 left ventricular failure, 1 craniocerebral injury, 1 colon cancer, 1 mixed connective tissue disease

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FRI0148 IS TREATMENT ADHERENCE OF RA PATIENTS TO MTX IMPROVED BY THE SWITCH FROM ORAL TO SUBCUTANEOUS ABMINISTRATION? RESULTS FROM THE PROSPECTIVE APRIM STUDY

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Background: Previous studies have shown, that switching from oral to SC MTX can lead to improved efficacy and bioavailability (especially for doses ≥15mg/wk.) as well as to a decreased frequency of adverse gastrointestinal effects in patients with RA. Furthermore, some reports consider that this switch may improve treatments adherence and persistence.

Objectives: The purpose of APRiM study was to investigate the treatment adherence of RA patients switching from oral to injectable MTX or between two different MTX prefilled syringes.

Methods: APRiM is a prospective, observational, multicentre study, which included adult patients with confirmed RA diagnosis (ACR/EULAR 2010 criteria) already treated by either oral MTX and requiring route modification (Gr1), or SC MTX in prefilled syringe (PFS) and eligible for a device switch (to another PFS) (Gr2). The primary criterion of the study was to estimate at 6 months the proportion of patients with strong or improved of at least 1 category treatment adherence evaluated by Morisky's self-assessment (8: strong/maximum adherence, 6-7: medium adherence, <6: poor adherence) in both groups.

Results: Between June 2016 and June 2017, 110 rheumatologists, at 90% with private practice, included 466 pts, 433 of which composed the analysable baseline set. Pts baseline characteristics Gr1/Gr2 were [mean (SD)]: age: 59.2 (13.0)/61.5 (12.2) yrs; RA duration: 6.5 (7.9)/9.9 (10.5) yrs; MTX use duration: 3.6 (4.6)/6.0 (5.1) yrs; DAS28: 3.9 (0.9)/3.2 (1.2); Erosive RA: 37%/53%. All pts were receiving MTX at a mean (SD) dose of 15.1 (4.0)/15.6 (4.0) mg/wk. Mean (SD) Morisky's scores were 6.5 (2.0)/6.6 (1.8) for respectively Gr1/Gr2 at baseline, they improved up to 6.9 (1.8)/7.0 (1.5) at 6 months. Adherence remained strong or improved of at least 1 category for respectively 56% and 60% of patients [Gr1/Gr2]. Proportion of patients with strong treatment adherence improved from 40% (V0) to 48% (M6) in both Gr1 and Gr2. Interestingly, when rheumatologists were asked to estimate their patients' adherence, they reported respectively 77% and 84% [Gr1/Gr2] of patients with "no missed injections". At baseline patients in the Gr1 (oral baseline) had a higher DAS28 than in Gr2, this difference was removed after 6 months of MTX SC treatment. No new safety signals were identified during this study.

Conclusion: The results of the observational study APRiM revealed that less than 50% of patients are perfectly adherent to injectable MTX treatment, irrespectively of whether was their previous MTX way of administration. Though, this proportion seems to be highly overestimated by the rheumatologists. This underlies the importance of patient/physician effective communication.

REFERENCES:

[1] Morisky DE, et al., Predictive Validity of a Medication Adherence Measure for in an Outpatient Setting. J Clin Hypertens 2008 May:348-354.
[2] Krousel-Wood M, et al., New Medication Adherence Scale Versus Pharmacy Fill Rates in Seniors with Hypertension. Am J Manag Care. 2009 Jan: 59-66.
[3] Morisky DE, et al., Improving the Measurement of Self-Reported Medication Nonadherence: Response to Authors. J Clin Epidemiol 2011 Mar: 255- 263.
[4] Morisky Widget™, MMAS™, MMAS4™, MMAS-8™, Morisky Medication Adherence Protocol™, and Morisky Medication Adherence Scale™ is

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FRI0149 DISEASE ACTIVITY IN ESCALATION OR DE-ESCALATION OF DOSAGE OF TOFACITINIB IN RHEUMATOID ARTHRITIS PATIENTS – THE FIRST RESULTS OF RUSSIAN NATIONAL REGISTER OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB

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Background: In previous studies tofacitinib (TF) had demonstrated efficacy of two dosages (10 and 20 mg/day) in patients with rheumatoid arthritis (RA). However, the expected results of switching of TF' dosages are unknown.
Objectives: The aim of the study was to evaluate the results of switching of TF's dosages in RA patients.
Methods: Were analyzed the data from Russian national register of patients with RA treated with TF (tofacitinib). 415 patients were involved in the register (aug 2018). In statistical analysis were included data from 41 patients with RA (EULAR 2010), who switched dosage of TF at visit 3 and had complete clinical and laboratory data from 5 consecutive visits with an interval of 3 months between the visits. Demographical (age, sex) data, disease activity data DAS28 (Disease activity score), C-reactive protein level were collected, table 1. Changes in disease activity were calculated to patients with switching of the tofa's dosage (the visit before and after the switching).
Results: 1.28 (68%) of patients were treated with NSAIDs, 24 (50%) with 5-10 mg of prednisolone, 34 (82.9) – with methotrexate (10-25 mg/week), biologics – 5 (4.2%).

Table 1. Baseline characteristics of the patients with RA included in the study (n=41)

Parameter	Characteristics
Male, n (%)	10 (24.3)
Caucasians, n (%)	41 (100)
Asians, n (%)	0 (0)
Age of disease onset, years (mean ±SD)	40.1±10.5
Symptoms duration, month (mean ±SD)	98.7± 87.1
Positive rheumatoid factor, n (%)	32 (78)
Positive antibodies to cyclic citrullinated peptide (anti-CCP), n (%)	37 (90.2)
BMI, kg/m^2(mean ±SD)	25.12±5.98
Smokers (current and in the anamnesis), n (%)	33 (80)

From 41 persons with RA 32 patients, who never achieved low disease activity (DAS28<3.2) or remission (DAS28<2.6) elevated the dosage of tofa from 10 to 20 mg/day and 9 patients with DAS28 < 3.2 decreased the dosage from 20 to 10 mg/day.
After escalation of TF dosage DAS28 decreased from 5.42±1.22 to 4.22 ±1.22 (p<0.00), n=32. In 10 patients escalation lead to DAS28-remission (DAS28 <2.6) and in 12 patients - to low disease activity (DAS28<3.2). 10 patients had no clinical or laboratory response on escalation of TF dosage. Interestingly, that responders before escalation of dosage had mean DAS28 3.54 (min 3.2 – max 4.9) and non-responders – 5.54 (min 5.3-max 6.9), p<0.000.
De-escalation of the dosage from 20 to 10 mg/day was not associated with significant changes of DAS28 (1.99 ± 1.25 increased to 2.1 ±0.96 respectively, p=0.82).
Conclusion: Escalation of dosage of TF in RA lead to improvement of the disease activity in non-complete responders, who achieved DAS 28 3.2-5.1, but not in patients with absence of any response (DAS28 before escalation 5.3-6.9). De-escalation of TF' dosage in patients with DAS28 < 2.6 dose not lead to significant changes of RA's activity.

REFERENCES:
[1] Fleischmann R, et al. Lancet. 2017 Jul 29;390(10093):457-468. doi: 10.1016/S0140-6736(17)31618-5.

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FRI0150 GS-9876, A NOVEL, HIGHLY SELECTIVE, SYK INHIBITOR IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: SAFETY, TOLERABILITY AND EFFICACY RESULTS OF A PHASE 2 STUDY

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Background: Spleen tyrosine kinase (SYK) mediates immunoreceptor signaling and is essential in activation of cells including B lymphocytes, monocytes, macrophages, dendritic cells, and osteoclasts. SYK may play an important role in the initiation and progression of autoimmune diseases, including rheumatoid arthritis (RA) and lupus. GS-9876 is a novel, potent, highly selective oral inhibitor of SYK in phase 2 trials for autoimmune diseases.
Objectives: To evaluate the efficacy, safety, and pharmacokinetics of GS-9876, and its impact on biomarkers relevant to RA as well as the SYK and JAK pathways.
Methods: Patients with active RA with prior inadequate response to methotrexate (MTX) or a biologic antirheumatic drug were randomized 1:1:1:1 to receive GS-9876 30 mg, GS-9876 10 mg, selective JAK1 inhibitor filgotinib (FIL) 200 mg, or matching placebo (PBO) once daily for 12 weeks on a stable background of oral MTX. The primary endpoint for GS-9876 was the change in DAS28(CRP) at week 12. Pharmacokinetics and various biomarkers were evaluated at several time points, including VectraDA and stimulation of whole blood in TruCulture (MyriadRBM) tubes.
Results: A total of 83 patients received the study drug and 79 completed the study. Fourteen patients (16.9%) were male and 69 (83.1%) were female. The majority were white (77, 92.8%). The mean (SD) age at baseline (BL) was 55 (11.5) years (range 18 to 73). The primary and secondary endpoints are reported in Table 1. For DAS28(CRP), the mean (SD) at BL was 5.75 (0.961) with a median of 5.69; a statistically significant reduction at week 12 was observed only in patients receiving FIL as compared to PBO (Table 1). Adverse events (AEs) were reported across all groups (37.5% in the combined GS-9876 arms, 38.1% in FIL, 40.9% in PBO). No deaths or serious AEs were reported. Plasma exposures of all study drugs were comparable to those observed in healthy subjects and historical data. *Ex vivo* stimulated whole blood identified differential responses between GS-9876 and PBO.

Table 1. Key endpoints at week 12.

	DAS28(CRP)[a] (mean change from BL to week 12)	ACR20/50/70[b] (% achieving at week 12)	HAQ-DI[b] (mean change from BL to week 12)
PBO	−1.36 (1.044)	40.9/22.7/13.6	−0.39 (0.389)
GS-9876 10 mg	−0.78 (1.119)	25.0/20.0/15.0	−0.18 (0.800)
GS-9876 30 mg	−1.26 (1.276)	35.0/20.0/5.0	−0.46 (0.480)
FIL 200 mg	−2.46 (1.242); *p=0.002	81.0/47.6/38.1	−0.70 (0.649)

[a]Primary endpoint; [b]Secondary endpoint; *p (compared to PBO).

Conclusion: Clinical efficacy of GS-9876 in RA was not observed, but GS-9876 was safe and well-tolerated over a 12-week period in patients with RA on MTX. FIL showed favorable safety and clinical efficacy consistent with prior data, validating the study concept and design. Additionally, biomarker changes with GS-9876 support the continuation of studies in lupus-related diseases.

REFERENCES:

[1] Kivitz AJ, et al. ACR 2018. Abstract 2518.

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FRI0151

THE RELATIONSHIP BETWEEN THE EFFECTIVENESS OF METHOTREXATE (MTX) IN RHEUMATOID ARTHRITIS (RA) AND MTX POLYGLUTAMATES LEVELS (MTXPGS) IN RED BLOOD CELLS BY TANDEM CHROMATOMASS SPECTROMETRY (PILOT STUDY)

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Background: Therapeutic control of the level of MTXPGs in erythrocytes may be an objective marker of its effective dose in RA treatment.

Objectives: To evaluate the relationship between the level of MTXPGs in erythrocytes and the effectiveness of the dose of MT used by RA patients.

Methods: The study included 60 random selected RA patients over the age of 18, 16 men and 44 women. The diagnosis in all cases met the criteria of ACR/EULAR 2010. All pts received MTX at a constant dose of at least 20 mg per week subcutaneously for at least the last 12 weeks. Patients were divided into 2 groups depending on the presence (group 1, n = 30) or absence (group 2, n = 30) of the therapeutic effect of MTX, according to the criteria of the EULAR response to therapy. The groups were comparable in age, sex, alcohol intake, smoking, body mass index (BMI), ACPP-positivity, incidence of unwanted reactions to MTX, single dose of MTX, duration of MTX treatment course. The groups differed in duration of the disease at the beginning of the current course of continuous therapy: 5.5 [2.0, 12.0] months in group 1 and 12.0 [3.0, 60.0] months in group 2; in group 2 patients received glucocorticoids (GK) orally 17 (57%) against 9 (30%) in group 1. Blood sampling was performed no later than 36 hours after the last administration of methotrexate. From each patient 2 ml of hemolysed blood were examined using an Agilent 6410 chromatograph (Agilent Technologies) - a quantitative measurement of methotrexate polyglutamate by liquid chromatography-spectrometry.

Results: It was established that the levels of total MTXPG and MTXPG1,2,3,5 in erythrocytes did not depend on the effectiveness of MTX, the dose of which was comparable in all patients. At the same time, the level of MTXPG4 was significantly higher (p = 0.023) in patients of group 1 (26.4 ± 6.1 nmol/l) compared with patients in group 2 (22.1 ± 6.8 nmol/l). Evaluation of the ROC curve showed that MTXPG4 values below 22.5 nmol/l corresponded to the absence of the therapeutic effect of MTX. The area under the curve was 0.672, (CI 95 0.536-0.808); p = 0.022. Sensitivity - 77%, specificity - 53.3%.

Conclusion: For effective treatment of RA patients, it is necessary to administer such doses of MTX so that the achieved level of MTXPG4 in erythrocytes is not less than 22.5 nmol/l.

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FRI0152

METHOTREXATE TREATMENT PATTERNS IN ADVANCED THERAPY–NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: CLINICAL CHARACTERISTICS AND OUTCOMES OF PATIENTS IN THE CORRONA REGISTRY

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Background: Methotrexate (MTX) is one of the most commonly used drugs in the treatment of rheumatoid arthritis (RA). Some patients may discontinue MTX therapy due to lack of efficacy or intolerance and may or may not restart MTX. There is a need to better understand the patterns of MTX use, the characteristics of these patients, and how the patterns of use are related to outcomes.

Objectives: To assess patterns of MTX use in a clinical practice setting, describe baseline demographic and clinical characteristics for groups defined by patterns of MTX use, and assess the association of patterns of MTX use with clinical outcomes and side effects during the 2 years after MTX initiation.

Methods: This observational study included patients from the US Corrona RA registry who initiated MTX from 01 October 2001 to 31 October 2018, were biologic/targeted synthetic disease-modifying antirheumatic drug (bDMARD/tsDMARD)–naïve and did not start bDMARD/tsDMARD through 2 years of follow-up. Patients were divided into 3 cohorts: those who discontinued and restarted MTX, those who discontinued without restarting MTX and those who persisted on MTX. Descriptive statistics were used to evaluate patient demographics and disease activity at MTX initiation and side effects during follow-up. Changes in clinical outcomes from baseline to 2 years were calculated for all groups. Differences in outcomes were assessed using Kruskal-Wallis one-way analysis of variance for continuous or ordinal-dependent variables and chi-square test for categorical variables.

Results: Among 785 MTX initiators, 34 (4.3%) discontinued/restarted MTX, 174 (22.2%) discontinued MTX, and 577 (73.5%) persisted on MTX within the 2-year follow-up period. Overall, mean age was 59.7 years; 72.7% were female; mean duration of RA was 4.8 years; and 52.9% were conventional synthetic DMARD–naïve. Generally, in patients who discontinued/restarted, discontinued, or persisted on MTX, those who discontinued/restarted therapy had more comorbidities at MTX initiation: hypertension (35.3%, 32.8%, or 29.3%, respectively), malignancy (14.7%, 9.2%, or 8.7%, respectively), chronic obstructive pulmonary disease (10.0%, 3.9%, 1.9%, respectively), or asthma (5.0%, 4.7%, or 2.9%, respectively). At end of follow-up, mean Clinical Disease Activity Index (CDAI) was 15.6, 10.1, and 8.8 for those who discontinued/restarted, discontinued, and persisted, respectively. Disease activity according to CDAI improved during the 2-year follow-up for all 3 groups, but less improvement was observed in those who discontinued/restarted MTX (**Table**). Overall, the most common side effects while on MTX therapy were elevated liver enzymes (65.4%) and fatigue (43.1%). Patients who discontinued/restarted MTX vs those who persisted had higher rates of hair loss (35.3% vs 18.9%), loss of appetite (32.4% vs 17.3%) stomach pain (26.5% vs 14.6%), mouth sores (20.6% vs 16.3%), diarrhœa (11.8% vs 9.5%), and myelosuppression (8.8% vs 2.1%).

Conclusion: More than 26% of patients who initiated MTX therapy either discontinued and did not restart or discontinued and restarted therapy during 2 years of follow-up. Patients who discontinued/restarted MTX therapy had less improvement in disease activity, experienced more side

effects, and tended to have more comorbidities at MTX initiation than those who persisted on therapy.

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Clinical Disease Characteristics and Outcomes by Pattern of MTX Use

	Discontinued/Restarted (N=34)	Discontinued (N=174)	Persisted (N=577)	*P*-value
CDAI change over 2-year follow-up				
Change from baseline in CDAI, mean ± SD	3.1 ± 15.6	7.4 ± 14.9	10.4 ± 13.6	<0.01
Achieved LDA,[a] n (%)	10 (29.4)	58 (33.3)	213 (36.9)	0.50
Achieved MCID,[b] n (%)	14 (41.2)	86 (49.4)	332 (57.5)	0.04
Outcomes at end of MTX use or 2-year follow-up				
CDAI, mean ± SD	15.6 ± 14.4	10.1 ± 9.3	8.8 ± 9.5	0.001
mHAQ, mean ± SD	0.5 ± 0.7	0.4 ± 0.5	0.2 ± 0.4	<0.001
Physician Global Assessment, mean ± SD	22.0 ± 20.6	18.1 ± 16.4	14.4 ± 15.4	<0.01
Patient Global Assessment, mean ± SD	39.4 ± 32.5	31.3 ± 26.7	25.2 ± 25.0	<0.01
Pain, mean ± SD	39.1 ± 32.5	33.9 ± 27.3	27.2 ± 26.2	<0.01
Fatigue, mean ± SD	44.0 ± 35.0	32.5 ± 29.5	27.2 ± 26.8	0.06
Morning stiffness, n (%)	23 (67.7)	127 (74.3)	359 (63.5)	0.03
Morning stiffness duration (h), mean ± SD	1.5 ± 4.0	1.3 ± 3.2	0.7 ± 1.9	<0.001

CDAI, Clinical Disease Activity Index; CPP, cyclic citrullinated peptide; LDA, low disease activity; MCID, minimum clinically important difference; mHAQ, modified Health Assessment Questionnaire; SD, standard deviation.

[a]Achievement of LDA (CDAI≤10) in those patients who initiated therapy in moderate (10<CDAI≤22) or high disease activity (CDAI>22).

[b]CDAI change >1 for those in LDA (CDAI≤10) at baseline, CDAI change >6 for those in moderate disease activity (10<CDAI≤22) at baseline, and CDAI change >12 for those in high disease activity (CDAI>22) at baseline.

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FRI0153 OPHTHALMOLOGICAL ADVERSE EVENTS UNDER JAK INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: CASE ANALYSIS OF THE EUROPEAN PHARMACOVIGILANCE DATABASE

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Background: Ophthalmological manifestations in rheumatoid arthritis (RA) include dry syndrome, scleritis, episcleritis, uveitis and peripheral ulcerative keratitis (PUK). Recently, a new class of synthetic molecules has been developed, called JAK inhibitors (JAKinhib). We observed one case of PUK occurring two months after the introduction of baricitinib treatment with corneal perforation with secondary improvement after discontinuation of JAKinhib.

Objectives: The aim of this study is to describe and characterize the ophthalmological side effects of JAK inhibitors (JAK inhib) in patients with rheumatoid arthritis (RA) from European pharmacovigilance (PV) data.

Methods: The ophthalmological manifestations that appeared under JAK inhib were extracted from the European PV database (May 2018), EUDRAVIGILANCE following a request addressed to the National Drug Safety Agency carried out according to the following MedDRA classification "SOC eye disorders and BARICITINIB" and "SOC eye disorders and TOFACITINIB".

Results: A total of 41 patients with ophthalmic adverse events (AEs) on JAK inhib were reported. Among patients, 12 were treated with BARICITINIB and 29 with TOFACITINIB. Of these AEs, 51% were reported by the medical profession, 39% by patients and 10% by paramedical teams. The database analysis revealed 4 scleritis, 3 uveitis, 1 PUK and 1 corneal ulceration. The average time to onset of AEs was 13.2 months. The infectious causes had been eliminated.

Ocular adverse events under JAK inhibitors

	BARICITINIB n=12	**TOFACITINIB** n=29	**Mean Delay** (in days)
Ophthalmological events	AEs	AEs	
Scleritis, n (%)**	2 (17)	2 (7)	344
Corneal ulceration, n (%)**	0	1 (3)	90
PUK, n (%)**	1 (8)	0	57
Uveitis, n (%)**	0	3 (10)	838
Blurry vision*, n (%)	3 (25)	8 (28)	9
Red eyes*, n (%)	3 (25)	1 (3)	33
Dry eyes*, n (%)	2 (17)	3 (10)	NA
Photophobia*, n (%)	0	1 (3)	NA
Decreased visual acuity*, n (%)	1 (8)	1 (3)	124
Retinal detachment**, n (%)	0	1 (3)	480
Retinal haemorrhage**, n (%)	0	2 (7)	541
Cataract**, n (%)	2 (17)	5 (17)	413
Glaucoma**, n (%)	0	4 (14)	489
Age related macular degeneration**, n (%)	0	1 (3)	NA

*Adverse event reported by the patient **Adverse event reported by the medical profession
PUK: Peripheral Ulcerative Keratitis NA: Not Available

Conclusion: Ophthalmological manifestations under JAKinhib seem to be rare but not exceptional, the rheumatologist must be aware of them in order to discuss the imputability of the treatment. A discontinuation of it seems justified pending an ophthalmological opinion.

Disclosure of Interests: None declared

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FRI0154 SAFETY AND EFFICACY OF FILGOTINIB IN PATIENTS AGED 65 YEARS AND OLDER: RESULTS FROM A PHASE 3 STUDY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDS (BDMARD-IR)

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Background: Filgotinib (FIL), an oral selective Janus kinase 1 (JAK1) inhibitor, demonstrated efficacy and safety vs placebo (PBO) in bDMARD-IR patients with active RA in a global phase 3 study (FINCH2, ClinicalTrials.gov NCT02873936).[1]

Objectives: We performed a prespecified subgroup analysis of the safety and efficacy of FIL in patients aged ≥65 years vs <65 years in FINCH2 to understand FIL effects in older patients.

Methods: 449 patients were randomized 1:1:1 to FIL 200 mg, FIL 100 mg, or PBO on a background of csDMARDs for 24 weeks. The primary efficacy endpoint was ACR20 response at week 12.

Results: Of 448 patients who received ≥1 dose of study drugs, 113 (25.2%) were ≥65 years of age; baseline disease characteristics were similar for both age groups. Safety and efficacy parameters by age group are in Tables 1 and 2. The most common treatment-emergent adverse events (TEAEs, by System Organ Class) category was infections and infestations; nasopharyngitis, upper respiratory tract infections, and bronchitis were the most common infections and infestations in the FIL arms in both age groups. There were no cases of opportunistic infection, active tuberculosis, malignancy, gastrointestinal perforation, or death. Efficacy outcomes were similar for both groups.

Conclusion: Overall, older age was not associated with higher incidence of safety events (serious infections, herpes zoster, MACE occurred in the group <65 yrs) and efficacy was similar in older and younger bDMARD-IR patients with active RA.

REFERENCE:

[1] MC Genovese, et al. ACR, 2018. Abstract L06.

Table 1. TEAEs and Key Safety Outcomes Week 0-24 by Age Group, n (%)

	<65 yrs (n=335)			≥65 yrs (n=113)		
Regimen	FIL 200 (n=112)	FIL 100 (n=117)	PBO (n=106)	FIL 200 (n=35)	FIL 100 (n=36)	PBO (n=42)
TEAE	72 (64.3)	81 (69.2%)	70 (66.0%)	30 (85.7%)	16 (44.4%)	30 (71.4%)
Serious AE	4 (3.6)	7 (6.0%)	4 (3.8%)	2 (5.7%)	1 (2.8%)	1 (2.4%)
TEAE leading to study drug discontinuation	4 (3.6)	6 (5.1%)	1 (0.9%)	1 (2.9%)	0	2 (4.8%)
Infection	39 (34.8)	47 (40.2%)	27 (25.5%)	14 (40.0%)	5 (13.9%)	11 (26.2%)
Herpes Zoster (uncomplicated)	2 (1.8)	2 (1.7)	0	0	0	0
Serious infection	1 (0.9)	3 (2.6)	2 (1.9)	0	0	0
MACE	0	1 (0.9)	1 (0.9)	0	0	0
Retinal vein occlusion	1 (0.9)	0	0	0	0	0

Table 2. Week 24 Key Efficacy Measures by Age Group

	<65 yrs (n=335)			≥65 yrs (n=113)		
Regimen	FIL 200 (n=112)	FIL 100 (n=117)	PBO (n=106)	FIL 200 (n=35)	FIL 100 (n=36)	PBO (n=42)
ACR20 n (%)[1]	78 (70)‡	60 (51)†	33 (31)	24 (69)*	24 (67)*	18 (43)
DAS28(CRP)<2.6 n (%)[1]	33 (30)‡	26 (22)*	11 (10)	12 (34)	14 (39)*	7 (17)
HAQ-DI mean CFB (SD)	–0.75 (0.66)‡	–0.60 (0.66)*	–0.40 (0.58)	–0.74 (0.48)*	–0.59 (0.67)	–0.48 (0.65)
SF-36 PCS mean CFB (SD)	9.4 (8.6)†	9.2 (8.7)†	6.2 (8.2)	9.4 (6.7)*	8.5 (7.8)	7.5 (7.4)
FACIT-Fatigue mean CFB (SD)	11.2 (11.6)†	9.6 (11.1)	7.2 (10.1)	12.9 (12.2)*	10.3 (8.3)	6.4 (10.7)

*p<0.05, †p<0.01, ‡p<0.001 CFB, change from BL. [1]Nonresponder imputation.

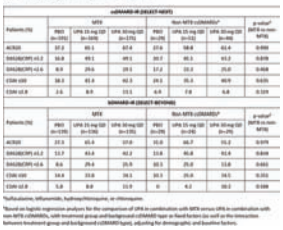
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FRI0155

A COMPARISON OF UPADACITINIB PLUS METHOTREXATE AND UPADACITINIB PLUS OTHER CSDMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN ANALYSIS OF TWO PHASE 3 STUDIES

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Background: Upadacitinib (UPA), a selective JAK1 inhibitor, has shown efficacy in patients with rheumatoid arthritis (RA) when combined with methotrexate (MTX) or other conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).[1,2] However, the efficacy of UPA plus MTX has not been directly compared with UPA plus other csDMARDs.
Objectives: To compare the efficacy of UPA in combination with MTX versus UPA in combination with other csDMARDs in patients with an inadequate response (IR) to csDMARDs (SELECT-NEXT[1]) or biologic DMARDs (bDMARDs; SELECT-BEYOND[2]).
Methods: 661 patients in SELECT-NEXT and 498 patients in SELECT-BEYOND received UPA 15 mg or 30 mg once daily (QD) or placebo (PBO) for 12 weeks; all patients received concomitant csDMARD(s). The primary endpoints for both studies were rates of ACR20 response and DAS28(CRP) ≤3.2. Additional endpoints included DAS28(CRP) <2.6, CDAI low disease activity (≤10), and CDAI remission (≤2.8). Patients were grouped according to concomitant csDMARD use (MTX vs non-MTX csDMARDs); patients receiving both MTX and a non-MTX csDMARD were included in the MTX group. p-values were calculated based on a logistic regression model with treatment group and type of background csDMARD as fixed factors, adjusting for demographic and baseline factors. p-values from the interaction between treatment group and background csDMARD were also calculated, to assess the consistency of the effects of study treatments for different background csDMARD type. Nonresponder imputation was used for missing data.
Results: In SELECT-NEXT and SELECT-BEYOND, 535 and 410 patients, respectively (80%), were receiving concomitant MTX (mean dose 17 mg/week), and 124 and 82 patients were receiving non-MTX csDMARDs. Demographics and disease characteristics were broadly similar between treatment groups; the majority of patients were female and of white ethnicity, and around half were using oral corticosteroids at baseline. Across all subgroups, the proportion of patients achieving efficacy outcomes was higher with both UPA doses compared with PBO (Table). There were no significant differences between efficacy outcomes with UPA in combination with MTX versus UPA in combination with non-MTX csDMARDs in either patient population. This included ACR20 response as well as low disease activity and remission defined by DAS28(CRP) and CDAI.



Conclusion: In this post hoc analysis, the efficacy of UPA in patients with RA appeared comparable whether administered in combination with MTX or non-MTX csDMARDs.

REFERENCES:
[1] Burmester GR, et al. Lancet 2018;391:2503–12;
[2] Genovese MC, et al. Lancet 2018;391:2513–24

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FRI0156 A PHASE 1, SINGLE AND MULTIPLE ASCENDING DOSE STUDY OF TAS5315—A NOVEL HIGHLY SELECTIVE INHIBITOR OF BRUTON'S TYROSINE KINASE—IN HEALTHY MALE VOLUNTEERS

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Background: Bruton's tyrosine kinase (BTK) is expressed in the cells of the immune system and osteoclasts, and plays an important role in inflammation and bone resorption[1]. TAS5315 is a novel, highly selective inhibitor of BTK. In animal models, TAS5315 suppressed the inflammation at the joints and significantly suppressed extreme bone destruction, in a dose-dependent manner. It has the potential to become a treatment option in patients with rheumatoid arthritis (RA).
Objectives: To evaluate the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of TAS5315 in healthy male volunteers.
Methods: The single ascending dose (SAD) study, which was the first-in-human study, and the multiple ascending dose (MAD) study were conducted as randomized, double-blind, placebo-controlled and parallel-group comparative studies in a single center. In the SAD study, 70 subjects were enrolled and received 0.01–8 mg of TAS5315 or placebo. In the MAD study, 31 subjects were enrolled and received 1–8 mg of TAS5315 or placebo once daily for 7 days. The allocation ratio (TAS5315: placebo) was 7:3 in the SAD study and 6:2 in the MAD study. The PD of TAS5315 was assessed by measuring the rate of BTK occupancy in peripheral blood mononuclear cells using a fluorescence probe. The expression level of CD203c in peripheral blood basophils treated with anti-IgE antibodies was also measured with a flow cytometer. The SAD and MAD studies were reviewed and approved by the IRB of Kitasato University Hospital.
Results: The observed PK profile of TAS5315 was linear in the dose range of 0.01–8 mg. TAS5315 was rapidly absorbed (median T_{max}: 0.5–1.5 hr) and eliminated (mean $T_{1/2}$: 1.00–1.37 hr). The maximum percentage of BTK occupancy by TAS5315 increased dose-dependently at 0.01–2 mg in SAD study. The occupancy rate of BTK peaked at 2 mg and was almost 100% at 2–8 mg, 6 hr after administration and remained almost 80% or higher for up to 24 hr. The expression level of CD203c after basophil activation decreased by 80% at 2–8 mg of TAS5315 6 hr after administration. No changes in the PD biomarkers were observed in the placebo group. The PD response was maintained after the reduction in the drug concentration. In the SAD and MAD studies, the incidence of adverse drug reactions (ADR) in the TAS5315 groups was 6.1% and 13.0%, respectively. Two subjects (8.7%) experienced subcutaneous hemorrhage in MAD study. No other ADR occurred twice in SAD and MAD studies. The severity of all ADR in SAD and MAD studies was mild and they were resolved without any treatment. There were no serious adverse events. None of the ADR showed a tendency towards a dose-dependent increase. The administration of TAS5315 resulted in a decrease in platelet aggregation and prolonged bleeding time. These changes returned to baseline level in the follow up measurement and there were no clinical safety concerns.
Conclusion: TAS5315 was tolerable when administered as repeated doses of up to 8 mg once daily for 7 days. The inhibitory effect of BTK by TAS5315 was demonstrated and this provides the basis for an early Phase II study to evaluate the efficacy of TAS5315 in patients with RA.

REFERENCE:
[1] Drug Discov Today. 2014;19,1200-4.

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FRI0157 OBSERVATIONAL STUDY OF HAIR FALL IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH LOW DOSE METHOTREXATE COMPARED TO HEALTHY CONTROLS

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Background: Chemotherapeutic drugs are known to cause of hair loss (typically anagen effluvium, starts at 2-4 weeks and most apparent at 1-2 months).(1) The effect of hair fall (or the perceived possibility of it) can be so distressing that up to 8% of patients may choose less effective chemotherapy regimens that do not cause hair loss.(2) Low dose methotrexate used in rheumatology has a different mode of action and side

effect profile compared to methotrexate at doses used in oncology.(3) Hence this study aimed to clarify whether low dose methotrexate carried a risk of hair fall.
Objectives: Determine the mean change in number of hair strands obtained by the hair pull test at the start of the trial and at 3 weeks, 2 months and 3 months among rheumatoid arthritis patients on methotrexate in comparison to healthy controls.
Methods: After ethics commitee approval and informed consent, consecutive patients attending a rheumatology OPD and who were planned to be initiated on methotrexate were enrolled into the study. Patient relatives, hospital staff and healthy blood donors were recruited as healthy controls. Patients with prior exposure to methotrexate in the last 6 months,currently on other medications known to cause hair fall or those suffering from diseases which could predispose to alopecia were excluded.
Results: During the 6 month enrollement phase 98 patients and 82 controls were enrolled. Patients were 85% female with a mean age of 48.1 +13.4. Rheumatoid factor positivity was seen in 56%. Average duration of the disease was 9.6 months (Range 15 days to 3 years) Pateints were started on 10 to 15 mg of methotrexate which was escalted at the 1st visit at 3 weeks. Only 3 patients had received prior DMARDs. Controls also constitued predominatly women (90%) with an slightly lower average age of 44.4 +10.9 years. The mean no of hair in the hair pull test at the start of the study was 1.21+2.01 (range 0-12) in pateints vs 0.84 +1.25 (range0-4)in controls. The mean change in the hair count in the same test repeated at 3 weeks, 2 months and 3 months was -0.29, -0.31 & -0.26 respectively.(i.e. reduction in hair fall). In comparison healthy controls showed values of 0.31,0.11, 0.1 at the same follow up points. There was no statistical significant difference in the proportion of patients having more that 5 hairs in the test at the onset of treatment vs healthy controls or during any point during the follow up period
Conclusion: Low dose methotrexate did not appear to predispose to increased hair fall during this short term study. In fact many patients showed reduction in the number of hair in the hair pull test on methotrexate

REFERENCES:

[1] Tosti A, Pazzaglia M. "Drug reactions affecting hair: Diagnosis." Dermatol Clin 2007;25:223-31.
[2] Malaviya AN, Sharma A, Agarwal D, Kapoor S, Garg S, Sawhney S. Low-dose and high-dose methotrexate are two different drugs in practical terms. International Journal of Rheumatic Diseases 2010; 13: 288–293.
[3] Batchelor D.Hair and cancer chemotherapy: consequences and nursing care-a literature study.Eur J Cancer Care (Engl). 2001 Sep;10(3):147-63.

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FRI0158 COMPARISON OF THE EFFICACY AND SAFETY OF TOFACITINIB AND UPADACITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: A class of targeted synthetic disease-modifying anti-rheumatic drugs (tsDMARDs) has emerged as an alternative treatment option for rheumatoid arthritis (RA). Tofacitinib is an orally administered JAK (Janus kinase) inhibitor with functional cellular specificity for JAK-1 and JAK-3 over JAK-2 and upadacitinib, a new JAK inhibitor, has been engineered to confer greater selectivity for JAK1 than for JAK2, JAK3, and Tyk2.
Objectives: The aim of this study is to assess the relative efficacy and safety of tofacitinib and upadacitinib at different doses were assessed in patients with RA with an inadequate response to conventional synthetic (cs) or biologic (b) DMARDs.
Methods: We performed a Bayesian network meta-analysis to combine direct and indirect evidence from randomized controlled trials (RCTs) to examine the efficacy and safety of tofacitinib and upadacitinib in combination with methotrexate (MTX) in RA patients with an inadequate cs- or b-DMARD response.
Results: Nine RCTs including 5,794 patients met the inclusion criteria. There were 15 pairwise comparisons including 10 direct comparisons of six interventions. Upadacitinib 15 mg+MTX and upadacitinib 30 mg+MTX were among the most effective treatments for active RA with an inadequate cs- or b-DMARD response, followed by tofacitinib 10 mg+MTX, tofacitinib 5 mg+MTX, and adalimumab 40 mg+MTX. Ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that upadacitinib 15 mg+MTX and upadacitinib 30 mg+MTX had the highest probability of being the best treatment in terms of the ACR20 response rate (SUCRA = 0.820, 0.762), followed by tofacitinib 10 mg+MTX (SUCRA = 0.623), tofacitinib 5 mg+MTX (SUCRA = 0.424), adalimumab+MTX (SUCRA = 0.371), and placebo+MTX (SUCRA = 0.001). No significant differences were observed in the incidence of serious adverse events after treatment with tofacitinib+MTX, upadacitinib +MTX, adalimumab+MTX, or placebo+MTX.
Conclusion: In RA patients with an inadequate response to cs- or b-DMARDs, upadacitinib 15 mg+MTX and upadacitinib 30 mg+MTX were the most efficacious interventions and were not associated with significant risks of serious adverse events.

REFERENCES:

[1] Kremer J, Li ZG, Hall S, et al. (2013) Tofacitinib in combination with non-biologic disease-modifying antirheumatic drugs in patients with active rheumatoid arthritis: a randomized trial. Ann Intern Med 159:253-261
[2] Catalá-López F, Tobías A, Cameron C, Moher D, Hutton B (2014) Network meta-analysis for comparing treatment effects of multiple interventions: an introduction. Rheumatology international 34:1489-1496
[3] Genovese MC, Fleischmann R, Combe B, Hall S, Rubbert-Roth A, Zhang Y, Zhou Y, Mohamed M-EF, Meerwein S, Pangan AL (2018) Safety and efficacy of upadacitinib in patients with active rheumatoid arthritis refractory to biologic disease-modifying anti-rheumatic drugs (SELECT-BEYOND): a double-blind, randomised controlled phase 3 trial. The Lancet

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FRI0159 REAL-WORLD EVIDENCE OF EFFECTIVENESS OF SWITCHING FROM TOFACITINIB 5MG BID TO TOFACITINIB 11MG QD IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS: A SINGLE-CENTER, OBSERVATIONAL STUDY IN TAIWAN

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder, precipitating chronic inflammation of the joints, also affecting organs throughout the body. For chronic conditions, such as RA, a once-daily (QD) dosing option has the potential to optimize patient adherence, and may enhance patient convenience and ease of use. Real-world data on effectiveness of switching from tofacitinib 5mg BID to 11mg QD is scarce.
Objectives: This study aimed at evaluating the effectiveness and safety of RA patients switching from tofacitinib 5mg BID to tofacitinib 11mg QD in a real-world setting.
Methods: A retrospective chart review of patients with RA was performed at the rheumatology department of an integrated secondary teaching hospital in Taiwan. The following cohorts were defined: RA patients who switched from tofacitinib 5mg BID to tofacitnib 11mg QD between 1 July 2018 and October 2018, and the follow-up period was at least 3 months. The clinical demographics and laboratory variables were obtained from clinic records.
Results: As of December 2018, 71 patients were included (85% of women), with a mean (SD) age of 57.4 (12.7) years, 70.1% were biologic-experienced; 78.9% rheumatoid factor positive and 80.3% anti- citrullinated peptide antibody (ACPA) positive. At baseline (before patients initiated tofacitnib 5mg BID treatment), the mean DAS28-ESR was 5.0 (8.4% patients with low disease activity, and 2.8% in clinical remission), the mean CDAI was 23.0 (11.2% patients with low disease activity, and 0% in clinical remission). After an average duration of 20 months treatment on tofacitinib 5mg BID treatment, the mean DAS28-ESR was 3.3 (29.6% patients with low disease activity, and 2.8% in clinical remission),

the mean CDAI was 7.5 (84.5% patients with low disease activity, and 2.8% in clinical remission). While switching to tofacitnib 11mg QD for 3 months, no significant difference was observed in terms of the ratio of DAS28-ESR LDA or CDAI LDA, but numerically more patients achieved DAS28-ESR LDA or CDAI LDA (32 and 64, respectively). During the 3-month follow-up period, no new adverse events were present.

Conclusion: Our study showed that RA patients switching from tofacitnib 5mg BID to tofacitnib 11mg QD sustained the effectiveness with no adverse clinical impact.

Table 1. Clinical demographics and laboratory variables

	Baseline	Before Switching to 11mg QD	After switching to 11mg QD
Age, mean (SD)	**57.4 (12.7)**		
Female proportion (%)	**85**		
RF positivity (%)	**78.9**		
ACPA positivity (%)	**80.3**		
Bio-exposed (%)	**70.1**		
DAS28-ESR, mean (SD)	**5.0 (1.1)**	**3.3 (0.3)**	**3.2 (0.4)**
CDAI, mean (SD)	**23.0 (8.7)**	**7.5 (2.8)**	**6.9 (2.7)**
DAS LDA (n,%)		**21 (29.6)**	**32 (45.0)**
CDAI LDA (n,%)		**60 (84.5)**	**64 (90.1)**

REFERENCES:

[1] Lamba M, Wang R, Fletcher T, et al. J Clin Pharmacol. 2016 Nov;56 (11):1362-1371

[2] Kuo CF, Luo SF, See LC, et al. Rheumatol Int. 2013 Feb;33(2):355-60.

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FRI0160 PREPARATION AND PROPERTY OF IGURATIMOD NANOSCALE SUSTAINED-RELEASE SYSTEM

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Background: Iguratimod, a methanesulfonanilide, has obvious anti-inflammatory function and has been developed exclusively in Asia-Pacific countries. As a novel disease-modifying anti-rheumatic drug, iguratimod is effective in the treatment of RA, but some side effects, such as liver damage and gastrointestinal discomforts are the main concerns in clinical application[1]. Currently, iguratimod is practically insoluble in aqueous solvents and only available in oral dosage forms. The low solubility of drugs leads to incomplete absorption and bioavailability, which affects the clinical efficacy and increases the gastrointestinal side effects of drugs[2].

Objectives: In order to improve the bioavailability and alleviate the side effect of gastrointestinal reaction, we changed the dosage form of iguratimod to NanoIguratimod-loaded Hydrogel Composite.

Methods: Iguratimod nanoparticles (NanoIguratimod) were prepared by using the high-gravity anti-solvent precipitation (HGAP) technique, and its properties were tested. The NanoIguratimod-loaded Hydrogel Composite was prepared and the delivery of the payload was demonstrated. In vitro, the biological effects of NanoIguratimod@Hydrogel on fibroblast-like synoviocytes (RA-FLS) were evaluated. In vivo, the pharmacokinetics of oral raw iguratimod or subcutaneous injection of NanoIguratimod@Hydrogel was carried out in the healthy rats. Further, we evaluated the efficacy of NanoIguratimod@Hydrogel in treating collagen-induced arthritis (CIA) rats.

Results: By the HGAP technique, we acquired the amorphous form NanoIguratimod with an average size of 295nm, which had higher dissolution rates and higher stability. The release of iguratimod from hydrogel composite in PBS was gradual and sustained for up to 48h compared with NanoIguratimod. NanoIguratimod@Hydrogel inhibited the proliferation, migration, and invasion of RA-FLS in a doses dependent manner. The pharmacokinetic parameters showed better bioavailability and longer half-life time with NanoIguratimod@Hydrogel by subcutaneous administration than oral raw iguratimod. Animal experiments confirmed that subcutaneous injection of NanoIguratimod@Hydrogel (10mg/kg every three days) and oral raw iguratimod (10mg/kg daily) showed similar efficacy in decreasing arthritis index score, pathological score, and expression of cytokines (IL-6, TNF-α and IL-1β).

Conclusion: Overall, our data suggested that NanoIguratimod@Hydrogel provided new administration routes and extended the administration interval, it may serve as a promising drug delivery approach for the treatment of RA.

REFERENCES:

[1] Hara M, Abe T, Sugawara S, et al. Long-term safety study of iguratimod in patients with rheumatoid arthritis[J]. Mod Rheumatol., 2007, 17(1):10-16.

[2] Zhou T, Ding L, Li X, et al. Determination of iguratimod in rat plasma by high performance liquid chromatography: method and application[J]. Biomed Chromatogr, 2010, 22(3):260-264.

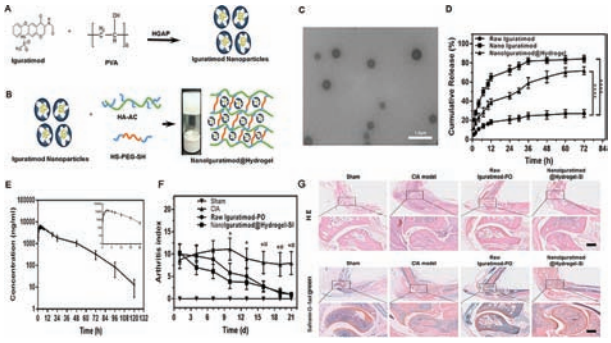


Figure: Preparation and Property of Iguratimod Nanoscale Sustained-Release System. **(A)**: Synthesis scheme of Hyaluronic acid–acrylate (HA-AC). **(B)**: Brief production process of NanoIguratimod@Hydrogel. **(C)** : TEM images of NanoIguratimod. **(D)**: Dissolution profiles of raw iguratimod, NanoIguratimod and NanoIguratimod-loaded Hydrogel. **(E)**: Plasma concentrations and pharmacokinetic parameters of raw Iguratimod and NanoIguratimod-loaded Hydrogel. **(F)**: Changes of arthritis index (AI) score in rats during drug intervention. **(G)**: Results of HE staining and saffron O-fixing green staining on the ankle joints of rats. *p<0.05,**p<0.01,***p<0.001, n=7 per group. Scar bar =200μm.

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FRI0161 PHARMACOKINETICS AND SAFETY OF A SINGLE ORAL DOSE OF PEFICITINIB (ASP015K) IN SUBJECTS WITH NORMAL AND IMPAIRED HEPATIC FUNCTION

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Background: Peficitinib (ASP015K), a novel oral Janus kinase inhibitor, demonstrated efficacy as once-daily therapy for moderate–severe rheumatoid arthritis in a phase 2b study (NCT01649999)[1] and 2 phase 3 studies (NCT02308163[2]; NCT02305849).[3] Mean urinary excretion of peficitinib accounted for 9–15% of the oral dose.[4] It produces 3 conjugated metabolites (H1, H2, H4), which show very weak in-vitro pharmacological action.

Objectives: To assess pharmacokinetics (PK) and safety of a single oral dose of peficitinib 150 mg in subjects with normal and impaired hepatic function.

Methods: This phase 1, open-label, single-dose, parallel-group study was conducted at six centres in Japan. Eligible subjects were aged 20–75 years, with body mass index $\geq$17.0–<30.0 kg/m^2. Hepatic impairment was defined at screening using Child-Pugh classification: Class A, mild (5–6 points); Class B, moderate (7–9 points). Subjects with severe hepatic impairment (Child-Pugh classification Class C, 10–15 points) were excluded. Subjects received a single oral dose of peficitinib 150 mg under fasting conditions, based on daily dose in the 2 phase 3 studies. Blood samples for plasma PK analysis of peficitinib and its metabolites were collected before and up to 72 h post dose. Safety was assessed throughout the study.

Results: 24 subjects were enrolled (70.8% male): 16 with impaired and 8 with normal hepatic function (**Table 1**); all received study medication

according to protocol. The peficitinib concentration-time profiles from dosing to 72 h (**Fig. 1**), extrapolated to infinity (AUC_{inf}), and maximum concentration (C_{max}) were similar in subjects with normal and mildly impaired hepatic function; however, AUC_{inf} and C_{max} were increased in subjects with moderate hepatic impairment (**Table 2**). There was a trend of greater exposure to H1, H2 and H4 metabolites in subjects with mild or moderate hepatic impairment, except for H2 in moderate hepatic impairment, although geometric mean ratios versus subjects with normal function were variable (**Table 2**). One subject in each group experienced a total of 5 TEAEs (**Table 3**), all of which were considered drug-related except back pain. No serious TEAEs, deaths or clinically significant mean changes from baseline in clinical laboratory parameters were reported during the study.

Table 1 Demographic characteristics (PKAS)

Parameter	Normal hepatic function (n=8)	Mild hepatic impairment[2] (n=8)	Moderate hepatic impairment[2] (n=8)	Total (n=24)
Male, n (%)	6 (75.0)	5 (62.5)	6 (75.0)	17 (70.8)
Median (min, max) age, y	60.0 (55, 68)	69.0 (48, 75)	60.5 (49, 67)	63.0 (48, 75)
Median (min, max) weight, kg	69.3 (48.8, 76.3)	69.0 (51.7, 81.2)	73.0 (43.3, 75.1)	71.3 (43.3, 81.2)
Median (min, max) BMI, kg/m^2	24.2 (20.8, 28.4)	27.3 (20.0, 29.7)	23.8 (18.6, 29.2)	24.5 (18.6, 29.7)
Median (min, max) prothrombin time, %	-	97.0 (70.2, 120.0)	65.2 (52.2, 101.0)	86.0 (52.2, 120.0)[1]

[1]Total number of subjects for which prothrombin time was calculated was 16.
[2]Hepatic impairment was defined at screening according to Child-Pugh classifications: Class A, mild, 5–6 points; or Class B, moderate, 7–9 points.

Table 2 Plasma PK parameters of peficitinib and its metabolites H1, H2 and H4 (PKAS)

Parameter		Normal hepatic function (n=8)[1]	Mild hepatic impairment[2] (n=8)	Moderate hepatic impairment[2] (n=8)
Peficitinib				
AUC_{inf}, ng.h/mL	Mean (SD)	1149 (231.1)	1435 (525.1)	2332 (895.6)
	GMR (90% CI)	--	1.19 (0.86, 1.64)	1.92 (1.39, 2.66)
C_{max}, mg/mL	Mean (SD)	350.4 (129.1)	371.6 (146.5)	673.8 (331.6)
	GMR (90% CI)	--	1.04 (0.71, 1.53)	1.82 (1.24, 2.69)
$t_{1/2}$, h	Mean (SD)	10.43 (6.215)	13.70 (9.934)	11.16 (8.881)
H1				
AUC_{inf}, ng.h/mL	Mean (SD)	372.1 (111.8)	887.9 (453.0)	1138 (1259)
	GMR (90% CI)	--	2.15 (1.01, 4.56)	1.65 (0.78, 3.50)
C_{max}, ng/mL	Mean (SD)	44.79 (23.87)	90.64 (50.46)	110.3 (107.2)
	GMR (90% CI)	--	1.95 (0.97, 3.92)	1.71 (0.85, 3.45)
$t_{1/2}$, h	Mean (SD)	12.50 (7.983)	9.939 (5.496)	14.11 (7.024)
H2				
AUC_{inf}, ng.h/mL	Mean (SD)	2707 (557.4)	4393 (2075)	2489 (2358)
	GMR (90% CI)	--	1.52 (0.86, 2.68)	0.62 (0.35, 1.10)
C_{max}, ng/mL	Mean (SD)	641.3 (174.0)	808.9 (247.1)	485.0 (426.3)
	GMR (90% CI)	--	1.25 (0.75, 2.09)	0.55 (0.33, 0.91)
$t_{1/2}$, h	Mean (SD)	10.77 (6.098)	7.743 (5.093)	12.24 (9.027)
H4				
AUC_{inf}, ng.h/mL	Mean (SD)	357.2 (143.1)	571.8 (281.1)	1346 (1011)
	GMR (90% CI)	--	1.51 (0.91, 2.49)	3.17 (1.92, 5.24)
C_{max}, ng/mL	Mean (SD)	35.57 (26.23)	53.46 (34.03)	110.5 (80.01)
	GMR (90% CI)	--	1.55 (0.85, 2.83)	3.05 (1.67, 5.56)
$t_{1/2}$, h	Mean (SD)	12.24 (6.956)	10.71 (4.767)	15.13 (7.502)

[1]Number of subjects available for AUC_{inf} and $t_{1/2}$ was 7.
[2]Hepatic impairment was defined at screening according to Child-Pugh classifications: Class A, mild, 5–6 points; or Class B, moderate, 7–9 points.
AUC_{inf}, area under the concentration–time curve from the time of dosing extrapolated to infinity; C_{max}, maximum concentration; GMR, geometric mean ratio; PKAS, pharmacokinetic analysis set (all subjects who received the study drug and provided at least one estimable PK parameter); SD, standard deviation; $t_{1/2}$, terminal elimination half-life; t_{max}, time of C_{max}.

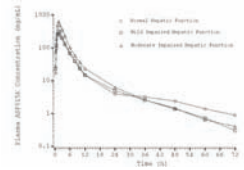
Table 3 Treatment-emergent adverse events (SAFI), by Preferred Term

n (%)	Normal hepatic function (n=8)	Mild hepatic impairment[2] (n=8)	Moderate hepatic impairment[2] (n=8)	Total (n=24)
Overall	1 (12.5)[3]	1 (12.5)[3]	1 (12.5)	3 (12.5)
Diarrhoea	0	1 (12.5)	0	1 (4.2)
Nausea	1 (12.5)	0	0	1 (4.2)
Blood urine present	0	1 (12.5)	0	1 (4.2)
Back pain	1 (12.5)	0	0	1 (4.2)
Hypotension	0	0	1 (12.5)	1 (4.2)

[2]Hepatic impairment was defined at screening according to Child-Pugh classifications: Class A, mild, 5–6 points; or Class B, moderate, 7–9 points.
[3]Adverse events of nausea and back pain were observed in a single subject with normal hepatic function.
[4]Adverse events of diarrhoea and presence of blood urine were observed in a single subject with mild hepatic impairment.
SAF, safety analysis set (all subjects who received the study drug)

Conclusion: Peficitinib exposure in subjects with mild hepatic impairment was similar to that in subjects with normal hepatic function; subjects with moderate hepatic impairment had greater exposure. A single dose of peficitinib was well tolerated.

Figure 1 Mean plasma peficitinib concentration over time by degree of hepatic impairment (semi-log scale; PKAS)



REFERENCES:

[1] Takeuchi T, et al. Ann Rheum Dis 2016; 75: 1057–64; 2. Tanaka Y, et al. ACR/ARHP Annual Meeting 2018: Abstract 887; 3. Takeuchi T, et al. ACR/ARHP Annual Meeting 2018: Abstract 888; 4. Cao YJ, et al. Clin Pharmacol Drug Dev 2016;5:435–49

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FRI0162

BASELINE CHARACTERISTICS AND OUTCOMES IN PATIENTS WITH ANAEMIA IN CLINICAL STUDIES OF TOFACITINIB IN RHEUMATOID ARTHRITIS

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).
Objectives: To describe the profile of patients (pts) with RA and clinically significant anaemia and the impact of treatment with tofacitinib on those with anaemia.
Methods: In this post hoc analysis, data were pooled from Phase (P)2, P3 and P3b/4 studies across the tofacitinib RA clinical programme. Pts received tofacitinib 5 or 10 mg twice daily (BID) with/without background conventional synthetic disease-modifying antirheumatic drugs, or placebo (PBO). Pts with grade $\geq$2 anaemia (G2A; haemoglobin [Hgb] <10 g/dL) at baseline (BL) were compared with pts without G2A (Hgb $\geq$10 g/dL) at BL. Demographic and BL characteristics, Hgb levels and efficacy (Disease Activity Score in 28 joints, erythrocyte sedimentation rate [DAS28-4(ESR)]) at Month (M)6 and treatment-emergent adverse events (TEAEs) were summarised descriptively.
Results: The proportion of pts with G2A at BL was similar for tofacitinib (3.2%, 152 of 4736 pts) and PBO (2.4%, 27 of 1125 pts) groups. Pts with G2A at BL were more often female, Asian, younger, had never smoked and had a lower body mass index (BMI) and higher C-reactive protein (CRP) and ESR vs pts without G2A at BL; RA duration was generally similar across groups (Table). Tofacitinib seemed to improve anaemia more rapidly than PBO: in pts with G2A at BL, a lower proportion of those receiving tofacitinib had G2A at M1 and M3 vs those receiving PBO (48.8% vs 75.0%, respectively, at M1 and 36.1% vs 57.1%, respectively, at M3), while the proportions were similar at M6 (28.9% vs 30.6%, respectively). In pts receiving tofacitinib, mean Hgb levels gradually increased from BL to M6 in those with G2A at BL (1.25 g/dL change), but were relatively stable in those without G2A at BL (0.15 g/dL change). In tofacitinib-treated pts, DAS28-4(ESR) scores decreased from BL to M6 by -2.40 in those with G2A at BL and -2.42 in those without G2A at BL. DAS28-4(ESR) low disease activity ($\leq$3.2) rate at M6 was lower in tofacitinib-treated pts with G2A at BL vs those without G2A at BL (18.3% vs 28.4%, respectively). Among pts receiving tofacitinib,

those with BL G2A had a higher incidence of TEAEs vs those without BL G2A in the following MedDRA system organ classes (with incidence >20% in pts who were either with or without BL G2A): gastrointestinal disorders (30.9% vs 22.5%, respectively) and infections and infestations (44.1% vs 39.0%, respectively).

Conclusion: In this post hoc analysis, more pts with BL G2A were female, Asian, younger, had never smoked, and had lower BMI and elevated ESR and CRP vs those without BL G2A. G2A resolved within 6 months in most pts with RA receiving tofacitinib, while inflammation and disease activity (assessed by DAS28-4[ESR]) decreased. G2A appeared to resolve more rapidly in pts receiving tofacitinib vs those receiving PBO. These data suggest that tofacitinib for the treatment of RA can be an option for pts who have anaemia, within prescribing guidelines.[1]

Table. Demographics and disease characteristics at baseline

	With baseline G2A (Hgb <10 g/dL)		Without baseline G2A (Hgb ≥10 g/dL)	
	Tofacitinib (N=152)	Placebo (N=27)	Tofacitinib (N=4584)	Placebo (N=1098)
Age group, years (%)				
18–45	40.8	63.0	27.3	24.3
>45–<65	46.1	25.9	58.6	59.7
≥65	13.2	11.1	14.1	16.0
Age, years (mean [SD])	48.9 (13.1)	45.1 (13.7)	52.0 (12.0)	53.1 (12.0)
Female (%)	96.1	96.3	82.7	81.2
BMI, kg/m^2 (mean [SD])	23.9 (5.3)	24.7 (7.1)	27.3 (6.5)	27.5 (6.7)
Race (%)				
White	39.5	37.0	64.4	66.9
Black	3.3	14.8	3.4	3.2
Asian	47.4	33.3	21.7	22.1
Other	9.9	14.8	10.5	7.7
Smoking status (%)				
Never smoked	85.5	85.2	65.2	56.0
Previous or current smoker	13.8	14.8	33.5	37.9
Unknown	<1.0	0.0	1.3	6.1
HAQ-DI (mean [SD])	1.7 (0.7)	1.6 (0.7)	1.5 (0.7)	1.4 (0.7)
DAS28–4(ESR; mean [SD])	6.9 (0.9)	7.0 (0.9)	6.4 (1.0)	6.3 (1.0)
Disease duration, years (mean [SD])	7.1 (7.8)	7.3 (7.0)	7.7 (7.9)	9.4 (8.6)
ESR, mm/hr (mean [SD])	77.8 (31.5)	69.7 (31.1)	49.5 (26.6)	45.4 (24.7)
CRP, mg/L (mean [SD])	39.1 (37.7)	34.7 (27.6)	17.7 (22.4)	16.0 (18.2)
RF+ (%)	73.4	65.2	72.3	68.6
Anti-CCP+ (%)	61.8	51.9	52.4	47.5
Hgb, g/dL (mean [SD])	9.4 (0.4)	9.3 (0.6)	12.8 (1.4)	12.9 (1.3)

Data were pooled from the following Phase 2, Phase 3 and Phase 3b/4 studies across the tofacitinib clinical programme: NCT00147498; NCT00413660; NCT00960440; NCT00550446; NCT00603512; NCT00687193; NCT00847613; NCT00814307; NCT00856544; NCT00853385; NCT01164579; NCT01039688; NCT00976599; NCT01059864; NCT01359150; NCT02147587; NCT02187055

Treatment groups are based on initial randomised study drug; tofacitinib was dosed at 5 or 10 mg BID

BID, twice daily; BMI, body mass index; CCP, cyclic citrullinated peptide; CRP, C-reactive protein; DAS28–4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; G2A, grade ≥2 anaemia; HAQ-DI, Health Assessment Questionnaire-Disability Index; Hgb, haemoglobin; RF, rheumatoid factor; SD, standard deviation

REFERENCES:

[1] US Food and Drug Administration. XELJANZ® (tofacitinib) highlights of prescribing information. Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=959 Accessed 28 January 2019.

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FRI0163

TIME TO DISCONTINUATION OF TOFACITINAB IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH AND WITHOUT METHOTREXATE: RESULTS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE (OBRI) COHORT

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Background: Tofacitinib (TOFA) is an oral, small molecule drug which can be used as an alternative to biologic disease modifying antirheumatic drugs (bDMARDs) for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX).

Objectives: We aimed to evaluate the discontinuation rate of this drug, with and without concurrent MTX, with and without prior biologic use, in patients with RA using real world data from a Canadian (Ontario) observational cohort.

Methods: Patients enrolled in the Ontario Best Practices Research Initiative (OBRI) who started TOFA after its approval in Canada (June 2014) were included in the analysis. Patients were followed from TOFA initiation until discontinuation, death, lost to follow-up, or last visit, whichever came first. Time to discontinuation of TOFA, due to any reason, in patients 1) with or without concurrent MTX use; 2) with or without prior biologic use was assessed using Kaplan-Meier survival analysis.

Results: Among the 131 patients, 70 (53.4%) received TOFA without MTX and 61 (46.6%) TOFA with MTX. Mean (SD) age and disease duration were 60.2 (0.90) years and 13.7 (0.80) years, respectively. The majority were females (89.3%) and most had prior biologic use history (74.0%). At baseline, no significant differences in disease activity and sociodemographic profiles were found between the two groups of patients with and without concurrent MTX use. Discontinuation was reported in 44 (33.6%) of all TOFA patients with a median survival of 31.3 months. Overall retention of TOFA at 6, 12 and 24 months was 80.5%, 63.1% and 53.5% respectively. These findings are very similar to the results reported from the RHUMADATA registry at ACR 2018.[1] Fifteen (34.0%) patients stopped their TOFA due to non-response/loss of response, 22 (50.0%) due to adverse events, and 7 (16%) due to other reasons.

At 6 and 12 months' follow-up, more patients remained on TOFA in the 'TOFA with MTX' group (88.3% and 73.1%, respectively) compared to the 'TOFA without MTX" group (73.9% and 54.6%, respectively) (Logrank p=0.05). There was no significant difference in TOFA discontinuation between the two groups of patients with and without prior biologic use (Logrank p=0.77).

Conclusion: We found that half of the RA patients remained on TOFA 31 months after initiation. Patients also stayed on TOFA longer when they concurrently used MTX compared to TOFA without MTX.

REFERENCE:

[1] Choquette D, Bessette L, Brown J, Haraoui B, Massicotte F, Pelletier JP, Raynauld JP, Rémillard MA, Sauvageau D, Turcotte A, Villeneuve É, Coupal L. Tofacitinib Show Similar Retention When Used with and without Methotrexate. Analysis from the Rhumadata® Clinical Database and Registry [abstract]. **Arthritis Rheumatol.** 2018; 70 (suppl 10).

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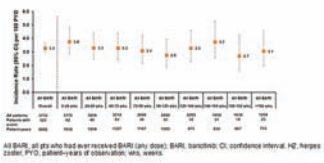
FRI0164

INCIDENCE RATE AND CHARACTERIZATION OF HERPES ZOSTER IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS: AN UPDATE FROM BARICITINIB CLINICAL STUDIES

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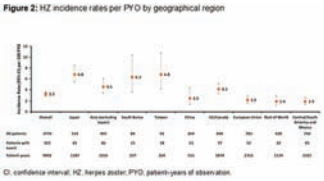
Background: Baricitinib (BARI) is a selective inhibitor of Janus kinase (JAK) 1 and JAK2, approved for the treatment of moderately to severely active rheumatoid arthritis (RA) in adults in over 50 countries, including the United States, Europe and Japan. Due to their disease and associated therapy with disease-modifying anti-rheumatic drugs (DMARDs), RA patients (pts) have an increased risk of herpes zoster (HZ) compared with the general population.[1] Furthermore, the incidence of HZ is increased in RA pts treated with BARI versus placebo (PBO).[2]
Objectives: To determine the long-term overall and geographical incidence, time to first event and risk factors for HZ in BARI-treated RA pts.
Methods: Data were pooled from nine completed Phase 1, 2, and 3 studies of BARI in RA pts, including six randomised, PBO-controlled studies (0–24 weeks in DMARD-inadequate responders, including RA-BUILD, RA-BEACON and the long-term extension study, RA-BEYOND [data cut off February 13, 2018]), and active-controlled studies with methotrexate (MTX; RA-BEGIN study in DMARD-naïve pts) and adalimumab (RA-BEAM study in MTX-inadequate responders). The HZ incidence was evaluated for all RA pts who had ever received BARI (any dose) and the HZ incidence rate (IR) was calculated as the number of pts with an HZ event per 100 patient–years of observation (PYO). Exposure included up to 28 days after treatment cessation, and was censored at the HZ event date. Univariate and multivariate Cox proportional hazard regression models were used to evaluate risk factors for HZ.

Figure 1: HZ incidence rates per PYO over time



All BARI, all pts who had ever received BARI (any dose); BARI, baricitinib; CI, confidence interval; HZ, herpes zoster; PYO, patient–years of observation; wks, weeks.

Figure 2: HZ incidence rates per PYO by geographical region



CI, confidence interval; HZ, herpes zoster; PYO, patient-years of observation.

Results: Of 3770 RA pts treated with BARI, median age at study entry was 54 years (range 20–90 years), approximately one-quarter were each from North America (n=840; 22%), EU (783; 21%), Asia (959; 25%) and Central America (760; 20%), median time from RA diagnosis was 5 years, 2938 (78%) and 1754 (47%) were on concomitant MTX or corticosteroids (CS; mean dose 6.2 mg/day), respectively. HZ was reported in 323 (9%) pts over 9892 PYO, with median BARI exposure of 1115 days. Of these pts, 12 (4%) had a history of HZ, and 256 (79%) and 168 (52%) were on concomitant MTX and CS, respectively. The median time to first HZ event was 538 days and the overall IR of HZ was 3.3/100 PYO, which did not increase significantly over time (Fig 1). Twenty-six (8%) cases were multidermatomal, and no visceral disease was reported. Eight (2%) pts showed involvement of the ophthalmic division of the Vth cranial nerve and 9 (3%) experienced recurrent HZ during observation. Only 11 HZ pts (4%) had received prior HZ vaccination. Multivariate analyses showed that older age (hazard ratio [HR] 1.30, 95% confidence interval [CI] 1.17, 1.43) and geographical region (Asia, especially Japan, Taiwan and South Korea; HR 1.82, 95% CI 1.28, 2.58; Fig 2) were associated with a higher risk of HZ.
Conclusion: HZ incidence in BARI-treated RA pts did not increase over time and the majority of HZ events were monodermatomal and uncomplicated. Pts who were older and those from Asia were at increased risk of a HZ event.

REFERENCE:

[1] Smitten AL, et al. Arthritis Rheum 2007;57:1431–1438. 2. Smolen JS, et al. J Rheumatol 2019;46:7–18.

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FRI0165 **PATIENT- AND PHYSICIAN-REPORTED OUTCOMES FROM RAJ4: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF THE EFFICACY AND SAFETY OF PEFICITINIB (ASP015K) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) WHO HAD AN INADEQUATE RESPONSE TO METHOTREXATE (MTX)**

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Background: The novel oral Janus kinase inhibitor, peficitinib, demonstrated efficacy and tolerability as once-daily combination therapy with MTX for moderate-to-severe RA in the RAJ4 phase 3 study (NCT02305849).[1] For the first time, we focussed on patient and physician outcome measures in this Japanese study.
Objectives: To assess health-related quality of life (HRQoL) of Japanese patients with RA who had an inadequate response to MTX.
Methods: This multicentre, randomised, double-blind, parallel-group, placebo-controlled, phase 3 study recruited patients in Japan with active RA and inadequate response to MTX.[1]Patients were randomised 1:1:1 to 52-week placebo+MTX (PBO), peficitinib 100 mg QD+MTX (PEFI 100 mg) or peficitinib 150 mg QD+MTX (PEFI 150 mg). The PBO group was switched to PEFI 100 mg or 150 mg at Week 12 (for non-responders) or Week 28 (for remaining patients). Patient- and physician-reported outcome assessments included: Physician's Global Assessment of disease activity (PGA); Subject's Global Assessment of disease activity (SGA); and Subject's Global Assessment of pain (SGAP) by visual analogue scale. Physical function was evaluated using Health Assessment Questionnaire-Disability Index (HAQ-DI). All assessments were conducted at each visit from baseline to the end of study.
Results: 519 patients were treated: PBO (n=170), PEFI 100 mg (n=175) and PEFI 150 mg (n=174). One PEFI 100 mg patient was excluded from the analysis due to protocol deviation. At Weeks 12/early termination (ET) and 28/ET, both PEFI groups were associated with significant improvements in PGA, SGA, SGAP and HAQ-DI (**Table 1**). These outcomes were maintained or improved at end of treatment (EOT; Week 52/ET), when mean change from baseline for PGA, SGA, SGAP and HAQ-DI in the PEFI 100 mg and PEFI 150 mg groups were: -38.41, -43.33; -29.34, -34.05; -28.94, -32.68; and -0.36, -0.51, respectively. Significantly greater proportions of patients achieved functional remission and a minimum clinically important (MCI) reduction in HAQ-DI score (≤0.5 and reduction of ≥0.22, respectively) at Weeks 12/ET and 28/ET in both PEFI groups than in the PBO group (p<0.001 vs PBO for both PEFI doses; **Table 1**). In the PEFI 100 mg and PEFI 150 mg groups at EOT, functional remission occurred in 105/172 (61.0%) and 106/171 (62.0%) patients and MCI reduction in HAQ-DI score occurred in 99/172 (57.6%) and 120/171 (70.2%) patients, respectively.

Table 1 Physician- and patient-reported outcome results at Week 12/ET and Week 28/ET

Outcome type	Result	Week 12/ET			Week 28/ET		
		PBO (n=168)[2]	PEFI 100 mg QD (n=172)	PEFI 150 mg QD (n=171)	PBO (n=168)[2]	PEFI 100 mg QD (n=172)	PEFI 150 mg QD (n=171)
Physician-reported	Mean (SD) change from baseline in PGA	-11.88 (21.46)	-28.83 (22.21)	-35.96 (25.00)	-12.55 (22.63)	-36.80 (23.57)	-40.61 (22.41)
	LS mean (SE) treatment difference vs PBO[2]	-	-17.67 (2.26)***	-24.09 (2.33)***	-	-25.11 (2.36)***	-28.07 (2.24)***
Patient-reported	Mean (SD) change from baseline in SGA	-7.11 (23.05)	-21.09 (23.63)	-26.57 (25.43)	-8.08 (25.99)	-27.70 (26.15)	-32.62 (26.60)
	LS mean (SE) treatment difference vs PBO[2]	-	-16.64 (2.26)***	-20.34 (2.40)***	-	-22.81 (2.47)***	-25.55 (2.57)***
	Mean (SD) change from baseline in SGAP	-6.64 (25.22)	-21.09 (27.04)	-26.87 (26.65)	-7.61 (27.81)	-26.33 (28.22)	-32.23 (27.59)
	LS mean (SE) treatment difference vs PBO[2]	-	-17.19 (2.44)***	-20.89 (2.50)***	-	-21.73 (2.59)***	-25.35 (2.63)***
	Mean (SD) change from baseline in HAQ-DI	0.01 (0.47)	-0.22 (0.44)	-0.37 (0.48)	0.00 (0.60)	-0.33 (0.51)	-0.47 (0.54)
	LS mean (SE) treatment difference vs PBO[2]	-	-0.27 (0.05)***	-0.39 (0.05)***	-	-0.38 (0.06)***	-0.48 (0.06)***
	Patients achieving HAQ-DI ≤0.5, n (%)	48 (28.4)	87 (50.6)****	85 (49.7)****	51 (30.2)	103 (59.9)****	100 (58.5)****
	Patients achieving HAQ-DI ≥0.22 reduction,[2] n (%)	53 (31.5)	85 (49.4)****	105 (61.4)****	57 (33.9)	95 (55.2)****	114 (66.7)****

Higher VAS score indicates greater disease activity.
Analysis of covariance models were used: 1Number of patients in PBO group assessed for HAQ-DI ≤0.5 reduction from baseline was 169; 2PGA (100 mm VAS) change = treatment + baseline PGA (100 mm VAS); 3SGA (100 mm VAS) change = treatment + baseline SGA (100 mm VAS); 4SGAP (100 mm VAS) change = treatment + baseline SGAP (100 mm VAS); 5HAQ-DI change = treatment + baseline HAQ-DI; 6Fisher's exact test; 7Reduction from baseline.
***p<0.005 vs PBO, with no adjustment made for multiplicity.
ET=early termination; HAQ-DI=Health Assessment Questionnaire – Disability Index; LS=least squares; PBO=placebo; PGA=Physician's Global Assessment of disease activity; SD=standard deviation; SGA=Subject's Global Assessment of disease activity; SGAP=Subject's Global Assessment of pain; SE=standard error; VAS=visual analogue scale.

Conclusion: Measures of PGA, SGA, SGAP and HAQ-DI in patients with RA who had an inadequate response to MTX demonstrated improved HRQoL with peficitinib; PEFI 150 mg QD showed similar or numerically greater changes in HRQoL than PEFI 100 mg QD. Improvements were maintained or improved to the EOT and demonstrated a significant benefit for patients with RA in Japan.

REFERENCE:
[1] Takeuchi T, et al. Arthritis Rheumatol 2018; 70 (Suppl. 10): Abstract 888.

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FRI0166 **RADIOSYNOVIOTHESIS WITH YTTRIUM90: A CANADIAN EXPERIENCE**

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Background: Radiosynovectomy (RSO) has been used since 1952 for treatment of refractory synovitis. ^{90}Yttrium in a colloidal form has been approved in several countries as a RSP radiopharmaceutical agent for intra-articular treatment of synovial hypertrophy. In comparison to surgical synovectomy, RSO produces equivalent results, costs less, allows the patient to remain ambulatory and can be repeated. However, there are currently no RSO radiopharmaceuticals approved in Canada.
Objectives: 1. Establish safety of Yttrium-90 citrate synovectomy in a Canadian cohort
2. Determine the therapeutic value of Yttrium-90 citrate in patients with refractory synovitis in a Canadian cohort.

Methods: Adult (≥18yo) patients with symptomatic, refractory inflammatory mono- or oligoarthritis were included for RSO with Yttrium-90 citrate as part of a phase-III, prospective, open-label non-controlled trial. All patients were required to have failed 6-months of medical therapy and 2 intraarticular injections and have minimal evidence of cartilage or bone destruction. Only large and medium-sized joints were included (i.e. knees, ankles, wrists and elbows). The dose of Yttrium was adjusted based on the size of joint. Follow-up evaluations were done at 3, 6 and 12 months after RSO. Safety was assessed by patient and clinician reported adverse events. Clinical response was measured by improvement in joint tenderness, effusion and range of motion.

Results: A total of 74 patients and 83 joints (88% knees) were treated with Ytrium-90 citrate. The underlying diagnosis included 25.7% RA, 34% SpA, 11% JIA, and 30.3% other inflammatory arthritis. Complications included 3 post-RSO flares, 1 septic joint and 2 injection site skin infections. Joint tenderness was reported in 93.8% of joints at baseline, compared to 50.0% at 3mo (p<0.001), 55.6% at 6mo (p<0.001) and 40.4% at 12mo (p<0.001). Joint effusion was present in 95.1% of joints at baseline, 44.3% at 3mo (p<0.001), 51.4% at 6mo (p<0.001) and 47.4% at 12mo (p<0.001). 73.9% of joints had improvement in range of motion at 3mo, 55.9% at 6mo and 60.7% at 12mo.

Conclusion: These results confirm the clinical efficacy and safety of Yttrium90-citrate RSO for refractory synovitis with a sustained clinical benefit at 12 months. This is the first such study in a Canadian cohort. RSO with Ytrium is a safe alternative to surgical synovectomy in refractory cases.

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FRI0167 DOES BARICITINIB HAVE A SPECIFIC EFFECT PATIENT'S REPORTED OUTCOME? COMPARISON OF EFFECTS ON PAIN AND PATIENT GLOBAL ASSESSMENT WITH TNF INHIBITORS

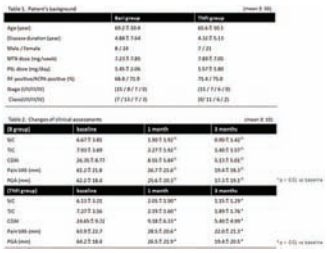
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Background: Baricitinib (bari) is approved for treating moderate–severe rheumatoid arthritis (RA) in many countries, including Japan. Bari is an oral Janus kinase (JAK1)/JAK2 selective inhibitor and has shown good efficacy in RA and an adequate response to conventional synthetic DMARDs in some clinical trials. Pain and patient global assessment (PGA) are common symptoms for patients with RA. Some trials suggest that bari may have a supplementary benefit on patients' reported outcomes (PRO). Our goal was to determine the impact of each treatment on pain and PGA.

Objectives: We evaluated and compared the impact of bari and TNF inhibitors (TNFi) on pain and PGA and correlation with PRO and clinical assessments for Japanese RA patients who have an inadequate response to csDMARDs in real world multicenter clinical data.

Methods: We included 60 Japanese RA patients with an inadequate response to csDMARDs. We classified patients into two groups, one treated with bari (B group; 24 females and 8 males) and the other with TNFi (TNFi group; 22 females and 6 males). Patients were scheduled to receive TNFi (GLM 50 mg/month or ETN 50 mg/week) in TNFi group or bari 4 or 2 mg/day in B group as a monotherapy or in combination with csDMARDs. We evaluated swollen joint counts on 28 joints (SJC), tender joint counts on 28 joints (TJC), visual analog scale of pain (VAS pain) (0–100 mm), PGA (0–100 mm), and Clinical Disease Activity Index (CDAI) at baseline, 4 weeks, and 12 weeks. First, we compared the changes in SJC, TJC, CDAI, VAS pain, and PGA at 4 and 12 weeks after treatments between the two groups. Second, we evaluated the correlation between PROs (VAS pain or PGA) and variations in clinical evaluation items (SJC, TJC, and CDAI).

Results: There were no significant differences in background at baseline between the two groups (Table 1). Baseline SJC, TJC, and CDAI scores; VAS pain; and PGA were 6.67 ± 3.81, 7.93 ± 3.69, 26.35 ± 8.77, 61.2 ± 21.8, and 62.2 ± 18.4 in the bari group, respectively, and 6.13 ± 3.21, 7.27 ± 3.56, 24.65 ± 9.72, 63.9 ± 22.7, and 64.2 ± 18.4 in the TNFi group, respectively. SLC, TJC, CDAI scores, VAS pain, and PGA in both groups were significantly improved 1 month after treatment. This tendency continued for 3 months after treatment. There were no significant differences in the improvement rate of SJC, TJC, CDAI scores, VAS pain, and PGA between the two groups at each follow-up time point after treatment. VAS pain scores were significantly correlated with SJC and CDAI scores in both groups (B group; r = 0.651, p < 0.01 and TNFi group; r = 0.688, p < 0.01). PGA scores were significantly correlated with SJC and CDAI scores in both groups (B group; r = 0.657, p < 0.01 and TNFi group; r = 0.613, p < 0.01).



Conclusion: Our results indicate that the effect of bari on pain and PGA is correlated with the improvement rate in disease activity. Bari treatment is not significantly different than TNFi, at least during the short term, in real world clinical data.

REFERENCE:

[1] Perricone C, et al. Rheumatology (Oxford) 2012;51:866-73

Disclosure of Interests: None declared

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FRI0168 POSITIVE EFFECTS OF AN ANTI-INFLAMMATORY DIET IN RHEUMATOID ARTHRITIS

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Background: Many patients with rheumatoid arthritis (RA) experience symptom relief of certain foods and earlier research has shown positive effects of food and food components on clinical outcomes of RA. Food components may potentiate each other in their effects on RA, but even so, studies combining foods and food components with probable effects on RA are scarce. Furthermore, comorbidities are common in RA and the risk of cardiovascular disease is elevated in this group. Assumed mechanisms include classical risk factors such as systemic inflammation, dyslipidemia as well as an unfavorable body composition.

Objectives: We investigated if a diet combining foods with anti-inflammatory effects, i.e. an anti-inflammatory portfolio diet, could reduce RA disease activity, markers of inflammation, body composition and blood lipid levels compared to a control diet.

Methods: In this controlled cross-over trial, 50 patients with RA were randomized to start with either intervention or control diet for ten weeks followed by a wash-out period of four months. The intervention diet was an anti-inflammatory portfolio diet containing foods rich in omega-3 fatty acids, fibers and probiotics. The control diet was a typical Swedish diet. Food equivalent to 50% of daily energy needs was delivered home weekly. For the remaining intake, participants were instructed to consume similar foods as the study diet regimen. Primary outcome measure was change in DAS28, using ESR. Secondary outcomes included changes in blood lipid levels, ESR and CRP as well as body composition.

Results: No significant difference in DAS28 between the groups was seen using Mixed Models analyze (p=0.116). However, DAS28 was significantly lower after the intervention diet compared to after control diet (p=0.04) and a significant reduction over time was seen in the intervention group (p=0.012) using Wilcoxon signed rank test. HDL-cholesterol was increased and TG were lowered after intervention compared to control, analyzed using Mixed Models (p=0.046 and p=0.006 respectively). In addition, there was a non-significant trend towards lowered LDL-cholesterol (p=0.077). Comparing after intervention to after control, there were non-significant lower weight, BMI and fat mass after the intervention (p=0.077, p=0.075 and p=0.058 respectively). None of the other outcomes changed significantly between groups.

Conclusion: This study showed positive effects on disease activity and blood lipid levels of a diet combining foods with anti-inflammatory properties, but the results must be confirmed in larger studies.

REFERENCES:

[1] Agca R, et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Annals of the rheumatic diseases. 2017;76(1):17-28.
[2] Piepoli MF, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). European heart journal. 2016;37(29):2315-81.
[3] Sköldstam L, et al. An experimental study of a Mediterranean diet intervention for patients with rheumatoid arthritis. Ann Rheum Dis. 2003;62(3):208-14.
[4] SLV. [Available from: https://www.livsmedelsverket.se/matvanor-halsa–miljo/kostrad-och- matvanor/matvanor—undersokningar/riksmaten-2010-11—vuxna.
[5] Tedeschi SK, et al. Diet and Rheumatoid Arthritis Symptoms: Survey Results From a Rheumatoid Arthritis Registry. Arthritis Care Res (Hoboken). 2017;69(12):1920-5.

Disclosure of Interests: Anna Vadell: None declared, Erik Hulander: None declared, Linnea Barebring: None declared, Inger Gjertsson: None declared, Helen Lindqvist Employee of: Yes, for Janssen-Cilag AB in 2001-2003, Before I was a phD-student and within a different field (dementia). My research field is within diet and Rheumatology., Anna Winkvist: None declared
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FRI0169 DOES INITIATING TOCILIZUMAB LEAD TO BETTER DISEASE CONTROL COMPARED TO INITIATING MTX WITH LOW-MODERATE DOSE PREDNISONE IN EARLY RHEUMATOID ARTHRITIS; AN INDIRECT COMPARISON OF U-ACT-EARLY AND CAMERA-II TREAT-TO-TARGET TRIALS

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Background: Treatment with methotrexate (MTX), often with concomitant glucocorticoids, is the cornerstone of early rheumatoid arthritis (RA) therapy. However, it may be less effective compared to (expensive) biological disease modifying anti-rheumatic drugs, such as tocilizumab (TCZ). Hitherto, the effectiveness and safety of MTX in combination with glucocorticoids have never been compared to TCZ with or without MTX.
Objectives: To compare effectiveness and safety of initiating TCZ, or TCZ with MTX (TCZ+MTX) to initiation of MTX with 10mg prednisone (MTX+Pred) all in a step-up treat-to-target treatment strategy in early RA patients.
Methods: Individual patient data of the U-Act-Early (*n=317*) and CAMERA-II (*n=236*) trials were used. Both were 2-year, double-blind, randomised, placebo-controlled studies evaluating step-up tight-control, treat-to-target treatment strategies with the opportunity to taper, in case of sustained remission, TCZ and/or MTX.[1,2] Using MTX (*n=108+119*) as the reference strategy, TCZ+MTX (*n=106*) and TCZ (*n=103*) were compared with MTX+Pred (*n=117*): primary outcome was the disease activity score (DAS28) over time. Secondary outcomes were remission, defined as DAS28<2.6, and the ConRew score (cumulative occurrence of remission and sustainment of remission). To assess the influence of acute phase reactants (APRs) on the results a disease activity outcome without APRs was also analysed (i.e. CDAI, modified due to lack of VAS physician in CAMERA-II). Multiple imputation was used for missing baseline data: HAQ, rheumatoid factor (RF) and smoking status. Multi-level models were used to account for clustering of patients within trials and for repeated measurements within patients over time. All models were corrected for baseline DAS28, HAQ, RF-status and smoking using fixed (and random) effects.
Results: Differences between U-Act-Early and CAMERA-II for RF seropositivity and DAS28 at baseline were observed; respectively 73% vs. 60% (p<0.01) and 5.2 vs. 5.7 (p=0.01). DAS28 was statistically significantly lower over time for TCZ+MTX compared to MTX+Pred (mean difference: -0.62 [95%CI -1.14 to -0.10]), but not for TCZ, Table 1. Remission occurred more often in TCZ+MTX and TCZ compared to MTX+Pred: relative risk 1.11 [95%CI 1.02 to 1.22] and 1.09 [1.00 to 1.20], respectively. ConRew scores were in line but not statistical significant different, Table 1. When using modified-CDAI, TCZ strategies did not show better control of disease activity over time than MTX+Pred (mean difference in log transformed values: TCZ+MTX vs. MTX+Pred: 0.10 [95%CI -0.16 to 0.36]; TCZ vs. MTX+Pred: 0.24 [95%CI -0.04 to 0.52]), Table 1. No differences in safety outcomes could be established, Table 2.

Table 1 Differences in effectiveness outcomes over 24 months between TCZ (U-Act-Early) and MTX+Pred (CAMERA-II) strategy arms.

	TCZ+MTX vs. MTX+Pred		TCZ vs. MTX+Pred	
Efficacy	**Mean difference (95% CI)**	**P-value**	**Mean difference (95% CI)**	**P-Value**
DAS28	-0.62 (-1.14 to -0.10)	0.02	-0.44 (-1.00 to 0.12)	0.08
ConRew	3.92 (-1.12 to 8.97)	0.14	4.73 (-0.41 to 9.88)	0.08
Modified CDAI*	0.10 (-0.16 to 0.36)	0.48	0.24 (-0.04 to 0.52)	0.09
	Relative Risk (95% CI)		**Relative Risk (95% CI)**	
Remission	1.11 (1.02 to 1.22)	0.01	1.09 (1.00 to 1.20)	0.05

*log transformed values. Multiplying the above regression coefficients by 100 leads to a difference on a modified percentage scale

Table 2 Differences in safety outcomes over 24 months between TCZ (U-Act-Early) and MTX+Pred (CAMERA-II) strategy arms.

	TCZ+MTX vs. MTX+Pred		TCZ vs. MTX+Pred	
Safety*	**Relative Risk (95% CI)**	**P-value**	**Relative Risk (95% CI)**	**P-value**
Elevated ALT	1.62 (0.66 to 3.97)	0.30	0.92 (0.33 to 2.53)	0.88
Elevated AST	1.48 (0.35 to 6.17)	0.60	0.55 (0.11 to 2.66)	0.48
Infections	0.99 (0.11 to 9.03)	1.00	1.05 (0.11 to 9.58)	0.96
Drop out due to AE	1.18 (0.39 to 3.63)	0.76	1.30 (0.43 to 3.90)	0.65

* occurrence of > 1 time

Conclusion: In early RA patients, TCZ-based strategies resulted in better DAS28 over time compared to MTX+Pred, as well as higher percentage of remission, part of these effects may be due to a specific effect of TCZ on APRs.

REFERENCES:

[1] Bijlsma JWJ, et al. Lancet. 2016;388:343-55.
[2] Bakker MF, et al. Ann Intern Med. 2012;156:329-339.

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FRI0170 PHYSICAL ACTIVITY LEVEL IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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Background: Rheumatoid arthritis (RA) is one of the most common inflammatory rheumatism characterized by an increased cardiovascular risk. Regarding the last EULAR recommendations, physical activity is an important part of the management of RA. The evaluation of Physical activity level is needed to know RA patients practices. However, to our knowledge, there is no consensual measure tool of the physical activity level for patients suffering RA.
Objectives: The aim of this study is to evaluate the different methods of measurement of physical activity levels in RA.
Methods: This is a systematic review of literature realized on the pubmed and Cochrane databases and meeting the PRISMA recommendations. We used the following key words: « physical activity », « physical activity level » AND « rheumatoid arthritis ». We included only article written in English language and with RA patients older than 18 years old.
Results: We identified 190 studies with the key words, 51 were selected on title and 23 articles have been identified as eligible. Finally, 19 studies were included in this review. In total, of the 19 selected studies, 13567 RA patients were evaluated on their level of physical activity. There were 73,4% female with a mean age of 56,1 years. In 10 studies, the BMI was available with results between 25 and 30 kg/m2. Two methods for measuring physical activity levels have been identified.

Questionnaires, a subjective tool, were used in 13 studies. It should be noted that 8 different questionnaires were used in these studies with recurrent use of the IPAQ (international validated questionnaire in general population) and SQUASH (validated in English language in RA). In these studies, patients were predominantly sedentary with a proportion of patients meeting WHO physical activity recommendations ranging from 20 to 77%. It appears that Scandinavian patients are clearly the most active.

Concerning objective measurement tools, 9 studies evaluated the level of physical activity using activity tracker. 7 studies used the accelerometer, 1 used the VO2 max, 1 used an actimeter. All studies showed a sedentary behavior. In these studies, the results were expressed as energy expenditure and not as a percentage of patients meeting WHO recommendations. Thus, the comparison between the two methods is difficult, but accelerometer showed a significant decrease in the level of physical activity in RA.

The oldest studies (2002 and 2007) showed that only 30% of patient met the WHO recommendations, but the recent studies (2017 and 2018) showed the same prevalence of sedentary behavior. The disease activity and the disease duration were comparable between the different studies.

Conclusion: Patients with rheumatoid arthritis present a sedentary behavior. Objective and subjective tools showed the low level of physical activity over the past decade. These data illustrate the necessity of the promotion of physical activity in rheumatoid arthritis.

Disclosure of Interests: None declared

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FRI0171 CLINICAL RESPONSES IN PATIENTS WITH INADEQUATE RESPONSE TO BDMARDS UPON TREATMENT WITH UPADACITINIB

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Background: Upadacitinib (UPA), a JAK1-selective inhibitor, demonstrated efficacy in the SELECT-BEYOND study in patients (pts) with moderate to severe rheumatoid arthritis (RA) on a stable dose of csDMARDs who had inadequate response (IR) or intolerance to bDMARDs,.

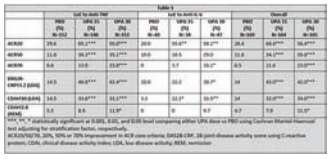
Objectives: In this analysis we evaluated clinical responses among pts receiving UPA and placebo (PBO) based on the number and mechanism of action (MOA) of prior bDMARDs.

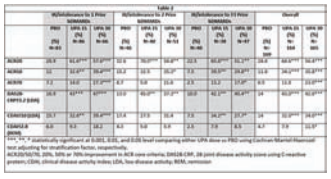
Methods: 498 pts were randomized to UPA 15mg or UPA 30mg once daily (QD) or PBO for 12 weeks (wks), after which pts on PBO received UPA 15 or 30mg QD from Wk 12 onwards.[1] Pts were subgrouped by the number and/or MOA of bDMARD(s) received prior to enrollment: 1) lack of efficacy (LoE) to $\geq$1 anti-TNF, 2) LoE to an anti-IL-6, and 3) the number of prior bDMARDs (1 vs 2 vs $\geq$3). ACR20/50/70 responses, DAS28-CRP low disease activity (LDA, ≤3.2), CDAI LDA (≤10), and CDAI remission (≤2.8) were evaluated at Wk 12. The frequency and percentage of treatment-emergent adverse events (TEAE) in each subgroup was assessed over the first 12 wks. Missing values of the efficacy endpoints were imputed using non-responder imputation (NRI). Nominal *P*-values are reported without multiplicity adjustment.

Results: Overall baseline disease duration was 13 years. The majority of pts had LoE to $\geq$1 anti-TNF (449, 90%); 88 (18%) had LoE to an anti-IL-6; 235 (47%), 137(28%), and 125 (25%) had been treated with 1, 2, or $\geq$3 prior bDMARDs, respectively.[1] At Wk 12, clinical responses were numerically, and often statistically, better for pts receiving either dose of UPA vs PBO, irrespective of their prior bDMARD exposure and the number of prior bDMARDs received. As most pts had LoE to $\geq$1 anti-TNF, responses in this group were comparable to the overall study population **(Table 1)**. Pts with LoE to an anti-IL-6 receiving UPA 15 or 30 mg QD experienced improvements vs PBO, particularly in achieving LDA and remission, although responses in these pts were generally lower compared to the overall study population. As expected, there was a trend towards lower responses as the number of prior bDMARDs increased **(Table 2).** Responses at Wk 24 were generally consistent with those at Wk 12 (data not shown). TEAEs across the subgroups were consistent with the overall study population (data not shown).

Conclusion: At Wk 12, treatment with UPA at either 15 or 30 mg QD led to significantly better clinical responses vs PBO in this treatment-refractory population, including in pts with LoE to an anti-TNF or an anti-IL-6, and those who had IR/intolerance to 1, 2 or $\geq$3 prior bDMARDs, with consistent safety profiles as to the overall study population.

Acknowledgement: AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barretto, PhD, of AbbVie, Inc.





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FRI0172 A PROSPECTIVE AUDIT OF A PATIENT COHORT PRESCRIBED HYDROXYCHLOROQUINE FOR RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY RHEUMATIC DISEASES IN ORDER TO PRIORITISE RETINOPATHY SCREENING AND ESTIMATE THE NEED FOR DRUG EDUCATION APPOINTMENTS

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Background: Hydroxychloroquine (HCQ) is prescribed for rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and inflammatory osteoarthritis (IOA). A potential side effect of HCQ is drug-induced retinopathy, with an increased risk reported for patients taking >5mg/kg/day and those who have renal impairment.

In the United Kingdom, the Royal College of Ophthalmologists (RCO) has published new screening guidelines for HCQ, recommending 1) patients receive doses <5mg/kg/day and 2) all patients planning to be on HCQ long term ($\geq$5 years) should receive baseline eye examination ideally within 6 months of starting HCQ and definitely within 1 year.

Objectives: This audit aimed to: 1) audit dose prescription by body weight, 2) estimate the screening burden on ophthalmology services, 3) estimate service needs for additional drug education appointments to counsel patients starting HCQ.

Methods: A list of all patients who were started on HCQ from January 2017 to February 2018 was obtained from the outpatient pharmacy at Salford Royal Hospital. Demographic and clinical data were extracted from electronic patient records. High-risk patients were defined as those who were prescribed an initial dose of >5mg/kg/day or those with an eGFR ≤50 ml/min/1.73m^2. Patients were followed until the most recent follow-up visit by July 2018 to determine drug persistence and reasons for HCQ cessation, if any.

Results: 177 patients were started on HCQ, with most (62%) diagnosed with rheumatoid arthritis (Table). Most patients were female (76%) and a third (35%) were older than 60 years old. 9 patients (5.1%) had impaired renal function. 83 patients (47%) were prescribed an initial daily dose of HCQ >5mg/kg/day. By July 2018 (follow-up duration 6-19 months), 127 patients (71.8%) remained on HCQ and will need baseline eye screening.

The remaining 50 patients (28.2%) stopped HCQ due to inefficacy (7.3%), GI disturbance (3.4%), rash (3.4%).

Table:

Patients prescribed hydroxychloroquine (HCQ) from Jan 2017 to Feb 2018	All indications N=177	Rheumatoid arthritis N=110	Connective tissue disease N=46	Inflammatory osteoarthritis N=21
Median age (interquartile range); years	54 (44-64)	55 (43-66)	54 (38-61)	57 (52-61)
Age >60 years; n (%)	61 (34.5)	42 (38.2)	13 (28.3)	6 (28.6)
Females; n (%)	134 (75.7)	74 (67.3)	41 (89.1)	19 (90.5)
eGFR ≤50; n (%)	9 (5.1)	4 (3.7)	3 (6.5)	2 (9.5)
Mean height (cm)	165	166	162	164
Mean weight (kg)	77	77	73	84
Mean BMI	29	29	27	32
Dose > 5mg/kg/day absolute body weight; n (%)	83 (46.9)	54 (49.1)	23 (50.0)	6 (28.6)
Proportion of patients still on HCQ by July 2018; n (%)	127 (71.8)	85 (77.3)	33 (71.7)	9 (42.8)
Reason for HCQ cessation; n (%)	G: 6 (3.4)	G: 3 (2.7)	G: 1 (2.2)	G: 2 (9.5)
-GI side effects (G)	R: 6 (3.4)	R: 4 (3.6)	R: 2 (4.4)	R: 0 (0)
-Rash (R)	I: 13 (7.3)	I: 6 (5.5)	I: 3 (6.6)	I: 4 (19.0)
-Ineffective (I)	O: 22	O: 10 (9.1)	O: 6 (13.0)	O: 6 (28.6)
-Other (O)	(12.4)	D: 2 (1.8)	D: 1 (2.1)	D: 0 (0)
-Death (D)	D: 3 (1.7)			

Conclusion: Clinicians need to be cognisant of recent guidelines and adjust HCQ dosing to the recommended 5mg/kg/day. Additional specialist pharmacist input for DED (12-13 extra appointments per month) is required. Almost a third of the patients had stopped HCQ by July 2018, mostly due to side effects and reported inefficacy. However, a large proportion (71%) of HCQ starters remain on the drug by 6-12 months and will need baseline screening. Ophthalmology services can estimate services and capacity required for baseline HCQ screening per annum.

REFERENCE:

[1] Royal College of Ophthalmology Guideline: Hydroxychloroquine and Chloroquine Retinopathy Screening 2018

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Disclosure of Interests: None declared
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SLE, Sjögren's and APS – treatment

FRI0173 HOW WELL DO CLINICAL TRIALS REPRESENT REAL WORLD LUPUS NEPHRITIS PATIENTS?

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Background: Lupus nephritis (LN) represents a serious manifestation of systemic lupus erythematosus (SLE). LN therapies include glucocorticoids and conventional immunosuppressants as standard of care (SOC) or biological therapies. Rituximab (RTX) is used in some patients but published clinical trials have failed to meet their primary end-points. SLE trials have limitations including stringent eligibility criteria in an attempt to achieve homogeneity, however poor recruitment can lead to early termination as such, clinical trials may not reflect the disease population of interest and outcomes can be difficult to generalise.
Objectives: Our aim was to apply published trial eligibility criteria to patients with LN in a large UK-wide register to quantify how accurately LN clinical trials represent a real-world cohort.
Methods: A literature review of recent major published LN clinical trials was performed (n=6). Inclusion and exclusion criteria common across trials were applied to all patients registered in the BILAG-Biologics Register (BILAG-BR) with active LN, a UK-wide registry of patients with SLE. Active LN was defined as a renal BILAG score A or B. We applied available data to inclusion criteria including ACR/SLICC criteria for SLE diagnosis, positive dsDNA or ANA antibodies and a UPCR>100mg/mmol. Available exclusion criteria were active CNS lupus, a history of hepatitis, malignancy or CKD 4/5, hypogammaglobulinaemia, and cyclophosphamide use within 30 days of entry or previous B cell therapy within 12 months of entry.
Results: As of July 2018, 259/897 (28.9%) patients in BILAG-BR had active LN. In the RTX and SOC groups, 70/230 (30.4%) and 10/29 (34.5%) respectively did not meet all inclusion criteria (Table 1). Meanwhile 118/230 (51.3%) of RTX patients and 6/29 (20.7%) of SOC patients met one or more exclusion criteria. Overall 131/259 (50.6%) did not satisfy all inclusion and exclusion criteria and thus were ineligible for clinical trial entry. Of those patients deemed ineligible, the RTX patients were younger (median age 36 vs. 49 in SOC group, p=0.653) and the majority were non-Caucasian (n=71/121 (58.7%), p=0.251). The majority of patients in both treatment groups were female (p=0.089). UPCR <100mg/mol (n=35) was the most common inclusion criteria missed whilst the commonest exclusion criteria were concomitant active CNS disease (n=22) and hypogammaglobulinaemia (n=24).

Inclusion criteria	**RTX**	**SOC**	**p**
Does not meet ACR/SLICC criteria for SLE	5	0	0.423
Negative dsDNA/ANA	30	4	0.910
UPCR ≤ 100mg/mmol	35	6	0.743
Total *(n)*	70	10	
Exclusion criteria	**RTX**	**SOC**	**p**
Active CNS lupus (BILAG A/B)	22	2	0.936
H/o hepatitis B or C	8	0	0.668
CKD 4 or 5	20	2	0.743
H/o malignancy	18	0	0.213
Cyclophosphamide <90 days before entry	13	0	0.189
B cell therapy <1 year before entry	14	0	0.172
Hypogammaglobulinaemia <6 (IgG)	24	2	0.550
Total *(n)*	118	6	
Total **NOT*** eligible for clinical trial *(n)*	**131 (50.6%)**		0.066

Conclusion: In a large national cohort of active LN we found that 50.6% of patients would not be eligible for clinical trial entry using published entry criteria. This poses significant implications on the study of LN treatment in patients with more severe disease. When designing clinical trials, the stringency of eligibility criteria should be reviewed in order to provide greater representation of the target disease population.
British Isles Lupus Assessment Group Biologics Register

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FRI0174 SUBCUTANEOUS DOSING OF THE NOVEL ANTI-CD40 ANTIBODY ISCALIMAB ACHIEVES TARGET DRUG EXPOSURE AND CLINICAL EFFICACY IN PRIMARY SJÖGREN'S SYNDROME; RESULTS OF A PHASE IIA RANDOMISED OPEN LABEL TWO ARM PARALLEL GROUP TRIAL

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Background: Primary Sjögren's syndrome (pSS) is a systemic progressive autoimmune disease characterised by formation of lymphoid structures and germinal centres within glandular tissue. Iscalimab (CFZ533) is a novel monoclonal antibody that potently and selectively blocks CD40, a co-stimulatory pathway receptor important for germinal centre reactions

and B cell activation. Iscalimab showed clinical efficacy in a Proof of Concept randomised controlled trial at a dose of 10 mg/kg intravenously (IV), whereas subcutaneous (SC) dosing at 3 mg/kg was associated with unexpectedly low plasma concentrations and reduced efficacy, likely due to efficient pre-systemic target-mediated clearance.

Objectives: To test IV versus SC loading doses of iscalimab followed by SC maintenance dosing, as a means of achieving target drug exposure and clinical efficacy.

Methods: Patients with clinically active pSS [EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) $\geq$6] were randomised to receive either 600 mg SC iscalimab weekly on 4 occasions, followed by 300 mg SC weekly until week 12, or a single IV dose of 10 mg/kg iscalimab on study Day 1, followed by 300 mg SC weekly until week 12. Subjects and investigator staff remained blinded to study treatment allocation until first dosing.

Results: Twenty-five patients were randomised; 13 in the SC loading and 12 in the IV loading arms. Baseline characteristics were similar to the previous phase IIa cohorts with mean ESSDAI scores of 12.7 (SD 6.1) and 10.4 (5.9) in the SC and IV loading arms respectively. In Arm 1 (SC) and Arm 2 (IV), the mean trough plasma concentrations were 169 µg/mL (SD 64.1, CV 38%) and 135 µg/mL (SD 70.9, CV 53%) on Day 85, respectively. Both values were well above levels previously reported to be sufficient for suppression of germinal centre development and T dependent antigen responses in cynomolgus monkeys. Consistent with this finding, clinically important improvements were seen in both arms with a mean decrease in ESSDAI scores of -5.5 (+/- SD: 5.5) and -7.6 (+/- 7.1) points from baseline to Day 85 in the SC and IV dosing arms. Improvements were also seen in EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) scores: -1.67 (+/- 1.8) and -1.17 (+/- 2.3), respectively. Other secondary efficacy outcomes showed similar patterns of improvement. Treatment with iscalimab was associated with a reduction in the germinal centre-related serum biomarker CXCL13 in both groups. Overall, iscalimab was safe and well-tolerated with no new safety signal emerging. One subject experienced three SAEs (hemarthrosis, worsening of right knee pain and swelling requiring arthroscopy) in the safety follow-up period, all unrelated to study drug.

Conclusion: These results further support the safety and efficacy of iscalimab in pSS and the suitability of SC dosing for future development.

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UCB Pharma (to University of Birmingham) and Roche, Consultant for: 2016-7: Novartis, Mitsubishi Tanabe Pharma
2017-8: AstraZeneca, MedImmune, GFK, Xtlbio, ONO Pharmaceutical
2018-9: Novartis, AstraZeneca, UCB Pharma, Pascal Espie Employee of: Novartis, Grazyna Wieczorek Employee of: Novartis, Pierre Moulin Employee of: Novartis, David Floch Employee of: Novartis, Cyrielle Dupuy Employee of: Novartis, Amanda Nguyen Employee of: Novartis, Andrew Wright Shareholder of: Novartis, Employee of: Novartis, Michael Rotte Employee of: Novartis, James Rush Employee of: Novartis, Peter Gergely Employee of: Novartis

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FRI0175 PREDICTORS OF LOW DISEASE ACTIVITY AND CLINICAL REMISSION FOLLOWING BELIMUMAB TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Post-hoc analyses of the pivotal phase III clinical trials of belimumab BLISS-52 and BLISS-76 have revealed superiority of belimumab over placebo in systemic lupus erythematsus (SLE) patients with high baseline disease activity, positive anti-double stranded (ds)DNA titres and low complement levels, as well as in patients receiving corticosteroids (1). Later, real-life observations demonstrated that established organ damage prior to treatment initiation predicted reduced belimumab efficacy based on the SLE Responder Index 4 (SRI-4) (2), which was recently corroborated in a post-hoc analysis of data from the BLISS trials (3). From a clinical point of view, clinical remission and low disease activity are more meaningful targets than reduced SLE activity (SRI-4).

Objectives: To identify predictors of low disease activity and clinical remission following belimumab treatment in patients with SLE.

Methods: SLE patients who received belimumab 10 mg/kg (N=563) in the BLISS-52 and BLISS-76 clinical trials were surveyed. Access to data was granted by GlaxoSmithKline. The performance of baseline factors in predicting attainment of low disease activity defined as Lupus Low Disease Activity State (LLDAS) (4) or clinical remission defined as clinical (c)SLEDAI-2K=0 at week 52 from treatment initiation was evaluated using logistic regression. Organ damage was assessed using the SLICC/ACR Damage Index (SDI).

Results: We demonstrated a negative impact of established organ damage on attainment of LLDAS (SDI>0; OR: 0.44; 95% CI: 0.22–0.90; P=0.024) and the primary LLDAS condition, i.e. SLEDAI-2K≤4 with no renal activity, pleurisy, pericarditis or fever (SDI>1; OR: 0.46; 95% CI: 0.27–0.77; P=0.004); cognitive impairment/psychosis was found to mainly account for the latter association. Baseline SDI scores>1 predicted failure to attain cSLEDAI-2K=0 (OR: 0.53; 95% CI: 0.30–0.94; P=0.030), with cutaneous damage mainly driving this association. Anti-dsDNA positivity increased (OR: 1.82; 95% CI: 1.08–3.06; P=0.025) and cardiovascular damage reduced (OR: 0.13; 95% CI: 0.02–0.97; P=0.047) the probability to attain cSLEDAI-2K=0 with the daily prednisone equivalent intake restricted to ≤7.5 mg.

Conclusion: Belimumab might be expected to be more efficacious in inducing low disease activity and clinical remission in SLE patients with limited or no organ damage accrued prior to treatment initiation. Patients with positive anti-dsDNA titers might be more likely to achieve clinical remission along with limited or no corticosteroid use. The findings contribute to a better selection of SLE patients expected to benefit from belimumab, and provide useful information towards refinement of SLE treatment recommendations.

REFERENCES:

[1] van Vollenhoven RF, Petri MA, Cervera R, et al. Ann Rheum Dis 2012.
[2] Parodis I, Sjowall C, Jonsen A, et al. Autoimmun Rev 2017.
[3] Parodis I, Gomez A, Emamikia S, et al. Ann Rheum Dis 2019.
[4] Franklyn K, Lau CS, Navarra SV, et al. Ann Rheum Dis 2016.

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FRI0176 PHASE 2, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY OF A REVERSIBLE B CELL INHIBITOR, XMAB®5871, IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: XmAb5871 is a humanized anti-CD19 antibody Fc-engineered for increased affinity to FcγRIIb. Co-ligation of CD19 and FcγRIIb inhibits B lineage cells key to SLE pathogenesis.

Objectives: This Phase 2 study was designed to minimize background medications and placebo responses to improve interpretation of a small trial in a complex, heterogenous disease.
Methods: SLE patients were enrolled with active disease, ameliorated during screening with ≥160 mg of IM Depo-Medrol. Improvement was required before randomization, defined by decrease in SLEDAI ≥4 points or ≥1 grade in a BILAG A or B score. Immunosuppressive drugs were stopped except antimalarials and/or ≤10 mg/day prednisone or equivalent. Subjects were randomized to IV XmAb5871 (5 mg/kg) or placebo and given Depo-Medrol 80 mg IM on Days 1 and 15, after which, steroid impact was expected to withdraw gradually. Study treatments were given Q14 days for up to 16 doses or ***loss of improvement*** **(LOI),** defined as SLEDAI increase ≥4 points OR new BILAG A or B, with investigator-determined significance. At LOI, patients could receive immediate standard treatments. The primary endpoint was the proportion with no LOI by Day 225 in the efficacy evaluable group (those completing Day 225 or withdrawn for LOI or drug-related adverse event).
Results: 104 subjects were randomized: 99 female, median age 45 (20-65). The primary endpoint was met by 21 (42%) of XmAb5871-treated patients vs 12 (28.6%) of the placebo group (p=0.18). All but one responder also fulfilled the SRI-4 response definition from screening to completion. Results did not differ in those with or without anti-dsDNA and/or ENA antibodies. Time to flare was significantly longer in the XmAb5871 group (p=0.025) **(figure 1)**. XmAb5871-treated patients with LOI had less recurrent disease after IM steroid cessation than those in the placebo group; 6 (20%) of placebo patients developed BILAG A scores vs 3 (13%) in the active arm. 9 (30%) of worsening placebo patients had SLEDAI increase ≥7 vs 0 in the XmAb5871 group. SLEDAI scores were higher and increased sooner after disease nadir with placebo vs XmAb5871 **(figure 2)**; 16 (30.8%) of XmAb5871 patients vs 7 (13.5%) placebo patients sustained LLDAS (low disease) during months 6-8 (p=0.0453). Transient, infusion-related gastrointestinal side effects occurred in XmAb5871-treated patients during the 1st or 2nd infusion. There were 8 SAEs in 7 XmAb5871-treated subjects, 5 in 4 placebo patients, no opportunistic infections, and no deaths. Infection rate was low compared to other SLE trials.
Conclusion: XmAb5871 was well-tolerated. Preliminary data from this small trial indicates suppression of disease recurrence after treatment withdrawal, supporting further evaluation of XmAb5871 in SLE.

Fig 1: Efficacy Evaluable Subjects: Time to Loss of Improvement
Kaplan-Meier probability plot (HR=0.53; Log-Rank p=0.025)

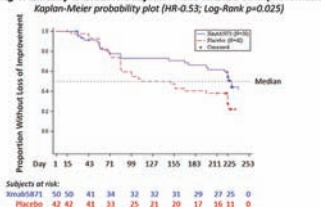
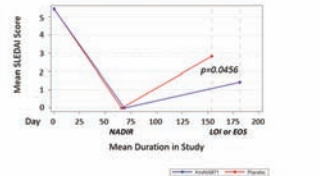


Fig 2: Change in SLEDAI From Disease NADIR to End of Study
Mean difference (95% CI) at last visit 1.404 (0.315, 2.493)



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FRI0177

THE ADDITIVE EFFECTS OF HYDROXYCHLOROQUINE TO MAINTENANCE THERAPY WITH STANDARD OF CARE IN PATIENTS WITH SYSTEMIC LUPUS: ERYTHEMATOSUS

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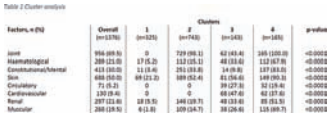
Background: Antimalarial agents such as hydroxychloroquine (HCQ) have long been used as effective therapies for skin and joint symptoms, as well as for the malaise associated with cutaneous lupus erythematosus and systemic lupus erythematosus (SLE). Furthermore, based on the various benefits demonstrated with these agents, the use of antimalarial agents was recently recommended for all patients with SLE. Whereas HCQ has been generally given to most of patients from the beginning of the treatment during the remission-induction therapy in multiple studies, its effects on maintenance therapy have not been sufficiently supported by evidence.
Objectives: We evaluated the additive effects of HCQ in maintenance therapy with standard of care (SoC) in 101 patients with SLE for 1 year.
Methods: The study included 101 patients diagnosed with SLE, whose course was followed for 1 year at our hospital and affiliated institutions. All patients were receiving maintenance therapy based on the SoC. The primary endpoint was the changes in the SLEDAI. The secondary endpoints were the proportion of emergence of new BILAG A or B organ domain score, and changes in anti-ds DNA Ab titre (U/mL), and serum complement activity (CH50, U/mL) up to year 1, as well as the CS-sparing effect. For these endpoints, the SoC+HCQ group (n = 42) was compared with the SoC group (n = 59) of patients matched for baseline characteristics. The Human Ethics Review Committee of our university reviewed and approved this study.
Results: In the SoC+HCQ group, the mean age was 42.2 years, and there were 3 male and 39 female. The mean disease duration was 157.9 months. In the SoC group, the mean age was 43.5 years, and there were 6 male and 53 female. The mean disease duration was 118.9 months. At baseline, no statistically significant differences between the two groups were observed in any baseline characteristics. The SLEDAI improved from 3.07 to 2.28 in the SoC+HCQ group, but significantly deteriorated from 2.73 to 4.8 in the SoC group. The CH50 levels, anti-dsDNA antibody titre, and concomitant CS dose were not significantly changed. The increase in the SLEDAI and concomitant CS dose after 1 year were all significantly greater in the SoC group, and the proportion of patients with SLEDAI flare was significantly lower in the SoC+HCQ group (4.76% vs 25.4%) (SLEDAI flare was defined as an increase of at least four points in the SLEDAI). Regarding the BILAG organ domain, there were no significant differences. SLEDAI flare were observed in 17 patients. When baseline characteristics were compared between patients with and without SLEDAI flare, HCQ was significantly more frequently used in patients without SLEDAI flare. In addition, univariate and multivariate logistic regression analyses were performed to identify the predictive factors for no SLEDAI flare. The univariate logistic analysis identified HCQ use, and immunosuppressant use with a P value of <0.3. Subsequently, multivariate logistic analysis was performed with these factors as dependent variables and identified the presence or absence of HCQ use as a predictive factor (P = 0.0041, odds ratio 6.66, 95% confidence interval 1.73–44.1). The retention rate of HCQ was 90.5%.
Conclusion: The comparison between the SoC+HCQ and SoC groups revealed that the addition of HCQ to maintenance therapy with low-dose CS for SLE is safe, and that HCQ was effective, not only for the suppression of disease activity based on the SLEDAI, but also for the prevention of the exacerbation of disease activity. Thus, the present study revealed that HCQ may be a useful mainstay for maintenance therapy based on SoC in patients with SLE.
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FRI0178 CLUSTER PROFILING OF PATIENTS IN A REAL-WORLD DATA SET WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND THEIR ASSOCIATED TREATMENTS

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Background: Previous systemic lupus erythematosus (SLE) studies have identified potential clusters of SLE clinical manifestations.
Objectives: To describe the presentation of SLE across different cohorts of patients and describe standard of care within clusters.
Methods: Cross-sectional study of 263 rheumatologists in the US and EU5. Data were collected from the Adelphi Real World 2015 Lupus Disease Specific Programme. Physicians completed patient record forms (PRFs) for the next 5 patients consulting with SLE; these patients completed patient self-completion (PSC) forms describing how SLE affected them. PRFs data include patient's characteristics and management history. PSCs focused on similar data collection, including patient reported outcome measures on the humanistic burden. Principal-component factor analysis reduced 39 unique SLE symptoms to 8 factors. These factors were used as covariates in latent class cluster analysis to provide discrete cohorts of patients. Chi-squared and Kruskal-Wallis tests compared patient outcomes across clusters.
Results: Data were extracted from 1376 PRFs. Factor analysis resulted in 8 clusters of concurrent symptoms; joint, haematological, constitutional/mental health, skin, circulatory, cardiovascular, renal, and muscular symptoms respectively. The four-cluster solution was selected.
Cluster 1 displayed the lowest symptom burden, characterised by low skin involvement. Cluster 2 is characterised by joint and skin involvement. Cluster 3 & 4 had a high frequency of all factors, with cardiovascular involvement high in cluster 3 and renal/constitutional involvement high in cluster 4 (table 1).
Significant between-cluster differences were observed when comparing clinical and humanistic outcomes; physician/patient satisfaction were greatest in cluster 1 (physician satisfied 94.2% vs. 2: 90.8%, 3: 85.2%, 4: 74.4%, p<0.0001; patient 94.7% vs. 2: 93.9%, 3: 91.5%, 4: 79.2%, p<0.0001), whilst disease progression (deteriorating slowly 2.5% vs. 2: 12.9%, 3: 9.8%, 4: 25.5%, p<0.0001) and flaring in the last 12 months (flared 30.0% vs. 2: 54.8%, 3: 62.2%, 4: 70.8%, p<0.0001) differed significantly with worst outcomes seen in cluster 4.
Significant differences were also observed between clusters in relation to treatment proportions; anti-malarials (highest cluster 1: 70.5%), biologic DMARD (highest cluster 3: 17.5%), glucocorticoid and immunosuppressants (highest cluster 4: 85.5%, 74.5%).
Conclusion: This study adds to the evidence demonstrating the heterogenous nature of SLE experienced within distinct patient clusters. Significant proportions of SLE patients experience high symptom burden and low levels of satisfaction. Additional analysis to understand limited biologic use in more severe patients is needed.



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FRI0179 PREDICTION OF RESPONSE TO RITUXIMAB IN SLE USING A VALIDATED TWO-SCORE SYSTEM FOR INTERFERON

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Background: Rituximab (RTX) is used for resistant SLE but clinical response varies. We previously validated two interferon-stimulated gene expression scores (IFN-Score-A and IFN-Score-B) that improved prediction of clinical outcomes in SLE. IFN-Score-A included most commonly reported ISGs and predicted flares and glucocorticoid requirements. IFN-Score-B included ISGs that respond to multiple IFN subtypes and predicted development of SLE in At-Risk individuals. Diagnosis of SLE was associated with both scores, while only IFN-Score-B was elevated in RA. The British Society for Rheumatology Biologics Registry (BILAG-BR) collects samples for RTX-treated patients in the UK. MASTERPLANS is a consortium to identify predictors of drug response.
Objectives: To investigate whether IFN-Score-A and IFN-Score-B predict BILAG response to RTX at 6 months.
Methods: This is a preliminary analysis of the first RTX-treated patients in the BILAG-BR with complete data. Patients were recruited if they were starting a first cycle of RTX for active SLE (BILAG A or 2xBILAG B) despite previous cyclophosphamide or mycophenolate mofetil. Disease activity was measured using BILAG-2004. Clinical response was defined as improvement by >=1 grade in active BILAG-2004 systems with no worsening in other systems. Whole blood was collected into TEMPUS tubes and RNA extracted. IFN-Scores were measured using a custom Taqman array as previously described [El Sherbiny et al., 2018]. Multivariate logistic regression was used to test IFN-Scores and baseline clinical covariates as predictors of BILAG response at 6 months.
Results: Samples were available from 147 patients, of whom 84 had complete baseline and 6 month clinical data available and were included in this analysis. 40/84 (47.6%) patients had BILAG response at 6 months. In univariate and multivariate analysis, high IFN-Score-B expression was significantly associated with clinical response (see table 1).

Predictor	Non-responders	Responders	Univariable OR (95% CI)	P	Multivariable OR (95% CI)	P
Age (mean, 95% CI)	40.5 (36.2,44.8)	40.9 (36.2,45.6)	1.015 (0.993,1.037)	0.188	0.994 (0.959,1.032)	0.765
Baseline organs affected	22/44	23/40	0.866 (0.468,1.601)	0.645	1.024 (0.381,2.750)	0.962
Mucocutaneous						
Musculoskeletal	21/44	18/40	0.728 (0.392,1.354)	0.728	0.424 (0.145,1.244)	0.118
Renal	21/44	16/40	0.869 (0.470,1.607)	0.654	0.290 (0.087,0.969)	0.044
Cardiovascular	9/44	5/40	1.250 (0.553,2.824)	0.591	0.627 (0.164,2.391)	0.494
Neurological	7/44	6/40	0.859 (0.358,2.065)	0.735	0.768 (0.170,3.473)	0.731
Antimalarial=Yes	41/44	39/40	1.458 (0.410,5.186)	0.560	0.073 (0.005,1.005)	0.050
IFN-Score-A (per unit)	2.49 (1.77,3.19)	1.74 (1.10,2.39)	0.845 (0.682,1.048)	0.126	1.601 (0.935,2.743)	0.086
IFN-Score-B (per unit)	2.36 (1.98,2.73)	1.76 (1.43,2.09)	0.606 (0.394,0.933)	0.023	0.267 (0.093,0.762)	0.014

Conclusion: This preliminary analysis suggests that assessment of IFN activity has a role in predicting response to RTX. A novel IFN score (Score B) was more predictive than classic ISGs (Score A). These results add to a body of work showing that IFN-Score-B predicts clinically significant outcomes independently of overall IFN activity. Future work will analyse this biomarker in a larger cohort of patients and integrate with other putative clinical and biological predictors of response.

REFERENCE:

[1] El-Sherbiny, Y. M.… E. M. Vital (2018). Sci. Rep. 8: 5793.

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FRI0180 OFF-LABEL USE OF RITUXIMAB IN RHEUMATIC DISEASES, A SWISS TERTIARY CENTRE EXPERIENCE

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Background: Rituximab (RTX), a monoclonal antibody targeting CD20, is licenced for the treatment of rheumatoid arthritis (RA) for many years and more recently for ANCA-associated vasculitis. RTX is frequently used off-label to treat other auto-immune diseases (AID), especially connective tissue diseases (CTD). There are no published data about off-label use of RTX in AID in Switzerland.

Objectives: To describe off-label use of RTX in a real-life setting, when treating AID.

Methods: Retrospective cohort study of all patients treated with RTX in the Rheumatology Department between 2005 and 2017. Clinical efficacy of RTX after 12 and 24 months of treatment was evaluated with a semi-quantitative scale (no response (NR), partial (PR) and complete response (CR)). RTX discontinuation rate was also analysed using Kaplan-Meier method and log rank test to evaluate the difference between survival curves. Adverse events (AE), serious AE (SAE) were included in the safety analysis. Occurrences of hypogammaglobulinemia and anti-rituximab antibodies (ADA) were also reported.

Results: 178 patients treated with RTX could be identified: 28% for CTD, 63% for RA and 10% for other AID.

Rituximab was used off-label in 73% of the patients according to official Swiss indications. No significant differences in terms of clinical response were observed in off-label indication after 12 months (NR: 15%/13%, PR:48%/52%, CR:37%/35%, n=108/31) and 24 months (NR:13%/9%, PR:37%/35%, CR:51%/57%, n=79/23) of treatment when compared with prescriptions following official Swiss indications, respectively. RTX discontinuation rate (HR 1.03 95% CI 0.71-1.49) was also similar between both groups.

Clinical response after RTX treatment did not differ significantly between patients with CTD and RA after 12 months (NR:10%/12%, PR:50%/52%, CR:40%/36%, n=42/n=84) and 24 months (NR:7%/9%, PR:32%/44%, CR:61%/47%, n=28/n=64), respectively. Detailed results are available in Table 1. Survival curves of rituximab treatment from CTD group closely matched that from RA group (HR 0.96 95% CI 0.65-1.44). Causes of RTX treatment discontinuation in patients with CTD (n=27) and RA (n=72) consisted of lack of efficiency (63%/56%), adverse event (19%/35%) and remission (19%/10%), respectively.

SAE (n=113) occurred in 33% of the patients and consisted mainly of infectious SAE (43%) and perfusion-related AE (6%). 6 patients died during RTX treatment. Low IgG levels were observed in 34% (50/149) of the patients graded as mild (20%), moderate (11%) or severe (3%). The nadir of IgG levels occurred after 4.5(3.5) years (mean (SD)) of RTX treatment. ADA were observed in 6/51 patients.

Conclusion: Off-label prescription of rituximab to treat AID was frequent. RTX discontinuation rate was comparable in patients treated for CTD and RA in our population.

Table 1

	Off-label prescription*	Partial or complete response after 12 months of RTX treatment	Partial or complete response after 24 months of RTX treatment	Rituximab discontinuation rate (95% CI), all causes, at :		
	n (%)	n=139 (%)	n=102 (%)	1 year	2 years	4 years
Connective tissue disease (n=49)	49/49 (100)	38/42 (90)	26/28 (93)	0.23 (0.13-0.37)	0.40 (0.27-0.55)	0.56 (0.42-0.71)
Overlap syndrome (n=14)		12/12 (100)	9/9 (100)			
Systemic lupus erythematosus (n=12)		8/10 (80)	7/8 (88)			
UCTD (n=8)		4/6 (67)	2/2 (100)			
Sjögren's syndrome (n=6)		6/6 (100)	4/4 (100)			
Dermato-, polymyositis (n=5)		5/5 (100)	2/3 (67)			
MCTD (n=3)		2/2 (100)	1/1 (100)			
Systemic sclerosis (n=1)		1/1 (100)	1/1 (100)			
Rheumatoid arthritis (n=112)	66/112 (59)	74/84 (88)	58/64 (91)	0.27 (0.20-0.36)	0.35 (0.27-0.44)	0.55 (0.46-0.65)
Other auto-immune diseases (n=17)	15/17 (88)	7/13(54)	6/10 (60)	0.35 (0.18-0.62)	0.76 (0.55-0.93)	-

RTX: rituximab; AE: adverse event, MCTD: Mixed connective tissue disease; UCTD: Undifferentiated connective tissue disease.
*off-label prescription according to Swiss Agency for Therapeutic Products (Swissmedic)

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FRI0181 THE PLUTO STUDY: INTRAVENOUS BELIMUMAB IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Belimumab (BEL), a monoclonal antibody targeting the B-lymphocyte stimulator, is approved in adults with active systemic lupus erythematosus (SLE). This is the first clinical trial of belimumab in pediatric patients with childhood-onset SLE (cSLE).

Objectives: PLUTO, a Phase 2, randomised, double-blind trial (BEL114055; NCT01649765), evaluated the efficacy, safety and pharmacokinetics (PK) of intravenous (IV) BEL vs placebo (PBO), plus standard of care (SoC), in cSLE.

Methods: Patients with cSLE 5–17 years of age were randomised to BEL 10 mg/kg IV or PBO every 4 weeks, plus SoC. Primary endpoint: SRI4 at Week 52. Major secondary endpoints: PRINTO/ACR 30 and 50 cSLE evaluation criteria for improvement at Week 52; cSLE core response variables at Week 52; and sustained SRI4 and ParentGA (patient well-being) responses (Weeks 44–52). Other endpoints: components of SRI4 at Week 52; and frequency of severe flares using the

modified SELENA-SLEDAI Flare Index. Safety and PK were assessed. Analyses were performed on the intent-to-treat population. The study was not powered to test for differences between groups; p-values were not calculated.

Results: 93 patients were included (BEL, n=53; PBO, n=40). Groups (BEL vs PBO) were balanced at baseline for age (mean [standard deviation] 13.5 [2.59] vs 14.8 [2.17] years, respectively) and SELENA-SLEDAI score (10.3 [3.34] vs 10.4 [3.63], respectively). Compared with PBO, there were more SRI4 responders (including all 3 components of SRI4), and PRINTO/ACR 30 and 50 responders in the BEL group (**Figure**). Likewise, more BEL than PBO recipients had sustained improvement of SRI and patient well-being (ParentGA) (**Figure**). Changes in cSLE core response variables are shown in the **Table**. Severe flares were 62% less frequent with BEL vs PBO (hazard ratio 0.38 [95% CI 0.18, 0.82]). PK: BEL exposures in cSLE were similar to adult SLE studies. 9/53 (17%) BEL patients had $\geq$1 serious adverse event vs 14/40 (35%) PBO patients. One PBO patient died of acute pancreatitis.

Conclusion: The benefit:risk profile of BEL IV plus SoC in cSLE is generally consistent with BEL in adult SLE. The 10 mg/kg IV dose used in adults may be an appropriate dose in cSLE.

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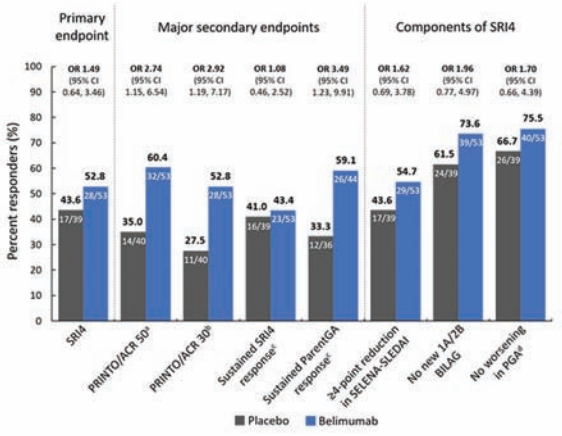
Disclosure of Interests: Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Carlos Abud-Mendoza: None declared, Diego O Viola: None declared, Inmaculada Calvo Grant/research support from: received research grants from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK, Consultant for: Advisory boards: Novartis, AbbVie, Speakers bureau: AbbVie, Roche, Novartis, SOBI, Deborah M Levy Consultant for: received consulting fees and/or honoraria from AbbVie and Janssen, Julia Calderon Gallegos: None declared, Manuel Ferrandiz: None declared, Vyacheslav Chasnyk: None declared, Vladimir Keltsev: None declared, Jordi Anton Grant/research support from: JA has received grant/research support, consulting fees and/or honoraria from AbbVie, Alexion, BMS, ChemoCentryx, Gebro, GSK, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Consultant for: JA has received grant/research support, consulting fees and/or honoraria from AbbVie, Alexion, BMS, ChemoCentryx, Gebro, GSK, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Maria Gastanaga: None declared, Michael Shishov: None declared, Alina Boteanu: None declared, Michael Henrickson: None declared, Damon Bass Shareholder of: GSK, Employee of: GSK, Ken Clark Shareholder of: GSK, Employee of: GSK, Anne Hammer Shareholder of: GSK, Employee of: GSK, Beulah Ji Shareholder of: GSK, Employee of: GSK, Antonio Nino Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK, Herbert Struemper Shareholder of: GSK, Employee of: GSK, Mei-Lun Wang Employee of: former employee of GSK, Alberto Martini Consultant for: I do not have any conflict of interest to declare since starting from 1 March 2016 I became the Scientific Director of the G. Gaslini Hospital; therefore, my role does not allow me to render private consultancies resulting in personal income.

I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:

AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.

The money received for these activities are directly transferred to the Gaslini Institute's bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Daniel J Lovell Consultant for: Consulting fees and/or honoraria from Astra Zeneca, Wyeth Pharma, Amgen, Abbott, Pfizer, F. Hoffmann-La Roche, Novartis, UBC, Takeda, GSK, Boehringer, and Celgene, Hermine Brunner Grant/research support from: Bristol-Myers Squibb, Pfizer, Consultant for: Pfizer, Bristol-Myers Squibb, Janssen, Novartis, Lilly, Roche, GlaxoSmithKline, Sanofi, Speakers bureau: Novartis, Roche

Figure. Primary and major secondary endpoints at Week 52 (N=93)



[a]At least 50% improvement in 2 of 5 cSLE core response variables, with no more than 1 of the remaining worsening by more than 30%; [b]at least 30% improvement in 3 of 5 cSLE core response variables, with no more than 1 of the remaining worsening by more than 30%; [c]Weeks 44–52; [d]Defined as increase of <0.30 points from baseline

ACR, American College of Rheumatology; BILAG, British Isles Lupus Activity Group; CI, confidence interval; OR, odds ratio; ParentGA, parent global assessment; PGA, Physician's Global Assessment; PRINTO, Pediatric Rheumatology International Trials Organisation; SELENA-SLEDAI, Safety of Estrogens in Systemic Lupus Erythematosus-National Assessment Trial-Systemic Lupus Erythematosus Disease Activity Index; SRI, SLE Responder Index

Table. Percent change from baseline in cSLE core response variables at Week 52

PRINTO/ACR variable	Placebo (n=40)	Belimumab (n=53)
ParentGA, median (range)	−23.6 (−95, 600)	−53.9 (−100, 900)
n	39	47
PGA, median (range)	−47.9 (−100, 61)	−76.1 (−100, 117)
n	40	53
SELENA-SLEDAI, median (range)	−50.0 (−100, 58)	−50.0 (−100, 150)
n	39	53
PedsQL (physical functioning), median (range)	12.5 (−53, 575)	10.5 (−100, 280)
n	40	53
Proteinuria, median (range)	7.1 (−91, 570)	−2.1 (−85, 1682)
n	40	53

PedsQL, Pediatric Quality of Life Inventory; PGA, Physician's Global Assessment

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FRI0182 FREQUENCY OF HYDROXYCHLOROQUINE RETINOPATHY IN THE HOPKINS LUPUS COHORT

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Background: The Kaiser-Permanente study projected hydroxychloroquine (HCQ) retinopathy rates of 40% after 20 years of use (1).

Objectives: We have prospectively followed SLE patients in the Hopkins lupus cohort to compare.

Methods: Patients in the Hopkins cohort are seen quarterly for assessment of disease activity and lupus complications. Yearly ophthalmology examinations are requested. Patients, if insurance allows, are referred to the Wilmer Retina group. Four tests are performed: OCT, ERG, MP-1 and FAF.

Results: Patients had a variety of retinal testing done, with optical coherence testing most frequent. Table 1 shows the concordance of a test abnormality with the retina expert opinion.

Table 1. – Performance of retinal imaging modalities relative to expert diagnosis

Test	Retinopathy N (%)	No Retinopathy N (%)
Ocular Coherence Tomography (OCT)		
Abnormal	25 (93%)	133 (16%)
Normal	2 (7%)	721 (84%)
Total	27	854
Electroretinogram (ERG)		
Abnormal	15 (100%)	195 (49%)
Normal	0 (0%)	201 (51%)
Total	15	396
Microperimetry (MP1)		
Abnormal	17 (100%)	144 (30%)
Normal	0 (0%)	331 (70%)
Total	17	475
Fundal Autoflourescence (FAF)		
Abnormal	19 (83%)	165 (24%)
Normal	4 (17%)	536 (76%)
Total	23	701

The concordance of the test abnormality with the retina expert opinion showed the following sensitivity and specificity, respectively: OCT 93%, 84%; ERG 100%, 51%; MP1 100%, 70%; and FAF 83%, 76%.

The frequency of retinopathy increased with years of HCQ use [number of retinopathies per total patients (percent frequency)]: 5 years or less, 1/103 (0.97%); 6-10 years, 2/109 (1.83%); 11-15 years, 3/91 (3.30%); 16-20 years, 11/96 (11.46%); and 21 or more years, 6/75 (8.00%).

Conclusion: In agreement with the American Academy of Ophthalmology, OCT appears to be the optimum test for yearly monitoring (2). The frequency of retinopathy was much lower in our prospective study than estimated by the Kaiser-Permanente study. Our data also show the need for ophthalmologists with retinopathy expertise to interpret retina testing, as screening tests are frequently abnormal due to causes other than HCQ retinopathy. Stopping HCQ based on an abnormal test without confirmation from a retinopathy expert could needlessly deprive an SLE patient of an important medication.

REFERENCES:

[1] Melles RB, Marmor MF. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. JAMA Ophthalmol 2014;132:1453–1460.

[2] Marmor MF, Kellner U, Lai TYY, Melles RB, Mieler WF. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (2016 revision). Ophthalmology 2016;123:1386–1394.

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FRI0183 STUDY DESIGN FOR A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF REPOSITORY CORTICOTROPIN INJECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DESPITE MODERATE-DOSE CORTICOSTEROIDS

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Background: Repository corticotropin injection (RCI) is a complex mixture containing purified porcine pituitary adrenocorticotropic hormone (ACTH)-analogue with potential anti–inflammatory and immunomodulatory effects through the melanocortin receptors (MC1R, MC3R-MC5R) and endogenous steroid production. RCI is approved by the US FDA for the treatment of acute exacerbations (ie, disease flares) or as maintenance therapy in patients with systemic lupus erythematosus (SLE). In a pilot study, RCI was well tolerated with improvements in disease activity for lupus patients treated with RCI compared to those who received placebo (Furie et al, 2016).

Objectives: To discuss the design, demographics, and baseline characteristics of a clinical trial evaluating the role of RCI in the treatment of patients with inadequately controlled SLE disease activity.

Methods: This is a multicenter, double-blind, randomized, placebo-controlled, 24-week clinical trial aiming to determine the effect of RCI in reducing disease activity for patients with persistently active SLE despite moderate-dose corticosteroids (CSs). Patients are required to have SLE ($\geq$4 of 11 ACR criteria from 1997) and active disease (moderate to severe rash and/or arthritis) despite stable dose CSs $\geq$ 4 weeks prior to screening (7.5 - 30 mg/day of prednisone or equivalent). Patients are treated with RCI 1 mL (80 U) subcutaneously (SC) or placebo 1 mL, every other day for 4 weeks followed by twice per week for 20 weeks. Randomization is stratified by study site location and prednisone or equivalent dose ($\leq$ 20 and > 20 mg/day). Patients remain on stable doses of CSs through Week 16, with tapering encouraged between Weeks 16 and 24. Efficacy is evaluated using the SLE Responder Index-4 (SRI-4) and changes from baseline in SLE Disease Activity Index-2000 (SLEDAI-2K), British Isles Lupus Assessment Group-2004 (BILAG-2004) scores, and Physician's Global Assessment (PGA). The primary efficacy endpoint is the proportion of SRI-4 responders at Week 16. Secondary and exploratory endpoints include changes in disease activity scores over time, prednisone dose, and biomarkers (ie, complements, autoantibodies, inflammatory, bone turnover).

Results: As of 14 December 2018, 124 patients comprised the intent–to–treat (ITT) population. Target enrollment is 270 patients, of which 162 patients are expected to be randomized at approximately 60 sites globally. Demographic and baseline characteristics (Table) were collected, including circulating lymphocyte profiles (CD19+ B Cells, CD3+ total T cells, and CD4 Treg cells), which are consistent with the pilot study of RCI (Furie et al, 2016).

Table. – Demographics and Baseline Characteristics

Characteristic	Patients (ITT Population; N=124)
Age, y, mean (SD)	40.6 (12.5)
Female, n (%)	114 (91.9)
Race, n (%)	
Caucasian	45 (36.3)
African American	15 (12.1)
American Indian or Alaska Native	25 (20.2)
Other	20 (16.1)
Ethnicity, n (%)	
Hispanic or Latino	85 (68.5)
Weight, kg, mean (SD)	73.3 (19.2)
SLEDAI-2K Total Score, mean (SD)	9.8 (3.0)
BILAG Total Score, mean (SD)	18.4 (5.6)
Physician's Global Assessment (100 mm), mean (SD)	62.1 (12.3)
Prednisone or Equivalent Daily Dosage, mg, mean (SD)	11.5 (5.2)
Antimalarials, n (%)	71 (57.3)
Immunosuppressants, n (%)	73 (58.9)
Bone Turnover Markers	
PINP, ng/mL, mean (SD)	44.0 (23.6)
CTX-I, ng/mL, mean (SD)	0.347 (0.175)

Conclusion: This on-going study assesses the efficacy and safety of RCI for the treatment of refractory SLE in a racially and ethnically diverse population. The rapid onset of action of RCI allows for a 16–week primary endpoint. Patients enrolled in this trial have moderate or high disease activity (as shown by the mean SLEDAI-2K, BILAG, and PGA) and are likely to provide valuable data on the role of RCI in refractory lupus. Bone turnover markers will further define the safety profile of RCI in lupus.

REFERENCE:

[1] Furie, et al. *Lupus Sci Med.* 2016 Oct 21;3:e000180.

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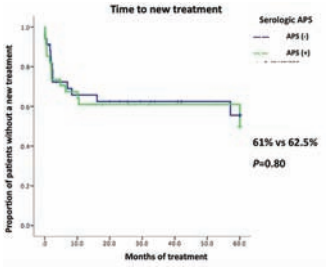
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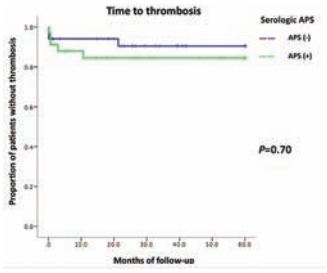
DOI: 10.1136/annrheumdis-2019-eular.5707

FRI0184 **SAFETY AND EFFICACY OF SPLENECTOMY IN THE TREATMENT OF ANTIPHOSPHOLIPID SYNDROME-ASSOCIATED CYTOPENIAS**

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Background: Thrombocytopenia and autoimmune hemolytic anemia (AIHA) are common hematologic manifestations in primary antiphospholipid syndrome (APS). Although splenectomy is considered a second-line treatment in both primary immune thrombocytopenia (ITP) and idiopathic AIHA, its role in APS patients with either one of these manifestations has not been adequately defined, mainly because of the theoretically increased risk of thrombosis for patients with APS who undergo surgery.
Objectives: To determine the safety and efficacy of splenectomy for steroid-refractory thrombocytopenia or autoimmune hemolytic anemia in patients with primary APS, when compared to patients with ITP or idiopathic AIHA.
Methods: We performed a retrospective, single-center, case-control study. We included patients with primary APS and either thrombocytopenia, or autoimmune hemolytic anemia/Evans syndrome who underwent splenectomy between 2000 and 2018. The control group was made up by patients with primary immune cytopenias (ITP or AIHA) who also underwent splenectomy during that period. Cases and controls were adjusted by age, the hematologic manifestation and date of splenectomy. We recorded demographic, clinical and serologic characteristics at the time of surgery and during follow-up.
Results: We included 34 patients in each group. Thrombocytopenia was the indication for splenectomy in 53% of patients, with AIHA or Evans syndrome comprising the remaining 47%. Most patients were female (78%) and median age was 37 years. Among APS patients, 41% had triple antibody positivity.
There were no differences regarding comorbidities between groups. Patients with APS received more immunosuppressive treatment lines before splenectomy compared to controls (p=0.02), and there was a trend for more high-dose steroid cycles in the APS group (p=0.07). Median time to splenectomy was 54 months in APS patients and 18 months in controls, but without statistical significance.
Regarding splenectomy, most were laparoscopic (88%) and surgical complications were similar between groups (18%). However, patients with APS had a higher incidence of global non-surgical complications in the first month (50 vs 23%, p=0.04), most of them being infections (21 vs 3%, p=0.05). There was no difference in the incidence of postsurgical thrombosis, venous or arterial, between groups.





Most patients achieved a global response after one month (85% in APS group, 91% in controls, p=0.7). Complete response was observed in 65% and 79% of cases and controls, respectively (p=0.27). Median follow-up time was 52 months for APS patients and 41 months for controls. There were no differences regarding relapse which required any treatment adjustment between cases and controls (44% and 38%, respectively, p=0.8, Fig 1). However, 47% of APS patients received a prolonged maintenance immunosuppressive treatment, compared with 6% of controls (p<0.01). The incidence of infections and thrombosis during follow-up was similar between groups (p=0.15 and p=0.7, respectively; Fig 2).
Conclusion: Splenectomy is associated with adequate and long-lasting responses in APS patients with cytopenias, which do not differ from patients with non-APS-associated thrombocytopenia and AIHA. Thrombosis was not a common complication in our patients; however, there was a higher incidence of infections in APS patients. This could be related to the higher steroid doses and more intensive previous immunosuppressive therapies. Splenectomy could be considered an earlier treatment option for APS patients with refractory cytopenias, and this could reduce infection risk and post-surgical morbidity.
Disclosure of Interests: Ana Barrera-Vargas: None declared, Juan Rangel Patiño: None declared, Samuel Govea-Peláez: None declared, Javier Merayo-Chalico Speakers bureau: Pfizer, Roberta Demichelis-Gómez: None declared, Jorge Alcocer-Varela: None declared
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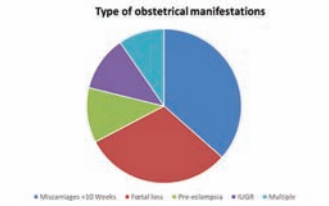
FRI0185 **HYDROXYCHLOROQUINE FOR THE PREVENTION OF RELAPSES IN A SERIES OF 812 PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME: THE HIBISCUS RETROSPECTIVE STUDY**

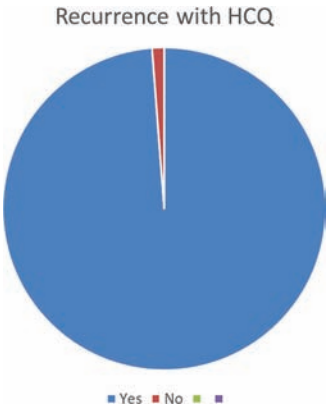
Cristina Belizna[1,2], Ljudmila Stojanovich[3], Patrick Saulnier[1], Francesca Pregnolato[4], Jaume Alijotas-Reig[5], Enrique Esteve-Valverde[6], Omar Latino[7], Sebastien Udry[8], Natasa Stanisavljevic[9], Alexander Makatsariya[10], Jamilya Khizroeva[10], Maarten Limper[11], Angela Tincani[12], Laura Andreoli[12], Francesca Regola[12], Cecilia Chighizola[4], Maria Orietta Borghi[13], Sule Apras Bilgen[14], Levent Kılıç[14], Arsene Mekinian[15], Valentina Canti[16], Katrien Devreese[17], Gilberto Pires Rosa[18], Laura Damian[19], Fatma Said[20], Yehuda Shoenfeld[21], Ricard Cervera[22], Pier Luigi Meroni[23], Zahir Amoura[24], HIBISCUS consortium. [1]*University Hospital Angers, Angers, France*; [2]*CNRS 6015 INSERM 1083, Angers, France*; [3]*Scientific Research Department, Internal Medicine-Rheumatology Bezhanijska Kosa, University Medical Center, Belgrade, Serbia*; [4]*Istituto Auxologico Italiano, Milan, Italy*; [5]*Vall d'Hebron University Hospital, Barcelona, Spain, BArcelona, Spain*; [6]*Althaia Healthcare Network of Manresa, Barcelona, Spain*; [7]*Hospital Carlos G. Durand, Buenos Aires, Argentina*; [8]*Hospital Carlos G. Durand, Buenos Aires, Buenos Aires, Argentina*; [9]*Bezhanijska Kosa, University Medical Center, Belgrade University, Serbia, Belgrade, Serbia*; [10]*I.M. Sechenow First Moscow State Medical University, Moscow, Moscow, Russian Federation*; [11]*UMC UTRECHT, UTRECHT, Netherlands*; [12]*Rheumatology and Clinical Immunology Unit, University of Brescia, Brescia, Italy, Brescia, Italy*; [13]*University of Milan, Milan, Italy*; [14]*Hacettepe University, Ankara, Ankara, Turkey*; [15]*APHP Saint Antoine, PAris, France*; [16]*Hospital San Raffaele, Milan, Italy*; [17]*Ghent University Hospital, Ghent, Belgium, Ghent, Belgium*; [18]*Sao Joao Hospital, Porto, Alameda, Porto, Portugal*; [19]*Emergency Clinical County, Cluj, Romania*; [20]*University Hospital La Rabta, TUNIS, Tunis, Tunisia*; [21]*The Zabludowicz Center for Autoimmune Diseases, affiliated to Sackler Faculty of Medicine, Tel-Aviv University, Israel, Tel Aviv, Israel*; [22]*University of Barcelona, Barcelona, Spain*; [23]*Istituto Auxologico Italiano, Milan, Italy*; [24]*APHP, PAris, France*

Background: The relapse rate in antiphospholipid syndrome (APS) remains high, 20% at 5 years in thrombotic APS and 28% in obstetrical APS *(1).* Hydroxychloroquine (HCQ) appears as an additional therapy, with immunomodulatory and antithrombotic effects *(2-5).*
Objectives: The main aim of this trial is to assess the efficacy of treatment with Hydroxychloroquine in preventing new events in primary antiphospholipid syndrome patients.
Methods: We have performed a retrospective multicentre open-labelled study (2002-2018).
Results: 812 patients with APS from 53 international centres from 16 countries were included. In all cases, the previous standard treatment was inefficient. The mean follow-up was 20.2 months (8- 144 mo), the mean age 39.5 years old. The type of clinical manifestations is described in figure 1.

Obstetrical	Thrombotic	Both
377	320	115
46,3%	39,7 %	14 %

Miscarriages 40%
Fœtal loss 31%
Preeclampsia 12%
IUGR 11%
Multiple type of obstetrical events 10%





The obstetrical manifestations were various as described in figure 2.
The number of thrombotic events were 190 arterial and 187 venous. Triple antiphospholipid antibody (tAPL) positivity was found in 20% of patients and lupus anticoagulant (LA) in 22%. No bleeding was registered in 99,6% of cases with treatment by HCQ. HCQ use was associated with favourable outcome in 96% of cases (figure 3).

In multivariate analysis, age more than 65 years was associated with arterial events (odds-ratio 0.13 95%CI 0.03-0.32, p 0.005).
Conclusion: HCQ could be effective in cases of refractory APS but prospective studies are necessary.

REFERENCES:

[1] Cervera R, Serrano R, Pons-Estel GJ, Ceberio-Hualde L, Shoenfeld Y, de Ramón E, Buonaiuto V, Jacobsen S, Zeher MM, Tarr T, Tincani A, Taglietti M, Theodossiades G, Nomikou E, Galeazzi M, Bellisai F, Meroni PL, Derksen RH, de Groot PG, Baleva M, Mosca M, Bombardieri S, Houssiau F, Gris JC, Quéré I, Hachulla E, Vasconcelos C, Fernández-Nebro A, Haro M, Amoura Z, Miyara M, Tektonidou M, Espinosa G, Bertolaccini ML, Khamashta MA. Morbidity and mortality in the antiphospholipid syndrome during a 10-year period: a multicentre prospective study of 1000 patients. Ann Rheum Dis. 2015;74:1011-8.

[2] Belizna C. Hydroxychloroquine as an anti-thrombotic in antiphospholipid syndrome. Autoimmun Rev. 2015;14:358–62.

[3] Nuri E, Taraborelli M, Andreoli L, Tonello M, Gerosa M, Calligaro A, Argolini LM, Kumar R, Pengo V, Meroni PL, Ruffatti A, Tincani A. Long-term use of hydroxychloroquine reduces antiphospholipid antibodies levels in patients with primary antiphospholipid syndrome. Immunol Res. 2017;65:17-24.

[4] Schmidt-Tanguy A, Voswinkel J, Henrion D, Subra JF, Loufrani L, Rohmer V, et al. Antithrombotic effects of hydroxychloroquine in primary antiphospholipid syndrome patients. J Thromb Haemost JTH. 2013;11:1927–9.

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FRI0186 HYDROXYCHLOROQUINE ON THE TOP OF STANDARD TREATMENT WITH LOW DOSE ASPIRIN AND LOW MOLECULAR WEIGHT HEPARIN SIGNIFICANTLY REDUCES THE PROBABILITY OF PREGNANCY MORBIDITY IN WOMEN WITH MULTIPLE POSITIVITY FOR ANTI-PHOSPHOLIPID ANTIBODIES

Cecilia Chighizola[1], Francesca Pregnolato[1], Francesca Bartoli[2,3], Maria Gerosa[2,3], Chiara Comerio[2,4], Maria Gabriella Raimondi[2,3], Laura Trespidi[4], Maria Orietta Borghi[1,2], Manuela Wally Ossola[4], Enrico Ferrazzi[2,4], Pier Luigi Meroni[1].
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Background: Hydroxychloroquine is an anti-malarial drug that not only exerts immunomodulatory and anti-thrombotic properties, but also has been shown to reverse several effects mediated by anti-phospholipid antibodies (aPL) in models of obstetric anti-phospholipid syndrome (APS). Not surprisingly, HCQ, whose prescription during gestation is perfectly safe, has been proposed as an additional therapeutic tool in obstetric APS, but evidence of ist efficacy is still scant.
Objectives: This study investigates how treatment with HCQ, prescribed in different combinations with low-dose aspirin (LDASA) and low-molecular weight heparin (LMWH), affects the probability of pregnancy morbidity (P_{PM}).
Methods: Data on pregnancies in women with persistent aPL positivity at any titre, with or without autoimmune diseases, were retrospectively collected at a single centre.
A weigthed generalized estimated equation (GEE) model was applied to quantify the effect of treatment with HCQ on P_{PM}, allowing to: i) evaluate pregnancy outcomes over time using available longitudinal data; ii) account that pregnancies of the same woman are not independent events; iii) consider that women had a different number of pregnancies; iv) estimate the role of several confounders and predictors.
The model envisaged as dependent variable pregnancy outcome as a binary outcome, defined for each pregnancy as "obstetric complication yes versus no" (pregnancy loss before 10 weeks, pregnancy loss after 10 weeks, premature birth before 34 weeks, according to updated APS classification criteria).
Results: Three-hundred-eighty-one women were recruited in this study: 155 women with aPL positivity (100 women with positivity for criteria aPL and 55 women with low titer aPL) and 226 women with autoimmune diseases but negative aPL. Data were collected on 847 pregnancies: 458 in women with positive aPL (172 in women with criteria aPL and 286 in women with low titer aPL) and 389 in women with autoimmune disease and negative aPL.
P_{PM} in untreated patients are presented in **Table 1. Table 2** reports P_{PM} in women receiving LDASA+/- HCQ, LDASA + LMWH +/- HCQ.
Conclusion: HCQ, when added to LDASA or on the top of standard treatment with LDASA and LMWH, allows to reduce P_{PM}. Most importantly, HCQ plus the combo LMWH + LDASA leads to a significantly

reduction of P_{PM} even in women at highest risk, namely those with multiple criteria aPL positivity.

REFERENCES:
[1] Miyakis S, et al. J Thromb Haemost. 2006;4(2):295-306
[2] Sciascia S, et al. Thromb Haemost. 2016;115(2):285-90.
[3] Ruffatti A, et al. Thromb Haemost. 2018;118(4):639-646.

Table 1. Probabilities of P_{PM} in untreated women with or without aPL.

	P_{PM}
aPL negative	38% (29-48)
Low titer single aPL positivity	62% (52-71)
Low titer double aPL positivity	83% (75-89)
Criteria single aPL positivity	80% (71-87)
Criteria multiple aPL positivity	89% (81-94)

Data are expressed as P_{PM} (95% confidence interval).

Table 2. Probabilities of P_{PM} in treated women with aPL.

	LDASA	LDASA + HCQ	LDASA + LMWH	LDASA + LMWH + HCQ
Low titer single aPL positivity	31% (23-41)	21% (14-30)	15% (9-23)	10% (6-17)
Low titer double aPL positivity	57% (47-66)	44% (35-54)	34% (26-44)	24% (17-33)
Criteria single aPL positivity	52% (42-62)	40% (31-50)	30% (22-40)	21% (14-30)
Criteria multiple aPL positivity	69% (59-77)	57% (47-66)	47% (38-57)	35% (26-45)

Data are expressed as P_{PM} (95% confidence interval).

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FRI0187

PRELIMINARY EXPLORATION OF NEW METHODS TREAT TO PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: REGULATING TH17/TREG CELL BALANCE BY RAPAMICIN AND ALL-TRANS RETINOIC ACID

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Background: Helper T cells 17 (Th17) and regulatory T cells (Treg)are two important immunoregulatory cells that act in opposite directions[1]. Previous study[2] has shown that Th17/Treg cell balance is one of the important pathogenesis of systemic lupus erythematosus(SLE). Further researches[3-5] believed that rapamycin(RAPA) alone or in combination with all-trans retinoic acid(ATRA) can regulate Th17/Treg cell balance, and then alleviate the condition of SLE.
Objectives: To investigate effect of the use of RAPA alone or combined ATRA on Th17/Treg cell balance in patients with SLE.
Methods: Seventy patients with SLE (64 females and 6 males, mean age 31.91±10.12 years, mean duration 61.14±53.64 months) in our hospital from March 2016 to June 2018 were enrolled. All of them were in line with the standard of ACR in 1997. The patients were randomly divided into RAPA group(RAPA0.5 mg/time, twice a week) and RAPA+ATRA group(RAPA and ATRA 10 mg/time, twice a week), 35 cases in each group. All were treated continuously for 24 weeks. The number of Th17 and Treg cells in peripheral blood before treatment and 6,12,24 weeks after treatment were measured. The SLEDAI scores and glucocorticoid dosage before and after the treatment were also observed to evaluate the differences of efficacy between the two groups.
Results: At different time in each group,the number of peripheral blood Th17 cells in SLE patients was decreased(P<0.05), the number of Treg cells was increased (P>0.05),the ratio of Th17/Treg cells induced(P<0.05), indicating a restored balance of them. The SLEDAI scores and the dosage of glucocorticoid were decreased significantly (P<0.001). There were no significant differences in the number of Th17 cells, Treg cells, SLEDAI scores and the dosage of glucocorticoid between two groups (P>0.05). Compared with pretreatment, the number of Th17 cells, the ratio of Th17/Treg cells and SLEDAI scores after24 weeks treatment in SLE patients was decreased in RAPA group(P<0.05). Compared with pretreatment, the SLEDAI scores and the dosage of glucocorticoid after24 weeks treatment in SLE patients was significantly reduced in RAPA+ATRA group (P<0.001).
Conclusion: Using RAPA or combined with ATRA could improve the condition of SLE patients by regulating Th17/Treg cells balance and reduce glucocorticoid dosage, which provided new directions for the pathogenesis and treatment of SLE.

REFERENCES:
[1] Lee GR. The balance of Th17versus Treg cells in autoimmunity[J]. Int J MolSci,2018,19(3): 730.
[2] Yang J, Yang X, Zou H, et al. Recovery of the immune balance between Th17 and regulatory T cells as a treatment for systemic lupus erythematosus. Rheumatology,2011,50(8):1366-1372.
[3] Lai Z-W, Borsuk R, Shadakshari A, et al. Mechanistic target of rapamycin activation triggers IL-4 production and necrotic death of double-negative T cells in patients with systemic lupus erythematosus[J]. J Immunol,2013,191(5): 2236-2246.
[4] Wang X, Wang W, Xu J, et al. All-trans retinoid acid promotes allogeneic corneal graft survival in mice by regulating Treg-Th17 balance in the presence of TGF-β[J]. BMC Immunol, 2015,16: 17.
[5] Beermann JL, Thiesler CT, Dringenberg U,et al. Migratory properties of ex vivo expanded regulatory T cells: Influence of all-trans retinoic acid and rapamycin[J]. Transpl Immunol, 2017,45: 29-34.

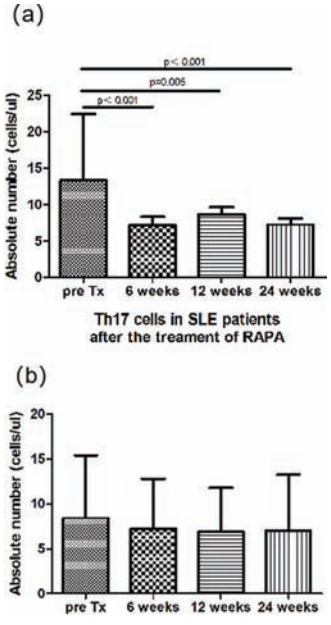


Figure 1. Changes in the number of Th17 cells (number/μl) before and after treatment in the two groups.

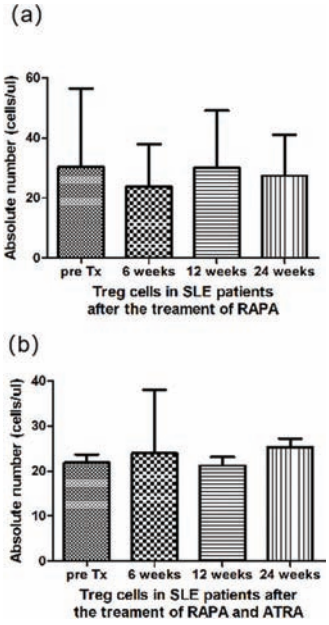


Figure 2. Changes in the number of Treg cells (number/μl) before and after treatment in the two groups.

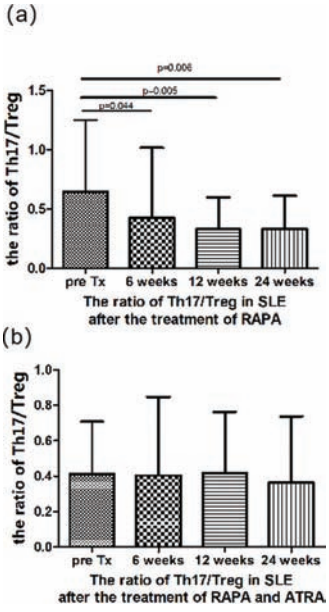


Figure 3. Changes in the ratio of Th17/Treg cells before and after treatment in both groups.

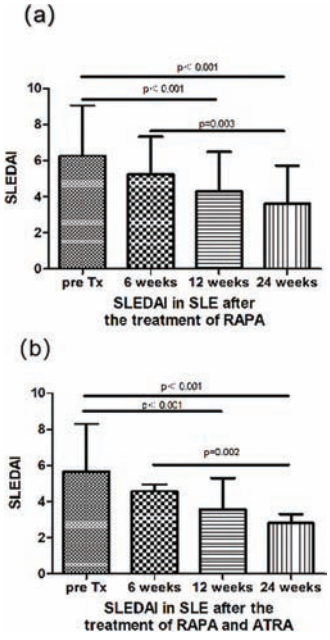


Figure 4. Changes in SLEDAI scores (minutes) before and after treatment in both groups.

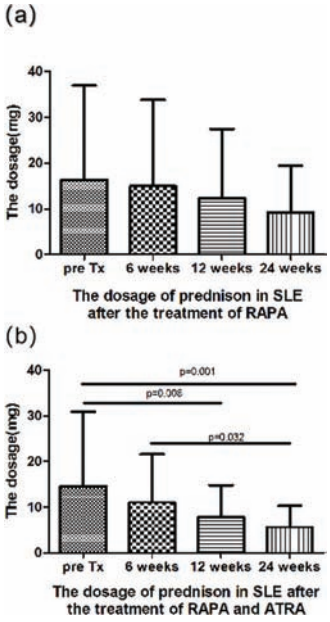


Figure 5. Changes in prednisone dosage (mg/d) before and after treatment in both groups

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Disclosure of Interests: None declared
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FRI0188 **EARLY RENAL IMPROVEMENTS FOLLOWING RITUXIMAB IN LUPUS NEPHRITIS**

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Background: Rituximab (RTX) is the monoclonal antibody of choice in patients with lupus nephritis (LN) who either fail to respond to, or cannot receive standard of care (SOC) therapy. Despite its continued use in clinical practice, published clinical trials regarding its use in LN management have failed to show any clear benefit.
Objectives: We aimed to analyse renal outcomes of LN patients in a large national register.
Methods: Patients with active LN on recruitment into the BILAG-Biologics Register (BILAG-BR) were included. Active LN was defined as a BILAG A or B score in the renal domain. Patients are eligible for RTX if they have failed either MMF or cyclophosphamide. We defined renal response at 6 and 12 months as a change in BILAG score from A to B/C/D or B to C/D. Non-renal disease activity was also described.
Results: Overall 259/897 patients in BILAG-BR had active LN at baseline. Of these, 230 received RTX and 29 received SOC. 109/159 (68.6%) RTX patients and 15/19 (78.9%) of SOC patients had a renal BILAG response at 6 months (p=0.792) (Table 1). In those with sufficient response data at 12 months, 31/98 (31.6%) and 7/15 (46.7%) (p=0.084) demonstrated continued renal response in the RTX and SOC groups respectively. Both groups made improvements or remained stable in all other renal domains (UPCR, eGFR, creatinine) at 6 and 12 months. Oral steroid doses decreased in both treatment groups. Of note, baseline steroid doses in the SOC group were higher than RTX patients (30mg (20-40) vs. 12.5mg (10-25), p<0.001). Non-renal disease activity measures improved in both cohorts.

Variable	RTX	SOC	p
Renal BILAG response*	109/159	15/19 (78.9%)	0.792
- 6m *(n=159 RTX, 19 SoC)*	(68.6%)	7 (46.7%)	0.084
- 6 to 12m *(n=98 RTX, 15 SoC)*	31 (31.6%)		
UPCR (median [IQR]) mg/mmol	215 (103-388)	173 (88-352)	0.2945
- 0m *(n=160)*	149 (54-404)	66 (21-92)	0.331
- 6m *(n=92)*	71 (42 -316)	18 (11-40)	0.0045
- 12m *(n=60)*			
Serum creatinine (median [IQR]) micromol/l	69 (58-97)	66 (52-90)	0.3864
- 0m *(n=239)*	70 (59-99)	70 (51-84)	0.4774
- 6m *(n=157)*	70 (59-100)	68 (60-95)	0.7651
- 12m *(n=105)*			
Oral steroid dose (median [IQR]) mg/day	12.5 (10-25)	30 (20-40)	<0.001
- 0m *(n=196 RTX, 29 SoC)*	10 (7-17.5)	12.5 (10-20)	0.1246
- 6m *(n=151 RTX, 19 SoC)*	10 (5-15)	8.5 (6.25-12.5)	0.9730
- 12m *(n=108 RTX, 16 SoC)*			
Non-renal BILAG	9 (1-12)	8 (1-10)	0.9310
- 0m *(n=230)*	1 (0-2)	1 (0-2)	0.6527
- 6m *(n=153)*	1 (0-2)	1 (0-2)	0.7803
- 12m *(n=101)*			
Non-renal SLEDAI (median [IQR])	3 (2-4)	2 (1-3)	0.0426
- 0m *(n=254)*	1 (0-2)	1 (0-2)	0.2845
- 6m *(n=183)*	1 (0-2)	1 (0-2)	0.6887
- 12m *(n=113)*			
SLICC DI ≥1	113 (50.2%)	14 (48.3%)	0.844
- 0m *(n=254)*			

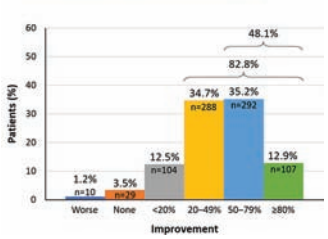
Conclusion: In a large UK-wide, real-world, observational LN cohort we have shown that RTX does improve renal outcomes at 6 and 12 months in refractory SLE patients. RTX is a valid treatment option for many patients with renal disease in SLE.
Disclosure of Interests: Sophie Collinson: None declared, Ben Parker Grant/research support from: GSK, Consultant for: AZ, UCB, GSK, Eoghan McCarthy: None declared, Ian N. Bruce Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, MedImmune, Merck Serono, Speakers bureau: GlaxoSmithKline, UCB Pharma
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FRI0189 **POOLED ANALYSIS OF THE REAL-WORLD EFFECTIVENESS OF BELIMUMAB IN TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS USING MULTI-COUNTRY DATA FROM THE OBSERVE STUDIES**

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Background: Real-world evidence of belimumab effectiveness in patients with systemic lupus erythematosus (SLE) has been reported separately for several countries through the OBSErve (evaluation Of use of Belimumab in clinical practice SEttings) programme.
Objectives: To evaluate the effectiveness of belimumab in patients with SLE using pooled data from the individual OBSErve studies.
Methods: This was a *post hoc* meta-analysis (GSK study 206351) of patient level data pooled from six retrospective observational cohort studies (Argentina, Canada, Germany, Spain, Switzerland, United States of America). Physicians provided data for adults (≥18 years; clinical diagnosis of SLE) who had initiated intravenous belimumab as part of their usual SLE care ≥6 months prior to enrolment and for whom reasons for belimumab initiation could be identified. Primary objective: physician-assessed overall clinical response to belimumab at Month 6, which reflected physicians' impression of change in overall clinical manifestations, categorised as worse, no improvement, and improvement of <20%, 20–49%, 50–79%, and ≥80%. Secondary objectives included a description of patient characteristics at belimumab initiation (index); treatment patterns during the 6 months after index; and patient and treatment characteristics associated with an overall clinical response. Safety was not assessed.
Results: Data were pooled from all 830 patients (89.3% female; mean [standard deviation] age 41.9 [12.6] years) included in each of the OBSErve studies. At index, most patients had moderate SLE (71.4%; physician-assessed) and serological indicators of high disease activity (82.8%; high anti-dsDNA and/or low complement). Of 345 patients for whom Safety of Estrogens in Lupus Erythematosus-National Assessment Trial-SLE Disease Activity Index baseline data were available, 60.0% had a score ≥10. At index, 72.0% of patients had musculoskeletal, 59.0% had mucocutaneous manifestations, and 16.5% had renal involvement. At Month 6, 82.8% of patients had ≥20% improvement and 48.1% had ≥50% improvement in their overall condition; only 4.7% had none or a worse response to belimumab therapy (**Figure**). At index, 81.4% of patients received steroids at a mean dose of 17.6 mg/day. At Month 6, the mean change in steroid dose was –9.7 mg/day. Of those receiving a dose >7.5 mg/day (78.4% of all patients receiving steroids at index), 54.5% had a dose reduction to ≤7.5 mg/day at Month 6. Ineffective previous treatment was the main reason for belimumab initiation (74.3%). Prior to Month 6, 4.4% of patients (n=12/270) in Argentina, Spain, Germany and Switzerland discontinued belimumab, most frequently due to lack of efficacy and patient request (both 33.3%); OBSErve US and Canada excluded patients with <6 months' belimumab treatment.
Conclusion: This study provides important insights into global real-world outcomes in a large number of patients with SLE treated with belimumab. After 6 months of treatment, most patients demonstrated clinical improvements in SLE; results were consistent across the pooled population and for patients with high disease activity. Belimumab was steroid sparing; most patients receiving steroids at belimumab initiation decreased their steroid dose after 6 months of belimumab treatment.

Figure. Overall improvement in disease activity at Month 6 (N=830)

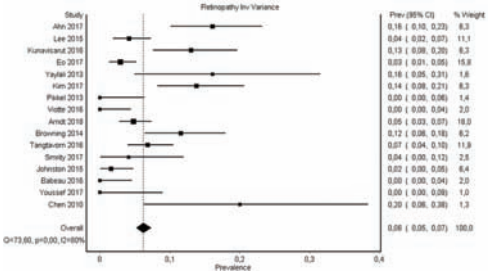


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FRI0190 INCIDENCE OF ANTIMALARIALS-INDUCED RETINOPATHY IN INFLAMMATORY RHEUMATIC DISEASES, USING OCT AND VISUAL FIELD TEST : A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Antimalarials (AM) are frequently used as first-line therapy in mild inflammatory diseases, because of a good benefit/risk ratio. Recently, their benefit on long term cardiovascular risk in RA patients has been demonstrated [1, 2]. Their most severe side effect is retinopathy, which can potentially lead to blindness, but remains reversible if detected early, provided the treatment is stopped. This complication has been described early [3], but its incidence remains uncertain. A recent update of the American Association of Ophtalmology (AAO) recommendations on screening for chloroquine and hydroxychloroquine retinopathy, suggests to screen patients under AM treatment, with a frequency depending on risk factors, and with the systematic and minimal use of Optical Coherence Tomography (OCT) and Visual Field (VF) test, completed by others tests if required [4].
Objectives: We aimed at estimating the exact incidence of AM-induced retinopathy, based on available published literature about this issue, with particular reference to detection performed with OCT and VF test.
Methods: A systematic literature search was conducted in Pubmed, Cochrane and Embase databases until April 6th 2018, completed by a manual search in references from the resulting selected articles. We first selected all publications about the incidence of AM-associated retinopathy in patients treated for inflammatory diseases and included them in the systematic literature search. Among them, and in order to minimize heterogeneity of results, we focused on those which had used at least OCT and VF test, as recommended by the AAO, to perform a meta-analysis. Analysis was conducted using MetaXL for Microsoft Excel, applying the Inverse of Variance method.
Results: Among the 3890 articles of potential interest, we selected 91 articles appropriately addressing the topic and included them in the systematic literature search. They were published between 1964 and 2018, with variable population sizes (10 to 3580 patients). Patients were treated with hydroxychloroquine, chloroquine or both for an inflammatory disease (usually lupus or rheumatoid arthritis). Mean treatment duration ranged from 1 to 14,1 years. Most of them were retrospectively designed, and diagnostic methods were diverse. For the aforementioned meta-analysis, we used data from 16 articles published between 2010 and 2018, in which every patient had at least OCT and VF Test. We found a pooled estimate of incidence of 6.05% (IC 95% [5.18 – 7.31]), with a I2 heterogeneity coefficient of 80%.



Conclusion: We found a pooled incidence of approximately 6% of AM-induced retinopathy when OCT and VF test are used. However diagnostic criteria are not consensually well-defined, leading to heterogeneous data.

REFERENCES:
[1] Rempenault C, Combe B, Barnetche T, et al. Metabolic and cardiovascular benefits of hydroxychloroquine in patients with rheumatoid arthritis: a systematic review and meta-analysis. Ann Rheum Dis2017.
[2] Mathieu S, Pereira B, Tournadre A, et al. Cardiovascular effects of hydroxychloroquine: a systematic review and meta-analysis. Ann Rheum Dis2017.
[3] Hobbs H, Sorsby A, Freedman A: Retinopathy following chloroquine therapy. Lancet 1959; II: 478.
[4] Marmor MF, Kellner U, Lai TY, et al, American Academy of Ophthalmology Statement. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (2016 revision).Ophthalmology. 2016;123:1386-1394.

Disclosure of Interests: Hélène DE CAGNY: None declared, Jacques Morel: None declared, Bernard Combe Consultant for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB, Cecile Gaujoux-Viala Consultant for: Speaking and/or consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Merck-Serono, Medac, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi and UCB Pharma., Speakers bureau: Speaking and/or consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Merck-Serono, Medac, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi and UCB Pharma., Cédric Lukas: None declared
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FRI0191 TREATMENT OF REFRACTORY POOR APL-RELATED OBSTETRIC OUTCOMES WITH TNF-ALPHA BLOCKERS: MATERNAL-FETAL OUTCOMES IN A SERIES OF 18 CASES

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Background: No absolute data on the treatment of antiphospholipid antibodies (aPL) related to refractory obstetric complications exist to date. TNF-α play a major role in this disorder.
Objectives: To assess the effectiveness of TNF-α blockers in 18 aPL-positive women with recurrent infertility after therapy with low-molecular-weight heparin (LMWH) plus aspirin (LDA) plus hydroxychloroquine (HCQ).
Methods: Prospective case-series of 12 women fulfilling Sydney criteria for obstetric antiphospholipid syndrome (OAPS) and 6 with incomplete forms (OMAPS). All women tested positive for aPL at least twice. Non-criteria aPL were tested in 15/18. Complement, TNF-α and IL-10 were also evaluated. Women were closely monitored for fetal well-being and possible malformations throughout gestation and the postpartum period.
Results: Sixteen patients were started on adalimumab and 2 on certolizumab. Twelve women completed gestation: 9 at term and 3 pre-term. Differences in laboratory categories and outcomes were observed when OAPS and OMAPS were compared. First trimester miscarriage or implantation failure recurred in 6 cases, all of the OAPS group. Malformations were not seen in the newborns.
Conclusion: Overall, good obstetric results were obtained in 70% of previous LMWH-LDA+HCQ refractory cases. TNF-α blockers were well tolerated without adverse effects. The combination of LMWH plus LDA plus TNF-α blockers appears to be a promising treatment for refractory obstetric complaints related to aPL; nevertheless, outcome differences between OAPS and OMAPS do exist.

REFERENCES:

[1] Yamaguchi Y, Noriyuki N, Kaburaki J, Kobayashi K, Matsuura E, Kuwana M. Excessive exposure to anionic surfaces maintains autoantibody response to B2-glycoprotein I in patients with antiphospholipid syndrome. Blood 2007;110:4312-18.

[2] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, Derksen RH, DE Groot PG, Koike T, Meroni PL, Reber G, Shoenfeld Y, Tincani A, Vlachoyiannopoulos PG, Krilis SA. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome. J Thromb Haemost 2006; 4:295-306.

[3] Alijotas-Reig J, Vilardell-Tarrés M. Is obstetric antiphospholipid syndrome a primary nonthrombotic, proinflammatory, complement-mediated disorder related to antiphospholipid antibodies? Obstet Gynecol Surv 2010: 65:39-45.

[4] Berman J, Girardi G, Salmon JE. TNF-alpha is a critical effector and a target for therapy in antiphospholipid antibody-induced pregnancy loss. J Immunol 2005;174:1222-1226.

[5] Meroni PL, Borghi MO, Raschi E,Tedesco F. Pathogenesis of antiphospholipid syndrome: understanding the antibodies. Nat Rev Rheumatol 2011;7:330-39.

[6] Brogin Moreli J, Cirino Ruocco AM, Vernini JM, Rudge MV, Calderon IM. Interleukin 10 and tumor necrosis factor-alpha in pregnancy: aspects of interest in clinical obstetrics. ISRN Obstet Gynecol. 2012;2012:230742.

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FRI0192

A SYSTEMATIC LITERATURE REVIEW TO INFORM THE 2019 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Culminating evidence over the past decade regarding management of systemic lupus erythematosus (SLE) called for an update of the 2008 EULAR recommendations for the treatment of the disease.
Objectives: Systematic review of the literature (SLR) to inform the 2019 EULAR recommendations for the management of SLE.
Methods: SLR of Pubmed from 01/2007 to 12/2017 for questions (selected through Delphi excercise) regarding: i) efficacy/safety of different drugs used in SLE, ii) treatment of specific manifestations, iii) monitoring and treatment goals and iv) comorbidities and adjunct therapy. Evidence was categorised based on design and validity of available studies [*Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence (LoE*)] and strength of statements was graded [*Grading of recommendation (GoR), assessment, development and evaluations, GRADE*)].
Results: Main topics supported by strong evidence base included: Association of hydroxychloroquine (HCQ) use with favourable outcomes (LoE 1b, GoR A), belimumab for extrarenal disease (LoE 1a, GoR A), efficacy of antimalarials in skin disease (LoE 1a, GoR A), mycophenolate mofetil (MMF) for induction and maintenance therapy of lupus nephritis (LN) and cyclophosphamide (CYC) in severe LN (LoE 1b, GoR A). Weak evidence supported the value of repeat kidney biopsy in refractory LN (LoE 4, GoR C), all second-line agents for skin disease (LoE 4, GoR C) and efficacy of most first and second-line treatments for thrombocytopenia (LoE 4, GoR C). Moderate LoE was found for all other questions (**Table**).
Conclusion: A SLR for the treatment of SLE found the highest LoE for benefits of HCQ, efficacy of belimumab for extrarenal disease and MMF and IV-CYC in LN.
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Table. Level of evidence for different items regarding treatment of systemic lupus erythematosus

Evidence Base	Topics in SLE treatment
A (strong)	• Association of HCQ use with favourable outcomes • Chronic exposure to GC and risk of organ damage • Gonadal toxicity of CYC • Efficacy and safety of belimumab in extrarenal SLE • Efficacy of antimalarials in skin disease • MMF for induction and maintenance therapy of LN and cyclophosphamide for severe LN • Immunosuppressive therapy for inflammatory neuropsychiatric manifestations • Association of aPL with adverse outcomes
B (moderate)	• HCQ cumulative exposure and retinal toxicity • Efficacy of MTX and MMF in extrarenal SLE • Comparable efficacy and less toxicity of lower-dose GC regimens • Efficacy of RTX in renal and extrarenal SLE • Efficacy of multitarget therapies for induction treatment in LN • Use of CNIs in refractory LN • Primary prophylaxis with low-dose aspirin in aPL(+) SLE patients
C/D (weak)	• Efficacy of AZA, CsA, and CYC in extrarenal SLE • Efficacy of second-line treatment in skin lupus • Efficacy of most first and second-line treatments for thrombocytopenia • Efficacy of vaccinations in SLE patients • Efficacy of primary cardiovascular protection with statins and low-dose aspirin in SLE

FRI0193

2019 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

Antonis Fanouriakis[1], Myrto Kostopoulou[2], Alessia Alunno[3], Martin Aringer[4], Ingeborg Bajema[5], John N. Boletis[6], Ricard Cervera[7], Andrea Doria[8], Caroline Gordon[9], Marcello Govoni[10], Frederic Houssiau[11], David Jayne[12], Marios Kouloumas[13], Annegret Kuhn[14], Janni Lisander Larsen[15], Kirsten Lerstrom[16], Gabriela Moroni[17], Marta Mosca[18], Matthias Schneider[19], Josef S. Smolen[20], Elisabet Svenungsson[21], Vladimir Tesar[22], Angela Tincani[23], Anne Troldborg[24], Ronald van Vollenhoven[25], Jörg Wenzel[26], George Bertsias[27], Dimitrios Boumpas[1]. [1]*"Attikon" University Hospital, Athens, Greece*; [2]*"G. Gennimatas" General Hospital, Athens, Greece*; [3]*University of Perugia, Perugia, Italy*; [4]*University Medical Center and Faculty of Medicine Carl Gustav Carus at the TU Dresden, Dresden, Germany*; [5]*Leiden University Medical Center, Leiden, Netherlands*; [6]*"Laikon" Hospital, National and Kapodistrian University of Athens, Medical School, Athens, Greece*; [7]*Hospital Clinic, Department of Autoimmune Diseases, Barcelona, Spain*; [8]*University of Padova, Padova, Italy*; [9]*Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom*; [10]*University of Ferrara, Azienda Ospedaliero-Universitaria Sant'Anna Ferrara, Ferrara, Italy*; [11]*Université catholique de Louvain, Louvain, Belgium*; [12]*Cambridge, Department of Medicine, Cambridge, United Kingdom*; [13]*Cyprus League Against Rheumatism, Aglantzia, Cyprus*; [14]*University Hospital Muenster, Muenster, Germany*; [15]*Rheumatology and Spine Diseases Centre, Rigshospitalet, Copenhagen, Denmark*; [16]*Lupus Europe, Farum, Denmark*; [17]*Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*; [18]*University of Pisa, Pisa, Italy*; [19]*UKD, Heinrich-Heine University, Düsseldorf, Germany*; [20]*Medical University of Vienna, Vienna, Austria*; [21]*Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden*; [22]*Charles University, Prague, Czech Republic*; [23]*University of Brescia, Brescia, Italy*; [24]*Aarhus University Hospital, Aarhus, Denmark*; [25]*Amsterdam University Medical Centers, Amsterdam, Netherlands*; [26]*University Hospital Bonn, Bonn, Germany*; [27]*University Hospital of Heraklion, Heraklion, Greece*

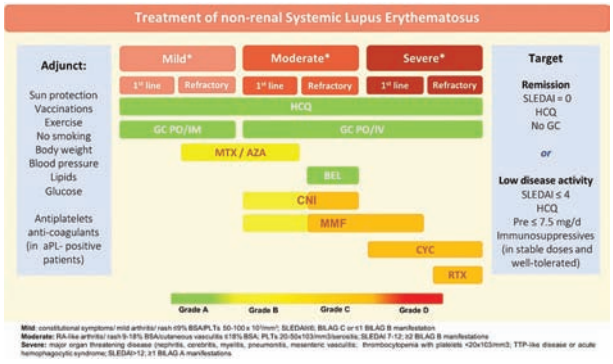
Background: Recommendations for the treatment of systemic lupus erythematosus (SLE) were published by EULAR in 2008. Advances in treatment strategies and goals called for an update of these recommendations, capitalizing on strengths and experience from previous projects.

Objectives: To update the EULAR recommendations for the management of SLE.

Methods: Systematic literature review (01/2007-12/2017) followed by Delphi method to form questions, elicit expert opinions and reach consensus.

Results: Treatment in SLE aims at remission or low disease activity and prevention of flares. Hydroxychloroquine is recommended in all lupus patients, at a dose not exceeding 5mg/kg real body weight. During chronic maintenance treatment, glucocorticoids should be minimized to less than 7.5 mg/day (prednisone equivalent) and, when possible, withdrawn. Prompt initiation of immunomodulatory agents (methotrexate, azathioprine, mycophenolate) can expedite tapering/discontinuation of glucocorticoids. In persistently active or flaring extrarenal disease, add-on belimumab should be considered; rituximab may be considered in organ-threatening, refractory disease. Specific recommendations are also provided for the management of cutaneous, neuropsychiatric, haematological and renal disease (including the use of calcineurin inhibitors). SLE patients should be assessed for their antiphospholipid antibody status, infectious and cardiovascular diseases risk profile, and preventative strategies be tailored accordingly.

Conclusion: Updated EULAR recommendations provide physicians and patients with updated consensus guidance on the management of SLE, combining evidence-base and expert-opinion.



Figure

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FRI0194 **INTEGRATED SAFETY PROFILE OF ATACICEPT FROM ALL CLINICAL STUDIES TO DATE**

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Background: We conducted an integrated analysis of pooled safety data from all 17 atacicept clinical studies across multiple indications to date.
Objectives: To characterize the overall safety profile of atacicept.
Methods: Analyses were based on 3 pooled datasets: double-blind placebo (PBO)-controlled set (DBPC-S) (n=1568; key endpoint: treatment-emergent AEs [TEAEs]); systemic lupus erythematosus set (SLE-S; n=761; key endpoints: IgG change and serious infection rates, and mortality); and full analysis set (FA-S; n=1845; key endpoint: exposure-adjusted mortality).
Results: Of 1568 patients (DBPC-S), 30.8% received PBO, and 8.2%, 24.5% and 36.5% received atacicept 25, 75 and 150 mg. Overall, baseline characteristics were balanced across treatment arms. Treatment exposure in patient-years (py) was similar with PBO and atacicept 75 and 150 mg but was lower with 25 mg (Table). Exposure-adjusted TEAE rates were generally higher with atacicept vs PBO; serious TEAE and infection rates were similar with atacicept and PBO (Table). TEAE-related discontinuation rates were higher with atacicept vs PBO (16.1 vs 10.9/100 py). In the SLE-S and DBPC-S, pharmacodynamic effects of atacicept (eg on IgG) were not associated with an increase in infection rates. Across all studies (FA-S), 11 patients died during treatment. Across all indications, exposure-adjusted mortality rates/100 py (95% CI) were 3.60 (0.90–14.38), 0.34 (0.05–2.43), 1.18 (0.49–2.82) for atacicept 25, 75 and 150 mg, and 0.44 (0.06–3.12) for PBO. In SLE patients, exposure-adjusted mortality rates/100 py were 1.45 (0.54–3.87) with atacicept 150 mg and 0.78 (0.29–2.07) across all atacicept-treated patients. The underlying disease and other causes were potential confounders in most cases.
Conclusion: In this integrated safety analysis of atacicept, no consistent association was found between atacicept dose and specific TEAEs or mortality. These results support further development and evaluation of atacicept in patients in whom potential benefits may outweigh risks.

Table.Exposure-adjusted TEAE rates by dose (DBPC-S)

	Placebo, n=483	Atacicept				Total, n=1568
		25 mg, n=129	75 mg, n=384	150 mg, n=572	All, n=1085	
Total number of py	278.3	51.5	225.0	286.7	563.2	841.4
TEAE, n (rate per 100 py)						
Hypersensitivity	37 (13.9)	8 (15.7)	40 (19.1)	55 (20.4)	103 (19.4)	140 (17.6)
Infections	211 (107.8)	43 (104.4)	180 (118.7)	281 (141.3)	504 (128.7)	715 (121.7)
Serious infection	20 (7.3)	1 (1.9)	23 (10.5)	22 (7.7)	46 (8.3)	66 (7.9)
Severe infection	9 (3.2)	0	11 (4.9)	16 (5.6)	27 (4.8)	36 (4.3)
Herpes zoster	13 (4.7)	2 (3.9)	10 (4.5)	17 (6.1)	29 (5.2)	42 (5.1)
Injection site reactions	54 (20.9)	27 (64.8)	109 (63.0)	156 (72.4)	292 (67.9)	346 (50.2)
Severe hypogammaglobulinemia (IgG <3 g/L)	0	0	2 (0.9)	4 (1.4)	6 (1.1)	6 (0.7)
Cardiac arrhythmias [all]	18 (6.6)	11 (22.4)	23 (10.6)	25 (8.9)	59 (10.8)	77 (9.4)
Ventricular arrhythmias	5 (1.8)	0	4 (1.8)	6 (2.1)	10 (1.8)	15 (1.8)
Ischemic heart disorders	11 (4.0)	3 (5.9)	13 (5.9)	11 (3.9)	27 (4.9)	38 (4.6)
Embolic and thromboembolic events	11 (4.0)	1 (2.0)	6 (2.7)	9 (3.2)	16 (2.9)	27 (3.2)
Vestibular disorders	19 (7.0)	5 (9.9)	18 (8.3)	26 (9.3)	49 (8.9)	68 (8.3)
Demyelination	1 (0.4)	1 (1.9)	0	5 (1.7)	6 (1.1)	7 (0.8)
Depression	14 (5.1)	3 (5.8)	8 (3.6)	11 (3.9)	22 (3.9)	36 (4.3)
Malignant tumor	0	1 (1.9)	1 (0.4)	3 (1.1)	5 (0.9)	5 (0.6)
Serious TEAE	51 (18.9)	15 (30.0)	51 (23.9)	61 (21.8)	127 (23.4)	178 (21.9)
Severe TEAE	28 (10.2)	10 (19.6)	45 (20.9)	56 (20.0)	111 (20.3)	139 (17.0)
Discontinuation of treatment due to TEAE	30 (10.9)	14 (27.6)	30 (13.4)	46 (16.1)	90 (16.1)	120 (14.3)
Infection-related deaths, n (%)						
Deaths	0	0	0	2 (0.3)*	0	0

*Acute respiratory failure and probable leptospirosis (n=1); pneumonia and pulmonary alveolar hemorrhage (n=1)

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FRI0195 **EFFICACY AND SAFETY OF DAPIROLIZUMAB PEGOL (DZP) IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A RANDOMISED, PLACEBO (PBO)-CONTROLLED STUDY**

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Background: CD40 ligand (CD40L) regulates interactions between T cells and CD40-expressing cells including antigen-presenting cells (APC) and B cells, thereby playing a critical role in autoimmune disease pathogenesis. DZP, a PEGylated monovalent Fab' antibody fragment with specificity for CD40L, prevents CD40L engagement of CD40 and thus blocks intracellular signalling and APC activation.
Objectives: To report the 24-week efficacy and safety interim data of DZP in a phase IIb, randomised, double-blind, PBO-controlled, dose-ranging study in patients with SLE (NCT02804763).
Methods: Patients with moderately to severely active SLE (SLEDAI-2K score $\geq$6; $\geq$1 BILAG grade A or $\geq$2 BILAG grade B organ domain scores at screening) despite stable non-biologic standard of care treatment were randomised 1:1:1:1 to receive iv DZP 6, 24 or 45 mg/kg or PBO every 4 weeks for 20 weeks. Patients receiving corticosteroids (CS) $\geq$10 mg/day prednisone equivalent were required to start tapering CS by Week 4; guidance was provided, but tapering schedules were ultimately determined by the investigators. The primary objective was to establish a dose-response relationship across three doses of DZP and PBO based on BICLA response rates at Week 24. Four pre-specified dose-response models were tested by a statistical method (MCP-Mod), to determine whether any of the models fit the observed data with statistical significance (at a one-sided p$\leq$0.05). The secondary endpoint was a pairwise comparison of BICLA response rates at Week 24. Other endpoints included the SRI-4 and BICLA response rates at 12 and 24 weeks, mean changes from baseline in SLEDAI-2K scores at 12 and 24 weeks, percentage of patients with daily CS dose $\leq$7.5 mg/day at 12 and 24 weeks, pharmacodynamic (PD) markers and safety.
Results: 182 patients were randomised; 167 (91.8%) completed Week 24 of the study. Baseline demographics were similar across treatment groups. The primary endpoint was not met as none of the pre-specified dose-response models fit the observed BICLA response rates at Week 24 with statistical significance (p=0.06 for the most applicable model). BICLA response rates and other efficacy outcome measures at Weeks 12 and 24, were numerically higher for all DZP groups vs PBO (Table 1). Favourable biological effects were observed with improvements in relevant PD markers, including anti-dsDNA antibody levels, in DZP groups vs PBO. Treatment-emergent adverse events (TEAEs) and serious TEAEs were generally balanced across treatment groups (Table 2). More upper

respiratory tract infections were observed in patients treated with DZP vs PBO; the majority were mild. We observed four thromboembolic events: one in the 24 mg/kg DZP group and three in the PBO group.



Table 1. Secondary and other efficacy endpoints at Weeks 12 and 24

		Week 12				Week 24			
Full analysis set		PBO n=43	DZP 6 mg/kg n=43	DZP 24 mg/kg n=44	DZP 45 mg/kg n=46	PBO n=43	DZP 6 mg/kg n=43	DZP 24 mg/kg n=44	DZP 45 mg/kg n=46
BICLA[a]	Responders, n (%)	11 (25.6)	21 (48.8)	25 (56.8)	20 (43.5)	16 (37.2)	21 (48.8)	25 (56.8)	24 (52.2)
	Difference vs PBO (95% CI)	–	23.3 (3.4, 43.1)	31.2 (11.6, 50.8)	17.9 (–1.5, 37.3)	–	11.6 (–9.2, 32.4)	19.6 (–1.0, 40.2)	15.0 (–5.5, 35.4)
SRI-4[a]	Responders, n (%)	13 (30.2)	23 (53.5)	21 (47.7)	27 (58.7)	22 (51.2)	29 (67.4)	23 (52.3)	29 (63.0)
	Difference vs PBO (95% CI)	–	23.3 (3.0, 43.5)	17.5 (–2.7, 37.7)	28.5 (8.7, 48.2)	–	16.3 (–4.2, 36.8)	1.1 (–19.9, 22.1)	11.9 (–8.6, 32.3)
SLEDAI-2K[a]	Change in total score from baseline, mean (SD)	–2.7 (3.8)[c]	–3.7 (3.2)	–3.8 (3.1)	–3.9 (2.7)[c]	–4.3 (4.1)[c]	–5.2 (3.4)[c]	–5.2 (3.5)[c]	–5.4 (3.4)[c]
	Patients with daily CS dose ≤7.5 mg/day prednisone equivalent,[d,e] n (%)	33 (76.7)	31 (72.1)	36 (81.8)	36 (78.3)	36 (83.7)	37 (86.0)	36 (81.8)	37 (80.4)
Safety set		n=45	n=45	n=45	n=47	n=45	n=45	n=45	n=47
Anti-dsDNA (IU/mL)[f] in patients with >10 IU/mL anti-dsDNA at baseline	n	17	23	19	19	17	23	18	19
	Change from baseline, mean (SD)	–37.4 (301.4)	–39.4 (190.4)	–83.4 (265.8)	–132.5 (260.2)	+32.9 (342.2)	–133.2 (372.1)[c]	–89.8 (267.9)	–256.3 (658.3)
	Patients with ≥50% reduction in anti-dsDNA,[e] n (%)	3 (18.8)	11 (52.4)	7 (41.2)	9 (50.0)	4 (25.0)	10 (45.5)[c]	11 (68.8)	11 (68.8)
C3 (g/L) in patients with C3 <LLN at baseline	n	18	16	16	17	17	16	16	17
	Change from baseline, mean (SD)	0.01 (0.12)[c]	0.04 (0.11)[c]	0.08 (0.13)	0.10 (0.13)	0.03 (0.13)	0.06 (0.11)[c]	0.10 (0.12)	0.12 (0.11)[c]
C4 (mg/L) in patients with C4 <LLN at baseline	n	28	26	23	26	26	26	23	26
	Change from baseline, mean (SD)	–1.5 (27.0)[c]	16.8 (32.9)[c]	23.9 (36.6)	30.8 (28.9)[c]	3.9 (31.3)[c]	28.2 (43.5)	15.5 (33.2)[c]	42.0 (65.0)[c]

BICLA, BILAG 2004-Based Composite Lupus Assessment; BILAG, British Isles Lupus Assessment Group; CS, corticosteroid; ds, double-stranded; DZP, dapirolizumab pegol; LLN, lower limit of normal; PBO, placebo; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SRI-4, SLE Responder Index 4; TEAE, treatment-emergent adverse event

[a] mNRI (modified non-responder imputation): patient was deemed a non-responder if >2 items were missing. If 1 item was missing, it could be imputed from the previous visit for one visit only. [b] Observed cases. [c] n=42; [d] n=43; [e] n=39; [f] LOCF (last observation carried forward). [g] Percentage of patients with baseline CS ≤7.5 mg/day prednisone equivalent: PBO 37.2%, DZP 6 mg/kg 34.9%, DZP 24 mg/kg 40.9%, DZP 45 mg/kg 47.8%. [h] anti-dsDNA measured by the Farr assay. [i] n=18; [j] n=21; [k] n=17. [l] n=18; [m] n=22. [n] or reverting to ≤10 IU anti-dsDNA. [o] n=25; [p] n=24

Table 2. Safety and tolerability of dapirolizumab pegol during the double-blind treatment period to Week 24 (safety set)

	PBO n=45	DZP 6 mg/kg n=45	DZP 24 mg/kg n=45	DZP 45 mg/kg n=47
Serious TEAEs, n (%)	5 (11.1)	1 (2.2)	4 (8.9)	3 (6.4)
TEAEs of interest, n (%)	9 (20.0)	8 (17.8)	11 (24.4)	9 (19.1)
Thromboembolic events	3 (6.7)	0	1 (2.2)	0
Moderate to severe infections	6 (13.3)	8 (17.8)[a]	11 (24.4)	8 (17.0)

DZP, dapirolizumab pegol; PBO, placebo, TEAE, treatment-emergent adverse event

[a] One TEAE was of mild intensity but was deemed to be a TEAE of interest by the investigator for the interim analysis

Conclusion: DZP appeared to be well tolerated as TEAEs were generally balanced across the treatment groups. Numerically greater improvements relative to PBO were observed consistently across multiple efficacy endpoints and biomarkers; however, for the primary endpoint no pre-specified dose-response relationship model fit the observed BICLA response rates at Week 24 with statistical significance. The potential for deriving clinical benefit from DZP in patients with SLE warrants further investigation.

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FRI0196

TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH THE IMMUNOPROTEASOME INHIBITOR KZR-616: RESULTS FROM THE FIRST 2 COHORTS OF AN OPEN-LABEL PHASE 1B DOSE ESCALATION TRIAL

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Background: Nonspecific proteasome inhibitors, e.g., bortezomib (BTZ), target both the constitutive and immuno- proteasomes and are standard of care for multiple myeloma. While BTZ has been used to treat refractory systemic lupus erythematosus (SLE) and lupus nephritis (LN), it is associated with adverse events (AEs) that limit its broad use. KZR-616, a first-in-class selective inhibitor of the immunoproteasome, is highly active and well tolerated in murine SLE[1]. In a Phase (Ph) 1 healthy volunteer (HV) study, KZR-616 subcutaneously (SC) at 30 and 45 mg weekly (QW) was shown to be safe, be well tolerated and achieve the target level of immunoproteasome inhibition[2]. We report here the preliminary safety and efficacy of KZR-616 in the Ph 1b portion of Study KZR–616–002 in active SLE patients (pts) (NCT03393013).

Objectives: The 1° objective of this first-in-patient study is to assess the safety and tolerability of KZR–616. The 2° objectives are to evaluate pharmacokinetics (PK) and determine the KZR-616 doses for the Ph 2 portion of the study. Pharmacodynamics (PD) and efficacy are also being assessed.

Assessments Mean (SD)	Timepoint	Cohort 1 n=6	Cohort 2 n=3
SLEDAI	BL	9.7 (1.97)	10.0 (2.00)
	W13	7.2 (3.35)	6.0 (2.83)
CLASI	BL	5.5 (2.07)	7.3 (1.16)
	W13	3.6 (1.95)	4.5 (2.12)
TJC	BL	14.3 (8.14)	11.7 (4.93)
	W13	7.6 (6.99)	8.5 (3.54)
SJC	BL	11.0 (6.03)	9.3 (3.06)
	W13	4.4 (6.07)	3.5 (4.95)
PhGA	BL	58.3 (19.24)	63.3 (26.50)
	W13	39.8 (24.67)	40.0 (14.14)
PtGA	BL	57.5 (25.79)	73.3 (11.59)
	W13	43.6 (31.64)	35.0 (7.07)

Methods: This open-label multicenter dose escalation trial enrolled SLE pts (per Systemic Lupus International Collaborating Clinics Classification Criteria) with SLE Disease Activity Index (SLEDAI) ≥4 despite stable background immunosuppressant, antimalarial, and/or corticosteroid (≤20 mg prednisone equivalent) therapy. Patients received KZR-616 at 45 mg (Cohort 1) or 60 mg (Cohort 2) SC QW through Week 13 (W13) with 12 weeks of follow up. Cohort 2a is currently enrolling pts using intrapatient dose escalation from 30 to 60 mg. Safety data include AEs, vitals, electrocardiograms and laboratory tests. Efficacy measures include the SLEDAI, Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), 28 tender (T) and swollen (S) joint counts (JC), Physician Global Assessment (PhGA), and Patient Global Assessment (PtGA) in evaluable pts (receive ≥1 month of KZR-616; non-evaluable pts can be replaced).

Results: We enrolled 13 pts: 8 in Cohort 1, 5 in Cohort 2. The pts were 100% female; Baseline (BL) median SLEDAI was 10.0. All pts received at least 1 dose of KZR-616. In each cohort, 3 pts withdrew due to withdrawal of consent prior to W13. Overall, the 45 mg dose was well tolerated with no SAEs; all AEs were mild in intensity. The most common AEs were injection site erythema (62.5%), nausea (25%), and injection site pruritus (25%).Cohort 2 (60 mg) enrollment was halted, as all pts experienced vomiting within 8-24 hours (h) of their first dose, which typically resolved within 24 h. One pt had an SAE of thrombotic microangiopathy. Two pts permanently reduced their dose to 45 mg. After 2 doses at 45 mg, another pt successfully re-escalated to 60 mg. In

Cohort 2a (n=5 to date), there has been 1 SAE of localized herpes zoster. In pts, PK and PD were similar to that achieved for the same doses in HV[1]. Efficacy data for evaluable pts are shown in the table. Two (33%) and 2 (67%) evaluable pts in Cohorts 1 and 2, respectively, had a SLEDAI improvement of ≥4 points from BL at W13.

Conclusion: KZR-616 dosed at 45 mg SC QW appears to be safe and well tolerated and showed evidence of disease suppression at W13 in active SLE pts on stable background therapy. The Ph 2 doses in the first randomized placebo-controlled trial with KZR-616 in active LN pts on mycophenolate and prednisone will be 30 and 45 mg. Efforts are ongoing to evaluate KZR–616 doses ≥60 mg using step–up dosing.

REFERENCES:
[1] Muchamuel, et al. ARD 2018. 77:A685.
[2] Lickliter, et al. ARD 2018. 77:A1413.

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FRI0197 EFFICACY DATA OF MC2–03 (CICLOSPORIN 0.03% AND 0.06% EYEDROPS) IN SJOGREN'S PATIENTS WITH SEVERE KERATITIS: OUTCOMES OF THE NORTHERN LIGHTS PHASE 2B TRIAL

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Background: Sjögren's syndrome is one of the most common rheumatic autoimmune disorders (1). It is a chronic systemic autoimmune disease in which immunomediated inflammation, characterized by lymphocytic infiltration of exocrine glands and epithelia, causes secretory gland dysfunction leading to dryness of the main mucosal surfaces (2) including dry eye with severe keratitis. Ciclosporin is a well-known immunosuppressant with anti-inflammatory properties through inhibition of cell-mediated reactions (inhibit the release of cytokines including IL-2).

Objectives: To report the clinical efficacy of MC2-03 (ciclosporin 0.03% and 0.06% eyedrops) in Sjogren's patients with severe keratitis from a 6-month clinical trial.

Methods: The NORTHERN LIGHTS trial is a randomized, double masked, controlled multicentre European trial that assessed MC2-03 0.03%, MC2-03 0.06%, vehicle and best-standard-of-care (BSC) for the treatment of moderate-to-severe dry eye disease (patients having baseline corneal fluorescein staining (CFS) score 3 or 4). The full analysis set consisted of a total of 255 patients with 66 patients having a documented history of Sjögren's syndrome. The objective of the trial was to evaluate safety and efficacy of MC2-03 after treatment once daily for 6 months followed by a 3 month safety follow-up. The primary efficacy endpoint was the proportion of patients achieving 2-grade improvement in CFS. CFS was evaluated using the modified Oxford grading system: a 7-point ordinal scale (0, 0.5, and 1 to 5), where grade 0 represents complete corneal clearing (absence of staining dots).

Results: The 66 patients with documented history of Sjögren's syndrome constituted 25.9% of the trial population with 90.9% of the patients being females (n=60). Among the Sjögren patients, 58% (n=38) had severe dry eye (CFS 4) at baseline. Data analyzed for observed cases showed that the proportion of Sjogren's patients achieving 2-grade improvement of CFS (baseline CFS 3 and CFS 4) was higher in MC2-03 groups compared to the control groups (Table 1). When patients treated with any active were compared to patients treated with any control, a 2-grade improvement of the CFS was observed in 51.9% patients in the combined active group vs. 26.7% for the combined control group (p=0.0620).

Table 1. Sjögren patients with 2-grade reduction in CFS

MC2-03 0.06%	MC2-03 0.03%	vehicle	BSC	Combined active	Combined control	Significance
7/16 (43.8%)	7/11 (63.6%)	4/14 (28.6%)	4/16 (25%)	14/27 (51.9%)	8/30 (26.7%)	p=0.0620

Using the same approach, the most severe patients, having CFS 4 at baseline, had a statistically significantly higher responder rate of 64.3% in the combined active group versus 21.1% in the combined control group (p=0.0286).

Table 2. Severe Sjögren patients with 2-grade reduction in CFS

Combined active	Combined control	Significance
9/14 (64.3%)	4/19 (21.1%)	p=0.0286

Conclusion: Data from the NORTHERN LIGHTS trial show that MC2-03 ciclosporin eyedrops has the potential to be a safe, well-tolerated and efficient treatment in Sjogren's patients.

REFERENCES:
[1] Fox, et al. 2000
[2] Kassan, et al. 2004

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FRI0198 ANTIMALARIAL AGENTS DIMINISH WHILE METHOTREXATE, AZATHIOPRINE AND MYCOPHENOLIC ACID INCREASE BAFF LEVELS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Elevated levels of the B cell activating cytokine BAFF (also known as BLyS) have been associated with active systemic lupus erythematosus (SLE), and the anti-BAFF monoclonal antibody belimumab has been approved as an add-on to standard-of-care SLE treatment, the latter mainly comprising glucocorticoids, antimalarial agents (AMA) and other immunosuppressive treatments.

Objectives: To investigate the effect of AMA and three other commonly used in SLE immunosuppressive agents (methotrexate, azathioprine, mycophenolate mofetil/sodium) on serum BAFF levels.

Methods: Access to data from the phase III clinical trials of belimumab BLISS-52 (n=865; NCT00424476) and BLISS-76 (n=819; NCT00410384) was granted by GlaxoSmithKline (Uxbridge, UK); a total of 1684 SLE patients were analysed. Serum samples obtained prior to belimumab initiation were stored at -80°C until BAFF level determination by ELISA. The non-parametric Mann-Whitney *U* test was used to compare BAFF level distributions between treatment groups. Linear regression models were applied to determine independence.

Results: BAFF levels (mean, SD; pg/mL) were higher in patients receiving methotrexate (1835, 1617; n=212; *P*=0.001), azathioprine (1901, 1472; n=364; *P*<0.001) or mycophenolate mofetil/sodium (1994, 1544; n=175; *P*<0.001) and no immunosuppressive treatment other than the one investigated compared with patients receiving no immunosuppressive treatment (1593, 1929; n=860); AMA were allowed in both groups, in all comparisons. In contrast, patients on AMA displayed lower BAFF levels (1654, 1318; n=1085) compared with patients who did not use AMA (1942, 2408; n=580; *P*=0.002). In linear regression, AMA use showed a consistent and independent association with lower BAFF levels in all models, whereas use of each one of methotrexate, azathioprine and mycophenolic acid was associated with higher BAFF levels. All models were adjusted for the use of immunosuppressive agents other than the one investigated.

Conclusion: Our data imply differential effects of antimalarial agents and other immunosuppressive treatments on BAFF levels; AMA diminished while methotrexate, azathioprine and mycophenolic acid increased BAFF levels. It is worth noting that methotrexate and mycophenolic acid are not approved for the treatment of SLE. Considering the importance of BAFF in B cell homeostasis and SLE pathogenesis, exploration of the biological significance of the differential effects of different immunosuppressive agents on BAFF levels is anticipated.

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FRI0199 **EFFECTIVENESS AND SAFETY OF BELIMUMAB IN PATIENTSWITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM A LARGE, NATIONWIDE, MULTICENTRIC STUDY**

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Background: Belimumab is the unique biologic therapy available for patients with SLE.

Objectives: To investigate effectiveness and safety of belimumab in SLE patients in clinical practice.

Methods: 458 active SLE patients (ACR criteria) from 24 Italian Centers, mean±SD age 43.5±11.3 years; mean±SD disease duration 12.3±8.7 years, were treated with belimumab (10 mg/kg day 0, 14, 28 and then every 28 days), as add-on therapy.

SLEDAI-2K, anti-dsDNA, C3, C4, prednisone daily dose, DAS-28, 24H proteinuria, CLASI, PGA, Fatigue (VAS 0-10) were recorded at baseline and every 6 months. Flares were defined according to SFI. Response was evaluated according to SRI-4. Statistics were performed by pairs T-test, chi-square test and multiple logistic regression (SPSS, version 22.0).

Results: Mean±SD follow-up was 21.2±15.3 months (range 3-60). Most common features treated with belimumab were articular in 67%, mucocutaneous in 55%, and renal in 17% of cases. Improvement of clinical and serological variables, including daily prednisone dosage, was observed (Table). SRI-4 is summarized in the Figure.

At the end of follow-up 293 patients (66%) were still on belimumab. Most common cause of discontinuation were inadequate response (36%), AEs (31%), and pregnancy (8%).

Mean number of flare during belimumab treatment compared with the corresponding period before belimumab initiation decreased (p<0.001). SLEDAI-2K $\geq$10 was an independent predictor of response by logistic regression at month 12 and 24 (p=0.003 and p=0.025).

9,998 infusions were analyzed. 784 AEs were observed in 330 patients, SAEs were 43 in 36 patients. No severe infusion reactions were observed; 16 patients had infective SAEs, and 22 non infective SAEs.

Conclusion: We confirmed the effectiveness, the steroid sparing effect and good safety profile of belimumab in our cohort.

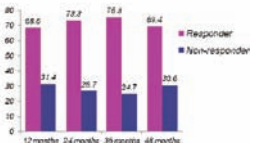
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Table. Variation of clinical and serologic disease activity variables in patients with active lupus treated with belimumab

	N° pts*	Baseline	6 months	12 months	18 months	24 months	30 months	36 months	48 months	p
SLEDAI-2K	458	8.1±3.4	4.9±3.3	3.8±2.7	3.8±3.2	3.5±2.8	2.6±2.8	2.8±2.4	2.7±2.1	<0.0001
Prednisone dosage (mg/day)	458	10.5±8.1	6.7±4.6	5.3±4.7	4.5±4.8	3.8±3.7	3.5±2.9	3.4±4.3	3.4±4.5	<0.0001
DAS-28	309	3.4±1.7	2.5±1.5	2.2±1.4	1.9±1.4	1.7±1.3	1.6±1.5	1.5±1.4	1.4±1.4	<0.0001
CLASI-a	254	3.3±4.7	1.9±3.3	1.1±2.2	0.8±2.1	0.6±1.8	0.6±1.4	0. 6±1.4	0.2±0.7	<0.0001
PGA (0-3)	356	1.8±0.6	1.2±0.7	0.8±0.6	0.8±0.7	0.8±0.6	0.7±0.6	0. 7±0.6	0.7±0.6	<0.0001
Fatigue (VAS 0-10)	197	5.2±3.0	4.3±2.8	3.3±2.6	2.8±2.7	2.8±2.6	2.5±2.9	2.3±2.7	2.4±2.9	<0.0001
Anti-dsDNA (ELISA, KUI/L)	131	230±354	144±217	118±179	107±164	99.2±162	71.5±104	74.4±145	23.0±56.2	<0.006
C3 (mg/dl)	458	50.1±38.8	57.9±41.0	61.2±41.8	59.9±43.1	62.1±41.8	59.2±43.2	64.9±42.6	73.3±45.5	<0.001
C4 (mg/dl)	458	7.7±7.7	10.1±8.5	11.2±9.3	11.2±9.1	11.9±9.3	11.0±9.3	13.8±10.1	13.6±9.7	<0.006
24-h proteinuria (g/die)	77	1.4±1.1	0.8±0.9	0.6±0.6	0.6±0.7	0.6±0.6	0.7±0.8	0.4±0.5	0.6±0.6	0.012

*Number of patients at baseline. p calculated using univariate analysis
SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index-2000; CLASI-a: Cutaneous Lupus erythematosus Area and Severity Index-activity; DAS-28: disease activity score-28 joints; anti-dsDNA: anti-double stranded DNA ELISA: Enzyme-Liked ImmunoSorbent Assay; pts: patients; CLIA: chemiluminescent immunoassay

Figure. SRI-4 after belimumab in 406 SLE patients



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FRI0200 REVIEW OF HYDROXYCHLOROQUINE USE AND DEVELOPMENT OF A REGIONAL STRATEGY TO MINIMISE RETINAL TOXICITY

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Background: Guidelines from the Royal College of Opthalmologists in February 2018 were developed for retinal screening for patients on hydroxychloroquine, as recent evidence suggests the risk of retinal toxicity is higher than previously reported. The prevalence of retinal toxicity in long term use appears to be 7.5% and depending on dose and duration of therapy can increase to 20-50% after 20 years of therapy. Risk is increased for patients taking more than 5mg per kg per day of hydroxychloroquine, patients on Tamoxifen and those with renal impairment. The guidelines recommend the use of a standardised referral proforma to help identify patients who are high risk.
Objectives: 1. Audit of Hydroxychloroquine use and retinal screening in the Belfast Health and Social Care Trust (BHSCT)
2. Develop a regional referral proforma and screening service for retinal toxicity
Methods: Patients who were treated with hydroxychloroquine, under the care of a consultant rheumatologist were identified on the database. A proforma was used to aid data collection and patients' electronic records were reviewed. We audited the use of hydroxychloroquine and retinal screening against current Royal College of Ophthalmology (RCO) guidelines. We designed a standardised referral proforma and regional screening strategy in conjunction with ophthalmology colleagues.
Results: There were 151 patients identified on hydroxychloroquine on the database. 40 of these patients had stopped hydroxychloroquine, 2 of which had retinal toxicity. Therefore the rate of retinal toxicity in this sample was 1.3% (2/151).
There were 111 patients who remained on hydroxychloroquine treatment with a female: male ratio of 9:1. Age range was from 22 to 84, with a mean age of 55. There were 44% of patients on hydroxychloroquine for rheumatoid arthritis, 25% had systemic lupus erythematosus, 8% had Sjogrens syndrome, 6% had pallindromic rheumatoid arthritis and 13% had other connective tissue diseases. The majority (79%) of patients were on 200mg hydroxychloroquine daily and 19% were on 400mg daily. 6% of patients had an eGFR<60. No patients were on tamoxifen. 73% of patients were on hydroxychloroquine treatment for over 5 years. Retinal screening was overdue in 64% of patients.
Conclusion: In this sample, only 1.3% of patients had evidence of retinal toxicity, although 64% of patients were overdue retinal screening. We developed a referral proforma and a regional screening strategy in line with RCO guidelines. In order to meet the RCO guidelines, we recognise the need for substantial investment in regional ophthalmology services.

REFERENCES:

[1] Royal College of Ophthalmologists. (2018) Clinical Guidelines. Hydroxychloroquine and Chloroquine Retinopathy:Recommendations on Screening.

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FRI0201 REAL WORLD MEDICATION USE IN INCIDENT SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that causes inflammation in connective tissues and can involve multiple organs systems. Lupus nephritis (LN) is an inflammatory kidney disease caused by SLE. There is a gap in the literature regarding the standard of care in SLE and LN patients.
Objectives: This study generated real world medication use among SLE and LN patients.
Methods: This retrospective study used data from two large administrative databases in the US: Truven Health MarketScan® and Optum® databases to identify adult patients (≥18 years of age) with ≥2 medical claims on different dates for SLE or LN diagnoses from 01JAN2013-31DEC2015. SLE was identified using the International Classification of Diseases, 9th and 10th Revision, Clinical Modification [ICD-9-CM] codes (710.0) OR ICD-10-CM (M32.10-M32.19, 32.8, 32.9). LN was captured as a subset of SLE using [ICD-9-CM: 710.0 AND (581.81 or 582.81 or 583.81); OR (ICD-10-CM:M32.14)]. The first SLE or LN diagnosis was designated as the index date. Patients were required to have continuous health plan enrollment for 1 year pre-index date (baseline period) and 1 year post-index date (follow-up period) and no prior SLE/LN diagnosis claims or belimumab medical/prescription claim during the baseline period to ensure incident patients were captured. The Truven Health MarketScan® and Optum® databases were pooled together and duplicates were identified and retained in MarketScan® only. Patient demographics and clinical characteristics during the baseline period were assessed. SLE treatment used during the follow-up period was evaluated and the proportion of patients that used SLE medications and average number of medical/prescription claims (#Rx) for each medication were provided.
Results: A total of 31,345 patients were identified including 30,086 SLE and 1,259 LN patients. Key results are shown in Table 1. The mean age was 52.7 years for SLE and 48.3 years for LN patients. Over 80% of the patients were female, with a mean Charlson Comorbidity Index (CCI) score of 1.1 and 1.8 for SLE and LN patients respectively. The most common comorbidities at baseline were hypertension and infections. Corticosteroids (SLE= 58.3%, #Rx=4.5; LN=66.2%, #Rx=6.5) and hydroxychloroquine (SLE=43.4%, #Rx=5.8; LN=40.7% #Rx=6.2) were the most commonly used SLE medications during 1-year follow up period. Approximately 2% of patients used biologics including belimumab (SLE=1.1%, #Rx=8.8; LN=1.4%, #Rx=8.3) and rituximab (SLE=0.9%, #Rx=4.2; LN=2.1%, #Rx=4.0).

Table 1. SLE Medications during 1 year of follow-up period

	Systemic Lupus Erythematosus (N=30,086)	Lupus Nephritis (N=1,259)
SLE Medications, N (%)		
Corticosteroids[a]	17533 (58.3%)	834 (66.2%)
Number of prescriptions, Mean (SD)	4.5 (5.0)	6.5 (6.0)
Hydroxychloroquine	13061 (43.4%)	513 (40.7%)
Number of prescriptions, Mean (SD)	5.8 (3.6)	6.2 (3.7)
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)[b]	11342 (37.7%)	271 (21.5%)
Number of prescriptions, Mean (SD)	3.6 (4.0)	3.0 (3.9)
Angiotensin Converting Enzyme Inhibitor (ACE)[c]	3827 (12.7%)	409 (32.5%)
Number of prescriptions, Mean (SD)	5.4 (3.7)	5.4 (3.7)
Angiotensin II Receptor Blockers (ARB)[d]	3376 (11.2%)	318 (25.3%)
Number of prescriptions, Mean (SD)	5.8 (3.7)	5.6 (4.0)
Methotrexate	2884 (9.6%)	62 (4.9%)
Number of prescriptions, Mean (SD)	5.5 (4.1)	4.9 (3.3)
Immunosuppressant[e]	1239 (4.1%)	83 (6.6%)
Number of prescriptions, Mean (SD)	4.8 (3.8)	4.1 (2.9)
Cyclosporine	1090 (3.6%)	40 (3.2%)
Number of prescriptions, Mean (SD)	2.7 (2.6)	3.8 (3.9)
Mycophenolate Mofetil	985 (3.3%)	397 (31.5%)
Number of prescriptions, Mean (SD)	5.2 (3.7)	6.0 (4.0)
Leflunomide	523 (1.7%)	15 (1.2%)
Number of prescriptions, Mean (SD)	4.3 (3.3)	4.7 (4.0)
Belimumab	306 (1.0%)	17 (1.4%)
Number of medical/prescription claims, Mean (SD)	8.8 (6.5)	8.3 (6.7)
Rituximab	275 (0.9%)	26 (2.1%)
Number of medical/prescription claims, Mean (SD)	4.2 (4.0)	4.0 (4.5)
Cyclophosphamide	98 (0.3%)	67 (5.3%)
Number of prescriptions, Mean (SD)	5.0 (5.0)	4.4 (2.7)

SD: Standard Deviation

[a]**Corticosteroids**: Prednisone, Betamethasone, Budesonide, Cortisone, Desoxycorticosterone, Dexamethasone, Fludrocortisone, Hydrocortisone, Methylprednisolone, Paramethasone, Prednisolone, Triamcinolone

[b]**NSAIDs**: Diclofenac, Bromfenac, Choline and Magnesium salicylate, Methanamine and sodium salicylate, Fenoprofen, Flurbiprofen, Ketoprofen, Naproxen, Oxaprozin, Sulindac, Piroxicam, Etodolac, Meloxicam, Nabumetone, Celecoxib/Celebrex, Indomethacin, Mefenamic acid, Meclofenamate, Diflunisal, Tolmetin, Salsalate, Aspirin, Ibuprofen, Ketorolac

[c]**ACE:** Captopril, Enalapril/ Enalaprilat, Fosinopril, Lisinopril, Moexipril, Perindopril, Quinapril, Ramipril, Trandolapril, Benazepril

[d]**ARB:** Candesartan, Eprosartan, Irbesartan, Losartan, Olmesartan, Telmisartan, Valsartan, Azilsartan

[e]**Immunosuppressant:** Azathioprine, 6 mercaptopurine

Conclusion: Our findings indicate a nominal use of biologics (2%) among SLE and LN patients. Corticosteroids and hydroxychloroquine were the most commonly used SLE treatments. These data reveal an unmet need for availability of advanced therapy to treat SLE and LN. Future studies are warranted to understand the underlying causes.

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FRI0202 SHORT AND LONG-TERM FOLLOW-UP OF APREMILAST THERAPY IN REFRACTORY SKIN LUPUS LESIONS

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Background: Treatment of skin lupus lesions (SLL) was based on topical therapy (corticosteroids, calcineurin inhibitors), systemic corticosteroids, antimalarials and immunomodulatory drugs including thalidomide. However, there are refractory patients to conventional treatment. Apremilast, an inhibitor of phosphodiesterase-4 (PDE-4), may be useful in these cases.

Objectives: Our objective was to assess the efficacy and safety of apremilast.

Methods: We set up an observational study of 8 patients with diagnosis of refractory SLL and treatment with apremilast at a standard dose of 30 mg/ 12 hours. The outcome was the presence of improvement and the appearance of side effects.

Results: 8 patients (7 female/1 male) with mean age of 39.9±10.6 years with SLL were studied. Patients were diagnosed as follows: discoid lupus (n=5) and systemic lupus erythematosus (SLE) (n=3). Patients with SLE were classified as lupus panniculitis (n= 1), polycyclic ring lupus (n=1) and psoriasiform lupus (n=1). All skin lesions were confirmed by biopsy (**table**).

Before apremilast, all patients had received conventional therapy without improvement: topical corticosteroids (n=8), topical tacrolimus (n=4), oral corticosteroids (n=5), antimalarials (n=8), thalidomide (n=1), belimumab (n=3) and rituximab (n=2).

The time between SLL diagnosis and apremilast beginning was 145.1 ±79.4 months. After a mean follow-up of 14.4±4.8 months, all patients presented improvement of skin lesions (4 of them with complete response). Due to the appearance of gastrointestinal symptoms (diarrhoea, vomiting) it was necessary to reduce the dose of apremilast to 30 mg/ day in one patient and finally, it was discontinued due to no improvement with antiemetic and probiotic treatment.

Conclusion: Apremilast seems useful and relatively safe in patients with refractory SLL to conventional treatment.

Table.

					Apremilast onset		Follow-up			
Patient	Age/Sex	Skin Lupus Lesions (SLL)	Previous treatment	Months from diagnosis to apremilast onset	Antinuclear antibody	Combined treatment	Months from apremilast onset	Side effects	Discontinued	Response
1	47 / Female	Polycyclic ring lupus	Prednisone Antimalarials Thalidomide Belimumab, RTX	300	ANA 1/1280	Prednisone	12	Diarrhoea	No	Partial
2	46 / Female	Lupus panniculitis	Prednisone Antimalarials	156	ANA 1/1280	Prednisone Antimalarials	17	No	No	Complete
3	37 / Male	Discoid lupus	Prednisone Antimalarials	ND	ANA (-)	Prednisone Antimalarials	16	Diarrhoea Vomiting	Yes	Complete
4	58 / Female	Discoid lupus	Prednisone Antimalarials	72	ANA (-)	Prednisone Antimalarials	16	No	No	Complete
5	38 / Female	Discoid lupus	Prednisone Antimalarials	120	ANA (-)	Prednisone Antimalarials	20	No	No	Complete
6	24 / Female	Psoriasiform lupus	Prednisone Antimalarials Tacrolimus Belimumab, RTX	92	ANA 1/160	Prednisone Antimalarials	15	No	No	Partial
7	34 / Female	Discoid lupus	Prednisone Antimalarials	89	ANA 1/320	Prednisone Antimalarials	5	No	No	Partial
8	42 / Female	Discoid lupus	Prednisone Antimalarials Tacrolimus Belimumab	187	ANA (-)	Prednisone Antimalarials Tacrolimus	5	No	No	Partial

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FRI0203 CONCORDANCE OF DORIS REMISSION CRITERIA WITH THE TREATING PHYSICIAN'S (DORIS-)INDEPENDENT REMISSION JUDGMENT IN A SLE-COHORT AT A TERTIARY CENTER

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Background: The definition of an accurate target for a treat to target (T2T) approach in SLE has been challenging over the past years. Recently four definitions of remission were presented by the international DORIS task force. [1]

Objectives: Aim of this study was to evaluate the frequency of remission in our outpatient SLE cohort and to assess feasibility and concordance of the remission definitions with the treating physician's opinion regarding the patient's state.

Methods: In this monocentric cross-sectional study patients with SLE according to the 1997 American College of Rheumatology (ACR) criteria were enrolled and assessed between September 2016 and December 2017. DORIS remission definitions were applied and demographic and laboratory data as well as disease activity (SLEDAI), steroid dosage and physician global assessment were evaluated. After the clinical consultation, the treating physicians answered the question if his/her patient was in remission.

Results: A total of 233 patients were included (87.6% female). 88 (37.8%) patients fulfilled any of the four DORIS remission definitions, while 129 patients were in remission according to their physician's judgement. Of the 88 in DORIS remission, 17 were in complete remission, 20 in clinical remission, 16 in complete remission on treatment (ROT) and 35 in clinical ROT. In most cases the treating physician agreed on their patient being in remission (94.1% for complete remission, 90.0% for clinical remission, 81.3% for complete ROT, 88.6% for clinical ROT). A total of 145 patient were not in any DORIS remission. We observed discordance in the assessment of remission in 58 patients (24.9%), 10/88 being not in remission according to their treating physician despite fulfilling the DORIS remission definition and 48/145 were considered in remission though not in DORIS remission. Reasons for failing DORIS remission in the patients with attested physician's remission were an elevated cSLEDAI Score (n=22), elevated (n=24) or missing (n=1) physician global assessment, and prednisolone dosage >5 mg (n=9).
Conclusion: DORIS remission proved an achievable target in our outpatient clinic. Still we found discordance regarding DORIS remission and the treating physician's judgement with a greater number of patients considered in remission by their physicians. Main reasons were a cSLEDAI>0 and physician global assessment >0.5. Further analyses are needed to better characterize cases of disagreement and to address the question, if the rather strict DORIS criteria are needed to improve long-term outcome.

REFERENCE:

[1] van Vollenhoven, Ronald; Voskuyl, Alexandre; Bertsias, George; Aranow, Cynthia; Aringer, Martin; Arnaud, Laurent, et al. (2017): A framework for remission in SLE: consensus findings from a large international task force on definitions of remission in SLE (DORIS). In: Annals of the rheumatic diseases 76 (3), S. 554–561. DOI: 10.1136/annrheumdis-2016-209519

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FRI0204 SAFETY, TOLERABILITY, PHARMACOKINETIC AND PHARMACODYNAMIC EFFECT OF BIIB059, A MONOCLONAL ANTIBODY TARGETING BDCA2 FOLLOWING ADMINISTRATION OF SUBCUTANEOUS SINGLE DOSES IN JAPANESE HEALTHY VOLUNTEERS

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Background: BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, when ligated inhibits the production of inflammatory mediators and Type I Interferon (INF), a major player in Systemic Lupus Erythemtosus's (SLE) pathogenesis. Hence, targeting BDCA2 with BIIB059 represents an attractive therapeutic strategy. BIIB059 was previously tested in a Phase 1 study in non-Japanese healthy volunteers (HV) (NCT02106897) and is currently in phase 2 development for the treatment of SLE and Cutaneous Lupus Erythematosus (CLE) (NCT02847598)*
Objectives: This phase 1 study evaluated the safety, tolerability, pharmacokinetics (PK) and pharmacodynamic (PD) of BIIB059 in Japanese HV (NCT03224793)
Methods: A total of 32 HV from Japanese descend were enrolled into 4 cohorts (6 BIIB059: 2 Placebo) to receive a single subcutaneous (SC) injection of 20-, 50-, 150- or 450 mg of BIIB059 or placebo. Blood samples were obtained to characterize PK and PD profiles and establish PK-PD relationships for BIIB059. Safety and tolerability data were monitored and reviewed by the Safety Surveillance Team.
Results: BIIB059 was generally well tolerated; no SAEs were observed. Adverse events were reported by 9 subjects (37.5%) and none (0.0%) in the BIIB059- and placebo-treated subjects, respectively. Overall, 95.8% and 4.2% subjects reported AEs that were mild or moderate in severity, respectively. Three subjects (12.5%) experienced AEs considered related to study drug and mild in severity. All AEs resolved without treatment. There were no clinically significant findings on laboratory or physical examination. Following single SC BIIB059 administration, Cmax and AUC (0-inf) increased in a dose-proportional manner. Mean t1/2 ranged from 10 to 27 days. Eleven subjects (45.8%) treated with BIIB059 tested positive for anti-BIIB059 antibodies at $\geq$ 1 postdose timepoint (ADA). There was no apparent relationship between incidence of ADA and dose, no apparent effect on drug exposure and no association with clinically relevant observations. Following BIIB059 administration, BDCA2 expression on pDCs sharply decreased with levels returning towards baseline in a dose-dependent manner as serum concentrations of BIIB059 decreased. Circulating pDC numbers were highly variable in individuals at baseline and overtime. pDCs transiently decreased following administration of BIIB059 and to a lesser extent placebo, and returned towards baseline levels at later timepoints. No consistent dose- or time-dependent effect on pDC numbers was observed in the BIIB059-treatment groups.
Conclusion:

- BIIB059 was well tolerated.
- BIIB059 exposure increased with dose in a dose–proportional manner.
- BDCA2 expression on pDCs decreased rapidly and sharply and returned to baseline levels in a dose–dependent manner.

Disclosures: CM, FG, HN, HC, AS, XH and NF are employees and shareholders of Biogen

REFERENCES:

[1] ***Martin D**, et al. Arthritis Rheumatol. 2016; 68 (suppl10): poster 774; **Naik H**, et al. Arthritis Rheumatol. 2017; 69 (suppl 10); poster 2607; **Furie R**, et al. J Clin Invest. 2019 Jan 15. pii: 124466. doi:10.1172/JCI124466. [Epub ahead of print]

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FRI0205 ANTIMALARIAL AGENTS IMPROVE PHYSICAL FUNCTIONING IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with systemic lupus erythematosus (SLE) suffer an impaired health-related quality of life (HRQoL), and the majority of them experience fatigue as a major problem. Traditionally, treatment of SLE has been symptomatic, and antimalarial agents (AMA) are considered a cornerstone of SLE treatment. In previous literature, results regarding the effect of antimalarial agents on HRQoL have been conflicting.
Objectives: In this study, we aimed at investigating the potential influence of AMA on SLE patients' self-perception of HRQoL aspects.
Methods: We utilised pooled baseline data from the BLISS-52 and BLISS-76 clinical trials of belimumab (n=1684). Access to data was granted by GlaxoSmithKline. The patients' HRQoL and fatigue were self-reported using the Medical Outcomes Study (MOS) short form 36 (SF-36) health survey, the functional assessment of chronic illness therapy (FACIT)-Fatigue scale and the three-level EuroQol- 5 Dimension (EQ-5D) questionnaire. Minimal clinically important difference (MCID) was set to $\geq$5.0 points for SF-36 subscales, $\geq$2.5 points for SF-36 component summary scores, and $\geq$4 points for FACIT-Fatigue scores. High disease activity was defined as a SELENA-SLEDAI score $\geq$10. Organ damage was assessed using the SLICC/ACR Damage Index (SDI). The non-parametric Mann-Whitney *U* test was used for comparisons between AMA users and non-users. Linear regression models were next used in order to adjust for possible confounding factors; these included age, sex, ethnic origin, SLE disease activity, SLE duration, organ damage, corticosteroid use and use of other immunosuppressive agents.
Results: Results are presented as mean values ± standard devation. Patients receiving AMA (n=1098) performed better than patients who did not receive AMA (n=586) with regard to SF-36 physical component summary (PCS) scores (39.6 ± 9.5 versus 38.1 ± 9.9; *P*=0.001), physical

functioning (61.1 ± 24.9 versus 55.0 ± 26.5; *P*<0.001), role physical (53.2 ± 26.9 versus 50.3 ± 27.7; *P*=0.036), bodily pain (49.5 ± 23.8 versus 47.1 ± 25.3; *P*=0.016), FACIT-Fatigue scores (30.5 ± 11.8 versus 29.3 ± 11.9; *P*=0.046), EQ-5D scores (0.75 ± 0.18 versus 0.72 ± 0.19; *P*=0.004) and EQ-5D visual analogue scale (VAS) scores (64.6 ± 19.4 versus 61.7 ± 18.6; *P*=0.001). The difference in SF-36 physical functioning was the greatest one among the SF-36 parameters, exceeding the corresponding MCID (≥5.0 points). The association between AMA use and better physical functioning was still significant after adjustment for potential confounding factors (standardised coefficient, β=0.08; *P*=0.001). In this analysis, Asian patients performed better in physical functioning (β=0.07; *P*=0.004) while African/African American patients performed worse (β=-0.07; *P*=0.003). High disease activity (β=-0.09; *P*<0.001) and organ damage (β=-0.12; *P*<0.001) were also independent factors of worse physical functioning, whereas corticosteroid use independently improved the outcome (β=0.06; *P*=0.022).

Conclusion: AMA use contributes to better physical functioning in patients with SLE, independently of other factors.

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FRI0206 HYDROXYCHLOROQUINE BLOOD LEVELS PREDICT RETINOPATHY IN SLE

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Background: Hydroxychloroquine (HCQ) retinopathy after 10 years or more of use is more frequent than previously appreciated. This led to new ophthalmology guidelines that changed the recommended dosing from 6.5 mg/kg to 5 mg/kg (1). However, it is not clear that the lower dose of hydroxychloroquine will have the same efficacy for SLE activity or the same protective role against cardiovascular risk factors and thrombosis.

Table 1. Risk of HCQ retinal toxicity (univariate)

	No	Yes		
Characteristic	n (%)	n (%)	p	P for Trend
Sex			0.1029	
Female	475 (96.2)	19 (3.8)		
Male	39 (90.7)	4 (9.3)		
Ethnicity			0.3804	
White	238 (94.4)	14 (5.6)		
Black	215 (96.4)	8 (3.6)		
Other	61 (98.4)	1 (1.6)		
Age			<0.0001	<0.0001
<45	215 (99.5)	1 (0.5)		
45-59	175 (95.6)	8 (4.4)		
60+	124 (89.9)	14 (10.1)		
HCQ max			0.0340	0.0143
1 (0 to 1182)	161 (98.8)	2 (1.2)		
2 (1183 to 1752)	157 (95.2)	8 (4.8)		
3 (1753 to 6281)	153 (93.3)	11 (6.7)		
HCQ duration			0.0006	0.0002
1 (0 to 8yrs)	158 (98.8)	2 (1.2)		
2 (9 to 15yrs)	139 (97.2)	4 (2.8)		
3 (16 to 48yrs)	154 (90.1)	17 (9.9)		
BMI			0.1701	0.0160
<20	50 (98.0)	1 (2.0)		
20-25	171 (97.7)	4 (2.3)		
25-30	159 (95.2)	8 (4.8)		
30-35	76 (95.0)	4 (5.0)		
35+	58 (90.6)	6 (9.4)		
HTN Ever			0.0020	
Yes	276 (93.2)	20 (6.8)		
No	238 (98.8)	3 (1.2)		

Objectives: We asked whether hydroxychloroquine blood levels could help identify those at greater future risk of retinopathy.

Methods: We analyzed data on 537 SLE patients from a clinical cohort who had repeated assessments of HCQ blood concentrations, and were evaluated one or more times for retinopathy (300 single retinopathy exam, 149 two and 88 three or more assessments). The patients were 92% female and 42% Caucasian. Hydroxychloroquine blood levels were performed as previously described. In our analysis, HCQ toxicity was defined dichotomously by a retina expert: all those with a value of "No" or "Possible" were categorized as not having HCQ toxicity, and those who had a "Yes" were categorized as having it. Mean and maximum HCQ blood concentration over all cohort visits prior to the final retinopathy assessment were calculated. Risk of HCQ toxicity was then assessed in tertiles defined by these variables.

Results:

Conclusion: Our data show that the risk of HCQ retinopathy is higher in men and Caucasians. As expected, it is higher in older patients and with greater duration. We also found that BMI and hypertension were predictive of HCQ retinopathy. For the first time, our data show the utility of HCQ blood levels in predicting retinopathy. This would allow clinicians to either decrease dose or increase monitoring in those with high blood levels.

REFERENCES:

[1] Marmor MF, Kellner U, Lai TYY, Melles RB, Mieler WF. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (2016 revision). Ophthalmology 2016;123:1386–1394.

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FRI0207 BASELINE LEVELS OF BAFF, APRIL AND CD8+ EFFECTOR MEMORY CELLS AS PREDICTORS OF SLEDAI RESPONSE TO BELIMUMAB THERAPY

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Background: Systemic lupus erythematosus (SLE) patients show high circulating levels of BLyS (B lymphocyte stimulator, also known as BAFF) and of other cytokines belonging to the tumor necrosis factor (TNF) superfamily [1]. Belimumab is a monoclonal antibody against soluble BLyS used for treatment of refractory SLE. Although B cells are the main target of this therapy, a BLyS-dependent T cell activation pathway has also been demonstrated [2]. Clinical studies showed that high levels of anti-DNA antibodies and low complement at baseline are predictors of response to Belimumab treatment.

Objectives: Our study aims at exploring the role of biomarkers belonging to the TNF superfamily and of effector T-lymphocytes as predictors of response.

Methods: Twenty-one patients with SLE received Belimumab. Clinical evaluation and laboratory test were performed at baseline and after six and twenty months of therapy. Biomarkers belonging to the TNF superfamily (BAFF, APRIL, sBCMA, sCD40L, sTACI, TWEAK) were tested by high-sensitivity ELISA in all patients and lymphocyte immunophenotyping was performed by flow cytometry in ten subjects. SLE-disease activity was assessed by SLEDAI-2K score.

Results: BAFF and APRIL baseline serum levels and the number of CD3+CD8+ effector memory T cells were correlated positively with SLEDAI-2K improvement after 12 months of treatment (Pearson correlation=0.535 (p=0.015), 0.504 (p=0.023) and 0.654 (p=0.040)). After backwards exclusion from linear regression analysis including SLEDAI-2K, effector T cell relative number and BAFF or APRIL at baseline, only APRIL remained as significant independent predictor of SLEDAI-2K improvement after 12 months of therapy (adjusted R square=0.649; p=0.025). Moreover, after comparing TNF-family members serum levels and SLEDAI-2K at baseline, only BAFF showed the best predictive value (adjusted R 0.564, p<0.001).

Conclusion: In our cohort of SLE patients, baseline serum level of APRIL together with percentage of CD3+CD8+ effector memory cells, or BAFF serum level alone resulted as best predictors of response to Belimumab. Considering that immunophenotyping is often not done in clinical practice, BAFF baseline serum levels alone could be used routinely as a good predictor of response to therapy, as suggested by post-hoc analyses of the BLISS study and showed by a recent "real-life" observational study [3].

REFERENCES:

[1] Ng LG, et al. J Immunol, 2004
[2] Samy E, et al. Int Rev Immunol, 2017
[3] Parodis I, et al. ACR, 2016

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FRI0208 IDENTIFYING LUPUS PATIENT SUBSETS AND SPECIFIC PHARMACODYNAMIC CHANGES THROUGH IMMUNE CELL DECONVOLUTION OF GENE EXPRESSION DATA IN ATACICEPT-TREATED PATIENTS IN THE APRIL-SLE STUDY

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Background: The Phase 2/3 APRIL-SLE study evaluated the safety and efficacy of atacicept, a dual inhibitor of the B lymphocyte stimulator (BLyS) and a proliferation-inducing ligand (APRIL), in systemic lupus erythematosus (SLE).
Objectives: The goal of this post-hoc analysis was to use cell-based gene signatures on gene expression data from the APRIL-SLE study to identify clusters of patients with potential to flare and to assess clusters for differences in treatment effects of atacicept vs placebo.
Methods: A published immune cell deconvolution algorithm (Abbas *et al*, 2009) was applied to whole-blood gene expression data from APRIL-SLE patients to identify relative proportions of 17 immune cell types. Patients were then grouped into clusters based on these immune cell profiles using a k-medoid clustering algorithm and were compared to each other based on patient characteristics, biomarkers and clinical efficacy. In addition, baseline expression and change in expression of putative APRIL-responder genes were compared among clusters. APRIL-responder genes were identified by combining differential expression results from the APRIL-SLE study (Week 52 vs Day 1 randomization) and tabalumab (targets BLyS only) Phase 3 studies (Week 52 vs baseline; GSE88887).
Results: Patient gene expression data (N=105; placebo, n=30; atacicept 75 mg, n=40; atacicept 150 mg, n=35) were used to group patients into five main clusters (P1-P5) by predominant characteristic cells: P1, T helper cells; P2, plasma cells; P3, neutrophils and B cells; P4, B cells; P5, activated dendritic cells. Patients in P2 and P5 were more likely to have positive anti-dsDNA antibodies ($\geq$30 IU/ml), elevated BLyS; $\geq$1.6 ng/ml, and high interferon gene signature in the blood than other those in other clusters. Patients in P2 were most likely to have low complement C3 and C4 levels. Placebo-group flare rates in P2 (100%), P4 (100%) and P5 (83%) were markedly higher than in P1 (33%) and P3 (29%). In P2, P4, and P5 the median time-to-flare was much lower with placebo (85, 98.5, and 115.5 days, respectively) than with atacicept 150 mg (over 364 days for all three clusters). A comparison of differentially-expressed genes from clinical studies of SLE patients treated with atacicept and tabalumab revealed possible APRIL-responder genes: SDC1, PARM1 and MZB1. These genes had a higher baseline expression in P2 and P4 compared with other clusters. SDC1 was reduced from baseline more in P2, P4, and P5 after atacicept treatment, while PARM1 and MZB1 decreased after atacicept treatment in P2 and P4.
Conclusion: These post-hoc analyses revealed different subsets of SLE patients based on their molecular profiles. Atacicept may have different treatment effects in the identified patient subsets vs placebo, providing insights into potential mechanisms of flare in SLE.

REFERENCES:

[1] Abbas AR, Wolslegel K, Seshasayee D, Modrusan Z, Clark HF. Deconvolution of blood microarray data identifies cellular activation patterns in systemic lupus erythematosus. PLoS ONE. 2009;4(7):e6098.

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Celgene – member, scientific advisory board, Julie DeMartino Shareholder of: Shares in Merck & Co, Employee of: Current employees of EMD Serono; Past employee of Merck & Co. & Roche, Robert Townsend Employee of: Current employees of EMD Serono

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FRI0209 LOW-DOSE GLUCOCORTICOID COULD AFFECT ADVERSE PREGNANCY OUTCOMES, ESPECIALLY IN PRETERM BIRTH, LIGHT-FOR-DATE NEWBORNS, PRETERM PREMATURE RUPTURE OF MEMBRANE IN CONNECTIVE TISSUE DISEASE PATIENTS

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Background: Connective tissue disease (CTD) often occurs in women of child-bearing age, and flare-ups during pregnancy. Therefore, it is important to manage their disease activities with the treatment which have no influence on fetal growth and development. Among the treatment during pregnancy glucocorticoid is most often used for maintain or control to flare-ups of CTD disease activities. However, prolonged use of glucocorticoid during pregnancy is considered to increase the risk of adverse pregnancy outcomes (APOs) including preterm birth, intrauterine growth restriction, and premature rupture of membrane (PROM) (1, 2).
Objectives: The aim of this study is to reveal the dose of glucocorticoid which influences on APOs.
Methods: We investigated 164 pregnant patients complicated with CTD from March 2006 to January 2019. All these patients were managed their disease activities throughout pregnancy in our institute. APOs including preterm births, light-for-date (LFD) newborns, PROMs in these pregnant patients were examined retrospectively. We analyzed the association between APOs and the incidence or mean dose of glucocorticoid use during pregnancy.
Results: Underlying CTD is Systemic lupus erythematosus (25.3%), Sjogren's syndrome (24.9%), rheumatoid arthritis (18.1%), Antiphospholipid syndrome (8.8%), mixed connective tissue disease (6.7%), and others. Glucocorticoid was administered in 96 cases, which tended to be earlier gestational week at delivery (37.5±3.0 vs. 38.9±1.5, P<0.01) and lower birth weight of newborns (2601.9±603.0 vs. 3019.0±480.8, P<0.01) significantly. Compared with full-term birth, the cases of preterm birth had higher dose of glucocorticoid during pregnancy significantly (P<0.01). Logistic regression analysis for preterm birth revealed the cut-off value of mean prednisolone dose as 7.5 mg per day (Figure 1). Similarly, the

patients who delivered LFD newborns had higher dose of prednisolone (P=0.04), and logistic regression analysis revealed cut-off value as 6.7 mg per day (Figure 2). The cases with preterm PROM also had higher dose of prednisolone (P=0.01), and logistic analysis revealed cut-off value as 5.0 mg per day (Figure 3).

Conclusion: Glucocorticoid is often used for CTD patients during pregnancy, however, CTD patients who were treated with continuing high dose of glucocorticoid during pregnancy had high risks for APOs such as preterm birth, low birth weight of newborns, preterm PROM. Our data indicated that the cut-off dose of prednisolone values of preterm birth, LFD, preterm PROM was 7.5 mg, 6.7 mg, 5.0 mg per day respectively. It is important for rheumatologists to pay much attention for these risk of glucocorticoid use to CTD patients who hope to conceive and to manage the disease activity with appropriate dose of glucocorticoid. Recently, many immunosuppressants including biologics have been reported to be available for the safety use during pregnancy, and might be helpful to reduce the risk of APOs by glucocorticoid use.

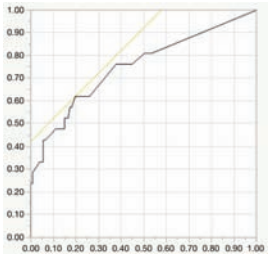


Figure 1. Logistic regression analysis for preterm birth (AUC=0.750, P<0.01, cut-off value=7.5mg/day)

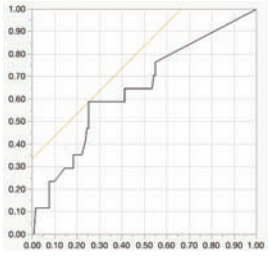


Figure 2. Logistic regression analysis for preterm birth (AUC=0.644, P=0.05, cut-off value=6.7mg/day)

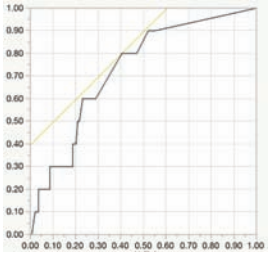


Figure 3. Logistic regression analysis for preterm birth (AUC=0.728, P=0.04, cut-off value=5.0mg/day)

REFERENCES:

[1] Østensen M, Forger F. How safe are anti-rheumatic drugs during pregnancy? Curr Opin Pharmacol 2013;13:470-5.

[2] Gur C, Diav-Citrin O, Shechtman S, et al. (2004) Pregnancy outcome after first trimester exposure to corticosteroids: a prospective controlled study. Reprod Toxicol 18:93-101

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FRI0210

EVALUATION OF THE IMPACT OF ROUTINE MONITORING OF BLOOD HYDROXYCHLOROQUINE LEVELS ON ADHERENCE TO TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: The usefulness of very low hydroxychloroquine (HCQ) blood levels to unmask severe non-adherence in patients with systemic lupus erythematosus (SLE) has been established, including in a recent prospective study. However, little is known on the individual impact of HCQ blood levels measurement.

Objectives: To assess the impact of HCQ blood levels measurements to detect patients with severe non-adherence and to assess its main causes.

Methods: Retrospective interviews about adherence to treatment were conducted by the same investigator in unselected consecutive SLE patients. Patients were classified as severely non-adherent (groups A and B) or not (group C). Group A included patients in whom the diagnosis of severe non-adherence was first made because of a blood HCQ level less than 200ng/ml at least once during follow-up, and group B because of the patient's acknowledgment of their complete interruption of HCQ treatment for at least one month. Mean HCQ blood levels were compared during the follow-up. The Medication Adherence Self-report Inventory scale (MASRI) was completed by each patient at the time of the interview (reflecting adherence in the last 30 days).

At the time of the interview	Group A (severe non adherence discovered by HCQ levels) N=12	Group B (severe non adherence discovered by regular discussion) N=16	Group C (not severely non-adherent) N=43
Duration of HCQ treatment (years), mean ±SD	6.2 ± 4.8	5.9 ± 3.1	6.4 ± 4.6
Nb of HCQ measurements, mean±SD	9.8 ± 5.5[1]	6.5 ± 3.7	6.0 ± 2.8
Mean HCQ levels during follow-up, mean±SD	662 ± 260[2]	866 ± 229	965 ± 281
MASRI < 80%, n (%)	3 (25)	6 (38)	0 (0)[3]

Results: 71 SLE patients who had a mean of 6.8 (±3.8) measurements of HCQ blood levels during a mean follow-up of 6.2 years (± 4.3) were included (Table). Twenty-eight patients (39%) had been diagnosed at some point with severe non-adherence: 12 in group A and 16 in group B (6 (38%) of them also had - at least - one HCQ blood level <200 ng/ml following the recognition of non-adherence). Demographic characteristics were similar between groups (p=NS, data not show). After the diagnosis of severe non-adherence, the mean±SD HCQ levels (including all the determinations of HCQ levels done before *versus* those done after this diagnosis) improved in Group A (from 232±249 ng/ml to 761±338 ng/ml; p<0.005) while they remained stable in Group B (p=NS). Non-acceptance of the disease was the leading cause of severe non-adherence to treatment in Group A (7 patients (58%) versus 2 patients in Group B (12.5%); p=0.02) while the boredom with chronic treatments was the main reported cause in Group B (9 patients (56%) versus 1 patient in Group A (8%); p=0.02).

Conclusion: We provide novel evidence that, in a real-life setting, HCQ blood level measurements are useful to diagnose severe non-adherence since 12 of 28 severly non-adherent patients were diagnosed because of HCQ levels. We confirm that discovering very low HCQ blood levels

leads to increase HCQ blood concentrations in the next samples after having stressed (and discussed!) the problem to the patient.

REFERENCES:

HCQ: hydroxychloroquine; [1-2] : *p*<0.005 *versus* Group C; [3] : p<0.0005 *versus* A and B Groups; other *p* values were non-significant; *p* values were calculated by unpaired t-tests and Fisher's exact tests, as appropriate.

Disclosure of Interests: None declared

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FRI0211 A LOW AND PROMPTLY TAPERED STEROID REGIMEN CAN ACHIEVE EXCELLENT RESULTS IN LUPUS NEPHRITIS, WITH LESS ADVERSE EVENTS

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Background: The optimal use of glucocorticoids (GC) in lupus nephritis (LN) remains a topic of debate, especially the tapering protocol and the duration of treatment. To date, only one randomized controlled trial, *MyLupus*, has compared two oral prednisolone (P) regimens in LN (0.5 *versus* 1mg/kg/d) in addition to mycophenolic acid. Although non-inferiority was not proven, this study demonstrated a similar rate of renal response at 24 weeks, with fewer side-effects in the 0.5mg/kg/d group.

Objectives: To determine by a retrospective study the efficacy and the toxicity of an even lower P regimen (20mg/d), very promptly tapered to 5mg/d at week 12 and stopped as early as at week 52.

Methods: Data from the last 30 consecutive proliferative LN patients diagnosed at the Louvain Lupus Clinic (between 2015 and 2018) were reviewed retrospectively. In these patients, the 10 last consecutive patients received a low fixed dose of P (20mg/d) for 4 weeks, rapidly tapered as follows: 15mg/d for 2 weeks, 12.5mg/d for 2 weeks, 10mg/d for 2 weeks, 7.5mg/d from for 2 weeks, 5mg/d for 3 months and 2.5mg/d for 6 months. GC were withdrawn at week 52. The baseline and the follow-up data of these 10 patients were compared to the 20 previous consecutive LN patients followed in the same center but given a standardized P dose of 0.5mg/kg/d. Both groups of patients received 750 mg methylprednisolone IV pulses on 3 consecutive days at baseline. The one-year renal response was defined by achieving a proteinuria target < 0.8g/d.

Results: Clinical (BMI, gender, age, mean serum creatinine, mean proteinuria, SLEDAI-2K, non-steroid immunosuppressants) and pathological (ISN/RPS class) characteristics did not differ at baseline between the two groups. As illustrated in the Table, the mean uP/C ratios measured at one year were similar, as were the percentages of patients who achieved the proteinuria target. Importantly, *Herpes zoster* infections were only observed in the higher P dose group, with the difference reaching almost statistical significance.

	High dose P 0.5mg/kg/d N=20	Low dose P 20mg/d; 5mg/d at w12 N=10	P value
Baseline BMI (kg/m²), mean ± SD	22.8 ± 4.0	23.4 ± 3.4	0.72
Baseline cumulative IV MP (g), mean ± SD	2.5 ± 1.9	2.1 ± 0.5	0.57
Baseline dose of oral P (mg), mean ± SD	39.5 ± 15.7	20 ± 0	0.0006
Baseline uP/C (g/g), mean ± SD	3.01 ± 2.30	2.05 ± 1.72	0.25
Month 12 dose of oral P (mg), mean ± SD	8.0 ± 6.5	0.8 ± 1.7	0.002
Month 12 uP/C (g/g), mean ± SD	0.61 ± 0.78	0.72 ± 1.23	0.75
Month 12 uP/C target (<0.8g/g), n (%)	16 (80)	8 (80)	1.00
Hesper zoster during GC treatment, n (%)	6 (30)	0 (0)	0.07

Conclusion: In patients suffering from proliferative LN, an induction protocol with a low and rapidly tapered dose of P may be as effective as higher dose regimen to achieve the proteinuria target at one year, with fewer *Herpes zoster* episodes. These results deserve to be confirmed in a controlled trial.

REFERENCES:

BMI: body mass index; IV MP: intravenous methylprednisolone; P: prednisolone; uP/C: urine protein to creatinine ratio; *P* values were calculated by unpaired *t*-tests and Fisher's exact tests, as appropriate.

Disclosure of Interests: None declared

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FRI0212 USE OF 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: THE RELATIONSHIP OF IMMUNOGENICITY WITH THERAPY

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Background: Immunization with pneumococcal vaccines is an important factor of the prevention of severe respiratory infections in patients with rheumatic diseases (RD). Vaccination in systemic lupus erythematosus (SLE) is designed to ensure the continuity of immunosuppressive therapy, reducing the risk of severe exacerbations and death, and is effective from a pharmaco-economical standpoint.

Objectives: Investigation of the immunogenicity of 23-valent polysaccharide pneumococcal vaccine (PPV-23) in patients with SLE, as well as the effect of immunosuppressive therapy on the vaccinal response.

Methods: 34 patients with a reliable diagnosis of SLE (30 women and 4 men aged 19 to 68 years) were included. The duration of the disease varied from 9 months to 20 years. At the time of vaccination, 3 patients had high, 4 – moderate, 22 – low disease activity, and 5 were in remission. Current therapy: 33 patients received glucocorticoids (GC) 5-30 mg/day in prednisolone equivalent, 27 – hydroxychloroquine, 17 – cytotoxic agents (CA) (7 – mycophenolate mofetil, 6 – methotrexate, 1 – mycophenolic acid, 3 – azathioprine,2 - cyclophosphamide),11 – biologics (BS): 5-rituximab (RTM), 6– belimumab (BLM). RTM was administered in doses of 500-1000 mg every 6-12 months, BLM – from 400 to 720 mg every month. 0.5 ml of PPV-23 (1 dose) was administered subcutaneously. During the visits standard clinical and laboratory tests were performed, as well as determination of antibody (AB) to *S.pneumoniae* serum level with VaccZymeTMPCPIg 2 sets (TheBindingSiteLtd, Birmingham, UK).

Results: 1 and 3 months after vaccination, most patients (82,4% and 96,7% respectively) had a significant (more than 2 times compared to baseline) increase of the concentration of AB to the S. pneumoniae cell wall polysaccharides. A year after the vaccination, 22 (64.7%) patients (responders) had a significant increase of the concentration of anti-pneumococcal AB. 12 (35,3%) patients were considered as non-responders, they did not have a significant increase of the AB level (table).

Table. Change of anti-pneumococcal antibody concentration in SLE patients during the first year after the vaccination (n=34).

	baseline	1 month	3 months	12 months
Antibody concentration mg/l	**83,5**[a]	**407,8**[b]	**311,4**[c]	**255,3**[d]
Me	(57,4; 117,4)	(195,5; 476,8)	(181,5; 423,8)	(109,6; 423,5)
(25;75 percentiles)				
responders		28	29	22
n		(82,4%)	(96,7%)	(64,7%)

p a–b=0,000002; p a–c=0,00009; p a–d=0,0002.

Among 11 patients receiving BS, a complete vaccinal response was observed much less frequently than in patients without these drugs, 36.4% and 78.3%, respectively, p=0.04.

In the group treated with RTM, the number of non-responders was greater than among patients receiving BLM (80% and 50%, respectively), but this difference is not significant, p=0.6.

The addition of CA to the treatment regimen did not have an additional negative effect on the vaccinal response.

Conclusion: Sufficient immunogenicity of PPV-23 was shown in patients with SLE, including those receiving combined immunosuppressive therapy.

At the same time, the use of anti-B-cell drugs in combination therapy resulted in a significant decrease of the vaccinal response
Disclosure of Interests: None declared
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FRI0213 RANDOMIZED PLACEBO CONTROLLED TRIAL OF ABATACEPT FOR NON-ORGAN THREATENING SYSTEMIC LUPUS WITH BACKGROUND MEDICATIONS WITHDRAWN

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Background: Abatacept (ABA) is a fusion protein of the extracellular domain of CTLA4 and the Fc domain of human IgG1, constructed to inhibit B/T cell co-stimulation. Previous studies of ABA in lupus failed to show benefit in overall disease activity, but improvement in arthritis was suggested.
Objectives: This 6-month randomized, double-blind, placebo-controlled (PBO) study withdrew background medications to facilitate the assessment of ABA in patients with SLE arthritis.
Methods: Patients were entered with moderate to severe arthritis [BILAG A or B with ≥3 swollen and ≥3 tender joints (28 joint count)]. All DMARDs except prednisone (up to 20mg daily) were withdrawn by baseline and patients were randomized 1:1 to weekly sc ABA or PBO. One or more DepoMedrol injections (≤320mg total) was allowed by end of Month 2. Additional steroids or immune suppressants (IMS) at any time, and transition to open label ABA at Month 3 or later, were allowed, but designated non-response. The primary endpoint was BICLA response at Month 6 compared to screening. Secondary objectives included SRI-4, SLEDAI 4-point improvement, SLEDAI arthritis resolution, BILAG A/B musculoskeletal (MSK) improvement, as well as low disease activity defined by either SLEDAI 2 or Lupus Low Disease Activity State (LLDAS) at Month 6. Flares were evaluated by the modified SELENA-SLEDAI flare index (1) in patients followed after baseline.
Results: 66 patients were randomized and received at least one dose of the study drug, 31 ABA and 35 PBO. 7 withdrew prior to Month 6. Placebo response rates were lower than in most SLE trials, but no primary or secondary endpoints were met, see table (Fischer's exact test).

	ABA (n=31)	PBO (n=35)	p value
BICLA	8(26%)	8(23%)	>0.999
SRI-4	9(29%)	8(23%)	0.587
SLEDAI 4-point improvement	9(29%)	8(23%)	0.587
SLEDAI arthritis improvement	9(29%)	8(23%)	0.587
BILAG A/B MSK improvement	9(29%)	8(23%)	0.587
SLEDAI 2	8(26%)	7(20%)	0.769
LLDAS	6(19%)	8(23%)	0.772

Flares were evaluable in 64 patients (31 on ABA, 33 on PBO). 14 (45%) patients on ABA vs. 18 (55%) on PBO had a moderate/severe flare by Month 6. 22 (71%) patients on ABA vs. 23 (70%) on PBO experienced flare or treatment failure (early drop off or off protocol steroids or IMS) by Month 6. Rates of flare and treatment failure by Month 6 did not differ between groups (Log-Rank test, p=0.688 and p=0.631, respectively). The safety profile of ABA was consistent with known effects of the treatment.
Conclusion: ABA did not demonstrate improvement vs placebo in controlling disease activity or flare in SLE patients in a protocol that mandated IMS withdrawal. Placebo response rates of ≤23% support the validity of these results. Since some evidence suggests potential efficacy of ABA for certain biologic subsets of SLE (2), immunophenotyping may prove helpful.

REFERENCES:

[1] Thanou A, Chakravarty E, James JA, Merrill JT. Rheumatology (Oxford) 2014;53(12):2175-81.
[2] Bandyopadhyay S, Connolly SE, Jabado O, Ye J, Kelly S, Maldonado MA, Westhovens R, Nash P, Merrill JT, Townsend RM. Lupus Sci Med. 2017 4 (1): e000206.

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FRI0214 EFFICACY OF RITUXIMAB AND CYCLOPHOSPHAMIDE TREATMENT IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME AND PAROTID GLAND MALT LYMPHOMA

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Background: Mucosa-associated lymphoid tissue (MALT) lymphoma occurred in a higher frequency and at an earlier age in primary Sjögren's syndrome (pSS) than reported for MALT lymphoma in the general population. The optimal treatment of MALT lymphoma in pSS has not been defined.
Objectives: to analyze retrospectively the long-term clinical course of pSS in patients with MALT lymphoma.
Methods: 63 SS patients with MALT lymphoma were retrieved from our pSS database. Most of the 63 pSS-lymphoma patients were female (n=60; 95%). pSS was diagnosed at a mean age of 51 (43-58) years and lymphoma at a mean of 7 (2-10) years later. Total mean follow-up was 5 years (2-8). 14 patients received immunomodulator agents for SS before the development of lymphoma (low doses of prednisone - 8 patients, **chlorambucil** – 7, cyclophosphamide – 3 patients). In 43 patients, the diagnosis of SS and MALT - lymphoma were established simultaneously. Clinical features and treatment outcome of MALT - lymphoma as well as SS activity was evaluated.
All patients had features of autoimmune disease (ANA-100%, RF-90%, anti-Ro or/and anti-La antinuclear antibodies-94%) and met the diagnostic criteria of the Association of Rheumatologists of Russia for primary Sjogren's syndrome: salivary gland involvement (stimulated parotid flow rate < 2,5 ml in 5 min, parotid sialography showing the presence of diffuse punctuate or globular shadows with a diameter > 1mm., histopathology: a focus score>2 per 4mm2 in minor salivary gland biopsy), keratoconjunctivitis sicca (stimulated Schirmer's test <10mm in 5 min, tear break-up time < 10 seconds, rose Bengal test or fluorescent test>1+), presence of abnormal concentrations of at least one of the serum autoantibodies (anti-Ro, anti-La, antinuclear antibodies, IgM-rheumatoid factor). The histologic and immunohistochemical diagnosis of lymphoma was performed with B-cell clonality determination in salivary gland tissue.
Patients were treated with RTX (25 patients) or RTX+CPH (38 patients). Patients received 2 1g intravenous infusions of RTX 2 weeks apart, then 375 mg every 3 months for 2 years. Cyclophosphamide 1000 mg was administered every two weeks for a period of 12 weeks.
Results: MALT lymphoma was localized in parotid glands in 60 cases, submandibular salivary glands – in 2 cases, lacrimal gland – in 1 case. Eleven patients showed systemic features (7-purpura, 1-peripheral neuropathy, 3 – nephritis). Blood serum and urine examination revealed monoclonal secretion in 16/56 patients (7-IgMk, 4-IgGk and IgG, 2-IgAk and 3 - BJk). Nineteen of 56 (34%) patients had cryoglobulinaemia.
After follow-up of 24 mo, complete clinical remission (CR) of MALT lymphoma (normalization of salivary gland size, disappearance of lymphadenopathy and cytopenia) was obtained in 25 (72%) in the group of RTX and 35 (92%) in the group of RTX+CPH (p=0.05). An incision biopsy of the parotid gland before and after therapy was made in 21 patients. Complete disappearance of histological pattern of MALT lymphoma was shown in 50% of the RTX treated patients and in 66% patients with combined therapy. B-cell clonality in parotid glands disappeared in 3/5 cases after RTX monotherapy and in 1/4 cases after RTX with CPH therapy. Cryoglobulinaemia disappeared in 33% patients in group of RTX and 46% in group of RTX+CPH (p=0.6).
Conclusion: Complete clinical remission of the lymphomas was achieved significantly more often in the group treated with RTX plus cytostatic agent in comparison with patients who had RTX monotherapy.
Disclosure of Interests: None declared
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FRI0215 **SIROLIMUS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS RELATED THROMBOCYTOPENIA (SLE-TP): A SINGLE-ARM, OPEN-LABEL CLINICAL TRIAL**

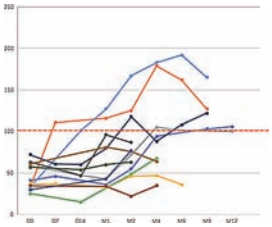
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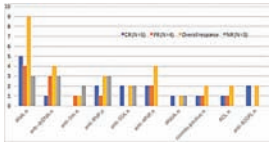
Background: Autoimmune thrombocytopenia (AITP) is common in systemic lupus erythematosus (SLE) patients and may be refractory to conventional therapies. SLE related thrombocytopenia (SLE-TP) patients have T-cell dysfunction that was reported to be associated with the activation of the mammalian target of rapamycin (mTOR). Rapamycin (RAPA) inhibits antigen-induced T-cell proliferation and has been developed as a medication named sirolimus.
Objectives: We assessed safety, tolerance, and efficacy of sirolimus in a prospective, open-label clinical trial.
Methods: We did a single-arm, open-label study of sirolimus in patients with refractory SLE-TP unresponsive to, or intolerant of, conventional medications at Peking Union Medical College Hospital (PUMCH, Beijing, China). We enrolled refractory TP patients (aged ≥18 years) with systemic lupus erythematosus (SLE) who visited our referral center since September 2017. We excluded patients with allergy or intolerance to sirolimus, patients with life-threatening manifestations of lupus, such as RPGN, NPLE or PAH and patients with uncured infection. All eligible participants had signed informed consents. Patients received oral sirolimus at a starting dose of 2 mg per day for 3 days and a sequential dose of 1mg per day, with dose adjusted according to tolerance and to maintain a therapeutic range of 6–15 ng/mL. Patients were treated with sirolimus for 6 months. Safety outcomes included tolerance as assessed by the occurrence of common side-effects. The primary efficacy endpoint was complete remission rate and partial remission rate at the sixth month. The secondary efficacy endpoint was thea remission rates at the third month. The efficacy endpoints were assessed in all patients who completed 3 or more months of treatment, and all patients who received at least one dose of treatment were included in the safety analyses.
Results: Between September 2017 and November 2018, 12 lupus patients (1 male and 11 female) were enrolled with an average age of 33.3y, average disease duration of 8.4 years. All patients haven't achieved remission with front-line therapy, including corticosteroids, intravenous immunoglobulin, and immunomodulatory agents, such as azathioprine, FK506, mycophenolate mofetil, and cyclosporine. After sirolimus therapy (2 weeks to 6 months), 5 of 12 patients achieved CRR. 11 patients have finished 4 months' assessment, and 9 of them achieved remission. One patient had mild oral ulcers and no other complications were noted. The study is still in regular follow-up. There will be more results and conclusions in the later period.

Table 1. Demographics and Characteristics for Patients With SLE-TP

Patient No.	Age (y)	Gender	Prior Therapies	Time to Sirolimus (y)	Duration of Sirolimus (m)	Therapy Outcome
1	36	F	GCs, MMF, AZA	15	12	CR
2	44	F	GCs, FK506	13	11	CR
3	48	F	GCs, MMF	7	11	CR
4	35	F	GCS, MMF	2	9	CR
5	31	F	GCs, FK506	7	9	CR
6	39	F	GCs, CTX	8	6	NR
7	30	F	GCs, MMF, CsA, CH	15	5	PR
8	29	F	GCs, FK506	7	6	NR
9	18	M	GCs, MMF, FK506, CsA	3	4	PR
10	20	F	GCs, CTX, FK506, CsA, MMF, IVIg	14	4	PR
11	31	F	GCs, FK506	6	4	PR
12	38	F	GCs, CsA	4	2	NR

AZA, azathioprine; CH, Chinese herbs; CR, complete response; CsA, cyclosporine; CTX, cyclophosphamide; FK506, tacrolimus; GCs, glucocorticoid; IVIG, intravenous immunoglobulin; MMF, mycophenolate mofetil; NR, no response; PR, partial response.





Conclusion: Sirolimus is effective for the treatment of refractory SLE-TP and can be a choice of the second-line treatment. Further prospective studies are needed to evaluate sirolimus as a therapeutic option for SLE-TP and to monitor for potential long-term side effects.

REFERENCES:

[1] Perl A. Nat Rev Rheumatol 2016; 12: 169–82.
[2] Morel L. Nat Rev Rheumatol 2017; 13: 280–90.
[3] Oaks Z, et al. Arthritis Rheumatol 2016; 68: 2728–39.
[4] Oaks Z, et al. Curr Rheum Rep 2016; 18: 73.
[5] Zhi-Wei Lai, et al. Lancet 2018 Mar 24;391(10126):1186-1196.
[6] Desmond Y.H. Yap, et al. J Rheumatol. 2018 Dec;45(12):1663-1670.

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Disclosure of Interests: None declared
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FRI0216 **IGURATIMOD MIGHT BE AN ALTERNATIVE OPTION FOR REFRACTORY LUPUS NEPHRITIS: A PRELIMINARY OBSERVATIONAL STUDY**

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Background: Despite significant advances in the management of patients with lupus nephritis (LN), a significant proportion of patients either do not respond to first-line immunosuppressive drugs, or relapse after initial remission. Iguratimod is a novel disease modifying anti-rheumatic drug that has been approved for treating rheumatoid arthritis in East Asia and has shown benefits in lupus animal model in our previous research.(1)
Objectives: The aim of the present study was to make a preliminary observation on the efficacy and safety of iguratimod in treating refractory LN patients.
Methods: We have enrolled adult refractory LN patients who were eligible if they experienced at least two times of failure or relapse before enrollment. Failure was defined as no response to one certain immunosuppressive drug for at least six months. After enrollment, we simply switched their previous immunosuppressant to daily iguratimod (25 mg twice per day), while keeping all other medications. Complete/partial remission (PR/CR) was used as the primary outcome. 24h urine protein, blood cell counts, liver and kidney function were routinely monitored.
Results: A total of 20 refractory LN patients had been enrolled (18 female and 2 male patients) since 2015. At enrollment, the median proteinuria was 2.588g/24h (range: 0.98-13.79g/24h). None of them had overt extra-renal involvement. All of them had biopsy-proven LN (class III/IV/V) and two patients agreed repeated biopsy before switching to iguratimod. The median prednisone dosage was 10mg/d (range: 5-35mg/d). One patient was lost to follow-up and one withdrew from the study. Of the remaining 18 patients, 16 patients achieved PR/CR and 2 did not respond to iguratimod. Of the 16 patients who achieved remission, 3 had renal relapse after initial PR and 1 had extra-renal flare after initial CR. One PR patient withdrew from the study due to severe anemia and another due to incompliance. For the remaining 10 patients who were still in follow-up, the median follow-up was 84 weeks (range: 28-144

weeks), with 4 having CR and 6 PR. The median response duration (MRD) was 12 weeks.
Conclusion: Out study provided preliminary but promising clinical evidence for iguratimod in treating refractory LN patients. A large randomized clinical trial is needed to establish its safety and efficacy for refractory LN.

REFERENCES:
[1] Yan Q, Du F, Huang X, Fu Q, Chen S, Dai D, et al. Prevention of immune nephritis by the small molecular weight immunomodulator iguratimod in MRL/lpr mice. PLoS One. 2014;9(10):e108273.

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FRI0216B **SELECTIVE IRAK4 INHIBITOR DAMPENS MYD88 SIGNALING AND AMELIORATES INFLAMMATION AND FIBROSIS IN A MOUSE MODEL OF LUPUS NEPHRITIS**

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Background: IRAK4 is an important signaling mediator of the innate immune system. IRAK4 initiates MyD88-dependent signaling from most TLRs and from IL-1Rs, resulting in downstream production of pro-inflammatory cytokines[1].
Objectives: Inhibition of IRAK4 kinase activity is a promising therapeutic approach for the treatment of autoimmune diseases, such as lupus. To this end, we identified a potent and highly selective inhibitor of IRAK4 kinase activity, BIIB-IRAK4i.
Methods: Recombinant kinase assays and DiscoveRx kinomescan were used to measure BIIB-IRAK4i kinase inhibition and selectivity, respectively. BIIB-IRAK4i -mediated proximal and distal pharmacodynamics effects (PD) were measured in both cell lines and whole blood assays. The ability of BIIB-IRAK4i to inhibit cytokine production induced by TLR ligands was measured *in vitro* and *in vivo*. Acute antibody-mediated lupus nephritis mouse model, which is a TLR-7 dependent and characterized by severe glomerular proliferative lesions with crescent formation, was used to determine the efficacy of BIIB-IRAK4i.
Results: BIIB-IRAK4i displayed equipotent proximal inhibition of MYD88 signaling and distal inhibition of cytokine production *in vitro*. BIIB-IRAK4i led to potent inhibition of cytokine production in whole blood assays stimulated with various synthetic TLR ligands as well as more physiological stimuli such as immune complexes, a hallmark of lupus pathogenesis. BIIB-IRAK4i inhibited TLR9-mediated cytokine production with same potency in vitro and in vivo. In addition, BIIB-IRAK4i decreased both inflammation and fibrosis in an acute antibody-mediated lupus nephritis mouse model. BIIB-IRAK4i inhibited crescent formation as well as markers of tubulointerstitial fibrosis., which are both associated with decreased survival and adverse outcomes in human lupus nephritis.
Conclusion: Our study highlights that pharmacological inhibition of IRAK4 can reverse two key components of lupus nerhrtis; the inflammatory and the fibrotic response.

REFERENCES:
[1] O'Neill LA and Bowie AG. The family of five: TIR-domain-containing adaptors in Toll-like receptor signaling. Nat Rev Immunol. 2007 May;7(5):353-64.

Disclosure of Interests: Dania Rabah Shareholder of: Employee and shareholder of Biogen, Employee of: Biogen, Ramon Bonegio Grant/research support from: Merck, Chugai Pharmaceuticals, Astra Zeneca, Aurinia Pharmacueticals, Consultant for: Merck, Chugai Pharmaceuticals, Agnes Gardet Shareholder of: Biogen, Employee of: Biogen, Holly Legault Shareholder of: Biogen, Employee of: Biogen, Ian Rifkin Grant/research support from: Chugai, Merck, Biogen, Kyowa Kirin, Consultant for: Eisai, Ti Wang Shareholder of: Biogen, Employee of: Biogen, Chris Roberts Shareholder of: Biogen, Employee of: Biogen, Jeffery Vessels Shareholder of: Biogen, Employee of: Biogen, Norm Alliare Shareholder of: Biogen, Employee of: Biogen, Andrea Bertolotti-Ciarlet Shareholder of: Biogen, Takeda, Employee of: Biogen, takeda, Kevin Guckian Shareholder of: Biogen, Employee of: Biogen
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SLE, Sjögren's and APS – clinical aspects (other than treatment)

FRI0217 **PREGNANCY OUTCOME IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN TERTIARY UNIVERSITY HOSPITAL IN EGYPT**

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Background: Pregnant systemic lupus erythematosus (SLE) patients have various risks to their fetus and themselves because a severe disease flare may be life-threatening, and some of the medications that are used to treat SLE adversely affect fetus.(1)
Objectives: To evaluate the pregnancy outcome in SLE patients and to determine the predictive factors for adverse fetal and maternal outcomes.
Methods: The study was conducted on the pregnant SLE patients attending Rheumatology department, Zagazig University hospitals in the period from January 2013 to January 2018. The data was collected retrospectively; demographic, laboratory and serological data on all patients, age at the onset of SLE, disease duration, systems affected, their disease activity using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), treatment received immunosuppressive regimen (dose and duration) before and during pregnancy, SLE flare during pregnancy, the fetal and the maternal outcomes.
Results: Fifty- two pregnancies were observed in 49 SLE patients with mean age of (27.5±5.6), mean SLE disease duration (3.7±2.2) and mean SLEDAI (5.4±6.1). 39 (75%) pregnancies with successful live births and 13(25%) fetal losses were observed. 36 of the live births (92.3%) were full-term and 3 (7.7%) were preterm births. Fetal losses included six spontaneous abortions, 3 stillbirths and 4 therapeutic abortions; 2 of them due to observed fetal anomalies and one due to life threatening lupus flare. We found SLEDAI significantly higher in patients with lost pregnancies ($p<0.0001$) than successful pregnancies. Proteinuria during pregnancy was a predictive factor for adverse fetal outcomes (odds ratio [OR] 19.7; $P < 0.0001$), also the presence of antiphospholipid antibodies (OR 15.3; $P<0.0001$), low C3 and C4 (OR 15.3; $P<0.0001$), anti-RO antibodies (OR 11.1; $P=0.02$), anti-LA (OR 4.7; $P=0.03$), chronic hypertension (OR 54.8; $p<0.0001$) and SLE flares(OR 32; $p=0.003$). SLE flares occurred in 10 pregnancies (19.2%), mostly during the second trimester (60%). Renal involvement (70%) was the most common SLE flare during pregnancy. SLE flares during pregnancy were highly associated by nephritis prior to pregnancy (adjusted OR 9; $P = 0.04$) and the presence of antiphospholipid antibodies (adjusted OR 12; $p=0.01$).
Conclusion: Favorable pregnancy outcome was observed in Egyptian SLE patients; particularly in those with longer period of remission. Planned pregnancy is very important to reduce undesirable fetal and maternal outcomes in SLE patients. The presence of lupus nephritis, chronic hypertension, antiphospholipid syndrome, active disease at the onset of pregnancy, and proteinuria were highly associated with bad outcome.

REFERENCES:
[1] Phansenee, S., Sekararithi, R., Jatavan, P., & Tongsong, T. (2018). Pregnancy outcomes among women with systemic lupus erythematosus: a retrospective cohort study from Thailand. Lupus, 27(1), 158–164.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8173

FRI0218 **IMMUNOPHENOTYPIC SUBGROUPS OF SLE DEFINED BY AUTOANTIBODIES, GENE EXPRESSION AND FLOW CYTOMETRIC ANALYSIS**

Marta Aguilar-Zamora[1,2], Hui Lu[3], Zoe Betteridge[3], Katie Dutton[4], MD Yuzaiful MD Yusof[4], Antonios Psarras[4], The Masterplans Consortium.[3,4], Neil Mchugh[3], Edward Vital[4]. *[1]Hospital Universitario Dr. Peset, Rheumatology, Valencia, Spain*; *[2]Fundación Valenciana de Reumatología, Valencia, Spain*; *[3]University of Bath, Bath, United Kingdom*; *[4]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), Leeds, United Kingdom*

Background: SLE may be stratified according to a range of different immune assessments but the relationships between these are less well defined. MASTERPLANS is an MRC-funded consortium that seeks to identify immunophenotypic subgroups of patients that predict response to therapy.

Objectives: Our objective here was to analyse a clinically well-phenotyped patients using a suite of immune assessments and identify inter-relationships between these features as well as subgroups of patients who may differ in response to therapy.
Methods: 143 SLE patients were evaluated for clinical phenotype using BILAG-2004, autoantibodies using radioimmunoprecipitation (IP, University of Bath), two interferon scores (IFN-Score-A and IFN-Score-B), flow cytometry for major circulating immune cell subsets, as well as the surface protein expression of tetherin on each subset, a cell-specific assay for IFN response.
Unsupervised hierarchical clustering was used to define autoantibody subgroups. IFN scores (reflected dCT) were compared between the groups using multivariate models. Other variables were compared using Kruskal-Wallis test with pairwise comparisons.
Results: Using IP, 141 patients could be divided into five subgroups: U1RNP/Sm+ only (n=23), Ro60+ only (n=8), U1RNP/Sm+Ro60+ (n=6), Ro60+Ro52+La+ (n=11), Ro52+ (n=16) and other ANA (n=77).
Antibody subgroups was strongly associated with IFN-Score-A (F=4.39, p=0.001). Expression was lowest for "other ANA", intermediate for single antibody groups, and highest with multiple positive antibodies. Multivariate linear regression, including interaction terms between antibody types, revealed that Ro60 and U1RNP/Sm were the independent predictors of IFN-Score-A level (p=0.051 and 0.009 respectively). There was no association between autoantibody status and IFN-Score-B (F=0.973, p=0.438).
In flow cytometry, the U1RNP/Sm group was notable for significantly lower numbers of CD4-T-cells and memory-B-cells. Memory -B-cells were also lower in antibody-positive groups compared to "other ANA". Tetherin expression was increased in antibody positive groups, but to a similar extent on most cell subsets. Memory B cell tetherin was significantly higher in the groups with multiple positive antibodies.
U1RNP/Sm+ was associated with renal involvement (p=0.004). Mucocutaneous involvement was greater in the Ro60+Ro52+La+ group (p=0.037).
Conclusion: This cohort revealed relationships between immune features. U1RNP/Sm antibody was notable for defining a group of patients with a cluster of immune abnormalities, including the greatest elevation of IFN activity, greater abnormalities on flow cytometry and clinical renal involvement. This was independent to the IFN-Score-B high status that predicts better clinical response to rituximab (presented elsewhere at this conference). Future work in MASTERPLANS will investigate the significance of these subgroups for response to therapy.

Table 1: Multivariate analysis of antibody status and IFN Score A

Predictor	Ab-Negative Score-A Mean(SD)	Ab-Positive Score-A Mean(SD)	Univariate OR (95% CI)	P	Multivariable OR (95% CI)	P
U1RNP/Sm	3.59 (2.89)	1.46 (1.53)	-2.4 (-2.7,-0.34)	0.012	-2.7 (-2.7, -0.4)	0.009
Ro60	3.75 (2.62)	1.83 (1.72)	-3.1 (-3.0,-2.83)	0.001	-2.0 (-2.7, 0.0)	0.051
La	3.39 (2.72)	1.51 (1.99)	-2.0 (-3.7,-0.4)	0.046	-0.35 (-2.7, 1.9)	0.73
Ro52	3.52 (2.80)	1.95 (1.53)	-2.1 (-2.9,-0.22)	0.023	-0.86 (-2.4, 0.9)	0.39
U1RNP*Ro60	N/A	N/A	N/A	N/A	0.05 (-2.1,3.21)	0.67
Ro60*Ro52	N/A	N/A	N/A	N/A	0.27 (-1.3,5.68)	0.21
Ro52*La	N/A	N/A	N/A	N/A	-0.41 (-10.5,1.26)	0.12

*Note these are untransformed dCT values, so numerically higher values represent lower gene expression

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FRI0219 CD4+CD25+FOXP3+ REGULATORY T CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: THE NEGATIVE ASSOCIATION WITH DISEASE ACTIVITY, ACUTE COURSE, TRANSITIONAL B CELLS AND IGG LEVELS

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Background: CD4+ CD25+ Foxp3+ regulatory T (Treg) cells play a key role in maintaining peripheral tolerance and preventing autoimmune disease. Quantitative and/or qualitative deficiencies of Treg have been associated with immune disturbances in systemic lupus erythematosus (SLE).
Objectives: The main goal of the study was to determine the relationship of CD4+CD25+FoxP3+Treg cells with clinical and immunological manifestations in SLE patients (pts).
Methods: Frequencies and absolute numbers of peripheral blood CD4 +CD25+FoxP3+Treg cells were assessed in 21 healthy donors and 20 SLE pts (2012 SLICC classification criteria); (1M/19F); age 32±13 years; disease duration median (25–75 percentile) 5(1-10) years; SLEDAI2K$\geq$10 - 15(10-22) (14 pts), <10 – 7(6-8) (6 pts). All pts were treated with prednisone, hydroxychloroquine, azathioprine, mycophenolate mofetil, cyclophosphamide. CD4+CD25+FoxP3+ Treg cells and B-cell subsets were analyzed using multicolor flow cytometry.
Results: Compared with healthy donors, SLE pts demonstrated significant lower the absolute number of Tregs (0.05; 0.04-0.06 vs 0.03;0.02-0.05x10^9/L, p<0,036), with a high percentage of Treg (8.8;7.5-10.5 vs 12.0;8.8-17.0%, p<0.02). The median percentage of Tregs was lower in pts with acute SLE compared to chronic SLE pts (9.0;8.3-9.9 vs 13.5;12.7-18.7%, p<0,02). SLE pts with high activity had a lower frequencies of Tregs (10.2;8.5-15.0 vs 15.8;12.7-20.4%, r=-0,51, p<0,05). Low count of Tregs correlated with elevated level of IgG (r=-0,52, p<0,05). Absolute number of Tregscorrelated negatively with percentage and absolute count of transitional (CD19+IgD+CD10+CD38++CD27-) B cells (r=-0,66 and r=-0,63, p<0,05).
Conclusion: Decreased amount of T regs in SLE is associated with high disease activity, acute course and expansion of autoreactive B cells.

REFERENCES:
[1] Zhang SX, Ma XW, Li YF, Lai NL, Huang ZH, Fan K, Wang CH, Li XF. The Proportion of Regulatory T Cells in Patients with Systemic Lupus Erythematosus: A Meta-Analysis. J Immunol Res. 2018 Sep 3;2018:7103219. doi: 10.1155/2018/7103219.
[2] Żabińska M, Krajewska M, Kościelska-Kasprzak K, Jakuszko K, Bartoszek D, Myszka M, Klinger M. CD4(+)CD25(+)CD127(-) and CD4(+)CD25(+) Foxp3(+) Regulatory T Cell Subsets in Mediating Autoimmune Reactivity in Systemic Lupus Erythematosus Patients. Arch Immunol Ther Exp (Warsz). 2016 Oct;64(5):399-407. doi: 10.1007/s00005-016-0399-5.

Disclosure of Interests: None declared
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FRI0220 OCULAR SURFACE INFLAMMATORY MARKERS CORRELATED WITH IMMUNOLOGICAL PARAMETERS IN PRIMARY SJÖGREN'S SYNDROME

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Background: In Sjögren's Syndrome (SS), ocular damage is mediated by inflammation induced by antibodies, enzymes, and other effectors that could be used as clinical indicators of the ocular surface damage. There is evidence suggesting that increased activity of matrix metalloproteinases (MMPs) is corelated with an increased ocular damage because of its potential inflamatory activity and could be used as a potential therapeutic target for dry eye[1,2]. Very few studies have addressed the rol betwen the ocular MMPS and the clinical parameters of SS.
Objectives: To determine the level of correlation between the serological profile of autoantibodies with ophthalmological parameters at the cornea level.
Methods: Cross-sectional, observational, and descriptive study. Sixty patients with a diagnosis of primary Sjögren's syndrome (pSS) classified according to the ACR/EULAR 2016 criteria were included. The following measurements were made: Schirmer test, lacrimal osmolarity, ocular staining score (OSS), and ocular surface disease index (OSDI) and metalloproteinase-9 (MMP-9) in tear and antibodies were measured in peripheral blood serum: RF isotypes (IgA, IgG, IgM), anti-SSA/Ro and anti-SSB/La in.
Results: Fifty-eight women participated (96.7%) with an average age of 53 years (± 13.01) (Table 1). We found a positive correlation between OSS and RF-IgM (rho=0.385 P=0.002), RF-IgA (rho=0.256 P=0.049), and anti-Ro/SSA (rho=0.302 P<0.019). We found a statistically significant association between the seropositivity of the Anti-SSA/Ro antibody and the presence of MMP-9 in tears (OR 4.38, CI 95% 0.877-21.92, P=0.057). A

Spearman correlation test and the association between MMP9 and serology were evaluated whit $\chi 2$ test.

Table 1. Demographic characteristics in Hispanic patients with primary Sjögren's Syndrome

Age, median (DS)	53.23 (13.0)
Female, n (%)	58 (96.7)
Anti-Ro/SSA, n (%)	41 (68.3)
Anti-La/SSB, n (%)	18 (31.6)
RF IgG, n (%)	13 (21.7)
RF IgM, n (%)	31 (51.7)
RF IgA, n (%)	24 (40.0)
Schirmer, n (%)	38 (63.3)
OSDI, n (%)	52 (86.7)
OSS, n (%)	43 (71.7)
Metalloproteinase 9, n (%)	14 (23.3)
Ocular Osmolarity >300, n (%)	45 (75.0)
Abnormal USF, n (%)	45 (75.0)
GSMB, n (%)	51 (85.0)

RF: Rheumatoid Factor, OSDI: Ocular Surface Disease Index, OSS: Ocular Staining Score, USF: Unstimulated Salivary Flow; MSGB: Minor Salivary Gland Biopsy.

Conclusion: A significant correlation was observed between serology, ocular surface damage (OSS), and ocular surface inflammation (MMP-9). The positivity of RF isotypes IgM and IgA could alert the clinician about the ocular damage to initiate a study directed to this organ. Nevertheless this present study shows preeliminary outcomes, we need to enroll more patients to obtain better outcomes.

REFERENCES:

[1] Aluri, H. S., et al. (2015). Role of Matrix Metalloproteinases 2 and 9 in Lacrimal Gland Disease in Animal Models of Sjögren's Syndrome. Investigative ophthalmology & visual science, 56(9), 5218-28.

[2] Messmer, E. M., et al. (2016). Matrix Metalloproteinase 9 Testing in Dry Eye Disease Using a Commercially Available Point-of-Care Immunoassay. Ophthalmology, 123(11), 2300–2308. https://doi.org/10.1016/j.ophtha.2016.07.028.

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FRI0221 CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME IN PREGNANCY: CASE SERIES

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Background: Catastrophic antiphospholipid syndrome (CAPS) is a rare condition associated with high mortality[1]. Prompt recognition and treatment is important for optimal outcomes. Clinical features of CAPS can overlap with obstetric complications, leading to diagnostic challenge[2].
Objectives: Describe two patients with CAPS during immediate post-partum period.
Methods: We report two cases in a single centre over two years.
Results: A 38 year old with obstetric Antiphospholipid syndrome (APS) presented with epigastric pain, transaminitis and thrombocytopenia in keeping with evolving HELLP syndrome. Spontaneous complete miscarriage ensued. Post-delivery, she developed worsening abdominal pain and transaminitis (Table 1). Imaging demonstrated hepatic infarcts and patchy ground glass lung opacities. She was treated for CAPS with intravenous steroids and anticoagulation, and recovered.
A 39 year old with primary APS (deep venous thrombosis and obstetric features) whose antenatal course was fraught with minor per vaginal bleeding (PVB) presented with heavy PVB at 22 weeks gestation requiring cessation of anticoagulation. She developed a deep venous thrombosis. Risk of clot propagation versus bleeding prompted cautious anticoagulation. Labour was induced for declining maternal health and poor foetal prognosis at 24 weeks, 3 days. Post-delivery, she developed abdominal pain, headache, transaminitis and worsening thrombocytopenia with heavy PVB requiring uterine artery embolization. Given features that were consistent with micro thrombi and ischaemia (Table 1), she was treated as for CAPS and HELLP syndrome with intravenous steroids, plasma exchange (PLEX) and intravenous immunoglobulin (IVIG), and recovered.

Table 1

	Case 1	Case 2
Gestational age on admission	17 weeks 5 days	22 weeks 5 days
Treatment during pregnancy prior to CAPS	LMWH^ once daily, Aspirin	LMWH twice daily, Aspirin, Steroids, Hydroxychloroquine, monthly IVIG
Time of onset of CAPS	2nd day after foetal loss	4th day after foetal loss
Organ involvement	Hepatic, Pulmonary, Placenta	Hepatic, Central nervous system, Placenta
Laboratory results at onsets of CAPS		
Haemoglobin (g/dL)	7.4	10.1
Platelets (x10^9/L)	82	28
AST°/ALT"/LDH◊ (U/L)	137/140/690	1199/1130/2206
Estimated proteinuria (g/day)	2.7	2.3
Positive serologies	Anti-Ro	Anti-nuclear antibody, Anti-double stranded DNA, Lupus anticoagulant, Anti-cardiolipin IgM/IgG, B2 glycoprotein IgM/IgG
Treatment	IV MP*, LMWH 1mg/kg/day twice daily	IV MP, PLEX, IVIG, LMWH 1mg/kg/day twice daily
Outcomes		
Obstetric	Intra-uterine foetal demise	
Maternal	Recovery	

^Low molecular weight heparin. °Aspartate aminotransferase. "Alanine aminotransferase. ◊Lactate dehydrogenase. *Intravenous Methylprednisolone
Conclusion: Recognition of CAPS is complex in pregnancy. Vigilance is required for urgent aggressive treatment to improve outcomes in this uncommon condition.

REFERENCES:

[1] Bucciarelli S, Espinosa G, Cervera R, et al. Mortality in catastrophic antiphospholipid syndrome: causes of death and prognostic factors in a series of 250 patients. Arthritis Rheum 2006; 54: 2568–2576.

[2] Silver RM. Catastrophic antiphospholipid syndrome and pregnancy. Semin Perinatol. 2018 Feb;42(1):26-32.

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FRI0222 ANALYSIS OF CLINICAL AND SEROLOGICAL PICTURE OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROMEAND AN EARLY DISEASE ONSET AT AGE BEFORE 35 YEARS

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Background: Primary Sjögren's Syndrome (pSS) is a chronic systemic autoimmune disease with diverse clinical picture, extending from exocrinopathy to systemic disease and non-Hodgkin's lymphoma (NHL). Usually, it affects middle aged women, but early disease onset (≤35 years old) has been also observed. So far, there is a limited number of studies to explore whether the age of SS onset affects the clinical SS phenotype[1]. To definitely answer this question a well-organized, large, harmonized cohort of patients with a continuous follow up is needed, through the ongoing European project (HarmonicSS, grant agreement no: 731944).
Objectives: To investigate whether the clinical and serological picture of pSS patients with early disease onset (≤35 years old) differs to that of middle-age onset.
Methods: Medical records of 717 pSS patients, included in two Greek cohorts fulfilling the 2002 revised European/American International classification criteria for SS, were evaluated. The study group included 133 (18,5%) patients with disease onset ≤35 years (median disease duration, range: 10, 0-32 years; group A) matched at 1:1 ratio according to gender and disease duration with 133 pSS patients with middle-age onset (mean

age at disease onset 52±5 years; median disease duration, range: 10, 0-30; group B). Clinical and laboratory data were collected through an extensive clinical chart review. All parameters were compared by chi-square or Fisher's exact test, when appropriate.
Results: The two pSS groups had similar frequencies of non-specific clinical findings (chronic fatigue, arthralgias-myalgias, arthritis, Raynaud's phenomenon), periepithelial manifestations (interstitial nephritis, lung and liver disease), splenomegaly, leucocyte and neutrophil counts. However, patients with disease onset ≤35 years old, exhibited increased proportion of salivary gland enlargement (SGE; 43,8% vs 25,4%, p=0,003), lymphadenopathy (18,2% vs 7,6%, p=0.016), palpable purpura (20,3% vs 9,8%, p=0,025), anti-Ro/SSA antibodies (90,2% vs 74%, p=0,001), rheumatoid factor positivity (73,3% vs 53,6% p=0,002), low C4 levels (64,5% vs 42,4%, p=0,001) and NHL (18% VS 8,3%, p=0.028).
Conclusion: Our findings suggest that young patients with pSS display increased prevalence of systemic features, B cell hyperreactivity, as well as heightened risk for lymphoma development. Further prospective studies with a larger number of patients are needed to address whether early disease onset may also serve as an additional risk factor for NHL development.

REFERENCES:
[1] Anquetil C et al, Rheumatology, 2019

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FRI0223 EXTRACELLULAR VESICLESAS A SOURCE OF BIOMARKERS IN SJÖGREN SYNDROME: A SWATH-MS PROTEOMIC APPROACH

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Background: Primary Sjögren's syndrome (pSS) is a multifactorial autoimmune disorder characterized by lymphocytic infiltration of the exocrine glands. In the recent past several proteomic studies attempted to look at valid biomarkers for pSS in whole saliva, however little is known about the composition of salivary extracellular vesicles (EVs), nor to what extent their content may reflect the phenotypic state of the disease.
Objectives: In this study, we search for pSS specific biomarkers by using a sequential window acquisition of all the theoretical fragment ion spectra (SWATH-MS) approach to monitor the dynamics of saliva EVs sub-proteome of pSS patients compared to healthy controls.
Methods: We included patients with a diagnosis of pSS made according to the AECG 2002 criteria and healthy volunteers as controls. Saliva was collected under standardized conditions. EVs were enriched by sequential ultracentrifugation steps from saliva samples. Peptide identification and quantitation was performed by matching SWATH data against an assay library of MS/MS spectra created from a previously acquired data-dependent acquisition (DDA) method. GO terms and protein-protein interaction network analysis were performed using Cytoscape software.
Results: We included 20 pSS patients (AECG 2002 criteria) and 10 healthy subjects. Quantitative data evidenced a distinct separation between the patient group and control group, indicating that pSS may modulate the phenotype of protein cargoes of salivary EVs. The majority of the proteins up-regulated in pSS compared to controls were found to be involved in several inflammatory processes. Particular emphasis was given to proteins converging to IL-12 signaling that included annexin A2, cofilin, macrophage migration inhibitory factor (MIF), S100A8-A9 and plastin-2 proteins.
Conclusion: Our results revealed that the inflammatory phenotype observed in pSS patients is also extended to salivary EVs, which protein content may represent a novel source for potentially useful biomarkers for pSS.
Disclosure of Interests: Chiara Baldini: None declared, Francesco Finamore: None declared, Francesco Ferro: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB, Stefano Bombardieri: None declared, Silvia Rocchiccioli: None declared, Antonella Cecchettini: None declared
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FRI0224 PREVALENCE OF SJÖGREN'S SYNDROME IN THE COMMUNITY OF MADRID

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Background: Several studies on the epidemiology of autoimmune diseases performed within the past several decades revealed a prevalence of Sjögren Syndrome (SS) between 0.3% and 4.83% (1). More recent studies revealed a lower prevalence between 31/100,000 to 49/100,000 (2 3). The exact prevalence of SS is unknown due to the heterogeneity of the populations and geographic areas studied, the utilization of different diagnostic tests or the lack of a unique classification criteria for the disease. Also, the disease may have an insidious onset and a variable course with a broad spectrum of clinical manifestations, so the diagnosis may be delayed or SS patients may be missed and misclassified as other rheumatic disease. Besides, SS can occur alone (primary SS) or in association with other specific systemic autoimmune rheumatic diseases (secondary SS).
Objectives: The aim of our study was to determine the prevalence of SS in the Community of Madrid (CM) and to describe the sociodemographic and clinical characteristics of these patients.
Methods: Population-based cross-sectional study in the CM, Spain. The information source for SS cases was the Registry of rare diseases in the CM (SIERMA).
A descriptive analysis of the main sociodemographic and clinical characteristics of SS cases was performed.
Prevalence per 10,000 inhabitants in people with 18 years of age and over, stratified by sex and their 95% confidence intervals (CI) were calculated for 2015. The denominator was the people registered at the Population Register in the middle of the period (July 2015).
Results: There were 4,778 cases of SS in SIERMA and 389 (8,1%) of them were already dead. 4434 (92.8%) were women. The median age was 64,7 years (15,4), and the maximum age was 103 years. The disease was most frequent in the sixth decade with 1079 cases (22,6%), in the seventh decade with 1120 cases (23,4%) and in the eighth decade with 935 cases (19,6).
3116 cases (65.2%) were classified as primary SS (pSS) and 1662 (34.8%) as secondary SS (sSS).
Among the sSS the main rheumatological conditions associated were rheumatoid arthritis (58%), lupus (24,5%), systemic Sclerosis (10,5%); mixed connective tissue (4%), inflammatory muscle disease (2%) and vasculitis (1%).
The prevalence of SS in adults (≥ 18 years of age) was 8.4/10,000 with a 95% CI: 8.2 – 8.7 (14.9% in women and 0,8% in men). The prevalence of pSS was 5.5/10,000 (CI 5,3 – 5,7) and for sSS was 2.8/10,000 (95%CI: 2.7-3).
Conclusion: SS mainly affects females during the sixth, seventh and eight decades of life, and shows a female:male ratio of 9:1. Two out of three cases of SS identified were classified as pSS. The main rheumatological conditions associated were rheumatoid arthritis and lupus. The estimated prevalence of SS in the Community of Madrid population is lower than the observed in previous studies whereas the prevalence of pSS is similar than the observed in current studies.

REFERENCES:
[1] Toms ̈ic ̆ M, Logar D, Grmek1 M, Perkovic T, Kveder T. Prevalence of Sjögren's syndrome in Slovenia. Rheumatology. 1999;38:164–70.
[2] Sardu C, Cocco E, Mereu A, Massa R, Cuccu A, Marrosu MG, et al. Population Based Study of 12 Autoimmune Diseases in Sardinia, Italy: Prevalence and Comorbidity. Ashour HM, editor. PLoS One [Internet]. 2012 Mar 2;7(3):e32487. Available from: http://dx.plos.org/10.1371/journal.pone.0032487
[3] Prevalencia de las enfermedades raras: Datos bibliográficos », Informes Periódicos de Orphanet, Serie Enfermedades Raras, Enero 2019, Número 1 : Listado por orden alfabético de enfermedades o grupo de enfermedades http://www.orpha.net/orphacom/cahiers/docs/ES/Prevalencia_de_las_enfermedades_raras_por_orden_alfabetico.pdf

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FRI0225

THE EULAR/ACR 2018 AND SLICC 2012 HAVE INCREASED SENSITIVITY AGAINST THE ACR 1997 CLASSIFICATION CRITERIA AND CLASSIFY NON-OVERLAPPING GROUPS OF SLE PATIENTS: SIMULTANEOUS APPLICATION ASSURES THE GREATEST CAPTURE OF PATIENTS IN CLINICAL PRACTICE

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Background: A joined EULAR/ACR initiative has proposed a new set of classification criteria for SLE based on weighted items and the use of ANA as an entry criterion.
Objectives: To compare the diagnostic performance of the old and new classification criteria against physician diagnosis in an early SLE cohort and examine phenotypic and prognostic differences among patients who are classified with the criteria.
Methods: Adult patients diagnosed by experienced physicians with SLE (n=690) or control diseases (n=301) during 2005-2016 and followed-up at least 6 months. All sets of criteria (ACR 1997, SLICC 2012, EULAR/ACR 2018) were applied. Hazard models were used to calculate elapsed time between the earliest item (of any criterion) and classification. Severity of SLE (BILAG-2004 glossary) and the SLICC/ACR organ damage index were determined.
Results: The SLICC and EULAR/ACR had increased overall sensitivity as compared to the ACR criteria (91.3%, 88.6%, 85.7%, respectively; p<0.01), especially in early-onset (<3 years) disease (91.4%, 87.3%, 79.9%, respectively; p<0.001), with comparable specificity rates (ranging 91.0–92.7%). By combining the three criteria sets, 97.1% of patients were classified. Both the EULAR/ACR and the SLICC enabled earlier SLE classification (median time-to-classification: 7.1 and 7.6 months, respectively) than the ACR criteria (median 9.1 months). Nevertheless, disease classification was delayed by >3 months in 17.3–19.9% of cases, particularly in neurological SLE (20.0–26.8%). Comparative analysis of patients who were missed by the criteria revealed significant differences in rates of individual clinical and serological features (**Table 1**) suggesting that existing criteria may classify non-overlapping groups of patients. Importantly, unclassified patients presented with a high prevalence of moderate/severe disease (43.3–60%) and organ damage (30–50%).
Conclusion: Despite improved sensitivity and earlier classification with the EULAR/ACR and the SLICC criteria, still SLE diagnosis may be missed or delayed even in patients with moderate to severe disease, especially neurological-dominant disease. Simultaneous application in clinical practice assures the greatest capture of patients.

Table 1. Prevalence of clinical and immunological features across groups of SLE patients who were not classified by the criteria

		Missed by the			
	ACR 1997	SLICC 2012	EULAR/ACR 2018	All three criteria	
	n=99	n=60	n=79	n=20	
SLICC 2012 items					**P value**
ACLE	49.5%	80.0%	72.2%	60.0%	<0.001
CCLE	10.1%	8.3%	17.7%	5.0%	0.206
Alopecia	42.4%	36.7%	63.3%	45.0%	0.008
Ulcers	12.1%	23.3%	51.9%	15.0%	<0.001
Synovitis	69.7%	86.7%	74.7%	65.0%	0.076
Serositis	6.1%	10.0%	12.7%	10.0%	0.506
Renal disorder	3.0%	3.3%	6.3%	10.0%	0.455
Neurologic disorder	8.1%	6.7%	6.3%	20.0%	0.232
Hemolytic anemia	3.0%	0.0%	2.5%	0.0%	0.503
Leukopenia	20.2%	15.0%	27.8%	10.0%	0.166
Thrombocytopenia	18.2%	6.7%	12.7%	10.0%	0.205
Anti-DNA	18.2%	3.3%	0.0%	0.0%	<0.001
Anti-Sm	2.0%	0.0%	1.3%	0.0%	0.664
Anti-phospholipid Ab	18.2%	1.7%	11.4%	5.0%	0.011
Low complement	43.4%	3.3%	21.5%	5.0%	<0.001
Coombs test	5.1%	0.0%	2.5%	0.0%	0.232
ANA	84.8%	56.7%	44.3%	50.0%	<0.001

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FRI0226

LOW EXPRESSION OF ESTROGEN RECEPTOR BETA IN RENAL TUBULAR EPITHELIAL CELL MAY CONTRIBUTE TO HYPERURICEMIA IN PREMENOPAUNITED STATES OF AMERICAL FEMALE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: We have reported that the incidence of hyperuricemia of young female systemic lupus erythematosus (SLE) patients was higher than that of healthy young women[1].Whether the estrogen receptor (ER) expressed in renal tubular tissue contributes to it? There are few reports yet.
Objectives: To investigate the expression of ERs in the renal tubular cells and their relationship with serum uric acid (UA) levels in premenopausal female SLE patients.
Methods: Eighteen kidney biopsy specimens of premenopausal female SLE patients served as the lupus nephritis group (LN group), and 12 specimens of premenopausal female IgA nephropaty patients served as the IgA group. Serum UA levels and kidney index were collected, and the expression of ERs in the renal tubular epithelial cell of the two groups were determined by immunohistochemistry. According to the

percentage of the positive stained cells, the semiquantitative analysis was made. The expressions of ERs, including ERα and ERβ, of the two groups were compared, and the relationship between the expression of ERs and serum UA levels were analyzed with linear regression analysis.

Results: 1. The mean ages of the LN group and the IgA group were 27.39±8.09 years and 33.08±5.45 years, respectively, with significantly different (t=2.128, p=0.042). There was no renal failure subject in both groups (CRE level above 120μmol/l), and all the SLE patients were at stage of onset.

2. Mean UA level of the LN group was significantly higher than that of the IgA group (t=-3.149, P=0.004), and the CRE level of the two groups were similar (t=-0.109, P=0.914) (table1).

3. In each group, ERβ was well expressed in the tubular epithelial cells, and no in kidney glomeruli. In contrast, ERα was not expresssed in the renal tissues of both groups (figure1).

4. The median score of ERβ expression in the LN group was remarkable lower than that of the IgA group (z=-2.080, P=0.038, table 1).

5.Linear regression analysis indicated that ERβ expression scores of the total 30 patients had significantly negative correlation with serum UA levels (t=-2.141, P= 0.041, table2).

Conclusion: 1. Low expression of ERβ in renal tubular epithelial cell may contribute to hyperuricemia in premenopausal female SLE patients.

2. ERα showed no expression in LN and IgA nephropaty kidney tissues.

REFERENCES:

[1] Haijun Liu, Xiaoyan Cai, Lie Dai, et al. Elevated uric acid levels in premenopausal female systemic lupus erythematosus patients: association with potential or existing renal damage. Eur J Inflamm,2018,16:1-6.

Table 1. Comparative analysis of main clinical biomarkers in LN groups and IgA group

	LN group (n=18)	IgA group (n=12)	P value
Age (year)	27.39±8.09	33.08±5.45	t=2.128 p=0.042
UA (μmol/L)	510.33±141.50	383.25±78.72	t=-3.149 p=0.004
CRE (μmol/L)	92.22±11.71	91.72±12.64	t=-0.109 p=0.914
ER α	0	0	
ER β	0.08(0.02,0.23)	0.20(0.10, 0.30)	z=-2.080 p=0.038

UA: uric acid; CRE: creatine; ER: estrogen receptor.

Table 2. The correlation of ERβexpression scores in the renal tubular epithelial cell with serum UA levels in premenopausal female SLE patients

Variable	Unstandardized Coefficients		Standardized Coefficients	t	P	95%CI	
	B	SEM					
ERβ	-317.004	148.040	-0.375	-2.141	0.041	-620.251	-13.757
Constant	516.455	148.040		14.641	0.000	444.198	588.712

ER: estrogen receptor

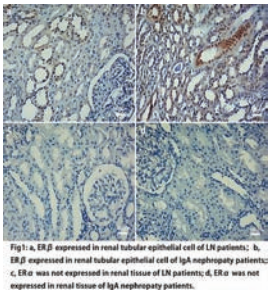


Fig1: a, ERβ expressed in renal tubular epithelial cell of LN patients; b, ERβ expressed in renal tubular epithelial cell of IgA nephropaty patients; c, ERα was not expressed in renal tissue of LN patients; d, ERα was not expressed in renal tissue of IgA nephropaty patients.

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FRI0227 **PREGNANCY OUTCOMES IN A LONG-TERM FOLLOW-UP COHORT OF PEDIATRIC ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (PSLE) AT A TERTIARY CARE CENTER IN NORTH-WEST INDIA**

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Background: Pediatric-onset SLE (pSLE) represents 10–20% of all SLE cases, and is associated with more severe disease as compared to adult onset SLE. pSLE patients are known to have more frequent systemic involvement especially related to kidneys, central nervous system and musculoskeletal system(1). Pregnant women with SLE have increased risk of adverse outcomes including disease flare, spontaneous abortion, preeclampsia/eclampsia, premature birth and maternal death(2). There is paucity of literature in pregnancy outcomes among women with pediatric onset SLE, especially from developing countries

Objectives: To evaluate pregnancy outcomes in a long term follow up cohort of pediatric SLE patients from a tertiary care center in North India

Methods: We have reviewed our previously published cohort of 27 pSLE patients who were diagnosed as SLE between 1998 and 2003. They were being followed-up at Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Postgraduate Institute of Medical education and research, Chandigarh, India. We have analyzed disease related complications, antiphospholipid antibody profile, pregnancy related complications and long-term outcomes in these patients.

Results: Follow up records of 27 pSLE patients were retrieved from the clinical files. Data are available for 14 patients (i.e. 52% of the original cohort). Six (22%) of 14 patients expired due to disease related complications (2 had end stage renal disease, 1 had pulmonary thromboembolism, 2 had pulmonary hemorrhage, 2 had sepsis). Eight patients have been on follow-up till date with mean duration of follow-up of 20 years (range:16-25 years). Total patient years of follow up was 160 years. Of the 8 patients on follow up, renal manifestations were seen in 4(50%), neuropsychiatric in 4(50%), severe hematologic in 3(37.5%), musculoskeletal in 1(12.5%), antiphospholipid antibody (APLA) positivity in 3(37.5%) patients. Disease and therapy related complications were seen in 3 patients (obesity in 2, osteopenia and avascular necrosis of femur in 1, hypertension in 1). Eight pregnancies were observed in 5 of these patients; 1 patient had primary infertility. Mean age at first pregnancy was 19 years (range: 21-25 years). All 5 patients received hydroxychloroquine throughout the pregnancy and disease activity was well controlled. APLA testing was done in 2 patients during pregnancy and both tested negative. Five live births and 3 fetal losses were observed. The fetal losses were spontaneous first trimester abortions. None had eclampsia/pre-eclampsia, ectopic pregnancy or adverse fetal outcomes (prematurity, intrauterine growth restriction, heart defects).

Conclusion: This is one of the longest follow-up studies in pSLE patients and probably the only one where pregnancy outcomes have been studied in a pediatric onset disease in context of a developing country. Our results show that in the presence of well controlled symptoms, pregnancy related outcomes are favorable with minimal fetal and maternal complications even in resource limited settings.

REFERENCES:

[1] Abujam B, Gupta A, Suri D, Rawat A, Singh S. Trends and predictors of mortality in childhood onset lupus in a single North-Indian centre over 23 years: a retrospective study. Clin Exp Rheumatol. 2016;34(3):554–9.

[2] Ling N, Lawson E, von Scheven E. Adverse pregnancy outcomes in adolescents and young women with systemic lupus erythematosus: a national estimate. Pediatr Rheumatol. 2018 Apr 16;16(1):26.

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FRI0228 **KL-6 AS A BIOMARKER OF DEVELOPING INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SJÖGREN SYNDROME**

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Background: Sjögren syndrome (SS) is an autoimmune disease presented with exocrine gland inflammation and extra-glandular involvement. The

prevalence of pulmonary involvement, including interstitial lung disease (ILD), in patients with primary SS widely varies from 8% to 20%.[1,2]Patients with SS with ILD have high morbidity and a fourfold increase in mortality.[3]

Objectives: Krebs von den Lungen-6 (KL-6) is a mucin-like, high-molecular-weight glycoprotein; it is expressed in regenerating type II pneumocytes. Serum KL-6 is highly associated with the activity of ILD in patients with radiation pneumonitis, idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, sarcoidosis, rheumatoid arthritis, polymyositis, dermatomyositis and systemic sclerosis.[4-8] The increase in serum KL-6 level might reflect the increase in the number of regenerating type II pneumocytes secondary to pulmonary damage.[8] We hypothesise that an early pulmonary damage occurs before clinical or radiological evidence of ILD in patients with SS.

Methods: In this retrospective case-control study, patients who were diagnosed with primary SS and fulfilled the American-European Consensus Group Criteria for Sjögren's Syndrome were included. Clinical information, laboratory results on inclusion, images and pulmonary functions test results were recorded via electronic medical records review. Pulmonary radiography including chest X-ray and chest computed tomography was reviewed by a chest physician.

Results: Of the 39 patients with SS, 21 (53.85%) developed ILD at the end of follow-up. The follow-up period was 2.65 ± 1.88 years. The time to diagnosis of ILD was 2.72 ± 1.74 years in the ILD group. The serum KL-6 level was 1920.10 ± 1974.26 U/ml in the ILD group and 894.11 ± 788.53 U/ml in the non-ILD group ($p = 0.001$). The diffusing capacity of the lungs for carbon monoxide was 70.76 ± 19.63 mmHg and 91.88 ± 12.02 mmHg in the ILD group and non-ILD group, respectively ($p < 0.001$).

Conclusion: Serum KL-6 level is significantly higher in patients with primary SS with developing ILD and may represent an early non-radiographic pulmonary damage. Serum KL-6 can be a valuable biomarker in predicting the development of ILD in patients with primary SS.

REFERENCES:

[1] Roca F, Dominique S, Schmidt J, et al. Interstitial lung disease in primary Sjogren's syndrome. Autoimmunity reviews. 2017; 16: 48-54.
[2] Kreider M and Highland K. Pulmonary involvement in Sjogren syndrome. Seminars in respiratory and critical care medicine. 2014; 35: 255-64.
[3] Palm O, Garen T, Berge Enger T, et al. Clinical pulmonary involvement in primary Sjogren's syndrome: prevalence, quality of life and mortality-a retrospective study based on registry data. Rheumatology *(Oxford, England)*. 2013; 52: 173-9.
[4] Hamada H, Kohno N, Akiyama M and Hiwada K. Monitoring of serum KL-6 antigen in a patient with radiation pneumonia. Chest. 1992; 101: 858-60.
[5] Kobayashi J and Kitamura S. Serum KL-6 for the evaluation of active pneumonitis in pulmonary sarcoidosis. Chest. 1996; 109: 1276-82.
[6] Oyama T, Kohno N, Yokoyama A, et al. Detection of interstitial pneumonitis in patients with rheumatoid arthritis by measuring circulating levels of KL-6, a human MUC1 mucin. Lung. 1997; 175: 379-85.
[7] Takanashi S, Nishina N, Nakazawa M, Kaneko Y and Takeuchi T. Usefulness of serum Krebs von den Lungen-6 for the management of myositis-associated interstitial lung disease. Rheumatology *(Oxford, England)*. 2019.
[8] Elhai M, Hoffmann-Vold AM, Avouac J, et al. Performance of candidate serum biomarkers for systemic sclerosis-interstitial lung disease. *Arthritis & rheumatology (Hoboken, NJ)*. 2019.

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FRI0229 SOLUBLE CD163 IS A BIOMARKER FOR ACCELERATED ATHEROSCLEROSIS IN SLE PATIENTS AT APPARENT LOW RISK FOR CARDIOVASCULAR DISEASE

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Background: Cardiovascular disease (CVD) due to accelerated atherosclerosis is the leading cause of death in SLE. Probably because they do not incorporate important risk factors such as overweight, chronic kidney disease or systemic inflammation, models for predicting CVD established in the general population (such as Framingham model) underestimate the cardiovascular risk in SLE. Identification of biological markers for CVD may help to classify high-risk subjects and set up targeted prevention in SLE.

Objectives: Our study aimed to determine whether sCD163, a soluble macrophage marker upregulated in numerous inflammatory disorders, might be predictive of accelerated atherosclerosis associated with SLE

Methods: Carotid ultrasound was prospectively performed in 63 consecutive SLE patients asymptomatic for cardiovascular disease (CVD) and 18 volunteer health-workers. Ultrasound was performed at baseline and during follow up. Serum level of sCD163 was determined at baseline using ELISA. The primary outcome was the presence of a carotid plaque. Factors associated with carotid plaques were identified through multivariate analysis.

Results: Despite a low risk for cardiovascular events according to Framingham score in both groups (2.1% ± 3.8 in SLE vs 2.1% ± 2.9 in controls; p=0.416), ultrasound study at baseline showed a carotid plaque in 23 (36.5%) SLE patients versus 2 (11.1%) controls (p=0.039). Multivariate analysis showed that SLE status increased the risk for carotid plaque by a factor of 9 (p=0.017). In SLE patients, sCD163 level was high (483.7ng/ml ± 260.8 versus 282.1ng/ml ± 97.5 in controls; p<0.001) and independently associated with carotid plaques as assessed by stratification based on sCD163 quartile values (p=0.009), receiver operating characteristic (ROC) (p=0.001) and multivariate analysis (p=0.015). Eventually, sCD163 at baseline was associated with the onset of carotid plaque during follow up (3±1.4 years) in SLE patients who had no carotid plaque at first evaluation (p=0.041)

Conclusion: sCD163 is associated with progressing carotid plaque in SLE and may be a useful biomarker for accelerated atherosclerosis in SLE patients at apparent low risk for CVD

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FRI0230 CLINICAL AND ECHOCARDIOGRAPHIC CHARACTERISTICS OF MYOCARDIAL INJURY IN SYSTEMIC LUPUS ERYTHEMATOSUS, CLASSIFIED ACCORDING TO CARDIAC MAGNETIC RESONANCECRITERIA

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Background: Lupus myocarditis (LM) occurs in 5-10% of patients with systemic lupus erythematosus (SLE). Subclinical myocardial inflammation occurs in 37% at post mortem.[1] Echocardiographic strain (STE) supports subclinical myocardial dysfunction in SLE.[2] Tissue characterisation by cardiac magnetic resonance (CMR) identifies myocardial inflammation, necrosis and/or fibrosis, detecting clinical and subclinical myocardial injury (MIN) in SLE. It's the non-invasive gold standard for diagnosing myocarditis (all types) based on the Lake Louise criteria (LLC).[3]

Objectives: Determine prevalence of MIN in SLE (LLC).
Compare clinical and echocardiographic (echo) features of patients with and without MIN.
Identify echo predictors of MIN.
Methods: A prospective crossectional study was done at Tygerberg Hospital, Western Cape, South Africa. Adult inpatients, fulfilling the 2012 SLICC criteria were screened. Echo analyses included STE and regional function (wall motion score (WMS)). Patients were grouped according to evidence of MIN (absent criteria [AC]; single criterion [SAC]; fulfilling LLC), comparing clinical, laboratory and echo data. Logistic regression and ROC were used to determine predictors of MIN.
Results: 49/106 SLE patients screened were included (Figure 1). 46.9% of patients had MIN (≥1 criterion): 12.2% fulfilled LLC for LM and 34.7% had a SAC. SLE disease activity (SLEDAI) (p=0.022) was higher in patients fulfilling LLC, but not in the SAC group. A clinical and echo diagnosis of LM was made in all patients fulfilling LLC, in 17.6% of patients in the SAC group and none in the AC group (Table 1). Anti-DsDNA and anti-B2GP1 were more frequently positive in SAC vs the AC group (p=0.054 and 0.081). WMS was higher in LLC and SAC groups (p=0.006;p=0.083) with mid and basal STE more impaired in patients with MIN (p=0.047;p=0.043). LVID and mid STE score combined was the best predictor of MIN (Table 2; Figure 2).
Conclusion: CMR evidence of MIN is common in SLE, even in the absence of clinical myocardial dysfunction or high lupus activity. Impaired echo regional and global function occurs more frequently in patients with MIN. STE combined with LVID predicts MIN detected by CMR and has potential as a cost effective screening tool. CMR is limited by a high exclusion rate in SLE, mainly due to renal impairment.

REFERENCES:

[1] Panchal L, et al. Cardiovascular involvement in systemic lupus erythematosus: an autopsy study of 27 patients in India. J Postgrad Med. 2006;52:5-10.
[2] Gusetu G, et al. Subclinical myocardial impairment in SLE: insights from novel ultrasound techniques and clinical determinants. Med Ultrason. 2016;18:47-56.
[3] Friedrich M, et al. Cardiovascular Magnetic Resonance in Myocarditis: A JACC White Paper. J Am Coll Cardiol. 2009;53:1475–87.

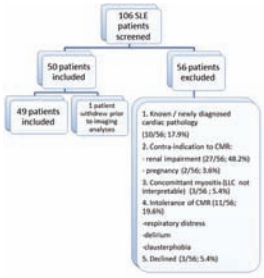


Figure 1

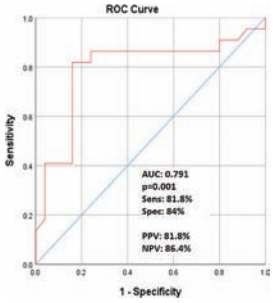
Table 1

	AC n=26	LLC n=6	p	SAC n=17	p
			Med (IQR)		
Age	27 (21-35)	27 (23-28)	1	29 (23-36)	0.542
SLE duration, days	114(6-1366)	35(31-44)	0.724	955(7-2101)	0.486
SLEDAI	13(9-15)	22(16-26)	0.022	12(9-20)	0.813
Antiphospholipid syndrome	2 (8)	0	0.483	4 (24)	0,085
			n (%)		
Female	24 (92)	5 (83)	0.497	14(82)	0.319
Cardiac risk factors	8 (31)	1 (17)	0.489	6 (35)	0.757
Nephritis	9(35)	3(50)	0.483	3(18)	0.225
Clinical LM	0	6(100)	<0.001	3(18)	0.026

Table 2

Logistic regression			
		Univariate	
Echo variable	**OR**	**95% CI**	**p**
LVID	2.6	0.8-8.4	0.109
LV ejection fraction	0.9	0.8-0.9	0.018
Wall motion abnormality	4.2	1.3-13.9	0.018
GLS	1.3	1-1.6	0.049
STE score Basal	1.6	0.9-2.7	0.068
Mid	1.9	1.2-3.2	0.006
Apical	1	0.9-3.9	0.083
		Multivariate	
LVID	3.5	0.9-13.3	0.070
Mid STE score	2.1	1.2-3.5	0.008

Figure 2



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FRI0231 IN PATIENTS WITH UCTD, IFN ACTIVITY IDENTIFIES PATIENTS THAT PROGRESS TO DEFINITIVE CTD CLASSIFICATION CRITERIA

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Background: Undifferentiated connective tissue disease (UCTD) is a term used to describe individuals with positive autoantibodies and symptoms but do not meet criteria for an established autoimmune CTD (AI-CTD). The prognosis of UCTD is unclear, could result in disease stability, remission or progression. As this condition is understudied, there is an unmet need for biomarkers to stratify those who progress to allow for a more aggressive therapy to be employed. IFN plays a major role in the pathogenesis of various AI-CTDs. However there are limited data on its role in AI-CTD.
Objectives: To determine whether IFN assays can predict progression from UCTD to meeting classification criteria of established AI-CTDs.
Methods: A prospective observational study was conducted on 43 consecutive patients with UCTD; as defined by Mosca criteria [1]. Progression was defined by meeting 2012 ACR/SLICC SLE, 2016 ACR/EULAR Primary Sjogren's, Bohan-Peter, 2013 ACR/EULAR Scleroderma, or 2006 Sydney Antiphospholipid syndrome criteria. For the interferon scores, RNA was extracted from PBMCs and a custom Taqman array was used to measure expression of 30 interferon stimulated genes (ISGs) as previously described [2]. A two-score system of ISGs (IFN-Score-A and Score-B), was calculated without the knowledge of participants' clinical status.
Results: Mean (range) age of the cohort was 48 (39-58) years; Female 36 (84%); mean disease duration 5.5 years; concomitant DMARDs including anti-malarials 38 (88%), concomitant corticosteroid 2(5%) and internal organ involvement 9 (21%). At the follow-up visit, 9/43 (21%) met established classification criteria for AI-CTD [SLE=6; IIM=2; and SSc=1]. Comparing the IFN scores between those who progressed (n=9) vs those remained undifferentiated (n=34); the IFN-Score-A was higher in the progressor group; fold difference (FD) 2.76 (95% CI 1.11-6.88); p=0.030. While for IFN-Score-B, there was a trend to association for higher expression in the progressor group vs remained undifferentiated; FD 1.74 (0.53-3.21); p=0.077.
Conclusion: IFN assays can identify progression to classifiable CTD within cohorts of UCTD. There is a potential role for the use of IFN biomarkers in the prognostication of patients with UCTD.

REFERENCES:
[1] Mosca M, Neri R & Bombardieri S. 1999. UCTD: a review of the literature and a proposal for preliminary classification criteria. Clin Exp Rheumatol; 17: 615-620
[2] El-Sherbiny YM, Psarras A, Yusof MY Md, Hensor EMA, Tooze R, Doody G, Mohamed AAA, McGonagle D, Wittmann M, Emery P & Vital E

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FRI0232 PATIENT PERCEPTION OF SLE BURDEN: THE ROLE OF ORGAN DAMAGE

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Background: physician-based assessment of Systemic Lupus Erythematosus (SLE) may not be able to capture the real disease impact on patients' life. In the literature, the impact of disease damage on patients' quality of life (QoL) is controversial.
Objectives: Objective of our study was to investigate the role of organ damage in determining patient perception of SLE burden.
Methods: this is a cross-sectional study that enrolls patients with a diagnosis of SLE (ACR 1997 criteria). For each patient, demographics, comorbidities, treatment, clinical and laboratory data were collected. Disease damage was evaluated with the SLICC-Damage Index (SDI) and a score >2 was defined as "severe damage". The BILD (Brief Index of Lupus Damage) was used for patient self-evaluation of organ damage. Finally, the Lupus Impact Tracker (LIT) questionnaire was used to assess patient perception of SLE burden.
Results: we included 246 adult SLE patients (94.7% Caucasian, 93.1% female, mean age 45.31±13.2 years, mean disease duration 14.3±9.8 years). As for cumulative organ involvement in our cohort, the most prevalent was articular involvement (67.5%), followed by cutaneous (54.1%), hematological (51.2%), renal (43.9%) and serositis (17.9%); 11.8% had a history of NPSLE. Among comorbidities, 10.9% of patients had a concomitant fibromyalgia. 48.8% of patients was presenting at least one organ damage; among those patients, the median SDI was 2 (IQR 1-3); 16.3% of patients had a "severe damage" and among them median SDI was 4 (IQR 3-6). The most frequent items of organ damage in our cohort were: cataract (19.9%), deforming or erosive arthritis (10.2%) and osteoporosis with fracture (8.5%). Moreover, a significant number of patients (18.3%) met the criteria for neuropsychiatric damage, mainly cerebrovascular accidents (7.3%), seizures (5.3%) and cognitive impairment (4.1%). Finally, a not negligible number of patients had premature gonadal failure (4.5%) and malignancy (6.5%).
As far as patients' perception is concerned, the median LIT score in the cohort was 22,5 (IQR 7.5-40) and median BILD was 1 (IQR 0-2).
In a multiple linear regression analysis, we found a direct positive correlation between the SDI score and age at enrollment and disease duration ($p<0,001$). Severe damage resulted associated with a history of serositis ($p<0,01$) and NPSLE ($p<0,001$). We also found a positive linear correlation between the SDI score and the patient's self- reported damage (BILD score; $p<0,001$) and with the patient's perception of disease burden (LIT; $p<0,01$), irrespective of age and disease duration. In particular, in the multivariate analysis, higher SDI scores were significantly associated with a poorer perception of disease burden in terms of: future planning ($p<0,001$), usual activities, family responsibilities, discomfort due to physical appearance ($p<0,01$) and drug side effects ($p<0,05$), irrespective of fibromyalgia and age at enrollment.
Among the different types of organ damage, we found that cognitive impairment, cerebrovascular accidents and premature gonadal failure mainly contribute to determine SLE burden. In fact, they were significantly associated with higher LIT scores ($p<0,05$).
Conversely, SDI score was not related with health-related quality of life and fatigue as measured by SF-36 and FACIT respectively, neither with fibromyalgia.
Conclusion: disease damage seems to have a role in determining patient perception of SLE burden, mainly affecting patients' ability to plan the future and to fulfill daily activities and family responsibilities. In particular, neuropsychiatric damage exerts the greatest influence on patient perception of SLE impact.

REFERENCES:
[1] Yazdany J. et al, Arthritis Care Res (Hoboken). 2011 Aug;63(8):1170-7

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FRI0233 MORTALITY IN SLE PATIENTS COMPARED TO POPULATION CONTROLS IN FINLAND IN YEARS 2000–2015

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Background: It is well established from a variety of studies that systemic lupus erythematosus (SLE) patients have a shortened life expectancy. The literature on SLE has highlighted the impact of cardiovascular diseases (CVD) on increased mortality [1,2]. However, there is lack of studies comparing results to the background population.
Objectives: Aim of the study was to clarify, whether incident SLE patients have an excess mortality compared to population controls.
Methods: The study included all adult (age $\geq$ 17 years), incident SLE patients who were entitled to a special reimbursement for SLE medication in years 2000 – 2014 in Finland. For each patient, the Population Register Centre identified 3 population controls matched for age, sex and place of residence. Comorbidities at baseline were obtained from the Care Register for Health Care of the National Institute for Health and Welfare. Data on education at baseline and deaths until the end of 2015 were retrieved from the Statistics Finland.
Results: A total of 1006 incident SLE patients (84% females) and 3005 population controls were found. During the follow-up (mean 8.6 years), 98 patients (mean age at death 70±14 years, 65% females) died. The 5 -, 10-, and 15-year survival rates in SLE patients were 95.0% (95%CI 93.3-96.2%), 88.8% (86.2-91.0%) and 82.1% (77.6-85.8%), respectively. The number of deaths among controls was 187. Crude hazard ratio (HR) was 1.61 (95% CI: 1.26 to 2.06), $p<0.001$, adjusted for education- and comorbidities 1.14 (95% CI: 0.88 to 1.48) $p=0.32$. Main causes of deaths in patients were CVDs (33%), malignancies (27%) and neurological diseases (10%). Ten-year cumulative mortality rate due to CVD was in SLE patients 3.3% (95CI 2.2 to 4.9%) and in controls 2.6% (2.0-3.3) and 15-year rate 6.7% (95C% CI 4.2 to 9.9) and 4.9% (3.6 to 12.0), respectively. Crude HR for CVD deaths was 1.28 (95% CI: 0.85 to 1.93), $p=0.24$, adjusted 0.88 (95% CI: 0.56 to 1.39), $p=0.58$.
Conclusion: SLE patients had a slightly increased risk for overall and cardiovascular related mortality compared to population controls. After adjusting for education and comorbidities, the difference was not statistically significant.

REFERENCES:
[1] Bernatsky S, et al. Mortality in systemic lupus erythematosus. Arthritis Rheum 2006;54:2550-7.
[2] Björnådal L, et al. Cardiovascular disease a hazard despite improved prognosis in patients with systemic lupus erythematosus: results from a Swedish population based study 1964-95. J Rheumatol 2004;31:713-9.

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FRI0234 **FACTORS ASSOCIATED WITH THE DEVELOPMENT OF NEOPLASIA IN PRIMARY SJOGREN'S SYNDROME**

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Background: Primary Sjögren's syndrome (pSS) is characterized by lymphocytic infiltration of the exocrine glands. These patients have a higher risk than the general population of developing non-Hodgkin lymphoma (NHL). This risk also increases with the time of evolution of the disease. pSS is also associated with the development of non-hematological cancer such as thyroid, digestive or gynecological among others.
Objectives: The aim of the study is to explore the association between the development of neoplasia and demographic, clinical or therapeutic factors in pSS.
Methods: The SJOGRENSER registry is a multicenter, cross-sectional study of patients with pSS who meet the American-European consensus criteria of 2002, of 33 Spanish rheumatology units. The demographic, clinical, analytical, therapeutic and neoplastic data were collected through review of the clinical records and interviews with the patients. Previously, all the patients signed informed consent and the approval of the local ethic committees was obtained. Descriptive statistics was used for the analysis of the data. The chi-squared test was used to establish the statistical associations and it was considered a p <0.05 as significant. Bivariate logistic regression models were used to identify the effect of each independent variable on the main variable (neoplasia); the multivariate analysis was used to establish the independent effect of the patient characteristics associated with the dependent variable.
Results: Four hundred and thirty-seven patients were included in SJOGREN-SER Registry (female gender 95.19%; median age 58.3 years). We found 30 patients (6.86%) with neoplasia (3 of them with more than one neoplasia): 7 with lymphomas (23.3%) (4 MALT lymphomas, 2 Hodgkin's lymphomas, 1 immunocytoma), 9 with gynecological neoplasia (30%), 2 with digestive malignancies, 2 with hematological, 2 with endocrine, 6 with malignancies in other locations, 3 with multiple mieloma and 2 patients with Waldenstrom macroglobulinemia. The results of the bivariate analysis are shown in the table. The factors significantly associated with the development of neoplasia were older age, glandular inflammatory involvement, lung involvement and use of rituximab. The age at diagnosis of the disease tended to be higher in the group with neoplasia (50.1 (± 12.9) vs 54.7 (± 11.7), p = 0.059). In the multivariate analysis, positive associations were found for the development of neoplasia in older patients (OR 1.045; CI95% 1.010-1.081), patients with glandular inflammation (OR 3.104; CI95% 1.396-6.906), and use of rituximab (OR 3.745; CI95% 1.386-10.118).

Variable	Neoplasia -	Neoplasia +	p
Age (years)	58.3	63.6	0.023
Glandular inflammation (%)	31	53.3	0.012
Lung involvement (%)	8.9	23.3	0.010
Rituximab (%)	6	23.3	<0.001

Conclusion: Thirty (6.86%) patients with pSS from the SJOGRENSER registry developed some neoplasia; the most frequent was gynecological, followed by lymphoproliferative processes. Older age, glandular inflammatory involvement and use of rituximab (presumably indication bias) were associated with the presence of neoplasia.

REFERENCES:

[1] Brito –Zeron, et al. Characterization and risk estimate of cancer in patients with primary Sjögren syndrome. Journal of hematology & oncology 2017;10:90.
[2] Liang Y, et al. Primary Sjögren syndrome and malignance risk: a systematic review and meta-analysis. Ann Rheum Dis 2014;73:1151

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FRI0235 **DIFFERENCES BETWEEN MALE AND FEMALE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE CENTER EXPERIENCE OVER 20 YEARS OF FOLLOW-UP**

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown etiology involving multiple organ systems. It affects predominantly women, and according to different reports only 4–22% of the lupus population is male. Sex differences may influence the clinical and serological expression, therapy and outcome, but the current results varies among different countries and different ethnic groups (1-3). Less is known about the clinical course of male SLE during the follow-up due to the small number of cases collected, but male sex might be a poor factor in SLE prognosis (4-9).
Objectives: The aim of this work was to analyze our male and female SLE patients with an ongoing follow-up.
Methods: Cumulative clinical, serological manifestations, concomitant diseases of patients belonging to the historical SLE cohort with at least one evaluation in the past 15 months were collected from clinical charts. For these patients data regarding the overall and ongoing treatments, damage index (SDI), activity index (SLEDAI-2K) during the last 12 months were collected. For statistical analysis was used Chi-squared test, Fisher exact test, Student T test or Wilcoxon-Mann Whitney when appropriated.
Results: Out of the 550 SLE patients registered until may 2018 we have included for this analysis 345 patients with an active follow-up, 31 males and 314 females, with a male to female ratio of 1:10. A higher number of SLE male had disease onset (13% vs 1.6%) and diagnosis (16% vs 1.6%) after 60 years compared to female (p=0.001; OR 9.1; 95%CI 1.92-42.56 and p<0.0001; OR11.8; 95% CI 2.73-51.56 respectively). The most relevant differences among male and female patients are reported in the table 1. Males more frequently presented discoid lesions, renal involvement, polyneuropathy and leukopenia compared to female SLE. No difference regarding disease activity during the last 12 months measured by SLEDAI was found. Regarding the damage index, males showed a higher mean SDI and number of patients with a severe damage (SDI>2) compared with women. Analyzing treatment prescribed since the diagnosis of SLE we collected some relevant differences: antimalarials were less prescribed in males than females (87%vs 97%, p=0.02; OR 0.19; 95%CI 0.051–0.825), whereas mycophenolate mofetil was more frequently used in males (63%vs36%, p=0.005 OR 3.0 95% CI1.3- 6.8). Finally, significant differences regarding the ongoing treatment are reported in table 1: mycophenolate mophetile was more frequently prescribed in males (84,2 vs 25,6) and a highly suggestive trend of significance toward a greater use of steroids in males was also found.

	SLE male N=31 (%)	SLE female N=314 (%)	P value
Clinical and serological manifestation			
Age at the onset (mean ±SD)	36.2±15	29±11.3	<0.001
Age at the diagnosis (mean ±SD)	39.13±13.8	30.5±11.4	<0.001
Discoid lesion	8 (34.8)	30 (11.5)	0.01, OR=3.29,95%CI 1.230-8.610
Renal involvement	18 (58.1)	116 (36.9)	0.035, OR 2.36, 95%CI 1.055–5.33
Neurological involvement	13 (41.9)	49 (15.3)	0.001, OR 4.9, 95%CI 1.716-9.205
Polyneuropathy	5 (38.5)	7 (14.6)	<0.001, OR 8.43, %CI 2.13-32.52
Leukopenia	12 (60)	60 (34.5)	0.02, OR 2.67, %CI 1.14–6.17
Damage			
SDI (mean ±SD)	1.94 (±1.83)	1.20 (±1.45)	0.018
Number of patients with SDI>=1	24 (77)	186 (59.2)	0.07
Number of patients with SDI >2	10 (32.2)	42 (13.3)	0.011, OR 3.08, 95%CI 1.25-7.48
Ongoing treatment			
Steroids	27 (87.1)	219 (69.7)	0.07
Mycophenolate mofetile	16 (84.2)	43 (25.6)	<0.0001,OR 6.72, 95% CI 2.90-15.62

Conclusion: Our study confirmed the presence of differences between male and female SLE patients, both on clinical manifestations and also during the disease course. Our results on currently followed male SLE confirmed that these patients have a more severe disease, in particular with renal or neurological manifestations, that could justify the higher use of mycophenolate mofetile and the higher SDI compared to female SLE.

REFERENCES:

[1] S.P. Ballou, et al.Arthritis Rheum. 25 (1) (1982) 55–60.

[2] L.J. Lu, et al., Lupus 19 (2) (2010)119–129.
[3] Isenberg DA, et al. Br J Rheumatol 1994;33:3078.
[4] Andrade RM, Arthritis Rheum (2007) 56(2):622–30
[5] Garcia MA, et al.. Lupus (2005) 14(12):938–46.
[6] Taraborelli M, et al. Lupus (2017) 11:1197-1204
[7] Tan TC, et al. J Rheumatol (2012) 39(4):759–69.
[8] Kamen DL, et al. Arthritis Rheum (2008) 58(5):1237-47

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FRI0236 MIGHT A 12-WEEK AEROBIC EXERCISE INTERVENTION IMPROVE PATIENT-REPORTED OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS?

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Background: Despite the relevant advance in treatment options and survival rates in systemic lupus erythematosus (SLE), patient's quality of life (QOL) and other patient-reported outcomes (PROs) do not seem to improve accordingly [1]. PROs provide valuable information about the patient's perceptions across a variety of domains that should be considered in a successful management of this condition [2]. Exercise seems to be a safe way to improve cardiorespiratory fitness [3], and could have also a positive influence on PROs in SLE.
Objectives: To evaluate the effects of 12-week aerobic exercise intervention on PROs (QOL, depression, stress, and fatigue) in women with SLE.
Methods: These are secondary outcomes of a non-randomized clinical trial [NCT03107442]. A total of 58 participants with SLE were assigned to exercise group (n=26) or control group (n=32). The exercise intervention followed the American College of Sports Medicine guidelines, and consisted of 12-week progressive aerobic exercise on a treadmill (2 sessions/week) between 40%-75% of the individual's heart rate reserve [3]. Attendance of $\geq$75% was set for inclusion in the analyses. The control group received verbal information about a healthy lifestyle. At baseline, and at week 12, PROs were assessed including the physical and mental summary scores of the 36-item Short-Form Health Survey (SF-36), depression (Beck Depression Inventory; BDI-II), perceived stress (visual analogue scale) and fatigue (Multidimensional Fatigue Inventory; MFI-20). A total of 49 women with SLE (age: 44.5±14.2 years) completed all the assessments (exercise=21; control=28) and were included in the per-protocol (primary) analyses. The exercise and control group were comparable in age, disease duration and SLE activity, sociodemographic characteristics, and BMI at baseline, although there were differences in BDI-II scores. Baseline values and BDI-II values were used as covariates in the analyses.
Results: In comparison to the control group, the exercise group showed a significant reduction in general fatigue (mean difference -2.11 units; 95% CI -4.18 to -0.04; P=0.046) and physical fatigue (mean difference -3.90 units; 95% CI -6.3 to -1.5; P= 0.002) following the intervention. There were no between-group differences in the changes from baseline to week 12 either in physical (P=0.828) or mental (P=0.767) QOL, depression (P=0.498), perceived stress (P=0.247) or other fatigue dimensions (mental, reduced motivation, reduced activity, all P>0.05).
Conclusion: The results of this study suggest that 12 weeks of progressive aerobic exercise might improve relevant dimensions of fatigue in women with SLE, despite absence of effects on QOL, depression or perceived stress.

REFERENCES:
[1] Mcelhone K, Abbott J, Teh L-S. A review of health related quality of life in systemic lupus erythematosus. Lupus. 2006;15: 633–643.
[2] Mahieu M, Yount S, Ramsey-Goldman R. Patient-reported outcomes in systemic lupus erythematosus. Rheum Dis Clin. Elsevier; 2016;42: 253–263.
[3] Soriano-maldonado A, Morillas-de-laguno P, Sabio M. Effects of 12-week Aerobic Exercise on Arterial Stiffness, Inflammation, and Cardiorespiratory Fitness in Women with Systemic LUPUS Erythematosus : Non-Randomized Controlled Trial. J Clin Med. 2018; 1–17.

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FRI0237 OMEGA-3 AND OMEGA-6 FATTY ACIDS IN SJÖGREN'S SYNDROME: CLINICAL IMPLICATIONS AND THEIR ASSOCIATION WITH INFLAMMATION

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Background: Essential ω-3 and ω-6 fatty acids (FA) are natural modulators of inflammation activity; however, their role in primary Sjögren's syndrome (pSS) is unknown.
Objectives: To evaluate the intake and serum levels of ω-3 and ω-6 FA in patients with pSS, and to correlate them with ocular and oral signs and symptoms, disease activity as well as with the presence of a panel of inflammatory chemokines/cytokines in saliva and tears.
Methods: We included 108 patients with pSS according to EULAR/ACG criteria. We excluded patients under ω-3 and ω-6 supplementation. Dietary information was obtained from a semiquantitative food frequency questionnaire of one-day reminder (applied by a trained interviewer), and processed using computerized nutritional analysis software. Fasting blood samples were collected. We measured the serum levels of ω-3 (α-linolenic acid [α-L], eicosapentaenoic acid [EPA], docosahexaenoic acid [DHA]) and ω-6 (linoleic acid [LA], arachidonic acid [AA]) using gas chromatography flame ionization. We assessed the ESSDAI score, ESPPRI, OSDI, tear film break-up time, Schirmer-I test and the SICCA Ocular Staining Score (OSS). In a subgroup of patients, we obtained tears and saliva samples that were frozen at -86°C until assayed. Once defrosted, the levels of CXCL8, CXCL10, CCL2, IL-22 and IL-21 in saliva and CXCL8, CXCL10, CCL2 and CXCL9 in tears were measured by Luminometry.
Results: The median age was 56.12 ± 13.7 years, 94.4% women and median disease duration 10 years. The FA ω-3 and ω-6 intake was 0.43 g/day and 3 g/d, respectively. The levels of α-L were 6.6 μg/mL, DHA 26 μg/mL, total ω-3 (α-L +DHA) 25.4 μg/mL, LA 168.5 μg/mL, AA 34 μg/mL, and total ω-6 (LA+AA) 205 μg/mL. We did not find a correlation among serum levels and food intake. Thus, further analyses were focused on serum results. We found a negative correlation between α-L and the OSDI (ρ= -0.42, p= 0.01) and ESSDAI (ρ= -0.26, p=0.03) as well of DHA and ESSDAI (ρ= -0.30, p= 0.01). The rest of the variables were not associated. In tears, there was a positive correlation of AA and CXCL9 (ρ= 0.48, p= 0.04), whereas in saliva, we observed a negative correlation between α-L, DHA and total ω3 (α-L+DHA) with CCL2. We also observed a negative correlation between total ω6 (LA+AA) and IL-21, and the ω6/ω3 ratio with IL-22.
Conclusion: Our pSS patients had deficient FA omega intake. We observed lower ocular symptoms, lower ESSDAI scores and salivary levels of CCL2 among patients with higher levels of FA ω-3. Our study suggest that low serum levels of ω-3 might be implicated in the perpetuation of chronic inflammation.
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FRI0238 **RISK OF THROMBOSIS IN PATIENTS RECEIVING STEROID PULSE THERAPY IN LUPUS NEPHRITISUSING JAPANESE HEALTH INSURANCE DATABASE**

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Background: Patients with systemic lupus erythematosus, especially lupus nephritis (LN), have higher risk of thrombosis than the general population [1]. Since use of corticosteroids also increase the risk of thrombosis [2], steroid pulse therapy (SPT) may increases the risk of thrombosis in patients with LN. However, few studies examined this association.
Objectives: To compare risk of thrombosis between patients with and without SPT in LN.
Methods: This retrospective, propensity score-matched cohort study was conducted using claims data provided by Medical Data Vision Co., Ltd (Tokyo, Japan). We defined individuals as LN cases if they met all of the following: 1) were diagnosed as LN; 2) had a dose of corticosteroids (CS) over 30 mg/day during hospitalization between April 2009 and January 2018; 3) were 16 years old or over. Cases with central neurological lupus, alveolar hemorrhage, or pregnancy at baseline were excluded. Cases with plasmapheresis or antiplatelet therapies at the start of observation, warfarin within a year, direct oral anticoagulants within a month, major surgery or lower limbs operation within three months, past thrombosis within a year, and prophylactic treatment of thrombosis from the observation starting month were also excluded from the study population. LN cases were divided into 2 groups; receiving SPT (SPT group, n=692) or not receiving SPT (non-SPT group, n=525). The start of observation was defined as commencement of CS treatment during hospitalization. Observation stopped either on April 2018 or the month cases were withdrawn from the database or developed first thrombosis, whichever came first. Thrombosis was defined as follows: at least one of three disease names (thrombosis, embolisms and infarction) and prescription of thrombolytic agents after the start of observation. After propensity-score matching, the incidence rate of thrombosis at Month 1, 2, 3, 4 was calculated using Kaplan–Meier methods. Univariate analysis were conducted by chi-squared test for categorical data and Mann-Whitney U-test for continuous data. Adjusted odds ratio (OR) was calculated using a multivariate logistic regression model.
Results: The mean age was 47 years old and the proportion of female was 76%. There were no statistically significant differences in baseline variables between the two groups after propensity-score matching (both groups: n=434). The percentage of cases with thrombosis in both groups at each month were similar (SPT vs non-SPT at Month 1, 2, 3, and 4; 3.0% vs 4.4% (p=0.28), 3.5% vs 5.1% (p=0.24), 3.9% vs 5.3% (p=0.331), and 4.6% vs 5.5% (p=0.536), respectively). There were no significant differences in cumulative incidence rates of thrombosis between the two groups (P=0.265 by log-rank test). Univariate analysis revealed five risk factors of thrombosis; activity of daily living (p=0.004), hepatic failure (p<0.0001), malignancy (p=0.02), and use of methotrexate (p=0.038) and oral contraceptive (p=0.037). After adjusting for covariates, OR of SPT was 0.82 [95%CI 0.44-1.52], which was not significantly elevated.
Conclusion: This study revealed that SPT did not increase the risk of thrombosis in patients with LN.

REFERENCES:

[1] J Rheumatol. 2016:576-86
[2] JAMA Intern Med 2013:743-52

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FRI0239 **HIGHER DOSE OF ADJUNCTIVE GLUCOCORTICOID THERAPY IS ASSOCIATED WITH MORTALITY OF PNEUMOCYSTIS PNEUMONIA IN PATIENTS WITH RHEUMATIC DISEASES**

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Background: Pneumocystis pneumonia (PCP) is a fatal complication in patients with rheumatic diseases, and prognostic factors are not well recognized.[1] Adjunctive glucocorticoid therapy is beneficial for PCP in patients with acquired immunodeficiency syndrome, but the role in patients with rheumatic diseases is debated.[2]
Objectives: To investigate the prognostic factors of PCP in patients with rheumatic diseases.
Methods: Retrospective data was collected for all subjects with rheumatic diseases and PCP between October 2015 and October 2018 in a tertiary referral center. PCP was diagnosed via a positive sputum *Pneumocystis jirovecii* PCR in the presence of a compatible clinical presentation. The clinical characteristic, underlying rheumatic diseases, comorbidity, immunosuppressants, adjunctive glucocorticoid dose, and outcome were evaluated. Chest X-ray (CXR) was evaluated as a radiographic score (0-18), and a higher score suggested a more severe lung involvement. The prognostic factors of mortality were analyzed by multivariate logistic regression analysis.
Results: 40 patients with PCP and rheumatic diseases were included. The mean age of the patients was 55.7 years, and twenty (50%) were female. The underlying rheumatic diseases were systemic lupus erythematosus (30%), rheumatoid arthritis (22.5%), Sjögren's syndrome (12.5%), systemic vasculitis (12.5%), antiphospholipid syndrome (10%), idiopathic inflammatory myopathies (10%), undifferentiated connective tissue disease (7.5%), and psoriatic arthritis (2.5%). All subjects were separated into survivors (n=17) and non-survivors (n=23) groups. The overall in-hospital mortality rate was 57.5%. The group of non-survivors had a higher adjunctive glucocorticoid dose (p=0.016), an older age (p=0.017), and a higher CXR radiographic score (p=0.029). In multivariate analysis, independent predictors of mortality were increased glucocorticoid dose (>10mg/day) as adjunctive therapy (odds ratio, OR=5.58, 95% confidence interval, C.I.=1.09-28.62; p=0.039), age (OR=1.06, 95% C.I.=1.00-1.11; p=0.037), and CXR radiographic score (OR=1.21, 95% C.I.=1.00-1.47, p=0.048).
Conclusion: Increased glucocorticoid dose (>10mg/day) as adjunctive therapy, older age, and CXR radiographic score were independently prognostic factors of mortality in PCP patients with rheumatic diseases.
Disclosure of Interest: None declared

REFERENCES:

[1] Teichtahl AJ, Morrisroe K, Ciciriello S, et al. Pneumocystis jirovecii pneumonia in connective tissue diseases: Comparison with other immunocompromised patients. Semin Arthritis Rheum 2015;45:86–90.
[2] Ando T, Abe Y, Endo Y, et al. Rapid glucocorticoid tapering therapy to reduce mortality from pneumocystis pneumonia in patients with rheumatic disease. Mod Rheumatol 2018;13:1–6.

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FRI0240

15-YEAR EXPERIENCE IN A MULTIDISCIPLINARY UNIT FOR THE FOLLOW-UP OF PREGNANCY IN RHEUMATIC INFLAMATORY AND AUTOIMMUNE DISEASES

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Background: Pregnancies in women with inflammatory and autoimmune diseases are considered high-risk pregnancies, so close and ideally multidisciplinary control is necessary. Given the advances in treatment and identification of risk factors a higher percentage of patients manifest gestational desire.

Objectives: To describe our experience in a multidisciplinary unit (integrated by Rheumatologists and Obstetrics) and assess the complications in the evolution of pregnancies and treatments used in patients with inflammatory and autoimmune diseases.

Methods: Retrospective study of pregnancy outcome in patients with rheumatic diseases and follow-up in a multidisciplinary unit for 15 years (January 2003-December 2018). Demographic characteristics, maternal disease, comorbidities, previous abortions, presence of autoantibodies (AAb), number of births, fetal losses and abortions during follow-up, previous treatment and treatment during pregnancy and maternal and fetal complications were collected.

Frequencies and percentages were used in qualitative variables, mean ±SD in quantitative and for the comparison between groups Chi2 test (or Fisher test if appropriate) was used in categorical variables and Student T test (or U of Mann-Whitney if appropriate) in quantitative variables. Data was analysed using IBM SPSS v23.

Results: 141 patients (194 pregnancies) were registered with maternal average age at rheumatic disease diagnosis of 29.14 ± 6.6 years and average age at abortion/childbirth of 34.82 ± 4.63 years. 12.8% were smokers and 21.1% had comorbidity (hypothyroidism:10.8%, dyslipidemia:2.1%). Maternal diseases are collected in table 1.

50 abortions were registered prior to follow-up in our unit (0.35 abortions/mother). During follow-up 19 abortions were registered (0.13 abortions/mother). Frequencies of abortions/births are specified in table 1.

13.5% of pregnancies were pre-term (< 37 weeks) and a caesarean section (C-section) was performed in 26% of cases. C-section was more frequent among asymptomatic women with positive autoantibodies (n:15, 30%), patients with SLE (n:13, 17.3%), RA (n:6, 37.5%) and PsA (n:6, 37.5%).

The frequency of different AAb is found in table 2.

Anti-Ro carriers (36.6%) did not have higher frequency of abortions (p = 0,798) and only one case of heart block was recorded among them. Abortions were more frequent among women with positive antiphospholipid antibodies (14.3% compared to 4.3%) (p = 0,013).

In inflammatory diseases (PsA, RA, spondyloarthropathies) no abortions were registered.

TABLE 1

MATERNAL DISEASE	n (%)	n abortions	n births
Systemic Lupus Erythematosus (SLE)	80 (42.1%)	5	75
Asymptomatic women with positive autoantibodies	52 (27.4%)	2	50
Antiphospholipid syndrome (APS)	19 (10%)	4	15
Rheumatoid Arthritis (RA)	17 (8.9%)	0	17
Sjögren Syndrome	8 (4.2%)	2	6
Psoriatic Arthritis (PsA)	5 (2.6%)	0	5
Mixed Connective Tissue Disease	3 (1.6%)	1	2
Behçet Syndrome	2 (1.1%)	0	2
Systemic Sclerosis	2 (1.1%)	0	2
Espondyloarthritis	2 (1.1%)	0	2

TABLE 2

ANTIBODIES	n (%)
Antinuclear antibodies	115 (62.8%)
Anti-Ro	67 (36.6)
Anticardiolipin antibodies IgG	51 (27.9%)
Antibodies to double-stranded DNA (anti-dsDNA)	35 (19.1%)
Anticardiolipin antibodies IgM	30 (16.4%)
Lupus Anticoagulant	25 (13.7)
Rheumatoid Factor	23 (12.6%)
Anti-La	15 (8.2%)
Anti-citrullinated protein antibodies	12 (6.6%)
Anti-β2-glycoprotein I IgM	8 (4.4%)
Anti-β-2 glicoprotein I IgG	1 (0.5%)

TABLE 3

PREVIOUS TREAMENT	n (%)	TREATMENT DURING PREGNANCY	n (%)
Hydroxychloroquine	97 (50%)	Acetylsalicylic acid	122 (62.9%)
Prednisone	23 (11.9)	Hydroxychloroquine	119 (61.3%)
Methotrexate	6 (3.1%)	Prednisone	66 (34%)
TNF inhibitors	4 (2.1%)	Heparin	34 (17.5%)
Sulfasalazine	2 (1%)	Antibiotics	3 (1.5 %)
Azathioprine	1 (0.5%)	Sulfasalazine	1 (0.5%)
Rituximab	1 (0.5%)	Chloroquine	1 (0.5 %)
Leflunomide	0 (0%)	Methylprednisolone	0 (0%)
Mycophenolate Mofetil	0 (0%)	TNF inhibitors	0 (0%)

Intrauterine growth restriction (IUGR) was observed in 7 cases (3.7%) and pre-eclampsia in 6 (3%) being more frequent among patients with SLE (n:3 and n:2 respectively), APS (n:1 and n:1) and asymptomatic women with positive autoantibodies (n:2 and n:1). No difference was observed in complications rate between anti-Ro positive and anti-Ro negative women (p = 0.047).

Treatments used prior to and during pregnancy are shown in table 3.

Conclusion: In our series, as previously described in the literature, women with systemic autoimmune and inflammatory diseases have higher risk of abortion, pregnancy complications and instrumental delivery than general population. SLE and APS are most associated with these complications. Multidisciplinary close follow-up of these patients improves pregnancy outcomes.

REFERENCES:

[1] - Pregnancy and reproduction in autoimmune rheumatic diseases. M. Ostenses, et al. Rheumatology, Volume 50, Issue 4, 1 April 2011, Pages 657-664

[2] - State of the art: Reproduction and pregnancy in Rheumatic diseases. M. Ostenses. Autoimmunity Reviews. Volume 14, Issue 5, May 2015, Pages 376-386.

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FRI0241

PREGNANCY RATES AND PERINATAL OUTCOMES AMONG WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN COMPARISON TO GENERAL POPULATION

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Background: Systemic lupus erythematosus (SLE) can affect people of all ages, but it occurs most often during childbearing ages. It has been documented that the fertility rates in women with SLE is similar to those

Table 1. Fertility rates in women with SLE compared with those of age-matched general population

Year	SLE			General population			IRR (95%CI)	
	Prevalent case, n	Pregnancy case, n	N. of pregnancy per 1,000 persons, IR (95%CI)	Total population†, n	Pregnancy case, n	N. of pregnancy per 1,000 persons, IR (95%CI)	unadjusted	Age-adjusted
2013	10,516	313	29.76 (26.47,33.06)	13,073,224	508,442	38.89 (38.78,39.00)	0.77 (0.69,0.86)	0.68 (0.61.0.76)
2014	11,205	331	29.54 (26.36,37.72)	12,992,974	512,712	39.46 (39.35,39.57)	0.75 (0.67,0.83)	0.66 (0.60.0.74)
2015	11,400	350	30.70 (27.49,33.92)	12,877,547	489,404	38.00 (37.90,38.11)	0.81 (0.73,0.90)	0.74 (0.66.0.82)

without SLE. On the other hand, the pregnancy adverse outcomes are common in pregnant women with SLE. However, the pregnancy rates in women with SLE was not fully understood. In addition, comparison of the pregnancy adverse outcomes with general population is limited.
Objectives: We estimated the pregnancy rates and adverse pregnancy outcomes in Korean women with SLE and compared them with women without SLE.
Methods: Among all women aged 15-49 years in the Korean National Health Insurance claim database from January 2013 to December 2015, pregnant women were identified by using ICD-10 code for delivery and abortion. Pregnant women were categorized into women with SLE and control group. Adverse pregnancy outcomes classified into five categories as follows: fetal loss, intrauterine growth retardation (IUGR), preterm delivery, pre-eclampsia or eclampsia, and gestational diabetes mellitus. Crude incidence rates (IRs) of pregnancy and adverse pregnancy outcomes were calculated. Incidence rate ratios (IRRs) of those were estimated and adjusted for age.
Results: In SLE, 994 pregnancy cases were observed during the study period. The crude estimated IRs of pregnancy were lower in SLE patients than general population (Table 1). Age-adjusted IRR was also lower in SLE patients (Table1). The adjusted-IRR of live birth in SLE pregnant women was 0.92 (95% CI 0.85 - 0.99) compared with control group. The adjusted-IRR of fatal loss, IUGR, and preterm delivery was 1.27 (95% CI 1.11 - 1.45), 4.52 (95% CI 3.45 - 5.91), and 3.25 (95% CI 1.62 - 6.52), respectively. The IRR of pre-eclampsia or eclampsia was 3.21 (95% CI 2.52 - 4.08), but those of gestational diabetes mellitus was not significant (IRR 0.89, 95% CI 0.80 - 1.00).
Conclusion: Pregnancy rates in SLE women were lower about 30% compared with general population. Pregnancy adverse outcomes were higher in SLE pregnant women with more than 4-fold IUGR and pre-eclampsia/eclampsia, 3.2-fold preterm delivery.

REFERENCES:

[1] EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome. Ann Rheum Dis. 2017 Mar;76(3):476-485.

Disclosure of Interests: None declared
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FRI0242 SUBPOPULATION COMPOSITION OF INFLAMMATORY INFILTRATES OF THE MINOR SALIVARY GLAND AS AN ADDITIONAL DIAGNOSTIC CRITERION FOR PRIMARY SJOGREN'S SYNDROME

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Background: Primary Sjogren's syndrome (pSS) is frequent nosological forms among the diffuse connective tissue diseases. Histological examination of the minor salivary gland (MSG) is important diagnostic method. The currently established histological criteria for pSS indicates 61.2-93.7% sensitivity and 61.2-100% specificity respectively, which makes the search for additional hallmark highly relevant. Immunohistochemical study of MSG is the most appropriate for this purpose.
Objectives: To study of the qualitative and quantitative compositions of cellular subpopulations minor salivary gland mononuclear foci as additional histological criteria of pSS.
Methods: The study included 56 patients with a definite diagnosis of pSS according to the criteria of ACR\EULAR 2016. The control group consisted of 19 healthy volunteers. The biopsy of the minor salivary gland was performed for all the subjects, followed by an immunohistochemical study to evaluate the expression of CD3, CD4, CD8, CD20, CD21, CD68, CD138. A statistical analysis of the data obtained during the study was carried out using the SPSS 23 statistical software for Windows (IBM, United States of America). Diagnostic threshold for each biomarker was determined by ROC analysis. Operating characteristic curve, area under the curve (AUC), specificity, sensitivity, diagnostic accuracy (DT), diagnostic thresholds (DP), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) were also calculated. The construction of classification models, including several markers, was performed using linear discriminant analysis.
Results: The largest AUC were observed in CD3 - 0.795 [95% confidence interval (CI) 0.697 - 0.893] and CD20 - 0.796 (95% CI 0.698 - 0.894), which at the specified DP corresponded to the sensitivity of 67.9% (95% CI 54.04 - 79.71) and 71.4% (95% CI 57.79 - 82.7), specificity of 95% (95% CI 73.97 - 99.87) and 95% (95% CI 73.97 - 99.87).
The CD21 marker was detected only in the PSS group. AUC for this biomarker was 0.652 (95% CI 0.525 - 0.778), sensitivity - 30.4% (95% CI 18,78 - 44.1), specificity - 100% (95% CI 82,35 - 100).
Using the method of discriminative analysis, we designed classification models that included various combinations of the markers under study. The combination of the decimal logarithms CD3 and CD68 had AUC 0.873 (95% CI 0.794 - 0.953), sensitivity - 76.8% (95% CI 63.58 - 87.02), specificity - 95% (95% CI 73.97 – 99.87).
Conclusion: CD3 and CD20 can be considered as additional histological criteria for pSS. CD21 was observed only in patients with pSS. The combined quantitative assessment of CD3 and CD68 had a greater diagnostic value compared to CD3 and CD68 separately.
Disclosure of Interests: None declared
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FRI0243 RECOVERY OF RENAL FUNCTION IN PATIENTS WITH LUPUS NEPHRITIS AND REDUCED RENAL FUNCTION

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Background: Reduced renal function is associated with worse renal outcome in patients with lupus nephritis (LN). However, there is insufficient knowledge regarding renal function recovery in patients with LN with reduced baseline renal function.
Objectives: The present study aimed to investigate renal function recovery and related factors in patients with reduced baseline renal function.
Methods: The present retrospective longitudinal cohort study included patients with LN and reduced renal function. Reduced renal function was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2. Recovery of renal function was determined by eGFR >60 mL/min/1.73 m^2 at 6 months after baseline, and factors associated with it were evaluated using logistic regression analysis.
Results: We included 90 patients with LN, with a mean eGFR value of 37.2 (± 13.9) mL/min/1.73 m^2. Forty-six patients (51.1%) recovered their renal function after 6 months. On multivariate analysis, hydroxychloroquine use (OR: 3.891, 95% CI: 1.196–12.653, p = 0.024), prolonged LN (OR: 0.926, 95% CI: 0.874–0.981, p = 0.009), and high-grade tubular atrophy (OR: 0.451, 95% CI: 0.208–0.829, p = 0.013) were associated with renal function recovery. During follow up, 25 patients were on end stage renal disease (ESRD). Kaplan-Meier analysis revealed that renal function recovery after 6 months and lower probability of ESRD are associated.
Conclusion: In patients with LN and reduced renal function, renal function recovery at 6 months was associated with use of hydroxychloroquine and inversely related to longer duration of LN and higher grade of tubular atrophy.
Disclosure of Interests: None declared
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FRI0244 MATHEMATICAL PROCESSING IS AFFECTED BY DAILY BUT NOT CUMULATIVE GLUCOCORTOCOID DOSE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: The impact of glucocorticoids on neurocognitive performance in patients with SLE is not fully understood.
Objectives: We aimed to study the effect of daily and cumulative doses of glucocorticoids on neurocognitive performance in patients with SLE using the computer-based Automated Neuropsychological Assessment Matric (ANAM).
Methods: Consecutive patients with SLE and gender- and age-matched (±5 years) healthy control subject (HC) were studied. In a quiet and comfortable room, each subject underwent the 45-minute ANAM test under supervision which comprises simple reaction time (SRT) that probes neuromuscular efficiency, and 8 domains of neurocognitive assessment including 3 code substitution tests (probing learning and recall), spatial processing (probing visual perception and mental rotation), matching to

sample (probing short-term memory and attention), continuous performance test (probing sustained attention), mathematical processing, and memory search (probing working memory). Anxiety and depression were assessed by the Hospital Anxiety and Depression scale (HADS). The total and individual-domain throughput scores (TPS) were compared between both groups using Student's t test. The presence of cognitive dysfunction, defined as total TPS <1.5 SD below the mean TPS of HC, was compared between both groups by χ^2 test. Within the SLE group, the relationships between prednisolone dose (daily [mg] or cumulative [gm]) and individual-domain TPS were first explored by bivariate correlations. Independent association between glucocorticoid dose and individual-domain TPS that showed significant bivariate associations with prednisolone dose was determined by multiple linear regression, with adjustment for potential clinically- and demographically-important cofounders.

Results: Ninety-six SLE patients and 96 HC were studied, 16 men (16.7%) were present in each group. The mean age±SD of SLE patients and HC were 36.57±11.4 and 33.61±10.6 years (p=0.073), respectively. The mean±SD duration of SLE, SLEDAI and daily and cumulative prednisolone doses were 98.85±87.4 months, 3.37±3.4, 11.01±13.6mg and 16.92±18.5gm, respectively. SLE patients had a significantly higher mean HADS-anxiety score than HC (6.25±3.3 vs 4.62±3.0, p=0.001) while the mean HADS-depression score was comparable between both groups (p=0.093). SLE patients had significantly shorter duration of education (12.92±3.92 vs 15.86±2.5 years, p<0.001), scored significantly worse across all the 8 ANAM domains, had a significantly lower mean total TPS [337.23±94.4 vs 395.62±87.6, p<0.001) and were significantly more prevalent of cognitive dysfunction as compared to HC (25.0% vs 7.3%, p=0.001). In SLE patients, a statistically significant negative correlation was found between daily prednisolone dose and TPS of mathematical processing (r=-0.248, p<0.015), while no significant correlation between cumulative glucocorticoid dose and any of the individual ANAM domain was found. In multivariate regression, daily prednisolone dose remained independently associated with lower TPS of mathematical processing (β=-0.208, p=0.024) after adjusting for age, gender, SLEDAI, total HADS, total TPS, serum albumin and 25-OH hydroxyvitamin D levels and duration of education in SLE patients.

Conclusion: Daily, but not cumulative glucocorticoid dose has an independent impact on the working memory of SLE patients. While how daily glucocorticoid dose affects working memory mechanistically requires further investigation, its impact on neurocognitive assessment in SLE patients cannot be underestimated.

Disclosure of Interests: None declared

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FRI0245 RHEUMATOID FACTOR IN IGA, IGG AND IGM IMMUNOGLOBULIN CLASES IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is an autoimmune disease with the autoantibodies overproduction, including rheumatoid factors (RF). An association of RFs with the disease activity has been already described, with RFs in IgA, IgG immunoglobulin classes suggested as potential biomarkers of immunological/clinical pSS features.

Objectives: Examining correlations of RF in IgM, IgA and IgG immunoglobulin classes with other autoantibodies, dry eye tests and histopathological assessment (focus score) of salivary gland inflammation.

Methods: We studied 76 patients, mean age 53 (SD=13); (67Female/9Male) with pSS diagnosis (criteria ACR/Eular 2017); mean disease duration from diagnosis 2,24 year. Laboratory tests performed: ESR, C-reactive protein(CRP), concentrations of gamma globulins (g/dl), RF serum concentration assessed using ImmuLisa Enhanced™ RF IgA, IgG, IgM Antibody ELISA IMMCO Diagnostics, Inc. As positive result of the RF-IgA and RF-IgG concentration > 25 EU/mL was considered, as positive RF-IgM > 12,5 EU/mL; a highly positive result set as > 100 EU/mL. Anti-Ro/SSA, and anti-La/SSB antibodies were detected by semiquantitative dot blot method. The eye dryness and keratoconjunctivitis sicca were confirmed with Schirmer's test (score of less than 5 mm/5') and the ocular staining score (OSS) using lissamine green and fluorescein staining and biopsy of minor salivary gland with the histopathological evaluation (focus score-FS). The study was approved by the proper ethics committee. Differences between groups were analyzed with U Mann-Whitney test (continuous variables). Correlations between quantative variables were assessed with the Spearman correlation coefficient. Statistical significance was set at p<0.05.

Results: The detection of RF in examined sera: RF- IgA: positive(+) 66% (n=50), negative (-) 34%(n=26); highly positive (++) 51%(n=39); RF-IgG: + 55% (n=42), - 45%(n=34), ++ 9% (n=7); RF-IgM: + 88% (n=67), - 12% (n=9), ++ 55% (n=42). In comparison of patients' groups: i/RF-IgA (+) vs. RF-IgA(-) : no difference in term of FS, OSS and Schirmer's test; in RF-IgA(+) group significantly higher anti SS-A antibodies (p=0,002); a significant difference in anti SS-A antibodies level (p=0.028) RF-IgA(++) and lower positive group (less than 100EU/mL); ii/RF-IgM(+) vs. RF-IgM(-): RF-IgM (+) significantly higher anti -SS-A antibodies (p=0.007); iii/RF-IgG (+) vs. RF-IgG(-): RF-IgG(+): RF-IgG(+) significantly higher anti SS-B antibodies (p=0.015). Positive correlation was found between: RF-IgA(+) and RF- IgG(+) (rho=0.647) and RF- IgM(+) (rho= 0.669); RF-IgG(+) and RF-IgM(-) (rho=0.429). Surprisingly no correlations found in studied group between concentrations of RF- IgA, IgG and IgM and WBC, C4, C3 complement component, FS, OSS, and Schirmer's test.

Conclusion: 1. rheumatoid factors in main three classes of gammaglobulins, particularly RF-IgA, strongly associate with anti-SSA and anti-SSB autoantibodies production. 2. RF – IgM and RF- IgA dominate over RF-IgG in pSS. 3. both RF-IgA and RF-IgM may be used as diagnostic tool for pSS. 4. Further research is needed to distinguish activity and role of RF- IgA based upon its presence in serum vs. in saliva.

REFERENCES:

[1] Peen E, Mellbye OJ, Haga HJ. IgA rheumatoid factor in primary Sjogren's syndrome. Scand J Rheumatol. 2009 Jan-Feb;38(1):46-9.

[2] García-Carrasco M, Mendoza-Pinto C, Jiménez-Hernández C, Jiménez-Hernández M, Nava-Zavala A, Riebeling C. Serologic features of primary Sjögren's syndrome: clinical and prognostic correlation. Int J Clin Rheumatol. 2012;7(6):651-659.

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FRI0246 CELLULAR/FIBROCELLULAR CRESCENT IS A 52-WEEK AND LONG-TERM POOR PROGNOSTIC FACTOR OF ACTIVE LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is one of the most serious manifestation of systemic lupus erythematosus (SLE), associated with poor prognosis. LN exhibits a variety of histological findings including both inflammatory lesions such as crescent formation and immune complex (IC) deposition lesions. In current INS/RPS 2003 classification, all of them are classified as class III, IV and V. Recently, in the 2016 update of Oxford classification of IgA nephropathy, crescent formation (C) was added as an independent prognostic factor. Further examination of pathological and clinical prognostic factors for LN is required.

Objectives: To identify renal remission rate and clinico-pathological characteristics associated with renal non-remission at 52 weeks (52w) in LN patients

Methods: A single center retrospective study. We enrolled Japanese 152 patients of LN class III, IV, and V those who could observe for 52 w out of 274 SLE cases performed renal biopsy in our department between 1995 to 2017. After 52w after biopsy, they were classified as complete remission (CR), partial remission (PR) and non-remission (NR) according to ACR and LUNAR remission criteria by estimated glomerular filtration rate (eGRF) or serum creatinine (sCre) and proteinuria. Overall renal remission is defined as RR (CR + PR). The primary endpoint was the RR achieving rate, and the secondary endpoints were the baseline histological and clinical factors related to NR. Clinical factors: albumin (alb), IgG, C3, C4, CH50, anti-nuclear antibodies (Abs), anti- dsDNA Abs, anti-Sm Abs, anti-RNP Abs in the sera, complete blood count, urinalysis, presence of comorbidities (antiphospholipid antibody syndrome, hypertension), disease activity score (SLEDAI and BILAG score) and therapeutic drug [prednisolone (PSL), intravenous cyclophosphamide (IVCY), etc]. Histological factors: endocapillary proliferation, cellular/fibrocellular crescents, wire-loop lesion, hyaline thrombi, karyorrhexis, tuft necrosis, segmental sclerosis, global sclerosis, interstitial inflammation and vascular lesion.

Results: Baseline data: mean age 39 years, 135 females, 18 men, histrogical class III, 53 cases, IV: 58 cases, pure V: 12 cases, III/IV + V: 30 cases. At 52w after biopsy, SLEDAI (16 → 2), BILAG (17 → 2) score is significantly decreased. Dose of PSL was reduced(48 → 9 mg). At 52w, all cases were classified as RR (125 cases, 82%) and NR (27 cases, 18%) by ACR/LUNAR remission criteria. Surprisingly, all cases of pure V reached remission. Class III or IV LN (RR 114 cases; 91% vs NR 27 cases; 100%, p = 0.01) and cellular/fibrocellular crescent formation (RR 51 cases; 40% vs NR 18 cases; 66% p = 0.01) were significantly higher in NR. Clinically, long disease duration (p = 0.02), coexisting hypertension (RR 7 cases; 6% vs NR 9; 33%, p <0.01) and TMA (RR 1 case;0.7%, NR 2 cases;7%, p = 0.02), baseline urine protein (RR 1.5g vs NR 2.2g, p<0.01), baseline low WBC (p = 0.03), baseline low IgG (p = 0.02) were detected. About therapeutic drugs, IVCY significantly improved remission rate (RR 84 cases 68% vs. NR 9 cases 41%, p = 0.03). After long-term observation, 52w NR was significantly lower eGFR level (RR 81 vs NR 50, p <0.01, median observation period of 138 months). 3 cases developed ESRD and all of those cases show crescent formation.

Conclusion: As histological factors contributing to 52w-NR, class III or IV and crescent formation were detected. This result suggested that the therapeutic response was relatively better in cases with IC deposition lesions than those with inflammatory lesions. In LN, more-detailed pathological classification which could extract crescent formation might be required.

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FRI0247 PROGNOSTIC ROLE OF TUBULO-INTERSTITIAL INFILTRATE IN PATIENTS AFFECTED BY LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) occurs up to 50% of patients affected by Systemic Lupus Erythematosus (SLE) representing one of the major causes of morbidity and mortality in lupus population (1). Kidney biopsy is a fundamental tool for the diagnosis and management of lupus nephritis. The presence of pathological changes such as inflammatory infiltrate in glomeruli and/or in tubulo-interstitium are relevant in terms of prognosis and response to therapy (2).

Objectives: The aim of the study was to correlate the clinical and laboratory findings and the response to therapy with presence of glomerular and/or interstitial infiltrate in kidney section of patients with a biopsy-proven LN.

Methods: Kidney sections of patients with SLE undergoing a renal biopsy for diagnostically purpose were studied; samples were classified according to the 2004 International Society of Nephrology/Renal Pathology Society classification criteria (3). Clinical, laboratory and histological data were collected in a standardized, computerized and electronically filled form, including demographics, past medical history, autoantibody profile, previous and concomitant treatments. We assessed the disease activity by using SLEDAI-2K and remission in response to therapy was defined as the absence of renal impairment and as a score 0 of renal SLEDAI (proteinuria <500mg/24 hours, absence of hematuria and urinary casts) (4). All patients underwent to cyclophosphamide or mycophenolate treatment (5, 6). Two to three micron thick sections from paraffin-embedded blocks routinely stained with hematoxylin-eosin (HE) and Periodic acid-Shiff (PAS) for light microscopy investigation were re-evaluated. Predictive value of the presence of interstitial infiltrate on renal remission was evaluated. The results were expressed as mean±standard deviation (SD) depending on the distribution of the variables. The values of P < 0.05 were considered statistically significant.

Results: We evaluated 53 kidney samples from patients with LN (F:M = 51:2, mean age at biopsy 35±7.7 years; mean disease duration at date of biopsy 8±8.3 years). Class IV (46%) was the most common class followed by class III (29%), class II (13%), class V (11.5%) and class VI (0,5%). Tubulo-interstitial infiltrate was found in 33 kidney specimens, with germinal centres (GC)-like features in 13 renal samples (Figure 1). During the follow up (6±3.8 years) the tubulo-insterstitial infiltrate, either diffuse or with GC-like feature, was negatively correlated with renal remission (P=0.03).

Conclusion: Assessment and management of patients with LN are greatly facilitated by information obtained by renal biopsy. In the present study we demonstrate that the presence of tubulo-interstital infiltrate is associated with a worse outcome in response to therapy. Our data highlight the importance of tubulo-interstitium damage, scarcely considered in the current classification criteria, since it represents a key point to predict long-term prognosis.

REFERENCES:

[1] Schwartz N, et al. Curr Opin Rheumatol. (2014)
[2] Giannakakis K, et al. Clinic Rev Allerg Immunol (2011)
[3] Weening JJ, et al. J Am Soc Nephrol (2004)
[4] Gladman DD, et al. J Rheumatol (2002)
[5] Houssiau FA, et al. Arthritis Rheum (2002)
[6] Hahn BH, et al. Arthritis Care & Research (2012)

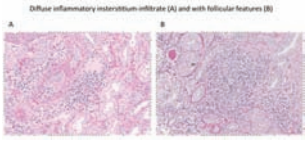


Figure 1

Disclosure of Interests: None declared

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FRI0248 ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY IN PRIMARY SJÖGREN SYNDROME: A MARKER OF EROSIONS ON HIGH RESOLUTION ULTRASOUND OF HANDS AND WRISTS

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Background: Cyclic citrullinated peptides antibodies (anti-CCP) were described in primary Sjögren's syndrome (pSS). However, its possible associations with joint erosions, synovitis and tenosynovitis on high resolution ultrasonography of hands and wrists (US) in pSS are uncertain.

Objectives: To assess in pSS the US findings, and their possible associations with anti-CCP.

Methods: We have evaluated 97 consecutive pSS patients (2016 ACR/EULAR Classification Criteria), of both sexes, aged 18-76 years, and without meeting the 1987 ACR classification criteria for rheumatoid arthritis (RA). Twenty RA patients (disease duration <5 years, and without joint deformities), and 80 healthy controls with comparable mean age, gender and ethnicity were also included in a case-control study. Clinical evaluation was performed through a standardized protocol with interview and physical examination. Disease activity was measured according to EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). US was done in 36 joints and 36 tendon areas of wrists and hands, by the same rheumatologist with expertise in ultrasound, and blinded to autoantibody profile. Patients and controls also underwent X-ray of hands and wrists. Anti-CCP was determined by ELISA using a commercially available kit.

Results: Frequency of tenosynovitis on US was higher in the pSS group than in healthy controls (36.1 vs. 3.8%, p<0.001). Moreover, the number of tenosynovitis was higher in the former group (p<0.001). Importantly, the presence of erosions on US (27.8 vs. 7.5%, p=0.001) and their number (p=0.005) were greater in the pSS group than in healthy controls, with predominance of small erosions (p=0.015). Comparative analysis between RA and pSS groups revealed that the frequency (p<0.001) and number (p<0.001) of synovitis on US were greater in the former group. The number of grade 1 synovitis was comparable between RA and pSS patients (p=0.354). However, the number of grade 2/3 synovitis were higher in RA than in pSS patients (p<0.001/p<0.001, respectively). Similarly, the number of erosions on US was higher in the RA group compared to pSS group (p<0.001), particularly of moderate/large erosions

(p<0.001/p<0.001, respectively). ESSDAI had moderate correlation with the number of synovitis (r=0.302, p=0.003) and tenosynovitis (r=0.343, p=0.001) on US. In pSS patients, US detected 225% more erosions than X-ray. Anti-CCP was more frequent in RA patients (85%) than in pSS (16.5%) (p<0.001). Anti-CCP was more frequent in pSS patients (16.5%) than in healthy controls (4.1%) (p=0.010). In addition, this reactivity was associated with higher mean numbers of erosions in wrists (p=0.018) and proximal interphalangeal joints (p=0.001) on US in pSS patients.
Conclusion: US detected higher frequencies of tenosynovitis and erosions in pSS patients than in healthy controls, and the numbers of synovitis and tenosynovitis correlated with ESSDAI, suggesting that US is an important tool for the evaluation of these patients. Moreover, grade 2/3 synovitis and moderate/large erosions appear to be relevant for the distinction between pSS and RA. The additional observation that erosions are associated with anti-CCP in pSS seems to characterize a subgroup of patients with a severe underlying mechanism of joint damage. Grant from FAPESP: 2015/03756-4.

REFERENCES:

[1] Riente L, Scirè CA, Delle Sedie A, et al. Ultrasound imaging for the rheumatologist. XXIII. Sonographic evaluation of hand joint involvement in primary Sjögren's syndrome. Clin Exp Rheumatol. 2009;27(5):747-50.

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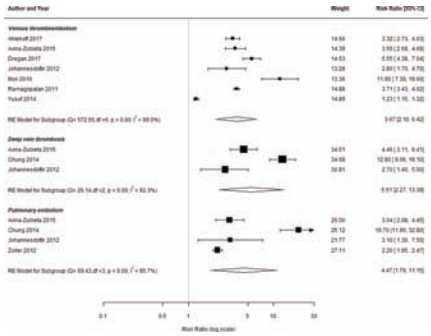
FRI0249 THE RISK OF VENOUS THROMBOEMBOLIC EVENTS IN ADULT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Although observational studies suggest people with systemic lupus erythematosus (SLE) have a heightened risk of venous thromboembolic events (VTE), meta-analyses that integrate evidence across studies to estimate the pooled risk have not been performed.
Objectives: To conduct a systematic review and meta-analysis to estimate the risk of VTE including pulmonary embolism (PE) and deep vein thrombosis (DVT) in patients with SLE.
Methods: We conducted a systematic review using MEDLINE and EMBASE from inception to March 2018 to identify observational studies (cohort and cross-sectional) that evaluated the risk of several major cardiovascular outcomes in patients with SLE compared to a general population or healthy controls (protocol published in PROSPERO 2018 CRD42018098690). Here we report the results for venous thromboembolic outcomes. Studies were included that provided effect estimates (relative risks or hazard ratios) for the calculation of pooled effect estimates. Random effects models were used to calculate pooled risk ratios (RR) and 95% confidence intervals (CI) separately for VTE, PE and DVT. Visualization of funnel plots and the Egger's test were used for evaluation of publication bias. The robustness of the results was tested using the leave one out function. Sensitivity analysis assessed the impact of removing high risk of bias studies (i.e. cross-sectional).
Results: A total of 9 studies were identified for inclusion into the meta-analysis; 7 for VTE (including two cross-sectional studies), 3 for DVT and 4 for PE. Meta-analysis of the VTE studies showed a significantly increased RR of 3.67 (95% CI: 2.10 to 6.42) for patients with SLE compared to a general population. Removing the two cross-sectional studies did not impact the results (RR 4.06 [95% CI: 3.12 to 5.28]). The pooled RRs for PE and DVT were 4.47 (95% CI: 1.79 to 11.15) and 5.51 (95% CI: 2.27 to 13.39), respectively. The statistical heterogeneity was high with an I^2 ranging between 92% and 99%. Visual examination of the funnel plots showed evidence of publication bias, however this was not supported by the Egger's test. The leave one out function confirmed the robustness of the results.
Conclusion: Overall, the risk of VTE was found to be significantly higher, over three- to six-fold higher, among patients with SLE compared with the general population. Future research should focus on assessing the impact of traditional and SLE-specific modifiable risk factors on VTE to further identify SLE patients most at risk to support targeting prevention and treatment strategies.

REFERENCES:

[1] Ahlehoff O, et al. *Lupus*. 2017;26:1435–1439. Avina-Zubieta JA, et al. *Semin Arthritis Rheum*. 2015;45:195–201. Chung WS, et al. *J Thromb Haemost*. 2014;12:452–458. Dregan A, et al. *Heart*. 2017;103:1867–1873. Johannesdottir SA, et al. *J Thromb Haemost*. 2012;10:815–821. Mok CC, et al. *Clin Rheumatol*. 2010;29:599–604. Ramagopalan SV, et al. *BMC Med*. 2011;9:1. Yusuf HR, et al. *J Thromb Thrombolysis*. 2014;38:306–313. Zoller B, et al. Lancet. 2012;379:244–249.



Abbreviations: RE, relative effects

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FRI0250 SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: COMPARABLE EFFECT OF TRADITIONAL CARDIOVASCULAR RISK FACTORS WITH RHEUMATOID ARTHRITIS

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Background: Both rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients are associated with an increased and premature

prevalence of atherosclerosis. This has been characteristically attributed to the inflammation present in both diseases

Objectives: To analyze the differences in the role of traditional cardiovascular risk factors in the subclinical atherosclerosis between the two diseases.

Methods: Cross-sectional study encompassing 602 subjects, 276 SLE and 326 RA patients. Carotid plaques were assessed by ultrasonography. A multivariable regression analysis was performed to evaluate if classic cardiovascular-related risk factors influence differentially on subclinical carotid atherosclerosis in SLE compared to RA patients.

Results: Traditional cardiovascular risk factors were found to be prevalent in RA and SLE patients. Age (interaction factor p=0.000), hypertension (interaction factor p=0.034), and diabetes (interaction factor p=0.037) were found to have a higher effect on cIMT in RA patients compared to SLE subjects. No differences between RA and SLE were discovered in the effect of traditional cardiovascular factors over the presence of carotid plaque when univariate interaction was performed. After final adjustment for demographics, the presence of others traditional cardiovascular factors, and disease related data, no differences were found in the influence of hypertension, diabetes, dyslipidemia or current smoking over cIMT or the presence of carotid plaque. Moreover, the effect of the addition of various cardiovascular risk factors on the subclinical carotid atherosclerosis did not differ between both diseases.

Conclusion: The influence of traditional cardiovascular risk factors (hypertension, diabetes, dyslipemia and smoking) over cIMT and carotid plaque is equal in RA and SLE. No interaction was found between traditional cardiovascular risk factors and disease related data in the effect of the former on subclinical atherosclerosis.

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FRI0251 SYSTEMATIC REVIEW OF PREDICTOR MARKERS OF POOR RENAL EVOLUTION IN PATIENTS WITH LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) affects 30-45% of patients with lupus and causes great morbidity and mortality. About 10-25% of patients will develop chronic kidney disease (CKD), and it has been described a mortality of 10-20% at 10 years[1-2]. Currently there is no ideal biomarker or composite indexes that help us to better assess and monitor.

Objectives: To identify and perform a critical analysis of the prognostic markers and indexes published through a systematic review of the literature in order to subsequently develop an index that helps us to estimate the prognosis of patients with LN.

Methods: We conducted a systematic review and meta-analysis according to the guidelines of the "Cochrane Collaboration" and our results are exposed in accordance with the "Preferred Reporting Items for Systematic Reviews and Meta-Analyzes PRISMA statement". We did an electronic search in MEDLINE, EMBASE, CINAHL and Web of Science using free text and MeSH terms. The selection was made by 2 independent authors using a bibliographic manager. First, a selection was made by title and if it seemed relevant, a review of the abstract was made. In case of doubt, the full text was evaluated for a possible inclusion. The articles had to fulfill the following criteria: marker or prognostic index of LN, longitudinal studies, to collect the prognostic factor retrospectively without variable biases suitable for good/poor renal prognosis and LN diagnosed by biopsy. Six authors independently extracted data from the articles on previously tested forms to determine their feasibility, and differences were discussed. The data included the general characteristics and results measured. Also adverse events were reported.

Results: We selected 1010 articles initially, of which we discarded 853 per title. Of the 157 remaining, 84 were selected per abstract, and finally, 62 articles were excluded after the review of the full text. In total, the 22 studies included 2301 patients, all older than 18 years. Most were single-center and retrospective (65%). Among the analytical markers, serum creatinine (Cr) was one of the most used variables as a predictor of time to CKD depending on the value, which varied according to the studies. It was also associated as a damage predictor according to the SLICC scale. Proteinuria appears in several studies as a marker of progression of LN, associating the amount with renal response, the development of end-stage renal disease (ESRD), the need for dialysis and the appearance of extrarenal events. Other variables analyzed were: demographic (ethnicity, socioeconomic level), immunological (anti-Ro, anti-DNA, anti-C1q and anti-CRP antibodies with poor renal evolution), histopathological (increased nedd for dialysis in glomerulonephritis IV, thrombotic microangiopathy, C4d deposits or tubular atrophy and association of chronicity index with remission) or therapeutic (hydroxychloroquine with remission).

Conclusion: Altough there are several biomarkers to evaluate the LN prognosis, we have no found indexes for LN prognosis assessment in literature. The development of easily reproducible compound index is necessary for the assessment of the prognosis and the severity of patients with LN on debut and during evolution.

REFERENCES:

[1] Carmona L, Gabriel R, Ballina J, Laffon A. Proyecto EPISER 2000: prevalencia de enfermedades reumáticas en la población española. Metodología, resultados del reclutamiento y características de la población. 2001;28:8.

[2] Austin HA, Boumpas DT, Vaughan EM, Balow JE. High-risk features of lupus nephritis: importance of race and clinical and histological factors in 166 patients. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 1995;10(9):1620-8.

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FRI0252 CLINICAL AND SEROLOGICAL LUPUS ACTIVITY BEFORE AND AFTER DEVELOPING END STAGE RENAL DISEASE

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Background: SLE disease activity tends to diminish after the development of end stage renal disease (ESRD)[1, 2]. Nonetheless, some patients continue to show signs of active disease and experience flares after ESRD[3]. To date, little is known about the evolution of SLE-related symptoms pre and post ESRD. Whether specific symptoms abate after ESRD or a shift towards different manifestations occurs deserves further study. Prompt identification of subtler SLE manifestations is further complicated by a trend towards poor rheumatology follow once ESRD develops. SLE manifestations post-ESRD may be underdiagnosed and undertreated contributing to increased morbidity and mortality.

Objectives: To study the different clinical manifestations and serological markers of SLE disease activity before and after ESRD development.

Methods: We performed a retrospective chart review of SLE patients with ESRD at a tertiary care center between the years of 2010 and 2017. SLE was defined by ACR and/or SLICC criteria. SLE ESRD patients were included if they had at least one visit with rheumatology, nephrology, or primary care pre- and post-ESRD. SLE-related symptoms and serologic markers of disease activity were identified from chart review before and after ESRD onset.

Results: Fifty-eight patients were included. Twenty-five patients had a least one clinical non-renal criteria documented pre-ESRD. Of them, 14 achieved complete clinical remission post-ESRD. Post-ESRD, cytopenias persisted in 49 of the 55 patients who were cytopenic pre-ESRD. Arthritis persisted in 3 of the 13 patients who had arthritis pre-ESRD. Of the 37 patients with hypocomplementemia pre-ESRD, 29 remained hypocomplementemic post-ESRD. Twenty-nine had elevated dsDNA pre-ESRD, of them, dsDNA remained elevated in 16 patients post-ESRD. Six patients developed at least one new clinical criteria post-ESRD. Three patients developed low complement, 5 developed elevated dsDNA, 3 developed new onset of serositis and 4 new osent of arthritis post-ESRD.

Conclusion: Lupus activity may diminish after ESRD onset. However, many patients experience persistent disease activity. New arthritis, serositis, low complements and elevated dsDNA may develop after ESRD. Limited evaluation and documentation of disease activity by non-rheumatology

providers may have resulted in under-reporting of SLE signs and symptoms on this study. SLE ESRD patients should be carefully evaluated for subtle signs of active SLE.

REFERENCES:

[1] Mattos P, Santiago MB. Clin Rheumatol. 2012; 31:897–905.
[2] Stone JH. Lupus. 1998; 7:654–659.
[3] Krane NK, Burjak K, Archie M, O'Donovan R. Am J Kidney Dis. 1999; 33:872–879.

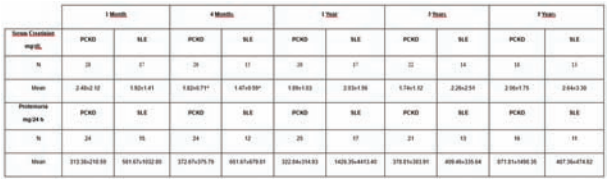
Disclosure of Interests: None declared
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FRI0253 RENAL TRANSPLANTATION IN LUPUS NEPHRITISVS NON-AUTOIMMUNE TRANSPLANTATION. LONG TERM FOLLOW-UP. STUDY FROM A SINGLE TERTIARY CENTER

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Background: Lupus nephritis (LN) is a severe complication of systemic lupus erythematosus (SLE), affecting up to 30-40% of patients. Unfortunately, approximately 10-20% of LN develop end stage renal disease (ESRD) and need replacement therapy. Renal transplantation may be a good option. However, concerns about LN recurrence after renal transplantation have been reported.
Objectives: In a series of patients with first renal transplantation due to LN our aim was to assess a) long-term post-transplant survival and, b) comparison of post-transplant survival with a control group due to a non-autoimmune nephropathy**,** the polycystic kidney disease (PCKD).
Methods: We study two groups of patients with first renal transplantation: **a)** LN and **b)** control group with PCKD. All these patients were transplanted in a single reference University Hospital. The main outcome variables were **a)** graft and patient survival up to 20 years and **b)** evolution of renal function (serum creatinine and proteinuria) in the first 5 years of follow-up. Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test. Mann-Whitney test was used to compare quantitative variables and chi^2/Fisher's exact test for qualitative variables.
Results: We included a total of 53 patients with renal transplant; a) LN group (n=21), b) PCKD group (n=32). No significant differences at baseline were observed between the 2 groups regarding sex and cardiovascular risk factors. Significant differences were found in terms of age at kidney transplantation, with a mean of 39.80±11.27 years in LN group and 46.59 ±5.01 years in the PCKD group (p=0.004). Renal biopsy had been performed in 16 patients with LN: type II LN (25%), type III (25%) and type IV (50%), (according to the World Health Organization and International Society of Nephrology/Renal Pathology Society classification). From 48 patients (of 53) in which a renal biopsy was performed during the first-year post-transplant, rejection was found in 21 patients (43.7%) without significant differences between the 2 groups (p=0.444). The evolution of serum creatinine and proteinuria after renal transplantation is shown in **TABLE-1**. Regarding serum creatinine, significant differences were found in creatinine levels only at the 6th month post-transplant (p=0.032) with no differences in the following measurements. In LN group, 3 patients (14.3%) developed a lupus flare: 2 cases presented as extrarenal disease and only 1 case with histological recurrence in the graft. No significant differences were found in terms of patient or graft survival between the two groups in 20 years of follow-up **(Figures 1 and 2).**
Conclusion: Despite concerns about LN recurrence after renal transplantation, data obtained in our sample indicate that this procedure as a safe alternative therapy for ESRD in this population and can provide a long-term survival.

TABLE 1. Evolution of creatinine and proteinuria levels after renal transplant in LN and PCKD.



*p<0.05

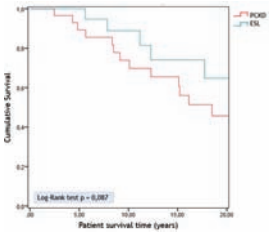


FIGURE 1. Patient survival

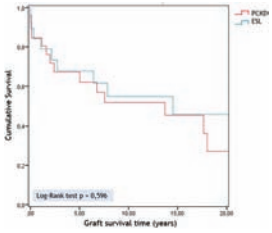


FIGURE 2. Graft survival

Disclosure of Interests: Lara Sánchez Bilbao: None declared, Iñigo González-Mazón: None declared, Marina de Cos-Gómez: None declared, Belén Atienza-Mateo: None declared, José Luis Martín-Varillas: None declared, Monica Calderón-Goercke: None declared, D. Prieto-Peña: None declared, Juan Carlos Ruiz-San Millán: None declared, Miguel Á. González-Gay: None declared, Ricardo Blanco Grant/research support from: Abbvie, MSD, and Roche, Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen
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FRI0254 COMBINED PANEL OF NINE TESTS HAS THE GREATEST SENSITIVITY BUT THE LOWEST SPECIFICITY TO DETECT ANTIPHOSPHOLIPID ANTIBODY SYNDROME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Antiphospholipid antibody syndrome (APS) is an autoimmune hypercoagulable state caused by antiphospholipid antibodies (aPL) which represent a diagnostic criterion and underlie significant comorbidities in patients with and without systemic lupus erythematosus (SLE). Although several tests exist for APS diagnosis, their utilization has been highly variable among laboratories and physicians.
Objectives: We have evaluated a panel of nine tests and conducted a retrospective study to determine their sensitivity and specificity for supporting the diagnosis of APS in SLE at our Institution between 2010 and 2018.
Methods: 1633 SLE patients, who satisfied the ACR criteria for a definitive diagnosis [1 2], were evaluated for the presence of APS as earlier described [3]. Lupus anticoagulants were assessed by Staclot LA hexagonal phase phospholipid neutralization assay (HPPNA; delta <8 seconds), Staclot diluted Russell viper venom test (dRVVT; <1.2 normalized ratio)

obtained from Stago (Parsippany, NJ, United States of America). Platelet neutralization procedure (PNP; delta < 1 second) has been performed using a STA-R Evolution instrument by Stago [4, 5]. IgG and IgM antibodies against β2-glycoprotein 1 (aβ2-IgG, aβ2-IgM) and cardiolipin (aCL-IgG, aCL-IgM) were measured in house while IgA isotypes (aβ2-IgA, aCL-IgA) were tested by LabCorp Diagnostics (Burlington, NC). Sensitivities, specificities, and positive (PPV) and negative predictive values (NPV) for detection of APS were calculated and compared by 2-tailed chi-square tests using GraphPad software.

Results: 222/1633 SLE patients had APS when using a combination of nine tests. Table 1 shows the frequency of positive and negative test results and p value for each assay. The greatest sensitivity was seen when all nine tests were performed together for detecting APS in SLE patients (74%; χ^2p=0.0003). In contrast, combining all tests had the lowest specificity (52%; p<0.0001). Importantly, the 2nd most sensitive test for detection of APS was the HPPNA at 52%, this tests also had the second lowest specificity (66%). Similar trends were seen when individual APS comorbidities, such as deep venous thrombosis (DVT), pulmonary embolism (PE), and stroke or TIA, were separately analyzed. Among the charts reviewed, the complete 9-test panel was only performed in 550 of 1633 patients (Table 1).

Table 1. Sensitivity and Specificity of Nine Tests for Detection of APS in SLE Patients

TEST	HPPNA	PNP	dRVVT	aβ2-IgG	aβ2-IgM	aβ2-IgA	aCL-IgG	aCL-IgM	aCL-IgA	All 9 tests
APS+ TEST+	102	35	36	15	14	13	21	28	8	73
APS+TEST-	96	77	155	191	192	175	195	185	181	26
APS-TEST+	395	78	96	43	57	47	81	123	41	215
APS-TEST-	777	536	1179	1285	1271	1110	1298	1245	1089	236
p value	<0.0001	<0.0001	<0.0001	0.0046	NS	NS	0.0316	NS	NS	<0.0001
Sensitivity (%)	52	31	19	7	7	7	10	13	4	74
p value vs	HPPNA	0.0096	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0003
PPV (%)	21	31	27	26	20	22	21	19	16	25
Specificity (%)	66	87	92	97	96	96	94	91	96	52
p value vs	HPPNA	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
NPV (%)	89	87	88	87	87	86	87	87	86	90
Number of Patients Tested	1370	726	1466	1534	1534	1345	1595	1581	1319	550

Conclusion: This study demonstrates that utilizing a combined 9-test panel has the greatest sensitivity but lowest specificity for detecting APS in SLE subjects. Thus, a failure to employ the complete panel may lead to exclusion of patients who may meet criteria for identifying patients with APS who need long-term anticoagulation for preventing life-threatening thrombotic events.

REFERENCES:

[1] Tan, E.M., et al., *The 1982 revised criteria for the classification of systemic lupus erythematosus*. Arthritis Rheum, 1982. 25(11): p. 1271-7.

[2] Hochberg, M.C., *Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus*. Arthritis Rheum, 1997. 40(9): p. 1725.

[3] Miyakis, S., et al., *International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS)*. J Thromb Haemost, 2006. 4(2): p. 295-306.

[4] Triplett, D.A., et al., *Laboratory diagnosis of lupus inhibitors: a comparison of the tissue thromboplastin inhibition procedure with a new platelet neutralization procedure*. Am J Clin Pathol, 1983. 79(6): p. 678-82.

[5] Genzen, J.R. and J.L. Miller, *Presence of direct thrombin inhibitors can affect the results and interpretation of lupus anticoagulant testing*. Am J Clin Pathol, 2005. 124(4): p. 586-93.

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FRI0255

LOW ATTENUATION NON-CALCIFIED CORONARY PLAQUES AND POSITIVE REMODELING INDEX: MARKERS OF VULNERABLE CORONARY PLAQUES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The presence of low attenuation noncalcified plaque (LANCP) and positive remodeling index (RI) are characteristic vessel changes in unstable coronary plaques.

LANCP (<30 Hounsfield Units) contain necrotic cores that are characterized by endothelial dysfunction, oxidative stress, and inflammation. They have been shown to be a better predictor of future cardiovascular events compared to traditional cardiovascular risk factors in the general population.

Coronary arterial remodeling describes changes of vessel size at the site of atherosclerotic lesions. Positive remodeling (expansion) of early lesions maintains lumen size despite plaque accumulation. This explains why these lesions might pass undetected by conventional angiography. Plaque rupture is often apparent at sites with only modest luminal stenoses but marked positive remodeling.

Accelerated atherosclerosis leading to premature coronary artery disease remains the major cause of late death in SLE.

Objectives: We sought to characterize LANCP and positive RI in patients with systemic lupus erythematosus.

Methods: A total of 72 patients who met the ACR or SLICC classification criteria for SLE had CT angiogram studies, 30 of which had follow up CT angiograms. A total of 100 healthy controls who had two CT angiograms were included in the study. Each noncalcified plaque (NCP) detected within the vessel wall was evaluated for minimum CT density and vascular remodeling index. A LANCP was defined as an NCP with a density <30 Hounsfield units. Lesions with remodeling 0% were considered to have positive RI. T-test was used to evaluate baseline characteristics between lupus patients and controls. Paired t-test or Wilcoxon signed ranks test was used to compare LANCP volume and RI between baseline and follow-up. Fisher's exact test was used to evaluate the association between change in LANCP, RI, demographic and clinical variables.

Results: Lupus patients had a significantly higher burden of LANCP at baseline compared to healthy controls in all age subgroups except in those >60 years of age. LANCP volume was associated with age (p<0.01) and body mass index (p<0.01). No significant differences were observed between RI in lupus and controls at baseline.

Despite a significant progression of the total noncalcified plaque burden in lupus compared to controls (p<0.0001), the LANCP in lupus patients regressed (p<0.001). No demographic or clinical differences were observed between lupus patients whose LANCP progressed and those whose LANCP regressed. Lupus patients who were not treated with statins had a more significant regression of their LANCP burden (p<0.01) compared to controls who were on statins, while lupus patients who were taking statins had a significant progression (p<0.01).

There were only 5 cardiovascular events in the studied group and there were no differences in remodeling index or low density noncalcified plaque observed but the number of events was small.

Conclusion: Lupus patients have a significantly higher burden of LANCP at baseline compared to healthy controls in all age subgroups except in those >60 years of age. The LANCP burden regresses more rapidly over time in lupus compared to controls. Surprisingly, the most significant LANCP plaque volume regression was seen in lupus patients who were never treated with statins, while the most significant progression was observed in those taking statins. Positive RI was ubiquitous, with no evidence of progression or differences compared to controls. These characteristic vessel changes may identify SLE patients at need for more frequent noninvasive cardiac monitoring.

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FRI0256

ASSESSING THE PREVALENCE AND USE OF VALIDATED SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY METRICS IN REAL WORLD PRACTICE

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Background: Disease activity metrics for systemic lupus erythematosus (SLE) are not widely used in real world clinical practice.

Objectives: To assess the use and drivers of SLEDAI and BILAG index in real world clinical practice.
Methods: A cross-sectional study of rheumatologists in the US and EU5. Data were collected from the Adelphi Real World 2010/2013/2015 Lupus Disease Specific Programmes (DSP). Physicians were asked to complete an attitudinal survey and patient record forms (PRFs) for the next 5 patients consulting with SLE; the same patients were asked to complete patient self-completion (PSC) forms describing how SLE affected them. PRFs collected data pertaining to the patient's diagnosis, disease history, current clinical outcomes, treatment and management history. PSCs focused on similar data collection and included patient reported outcome measures (PROs) to assess the humanistic burden. 2015 DSP data was used to assess the profile of patients with a SLEDAI assessment were compared to those without a SLEDAI assessment, using Fisher's Exact and Mann-Whitney tests. Similar analysis was also conducted for those with/without BILAG index assessments. 2013 & 2010 DSP datasets were merged, and multiple linear regression was used to assess drivers of SLEDAI and BILAG index utility, respectively.
Results: Physicians provided 263 surveys, extracted from the 2015 DSP, indicating that 131 were aware of but did not use the BILAG index, and 92 of physicians were aware of but did not use the SLEDAI.
Physicians provided 1376 record forms for SLE patients, extracted from the 2015 DSP; 71 (5.2%) had a BILAG index (1305, 94.8% had no BILAG index), and 373 (27.1%) had had a SLEDAI calculated prospectively (1003, 72.8% had No SLEDAI). Patients with SLEDAI had longer disease duration that patients who did not have a SLEDAI (mean: 6.3 vs. 5.2 years, p=0.007), were less likely to have been described as mild at diagnosis (no SLEDAI mild: 18.7%; SLEDAI mild: 11.3%, p=0.0004) and consulted more with health care professionals in the past 12 months (no SLEDAI mean visits: 6.5, SLEDAI mean: 7.7, p<0.001).
Patients with a BILAG index had flared more in the last 12 months (no BILAG: 30.6%, BILAG: 45.1%, p=0.0126).
Physicians provided data on 220 SLEDAI and 75 BILAG assessments, extracted from the 2010 & 2013 DSPs. Multiple linear regression analyses revealed that flaring in the last 12 months (Coef: 3.27 [0.36 – 6.18], p=0.028), renal symptoms (Coef: 5.67 [1.84-9.51], p=0.004), and muscular symptoms (Coef: 4.58 [1.22-7.94], p=0.008) were all associated with a higher SLEDAI score, with r-squared 0.1948.
Multiple linear regression showed that renal symptoms (Coef: 3.87 [1.00 – 6.75], p=0.009) were associated with a higher BILAG score, with r-squared 0.3717.
Conclusion: The use of SLEDAI and BILAG index in clinical practice is limited and seemingly reserved for use in more severe patient cohorts; understanding the ongoing impact of this selective use on the treatment and management of SLE would be beneficial. Additionally, understanding the drivers and barriers to the use of disease activity metrics is important to improve the management of SLE in the future.
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FRI0257 PROLACTIN AND DEHYDROEPIANDROSTERONE SULFATE IN WOMEN WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS OF RECENT ONSET VERSUS CHRONIC INACTIVE PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease, typically affecting young women at reproductive age. Prolactin (PRL) levels have shown direct correlation with clinical and serological disease activity. Hyperprolactinemia has been reported in a wide range of SLE patients (15–33%). Dehydroepiandrosterone (DHEA) and its sulfated form dehydroepiandrosterone sulfate (DHEAS) are the most abundant circulating steroid hormones in humans. The level of both metabolites is lower in patients with active SLE compared with patients with inactive disease, which suggests a potential role of low levels of DHEAS in the pathogenesis of SLE.
Objectives: To evaluate serum PRL levels and DHEAS levels in patients with active SLE of recent onset vs patients with inactive chronic and healthy controls and their correlation with activity and chronicity scores
Methods: Serum PRL levels and DHEAS levels were studied, as well as their correlation with SLEDAI and SLICC scores. Group 1: 15 patients with SLE of recent onset (active SLEDAI >3) Group 2: 20 patients with inactive chronic SLE (SLEDAI<3) and Group 3: 20 healthy controls. SLEDAI and SLICC were calculated in group 1 and group 2 respectively. PRL and DHEAS was measurement by radioimmunoassay in all groups. Statistical analysis: U-Mann Whitney and Spearman correlation.
Results: Group 1: serum PRL levels were 27.82±9.96 ng/dl vs group 2: 20±5.02 ng/dl (p= 0.004) and group 3:19.58±4.57 ng/dl (p=0.004). Group 1: serum DHEAS levels were 14.58±9.26 µg/dl, group 2: 19.36±7.21 µg/dl (p=0.04) and group 3: 154.43±50.88 µg/dl (p =0.001). The average DHEAS was lower in patients with chronic SLE vs controls (p = 0.001). A positive linear correlation was found between serum PRL levels and SLEDAI score (Rho 0.92, p=0.001). No correlation was found between PRL and SLICC score. A negative linear correlation was shown between DHEAS concentration and SLICC score (Rho-0.46, p =0.03).
Conclusion: PRL levels were higher in active SLE patients VS. chronic inactive SLE and healthy controls. In contrast, serum DHAS levels were lower in patients with active SLE vs. inactive chronic SLE. We found a positive correlation between SLEDAI score and PRL serum concentrations and an inverse correlation between SLICC score and DHAS serum levels.

REFERENCES:
[1] Borba VV, Zandman-Goddard G, Shoenfeld Y. Prolactin and Autoimmunity. Front Immunol 2018; 12:73.
[2] Rutkowski K, Sowa P, Rutkowska-Talipska J, et al. al. Dehydroepiandrosterone (DHEA): hypes and hopes Drugs. 2014;74:1195-207.
[3] Robeva R, Tanev D, Andonova S, et al. Androgen receptor (CAG)n polymorphism and androgen levels in women with systemic lupus erythematosus and healthy controls. Rheumatol Int. 2013;33:2031-8.

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FRI0258 ANTI-RO/SSA POSITIVITY, ANTI-AQUAPORIN4 ANTIBODIES AND CENTRAL NERVOUS SYSTEM INVOLVEMENT: A RETROSPECTIVE STUDY ON A CONTROVERSIAL CORRELATION

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Background: Different neurological manifestations have been observed in 20-25% of patients affected by Sjögren's syndrome (SS). Among them, CNS demyelinating diseases, Neuromyelitis optica (NMO) and NMO spectrum disorders (NMOSD) with anti-aquaporin4 antibodies (anti-AQP4) positivity have been described.
Objectives: The aim of the present study was to assess the clinical charachteristics and seroimmunological correlations in patients with Ro-SSA antibodies and Central and peripheral nervous system (CNS and PNS) involvement.
Methods: We retrospectively reviewed clinical records, laboratory and Magnetic Resonance Imaging (MRI) reports of patients followed-up at a tertiary level immunorheumatology and neuroimmunology clinic. We included patients showing an anti-SSA antibodies positivity and concomitant neurological symptoms at diagnosis. We excluded patients fulfilling SLICC criteria for SLE. We recorded clinical and laboratory and MRI data for all patients.
Results: Out of 9598 clinical records reviewed, we identified 511 patients with anti Ro/SSA positivity. 11 patients had prevalent neurological manifestations. 8 (72.7%) patients were women. The median age was 56 [IQR 31] years. CNS involvemente was the main clinical feature in 7 patients (63.6%); 3 of them (27.3%) also had PNS manifestations. 4 patients showed exclusively PNS involvement.
3 subjects fulfilled criteria for SS while 8 patients were classified as undifferentiated connective tissue disease. 7 patients underwent spinal tap

which reported inflammatory alterations (high levels of CSF proteins in 2 subjects and oligoclonal bands in 4 patients).
Median Erythrocyte sedimentation rate (ESR) was 12 mm/h [IQR 18] while median C- Reactive protein was 0.34 mg/dL [IQR 0.32]. There was not complement deficiency in any patient. With regard to the tested auto-antibodies, 2 subjects showed also anti-La positivity. Out of the 4 patients tested for anti-AQP4 none was positive, even if 2 patients had NMODSD.
Conclusion: Anti-SSA positive may show a wide spectrum of neurological manifestations; CNS involvement was not associated to anti-AQP4 positivity in our cohort, even in patients with NMO/NMOSD. Further investigations are required to better disclose this association and to search for novel autoantibodies.
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FRI0259 **SEROLOGICAL IMMUNE ABNORMALITIES ASSOCIATE WITH SPECIFIC PATHOLOGICAL ACTIVE LESIONS IN LUPUS NEPHRITIS**

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Background: Serological immune abnormalities such as anti-double strand DNA (dsDNA) antibodies (Abs) and hypocomplementemia (HC) are characteristic of lupus nephritis (LN). International Society of Nephrology/Renal Pathology Society (ISN/RPS) Classification of LN defines pathological active lesions (ALs) as including endocapillary hypercellularity, karyorrhexis, fibrinoid necrosis, cellular/fibrocellular crescents, and wire-loop lesion/hyaline thrombi [Reference 1]. Few reports have focused on the clinicopathological impact of serological immune abnormalities on pathological ALs.
Objectives: To identify the clinicopathological association between serological immune abnormalities and pathological ALs in LN.
Methods: We enrolled 126 Japanese LN patients who were subjected to renal biopsy in 11 hospitals from 2000 to 2018. We determined various clinical parameters at the time of renal biopsy, including creatinine (Cr), estimated glomerular filtration rate (eGFR), total protein (TP), IgG, IgA, IgM, C3, C4, CH50, anti-nuclear antibodies (Abs), anti-double strand DNA (dsDNA) Abs, anti-Sm Abs, anti-RNP Abs in the sera, urinalysis findings, presence of comorbidities (antiphospholipid antibody syndrome, hypertension, hyperlipidemia, diabetes mellitus, and hyperuricemia), and use of any immunosuppressive medications before renal biopsy. Renal biopsy findings were classified by ISN/RPS Classification including ALs. Immune deposits were evaluated by immunofluorescence. Elevation of serum anti-dsDNA Abs level [dsDNA Abs (+)] was defined as >12 IU/mL. HC was defined by C3 <60 mg/dL. In patients of all pathological classes, we analyzed the association between serological abnormalities and ALs by univariate and multiple regression analyses.
Results: Of 126 patients (104 females; mean age 41.8 years), dsDNA Abs (+) and HC (+) were found in 83 (65.9%) and 80 (63.5%), respectively. There were no significant differences in renal function, comorbidities, immune deposits or immunosuppressive medications before renal biopsy between dsDNA Abs (+) and dsDNA Abs (-), or between HC (+) and HC (-) patients. In pathological study, endocapillary hypercellularity, karyorrhexis, fibrinoid necrosis, cellular or fibrocellular crescents, and wire-loop lesion/hyaline thrombi were found in 81 (64.3%), 33 (26.2%), 19 (15.1%), 51 (40.5%), and 41 (32.5%), respectively. dsDNA Abs (+) had a higher frequency of endocapillary hypercellularity, karyorrhexis, fibrinoid necrosis, and wire-loop lesion/hyaline thrombi than dsDNA Abs (-). HC (+) had a higher frequency of endocapillary hypercellularity, karyorrhexis, fibrinoid necrosis, cellular or fibrocellular crescents, and wire-loop lesion/hyaline thrombi than HC (-). On multiple regression analysis dsDNA Abs and C3 associated with fibrinoid necrosis and karyorrhexis, respectively (β=0.25, p=0.049; β=-0.31 p=0.01).
Conclusion: Serum anti-dsDNA Abs and HC were associated with fibrinoid necrosis and karyorrhexis, respectively. These results document that individual serological immune abnormalities associate with specific AL, suggesting that pathophysiological differences underlie each AL.

REFERENCES:
[1] J Am Soc Nephrol. 2004;15:241-50.

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Vasculitis

FRI0260 **THE INPATIENT BURDEN OF TAKAYASU'S ARTERITIS IN THE UNITED STATES: A NATIONWIDE ANALYSIS**

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Background: Takayasu's Arteritis (TAK) is a rare granulomatous inflammation of the large vessels. Its incidence has been reported to be 2-3 cases per million people in the United States. To our knowledge an inpatient nationwide study of TAK in the United States has not been conducted to date. The aim was to evaluate the demographic characteristics, reason for admission, procedures, mortality and resource utilization of patients with TAK using a national database.
Objectives: The primary goal was to estimate the national inpatient prevalence of admissions involving patients with TAK. Secondary outcomes were top reasons for admission, mortality, morbidity, resource utilization, length of hospital stay (LOS), and total hospitalization charges and costs, adjusted for inflation using the Consumer-Price Index.
Methods: All patients with a principal ICD9 diagnosis code for TAK were included using the NIS 2013 and 2014, the largest publically available inpatient database in the US. Controls were 1:1 matched using a propensity score including age, gender, and Charlson Comorbidity Index (CCI). Multivariate logistic regression models were used to adjust for race, sex, patient zip code, income, CCI, hospital region, location, size and teaching status.
Results: Of a total of 2,840 hospital admissions for patients with TAK, 2,680 were propensity-matched to admissions without TAK and included in the study. Mean age was 49 years, 81% were female. The inpatient prevalence of TAK was 4.6/100,000 admissions. After adjusting for confounders, patients with TAK had propensity-matched mortality odds of 1.44 (p=0.43) when compared to patients without TAK. The top reasons for admission were large vessel vasculitis, sepsis secondary to pneumonia and urinary tract infection, carotid artery stenosis/occlusion, and arthralgias. For secondary outcomes, patients with TAK displayed increased odds of stroke, aortic aneurysm, peripheral vascular disease and aortic valvulopathy when compared to patients without TAK. When CCI was evaluated it was noted that all the patients had an index lower than 4 and the great majority lower than 2 which could be related to the young age of this population. Despite the low CCI, these patients had 7.35 days of in-hospital stay which represented 2.1 days more when compared to non-TAK patients. For resource utilization, patients with TAK displayed higher odds of peripheral vascular intervention and arteriography when compared to patients without TAK. Patients with TAK displayed significantly higher adjusted total hospital costs, charges and LOS compared to patients without TAK.
Conclusion: The inpatient prevalence was higher than suspected and could be related to the severity of the disease and complications associated with TAK. TAK was associated with an increased risk of stroke, aortic aneurysm, peripheral vascular disease and vascular interventions, but no increase mortality in this group of patients. The costs associated with hospitalization were substantial.

REFERENCES:
[1] Watanabe Y, Miyata T, Tanemoto K. Current Clinical Features of New Patients With Takayasu Arteritis Observed From Cross-Country Research in Japan: Age and Sex Specificity. Circulation. 2015;132(18):1701-9.
[2] Schmidt J, Kermani TA, Bacani AK, Crowson CS, Cooper LT, Matteson EL, et al. Diagnostic features, treatment, and outcomes of Takayasu arteritis in a US cohort of 126 patients. Mayo Clinic proceedings. 2013;88 (8):822-30.

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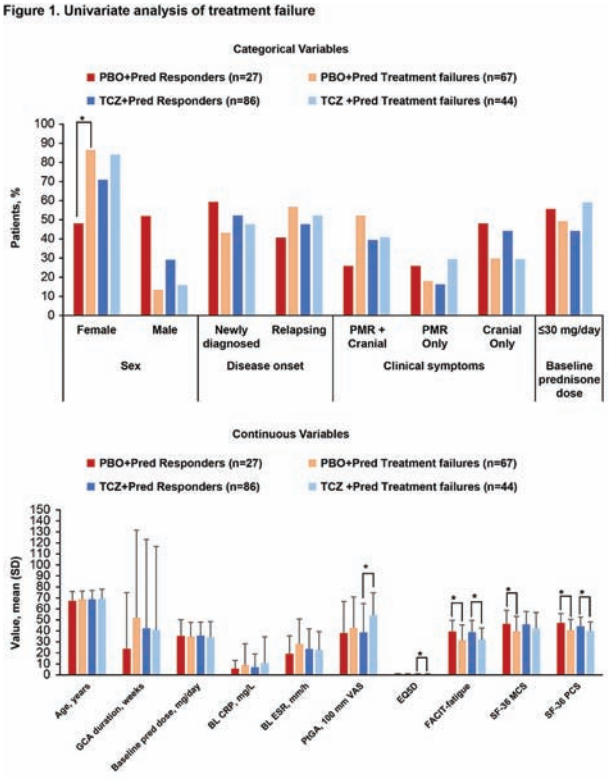
FRI0261

RISK FACTORS FOR TREATMENT FAILURE IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB PLUS PREDNISONE VERSUS PREDNISONE ALONE

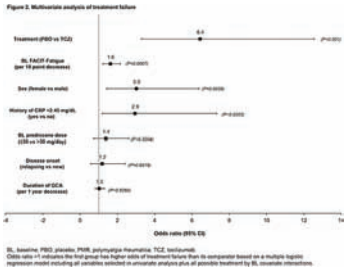
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Background: Risk factors for treatment failure in patients with giant cell arteritis (GCA) are poorly understood.
Objectives: To identify predictors of treatment failure in GCA patients receiving tocilizumab (TCZ) or placebo (PBO) in combination with prednisone in a randomized controlled trial.[1]
Methods: Two hundred fifty GCA patients received weekly or every-other-week TCZ plus a 26-week prednisone taper (TCZ+pred) or PBO plus a 26- or 52-week prednisone taper (PBO+pred). Patients who achieved and maintained clinical remission (CR) from week 12 to week 52 while adhering to the protocol prednisone taper were classified as responders. CR, adjudicated by investigators, was defined as the absence of disease flare (GCA signs or symptoms, and/or ESR elevation attributable to GCA that required further treatment [eg, rescue prednisone]) regardless of CRP level. Treatment failure was defined as failure to achieve CR by week 12 or occurrence of flare between weeks 12 and 52. Both TCZ groups and both PBO groups were combined for this analysis. Potential predictors investigated included baseline demographics, disease- and treatment-related factors, and health-related quality of life (HRQOL) measures. Univariate and multivariate analyses were performed.
Results: Overall, 45% (113/250) of patients were responders: 27% (27/101) in the PBO+pred groups and 58% (86/149) in the TCZ+pred groups. In contrast, 44% (111/250) of patients experienced treatment failure: 66% (67/101) in the PBO+pred group and 30% (44/149) in the TCZ +pred group. The other 10% (26/250) of patients were nonresponders for reasons other than treatment failure: 7 in the PBO+pred group and 19 in the TCZ+pred group. In univariate analysis, female sex and lower baseline SF-36 Physical Component Summary (PCS), Mental Component Summary, and FACIT-Fatigue scores were associated with treatment failure among PBO+pred–treated patients, whereas higher patient global assessment of disease activity scores and lower SF-36 PCS, FACIT-Fatigue, and EQ-5D scores were associated with treatment failure among TCZ +pred–treated patients (Figure 1). Among TCZ+pred–treated patients, no treatment response difference according to sex was observed. Age, previous relapse, starting prednisone dose, and GCA clinical features (cranial or polymyalgia rheumatica symptoms) were not associated with treatment failure in either group based on univariate analysis. Multivariate logistic regression demonstrated that PBO+pred treatment, female sex, worse FACIT-Fatigue scores at baseline, and historical CRP >2.5 mg/dL all independently increased the risk for treatment failure (Figure 2).
Conclusion: Female GCA patients responded particularly poorly if treated with prednisone alone according to univariate analysis. Female sex, impaired HRQOL at baseline, history of elevated CRP, and treatment with prednisone alone are independent risk factors for treatment failure in GCA. These factors may be considered when determining which treatment would be best for a particular patient.

Figure 1. Univariate analysis of treatment failure



BL, baseline; CRP, C-reactive protein; EQ-5D, Euro-Qol 5D; ESR, erythrocyte sedimentation rate; GCA, giant cell arteritis; MCS, Mental Component Summary; PBO, placebo; PCS, Physical Component Summary; PMR, polymyalgia rheumatica; Pred, prednisone; PtGA, patient global assessment; SF-36, Short Form 36; TCZ, tocilizumab; VAS, visual analog scale.
14 patients in the PBO+prednisone group and 23 patients in the TCZ+prednisone group were nonresponders for reasons other than treatment failure. Percentages are based on number of responders/treatment failures (n).
*p<0.05 treatment failures vs responders (based on χ^2 test for categorical variables and *t* test for continuous variables).



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REFERENCES:

[1] Stone JH, et al. N Engl J Med. 2017;377:317-328.

FRI0262

CLINICAL OUTCOMES OF PATIENTS WITH GIANT CELL ARTERITIS WITH POLYMYALGIA SYMPTOMS ONLY VS CRANIAL SYMPTOMS ONLY TREATED WITH TOCILIZUMAB OR PLACEBO IN THE GIACTA TRIAL

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Background: GiACTA, a randomized, double-blind, placebo (PBO)–controlled study, demonstrated the efficacy and safety of tocilizumab (TCZ) in patients with giant cell arteritis (GCA).[1] Growing evidence has shown that TCZ is also effective for the treatment of polymyalgia rheumatica (PMR); however, data on this are limited.[2,3]

Objectives: To evaluate the efficacy of TCZ in patients with GCA presenting with cranial symptoms only or PMR symptoms only in GiACTA.

Methods: GiACTA randomized 251 GCA patients to receive weekly or every other week TCZ plus a 26-week prednisone taper (TCZ + prednisone) or PBO plus a 26- or 52-week prednisone taper (PBO + prednisone).[1] In this post hoc analysis, baseline characteristics, sustained remission rate, number of flares, annual flare rate, time to flare, cumulative prednisone dose and safety were assessed in patients with PMR symptoms only and patients with cranial symptoms only at diagnosis. Disease flare was defined as the recurrence of signs or symptoms of GCA (including PMR) or an elevation in erythrocyte sedimentation rate attributable to GCA.

Results: Of 146 patients included in the analysis, 52 had PMR symptoms only and 94 had cranial symptoms only at diagnosis. Demographics and other patient characteristics are shown in **Table 1**. The hazard ratios for flare in patients receiving TCZ vs PBO were 0.77 (99% CI, 0.26-2.32) for patients with PMR symptoms only and 0.37 (99% CI, 0.13-1.01) for patients with cranial symptoms only. Of patients with PMR symptoms only, 18 flares occurred in 13/31 patients (41.9%) in the TCZ group and 20 flares occurred in 12/21 patients (57.1%) in the PBO group. Of patients with cranial symptoms only, 19 flares occurred in 12/58 patients (20.7%) in the TCZ group and 25 flares occurred in 17/36 patients (47.2%) in the PBO group (**Table 2**). For both the PMR and cranial symptoms only groups, annual flare rates were lower in patients receiving TCZ compared with those receiving PBO. The occurrence of adverse events and serious adverse events was similar between groups (**Table 2**).

Conclusion: TCZ improved clinical outcomes in patients who presented with PMR symptoms only or cranial symptoms only at diagnosis as indicated by a reduced incidence of flares. These findings suggest that TCZ is effective in patients with GCA with PMR or cranial symptoms.

REFERENCES:

[1] Stone JH, et al. N Engl J Med. 2017;377(4):317-328.
[2] Lally L, et al. *Arthritis Rheumatol.* 2016;68(10):2550-4.
[3] Devauchelle-Pensec V, et al. Ann Rheum Dis. 2016;75(8):1506-10.

Table 1. Patient Characteristics and Treatment at Study Baseline

	PMR Symptoms Only at Diagnosis (n = 52)	Cranial Symptoms Only at Diagnosis (n = 94)
Age, mean (SD), y	64.5 (8.3)	70.8 (7.8)
Female, n (%)	39 (75.0)	64 (68.1)
White, n (%)	51 (98.1)	91 (96.8)
Weight, mean (SD), kg	70.06 (14.09)	71.78 (16.10)
Body mass index, mean (SD), kg/m^2	24.81 (3.95)	26.36 (5.44)
GCA diagnosis, n (%)		
Newly diagnosed	27 (51.9)	41 (43.6)
Relapsing	25 (48.1)	53 (56.4)
Disease duration, mean (SD), days	327.04 (600.89)	239.05 (404.94)
ESR, mean (SD), mm/h	24.98 (20.21)	24.56 (19.92)
CRP, mean (SD), mg/L	6.51 (9.44)	7.73 (12.70)
Diagnosis, n (%)*		
Positive temporal artery biopsy	9/12 (75)	72/79 (91.1)
Positive imaging	44/52 (84.6)	31/94 (33.0)
Prednisone dose, n (%)		
≤ 30 mg/d	27 (51.9)	53 (56.4)
> 30 mg/d	25 (48.1)	41 (43.6)
Treatment group, n (%)		
TCZ†	31 (59.6)	58 (61.7)
Placebo‡	21 (40.4)	36 (38.3)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PMR, polymyalgia rheumatica; TCZ, tocilizumab.
* Of patients with available results.
† TCZ 162 mg weekly or every other week with a 26-week prednisone taper.
‡ Placebo with a 26- or 52-week prednisone taper.

Table 2. Clinical and Safety Outcomes

	PMR Symptoms Only at Diagnosis (n = 52)		Cranial Symptoms Only at Diagnosis (n = 94)	
	TCZ* (n = 31)	Placebo† (n = 21)	TCZ* (n = 58)	Placebo† (n = 36)
Patients with ≥ 1 flare, n (%)	13 (41.9)	12 (57.1)	12 (20.7)	17 (47.2)
with PMR symptoms, n/N (%)	8/13 (61.5)	7/12 (58.3)	7/12 (58.3)	9/17 (52.9)
with cranial symptoms, n/N (%)	10/13 (76.9)	6/12 (50.0)	10/12 (83.3)	10/17 (58.8)
No. of flares	18	20	19	25
with PMR symptoms, n/N (%)	10/18 (55.6)	10/20 (50.0)	7/19 (36.8)	11/25 (44.0)
with cranial symptoms, n/N (%)	12/18 (66.7)	8/20 (40.0)	15/19 (78.9)	11/25 (44.0)
Annual flare rate, mean (SD)‡	0.64 (0.85)	0.95 (1.24)	0.40 (0.93)	0.93 (1.81)
Patients with flare following remission, n (%)	11 (35.5)	11 (52.4)	11 (19.0)	16 (44.4)
Cumulative prednisone dose, median, mg	1862.0	3671.5	1842.0	2985.5
Patients with ≥ 1 AE, n (%)§	30 (96.8)	20 (95.2)	55 (94.8)	36 (100)
Patients with ≥ 1 SAE, n (%)§	5 (16.1)	3 (14.3)	10 (17.2)	12 (33.3)

AE, adverse event; GCA, giant cell arteritis; PMR, polymyalgia rheumatica; SAE, serious adverse event; TCZ, tocilizumab.
* TCZ 162 mg weekly or every other week with a 26-week prednisone taper.
† Placebo with a 26-week or 52-week prednisone taper.
‡ Annualized flare rate is calculated as the number of flares between the first clinical assessment of GCA and the final clinical assessment prior to entry into Part 2, divided by the time period between the 2 days, multiplied by 365.25.
§ Multiple occurrences of AEs are included. Denominators are all AEs or SAEs.

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FRI0263

GRANULOMATOSIS WITH POLYANGIITIS, (GPA): CARDIOVASCULAR MORBIDITY AND MORTALITY IN A POPULATION-BASED COHORT. A DANISH REGISTER STUDY

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Background: In order to understand and ultimately prevent cardiovascular (CV) morbidity and mortality in systemic inflammatory disorders we studied the epidemiology of CV disease in ANCA associated Vasculitis (AAV). There is growing evidence that both premature and pronounced atherosclerosis is associated with ANCA associated vasculitis (AAV) [1-3]. However, the exact mechanisms for CV involvement are unknown and probably multiple.

Objectives: To investigate if CV related comorbidity and death were increased among Danish AAV patients registered with a diagnosis of granulomatosis with polyangiitis (GPA) in Denmark.

To investigate if there was a temporal relation between diagnosis of GPA and CV disease and death.

Methods: A population-based cohort study was performed using the Danish Civil Registration System, the Danish National Patient Registry (all in-patient and out-patient contacts are registered with ICD diagnosis since 1995) and the Danish Cause of Death Register. Patients registered twice or more with a diagnosis of GPA (ICD8: 446.29 and ICD10: M313) during 1995-2016 were included. Annual incidence rate (IR), point prevalence (PP) and standardized mortality rate (SMR) were calculated. The entire adult population in Denmark served as control population. CV morbidity was divided into heart failure (HF) (ICD-10 code I42, I50, J81 and I110) and myocardial infarction (MI) (ICD-10 code I21-25). Death caused by CV disease (ICD-10 code I1-999) was registered.

Results: We identified 1829 individuals with GPA. The median annual IR was 20.5/1,000,000 and PP was 277/1,000,000 in 2015. Overall SMR was 2.14.

Among patients with GPA 171 had a hospital diagnosis of MI. Compared to the control population, the hazard ratio (HR) of MI was 2.47 (95% CI 4.55-11.46) during the first 3 months after the GPA diagnosis. From 3 months to one year declining to 1.41 (95%CI 0.80-2.49) and after 10 years the HR was still slightly increased to 1.64 (95%CI 1.20-2.23). The risk of a diagnosis of HF was markedly increased with a HR at 7.22 (95% CI 4.55-11.46) during the first 3 months after a GPA diagnosis, after three months up to one year 2.94 (95%CI 1.87-4.69), and 2.07 (95% CI 1.54-2.78) after 10 years.

The total number of CV deaths in the GPA cohort was 307. During the first three months after a GPA diagnosis, the HR was increased to 9.51 (95%CI 7.12-12.70) declining to 2.51 (95% CI 1.77-3.58) after one year, but still increased to 1.56 (95% CI 1.23-1.98) after 10 years.

Conclusion: In a population-based study we found an overall increased SMR. The risk of CV comorbidity and of CV death among patients with a register diagnosis of GPA was increased.
There was a striking temporal relation between a high HR of CV morbidity and mortality during the first year after the diagnosis of GPA. Nevertheless, the HR of CV morbidity and mortality was albeit lower still increased after 10 years with a diagnosis of GPA.
The result indicates a strong association between systemic vascular inflammatory disease and CV involvement. A the time of diagnosis of GPA systemic inflammatory activity usually is present and the results point towards an association of inflammation with CV risk-factors probably including premature and pronounced atherosclerosis. The persistence of increased HR of CV involvement after 10 years indicates a permanent influence on the risk factors.

REFERENCES:
[1] Mayo Clin Proc 2018; 93(5):597-606.
[2] Arthritis Rheum 2009; 60(4):1187-1192.
[3] J Autoimmun 2019; 96:134-141.

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FRI0264 ADVERSE EVENTS DUE TO HIGH DOSE GLUCOCORTICOIDS – LESSONS FROM ANCA-ASSOCIATED VASCULITIS AND OTHER INFLAMMATORY DISEASES

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Background: High dose glucocorticoids (GCs) are a component of induction remission and maintenance regimes in ANCA-associated vasculitis (AAV) and are used in other inflammatory disorders. The adverse event (AE) profile of GC is well known and in AAV is believed to link to early mortality risk from infection as well as long term organ/tissue damage. However, it is known GC AE reporting is incomplete and EULAR made specific recommendations for such reporting in clinical trials (Van der Goes 2010).
Objectives: This systematic literature review aimed to examine AE rates and outcomes related to high dose GC use in AAV and to quantify AE risk in terms of GC dose and duration.
Methods: A systematic literature review was performed of studies published between 1 Jan 2007 and 30 January 2018. Data on GC-related AEs (defined as any untoward medical occurrence) and serious AEs (defined in European Medicines Agency CPMP/ICH/377/95) which threaten life or function were extracted from identified trials. The initial AAV search demonstrated incomplete GC data collection compared to EULAR recommendations in most AAV studies so the search strategy was extended to include other inflammatory disorders in which similar GC regimes and doses are used namely systemic lupus erythematosus, glomerulonephritis, pemphigus and giant cell arteritis.
Results: Three hundred and eleven studies of these 5 conditions were identified in which GC-related AEs were published. 38 studies were selected for a detailed AE analysis on the basis of their inclusion of full description of GC regime, actual delivered GC dose and patient exposure. Of the 62,630 patients enrolled in the 38 studies, 35,587 were exposed to GCs. 21 studies reported serious AEs, while 17 studies reported AEs only. The most common serious AEs related to specific organ damage - particularly musculoskeletal, ocular and neuropsychiatric - but mortality and infection were also observed. The most common AEs were metabolic conditions, with diabetes related events comprising 72% of the metabolic AEs, and weight gain comprising 15%.

	Serious adverse events	Adverse events
Number of patients in studies reporting GC-related events	2340	9602
Events reported (n)/%	840/36%	2479/26%
Most common events%	Mortality 14% Infection 7% Organ damage 49%	Metabolic 50% Musculoskeletal 16% Ocular 14% Infections 12%

Correlation analysis demonstrated mean total GC dose was positively related to risk of death (r = 0.51) and infection (r = 0.49) while GC therapy duration was related to risk of infection (r = 0.62).

Conclusion: GC-related AE reporting in clinical studies of high dose GCs could be improved. Serious AEs including organ damage, infection and mortality were reported and both total GC dose and therapy duration are important risk factors mortality and infection. Metabolic and musculoskeletal events are a particular patient burden. New therapeutic options for AAV and other disorders should aim to reduce this AE profile.

REFERENCES:
[1] Van der Goes, et al. Ann Rheum Dis 2010; 69: 1913-19

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FRI0265 ANTI-IGE AND ANTI-IL5 THERAPY FOR EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA), formerly Churg-Strauss syndrome, is a rare type of anti-neutrophil cytoplasm antibody-associated vasculitis, associated with asthma, nasal poliposis and rinosinusitis, in which eosinophils paly a key role.
Eosinophil targeted therapies alone or associated to conventional treatment with corticosteroids and immunosuppressant drugs may be useful in patients with refractory disease or asthma difficult to treat.
Objectives: To describe the efficacy and safety of eosinophil targeted therapies in patients with relapsing or refractory EGPA
Methods: Retrospective study including all patients with EGPA included at the REVAS Registry, who were treated with omalizumab, mepolizumab or resilizumab. Complete response (CR) was defined as the absence of asthma and/or sinonasal exacerbations with a prednisone dosage of $\leq$ 7.5 mg/day, and partial response (PR) when the prednisone dosage was $\geq$ 7.5 mg/day. Statistical analysis was performed using SSPS 20 package.
Results: Seventeen patients (median age 49 years) received omalizumab (n=9) for a mean period of 53.4 (5-91) months, mepolizumab (n=7) for a mean period of 13.6 (5-16) months, or resilizumab (n=1) for a mean period of 7 months, for severe steroid-dependent asthma (94.1%) and/or sinonasal involvement (82.4%). ANCA were positive in 8 (47.1%) cases with MPO specificity in 7 cases. All patients were receiving corticosteroids with a mean dosage of 15 mg/day prior to eosinophil targeted therapies institution. Four (57.1%) patients treated with omalizumab achieved a CR, 1 a PR, and 2 had no improvement. The median dosage of prednisone 6 months after omalizumab initiation was 10 (2.5-10) mg/day and the median dosage after 12 months 5 (0-10) mg/day. The median number of exacerbations decreased from 4 over the 6 months previous to therapy startment to 2 in the following 12 months. Both patients refractory to omalizumab were treated with mepolizumab with CR at 6 months in 1 case. Treatment with mepolizumab was also started in 4 patients treated with omalizumab after a prolonged period of treatment (72.4 months), due to recurrence of asthma and/or sinusitis, and peripheral blood eosinophilia >10%. Three (75%) patients achieved a CR, and 1 patient experienced a major vasculitis relapse needing immunosuppressant drugs. Six (85.7%) patients initially treated with mepolizumab achieved a complete remission after 6-12 months of treatment. One patient achieved a PR. The median dosage of prednisone 6 months after mepolizumab initiation was 5 (3.1-6.8) mg/day and the median dosage after 12 months 3.5 (0-5) mg/day. The median number of exacerbations decreased from 2.5 over the 6 months previous to therapy startment to 1 in the following 12 months. The patient treated with resilizumab achieved a CR at 6 months of therapy. All 3 drugs were safe and well tolerated.
Conclusion: The results of the present study suggest that eosinophil targeted therapies have a corticosteroid-sparing effect in EGPA patients with asthmatic and/or sinonasal manifestations, and that may be used sequentially in refractory cases. However, reducing the corticosteroid dosage may also increase the risk of severe EGPA flares. More data are needed to widely recommend this therapy in EGPA patients.

REFERENCES:
[1] AntiIgE monoclonal antibody (omalizumab) in refractory and relapsing Eosinohilic granulomatosis with polyangiitis (Churg-Struss). Arthritis Rheum 2016; 68: 2274-82

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FRI0266 ABERRANT PD-1 AND VISTA EXPRESSION ON CD4+ TH-CELLS IN GIANT CELL ARTERITIS

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Background: The immune system controls immune responses by balancing positive and negative immune checkpoint (IC) molecules in cell-cell interactions. These co-stimulatory and co-inhibitory molecules allow complete T-cell activation and T-cell effector functions giving rise to an optimal immune response while preventing autoimmunity (1). Failure of tolerance results in the initiation and propagation of pathogenic T-cell responses leading to the development of autoimmune diseases such as Giant Cell Arteritis (GCA). The latter is a complex illness of multiple pathogenic factors with important contributions of both innate and adaptive immunity in its initiation and perpetuation (2,3). Recently, a loss of inhibitory checkpoints on immune cells has been implicated in the immunopathology of GCA (4,5). The possible contribution of IC pathways to the dysregulation of Th-cells in GCA could aid in our understanding of GCA immunopathology.
Objectives: In this study, we aimed to investigate the expression of different IC molecules and their ligands by circulating monocytes, and functionally distinct populations of CD4+T-cells in peripheral blood samples from GCA-patients in comparison to healthy controls (HCs).
Methods: In a cross-sectional study, fresh blood samples were obtained from 30 GCA-patients with/without immunosuppressive treatment (glucocorticoids) and 18 sex and age-matched HCs. The frequency of the expression of different IC including CD80/86, PD-L1, PDL2 and V-domain Ig suppressor of T-cell activation (VISTA) were determined on total monocytes and subsets (classical, intermediate and non-classical). In parallel, expression of the corresponding receptors CD28, Cytotoxic T-Lymphocyte-associated antigen-4 (CTLA-4), Programmed death- 1 (PD-1), and VISTA were determined on total CD4+ and subsets of Th-cells defined by CD45RA and CD25 expression of GCA-patients and HCs by flow cytometry.
Results: The frequencies of CD80/CD86+ and VISTA+ monocytes were decreased in GCA-patients compared to HCs. Proportions of circulating CD4+ Th-cells in GCA-patients were not different when compared to HCs. The frequencies of CD28 and CTLA-4 expressing CD4+Th-cells did not differ between GCA-patients and HCs. In contrast, proportions of PD-1 and VISTA expressing Th-cells were significantly decreased in GCA patients. Memory T-cells showed decreased expression of IC molecules. Interestingly, naïve T-cell populations already demonstrated loss of PD-1 and VISTA.
Conclusion: In GCA, lower frequencies of CD80/CD86+ and VISTA+ circulating monocytes were found. Likewise, decreased proportions of PD-1 +CD4+ and VISTA+CD4+ Th-cells were noted. Decrease of negative IC on the surface of immune cells could add to the persistent activation of CD4+T-cells seen in GCA.

REFERENCES:
[1] Ceeraz S, Nowak EC, Noelle RJ. B7 family checkpoint regulators in immune regulation and disease. Trends in Immunology. 2013.
[2] Samson M, Corbera-Bellalta M, Audia S, Planas-Rigol E, Martin L, Cid MC, et al. Recent advances in our understanding of giant cell arteritis pathogenesis. Autoimmun Rev [Internet]. 2017 Aug;16(8):833–44.
[3] Weyand CM, Goronzy JJ. Immune mechanisms in medium and large-vessel vasculitis. Nat Rev Rheumatol. 2013;9(12):731–40.
[4] Watanabe R, Zhang H, Berry G, Goronzy JJ, Weyand CM. Immune checkpoint dysfunction in large and medium vessel vasculitis. Am J Physiol - Hear Circ Physiol [Internet]. 2017 May 1;312(5):H1052–9.
[5] Zhang H, Watanabe R, Berry GJ, Vaglio A, Liao YJ, Warrington KJ, et al. Immunoinhibitory checkpoint deficiency in medium and large vessel vasculitis. Proc Natl Acad Sci {United States of America} [Internet]. 2017;201616848.

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FRI0267 DIAGNOSING POLYMYALGIA RHEUMATICA: THE IMPACT OF FAST-TRACK CLINIC AT HOSPITALIZATION RATES

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Background: Polymyalgia Rheumatica (PMR) is a common inflammatory autoimmune rheumatic disease, with the highest incidence rates seen in Scandinavia.
One of the challenges in the diagnosis of PMR is the lack of diagnostic tests specific for the disease. The diagnosis may require exclusion of other conditions that can present with polymyalgia symptoms and may lead to hospitalization. Only limited data on hospitalization rates among patients with PMR exists (1).
Ultrasound (US) may be useful in differentiating PMR from non-inflammatory conditions and can also be used for the diagnosis of concomitant Giant Cell Arteritis (GCA)
GCA Fast Track Clinics (FT) using US as the main diagnostic tool have shown both improvement in patient outcomes and decrease in the cost of care(2)
Objectives: To investigate the admission rates of patients diagnosed with PMR and the impact of the FT on these rates.
Methods: A FT clinic for patients suspected to have PMR was established at rheumatological outpatient clinic of South-West Jutland Hospital (serving 250.000inhabitants) in January 2018. Collaboration with the Emergency Medical department was established and patients with PMR symptoms referred to the hospital were examined at FT within 0-1 days, thereby avoiding hospitalization. Similarly, patients referred with PMR symptoms to the outpatient clinic by a GP, were examined at FT within 1-2 days. At FT a thorough history and clinical examination were performed including musculoskeletal and vascular US. Retrospectively data from patients diagnosed with PMR from 2013-2018 was analyzed.
Results: In a 6 years' period, 336 patients were diagnosed with PMR. 54 patients were diagnosed during hospitalization. Hospitalized patients were older (mean values ± standart deviaton-sd) 73,61±8,96 vs 70,94 ±7,97 years, p=0,024, with significantly higher initial C-reactive protein (CRP, mg/l) levels 99±58,8 vs 43,9±37,p<0,0001 and a shorter duration of symptoms(6,92±5,5 vs 13,6±13,7 weeks, p=0,0018). No differences were found regarding gender, PMR related symptoms, initial prednisolone dose and response to treatment. An equal annual distribution of the number of new diagnosed cases and hospitalizations rates during the first 5 years was found. After the implementation of the FT at January 2018 a significant decrease in hospitalization rates (19,4% vs 3,5% p=0,001) and inpatient days of care (4,15±3,1 vs 1±0, p<0,0001) was observed. The time from symptoms debut to diagnosis was also significantly decreased from 13, 74 to 6, 79 weeks (Table)

	Diagnosed at 2013-2017 N 268	Diagnosed at 2018 N 56	P values
Age (years) mean ± sd	71,3 ± 8,5	71,79 ± 6,6	n.s*
Gender (female)	58,2%	48,2%	n.s
Duration of symptoms (weeks) mean± sd	13,74± 13,74	6,79 ± 4,72	0,001
Bilateral shoulder pain	95,9%	98,2%	n.s
Abnormal CRP and/or SR at debut	91,8%	100%	0,03
CRP (mg/lt) mean± sd	52,82 ± 48,3	56,5 ± 37,2	n.s
Morning stiffness	90,3%	92,7%	n.s
Hip pain or limited range of motion	71,4%	61,8%	n.s
RF and aCCP negative	95,1%	100%	n.s
Absence of other joint involvement	72%	75%	n.s
Initial prednisolone dose (mg) mean± sd	18,44 ± 8,41	19,2 ± 9,25	n.s
Hospitalized n(%)	52 (19,4%)	2 (3,5%)	0.01
Inpatient days of care mean± sd	4,15 ± 3,1	1 ± 0	0,0001

*n.s=non-significant

Conclusion: The annual hospitalization rates in connection with PMR diagnosis at South-west Denmark during a 5 year period were estimated to be 19,2%. The implementation of a FT ultrasound clinic decreased significantly the hospitalization rates among patients with PMR.

REFERENCES:

[1] Gran JT,Myklebust G. The incidence of PMR and temporal arteritis in the county of Aust Agder, South Norway: a prospective study 1987–94. J Rheumatol 1997.
[2] Diamantopoulos AP et.al. The fast-track ultrasound clinic for early diagnosis of GCA significantly reduces permanent visual impairment: towards a more effective strategy to improve clinical outcome in giant cell arteritis? Rheumatology (Oxford)55:66–70

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FRI0268 CLINICAL FEATURES OF TAKAYASU'S ARTERITIS FROM AN INCEPTION COHORT: EARLY DISEASE IS CHARACTERIZED BY 'SYSTEMIC INFLAMMATION'

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Background: There is only retrospective and very limited data for the long term prognosis of Takayasu's Arteritis (TAK), a rare large-vessel vasculitis.
Objectives: In this study, we aimed to present the preliminary results of a Takayasu Inception Cohort settled for long term, prospective follow-up of only newly-diagnosed patients with TAK.
Methods: Patients fullfilling the American College of Rheumatology 1990 criteria for TAK and diagnosed in the last 12 months were included to the study. Patients' data were recorded in an electronic database of an international "Takayasu's Arteritis Registry" requiring baseline and at least annual visits. Data is compared with an historical Turkish cohort previously published (*Bıçakçıgil, et al, 2009).*
Results: The study included 170 patients (age: 38.5±13.1 years, F/M: 143/27) with TAK from 15 tertiary Rheumatology centers in Turkey. The mean symptom duration of patients was 5.2 years at diagnosis. According to the angiographic classification, 68.2% of the study group had type I and only 18.3% had type V disease. When we compared our results to our retrospective cohort (previously published by Turkish Takayasu Arteritis Study Group), constitutional symptoms (115/165= 69.6% vs 66%) and limb claudication (87/131= 66.4% vs 48%) were observed to be more frequent, whereas pulselessness (45/130=34.6%vs 88%) was less in the inception cohort.(Table 1) Carotidynia was present only in the inception cohort. Similarly, mucocutaneous symptoms also seem to be a feature of newly-diagnosed disease (30/162=18.5% vs 8.8%).
Regarding comorbidities at diagnosis, the rate of dyslipidemia was 17.6 (30/165)%, diabetes mellitus 15.1(25/165)%, smoking 20 (34/164)% and obesity (BMI>30) 14 (22/157)% among TAK patients. All patients were given oral corticosteroid (CS) therapy (0.5-1 mg/kg) at diagnosis, 17 patients (17/170=10%) also having CS pulses. In addition to CSs, 86 patients (50.6%) were given methotrexate, 31patients (18.2%) azathioprine, 6 (3.5%) cyclophosphomide, 12 patients (7.1%)leflunamide, 2(1.2%) patients mycophenolate mofetil and 5(2.9%) patients biologics at disease-onset(2 tocilizumab, 2 infliximab, 1 adalimumab). Biologic agents were chosen for 7 patients (7/32) at last vizit(1 adalimumab, 4 tosiluzumab, 2 infliximab).
Seventy-three patients (42.9%) had follow-up > 3 months. Remission was observed 78% of patients. At least one relaps was observed 40% of these patients. Mortality rate was 4.1% (3/73 patients) during a mean 25.7 months follow-up.
Conclusion: Our results suggest that, in an inception cohort, signs and symptoms of 'systemic inflammation' is more prominent in newly-diagnosed TAK patients, whereas vascular extent and damage accumulates during the disease course. The long term follow-up of our inception cohort shows that 40% of patients relapse within 2 years after diagnosis in spite of IS treatments.

REFERENCES:

[1] Bicakcigil M, Aksu K, Kamali S, et al. (2009) Takayasu's arteritis in Turkey - clinical and angiographic features of 248 patients. Clin Exp Rheumatol. 27, 59-64.

Table 1. Clinical characteristics of Inception and Retrospective Cohorts from Turkey

	Inception Cohort (n=170)	Retrospective Cohort (*Bıçakçıgil, et al*) (n=248)
Constitutional symptoms	115/165(69.6%)	163/248/ (66%)
Limb claudication	87/131(66.4%)	119/248 (48%)
Carotidynia	31/130 (18.2%)	-
Pulseless	45/130(34.6%)	218/248 (88%)
Musculoskeletal manifestations	90/163 (52.9%)	104/248 (42%)
Mucocutaneous manifestations	30/162 (17.6%)	22/248 (8.8%)
Respiratory manifestations	47/163 (28.8%)	22/184 (12%)
Neurologic manifestations	69/163 (40.6%)	156/248 (63%)
Cardiac involvement	64/146 (43.8%)	141/248 (57%)
Ophthalmologic involvement	27/166 (16.2%)	57/248 (36%)

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FRI0269 COMPARATIVE STUDY OF INFLIXIMAB VERSUS ADALIMUMAB IN REFRACTORY UVEITIS DUE TO BEHÇET'S DISEASE. NATIONAL MULTICENTER STUDY OF 177 CASES

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Background: Uveitis is one of the major causes of disability of Behçet's disease (BD). According to the "Expert panel recommendations", anti-TNF therapy with infliximab (IFX) or adalimumab (ADA) may be considered as first- or second-line therapy for patients with BD-ophthalmic manifestations.
Objectives: To compare IFX versus ADA as first biologic drug in refractory uveitis due to BD for 1-year period.
Methods: Multicenter study of BD-associated uveitis refractory to conventional non-biologic treatment. Dosing schedule: IFX 3-5 mg/kg iv at 0, 2 and 6 weeks and then every 4-8 week, and ADA 40 mg/sc/every other week without loading dose. Main comparative outcome measures: safety and efficacy, assessing the intraocular inflammation, macular thickness, visual acuity, degree of immunosuppression load, drug retention, and glucocorticoid-sparing effect.
Results: 177 patients (316 affected eyes) were included. IFX was used in 103 and ADA in 74. No significant differences at baseline were observed regarding main demographic features, previous therapy and ocular severity. After 1 year of therapy, we observed an improvement in all ocular parameters in IFX vs ADA groups: AC inflammation (78.18% vs 92.31%), vitritis (78.95% vs 93.33%), retinal vasculitis (97% vs 95%), macular thickness (264.89±59.74 vs 250.62±36.85), and BCVA (0.67±0.34 vs 0.81±0.26). Drug withdrawal was observed in 57 (55.33%) of IFX group and in 21 (28.37%) of ADA group.
Conclusion: After 1 year of therapy in refractory BD-associated uveitis, ADA showed a statistically better outcome than IFX in improvement of BCVA, vitritis and drug retention.

REFERENCES:

[1] Levy-Clarke G, et al. Expert panel recommendations for the use of anti-tumor necrosis factor biologic agents in patients with ocular inflammatory disorders. Ophthalmology. 2014; 121:785-96.

[2] Santos-Gómez M, et al. The effect of biologic therapy different from infliximab or adalimumab in patients with refractory uveitis due to Behçet's disease: results of a multicentre open-label study. Clin Exp Rheumatol 2016; 34 (6 Suppl 102): S34-40
[3] Atienza-Mateo B, et al. Anti-IL6-Receptor Tocilizumab in Refractory Uveitis Associated With Behçet's Disease. Multicenter Retrospective Study. Rheumatology (Oxford). 2018 May 1;57(5): 856-864.
[4] Martín-Varillas JL, et al. Successful Optimization of Adalimumab Therapy in Refractory Uveitis Due to Behçet's Disease. Ophthalmology. 2018 Mar 27.

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TABLE 1. Main baseline features and follow-up of a series of 177 patients with refractory uveitis due to Behçet's disease undergoing infliximab (IFX) or adalimumab (ADA) therapy.

	IFX group (N=103)	ADA group (N=74)	p
Number of patients/affected eyes, (n/n)	103/186	74/131	
Age, mean (SD) years	40.4 (10.1)	38.7 (11.3)	0.29
Sex, men/women, n/n	55/48	39/35	0.92
HLA-B51 positive, (%)	69.4	68.9	0.74
Duration of uveitis before anti-TNFα, median [IQR] months	36 [12-72]	24 [12-60]	0.69
Ocular features at the time of anti TNF-α onset			
AC cells, median [IQR]	1 [0-2]	1 [0-2]	0.25
Vitritis, median [IQR]	1 [0-2]	1 [0-2]	0.12
BCVA, mean (SD)	0.90 (0.35)	0.96 (0.34)	0.08
Macular thickness, mean (SD)	331.11 (131.97)	346.37 (136.14)	0.49
Presence of retinal vasculitis, n (%)	114 (58)	78 (55)	0.51
Presence of choroiditis, n (%)	41 (21)	10 (7)	**<0.01**
Pattern of uveitis, n (%)			
Bilateral	82 (79.61)	57 (77.03)	0.68
Unilateral	21 (20.39)	17 (22.97)	0.68
Anterior	11 (10.68)	14 (18.92)	0.19
Posterior	28 (27.18)	14 (18.92)	0.19
Panuveitis	64 (62.14)	45 (60.81)	0.19
Intermediate	0 (0)	1 (1.35)	0.19
Treatment before anti TNF-α onset, %			
Oral corticosteroids	95	88	0.08
Intravenous pulses of MP	31	31	0.98
CsA	75	76	0.65
AZA	57	42	**0.049**
MTX	44	42	0.77
Other treatments	3.84	1.92	0.41
Prednisone dose at anti TNF-α onset, mean (SD), mg/d	54.35 (15.84)	53.37 (17.52)	0.37
Combined treatment, %	**76.5**	**70.3**	
AZA	21.8	19.2	
CsA	41.1	55.7	
MTX	33.3	21.1	
CFM	1.3	0.0	
MMF	1.3	3.8	
FK-506	1.3	0.0	0.35
Follow-up on anti TNFα therapy, mean (SD), months	31.52 (23.51)	26.48 (18.57)	0.13
Remission, n (%)	78 (76.47)	61 (82.43)	0.34
Relapses, mean (SD)	1.13 (2.62)	1.66 (8.62)	0.61
Drug withdrawal, n (%)	57 (55.33)	21 (28.37)	**<0.01**
.....remission, n (%)	20 (19.41)	6 (8.45)	0.58
.....inefficacy, n (%)	18 (17.47)	11 (14.86)	0.09
.....severe side-effects/toxicity, n (%)	8 (7.76)	4 (3.88)	0.56
.....others, n (%)	11 (10.68)	0 (0)	**0.03**
Serious side-effects, n (per 100 patients/year)	4 (1.48)	4 (2.46)	0.40

Abbreviations: ADA, adalimumab; AZA, azathioprine; CFM, cyclophosphamide; CsA, cyclosporine A; FK-506, tacrolimus; IFX, infliximab; IQR: interquartile range; MMF, mycophenolate mofetil; MTX, methotrexate; MP, methylprednisolone; SD: standard deviation; TNF-α: tumor necrosis factor alpha.

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FRI0270

APREMILAST IN NON-ULCER MANIFESTATIONS IN BEHÇET'S DISEASE. MULTICENTER STUDY OF 32 CASES IN CLINICAL PRACTICE

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Background: Behçet´s disease (BD) is a variable vessel vasculitis with a wide and heterogeneous set of signs and symptoms. The inhibitor of phosphodiesterase-4 Apremilast (APR) has demonstrated efficacy in the treatment of oral and/or genital ulcers.
Objectives: To assess the efficacy and safety of APR in BD patients with manifestations different from mucocutaneous ulcers.
Methods: National multicenter retrospective study on 32 BD patients treated with APR at maintained standard dose of 30 mg twice daily.
Results: From a cohort of 49 patients with oral and/or genital ulcers related to BD and refractory to conventional and/or biological treatment, we selected the cases with another clinical manifestation/s (n=32, 23 women/9 men), mean age of 46.35±15.05 years. Non-aphthous manifestations present at apremilast onset were: arthralgia/arthritis (15), folliculitis/pseudofolliculitis (12), asthenia (7), erythema nodosum (3), furunculosis (2), paradoxical psoriasis by TNFi (2), ileitis (2), deep venous thrombosis (2), erythematosus and scaly skin lesions (1), fever (1), eating disorder (1), fibromyalgia (1), unilateral anterior uveitis (1) and neurobehçet (1). APR was used in monotherapy (n=3) or combined (n=29) with oral corticosteroids (20), colchicine (17), methotrexate (5), azathioprine (3), dapsone (1), tocilizumab (1), hydroxychloroquine (1) and/or mesalazine (1).
The outcome of the different clinical symptoms is shown in TABLE. The patient with neurobehçet kept stable (paresthesias) during the 6 months of follow-up. The 2 cases of deep venous thrombosis and the case of anterior uveitis resolved with anticoagulants and adjuvant topical treatment, respectively. Furunculosis, folliculitis/pseudofolliculitis and ileitis were the manifestations that improved completely and rapidly. The cases of arthritis experienced improvement, while those with arthromyalgias presented a torpid evolution.
Conclusion: Our data show an improvement of the cutaneous follicular and intestinal clinic with APR and a stability of the neurological clinic, while the musculoskeletal manifestations were mostly refractory.

REFERENCES:

[1] Davatchi F et al. The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. J Eur Acad Dermatology Venereol. 2014;28(3):338–47.
[2] Atienza-Mateo B et al. Anti-interleukin 6 receptor tocilizumab in refractory uveitis associated with Behçet's disease: multicentre retrospective study. Rheumatology (Oxford). 2018 May 1;57(5):856-864.
[3] Santos-Gómez M et al. The effect of biologic therapy different from infliximab or adalimumab in patients with refractory uveitis due to Behçet's disease: results of a multicentre open-label study. Clin Exp Rheumatol 2016; 34 (6 Suppl 102): S34-40.
[4] Gulen Hatemi et al. Apremilast for Behçet's Syndrome — A Phase 2, Placebo-Controlled Study. N Engl J Med 2015; 372:1510-1518.

TABLE. Outcome of non-aphthous clinic with apremilast.

Non-aphthous manifestations at APR onset (n)	1-2 Weeks	4 Weeks	3 Months	6 Months	12 Months	18 Months	24 Months
Neurobehçet (NCS vasculitis) (1)	NC	NC	NC	NC			
Unilateral anterior uveitis (1)	CR	CR					
Deep venous thrombosis (2)	CR (2)	CR (2)	CR (2)	CR (2)	CR (1)	CR (1)	CR (1)
Arthromyalgias (11)	CR (1) NC (10)	CR (1) PR (2) NC (8)	PR (4) NC (1)	PR (5) NC (1)	PR (5) NC (1)	NC (1)	NC (1)
Arthritis (4)	NC (3) ND (1)	PR (2) NC (1) ND (1)	CR (1) PR (1) ND (1)	CR (1) PR (1) ND (1)	CR (1)		
Folliculitis/pseudofolliculitis (12)	CR (5) PR (2) NC (5)	CR (8) PR (3) NC (1)	CR (9) PR (3) NC (1)	CR (5) NC (1)	CR (2)	CR (1)	
Furunculosis (2)	CR (2)	CR (2)	CR (1)	CR (1)			
Erythema nodosum (3)	PR (1) ND (2)	PR (1) NC (1) ND (1)	CR (1)	NC (1)			
Psoriasis/ erythematosus-scaly skin lesions (3)	NC (2) ND (1)	NC (2) ND (1)	PR (3)	PR (2)	PR (2)	PR (1)	PR (1)
Ileitis (2)	CR (1) PR (1)	CR (2)	CR (2)	CR (2)	CR (1)		
Asthenia (7)	CR (1) NC (6)	CR (1) NC (6)	CR (1) NC (6)	NC (4)	NC (2)	NC (1)	NC (1)
Fever (1)	ND	ND					
Eating disorder (1)	ND	ND	ND				
Fibromyalgia (1)	NC	NC	NC				

Abbreviations: CR= complete response; (n)= number of cases; ND= non-data available; NC= no changes observed; PR = partial response.

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FRI0271 USE OF CONTRAST ENHANCED ULTRASOUND SONOGRAPHY (CEUS) IN LARGE VESSEL VASCULITIS (LVV)

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Background: C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are important parameters in the monitoring of LVV. Since Tocilizumab is approved for treatment of LVV these cheap and easy repeatable parameters are worthless because of their normalisation by Tocilizumab. MRI and PET-CT as an alternative are not only much more expensive, they are also not arbitrarily repeatable and available. Thus, monitoring of LVV-Patients undergoing a Tocilizumab therapy remains unclear – especially upon showing a persisting thickened vessel wall.
Objectives: CEUS can increase the visibility of tissue perfusion, particularly if there is a very slow bloodflow, which cannot be detected by (power)-doppler sonography.
Methods: In this proof of concept study we investigated patients with active and inactive LVV (aLVV/iLVV) with CEUS. After injection of ultrasound contrast agent we measured the contrasted area of large vessels in a transverse section first if the lumen was completely contrasted and once again 4-8 seconds later. If the vessel wall incorporated the contrast agent the contrasted area increased (Fig 1). The increase of the contrasted area (CA) was correlated with CRP and ESR. Patients were only included if they were not treated with Tocilizumab and therefore ESR and CRP were usable to evaluate the disease activity.
Results: Investigated were 16 patients (13 female, 3 male), 8 with aLVV and 8 with iLVV, respectively. The mean CRP was 85±69 (aLVV) vs. 4 ±2 mg/l (iLVV) ($p<0.0001$), the ESR 80±28 (aLVV) vs. 7±4 (iLVV) mm/h ($p< 0.0001$). The mean age was 74.6±8.4 y (range 56-82). The increase of the CA was 66.6±44.6 (aLVV) vs. 2.4±6.6% (iLVV) ($p<0.0001$). The increase correlated significantly with the CRP $r=0.87$, $p<0.0001$. An increase of CA of ≥20% has a sensitivity of 92,3% and a specificity of 90% for active LVV.
Conclusion: The results of our proof of concept study demonstrate, that CEUS can detect aLVV with a good sensitivity and specificity. Including CEUS in clinical routine will be much easier repeatable, save, quicker and by far more cost-effective then MRI or PET-CT. CEUS might be a good method for monitoring disease activity in LVV treated with Tocilizumab. The limitation of our study is the small number of patients, the missing blinding of the investigator and the method intrinsic fact, that you can't investigate all involved vessels by ultrasound/CEUS.

REFERENCES:
None

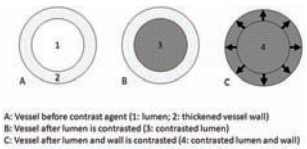


Fig.1

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FRI0272 RISK OF POTENTIAL GLUCOCORTICOID-RELATED ADVERSE EVENTS IN PATIENTS WITH GIANT CELL ARTERITIS: RESULTS FROM A US-BASED ELECTRONIC HEALTH RECORDS DATABASE

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Background: Oral glucocorticoids (OGC) have been the mainstay of treatment for giant cell arteritis (GCA). However, OGCs are associated with several adverse events (AEs).
Objectives: To estimate the risk of potential OGC-related AEs in patients with GCA.
Methods: This retrospective, observational cohort study utilized the 2008-2017 IBM Explorys Electronic Health Records database which includes lab values. Inclusion criteria included age ≥ 50 years with ≥ 2 GCA diagnoses ≥ 7 days apart, 1 OGC prescription within 6 months of the first GCA diagnosis (index date = date of first OGC prescription) followed by a second OGC prescription, no other autoimmune disease requiring high-dose OGCs, no exposure to anti-tumor necrosis factor or anti-interleukin-6 therapies, ≥ 1 C-reactive protein (CRP)/erythrocyte sedimentation rate (ESR) lab test and 12 months of data available pre- and post-index. Potential AEs assessed during the 12 months post-index were descriptively summarized across cohorts of patients based on quartiles (Q) of mean daily dose of OGCs measured over 6 months post-index among this patient sample (Q1: ≥ 1.00 to ≤ 13.75 mg; Q2: > 13.75 to ≤ 25.00 mg; Q3: > 25.00 to ≤ 40.00 mg; Q4: > 40.00 mg). Potential AEs included type 2 diabetes (T2D) diagnosis, hemoglobin A1c (HbA1c), blood glucose level, serious infections, cataracts, gastrointestinal bleeding or ulcer and increases in body mass index (BMI). Actual OGC use by patient could not be confirmed and is a limitation of this study.
Results: Mean age of the 785 eligible patients was 76 years (SD 9); 70% were female. Mean Deyo Charlson Comorbidity Index score at baseline was 1.57 (SD 2.01). The most common baseline comorbid conditions were cerebrovascular disease, diabetes, chronic pulmonary disease, and renal disease. Mean daily OGC dose was 28.9 mg during the first 6 months post-index. Mean (SD) CRP and ESR during the 12-month follow-up was 5.1 (13.6) and 26.5 (20.7), respectively. The proportion of patients with newly diagnosed T2D or with HbA1c ≥ 7.5 during the 12-month follow-up ranged from 7.5% to 24.5% from OGC daily dose Q1 to Q4 cohorts. The proportion of patients with glucose ≥ 200 mg/dL ranged from 7.5% to 15.0% from Q1 to Q4. Serious infections ranged from 16.8% to 24.8% from Q1 to Q4 and cataract ranged from 12.0% to 21.7% from Q1 to Q4. The proportions of patients with gastrointestinal bleed/ulcer ranged from 6.0% in Q1 to 11.8% in Q4. An increase in BMI of 5 ranged from 4.1% to 6.4% from Q1 to Q4.
Conclusion: In patients with GCA, potential OGC-related AEs increased with increased daily OGC dose. This highlights the need for effective therapies that reduce the exposure and potential risk of OGCs.
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Table 1. Adverse Events During the 12-Month Post-Index Period, Stratified by OGC Daily Dose

	Dose Q1 ≥ 1.00 to ≤ 13.75 mg N = 184	Dose Q2 > 13.75 to ≤ 25.00 mg N = 184	Dose Q3 > 25.00 to ≤ 40.00 mg N = 198	Dose Q4 > 40 mg N = 161
Patients without type 2 diabetes and without HbA1c ≥ 7.5 in the pre-index period, n	120	136	130	110
With type 2 diabetes diagnosis or HbA1c ≥ 7.5 in the post-index period, n (%)	9 (7.5)	16 (11.8)	16 (12.3)	27 (24.5)
Maximum HbA1c value across HbA1c lab results during post-index, mean (SD)	7.75 (2.46)	8.30 (2.86)	8.25 (2.42)	8.61 (3.09)
Patients with diabetes diagnosis in the pre-index period but without HbA1c ≥ 7.5 in the pre-index period, n	31	18	40	15
With worsening diabetes with HbA1c ≥ 7.5 in the post-index period, n (%)	10 (32.3)	6 (33.3)	20 (50.0)	4 (26.7)
Patients without blood glucose level ≥ 200mg/dL in the pre-index period, n	173	169	179	147
With blood glucose level ≥ 200mg/dL in the post-index period, n (%)	13 (7.5)	15 (8.9)	24 (13.4)	22 (15.0)
Adverse events in the post-index period, n (%)				
Serious infection requiring hospitalization for infection and/or IV antibiotics	31 (16.8)	39 (21.2)	44 (22.2)	40 (24.8)
Serious infection requiring IV antibiotics	29 (15.8)	33 (17.9)	42 (21.2)	35 (21.7)
Serious infection requiring hospitalization for infection	6 (3.3)	12 (6.5)	12 (6.1)	8 (5.0)
Cataracts	22 (12.0)	27 (14.7)	34 (17.2)	35 (21.7)
Gastrointestinal bleeding or ulcer	11 (6.0)	11 (6.0)	13 (6.6)	19 (11.8)
Patients with BMI in pre- and post-index, n	171	162	181	141
Increase in BMI by 5, n (%)	7 (4.1)	5 (3.1)	9 (5.0)	9 (6.4)

BMI, body mass index; HbA1c, hemoglobin A1c; IV, intravenous; Q, quartile.

FRI0273 **SURVEYING PATIENTS WITH TAKAYASU ARTERITIS WITH A DELAYED DIAGNOSIS**

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Background: Takayasu arteritis (TA) is a well known, but rarely identified variety of large vessel vasculitis. Frequency of initial misdiagnosing in TA patients has been reported to reach 80%. Up to 80% of TA cases are correctly diagnosed only 2 to 11 years after the symptoms presentation.
Objectives: to study possible reasons for misdiagnosing in TA patients with a delayed diagnosis.
Methods: cross-sectional survey included 30 TA patients. All subjects met ACR criteria for TA and more than 12 months since the onset of the clinical manifestations delayed diagnosis. The subjects were asked to recall if vessels auscultation (VA), measurement of both arms and legs blood pressure (BP), assessment of BP and pulse asymmetry (PA) were performed during their first physician visit following the symptoms onset.
Results: 19 (67%) patients reported no VA during the initial examination, only 3 (10%) subjects confirmed the test performed, 5 (17%) were not sure and 3 (10%) did not apply for medical aid during the first year of the symptoms occurrence. Arms BP asymmetry was not assessed in 13 (43%) patients, in 6 (20%) subjects correct BP tests were performed, 8 (27%) responders were not sure and 3 (10%) had not consulted any physician timely. PA was assessed in7 (23%) cases, PA was not tested in 12 (40%) patients, and 8 (27%) subjects were not sure. Arms and legs BP was not assessed in 26 (87%) patients during their initial examination.
Conclusion: the data obtained confirm paramount importance of proper physical examination during initial physician's consultation for timely and correct Takayasu arteritis diagnosis.

REFERENCES:

[1] Arend W.P., Michel B.A., Bloch D.A., et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis Rheum. 1990; 33(8): 1129-1134.
[2] Pokrovskiĭ AV, Zotikov AE, Kul'bak VA, Burtseva EA. Problems of diagnostics and treatment strategy in patients with Takayasu' arteries. Vestn Ross Akad Med Nauk. 2010;(10):9-19.
[3] Ringleb PA, Strittmatter EI, Loewer M, et al. Cerebrovascular manifestations of Takayasu Arteritis in Europe. Rheumatology 2005; 44 (8): 1012–5.

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FRI0274 **ULTRASOUND CUT-OFF VALUE FOR INTIMA-MEDIA THICKNESS OF THE AXILLARY ARTERIES IN PATIENTS WITH CHRONIC LARGE-VESSEL GIANT CELL ARTERITIS**

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Background: The European League Against Rheumatism (EULAR) recently recommended the use of ultrasound for the detection of inflamed artery walls in giant cell arteritis (GCA) for diagnostic purposes. Intima media thickness (IMT) values, defining the "halo" sign in acute GCA patients, have also recently been proposed. In patients with chronic GCA, already receiving a treatment, the ultrasound appearance of inflamed artery walls changes and becomes difficult to detect.(1-4)
IMT measurement may help to identify patients with chronic large-vessel GCA (LV-GCA) by assessing the axillary arteries; however, a cut-off for distinguishing between chronically affected arteries and unaffected ones is not yet available.
Objectives: To determine an ultrasound IMT cut-off value for axillary arteries in patients with chronic LV-GCA.
Methods: Ultrasound of temporal and axillary arteries was performed in 127 GCA patients at the time of diagnosis and at one or two follow-up visits. Axillary arteries of GCA patients with sonographic signs of inflammation at the time of diagnosis were compared to unaffected axillary arteries of GCA patients and to axillary arteries of healthy controls. Receiver operating curves (ROC) were calculated using follow-up data to identify the optimal IMT cut-off.
Results: 148 axillary arteries of GCA patients showed signs of ultrasound inflammation at baseline (=LV-GCA group). The control group consisted of 162 axillary arteries, including 82 (50.6%) axillary arteries of GCA patients without signs of ultrasound inflammation at baseline or follow-up exam and 80 (49.4%) axillary arteries of 40 healthy controls. The mean age and gender distribution of the two groups at follow-up were 71 years (S. D. 7.9) with 69.9% females, respectively in the chronic LV-GCA group and 74 years (S.D. 6.9) with 59.8% females, respectively in the control group. The mean IMT values in the LV-GCA group were 1.14 (S.D. 0.38, n=78) for the right and 1.18 (S.D. 0.47, n=70) for the left axillary arteries as compared to 0.60 (S.D. 0.11, n=77) for the right and 0.62 (S. D. 0.11, n=85) for the left axillary arteries in the control group. Intervals from diagnosis to follow-up were 0.5-3 years, 3-6 years and >6years, with a distribution of 96 (65%), 32 (22%) and 20 (13%) exams in the LV-GCA group and 29 (35%), 41 (50%) and 12 (15%) exams in the control group (excluding healthy controls), respectively.
The optimal IMT cut-off value for the axillary arteries in patients with chronic LV-GCA was 0.87 mm with 75.0% sensitivity and 99.4% specificity (see figure 1). Sensitivity analysis (comparing patients with and without an involvement of the temporal artery at the time of diagnosis) validated this cut-off value.
Conclusion: An ultrasound IMT cut-off value for the axillary arteries can distinguish between patients with chronic LV-GCA and patients without chronic large vessel involvement.

REFERENCES:

[1] Dejaco C, Ramiro S, Duftner C, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheum Dis 2018;77:636-43.
[2] Schäfer VS, Juche A, Ramiro S, et al. Ultrasound cut-off values for intima-media thickness of temporal, facial and axillary arteries in giant cell arteritis. Rheumatology 2017;56:1479-83.
[3] De Miguel E, Beltran LM, Monjo I, et al. Atherosclerosis as a potential pitfall in the diagnosis of giant cell arteritis. Rheumatology 2017;57:318-21.
[4] Czihal M, Schrottle A, Baustel K, et al. B-mode sonography wall thickness assessment of the temporal and axillary arteries for the diagnosis of giant cell arteritis: a cohort study. Clin Exp Rheumatol 2017;35 Suppl 103:128-33.

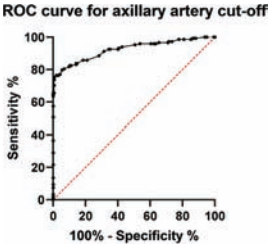


Figure. 1. Receiver operating curve for the axillary artery cut-off in chronic large-vessel giant cell arteritis.

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FRI0275 **HIGH ANGIOPOIETIN-2 LEVELS ASSOCIATE WITH ARTERIAL INFLAMMATION AND LONG-TERM GLUCOCORTICOID REQUIREMENT IN POLYMYALGIA RHEUMATICA**

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Background: Polymyalgia rheumatica (PMR) frequently co-occurs with giant cell arteritis (GCA). So far, a simple biomarker for detecting concomitant arterial inflammation in PMR patients is lacking. Furthermore, biomarkers predicting disease course in PMR are awaited.
Objectives: We here investigated the diagnostic and prognostic value of acute-phase markers (ESR, CRP, IL-6, serum amyloid A) and angiogenesis markers (VEGF, soluble Tie2, angiopoietin-1, angiopoietin-2) in isolated PMR and PMR/GCA overlap patients.
Methods: We prospectively included 39 treatment-naive PMR patients, of which 10 patients also showed evidence of large vessel GCA on FDG-PET/CT. Age-matched healthy controls (N=32) and infection controls (N=13) were included for comparison. Serum marker levels were measured by ELISA or Luminex. ROC and Kaplan Meier analyses were used to asses diagnostic and prognostic accuracy, respectively.
Results: All acute-phase and angiogenesis markers, except angiopoietin-1, were higher in isolated PMR patients compared to HCs. Angiopoietin-2, ESR and soluble Tie-2 were significantly higher in patients with PMR/GCA overlap compared to isolated PMR patients. Angiopoeietin-2, but not soluble Tie2, outperformed ESR and CRP in discriminating patients with and without overlapping GCA (AUC 0.90). Moreover, high angiopoietin-2 levels were associated with long-term glucocorticoid requirement.
Conclusion: Assessment of angiopoietin-2 at baseline may assist diagnosis of concomitant vasculitis in PMR. Moreover, high levels of angiopoietin-2 were associated with a unfavorable disease course in isolated PMR patients. These findings imply that angiopoietin-2 could be an interesting diagnostic and prognostic biomarker in PMR.
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FRI0276 **TIME OF DISEASE EVOLUTION AND EFFICACY OF TOCILIZUMAB IN GIANT CELL ARTERITIS**

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Background: Tocilizumab (TCZ) has proved to be effective in the management of Giant Cell Arteritis (GCA). Based on results of the GiACTA trial, it has been approved by the FDA and the European Commission for GCA treatment. Nevertheless, almost half of the GiACTA trial patients presented a short time evolution disease.
Objectives: Our aim was to evaluate the efficacy of TCZ according the time of disease evolution.
Methods: Retrospective, multicenter study of 134 patients with GCA in treatment with TCZ. A comparative study between two groups according to the time from disease diagnosis and TCZ onset was performed.
Results: Our study included 134 GCA patients. **TABLE 1** summarizes a comparative study between: a) ≤ 6 months of disease evolution, and b) > 6 months of disease evolution. Non-significant difference in baseline characteristics was found. In terms of visual involvement, we observed more patients affected in the first group (≤ 6 months) (p=0.30). Analyzing clinical improvement non-significant difference was seen during follow-up. At TCZ onset, in the group of ≤ 6 months of evolution, the prednisone dose was higher with a mean dose of 31.3±16.5 mg/d vs 17.7±14.2 mg/d (p<0.001), however, a similar reduction of corticosteroids was achieved in both groups after 6 months of follow-up. The incidence of adverse events and severe infections was similar in both groups (p=0.132 and p=0.672 respectively).
Conclusion: In this retrospective analysis, our results support the previously reported efficacy and safety profile of TCZ. We can conclude that TCZ can be used in GCA independently the time of disease evolution.

REFERENCES:

[1] Calderón-Goercke M. Tocilizumab in giant cell arteritis. Observational, open-label multicenter study of 134 patients in clinical practice. Semin Arthritis Rheum. 2019 Jan 5. pii: S0049-0172(18)30571-7. Doi: 10.1016/j.semarthrit.2019.01.003. [Epub ahead of print]
[2] Salvarani C, Magnani L, Catanoso M, Pipitone N, Versari A, Dardani L, et al. Tocilizumab: a novel therapy for patients with large-vessel vasculitis. Rheumatolgy (Oxford). 2012; 51:151-6.
[3] Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, et al. Trial of Tocilizumab in Giant-Cell Arteritis. N Engl J Med. 2017; 377:317-28.

	GCA ≤ 6 MESES (n=44)	GCA > 6 MESES (n=90)	p
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	31.3 ± 16.5	17.7 ± 14.2	**<0.001**
EFFICACY AND SAFETY AFTER TCZ			
Prolonged remission n (%)			
Month 6	16 (57.1)	42 (58.3)	0.272
Month 12	11 (64.7)	35 (67.3)	0.843
Month 24	6 (66.7)	21 (67.7)	0.952
Relapses n (%)			
Month 1	2 (4.9)	2 (2.3)	0.593
Month 3	4 (10.8)	3 (3.5)	0.197
Month 6	1 (3.6)	4 (5.6)	1.000
Month 12	2 (11.8)	7 (13.5)	0.857
Month 24	1 (11.1)	6 (19.4)	0.567
CORTICOSTEROIDS SPARING EFFECTS, median [IQR]			
Month 1	18.8 [10-30]	10 [5-15]	**<0.001**
Month 3	12.5 [7.5-20]	7.5 [5-10]	**<0.001**
Month 6	5 [4.4-10.6]	5 [2.5-7.5]	0.202
Month 12	5 [0-5]	2.5 [0-5]	0.335
Month 24	0 [0-4.4]	0 [0-5]	0.724
SIDE EFFECTS, n (%)			
Relevant adverse events	14 (31.8)	18 (24)	0.132
Serious infections	6 (13.6)	10 (11.1)	0.672

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FRI0277 ISCHEMIC AND SYSTEMIC SYMPTOMS IN GIANT CELL ARTERITIS PATIENTS, RESPONSE TO TOCILIZUMAB

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Background: In Giant Cell Arteritis (GCA) two dominant cytokine clusters have been linked to disease activity, IL-6 – IL-17 axis (Th17) and IL-12 – IFN γ axis (Th1). The first one related to systemic symptoms and the second route responsible for ischemic symptoms. Tocilizumab (TCZ) performs its effect mainly by inhibiting Th17 axis and terminally Th1 route.
Objectives: Our aim was to evaluate the effect of TCZ on ischemic and systemic symptoms throughout the follow-up.
Methods: Retrospective, multicenter study of 134 patients diagnosed of GCA on treatment with TCZ. We evaluate the efficacy of TCZ by improving ischemic (visual involvement, headache, jaw claudication) and systemic symptoms (fever, constitutional syndrome, polymyalgia rheumatica (PMR)).
Results: We evaluated 134 patients (101 w/33 m) and its main symptoms at TCZ onset, **TABLE**. 73 (54.5%) patients presented PMR followed by headache in 70 (52.2%) cases, constitutional syndrome in 31 (23.1%) and visual involvement in 28 (20.9%) patients. After one month of treatment there was an important clinical improvement, persisting in 13,6% of patients PMR, 10.6% headache and 10.6% visual involvement. Throughout the follow-up, the improvement of ischemic symptoms was slower. At month 12, in 5.6% (4) of patients persisted with visual impairment, and 2.8% (2) patients presented headache and constitutional syndrome. However, the analytical improvement was statistically significant from the first month and sustained during follow-up.
Conclusion: According to the results of our study, we can conclude that in clinical practice, ischemic symptoms take longer to improve than systemic symptoms; being visual affectation the most frequent symptom after 12 months of follow-up.

REFERENCES:

[1] Soriano A, Muratore F, Pipitone N, Boiardi L, Cimino L, Salvarani C. Visual loss and other cranial ischaemic complications in giant cell arteritis. Nat Rev Rheumatol. 2017; 13:476-84.
[2] Ciccia F, Rizzo A, Ferrante A, Guggino G, Croci S, Cavazza A, et al. New insights into the pathogenesis of giant cell arteritis. Autoimmun Rev. 2017; 16:675-83.
[3] Calderón-Goercke M. Tocilizumab in giant cell arteritis. Observational, open-label multicenter study of 134 patients in clinical practice. Semin Arthritis Rheum. 2019 Jan 5. pii: S0049-0172(18)30571-7. Doi: 10.1016/j.semarthrit.2019.01.003. [Epub ahead of print]

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	Basal	Month 1 n=132	Month 3 n=122	Month 6 n=99	Month 12 n=71
SYSTEMIC MANIFESTATIONS					
Fever, n (%)	9 (6.7)	0	1 (0.8)	1 (1.0)	1 (1.4)
Constitutional syndrome, n (%)	31 (23.1)	12 (9.1)	6 (4.9)	2 (2.0)	2 (2.8)
PMR, n (%)	73 (54.5)	18 (13.6)	14 (11.5)	4 (4.0)	0
ISCHEMIC MANIFESTATIONS					
Visual involvement, n (%)	28 (20.9)	14 (10.6)	9 (7.4)	5 (5.1)	4 (5.6)
Headache, n (%)	70 (52.2)	14 (10.6)	7 (5.7)	6 (6.1)	2 (2.8)
Jaw claudication, n (%)	14 (10.4)	0	0	1 (1.0)	1 (1.4)
ACUTE PHASE REACTANTS					
ESR, mm/1st hour, mean (SD)	33 [14.5-61] ** (129)	6 [2-12] ** (102)	4 [2-7.5] ** (116)	4 [2-8] ** (93)	4 [2-8] ** (71)
CRP, mg/dL mean (SD)	1.7 [0.4-3.2] **_(131)	0.1 [0-0.5] ** (98)	0.1 [0-0.4] ** (110)	0.1 [0.-0.2] ** (92)	0.1 [0-0.2] ** (67)

**p<0.001

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FRI0278 OFF-LABEL USE OF BIOLOGICAL THERAPIES IN RELAPSING AND/OR REFRACTORY EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (CHURG-STRAUSS)

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA), formerly named Churg-Strauss syndrome, is a small-vessel necrotizing vasculitis associated with eosinophilia and asthma. Glucocorticoids (GCs) usually control the disease, but relapses and GC-dependant asthma are frequent, leading to potential biological therapy use.

Objectives: We examined off-label biological therapy use for relapsing/ refractory EGPA.

Methods: Remission was defined as the absence of asthma and vasculitis manifestations with a prednisone dose ≤5 mg/day, and partial response as the absence of manifestations requiring prednisone dose between 6 and 10 mg/day.

Results: One hundred and eigteen patients (66 men, 52 women; median age 50.5 years) were included. Fifty (42%) patients received rituximab (RTX), 38 (32%) mepolizumab (MEPO), and 30 (26%) omalizumab (OMA).

Previous treatments were: oral GCs (98%), methylprednisolone infusions (51%), azathioprine (68%), cyclophosphamide (47%), methotrexate (30%), mycophenolate mofetil (8%).

At inclusion, median (interquartile range) BVAS in the RTX, OMA and MEPO groups were 8 (4.5-13), 2 (1.5-4) and 2 (2-5), respectively, median (IQR) daily GCs dose were 20 mg/day (15-40), 20 mg/day (10-37.5), 10 mg/day (7.5-20). GC-dependant asthma was found in 39 (78%) of the RTX group, 36 (95%) in the MEPO group and 28 (93%) in the OMA group.

After median follow-up of 22.8 months (IQR 10-47), remissions, partial responses and therapeutic failures, respectively, were noted in 50%, 16% and 34% for RTX recipients, 17%, 38% and 45% for the OMA group and 84%, 3% and 13% for the MEPO group.

Median BVAS dropped to 0 at 6 and 12 months and at last follow-up in all groups. A GC-sparing effect seemed more important with RTX and MEPO. Median GCs dose decreased from the baseline 20 mg/day to 8.5 at 6 months, 7.5 at 12 months and 5 at last follow-up in the RTX group, from 20 mg/day to 12 at 6 months, 10 at 12 months and 10 at last follow-up in the OMA group, and from 10 mg/day to 5 at 6 months, 3 at 12 months and 5 at last follow-up in the MEPO group. In the MEPO group, no difference was noted between patients receiving 100 mg and those 300 mg monthly.Nine (18%) patients stopped RTX because of refractory disease, and 12 (24%) experienced adverse events, including severe infections in 5. Thirteen (43%) stopped OMA because of severe infusion reaction in one and refractory disease in 12, and 4 (13%) patients receiving OMA experienced adverse events. Three (8%) patients stopped MEPO because of adverse events in 2 (one severe infusion reaction and one because of paresthesia), because of pregnancy in one. Seven (18%) additional patients receiving MEPO experienced adverse events, mainly asthenia.

Conclusion: The results suggest that RTX may be effective in 50% of patients with vasculitis relapses related to EGPA, with an acceptable safety profile, while MEPO is highly effective with a good GCs-sparing effect and safety profile in patients with steroid-dependant asthma.

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FRI0279 MYCOPHENOLATE MOFETIL IN THE TREATMENT OF MAJOR ORGAN INVOLVEMENT OF PATIENTS WITH BEHÇET'S SYNDROME

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Background: Mycophenolate mofetil (MMF) has been increasingly used in various rheumatic diseases. It may also be a safe and effective treatment option for Behçet's syndrome (BS) where oral immunosuppressives other than azathioprine and cyclosporine are not available.

Objectives: We aimed to report our experience with MMF in BS patients with major organ involvement.

Methods: We retrospectively reviewed the charts of all BS patients who started using MMF between 2016 and 2018. Demographic characteristics, MMF indication, history of previous immunosuppressive agents, concomitant therapies with MMF, adverse events and outcome were recorded from the chart review.

Results: We evaluated 39 BS patients (M/W: 30/9, mean age: 39 ± 8 years) treated with MMF during a mean follow-up of 18 ± 13 months. Of 39 patients, 31 received MMF for maintenance of remission therapy, while 8 had active disease at the initiation of MMF. The main indications were vascular involvement in 26, eye involvement in 11, and neurologic involvement in 2 patients. Among the 26 patients with vascular involvement, 13 had deep vein thrombosis, 6 had pulmonary artery involvement, and 3 had arterial involvement.

Twenty-nine patients started MMF after azathioprine due to adverse events such as leucopenia, gastrointestinal intolerance and elevation of liver enzymes. MMF was chosen in 2 patients because of concomitant use of warfarin, that may be problematic with azathioprine. The remaining 8 patients were treated with MMF due to active disease despite azathioprine.

In 20/39 (50%) patients MMF was used concomitantly with biologics (infliximab in 15 and adalimumab in 5). One patient additionally used cyclosporine-A and 7 patients used low-dose prednisolone.

At the end of follow-up, 33 of the patients were still using MMF. The reasons for MMF discontinuation were recurrent superficial thrombophlebitis in 3 patients with previous lower extremity deep vein thrombosis, fear from adverse events, desire of pregnancy and itching in 1 patient each. There were no serious adverse events or adverse events leading to discontinuation except for itching. None of the patients experienced exacerbation of mucocutaneous lesions during MMF treatment.

Conclusion: MMF seems to be a safe and effective alternative especially when used for maintenance of remission or in addition to biologic agents in active patients with major organ involvement.

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FRI0280 **BAFF AND APRIL GENE EXPRESSION IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS**

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Background: Neutrophil activation is the central step in the pathogenesis of ANCA associated vasculitis (AAV). Activated neutrophils are an important source of tumor necrosis factor (TNF) ligands involved in the B cell development and survival, namely, B cell activating factor (BAFF) and a proliferating ligand (APRIL)[1]. They have been postulated to have a role in the pathogenesis of AAV but presently there is limited data[2, 3].
Objectives: To study the expression of BAFF and APRIL genes in patients with AAV and healthy controls and their correlation with disease activity.
Methods: This was a prospective case-control study. Gene expression of BAFF and APRIL was studied in 20 patients of AAV (10 each with active disease and in remission) and 20 healthy age and sex matched controls. Blood samples were collected after taking due consent. Following RNA extraction (QIAamp RNA blood mini kit) and cDNA synthesis ("Thermo Scientific™ RevertAid™ First Strand" cDNA Synthesis Kit), quantitative real time polymerase chain reaction (qRT-PCR) using SYBR Green I Chemistry was carried out to study relative mRNA expression of BAFF and APRIL. β actin (ACTB) a housekeeping gene was taken as a reference gene.
Results: Out of 20 AAV patients 16 were GPA and 4 MPA. Mean age of patients in active (8 GPA and 2 MPA) and remission (8 GPA and 2 MPA) group was 34.5 ± 16.1 and 39.9 ± 16.6 years respectively. The sex distribution in both groups was 1:1. Mean BVASv3, ESR and CRP in active AAV patients were 18.8 ± 8.5, 54 ± 10.8 mm/h and 41.75 (7.07- 402) mg/l respectively. BAFF gene expression was significantly higher in both active AAV group and remission AAV group compared to controls ($p < 0.01$, Figure 1). The BAFF expression was significantly higher in AAV patients in remission compared to active AAV patients ($p=0.008$). In contrast, the APRIL expression did not differ between AAV patients and controls ($P = 0.829$) or between active and inactive AAV patients ($p = 0.166$). There was no significant correlation of both BAFF and APRIL expression with disease activity markers (ESR, CRP, platelets and BVASv3).

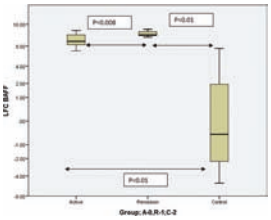


Figure 1. Box and whisker plot of BAFF expression in active AAV patients, AAV in remission and controls

Fig 1- X axis shows the patients groups A-0(active), R-1(remission), C-2(control); Y axis shows the log fold change (LFC) of BAFF expression
Conclusion: BAFF gene is significantly expressed in patients with ANCA associated vasculitis. Among AAV patients there is significantly higher expression of BAFF in patients with inactive disease than active disease. There is no significant APRIL gene expression in patients with AAV.

REFERENCES:

[1] Mackay F, Schneider P, Rennert P, Browning J. BAFF AND APRIL: a tutorial on B cell survival. Annu Rev Immunol. 2003; 21:231–64.
[2] Krumbholz M, Specks U, Wick M, Kalled SL, Jenne D, Meinl E. BAFF is elevated in serum of patients with Wegener's granulomatosis. J Autoimmun. 2005; 25:298–302.
[3] Schneeweis C, Rafalowicz M, Feist E, Buttgereit F, Rudolph PE, Burmester GR, et al. Increased levels of BLyS and sVCAM-1 in anti-neutrophil cytoplasmatic antibody (ANCA)-associated vasculitides (AAV) Clin Exp Rheumatol. 2010; 28:62–6.

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FRI0281 **MACRO AND MICRO-VASCULAR AFFECTION IN CORRELATION TO HLA-B51 IN EGYPTIAN PATIENTSWITH BEHÇET'S DISEASE**

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Background: Behçet's disease is a multisystem inflammatory disorder with unknown etiology.HLA-B51 antigen has been known as a genetic factor associated with B D(1). Vascular involvement in Behcet has been widely described to affect large & medium vessels Vascular involvement in Behcet has been widely described to affect large & medium vessels however, few studies demonstrated micro vascular affection through nailfold capillaroscopy examination (2).
Objectives: Objective was to highlights HLA role in different clinical presentation of BD, especially the vascular point of view.
Methods: 40 Egyptian Behçet's disease patients (according to the international study group of Behçet's disease, 1990), and 30 age and sex matched healthy controls where enrolled in our study. All patients were subjected to history taking and clinical examination. BDCAF, CBC, ESR, CRP, liver function and lipid profile.
Genetic typing HLA B51 by PCR, carotid intima media thickness, Capillriscopy of nail capillary fold and ankle brachial index were done to both patients and controls.

Comparison of Doppler& capillaroscopy parameters between the studied groups

				Behçet's group(N=50)	Control (N=30)	p-value
Carotid artery	**Intima media thickness (mm) (mean±SD)**		**Rt**	0.09±0.12	0.07 ±0.01	< 0.001
		Lt		0.08±0.01	0.07 ±0.01	0.009
	Peak systolic velocity (mm/s) (mean±SD)		**Rt**	82.49±22.82	93.46 ±19.79	0.007
		Lt		86.24±19.65	87.85 ±14.06	0.684
	End diastolic volume (mean±SD)		**Rt**	27.94±10.34	37.05 ±18.18	0.002
		Lt		27.29±6.35	33.81 ±13.48	0.021
	Resistivity index (mean±SD)		**Rt**	0.67±0.08	0.60 ±0.17	0.097
		Lt		0.69±0.07	0.62 ±0.13	0.005
Posterior tibial artery diameter(mm) (mean±SD)			**Rt**	0.24±0.07	0.27 ±0.08	0.079
		Lt		0.23±0.08	0.26 ±0.08	0.083
Anterior tibial artery diameter(mm) (mean±SD)			**Rt**	0.25±0.10	0.28 ±0.06	0.144
		Lt		0.24±.0.10	0.27 ±0.08	0.028
Ankle brachial index (mean±SD)			**RT ATA**	1.20±0.25	1.21 ±0.20	0.445
			RT PTA	1.20±0.25	1.24 ±0.23	0.419
			LT ATA	1.18±0.22	1.19 ±0.18	0.490
			LT PTA	1.19±0.25	1.20 ±0.23	0.722
Attenuated arterial wall of tibialis N (%)				10 (20)	1(2)	0.004
Capillaroscopy	**Arterial limb (mean ±SD)**			10.84±3.61	12.53 ±3.16	0.007
	Posterior limb (mean±SD)			16.04±6.04	17.13 ±4.47	0.050
	Capillary loop (mean±SD)			19.35±6.32	22.23 ±5.98	0.014
	Capillary length (mm) (mean±SD)			185.79±88.60	222.17 ±78.15	0.020
	Morphology N (%)	**Abnormal shape**		2(4%)	0	0.044
		Scanty		3(6%)	0	
		Scarring		3(6%)	0	
		Elongated		5(10%)	1(2%)	
		Crossed		7(14%)	9(18%)	
		Hemorrhage		3(6%)	6(12%)	
		No		27(54%)	34(68%)	

Results: There was no statistically significant correlation between HLA B51 and systemic manifestations or disease activity or Doppler findings nor capillary parameters and morphology. There was statistically significant relation between HLA B51 and ankle brachial index.
There was statistically significant difference between patients and controls in EDV, RI of the carotid artery, and arterial, venous limb of the capillary, also the capillary lobe and length with lower values in the patients. There was statistically significant difference between patients and controls in carotid intima media thickness with higher values in patients, insipte of the absence of significant difference in lipid.
Conclusion: HLA B51 didn't link to different clinical presentation in BD; it is related to peripheral arterial affection only. BD patients had poor arterial compliance and increased arterial stiffness, there is preclinical atherosclerosis in BD not to related to the level of lipid profile.

REFERENCES:

[1] Marshall SE. bechet's disease. Best Pract Res Clin Rheumatol. 2004 Jun 1;18(3):291–311.
[2] Hegab S, Al-Mutawa S. Immunopathogenesis of Behçet's Disease. Clin Immunol. 2000;96(3):174–86.

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FRI0282 STATINS REDUCE RELAPSE RATE IN TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) is a chronic inflammatory disease, mainly affecting aorta and its major branches. Despite treatment with glucocorticoid and adjunctive immunosuppressive agent, relapse is common. Considering the high relapse rate, it is important to identify additional medications that may help sustain remission. Statins, as having anti-inflammatory and immunomodulartory effects, may be one such possibility.
Objectives: To investigate the effect of statins on relapse of Takayasu arteritis (TAK), which frequently occurs after achievement of remission.
Methods: We conducted a retrospective study on TAK patients with active disease, diagnosed between 2012 and 2017. Relapse was defined as recurrence of active disease after achieving remission. Demographic and clinical parameters of patients who experienced relapse were compared to those who did not. To identify factors associated with relapse, multivariate Cox regression analysis with stepwise backward elimination was performed. Inverse probability of treatment weighting (IPTW)-adjusted analysis was used to evaluate the influence of statins on relapse.

Table. Multivariate Cox proportional hazard regression analysis estimating risk of relapse

	Adjusted hazard ratio	95% confidence interval	P value
Age	0.974	0.942–1.008	0.130
Hypertension	0.776	0.309–1.951	0.590
Carotidynia	2.348	1.002–5.505	0.050
LDL-cholesterol	1.007	0.986–1.028	0.510
Statin use	0.260	0.120–0.563	**0.001**

Abbreviation: LDL; low density lipoprotein

Results: Of the total 74 TAK patients, 40 (54.1%) patients received statins, whereas 34 (45.9%) patients did not. Relapse was observed in 36 (48.6%) patients of the total 74 TAK patients. Compared with patients who did not experience relapse, patients who experienced relapse were younger (44.5±13.5 years vs 34.1±12.6 years, p=0.001), had lower prevalence of hypertension (63.2% vs 38.9%, p=0.037), more commonly had carotidynia (7.9% vs 27.8%, p=0.025), had higher LDL-cholesterol (84.8 ±18.8 mg/dl vs 100.5±26.1 mg/dl, p=0.010), and were less commonly taking statins (71.1% vs 36.1%, p=0.003). These variables were included in multivariate Cox regression analysis. The use of statins was significantly associated with lower risk of relapse (adjusted hazard ratio 0.260, 95% confidence interval 0.120–0.563, p=0.001). Furthermore, IPTW-adjusted analysis confirmed that statin use was associated with a lower risk of relapse (IPTW-adjusted hazard ratio 0.153, 95% confidence interval 0.038–0.616, p=0.008).
Conclusion: In TAK, statins can be beneficial in reducing relapse rate after achieving remission.
Covariates: age (continuous), hypertension (yes/no), carotidynia (yes/no), LDL-cholesterol (continuous), and statin use (yes/no)
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FRI0283 PRESENTATION AND MANAGEMENT OF GIANT CELL ARTERITIS IN A REAL-WORLD SETTING (ARTEMIS STUDY)

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Background: We have little real-world data in France on the natural history and management of patients with GCA.
Objectives: The objective of this observational study, named ARTEMIS, was to describe the characteristics and management of patients with GCA in real-life settings in France.
Methods: This was a cross-sectional, non-interventional, multicentre, single-visit survey, conducted among hospital-based physicians specialized in internal medicine or rheumatology. Investigators enrolled consecutive patients $\geq$ 50 years old seen for GCA and currently under treatment. Information on medical practices, such as patient characteristics and diagnostic journey, diagnostic methods and specific GCA treatments, were collected on an eCRF. GCA activity was assessed on a 100-mm VAS completed by the patients (PtGA) and physicians (PGA). GCA was considered active for VAS scores $\geq$10 mm. Newly diagnosed GCA was defined as diagnosis (Dg)-to-visit interval <6 weeks. Onset of symptoms-to-Dg interval was classified as "short" (<1 month), "intermediate" (1–3 months) and "long" (>3 months). Descriptive statistics were used for quantitative and qualitative variables.
Results: Over the 3-month inclusion period (August–November 2018), 306 patients were recruited (females: 67.3%, age at Dg $\geq$70 years: 72.5%); 260 (85.0%) and 46 (15.0%) were followed by internists or rheumatologists, respectively. Overall, 39 (12.7%) had newly diagnosed GCA, 267 (87.3%) had a GCA duration $\geq$ 6 weeks (mean follow-up 24.0±27.0 months). Original referral of patients to specialized centres was from GPs (55.9%), ophthalmologists (10.1%), neurologists (6.9%), emergency physicians (5.6%), internists (4.2%) and rheumatologists (4.9%). Mean time to Dg was 3.3±6.9 months, with an "intermediate" Dg interval for 57.5% of patients. The most common prior medical histories were hypertension (45.8%), psychiatric disorders (10.1%), dyslipidemia (11.8%), diabetes (9.5%) and osteoporosis (5.9%); during follow-up psychiatric disorders, diabetes and osteoporosis were more often reported: 12.1%, 14.7% and 8.5% of patients respectively. Initial GCA presentations included cranial symptoms (89.5% of patients), constitutional symptoms (73.9%), polymyalgia rheumatica (48.4%), and other extra-cranial manifestations (34.0%). Initial mean ESR and CRP level were 73.0±30.7 mm/hr and 87.3±68.3 mg/l. Temporal artery biopsy, high-resolution temporal artery Doppler ultrasonography, ^{18}FDG-PET and aortic angio-CT were performed for 84.7%, 31.2%, 26.4% and 29.7% of patients, respectively, and contributed to GCA Dg for 67.1%, 52.7%, 70.3% and 36.8%. At study visit, PtGA was 28.1±26.4 and PGA was 13.1±21.4. Ongoing medications included glucocorticoids (GC) for 273 (89.2%) patients (mean dose: 14.9±16.7 mg/d), methotrexate for 35 (11.4%) and tocilizumab for 44 (14.4%). In total, 122 (39.9%) patients had $\geq$1 relapse (mean number of relapses: 1.7±1.0) after a mean time to a first relapse of 13.3±12.8 months. Total cumulative oral GC dose was 5179±4987 mg. GCA-related complications occurred in 48 (15.7%) pts with eye disorders in 15 (5.2%).
Conclusion: This observational, cross-sectional study of a large number of patients provides insight into current medical practices for GCA in France. Despite extensive use of large-vessel imaging, the proportion of patients diagnosed with non-cranial GCA is small (10%). The substantial proportion of patients with relapsing disease results in high cumulative doses of glucocorticoids. The number of patients with tocilizumab treatment was slightly greater than that with methotrexate treatment.
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Isabelle Idier Employee of: ChugaiPharma france, Valerie Devauchelle-Pensec Grant/research support from: Roche-Chugai, Speakers bureau: MSD, BMS, UCB, Roche

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FRI0284 RESULTS OF A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2018 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF LARGE VESSEL VASCULITIS: EVIDENCE TO GUIDE THE MANAGEMENT OF GIANT CELL ARTERITIS

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Background: The latest EULAR recommendations for the management of large vessel vasculitis (LVV) were published in 2009 (1). Since then, imaging has become a reliable diagnostic tool and new therapeutic options are available for giant cell arteritis (GCA), supporting the need to update the recommendations.

Objectives: To analyse the current evidence for the management (diagnosis/monitoring and treatment) of LVV to inform the 2018 update of the EULAR recommendations.

Methods: A systematic literature review (SLR) dealing with diagnosis/monitoring and treatment strategies for LVV, respectively, was performed. Medline, Embase and Cochrane databases were searched from inception until 31st December 2017. Evidence on imaging was excluded in light of recently published EULAR recommendations (2). We reviewed data relevant to GCA. Level of Evidence (LoE), was assessed in accordance with the 2009 Oxford Centre for Evidence-based Medicine.

Results: We identified 283 papers from the SLR. The implementation of a fast-track approach to diagnosis significantly lowered the risk of permanent visual loss compared to historical cohorts (Level of evidence – LoE 2b). The SLR confirmed the efficacy of prompt initiation of glucocorticoids (GC). There was no high-quality evidence on the most appropriate starting dose, route of administration, tapering and duration of GC (LoE 4). Patients with GCA are at increased risk of dose-dependent GC-related adverse events (LoE 3b). The addition of methotrexate (MTX) (LoE 1a) or tocilizumab (TCZ) reduced relapse rates and GC requirements (LoE 1b). There was no consistent evidence that anti-platelet agents given at the time of GCA diagnosis prevented future ischaemic events (LoE 2a). There was little evidence to guide monitoring of patients with GCA.

Conclusion: Results from a SLR confirmed the importance of a prompt diagnosis and rapid initiation of GC therapy. Patients with GCA are at an increased risk for GC-related comorbidities. MTX and TCZ can reduce GC exposure and relapse rates. There are yet no high-quality data to guide monitoring and duration of treatment in GCA.

REFERENCES:

[1] Mukhtyar C, et al. EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis 2009;68:318-23.

[2] Dejaco C, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheum Dis. 2018;77:636-43.

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FRI0286 CUTANEOUS POLYARTERITIS NODOSA: A SUBSET OF SYSTEMIC PAN OR A DISEASE APART?

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Background: Cutaneous Polyarteritis Nodosa (cutaneous PAN) is a rare form of necrotizing vasculitis involving predominantly medium and small arteries. It is limited to the skin. The clinical course is mostly chronic, however it has a more favourable prognosis than systemic PAN. Cutaneous PAN may be preceded by infection, drugs intake or may reflect underlying inflammatory or autoimmune disease. The diagnostic criteria are controversial and in some cases overlapping with those of systemic PAN. Cutaneous PAN is limited to the skin, but occasionally patients present extracutaneous symptoms, namely: myalgia, arthralgia or multineuritis

Objectives: To describe the clinical manifestations of cutaneous PAN, emphasizing the extracutaneous manifestations, as well as comorbid associations.

Methods: Retrospective study (1989-2018) of patients with cutaneous PAN seen in a tertiary center: referral area 800.000 inhabitants. All the cases were reviewed regarding epidemiological, clinical, electromyographic, histopathological and laboratory findings. Infections and comorbid diseases were also reviewed.

Results: Twenty-three cases were recruited: 8 male (34.78%) and 15 female (65.22%) patients. Mean age at onset: 47 years (range 18-76). Mean follow-up period :105 months (range 12-380). Cutaneous manifestations included: subcutaneous nodules (95.65%), ulcers (52.17%), livedo *reticularis (*60.87%), livedo *racemosa* (8.70%), *atrophie blanche* (39.13%) and purpura (4.34%). Cutaneous PAN most commonly occurred on the legs (100%), followed by the thighs (47.83%), the upper limbs (39.13%) and the trunk (17.39%). The most frequent extracutaneous symptom were asthenia (78.26%). Extracutaneous manifestations, limited to the same area of cutaneous lesions, were myalgia (60.87%) and paraesthesia (56.52%). An electromyography was performed in 14/23 patients and mononeuritis multiplex was observed in 7 patients. Only one patient progressed to systemic PAN, with development of renal disease 12 month after the diagnosis. The following infections were identified: hepatitis C (2), tuberculosis (1), *Streptococcus pyogenes* (1) and rickettsia (1). Comorbid diseases included: autoimmune hypothyroidism (2), cutaneous psoriasis (1), recidivant polychondritis (1), adult onset Still´s disease (1), ulcerative colitis (1), pulmonary idiopathic fibrosis (1) and acute myeloid leukaemia (1). Glucocorticoids were used at medium-high doses (20-40 mg/day) in 20 patients as induction therapy, and NSAIDs at full doses in the remaining 3. Thirteen patients (56.52%) developed relapsing forms. Of this, 12 patients (52%) needed associated immunosuppressive treatment to prevent relapse. The most widely used immunosuppressant was methotrexate, followed by mycophenolate or azathioprine.

Conclusion: A long-term follow-up, with careful anamnesis and examination, including electromyography, is necessary to better characterize the cutaneous and extracutaneous manifestations of cutaneous PAN. The progression to systemic involvement is infrequent and cutaneous PAN has a more benign course from a clinical, and prognostic point of view.

REFERENCES:
[1] Diaz-Perez JL, De Lagran ZM, Diaz-Ramon JL, Winkelmann RK. Cutaneous polyarteritis nodosa. Semin Cutan Med Surg. 2007 Jun;26:77–86.
[2] Morgan AJ, Schwartz RA. Cutaneous polyarteritis nodosa: a comprehensive review. Int J Dermatol. 2010 Jul;49:750–6.
[3] Daoud MS, Hutton KP, Gibson LE. Cutaneous periarteritis nodosa: a clinicopathological study of 79 cases. Br J Dermatol. 1997 May;136:706–13.
[4] Nakamura T, Kanazawa N, Ikeda T, Yamamoto Y, Nakabayashi K, Ozaki S, et al. Cutaneous polyarteritis nodosa: revisiting its definition and diagnostic criteria. Arch Dermatol Res. 2009 Jan;301:117–21.

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FRI0287 EFFICACY OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS TREATMENTS ACCORDING TO THE TYPE OF MANIFESTATIONS BASED ON ANALYSIS OF 636 PATIENTS

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss) is a small-vessel necrotizing vasculitis characterized by blood and tissue eosinophilia and asthma. Glucocorticoids (GCs) represent the treatment cornerstone. So far, EGPA management has been based on conventional immunosuppressants, but GC-dependence remains frequent. Recently, therapies targeting B cells and interleukin-5 have been prescribed, but data on large cohorts are lacking.
Objectives: This study aimed to describe therapeutic management and efficacy of treatments in EGPA patients.
Methods: We set up a multicenter European cohort that included 636 EGPA patients. Treatments used, complete remission rates and vasculitis relapse-free survival were recorded. Complete remission was defined as absence of vasculitis relapse and prednisone dose <5 mg/d at last follow-up. Efficacy to treat GC-dependent asthma/ENT signs was defined as the absence of asthma/ENT symptoms and prednisone dose ≤7.5mg/d within the 6 months after initiation.
Results: For induction, cyclophosphamide (CYC) was the most frequently prescribed immunosuppressant (36.2%), more often in patients with FFS ≥1 (P<0.0001). GCs alone were used in 37.3%, azathioprine (AZA) in 14.4% and methotrexate (MTX) in 6.2%. No difference was found in the 10-years overall survival between patients with FFS=0, FFS=1 and FFS≥2.
Complete remission rates were similar between conventional immunosuppressants (CYC, AZA or MTX) and GCs alone. Vasculitis relapse-free survival was also similar between CYC, AZA or MTX and GCs alone. Similar results were observed for first vasculitis relapse treatments.
During follow-up, GC-dependent asthma and/or ENT manifestations were treated with AZA (40%), MTX (25%), mycophenolate mofetil (16%), rituximab (RTX) (21%), CYC (19%), cyclosporine (6%), omalizumab (5.9%) and mepolizumab (5.5%), allowing GC-tapering ≤7.5mg/in 23%, 31%, 17%, 43%, 5%, 71%, 25% and 50%, respectively. Conventional immunosuppressants were mostly used in first and second line, while eosinophil-targeted biotherapies were used in 4th or 5th lines.
Conclusion: In EGPA patients, the response to conventional immunosuppressants, in addition to GCs, is often disappointing compared to GCs alone, without clear benefit on complete remission rates and relapse-free survival. In contrast, notwithstanding a small number of treated patients, eosinophil-targeted therapies seemed promising to treat asthma and/or ENT manifestations.
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FRI0288 OPHTHALMOLOGICAL MANIFESTATIONS AND ENDOTHELIN-1 PLASMA LEVELS IN PATIENTS WITH SYSTEMIC NECROTIZING VASCULITIS (SNV)

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Background: Inflammatory eye disease is described in 50% to 60% of patients with ANCA-positive vasculitis and in 10–20% of patients with polyarteritis nodosa, and for 8% to 16% of patients it is an initial manifestation [1,2]. Endothelin-1 (ET-1) as a potential participant in the local regulation of intraocular pressure, ocular blood vessel tone, and iris smooth muscle tone, suggesting that it may be an important mediator in the development of ocular pathologic conditions [3]. The lower ET-1 plasma levels were found in the optic neuropathy [4].
Objectives: to provide a more complete description of the ocular disease in patients with systemic necrotizing vasculitis (SNV), to evaluate the serum level of ET-1 in patients with SNV with and without eye involvement.
Methods: The study included 36 patients with SNV (polyarthritis nodosa - 8, ANCA - associated vasculitis - 28) and healthy controls (n=26). The 17 patients with SNV had ophthalmological manifestations. Clinical activities of patients were calculated according to the Birmingham Vasculitis Activity Score (BVAS). The serum levels of ET-1 (pmol/L) were determined by immunoassay analysis using the kits of Biomedica. The outcomes of this study were the differences in marker levels between SNV patients with and without eye involvement and healthy controls estimated by analysis of the absolute changes in marker levels and the areas under receiver operating characteristic (ROC) curves (AUC).
Results: The ocular manifestation of patient with SNV included episcleritis (n=10), anterior uveitis (n=3), ischaemic optic neuritis (n=3) and occlusive retinal vasculitis (n=1). All patients had active disease (BVAS>11). There were no significant differences of BVAS, ESR and CRP between SNV patients with and without eye involvement. In 14% patients with SNV eye involvement was an initial manifestation. The level of ET-1 (M ± σ) in group of SNV patients with eye involvement (n=17) was 0.28 ± 0.13 and did not differ significantly from the control group (0.27 ± 0.10, p> 0.05). At the same time, in patients without eye involvement (n=19), it was significantly elevated (0.36 ± 0.34) compared with control group and with group of SNV patients with eye involvement (p < 0,001). ROC analysis showed that the AUC for ET-1 is 0.5±0.10 (p=0.98), which indicates not acceptable capacity for ET-1 differentiate groups of patients with ocular involvement and patients without ocular involvement (sensitivity - 59%, specificity - 57%).

Conclusion: The most common ocular manifestation in patients with SNV was episcleritis, which occurred in almost one third of patients. The serum levels of ET-1 were decreased in patients with SNV with eye involvement compared with patients without eye involvement, but this cannot be used for diagnostic purposes.

REFERENCES:

[1] Pakrou N, Selva D, Leibovitch I. Wegener's granulomatosis: ophthalmic manifestations and management. Semin Arthritis Rheum. 2006;35(5):284–92.

[2] Pagnoux, C., Seror, R., Henegar, C., Mahr, A., Cohen, P., Le Guern, V., Bienvenu, B., Mouthon, L., and Guillevin, L. (2010). Clinical features and outcomes in 348 patients with polyarteritis nodosa: a systematic retrospective study of patients diagnosed between 1963 and 2005 and entered into the French Vasculitis Study Group Database. Arthritis and Rheumatism, 62, 616–26

[3] Sugiyama T. Involvement of Endothelin-1 in the Pathophysiology of Normal-Tension Glaucoma. International Journal of Ophthalmic Research 2015; 1(2): 36-40 Available from: URL: http://www.ghrnet.org/index.php/ijor/article/view/1221.

[4] Ohguro I, Ohguro H, Ohkuro K, Nakazawa M: Study of contribution of low levels of plasma endothelin-1 concentrations to pathogenesis of glaucomatous optic neuropathy. Hirosaki Med J, 2006; 57: 59–64

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FRI0289 THE CYCLOPHOSPHAMIDE-SPARING ROLE OF AN INTENSIFIED B-CELLS DEPLETION PROTOCOL IN ANCA-ASSOCIATED VASCULITIS

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Background: ANCA-associated vasculitis (AAV) are systemic diseases with relapsing chronic course. The management of AAV requires the use of immunosuppressive drugs whose use is associated with potential toxicity.
Objectives: This case-control study aims to evaluate the immunosuppressive-sparing effect of rituximab (RTX) used with cyclophosphamide (CYC), compared to a traditional regimen based on high-dose CYC.
Methods: 26 patients (pts) with AAV with a necrotising extracapillary glomerulonephritis were prospectively enrolled. 13 pts received the intensified protocol of B-lymphocyte depletion therapy (IBCDT) "4+2" with RTX and CYC (4 weekly infusions of RTX followed by 2 monthly followed by prednisone tapered to 5 mg/day in 3 months). 13 pts treated with the high-dose CYC treatment protocol followed by azathioprine as maintenance therapy were enrolled as controls.
Results: In the 13 cases treated with the IBCDT we observed a significant reduction in mean values of parameter of disease activity. After administration of RTX, a significant reduction of the mean s-creatinine values and BVAS was observed. All pts had full B-cell depletion on peripheral blood after the first IBCDT protocol after 1 year. No further maintenance therapy was given. In the cases, a response was observed in 8/13 cases. 4 pts did not respond and a death was observed for cardiovascular causes. No significant difference was observed in terms of response to therapy between the two groups. The IBCDT allows a significant reduction in the cumulative dose of CYC to which each patient was exposed during follow-up, reaching statistical significance levels ($p < 0.001$). Calculated on a monthly basis, the "4+2" protocol allowed an average reduction in the CYC cumulative dose equivalent to 827 mg/month.
Conclusion: In a selected sample of patients with AAV with renal involvement, the IBCT regimen appeared to be non inferior in terms of the efficacy when compared to CYC-based standard regimens. Moreover, the IBCDT regimen allowed a net reduction in the cumulative average dose of CYC to which pts are exposed, quantifiable in approximately 1g/month.

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FRI0290 EFFICACY AND SAFETY OF TOCILIZUMAB IN PATIENTS WITH GIANT CELL ARTERITIS AND VISUAL DISTURBANCES

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Background: Giant cell arteritis (GCA) affects cranial arteries and, as a complication, may lead to visual disturbances and ultimately blindness. Tocilizumab (TCZ) has recently been approved for treatment of GCA. Data on its efficacy and safety in patients who present with visual affection are limited.
Objectives: To study the outcome of patients with GCA and visual affection treated with TCZ.
Methods: We performed this retrospective single center study of all patients with GCA and visual disturbances consecutively seen in our clinic between April 2013 and January 2019 who underwent treatment with tocilizumab in addition to glucocorticosteroids (GC).
Results: 16 GCA patients (13 women, 3 male) with a mean age of 76.3 ± 9.7 yrs at GCA diagnosis and 25 affected eyes were treated with tocilizumab in addition to GC.
2/16 patients presented with visual disturbances under treatment with under prednisone, and 1/16 patient under leflunomide for polymyalgia. 2 patients experienced unilateral blindness while receiving iv pulse GC. AAION was diagnosed in 20/25 eyes, PION in 1/25 eyes and occlusion of the central retinal artery in 4/25 eyes. Loss of vision below 10% occurred in 12/25 eyes. None of the patients had bilateral blindness at baseline. 5/25 eyes were affected by hemi- or sectorial anopsia, blurred vision was reported in 8/25 eyes. 14 patients were treated with TCZ iv 8mg/kg every 4 weeks, 2 patients received sc TCZ at 162mg every 2 weeks.
All patients with visual symptoms received intravenous GC boluses, followed by prednisone 1mg/kg/day with subsequent stepwise reduction. Concomitant treatment consisted of low dose ASS in 11/16 and anticoagulants/NOAKs in 5/16 patients. Statins were used in 9/16 patients. Mean disease duration before initiation of tocilizumab was 3.8 ± 5.7 months. 13/16 patients started with TCZ within 2 months after diagnosis of GCA, in 3 patients TCZ was started because of refractory and/or relapsed disease.
Mean duration of TCZ therapy was 14.8 ± 9.4 months. 9/16 patients were able to stop GC after a mean duration of 14.8 ± 9.5 months and have been steroid-free for an average time of 14.7 ± 10 months (as of January 2019). 4/7 patients with a disease duration of less than 6 months are still on a GC taper at present. In addition to cessation of GC, 4 patients have discontinued TCZ and are drug-free at present for 4, 9, 31 and 35 months, respectively. In 2 additional patients, TCZ dose was decreased and/or the dosing interval extended. None of the 12 eyes with vision < 10% have recovered, but no new vision disturbances occurred during TCZ or after cessation of either TCZ/or GC.
Overall, TCZ was well tolerated with no major side effects. 22 patients experienced vascular complications (stroke, development of an aortic aneurysm) during treatment with TCZ.
Conclusion: Although TCZ was unable to reverse unilateral blindness, no new visual symptoms occurred during or after TCZ treatment and the majority of patients were able to stop or reduce GC.

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FRI0291

RENAL TRANSPLANTATION DUE TO RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (RPGN). COMPARATIVE STUDY WITH NON-AUTOIMMUNE TRANSPLANTATION AND LONG-TERM FOLLOW-UP. STUDY FROM A SINGLE TERTIARY CENTER

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Background: Rapidly Progressive Glomerulonephritis (RPGN) is characterized histology by the presence of crescents and clinically by a rapid and severe decline in kidney function. Thus, this entity may lead to an end stage renal disease, with kidney transplantation. RPGN can be primary, without extra-renal involvement (RPGN-renal-limited), or secondary to systemic autoimmune disorders (RPGN-SAD), infectious diseases or drugs. Kidney transplantation in RPGN-SAD may be associated to a worse outcome.

Objectives: In a series of patients with first transplantation due to RPGN our aim was to assess a) long-term post-transplant survival in RPGN-SAD, b) comparison of post-transplant survival between RPGN-SAD and RPGN-renal-limited and c) comparison of both RPGN (SAD and renal-limited) with a control group of non-immunological disorder, the polycystic kidney disease (PCKD).

Methods: We study three groups of patients: a) RPGN-SAD due to granulomatosis with polyangiitis (n=3), microscopic polyangiitis (n=6) or Goodpasture syndrome (n=2), b) RPGN-renal-limited and c) control group of patients with PCKD. All these patients were transplanted in a single reference University Hospital. The main outcome variables were a) graft and patient survival up to 20 years and b) evolution of renal function (serum creatinine and proteinuria) in the first 5 years of follow-up. Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test. Kruskal-Wallis test was used to compare quantitative variables and chi^2/Fisher's exact test for qualitative variables.

Results: We included a total of 100 patients with renal transplant; a) RPGN-SAD group (n=11), b) RPGN-renal-limited group (n=32), and c) PCKD group (n=57). No significant differences at baseline were observed between the two RPGN groups regarding sex, age and cardiovascular risk factors. Compared to the PCKD group, patients with RPGN presented higher cholesterol levels at the time of the transplant (p=0.041) with no other significant differences. Renal biopsy had been performed in the 43 patients with RPGN: type I (27.9%), type II (4.7%), type III RPGN (41.9%) and 25.6% of patients had not classified RPGN (no immunofluorescence was performed at the time of the biopsy). From 89 patients (of 100) in which a renal biopsy was performed during the first-year post-transplant, rejection was found in 33 patients (37.1%) without significant differences between the 3 groups (5 cases in the RPGN-SAD group, 11 cases in the RPGN-renal-limited group and 17 cases in the PCKD group; p=0.592). The evolution of serum creatinine and the proteinuria after the transplant is shown in **TABLES 1-2**. There were no significant differences between the three groups in the serum creatinine values during at 1st, 6th, 12th, 36th and 60th months post-transplant. Neither differences were found in terms of graft and patient survival between the 3 groups in 20 years of follow-up **(Figures 1 and 2).**

Conclusion: Our study shows similar graft and patient survival as well as renal outcome in renal transplant due to RPGN-SAD and RPGN-renal-limited. These outcomes were also similar in non-immune renal disease. Therefore, renal transplantation could be the best option for patients with end stage renal disease due to RPGN regardless of systemic manifestations.

Table 1. Evolution of creatinine and proteinuria levels after renal transplant in RPGN and PCKD.

	1 Month				6 Months				1 Year			
Serum Creatinine mg/dL	RPGN-renal-limitedl	RPGN-SAD	PCKD	Total	RPGN-renal-limitedl	RPGN-SAD	PCKD	Total	RPGN-renal-limitedl	RPGN-SAD	PCKD	Total
N	27	11	51	89	24	9	48	81	24	8	46	78
Mean±SD	1.81±0.9	2.09±1.65	2.23±1.75	2.08±1.52	1.97±1.34	1.54±0.37	1.74±0.77	1.79±0.95	1.80±1.11	1.48±0.40	1.74±0.88	1.73±0.92
Proteinuria mg/24 h	RPGN Renal	RPGN Systemic	PCKD	Total	RPGN Renal	RPGN Systemic	PCKD	Total	RPGN Renal	RPGN Systemic	PCKD	Total
N	22	9	45	76	23	6	45	74	20	7	41	68
Mean±SD	474.86±432.03	1127.67±290.44	408.22±449.00	512.71±988.84	611.87±832.20*	797.00±556.29*	362.98±323.38*	475.53±561.34*	656.10±1206.68	340.57±175.22	282.54±272.35	398.38±698.81

*p < 0.05

Table 2.

	3 Years				5 Years			
Serum Creatinine mg/dL	RPGN-renal-limitedl	RPGN-SAD	PCKD	Total	RPGN-renal-limitedl	RPGN-SAD	PCKD	Total
N	20	9	41	70	14	10	36	60
Mean±SD	1.69±0.76	1.70±0.69	1.69±0.91	1.69±0.83	1.64±0.80	1.81±0.99	1.82±1.29	1.77±1.13
Proteinuria mg/24 h	RPGN Renal	RPGN Systemic	PCKD	Total	RPGN Renal	RPGN Systemic	PCKD	Total
N	19	7	40	66	13	8	31	52
Mean±SD	510.79±832.90	272.57±291.20	340.65±344.17	382.41±527.44	238.23±311.19	443.88±300.87	579.26±111 4.5	473.17±887.08

	3 Years				5 Years			
Serum Creatinine mg/dL	RPGN-renal-limitedl	RPGN-SAD	PCKD	Total	RPGN-renal-limitedl	RPGN-SAD	PCKD	Total
N	20	9	41	70	14	10	36	60
Mean±SD	1.69±0.76	1.70±0.69	1.69±0.91	1.69±0.83	1.64±0.80	1.81±0.99	1.82±1.29	1.77±1.13
Proteinuria mg/24 h	RPGN Renal	RPGN Systemic	PCKD	Total	RPGN Renal	RPGN Systemic	PCKD	Total
N	19	7	40	66	13	8	31	52
Mean±SD	510.79±832.90	272.57±291.20	340.65±344.17	382.41±527.44	238.23±311.19	443.88±300.87	579.26±111 4.5	473.17±887.08

Figure 1. Patient survival.

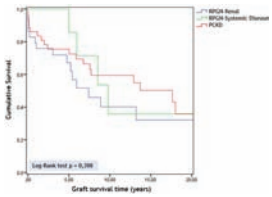


Figure 2. Graft survival.

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FRI0292

A MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY TO EVALUATE THE EFFICACY AND SAFETY OF SIRUKUMAB IN THE TREATMENT OF PATIENTS WITH GIANT CELL ARTERITIS

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Background: Sirukumab (SIR), a selective, high-affinity human monoclonal antibody to the interleukin-6 (IL-6) cytokine, was under development for giant-cell arteritis (GCA) and other diseases.
Objectives: To evaluate the efficacy and safety of sirukumab (SIR) in subjects with GCA.
Methods: This 2-part phase 3 study enrolled subjects with active GCA (NCT02531633). Subjects were randomized in a 3:3:2:2:2 ratio to one of 5 treatment arms: SIR 100 mg SC q2w + 6-mo prednisone taper (SIR100+6mo), SIR 100 mg SC q2w + 3-mo prednisone taper (SIR100 +3mo), SIR 50 mg SC q4w + 6-mo prednisone taper (SIR50+6mo), placebo (PBO) SC q2w + 6-mo prednisone taper (PBO+6mo), PBO SC q2w + 12-mo prednisone taper (PBO+12mo), for 52-week treatment(Part A). Following completion of Part A, subjects could enroll into the study extension with option for open label SIR treatment (Part B). The primary endpoint was the proportion of subjects in sustained remission at Week 52. Secondary endpoints included sustained remission over time, disease flare, and safety. As a result of the early study termination due to administrative reasons, the revised primary endpoint intent-to-treat analysis (revised ITT, N=55) included only subjects who received at least 1 dose of the SC investigational product and had completed 52 weeks (N=28) or had discontinued the study prior to study termination (n=27).
Results: A total of 161 of planned 204 subjects were randomized (mean age 69.6 years, 77.0% female, 98.1% white, 55.9% with new-onset disease). Baseline prednisone dose was ≥30 mg/day in 50.9% of subjects. The proportions of subjects with disease flares from Week 2 (N=155) to Week 52 were lower in the SIR100+6mo (18.4%), SIR 100+3mo (28.2%) and SIR50+6mo (30.8%) arms compared to the PBO+6mo (40%) and PBO+12mo (37%) arms.

Table 1. REVISED ITT*: Summary of Sustained Remission at Week 52 – Part A

Sustained Remission Disposition	SIR100 mg SC q2w + 6 mo prednisone (N=17) n (%)	SIR 100 mg SC q2w + 3 mo prednisone (N=13) n (%)	SIR 50 mg SC q4w + 6 mo prednisone (N=9) n (%)	PBO SC q2w + 6 mo prednisone (N=9) n (%)	PBO SC q2w + 12 mo prednisone (N=7) n (%)
Sustained remission	3 (17.6)	2 (15.4)	1 (11.1)	0	0
Early study withdrawal	8 (47.1)	8 (61.5)	4 (44.4)	4 (44.4)	3 (42.9)
Not in remission at Week 12:	4 (23.5)	6 (46.2)	1 (11.1)	8 (88.9)	4 (57.1)
Reasons for not in remission					
• Presence of signs and symptoms	4 (23.5)	6 (46.2)	1 (11.1)	4 (44.4)	2 (28.6)
• CRP ≥1 mg/dL	4 (23.5)	6 (46.2)	1 (11.1)	7 (77.8)	4 (57.1)
• ESR ≥30 mm/h	4 (23.5)	6 (46.2)	1 (11.1)	7 (77.8)	4 (57.1)

*Including subjects who received at least 1 dose of the SC investigational product and had completed 52 weeks (N=28) or had discontinued the study prior to study termination (n=27).

In Part A, 152 subjects (94.4%) experienced at least 1 treatment-emergent adverse event (TEAE), with similar proportions of subjects across the treatment arms. The most common TEAE's (>10% total subjects) were headache, arthralgia, back pain, cough, upper respiratory tract infection. Treatment-emergent serious adverse events (TESAE) were reported for 31 subjects with similar incidence across all treatment arms. There were no reported deaths, GI perforations or TB activation. Infections and infestations were the most common TESAE, 6 subjects, with no clear difference between SIR and PBO. Two subjects had new onset GCA-related vision loss (SIR100+3mo, n=1; SIR50+6mo, n=1). There were 3 subjects with adjudicated major adverse cardiovascular events (SIR100 +3mo, n=2; PBO+12mo, n=1). NCI CTCAE Grade 3 or 4 laboratory abnormalities of increased ALT, bilirubin, cholesterol, triglycerides and decreased leukocytes, neutrophils, and platelets occurred only in SIR treatment arms (0.6 to 2.5% of total subjects).
Conclusion: As a result of early study termination, only a few subjects, all in SIR treatment arms, achieved the primary endpoint of sustained remission at Week 52. The proportion of subjects with flares from Week 2 – 52 were higher in the PBO arms compared to SIR arms. The overall safety was consistent with the known SIR safety profile.
Study funded by GSK
Disclosure of Interests: Wolfgang Schmidt Grant/research support from: GSK, Roche, Novartis, Sanofi, Consultant for: GSK, Roche, Novartis, Sanofi, Bhaskar Dasgupta Consultant for: Roche, GSK, Sanofi, BMS, Abbvie, Speakers bureau: Roche, Raashid Luqmani Grant/research support from: Roche, Vifor and GSK, Sebastian Unizony Grant/research support from: F. Hoffmann-La Roche, Genentech, Consultant for: Kiniksa, Sanofi, GSK, Zhihong Lai Shareholder of: GSK, Employee of: GSK, Regina Kurrasch Shareholder of: GSK, Employee of: GSK, Ivana Lazic Shareholder of: GSK, Employee of: GSK, Kurt Brown Shareholder of: GSK, Employee of: GSK, Ravi Rao Shareholder of: GSK, Employee of: GSK
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FRI0293

FACTORS ASSOCIATED WITH FIRST-YEAR AND OVERALL MORTALITY IN ANCA ASSOCIATED VASCULITIS; PATIENTS WITH RENAL LIMITED VASCULITIS MAKES NO BETTER THAN MICROSCOPIC POLYANGIITIS

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Background: Overall mortality in ANCA-associated vasculitis (AAV) over the last two decades has been reported to be decreasing with the use of immunosuppressive therapies. However, mortality rates remain high and most of the deaths occur in the first year after diagnosis despite treatment.
Objectives: In this study, we aimed to determine the prevalence of mortality in our AAV patients and to investigate the factors that may be associated with first-year and overall mortality.
Methods: Patients followed up in one center with the diagnosis of AAV were included in the study. Diagnostic subgroups were; granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), and renal-limited vasculitis (RLV). The clinical and demographic characteristics of the patients were collected retrospectively. Factors predictive of mortality were evaluated by Kaplan-Meier method and the Cox proportional hazard model.
Results: In total 104 (45 [43%] female and mean age 54.9 ± 15.4 years) AAV patients (51 GPA; 25 MPA; 27 RLV and 1 EGPA) were included in the analysis. ANCA positivity was detected in 81 (77.9%) patients with IIF and/or ELISA. ESRD had developed in 31 (32.3%) of AAV patients and in 37.8% of patients with renal involvement. Mortality rate was 14.4% in the first year after diagnosis and 27.9% during a median follow-up period of 1289 (5-5804) days. The age at diagnosis was the only significant predictor of first-year mortality (p=0.006). Univariate analysis revealed that overall mortality was associated with AAV subgroups (p = 0.035), renal (p = 0.046) (figure) and, ENT (ear-throat) involvement (p = 0.025), ESRD (p = 0.025) and hemodialysis at the time of diagnosis (p = 0.040). However Cox regression analysis showed age at diagnosis as the only significant predictor also of the overall mortality (*P*=0,001).
Conclusion: Our findings suggest that there could be some survival differences between AAV subgroups and patients with or without renal and ENT involvement. However, the age at diagnosis seems to be the only significant predictor of first-year and overall mortality in our AAV patients.

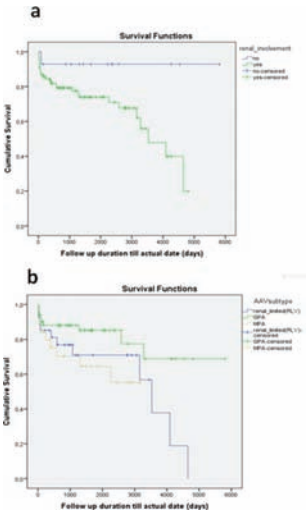


Figure. The results of the Kaplan-Meier analysis. Overall mortality was significantly associated with renal involvement (a) and AAV subgroups (b).

*AAV: ANCA-Associated Vasculitis; GPA: Granulomatosis with PolyAngiitis; MPA: Microscopic PolyAngiitis; RLV: Renal Limited Vasculitis

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FRI0294 CHEMOTHERAPY AND G-CSF INDUCED LARGE VESSEL VASCULITIS AND CAROTIDYNIA – SIX PATIENT CASES AND A SYSTEMATIC LITERATURE REVIEW

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Background: Large vessel vasculitis (LVV) and neutropenic infection in patients receiving chemotherapy present similar clinical symptoms with fever and high inflammation parameters. Infection is more frequent but LVV should be kept in mind as differential diagnosis. LVV is a serious condition which may lead to vessel wall damage. Published few case reports and adverse event reports suggest causal association between LVV and use of granulocyte colony-stimulating factor (G-CSF) and/or chemotherapy (1).

Objectives: To evaluate the rare connection of LVV and anticancer therapy by describing our six patient cases and a systematic review of the literature.

Methods: Between 2016-2018 we identified six patients with probable drug induced LVV associated with chemotherapy and G-CSF. All patients had breast cancer. Systematic literature review was performed according to PRISMA guidelines using comprehensive search terms for breast cancer, chemotherapy, LVV and G-CSF.

Results: In our case series, 5/6 patients developed LVV symptoms within two weeks after administration of docetaxel and G-CSF. Vasculitis symptoms disappeared after drug cessation or drug change.

Literature search identified 16 published case reports with association of LVV and chemotherapy fulfilling our study criteria. Altogether 22 cases were analyzed. Mean age was 59 years (range 40-77 years). In 14/22 cases data from G-CSF administration was available. Time delay from drug administration to LVV symptoms was average 10 days (range 1-42 days) with G-CSF and median 12 days (range 2-310 days) with chemotherapy. Most prevalent cancer types were breast cancer (8/22), hematological malignancies (7/22) and lung cancer (3/22). Most common clinical LVV symptom were fever (18/22), neck pain (11/22) and chest pain (8/22). Diagnosis was confirmed with imaging studies showing vasculitis in various large vessels in upper body. Notably, four cases had vascular inflammation only in carotid region and this was recognized by radiologist as carotidynia/transient perivascular inflammation of the carotid artery (TIPIC) syndrome.

Conclusion: Large vessel vasculitis is a possible serious rare adverse event associated with chemotherapy (possibly docetaxel) and G-CSF. Since signs and symptoms are non-specific, we assume this condition is underdiagnosed and should be kept in mind when treating oncological patients. Successful management requires early identification and cessation of the drug. When diagnosed and treated properly, the recovery is usually fast.

REFERENCE:

[1] Lardieri, A., McCulley, L., Christopher Jones, S. & Woronow, D. Granulocyte colony-stimulating factors and aortitis: A rare adverse event. Am. J. Hematol. 93, E333–E336 (2018).

Disclosure of Interests: Kirsi Taimen Speakers bureau: Pfizer, Novartis, Abbvie, Roche (lectures), Samu Heino: None declared, Ia Kohonen: None declared, Heikki Relas Speakers bureau: Pfizer, Riikka Huovinen Consultant for: Roche, Amgen, Novartis, Pfizer, Speakers bureau: Roche, Amgen, Novartis, Pfizer, Arno Hänninen Speakers bureau: Roche, Laura Pirilä Consultant for: Abbvie, Novartis, Eli Lilly, MSD Finland, Pfizer, UCB, Roche, Jansen- Cilag, Sandoz, Speakers bureau: Pfizer,

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FRI0295 EVALUATION OF CLINICAL CHARACTERISTICS IN BEHCET SYNDROME BY GENDER AND AGE; A SINGLE CENTER EXPERIENCE WITH 665 PATIENTS

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Background: To evaluate clinical characteristics according to age and gender in patients with Behcet's Syndrome (BS).

Objectives: BS is a systemic vasculitis that affects mucosa, skin, joint, eye, vessels, gastrointestinal system, and central nervous system. The disease characterizes by relapses and remissions, and it is known that prognosis is worse in young males. The aim of this study was to reinvestigate the relationship between the clinical features of BS according to gender and age.

Methods: The data of 665 patients (282 male, 383 female), diagnosed as BS according to the ISG-1990 Behçet's Disease classification criteria, were retrospectively evaluated.

Results: All patients had oral aphthous (OA) ulcers (100%). Eighty-five percent of patients had a genital ulcer (GU), 56.5% had erythema nodosum (EN), 65.9% had papulopustular lesions (PPL), 32.6% had ocular involvement, 49.3% had joint involvement, and 21.7% vascular involvement, and 4.8% had neurobehcet. The incidence rates of PPL, ocular involvement, and vascular involvement were significantly higher in males ($p < 0.001$, $p = 0.004$ and $p < 0.001$, respectively). GU, joint involvement, headache, and pathergy positivity were more common in women ($p = 0.006$, $p < 0.001$, $p < 0.001$ and $p < 0.001$, respectively). Table 1 shows the comparison of the clinical features according to gender. When we compare the mean age of the patients according to the presence or absence of clinical findings; patients with GU, EN, and vascular involvement were found to be younger than those without ($p = 0.006$, $p = 0.025$ and $p = 0.007$, respectively) (Table-2).

Conclusion: Clinical features of BS may vary according to age and gender. Variations can be observed depending on the size of the population, the center where the study is conducted, and the selected-criteria for inclusion. In our study, PPL, ocular involvement and vascular involvement were more frequent in men, whereas GU, joint involvement, headache, and pathergy positivity were more common in women. In addition, GU, EN, and vascular involvement were related to younger ages. Our results were compatible with the BS literature.

REFERENCES:

None

Table 1. Characteristics of patients according to gender

Findings	Patients, n (%)	Male (n=282)	Female (n=383)	OR (95%CI)	p
GU, n (%)	571, (85.9)	230 (81.6)	341 (89)	1.84 (1.18-2.85)	**0.006**
EN, n (%)	376, (56.5)	151 (53.5)	225 (58.7)	1.24 (0.91-1.69)	0.181
PPL, n (%)	438, (65.9)	215 (76.5)	223 (58.2)	0.43 (0.30-0.60)	**< 0.001**
Ocular, n (%)	217, (32.6)	109 (38.7)	108 (28.2)	0.62 (0.45-086)	**0.004**
Joint involvement, n (%)	328, (49.3)	114 (40.4)	214 (55.9)	1.87 (1.37-2.55)	**<0.001**
Vascular involvement, n (%)	144, (21.7)	99 (35.1)	45 (11.7)	0.25 (0.17-0.37)	**<0.001**
GI involvement, n (%)	18, (2.7)	8 (2.8)	10 (2.6)	0.92 (0.36-2.36)	0.859
Headache, (n = 581), n (%)	200 (34.4)	46 (19)	154 (45.4)	3.55 (2.41-5.22)	**<0.001**
Neurobehçet's disease, n (%)	32, (4.8)	13 (4.6)	19 (5.0)	1.07 (0.52-2.21)	0.850
Pathergy positivity (n = 384), n (%)	233 (60.7)	91 (54.5)	142 (65.4)	1.58 (1.05-2.39)	0.029

Table 2. Comparison of the age according to the presence of clinical findings

Findings	n	Median age, years (IQR)	p
GU	(+) = 571	30.4 (11.7)	**0.006**
	(-) = 94	34.1 (12.5)	
EN	(+) = 376	30.3 (11.4)	**0.025**
	(-) = 289	31.5 (13.3)	
PPL	(+) = 438	30.5 (12.0)	0.569
	(-) = 227	30.5 (11.1)	
Ocular	(+) = 217	30.5 (12.0)	0.699
	(-) = 448	30.5 (11.5)	
Joint involvement	(+) = 328	30.5 (12.5)	0.723
	(-) = 337	31.1 (11.4)	
Vascular involvement	(+) = 144	29.6 (10.8)	**0.007**
	(-) = 521	31.2 (12.0)	
GI involvement	(+) = 18	27.8 (10.9)	0.211
	(-) = 647	30.5 (11.8)	
Headache, (n = 581)	(+) = 200	30.4 (12.9)	0.374
	(-) = 381	31.0 (11.6)	
Neurobehçet's disease	(+) = 32	29.5 (7.7)	0.160
	(-) = 633	30.5 (11.8)	
Pathergy (n = 384)	Pozitive:233	30.8 (12.6)	0.446
	Negative:151	30.5 (11.8)	

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.4612

FRI0296 INPATIENT PREVALENCE, MORTALITY, EXPENDITURES AND COMORBIDITIES OF POLYARTERITIS NODOSA: NATIONWIDE INPATIENT SAMPLE 2014

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Background: Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis that characteristically affects medium-sized arteries of the intestine, kidneys and soft tissue [1]. Little is known about the inpatient burden, expenditures and association with comorbidities of PAN.
Objectives: To investigate the inpatient prevalence, expenditures and comorbidities of patients with PAN using a national inpatient database.
Methods: Patients with PAN were identified from the Nationwide Inpatient Sample (NIS) database of the years 2014 using ICD-9 diagnostic code. NIS is a publicly available inpatient database that contained data of over 7 million hospital stays, which are a 20% stratified sample of over 4,000 non-federal acute care hospitals across all the regions of the United States (US). Data on patient characteristics, comorbidities, resource utilization and expenditures was collected. The primary outcome was determining the inpatient prevalence of PAN in hospitalized patients in the US. Secondary outcomes included determining inpatient mortality, inpatient morbidity (measured by shock, ICU admission and multi-organ failure), comorbidities, hospital length of stay (LOS) and total hospital costs and charges. The most common reasons for hospitalization were abstracted utilizing the top principal diagnoses in patients with PAN. A cohort of patients without PAN was also identified from the same database to serve as comparators for analysis of comorbidities. Multivariate regression analysis was used to adjust for age, gender, ethnicity, Charlson Comorbidity Index, income, hospital region, location, size and teaching status.
Results: A total of 5,255 patients with PAN were included in the study. The mean age was 58.8 years, and 57% were female. The top reasons for hospitalization were PAN itself (15.3%), sepsis (6.9%), acute kidney injury (4.8%) and acute respiratory failure (2.5%). For the primary outcome, the inpatient prevalence of PAN was found to be 14.9 cases per 100,000 admissions. For secondary outcomes, patients with PAN displayed increased adjusted odds of mortality (OR:1.60, p<0.01), shock (OR:1.81, p<0.01), ICU admission (OR:2.06, p<0.01) and multiorgan failure (OR:3.45, p<0.01) compared to patients without PAN. Patients with PAN also displayed significantly higher hospital costs (additional adjusted mean [aAM]: $10,780, p<0.01), hospitalization charges (aAM: $39,915, p<0.01) and LOS (aAM: 4.2 days, p<0.01) compared to patients without PAN. Patients with PAN displayed a significant association with several comorbidities (Table 1).
Conclusion: The inpatient prevalence of PAN was higher than what would be expected from the overall prevalence. The mean total hospital costs and total hospitalization charges for patients with PAN were higher than patients without PAN. Analysis of comorbidities found significantly higher odds of several comorbidities even after adjusting for potential confounders.

REFERENCE:

[1] Forbess L, Bannykh S. Polyarteritis nodosa. Rheum Dis Clin N Am 2015;41:33-46

Table 1. Adjusted ORs comparing the prevalence of comorbidities between patients with PAN versus patients without PAN

	Adjusted odds ratio	95% CI	*p*-value
DVT	2.07	1.60-2.66	<0.01
PE	2.12	1.62-2.78	<0.01
AMI	1.27	0.79-2.04	0.32
CHF	1.10	0.92-1.32	0.32
Arrythmia	1.05	0.86-1.29	0.61
Peripheral vascular disease	0.86	0.61-1.19	0.36
Acute kidney injury	4.14	3.54-4.85	<0.01
Chronic kidney disease	9.70	7.69-12.22	<0.01
ESRD	5.51	4.41-6.88	<0.01
Intestinal perforation	3.78	1.59-9.01	<0.01
HBV infection	5.01	2.80-8.95	<0.01
HCV infection	1.65	1.12-2.42	0.01
Sepsis	1.87	1.54-2.28	<0.01

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.6577

FRI0297 CLINICAL FEATURES, TREATMENT MODALITIES AND RELAPSE RATES IN GREEK PATIENTS WITH RETROPERITONEAL FIBROSIS

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Background: Retroperitoneal fibrosis (RPF) is a rare disease of unknown etiology characterized by deposition of fibro-inflammatory tissue around the infra-renal abdominal aorta. The process may involve adjacent structures leading to complications, the most frequent being ureteral obstruction [1]. RPF is mainly idiopathic (iRPF), yet it might be secondary to malignancies, infections, drugs, or radiotherapy [2]. Recent data argue that iRPF could be part of the IgG_4-related diseases [3]. Diagnosis is aided by imaging studies (abdomen CT/MRI), but in patients with newly diagnosed RPF, excluding malignancy is mandatory [2].
Objectives: The aim of our study was a) to describe the presenting clinical, laboratory, imaging features and treatment modalities used in patients

with iRPF from four tertiary medical units in Greece and b) to evaluate **factors potentially associated** with **disease relapse.**
Methods: Medical records of patients diagnosed with RPF from 2000-2018 in four rheumatology units (Laiko, Euroclinic, Sismanoglion and Sotiria Hospitals) were retrospectively evaluated. Sixty-seven patients with iRPF were included in the study.
Results: The median age at diagnosis was 56 years (IQR:52.0–60.0), with median disease duration 8.0 years (IQR:3.0-11.0), 58% were smokers and 73% males. Patients more often presented with constitutional symptoms (57%), low back pain (63%), raised inflammatory markers (78%), anemia (43%) and compromised renal function (15%). Commonest imaging findings were periaortic-periiliac mass (46%), periaortic mass (33%), periaortitis (25%) and hydronephrosis (36%) with envelopment of one (31%) or both ureters (18%). Tissue biopsy was requested in all patients, but was performed in only 10, with 3 having marked numbers of IgG4-positive plasma cells. Serum IgG4 was measured in 36/67 and 36% had elevated levels at diagnosis (median 224 mg/dL, IQR:174-328). Clinical/laboratory/radiological presentation did not differ between patients with elevated and normal serum IgG_4 levels. Steroids were first-line treatment in 93% of patients. Other immunosuppressives used as steroid-sparing agents were azathioprine (70%), cyclophosphamide (19%), mycophenolate-mofetil (18%), D-penicillamine (12%) and methotrexate (8%). Relapse occurred in 19% of patients at a median of 36 months (IQR:18-66) after diagnosis with 69% of them being under therapy. Relapse did not correlate to initial imaging findings or to any treatment modality, yet patients with increased serum IgG4 tended to have higher relapse rate (26% vs 11%, p=0.071).
Conclusion: Diagnosis of iRPF was mostly based on imaging studies in our cohort. Steroids were used as first-line treatment. Relapse occurred in one-fifth of patients independently of initial clinical/radiographic presentation or treatment modality used. RPF patients with initially elevated serum IgG_4 levels tended to have a higher relapse rate.

REFERENCES:
[1] Vaglio A, Salvarani C, Buzio C. Retroperitoneal fibrosis. Lancet 2006; 367:241–51.
[2] Brandt AS, Kamper L, Kukuk S, Haage P, Roth S. Associated findings and complications of retroperitoneal fibrosis in 204 patients: results of a urological registry. J Urol. 2011; 185:526-31.
[3] Khosroshahi A, Carruthers MN, Stone JH, Shinagare S, Sainani N, Hasserjian RP, Deshpande V. Rethinking Ormond's disease: "idiopathic" retroperitoneal fibrosis in the era of IgG4-related disease. Medicine (Baltimore). 2013; 92:82-91.

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FRI0298 ABNORMALITY OF PERCENTAGES AND ABSOLUTE NUMBERS OF CD4+T SUBSETS IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND ITS CORRELATIONS WITH CLINICAL INDICATORS

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Background: ANCA-associated vasculitis (AAV) is a heterogenous autoimmune disease with unknown etiology [1-2]. During the last decade, a panel of CD^+ T subsets have been identified. However, the exact role and quantitative status of these subsets in AAV patients remains unclear.
Objectives: We therefore investigated these T cell subsets in AAV patients.
Methods: AAV patients (n = 54) and healthy controls (HCs) (n = 19) were enrolled. Of them, ten patients initially presenting with active disease were assessed again after remission was achieved. In addition, 38 patients were renal vasculitis. Proportions and absolute numbers of peripheral CD4+T cell subsets and expression of multiplex cytokines were determined by flow cytometry (FCM). Correlations of clinical indicators with the CD4+ T cell subsets were systematically analyzed.
Results: Percentages of naive T cells (TN) (p<0.001), terminally differentiated effector (TEMRA) T cells (p=0.027) and activated Treg cells (aTreg) in AAV patients were decreased, but those of effector memory T-cell subpopulation (TEM) (p<0.001), regulatory T cell (Treg) cells and Fox-P3lowCD45RA- T cells were increased. Similar results were observed when we compared absolute numbers of the above corresponding cells in AAV patients and HCs, except TEM. Furthermore, the percentage of aTreg (p=0.043) was decreased while that of Th17 cells (p=0.027) was increased in renal vasculitis patients. A significant correlation was observed between the ratio of Th17 to Treg subset and creatinine or BUN, as well as the ratio of Th17/aTreg was significantly increased in active and renal vasculitis patient. In addition, we found that cytokine IL-2 and IL-4 exhibited a downward while IL-6, IL-10, TNF, IFN-γ and IL-17A trend upward in AAV patients.
Conclusion: There were abnormally quantitative changes in CD4+ T subsets and cytokines in AVV patients, especially the decrease in the relative and absolute number of aTreg (activated Tregs), which indicates an imbalance of pro- and anti-inflammatory T cells. These T subsets might be associated with the ANCA-related autoimmune response and can be used as diagnosis markers for disease activity and as targets for potentially powerful therapy of AAV.

REFERENCES:
[1] Hutton H L, Holdsworth S R, Kitching A R. ANCA-Associated Vasculitis: Pathogenesis, Models, and Preclinical Testing [J]. Seminars in Nephrology, 2017, 37(5):418.
[2] Kerstein A, Silke Schüler, Otávio CabralMarques, et al. Environmental factor and inflammation-driven alteration of the total peripheral T-cell compartment in granulomatosis with polyangiitis [J]. Journal of Autoimmunity, 2016, 78:79.

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FRI0299 THE PREVALENCE OF NON-VASCULAR PULMONARY MANIFESTATIONS IN PATIENTS WITH TAKAYASU' ARTERITIS: A RETROSPECTIVE MULTI-CENTERED COHORT STUDY

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Background: Takayasu' arteritis (TAK) is a rare vasculitis characterized by inflammation and obliteration of intermediate to large-size arteries. Even though more than 50% of patients with TAK have pulmonary artery involvement, non-vascular involvement and symptoms are uncommon.
Objectives: We aimed to investigate the frequency of non-vascular pulmonary involvement in TAK.
Methods: We assembled a retrospective cohort of patients with TAK from six different centers in Turkey. The demographics, clinical characteristics, treatment and outcomes of patients were abstracted from medical records, and the computed tomography findings were evaluated for pulmonary manifestations.
Results: As of January 2019, 197 TAK patients were recruited (mean age: 42.7±13.9 years [min-max: 17-75]) to the cohort, and 88.3% of them were female. Twenty-four patients had cough and/or dyspnea and four had hemoptysis as pulmonary symptoms. In CT assessment, parenchymal infiltrations were present in four (2%), pleural effusion in five (2.5%), nodule/cavity in one (0.5%), and pulmonary hemorrhage in one patient (0.5%). The patient who had pulmonary hemorrhage had also pleural effusion at the same time. In the whole cohort, 11.2% of patients (n=22) had pulmonary hypertension (PAH), three of them had cough and/or dyspnea and four of them had hemoptysis as a pulmonary symptom. Among patients with PAH, any pulmonary involvement in CT was more frequent compared to the rest of the patients (22.7% vs 5.1%, p<0.0001) (Table 1).
Conclusion: In this first assessment of Turkish TAK cohort, we observed non-vascular pulmonary involvement in about 5% of our patients and half of them were pleural effusions. The second most common manifestation was parenchymal infiltration with a frequency of 2%. Although rare, non-vascular pulmonary manifestations should also be investigated in TAK patients, especially in patients with pulmonary hypertension.

REFERENCES:
[1] Nakajima N. Takayasu Arteritis: Consideration of pulmonary involvement. Ann Vasc Dis 2008;1(1):7-10.
[2] Elsasser S, Soler M, Bollinger CT, et al. Takayasu disease with predominant pulmonary involvement. Respiration 2000;67(2):213-5.

Table 1. The frequencies of non-vascular pulmonary manifestations in patients with Takayasu' arteritis

n (%)	All Patients n=197	Patients with PAH n=22	p
Symptoms	24 (12.2)	3 (13.6)	0.049
Cough/Dyspnea	4 (2)	3 (13.6)	0.000
Hemoptysis			
Pulmonary involvement in	10 (5.1)	5 (22.7)	0.000
CT	4 (2)	1 (4.5)	0.000
Pulmonary infiltrates	1 (0.5)	1 (4.5)	0.000
Nodules/cavities	1 (0.5)	1 (4.5)	0.000
Pulmonary hemorrhage	5 (2.5)	2 (9.1)	0.000
Pleural effusion			

(PAH: pulmonary arterial hypertension, CT: computed tomography)

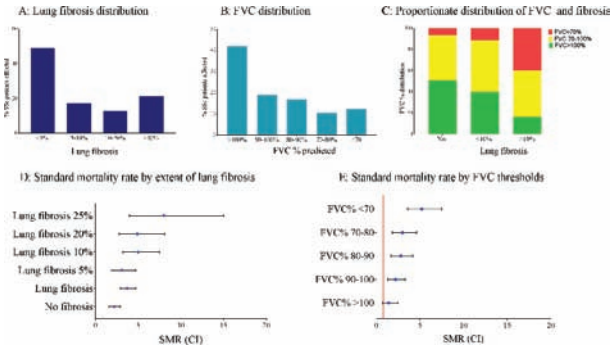
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Scleroderma, myositis and related syndromes

FRI0300 **IMPACT OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS IN A COMPLETE, NATIONWIDE COHORT**

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Background: Interstitial lung disease (ILD) represents a clinical challenge in systemic sclerosis (SSc) and associates with high mortality. The presence of severe lung fibrosis is a strong predictor for early mortality. There is substantial progress in SSc-ILD research, but precise, population-based data on cumulative incidence, range of severity and predictive value of clinical risk factors are lacking. Such data are vital for clinical decision making, and highly warranted as background information for appropriate development of screening and management strategies for SSc-ILD.
Objectives: To assess cumulative incidence of ILD, range of ILD severity and mortality risk predicted by baseline pulmonary function tests (PFT) and ILD extent by CT in a complete, nationwide SSc cohort.
Methods: The Norwegian SSc cohort study (Nor-SSc) includes all the 630 incident and 185 prevalent SSc patients from 2000-2012 meeting SSc classification criteria. A baseline PFT was recorded in 703 (86%) patients, and 650 (80%) had high resolution computed tomography (HRCT) images available for analyses. Extent of fibrosis was scored on 10 sections from every HRCT and expressed as percentage of total lung volumes. For the survival and mortality analyses, all Nor-SSc patients diagnosed from 2000-2012 (the 630 incident cases) were included and compared with 15 age- and gender matched controls per patient drawn from the national population registry. Vital status was available for all patients and controls at study end (January 2018). Descriptive statistics and standardized mortality rates (SMR) were estimated.
Results: Of the 815 patients in the total Nor-SSc cohort, 682 (84%) were female and 629 (77%) had limited cutaneous SSc. Mean age at SSc diagnosis was 53 yrs, with mean time from SSc onset to diagnosis of 3.8 yrs. We observed ILD on HRCT in 324/650 patients (50%), and the majority of these had <5% lung fibrosis (Figure 1A). Mean FVC at baseline was 94% of expected value, and nearly half of the patients (42%) had an FVC>100% (Figure 1B). Proportionate distribution of FVC values in patients with no lung fibrosis, <10% lung fibrosis of total lung volume and >10% lung fibrosis is shown in Figure 1C. During the mean 8.6 yrs observation period of this study, 148 of the 630 incident SSc patients died, corresponding to an overall SMR of 2.4. Separate analyses of the 650 patients with baseline HRCT data showed that the SMR correlated with presence and extent of lung fibrosis, from SMR 2.2 in patients with no fibrosis to SMR 8 in patients with >25% lung fibrosis (Figure 1D). Correspondingly, we found that the SMR changed across patient groups stratified by baseline FVC%, with increased mortality evident already in the FVC 90-100% group (Figure 1E).
Conclusion: The results from this population based SSc cohort study provide new, unbiased data regarding the impact of ILD. Our results indicate a dose-response relationship between lung fibrosis extent and SMR; and between FVC% and SMR. Importantly, this relationship was evident even in groups with limited lung fibrosis and groups with normal range FVC%, strongly suggesting that all SSc patients should be screened with PFT and HRCT at baseline, to diagnose ILD early and tailor further management.



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FRI0301 **GASTROINTESTINAL ADVERSE EVENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) TREATED WITH NINTEDANIB: DATA FROM THE SENSCIS TRIAL**

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Background: In patients with idiopathic pulmonary fibrosis (IPF), nintedanib has a manageable adverse event (AE) profile characterised predominantly by gastrointestinal (GI) events. The efficacy and safety of

nintedanib versus placebo in patients with SSc-ILD were investigated in the SENSCIS trial (NCT02597933).
Objectives: To characterise GI AEs associated with nintedanib therapy in the SENSCIS trial.
Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom <7 years were randomised to receive nintedanib 150 mg bid or placebo double-blind. Dose reductions to 100 mg bid and treatment interruptions were allowed to manage adverse events. AEs reported over 52 weeks of treatment were coded using preferred terms in the Medical Dictionary for Regulatory Activities and analysed descriptively. A questionnaire was used to collect additional information on diarrhoea AEs.
Results: A total of 576 patients (288 per group) received ≥1 dose of nintedanib or placebo. Over 52 weeks, 13.9% and 7.3% of patients treated with nintedanib and placebo discontinued study treatment due to AEs. The most frequent AEs in patients treated with nintedanib were diarrhoea (75.7% vs 31.6%), nausea (31.6% vs 13.5%) and vomiting (24.7% vs 10.4%). Serious diarrhoea AEs were reported in 2 patients (0.7%) in each group, and serious vomiting AEs were reported in 2 patients (0.7%) in the placebo group and none in the nintedanib group. Of the 218 nintedanib-treated patients who experienced a diarrhoea AE, most experienced events that were at worst of mild (49.5%) or moderate (45.0%) intensity, most (70.2%) experienced 1 or 2 events, and the duration of diarrhoea AEs was ≤9 days for 50% of the events reported over 52 weeks. Among nintedanib-treated patients who experienced ≥1 diarrhoea AE, 26.1% had a permanent dose reduction and 9.2% discontinued study drug due to the AE. Among the 91 patients in the placebo group who experienced ≥1 diarrhoea AE, the duration of diarrhoea AEs was ≤3 days for 50% of the events reported over 52 weeks, 2.2% had a permanent dose reduction and 1.1% discontinued study drug due to the AE.
Conclusion: In patients with SSc-ILD, the gastrointestinal AEs associated with nintedanib were manageable for most patients and consistent with its known safety and tolerability profile in patients with IPF.
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FRI0302 **SAFETY AND EFFICACY OF RITUXIMAB BIOSIMILAR IN SYSTEMIC SCLEROSIS: AN ITALIAN MULTICENTER STUDY**

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Background: recent data support the use of rituximab(RTX) in Systemic Sclerosis(SSc). RTX biosimilar(RTX-B) offers a more affordable option but its efficacy and safety have not yet been evaluated.
Objectives: To assess the safety and efficacy of RTX-B in SSc.
Methods: Data about SSc patients treated with RTX-B(1gr repeated after 2 weeks) and with a follow-up ≥6 months were retrospectively collected from 5 Italian centres. Both SSc patients naïve to RTX(RTX-Bn) or already treated with ≥1 course of RTX originator(RTX-O) and switched to RTX-B(RTX-Bs) were considered. A comprehensive assessment of disease features and organ involvement was available at baseline and at final follow-up for all patients. Non parametric tests were used.
Results: Data of 21 SSc patients(20 female, mean age 50.5±11.8 years) were collected;mean disease duration at RTX-B therapy was 7.6±4.8 yrs. Eleven patients(52%) had diffuse cutaneous SSc(dcSSc), 12(57%) were anti-topoisomeraseI+, 5 anti-RNA-polymeraseIII+ and 4 anti-centromere+. Twelve patients(57%) were RTX-Bn and 9 RTX-Bs(43%). In RTX-Bs patients, the median number of previous RTX-O courses was 3(range 1 – 8). RTX was decided because of skin progression in 11(52%), interstitial lung disease(ILD) worsening in 9(43%), arthritis in 6(29%), myocarditis and myositis in 1 patient each. All patients had been previously treated with immunosuppressants: mycophenolate mofetil(MMF) 14(67%), methotrexate(MTX) 7(33%), cyclophosphamide 6(29%), azathioprine 4(19%), tocilizumab and etanercept 1(5%) patient each. At RTX-B introduction, 14 (67%) patients were on concomitant immunosuppressant: 10(48%) MMF and 4(19%) MTX; 15 patients(71%) were also on steroids(mean dose:3.1 ±2.1mg/day). At 6 months after RTX-B treatment, a significant reduction of the modified Rodnan skin score(mRSS), DAS28 and erythrocyte sedimentation rate(ESR) was observed in the entire cohort ($p<0.001$,$p<0.028$, $p<0.003$, respectively); mRSS was significantly reduced also in RTX-Bn ($p<$**0.011**) and RTX-Bs patients($p<$**0.046**)(Table 1). No significant changes were observed for lung function tests. Only 1 RTX-Bs patient experienced a transient neutropenia 3 months after the 2nd RTX-B infusion whilst also on MTX.
Conclusion: in agreement with previous data published on RTX-O, also RTX-B seem efficient in improving skin and joint involvement and in stabilizing lung function, either in RTX-Bn and in RTX-Bs SSc patients.

REFERENCE:
[1] JordanS,et al.AnnRheumDis.2015;74(6):1188-94.

Table 1. Clinical, laboratory and lung functions tests of patients treated with RTX-B. Data expressed as mean±SD. FVC=forced vital capacity(% predicted); TLC=total lung capacity(% predicted); DLCO=diffusion lung CO(% predicted); DAS28=disease activity score 28 (3 RTX-Bn, 3 RTX-Bs) patients with arthritis);ESR(mm/1h).

Overall	Time 0	6 Months	p value
mRSS	11.8±9.3	8.8±7.7	**0.001**
FVC	89.7±21.1	92.8±20.4	0.089
TLC	86.3±19.4	87.9±18.9	0.219
DLCO	62.3±21.0	60.7±18.8	0.542
DAS28	3.6±1.1	2.2±0.9	**0.028**
ESR	21.3±13.0	16.9±9.7	**0.003**
RTX-Bn			
mRSS	12.3±10.6	9.2±8.3	**0.011**
FVC	91.3±22.3	95.3±18.8	0.100
TLC	89.60 ±21.16	93.3±18.5	0.172
DLCO	67.5±19.1	64.3±15.4	0.422
DAS28	4.3±0.4	2.1±1.1	0.109
ESR	21.9±14.8	17.4±11.2	**0.017**
RTX-Bs			
mRSS	11.0±7.8	8.2±5.9	**0.046**
FVC	87.6±20.4	89.4±23.1	0.546
TLC	82.1±17.4	80.1±18.0	0.750
DLCO	56.00 ±22.54	56.33 ±22.49	0.799
DAS28	3.0±1.3	2.4±0.9	0.109
ESR	20.5±11.0	16.2±7.8	0.066

Disclosure of Interests: Corrado Campochiaro Consultant for: Dr Corrado Campochiaro received consultation honoraria from Pfizer., Giacomo De Luca Consultant for: Dr Giacomo De Luca received consultation honoraria from Pfizer and SOBI., Maria Grazia Lazzaroni: None declared, Silvia Laura Bosello: None declared, Maria De Santis: None declared, adriana cariddi: None declared, Carlo Selmi Grant/research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, Alfa-Sigma, Biogen, Bristol-Myrs Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Speakers bureau: AbbVie, Alfa-Sigma, Biogen, Bristol-Myrs Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Elisa Gremese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Paolo Airò: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS; MSD, Janssen, Lorenzo Dagna Consultant for: Prof Lorenzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI.

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FRI0303

THE EFFECTS OF RIOCIGUAT ON RAYNAUD'S PHENOMENON AND DIGITAL ULCERS IN PATIENTS WITH DIFFUSE SYSTEMIC SCLEROSIS: RESULTS FROM THE PHASE IIB RISE-SSC STUDY

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Background: Riociguat is a soluble guanylate cyclase stimulator approved for treatment of pulmonary arterial hypertension associated with connective tissue disease. Through its vasodilatory and anti-remodeling properties, it was predicted that riociguat might relieve Raynaud's phenomenon (RP) attacks and reduce net digital ulcer (DU) burden in patients with diffuse cutaneous systemic sclerosis (dcSSc).

Objectives: We present exploratory endpoints from the RISE-SSc study (NCT02283762) on the effects of riociguat on RP and DUs in early dcSSc patients.

Methods: RISE-SSc was a Phase IIb, multicenter, randomized, double-blind, placebo-controlled study. Inclusion criteria were: SSc fulfilling ACR/EULAR criteria, diffuse cutaneous involvement, disease duration ≤18 months, and modified Rodnan skin score 10−22 units. Patients were assigned to placebo or riociguat individually adjusted from 0.5 mg up to 2.5 mg, 3 times daily. Exploratory efficacy endpoints included 1) change in Raynaud's attacks from baseline to Week 14, assessed by: Raynaud's condition score; patient/physician assessment of RP; attack symptoms, attack duration, and average number of attacks per day; and 2) change in net DU burden from baseline to Week 52, assessed by ulcer count, ulcer burden, and visual analog score for patient-reported severity. Blood samples for exploratory evaluation of biomarkers were taken on Day 0, Week 14 and for discontinuation before Week 14.

Results: 60 patients were treated with riociguat and 61 with placebo. None of the effects of riociguat on RP or DUs were statistically significant vs placebo. However, there was a greater relative reduction in attack duration, attack frequency, pain, numbness, tingling, and patient/physician global assessment in the riociguat group vs placebo, from baseline to Week 14. Reductions in net DU burden were –0.09±0.50 for riociguat and –0.08±1.47 for placebo (estimated treatment difference: –0.11 [95% CI: –0.38, 0.17; p=0.44]) at Week 52. At Week 14, 2 patients in the riociguat group and 6 in the placebo group had developed new DUs. At Week 52, 5 and 12 patients, respectively, had developed new DUs. The total numbers of new DUs were 4 and 6 with riociguat and placebo, respectively, at Week 14, and 12 and 65, respectively, at Week 52 (Figure). Riociguat was associated with reductions vs placebo in serum sPECAM-1 (p=0.004) and CXCL-4 (p=0.008), potentially indicating anti-vasculopathy properties of riociguat.

Conclusion: Riociguat did not produce statistically significant changes in DUs. Riociguat may reduce the development of new DUs in patients with early dcSSc and may favourably improve cytokine vasculopathy.

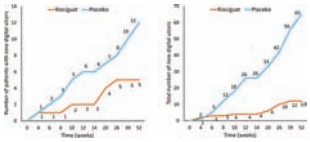


Figure. Development of new digital ulcers

Left: Number of patients with new digital ulcers
Right: Total number of new digital ulcers
New digital ulcers are defined as ulcers not existing at baseline.

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FRI0304 **DEFINITION AND STANDARDIZATION OF INTERSTITIAL LUNG DISEASE ASSESSMENT BY ULTRASOUND: RESULTS FROM A DELPHI PROCESS AND WEB-RELIABILITY EXERCISE BY THE OMERACT ULTRASOUND WORKING GROUP (WG)**

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Background: Interstitial lung disease (ILD) evaluation is challenging, given the low sensitivity of X-ray and pulmonary function tests, and limited accessibility and radiation linked to repetitive HRCT. Lung Ultrasound (US) has shown potential in the evaluation of ILD of autoimmune diseases including systemic sclerosis.
Objectives: To define and asses the reliability of definitions of US-detected findings in ILD.
Methods: A taskforce (TF) within the OMERACT US WG performed a literature review (LR) to identify US lesions in ILD, a Delphi exercise to define these lesions and a web-based exercise to test the reliability of these definitions by using either intraclass correlation coefficient (ICC) or kappa statistics. Prior to the Delphi exercise all participants received training files and were subsequently asked to provide clips on BL, PLI and normal findings. Based on the results of the LR, which identified B-lines (BL) and pleural line irregularity (PLI) as main US findings in ILD, the Delphi exercise contained statements on US definitions on BL and PLI. After reaching agreement (> 75%) on the above mentioned items, a set of 80 high-quality clips (30 for PLI, 50 for BL), was selected and distributed to the TF members in order to score them (semiquantitatively, 0-2 for PLI and total number for BL)
Results: The 3 Delphi rounds and the web-based exercise were completed by 24 and 22 sonographers, respectively. Final definitions are reported in Table I. The web-based exercise showed moderate inter-reader reliability for both BL (ICC=0.61) and PLI (kappa=0.69).
Table I: definitions of PLI and BL
Pleural line irregularity (PLI): a loss of regularity that may be associated with an increase in thickness, focal, diffuse, or nodular
B-line (BL): a vertical hyperechoic reverberation artifacts that arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with lung sliding
Conclusion: US is a candidate imaging modality to identify and monitor ILD in rheumatic diseases; US consensus based definitions of main US findings were defined and endorsed. Further development is planned for validating US as an outcome measurement instrument for ILD.
Disclosure of Interests: Andrea Delle Sedie Speakers bureau: Abbvie, UCB, Celgene, MSD, Lene Terslev Speakers bureau: Speakers fee from : Roche, Novartis, Pfizer, MSD, BMS, Celgene, George Bruyn : None declared, Tomás Cazenave: None declared, stavros chrysidis: None declared, Mario Diaz: None declared, Marco Di Carlo: None declared, Marilena Frigato: None declared, Luna Gargani: None declared, Marwin Gutierrez: None declared, ALOJZIJA HOCEVAR: None declared, Annamaria Iagnocco: None declared, Aaron Juche: None declared, Peter Mandl: None declared, Esperanza Naredo Consultant for: Abbvie, Speakers bureau: AbbVie, Roche, Bristol-Myers Squibb, Pfizer, UCB, Lilly, Novartis, Janssen, and Celgene GmbH, Mohammed A Mortada: None declared, Carlos Pineda: None declared, Francesco Porta: None declared, Viviana Ravagnani: None declared, Carlo Alberto Scirè: None declared, Teodora Serban: None declared, Kate Smith: None declared, Maria Stoenoiu Grant/research support from: Abbvie, Roche, Wyeth, Marika Tardella: None declared, Karina Torralba: None declared, Richard Wakefield: None declared, Maria-Antonietta d'Agostino: None declared
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FRI0305 **PREDICTIVE VALUE OF INNATE LYMPHOID CELLS IN SYSTEMIC SCLEROSIS**

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease with a high morbidity and mortality. Activation of the immune system is a characteristic feature of SSc. Numerous studies have suggested that type 2 and type 3 cytokines are key drivers of progressive fibrosis. Recently, innate lymphoid cells (ILC) are emerging as an important cellular source of type 2 and type 3 cytokines triggering fibrotic tissue remodeling independently of the adaptive immune system. ILCs are characterized by the absence of conventional lineage markers. Similar to T cells, they are categorized into three groups (ILC1, ILC2, ILC3), according to distinct pattern of cytokine production and the requirement of specific transcription factors guiding their development and function. Increased levels of ILC2 were found in patients with SSc. However, the contributive role of ILC2 and ILC3 in pathogenesis of SSc is not completely understood.
Objectives: We aim in our study to evaluate the predictive role of ILC2 and ILC3 in SSc patients.
Methods: We conducted an observational retrospective study on 52 patients with SSc fulfilling the 2013 ACR/EULAR classification criteria. Yearly clinical, laboratory and investigational data according to EUSTAR recommendations were collected. Blood samples collected between 15.09.2014 and 15.01.2015 were analyzed by flow cytometry and ILC2 and ILC3 counts were measured. The predictive value of ILC2 and ILC3 during a 2-year follow-up was analyzed using SPSS 21.0. ILC3 counts were also analyzed in skin sections (10 patients with SSc and 10 healthy controls) by immunofluorescence (IF) staining using two complementary panels of markers. Cytokine production of skin resident ILC3s was additionally analyzed by IF staining.
Results: 52 patients were included in the study, 78% female, 63% limited cutaneous SSc with a mean follow-up time of 2.85 ± 1.28 years. At baseline we have shown that circulating ILC2s are significantly increased compared to gender and age-matched healthy controls. Increased numbers of ILC2s significantly correlated with worsening of mRSS calculated by five point increase in mRSS or 25% increase from baseline ($p < 0.001$; 95% CI 1.39 – 3.26). ILC2 counts also correlated with 5% decrease of diffusion capacity of carbon monoxide (DLCO) during the follow-up time ($p < 0.0001$; 95% CI 1.83 – 3.49). Worsening of forced vital capacity (FVC) assessed as 5% decrease over 2 years was also significantly correlated with an increased number of ILC2s ($p < 0.0001$; 95% CI 1.27 – 3.04). In contrast, we did not find any correlation regarding increase in pulmonary arterial pressure assessed by echocardiography. Although new appearance of digital ulcers could not be predicted by ILC2 counts, increased numbers of ILC2s were correlated with digital ulcers at follow-up. ILC2s did not have a predictive value for death during the follow-up time. In contrast to ILC2, circulating ILC3s were not found to be correlated with worsening of disease activity. However, ILC3s were prominent in fibrotic skin of SSc patients compared to healthy controls, and showed strong production of IL-17.
Conclusion: Here, we provide first evidence for a role of ILC2s as potential prognostic marker of disease progression in SSc. Circulating ILC3 counts were not elevated in SSc. However, ILC3s showed strong cytokine production in the fibrotic skin of SSc patients. The functional impact has to be further evaluated.
Disclosure of Interests: Alina Soare: None declared, Stefanie Weber: None declared, Markus Luber: None declared, Simon Rauber: None declared, Thomas Wohlfahrt: None declared, Georg Schett: None declared, Jörg Distler: None declared, Andreas Ramming Grant/research support from: Novartis
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FRI0306 **IDIOPATHIC INFLAMMATORY MYOPATHIESAND ANTISYNTHETASE SYNDROME: CONTRIBUTION OF ANTISYNTHETASE ANTIBODIES TO IMPROVE CURRENT CLASSIFICATION CRITERIA**

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Background: The presence of muscle weakness and anti-Jo1 anti-amino-acyl transfer RNA synthetase (ARS) autoantibodies, are evaluated in the new EULAR/ACR proposed classification criteria for adult and juvenile idiopathic inflammatory myopathies (IIM), as well as in the Solomon proposed criteria for antisynthetase syndrome (ASSD) diagnosis (1, 2). That favors an overlapping in both criteria fulfillment; however, the ASSD are not considered among the IIM subgroups classification. Anti-Jo1 ARS positivity is the highest weighted criterion in the EULAR/ACR criteria; nevertheless, other ARS were not included. Any ARS positivity is considered in Solomon´s criteria.
Objectives: To evaluate if the detection of non-anti-Jo1 ARS could improve the EULAR/ACR criteria performance, and additionally to contribute to a better classification of the antisynthetase syndromes.
Methods: We performed an observational retrospective study in 2 centers. All patients with clinical suspicion of ASSD or myositis, and positive ARS in the myositis immunoblot (Euroimmun assay) were included. We assessed: 1) The rate of patients meeting EULAR/ACR and Solomon´s criteria; 2) The rate of patients with anti-Jo1 and with non-anti-Jo1 ARS that fulfilled them; and 3) The rate of patients with non-anti-Jo1 ARS meeting the EULAR/ACR criteria if we assign to these antibodies the same weight as anti-Jo1 ARS.
Results: A total of 37 patients were included; 70.3% woman, with a mean age at the moment of the ARS detection of 51.4 (SD±14.0) years. The frequency of ARS was: anti-Jo1 (n=17), anti-PL-12 (n=8), anti-PL-7 (n=4), anti-EJ (n=4), and anti-OJ (n=4).
Twenty-two of 34 patients (59.5%) met EULAR/ACR criteria and 17 (45.9%) met Solomon's criteria. Thirteen patients (35.1%) fulfilled both criteria, representing the 59.1% of those who met EULAR/ACR criteria and the 76.5% of those who met Solomon´s criteria.
Analyzing by antibodies, all patients with anti-Jo1 ARS (n=17) met EULAR/ACR criteria. Among the patients with non-anti-Jo1 ARS (n=20), only 5 (25%) met the criteria; however, if we gave the anti-Jo1 weight to the other ARS when applying the EULAR/ACR criteria, 19 of the 20 cases (95%) would meet them.
Besides, considering the clinical features, 10 of the 20 patients with non-anti-Jo1 ARS (50%) presented clinically objectified muscle weakness, and only 4 of them met EULAR/ACR criteria; nevertheless, weighing any ARS as anti-Jo1, the other 6 cases would be reclassified as IIM.
Conclusion: All cases with anti-Jo1 positivity met EULAR/ACR criteria, but not those with other ARS. Nevertheless, when we applied the EULAR/ACR criteria assigning to all ARS the same weight as anti-Jo1, all except one patient fulfilled the criteria; thus, the most important result was that all patients with clinically objectified muscle weakness and non-anti-Jo1 ARS that initially did not meet the EULAR/ACR criteria could be re-classified as IIM.
In this way, our results suggests that the detection of non-anti-Jo1 ARS in patients with myopathy suspicion, could increase the sensitivity of the EULAR/ACR classification criteria; and that the ASSD, when presents myositis, should be considered among the IIM classification subgroups.

REFERENCES:

[1] Lundberg IE, et al. Annals of the rheumatic diseases. 2017;76(12):1955-64.
[2] Solomon J, et al. Jornal brasileiro de pneumologia. 2011;37(1):100-9.

Disclosure of Interests: Martín Greco: None declared, María Jesús García de Yébenes: None declared, Inmaculada Alarcón: None declared, Anahy Brandy-Garcia: None declared, Iñigo Rua-Figueroa: None declared, Estíbaliz Loza Grant/research support from: Roche, MSD, Pfizer, Abbvie, BMS, UCB, Actelion, Celgene, Grunenthal and Sanofi, Loreto Carmona Grant/research support from: Abbvie, Actelion, Astellas, BMS, Eisay, Gebro Pharma, Grünenthal, Leo Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis and UCB Pharma, Paid instructor for: Novartis
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FRI0307 **LENABASUM, A CANNABINOID TYPE 2 RECEPTOR AGONIST, REDUCES CD4 CELL POPULATIONS AND DOWNREGULATES TYPE 1 AND 2 INTERFERON ACTIVITIES IN LESIONAL DERMATOMYOSITIS SKIN**

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Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 (CB2) agonist that activates resolution of innate immune responses. CB2 is a G-protein coupled receptor found primarily on activated immune cells. In vitro, it has shown to affect T-cell activity, alter Th1 and Th2 cytokine production, and decrease type 1 interferon activity.
Objectives: We sought to characterize the in vivo effect of lenabasum on inflammatory cells and cytokines thought to be involved in the itch and disease pathogenesis of dermatomyositis (DM).
Methods: 22 adult patients with refractory, skin-predominant DM on stable standard-of-care treatments were recruited for a double-blind, placebo-controlled, randomized trial. Treatment was initially administered orally at a dose of 20 mg a day for 4 weeks, and subsequently raised to 20 mg twice a day for an additional 8 weeks. In a subset of subjects, lesional skin biopsies were collected at baseline and at Week 12. Tissues were stained via immunohistochemistry for IFN-beta, IFN-gamma, IL-4, IL-13, IL-33, IL-31, IL-31 RA, CB2 receptor, PPAR-gamma, CD4, CD8, CD69, CD11c, and mast cells. RT-PCR for IFN-beta, IFN-gamma, IL-31, IL-4, STAT6, and ST2 was performed on tissue RNA. Protein expression was quantified either by percent area positive or cells per HPF in the dermis. Statistical analyses were performed using the Wilcoxon signed-rank test.
Results: CD4 expression in the skin biopsies from lenabasum-treated subjects significantly decreased at Week 12 compared to the placebo group ($p<0.05$). There were significant reductions in IFN-beta mRNA and protein, as well as IFN-gamma mRNA and protein at Week 12 in subjects on lenabasum compared to placebo ($p < 0.05$). IL-31 protein ($p < 0.01$) was reduced at Week 12 in subjects who received lenabasum, but IL-31RA protein did not change. CB2 protein decreased significantly in the lenabasum group compared to placebo. There were no changes in IL-4, IL-13, IL-33, and PPAR-gamma protein, or the number of CD8, CD69, CD11c, or mast cells in either group. There was no significant difference in IL-31, IL-4, STAT6, or ST2 mRNA expression.
Conclusion: Lenabasum reduces Type 1 and 2 interferon levels as well as T-helper cell inflammation in subjects with DM. These effects have the potential to inhibit underlying disease pathways in DM, thus contributing to clinical improvement.

REFERENCES:

[1] Kim, H.J., Zeidi, M., Bonciani, D., Pena, S.M., Tiao, J., Sahu, S. and Werth, V.P. Itch in dermatomyositis: the role of increased skin interleukin-31. British Journal of Dermatology. 2018;179(3):669-678.
[2] Robinson ES, Alves P, Bashir MM, Zeidi M, Feng R, Werth VP. Cannabinoid Reduces Inflammatory Cytokines, Tumor Necrosis Factor-α, and Type I Interferons in Dermatomyositis In Vitro. J Invest Dermatol. 2017;137 (11):2445
[3] Wong D, Kea B, Pesich R, Higgs BW, Zhu W, Brown P, et al. Interferon and biologic signatures in dermatomyositis skin: specificity and heterogeneity across diseases. PLoS One. 2012;7(1):e29161.

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FRI0308 **HIGH LEVEL OF SERUM NEOPTERIN IS ASSOCIATED WITH RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE AND REDUCED SURVIVAL IN DERMATOMYOSITIS**

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Background: Neopterin is primarily synthesized and released by activated macrophages/monocytes upon stimulation with interferon-γ and is considered as a marker for macrophage activation.

Objectives: This study aimed to analyze the serum levels of neopterin in patients with dermatomyositis (DM) in association with clinical manifestations, laboratory data and patient prognosis.
Methods: One hundred and eighty-two consecutive DM patients and 30 healthy controls were retrospectively enrolled in the study. Serum levels of neopterin were detected by using the ELISA method. Clinical and laboratory data and patient prognosis were obtained and analyzed in association with serum neopterin.
Results: Serum levels of neopterin were significantly increased in DM patients (median 21.2 nmol/L, IQR 13.9-35.2 nmol/L) compared to healthy controls (median 4.3 nmol/L, IQR 2.9-5.6 nmol/L, P<0.01). High serum neopterin levels were associated with anti-MDA5 antibody, rapidly progressive interstitial lung disease (RP-ILD), and cutaneous involvement including skin ulcer and heliotrope rash. Longitudinal assessment of serum samples revealed that the serum neopterin levels were closely correlated with disease severity. In addition, a significant increase in serum neopterin concentration of non-survivors (median 38.7 nmol/L, IQR 23.5-65.3 nmol/L) was observed when compared to that of survivors (median 19.0 nmol/L, IQR 12.5-29.0 nmol/L) (P<0.01). ROC curves showed that serum neopterin could distinguish non-survivors and survivors at an optimal cut-off level of 22.1 nmol/L with a sensitivity and specificity of 0.804 and 0.625 respectively (P<0.01). Kaplan-Meier survival curves revealed that DM patients with serum neopterin > 22.1 nmol/L had a significantly higher mortality compared to patient group with serum neopterin <22.1 nmol/L (logrank P<0.01). Multivariate Cox regression analysis identified high serum neopterin concentration to be an independent risk factor for poor prognosis in DM (adjusted HR=4.619, 95%CI: 2.092-10.195, P<0.01).
Conclusion: Increased serum levels of neopterin were significantly associated with RP-ILD and reduced survival in DM patients, suggesting it as a promising biomarker in the disease evaluation of DM. These findings highlight the role of cellular immune activation and macrophage activity in the pathogenesis of DM.

REFERENCE:

[1] Murr C, Widner B, Wirleitner B, et al. Neopterin as a marker for immune system activation. Current drug metabolism 2002; 3: 175-87.

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FRI0309 SEVERE ABDOMINAL MANIFESTATIONS IN JUVENILE DERMATOMYOSITIS

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Background: Juvenile dermatomyositis (JDM) is a rare and heterogeneous children-onset idiopathic inflammatory myopathy. It primarily affects skeletal muscle and skin, but also pulmonary, cardiac and gastrointestinal systems in a subset of patients. Gastrointestinal (GI) involvement occurs in 22 to 37% of JDM patients and have been described only in a few case reports.
Objectives: To describe causes of severe abdominal manifestations in JDM patients.
Methods: Retrospective monocentric study. Inclusion criteria were (i) diagnosis of JDM according to the modified Bohan and Peter criteria before 16 years of age, (ii) occurrence of severe involvement of any intra-abdominal organ, (iii) follow-up at Necker Hospital from 2005 to 2018. Severe abdominal manifestation was defined as a potential life-threatening abdominal organ event, need for abdominal surgery and/or parenteral nutrition. Gastrointestinal (GI) involvement was defined by severe abdominal pain, dysphagia, digestive hemorrhage, obstruction, ulceration and/or perforation. Severe hepatitis was defined by an elevation of liver enzymes exceeding five times the upper limit associated with an elevation of γ-glutamyl transferase (γGT) activity and/or liver failure. Abdominal manifestations were classified as certain or probable primary JDM involvement, therapy-related event or infection-related event.
Results: Nine patients with 19 abdominal complications were identified among 110 JDM patients followed during the study period (8,3%). Diagnosis of JDM was made at a median age of 10.7 years-old [range, 3.7 – 14.4], with a median CMAS of 7 [range, 2 – 48], median MMT of 47 [range, 38 – 76], a median creatine kinase level of 3 812 UI/L [range, 170 – 14 054], and a median follow-up of 3 years [range, 0.4 – 6.3]. Seven patients were positive for either anti-NXP2 (n = 4), anti-TIF1-γ (n = 2) or anti-MDA5 (n = 1) antibodies. JDM-related abdominal disease comprised GI involvement (n = 10), acute pancreatitis (n = 4) and hepatitis (n = 3). The revealing symptom for GI involvement and acute pancreatitis was abdominal pain. Five patients with severe abdominal pain, vomiting and/or obstruction, underwent abdominal imaging revealing thickening of colon (n = 2) and/or ileum mucosa (n = 2). Hepatitis was found in 3 patients with an uncommon extensive steatosis with moderate inflammation and perisinusoidal fibrosis (n = 2). Treatment-related complications were considered certain for methotrexate-induced liver toxicity (1 patient) and possible for duodenal perforations (1 patient) 3 days after a methylprednisolone pulse. At last visit, JDM was clinically inactive in four patients. Three patients died from refractory JDM, 2.9 years [range, 2 – 3.6] after the JDM diagnosis, among the 9 patients identified in this study *versus* only 1/92 of the other JDM patients from our cohort.
Conclusion: Primary JDM involvement was the main cause of severe abdominal manifestations and associated to a high mortality rate. We highlight for the first time that pancreatitis should be considered as a main diagnosis in JDM patients who develop severe and/or sustained abdominal pain.
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FRI0310 UNIVERSITY OF CALIFORNIA LOS ANGELES SCLERODERMA CLINICAL TRIALS CONSORTIUM GASTROINTESTINAL TRACT 2.0 REFLUX-SCALE ASSOCIATES WITH IMPAIRED ESOPHAGEAL SCINTIGRAPHY FINDINGS IN SYSTEMIC SCLEROSIS

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Background: The University of California Los Angeles Scleroderma Clinical Trials Consortium gastrointestinal tract 2.0 (UCLA SCTC_GIT 2.0) questionnaire is a self-reported tool including 7-multi-item scales and measuring GI quality of life both in clinical trials and day-to-day clinic care of systemic sclerosis (SSc) patients (1). Scarce data are available on the correlation between patient reported GI symptoms and motility dysfunction as assessed by esophageal scintigraphy.
Objectives: To evaluate the UCLA SCTC_GIT 2.0 score in SSc patients undergoing esophageal scintigraphy and correlate their findings.
Methods: Data of SSc patients admitted to our clinic, undergoing esophageal scintigraphy, were reviewed. The score of UCLA SCTC_GIT 2.0, usually administered to all attending SSc patients, was calculated. Data were expressed as percentage (%) and mean ± standard error. Pearson's test was used for Prism 7 correlation analysis. P < 0.05 was considered significant.
Results: Of all the SSc patients admitted to our clinic from 1stSept 2017 to 31st December 2018, twenty underwent esophageal scintigraphy. Seventeen were female, 4 with diffuse subset, mean age was 51 (± 3.4) years, disease duration of 6.8 (± 1.2 years) years. Twelve (60%) patients reported esophageal (reflux, dysphagia) symptoms, 5 (25%) stomach (early satiety, vomiting) and 9 (45%) intestinal (bloating, diarrhea, constipation) symptoms while 3 (15%) reported no symptoms. Mean ± SE scores of UCLA SCTC_GIT 2.0 items were: reflux 0.8 ± 0.2, distention 0.9 ± 0.2, fecal soiling 0.5 ± 0.2, diarrhea 0.5 ± 1, social 0.5 ± 0.1, emotional 0.5 ± 0.2, constipation 0.5 ± 0.1, and total UCLA SCTC_GIT 2.0 0.6 ± 0.1. Nine (45%) patients had no-mild, 4 (20%) moderate and 7 (35%) severe to very-severe reflux score. Esophageal scintigraphy showed hypomotility in 16 (80%) patients who had a higher UCLA SCTC_GIT 2.0 reflux score compared with the remaining 20% patients (1

± 0.2 vs 0.3 ± 0.2). Fifteen/20 (75%) had an abnormal (<90% within 10 sec) esophageal emptying activity. Percentage of esophageal emptying activity negatively correlated with reflux score (r = - 0.52, p = 0.02) while it did not correlate with the other items scales and the total UCLA SCTC_GIT 2.0 score (p > 0.05).

Conclusion: SSc patients with impaired esophageal scintigraphy findings have a higher GIT2 reflux score. The lack of correlation with UCLA SCTC_GIT 2.0 total score may be related to the composite nature of the score capturing overall GI disease aspects. The UCLA SCTC_GIT 2.0 is a complementary tool for objective measurement of esophageal involvement which can be easily administered in day-to-day clinical assessment. A larger number of SSc patients is needed to confirm these preliminary findings.

REFERENCE:

[1] Khanna D, Hays RD, Maranian P, et al. Reliability and validity of the University of California, Los Angeles Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument. Arthritis Rheum 2009;61:1257-63.

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FRI0311 PREVALENCE AND CLINICAL MANIFESTATIONS OF ERASMUS SYNDROME IN SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY

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Background: Erasmus syndrome (ErS) is defined by the association of exposure to silica with the subsequent development of systemic sclerosis (SSc), with or without associated silicosis.

Objectives: The objectives of this study were, on one hand, to evaluate the prevalence of ErS in a population of SSc patients and to characterize the cases and, on the other hand, to evaluate the clinical and laboratory characteristics of SSc patients with or without exposure to silica.

Methods: We performed a cross-sectional study of the patients with SSc in our department. Demographics, clinical and laboratory data were collected from all patients with SSc diagnosed according to ACR/EULAR criteria. Moreover, a telephone call was made in order to detail the professional activity and possible exposure to silica.

Results: The prevalence of ErS in this population was 15.3% (9/59). All cases identified were male, corresponding to 75% of men with SSc followed at our department. There was a statistically significant association between ErS and male gender (p<0.001), initial pulmonary manifestation (p=0.025), history of digital ulcers (p=0.014) and smoking (p=0.047). On the other hand, a lower risk of gastrointestinal involvement was found in ErS cases (p=0.008). All patients with ErS had positive autoantibodies (mainly anti-Scl70 and anti-centromere) with titters tending to be higher than SSc without ErS, although without statistically significant differences. In addition, although with no statistical significance, we found that pulmonary artery systolic pressure (PASP) estimated by echocardiogram was higher in patients with ErS.

Conclusion: In our study, prevalence of ErS was higher than data from previously published literature. For a more accurate ErS diagnosis it is necessary to be aware of and investigate less intense silica exposures, which may have occurred many years before diagnosis.

Statistically significant differences were found between ErS and SSc without exposure to silica; this fact may have impact in diagnosis, treatment and prognosis.

REFERENCES:

[1] Erasmus L.D. et al.
[2] Pollard K. M. et al.
[3] West S. G.et al.
[4] Elhai M et al.
[5] Ferri C etal
[6] Mora G. F. et al.
[7] Haustein UH et al.
[8] Rosenman KD et al.
[9] Van Loveren H et al.
[10] Rocha L.F. et al.
[11] Sharma RK et al.
[12] Rustin M. H. et al.
[13] Marie I et al.
[14] Magnant J et al.
[15] Van den Hoogen F et al.
[16] Sebastiani M et al.
[17] Leroy EC et al.
[18] Marie I, et al.
[19] Elhai M et al.
[20] Makol A. et al.
[21] Rodnan G.P. et al.
[22] Subrata Chakrabarti et al.
[23] Bello S et al.
[24] Burns C.J. et al.
[25] Galluccio F et al.
[26] Forbes A et al.
[27] MacHugh NJ et al.
[28] Czirjak L et al.

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FRI0312 HYDROXYCHLOROQUINE SIGNIFICANTLY REDUCES SERUM MARKERS OF ENDOTHELIAL INJURY AND NEMO VIDEOCAPILLAROSCOPY SCORE IN SYSTEMIC SCLEROSIS: A 3-MONTHS PROSPECTIVE OBSERVATIONAL STUDY

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Background: The most-commonly postulated model of disease progression in Systemic sclerosis (SSc) is based on the interplay between endothelial damage and tissue repair. Hydroxychloroquine (HCQ) is commonly used in systemic sclerosis (SSc) for the management of joint involvement [1]. In addition, HCQ showed to exert a protective role on endothelial dysfunction in several pathologic conditions [2] but no data exist in SSc.

Objectives: aim of our study was to assess the effect of 3-months HCQ administration on serum levels of markers of endothelial injury and microvascular changes, assessed with NEMO score.

Methods: 20 SSc patients considered for treatment with HCQ 400 mg/day and 16 SSc patients not treated with HCQ were consecutively recruited, having clinical assessment, blood samples and nailfold capillaroscopy (NVC) at recruitment and after 3 months. Median age was 51.5 (19.5). Median onset of Raynaud's phenomenon was 83 (66) months. 29 patients had lSSc and 7 patients dSSc. Both groups had comparable vasoactive drugs, disease activity, duration and subtype. Any kind of overt vasculopathy was an exclusion criteria. The NEMO score was calculated as the total number of micro-haemorrhages (MHE) and microthrombosis (MT) and the giant capillaries (GC) score was calculated as the total number of GC [3]. Serum E-selectin, Endothelin-1 (ET-1), Vascular cell adhesion molecule-1 (VCAM-1), vascular endothelial growth factor (VEGF-A) levels were assayed by Magnetic Luminex Assay, Human Premixed Multi-Analyte Assay (R&D Systems). Plasma dimethyl arginine (ADMA) levels were determined by competitive ELISA (DLD Diagnosticka GMBH). Data were assessed with SPSS software version 25.0 and expressed as median and interquartile range. Wilcoxon rank-sum test, Mann-Whitney U test and Fisher's exact test were used for statistical evaluation. P values < 0.05 were considered significant.

Results: in the group treated with HCQ serum levels of E-Selectin (35.28 (16.88) ng/ml vs 30.84 (12.60) p = 0.004), VCAM-1 (847.30 (344.85) ng/ml vs 761.55 (396.87) p = 0.014) and ET-1 (12.25 (5.53) pg/ml vs 10.94 (4.35) pg/ml (p = 0.022) decreased significantly, as well as NEMO Score (7.5 (11.25) vs 6.5 (8) p = 0.001), MHEs (6 (7) to 5 (5.75) p = 0.003) and MTs (1 (4.5) to 0.5 (2) (p = 0.003). VEGF-A (p = 0.68), ADMA (p = 0.91) and GCs (p = 0.30) were unaffected. No significant improvements were observed among patients not treated with HCQ.

Conclusion: a significant improvement in endothelial function and microvascular involvement was achieved after three months of HCQ treatment. It is a novel finding in SSc which can represent a new therapeutic possibility for the prevention of microvascular complications of the disease

REFERENCES:

[1] Fernández-Codina A, Walker KM, Pope JE; Scleroderma Algorithm Group. Treatment Algorithms for Systemic Sclerosis According to Experts. Arthritis Rheumatol. 2018;70:1820-1828. Doi: 10.1002/art.40560.

[2] Virdis A, Tani C, Duranti E, Vagnani S, Carli L, Kühl AA, et al. Early treatment with hydroxychloroquine prevents the development of endothelial dysfunction in a murine model of systemic lupus erythematosus. Arthritis Res Ther. 2015;17:277.

[3] Andracco R, Irace R, Zaccara E, Vettori S, Maglione W, Riccardi A, et al. The cumulative number of micro-haemorrhages and micro-thromboses in nailfold videocapillaroscopy is a good indicator of disease activity in systemic sclerosis: a validation study of the NEMO score. Arthritis Res Ther. 2017;19:133.

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FRI0313 DIFFERENTIAL PERFORMANCE OF NAILFOLD VIDEO CAPILLAROSCOPIC PARAMETERES IN THE DIAGNOSIS AND PROGNOSIS OF SYSTEMIC SCLEROSIS

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Background: The role of Nailfold Video Capillaroscopy (NVC) in the identification of patients with Raynaud phenomenon (RP) at risk to develop systemic sclerosis (SSc) is well established. However, it is not clear if certain capillaroscopic indices perform better than others at predicting SSc development and which NVC parameters have a prognostic value in established SSc.
Objectives: To comparatively assess the performance of different NVC parameters in predicting development of SSc, very early diagnosis of SSc (VEDOSS), or mixed connective tissue disease (MCTD) in patients with RP. Also, to longitudinally examine the consistency of clinical correlations of NVC parameters in SSc patients at two different time points and evaluate the prognostic capacity of NVC in SSc.
Methods: Consecutive RP patients referred to our department for NVC (138 with SSc, 12 with VEDOSS, 6 with MCTD, 36 with primary RP, and 50 with non-SSc secondary RP) were evaluated at baseline, both clinically and capillaroscopically; 175 were reevaluated after a mean±SD of 3.34±1.48 years. Sixty-two healthy volunteers served as controls. Qualitative assessment of NVC images permitted categorization of patients to a normal, early, active or late capillaroscopic pattern. Capillary loss, dilated, giant or ramified capillaries and micro-hemorrhages were evaluated by a semi-quantitative score (0-3), derived as the mean of three 1mm fields in each of the 2nd, 3rd, 4th and 5th finger of both hands. FVC and DLCO were recorded, if performed within 6 months of NVC. FVC and DLCO deterioration were considered clinically significant if >10% and >15%, respectively. Skin thickening was measured using the modified Rodnan Skin Score (mRSS). MRSS deterioration was considered clinically significant if >3.5. First occurrence of digital ulcers in patients with no prior such history and vital status were also recorded at follow-up.
Results: Capillary loss score had the highest diagnostic accuracy at discriminating patients with an SSc-spectrum disorder from patients with RP of different etiology and from controls, as defined by ROC curve analysis [AUC (95% CI)=0.925 (0.893-0.956)], followed by dilatation score [AUC (95% CI)=0.904 (0.807- 0.938)] and giant score [AUC (95% CI)=0.856 (0.810-0.902)]. By contrast, micro-hemorrhages [AUC (95% CI)=0.727 (0.669-0.786)] and ramification scores [AUC (95% CI)=0.588 (0.521-0.654)] did not perform equally well. Notably, clinical correlations of capillaroscopic parameters in SSc were found not to be consistent over time, when longitudinally assessed at two different time points by univariate and multivariate analysis. Binary logistic regression analysis indicated that baseline capillaroscopic pattern could predict occurrence of a combined adverse disease outcome (FVC deterioration>10% and/or DLCO deterioration>15% and/or mRSS deterioration>3.5 and/or first occurrence of digital ulcers and/or death), after a mean±SD follow up of 3.28±1.45 years in 94 SSc patients with available follow-up data (OR=3.43, p=0.031 for active versus early pattern, OR=8.778, p=0.007 for late versus early pattern).
Conclusion: Dilatation score performs best of all semi-quantitative NVC parameters in diagnosing SSc and although clinical correlations of capillaroscopic findings change over time, an active or late capillaroscopy pattern at baseline is associated with an adverse prognosis.

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FRI0314 SENSITIVITY TO CHANGE AND RESPONSIVENESS TO TREATMENT OF RENAL RESISTIVE INDEX (IRR) IN SYSTEMIC SCLEROSIS (SSC)

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Background: RRI may identify any problem with the blood flow in the renal artery and in the parenchyma. It was shown to be increased in SSc patients and being in relationship with both vascular and fibrotic SSc-related manifestations.
Objectives: to test sensitivity to change and responsiveness to treatment of RRI in SSc.
Methods: patients fulfilling the 2013 ACR/EULAR classification creteria for SSc were enrolled from two SSc-care units, if RRI was determined at least twice since being diagnosed. Data regarding SSc clinical manifestations, instrumental and laboratory evaluation for renal, cardiac and cardiovascular involvement, as well as ongoing immunosuppressive and vasoactive/vasodilating treatment, were collected both at baseline and follow-up RRI measurements.
Results: 230 patients [aged 57 (48-67) years, 12.6% males] were enrolled in the study, with baseline RRI value of 0.68 (IQR 0.07). In a mean 3.4 years follow-up, RRI showed a median change (ΔRRI) of +0.02 (IQR 0.05). ΔRRI was significantly correlated with ΔsPAP (R=0.173, p=0.023) and it was significantly higher in patient with new onset of pulmonary arterial hypertension (0.08 ± 0.02 vs 0.03 ± 0.05; p=0.038). On Cox univariate regression analysis, time from disease onset, ΔssPAP and ΔRRI predicted new PAH, while ΔsPAP was the only independent predictors at multivariate regression analysis. Regarding treatment, Sildenafil exposure determined a significantly lower increase in ΔRRI, with a progressive long-term effect. Conversely, CCBs and Iloprost treated patients showed a significantly higher increase of ΔRRI, which was determined by a higher DU burden. No difference was seen when immunosuppressive treatment was evaluated.
Conclusion: RRI is sensitive to change and reflects, in particular, the worsening of cardio-pulmonary vascular involvement (increase in ΔsPAP and new PAH onset). Moreover, it shows a possible protective effect of Sildenafil in reducing pulmonary vasculature manifestations.

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FRI0315 **SERUM INTERFERON SCORE PREDICTS CLINICAL OUTCOME AT 12 MONTHS IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS AS MEASURED BY GLOBAL RANKED COMPOSITE SCORE (GRCS) AND COMPOSITE RESPONSE INDEX IN SSC(CRISS)**

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Background: Systemic sclerosis (SSc) is a disease orphan of effective disease modifying agents. The diffuse cutaneous subset (dcSSc) is targeted in most clinical trials. Nevertheless, the high variability in clinical outcome at 12 months is limiting effective RCTs design and interpretation. The Global Ranked Composite Score (GRCS) and the Composite Response Index in SSc (CRISS) are the most recent attempts to capture overall response to treatment in dcSSc [1, 2]. Activation of interferon type 1 (IFN) pathway is associated with severe clinical manifestations in SSc. Several studies have indicated that the serum concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10 and CXCL11 are the most relevant to measure IFN induced activation of PBMCs [3-4].
Objectives: Here we aimed to determine whether IFN pathway activation measured by a serum test could be used to stratify patients with dcSSc for severe clinical outcome at 12 months as measured by GRCS and CRISS.
Methods: Serum concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10, and CXCL11 was measured by Luminex xMAP technology (Myriad RBM) in 143 SSc patients and 35 healthy controls (HC). IFN score was calculated as the average of the natural logarithm of the above chemokines. IFN score mean + 2STDV in the HC sera was adopted as cut off for IFN LO (within this range) or HI (above) [5]. Clinical outcomes at baseline and at 12 months were recorded. GRCS and CRISS were calculated at 12 months. GRCS were compared by Mann Whitney test. Fisher exact test was used to analyse the proportion of patients with CRISS of 0% or >0%. CRISS and GRCS correlation was tested by Spearman's rank correlation.
Results: All chemokines had a higher serum concentration in SSc vs HC ($p<0.0001$ for all). Median IFN score was higher in SSc than HC (5.26 vs 4.70, $p<0.0001$). There was no difference associated with disease subset or duration. To simulate enrollment criteria in a RCT we analyzed the 12 months outcomes of the dcSSc patients with ≤6 years disease duration. Sixty six 12-month outcome data were available. 37 were IFN HI and 29 IFN LO at baseline. The IFN HI group had a higher mRSS (median 9.5 vs 5, p= 0.03), CRP (10.2 vs 5, p=0.0003) and NT-proBNP (195 vs 50.5, p=0.001). We recorded 7 deaths for SSc and 5 lung failures (3 FVC drop, 2 DLCO drop); 3 had worsening of FVC, 4 improvement and 49 no change; 11 had worsening of HAQ-DI, 5 improvement and 43 no change; 9 had worsening of mRSS, 7 improvement and 43 no change (table 1). GRCS ranged from -59 to 64 and was negative in 29 (21 IFN HI, 8 IFN LO) and positive in 37 (16 IFN HI, 21 IFN LO). IFN HI patients had a worse outcome at 12 months with GRCS median score of -12 vs 15 in IFN LO (p=0.0271)(fig. 1). Accordingly, GRCS favored IFN LO in 68.4% of 1073 (37*29) pairwise comparisons versus 31.6% of IFN HI (p=0.0001). CRISS was 0 in 46 (28 IFN HI, 18 IFN LO) and >0 in 20 (9 IFN HI, 11 IFN LO). Spearman's rank correlation of the two scores was r= 0.5113. Consistent with GRCS data, CRISS was 0 in 76% of IFN HI vs 62% of IFN LO (P=0.046).
Conclusion: Serum IFN Score predicts worse clinical outcome at 12 months in dcSSc. Stratification for IFN score could aid both in clinical trial design and clinical management. Moreover, here we show that GRCS and CRISS may be sufficiently sensitive to measure difference in composite outcome at 12 months in dcSSc in an observational setting and they correlate with each other in this observational setting.

REFERENCES:

[1] Sullivan KM. N Engl J Med 2018
[2] Khanna D. Arthritis Rheumatol 2016
[3] Liu X. Arthritis Rheum 2013
[4] Maija-Leena Eloranta. Ann Rheum Dis 2010
[5] Bauer JW. PLoS Med 2006

Tab 1

Death		Organ Failure			FVC		HAQ		mRSS	
IFN HI	IFN LO	IFN HI	IFN LO		IFN HI	IFN LO	IFN HI	IFN LO	IFN HI	IFN LO
6	1	4	1	Worsening	1	2	7	4	8	1
				No change	26	23	23	20	20	23
				Improvement	2	2	1	4	3	4

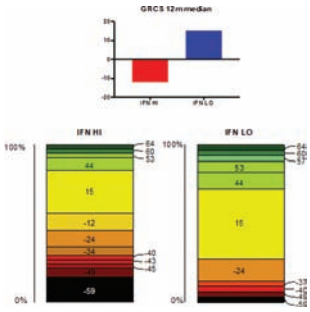


Fig 1

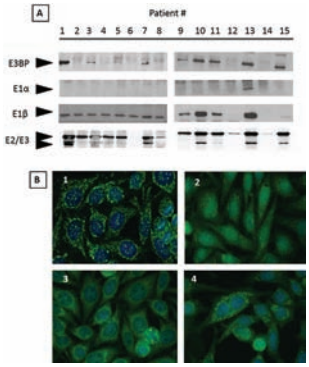
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FRI0316 **SERUM ANTI-MITOCHONDRIAL ANTIBODIES IN SYSTEMIC SCLEROSIS RECOGNIZE VARIABLE PYRUVATE DEHYDROGENASE COMPLEX ANTIGENS**

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Background: Serum anti-mitochondrial antibodies (AMA) are the hallmark of primary biliary cholangitis (PBC) and are identified also in systemic sclerosis (SSc) patients with limited variant and serum anti-centromere antibodies (ACA). Indirect immunofluorescence (IIF) shows the cytoplasmic pattern that characterizes AMA positivity, but it is usually performed when a suspect of PBC is already present. Protein-immunoprecipitation (IP) and IP-Western Blot (WB) have the advantage of 1) identify AMA in an early screening phase, before the onset of PBC and liver function abnormalities; 2) detect the proteins that constitute the pyruvate dehydrogenase complex (PDC) complex (the subunits E1α, E1β, E2/E3, and E3BP) which seem to be associated to different risk of PBC onset.
Objectives: To determine the prevalence and clinical significance of the PDC complex subunits in AMA positive SSc patients with and without PBC.
Methods: Sera from 279 consecutive patients with rheumatic disease (146 with SSc, 77 with undifferentiated connective tissue disease –UCTD-, and 56 with polymyositis/dermatomyositis -PM/DM) were tested by protein-IP for the screening of serum autoantibodies. In 58/279 (21%) sera we report a complete or partial protein-IP pattern of 75-50-40-34kD bands corresponding to the 4 proteins of the PDC complex recognized by AMA. In these sera we performed IIF and IP-WB to confirm the identity of these bands, by using established protocols. Clinical charts were used to analyze clinical and laboratory data for possible statistical correlation.
Results: In 15/58 (26%) patients with protein-IP AMA pattern we confirm a diagnosis of PBC, and all of them had a diagnosis of SSc without additional rheumatic disease. Their expression of the PDC subunits is variable by IP-WB (Figure panel A), but this variability is not associated with specific clinical and laboratory features. In the 42/58 (72%) cases with AMA protein-IP pattern but without clinical and histological evidence of PBC, the E2 component of the PDC was detected in all except one patient, while the expression of the other proteins of the PDC was significantly less represented, i.e. E3BP in 14/42 (33%), E1β in 13/42 (31%), E3 in 6/42 (14%), and E1α in 4/42 (10%) patients. The IIF analysis on Hep2 cells of AMA positive samples also shows different patterns of expression, which spans from cytoplasmic positive staining with a reticular pattern in AMA positive sera for all the PDC proteins recognized by AMA, to cytoplasmic speckled pattern in cases with incomplete expression of PDC antigens (Figure panel B). So far, no specific clinical correlation was identified in these patients, as they did not have a diagnosis of

PBC or other autoimmune liver disease or manifested elevated liver function tests.



Conclusion: The expression of the PDC antigenic components is variable both in SSc patients with AMA positive PBC and in SSc patients AMA positive without PBC or altered liver function tests, but we could not identify a clinical significance of this variability. It may be necessary to maintain a strict follow-up of these patients and to perform longitudinal studies to determine the prognostic value of this variable expression of PDC components in the onset of PBC.

REFERENCES:

[1] Fujimoto M, et al. Arthritis Rheum. 1995 Jul; 38(7): 985-9
[2] Ceribelli A, et al. J Immunol Methods. 2018 Jan; 452: 1-5

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FRI0317 NOVEL CLASSIFICATION OF IDIOPATHIC INFLAMMATORYMYOPATHIES BASED ON DISTINCTIVE FEATURES AND AUTOANTIBODIES: ANALYSIS OF 67 KOREAN PATIENTS

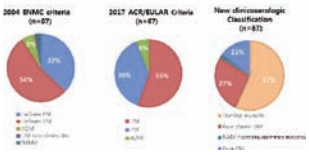
Sang Wan Chung[1], In Seol Yoo[2], Su-Jin Yoo[2], Jinhyun Kim[2], Seong Wook Kang[2], Seungcheol Shim[2], Mihye Kwon[3], Chung-Il Joung[3], Seung-Jae Hong[1], Yeon-Ah Lee[1]. *[1]Kyung Hee University Medical Center, Seoul, Korea, Rep. of (South Korea); [2]Chungnam National University College of Medicine, Daejeon, Korea, Rep. of (South Korea); [3]College of Medicine, Konyanguniversity, Daejeon, Korea, Rep. of (South Korea)*

Background: SinceBohan and Peter first described their diagnostic criteria foridiopathic inflammatorymyopathies (IIM) in 1975, new discoveries suchas myositis-specific and myositis-associated autoantibodies (Abs) have been made.
Objectives: To investigate correlations between specificmyositis Abs and their frequenciesand clinical associationsacross different IIM groups, collectively demonstrating theutility of the new clinicoserologic classification in Koreanadult patients with IIM.
Methods: We conducted a multicenter cohort study including 67adult patients (age≥18 years) who have been diagnosed as IIM by ENMC criteria.Immunoblot assay with Euroline strip(EUROIMMUN, Germany)was performed using the sera of definite deramatomyositis (DM, n=36), definite polymyositis (PM, n=25), amyopathic DM (n=4), DM sine dermatitis (n=1), and immune mediated necrotizing myopathy (IMNM, n=1). Patients were classifiedbased on three classifications: 1) novel clinicoserologic classification suggested by Troyanov et al. in 2017. 2) 2017 EULAR/ACR classification criteria. 3) 2004 European neuromuscular center (ENMC) criteria. Associations ofmyositis Absand clinical subsets of IIM were investigated.
Results: The distribution of the various IIM differed strikingly from those using the 3 classifications (Fig1). According to the 2004 ENMC classification and 2017 EULAR/ACR classification criteria, DM and PM was the most and the second frequent entities (DM: 55.2%, 56.7%; PM: 35.8%, 37.3%). But, using the new clinicoserologic classification,overlapmyositis (OM) is the major type of IIM and the frequency of PM is significantly decreased.Anti-ARS Abs specificity included anti-Jo-1(16.4%), -OJ(4.6%), -EJ(6.2%) -PL-7(3.1%), and -PL-12(4.6%). Interstitial lung disease was closely associated with anti-MDA5,and anti-ARS Abs, while DM-specific skin lesion was frequently observed in patients with anti-TIF1γ and anti-ARS Abs. Sevenpatients with cancer-associated DM were identified. They were positive for anti-TIFγ (5/7) and anti- SRP(3/7) (table 1).

Table 3. Associations between myositis autoantibodies and distinctive clinical features

	Anti-ARS N=21	Anti-SRP N=14	Anti-MDA5 N=14	Anti-TIF1-γ N=9	Anti-Mi2 N=8	Anti-SAE N=3	Total N=67
ILD	20*	5	13†	0	3	1	36
Malignancy	1	3	0	5*	1	0	7
DM specific skin lesion	8*	6	10	9*	5	2	39
Dysphagia	2	2	2	3	2	1	16

Fig 1. Distribution of 67 patients according to 3 classifications for idiopathic inflammatory myopathies



Conclusion: Novel classification based on distinctive features and new myositis Absreflects the clinical phenotype of IIM better. Establishment of a system routinely available to screen myositis Abs is needed. Thiswill be beneficial to providemore precise diagnosis and proper management for patients with IIM.

REFERENCE:

[1] Jean-Luc Senecal, Jean-Pierre Raynauld, Yves Troyanov. A New Classification of Adult Autoimmune Myositis. Arthritis Rheum 2017;69:878-884.

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FRI0318 THROMBOCYTOPENIA AND MULTI-ORGAN INVOLVEMENT MIGHT BE POOR PROGNOSTIC FACTORS FOR SYSTEMIC SCLEROSIS CARDIOMYOPATHY

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Background: Systemic Sclerosis (SSc)-cardiomyopathy is associated with a high mortality in SSc. It is important to identify potential prognostic factors for SSc-cardiomyopathy.
Objectives: To describe the clinical characteristics and identify potential prognostic factors for patients with SSc-cardiomyopathy.
Methods: We retrospectively reviewed the clinical data of SSc-cardiomyopathy patients hospitalized at Sun Yat-Sen Memorial Hospital from January 1992 to November 2018. SSc-cardiomyopathy was defined as structurally and functionally abnormal of heart muscle in SSc patients with cardiac symptoms. Coronary artery disease, hypertension, valvular disease and congenital heart disease were excluded.The Chi-square test was used to compare the differences between the death group and the survival group.
Results:

1. There were 903 SSc patients recruited and 20 patients (2.2%) of them were SSc–cardiomyopathy. Among these 20 patients, 65% were females, age was 52.8±13.2 years, disease duration was 3.1±2.3 years, duration from SSc onset to cardiomyopathy occurred was 2.8±2.3 years.
2. SSc–cardiomyopathy developed in 18 patients (90%) with diffuse cutaneous SSc (dcSSc), and in 2 patients (10%) with limited cutaneous SSc (lcSSc). Eleven patients (55%) had pulmonary fibrosis, 7 patients (35%) had pulmonary arterial hypertension (PAH), 5 patients (25%) had scleroderma renal crisis (SRC) and esophageal involved respectively, 6

patients (30%) manifested thrombocytopenia and 4 patients (20%) manifested anemia.

3. Cardiac symptoms included shortness of breath (n=18), palpitation (n=6), edema of lower extremity (n=4), fatigue (n=5) and/or cough (n=3). All patients were found to have cardiomegaly by echocardiography (UCG) or chest radiography. Left ventricular ejection fraction (47±15%) were decreased. Ventricular wall motion abnormality was found in 5 patients (25%) by UCG. 15 patients (75%) manifested cardiac arrythmia in electrocardiogram, with frequent premature ventricular contractions were the most common (n=10, 50%). Myocardial injury was found in 14 patients (70%) by electrocardiogram. Myocarditis was found in 7 patients (35%) by myocardial enzyme assay.
4. Nine patients (45%) died, the causes of death were heart failure (n=4, 45%), sudden death (n=3, 33%) and ventricular tachycardia (n=2, 22%). 5 patients (55.6%) died within 1 month after the onset of cardiac symptoms. 3 patients died within 2 month, and one patient with implantable cardioversion defibrillation (ICD) died 2 years after ICD implanted. Ten patients survived in a mean 6 (1 10) years follow–up.
5. Six patients (67%) manifested thrombocytopenia and 4 patients (44%) manifested anemia in the death group. However, only one patient (9.1%) in survival group manifested thrombocytopenia (p=0.007) and anemia (p=0.069). There were more organs and systems involved in the death group, compared to the survival group (4±2 vs 2±1, p=0.044). 4 patients had SRC in death group, while 2 patients had SRC in survival group. 6 patients had pulmonary fibrosis in death group, while 5 patients in survival group (Table 1).

Table 1. Comparison between the death group and the survival group in Systemic Sclerosis cardiomyopathy patients.

	Death group (n=9)	Survival group (n=11)	p
Thrombocytopenia, n (%)	6(66.7)	1(9.1)	**0.007**
Anemia, n (%)	4(44.4)	1(9.1)	0.069
Pulmonary fibrosis, n (%)	6(66.7)	5(45.5)	0.343
Pulmonary arterial hypertension, n (%)	3(33.3)	4(36.4)	0.888
Scleroderma renal crisis, n (%)	4(44.4)	2(18.2)	0.202
Esophageal involvement, n (%)	3(33.3)	2(18.2)	0.436
Anti-SCL 70 positive, n (%)	5(55.6)	5(50)	0.653
Myocarditis, n (%)	4(44.4)	3(27.3)	0.423
Numbers of organ involved, mean (SD)	4(2)	2(1)	**0.044**

Conclusion: Thrombocytopenia and multi-organ involvement might be poor prognostic factors for patients of SSc-cardiomyopathy.
Disclosure of Interests: None declared
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FRI0319 ESOPHAGEAL EROSIONS PREDICT PROGRESSION OF LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Interstitial lung d isease (ILD) is the leading cause of death in Systemic Sclerosis (SSc) but its pathogenesis is not fully understood. Esophageal disease is common in SSc and micro aspiration of both acid and non-acid gastroesophageal reflux could be involved in the pathogenesis of ILD. Esophagogastroduodenoscopy (EGD) is an essential tool to evaluate disease severity of upper gastrointestinal tract involvement in SSc.
Objectives: The objective of the present study is to assess the role of EGD in predicting pulmonary functional deterioration in SSc patients.
Methods: One hundred and fifty patients with SSc and suspected esophageal involvement underwent EGD. Pulmonary function tests were performed at baseline and after a 36-months follow-up. Patients were characterized for disease phenotype, BMI, smoking exposure and medication history. A significant ILD progression was defined as a relative decline >= 10% of FVC or a concomitant decline >= 5% of FVC and >= 15% of DLCO.
Results: One hundred and thirty-six patients (90.5%) were female with a mean age of 55.6 ± 13.8 years and 12.1% were active smokers. Fifty patients (33.3%) had a diffuse cutaneous disease; 37.4% and 40.8% were positive for anti-centromere and anti-Scl70 antibodies respectively. The mean disease duration from the first non-Raynaud symptom was 5.9 ±6.7 years. Sixty-one patients (40.8%) showed EGD signs of reflux esophagitis. Among them, 31.3% had an erosive form (9.5% grade A, 15.6% grade B, 4.8% grade C and 1.4% grade D according to Los Angeles classification). At the baseline, 23.1% of the patients had a FVC <= 80% and 45.6% had a DLCO <= 50%. Patients with erosive esophagitis did not differ in terms of sex, age, duration and disease variant, positivity for anti-centromere, skin score values, FVC and DLCO at baseline compared to patients without erosions, but had a lower prevalence of anti-Scl70 (28.3 vs 52.5%, p=0.005) and active smoking (20.0 vs 8.4%, p=0.05). At follow-up, patients with esophageal erosions showed a greater relative decrease in FVC (3.4%±9.3% vs 1.7%±12.0%; p=0.013) without significant differences in the DLCO change. Overall, 11.0% of patients presented pulmonary disease progression. The presence of esophageal erosions was associated with a significantly greater risk of lung disease progression (OR 5.3, 95% CI 1.7-16.8, p=0.004) after paired correction for sex, age, duration of disease, auto-antibodies, skin involvement variant, baseline FVC and DLCO, smoke exposure and therapy with immunosuppressants, proton pump inhibitors, prokinetics, antiplatelet agents and prostanoids.
Conclusion: SSc patients with erosive esophagitis present a higher risk of progression of interstitial lung disease. This evidence supports a role of micro-aspiration of gastric contents in the development of inflammation and fibrosis of the airways.
Disclosure of Interests: Enrico De Lorenzis: None declared, Gerlando Natalello: None declared, Laura Gigante: None declared, Lucrezia Verardi: None declared, Umberto La Porta: None declared, Giovanni Battista Canestrari: None declared, Ludovica Berardini: None declared, Silvia Laura Bosello: None declared, Elisa Gremese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer
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FRI0320 CN-1A AUTOANTIBODIES ARE SPECIFIC FOR SPORADIC INCLUSION BODY MYOSITIS

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Background: Sporadic inclusion body myositis (sIBM) is a subgroup of the idiopathic inflammatory myopathies (IIMs) and is characterized by both degenerative and autoimmune features. Unlike other IIMs, myositis-specific autoantibodies had not been found in sIBM patients until recently.
Objectives: We aimed to establish the prevalence and clinical associations of anti-cN-1A in a large Danish cohort with connective tissue diseases (CTD).
Methods: In a cross-sectional study design, a total of 568 participants (183 IIMs (55 sIBM, 128 non-sIBM: dermatomyositis (DM), polymyositis (PM), immune-mediated necrotizing myopathy (IMNM)), 164 systemic lupus erythematosus (SLE), 121 systemic sclerosis (SSc), and 100 blood donors (BD)) were tested for the presence of: a) cN-1A autoantibodies using a commercial Anti-cN-1A ELISA and b) myositis specific and associated autoantibodies (anti-Jo-1, anti-PL-7, anti-PL-12, anti-OJ, anti-EJ, anti-SRP, anti-Mi-2α/β, anti-MDA5, anti-TIF1γ, anti-NPX2, anti-SAE1, anti-PM-Scl75, anti-PM-Scl100, anti-Ro52, anti-Ku) using a commercial lineblot kit. The patients were classified according to the ACR classification criteria for IIMs (2017), SLE (1997) and SSc (1980), respectively. Clinical features were compared between anti-cN-1A positive and anti-cN-1A negative sIBM patients using two-sample t-test and Mann-Whitney test for continuous normally and non-normally distributed data and Chi-square test for categorical data, as appropriate.
Results: cN-1A antibodies were predominantly found in IIM patients. In the sIBM cohort, 24 patients (43.6%) were anti-cN-1A positive vs. 25 (19.5%) in the non-sIBM myositis cohort and 17 (10%) in the SLE cohort. None of the participants in the SSc or the BD cohorts had

presence of anti-cN-1A. Anti-cN-1A positivity had a sensitivity of 43.6% and a specificity of 91.8% for sIBM. The positive and negative predictive values were 36.4% and 93.8%, respectively.
There was no significant difference in gender, age at study entry, age at symptom onset, duration of symptoms or max creatine kinase (CK) levels during disease course between the anti-cN-1A positive and negative sIBM patients. Dysphagia was present in 19 (79%) of the anti-cN-1A positive and in 17 (55%) of the anti-cN-1A negative sIBM patients (P = 0.06).
Conclusion: Antibodies against cN-1A are the first and so far the only serological marker for sIBM. Our data showed that cN-1A autoantibodies are specific for sIBM and further corroborate the potential diagnostic role of cN-1A autoantibodies in this distinct subgroup of myositis.
Disclosure of Interests: Louise Pyndt Diederichsen: None declared, Sine Søndergaard Korsholm: None declared, Line Vinderslev Iversen: None declared, Christoffer Tandrup Nielsen: None declared, Marie-Louise From Hermansen: None declared, Søren Jacobsen: None declared, Nanna Witting: None declared, Markus E. Krogager: None declared, Tina Friis Grant/research support from: Anti cN-1A ELISA kits and EUROLINE Autoimmune Inflammatory Myopathies 16 AG kits have been provided for a project free of charge from Euroimmun.
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FRI0321 PERFORMANCE OF DIFFERENT PULMONARY HYPERTENSION SCREENING ALGORITHMS IN PATIENTS WITH SYSTEMIC SCLEROSIS PATIENTS

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Background: Pulmonary hypertension (PH) is an important cause of morbidity and mortality in patients with systemic sclerosis (SSc). Different screening algorithms have been proposed for identifying patients who have a high probability of PH and require right heart catheterization (RHC), which is the gold standard for diagnosing PH.
Objectives: To compare the performance of PH screening algorithms in our patients with SSc.
Methods: Forty-eight consecutive patients, fulfilling ACR/EULAR 2013 SSC criteria, were screened for PH using the, 2015 ESC/ERS, DETECT and ASIG algorithms. Pulmonary function tests (PFT), diffusing capacity of the lung for carbon monoxide (DLCO), trans-thoracic echocardiography, serum NT-proBNP, uric acid assay and high-resolution computed tomography (HRCT) were performed as needed. Patients with known PH, severe interstitial lung disease and severe left ventricular dysfunction were not included. RHC was performed in all patients with positive screening according to any one of the screening algorithms. Patients with PH were classified according to the updated PH classification criteria. Sensitivity and specificity of the 3 screening algorithms were evaluated according to the established cut-off value of 25 mmHg for mean systolic pulmonary artery pressure and for the recently proposed cut-off value of 20 mmHg.
Results: Among the 48 SSc patients, 15 were excluded due to already diagnosed PH (n=4), left ventricular dysfunction (n=4), no measurable tricuspid regurgitation velocity (TRV) (n=5) and coexisting lung cancer (n=2). Among the remaining 34 patients, 16 required RHC according to at least one of the screening algorithms. Demographic and clinical features of remaining 34 patients were summarized in Table 1. Number of patients who had suspected pulmonary hypertension and required RHC according to ESC/ERS 2015, DETECT and ASIG were 8 (%25), 9 (% 27), and 13 (%41) respectively (Figure 1). Among the 14 who had RHC, PH was present in 3 patients according to the 25-mmHg cut-off (Group1 in 1, Group 2 in 1, Group 3 in 1) and in 8 patients according to the 20-mmHg cut-off (Group 1 in 5, Group 2 in 2, Group 3 in 1). The sensitivity and specificity of each algorithm is presented in Table 2. Sensitivity was similar at 100% for the 3 algorithms, but the ESC/ERS algorithm had better specificity, when PH was diagnosed with the 25-mmHg cut-off. For the 20-mmHg cut-off, both the sensitivity and the specificity were better with the ESC/ERS algorithm.
Conclusion: The ESC/ERS algorithm seems to have a better performance for detecting PH in patients with SSc. A limitation of this study was that RHC was not performed in patients who did not fulfill criteria according to any of the screening algorithms. The sensitivities may be lower than what we propose if there are patients with PH who are asymptomatic and not captured with any of the algorithms.

Table 1. Demographic and Clinical Features of Patients

	All Patients n=33	ESC/ESR screen positive, n=8 (25%)	ESC/ESR screen negative, n=24 (75%)	DETECT screen positive, n=9 (27%)	DETECT screen negative, n= 24 (63%)	ASIG screen positive, n=13(41%)	ASIG screen negative, n=19 (59%)	Any of the algorithms, n=14 (41%)	Any of the algorithms, n=20 (59%)
Age, median [IQR]	51 [46.75-59.75]	66.5 [59-69.75]	48 [38.75-52]	66.5 [58.25-69.75]	48 [38.5-51.5]	61 [52.75-68.5]	48 [38-51]	57 [50.5-68]	48 [38-51]
Male, n (%)	-	-	-	-	-	-	-	-	-
Female, n (%)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)
Duration of SSc symptoms, year [IQR]	13.5 [5-20.75]	52 [39-57]	65 [51-79.5]	24 [5-38]	12 [5.25-16.75]	14 [5-37]	13 [5-19]	14 [5.25-35.25]	12 [5-17.5]
SSc pattern, n (%)									
Diffuse	10/34 (29)	2/8 (75)	8/26 (31)	1/8 (13)	9/24 (27)	4/13 (31)	6/21 (29)	4/14 (29)	6/20 (30)
Limited	24/34 (71)	6/8 (75)	18/26 (69)	7/8 (87)	15/24 (63)	8/13 (69)	8/23 (61)	10/71	14/20 (70)
SSc related serology, n (%)									
Anti-Scl70 (+)	18/34 (69)	3/6 (50)	15/20 (75)	5/7 (71)	13/18 (72)	6/10 (60)	12/16 (75)	6/10 (60)	12/16 (75)
Anticentromere (+)	3/34 (9)	**3/7 (43)**	**0/20 (0)**	**2/5 (40)**	**1/20 (5)**	**3/10 (30)**	**0/17 (0)**	**3/10 (30)**	**0/17 (0)**
Presence of ILD, n (%)	17/34 (50)	4/8 (50)	13/23 (57)	4/9 (44)	12/24 (50)	7/13 (54)	10/23 (48)	7/14 (50)	10/20 (50)
Presence of digital ulcer(ever), n (%)	21/34 (66)	**4/8 (50)**	**17/24 (71)**	6/9 (67)	14/22 (64)	8/13 (62)	13/19 (68)	9/14 (64)	12/20 (60)
Presence of GIS involvement, n (%)	14/34 (41)	**6/8 (75)**	**8/22 (36)**	**4/9 (44)**	**12/24 (50)**	**7/13 (54)**	**7/21 (33)**	**7/14 (50)**	**7/20 (35)**
Presence of telangiectasia, n (%)	14/34 (41)	5/8 (63)	9/19 (47)	4/9 (44)	10/24 (42)	7/13 (54)	7/21 (33)	**7/14 (50)**	**7/20 (35)**
sPAP on TTE, median (mmHg) [IQR]	28.5 [23.5-33]	36.5 [29.25-46.25]	27 [21.75-31]	33 [29.5-44]	27 [21-31]	30 [25.5-40.5]	27 [19.5-31]	30 [25.75-40.25]	27 [18.75-31]
FVC, median (% predicted) [IQR]	86 [69.5-102.5]	**92 [58.25-115.25]**	**83 [70-99]**	92 [63.5-114]	79 [69.25-100]	92 [67-108.75]	76 [69.5-99]	90 [72-107.5]	74 [69.25-100]
DLCO, median (% predicted) [IQR]	53.5 [41.25-71]	**47 [33.75-56.5]**	**62 [45-76.5]**	55 [36-71]	52 [43-71.75]	50 [35.5-58.5]	63 [46-79]	53 [37.25-62.5]	62 [44-27]
FVC / DLCO ratio, median [IQR]	1.4 [1.1-1.74]	**2.11 [1.58-2.18]**	**1.3 [1-1.4]**	1.6 [1.28-2.18]	1.40 [1.11-1.58]	1.78 [1.35-2.12]	1.35 [1-1.43]	1.71 [1.29-2.12] 1.36 [1.4-1.44]	1.36 [1.04-1.44]
NT-proBNP, median (pg/mL) [IQR]	137 [63-258]	**284 [162-778]**	120 [52-165]	451 [210-887]	120 [52-158]	284 [124.25-695]	120 [38-158]	284 [124.25-695]	120 [38-158]
Presence of dyspnea, n (%)		7/8 (88)	7/26 (27)	**5/9 (56)**	**9/24 (38)**	**7/13 (54)**	**7/21 (33)**	**7/14 (50)**	**7/20 (35)**
WHO-FC, n (%)									
Class 1		1 /14)	-	-	-	-	-	-	-
Class 2		5 (72)	7 (100)	4/5 (80)	9 (100)	6/7 (86)	7/7 (100)	6/7 (86)	7/7 (100)
Class 3		1 (14)	-	1/5 (20)	-	1/7 (14)	-	1/7 (14)	-
Class 4		-	-	-	-	-	-	-	-

GIS: Gastrointestinal system, ILD, Interstitial Lung Disease, Ssc: Systemic Sclerosis, TTE: Transtorasic Echocardiography, WHO-FC: World Health Organization Functional Capacity

Table 2. Performance of the PAH screening algorithms

	Performance for 25-mmHg cut-off			Performance for 20-mmHg cut-off		
	ESC/ESR	ASIG	DETECT	ESC/ESR	ASIG	DETECT
Sensitivity, %	100	100	100	75	100	50
Specificity, %	54	0	40	67	17	0
PPV, %	37.5	29	33	75	41	44
NPV,%	100	100	100	67	0	0

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FRI0322 AUTOANTIBODIES PROFILE INFLUENCE ON SYSTEMIC SCLEROSIS INTERSTITIAL LUNG DISEASE. A TERTIARY SPANISH HOSPITAL EXPERIENCE

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Background: Systemic Sclerosis (SSc) is a rare and heterogeneous connective tissue disease (CTD) characterized by skin fibrosis, vasculopathy/vascular damage and potential visceral impairment. Interstitial lung disease (ILD) constitutes the leading cause of mortality and requires close periodical assessment and follow-up. Diffuse cutaneous sclerosis and specific autoantibody profile (anti SCL70, anti Th/To, Anti U3 RNP and anti PmScl) are considered ILD development risk factors. In contrast, positivity to anticentromere has been considered as a protective factor to develop a clinical significant ILD.
Objectives: To assess ILD frequency and severity (extension and functional impairment) in SSc patients, analyzing the association with the different autoantibodies.
Methods: Retrospective, descriptive study of patients meeting EULAR/ACR 2013 SSc criteria and had a HRTC performed at a tertiary Spanish hospital from 1975 to 2018. One hundred and eight patients were included. HRCTs were graded by two radiologists according to Goh et al semiquantitative score. Three groups were established according to the presence of different autoantibodies: anticentromere (ACA), antitopoisomerase (ATA), and positivity to other ANAs (nucleolar pattern and other specificities).
Results: Clinical and laboratory characteristics are presented in table 1. Thirty-three patients had pulmonary involvement, 6 were ACA+, 18 ATA+ and 9 had other ANA specificities. The probability of not having pulmonary involvement among ACA+ and of having pulmonary involvement among ATA + showed statistic significance ($p<0.001$ and $p<0.001$). Usual intestinal Pneumonia (UIP) was the most frequently reported pattern (6 patients), followed by Non-Specific Interstitial Pneumonia (NSIP 11 patients); Six patients did not meet the radiological criteria for neither UIP or NSIP. No statistical significant difference was found among radiological pattern and autoantibody profile. Regarding extension: 15 patients

had non-extensive involvement (ACA: 2, ATA: 7, "other ANAs": 6) performing Goh et al score with the FVC correction. Extensive ILD was found among 18 patients (ACA: 4, ATA: 11, "other ANAs": 3). Despite the fact that ATA+ group was more likely to have an extensive involvement no statistical significance was met. About pulmonary function tests (PFT) the mean FVC was 98,45% on ACA group, whereas on ATA and other ANAs groups the mean FVC were 88,97% and 81,43% respectively. Statistical differences were found between first and third group, However this difference was not found when only patients with pulmonary involvement were analyzed.

Conclusion: In our cohort, ATA and other ANAs groups were more likely to develop pulmonary interstitial disease and to need inmunosuppressant treatment. Although the prevalence of ILD among ACA+ was only 10%, 50%of them required, due to the functional impairment or extension, inmunosuppressant treatment. In spite of the low ILD-ACA+ incidence this complication should be kept in mind and periodical screening and assessment must be carried out as in other autoantibodies profiles.

Disclosure of Interests: None declared

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Table 1. ACA ATA Other ANA[1]

Table 1	ACA	ATA	Other ANA
Patients, n (%)	60 (55,6)	22 (20,4)	26 (24,1)
Sex Female (%) Male (%)	 57 (95) 3 (5)	 18 (81,8) 4 (18,2)	 21(80,8) 5 (19,2)
Age at diagnosis, median (years)	59	55	61,5
Smoke Active (%) Former (%)	 1,7 23,3	 4,5 4,5	 11,5 26,9
DIAGNOSIS lcSSc (%) dcSSc (%)	 55 (91,7) 4 (6,7)	 4 (18,2) 17 (77,3)	 11 (42,3) 11 (42,3)
Time from diagnosis to ILD, mean (months)	6	5	0
Death,n (%)	8 (57,2)	2 (14,2)	4 (28,6)
PCR, mean (DS)	4,69 (3,9)	5,25 (3,75)	8,08 (8,34)
VSG, median (mm/h)	18	20.5	21
PH (%)	23.7	18.2	19.2
GERD (%)	72,9	77,3	57,7
ILD, n (%)	6 (10)	18 (81,8)	9 (34,6)
FVC, mean (DS)	98,4 (18,5)	88,9 (21,7)	81,42 (22,8)
DLCO, mean (DS)	72,5 (20,4)	75,5 (35,9)	73,4 (20,7)

FRI0323 EVALUATION OF LIPID PROFILE AND ATHEROSCLEROSIS IN TREATMENT-NAÏVE PATIENTS DIAGNOSED WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE (UCTD)

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Background: Patients with UCTD cannot be definitely diagnosed with a **well-characterized systemic rheumatic disease. These patients** often exhibit one of several disease patterns, manifesting multiple nonspecific clinical or serologic abnormalities, sometimes of more than one defined rheumatic disorder.

Objectives: The aim of this study is to investigate lipid profile and atherosclerosis in UCTD patients.

Methods: This is a prospective, observational study which included 30 treatment-naïve UCTD patients. Thirty patients and 30 healthy matched-controls were compared for total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and triglycerides (TGs). Furthermore, in order to describe endothelial dysfunction and presence of atherosclerosis, we assessed intima-media thickness (IMT) of common carotid artery with the contribution of an experienced sonographer. We also measured Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB), Apolipoprotein E (ApoE), Lipoprotein A (LpA), erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (HSCRP) and fibrinogen in the group of patients only.

Results: Thirty UCTD patients were studied. There were 11(36.7%) men, 19(63.3%) women and 7(23.3%) smokers. The mean (SD) age was 54.4 (13.1) years and disease duration was 17.3(10.4) years. All reported Raynaud's phenomenon, 22(73.3%) had esophagus disorders, 21(70%) had pulmonary fibrosis and 3(10%) pulmonary hypertension. Arthritis was present in a great majority of these patients (93%). The immunological evaluation of the patients showed that 4(13.3%) had positive anticardiolipin antibodies and 11(36.7%) had scl-70 (+).

The comparison of IMT between patients and matched-controls revealed an increased IMT in UCTD patients [0.82 (0.32) vs 0.6 (0.13) mm; p<0.001]. There was also a significant difference in mean (SD) TC [204.4(43.03) in patients vs 238(41.4) in controls; p value<0.004] with respective reduced levels of mean(SD) HDL in patients [50.6(9.5) vs 61.3 (13.3); p value<0.002]. No statistically significant difference was found for LDL-c and TGs.

These patients had mean (SD) ApoA1 146.9(27.6), ApoB 94.9(25.6), ApoE 42.1(10.7), LpA 12.8 (15.9), HSCRP 7.5(13.5), ESR 28.9 (22.6) and fibrinogen 422.9(101.3).

Conclusion: IMT measurement confirmed that UCTD patients are prone to endothelial dysfunction and consequently to atherosclerosis. Treatment-naive patients had reduced TC levels in combination with low levels of HDL-c reflecting high disease activity. Control of the disease and initiation of specific therapy may induce an improved lipid profile.

Disclosure of Interests: None declared

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FRI0324 DISEASE ACTIVITY INDICES IN SYSTEMIC SCLEROSIS-WHICH TO USE IN DAILY PRACTICE?

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Background: Currently there is no fully validated index for assessing overall disease activity in patients with systemic sclerosis (SSc).

Objectives: To estimate the effect of disease activity as measured by 4 disease activity indices on the risk of subsequent organ damage in a EUSTAR center cohort.

Methods: Longitudinal observational study; European Systemic sclerosis study group disease activity index (EScSG DAI), revised EUSTAR disease activity index (r-EUSTAR DAI), 12 point activity index proposed by Minier (12point DAI) were calculated for all patients; the CRISS (The Combined Response Index for Systemic Sclerosis) only for patients included after 2016. Student t-test/Mann-Whitney test, chi-square test were used to evaluate differences across subgroups; Pearson's bivariate correlation/Spearman's rank correlation coefficient to evaluate the association between variables. The predictive value of various variables for major organ involvement was assessed by Roc curves and univariate regression.

Results: 91 patients were selected,77 females (84,61%), 51,65(13,20) years old at diagnosis, 49,45% diffuse subset.

Disease activity scores were all higher in male patients and in patients with diffuse cutaneous involvement, digital ulcers(DU), lung fibrosis, sclerodema renal crisis (SRC), arrythmias, muscle atrophy, gastric involvement, antitopoisomerase-1 positive, EscSG DAI correlated with forced vital capacity (FVC)(r=0.73,p<0.001), DLCO(r=0.68,p<0.001), DU(x2= 3.08, p=0.05), lung fibrosis(x2=10.90,p<0.0), systolic pulmonary arterial pressure (sPAP) (r=0.54,p<0.001), muscle atrophy (x2=11,58,p=0.001), diffuse subset (x2=11,46,p=0.001).

R- EUSTAR DAI correlated with FVC(r=0.6,p<0.001), DLCO(r=0,58, p<0.001), diffuse subset(x2=9,52,p<0.01), contractures(x2=11,23,p=0.001), muscle weakness(x2= 6,61,p=0.01), muscle atrophy (x2=10,19, p<0.001), SRC (x2=4,74, p=0.02) and sPAP(r=0.5,p<0.001).

12 point DAI correlated with FVC(r=0.57,p<0.001), DLCO(r=0.66,p<0.001) and sPAP(r=0.42,p<0.001).

EscSG predicted well lung fibrosis (AUC=0.79,p<0.001), DU (AUC=0.66, p<0.001), gastric involvement (AUC=0.73, p<0.01) and SRC (AUC=0.9, p=0.01). R-EUSTAR index also lung fibrosis (AUC=0.76,p<0.001), DU (AUC=0.82,p<0.01) and SRC (AUC=0.84,p=0.04).

12point DAI was a good predictor for lung fibrosis(AUC=0.74,p<0.01), DU (AUC=0.78,p=0.05), gastric involvement(AUC=0.76,p=0.01).

In the regression analysis, lung fibrosis(beta=0.5,95%CI=1,21-2,58,p<0.01), muscle atrophy (beta=1.49, 95%CI=1.02-2.19,p=0.03) and rhythm and conduction disturbancies (beta=1.98, 95%CI=1.31-2.99,p<0.001) were independent predictors for disease activity evaluated by EScSG. For 12-EUSTAR DAI none of the evaluated parameters proved to independently contribuite to disease activity. For 12point DAI items independently

contributing to disease activity were gastric involvement (beta=2.46,95% CI=1.19-5.09, p=0.01) and muscle atrophy (beta=2.05, 95%CI=1.03-4.08, p=0.03).
The CRISS cohort included 35 patients, 32 females(91,42%), 48.48(14.24) years old, 62.85% diffuse subset, medium disease duration 11.88(7.9) months. 8 patients were excluded due to new onset or worsening of lung fibrosis or SRC. None of the patients had a CRISS score with a probability of improvement>0.6.
Conclusion: We could not conclude that there is a gold standard to measure disease activity; for daily practice especially EscSG and r-EUSTAR DAI quantify and predict major organ involvement. CRISS can be useful as an outcome measure for patients with short disease duration and closely monitored in clinical studies.

REFERENCES:

[1] K. Melsens, et al. Disease activity indices in systemic sclerosis: a systematic literature review Clin Exp Rheumatol 2016; 34 (Suppl. 100):S186-S192.

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FRI0325 **IDENTIFYING SYSTEMIC SCLEROSIS PATIENTS AT RISK OF PROGRESSIVE LUNG FIBROSIS – A EUSTAR DATABASE ANALYSIS**

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Background: Early identification of patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) at risk of progression could help tailor management and aid cohort enrichment in clinical trials to improve outcome.
Objectives: To assess the frequency of progressive SSc-ILD in the total ILD cohort and in subgroups enriched by risk factors in the EUSTAR database.
Methods: Patients from the EUSTAR database registered after 2010, ≥18 yrs old, fulfilling SSc classification criteria, with serial lung function and HRCT assessments were eligible. The following risk factors for progressive SSc-ILD available in the EUSTAR database were chosen as enrichment criteria: low forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DL_{CO}), diffuse cutaneous SSc, anti-topoisomerase I antibody (ATA), short disease duration, older age, male sex, increased C-reactive protein, and presence of respiratory symptoms and reflux disease. Eligible patients with progressive ILD were assessed in the cohort and in subgroups enriched by the risk factors. Progressive SSc-ILD was assessed as absolute changes in%predicted and defined as: significant progressive (FVC decline >10%, or FVC decline 5−10% and DL_{CO} decline ≥15%), moderate progressive (FVC decline 5−10%) or stable (<5% FVC change in either direction). The follow-up period was defined as time from baseline to last available lung function test.
Results: 6004 patients fulfilled the main entry criteria; of these, 1822 (30.3%) had ILD. At baseline, mean age was 57 yrs, 17.4% were male, 48.2% had diffuse SSc, 53.5% were ATA-positive, mean baseline FVC 86% and DL_{CO}59%, mean disease duration 9.8 yrs, and follow-up was 2.5 yrs. In the total ILD cohort (30% eligible patients), 21% showed progressive ILD. Enriching with single risk factors reduced the number of eligible patients down to 6%, while the frequency of progressive ILD stayed stable (Figure). Combinations of risk factors did not result in increasing numbers of progressive ILD patients, but in further decreasing numbers of eligible patients.
Conclusion: There is still an unmet need to identify SSc-ILD patients at risk of progression with efficient risk factors. For clinical trials, it is a challenge to balance feasibility of recruitment and enrichment.
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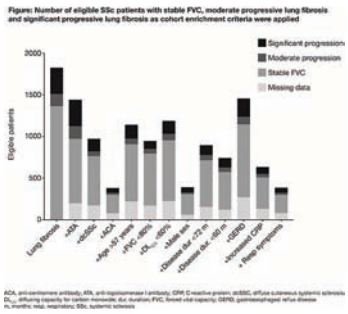


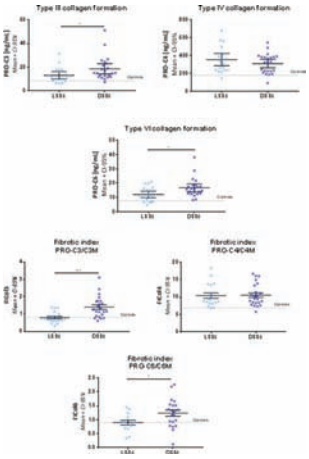
Figure: Number of eligible SSc patients with stable FVC, moderate progressive lung fibrosis and significant progressive lung fibrosis as cohort enrichment criteria were applied

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FRI0326 **SEROLOGICAL ASSESSMENT OF THE FIBROTIC INDEX IN SCLEROSIS: A CROSS SECTIONAL STUDY**

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Background: The hallmark of systemic sclerosis (SSc) is fibrosis of the skin. The interstitial matrix is rich in type I and III collagen while type IV collagen is the main collagen of the basement membrane. These two types of matrix are anchored together by other matrix proteins such as type VI collagen. Tissue turnover is in a delicate equilibrium of tissue formation and degradation, which may be altered in pathologies such as SSc, in which there is a net increase in tissue. By using advanced serological biomarkers tissue turnover, tissue formation and tissue degradation may be assed separately, to quantify the tissue balance. The hypothesis of the current study was that the tissue balance was altered in SSc as compared to healthy, and that limited and diffuse SSc would present with different turnover rates.
Objectives: The objective was to quantify the tissue turnover balance in a cross-sectional study in limited and diffuse SSc.
Methods: Forty-three patients fulfilling the 2013 ACR/EULAR criteria for SSc were included. The study included limited (lcSSc, n= 20) and diffuse SSc (dcSSc, n=23) (recruited at Lund University, approval number Dnr 590/2008). Ten healthy controls were included.
Biomarkers of type III, IV and VI collagen formation (PRO-C3, PRO-C4, PRO-C6) and degradation (C3M, C4M, C6M) were measured cross sectional in serum samples by competitive ELISAs. The fibrotic index of collagens (FICol) were examine (formation/degradation). Difference between groups were tested by Mann-Whitney U test and correlations by Spearman's correlation.
Results: There was no significant difference in gender, age or BMI between lcSSc and dSSc. The mean age of the population was 53.5 years and 79% were female. LcSSc had a longer disease duration (lcSSc: 32.3 month (SD: 41.0), dcSSc: 13.5 month (SD 14.9), P=0.05) and a lower modified Rodnan skin score (mRSS, lcSSc: 4.25 points (SD: 3.1), dcSSc: 20.3 points (11.7), P<0.0001) compared to dcSSc as expected.
Type III and VI collagen formation were both significantly increased in dcSSc compared to lcSSc (PRO-C3: 18.6 ng/ml (SD: 10.0) vs 13.0 ng/ml (SD: 6.5) (P=0.01), PRO-C6: 16.7 ng/ml (SD: 6.6) vs 12.1 ng/ml (SD: 4.9) (P=0.01), Figure 1). Type III collagen degradation were decreased in dcSSc compared to lcSSc (C3M: 13.3 ng/ml (SD: 2.9) vs 17.4 ng/ml (SD: 7.5) (P=0.03)). Neither type IV collagen formation nor type III, IV or VI collagen degradation were significantly different. The fibrotic index of type III and VI collagen (FICol3 and FICol6) were significantly increased in dcSSc compared to lcSSc (FICol3: 1.4 (SD: 0.6) vs 0.8 (SD: 0.3) (P=0.0001), FICol6: 1.2 (SD: 0.5) vs 0.9 (SD: 0.3) (P=0.03), Figure 2). The fibrotic index of type IV collagen (FICol4) were not different between the two groups but were both 1.5 times higher than the levels of healthy (healthy: 6.9, lcSSc 10.4 (SD: 3.3), dcSSc: 10.5 (SD:3,1)).
Both type III and VI collagen formation correlated moderately with mRSS with rho's of 0.53 (P=0.0003) and 0.4 (p=0.008), respectively. FICol3 correlated with a rho of 0.59 (P<0.0001) and FICol6with a rho of 0.35 (P=0.04).



Conclusion: The tissue turnover balance was clearly altered in both limited and diffuse SSc as compared to healthy controls. In addition, diffuse SSc presented with a more screwed balance in the fibrotic index towards tissue formation and disease progression. This study shows the importance of looking at both collagen formation and degradation. The collagen tissue turnover could be beneficial in following patients' fibrosis development and possibly identifying if they are progressing or in remission.
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FRI0327 **EVALUATION OF AMERICAN COLLEGE OF RHEUMATOLOGY PROVISIONAL COMPOSITE RESPONSE INDEX IN SYSTEMIC SCLEROSIS IN A PHASE II TRIAL OF ABATACEPT VS. PLACEBO**

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Background: Treatment with CTLA4Ig, abatacept (ABA), in early diffuse systemic sclerosis (dcSSc; a Phase 2 ASSET trial) showed evidence of improvements in modified Rodnan skin score (mRSS) and secondary outcome measures at month 12[1]; however, statistical significance was not always shown vs. placebo. The ACR CRISS index, a composite outcome measure for trials in SSc[2], is a 2-step process that assigns a probability of improvement for each subject ranging from 0 [no improvement] to 1 [marked improvement]. Step 1 assesses clinically meaningful decline in cardio-pulmonary-renal involvement with a probability of 0. For remaining subjects, probability of improvement is based on 5 variables: changes from baseline to month 12 in FVC%, mRSS, patient (PTGA) and physician global assessments (MDGA), and HAQ-DI.
Objectives: We assessed the performance of ACR CRISS, a secondary outcome measure, in ASSET at month12.
Methods: ASSET was a multicenter double-blind, randomized placebo-controlled trial. Eligible subjects were randomized in a 1:1 ratio to either 12 months of 125 mg SC ABA or matching placebo, stratified by duration of dcSSc (≤18 vs >18 to ≤36 months). Investigators reported SSc end organ involvement (Step 1 for ACR CRISS) prospectively using a case report form. All AEs and SAEs were reviewed for cardio-pulmonary and renal involvement by the study PI. Step 2 calculated the ACR CRISS index as previously defined. Treatment differences, adjusted for duration of dcSSc, in the CRISS score were assessed by the non-parametric Van Elteren test and by ANCOVA for individual CRISS components. We calculated Spearman's correlation coefficients to assess the relationship between the ACR CRISS score and individual components. Multiple imputation was used for analysis, creating 25 complete datasets with estimates, standard errors and p-values pooled over each imputed dataset.
Results: 88 subjects (44 ABA, 44 PBO) were randomized; 63 (72%) had complete data for all relevant outcomes at month 12. 5 PBO and 5 ABA subjects met the pre-defined definition of worsening cardio-pulmonary-renal involvement (Step 1) and were given a score of 0. There is evidence of improved ACR CRISS scores on ABA compared to the PBO at month 12 and the difference was statistically significant (p=0.03; Table). Most variables, except HAQ-DI and PTGA, had statistically significant correlations with the ACR CRISS (Table).
Conclusion: In ASSET trial, the ACR CRISS was more sensitive to clinically meaningful treatment changes than the skin score and provides further validation of ACR CRISS as an independent primary endpoint for clinical trials.

REFERENCES:
[1] Khanna D. ACR Presentation 2018
[2] Khanna D. Arthritis Rheumatol. 2016

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Table. Spearman Correlations between CRISS and individual components at 12 months and Comparison of ABA and PBO using CRISS index and individual components at 12 months;

Outcome		ABA N=44	PBO N=44	Treatment Difference (ABA-PBO)	P-value^
ACR CRISS (0.0-1.0) median (IQR)		0.68 (1.00)	0.01 (0.86)		0.03
	Spearman Correlation	LS mean (SE)	LS mean (SE)	LS mean (SE)	P-value^^
ΔmRSS (0-51)	-0.75*	-6.7 (1.30)	-3.8 (1.23)	-2.9 (1.75)	0.10
ΔFVC% predicted	0.36*	-1.4 (1.30)	-3.1 (1.20)	1.7 (1.72)	0.32
ΔPTGA (0-10)	-0.17	-0.50 (0.392)	-0.30 (0.385)	-0.20 (0.557)	0.73
ΔMDGA (0-10)	-0.47*	-1.34 (0.282)	-0.18 (0.284)	-1.16 (0.403)	0.004
ΔHAQ-DI (0-3)	-0.21	-0.11 (0.079)	0.11 (0.076)	-0.22 (0.108)	0.05

^p-value for treatment comparisons based on Van Elteren test^^p-value for treatment comparisons based on ANCOVA model with treatment, duration of SSc and baseline value as covariates*p< 0.01 using Spearman correlation coefficientNegative score denotes improvement, except for FVC% where negative score denotes worsening; LS mean = least squares mean; SE = standard error

FRI0328 BRANCHED CHAIN AMINO ACIDSIN THE TREATMENT OF POLYMYOSITIS AND DERMATOMYOSITIS: RESULTS FROM THE BTOUGH STUDY

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Background: Muscle functions of patients with polymyositis and dermatomyositis (PM/DM) remain often impaired even after successful control of the immune-mediated muscle injury by immunosuppressive therapy. The only effort at the present to regain muscle functions except for the immunosuppression is rehabilitation, which is carried out systematically in limited institutes. No medicines for rebuilding muscles have been approved. Branched chain amino acids (BCAA) promote skeletal muscle protein synthesis and inhibit muscle atrophy. They thus have positive effects on muscle power, but have never been examined for the effects on PM/DM patients.
Objectives: To assess the efficacy and safety of BCAA in the treatment of PM/DM for official approval of their use in Japan.
Methods: Untreated adults with PM/DM were enrolled in a randomized, double-blind trial to receive either TK-98 (drug name of BCAA) or placebo in addition to the conventional immunosuppressive agents. One package of TK-98 (4.15g) contained L-isoleucine 952mg, L-leucine 1904mg, and L-valine 1144mg (molar ratio is 1:2:1.35), and 6 packages were administered daily in 3 divided doses. After 12 weeks, patients with average manual muscle test (MMT) score less than 9.5 were enrolled in an open label extension study for 12 weeks. The primary end point was the change of the MMT score at 12 weeks. The secondary end points were the disease activity evaluated with myositis disease activity core set (MDACS) and the change of functional index (FI), which evaluates dynamic repetitive muscle functions.
Results: Forty-seven patients were randomized to the TK-98 (24 patients [12 with PM and 12 with DM]) and placebo (23 patients [11 with PM and 12 with DM]) groups. The baseline MMT scores were equivalent (7.97±0.92 [mean±SD] in the TK-98 group and 7.84±0.86 in the placebo group). The change of MMT scores at 12 weeks were 0.70±0.19 (mean ±SEM) and 0.69±0.18, respectively (P = 0.98). Thirteen patients from the TK-98 group and 12 from the placebo group were enrolled in the extension study. The MMT scores in both groups improved comparably throughout the extension study. The increase of the FI scores of the shoulder flexion at 12 weeks was significantly larger in the TK-98 group (27.9±5.67 and 12.8±5.67 in the right shoulder flexion [P < 0.05], 27.0 ±5.44 and 13.4±5.95 in the left shoulder flexion [P < 0.05]). The improvement rate of the average FI scores of all tested motions (head lift, shoulder flexion, and hip flexion) through the first 12 weeks was larger in the TK-98 group. No difference was found in the disease activity throughout the study period. Frequencies of the adverse events until 12 weeks were comparable.
Conclusion: Although BCAA exerted no effects in the improvement of the muscle strength evaluated with MMT, they were effective in the improvement of dynamic repetitive muscle functions in patients with PM/DM without significant increase of adverse events.
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FRI0329 ANALYSIS OF 11 CASES OF ANTI-PL-7 ANTIBODY POSITIVE PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES. MALIGNANCY MAY NOT BE UNCOMMON COMPLICATION IN ANTI-PL-7 ANTIBODY POSITIVE MYOSITIS PATIENTS

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Background: Various autoantibodies are known to be related to idiopathic inflammatory myopathies (IIM). Anti-PL-7 antibody is anti-threonyl-tRNA synthetase antibody associated with antisynthetase syndrome (ASS). Since anti-PL-7 antibody is rare (mostly 1-4% of myositis, while a Japanese study reported 17%), little is known as to clinical characteristics of it (1).
Objectives: To analyze clinical characteristics of anti-PL-7 positive IIM patients.
Methods: Anti-PL-7 antibody was detected by EUROLINE Myositis Profile 3. IIM diagnosis was made by the 2017 EULAR/ACR classification criteria (2) and/or Bohan And Peter classification (3). Eleven anti-PL-7 antibody positive adult patients (all female), age at onset (61.5±12.6 years) were enrolled in this study between 2009 and 2018. Clinical manifestations, laboratory and instrumental data were reviewed in this single centre retrospective cohort.
Results: Characteristic symptoms were identified at diagnosis: skin manifestations (7/11 cases, 63.6%), muscle weakness (8/11 cases, 72.7%), arthralgia (5/11 cases, 45.5%) and Raynaud's phenomenon (4/11 cases, 36.4%). Myogenic enzymes were elevated in most cases (10/11 cases, 90.9%). ILD was detected in all patients (11/11 cases, 100%) and 2 patients (18.2%) developed rapidly progressive ILD. Largest IIM subtype was polymyositis (PM, 5/11 cases), followed by dermatomyositis (DM, 3/11 cases) and amyopathic dermatomyositis (ADM, 3/11 cases). Five patients (45.5%) complicated with malignancy within 3 years from the diagnosis of IIM. Though clinical manifestations and laboratory data showed any difference between malignancy group and non-malignancy group, all 3 ADM cases but no DM cases complicated with malignancy in this study.
Conclusion: Anti-PL-7 antibody positive IIM patients frequently complicated with ILD. Frequency of cancer in ASS patients within three years from diagnosis was 1.7% and not much different from the general population in previous report from France (4). Though this study only included IIM patients and may have selection bias, careful malignancy survey may be essential in Anti-PL-7 antibody positive IIM patients.

REFERENCES:

[1] Y Yamazaki, et al. Unusually High Frequency of Autoantibodies to PL-7 Associated With Milder Muscle Disease in Japanese Patients With Polymyositis/DermatomyositisARTHRITIS & RHEUMATISM Vol. 54, No. 6, June 2006, pp 2004–2009
[2] Lundberg IE, Tjärnlund A, Bottai M, et al. EULAR/ACR classification criteria for adult and juvenile idiopathic inflammatory myopathies and their Major Subgroups. Ann Rheum Dis. 2017;76:1955–64.
[3] Bohan A, Peter J. Polymyositis and dermatomyositis. N Engl J Med 1975, 292: 344-347; 403-407.
[4] Hervier B, et al. Hierarchical cluster and survival analyses of antisynthetase syndrome: phenotype and outcome are correlated with anti-tRNA synthetase antibody specificity. Autoimmunity reviews. 2012; 12:210–217.

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FRI0330 **MALIGNANCIES IN SYSTEMIC SCLEROSIS PATIENTSWITH ANTI-PM/SCL ANTIBODIES: AN EUSTAR CASE- CONTROL STUDY**

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Background: The main clinical associations of anti-PM/Scl in Systemic Sclerosis (SSc) include calcinosis, joint and muscle involvement, interstitial lung disease (ILD), and, possibly, scleroderma renal crisis (1,2). A possible association of anti-PM/Scl with cancer was reported in single-centre SSc series (2,3), but was never analysed in large multicentre studies. Moreover, the characteristics of malignancies, in particular their temporal association with the onset of SSc, were not explored.
Objectives: To evaluate the association of anti-PM/Scl with malignancies in a large, international, multicentre cohort.
Methods: 16 EUSTAR centres provided data on anti-PM/Scl+ SSc patients in their cohorts (cases), and on anti-PM/Scl-negative controls, matched for sex, age at onset (±5 years), cutaneous subset, and disease duration (±24 months). Only SSc patients with age >16 years at disease onset were included in this analysis. Anti-RNA Polymerase3+ patients were not included in controls, given the known association with synchronous cancer. Malignancies diagnosed between 2 years before and after the onset of SSc were defined as "synchronous to the onset of SSc".
Results: 123 anti-PM/Scl+ SSc patients and 160 matched anti-PM-Scl-controls (28% anti-Topoisomerase I, 40% anti-centromere, 32% others) were compared (Table 1): anti-Pm/Scl+ patients had a higher prevalence of myositis (p<0.0001) and ILD (p<0.0001), and a lower prevalence of oesophageal symptoms (p<0.0001). The frequency of malignancies was not significantly different between the 2 groups (14/120 (12%) vs. 9/155 (6%), p:0.12). Only 7 malignancies synchronous to SSc onset were identified: 4 among anti-PM/Scl+ cases and 3 among controls (3 breast cancers; 3 other solid tumours; 1 multiple myeloma). Mean age at SSc onset was significantly higher in patients with synchronous malignancies compared to those without (64.9±7.2 vs. 48.4±14.5 years; p:0.003), irrespective of the anti-PM/Scl status.

	anti-Pm/Scl +	anti-Pm/Scl-	p-value
Age at disease onset (years) (mean (SD)) (n available)	47.9 (15.4) (123)	49.5 (14.3) (160)	0.36
Disease duration (months) (mean (SD)) (n available)	124.9 (87.2) (123)	111.3 (77.1) (160)	0.17
Male sex	21/123 (17.1)	19/160 (11.9)	0.23
Limited cutaneous subset	92/123 (74.8)	119/160 (74.4)	1.00
Smoke (current/previous)	32/121 (26.4)	60/157 (38.2)	0.04
Caucasian ethnicity	110/114 (96.5)	133/143 (93.0)	0.27
Raynaud's phenomenon	115/118 (97.5)	158/159 (99.4)	0.32
Esophageal symptoms	69/123 (56.1)	121/160 (75.6)	<0.0001
Scleroderma renal crisis	5/123 (4.1)	3/153 (2.0)	0.25
Active digital ulcers	13/123 (10.6)	22/160 (13.8)	0.47
Joint synovitis	23/123 (18.7)	36/158 (22.8)	0.46
Arrythmia requiring specific therapy	7/122 (5.7)	22/159 (13.8)	0.03
Lung fibrosis on HRCT	78/119 (65.5)	53/152 (34.9)	<0.0001
PAH confirmed on RHC	4/123 (3.3)	12/158 (7.6)	0.19
Clinical signs of myositis	45/123 (36.6)	17/160 (10.6)	<0.0001
Calcinosis	42/123 (34.1)	34/157 (21.7)	0.02
Death (any cause)	8/123 (6.5)	7/160 (4.4)	0.44
GAVE	3/123 (2.4)	0/160 (0)	0.08
Malignancies (ever)	14/120* (11.7)	9/155* (5.8)	0.12
Malignancies synchronous (±2 years)	4/120* (3.3)	3/155* (1.9)	0.70

Table 1. Univariate analysis comparing anti-Pm/Scl+ (cases) and anti-Pm/Scl- (controls) SSc patients. *patients with <2 years follow-up were excluded. Results are presented as number/number available data (%) unless stated otherwise. P-Value after Bonferroni correction was obtained for a p value <0.0025

Conclusion: in this EUSTAR multicentre case control-study, the association of anti-Pm/Scl with malignancies in SSc patients could not be confirmed. Patients with older age at SSc onset seems to be at higher risk for synchronous malignancies, regardless the autoantibody status.

REFERENCES:

[1] Lazzaroni MG, et al. Ann Rheum Dis 2018; 77:(Suppl 2), 421-422.
[2] Bruni C, et al. Rheumatology (Oxford). 2017;56:317-8.
[3] Bernal-Bello D, et al. Autoimmun Rev 2017;16:461-8.

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FRI0331 **HISTORY OF SILICA DUST EXPOSURES AND ASSOCIATION WITH CHEST HRCT AND CLINICAL CHARACTERISTICS IN SYSTEMIC SCLEROSIS**

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Background: The association of a history of silica exposure with precise chest high-resolution computed tomography (HRCT) features are still to be determined in SSc patients fulfilling the 2013 EULAR/ACR classification criteria. A recent study highlighted that mediastinal lymph nodes were associated with worse prognosis in all-cause interstitial lung diseases (ILD) (1). Nonetheless, the links between mediastinal lymphadenopathies (LA) and silica exposure in SSc patients have never been studied to date.
Objectives: The aim of this study was to assess the association of exposures to inorganic particles on the whole life course, with the HRCT characteristics in an unselected population of SSc patients.
Methods: A specific questionnaire based on a multidisciplinary approach (social sciences, epidemiology, occupational health and medicine) was used to assess occupational and non-occupational exposures to inorganic particles, with a specific interest on silica exposures in 100 SSc patients fulfilling the 2013 EULAR/ACR classification criteria. Clinical characteristics and chest HRCT at diagnosis were evaluated to assess the association of dust exposure with disease characteristics. The most recent chest HRCT was also evaluated and compared to HRCT at diagnosis to assess pulmonary evolution. All HRCT were evaluated by 3 experts, blinded for the results form dust exposure questionnaire.
Results: Men had significantly higher global and occupational dust-exposure scores than women. Sixty-five percent of men with SSc (n=17) had an occupational exposure to silica. Thirty-five percent of patients had thoracic LA and 12% an association of mediastinal and hilar LA. Male gender, history of tobacco use, dcSSc, positivity for ATA, thoracic LA and pneumoconiosis were significantly associated with occupational exposure to silica (p<0.05 for all). The presence of mediastinal and hilar LA was also associated with occupational exposure to silica (p=0.0001, OR=13.45, 95%CI=3.46-52.27). After stratification on gender, higher occupational dust-exposure score in men remained associated with mediastinal and hilar LA (p=0.046, OR=6.5, 95%CI=1.09-38.63). Mediastinal and hilar LA were also significantly associated with a more severe evolution of pulmonary involvement in SSc when considering extensive ILD at diagnosis, the use of immunosuppressive drugs, a fibrotic evolution with change of SSc-ILD pattern in the course of the disease, and an increase of pathological parenchyma extent above 10% since diagnosis.
Conclusion: By using a dedicated highly detailed questionnaire, this study underscores the high prevalence of silica exposure in SSc patients, especially in men. Mediastinal and hilar LA, considered as a bad prognostic factor in ILD, were frequent and associated with silica exposure.

REFERENCES:
[1] Adegunsoye A, et al. Prognosticating Outcomes in Interstitial Lung Disease by Mediastinal Lymph Node Assessment: An Observational Cohort Study with Independent Validation. Am J Respir Crit Care Med. 2018 Sep 14.

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FRI0332 IL-2 RESTORED THE REDUCED ABSOLUTE NUMBER OF TREG CELLS IN THE PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY

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Background: Idiopathic inflammatory myositis (IIM) is a group of skeletal muscle non-suppurative inflammatory disease, including polymyositis (PM), dermatomyositis (DM), inclusion body myositis (IBM), DM/PM associated with malignancy and so on. The latest studies suggest that there is an increase of Th17 cells levels and a decrease of regulatory T cells (Tregs) levels in IIM, which lead to the Th17/Treg imbalance. IL-2 promotes the proliferation and differentiation of several subsets of $CD4^+$T cells and inhibits Th17 cells. It is provided to Tregs from IL-2-producing cells such as activated $CD4^+CD25^{low}$ T cells, NK and NKT cells. Tregs express IL-2R$\alpha\beta\gamma$, a high affinity IL-2 receptor complex. Therefore, Tregs may be selectively stimulated by low-dose IL-2 and amplified.
Objectives: To explore the quantitative changes of peripheral Th17 cells and Tregs in IIM before and after receiving treatment with low-dose interleukin-2 (IL-2) and analyze the relationship between peripheral Th17 cells and Tregs and clinical indicators disease activity.
Methods: Total 151 IIM patients were enrolled, and 196 healthy adults were used as normal controls. Of them, 76 cases were treated with low dose IL-2 ($5.0*10^5$ international units (IU) for 5 days). The absolute number of peripheral T, $CD4^+$ T, $CD8^+$ T, Th1, Th2, Th17 and Treg subsets were analyzed by flow cytometry. Laboratory examinations were analyzed retrospectively. Since the data was disregarded from the normal distribution, the median four quantile method was used for statistical description. Multiple samples were compared with Kruskal-Wallis H test, and the correlation between variables was Spearman rank correlation analysis.
Results: (1) In the patients, the absolute number of Treg cells was significantly decreased as compared with that in the control group ($P<0.05$) and increased by treated with a low dose IL-2. After IL-2 treatment, the absolute numbers of T, $CD4^+$ T, $CD8^+$ T, Th1, Th2 and Th17 cells and the ratio of Th17/Treg were still significantly lower than that in the control group ($P<0.05$); the ratio of Th17/Treg in the patients was not significantly different from that in the control group ($P>0.05$). (2) The peripheral Th17 cells levels were negatively correlated with ESR, CRP, LDH and HBDH ($r=-0.42$, $r=-0.28$, $r=-0.21$, $r=-0.20$, $P<0.05$); the peripheral Treg cells levels were negatively correlated with ESR, CRP, LDH and HBDH ($r=-0.18$, $r=-0.20$, $r=-0.18$, $r=-0.20$, $P<0.05$); the ratio of Th17/Treg was negatively correlated with ESR ($r=-0.23$, $P<0.05$).
Conclusion: The absolute number of peripheral Th17 cells and Tregs declined significantly in IIM, and had correlation with ESR, CRP, LDH and HBDH. However, after receiving treatment with low-dose IL-2, the Tregs levels elevated, which means that IL-2 may plays an essential role in the differentiation and development of Tregs. It also provides new thought and strategy for the therapy of IIM.

REFERENCES:
[1] Noack M, Miossec P. Th17 and regulatory T cell balance in autoimmune and inflammatory diseases [J]. Autoimmunity reviews, 2014, 13(6): 668-677.
[2] Bluestone J A, Trotta E, Xu D. The therapeutic potential of regulatory T cells for the treatment of autoimmune disease[J]. Expert opinion on therapeutic targets, 2015, 19(8): 1091-1103.
[3] Peterson, L. B., Bell, C. J. M., Howlett, S. K. A long-lived IL-2 mutein that selectively activates and expands regulatory T cells as a therapy for autoimmune disease[J]. Journal of Autoimmunity, 2018, 95: 1-14.
[4] Fan, M. Y., Low, J. S., Tanimine, N. Differential Roles of IL-2 Signaling in Developing versus Mature Tregs[J]. Cell Reports, 2018, 25(5): 1204-1213.

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FRI0333 ASSESSING SYSTEMIC SCLEROSIS CARDIAC INVOLVEMENT USING MAGNETIC RESONANCE T1-MOLLI MAPPING

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Background: Patients with systemic sclerosis (SSc) and symptomatic cardiac involvement have a disease-associated mortality of 20% in 10 years. Prevalence of subclinical cardiac involvement is 15%-35%. Early diagnosis and monitoring is therefore critical in the management of SSc-associated cardiac involvement. Conventional cardiac magnetic resonance imaging (cMRI) T1-weighted sequence with late gadolinium contrast has good accuracy for detecting localized fibrosis but not diffuse fibrosis that occurs in SSc. Modified look-locker inversion recovery (T1-MOLLI) mapping, a novel cMRI sequence, has been used to detect and quantify diffuse fibrosis in aortic stenosis. T1-MOLLI values have also been correlated with the degree of biopsy-quantified fibrosis.
Objectives: To investigate whether cMRI T1-MOLLI is able to detect fibrosis associated with SSc cardiac involvement.
Methods: We recruited 16 patients fulfilling the 2013 ACR/EULAR criteria for SSc and 17 healthy age-matched (within 5 years) controls. Patients underwent cMRI T1-MOLLI mapping on the Siemens Biograph mMR 3.0T (Erlanger, Germany).
T1-MOLLI values were compared between SSc patients and healthy controls using student t-test and statistical significance was taken to be $p<0.05$.
Results: Demographics and clinical features of our study cohort are as shown in Table 1. Two (12.5%) SSc patients were symptomatic with palpitations or had arrhythmia requiring treatment. Eleven (68.8%) SSc patients had elevated T1 MOLLI values, using a normal cut-off threshold of 1284 ms.
Mean cardiac T1 values were significantly higher in SSc patients (1329 ± 88.0 ms) than in controls (mean T1 = 1238 ± 93.7 ms, $p=0.0075$), indicating the presence of cardiac fibrosis.
Conclusion: cMRI T1-MOLLI mapping demonstrated that SSc patients who were predominantly asymptomatic showed evidence of cardiac fibrosis. cMRI T1-MOLLI is potentially a useful diagnostic and monitoring tool for SSc cardiac disease.

Table 1. Demographics and clinical features

	SSc patients (n=16)	Controls (n=17)
Limited/Diffuse SSc, n	11/5	Not applicable
Female, n (%)	14 (87.5%)	14 (82.3%)
Age, years	49.2 ± 13.9	51.5 ± 14.8
Mean disease duration from Raynaud's phenomenon onset, years	6.1 ± 7.3	Not applicable
Mean disease duration from non-Raynaud's phenomenon onset, years	6.6 ± 7.4	Not applicable
Hypertension, n (%)	4 (25%)	1 (5.9%)
Palpitations, n (%)	2 (12.5%)	0
Arrhythmia requiring treatment, n (%)	2 (12.5%)	0
Anti-centromere positivity, (n)	3	Not applicable
Anti-Topo-I positivity, (n)	4	Not applicable

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.6892

FRI0334 PERFORMANCE OF THE SCLERODERMA SKIN PATIENT-REPORTED OUTCOME (SSPRO) IN A PHASE 2 TRIAL WITH LENABASUM

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Background: Skin thickening is a distressing feature of systemic sclerosis (SSc). The severity and extensiveness of skin thickening, as traditionally

assessed by mRSS, may not directly correlate with its effect on patients' health related quality of life (HRQoL). The Scleroderma Skin Patient-reported Outcome (SSPRO) was specifically developed to assess the skin-related HRQoL in SSc. No skin-specific PRO in SSc has been prospectively validated in a clinical trial.

Objectives: Validate the SSPRO prospectively in a clinical trial.

Methods: The SSPRO, Patient Global Assessment (PtGA), Physician Global Assessment (MDGA), HAQ-DI, mRSS, FVC% predicted, PROMIS-29 questionnaire, and ACR CRISS were assessed prospectively in a Phase 2 study of lenabasum in dcSSc. SSPRO has 18 items that assess four SSc skin-related HRQoL domains. The Phase 2 study of lenabasum had a 4-month double-blinded portion (N = 41 completers) followed by an open-label extension (N = 38 entered). Spearman correlations of baseline values and change values were determined for SSPRO and other outcome measures. Mean change in SSPRO scores were determined in subjects with increasing levels of improvement in other efficacy outcomes.

Results: At baseline, SSPRO correlated moderately with all other outcome measures except for FVC%, as expected, with strongest correlations with PtGA, HAQ-DI, and PROMIS-29 pain interference and social role domains (**Table 1**). The mean change in SSPRO scores at 3 and 12 months correlated mostly moderately (r = 0.25 to 0.62) with the mean change in other outcome scores, but correlations were low or inconsistent with mRSS, FVC%, and PROMIS-29 anxiety domain (**Table 1**). Significance of correlations in some outcomes was hampered by small magnitudes of change.

Mean SSPRO generally increased in subjects with increasing levels of improvement in HAQ-DI, PtGA, mRSS, and ACR CRISS, although less consistently with mRSS and ACR CRISS at 3 months (**Table 2**).

Conclusion: SSPRO score correlates with both physician and patient-reported outcomes at baseline, though correlations with the latter were stronger. Change in SSPRO reflects changes in how the patient feels (PtGA, PROMIS-29 pain interference and depression domains) and functions (HAQ-DI, PROMI-29 physical function and social role domains) and less consistently with physician-assessed outcomes. Subjects with improvement $\geq$ MID levels of –0.250 in HAQ-DI, -1 in PtGA, and –5 in mRSS had SSPRO improvements of -22 to -23 points at 12 months.

Disclosure of Interests: Ada Man Consultant for: Advisory Board Fee: Abbvie, Janssen, Boeringer Ingelheim, Nancy Dgetluck Employee of: Corbus Pharmaceuticals, Inc., Brian Conley Employee of: Corbus Pharmaceuticals, Inc., Barbara White Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc.

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FRI0335

PROGNOSTIC IMPACT AND CLINICAL CHARACTERISTICS OF INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES IN A MULTIDISCIPLINARY SETTING

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Background: Interstitial Pneumonia with Autoimmune feature (IPAF) is a recently defined disease that includes Interstitial Lung Disease (ILD) patients with features of autoimmunity, not satisfying any of the established classification criteria for connective tissue diseases (CTD). Even if IPAF pateints share clinical and serological findings with CTD, we are unaware about the clinical evolution of IPAF pateints.

Objectives: To define the characteristics and evolution of IPAF patients in a multidisciplinary setting.

Methods: We selected patients with a diagnosis of IPAF referring to a multidisciplinary Rheumatology/Pneumology/Radiology team at our hospital. We excluded from the analysis patients positive for antisynthetase antibodies, as diagnosed with antisynthetase syndrome. Data were retrospectively collected from our hospital medical records.

Results: We analyzed 25 patients (19 females, 76%, 6 males, 24%), with a median onset age of 67 years (interquartile range, IQR, 59-74) and a follow-up of 32 months (IQR 22-69). ANA test was positive in 23 (92%) cases (fig 1), whereas cytoplasmic positivity was observed in 17 (68%). Anti-ENA screen was positive in 9 patients (36%) (7 [28%] anti-Ro52 and 2 [8%] anti-RNP). One patient (4%) was positive for anti-PM-Scl, 1 (4%) for anti-Mi2 and 1 (4%) for anti-Ku antibodies. These 2 latter antibodies are not included in the serological domain of IPAF. Patients had mainly a Non Specific Interstitial Pneumonia (NSIP) pattern (19 [76%]; fibrosing in 7 [28%], and with concomitant organizing pneumonia (OP) in 3 [12%]). Three (12%) patients had Usual Interstitial Pneumonia-like and 3 (12%) an OP pattern. The majority of patients (15 [60%]) satisfied only the morphological and serological domains. Clinical domains satisfied were: arthritis (4 [16%]), Raynaud's phenomenon (5 [20%]), palmar telangiectasias (2 [8%]), mechanic's hands (1 [4%]) and hiker's feet (1 [4%]). We observed other findings not included in IPAF criteria but suggestive for CTDs, both clinical (inflammatory myopathy 3 [12%]; dry eye1 [4%]; sclerodactyly 1 [4%]), and instrumental (scleroderma pattern at naifold capillaroscopy 1 [4%]; dilated esophagus at barium X-rays 2 [8%]). Clinical spectrum time course was variable in 5 (20%) cases: 3 (12%) patients developed arthritis after ILD, and 2 (8%) developed ILD respec-

Table 1. Spearman Correlations for SSPRO and Other Efficacy Outcomes at Baseline and for Change in SSPRO and Other Efficacy Outcomes at 3 and 12 months (r, P-value)

Time	PtGA	MDGA	HAQ-DI	mRSS	FVC,%	ACR CRISS	PROMIS-29 Domain				
							Pain Interference	Social Role	Physical Function	Depression	Anxiety
Baseline	0.61	0.51	0.52	0.44	-0.07		0.62 <0.0001	-0.57 0.0001	-0.33 0.034	0.51 0.0007	0.41
	<0.0001	0.0007	0.0005	0.004	0.670						0.008
Change 3 months	0.26 0.124	0.30 0.067	0.29 0.083	0.02	-0.12	-0.20 0.235	0.46 0.005	-0.40 0.015	-0.46 0.004	0.33 0.044	0.14
				0.932	0.483						0.395
Change 12 months	0.28 0.103	0.15 0.394	0.25 0.145	0.20	-0.53	-0.48 0.004	0.41 0.014	-0.62 <	-0.25 0.152	0.27 0.119	0.21
				0.251	0.001			0.0001			0.234

Table 2. Mean Change in SSPRO Associated with Increasing Levels of Improvement in Other Outcomes

Efficacy Outcome	HAQ-DI improvement				PtGA improvement			mRSS improvement				ACR CRISS[1]			
Improvement at least	None	-0.125	-0.250	-0.500	None	-1	-2	None	-3	-5	-8	< 0.30	$\geq$ 0.30	$\geq$ 0.60	$\geq$ 0.90
3 months (N=37)	-9.9	-17.6	-20.2	-22.5	-11.9	-15.3	-16.5	-11.0	-14.7	-16.3	-10.3	-10.2	-17.8	-17.1	-14.5
12 months (N=35)	-17.9	-20.2	-22.7	-27.2	-16.5	-21.9	-21.5	-11.6	-19.6	-23.2	-23.1	-13.0	-23.5	-26.6	-27.3

[1]ACR CRISS score is absolute, not change, score.

tively after arthritis and inflammatory myopathy onset. Three (12%) patients were admitted to the Intensive Care Unit for Rapidly Progressive (RP) ILD and 2 died (respectively 2 months and 54 months after ILD onset), whereas the alive patient had 2 ICU admission for RP-ILD. Five (20%) patients, including the only 1 dismissed from ICU, needed home O_2 therapy. Ongoing and previous therapies are reported in figure 2.

Conclusion: We showed that the prognosis of IPAF is highly variable, with patients experiencing RP ILD, other slow progressive worsening of respiratory functions and other a substantially stable disease. Furthermore, we showed other findings, laboratory, clinical and instrumental, that could help clinicians in a better identification and stratification of IPAF patients. As a matter of fact, at present, IPAF appears as a generic term including very different conditions that can be further differentiated according to clinical and serological data.

REFERENCES:

[1] Fischer A, et al. Eur Respir J 2015
[2] Sciré CA, et al. Resp Med 2017
[3] Sambataro G, et al. Eur Resp Rev 2018
[4] Cavagna L, et al. Eur Resp Rev 2018

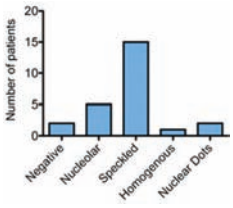


Figure 1. Antinuclear antibodies determination results

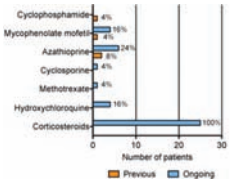


Figure 2. Ongoing (at last follow-up) and previous treatments

Disclosure of Interests: Emiliano Marasco: None declared, Federica Meloni: None declared, Giovanni Zanframundo: None declared, Adele Valentini: None declared, Valentina Morandi: None declared, Veronica Codullo: None declared, Lorenzo Volpiano: None declared, Claudia La Carruba: None declared, Francesca Motta: None declared, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Lorenzo Cavagna: None declared
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FRI0336 INCIDENCE OF IDIOPATHIC INFLAMMATORY MYOPATHIES (IIM) IN ADULTS IN FIFE, SCOTLAND, UK

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Background:
Objectives: To determine the Adult incidence of IIM in the Kingdom of Fife, Scotland. The Fife population is 370,000 and constitutes 6.8% of the Scottish Population (5,425,000). 98% of the Fife population is Caucasian. We also sought to characterise the incident IIM cases in terms of subtype and autoantibody profile.
Methods: All newly diagnosed Adult cases ($\geq$ 18 years) of IIM between 01.03.17 and 30.11.18 were recorded (11.75 year period). The cases were identified by a search of the Fife Rheumatic Diseases Unit Database using IIM-specific ICD-10 codes. These were cross-referenced with a prospective personal database of IIM cases established by the Lead Author (JMcL) on 26.02.17. In addition a search of all Fife patients enrolled in the UKMYONET study was also performed. All patients with 'definite' or 'probable' IIM by the Bohan & Peter 1977 criteria; Clinically defined Inclusion Body Myositis (IBM) by the ENMC 2011 criteria; or other specific criteria in the case of Clinically Amyopathic Dermatomyositis (CADM) and Immune-mediated Necrotising myopathy (IMNM) were included.
Results: 53 newly diagnosed Adult IIM cases were identified. 11 Dermatomyositis (DM) (3 NXP2; 2 Jo-1; 2 TIF1-G; 1 Mi-2; 3 Myositis-specific antibody (MSA) not tested). 4 Polymositis (PM) (1 Jo-1; 1 MDA5; 1 MSA/Myosits-associated antibody (MAA) negative; 1 MSA not tested). 12 Anti-synthetase syndrome (8 Jo-1; 3 PL7; 1 PL12) and 3 patients with Jo-1 isolated Interstitial lung disease (ILD). 5 Overlap Connective tissue disease (CTD) : 2 Systemic Lupus Erythematosus; 2 Systemic sclerosis; 1 Mixed CTD. 5 Cancer-associated myositis (CAM) : 2 lung (1 NXP2 DM & 1 SRP PM); 1 ovarian (DM, MSA not tested); 1 Breast (DM, TIF1-G); 1 Prostate (DM, Mi-2). 5 CADM (2 MDA5; 1 TIF1-G; 1 NXP2; 1 MSA not tested). 4 IMNM (2 HMGCR; 1 HMGCR overlap with IBM; 1 SRP overlap with IBM who developed bladder cancer < 3 years after diagnosis). 4 sporadic IBM (2 cN-1A/Mup44 of which 1 overlap with Primary Sjogren's Syndrome; 2 MAA not tested).
Conclusion: The incidence of IIM in Fife, Scotland is 4.5 cases per year which equates to an annual incidence of 12.2 cases per million population. This is comparable with the incidence data published for Salford in the UK (17.6). However the IIM subtypes differed from Salford in that Fife has a much lower incidence of PM. 40/49 (82%) of Fife patients who were tested were found to be MSA positive.
Disclosure of Interests: None declared
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FRI0337 INCIDENCE AND PREVALENCE OF MYOSITIS ASSESSED BY MULTI-SOURCES CAPTURE-RECAPTURE METHODOLOGY

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Background: Precise epidemiology of myositis epidemiology remains largely unknown (1). Surveys based solely on administrative claims benefit from large case ascertainment but may be influenced by miscoding and misdiagnosing. The use of medical records with charts review benefit from accurate diagnosis but exhaustive ascertainment is difficult to achieve because numerous specialists are involved and cases may concern both inpatients and outpatients.
To overcome these difficulties we undertook a capture–recapture survey that takes advantage of a multi-sources case ascertainment to estimate the number of cases missed by any one source and to correct the prevalence rate (2).
Objectives: To assess the incidence and prevalence of myositis in Alsace, a region of eastern France.
Methods: Alsace, region of eastern France, is home to about 2 million inhabitants benefiting from high access to healthcare and a labialized referral center for myositis. Seeking care outside is uneasy because of peculiar geography. Myositis patients were retrieved through three separate sources: i) all general practitioners and community specialist ii) Muscle pathology center records, iii) all public and private hospitals records, vi) all public and private laboratory records. Incident and prevalent cases fulfilling the ACR/EULAR criteria for myositis were included.
Results: The responses to the questionnaires sent to the physicians (n=3452), yielded 105 potential myositis cases. All hospital centres contacted (n=13) participated in the study and 1335 potential myositis patients were recorded by this source. 263 potential myositis cases were identified through muscle pathology center records. 13 laboratories participate in the studies and 324 potential myositis patients were recorded by this source. We thus received 1863 records of suspected myositis after excluding duplicates within each sources. The thorough review of the corresponding medical charts is currently ongoing and at this stage 10% of the potential cases fulfilled the ACR/EULAR criteria for myositis.
Conclusion: This first study based on a multi-sources capture-recapture methodology and ACR/EULAR criteria is very likely to provide an accurate estimation of myositis epidemiology.

REFERENCES:

[1] Incidence and prevalence of inflammatory myopathies: a systematic review.
[2] Meyer A, Meyer N, Schaeffer M, Gottenberg JE, Geny B, Sibilia J.
[3] Rheumatology (Oxford). 2015;54:50-63.
[4] Brief Report: Spatial Heterogeneity of Systemic Sclerosis in France: High Prevalence in the Northeast Region.
[5] Meyer A, Chifflot H, Chatelus E, Kleinmann JF, Ronde-Ousteau C, Klein D, Jégu J, Geny B, Hirshi S, Canuet M, Blaison G, Kieffer P, Lipsker D,

Martin T, Sauleau E, Velten M, Sibilia J. Arthritis Rheumatol. 2016;68:1731-7.

Disclosure of Interests: None declared
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FRI0338 **ANTI-MDA5 IDIOPATHIC INFLAMMATORY MYOSITIS (IIM) CONFERS POOR PROGNOSIS BUT NEGATIVE MYOSITIS SPECIFIC ANTIBODY (MSA) IS NOT BENIGN EITHER**

Sin Ngai Ng, Chun Man Ng, Chu Oi Ciang, Moon Ho Leung. *Queen Elizabeth Hospital, Medicine, Hong Kong, Hong Kong (SAR)*

Background: MSA test is useful to diagnose IIM and subcategorize patients by disease phenotypes.
Objectives: The study aims to evaluate the survival of IIM patients of different MSA patterns.
Methods: An IIM registry had been set up in a tertiary referral centre since 2014 by recruiting prevalent and incident cases. Patients were followed-up prospectively. This study included patients fulfilling the 2017 EULAR/ACR classification criteria for IIM[1] and excluded those aged < 18 at disease onset. Immunoblot EUROLINE autoimmune inflammatory myopathies 16 antigens strip (EUROIMMUNE AG, Lubeck, Germany) was used. Information including baseline demographic data, disease manifestations, MSA results, co-existing malignancy, duration of survival and causes of death were collected. IIM patients were divided into seven groups, which included 1) anti-aminoacyl tRNA synthetase (ARS) 2) anti-MDA5, 3) anti-TIF1γ/anti-NXP2, 4) double positive MSA, 5) other MSAs, 6) negative MSA/MAA (myositis associated antibodies) and 7) positive MAA only. Survival probabilities were compared among different MSA groups by using the Kaplan-Meier method and log-rank test. A two-tailed probability value (p) < 0.05 was considered significant. The study was approved by Kowloon Central Cluster Ethic Committee (ref.: KC/KE-17-0177/ER-3)
Results: Among 112 IIM patients, 79 (70.5%) were female, and the median age of onset was 55 (18-90) years old; 63.4% were dermatomyositis (DM), 17.9% polymyositis (PM) and 18.8% clinically amyotrophic DM (CADM). Co-existing interstitial lung disease (ILD) was common and found in 65 (58%) patients; 16 (14.3%) had rapidly progressive interstitial lung disease (RPILD), and 16 (14.3%) died within the observed period. Overall, the commonest cause of death was RPILD, followed by infection and malignancy. While anti-MDA5 was strongly associated with RPILD (odds ratio = 33.0 [95% CI: 7.2-151.8], p<0.001), anti-MDA5 group had the worst survival, with 1-year and 5-year survival both at 43%, compared to above 80% in all other groups (log-rank test p<0.001) (Table 1). There were nine patients with double positive MSA and 28 had negative MSA/MAA. Analysis between MSA sub-groups found that the double positive MSA, MAA only and other MSAs group had no mortality during study period while the negative MSA/MAA group had the second highest mortality following the anti-MDA5 group (Figure 1). Infection and malignancy were the two major causes of death in the MSA/MAA negative group.
Conclusion: Anti-MDA5 associated RPILD was the leading cause of mortality in IIM. However, those tested negative for both MSA and MAA by current immunoblot technique also had guarded prognosis related to the risk of infection and malignancy.

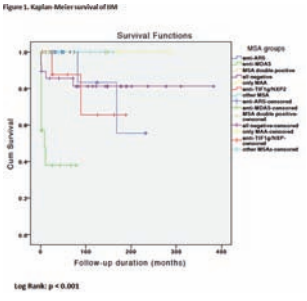


Figure 1. Kaplan-Meier survival of IIM

Table 1. Survival rates in different MSA groups

Survival	1 year	5 years
Anti-ARS	100%	92%
Anti-MDA5	43%	43%
Double positive	100%	100%
Negative MSA/MAA	89%	82%
Only positive MAA	100%	100%
Anti-TIF1γ/anti-NXP2	100%	88%
Other MSAs	100%	100%

REFERENCES:

[1] Lundberg IE, et al.. ARD 2017;76(12):1955-1964.

Disclosure of Interests: None declared
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FRI0339 **CLINICAL CHARACTERISTICS OF ANTI-RO52A AND ANTI-RO52B ANTIBODIES IN DERMATOMYOSITIS/ POLYMYOSITIS**

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Background: The anti-Ro52 antibody, found in numerous systemic autoimmune conditions, is one of the most common autoantibodies in inflammatory myositis. It is known to be associated with interstitial lung disease (ILD) and to coexist with anti-Jo-1[1]. There are two spliced forms: Ro52α and Ro52β. Ro52β was originally reported in 1995 as a spliced form of Ro52α in the human heart[2]. Ro52β antigen cDNA has a defective exon 4, which encodes part of an autoepitope hotspot[2].
Objectives: We investigated the clinical and laboratory characteristics of anti-Ro52α and anti-Ro52β. We also analyzed the characteristics of anti-Ro52α/β within each coexisting inflammatory myositis specific autoantibody (MSA) group to reduce the influences of coexisting MSA characteristics.
Methods: Among 229 dermatomyositis (DM) and polymyositis (PM) patients, 167 patients (DM 152, PM 10, juvenile DM 5) fulfilled the criteria of Bohan and Peter, and 62 clinical amyopathic DM cases fulfilled the criteria of Sontheimer. Anti-Ro52α and anti-Ro52β antibodies were detected by ELISA.
Results: 46 of the 229 patients were anti-Ro52α-positive (20%). ILD was a frequent complication in the anti-Ro52α-positive patients (35/42: 76%) (P=0.0016), and anti-Ro52α was highly positive in the anti-aminoacyl tRNA synthetase (ARS) antibody-positive group (19/32: 60%) (P<0.0001) (Table 1). However, the ILD frequencies of anti-Ro52α-positive and anti-Ro52α-negative patients within each group of coexisting MSA (anti-ARS, anti-TIF, anti-MDA5, etc.) were almost same (P=1). The anti-Ro52α-positive rates were similar to the positive rates of anti-Jo1 (61%) and other anti-ARSs (52%) (P=0.7).
Of the 46 anti-Ro52α-positive patients, 26 patients were anti-Ro52β-positive. No patient was only anti-Ro52β positive. The anti-Ro52α-positive and anti-Ro52β-positive groups were older than the anti-Ro52α-only-positive group (P=0.009), and the average of maximum creatine kinase was higher in both of the positive groups (P=0.065). The 6 patients without coexisting MSA were all both anti-Ro52α-positive and anti-Ro52β-positive (P=0.03) (Table 2).
Conclusion: Anti-Ro52 is highly positive when anti-ARS antibodies are present, but it is not anti-Jo-1-specific. Anti-Ro52 positivity is not associated with elevated risk of ILD in any of the MSA-positive groups. The anti-Ro52β antibody might be an indicator of myositis.

REFERENCES:

[1] Lee AYS. A review of the role and clinical utility of anti-Ro52/TRIM21 in systemic autoimmunity. Rheumatol Int. 2017;37(8):1323-1333.
[2] Chan EK, Di Donato F, Hamel JC, Tseng CE, Buyon JP. 52-kD SS-A/Ro: genomic structure and identification of an alternatively spliced transcript encoding a novel leucine zipper-minus autoantigen expressed in fetal and adult heart. J Exp Med. 1995;182(4):983-92.

Table 1. Clinical and laboratory characteristics with anti-Ro52α

	anti-Ro52α (+) N=46	anti-Ro52α (-) N=183	P value
age	54.6 ± 14	53.1 ± 19	0.89
sex (female)	35 (76%)	126 (69%)	0.37
cancer	6 (13%)	43 (23%)	0.15
ILD	32 (76%)*	78 (49%)**	0.0016
creatine kinase	974.3***	1274****	0.40
MSA			
MDA5	12 (26.1%)	36 (19.6%)	0.41
ARS	19 (41%)	13 (7.1%)	<0.00001
TIF1γ	4 (8.7%)	37 (20%)	0.084
Mi-2	1 (2.1%)	12 (6.5%)	0.47
MJ	1	11 (6%)	0.46
SAE	2	5 (2.1%)	0.63
PM/Scl	1	5 (2.1%)	1
SRP	0	4	0.58
non	6 (13%)	56 (30%)	0.016

*4 patients excluded with insufficient data. **23 excluded. ***2 excluded. ****16 excluded.
ILD: interstitial lung disease. MSA: myositis specific autoantibodies

Table 2. Clinical and laboratory characteristics in patients with anti-Ro52α and anti-Ro52β

	anti-Ro52α with anti-Ro52β (N=26)	Anti-Ro52α without anti-Ro52β (N=20)	P value
age	59.8±12.5	47.85±13.5	0.009
sex (female)	21 (81%)	14 (70%)	0.49
cancer	4 (15%)	2 (10%)	0.68
creatine kinase	1267.52	588.4	0.065
ILD	17 (71%) *	16 (89%)**	0.25
MSA			
MDA5	5	7	0.31
ARS	9	10	0.74
TIF1	3	1	0.62
SAE	1	1	1
Mi-2	1	0	1
MJ	1	0	1
PM/ScL	0	1	0.45
non	6	0	0.03

*4 cases excluded with insufficient data. **2 cases excluded.

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FRI0340 LONG-TERM FOLLOW-UP OF PRIMARY RAYNAUD´S PHENOMENON COHORT OF 248 PATIENTS

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Background: Raynaud's phenomenon (RP) is frequently associated with the presence of scleroderma or other connective tissue diseases (CTD). Identify the presence of secondary RP is important to perform an adequate therapeutic management and to achieve the early control of these patients. Nailfold capillaroscopy is safe, economic, easy to perform and has proven to be useful in identifying patients with secondary RP.
Objectives: To assess a long-term follow-up primary RP patient's cohort.
Methods: Retrospective observational study of a wide and unselected series of patients diagnosed as primary RP from a single university hospital from January 2012 to December 2018. Patients were classified as primary RP after the presence of CTD at the onset was excluded.
Results: We studied 248 patients (210 women/38 men), with a mean age of 46.3±15.2 years (range 15-88). After a mean follow-up period of 57.2±21.6 months, 9 (3.6%) patients were diagnosed of a CTD. The remaining 239 (96.4%) patients continued classified as primary RP. The main pathologies observed after follow-up were: Scleroderma/Systemic sclerosis (n=3), Systemic Lupus Erythematosus (n=3), Rheumatoid arthritis (n=1), Sjogren's syndrome (n=2). The main capillaroscopic patterns observed were: Normal (n=175), Unspecific (n=64), Scleroderma pattern (n=3) and suggestive of other rheumatic diseases pattern (n=6). All the patients who developed a CTD during follow-up showed changes at successive nailfold capillaroscopic examinations. 28 of 239 patients who remained primary RP showed minor changes at successive nailfold capillaroscopy. The main capillaroscopic changes detected on this group were: Presence of capillary tortuosity (n=6), presence of a decreased capillary density (2) and the presence of capillary bleeding (n=20). Antinuclear antibodies (ANA) were positive at he onset in 46 patients (16.9%) and after follow-up in 44 (17.7%) patients.
Conclusion: After a mean follow-up period next to 5 years, most of our primary RP patients remained free of CTD. A minority of our patients showed changes at nailfold capillaroscopy exam or positivity of ANA.
Disclosure of Interests: None declared
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FRI0341 LOWER URINARY TRACT SYMPTOMS PREVALENCE IN SYSTEMIC SCLEROSIS PATIENTS: RESULTS FROM A COMPREHENSIVE ANALYSIS

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Background: Lower urinary tract symptoms (LUTS) are a seldom-reported manifestation of systemic sclerosis (SSc). Although LUTS have been described in SSc patients with a higher prevalence than in the general population, no controlled studies have been reported to date [1–3].
Objectives: To compare LUTS prevalence and severity in SSc patients and in healthy subjects and mainly to explore their association with SSc clinical and diagnostic parameters.
Methods: This study evaluated 42 SSc consecutive patients (median age 61 years, range 21-85) and 50 matched healthy subjects (median age 57 years, range 28-93). SSc diagnosis was based on the 2013 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria. LUTS were assessed through validated self-reported questionnaires derived from the International Conference on Incontinence (ICIQ-FLUTS, ICIQ-MLUTS and ICIQ-OAB) [4]. General comorbidities and/or medication potentially related to LUTS, as well as lower urinary tract infections, were evaluated in order to exclude confounding factors. Non-parametric tests and chi-squared test were performed to compare LUTS distribution, namely of urinary incontinence (UI) and overactive bladder (OAB), in the two populations, then linear and logistic regressions were used to test the association between SSc disease and LUTS prevalence and severity. In SSc population, linear and logistic regressions were performed to test the association between LUTS and SSc variables, including nailfold videocapillaroscopy (NVC) patterns ("Early", "Active", "Late"), SSc-related autoantibodies and dual X-ray absorptiometry (DXA) parameters. Multivariate analysis was performed to adjust the associations for potential confounders. A p value < 0.05 and a confidence interval (CI) of 95% were considered statistically significant.
Results: SSc patients showed significantly higher prevalence and severity of UI and OAB than healthy controls (p< 0.005, p< 0.01). SSc was a strong predictor of LUTS, independent of demographic data, comorbidities and treatments (OR 5.57, 95% IC 1.64-18.88). In SSc patients sarcopenia positively correlated with OAB (p< 0.001) and reduced bone mineral density (BMD) positively correlated with OAB (p< 0.05) and UI (p= 0.001). UI positively correlated with anti Scl70 Abs (p< 0.05) and cyclosporine treatment (p= 0.001) and negatively with anti RNA polymerase III Abs (p< 0.05); OAB positively correlated with calcinosis (p< 0.005) and negatively with methotrexate treatment (p< 0.05). NVC "Active" and "Late" patterns were predominant among SSc patients presenting LUTS (both UI and OAB), although not any statistical correlation was found.
Conclusion: For the first time urinary tract involvement was found to be significantly higher in SSc patients than in healthy matched controls. In addition, sarcopenia, bone damage and calcinosis appeared significantly correlated with LUTS, suggesting a possible interplay.

REFERENCES:

[1] John G, et al. Arthritis Care Res. 2018;70:1218–27.
[2] Sanchez K, et al. Press Medicale [Internet]. 2016;45(4):e79–89.
[3] Adler BL, et al. J Rheumatol. 2018;45:1145–52.
[4] Abrams P, et al. J Urol. 2006;175:1063–6.

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FRI0342 EROSIVE OSTEOARTHITIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Erosive osteartritis (EO) is a rare but aggressive variant of hand osteoarthritis. Its prevalence in Europe is 3.3% in men and 9.9% in women, affecting 15.5% of patients with hand osteoarthritis[1,2]. EO causes a significant loss of function in the hands, with more severe inflammatory signs and affecting almost exclusively the PIP and DIP joints, usually avoiding the TM and MCP. In systemic sclerosis (SSc), hands are commonly affected with pain and joint deformity that, added to sclerodactyly and the presence of digital ulcers, produce an important functional limitation. It has not been established yet whether the presence of the disease determines an increased risk for the development of erosive osteoarthritis.
Objectives: To determine the frequency of EO in patients with SSc seen in a tertiary hospital in Madrid and to compare it with the frequency observed in the large cohorts of healthy population (Framingham study[1]). Secondly analyze both the clinical and analytical factors that may be related to the presence of EO in these patients.
Methods: A descriptive, observational cross-sectional study was conducted. We included all patients with a diagnosis of systemic sclerosis attended in our Rheumatology Unit. A database was created including clinical and epidemiological data and all the available imaging tests to assess the presence of findings compatible with EO in interphalangeal hand joints were reviewed. Acroosteolysis lesions were not considered as EO. Finally, a descriptive analysis was carried out.
Results: The prevalence of EO in our cohort of SSc patients, although low, is higher than the estimated in general healthy population according to the large European studies, with 8.16% (12/147) of the patients affected. All the patients with EO were female, wih a higher age of presentation of SSc compared to patients without EO (66.72 vs 50.72 years). EO was more prevalent in patients with limited skin involvement (75% vs 62%) and they had a higher frequency of telangiectasias in the typical locations. Likewise, patients with EO had more frequently positive AMA (25% vs 8.88%) and calcinosis (33% vs 17.77%). The frequency of ANA, Raynaud's phenomenon and interstitial lung disease was similar in both groups. No patients with positive Ro or La presented EO.
Conclusion: Although it is an uncommon variant of hand osteoarthritis, in our cohort a higher prevalence of EO was observed in patients with SSc compared to the healthy general population. In our group, the most associated risk factors were female sex, advanced age at the diagnosis of SSc, the presence of AMA and calcinosis, regardless of its location. The frequency of pulmonary involvement and Raynaud's phenomenon was similar in both groups.

REFERENCES:

[1] I.K. Haugen, M. Englund, P. Aliabadi, et al. Prevalence, incidence and progression of hand osteoarthritis in the general population: The Framingham Osteoarthritis Study. Ann Rheum Dis, 70 (2011), pp. 1581-1586.
[2] W.Y. Kwok, M. Kloppenburg, F.R. Rosendaal, et al. Erosive hand osteoarthritis: Its prevalence and clinical impact in the general population and symptomatic hand osteoarthritis. Ann Rheum Dis, 70 (2011), pp. 1238-1242.

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FRI0343 EVALUATION OF CAROTID HEMODYNAMIC PARAMETERS AND PLAQUES BY DOPPLER ULTRASOUND IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Carotid Doppler-ultrasound is useful for the detection of subclinical atheromatosis(1), and also for the evaluation of hemodynamic characteristics of carotid arteries(2).

Objectives: The aim of this study is to evaluate the hemodynamic parameters of carotid arteries and its relation with vascular related Systemic Sclerosis (SSc) complications and subclinical atheromatosis.
Methods: 157 patients with SSc of the cohort of Vall d'Hebron Hospital were included according to the ACR/EULAR 2013 criteria and LeRoy classification.
The left and right common carotid arteries (CCA), bulb and internal carotid arteries (ICA) were scanned using Doppler ultrasound for the detection of plaques and for the measurement of the Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV), Pulsatility Index (PI), Resistance Index (RI) and Systole/Diastole ratio (S/D), using the software incorporated in GE Healthcare's Vivid I equipment.
Results: 157 patients were included, 132 women (84.1%), the mean age was 56 years old (range 20-83) and the mean of years of disease evolution was 19 years (range 3-57). 64.2% were SSc limited subset, 20.9% SSc diffuse subset, 9.5% SSc *sine scleroderma* and 4.7% early SSc subset. 49.3% had digital ulcers, 41.9% had interstitial lung disease and 14.2% had pulmonary hypertension.
There were no statistically significant differences in hemodynamic parameters in relation to Raynaud´s phenomenon, digital ulcers or pulmonary hypertension.
Seventy-five patients (47.7%) had carotid plaques. Patients with plaques had lower CCA PSV (66.8cm/s vs 76.7cm/s, p <0.01, CI 4.62-14.5), lower CCA EDV (15.3 cm/s vs 19.99cm/s p <0.01, CI 2.88-6.49), higher CCA PI (1.69 vs. 1.55, p <0.05; CI 0.02-0.26) and higher CCA RI (0.77 vs 0.73 p <0.01 CI 0.02-0.05). These patients also had lower ICA EDV (22.9cm/s vs 26.5cm/s, p <0.01; CI 1.01-6.11), higher ICA PI (1.43 vs 1.32, p <0.05 CI 0.01-0.22) and higher RI0.71 vs 0.68 p <0,05 CI 0.01-0.05), without statistically significant differences in ICA PSV (79.75cm/s vs 84.24cm/s p: 0.21) nor in the ratio PSV/EDV.
Ratio ICA PSV/CCA PSV was calculated, without showing significant differences in the presence of plaques or vascular manifestations of the SSc.
The PSV greater than 120m/s, as an isolated measure, did not show statistically significant differences related to the presence of plaques. The PSV greater than 150 showed statistically significant differences (p <0.01, CI 0.05-0.23), showing a large specificity 0.98 but a very low sensitivity 0.15 for the detection of plaques.
Conclusion: In our study we have not found relation between carotid hemodynamic parameters and microvascular related SSc complications such as Raynaud's phenomenon, the presence of digital ulcers or pulmonary hypertension.
Patients with SSc and atheromatous disease have a characteristic carotid hemodynamic profile consisting in lower PSV and EDV, and higher PI and RI, both at CCA and at ICA. The presence of increased PI and RI in patients with plaques, could suggest a primary damage of the vascular wall in patients with SSc. More studies are needed to determine if these data are the cause or a consequence of the presence of plaques.
In our study the PSV greater than 150 cm/s isolated shows a high specificity for the presence of plaques.

REFERENCES:

[1] Sanz Pérez I. et al. Subclinical cardiovascular disease and Systemic Sclerosis: A comparison between risk charts, quantification of coronary calcium and carotid ultrasonography. Autoimmun Rev. 2018;17(9):900–5.
[2] Staub D. et al. Prediction of cardiovascular morbidity and mortality: Comparison of the internal carotid artery resistive index with the common carotid artery intima-media thickness. Stroke. 2006;37(3):800–5.

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FRI0344 SEXUAL FUNCTION IN GERMAN WOMEN WITH SYSTEMIC SCLEROSIS COMPARED TO WOMEN WITH SYSTEMIC LUPUS ERYTHEMATODES AND EVALUATION OF A SCREENING TEST

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Background: Few studies have been conducted to address the impact of systemic lupus erythematodes (SLE) or systemic sclerosis (SSc) on sexual function (1,2), and so far none in Germany.

Objectives: To assess and compare sexual dysfunction (SDF) in female patients with SLE or SSc, to correlate sexual function with disease characteristics and depression, and to evaluate a short questionnaire (Qualisex) as a screening test.
Methods: Female patients with systemic lupus erythematodes or systemic sclerosis in two German tertiary university hospitals were evaluated with a self-designed questionnaire on various sexual and gynaecological aspects, a 19-item version of the Female Sexual Function Index (FSFI), the 9-item questionnaire Qualisex, and the Beck's depression inventory in a prospective study.
Results: 171 female patients were included into the study. Among them 83 suffered from SSc (mean age 48.50 years), and 88 from SLE (mean age 39.65 years). Organ involvement and immunosuppressive medication was frequent in both groups. 34.9% of SSc patients and 28.4% of SLE patients ever received cyclophosphamide. Disease duration was significantly longer in SLE patients (13.17 vs 9.85 years in SSc patients, p=0.021). No significant differences between SSc and SLE were found as to educational background, BDI depression categories, marital status, or number of children. Only 9.6% of SSc patients and 14.8% of SLE patients had ever discussed sexual problems with their physician, whereas 52% of all patients thought that these were relevant in relation to their disease. Significantly more SSc patients would wish to discuss sexuality with their physician more intensively (37.3% vs 28.4% in SLE patients, p=0.011). 79.5% of SSc patients and 79.4% of SLE patients were in a constant relationship; 62.6% (52 of 83) of SSc patients and 67.0% (59 of 88) of SLE patients were sexually active. Impeding factors like vaginal stenosis, sicca, impaired mobility of pelvis, or pain did not differ significantly between SSc and SLE. Among the 51 sexually active and evaluable SSc patients a mean FSFI of 25.53 (±5.06) was found, with a FSFI value below the cut off defining SDF (<26.55) in 49% of patients, which did not differ significantly compared to SLE patients (n=59, mean FSFI 26.92 (±5.17), SDF in 45.8%). More patients who suffered from SDF had at least mild depression defined by BDI than patients without SDF (71.2% vs. 46.4%, p=0.016). SSc patients showed a numerically better Qualisex than SLE patients (2.98 (±2.24) vs. 3.16 (±2.45) with 0 meaning no impairment and 10 severe impairment). The Qualisex correlated significantly with the FSFI (r=-0.367; p<0.001) with numerically better correlation in SSc patients (r=-0.407, p=0.001 vs r=-0.340, p=0.004).
Conclusion: Sexual Dysfunction (SDF) is a frequent problem in female patients with SSc and SLE. Frequency and nature are comparable between the two entities. Addressing sexual issues during medical consultation is an unmet need. The Qualisex constitutes a short questionnaire, which is suitable for SDF screening.

REFERENCES:

[1] Rosato E, Rossi C, Molinaro I, Digiulio M, Trombetta A, Marra A, et al. Sexual distress, sexual dysfunction and relationship quality in women with systemic sclerosis: correlation with clinical variables. International journal of immunopathology and pharmacology. 2014;27(2):279-85.
[2] Yin R, Xu B, Li L, Fu T, Zhang L, Zhang Q, Li X, Shen B. The impact of systemic lupus erythematosus on women's sexual functioning: A systematic review and meta-analysis. Medicine (Baltimore). 2017 Jul;96(27): e7162.

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FRI0345 **CAPILLAROSCOPY IN SYSTEMIC SCLEROSIS RELATED PULMONARY ARTERIAL HYPERTENSION**

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Background: Despite its importance in diagnosing SSc, the role of nailfold videocapillaroscopy (NVC) in evaluating SSc related PAH (SSc-PAH) using standardized NVC definitions has not yet been the subject of a systematic literature review.
Objectives: To identify and critically appraise all currently available literature evaluating NVC in SSc-PAH according to the standardized definitions of the EULAR Study Group on Microcirculation in Rheumatic Diseases (EULAR SG MC/RD).
Methods: Original longitudinal or cross-sectional studies, documenting an association between NVC parameters and SSc-PAH (confirmed on right heart catheterization) were identified, by means of a systematic literature search in PubMed, EMBASE and Web of Science. All retrieved records were screened by two raters based on title, abstract and full-text level to finally include manuscripts eligible for quality appraisal and data extraction. NVC parameters were evaluated as proposed by the EULAR SG MC/RD as follows: quantitative (capillary density, dimension, morphology and haemorrhages), semiquantitative and qualitative assessment (NVC pattern).

CAPILLAROSCOPIC PARAMETER			SIGNIFICANT ASSOCIATION	NON-SIGNIFICANT ASSOCIATION	CONCLUSION
QUANTITATIVE	Density	Mean density	Inverse correlation with SSc-PAH (3,4)	N/A	Density unequivocally associated with (incident) SSc-PAH in 2 longitudinal and 2 cross-sectional studies
		Capillary loss	Incident SSc-PAH (1,2)	N/A	
	Dimension	Width	SSc-PAH (4)	SSc-PAH (3)	No unequivocal findings
		Giant	SSc-PAH (4)	Incident SSc-PAH (1)	
	Morphology	Abnormal	Incident SSc-PAH (1,2) SSc-PAH (4)	N/A	Abnormal morphology unequivocally associated with incident SSc-PAH in 2 longitudinal studies and was found to be more present in SSc-PAH in 1 cross-sectional study
	Haemorrhages		N/A	Incident SSc-PAH (1) SSc-PAH (4)	No association
SEMI QUANT	NVC score		SSc-PAH (5)	N/A	Both NVC score and avascular area grade were found to be more commonly associated with SSc-PAH in 1 cross-sectional study
	Avascular area grade		SSc-PAH (5)	N/A	
QUALITATIVE	Severe NVC patterns (active or late vs normal or early)		Incident SSc-PAH (2) SSc-PAH (4,5)	N/A	More severe NVC patterns (active or late) were found to be more commonly associated with incident SSc-PAH in 1 longitudinal study and were unequivocally associated with SSc-PAH in 2 cross-sectional studies
	Worsening to a late NVC pattern		Incident PAH (1)	N/A	Worsening from a normal/early/active to a late NVC pattern was found to be more commonly associated with incident SSc-PAH in 1 longitudinal study

Longitudinal studies, Unequivocal association

Results: The systematic search retrieved 316 records, of which a total of 234 unique titles were screened. Of those, 28 records eligible for full-text review. Finally, only 5 fulfilled the predetermined eligibility criteria.
Two high-quality longitudinal studies were identified [1,2]. Both baseline and progression of capillary loss were found to be associated with incident SSc-PAH [1,2]. Both studies reported an association between baseline abnormal capillary morphology and incident SSc-PAH [1,2]. No association with incident SSc-PAH was found between capillary dimension nor presence of haemorrhages [1]. Concerning qualitative assessment, Avouac et al. reported worsening to a late NVC pattern over time to be more commonly associated with incident SSc-PAH [1]. Finally, Sulli et al. found severe NVC patterns (i.e. active or late) to be more commonly associated with incident SSc-PAH [2].
Three fair-quality cross-sectional studies were identified [3-5]. Capillary density has been unequivocally inversely associated with SSc-PAH [3,4].

Capillary dimension has been evaluated in 2 studies, with no unequivocal results [3,4]. Corrado et al. found abnormal morphology to be more commonly associated with SSc-PAH [4]. No association was found between presence of haemorrhages and SSc-PAH [4]. Riccieri et al. found that NVC score and avascular area grade were more commonly associated with SSc-PAH [5]. Concerning qualitative assessment, severe NVC patterns have been unequivocally found to be more commonly associated with SSc-PAH [4,5].

Conclusion: This is the first systematic literature review to investigate the role of NVC in SSc-PAH using standardized definitions as proposed by the EULAR SG MC/RD. Unequivocal associations with incident SSc-PAH were found in longitudinal studies between capillary density, abnormal morphology and NVC pattern. Unequivocal associations with SSc-PAH were found in cross-sectional studies between capillary density and severe NVC pattern.

REFERENCES:

[1] Avouac. Semin Arthritis Rheum 2017;47(1):86-94.
[2] Sulli. Arthritis Rheumat 2012;64(3):821-5.
[3] Hofstee. Ann Rheum Dis 2009;68(2):191-5.
[4] Corrado. Microvasc Res 2017;114:46-51.
[5] Riccieri. Rheumatology 2013;52(8):1525-8.

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FRI0346 PERFORMANCE OF THE 2017 EUROPEAN LEAGUE AGAINST RHEUMATISM/AMERICAN COLLEGE OF RHEUMATOLOGY (EULAR/ACR) CLASSIFICATION CRITERIA FOR ADULT IDIOPATHIC INFLAMMATORY MYOPATHIES IN A HONG KONG COHORT

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Background: The new classification criteria for idiopathic inflammatory myopathy (IIM) endorsed by the European League Against Rheumatism and American College of Rheumatology (EULAR/ACR) were published in 2017 [1]. However, the majority of the patients in the development cohort were Caucasians. External validation in other populations were advised. With the increasing availability and experience of myositis specific autoantibodies (MSAs) testing, the inclusion only anti-Jo-1 antibody is apparently insufficient.

Objectives: The objective of the study was to evaluate the performance of the 2017 EULAR/ACR classification criteria in a cohort of Hong Kong adult IIM patients. The secondary objectives included examining the level of agreement between the new criteria and the traditional criteria and assessing the effect of including other MSAs into the criteria.

Methods: This was a multi-centre retrospective cross-sectional study. Consecutive patients with a clinical diagnosis of IIMs and MSA tested seen in the rheumatology clinic or admitted to the rheumatology wards of the participating hospitals in Hong Kong up till August 2018 were recruited. Patients with juvenile onset myositis were excluded. Clinical parameters required by the two criteria will be collected by reviewing the medical records. A commercial line blot immunoassay kit (EUROIMMUN) was used to detect the MSAs.

Results: Two hundred and four patients with IIM were recruited. The mean age was 59.3 years. There was a female predominance of 76.5%. The subgroups of the patients were: polymyositis 40.7%, dermatomyositis 38.2%, clinically amyopathic dermatomyositis patients 21.1%. MSAs were detected in 59.3% of the patients with anti-Jo-1 antibody being the commonest (13.2%). The new 2017 EULAR/ACR Criteria could classify 96.1% of the patients as having definite or probable IIM. The Bohan and Peter criteria could only classify 76.0% of the patients. When combining with the Sontheimer's criteria for CADM, 93.1% of the patients could be classified. The percentage agreement of the new and the Bohan and Peter criteria also increased from 77.0% to 93.1% when the latter was supplemented by the Sotheimer's criteria. If the presence of any MSAs is considered one of the criteria, the performance of the 2017 criteria improved to 97.5% while the combined Bohan and Peter/Sontheimer's criteria to 96.1%. However, the new criteria still failed to highlight the important subtype of IIM associated with anti-MDA5 autoantibody.

Conclusion: In a population with a significant proportion of CADM patients, the new 2017 EULAR/ACR classification criteria outperformed the old criteria. Finally, a clinico-serological criteria for "anti-MDA5 syndrome" is proposed in which a patient must have positive serologic testing for an anti-MDA5 autoantibody, plus one of the following conditions: myositis by the new EULAR/ACR criteria, interstitial lung disease or typical rash (skin ulceration, palmer papules).

REFERENCE:

[1] Lundberg IE, Tjarnlund A, Bottai M, Werth VP, Pilkington C, Visser M, et al. European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. Ann Rheum Dis. 2017;76:1955–64.

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FRI0347 TUBERCULIN SKIN TEST FOR DETECTION OF TUBERCULOSIS IN SYSTEMIC SCLEROSIS

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Background: The tuberculin skin test (TST) is a screening tool for detection of occult or remote tuberculosis infection. Although skin tightness is a classic manifestation in systemic sclerosis (SSc), there are no reports vis-à-vis any limitation of the TST in SSc patients nor a definition on the cut-off for a positive TSTtest size for a diagnosis of tuberculosis.

Objectives: Our aims were to determine (a) the indurated reaction size of the TST; (b) the cut-off size for the indurated TST; and, (c) the sensitivity and specificity of the test for the diagnosis of tuberculosis in SSc patients.

Methods: A cross-sectional study was conducted among Thai adult SSc patients, followed up at the Scleroderma Clinic, Khon Kaen University, Thailand between November 1, 2016 and November 30, 2017. The TST was performed using 0.1 ml purified protein derivatives (PPD) injected intradermally (Figure 1), and interpreted 72 hours after testing.

Results: A total of 168 SSc patients were enrolled (female to male ratio = 1.8:1). The median age and duration of disease was 57.2 and 6.4 years, respectively. The majority (71.8%) was the diffuse cutaneous SSc subset. Seventeen cases (10.1%) were defined as tuberculosis infection. All of the patients had a history of BCG vaccination at birth. An indurated skin reaction size TST of 20 U/L had a high specificity for tuberculosis (99.3%: 95%CI 96.4-100) (Kappa 0.86; p=0.03). The modified Rodnan skin score (mRSS) had a significant negative correlation with the indurated skin reaction size (Rho -0.23; p=0.003). While other clinical parameters—such as BMI, SSc subset, serum albumin level, steroid or immunosuppressant use—were not correlated with the TST result (p=0.06, 0.14, 0.09, 0.23 and 0.89, respectively).

Conclusion: Indurated skin $\geq$ 20 mm indicated a high specificity for tuberculosis infection in SSc patients with history of BCG vaccination. The high mRSS resulted in a smaller skin reaction size when using the TST. The TST is thus less useful as a diagnostic tool for tuberculosis among SSc patients, especially among those with severe skin tightness.



Figure 1. Tuberculin skin test in a systemic sclerosis patient

REFERENCES:

[1] Foocharoen C, Nanagara R, Foocharoen T, Mootsikapun P, Suwannaroj S, Mahakkanukrauh A. Clinical features of tuberculous septic arthritis in Khon Kaen, Thailand: a 10-year retrospective study. Southeast Asian J Trop Med Public Health. 2010 Nov;41(6):1438–46.
[2] Rose DN, Schechter CB, Adler JJ. Interpretation of the tuberculin skin test. J Gen Intern Med. 1995 Nov;10(11):635–42.
[3] Jamil B, Qamruddin S, Sarwari A, et al. An assessment of Mantoux test in the diagnosis of tuberculosis in a BCG-vaccinated, tuberculosis endemic area. Journal of Infectious Disease Parkistan. 2008;17(1):18–22.
[4] Liam C, Lim K, Wong C. Changes in serum proteins, erythrocyte sedimentation rate and Mantoux tuberculin skin test reactivity in active tuberculosis. JUMMEC. 1998;3(1):47–53.

[5] Wang L, Turner MO, Elwood RK, Schulzer M, FitzGerald JM. A meta-analysis of the effect of Bacille Calmette Guérin vaccination on tuberculin skin test measurements. Thorax. 2002 Sep;57(9):804–9.
[6] Araujo Z, de Waard JH, de Larrea CF, Borges R, Convit J. The effect of Bacille Calmette-Guérin vaccine on tuberculin reactivity in indigenous children from communities with high prevalence of tuberculosis. Vaccine. 2008 Oct 16;26(44):5575–81.
[7] Farhat M, Greenaway C, Pai M, Menzies D. False-positive tuberculin skin tests: what is the absolute effect of BCG and non-tuberculous mycobacteria? Int J Tuberc Lung Dis. 2006 Nov;10(11):1192–204.
[8] Abdel-Samea S, Ismail Y, Fayed S, Mohammad A. Comparative study between using QuantiFERON and tuberculin skin test in diagnosis of Mycobacterium tuberculosis infection. EJCT. 2013;62:137–43.

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FRI0348 USE OF INTRAVENOUS IMMUNOGLOBULIN THERAPY IN PATIENTS WITH SYSTEMIC SCLEROSIS: A SPANISH MULTICENTER EXPERIENCE

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Objectives: To describe the efficacy of intravenous immunoglobulin (IVIG) therapy in different organic conditions of Systemic Sclerosis (SSc).
Methods: Retrospective multicenter observational study that enrolled patients with SSc treated with IVIG. We collected epidemiological data, SSc complications, treatments and functional tests. Regarding IVIG treatment we recorded the reason to use, number of cycles, and the clinical efficacy at the end of the last IVIG cycle were collected at investigator's discretion. For the comparison of variables, the Chi-square, Fisher's F test and the T test was used.
Results: 41 patients (83% women) were recruited, with a mean age of 58 ± 18.2 years old. The age of diagnosis was 48 ± 8 years old. The diffuse cutaneous SSc was the most frequent in the sample (61%) and 24/41 had Overlap syndrome (49% myositis). Regarding the different SSc complications in treated patients the most frequent were digestive involvement, arthritis and interstitial lung disease (78%, 73%, and 63% respectively). 12% of patients developed cancer and 25% died during the follow-up. The most frequent indication IVIG was myositis (51%) followed by cutaneous (17%). The mean of cycles was 10. 37% of patients had previously undergone treatment with biological therapy, being RTX the most used therapy. 80% of patients had a history of use with corticosteroid therapy. When evaluating the degree of skin involvement (mRSS) patients showed a significant improvement of -2.89 ± 5.2(p <0.03) at the end of the follow-up. Indeed we observed better results in the groups of patients with myositis. No differences were observed in the% FVC or% DLCO outcomes during the follow-up. However, when we compared patients with or without overlap syndrome we found differences in%FVC values at the beginning of the study that were not present at the end of the follow-up. Patients with antiScl70 seemed to have less response to IVIG therapy.
Conclusion: Our results suggest that IVIG can be useful for the management of some conditions in specific profiles of patients with SSc. Prospective studies and randomized clinical trials are necessary to establish the efficacy and safety of IVIG to treat the different conditions of SSc.

	IVIG N=41(%)	Difuse n=25 (%)	Limited n=16(%)
Women	34(83)	21(84)	13(81)
Age	58 ± 18		
Overlap	24(59)	11(44)	13(81)
Clinical manifestations			
Joint	30(73)	22(88)	8(50)
Muscular	30(73)	16(64)	14(88)
Reflux GE	32(78)	20(95)	12(75)
Interstitial lung disease	26(63)	16(64)	10(63)
Pulmonary hypertension	5(12)	2(8)	3(19)

	myositis	Overlap	AntiScl70	PM/Scl
Initial mRss	16±12	13±11	29±9	15 ±10
Final mRss	12±12	7±7	32±7	13 ±15
Initial FVC	68±25	64±24	56±23	60 ±13
Final FVC	73±26	72±25	58±20	67 ±18
Initial DLCO	56±16	56±17	55±16	49 ±13
Final DLCO	68±25	71±24	45±12	69 ±18

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FRI0349 RELATIONSHIPS BETWEEN BODY COMPOSITION AND NAILFOLD VIDEOCAPILLAROSCOPY PATTERNS IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease, characterized by microvascular damage and progressive fibrosis. Among clinical complications, abnormal body composition and sarcopenia have been reported in SSc patients(1,2). Nailfold videocapillaroscopy (NVC) is a safe diagnostic tool to assess microvascular progressive damage and may predict severe organ involvement in SSc(3).
Objectives: The aim of this study was to evaluate body composition in SSc patients and assess possible differences between patients with specific NVC patterns of microangiopathy.
Methods: 38 patients (6 men and 32 women) fulfilling ACR 2013 criteria for SSc underwent NVC to assess their NVC patterns ("Early", "Active" and "Late" pattern)(4) and DXA to evaluate body composition(5). In particular we analyzed: total mass, total lean mass, total fat mass, bone

mineral content(BMC), and bone mineral density(BMD) in seven body areas(head, upper limbs, lower limbs, trunk, spine, ribs, pelvis). Sarcopenia was diagnosed in patients with reduced skeletal muscle index (RSMI) below 5.45 Kg/m^2 for females and 7.25 Kg/m^2 for males(6). Statistical analysis was performed by non parametric tests.

Results: The mean age of patients was 64±11 years, mean disease duration 19.2 ±7.6 years, mean Rodnan skin score(mRSS) 11.5±9.3, and mean RSMI 6.3±1.05 g/cm^2. All the patients showed a NVC "scleroderma pattern": in particular 15 patients showed the "Late" pattern, 15 patients the "Active" pattern and 8 patients the "Early" NVC pattern. The "Late" NVC pattern group comparing to "Early/Active" group showed significantly lower total mass(58287±8217 *vs* 67238±11437 gr, p=0.01), lean mass (35249±3646 *vs* 41230±7954 gr, p= 0.05), RSMI(5.8±0.92 *vs* 6.6±1.02 g/cm^2, p=0.02), BMC(1839±339 *vs* 2183±502 gr, p= 0.04), trunk BMD(0.70 ±0.12 *vs* 0.87±0.13 g/cm^2, p=0.05) and spine BMD(0.91±0.17 *vs* 1.08 ±0.18 g/cm^2, p=0.008). No statically significant difference between the two group was observed regarding total fat mass, total body BMD and BMD at upper limbs, lower limbs, head, ribs and pelvis. Interestingly, 24% of SSc patients were found affected by sarcopenia, and the most of sarcopenic patients showed the "Late" NVC pattern(67%). Comparing age, disease duration, mRSS between sarcopenic and non sarcopenic patients there was no difference between the groups, but sarcopenic patients presented a statistically significant lower BMI(p=0.02).

Conclusion: This study demonstrates in SSc patients a relationship between a more severe microvascular damage ("Late" SSc pattern) and the body composition, characterized by lower weight, total lean mass, bone mineral content and sarcopenia, without any significant variation in total fat mass. These clinical conditions seem not to be associated with severity of skin involvement and/or disease duration.

REFERENCE:

[1] Caimmi C, et al. Clinical Rheumatology 2018;37:987-997.2.Thais FM, et al. Clin Rheumatol 2013;32:1037-44.3.Smith V, et al. J Rheumatol. 2013;40:2023-8.4.Cutolo M, et al. J Rheumatol 2000;27:155-60.5.Haarbo J, et al. Clin Physiol 1991;11:331-41.6.Baumgartner RN, et al. Am J Epidemiol 1998;147:755-63.

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FRI0350 THE FREQUENCY OF LOW MINERAL DENSITY, FALLS AND FRACTURES IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a severe connective tissue disorder causing vascular, immune, and fibrotic changes in the skin and internal organs. Patients with SSc may have an increased risk of osteoporosis (OP) and fractures due to a chronic inflammatory state, latent malabsorption or malnutrition, immobilization, and use of corticosteroid therapy.

Objectives: to determine the frequency of low mineral density, falls, low energy fractures and 10-year probability of new fracture in patients with SSc.

Methods: 191 patients with SSc were enrolled in the study: 160 women (mean age 51±13 yrs), among them 107 postmenopausal, and 31 men (mean age 53±14 yrs). Bone mineral density (BMD) was measured at lumbar spine (LS), femoral neck (FN) and total hip (TH) by dual energy X-ray absorptiometry (DXA, Hologic 4500A). BMD decreasing grade was determined in accordance to WHO criteria. All patients were interviewed on a special questionnaire and assessment of 10-year probability of new fracture by FRAX® was performed. Vitamin D level was measured in 104 patients.

Results: Low BMD was found in 68% women and 55% men: osteopenia in 30% and 32% and OP in 38% (21% in reproductive age and 50% in postmenopausal) and 23%, respectively. BMD in LS, FN and TH associated with body mass index (r=0,3, p=0,030; r=0,41, p=0,0027; r=0,49, p=0,0002, respectively) and duration of postmenopausal period in women (r=-0,56, p=0,023; r=-0,66, p=0,006; r=-0,63, p=0,009, respectively). BMD of LS and FN correlated with age (r=-0,22, p=0,045; r=-0,23, p=0,016, respectively), duration of SSc (r=-0,32, p=0,037; r=-0,31, p=0,046, respectively), glucocorticoid cumulative dose for LS only (r=-0,31, p=0,024). Mean 25(OH)D level was 19,83±11,06 ng/ml. Normal vitamin D level had 9% of SSc patients. No correlation between BMD and 25(OH)D level was found.

46 (24%) patients reported falls in the year prior to the interview, among them in 2 patients the fall led to fracture. A total of 48 (25%) patients had low energy fractures in the past, among them 8 (4%) of women had two or more fractures. Frequency of low energy fractures was 35%, 8% and 25% among postmenopausal women, women of reproductive age and men, respectively. The mean age at which the fracture occurred was 55±11 yrs. in postmenopausal women, 30±12 yrs. in young women and 60±12 yrs. in men. The most frequent were the fractures of distal forearm and vertebrae: 13 (7%) and 26 (14%) patients, respectively. Five patients each (3%) had ankle and humerus neck fractures and 7 – other localizations. Nobody reported the fracture of the proximal femur. Patients with abnormal BMD (OP or osteopenia) had a risk of falls and low energy fractures more than 2 times higher than patients with normal BMD (OR 2.93 [95% CI 1.11; 8.01], *p*=0,016 and OR 2.58 [95% CI 1.04; 6.6], *p*=0,025, respectively). 10-year probability of any major osteoporotic fracture was 18.4 ± 9.6% in women and 9.7 ± 8.6% in men and of hip fracture - 3.5 ± 3.7% and 1.5 ± 3.9%, respectively. Among all patients, 55% of women and 4% of men had a high risk of subsequent fractures using the FRAX® algorithm.

Conclusion: Low BMD was diagnosed in 68% of women and 55% of men with SSc. The correlations between BMD and age, body mass index, the duration of postmenopause were revealed. Additionally, we found associations with risk factors related to the disease itself: disease duration and glucocorticoid cumulative dose. Reduced BMD was associated with an increased risk of falls and fractures. 55% of women and 4% of men had a high risk of further fractures.

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FRI0351 DISTINCTION BETWEEN TELANGIECTASIA SECONDARY TO CONNECTIVE TISSUE DISEASE AND CUTANEOUS COLLAGENOUS VASCULOPATHY

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Background: Cutaneous collagenous vasculopathy (CCV), a recently described, rare, superficial dermal microangiopathy of unknown etiology, shares clinical and histopathological features in common with cutaneous lupus erythematosus and dermatomyositis. Fewer than 50 cases have been reported in the literature. Concurrence of CCV and connective tissue diseases (CTD) may present a diagnostic quandary.

Objectives: To determine whether CCV cases at our center were associated with CTD and to identify distinguishing features between CCV and cutaneous manifestations of CTD.

Methods: The laboratory information system at a single academic health care center (2000-2018) was searched to identify cases with a diagnosis of CCV. All pathological material and clinical charts were reviewed. The demographic, clinical and pathological data were documented.

Results: We identified 6 cases of CCV (4 female, 2 male; median age 57 years). Clinically, a telangiectatic eruption was present in all patients, affecting the lower limbs and other sites (N= 5) and the abdomen and arms (N=1). All patients had been seen by a dermatologist and 3 by a rheumatologist. A concurrent CTD was present in 2 cases; Sjogren's syndrome (N=1) and undifferentiated connective tissue disease (N=1). In both, the clinical differential diagnosis included CCV and cutaneous involvement by the CTD. In all 6 cases, histopathological examination revealed a non-inflammatory vasculopathy, with PAS-positive, diastase resistant, hyaline thickening of ectatic superficial capillary walls, and loss of pericytes. These hallmarks of CCV excluded skin disease attributable to CTD in the two relevant cases.

Conclusion: Concurrence of CCV and CTD, though uncommon, presents a diagnostic challenge. The clinical distribution of the CCV eruption, favouring the lower limbs, and its non-inflammatory character histopathologically distinguish it from cutaneous involvement by a CTD.

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FRI0352 **DIFFERENCES IN ANTISYNTHETASE SYNDROME DEFINITION AND RELATED DIAGNOSTIC PERFORMANCE. A SYSTEMATIC LITERATURE REVIEW INFORMING THE NEW ACR/EULAR CLASSIFICATION CRITERIA**

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Background: Antisynthetase syndrome (ASSD) lacks of established clinico-serological classification criteria. A taskforce by EULAR and ACR is working on to develop and validate classification criteria for ASSD.
Objectives: To systematically upraise literature to retrieve the available definitions of ASSD and to evaluate their diagnostic performance.
Methods: This systematic review followed a pre-specified protocol. Two research questions (Q1: how is ASSD defined; Q2: what is the diagnostic performance of the definitions) were rephrased into PICOs terms to create search strategies. Studies on patients with suspect or confirmed ASSD, including a definition of the disease with any study design, excluding case-reports and narrative reviews, were eligible for inclusion. The diagnostic performance had to be tested against the reference standard of expert opinion. PubMed and Embase were searched from 01/01/1984 to 06/11/2018. Moreover, the ACR and EULAR congress abstracts (2017-2018) were hand searched. The titles and abstracts of the retrieved studies were screened by pairs of reviewers, the full-text of studies fulfilling the inclusion criteria was assessed to confirm eligibility. The references of the included studies were also evaluated in search of additional studies. Data from primary studies were extracted into a pre-specified extraction form and, if possible, 2x2 tables to assess diagnostic performance were completed. Sensitivities, specificities, positive and negative likelihood ratios (LR) were calculated for each study. If the diagnostic performance of a definition or variable was assessed in at least 4 studies, a meta-analysis of diagnostic performance was undertaken. The risk of bias (RoB) was assessed using the most appropriate tool depending on study design.
Results: After the exclusion of duplicates, the searches retrieved 4358 studies, of which 375 suitable for full-text review. Finally, 77 studies were included, along with 1 additional study from hand search and 3 congress abstracts. 72 studies were included in Q1 and 9 in both Q1 and 2. The presence of antisynthetase antibodies (70 studies), mainly anti-Jo1 (57 studies); myositis (51 studies), mainly defined clinically (32 studies); and interstitial lung disease (38 studies) were the variables most frequently used to define ASSD. Other variables, such as arthritis (19 studies), Raynaud's phenomenon and skin manifestations (10 studies each) were included less frequently. Most commonly, ASSD was defined by a combination of clinical and serological variables. However, no study evaluated the diagnostic performance of such combined definitions. Most of the studies included in Q2 (6) evaluated specific variables of muscle biopsy, one evaluated MRI and 2 clinical variables, with a wide variability in the performance of each item. It was possible to meta-analyze data only to assess the performance of perifascicular necrosis/atrophy: pooled sensitivity (95%CI) was 0.53 (0.33,0.72) and specificity 0.63 (0.47,0.76), pooled LR+ 1.45 (0.72,2.89) and LR- 0.73 (0.40,1.34).
Conclusion: ASSD is defined according to a variety of combinations of serological, clinical and histological variables. The performance of these combined definitions however has not been tested, and from the limited evidence available single muscle biopsy variable (perifascicular necrosis/atrophy) seem to perform poorly. The systematic review confirms the need of data and consensus driven classification criteria for ASSD.
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FRI0352B **COMPARISON OF TWO ILOPROST REGIMENS IN TERMS OF ECONOMIC IMPACT AND EFFECTIVENESS**

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Background: Systemic sclerosis (SSc) is an autoimmune chronic disease characterized by prominent vascular involvement. Intravenous iloprost (IV ILO), according to the recently updated EULAR recommendations, is indicated for Ssc Raynaud's phenomenon (RP) after failure of oral therapy. Moreover, IV ILO could be useful in DU healing and may represent a potential disease modifying medication. However, there are no uniform data regarding type of regimen (dosage, duration and frequency) and infusion modality.
Objectives: The purpose of this study was to compare effectiveness (in terms of Dus) and direct costs, of two regimens of IV ILO infusion in the same cohort of consecutive SSc subjects.
Methods: Protocol A (A): the patient was admitted and 100 mcg of ILO was diluted in 500 ml of normal saline or 5% dextrose solution and infused continually at the maximum tolerated dose until exhaustion.
Protocol B (B): the patient was followed as outpatient at infusion clinic and 50 mcg of ILO was diluted in 250 of normal saline or 5% dextrose and infused at a dose range from 0.5 to 1.5 ng/Kg/min. The dose was escalated at 30 minutes intervals and maintained at the maximum tolerated dose for 5 consecutive hours for two consecutive days. The intervals between the infusions were between 6-8 weeks in both protocols depending on clinical response and availability of places at the Unit.
44 patients who received long term IV ILO as inpatients (Cohort A), after a wash out of 3 months, were switched to ambulatory administration (Cohort B). Thereafter, after one year of follow-up 24 patients of the protocol B were lost to follow-up and 20 patients were maintained on this regimen. Comparison was made between Cohort A (44 patients=A44) in the period between march 2015 and October 2016 (period A), Cohort B (44 patients=B44) between October 2016 and March 2017 (period B44), Cohort B (20 patients=B20), between October 2017 and March 2018 (period B20). Comparison between groups was made by non parametric tests and contingency table analysis when appropriate. Costs were estimated multiplying data related to resource use (drug consumpion, hospital stay, outpatient visits, management of complications, etc) by unit cost obtained from the accounting office of the Hospital. All costs were expressed in Euro
Results: Mean number of DUs at the end of period A was 0,37±0,98 in A44 as compared to 0,90±1,39 of period B44 cohort B44 (p=0,045) and 0,55±0,95 of period B20 Cohort B20 (p=n.s.). Cumulative number of DUs was 9/44 in Cohort A (20.5%) as compared to 20/44 in Cohort B44 (45% p=0.002) and 7/20 in cohort B20 (35% p=0,05). High number of drop outs (24/44) in protocol B was due mainly to statistical significant difference in tolerability (adverse events 11% protocol A vs 42% protocol B p < 0,01). Direct costs were higher in protocol A (3132±883 Euros vs 2687±556 Euros) as compared to protocol B, despite the differences were not statistically significant between the two modalities
Conclusion: Protocol A seems to represent a regimen better tolerated and more effective than protocol B. Moreover, protocol B is affected by high rate of drops out due mainly to worse tolerability. Admitting SSc-patients for continuous IV ILO infusion seems to represent a better tolerated and more effective choice than following them as outpatients at infusion clinic, with substantially comparable direct costs in the same SSc cohort.
Disclosure of Interests: Alessandra Della Rossa: None declared, Simone Barsotti: None declared, Marco Di Battista: None declared, Lorenzo Puccetti: None declared, Valentina Lorenzoni: None declared, Giuseppe Turchetti: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB
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Spondyloarthritis – etiology, pathogenesis and animal models

FRI0353 MISREGULATION OF BMP/TGFB SHEDS LIGHT ON THE PATHOGENICITY OF HLA-B27 IN SPONDYLOARTHRITIS

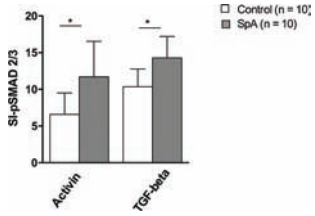
Benjamin Grandon[1], Auroe Rincheval[1], Nadège Jah[2,3], Jean-Marc Corsi[1], Luiza M. Araujo[2,3], Simon Glatigny[2,3], Delphine Roche[1], Gilles Chiocchia[2,3], Isabelle Guénal[1], Sébastein Gaumer[1], Maxime Breban[2,3,4]. [1]*University of Versailles-saint-Quentin, LGBC, Montigny-le-Bretonneux, France*; [2]*UMR 1173 University of Versailles Saint-Quentin-INSERM, Team Chronic Inflammation and Immune System, Montigny-le-Bretonneux, France*; [3]*University Paris Diderot, Sorbonne Paris Cité, INFLAMEX, Laboratoire d'Excellence, Paris, France*; [4]*Ambroise Paré Hospital, Rheumatology, Boulogne-Billancourt, France*

Background: The class I MHC allele, HLA-B27 is the main genetic factor predisposing to ankylosing spondylitis (AS) and related spondyloarthritis (SpA), a group of osteo-articular disorders combining inflammation with ossification. Until now, hypotheses to explain such striking association discovered 45 years have speculated either on the presentation of particular peptides to $CD8^+$ T cells or on aberrant behaviors of the HLA-B27 molecule independent of its antigen presenting function, including slow folding and homodimers formation

Objectives: To unravel aberrant function(s) of HLA-B27 independent of antigen presentation that may explain its pathogenicity.

Methods: *Drosophila* transgenic for SpA-associated HLA-B*27:04 or HLA-B*27:05 or non-SpA -associated HLA-B*07:02, alone or in combination with human β2-microglobulin (hβ2m) were produced. Genetic interaction tests were used to identify altered pathway(s). Protein-protein interactions were evidenced by proximity ligation assay. Phosphorylation of Smad2/3 was tested on CD4+ T cells from HLA-B27+ SpA patients and HLA-B27- neg healthy controls (6-10/group) by PhosFlow.

Results: *Drosophila* transgenic for HLA-B*27:04 or HLA-B*27:05 but not for control HLA-B*07:02 allele, in the presence of hβ2m that allows expression of well-folded HLA-B molecules at the cell surface, developed *crossveinless* phenotype. This was due to a disturbance of BMP signaling by HLA-B27/hβ2m which repressed Saxophone (Sax) BMP type I receptor (BMPR1) function, resulting in widening of phosphorylated Mad, the *Drosophila* receptor-mediated Smad, gradient, and increased expression of its target genes *dpp* and *omb*. Consistently, HLA-B27/hβ2m well-folded conformers co-localized with Sax at the surface of *Drosophila* cells and also with Sax mammal ortholog ALK2, on immune cells from SpA patients. As predicted, given that Sax orthologs ALK1 and ALK2 are known to exert antagonistic function on TGFβ/BMP signaling, we found heighthened p-Smad in response to TGFβ or Activin A in CD4+ T cells from HLA-B27+ SpA patients ($p<0.05$).



Conclusion: The pathogenic role of HLA-B27 in SpA may result from a TGFβ/BMP signaling misregulation due to specific antagonistic interaction with ALK1/ALK2 BMPR1, at the crosstalk between inflammation and ossification. Interestingly, ALK2 mutations are responsible for the rare mendelian disorder, Fibrodysplasia Ossifians Prgogressiva that mimicks AS (Ref).

REFERENCES:

[1] Hatsell, S. J. et al. ACVR1R206H receptor mutation causes fibrodysplasia ossificans progressiva by imparting responsiveness to activin. Science Translational Medicine 7, 303ra137-303ra137 (2015).

Disclosure of Interests: Benjamin Grandon: None declared, Auroe Rincheval: None declared, Nadège Jah: None declared, Jean-Marc Corsi: None declared, Luiza M. Araujo: None declared, Simon Glatigny: None declared, Delphine Roche: None declared, Gilles Chiocchia: None declared, Isabelle Guénal: None declared, Sébastein Gaumer: None declared, Maxime Breban Grant/research support from: Pfizer, UCB, Novartis, MSD, Consultant for: UCB

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FRI0354 ASSESSING THE ROLE OF TENDON-T CELL INTERACTIONS IN THE DEVELOPMENT OF CHRONICITY IN SPONDYLOARTHRITIS

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Background: Enthesitis is a hallmark of spondyloarthropaties[1], with mechanical stress or damage in the tendon being proposed as a trigger for the development of inflammation at the enthesis that propagates to the synovial compartment through what has been termed "synovio-entheseal complex"[2]. Increasing evidence supports the role that stromal cells play in the shift of the inflammatory process towards chronicity promoting T cell migration, retention and survival[3]. Therefore, we hypothesize that after tendon damage the crosstalk between stromal and immune compartments contributes to the development of chronic inflammation.

Objectives: We aimed to assess the effect of tendon stromal cells (tenocytes) on T cell migration and activation and the impact of these activated T cells on the stroma.

Methods: Tenocytes were explanted from tissue obtained from anterior cruciate ligament (ACL) reconstructions. The effect of damage on tenocytes after stimulation with conditioned media from tendon explants or IL-1ß was evaluated by qPCR. A transwell membrane system was used to test the impact of conditioned media from tenocytes on T cell migration. T cells and tenocytes were co-cultured with or without the presence of a transwell membrane to quantify T cell activation (CD69 by FACS and IFN-γ by ELISA). Changes in gene expression on tenocytes after co-culture with activated T cells were analysed by qPCR.

Results: In the presence of damage, tenocytes upregulated inflammatory mediators (IL-6, COX2), chemokines (CCL2, CCL5, CXCL10, CXCL12) and adhesion molecules (ICAM-1). Conditioned media, particularly after stimulation with IL-1ß, from tenocytes induced T cell migration. Co-cultures of tenocytes and T cells resulted in activation of T cells that was contact dependant. In turn, these activated T cells upregulated the production of inflammatory mediators in tenocytes and increased the COL3/COL1 ratio.

Conclusion: Our results support a communication between the stromal and immune compartment within the tendon that could be involved in the progression towards chronicity in the context of spondyloarthritis. Following damage, tendon stromal cells are able to induce the recruitment of T cells, that once enter the tissue interact with the stroma. Stromal cells are then further activated to produce inflammatory cytokines and chemokines that amplify and maintain this inflammatory response.

REFERENCES:

[1] G. Schett, et al., "Enthesitis: from pathophysiology to treatment," *Nat. Rev. Rheumatol.*, vol. 13, no. 12, pp. 731–741, 2017.

[2] D. McGonagle, S. Z. Aydin, and A. L. Tan, "The synovio-entheseal complex and its role in tendon and capsular associated inflammation," *J. Rheumatol.*, vol. 39, no. SUPPL. 89, pp. 11–14, 2012.

[3] C. D. Buckley, "Why does chronic inflammation persist: An unexpected role for fibroblasts," Immunol. Lett., vol. 138, no. 1, pp. 12–14, 2011.

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FRI0355 MUCOSAL ASSOCIATED INVARIANT T-CELLS ARE ENRICHED AT THE HUMAN ENTHESIS AND HAVE A RESIDENT MEMORY PHENOTYPE

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Background: Mucosal associated invariant T-cells (MAITs) are innate-like T lymphocytes that express a semi-invariant TCR repertoire. They are activated by microbial ligands or cytokines including IL-23 and secrete inflammatory cytokines, including IFNγ and IL-17A. MAIT cells are enriched at mucosal surfaces and have been implicated in the pathogenesis of spondyloarthritis (SpA) (1) and inflammatory bowel disease (IBD). Although the human enthesis is not a mucosal surface it is the primary site of inflammation in SpA which has strong association with IBD.
Objectives: To investigate if a population of MAITs is present at the normal human enthesis thereby establishing a potential link between gut and joint inflammation.
Methods: Healthy interspinous ligament and spinous process were harvested from patients undergoing elective surgery for the correction of mechanical spinal defects. Entheseal soft tissue (EST) and peri-entheseal bone (PEB) were separated and cells were harvested by enzymatic and mechanical digestion respectively. The proportion of cells expressing markers consistent with MAITS (CD45+, CD3+, CD161+, TCRVα7.2+) were measured by flow cytometry in EST, PEB and matched blood. Expression of CD69 and CD45RA were examined for phenotypic analysis. Transcript analysis for IL-23/IL-17 axis and immunomodulatory genes was performed on sorted entheseal MAITs and analysed by TaqMan array.
Results: As a proportion of total T-cells, MAITs were of approximately 3 fold and 2.5 fold greater abundance in EST and PEB respectively in comparison to matched peripheral blood (both p=0.034). MAITs in entheseal tissue had an overwhelming resident memory phenotype (CD69+, CD45RA-) median 53.2% (range 42.4 – 78.6%) in EST and 54.9% (45.2 - 82.1%) in PEB compared to those from blood 17.7 (6.8 – 69.4). MAITs robustly expressed RORC, CCR6 and IL-23R transcript. Compared to conventional entheseal T-cells, MAITs expressed significantly less TGFβ (6-fold, p>0.001) and significantly more IL-23R (29-fold, p=0.004).
Conclusion: Healthy human entheseal tissue contains an enriched population of MAITs that strongly express IL-23R transcript at a frequency comparable to that reported in the colon (2). The majority of these cells express a resident memory phenotype suggesting that they are a distinct population residing in entheseal tissue. These observations are potentially relevant to SpA pathogenesis and the observed link between SpA and IBD.

REFERENCES:

[1] Gracey E, Qaiyum Z, Almaghlouth I, Lawson D, Karki S, Avvaru N, et al. IL-7 primes IL-17 in mucosal-associated invariant T (MAIT) cells, which contribute to the Th17-axis in ankylosing spondylitis. Annals of the rheumatic diseases. 2016:annrheumdis-2015-208902.
[2] Salou M, Franciszkiewicz K, Lantz O. MAIT cells in infectious diseases. Current opinion in immunology. 2017;48:7-14.

Disclosure of Interests: Richard Cuthbert: None declared, Qiao Zhou: None declared, Abdulla Watad: None declared, Robert Dunsmuir: None declared, Peter Loughenbury: None declared, Almas Khan: None declared, Peter Millner: None declared, Charlie Bridgewood: None declared, Dennis McGonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB
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FRI0356 DIFFERENTIAL EXPRESSION OF HUMAN ENDOGENOUS RETROVIRUSES IN PSORIATIC DISEASE

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Background: Human endogenous retroviruses (HERV) are the stably inherited remnants of ancient retroviruses that infected the ancestral germline. A growing body of research has associated the differential expression and regulation of HERVs with a number of diseases, including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). HERVs are thought to contribute to the pathogenesis of autoimmune diseases by modulating the expression of host immune-related genes, molecular mimicry, or cross reactivity of host proteins with HERV encoded products.
Objectives: To compare the expression of 4 HERVs previously associated with autoimmune disorders (HERV-K, HERV-K10, HERV-W, and HERV-H) in whole blood, CD3+ T cells, and CD14+ monocytes of patients with cutaneous psoriasis without arthritis (PsC), psoriatic arthritis (PsA), and healthy controls.
Methods: PsC, PsA patients satisfying the CASPAR criteria, and healthy controls were recruited for the study. RNA was extracted from whole blood collected in Tempus tubes and HERV expression was measured by quantitative real time PCR (qRT-PCR) or droplet digital (dd)PCR with normalization to *GAPDH*. HERV expression in whole blood RNA from 40 PsA patients was compared to 40 age and sex matched PsC patients and 40 age and sex matched healthy controls. Subsequently, HERV expression in 55 PsC patients who progressed to develop PsA (converters) was compared to 55 age and sex matched PsC patients who did not develop PsA over the same duration of follow-up (non-converters). Finally, HERV expression in RNA isolated from CD3+ T cells and CD14+ monocytes from 19 PsA patients was compared to 13 PsC and 8 healthy controls. Expression differences between groups were determined by one-way ANOVA, Kruskal-Wallis and Mann-Whitney tests where appropriate.
Results: In whole blood, HERV-K was significantly differentially expressed between 40 PsA and 40 PsC patients (fold change [FC]=1.57, p=0.008). HERV-K was also significantly differentially expressed in baseline samples from 55 converters compared to 55 non-converters (FC=1.93, p=0.03). No other HERV genes were differentially expressed between these groups in whole blood. Significant expression differences were more evident in purified cells (Table 1).

Table 1. Differential expression of HERVs in purified T cells and monocytes.

	PsA vs. PsC		PsA vs. Controls		PsC vs. Controls	
	CD3+ T cells FC, p value	CD14+ Monocytes FC, p value	CD3+ T cells FC, p value	CD14+ Monocytes FC, p value	CD3+ T cells FC, p value	CD14+ Monocytes FC, p value
HERV-K	0.43, p=0.02	0.30, p<0.01	ns	0.17, p<0.01	2.18, p=0.02	ns
HERV-K10	2.94, p=0.02	ns	6.87, p<0.01	2.60, p=0.04	ns	ns
HERV-H	ns	ns	3.19, p<0.01	0.36, p=0.02	2.67, p=0.01	0.27, p<0.01
HERV-W	1.27, p=0.04	ns	4.12, p<0.01	ns	3.24, p=0.01	0.47, p=0.04

Ns, not significant.

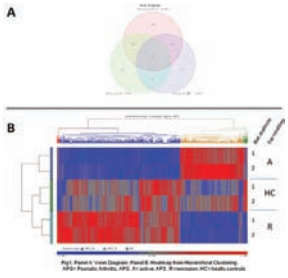
Conclusion: In whole blood, expression of HERV-K differentiates PsA and PsC patients, and its expression is significantly elevated in PsC patients prior to the development of PsA. HERV expression differences between the groups are also evident in purified T cells and monocytes. These data suggest a role for HERVs in the pathogenesis of psoriatic disease and their potential use as prognostic markers of arthritis in patients with psoriasis.
Disclosure of Interests: Remy Pollock: None declared, Rohan Machhar: None declared, Laila Zaman: None declared, Dafna D Gladman Grant/research support from: AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB, Vinod Chandran: None declared
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FRI0357 DRUG-INDUCED REMISSION AND SUBCLINICAL ACTIVITY IN PSORIATIC ARTHRITIS: TRANSCRIPTIONAL PROFILING TO CHARACTERIZETHE DISEASE STATE

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Background: Remission is an important goal of therapy in psoriatic arthritis (PsA), but data on molecular players of clinical remission and effective

disease inactivation are scarce. Gene expression profiling analysis could be useful to elucidate the pathogenic mechanisms of diseases, and differential gene expression analysis between diverse disease conditions produces gene signatures characteristic of the state or disease being studied.
Objectives: Our aim was to compare the transcriptional profiles of patients with clinically active versus inactive (remission state) PsA (peripheral joint subset), and healthy controls (HCs).
Methods: From a cohort of around 300 patients affected by PsA according to CASPAR criteria, we first selected 20 patients (peripheral arthritis subset) with active disease state (without biologic treatment ongoing) (A) and 20 patients with >1-year remission induced by TNFα antagonism (R), as assessed by DAPSA > 14, and DAPSA ≤ 4 scores respectively, and from 20 HCs matching for age and gender ratio. Both PsA groups were not on corticosteroid treatment. RNA from peripheral blood was extracted and, following quality analysis by Agilent Bioanalyzer, each condition has been profiled using RNAs pools in biological duplicates by distinct Affymetrix Human GeneChip HTA 2.0, for a total of 6 arrays. Data analysis was performed using the commercial software Partek Genomics Suite, V 6.6. To identify a transcript as differentially expressed, a value of fold change 1.5 and *p-value* 0.05 has been set.
Results: The Venn diagram shows all comparative groups (A vs R, A vs HC, R vs HC) with their relative amount of transcripts differentially expressed, generated using abovementioned parameters, and the relationship between sets (fig1, panel A). Using the list of transcripts differentially expressed in at least one of the aforementioned comparison, a hierarchical clustering was carried out to highlight the intra-condition expression profile. We have identified (arbitrarily) 4 clusters of transcripts with analogous transcriptional profile and to each of them a color code has been assigned (Heatmap in Fig1, panel B). For these clusters and for all lists of transcripts differentially expressed founded by our comparative study, we carried out the Gene Set Enrichment Analysis by Gene Ontology (GO), in order to identify how molecular functions, cellular components or biological processes occurs more frequently than expected in a reference list of transcripts.



Conclusion: Observing the amount of differentially expressed transcripts, is evident that while active disease state (A) has a clear-cut different profile, the drug-induced remission (R) is more similar with HCs condition. However, in the hierarchical clustering this trend of similarity does not appear in all clusters of transcripts, as shown particularly in the red, orange and green clusters. Again, the Gene Set Enrichment Analysis Score showed us that mRNA transcripts dysregulated in the R condition vs HCs, are involved in several biological processes related to immune system, development, response to stimulus, localization and others. Our next step will be to validate, by Real Time PCR in a large cohort of patients, the most interesting dysregulated genes covering biological functions eventually sustaining subclinical activity in PsA.
Disclosure of Interests: None declared
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FRI0358 ROLE OF MIRNA-21-5PAS A POTENTIAL BIOMARKER FOR THE INFLAMMATION PATHWAY IN PSORIATIC DISEASE AND RESPONSE TO METHOTREXATE TREATMENT

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Background: Psoriatic arthritis (PsA) is an inflammatory arthritis occurring in patients with psoriasis. Several studies have shown links between altered miRNA expression with the pathogenesis of several autoimmune disorders. We previously demonstrated that miR-21-5p was upregulated in PsA compared to psoriasis without arthritis (PsC) and healthy controls (HC) and is thus a potential biomarker for PsA.
Objectives: 1) To determine whether miR-21-5p is differentially expressed in PsC patients who convert to PsA vs non-convertors and validate the previous results in an independent cohort. 2) To determine the role of miR-215p in the response to methotrexate treatment (MTX) 3) To determine whether miR-21-5p modulates inflammation in psoriatic disease.
Methods: Serum & whole blood RNA samples were collected from 54 convertors and 54 non- convertors (matched for age, sex, psoriasis duration), 40 patients with early PsA (<2 years' disease duration and not receiving biologic therapy), 40 patients with PsC (>10 years disease duration, not receiving biologic therapy, and matched to PsA patients on age, sex, psoriasis duration, and age of psoriasis onset), and 40 HC (matched to patients based on age, sex). RNA was extracted using the Tempus Spin RNA Isolation Kit. miR-21-5p was validated using droplet digital PCR (ddPCR). Serum Il-17, CXCL10, IL-23, TGFβ1 were measured by commercially available ELISA kits. Mann- Whitney test, Kruskal-Wallis test, Wilcoxon signed rank test and Spearman correlations were performed.
Results: The expression of miR-21-5p was significantly higher in convertors compared to non-convertors (Fold change(FC)=2.16, p=0.002). miR-21-5p was upregulated in PsA compared to PsC (FC=2.32, p=0.001) and HC (FC=15.7, p=<0.0001) in the validation cohort. miR-21-5p was significantly down regulated 24 weeks post-MTX treatment in 30 PsA patients (FC=1.9, p< 0.008), which correlated with swollen (r=0.49, p=0.003) and tender joint counts (r=0.41, p=0.02) supporting a possible role in inflammation pathway in PsA patients. IL-17 levels in PsA & PsC were significantly higher from HC (p= 0.03), but not different between PsA & PsC. IL-17 levels were down- regulated post MTX treatment and correlated with miR-21-5p (r=0.56, p=<0.001), CXCL10 levels (r=0.48, p=0.01), IL-23 levels (r=0.43, p=0.02), TGFβ1 (r= -0.45, p=0.04) and total active joint counts (r=0.40, p=0.016).
Conclusion: Up regulated expression levels of miR-21-5p in convertors and in PsA patients suggests a role as a potential biomarker for PsA. In the presence of upregulated miR-21-5p, IL-17 and IL-23 are upregulated while TGFβ1 is down regulated. When miR-21-5p is decreased IL-17 and IL-23 downregulate, with up regulation of TGFβ1. We have thus determined the role of miR21-5p as a potential biomarker for inflammation pathway in psoriatic disease and response to MTX possibly through modulation of CXCL10 and IL-17/IL-23 axis.
Disclosure of Interests: Rohan Machhar: None declared, Remy Pollock: None declared, Justine Ye: None declared, Vinod Chandran: None declared, Dafna D Gladman Grant/research support from: AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB
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FRI0359 KRT77 DELETIONS IN FAMILIAL INFLAMMATORY BOWEL DISEASE MAY OFFER A NOVEL LINK TO FAMILIAL SPONDYLOARTHROPATHY

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Background: Inflammatory bowel disease, either clinical or subclinical is a cardinal pathological process that is central to the spondyloarthropathy (SpA) category of disease that also includes psoriasis, psoriatic arthritis, uveitis and ankylosing spondylitis.
Objectives: To look for novel genes in familial SpA in large multcase families using a whole genome sequencing approach.
Methods: We used Whole Genome Sequencing to screen SpA family members with different disease manifestations. We screened 5 multicase SpA families (up to 8 members) with different disease manifestations.
Results: We found a 1.5MB deletion of the KRT77 gene in 3 of 7 families that segregated with SpA phenotype. Given that KRT77 is a barrier protein and given that tagging SNPs from GWAS studies do not cover the region, and given that both IBD and psoriasis are associated with barrier defects, we looked for an association with KRT77 deletion in

1,000 cases of Psoriasis, 1,000 Crohn's disease (CD) and 1,001 healthy controls. Deletion genotyping was performed using TaqMan RealTime-PCR assays. The deletion genotype frequencies in controls did not deviate from Hardy-Weinberg Equilibrium ($p > .1$). We found an association between KRT77 deletion and CD risk ($p = 0.03$) and also a putative association with pustular psoriasis ($p < 0.05$). We also demonstrated that the KRT77 protein is expressed in the intestinal lumen and Peyers Patches in addition to the know skin expression.

Conclusion: Given the strong association between SpA and subclinical gut inflammation and barrier defects in IBD these findings suggest that KRT77 heterozygous deletions with dysregulated gut permeability may play a role in IBD and the wider SpA phenotype.

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FRI0360 ANALYSIS OF BLOOD MONOCYTE TRANSCRIPTOMES AND BONE MARROW SAMPLES OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS REVEALS THEIR CHANGES RELATED TO ACTIVATION AND MYELOPOIESIS

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Background: Axial spondyloarthritis (axSpA) is characterized by inflammation within the axial skeleton. Previously, we observed preactivation of circulating monocytes of axSpA patients suggesting systemic immune activation apart from local skeletal inflammation.

Objectives: The aim of this study was to characterize systemic immune activation in axSpA by analyzing axSpA-specific monocyte transcriptomes and changes in myelopoiesis.

Methods: We performed transcriptomic analyses using GeneChip HG-U133 Plus2.0 arrays of CD14+ monocytes isolated from peripheral blood of 25 HLA-B27+ axSpA patients and 10 healthy controls (HC). 10 patients were classified as non-radiographic axSpA (nr-axSpA) and 15 patients as ankylosing spondylitis (AS). Robust Multichip Averaging Algorithm normalization and high performance chip data analysis were used to select differentially expressed transcripts that define 1) axSpA-gene-expression profile and 2) profile that discriminates nr-axSpA from AS patients. Functional analysis of significant IDs was performed with Gene ontology (GO) and reference transcriptomes that portrayed myelopoiesis in bone marrow and monocytes activation with TNF, LPS, IFN and G-CSF. Myelopoiesis in bone marrow was studied by immunohistology according to MPO and CD15 expression in sections from facet joints of AS patients and controls (CO) without skeletal disease (n=6/group).

Results: Comparison between axSpA and HC monocyte transcriptomes identified 957 differentially expressed transcripts that allowed separation of both groups by hierarchical clustering. GO analysis revealed associations of axSpA related transcripts with cell-cell adhesion, immune responses including Ras-signalling, Jak-STAT-signalling, innate immunity. Comparison of axSpA related transcripts with reference transcriptomes identified overlap with late myelopoiesis, pronounced mobilisation of monocytes from bone marrow into blood triggered by G-CSF and weak TNF/LPS activation.

Nr-axSpA and AS monocytes differed in 562 transcripts. GO analysis of these transcripts suggested alterations in mitochondrial activity, peptide transport and DNA repair. According to reference transcriptomes, profiles of nr-axSpA monocytes differed from those in AS by gene patterns of late myelopoiesis and G-CSF triggered mobilisation from bone marrow.

In histological analyses of bone marrow a significantly higher percentage of MPO+ cells indicative of left shifted granulopoiesis was found in AS vs. CO facet joints ($p<0.01$).

Conclusion: AxSpA monocyte transcriptomes reflect weak immune activation by cytokine and/or LPS and premature release from bone marrow into blood. Bone marrow analysis shows a left shifted granulopoiesis in AS – both of which may contribute to pathological immune response within the skeleton in axSpA.

REFERENCE:

[1] Conrad K, Wu P, Sieper J, Syrbe U. In vivo pre-activation of monocytes in patients with axial spondyloarthritis. Arthritis Res Ther. 2015 Jul 16;17:179. Doi: 10.1186/s13075-015-0694-2. PubMed PMID: 26178906

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FRI0361 INNATE VERSUSADAPTIVE IL-17A PRODUCING CELLS IN AXIAL SPONDYLOARTHRITIS

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Background: IL-17A-inhibition has been very successful in AxSpA but the cell populations targeted by this new therapeutic remain unknown. This question is relevant because the recent failure of anti-IL-23 in AxSpA demonstrated that IL-23-independent IL-17-producing cells may be of particular relevance for SpA pathogenesis. Some data from literature suggests the involvement of MAIT, γδ T, and neutrophils as IL-17A producing cells in AxSpA (1–3). However, even though they may be responsible for IL-17A-mediated inflammation, it is still unclear which is the major IL-17A-producing cell population in this disease.

Objectives: To assess and compare gene expression profiles of neutrophils, MAIT, γδ, CD4+ and CD8+ T cells from AxSpA patients.

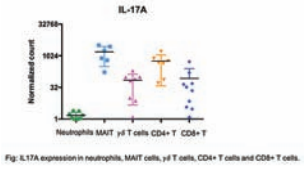


Fig: IL17A expression in neutrophils, MAIT cells, γδ T cells, CD4+ T cells and CD8+ T cells.

Methods: We recruited 5 healthy donors and 10 patients with a diagnosis of AxSpA according to the ASAS criteria. We compared the gene expression profiles of 5 sorted cell populations: 3 innate cell populations (neutrophils, MAIT and γδ T cells) and 2 adaptive cell populations (CD4+T and CD8+T) after cell stimulation by PMA + A23187 (calcium ionophore) + β1,3 glucan (extracted from *Aspergillus fumigatus* hyphae). Published data suggested that neutrophils stimulation by *Aspergillus fumigatus* induces IL-17A production by these cells(4). For each of these cell populations, cytokine production and the expression of a panel of 755 genes (Autoimmune discovery panel from Nanostring including 43 genes for which a polymorphism was associated with AS) were assessed. Patient and control groups were compared with a Mann-Whitney test and comparison of cell populations was performed by a multigroup comparison.

Results: There was no significant difference between patients and controls regarding gene expression profile of neutrophils, γδ T, CD4+T and CD8+T. We observed that 34 genes were differentially expressed between patients and controls in MAIT cells ($p = 0.03$, $q = 0.1$). In particular, T cell activation genes (*TBX21, AHR, ZAP70*) and cell interaction genes (*ITAG6, CTNNB1, ICAM2, ITGB2, SELL*) were decreased in patients. Among AxSpA patients, MAIT cells were those significantly showing the highest level of IL-17A expression. *IL23R* and *RORC* were also more expressed by MAIT compared to others cell populations. IL-17A expression was very low in neutrophils but we observed that 18 out of the 43 AS associated genes were mainly expressed by neutrophils (p

<0.05, q = 0.02), supporting the idea that they should be involved in the pathophysiology of the disease.
Conclusion: These preliminary data confirm that the innate immune cells could play an important role in AxSpA. MAIT cells are at the forefront of the expression of IL-17A before γδ T, CD4+T and CD8+T. Neutrophils do not appear to participate in the production of IL-17A, but the high expression of AS linked genes in these cells suggests their involvement in AxSpA.

REFERENCES:

[1] Appel H, et al. Analysis of IL-17(+) cells in facet joints of patients with spondyloarthritis suggests that the innate immune pathway might be of greater relevance than the Th17-mediated adaptive immune response. Arthritis Res Ther. 2011
[2] Kenna TJ, et al. Enrichment of circulating interleukin-17-secreting interleukin-23 receptor-positive γ/δ T cells in patients with active ankylosing spondylitis. Arthritis Rheum. 2012
[3] Gracey E, et al. IL-7 primes IL-17 in mucosal-associated invariant T (MAIT) cells, which contribute to the Th17-axis in ankylosing spondylitis. Ann Rheum Dis. 2016
[4] Taylor PR, et al. Activation of neutrophils by autocrine IL-17A-IL-17RC interactions during fungal infection is regulated by IL-6, IL-23, RORγt and dectin-2. Nat Immunol. 2014

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FRI0362 HIGH-DIMENSIONAL MULTIPARAMETRIC CHARACTERIZATION OF THE REGULATORY T CELLS LANDSCAPE IN SPONDYLOARTHRITIS

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Background: The Spondyloarthritides (SpA) are immune-mediated conditions characterised by spinal and joint inflammation. The pathogenic role of Th17 lymphocytes has been shown by multiple studies but few reports exist on the phenotype of regulatory T cells (Tregs) and their role in the course of the disease. Studying Tregs is particularly challenging because of their heterogeneous phenotype and potential plasticity at the site of inflammation. Given the complexity of the Treg landscape, a multi-dimensional approach, including both protein and gene analysis, offers novel mechanistic insights that can be leveraged to develop new treatments.
Objectives: 1) To describe the Treg phenotype in SpA patients compared to controls. 2) To identify differential expression of markers, such as trafficking molecules or co-inhibitory molecules, within Tregs at the inflammatory site. 3) To define the gene expression landscape in Tregs in the peripheral blood and synovial fluid in patients with active SpA.
Methods: A total of 61 patients with SpA (38 with Ankylosing Spondylitis (AS), 23 with Psoriatic Arthritis (PsA)) and 16 age-matched healthy controls were recruited. Peripheral blood (PB) and paired synovial fluid (SF) mononuclear cells (n=8) were also analyzed. Isolated mononuclear cells were stained with 3 multicolor flow cytometry panels, including a total of 35 surface and intracellular protein markers. Manual gating was done in parallel with unsupervised data analysis using FlowSOM and SPADE. Cells from blood and synovial fluid from three treatment-naive PsA patients were isolated and their RNA sequenced at a single cell level with the 10x Genomics platform.
Results: Whereas no major difference in the Treg frequency was observed comparing the PB of SpA patients and healthy controls, in the SF we observed a higher Treg frequency, with a striking prevalence of the memory (CD45RA-) compartment (mean: 11.7 vs 4.7%; p=0.01) and a higher expression of Foxp3 (p=0.04). Trafficking markers demonstrated considerable heterogeneity, as visualized on SPADE analysis, mirroring the classification of T helper cells, but little difference in terms of relative frequency compared to healthy controls. Within the Treg compartment we identified populations of Helios-negative Th17-like cells able to secrete higher levels of IL-17A (mean: 2.8 vs 1.2%; p=0.02) while expressing normal levels of Foxp3; and putative regulatory CD8+ T cells expressing classical Treg features (Foxp3, CTLA4).
The analysis of the single cell transcriptomic data confirmed a high degree of heterogeneity, both in the SF and the PB, with consistent findings across patients. Unsupervised clustering identified different subsets that share a core of regulatory transcripts, onto which additional programs are added, including a very distinct Th17-like module. Of note, various Treg subsets express preferentially different co-inhibitory genes, suggesting a functional specialization.
Conclusion: High-dimensional immunoprofiling in SpA patients shows normal frequency of Tregs in the PB, but increased Tregs with activated phenotype in the inflammatory site. The presence within the Treg population of Th17-like and CD8+ populations are intriguing preliminary findings that require further evaluation. Preliminary transcriptomic analysis confirms the presence of specialized subsets within the Treg compartment.
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FRI0363 AUTOANTIBODIES TO THREE NOVEL PEPTIDES IN EARLY AXIAL SPONDYLOARTHRITIS IN TWO INDEPENDENT COHORTS

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Background: Diagnosis of axial spondyloarthritis (axSpA) is challenging since clinical manifestations, such as inflammatory back pain, peripheral arthritis, enthesitis and inflammatory bowel disease, often overlap with other disorders. Current laboratory markers for axSpA, Human Leukocyte Antigen (HLA)-B27 and C-reactive protein (CRP) are not sufficiently specific for diagnosis. Despite being considered a "seronegative" disease, emerging evidence supports the involvement of antibodies in axSpA. In order to identify novel autoantibodies in axSpA patients, we recently screened an axSpA cDNA phage display library for reactivity with immunoglobulin G (IgG) antibodies in plasma of early axSpA patients. This resulted in autoantibodies to 9 novel University of Hasselt (UH) axSpA peptide targets, corresponding to fragments of known proteins and novel lineair peptides.
Objectives: The aim of this study was to determine the diagnostic potential of autoantibodies to the 9 novel UH axSpA peptides in axSpA patients and controls from 2 independent cohorts.
Methods: Using enzyme-linked immunosorbent assays (ELISA), presence of antibodies to the 9 UH axSpA peptides expressed on phage particles was determined in 76 early axSpA patients, 75 chronic low back pain patients (LBP), 60 early rheumatoid arthritis patients (RA) and 94 healthy controls (HC) from the UH cohort. Antibody reactivity was further validated in 174 patients from the **Leuven** Spondyloarthritis (Biologics) Cohort ((**Bio)SPAR**), including 79 early axSpA patients.
Results: Antibody reactivity against at least one of 9 novel UH axSpA peptides was found in 54% (41/76) of early axSpA patients, 26% (24/94) of HC (*p=0.0002*), 39% (29/75) of LBP (*p=0.0731*) and 38% (23/60) of RA patients (*p=0.0845*) from the UH cohort, as compared to 43% (74/174) of the axSpA patients from the (Bio)SPAR cohort. By combining the three UH axSpA peptides with highest positive likelihood ratios (LR+) into a panel, antibodies against these 3 peptides were detected in 14.2% (22/155) of early axSpA patients from the combined UH and (Bio)SPAR cohorts and in only 5% (4/75) of persons with LBP (*p=0.*0484), resulting in a specificity of 95%.. The LR+ for confirming axSpA using antibodies to these 3 UH axSpA peptides was 2.7, which is the same as for the currently used laboratory marker CRP. Assuming a 5% pretest probability of axSpA in persons with LBP, a combination of the presence of inflammatory back pain (LR+ 3.1) and a positive test result for the laboratory markers HLA-B27 (LR+ 9.0) and CRP (LR+ 2.5) provides a disease (posttest) probability of 79%. When we added a positive test result for the presence of antibodies to the 3 UH axSpA peptides (LR+ 2.7), posttest probability could be increased to 91%.
Conclusion: Antibodies to 3 UH axSpA peptides were significantly more present in early axSpA patients compared to LBP and could provide a novel tool for objective diagnosis of a subset of axSpA patients.
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FRI0364 T REGULATORY CELLS AS BIOMARKER OF DISEASE ACTIVITY AND RESPONSE IN PSORIATIC ARTHRITIS PATIENTS: RESULTS FROM APREMILAST-TREATED COHORT

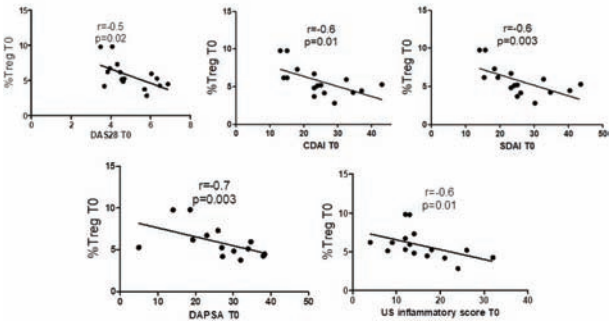
Fulvia Ceccarelli[1,1], Ilenia Pacella[2], Ramona Lucchetti[1], Arianna Forniti[2], Francesca Spinelli[1], Enrica Cipriano[1], Carlo Perricone[1], Simona Truglia[1], Francesca Miranda[1], Rossana Scrivo[1], Cristiano Alessandri[1], Vincenzo Barnaba[2], Guido Valesini[1], Silvia Piconese[2], Fabrizio Conti[1]. [1]*Sapienza Università di Roma, Sapienza Arthritis Center, Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Roma, Italy*; [2]*Sapienza Università di Roma, Cellular and Molecular Immunology Unit, Dipartimento di Medicina Interna e Specialità Mediche, Roma, Italy*

Background: The PDE4-inhibitor apremilast has been recently introduced in the treatment of Psoriatic Arthritis (PsA). It acts by down-regulating intracellular inflammatory mediators synthesis by elevating cAMP levels. Tregs, a subset of FOXP3+ CD4 T cells, play a key role in preventing immune responses and could exert their suppressive function via cAMP (1). Reduced frequencies of circulating Tregs have been observed in inflammatory disorders, nonetheless very few data are available on PsA patients.

Objectives: We evaluated peripheral Tregs in a cohort of PsA patients treated by apremilast.

Methods: Seventeen PsA patients (M/F 3/14; median age 56.0 years, IQR 20.0; median disease duration 15.0 years, IQR 11.0) with polyarticular subset treated by apremilast, were evaluated at baseline (T0) and after 6 (T1) and 12 weeks (T1). Clinimetric evaluation included DAS28, DAPSA, CDAI, and SDAI. Moreover, US assessment was performed at wrists, metacarpophalangeal (MCP), and proximal interphalangeal (PIP) joints: synovial effusion/hypertrophy and power Doppler were scored by a semi-quantitative scale (0-3), obtaining a total score (0-198). Treg frequency was assessed in peripheral blood mononuclear cells by flow cytometry, as the percentage of CD127low FOXP3+ in live CD4+ T cells (%Treg).

Figure 1: Correlation between %Treg and disease activity indices (DAS28, CDAI, SDAI, DAPSA, US inflammatory score.



Results: At baseline we identified a median%Tregs of 4.6 (IQR 1.1), inversely correlating with DAS28 (r=-0.5, p=0.02), DAPSA (r=-0.7, p=0.003), CDAI (r=-0.6, p=0.01), SDAI (r=-0.6, p=0.003 and US inflammatory score (r=-0.6, p=0.01) (Figure 1). Treatment with apremilast was able to induce a significant improvement in all activity indices at T1 (DAS28, P=0.009; DAPSA, P=0.01; CDAI, P=0.005; SDAI, P=0.006; US score, P<0.0001) and T2 (DAS28, P<0.0001; DAPSA, P=0.007; CDAI, P=0.008; SDAI, P=0.006; US score, P=0.0005). Furthermore, responding patients according with EULAR criteria at T2 showed significantly higher%Treg at baseline in comparison with non-responder patients (median 4.8, IQR 1.2 versus median 2.9, IQR 1.1; P=0.02).

Conclusion: The results of our study demonstrate that%Treg is a marker of disease activity in PsA patients. Moreover, the baseline value of Tregs could predict the response to apremilast after 12 weeks of treatment.

REFERENCE:

[1] Chavele KM et al, FEBS Lett 2011.

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FRI0365 PDE4 TARGETING SELECTIVELY INHIBITS INFLAMMATORY-DRIVEN OSTEOCLASTOGENESIS

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Background: Patients suffering from Psoriatic arthritis (PsA) commonly develop bone erosions and inflammatory-induced bone loss. This process is mediated by osteoclasts derived from monocytic precursors, and modulated by inflammatory cytokines (i.e. TNF, IL-1, IL-6, IL-17, IL-10 and GM-CSF) from immune and stromal cells. In immune cells (including $CD14^+$ osteoclast pre-cursors), PDE4, an enzyme responsible for hydrolysing cyclic AMP to inactive AMP, drives inflammatory effects [1]. Importantly, Apremilast (APR; a selective PDE4 inhibitor) has known efficacy in PsA [2], and decreases pro-inflammatory mediators whilst increasing anti-inflammatory mediators (IL-10) [3]. Although published data indirectly suggest a positive impact of APR on bone in PsA, data is lacking with regard to the impact on bone resorption.

Objectives: To evaluate the impact of a selective inhibition of PDE4 by APR on osteoclastogenesis from human $CD14^+$ precursors.

Methods: Osteoclasts were differentiated from primary human $CD14^+$ blood monocytes (healthy controls) with RANKL and MCSF, in the presence or absence of APR. To specifically study the impact of APR on osteoclastogenesis in an inflammatory context, osteoclastogenesis was also undertaken in the presence of: ***(i)*** TNF, ***(ii)*** Supernatants from activated Peripheral Blood Mononuclear Cells (PBMC) or activated CD3 cells, treated with or without APR, ***(iii)*** Co-culture with activated PBMC or activated CD3 cells, treated with or without APR. $TRAP^+$ multinucleated cells (mature osteoclasts) were enumerated via microscopy.

Results: In a non-inflammatory context, PDE4 inhibition by APR did not affect the differentiation of $CD14^+$ precursors into mature osteoclasts. However, TNF-enhanced osteoclastogenesis was significantly decreased by APR (-30.0% +/- 14.9; p=0.0279).The treatment of either activated PBMCs or purified $CD3^+$ T cells with APR substantially reduced cellular activation. In PBMCs this decrease in cellular activation resulted in a decrease in conditioned media-driven osteoclastogenesis (-49.7% +/- 13.2; p=0.0385). In comparison, APR treatment of purified $CD3^+$ T cells did not reduce their osteoclastogenic potential.

Conclusion: The results of this study reveal that PDE4 targeting potently inhibits inflammatory-driven osteoclastogenesis. Moreover, these data also suggest that $CD3^+$ T cells are not the main target of PDE4 inhibition in this context. In summation, our study supports the hypothesis that APR can modulate bone integrity in inflammatory condition such as PsA.

REFERENCES:

[1] Houslay. Drug Discov Today. 2005 Nov 15;10(22):1503-19.
[2] Edwards. Ann Rheum Dis. 2016 Jun;75(6):1065-73. Doi: 10.1136/annrheumdis-2015-207963.
[3] Schafer. J Immunol Res. 2015;2015:906349. Doi: 10.1155/2015/906349.

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FRI0366 SUBSTANTIAL CHANGES IN BONE FORMATION REGULATORS BIOMARKERS IN EARLY AXIAL SPONDYLOARTHRITIS – ROLE OF TNF INHIBITORS

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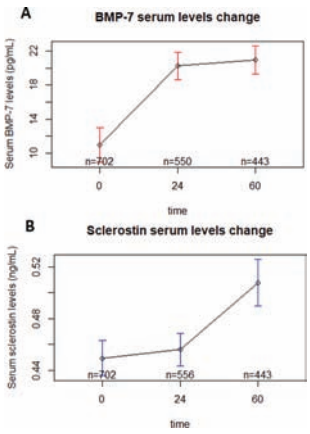
Background: The hallmark of advanced axial spondyloarthritis (SpA) is spine ankylosis, due to an excess of bone formation. Our hypothesis was that pathways of bone formation regulators changed over time and that their changes were related to inflammation or use of "anti-inflammatory" drugs (like non-steroidal anti-inflammatory drugs (NSAIDs) and/or Tumor Necrosis Factor inhibitors (TNFi).
Objectives: This prospective study aimed to describe the 5-year serum changes of bone formation regulators markers (sclerostin, bone morphogenetic protein 7 (BMP-7) and Dickkopf-1 (DKK-1)) in early axial SpA and to assess determinants of their changes.
Methods: The DESIR cohort is a prospective, multicentre French study of 708 patients (34 ± 9 years, 58% HLA B27 positive, BASDAI 45 ± 20) with early (> 3 months and < 3 years) inflammatory back pain suggestive of axial SpA. Sclerostin, BMP-7 and DKK-1 serum levels were assessed at baseline, two and five years. Change in bone formation regulators over time was analysed using mixed linear models, first in complete-cases and then in available-cases analysis. Determinants of serum biomarkers change were analysed using mixed linear models and we searched for an interaction between time and determinants of serum biomarkers.
Results: Serum levels of each biomarkers at baseline, two and five years are reported in Table 1. Serum BMP-7 significantly increased over time, with a mean of 0.17 pg/mL per month (Figure 1A). Median relative change of BMP-7 at five years was 53.0% [IQR -31.6%, 286.8%]. Serum BMP-7 levels was undetectable in 337 patients (59.6%) at baseline, in 111 patients (48.0%) at two years and in 59 patients (20.2%) at five years. At baseline, serum sclerostin was significantly correlated with age ($r = 0.28$, $p < 0.001$), weight (kg) ($r = 0.10$, $p = 0.007$), CRP level (mg/mL) ($rS = -0.14$, $p < 0.001$), mSASSS ($r = 0.08$, $p = 0.03$), number of syndesmophytes ($r = 0.15$, $p < 0.001$), bone mineral density in hip and lumbar spine ($r = 0.19$, $p < 0.001$ and $r = 0.18$, $p = 0.001$ respectively). Serum sclerostin significantly increased over time, with a mean of 0.001 ng/mL per month (Figure 1B). Median relative change of sclerostin at five years was 14.8% [-7.9%, 41.4%]. Serum DKK-1 did not significantly vary over time. In multivariate analysis, serum BMP-7 increased with moderate or high disease activity (ASDAS-CRP) (0.19 pg/mL per month, $p = 0.01$), in men (5.3 pg/mL, $p = 0.004$) and decreased with the duration of TNFi use (-0.04 per month of TNFi use, $p < 0.001$). Unlike in serum BMP-7, there was not a significant interaction between time and determinants of serum sclerostin. In multivariate analysis, serum sclerostin increased with time (0.001 ng/mL per month, $p < 0.001$), age (0.007 ng/mL per year, $p < 0.001$) and in men (0.05 ng/mL, $p = 0.001$) but decreased with the use of TNFi (-0.037 ng/mL, $p < 0.001$), in patients with a Z score ≤ -2 at at least one site (-0.036 ng/mL, $p = 0.005$) and with serum BMP-7 levels (-0.0006 ng/mL per unit of serum BMP-7, $p = 0.03$).
Conclusion: Serum BMP-7 levels significantly increased over time with a rapid and substantial change. Serum sclerostin levels significantly increased over time but to a lesser degree than serum BMP-7. Serum BMP-7 changes were related to the use of TNFi.

Table 1. Serum levels of bone biomarkers over time

	SOST (ng/mL)	DKK-1 (pg/mL)	BMP-7 (pg/mL)
Baseline	0.45 ± 0.18	5413.0 ± 2370.0	11.0 ± 27.5 2.1 [0 – 15.7]
Two years	0.46 ± 0.15	5621.3 ± 2571.0	20.3 ± 19.2 16.2 [5.2 – 27.7]
Five years	0.51 ± 0.19	4998.2 ± 2889.3	20.9 ± 17.6 19.5 [7.2 – 30.6]

Results are expressed by mean ± standard deviation and median [IQR]

Figure 1:



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FRI0367 INFLAMMATORY PROCESSES IN EXPERIMENTAL SPONDYLOARTHRITIS ARE ACCOMPANIED BY FORMATION OF ECTOPIC LYMPHOID STRUCTURES IN THE BONE MARROW AND ALTERATIONS IN THE B CELL LINEAGE

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Background: Tumour necrosis factor (TNF) is important in immune-mediated inflammatory diseases such as spondyloarthritis (SpA). SpA patients have extensive angiogenesis in inflammatory and bone forming regions. Transmembrane (tm)TNF-transgenic (tg) mice (1) that overexpress tmTNF develop SpA symptoms, including inflammation, bone destruction and bone formation. Interestingly, these mice also develop lymphoid aggregates in the bone marrow (BM) of the axial and peripheral skeleton.
Objectives: Characterization of lymphoid aggregates in tmTNF tg mouse BM in the context of angiogenesis and bone formation.
Methods: Ankles, femora, tibiae, vertebrae and spleens from tmTNF tg mice and wild-type (WT) littermates (6 weeks, 12 weeks, and 8 months old; n=5 per age per group) were dissected and analyzed by confocal microscopy. In addition, 12 week old mice (n=5 per group) were analyzed by flow cytometry. To study the importance of TNF-R signaling in these processes, tmTNF tg mice lacking TNF-RI (tmTNF tgxTNF-RI$^{-/-}$) or TNF-RII (tmTNF tgxTNF-RII$^{-/-}$) (n=4 per group) were investigated.
Results: Immunofluorescent (IF) evaluation demonstrated that BM of tmTNF tg mice contained extensive lymphoid aggregates, both in the vertebrae and the ankles, but not in the femurs or spleen. IF microscopy demonstrated that the aggregates in the BM contain characteristics of ectopic lymphoid structures (ELS) and consisted of B220^{+} B cells and FDC-M1^{+} follicular dendritic cells that are in close proximity of MECA79^{+-} high endothelial venules (HEVs). Flow cytometric analysis revealed that most B220^{+} B cells are IgD^{+} naive B cells and that tmTNF tg vertebrae

contain significantly more IgD^-CD95^+ germinal center B cells (P< 0.01) with a higher expression of the costimulatory molecules CD80 and CD86 compared to WT. The vertebrae also contained more $CXCR5^+PD\text{-}1^+FoxP3^+CTLA4^+$ T regulatory cells and a trend towards an increase in $CXCR5^+PD\text{-}1^+FoxP3^-CTLA4^-$ T follicular helper cells in tmTNF tg mice. Meanwhile, B cell development in the BM of tmTNF tg hind limbs was not altered. Furthermore, BM, spleen and vertebrae from tmTNF tg mice contained significantly more IgA^+ plasma cells compared to WT littermates. Of note, tmTNF tgxTNF-$RI^{-/-}$ mice did not display lymphoid aggregates or HEVs in the BM, while tmTNF tgxTNF-$RII^{-/-}$ mice did, although to a lesser extent than tmTNF tg mice.

Conclusion: tmTNF overexpression in mice results in extensive lymphoid aggregates in the BM that are often organized in ELS, which may be mediated via TNF-RI signaling. These ELS might result in an increase of IgA^+ plasma cells in tmTNF tg mice. Ongoing studies will look further into this and may indicate whether these findings contribute to the pathology observed in these mice.

REFERENCE:

[1] Alexopoulou L, et al. Eur J Immunol 1997; 27(10):2588-92

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FRI0368 VASCULAR CALCIFICATION BY INFLAMMATION COULD BE AN IMPORTANT CAUSE OF CARDIOVASCULAR DISEASE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Patients with ankylosing spondylitis (AS) have a higher risk of cardiovascular disease. Atherosclerosis is a main pathological process of cardiovascular disease and calcified plaque is a characteristic feature of atherosclerosis. Inflammation plays a potential role in vascular calcification. There is no previous study revealing the mechanism of vascular calcification in AS.

Objectives: We investigated the relationship between vascular calcification and inflammation in patients with AS.

Methods: Sixteen male patients aged over 20 years with AS were enrolled. They fulfilled the modified New York criteria and each of their ankylosing spondylitis disease activity score was more than 2.1. Sex and age matched nine healthy controls were also recruited. Mouse MOVAS (American Type Culture Collection, ATCC®, CRL-2797TM) vascular smooth muscle cells were stabilized in maintenance medium for 24 hours. Then the amount of serum equivalent to 10% of maintenance medium from subjects was added and cells were stimulated for another 72 hours. We exchanged this medium with calcification medium every third day and cells were cultured for another 11 days. After 2 weeks, cells were stained with Alizarin Red S and the optical density (OD) was measured while being compensated by cell viability. For Western blotting, cells were stabilized for 24 hours and stimulated for another 72 hours through the same procedure as that of Alizarin Red S staining. Then we measured the level of protein expression in PPAR-gamma, beta-catenin, TNF-a, interleukin (IL)-23, and MMP7.

Results: The level of OD of MOVAS cells treated with serum from AS patients (19.503 ± 6.422, mean ± SD) was significantly higher than that from controls (12.724 ± 5.746) (P=0.027, Mann-Whitney test). The level of MMP7 expression of MOVAS cells treated with serum from AS patients (1.921 ± 0.702) was significantly higher than that from controls (0.779 ± 0.191) (P=0.000, Mann-Whitney test). The level of beta-catenin expression of MOVAS cells treated with serum from AS patients (1.292 ± 0.356) was significantly higher than that from controls (0.887 ± 0.310) (P=0.025). There was negative correlation between PPAR-gamma and TNF-a (rho=-0.762, p=0.028, Spearman rank correlation coefficient), and between PPAR-gamma and IL-23 (rho=-0.601, p=0.039); positive correlation between MMP7 and TNF-a (rho=0.833, p=0.010), and between MMP7 and IL-23 (rho=0.797, p=0.002).

Conclusion:

1. Serum from AS patients showed increased calcification of vascular smooth muscle cells than serum from controls.
2. The level of vascular calcification marker from vascular smooth muscle cells treated with serum from AS patients was significantly higher than that from controls.
3. There were negative relationship between inflammatory markers and inhibitory marker of vascular calcification but positive relationship between inflammatory markers and stimulatory marker of vascular calcification.

These findings suggest that vascular calcification by inflammation could be an important cause of cardiovascular disease in AS patients.

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FRI0369 TOWARDS MORE PRECISE ESTIMATES OF THE FAMILIAL AGGREGATION AND HERITABILITY OF ANKYLOSING SPONDYLITIS – A SWEDISH NESTED CASE-CONTROL STUDY

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Background: Ankylosing spondylitis (AS) is known to have strong familial aggregation, but studies quantifying the familial risk are few and have reached varying results. Familial risks reported from population-based studies range from 17 to 94 in first-degree relatives of AS cases.[1] [2] The heritability (i.e., the proportion of variance in AS liability explained by genetic variation) has been reported to >90%, based on very small studies of twins.[3]

Objectives: To assess the familial aggregation and heritability of AS among all Swedish AS patients, and to investigate if risks vary by type of first-degree relative or sex.

Methods: We identified all patients with an ICD-10 code of AS in the Swedish National Patient Register (NPR) between 1 January 2001 and 31 December 2016. To increase validity, index patients were required to have two or more visits listing an AS diagnosis, and at least one of the visits being to a specialist in rheumatology or internal medicine. Each index patient was matched on sex and birth year to 50 general population controls from the Total Population Register. First-degree relatives of index patients and controls were identified through the Multi-generation register. Their disease status was ascertained from the NPR in a similar manner as for index patients. Familial risks of AS among first-degree relatives were calculated as odds ratios (ORs) with conditional logistic regression. Based on the familial risks, the corresponding heritability was calculated for a range of plausible prevalence estimates.

Results: We identified 13 795 patients that met the inclusion criteria. Of their siblings, parents, and children, 3.6, 2.3, and 2.1% respectively also had AS. The overall familial OR when having one affected relative was 19.4 (95% CI 18.1-20.8). The estimates were similar for relatives of different kinds (see table), but having more than one affected relative resulted in a higher risk (OR 68.0 (95% CI 51.3-90.1)). Heritability, estimated from sibling risk, was 77%. There were no clear-cut differences between the sexes, but women tended to have an elevated familial risk if the affected relative was female, and slightly lower heritability compared to males. These estimates can be considered as an upper limit of heritability, as shared environmental factors have not been taken into account in calculations.

Conclusion: Familial risks of AS were similar between different types of first-degree relatives, and no significant gender difference was seen on the heritability scale. Although high compared to most other diseases, the familial risks and heritability were lower than previous reports from other countries, though in line with earlier Swedish findings using in part the same data source. The heritability proposed here might still be an overestimate of the true influence of genetics on disease risk. Thus, efforts should also be directed at identifying other risk factors for AS that are not of genetic origin.

REFERENCES:

[1] Sundquist K, et al. Rheumatology 2008;47(8):1199-202.
[2] Geirsson AJ, Kristjansson K, Gudbjornsson B. Ann Rheum Dis 2010;69 (7):1346-8.
[3] Brown MA, et al. Arthritis Rheum 1997;40(10):1823-8.

Table. Familial risks and heritability of AS by type of first-degree relative (FDR) and sex

	Overall	Male-male	Male-female	Female-male	Female-female
Relative with AS	Familial risk, odds ratio (95% CI)				
Sibling	19.5 (16.9 - 22.4)	19.9 (16.1 - 24.7)	20.9 (16.0 - 27.4)	20.5 (16.0 - 26.5)	21.0 (13.3 - 33.2)
Parent	19.1 (17.2 - 21.3)	18.3 (15.5 - 21.6)	20.8 (16.3 - 26.4)	14.1 (11.3 - 17.5)	34.2 (26.1 - 44.9)
Child	20.6 (18.2 - 23.3)	20.5 (16.8 - 25.1)	16.0 (12.2 - 21.0)	19.9 (15.0 - 26.4)	26.2 (18.5 - 37.2)
Any FDR	19.4 (18.1 - 20.8)	19.0 (17.2 - 21.1)	18.2 (15.9 - 21.0)	17.7 (15.4 - 20.3)	26.9 (22.0 - 32.9)
>1 relative	68.0 (51.3 - 90.1)				
	Heritability (95% CI)				
Siblings	0.77 (0.73 - 0.80)	0.80 (0.74 - 0.85)	0.73 (0.67 - 0.78)	0.77 (0.72 - 0.83)	0.71 (0.61 - 0.81)

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FRI0370 ACCELERATED EXTRACELLULAR MATRIX REMODELING IN PSORIATIC ARTHRITIS & VALUE OF ECM-RELATED BIOMARKERS

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Background: With our increasing understanding of cross-talk between the immune system (immune cells, cytokines) and extracellular matrix (ECM) of the affected tissues, ECM destruction and turnover has gained a lot of attention in inflammatory arthritis. ECM mainly consists of interstitial matrix (rich in type I and III collagens) and basement membrane (mainly composed of type IV collagen), both of which are affected in inflammatory arthritis. We hypothesize that inflammatory milieu in Psoriatic Arthritis (PsA) leads to accelerated ECM destruction and remodeling, and the release of ECM metabolites into circulation, that can be measured in serum as biomarkers of tissue remodeling and may give insight to pathological process at the tissue level.
Objectives: This prospective study aimed to use serological biomarkers for evaluation of the extent of damage to, and changes in turnover of ECM in patients with PsA and to investigate their relation to inflammatory biomarkers and disease activity.
Methods: Patients with PsA (n=145) fulfilling the CASPAR criteria and above 18 years of age with any disease activity were recruited through outpatient department in Aalborg University Hospital, Denmark. Exclusion criteria were pregnancy, treatment with biological DMARD, or with oral corticosteroids and other comorbidities. Clinical disease parameters were recorded, and blood samples were collected at baseline and 24 weeks follow-up. Inflammation-related ECM remodelling was measured by serological biomarkers of type I, III and IV collagen formation (Pro-C1, Pro-C3 and Pro-C4, respectively) and MMP-mediated degradation (C1M, C3M and C4M respectively). The chronic inflammation was measured by CRPM (MMP degraded metabolite of CRP). All biomarkers were measured by competitive ELISAs and levels were compared to the reference levels of healthy individuals. The biomarker data was log_2 transformed for normalization and standard parametric statistical methods were applied.

Biomarkers	PsA patients			Reference values*			Statistics	
(ng/ml)	Mean	SD	n	Mean	SD	n	Difference	P Value
C1M	50.00	32.18	145	24.8	10.8	29	25.2	<0.0001
C3M	10.94	3.15	145	9.69	2.59	127	1.25	0.0004
C4M2	29.57	10.51	145	21.33	5.64	89	8.24	<0.0001
Pro-C1	79.20	38.85	145	104.77	54.17	119	-25.57	<0.0001
Pro-C3	11.49	3.56	145	11.28	3.56	111	0.21	ns
Pro-C4	304.07	120.17	145	204.88	63.54	127	99.19	<0.0001

*Table 1. Comparison of ECM turnover biomarkers in PsA patients (at baseline) and healthy individuals (*internal laboratory data)*

	Log_2 ΔC1M	Log_2 ΔC3M	Log_2 ΔC4M	Log_2 ΔPro-C1	Log_2 ΔPro-C3	Log_2 ΔPro-C4
ΔCRP	0.621‡	0.53‡	0.341‡	-0.062	0.098	0.267†
Log_2 ΔCRPM	0.436‡	0.615‡	0.415‡	0.097	0.208	0.393‡
ΔASDAS	0.202*	0.21*	0.207*	0.042	0.104	0.204*
ΔBASDAI	0.032	0.102	0.148	0.03	0.057	0.117
ΔBASMI	0.015	0.005	0.107	-0.015	-0.061	0.175*
ΔPASI	-0.076	-0.033	-0.001	-0.09	-0.053	0.008
ΔLEI	-0.024	0.027	0.246†	0.108	-0.043	0.094
ΔSPARCC	0	0.152	0.163	0.018	-0.049	0.174
ΔSJC	-0.015	-0.144	0.153	-0.011	0.019	0.062
ΔTJC	-0.039	0.037	0.062	0.006	-0.006	0.077
ΔVAS-Pain	0.07	0.104	0.138	0.075	0.087	0.198*

Results: We found that there was an increase in the degradation of interstitial matrix (represented by C1M and C3M) which was uncompensated with either decreased (Pro-C1) or unaltered (Pro-C3) formation in patients with PsA as compared to healthy individuals. On the contrary, there was a compensated increase in basement membrane remodeling in patients with PsA as represented by increase in both C4M and Pro-C4 in comparison to healthy individuals (Table 1). Interestingly, there was a strong correlation between baseline C4M and Pro-C4 ($r=0.703$, $p<0.0001$), and 24-week changes in both biomarkers ($r=0.468$, $p<0.0001$) pointing towards coupling between the two processes which was either lost or was weak in case of interstitial collagens. As baseline values and changes in C1M, C3M, C4M and Pro-C4 showed a strong correlation with changes in inflammatory biomarkers, we believe that ECM remodeling in PsA is, at least partly, driven by inflammation. Furthermore, baseline values and changes in these ECM turnover biomarkers correlated positively with changes in composite disease activity scores (Table 2) that may indicate their clinical importance as potential diagnostic or disease activity markers.
Conclusion: Chronic inflammation underlying PsA pathology results in an increased amount of ECM turnover that correlates with clinical progression and can be measured by serological biomarkers.

REFERENCES:
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Disclosure of Interests: Samra Sardar Employee of: I am a full time employee at Nordic Bioscience, Salome Kristensen: None declared, Anne Sofie Siebuhr Employee of: I am a full-time employee in Nordic Bioscience, Jeppe Christensen: None declared, Morten Karsdal Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Annette Mortensen: None declared, Anne-Christine Bay-Jensen Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience
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FRI0371 ALTERED EXPRESSION OF LNCRNA NR_003542 AND NR_026756 IN ANKYLOSING SPONDYLITIS MIGHT BE ASSOCIATED WITH THE DISEASE ACTIVITY

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Background: lncRNAs have been recognized as powerful regulators of numerous genes and pathways in the pathogenesis of inflammatory and autoimmune diseases, including SLE, RA, T1DM, MS, autoimmnue thyroid disease, Sjögren's syndrome psoriasis, and Crohn's disease[1]. The role of lncRNAs in the pathogenesis of Ankylosing Spondylitis (AS) is just beginning to be investigated
Objectives: To determine whether the altered expression of lncRNA NR_003542 and NR_026756 in peripheral blood of AS patients could provide insights into the pathogenesis of AS.
Methods: Peripheral blood mononuclear cells (PBMCs) lncRNA NR_003542 and NR_026756 expression were measured in 30 active AS (AAS)group, 30 inactive AS (IAS) group and 30 healthy control (HC) subjects. Clinical characteristics of the subjects are summarized in Table1.
Results: 1. Clinical and laboratory characteristics of the three groups (Table 1)

Table 1. Clinical and laboratory characteristics of subjects studied

	AAS(*n*=30)	IAS(*n*=30)	HC(*n*=30)	*P* value
Gender, F/M	8/22	8/22	10/20	0.805
Age, mean±SD (years)	36.23±10.86	33.47±10.42	35.8±10.84	0.467
Disease duration, mean±SD(years)	9.55±6.34	7.8±6.55	-	0.205
Family history,positive/tested (%)	4/30(13.33%)	2/30(6.67%)	-	0.667
BASDAI, mean±SD	5.2±0.98	2.24±1.31	-	0.000
BASFI, mean±SD	3.2±2.34	0.74±0.99	-	0.000
Uveitis,positive/tested (%)	6/30(20%)	3/30(10%)	-	0.470
CT grading of sacroiliac arthritis, II/III/IV	5/14/11	12/14/4	-	0.014[a]
HLA-B27,positive/tested (%)	29/30(96.67%)	25/30(83.33%)	-	0.000
ESR, mean±SD (mm/h)	58.83±27.04	15.63±12.75	5.97±3.18	0.000
hsCRP, mean±SD (mg/L)	36.6±31.14	5.9±5.54	1.09±2.11	0.000
WBC, mean±SD (10^9*/L)	7.99±1.62	6.98±1.81	5.94±1.09	0.028
GLOB, mean±SD (g/L)	40.3±6.08	33.44±3.93	32.85±4.55	0.000

BASDAI: bath ankylosing spondylitis disease activity index, *BASFI*: bath ankylosing spondylitis functional index,*HLA-B27*:Human leukocyte antigen B27.*ESR*: erythrocyte sedimentation,*WBC*:leukocyte, *GLOB*: globulin, a: the *P* value of the non-parametric Mann-Whitney test.

2. Comparison of the two lncRNAs expression among the three groups (Figure 1)

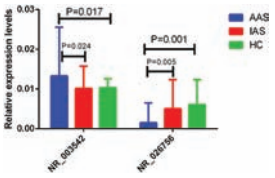


Figure 1. Expression of lncRNA-NR_003542 and NR_026756 among three groups

3. Correlations between levels of two lncRNAs expression s and clinical data in AS patients (Figure 2)

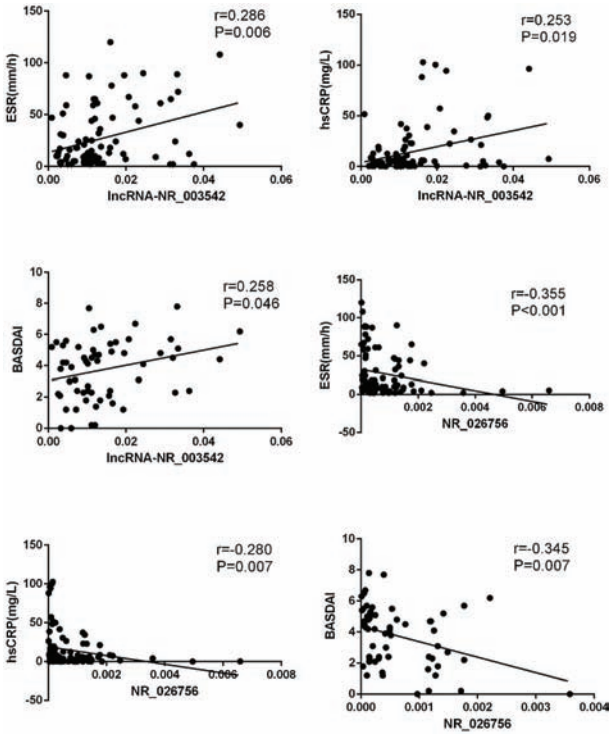


Figure 2. Correlations between levels of two lncRNAs expression and clinical data in AS patients

Conclusion: Altered expression of lncRNA-NR_003542 and NR_026756 in peripheral blood of AS patients might be involved in the pathogenesis of AS, higher expression of lncRNA-NR_003542 and lower expression of NR_026756 might be as the biomarkers for the disease activity of AS, further study would be needed to expound on the exact role of the two lncRNAs in AS.

REFERENCES:

[1] Chatenoud, L. Immune therapies of autoimmune diseases: are we approaching a real cure? Curr Opin Immunol 18, 710-7 (2006).

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Spondyloarthritis – treatment

FRI0372 **DMARD TREATMENT AND OPIOID USE IN EARLY SPONDYLOARTHRITIS IN FINLAND**

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Background: Disease-modifying anti-rheumatic drugs (DMARDs) are introduced for the treatment of spondyloarthritis (SpA) after failure of non-steroidal anti-inflammatory drugs (NSAIDs). In Finland, try out with a conventional synthetic DMARD (csDMARD) is required before initiation of biologicals (bDMARD). The patients with DMARDs are eligible for a higher reimbursement for the cost of medication. Opioids are not recommended for arthritis pain.

Objectives: To report the current DMARD and pain medication use among newly-onset SpA patients in Finland.

Methods: From the nationwide reimbursement register maintained by the Social Insurance Institution of Finland we collected all incident adult patients with SpA (ICD-10 codes M45-46) between 2010-14 and divided them into two groups depending on whether bDMARDs were subsequently initiated (group B) or not (group A). Patients' drug purchases between 2009-15 were obtained from the Drug Purchase Register. Opioid use by these patients was evaluated one year before and after the index date (ID; the date when special reimbursement for antirheumatic drugs became effective), and compared to age, sex, and place of residence matched population controls. Intravenously administered bDMARDs (e.g. infliximab) were not included.

Results: We identified 3577 SpA patients, 23% of which started a self-injected bDMARD during the observation period. More of the patients in group B needed pain medication, prednisolone, methotrexate, or other csDMARDs than sulphasalazine, which was more frequent in group A (table 1). Fifty-eight percent of the patients in group B started their bDMARD already within one year from ID (table 1). Overall, 29.8% of the SpA patients compared to 8.1% of the controls purchased opioids at least once during the year before ID. Patients' opioid purchases peaked during the last 3-month period before ID; risk ratios (RR) were 4.23 (95% confidence interval (CI) 3.63 to 4.84) and 6.23 (5.23 to 7.41) in patient groups A and B, respectively, compared to controls. SpA patients who had at least one opioid purchase during 12 months preceding the ID were 1.58 times more likely to start a bDMARD than those who did not purchase any opioids.

Conclusion: Only one of four early SpA patients in Finland were initiated a self-injected bDMARD during 2010-15. The use of opioids before SpA diagnosis appears to be nearly four times more common among SpA patients compared to population controls, and early opioid purchases may act as a surrogate marker for further bDMARD initiation.

Table 1. Data on incident SpA patients between 2010-14, divided into two groups depending on whether bDMARDs were introduced (group B) or not (group A). Pain medication and DMARD use during the whole first year after the ID are shown.

	Group A N=2741	Group B N=836	p-value
Age, mean (SD)	39 (13)	38 (11)	0.16
Proportion of females,%	53	49	0.048
Pain medication,%			
Paracetamol	21.1	24.9	0.020
NSAID	71.9	78.5	<0.001
Opioid	18.2	33.0	<0.001
DMARDs			
None	3.6	0.2	
Methotrexate	29.9	53.8	<0.001
Sulphasalazine	84.5	78.6	<0.001
Prednisolone	33.8	47.0	<0.001
Other csDMARDs	6.5	9.8	<0.001
BDMARDs	0	58.0	..

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FRI0373 5-YEARS TREATMENT EFFECT OF TNF ALPHA INHIBITOR IN EARLY AXIAL SPONDYLOARTHRITIS AND ASSOCIATED FACTORS: AN INVERSE PROBABILITY WEIGHTING ANALYSIS OF THE DESIR COHORT

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Background: Only scarce data is available on the long-term treatment effect in a real-life setting (i.e. effectiveness) of TNFi in early axial SpA forms and its predisposing associated factors; furthermore, unbiased evaluation of treatment effect in non-randomized clinical trials is challenging, and new methods have been developed to overcome prescription bias.
Objectives: a) to estimate the probability to initiate a TNFi over 5 years of follow up in real life setting using novel statistical methods to overcome prescription bias; b) to determine the long-term effectiveness of first TNFi and its predictive factors.
Methods: Observational prospective French cohort (DESIR) with 5 years of follow-up, including 708 TNFi-naïve patients early axial spondyloarthritis. Study visits were scheduled every 6 months in the first two years of follow up then yearly up to 5 years. Treatment (TNFi or other) was at the discretion of the treating rheumatologist's. The probability to initiate a TNFi was estimated by the Kaplan Meier Method, assuming non informative dropouts. Effectiveness of the first TNFi was defined as the probability to reach an ASAS40 response in both groups (TNFi vs. any other treatment) after at least 10months of exposure. To evaluate treatment effect and overcome prescription bias repeatedly occurring over time, we have applied an iterative method based on inverse propensity score (PS) weighting using a marginal structural model, that allows the integration of the repeated weights derived from the propensity score at each visit (i.e. the probability to receive the treatment at each visit). The structural model used for this analysis was a PS-weighted cox regression, to estimate the probability to present an ASAS40 response after at least 10 months of treatment. Factors predicting first TNFi effectiveness, were explored by Cox (univariate and then multivariate) regression models.
Results: Of the 708 patients included in the analysis, 258 patients initiated a first TNFi during the first five years of follow up. The probability to initiate a TNFi treatment was 41.3% [95%CI 37.2-45.1]. Among the 258 patients who received a first TNFi, 163 (63.2%) were exposed for at least 10 months. On the original data, ASAS40 response was observed in 50/163(30.7%) vs. 58/450(12.9%) patients from the TNFi and usual care groups, respectively. The likelihood of an ASAS40 response was greater in the TNFi exposed group (HR= 3.3[95%CI 2.9-3.8], p <0.0001). Male gender (HR=1.5[95%CI 1.1-2.1]), HLAB27+ (HR= 1.4 [95%CI 1.1-2.0]) and the presence of at least one objective sign of inflammation (MRI or CRP) or structural damage (radiographic sacroiliitis) (HR= 1.7 [95%CI 1.2-2.4]) were jointly predictive of an improved outcome.
Conclusion: Our study, applying novel statistical techniques to overcome prescription bias, confirms the 5-year effectiveness of TNF alpha inhibitors (TNFi) in patients with early axial Spondyloarthritis (axSpA), and we confirm that male gender, with HLAB7 positive and the presence of at least one objective sign of inflammation or structural damage are more frequently associated with such effectiveness.

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FRI0374 THE RISK OF INFECTION BY TUMOR NECROSIS FACTOR INHIBITORS AND ITS ASSOCIATED FACTORS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULT FROM KOREAN NATIONAL HEALTH INSURANCE DATA

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Background: Tumor necrosis factor inhibitors (TNFi) are effective in patients who do not respond to non-steroidal anti-inflammatory drugs, or disease modifying anti-rheumatic drugs, and have been widely used in patients with ankylosing spondylitis (AS). However, there is some evidence that treatment with TNFi can increase the risk of infection in patients with AS.
Objectives: The aim of this study was to investigate the risk of infection in patients with AS treated with TNFi.
Methods: Data was obtained from insurance claims database of the Health Insurance Review & Assessment Service (HIRA) in South Korea. Patients who have been prescribed a TNFi such as etanercept (ETN), adalimumab (ADA), golimumab (GLM), and infliximab (IFX) to treat AS from 1 July 2012 to 30 June 2017 were enrolled. We evaluated the incidence rate (IR) and hazard ratio (HR) of serious infections including pneumonia, tuberculosis, and herpes zoster in each TNFi treatment group by using cox proportional hazard model. We further analyzed the HR of infection by sex.
Results: A total of 2,515 patients were included in the study, and they were prescribed ETN (n=528), ADA (n=914), GLM (n=628), or IFX (n=445). The IRs of serious infection were 1668.63, 1489.88, 1457.58, and 1399.16 per 1,000 person years (pys) in ETN, ADA, GLM, and IFX treated groups, respectively. There was no significant difference in HR of serious infection between the TNFi groups. In the subgroup analysis of major infections, there was no difference in the HR of pneumonia between TNFi groups. However, the HR of tuberculosis with IFX group was significantly higher than that with ETN (adjusted HR 8.95, 95% CI: 1.12-71.4). In herpes zoster infection, there was no difference between TNFi groups in all patients, but the adjusted HRs significantly increased with GLM (adjusted HR 15.40, 95% CI: 1.64-144.34) and IFX (adjusted HR 10.02, 95% CI: 1.12-89.9) treatment as compared to ETN in female patients.
Conclusion: Patients receiving IFX had a higher risk of contracting tuberculosis than those receiving ETN. Moreover, the risk of herpes zoster was higher in female patients treated with GLM and IFX than in those treated with ETN in Korea.

REFERENCES:

[1] Kim JA, Yoon S, Kim LY, Kim DS. Towards Actualizing the Value Potential of Korea Health Insurance Review and Assessment (HIRA) Data as a Resource for Health Research: Strengths, Limitations, Applications, and Strategies for Optimal Use of HIRA Data. J Korean Med Sci 2017;32:718-728.

[2] Fouque-Aubert A, Jette-Paulin L, Combescure C, et al. Serious infections in patients with ankylosing spondylitis with and without TNF blockers: a

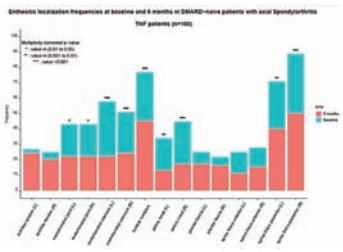
systematic review and meta-analysis of randomised placebo-controlled trials. Ann Rheum Dis 2010;69:1756-1761.

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FRI0375 SITE-SPECIFIC EFFECTIVENESS OF TNF INHIBITORS FOR ENTHESITIS IN DMARD-NAIVE PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Enthesitis is a hallmark of spondyloarthritis (SpA), with substantial impact on quality of life. Although pathophysiological mechanisms of enthesitis may include both mechanical and autoimmune features, improvements upon initiation of TNF-inhibitors (TNFi) across individual enthesitis sites have not been reported in real-world patients with axial spondyloarthritis (axSpA).
Objectives: To investigate the effectiveness of TNFi in axSpA patients without prior DMARD treatment at specific enthesitis sites, including spine, thoracic cage, Achilles tendon and the plantar fascia.
Methods: This was a retrospective cohort study using the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry. AxSpA patients initiating TNFi without previous DMARD (biologic or conventional synthetic DMARD [csDMARD]) use and with available Maastricht Ankylosing Spondylitis Enthesitis Score, modified to include the plantar fascia, (MASES) at start of treatment ('baseline') and after 6 months (± 3 months) of follow up were included. Presence of enthesitis was defined as at least 1 inflamed enthesis. Among patients with any enthesitis present at baseline, the number of patients with enthesitis at each MASES site was assessed at baseline and the 6 month follow up. Fisher's exact test was used to assess significant enthesitis resolution at each enthesitis site between baseline and 6-month follow up. The Holm-Bonferroni method was used for multiplicity correction of p-values.
Results: 781 DMARD-naive patients with axSpA who initiated TNFi were identified. At baseline, patients (57% male) were a median of 40 (interquartile range [IQR]) = 31-50) years of age with a median disease duration of 9 (IQR = 3-18) years and median Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) of 3.4 (IQR = 2.8-3.9) at treatment initiation. A subgroup of 160 TNFi patients had active enthesitis at baseline (MASES: mean = 4.14, standard deviation [sd] = 2.87) and a 6-month follow-up visit with MASES available (MASES: mean = 2.07, sd = 2.82), with a mean MASES reduction at the follow-up visit of 2.07 (sd = 3.06). At the 6-month follow up, complete enthesitis resolution was observed for 72 (45.0%) of patients. Enthesitis resolution was most frequent at the following sites: the costochondral sternum, the costochondral joint, the lumbar vertebra, the pelvic crest, and spina iliaca posterior (Figure 1). Limited resolution of enthesitis was observed in the spina iliaca anterior, plantar fascia, and the Achilles tendon.



Conclusion: Our results suggest that for real-world DMARD-naïve axSpA patients, TNFi are generally effective for resolving enthesitis. Significant resolution was observed for enthesitis of the spine and thoracic cage though resolution was more limited for plantar fascia or Achilles tendon enthesitis. Lower limb entheses are more prone to mechanical strain and may therefore require alternative or more prolonged therapy.
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Disclosure of Interests: Thomas Huegle Grant/research support from: AbbVie, Lilly, Novartis and Pfizer, Speakers bureau: AbbVie, Lilly, Novartis and Pfizer, Burkhard Moeller Consultant for: Swissmedic Human Medicines Expert Committee Member (regulatory agency), Adrian Ciurea Consultant for: AbbVie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Michael Nissen Consultant for: AbbVie, Lilly, Novartis, and Pfizer, Patrick Zueger Shareholder of: AbbVie, Employee of: AbbVie, Martin Schulz Shareholder of: AbbVie, Employee of: AbbVie, Fabiana Ganz Shareholder of: AbbVie, Employee of: AbbVie, Almut Scherer Grant/research support from: Almut Scherer is an employee of SCQM, which receives funding from AbbVie, Celgene, iQONE, Lilly, MSD, Novartis, Pfizer, Roche, Sandoz, Sanofi Genzyme, and UCB., Consultant for: Consultant for Pfizer, MSD, and AbbVie, Eleftherios Papagiannoulis: None declared
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FRI0376 DIFFERENCES IN PHYSICAL ACTIVITY BETWEEN AXIAL SPONDYLOARTHRITIS PATIENTS WITH AND WITHOUT PHYSICAL THERAPY

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Background: Physical activity (PA) according to public health guidelines is effective and safe for people with rheumatic and musculoskeletal diseases, including axial spondyloarthritis (axSpA), and should be promoted by healthcare providers.[1] In axSpA, in particular high intensity aerobic PA is beneficial, yet this was found to be incompletely implemented in physical therapy programs.[2] Studies describing aerobic PA in axSpA patients with and without physical therapy are lacking.
Objectives: To describe the amount, frequency and intensity of aerobic PA in axSpA patients with and without physical therapy treatment.
Methods: A survey, which included questions on patient characteristics, current physical therapy use (individual or group), PA (Short QUestionnaire to ASess Health-enhancing PA (SQUASH)) and health status (Assessment of Spondyloarthritis International Society Health Index (ASAS HI)), was sent by postal-mail to 458 axSpA patients registered in three hospitals in the Netherlands. From the SQUASH, besides amount (minutes/week) of all PA and meeting the PA guideline ($\geq$30 minutes $\geq$moderate PA on $\geq$5 days/week; yes/no), also the amount and frequency (sessions/week) of moderate and vigorous intensity aerobic PA during commuting and leisure (including sports) were extracted. Differences in PA behaviour between patients with and without current physical therapy were analyzed with the Mann-Whitney U or Chi-square test, where appropriate.
Results: The questionnaire was returned by 206 axSpA patients (response rate: 45%) of whom 200 completed the SQUASH correctly. Overall, 64% met the PA guideline. Half of the patients were using physical therapy (n=99; 77 individual, 11 group and 11 both); these patients had a significantly longer disease duration. Regarding overall PA, there were no differences in the total amount and the proportion meeting the guideline between patients with and without physical therapy. For moderate intensity aerobic PA, both the amount and frequency were significantly greater in the group with physical therapy, whereas for vigorous intensity aerobic PA there were no differences between the groups (Table 1).
Conclusion: More than half of people with axSpA were physically active according to public health PA guidelines. People using physical therapy engaged in significantly more moderate intensity, but not high intensity aerobic PA than those without physical therapy. These results indicate that high intensity aerobic PA should be more intensively advocated and implemented, also in physical therapy treatment.

REFERENCES:
[1] Rausch Osthoff, et al. Ann Rheum Dis. 2018;77:1251-1260.
[2] Niedermann, et al. Arthritis Care Res. 2018. Doi: :10.1002/acr.23705

Table 1. Characteristics and total, moderate and vigorous PA of Dutch axSpA patients with and without current physical therapy (PT)

	With PT (n=99)	Without PT (n=101)	*p*-value*
Gender, male,%	71	68	.679
Age, years, median (IQR)	59 (46-69)	54 (45-67)	.260
Disease duration, years, median (IQR)	25 (11-37)	17 (7-34)	**.034**
DMARDs or biological use,%	46	48	.769
ASAS HI score, median (IQR)	6.0 (3.0-8.0)	5.0 (2.0-8.0)	.295
Meeting PA guideline,%	67	60	.357
Total PA, minutes/week, median (IQR)	2470 (995-3420)	2280 (1050-3147)	.460
Moderate intensity aerobic PA			
Minutes/week, median (IQR)	240 (85-435)	140 (0-300)	**.007**
sessions/week, median (IQR)	4 (2-8)	2 (0-6)	**.005**
Vigorous intensity aerobic PA			
Minutes/week, median (IQR)	120 (0-390)	40 (0-360)	.367
sessions/week, median (IQR)	2 (0-5)	1 (0-5)	.380

* *P*-value of Chi-square (for nominal variables) or Mann-Whitney U (for continuous variables) tests.

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FRI0377

IDENTICAL TWO-YEAR TREATMENT RETENTION OF ORIGINATOR AND BIOSIMILAR INFLIXIMAB. RESULTS OF A NORDIC COLLABORATION INCLUDING 1319 PATIENTS WITH SPONDYLOARTHRITIS

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Background: The first infliximab biosimilar (CT-P13) was introduced in Europe in 2014, followed by a rapid, but differential, uptake across the Nordic countries [1]. Pre and post-marketing randomized controlled trials have shown similar efficacy and safety of originator infliximab (INF) versus CT-P13, but a number of observational studies have indicated potential differences in long-term treatment retention. However, no large observational study has hitherto directly compared the treatment retention of INF with CT-P13 in bio-naïve patients with spondyloarthritis (SpA) starting infliximab during the same calendar-time period.

Objectives: To compare one- and two-year treatment retention of INF versus CT-P13 in SpA, when used as a first line biologic, and to explore baseline characteristics in the two cohorts.

Methods: Observational cohort study. Bio-naïve patients with ankylosing spondylitis (AS), non-radiographic axial SpA (nrax-SpA) or undifferentiated SpA (uSpA), starting INF or CT-P13 as their first ever TNFi during the time-period Jan 2014 through Jun 2017 were identified in biological registers in the five Nordic countries. SpA comorbidities were identified through linkage to national registers. Treatment retention of INF versus CT-P13 was assessed through survival probability curves and one- and two-year retention rates.

Results: In total 1319 bio-naïve patients with SpA started infliximab during the time-period, 24% started INF and 76% CT-P13. Baseline characteristics of patients in the two treatment groups were comparable (Table 1).

The survival probability curves were identical for INF compared to CT-P13 (Figure 1), and the proportion of patients remaining on treatment after one and two years were similar: one year INF 62% (95%CI 57-68%), CT-P13 63% (95%CI 60-66%); two years: INF 44% (95%CI: 38-50%) and CT-P13 46% (95%CI: 42-51%). Further confounder-adjusted analyses, are planned and will be presented at the conference.

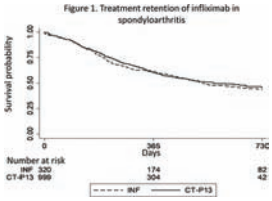


Table 1. Baseline characteristics of infliximab treated SpA patients.

	INF (N=320)	CT-P13 (N=999)
Age at start, years	42 (14)	42 (13)
Disease duration, years	13 (12)	10 (11)
Sex, men,%	57	58
AS,%	57	46
nrax-SpA/uSpA,%	43	54
Psoriasis*,%	6	3
Inflammatory bowel disease*,%	10	11
CRP, mg/L	15 (21)	13 (22)
VAS-pain, mm	62 (23)	59 (24)
ASDAS	3.37 (1.02)	3.35 (0.97)
BASDAI, mm	6.0 (2.0)	5.6 (2.0)
BASFI, mm	4.4 (2.5)	4.8 (2.4)
Concomitant csDMARD,%	44	31

Numbers are means (standard deviations) unless otherwise stated
INF= infliximab originator; CT-P13= infliximab biosimilar.
*comorbidities only available from Sweden, Denmark and Finland.
csDMARD = conventional synthetic Disease Modifying anti-Rheumatic Drugs.

Conclusion: We found remarkably similar treatment retentions for the infliximab originator and biosimilar when used as the first line biologic in 1319 patients with SpA. The baseline characteristics of the patients starting the originator and the biosimilar suggest that the cohorts are comparable, and the results thus supports the equivalence of the treatments.

REFERENCE:

[1] Glintborg, et al. Biological treatment in ankylosing spondylitis in the Nordic countries during 2010-2016: a collaboration between five biological registries. Scand J Rheumatol. 2018;47:465-74.

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FRI0378

DOES DRUG EFFECTIVENESS OF 2ND AND 3RD TNF INHIBITORS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS DEPEND ON THE REASON FROM WITHDRAWAL FROM THE PREVIOUS TREATMENT? – RESULTS FROM THE EUROSPA RESEARCH COLLABORATION

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Background: Tumour necrosis factor inhibitors (TNFi) are efficacious in patients with axial spondyloarthritis (axSpA), but some patients switch to a different TNFi because of adverse effects (AE) or lack of effect (LOE). The EuroSpA Collaboration has previously demonstrated a 1-year retention rate of 79% and 6 months LUNDEX adjusted BASDAI<4 of 59%[1] in patients initiating the first TNFi treatment. Little is known about the effectiveness of switching to a second and third TNFi in patients with axSpA.
Objectives: Firstly, to investigate retention and response rates at 6, 12 and 24 months in patients with axSpA initiating the 2nd and 3rd TNFi in clinical practice across Europe. Secondly, to investigate whether the outcomes were associated with the reason for withdrawal (AE or LOE) from the previous treatment.
Methods: Prospectively collected data on axSpA patients in routine care from 12 European registries were pooled. Kaplan-Meier estimation was used to investigate TNFi retention rates. LUNDEX adjusted[2] response rates were calculated for BASDAI<4 and ASDAS inactive disease (ASDAS<1.3). Group comparisons were performed by Chi-square test.
Results: A total of 7953 patients initiating their 2nd TNFi and 2782 patients initiating 3rd TNFi were included. Baseline characteristics are shown in the Table.
The overall retention rates for both 2nd and 3rd TNFi at 12 months were 72% (**Figure**). Corresponding retention rates for the individual registries ranged from 52-90% and 54-89%, respectively. In both patients who stopped 1st TNFi due to AE or LOE, 12-month retention rate for the 2nd TNFi treatment was 68%. In patients who stopped the 2nd TNFi due to AE or LOE, 12-month retention rates for the 3rd TNFi treatment were 68% and 69%, respectively.
For the 2nd and 3rd TNFi, 6 months LUNDEX adjusted BASDAI<4 were 44% and 37% (p<0.001), respectively, and for ASDAS inactive disease 18% and 13% (p=0.003) (**Table**).

Table: Baseline characteristics, retention and remission rates of axSpA patients initiating 2nd and 3rd TNFi overall and stratified by reason of withdrawal from the previous TNFi (AE or LOE)

	2nd TNFi (n=7953)*		3rd TNFi (n=2782)**	
	Baseline characteristics			
Age, years	43(35-52)		44(36-53)	
Male	55%		52%	
HLA-B27	66%		66%	
Concomitant csDMARD/prior csDMARD	28% / 68%		30% / 74%	
Disease duration, years	5(2-11)		6(3-12)	
First TNFi drug: Infliximab/ Etanercept / Adalimumab / Certolizumab / Golimumab	14% / 34% / 32% / 5% / 16%		19% / 24% / 28% / 7% / 23%	
BASDAI	56(37-71)		59(40-74)	
BASFI	44(23-65)		47(27-70)	
BASMI	20(10-40)		30(10-50)	
	Retention rates			
6 / 12 / 24 months (95% CI)	81% (80-82%) / 72% (71-73%) / 64% (62-65%)		81% (80-83%) / 72% (70-73%) / 62% (60-64%)	
	Initiating 2nd TNFi because of AE on 1st TNFi	Initiating 2nd TNFi because of LOE on 1st TNFi	Initiating 3rd TNFi because of AE on 1st TNFi	Initiating 3rd TNFi because of LOE on 1st TNFi
6 months (95% CI)	77% (75-79%)	78% (77-80%)	77% (73-80%)	80% (78-82%)
12 months (95% CI)	68% (66-70%)	68% (66-69%)	68% (64-72%)	69% (67-72%)
24 months (95% CI)	61% (58-63%)	58% (56-60%)	61% (56-65%)	58% (56-61%)
	Response rates			
	LUNDEX adjusted ***		LUNDEX adjusted ***	
BASDAI<4 at 6 / 12 / 24 months	44% / 36% / 27%		37% / 30% / 21%	
ASDAS inactive disease at 6 / 12 / 24 months	18% / 15% / 11%		13% / 10% / 7%	
	Initiating 2nd TNFi because of AE on 1st TNFi	Initiating 2nd TNFi because of LOE on 1st TNFi	Initiating 3rd TNFi because of AE on 1st TNFi	Initiating 3rd TNFi because of LOE on 1st TNFi
	LUNDEX adjusted ***			
BASDAI<4 at 6 / 12 / 24 months	46% / 37% / 29%	39% / 32% / 23%	39% / 28% / 25%	35% / 28% / 19%
ASDAS inactive disease at 6 / 12 / 24 months	21% / 16% / 14%	13% / 11% / 8%	15% / 13% / 9%	11% / 8% / 6%

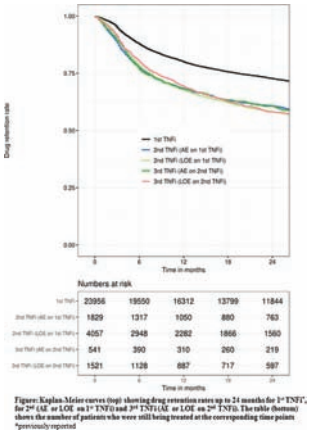


Figure: Kaplan-Meier curves (top) showing drug retention rates up to 24 months for 1st TNFi, for 2nd (AE or LOE on 1st TNFi) and 3rd TNFi (AE or LOE on 2nd TNFi). The table (bottom) shows the number of patients who were still being treated at the corresponding time points
*previously reported

Conclusion: Data from 12 European countries demonstrated decreasing response rates with increasing number of previous TNFi, although with only minor difference between 2nd and 3rd. Patients who had withdrawn from the previous TNFi due to LOE had retention rates and remission rates similar to those who had withdrawn due to AE.

REFERENCES:

[1] Brahe, et al. ACR 2018
[2] Arthritis Rheum, 2006, 54(2), p:600-6.

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FRI0379 LONG-TERM EVALUATION OF SECUKINUMAB 150 MG IN ANKYLOSING SPONDYLITIS: 5-YEAR END-OF-STUDY EFFICACY AND SAFETY RESULTS FROM A PHASE 3 TRIAL

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Background: Evaluation of long-term efficacy and safety for treatments for ankylosing spondylitis (AS) is important. Secukinumab, a fully human monoclonal antibody that directly inhibits interleukin-17A, has shown significant and sustained improvement in the signs and symptoms of AS through 3 years in the MEASURE 2 study (NCT01649375).[1]

Objectives: We report the 5-year end-of-study results of subcutaneous (s.c.) secukinumab 150 mg in the MEASURE 2 study.

Methods: AS patients (pts; N = 219) were randomised to receive s.c. secukinumab 150 mg, 75 mg or placebo at baseline, Weeks (Wks) 1, 2 and 3 and every 4 wks from Wk 4. At Wk 16, placebo-treated pts were re–randomised to receive secukinumab 150/75 mg. Efficacy results are reported for pts initially randomised to secukinumab 150 mg and those who switched from placebo to secukinumab 150 mg at Wk 16 (N = 106). An optional dose escalation from secukinumab 75 mg to 150 mg was initiated beginning Wk 140. Outcome measures at Wk 260 included ASAS20/40, BASDAI50, BASMI, BASFI, SF-36 PCS and ASAS partial remission. Analyses stratified by anti-TNF status (anti–TNF-naïve and anti-TNF inadequate response [IR]) were performed. Safety analysis included all pts who received ≥1 dose of secukinumab. Results are reported as observed.

Results: The retention rate to Wk 260 was 77% (82/106) for secukinumab 150 mg. Sustained efficacy was observed with secukinumab 150 mg across all endpoints through 5 years (Table). Improvements were maintained regardless of prior exposure to anti–TNF therapy with greater responses in anti–TNF-naïve pts. A total of 49 pts on secukinumab 75 mg (46.7%) escalated dose to 150 mg after Wk 140; efficacy responses improved in pts whose dose was escalated. Over the entire study period, the mean exposure (±SD) to secukinumab was 1459.1 ± 597.8 days. Exposure-adjusted incidence rates (per 100 pt-years) with any secukinumab dose for selected adverse events were: *Candida* infections (1.0), Crohn's disease (0.5), major adverse cardiovascular events (0.7), uveitis (0.5), and malignant/unspecified tumours (0.5).

Conclusion: Secukinumab 150 mg provided sustained improvement in the signs, symptoms, and physical function in pts with AS through 5 years of treatment. The safety profile of secukinumab remained consistent with previous reports.[1–3]

REFERENCES:

[1] Marzo-Ortega, et al. *RMD Open.* 2017;3:e000592; 2. Marzo-Ortega, et al. *Ann Rheum Dis.* 2016;75:812–3; 3. Baraliakos X, et al. Clin Exp Rheumatol 2017.

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Table. Efficacy Endpoints with Secukinumab 150 mg at Week 260 (5 year)

Variable	Secukinumab 150 mg[1]		
	Total N = 106	Anti–TNF-naïve N = 66	Anti–TNF-IR N = 40
ASAS20[2]	69.9 (83)	73.7 (57)	61.5 (26)
ASAS40[2]	54.2 (83)	63.2 (57)	34.6 (26)
ASAS-Partial Remission[2]	25.3 (83)	28.1 (57)	19.2 (26)
BASDAI50[2]	53.0 (83)	56.1 (57)	46.2 (26)
BASMI[3]	-0.7±1.2 (80)	-	-
BASFI[3]	-2.8±2.6 (83)	-	-
SF-36 PCS[3]	8.0±8.5 (79)	8.5±8.9 (56)	6.8±7.4 (23)

Data are reported as observed; [1]Includes placebo switchers; [2]% responders (n); [3]mean change from baseline ± SD (n); IR, inadequate response; N, total number of randomised patients; n, number of evaluable patients; TNF, tumour necrosis factor

FRI0380 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENT OF ENTHESITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: POOLED ANALYSIS OF FOUR PIVOTAL PHASE 3 STUDIES

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Background: Enthesitis can be a debilitating extra-articular spondyloarthritis (SpA) manifestation and cause of considerable pain and reduced quality of life/physical function.[1,2]

Objectives: To evaluate the effect of secukinumab (SEC) on axial and peripheral enthesitis in ankylosing spondylitis (AS) patients (pts) with baseline enthesitis (BLE) across all Maastricht AS EnthesiS (MASES) sites (N=13), axial MASES sites [N=11; 13 MASES minus Achilles tendons (AT); AxS], peripheral sites (N=6; AT + lateral condyles of humerus/femur; PS) and the AT (N=2; AT) at Weeks (W) 16 and 52.

Methods: This post hoc analysis pooled data across 4 SEC studies in AS (MEASURE 1-4) from pts originally randomised to SEC 150mg (approved dose in AS), 300mg (MEASURE 3 only), or placebo (PBO) with BLE (MASES >0). Study designs have been reported previously. Evaluations include mean change from BL in MASES score, complete resolution (CR; MASES=0) and improvement from BL in MASES score of ≥5 counts. Mixed-effect model repeat measurement (MMRM) analysis was done on change from BL in MASES score and non-responder imputation for resolution of enthesitis at W16; data are reported as observed at W52.

Results: A total of 355 (70.4%), 58 (76.3%), and 280 (72%) pts had BLE in 150mg, 300mg and PBO groups, respectively. BL characteristics were generally comparable across groups. At W16, mean change from BL for overall MASES and at AxS was greater for SEC 150mg (-2.4 and -2.3) and 300mg (-2.9 and -2.9) vs PBO (-1.9 and -1.8; $P<0.05$ and <0.01). At W16, pts treated with SEC 150mg (40.8% and 42.7%) and 300mg (36.2% and 42.1%) vs PBO (28.9% and 30.1%) achieved CR of enthesitis based on overall MASES and at AxS. SEC150mg and 300mg were also consistently associated with higher mean change in MASES and CR of enthesitis at PS and individually at AT vs PBO. A higher proportion of pts treated with SEC 150/300mg vs PBO achieved a higher threshold of improvement (≥5 counts) in overall MASES at W16. Further improvements were observed for all endpoints at W52 (Table).

Conclusion: Secukinumab was associated with higher mean change in MASES and complete resolution of enthesitis compared to placebo at Week 16, which further improved through Week 52.

REFERENCES:

[1] Braun J, et al. *Nat Clin Pract Rheumatol.* 2006;2:536-45; 2. Schett G, et al. Nat Rev Rheumatol. 2017;13:731-741.

Table. Summary of results

	SEC 150 mg N=355		SEC 300mg N=58		PBO N=280
	W16	W52^{o}	W16	W52^{o}	W16
LS mean change from BL in MASES score*					
Overall MASES[a]	-2.4‡	-3.5	-2.9§	-3.9	-1.9
AxS[b]	-2.3‡	-3.2	-2.9§	-3.6	-1.8
PS[c]	-1.3	-1.9	-1.6	-2.1	-1.2
AT[d]	-1.0	-1.2	-1.0	-1.3	-0.8
Complete resolution of enthesitis (MASES=0)#,%					
Overall MASES[a]	40.8§	56.4	36.2	52.9	28.9
AxS[b]	42.7§	58.6	42.1	60.0	30.1
PS[c]	46.3	65.5	52.5	69.7	38.3
AT[d]	57.0	78.4	55.0	77.8	48.0
Improvement from BL in MASES score (≥5 counts)#,%					
Overall MASES[a]	23.7	34.1	27.6	43.1	16.1
AxS[b]	20.1	28.0	22.8	32.0	15.4

$^{§}P<0.01$; $^{‡}P<0.05$ vs PBO. $^{*}P$-values from repeated MMRM until Week 16. $^{\#}P$-values from logistic regression model. SEC 150mg (n=^{a}355, ^{b}344, ^{c}229, ^{d}128); 300mg (n=^{a}58, ^{b}57, ^{c}40, ^{d}20) and PBO (n=^{a}280, ^{b}272, ^{c}188, ^{d}98). ^{o}Observed data. LS, least squares; N, number of patients analysed; n, number of patients with measurement.

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FRI0381 TROUGH SERUM DRUG LEVELS AND DISEASE ACTIVITY IN AXIAL SPONDYLOARTHRITIS PATIENTS ON LONG-TERM TREATMENT WITH TNF-A INHIBITORS

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Background: In approximately 50% of patients with axial spondyloarthritis (ax-SpA) treated with TNF-α inhibitors, treatment loses efficacy after a period of time.[1] Previous research has shown that high disease activity is associated with low serum drug levels after 6 months of treatment with TNF-α inhibitors.[2] There is limited literature regarding this subject in axial SpA patients on long-term treatment with TNF-α inhibitors.
Objectives: To investigate the association between trough serum drug level of TNF-α inhibitors and disease activity in axial SpA patients.
Methods: All consecutive ax-SpA patients of the Groningen Leeuwarden Axial SpA (GLAS) cohort, fulfilling the ASAS classification criteria, treated with TNF-α inhibitors and visiting the out-patient clinic in Groningen between the 1st of June 2015 until the 31st of May 2016 were approached to have a trough serum drug level measurement within two months from the out-patient visit. Serum trough levels were stratified in a 'therapeutic' and 'below-therapeutic' range according to the reference values of Sanquin[3]. Disease activity was assessed with the ASDAS, BASDAI and CRP.
Results: 67 (60%) of the 112 approached patients were eligible for analyses. Thirty-one (46%) were male, mean age was 45±12 years, 48 patients (72%) were HLA-B27 positive, mean symptom duration was 20 ±12 years and median duration of TNF-α inhibitor treatment was 49 months (IQR 14-64). 34 patients were on adalimumab (51%), followed by 21 on etanercept (31%) and the remaining 12 patients (18%) were on infliximab, certolizumab or golimumab. 32 of the 67 patients (48%) had a 'therapeutic' serum trough drug level and 35 (52%) were 'below-therapeutic', with no significant difference in patient characteristics between these 2 groups, including disease activity (ASDAS 2.2±1.0 vs. 2.3±0.8; BASDAI 3.9±2.4 vs. 4.1±2.1; CRP 4.5, IQR 2.0-6.6 vs. 3.0, IQR 2.0-6.0). No significant correlations for ASDAS, BASDAI and CRP with adalimumab or etanercept drug level were found (adalimumab r=-0.164, p=0.36; r=-0.191, p=0.29; r=-0.041, p=0.83 resp.; etanercept r=-0.185, p=0.42; r=-0.113, p=0.63; r=-0.216, p=0.36 resp.).
Stratified by gender, only women on adalimumab showed a weak significant negative correlation between serum level and ASDAS and BASDAI (r=-0.444, p<0.05; r=-0.497, p<0.05 resp.) but not for CRP (r=0.038, p=0.87). Compared to men, women had a significantly higher ASDAS and CRP. BASDAI was not significantly different (data not shown). Patient characteristics between patients with and without serum trough level measurements did not differ significantly.
Conclusion: In daily clinical practice random serum trough levels in ax-SpA patients are relatively low according to reference values of Sanquin. Furthermore, only for women on adalimumab a weak correlation was found between trough serum drug level and ASDAS and BASDAI but not for CRP.

REFERENCES:

[1] Arends S., Brouwer E., Efde M. et al. Long-term drug survival and clinical effectiveness of etanercept treatment in patients with ankylosing spondylitis in daily clinical practice. Clin Exp Rheumatol 2017;35:61-68.
[2] Kneepkens E.L., Wei J.C.C., Nurmohamed M.T, et al. Immunogenicity, adalimumab levels and clinical response in ankylosing spondylitis patients during 24 weeks of follow-up. Ann Rheum Dis 2015;74:396-401.
[3] Sanquin Amsterdam. Diagnostische testen. Available via: www.sanquin.org/nl/producten-en-diensten/diagnostiek/diagnostische-testen/index. Consulted on April 28th 2018.

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FRI0382 TEN-YEAR RETENTION RATES OF FIRST-LINE BIOLOGICAL AGENT IN AXIAL SPONDYLARTHRITIS IN DAILY PRACTICE: A ROMANIAN MULTICENTRE EXPERIENCE

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Background: Although the efficacy and long-term persistence of TNF inhibitors (TNF-i) are widely recognized in axial spondyloarthritis (axSpA), up to about one third of patients experience failure (loss of therapeutic response or toxicity) with the first biological agent requiring switching to another drug.

Objectives: The aims of our study were to assess the 10-year survival of the first TNF-i, to compare retention rates of different anti-TNF drugs in real life settings and to identify factors associated with drug retention in active axSpA.
Methods: We performed a hospital-based retrospective cohort study on consecutive adult axSpA suboptimally controlled by standard therapy, starting their first biological agent with infliximab (IFX), adalimumab (ADA), etanercept (ETA) or golimumab (GLM) according to local policy, recruited at three academic centres between 2003 and July 2018.
Drug efficacy (BASDAI, ASDAS-CRP) as well as reasons for discontinuation were evaluated every 24 weeks. Drug survival was calculated using the Kaplan-Meier analysis, while univariate and multivariate regression was used for predictors of persistence and withdrawal ($p<0.05$). Subanalysis was done according to discontinuation reasons.
Results: Of the 241 axSpa were recruited, 104 (43.15%) cases received ETA (original, biosimilar), 100 (41.49%) ADA, 26 (10.78%) IFX (original and biosimilar) and 11 cases (4.56%) GLM.
Statistical significant improvement was demonstrated (ASDAS-CRP, BASDAI, BASFI) in all patients, those with higher disease activity and functional impairment at baseline presenting earlier and higher response rate ($p<0.05$).
We reported high long-term persistence of the first TNF-i with a median survival rate of 8.1±2.1 years for IFX, ADA and ETA; furthermore, at 10 years, up to one third (36%) of axSpA remained on the initial drug achieving either stable remission (62.24%) or low disease activity (37.76%), while one out of five patients on the same drug after 140 months. The retention rates of ETA, ADA and IFX were 70%, 68% and 57% after 3 years; 68%, 48% and 53% after 5 years; 35%, 30% and 27% after 10 years. Overall, retention to ETA was superior to that of monoclonal antibodies ($p<0.05$), with a total drug-exposure of 625.43 patient-years for ETN, 415.26 for ADA, 221.53 for IFX.
In addition, survival of the second TNF drug was good but inferior to the first TNF-I ($p<0.05$).
Male sex, age under 40, high baseline C reactive protein, low initial BASFI and disease duration under 5 years were associated with retention rate in multivariate analysis ($p<0.05$), while the presence of syndesmophytes and obesity with higher withdrawal ($p<0.05$).
Conclusion: We reported high long-term persistence of the first biological agent in axSpA, with superior retention for ETA compared to monoclonal antibodies. Predictors for high retention rate advocate the rationale for the drug choice in different axSpA settings.
Disclosure of Interests: CODRINA ANCUTA Speakers bureau: Abbvie, Pfizer, Novartis, MSD, Roche, Biogen, UCB, Lilly, Cristina Pomirleanu Speakers bureau: Abbvie, Pfizer, UCB, Raluca Paiu: None declared, Georgiana Strugariu Speakers bureau: Abbvie, Pfizer, UCB, Luiza Petrariu Speakers bureau: Abbvie, Pfizer, Novartis, Eugen Ancuta: None declared, Codruta Bran Speakers bureau: Abbvie, Pfizer, Novartis, Lilly, Roche, Rodica Chirieac: None declared, Claudia Mihailov Speakers bureau: Abbvie, Pfizer, Novartis, MSD, Roche, Biogen, UCB, Lilly
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FRI0383 PAMIDRONATE IN CHRONIC NON-BACTERIAL OSTEOMYELITIS: A RANDOMIZED, PLACEBO-CONTROLLED PILOT TRIAL

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Background: Chronic non-bacterial osteitis (CNO) is an autoinflammatory disease often associated with seronegative spondyloarthritides. Osteitic bone lesions in adults are predominantly located in the anterior chest wall, the spine and pelvis. Case series suggest that the amino-bisphosphonate pamidronate may be effective in improving bone inflammation, pain, and disability. No randomized controlled trials have been conducted in CNO.
Objectives: In a randomized double-blinded, placebo-controlled trial we hypothesized that pamidronate reduces radiological signs of bone inflammation assessed by whole-body magnetic resonance imaging, improve pain, disability and reduces systemic markers of bone inflammation and bone turnover in blood.
Methods: Patients with an established diagnosis of CNO were assessed for eligibility. Inclusion criteria were 1. Mono- or multifocal bone inflammation (osteitis with or without sclerosis) 2. Jansson clinical score for CNO in children and adults ≥ 39[1] or malignancy and infection excluded by biopsy and 3. Symptoms duration > 6 weeks. Patients were randomized 1:1 to receive placebo or pamidronate 1 mg/kg, max 60 mg, given for three consecutive days at baseline, week 12 and week 24. Whole-body MRI was performed at baseline, week 12 and 36. CT scan of the anterior chest wall was performed at baseline and week 36. Changes in active and chronic radiological bone inflammation in the ACW and spine were systematically scored.[2, 3] Patient-reported outcome were measured at baseline and week 1,4,12,24 and 36 using a visual analogue scale for pain and global health assessment, Health Assessment Questionnaire for physical functioning and, EuroQoL- 5 Dimension-3 Level and The Short Form (SF)-36 questionnaire for Quality of life. Biomarkers of bone turnover and inflammation in blood were measured at baseline and week 1,4,12,24 and 36.
Results: Analyses were performed in 12 patients with CNO, mean age 32 (range 20-63) years. From baseline to week 36 the radiological score of active bone inflammation decreased from 4,8(SD 2.2) to 2,5(SD 1.6) in the pamidronate group (p=0,01). This differed significantly from the placebo group in which no change from baseline was observed (p=0.04). We observed a decreasing trend in VAS pain from mean 38(SD 23)mm to 19(SD 18)mm and VAS global from 32(SD 22)mm to 13(SD 18)mm.
Conclusion: This study is the first randomized double-blinded, placebo-controlled trial in CNO. Treatment with pamidronate improved bone marrow oedema in the anterior chest wall assessed by whole-body magnetic resonance imaging. This pilot study points out methodological considerations in relation to study design and outcome measures in CNO.

REFERENCES:

[1] Jansson AF, Müller TH, Gliera L, Ankerst DP, Wintergerst U, Belohradsky BH, et al. Clinical score for nonbacterial osteitis in children and adults. Arthritis Rheum 2009;60:1152–9.
[2] Weber U, et al. Anterior chest wall inflammation by whole-body magnetic resonance imaging in patients with spondyloarthritis: lack of association between clinical and imaging findings in a cross-sectional study. Arthritis Res Ther 2012;14:R3.
[3] Madsen KB, Jurik AG. MRI grading method for active and chronic spinal changes in spondyloarthritis. Clin Radiol 2010;65:6–14.

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FRI0384 IMPACT OF INTERLEUKIN 17 BLOCKING AGENT ON CLINICAL OUTCOME IN SAPHO PATIENTS

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Background: SAPHO syndrome has to be considered as a rare subtype of seronegative spondyloarthritis (SpA) showing typical manifestations with palmoplantar pustolosis and osteitis with hyperostosis; the clinical response of conventional or biological disease modifying drugs (DMARDs) in SAPHO syndrome are often disappointing. Whereas in SpA peripheral arthritis and inflammatory back pain represent the leading symptoms, the SAPHO patients often complain painful osteitis with hyperostosis in the sternal region as well as the palmoplantar pustulosis accompanied by synovitis preferentially in large joints including sacroiliitis. Recently, the detection of higher numbers of CD4+IL17+ lymphocytes in the peripheral blood of SAPHO patients has arisen the hypothesis that Th4/17 helper cells with their secretion of interleukin 17 (IL17) could be involved in the development of inflammation in SAPHO syndrome (1)
Objectives: Here we present an observational study of 12 SAPHO patients which were treated with the IL 17 blocking agent secukinumab. In addition, the fraction of CD4/17+ lymphocytes in peripheral blood specimen has been monitored on treatment.
Methods: Between January 2015 and February 2017 clinical activity of disease were measured in 37 SAPHO patients with a disease duration of 11 years (median). The disease activity were evaluated by the osteitis

score and skin score (ranging from 0 to 6, assessed by physician), the HAQ score (ranging from 0 to 3, assessed by patient), and MRI of the osteitis lesion (activity score 0-3, analogously to 3 domains of OMERACT RAMRIS scoring synovitis, bone marrow edema, and erosions; assessed by radiologist). In this period of time 12 of them showed disease activity due to osteitis and/or skin disease, at which time the treatment of secukinumab at dosage of 300mg as monotherapy has been started, re-evaluated after at least 12 weeks (ranging from 12 to 18 weeks). For monitoring blood specimens were derived to assess the CD4+/IL17+ lymphocyte subpopulation using immunofluorescence technique commercial antibodies for CD4, IL17 (Boehringer Ingelheim, Germany). To analyse the differences between the disease activity scores prior to secukinumab treatment and after treatment we applied the nonparametric analysis according to Wilcoxon test. The p-value < 0.05 was considered as significant.

Results: Secukinumab improved osteitis and palmoplantar pustolosis (osteitis score 3.8 to 2.4; p=0.007; PPP 3.4 to 2.4; p=0.071), the HAQ score was reduced from 1.25 to 1.0 (p=0.018), the MRI score from 2.08 to 1.58 (p=0.034). The reduction of at least two clinical activity parameters (osteitis, HAQ and/or MRI) after secukinumab treatment could be documented in all SAPHO patients who showed CD4+IL17+ lymphocytes in higher frequency of 0.4% of leukocytes of peripheral blood.

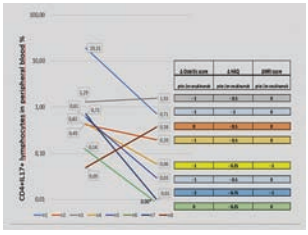


Figure: SAPHO patients n1-8 and their CD4/17+ lymphocytes fraction in peripheral blood.

Conclusion: Secukinumab seems to control osteitis and PPP in SAPHO syndrome resulting in reduced burden of disease. High Th17 lymphocytes numbers seems to be associated with higher probability of clinical response to secukinumab.

REFERENCE:

[1] Firinu D, Barca MP, Lorrai MM, Perra S, Cabras S, Muggianu E, Di Martino ML, Manconi PE, Del Giacco SR. TH17 cells are increased in the peripheral blood of patients with SAPHO syndrome. Autoimmunity. 2014 Sep;47(6):389-94

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FRI0385

LONG-TERM CERTOLIZUMAB PEGOL TREATMENT OF AXIAL SPONDYLOARTHRITIS IS ASSOCIATED WITH RAPID AND SUSTAINED REDUCTION OF ACTIVE INFLAMMATION AND MINIMAL STRUCTURAL CHANGES IN THE SPINE: 4-YEAR MRI RESULTS FROM RAPID-AXSPA

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Background: In patients (pts) with axial spondyloarthritis (axSpA), inflammation of the spine is believed to trigger a repair mechanism that results in syndesmophyte formation.[1]Fatty lesions (FLs) in the bone marrow and erosions in the axial skeleton, both visible on magnetic resonance imaging (MRI) T1 sequences, are post–inflammatory changes that have been shown to contribute significantly to models predicting new bone formation.[2] It has previously been shown that resolution of inflammatory lesions (INFLs) in pts with axSpA treated with anti–TNF therapy may be associated with an increase in FLs.[3,4] RAPID–axSpA was a long–term study in pts with radiographic (r)–axSpA (also known as ankylosing spondylitis) or non–radiographic (nr)–axSpA treated with certolizumab pegol (CZP), which rapidly suppressed active inflammation of the spine, with pts showing limited spinal radiographic progression over 4 years.[5] However, it is not known whether CZP treatment coincides with changes in FLs, sclerosis, and erosions.

Objectives: To report the incidence and association of active inflammation and chronic lesions in the spine of pts with axSpA treated with CZP over 4 years

Methods: RAPID–axSpA (NCT01087762) was double–blind and placebo (PBO)–controlled to Week (Wk)24, dose–blind to Wk48, and open–label to Wk204. CZP–randomised pts (either 200mg every 2 weeks [Q2W] or 400 mg Q4W) continued their assigned dose throughout; PBO–randomised pts received CZP from Wk24, or if non–responders, from Wk16 onwards. Blinded spinal MRI scans at baseline (BL) and Wk12, 48, 96, and 204 were assessed by 2 central readers to evaluate the presence/absence of active INFLs (Short T1 Inversion Recovery [STIR] sequence) and FLs, sclerosis and erosions (T1 sequence) in vertebral edges (VEs) (present if recorded so by both readers). Pts (r–axSpA and nr–axSpA combined) with valid assessments at BL and at least once post–BL were included. Mean lesion counts at the pt level were estimated from mixed models with repeated measures (MMRM), fitted on observed data from CZP–randomised pts. Associations between INFLs and FLs at the VE level for CZP–and PBO–randomised pts were described using cross–tabulations.

Results: Of 325 randomised pts, 136 were eligible for these analyses. In pts randomised to CZP at Wk0 (n=89), active INFLs were reduced, and FL counts only slightly increased by Wk12; both were sustained at a low level to Wk204 (**Table A**). Very few VEs with sclerosis and erosions were observed at BL, and no changes in their frequency were observed over 4 years' treatment (**Table A**). Over 4 years' CZP treatment, the risk of developing a new FL was greater in VEs with vs without INFLs at BL, regardless of changes to INFLs in these VEs post–BL (**Table B**). The prevalence of FLs was greater in pts with >3 vs ≤3 years' symptom duration and there were more new FLs in the >3 years subgroup during CZP treatment (data not shown)

Conclusion: Long–term CZP treatment in axSpA pts was associated with rapid and sustained reduction in active inflammation and a negligible increase in FLs in VEs. More FLs developed in VEs with INFLs at BL than without, but this was not affected by resolution of INFLs. There was no increase in sclerosis and erosions in VEs over 4 years' CZP treatment.

REFERENCE:

[1] Appel H. Curr Rheumatol Rep 2008;10:356–63; 2. Poddubnyy D. Arthritis Rheum 2016;68:1899–903; 3. Maksymowych W. Ann Rheum Dis 2013;72:23–8; 4. Song I. Ann Rheum Dis 2011;70:1257–63; 5. van der Heijde D. Ann Rheum Dis 2018;77:699–705.

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Table: A) Counts of inflammatory lesions, fatty lesions, sclerosis and erosions at the patient level[a] through 204 weeks' CZP treatment (MMRM estimates)

LS mean (SE)	Week 0	12	48	96	204
Inflammatory lesion count	**4.9 (0.5)**	**2.8 (0.4)**	**2.5 (0.3)**	**2.7 (0.3)**	**2.8 (0.4)**
Patients observed, n	89	88	68	70	55
Fatty lesion count	**6.9 (0.7)**	**7.3 (0.7)**	**7.3 (0.8)**	**7.5 (0.8)**	**7.4 (0.8)**
Patients observed, n	89	88	69	69	55
Sclerosis count	**0.1 (0.1)**	**0.1 (0.1)**	**0.1 (0.1)**	**0.1 (0.1)**	**0.1 (0.1)**
Patients observed, n	89	88	69	69	55
Erosion count	**0.0 (0.0)**	**0.0 (0.0)**	**0.0 (0.0)**	**0.0 (0.0)**	**0.0 (0.0)**
Patients observed, n	89	88	69	69	55

B) Presence/absence of fatty lesions in vertebral edges[b] through 204 weeks' CZP treatment by baseline MRI lesion type (observed cases)

% of VEs observed [c]		Week 12 FL+	12 FL−	48 FL+	48 FL−	96 FL+	96 FL−	204 FL+	204 FL−
FL− INFL+ at baseline n=346	VEs observed, n	338		243		278		205	
	INFL+	**8.9**	**39.3**	**9.1**	**26.3**	**9.4**	**18.3**	**11.2**	**20.5**
	INFL−	**13.0**	**38.8**	**14.0**	**50.6**	**22.3**	**50.0**	**22.4**	**45.9**
	New FLs, n [d]	74	–	56	–	88	–	69	–
FL− INFL− at baseline n=1866	VEs observed, n	1797		1429		1418		1018	
	INFL+	**0.2**	**4.2**	**0.5**	**5.3**	**0.5**	**4.2**	**0.4**	**5.2**
	INFL−	**4.7**	**90.9**	**6.3**	**87.9**	**7.1**	**88.2**	**6.9**	**87.5**
	New FLs, n [d]	89	–	97	–	107	–	74	–
FL+ INFL+ at baseline n=329	VEs observed, n	326		220		293		220	
	INFL+	**42.9**	**4.9**	**34.5**	**4.5**	**31.1**	**1.4**	**30.9**	**1.8**
	INFL−	**46.9**	**5.2**	**57.3**	**3.6**	**61.4**	**6.1**	**60.5**	**6.8**
FL+ INFL− at baseline n=586	VEs observed, n	575		424		494		337	
	INFL+	**10.6**	**0.9**	**6.1**	**1.2**	**7.3**	**1.4**	**7.4**	**1.2**
	INFL−	**76.7**	**11.8**	**78.8**	**13.9**	**78.1**	**13.2**	**75.1**	**16.3**

MRI Set. [a] Week 0 CZP patients only (n=89). [b] All CZP-treated patients, including those switching from PBO to CZP treatment at Weeks 16/24. [c] Unless stated otherwise. [d] The number of observed VEs FL− at BL recorded as FL+ post-BL. CZP: certolizumab pegol; FL: fatty lesion; INFL: inflammatory lesion; LS: least squares; MMRM: mixed model repeated measures; MRI: magnetic resonance imaging; PBO: placebo; SE: standard error; VE: vertebral edge.

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FRI0386

RELATIONSHIP BETWEEN ASDAS STATES AND INHIBITION OF STRUCTURAL DAMAGE PROGRESSION WITH SECUKINUMAB IN ANKYLOSING SPONDYLITIS: DATA FROM MEASURE 1 TRIAL

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Background: The primary treatment goal in patient with axial Spondyloarthritis (axSpA) is to optimize health-related quality of life through control of signs and symptoms, no structural damage progression and preservation of function.[1] The 2017 Treat to Target recommendations (T2T) outlined Ankylosing Spondylitis Disease Activity Score (ASDAS) -inactive disease (ID) as an optimal treatment target for axSpA patients.[1] ASDAS states were shown to correlate with syndesmophyte formation as assessed with X-Ray and MRI changes.[2] Secukinumab, a fully human monoclonal antibody that directly inhibits IL-17A, demonstrated sustained efficacy and low radiographic progression through 4 years in patient with ankylosing spondylitis (AS) in MEASURE 1 study (NCT01863732).[3]

Objectives: To investigate the relationship between ASDAS states and inhibition of radiographic structural progression in patient with AS treated with secukinumab 150 mg from the MEASURE 1 study over 4-years using *post hoc* analysis.

Methods: Lateral radiographs of the cervical and lumbar spine were assessed using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS: range 0-72). Images were scored twice at baseline/Week (Wk) 104 and baseline/Wk 208 by 2 central readers blinded to treatment/visit; mean change from baseline to Wk 104 or 208 in mSASSS scores were used. The ASDAS-CRP was used to define the disease activity states at Wks 16, 52, 104, and 208: ID (ASDAS-CRP < 1.3), Low Disease Activity (LDA, 1.3 ≤ ASDAS-CRP < 2.1) or pooled High/Very High Disease Activity (HDA/VHDA, ASDAS-CRP ≥ 2.1) given low number of patients with VHDA. Sustained ASDAS state at Wk 104 was defined as reaching the same state at Wk 104 and Wk 16 and/or 52. Sustained ASDAS state at Wk 208 was defined as reaching the same state at Wk 208 and Wk 16 and/or 52. Overall, 87 patients on secukinumab 150 mg were in the extension trial; of these, 57 and 71, respectively, had evaluable X-rays at Wks 104 and 208.

Results: The proportion of patients achieving each ASDAS state are shown in **Table**. Patients with ASDAS-ID were associated with numerically lower mSASSS mean change from baseline to Wks 104/208 compared to other ASDAS states (**Figure**).

Conclusion: In this *post hoc* analysis, patients with ASDAS-ID state and sustained ASDAS-ID state had lower radiographic progression than patients with higher disease activity at 2 and 4-years suggesting a potential relationship between ASDAS state and structural progression in patients with AS. Further confirmation is needed in larger prospective studies.

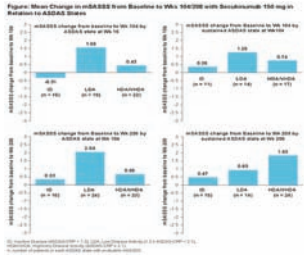
REFERENCES:

[1] Smolen JS, et al. Ann Rheum Dis. 2018;77:3-17.
[2] Poddubnyy D, et al. Ann Rheum Dis. 2014;73:422.
[3] Braun J, et al. *Rheumatology (Oxford)* 2018. Doi: 10.1093/rheumatology/key375.

Table: Proportion of Patients with ASDAS States through Wk 208

ASDAS states	Wk 16 N = 86	Wk 52 N = 84	Wk 104 N = 80	Wk 208 N = 78
ID	24.4	25.0	30.0	26.9
LDA	34.9	39.3	38.8	33.3
HDA/VHDA	40.7	35.7	31.3	39.7

ID, Inactive Disease (ASDAS-CRP < 1.3); LDA, Low Disease Activity (1.3 ≤ ASDAS-CRP < 2.1); HDA/VHDA, High/very high Disease Activity (ASDAS-CRP ≥ 2.1)
N, total number patients with ASDAS



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FRI0387

DISEASE COURSE AND OUTCOMES DURING PREGNANCY IN PATIENTS WITH AXIAL SPONDILOARTHRITIS: COMPARISON BETWEEN TNFI USERS AND NAIVE PATIENTS

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Background: Axial Spondiloarthrtis (AxSpA) can be active during pregnancy, especially in those patients who discontinued TNFi at the beginning of pregnancy. The severity of flare during pregnancy can influence the gestational outcome and the attitude of the physician towards treatment.

Objectives: To describe: 1)the disease course of AxSpA during pregnancies in patients who never used TNFi (bio-naïve) and those who were TNFi users; 2)the severity of flares; 3)the impact of resuming TNFi in patients who experienced a flare during pregnancy (on both maternal disease control and gestational outcome).

Methods: Retrospective analysis of 18 prospectively-followed pregnancies from 2010 to 2018 in 15 patients with AxSpA. Two pregnancies ended in miscarriage, so they weren't considered for the analysis of flares during pregnancy. Active disease was defined as ASDAS-CRP >2.1. Flare was defined as an increase of ASDAS-CRP greater than 0.6 with CRP elevation and one of the followings: introduction or increase above 5mg/day of prednisone, introduction of cDMARD or bDMARD.

Results: At preconception visit, 2 patients were on treatment only with steroids, 1 with sulfasalazine and steroids and 9 with bDMARDs (5 etanercept, 2 adalimumab, 2 golimumab; 2 with steroids). At conception, 3 patients presented active disease. TNFi was stopped at positive pregnancy test in 7 pregnancies; 1 patient continued TNFi over pregnancy.

Twelve out of 16 (75%) patients had at least one disease flare (4, 10 and 3 during 1st, 2nd and 3rd trimester respectively). Among pregnancies with flare, medication resumed during pregnancy were steroids (7, 58%), cDMARDs (1 salazopyrine and 1 cyclosporine A, 17%) and bDMARDs (4 etanercept and 1 certolizumab, 42%). Six patients (38%) had a flare in postpartum period. Table 1 shows the comparison between pregnancies with and without flares during pregnancy.

By comparing the pregnancies of patients with and without history of TNFi use (table 2), we have registered 8 flares (8/11, 73%) in the first group and 4 flare (4/5, 80%) in the second one. In the group of TNFi users, medications resumed during pregnancy were steroids in 5/11 (46%) and bDMARDs in 5/11 (46%), whereas in the group TNFi naïve only in 1 pregnancy steroids was resumed and no bDMARDs were started. Mean ASDAS-CRP was higher in the group of TNF user.

For what concerned gestational outcome, we did not observe any SGA, pre-eclampsia and eclampsia. Two pregnancies ended with miscarriage and 2 with preterm birth (at 36 and 34 gestational weeks). Two patients had PROM and 1 pPROM (this patient refused to resume TNFi during pregnancy and her flare was treated with medium doses of prednisone).

Conclusion: Three out of 4 AxSpA patients with severe disease phenotype and history of TNFi use prior to pregnancy experienced a disease flare after TNFi discontinuation at conception. Conversely, AxSpA patients with mild disease phenotype had a similar rate of flare during pregnancy but less severe and without the need for chronic treatment during pregnancy. When resumed during pregnancy TNFi was able to control disease activity and to favor a good gestational outcome. In preconception counselling the continuation of TNFi during pregnancy should be discussed with the patients.

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Table 1: clinical features, medication and disease activity in pregnancies with flare vs pregnancies without flares

	FLARE YES (12)	FLARE NO (4)
CLINICAL FEATURES		
Mean age at conception, years (SD)	33 (5.12)	32.7 (6.7)
Mean Disease duration, months (SD)	74.8 (52)	93 (122.1)
Peripheral arthritis, n (%)	4 (33)	2 (50)
Enthesitis, n (%)	3 (25)	2 (50)
Dactilitis, n (%)	1 (8)	0 (0)
Psoriasis, n (%)	3 (25)	1 (25)
IBD, (%)	2 (17)	1 (25)
Uveitisi, n(%)	1 (8)	0 (0)
MEDICATION		
History of TNFi, n (%)	8 (67)	3 (75)
History of TNFi >1, n (%)	2 (17)	2 (50)
TNFi at preconception visit, n (%)	6 (50)	2 (50)
TNFi stopped at pregnancy test+, n (%)	3 (25)	1 (25)
cDMARDs history, n (%)	9 (75)	3 (75)
cDMARDs >1, n (%)	2 (17)	1 (25)
DISEASE ACTIVITY		
ASDAS-CRP >2.1 at preconception visit, n (%)	2 (17)	1 (25)
Elevated CRP at preconception visit, n (%)	0 (0)	1 (25)
ASDAS-CRP >2.1 during 1st trimester, n (%)	4 (33)	0 (0)
Elevated CRP during 1st trimester, n (%)	3 (25)	1 (4)

Table 2: flare, medications at preconception visits and medications initiated during pregnancy in pregnancies of patients with history of TNFi use or not.

	TNFi users	TNFi naive
FLARE AND ASDAS-CRP		
Flare during pregnancy *	8/11 (73%)	4/5 (80%)
Flare in post partum period	5/12 (42%)	1/6 (17%)
ASDAS-CRP 1st TRIMESTER (mean)	2.04 (SD 1.23)	0.82 (SD 0.39)
ASDAS-CRP 2ndTRIMESTER (mean)	2.54 (SD 1.31)	1.55 (SD 0.82)
ASDAS-CRP 3rdTRIMESTER (mean)	1.56 (SD 0.64)	1.02 (SD 0.99)
ASDAS-CRP post partum (mean)	2.46 (SD 0.73)	1.53 (SD 1.34)
MEDICATION AT PRECONCEPTIONAL VISIT		
TNFi	6/12 (55%)	0/6 (0)
Prednisone	2/12 (18%)	1/6 (17%)
cDMARDs	0/12 (0)	2/6 (33%)
MEDICATION RESUMED DURING PREGNANCY *		
TNFi	5/11 (46%)	0/5 (0)
Prednisone	5/11 (46%)	1/5 (20%)
cDMARDs	1/11 (9%)	1/5 (20%)

*two pregnancies ended in miscarriage were not considered

FRI0388

SECUKINUMAB IMPROVES HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS, IRRESPECTIVE OF TIME SINCE FIRST DIAGNOSIS: POOLED RESULTS FROM THE SECUKINUMAB PHASE 3 TRIAL PROGRAM

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Background: Ankylosing spondylitis (AS) is a chronic rheumatic condition that has a negative impact on health-related quality of life (HRQoL). Secukinumab (SEC), a fully human anti-IL-17A monoclonal antibody, has been shown to effectively control AS symptoms and improve HRQoL.

Objectives: To evaluate the impact of SEC on HRQoL, assessed by the Short Form-36 Health Survey (SF-36), in pts with active AS stratified by time since first diagnosis (<2 or ≥2 yrs).

Methods: Pts were randomized to placebo (PBO) or SEC in MEASURE 1 (10 mg/kg intravenously followed by 150 or 75 mg SC), MEASURE 2 (150 or 75 mg SC) and MEASURE 4 (150 mg SC with/without SC loading). At Wk 16 or Wk 24, depending on ASAS 20 response, pts on PBO were re-randomized to SEC. Mixed-models for repeated measures were used to evaluate changes in SF-36 from baseline (BL) to Wk 16; observed data are presented at Wk 52. The proportion of pts reporting improvements meeting/exceeding the minimal clinically important differences (MCID) for SF-36 physical (PCS responders) and mental component summary (MCS responders), and individual SF-36 domains was also

assessed. Missing data were recorded as non-response and Fisher's exact test was used to compare the proportion of responders between groups at Wk 16. Only pooled data for pts receiving the licensed dose of SEC (150 mg) are shown.

Results: Overall 739 patients were included, with 427 and 312 in the SEC 150 mg and PBO groups, respectively. Of those, 37% and 36% of the SEC and PBO groups, respectively, were classified as <2 yrs since first AS diagnosis (Overall: 37%). The mean time since AS diagnosis was similar for the PBO and SEC treatment groups in both the <2 yrs (approx. 0.80 yrs) and the ≥2 yrs subgroups (approx.11 yrs). The least squares mean (LSM) changes in PCS from BL to Wk 16 were increased with SEC 150 mg compared with PBO, in both <2 yrs (PBO: 2.11; 150 mg: 6.44, p<0.0001) and ≥2 yrs since diagnosis (PBO: 3.03; 150 mg: 5.82, p<0.0001) groups. Significant increases were also reported in LSM changes in MCS scores from BL to Wk 16 with SEC 150 mg in patients <2 yrs since diagnosis (PBO: 2.10; 150 mg: 5.53, p<0.01), but not in the ≥2 yrs group. Analysis of individual SF-36 domain scores showed improvements with SEC vs PBO in the overall population and in both time since diagnosis subgroups, except Role-Emotional and Mental Health in the ≥2 yrs group (Figure). At Wk 16, the proportions of PCS responders were significantly higher with SEC 150 mg vs PBO, regardless of time since diagnosis (<2 yrs: PBO = 50.0%, SEC = 73.6%, p<0.01; ≥2 yrs: PBO = 45.0%, SEC = 69.8%, p<0.0001). MCS responses were not significantly different with SEC vs PBO in either subgroup. Overall, improvements in SF-36 scores and clinically meaningful MCID responses with SEC were more prominent in the <2 yrs since diagnosis compared with the ≥2 yrs group. Improvements in PCS, MCS, individual SF-36 domains and overall MCID responses were sustained to Wk 52 with SEC 150 mg.

Conclusion: Treatment with SEC 150 mg resulted in significant, clinically meaningful, and sustained improvements in HRQoL. Although reported irrespective of time since AS diagnosis, improvements were more prominent in earlier diagnosed pts.

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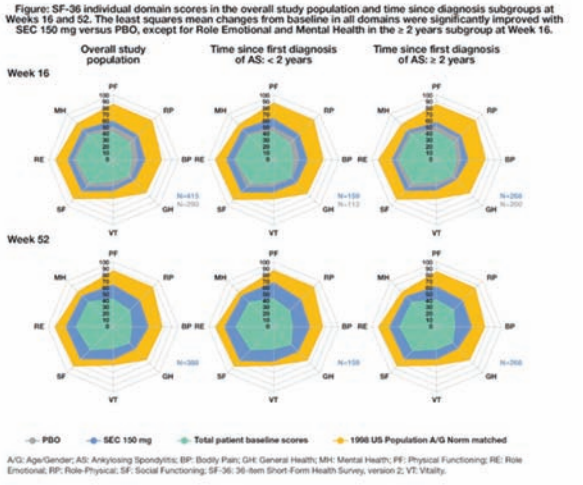


Figure: SF-36 individual domain scores in the overall study population and time since diagnosis subgroups at Weeks 16 and 52. The least squares mean changes from baseline in all domains were significantly improved with SEC 150 mg versus PBO, except for Role Emotional and Mental Health in the ≥ 2 years subgroup at Week 16.

A/G: Age/Gender; AS: Ankylosing Spondylitis; BP: Bodily Pain; GH: General Health; MH: Mental Health; PF: Physical Functioning; RE: Role Emotional; RP: Role-Physical; SF: Social Functioning; SF-36: 36-Item Short-Form Health Survey, version 2; VT: Vitality.

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FRI0389

EFFECTIVENESS OF BIOLOGIC THERAPY ON DISEASE ACTIVITY IN ANKYLOSING SPONDYLITIS: A BIOBADASER III OBSERVATIONAL STUDY

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Background: The advent of biologic therapy (BT) in ankylosing spondylitis (AS) has substantially benefited patients with inadequate response to conventional therapy. However, it is known patients with inadequeate response to a 1st BT have worse response to 2nd and further lines.

Objectives: To analyze the effectiveness of BT in biologic-naïve and biologic-experienced real-world AS patients, measuring response through change in activity indexes (ASDAS-CRP and BASDAI) and percentage of low activity and inactive disease at 12 months.

Methods: Data were obtained from BIOBADASER III, an ongoing observational longitudinal multicenter cohort of patients with rheumatic diseases treated with BT or targeted synthetic DMARDs. Patients were divided into 2 groups, according to their state before entering the study: BT-naïve (BTn) receiving their 1st BT, and BT-experienced (BTe) receiving their 2nd or further BT; regardless of the specific drug they received. Disease activity indexes (DAI) were collected at baseline and after 12 months of BT; mean and SD was calculated for each group and interpreted according to ASDAS disease activity states and, since not established, analogous categories previously used for BASDAI (<2 inactive, ≥2 <4 low, ≥4 <6 high, ≥6 very high)[1]. Clinical response was assessed by ASDAS improvement cut-offs (≥1.1 clinically important improvement (CII), ≥2 major improvement (MI)) and BASDAI CII (≥1.1)[2], BASDAI change (Δ) ≥2 or BASDAI50.

Results: 846 patients, (29.3% women, mean age 47.6 years) were included, 422 BTn and 424 BTe. Mean DAI results (table 1): at baseline, AS had high disease activity by BASDAI (>4) and ASDAS (>2.1 to <3.5). At 12 months, disease activity was low on both groups (BASDAI<4, ASDAS >1.3 to <2.1), reaching BASDAI CII; ΔBASDAI≥2 was only achieved in BTn. No group reached BASDAI50. ASDAS CII was reached in all groups, but MI was not seen. Percentage of patients achieving low disease activity and inactive disease are summarized at table 2, being overall higher for the BTn compared to the BTe group.

Table 1. Mean disease activity indexes evolution

Activity index	*Biologic-naïve (BTn)*			*Biologic-experienced (BTe)*		
	Baseline (SD)	12 months (SD)	Δ	Baseline (SD)	12 months (SD)	Δ
BASDAI	5.5 (2.0) *n=422*	3.2 (1.0) *n=287*	2.3	5.6 (2.3) *n=424*	3.9 (2.3) *n=244*	1.7
ASDAS-PCR	3.2 (1.4) *n=120*	1.7 (1.0) *n=64*	1.5	3.4 (1.5) *n=95*	2.0 (0.9) *n=50*	1.4

Table 2. Percentage of low disease activity and inactive disease by BASDAI and ASDAS

Disease activity states	n,% achieved at 12 months on BTn	n,% achieved at 12 months on BTe
BASDAI low activity	120, 41.8%	72, 29.5%
BASDAI inactive disease	73, 25.4%	58, 23.8%
ASDAS low activity	21, 32.8%	11, 22%
ASDAS inactive disease	23, 35.9%	15, 30%

Conclusion: The mean disease activity on patients starting biologic therapy is high. A clinically important improvement is met after 12 months of therapy, irrespectively of the index used or the prior use of biologics. The delta in DAI is bigger in the biologic-naïve group who receive the 1st BT. The biologic-naïve group also reaches a higher percentage of low disease activity and inactive disease. Further analysis is needed to see if these tendencies remain after separating the groups per type of biologic drug.

REFERENCES:

[1] Ramiro S, et al. Ann Rheum Dis 2014;73:1455-61.

[2] Kviatkovsky MJ, et al. J Rheumatol 2016;43:1680-6.

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FRI0390 DRUG THERAPY OF ANKYLOSING SPONDYLITIS (AS) DURING PREGNANCY IN REAL CLINICAL PRACTICE

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Background: The emergence of new drugs for the treatment of AS and improvement of life quality of patients led to an increase in the number of pregnancies and births in women with AS. However, the prescription of medication during pregnancy is still a difficult decision for both doctors and patients, and the unreasonable abolition of therapy can lead to increased activity of the AS.

Objectives: was described the frequency of use of various groups of drugs before and during pregnancy, determine the relationship between the abolition or change in the mode of taking nonsteroidal anti-inflammatory drugs (NSAIDs) and the dynamics of back pain.

Methods: the survey involved 86 women with AS, having pregnancies that ended in childbirth, not earlier than 2016. The average age is 34.0 ± 5.8 years and the average duration of the AS is 120 ± 73.5 months. The median term of delivery is 39 [38; 40] weeks, the weight of newborns is 3241.1 ± 484.6 g. During pregnancy, 58 (67.4%) women noted deterioration of health. Among them: increased back pain in the first trimester was 66.7%, in II – 84.6%, in III – 72.2%.

Results: Before pregnancy, NSAIDs were taken by more women (63.4%) as compared to taking in a month of conception (37.2%) and taking during gestation (in trimesters - 25.6%; 34.8%; 9.3%, respectively), p <0.05 in both cases. "On demand", NSAIDs were taken before pregnancy by 41.8% of women, at conception - 37.5%, in trimesters — 50%, 40% and 25%, respectively. There was a tendency for more frequent increase of back pain during pregnancy in women who abolished NSAIDs in the month of conception, or switched to "on demand" (65%), compared with taking NSAIDs daily (50%). Patients who took NSAIDs "on demand" in the first trimester (group 1), more often noted deterioration of health in the second trimester - 34.6%, compared with patients constantly taking NSAIDs (group 2) - 18.2%. In addition, patients in group 1, as well as women who didn't take NSAIDs in the first trimester, more often complained of back pain (54.6% and 53.1%) during gestation compared with patients in group 2 (36.4%). Group 1 patients in the second trimester noted increased back pain during pregnancy in 83.3%, whereas group 2 patients - in 58.3% (p<0.01).Glucocorticoids were taken more often during pregnancy (16.3%; 20.9%; and 22.1% - in trimesters) than before (7%) and at conception (9.3%), p<0.01 in both cases. Sulfasalazine before pregnancy was taken by 16% of women, at conception - 8%, during pregnancy - 3.5% (p<0.01 in both cases). Before pregnancy, only 12.8% of women received biological therapy; at the time of conception (adalimumab, etanercept) – 6.9%, in I and II trimesters – by 2.3% (p<0.01).

Conclusion: During pregnancy and the month of conception, the number of women receiving NSAIDs, sulfasalazine, biological therapy, decreases compared to the period before pregnancy. Glucocorticoids in preparation for pregnancy and gestation are prescribed more often than before pregnancy. Withdrawal of NSAIDs or switch to mode "on demand" in the first trimester is associated with an increase in the frequency of back pain during pregnancy, but due to discrepant data on the safety of continuous use of NSAIDs in the first trimester, correction of therapy with the prescription of low-risk drugs is necessary.

Disclosure of Interests: None declared

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FRI0391 NETAKIMAB IMPROVES PATIENT-RELATED OUTCOMES IN PATIENTS WITH RADIOLOGICAL AXIAL SPONDYLOARTHRITIS: RESULTS FROM RANDOMISED PHASE 3 TRIAL (ASTERA)

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Background: chronic pain, stiffness, fatigue and limited spinal mobility significantly affect quality of life (QoL) in patients (pts) with axial spondyloarthritis (axSpA). There is increasing evidence that IL-17 blockade is highly effective in this pts' population and show benefits in terms of multiple patient-reported outcomes (PROs) in both non-radiological (nr) and radiological (r) axSpA.

Objectives: To evaluate early effects of netakimab (NTK) on PROs in pts with active r-axSpA, based on data of 16-week observation from ongoing phase 3 ASTERA study (NCT03447704).

Methods: ASTERA is a phase 3 international double-blind placebo(PBO)-controlled clinical study. After completion of screening 228 eligible adult pts with r-axSpA (mNew York criteria, 1984), which remained active (BASDAI $\geq$ 4.0) despite the standard non-steroidal anti-inflammatory drugs (NSAIDs), were randomly assigned (1:1) to receive 120 mg NTK or placebo (PBO) at Week (Wk) 0, 1, 2 and then q2wk through Wk 16. After Wk 16 all patients will continue/be switched to receive NTK up to week 52. PROs were total back pain (10-item numerical range scale), BASDAI, BASFI. Work productivity and QoL were also assessed by Work Productivity and Activity Impairment (WPAI) and 36-item Short Form Health Survey (SF-36), respectively.

Results: Baseline characteristics were similar between treatment arms. The mean age at baseline was 39.14±9.99 years, 75.88% of patients were male and the mean symptoms duration was 4.3±4.48 years. All patients had active (mean BASDAI: 6.21±1.55) r-axSpA, 76.8% of patients were naïve to any biological treatment. Mean total back pain score at baseline was 6.7±1.6 in NTK group and 6.8±1.5 in PBO arm. At Wk1 the difference in total back pain score between study arms became statistically significant (Figure 1). At Wk 16 use of NTK was associated with statistically significant improvements from baseline in BASDAI (-2.8 vs 0.2, p<0.0001), BASFI (-0.9 vs 0.9, p<0.0001) and physical component of SF36 (6.3 vs. -2.6, p<0.0001) (Figure 2). WPAI response in NTK arm was significantly better at Wk 16, as compared with PBO (Table 1).

Conclusion: NTK in treatment of patients with r-axSpA showed rapid improvement in PRO, WP and QoL and was accompanied with improvement in physical function and disease activity.

Table 1. Change in WPAI at week 16 (medians; upper and lower quartiles)

Parameter	NTK (n=114)		PBO (n=114)	
	Baseline	Change from baseline to Wk16	Baseline	Change from baseline to Wk16
% work time missed due to health	0 [0; 18.4]	0 [-11,1; 0]	0 [0; 15.8]	0 [0; 29.9]
% impairment while working due to health	50 [30; 70]	-80 [-40; 0]	50 [40; 70]	10 [-10; 20]
% overall work impairment due to health	55.1 [40; 84]	-15.6 [-40; 0]	60 [50; 75]	1.2 [-10.3; 20]
% activity impairment due to health	60 [40; 80]	-20 [-40; - 10]	60 [50; 70]	0 [-10; 20]

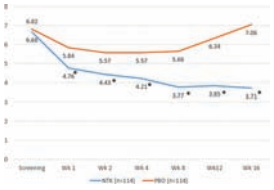


Figure 1. Total back pain score within 16 weeks of ASTERA study (means) (* P<0.05 for the comparison with placebo).

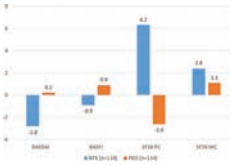


Figure 2. Change in BASDAI, BASFI and QoL at Wk 16 (means)

Disclosure of Interests: Inna Gaydukova Grant/research support from: JSC BIOCAD, Speakers bureau: paiment from Pfizer, Novartis, Abbvie, Biocad, Selgene, MSD, Sanofy does not exceed 10 000 euros, V Mazurov Grant/research support from: JSC BIOCAD, Shandor Erdes Grant/research support from: JSC BIOCAD, Speakers bureau: JSC BIOCAD, Tatiana Dubinina: None declared, Olga Nesmeyanova Grant/research support from: JSC BIOCAD, Elena Ilivanova Grant/research support from: JSC BIOCAD, Alena Kundzer: None declared, Nikolaj Soroka: None declared, Ekaterina Dokukina Employee of: JSC BIOCAD, Anna Eremeeva Grant/research support from: JSC BIOCAD, Ekaterina Chernyaeva Employee of: JSC BIOCAD, Roman Ivanov Employee of: JSC BIOCAD

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FRI0392 **EVIDENCE BASED RECOMMENDATIONS FOR THE MANAGEMENT OF ENTEROPATHIC ARTHRITIS: A RHEUMATOLOGY, GASTROENTEROLOGY COLLABORATIVE INITIATIVE**

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Background: Management of enteropathic arthritis may be challenging due to differences in treatment response of inflammatory bowel diseases and arthritis to different therapeutic modalities, which may even cause worsening of some manifestations while improving others. Enteropathic arthritis was not addressed in the management recommendations for spondyloarthritis.

Objectives: The aim of this project was to develop a set of evidence based recommendations for the management of patients with enteropathic arthritis.

Methods: A task force was formed that included ten rheumatologists and 8 gastroenterologists. Research questions were determined using a Delphi approach. A systematic literature search, data extraction, and statistical analyses were performed according to a pre-specified protocol. Studies that assessed the efficacy of an intervention on inflammatory bowel disease related outcomes and/or spondyloarthritis relates outcomes in patients with enteropathic arthritis were included. Risk ratios were calculated for binary outcomes and mean difference for continuous outcomes, whenever possible. Results of the systematic literature review were presented to the experts and recommendations were formulated after thorough discussions and voting.

Results: A total of 4 overarching principles and 10 recommendations were formulated. The recommendations addressed the use of NSAIDs, corticosteroids, sulfasalazine and 5-ASA derivatives, TNF inhibitors, tofacitinib, secukinumab, ustekinumab and vedolizumab among patients with active inflammatory bowel disease, active arthritis, active disease regarding both inflammatory bowel disease and arthritis, and among patients in remission. Final voting showed good agreement among the group on all recommendations.

Conclusion: These recommendations are intended to help rheumatologists, gastroenterologists and other clinicians dealing with enteropathic arthritis and to point out to the shortcomings of the available data on the management of this challenging condition.

Disclosure of Interests: Gulen Hatemi Consultant for: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Servet Akar Grant/research support from: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Speakers bureau: Pfizer, Hale Akpinar: None declared, Pamir Atagündüz: None declared, Goksel Bengi: None declared, Gerçek Can: None declared, Aykut Ferhat Celik: None declared, Sinem Nihal Esatoglu: None declared, Önay Gerçik: None declared, Hulya Hamzaoglu: None declared, Murat Inanc: None declared, Gokhan Kabacam: None declared, Ismail Hakkı Kalkan: None declared, Levent Kılıç: None declared, Fatos Onen: None declared, Ahmet Tezel: None declared, Murat Toruner: None declared, Sedat Kiraz: None declared

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FRI0393 **PATIENTS' SATISFACTION AND PREFERENCES TOWARDS SUPERVISED GROUP EXERCISE FOR PEOPLE WITH AXIAL SPONDYLOARTHRITIS**

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Background: Supervised group exercise (SGE) is proven effective in patients with axial spondyloarthritis (axSpA), but its contents and dosage do not always comply with current scientific insights.[1]

In particular vigorous intensity cardiorespiratory exercise is considered to be an important element of exercise programs in axSpA.[2] For successful implementation of any adjustments, axSpA patients' satisfaction and preferences towards SGE needs to be determined.

Objectives: This study aimed to describe axSpA patients' satisfaction with current SGE and perspective on potential, evidence-based SGE enhancements.

Methods: AxSpA patients participating in SGE in four regions in the Netherlands (n=118) completed a survey on their satisfaction with features of current SGE (eight questions, 3-point Likert scale, and one overall grade, 11-point scale) and their perspective on introducing appropriately dosed cardiorespiratory and strengthening exercise, monitoring exercise intensity, periodic (re)assessments, patient education and supervision by physical therapists with specific expertise (four dichotomous questions and one 5-point Likert scale). In addition, sociodemographic and disease characteristics were recorded.

Results: The patients' mean age was 60 years (SD ±12), 64% was male and they participated in SGE for 25 years (SD ±14) on average. The SGE programs in the four regions all took place once weekly between 90 to 135 minutes and all consisted of mobility exercises, sports activities and hydrotherapy. Two regions also focused on strengthening and only one specifically addressed cardiorespiratory exercise.

Most patients were satisfied with the current total intensity (n=84/112, 75%), duration (n=93/111, 84%) and load (n=89/117, 76%) of the program and the proportion of mobility (n=102/114, 90%), strengthening (n=90/115, 78%) and cardiorespiratory exercise (n=82/114, 72%). The median overall grade of the program was a 7 (IQR=7-8). Most patients agreed with the implementation of more frequent (home) exercise (n=73/117, 62%), heartrate monitoring (n=97/117, 83%) and periodic (re)assessments (n=97/118, 82%), whereas 50% agreed with the addition of structured patient education (n=37/74). The majority found supervision by therapists specialized in axSpA highly important (n=105/118, 89%).

Conclusion: The majority of axSpA-specific SGE participants was satisfied with current SGE, but also agreed with enhancements in line with scientific evidence. The high satisfaction levels with the amount of cardiorespiratory exercise, despite only being targeted in one SGE region, suggests a knowledge gap regarding its (health) benefits. Current satisfaction levels indicate that a planned implementation strategy, including education and addressing potential barriers and facilitators for the uptake of enhancements, is warranted.

REFERENCES:
[1] Dagfinrud, et al. Arthritis Care Res. 2011;63(4):597-603.
[2] Niedermann, et al. Arthritis Care Res. 2018. Doi: :10.1002/acr.23705

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FRI0394 MAINTAINED CLINICAL REMISSION IN ANKYLOSING SPONDYLITIS PATIENTS SWITCHED FROM REFERENCE INFLIXIMABTO ITS BIOSIMILAR. AN 18-MONTH COMPARATIVE OPEN-LABEL STUDY

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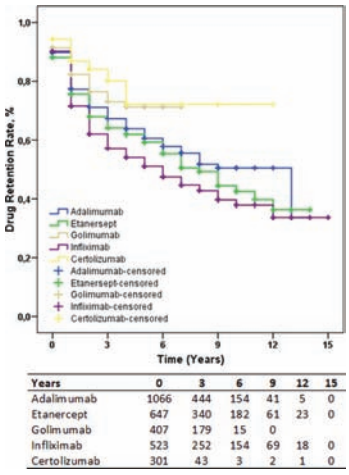
Background: switching from reference infliximab (RI) to biosimilar infliximab (BI) had no detrimental effects on efficacy and safety compared to continuous RI. However, long-term follow-up data is missing.
Objectives: the aim of this study was to evaluate if BI is equivalent to RI to maintain patients with Ankylosing Spondylitis (AS) in clinical remission, in a long-term fashion.
Methods: one hundred and nine consecutive unselected AS patients were investigated. All, followed-up at predefined times receiving RI (5mg/kg/8 weeks) and were naïve to other biologics. Patients who were in clinical remission were asked to switch from RI to BI using the same therapeutic dose. Patients switched to BI were compared with a match control group receiving continuous RI. During follow-up the demographic, clinical, laboratory parameters and comorbidities were all recorded for at least 18 months. Disease activity was measured using the Bath Ankylosing Spondylitis activity index (BASDAI), and the Ankylosing Spondylitis disease activity score (ASDAS), using the C-reactive protein. Remission was defined if patients achieved BASDAI <4 and ASDAS <1.3.
Results: twenty-one patients were excluded, nine because had no clinical remission and twelve because refused to switch. Thus, 88 were evaluated. From those, 45 switched to BI, while 43 continued receiving RI. There were no differences between groups regarding demographic, clinical and laboratory parameters. All patients were in clinical remission (BASDAI <4 and ASDAS <1.3). During follow-up, five patients from the switched group and three from the maintenance group discontinued the study. Four patients receiving BI presented nocebo effects and were switched back to the RI. Three responded well, while the fourth did not. After 18 months of treatment, all patients in both groups remained in clinical remission. No significant adverse events were noted between groups.
Conclusion: BI is equivalent to RI in maintaining AS in clinical remission for at least 18 months.
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Disclosure of Interests: None declared
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FRI0395 SWITCHING RATE OF ANTI-TNF AGENTS IN SPONDYLOARTHRITIS PATIENTS: TREASURE – REAL LIFE DATA

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Background: In spondyloarthritis (SpA), biologic DMARDs are important treatment options in resistant patients. Inefficacy or side effects may cause switching between these drugs.
Objectives: This study aimed to determine features of patients switching from one biologic agent to another in SpA treatment and to investigate associated reasons.
Methods: This multicenter, prospective observational cohort study used the TReasure database in which web-based registration of rheumatoid arthritis and SpA patients are being performed in 15 centers across different regions of Turkey. In this study, data of SpA patients switching from one biologic agent to another were analyzed. Demographic and clinical data, follow-up duration, time to switch, and reasons for switching were retrieved from the database. Kaplan-Meier analysis was performed to show drug retention rates and Cox regression analysis was performed to investigate the factors affecting switching.
Results: Of the included 3138 SpA patients, 1165 (37.1%) switched to another biologic agent (switched group) and 1973 (62.9%) continued to receive their current therapies (continued group). The median follow-up duration of all patients was 3.8 years and the median time to switch was 1.0 years (0-13.4 years). According to the distribution of comorbidities, the rates of patients having diabetes mellitus, hyperlipidemia, asthma, gastrointestinal bleeding, and cancer were significantly higher in the switched group than those of in the continued group (8.4% vs. 5.8%, p=0.006; 14.5% vs. 9.2%, p<0.001; 15.6% vs. 6.2%, p<0.001; 3.2% vs. 1.8%, p=0.018; and 1.0% vs. 0.3%, p=0.019; respectively). Features of the patients are presented in Table 1. Cox regression analysis revealed that female gender HR 1.47 (95% CI 1.24-1.75), p<0.001, disease duration HR 1.016 (95%CI 1.00-1.03), p=0.009, and BASDAI score HR 1.095 (95%CI 1.05-1.14), p<0.001 were the significant increasing factors for switching from one biologic agent to another.
In the switched group (n=1165), the main reasons for switching were secondary inefficacy (n=351), primary inefficacy (n=328), and side effects (n=267) followed by primary or secondary unknown inefficacy (n=57), physician's request (n=45), patient's demand (n=36), willing to be pregnant (n=9), other (n=37), and unknown (n=70).

	Adalimumab	Etanersept	Golimumab	Infliximab
Etanersept	0,329			
Golimumab	**0,016**	**0,004**		
Infliximab	**0,003**	0,069	**<0,001**	
Certolizumab	**0,002**	**<0,001**	0,197	**<0,001**



Years	0	3	6	9	12	15
Adalimumab	1066	444	154	41	5	0
Etanercept	647	340	182	61	23	0
Golimumab	407	179	15	0		
Infliximab	523	252	154	69	18	0
Certolizumab	301	43	3	2	1	0

Figure 1. Kaplan-Meier curve for drug retention rates in the switched group

Conclusion: In SpA patients, switching was frequent between anti-TNF agents and the median time to first switch was 1 year. Female gender, short disease duration, and lower BASDAI score were found to be the significant factors affecting switching from the anti-TNF agent used at first. The main reasons for this switching were primary (29.0%) and secondary (31.0%) inefficacy followed by side effects (23.6%). Switching between subcutaneous anti-TNF agents is generally less than switching from infliximab to another biologic agent.
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Roche, Pfizer, Abbvie, Consultant for: Novartis, Roche, Speakers bureau: MSD, Roche, Pfizer, Abbvie,Celltrion, Novartis, Pamir Atagündüz: None declared, Belkıs Nihan Coşkun: None declared, Burcu Yağız: None declared, Süleyman Serdar Koca: None declared, Muhammet Çınar: None declared, Aşkın Ateş: None declared, Servet Akar Grant/research support from: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Speakers bureau: Pfizer, Onay Gercik: None declared, Duygu Ersözlü: None declared, Veli Yazısız: None declared, Gezmiş Kimyon: None declared, Müge Aydın: None declared, Rıdvan Mercan: None declared, Burak Öz: None declared, Nazife Sule Yasar Bilge: None declared, Zeynel Abidin Akar: None declared, Omer Karadag: None declared, Ayse Bahar Kelesoglu Dincer: None declared, Sedat Yilmaz: None declared, Ufuk İlgen: None declared, Yavuz Pehlivan: None declared, Ender Terzioğlu: None declared, Levent Kılıç: None declared, Şükran Erten: None declared, Ali İhsan Ertenli: None declared

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FRI0396 CHARACTERIZATION OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN THE ANKYLOSING SPONDYLITIS COHORT PRIOR AND DURING ADALIMUMAB TREATMENT: DATA FROM A LARGE GERMAN NON-INTERVENTIONAL STUDY

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Background: Spondylarthritidies (SpA) are characterized by different disease manifestations such as arthritis, enthesitis, dactylitis and associated to concomitant diseases like Inflammatory bowel diseases (IBD) including ulcerative colitis (UC) and crohn's disease (CD). IBD might have a specific role to SpA due to common pathophysiological pathways. Characteristics of the rheumatic disease and response to treatment may differ within the phenotypic manifestation and with and without associated diseases. Adalimumab (ADA) is a monoclonal antibody inhibiting TNF alpha which has demonstrated efficacy in both, nraxSpA and ankylosing spondylitis (AS) as well as for UC and CD.

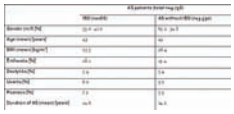
Objectives: To evaluate patient baseline characteristics prior to and treatment response on different disease manifestations in a cohort of AS patients with IBD compared to an AS without IBD during ADA treatment.

Methods: Data from a large German multicenter prospective observational non-interventional study (n=3.756) of patients with active AS who initiated ADA therapy during routine clinical care were analyzed with focus on specific patient groups: (1) patients with AS and IBD at baseline (n=166) and (2) patients with AS without IBD at baseline (n= 3.590). Patient characteristics and data of efficacy on different disease manifestations and prevalence of concomitant IBD over 24 months were analyzed.

Results: Of 3.756 patients in the main analysis set, 166 (4.4%) were identified to suffer from concomitant IBD at baseline. Baseline characteristics showed differences in gender distribution, proportion of patients with enthesitis, psoriasis and uveitis showing a higher proportion of each for the IBD group (Table). After 24 months of ADA treatment, both groups had similar decreases for BASDAI, BASMI, BASFI and dactylitis improvement. The IBD group had a fast decrease in BASDAI at M6 to its maximum improvement (delta of 1.9) which was kept stable until M24. For clearance of enthesitis, ADA had its largest therapeutic effect at M6 in the IBD group (clearance in 15.3% of the patients) while the AS without IBD group had the largest decrease of 10.2% at month 24. Resolving of uveitis with ADA therapy was more often seen in the IBD group compared to the AS without IBD (delta of 6% at M12 compared to delta of 2.6% at M12, respectively). The prevalence of IBD in AS in patients treated with ADA changed from 4.4% at baseline to 1.9% at M24.

Conclusion: Within the cohort of AS, patients' characteristics of manifestations are associated to different treatment responses: Patients identified to have IBD at baseline respond better for resolving of enthesitis and show a faster response in BASDAI compared to the group without IBD. Overall a significant reduction in the prevalence of clinically relevant IBD was seen earliest at month 3 after ADA initiation.

Table. Baseline characteristics of patients with IBD within the documented AS cohort treated with ADA



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FRI0397 EFFICACY AND SAFETY OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH CERTOLIZUMAB PEGOL: RESULTS FROM THE 48-WEEK RUN-IN PART OF C-OPTIMISE

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CA, United States of America

Background: C-OPTIMISE is the first trial to evaluate whether certolizumab pegol (CZP) can be reduced/discontinued in patients with radiographic(r)-axSpA/ankylosing spondylitis (AS) and non-radiographic(nr)-axSpA achieving sustained remission after 48 weeks' (wks') treatment.

Objectives: Here, we report interim efficacy and safety data for both subpopulations from the ongoing trial.

Methods: Up to Wk48**,** C-OPTIMISE (NCT02505542) was open-label (Part A), followed by 48-wk parallel-group, double-blind, placebo-controlled treatment (full dose and half dose) to Wk96 (Part B). Patients with adult-onset axSpA of <5 years' duration, fulfilling Assessment of SpondyloArthritis international Society (ASAS) classification criteria, were recruited. Part A: patients received CZP 400mg at Wks0/2/4, then 200mg every 2 weeks [Q2W]); patients achieving sustained remission (Ankylosing Spondylitis Disease Activity Score [ASDAS]<1.3 at Wk32 and <2.1 at Wk36 [or vice versa], and <1.3 at Wk48) were eligible for Part B (secondary outcome). Primary outcome (not reported): percentage of patients in Part B not experiencing a flare. Missing values were imputed using non-responder imputation (NRI) and last observation carried forward (LOCF).

Results: Part A: Of 736 patients (**Table A**), 43.9% achieved sustained remission (r-axSpA/AS: 42.8%; nr-axSpA: 45.3%; NRI). At baseline, 98.5% patients had high/very high disease activity (ASDAS≥2.1); at Wk48,

52.7% (r-axSpA/AS: 52.6%; nr-axSpA: 52.9%) had inactive disease (ASDAS<1.3; LOCF; **Table B**). The treatment-emergent adverse event (TEAE) rate/100 patient-years' exposure was 224.2; 3.9% patients discontinued CZP due to TEAEs. No new safety signal was identified.

Conclusion: The run-in phase of C-OPTIMISE shows that similar and substantial proportions of patients with r–axSpA/AS and nr-axSpA achieved sustained remission during 48 wks' CZP treatment. No new safety signal was identified.

Table: A) Baseline Characteristics

	axSpA (N=736) [a]	r-axSpA/AS (n=407) [b]	nr-axSpA (n=329) [b]
Age (years), mean (SD)	32.9 (7.0)	33.7 (6.8)	32.1 (7.1)
Male, n (%)	513 (69.7)	318 (78.1)	195 (59.3)
Symptom duration (years), mean (SD) [c]	2.2 (1.7)	2.5 (1.8)	1.8 (1.6)
HLA-B27 positive, n (%)	597 (81.1)	354 (87.0)	243 (73.9)
Sacroiliitis on imaging, n (%) [d]	691 (93.9)	401 (98.5)	290 (88.1)
Prior anti-TNF treatment, n (%)	31 (4.2)	20 (4.9)	11 (3.3)

B) Clinical Outcomes

	axSpA (N=736)		r-axSpA/AS (n=407)		nr-axSpA (n=329)	
%	BL	Wk48 (NRI)	BL	Wk48 (NRI)	BL	Wk48 (NRI)
ASAS20	–	79.6	–	79.9	–	79.3
ASAS40	–	72.0	–	71.3	–	72.9
ASAS-PR	–	57.3	–	55.8	–	59.3
BASDAI 50	–	71.7	–	71.3	–	72.3
Mean [e]	**BL**	**Wk48 (LOCF [e])**	**BL**	**Wk48 (LOCF [e])**	**BL**	**Wk48 (LOCF [e])**
ASDAS	3.7	1.6	3.8	1.6	3.6	1.5
HDA/VHDA,%	98.5	24.7†	98.5	25.8	98.5	23.2‡
ID, %	–	52.7†	–	52.6	–	52.9‡
CII, % [f]	–	76.5	–	78.6	–	73.9
MI, % [f]	–	56.3	–	58.7	–	53.2
BASDAI	6.7	2.1	6.7	2.1	6.7	2.2
BASFI	5.3	1.7	5.4	1.7	5.1	1.6
BASMI	3.1	2.3	3.5	2.6	2.7	1.9
Nocturnal back pain	6.9	1.8	7.0	1.8	6.8	1.8
Fatigue	7.1	2.6	7.1	2.5	7.1	2.6
CRP (mg/L), median [g]	7.8	2.0	10.7	2.0	4.5	2.0

[a] Patients with prior exposure to >1 anti-TNF excluded. [b] Central reading of patients' sacroiliac joint x-rays was used to stratify patients into r-axSpA/AS and nr-axSpA subpopulations. [c] Time since diagnosis of disease. [d] MRI or x-ray. [e] Unless stated otherwise. [f] NRI. [g] Values below the limit of quantification were set to half of the limit. †n=734. ‡n=327. AS: ankylosing spondylitis; ASAS20/40: ≥20%/≥40% improvement in Assessment of SpondyloArthritis international Society response criteria; ASAS PR: ASAS Partial Remission; ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASDAI 50: ≥50% improvement in BASDAI; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BL: baseline; CII: ASDAS Clinically Important Improvement (RFB ≥1.1); CRP: C-reactive protein; CZP: certolizumab pegol; HDA/VHDA: ASDAS High/Very High Disease Activity (ASDAS≥2.1); ID: ASDAS Inactive Disease (ASDAS <1.3); LOCF: last observation carried forward; MI: ASDAS Major Improvement (RFB ≥2.0); MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axSpA; NRI: non-responder imputation; r-axSpA: radiographic axSpA; RFB: reduction from baseline; Wk: week.

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FRI0398

IXEKIZUMAB IS EFFECTIVE IN THE TREATMENT OF RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS REGARDLESS OF THE LEVEL OF C-REACTIVE PROTEIN OR MAGNETIC RESONANCE IMAGING SCORES: 16-WEEK DATA FROM COAST-V AND COAST-W

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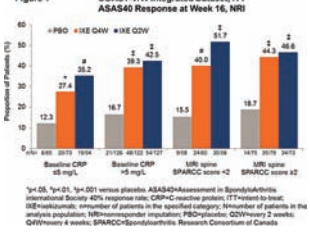
Background: Radiographic axial spondyloarthritis (r-axSpA) is a chronic inflammatory disease of the axial skeleton, and interleukin (IL)-17 plays an important role in the pathogenesis. Elevated C-reactive protein (CRP) levels in serum predict response to tumor necrosis factor inhibitors (TNFi)[1-4] but not to secukinumab.[5] The role of baseline spine magnetic resonance imaging (MRI) as a predictor of response has not been investigated for IL-17 inhibitors.

Objectives: To evaluate response rates at week (wk) 16 with ixekizumab (IXE), an IL-17A antagonist, in patients with ankylosing spondylitis (AS)/r-axSpA and elevated or normal/low inflammation as measured by CRP or spinal MRI.

Methods: Two Phase 3, randomized, double-blind, placebo (PBO)-controlled trials (COAST-V, NCT02696785; COAST-W, NCT02696798) enrolled patients who were biologic-naive or TNFi-experienced, respectively, with active disease (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] ≥4 and spinal pain ≥4 on a numeric rating scale) and an established diagnosis of r-axSpA and fulfilling Assessment of SpondyloArthritis international Society (ASAS) criteria (sacroiliitis on radiograph by modified New York [mNY] criteria and ≥1 spondyloarthritis feature). All patients fulfilling ASAS criteria also fulfilled mNY criteria for AS. Patients were treated with IXE (80 mg every 2 or 4 wks [Q2W, Q4W]) or PBO; adalimumab (40 mg Q2W) was an active reference arm in COAST-V. We examined ASAS 40% (ASAS40) response rates at wk 16 for the intent-to-treat population by CRP (≤5 or >5 mg/L) or MRI spine inflammation (Spondyloarthritis Research Consortium of Canada [SPARCC] spine score, <2 or ≥2). Baseline spine MRI was available in 96% of patients in COAST-V and 51% of patients in COAST-W; scoring was done by central readers. Higher scores reflect greater baseline disease activity. Sacroiliac joint MRIs were not assessed. Missing data for ASAS40 were imputed by nonresponder imputation.

Results: In the COAST-V/W integrated dataset that combined biologic-naive and TNFi-experienced populations, significantly more patients treated with IXE achieved ASAS40 response at wk 16 than with PBO in the elevated (>5 mg/L) baseline CRP group (39.3%, 42.5%, and 16.7% for IXE Q4W, IXE Q2W and PBO, respectively; p<.001 for IXE Q4W, IXE Q2W vs PBO) and in the normal (≤5 mg/L) baseline CRP group (27.4%, 35.2%, and 12.3% for IXE Q4W, IXE Q2W and PBO, respectively; p<.05 for IXE Q4W, p<.01 for IXE Q2W vs PBO, Fig 1), and the magnitude of response with IXE between elevated vs normal CRP groups was not statistically significant. Notably, a significantly higher proportion of patients achieved ASAS40 at wk 16 with IXE than with PBO, regardless of whether MRI spine SPARCC scores were <2 (40%, 51.7%, and 15.5% for IXE Q4W, IXE Q2W and PBO, respectively; p<.01 for IXE Q4W, p<.001 for IXE Q2W vs PBO) or ≥2 (44.3%, 46.6%, and 18.7% for IXE Q4W, IXE Q2W and PBO, respectively; p<.001 for IXE Q4W, IXE Q2W vs PBO, Fig 1).

Figure 1



Conclusion: IXE demonstrated rapid efficacy in the treatment of AS/r-axSpA at wk 16 irrespective of baseline serum CRP levels or spinal MRI score.

REFERENCES:

[1] Inman, et al. 2008
[2] Braun, et al. 2016
[3] de Vries, et al. 2009
[4] Vastesaeger, et al. 2011
[5] Braun, et al. 2018

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FRI0399 INFLIXIMAB TROUGH LEVELS AND DISEASE ACTIVITY PREDICT EARLY CLINICAL RESPONSE IN PATIENTS WITH AXIAL SPONDYLOARHTRITIS

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Background: Infliximab (Ifx) has proven to be effective in patients with axial spondyloarthritis (axSpA). Several variables may affect pharmacokinetic-pharmacodynamic of Ifx and its relation with clinical response, such as: disease activity (inflammatory burden), the development of anti-drug antibodies (ADA) and the concomitant use of conventional synthetic disease modifying anti-rheumatic drugs The improvement of patient's management by achieving optimal serum drug concentration associated with good clinical response is the main goal of therapeutic drug monitoring (which can be helpful in the prediction of clinical response to biological treatment.
Objectives: To identify clinical and serological variables at early stages of treatment that can predict clinical response in patients with axSpA treated with Ifx.
Methods: Observational study including 81 patients with axSpA recruited from the axSpA-Paz cohort treated with Ifx and monitored during 24 weeks (W). Serum Ifx levels and ADA were measured by capture ELISA and by bridging ELISA respectively at baseline, W2, W6, W14 and W24. Disease activity was assessed at baseline and W24 by the Ankylosing Spondylitis Disease Activity Score (ASDAS) and clinical response was defined by $\Delta ASDAS \geq 1.1$ (clinically important improvement). The association between clinical response at W24 and clinical and serological variables was evaluated by univariable and multivariable logistic regression analyses. Serum Ifx levels at W2, 6 and 14 as a categorical variable (above o under the corresponding median value of levels at each time week), age, sex, HLA-B27, methotrexate (MTX), sulfasalazine, body mass index, smoke status, prednisone, C-reactive protein and ASDAS at baseline were included as independent variables. Receiver operating characteristic (ROC) curves for the outcome of clinical response after 24 weeks of treatment were employed to determine the best cut-off values for the predictors (serum Ifx concentrations and baseline ASDAS). Ifx survival was evaluated through Kaplan-Meier curves.
Results: In the univariable analyses, higher serum Ifx trough levels at W14 (OR: 3.9; 95%CI: 1.5-10.4); higher baseline ASDAS (OR: 1.9; 95% CI: 1.1-3.1) and MTX use (OR: 3.3; 95%CI: 1.2-8.7) were associated with a better clinical response at W24. Patients with concomitant MTX had higher serum Ifx trough levels (median and IQR) than patients without MTX and these differences were significant at W6: 26.37(16-41.4) versus 16.9(11.4-26.9); p=0.008; at W14: 8.4(5.4-13.9) versus 4.1(1.8-7.8); p=0.003 and at W22: 5.1(2.2-8.3) versus 3.1(0.6-5.4); p=0.006 and; respectively). In the multivariable analysis, higher ASDAS at baseline (OR: 1.8; CI 95%: 1.1-3.0) and higher serum Ifx trough levels at W14 (OR: 3.6; CI 95%: 1.3-10.4) remained significantly associated. Serum Ifx concentration at W14 $\geq$ 6.7 μg/mL and a disease activity score at baseline $\geq$ 3.5 were found to be associated with higher ΔASDAS at W24 (OR: 16; 95%CI: 3.6-71.7). No patient with Ifx levels at W14 $\geq$ 6.7 μg/mL developed ADA during the 24 weeks follow up. The combination of both variables was used to predict clinical response with a sensitivity of 87.5%, specificity of 69.6%, PPV of 75% and NPV of 84.2%.
Conclusion: Elevated baseline ASDAS and high serum Ifx trough levels at W14 are associated with better clinical response at 24 weeks in patients with axSpA under Ifx therapy. A predictive model based on these variables is suggested to identify early responders to Ifx treatment.
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FRI0400 LONG-TERM SAFETY OF IXEKIZUMAB IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS/ ANKYLOSING SPONDYLITIS: AN INTEGRATED ANALYSIS OF COAST-V AND COAST-W

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Background: The efficacy and safety of ixekizumab (IXE) in patients with radiographic axial spondyloarthritis (r-axSpA) were investigated in the COAST trial program.
Objectives: To report the long-term safety of IXE in r-axSpA patients using integrated safety data from the COAST trials program.
Methods: Safety data for r-axSpA patients treated with IXE were integrated from COAST-V (biologic-naïve; NCT02696785) and COAST-W (Inadequate responders or intolerant to 1 or 2 TNF inhibitors; NCT02696798) studies. Patients fulfilled ASAS criteria for r-axSpA and mNY criteria for ankylosing spondylitis. Trial eligibility criteria were previously reported.[1,2] In these studies, participants were randomized to placebo (n=191), adalimumab (n=90, active reference arm, COAST-V only), or ixekizumab (n=376). Study participants initially randomized to IXE in both trials were treated with a starting dose (80-mg or 160-mg) and then 80-mg IXE every 2 weeks (IXEQ2W) or 4 weeks (IXEQ4W). Patients initially treated with placebo or adalimumab were re-randomized at Week 16 to receive either IXEQ2W or IXEQ4W following a 160-mg starting dose. The analysis population included all ixekizumab-exposed patients in both trials. Incidence rates (IR) per 100 person years with 95% confidence intervals (CI) and the number of patients are reported. Adverse Event (AE) codes were derived from MedDRA (v21.0). Integrated safety data presented here include all data collected between May 6. 2016 and Sept. 20, 2018.
Results: The integrated population consisted of 641 patients with 749.6 total patient-years of exposure to IXE. Mean follow up time was 427 days. Mean baseline age was 43.8±12.3 years. Mean and median baseline disease symptom duration (since onset) were 17.2±10.8 years and 15.5 years (Min: 1.1, Max: 56.2), respectively. Safety data are presented in Table 1. Among these patients, 489 (76.3%) reported $\geq$1 treatment

emergent AEs with an IR of 65.2. Serious AEs (≥1) were reported for 51 (8.0%) patients with an IR of 6.8. Discontinuations due to AEs were reported for 38 (5.9%) patients with an IR of 5.1. One death was reported, a suicide, in a patient with a documented prior history of depression and judged by the blinded principal investigator to be unrelated to the investigational product. The overall infection IR was 39.4, with both serious and opportunistic infections reported with an IR of 1.7. Among opportunistic infections, no *Tuberculosis* infections or reactivations were reported and the *Candida* infection IR was 1.2. No infections were associated with grade 3 or 4 neutropenia. The confirmed major adverse cardiovascular events IR was 0.1. The malignancy IR was 0.4 with acute promyelocytic leukemia, bladder cancer, and ovarian cancer reported. The depression IR was 0.8. The adjudicated inflammatory bowel disease (IBD) IR was 1.5 with 4 of 11 patients having prior history of IBD. The Anterior uveitis (AU) IR was 3.9 with 24 of 29 patients having prior history of AU. The injection site reaction IR was 11.3.

Table 1. Integrated Safety Outcomes

	n (%)	IR (CI)
Treatment Emergent AEs	489 (76.3%)	65.2 (59.7, 71.3)
Serious AEs	51 (8.0%)	6.8 (5.2, 9.0)
Discontinuation due to AEs	38 (5.9%)	5.1 (3.7, 7.0)
Death	1 (0.2%)	0.1 (0.0, 0.9)
Infections[a]	295 (46.0%)	39.4 (35.1, 44.1)
Serious Infections	13 (2.0%)	1.7 (1.0, 3.0)
Opportunistic Infections	13 (2.0%)	1.7 (1.0, 3.0)
Candida	9 (1.4%)	1.2 (0.6, 2.3)
Tuberculosis	0	0
Confirmed MACE	1 (0.2%)	0.1 (0.0, 0.9)
Malignancies	3 (0.5%)	0.4 (0.1, 1.2)
Depression	6 (0.9%)	0.8 (0.4, 1.8)
Adjudicated IBD	11 (1.7%)	1.5 (0.8, 2.6)
Anterior Uveitis	29 (4.5%)	3.9 (2.7, 5.6)
Injection Site Reactions	85 (13.3%)	11.3 (9.2, 14.0)

[a]Infections reported with frequencies ≥2.5% included nasopharyngitis (12.2%), upper respiratory tract infection (10.9%), pharyngitis (4.2%), bronchitis (3.6%), urinary tract infection (2.7%), and gastroenteritis (2.5%).

MACE, major adverse cardiovascular events; IBD, inflammatory bowel disease; AE, adverse event; n, number of patients; IR, incidence rate; CI, 95% confidence interval

Conclusion: The reported safety profile for IXE in r-axSpA is consistent with the profile reported for other indications. During the extension period, the overall safety profile of ixekizumab remained consistent with that observed during the double-blind period of COAST-V and COAST-W.[1,2]

REFERENCES:

[1] [Van der Heijde et al Lancet 2018 2Deodhar et al Arthritis Rheumatol 2018]

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FRI0401 EFFECT OF LONG-TERM TREATMENT WITH SECUKINUMAB ON LIPID PROFILE IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS: POOLED 4 YEAR ANALYSIS

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Background: Systemic inflammation may adversely affect the lipid profile in AS and PsA patients (pts)[1]. Treatment with some TNF and JAK inhibitors have reported increased total cholesterol (TC) and triglycerides (TG) despite reduction in inflammation[2-3]. Secukinumab (SEC), a fully human monoclonal antibody that directly inhibits IL-17A, has demonstrated a sustained efficacy and consistent safety profile in pts with AS and PsA[4]

Objectives: To evaluate the long-term effect of SEC on key lipid parameters in AS and PsA pts from pooled phase 3 clinical trials, through 208 weeks (wks)

Methods: This *post hoc* analysis included pooled data from MEASURE 1-4 (SEC 150 mg) in AS (N = 892) and FUTURE 2-5 studies (SEC 150/300 mg) in PsA (N = 2049), from pts treated with SEC or placebo (PBO). Serum TC, TG, LDL- and HDL-cholesterol and TC/HDL-C levels were assessed at baseline (BL), Wks 16, 104 and 208 in overall population and in sub-groups by prior anti-TNF therapy, concomitant methotrexate (MTX) and BL statin usage. Shift of common terminology criteria for adverse events (CTCAE) grade from BL through Wk 208 were also analysed

Results: BL characteristics were comparable across SEC and PBO groups. Lipid levels were stable in SEC treated AS and PsA pts through Wk 208 (**Table**) with mean change (mmol/L) from BL in AS: TC = ±0.1, TG = 0.1-0.2, LDL-C = ±0.1, HDL-C = ±0.04 and TC/HDL-C = ±0.2 and PsA: TC = ±0.2, TG = 0.001-0.2, LDL-C = ±0.2, HDL-C = ±0.06 and TC/HDL-C = ±0.2. Stable lipid values were also seen across key subgroups by prior anti-TNF therapy, concomitant MTX and BL statin usage, which remained stable through Wk 208. No Change in CTCAE lipid grades was observed in >90% of SEC-treated pts through Wk 208

Conclusion: SEC did not adversely affect the lipid profile and TC/HDL-C ratio in pts with AS and PsA, over 4 years. The lipid profile remained stable with SEC treatment and was sustained irrespective of prior anti-TNF status, concomitant MTX and BL statin usage

REFERENCES:

[1] Papagoras C, et al. Joint Bone Spine 2014;81:57-63
[2] Wolk R, et al. J Clin Lipidol.. 2017;11:1243-56
[3] Agca R, et al. J Rheumatol. 2017; 44(9):1362-8
[4] Lubrano E and Perrotta FM. Ther Clin Risk Manag. 2016;12:1587-92

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Lipid levels in AS and PsA pts through Wk 208

Parameters (Normal level[5])	Wk	AS		PsA		
		SEC 150 mg (N=504)	PBO (N=388)	SEC 300 mg (N=461)	SEC 150 mg (N=907)	PBO (N=681)
TC (<5.2)*	BL	4.92 (502)	4.90 (387)	4.99 (459)	5.07 (905)	5.12 (675)
	16	5.03 (486)	4.87 (362)	5.08 (448)	5.14 (879)	5.03 (634)
	104	4.91 (390)		5.02 (199)	5.13 (350)	
	208	4.91 (135)		4.88 (74)	5.06 (72)	
TG fasting (<1.7)*	BL	1.29 (502)	1.31 (387)	1.48 (460)	1.53 (905)	1.59 (675)
	16	1.40 (486)	1.31 (362)	1.62 (448)	1.64 (879)	1.54 (634)
	104	1.42 (390)		1.61 (199)	1.60 (350)	
	208	1.44 (136)		1.66 (74)	1.67 (72)	
LDL-C (<2.6)*	BL	3.09 (502)	3.08 (387)	3.11 (460)	3.18 (905)	3.17 (675)
	16	3.12 (486)	3.02 (362)	3.16 (448)	3.20 (879)	3.11 (634)
	104	3.08 (390)		3.15 (199)	3.24 (350)	
	208	3.08 (135)		3.03 (74)	3.24 (72)	
HDL-C (>1.5)*	BL	1.44 (502)	1.43 (387)	1.43 (460)	1.44 (905)	1.47 (675)
	16	1.46 (486)	1.43 (362)	1.43 (448)	1.45 (879)	1.43 (634)
	104	1.47 (390)		1.40 (199)	1.49 (350)	
	208	1.41 (135)		1.42 (74)	1.38 (72)	
TC/HDL-C ratio	BL	3.67 (502)	3.68 (387)	3.72 (459)	3.79 (905)	3.75 (675)
	16	3.72 (486)	3.61 (362)	3.81 (448)	3.88 (879)	3.77 (634)
	104	3.58 (390)		3.82 (199)	3.76 (350)	
	208	3.72 (135)		3.69 (74)	3.94 (72)	

n, number of pts with data at both BL and at that time point; N, total number of pts
*mmol/L (n). [5]https://optimalhealthsolutions.ca/cholesterol-ratio/

FRI0402

SECUKINUMAB FOR AXIAL SPONDYLOARTHRITIS: DRUG SURVIVAL IN REAL-WORLD SETTING AND RESPONSE FACTORS

Carolina Merino Argumánez[1], Valentina Emperiale[2], María Martín[3], Marta Valero[4], Javier Bachiller-Corral[4], Beatriz Joven-Ibáñez[5], Ana Pérez Gómez[6], Jose Campos Esteban[1]. [1]*Hospital Puerta de Hierro, Majadahonda (Madrid), Spain*; [2]*Hospital Príncipe Asturias, Alcalá de Henares, Spain*; [3]*Hospital Doce de octubre, Madrid, Spain*; [4]*Hospital Ramón y Cajal, Madrid, Spain*; [5]*Hospital Doce de Octubre, Madrid, Spain*; [6]*Hospital Príncipe Asturias, Alcalá de Henares, Spain*

Background: IL-17 inhibition has been proved effective in patients with ankylosing spondylitis (AS) in clinical trials and it has been added to the most recent national and international treatment guidelines. However, real-world data of its use is still scarce.
Objectives: This study aims to analyze drug survival of secukinumab for axial spondyloarthritis (AxSpA) in a real world setting and identify response factors.
Methods: Multicentric observational, retrospective, longitudinal study conducted in 4 tertiary hospitals of the Madrid region. Patients over 18 y.o. with clinical diagnosis of AxSpa and having received at least one dose of secukinumab between January 2016 and October 2018 were included. Medical records were reviewed to collect demographic and clinical data related to AxSpA, its features and treatment. Statistical analysis was performed including bivariate analisys (considering withdrawal of drug during study period or not) and survival analysis with Kaplan-Meier and Cox regression. Reasons for discontinuating therapy are described. To detect inffluential variables, demographic characteristics, HLA-B27 positivity, radiographic features, previous biologic therapies, comorbidities and extra-articular involvement were analyzed.
Results: Out of 143 patients included, 89 (62%) mantained secukinumab therapy at the end of the observation period (Dec 31, 2018), with an average drug survival time of 17 ± 8,2 months. 54 patients (38%) withdrawn therapy, due to primary ineffectiveness (26), secundary ineffectiveness (14), adverse events (7) and other reasons (7). Median time to withdrawal was 6 months (0-21). No significative differences were found between groups, but a tendency to higher number of female patients (55% vs 41%, p 0,07), non radiographic AxSpA (35% vs 27%, p 0,053) and lower HLA-B27 positivity (50% vs 65%, p 0,052) was noted in the group withdrawing therapy. Previous exposure to biologic therapy did not differ (75% vs 71%, p 0,37). Number of bDMARDs before Secukinumab therapy was also similar in both groups; the proportion of patients with previous exposure to 2 or more bDMARDs were 17% vs 22% (p 0.373). Neither differences were found in all other variables studied (demographic, hip arthropathy, syndesmophytes, extra-articular involvement -uveitis, psoriasis, inflammatory bowel disease- nor in comorbidities (tobacco exposure, hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, malignancy)



Conclusion: This study assesing drug survival of secukinumab in real-world setting showed a trend to lower drug survival in comparison to clinical trial data. No differences were found in the treatment withdrawal group. Population in which secukinumab is prescribed in real-world setting differs from clinical trials, with higher previous exposure to bDMARDs and higher comorbidity.
Disclosure of Interests: Carolina Merino Argumánez: None declared, Valentina Emperiale: None declared, María Martín: None declared, Marta Valero: None declared, Javier Bachiller-Corral: None declared, Beatriz Joven-Ibáñez Speakers bureau: Celgene, Novartis, MSD, Pfizer, AbbVie, and Janssen, Ana Pérez Gómez: None declared, Jose Campos Esteban: None declared
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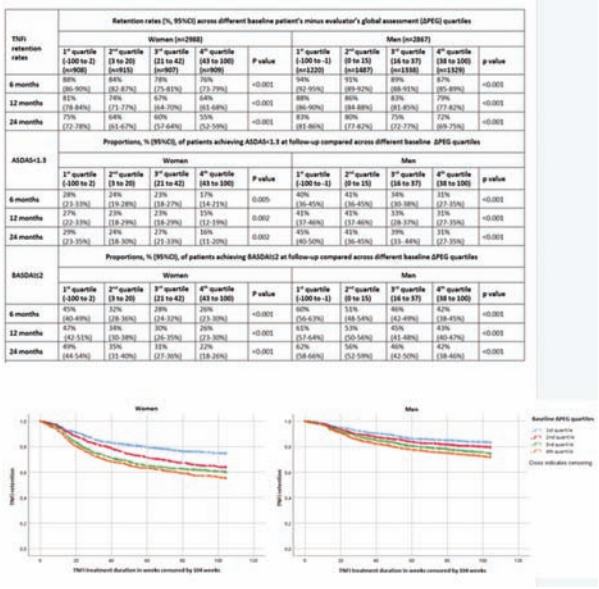
FRI0403

HIGH BASELINE PATIENT'S COMPARED WITH EVALUATOR'S GLOBAL ASSESSMENT IS ASSOCIATED WITH LOWER RETENTION AND REMISSION RATES OF FIRST TNF INHIBITOR IN AXSPA PATIENTS – DATA FROM THE EUROSPA COLLABORATION

Brigitte Michelsen, Lykke Ørnbjerg, Anne Gitte Loft, Joseph Sexton, Adrian Ciurea, Heřman Mann, Kari Eklund, Ayten Yazici, Maria Jose Santos, Johan Askling, Ziga Rotar, Björn Gudbjornsson, Manuel Pombo-Suarez, Catalin Codreanu, Irene van der Horst-Bruinsma, Eirik Kristianslund, Michael Nissen, Karel Pavelka, Nina Trokovic, Nevsun Inanc, Elsa Vieira-Sousa, Daniela DI Giuseppe, Matija Tomsic, Arni Jon Geirsson, Ruxandra Ionescu, Marleen van de Sande, Florenzo Iannone, Carlos Sánchez-Piedra, Gareth T. Jones, Lise Hyldstrup, Niels Steen Krogh, Merete L. Hetland, Mikkel Østergaard. *EuroSpA Research Collaboration, on behalf of DANBIO (Denmark), ARTIS (Sweden), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), biorx.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RRBR (Romania), ARC (Netherlands), BSRBR-AS (UK), GISEA (Italy), Denmark*

Background: Discordance between baseline patient's and evaluator's global assessment of disease activity is common.[1] However, the impact of such discordance on retention and remission rates of TNF inhibitor (TNFi) therapy in axial spondyloarthritis (axSpA) patients remains unexplored.
Objectives: To assess the impact of baseline discordance, defined as "patient's minus evaluator's global assessment of disease activity" (ΔPEG), on retention and remission rates of first TNFi in female and male axSpA patients across Europe.
Methods: AxSpA patients from 10 European registries participating in the European Spondyloarthritis Research Network Collaboration (EuroSpA) were included. Retention rates after 6/12/24 months' treatment with first TNFi were assessed with Kaplan-Meier analyses, with comparison between baseline ΔPEG quartiles with log rank test, stratified by gender. Proportions of patients in BASDAI remission (≤2) and ASDAS inactive disease (<1.3) after 6/12/24 months for different ΔPEG quartiles were compared with Chi-square test, stratified by gender.
Results: A total of 9013 axSpA patients were included. Mean(SD) age for women(n=3639)/men(n=5374) were 42.7(12.0)/41.7(12.0) years, disease duration 5.1(7.4)/6.9(8.7) years, median(25-75 percentiles) baseline ΔPEG

20(3-42)/15(0-37) mm. TNFi retention rates and proportions of patients achieving BASDAI≤2 and ASDAS<1.3 after 6/12/24 months were lower for higher quartiles of ΔPEG (table, figure).



Conclusion: In patients receiving their first TNFi, high baseline patient's compared with evaluator's global assessment is negatively associated with retention rates as well as proportions of patients achieving BASDAI remission and ASDAS inactive disease after 6, 12 as well as 24 months follow-up, both in female and male axSpA patients.

REFERENCES:

[1] Lindström, et al., J Rheumatol 2015;42:1781-5.

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FRI0404

POOLED 6-MONTH TREATMENT OUTCOMES AND DRUG RETENTION RATES IN 1556 PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH SECUKINUMAB IN ROUTINE CLINICAL PRACTICE IN 12 EUROPEAN COUNTRIES IN THE EUROSPA RESEARCH COLLABORATION

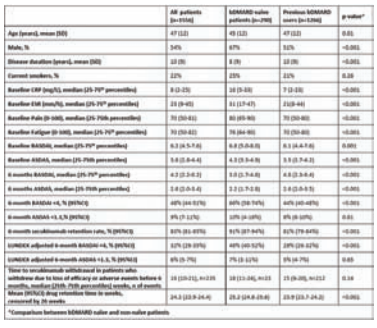
Brigitte Michelsen, Cecilie Heegaard Brahe, Johan Askling, Catalin Codreanu, Adrian Ciurea, Anne Gitte Loft, Heřman Mann, Manuel Pombo-Suarez, Fatos Onen, Joe Sexton, Ziga Rotar, Maria Jose Santos, Kari Eklund, Björn Gudbjornsson, Florenzo Iannone, Daniela DI Giuseppe, Ruxandra Ionescu, Michael Nissen, Karel Pavelka, Carlos Sánchez-Piedra, Servet Akar, Eirik Kristianslund, Matija Tomsic, Helena Santos, Nina Trokovic, Arni Jon Geirsson, Ennio Giulio Favalli, Irene van der Horst-Bruinsma, Gary Macfarlane, Lise Hyldstrup, Niels Steen Krogh, Mikkel Østergaard, Merete L. Hetland. *EuroSpA Research Collaboration, on behalf of DANBIO (Denmark), ARTIS (Sweden), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), biorx.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RRBR (Romania), ARC (Netherlands), BSRBR-AS (UK), GISEA (Italy), Denmark*

Background: There is a lack of real-life data on secukinumab exposure, treatment outcomes and retention rates in axial spondyloarthritis (axSpA) patients.

Objectives: Primary objective: To assess the proportion of axSpA patients in BASDAI low disease activity (<4) and ASDAS inactive disease (<1.3) after 6 months of secukinumab treatment across Europe. Secondary objectives: To compare baseline characteristics, crude and LUNDEX adjusted 6-month BASDAI <4 and ASDAS <1.3 rates, retention rates and median time to secukinumab withdrawal (due to loss of efficacy/adverse events) between biologic DMARD (bDMARD) naïve and non-naïve patients, as well as across the participating registries.

Methods: Data from axSpA patients treated with secukinumab in routine care from 12 countries in the European Spondyloarthritis Research Collaboration (EuroSpA) were pooled. Time from treatment initiation to data cut was >= 6 months. Group comparisons were performed with independent t-test, Mann-Whitney U-test, ANOVA, Kruskal-Wallis and Chi-square test, as appropriate. Kaplan-Meier analyses with log rank test were performed for comparison of secukinumab drug survival.

Results: A total of 1556 axSpA patients were included. Overall 6-month BASDAI<4 was achieved by 49% and ASDAS<1.3 by 9% of the patients. bDMARD naïve compared with non-naïve secukinumab starters had shorter disease duration, higher baseline disease activity, a higher proportion were men and a higher proportion achieved crude and LUNDEX adjusted 6-month BASDAI<4 but not ASDAS<1.3 (table).



Drug retention was higher for bDMARD naïve compared with non-naïve patients (figure 1a). Baseline characteristics and disease activity (data not shown) as well as drug retention differed in-between the European registries (figure 1b).

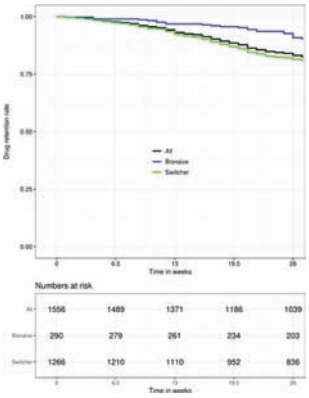


Figure 1a. Pooled 6-month secukinumab retention rates for axSpA patients in EuroSpA, as well as compared between the bDMARD naïve and non-naïve patients (log rank test; p<0.001).

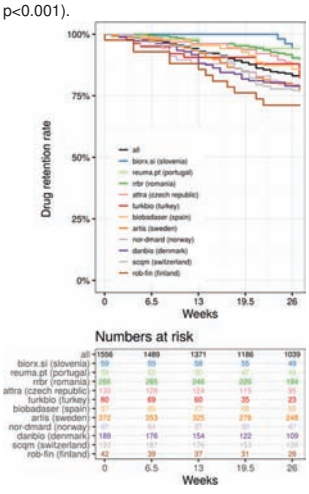


Figure 1b. Pooled 6-month secukinumab retention rate as well as compared across 11 registries in EuroSpA (log rank test; p<0.001). ICEBIO was excluded from the Kaplan-Meier plot (<10 patients).

Conclusion: This study of >1500 patients in 12 European countries provides real-world data on the effectiveness of secukinumab in patients with axSpA, adding evidence to existing RCTs. A majority of the patients was previous bDMARD users and had long disease duration. BASDAI <4 was achieved by 49% of the patients and ASDAS <1.3 by 9% at 6 months. Overall retention rate was 83% at 6 months, with significant differences across the registries and higher retention rates for bDMARD naïve compared with non-naïve axSpA patients.

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FRI0405

AQUILA STUDY IN GERMANY – REAL WORLD DATA ON SECUKINUMAB´S EFFECTIVENESS IN PSORIATIC ARTHRITIS PATIENTS – RESULTS FROM AN INTERIM ANALYSIS

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Background: Psoriatic arthritis (PsA) is a chronic, progressive, inflammatory disorder of skin and joints, it impacts both physical and emotional well-being, and increases the risk of comorbidities. Thus, improvement of disease activity as well as emotional well-being is of utmost importance in treatment of PsA patients (pts). In clinical trials, secukinumab, an anti-interleukin (IL)-17A monoclonal antibody, has shown to significantly improve signs and symptoms of PsA[1].

Objectives: To evaluate real-world interim data on the effectiveness of secukinumab on treatment outcomes and quality of life (QoL) in pts with active PsA.

Methods: AQUILA is an ongoing, 52-week (wk) non-interventional study enrolling 2000 pts with active PsA and ankylosing spondylitis. Here, we report interim results of effectiveness in a subgroup of PsA pts treated with secukinumab.

Validated questionnaires were used to measure effectiveness of secukinumab on:

- disease activity
  - Physician´s Global Assessment (PhGA, 0=no disease activity, 10=most intense disease activity),
  - Psoriasis Area and Severity Index (PASI),
  - American College of Rheumatology (ACR) joint count and
  - C–reactive protein (CRP);
- and QoL
  - Psoriatic Arthritis Impact of Disease 12–item score (PsAID–12),
  - Medical Outcomes Study (MOS) Sleep scale and
  - Beck´s Depression Inventory II (BDI–II).

Pts who were already under secukinumab treatment or just about initiating secukinumab therapy, based on medical therapeutic need, were included; in both scenarios, disease activity at start of secukinumab treatment was used as starting point for analysis. Treatment decision was made independently of participating in this study. Pts were observed from

BL up to wk 52 according to clinical routine. Real-world effectiveness of secukinumab was assessed prospectively and analyzed as observed.
Results: At BL, 641 PsA pts were included of whom 385 (60.1%) completed 52 wks so far (i.e. at the time of data cut-off for this interim analysis). 58.5% (n=375) of the pts were female and 41.5% (n=266) were male, mean age was 52.6 years. About 66% (n=424) were pre-treated with biologics. Mean PhGA improved from 5.3 at BL (n=571, 89.1%) to 2.5 at wk 52 (n=341, 53.2%). Mean absolute PASI improved from 8.1 at BL (n=211, 32.9%) to 1.2 at wk 52 (n=147, 22.9%). More than half of the documented pts (51 out of 94) achieved a 100% reduction (PASI 100) in skin symptoms at wk 52. The mean number of tender/swollen joints (ACR) was reduced from 7.6 (n=436, 68.0%)/3.9 (n=437, 68.2%) to 3.0 (n=241, 37.6%)/0.7 (n=242, 37.8%) at wk 52. The percentage of pts with CRP >5mg/L dropped from 43.0% at BL (n=230) to 36.6% at wk 52 (n=112). Mean PsAID-12 improved from 5.0 at BL (n=602, 93.9%) to 3.3 at wk 52 (n=343, 53.5%). The percentage of PsA pts with high disease activity (score $\geq$ 5) assessed by PsAID-12 dropped from 61.0% at BL (n=367) to 26.2% at wk 52 (n=90). MOS sleep scales did not change relevantly over time. With respect to pts with a BDI-II reduction of at least 3 score points, the mean value improved from 16.4 (mild depression) at BL to 8.0 (no depression) at wk 52 (n=123, 19.2%).
Conclusion: Secukinumab reduced disease activity and improved QoL already within this subgroup of PsA pts. Thus, real-world data from the AQUILA study show that, in clinical routine, secukinumab treatment up to one year provides a clear benefit for PsA pts in clinical and QoL parameters.

REFERENCES:
[1] Mease PJ, et al. N Engl J Med. 2015;373:1329–39

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FRI0406 AQUILA STUDY IN GERMANY – REAL WORLD DATA ON SECUKINUMAB´S EFFECTIVENESS IN ANKYLOSING SPONDYLITIS PATIENTS – RESULTS FROM AN INTERIM ANALYSIS

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Background: Ankylosing spondylitis (AS) is characterized by chronic inflammation of the spine and is at high risk to cause inflammation, pain, and stiffness extraspinal as well. Thus, important aims in therapy of AS are pain reduction and maintenance of physical functioning. Secukinumab, a fully human monoclonal antibody that selectively neutralizes interleukin (IL)-17A, has already shown significant efficacy in the treatment of AS in clinical trails[1].
Objectives: The aim of this interim analysis is to evaluate the effectiveness of secukinumab on disease activity, physical functioning and quality of life in AS patients (pts) in a real world setting.
Methods: AQUILA is an ongoing, multi-center, 52-week (wk) non-interventional study enrolling 2000 pts with active AS and psoriatic arthritis in Germany. Here, we report interim results of effectiveness in a subgroup of AS pts treated with secukinumab.
Validated questionnaires were used to measure the effectiveness of secukinumab on:

- disease activity
- o Physician´s Global Assessment (PhGA: 0=no disease activity, 10=most intense disease activity),
- o Bath Ankylosing Disease Activity Index (BASDAI),
- o C–reactive protein (CRP)
- physical functioning
- o global functioning: Assessment of Spondyloarthritis Health Index, (ASAS–HI),
- and key aspects of sleep
- o Medical outcomes Study Sleep Scale (MOS),
- severity of depression
- o Beck´s Depression Inventory Version II (BDI–II).

Pts who were already under secukinumab treatment or just about initiating secukinumab therapy, based on medical therapeutic need, were included; in both scenarios, disease activity at start of secukinumab treatment was used as starting point for analysis. Treatment decision was made independently of participating in this study. Pts were observed from BL up to wk 52 according to clinical routine. Real-world effectiveness of secukinumab was assessed prospectively and analyzed as observed.
Results: This interim analysis describes 311 AS pts who were included at BL and of whom 178 (57.2%) have completed wk 52 so far (i.e. at the time of data cut-off for this interim analysis). 63.3% (n=197) of the pts were male and 36.7% (n=114) female, mean age was 47 years. About 70% (n=221) of the pts were pre-treated with biologics. Physicians reported a mean PhGA value of 5.9 at BL (n=282, 90.7%) which improved to 2.6 at wk 52 (n=168, 54.0%). Mean BASDAI value was reduced from 5.6 at BL (n=301, 96.8%) to 4.0 at wk 52 (n=171, 55.0%). With regard to inflammation parameters, the percentage of pts with a CRP of >5mg/L decreased from 54.7% (n=140) to 40.0% (n=58) at wk 52. Further, mean ASAS-HI value decreased over time from 8.2 at BL (n=274, 88.1%) to 6.3 at wk 52 (n=156, 50.2%). MOS sleep scale did not change over time, yet only few BL documentations for these scales were available (range n=26 to 44). Regarding depressive mood of the pts, while at BL 40.7% (n=101) of the pts suffered from mild to severe depression (BDI-II score between 14 and 63), 30.3% (n=46) did so in wk 52. This is reflected by a drop of mean BDI-II value from 13.0 at BL (n=248, 79.7%) to 10.6 at wk 52 (n=152, 48.9%).
Conclusion: Within this limited subset of AS pts, secukinumab reduced disease activity and improved quality of life for up to one year as assessed by validated physicians' as well as pt-reported outcomes. Overall, this interim analysis gives promising insights into treatment effects of secukinumab on pts' physical and mental well-being under real-world conditions.

REFERENCES:
[1] Baeten D, et al. N Engl J Med. 2015;373:2534-4

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FRI0407 TWO-YEAR ULTRASOUND CONTROLLED STUDY OF HYALINE CARTILAGE AND SYNOVIAL LAYER STRUCTURE OF HIP JOINTS IN PATIENTS WITH ANKYLOSING SPONDYLITIS DURING TREATMENT WITH ADALIMUMAB

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Background: The impairment of hip joints has significant prognostic value on functional status of patients with Ankylosing spondylitis (AS) [1]. One of possible yearly marker of hip joints structure damage in patients with AS may be changing in volume of hyaline cartilage [2]. Objectives.
Objectives: To investigate changes in width of hyaline cartilage and synovial layer of hip joints in patients with coxitis, associated with AS under treatment with adalimumab (ADA) during 2 years.
Methods: The 28 patients with AS and clinical, ultrasound and radiographic signs of coxitis (21 male, 7 female, average age is 35.4 years old, duration of disease is 12-132 month) were included into study. All patients were being treated by NSAIDs at least 3 months before they started to take ADA (40 mg subcutaneously every 2 weeks). Treatment with ADA was continued during 24 months. Patients were observed at month 0, 12 and 24 months of treatment including measurements of pain visual analog scale (VAS) in hip movements, maximal distance between ankles, pelvic X-ray and sonography of hip joints by 10-18 MHz probe. BASRI-Hips index was applied for radiographic estimation of structural damage of hip joints [3]. During sonography width of hip joint capsule and hyaline cartilage were measured. The Mann-Whitney-U test was used for comparison of changes in clinical and sonographic data between two groups of patients.

Results: It was determined that pain VAS at hip movements was decreased (23.1 [12.3; 32.3] mm at month 12 and 19.7 [11.8; 32.9] mm at month 24 vs 73.7 [59.5; 82.6] mm at month 0, p<0.05) and maximal distance between ankles was increased (112.5 [94.7; 122.2] mm at month 12 and 116.2 [91.2; 125.0] mm at month 24 vs 78.7 [63.4; 98.5] mm at month 0, p<0.05) in observed patients under treatment with ADA. It was also found that ultrasound measured width of hip joint capsule was decreased from 11.8 [10.3; 12.7] mm at month 0 to 8.7 [8.1; 9.4] mm at month 12 (p<0.05) and 7.5 [6.6; 8.5] mm at month 24 (p<0.05). The ultrasound measured width of hyalinic cartilage in observed patients was increased from 0.8 [0.6; 1.1] mm at month 0 to 1.0 [0.8; 1.2] mm at month 12 (p>0.1) and 1.2 [1.0; 1.7] mm at month 24 (p<0.05) under treatment with ADA. The BASRI-Hips index had not changed in observed patients at the end of 24-months period. The differences in changes of hip cartilage width between patients with joint capsule width at month 24 less than 9 mm and more than 9 mm was determined (p<0.05): +0.6 [0.3; 0.8] mm vs +0,1 [-0.1; 0.2] mm.

Conclusion: Treatment with ADA leads to decrease of clinical and sonographic signs of coxitis in patients with AS and improves of hyaline cartilage structure. The increase of width of hip hyalinic cartilage was observed in patients with absence of ultrasound signs of hip joints synovial inflammation in patients with AS. MRI-controlled studies are needed to confirm ability of THFα inhibitors to restore cartilage volume in patients with coxitis, associated with AS.

REFERENCES:

[1] Baraliakos X., Braun J. Hip involvement in ankylosing spondylitis: what is the verdict? Rheumatology 2009;49(1):3–4.
[2] Maksymowych W.P. Ankylosing spondylitis – at the interface of bone and cartilage. J Rheumatol 2000;27(10):2295–301.
[3] MacKay K, Brophy S, Mack C, et al. The development and validation of a radiographic grading system for the hip in ankylosing spondylitis: the bath ankylosing spondylitis radiology hip index. J Rheumatol. 2000;27:2866–72.

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FRI0408

EARLIER TREATMENT OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS WITH CERTOLIZUMAB PEGOL RESULTS IN IMPROVED CLINICAL OUTCOMES

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Background: Patients (pts) with axial spondyloarthritis (axSpA) often experience delayed diagnosis, which leads to treatment delay.[1]Whilst certolizumab pegol (CZP) has been shown to improve the signs and symptoms of non-radiographic (nr)-axSpA,[2] whether earlier CZP treatment is beneficial in these pts is unclear.

Objectives: To report clinical outcomes in pts with nr–axSpA treated with CZP or placebo (PBO) over 52 weeks (wks) by their symptom duration.

Methods: Post-hoc analyses of disease outcomes in pts stratified by symptom duration (<5 vs ≥5 yrs at baseline [BL]) from C-axSpAnd (NCT02552212) were performed. In this 52–week, phase 3, multicentre, double-blind, PBO-controlled study, pts were randomised 1:1 to PBO or CZP (400mg at Wks 0/2/4, then 200mg every 2 wks), and could adjust non-biologic background medication or switch to open-label biologics at any point.[2] Outcomes reported: responder rates for Ankylosing Spondylitis Disease Activity Score – major improvement (ASDAS-MI), ASAS 40% improvement (ASAS40) and ASAS partial remission (ASAS-PR); the proportion of pts who reached ASDAS-inactive/low disease (ASDAS-ID/LD) or ASDAS<2.1; and change from BL (CFB) in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Missing values or values observed after discontinuing double-blind study treatment were considered to be non-response for categorical measures or, for quantitative measures, imputed by carrying forward the last observation from double–blind treatment.

Table: Clinical outcomes in patients treated with PBO or CZP stratified by symptom duration

		CZP (n=159)		PBO (n=158)	
	Wk	Symptom duration: <5 yrs (n=80)	Symptom duration: ≥5 yrs (n=79)	Symptom duration: <5 yrs (n=77)	Symptom duration: ≥5 yrs (n=81)
ASDAS-MI [a]	**0**	–	–	–	–
% (n)	12	46.3 (37)	24.1 (19)	9.1 (7)	3.7 (3)
	52	55.0 (44)	39.2 (31)	7.8 (6)	6.2 (5)
ASAS40 [a]	**0**	–	–	–	–
% (n)	12	58.8 (47)	36.7 (29)	11.7 (9)	11.1 (9)
	52	65.0 (52)	48.1 (38)	18.2 (14)	13.6 (11)
ASAS-PR [a]	**0**	–	–	–	–
% (n)	12	32.5 (26)	12.7 (10)	3.9 (3)	1.2 (1)
	52	43.8 (35)	24.1 (19)	2.6 (2)	6.2 (5)
ASDAS-ID [b]	**0**	–	–	–	–
% (n/N)	12	20.3 (16/79)	12.8 (10/78)	1.3 (1/77)	1.2 (1/81)
	52	40.5 (32/79)	17.9 (14/78)	2.6 (2/77)	6.2 (5/81)
ASDAS-LD [b]	**0**	–	–	–	–
% (n/N)	12	39.2 (31/79)	24.4 (19/78)	14.3 (11/77)	9.9 (8/81)
	52	25.3 (20/79)	34.6 (27/78)	16.9 (13/77)	11.1 (9/81)
ASDAS<2.1 [b]	**0**	–	–	–	–
% (n/N)	12	59.5 (47/79)	37.2 (29/78)	15.6 (12/77)	11.1 (9/81)
	52	65.8 (52/79)	52.6 (41/78)	19.5 (15/77)	17.3 (14/81)
BASDAI [b]	**0**	6.7 (1.3; 80)	7.0 (1.5; 79)	6.9 (1.3; 77)	6.7 (1.3; 81)
Mean (SD; n)	12	3.4 (2.1; 79)	4.5 (2.2; 78)	5.8 (2.1; 77)	5.6 (2.1; 81)
	52	2.8 (2.3; 79)	3.7 (2.5; 78)	5.5 (2.4; 77)	5.4 (2.2; 81)

[a] Missing values imputed using non-responder imputation; [b] Missing values imputed using double-blind last observation carried forward. ASAS: Assessment in SpondyloArthritis international Society; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-ID: ASDAS inactive disease (ASDAS<1.3); ASDAS-LD: ASDAS low disease (ASDAS ≥1.3, <2.1); ASDAS-MI: ASDAS major improvement (ASDAS reduction of ≥2.0 or lowest possible score [0.6]); ASAS40: ASAS 40% improvement; ASAS-PR: ASAS partial remission (score ≤2 in all 4 domains); BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CZP: certolizumab pegol; PBO: placebo; pt: patient; yrs: years.

Results: Of 317 recruited pts, 159 were randomised to CZP, and 158 to PBO. The mean (standard deviation [SD]) BL symptom duration was 7.8 (7.7) yrs for CZP-treated pts and 8.0 (7.5) yrs for PBO pts. 50.3% (80/159) CZP pts and 48.7% (77/158) PBO pts had a symptom duration <5 yrs. At Wks 12 and 52, ASDAS-MI, ASAS40 and ASAS-PR responder rates, the proportions of pts reaching ASDAS-ID and ASDAS<2.1, and mean CFB in BASDAI, were substantially better among CZP-treated pts with shorter symptom duration (<5 yrs at BL) vs longer symptom duration (**Table**). Amongst PBO pts, responses were low and there was no consistent trend in outcomes by symptom duration (**Table**).

Conclusion: In this post-hoc analysis, CZP-treated nr-axSpA pts with shorter symptom duration (<5 vs ≥5 yrs) showed greater improvements across multiple signs and symptoms of disease. These results indicate that early CZP treatment for nr-axSpA may be beneficial to pts.

REFERENCES:

[1] Rudwaleit M. Arthritis Rheum 2009;60:717–27; 2. Deodhar A. Arthritis Rheumatol 2018;70(S9):2073–4.

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FRI0409 **FEMALE ANKYLOSING SPONDYLITIS PATIENTS HAVE A SUBSTANTIALLY LOWER TNFI TREATMENT RESPONSE THAN MEN**

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Background: Accumulating data revealed difference in treatment efficacy in biologicals in women with axial spondyloartritis (axSpA) (1).
Objectives: The aim of this study was to assess gender differences in TNF inhibitor treatment response up to a five year biological treatment
Methods: Radiographic axSpA patients (AS) were recruited from the Amsterdam Spondyloarthritis cohort (the AmSpA cohort) of the VU University center and Reade. This prospective, observational cohort study included consecutive AS patients who were treated with TNF inhibitors (TNFi) (infliximab, adalimumab, etanercept or golimumab). Data of this cohort were collected between January 2000 until December 2018. Inclusion criteria were: AS diagnosis according to the modified New York criteria and start with a first TNFi. Patients were evaluated at baseline, three months, six months and once yearly up to five years follow-up. Disease activity was determined with the Ankylosing Spondylitis Disease Activity Score (ASDAS) and the Bath Ankylosing Spondyloartritis Index (BASDAI). Generalized equation estimation (GEE) analyses were performed to correct for multiple measurements. Linear ad logistic regression analyses were performed to assess the delta difference between baseline and 1 year.
Results: 389 AS patients were included in the AmSpA cohort. Thirty-three of these 389 patients were excluded since they were not TNFi naive or their treatment status was unknown (7.5%), of whom the majority was female: 14/135 females (10.5%) vs. 15/250 males (6.0%). Overall 182 patients (51.1%) dropped out over the study period, with a statistically significant higher percentage of females: 46.4% vs. 60.3% (OR= 1.8, 95%CI [1.4;2.4] *p*= 0.01). Adjusted models for ASDAS-CRP at six and twelve months showed that female patients had a 1.4 and 1.5 point higher mean ASDAS-CRP (β = 1.4, 95%CI [0.17;2.5] *p*=0.03) and (β = 1.5, 95%CI [0.41;2.8] *p*=0.007), respectively, compared to males. Adjusted models for BASDAI at six and twelve months showed no statistical significant differences for gender. After one year up to five year follow-up, no statistical significant gender differences were observed in both the mean BASDAI and mean ASDAS-CRP
Conclusion: In radiological axial SpA, female patients had significantly lower level of TNFi treatment response at six and twelve months on the ASDAS-CRP and had a higher drop-out rate compared to males. This strongly indicates an important gender difference in especially the twelve first months of TNFi treatment.

REFERENCES:

[1] Rusman, T. Curr Rheumatol Rep. 2018 May 12;20(6):35

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FRI0410 **TNF INHIBITORS REDUCE SPINAL RADIOGRAPHIC PROGRESSION IN AXIAL SPONDYLOARTHRITIS (PARTIALLY) BY DECREASING DISEASE ACTIVITY**

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Background: Recent observational data suggest that TNFi reduce spinal radiographic progression in radiographic axial spondyloarthritis (r-axSpA) mostly by inhibiting disease activity[1]. Yet, resolution on the controversial effect of TNFi on structural progression is yet to be achieved.
Objectives: To investigate whether in r-axSpA TNFi have an indirect (through ASDAS) and/or direct effect on spinal radiographic progression.
Methods: Patients (pts) with axial spondyloarthritis (axSpA) fulfilling the modified New York criteria (mNY) were included in this prospective, observational cohort (ALBERTA FORCAST). Clinical and imaging data were collected at baseline and every 2 years up to 10 years of follow-up. Radiographs of the spine were independently scored by 2 central readers and one adjudicator (if disagreement), with known chronological order but blinded to clinical data, using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The indirect effect of TNFi on mSASSS progression was evaluated by testing the interaction between TNFi and ASDAS at the start of each 2-year interval (t). If significant ($p<0.15$) the association between ASDAS at t and mSASSS at the end of the interval (t+1) was assessed in 3 groups of exposure to TNFi: i. treatment in all visits; ii. treatment in some visits and iii. Never treated. The direct effect of TNFi on mSASSS progression was evaluated by testing the association between TNFi at t and mSASSS at t+1 (adjusting for ASDAS at t). Multivariable GEE models adjusted for mSASSS at t (autoregression) and for a set of potential confounders defined a priori on clinical grounds (Figure). In a sensitivity analysis, the direct effect of TNFi was also tested after adjusting for a propensity score (PS), to take confounding by indication into account.

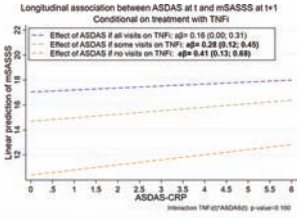


Figure. Longitudinal effect of ASDAS at the beginning of each 2-year interval on mSASSS 2 years later conditional on TNFi treatment group (multivariable linear GEE model with autoregression adjusted for symptom duration, gender, HLA-B27 and number of previous TNFi).

Results: In total, 314 pts were included [74% males, mean symptom duration 17.8 (SD 11.7) years, 83% HLA-B27 positive and 7% previously treated with ≥1 TNFi]. The interaction between ASDAS and TNFi at t was significant (p=0.10). A gradient was seen for the effect of ASDAS at t on mSASSS at t+1, which was more than 2 times higher in patients never treated with TNFi (β (95% CI): 0.41 (0.13; 0.68) compared to those always treated [β (95% CI): 0.16 (0.00; 0.31)] (Figure), showing that treatment with TNFi diminishes the effect of ASDAS on mSASSS. In addition to the indirect effect, TNFi also directly associated with less mSASSS progression: Pts receiving TNFi at t had on average 0.87 mSASSS-units less on t+1 compared to those not treated [β (95% CI): -0.85 (-1.35; -0.35)] and this was noted independently of ASDAS. Importantly, this effect remained significant after PS-adjustment [β (95% CI): -0.80 (-1.37; -0.22)].
Conclusion: This data is in in agreement with previous evidence showing that treatment with TNFi limits spinal radiographic progression in pts with r-axSpA by decreasing disease activity. Additionally, a direct effect of TNFi reducing mSASSS progression, and independent of ASDAS inflammation, is also seen suggesting that other mechanisms also contribute to the structural effect of TNFi.

REFERENCES:
[1] Molnar C, et al. Ann Rheum Dis 2018;77:63-69.

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FRI0411 COMPARABLE CLINICAL RESPONSES BUT HIGHER TREATMENT ADHERENCE OF SECUKINUMAB COMPARED TO TNF INHIBITORS IN SPONDYLOARTHRITIS PATIENTS: LONG TERM PROSPECTIVE OBSERVATIONAL STUDY IN A TERTIARY HOSPITAL OF GREECE

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Background: Data regarding effectiveness and persistence to therapy with anti-IL17 agent secukinumab (SEC) in spondyloarthritis (SpA) patients of real world clinical practice are very limited.
Objectives: To assess characteristics of SpA patients starting therapy with SEC versus tumor necrosis factor inhibitors (TNFis) in routine clinical care and compare clinical responses and treatment retention at 2 years.
Methods: All patients starting a bDMARD in the Rheumatology Department of the University Hospital of Heraklion, Crete, are included in a prospective observational study after their written informed consent. Data concerning disease activity at pre-specified time-points, drugs, comorbidities and any adverse events are recorded. For the present study we analyzed all consecutive patients with axial (AxSpA) or peripheral SpA (pSpA) starting or switching bDMARD therapy, either a TNFi or SEC from 1/2015 till 12/2018. We excluded patients with IBD-related SpA, patients starting ustekinumab (or apremilast) and patients switching from a bio-originator to a biosimilar TNFi. We compared disease activity scores improvement at 6 months using linear regression analysis and treatment retention using Kaplan-Meier survival curves with log-rank test and Cox regression. Inverse propensity score weighting (IPW) was used to adjust for the potential confounding of gender, age, disease duration, previous bDMARDs and csDMARDs number, diagnosis (AxSpA vs pSpA), presence of peripheral arthritis and co-therapy with csDMARDs.
Results: A total of 239 patients with SpA started/switched bDMARD (SEC:69, TNFis:170). SEC was the $\geq 3^{rd}$ bDMARD in 63% of patients compared to 17% of TNFis (p<0.001). Patients' characteristics at baseline were comparable except for disease duration (median (IQR): 5 (1.5-11) years in SEC vs. 0.9 (0.2-4.6) in TNFis, p<0.001). AxSpA was the diagnosis in 78% patients starting SEC and 79% starting TNFis while peripheral arthritis was slightly more common with SEC (81% vs 76% in TNFis). Monotherapy tended to be more common with SEC compared to TNFis (52% vs 42%, p=0.16). Baseline disease activity regarding both axial and peripheral arthritis was comparable in the two groups.
Unadjusted 2-year treatment retention was similar in the two groups, both overall (SEC: 63%, TNFi: 56%, p=0.18) and due to failure or adverse events. However, when we selected only patients on 1^{st} or 2^{nd} bDMARD (SEC:26, TNFis:131), 2-year survival of SEC was higher than that of TNFis (95% vs. 57%, p=0.027). Similarly, SEC tended to have higher survival than TNFis in patients with pSpA (p=0.11). After IPW, SEC administration was an independent predictor for higher bDMARD retention overall [HR (95%CI)=0.48(0.33-0.69), p<0.001] and specifically due to discontinuation for failure [HR=0.58 (0.38-0.88), p=0.011] and for adverse events [HR=0.21 (0.08-0.62), p=0.004].
Mean BASDAI and ASDAS improvements at 6 months were similar in patients with AxSpA receiving SEC or TNFis [Mean(SD) δBASDAI: 1.6 (2.5) vs 1.4(2.5) respectively (p=0.78) and δASDAS: 0.7 (1.4) vs 1.0 (1.5), p=0.44]. Similarly, in patients with peripheral arthritis, δDAS28 at 6 months was comparable in the two groups (p=0.88). Adjusted linear regression with IPW provided similar results to the unadjusted analyses in both axial and peripheral disease.
Conclusion: In SpA patients of real-world, administration of SEC results in similar clinical responses but higher treatment adherence compared to TNFis, especially if Secukinumab is the 1^{st} or 2^{nd} bDMARD. Larger number of patients and longer follow-up is needed to confirm these data.
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FRI0412 SPINAL AND SACROILIAC JOINTS INFLAMMATION IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TREATED WITH NETAKIMAB – 16-WEEKS RESULTS OF MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III ASTERA STUDY

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Background: Efficacy and safety of netakimab (NTK), a humanized anti-interleukin 17A antibody, have been previously established in two phase 2 clinical trials in patients with radiographic axial spondyloarthritis (r-axSpA)[1] and psoriasis[2]. ASTERA is a randomized, double-blind, placebo (PBO)-controlled phase III trial, aimed to demonstrate efficacy and safety of NTK in subjects with r-axSpA (NCT03447704).
Objectives: To evaluate the effect of NTK on inflammation in spine and sacroiliac joints (SIJ) at Week (Wk) 16 in ongoing ASTERA study in patients with active r-axSpA.
Methods: 228 eligible adults with active r-axSpA were randomized into 2 study arms (1:1) to receive 120 mg of NTK or PBO, administered as SC injections at Wk 0, 1, 2 and then q2wk through Wk 16. After Wk 16 all patients will start to receive NTK up to week 52. Inflammation in spine and SIJ was assessed with magnetic resonance imaging (MRI) at baseline and Wk 16. The following scoring methods were used: the Berlin spine score (derived from Ankylosing Spondylitis Spine MRI Activity (ASspi-MRI-a) Score for spine assessment and the SPARCC score for SIJ assessment. All images were evaluated by central reader, blinded to treatment.
Results: Both arms were comparable in the Berlin spine score (4.18 ± 4.58 in NTK arm vs. 4.19 ± 4.32 in PBO arm) and the SPARCC score (5.67 ± 8.33 in NTK arm vs. 5.23 ± 7.86 in PBO arm) at baseline ($p \geq 0.05$). Data analysis at Wk16 revealed that NTK arm achieved significant decline in bone marrow edema in direct comparison with PBO arm: by Wk 16 the mean change from baseline in the Berlin spine score was -2.16 ± 2.87 in NTK arm vs. -0.30 ± 1.55 in PBO arm (p<0.0001) and the mean change from baseline in the SPARCC score was -3.80 ± 6.68 in NTK arm vs. -1.82 ± 4.12 in PBO arm (p<0.01).
Conclusion: the treatment with NTK at a dose 120 mg leads to improvement in spine and SIJ inflammation in patients with active r-axSpA by Wk16, as compared with PBO.

REFERENCES:
[1] Mazurov V, Erdes S, Kunder E, et al.: OP0028|Efficacy and safety of BCD-085, a novel il-17 inhibitor, in ankylosing spondylitis. Results of phase 2 clinical study. Ann Rheum Dis 2018; 77: A64.
[2] Samtsov A, Khairutdinov V, Bakulev A, *et al.:* Efficacy and Safety of BCD-085, a Novel Interleukin-17 Inhibitor. Results of Phase II Clinical Trial in Patients with Moderate-to-Severe Plaque Psoriasis. *Vestn Dermatol Venerol* 2017; 0(5):52-63.

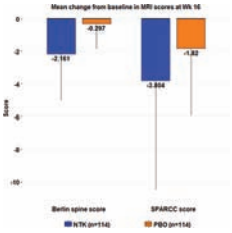


Figure 1. Change from baseline in MRI scores

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FRI0413 EFFICACY, PHARMACOKINETICS, SAFETY AND IMMUNOGENICITY OF THE BIOSIMILAR HS016 IN COMPARISON WITH ADALIMUMAB IN CHINESE PATIENTS WITH ANKYLOSING SPONDYLITIS: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP, PHASE 3 TRIAL

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Background: HS016, a proposed biosimilar to adalimumab, has an identical amino acid sequence, similar physicochemical and in vitro functional properties to adalimumab originator.
Objectives: To assess the efficacy, pharmacokinetic (PK) equivalence, safety and immunogenicity of HS016 compared with adalimumab in Chinese patients with ankylosing spondylitis (AS).
Methods: In a multicenter, randomized, double-blind, parallel-controlled phase 3 study, patients with AS fulfilled with the Modified New York Criteria in 1984 in China were randomized 2:1 to receive HS016 or adalimumab with a dose of 40mg every other week for 24 weeks. Blood samples for PK analyses were collected in about half of AS patients pre-dose every other week and during week 12 and week 14. Samples for anti-drug antibodies (ADA) and neutralizing antibodies (NAb) were analyzed in all patients. The primary endpoint was the proportion of patients achieving 20% improvement in Assessment in SpondyloArthritis International Society (ASAS 20) at week 24. Equivalent efficacy was concluded if 90% confidence interval (CI) of the difference in ASAS 20 response rate was between -15% and 15%. The secondary endpoints included the ASAS 20 response rate at week 12, ASAS 40, 50% improvement in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI 50), ASAS5/6 response rate at week 12 and week 24, PK, safety and immunogenicity.
Results: 416 patients were randomly assigned to receive HS016 and 232 to receive adalimumab. The ASAS 20 response rates at week 24 were 87.50% and 90.09% in HS016 and adalimumab groups, respectively, and the difference was -2.59% (90%CI, -6.77% to 1.60%), demonstrating clinical equivalence between HS016 and adalimumab. No significant difference of the proportion of ASAS 40, BASDAI 50 and ASAS 5/6 between the two groups were detected at week 12 or week 24 (table 1).

Table 1. Response rates (%) at week 12 and week 24.

	Week 12			Week 24		
	HS016 (N=416)	Adalimumab (N=232)	P value	HS016 (N=416)	Adalimumab (N=232)	P value
ASAS 20	79.57	81.03	0.65	87.50	90.09	0.32
ASAS 40	58.65	61.64	0.35	71.15	75.43	0.18
BASDAI 50	61.78	61.21	0.96	76.44	78.45	0.52
ASAS 5/6	57.45	58.62	0.86	62.98	67.24	0.37

ASAS, the Assessment in SpondyloArthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index.

Pharmacokinetic values from 188 AS patients in HS016 group and 109 in adalimumab group were analyzed. The geometric means for steady-state maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve from time zero to infinity (AUC_{inf}) were similar between HS016 group and adalimumab group. The proportions of treatment-emergent adverse events, serious adverse events and injection site reactions were similar between the two groups (table 2).**Table 2**. Adverse events in AS patients with HS016 or adalimumab.

Adverse events N (%)	HS016 (N=416)	Adalimumab (N=232)
TEAEs	352 (84.62)	200 (86.21)
TEAEs related to study drug	267 (64.18)	154 (66.38)
TEAEs leading to discontinuation	22 (5.29)	15 (6.47)
SAEs	18 (4.33)	6 (2.59)
Injection site reactions	21 (5.05)	11 (4.74)

TEAE, treatment-emergent adverse event; SAE, serious adverse event.

The frequencies of ADA and NAb positive were similar between the two groups at different time points. Through week 24, 79.13% of 412 patients in HS016 and 79.91% of 229 patients in adalimumab group developed ADAs, and 17.48% of 412 in HS016 and 18.78% of 229 in adalimumab group developed NAbs.
Conclusion: The results of efficacy, PK, safety, immunogenicity from the study conducted in Chinese AS patients support a high similarity between HS016 and the adalimumab.
Acknowledgement: In addition to Peking Union Medical College Hospital, another 27 sites from China were also involved in the study. The authors thank the investigators who made the study possible.
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FRI0414 SECUKINUMAB PROVIDES RAPID AND SIGNIFICANT IMPROVEMENT IN THE SIGNS AND SYMPTOMS OF ANKYLOSING SPONDYLITIS: PRIMARY (16-WEEK) RESULTS FROM A PHASE 3 CHINA-CENTRIC STUDY, MEASURE 5

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Background: Secukinumab (SEC), a fully human monoclonal antibody to IL-17A, has demonstrated significant and sustained efficacy in patients (pts) with ankylosing spondylitis (AS) across several phase 3 studies.[1-3] MEASURE 5 (NCT02896127) is a placebo (PBO)-controlled phase 3 China centric 1-year study in pts with active AS.
Objectives: To present the primary efficacy and safety results of the MEASURE 5 study.
Methods: Pts were randomised (2:1) to receive subcutaneous (s.c.) SEC 150 mg or PBO at baseline (BL), Weeks (Wks) 1, 2, 3, and 4, and then every 4 wks (q4w) thereafter through Wk 52. All PBO pts were switched to s.c. SEC 150 mg q4w starting at Wk 16. Primary endpoint was ASAS20 at Wk 16. Key secondary endpoints were ASAS40, hsCRP, ASAS5/6, BASDAI, SF-36 PCS, ASQoL and ASAS partial remission (PR). Randomisation was stratified by geographic location (China vs. non-China). Statistical analyses used non-responder imputation (NRI) for binary and mixed-effect model repeated measures (MMRM) for continuous variables. A pre-defined hierarchical testing strategy was used for overall population to adjust multiplicity. Safety analysis included all pts who received $\geq$1 dose of SEC.
Results: A total of 458 pts were randomised; 327 (71.4%) from China and 131 (28.6%) from Czech Republic, South Korea and UK. Overall, 97.7% (298/305) and 97.4% (149/153) pts in the SEC and PBO groups, respectively, completed 16 wks. BL characteristics were comparable between groups. Approximately 24% of pts were anti-TNF-inadequate responders/intolerant. The primary endpoint was met; SEC (58.4%) significantly improved ASAS20 response at Wk 16 vs. PBO (36.6%; $P < 0.0001$); corresponding rates were 56.0% vs. 38.5% ($P < 0.01$) in the Chinese population. Improvements were demonstrated in all secondary

endpoints at Wk 16 for SEC vs. PBO (overall and Chinese populations; Table). Serious AE rates were reported in 3.3% and 2.0% of SEC and PBO pts, respectively. Uveitis was reported in 1.0% (SEC) and 0.7% (PBO) of pts. No MACE, IBD or deaths were reported.

Conclusion: SEC demonstrated rapid and significant improvement in the signs and symptoms of AS in both the overall and Chinese populations. Secukinumab was well tolerated with no new safety signals identified.

REFERENCES:

[1] Baeten D, et al. N Engl J Med. 2015;373:2534-48.
[2] Pavelka K, et al. Arthritis Res Ther. 2017;19:285.
[3] Kivitz AJ, et al. *Rheumatol Ther.* 2018;5:447-62.

Table. Wk 16 data

	Overall		Chinese	
	SEC 150 mg (N=305)	PBO (N=153)	SEC 150 mg (N=218)	PBO (N=109)
ASAS20[1]	58.4*	36.6	56.0§	38.5
ASAS40[1]	43.9*	17.0	41.7*	16.5
hsCRP[2,3]	0.39*	1.05	0.33*	0.97
ASAS5/6[1]	47.2*	17.6	45.9*	17.4
BASDAI[2]	-2.79*	-1.50	-2.63*	-1.37
SF-36 PCS[2]	7.43*	4.60	7.18*	4.07
ASQoL[2]	-4.83*	-2.93	-4.50†	-2.50
ASAS PR[1]	16.7§	6.5	15.1‡	6.4

*$P < 0.0001$; †$P < 0.001$; §$P < 0.01$; ‡$P < 0.05$ vs. PBO (*P*-values are adjusted for overall and un-adjusted for Chinese populations). NRI for binary and MMRM for continuous variables.

[1]% responders; [2]LS mean change from BL; [3]ratio of post-BL/BL; LS, least squares; N, total number of randomised pts

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FRI0415 BIOSIMILAR BAT1406 VERSUS ADALIMUMAB THERAPY ON ACTIVE ANKYLOSING SPONDYLITIS: A RANDOMIZED, DOUBLE-BLINDED, MULTICENTER, CONTROLLED PHASE 3 TRIAL

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Background: Adalimumab has been proved to be effective and safety in management of ankylosing spondylitis (AS) in several clinical trials. In China, small proportion of AS patients had ever used TNF inhibitors and most of them discontinued because of expensive cost. BAT1406 and ADA have demonstrated comparable in protein structure, physicochemical properties, biological activity and immunological characteristics.

Objectives: To compare the effects, safety and immunogenicity of biosimilar BAT1406 vs adalimumab (ADA) in patients with active AS.

Methods: A multicenter, randomized, non-inferiority, double-blinded, ADA controlled clinical trial with 24 weeks of follow-up was conducted in China. Participants with active AS defined as BASDAI $\geq$4 and average back pain score (VAS 0-10) $\geq$4 were eligible for participation. Participants were randomly assigned to receive BAT1406 (40mg q2w) or adalimumab (40mg q2w) at a ratio of 2:1 for 24 weeks. Primary outcome was the proportion of patients achieving ASAS20 response at 12 weeks. Inclusion of the 95% CI of the ASAS20 response difference within a ± 15% margin was required for equivalence. Secondary outcomes included ASAS40, ASAS5/6, BASDAI50 response, patient reported outcomes, safety and immunogenicity. This trial is approved by China Food and Drug Administration (number 2015L05751).

Results: 554 eligible patients were enrolled from Jan 2017 to Aug 2017 and randomly assigned to receive BAT1406 (n=363) or Adalimumab (n=191) participants, 514 completed the study. Patients (86.5% of whom were male and whose mean age was 31.6 years) had a mean disease duration was 5.82 years. Over 12 weeks, 75.69% of patients in BAT1406 group and 73.68% in ADA group (between group difference 1.6%, 95% CI [-6.82% to 10.03%]) achieved ASAS20 response (per-protocol set; adjusted treatment difference 2.16%, 95% CI [-6.9% to 11.22%]). Outcomes for secondary end points were consistent with the primary efficacy findings. The frequency of adverse events (AEs) was comparable between groups ((BAT1406 316[87.1%] vs ADA 162 [85.3%]), as well as serious AEs, adverse drug reactions and discontinuations due to AEs. Similar positive rate was found in two groups for anti-drug antibodies up to week 24.

Conclusion: The study met the primary endpoint of demonstrating equivalent efficacy of BAT1406 and ADA. BAT1406 was comparable in tolerance, safety and immunogenicity with ADA in active AS patients.

REFERENCES:

[1] Park W, Yoo DH, Miranda P, et al. Efficacy and safety of switching from reference infliximab to CT-P13 compared with maintenance of CT-P13 in ankylosing spondylitis: 102-week data from the PLANETAS extension study. Annals of the rheumatic diseases. 2017;76(2):346-354.
[2] Park W, Yoo DH, Jaworski J, et al. Comparable long-term efficacy, as assessed by patient-reported outcomes, safety and pharmacokinetics, of CT-P13 and reference infliximab in patients with ankylosing spondylitis: 54-week results from the randomized, parallel-group PLANETAS study. Arthritis research & therapy. 2016;18:25.
[3] Chingcuanco F, Segal JB, Kim SC, Alexander GC. Bioequivalence of Biosimilar Tumor Necrosis Factor-alpha Inhibitors Compared With Their Reference Biologics: A Systematic Review. Ann Intern Med. 2016;165(8):565-574.
[4] Kneepkens EL, Wei JC, Nurmohamed MT, et al. Immunogenicity, adalimumab levels and clinical response in ankylosing spondylitis patients during 24 weeks of follow-up. Annals of the rheumatic diseases. 2015;74(2):396-401.
[5] Kanters TA, Stevanovic J, Huys I, Vulto AG, Simoens S. Adoption of Biosimilar Infliximab for Rheumatoid Arthritis, Ankylosing Spondylitis, and Inflammatory Bowel Diseases in the EU5: A Budget Impact Analysis Using a Delphi Panel. Front Pharmacol. 2017;8:322.

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FRI0416

THE EFFICACY AND SAFETY OF ANTI-TNF A TREATMENT IN ANKYLOSING SPONDYLITIS PATIENTS WITH LATE ONSET COMPARED TO THOSE WITH ADULT ONSET; THE DATA FROM TURKBIO REGISTRY

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Background: The first symptoms of ankylosing spondylitis (AS) patients usually begin prior to 45 years, but can occur later in life.
Objectives: The purpose of this study is to evaluate the efficacy and safety of anti-TNFα treatment in late-onset AS (LoAS) patients in comparison to those with adult onset AS (AoAS).
Methods: We studied AS patients in TURKBIO registry between the dates of January 2011 and November 2018. All the patients fulfilled the modified New York criteria for AS [1] and were classified into 2 groups based on their age at symptom onset: AoAS (age>16 but ≤45 years); and LoAS (age>45 years). In both groups, the following data were compared: (1) epidemiological variables (2) clinical manifestations, including signs and symptoms at diagnosis; (3) laboratory results (4) disease activity markers and follow-up parameters (BASDAI, ASDAS-CRP and HAQ); (5) previous and current treatments (6) adverse events.
Results: A total of 2551 AS patients (91,1% with AoAS and 8.9% with LoAS) were included in the study. LoAS group had more female patients, older age, shorter disease duration and diagnostic delay, higher initial ESR and less HLA-B27 positivity compared to the AoAS (Table 1). Peripheral arthritis (not statistically significant) and dactylitis was seen more common in the LoAS. The frequency of other involvements was similar between the groups (Table1). The frequency of using drugs was similar between each groups although the use of glucocorticoids and sulphasalazine was more common in the LoAS. Switching from the first anti-TNFα treatment to the second one was more common in the AoAS. However, there was found no significant difference between the two groups in 2 or more switch ratios (Table 1). At the latest visit after the anti-TNFα therapy, the mean improvement in BASDAI was significantly higher in the AoAS (Table 2). A total of 10 (4.4%) serious adverse events were reported in LoAS and 39 (1.7%) in AoAS patients in the follow-up (HR: 2.62; 95% CI: 1.32–5.18). Severe infections were the most commonly seen serious adverse events (1.3% in LoAS and 0.8% in AoAS), followed by allergic reactions (0.9% in LoAS and 0.3% in AoAS). Tuberculosis was observed in 2 patients (0.9%) in LoAS and 9 (0.4%) in AoAS, malignancy in 3 patients (1.3%) in LoAS and 6 (0.3%) in AoAS.
Conclusion: Our data showed that almost 8.9% of the patients with AS had late-onset of symptoms. The results suggested that LoAS patients might have different demographic, clinical features, disease activity parameters at baseline. The frequency of anti-TNFα use and response rate to the treatment was also similar in LoAS to those in AoAS patients. The LoAS patients seem to have more common severe adverse events compared to the AOAS patients possibly related to their older age.

Table 1. Demographic and clinical characteristics of patients with AoAS and LoAS

	AoAS (≤45 yrs)	LoAS (>45 yrs)	p-value
N	2324	227	
Sex (male), n (%)	1411 (61)	109 (48)	0.000
Age, yrs	43.07 ± 10.26	62.10 ± 8.59	0.000
Duration of disease, yrs	14.50 ± 9.42	8.53 ± 6.27	0.000
Delay of diagnosis, yrs	6.12 ± 6.61	3.59 ± 4.37	0.000
HLA-B27 positivity, (%)	64	44	0.000
C-reactive protein (mg/L)	16.66 ± 24.32	19.20 ± 26.37	0.169
Erythrocyte sedimentation rate (mm/hr)	26.83 ± 21.56	34.47 ± 24.56	0.000
BASDAI	38.9±22.6	34.6±22.1	0.007
BASFI	29.3±22.7	30.4±23.8	0.535
ASDAS-CRP	2.70 ± 1.19	2.69 ± 1.21	0.454
HAQ	0.78±0.60	0.92±0.69	0.008
Uveitis, n (%)	192 (8)	14 (6)	0.328
Peripheral arthritis, n (%)	389 (17)	50 (22)	0.055
Enthesitis, n (%)	339 (15)	31 (14)	0.779
Dactylitis, n (%)	77 (3)	15 (7)	0.019
Inflammatory bowel disease, n (%)	41 (2)	7 (3)	0.254
Psoriasis, n (%)	30 (1)	0 (0)	0.162
Treatment, n (%)			
NSAIDs	762 (33)	70 (31)	0.600
Sulphasalazine	176 (8)	35 (15)	0.000
Methotrexate	111 (5)	16 (7)	0.179
Glucocorticoid	62 (3)	15 (7)	0.002
Anti-TNFα	1467 (63)	134 (59)	0.252
Secukinumab	31 (1)	2 (1)	0.788
Anti-TNFα switch, n (%)			
One switch	359 (15)	22 (10)	0.026
Two switch	113 (5)	7 (3)	0.297
Three switch	25 (1)	3 (1)	0.996
Four switch	8 (0.3)	0 (0)	0.792

AoAS: adult-onset ankylosing spondylitis, LoAS: late-onset ankylosing spondylitis
*Continuous variables were presented as mean ±SD for both tables

Table 2. Changes in follow-up parameters between the baseline and the latest visits in patients on biologicals

	AoAS (≤45 yrs)			LoAS (>45 yrs)		
	Baseline (mean±SD)	Latest follow-up (mean±SD)	Change (mean±SD)	Baseline (mean±SD)	Latest follow-up (mean±SD)	Change (mean±SD)
BASDAI	38.9±22.6	23.7±21.6*	15.2±23.6	34.6±22.1	23.4±21.1*	11.2±20.8**
BASFI	29.3±22.7	20.9±19.9*	8.3±20.2	30.4±23.8	24.1±23.4*	6.3±20.3
ASDAS-CRP	2.70 ± 1.19	1.98 ± 1.08*	0.72 ± 1.23	2.69 ± 1.21	2.03 ±1.08*	0.65 ± 1.17
CRP (mg/L)	16.66±24.32	11.33±18.87*	5.33±24.60	19.20±26.37	13.71±18.27*	5.49±25.25
HAQ	0.78±0.60	0.59±0.47*	0.19±0.52	0.92±0.69	0.71±0.58*	0.21±0.55

*Baseline vs the latest visits, p<0.05
**Change between the baseline and the latest visits in AoAS vs LoAS groups, p<0.05

REFERENCES:
[1] Van der Linden S, Valkenburg HA. Evaluation of diagnostic criteria for AS. Arthritis Rheum 1984; 27: 361–368.

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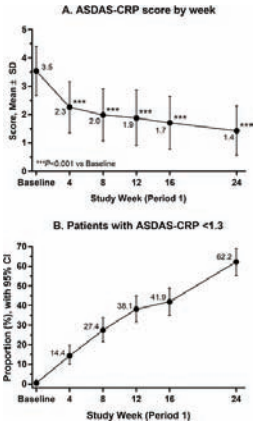
FRI0417

ETANERCEPT TREATMENT IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND AN INADEQUATE RESPONSE TO NONSTEROIDAL ANTI-INFLAMMATORY DRUGS: PERIOD 1 RESULTS FROM THE RE-EMBARK TRIAL

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Background: Etanercept (ETN) is efficacious in patients with non-radiographic axial spondyloarthritis (nr-axSpA).[1] However, little is known[2] about the effect of ETN withdrawal in patients with nr-axSpA who achieved a significant clinical response.
Objectives: The primary objective of this ongoing, 3-period study is to estimate the proportion of patients with nr-axSpA who experienced a flare (Ankylosing Spondylitis Disease Activity Score with erythrocyte sedimentation rate [ASDAS-ESR] ≥2.1) within 40 weeks post-ETN withdrawal, after achieving inactive disease (ASDAS with C-reactive protein [ASDAS-CRP] <1.3). Here, we report results of the 24-week Period 1, whose goal was to generate a population of ETN-treated patients with inactive disease.
Methods: RE-EMBARK (NCT02509026) is a multicenter, open-label trial in 18-50-year-old patients with active nr-axSpA (defined as fulfillment of Assessment in Spondyloarthritis International Society [ASAS] criteria, but not modified New York criteria, plus ASDAS-CRP ≥2.1), with an inadequate response to ≥2 nonsteroidal anti-inflammatory drugs (NSAIDs),

who were on a stable NSAID dose for ≥2 weeks. In Period 1, all patients received ETN (50 mg/week) plus NSAID for 24 weeks. At week 24, patients who achieved inactive disease qualified for Period 2 and were withdrawn from ETN treatment for 40 weeks. In Period 3, patients who experience a flare during Period 2 will be retreated with ETN for 12 weeks. Efficacy outcomes for Period 1 included the proportions of patients achieving inactive disease and 20% and 40% improvements in ASAS disease activity (ASAS20 and ASAS40), as well as the changes from baseline in the Spondyloarthritis Research Consortium of Canada (SPARCC) scores for the sacroiliac joint (SPARCC-SIJ) and the spine (SPARCC-Spine). Efficacy analyses presented here were performed on the observed cases.



Results: Of 209 treated patients, 112 (54%) were men, 186 (89%) white, 142 (68%) had MRI-evident sacroiliitis, and 162 (78%) were HLA-B27-positive. The mean baseline score for ASDAS-CRP was 3.5, 8.5 for SPARCC-SIJ, and 2.7 for SPARCC-Spine. Twenty-one (10%) patients discontinued the trial. A significant decrease in ASDAS-CRP score was observed at all post-baseline visits (Panel A). At Week 24, 62% (117/188) of patients achieved inactive disease (Panel B), 86% (163/190) and 76% (144/190) achieved ASAS20 and ASAS40, respectively, and there was a significant reduction from baseline in SPARCC-SIJ (-5.8; *P*<0.001) and SPARCC-Spine (-1.5; *P*=0.002). Seventy-nine (38%) patients experienced TEAEs, and 1 (0.5%) patient experienced a serious TEAE (cellulitis).
Conclusion: Majority of patients with active nr-axSpA and an inadequate response to NSAIDs achieved inactive disease and reduction of inflammation in both the SIJ and the spine with 24-week open-label ETN treatment. There were no unexpected safety signals.

REFERENCES:

[1] Dougados M et al, *Arthritis & Rheumatology*. 2014;66:2091-2102. 2. Song IH et al, Ann Rheum Dis. 2012;71:1212-1215.

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FRI0418

SECUKINUMAB PROVIDED SIMILAR EFFICACY IN MALES AND FEMALES WITH ACTIVE ANKYLOSING SPONDYLITIS OVER 52 WEEKS: POST HOC POOLED ANALYSIS OF THE MEASURE TRIALS

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Background: The burden of ankylosing spondylitis (AS) is reported to be higher in female patients (pts). In addition, females show less improvement in AS outcome measures as compared to males when treated with tumour necrosis factor (TNF) inhibitors.[1,2] Currently, there are no data available on the efficacy of secukinumab (SEC) in males versus females.
Objectives: To compare the efficacy of SEC in pts with active AS by gender (male vs female) from data pooled from four phase 3 studies (MEASURE 1-4).
Methods: This *post hoc* analysis pooled data from the MEASURE 1-4 trials. Baseline (BL) demographics and disease characteristics were summarized across genders. Efficacy outcomes assessed at Week (Wk) 16 and 52 were ASAS20, ASAS40, ASDAS-ID, BASDAI, BASMI, BASFI, SF-36 PCS and FACIT-F. BL predictor analysis used multivariable logistic regression (binary variables) or generalized linear model (continuous variables) to assess the impact of gender as an independent variable on ASAS40, ASDAS-ID, and BASDAI at Wk 52, after adjusting for treatment group and other baseline factors in a pooled analysis across studies and treatment groups.
Results: Overall, 647 males and 322 females who received SEC 300mg IV load (LD) (n=76), 150mg IV LD (n=199), 150mg s.c. LD (n=188), 150mg no LD (n=117), and placebo (n=389), respectively, were included in the analysis. At BL, significant differences in TNFi, HLA-B27, and smoking status were observed between genders. MASES scores were significantly higher in females; hs-CRP, BASMI-occiput to wall, and BASMI tragus to wall distance scores were significantly higher in males. Efficacy outcomes were generally similar in males and females (Figure 1). There was no significant impact of gender as an independent predictor of SEC efficacy at Wk 52 as measured by ASAS40 (Odds ratio [OR] 1.1; P=0.50), ASDAS-ID (OR 1.32; P=0.16) or change in BASDAI (treatment effect, -0.17; P=0.82).
Conclusion: Similar efficacy outcomes were observed in male and female patients with active ankylosing spondylitis treated with secukinumab over 52 weeks.

REFERENCES:

[1] Rusman T et al, Int J Rheum Dis. 2018; 21: 836–42.
[2] van der Horst-Bruinsma IE et al, Ann Rheum Dis. 2013;72:1221–4.

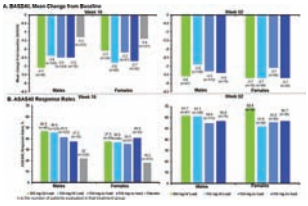


Figure 1. Summary of Efficacy Responses by Gender: A. BASDAI Mean Change from Baseline and B. ASAS40 Response Rates

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FRI0419 OUTCOMES OF DOSE REDUCTION OF TNF-INHIBITORS IN AXIAL SPONDYLOARTHRITIS AT 24 MONTHS

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Background: Some patients with inflammatory arthritis who respond well to TNF inhibitor (TNFi) treatment continue to do so after dose reduction. In Axial Spondyloarthritis (axSpA) dose optimisation is desirable but the extent of benefit is unclear and predictors of therapeutic response to dose reduction are unknown.

Objectives: To observe responses to dose reduction of TNFi treatment in axSpA patients and to seek preliminary predictors of low-dose therapeutic response.

Methods: AxSpA Patients at 4 UK centres were allowed to reduce their doses of TNFi therapy if they had met UK (NICE) response criteria and remained well for at least 6 months and wished to do so. There was no predetermined dose-reduction schedule. The proportion of dose reduction was calculated as a percentage, in mg per month, of the original, standard dose. All patients completed BASDAI and BASFI questionnaires at each visit with annual BASMI measurement. CRP levels were measured frequently. Individuals who continued to take reduced-dose treatment throughout the 24-month period were designated "Remainers" (REM) and those who reverted to full-dose treatment were designated "Reverters" (REV). Data were collected at 6 timepoints; 1: immediately before starting TNFi therapy; 2: at the point of dose reduction; 3: at the point of reversion to full-dose treatment (REV only); 4: 6 months after dose reduction; 5:12 months after dose reduction; 6: 24 months after dose reduction.

Results: 58 patients (86%male) who had reduced their dose of TNFi treatment were observed for 24 months. 47 (81%) were REM and 11 (19%) were REV. Mean disease duration prior to biologic therapy was 22.6 years for remainers and 18.6 years for reverters. Mean dose reduction was 38% and 41%, respectively. These 47 REM (85%male) were of mean age 53.6 (range 36 to 71) years, compared with the 11 REV (63.6%male) whose mean age was 51.9 (range 39 to 71) years.

Mean BASDAI, BASFI and BASMI scores and CRP levels at the designated time points are shown in table1.

REM mean BASDAI scores reduced from 1.9 to 1.4 (28%) from dose reduction to 24 months whereas REV mean BASDAI scores increased from 1.8 to 2.4 (34%) from dose reduction to dose reversion.

REM mean BASFI scores reduced from 2.5 to 1.4 (43%) from dose reduction to 24 months whereas REV mean BASFI scores increased from 2.6 to 3.0 (17%) from dose reduction to dose reversion.

REM mean BASMI scores reduced from 3.4 to 2.3 (32%) from dose reduction to 24 months whereas REV mean BASMI scores increased from 2.8 to 3.3 (19%) from dose reduction to dose reversion.

REM mean CRP scores decreased from 4.1 to 0.7mg/dl (83%) from dose reduction to 24 months and REV mean CRP scores also decreased from 4.7 to 3.5mg/dl (25%) from dose reduction to dose reversion.

Conclusion: Amongst these selected patients with axSpA 85% continued to respond to TNFi treatment in spite of 38% dose reduction. Reverters were more likely to be female and to have relatively low CRP levels at the initiation of TNFi treatment; reversion was preceded by modest rises in BASDAI, BASFI and BASMI but by continued fall in CRP levels.

There is a need for randomised dose-reduction studies in axSpA and further research to understand the factors that lead to dose-reversion.

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TABLE

	No	T/P1	T/ P2	T/ P3	T/ P4	T/ P5	T/P 6
BASDAI REM	47	5.8	1.9	n/a	1.2	1.3	1.4
REV	11	5.2	1.7	2.4			
BASFI REM	47	4.5	2.5	n/a	1.6	1.4	1.4
REV	11	4.4	2.6	3.0			
BASMI REM	47	3.9	3.4	n/a	1.8	2.0	2.3
REV	11	4.0	2.7	3.3			
CRP REM	47	12.8	4.1	n/a	0.8	1.4	0.7
REV	11	6.7	4.7	3.5			

T/P Timepoint

FRI0420 IXEKIZUMAB SIGNIFICANTLY IMPROVES SELF-REPORTED OVERALL HEALTH IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS/RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: SF-36 RESULTS OF TWO PHASE 3 TRIALS

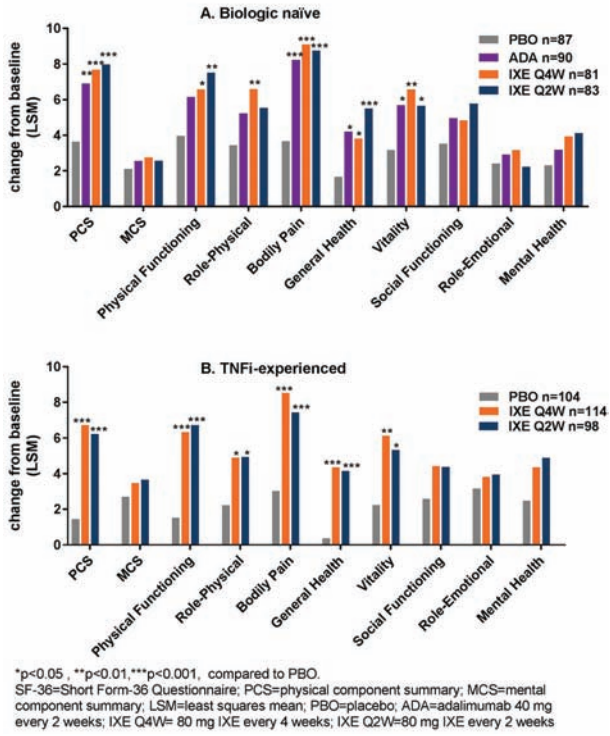
Jessica A. Walsh[1,2], Uta Kiltz[3,4], James Cheng-Chung Wei[5], Filip van den Bosch[6], Theresa Hunter[7], Yan Dong[7], LI Xiaoqi[7], David Sandoval[7], Luis Leon[7], Vibeke Strand[8]. [1]*University of Utah, Salt Lake City, United States of America*; [2]*Veterans Affairs Medical Center, Salt Lake City, United States of America*; [3]*Rheumazentrum Ruhrgebiet, Herne, Germany*; [4]*Ruhr-Universität Bochum, Bochum, Germany*; [5]*Chung Shan Medical University Hospital, Taichung City, Taiwan, Republic of China*; [6]*Ghent University Hospital, Ghent, Belgium*; [7]*Eli Lilly and Company, Indianapolis, United States of America*; [8]*Biopharmaceutical Consultant, Portolo Valley, United States of America*

Background: Using the Short Form-36 (SF-36) questionnaire, previous studies have determined that ankylosing spondylitis/radiographic axial spondyloarthritis (AS/r-axSpA) significantly impairs patients' health-related quality of life (HRQoL).[1] Ixekizumab (IXE), a humanized anti-interleukin-17A monoclonal antibody, improves disease signs and symptoms in patients with AS/r-axSpA.[2,3] Week 16 SF-36 results from two clinical trials with IXE are presented here (NCT02696785 and NCT02696798).

Objectives: To evaluate the efficacy of IXE versus placebo (PBO) in improving HRQoL assessed by the SF-36 questionnaire in patients with active AS/r-axSpA who were either naïve to biologic therapy or have failed or been intolerant of one or two TNF inhibitors (TNFi).

Methods: COAST-V and -W are randomized, double-blind, placebo-controlled clinical trials. Enrolled patients were adults with active AS/r-axSpA classified by ASAS criteria who fulfilled mNY of sacroiliitis (central reading), with Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and back pain $\geq$4. In COAST-V, patients naïve to biologic agents were randomized 1:1:1:1 to receive 80 mg IXE every 4 weeks (Q4W), 80 mg IXE every 2 weeks (Q2W), adalimumab 40 mg Q2W (ADA), or PBO. In COAST-W, patients who had failed on or were intolerant of one or two TNFi were randomized 1:1:1 to 80 mg IXE Q4W, 80 mg IXE Q2W, or PBO. In both studies, patients in the IXE arms were randomized to receive either 80 mg or 160 mg IXE as the starting dose. Comparisons of change from baseline to Week 16 in norm-based SF-36 scores between active groups and PBO were performed using mixed model for repeated measures.

Figure. Change from baseline in SF-36 at 16 weeks in (A.) biologic naïve patients and (B.) TNFi-experienced patients



*p<0.05 , **p<0.01,***p<0.001, compared to PBO.
SF-36=Short Form-36 Questionnaire; PCS=physical component summary; MCS=mental component summary; LSM=least squares mean; PBO=placebo; ADA=adalimumab 40 mg every 2 weeks; IXE Q4W= 80 mg IXE every 4 weeks; IXE Q2W=80 mg IXE every 2 weeks

Results: Biologic naïve and TNFi-experienced patients treated with IXE reported significantly greater improvement than PBO patients in SF-36 Physical Component Summary and the physical functioning, bodily pain, general health, and vitality domains. No changes between treatments groups were reported in Mental Component Summary scores. The greatest numerical improvements with IXE were observed in the bodily pain domain. Similar improvements were reported in the IXE Q4W, IXE Q2W, and ADA groups.
Conclusion: IXE improved self-reported HRQoL, as measured by the SF-36 questionnaire, at Week 16 in patients with active AS/r-axSpA who were naïve or experienced with biologic treatments.

REFERENCES:

[1] Yang, et al. (2016). Qual Life Res. 25:2711-23.
[2] van der Heijde, et al. (2018). Lancet. 392(10163):2441-51.
[3] Deodhar, et al. (2018). *Arthritis Rheumatol.* Doi: 10.1002/art.40753.

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FRI0421

IXEKIZUMAB SIGNIFICANTLY REDUCED PAIN, INFLAMMATION, AND FATIGUE IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLARTHRITIS (R-AXSPA)/ANKYLOSING SPONDYLITIS (AS)

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Background: Chronic pain, inflammation, and fatigue are among the most common symptoms of radiographic axial spondyloarthritis (r-axSpA)/ankylosing spondylitis (AS).[1,2] Efficacy data for ixekizumab (IXE), a high affinity monoclonal antibody that selectively targets interleukin-17A,compared to placebo (PBO) in patients with r-axSpA have been reported.[3,4]
Objectives: The purpose of this analysis was to evaluate the impact of IXE on pain, inflammation, and fatigue in patients with r-axSpA treated with IXE versus PBO over 16 weeks.
Methods: This was a prespecified analysis from two Phase 3, multicenter, randomized, placebo-controlled studies comparing the efficacy and safety of IXE 80 mg every 2 weeks (Q2W) or every 4 weeks (Q4W) to PBO or reference, adalimumab (ADA), over 16 weeks in biologic-naive (COAST-V; NCT02696785) and to PBO in tumor necrosis factor inhibitor (TNFi)-experienced (COAST-W; NCT02696798) patients with active r-axSpA per Assessment of Spondyloarthritis (SpA) international Society (ASAS) criteria (sacroillitis modified New York criteria and $\geq$1 SpA feature). Patient global, spinal pain, spinal pain at night, and inflammation (average of BASDAI Q5&6) data were collected at baseline and Weeks 1, 2, 4, 8, 12, and 16. Fatigue Numeric Rating Scale data were collected at baseline, Week 8, and Week 16. Changes from baseline were analyzed using mixed-effects model of repeated measures.
Results: In biologic-naive (COAST-V) and TNFi-experienced (COAST-W) patients, significant improvements from baseline in patient global, spinal pain, spinal pain at night, and inflammation were observed as early as Week 1 (Table 1, Figure 1). Significant reductions in fatigue as early as Week 8 (first measurement) were seen in patients receiving IXE Q2W and Q4W and maintained up to Week 16 (Table 1; P<.05).

Table 1. Change from baseline in patient global, inflammation, and fatigue in patients with r-axSpA with IXE, ADA, and PBO in biologic-naive (COAST-V) and TNFi-experienced (COAST-W) patients

			Least Squares Mean (Standard Error)			
Parameter	**Study**	**Week**	**IXE Q2W**	**IXE Q4W**	**ADA**	**PBO**
Patient Global	COAST-V	1	-1.3 (0.17)	-1.3 (0.18)	-1.4 (0.17)	-0.6 (0.17)
		16	-2.8 (0.25)*	-2.5 (0.25)	-2.6 (0.24)*	-1.4 (0.24)
	COAST-W	1	-1.3 (0.18)*	-1.1 (0.16)	–	-0.4 (0.16)
		16	-2.1 (0.24)*	-2.4 (0.22)*	–	-0.7 (0.23)
Inflammation (average of BASDAI Q5/Q6)	COAST-V	1	-1.5 (0.18)*	-1.6 (0.18)*	-1.4 (0.17)*	-0.4 (0.18)
		16	-2.9 (0.23)*	-3.2 (0.24)*	-2.7 (0.22)*	-1.3 (0.23)
	COAST-W	1	-1.4 (0.17)*	-1.3 (0.15)*	–	-0.4 (0.16)
		16	-2.4 (0.25)*	-2.4 (0.23)*	–	-0.7 (0.24)
Fatigue NRS	COAST-V	8	-1.7 (0.23)†	-2.0 (0.23)	-2.1 (0.22)*	-0.9 (0.22)
		16	-2.1 (0.24)†	-2.5 (0.24)	-2.2 (0.23)†	-1.4 (0.23)
	COAST-W	8	-1.5 (0.23)	-1.8 (0.21)*	–	-0.5 (0.22)
		16	-1.7 (0.25)	-2.0 (0.23)*	–	-0.7 (0.24)

*p<0.001 vs PBO; p<0.01 vs PBO; †p<0.05 vs PBO.
ADA, adalimumab; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IXE, ixekizumab; NRS, Numeric Rating Scale; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks.

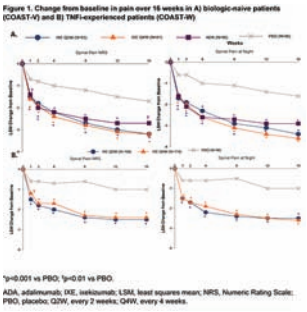


Figure 1. Change from baseline in pain over 16 weeks in A) biologic-naive patients (COAST-V) and B) TNFi-experienced patients (COAST-W)

*p<0.001 vs PBO; †p<0.01 vs PBO.
ADA, adalimumab; IXE, ixekizumab; LSM, least squares mean; NRS, Numeric Rating Scale; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks.

Conclusion: IXE significantly improved pain, inflammation, and fatigue in patients with r-axSpA.

REFERENCES:

[1] Sieper J, et al. Lancet. 2017;390:73–84.
[2] Stebbings SM, et al. Clin Rheumatol. 2014:33:1467–74.
[3] Van der Heijde D, et al. Lancet. 2018;392:2411–51.
[4] Deodhar A, et al. Arthritis Rheumatol. 2018 Oct 20. Doi: :10.1002/art.40753.

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FRI0422

HS016, A PROPOSED ADALIMUMAB BIOSIMILAR, SHOWED EQUIVALENT PHARMACOKINETICS AND SIMILAR SAFETY, IMMUNOGENICITY AND TOLERABILITY TO CHINA-LICENSED ADALIMUMAB IN HEALTHY MALE SUBJECTS, ACCORDING TO A 2.3-MONTHS PHASE I STUDY

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Background: HS016, a biosimilar to China-licensed adalimumab, has an identical amino acid sequence, similar physicochemical and in vitro functional properties to China-licensed adalimumab.
Objectives: The primary objective of this study was to demonstrate PK equivalence between HS016 and China-licensed adalimumab.
PK characteristics, safety, tolerability and immunogenicity were investigated as secondary objectives.
Methods: The first-in-human study was a randomized, double-blind, parallel-control, single-dose study conducted in 136 healthy male subjects at 1 site in China. Subjects were randomized to receive a 40 mg subcutaneous injection of either HS016 or China-licensed adalimumab and were followed up for 70 days. Blood samples were taken pre-dose and at multiple intervals to day 70.
The primary outcomes were area under the concentration-time curve from time zero to time t (AUC_{0-t}) area under the concentration-time curve from time zero to infinity ($AUC_{0-\infty}$), and maximum concentration (C_{max}). The secondary endpoints were the time taken to reach the maximum concentration($^*T_{max}$), elimination half-life ($T_{1/2}$) etc. Equivalence for the primary outcomes were to be concluded if the 90% confidence intervals (CIs) for the ratio of geometric least squares means (LS Means) of the groups compared were completely contained within the pre-defined equivalence margin of 0.8 to 1.25 using analysis of variance (ANOVA).
Safety indicators mainly included physical examination, vital signs, laboratory examination, electrocardiogram, chest X-ray, etc. Immunogenicity evaluation explored kinetics and magnitude of anti-drug antibody (ADA) and its neutralizing ability of Neutralizing ADA.
Results: The 90% confidence intervals of geometric least squares means ratios (GMR) of C_{max}, $AUC_{0-\infty}$and AUC_{0-t} between HS016 and China-licensed adalimumab arms were (0.9855,1.1359),(0.8743,1.0841) and (0.8724, 1.0605). The 90% confidence intervals of all GMRs fell within pre-specified confidence bounds of 80% to 125%.

Table 1. Statistical Analysis of Bioequivalence-Pharmacokinetic Analysis Set

	Statistic	lsmeans	95% CIs	GLSM	95% CIs	HS016 compare with adalimumab 90% CIs
HS016 (N=68)	AUC_{0-t} (hr·ng/mL)	14.66	(14.58, 14.74)	2326562.38	(2142491.09, 2526448.09)	(0.8724, 1.0605)
	$AUC_{0-\infty}$ (hr·ng/mL)	14.73	(14.63, 14.82)	2484615.56	(2268102.44, 2721797.02)	(0.8743, 1.0841)
	C_{max} (ng/mL)	8.3	(8.24, 8.36)	4034.86	(3799.95, 4284.29)	(0.9855, 1.1359)
adalimumab (N=68)	AUC_{0-t} (hr·ng/mL)	14.7	(14.62, 14.78)	2418702.15	(2227341.01, 2626504.01)	
	$AUC_{0-\infty}$ (hr·ng/mL)	14.75	(14.66, 14.84)	2552064.12	(2331241.56, 2793803.70)	
	C_{max} (ng/mL)	8.25	(8.19, 8.31)	3813.61	(3591.58, 4049.36)	

Of the 136 subjects, 128 had adverse events (AEs) with 63 (92.6%) and 65 (95.6%) AEs occurring in the HS016 and China-licensed adalimumab, respectively. Among these AEs, 172 from 50 subjects (73.5%) in HS016 group and 148 from 55 subject (80.9%) in China-licensed adalimumab were treatment emergent adverse event.
The proportion of confirmed anti-drug antibody responses in the 2 study arms were, 25.0% (17 cases) and 22.1% (15 cases) at day 14, 50.0% (34 cases) and 42.6% (29 cases) at day 42, for the HS016 and China-licensed adalimumab arms, respectively. Neutralizing antibodies were all negative at day 14 for both groups, except 2 cases (3.7%) and 1 case (1.6%) at day 42, for the HS016 and China-licensed adalimumab arms, respectively.
Conclusion: It is concluded that HS016 have shown a similar PK to china -licensed adalimumab in healthy male subjects, and no meaningful differences in safety of immunogenicity were observed.
Disclosure of Interests: None declared
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Psoriatic arthritis

FRI0423

NAIL ULTRASONOGRAPHY FINDINGS IN GRAYSCALE AND POWER DOPPLER TO DIFFERENTIATE PSORIATIC ARTHRITIS, PSORIASIS AND CONTROL INDIVIDUALS

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Background: The early diagnosis of psoriatic arthritis (PsA) on patients with psoriasis (PsO) is challenging, but may prevent functional impairment. Patients with nail psoriasis have an odds ratio of nearly 3.0 of developing psoriatic arthritis. Ultrasonography is a replicable, radiation-free method that could be used to identify nail changes before clinical manifestations.
Objectives: To verify if nail changes identified via ultrasonography can differentiate between PsA and PsO patients as well as between PsA/PsO patients and a control group.

Methods: Single-center, cross-sectional study. PsA patients were consecutively enrolled, PsO and controls were matched by age and gender with the PsA group. PsO patients must have had the diagnosis of psoriasis of any subtypes. PsA patients had to fulfill the CASPAR criteria. Exclusion criteria, for all groups included: other joint inflammatory disease; dermatological or systemic disease that could modify the nail structure. Ultrasound examination was performed using a MyLab 50 system (Esaote Biomedica, Genova, Italy), equipped with a linear probe of 18 MHz in greyscale (GS) and 8.0 MHz in power doppler (PD). The exams were performed in a room with temperature between 22°C and 26°C, after a 10 minutes rest period. Patients were seated, with hands and fingers in a neutral position over the table. The nails were scanned on a longitudinal plane. The 2nd and 3rd fingernails of both hands were examined. Through GS, the following characteristics were assessed: 1) the trilaminar appearance of the nail plate (NP), that was classified according to Wortsman characterization of changes on psoriatic nails (I – IV), 2) the nail plate thickness (NPT), 3) the nail bed thickness (NBT), and 4) the nail matrix thickness (NMT). The signal of PD in the nail matrix and in the nail bed were evaluated together and classified according to Gutierrez *et al.*'s score (1-3). Comparisons between independent means were analyzed using ANOVA or Kruskal-Wallis test. The association between categorical variables was calculated by chi-squared test or Fisher's exact test.
Results: In the trilaminar structure (TS) evaluation, 137(99.3%) of the nails from control group had no change in the TS; for PsO group, 32 of the analyzed nails presented TS alterations, as follows: 9 type I, 5 type II, 7 type III and 11 type IV. For PsA group, there were also 32 of the analyzed nails that presented TS changes; 4 type I, 15 type II, 9 type III and 4 type IV. The mean NPT± SD (mm) was higher on both PsA and PsO groups when compared to the control group: 0.73 ±0.14 and 0.72 ±0.15 vs.0.67±0.10 (p=0.001), respectively. NBT and NMT means did not differ among groups. There was also no statistical difference between groups regarding the degree of nail PD, as well as no difference in the grayscale and PD evaluated parameters between PsA/PsO nails both with or without clinical involvement.
Conclusion: Alterations of the trilaminar structure of the NP and the NPT show differentiation between psoriatic nails and the control group, but no differentiation between PsO and PsA nails. PD, NMT and NBT means also had no differences between groups. Studies with larger sample sizes are necessary to clarify the utility of these parameters in the evaluation of psoriatic patients.

REFERENCES:

[1] Wortsman C X, Holm EA, Jemec GB, Gniadecka M, Wulf HC. Ultrasonido de Alta Resolucion en el estudio de la uña psoriatica. *Rev Chil Radiol.* 2004;10(1).
[2] Gutierrez M, Di Geso L, Salaffi F, Bertolazzi C, Tardella M, Filosa G, Filippucci E, Grassi W. Development of a preliminary US power Doppler composite score for monitoring treatment in PsA. Rheumatology. 2012 Jul;51 (7):1261-8.

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FRI0424 **DIFFERENCES AND SIMILARITIES ACCORDING TO GENDER IN PATIENTS WITH PSORIATIC ARTHRITIS INITIATING BIOLOGICAL THERAPY**

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Background: The evolution of the disease is heterogeneous among patients with psoriatic arthritis (PsA). Specifically, the influence of gender on the disease outcomes (and the need of a more intensive treatment) has been pointed. However, data regarding this are scarce.
Objectives: to analyse the disease profile in male and female patients with PsA starting biological treatment.
Methods: Data from an observational prospective cohort including all patients with PsA initiating biological therapy from 2002-2018 in a university hospital was conducted. Demographic information, laboratory tests, disease presentation (axial presentation, including oligoarticular affection, and poliarticular presentation), disease activity indexes (ASDAS and DAPSA for axial and peripheral-only presentations, respectively) and concomitant treatment were collected before starting biological drug. Patients were stratified by gender to compare the characteristics of the populations. Chi-squared for categorical and tstudent tests for continuous variables were used to analyse the differences between groups.
Results: Out of 109 included patients, 55 (51%) were males and 54 (49%) females. Baseline gender-stratified characteristics are shown in Table 1. Including the whole population of the study, mean age at diagnosis was 57 ± 14.6 years, mean PsA duration was 17.7 ± 9.2 years, and mean Body Mass Index (BMI) was 27.2 ± 4.9. Axial or oligoarticular presentation was shown in 57 patients (52%), whereas 52 patients (48%) had poliarticular manifestations. Mean baseline ASDAS was 3.2 ± 1.0 and mean baseline DAPSA was 25.4 ± 13.6. Biological therapies initiated included etanercept in 42% of the cases, infliximab in 25%, adalimumab in 19%, golimumab in 7% and secukinumab in 6%. No significant differences were observed between genders for most of the characteristics including: age at starting biologic, disease duration, BMI, smoking habit, positive HLA B27 and rheumatoid factor, baseline activity, baseline ESR, baseline CRP, baseline sulfasalazine (SSZ), baseline prednisone (PRD), baseline patient global assessment and biological drug use. However, there were substantial differences between gender in some other characteristics. While males had more frequently a predominant axial disease (p=0.01), females more frequently presented a poliarticular disease (p=0.02) and received methotrexate more frequently (p=0.02). These differences in methotrexate use might be explained by the predominance of peripheral presentation in female patients.
Conclusion: In clinical practice, biological therapy (TNFi and IL-17i) is prescribed in a similar frequency in male and female patients with PsA. Nevertheless, the predominant articular manifestation behind the prescription of the biological therapy is different among genders: while men have predominant axial disease, women have predominant peripheral manifestations. These differences in clinical presentation in both genders may contribute to differences in therapeutic management, such as increased use of methotrexate in women with PsA who initiate biological therapy.

Table 1. Gender-stratified characteristics at the visit starting the biological therapy. Results are shown as mean (standard deviation) or absolute number (percentage).

	Male n=55 (51 %)	Female n= 54 (49 %)	p-value
Age (years)	55.8 (12.2)	58.3 (16.7)	0.2
Disease duration (years)	17.3 (7.3)	18.1 (10.9)	0.6
BMI	27.7 (3.8)	26.7 (5.9)	0.3
Smokers & ex smokers	19 (34.5%)	19 (35.2 %)	1.0
HLA B27	8/28 (28.6 %)	3/20 (15.0 %)	0.3
RF	2/47 (4.3%)	4/48 (8.3%)	0.4
Axial and/or Oligoarticular manifestations	37 (67.3%)	20 (37.2 %)	**0.01**
Poliarticular manifestations	18 (32.0%)	34 (63.1 %)	**0.02**
bASDAS	3.1 (1.0)	3.3 (1.0)	0.5
bDAPSA	21.3 (11.8)	29.4 (15.5)	0.08
bESR	19.8 (19.2)	31.6 (19.7)	0.2
bCRP mg/L	11.9 (16.16)	9.6 (10.7)	0.1
Baseline PGA	45.1 (20.8)	50.4 (20.8)	0.4
Baseline MTX	27 (49.1 %)	38 (70.4 %)	**0.02**
Baseline SSZ	10 (18.2 %)	8 (14.8 %)	0.6
Baseline PRD	14 (25.5%)	20 (37.1 %)	0.2
Infliximab	15 (27.3 %)	12 (22.2 %)	0.9
Adalimumab	6 (10.9 %)	15 (27.8 %)	0.2
Etanercept	24 (43.6 %)	22 (40.7 %)	0.8
Golimumab	6 (10.9 %)	2 (3.7 %)	0.4
Secukinumab	4 (7.3 %)	3 (5.6 %)	0.9

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FRI0425 **LITERATURE REVIEW OF PATIENT PERSPECTIVES ON THE MANAGEMENT AND TREATMENT OF PSORIATIC ARTHRITIS**

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Background: A patient-centred approach to the management and drug treatment of psoriatic arthritis (PsA) has been advocated by a multidisciplinary group of experts to improve skin and joint symptoms and health-related quality of life (HRQoL).[1]
Objectives: To examine perspectives of patients with PsA on: (1) disease management and treatment goals, (2) disease management and treatment satisfaction, and (3) treatment adherence, including reasons for discontinuation. Areas of interest were those related to medication, symptom resolution, everyday living and overall HRQoL.
Methods: A targeted literature review was conducted to identify peer-reviewed literature on patient experience with PsA management and drug-treatment. English-language articles published between 1 January 2010–8 October 2018 reporting qualitative or quantitative evidence from cross-sectional or longitudinal observational studies were identified from searches conducted using MEDLINE (via PubMed) and Embase. Selection criteria included adult patients with PsA (self-reported or clinician-diagnosed); drug-treatment studies could consider only regulatory-approved treatments for PsA and other studies had to provide evidence of patient perspectives on disease management and treatment goals, experiences and/or satisfaction. Studies involving paediatric/adolescent populations were excluded, as were results for PsA were not distinguishable from other diseases.
Results: The literature search identified 266 titles, of which 48 duplicates were removed. The remaining 218 abstracts were screened: 58 full-text articles were assessed for eligibility and 16 articles were selected for full-text review. Of these 16 articles, 9 were primarily related to patient perspective on disease management, 6 to patient satisfaction and 1 to treatment adherence; some articles covered more than one of these objectives. None of the articles studied whether explicit consideration of treatment goals from the patient perspective would influence management or outcome of care. Symptom resolution, reduced fatigue, improved sexual relations, improved HRQoL and ability to participate in daily activities were consistently identified by patients as important aspects for disease management and daily living with PsA. Articles on patient satisfaction focused largely on general satisfaction with medication rather than satisfaction specifically with holistic PsA management. Notwithstanding, symptom resolution was clearly linked to greater patient satisfaction with medication. Patient dissatisfaction with PsA treatment was influenced by their attitude towards treatment, concerns about PsA medication, the physician-patient relationship and lack of patient involvement in decision-making. Treatment adherence has not been widely explored but mainly relates to perceptions about, and experiences with, medications, including efficacy and adverse events.
Conclusion: This literature review identified a lack of research on patient perspectives of PsA management and treatment goals. It also highlighted the lack of patient involvement in determining management and/or setting personal goals, which may ultimately affect satisfaction. There remains a lack of clarity on PsA symptoms and other disease- or patient-related parameters that impact patient satisfaction/dissatisfaction and patient-centred reasons for treatment discontinuation. The findings of this review will be used to develop a PsA patient survey to further explore patient perspectives to improve care in PsA.

REFERENCES:

[1] Betteridge N, et al. J Eur Acad Dermatol Venereol 2016; 30: 576–85.

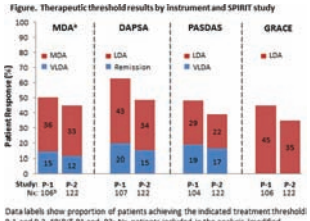
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FRI0426 **IXEKIZUMAB MAKES REMISSION AND LOW DISEASE ACTIVITY POSSIBLE IN PATIENTS WITH PSORIATIC ARTHRITIS: TWO-YEAR RESULTS IN TNF INADEQUATE RESPONDERS OR BIOLOGIC-NAÏVE PATIENTS**

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Background: Psoriatic arthritis (PsA) is a heterogeneous inflammatory disease that can involve peripheral and axial joints, skin, and entheses. A number of validated composite indices have been developed, not only to measure overall disease activity for PsA, but also to provide thresholds for treat-to-target goals. These include MDA (Minimal Disease Activity), DAPSA (Disease Activity in PsA), and PASDAS (PsA Disease Activity Score). We have previously demonstrated that higher proportions of PsA patients treated with ixekizumab (IXE), a monoclonal antibody that selectivity targets interleukin-17A, achieved therapeutic thresholds defined by MDA, DAPSA, and PASDAS versus placebo (PBO) up to Week 24.[1]
Objectives: To explore the extent to which IXE can help biologic-naïve and tumor necrosis factor inhibitor (TNFi) inadequate responder patients achieve treat-to-target goals, as defined by composite indices incorporating multiple disease domains, through 108 weeks of treatment.
Methods: Data were analyzed from all patients initially randomized to 80 mg IXE every 4 weeks after a 160-mg starting dose in 2 double-blind, PBO-controlled phase III trials investigating the efficacy and safety of IXE. For SPIRIT-P1 (NCT01695239), patients (N=107) were bDMARD naïve. For SPIRIT-P2 (NCT02349295), patients (N=122) had an inadequate response or were intolerant to TNFis. The following composite measures and definitions were used: MDA and Very Low Disease Activity (VLDA) (see Figure); DAPSA Low Disease Activity (LDA) (≤14 and >4) and remission (≤4); PASDAS LDA/VLDA (≤3.2/≤1.9); and GRACE (GRAppa Composite score) LDA (≤2.3). Modified nonresponder imputation (mNRI; missing data treated as nonresponse for patients discontinued due to lack of efficacy or adverse events; multiple imputation for all other missing data) was used for all analyses.
Results: Therapeutic threshold results at Week 108 are summarized in the Figure. Whether measured using MDA, DAPSA, PASDAS, or GRACE, the proportions of IXE-treated patients achieving designated therapeutic thresholds were sustained through 2 years of treatment. Efficacy was similar between SPIRIT-P1 and SPIRIT-P2.

Figure. Therapeutic threshold results by instrument and SPIRIT study



Data labels show proportion of patients achieving the indicated treatment threshold. P-1 and P-2, SPIRIT-P1 and -P2; Nx, patients included in the analysis (modified nonresponder imputation applied). †MDA was achieved if 5 to 6, and VLDA was achieved if 7 of 7, of the following criteria were met: tender joint count ≤1; swollen joint count ≤1; Psoriasis Area and Severity Index total score ≤1 or body surface area ≤3%; patient's assessment of pain visual analog scale (VAS) ≤15; patient's global assessment of disease activity VAS ≤20; Health Assessment Questionnaire Disability index ≤0.5; and tender entheseal points ≤1 (assessed by the Leeds Enthesitis Index). *Nx=106 for MDA; 107 for VLDA.

Conclusion: High proportions of IXE-treated patients, whether biologic naïve or TNFi inadequate responders, achieved treat-to-target goals, as defined by composite indices incorporating multiple disease domains, through 2 years of treatment.

REFERENCES:

[1] Coates L, et al. Ann Rheum Dis. 2018;77(Suppl):A375.

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FRI0427 IS THE CLINICAL AND THERAPEUTIC PROFILE RELATED TO SATISFACTORY RESPONSE TO APREMILAST IN PSORIATIC ARTHRITIS?

Isabel de la Morena[1], María Espinosa[2], Hilda Godoy Tunidor[3], À Martínez-Ferrer[4], Carlos Santos Ramirez[5], Anna Martinez[6], Meritxell Fernandez Matilla[7], Nagore Fernández-Llanio[7], Deseada Palma Sanchez[8], Maria Jose Moreno[8], Ana Haro[8], Arantxa Conesa[9], Javier Calvo[10]. *[1]Hospital Clinico Universitario de Valencia, Valencia, Spain*; *[2]Hospital Puerta de Hierro, Madrid, Spain*; *[3]Hospital Puerta de Hierro, Rheumatology, Madrid, Spain*; *[4]Hospital Doctor Peset, Rheumatology, Valencia, Spain*; *[5]Hospital Virgen de los Lirios, Alcoy, Spain*; *[6]Hospital de la Ribera, Rheumatology, Alzira, Spain*; *[7]Hospital Arnau de Vilanova, Valencia, Spain*; *[8]Hospital Rafael Mendez, Lorca, Spain*; *[9]Hospital General de Castellón, Castellón, Spain*; *[10]Hospital General Universitario de Valencia, Valencia, Spain* **Objectives:** To identify the factors that are related with response to Apremilast(APR) in Psoriatic Arthritis(PsA).

Methods: An observational and analytical multicenter retrospective study. There are included PsA patients treated with APR after two years of commercialization. Clinical and demographic data were collected: disease duration, previous treatments, cutaneous and joint involvement pattern defined as: joint exclusively, non joint and mixed (by several domains combination). It was collected: duration of treatment, tolerance, adverse events, and reason for APR choice: intolerance or toxicity to csDMARD, preference before bDMARD contraindication or caution to bDMARD, csDMARD and bDMARD inefficacy, csDMARD and bDMARD intolerance. The effectiveness was considered as a dicotomic variable (Yes/No) by clinical criteria.

Results: There were included 89 patients, 46(51.7%) males, the mean age was 53.99±12.3 years, and the PsA disease duration was 7.28±6.25 years. The PsA pattern was: joint 29(32.6%), non joint, 12(13.5%) and mixed 48(53.9%). The reason for APR choice was: intolerance or toxicity to cDMARD 13 patients, preference before BT 28, contraindication or caution to BT 22, inefficacy to cDMARD or BT 18, intolerance to cDMARD and BT 1, and due to clinical profile 1. After a mean treatment duration with APR of 8.13(0-23) months a total of 33 withdrawals were found (17 due to inefficacy and 16 due to intolerance), treatment was mantained on them a mean of 4.3(0-12) months. 56 patients keep with APR a mean of 10.4(2-23) months, 22 of them among 1 and 2 years of evolution. The treatment was effective in 61(68.5%) patients. Comparisons of the different variables analyzed did not show significative differences among the responders and non responders patients.

Conclusion: We have not found a specific profile that relates with a satisfactory response to APR.

Disclosure of Interests: Isabel de la Morena Speakers bureau: Abbvie, Celgene, Pfzier, UCB, Ghebro, Roche, Sanofi, Janssen., María Espinosa: None declared, Hilda Godoy Tunidor: None declared, À Martínez-Ferrer: None declared, Carlos Santos Ramirez: None declared, Anna Martinez: None declared, Meritxell Fernandez Matilla: None declared, Nagore Fernández-Llanio: None declared, DESEADA PALMA SANCHEZ: None declared, Maria jose Moreno: None declared, Ana HARO : None declared, Arantxa Conesa: None declared, Javier Calvo Consultant for: Abbvie, Celgene, Pfzier, UCB, Ghebro, Roche, Sanofi, Janssen, Novartis, Amgen., Speakers bureau: Abbvie, Celgene, Pfzier, UCB, Ghebro, Roche, Sanofi, Janssen, Novartis, Amgen.

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FRI0428 PSORIATIC ARTHRITIS AND DEPRESSIVE SYMPTOMS: DOES SYSTEMIC INFLAMMATION PLAY A ROLE?

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Background: Depression is one of the most common comorbidities in patients with Psoriatic Arthritis (PsA) but risk factors for mood disorders in these patients are still largely unrecognized. Pro-inflammatory cytokines involved in the pathogenesis of PsA have been also associated with depressive symptoms in patients without systemic autoimmune diseases.

Objectives: The aim of this study is to determine risk factors for depressive symptoms and compare serum cytokines concentrations in subjects with and without depressive symptoms in a court of PsA patients.

Methods: Eighty consecutive patients with PsA were screened for depressive symptoms with depression subscale of the Hospital Anxiety and Depression Scale (HADS-D). A validated cut-off of 8 was used to define patients with significative depressive mood. Patients with and without depressive symptoms were compared for the prevalence of general risk factors for depression, comorbidity, psoriatic disease age of onset, duration, activity and domains affected, treatment and serum levels of IL-6, TNF-α and IL-17A.

Results: Mean disease duration of skin disease and articular disease was 18.8 ± 15.3 years and 9.0 ± 11.1 years, respectively. All patients had a history of peripheral arthritis, 41.3% had dactylitis, 38.8% had enthesitis, 21.3% had spondylitis 82.5% had a psoriatic skin disease and 51.2% had psoriatic nail disease. According to DAPSA index, 20.0% were in remission, 50.0% in Low Disease Activity, 20.0% in Moderate Disease Activity and 10.0% in High Disease Activity. Thirty-five (43.8%) were in Minimal Disease Activity. Thirty-three patients (41.3%) had depressive symptoms according to HADS. Patients with and without depressive symptoms did not differ in terms of age, gender, comorbidity, general risk factors of depression, psoriatic disease age of onset, duration, domains affected, DAPSA activity, MDA achievement, PASI, HAQ, VAS pain, the intensity of treatment, serum TNF-α IL-17A and IL-23. Serum levels of IL-6 were higher in patients with depressive symptoms. (2.99±2.58 vs 1.54±1.60 pg/dl; p=0.006). A cut-off of 2.27 pg/ml of serum IL-6 had the best ability to predict a HADS$\geq$8 according to higher Youden Index of the ROC curve (AUC 0.682±0.061; p=0.006). Multivariate logistic regression analysis revealed that serum IL-6$\geq$2.27 pg/ml was a predictor of depressive symptoms even when adjusted for DAPSA, HAQ and PASI (OR 3,06; CI 1.14-8.20; p = 0.026).

Conclusion: Higher serum Il-6 is associated with depressive symptoms independently from articular and cutaneous disease activity and degree of disability. This association suggest a direct role of systemic inflammation in the modulation of mood in PsA patients.

REFERENCES:

[1] Husni ME, et al. The psychosocial burden of psoriatic arthritis. Semin Arthritis Rheum 2017.
[2] Ogata A, et al. Pathological Role of Interleukin-6 in Psoriatic Arthritis. Arthritis 2012.
[3] Hodes GE et al. Integrating Interleukin-6 into depression diagnosis and treatment. Neurobiol Stress 2016.
[4] Zigmond AS et al. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983.

Disclosure of Interests: Enrico De Lorenzis: None declared, Gerlando Natalello: None declared, Dario Bruno: None declared, Giacomo Tanti: None declared, Giovanni Battista Canestrari: None declared, Maria Rosaria Magurano: None declared, Clara Di Mario: None declared, Barbara Tolusso: None declared, Giusy Peluso: None declared, Elisa Gremese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer

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FRI0429

NON TOPICAL PHARMACOLOGICAL TREATMENT OF EARLY, UNTREATED (DMARD-NAÏVE, SYSTEMIC THERAPY-NÄIVE) PSORIATIC DISEASE: A SYSTEMATIC REVIEW

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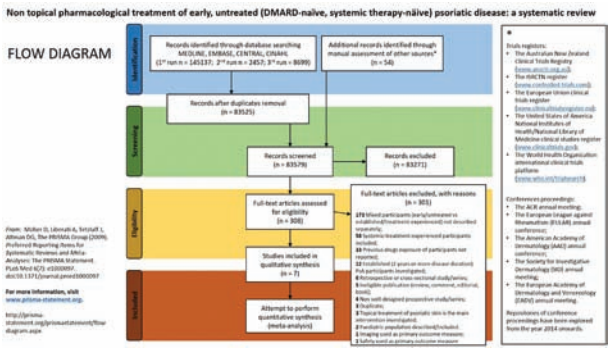
Background: Psoriatic disease (PsD) refers to a systemic condition, probably driven by chronic and complex inflammatory mechanisms. PsD patients experience a fickle mixture of cutaneous (nail dystrophy, psoriatic lesions spectrum) and musculoskeletal (MSK: arthritis, enthesitis, dactylitis, spondylitis) inflammatory features, variously associated with other co-morbidities (ocular or bowel inflammatory disease, increased cardiovascular risk and metabolic syndrome).
Current evidence is limited in respect of the management of early, treatment-naïve PsD.
Objectives: To assess the literature with a focus on pharmacological interventions in early, treatment-naïve PsD.
Methods: Seven research questions were formulated according to the PICO approach: are interventions effective in obtaining control of overall PsD activity? Are interventions effective on peripheral arthritis? On dactylitis? On spondylitis? On enthesitis? On skin and nails?
The search was designed as a systematic review of the literature. Early PsD was defined as disease duration ≤2 years, except for studies investigating outcomes restricted to the skin.
Criteria for including records were: adult human participants; participants with cutaneous features of PsD; participants with MSK features of PsD; double blind, single blind and non-blinded RCT; well-designed prospective studies/series.
The search protocol was registered on PROSPERO [1], the search was performed between June 2018 and January 2019.
Results: Resources available were widely explored (4 databases, 5 trial registers, 5 conference archives; see figure). The search retrieved 156,348 references (publication range 1946–2019) of which 308 (0.2%) qualified for full-text-assessment (FTA, figure); 7 (0.0004%) fulfilled the selection criteria and only 4 underwent data extraction.

Ref. type	PsD feature targeted	Intervention (success)	Primary outcome
1 RCT	Skin	Secukinumab (yes) vs fumarates (no)	PASI75
2 cohort	MSK	MTX part of T2T (yes)	Unclear
3 RCT	MSK	MTX (partial)	Joint count
4 RCT	Skin	Apremilast (yes)	PGAxBSA

Meta-analysis was impossible due to data heterogeneity (disease classification criteria, outcome measures and intervention durations). Although no clinical study adopted comprehensive composite indexes as primary outcome measures, 40% of FTA references described more than one component of PsD (i.e.: cutaneous and MSK) at least within the baseline characteristics. A substantial proportion of FTA references did describe, among participants recruited, many who were early untreated PsD at baseline. Unfortunately, separate analyses were not possible due to unavailability of the original datasets. A subset (10%) of the FTA references did not report on the participants' exposure to previous treatment.
Conclusion: Few studies addressed early, treatment naïve PsD. The underrepresentation of such data may be related to trial-enrolment criteria. More studies are needed to investigate this identified unmet need.

REFERENCES:

[1] http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018097366



Figure

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FRI0430

IXEKIZUMAB IMPROVES THE SIGNS AND SYMPTOMS OF PSORIATIC ARTHRITIS REGARDLESS OF SEX, DURATION OF DISEASE, OR BODY MASS INDEX IN TWO RANDOMIZED, PHASE 3 CLINICAL TRIALS

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Background: Ixekizumab (IXE) is a high-affinity monoclonal antibody that selectively targets interleukin-17A. During 24 weeks (wks) of treatment, IXE resulted in significantly greater improvements versus placebo (PBO) in the signs and symptoms of active psoriatic arthritis (PsA) in two randomized Phase 3 studies.[1,2]
Objectives: To evaluate the consistency of clinical response with IXE in demographic subsets of patients (pts) with active PsA.
Methods: Clinical response to IXE was analyzed from an integrated database of 2 randomized, double-blind, Phase 3 studies in biologic Disease

Modifying Anti-Rheumatic Drug (bDMARD)-naïve (SPIRIT-P1) pts or in pts with prior inadequate response or intolerance to TNF inhibitors (SPIRIT-P2). Analyses were conducted on subgroups defined by sex, body mass index (BMI), and duration of disease (<5 or ≥5 years) at baseline for pts who were randomly assigned to either PBO or the approved dosing regimen of IXE (80 mg IXE every 4 wks [IXE Q4W] with a starting dose of 160-mg IXE). Efficacy in each subgroup was evaluated as the percentage of pts at Wk 24 achieving ≥20%, 50%, or 70% improvement from baseline in the American College of Rheumatology criteria (ACR20/50/70) or minimal disease activity. Missing data were imputed using nonresponder imputation (NRI).

Clinical responses in demographic subgroups at Week 24 (NRI)

	ACR20		ACR50		ACR70		MDA	
	PBO (N=224)	IXE Q4W (N=229)	PBO (N=224)	IXE Q4W (N=229)	PBO (N=224)	IXE Q4W (N=229)	PBO (N=224)	IXE Q4W (N=229)
Sex								
Male	23/104 (22)	67/108 (62)†	12/104 (12)	51/108 (47)†	3/104 (3)	31/108 (29)†	9/104 (9)	38/108 (35)†
Female	32/120 (27)	60/121 (50)†	10/120 (8)	35/121 (29)†	3/120 (3)	21/121 (17)†	11/120 (9)	28/121 (23)‡
Time since symptom onset, years								
0 to <5	21/63 (33)	39/71 (55)*	11/63 (18)	28/71 (39)‡	3/63 (5)	18/71 (25)†	11/63 (18)	24/71 (34)*
≥5	34/161 (21)	88/158 (56)†	11/161 (7)	58/158 (37)†	3/161 (2)	34/158 (22)†	9/161 (6)	42/158 (27)†
BMI category, (kg/m²)								
Underweight (<18.5)	0/0 (0)	0/3 (0)	0/0 (0)	0/3 (0)	0/0 (0)	0/3 (0)	0/0 (0)	1/3 (33)
Normal (≥18.5 and <25)	13/39 (33)	30/49 (61)*	6/39 (15)	20/49 (41)*	4/39 (10)	11/49 (22)	7/39 (18)	15/49 (31)
Overweight (≥25 and <30)	19/90 (21)	37/67 (55)†	10/90 (11)	29/67 (43)†	2/90 (2)	20/67 (30)†	9/90 (10)	25/67 (37)†
Obese (≥30 and <40)	18/74 (24)	47/84 (56)†	6/74 (8)	29/84 (35)†	0/74 (0)	18/84 (21)†	4/74 (5)	21/84 (25)†
Extreme Obese (≥40)	5/20 (25)	11/24 (46)	0/20 (0)	6/24 (25)*	0/20 (0)	2/24 (8)	0/20 (0)	3/24 (13)

Data are provided as n/Ns (%) where n=number of responders and Ns=number of patients in each subgroup
p-values from Fisher's exact test. *=p<0.05, ‡=p<0.01, †=p<0.001
ACR20/50/70 = ≥20%, 50%, or 70% improvement from baseline in the American College of Rheumatology criteria; BMI = body mass index; IXE Q4W = 80 mg IXE every 4 wks, MDA = minimal disease activity; NRI = nonresponder imputation; PBO = Placebo

Results: Response rates at Wk 24 (Table) were significantly (p<0.05) greater in pts receiving IXE versus PBO across all endpoints assessed in subgroups defined by sex, disease duration, and in pts with overweight and obese BMI at baseline. Response rates were significantly greater with IXE compared to PBO for ACR20 and ACR50 in the normal BMI subgroup and for ACR50 in the extreme obese BMI subgroup. Assessment of superiority of IXE versus PBO in underweight and extreme obese subgroups was limited by small sample sizes; only three patients (all receiving IXE Q4W) had underweight BMI at baseline. For all endpoints assessed, numerically greater response rates were observed with IXE Q4W in male versus female pts.

Conclusion: IXE was superior to PBO in the treatment of pts with active PsA at Wk 24 regardless of sex or disease duration, as well as in normal, overweight, and obese BMI subgroups.

REFERENCES:

[1] Mease, et al. Ann Rheum Dis. 2017
[2] Nash, et al. Lancet. 2017

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FRI0431 EFFECT OF PHOSPHODIESTERASE 4 INHIBITION WITH APREMILAST ON BODY WEIGHT AND VASCULAR FUNCTION IN PSORIATIC ARTHRITIS – INITIAL RESULTS FROM THE IMMUNE METABOLIC ASSOCIATIONS IN PSORIATIC ARTHRITIS (IMAPA) STUDY

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Background: Psoriatic arthritis (PsA) is associated with obesity and increased cardiometabolic risk. Weight loss is associated with improved disease activity and has been noted with the phosphodiesterase 4 (PDE4) inhibitor apremilast.

Objectives: To investigate the effects of PDE4 inhibition with apremilast on body weight, vascular function and disease activity in psoriatic disease.

Methods: The Immune Metabolic Associations in Psoriatic Arthritis (IMAPA) study is a prospective, open label study of adults receiving apremilast 30mg BD as part of routine care for psoriasis and/or PsA. Cardiometabolic, anthropometric, and disease activity assessments were performed at baseline, months 1, 3, and 6. A subgroup underwent endothelial function assessment by Endo-PAT at baseline and month 3. Repeated measures mixed models were used to compare changes in body weight, waist circumference, systolic & diastolic BP, reactive hyperaemia index (RHI), and disease activity markers with apremilast.

Results: 53 participants were recruited; mean age (SD) 52 (13) years, 64% female, mean disease duration (SD) 9.3 (8.1) years. To date, data available for n=47 at month 1, n=42 month 3, and n=29 at month 6. Mean weight loss after 6 months apremilast was -1.9kg (95% CI -2.8, -1.0); 13% (7/53) lost ≥5% body weight. Statistically significant improvements in 66/68 joint count, DAS28-ESR, PtGA, PGA, pain-VAS, LEI, and ESR were seen at month 6. There was no statistically significant change in RHI, SBP, or DBP (table 1). Weight change showed no statistically significant correlation with change in joint or skin disease activity markers.

Conclusion: Apremilast was associated with modest weight loss and reduced disease activity over 6 months. There did not appear to be any significant alteration in endothelial function, however this was assessed in relatively small numbers and many patients had baseline results within normal range. Improvements in disease activity with apremilast appear largely independent of weight change in this cohort.

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Table 1. Baseline and follow-up metabolic, vascular, and disease activity markers. Values are mean (SD) or mean (95% CI).

Variable	Baseline N=52	Change at Month 1* N=47	Change at Month 3* N=42	Change at Month 6* N=29
Weight (kg)	95.8 (23.1)	-1.1 (-1.9, -0.4)‡	-1.3 (-2.1, -0.5)‡	-1.9 (-2.8, -1.0)‡
BMI (kg/m^2)	34.3 (8.7)	-0.4 (-0.7, -0.05)‡	-0.3 (-0.7, 0.02)	-0.7 (-1.0, -0.3)‡
Waist circumference (cm)	107.8 (18.0)	-1.6 (-3.3, 0.2)	-1.0 (-2.9, 0.8)	-0.9 (-3.1, 1.2)
SBP (mmHg)§	132.9 (20.7)	-1.5 (-5.8, 2.8)	-0.6 (-5.1, 3.8)	-2.1 (-7.2, 3.0)
DBP (mmHg)	77.7 (12.2)	2.5 (-0.2, 5.2)	1.7 (-1.1, 4.5)	0.5 (-2.7, 3.7)
RHI†	2.33 (0.55)	-	-0.15 (-0.38, 0.09)	-
66 Swollen Joint Count	8.7 (6.1)	-3.0 (-4.9, -1.1)‡	-2.5 (-4.5, -0.5)‡	-2.7 (-4.9, -0.4)‡
68 Tender Joint Count	12.5 (9.8)	-2.3 (-4.5, -0.1)‡	-0.7 (-3.0, 1.5)	-2.9 (-5.5, -0.3)‡
DAS28-ESR	4.3 (1.2)	-0.3 (-0.6, 0.0)	-0.3 (-0.6, 0.0)	-0.4 (-0.7, -0.03)‡
Patient global assessment	56.4 (23.8)	-7.5 (-15.0, 0.0)	-7.6 (-15.4, 0.2)	-9.7 (-18.5, -0.8)‡
Physician global assessment	55.2 (20.2)	-18.2 (-24.9, -11.5)‡	-23.4 (-30.4, -16.4)‡	-24.4 (-32.5, -16.4)‡
Pain VAS	52.3 (24.8)	-7.8 (-15.8, 0.2)	-9.0 (-17.3, -0.6)‡	-12.2 (-21.7, -2.8)‡
LEI	1.6 (1.6)	-0.3 (-0.6, 0.1)	-0.6 (-1.0, -0.2)‡	-0.6 (-1.1, -0.2)‡
PASI	6.2 (8.5)	-2.4 (-3.8, -1.0)‡	-2.6 (-4.0, -1.2)‡	-1.5 (-3.1, 0.2)
CRP (mg/dl)	12.3 (20.8)	-3.7 (-7.6, 0.2)	-5.8 (-9.9, -1.8)‡	-2.7 (-7.2, 1.8)
ESR (mm/hour)	18.3 (13.7)	-0.3 (-0.6, 0.0)	-0.3 (-0.6, 0.0)	-0.4 (-0.7, -0.03)‡

*All changes compared to baseline. †RHI: reactive hyperaemia index, normal >1.67. n=32 at baseline, n=26 at month 3. §26% (14/53) on antihypertensives. ‡ p<0.05.

FRI0432 **CLINICAL EXAMINATION AND ULTRASOUND IN THE ASSESSMENT OF PATIENTS WITH PSORIATIC ARTHRITIS WITH AND WITHOUT FIBROMYALGIA**

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Background: Evaluating psoriatic arthritis (PsA)-related enthesitis is diagnostically and therapeutically essential, but may be very complex because of the wide range of signs and symptoms that partly overlap or co-exist with the clinical features of fibromyalgia (FM) [1,2].
Objectives: The primary aim was to compare the prevalence of clinical and ultrasonographic signs of enthesitis in patients with PsA, FM, or both. The secondary aim was to assess the impact of FM on disease activity and clinimetric scores.
Methods: This single-centre, observational cross-sectional study involved 101 consenting patients: 39 with PsA (CASPAR criteria), 23 with FM (2016 criteria), and 39 with both. Standard PsA and FM clinical, laboratory and clinimetric data were recorded. Disease activity in PsA and PsA-FM patients was assessed using BASDAI and ASDAS. The entheses were assessed using LEI and MASES score. All of the patients underwent B mode (grey scale) ultrasonography, the US findings were scored using the GUESS.
Results: The mean age of the patients was 53.6 years, SD ± 9.47. Females accounted for 64.1% of the PsA patients (disease duration 9.13 years, SD ± 5.9), 95.6% of FM patients (disease duration 5.09 years, SD ± 3.6), and 92.3% of the patients with PsA-FM (disease duration 7.9 years, SD ± 5.5). There were no between-group differences in the patients' BMI. None of the FM subjects reported any personal or family history of psoriasis. The mean PASI was 2.3 ± 3.1 in the PsA group, and 1.2 ± 2.45 in the PsA-FM group. The median BASDAI was significantly higher in PsA-FM vs PsA group (7.7 [IQR 2.1] *vs* 5.0 [IQR 3.8]; p<0.001), as well the median ASDAS score ESR-assessed (3.69 [IQR 1.00] *vs* 2.82 [IQR 1.55]; p=0.004), or PCR- assessed (median 3.27 [IQR 1.07] *vs* 2.66 [IQR 1.26]; p = 0.006). Clinical evidence of enthesopathy was found in 43% of PsA, 51.3.8% of PsA-FM, and 50.8% of FM, while US entheseal abnormalities were detected in respectively 65%, 54.6% and 30%. The median MASES was significantly higher in FM or PsA-FM than in PsA group (p<0.001), no statistically significant difference between FM *vs* PsA-FM groups (6 [IQR 2] *vs* 7 [IQR 3]; p=0.737). The median LEI was significantly higher in FM or PsA-FM groups(p<0.001),with no statistically significant difference between these two groups(6 [IQR 2] *vs* 7 [IQR 3]; p=0.658). The median GUESS was significantly higher in PsA *vs* FM group (9 [IQR 7.5] *vs* 3 [IQR 2]; p<0.001), and in PsA-FM vs FM group (8 [IQR 4.5] *vs* 3 [IQR 2]; p<0.001). No statistically significant difference between PsA and PsA-FM group (9 [IQR 7.5] *vs* 8 [IQR 4.5]; p<0.112). No statistically significant Spearman correlation coefficient(rho) was found between GUESS and MASES/LEI in any of the groups. There was a correlation between GUESS scores and disease duration in PsA (rho=0.37; p=0.019, 95% CI 0.10-0.61) or PsA-FM (rho=0.38; p=0.016, 95% CI 0.10-0.61), but not in the FM group, and GUESS scores correlated with BMI (rho=0.2; p=0.05, 95% CI 0.00-0.37) and dyslipidemia (rho=0.34; p=0.006, 95% CI 0.11-0.58) in all groups.
Conclusion: The use of a clinical examination and clinimetric scores alone may overestimate active enthesitis in FM patients. As US was more frequently positive in patients with PsA and PsA-FM than in those with FM, it may be useful in differentiating pain due to enthesitis from entheseal pain due to FM.

REFERENCES:

[1] Marchesoni A, et al. The problem in differentiation between psoriatic-related polyenthesitis and fibromyalgia. Rheumatology. 2018;57:32-40
[2] McGonagle D. Enthesitis: an autoinflammatory lesion linking nail and joint involvement in psoriatic disease.J Eur Acad Dermatol Venereol 2009;23:9–13

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FRI0433 **EFFECTS OF DISEASE MODIFYING DRUGS ON BONE MINERAL DENSITY, FRACTURE INCIDENCE, BACK PAIN AND PHYSICAL ACTIVITY IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS**

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Background: Reports on the prevalence of osteoporosis, osteoporotic fractures and risk factors for osteoporosis in patients with psoriasis (PSO) or psoriatic arthritis (PSOA) are scarce, and the published results on this are, at least in part, contradictory. [1] Despite the fact that IL-17 is involved in bone homeostasis under both physiologic and pathologic conditions, there is no detailed knowledge of the direct and indirect impact an IL-17 antagonist like secukinumab (SEC) has on bone mineral density (BMD).
Objectives: Rh-GIOP (ClinicalTrials.gov Identifier NCT02719314) is an ongoing prospective study monitoring glucocorticoid (GC)-induced osteoporosis of rheumatic patients, established in 2015 at the Charité University Hospital. For this analysis, clinical data and bone mineral density data measured by dual x-ray absorptiometry (DXA) of 936 patients with inflammatory rheumatic diseases provided the basis. The main objective of this cross-sectional analysis was to evaluate the prevalence of osteoporosis and the frequency of fractures in patients with PSO or PSOA. Additionally, patients treated with secukinumab were compared to those with methotrexate (MTX) with regard to BMD, fracture incidence, physical activity, and back pain
Methods: We analyzed the initial visit of 103 patients with PSO (n= 31, 74% female) or PSOA (n=72, 64% female). Descriptive analyses were performed, and values are displayed as means and standard deviations. For subgroup analyses non-parametric tests were used.
Results: The prevalence of osteoporosis in our patient group (mean age: 62±10 years; 67% female; mean disease duration: 17±13 years) was 19%. The prevalence of osteopenia was 26%, 34% (n=35) reported peripheral fragility fractures, and 11% (n=11) had vertebral fractures in history. Regular physical activity was reported by 41% (n=42), while 53% (n=55) suffered from movement restrictions. Back pain was present in 68% (n=70) of patients with a mean numeric rating scale of 5 (NRS; 0-

10). SEC was used by 18% (n=19), and MTX by 42% (n=43, 25% sc, 13% oral, 4% unknown), respectively. Eight percent had a combination therapy of MTX and SEC. Twenty-seven percent used GC and/or other biologics/conventional disease modifying antirheumatic drugs (DMARDs). Mean glucocorticoid cumulative dose (GCCD) was 12.8±22.0g. Patients with SEC showed a significantly longer disease duration (median: 24 years vs. 13 years) compared to MTX, but showed no other differences in baseline-characteristics or risk factors. T-Scores of both femora were significantly higher in the MTX versus the SEC group. We could not find significant differences between these groups with regard to physical activity, back pain, movement restriction, fracture rates or GCCD. Twenty-five percent of the MTX users and 27% of the patients in the SEC group additionally had GC while; in contrast to no patient in the combination group.

Conclusion: The prevalence of osteoporosis in patients with PSO or PSOA was found to be as high as in the normal population. However, there was a high frequency of peripheral fragility, but not vertebral fractures. Patients with PSO or PSOA patients treated with SEC had a longer disease duration and lower hip BMD, but showed no differences in back pain, physical activity or movement restrictions compared to MTX users.

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REFERENCES:

[1] Frediani, B., et al., Bone mineral density in patients with psoriatic arthritis. J Rheumatol, 2001. 28(1): p. 138-43.

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FRI0434 THE RELATIONSHIP BETWEEN SYMPTOMS OF AUTONOMIC DYSFUNCTION AND CARDIOVASCULAR INVOLVEMENT IN PSORIATIC ARTHRITIS

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Background: The incidence of cardiovascular disease (CVD), diabetes mellitus, metabolic syndrome and subclinical atherosclerosis is markedly increased in patients with psoriatic arthritis (PsA). The autonomic nervous system is the visceral nervous system of the body consisting of two parts; sympathetic and parasympathetic. Patients with PsA have predominantly parasympathetic involvement autonomic nervous system.

Objectives: The aim of this study was to evaluate the symptoms of autonomic dysfunction and their relationship with cardiovascular involvement and other clinic parameters in patients with PsA.

Methods: The study included patients diagnosed with PsA according to the CASPAR criteria. For evaluation of cardiovascular involvement, body mass index (BMI), abdominal obesity, hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), metabolic syndrome, fasting glucose levels, lipid levels, systolic and diastolic blood pressures (SBP-DBP) were assessed. DAPSA (Disease Activity in Psoriatic Arthritis), BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), Leeds enthesitis index, Psoriasis Area Severity Index (PASI), Psoriatic Arthritis Quality of Life (PsAQoL) and Health Assessment Questionnaire (HAQ) were used to assess patients clinical situations. The Composite Autonomic Symptom Score (COMPASS-31) (range:0-100) consisting of 6 subdivisions including orthostatic, vasomotor, secretomotor, gastrointestinal (GIS), bladder and pupillomotor was used for the symptoms of autonomic dysfunction. The Mann-Whitney U-test, student's t-test and Spearman's correlation coefficient were used for statistical analysis. P<0.05 was considered statistically significant.

Results: A total of 64 subjects (43 female, 21 male) with a mean of age 49 years (SD:12.3) and disease duration of 59 months (SD:71.3) were recruited into the study. The patients had HT (23.4%), DM (17.2%), abdominal obesity (62.5%), metabolic syndrome (45.3%) and dyslipidemia (42.2%). The mean total COMPASS-31 score was 19.7 (SD:8.3). There was no significant difference in COMPASS-31 scores in patients with or without HT, DM, dyslipidemia. Bladder scores were significantly higher in patients with abdominal obesity and metabolic syndrome (p<0.05). GIS and pupillomotor scores were significantly higher in patients with enthesis (p<0.05). Significant correlations were found between: LDL and bladder (r=0.392) scores; enthesis and GIS (r= 0.303), pupillomotor (r=0.365) scores; DAPSA and total COMPASS-31 (r=0.310), secretomotor (r=0.359) scores; BASDAI and total COMPASS-31 (r=0.483), GIS (r=0.327), secretomotor (r=0.309), pupillomotor (r=0.302) scores; fatigue and total COMPASS-31 (r=0.503), GIS (r=0.377), pupillomotor (r=0.302) scores; HAQ and total COMPASS-31 (r=0.476), orthostatic (r=0.388), bladder (r=0.371) scores; PsAQoL and total COMPASS-31 (r=0.601), orthostatic (r=0.549), secretomotor (r=0.414), pupillomotor (r=0.380) scores.

Conclusion: The total score of COMPASS-31 and its subdivisions were high in PsA patients as compared with literature data on healthy subjects. The symptoms of autonomic dysfunction were increased in PsA patients. Disease activity, functional impairment, fatigue, LDL and quality of life are associated with autonomic dysfunction. Autonomic symptoms improve with disease control.

REFERENCES:

[1] Sletten, D.M., et al., COMPASS 31: a refined and abbreviated Composite Autonomic Symptom Score. Mayo Clinic Proceedings, 2012. 87(12): p. 1196-1201.

[2] Syngle, A., et al., Autonomic dysfunction in psoriatic arthritis. Clin Rheumatol, 2013. 32(7): p. 1059-64.

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FRI0435 INFLUENCE OF BASELINE DEMOGRAPHICS AND DISEASE CHARACTERISTICS ON EFFICACY OF AN ORAL, SELECTIVE TYK2 INHIBITOR, BMS-986165, IN PATIENTS WITH PLAQUE PSORIASIS IN A PHASE 2 TRIAL

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Background: BMS-986165 is an oral, selective inhibitor of tyrosine kinase 2 (TYK2), an enzyme that activates signal transducer and activator of transcription (STAT)-dependent cytokine signalling pathways involved in the pathophysiology of psoriasis (PsO). In a 12-week, Phase 2 trial of BMS-986165 in patients with moderate to severe plaque PsO, including those with baseline (BL) musculoskeletal symptoms, Psoriasis Area and Severity Index (PASI) 75 responses (primary endpoint) were highest at doses ≥3 mg twice daily (BID; 67–75%) vs placebo (7%; *P*<0.001), with a favourable safety profile.[1]

Objectives: To evaluate the influence of BL demographics (weight, body mass index, age) and disease characteristics (age of onset, presence of musculoskeletal symptoms, disease duration, previous biologic use, PASI score, static Physician Global Assessment [sPGA] score, Dermatology Life Quality Index [DLQI] score) on Week 12 efficacy for the 3 most effective doses of BMS-986165 (3 mg BID, 6 mg BID, and 12 mg once daily [QD]) in the trial.

Methods: Adults with moderate to severe plaque PsO (body surface area [BSA] ≥10%, PASI score ≥12, sPGA score ≥3) were randomised equally to 1 of 5 oral doses of BMS-986165 (3 mg every other day, 3 mg QD, 3 mg BID, 6 mg BID, 12 mg QD) or placebo for 12 weeks.

Results: A total of **267 patients were treated; subgroup analyses based on BL characteristics are reported for patients treated with the most effective doses of BMS-986165 (≥3 mg BID; n=134). BMS-986165 showed no meaningful differences in efficacy among almost all of the 3 subgroups, including age of onset, presence of musculoskeletal symptoms, and disease duration (Table), with some variability across subgroups.** Small patient numbers may underlie observed fluctuations in results. **Similar consistency in responses was seen regardless of BL age (18–<45 years, n=66; ≥45 years, n=68), weight**

(<90 kg, n=81; ≥90kg, n=53), PASI score (<20, n=96 vs ≥20, n=38), DLQI score (<10, n=52; 10–<20, n=62; ≥20, n=20), sPGA score (<4, n=89; ≥4, n=44), and BSA (<20, n=73; ≥20, n=61).

Conclusion: In patients with moderate to severe plaque PsO, BMS-986165 demonstrated consistent efficacy at doses ≥3 mg BID regardless of many BL characteristics, including presence of musculoskeletal symptoms, that may impact results. These observations will be evaluated further in ongoing Phase 3 studies (POETYK PSO Phase 3 programme; ClinicalTrials.gov identifiers: NCT03611751 and NCT03624127).

REFERENCES:

[1] Papp K, et al. N Engl J Med 2018;379:1313–1321.

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Table 1. Efficacy of BMS-986165: endpoints at Week 12 by select baseline disease characteristics

Endpoint	Dose	Age of onset			Musculoskeletal symptoms		Disease duration	
		<18 years	18–<45 years	≥45 years	No	Yes	<15 years	≥15 years
PASI 75	3 mg BID	n=13 76.9 (46.2–95.0)	n=21 71.4 (47.8–88.7)	n=11 54.5 (23.4–83.3)	n=34 64.7 (46.5–80.3)	n=11 81.8 (48.2–97.7)	n=25 72.0 (50.6–87.9)	n=20 65.0 (40.8–84.6)
	6 mg BID	n=16 50.0 (24.7–75.3)	n=26 76.9 (56.4–91.0)	n=3 66.7 (9.4–99.2)	n=34 67.6 (49.5–82.6)	n=11 63.6 (30.8–89.1)	n=22 68.2 (45.1–86.1)	n=23 65.2 (42.7–83.6)
	12 mg QD	n=9 77.8 (40.0–97.2)	n=29 75.9 (56.5–89.7)	n=6 66.7 (22.3–95.7)	n=29 75.9 (56.5–89.7)	n=15 73.3 (44.9–92.2)	n=13 61.5 (31.6–86.1)	n=31 80.6 (62.5–92.5)
	Combined*	n=38 65.8 (48.6–80.4)	n=76 75.0 (63.7–84.2)	n=20 60.0 (36.1–80.9)	n=97 69.1 (58.9–78.1)	n=37 73.0 (55.9–86.2)	n=60 68.3 (55.0–79.7)	n=74 71.6 (59.9–81.5)
PASI 90	3 mg BID	n=13 53.8 (25.1–80.8)	n=21 42.9 (21.8–66.0)	n=11 36.4 (10.9–69.2)	n=34 47.1 (29.8–64.9)	n=11 36.4 (10.9–69.2)	n=25 48.0 (27.8–68.7)	n=20 40.0 (19.1–63.9)
	6 mg BID	n=16 18.8 (4.0–45.6)	n=26 61.5 (40.6–79.8)	n=3 33.3 (0.8–90.6)	n=34 44.1 (27.2–62.1)	n=11 45.5 (16.7–76.6)	n=22 54.5 (32.2–75.6)	n=23 34.8 (16.4–57.3)
	12 mg QD	n=9 44.4 (13.7–78.8)	n=29 48.3 (29.4–67.5)	n=6 16.7 (0.4–64.1)	n=29 44.8 (26.4–64.3)	n=15 40.0 (16.3–67.7)	n=13 23.1 (5.0–53.8)	n=31 51.6 (33.1–69.8)
	Combined*	n=38 36.8 (21.8–54.0)	n=76 51.3 (39.6–63.0)	n=20 30.0 (11.9–54.3)	n=97 45.4 (35.2–55.8)	n=37 40.5 (24.8–57.9)	n=60 45.0 (32.1–58.4)	n=74 43.2 (31.8–55.3)
sPGA 0/1	3 mg BID	n=13 84.6 (54.6–98.1)	n=21 71.4 (47.8–88.7)	n=11 72.7 (39.0–94.0)	n=34 70.6 (52.5–84.9)	n=11 90.9 (58.7–99.8)	n=25 68.0 (46.5–85.1)	n=20 85.0 (62.1–96.8)
	6 mg BID	n=16 56.3 (29.9–80.2)	n=26 69.2 (48.2–85.7)	n=3 66.7 (9.4–99.2)	n=34 67.6 (49.5–82.6)	n=11 54.5 (23.4–83.3)	n=22 63.6 (40.7–82.8)	n=23 65.2 (42.7–83.6)
	12 mg QD	n=9 77.8 (40.0–97.2)	n=29 75.9 (56.5–89.7)	n=6 66.7 (22.3–95.7)	n=29 75.9 (56.5–89.7)	n=15 73.3 (44.9–92.2)	n=13 53.8 (25.1–80.8)	n=31 83.9 (66.3–94.5)
	Combined*	n=38 71.1 (54.1–84.6)	n=76 72.4 (60.9–82.0)	n=20 70.0 (45.7–88.1)	n=97 71.1 (61.0–79.9)	n=37 73.0 (55.9–86.2)	n=60 63.3 (49.9–75.4)	n=74 78.4 (67.3–87.1)

Data are shown as response rate, % (95% exact CI).
Data for the placebo arm are as follows.
Age at onset: <18 years (n=14): PASI 75, 0.0 (0.0–23.2); PASI 90, 0.0 (0.0–23.2); sPGA 0/1, 0.0 (0.0–23.2); 18–<45 years (n=27): PASI 75, 11.1 (2.4–29.2); PASI 90, 3.7 (0.1–19.0); sPGA 0/1, 11.1 (2.4–29.2); ≥45 years (n=4): PASI 75, 0.0 (0.0–60.2); PASI 90, 0.0 (0.0–60.2); sPGA 0/1, 0.0 (0.0–60.2).
Musculoskeletal symptoms: no (n=24): PASI 75, 12.5 (2.7–32.4); PASI 90, 4.2 (0.1–21.1); sPGA 0/1, 12.5 (2.7–32.4); yes (n=21): PASI 75, 0.0 (0.0–16.1); PASI 90, 0.0 (0.0–16.1); sPGA 0/1, 0.0 (0.0–15.1).
Disease duration: <15 years (n=16): PASI 75, 6.3 (0.2–30.2); PASI 90, 0.0 (0.0–20.6); sPGA 0/1, 12.5 (1.6–38.3); ≥15 years (n=29): PASI 75, 6.9 (0.8–22.8); PASI 90, 3.4 (0.1–17.8); sPGA 0/1, 3.4 (0.1–17.8).
*BMS–986165 3 mg BID, 6 mg BID, and 12 mg QD combined.
BID=twice daily; CI=confidence interval; PASI 75=≥75% improvement in Psoriasis Area and Severity Index score; PASI 90=≥90% improvement in Psoriasis Area and Severity Index score; QD=once daily; sPGA 0/1=static Physician Global Assessment score of 0 or 1.

FRI0436

ACHIEVING THE TREATMENT TARGETS OF REMISSION OR LOW DISEASE ACTIVITY (LDA) IN PSORIATIC ARTHRITIS (PSA) IS ASSOCIATED WITH SIGNIFICANTLY IMPROVED QUALITY OF LIFE, FUNCTION AND PAIN

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Background: The link between reaching a state of remission or LDA[1,2] and patient-reported outcomes in PsA has been little explored in an observational setting.

Objectives: This analysis investigates the potential effect of reaching remission or LDA according to cDAPSA and achievement of VLDA/MDA on patient-reported outcomes such as HRQoL, functioning and pain in an observational cohort of PsA patients.

Methods: PsABio (NCT02627768) is an ongoing real-world observational study in 8 European countries where PsA patients receive 1st-, 2nd- or 3rd-line biologics (starting either ustekinumab [UST] or a TNFi. Of 563 UST- or TNFi-treated patients enrolled Dec 2015 – Aug 2017, 303 had data available from their 6-month follow-up. Disease states were defined using cDAPSA ≤4 for remission and ≤13 for LDA (data available for 250 patients) and VLDA 7/7 and MDA 5/7 criteria (data available for 206 and 260 patients, respectively). HRQoL was assessed by the generic instrument EQ5D and the PsA specific tool PsAID-12. Physical functioning was measured by the HAQ-DI and pain with a Pain VAS (0–100). Assessment of Psoriasis Skin Disease (68/299=22.7%) was the most frequently missed MDA component, while enthesitis was the least frequently missed (6/299=2.0%). The other 5 components were all missed with equal frequency (8–9%). Available observed data on univariate associations are presented, with no imputation of missing data or adjustment for baseline imbalances.

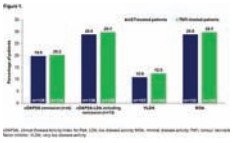
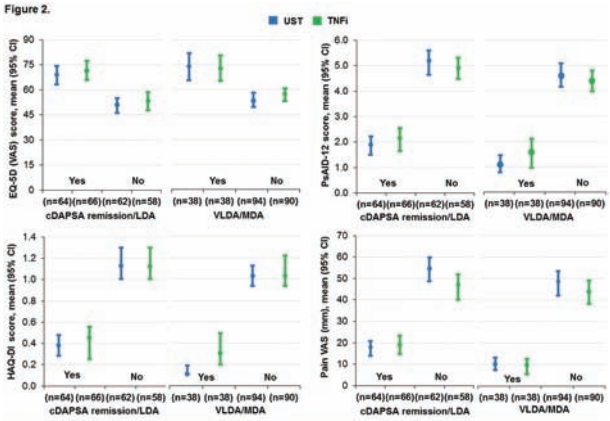


Figure 2.



cDAPSA, clinical Disease Activity Index for psoriatic arthritis; CI, confidence interval; EQ-5D, EuroQoL 5-dimension questionnaire; HAQ-DI, Health Assessment Questionnaire – Disability Index; LDA, low disease activity; MDA, minimal disease activity; PsAID-12, Psoriatic Arthritis Impact of Disease 12-item questionnaire; VAS, visual analogue scale; VLDA, very low disease activity

Results: For the 303 patients, mean age was 49.7 (standard deviation [SD] 12.8) years, mean disease duration was 7.2 (SD, 8.2) years, and 50.5% were women. Figure 1 shows data at 6 months for cDAPSA remission, cDAPSA LDA, VLDA, and MDA in UST- and TNFi-treated patients. Start of treatment with either UST or TNFi did not significantly influence the rates of these outcomes at 6 months. cDAPSA remission/LDA and VLDA/MDA achievement (Yes vs No) was associated with better general and disease-specific HRQoL assessments, (EQ5D VAS, PsAID-12) physical function (HAQ-DI) and Pain (VAS) shown by non-overlapping confidence intervals in Figure 2.

Conclusion: In real-life, treatment with either UST or a TNFi leads to considerable and comparable numbers of patients reaching LDA or remission. Reaching such LDA is associated with clinically important improvements exceeding minimal clinically important differences for QoL, functioning and pain experience. Our data therefore strongly support a treat-to-target strategy in routine care for PsA.

REFERENCES:

[1] Gossec L, et al. Ann Rheum Dis. 2016;75:499–510; 2. Smolen JS, et al. Ann Rheum Dis. 2018;77:3–17.

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FRI0437

PATIENT-DEFINED FLARES IN IN PSORIATIC ARTHRITIS: WHAT DO THEY MEAN? AN ANALYSIS OF CHANGE BETWEEN 2 VISITS IN 222 PATIENTS

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Background: In psoriatic arthritis (PsA), disease fluctuations lead to periods of flares which impact patients' lives and treatment retention, these flares have been little studied.

Objectives: To explore the frequency of flares in patients with PsA, and to assess the validity of patient-defined flares against PsA disease activity.
Methods: ReFlap (NCT03119805, ref) was a longitudinal study in 14 countries of consecutive adult patients with definite PsA and more than 2 years of disease duration. Patients were seen twice in the context of usual care, around 4 months apart. The proportion of flares was computedat the second visit according to a patient-reported question: "At this time, are you having a flare of your psoriatic arthritis, if this means the symptoms are worse than usual?" and a symmetrical physician question. These definitions were compared with a change in disease activity defined as transition to a more active disease category based on the Disease Activity in PSoriatic Arthritis (DAPSA) categories. Agreement was calculated using prevalence-adjusted kappas. Validity of patient-reported flares was assessed by comparing patients who flared with patients who did not flare at the second visit using clinical and patient-reported variables. Finally, for patients flaring, effect sizes corresponding to a patient transition to flare state were calculated by standardized response means (SRMs) for continuous outcomes, with p values based on McNemar test or rank signed test. There was no imputation of missing data.
Results: Overall, 222 patients were analysed: 127 (58.8%) were male, mean age was 53.5±12.3 years, mean disease duration was 10.8±8.3 years; 66.3% received a biologic and 13.8% oral glucocorticoids. Disease activity was moderate: 35.9% had no current psoriasis skin lesions, mean tender joint count (TJC, 0-68) was 3.0±7.5, mean swollen joint count (SJC, 0-66) was 1.6±6.6, and mean DAPSA was 11.5±14.0. At 4.5±2.2 months follow-up, the proportion of patient-reported flares was 27.0% (n=60), compared to 17.6% (n=39) physician-reported flares); there was a worsening in DAPSA category in 40.1% (n=89) patients. Agreements between definitions were moderate (range of kappas, 0.32-0.59). Patients in flare had significantly more active disease than patients not in flare using all outcomes (all p<0.001 except skin lesions, p=0.01, perhaps due to the fact that the majority of patients were included in rheumatology departments and had mild skin involvement at visit 1). Finally, among patients self-describing as in flare (N=60), all outcomes were worse than at the first visit; changes from the first visit were most notable for patient global (SRM 1.22), pain (0.92), physician global (0.85), DAPSA (0.83) and PsAID12 (0.80).
Conclusion: Patient-reported flares occurred in 27% of these PsA patients at 4 months follow-up, which was more than the proportion of physician-reported flares but less than the proportion of patients showing worsening of DAPSA category. Patient flares were associated with more active disease for all PsA manifestations; and at the patient-level, to a clear worsening in disease activity. A single question for flares is feasible, easy to understand for patients and not time consuming. These findings provide preliminary validation of the notion of patient-reported flares.

REFERENCES:
[1] Gorlier C, et al. Ann Rheum Dis. 2019;78(2):201-208.

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FRI0438 TREATMENT UTILISATION PATTERNS OF ADVANCED THERAPIES IN PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy typically associated with psoriasis. Little is known regarding the pattern of advanced therapy use, such as biologics and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs), and how the characteristics of patients with PsA initiating these therapies differ by line of therapy.
Objectives: To characterise the prescribing frequency of medication classes and compare characteristics across line of therapy groups among patients with PsA who initiated a biologic/tsDMARD.
Methods: This observational study included patients with PsA in the US Corrona PsA/SpA Registry who initiated a biologic/tsDMARD between 31 March 2013 and 31 October 2018. Patients were grouped by line of therapy at time of drug initiation: 1st, 2nd, 3rd, or 4th-or-higher. For each group, frequencies of medication classes were calculated, and proportions (categorical variables) and means with standard deviations (continuous variables) were determined for patient demographic, clinical and disease activity characteristics, patient-reported outcome measures, history of medication use, and concomitant medication use at the time of therapy initiation. Comparisons across groups were made with chi-square tests and one-way analysis of variance.
Results: Data from 1516 initiators (396 (26%), 453 (30%), 333 (22%), 334 (22%) in the 1st, 2nd, 3rd, or 4th-or-higher line groups, respectively) were examined. Mean age was 53.1 years, mean time since PsA diagnosis was 8.1 years and mean time from PsA diagnosis to 1st line therapy initiation was 5.2 years. TNFi therapy was commonly initiated earlier, while initiation of the other classes as a proportion of total line-specific initiations increased in later lines of therapy (TNFi: 77%, 61%, 41%, and 30%; tsDMARDs: 16%, 18%, 19%, and 22%; IL-17: 4%, 12%, 25%, and 34%; non-TNFi/non-IL-17: 3%, 8%, 14%, and 14% for the 1st, 2nd, 3rd, and 4th-or-higher lines of therapy, respectively). Among all initiators, 72% had a history of methotrexate (MTX) use and 35% had concomitant MTX use at drug initiation. Most patients had moderate to high disease activity at therapy initiation based on the proportion of patients reporting minimal disease activity (20%) (**Table**); 30% had enthesitis and 15% had dactylitis. Across therapy lines, statistically significant differences in minimal disease activity, HAQ, fatigue, pain and morning stiffness (P<0.05) were seen. Generally, scores were lower for those receiving 1st line therapy relative to the 4th-or-higher line group; fatigue scores ranged from 45.1 to 56.8, pain scores ranged from 46.6 to 58.2, and the percentage of patients with morning stiffness $\geq$30 minutes ranged from 72% to 80%.
Conclusion: Patients with PsA who initiated biologic/tsDMARD therapies in a large, national US based registry frequently exhibited significant disease activity, as demonstrated by patient-reported outcome measures and validated disease activity measures. On average, disease activity was worse in later lines of therapy. Enthesitis and dactylitis were highly prevalent in this population. TNFi was the most common 1st line therapy while newer agents such as IL-17 inhibitors were most commonly initiated as 4th line therapy or higher. In light of the newly published guidelines, it appears that rheumatologists are treating in a manner aligned with the guidelines based on the characteristics of patients observed across the different lines of therapy.
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Employee of: AbbVie, Patrick Zueger Shareholder of: AbbVie, Employee of: AbbVie, Jacqueline O'Brien Employee of: Corrona, Heather J. Litman: None declared, Hua Feng Employee of: Corrona, Robert McLean: None declared

Patient clinical and disease activity characteristics at drug initiation by line of therapy

Variable	All (n=1516)	Line of Therapy 1st (n=396)	2nd (n=453)	3rd (n=333)	4th-or-Higher (n=334)	P-value*
Minimal Disease Activity, n (%)	235 (20.3)	73 (23.9)	83 (23.2)	44 (17.4)	35 (14.4)	0.01
Tender Joint Count 28, mean±SD	4.5±5.8	4.2±5.3	4.3±6.0	4.8±6.2	4.7±5.7	0.21
Swollen Joint Count 28, mean±SD	2.5±3.6	3.0±4.0	2.5±3.7	2.3±3.5	2.3±3.1	0.01
Enthesitis category >0, n (%)	380 (30.1)	96 (27.7)	102 (26.4)	96 (35.8)	86 (33.1)	0.03
Dactylitis category >0, n (%)	190 (15.1)	70 (20.2)	49 (12.7)	34 (12.7)	37 (14.2)	0.02
HAQ >1, n (%)	483 (39.1)	108 (32.3)	146 (38.2)	104 (39.7)	125 (48.8)	0.001
Body surface area ≤3% affected by psoriasis, n (%)	790 (64.2)	215 (64.8)	239 (62.9)	165 (62.7)	171 (67.1)	0.69
Patient reported fatigue 0–100, mean±SD	50.7±28.2	45.1±28.7	49.7±29.4	53.4±25.8	56.8±26.4	<0.001
Patient overall pain 0–100, mean±SD	51.5±28.2	46.6±29.0	49.2±28.6	54.8±26.4	58.2±27.0	<0.001
Morning stiffness ≥30 min, n (%)	950 (77.2)	241 (72.2)	293 (77.1)	212 (80.9)	204 (80.0)	0.046

HAQ, Health Assessment Questionnaire; SD, standard deviation.
*P-values from chi-square tests (categorical variables) and one-way analysis of variance (continuous variables) across lines of therapy.

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FRI0439

PERCEIVED INFLUENCE OF HEALTH STATUS ON SEXUAL ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS IS ASSOCIATED WITH MUSCULOSKELETAL MANIFESTATIONS BUT NOT WITH PSORIASIS SKIN MANIFESTATIONS

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease involving multiple domains including the musculoskeletal system and the skin. The disease may have a significant impact on various aspects of quality of life including sexuality.
Objectives: To explore the prevalence of self-reported problems with sexual activity in patients with PsA, and any associations with demographic and disease related variables as well as treatment.
Methods: PsA patients were consecutively recruited from a Norwegian rheumatology outpatient clinic. Data collection included information on demographics, measures of PsA disease activity (both skin and musculoskeletal manifestations), patient reported outcome measures and treatment. The perceived effect of health status on sexual activity was assessed using question 15 in the Health Related Quality of Life (HRQoL) instrument 15D. The question reads: My state of health: 1. Has no adverse effect on my sexual activity. 2. Has a slight effect on my sexual activity. 3. Has a considerable effect on my sexual activity. 4. Makes sexual activity almost impossible. 5. Makes sexual activity impossible. For analytical purposes the answers were dichotomized into "no/little negative effect" (answers 1 and 2) and "large negative effect" (answers 3-5). For group comparisons we used Chi-square test for categorical variables and student t-test for continuous variables. Adjusted logistic regression models were also applied.
Results: Among the 135 PsA patients assessed mean (SD) age was 52.1 (10.2) years and 51.1% were men. The majority of patients (111 patients, 82.2%) reported their state of health to have no/little effect on their sexual activity and 24 patients (17.8%) reported their state of health to have large negative effect on their sexual activity.
Patients with a large negative effect of their health status on sexual activity had significantly longer disease duration as well as higher DAPSA, MASES and fatigue score compared with the patients reporting no/little impact of their health status on sexual activity (table).
In adjusted logistic regression models with disease duration, DAPSA, MASES and fatigue in the model, only disease duration and MASES were independently associated with a large negative effect on sexual activity, this also when adjusting for age and sex.
Conclusion: Approximately 20% of the PsA patients reported their health status to have a large negative effect on their sexual activity. Only disease duration and measures reflecting musculoskeletal disease were found to have a negative effect on sexual activity among PsA patients; skin psoriasis did not have an impact.

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	Total (n=135)	No/little effect (n=111)	Large negative effect (n=24)	P-values
Age (SD) years	52.1 (10.2)	51.8 (10.3)	53.3 (10.3)	0.54
Men, n (%)	69 (51.1%)	58 (52.3%)	11 (45.8%)	0.57
BMI (SD) kg/m2	28.2 (4.4)	28.1 (4.2)	29.1 (5.0)	0.34
Smoking	21 (15.6%)	16 (14.4%)	5 (20.8%)	0.43
Disease duration (SD) years	8.7 (6.7)	8.1 (6.6)	11.6 (6.5)	0.02
68 Tender Joint Count	10.1 (11.1)	9.1 (10.2)	14.7 (13.8)	0.07
66 Swollen Joint Count	0.6 (1.1)	0.6 (1.1)	0.6 (0.9)	0.96
DAPSA	18.2 (14.2)	16.8 (13.3)	24.8 (16.6)	0.01
MASES	2.9 (3.1)	2.5 (2.9)	4.4 (3.5)	0.01
Fatigue (VAS 0-100)	45.1 (32.4)	42.2 (32.4)	58.1 (29.6)	0.03
Pain (VAS 0-100)	33.7 (23.1)	32.1 (22.8)	41.3 (23.5)	0.08
MHAQ	0.42 (0.40)	0.39 (0.34)	0.58 (0.58)	0.12
PASI skin score	2.5 (3.6)	2.4 (3.6)	3.1 (4.0)	0.38
Current Biologics	44 (32.6%)	36 (32.4%)	8 (34.8%)	0.83
Current DMARDs	79 (58.5%)	68 (61.3%)	11 (45.8%)	0.16

FRI0440

THE EFFECT OF GUSELKUMAB ON PASDAS, GRACE INDEX, MCPDAI, AND DAPSA: RESULTS FROM A PHASE 2 STUDY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Psoriatic ArthritiS Disease Activity Score (PASDAS), GRAppa Composite scorE (GRACE) Index, modified Composite Psoriatic Disease Activity Index (mCPDAI), and Disease Activity Index for PSoriatic Arthritis (DAPSA) are composite indices recently developed to assess disease activity in psoriatic arthritis (PsA).[1,2]
Objectives: The effect of guselkumab (GUS) on these indices was evaluated in a phase 2 study in patients with active PsA.
Methods: Patients with ≥3 tender and ≥3 swollen joints, C-reactive protein ≥3 mg/L, and ≥3% body surface area (BSA) of plaque psoriasis despite treatment were randomized 2:1 to receive GUS 100 mg subcutaneously (N=100) or placebo (PBO, N=49) at Weeks 0, 4, and every 8 weeks thereafter through Week44. At Week16, patients with <5% improvement in both swollen and tender joint counts were eligible for early escape (EE) to open-label ustekinumab. All remaining PBO patients crossed-over to receive GUS 100 mg at Weeks 24, 28, 36, and 44 (PBO→GUS). The PsA composite indices through Week24 were analyzed using last-observation-carried-forward for missing data and data post EE. After Week24, observed data were used. Missing baseline data were excluded in the analyses.
Results: Baseline PASDAS, GRACE, mCPDAI, and DAPSA showed moderate to high disease activity (mean (SD): 6.53 (1.079), 6.08 (1.208), 7.6 (2.15), and 46.65 (20.391), respectively), and were generally comparable between PBO and GUS. At Week24, GUS significantly decreased PASDAS, GRACE, mCPDAI, and DAPSA scores (mean (SD) change from baseline: -2.50 (1.59), -2.73 (1.76), -3.8 (2.72),

-23.08 (20.21), respectively) vs PBO (mean (SD) change from baseline: -0.49 (1.33), -0.35 (1.39), -0.8 (2.16), -4.97 (20.11), respectively, all p<0.001). Significantly more GUS-treated patients achieved a low or very low disease activity state defined by PASDAS, GRACE, and mCPDAI (35.0%, 29.6%, and 45.9%, respectively) vs PBO (4.1%, 2.1%, and 10.4%, respectively, all p<0.001). In addition, 12% of GUS- vs 0% of PBO-treated patients achieved DAPSA remission (p<0.01). Post Week24, improvements in PASDAS, GRACE, mCPDAI, and DAPSA were also observed in PBO→GUS patients (39.3%, 39.3%, 71.4%. and 50.0% achieved disease activity states of low, very low, or remission at Week 44, respectively), and were maintained through Week44 in GUS patients (45.8%, 42.2%, 62.7%, and 51.1% achieved disease activity states of low, very low, or remission, respectively).

Conclusion: GUS demonstrated consistent improvements based on all PsA composite indices evaluated, and efficacy was maintained through Week44.

REFERENCES:

[1] Helliwell PS, FitzGerald O, and Fransen J. JRheumatol 2014;41:1212-1217.
[2] Scholes MM, Aletaha D, Alasti F, Smolen JS. AnnRheumDis 2016;75:811-818.

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FRI0441 LONG DISEASE DURATION PREDICTED NON-ALCOHOLIC FATTY LIVER DISEASE IN PSORIATIC ARTHRITIS

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Background: Psoriasis is known to be associated with non-alcoholic fatty liver disease (NAFLD). Previously studies showed that patients with psoriatic arthritis (PsA) were of higher risk of developing NAFLD compared to non-PsA individuals.

Objectives: To study the prevalence of NAFLD among patients with PsA and factors predicting the development of NAFLD.

Methods: This retrospective study was carried out in a tertiary hospital. Adult patients (>18-year-old) with PsA who attended rheumatology specialist outpatient clinic between 1st Jan 2016 and 31st Dec 2018 were included. Demographic and clinical (disease duration, comorbidities, investigation results and treatment profile) data of these patients were obtained. NAFLD was diagnosed by either imaging or histology. Logistic regression was used to identify factors predicting NAFLD.

Results: 223 patients (male 53%, female 47%) with a mean age of 58-year-old and mean disease duration of 10.5 years were included in the study. Patients with NAFLD (n= 58, 26%), compared to those without, tended to be older (mean age 59.0-year-old vs 57.6-year-old) and had higher proportion of male (64% vs 51%).

Among the patients with NAFLD, 30 (51.7%) had transient abnormal liver function test but none resulted in hepatic failure or death. 10 patients (17.2%) had their treatment for PsA withheld or changed as a result of abnormal liver function due to NAFLD.

Long disease duration (OR 1.005, p<0.01), but not age, predicted NAFLD. In particular, those with disease duration of 10 years or more were of higher risk (OR 2.79, p<0.001). Cardiovascular risk factors including hypertension, diabetes mellitus, dyslipidaemia, and established cardiovascular diseases were not found to be predictors of NAFLD among PsA. None of the treatment agents including steroid, conventional synthetic or biological disease modifying anti-rheumatic durgs (DMARDs) was found to be risk factor for NAFLD.

Conclusion: NAFLD was common among patients with PsA, though it seldom led to significant hepatic impairment or interruption of treatment of PsA. Patients with longer duration of psoriatic arthritis were at risk of developing fatty liver. Traditional cardiovascular risk factors, established cardiovascular diseases or use of any particular treatment agent were not found to be predicting factor of development of NAFLD in PsA.

REFERENCES:

[1] Aliment Pharmacol Ther. 2015 Feb;41(3):293-300
[2] J Invest Dermatol. 2018 Apr;138(4):760-767

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FRI0442 EFFECTIVENESS OF YTTRIUM KNEE SYNOVECTOMY IN PSORIATIC OR SERONEGATIVE ARTHRITIS WHO HAVE FAILED CONVENTIONAL THERAPY

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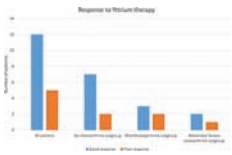
Background: Radiation synovectomy with Yttrium 90Y is indicated for refractory arthritis of various aetiologies e.g. inflammatory joint diseases such as rheumatoid arthritis, seronegative arthritidies such as psoriatic arthritis and reactive arthritis, Haemophilic arthritis, Calcium pyrophosphate dihydrate (CPPD) arthritis and pigmented villonodular synovitis (PVNS)[1].

Treatment of inflammatory arthritis has improved due to more effective therapy and earlier treatment therefore Yttrium therapy is less commonly used.

Objectives: To assess the response to Yttrium 90Y synovectomy in patients with Psoriatic arthritis or seronegative arthritis with synovitis affecting the knee joint in a cohort of patients who had failed conventional DMARDs, biological DMARDs or intra-articular steroid injections. To identify any possible predictors of good or poor response. To develop a standard operating procedure to improve consistency and also allow service to be potentially expanded.

Methods: Retrospective chart and electronic care record review of all patients receiving Yttrium therapy in Northern Ireland from March 2016 to April 2018. Patient demographics, MRI findings, conventional and biological DMARD use, previous intra-articular steroid use were recorded. Patients were reviewed approximately six months following treatment. The medical notes were reviewed to decide whether there had been a good or poor response to treatment and data analyzed to look for factors that may predict response. The process was evaluated and we developed a standard operating procedure to improve consistency and safety going forward.

Results: 17 patients in total received Yttrium therapy, 9 males. Age range was 18-75 with a mean 41. 10 patients were diagnosed with seronegative arthritis and 7 with psoriatic arthritis. All patients had an MRI of the affected joint(s) which confirmed synovitis in all cases. 9 MRIs showed no significant degenerative changes, 5 showed mild degenerative changes and 3 moderate/severe. All patients had previously received intra-articular steroid injection. 12 patients also were receiving or had failed treatment with a conventional or biological DMARD.



Each knee received a dose of 180MBq Yttrium under direct ultrasound guidance in addition to Triamcinolone 40mg and using Lidocaine 1% local anaesthesia. 3 patients received treatment for both knees.

Reviewing all patients 71% (12/17) reported good efficacy. 78% (7/9) of patients reported good efficacy in group with no osteoarthritis on MRI, 60% (3/5) in the mild osteoarthritis group and 67% (2/3) in the moderate to severe osteoarthritis group. BMI, Age, sex or underlying diagnosis did

not appear to predict response in this group. There were no adverse events reported

Conclusion: Yttrium therapy is not widely used with only one unit in Northern Ireland performing the procedure. The use of effective DMARDs and biological therapy has improved management of psoriatic and rheumatoid arthritis. In spite of this some patients still have refractory disease. We have shown in this observational study that in patients with knee synovitis despite treatment with DMARDs, biologics and intra-articular steroids, Yttrium synovectomy shows good efficacy, is a relatively low cost and generally safe treatment option for these patients.

Going forward this study and our standard operating procedure will allow us to develop criteria to help select patients for Yttrium therapy and standardize our treatment.

REFERENCES:

[1] Clunie G, Fischer M (2003) EANM procedure guidelines for radiosynovectomy. Eur J Nucl Med 30:BP12–BP16

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FRI0443 IMPACT OF APREMILAST ON PSAID CORE COMPONENTS IN PATIENTS WITH A LIMITED NUMBER OF ACTIVE JOINTS: RESULTS FROM THE REAL-WORLD, PROSPECTIVE, MULTICENTRE REWARD STUDY

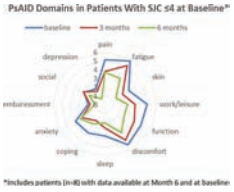
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Background: Recent data suggest that patients with moderately active psoriatic arthritis (PsA) and a limited number of active joints have a high likelihood of achieving treatment goals with apremilast treatment.[1,2] Real-world evidence on the effect of apremilast on patients' perception of the impact of their disease is limited.

Objectives: To describe the effects of apremilast on the impact of disease in the real world as measured by the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire in PsA patients with SJC ≤4 at baseline.

Methods: The prospective, multicentre, observational REWARD study (The Netherlands) is investigating apremilast treatment in real-world patients with PsA. Descriptive statistics were assessed for disease measures, including swollen joint count (SJC; 0-66) and tender joint count (TJC; 0-68), PsAID (0-10) and patient's perception of pain based on the visual analog scale (VAS; 0-100 mm) among patients with limited number of swollen joints (SJC ≤4) at baseline. We report the effects of apremilast on these disease measures at treatment initiation and at the first 6 months of treatment with a data cutoff of December 2018.

Results: A total of 48 patients from 9 clinics who were receiving apremilast were included in this interim analysis. Among these patients, 31 (65%) had SJC ≤4 and 17 (35%) had SJC >4 at baseline. Of patients with SJC ≤4 at baseline, 18 and 8 had at least 3 and 6 months of follow-up, respectively, at the time of data cutoff. Results are reported for patients with available data at each time point. Baseline characteristics for patients with SJC ≤4 included a mean age of 54 years, mean BMI of 29.1 and mean years since PsA diagnosis of 7.0 years; 58% of patients were female, 90% had prior cDMARD use and 29% had prior biologic use. For patients with SJC ≤4, disease measures were reported as follows: The mean SJC at baseline, 3 and 6 months were 1.1, 0.6 and 0.1 and the mean TJC at baseline, 3 and 6 months were 4.5, 3.6 and 1.5. The mean PsAID scores at baseline, 3 and 6 months were 4.2, 3.4 and 2.6. Individual PsAID domain scores by time points are shown (Figure). Patients with a limited number of swollen joints showed gradual improvements in all domains of the PsAID. Mean Pain VAS scores at baseline, 2 weeks, 6 weeks, 3 months and 6 months were 47, 48, 39, 29 and 26 in these patients.



Conclusion: Results from the real-world, prospective, multicenter, observational REWARD study suggest that PsA patients with a limited number of active swollen joints may benefit from apremilast treatment. Apremilast was associated with improvements in the perceived impact of disease, as observed by reductions in the PsAID and its core components.

REFERENCES:

[1] McInnes I, et al. Ann Rheum Dis. 2018;77(Suppl 2). Abstract 0927. 2. Coates LC, et al. *Arthritis Rheumatol.* 2018;70(Suppl 10). Abstract 1607.

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FRI0444 EFFICACY AND SAFETY OF SECUKINUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS FOLLOWING INADEQUATE RESPONSE TO SYNTHETIC OR BIOLOGICAL DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN REAL-LIFE SETTINGS

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Background: The data regarding the efficacy and safety of Secukinumab (SEC) in patients with psoriatic arthritis (PsA) in daily clinical practice are scarce.

Objectives: To assess the **safety and efficacy of** SEC in patients with PsA in real life settings.

Methods: All PsA patients treated with SEC in the Rheumatology Units of 2 referral University Hospitals were prospectively included (from 3/2016-12/2018). Patients' characteristics, treatments and indices of disease activity (DAPSA, DAS28-CRP, BASDAI) and function (HAQ, BASFI) as well as the extent of skin disease (BSA) were recorded at baseline and during therapy.

Results: 79 patients treated with SEC were included; 75% were females (n=59) with a mean age of 54±13.4 years, a median disease duration of 7.8 years and a median SEC treatment duration of 10 months (IQR 13). At baseline, 42% had axial involvement, 25% enthesitis and 13% dactylitis. The majority of patients had previously failed anti-TNFs (91%, n=72; n=1: 32%, n=2: 43% or n≥3: 25%), anti-IL12/23 (37%), both biologic agents (34%) or apremilast (5%). SEC was administered in combination with csDMARDs in 55% and corticosteroids in 40% of patients, respectively. At the end of the **follow-up** period (median: 15 months), patients' disease activity (median DAPSA: 29 → 18.5, p<0.001, DAS28-CRP: 4.6 → 3.7, p=0.05, BASDAI: 5.5 → 3.2, p=0.15), function (median HAQ: 1 → 0.38, p=0.07, BASFI: 7 → 3.2, p=0.14) and skin psoriasis (median BSA: 2 → 0%, p=0.005) improved. Drug survival at the last follow-up visit was 63% (n=50). Reasons for SEC discontinuation were inadequate response (25%, n=20), serious adverse events (7%, n=5) or other reasons (5%, n=4). During follow-up there were 12 adverse events (1.2/100 patient-years); among them 5 were serious (0.5/100 patient-years). The rate of serious infections was 0.1/100 patient-years. Two fungal infections (one oral-genital and one inguinal that improved with local therapy) and three cases of cancer were also recorded (two colon cancers/one fatal and one endometrial cancer).

Conclusion: In a large, real life, cohort of patients with PsA, resistant to different biologics (anti-TNFs and/or anti-IL12/23), SEC displayed a high retention rate (63% after a median follow-up of 15 months) without significant side effects. These data emphasize the role of SEC as a viable therapeutic option even in patients with difficult to treat, multi-resistant PsA in daily clinical practice.

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Disclosure of Interests: None declared

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FRI0445 **IDENTIFICATION OF PSORIATIC ARTHRITIS USING AN ADMINISTRATIVE CLAIMS-BASED ALGORITHM**

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Background: Accurately identifying psoriatic arthritis (PsA) in large electronic healthcare database is critical for epidemiological studies.
Objectives: To develop and validate a claims-based algorithm to identify patients with PsA.
Methods: We conducted a retrospective chart review of the Partners Healthcare electronic medical record linked to Medicare claims from year 2012 to 2014. 7 claims-based algorithms were developed to identify PsA: 1) ≥2 International Classification of Diseases, Ninth Revision (ICD-9) codes for PsA (696.0) and at least one diagnosis of psoriasis (696.1) by any physician; 2) ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist; 3) ≥2 PsA diagnosis with at least 1 diagnosis by rheumatologist and ≤1 diagnosis of rheumatoid arthritis (714.0); 4) ≥2 diagnosis of PsA and at least 1 diagnosis of psoriasis by dermatologist; 5) ≥1 diagnosis of PsA by rheumatologist and ≥1 diagnosis of psoriasis by dermatologist; 6) ≥2 diagnosis of PsA by any physician and ≥1 claims for PsA medication; 7) ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist and ≥1 claims for PsA medication. The ICD-9 codes were separated by ≥7 days but <365 days. Medical record by the treating physician was considered as the gold standard, and two independent physicians confirmed the presence of PsA. Positive predictive value (PPV) and 95% confidence intervals (CI) of the algorithms were calculated.
Results: The 7 algorithms identified 357, 399, 315, 223, 215, 372, and 276 records, respectively. Approximately 45% of the identified records with adequate data were reviewed. The PPV of the algorithms ranged from 75.2% to 88.6% (**Table 1**). Mean age of identified PsA patients ranged from 72.6 to 73.5 years old. Presence of psoriasis 1 year prior to index date of PsA ranged from 54.2% to 89.2%. Algorithm 6 which captured ≥2 diagnosis of PsA and ≥1 claims for PsA-related medications identified second highest number of patients (n=372) yet still yielded high PPV of 82.4% (95% CI 76.5, 88.3).
Conclusion: All seven claims-based algorithms had a high PPV of 75-89% in identifying PsA. A claims-based algorithm utilizing two or more diagnosis codes of PsA by any physician with a claim for PsA medication can be a useful and efficient tool to identify the PsA population in large claims databases.

REFERENCES:

[1] Ciccia F, et al. The New England journal of medicine. May 25 2017;376 (21):2094-2095.

Table 1. Predictive Values of Proposed Algorithms for Identifying Psoriatic Arthritis

Algorithms	Records Identified	Charts Reviewed (%)	PsA per treating MD, PPV% (95% CI)
Diagnosis only			
1. ≥2 diagnosis of PsA and ≥1 diagnosis of psoriasis by any physician	357	141 (39.5)	75.2 (68.0, 82.3)
Diagnosis with Specialist Visit			
2. ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist	399	185 (46.4)	80 (74.2, 85.8)
3. ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist and ≤1 diagnosis of RA	315	147 (46.7)	81.6 (75.4, 87.9)
4. ≥2 diagnosis of PsA and at least 1 diagnosis of psoriasis by dermatologist	223	95 (42.6)	77.9 (69.6, 86.2)
5. ≥1 diagnosis of PsA by rheumatologist and ≥1 diagnosis of psoriasis by dermatologist	215	114 (53.0)	85.1 (78.5, 91.6)
Diagnosis and Medication Dispensing			
6. ≥2 diagnosis of PsA and at least 1 medication dispensing for PsA	372	159 (42.7)	82.4 (76.5, 88.3)
7. ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist and at least 1 medication dispensing for PsA	276	123 (44.6)	88.6 (83.0, 94.2)

***** PsA, Psoriatic arthritis; MD, Medical doctor; PPV, Positive predictive value; ICD, International Criteria of Diagnosis; RA, Rheumatoid arthritis

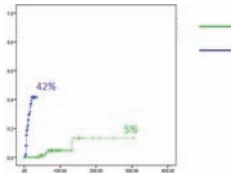
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FRI0446 **ATTAINMENT OF MINIMAL DISEASE ACTIVITY (MDA) IN PSORIATIC ARTHRITIS (PSA) PATIENTS (PTS) DEPENDING ON THE TIME OF SYNTHETIC (S) DMARDS INITIATION IN CLINICAL PRACTICE: RUSSIAN PSA REGISTRY (RU-PSART) DATA**

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Background: According to the EULAR recommendations and treat to target strategy sDMARD are the first line of PsA therapy. The goal of PsA treatment is attaining MDA. But there are contradictory data about the efficacy of sDMARDs in PsA pts. Data was collected from 25 rheumatology clinics of the Russian Federation.
Objectives: To investigate the cumulative frequency and the time of MDA attainment in early and long-term PsA after starting sDMARDs in clinical practice.
Methods: 253 (M/F–93/160) PsA pts according to CASPAR criteria were included in the RU-PsART, after signing consent participation forms; median (Me) age 47 [Min 20 – Max 82] years (yrs.). All patients were divided into two groups according to disease duration at time of sDMARDs initiation: early PsA ≤2 yrs. (165pts) and long-term PsA>2 yrs (88pts). All pts underwent standard clinical examinations of PsA and psoriasis activity. All pts were treated with the following sDMARDs: Oral Methotrexate (MTX) (103pts), intramuscular MTX (30pts), subcutaneous MTX (78pts), Leflunomide (7pts), Sulfasalazine (24pts), Apremilast (10pts), Tofacitinib (1pts). MDA was defined as ≥ 5 of the following criteria: tender joint count ≤1, swollen joint count ≤1, PASI≤1 or BSA≤3, patient pain global assessment VAS≤15, patient´s global disease activity VAS≤20, HAQ≤0,5, enthesitis count ≤1. The cumulative frequency and the time of MDA attainment were calculated in both groups. Kaplan-Meier cumulative analysis, Me [Min-Max], ORs with 95% CI,%, Breslow, Tarone-Ware, Log Rank tests were performed. All CI>1, p<0.05, were considered to indicate statistical significance.
Results: MDA has been achieved by the use of sDMARDs treatment in 39 out of 165 (24%) pts with early PsA and in 4 out of 88 (5%) pts with long-term PsA. Early PsA pts have more chance to achieve MDA in comparison to long-term PsA pts, OR=6.5 [CI 95% 2.2-18.9]. Comparative analysis has shown that cumulative frequency of MDA achievement after sDMARDs initiation was significantly higher (42% vs 5%) and faster (21 months vs 11 yrs.) in early PsA than in long-term PsA (p<0.05 for Breslow, Tarone-Ware and Log Rank tests) (Fig. 1). **Fig. 1.** Cumulative frequency and the time of MDA achievement after starting sDMARDs in early and long-term PsA.

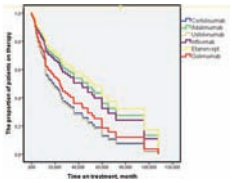


Conclusion: Our study suggests that sDMARDs initiation (mostly MTX-monotherapy) at an early stage of PsA allows to achieve MDA significantly faster and more often than in long-term PsA.
Disclosure of Interests: Elena Loginova Speakers bureau: Novartis, Celgene Corporation, Biocad, Janssen, AbbVie Inc, Tatiana Korotaeva Speakers bureau: Novartis, Celgene Corporation, AbbVie Inc, Biocad, Janssen, Pfizer, UCB, Lilly, Anastasia Koltakova: None declared, ELENA GUBAR: None declared, Yulia Korsakova Speakers bureau: Celgene Corporation, Janssen, Maria Sedunova: None declared, Igor Pristavsky: None declared, Irina Umnova: None declared, Irina Bondareva: None declared, Snezana Kudishina: None declared, Alexander Lila Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc.
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FRI0447 **THE SURVIVAL OF BIOLOGICS IN PSORIATIC ARTHRITIS – THE FIRST DATA FROM MOSCOW UNIFIED REGISTER OF ARTHRITIS (MUAR)**

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Background: Early started therapy of psoriatic arthritis with the goal to achieve minimal disease activity can slow the joint damage progression. Data concerning the persistence of psoriatic arthritis (PsA) patients on biologics in real clinical practice are insufficient.
Objectives: to analyze the survival of biological treatment of PsA and detect possible predictors of persistence on biologics.
Methods: PsA patients from Moscow Unified Arthritis Registry (MUAR) treated with biologics were included in study. Unadjusted survival analysis was performed by the Kaplan-Mayer method. The search for independent risk predictors of the therapy discontinuation was carried out by the multivariate Cox regression.
Results: We analyzed 236 treatment episodes in 141 PsA patients enrolled in MUAR, 61 men (43%); mean age was 50.1 ± 11.5 years. We used the following biologics: etanercept (71 patients), infliximab (51), adalimumab (50), ustekinumab (35), golimumab (11), cerolizumab pegol (7).
In unadjusted analysis mean treatment survival was longer with etanercept, adalimumab and infliximab. As significant independent predictors of withdrawal risk (potential confounders) low education, mutilating or polyarticular form of PsA, heel pain, shoulder joints swelling and absence of neck pain at the disease onset were detected.
After the adjusting data for cofounders there was no significant difference in risk of withdrawal between different biologics. Neither the year of onset of the case of treatment nor the number of previous bDMARDs show a significant relation with the risk of drug withdrawal (Picture 1). This data show the difference between the patterns of treatment survival of rheumatoid arthritis and psoriatic arthritis
Conclusion: our analysis of PsA treatment persistence in real clinical practice detected several factors associated with withdrawal risk. These data can provide specialists with a tool for personalized treatment



Picture 1. Adjusted analysis of persistence of bDMARDs

Disclosure of Interests: None declared
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FRI0448 **REAL-WORLD EXPERIENCE OF SECUKINUMAB FOR PSORIATIC ARTHRITIS**

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Background: Secukinumab, an inhibitor of IL-17, is a new option for the treatment of Psoriatic Arthritis (PsA) which has showed efficacy in clinical trials. However, real-world data of its use is still scarce.
Objectives: This study aims to analyze the experience of using secukinumab for PsA in four tertiary hospitals.
Methods: Multicentric observational, longitudinal, retrospective study conducted in 4 tertiary hospitals of the Madrid region. Patients with clinical diagnosis of PsA and having received at least one dose of secukinumab were included. Medical records were reviewed to collect demographic and clinical data (body mass index, BMI, risk factors cardiovascular disease, cancer, HBV/HCV infection), features of PsA (extra-articular involvement, radiological damage), previous therapies, assessment of the disease and response data at 6 months of secukinumab (joint counts, CRP, DAPSA, reasons for discontinuation, adverse events). Descriptive statistic analysis using mean and standard deviation was performed.
Results: 177 patients, of which 115 female (65%) were included. Mean age was 53 y.o.(SD 15) and average duration of the disease was 9 years (SD 7). 169 patients (95%) had peripheral disease (34% joint erosions), 84 (47%) had axial disease (68 with radiological damage), 148 (84%) had psoriasis, 61 (34%) showed dactilitis and 111 (63%) had enthesitis. Average BMI was 28.4 (SD 6), with an obesity rate of 37% (52 pt). Observed comorbidities were hypertension (22 pt, 12%), diabetes mellitus (22 pt, 12%), dyslipidemia (58 pt, 33%), active smoking (55 pt, 31%) and others: 20 patients had HBV infection, 5 had HCV infection and 12% had malignancy.
Regarding previous treatments, 90% had received cDMARDs, particularly methotrexate (77%) and 119 (67%) had been exposed to at least one bDMARD (32% to one, 25% to two, 20% to three and 21% to four or more). 69% were on 150 mg dose and 31% on 300 mg dose.
At baseline, average tender joint count was 7 (SD 8), swollen joint count was 4 (SD 4), CRP 7 mg/l and DAPSA 26. At 6 months of secukinumab therapy, tender joint count had decreased to 5 (SD 8), swollen joint count 2 (SD 3), CRP 5 mg/l and DAPSA 17. Thirty-eight (47%) of the patients with the data available (80) had DAPSA ≤14 (low activity) and 9 DAPSA ≤4 (remission). In naïve to biologic patients, DAPSA varied from 27 in the baseline visit to 16 at 6 months, and in the other group of patients with biologic experience, DAPSA varied from 24 to 17 at 6 months (if they had been exposed to 3 or more biologics, DAPSA from 18 to 10 at 6 months).
Average drug survival time was 20 months (1-34). 79 patients (44.6%) withdrawn therapy, due to primary ineffectiveness (40), secondary ineffectiveness (26), adverse events (9) and other reasons (3). Adverse events do not differ from those reported in clinical trials.
Conclusion: Secukinumab in real-world setting had been indicated in a population of PsA with a high percentage of axial involvement (47%), with an important previous exposure to biologics, and with higher comorbidity than that reported in clinical trials. Response data were favorable, 47% of patients achieved remission or low activity by DAPSA, and similar profile of adverse events to the one reported in the clinical trials was observed.

REFERENCES:

[1] Mease PJ, McInnes IB, Kirkham B, Kavanaugh A, Rahman P, van der Heijde D, et al. for the FUTURE 1 Study Group* Secukinumab Inhibition of Interleukin-17A in Patients with Psoriatic Arthritis. N Engl J Med 2015;373:1329-39

Disclosure of Interests: MARIA MARTIN LOPEZ: None declared, Marta Valero: None declared, Valentina Emperiale: None declared, Carolina Merino Argumánez: None declared, Javier Bachiller-Corral: None declared, Jose Campos Esteban: None declared, Ana Pérez Gómez: None declared, Beatriz Joven-Ibáñez Speakers bureau: Celgene, Novartis, MSD, Pfizer, AbbVie, and Janssen
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FRI0449 **EFFECTIVENESS OF BIOLOGIC DRUGS WITH DIFFERENT MECHANISM OF ACTION IN PSORIATIC ARTHRITIS. AN APPRAISAL FROM THE APULIAN REGISTRY BIOPURE**

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Background: In the last decade, the number of drugs available for patients affected with psoriatic arthritis (PsA) is increased and rheumatologists have multiple choices to manage PsA refractory to conventional disease modifying anti-rheumatic drugs (cDMARDs). However, the possibility

of identifying disease's or patient's related characteristics to drive the optimal choice is still under investigation.

Objectives: We aimed at evaluating the effectiveness and drug survival of the biological drugs (bDMARDs) and apremilast indicated for the treatment of PsA patients with inadequate response to cDMARDs. To this purpose, PsA patients on treatment with bDMARs or Apremilast recorded into the Apulian BIOPURE registry have been retrospectively analyzed.

Methods: We retrospectively assessed PsA patients, fulfilling CASPAR criteria, starting a biologic drug or apremilast from June 2016 through December 2017. At baseline and at last observation within the time frame of the study, DAPSA, PASI, ASDAS-CRP, the presence of enthesitis and dactylitis were collected. Rate of patients achieving DAPSA based remission was assessed at last observation. The persistence on the first treatment was evaluated by Kaplan-Meier survival curves. Estimated hazard ratios (HRs) of discontinuing therapy or achieving remission were assessed by multivariate stepwise backward Cox regression models, adjusting for patient demographics (gender, age) and disease characteristics (disease duration, number of prior bDMARDs, baseline DAPSA, PASI, presence of enthesitis and dactylitis, type of current drug).

Results: We recruited 450 PsA patients (268, 60% female) with mean age 53 (±11) years, disease duration 19 (±13) months, 337 (75%) naïve to bDMARDs. At baseline, 404 had peripheral joint involvement and 46 axial disease, DAPSA was 18 (±10), PASI 1.6 (±3), ASDAS-CRP 2.5 (±1), 48/355 (13.5) had dactylitis and 78/231 (33%) showed enthesitis. Table 1 shows the type of drugs. At last observation, the rate of patients who achieved the DAPSA remission was significantly higher in naïve patients (25%) than in those bDMARDs experienced (14%, p=0.02). The rate of drug survival was not significantly different among drugs (Figure 1). Cox-regression multivariate models showed that independent baseline factors negatively associated to drug persistence were prior bDMARD treatment (HR 0.70, 0.50-0.97 (95% CI), p=0.03) and the absence of axial disease (HR 0.56, 0.35-0.91 (95% CI), p=0.02). Negative predictors of DAPSA remission were prior bDMARD treatment (HR 0.40, 0.19-0.83 (95% CI), p=0.01), gender female (HR 0.51, 0.29-0.91 (95% CI), p=0.02), and the absence of dactylitis(HR 0.36, 0.19-0.68 (95% CI), p=0.002).

Conclusion: A good rate of DAPSA remission is achievable with all the current available drugs in PsA in settings of real life. Predictors of remission and persistence on treatment were being male and naïve to prior bDMARDs. No difference among drugs was detected.

Table 1. Treatments

	Frequency	Percentage
Adalimumab	80	17.8
Certolizumab	56	12.4
Golimumab	61	13.6
Etanercept	65	14.4
Secukinumab	104	23.1
Ustekinumab	43	9.6
Apremilast	41	9.1
All	450	100

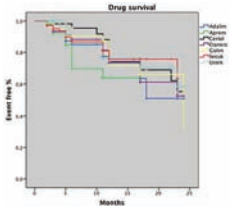


Figure 1. Kaplan-Meier curves of drug survival of PsA patients on different therapies.

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FRI0450 PROBABILITY OF ACHIEVING LOW DISEASE ACTIVITY OR REMISSION IN SUBJECTS WITH ACTIVE PSORIATIC ARTHRITIS TREATED WITH APREMILAST

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Background: Therapeutic targets for long-term control of psoriatic arthritis (PsA) include the achievement of remission (REM) or low disease activity (LDA), as measured by the Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA).[1]

Objectives: This post hoc analysis was conducted to (1) assess the predictive values of baseline clinical disease status on achieving long-term Clinical Disease Activity for Psoriatic Arthritis (cDAPSA) targets at Week 52 and (2) examine the association between early response to APR at Week 16 and the achievement of cDAPSA targets at Week 52.

Methods: Pooled analyses of 3 phase III trials (PALACE 1-3) were performed among subjects assigned to receive APR 30 mg twice daily at baseline. Data were analyzed using multiple imputation to account for subjects who discontinued or had missing values, using all available cDAPSA scores. The probabilities of shifting across different cDAPSA categories from baseline or Week 16 responses to Week 52 were calculated within these subjects. Binary logistic regression was also performed to confirm the results. We also analyzed mean cDAPSA from baseline to Week 52 by cDAPSA category at Week 52 among subjects with moderate or high disease activity (HDA) at baseline.

Results: A total of 494 subjects who received APR were included in the analyses; at baseline, 74.3% were in HDA, 24.5% in moderate disease activity, and 1.2% in LDA. Most subjects had $\geq$1 of the following conditions at baseline: affected body surface area $\geq$3%, dactylitis >0 based on the dactylitis severity score, enthesitis >0 based on the Maastricht Ankylosing Spondylitis Enthesitis Score or pre-existing axial PsA (physician determined) (HDA: 93.5%; moderate disease activity: 82.6%; LDA: 100%). The estimated probabilities of achieving either cDAPSA LDA or REM at Week 52 were 46.9% in subjects with baseline moderate disease activity (cDAPSA >13 to ≤27) and 71.1% in subjects with baseline LDA (cDAPSA >4 to ≤13) (Figure). In subjects with baseline HDA (cDAPSA >27), the probability of achieving LDA or REM by Week 52 was 24.9%. Subjects with moderate disease activity at baseline and improved to LDA or REM by Week 16 had high probabilities (58.9% and 88.5%) of remaining in target at Week 52. Among the subjects with moderate disease activity at baseline, a mean cDAPSA improvement of $\geq$30% by Week 16 was associated with achievement of LDA or REM at Week 52.



Conclusion: Subjects with low or moderate disease activity at baseline exhibited the highest likelihood of achieving and maintaining an improvement in LDA or REM with continued APR treatment to Week 52. In these patients, a partial response with apremilast by Week 16 was associated with higher achievement or maintenance of cDAPSA LDA or REM by Week 52.

REFERENCES:

[1] Smolen J, et al. Ann Rheum Dis. 2018;77:3-17.

Disclosure of Interests: Philip J Mease Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Consultant for: AbbVie, Amgen, BMS, Galapagos, Gilead Sciences, Inc., Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer and UCB, Frank Behrens Grant/research support from: AbbVie, Pfizer, Roche, Chugai, Prophylix, Bioline, Novartis, Consultant for: AbbVie, Pfizer, Roche, Chugai, UCB, Bristol-Myers Squibb, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Eli Lilly, Speakers bureau: Ad board: AbbVie, Pfizer, Roche, Chugai, UCB, Bristol-Myers Squibb, Celgene, Novartis, Biotest, Janssen, Genzyme, Eli Lilly, Dafna D Gladman Grant/research support from: AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB, Arthur Kavanaugh Grant/research support from: UCB Pharma, Michele Brunori Employee of: Celgene Corporation, Lichen Teng Employee of: Celgene Corporation, Benoit Guerette Employee of: Celgene Corporation, Ruben Queiro Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Takeda, Alexis Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer Inc, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda

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FRI0451

SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS IN PSORIATIC ARTHRITIS: FINAL 5 YEAR EFFICACY AND SAFETY RESULTS FROM A PHASE 3 TRIAL

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Background: Secukinumab (SEC) provided rapid and significant improvements in all key clinical domains of psoriatic arthritis (PsA) in the FUTURE 1 study (NCT01392326) with improvements sustained through 3 years.[1]

Objectives: We present the final 5 year efficacy and safety results of the study.

Methods: Overall, 606 adults with active PsA were randomised to SEC 10 mg/kg intravenously at baseline, and at weeks (wks) 2 and 4, followed by 150 mg or 75 mg subcutaneously (SC) every 4 wks, or matching placebo. Placebo patients (pts) were re-randomised to SEC 150 mg or 75 mg SC from Wk 16 or 24, depending on clinical response.[1] At Wk 104, 460 pts entered the 3-year extension study. Pts could have SEC dose escalated from 150 to 300 mg and from 75 mg to 150/300 mg starting from Wk 156, based on physician's judgement. Assessments at Wk 260 included ACR20/50/70, PASI 90, HAQ-DI, SF-36 PCS, and resolution of dactylitis and enthesitis and are reported for pts originally randomised to the SEC 150 mg and 75 mg groups (observed data). Safety is reported as exposure adjusted incidence rate/100 patient-years (EAIR) for all pts (n = 587) who received ≥1 dose of study treatment.

Results: Overall, 132/161 (82%) and 124/147 (84.4%) pts originally randomised to SEC 150/75 mg, respectively, who entered the extension study, completed 260 Wks of treatment. A total of 86/236 (36.4%) pts on SEC 150 mg were escalated to 300 mg, while 180/221 (81.4%) pts on SEC 75 mg were escalated to 150/300 mg. Clinical responses were sustained or further improved through 5 years treatment (Table 1). Over the entire study period (SEC mean exposure of 2320 patient-years), the safety profile of SEC was consistent with previous reports.[1] EAIR of selected adverse events for SEC were serious infections (1.8), ulcerative colitis (0.04), Crohn's disease (0.1), and MACE (0.5). Six deaths (3 in each dose group) were reported in any SEC group through 5 years.

Conclusion: SEC provided sustained improvements in the signs and symptoms in the major clinical domains of PsA through 5 years. SEC was well tolerated with a safety profile consistent with that previously reported.

REFERENCES:

[1] Mease PJ, et al. Ann. Rheum. Dis. 2017; 76 (suppl 2): 952.

Table 1. Summary of Efficacy Results at Week 260

Efficacy endpoints (n/M (%) unless otherwise stated)	SEC 150 mg Group (N=161)[1]	SEC 75 mg Group (N=147)[1]
ACR20	89/131 (67.9)	98/127 (77.2)
ACR50	69/131 (52.7)	65/127 (51.2)
ACR70	49/131 (37.4)	43/127 (33.9)
PASI90[2]	48/72 (66.7)	47/71 (66.2)
HAQ-DI, mean change from baseline (SD)	–0.4 (0.58) n=131	–0.5 (0.61) n=126
SF-36 PCS, mean change from baseline (SD)	6.6 (8.33) n=131	5.9 (9.36) n=123
Resolution of enthesitis[3]	67/81 (82.7)	60/77 (77.9)
Resolution of dactylitis[4]	63/67 (94.0)	63/70 (90.0)

[1]Secukinumab 150 and 75 mg arms include 60 and 121 pts, respectively, who were dose escalated to 150 and/or 300 mg at Wk 156 or later

[2]Pts with psoriasis affecting ≥3% body surface area at baseline (150 mg: N = 89; 75 mg: N = 82)

[3]Pts (N = 99 [150 mg], and 91 [75 mg]) with enthesitis at baseline

[4]Pts (N = 83 [150 mg], and 77 [75 mg]) with dactylitis at baselineM, number of evaluable pts; N, total number of randomised pts; n, number of responders

Disclosure of Interests: Philip J Mease Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Consultant for: AbbVie, Amgen, BMS, Galapagos, Gilead Sciences, Inc., Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer and UCB, Arthur Kavanaugh Grant/research support from: UCB Pharma, Andreas Reimold Grant/research support from: AbbVie, Hasan Tahir: None declared, Jürgen Rech Grant/research support from: Bristol-Myers Squibb and Celgene (greater than $10,000), Consultant for: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Speakers bureau: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Stephen Hall Grant/research support from: AbbVie Inc, BMS, Lilly, Janssen, Pfizer, UCB, and Novartis, Consultant for: AbbVie Inc, BMS, Lilly, Janssen, Pfizer, UCB, and Novartis
, Piet Geusens Grant/research support from: Research support, consultant and/or speaker fees from: Pfizer, Abbott, Eli Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, Will-Pharma, Grant/research support from: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Bio Minerals and Roche, Consultant for: Research support, consultant and/or speaker fees from: Pfizer, Abbott, Eli Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, Will-Pharma, Speakers bureau: Research support, consultant and/or speaker fees from: Pfizer, Abbott, Eli Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, Will-Pharma, Speakers bureau: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Bio Minerals and Roche, Pascale Pellet Shareholder of: Novartis, Employee of: Novartis, Eumorphia Maria Delicha Employee of: Novartis, Luminita Pricop Shareholder of: Novartis, Employee of: Novartis, Shephard Mpofu Employee of: Novartis

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FRI0452 **TOFACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS: ANALYSIS OF DERMATOLOGIC ENDPOINTS FROM 2 PHASE 3 STUDIES**

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Background: Psoriatic arthritis (PsA) is a chronic, systemic inflammatory disease; the onset of dermatologic symptoms often precedes rheumatic manifestations.[1] Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. It has been shown that tofacitinib can improve dermatologic symptoms in patients (pts) with PsA.[2,3]

Objectives: To investigate the efficacy of tofacitinib in improving additional dermatologic endpoints in adult pts with active PsA.

Methods: This analysis included data from 2 placebo (PBO)-controlled, double–blind, Phase 3 studies in pts with active PsA and an inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD) who were tumour necrosis factor inhibitor (TNFi)-naïve (OPAL Broaden [12 months; NCT01877668]; N=422)[2] or had an IR to ≥1 TNFi (OPAL Beyond [6 months; NCT01882439]; N=394).[3] Pts must have had active plaque psoriasis at screening only and were required to receive a stable dose of 1 csDMARD. Pts were randomised to tofacitinib 5 mg twice daily (BID), 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks (OPAL Broaden only) or PBO (advanced to tofacitinib 5 or 10 mg BID at Month [M]3). Percentage (%) change from baseline (BL) (Δ) in Psoriasis Area and Severity Index (PASI) total score, % of pts achieving ≥75% PASI improvement from BL (PASI75) stratified by BL PASI severity (>0 to ≤10, or >10), and ΔPatient's Global Joint and Skin Assessment-Visual Analogue Scale Psoriasis question (PGJS–VAS Psoriasis) were measured at M1, 3, 6, and at M9 and 12 (OPAL Broaden only).% ΔPASI total score and PASI75 were measured only in pts with BL affected body surface area (BSA) ≥3% and PASI >0. Safety endpoints were also analysed.

Results: BL demographics were similar between treatment groups and studies. BL median PASI scores (pts with BL BSA ≥3% and PASI >0) ranged from 5.6 to 7.8 (OPAL Broaden) and 7.1 to 8.8 (OPAL Beyond). BL mean PGJS–VAS Psoriasis ranged from 51.0 to 54.8 (OPAL Broaden) and 53.5 to 58.9 (OPAL Beyond). At M1 and 3,% ΔPASI total score, PASI75 response rates in pts with mild or moderate/severe dermatologic symptoms at BL, and ΔPGJS–VAS Psoriasis were improved vs PBO in tofacitinib-treated pts; these improvements were maintained to M12 in OPAL Broaden and M6 in OPAL Beyond (Table). Similar effects were observed in adalimumab-treated pts vs PBO in OPAL Broaden across these endpoints. Serious adverse events (AEs) and discontinuations due to AEs were similar across treatment groups up to M6 in OPAL Beyond and M12 in OPAL Broaden.

Conclusion: In pts with PsA (TNFi-naïve or TNFi-IR), tofacitinib improved dermatologic endpoints, and responses were maintained to the end of each study. Tofacitinib may provide a treatment option for pts with active PsA, including the dermatologic symptoms of PsA.

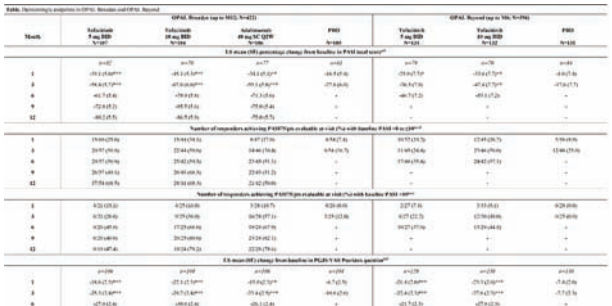
REFERENCES:

[1] Gladman DD, et al. Ann Rheum Dis 2005;64:ii14-7.
[2] Mease P, et al. N Engl J Med 2017;377:1537-50.
[3] Gladman D, et al. N Engl J Med 2017;377:1525-36.

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FRI0453 **DOES DISCORDANCE BETWEEN BASELINE PATIENT'S AND EVALUATOR'S GLOBAL ASSESSMENT OF DISEASE ACTIVITY IMPACT RETENTION AND REMISSION RATES OF TNF INHIBITORS IN PATIENTS WITH PSORIATIC ARTHRITIS? DATA FROM THE EUROSPA RESEARCH COLLABORATION**

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Background: Discordance between baseline patient's and evaluator's global assessment of disease activity is common[1] and may reduce the likelihood of remission following tumor necrosis factor inhibitor (TNFi) treatment in patients with psoriatic arthritis (PsA).[2] However, the impact of such discordance on retention rates of TNFi in PsA patients remains unexplored.

Objectives: To explore the impact of discordance, defined as patient's minus evaluator's global assessment (ΔPEG), on retention rates and remission rates (DAS28(3)CRP (which does not include patient's global) and DAS28(4)CRP (which includes patient's global)) in PsA patients initiating their first TNFi treatment. We used pooled data from the European Spondyloarthritis Research Collaboration (EuroSpA).

Methods: TNFi naïve PsA patients from 11 European registries in EuroSpA were included. Kaplan-Meier analyses were used to estimate TNFi retention rates after 6/12/24 months, with comparison between baseline ΔPEG quartiles using the log rank test, stratified by gender. Remission rates were compared between different ΔPEG quartiles with Chi-square test, stratified by gender.

Results: A total of 5422 PsA patients were included. Mean (SD) age for women(n=2988)/men(n=2867) were 49.3(12.5)/47.4(11.7) years, disease duration 6.6(7.3)/6.7(7.2) years, median(25-75 percentiles) baseline ΔPEG 17(0-38)/10(0-30) mm. Retention rates and DAS28(4)CRP but not DAS28 (3)CRP remission rates were lower for higher quartiles of baseline ΔPEG (table, figure).

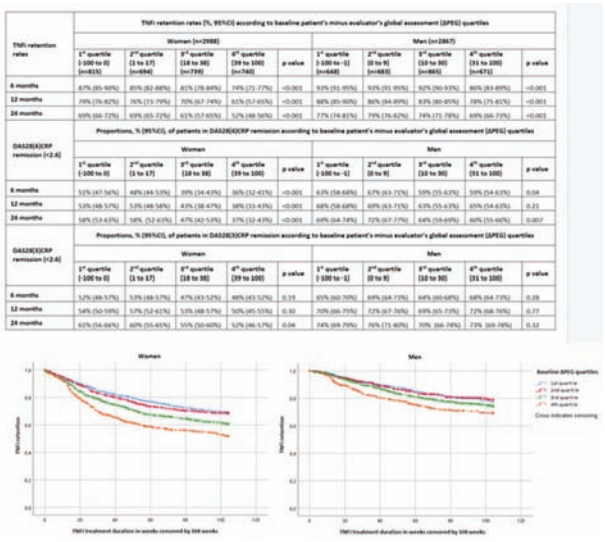
Conclusion: High baseline discordance (ΔPEG) was associated with lower TNFi retention rates and with DAS28(4)CRP but not DAS28(3)CRP remission rates after 6, 12 and 24 months' follow-up in both male and female PsA patients. The choice of remission criteria in the follow-up of PsA patients may affect important treatment decisions, and may be of particular impact in patients with high baseline ΔPEG.

REFERENCES:

[1] Lindstrom, et al., J Rheumatol 2015;42:1781-5; 2 Michelsen, et al. Ann Rheum Dis 2016;76:708-11.

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FRI0454 **EVOLUTION OF SUBCLINICAL ATEROSCLEROSIS IN PATIENTS WITH PSORIASTIC ARTHROPATHY**

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Background: Patients with psoriatic arthritis (PsA) have a higher prevalence of classical vascular risk factors (CVRF) and early atherosclerosis determined by chronic inflammation.

Objectives: To study the evolution over time of different vascular damage evaluation measures in patients with PsA and investigate the factors related to these changes.

Methods: Pre-post longitudinal study with analytical components. PsA patients with peripheral joint involvement were included. Demographic (sex, age), clinical [duration of the disease, DAS28, current treatment, body mass index (BMI), CVRF, vascular events] and analytical variables [atherogenic index, glomerular filtration (GF-MDRD), fibrinogen, glycosylated hemoglobin (HbA1c), CRP, ESR, ultrasensitive CRP, Apolipoprotein A1, apolipoprotein B] were collected. Other variables were collected from the clinical history retrospectively. Basal vascular risk was estimated through SCORE tool. Extracranial carotid artery was explored with an Esaote MyLab70XVG ultrasound with linear probe (7-12mHz) and an

automated program that measures intima media thickness (IMT) by radiofrequency ("Quality intima media thickness in real-time), and the presence of ateroma plaques was evaluated following Mannheim consensus. Pulse wave velocity (PWV) was measured through Mobil o graph® dispositive. We repeat vascular study 3 years later. IMT≥900 µ and PWV≥ 10m/s were considered as pathological values. Statistical analysis were performed using SPSS 22.0 program.

Results: 108 patients were included. Twelve patients excluded due to high vascular risk [previous event and/or diabetes type II or type I with target organ injury]. Repeated VOP measurement was only available in 49 patients. 64.2% of patients were women and the mean age was 54.2 (SD 1,3) years. Mean disease duration was 93.1 (SD 12.7) months and mean DAS28 was 1.7 (SD 0.1). 22.4% of patients received glucocorticoids, 47.8% NSAIDs, 83.6% DMARDs and 37.3% biological drugs. Mean BMI was 26.5 (SD 0.5) kg/m². 38.8%, 28.4% and 43.3% of patients were smokers, hypertensive (11.9% on ARA2, 3% on IECA, 1.5% on calcium channel blockers, 10.4% on combined treatment) and 43.3% dyslipidemic [most of them (38.8%) on statins]. Mean CRP and ESR were 6.2 (SD 0.4) mg/l and 9.9 (SD 1) mm/h, respectively. Mean SCORE was 1.06 (SD 0.1). Baseline, 23.9% of patients had atheromatous plaques, and 13.4% and 20.4% had a pathological IMT or PWV, respectively. Three years later, we detected new and/or atheromatous plaques rises in 19.4% of patients and PWV and IMT worsening in 10.2% and 1.5% of patients, respectively. As per logistic regression analysis, high baseline SCORE (16.9%), high systolic blood pressure (8.6%), GF-MDRD (8.2%), fibrinogen (6.8%) and the presence of dyslipidemia were the factors that most contributed to the progression of vascular damage, with independence of the therapeutic objective used for their treatment.

Conclusion: Progression of vascular damage is mainly related to CVRF in patients with PsA, therefore it is essential to intervene on CVRF early.

Disclosure of Interests: None declared

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FRI0455 USE OF SECUKINUMAB IN PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS….REAL WORLD DATA

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Background: Secukinumab was the IL-17 inhibitor licensed for use in Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS). The aim of this study was to evaluate the effectiveness and safety of Secukinumab in our cohort of patients.

Objectives: In order to assess the effectiveness and safety of Secukinumab, a retrospective analysis of patients treated with this drug in the Northern Health and Social Care Trust was undertaken.

Methods: Retrospective data was collected from the Local Biologic database. All patients who were on Secukinumab were selected. They were divided into two arms, Psoriatic Arthritis and Ankylosing Spondylitis. From this baseline disease severity was sought, baseline inflammatory markers and patient cohort data was collected. Patients were seen routinely at three monthly intervals and outcomes were collected up to a 12 month period. From patient notes drug response and adverse effects were recorded.

Results: A total of 41 patients with psoriatic arthritis were treated with Secukinumab over the 12-month period studied. Twenty-six patients were female and fifteen were male, with ages ranging from 26 to 70. Only 12 of the patients were on concomitant methotrexate, all met the NICE start criteria with required DAS 76 scores. Seven of the patients were biologic naïve (17%) at commencement of drug.

Of all the patients who responded, most had some response by 3 months, and all had further response by six months.

Sixteen patients (39%) discontinued treatment due to no response, one due to increasing shortness of breath, wheeze and rash, and one patient developed colitis.

Other side effects were noted, which did not cause the drug to be discontinued. Five patients had rash and urticaria, three reported headaches. Infections were fairly common, five patients had chest infections, four had sinusitis and three had urinary tract infections. Four patients reported thrush, one oral thrush and three vaginal.

A total of 18 patients with Ankylosing Spondylitis were commenced on Secukinumab. 11 males and 7 females. A third (6/18) were biologic naïve. Ages ranged from 27 to 65.

In the first three months of commencement there was a reduction in BADSAI scores of all patients. This remained at six months. Inflammatory markers CRP and ESR were also reduced.

Seven patients discontinued Secukinumab after six months due to side effects or lack or perceived response by the patient (seen in 1 patient). Two patients had a loss of efficacy. The remaining four patients noted cutaneous skin infections, sinus symptoms or headaches as noted in the PsA arm of the audit.

Conclusion: Patients in the Northern Trust starting Secukinumab generally have severe disease and most have had prior treatment with biologics. There was a high incidence of non responders in this group, however in those patients who responded there was a good response rate at 3 months, and these patients were still on treatment at 12 months. Side effects were as expected, with infections being the most commonly reported side effect.

REFERENCES:

[1] Robertson J, Tindell A, Crosbie D, Siebert S. Real-world experience of secukinumab for psoriatic arthritis and axial spondyloarthritis. Rheumatology. Volume 57. Issue suppl_3, April 2018.

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FRI0456 THE EFFECT OF GENDER ON DISEASE ACTIVITY, FUNCTIONAL INDEX AND QUALITY OF LIFE IN PATIENTS WITH AXIAL SPA. THE DATA OF TLAR-NETWORK PSA STUDY

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Background: PsA is a chronic musculoskeletal disease. The prevalence of axial involvement in PsA varies according to the duration of the disease. In early stage the incidence varies between 5% and 28%, but it increases up to 25-70% in later stages of the disease. In the literature, there is limited data on the differences in disease activity, functional status and quality of life of men and women with axial PsA.

Objectives: In this study, we aimed to evaluate the effect of gender difference on clinical findings, disease activity, functional status and quality of life in patients with axial involvement in Turkey.

Methods: Patients with PsA who met the CASPAR classification criteria were enrolled consequently in this cohort. Turkish League Against Rheumatism (TLAR)- Network was formed with the participation of 25 centers. The demographic variables, fatigue, diagnostic delay, the beginning of peripheral arthritis, enthesitis, dactylitis and spine involvement, inflammatory lumbar pain, patients' quality of life, BASFI, HAQ, HAQ-s,VAS pain, anxiety, depression and disease activity parameters (TJC, SJC, ESH, DAS28, BASDAI), were recorded. Student's t test and Chi-square test were used to compare variables in SPSS v.22 program.

Results: A total of 1130 patients (36.0% male, 64.0% female) with PsA included in this study. In this cohort, 169 male (46 ± 12.29) and 251 female (47.4 ± 12.11) had axial involvement. VAS pain ($p < 0.001$), fatigue ($p < 0.001$), ESR ($p < 0.001$), DAS28 ($p < 0.001$), BASDAI score ($p < 0.001$), PsAQoL ($p < 0.001$), HAQ score ($p < 0.001$), HAQ-S score ($p < 0.001$), anxiety ($p < 0.001$), depression ($p < 0.020$), FACIT ($p < 0.001$) and FIRST ($p < 0.001$) scores were statistically significantly worse in women than males with axial PsA (Table 1). However, SF-36 physical component score ($p < 0.001$), SF-36 mental component score ($p < 0.001$) and PASI score ($p < 0.005$) were statistically worse in male patients than in female patients with axial involvement.

Conclusion: This study shown that the burden of disease in axial PsA has a significantly different between genders. Female patients with PsA who have axial involvement have higher disease activity, physical disability, functional limitation and higher depression and anxiety risk than male patients. Therefore, we suggest that new strategies should be developed for more effective treatment of axial PsA in female patients.

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FRI0457

SECUKINUMAB PROVIDES SIGNIFICANT AND SUSTAINED IMPROVEMENT IN NAIL PSORIASIS AND SIGNS AND SYMPTOMS OF PSORIATIC ARTHRITIS IN PATIENTS WITH NAIL PHENOTYPE: 52-WEEK RESULTS FROM THE PHASE III FUTURE 5 STUDY

Peter Nash[1], Philip J. Mease[2], Bruce Kirkham[3], Alejandro Balsa[4], Atul Singhal[5], Erhard Quebe-Fehling[6], Luminita Pricop[7], Corine Gaillez[6]. *[1]University of Queensland, Brisbane, Australia*; *[2]Swedish Medical Center and University of Washington, Seattle, United States of America*; *[3]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom*; *[4]Hospital La Paz – IdiPAZ, Madrid, Spain*; *[5]Southwest Rheumatology, Dallas, United States of America*; *[6]Novartis Pharma AG, Basel, Switzerland*; *[7]Novartis Pharmaceuticals Corporation, East Hanover, United States of America*

Background: Nail psoriasis (PsO) is present in up to 80% in psoriatic arthritis (PsA) patients (pts) and associated with significant pain, psychosocial disability, decreased physical function and quality of life (QoL).[1] Nail PsO is considered as one of the six core PsA domains by GRAPPA[2] and is a predictor of severe disease with joint involvement and structural damage. Secukinumab (SEC) has demonstrated efficacy for pts with nail PsO in the TRANSFIGURE study[3] and significant improvement in signs and symptoms of PsA in the FUTURE 5 study[4]

Objectives: To evaluate the efficacy of SEC on nail PsO and other facets of disease in the nail subset from the FUTURE 5 study through 52 weeks (wks).

Methods: Pts (N=996) with active PsA, were randomised to subcutaneous SEC 300 mg loading dosage (LD; 300 mg), 150 mg LD (150 mg), 150 mg no LD or placebo (PBO). All groups received SEC or PBO at baseline (BL), Wks 1, 2, 3, and 4, and then every 4 wks. Efficacy assessments through Wk 52 included mNAPSI, ACR, PASI, HAQ-DI, SF-36 PCS, PsAQoL and resolution of dactylitis and enthesitis. Analyses through Wk 16 used non-responder imputation (NRI) for binary and mixed-effect model repeated measure (MMRM) for continuous variables. Observed data are presented from Wk 20-52.

Results: A total of 663/996 (66.6%) PsA pts had concomitant nail PsO at BL. Demographics and BL disease characteristics were balanced between treatment groups in the nail subset, which were comparable with overall population. The total mean mNAPSI score at BL was 16.4. SEC 300 and 150 mg doses improved nail PsO vs. placebo (PBO) at Wk 8, 12 and 16 ($P < 0.0001$), with further improvements through Wk 52 (Figure). ACR20/50 and PASI 90 responses, resolution of dactylitis and enthesitis, physical function and QoL were also improved with SEC vs. PBO at Wk 16 with sustained improvements through 52 wks (Table).

Conclusion: Secukinumab provided sustained improvements in nail disease, signs and symptoms of PsA, physical function and QoL through 52 wks in pts with PsA and moderate to severe nail PsO.

REFERENCES:

[1] Baran R. Dermatology 2010;221(Suppl1):1-5.
[2] Coates LC, et al. *Arthritis Rheumatol.* 2016;68:1060-71.
[3] Reich K, et al. Br J Dermatol. 2018. Doi: 10.1111/bjd.17351.
[4] Mease PJ, et al. Ann Rheum Dis. 2018;77:890-7.

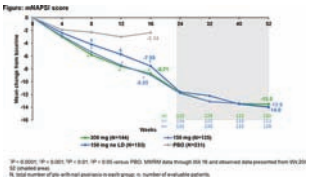


Table: Summary of results

Variable	Wk	SEC 300 mg N=144	SEC 150 mg N=135	SEC 150 mg no LD N=153	PBO N=231
ACR20[1]	16	66.7*	60.0*	61.4*	29.0
	52	81.2 (133)	73.7 (118)	77.9 (136)	-
ACR50[1]	16	43.1*	40.7*	32.0*	9.1
	52	54.1 (133)	45.8 (118)	50.7 (136)	-
PASI 90[1,2]	16	52.0*	36.8*	31.0*	7.6
	52	62.3 (69)	50.7 (75)	49.3 (75)	-
HAQ-DI[3]	16	-0.6*	-0.5*	-0.5*	-0.2
	52	-0.6 (132)	-0.6 (117)	-0.6 (136)	-
SF-36 PCS[3]	16	7.82*	6.90*	6.00*	2.29
	52	8.0 (134)	6.71 (123)	7.93 (137)	-
PsAQoL[3]	16	-3.6*	-3.6*	-3.0†	-1.1
	52	-3.9 (134)	-4.2 (122)	-3.8 (137)	-
Resolution of enthesitis, %[4]	16	58.2†	56.8†	47.2‡	34.3
	52	81.5 (92)	68.7 (80)	70.7 (82)	-
Resolution of dactylitis, %[4]	16	63.8†	52.6‡	59.2†	32.4
	52	78.8 (52)	79.6 (49)	80.3 (66)	-

*P<0.0001; †P<0.001; §P<0.01; ‡P<0.05 vs. PBO. NRI data for binary and MMRM data for continuous variables presented at Wk 16. Observed data presented at Wk 52.
[1]% responders (n); [2]Data from pts with BL psoriasis ≥3% BSA: N=75 [300 mg]; 87 [150 mg], 84 [150 mg no LD] and 118 [PBO]; [3]Mean change from baseline (n); [4]Data from pts with enthesitis/dactylitis at BL: N=98/58 [300 mg]; 88/57 [150 mg], 89/76 [150 mg no LD] and 140/102 [PBO]; N, number of pts with nail PsO in each group; n, number of evaluable pts at Wk 52

Table. Summary of results

Variable	Wk	SEC 300 mg N=144	SEC 150 mg N=135	SEC 150 mg no LD N=153	PBO N=231
ACR20[1]	16	66.7*	60.0*	61.4*	29.0
	52	81.2 (133)	73.7 (118)	77.9 (136)	-
ACR50[1]	16	43.1*	40.7*	32.0*	9.1
	52	54.1 (133)	45.8 (118)	50.7 (136)	-
PASI 90[1,2]	16	52.0*	36.8*	31.0*	7.6
	52	62.3 (69)	50.7 (75)	49.3 (75)	-
HAQ-DI[3]	16	-0.6*	-0.5*	-0.5*	-0.2
	52	-0.6 (132)	-0.6 (117)	-0.6 (136)	-
SF-36 PCS[3]	16	7.82*	6.90*	6.00*	2.29
	52	8.0 (134)	6.71 (123)	7.93 (137)	-
PsAQoL[3]	16	-3.6*	-3.6*	-3.0†	-1.1
	52	-3.9 (134)	-4.2 (122)	-3.8 (137)	-
Resolution of enthesitis,%[4]	16	58.2†	56.8†	47.2‡	34.3
	52	81.5 (92)	68.7 (80)	70.7 (82)	-
Resolution of dactylitis,%[4]	16	63.8†	52.6‡	59.2†	32.4
	52	78.8 (52)	79.6 (49)	80.3 (66)	-

*P<0.0001; †P<0.001; §P<0.01; ‡P<0.05 vs. PBO. NRI data for binary and MMRM data for continuous variables presented at Wk 16. Observed data presented at Wk 52.
[1]% responders (n); [2]Data from pts with BL psoriasis ≥3% BSA: N=75 [300 mg]; 87 [150 mg], 84 [150 mg no LD] and 118 [PBO]; [3]Mean change from baseline (n); [4]Data from pts with enthesitis/dactylitis at BL: N=98/58 [300 mg]; 88/57 [150 mg], 89/76 [150 mg no LD] and 140/102 [PBO]; N, number of pts with nail PsO in each group; n, number of evaluable pts at Wk 52

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FRI0458 OBJECTIVE MEASURES OF PSORIASIS SEVERITY AND THE RISK FOR PSA: RESULTS FROM THE INCIDENT HEALTH OUTCOMES AND PSORIASIS EVENTS PROSPECTIVE COHORT STUDY

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Background: Psoriasis severity is a presumed risk factor for development of psoriatic arthritis (PsA) but most studies have examined this question retrospectively. Additionally, it remains unclear whether obesity and body surface area of psoriasis (BSA) are independent risk factors for PsA.
Objectives: We examined the association of psoriasis severity, obesity and other potential risk factors for the development of PsA in patients with psoriasis.
Methods: Between 2008-2011, patients with at least one code for psoriasis aged 25-60 years in The Health Improvement Network were randomly selected and questionnaires were sent to their general practitioners (GPs). GPs were asked to confirm the diagnosis of psoriasis and provide the patient's approximate BSA that the patient typically demonstrates based on categories commonly used for epidemiological studies. Data through 2015 were used in the current analysis. After excluding patients with PsA at baseline, the incidence of PsA among patients with psoriasis was calculated. Cox proportional hazard ratios were used to examine the risk of developing PsA among patients with mild (<3%), moderate (3-10%) and severe (>10%) psoriasis. We also examined other covariates including obesity, depression, recent infections, smoking, and comorbidities in univariable models. Factors significant at the unviariable level were included in multivariable models. We additionally tested an interaction between BSA and obesity.
Results: Among 10,474 questionnaires sent, 9,987 (95%) were returned and, of those, 9,069 (91%) had confirmed psoriasis. The mean age was 46 and 53% were female. BSA was provided for 8,881 patients of which 52% had mild psoriasis, 36% moderate psoriasis, and 12% severe psoriasis. Mean follow up time was 4.2 years (SD 2.1); the incidence of PsA was 5.4 cases per 1,000 person years. In univariable models, age and sex were not associated with PsA but obesity, BMI (continuous), BSA (continuous and category) and depression were significantly associated with development of PsA. The final multivariable model included BSA category (ref mild, moderate: HR 1.44, 95%CI: 1.02-2.03; severe HR 1.99, 1.28-3.11), history of depression (1.69, 1.22-2.34), obesity (1.64, 1.19-2.25), age (HR 0.99, 0.98-1.00) and female sex (HR 0.72, 0.52-0.99). There was not a statistically significant interaction between BSA and obesity although patients that were obese and had $\geq$10% BSA had the highest risk (HR 3.90, 2.22-6.85).
Conclusion: In this large prospective cohort study, we found that body surface area is a strong predictor of developing psoriasis over the next 4-7 years and obesity is an additive risk factor.

REFERENCES:

[1] Scher JU, et al. Nat Rev Rheumatol 2019 In Press.

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	Univariable	Multivariable
	HR (95% CI)	**HR (95% CI)**
Age	0.99 (0.98-1.00)	0.99 (0.98-1.00)
Female Sex	0.83 (0.63-1.09)	0.72 (0.52-0.99)
Body Mass Index (per 1 unit)	1.04 (1.02-1.07)	
Obese BMI (BMI>30 vs <=30)	1.62 (1.20-2.17)	1.64 (1.19-2.25)
Smoking		
Never	Ref	
Current	0.90 (0.64-1.27)	
Past	1.30 (0.95-1.79)	
Body Surface Area Category		
Mild (<3)	Ref	
Moderate (3-10)	1.55 (1.13-2.14)	1.44 (1.02-2.03)
Severe (>10)	2.40 (1.60-3.59)	1.99 (1.28-3.11)
Anxiety	0.94 (0.67-1.32)	
Depression	1.45 (1.09-1.92)	1.69 (1.22-2.34)
Any diarrheal illness	1.28 (0.93-1.75)	
Disabled	1.41 (0.75-2.67)	
Prior light therapy	2.29 (1.33-3.93)	
Hyperlipidemia	0.94 (0.60-1.48)	
Hypertension	1.04 (0.72-1.49)	
Diabetes	0.72 (0.40-1.30)	

FRI0459 PREVALENCE OF DISEASE DOMAIN PRESENTATIONS AMONG PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM THE CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

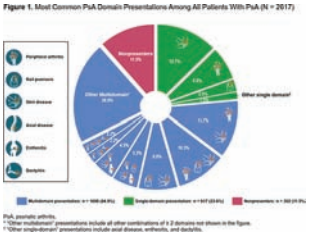
Alexis Ogdie[1], Peter Hur[2], Mei Liu[3], Sabrina Rebello[3], Robert Mclean[3], Blessing Dube[3], Meghan Glynn[3], Philip J. Mease[4]. *[1]Perelman School of Medicine at the University of Pennsylvania, Philadelphia, United States of America*; *[2]Novartis Pharmaceuticals Corporation, East Hanover, United States of America*; *[3]Corrona, LLC, Waltham, United States of America*; *[4]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, United States of America*

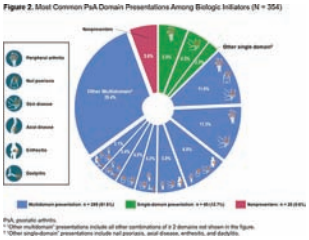
Background: Psoriatic arthritis (PsA) is a heterogeneous, chronic inflammatory disease of the skin and musculoskeletal system. Six key domains of PsA have been identified to help guide treatment: peripheral arthritis, axial disease, enthesitis, dactylitis, and psoriatic skin and nail disease.[1] Understanding the epidemiology of these different disease presentations is important for the management and treatment of PsA, yet there is limited evidence available.
Objectives: To describe the prevalence of disease domain presentations among patients with PsA at enrollment in the Corrona PsA/SpA Registry.
Methods: This study included adult patients with PsA enrolled in the Corrona PsA/SpA Registry between March 2013 and August 2018. Patients were evaluated for the presence of 6 disease domains at enrollment: enthesitis (Spondyloarthritis Research Consortium of Canada enthesitis count > 0), dactylitis (dactylitis count > 0), peripheral arthritis (PA; tender and/or swollen joint count > 0), nail psoriasis (global nail psoriasis visual analog scale > 0), axial disease (physician-reported presence of spinal involvement, based on clinical judgment and/or radiographs or MRI showing sacroiliitis), and skin disease (BSA > 0%). The most common mutually exclusive disease presentations were summarized among all patients

with PsA and those who initiated biologics using frequency counts and percentages.

Results: Of 2617 patients with PsA enrolled in the Corrona PsA/SpA Registry, 1698 patients (64.9%) had multidomain disease presentations, 617 (23.6%) had single-domain presentations, and 302 (11.5%) had no presentations. Overall, 1814 (69.3%) patients presented with skin disease, 1523 (68.2%) with PA, 1042 (39.8%) with nail psoriasis, 539 (20.6%) with enthesitis, 319 (12.2%) with axial disease, and 235 (9.0%) with dactylitis at enrollment. Among all patients with PsA, the most common disease presentations were skin disease (2.7%), PA + skin disease (11.7%), and PA + nail psoriasis + skin disease (10.3%) (**Figure 1**).. A total of 354 patients initiated biologics at enrollment. Of these, 289 patients (81.6%) had multidomain disease presentations, 45 (12.7%) had single-domain presentations, and 20 (5.6%) had no presentations; 273 patients (77.1%) presented with PA, 267 (75.4%) with skin disease, 159 (44.9%) with nail psoriasis, 115 (32.5%) with enthesitis, 70 (19.8%) with dactylitis, and 64 (18.1%) with axial disease at enrollment. The most common disease presentations were PA + nail psoriasis + skin disease (11.6%), PA + skin disease (11.3%), and enthesitis + PA + nail psoriasis + skin disease (8.8%), and enthesitis + PA + skin disease (5.9%) (**Figure 2**).

Conclusion: The majority of patients with PsA presented with multiple disease domains. Biologic initiators generally had a higher prevalence of all disease features. These results may increase the physician awareness of the heterogeneity of disease presentations among patients with PsA, which can be important for the development of an effective management plan.





REFERENCES:

[1] Coates LC, et al. *Arthritis Rheumatol.* 2016;68(5):1060-71.

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FRI0460 IMPACT OF MULTIDOMAIN DISEASE PRESENTATIONS ON OVERALL DISEASE BURDEN AMONG PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM THE CORRONA PSORIATIC ARTHRITIS/ SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease with heterogeneous presentations that may involve peripheral arthritis, axial disease, enthesitis, dactylitis, and psoriatic skin and nail disease, either alone or in combination. Prior studies have characterized patients affected in one domain[1,2]; however, there is limited evidence in understanding the differential impact of multidomain vs single-domain presentations on the overall disease burden in PsA.

Objectives: To compare disease characteristics, quality of life, and work productivity at enrollment among patients with PsA who have multidomain vs single-domain presentations in the Corrona PsA/SpA Registry.

Methods: This study included adult patients with PsA enrolled in the Corrona PsA/SpA Registry between March 2013 and August 2018. Patients were evaluated for the presence of 6 disease domains at enrollment: enthesitis (SPARCC enthesitis count > 0), dactylitis (dactylitis count > 0), peripheral arthritis (PA; tender and/or swollen joint count > 0), nail psoriasis (global nail psoriasis VAS > 0), axial disease (physician-reported presence of spinal involvement, based on clinical judgment and/or radiographs or MRI showing sacroiliitis), and skin disease (BSA > 0%), and were further classified as having multidomain or single-domain disease presentations. Separate multivariable linear regression models evaluated the association of the presence of multidomain presentations with selected PsA disease characteristics, quality of life, and work productivity measures relative to single-domain presentations. Models were adjusted for age, sex, race, BMI, disease duration, and current and prior biologic, conventional synthetic disease-modifying antirheumatic drug, and prednisone use.

Results: Of 2315 patients with PsA enrolled in the Corrona PsA/SpA Registry who had $\geq$ 1 disease domain presentation, 1698 patients (73.3%) were classified as having multidomain disease presentations and 617 (26.7%) as single-domain presentations. The most common single-domain and multidomain presentations, respectively, were skin disease (12.7%) and PA + skin disease (11.7%). At enrollment, patients with multidomain presentations had higher BMI; shorter disease duration; were more likely to have fibromyalgia, depression, and anxiety; and were more likely to have prior biologic use vs those with single-domain presentations (**Table 1**). In adjusted analyses, the presence of multidomain presentations was associated with significantly worse patient and physician global assessment of disease, pain, fatigue, HAQ-DI and EQ-5D scores, and work productivity and activity at enrollment (**Table 2**).

Conclusion: In this US real-world cohort, nearly three-quarters of patients with PsA had multidomain disease presentations, which were associated with worse disease activity, quality of life, and work productivity measures compared with single-domain disease presentations. Assessing all PsA domains is critical for developing a comprehensive management plan and reducing the impact of PsA on patients' lives.

REFERENCES:

[1] Mease PJ, et al. *Arthritis Care Res (Hoboken).* 2017;69(11):1692-9.

[2] Mease PJ, et al. J Rheumatol. 2018;45(10):1389-96.

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companies. The abstract was a collaborative effort between Corrona and Novartis, with financial support provided by Novartis.

Table 1. Demographics, Treatment Profiles, Disease Activity, Quality of Life, and Work Productivity at Enrollment for Patients With Multidomain vs Single-Domain PsA Disease Presentations

Characteristic*	Multidomain (N = 1698)	Single Domain† (N = 617)	*P* Value‡
Age, years	53.5 (13.2) [1678]	54.5 (12.9) [607]	0.20
Female, n/m (%)	907/1689 (53.7)	314/610 (51.5)	0.35
Race, n (%)	n = 1655	n = 596	0.04
White	1548 (93.5)	572 (96.0)	
Black	9 (0.5)	4 (0.7)	
Other	98 (5.9)	20 (3.4)	
BMI, kg/m^2	32.0 (7.4) [1658]	31.3 (7.6) [600]	< 0.01
Symptom duration, years	11.3 (10.7) [1651]	11.0 (9.7) [594]	0.51
Disease duration, years	7.7 (8.8) [1662]	8.5 (8.1) [598]	< 0.01
Select comorbidities, n (%)			
Psoriasis	1537 (90.5)	520 (84.3)	< 0.01
Nail psoriasis	602 (35.5)	81 (13.1)	< 0.01
Depression	280 (16.5)	57 (9.2)	< 0.01
Fibromyalgia	114 (6.7)	23 (3.7)	< 0.01
Anxiety	65 (3.8)	12 (1.9)	0.03
History of biologic use, n (%)	561 (33.0)	151 (24.5)	< 0.01
History of csDMARD use, n (%)	478 (28.2)	151 (24.5)	0.08
History of prednisone use, n (%)	230 (13.5)	83 (13.5)	0.95
Current biologic use, n (%)	980 (57.7)	378 (61.3)	0.13
Current csDMARD use, n (%)	859 (50.6)	339 (54.9)	0.06
Current prednisone use, n (%)	122 (7.2)	42 (6.8)	0.75
Physician global assessment (VAS 0-100)	24.3 (21.4) [1686]	10.9 (15.0) [612]	< 0.01
Physician global assessment of psoriasis (VAS 0-100)	28.0 (22.6) [1661]	12.9 (15.0) [594]	< 0.01
Patient pain (VAS 0-100)	44.8 (29.2) [1590]	28.6 (26.9) [580]	< 0.01
Patient-reported fatigue (VAS 0-100)	45.9 (29.2) [1676]	33.8 (28.4) [602]	< 0.01
Patient global assessment (VAS 0-100)	43.1 (28.4) [1669]	36.8 (31.5) [605]	< 0.01
HAQ-DI (0-3)	0.8 (0.7) [1600]	0.5 (0.6) [586]	< 0.01
EQ-5D (0-1)	0.7 (0.2) [1592]	0.8 (0.2) [579]	< 0.01
EQ VAS (0-100)	67.4 (21.5) [1667]	75.5 (19.8) [606]	< 0.01
WPAI domains			
Current employment, n/m (%)	987/1646 (60.0)	381/595 (64.0)	0.08
% Work time missed	6.2 (17.5) [842]	2.7 (11.3) [323]	< 0.01
% Impairment while working	22.9 (24.4) [887]	12.4 (18.9) [344]	< 0.01
% Overall work impairment	26.2 (26.8) [798]	13.0 (19.5) [306]	< 0.01
% Activity impairment	34.7 (29.9) [1530]	19.1 (24.3) [549]	< 0.01

BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; EQ-5D, EuroQol-5 Dimensions; EQ VAS, EuroQol visual analogue scale; HAQ-DI, Health Assessment Questionnaire Disability Index; PsA, psoriatic arthritis; WPAI, Work Productivity and Activity Impairment questionnaire; VAS, visual analog scale.
* All values were calculated based on available data and are presented as "mean (SD) [n]" unless otherwise stated.
† Single-domain disease presentations for PsA overall (N = 617) included skin disease (53.8%), peripheral arthritis (29.0%), nail psoriasis (10.9%), axial disease (3.4%), enthesitis (1.8%), and dactylitis (1.1%).
‡ *t*-test or Wilcoxon rank-sum test for continuous variables and χ^2 or Fisher's exact test for categorical variables.

Table 2. Multidomain vs Single-Domain Impact on Outcomes—Multivariable Regression Coefficients Estimating the Association of Presence of Multidomain Presentations With Selected PsA Disease Activity, Quality of Life, and Work Productivity and Activity Measures Relative to Single-Domain Presentations in Patients With PsA

Outcomes*	β Coefficient (95% CI)	*P* Value
Physician global assessment	12.16 (10.30, 14.01)	< 0.001
Physician global assessment of psoriasis	14.03 (12.03, 16.04)	< 0.001
Patient pain	14.02 (11.26, 16.78)	< 0.001
Patient-reported fatigue	10.09 (7.38, 12.81)	< 0.001
Patient global assessment	5.65 (2.81, 8.49)	< 0.001
HAQ-DI	0.26 (0.20, 0.32)	< 0.001
EQ-5D	−0.07 (−0.09, −0.06)	< 0.001
% Work time missed	2.71 (0.57, 4.84)	0.013
% Impairment while working	8.63 (5.72, 11.55)	< 0.001
% Overall work impairment	11.02 (7.69, 14.36)	< 0.001
% Activity impairment	13.47 (10.65, 16.29)	< 0.001

BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; EQ-5D, EuroQol 5-Dimensions; HAQ-DI, Health Assessment Questionnaire Disability Index; PsA, psoriatic arthritis.
* Single-domain disease is the reference group. Adjusted for age, sex, race, BMI, disease duration, and current and prior biologic, csDMARD, and prednisone use.

Disclosure of Interests: Alexis Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer Inc, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Peter Hur Employee of: Peter Hur is an employee of Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, USA, Mei Liu Employee of: M. Liu is an employee of Corrona, LLC., Sabrina Rebello Employee of: Corrona, LLC, Robert McLean: None declared, Blessing Dube Employee of: B. Dube is an employee of Corrona, LLC., Meghan Glynn Employee of: M. Glynn is an employee of Corrona, LLC., Philip J Mease Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Consultant for: AbbVie, Amgen, BMS, Galapagos, Gilead Sciences, Inc., Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer and UCB

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FRI0461 GENETIC ANALYSIS OF THE NF-KB PATHWAY CAN BE USEFUL TO DISTINGUISH PATIENTS AT RISK OF PSORIATIC ARTHRITIS WITHIN THE SPECTRUM OF PSORIATIC DISEASE

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Background: Psoriasis and psoriatic arthritis (PsA) are the main manifestations of what is now known as psoriatic disease. Both entities share common genetic pathways, but they also differ. The NF-Kb pathway has been implicated in the genesis of psoriatic disease, but the differential contribution of this genetic pathway to the risk of psoriasis and PsA is not fully understood[1].
Objectives: Our aim was to study the association of common polymorphisms at genes of the NF-Kb pathway in patients with psoriatic disease.
Methods: The study involved a total of 690 psoriatic disease patients (187 of them with PsA) and 550 controls. We genotyped three common polymorphisms in *NFKB1* (rs230526), *NFKBIA* (rs7152376) and *NFKBIZ* (rs3217713 indel) and compared allele and genotype frequencies between cases and controls.
Results: The rare *NFKBIA* rs7152376 C was significantly more frequent in the PsA group vs. controls (0.42 vs. 0.36; p=0.04, OR=1.29, 95% CI=1.02-1.63). Compared to skin psoriasis, PsA patients showed a significantly higher frequency of the rs7152376 C (0.42 vs. 0.31; p<0.001). In reference to the genotypes, carriers of rs7152376 C (CC+CT) were non-significantly more frequent in PsA compared to controls (0.66 vs. 0.58; p=0.06). However, the frequency of these carriers was significantly higher in PsA vs. skin psoriasis (p=0.004). Thus, our data showed significant association between the rare *NFKBIA* rs7152376 C allele and PsA, and a trend toward the opposite effect for skin psoriasis. Neither *NFKB1* rs230526 or *NFKBIZ* rs3217713 indel were associated with the risk of developing psoriasis or PsA.
Conclusion: We found a significant association between *NFKBIA* variants and PsA. Our study shows that alterations in the same genetic pathway may have differential effects on different manifestations of psoriatic disease. Additional studies from larger cohorts and different populations are necessary to validate these results.

REFERENCES:

[1] Nair RP, Duffin KC, Helms C, et al. Genome-wide scan reveals association of psoriasis with IL-23 and NF-kappaB pathways. Nat Genet 2009; 41: 199-204.

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FRI0462 UNDERSTANDING MEDIATORS OF PAIN REDUCTION IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH TOFACITINIB: ROLE OF INFLAMMATION

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Background: Pain is a priority for patients (pts) with psoriatic arthritis (PsA) and physicians. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. As pain is a multidimensional phenomenon, there is growing interest in understanding mechanisms of pain relief during treatment.
Objectives: To examine the potential role of inflammation in the effect of tofacitinib on pain in pts with PsA, using mediation modelling.
Methods: Data were from the Phase 3 OPAL Broaden (NCT01877668) and OPAL Beyond (NCT01882439) studies of pts with active PsA treated

with tofacitinib 5 mg twice daily (BID) or placebo; pts were tumour necrosis factor inhibitor (TNFi)-naïve or had previous inadequate response (IR) to ≥1 TNFi. All pts continued on a stable dose of a single conventional synthetic DMARD. Analyses used pooled and individual trial data (mean scores from Months 1, 2 and 3). Mediation modelling seeks to explain mechanisms underlying an observed relationship between independent and dependent variables via other explanatory variables (mediators). In this model, pain (100 mm visual analogue scale) was the designated dependent variable, treatment (tofacitinib 5 mg BID vs placebo) the independent variable and inflammation, measured by swollen joint count (SJC) and C-reactive protein (CRP), was a mediator. The primary model designated treatment effect on pain mediated via CRP/SJC as an indirect effect and treatment effect not attributable to CRP/SJC as a direct effect. Models were re-specified based on initial results; model invariance by population (TNFi-naïve vs TNFi-IR pts) was assessed.

Results: In the pooled analysis (N=469), 25.9% ($p<0.01$) of the tofacitinib treatment effect on pain was mediated by CRP/SJC (indirect effect), of which changes via CRP and SJC were 17.8% ($p<0.01$) and 8.1% ($p>0.05$), respectively. The treatment effect on pain not attributable to CRP/SJC (direct effect) was 74.1% ($p<0.0001$). In TNFi-naïve and TNFi-IR pts, indirect effects via SJC were not statistically significant. In the re-specifed model with CRP as sole mediator, the indirect effect was 21.3% for pooled data ($p<0.01$; Figure A) and 36.1% ($p<0.05$) and 16.7% ($p<0.05$) for TNFi-naïve and TNFi-IR pts, respectively (Figures B, C); the 19.4% difference between TNFi-naïve vs TNFi-IR pts was not statistically significant.

Conclusion: While inflammation, as assessed by CRP/SJC, was a significant mediator of the overall treatment effect on pain in tofacitinib-treated pts with PsA, the majority of the treatment effect was not attributable to CRP/SJC changes. When mediators were assessed individually, only CRP was a significant mediator in the pooled analysis. In the re-specified model, CRP-mediated effects differed in TNFi-naïve vs TNFi-IR pts, but this was not statistically significant. These results suggest that CRP/SJC-associated inflammation only partially explains pain in PsA; other potential mediators need to be identified to better understand the treatment effect of tofacitinib on pain.

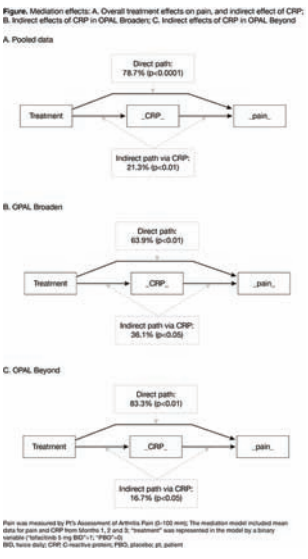


Figure. Mediation effects: A. Overall treatment effects on pain, and indirect effect of CRP; B. Indirect effects of CRP in OPAL Broaden; C. Indirect effects of CRP in OPAL Beyond

Pain was measured by Pt's Assessment of Arthritis Pain (0-100 mm); The mediation model included mean data for pain and CRP from Months 1, 2 and 3; "treatment" was represented in the model by a binary variable (Tofacitinib 5 mg BID=1; "PBO"=0).
BID, twice daily; CRP, C-reactive protein; PBO, placebo; pt, patient

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FRI0463

ENTHESITIS, DACTYLITIS, AND AXIAL DISEASE IN PSORIATIC ARTHRITIS (PSA): IMPACT ON PATIENT QUALITY OF LIFE AND WORK PRODUCTIVITY

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Background: PsA is a chronic, inflammatory disease characterised by peripheral arthritis, axial disease, dactylitis, enthesitis and skin and nail psoriasis. The impact of skin and joint components of the disease on quality of life and work productivity has been studied (1,2) but the impact of other manifestations has not.

Objectives: To assess the impact of enthesitis, dactylitis, and axial disease on quality of life and work productivity in PsA patients.

Methods: Cross-sectional study among patients with PsA recruited by rheumatologists and dermatologists in France, Germany, Italy, Spain, UK, and US. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Physicians recorded (Yes/No) if patients currently presented with enthesitis, dactylitis, inflammatory back pain (IBP), and sacroiliitis (identified by x-ray or MRI). Multiple linear regression analyses were used to examine the impact of these manifestations on patient reported outcomes (PROs) including EQ-5D index, EQ-5D VAS, HAQ-DI, PsAID12, and WPAI. Models were adjusted for age, gender, number of joints affected, and time since diagnosis. There was no imputation of missing data.

Results: The sample included 1103 patients: mean age 47.6 [SD 13.2] years, 46% were female, 58% were working full time. Mean number of joints affected by PsA was 3.8 (SD 5.2), and 54.9% were receiving biologic treatment. Enthesitis (present in 6.3% of patients), dactylitis (8.0%) and IBP (12.6%) were associated with worse outcomes overall (Table 1); sacroiliitis (3.9%) was linked to worse physical function and quality of life.

Conclusion: In a multi-national, real-world PsA population, enthesitis, dactylitis, IBP, and sacroiliitis were significantly associated with worse patient quality of life and/or work productivity across a range of PROs independent of the number of joints affected. These manifestations should be considered alongside skin and joint components in order to optimize patient outcomes.

REFERENCES:

[1] Borman P, et al. Clin Rheumatol. 2007;26(3):330–4.
[2] de Vlam K, et al. *Rheumatol Ther.* 2018;5(2):423–36.

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Table 1. Impact of manifestations on PROs: Adjusted* regression coefficient and p-values

Outcome measure (N patients with data available)	Manifestation	Coef.	P value
EQ-5D Index (N=771)	Enthesitis	-0.12	0.002
	Dactylitis	-0.07	0.010
	IBP	-0.07	0.001
	Sacroiliitis	-0.06	0.259
EQ-5D VAS (N=784)	Enthesitis	-8.86	0.013
	Dactylitis	-4.31	0.123
	IBP	-4.10	0.073
	Sacroiliitis	-10.19	0.043
HAQ DI (N=744)	Enthesitis	0.17	0.096
	Dactylitis	0.17	0.024
	IBP	0.20	0.003
	Sacroiliitis	0.30	0.035
PsAID12 (N=750)	Enthesitis	1.32	0.002
	Dactylitis	1.09	0.003
	IBP	0.47	0.060
	Sacroiliitis	0.59	0.243
WPAI: Productivity (N=485)	Enthesitis	14.40	0.034
	Dactylitis	4.36	0.128
	IBP	4.07	0.185
	Sacroiliitis	-3.86	0.332

*Adjusted for age, gender, number of joints affected, time since diagnosis.

FRI0464

EFFECT OF BIOLOGICS ON ENTHESITIS AND DACTYLITIS IN PATIENTS WITH PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Enthesitis and dactylitis are hallmarks for patients with psoriatic arthritis and mechanical injury are common risk factor for enthesitis and dactylitis [1-4]. Biologic disease modifying anti-rheumatic drugs (bDMARDs), including tumor necrosis factor alpha (TNF-α), interleukin (IL), phosphodiesterase type 4(PDE-4), Janus kinase (JAK) blockers and abatacept have shown efficacy on enthesitis and dactylitis in patients with PsA.

Objectives: The aims of this study are to summarize the efficacy of the bDMARDs on enthesitis and dactylitis in patients with PsA.

Methods: Systematically review of articles published up to Jan 2019 in Medline and Web of Science, and abstracts from the two last EUropean League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) meetings. Primary endpoint was the proportion of patients with resolution of enthesitis or dactylitis from week 12 to 24. Secondary endpoint was the mean change in different enthesitis score (Leeds Enthesitis Index [LEI, 0-6], Maastricht Ankylosing Spondylitis Enthesitis Score [MASES, 0-13], PsA modified MASES [0-15]) and dactylitis score (Leeds Dactylitis Index [LDI, 0-60], dactylitis severity score [DSS, 0-60], [DSS, 0-20]) from week 12 to 24. Odds ratio (OR) and standardized mean difference (SMD) with 95% CIs across studies were synthesized.

Results: Nineteen studies (8,208 patients), 10 drugs (adalimumab, infliximab, certolizumab pegol, golimumab, secukinumab, ustekinumab, ixekizumab, abatacept, tofacitinib and apremilast) and 22 treatments were evaluated. Patients treated with bDMARDs were more likely to achieve resolution of enthesitis compared with placebo (OR for pooled: 1.99, 95% CI:1.74, 2.27; OR for IL blocker: 2.06, 95%CI:1.78, 2.38; OR for abatacept:1.82, 95%CI:1.05,3.14; OR for PDE4 blocker:1.67, 95%CI:1.14, 2.45) (Figure 1) and have significant improvement in terms of LEI (SMD for pooled: -2.17, 95%CI: -2.87, -1.46; SMD for tofacitinib: -3.83, 95%CI: -5.24, -2.43; SMD for TNF blocker: -1.43, 95%CI: -2.38, -0.48; SMD for ixekizumab: -1.47, 95%CI: -2.42, -0.52; Figure 2A), MASES (SMD for apremilast: -1.50, 95%CI: -2.80, -0.21; Figure 2B), PsA modified MASES (SMD for golimumab: -0.32, 95%CI: -0.52, -0.12; Figure 2C) compared with placebo. Patients treated with bDMARDs were more likely to achieve resolution of dactylitis compared with placebo (OR for pooled: 3.26, 95% CI:2.45, 4.33; OR for IL blocker: 3.88, 95%CI:2.97, 5.06; OR for abatacept:1.54, 95%CI:0.71, 3.34; OR for PDE4 blocker:1.50, 95%CI:0.97, 2.33) (Figure 3) and have significant improvement in terms of LDI (SMD for pool: -1.73, 95%CI: -3.07, -0.40; SMD for TNF blocker: -1.67, 95%CI: -3.72, 0.38; SMD for ixekizumab: -1.67, 95%CI: -3.69, 0.12; Figure 4A), DSS [0-60] (SMD for pool: -2.10, 95%CI: -3.11, -1.10; SMD for tofacitinib: -3.39, 95%CI: -4.95, -1.83; SMD for TNF blocker: -0.84, 95%CI: -1.48, -0.20; Figure 4B), DSS [0-20] (SMD for apremilast: -1.20, 95%CI: -2.07, -0.34; Figure 4C) compared with placebo.

Conclusion: Biologic DMARDs was effective for PsA patients with enthesiitis and dactylitis. IL blocker is probably the optimal option to consider when patients present with predominant enthesitis and dactylitis

REFERENCES:

[1] Kaeley GS et al, Semin Arthritis Rheum. 2018 Aug;48(1):35-43
[2] Kaeley GS et al, Semin Arthritis Rheum. 2018 Oct;48(2):263-273
[3] Schett G et al, Nat Rev Rheumatol. 2017 Nov 21;13(12):731-741
[4] McGonagle D et al, Nat Rev Rheumatol. 2019 Feb;15(2):113-122

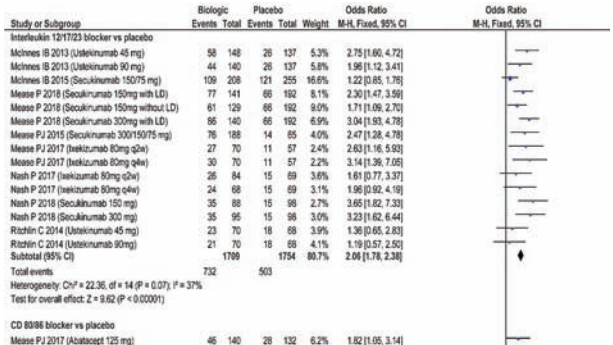


Figure 1. Risk estimates of resolution of enthesitis

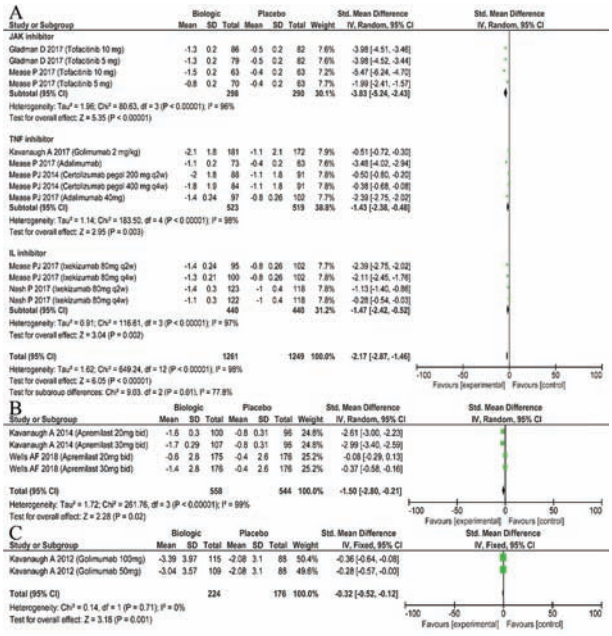


Figure 2. Standardized mean difference of different enthesitis score

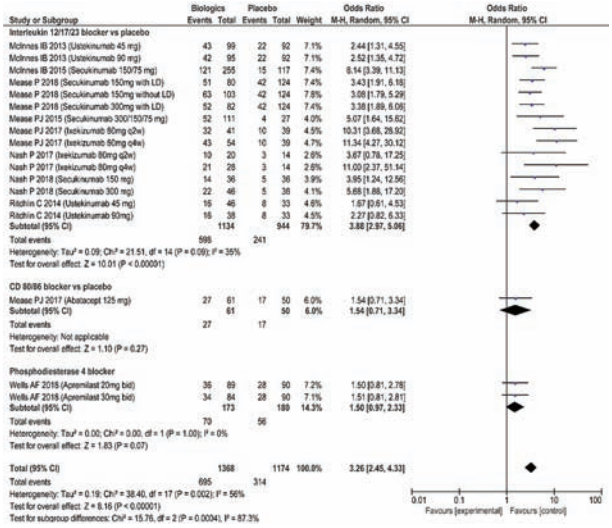


Figure 3. Risk estimates of resolution of dactylitis

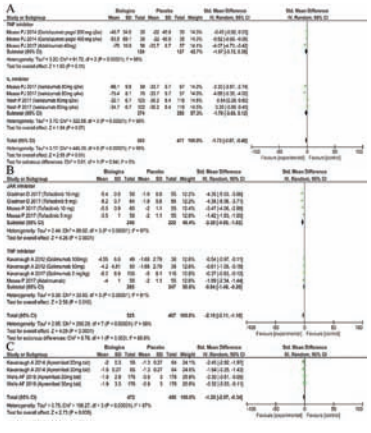


Figure 4. Standardized mean difference of different dactylitis score

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multicentre clinical study, REMS T-score values were highly correlated with Dual-energy X-ray absorptiometry (DXA) T-scores [1].

Objectives: To determine the predictive value in term of fragility fracture risk reduction of the REMS T-score compared to DXA T-score in a representative female population.

Methods: We enrolled 1370 women (30-90 y, BMI ≤ 35 kg/m^2) from 2013 to 2017. We performed in all patients both DXA and REMS lumbar scans. All analyses were performed under the strictest adherence to the corresponding guidelines. All patients underwent a follow-up lasting up to 5 years to assess the incidence of fragility fractures. Patients were stratified in two groups: patients who suffered a fragility fracture during the follow-up period (Group X) and those who did not (Group Y). Through an iterative process, the two groups were then age-matched with an enrolment proportion of 1:2. The finally obtained groups were identified as Group A (with incident fractures) and Group B (without incident fractures). The performance of REMS T-score in discriminating between Group A and Group B was quantitatively assessed and compared with DXA.

Results: Fragility fractures incidence was 14.0% (192 out of 1370 patients, mean follow-up 3.6 ± 0.8 years). Group A included 180 patients (mean age 67.2 ± 7.2 years) and Group B included 360 patients (mean age 67.3 ± 3.5 y). Group A and Group B did not show significant differences with respect to height (p=0.41), weight (p=0.68) and BMI (p=0.32). As expected we found significant differences in REMS T-score (-2.68 ± 1.28 in Group A vs -2.03 ± 1.23 in Group B, p<0.001) and DXA T-score (-2.52 ± 1.20 in Group A vs -2.08 ± 1.17 in Group B, p<0.001). REMS T-score ≤ -2.5 identified Group A patients with sensitivity = 65% and specificity = 58% (OR=2.6). DXA T-score identified Group A patients with sensitivity = 57% and specificity = 57% (OR=1.7).

Conclusion: REMS T-score resulted an effective predictor for the risk of incident fragility fractures in a representative population-based sample of female subjects. Reported OR values showed also that REMS had a better performance than DXA in the considered population, showing higher values for both sensitivity and specificity in the identification of fragile patients.

REFERENCES:

[1] Di Paola M, Gatti D, Viapiana O, et al. Radiofrequency echographic multispectrometry compared with dual X-ray absorptiometry for osteoporosis diagnosis on lumbar spine and femoral neck. Osteoporos Int Published Online First: 4 September 2018. Doi: :10.1007/s00198-018-4686-3

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Osteoporosis

FRI0465 PREDICTION OF INCIDENT FRAGILITY FRACTURES THROUGH RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY(REMS)

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Background: Radiofrequency Echographic Multi Spectrometry (REMS) is an innovative non-ionizing technique used for diagnosing osteoporosis at lumbar spine and femoral neck sites. In accordance with the results of a

FRI0466 RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF FRACTURES IN GLUCOCORTICOID TREATED PATIENTS. THE ROLE OF HYPOGONADISM

Helena Florez[1], José Hernández-Rodríguez[2], Africa Muxi[3], Josep Lluís Carrasco[4], Sergio Prieto-González[2], Silvia Ruiz-Gaspà[1], Maria C. Cid[2], Ana Monegal[1], Núria Guañabens[1], Pilar Peris[1]. [1]*Hospital Clinic, University of Barcelona, Metabolic Bone Diseases Unit. Department of Rheumatology, Barcelona, Spain*; [2]*Hospital Clínic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Vasculitis Research Unit, Department of Autoimmune Diseases, Barcelona, Spain*; [3]*Hospital Clinic, University of Barcelona, Department of Nuclear Medicine, Barcelona, Spain*; [4]*University of Barcelona, Biostatistics, Department of Basic Clinical Practice, Barcelona, Spain*

Background: Glucocorticoid-induced osteoporosis (GIOP) is a common form of secondary osteoporosis (OP). Fractures in GIOP frequently occur with higher bone mineral density (BMD) than expected and typically at treatment initiation, complicating the identification of patients at risk for fracture.

Objectives: Identify risk factors associated with fragility fracture development in GC-treated patients.

Methods: 127 patients (aged 62±18years, 63% women, 46% postmenopausal) on GC treatment (prednisone ≥5mg/day, >3months) were included. Clinical data collected included: risk factors for OP and fractures, dose and GC-treatment duration, previous fractures and disease activity, anthropometric data, bone metabolism parameters (including gonadal axis study), BMD analysis (DXA; OP: T-score ≤-2.5), TBS (degraded microarchitecture [DMA]:<1.230), dorsolumbar X-ray (assessing vertebral fractures [VF]) and FRAX risk (GC-adjusted)[1].
Results: Most patients received GC treatment for vasculitis or polymyalgia rheumatica during 47.7±69 months (mean daily dose: 14.5mg). 17% had VF, 28% had fragility fracture (VF + non-VF), 29% OP and 71% DMA. Patients with VF received more GC-boluses (57.1% vs. 29.5%,p=0.03), were older (68±13 vs. 60±19 years, p=0.02), postmenopausal (100% vs. 67%, p=0.015) and/or men with testosterone <250ng/dL (57% vs. 11%, p=0.017) and had lower TBS values (1.100 vs. 1.220, p<0.001) and higher FRAX risk (17 vs. 9, p=0.003); patients with fragility fractures showed higher accumulated GC-doses (6.1±13 vs. 8±18g, p=0.046). On multivariate analysis, hypogonadism (OR 14.3; IC95% 2.2->100, p=0.01) and having received GC-boluses (OR 3.40; IC95% 1-11.8, p=0.01) were the principal factors associated with VF. Hypogonadism (OR 7.1; IC95% 1.5-38.7, p=0.01) and having a FRAX >20 (OR 6.97; IC95% 1.3-51.7, p=0.02) were factors related to the presence of fragility fractures. Men with testosterone <250ng/dL had higher BMI (29.4 vs. 26.3, p=0.005) and disease activity (ESR 23 vs. 12, p=0.005) and lower TBS (1.050 vs. 1.210, p<0.001); age, daily and cumulated GC doses were similar to subjects with normal testosterone levels.
Conclusion: Hypogonadism is a major risk factor for developing fractures in GC-treated men and women, whereas receiving GC-boluses is related to VF, indicating the importance of evaluating the gonadal axis in these patients.

REFERENCES:
[1] Buckley L, et al. Arthritis Care Res. 2017

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FRI0467 **THE DISTRIBUTION OF PREVALENT AND INCIDENT VERTEBRAL FRACTURES IN THE TERIPARATIDE VERSUS RISEDRONATE "VERO" CLINICAL TRIAL**

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Background: Biomechanical analyses indicate that compressive load is heterogeneous throughout the thoraco-lumbar spine, with maximal loads during daily activities on T_7-T_8 and T_{11}-L_1. Population-based studies have shown a bimodal spinal distribution of prevalent and incident vertebral fractures (VFxs) at the mid-thoracic and thoraco-lumbar junction levels. However, prevalence and incidence of individual VFxs according to both their location and severity have not been reported in randomised clinical trials with anti-osteoporosis drugs.
Objectives: The aim of this study was to describe the distribution of prevalent and 12- and 24-month incident new and/or worsening VFxs according to location and severity in the teriparatide versus risedronate VERO clinical trial[1].
Methods: 1360 postmenopausal women with at least 2 moderate (SQ2: 25% ≤ vertebral body height loss ≤ 40%) or 1 severe (SQ3: vertebral body height loss > 40%) VFx according to the semiquantitative (SQ) scale by Genant [2], and a BMD T-score ≤ -1.50 were randomised to SC daily teriparatide (20 µg) or oral weekly risedronate (35 mg) in a double-blind, double-dummy 2-year trial. A new VFx was defined as a vertebral body height loss of at least 20% (and 4 mm) of a vertebra that was unfractured at baseline, based on a 6-point placement of the vertebral bodies from T4 to L4, and confirmed by an increase by 1 or more severity grades according to the SQ scale[2]. Worsening of a baseline pre-existing fracture was diagnosed if the decrease in vertebral height was at least 1 severity grade in the SQ assessment. Vertebrae with Schmorl's nodules, Scheuermann's disease and platyspondyly were excluded. Spine x-rays were centrally assessed by radiologists at BioClinica.
Results: Mean (SD) age was 72.1 (8.7) years (min-max: 45-93 years). Spine x-rays were available at baseline, 12, and 24 months for 1,360, 1,159 and 1,049 patients respectively, for a total of 17,413, 14,987 and 13,454 evaluable vertebral bodies. The location of the prevalent VFx by SQ severity degree is shown in Fig.1. At baseline, VFxs were preferentially located at L_1, T_{12}, L_2, T_{11} and T_8 (38.5%, 37.4%, 25.3%, 23.5% and 23.1% of the patients, respectively). A total of 524 (3.0%) of all the assessed vertebral bodies had a fracture at L_1, the most frequently affected level. There were 126 new and/or worsened incident VFxs during the course of the study (35 in the teriparatide and 91 in the risedronate groups) affecting 100 patients (9.5%) at 24 months. Eighty-nine of these patients presented a new moderate (SQ2) or severe (SQ3) incident VFx. The most frequently fractured vertebral body was T_{12} (1.6% of patients), followed by L_1 and T_{11} (1.3% both), T_9 (1.2%) and T8 (1.1%). The frequency of incident VFx was lower at all levels with teriparatide (Fig.2). T_{12} was also the most frequently fractured vertebral body at 12 months of follow-up (0.7% of patients).
Conclusion: These results from the VERO clinical trial confirm previous results from epidemiological studies that VFxs occur most frequently in the mid-thoracic and thoraco-lumbar regions of the spine. Given the study eligibility criteria, mild (SQ1) VFxs are likely under-represented. Teriparatide is more effective in reducing the incidence of the commonest VFxs (T_{12}, L_1) as compared to risedronate.

REFERENCES:
[1] Kendler DL, et al. Lancet (2018);391:230.
[2] Genant HK, et al. J Bone Miner Res (1993);8:1137.

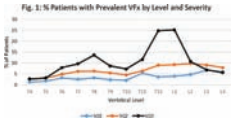
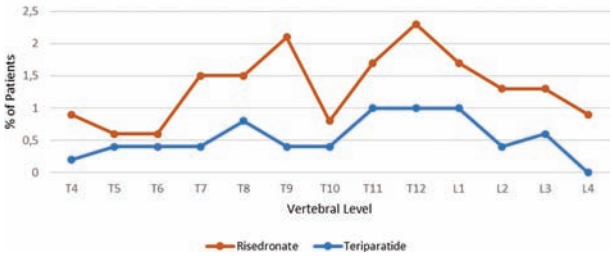


Fig. 2: % Patients with Incident VFx by Level and Treatment Arm



Disclosure of Interests: Piet Geusens Grant/research support from: Research support, consultant and/or speaker fees from: Pfizer, Abbott, Eli Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, Will-Pharma, Grant/research support from: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Bio Minerals and Roche, Consultant for: Research support, consultant and/or speaker fees from: Pfizer, Abbott, Eli Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, Will-Pharma, Speakers bureau: Research support, consultant and/or speaker fees from: Pfizer, Abbott, Eli Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, Will-Pharma, Speakers bureau: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Bio Minerals and Roche, David Kendler Grant/research support from: Research grants, and/or consultant fees from: Amgen, Lilly, AstraZeneca, Astellas, UCB, Consultant for: Research grants, and/or consultant fees from: Amgen, Lilly, AstraZeneca, Astellas,

UCB, Speakers bureau: Research grants, and/or consultant fees from: Amgen, Lilly, AstraZeneca, Astellas, UCB, Astrid Fahrleitner-Pammer Speakers bureau: Speaker fees from: Amgen, Alexion, BMS, Lilly, Fresenius, Pedro López-Romero Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Fernando Marin Shareholder of: Lilly, Employee of: Lilly

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FRI0468 EFFECTS OF DIFFERENT VITAMIN D SUPPLEMENTATION SCHEMES IN POSTMENOPAUSAL WOMEN

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Background: Vitamin D exerts different extra-skeletal effects, including a positive effect on muscle function. Circulating levels of the 25 hydroxylated Vitamin D - 25(OH)D - reflect the body Vitamin D reserves; to reach the optimal serum 25(OH)D threshold, Vitamin D supplementation is often requested. The commonest Vitamin D supplementation is represented by cholecalciferol (D3), but the hydroxylated Vitamin D metabolite calcifediol (HyD) represents a therapeutic alternative.

Objectives: The aim of the study was to evaluate the efficacy of the calficediol supplementation compared to various cholecalciferol administration schedules in increasing the 25(OH) vitamin D serum levels and the effects on muscular function in post-menopausal women.

Methods: 60 post-menopausal women aged ≤ 65 years with low serum 25(OH)D levels (8-24 ng/ml) were included in the study. Recruited patients were randomly assigned to receive oral Vitamin D 1000 UI/ day according to four different regimens. 1) cholecalciferol (D3) 300.000 UI, single oral dose; 2) monthly cholecalciferol 100.000 UI for three consecutive months; 3) weekly cholecalciferol 7000 UI; 4) weekly HyD 7000 UI. At baseline and every three months, for 12 months, the following parameters were evaluated: serum levels of 25(OH)D; PTH, calcium, phosphates; at baseline and every 15 days muscular function was evaluated using the Timed Up and Go (TUG) and the Sit to Stand test.

Results: Weekly administration of HyD induced a significantly faster and greater increase of 25(OH)D levels, compared to the other treatment groups (at 12 months: +384% vs +145%, + 220%, + 248% in groups 1, 2, 3, respectively); the increase appeared after 1 month from baseline. D3 300.000 UI single dose induces a slower increase of 25(OH)D compared to monthly and weekly supplementation. An increase of muscular strength was observed after 12 months in all supplementation groups, starting from 1 months from baseline, with a greater effect in subjects treated with weekly HyD compared to D3 treated subjects (TUG 6 second vs 7.3, 7.7, 7.9 in groups 1, 2, 3, respectively; Sit to Stand 16,2 vs 15.4, 15.3, 15.7 in groups 1, 2, 3 respectively). Overall, the effects on 25(OH)D levels and on muscular function were greater in subject treated with weekly D3 compared to subject treated with monthly or single dose D3. No differences in PTH, calcium and phosphate serum levels were found between supplementation groups.

Conclusion: Supplementation with calcifediol is more effective and faster compared to cholecalciferol in increasing 25(OH)D serum levels; further, weekly cholecalciferol is more effective and faster compared to single dose or monthly administration. Increase in circulating levels of 25(OH)D is associated to an improvement of muscular strength.

REFERENCES:

[1] Bischoff-Ferrari, et al., Oral supplementation with 25(OH)D3 versus Vitamin D3: effects on 25(OH)D levels, lower extremity function, blood pressure, and markers of innate immunity. Journal for bone and mineral Research, Vol. 27, N. 1, January 2012, pp 160-169.

[2] Bischoff – Ferrari, Which vitamin D oral supplement is best for Postmenopausal women? CurrOsteoporos Rep (2012) 10:251-257.

Disclosure of Interests: Stefano Berardi: None declared, Addolorata Corrado: None declared, Angiola Mele: None declared, Cinzia Rotondo: None declared, Antonello Trotta: None declared, Natalia Mansueto: None declared, Francesco Paolo Cantatore Speakers bureau: PFIZER, ROCHE

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FRI0469 CHANGES IN DKK-1, SCLEROSTIN, AND RANKL SERUM LEVELS FOLLOWING DISCONTINUATION OF LONG-TERM DENOSUMAB TREATMENT IN POSTMENOPAUSAL WOMEN

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Background: The positive effects of denosumab (DMAb) on bone mineral density (BMD) are quickly reversible after its discontinuation and concerns about the possible increase in vertebral fracture after stopping denosumab have been recently raised. Indeed, a rebound in bone turnover markers have been described after DMAb discontinuation. Dickkopf-1 (Dkk-1), and sclerostin, Wnt inhibitors, are considered master regulators of bone remodeling and directly influence the Receptor Activator of Nuclear factor Kappa B Ligand (RANKL) serum levels.

Objectives: We sought to determine whether the rebound of bone turnover following DMAb discontinuation is associated with dysregulation of the Wnt canonical pathway and/or with the increase in the receptor-activator of nuclear factor-kappa B ligand (RANKL) serum levels in long-term DMAb postmenopausal users.

Methods: The present study included patients (n = 15) with postmenopausal osteoporosis to whom DMAb was administered for 78 months and then discontinued. We collected BMD data at DMAb administration month 60 (M60), M84 (6 months after last DMAb administration, coinciding when the next DMAb dose would typically be due), and after discontinuation, 3 and 12 months of follow-up (FU-M3 and FU-M12, respectively). Serum C-terminal telopeptide of type 1 collagen (CTX-I), Dkk-1, and sclerostin were measured at M60, M84, FU-M3, and FU-M12. Serum N-terminal propeptide of type 1 procollagen (PINP) and RANKL were dosed at M60, M84, FU-M3, and FU-12.

Results: We found a significant decrease in the T- score at all sites at FU-M12, when compared to M84 (-0.51 ± 0.91 at the lumbar spine; -0.72 ± 0.33 at the total hip; and -0.42 ± 0.27 at the femoral neck, $p<0.05$). After DMAb discontinuation (M84 vs FU M12), RANKL, CTX-I and PINP significantly increased (+0.041 ± 0.062 ng/mL; +0.846 ± 0.590 and +124.6 ± 62.72, $p<0.05$, respectively), while Dkk-1 and sclerostin significantly decreased (-10.90 ± 11.80 and -13.00 ± 10.52 pmol/L, respectively, $p<0.01$) (Figure 1). No changes in BMD or any of the markers were found between M60 and M84.

Conclusion: RANKL serum levels progressively increased after discontinuation of long-term DMAb while Dkk-1 and sclerostin serum levels decreased. The increase in RANKL serum levels supports the hypothesis of a sudden loss of inhibition of the resting osteoclast line after DMAb clearance, with a hyperactivation of these cells. Our results suggest that the decrease in serum Wnt inhibitors after DMAb suspension might represent a mere feedback response to the increased bone turnover.

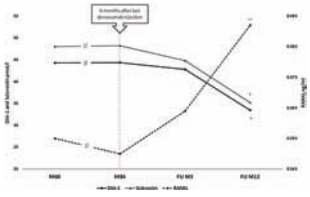


Figure 1. Absolute values of Dickkopf-1 (Dkk-1), sclerostin and Receptor Activator of Nuclear factor Kappa B Ligand (RANKL) following discontinuation. * $p<0.01$ vs M84; ** $p<0.05$ vs M84

Disclosure of Interests: Giovanni Adami: None declared, Angelo Fassio Speakers bureau: Abiogen Pharma, Camilla Benini: None declared, Elisabetta Vantaggiato: None declared, Kenneth Saag Grant/research support from: Amgen, Ironwood/AstraZeneca, Horizon, SOBI, Takeda, Consultant for: Abbvie, Amgen, Ironwood/AstraZeneca, Bayer, Gilead, Horizon, Kowa, Radius, Roche/Genentech, SOBI, Takeda, Teijin, Alessandro Giollo: None declared, Irma Lippolis: None declared, Luca Idolazzi: None declared, Giovanni Orsolini Speakers bureau: Grunenthal, Maurizio Rossini: None declared, Davide Gatti Speakers bureau: Abiogen, Amgen, Janssen-Cilag, Mundipharma, Pfeizer

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FRI0470 **EFFECT OF DISCONTINUATION OF DENOSUMAB IN SUBJECTS WITH RHEUMATOID ARTHRITIS TREATED WITH GLUCOCORTICOIDS**

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Background: Denosumab, a monoclonal antibody against RANKL, is approved for the treatment of glucocorticoid (GC) induced osteoporosis (GiOP). In postmenopausal women with osteoporosis, denosumab discontinuation leads to a transient increase in bone turnover above baseline, peaking at 12 months from the last dose, and a corresponding decline in bone mineral density (BMD). To better understand the effects of denosumab discontinuation in GC-treated patients, we analyzed a subgroup receiving GCs at baseline from a phase 2 study of denosumab in subjects with rheumatoid arthritis (RA), followed for 12 months after denosumab discontinuation.

Objectives: To evaluate changes in bone turnover and BMD in subjects with RA on GCs treated with denosumab, after discontinuing denosumab for 12 months.

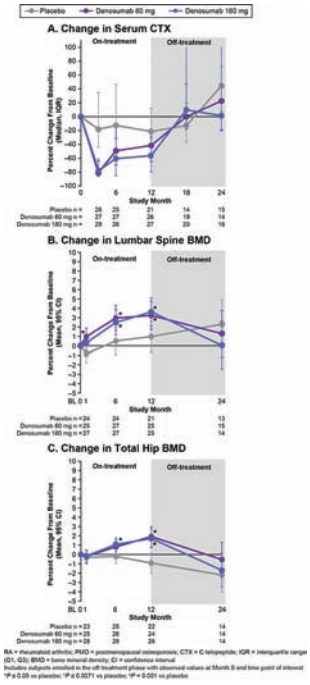
Methods: This double-blind, placebo-controlled study enrolled subjects with RA who were randomized to receive denosumab 60 mg, denosumab 180 mg, or placebo subcutaneously for 12 months, and followed for progression of structural damage. Subjects were followed for an additional 12 months after denosumab discontinuation. Outcome measures in this subgroup analysis of subjects treated with GCs at study baseline included percent change from baseline in serum C-terminal telopeptide of type I collagen (CTX) and lumbar spine (LS) and total hip (TH) BMD on- and off-treatment. Baseline mean (SD) prednisone equivalent dose (mg/day) was 6.1 (2.4), 5.2 (2.1), and 6.1 (3.2) in the placebo, denosumab 60 mg, and denosumab 180 mg groups, respectively. Data on CTX are reported as median and interquartile range. Percent changes in LS and TH BMD at each time point were assessed based on a repeated-measures model adjusting for treatment, baseline use of steroids, previous use of biologics, and baseline BMD value.

Results: Among 218 subjects in the phase 2 study, 82 (26 placebo, 27 denosumab 60 mg, and 29 denosumab 180 mg) were included in this analysis. After 12 months of denosumab treatment, CTX decreased from baseline in both groups (Figure); in the off-treatment period, CTX returned to baseline by 18 months and was overall similar to placebo at 24 months. BMD increased at the LS and TH at 12 months with denosumab treatment (Figure) and returned to baseline levels after 12 months of discontinuation.

Conclusion: Like all non-bisphosphonate medications for osteoporosis, denosumab is reversible with discontinuation. In this small subgroup of GC-treated subjects with RA, BMD gains achieved with denosumab were lost upon discontinuation, consistent with observations in postmenopausal women receiving denosumab for osteoporosis. In this analysis of short-term denosumab use in subjects with RA receiving GCs, bone turnover was reduced with denosumab and gradually returned to baseline upon discontinuation, without a clear increase to above-baseline levels in the off-treatment period.

Disclosure of Interests: Kenneth Saag Grant/research support from: Amgen, Ironwood/AstraZeneca, Horizon, SOBI, Takeda, Consultant for: Abbvie, Amgen, Ironwood/AstraZeneca, Bayer, Gilead, Horizon, Kowa, Radius, Roche/Genentech, SOBI, Takeda, Teijin, Michele McDermott Shareholder of: Amgen Inc., Employee of: Amgen Inc., Jonathan Adachi Grant/research support from: Amgen Inc, Consultant for: Amgen Inc, Eli Lilly, Speakers bureau: Amgen Inc., Willem Lems Speakers bureau: Amgen Inc., Merck, Eli Lilly and Pfizer, Nancy Lane Consultant for: Samumed, LLC, Piet Geusens Grant/research support from: Research support, consultant and/or speaker fees from: Pfizer, Abbott, Eli Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, Will-Pharma, Grant/research support from: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Bio Minerals and Roche, Consultant for: Research support, consultant and/or speaker fees from: Pfizer, Abbott, Eli Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, Will-Pharma, Speakers bureau: Research support, consultant and/or speaker fees from: Pfizer, Abbott, Eli Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, Will-Pharma, Speakers bureau: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Bio Minerals and Roche, Peter Butler Shareholder of: Amgen Inc., Employee of: Amgen Inc., Li Chen Shareholder of: Amgen Inc., Employee of: Amgen Inc., Daria B Crittenden Shareholder of: Amgen Inc., Employee of: Amgen Inc., Robin Dore Grant/research support from: Amgen Inc., AbbVie, Biogen, Gilead, Pfizer, Eli Lilly, Novartis, and UCB, Consultant for: Amgen Inc., AbbVie, Gilead, Pfizer, Eli Lilly, Novartis, and UCB, Speakers bureau: Amgen Inc., AbbVie, Pfizer, BMS, Eli Lilly, Novartis, UCB, and Radius, Stanley Cohen Grant/research support from: AbbVie, Amgen Inc., AstraZeneca, Biogen-IDEC, Bristol Meyer Squibb, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Merck, and Roche, Consultant for: Abbvie, Amgen, AstraZeneca, Biogen-IDEC, Bristol Meyer Squibb, Genentech, Janssen, Lilly, Novartis Pfizer, Merck and Roche

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FRI0471 **BONE QUALITY ASSESSMENT IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

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Background: Type 2 diabetes mellitus (T2DM) is a risk factor for osteoporotic fractures although bone mineral density is normal or even increased, Thus, diabetes may be associated with a reduction of bone strength that is not reflected in the measurement of bone mineral density (BMD)

Objectives: The aim of this study was to compare BMD with a non invasive assessment of trabecular microarchitecture, (Trabecular bone score) TBS, in patients with T2DM

Methods: In a prospective cross-sectional study, trabecular microarchitecture was examined in patients with T2DM and non diabetic control subjects. The exclusion criteria were diseases (hyperthyroidism, Cushing's syndrome, primary hyperparathyroidism, renal failure, malabsorption), rheumatic diseases and/or medications that might affect bone and mineral metabolism,post menopausal women. Lumbar spine BMD was measured by dual-emission x-ray absorptiometry (DXA), and TBS was calculated by examining pixel variations within the DXA images using TBS iNsight

Results: 205 patients (108 male, 97 female), aged 25 to 60 years with T2DM and 205 non diabetic control subjects ((105 male, 100 female) Mean TBS was lower in T2DM (1.256±0.103 vs. 1.291±0.101, p=0.001). Mean BMD was higher in T2DM Z score (0.516±1.346 vs. -0.8151 ±1.153, p= 0.016).

Conclusion: In T2DM,TBS is lower than control subjects. Abnormal trabecular microarchitecture may help explain the paradox of increased fractures at a higher BMD in T2DM

REFERENCES:

[1] Dhaliwal R, Cibula D, Ghosh C, Weinstock RS, Moses AM. Bone qualityassessment in type 2 diabetesmellitus. OsteoporosInt.2014;25:1969-73. -

Leslie WD, Aubry-Rozier B, Lamy O, Hans D. TBS (Trabecular Bone Score) and Diabetes-Related Fracture Risk. J Clin EndocrinolMetab.2013;98:6029. -Kim JH, Choi HJ, Ku EJ, Kim KM, Kim SW, Cho NH, et al. Trabecular Bone Score as an Indicator for Skeletal Deterioration in Diabetes. J Clin EndocrinolMetab.2015;100:475-82.

Disclosure of Interests: None declared
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FRI0472 COMPARISON OF THE THERAPEUTIC EFFICACY OF DAILY VERSUS WEEKLY DOSE OF TERIPARATIDE FOR PREVENTING BONE FRACTURE IN PATIENTS WITH OSTEOPOROSIS – A SINGLE CENTRE, PROSPECTIVE OPEN-LABEL STUDY

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Background: In Japan, teriparatide (20 μg) and teriparatide acetate (56.5 μg) have been approved for treatment of osteoporosis. Teriparatide is a recombinant human parathyroid hormone (PTH) administered as daily subcutaneous injections, whereas teriparatide acetate is a biologically active fragment containing the N-terminal 34 amino acids of human PTH administered as weekly subcutaneous injections. To the best of our knowledge, a study comparing the therapeutic effects of these two teriparatide preparations does not exist.
Objectives: We aimed to compare the therapeutic effects of the two teriparatide preparations that varied in dose interval.
Methods: We prospectively enrolled 55 osteoporotic patients with vertebral fracture who needed bone-strengthening therapy in a single-centre cohort. The patients randomly selected either daily injection of teriparatide for 2 years or weekly injection of teriparatide acetate for 72 weeks. The primary endpoint was comparison of the new fracture onset ratio at 18 months, based on the approval for use of teriparatide and teriparatide acetate for up to 2 years and 72 weeks, respectively at the time of the trial. However, since May 2017, teriparatide acetate use for osteoporosis treatment has been approved for up to 24 months in Japan. We evaluated their background data (age, sex, bisphosphonate use, basal disease, glucocorticoid use, vertebral and femoral bone marrow density (BMD), number of thoracic and lumbar vertebral fractures, levels of tartrate-resistant acid phosphatase 5b (TRACP-5b), total procollagen type 1 amino-terminal propeptide (total P1NP), 1,25(OH)2-vitamin D3(1,25(OH) 2D3), total serum calcium corrected for albumin level (cCa), inorganic phosphorus(IP), homocysteine, whole PTH and estimated glomerular filtration rate, ankle-brachial index(ABI), and brachial-ankle pulse wave velocity (baPWV)). IP levels were observed until month 1, while levels of TRACP-5b, total P1NP, cCa, 1,25(OH)2D3, BMD, number of fractured vertebrae, ABI, and baPWV were observed until month 18.
Results: The background factors were not significantly different between the groups. The onset rates of new vertebral fractures until 18 months were 50% and 52% for teriparatide and teriparatide acetate, respectively. However, we did not observe the onset of new non-vertebral fracture in the two groups for 18 months. Survival rates in new bone fracture onset (teriparatide vs teriparatide acetate) were 71.4% vs. 60.0% at month 6, 57.1% vs. 52.2% at month 12, and 46.4% vs. 52.2% at month 18. The survival curve showed no significant difference in new bone fracture onset between the groups using the log rank test (p=.976) with a hazard ratio (teriparatide vs. teriparatide acetate) of 0.867 (95% confidential interval; 0.291-2.582) (p=.797) (see Fig.1). No significant differences were seen in the continuation rates for 18 months for teriparatide (93.3%) and teriparatide acetate (96.0%) (p=.669). Statistically significant differences in %Δ vertebral BMD at month 6 and baseline (p<.01); TRACP-5b at months 12 and 18 (p<.05); total P1NP at months 1,6,12, and 18 (p<.01); and cCa at month 6(p<.01) were seen between the groups. Moreover, levels of 1,25(OH)2D3 at months 6, 12, and 18 were lower with teriparatide acetate than those of teriparatide (p<.01).
Conclusion: The protective efficacy of the teriparatide preparations to prevent bone fracture showed no difference. In osteoporosis treatment with vertebral fracture, teriparatide preparation daily or weekly may be selected based on the patient's choice.
[UMIN000024503]

REFERENCES:

[1] J Clin Endocrinol Metab. 2012 Sep;97(9):3097-106.
[2] Arthritis Rheum. 2009 Nov;60(11):3346-55.

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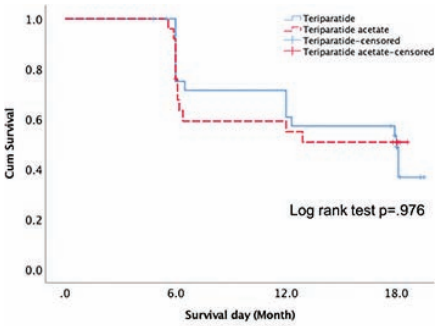


Figure. 1 Survival curve in new bone fracture onset of teriparatide and teriparatide acetate.

FRI0473 ASSESSING THE CLINICAL RELEVANCE OF BONE DENSITOMETRY SCREENING IN PATIENTS UNDER 40 YEARS OF AGE: INDICATIONS AND RESULTS

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Background: Guidelines for the diagnosis and treatment of osteoporosis in patients under the age of 40 years are lacking. The International Osteoporosis Foundation (IOF) working group has recommended dual-energy X-ray absorption (DXA) screening should only be performed in this age group if patients have an associated chronic disease such as inflammatory bowel disease (IBD) in conjunction with a vertebral fracture or multiple fractures elsewhere.[1] For these patients, a T-score of <-2.5 can be used to diagnosis low BMD but the term osteoporosis may not be appropriate and there is minimal evidence supporting the use of bisphosphonates (BPs).
Objectives: In patients under 40 years of age undergoing DXA screening, to determine (1) the indication and (2) the DXA results (age adjusted Z score and standard T score), in order to conclude whether DXA screening in this group was appropriate and relevant for making meaningful treatment decisions.
Methods: Clinical details for all DXA scans requested for patients less than 40 years of age were obtained from the Mid Cheshire Hospital NHS Trust radiology department for a 6 month period from July to December 2018 inclusive. Descriptive data was produced regarding basic patient demographics, DXA indication and DXA results in the form of Z- and T-scores at the neck of femur (NOF) and spine.
Results: In total, 35 patients under the age of 40 years underwent DXA screening in the defined time period. The mean age of patients was 30.5 years (s.d. 6.0) and 24 patients (69%) were female. The youngest patients were 19 years. Regarding indications, only two patients (6%) were appropriate for DXA screening according to the IOF suggested guidelines, both of whom had vertebral fractures. Twenty seven patients (77%) had an established diagnosis of a disease known to cause OP but no history of fracture. Regarding results, at the NOF and spine respectively mean Z-scores were -0.77 (s.d. 1.19) and -0.96 (s.d. 0.97), and mean T-scores were -0.88 (s.d. 1.19) and -0.945 (0.93). Only three patients (9%) had Z- or T-score of <-2.5; two patients who had a history of thoracic vertebral fracture, and a patient with high steroid use for IBD but no fracture history.
Conclusion: The majority of patients aged less than 40 years referred for DXA screening are being referred due to associated diagnoses with no history of fracture, not in keeping with IOF recommendations. Of the 33 patients with no history of fracture, only one patient (3%) had a T-score consistent with low BMD. There is little evidence to support bisphosphonate use in this group. We therefore conclude that DXA screening in patients less than 40 years should be reserved for those with a history of fracture.

REFERENCES:

[1] Ferrari, S. et al. (2012). Osteoporosis in young adults: pathophysiology, diagnosis and management. *Osteoporosis Int.* 23:2735-2748

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FRI0474 **FRACTURE RISK FOLLOWING BARIATRIC SURGERY: A SELF-CONTROLLED CASE SERIES AND RISK PREDICTION ALGORITHM**

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Background: Bariatric surgery is increasingly common due to the obesity epidemic. However, there is controversial evidence about the association between bariatric surgery and fracture risk. This may be due to the fundamental differences between patients undergoing bariatric surgery with patients who do not, raising the question: within patients who fracture, are they are at increased risk of fracture after surgery? And if so, who is at risk of fracture?

Objectives: 1. To investigate the association between bariatric surgery and risk of three fracture locations using a within person study design comparing a) the 5 year incidence post surgery to the 5 year pre surgery, b) splitting the 5 year post surgery risk into two windows 0-2 and 2.01 – 5 years. 2. To predict who is at risk of fracture following bariatric surgery.

Methods: A self-controlled case series analysis (SCCS) and Stepwise logistic regression (LR) were conducted. Patients undergoing bariatric surgery were identified in the clinical practice research datalink (CPRD) GOLD dataset and linked to hospital episode statistics (HES) data. Primary outcome was any fracture (any skeletal sites except skull and digits). Secondary outcomes were major (hip, spine, forearm and humerus) and peripheral fractures (forearm and lower leg). For the SCCS, Poisson models in those who fractured were fit to calculate Incidence Rate Ratios (IRR) for the aforementioned time windows. Potential predictors were selected with an exit p-value of 0.157 and their predictive performance was reported using a C-statistic.

Results: Of 5,492 patients undergoing bariatric surgery, 252 patients had 272 any fractures, 75 (80) major fractures and 126 (135) peripheral fractures. Average BMI was 43.9. Major fracture risk increased nearly threefold following surgery: IRR (95% CI) 2.70 (1.31, 5.57). Conversely, the incidence of any and peripheral fractures did not change: IRRs 1.17 (0.86, 1.60) and 0.92 (0.60, 1.42) respectively. Any and major fracture risk increased in the 3rd to 5th year post-surgery: IRRs of 1.73 (1.08, 2.77), 4.98 (1.94, 12.78) respectively. 7 variables were identified which may predict major fracture with a high c-statistics of 0.77 (0.71, 0.88).

Conclusion: Few patients had fractures (252/5492). The incidence of major osteoporotic fracture is increased after bariatric surgery by nearly 3 fold, to then increase to 5 fold in the 2-5 year window. Multiple factors were identified for patients at risk of major fracture post-operatively. External validation is needed. Further research is needed on post-bariatric surgery care to minimise fracture risk.

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FRI0475 **TITLE: LUMBAR SPINE AND PROXIMAL FEMUR OSTEOPOROSIS DIAGNOSIS: REMS TECHNOLOGY IN A MULTICENTER CLINICAL STUDY**

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Background: To date numerous quantitative methods to diagnose osteoporosis at peripheral sites have been developed. REMS (Radiofrequency Echographic Multi Spectrometry) is a non-ionizing instrument used to quantitatively evaluate bone mineral density at lumbar spine and femoral neck sites [1].

Objectives: To assess the accuracy of REMS in osteoporosis diagnosis at axial sites (lumbar spine and hip) compared with the gold standard, Dual-energy X-ray absorptiometry (DXA).

Methods: We enrolled patients aged from 50 to 75 years and perfomed a total of 1,699 and 1,794 lumbar spine and proximal femur scans with REMS and DXA. A quality checks on DXA and REMS acquired data were performed through direct examination of scans by experienced operators. We investigated the agreement between the two techniques calculating: Pearson`s correlation coefficient (r), Standard Error of the Estimate (SEE) and efficiency (sensitivity and specificity) in identifying osteoporotic individuals (i.e. T-score $\leq$ -2.5).

Results: We found a good linear correlation between REMS and DXA BMD estimation, Pearson coefficient r=0.938 for lumbar spine and r=0.933 for proximal femur (p<0.001 for both). SEE values were 5.2% and 5.8% for lumbar spine and femoral site, respectively. In addition, REMS demonstrated a high sensitivity (92.9% and 92.3% for spine and femur) and specificity (93.5% for spine and 92.6% for femur) for the discrimination of osteoporotic patient. Moreover, considering together all the diagnostic classification categories (healthy, osteopenia and osteoporosis), the diagnostic agreement between REMS and DXA was 90.2% and 89.3% for lumbar spine and proximal femur sites, respectively.

Conclusion: REMS exhibited a high sensitivity and specificity in identifying osteoporotic patients at lumbar spine or proximal femur sites compared with gold-standard DXA. REMS accurately diagnosed osteoporotic patients in clinical routine, at both lumbar spine and proximal femur sites, without using ionizing radiation.

REFERENCES:

[1] Di Paola M, Gatti D, Viapiana O, et al. Osteoporos Int, 2018

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FRI0476 **ISCHEMIA MODIFIED ALBUMIN IN OSTEOPOROSIS**

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Background: Osteoporosis is a common bone metabolism disease, characterized by low bone mass and pathological fractures. This disease is caused by loss of balance in bone resorption and formation. It is thought that this imbalance is associated with increasing in reactive oxygen species (ROS) and/or insufficiency of antioxidant defense (1). ROS adversely affect the formation and life cycle of osteoclasts, osteoblasts and osteocytes (2).
Albumin has many functions such as the transport of molecules, the oncotic pressure of plasma and antioxidation. The damage of the ROS to the N-terminal of the albumin reduces the carrying capacity of the albumin and thus the antioxidant capacity. This damage is evaluated by decreasing the cobalt binding capacity of albumin called ischemia modified albumin (IMA), and IMA shows oxidative damage (3).
Objectives: The aim of this study was to determine IMA levels of patient with osteoporosis.
Methods: OP was diagnosed by t score of bone mineral density (BMD). IMA, albumin levels and IMA/Albumin ratio (IMAR) were studied from the sera of patients with osteoporosis (OP) and healthy volunteers (control) (4). Patients who had any chronic disease such as diabetes mellitus, hypertension, and etc. and any acute disease such as infection were excluded from study. Results were shown as mean ± standard deviation or median (IQR) according to the distribution of variables. p<0.05 was considered significant.
Results: The study included 28 female patients in OP group and 26 female volunteer in control groups. The mean age was 65.5 ± 5.4 and 66.4 ± 7.4 for OP and control groups, respectively (p:0.616). Median (IQR) lumbar t scores of BMD of OP group were -3.1 (-3.32; -2.85). The albumin values of OP and control groups were 4.38 ± 0.13 and 4.40 ± 0.11, respectively; and no significant difference was found between the groups (p = 0.441). The IMA and IMAR results of the OP group were 0.65 (0.61; 0.74) and 0.15 (0.14; 0.17), respectively; and 0.46 (0.40, 0.55), and 11 (0.09; 0.13) in the control group, respectively. (Figure 1). Both IMA and IMAR results were significantly lower in the OP group than in the control group (high ABSU) (p <0.001; for all).
Conclusion: Cobalt binding capacity of albumin was decreased in patients with osteoporosis. To the best of our knowledge, this study is the first determining IMA levels in osteoporosis. It is known that the cobalt binding capacity of albumin decreased after oxidative damage. It is shown that IMA is increased in some diseases associated with oxidative stress. Similarly, it was showed that thiol-disulphide balance was shifted to disulphide side in postmenopausal osteoporosis and it was an indicator of oxidative stress (1, 2). In the light of these results, oxidative stress is thought to play role in the pathophysiology of osteoporosis. As a result, antioxidant replacement such as N-acetyl cysteine, lipoic acid, vitamin C, etc. may be recommended to the patients with osteoporosis.

REFERENCES:

[1] Altindag O, Erel O, Soran N, Celik H, Selek S. Total oxidative/anti-oxidative status and relation to bone mineral density in osteoporosis. Rheumatology international. 2008;28(4):317-21.
[2] Korkmaz V, Kurdoglu Z, Alisik M, Turgut E, Sezgin OO, Korkmaz H, et al. Thiol/disulfide homeostasis in postmenopausal osteoporosis. Journal of endocrinological investigation. 2017;40(4):431-5.
[3] Ellidag HY, Eren E, Yilmaz N, Cekin Y. Oxidative stress and ischemia-modified albumin in chronic ischemic heart failure. Redox report : communications in free radical research. 2014;19(3):118-23.
[4] Bar-Or D, Lau E, Winkler JV. A novel assay for cobalt-albumin binding and its potential as a marker for myocardial ischemia-a preliminary report. The Journal of emergency medicine. 2000;19(4):311-5.

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FRI0477 **STUDY OF CORTICAL AND TRABECULAR COMPARTMENTS THROUGH 3D-SHAPER IN LUNG TRANSPLANTED PATIENTS**

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Background: Osteoporosis in lung transplant (LT) patients is a frequent complication. Glucocorticoid treatment (GC) is a prominent risk factor (RF) that alters both bone mass and architecture. Studying the volumetric BMD using 3D-SHAPER software would help the study of architecture.
Objectives: To study the change in cortical surface density, volumetric trabecular density and integral volumetric density measured by 3D-SHAPER before and after LT as well as changes in bone mineral density (BMD) measured by densitometry (DXA).
Methods: LT patients assessed in Rheumatology are included. The demographic characteristics, diagnosis of lung disease and RF of low bone mass prior to LT are collected. Patients were grouped into 3 groups according to the type of disease, these being: Chronic Obstructive Pulmonary Disease (COPD), Interstitial Lung Diseases (ILD) and OTHER pathologies. Bone mass was evaluated by DXA (GE-LUNAR) before and 6 months after LT and 3D-SHAPER software (v2.7, Galgo Medical) was applied in all DXAs.
Results: 49 LT patients were included (46.9% women), with an average age of 56.9 ± 8.7 years. In the ILD group, a higher proportion of patients with a low calcium intake (p = 0.027) and with high doses of GC (p = 0.001) was observed. COPD group presented the highest proportion of smokers (p = 0.027). Prevalence of osteoporosis prior to LT was 24.5%, higher in COPD (p=0.007). Values of BMD and 3D-SHAPER as well as the percentage of post-transplant variation are shown in Table 1. Of the 47 patients, 19 (38.8%) started osteoactive treatment before LT, with a higher percentage of patients treated in the COPD group (p = 0.007). Of 42 patients, we have DXA at 6 months post-transplant, with a prevalence of osteoporosis of 23.8%. 27/42 patients underwent post-transplant osteoactive treatment, with an average treatment time until DXA was 19.2 ± 26.1 months, with no differences between groups.
Conclusion:

- Prevalence of low bone mass is high both before and after the transplant.
- Prevalence of some osteoporosis RFs was different between the lung disease groups.
- COPD group presented a worse bone mass before LT. Subsequently, they experienced a significant improvement in BMD and volumetric measurements with respect to the other two groups, which showed losses of these parameters. COPD was the group most treated for osteoporosis and with a lower proportion of patients with GC at high doses.
- Trabecular BMDv was the most altered measure of 3D-SHAPER, with greater decrease in patients with GC at high doses and lower in those with osteoactive treatment.

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PRE-TRASPLANT	**TOTAL (n=47)**	**COPD (n=11)**	**ILD (n=30)**	**OTHERS (n=8)**
BMD pre-trasplant (mean)	**g/cm² (T-score)**	**g/cm² (T-score)**	**g/cm² (T-score)**	**(g/cm² (T-score)**
. Lumbar Spine	1,074 (-1,02)	0,927**(2,18**)	1,131(-0,55)	1,051(-1,18)
. Femoral Neck	0,868 (-1,28)	0,798 (-1,89*)	0,899(-1,04)	0,846(-1,35)
. Total Hip	0,907 (-1,15)	0,812*(-2,07**)	0,950(-0,79)	0,878(-1,27)
3D-SHAPER (mean)	155,6 (-1,19)	143,9 (-1,90*)	163,3 (-0,97)	142,7 (-1,26)
. BMDs Cortical; g/cm² (T-score#)	146,1 (-1,69)	115,4**(-2,65)	155,3 (-1,64)	153,6† (-1,06†)
. BMDv Trabecular; g/cm³ (T-score#)	296,0	258,4*	309,4	297,5
. BMDv Integral; g/cm³				
6 m POST-TRASPLANT	**TOTAL (n=42)**	**COPD (n=10)**	**ILD (n=25)**	**OTHERS (n=7)**
% change BMD (mean±DE)	- 1,26 ± 10,3	9,38 ± 11,6**	- 3,92 ± 7,3	- 7,03 ± 7,7†
. Lumbar Spine	- 4,34 ± 7,3*	- 0,74 ± 6,5	- 5,43 ± 6,9	- 5,57 ± 9,3
. Femoral Neck	- 3,22 ± 6,0^^	1,18 ± 3,5*	- 4,07 ± 6,2	- 6,58 ± 5,6††
. Total Hip				
% change 3D-SHAPER (mean±DE)	- 1,59 ± 5,9	0,14 ± 4,9	- 2,53 ± 6,5	- 0,59 ± 4,9
. BMDs Cortical	- 4,42 ± 11,6^^	8,63 ± 8,6**	- 8,12 ± 9,5	- 11,66 ± 5,1††
. BMDv Trabecular	1,87 ± 4,3*		- 4,67 ± 6,5	- 5,20 ± 3,9†
. BMDv Integral	- 3,11 ± 6,3^^			

^p<0.05, ^^p<0.01 respect previous, *p<0.05, **p<0.01 COPD vs. ILD; †p<0.05, ††p<0.01 COPD vs. OTHERS; # only in women.

FRI0478 **SPINAL MOBILITY AND BONE MINERAL DENSITY IN SPONDYLOARTHRITIS**

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Background: Osteoporosis is the most frequent comorbidity in axial spondyloartritis (axSpA). The change in spinal mobility (traditional measures) in patients with axSpA has been associated with low bone mineral density (BMD) although the data are variable (DIM, lateral flexion, BASMI).
Objectives: The aim of our study is to understand the relationship between spinal mobility, BMD and fragility fractures.
Methods: Analytical, observational, longitudinal, and retrospective study of a cohort of patients with axSpA (ASAS criteria). Perimenopausal or menopausal women, diseases and/or osteopening treatments, biological drugs, immunosuppressive drugs (at least one year before), and treatment with drugs that interfere in the bone metabolism were excluded; bisphosphonates, ranelate of strontium, selective modulators of the estrogen receptor, calcitonin, hormone therapy, denosumab and teriparatide, among others.
Results: 74 patients were studied, 67 were clasified as axSpA and 7 as peripheral SpA. Bivariate analysis showed that the group of patients with osteoporosis (14,86%) had a worse DIM (p = 0.001), tragus-to-wall distance (p = 0.001) and lateral flexion (p = 0.045) than patients who did not have osteoporosis. The multiple regression analysis indicated that lumbar spine t/zscore was independently associated with BASMI index (B 0,682, p=0,013), femoral neck t/zscore was independently associated with BASFI index (B 1,575, p=0,007) and with lower levels of 25 OH vitamin D (B 0,895, p=0,028).
Conclusion: UCOASMI is a validated metrological index with three-dimensional measurements of human spinal mobility that shows higher levels of objectivity and precision than traditional measures. Subsequent studies will compare mobility parameters (UCOASMI) and BMD of patients with axSpA. Clarifyng the relationship between spinal mobility, BMD and fragility fractures would help us to better understand the course of the disease in axSpA.

REFERENCES:

[1] Moltó A, et al. Ann Rheum Dis. 2016 Jun;75(6):1016-23.
[2] Weijden MA,et al. Clin Rheumatol. 2011;30(4):497–503.
[3] Venceviciene, et al. Medicine,2015; 51(5): 272-279

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FRI0479 **TRENDS IN LOW TRAUMA DISTAL FOREARM FRACTURE INCIDENCE IN WOMEN AND MEN OVER 1995-2015 IN OLMSTED COUNTY, MINNESOTA, USA**

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Background: It is unclear how recent practice changes of decreased use of hormone replacement therapy and drug holidays from bisphosphonate therapy have impacted incidence of fragility fractures. Fragility (low trauma) fractures at the distal forearm in women may be more likely to be impacted by these changes as compared with men.
Objectives: We examined the trends in distal forearm fracture incidence over 1995-2015, in both women and men, from Olmsted County, Minnesota, USA.
Methods: Using the Rochester Epidemiology Project, a unique medical records linkage system that allows access to all (inpatient and outpatient) community medical records for Olmsted County residents, we identified all incident distal forearm fractures among residents age ≥18 years between 1995-2015. Available medical records were reviewed by trained nurse abstractors to validate distal forearm fractures identified and to determine their antecedent cause (pathological process [e.g., malignancy], severe trauma [e.g., motor vehicle accidents, sports/other recreational activities] and low trauma [by convention, equivalent to a fall from standing height or less]). Overall incidence rates were summarized separately for women and men, as well as by 5 year strata for different age groups (ages 18-39, 40-59, 60-79 and ≥ 80 yrs). Rates for women and men were each directly age-adjusted to the population distribution of US whites in 2010.
Results: Between 1995-2015, we identified 2727 distal forearm fractures in women (70%, median age 62 yrs; 1915 due to low trauma) and 1193 distal forearm fractures in men (30%, median age 48 yrs; 450 due to low trauma), 92.3% of which were in whites. The overall age-adjusted annual incidence of first distal forearm fracture over 1995-2015 was 233 per 100,000 person-years (p-y) for women and 113 per 100,000 p-y for men. When considering only fractures due to low trauma, the overall age-adjusted annual incidence of first distal forearm fracture over 1995-2015 was 169 per 100,000 p-y for women and 49 per 100,000 p-y for men. Rates of low trauma distal forearm fracture appear to be stable in younger (18-39 yrs) women, but since 2005, seem to be increasing in women age 40-59 yrs (Table). In contrast, rates in older women appear to be decreasing or are stable since 2005. In men, the rates of low trauma distal forearm fracture have been relatively unchanged over the past 20 years, except in men age ≥ 80 yrs where the rates have generally been lower since 2005 (Table).

Distal Forearm Fracture* Incidence per 100,000 p-y by Age Group

	18-39 yrs		40-59 yrs		60-79 yrs		≥ 80 yrs	
Years	Women	Men	Women	Men	Women	Men	Women	Men
1995-99	33	10	131	46	370	81	571	299
2000-04	27	17	102	40	415	72	690	297
2005-09	25	22	126	44	327	89	650	128
2010-15	30	10	145	43	332	75	594	161

*Incidence of fragility (low trauma) fractures at the distal forearm

Conclusion: The trend for increasing low trauma distal forearm fractures in women age 40-59 yrs may reflect the decreased use of hormone replacement therapy, which would likely have particularly impacted this age group. The decrease in fractures in men age ≥ 80 yrs may reflect greater recognition, in recent years, of osteoporosis in older men and initiation of treatment. Whether changes in practice patterns are actually contributing to these observed trends warrants further review.

REFERENCES:

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FRI0480 **CHANGES IN CIRCULATING SCTLA-4 FOLLOWING ZOLEDRONIC ACID INFUSION**

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Background: Acute phase response (APR) is a transient, flu-like reaction to first exposure to intravenous nitrogen-containing bisphosphonate (NBP). APR is characterised by a strong inflammatory response, associated with increases in circulating levels of IL-6 and TNF-, that is thought to be due to activation and increased proliferation of γδ T cells related to the molecular mechanism of action of NBP.
Cytotoxic T-Lymphocyte Antigen-4 (CTLA-4), in both its soluble (s) and membrane-bound forms, is involved in the downregulation of T cell proliferation, cell cycle progression and cytokine production. High levels of serum sCTLA-4 have been reported in several autoimmune diseases, and its role as both inhibitor and enhancer of the immune response has been proposed.
Objectives: To evaluate the potential relationship between sCTLA-4 and the development of APR in patients treated with zoledronic acid (ZOL).

Methods: Included in the study were patients treated with a single intravenous ZOL infusion 5 mg. Exclusion criteria were previous treatment with ZOL, treatments interfering with CTLA-4, and estimated glomerular filtration rate <35 ml/min. APR was defined as a rise in axillary temperature above 38°C at any time during the first 48 hours and an increase in musculoskeletal pain by more than 10 mm in a visual analogue scale (VAS, from 0 to 100 mm). Clinical and laboratory parameters were assessed at baseline, before ZOL, and at 24, 48 and 72 hours after the infusion.

Results: Ten female patients (mean age 73-10 years) were included (2 had vertebral fractures and the remaining had osteoporosis), 5 of whom experienced APR (APR+) associated with the expected increases in serum CRP and IL-6. Baseline levels of sCTLA-4 did not differ between APR+ and APR- patients and decreased significantly in all from 32-9 ng/ml to 24-9 ng/ml (p=0.007) at 24 hr, 16-8 ng/ml (p=0.004) at 48 hr and 7-6 ng/ml (p<0.001) at 72 hr. Absolute value of sCTLA-4 and mean% change of sCTLA-4 after ZOL were not statistically different between APR+ and APR- patients. At 72 hr, sCTLA-4 decreased by 77% (-23%) in APR+ and by 81% (-20%) in APR- (p=0.786). There were no statistically significant correlations between serum sCTLA-4 levels with any clinical or biochemical parameter of APR.

Conclusion: Contrary to our hypothesis, sCTLA-4 was not related to the occurrence of APR after ZOL. The significance of the substantial decrease of circulating levels of sCTLA-4 after ZOL in all studied patients warrants further investigation.

Disclosure of Interests: Gerolamo Bianchi Consultant for: Alfa-Sigma, Amgen, BMS, Celgene, Medac, UCB, Speakers bureau: Abbvie, Abiogen, Alfa-Sigma, Amgen, BMS, Celgene, Daniele Saverino: None declared, Dario Camellino Consultant for: Janssen-Cilag, Novartis, AbbVie, Sanofi, Paid instructor for: Mylan, Andrea Giusti Grant/research support from: Abiogen Pharma, Consultant for: EffRx, Speakers bureau: Abiogen Pharma, Eli Lilly, AMGEN, Erika Iervasi: None declared, Giuseppe Girasole: None declared, Socrates Papapoulos Grant/research support from: No in the last 3 years, Consultant for: Amgen, Axsome, Gador, Radius Health, UCB, Speakers bureau: Amgen, UCB

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FRI0481 MEDIATORS OF BONE METABOLISM (DKK1, OPG SCLEROSTIN AND RANKL) IN A COHORT OF PATIENTS WITH ELDERLY-ONSET ARTHRITIS

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Background: Patients with elderly-onset arthritis have greater comorbidity than young patients, with a higher incidence of osteoporosis (OP), probably mediated by increased bone resorption. However, there are few data on bone metabolism mediators in this population.

Objectives: To analyze bone remodeling mediators (DKK1, sclerostin, osteoprotegerin [OPG], and RANKL) in patients with elderly-onset arthritis and its relationship with bone mineral density.

Methods: Longitudinal observational study that included patients with elderly-onset arthritis (> 65 years) without diagnosis of OP or on antiosteoporotic treatment. Phospho-calcium metabolism, quantification of bone remodeling mediators (ELISA, R&D systems) and bone densitometry, were determined in all patients at diagnosis and at 12 months. The results were compared with a control group of the same age and sex (n=14). The statistical study was performed using SPSS.

Results: We included 73 patients (37F: 36M), with a mean age of 75±7 years. Most were diagnosed with rheumatoid arthritis (RA) (n=43), followed by polymyalgia rheumatica (n=16) and others (n=14). Fifteen patients were rheumatoid factor (RF) positive and 23 were ACA positive. Five patients had erosions at the diagnosis. 88.64% of patients with RA had an initial DAS28-VSG >5.1. Only 3 patients had previous fragility fractures (2 vertebral and 1 femur fractures).

At diagnosis, patients with elderly-onset arthritis had higher levels of DKK1 and CTX than the control group, with no statistically significant differences in sclerostin, OPG, and RANKL values (table 1). In addition, DKK1 values were negatively correlated with sclerostin (r=-0.286, p=0.016) and OPG (r=-0.276, p=0.020). 31.9% had densitometric OP. We found no significant differences in bone remodeling mediators between patients with/without basal OP.

At 12 months, DAS28-VSG was <2.6 in 38.1%. The mean corticosteroid dose was 5.5 mg/day with a cumulative dose of 1630±426 mg. 45.8% received antiosteoporotic treatment (28 patients' bisphosphonates and 5 denosumab). The prevalence of OP at 12 months was 31.3% and 4 patients had new fractures (4 vertebral and 1 femur fractures). We observed a marked decrease in the values of DKK1 (-18.89%, p<0.001) and sclerostin (-46.76%, p<0.001) and an increase in OPG (11.97%, p=0.018).

We didn´t found relationship between bone metabolim mediators and cumulative corticosteroid dose. There were not differences in terms of diagnosis (RA or PRM), ACPA positivity, activity scores or treatment with bisphosphonates.

Conclusion: Patients with elderly-onset arthritis have higher Dkk1 values than the control group, and this correlate negatively with sclerostin and OPG. The marked decrease in Dkk-1 and sclerostin at 12 months, and the increase in OPG, suggests a role for these mediators in the bone metabolism of this population. It is important to note the high prevalence of OP in this group of patients.

Table 1. *We excluded patients treated with denosumab. † p<0.005 with respect to the control group. ‡ p<0.05 with respect to baseline

Variables	Control N=14	Basal patients N=73	12 months patients* N=72
VSG(mm/h)	14±10	55±27†	27±18†‡
PCR(mg/L)	3.6±6.6	38,1±50,6 †	4,9±5,5 †‡
HAQ	-	1,6±0,75	0,51±0,57 ‡
DAS28-VSG(in RA) {n=43}	-	6,32±1,04	3,10±1,30 ‡
CTX(ng/mL)	0,33±0,18	0,49±0,19 †	0,26±0,13 ‡
OPG(pg/ml)	3127±948	3319±1134	3647±1466 ‡
DKK-1(pg/ml)	1558±555	2740±1611 †	1516±985 ‡
Sclerostin(pg/ml)	1299±961	1189±626	515±333 †‡
RANKL(pg/ml)	122±184	101±102	-
RANKL indetectable n (%)	9(64.3)	16(22.5)	72(100)

Disclosure of Interests: None declared

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FRI0482 RISK FACTORS FOR FRAGILITY FRACTURE IN PATIENTS WHO SMOKE: AN OBSERVATIONAL STUDY

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Background: Smoking is a risk factor for osteoporosis and increases the likelihood of a fragility fracture. It is included in the FRAX™ tool, which is used as an aid for bone mineral density (BMD) referral and as a risk stratification for the propensity of developing a fragility fracture. The additive effect of other risk factors including demographics increasing the risk of fracture has not been explored in a large cohort.

Objectives: To investigate the additive predictors of fracture in patients who have smoking as their only risk for fracture, referred for BMD estimation.

Methods: Patients who were referred for bone mineral density (BMD) estimation in a scanner in the North West of England between June 2004 and October 2015 were included in the analysis. Patients with only smoking as a FRAX™ risk factor were then analysed. All patients have their other risk factors for fracture and demographics recorded at time of scan. All patients with other FRAX™ indications for scanning were excluded including Rheumatoid Arthritis, Excess Alcohol, Steroids, family history of fracture and Secondary Osteoporosis. Patients in the smoking group were divided into those that had experienced a fracture and those that had not before comparing with Chi-squared test for categorical variables and T-test for continuous variables. Univariate and multivariate logistic models were then fitted to examine predictors of fracture in this group.

Results: 35,759 patients were referred for scanning during the period. 4096 (11.45%) were referred with smoking as their only indication for scanning. Mean age at scan was 64.43 (SD 12.38) and 3244 (79%) of the cohort were females. 1663(40.60%) had a fracture. Fractures were more prevalent in males with 383 (44.95%) compared to 1280 (39.46%) in females (p=<0.05).

Univariate predictors shown in the Table 1 below.

Table 1. Univariate predictors of fracture in the smoking cohort * denotes significant prediction

Predictor	Fracture (n=1663)	No Fracture (n=2433)	Odds ratio	95% CI
Age (years)	66.58	62.97	1.03*	[1.02, 1.03]
Gender (no. of patients)	Male (383) Female (1280)	Male (469) Female (1964)	0.80*	[0.69, 0.93]
Height (cm)	162.26	162.41	1.00	[0.99, 1.01]
Weight (kg)	71.16	71.16	1.00	[1.00, 1.00]
L1-L4 BMD (g/cm^2)	1.04	1.10	0.19*	[0.13, 0.26]
Femoral neck BMD (left) (g/cm^2)	0.82	0.87	0.08*	[0.05, 0.12]
Total femur BMD (left) (g/cm^2)	0.87	0.92	0.10*	[0.07, 0.16]
% Body fat (g)	308.15	299.89	1.00*	[1.00, 1.00]

In the multivariate model, the only variables associated with increased fracture risk was increasing age at scan decreased BMD total left and increased percentage body fat. All other factors did not significantly increase fracture risk in this cohort.

Conclusion: Our study suggests that many risk factors are associated with fragility fractures in those with smoking as their only risk factor; the best predictor was age at scan, BMD and gender. The percentage body fat association with increased fracture risk is quite surprising and would need further study. Percentage body fact is not currently included in the FRAX™ tool.

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FRI0483 INTEREST OF A SYSTEMATIC SCREENING OF OSTEOPOROSIS IN HEART TRANSPLANT PATIENTS

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Background: Osteoporosis is common among patients with end-stage heart disease. A rapid decrease of bone mineral density (BMD) is usually observed after heart transplantation. Bone loss is probably linked to glucocorticoids and calcineurin inhibitors use and vitamin D deficiency.

Objectives: The aim of this study was to evaluate the interest of a systematic screening of osteoporosis in heart transplant patients.

Methods: We performed a prospective monocentric study including patients, who had of heart transplantation in our hospital, from December 2016 to January 2019.The following parameters were systematically assesses: history of cardiac disease, immunosuppressive therapies, glucocorticoids, previous history of low trauma fracture, known risk factors of osteoporosis, treatment received for bone disease management (calcium, vitamin D and bisphosphonates). Blood tests with creatinine clearance, calcium and vitamin D levels, were assessed. Bone densitometry and spine radiographs (to search asymptomatic vertebral fractures) were assessed in all patients. Osteoporosis was defined respectively for patients $\geq$50 years and <50years as a T-score$\leq$-2.5 SD and Z-score$\leq$-2 SD either at lumbar spine (L2-L4), femoral neck or hip.

Results: A total of 42 patients were included (76.7% male), mean age was 58.1±10.6 years, mean duration after transplantation was 2.6±3.1 years. Past or active smoking statues were observed in 26 patients (mean 23.9 pack-years). Calcium, vitamin D and bisphosphonates were administered in 13 (30.9%), 10 (23.8%) and one patients, respectively. All patients received prednisone (mean dose: 10.7±4.9 per day). Mean lumbar spine BMD was 1.03±0.25 g/cm² and left femoral neck BMD 0.85 ±0.15g/cm². Osteoporosis was observed in 18 (45%) patients. Only one hip fracture was known before heart transplantation. Incidental low trauma fractures after transplantation were diagnosed in 14 patients (33.3%): 11 patients with vertebral fractures (mean 2 vertebral fractures per patient) including 4 patients with asymptomatic vertebral fractures. Others low trauma fractures were hip fracture, proximal humerus and fibula for one patient each. Mean duration between transplantation and the first low trauma fracture was 7.5±3.7 months. Low level of calcemia was found in 20 patients (47.6%) and low level of vitamin D (≤30mg/l) in 32 patients (76.2%) associated with secondary hyperparathyroidism in 21 patients (51.2%), mean creatinine clearance was 51.7±19.9ml/min. After evaluation, specific treatment of osteoporosis was started for 33 patients (78.6%): zoledronic acid (n=20), denosumab (n=8), alendronate (n=4) and teriparatide (n=1).

Conclusion: Systematic screening of osteoporosis seems to be useful in heart transplant patients. Osteoporosis was observed in half of these patients with a high frequency of low trauma fracture after heart transplantation, particularly in the first year.

Disclosure of Interests: None declared

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FRI0484 RESULTS OF BONE MINERAL DENSITY DURING CELIAC DISEASE: ABOUT 83 CASES

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Background: The prevalence of osteopenia during celiac disease (CD) can range from 38% to 72%. In fact, it is a pathology that causes bone loss and is associated with a higher fracture risk compared to the general population.

Objectives: The aim of this work is to determine the frequency and factors associated with the decline in bone mineral density in adult subjects with CD.

Methods: This is a retrospective study, over a period of 4 years (from January 2014 to December 2018) and including patients followed for MC who had a measurement of bone mineral density (BMD) by DEXA.

Clinical, anthropometric and densitometric data (BMD at the femoral and vertebral site) were recorded.

The WHO criteria for the definition of osteoporosis and osteopenia have been used.

Results: 83 patients were collected among them 12 were men (sex ratio = 0.16). The average age was 38.2 years old. The average body mass index (BMI) was 21.64 kg/m² [13.05-31.9 kg/m²]. Undernutrition (BMI <19 kg/m²) was found in 24 cases. It was associated with hyperthyroidism in 5 cases, autoimmune hepatitis in 1 case and primary amenorrhoea in 2 cases. 2 patients had a history of fragility fracture, and 5 patients had a history of fragility fracture in a first-degree relative.

Osteodensitometry showed low bone mass in 36 cases: osteoporosis in 23 patients (27.7%) and osteopenia in 13 cases. Osteoporosis was found in 21 patients: 1 man and 20 women. Mean femoral BMD was 0.887 g/cm3 and vertebral BMD was 0.999 g/cm3. The mean T-score at the femoral site and the vertebral site were -1.28 SD and -1.26 SD, respectively. No correlation was found between age and BMD and bone status. Comparing patients with a BMI <19 kg/m² to those with a BMI $\geq$ 19 kg/m², BMD at the vertebral site was significantly lower in malnourished subjects (p = 0.01). a significant correlation was found between BMI and vertebral BMD (p=0.000)

Conclusion: The decline in BMD was observed in third of our patients. It seems to be favored by a low BMI, which is common during CD in relation to the associated malabsorption. Thus, screening for osteoporosis should be advocated early in the course of CD.

Disclosure of Interests: None declared

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FRI0485 TIMED UP AND GO TEST FOR VERTEBRAL FRACTURE PREDICTION

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Background: Sarcopenia describes the age related loss of skeletal muscular mass and function. The development of sarcopenia may confer an increased risk of falls which leads to a potential increase in fracture. The Timed Up and Go (TUG) Test is one of clinical tools used to assess sarcopenia.

Objectives: We hypothesized that slow TUG test performance would predict vertebral fracture (VF) in post-menopausal women independently of bone mineral density (BMD) and other risk factors.

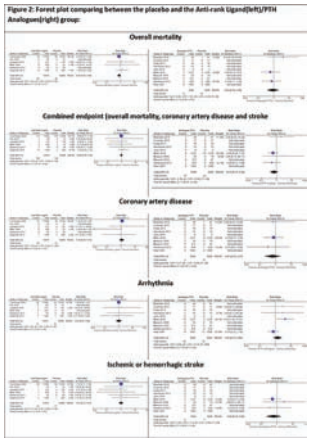
Methods: This is a cross sectional study enrolled from September 2018 to December 2018, including post-menopausal women referred to rheumatology department for measure of BMD. All subjects underwent dual energy X-ray absorptiometry (DeXA) and physical performance tests

including the TUG test. TUG performance was considered low if it took, 15 seconds or longer. A vertebral fracture assessment (VFA) image was obtained which was subsequently scored for the presence of significant vertebral deformities. VF grade 1 were excluded.
Results: Eighty four patients were included. The mean age of our patients was 62.29±8.27 years with an average body mass index (BMI) of 31.45±6.21 kg/m^2 [18.18-44.38]. According to the WHO classification 42 patients (50%) had osteoporosis. Among 84 women, 47 had a low TUG performance. Subjects with low TUG performance had an older age (57.94 vs 65.71 years) (p<0.001), and had a significantly lower BMD at femoral neck (0.825 g/cm^{3}vs 0.752 g/cm^3) (p<0.001). There was no significant difference between the two groups regarding duration of menopause, history of previous fragility fracture, body mass index and BMD at total hip and at vertebral site. Osteoporosis was found in 30 patients who had low TUG performance and in 12 patients who had normal TUG performance without statistically significant difference (p=0.08).VF were assessed in 22 subjects. VF were found in 20 patients with low TUG performance (42.55%). Compared with the group with normal TUG performance, subjects with low TUG performance had significantly higher number of fracture (p<0.001).A significant correlation was found between the number of VF and the score of get up and go test (Khi-2 test, p<0.001).
Conclusion: Our study found a strong relationship between TUG performance and prevalent vertebral fracture. Therefore evaluation of additional risk factors may improve the prediction of vertebral fracture in post-menopausal women.
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FRI0486 NO IMPACT OF ANTI-RANK LIGAND AND PTH ANALOGUES ON CARDIOVASCULAR RISK IN IDIOPATHIC AND POSTMENOPAUSAL OSTEOPOROSIS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Background: Emerging evidence suggests a possible association between osteoporosis and cardiovascular disease[1,2]. The mutual effects of drugs used in these two diseases are now a point of interest. Two meta-analyses have been conducted to explore the cardiovascular effects of bisphosphonates[3,4]. There is no review for other osteoporosis treatments, such as anti-rank ligand antibody and parathyroid hormone analogues.
Objectives: A literature review and meta-analysis of randomized controlled trials was conducted to address the impact of PTH analogues and anti-Rank Ligand on cardiovascular events and overall mortality in individuals with idiopathic osteoporosis.
Methods: A systematic literature review was conducted in December 2017 in the PubMed, Embase, Cochrane databases, and updated on PubMed in December 2018, by selecting trials including a treatment (anti-Rank Ligand or PTH analogue) and a control group. We also conducted a search for abstracts of the French Rheumatology Society, American College of Rheumatology and European League Against Rheumatisms annual meetings over the past 3 years. Relative risks and 95% confidence intervals for each event were estimated using the Inverse Variance fixed effects method. The main endpoints were the occurrence of cardiovascular events and all-cause of mortality.
Results: Of the 2782 reports initially found (503 articles via PubMed, 1309 via Embase, 474 via the Cochrane Library and 15 abstracts from annual meetings, 16 articles were used for the meta-analysis. All studies were randomized; no exploitable prospective cohort study was found. The number of adverse events of interest was available for 6 studies for the anti-Rank Ligand corresponding to 26 864 patient-years. After meta-analysis, there was no significant difference between the placebo group and the anti-Rank Ligand group for overall mortality (RR 0.79, 95% CI (0.60-1.04)), the combined cardiovascular endpoint (overall mortality, coronary artery disease and stroke: RR 0.95, 95% CI (0.78-1.16)), and the individual risk of coronary artery disease (RR 1.14, 95% CI (0.76-1.73)), arrhythmia (RR 1.03, 95% CI (0.63-1.68)) and ischemic or hemorrhagic stroke (RR 1.03, 95% CI (0.72-1.47)). The number of adverse events of interest was available for 10 studies for the PTH analogue group, corresponding to 6 220 patient-years. After meta-analysis, there was no significant difference between the placebo group and the PTH analogue group for overall mortality (RR 0.89, 95% CI (0.35-2.29)), the combined endpoint (overall mortality, coronary artery disease and stroke: RR 0.71, 95% CI (0.37-1.36)), and the individual risk of coronary artery disease (RR 0.65, 95% CI (0.19-2.27)), arrhythmia disorders (RR 1.43, 95% CI (0.73-2.80)) and ischemic or hemorrhagic stroke (RR 0.60, 95% CI (0.19-1.96)).
Conclusion: The anti-Rank Ligand and the PTH analogues have no short-term impact on the cardiovascular risk and the overall mortality in postmenopausal osteoporosis. To better answer the question whether these treatments are able to reduce the long-term cardiovascular risk, further comparative studies with longer duration are required.



REFERENCES:
[1] von der Recke P, et al. The association between low bone mass at the menopause and cardiovascular mortality. Am J Med. 1999;106(3):273-278.
[2] Veronese N, et al. Relationship Between Low Bone Mineral Density and Fractures With Incident Cardiovascular Disease: A Systematic Review and Meta-Analysis. J Bone Miner Res Off J Am Soc Bone Miner Res. 2017;32 (5):1126-1135.
[3] Kim DH, et al. Bisphosphonates and Risk of Cardiovascular Events: A Meta-Analysis. Pizzi C, ed. PLOS ONE. 2015;10(4):e0122646.
[4] Kranenburg G, et al. Bisphosphonates for cardiovascular risk reduction: A systematic review and meta-analysis. Atherosclerosis. 2016;252:106-115.

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FRI0487 UTILITY OF TRABECULAR BONE SCORE(TBS) FOR FRACTURE RISK ASSESSMENT IN GLUCOCORTICOID-INDUCED OSTEOPOROSIS

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Background: Glucocorticoid-induced osteoporosis (GIOP) is the one of the most common forms of secondary osteoporosis (OP). Fractures in GIOP frequently occur with higher than expected bone mineral density (BMD) values. The Trabecular Bone Score (TBS) is a gray-level textural index derived from DXA images that provides information about bone microarchitecture and fracture risk independently of BMD; therefore, TBS measurement could be useful for identifying patients with high fracture risk associated with glucocorticoid (GC) treatment.
Objectives: To analyse the clinical utility of TBS for fracture risk assessment in GC treated patients and compare it with BMD assessment, the gold-standard diagnostic test.
Methods: 127 patients on chronic GC treatment (≥5mg/day) were included (mean age 62±18 years, 63% women) in this cross-sectional study. The medical history and anthropometric data were collected, as well as measurements of bone metabolism parameters, bone densitometry (DXA) at lumbar spine and femur (considering OP when T-score ≤-2.5), TBS (considering degraded microarchitecture [DMA] with values <1.230) and dorsolumbar X-ray to assess vertebral fractures (VF). BMD and TBS

sensitivity, specificity and positive and negative predictive values (PPV, NPV) were evaluated to determine the diagnostic accuracy of the two methods.

Results: Most of the patients were receiving GC treatment for vasculitis or polymyalgia rheumatica over a mean period of 47.7±69 months at a mean daily dose of 14.5mg. 17% had VF, 28% any type of fragility fracture (VF + no-VF), 29% OP and 71% DMA. In patients with VF, low TBS (DMA) was more common than densitometric OP (76%, p=0.03 *vs.* 38%, p=n.s). Similar results were observed when analysing patients with any fragility fracture (69%, p=0.02 *vs.* 36%, p=n.s). The diagnostic accuracy of TBS was greater than BMD on evaluating VF, with a sensitivity, specificity, PPV and NPV of 0.76, 0.53, 0.25 and 0.92 for TBS and 0.38, 0.72, 0.22, and 0.85 for BMD, respectively. Specificity increased to 0.89 for VF and 0.9 for any fragility fracture on combining both assessments (OP+DMA).

Conclusion: TBS has greater discriminative power than BMD measurement and could be useful as a complementary tool for fracture risk assessment in GIOP.

Disclosure of Interests: Helena Florez: None declared, José Hernández-Rodríguez : None declared, Africa Muxi: None declared, Josep Lluís Carrasco: None declared, Sergio Prieto-González: None declared, Silvia Ruiz-Gaspà : None declared, Maria C. Cid Grant/research support from: Kiniksa Pharmaceuticals, Consultant for: Roche, GSK, Janssen, Abbvie, Speakers bureau: Boehringer-Inhelheim, Vifor, Ana Monegal Speakers bureau: Eli Lilly, Amgen, Núria Guañabens Consultant for: Advisory Boards from Amgen, Alexion and UCB, Speakers bureau: Fees and lectures from Eli Lilly, Pilar Peris Speakers bureau: Personal Fees and Non-financial support (attendance to congresses) from Amgen and Eli Lilly

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FRI0488 ROLE OF DUAL-PHOTON X-RAY ABSORPTIOMETRY (DXA) IN PREDICTION OF REFRACTURE AND MORTALITY

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Background: The presence of a fragility fracture leads to a high risk for a subsequent fracture and mortality. Although bone mineral density (BMD) does not reflect the real fracture risk in many conditions, it is a well-established predictor of fracture risk and for many years, dual-photon X-ray absorptiometry (DXA) has been the reference standard for measuring BMD.

Objectives: To evaluate the predictive significance of femur BMD and T-score obtained by DXA in the outcomes refracture and mortality of elderly patients with a previous fragility hip fracture.

Methods: Longitudinal retrospective study of patients referred to the Rheumatology department's Fracture Liaison Service (FLS) from march 2015 until march 2017 aged ≥65 years old. Demographic and clinical data were collected including DXA results. Statistical analysis was performed with STATA. Hazard ratios (HR) were calculated through cox regression, adjusted to age and degree of dependence.

Results: From a total of 522 patients, 214 performed DXA (77.6% female; median (min-max) age 82 (65-99) years; 65.4% autonomous). Twenty seven patients died (median days until death=457, min 160, max 1049) and 18 had a subsequent fracture (median days until refracture 343.5, min 160, max 1049); 129 patients maintained follow-up. Mean serum total femur BMD, g/cm^2 (SD) was 0.7 (0.14) and mean total femur T-score (SD) was -2.6, (1.1). 127 (59.3%) patients had T-score ≤-2.5. After multivariable analysis, higher femur BMD and T-score were predictors of better survival outcome (HR 0.01, *p*=0.023; HR 0.67, p=0.038, respectively). Nevertheless, none of them predicted refracture outcome. (HR: 0.08; 95%CI [0.01-5.16]; *p*=0.240); HR: 0.81; 95%CI [0.51-1.28]; *p*=0.361).

Conclusion: DXA is important in the management of patients with bone fragility syndromes. Our sample suggests that femur BMD/T-score had significant impact on survival outcome. Thus it can be a predictor of mortality with relevant role in daily practice.

REFERENCES:

[1] Browner WS, Seeley DG, Vogt TM, Cummings SR. Non-trauma mortality in elderly women with low bone mineral density. Study of Osteoporotic Fractures Research Group. Lancet 1991;338:355–8.

[2] Trivedi DP, Khaw KT. Bone mineral density at the hip predicts mortality in elderly men. Osteoporos Int 2001;12:259–65.

[3] Cortet B. Does low bone mineral density predict mortality? Joint Bone Spine. 2016 Dec;83(6):623-624

[4] Roux C[1], Briot K[2]. Current role for bone absorptiometry. Joint Bone Spine. 2017 Jan;84(1):35-37.

[5] Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K,et al. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. Lancet. 1993;341:72–75.

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FRI0489 THE ASSOCIATION BETWEEN CT-MEASURED BONE ATTENUATION AND PREVALENT VERTEBRAL FRACTURES IN THE THORACIC SPINE DIFFERS ACCORDING TO VERTEBRAL FRACTURE LOCATIONS

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Background: Subjects with prevalent vertebral fractures (VFs) have lower bone mineral density (BMD) in the lumbar spine and hip than subjects without prevalent VFs. However, VFs are not equally distributed across the thoracic spine. They occur preferentially at T7-T8 and T11-T12, which are the highest loaded vertebral regions during daily activities (1).

Objectives: We evaluated the association of BMD with prevalent VFs at non-preferential locations (nprVFs: T4-T6 and T9-T10) and at preferential locations (prVFs: T7-T8 and T11-T12).

Methods: Baseline CT images of T4-T12 in smokers with and without COPD were analysed for the presence of VFs according to Genant. Bone attenuation (BA), expressed in Hounsfield units (HU), was measured in all non-fractured vertebrae. Linear regression was used to compare mean BA and logistic regression was used to estimate the association between BA and prevalent VFs. All analyses were adjusted for age and sex.

Results: Prevalent VFs were most frequently located at T7-T8 (in >6% of vertebrae) and T11-T12 (in >4% of vertebrae).

At subject level and compared to subjects without prevalent VFs, mean BA of all non-fractured vertebrae was significantly lower in subjects with any prevalent VFs (-21%, p<0.0001). There was a significant progressive trend (p<0.0001) in decrease in mean BA of all non-fractured vertebrae between subjects with only prVFs (-15%), with only nprVFs (-25%, p<0.05 vs prVFs) and with both nprVFs and prVFs combined (-32%, p<0.0001 vs prVFs) (all p<0.0001 compared to subjects without VF).

At each individual non-fractured vertebral level, each BA decrease of 50 HU was associated with a 2.0-2.5 increased odds of any prevalent VF, a 1.5-1.9 increased odds of only prVF, a 2.2-3.4 increased odds of only nprVF and a 3.8-4.6 increased odds of nprVF and prVF combined.

Conclusion: In addition to BA, other factors such as vertebral load during daily activities may determine the location of a VF. The location of a VF may be a potential *in vivo* marker of the load/strength ratio of bone.

REFERENCES:

[1] Bruno AG, Burkhart K, Allaire B, Anderson DE, Bouxsein ML. Spinal Loading Patterns From Biomechanical Modeling Explain the High Incidence of Vertebral Fractures in the Thoracolumbar Region. J Bone Miner Res. 2017 Jun;32(6):1282-1290

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FRI0490 GOAL-DIRECTED TREATMENT OF OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS USING DENOSUMAB FOR THREE YEARS

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Background: Osteoporosis (OP) is frequently concomitant with rheumatoid arthritis (RA). Effective treatment have to be performed in OP in RA (RAOP). Denosumab (DMB) is one of the promising drugs for the treatment of RAOP. We reported results of 12-month DMB treatment for RAOP from Japanese multicenter registry study (TBCR-BONE) in EULAR2016 [1)]. Recently treatment goal of OP was reported from American society for bone and mineral research and National Osteoporosis Foundation (ASBMR-NOF) working group (Goal-Directed Treatment) [2)]. This progress report advocated that the goal of treatment is a T-score>-2.5 at femoral neck, total hip (TH) or lumbar spine (LS) by DXA if the primary reason for starting treatment was T-score -2.5 at that skeletal site. The Working Group judged that it was intuitively reasonable to expect that initial treatment should offer at least a 50% chance of achieving the treatment goal within 3 to 5 years of starting therapy.
Objectives: The aim of this retrospective study is to evaluate whether 3-year DMB treatment can achieve treatment goal of OP reported recently from TBCR-BONE.
Methods: This study used 78 female RAOP patients who completed 3-year DMB treatment for RAOP. 36 patients in whom baseline T-score of LS-BMD were -2.5 or less were included in LS-BMD analysis. 52 patients in whom baseline T-score of TH-BMD were -2.5 or less were included in TH-BMD analysis in the same way. As was in clinical setting in Japan, 60mg DMB was administered every 6 months with vitamin D3 agent. Patients' characteristics, time course of T-score and baseline characteristics related to achievement of treatment goal (T-score>-2.5) were investigated.
Results: Baseline characteristics of 78 patients: Mean age was 71 years. RA duration was 17 years. Prednisolone user was 32%. LS-BMD analysis (n=35) T-score was significantly increased (-3.5 at baseline, -3.0 at 1 year, -2.9 at 2 years, -2.8 at 3 years). The rates of patients who achieved treatment goal were 30.6% at 1 year, 38.9% at 2 years and 44.4% at 3 years (Fig1A). The achiever had significant lower baseline fracture risk by FRAX (20.1% vs. 33.9%: p=0.013), significant lower baseline mHAQ (0.45 vs. 1.05: p=0.03) and significant lower baseline T-score of LS-BMD (-3.0 vs. -3.9: p<0.01) than the non-achiever did. TH-BMD analysis (n=52) T-score was significantly increased (-3.2 at baseline, -3.0 at 1 year, -2.9 at 2 years, -2.9 at 3 years). The rates of patients who achieved treatment goal were 19.2% at 1 year, 28.8% at 2 years and 25.0% at 3 years (Fig1B). The achiever had significant lower baseline bone turn over marker (P1NP and TRACP-5b) and significant lower baseline T-score of TH-BMD (-2.6 vs. -3.3: p<0.01) than the non-achiever did. Cut-off values at baseline for achievement of treatment goal calculated using receiver operating characteristic analysis was -3.4 in LS-BMD and -2.7 in THBMD.
Conclusion: This study suggested that achievement of treatment goal in RAOP is not possible in LS-BMD and in TH-BMD when 3-year DMB was used as treatment for RAOP. Longer duration or earlier initiation of DMB treatment is necessary to achieve the goal. Although response in LS-BMD was related to fracture risk and physical function, response in TH-BMD was related to bone turnover. We will report 5-year results in the future.

REFERENCES:

[1] Hirano, et al. Ann Rheum Dis 2016; 75 (Suppl2): 94
[2] Cummings, et al. J Bone Miner Res 2017; 32: 3-10

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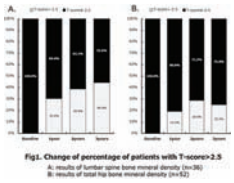


Fig1. Change of percentage of patients with T-score>-2.5
A: results of lumbar spine bone mineral density (n=36)
B: results of total hip bone mineral density (n=52)

FRI0491 MANAGEMENT OF SECONDARY OSTEOPOROSIS FRACTURES IN FRACTURE LIAISON SERVICE OF REIMS HOSPITAL IN FRANCE: STUDY AT 25 MONTHS OF FOLLOW-UP

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Background: Osteoporosis is a major public health issue, progressing with the aging of the population and responsible for nearly 400,000 fractures/year in France. Fracture Liaison Services (FLS) are systems of detection and secondary prevention of osteoporotic fractures. These systems are recognized as effective by international scientific societies.
Objectives: The aim of this study was to evaluate the efficiency of Reims Hospital FLS protocol after 25 months of implementation.
Methods: We performed an ambispective monocentric observational study at the Reims Hospital between April 2016 and May 2018. We included patients over 50 years who were hospitalized in the orthopedic department for osteoporotic fractures. These patients were evaluated clinically, biologically and radiographically during a one-day hospitalization in the rheumatology unit. Therapeutic compliance and fracture recurrence were assessed in consultation at 3-month and 1-year telephone interviews.
Results: Sixty-four/242 patients (26.4%) identified in orthopedic service were included. The average age was 72 years old with a sex ratio of 1:10. The most common fracture was the proximal end of the femur for 25 patients (39%). Fifty-five patients (85.9%) had an indication for osteoporosis treatment, the most prescribed was zoledronic acid for 45 patients (81.9%). Twenty-four/55 patients (43.6%) started their treatment and 22/24 (91.7%) were still treated at one year.
One patient (1.63%) died within the follow-up period. Twelve/55 patients (21.8%) presented a new fall and 7/55 patients (12.7%) experienced a new fracture.
Comparative analysis of observant versus non-observant population groups at 1 year showed that non-observant patients had significantly more recurrent falls (93.54% versus 68.18%, p = 0.024) and received treatment of zoledronic acid (93.56% versus 63.64%, p = 0.010).
Further analysis showed that our low rate of initiation treatment was due to difficulties in implementing bisphosphonates, mainly because of the dental care needed. However, we observed a high rate of treatment adhesion at 1 year, once the treatment is started. During this study, we identified 2 areas of improvement: therapeutic education to improve patient adherence and fall risk factors to decrease recurrent fall rate.
Conclusion: There is a real benefit to the establishment of this FLS with a high rate of therapeutic compliance at 1 year follow-up. However there are opportunities for improvements in treatment initiation through patients therapeutic education.

REFERENCES:

[1] Lems WF, Dreinhöfer KE, Bischoff-Ferrari H, Blauth M, Czerwinski E, da Silva J, et al. EULAR/EFORT recommendations for management of patients older than 50 years with a fragility fracture and prevention of subsequent fractures. Ann Rheum Dis. mai 2017;76(5):802–10.

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FRI0492 CALCULATING FRAX SCORE IN CLINICAL PRACTICE: PITFALLS AND PROBLEMS

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Background: Osteoporosis related fractures cause significant morbidity and mortality. FRAX score uses clinical risk factors and country-specific data in addition to Bone Mineral Density (BMD) to assess patients with high 10-year risk of hip (>3%) or major osteoporotic (>20%) fracture. We noticed discrepancies between radiologist reported and physician calculated FRAX scores at our hospital. We hypothesized that providers are calculating FRAX score differently as BMD in the FRAX calculator is an optional input variable.
Objectives: This study was initiated to see the differences in results when FRAX score is calculated using T-score, BMD and no BMD and how this difference can influence treatment.
Methods: Retrospective chart review of 1200 DEXA reports from 2013 to 2015 was done. Patients between ages of 40-90 years with T-score ranging from ≤ -1 to >-2.5 at femoral neck were included in the study. Patients already on osteoporosis therapy and/or with T-score ≤ -2.5 or >-1 were excluded.
Pertinent risk factors were obtained from chart review. 237 patients met inclusion criteria and 3 separate FRAX scores were calculated using a) Femoral neck BMD b) T-score c) no BMD value. FRAX score reported by radiologist in the chart was also reviewed. Subsequently, FRAX scores obtained using T-score, no BMD value and radiology reported scores were compared against FRAX score calculated using femoral neck BMD (gold standard)
Results:

Table 1. shows demographic information for 237 patients who met inclusion criteria.

Demographics	
Race	
Hispanic	131 (54.8%)
Black	71 (29.9%)
Caucasian	15 (6.3%)
Asian	20 (8.5%)
Average Age	67±10.5 years
Sex	
Male	11 (4.7%)
Female	226 (95.3%)
Average Height	159.3 ± 7.6 cm
Average Weight	71 ± 13 kg
BMI	27.9 ± 4.9
Previous fracture	13 (5.4%)
Current smoking	14 (5.9%)
Steroid use	48 (20.3%)
RA	26 (11%)
Secondary osteoporosis	8 (3.4%)
Alcohol use	3 (1.3%)

When FRAX score calculated using BMD was compared with FRAX score calculated without BMD, number of patients with high 10-year fracture probability decreased from 49 to 11 patients, which was a statistically significant decrease of 77.6% (p<0.001).
When data was stratified according to age, there was significant overestimation of risk in patients >65 years(p<0.0001) when FRAX was calculated without BMD.
Conclusion: FRAX score calculation without BMD leads to both statistically and clinically significant overdiagnosis especially in elderly.
Interchanging T score and BMD to calculate FRAX score leads to same treatment decision.
Further education of providers regarding FRAX score is needed.
Many providers are not aware that if BMD column is left blank, it defaults the calculation to no BMD. A pop up alerting the user "no machine was selected so the calculation will default to no BMD which can lead to overestimation of risk" in FRAX tool might be helpful to avoid miscalculation.

REFERENCES:

[1] https://www.sheffield.ac.uk/FRAX/tool.jsp
[2] Prawiradilaga, RS, et al., "FRAX Calculated without BMD Resulting in a Higher Fracture Risk Than That Calculated with BMD in Women with Early Breast Cancer," Journal of Osteoporosis, vol. 2018, Article ID 4636028.

Table 2. shows difference in risk estimation when different FRAX score assessments were compared against gold standard femoral neck BMD.

FRAX Scores Compared	Discrepancy in Risk estimation	Overestimation	Underestimation	McNemar's test
No BMD vs. BMD FRAX	52/237 (16%)	52	0	p<0.0001
Reported FRAX vs. BMD FRAX	6/237 (2.4%)	2	4	p=0.414
T-score vs. BMD FRAX	1/237 (0.4%)	1	0	p= 0.317

McNemar's test was used to compare difference in risk estimation and although the difference in absolute FRAX score values was statistically significant in all groups (p<0.0001), difference in risk estimation based on FRAX score was statistically significant only in BMD vs. no BMD comparison.

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FRI0493 CLINICLAL EFFICACY OF DENOSUMAB IN PATIENTS WITH OSTEOPOROSIS BETWEEN RHEUMATOID ARTHRITIS AND PRIMARY OSTEOPOROSIS; 24 MONTHS OF FOLLOW-UP

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Background: Denosumab (DMB) is a fully human monoclonal antibody to the receptor activator of nuclear factor-kappaB ligand (RANKL) that blocks its binding RANK, inhibiting the development and activity of osteoclasts, decreasing bone resorption, increasing bone density and reducing fracture risk. Also DMB is a useful therapeutic agent for both rheumatoid arthritis (RA-OP) and primary osteoporosis (P-OP). However there is still few comparative study of clinical efficacy of DMB between RA-OP and P-OP.
Objectives: To compare the clinical efficacy of DMB in patients with osteoporosis between rheumatoid arthritis and primary osteoporosis for 24 months.
Methods: RA patients diagnosed according to the 2010 ACR/EULAR criteria. RA-OP and P-OP patients met at least one of the following criteria were eligible; a bone mineral density T score of -2,5 or less at the lumber spine or total hip and either one or more moderate or severe vertebral fractures or two or more mild vertebral fractures. All patients were initiated DMB from between October, 2013 and August, 2016. The final study cohort of 61 RA- OP and 50 P-OP patients received continuous DMB therapy more than 24 months. The DMB dose was 60mg at once every 6 months. In all cases native or activated vitamin D has been used. We reviewed the results for 24 months about the increase and decrease of bone mineral density(BMD) of lumbar spine(LS) and total hip (TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen(PINP) and tartrate-resistant acid phopshatate form 5b (TRACP-5b).
Results: In the patients of RA-OP (n=61) and P-OP (n=50), the number of female was each 56(92%) and 45(90%) cases(p=0.741). The mean age was 72.7 ± 7.5 and 76.8 ± 7.8 years old (p=0.006); disease duration of RA-OP patients was 12.6 ± 12.9 years; the body mass index was 20.4 ± 2.7 and 20.3± 3.0 (p=0.687) and the FRAX was 27.2 ± 15.7 and 24.6 ± 11.1 (p=0.745). Clinical findings related to RA-OP at baseline were as follows; CRP 0.8 ± 1.1; DAS-CRP 3.28 ± 1.36; HAQ 1.16 ± 1.04 in RA-OP patients and in the patients of RA-OP and P-OP, bone turnover markers and bone mineral density at baseline were as follows; P1NP 57.7 ± 32.2 and 64.0 ± 32.7 μg/l(p=0.151); TRACP-5b 563

± 237 and 570 ± 217 mU/dL (p=0.674); LS-BMD 0.85 ± 0.16 and 0.74 ± 0.13 g/cm^2(p<0.001) and TH-BMD 0.62 ± 0.09 and 0.60 ± 0.08 g/cm^2 (p=0.110). The rate of decreased P1NP from baseline to 6, 12 and 24 months were each -43.7% vs -61.3% (p=0.015) at 6 month, -40.2% vs -55.2% (p<0.001) at 12 month and -43.5% vs -67.9% (p<0.001) at 24 month and TRAC-5b were -44.6% vs -51.5% (p=0.225) at 6 month, -39.5% vs -53.0% (p=0.007) at 12 month and -41.3% vs -54.2% (p=0.663) at 24 month in the RA-OP vs P-OP group. The rate of increased LS-BMD from baseline to 6, 12 and 24 months were each 4.3% vs 4.5% (p=0.743) at 6 month, 6.3% vs 6.9% (p=0.575) at 12 month and 9.3% vs 11.1% (p=0.300) at 24 month and TH-BMD were 2.5% vs 2.6% (p=0.583) at 6 month, 3.3% vs 3.2% (p=0.683) at 12 month and 5.7% vs 4.2% (p=0.403) at 24 month RA-OP vs P-OP group.
Conclusion: DMB was effective for both RA-OP and P-OP, and the clinical efficacy was almost similar between the two groups.
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FRI0494 CORRELATION OF METACARPAL BONE MASS MEASURED EITHER BY DUAL X-RAY DENSITOMETRY OR DIGITAL X-RAY RADIOGRAMMETRY WITH SEVERITY OUTCOMES IN PATIENTS WITH EARLY ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disorder that predominantly affects small joints of the hands and feet. X-ray digital radiogrammetry (DXR) is a validated technique for the evaluation of bone mineral density (BMD) in the diaphysis of metacarpals (MC) that has demonstrated that low bone mass at this location correlates with worse radiographic progression (1). However, this technique is not available in our environment. Dual X-ray densitometry (DXA) is a simple, accessible and widely validated technique for the study of osteoporosis. Our group has previously validated the reproducibility of MCP measurements by DXA (2).
Objectives: To study the relationship between baseline MC BMD measured by DXA or DXR and disease severity in patients with early arthritis at 2 years follow-up.
Methods: 202 patients belonging to PEARL (Princess Early Arthritis register longitudinal) study were included. Demographic, laboratory, radiographic and therapeutic data were recorded by protocol. Most patients (87%) were women, 59% fulfilled 2010 ACR criteria and 41% were classified as undifferentiated arthritis. More than 60% were seropositive (60% RF; 58% anti-CCP). Median disease duration at first visit was 4.6 months, median DAS28 4.2 and HAQ 0.875. The BMD of 2th to 4th MC was measured by DXR through the standardized software by Sectra (Linköping, Sweden) applied on radiographs of hands submitted in digital format (GE© DX Definium 8000). Baseline non-dominant hand DXA was performed using a densitometer Hologic© QDR4500. To analyze 2th to 4th MC BMD, we created 3 regions of interest (ROI) similar to that generated in the DXR measurements; briefly, the ROIs cover the mid-third of each MC diaphysis, avoiding overlapping of ROIs. The statistical study was performed with Stata 12 for Windows, including linear correlation between MC-BMD values measured by DXR and DXA (Pearson's test), and different multivariate analyses in which MC-BMD measured either by DXR or DXA were included as dependent variable and sex, age and body mass index (BMI) as independent confounding variables. Then in these models different subrogate variables of disease severity such as disease activity (DAS28), disability (HAQ) or cumulative DMARD treatment after 2 years of follow-up were included in order to determine whether there was an association with MC-BMD.
Results: The MC-BMD measured by DXA and DXR at baseline showed a good correlation (r=0.87, p <0.001). As expected, being female (ß coefficient -0.0381, p=0.0001) and age > 65 years (ß coefficient -0.076, p=0.0001) were associated with lower BMD, whereas high body mass index (ß coefficient 0.002 x kg/m^2, p=0.004) was associated with higher BMD. Adjusting by this confounding variables, the multivariate analyses did not show any significant association between MC-BMD and DAS28, HAQ or treatment intensity, neither with the DXA or DXR measurements.
Conclusion: Despite of the good correlation between DXR and DXA, our data obtained either with DXA or DXR do not confirm the association of low MC-BMD measured with DXR and more aggressive disease in patients with early arthritis.

REFERENCES:
[1] Forslind K, Boonen A, Albertsson K, et al. Scand J Rheumatol 2009;38:431-438.
[2] Castañeda S, González-Álvaro I, Rodríguez-Salvanés F, et al. J Clin Densitom 2007;10:298-305.

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FRI0495 FRAGILITY FRACTURE IN MALE; EXPERIENCE OF A FRACTURE LIAISON SERVICE

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Background: Secondary prevention of osteoporotic fracture is more efficient with the *Fracture Liaison Service* (FLS) model.
Objectives: To describe the characteristics of male patients attended in a FLS
Methods: Prospective observational study. The program consists of: 1) recruitment from the emergency records, hip fracture admitted or referral to outpatient rheumatology; 3) baseline visit: questionnaire including demographCI variables, FRAX and previous treatments; 4) DXA; 5) patient education; 6) report of results to the patient and the PC doctor, with specifCI management recommendations; complex patients are referred to rheumatology; and 7) follow-up through telephone survey plus prescription check in electronCI records. The characteristCIs of male patients are described and compared with women.
Results: 2,135 patients have been included, 382 male (18%). The recruitment was in 300 cases (78%) from the emergency list, in 55 cases (14%) admission for hip fracture and in 25 cases (6%) from outpatient clinCI. The characteristCIs of the patients are shown in the table.
The average age was similar in men and women. Hip fracture was more frequent in men (34% vs. 25%, OR 1.63 CI 95% 1.50-1.75) as opposed to forearm fracture (18% vs. 33%, OR 0.46 CI 95% 0.32-0.60). Male had previous DXA (6% vs 25%, OR 0.22 CI 95% 0.00-0.43) and previous treatment with bisphosphonate (4% vs 19%, OR 0.17 CI 95% 0, 0-0.44) less frequently.
Of the variables included in the FRAX, in men was less frequent the previous fracture (13% vs 24%, OR 0.48 CI 95% 0.32-0.64), the hip fracture of the parents (9% vs. 13%; OR 0.66 CI 95% 0.47-0.85) and the use of corticoids (6% vs 10%, OR 0.61 CI 95% 0.39-0.84). However, active smoking was more frequent in men (21% vs 14%, OR 1.67 CI 95% 1.53-1.81) as well as consumption >2 daily units of alcohol (18% vs 5%; OR 3.96 CI 95% 3.78-4.13).
The percentage of osteoporosis was lower in men compared to women (30% vs 46%, OR 0.49 CI 95% 0.30-0.68) as well as the percentage of patients with >1 fall in the last year (29% vs 45%, OR 0.51 CI 95% 0.30-0.71).
In addition, after the visit to the FLS, a bisphosphonate was indicated less frequently to men than to women (68% vs. 77%, OR 0.64 CI 95% 0.51-0.76) and were referred less frequently to PC (64% vs. 76%; OR 0.55 95% CI 0.41-0.70). Finally, persistence at 12 months was lower in men than in women (53% vs. 68%, OR 0.53 CI 95% 0.30-0.76).
Conclusion: Compared with women, men seen in an FLS present hip fracture more frequently and a forearm fracture less frequently. Men also have a lower frequency of personal and family history of fracture and a greater frequency of smoking and alcohol intake. The percentage of patients who are candidates for treatment and persistence is lower than in women. These data should be taken into account in the identification and treatment of fragility fracture in men.
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Table

Age, mean (SD)	73.4 (10)
BMI, mean	27.4
Fracture type, N (%)	
Forearm	71 (18)
Hip	132 (34)
Humerus	77 (20)
Vertebra	52 (13)
Others	49 (13)
FRAX items, N (%)	
Previous fracture	51 (13)
Hip fracture of parents	36 (9)
Smoking	81 (21)
Corticoids	24 (6)
Rheumatoid arthritis	4 (1)
Secondary osteoporosis	17 (4)
Alcohol	68 (18)
Densitometry (%)	
Normal	30
Osteopenia	43
Osteoporosis	26
FRAX, mean (SD)	
Major fracture	8,4 (5)
Hip fracture	4,3 (4)
Treatment prescribed, (%)	
Bishoshonate or equivalent	68
Refferal to primary care	64
Persistence at 12 months	53

FRI0496 OSTEOPOROSIS IN PRIMARY CARE – ARE WE MISSING A TRICK?

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Background: Globally various incentive schemes have been employed in primary care to improve early diagnosis and management of several rheumatic conditions. In the UK, the Primary Care Quality and Outcomes Framework (QOF) rewards general practices for the provision of 'quality care' and helps to fund further improvements in the delivery of clinical care. Currently, there is one quality indicator in place for secondary prevention of osteoporosis. In order to help establish an integrated care pathway encompassing the whole patient journey between primary and secondary care, we undertook a detailed survey of two GP practices.
Objectives: The aims of the exercise were to identify the utility of quality indicator and any gaps in the model of care for the high-risk osteoporosis patients.
Methods: An independent service evaluation tool was employed to interrogate the IT system used in the GP surgeries. All patients over the age of 65 were extracted from the database and FRAX analysis was undertaken. Those with medium to high FRAX score (i.e. ten-year risk of >20% for major osteoporotic fracture and/or >5% for hip fracture) were captured to explore whether they were offered further evaluation and bone-sparing therapy as necessary.
Results: Of 18,248 patients registered in the multi-cultural urban practices, 6796 were >65 years old. 793 had pre-defined moderate-high FRAX score. 300 (37%) had a confirmed diagnosis of osteoporosis. Median age was 78 (range 65-103 years). 249 (83%) were women. 88.5% were White and remaining of other ethnicities.
20/300 (6.6%) had been coded to have ever sustained a fragility fracture. 178 (59.3%) were prescribed bone-sparing therapy with five people taking it for over five years. 91% were prescribed oral therapy (78% alendronic acid, 10% risedronic acid and 3% others) and remaining had parenteral therapies. Of the 27 patients not receiving any treatment, 11 (30%) were incorrectly coded. The remainder's reasons for lack of treatment include intolerance, poor adherence and comorbidities.
Conclusion: This study highlights the inadequacy of quality indicators in the overall management of osteoporosis burden in primary care. It relies heavily on active identification process for high-risk individuals and correct coding of fragility fracture. However the vast majority of patients with moderate-high risk, based on case finding strategy advised by international bodies e.g. FRAX, remain hidden. Less than 10% of patients with confirmed osteoporosis fulfil the quality outcome in this survey. The QOF hence fails to reflect the nature of disease burden in the primary care thereby risking the management strategies skewed towards too small a cohort and missing the big picture. It is clear that quality indicators for osteoporosis need to be aligned to risk stratification model. This will allow better identification of at-risk individuals and improved care pathway for patients requiring bone active therapies.
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FRI0497 TRABECULAR BONE SCORE AND MALNUTRITION IN A COHORT OF SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic sclerosis (SSc) is a connective tissue disease characterized by initial microvascular damage, immune system activation and progressive fibrosis of the skin and internal organs.Gastrointestinal (GI) involvement induce malnutrition due to gastroesophageal symptoms, GI dismotility and malabsorption that are related to fibrosis of bowel wall and bacterial overgrowth(1).Therefore the disease is associated with secondary osteoporosis with a few studies evaluating the bone microarchitecture(2).
Objectives: To evaluate a relationship between malnutrition and bone microarchitecture detected by trabecular bone score (TBS) in SSc patients.
Methods: 38 patients(6 male and 32 female) fulfilling ACR 2013 criteria for SSc underwent DXA to detect quantitative lumbar spine bone mineral density and TBS. DXA also assess body composition with a software that provides the physician quantitative parameters, including free fat mass index (FFMI), that identifies the patient with malnutrition(values <15 kg/m2 in women and 17 kg/m2 in men), according to the ESPEN criteria (3).Body mass index was calculated for all SSc patients and every patient completed a diary reporting GI symptoms possibly related to intestinal disbiosis.Fasting blood samples were obtained in order to analyse some biochemical parameters of malnutrition (total proteins(g/L), albumin(g/L), serum total cholesterol(mg/dl) and blood lymphocyte count (N/mm3). Continue variables were summarized as mean and standard deviation(SD) or median and inter quartile rang (IQR), discrete variables were summarized with count and percentage. Correlation was tested with Pearson or Spearman method. T-test was used to compare TBS between dichotomic groups Uni and multivariate linear regression models were used as well the Multiple R-squared variation was applied. The multivariate linear regression was performed with a stepwise approach to select the best model using highest AIC criteria.
Results: The mean age of patients was 64.2±11.3 years with mean disease duration 19.2±7.6 years. 36.8% of patients was found malnourished. The univariate analysis showed that only higher age of patients correlated to lower TBS($p<0.001$). The R-squared of multivariate linear regression showed that about 45% of the TBS variations(TBSv) can be explained by the variation of the following variables(age, disease duration, lymphocyte count).Age explains about 25% of the TBSv.Older patients had lower TBS, with approximately 0.05 points of TBS loss every decade($p = 0.001$).The presence of symptom possibly related to intestinal disbiosis, added to the model, might explains about 12% more of TBSv. Patients with symptom related to bacterial overgrowth had lower TBS respect to patients without(-0.08), regardless of other variables($p=0.002$).Disease duration, added to the model, further explains about 4% more of TBSv and suggest a trend between highest disease duration (regardless of other variables) and higher TBS($p = 0.103$).Lymphocyte count added to

the model also seems to explain about 4% more of TBSv, in fact lowest number(regardless of other variables) appear to have interference on TBS (p = 0.020)

Conclusion: This study shows that a more severe microarchitectural bone defect correlates with gastrointestinal involvement in term of symptom related to intestinal disbiosis and with selected blood biochemical markers of malnutrition.

REFERENCES:

[1] Caimmi C et al. 2017 Clin Rheumatol 37(4):987–997.
[2] Ruaro B et al. 2018 Rheumatology (Oxford) 1;57(9):1548–1554.
[3] Cederholm T et al. 2015 Clin Nutr 34(3):335–340.

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FRI0498 HIGH SERUM URIC ACID LEVEL IS ASSOCIATED WITH LOWER INCIDENCE OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN: DATA FROM THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

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Background: Osteoporosis is one of the most common morbidities in postmenopausal women. Although serum uric acid (SUA) accounts for about 50% of extracellular antioxidant activity, the role of hyperuricemia in osteoporosis, a condition characterized by high oxidative stress level, has not been investigated in a Nation-wide scale.

Objectives: The aim of this study is to evaluate an association between SUA and incidence of osteoporosis in postmenopausal women.

Methods: Data of postmenopausal women from the 2016 Korean National Health and Nutrition Examination Survey were included and retrospectively analyzed. Weighted prevalence and logistic regression analysis were used to determine the incidence of osteoporosis and the effect of SUA on osteoporosis in postmenopausal women.

Results: One-thousand three-hundred eighty-two (weighted n = 7,064,137) of postmenopausal women were observed. Of these, 401 (29.0%, weighted n = 1,880,586) women developed osteoporosis. Mean age of participants was 63.2 years and mean of SUA was 4.4 mg/dL. The effect of SUA on osteoporosis in postmepausal women was not statistically significant according to univariable logistic regression (OR 0.977, 95% CI 0.855-1.116, *p* = 0.729). However, SUA was negatively associated with incidence of osteoporosis in postmenopausal women with statistical significance after adjusting for age, obesity, amount of drink, smoking, intake of calcium, rheumatoid arthritis, thyroid diseases, and loss of activity (OR 0.867, 95% CI 0.752-0.999, *p* = 0.048).

Conclusion: Our data demonstrated that high SUA is associated with lower incidence of osteoporosis in postmenopausal women. This result suggests a protective role of SUA in metabolic bone diseases.

REFERENCES:

[1] Hernlund E, Svedbom A, Ivergard M, Compston J, Cooper C, Stenmark J, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). Arch Osteoporos. 2013;8:136.
[2] Varacallo MA, Fox EJ. Osteoporosis and its complications. Med Clin North Am. 2014;98(4):817-31.
[3] Wauquier F, Leotoing L, Coxam V, Guicheux J, Wittrant Y. Oxidative stress in bone remodelling and disease. Trends Mol Med. 2009;15 (10):468-77.
[4] Lee NK, Choi YG, Baik JY, Han SY, Jeong DW, Bae YS, et al. A crucial role for reactive oxygen species in RANKL-induced osteoclast differentiation. Blood. 2005;106(3):852-9.
[5] Bai XC, Lu D, Liu AL, Zhang ZM, Li XM, Zou ZP, et al. Reactive oxygen species stimulates receptor activator of NF-kappaB ligand expression in osteoblast. J Biol Chem. 2005;280(17):17497-506.

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FRI0499 EFFICACY OF POSTMENOPAUSAL OSTEOPOROSIS TREATMENT BY COMBINATION OF DENOSUMAB WITH PLAIN VITAMIN D OR WITH ANALOG OF VITAMIN D ALFACALCIDOL

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Background: The superiority of the treatment of osteoporosis (OP), using the combination of alendronate (ALN) and alfacalcidol (1αD3) to ALN treatment with cholecalciferol (D3) in both genders, has been demonstrated[1].

Objectives: To compare the efficacy of two-year OP treatment with denosumab (DMAb) with D3 to the treatment of DMAb with 1αD3.

Methods: Retrospective study included 58 postmenopausal OP patients treated at the Institute of Rheumatology in Belgrade. Average age was 74.5 ± 16.22 years, bone density (BMD) on the lumbar spine (L1L4) was 1.102 ± 0.0878g/cm^2, total hip (TH) 0.728 ± 0.0324g/cm^2, femoral neck (FN) was 0,600 ± 0.1281g/cm^2, and the bone quality expressed as trabecular bone score (TBS) was 1.222 ± 0.3457, at study inclusion. BMD and TBS were measured using Hologic Prodigy DXA device. All women had primary OP, and 50% had fracture in the adult age. Average serum level 25 (OH) D3 was 29.8 ± 6.67ng/mL. Out of all, 68.4% patients had previous OP treatment, during 4.2 ± 3.45 years, 55.2% had used oral bisphosphonates (BF), 8.62% parenteral BF, 3.44% strontium ranelate, while one patient (1.72%) received a full course of teriparatide. Patients were asigned by the doctor's decision to be treated either by combination of DMAb 60mg s.c. every 6 months and D3 800-1000 IU daily (N = 29) or DMAb and 1αD3 1μg daily (N = 29). Safety was monitored clinically and laboratory at six-month intervals - serum calcium (Ca), ionised Ca, phosphorus, 24 hours of calciuria, incidence of falls and fractures. Serum 25 (OH) D3 and parathormone (PTH) were observed once a year, as well as BMD and TBS. Analytical statistical analysis was done by student t - test and Fisher 's test.

Results: The patients were mutualy comparable in term of age, previous fractures, BMD and TBS, laboratory findings, previous OP treatment. After 2 years of study treatment, there was no significant difference in the increase in BMD on the L1L4 between DMAb plus D3 and DMAb plus 1αD3 group (6.4% vs. 6.5%), as well as on the TH (3.3% vs 3.4%). Statistically significantly higher BMD on FN (2.0% vs 5.9%, p<0.001), as well as TBS increase (2% versus 6.7%, p < 0, 05) in DMAb plus 1αD3 group was found. Serum calcitriol was higher (30.54 vs 35.1 ng/mL), while PTH was statistically significant in DMAb plus 1αD3 group (48.6 vs 31.2 pg/mL, p <0.001) at the ed of study. The incidence of hypocalcaemia was 2.3% in the DMAb plus D3 group, and 1.0% in the DMAb plus the 1αD3 group, hyperchalcemia was not found in any. The clinical fractures incidence after 2 years of follow-up was 6.9% in DMAb with D3 and 3.44% in the DMAb plus 1αD3 group, which was not statistically significant, as well as occurence of falls, recorded more frequently in DMAb plus D3 group (31% vs. 13.8%).

Conclusion: DMAb in combination with 1αD3 is more effective and equally safe OP treatment compared to DMAb with D3, in term of increasing FN BMD and improvement of bone micro-architecture.

REFERENCES:

[1] Ringe JD, Farahmand P, Schacht E, Rozehnal A. Superiority of a combined treatment of Alendronate and Alfacalcidol compared to the combination of Alendronate and plain vitamin D or Alfacalcidol alone in established postmenopausal or male osteoporosis (AAC-Trial). Rheumatol Int.2007;27 (5):425-34

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FRI0500 **INCIDENCE OF CLINICAL FRACTURES IN ADULTS WITH KIDNEY TRANSPLANT**

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Background: Chronic kidney disease is associated with an increased risk of fractures. However, the existing evidence investigating the incidence of fractures after kidney transplant is scarce.
Objectives: To evaluate the incidence of clinical fractures in patients with kidney transplant and analyze the possible factors that may influence its occurrence.
Methods: A retrospective observational study of patients who underwent kidney transplant between 2005 and 2015 in a tertiary hospital was conducted. A minimum follow.up period of 6months after transplant was required. Sociodemographic and anthropometric data, clinical risk factors for bone fractures, drugs use (steroids, immunosuppressive drugs, vitamin D analogues, calcium and vitamin D supplements and calcimimetics), as well as biochemical and densitometric data to assess bone metabolism were retrieved from medical records. The occurrence of new clinical fractures after the transplant and throughout the follow-up period was recorded. The statistical analysis included univariable analysis using chi-square and Fisher's exact tests for the qualitative variables and T-Student and Mann-Whitney U for the quantitative variables. Subsequently, logistic regression multivariable analysis was carried out to investigate which factors were associated with fractures occurrence.
Results: A total of 163 patients were included, 63 (38%) females, with a mean age of 51 ± 14.6 years. The etiology of kidney disease was polycystic kidney disease (24.2%), glomerulonephritis (23.6%), diabetes mellitus (5.5%), vasculopathy (5.5%), connective tissue disorders (2.4%) and miscellany (38.7%). The daily average dose of steroids one year after transplant was 5.8 ± 4.4 mg. Bone densitometry was performed before transplant in 27 patients (19.6%), ten of whom (37%) presented osteopenia and 7 (26%) osteoporosis. The ten-year probability of bone fracture risk (FRAX) before transplant was 2.6 ± 2.6. Mean follow-up after transplant was 8.7 ± 3.5 years. During this period, 23 (13.9%) patients suffered a clinical fracture, with an average time of appearance after transplant of 5.5 ± 3.3 years. These were located in hip (6 - 26.1%), vertebrae (2- 8.7%), extremities (9 – 39.1%) and hands and feet (6 – 26%). One year after transplant, 65.6% had vitamin D deficiency (<30 ng/dl serum calcidiol leves) and 12.2% had levels compatible with osteomalacic range (<10ng/dl). The data of the descriptive study stratified by the fracture occurrence are shown in Table 1. Compared with the subgroup patients without (Fx -), patients with (Fx +) post-transplant fractures showed to be more frequely female (60.9% vs 34.5%, p=0.01), older (50.1 ± 14.6 vs 56.3 ± 14.1 p=0.03), had more pre-transplant major clinical FRAX ((2.4 ± 1.9 vs 4 ± 4.7, p=0.03), and higher levels of PTH (98.2 ± 75.7 vs 140.1 ± 86.9 p=0.02) and serum alkaline phosphatase [ALP] (90.2 ± 37 vs 117.8 ± 60.4, p=0.02) after one year of transplant. Also, a trend to present a higher prevalence of pre-transplant clinical fractures was observed in the second group (5.6% vs 17.4%, p=0,06). No difference in the use of immunosupressants were detected. The multivariable analysis showed a significant association between post-transplant fractures and female gender (OR of 3.8, p=0.03) and higher levels of ALP (OR of 1.01, p=0.03).
Conclusion: In patients with kidney transplant, an incidence of clinical fracture of 13.9% is observed after a mean follow-up of 8.7 year. The female population seems especially susceptible to present fractures. The persistence of a possible pre-transplant autonomous secondary hyperparathyroidism one year after kidney transplant seems to influence the risk of fracture.
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Table 1. Descriptive study and comparison between groups (FX – and FX +). The data are shown as N(%) and mean (±SD).

	Total	Fx -	Fx +	P
Total (n)	165	142	23	
Mean age (years) Gender (female) BMI	51 ± 14.6 63 (38.%) 25.5 ± 4.1	50.1 ± 14.6 49 (34.5%) 25.5 ± 4	56.3 ± 14.1 14 (60.9%) 25.6 ± 4.7	**0.03** **0.01** 0.8
Smoking habit	23 (13.9%)	20 (14.1%)	3 (13%)	0.8
Diabetes mellitus	19 (11,5%)	15 (10.6%)	4 (17.4%)	0.2
Presence of fracture before transplant	12 (7.3%)	8 (5.6%)	4 (17.4%)	0,06
Major clinical FRAX at transplant Major densitometric FRAX at transplant	2.6 ± 2.6 5.6 ± 4.6	2.4 ± 1.9 4.9 ± 3.7	4 ± 4.7 7.6 ± 6.4	**0.03** 0.2
Average steroid dose 1y after transplant (mg/d)	5.8 ± 3,4	5.9 ± 3.5	5.9 ± 2.6	0.8
Use of Calcitriol 1y after transplantation	53 (32.1%)	44 (42.3%)	9 (56.3%)	0.2
Use of Cinacalcet 1y after transplantation	19 (11.5%)	16 (16.3%)	3 (13%)	0.8
Use of Calcidiol 1y after transplantation	48 (29.1%)	42 (29.6%)	6 (26.1%)	0.4
Serum calcium 1y after transplantation	9.6 ± 2.1	9.7 ± 2.3	9.6 ± 0.4	0.1
Serum phosphate 1y after transplantation	3.2 ± 0.9	3.2 ± 0.9	3.1 ± 0.6	0.9
iPTH 1y after transplantation (pg/ml)	104,3 ± 78,5	98.2 ± 75.7	140.1 ± 86.9	**0.02**
Serum calcidiol 1y after transplantation (ng/ml)	26.5 ± 22.8	27.6 ± 23.9	20.4 ± 13.5	0.15
Stratified serum calcidiol (>30/29-20/19-10<10)	31 (34.4%) 19 (21.1%) 29 (32.2%) 11 (12.2%)	28 (36.4%) 17 (22.1%) 24 (31.2%) 8 (10.4%)	3 (23.1%) 2 (15.4%) 5 (38.5%) 3 (23.1%)	0.3
Serum alkaline phosphatase (U/L)	94 ± 42	90.2 ± 37	117.8 ± 60.4	**0.02**
T-Score Spine Pretransplante	-1.3 ± 1.4	-1.4 ± 1.3	-1.3 ± 1.7	1
BMD Spine Pretransplante (g/cm²)	0.793 ± 0.684	0.932 ± 0.163	0.904 ± 0.181	0.6
T-Score Neck before transplantation	-1.9 ± 1.1	-1.8 ± 1.2	-2.3 ± 1.1	0.4
BMD Neck before transplantation (g/cm²)	0.697 ± 0.116	0.709 ± 0.121	0.659 ± 0.098	0.3
Stratified DXA (normal/osteopenia/osteoporosis)	10 (37%) 10 (37%) 7 (25.9%)	7 (35%) 8 (40%) 5 (25%)	3 (42.9%) 2 (28.6%) 2 (28.6%)	0.5

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FRI0501 **EVALUATION OF BONE QUALITY BY TRABECULAR BONE SCORE (TBS) IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS**

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Background: Systemic lupus erythematosus (SLE) patients shown an increased risk of low bone mass as a result of multifactorial events: physical inactivity, persistent inflammation, low vitamin D levels (photosensitivity) and glucocorticoid treatment. Trabecular Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) that provides an indirect measurement of bone axial microarchitecture and allows to get information about bone quality in several rheumatic diseases (1-4).
Objectives: The aims of this study were to examine the prevalence and risk factors for low bone mineral density (BMD) (osteoporosis or osteopenia) in female patients affected by SLE and to compare with matched healthy subjects (CNT).
Methods: 40 female patients (mean age 47±14 years) affected by SLE and 40 age- matched CNT (mean age 49±8 years) were enrolled. Bone Mineral Density (BMD, g/cm^2) of the lumbar spine (L1-L4) was analyzed using a DXA scan (GE, Lunar Prodigy) Lumbar spine TBS was derived for each spine DXA examination using the TBS index (TBS iNsight Medimaps).
Results: The mean BMD±SD was 0.85±0.22 g/cm^2 at the lumbar spine and 0.64 ± 0.32 g/cm^2 at the hip in SLE patients. The prevalence of osteopenia was 39.0% and 16.4% of osteoporosis in SLE patients. Most of SLE patients (70%) presented a bone loss that was significantly lower when compared with control group (p<0.001). Likewise, lumbar spine TBS

score was found significantly lower in SLE patients compared with CNT (0.868±0.227 vs 1.482±0.113,p<0.001, respectively). An history of high-dose oral glucocorticoids (> 10 mg/day) was associated with the preservation of BMD at the lumbar spine but not in spinal trabecular bone as observed by TBS analysis.
Conclusion: SLE is associated with significant trabecular bone loss, which could not be caused by glucocorticoid therapy. This study confirms the role of TBS as new and safe diagnostic tool for the quantification of the bone quality in chronic and systemic inflammatory rheumatic diseases, such as SLE.

REFERENCES:

[1] Cutolo M, et al. Ann Rheum Dis. 2009;68 446-7; 2 Dey M, et al. Lupus. 018;271547-1551; 3 Ruaro B, Casabella A, et al. Rheumatology (Oxford). 2018;57:1548-1554. 4 Ruaro B, Casabella A, et al. Clin Rheumatol. 2018 Nov;37(11):3057-3062.

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FRI0502 CORRELATION OF THE DAILY DIETARY INTAKE OF CALCIUM WITH THE LEVEL OF BONE MINERAL DENSITY IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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Background: There are few studies in which the relationship between daily calcium intake and bone mineral density (BMD) in patients with human immunodeficiency virus (HIV) infection has been evaluated, as well as its correlation with other factors of risk for the development of fragility fractures in this population.
Objectives: To determine the correlation of daily calcium intake with the most predictive risk factors for fragility fracture in patients with HIV infection, as well as BMD values in a cohort of patients followed in a Tertiary Madrid hospital.
Methods: Cross-sectional evaluation of a prospective study carried out in a specialized unit in HIV/AIDS of a tertiary Madrid hospital. We included asymptomatic consecutive patients with HIV infection, older than 50 years, followed regularly between January 2014 and December 2016.
Results: A total of 128 patients were included (35 women, 27%), with a mean age of 57 years (range: 50-83) and body mass index of 23.8 kg/m2 (range: 15.6-33.5). The mean time of HIV infection was 256 months (range: 202-306) and of antiretroviral therapy (ART) 219.7 months (range: 156-247). The average calcium intake obtained by dietary calculation (without supplementation) was 563.8 g/day (462-2772). Among the risk factors for fragility fracture (included in the FRAX): 44 (34%) reported smoking, 11 (9%) family history of fracture, 54 (42%) previous history of fracture, 8 (6%) significant alcohol consumption and 25 (21%) renal tubular dysfunction. According to the WHO classification based on BMD at the level of lumbar spine (LS) 50 (39%) were classified as osteopenia and 43 (34%) as osteoporosis, while at the femoral neck level said proportions were 83 (65%) and 9 (7%), respectively. A correlation was found between higher calcium intake with a longer time of ART (rho = 0.2, p = 0.02), but not with the age or time of HIV infection. The calcium intake showed no correlation with serum calcium levels (rho = 0.05, p = 0.72), serum phosphorus levels or bone biomarkers such as alkaline phosphatase, osteocalcin or P1NP, but an inverse relationship with the levels of βcrosslaps (rho = -0.21; p = 0.02). Calcium intake was associated with greater exercise, assessed by the International Physical Activity Questionnaire (IPAQ) (rho 0.23; 0 = 0.01). The calcium intake was lower in patients with osteoporosis with respect to osteopenia or normal (hip 500 vs 580 vs 573, LS 507 vs 635 vs 585, respectively, p = 0.04 between osteoporosis/osteopenia). Although a lower calcium intake was found in patients with vertebral fractures, this was not significant (486 (236) vs 583 (317), p = 0.09).
Conclusion: Although recent meta-analyzes show that calcium intake in non-HIV population is not related to the development of fragility fractures, in our cohort (with the limitations of a cross-sectional study) a probable association of daily calcium intake with a low BMD is evidenced. These findings should be confirmed in the longitudinal analysis of the data of the cohort.

REFERENCES:

[1] Compston J. Osteoporosis and fracture risk associated with HIV infection and treatment. Endocrinol Metab Clin North Am. 2014

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FRI0503 USING BONE MINERAL DENSITY VERSUS THE RATIO OF BODY MASS INDEX TO BONE MINERAL DENSITY TO PREDICT FRACTURE RISK IN HYPERTHYROIDISM

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Background: Euthyroidism is important in the development of a normal skeletal system, with thyroid hormones acting as important regulators of bone homeostasis in adults[1]. Hyperthyroidism, whether current or previous, increases the risk of developing osteoporotic fractures by stimulating osteoclastic bone resorption and hence bone remodelling, which overall results in decreased bone mineral density (BMD)[2]. Generally, BMD is used as a predictor of fracture risk; however there has been recent research that suggests using the ratio of BMD to Body Mass Index (BMI) is a better marker of predicting fracture risk in obese patients than BMD alone[3].
Objectives: Our research set out to find whether BMD alone or the ratio of BMI to BMD is a better predictor of fracture risk in patients with current or previous hyperthyroidism.
Methods: Data were used from a cohort of patients with current or previous hyperthyroidism, referred for DEXA scan to a District General Hospital between June 2004 and October 2010. The following were recorded: age, sex, whether a fracture was sustained, whether they had had steroid therapy at any point, BMI, BMD at L1-L4, BMD at femoral neck (left and right) and BMD at hip (left and right). Logistic regression models were fitted using fracture as the dependent variable. The independent variables for the first set of logistic regression models were BMD at each level and for the second set BMI:BMD ratio at the same levels. Data were adjusted for sex and age at scan. The fit of logistic models were compared using area under the ROC curves (AUC).
Results: 720 patients were used in the study, of whom 643 (89.3%) were female. Mean age was 63.6 years (SD 11.6) with age range of 28.4 to 89.6 years. 120 (16.7%) were recorded to have had steroid therapy at any point. Mean BMI was 25.9 kg/cm^2 (SD 4.77). 274 (38.1%) had sustained a fracture. Odds ratios and AUC values for each level were as shown in the table. The fit of the models using the ratio was generally superior to the fit of the models using BMD alone at the hips and femurs, as AUC values were generally greater for the ratio. At each individual level of the lumbar spine the BMD alone provided a better fit, however overall the ratio gave a slightly better fit.

Table 1. – Odds ratios (age- and sex-adjusted) and AUC values

Level	Odds Ratio and CI (BMD)	AUC (BMD)	Odds Ratio and CI (BMI:BMD)	AUC (BMI:BMD)
L1	0.128 (0.0510, 0.324)	0.6277	1.07 (1.04, 1.09)	0.6305
L2	0.161 (0.0697, 0.374)	0.6277	1.06 (1.03, 1.09)	0.6250
L3	0.128 (0.0510, 0.324)	0.6418	1.06 (1.04, 1.09)	0.6307
L4	0.188 (0.0879, 0.401)	0.6282	1.06 (1.03, 1.09)	0.6249
L1 to L4	0.120 (0.0496, 0.291)	0.6282	1.07 (1.04, 1.10)	0.6309
L FEMORAL NECK	0.0988 (0.0290,0.336)	0.6219	1.05. (1.02, 1.07)	0.6285
R FEMORAL NECK	0.0450 (0.0877, 0.231)	0.6776	1.06 (1.03, 1.09)	0.6798
L TOTAL	0.0980 (0.0233, 0.412)	0.6812	1.07 (1.03, 1.10)	0.6936
R TOTAL	0.0623 (0.0136, 0.285)	0.6778	1.07 (1.03, 1.10)	0.6850

Conclusion: This study identifies that the BMI:BMD ratio does not provide better indication of fracture risk than BMD alone in our cohort of patients with current or previous hyperthyroidism. We have previously shown that the same is true for patients with rheumatoid arthritis. A limitation of this study is not stratifying by presence of other diseases or steroid use.

Further work will be done to study the role of the ratio in predicting fracture risk in patients with other conditions.

REFERENCES:
[1] Williams, GR., & Bassett, JHD. (2018). Thyroid diseases and bone health. Journal of Endocrinological Investigation, 41(1), 99-109.
[2] Saito, J., & Nishikawa, T. (2009). Osteoporosis treatment in patients with hyperthyroidism. *Nishon Rinsho (Japanese journal of clinical medicine)*, 67 (5), 1011-6.
[3] Tucker, M., (2018, May 18). *Simple Ratio May Predict Fracture Risk in Obese Patients*. Retrieved from https://www.medscape.com/viewarticle/896882.

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Cartilage, synovium and bone

FRI0504 TOCILIZUMAB CONTROLS BONE TURNOVER IN EARLY POLYMYALGIA RHEUMATICA

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Background: Tocilizumab has been proved to be an alternative to corticosteroids in treating polymyalgia rheumatica. Considering the action on interleukin-6 on bone turnover an effect of tocilizumab is supposed. Few data are available about bone turnover in rheumatoid arthritis patients treated with tocilizumab but no data are available in polymyalgia rheumatica patients.
Objectives: This study explores changes in the bone homeostasis by testing the N-terminal collagen type I extension propeptide (PINP) marker for osteo-formation and the carboxy-terminal region of collagen type I (CTX-I) marker for osteo-resorption in patients taking tocilizumab for polymyalgia rheumatica (PMR).
Methods: Twenty patients were included in the prospective open-label TENOR study (Clinicaltrials.gov NCT01713842) and received three monthly tocilizumab infusions, followed by corticosteroids starting at week (W)12. PINP and CTX-I were tested at inclusion (W0), after tocilizumab but before steroid initiation (W12), at the end of the protocol (W24) and were compared to healthy controls. Information regarding disease activity, inflammatory parameters and interleukin (IL)-6 levels were collected during the follow-up of the patients.
Results: Polymyalgia rheumatica patients were characterized by higher levels of CTX-I relative to healthy controls matched in age and sex at baseline. PINP levels increased at W12 (p=0.0008, *versus* W0) following tocilizumab introduction and CTX-I levels decreased at W24 and after steroid initiation (p=0.001, *versus* W0) (figure 1). Such modifications explain the altered correlation observed between PINP and CTX-I at W0 (r=0.255 at W0 *versus* r=0.641 in healthy controls) and its correction after treatment (r=0.760 at W12 and r=0.767 at W24). Finally, greater changes in PINP were observed in patients whose circulating IL-6 levels decreased after tocilizumab therapy.

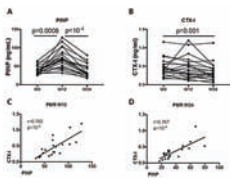


Figure 1. Evolution of PINP (A) and CTX-I (B) in polymyalgia rheumatica patients under tocilizumab therapy (W0-W12) and under corticosteroids (W12-W24). Correlation between CTX-I and PINP in polymyalgia rheumatica patients at week 12 (C) and 24 (D)

Conclusion: Control of bone turnover, in part through the inhibition of the IL-6 axis, is observed during tocilizumab and subsequent steroid treatment of polymyalgia rheumatica.

Disclosure of Interests: : Guillermo CARVAJAL ALEGRIA: None declared, Eleonore Bettacchioli: None declared, Alain Saraux Consultant for: Roche SAS, Speakers bureau: Chugai Pharma France, Divi Cornec: None declared, Valerie Devauchelle-Pensec Grant/research support from: Roche-Chugai, Speakers bureau: MSD, BMS, UCB, Roche, Yves Renaudineau: None declared
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FRI0505 CORRELATIONS BETWEEN CARTILAGE MOLECULAR COMPOSITION DETERMINED BY RAMAN SPECTROSCOPY AND MANKIN SCORE: IMPACT OF INTER AND INTRA-VARIABILITY

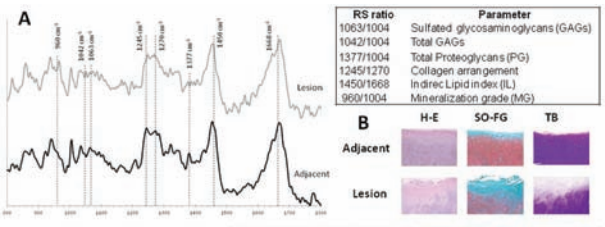
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Background: Osteoarthritis (OA) is an incurable disease and methods for its early diagnosis are still an unmet clinical need. Raman spectroscopy (RS) presents potential as a diagnosis technique based on the detection of peaks that can be assigned to cartilage components and molecular rearrengements during disease progression.[1]Mankin score (MS) is the main validated method to evaluate severity of cartilage degradation considering structure, cell distribution, Safranin-O staining and tidemark integrity.[2]
Objectives: To evaluate the correlations between OA cartilage RS assigned peaks and MS, considering the inter- and intra-variability of different observers.
Methods: MS analysis (Subscore-I, structure: 0-6; -II, cellularity: 0-3; and -III, safranin-O staining: 0-4; Total Score: 0-13) of human OA cartilage explants from 22 donors (age range: 32-92), obtained from lesion (n=22) and/or adjacent tissues (n=14), was performed by 3 blinded observers (O1, 2 and 3). Moreover, one of the observers performed the scoring in triplicate, with at least one month between observations. Inter- and intra-observer variability was determined by kappa and intraclass correlation (ICC) coeficients. Raman spectra were obtained with a FT-Raman Bruker RFS100 (λ=1064nm) and main peaks assigned (6 ratios related to proteoglycans, collagen, lipid index or calcium phosphate). Spearman's non-parametric correlation coefficient rho was used to compare MS and RS assigned peaks.
Results: Inter-observers variability indicated good (ICC>0.74) or moderate agreement (ICC>0.5) for all scores in lesions, whilst only a good agreeement (ICC=0.70) was found for subscore-I, in adjacent tissues, and no agreeement for the remaining parameters (subscores -II, -III, and total scoring). However, when performing analysis using kappa coefficients, a simultaneous agreement between the 3 observers was not observed. Intra-observer variability revealed good concordance (ICC>0.6) for all subscores and total scoring in cartilage for both sites, except for subscore –III, in adjacent tissues. In this case, ICC results were confirmed by kappa coefficients. Spearman's correlation coefficient between cartilage main peaks assigned by RS and MS indicated significant differences between observers(Fig.1). Correlations were found for a greater number of MS subscores in O1 (6) regarding O2 (4) or O3 (3) which could be related to the observers' experience (being O1>O2>O3). These correlations were mostly found in lesions (5, 3 and 1 for O1, 2 and 3, respectively) in comparison to adjacent tissues (2, 1 and 2 for O1, 2 and 3, respectively).
Conclusion: Eventhough inter-observation correlations for MS were in the moderate- good range, when analyzing kappa coefficients (categorical variables) these were not maintained. In addition, inter- and intra-observer variability results for adjacent tissues revealed possible limitations when characterizing early to mild OA. In view of MS-RS correlations, a reader dependency is underlined, indicating MS subjectivity and further limitations in the validation of RS using MS.

REFERENCES:
[1] Esmonde-White, et al. Analyst 2011,136(8),1675-1685;
[2] Mankin, et al. *J. Bone Jt. Surg.* 1971,53,3,523-537.

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C

		Total Mankin Score lesion (n=22)			Total Mankin Score adjacent (n=14)		
		O1	O2	O3	O1	O2	O3
Sulfated GAGs	Correlation coeficient	-,566*	-0.473	-0.346	-0.293	-,667*	-0.034
	Significance	0,028	0.075	0.207	0.444	0,05	0.931
Total GAGs	Correlation coeficient	-,547*	-0.326	-0.405	0.138	0.017	-0.373
	Significance	0,035	0.295	0.134	0.723	0.905	0.323
Total PG	Correlation coeficient	-0.479	-,545*	-0.481	-0.121	-0.427	-,746*
	Significance	0.071	0,036	0.069	0.757	0.251	0,021
Colagen arrangement	Correlation coeficient	,597*	0.171	0.336	0.328	0.487	0.237
	Significance	0,019	0.542	0.22	0.389	0.183	0.539
IL	Correlation coeficient	0.043	-0.074	0.038	,673*	0.445	0.407
	Significance	0.879	0.794	0.893	0,047	0.231	0.277
MG	Correlation coeficient	0.104	-0.301	0.092	0.362	0.368	-0.17
	Significance	0.711	0.276	0.744	0.338	0.33	0.663

Figure 1. A: Raman spectra (RS) for lesion and adjacent cartilage tissue and assigned peaks; B: Histological stainings (Hematoxilin-eosin (H-E) Safranin-O/Fast-Green (SO-FG) and Toluidin Blue (TB)) used for MS analysis from the adjacent and lesion sites from a selected donor; C: rho Spearman's correlation coeficients and significance between RS and MS (total scoring) in lesion and adjacent sites for Observer 1, 2 and 3 (O1, 2 and 3).

FRI0506 ROLE OF MITOCHONDRIA FROM PATIENTS WITH OA IN CELLULAR SENESCENCE

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Background: Chondrosenescence, chondroptosis and autophagy contribute to cell death and tissue damage in OA. The mitochondria are related with these three process implicated in the cartilage degeneration. Mitochondrial dysfunction is well documented in OA and has the capacity to promote abnormalities in chondrocyte viability contributing to cartilage degeneration. Cybrids are optimal cellular models to study the mitochondrial function, since they carry different mitochondrial variants with the same nuclear background, therefore, excluding the variations because of nuclear genome.
Objectives: The aim of this work is to study the role of human OA mitochondria in the cellular senescence, apoptosis and autophagy.
Methods: Cybrids were developed using 143B.TK$^-$ Rho-0 cell line (nuclear donor) and platelets (mitochondrial donors) from healthy (N) and knee OA donors. Senescence level was measured by real-time PCR method The percentage of mitochondrial depolarized was evaluated incubating cells with DilC1(5) in presence of FCCP 1μM using Flow Cytometer. The percentage of apoptotic cells was measured by Flow Cytometry using Annexin-V. Autophagy was evaluated through the developed of Microtubule-associated protein 1A/1B-light chain 3 (LC3) WB. Appropriate statistical analyses were performed with GraphPad Prism v6.
Results: The gene expression corresponding to senescence marker protein (SMP30) showed higher levels in OA cybrids than in N (4.535±1.63; 1.21±0.42 respectively, p≤0.0005). OA cybrids showed higher increment depolarized mitochondria under negative stimuli in comparison with basal condition than N (2.57±1.20; p≤0.0005; 1.76±0.99; p≤0.05 respectively). The analysis of apoptotic levels, when the cells were submitted for a positive stimuli with staurosporine (2 μM) and an inflammatory environment with IL-1β (10 ng/ml), OA cybrids reflected a statistically significant increase in positive cells for Anexine-V in comparison with N cybrids in both conditions (staurosporine 15.68±6.39; 6.41±4.88 respectively, p≤0.05. IL-1β 0.924±0.19; 0.47±0.24 respectively, p≤0.05). Autophagy was analyzed studying LC3 a marker for autophagosome formation and the results showed that LC3 activation was reduced in OA cybrids (1.19 ±0.24; 1.41±0.21 respectively, p≤0.05).
Conclusion: Mitochondria from OA patients is involved in cellular senescence, apoptosis and autophagy (three relevant processes involved in OA).
Disclosure of Interests: Andrea Dalmao-Fernandez: None declared, Tamara Hermida Gómez: None declared, Maria Eugenia Vazquez Mosquera: None declared, Sara Relaño-Fernandez: None declared, Ignacio Rego-Perez: None declared, Francisco J. Blanco Consultant for: AbbVie, Bioiberica, BMS, GSK, Grünenthal, Janssen, Lilly, Pfizer, Regeneron, Roche, Sanofi, TRB Chemedica, and UCB, Mercedes Fernandez-Moreno: None declared
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FRI0507 THE HUMAN-BASED IN VITRO 3D ARTHRITIC JOINT MODEL

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Background: Our ultimate goal is to develop a valid human *in vitro* 3D joint model to simulate the pathogenesis of arthritis. The model consists of different components including an osteogenic and chondrogenic part, the joint space with synovial fluid and the synovial membrane. It contains all involved cell types and thus, to allow interactions between cells by cell contacts and signaling molecules. The arthritic joint is simulated by the application of sorted immune cells and typical cytokines. As an alternative experimental setup for animal models, our *in vitro* 3D joint model will enable us to study the influence and efficacy of potential drug candidates. Currently, there is no valid 3D model, which is able to mimic an arthritic joint.
Objectives: Here, we aimed to develop the single joint components, namely the osteogenic and chondrogenic part, the joint space with synovial fluid and the synovial membrane, separately and in co-culture without and with the application of neutrophils (PMNs) and cytokines.
Methods: We have used human bone marrow derived mesenchymal stromal cells (hMSCs) to develop the different 3D tissue components that are characterized in detail (e.g. cell vitality, structural integrity) using histological, biochemical and molecular biological methods as well as μCT and scanning electron microscope (SEM). For the osteogenic component, we populated β-tricalcium phosphate (TCP) – mimicking the mineral bony part – with hMSCs, while the scaffold-free 3D cartilage component was generated from a marrow tissue exclusively consisting of hMSC under intermittent mechanical stimulation (fzmb GmbH). Simulating the synovial fluid, non-animal stabilized hyaluronic acid was applied to the osteochondral model. In order to model the synovial membrane, a confluent hMSC layer was formed on a polycarbonate membrane. Subsequently, we applied sorted CD15$^+$ cells to the synovial membrane and cytokines (e.g. TNF, MIF, IL6) into the synovial fluid, analyzed using qPCR, multiplex immunoassay and flow cytometry.
Results: We developed an *in vitro* 3D bone model by successfully seeding hMSC on a β-TCP scaffold. Cells consistently adhere onto the scaffold for up to 6 weeks as observed by SEM. The analysis of cell viability via LDH detection and LIVE/DEAD staining showed no toxic effects on the cells even after 3 weeks of incubation as compared to the corresponding control. mRNA expression of bone-related genes such as *RUNX2*, *SPP1* and *COL1A1* as well as μCT analysis confirmed the osteogenic phenotype of hMSC grown in 3D. Mimicking the articular cartilage component, we verified its chondrogenic phenotype by HE and Alcian Blue staining as well as by the reduced mRNA expression of *COL1A1* and an abundant expression of *COL2A1*. Interestingly, co-cultivation of the osteogenic and chondrogenic part looks promising showing a close alignment and cell interaction between both components. Modelling the synovial membrane, we successfully and reproducibly created a confluent hMSC cell layer, with a high cell viability even after 3 weeks of incubation. In addition, we injected cytokines into the synovial fluid. In response, the simulated synovial membrane showed an upregulation of *IL6, HIF* and *MMP13* expression on mRNA level. Furthermore, under co-cultural conditions the hMSCs enhanced the survival of the PMNs.
Conclusion: Results from the analysis of the single components confirmed viability, integrity and morphology pointing towards an ultimately successful development of the anticipated *in vitro* 3D model. By combining the different components in a standard 96 well format, we aim to provide a mid-throughput system for preclinical drug testing as well as a valid *in vitro* human-based 3D disease model to study the pathogenesis of arthritis.

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FRI0508 OLIVE OIL POLYPHENOLS AS NOVEL NUTRACEUTICALS IN TREATMENT OF OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a degenerative disease of the joints characterised by the imbalance of anabolic and catabolic processes in articular cartilage. It is one of the most significant causes of disability in the world affecting over 60% of people over the age of 60, causing joint stiffness, pain and a decrease in the quality of life. Currently no successful disease-modifying agent has been found to prevent or treat the condition. To address this unmet need, alternative approaches, including the use of nutraceuticals as a novel therapeutic intervention are under examination.
Objectives: To analyse if nutraceutical are able to reverse the catabolic activity that contribute to cartilage destruction in OA. Here two polyphenols from extra virgin olive oil (EVOO), oleocanthal (OLC) and ligstroside aglycone (LA), plus a chemically modified acetylated ligstroside aglycone (A-LA), and two marine polyunsaturated fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), were examined as potential anti-inflammatory agents for OA.
Methods: Human chondrocytes and cartilage explants were extracted from OA femoral heads, cultured and incubated with increasing concentrations of select compounds in combination with the pro-inflammatory cytokines IL-1β and oncostatin M (OSM). Gene expression levels were analysed by qPCR; nitric oxide (NO), GAG release and cytokines were measured in supernatants by colorimetric assays and Luminex technology respectively. Safranin-O and Alcian blue/Sirius red staining were done to quantify extracellular matrix components from cartilage.
Results: Acetylated ligstroside showed the most promising results for implementation in treating OA as it reduced the expression of pro-inflammatory genes such as inducible nitric oxide (*iNOS*), matrix metalloprotease-13 (*MMP13*) and interleukin-1β (*IL1B*) at both RNA and protein levels; decreased nitric oxide (NO) levels from cartilage explants and also reduced proteoglycan (PG) losses in human osteoarthritic cartilage explants and chondrocytes (Figure 1).
Conclusion: These results substantiate the role of nutraceuticals in OA with implications for therapeutic intervention and our understanding of OA pathophysiology.

REFERENCES:

[1] Castrogiovanni*et al.* Nutraceutical supplements in the management and prevention of osteoarthritis. *Int. J. Mol. Sci.* 17, (2016).
[2] Rigacci & Stefani. Nutraceutical Properties of Olive Oil Polyphenols. An Itinerary from Cultured Cells through Animal Models to Humans. *Int. J. Mol. Sci.* 17, 1–28 (2016).
[2] Aparicio-Soto, et al. Extra virgin olive oil: a key functional food for prevention of immune-inflammatory diseases. *Food Funct.* 7, 4492–4505 (2016).

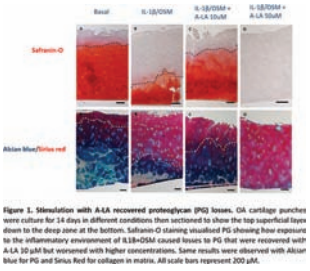


Figure 1. Stimulation with A-LA recovered proteoglycan (PG) losses. OA cartilage punches were culture for 14 days in different conditions then sectioned to show the top superficial layer down to the deep zone at the bottom. Safranin-O staining visualised PG showing how exposure to the inflammatory environment of IL1B+OSM caused losses to PG that were recovered with A-LA 10 μM but worsened with higher concentrations. Same results were observed with Alcian blue for PG and Sirius Red for collagen in matrix. All scale bars represent 200 μM.

Disclosure of Interests: None declared
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FRI0509 3D MICROSTRUCTURE OF INTACT AND OSTEOARTHRITIC HUMAN MENISCUS USING MICRO-COMPUTED TOMOGRAPHY

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Background: Degenerative meniscal lesions are highly prevalent in the general population and are associated with increased risk of knee osteoarthritis (OA). Development of novel methods for visualization of the early degenerative changes in the meniscus could help us better understand meniscal degradation and the onset of OA.
Objectives: To develop and perform *ex vivo* 3D imaging of meniscus posterior horn microstructure with micro-computed tomography (μCT), and to compare specimens from healthy references with end-stage OA using histology and qualitative μCT.
Methods: Medial and ipsilateral lateral menisci were retrieved from 10 patients undergoing total knee arthroplasty for medial compartment knee OA (age range 50 to 75 years, 5 women). Additionally, medial menisci were obtained from 10 cadaveric donors without known OA, to serve as reference (age range 18 to 77 years, 5 women). The samples were freshly frozen in -80°C. After thawing, the posterior horns were dissected and fixed, followed by excision of a piece for μCT imaging (Fig. 1A). The μCT samples were dehydrated in ascending ethanol concentrations, treated with hexamethyldisilazane (HMDS), and dried in room temperature. They were then imaged with a desktop μCT (scanning parameters: 40 kV, 250 μA, 2.0 μm pixel size, 1815 ms, no additional filtering). For histological analysis, Pauli's histopathological scoring[1] was performed independently by two graders on sections from three regions (Fig. 1A). The graders' consensus was given for each sub-score, from which the final overall consensus scores were calculated for each region. The mean difference in consensus scores (95% CI), adjusted for age and sex, were estimated between the menisci from OA knees and the reference menisci (medial OA menisci vs reference menisci, and lateral menisci from OA patients vs reference menisci) using a mixed linear regression model. The mean difference in consensus scores between the medial and lateral menisci from the same OA patient was calculated using a linear fixed effects model. The models were fitted on all three histological regions, but here we report histology results from region 2, because this region is adjacent to the piece analyzed by μCT (Fig 1A).

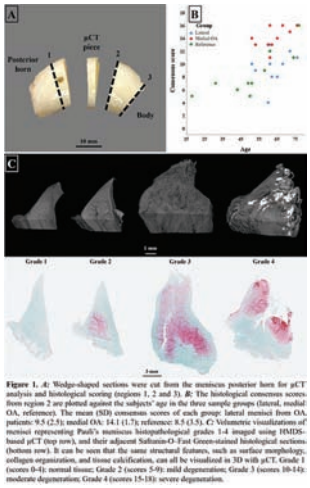


Figure 1. *A:* Wedge-shaped sections were cut from the meniscus posterior horn for μCT analysis and histological scoring (regions 1, 2 and 3). *B:* The histological consensus scores from region 2 are plotted against the subjects' age in the three sample groups (lateral, medial OA, reference). The mean (SD) consensus scores of each group: lateral menisci from OA patients: 9.5 (2.5); medial OA: 14.1 (1.7); reference: 8.5 (3.5). *C:* Volumetric visualizations of meniscal tissue representing Pauli's meniscus histopathological grades 1-4 imaged using HMDS-based μCT (top row), and their adjacent Safranin-O–Fast Green-stained histological sections (bottom row). It can be seen that the same structural features, such as surface morphology, collagen organization, and tissue calcification, can all be visualized in 3D with μCT. Grade 1 (scores 0-4): normal tissue; Grade 2 (scores 5-9): mild degeneration; Grade 3 (scores 10-14): moderate degeneration; Grade 4 (scores 15-18): severe degeneration.

Results: 3D visualization of the meniscus with μCT revealed similar structural changes as histological analysis (Fig. 1C). The histopathological consensus scores were generally higher in medial OA samples as compared to both lateral menisci from OA patients and the reference menisci (Fig. 1B). The mean difference in histological scores (95% CI) was 4.3 (2.5, 6.1) for medial OA menisci vs reference menisci, -0.3 (-2.2, 1.5) for lateral menisci from OA patients vs reference menisci, and 4.6 (3.0, 6.2) for medial OA menisci vs lateral menisci from OA patients.
Conclusion: An HMDS-based 3D μCT protocol allows unique 3D visualization of meniscus microstructures. The method enables the visualization of considerably large volumes and evaluation of the tissue's 3D

organization. Therefore, it may provide additional, important information compared to conventional section-based histology. Moreover, analyzing patients with medial compartment knee OA, we found that the medial OA menisci had higher histopathological scores than both reference medial menisci, as well as the lateral meniscus from the same knee.

REFERENCES:

[1] Pauli C, Grogan SP, Patil S, Otsuki S, Hasegawa A, Koziol J, et al. Macroscopic and histopathologic analysis of human knee menisci in aging and osteoarthritis. Osteoarthritis Cartilage 2011;19:1132-41. Doi: 10.1016/j.joca.2011.05.008 [doi]

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FRI0510 THE EFFECT AND MECHANISM OF HUMAN UMBILICAL CORD MESENCHYMAL STEM CELLS-DERIVED EXOSOMES ON BONE DESTRUCTION OF COLLAGEN INDUCED ARTHRITIS RATS

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Background: Rheumatoid arthritis (RA) is a highly disabling autoimmune disease, characterized by destruction of the cartilage and bone, which is difficult to reverse. mesenchymal stem cells-derived exosomes (Mesenchymal stem cells-derived Exos) is a kind of extracellular vesicle, produced by MSCs in resting or stress state, which can simulate the tissue repair effect of its maternal cells and may be a new breakthrough point in the treatment of RA bone destruction.
Objectives: Study the effect of human umbilical cord mesenchymal stem cells derived exosomes(hUCMSC-exos) on bone destruction in Collagen induced arthritis (CIA) rats.
Methods: 1. After isolated by differential centrifugation, hUCMSCs was cultured in vitro, which was identified by morphology and surface markers.2. Grouping: The CIA rats were randomly divided into CIA group, MTX group, hUCMSCs group, hUCMSC-exos low concentration group, hUCMSC-exos medium concentration group, hUCMSC-exos high concentration group, and a healthy control group.3. Efficacy evaluation: the efficacy of hUCMSC-exos on CIA rats was evaluated by measuring joint swelling, arthritis index, micro-ct scanning and pathological score. The expression levels of RANKL and OPG in the serum of rats in each group were detected by high-throughput flow,multi-factor detection technique or ELISA method, and the levels of the above factors in the synovial tissue of the ankle were detected by immunohistochemical detection technique, and the mRNA levels were detected by RT-PCR.
Results: 1. Effect evaluation: hUCMSC-exos can improve the arthritis index (AI) of CIA rats, and no definite side effect been find. In addition to hUCMSC-exos low concentration group, the joint synovial hyperplasia and inflammatory cell infiltration degree of each treatment group were significantly improved, comparing with that of CIA group. The Results of Micro-ct scanning suggested that the degree of osteoporosis in each intervention group was significantly improved comparing with that in the CIA group, and the improvement degree of hUCMSCs groups,MTX groups and hUCMSC-exos high concentration group was similar.2.The detection of bone metabolism factor in Serum and synovial tissue: medium and high concentrations of hUCMSC-exos, hUCMSCs group and MTX group could down-regulate the level of RANKL in serum and synovial tissues of CIA rats, and raise the level of OPG, and the effect of hUCMSC-exos in high concentration group was slightly obvious.
Conclusion: hUCMSC-exos can improve bone destruction in CIA rats, and it is safe. hUCMSC-exos can mimic its mother cells and exert an inhibitory effect on bone destruction by regulating the imbalance of RANKL/OPG, and the effect is equal or better than its mother cells, and the high concentration group is superior to the low concentration group.

REFERENCES:

[1] Aghajani NA, Lerman LO, Eirin A. Mesenchymal stem cell-derived extracellular vesicles for kidney repair: current status and looming challenges. STEM CELL RES THER 2017;8(1):273.
[2] Calabresi E, Petrelli F, Bonifacio AF, Puxeddu I, Alunno A. One year in review 2018: pathogenesis of rheumatoid arthritis. CLIN EXP RHEUMATOL 2018;36(2):175-84.
[3] Emori T, Hirose J, Ise K, Yomoda JI, Kasahara M, Shinkuma T, Yoshitomi H, Ito H, Hashimoto M, Sugahara S, Fujita H, Yamamoto N, Morita Y, Narumiya S, Aramori I. Constitutive Activation of Integrin alpha9 Augments Self-Directed Hyperplastic and Proinflammatory Properties of Fibroblast-like Synoviocytes of Rheumatoid Arthritis. J IMMUNOL 2017;199(10):3427-36.
[4] Potter DR, Miyazawa BY, Gibb SL, Deng X, Togaratti PP, Croze RH, Srivastava AK, Trivedi A, Matthay M, Holcomb JB, Schreiber MA, Pati S. Mesenchymal stem cell-derived extracellular vesicles attenuate pulmonary vascular permeability and lung injury induced by hemorrhagic shock and trauma. J Trauma Acute Care Surg 2018;84(2):245-56.

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FRI0511 LOW Ω6-Ω3 RATIOS CAUSED REDUCTION IN CELLULAR INFLAMMATION IN HUMAN SYNOVIOCYTES CELL LINE (SW982): GENE EXPRESSION STUDY

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Background: Alarming global increase in osteoarthritis (OA), coupled with off target existing palliative care poses nutraceuticals an extremely attractive alternative in this respect. Beyond meeting the basic nutritional demands, nutrition is thought to play a beneficial role in the management of chronic diseases. Interestingly, the off target effects of nutriceuticals are beneficial in reducing co-morbidities. Skewed ratio of ω-6: ω-3 fatty acids (FAs) in modern diets has been shown associated with increased number of inflammatory diseases including bone and cartilage metabolism. Considering this, due to their disease modifying actions, ω-3 FAs are thought to serve better in OA management.
Objectives: We here investigated the effect of different ω-6: ω-3 ratios on synovitis, a prominent OA pathology. The selected ratios are generally found in global diet.
Methods: Selected ω-6FAs - arachidonic acid (AA), eicosadienoic acid (EDA), linolic acid (LA) and dihomo gamma linoleic acid (DGLA) along with selected ω-3 FAs docosapentaenoic acid 5 (DPA) and α-linolenic acid (ALA) were tested on induced SW-982 cells, in common dietary ratios of 16:1, 8:1, 4:1, 2:1 and 1:1 for their effect on synovial inflammation. For induction, 50ng/ml tumor necrosis factor-α (TNF-α) was used for 72 hrs and the PUFAs were added in the culture media in the selected ratios (concentration of each PUFA - 50μM). Finally, isolated cDNA was used to run quantitative RT-PCR for superoxide dismutase (SOD), interleukin-15 (IL-15), matrix metalloproteinase-1 (MMP-1) and vascular endothelial growth factor (VEGF).
Results: All the ratios LA:ALA of caused a remarkable reduction in MMP-1($P<0.001$). Marginal reduction in VEGF was noted with1:1, 4:1 and 8:1 ratios ($P<0.005$); 8:1 and 16:1 showed a significant increase ($P<0.001$). SOD did not show any particular trend but noteworthy increase was observed with 2:1, 8:1 and 16:1 ratios ($P<0.001$) while reduction with 1:1 and 4:1 ratios ($P<0.001$). IL-15 remained low for 1:1, 2:1and 4:1 while a marked up-regulation was noted for 8:1 and 16:1 ratios ($P<0.001$). In case of EDA:DPA, a consistent down-regulation of MMP-1was found with all the ratios excluding 4:1. The selected ratios were efficient against VEGF ($P<0.001$). A consistent high SOD was revealed by all the ratios of EDA:DPA, which remained comparable to control. Marginal reduction in IL-15 was noted with 1:1, 8:1 and 16:1 ($P<0.05$). Lastly, a significant MMP-1 reduction was caused by all the ratios of DGLA:DPA, except 2:1. Excluding 2:1, all the ratios were efficient against VEGF ($P<0.001$). Increased levels of SOD remained comparable with TNF-α for 1:1 and 4:1; a trivial drop was noted with 2:1 and 8:1, followed by a noticeable reduction with 16:1. IL-15 showed a down-regulation with 1:1, 4:1, 8:1 ratios of DGLA: DPA.
Conclusion: Consequence of synovial inflammation in typical and atypical forms results in cartilage-loss, osteophytes and pain. FA ratios when used in equivalent, was found highly effective against IL 15, MMP1 and VEGF, whereas inflammation increases with increase in their proportions. Low SOD indicated lower oxidative-stress while it was up-regulated in response to high stress. FAs work in two distinct ways, membrane incorporation and metabolic modulation. Unsaturated fatty acid increase membrane fluidity and thus improves cell signaling. Analysis of treated and untreated cells showed incorporation of FAs in cell membrane, which improves membrane fluidity and status of signal transduction.
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Disclosure of Interests: None declared
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FRI0512 RETRO-INVERSO TAT-BECLIN-1 INDUCES SYNOVIAL FIBROSIS AND DOES NOT PROTECT CARTILAGE FROM DEGENERATION IN A MOUSE MODEL OF OA

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Background: Beclin-1 is a component of the autophagy pathway necessary for formation of autophagosomes, contributing to autophagy-mediated cellular homeostasis. Enhancing autophagy through inhibition of mTOR activity, either via genetic deletion in chondrocytes or intra-articular injection of rapamycin, attenuates progression of surgically-induced models of osteoarthritis (OA). Retro-inverso TAT-Beclin-1 is a cell-permeable peptide which competes for binding to the endogenous Beclin-1 inhibitor GAPR-1, thus promoting autophagy. It is unknown whether activation of Beclin-1 is sufficient to protect joints from osteoarthritis progression.
Objectives: For this study, we sought to determine if retro-inverso TAT-Beclin-1 could attenuate OA progression in a surgically-induced mouse model.
Methods: Eight-week old C57BL/6 mice underwent destabilization of the medial meniscus (DMM) surgery to induce OA, or sham surgery as a control. Mice were injected intra-articularly with retro-inverso TAT-Beclin-1 (2 mg/kg in 5µl) twice weekly for 2 or 9 weeks. Mice were sacrificed at 10-weeks post-surgery. Knee joints were stained with Safranin-O/Fast-green to evaluate cartilage degeneration and Masson's trichrome to determine degree of synovitis using OARSI scoring for mice. Sections were stained for α-SMA (myofibroblast) and CD45 (hematopoietic-origin cell) to evaluate changes in markers of fibrosis and inflammation, respectively.
Results: As opposed to the effects of mTOR deletion in cartilage or rapamycin treatment in joints, injection of retro-inverso TAT-Beclin-1 for 2 into knee joints of mice with DMM-induced OA had no effect on the degree of articular cartilage degeneration in the tibia or femur as compared to PBS-injected controls. However, in both sham and DMM mice, retro-inverso TAT-Beclin-1 for 2 or 9 weeks of treatment induced a pronounced thickening of the synovium with increased cell numbers and collagen deposition compared to PBS-treated mice. The increased number of synovial cells in 9-week treated mice did not show substantial expression of α-SMA+ or CD45+ cells, suggesting the increased number of cells and matrix in the synovium was independent of myofibroblast differentiation or inflammatory influx.
Conclusion: Contradictory to our expected results, retro-inverso TAT-Beclin-1 did not attenuate cartilage degeneration. Rather, it promoted substantial synovial thickening that likely involved cell proliferation and collagen deposition. This severe fibrotic phenotype appears independent of myofibroblast differentiation or inflammation, normally associated with typical fibrotic responses. To evaluate the potential for dose responses with retro-inverso TAT-Beclin-1 in synovial joints, we are currently modifying our dosing strategy in an effort to determine possible disease modifying effects of this novel Beclin-1 activator.
Disclosure of Interests: None declared
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FRI0513 HISTONE-ACETYLTRANSFERASES CBP AND P300 REGULATE AUTOPHAGY AND PROTEASOMAL DEGRADATION IN SYNOVIAL FIBROBLASTS

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Background: Proteasomal degradation and autophagy are the major catabolic pathways that maintain the homeostasis of cells and are associated with cell survival. The histone acetyltransferases cAMP-response element binding protein binding protein (CBP) and p300 are close homologues and widely accepted as redundant proteins.
Objectives: To analyse individual functions of CBP and p300 in catabolic pathways in rheumatoid arthritis (RA) synovial fibroblasts (SF).
Methods: SF were isolated from knee, shoulder and hand joints of RA patients undergoing joint replacement surgery. The expression of CBP and p300 was silenced by transfection of antisense LNA gapmeRs (12,5 nM). 24h after transfection cells were stimulated with TNF-α (10 ng/ml, 24h). Transcriptomes were determined by RNA-seq (Illumina NovaSeq 6000, n=6). Pathway enrichment analysis of RNA-seq data (fold change >1.5, FDR <0.05) was performed using DAVID bioinformatic resources. Autophagy was assessed by Western blotting using LC3B conversion and p62 as autophagy markers (n=4) in presence and absence of bafilomycin A1 (100 nM, 4h), a lysosomal inhibitor. Cell death was analysed using the CytoTox-Glo cytotoxicity assay.
Results: The top pathway identified after silencing of p300 in SF in presence ($p=1.33x10^{-10}$) and absence of TNF-α ($p=1.76x10^{-10}$) was 'proteasome', with an enrichment of genes contributing to 'proteasome assembly' and 'proteasome regulation'. The expression of several genes encoding proteasome subunits was increased after p300 silencing but unaffected by silencing of CBP. Genes contributing to the biological processes 'autophagy' ($p<0.05$) and 'regulation of autophagy' ($p<0.05$) were enriched after silencing of CBP and p300, whereas 'autophagy assembly' was only affected by CBP silencing. In RNA-seq data, the expression of MAP1LC3B, encoding the autophagy marker LC3B, and the autophagy substrate p62, was increased by p300 silencing but slightly decreased by CBP silencing. In line with the RNA expression, silencing of CBP reduced the conversion of LC3B and the protein expression of p62 in presence and absence of TNF-α. Results were similar in presence of bafilomycin A1, indicating a decrease in autophagosome synthesis. In contrast, the conversion of LC3B and p62 expression were increased after silencing of p300 in unstimulated SF, indicating increased autophagy. This effect was lost for LC3B after treatment with TNF-α, and LC3B conversion was even decreased in presence of bafilomycin A1. This indicates a late stage block of autophagy after silencing of p300 in TNF-α-stimulated SF. In line with this, silencing of p300 in SF (n=6, $p<0.05$) increased cell death only in presence of TNF-α. Viability of SF was not affected by silencing of CBP.
Conclusion: Here we identified p300 as a major regulator of the proteasome in SF and provide first evidence for individual functions of CBP and p300 in regulating autophagy in SF.
Disclosure of Interests: Monika Krosel: None declared, Marcel Gabathuler: None declared, Christoph Kolling: None declared, Matija Tomsic: None declared, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Caroline Ospelt: None declared, Kerstin Klein: None declared
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FRI0514 NEW DIAGNOSTIC BIOMARKER OF BONE TISSUE METABOLISM DISORDERS IN RHEUMATOID ARTHRITIS

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Background: Bone mineral density and proteins/peptides determination in blood and urine as markers of bone resorption and formation are currently used to diagnose osteoporosis (OP) and metabolic bone diseases. However, these methods have some disadvantages for bone turnover evaluation. Recent evidence suggests that in RA changes in the secretion of hormones of white adipose tissue can be revealed [1,2,3,4]. One of them is Adiponectin possessing anti-inflammatory, anti-diabetic and anti-atherogenic properties. Changes in Adiponectin levels may reflect influence of immune inflammation on bone turnover.
Objectives: To study the clinical and diagnostic value of serum Adiponectin determination in RA patients complicated by OP.
Methods: We examined 88 women with documented diagnosis of RA and mean disease duration of 6.56±0.88 years. We used EULAR/ARA 2010 criteria to diagnose the patients. Female patients with II degree of disease activity (DAS28), Steinbrocker stage II (erosive), rheumatoid factor- and anti-cyclic-citrullinated peptide antibody-positive were prevalent. We excluded patients who had surgery or developed an infection within the last 8 weeks, pregnant and breast-feeding women, those with severe heart, liver or kidney disease, immune deficiency, leukopenia or chronic infection. A control group of 45 healthy females aged of 25 and 59 years were included in the study. There were no reported findings of

joint pain and RA symptoms in the group. The groups were adjusted for age (p>0.05) and showed no statistically significant differences.
We measured serum Adiponectin levels (μg/ml) using Human Adiponectin ELISA commercial test systems (BioVendor, Czech Republic, cat № RD195023100). We used spectrophotometer with wavelength of 450 nm to detect the test results («Multiskan» immunoenzyme analyzer, Finland). We plotted a curve using computer software. We diagnosed OP using dual-energy X-ray absorptiometry with LUNAR DPX PRO (GE, USA).
Results: Serum adiponectin levels in the control group were 12.5±0.9 μg/ml (M±m). Adiponectin levels in healthy subjects measured as M ± 2δ, ranged between 0.44 and 24.56 μg/ml. Patients with OP and RA had significantly higher levels of serum Adiponectin (p<0.001). Mean serum Adiponectin levels in RA patients who had normal bone density and had no OP were 35.21±0.6 μg/ml. Mean serum Adiponectin levels in RA/OP patients with low bone mineral density were 52.42±0.69 μg/ml. Adiponectin levels of 44 μg/ml and higher were associated with osteoporosis. Adiponectin levels of 43.9 μg/ml and lower were associated with normal bone density.
Conclusion: Thus, we revealed that Adiponectin levels depend on osteoporosis presence in RA patients. We suppose that Adiponectin determination may be useful laboratory marker for OP diagnosis. The test may be used to reduce the risk of low-energy fractures and to improve the quality of life in RA.

REFERENCES:
[1] Akhverdyan Y. et al. Laboratory markers of inflammation and serum nicotinamide phosphoribosyltransferase level in rheumatoid arthritis patients// Ann. Rheum. Dis., 2017, vol.76, suppl.2, p.1149.
[2] Kvlividze Z. et al. Elevated nesfatin-1 levels in patients with rheumatoid arthritis//Ann Rheum Dis, 2018, vol.77, p.A1762.
[3] Papichev E. et al. Fetuin-A: clinical and laboratory associations in women with rheumatoid arthritis//Ann Rheum Dis, 2018, vol.77, p.A1228.
[4] Polyakova J. S. et al. Serum visfatin determination in rheumatoid arthritis // Ann. Rheum. Dis. 2014; 73 (Suppl2).

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FRI0515 HSP90AA1, A CHAPERONE-MEDIATED AUTOPHAGY, IS A BIOMARKER ASSOCIATED WITH DEFECTIVE AUTOPHAGY IN OSTEOARTHRITIS

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Background: In osteoarthritis (OA), defects in cellular homeostasis, such as autophagy, are evident and precede joint damage (1). We have shown that there is a defect in autophagy in OA human chondrocytes and cartilage (2). Indeed, pharmacological activation of autophagy protects against joint damage (3). Our working hypothesis is that joint damage in OA could be due to a failure of autophagy that can be detected in the blood and tissue of patients.
Objectives: The objective of this study is to identify biomarkers associated with autophagy defects that could facilitate the development of personalized therapeutic strategies to prevent OA progression.
Methods: A comparative analysis of 35 autophagy genes was performed in blood from a Prospective OA Cohort of A Coruña (PROCOAC) of Non-OA and knee OA patients. Non-OA patients (Age: 61,44 ± 1,16 years; BMI: 25,25 ± 0,52; Females, n=18) and Knee OA patients (Age: 65,50 ± 1,05 years; BMI: 29,55 ± 0,67; Females, n=18, OA grade III-IV) were profiled using PrimePCR autophagy human panel array (Bio-Rad). Confirmatory studies of the candidate genes were performed in blood from Non-OA patients (Age: 60,13 ± 1,12 years; BMI: 24,85 ± 0,59; Females; n=30) and Knee-OA patients (Age: 68,4 ± 1,11 years; BMI: 29,65 ± 0,55; Females; n=30, OA grade III-IV) by Taqman Technology. A quantitative proteomic analysis of defective autophagy genes regulated upon deletion of Atg5 in human OA chondrocytes was performed by iTRAQ analysis. Moreover, the candidate gene was evaluated as a potential biomarker in human cartilage from Normal (n=19) and Knee-OA (n=20) patients and in both spontaneous aging (6, 12, 18, and 30 months old, n=3) and surgically-induced OA (10 weeks after surgery, n=4) in mice by immunohistochemistry. Remarkably, the consequences of candidate gene silencing on autophagy, FOXO signaling, inflammation, senescence and cell death by apoptosis was investigated by gene expression and flow cytometry.
Results: 15 autophagy-related genes were downregulated in blood from knee OA patients compared to non-OA patients (p<0.05). Importantly, key autophagy-related genes, including ATG16L2, ATG12, ATG4B and MAP1LC3B, involved in relevant process including initiating autophagy, phagophore extension and autophagosome formation, were significant downregulated in knee OA patients (p<0.05). Interestingly, HSP90AA1 and HSPA8, chaperone-mediated autophagy genes involved in stress response and protein folding, were significant downregulated (p<0.001). In addition, several regulators of autophagy and apoptosis, such as BNIP3, BCL-2 and BCL2L1 were downregulated (p<0.01). Confirmatory studies for MAP1LC3B and HSP90AA1, showed a significant downregulation (p<0.001) in blood from knee OA patients. Remarkably, total proteome screening of human OA chondrocytes with defective autophagy, showed a significant reduction of HSP90AA1 (p<0.05). Remarkably, HSP90AA1 expression was reduced in OA cartilage ($p < 0.01$) and in spontaneous aging and surgically-induced OA in mice ($p < 0.05$). Interestingly, HSP90AA1 silencing increased LC3 and FOXO1 expression ($p > 0.01$), might be as a protective response, and increased NFκB and p16 expression ($p < 0.05$) at 48 hours. In addition, genetic deletion of HSP90AA1 increased cell death by apoptosis ($p < 0.05$). These data indicate that HSP90 might be a potential biomarker associated with defective autophagy in OA.
Conclusion: We identified biomarkers of defective autophagy as a mechanism of central homeostasis, which gives us a general vision of the disease mechanisms linked to OA clinical reality.

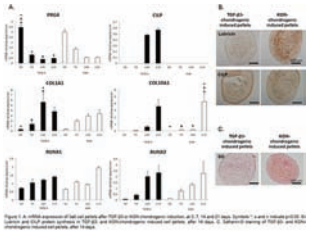
REFERENCES:
[1] Lotz MK, Caramés B. Nat Rev Rheumatol. 2011;7:579-87
[2] Caramés B, et al. Arthritis Rheum. 2010;62:791-801.
[3] Caramés B, et al. Ann Rheum Dis. 2012;71:575-81.

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FRI0516 CHONDROGENIC EFFECT OF KARTOGENIN ON AN IMMORTALIZED CELL LINE DERIVED FROM MESENCHYMAL STROMAL CELLS ISOLATED FROM HUMAN BONE MARROW

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Background: Mesenchymal stromal cells (MSCs) currently tested in regenerative medicine approaches for osteoarthritis (OA) present limitations in obtaining stable hyaline-like cartilage phenotype. Kartogenin (KGN) has been recently described to promote both reparative and protective effects hampering the hypertrophic effects of chondrogenesis.[1]
Objectives: The aim of this study is to evaluate the chondrogenic effect of kartogenin on an immortalized cell line (3a6), using a conventional cell pellet model and gold-standard chondroinductor transforming growth factor 3 (TGF-β3), as positive reference.
Methods: 3a6 cells, originally obtained from a 61-year old Asian woman bone marrow, was cultured under pellet culture system with basal (DMEM, low glucose) or commercial chondrogenic medium, supplemented with 10 ng/ml TGF-β3 or 100nM KGN for 3, 7, 14 and 21 days. Total RNA was isolated and real-time quantitative reverse transcription-polymerase chain reaction (RT-qPCR) was performed, using custom-made primers for runt-related transcription factor 1 (RUNX1), proteoglycan 4 (PRG4), cartilage intermediate layer protein (CILP), collagens type-II (COL2A1), -X (COL10A1) and -I (COL1A1), using RPL13A as housekeeping. Proteoglycans and zonal markers protein synthesis was evaluated by safranin-O (SO) staining and lubricin/PRG4 and CILP immunohistochemical analysis (both 1:500), respectively. The experiment was performed in triplicate and differences judged using one-way ANOVA with Bonferroni's corrections, considering p<0.05 significantly different.



Results: The molecular analysis of KGN- and TGF-β3-chondrogenic induced 3a6 pellets is depicted in figure 1A. For zonal markers expression, both conditions showed a significant downregulation in PRG4 with time, concomitant with an upregulation of CILP, for TGF-β3 but not for KGN-induced cells. However, PRG4 and CILP were found on the protein level (Figure 1B) for both conditions. The studied zonal markers were found heterogeneously distributed for KGN-induced pellets (Figure 1C). This difference is also supported by proteoglycans SO staining, with an earlier formation of a more mature tissue for KGN- than TGF-β3-induced pellets. No expression was found for the main hyaline-like cartilage collagen (COL2A1). RUNX1 was practically unaltered in both conditions. For hypertrophic markers, RUNX2 was upregulated at 14 days in TGF-β3- whilst, in KGN-induced cells its expression seems to be delayed, although no significant differences were found. In both conditions, COL10A1 was very low, until 21 days. COL1A1 presented a significant upregulation at 14 days for TGF-β3- whilst in KGN-induced cells expression was non-significant.
Conclusion: This is the first study to report the chondrogenic effect of kartogenin on 3a6 immortalized human bone marrow MSCs line. On the molecular level, no significant differences were found between KGN- and TGF-β3 chondroinduction, although transition into a hypertrophic phenotype seems to be delayed. On the protein level, zonal markers and proteoglycan synthesis were found improved by kartogenin after 14 days.

REFERENCE:
[1] Johnson K, et al. Science 2012, 11;336(6082):717-21.

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FRI0517 ANTI-CARBAMYLATED PROTEINS ANTIBODIES INDUCE OSTEOCLASTOGENESIS

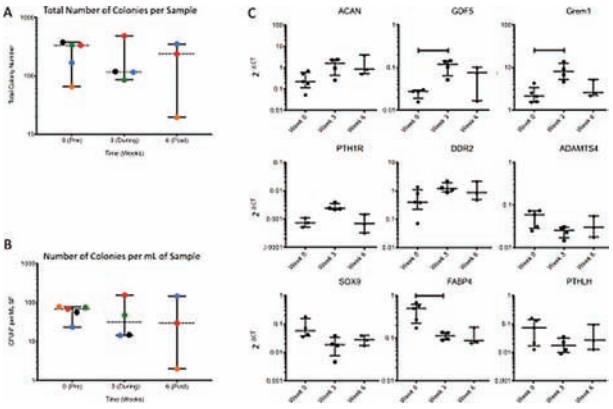
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Background: Post-translational-modifications (PTMs) are implicated in the pathogenesis of autoimmune diseases, leading to the break of self-tolerance, generation of new autoantigens and production of autoantibodies. Anti-citrullinated-proteins antibodies (ACPA) play a key role in the pathogenesis of rheumatoid arthritis (RA) and many evidences showed that they are related to bone loss in RA. Osteoclasts are the primary targets of ACPA in the joint site, displaying citrullinated antigens on their surface. Carbamylation is another PTM generating the production of anti-carbamylated proteins antibodies (anti-CarP), recently proposed as a new biomarker for RA. Anti-CarP have been also studied in patients with systemic lupus erythematosus (SLE) with predominant joint involvement, showing a prevalence of 46.1%. Moreover, in SLE patients these autoantibodies have been also associated to bone erosive damage. The pathogenic mechanism of these autoantibodies is not completely clarified so far.
Objectives: The aim of the present study was to investigate the possible pathogenic role of anti-CarP in the induction of osteoclastogenesis.
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from a buffy coat from healthy donors using a Ficoll Hypaque gradient. Cells were cultured for 14 days in α-MEM complete medium, supplemented with 25 ng/ml of macrophage-colony-stimulating-factor (MCSF) and 30 ng/ml of receptor activator of nuclear-factor-kappa-B-ligand (RANKL), for the differentiation of monocytes in osteoclasts. Simultaneously, PBMCs were co-cultured in presence of anti-carbamilated-vimentin autoantibodies (anti-Vim CarP) purified from sera of 3 patients with RA and 3 patients with SLE with a predominant joint involvement at 100 ng/ml and 1 μg/ml. As control, intravenous immunoglobulin (IVIg) were used at the same concentrations. After 14 days, osteoclast differentiation was evaluated by staining cells for tartrate-resistant acid phosphatase (TRAP), using leukocyte acid phosphatase kit.
Results: Anti-VimCarP purified from RA patients at 100 ng/ml were able to increase the median number of osteoclasts per well significantly more than untreated and IVIg at 100 ng/ml and 1 μg/ml (P=0.0008; P=0.0009 and P=0.0009, respectively). The same results were observed treating cells with 1 μg/ml of anti-VimCarP from RA patients (P=0.0008, P=0.002 and P=0.002, respectively). Similarly, anti-VimCarP purified from SLE patients at 100 ng/ml significantly increased the median number of osteoclasts than untreated and IVIg at 100 ng/ml and 1 μg/ml (P=0.002, P=0.004 and P=0.003, respectively). Analogously, we observed similar results co-culturing cells with 1 μg/ml of anti-VimCarP from SLE patients (P=0.002, P=0.02 and P=0.006, respectively).
Conclusion: For the first time, we demonstrated that anti-Vim CarP purified from RA and SLE patients are able to induce osteoclastogenesis, suggesting their potential role as a biomarker of joint erosiveness in these autoimmune diseases.
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FRI0518 LONGITUDINAL EVALUATION OF SYNOVIAL FLUID AND SYNOVIAL FLUID MSC TRANSCRIPT CHANGES IN SUBJECTS UNDERGOING JOINT DISTRACTION

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Background: In relatively young patients with end-stage knee osteoarthritis (OA), total knee arthroplasty (TKA) comes with the risk of future revision surgery [1]. Knee joint distraction (KJD) is a joint preserving surgical technique, which has been shown to provide clinical and structural improvement for over five years [2,3] and postpones the need for TKA. The underlying mechanism however, is largely unknown. It is anticipated that an alteration of joint homeostasis including synovial fluid resident mesenchymal stem cells (MSCs), and their access to the superficial arthritic surface, is key to the regenerative process seen with KJD.
Objectives: To evaluate the longitudinal changes in synovial fluid MSC numbers and their gene expression profile upon KJD.
Methods: Patients with established symptomatic radiographic knee OA undergoing KJD gave written informed consent to participate. Synovial fluid (SF) was sampled at baseline (before distraction; pre), at midpoint (after 3 weeks; during) and at endpoint of distraction (6 weeks; post). MSCs were isolated and Colony Forming Units (CFU; MSCs) were determined. Moreover, gene expression profiles in isolated synovial fluid (SF) MSCs was determined by Realtime PCR for genes known to be involved in joint morphogenesis, cartilage homeostasis and OA, which included: Aggrecan (ACAN), Growth/Differentiation Factor 5 (GDF5), Gremlin 1 (Grem1), Parathyroid Hormone 1 receptor (PTH1R), Discoidin Domain receptor 2 (DDR2), A disintegrin and metalloproteinase with thrombospondin motifs 4, Aggrecanase 1 (ADAMTS4), SRY-related proteins 9 (SOX9), Fatty acid binding protein 4 (FAB4), and Parathyroid hormone related protein (PTHLH). All data were normalized to HPRT (2-ΔCt).



Results: Participants had a mean age 47±9 yrs and 6 out 7 (86%) were female. All had KL grade≥2 with substantial knee pain at baseline. Enough SF (>500 µll) could be obtained from n=7 at baseline, n=4 at midpoint, and n=3 at endpoint of distraction. For the first time in this same group, we show how MSC number initially decline upon KJD (figure 1A-B) as seen previously in our animal study [4]. Also, MSCs present in the SF showed changes in their gene expression profile upon KJD, most clearly observed during the treatment (3 weeks; figure 1C). GDF5 and Grem1 presented with a statistically significant increased expression ($p<0.05$) during treatment while FAB4 expression was decreased. ACAN, PTH1R, and DDR expression had the tendency to increase over time. ADAMTS4, SOX9 and PTHLH expression showed a trend to decrease over time.

Conclusion: This explorative study provides for the first-time data on changes in SF MSC number and their gene expression profiles upon knee joint distraction. As such, first clues are provided for the involvement of MSCs in the regenerative process induced by joint distraction for end-stage knee OA. The fall in SF MSCs number during distraction suggests adhesion to the arthritic surfaces in the KJD environment as found in our previous work in canine KJD [4]. Further studies are necessary to unravel the processes involved.

REFERENCES:

[1] SM Kurtz, et al. Clin Orthop Relat Res 2009, 467(10):2606-
[2] J-TAD van der Woude, et al. Cartilage 2017, 8(3):263–
[3] MP Jansen, et al. Osteoarthritis Cartilage. 2018; 26(12):1604-
[4] T Baboolol, et al. Ann Rheum Dis. 2016;75(5):908-

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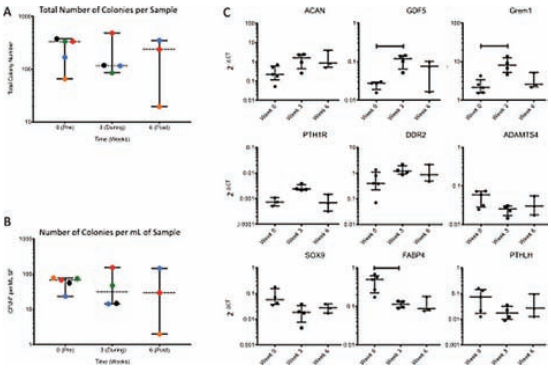


Figure 1. Changes in synovial fluid MSCs numbers and gene expressing profiles upon knee joint distraction. Bar indicates statistically significant changes ($p<0.05$).

FRI0519

IDENTIFICATION OF CELLULAR TARGETS FOR ANTI-CITRULLINATED PROTEIN ANTIBODIES (ACPAS)

Bence Réthi, Meng Sun, Alexandra Circiumaru, Akilan Krishnamurthy, Heidi Wähämaa, Jimmy Ytterberg, Vivianne Malmström, Lars Klareskog, Anca Catrina. *Karolinska Institutet and Karolinska University Hospital, Department of Medicine, Solna, Stockholm, Sweden*

Background: Autoantibodies against citrullinated proteins (ACPAs) have been suggested to play important roles in RA pathogenesis (1-3).

Objectives: In order to further dissect how ACPAs influence bone homeostasis and inflammation in the joints we analyzed the binding of different ACPA clones to target antigens produced by synovial fibroblasts, osteoclasts (OCs) or neutrophil granulocytes.

Methods: Fibroblasts were isolated from synovial tissue of RA patients by enzymatic digestion. Monocytes and neutrophil granulocytes were isolated from the peripheral blood of healthy individuals. Osteoclasts were generated from monocyte-derived dendritic cells in the presence of M-CSF and RANK-L. Polyclonal ACPAs were purified from pooled serum samples of RA patients using protein G and Cyclic Citrullinated Peptide-based affinity chromatography. Monoclonal ACPAs were isolated from synovial plasma cells of RA patients, as described (4). Protein citrullination was analyzed with mass spectrometry. ACPA binding was analyzed using confocal microscopy and flow cytometry. Neutrophil extracellular trap (NET) formation was monitored using IncuCyte and confocal microscopy.

Results: Synovial fibroblasts expressed surface antigens to the ACPA clone 1325:01B09 following exposure to cellular stress (serum withdrawal) or IL-8 stimulation. Osteoclasts and their precursors were characterized by steady state protein citrullination and these cells were recognized by another distinct ACPA clone 1325:04C03. Using mass spectrometry, we detected citrullinated actin and vimentin in developing OCs. Interestingly, both proteins were present on the cell surface, showing a partial colocalization with the cell-bound 1325:04C03 antibodies.

Neutrophil granulocytes exposed a large amount of citrullinated targets for both 1325:04C03 and 1325:01B09 as well as for polyclonal ACPAs in neutrophil extracellular traps (NETs), irrespectively of the stimulus that triggered NETosis. Activation of the cells by Ca2+ ionophores triggered a rapid NETosis and cellular disintegration, in parallel with a profound reactivity of all tested ACPAs with both intracellular or surface antigens. Other activation signals, e.g. PMA, nigericin, zymosan or IL-8 did not induce protein citrullination in the cells, even in conditions where citrullinated proteins were detected in NETs.

Conclusion: Distinct monoclonal ACPAs target different cell types, suggesting unique pathological roles for individual ACPA clones. OCs might be among the earliest ACPA targets due to their physiological protein citrullination. Fibroblasts, on the contrary, acquired ACPA sensitivity only following cellular stress signals. Intact neutrophils were not targeted by ACPAs, whereas damaged cells and the extruded NET products might be important sources of citrullinated antigens that form immune complexes with ACPAs.

REFERENCES:

[1] Harre, U. et al. J Clin Invest (2012)
[2] Krishnamurthy, A. et al. Ann Rheum Dis (2016)
[3] Wigerblad, G. et al. Ann Rheum Dis (2016)
[4] Steen, J. et al. Arthritis Rheumatol (2018)

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FRI0520

THE HUMAN ENTHESIS CONTAINS POPULATIONS OF MESENCHYMAL STEM CELLS WITH DISTINCT FUNCTIONAL CHARACTERISTICS

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Background: Ankylosing spondylitis (AS) is associated with entheseal inflammation and new bone formation. Resident populations of lymphocytes have been identified at the enthesis that on stimulation with IL-23 produce pro-inflammatory cytokines including IL-17A and IL-22 (1) which drive inflammation and may also influence osteogenesis. Surprisingly, enthesis resident mesenchymal stem cells (MSCs) have not been phenotypically or functionally characterised.
Objectives: To determine if human enthesis including entheseal soft tissue and peri-entheseal bone harbours a population of MSCs. Furthermore, to investigate the effect of spondyloarthritis associated pro-inflammatory cytokines on MSC osteogenesis.
Methods: Samples from healthy the spinous process and interspinous ligament (male = 5, female = 10, median age = 19) were divided into entheseal soft tissue (EST) and peri-entheseal bone (PEB) and enzymatically digested (1). MSCs content was assessed using a CFU-F assay. Flow cytometry was used to examine expression of MSCs specific markers in plastic adherent cultures. Following osteogenic, chondrogenic and adipogenic inductions, osteogenesis was qualitatively by alkaline phosphatase and alizarin red staining and quantitatively by measurement of calcium accumulation. Chondrogenesis and adipogenesis were assessed using glycosaminoglycan assay and oil red o staining respectively. Osteogenic cultures were also supplemented with IL-17A (50ng/ml), IL-22 (10ng/ml) or TNF-α (1ng/ml).
Results: As a proportion of total cellularity EST developed approximately 5 fold more colonies than matched PEB ($p<0.0001$). Cultured cells were overwhelmingly positive for expression of MSC markers CD73, CD90, CD105 (PEB median 98.66% range: 95.17-98.96%, EST median 98.42% range: 87.69-98.7%) and negative for CD14, CD19, CD45 and HLA-DR (PEB median 0.34% range: 0-2.91%, EST median 1.1% range: 0-2.53%) however some CD34 expression was noted particularly in EST cultures (median 3.74% range: 0-29%). Both populations were capable of tri-lineage differentiation, although PEB MSCs had greater osteogenic ($p<0.025$) and lower adipogenic ($p<0.05$) potential than matched EST MSCs. Addition of IL-22 ($p<0.01$) or IL-17A ($p<0.005$) caused a significant decrease in the calcium deposited in PEB MSCs but not in EST MSCs.
Conclusion: Both the EST and PEB contain cells that meet the ISCT criteria defining MSCs. However, MSCs from these sources are functionally distinct in terms of their differentiation potential and response to inflammatory cytokines. The cytokines tested had a negative influence on osteogenesis in the conditions tested.

REFERENCES:

[1] CUTHBERT, R.J., E.M. FRAGKAKIS, R. DUNSMUIR, Z. LI, M. COLES, H. MARZO-ORTEGA, P.V. GIANNOUDIS, E. JONES, Y.M. EL-SHERBINY and D. MCGONAGLE. Brief Report: Group 3 Innate Lymphoid Cells in Human Enthesis. *Arthritis Rheumatol*, 2017, 69(9), pp.1816-1822.

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FRI0521

MIRNA-150 AS A NOVEL REGULATOR OF POST-TRAUMATIC OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a chronic joint disease causes irreversible damage to the articular cartilage resulting in loss of joint function and subchondral bone remodeling. There is no cure for OA and currently the available treatment like pain management, and joint replacement surgery is used to treat this disease. MiRNAs are small non-coding RNAs consist of 21-29 nucleotides which regulate gene expression by targeting the 3' untranslated region (UTR) leading to translation inhibition. In recent years, many studies showed that microRNAs could be a target for many diseases including OA. Our preliminary data on osteoactivin showed that the GPNMB acts as a protective protein in osteoarthritis by reducing catabolic gene expression. Our lab group results have been shown that miRNA-150 targets the 3'UTR of osteoactivin in osteoblast cells.
Objectives: There is no study regarding the role of miRNA 150 on cartilage homeostasis and because the miRNA 150 targets osteoactivin in lung and bone cells, we hypothesized that miRNA-150 targets osteoactivin in chondrocytes and protect cartilage ECM degradation.
Methods: RNAs were isolated from primary chondrocytes of miRNA- 150 knockout pups, then was used in qPCR to measure gene expression. Western blot used to detect MMP-3, MMP-9, MMP-13, IL-6, collagen type-II and aggrecan. In addition, histological analysis was used to test the role of miRNA-150 vivo through evaluating proteoglycan degradation by toluidine blue staining and immunohistochemistry after 12 weeks from DMM surgery. PCR transcription factors and signaling pathway finder array were used to elucidate the altered genes and transcriptions factors compared to the wild type in primary chondrocytes culture.
Results: Primary chondrocytes from 150 KO mice showed high mRNA expression levels of GPNMB compared to the wild type mice. Medial tibia plateau (MTP) and medial femur condyle (MFC) have been graded by OARSI scoring system after 12 weeks of DMM surgery. Histological results showed that the 150 KO mice have less cartilage damaged compared to the wild type. To determine whether epigenetic modifiers (miRNAs) regulating GPNMB/Osteoactivin expression can modulate the cartilage protective effects of GPNMB/Osteoactivin, we found that miRNA 150 targets GPNMB/Osteoactivin in chondrocytes. Next, we examined the effects of miRNA 150 deficiency on the OA progression in vivo and found that miRNA 150 KO are more protected against post-traumatic OA compared to WT mice. Furthermore, we assessed the expression of GPNMB/Osteoactivin in miRNA 150 KO chondrocytes and showed a significant increase compared to WT cells.
Conclusion: These results showed that miRNA is negative regulator of cartilage homeostasis and blocking miRNA might have therapeutic potential fort he treatment of age-related osteoarthritis and post-traumatic induced osteoarthritis.

REFERENCES:

The surgical destabilization of the medial meniscus (DMM) model of osteoarthritis in the 129/SvEv mouse. Methods in Molecular Biology: Osteoporosis and Osteoarthritis. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: A disease of the joint as an organ. Arthritis and Rheumatism. 2012. pp. 1697–1707.
[1] Zhou, L., Zhuo, H., Ouyang, H., Liu, Y., Yuan, F., Sun, L.,. .. & Liu, H. (2017). Glycoprotein non-metastatic melanoma protein b (Gpnmb) is highly expressed in macrophages of acute injured kidney and promotes M2 macrophages polarization. Cellular immunology, 316, 53-60.
[2] Ripoll, V.M., et al., Gpnmb is induced in macrophages by IFN-gamma and lipopolysaccharide and acts as a feedback regulator of proinflammatory responses. J Immunol, 2007. 178(10): p. 655766.

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FRI0522

MITOCHONDRIAL BACKGROUND IMPACT ON THE JOINT DEGENERATION PROCESS DURING AGING AND FORCED EXERCISE: A CONPLASTIC MOUSE MODEL

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Background: Several studies indicated that osteoarthritis has a strong genetic component with a prevalent role of mitochondria and mtDNA variations (1).

Objectives: In the present study, we aimed to investigated the influence of the mtDNA variation in the joint deterioration using mice with the same nuclear genome but different mtDNA variants (named conplastic mice) (2) during aging and forced exercise.

Methods: Conplastic mice (BL/6^{NZB}) strain was developed with the C57BL/6JOlaHsd nuclear genome and the NZB/OlaHsd mtDNA to compare with the original C57BL/6JOlaHsd strain (BL/6^{C57}). Knee joints from BL/6^{NZB} mice as well as from BL/6^{C57} mice were processed and cut into coronal sections. The mice were sacrificed at 25, 75 and 90 weeks of age and knee joints were collected for histological analysis. All sections were stained with Hematoxylin-Eosine and Safranin O-fast green and graded using a Mankin scoring system. Another group of mice from both BL/6^{NZB} and BL/6^{C57} strains were subjected to exercise by running in a treadmill 400m/day three times a week. After 75 and 90 weeks of age, mice were sacrificed and knee joints were processed for histological analysis. Cartilage expression of markers of autophagy like LC3 and metalloproteinases like MMP-13 were also analysed by immunohistochemistry in both strains. The results are given as mean ± SEM and statistical analysis was performed using non parametric unpaired t-test (Graph Pad Prism v 6.0).

Results: In response to aging, conplastic mice BL/6^{NZB} presented reduced cartilage Mankin score at 25 (p=0.0079), 75 (p=0.0087) and 90 (p=0.064) weeks when compared with mice of the original strain BL/6^{C57} at the same age. Specifically, we showed a reduced score in both femoral condyle (FC) and tibial plateau (TP) of BL/6^{NZB} mice that reached the statistical significance at 25 (FC: p=0.0317; TP: p=0.0079), 75 (FC: p=0.0411; TP: p=0.0238) and borderline the statistical significance at 90 (FC: p=0.0649; TP: p=0.0628) weeks of age. These results were accompanied with more expression of LC3 in cartilage from BL/6^{NZB} mice at 75 weeks when compared with cartilage from BL/6^{C57} at the same age (p=0.0152). We also reported a significant decrease of LC3 expression in cartilage from mice at 75 weeks when compared with mice at 25 weeks in both strains confirming the decrease of autophagy with aging. Difference in MMP13 cartilage expression between the two mice strains were also found. In the mice subjected to exercise, BL/6^{C57} presented an increased cartilage score in the medial compartment (p=0.0286) and lateral compartment (p=0.057) of the joint at 90 weeks when compared with BL/6^{NZB} mice at the same age.

Conclusion: This study demonstrated that aging and forced exercise in conplastic mice BL/6^{NZB} are associated with a reduced joint deterioration compared with the original strain BL/6^{C57}. Moreover, we showed that mtDNA variants can improve the aging process at joint level through the modulation of autophagy. These results support the hypothesis that mtDNA background has a role in the process of joint damage, suggesting that mtDNA has potential as novel therapeutic target in OA associated to aging.

REFERENCES:

[1] Mitochondrial DNA variation and the pathogenesis of osteoarthritis phenotypes. Nat Rev Rheumatol. 2018 Jun;14(6):327-340

[2] Mitochondrial and nuclear DNA matching shapes metabolism and healthy ageing; Latorre-Pellicer, et al. Nature2016;535(7613):561–5

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FRI0523

TLR-1/2 SIGNALING IMPAIRS MITOCHONDRIAL OXIDATIVE PHOSPHORYLATION IN CHONDROCYTES VIA THE INDUCTION OF NITRIC OXIDE

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Background: Osteoarthritis (OA) is a degenerative disease that causes progressive loss of joint function, representing a severe health problem plaguing this ageing world. Cartilage matrix degradation and catabolic factor production are closely associated with OA clinical symptoms[1]. Recent studies suggest that, metabolism is important for maintaining cartilage function, and aberrant metabolic activities in chondrocytes have been shown in various OA animal models and patients[2]. Despite the severity of OA, the initial triggers of this disease are mostly unknown. Small molecules generated during physiological catabolic reactions often function as damage-associated molecular patterns (DAMP) to activate innate immunity through receptors such as Toll-like receptors (TLR), resulting in enhanced expression of matrix metalloproteinases (MMP) and catabolic factors[3]. Here we studied the effect of various TLR signaling on chondrocyte protein production and mitochondrial oxidative phosphorylation (OXPHOS). We furthermore establish connections between catabolic factors and altered OXPHOS of chondrocytes, aiming to understand the underlying molecular mechanisms.

Objectives: This project is designed to investigate the roles of TLR signaling in the development of OA and the involved molecular mechanisms

Methods: Chondrocytes were obtained from the femural condyles of OA patients that underwent total knee arthroplasty in the Charité hospital. 3D spheroids were generated and cultured under physioxia (4.2% O2) with addition of TGF-β3. PGN, PolyI:C, LPS, Flagellin, FSL-I, Imiquimod, ssRNA, or CpG were used as agonist of TLR-1/2, -3, -4, -5, -2/6, -7, -8, or -9, respectively. Supernatants were collected, and culture medium were renewed twice per week. Pellets were weighted and processed for Alcian blue staining, or mRNA detection, or OXPHOS assay using Seahorse XFe96 Spheroid Mito Stress Test Kit. We used Griess reaction to quantify nitric oxide (NO) in the supernatant and L-NAME to block NO production. We used One-way ANOVA and t test for statistical analysis.

Results: TLR-1/2 and TLR-2/6 stimulation drastically impaired the cartilage matrix production, as they imposed the slowest pellet growth, lowest expression of matrix proteins COL2 and AGC1, but highest expression of matrix degrading enzymes MMP3, ADAMTS5, and the catabolic factor NO. Remarkably, this phenomenon is associated with drastically diminished OXPHOS activity, as shown by the reduction of both basal and maximal respiratory capacity. Moreover, blockade of NO production reversed the adverse effect imposed by TLR-1/2 stimulation, namely restored their OXPHOS activities and Col2 and AGC1 production in a dose-dependent manner.

Conclusion: Among the whole spectrum of TLR signaling, stimulation of TLR-1/2 and -2/6 impose the strongest inhibition on chondrocyte pellet growth by suppressing matrix protein synthesis and facilitating matrix degradation. TLR-1/2 stimulation causes the reduction of OXPHOS capacity, which is mediated by the induction of NO. Thus, TLR-1/2 stimulation, via inducing NO production, impairs the mitochondrial respiration in chondrocytes and thus possibly promotes the development of OA.

REFERENCES:

[1] Piotr Wojdasiewicz. et al. The Role of Inflammatory and Anti-Inflammatory Cytokines in the Pathogenesis of Osteoarthritis. Mediators Inflamm. 2014: 561459.

[2] Mobasheri A. et al. The role of metabolism in the pathogenesis of osteoarthritis. Nat Rev Rheumatol. 2017 13(5):302

[3] Orlowsky EW, Kraus VB. The role of innate immunity in osteoarthritis: when our first line of defense goes on the offensive. J Rheumatol. 2015 42 (3):363

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FRI0524 **HUMAN MONOCLONAL ACPAS INDUCE MOBILITY OF PRIMED SYNOVIAL FIBROBLAST IN A PAD-DEPENDENT PATHWAY**

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Background: Anti-citrullinated protein antibodies (ACPA) play an important role in rheumatoid arthritis (RA) pathogenesis. They recognize a wide number of citrullinated targets and show limited cross-reactivity to acetylated ones(*1*).
Objectives: We aimed to investigate the effect of monoclonal ACPAs with different binding patterns on RA synovial tissue derived fibroblasts (SF).
Methods: Synovial fibroblasts were isolated from synovial tissue of RA patients by enzymatic digestion. ACPA and control monoclonal antibodies (mAbs) were derived from single B cells isolated from RA patients. Two monoclonal ACPA (1325:01B09 and 1325:05C06) showed cross-reactivity to acetylated-targets while four of them (1325:04C03, 1325:07E07, 14CFCT2D09, 14CFCT2H12) did not(*1*). mAbs were tested in synovial fibroblast migration (Incucyte live time image analysis) and osteoclast formation (TRAP) assays. The role of mAbs cross-reactivity was tested in fibroblast migration assays using inhibitors of peptidylarginine deiminases (Cl-amidine), histone acetyltransferase (anacardic acid) and histone deacetylase (trichostatin A). Binding patterns of monoclonal ACPAs were tested in synovial biopsies obtained from both healthy donors and RA patients.
Results: One acetylation cross-reactive ACPA (1325:01B09) and two with no cross reactivity (14CFCT2D09 14CFCT2H12) significantly enhanced fibroblast migration (mean±SD fold increase of 1.9±0.5, 1.7±0.4 and 1.8±0.6, respectively) compared to control mAb 1362:01E02 ($p<0.05$), while having no effect on osteoclast formation. In contrast, one acetylation non-cross-reactive ACPA (1325:04C03) promoted osteoclastogenesis (mean±SD fold increase of 1.6 ±0.05) compared to control mAb 1362:01E02 ($p<0.05$), while having no effect on fibroblast migration. Cl-amidine completely abolished the effect of 1325:01B09, while neither anacardic acid nor trichostatin A had any effect. Moreover, the fibroblast-promoting ACPA (1325:01B09) but not the osteoclastogenic ACPA1325:04C03 co-localize with CD55-positive SF in the inflamed rheumatoid synovium. No detectable signals were found in healthy synovium.
Conclusion: Monoclonal ACPAs have distinct cellular effects on synovial fibroblasts and osteoclasts that are not related to cross reactivity towards acetylated targets

REFERENCES:

[1] K. A. Lloyd, G. Wigerblad, P. Sahlstrom, M. G. Garimella, K. Chemin, J. Steen, P. J. Titcombe, B. Marklein, D. Zhou, R. Stalesen, E. Ossipova, C. Lundqvist, O. Ekwall, J. Ronnelid, D. L. Mueller, M. C. I. Karlsson, M. J. Kaplan, K. Skriner, L. Klareskog, F. Wermeling, V. Malmstrom, C. Gronwall, Differential ACPA Binding to Nuclear Antigens Reveals a PAD-Independent Pathway and a Distinct Subset of Acetylation Cross-Reactive Autoantibodies in Rheumatoid Arthritis. Front Immunol 9, 3033 (2018).

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VISAFTIN-MEDIATED OSTEODESTRUCTIVE EFFECTS ARE REDUCED

FRI0525 **DURING ADIPOGENIC DIFFERENTIATION OF MSC ON MINERALIZED BONE FRAGMENTS**

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Background: Osteoporosis (OP), as an age-related disease, is characterized by bone loss, increased fracture risk and poor regeneration. During aging and OP bone marrow adiposity is increased due to a shift of osteogenic towards adipogenic differentiation of bone marrow mesenchymal stem cells (MSC). The differentiation of MSC into adipocytes or osteoblasts is an important determinant of bone structural integrity. It is known, that fatty tissue not simply functions as energy storage but is metabolically highly active. Therefore, adipocyte-derived factors such as adipokines might influence MSC differentiation.
Objectives: The role of interactions between adipocyte-derived factors and MSC in the pathogenesis of OP is not fully elucidated. Thus, we analyzed the presence of the adipokine visfatin in bone tissue and its effects on MSC differentiation in standard culture vs. spongiosa.
Methods: The spongiosa of femoral heads of patients with osteoarthritis (OA) after hip replacement surgery, or after osteoporotic femoral neck fracture were used for RNA- and MSC-isolation. Adipogenic MSC differentiation was performed with/without visfatin and its inhibitor Apo866 as well as SB203580 p38-MAPK inhibitor. For the transfer and differentiation of MSC on cancellous bone, bone fragments were purified and sterilized. Gene expression was measured by Realtime PCR. Protein production was evaluated by ELISA.
Results: Elevated visfatin-level were observed in OP compared to non-osteoporotic OA bone. Visfatin-induced secretion of proinflammatory factors was lower during adipogenesis on cancellous bone then in standard cell culture (e.g. 14d IL6, x-fold: standard culture 151±110, spong. 40±30, n=7). Significantly elevated MMP13 mRNA as well as protein expression induced by visfatin could be detected during adipogenesis on spongiosa as well as in standard cell culture. However visfatin-mediated MMP13 expression was markedly reduced in the presence of cancellous bone (e. g. 21d, x-fold: standard culture 81±89, spong. 13±21, n=7). Inhibition of visfatin by Apo866 decreased the visfatin-induced cytokine release but not the MMP13 expression during adipogenesis in culture (n=4). In contrast to Apo866, the p38-MAPK inhibitor did not influence cytokine release but reduced MMP13 expression in a time dependent manner.
Conclusion: Visfatin level was elevated in osteoporotic vs OA bone. Therefore, visfatin-mediated increase of MMPs and proinflammatory cytokines during adipogenic differentiation might influence bone turnover at the adipose tissue/bone interface. Our results support the idea that the extracellular matrix attenuates visfatin-mediated detrimental effects during adipogenesis. The observed visfatin-mediated effects most likely depend on different signaling pathways.
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FRI0526 **IL37 AMELIORATES EXPERIMENTAL MURINE OSTEOARTHRITIS**

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Background: Osteoarthritis (OA) is the world's most common degenerative joint disorder and leads to pain and disability. Currently, no disease-modifying drugs are available, resulting in a large unmet clinical need. Recently, we have shown that the anti-inflammatory cytokine IL37 lowers pro-inflammatory cytokine production, MMP3 activity and sulfated glycosaminoglycan loss from *ex vivo* cultured chondrocytes and human cartilage explants. In this study, we further explored the ability of IL37 to ameliorate OA pathology by studying its effects both *in vitro* on synovial fibroblasts and *in vivo* in collagenase-induced OA
Objectives: To establish if IL37 can ameliorate experimental OA pathology
Methods: Primary synovial fibroblasts were obtained from synovial biopsies of 10 patients undergoing total joint replacement surgery. IL37 was overexpressed in these cells using an adenovirus and subsequently cells were challenged with IL1β or OA-synovium conditioned medium. Collagenase-induced OA (CiOA) was induced by injecting 10 weeks old female C57BL/6J with a single intra-articular injection of 3 units of collagenase type VII. Four days after collagenase injection, Ad-IL37 or Ad-Luc (= control) was intra-articular injected in the right knee joint of mice. Two weeks later this injection was repeated. Mice were sacrificed on day 7, 28 and 42 after collagenase-injection. Synovial thickening, cartilage damage and osteophyte formation were measured histologically. IL37, MMP3 and VDIPEN expression were investigated by immunohistochemistry.

Results: In primary synovial fibroblasts, IL37 overexpression significantly reduced IL1β- and OAS-CM-induced expression of MMP1, MMP3, IL1B and IL6 by more than 50%. In naïve knee joints, IL-37 overexpression did not induce synovial thickening, cartilage damage or osteophyte formation and no overt immune response was detected after 28 days. Strikingly, in CiOA, at day 7, IL37 overexpression significantly reduced synovial thickening and the presence of the metalloproteinase-generated aggrecan-degradation neoepitope VDIPEN in cartilage. At day 28 of CiOA, cartilage degradation was significantly reduced by IL37 treatment at the lateral and medial femur by respectively 46% and 41%, and osteophyte size at the medial femur was reduced by 70%. At day 42 of CiOA, IL37 overexpression could no longer be detected. Osteophyte size formation at the medial femur was still significantly reduced by 46% at this time point, but only a trend (p = 0.06) towards reduced cartilage damage was observed on both femur and tibia.
Conclusion: Our results show that IL37 inhibits the production of catabolic mediators in synovial fibroblasts, similar to our previously obtained results in cartilage. Furthermore, IL37 clearly lowered synovial thickening and ameliorated cartilage damage and osteophyte formation in murine experimental OA. These results indicate that IL37 acts on multiple tissues and OA-related processes, which supports IL37 as a potential therapeutic agent for OA
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FRI0527 HIGH LDL LEVELS LESSEN BONE DESTRUCTION DURING ANTIGEN-INDUCED ARTHRITIS BY INHIBITING OSTEOCLAST FORMATION AND FUNCTION

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease with severe joint inflammation and bone destruction resulting from increased numbers and activity of osteoclasts as important hallmarks. RA is often associated with the metabolic syndrome, characterized by elevated levels of low-density lipoprotein (LDL), which in inflammatory environments is oxidized into oxLDL. However, the effects of high (ox)LDL levels on osteoclasts remains elusive.
Objectives: Here, we investigated the effects of high LDL and oxLDL levels on osteoclast differentiation and bone destruction.
Methods: Antigen-induced arthritis (AIA) was induced in *Apoe*$^{-/-}$ mice that spontaneously develop high LDL levels. Bone erosion was assessed with histology and numbers of osteoclasts were determined with staining for tartrate-resistant acid phosphatase (TRAP). Numbers of CD11b^{+}/Ly6C^{high} and CD11b^{-}/Ly6C^{high} osteoclast precursors were determined by flow cytometry. *In vitro* osteoclast differentiation from bone marrow cells was induced with macrophage colony-stimulating factor (M-CSF) and receptor activator of nuclear factor kappa-B (RANK) for 7 days. Pre-osteoclasts from day 3 and mature osteoclasts from day 6 of differentiation were exposed to LDL/oxLDL. Gene expression was determined with qPCR.
Results: Whereas basal levels of bone resorption were comparable between WT and *Apoe*$^{-/-}$mice, induction of AIA resulted in significantly lower bone resorption in *Apoe*$^{-/-}$ mice as compared to WT mice, which was associated with lower number of TRAP^{+} osteoclasts along the bone surface. However, the absence of *Apoe* did not result in altered numbers of osteoclast precursors in the bone marrow of naïve mice, whereas even increased numbers were observed in *Apoe*$^{-/-}$ mice during AIA. Moreover, *in vitro* osteoclastogenesis showed comparable numbers and mRNA expression of osteoclast markers, such as c-Fms, RANK, NFATc1, DC-STAMP, TRAP, CTR, ClC-7, CA-II, Cat K and MMP-9. Together, this showed that the absence of *Apoe* by itself does not affect osteoclastogenesis. Therefore, we determined whether high levels of LDL cholesterol, a characteristic of *Apoe*$^{-/-}$ mice, or oxLDL as the result of LDL oxidation by inflammation led to decreased osteoclast differentiation. Addition of oxLDL, but not LDL, to pre-osteoclasts from day 3 and mature osteoclasts from day 6 of osteoclastogenesis strongly reduced the number of TRAP^{+} osteoclasts and their resorptive capacity. This was accompanied by a decreased expression of various osteoclast markers. To determine the mechanism of how oxLDL stimulation might reduce the osteoclast differentiation, we determined the expression of RANK and various members of the co-stimulatory pathway that promotes osteoclast formation. Interestingly, whereas RANK expression was not affected upon oxLDL exposure, we observed decreased expression of osteoclast -associated receptor (*Oscar*) and the DNAX adaptor protein-12 encoding gene *Tyrobp*, which regulate the immunoreceptor tyrosine-based activation motif (ITAM) mediated co-stimulation signaling pathway.
Conclusion: *Apoe*$^{-/-}$ mice have decreased bone resorption during experimental RA, probably via oxLDL-mediated interference in the co-stimulatory pathway during osteoclastogenesis.
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FRI0528 HIGH INTENSIVE THERAPEUTIC LOWERING OF SYSTEMIC CHOLESTEROL DOES NOT AMELIORATE OA DEVELOPMENT IN KNEE JOINTS OF HUMANIZED DYSLIPIDEMIC MICE

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Background: High systemic cholesterol levels have been associated with osteoarthritis (OA) development and lowering cholesterol using statins has been suggested as a potential treatment for OA[1]. Recently, novel therapeutic high-intensive cholesterol-lowering treatment has been shown to regress Western-type diet (WTD)-induced atherosclerosis in dyslipidemic APOE*3Leiden.CETP mice, a translational model with a human-like lipoprotein metabolism[2].
Objectives: Here, we investigated the potency of these therapeutic cholesterol-lowering strategies to attenuate OA development in dyslipidemic APOE*3Leiden.CETP mice.
Methods: Female mice (n=13-16 per group) were fed a cholesterol-supplemented WTD for 38 weeks. After 13 weeks, mice were matched into a baseline group (sacrificed at t=13w) and 5 groups that received WTD alone or with treatment for 25 weeks: atorvastatin alone (A), in combination with PCSK9 inhibitor alirocumab (AA) or ANGPTL3 inhibitor evinacumab (AE) or triple treatment (AAE). Plasma lipids were monitored to assess metabolic dysfunction. Knee joints were analysed for cartilage degradation, synovial inflammation and osteophyte formation. Aggrecanase activity and S100A8 expression were determined using immunohistochemistry.
Results: Systemic administration of cholesterol-lowering interventions resulted in a significant reduction of body weight (A: -16%; AA: -8%; AE: -12%; AAE: -18% at end point) without changes in food intake. WTD-feeding manifested itself in dyslipidemia, with high cholesterol levels that were significantly reduced after administration of therapeutic cholesterol-lowering interventions (A: -46%; AA: -74%; AE: -74%; -AAE: 86% at end point). Using detailed OARSI scoring, dyslipidemic mice showed a mild but significant increase in cartilage degeneration at end point (7.8 ± 1.9) compared to baseline controls (3.8 ± 1.8, 2.1-fold increase, p=0.001), and a strong 52-fold increase in NITEGE staining, representing proteolytic activity by aggrecanases[3]. However, therapeutic cholesterol lowering did not ameliorate further progression of cartilage destruction. This was supported by comparable NITEGE staining in all treatment groups at end point. Dyslipidemic APOE*3Leiden.CETP mice developed minor synovial inflammation which was not affected by cholesterol-lowering interventions. Alarmin S100A8, a marker for macrophage activation, showed minor expression in the synovial lining of all treatment groups, supporting the absence of joint inflammation in this model[4]. Finally, we determined whether high plasma cholesterol levels promoted osteophyte formation. The total number of osteophytes and osteophyte maturation stage was comparable between all groups despite reduction of systemic cholesterol levels.
Conclusion: Therapeutic cholesterol-lowering interventions did not slow the progression of cartilage degradation and osteophyte formation in dyslipidemic APOE*3Leiden.CETP mice with minor joint inflammation. These findings suggest that therapeutic cholesterol-lowering interventions in the absence of local inflammation within the knee joint cannot prevent progression of OA.

REFERENCES:
[1] Gierman, LM, Ann Rheum Dis, 2014; 73, 921-927.
[2] Dewey, F.E., *New Engl J Med* 2017; 377, 211-221.
[3] van Meurs JB, Arthritis Rheum 42, 1999; 42, 1128-1139.
[4] van Lent PL, *Arthritis & Rheumatism* 2012; 64, 1466-1476.

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FRI0529 SPREAD OF SENESCENCE AND JOINT INFLAMMATION VIA CONNEXIN43-POSITIVE EXOSOMES RELEASED BY OSTEOARTHRITIC CHONDROCYTES

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Background: Chondrocytes (CHs) in articular cartilage undergo phenotypic changes and senescence, restricting cartilage regeneration and favoring osteoarthritis (OA) progression. CHs and synovial cells from OA patients show a chronic increase in the channel protein connexin43 (Cx43), which regulates signal transduction. Extracellular vesicles (EVs), including exosomes, have been shown to play important roles in many biological functions and harbour Cx channels that allow the formation of gap junctions (GJs) between the exosome and the target cell, but the role of these EVs and exosomal-Cx43 in OA progression has not been studied yet.
Objectives: The objective of this study was to investigate the role of EVs released by OA chondrocytes (OACs) in cellular plasticity, inflammation and senescence of surrounding joint tissues.
Methods: CHs, bone and synovial cells were isolated from healthy and OA donors. EVs were obtained by ultracentrifugation and their protein content was analysed by LC-MS/MS. Protein levels were evaluated by western blot, immunofluorescence and flow cytometry. RNA expression was evaluated by RT-qPCR. Senescence and GJ intercellular communication was studied by flow cytometry and scrape loading assay, respectively.
Results: OACs showed increased levels of Cx43 within their EVs in comparison to the EVs isolated from healthy donors. Overexpression of Cx43 in CHs increased senescence and exosomal Cx43 levels. Interestingly, the treatment of CHs, bone cells and synoviocytes (target cells) with Cx43-EVs released by OACs, led to a significant increase in both Cx43 mRNA and protein levels in the recipient cells. The increase of Cx43 in target cells acted as a positive regulator of the reversion to a less differentiated state via EMT by activation of Twist-1, associated with increased levels of the mesenchymal markers, as CD105/CD166. The phenotypic changes detected in OACs lead to a decrease in Col2A1 and aggrecan expression in CHs, and increased the levels of cellular senescence and the senescence associated secretory phenotype (SASP) in the target cells in target cells via p53/p16 and NF-kß. These results were corroborated by analysing the protein cargo of these Cx43 positive EVs by LC-MS/MS, finding enrichment in proteins related with catabolic, senescence and wound-healing pathways.
Conclusion: Our results indicate that Cx43-positive exosomes released by OACs may be involved in the spread of cellular senescence and inflammation involved in wound healing failure. Further understanding of the role of exosomal Cx43 in OA will help to halt the disease spread and progression.
Disclosure of Interests: : None declared
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FRI0530 ADIPOSE DERIVED STEM CELLS TRANSPLANTATION AMELIORATES OSTEOARTHRITIS THROUGH AUTOPHAGY INDUCING VIA PI3K/AKT/MTOR SIGNALING

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Background: Osteoarthritis is characterized by joint inflammation and cartilage degradation. Adipose derived stem cells (ADSCs), as a source of adult mesenchymal stem cells, display similar multiple-linage differentiating potentials to bone marrow MSCs, only are much more abundant, much easier to isolate and expand, have been suggested for suppressing inflammatory responses and repairing cartilage damage. Autophagy are known to be take part in the pathogenesis of OA. Aging related changes of chondrocytes were related to increased mammalian target of rapamycin (mTOR) signaling and defective autophagy (1). We aim to determine the effect of ADSC on autophagy and its underlying mechanism.
Objectives: To investigate the effect of ADSCs on autophagy in a rat osteoarthritis model and IL-1-induced chondrocytes, and to ascertain whether it regulates autophagy via PI3K/AKT/mTOR signaling.
Methods: ADSCs and chondrocytes were isolated from SD rats. Flow cytometry was performed for ADSC phenotypic characterization. ADSCs and chondrocytes coculture were established in the presence of IL-1β. A rat anterior cruciate ligament transection (ACLT) OA model were established. ADSCs or irrelevant cell lines of similar number were injected in the osteoarthritis-affected joints. Autophagic activation was determined by Western blotting for LC3-II, p62, MDC (monodansylcadaverine) staining and GFP-LC3 fluorescence microscopy. Autophagy inhibition was mediated by siRNA knockdown of ATG5. Relevant proteins in the PI3K/AKT/mTOR signaling pathway were detected by western blotting. IL-1β, IL-6, TNFα, IFN-γ, Col2, MMP-1, 3 and -13 were measured. Histology of the target joints were evaluated.
Results: Application of ADSCs resulted in downregulation of MMP13 and upregulation of Col2 in OA model cartilage and IL-1β induced chondrocytes. ADMSCs decreased pro-inflammatory cytokines IL-1β, IL-6, and TNF-α in rat OA and IL-1β-induced chondrocytes. Autophagy was inhibited in OA model and IL-1β induced chondrocytes. ADSCs increased cell viability and autophagy-related proteins levels in vitro and in vivo. In IL-1β induced chondrocytes with ATG5 knockdown by siRNA, the effect of ADSCs on autophagy activation and its function as suppression of IL-1β induced pro-inflammatory cytokines was undermined. Furthermore, ADSCs remarkably decreased the expressions of phosphorylated (p)-PI3K, p-AKT and p-mTOR in IL-1β induced chondrocytes.
Conclusion: ADSCs inhibited the progression of cartilage degeneration in a rat OA model and provide an effective approach to decrease the pro-inflammatory cytokines secretion. ADSCs' anti-inflammatory effect was associated with cell autophagy and these roles of ADSCs may be associated with PI3K/AKT/mTOR signaling pathway.

REFERENCES:

[1] Alvarez-Garcia O, Olmer M, Akagi R, Akasaki Y, Fisch KM, Shen T, Su AI, Lotz MK. Suppression of REDD1 in osteoarthritis cartilage, a novel mechanism for dysregulated mTORsignaling and defective autophagy.Osteoarthritis Cartilage. 2016; 24(9):1639-47.

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FRI0531 THE ARTICULAR PROTECTION EFFECT OF ISORHAMNETIN IN THE RATS OF MONOSODIUM IODOACETATE-INDUCED OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a degenerative joint disease with damage to the articular cartilage. Active production of inflammatory cytokine/chemokine and matrix metalloproteinases may be found during the progression of OA. Isorhamnetin had the effects of anti-inflammatory, antioxidant, anti-ischemia, anti-atherosclerotic hepatoprotective and anticancer activities.
Objectives: Our study was focused on the effects of isorhamnetin treatment in OA.
Methods: We used monosodium iodoacetate (MIA)-induced OA rats to evaluate the effects of isorhamnetin related anti-inflammatory process. The rats in all groups were sacrificed on four weeks post-MIA injection. The measurements of knee joint swelling, histological analysis, serum inflammatory biomarkers and Western blot were evaluated.
Results: We found that isorhamnetin may reduce MIA-induced knee swelling by significantly reduction of articular cartilage damage in rats. The severity of OA lesion was graded using the modified Mankin scoring system, and we found that the overall modified Mankin's scores were significantly decreased after isorhamnetin treatment compared with a MIA-treated group. The production of IL-1β, IL-6, and TNF-α decreased in isorhamnetin treatment group compared with MIA alone group.

Isorhamnetin inhibited the production of NO and PGE2, and the expression of iNOS and COX-2. The production of COMP and CTX-II were also inhibited in MIA-induced OA rats.
Conclusion: Isorhamnetin may modulate the inflammatory progression of OA in MIA-induced OA rats. The prevention of cartilage damage was found in OA after adequate isorhamnetin treatment. Isorhamnetin may serve as a potential agent for the management of OA.

REFERENCES:
[1] Sellam J, Berenbaum F. The role of synovitis in pathophysiology and clinical symptoms of osteoarthritis. Nat Rev Rheumatol 2010; 6: 625-635.
[2] Manu KA, Shanmugam MK, Ramachandran L, et al. Isorhamnetin augments the anti-tumor effect of capeciatbine through the negative regulation of NF-kappaB signaling cascade in gastric cancer. Cancer Lett 2015; 363: 28-36.
[3] Chen TL, Zhu GL, Wang JA, et al. Protective effects of isorhamnetin on apoptosis and inflammation in TNF-alpha-induced HUVECs injury. Int J Clin Exp Pathol 2015; 8: 2311-2320.

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FRI0532 SONIC HEDGEHOG PROMOTES PROLIFERATION, MIGRATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS VIA P38-MAPK SIGNALING

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Background: Abnormal activation of Sonic hedgehog (Shh) signaling has been found in synovium from patients with rheumatoid arthritis and inhibition of Shh signaling pathway suppresses the proliferation and migration of fibroblast-like synoviocytes in rheumatoid arthritis (RA-FLS). However, the mechanism how Shh signaling promotes tumor-like behavior of RA-FLS is not well elucidated.
Objectives: In this study, we aimed to investigate the effect of Shh on p38 MAP kinase signaling and hypothesized that Shh promotes proliferation, migration and invasion of RA-FLS via p38-MAPK signaling.
Methods: Cultured RA-FLSs were treated with Smoothened agonist (SAG) or IL-1β combined with Smoothened antagonist (Cyclopamine). The levels of phosphorylation of p38, its upstream kinases including TGFβ activated kinase 1 (TAK1), MKK3, MKK6 and downstream target MAPKAPK2 (MK-2) were determined by western blot. The functional state of p38 was determined using in vitro kinase assay. Cell proliferation was evaluated by Cell Counting Kit -8 assay. Cell migration and invasion were performed by Transwell assay. The expression of matrix metalloproteinase proteins (MMPs), IL-6 and IL-8 was examined by real-time PCR.
Results: SAG rapidly increased phosphorylation of p38, TAK1, MKK3, MKK6 and MK2 in RA-FLS and combination of SAG and p38 inhibitor significantly decreased the phosphorylation of these kinases (P<0.01). Inhibition of Shh significantly decreased the levels of phosphorylation of p38, TAK1, MKK3, MKK6 and MK2 in IL-1β stimulated RA-FLS (P<0.05). In vitro kinase assay showed that stimulation of SAG significantly increased the kinase activity, and the kinase activity was inhibited by p38 inhibitor. Furthermore, SAG increased cell proliferation, migration, invasion and production of MMP1, MMP3, MMP13, IL-6 and IL-8. However, these enhanced activities of RA-FLS were inhibited in the presence of p38 inhibitor.
Conclusion: The study indicates that Shh is associated with activation of p38 MAPK signaling in RA-FLS and Shh may promote the tumor-like behavior of RA-FLS via p38 signaling.
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Paediatric rheumatology

FRI0533 ETHNICITY AND NEONATAL LUPUSRISK IN A LARGE MULTI-ETHNIC COHORT

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Background: Neonatal Lupus (NL) is an acquired autoimmune disorder of newborns secondary to the transplacental passage of maternal anti-Ro and/or anti-La. Approximately 2% of children exposed to these antibodies develop NL. Prior studies have suggested that babies of non-European ancestry have a higher proportion of cardiac NL when compared to babies of European ancestry. This finding has not been consistently replicated.
Objectives: To examine the association between ethnicity and clinical manifestations of NL in our multi-ethnic population.
Methods: We conducted a cohort study of our large, multi-ethnic NL clinic population. The Neonatal Lupus clinic at the Hospital for Sick Children, Toronto, Canada was established in 1986. Children born to anti-Ro and/or anti-La antibody positive mothers are referred to the NL clinic. Antenatal testing is completed due to maternal rheumatologic diagnosis, a prior child born with NL and/or a history of symptoms that prompted physician testing for these antibodies. Beginning in 2011, families routinely reported ethnicity (Canadian census categories). We divided our NL patient cohort in European and non-European groups; the non-European group includes patients of African, Latin American, East Asian, South Asian and Mixed non-European ancestry (i.e. combination of two or more of non-European ethnicities). We included children assessed in the NL clinic ≤ 1 year of age between January 2011 to April 2018. There were 59 children censored for this analysis (7 missing ethnicity and 52 Mixed European-Non European ancestry). We analyzed prospectively collected data from our NL database, on specific NL manifestations: cardiac (heart block, myocarditis, endocardial fibroelastosis), dermatologic (typical rash of NL), hematologic (cytopenias), hepatic (transaminitis) and neurologic (macrocephaly). The frequency of NL clinical manifestations was compared among ethnicity groups (Fisher's exact test). We tested the association between ethnicity and NL clinical manifestations in logistic models.
Results: Our study included 301 children, 149 (50%) female and 164 (55%) with NL (Table 1). The median follow-up period was 12.2 months (IQR: 4.8, 28.8 months). Ethnicity data was available for 294 (98%) of the children. The non-European group (40%) was comprised of East Asian (14%), South Asian (13%), African (10%), Latin American (2%) and Mixed Non-European ancestry (17%). We did not observe a difference between European and Non-European babies in the proportion with NL, nor any difference in the frequency of specific NL manifestations (p-values > 0.3).
Conclusion: In our multiethnic NL cohort of children born to mothers with positive anti-Ro and/or anti-La antibodies, there was no association between ethnicity and NL, nor specific NL manifestations. Future analyses will examine the effect of maternal ethnicity and rheumatic disease status on the risk of NL and specific NL manifestations.

REFERENCES:
[1] Neiman AR, Lee LA, Weston WL, Buyon JP. Cutaneous manifestations of neonatal lupus without heart block: Characteristics of mothers and children enrolled in a national registry. J Pediatr. 2000;137(5):674–80.
[2] Izmirly PM, Saxena A, Kim MY, Wang D, Sahl SK, Llanos C, Friedman D, Buyon JP. Maternal and fetal factors associated with mortality and morbidity in a multi-racial/ethnic registry of anti-SSA/Ro associated cardiac neonatal lupus. Circulation. 2011;124:1927–1935.

Table 1. Neonatal Lupus Clinical Manifestations in European and non-European children.

	European n = 99 (%)	Non-European n = 143 (%)	p-value
Female	45 (45%)	72 (50%)	0.51
NL	48 (48)	80 (56)	0.29
Cardiac	10 (21)	11 (14)	0.32
Dermatologic	11 (23)	19 (24)	1.00
Hematologic	18 (38)	33 (41)	0.71
Hepatic	26 (54)	42 (53)	1.00
Neurologic	6 (13)	4 (5)	0.17

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FRI0534 ORAL GLUCOCORTICOIDS AND NEWLY TREATED DIABETES MELLITUS, HYPERTENSION, AND THROMBOSIS IN CHILDREN WITH CHRONIC DISEASES

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Background: Systemic glucocorticoid use is associated with a well-known spectrum of toxicities. Nonetheless, the risks of cardiometabolic complications in children are poorly understood.

Objectives: We sought to quantify rates of newly treated diabetes mellitus, hypertension, and venous thromboembolism (VTE) associated with oral glucocorticoid exposure in children. We hypothesized that oral glucocorticoids were associated with each complication in a dose-dependent manner, most strongly with current or recent glucocorticoid exposure.

Methods: Using Medicaid claims data (2000-2010), we identified children ages 1-18 diagnosed with immune-mediated diseases (inflammatory bowel disease, juvenile idiopathic arthritis, or psoriasis) or a non-immune comparator condition (attention-deficit/hyperactivity disorder) based on diagnostic codes ± pharmacy claims. We studied time-varying oral glucocorticoid exposures using pharmacy claims after a ≥6-month glucocorticoid-free baseline period, categorizing dose as low (<0.25 mg/kg/day), medium (0.25-0.99 mg/kg/day), or high (≥1 mg/kg/day) based on prescribed prednisone-equivalent dosage and age-/sex-imputed weights. Primary outcomes were incident treatment of diabetes (type 1 or 2), hypertension, and VTE. We used Cox regression and weighted cumulative exposure models[1] to estimate adjusted hazard ratios (aHRs) and number needed to harm (NNH) for varying patterns of glucocorticoid exposure.

Results: We followed 932,517 children (21.3% glucocorticoid-exposed) for 1.6 million person-years. Glucocorticoid usage varied by disease (Table). After adjusting for age, sex, race/ethnicity, calendar year, inclusion diagnosis, comorbidities, other medications, and healthcare usage, we found strong dose- and time-dependent relationships between glucocorticoid exposure and rates of newly treated diabetes, hypertension, and VTE (Figure 1). These effects increased with longer durations of exposure and declined within 6 months after stopping (Figure 2). Sustained low-dose exposures (e.g., 0.1 mg/kg/day) appeared relatively safe (aHR<1.2), but risks increased even with brief high-dose exposures (2 mg/kg/day x7 days) (aHR 1.7-2.2). Risk differences were highest for hypertension (number needed to harm [NNH]: 2 mg/kg/day x7 days, 6,206-17,894; 2 mg/kg/day x30 days, 233-671) and lowest for VTE (NNH: 2 mg/kg/day x7 days, 54,886-612,350; 2 mg/kg/day x30 days, 1,977-22,045). Absolute risks were higher for children with immune-mediated diseases (e.g., diabetes, 2 mg/kg/day x30 days, NNH: 424-691) than for those with ADHD (NNH: 959).

Table. Distribution of dose and duration of oral glucocorticoids by disease cohort.

Cohort	Aspect	25th %	50th %	75th %
ADHD	Duration	5	5	7
ADHD	Dose	0.41	0.74	1.24
IBD	Duration	5	27	47
IBD	Dose	0.29	0.59	0.92
JIA	Duration	5	9	30
JIA	Dose	0.16	0.33	0.88
PSO	Duration	5	6	10
PSO	Dose	0.3	0.63	1.14

Units: duration, days; dose, mg/kg/day.

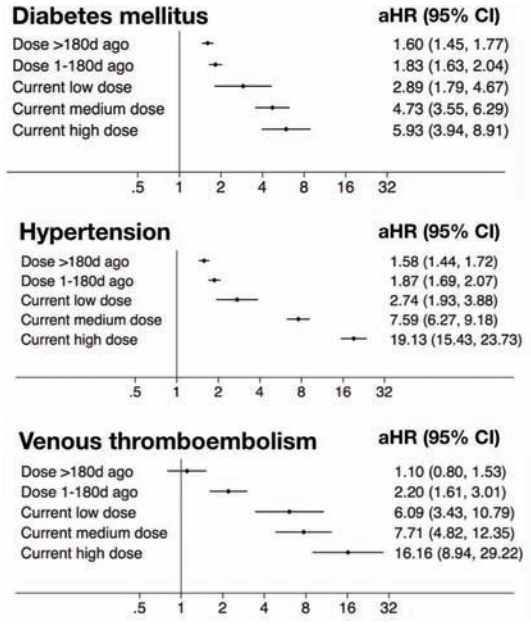


Figure 1. Associations of glucocorticoid timing and dose with newly treated outcomes based on Cox regression models.

aHR, adjusted hazard ratio; CI, confidence interval

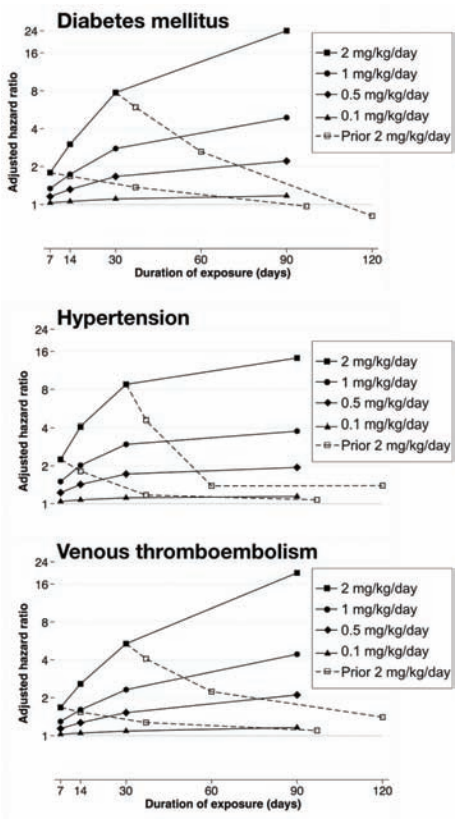


Figure 2. Associations of glucocorticoid timing and dose with newly treated outcomes based on weighted cumulative exposure models.

Line plots show associations of daily glucocorticoid dose, duration, and recency with outcomes.

Conclusion: In children with various chronic conditions, current oral glucocorticoid use is strongly associated with newly treated diabetes, hypertension, and VTE in a dose- and duration-dependent fashion. Hypertension is a more common glucocorticoid-related complication than diabetes or VTE, but in absolute terms, all of these complications are uncommon in children.

REFERENCES:

[1] Sylvestre MP, Abrahamowicz M. Stat Med. 2009;28(27):3437-3453.

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FRI0535

COMPARISON OF SERUM BIOMARKERS FOR THE DIAGNOSIS OF MACROPHAGE ACTIVATION SYNDROME COMPLICATING SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: CLINICAL SIGNIFICANCE OF SERUM NEOPTERIN LEVELS

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Background: Macrophage activation syndrome (MAS) is a severe life-threatening condition that complicates systemic juvenile idiopathic arthritis (s-JIA). Differentiating MAS from these conditions is essential for selecting appropriate therapeutic interventions in a timely manner. However, there is no definite biomarkers that can effectively diagnose MAS.

Objectives: Our study aimed to compare the accuracy of serum biomarkers for the diagnosis of MAS complicating s-JIA and to investigate the clinical significance of serum neopterin levels as an indicator of disease activity and diagnosis of MAS complicating s-JIA.
Methods: Serum cytokine levels (neopterin, IL-18, and CXCL9 and soluble tumor necrosis factor receptor type I (sTNFR-I) and II were determined by enzyme-linked immunosorbent assay in 78 patients with s-JIA, including 21 with MAS. The accuracy of these levels for the diagnosis of MAS were compared. Next, serum neopterin levels, in total 125 patients with s-JIA, including 30 with MAS, 15 with Epstein–Barr virus-induced hemophagocytic lymphohistiocytosis (EBV-HLH), and 15 with Kawasaki disease (KD), as well as 28 healthy controls (HCs) were analysed. Results were compared with the clinical features of MAS.
Results: Receiver operating characteristic curve analysis revealed area under the curve values and cut off values of neopterin, IL-18, CXCL9, sTNFR-II/I ratio and ferritin were 0.9465/19.5nmol/l, 0.8895/69250ng/ml, 0.9333/3130pg/ml, 0.9395/3.796 and 0.8671/2560ng/ml, respectively. Serum neopterin levels were significantly elevated in patients with MAS and EBV-HLH compared with those in patients with acute-phase s-JIA and KD. Serum neopterin levels profoundly and rapidly increased as MAS developed and correlated positively with disease activity.
Conclusion: Serum neopterin levels may be used as a promising indicator of disease activity in s-JIA and MAS and for evaluating it. It may also be a useful marker to diagnose the transition to MAS from active-phase s-JIA.

REFERENCES:
[1] Huber C, et al. J Exp Med 1984;160:310-6.
[2] Bracaglia C, et al. Ann Rheum Dis 2017;76:166-72.
[3] Shimizu M, et al. Clin Exp Immunol 2018;191:349-355.

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FRI0536 FAMILIAL MEDITERRANEAN FEVER (FMF): A SINGLE CENTEREXPERIENCE FROM TURKEY

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Background: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease mainly affecting ethnic groups living at Mediterranean region. Since the discovery of the *Mediterranean FeVer* (*MEFV*) gene, molecular genetic testing has been used as a diagnostic adjunct especially in atypical cases (1, 2). Although substantial progress had been achieved about the etiopathogenetic mechanisms of FMF during the past 20 years, the diagnosis is still based on clinical criteria.
Objectives: To define the demographic, clinical and laboratory characteristics of children with FMF and then to compare the identification capacity of 3 validated FMF diagnostic criteria (Tel-Hashomer, Livneh and Pediatric) at our cohort (3-5).
Methods: The medical records of 1685 children diagnosed and followed up as FMF were reviewed retrospectively. All patients were evaluated for three diagnostic criteria.
Results: A total of 1685 children (839 girls, 846 boys) were involved to the study. Family history of FMF was positive in 46.1%. The mean ±standard deviation of current age, age at symptom onset, age at diagnosis were 13±5.4, 5.4±4.05, 7.9±4.1 years, respectively. Median (min-max) follow-up period was 3 (0.5-18) years. Among 1685 patients, 82.8% had fever, 78.2% had abdominal pain, 36.1% had arthritis, 22.6% had chest pain and 16.6% had erysipelas-like erythema. Three patients had biopsy proven amyloidosis. Concomitant disease was present in 140 (8.3%) patients. Most of them (40.7%) were diagnosed with juvenile idiopathic arthritis and FMF. Henoch-Schönlein vasculitis was observed in 35 (25%) patients. Median (min-max) PRAS score was 7 (3-13). Forty-four patients (2.6%) were unresponsive to adequate doses of colchicine. Among them, 16 (36.4%) were treated with anakinra and 28 (63.6%) received canakinumab. Children homozygous for *M694V* were found to have more severe course of disease and higher PRAS scores ($p<0.001$). Furthermore, 34 (77.3%) of colchicine resistant patients carried at least one *M694V* variant. When we applied the diagnostic criteria to our cohort, 99.5% met the Livneh criteria, 91.6% fulfilled the pediatric criteria and 82.9% satisfied the Tel-Hashomer criteria.
Conclusion: This is the largest pediatric cohort studied and presented since now. We believe that the large number of our cohort is convincing at the point of discussing phenotype-genotype relations. We confirmed that carrying *M694V* mutation is associated with increased disease severity. On the other hand, we compared two adult and one pediatric validated diagnostic criteria at a largest group of children with FMF.

REFERENCES:
[1] Ancient missense mutations in a new member of the RoRet gene family are likely to cause familial Mediterranean fever. The International FMF Consortium (1997). Cell 90:797-807
[2] A candidate gene for familial Mediterranean fever (1997). Nat Genet 17:25-31.
[3] Sohar E, Gafni J, Pras M, Heller H (1967) Familial Mediterranean fever. A survey of 470 cases and review of the literature. The American journal of medicine 43:227-253
[4] Livneh A, Langevitz P, Zemer D, Zaks N, Kees S, Lidar T, Migdal A, Padeh S, Pras M (1997) Criteria for the diagnosis of familial Mediterranean fever. Arthritis and rheumatism 40:1879-1885.
[5] Yalcinkaya F, Ozen S, Ozcakar ZB, Aktay N, Cakar N, Duzova A, Kasapcopur O, Elhan AH, Doganay B, Ekim M, Kara N, Uncu N, Bakkaloglu A (2009) A new set of criteria for the diagnosis of familial Mediterranean fever in childhood. Rheumatology (Oxford, England) 48:395-398.

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FRI0537 LONG-TERM OUTCOMES AND TREATMENT EFFICACY IN PATIENTS WITH TNF RECEPTOR-ASSOCIATED AUTOINFLAMMATORY SYNDROME (TRAPS): A SERIES OF 290 CASES FROM THE EUROFEVER/EUROTRAPS INTERNATIONAL REGISTRY

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Background: Tumour necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) is one of the best known monogenic auto-inflammatory disorder resulting from an autosomal dominant variation in the TNF super family receptor 1A (*TNFRSF1A*) gene.
Objectives: To define best treatment approach in patients with TRAPS and effect on long-term outcomes.
Methods: We reviewed all data on patients with *TNFRSF1A* variants enrolled in the Eurofever/EUROTRAPS international registry.
Results: Data on 290 patients were available. Patients with R92Q, P46L or intronic variants (49%) displayed milder disease than 147 patients with mutations affecting other coding regions, with less frequent abdominal pain and skin rashes ($P<0.01$), higher efficacy rate of colchicine as maintenance treatment, and none developed AA amyloidosis. Almost 90% of patients with exon mutations required maintenance therapy. Anti-interleukin (IL) 1β drugs were the most frequently used (47 patients), with the highest efficacy rate (>90% complete response), while Etanercept was less effectively used and discontinued in 72% of patients. No patients on anti-IL1β treatment developed amyloidosis and 10 patients with amyloidosis have been successfully treated with anti IL-1 agents with preservation of native renal function in 7 and excellent long-term transplant function in 2. Nine women had a history of failure to conceive and seven had successful pregnancies without fertility treatment following complete disease control with anti-IL1β drugs. Long term safety profiles for anti IL-1 agents were excellent even in the presence of comorbidity.
Conclusion: Anti-IL1β drugs are the best maintenance treatment in TRAPS with potential to reverse the most serious disease complications of AA amyloidosis and infertility. The diagnosis of TRAPS should be considered very carefully in patients carrying R92Q, P46L or intronic *TNFRSF1A* variants.

REFERENCES:
[1] Lachmann HJ, Papa R, Gerhold K, Obici L, Touitou I, Cantarini L, et al. The phenotype of TNF receptor-associated autoinflammatory syndrome (TRAPS) at presentation: a series of 158 cases from the Eurofever/EUROTRAPS international registry. Annals of the rheumatic diseases. 2014;73 (12):2160-7.
[2] Papa R, Doglio M, Lachmann HJ, Ozen S, Frenkel J, Simon A, et al. A web-based collection of genotype-phenotype associations in hereditary

recurrent fevers from the Eurofever registry. Orphanet Journal of Rare Diseases. 2017;12(1):16.
[3] Papa R, Lachmann HJ. Secondary, AA, Amyloidosis. Rheum Dis Clin North Am. 2018;44(4):585–603.

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FRI0538 MAY SOME OF THE MEFV GENE VARIANTS CAUSE PFAPA SYNDROME LIKE SYMPTOMS?

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Background: PFAPA syndrome is characterized by periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis. As diagnosis usually depends on clinical diagnostic criteria, sometimes it can be difficult to distinguish this clinical entity from the other periodic fever syndromes, especially in regions endemic for FMF.
Objectives: The objective of the study is to evaluate the PFAPA patients' *MEFV* gene variation frequencies (if it was performed) and relations between detected variants and clinical manifestations in pediatric PFAPA patients.
Methods: Nine hundred and thirty-seven patients that were recorded to our database as PFAPA syndrome were evaluated. Patients were reached by phone and asked about characteristics of their fever episodes, presence of acute phase reactant elevation, pharyngitis, aphthous stomatitis/cryptic tonsillitis, cervical lymphadenopathy, arthralgia, arthritis, abdominal pain, headache, nausea or vomiting, chest pain, diarrhea, skin changes, myalgia and conjunctivitis in the course of fever attack, if they had tonsillectomy, if they were attack-free after tonsillectomy and if they had clinical response to steroid or colchicine.
Results: There were 937 PFAPA patients in our database. *MEFV* gene analysis was performed in 407 (%43) of PFAPA patients and 305 of them had at least one mutation. Most common *MEFV* mutations of patients were: R202Q heterozygotes (25,9%), M694V heterozygotes (24,2%), E148Q heterozygotes (13,4%), P369S heterozygotes (9,8%) and V726A heterozygotes (8,6%), respectively.%45.8 of detected mutations were located in exon 2,%40,3 of them were located in exon 10 and% 13,9 of them were located in exon 3 of the *MEFV* gene. Patients were divided into five groups according to their mutations' localization and groups were compared according to clinical features. There were significant differences between groups according to presence of pharyngitis, arthralgia, abdominal pain, myalgia and tonsillectomy history (**Table 1**).

Table 1. Comparison of patients according to their mutations' location and clinical features.

		Exon 2	Exon 3	Exon 10	No Mutation	MEFV study not performed	p
Pharyngitis	*Yes*	21	9(40,9)	45	28 (87,5)	168(87,5)	**<0,05**
	No	(87,5)	13	(80,4)	4(12,5)	24(12,5)	
		3(12,5)	(59,1)	11			
				(19,6)			
Aphthous stomatitis/Cryptic tonsillitis	*Yes*	15	8(36,4)	21	17 (53,1)	102(53,1)	0,11
	No	(62,5)	14	(37,5)	15(46,9)	90(46,9)	
		9(37,5)	(63,6)	35			
				(62,5)			
Cervical lymphadenopathy	*Yes*	10	8(36,4)	21	14(56,3)	77(40,1)	0,97
	No	(41,7)	14	(37,5)	18(43,7)	115(59,9)	
		14	(63,6)	35			
		(58,3)		(62,5)			
Arthralgia	*Yes*	5(20,8)	11(50)	22	19(59,4)	66(34,5)	**0,02**
	No	19	11(50)	(39,3)	13(40,6)	126(65,5)	
		(79,2)		34			
				(60,7)			
Abdominal Pain	*Yes*	17	12	27	16(50)	56(70,8)	**<0,05**
	No	(70,8)	(54,5)	(48,2)	16(50)	136(29,2)	
		7(29,2)	10	29			
			(45,5)	(51,8)			
Myalgia	*Yes*	0(0)	8(36,4)	9(16,1)	7(21,9)	24(12,5)	**0,006**
	No	24(100)	14	47	25(78,1)	168(87,5)	
			(63,6)	(83,9)			
Tonsillectomy	*Yes*	14	5(22,7)	21	20(62,5)	109(57,1)	**0,005**
	No	(58,3)	17	(38,9)	12(37,5)	82(42,9)	
		10	(77,3)	33			
		(41,7)		(66,1)			

Conclusion: In this study, we reported increased frequency of *MEFV* mutations in a large PFAPA patients cohort. Frequency differences of clinical features between groups suggest that some of the *MEFV* gene mutations may modify phenotype of PFAPA syndrome. Furthermore, underlying *MEFV* gene mutations possibly lead to PFAPA like clinical presentation in FMF patients. Another remarkable finding of this study is the relatively high P369S mutation rates in patients with PFAPA syndrome.

REFERENCES:

[1] Pehlivan E, Adrovic A, Sahin S, et al. (2018). PFAPA Syndrome in a Population with Endemic Familial Mediterranean Fever. The Journal of pediatrics, 192, 253-255.
[2] Yamagami K, Nakamura T, Nakamura R, et al. (2017). Familial Mediterranean fever with P369S/R408Q exon3 variant in pyrin presenting as symptoms of PFAPA. Modern rheumatology, 27(2), 356-359.

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FRI0539 WNT6 MUTATION CAUSES AN EARLY ONSET GRANULOMATOSUS INTESTINAL DISEASE WITH RECURRENT HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

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Background: Use of NGS in patients with unclassifiable disease lies a possible approach to the identification of novel disease causing genes.
Objectives: We report a patient with an early onset inflammatory bowel disease with granulomatous lesions and recurrent HLH episodes carrying a missense mutation in the *WNT6* gene.
Methods: A trio based Whole Exome Sequencing (WES) approach was used. Cytokine levels were measured by multiplex assay and by specific ELISAs.
Results: Ten years old Caucasian boy affected by early onset pan-colitis from 9 months of age. Since the disease onset the patient is on glucocorticoid treatment with amino acidic enteral nutrition and oligo antigenic diet. Because of recurrent disease relapses at any attempt of glucocorticoid withdrawal, azathioprine and cyclosporine treatments were also added. At 2 years of age he received total colectomy with ileostomy.

Because of insufficient disease control, treatment with a TNF-inhibitor (infliximab) was started with apparent improvement of intestinal symptoms. However, persistent granulomatous inflammatory disease of the distal portion of the ileus-rectal anastomosis persisted. Moreover, the patient presented recurrent HLH episodes that required high dose of glucocorticoid and cyclosporine-A treatment. Except one HLH episode related to a varicella zoster infection, the other HLH events were most likely triggered by his underlying inflammatory condition. During the HLH episodes levels of IL-18 were moderately elevated (10.880 pg/ml) the IFN-gamma induced chemokine CXCL9 was markedly high (21.871 pg/mL) and remained markedly elevated also during clinical and laboratory HLH remission (3.121 pg/ml and 9.929 pg/ml respectively). Considering the early disease onset, primary immunodeficiency and early intestinal bowel disease onset were genetically ruled out as well as chronic granulomatosis diseases through extensive NGS panels. WES revealed carriage of a private (MAF: 1/125568, TOPMED), predicted pathogenic (CADD: 31), homozygous variant of WNT6 (c.793G>C; p.(Asp265His); NM_006522.3). The patient is now partially controlled on low dose of oral glucocorticoid (0.1 mg/kg), cyclosporine-A (5mg/kg) and antimicrobic treatment.

Conclusion: WNT signalling has been primarily described as a regulatory pathway in ontogeny and homeostatic processes. Schaale at al. demonstrated that WNT6 is expressed in granulomatous lesions in the lung of *Mycobacterium tuberculosis*–infected mice. Moreover, they found that the transcription factor c-Myc is significantly induced in murine macrophages by WNT6. This identifies WNT6 as a novel factor driving macrophage polarization toward an M2-like phenotype, suggesting a role for WNT6 in macrophage differentiation. Our case suggests defective function of WNT6 might be involved in the development of a granulomatous disease. WNT6 role in macrophage differentiation and polarization might also be important in the activation of the IFN-gamma pathway and in recurrent HLH episodes.

REFERENCES:

[1] K. Schaale, et al. Wnt6 Is Expressed in Granulomatous Lesions of Mycobacterium tuberculosis–Infected Mice and Is Involved in Macrophage Differentiation and Proliferation. J Immunol 2013; 191:5182-5195.

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FRI0540

A NOVEL AUTOINFLAMMATORY DISEASE CHARACTERIZED BY NEONATAL-ONSET CYTOPENIA WITH AUTOINFLAMMATION, RASH, AND HEMOPHAGOCYTOSIS (NOCARH) DUE TO ABERRANT CDC42 FUNCTION

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Background: Despite continuous advances in the identification of novel causative genes, several patients with a clinical autoinflammatory phenotype remain unclassifiable

Objectives: to describe a novel hematological and autoinflammatory disorder in three unrelated patients caused by a *de novo* missense mutation of *CDC42*

Methods: Whole exome sequencing was used to identify the novel variant. The functional impact of altered CDC42 function on hematopoiesis and inflammation was assessed through patient peripheral blood and bone marrow analyses, protein behavior and immune and non-immune cell functioning through *in vitro* biochemical and functional assays and *in vivo C. elegans* modeling

Results: Patients shared the same *de novo* missense mutation of *CDC42* (NM_001791, Chr1:22417990, c.556C>T, p.R186C). Disease features included neonatal-onset cytopenia with dyshematopoiesis, autoinflammation, rash, and hemophagocytosis (collectively termed NOCARH syndrome) (Table). An altered hematopoietic compartment (prevalence of early differentiation elements and substantially decreased clonogenic progenitors) was demonstrated. Complementary assays documented the unique consequences of this mutation on CDC42 localization and function, and its disruptive effect on cell behavior and developmental processes, possibly linked to actin dysregulation. Increased secretion of IL-1β, and particularly of IL-18, was observed via *ex vivo* spontaneous release from unstimulated bone marrow mononuclear cells and by high levels in bone marrow supernatants and plasma. IFNγ was also increased and correlated to CXCL9 levels which were strictly related to ferritin levels. Treatment with anakinra and emapalumab, a monoclonal antibody to iIFNγ, was identified as critical in the survival of one patient, who underwent successful hematopoietic stem cell transplantation

	Patient 1	Patient 2	Patient 3
Outcome and status	Alive, 6 yrs	Dead, 6 mos	Dead, 1.5yrs
Fever	+	+	+
Skin rash	+	+	+
Hepato-Splenomegaly	+	+	+
Hemophagocytic lymphohistiocytosis	+	+	+
Gastrointestinal symptoms	+	+	+
Cytopenia	+	+	+
Acute phase response	+	+	+
Bone marrow dysplasia	+	+	+

Conclusion: The p.R186C amino acid substitution in CDC42 underlies a novel, unique syndrome where CDC42 functional dysregulation has pleiotropic effects, causing hematopoietic disturbance, hyperinflammation, and immune impairment. Early recognition and control of HLH, through neutralization of IFNγ, followed by hematopoietic stem cell transplantion, appear to be crucial to survival.

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FRI0541 **HIGHLY ELEVATED FERRITIN LEVELS ARE ASSOCIATED WITH HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS/MACROPHAGE ACTIVATION SYNDROME – ARE WE MISSING TREATABLE DIAGNOSES? A RETROSPECTIVE SERVICE EVALUATION OF DIAGNOSIS IN PATIENTS WITH FERRITIN >10,000 MICROGRAM/L**

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Background: Haemophagocytic lymphohistiocytosis (HLH)/macrophage activation syndrome (MAS) is a hyperinflammatory syndrome potentially leading to critical illness. Early treatment reduces mortality but diagnosis requires a high index of suspicion. Highly elevated ferritin levels (HEF) >10,000 μg/L are highly specific for HLH/MAS [1] and should prompt consideration of hyperinflammation. Diagnostic guidelines for HLH, requiring the presence of ≥5/8 criteria [2], and classification criteria for MAS complicating systemic juvenile idiopathic arthritis (sJIA) have been published [3].
Objectives: To assess recognition of HLH/MAS in a paediatric population with HEF.
Methods: This retrospective study was conducted at 11 centres under local service evaluation permissions. Biochemistry databases identified patients ≤16 years with serum ferritin >10,000 μg/L during a 3-year period. Each case was assessed against the 2004 HLH criteria and, for patients with sJIA, the 2016 MAS criteria. Due to limited access to some of the laboratory tests, previously-published modified HLH criteria using a threshold of ≥4/5 (excluding tissue haemophagocytosis, decreased natural killer cell function, increased soluble interleukin-2 receptor) were also applied to all patients [4].
Results: 153 patients (55.6% male) were identified. Patient diagnoses included: infections (29.4%), rheumatological (17.0%) and malignancies (17.0%). A diagnosis of HLH/MAS was made by the treating clinical team in 39.9% and considered in a further 16.3%. Using all available data, 30/153 (19.6%) met ≥5/8 criteria and 93.3% of these patients were diagnosed with HLH/MAS by the treating team. 56 (36.6%) met ≥4/5 criteria and 33 (58.9%) of these were diagnosed with HLH/MAS by clinicians. HLH/MAS was not documented as being considered in the differential in 23.2%. Of 23 patients with sJIA, 82.6% met MAS classification criteria and 89.5% of these were diagnosed with MAS by the treating clinicians. Overall mortality was 32.7% (50/153) and was 27.9% (17/61) in patients diagnosed with HLH/MAS during their admission.
Conclusion: Although HEF is highly specific for HLH/MAS, the diagnosis was only made or considered in just over half of paediatric patients with this laboratory result. Increased awareness of this potentially-lethal condition is likely to lead to earlier treatment and reduced mortality.

REFERENCES:
[1] Allen CE, et al. 2008;50:1227-35.
[2] Henter JI, et al. 2007;48:124-31.
[3] Ravelli A, et al. 2016;75:481-9.
[4] Davì S, et al. 2014;66:2871-80.

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FRI0542 **CLINICAL PRESENTATION, GENETIC ANALYSIS AND IFN-SCORE IN PATIENTS WITH UNDEFINED INTERFERONOPATHIES**

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Background: In the last years, an expanding group of complex genetic disorders characterized by disturbance of the homeostatic control of IFN-mediated immune responses, have been identified, so called type I interferonopathies. An increased expression of type I IFN regulated genes, IFN signature (IS), is described in these conditions. IS represent a useful tool in clinical practice to classify patients with suspected interferonopathies.
Objectives: To evaluate the correlation between clinical presentation, genetic analysis and IFN-score in 10 patients with undefined interpheronopathies
Methods: Patients with suspected interferonopathy based on the presence of typical clinical manifestations (neurological, muco-cutaneous symptoms), laboratory parameters (complement deficiency, low platelet count, presence of autoimmunity), instrumental abnormalities (cerebral calcification), were screened for the IFN-score. Defined IFN-mediated diseases were excluded. Patients presenting with a high IFN-score value (above a fixed cut-off of 10) underwent genetic screening by running a panel of 24 genes known to be involved in interferonopathies
Results: 10 patients with suspected interferonopathy followed in a single pediatric rheumatology center were included. 7/10 presented with recurrent episodes of fever (table). Patient 2, 3 and 7 displayed neurological manifestation, respectively epilepsy, epilepsy and mental retardation and progressive hemiplegia. To note epilepsy in patient 2 might be correlated to a bilateral intraventricular hemorrhage presented at birth. In two patients (1,4) gastrointestinal manifestation resembling inflammatory bowel diseases were described while patients 5,7 and 10 suffered from recurrent abdominal pain, diarrhea and patient 10 from hypertransaminasemia. Half of the patients complained arthromyalgia; arthritis developed in patient 2. Cutaneous involvement presented in 3 patients (1,3,6) respectively with a widespread panniculitis of trunk and limbs, aspecific vasculitis and Schonlein Henoch purpura. Other cutaneous manifestation were urticarial rash (pt 2) and an erythematous, desquamative confluent eczema (pt 4). Autoimmunity was confirmed in 2/10 patients. Two patients (4, 8) had an immunological defect with recurrent infections. The genetic analysis resulted negative in patients 1 and 7 and is still ongoing in patients 5, 6 and 8. Patients 2,3,4,9 and 10 carried one mutation in at least one IFN correlated gene not confirming the diagnosis. All patients presented an increased IS ranging from 14,2 to 172,5

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8	Pt 9	Pt 10
Systemic symptoms	Fever		Fever			Fever	Fever	Fever	Fever	Fever, hemophagocytic lymphohistiocytosis
CNS involvement Cerebral calcifications		Epilepsy (bilateral intraventricular hemorrhage at birth)	Epilepsy, mental retardation		/			Hemiplegia		
Gastrointestinal involvement	Eosinophilic gastritis, aspecific IBD			Histological findings simil-RCU	Abdominal pain, diarrhoea		Abdominal pain	/		Hypertransaminasemia
Skin/mucocutaneous involvement	Arthromyalgia, arthritis, urticarial rash	Arthromyalgia, arthritis, urticarial rash	Arthromyalgia, vasculitis	Erythematous, desquamative confluent eczema	Arthromyalgia	erythema polymorphe, Shonlein Henoch purpura in infancy	Arthromyalgia	/		
C3 (90-180 mg/dl) C4 (10-40 mg/dl)	144 34	127 24	81 6	133 23	53 20	137 54	96 17	203 38	97 28	83 16
Immunodeficit autoimmunity		ANA 1:2.560 Anti ds-DNA 1:640	ANA 1:10.240 Anti dsDNA 1:1280	Immunodeficit ANA neg	Neg	/	Neg	Neg	Immunodeficit	/
WBC/ mm³ Hb g/dl PLT/mm³	5,2 10,4 199	4,4 12 381	9,8 12,9 194	3,9 10,2 86	4,6 13 110	8,1 11,1 277	6,4 14,1 214	4,4 12,1 358	3,5 16,5 150	1,7 9,7 56
IFN signature	14,2	171,5	54,73	60,09	27,8	17,2	53,9	40,6	32,6	18,19
Genetic analysis	Neg	PSMB8: p.Arg68Cys OAS1/2/L: p.Gln115His	CARD8: p.Leu426Phe	IFIH1: p.Arg374His	/	/	Neg	/	RCP2: p.Arg269Tr	DOCK2: p.Ala45Gly

Conclusion: An elevated IFN-score represent a useful instrument in the clinical practice to classify patients with suspected interferonopathy. It may represent an important tool to select those patients to be genetically screened with a defined panel of interferonopathies correlated genes. In those patients in which the genetic analysis result negative, the presence

of a positive IFN-score, confirming an activation of this inflammatory pathway, may guide the clinicians in the management of these patients and may support therapeutic decisions

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FRI0543 EFFICACY AND SAFETY OF INTRAVENOUS GOLIMUMAB IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM A PHASE 3 OPEN-LABEL STUDY

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Methods: A multicenter, Phase 3, single arm, open-label trial was conducted using intravenous golimumab at a dose of 80mg/m^2 given at weeks 0 & 4, then every 8 weeks thereafter, in pediatric patients ages 2-17 years old with active polyarticular course juvenile idiopathic arthritis despite methotrexate therapy. Patients received commercial MTX weekly at same BSA-based dose as at time of study entry. All the results below are based on full analysis set which includes all patients who received at least 1 dose of study agent.

Results: 180 patients were screened (130 enrolled, 127 treated) with the first patient screened on 22Dec2014; last patient first treated 26Dec2017, & last patient's Wk28 visit was 09Jul2018.

Proportion of JIA ACR 30,50,70, & 90 responders at Wk28 was 83.5%,79.5%,70.1%, & 46.5%, respectively. 29.1% of patients met criteria for inactive disease at Wk28. Median change from baseline for JASDAS 10, 27, & 71 was -14.20, -16.60, & -20.32, respectively at Wk28. JADAS 10, 27, & 71 minimal disease activity was met by 15% of patients at Wk28.

Proportion of patients experiencing at least 1 treatment-emergent AE through Wk28 was 77.2%. MedDRA system organ class with highest incidence of AEs was Infections & infestations (57.5%);most commonly reported AE upper respiratory tract infection(17.3%), then nasopharyngitis (15.0%).Six patients experienced serious AEs through Wk28: Herpes zoster disseminated, Infective exacerbation of bronchiectasis, Sepsis, Varicella, Mycosis fungoides, & Suicidal ideation. These events resulted in permanent discontinuation of intravenous golimumab, except for Varicella.

Conclusion: Intravenous golimumab delivered at a dose of 80mg/m2 at weeks 0 & 4, then every 8 weeks thereafter and appears to be effective in these patients with a safety profile similar to other TNF inhibitor therapies.

Disclosure of Interests: Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Alberto Spindler: None declared, Cesar Francisco Pacheco Tena Grant/research support from: Janssen Research & Development, LLC, Ingrid Louw Consultant for: Advisory committee: Roche, Novartis, Pfizer, Gabriel Vega Cornejo Grant/research support from: I currently have no conflicts of interest, I am only setting protocols for the pharmaceutical industry with Parexel, Sanofi and Bristol-Myers Squibb., Daniel Kingsbury Grant/research support from: Clinical trial support from Bristol-Myers Squibb, Michael Clark Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Karen Bensley Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Devvelopment, LLC, Xiaoming Li Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Hermine Brunner Grant/research support from: Bristol-Myers Squibb, Pfizer, Consultant for: Pfizer, Bristol-Myers Squibb, Janssen, Novartis, Lilly, Roche, GlaxoSmithKline, Sanofi, Speakers bureau: Novartis, Roche

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FRI0544 EFFICACY AND SAFETY OF CANAKINUMAB IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS – EXPERIENCE USING DATA OF THE BIKER REGISTRY

Gerd Horneff[1,2], Eggert Lilienthal[1], Ralf Trauzeddel[1], Toni Hospach[1], Tilmann Kallinich[1], Frank Dressler[1], Michaela Sailer-Hoeck[1], Gerd Ganser[1], Frank Weller-Heinemann[1], Georg Heubner[1], Andreas Urban[1], Michael Rühlmann[1], Christoph Rietschel[1], Markus Hufnagel[1], Wolfgang Emminger[1], Ariane Klein[1]. [1]*BIKER-Registry, Sankt Augustin, Germany*; [2]*Asklepios Clinic Sankt Augustin, General Paediatrics, Sankt Augustin, Germany*

Background: Canakinumab is approved for the treatment of systemic juvenile idiopathic arthritis (sJIA) older than 2 years.

Objectives: The aim of the German Biologics Registry (BiKeR) is the surveillance of JIA patients exposed to biologics.

Methods: Baseline demographics and disease activity parameters were documented. Efficacy was determined using the JADAS and the proposed criteria for inactive disease on medication. Safety assessments were based on reports of adverse events (AE). All reports have been coded according to MedDRA ®.

Results: 48 sJIA patients with 82.5 patient-years (PY) of exposure to Canakinumab were recorded in the German BiKeR registry. The total observation time (from date of first dose until last follow-up, censored, if another biologic was started) was calculated with 109.9 PY.

The cohort treated with Canakinumab had experienced long disease duration of 2.9+/-3.8 years (mean +/- SD). 21 (44%) were pre-treated with methotrexate, 10 (21%) with Etanercept, 3 (6%) with Adalimumab, 18 (38%) with Anakinra and 19 (40%) with Tocilizumab. Concomitantly, 9 (18.8%) received methotrexate, 22 (45.8%) NSAIDs and 23 (48%) systemic corticosteroids.

At last follow up upon treatment, 48%/44%/42%/38% of patients reached PedACR30/50/70/90 improvement. 8 patients (16.7%) had inactive disease according to the Wallace criteria. The median (IQR1-IQR3) JADAS10 score decreased from 12.6 (6.2-15.8) at baseline to 0.5 (0.0-2.8). During ongoing treatment, approximately 82% of patients achieved a JADAS defined minimal disease activity; while 64% reached a JADAS defined remission at last follow-up.

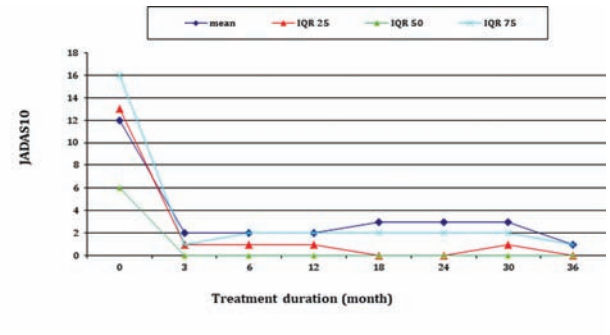
125 adverse events (AE) were recorded (114 events/100PY [95% CI 96-136]). Of these, 22 qualified as serious adverse events (SAE) (20/100PY [13-30]). 100 AEs were observed during exposure or up to 90 days follow up after the last exposure to Canakinumab (121/100PY [99-147]). 19 qualified as SAE (23/100PY [15-36]).

Adverse Events of Special Interest were serious and medically important infection (n=4), cytopenia (n=4), macrophage activation syndrome (n=3). There was no opportunistic infection, intestinal perforation, anaphylaxis or other hypersensitivity, thrombotic event, evolving autoimmune disease, cardiac or cerebral event, bleeding, malignancy, or death. A total of 38 patients (79%) discontinued treatment, 8 (17%) due to lack or efficacy, 16 (33%) due to remission and 2 (4%) because of intolerance.

Conclusion: The current analysis adds to the established safety profile of Canakinumab and demonstrates that safety was comparable and consistent with the overall AE profile of Canakinumab in paediatric patients. MAS occurred in three sJIA patients and might be a JIA-associated feature. Infections were the most frequent AE, but only two serious infections were reported. No new safety signals specific to the paediatric population were identified for Canakinumab; the risk profile of Canakinumab remains positive for the approved paediatric indication sJIA.

REFERENCES:

[1] Horneff G, Klein A, Klotsche J, Minden K, Huppertz HI, Weller-Heinemann F, Kuemmerle-Deschner J, Haas JP, Hospach A. Comparison of treatment response, remission rate and drug adherence in polyarticular juvenile idiopathic arthritis patients treated with etanercept, adalimumab or tocilizumab. Arthritis Res Ther. 2016 Nov 24;18(1):272



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FRI0545 HEMODYNAMIC MEASUREMENTS AND ARTERIAL STIFFNESS IN PATIENTS WITH JUVENILE IDIOPATIC ARTHRITIS COMPARED TO CHILDREN WITHOUT JUVENILE IDIOPATIC ARTHRITIS

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Background: Juvenile Idiopathic Arthritis (JIA) can cause long-term cardiovascular complications. There are non-invasive, validated, easy to perform methods for cardiovascular testing, such as: carotid intimal-media thickness (cIMT), and measurement of arterial rigidity through carotid distensibility, carotid-femoral pulse wave velocity (cfPWV) and the augmentation index (AIx).
Objectives: To compare the main hemodynamics measurements (cIMT, carotid distensibility, cfPWV and AIx) between JIA and non-JIA subjects.
Methods: Analytical cross-sectional study in subjects 5 to 16 years of age. Two groups: patients with JIA according to the ILAR classification without any other condition *vs* healthy children. Measurements: somatometry, laboratory (glucose, creatinine, lipid profile), disease activity index (JADAS-27) and hemodinamic variables (cIMT, carotid distensibility, cfPWV and AIx).
Results: 63 JIA subjects and 50 healthy controls were included, mean age 11.5 ± 2.8 *vs* 10.7 ± 3.2 years (p = 0.17) and 70% vs 54% females, respectively. Both groups were also similar (p > 0.05) for nutritional state, sedentary lifestyle, smoking habits and family history of cardiovascular risk. Table 1 show lipid profile of both groups. Subtypes of JIA were: RF positive polyarthritis (29%), RF negative polyarthritis (29%), oligoarthritis (19%), enthesitis-related arthritis (14%) and systemic arthritis (9%). Mean time of disease evolution was 4 ± 3 años. There were no significant differences between groups in the main hemodinamic parameters (table 2). When comparing inactive *vs* active disease and active disease *vs* controls there were no differences either, we found a discrete trend to less carotid distensibility and higher cfPWV in patients with active disease compared to controls [0.63 ± 0.17 mm vs 0.66 ± 0.15 mm (p = 0.94) and 6.12 ± 2.88 m/s *vs* 5.42 ± 0.75 m/s (p = 0.33), respectively]. 59% of subjects with JIA were inactive according to JADAS-27. When considering time of disease evolution, children with 0-4 years *vs* children with >4 years and children with >4 years *vs* controls, we found differences in cIMT [0.41 ± 0.62 mm *vs* 0.44 ± 0.50 mm (p = 0.02) and 0.44 ± 0.50 mm vs 0.40 ± 0.70 mm (p = 0.01), respectively]. Finally, cfPWV was higher in patients with 0-4 years than in patients with >4 years of evolution (p = 0.01).

TABLE 1. LIPID PROFILE

LIPID	JIA	CONTROLS	p†
Triglicerides	94 ± 56	85 ± 36	0.22
Total cholesterol	141 ± 27	152 ± 26	0.06
HDL cholesterol	45 ± 12	47 ± 10	0.36
LDL cholesterol	77 ± 21	87 ± 22	0.01
VLDL cholesterol	18 ± 11	17 ± 7	0.52

†Mann-Whitney U test.

TABLE 2. HEMODINAMIC MEASUREMENTS

MEASUREMENT	JIA	CONTROLS	p†
cIMT (mm)	0.42 ± 0.59	0.40 ± 0.70	0.11
Carotid distensibility (mm)	0.64 ± 0.16	0.66 ± 0.15	0.78
cfPWV (m/s)	5.77 ± 2	5.42 ± 0.75	0.66
AIx (%)	69 ± 15	69 ± 12	0.64

†Mann-Whitney U test.

Conclusion: We found a tendency to increased cardiovascular risk when the disease has more than 4 years of evolution, specially in patients with persistent active disease. Traditional and non-traditional cardiovascular risk factors add up in this population. We need longterm follow-up studies.

REFERENCES:

[1] Bohr AH, Fuhlbrigge RC, Pedersen FK, De Ferranti SD, Müller K. Premature subclinical atherosclerosis in children and young adults with juvenile idiopathic arthritis. A review considering preventing measures. *Pediatr Rheumatol* 2016; 14: 1-5.
[2] Sozeri B, Atikan BY, Ozdemir K, Mir S. Assessment of vascular function in systemic onset juvenile idiopathic arthritis. Clin Rheumatol 2016; 35: 1699-1703.

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FRI0546 TRAJECTORIES OF DISEASE ACTIVITY OVER THE FIRST THREE YEARS FOLLOWING JUVENILE IDIOPATHIC ARTHRITIS DIAGNOSIS

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Background: The advent of biological therapies and early aggressive treatment strategies have drastically changed prognoses for children and young people (CYP) with juvenile idiopathic arthritis (JIA). Clinical trials and observational research have demonstrated improvements in disease for the majority, but not all, CYP over time. It is not currently known what the patterns of disease activity are in CYP with JIA and how these cluster over time.

Objectives: To explore latent patterns of clinical juvenile arthritis disease activity scores (cJADAS) following a diagnosis of JIA.
Methods: CYP with JIA were selected if enrolled in the Childhood Arthritis Prospective Study (CAPS), a UK multicentre inception cohort, before January 2015. cJADAS10 scores were calculated based on components (active joint count up to 10, physician global, patient/parent global) collected at diagnosis, six months, one year and then annually to three years. CYP were excluded if no cJADAS10 scores were available within this time frame.
Group-based trajectory models were constructed to model latent groups of cJADAS10 scores. Linear, quadratic and cubic polynomials were tested, with one to six trajectories tested within each polynomial group. An optimal model within each polynomial group was selected using Bayesian Information Criteria. The final model was then selected from this shortlist based on model parsimony and clinical plausibility.
Results: Of 1183 CYP selected, the majority were female (65%) and of white ethnicity (90%) with oligoarticular JIA the most common JIA category (45%).
The optimal model identified five cJADAS10 quadratic trajectories (Figure 1): Low-low (59%, initial cJADAS10 median: 6.1), moderate-low (16%, initial cJADAS10 median: 11.5) and three groups with high disease activity at initial presentation (initial median cJADAS10: 17.7 to 19.1). A high-low group experienced the greatest improvement (15%, median improvement 17.2 (IQR 13.7 to 20.1)), and a high-moderate group lesser improvement (5%, median improvement 7.3 (IQR 0.8 to 9.0)). A final high-low-high group experienced improvement to one year followed by disease relapse (5%).
Conclusion: Disease activity in CYP with JIA does not improve in a uniform manner following initial presentation to paediatric rheumatology. Five latent trajectory groups have been identified, with three of these displaying different patterns following initial high disease activity at diagnosis. Identifying distinguishing characteristics for each group may aid the stratification of different treatment strategies to facilitate personalised medicine in JIA.

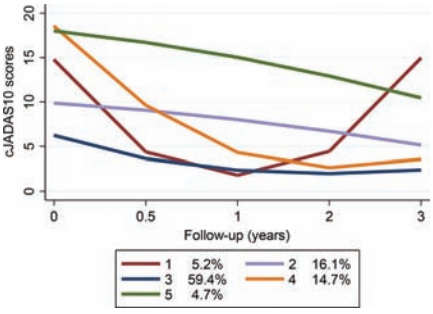


Figure 1. Latent trajectories of cJADAS10 scores in young people with JIA over the first three years following diagnosis

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FRI0547

DEVELOPMENT AND INITIAL VALIDATION OF THE SYSTEMIC JADAS, A NEW COMPOSITE DISEASE ACTIVITY SCORE FOR SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Arthritis Disease Activity Score (JADAS) has gained increasing popularity for the measurement of the level of disease activity in patients with juvenile idiopathic arthritis (JIA). However, so far the JADAS has been validated only in children with the non-systemic categories of JIA.
Objectives: To develop and validate the systemic JADAS (sJADAS), a new version of the JADAS specific to systemic JIA (sJIA).
Methods: The sJADAS is made up by adding a fifth item, named Systemic Manifestation Score (SMS), to the four items included in the original tool (physician global assessment of disease activity, parent/patient global assessment of well-being, active joint count and erythrocyte sedimentation rate). The SMS ranges from 0 to 10 and is aimed to quantify the activity of systemic features. The sJADAS score ranges from 0 to 50. The validation sample included patients with definite and possible/probable sJIA with active systemic manifestations, which should comprise fever, who were assessed at baseline and then at a subsequent visit, 2 weeks to 3 months after initial evaluation. Validation procedures included assessment of concurrent, construct and discriminant validity, internal consistency and responsiveness to clinical change.
Results: A total of 161 patients, 86.7% (n=137) with definite sJIA and 13.3% (n=21) with possible/probable sJIA, assessed at disease onset (n=90; 56.6%) or at time of a disease flare (n=69; 43.4%), were enrolled at 57 centers in 10 countries from February 2017 to December 2018. Median age at disease onset was 5.0 years (interquartile range, IQR 2.8 - 8) and median age at study entry was 6.9 years (IQR 3.8–10.8). Median disease duration from onset to study entry was 0.2 years (IQR 0.1–1.9). The median sJADAS at baseline visit was 28.2 (IQR 22.8–35.0). The sJADAS correlated strongly with JADAS10 (r_s=0.98) and clinical JADAS10 (cJADAS10) (r_s=0.91); moderately with functional ability scales (JAFS and CHAQ) (r_s=0.69; r_s=0.62) and total score (r_s=0.57) and physical (r_s=0.60) and psychosocial (r_s=0.40) subscale scores of the health-related quality of life tool (PRQL) and with pain VAS (r_s=0.57); and mildly with the CRP (r_s=0.42). The sJADAS discriminated well between patients with or without morning stiffness (p<0.0001), with different levels of disease activity defined subjectively by the physician (p<0.0001) and with different degrees of pain (p<0.0001). The internal consistency was good (Cronbach's alpha=0.64) and comparable to that of JADAS10 (Cronbach's alpha=0.59,) and cJADAS10 (Cronbach's alpha=0.63). Responsiveness to change, measured on all patients (SRM=2.23) and on patients classified as improved at second visit (SRM=2.41), was strong and superior to that of JADAS10 (SRM=1.92 and 2.14, respectively).
Conclusion: The sJADAS was found to be a valid instrument for the assessment of disease activity in sJIA. This composite score is feasible and easily applicable in standard clinical practice, which should result in its widespread acceptance and use. The strong responsiveness to clinical change over time indicates that the sJADAS is suitable to assess therapeutic response in sJIA clinical trials.
Disclosure of Interests: : Jessica Tibaldi: None declared, Yasser El Miedany: None declared, Priyankar Pal : None declared, Soamarat Vilaiyuk: None declared, Raju Khubchandani: None declared, Claudia Bracaglia: None declared, Tapas K Sabui : None declared, Sujata Sawhney: None declared, Riccardo Russo Speakers bureau: Novartis, Abbvie, Flávio R. Sztajnbok: None declared, Rolando Cimaz: None declared, Francesca Minoia: None declared, Motasem O. Alsuweiti: None declared, Ekaterina Alexeeva: None declared, Mikhail Kostik: None declared, Maria Cristina Maggio: None declared, Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Alessandro Consolaro Grant/research support from: AbbVie, Pfizer, Angelo Ravelli Grant/research support from: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benkiser, and Roche, Consultant for: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benkiser, and Roche, Speakers bureau: Angelini, AbbVie, Bristol-Myers

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FRI0548 EFFICACY AND SAFETY OF TOCILIZUMAB IN SYSTEMIC AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS – DATA OF THE BIKER REGISTRY

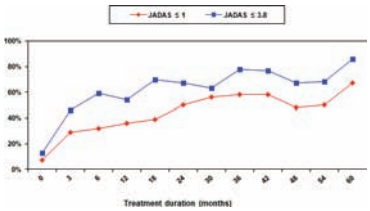
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Background: Since 2011 Tocilizumab is approved for systemic juvenile idiopathic arthritis (JIA) and since 2013 for polyarticular JIA
Objectives: To describe efficacy and safety of Tocilizumab in clinical practice in polyarticular (pJIA) and systemic JIA (sJIA) patients using the German Biologics registry (BiKeR)
Methods: Baseline demographics and disease activity parameters have been documented. Efficacy was determined using the JADAS10 prospectively. Safety assessments were based on adverse events reports (AE) processed according to MedDRA
Results: Until October 1, 2018, 345 JIA patients treated with Tocilizumab were registered, representing 635 patient-years (PY) of observation. The cohort treated with Tocilizumab had experienced disease duration of 5.5 +/-4.3 years (mean+/-SD) for sJIA and 5.9+/-4.1 years for pJIA. sJIA/pJIA patients received pretreatment with MTX 72%/96%, Anakinra 23%/1%, Adalimumab 4%/60%, Etanercept 30%/69%, Canakinumab 2%/0%. Concomitantly, sJIA/pJIA patients received NSAIDs 64%/57%, systemic steroids 72%/35%, MTX 55%/54%, other DMARDS 4%/8%. At last follow-up, 63%/60%/51%/43% of sJIA and 56%/49%/40%/30% of pJIA patients reached JIAACR30/50/70/90 criteria. After 2 years of treatment JADAS remission was reached by 50%/43% and JADAS minimal disease activity by 67%/67%.
586 AE were reported during exposure plus 90 days of observation. The rate was significantly higher in sJIA (104/100PY [95% CI 92-119]) than in pJIA patients (79 [79-90]; RR 1.3; p=0.003). 75 qualified as serious AE (SAE) with a higher rate in sJIA (22[16-29] vs. 8 [5-12], RR 2.6; p<0.001). The most frequent AE in the sJIA/pJIA cohort were grouped in the MedDRA SOC infections and infestations (n=92/76). Compared to pJIA, rates were significantly higher in sJIA patients for blood and lymphatic (RR 2.4; p=0.019), immune system (RR 2.6; p=0.04), infections & infestations (RR 1.7, p<0,001) and nervous system disorder (RR 2.6, p=0.012) and lower for general and administration site (RR 0.4; p=0.023). 169 patients (49%) discontinued treatment, 17% due to remission, 22% due to lack of efficacy and 9% because of intolerance.
Conclusion: The analysis adds to the established safety profile of tocilizumab in paediatric patients with systemic & polyJIA. Differences were noted between pJIA and sJIA cohorts, the latter with higher rates of total number of adverse events, serious AE, infections and cytopenias, probably due to higher doses or shorter application intervals. No new safety signals specific to the paediatric population were identified in this large cohort of JIA patients.

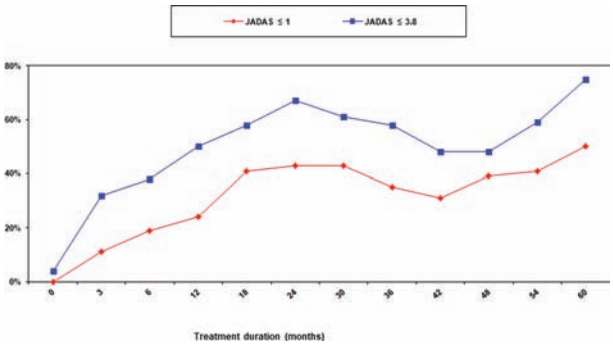
	sJIA (n=109)	pJIA (n=239)	RR/p
All AE (rate[95%CI])	234(104[92-119])	252 (79[70-90])	0.76/ 0.003
SAE	49 (22[16-29])	26 (8[5-12])	0.38/ <0.001
blood & lymphatic system [1]	20 (9[6-14])	12(4[2-7])	0.42/ 0.019
gastrointestinal disorders	13 (6[3-10])	30(9[7-14])	n.s.
general disorder & administration site condition[2]	9 (4[2-8])	30 (9(7-14])	2.4/ 0.023
immune system disorders[3]	13 (6[3-10])	7 (2[1-5])	0.38/ 0.040
infections and infestations[4]	92 (41[33-50])	76 (24[19-30])	0.59/ <0,001
injury, poisoning and procedural complications	7 (3[1-7])	10 (3[2-6])	n.s.
neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (0[0-3])	2(1[0-3]	n.s.
nervous system disorders[5]	20 (9[6-14])	11(3[2-6])	0,39/ 0.012
skin and subcutaneous tissue disorders	11(5[3-9])	11(3[2-6])	n.s.

MedDRA-SOC: Rates are outlined as number during exposure + 90 days follow up, censored if an alternative biologic has been applied. 1 MAS, neutron-, thrombocytopenia; 2 nausea, aphthosis; 3 allergic reactions; 4 viral and bacterial infections; 5 seizures

REFERENCES:
[1] Horneff G, et al. Arthritis Res Ther. 2016 Nov 24;18(1):272



sJIA



polyJIA

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FRI0549 SARILUMAB, A HUMAN MONOCLONAL ANTIBODY TO THE INTERLEUKIN-6 (IL-6) RECEPTOR, IN POLYARTICULAR-COURSE JUVENILE IDIOPATHIC ARTHRITIS (PCJIA): A 12-WEEK MULTINATIONAL OPEN-LABEL DOSE-FINDING STUDY

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Background: Sarilumab blocks IL-6 from binding to membrane and soluble IL-6 receptor-á. Sarilumab is approved for adults with rheumatoid arthritis (RA) and is being investigated in a Phase 2 trial (NCT02776735)

in 2–17-year-old patients (pts) with pcJIA, comprising rheumatoid-factor (RF)-positive and RF-negative polyarticular and extended oligoarticular JIA.
Objectives: Evaluation of pharmacokinetics (PK), pharmacodynamics (PD), safety, and efficacy of 3 subcutaneous (SC) sarilumab doses in pcJIA.
Methods: A 12-week dose-finding study was performed to identify an appropriate sarilumab dose for use in the pcJIA population. Pts were divided by body weight into 2 groups: A (30–60 kg) and B (10–<30 kg), and received sequential ascending doses of sarilumab, Dose 1 (Group A/B): 2.0/2.5 mg/kg q2w; Dose 2 (Group A/B): 3/4 mg/kg q2w; and Dose 3 (Group A/B): 2.0/2.5 mg/kg qw. pcJIA doses were targeted to achieve similar exposure to adult RA doses (150 mg q2w, 200 mg q2w, and 150 mg qw). Primary outcome was PK; secondary outcomes were safety, PD, and efficacy of sarilumab.
Results: 42 pts enrolled (20/22 in Groups A/B); mean age was 13.0/5.2 years. At baseline, mean pcJIA duration, number of active joints, and JADAS27-CRP were 4.6/1.7 years, 17.2/11.0, and 22.2/19.1, in Groups A/B, respectively. As in adult pts, sarilumab exhibited nonlinear PK with target-mediated drug disposition (TMDD). Following repeated SC administrations, exposure increased in a greater than dose-proportional manner and accumulated 1.9–4.5-fold over 12 weeks. Sarilumab exposure was similar in both weight groups for each dose (Figure), and comparable to corresponding adult doses. Treatment-emergent adverse events (AEs) were reported in 36/42 (85.7%) pts (comparable across dose and weight groups); infections (28/42, 66.7%) were the most frequently reported AE. 12 grade 3/4 neutropenias were identified, mostly in Dose 3 (n=6) and in Group B (n=8). None was associated with infection; all resolved in a few days. Overall, 4 pts discontinued due to neutropenia and 1 due to alanine aminotransferase increase. There were no serious AEs, no cases of GI perforation, and no deaths. By Week 12, as observed while on-treatment: all pts attained JIA ACR30; 50%, 62%, and 100% of pts attained JIA ACR70 with Doses 1, 2, and 3, respectively; JADAS27-CRP mean % changes from baseline in Doses 1, 2, and 3 were -74.6%, -73.1%, and -87.9%, respectively.

Figure. Mean (CV%) individual sarilumab exposure, following first SC dose, and after repeated SC administration at Weeks 10–12 or Weeks 11–12, in patients with pcJIAFirst

pcJIA treatment		First SC administration			Repeated SC administration (Weeks 10–12 or Weeks 11–12)		
Patient weight group	Sarilumab dose	N	C_{trough} mg/L (CV%)	$AUC_{\tau,ss}$ day mg/L (CV%)	N	C_{trough} mg/L (CV%)	$AUC_{\tau,ss}$ day mg/L (CV%)
10–<30 kg (Group B)	2.5 mg/kg q2w	6	0.54 (48)	63 (30)	5	1.83 (101)	118 (37)
	4.0 mg/kg q2w	7	3.77 (43)	167 (26)	7	11.90 (41)	310 (26)
	2.5 mg/kg qw	9	5.22 (39)	45 (36)	5	25.10 (29)	203 (25)
30–60 kg (Group A)	2.0 mg/kg q2w	7	0.63 (63)	53 (46)	5	1.99 (86)	114 (18)
	3.0 mg/kg q2w	7	1.84 (69)	123 (24)	6	8.46 (68)	269 (34)
	2.0 mg/kg qw	6	8.07 (32)	61 (22)	6	30.40 (28)	250 (24)

AUC, area under the serum concentration versus time curve, calculated using trapezoidal method during a dose interval; C_{trough}, serum concentration observed before treatment administration during repeated dosing; CV, coefficient of variance; N, number of patients; pcJIA, polyarticular-course juvenile idiopathic arthritis; qw, every week; q2w, every 2 weeks; SC, subcutaneous.
Dose interval (τ) was 2 weeks for q2w, or 1 week for qw regimen.

Conclusion: Sarilumab exhibited nonlinear PK with TMDD. Doses tested in pcJIA yielded similar exposure in both weight groups and were comparable to equivalent doses in adults with RA. All dose regimens proved effective for decreasing disease activity. Safety profile was consistent with class effects; higher incidences of neutropenia were observed with Dose 3, and in pts weighing 10–<30 kg.
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FRI0550

JIA DISEASE ACTIVITY OUTCOMES ACROSS A MULTI-CENTER COHORT: ANALYSIS OF THE PEDIATRIC RHEUMATOLOGY CARE AND OUTCOMES IMPROVEMENT NETWORK (PR-COIN) REGISTRY

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Background: Clinical remission is widely accepted as the primary target outcome for juvenile idiopathic arthritis (JIA). PR-COIN is a quality improvement collaborative that serves as a sample of pediatric rheumatology centers in North America. By measuring disease activity in practice using the ACR provisional criteria for Clinical Inactive Disease (CID), variation in patient outcomes has been previously observed between centers.
Objectives: The objective of this study was to evaluate differences in patient-level factors that may be driving center-level variation in JIA outcomes.
Methods: This study used cross-sectional data provided by PR-COIN that was collected by PR-COIN centers from March 2015 to May 2016. For each patient, sociodemographic, clinical, patient-reported, disease activity, and medication variables were extracted from the most recent encounter. Patients with disease duration less than 9 months were excluded. Patients were grouped by CID status (inactive vs active disease) and then compared using descriptive statistics, chi-square for categorical variables, and independent t-tests for continuous variables. Missing data were excluded with each analysis. Analyses were performed using R software.
Results: There were 2751 patients eligible for analysis from 14 centers, with 33 to 394 patients per center. We identified 1249 patients with inactive disease (47%) and 1428 patients with active disease (53%). Patients with inactive disease were younger (12 vs 13 years), more likely to have persistent oligoarticular subtype (33% vs 23%), and less likely to have enthesitis related arthritis (9% vs 14%). Patients with active disease had higher patient-reported measures of global assessment of disease activity, pain, and functional disability, as well as disease activity measures per definition. More medication usage was observed in patients with active disease compared to inactive disease across multiple categories, including both non-biologic DMARDs (45% vs. 32%) and biologic DMARDs (48% vs 35%).
Conclusion: This study demonstrates differences in sociodemographic, clinical, and medication factors between patients with inactive and active JIA. Further analysis is needed to adjust center-level measures of JIA disease activity using the observed differences in patient case-mix. By using population data to identify predictors of inactive disease in JIA, there is potential to develop and implement targeted clinical interventions to directly impact care and improve outcomes.
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Burnham: None declared, Julia G. Harris: None declared, Judyann C. Olson: None declared, Mileka Gilbert: None declared, Michelle Batthish Speakers bureau: Novartis, Abbvie, Michael Shishov: None declared, Dustin Fleck: None declared, Esi Morgan: None declared
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FRI0551 IDENTIFYING RESEARCH PRIORITIES FOR JUVENILE IDIOPATHIC ARTHRITIS TOGETHER WITH PATIENTS, CARERS AND CLINICIANS THROUGH THE JAMES LIND ALLIANCE METHOD: PRELIMINARY RESULTS

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Background: Research on Juvenile Idiopathic Arthritis (JIA) should have the primary goal to ultimately improve the lives of the affected patients, and help health professionals provide the best care for them. Therefore, these end users of research evidence – patients, carers (parents/caregivers) and clinicians – should be included in the process of identifying research priorities. Importantly, patients and carers can use their unique experiential knowledge from living with the disease to give vital input to researchers in designing a study. Combining this input with the goal of research(ers) to make a true impact on patients' lives, will result in research that is more effective and meaningful, and thereby increases research value [1]. To this end, we initiated the project of establishing a research agenda for JIA jointly by patients, carers and clinicians [2].
Objectives: The objective of this project is to bring patients, carers and clinicians together to identify research priorities and create a research agenda for JIA, such that future research into JIA is guided to the issues that matter most.
Methods: The method for research priority setting developed by the James Lind Alliance (JLA) is used [3]. This method consists of several steps with the end goal of creating a top 10 list of research priorities agreed on by all parties. First, a steering group with equal representation of patients, parents and clinicians was assembled. We are now in the process of collecting research questions through an online survey. Focus groups are being held to ensure the inclusion of younger patients. Questions will be clustered and checked against the evidence. Next, the process of interim priority setting will follow, in which a shortlist of up to 30 questions will be assembled. During a final workshop in which all parties are equally represented, the top 10 research priorities will be established. This workshop is scheduled for the end of 2019. A process evaluation is conducted to monitor ethical aspects in the decision-making process.
Results: The first step of collecting research questions is performed until the end of March 2019. We will be able to present preliminary results on the questions gathered from the online survey and focus groups by June 2019. Furthermore, we will discuss the effects of our efforts to be inclusive and representative of every party involved.
Conclusion: Through this project, patients, carers and clinicians are brought together to define the most important unanswered questions for JIA. Engaging patients and stakeholders in this crucial phase is the next step in performing more meaningful and effective research.

REFERENCES:

[1] Chalmers I, Bracken MB, Djulbegovic BD, et al. How to increase value and reduce waste when research priorities are set. Lancet 2014; 383;156-165.
[2] Schoemaker CG, Armbrust W, Swart JF, et al. Dutch juvenile idiopathic arthritis patients, carers and clinicians create a research agenda together following the James Lind Alliance method: a study protocol. Pediatr Rheumatol Online J 2018;16(1):57.
[3] James Lind Alliance. Guidebook. 2018; Available from: www.jla.nihr.ac.uk/jla-guidebook. Accessed 4 January 2018.

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FRI0552 PERFORMANCE OF NEWLY PROPOSED PERIODIC FEVER, APHTHOUS STOMATITIS, PHARYNGITIS AND CERVICAL ADENITIS (PFAPA) SYNDROME CRITERIA IN REGIONS ENDEMIC FOR FAMILLIAL MEDITERRANEAN FEVER (FMF)

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Background: The periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome is an autoinflammatory condition characterized by regularly recurrent episodes of high fever lasting 3 to 6 accompanied by aphthosis, cervical adenitis, and pharyngitis, in the absence of upper respiratory tract infections. A relevant number of patients with monogenic periodic fevers also meet the diagnostic criteria for PFAPA syndrome. Especially in regions endemic for familial Mediterranean fever (FMF), it would be important to avoid useless genetic testing and to be able to identify PFAPA patients by using clinical classification criteria. Despite the high specificity, widely used Marshall's criteria have been shown to have low specificity. An international consensus among experts has been established recently, in order to define a set of classification criteria for PFAPA syndrome with a better performance in term of sensitivity and specificity.
Objectives: We aimed to evaluate the performance of recently proposed PFAPA criteria, in order to assess their utility in regions endemic for FMF.
Methods: Patients diagnosed with PFAPA syndrome, FMF and juvenile idiopathic arthritis (JIA) were consecutively included in the study. PFAPA diagnosis has been established by Marshall's criteria. Patients with FMF and JIA were diagnosed according to Turkish pediatric FMF criteria and ILAR criteria, respectively. Two investigators blindly evaluated all of patients for the newly proposed PFAPA criteria.
Results: A total of 321 PFAPA, 118 FMF and 45 JIA patients with mean age of 7.23±2.9, 14.7±3.09, 13.5±4.6 years, respectively, were included in the study. A 45% (146/323) of PFAPA, 50% (59/118) of FMF and 58% (23/45) of JIA patients were female. We found quite high sensitivity (90%) of newly proposed PFAPA criteria: 289 out of 321 (90%) patients followed up as PFAPA syndrome fulfilled newly proposed PFAPA criteria, as well. When applied to patients diagnosed with FMF and JIA, 46 out of 118 (39%) FMF and 10 out of 45 (22%) JIA patients also fulfilled newly proposed PFAPA criteria. Specificity of recently proposed PFAPA criteria was found to be 61% and 77%, among FMF and JIA patients, respectively. Positive predictive value was 86% and 97%, negative predictive value was 69% and 50% for FMF and JIA patients, respectively.
Conclusion: Recently proposed PFAPA criteria have satisfactory high sensitivity. Specificity of recently proposed criteria is still under expectation in regions endemic for FMF. Multicentric studies with higher patients' number in different regions are needed in order to provide more relevant data on performance of newly proposed PFAPA criteria.

REFERENCES:

[1] Marshall GS, Edwards KM, Butler J, Lawton AR. Syndrome of periodic fever, pharyngitis, and aphthous stomatitis. J Pediatr. 1987;110(1):43– 46
[2] Adrovic A, Sahin S, Barut K, Kasapcopur O. Familial Mediterranean fever and periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome: shared features and main differences. Rheumatol Int. 2019;39 (1):29-36.
[3] Vanoni F, Federici S, Antón J, et al. An international delphi survey for the definition of the variables for the development of new classification criteria for periodic fever aphtous stomatitis pharingitis cervical adenitis (PFAPA). Pediatr Rheumatol Online J. 2018;16(1):27
[4] Vanoni F, Caorsi R, Aeby S, et al. Towards a new set of classification criteria for PFAPA syndrome. Pediatr Rheumatol Online J. 2018;16(1):60.
[5] Pehlivan E, Adrovic A, Sahin S, et al. PFAPA Syndrome in a Population with Endemic Familial Mediterranean Fever. J Pediatr. 2018;192:253-255.

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FRI0553

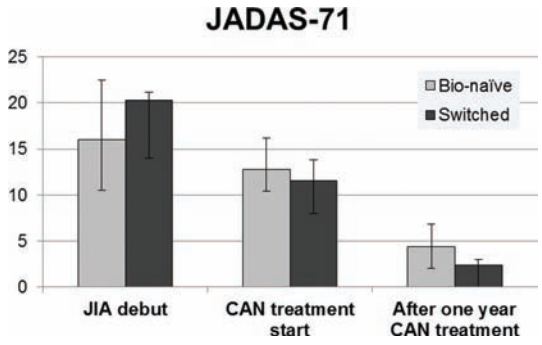
CANAKINUMAB AS A FIRST-LINE AND SECOND-LINE BIOLOGIC FOR TREATMENT OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN CHILDREN UNDER 4 YEARS OF AGE

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Background: Development of biologics and their launching into clinical practice has yielded significant progress in pediatric rheumatology. Nevertheless, treatment of severe disorders, and systemic JIA in particular, still remains a challenge. JIA often has the early-onset form. If its course is aggressive and persistent, patients exhibit poor response to treatment with first-line biologics. Effectiveness of the second-line and subsequent biologics, as well as the optimal sequence of prescribing drugs belonging to different classes to children younger than 4 years, remains an open question

Objectives: To compare the efficacy of canakinumab (CAN) in children with sJIA younger than 4 years (in biologic-naïve patients and when prescribed as a second-line biologic).

Methods: The study was conducted as a subanalysis of the prospective cohort study to evaluate the efficacy of biologics in children with sJIA. Comparative analysis involved 17 patients who had initiated CAN treatment at the National Medical Research Center of Children's Health (Moscow, Russia) when aged < 4 years (9 biologic-naïve patients (the naïve group) and 8 patients switched from tocilizumab therapy (the switched group)). Treatment efficacy was evaluated according to the dynamics of clinical and laboratory signs using the ACRPedi criteria. The Wallace criteria were used to evaluate whether or not remission had been achieved. Treatment safety was evaluated according to the data presented in the Adverse Event Reports



Results: At baseline, patients had comparable duration and severity of the disease. The biologic proved efficacious already after 4 weeks of treatment. Five (55.6%) patients in the naïve group and 4 (50%) patients in the switched group achieved ACR90 (p>0.999) within one year of treatment. A state of inactive disease according to the Wallace criteria was achieved in one patient in each group, (12.5% and 11.1%, respectively (p>0.999). JADAS-71 decreased significantly from 12.8 (IQR 10.4-16.2) to 4.4 (IQR 2-6.8) in the naïve group (p=0.012) and from 11.6 (IQR 8-13.88) to 2.35 (IQR 1-3.03) in the switched group (p=0.017).

Conclusion: CAN was found to be highly efficacious and have a good safety profile in children younger than 4 years regardless of prior biologic treatment.

Disclosure of Interests: : None declared

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FRI0554

DNASE1L3 VARIANT IN HYPOCOMPLEMENTEMIC URTICARIAL VASCULITIS SYNDROME IDENTIFIES A DIFFERENT CLINICAL PHENOTYPE

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Background: Hypocomplementemic urticarial vasculitis syndrome (HUVS) is a rare disease characterized by persistent urticarial lesions and hypocomplementemia associated with systemic features involving musculoskeletal, pulmonary, renal and gastrointestinal systems. Systemic lupus erythematosus (SLE) develops in >50% of patients with HUVS, although the pathogenesis is unknown.

Objectives: We describe 6 paediatric patients with HUVS, three of whom carry a homozygous variant of *DNASE1L3* and present a peculiar clinical phenotype.

Methods: A Targeted Resequencing using a panel including genes already known to be mainly associated to Interferonopathies Lupus-like (*DNASE1*, *DNASE2*, *DNASE1L3*, *TREX1*) on the Illumina NextSeq® platform was performed. All variants identified were confirmed by Sanger sequencing and, when possible, family members were tested to study the segregation of identified variants. We applied in silico studies only to variants with an allelic frequency ≤1%.

Results: All patients described are Caucasian and 3 of them are female. Two patients presented at onset with extended cutaneous manifestation, joints and abdominal involvement with cholecystitis. They did not develop renal or pulmonary involvement. In contrast, the other four patients presented a more severe disease. All of them developed renal involvement (from microhaematuria up to nephrotic syndrome) with renal biopsy showing mesangial glomerulonephritis in three patients and pauci-immune glomerulonephritis (ANCA negative) in one. Moreover, two of them developed also pulmonary vasculitis (Table 1). A homozygous *DNASE1L3* variant (c.290_291delCA) was identified in three of these patients. All of them were treated with glucocorticoid and dapsone at onset. Cyclophosphamide, mycophenolate mofetil and azathioprine were used in patients with renal involvement. None of them developed SLE.

Table 1. Patients' clinical characteristics

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6
Age at onset	9 y 6/12	3 y 10/12	9y 5/12	14y 3/12	3y 6/12	3y 1/12
Joints	Yes	Yes	Yes	No	Yes	Yes
Ocular	No	Yes	No	No	No	No
Abdominal	Yes	Yes	Yes	No	Yes	Yes
Pulmonary	No	Yes	Yes	No	No	No
Renal	Yes	Yes	Yes	Yes	No	No
Antibody anti-C1q	+	+	+	+	+	+
Anti-dsDNA	absent	absent	absent	absent	absent	absent
C3 (nv 90-180 mg/dl)	57	63	52	57	19	57
C4 (nv 10-40 mg/dl)	7	6	2	7	1	1
DNASE1L3 variant	+	+	Ongoing	+	-	-

Conclusion: HUVS is very rare disease in childhood. Approximately 50% of HUVS patients develop SLE. Genetic susceptibility to SLE is recognized and *DNASE1L3*-related SLE have been reported. Özçakar et al. have described 5 children from two families with HUVS who carry the same variant on *DNASE1L3* that we report here (1). Our patients confirm that variant in *DNASE1L3* can cause HUVS and support the hypothesis that this variant is responsible of a more severe phenotype with major organ involvement (renal and pulmonary). Patients with HUVS need to be followed very strictly for the risk to develop SLE. Presence of variant in *DNASE1L3* can identify patients with more severe disease and high risk to develop major organ involvement. These patients need more aggressive and possibly life-long immunosuppressive treatment.

REFERENCES:

[1] Ozçakar ZB, et al. *DNASE1L3 Mutations in Hypocomplementemic Urticarial Vasculitis Syndrome*. Arthritis Rheum. 2013 Aug;65(8):2183-9.

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FRI0555

INFLUENCE OF ANTI-TUMORNECROSIS FACTOR (TNF) DRUG IMMUNOGENICITY ON THE TREATMENT EFFECTIVENESS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) USING SERUM CALPROTECTIN AS A DISEASE ACTIVITY MARKER. MULTICENTER STUDY. ITACA STUDY

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Background: There is a lack of evidence about the loss of efficacy of anti-TNF agents in JIA and its possible relation to the immunogenicity generated. In the last years there has been interest in the role of serum calprotectin in children diseases, including JIA.
Objectives: To assess the immunogenicity and bioavailability of anti-TNF drugs, their relationship with disease activity and the clinical utility of serum calprotectin in monitoring JIA patients.
Methods: This is a 12-month prospective, multicenter, non-interventional, observational study. Patients from 2 to 18 years diagnosed with non-systemic JIA according to ILAR criteria and receiving treatment with IFX, ADA or ETN were included. The patients were evaluated using the CHAQ and the juvenile arthritis disease activity score (JADAS 71) and determination of anti-TNF drug, anti-drug antibody and calprotectina serum levels were performed.
Results: 222 patients were included. At month 12, 181 (81.5%) continued receiving treatment, and 205 (94.5%) had positive serum levels of anti-TNF drug (96.2% of ETN, 93.5% of ADA and 66.7% of IFX) at baseline and at 12 months serum levels were positive in 161 (95.3%) patients (97.5% ETN, 93.2% ADA and 100% IFX). In total, 16 (7.3%) patients presented anti-drug A (1 of 106 anti-ETN, 13 of 109 anti-ADA, 2 of 3 anti-IFX) at baseline and 4 patients (2.4%) (0 of 81 anti-ETN, 4 of 88 anti-ADA, 0 of 1 anti-IFX) at 12 months. Regarding the relationship between anti-TNF levels or anti-drug Abs, disease activity, and functional disability overall, statistically significant differences were not observed between the groups. Patients with high levels of serum calprotectin at the baseline visit (16 of 216) showed higher JADAS-71 score [1.23 (2.06 SD) vs. 2.06 (3.44 SD)] and CHAQ [0.11 SD (0.28 SD)] vs 0.17 (0.40 SD)] compared with normal calprotectin group, although no statistically significant differences were observed (p = 0.066 and p = 0.288) between the groups with a normal and high level of serum calprotectin and the number of patients was small.
Conclusion: The low prevalence of anti-drug Abs observed was in consonance with the high proportion of patients with a positive serum level of anti-TNF drug. These data suggest an appropriate management of the long-term treatment of Spanish JIA patients, who showed a maintained inactive disease/low disease activity state and a very low functional disability state as a consequence of a low immunogenicity and good bioavailability of anti-TNF drugs.

. **Baseline patients' characteristics**.

	Total
Sex	
Female, n (%)	156 (70.3)
Age (years)	
Mean (SD)	10.77 (4.27)
Age at onset of symptoms	
Mean (SD)	4.61 (3.65)
Age at diagnosis, Diagnosis	
Mean (SD)	5.01 (3.90)
Uveitis episode prior to the study	
N (%)	76 (34.7)
Antinuclear antibodies (+)	
N (%)	155 (69.8)
Rheumatoid factor(+)	
N (%)	10 (6.0)
Anti-cyclic citrullinated peptide antibody(+)	
N (%)	14 (6.4)
HLA B27(+)	
N (%)	5,01 (3,90)
JIA subtypes according ILAR	
oligoarthritis(%)	69 (31,1)
Oligoarthritis (%)	25 (11,3)
polyarthritis FR positive (%)	7 (3,2)
polyarthritis FR negative (%)	62 (27,9)
Psoriatic (%)	10 (4,5)
arthritis-enthesitis (%)	33 (15,3)
Undifferentiated (%)	15 (6,8)

Table 2. JADAS -71 score according to immunogenicity and bioavailability of anti-TNF drugs

	Serum anti-TNF (Negative)	Serum anti-TNF (Positive)	Anti-drug antibodies (Negative)	Anti-drug antibodies (Positive)	Total
Baseline					
N	22	197	200	19	221
Mean (SD)	1.52 (2.66)	1.35 (2.29)	1.30 (2.28)	1.99 (2.66)	1.38 (2.34)
p value	0.743		0.216		
Month 12					
N	20	178	182	16	199
Mean (SD)	2.19 (2.61)	0.94 (1.90)	0.98 (1.97)	2.06 (2.22)	1.08 (2.01)
p value	0.009		0.039		

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FRI0556 **GENETIC SCREENING IN PATIENTS WITH UNDIFFERENTIATED PERIODIC FEVER SYNDROME**

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Background: Autoinflammatory diseases (AID) are a group of hereditary diseases characterised by inflammation periods accompanied with clinical findings such as fever, skin rash, lymphadenopathy, abdominal pain, musculoskeletal symptoms, and with sign of inflammation in the blood. Each disease has own typical clinical findings and they are associated with mutations in specific genes such as in MEFV gene in familial Mediterranean fever (FMF), MVK gene in hyperimmunglobulin D syndrome (HIDS), TNFRSF1A gene in tumor necrosis factor-alpha receptor associated periodic fever syndrome (TRAPS) and NLRP3 gene in cryopyrin associated periodic fever syndrome (CAPS) (1,2). Also in some patients with periodic fever syndrome (PFS), clinical signs of these diseases can be seen but no mutation can be detected in the related genes (3,4). There are also patients exhibit the incomplete phenotype of a disease or overlap signs of more than one AID. The diagnosis of these undifferentiated patients have difficult and may not be possible by a single target gene analysis (5). Screening of the periodic fever syndrome (PFS) panel including various AID genes may be beneficial to define the atypical cases. Molecular genetics has an important role for lead to diagnosis in these patients.
Objectives: The aim of this study was to investigate the genotypic diagnosis in patients with non-characteristic PFS findings for any AID.
Methods: This is a prospective study and conducted between June 2016 and December 2018. Next-generation sequencing (NGS) analysis was performed by using "Fever and AutoInflammatory Syndrome panel: Panel by Sophia Genetics" including 8 genes (MEFV, MVK, NLRP3, NLRP12, TNFRSF1A, TNFRSF11A, LPIN2 and PSTPIP1) in 30 patients with undifferentiated PFS. Clinical features and genetic results were evaluated together and final diagnoses were determined.
Results: Thirty patients included in the study did not have typical clinical features for any of the eight monogenic diseases in the PFS panel. In the result of the genetic screening; disease-causing mutation was found in MEFV gene in 12 patient, in NLRP3 gene in four patient, in NLRP12 gene in two patient and in MVK gene in one patient. Also, genetic variants of uncertain significance (VUS) in different genes were shown in five patient. No mutation was detected in remaining six patient. The final diagnosis was made by both phenotypic and genotypic data. 12 patients were diagnosed with FMF, four were FCAS, two were FCAS2, one was TRAPS and one was HIDS. Patients with negative genetic screening or had mutation as VUS, were followed as **undifferentiated** PFS.
Conclusion: Autoinflammatory diseases may not always be appear with typical clinical findings of related disease. In such patients, target gene sequencing and detection of underlying disease can be challenging. Our study has shown that the NGS analysis may help to determined the diagnosis in patients with non-characteristic PFS findings for any AID.

REFERENCES:

[1] Federici S, et al, An International Delphi Survey for the Definition of New Classification Criteria for Familial Mediterranean Fever, Mevalonate Kinase Deficiency, TNF Receptor-associated Periodic Fever Syndromes, and Cryopyrin-associated Periodic Syndrome. J Rheumatol. 2018 Nov 1.

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FRI0557 **NOVEL G-CSF RECEPTOR MUTATION CAUSING NEUTROPAENIA AND AUTO-IMMUNE DISEASE**

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Background: Novel G-CSF receptor mutation causing neutropaenia and auto-immune disease:
We present 2 brothers, born to consanguineous (second cousin) parents, with persistent, moderate neutropaenia secondary to a previously undescribed mutation in the *CSF3R* gene.
Objectives: Both brothers had associated autoimmune phenomena – one with poly-articular arthritis and the other with kerato-conjunctivitis.
Methods: Patient A is a 13-year old boy who was referred with a history of recurrent knee swelling. His father described that, from an early age, whenever he had a viral illness he developed marked swelling of his knee which settled spontaneously over a few days. In between episodes he remained completely well and fully active. Growth was normal and there was no history of recurrent or unusual infections. USS & MRI confirmed the presence of large effusions in the knees during these episodes.
On examination A had clinical evidence of synovitis in his right knee which settled spontaneously over 3 weeks. However a few months later his arthritis subsequently extended to involve his other knee, both hips, elbow and shoulder. He was treated with Etanercept with good clinical response.
Patient H is the younger brother of A. He was diagnosed with severe eczema at age 3 which needed treatment with topical steroids & tacrolimus, along with oral montelukast, to control. He subsequently developed vernal kerato-conjunctivitis which required high-dose cyclosporine & steroid eye-drops to control.
Initial Investigations: Both A and H had been noted from an early age to have neutropaenia. This was initially noted during admission for a viral illness but repeat samples over several years showed persistent neutropaenia (Patient A 0.27 – 0.94, patient H 0.9 - 1.1). Patient A also had markedly raised ESR (range 27 – 120mm/hr) noted during episodes of arthritis. All other investigations were reported as normal
Results: Whole exome sequencing of patient A revealed a novel homozygous single nucleotide variant c.909C>A affecting exon 8 of the *CSF3R* gene on Chr. 1. This was confirmed by Sanger sequencing, and the same homozygous mutation was found in patient H.
CSF3R encodes the receptor for Granulocyte Colony Stimulating Factor (G-CSF). This receptor consists of an extracellular Ig-like domain, a cytokine receptor homology domain, 3 fibronectin domains, a trans-membrane domain, and a cytoplasmic domain that couples to Janus Kinases for signal transduction. The c.909C>A variant leads to a premature stop codon, p.Tyr303*. Residue Y303 is located in the 2nd extracellular fibronectin type III domain. Truncation thereafter leads to a protein that, if expressed at all, would lack its transmembrane and cytoplasmic domains. Homozygous Y303X is thus predicted to be a null mutation.
Conclusion: G-CSF is a crucial cytokine that induces proliferation, differentiation, & survival of myeloid progenitors. This variant has not, to our knowledge, been previously described. It is compatible with low level neutrophil production, as in our patients, which may be boosted by GM-CSF, but not G-CSF.
Other recessive loss-of-function mutations in *CSF3R* have been found in patients with severe congenital neutropenia. These patients are, unsurprisingly, refractory to rhG-CSF treatment.
It is not clear how this mutation is linked to autoimmunity in these 2 boys. Theoretically both G-CSF, which is likely to be circulating in high concentrations, and GM-CSF, which may be increased to stimulate neutrophil production, have been shown to have pro-inflammatory effects, and indeed are potential targets for future treatment modalities in autoimmune diseases.
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FRI0558 **PREVALENCE OF SUBCLINICAL SACROILIITIS IN YOUNG PATIENTS WITH INFLAMMATORY BOWEL DISEASE REVEALED BY ENTERO-MRI**

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Background: Sacroiliitis is one of the extraintestinal manifestations associated with inflammatory bowel disease (IBD), and may be underdiagnosed especially in the pediatric age. MR-enterography (Entero-MRI) is currently

the imaging gold standard to assess intestinal disease activity and to detect complications in patients with IBD. Only few studies have been conducted on adult patients with IBD in order to define the role of this technique in assessing sacroiliitis, while no data are available on pediatric patients.

Objectives: To study the prevalence of inflammatory sacroiliitis on MRI performed for intestinal investigation in an IBD pediatric population.

Methods: This is a retrospective study conducted on patients suffering from IBD followed in our gastroenterology department between 2010 and 2018 whose entero-RM (1.5 or 3 Tesla, Philips depending from year of scanning) were blindly and independently scored by two readers experienced in pediatric musculoskeletal imaging. Each sacroiliac joint was divided into 4 quadrants. Signs of sacroiliitis were identified according to the ASAS criteria, with a particular attention to the presence of bone marrow edema (using T2 weighted sequences with fat suppression), diffusion restriction in DWI sequences (Diffusion Weighted Imaging) or DWIBS (Diffusion Weighted Imaging with Background Suppression) and post-contrastographic uptake in dynamic acquisitions. Demographics, IBD characteristics, clinical, radiological, and laboratory data were recorded and a dedicated Excel database was constructed. Results were elaborated using descriptive statistics.

Results: 34 patients (10 F, 24 M, age at scanning range 5-20 yrs, median 15) were included in the study, for a total of 59 entero-MRI evaluated (some patients were subjected to more than one scan). Two out of 34 patients were affected by Ulcerative Colitis, 32 by Crohn disease. Joint examination resulted negative in all patients, and none complained of articular symptoms including back pain.

In 5 IBD patients (4 CD, 1 UC) a monolateral slight degree of sacroiliitis (grade 1) was radiologically identified. They were all males, without clinical-laboratory-radiologic inflammatory signs of intestinal activity, with the exception of a patient who presented signs of intestinal and sacroiliac inflammation at his first entero-MRI, while 18 months later, at his MRI control under pharmacological treatment, signs of sacroiliitis were still present in the absence of intestinal signs of inflammation.

Conclusion: Asymptomatic sacroiliitis was observed in about 15% of our IBD patients. Sacroiliac involvement therefore can be underdiagnosed in these patients. Entero-MRI with specific sequences could be a good tool to detect early signs of sacroiliac inflammation.

REFERENCES:

[1] S.Lecler-Jacob,G.Lux, A.C.Rat, V.Laurent, A.Blum, I. Chary-Valckenaere, L.Peyrin-Biroulet & D. Loeuille. The prevalence of inflammatory sacroiliitis assessed on magnetic resonance imaging of inflammatory bowel disease: a retrospective study performed on 186 patients. Aliment Pharmacol Ther 2014; 39: 957-962.

[2] Timothy J.P. Bray, Nicola Ambrose, David Atkinson, Debajit Sen, Yiannis Ioannou and Margaret A. Hall-Craggs Diffusion-weighted imaging is a sensitive biomarker of response to biologic therapy in enthesitis-related arthritis. Rheumatology 2017; 56: 399-407.

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FRI0559 **VALIDATION OF NORDIC JUVENILE IDIOPATHIC ARTHRITIS CLINICAL PREDICTION MODELS IN A CANADIAN COHORT**

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Background: Validation of clinical prediction tools for juvenile idiopathic arthritis (JIA) in populations different than those in which they were first developed is essential to understand their applicability across healthcare settings.

Objectives: To determine if clinical prediction tools to predict 1) non-achievement of remission off medication and 2) functional disability, developed in the Nordic cohort[1] can be directly applied to JIA patients in the Canadian Research in Arthritis in Canadian Children emphasizing Outcomes (ReACCh-Out) cohort; and to assess performance of the prediction tools if model parameters are fine-tuned to the Canadian cohort.

Methods: Since the Nordic models were developed to predict outcomes 8 years after disease onset but the follow-up of the ReACCh-Out cohort was shorter, we chose to cross-validate the tools in a subpopulation of 513 subjects at the 3 years follow-up (3.75 years after onset). Attainment of remission off medications was determined by a panel of 3 pediatric rheumatologists as previously described[2] and functional disability was defined as a Childhood Health Assessment Questionnaire Disability Index (CHAQ)>0. Missing data was handled with multiple imputation by chained equations and prediction ability was assessed with c-index and Receiver Operator Characteristic (ROC) curves. The Nordic models were first evaluated exactly as published on the entire Canadian cohort. Then we fine-tuned the model coefficients using repeated runs of cross-validation in the Canadian cohort. This way, fine-tuned models were tested in patients not included in the fine-tuning process while also minimizing the standard error of prediction.

Results: In total, 408 of 506 evaluable patients (81%) were not on remission and 137 of 361 evaluable patients (38%) had functional disability at the 3-year visit. The Nordic model for predicting non-achievement of remission had a c-index of 0.68 (95%CI 0.62-0.74) when directly applied, and a c-index of 0.74 (0.70-0.78) when it was fine-tuned for the Canadian population. The latter values are comparable to those reported in the Nordic cohort (median AUC 0.78, IQR 0.72-0.82). Table 1 shows fine-tuned coefficient values along-side the original values. The Nordic model for predicting functional disability had a c-index of 0.57 (0.50-0.63) when directly applied, and fine-tuning failed to improve its performance, a c-index of 0.53 (0.43-0.63). Figure 1 shows ROC curves for fine-tuned models in the multiple splits.

Conclusion: After fine-tuning of coefficients, the Nordic model for prediction of non-achievement of remission had similar prediction ability in Canadian patients with JIA. We could not confirm the validity of the Nordic model for prediction of functional disability in Canadian patients.

REFERENCES:

[1] Rypdal V, Arnstad ED, Aalto K, et al. Predicting unfavorable long-term outcome in juvenile idiopathic arthritis: results from the Nordic cohort study. Arthritis Research & Therapy 2018;20:91

[2] Guzman J, Oen K, Tucker LB, et al. The outcomes of juvenile idiopathic arthritis in children managed with contemporary treatments: results from the ReACCh-Out cohort. Ann Rheum Dis.2015;74:1854-60

Table 1. Prediction models for non-remission off medications 3.75 years after JIA onset

Variable	Original Nordic	Fine-tuned Canada
Constant	1.58 (SE 0.44)	0.26
Cumulative active joint count	0.04 (SE 0.05)	0.13
ESR in mm/h	0.03 (SE 0.02)	-0.01
CRP> 10 mg/L	-0.07 (SE 0.69)	0.12
Morning stiffness > 15 min	1.16 (SE 0.45)	0.36
Physician global assessment	0.16 (SE 0.46)	0.15
ANA positive	1.25 (SE 0.50)	-0.02
HLA-B27 positive	1.37 (SE 0.54)	0.84
Ankle joint arthritis	1.10 (SE 0.49)	0.67

SE= Standard Error

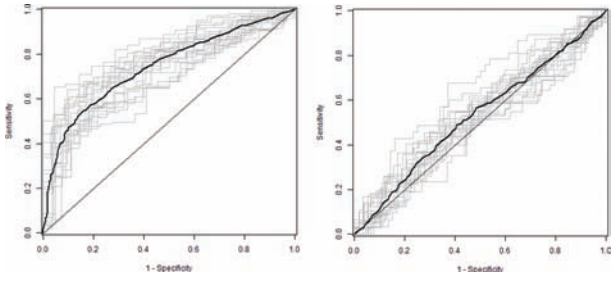


Figure 1. ROC curves for the multiple fine-tuning splits

Disclosure of Interests: None declared
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FRI0560 EFFICACY AND SAFETY OF ANAKINRA IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS – DATA OF THE BIKER REGISTRY

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Background: Anakinra (ANA) is recommended for treatment of systemic juvenile idiopathic arthritis (sJIA) and has recently received EMA approval.
Objectives: To describe safety and effectiveness of ANA in clinical practice in sJIA patients documented in the German Biologics registry (BiKeR).
Methods: Demographic and clinical parameters of the patients were recorded at BiKeR enrollment, ANA effectiveness was evaluated by half-yearly evaluation of disease activity using JADAS-10. Safety assessments were based on MedDRA-coded adverse events (AE) reports.
Results: Until December 1 2018, 50 sJIA patients treated with ANA were registered, representing 113.4 patient-years (PY) of observation, with 10 patients (20%) receiving ANA for at least 4 years. The cohort treated with ANA had experienced a prior disease duration of 3.5+/-3.8 years (mean+/-SD).
Most sJIA patients treated with ANA received pretreatment: 35 patients (70%) were pretreated with at least one other biologic, mostly etanercept (n=28), followed by tocilizumab (6) and canakinumab (1). Further pretreatments included methotrexate (MTX, n= 35), ciclosporine A (n=13), azathioprine (n=8) and other DMARDs at lower frequency. 39 patients had received corticosteroids. Concomitant treatment consisted of NSAIDs (n=20), systemic steroids (n=35), MTX (n=29) and other DMARDs (n=8).
At month 3, JADAS minimal disease activity (MDA)/JADAS remission and inactive disease according to Wallace [1] were observed in 42%/37%and 47%, respectively. After one year of treatment, the rates were 62%/45% and 56%, respectively (Figure 1).
Conclusion: The current analysis adds to the established safety profile of Anakinra and demonstrates that in ANA treated patients with sJIA the rate of SAEs was comparable and consistent with the overall AE profile of ANA in pediatric patients. Hospitalisation was the usual reason for classification as serious AE. No new safety signals specific to the paediatric population were identified in this large cohort of JIA patients.

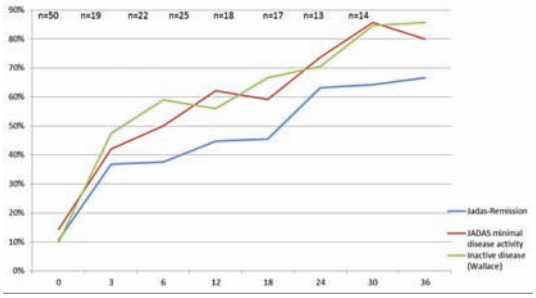


Figure 1: Efficacy parameter over time (months) in JIA patients treated with Anakinra

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FRI0561 COMPARISON OF INITIAL PRESENTATIONS BETWEEN JUVENILE IDIOPATHIC ARTHRITIS CHILDREN WITH SYSTEMIC ONSET WITH NON-BIOLOGIC MONOCYCLIC AND PERSISTENT COURSES

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Background: Juvenile idiopathic arthritis with systemic onset (soJIA) may have monocycling, polycycling or relapsed course [1]. There were not known soJIA course predictors.
Objectives: The aim of our study was to evaluate initial clinical or laboratory features of the patients with soJIA who had monocyclic course without biologics.
Methods: In the present study were included data about 130 soJIA patients. After selection we identified a subgroup of the soJIA patients (n=22) who successfully achieved remission without any biologic medication and were stable in the remission off-medication at least two years. The second group consisted of the patients with chronic persistent course (n=83). The remained 25 patients were excluded due to missing data or who did not meet the selection criteria. We evaluated routine clinical (fever, rash, hepatosplenomegaly, serositis, lymphadenopathy, MAS, joint involvement) and laboratorial (WBC, PLT, Hb, ferritin, ALS, AST, LDH, GGTP, ALP, albumin, Na, triglycerids, ESR, CRP, prothrombin, fibrinogen) soJIA features in the onset of the disease.
Results: Patient with monocycling course have no any differences except the ferritin level: 275 (133; 698) ng/ml vs 950 (150; 3240) ng/ml, (p=0.04), time to achievement remission 17.7 (8.2; 38.0) months vs 60.2 (36.0; 99.0) months (p=0.00002) and rare elbow involvement 4.6% vs 30.9% (p=0.01). The parameters, associated with possible monocycling course are in the table.

Table. The parameters, associated with possible monocyclic course in soJIA patients.

Parameter	AUC (95%CI)	Se	Sp	OR (95% CI)	p
CRP≤3.1 mg/dl	0.59 (0.48; 0.69)	0.53	077	3.6 (1.3; 10.3)	0.014
ESR≤ 53 mm/h	0.62 (0.51; 0.71)	0.9	0.43	6.8 (1.5; 31.3)	0.006
Ferritin ≤1340 ng/ml	0.69 (0.58; 0.79)	1.0	0.46	-	0.003
Active joints < 8	0.5 (0.4; 0.6)	0.82	0.39	4.6 (1.3; 16.8)	0.013
Onset age <7 years	0.57 (0.47; 0.66)	0.86	0.4	4.2 (1.5; 15.3)	0.022
No elbow involvement, n (%)	-	0.96	0.31	9.4 (1.2; 73.6)	0.012

Conclusion: Patients with soJIA initially have quit similar clinical presentations independently the further clinical course. The prediction of possible course of soJIA is a difficult problem. Patients with soJIA with monocycling course were younger and had less impressive laboratory activity. Further investigations required.

REFERENCE:

[1] Cimaz R. Systemic-onset juvenile idiopathic arthritis. Autoimmun Rev. 2016;15(9):931-4.

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FRI0562 CONCENTRATION OF SURVIVIN IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS(JIA) – DIAGNOSTIC AND PROGNOSTIC VALUE

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Background: Survivin is an anti-apoptotic protein that has been suggested as a predictive marker of severe course of adult rheumatoid arthritis and could be used for preclinical recognition of rheumatoid process.
Objectives: The goal of the study was to evaluate the diagnostic and prognostic value of survivin in Juvenile Idiopathic Arthritis (JIA).

Methods: Sixty three children with newly diagnosed JIA (46 girls and 17 boys) aged 1.5-17 years and 32 healthy children as a control group appropriately matched in terms of sex and age, hospitalized in the Department of Pediatric Cardiology and Rheumatology, Medical University of Lodz due to functional disorders of the cardiovascular system were included into the study. Concentration of survivin was assessed by an ELISA test in blood and 18 matched synovial fluid samples collected from JIA patients and in sera of children from control group.
Results: Children with JIA were divided according to the subtype of the JIA. In 68,2% of patients oligoarthritis was diagnosed. The disease activity was established on the basis of JADAS-27 criteria, distinguishing three levels of rheumatoid process activity: low, medium and high. The largest group comprised children of low activity (56%). The concentration of survivin was significantly higher in JIA compared to the controls (p=0.00041). Higher concentration of survivin correlated positively with the presence of anti-CCP antibodies (p=0.004) and with higher disease activity (p=0.0014). The higher survivin concentration was found more often in polyarticular and systemic JIA onset. In all synovial fluid samples the concentration of survivin was higher than in matched blood (p=0.0002).
Conclusion: On the basis of the conducted study, it could be concluded that the higher concentration of survivin is being associated to more severe course of the JIA. Determination of survivin may be helpful in the diagnosis of JIA and may be used to identify a group of children with early arthritis and JIA with bad prognosis who should be treated more aggressively early from the disease onset.

REFERENCES:

[1] Galeotti L, Adrian K, Berg S, Tarkowski A, Bokarewa M. Circulating survivin indicates severe course of juvenile idiopathic arthritis. Clin Exp Rheumatol. 2008;26(2):373-8.
[2] Erlandsson MC, Turkkila M, Siljehult F, Pullerits R, Eriksson C, Rantapää-Dahlqvist S, Bokarewa MI. Survivin improves the early recognition of rheumatoid arthritis among patients with arthralgia: A population-based study within two university cities of Sweden. Semin Arthritis Rheum. 2018;47 (6):778-785.

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FRI0563 A NATIONAL SURVEY ACROSS GENERAL PAEDIATRICIANS REGARDING IMMUNIZATION PRACTICES IN CHILDREN WITH RHEUMATIC DISEASES

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Background: Robust scientific evidence on the safety and efficacy of certain vaccines in patients with rheumatic diseases is available; therefore guidelines regarding immunizations in this vulnerable group of children are published via a variety of official health organizations/societies including the Greek Rheumatology Society. Nonetheless, the uptake of specific immunizations is suboptimal. In Greece, vaccinations are mainly delivered by primary care Paediatricians.
Objectives: The purpose of this study was to describe the knowledge, attitude and current practice of General Paediatricians working in primary care regarding vaccination in children with rheumatic diseases on immunosuppressive medication across Greece and to identify barriers and facilitators that could be used to promote uptake.
Methods: This was a cross-sectional survey, conducted with an anonymous questionnaire of 25 items distributed to Paediatricians via an online platform. Data collected included demographics, questions on knowledge, perceptions and opinions as well as advice given to families. Additionally, questions addressed three specific categories: live-vaccines, non-live vaccines and annual influenza vaccine. This study was approved by the "P. & A. Kyriakou" Children's Hospital Research and Ethics Committee.
Results: Out of 400 questionnaires sent out, 256 were returned. Mean age was 48 years age ((+/-8.2) mean duration of working as a Pediatrician was 15 years (+/-6.7). 25% of the responders worked in rural areas and the remaining in urban areas. 67% worked in the private sector. The majority (78%) of doctors felt that vaccination in children with rheumatic diseases is of pivotal importance. 50% gave specific advice on immunisations at initial diagnosis and 25% checked vaccination status at regular intervals. Responders were using a variety of guidelines in order to reach a clinical decision; still 45% were unaware of the existing national guidelines. 50% were hesitant to adhere to the national vaccination scheme without expert input. Reasons were: not convinced from current literature that the vaccine is safe (32%), afraid to cause disease flare (43%), unable to deal with parental concerns/refusal (54%). 12% of responders felt that the rheumatic disease may have been triggered by a vaccine. The majority (95%) were pro annual influenza vaccination, while a minority (15%) was against live vaccines administration even if the patient was not on immunosuppressive treatment. 75% of doctors were keener to administer booster doses rather than primary ones, whlie 75% of respondents would postpone vaccinations in all cases if disease was active.
Conclusion: Variation in opinion and clinical practice exists. Overall, although Greek Paediatricians are well informed regarding efficacy and side effects of immunizations, there are steps to be made form principle to practice. Further research will allow the development of clear guidelines to aid in the management of increasing numbers of children with rheumatic diseases.
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FRI0564 PSTPIP1- ASSOCIATED MYELOID-RELATED PROTEINEMIA INFLAMMATORY SYNDROME/PAMI SYNDROME: CASE REPORT AND REVIEW OF THE LITERATURE

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Background: PAMI syndrome is a recently described condition, previously known as Hyperzincemia/Hypercalprotectinemia (Hz/Hc) syndrome. It is a very rare auto-inflammatory disorder characterized by a chronic systemic inflammation, cutaneous and osteo-articular manifestations, hepatosplenomegaly, anemia and neutropenia. Increased blood levels of MRP 8/14 (S100A8/A9 or calprotectin) and zinc distinguish this condition. Specific pathogenic mutations in PSTPIP1 gene (p.E250K and p.E257K) were identified as the genetic cause of this condition.
Objectives: Case presentation and review of literature
Case Presentation: We report a case of 13 months age female referred to our unity for recurrent episodes of osteoarthritis. Physical examination showed hepatosplenomegaly. Blood work revealed a systemic inflammation, a microcytic anemia and neutropenia. A complete workup for metabolic disorders, oncologic processes and uncommon infections was negative. Because of history of recurrent osteoarthritis, a whole-body MRI was performed and confirmed a multifocal osteomyelitis. Whole exome sequencing identified the missense p.E250K in the PSTPIP1 gene.
Methods: A literature search on PAMI syndrome was performed until the15 October 2018. Pubmed was screened using a combination of the following terms: Hyperzincemia, Hypercalprotectinemia, E250K mutation, PSTPIP1 mutation, PAPA with E250K mutation.
Results: We identified 20 cases of PAMI syndrome in the literature. PAMI syndrome is an early onset inflammatory disease with a median age of 2.4 years. Clinical manifestations include Osteo-articular manifestations (80%), skin lesions (71%), splenomegaly (89%), hepatomegaly (68%), lymphadenopathy (42%), growth failure (58%) and hemorragic diasthesis with recurrent epistaxis and/or haematoma tendency in 5 patients. All cases had relevant abnormalities in hematologic parameters: mild to severe neutropenia and anemia (100%). Thrombocytopenia (42%). Systemic inflammation was confirmed in 94% using the monitoring of CRP, ESR or SAA. Zinc and MRP 8/14 blood concentrations were markedly elevated in all tested patients. Genetic analyses of PSTPIP1 gene revealed the two specific identified mutations (p.E250K and p.E257K) in all patients. Response to the treatment was variable with no consistently effective therapy. Most common therapeutic options were AINS, Corticosteroids (n=9), Anakinra (n=9), Anti-TNF (n=6) and Cyclosporine A (n=4).
Conclusion: PAMI syndrome is a rare auto inflammatory condition which should be considered in patients with undefined systemic inflammation and neutropenia, even without skin or osteo-articular manifestations. Zinc and serum MRP 14/8 measurement may be helpful tools for the diagnostic orientation in these cases.

REFERENCES:

[1] HOLZINGER D, FASSL SK, de JAGER D, et al.: Single amino acid charge switch defines clinically distinct proline-serine-threonine phosphatase- interacting protein 1 (PSTPIP1)- associated inflammatory diseases.
[2] E. BELELLI, C.PASSARELLI, M.PARDEO, et al: Haematological involvement associated with a mild autoinflammatory phenotype, in two patients carrying the E250K mutation of PSTPIP1

[3] SAMAN K. HASHIMI, KATIE BERGSTROM, ALISON A BERTUCH, et al: *PSTPIP1*-associatedmyeloid-related proteinemia inflammatory syndrome: A rare cause of childhood neutropenia associated with systemic inflammation and hyperzincemia
[4] SAMPSON B, FAGERHOL MK, SUNDERKOTTER C, et al.: Hyperzincemia and hypercalprotectinemia: a new disorder of zinc metabolism.
[5] FESSATOU S, FAGERHOL MK, ROTH J, et al.: Severe anemia and neutropenia associated with hyperzincemia and hypercalprotectinemia.

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FRI0565 A MULTINATIONAL STUDY OF THROMBOTIC MICROANGIOPATHY IN MACROPHAGE ACTIVATION SYNDROME: A DREADFUL CONDITION WHICH IS LIKELY UNDER-RECOGNIZED

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Background: Macrophage activation syndrome (MAS) is a severe complication of rheumatologic conditions, mainly systemic juvenile idiopathic arthritis (sJIA), and is classified as a secondary form of hemophagocytic lymphohistiocytosis (HLH). Thrombotic microangiopathy (TMA) is a heterogeneous group of potentially fatal diseases characterized by microangiopathic hemolytic anemia, thrombocytopenia and organ injury. The association between TMA and HLH has been described only in single reports in renal transplant recipients[1] and in two cases of virus-induced HLH[2]. TMA associated with MAS has never been reported so far
Objectives: To present the preliminary data from a multinational cohort of pediatric patients with MAS and TMA
Methods: The clinical charts of patients with MAS were retrospectively reviewed to identify the instances that were associated with TMA. Demographic, clinical and laboratory features at MAS and TMA onset, therapeutic interventions and outcome were collected.
Results: A total of 14 patients, 71.4% females, with MAS and TMA were collected. An underlying rheumatologic disease was reported in 9/14 (8 sJIA or sJIA-like illness and 1 systemic lupus erythematosus). The median age at MAS onset was 8.6 years. In 5 patients MAS and TMA occurred simultaneously, whereas in 4 TMA preceded and in 5 followed MAS. The main features at MAS and TMA onset are presented in Table. Low complement levels and reduced ADAMTS13 activity were observed in 75% and 43% of patients respectively. For MAS management, 85.7% of patients received high-dose corticosteroids and 71.4% cyclosporine; in 5 cases anakinra was added. TMA episodes were treated with plasma-exchange in 57.1% of patients; 7 patients were given biologics (1 rituximab and 6 eculizumab) with good results. Admission to the Intensive Care Unit was required in 85.7% of cases. All patients survived.
Conclusion: The association of MAS and TMA is a life-threatening condition, likely under-recognized. Clues to suspect TMA in a patient with MAS are the increase in LDH and decrease in platelet count out of proportion of other laboratory abnormalities, the drop in haptoglobin level, the finding of schistocytes in blood smear and the new onset of hematuria. Biologics, particularly rituximab and eculizumab, may offer an adjunctive therapeutic option for refractory cases.

REFERENCES:

[1] Esmaili H, et al. An update on renal involvement in hemophagocytic syndrome. J Nephropathol 2016; 2Fraga-Rodriguez GM, et al. Eculizumab in a child with atypical haemolytic uraemic syndrome and haemophagocytic lymphohistiocytosis triggered by cytomegalovirus infection. *BMJ Case Rep* 2017.

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	Features at MAS onset	Features at TMA onset	p
Fever, n (%)	14/14 (100)	10/14 (71.4)	0.0978
Hepatomegaly, n (%)	10/14 (71.4)	7/13 (53.8)	0.5847
Splenomegaly, n (%)	8/13 (61.5)	6/13 (46.2)	0.6940
CNS involvement, n (%)	8/14 (57.1)	12/14 (85.7)	0.2087
Kidney involvement, n (%)	6/14 (42.9)	13/14 (92.9)	**0.0128**
Median values			
Hemoglobin, g/dl	9.6	8.5	0.7263
Platelet count, x 10^9/l	117	34	**0.0031**
Aspartate aminotransferase, U/l	109	159	0.6455
Lactate dehydrogenase, U/l	1,997	3,188	0.2585
Fibrinogen, mg/dl	273	252	0.6599
Ferritin, ng/ml	13,974	11,116	0.5485
BUN, mg/dl	42	86	**0.0076**
Creatinine, mg/dl	1.3	1.5	0.6031
Hematuria	-	11/14 (71.4)	-
Schistocytes on blood smear	-	8/8 (100)	-
Low haptoglobin levels	-	9/9 (100)	-

FRI0566 STUDY ON SERUM DNAASE1 ACTIVITY IN PEDIATRIC ONSET SYSTEMIC LUPUS ERYTHEMATOSUS FROM A TERTIARY CARE CENTRE IN NORTH WEST INDIA

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Background: DNAase is an apoptotic endonuclease responsible for degradation of chromatin released by inappropriately cleared dead cells. DNAase1 activity in systemic lupus erythematosus (SLE) patients is lower than that in inactive disease in studies conducted in adult SLE patients from developed country. There is a paucity of data on DNAase1 activity in paediatric SLE from India.
Objectives: To measure the serum level of DNAase1 in pediatric-onset lupus patients and to correlate with the disease activity.
Methods: A cross-sectional observational study was conducted over a period of 1 year. Thirty-three consecutive children with pediatric-onset SLE were enrolled and divided into active and inactive disease activity groups based on Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score and compared the serum DNAase1 level between the two groups.
Results: Out of 33 children enrolled, 13 (39.3%) had active disease (SLEDAI score $\geq$ 3) and 20 (60.6%) had inactive disease activity. Mean age at diagnosis was 8.5 years and 10.2 years in active and inactive groups respectively. There is female preponderance (66.7%) in the enrolled patients. Anti nuclear antibody (ANA) was positive in 90.9% of patients. The most common pattern of ANA was diffuse pattern (48.4%). The patients in active disease activity group presented most commonly with nephritis (53.8%), rash (53.8%), arthralgia (38.5%), oral ulcer (30.8%) and central nervous system (CNS) involvement (38.4%) while patients in inactive disease activity group presented with nephritis (35%), arthralgia (35%), rash (25%) and CNS involvement (30%). Class III/IV lupus nephritis was present in 25% in active disease activity group while it was present in 23.1% in inactive disease activity group. Anti-double stranded DNA (anti dsDNA) was elevated in 53.8% in active group and 50% in

inactive group. Antiphospholipid antibody was present in 3 (23.1%) in active disease activity group and 5 (25%) in inactive disease activity group. The mean serum concentrations of DNAase1 were 15.394 ng/ml in active disease group and 15.205 ng/ml in inactive disease group. There was no statistically significant difference in the serum DNAase1 concentrations between the two groups (p=0.943). There was also no significant difference in the mean serum concentration of DNAase1 in patients with or without nephritis (p= 0.080).
Conclusion: The present study could not established any correlation between serum DNAase1 levels and disease activity in pediatric-onset SLE. There was no association between serum DNAase1 levels and organ involvement such as nephritis in the enrolled patients

REFERENCES:

[1] Skiljevic D, Jeremic I, Nikolic M, Andrejevic S, Sefik-Bukilica M, Stojimirovic B, et al. Serum DNase I activity in systemic lupus erythematosus: correlation with immunoserological markers, the disease activity and organ involvement. Clin Chem Lab Med. 2013 May;51(5):1083–91.

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FRI0567 ABATACEPT THERAPY EXPERIENCE IN THE CASE SERIES OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED WITH OVERLAP SYNDROME AND/OR SJOGREN'S SYNDROME

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Background: The choice of Biologics in patients with juvenile idiopathic arthritis (JIA) who have overlap syndrome with juvenile onset of systemic lupus erythematosus (JSLE), juvenile dermatomyositis (JDM), juvenile systemic sclerosis (jSSc) and juvenile Sjogren's syndrome (jSS) is difficult. TNF inhibitors are limited in this kind of disorders and abatacept (ABA) seems to be the favorable option for children, but there are not enough studies in pediatric overlap syndrome and jSS.
Objectives: The evaluation of the abatacept therapy in case series of patients with JIA associated with overlap syndrome and/or jSS.
Methods: Patients who fulfilled the criteria for JIA and the criteria of above mentioned rheumatic disorders and received abatacept therapy according to JIA indication in real clinical practice of our rheumatological clinic.
Results: 11 patients included in the retrospective study (8 girls, 3 boys). The average age of patients was 15.1 years (from 7 to 18 years). Mean duration of disease was 5.4 years. 9 patients were RF positive, 4 patients had ACCP. All of the patients had antinuclear antibody (from 1:320 to 1:2560), 3 patients had positive anti-Ro antibody. Sjogren's syndrome was the most common concomitant autoimmune disorder (**n** = 8), JDM (**n** = 2), jSSc (**n** = 2), JSLE (**n** = 1). 7 patients were treated by a low dose of prednisolone (median 5.7 mg/day). All patients received methotrexate in dose 10-15 mg/m^2/week. ABA was indicated as first line of biology therapy in 10 patients, in one patient after adalimumab withdrawn due to severe flare. Mean duration of abatacept treatment was 23.7 month (from 6 to 78). The most of the patients (82%) had excellent stable effect of ABA treatment, but two patients needed to be switched to rituximab due to secondary inefficacy. We observed wonderful result of treatment with full remission of arthritis, calcinosis regression and resolving of Sjogren's syndrome in the boy with overlap syndrome treated by ABA for 78 months. The seroconversion from initial levels of RF 32.9 IU/ml (>2N), antinuclear antibody 1:640, anti-Ro antibody 200 U/ml (>9N) to negative results was registered. The ABA was good tolerated in all patients. In one case it was canceled due to pregnancy.
Conclusion: ABA is efficacy and safety option in patients with pediatric overlap syndrome and jSS. ABA is good alternative to anti-B cell therapy and preferable choice among Biologics in such category of patients.

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FRI0568 THE USE OF NEXT GENERATION SEQUENCING PANEL IN UNDIFFERENTIATED AUTOINFLAMMATORY DISEASES IDENTIFY A SEPARATE SUBSET OF COLCHICINE-RESPONDER RECURRENT FEVERS DISTINCT FROM PFAPA SYNDROME

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Background: The number of monogenic innate immune system disorders classified as systemic autoinflammatory diseases (SAID) has increased during the recent years. However, more than 70% of patients with clinical manifestations of SAID not achieved a molecular diagnosis, thus getting into the so-called undifferentiated or undefined SAID (uSAID).
Objectives: The aim of the present study is to characterize a subgroup of patients with recurrent fever episodes distinct to PFAPA that turned out to be negative to a large 41-gene NGS panel.
Methods: We designed an NGS panel including 41 genes clustered in seven subpanels.
Results: Fifty patients were enrolled in the study. 34 patients (72%) displayed recurrent fevers and sixteen presented a chronic inflammatory disease course. A total of 100 gene variants were found (mean 2 per patient; range 0-6). Mutations with a sure or possible diagnostic impact were detected in five patients (10%). Differently from PFAPA syndrome (table), genetically negative patients with recurrent fevers presented episodes that lasted on average of six days (P<0.0001). Abdominal pain and limb pain were the most common symptoms. The classic PFAPA triad (pharingotonsillitis, aphthosis and cervical lymphadenopathy) was less frequently reported (P<0.0001) while skin rash and arthritis were more frequent (P<0.0001). Eighteen patients were exclusively treated with steroid on demand with a high response rate (94%). In 18 patients, colchicine treatment was used with an overall complete or partial response of 78%.
Conclusion: Even with a low molecular diagnostics rate, an NGS-based approach is able to provide a final diagnosis in a proportion of uSAID patients. It also allows the identification of a subgroup of genetically negative patients with recurrent fever responding to steroid on demand and colchicine.

REFERENCES:

[1] Rusmini M, et al. Next-generation sequencing and its initial applications for molecular diagnosis of systemic auto-inflammatory diseases. Ann Rheum Dis. 2016 Aug;75(8):1550-7.

Table. Clinical features of patients with undifferentiated recurrent fevers compared to PFAPA syndrome. *Values are number of patient (%) when not specified. NR = not reported. NS = not significant. P values were assessed using Chi square test or T-test as appropriate. If significant interactions were determined, a post-hoc test for multiple comparison was performed.*

Clinical features	Our cohort (34 patients)	Thomas et al. (82 patients)	Hofer et al. (301 patients)	Batu et al. (131 patients)	Pehlivan et al. (359 patients)	P value
Mean duration of episodes (days; ±SD)	5.9 ± 1.4	NR	NR	NR	4.0 ± 3.1	<.0001
Median interval between episodes (weeks; ±SD)	3.0 ± 0.3	NR	NR	NR	3.3 ± 1.5	NS
Abdominal pain	17 (50)	40 (49)	136 (45)	60 (46)	102 (29)	NS
Arthritis	7 (21)	NR	8 (3)	NR	7 (0)	<.0001
Skin rash	11 (32)	7 (9)	38 (13)	7 (5)	NR	<.0001
Pharyngotonsillitis	13 (38)	59 (72)	271 (90)	126 (96)	359 (100)	<.0001
Cervical lymphadenopathy	6 (18)	72 (88)	236 (78)	70 (53)	215 (60)	<.0001
Oral aphthosis	13 (38)	57 (70)	171 (57)	56 (43)	317 (88)	<.0001
Response to colchicine	14/18 (78)	0/1 (0)	NR	5/11 (45)	24/45 (53)	NS

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FRI0569 WHAT DOES IT MEAN TO BECOME PREGNANT WITH JUVENILE IDIOPATHIC ARTHRITIS? A MONOCENTRIC EXPERIENCE IN A TERTIARY CENTRE OF MILAN DEDICATED TO YOUNG ADULTS AFFECTED BY JIA

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Background: During the last seventeen years, biological and non-biological therapies have been used in our center in an open prospective study for the treatment of refractory JIA not only in paediatric age but also in young adults. The availability of more effective drugs for JIA has dramatically increased the number of patients willing to become pregnant. Data regarding the effect of JIA on pregnancy outcome are scant.
Objectives: The study aims to evaluate the capability of JIA patients to become pregnant, the effects of drugs on pregnancy outcome and the impact of gestation on the disease course.
Methods: JIA patients regularly followed up in our Transition Clinic of the Division of Rheumatology, Gaetano Pini Institute of Milan, were enrolled in the study at positive pregnancy test. During the whole pregnancy patients underwent monthly clinical examination and obstetric ultrasound. Data regarding disease activity and pregnancy course (fetal morphometric parameters, fetal heart rate, fetal growth, Doppler velocimetry) were collected. Gestational age, birth weight and APGAR score were also recorded.
Results: 29 pregnancies in 23 women affected by refractory JIA became pregnant during a 17 years follow up. All patients had a long lasting polyarticular disease (median duration of 23 years) not responsive to DMARDs, and became pregnant during biologic therapy. Patients were treated with Etanercept (11 patients), Golimumab (4 patients), Rituximab (3 patients), Adalimumab and Certolizumab (2 patients respectively) as monotherapy, and in most of the cases after multiple switches. One woman was treated with Etanercept during the first pregnancy and Adalimumab during her second pregnancy. Three patients decided for an elective termination and 3 experienced an early miscarriage; among 23 pregnancies resulting in live born infants, only 3 had premature births and 1 cleft palate. A pregnancy was complicated by gestosis, two by placental detachment. All the babies were followed up during the 17 years of observation and did not experience any major late complication. Eight patients were subjected to intra-articular infiltrations during pregnancy to switch off the disease, 18 patients resumed therapy shortly after childbirth and only 7 patients decided to breastfeed.
Conclusion: despite a large amount of studies demonstrating the safety of anti-TNF during pregnancy, data regarding the effects of biologics on pregnancy outcome in JIA are still lacking. The very low number of patients treated with traditional DMARDs achieving low disease activity underline the pivotal role of new biologic drugs in the management of aggressive long standing JIA, to improve the quality of life of these patients, including family planning. In our experience, no greater number of unexpected complications or side effects were observed in JIA patients during pregnancy compared to the other autoimmune diseases. Discontinuation of therapy has increased the risk of flare, requiring local therapy, confirming that EULAR recommendations for the use of biologics during pregnancy can be applied also in JIA.

REFERENCES:

[1] Bazzani C, et al. Prospectively-followed pregnancies in patients with inflammatory arthritis taking biological drugs: an Italian multicentre study. Clin Exp Rheumatol. 2015 Sep-Oct;33(5):688-93. Epub 2015 Aug 25.

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FRI0570 CLINICAL CHARACTERISTICS IN PATIENTS WITH PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUSDIAGNOSED BEFORE 6 -YEARS OLD IN A THIRD-LEVEL HOSPITAL IN MEXICO

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Background: Pediatric-onset Systemic Erythematosus Lupus (pSLE) is known to be more aggressive than adult-onset SLE. The disease is extremely rare under the age of 5 years and with severe course.
Another big difference is the association of pSLE with monogenic primary immune deficiencies (PID). Some PIDs have been associated with SLE or lupus-like manifestations: deficiencies of the classical complement pathway, female carriers of X-linked chronic granulomatous disease, IgA deficiency (present in 5% of pSLE).
It is important to consider PIDs in patients with severe manifestations in pSLE, in our country there are no studies of this association.
Objectives: To describe the clinical manifestations, laboratory features, characteristics and therapeutics of patients with diagnosis of SLE before 6 years of age at National Institute of Pediatrics in Mexico City
Methods: This is a retrospective study with the review of the patient's records with diagnosis of SLE before 6 years old, from the Immunology department between January 2005 and December 2016 at National Institute of Pediatrics in Mexico City.
Results: Between 2005-2016 there were 295 newly patients diagnosed with pediatric Systemic Lupus Erythematosus (pSLE) at our hospital, from these patients 2.7% (8) were diagnosed with pSLE before 6 years of age. According to this, 7 (87.5%) were female. The youngest patient was 26 months at moment of diagnosis.
Every patient had at least 4 criteria of the ACR classification for SLE. Only 2 (25%) had malar rash at diagnosis, and 1 (12.5%) presented discoid rash. Seventy-five percent of patients presented glomerulonephritis at diagnosis and also 75% had an Hematological disorder.
In terms of serology, 37.5% had positive native DNA antibody, 37.5% antibody to Sm protein and 37.5% antiphospholipid antibodies. One hundred percent of patients had presence of antinuclear antibody (ANA) at moment of diagnosis.
Conclusion: During 2005-2016 we found 295 newly patients with diagnosis of pediatric Systemic Erythematosus Lupus (pSLE), from these, eight patients (2.7%) were diagnosed before 6 years of age. Seventy-five percent presented recurrent infections and 50% with severe infections, and one patient died due to septic shock.
Systemic erythematosus lupus with an early onset has a more severe phenotype and has been associated with monogenic primary immune deficiency, presenting with severe infections and higher mortality.
In our country, we do not have genetic testing to help us determine the endless monogenic defects associated with early-onset SLE, being necessary to determine etiology and specific treatment as needed.
We recommended that in every patient with severe pSLE who develops life-threatening, infections or due to unusual germs, associated with hypocomplementemia and/or consanguinity, to perform an approach to rule out any primary immune deficiency.

REFERENCES:

[1] Levy, D. Kamphuis Systemic Lupus Erythematosus in Children and Adolescents. Pediatr Clin North Am. 2012 April; 59(2): 345–364
[2] F.Rivas-Larrauri, M.A.Yamazaki-Nakashimada. Lupus eritematoso sistémico: ¿es una sola enfermedad? Reumatol Clin. 2016;12(5):274–281
[3] Carneiro M, Understanding Systemic Lupus Erythematosus Physiopathology in the Light of Primary Immunodeficiencies J Clin Immunol (2008) 28 (Suppl 1):S34–S41
[4] G. Tsokos, K. Sullivan, New insights into de immunopathogenesis of systemic lupus erythematosus. Nature Reviews (2016) 10.1038

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FRI0571 MEASUREMENT PERFORMANCE OF REDUCED VERSIONS OF MUSCLE STRENGTH TOOLS IN JUVENILE DERMATOMYOSITIS

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Background: Assessment of muscle strength is a fundamental component of the clinical evaluation of children with juvenile dermatomyositis (JDM). Regular measurement of muscle strength in daily care requires the availability of simple and quick muscle assessment tools.
Objectives: To investigate whether reduced versions of the MMT8 and CMAS are equally reliable as the original tools.
Methods: The following 4 reduced instruments were devised: 1) MMT4 (score 0-40), including 4 items of MMT8 (neck flexors, deltoid middle, gluteus maximus, and gluteus medius); 2) MMT6 (score 0-60), composed of the same items of MMT4 plus biceps brachii and quadriceps; 3) head lift time of CMAS (0-120 seconds or 0-5 points); 4) sum of CMAS head lift time in points and the 6 sit-ups maneuvers of CMAS (score 0-11). Validation was conducted according to OMERACT filter on 213 patients followed in standard clinical care at 13 international pediatric rheumatology centers and evaluated at baseline and after a median of 5.9 months.
Results: All reduced instruments revealed strong correlations ($r > 0.7$) with muscle activity VAS and total DAS, moderate correlations ($r = 0.4$-0.7) with physician's global VAS, muscle DAS, skin activity VAS, pain VAS, parent's overall wellbeing VAS, and CK. Correlations with skin DAS and fatigue VAS were low ($r < 0.4$). Cronbach's alpha was excellent (0.92-0.95) for all reduced tools for which this property could be assessed. SRM was good-to-moderate (0.60-0.91) for all reduced instruments in patients judged as improved by the physician. All reduced tools discriminated strongly between patients classified in different disease activity states by the physician ($p < 0.0001$), and between patients whose parents were satisfied or not satisfied with their children's disease status ($p < 0.0001$). Overall, the metrologic performance of the reduced instruments was comparable to that of MMT8 and CMAS.
Conclusion: We found that reduced versions of the MMT8 and CMAS have good metrologic properties and perform similarly to the original tools in a population of patients followed in standard clinical care. Our results suggest that these simplified and shortened instruments could serve as surrogate for the complete measures in routine practice, particularly in a busy clinical setting.

REFERENCES:

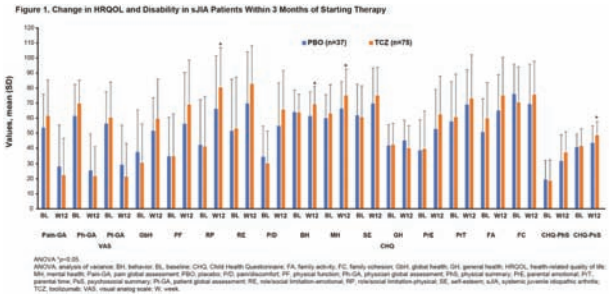
[1] Measures of adult and juvenile dermatomyositis, polimyositis, and inclusion body myositis. Rider LG, Werth VP, Huber AM, Alexanderson H, Rao AP, et al. Arthritis Care Res (Hoboken) 2011;63:S118-57.
[2] Clinical assessment in juvenile dermatomyositis. Ravelli A, Ruperto N, Trail L, Felici E, Sala E, et al. Autoimmunity 2006;39:197-203.

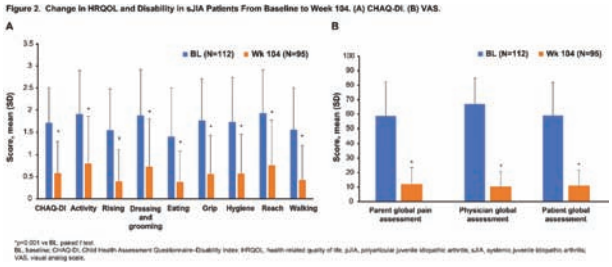
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FRI0572 DISABILITY AND HEALTH-RELATED QUALITY OF LIFE OUTCOMES IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH TOCILIZUMAB IN A PHASE 3 RANDOMIZED CONTROLLED TRIAL

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Background: Tocilizumab (TCZ) intravenous (IV) formulation was approved for the treatment of patients with systemic juvenile idiopathic arthritis (sJIA) based on the results of a large phase 3 clinical trial. Physical function, measured by the Childhood Health Assessment Questionnaire–Disability Index (CHAQ-DI), and health-related quality of life (HRQOL), measured by the Child Health Questionnaire (CHQ), were evaluated.
Objectives: To examine measures of disability and HRQOL in patients with sJIA treated with TCZ IV for up to 2 years in post hoc analysis of data from the phase 3 trial of TCZ.
Methods: Changes within 3 months of treatment initiation with TCZ (baseline) were compared between TCZ- and placebo (PBO)–treated patients using CHAQ-DI, pain global assessment (Pain-GA), physician global assessment, and patient global assessment (Pt-GA) using analysis of variance adjusted for treatment group. Changes in CHAQ-DI overall and domain scores and changes in CHQ domain and summary scores from baseline to 2 years were compared for patients treated with TCZ using the unpaired *t* test.
Results: Patients with sJIA experienced clinically relevant improvement in physical function (CHAQ-DI) and reduction of pain (Pain-GA). Mean (SD) CHAQ-DI scores for patients treated with PBO and TCZ were 1.7 (0.8) for both groups at baseline and 1.2 (1.0) and 0.9 (0.8), respectively, at week 12 (week 12 mean difference, –0.2; median [range] change from baseline to week 12 difference, –0.3 [–0.6 to 0.0]). These patients also had significantly improved CHQ socialization, behavior, mental health, and psychosocial summary scores after 3 months compared with those receiving PBO (Figure 1). Improvement in all CHAQ-DI domains over 2 years was observed with TCZ treatment (Figure 2); improvement rates in patient well-being (Pt-GA) were 87.7%. Similar improvements in physical function were observed in patients with polyarticular JIA in the phase 3 trial that led to approval of TCZ IV in these patients (not shown). There was also significant improvement ($p<0.05$) in most domains of HRQOL (CHQ domain scores) in patients with sJIA; of note, patients experienced marked improvement in mean scores from baseline to week 104 for pain/discomfort (31.7 to 75.3), self-esteem (61.0 to 76.0), mental health (62.1 to 76.8), and social limitation-emotional (52.6 to 86.2).
Conclusion: Two years of TCZ treatment resulted in statistically significant and clinically relevant improvements in function and HRQOL in patients with sJIA.





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FRI0573

COGNITIVE IMPAIRMENT IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: EARLY DETECTION WITH MR SPECTROSCOPY AND ITS ASSOCIATION WITH MOG ANTIBODIES

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease characterized by the presence of various autoantibodies. Unnoticed and progressive cognitive impairment may develop in the course of disease even without overt neuropsychiatric (NP) features. Some authors attributed this mild impairment to the immune-mediated myelinopathy. Evidence exists that myelin oligodendrocyte glycoprotein (MOG) might act as a mediator of interactions between myelin and the immune system.

Objectives: To detect the role of MOG-Ab in neurologic manifestations of childhood-onset SLE (cSLE) and to better delineate the actual grade of cognitive dysfunction by neurocognitive tests in patients without overt NP features (non-NPSLE). Moreover, we aimed to identify the localization of pathology at molecular level by analyzing the presence of any correlation between various metabolite peaks in MR spectroscopy (MRS) and the severity of cognitive dysfunction in non-NPSLE children.

Methods: MOG-Ab levels were studied in all healthy subjects (n=28) and in all patients with (NPSLE =9) and without (non-NPSLE=36) overt neuropsychiatric manifestations. All of the non-NPSLE group and healthy group underwent brain MR and MRS examination. However, only 20 subjects in each group met the MRS imaging standards for evaluation. In the non-NPSLE group, 29 cSLE patients were further evaluated by neurocognitive tests. Sixteen children with non-NPSLE were assessed by both MRS and neurocognitive tests.

Results: The mean age of the SLE patients at study time was 16.22± 3.22 years. MOG-Ab was detected positive neither in cSLE nor in healthy group.

In children with non-NPSLE, verbal IQ ranged from 40 to 108 (mean: 79.06±17.66), performance IQ ranged from 42 to 111 (mean: 92.03 ±16.28), and full-scale IQ ranged from 40 to 106 (mean: 84.31±16.39). There were 15 patients (51%) in non-NPSLE group with a full-scale IQ under 85. There was no significant difference between the non-NPSLE group and healthy subjects in terms of choline, N-aspartic acid (NAA), creatine, NAA/creatine and choline/creatine.

A negative correlation was observed between the NAA/Creatine level of the left frontal white matter in MRS and the stroop test time (measures the ability to shift a perceptual set with changing demands which is a function of the frontal lobes) (p=0.015; r=0.596).

Conclusion: More than a half of our patients in non-NPSLE group were found to have a full-scale IQ under 85. Cognitive impairment may develop insidiously in cSLE children even without any overt symptom or sign. There was no association of MOG-Ab with cSLE, whether neuropsychiatric manifestations present or not. A causal relationship between immune-mediated myelinopathy and neuropsychiatric involvement/cognitive impairment could not be suggested, since there has been no patient with positive MOG-Ab and there has been no difference in choline, cholin/creatine between cSLE patients and healthy subjects. Decrease in the NAA/Creatine level of the left frontal white matter in MRS, which is a finding of neuronal loss, may be used as a first sign of cognitive impairment in patients with cSLE.

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FRI0574 **CLINICAL RESPONSE TO HIGH-DOSE INTRAVENOUS METHYLPREDNISOLONE IN CHILDHOOD AUTOIMMUNE UVEITIS: A RETROSPECTIVE ANALYSIS**

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Background: Intraocular inflammation accounts for up to 10-15% of total blindness cases [1]. The incidence of uveitis in children ranges around 4.9/100.000, and a significant number of patients develop chronic courses and irreparable complications [2]. An impressive 74% of children with juvenile idiopathic arthritis (JIA)-associated uveitis are legally blind at diagnosis [3]. This underscores the importance of timely diagnosis and effective anti-inflammatory treatment.
Objectives: To evaluate the clinical response to high-dose intravenous methylprednisolone (IVMP) in children and adolescents with autoimmune uveitis.
Methods: A retrospective chart review was conducted in two tertiary referral centers in Germany (TU Dresden and University of Würzburg) to investigate treatment responses to IVMP (10-30mg/kg/day on three successive days with a total of one to five IVMP at monthly intervals) in children and adolescents (<16 years) with autoimmune uveitis diagnosed between 2003 and 2016. Clinical features of uveitis, disease activity, outcomes, and concomitant anti-inflammatory treatment were documented at treatment initiation, after 3 and 6 months.
Results: Fifty-six patients (93 affected eyes) with a median age of 7.4 (range: 2.5-16.7) years were included. In 29% of patients uveitis was associated with JIA. Uveitis was predominately located in the anterior segment (43%), bilateral (66%) and recurrent (43%). Complications occurred in 77% of patients and included visual loss, synechiae, cataract and/or retinal lesions. Patients with active uveitis received between 1 and 5 IVMP. Visual acuity improved significantly (0.52±0.33 to 0.69±0.30 at 3 months (p<0.001), 0.78±0.31 at 6 months (p<0.001)) independent of the number of IVMP. Furthermore, anterior chamber cells (45% to 18%, p=0.01), synechiae (47% to 32%, p<0.005), keratic precipitates (27% to 18%, p<0.001), papillary edema (30% to 13%, p<0.001) and/or macular edema (15% to 4%, p=0.01) improved 3 months after IVMP. Over all, children treated with 3 or more IVMP (n=27) (as compared to 1 IVMP (n=18)) experienced fewer relapses (Median 1 [0-6] vs 3 [0-13], p=0.186), developed fewer cataracts (7% vs 39%, p<0.02) and less frequently required treatment with biologics (19% vs 39%, p=0.174).
Conclusion: High-dose IVMP induces rapid improvement in children with autoimmune uveitis. Data suggest improved outcomes in children treated with three or more courses of IVMP when compared to one course (without reaching statistical significance). Prospective randomized trials in larger cohorts are required to confirm results.

REFERENCES:

[1] Nussenblatt RB. The natural course of uveitis. Int Ophthalmol. 1990; 141:303–8.
[2] [2] Päivönsalo-Hietanen T et al. Uveitis in children: population-based study in
[3] Finland. Acta Ophthalmol Scand. 2000; 78(1):84-8.
[4] [3] Woreta F at el. Risk factors for ocular complications and poor visual acuity at presentation among patients with uveitis associated with juvenile idiopathic arthritis (JIA). Am J Ophthalmol 2007; 143:647–55.

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Local Principal Investigator in a Clinical Trial DAP-PEDOST-11-03 supported by Merck (Trial Registration EUDRACT 2013-000864-28), Anna Leszczynska: None declared, Christian Hedrich Grant/research support from: Novartis Pharmaceuticas for Research study on effector T cells in psoriasis, Speakers bureau: In 2016: Roche Pharmaceuticals, Rheumato-Logisch, Dresden, Germany; Novartis, Advisory board > Travel costs.
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FRI0575 **PREVALENCE OF OVERWEIGHT AND OBESITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS**

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Background: Children with juvenile idiopathic arthritis (JIA) may have an increased risk for overweight and obesity, which could be an additional risk factor for inflammatory arthritis.
Objectives: The aims of this study were to determine the prevalence of overweight and obesity in children and adolescents with JIA, and to assess the association between overweight and disease parameters in this population.
Methods: We assessed the weight (kg) and height (cm) according to the standard deviation score (SDS) in a cross-sectional study of JIA children. The diagnosis of JIA was based on the International League of Association of Rheumatology (ILAR) criteria. Overweight and obesity were defined by the Body Mass Index (BMI) (weight/height^2) matched on age and sex and in reference to the French curves. Children were classified as obese if their BMI was $\geq$ 95th percentile, overweight if their BMI was between the 85th and 94th percentile, and healthy weight if their BMI was between the 5th and the 84th percentiles. Functional disability was determined by the Childhood Health Assessment Questionnaire (CHAQ). Disease activity was assessed using a validated score, Juvenile Arthritis Disease Activity Score 27 (JADAS- 27).
Results: Fifty-five patients (38 boys and 17 girls) with JIA were enrolled in this study. The median age was 8.5 ± 4.12 years (range 6–14). Thirty-one patients (53%) had persistant oligoarticular JIA, 15 (27%) had polyarticular JIA, 5 patients (9%) had systemic JIA, and 4 (7%) had enthesitis-related arthritis. The median disease duration was 3.2 ± 2.8 years. Twelve patients had active disease at the time of the study with a mean JADAS 27 of 6.9 ± 2.7. The mean CHAQ was 1.4 ± 0.5. Nineteen children (52.7%) had received corticosteroids during an average period of 1.7 years [0.6-3] with a mean of 10mg/day of prednisone or equivalent. The mean BMI was 14.56 ± 2.1 kg/m^2. Twenty-two patients (40%) were overweight, 15 (27%) were obese and 18 (33%) have normal weight. Patients with normal weight, overweight and obese represented respectively 60%, 20% and 20% of systemic forms, 53%, 27% and 20% of polyarticular form, 39%, 32% and 29% of persistent oligoarticular forms, and 50%, 25% and 25% of enthesitis-related arthritis forms. Obesity was more frequent in older patients (p=0.021), with significant functional impairment (p<0.001) and with active disease (p<0.001). Only systemic JIA was more likely to be associated with overweight (p=0.031) and obesity (p=0.024). There was no relationships with other subtypes of JIA (p=0.428) or with corticosteroid treatment (p= 0.636).
Conclusion: In our study, more than 60% of patients were overweight. Severe functional limitation, systemic JIA, and active disease were the most correlated parameters with obesity. Better management of the activity and functional status of the disease may reduce overweight in children with JIA.

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FRI0576 **PULSE WAVE VELOCITY EVALUATING ARTERIAL STIFFNESS IN FAMILIAL MEDITERRANEAN FEVER**

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Background: Chronic inflammation leads to atherosclerosis, resulting in increased arterial stiffness. Familial Mediterranean Fever (FMF) patients, experiencing recurrent inflammatory process during the attacks, are at increased risk for atherosclerosis and cardiovascular disease. Carotid-femoral Pulse Wave Velocity (cf-PWV) is considered the gold standard for arterial stiffness evaluation. There are few studies investigating arterial stiffness with the use of PWV only in adult patients with FMF, but none in children.
Objectives: In the present study we aimed to investigate indices of arterial stiffness, cf-PWV and aortic augmentation index (AIx75), measured with the SphygmoCor XCEL device, in patient with FMF -mostly of childhood- and their associations with disease-related factors and colchicine treatment.
Methods: A total of 85 individuals were enrolled in the study, 43 FMF patients, including 30 children, in attack free period, attending the outpatient clinic of a paediatric rheumatology referral center in Northern

Greece, between September 2015 and June 2018 and 42 healthy controls.

Results: Patients with FMF presented similar systolic Blood Pressure (sBP), central Systolic Pressure (cSP) and cf-PWV values to controls, but significantly higher AIx75 values (patients vs. controls, 19.76% and 9.96%, p<0.05). Only one FMF patient had cf-PWV > 95th percentile. Statistical analysis in FMF patients showed that AIx75 adjusted for age and sew associated with complete response compared to partial response to treatment (B=-17.78 95% CI -31.17-(-4.40), P<0.05) and the presence of M694V.M680I genotype (B=-16.75 95% CI -33.81 -0.30, P=0.05). Cf-PWV presented an inverse relationship with colchicine treatment duration (B=-0.003, 95% CI (-0.006)-0.00, P<0.05). Cf-PWV values adjusted for age and sBP associated with attacks frequency (for <2 months vs. > 2 months, B= 0.48 95%CI 0.01-0.96, P<0.05). Addition of colchicine treatment duration to the model, attenuated the association between cf-PWV and attack frequency, supporting the protective role of colchicine.

Conclusion: The normal values of cf-PWV in FMF patients may reflect the compliance to colchicine treatment, that seems to have a protective role against vessel inflammation. However, the increased values of AIx75 need further investigation.

REFERENCES:

[1] Mustafa Cakar, Muharrem Akhan, Tolga Dogan, Gurhan Taskin, Kadir Ozturk, Muhammet Cinar, Erol Arslan, Sedan Yilmaz, Investigation of the arterial stiffness and associated factors in patients with familial Mediterranean fever, Anatol. J Cardiol 2017; 17:132-8

[2] O. Kukuy, a. Livneh, L. Mendel, A. Benor, E. Giat, O. Perski, O. Feld, Y. Kassel, I. Ben-Zvi, M. Lidar, E. J. Holtzman, A. Leiba, Normal arterial stiffness in familial Mediterranean fever. Evidence for a possible cardiovascular protective role of Colchicine, Clin Exp Rheumatol 2017; 35 (Suppl. 108): S32-S37

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FRI0577 **ANTIPHOSPHOLIPID SYNDROME SECONDARY TO PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS. EXPERIENCE IN A THIRD-LEVEL HOSPITAL IN MEXICO CITY**

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Background: Antiphospholipid syndrome (APS) is a multisystemic autoimmune disease that is characterized by thromboembolic events, pregnancy morbidity and other manifestations in the presence of elevated titers of antiphospholipid antibodies.(1)

APS can be either primary, occurring as an isolated clinical entity, or secondary to other diseases including infections, malignancy or autoimmunity, the latter associated in particular with systemic lupus erythematosus (SLE).(1)

Patients with SLE can produce a great variety of autoantibodies, including the so called antiphospholipid antibodies (aPLs), such as lupus anticoagulant (LA); anti-cardiolipin antibodies (aCL) or anti-β_2Glycoprotein-I antibodies (anti-β_2GPI).(2) These aPLs have been described in 20-40% of SLE patients.

Objectives: To report frequency of patients with antiphospholipid syndrome secondary to pediatric systemic lupus erythematosus (pSLE) at National Institute of Pediatrics in Mexico City from 2005-2016. In addition, describe their clinical manifestations and laboratory features.

Methods: Retrospective study that included all pediatric systemic lupus erythematosus (pSLE) patients diagnosed at National Institute of Pediatrics in Mexico City from 2005 to 2016. We then identified patients with positive antiphospholipid antibodies (aPLs) and/or clinical manifestation of antiphospholipid syndrome (APS). Demographic, clinical and laboratory features were extracted from their clinical records. Study approved by the local Ethics Committee.

Results: Over the 12-year study period, we collected 295 patients with a new diagnosis of pediatric systemic lupus erythematosus (pSLE). Eighty patients (27.11%) had at least a positive antiphospholipid antibody (aPL) or a clinical manifestation of antiphospholipid syndrome (APS). Figure 1 shows our study population. Of these 80 patients, 75 (93.75%) had a positive aPL at moment of pSLE. With respect to the remaining 5 cases, 3 of them developed a positive aPL during follow-up, while the remaining 2 cases presented a clinical feature of APS simultaneously to pSLE diagnosis and their serology persisted negative during follow-up.

Twenty (25%) patients had a clinical manifestation associated to APS. Concerning these patients, 11 (55%) patients presented clinical features of APS at time of pSLE diagnosis, 6 (30%) patients developed it during follow-up and the remaining 3 (15%) patients had previous history of a clinical manifestation associated to APS prior to pSLE diagnosis. Nevertheless, 2 of these 20 patients never reported positive antiphospholipid antibodies.

According to clinical manifestations 11 (55%) patients had venous thrombosis, 7 (35%) patients with arterial thrombosis, one patient identified with chorea and one showed evidence of thrombosis in a skin biopsy.

Characteristics of the patients are shown in Table 1.

Conclusion: Antiphospholipid syndrome (APS) secondary to pediatric systemic lupus erythematosus (pSLE) is a very common entity and is increasingly diagnosed. This study allowed us to report frequency and describe clinical manifestations of pSLE patients presenting with secondary APS from Mexico City.

Figure 1. Patients with pediatric systemic lupus erythematosus at National Institute of Pediatrics from 2005-2016.

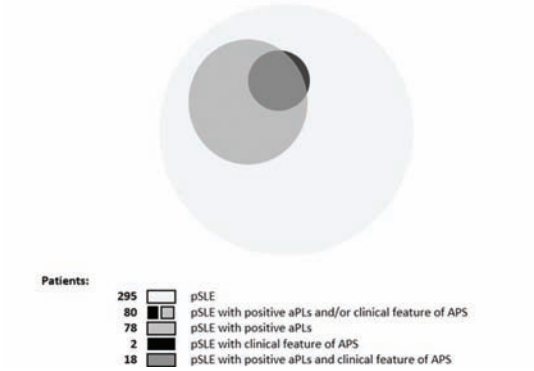


Table 1. Characteristics of patients with clinical features of APS secondary to pSLE.

Case	Sex	Age at pSLE diagnosis	Clinical manifestation of APS according to pSLE diagnosis	APS clinical manifestation	Anti-B2GPI-IgG/IgM	Anti-aCL-IgG/IgM	LA
1	F	12 y 4 mo	Follow-up	Venous thrombosis of LL	+/+	+/+	+
2	F	5 y 9 mo	At diagnosis	Skin biopsy with thrombosis	-/+	+/+	-
3	F	9 y 10 mo	Follow-up	Venous thrombosis of LL	-/-	-/+	+
4	F	10 y 0 mo	Follow-up	Stroke	-/+	-/-	-
5	F	8 y 2 mo	At diagnosis	Stroke	-/-	-/+	+
6	F	12 y 5 mo	At diagnosis	Venous thrombosis of LL	+/-	+/-	+
7	M	14 y 11 mo	At diagnosis	Splenic vein thrombosis	-/+	-/-	-
8	F	5 y 6 mo	Previous history	Stroke	-/+	+/-	-
9	F	7 y 10 mo	Follow-up	Chorea	+/+	+/+	+
10	F	13 y 5 mo	At diagnosis	Digital ischemia	+/+	+/+	+
11	F	14 y 2 mo	At diagnosis	Venous thrombosis of LL	ND	+/ND	+
12	F	13 y 5 mo	Follow-up	Pulmonary thromboembolism	-/+	+/-	+
13	F	16 y 5 mo	At diagnosis	Venous thrombosis of LL	+/+	+/+	+
14	M	10 y 6 mo	At diagnosis	Digital ischemia	+/+	+/+	+
15	F	14 y 9 mo	Follow-up	Venous thrombosis of UL	-/+	-/+	+
16	F	15 y 8 mo	Previous history	Arterial pancreatic thrombosis	-/+	-/-	-
17	F	13 y 7 mo	Previous history	Stroke	+/+	-/-	ND
18	F	13 y 9 mo	At diagnosis	Stroke	ND	-/+	ND
19	M	16 y 2 mo	At diagnosis	Venous thrombosis of LL	-/-	-/-	-/-
20	F	15 y 1 mo	At diagnosis	Venous thrombosis of LL	-/-	-/-	-/-

Anti-aCL: anticardiolipin antibodies; anti-B2GPI: anti-β2 glycoprotein-I antibodies F: female; LA: lupic anticoagulant; LL: lower limb; M: male; mo months; UL: upper limb; ND: no data; y:years

Antiphospholipid antibodies (aPLs) were positive in 27% of cases with pSLE. And more than 90% of cases had positive aPLs at moment of pSLE diagnosis, which is why we strongly agree with international recommendations of performing aPLs screening simultaneously to pSLE diagnosis.

REFERENCES:

[1] Meroni PL, Argolini LM, Pontikaki I, P.l M, L.m A, I P. What is known about pediatric antiphospholipid syndrome? Expert Rev Hematol. 2016;9 (10):977–85.

[2] Taraborelli M, Lazzaroni MG, Martinazzi N, Fredi M, Cavazzana F. The role of clinically significant antiphospholipid antibodies in systemic lupus erythematosus. Reumatismo. 2016;68(3):137–43.

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FRI0578 **LACC1 MUTATION IN THREE SIBLINGS WITH POLYARTHRITIS WITHOUT SYSTEMIC MANIFESTATIONS**

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Background: Juvenile idiopathic arthritis (JIA) is a complex group of disorders characterized by wide phenotypic diversity and genetic heterogeneity. It has multifactorial etiology varying among different subtypes. There are emerging reports on new gene loci being identified especially in families with many affected members (1,2)
Objectives: To report 3 siblings with polyarthritis who were detected to have mutation in Laccase domain containing 1 (*LACC 1*) gene.
Methods: We reviewed case records of 3 siblings with infantile onset polyarthritis and performed whole exome sequencing on their DNA samples for *LACC1*, *MMP2* and *WISP* genes.
Results: A non-consanguineous family from north-western part of India reported with 3 daughters having polyarticular joint disease. The chronology of symptoms was similar in all 3 children. Joint symptoms started in later half of infancy with swelling of knee and ankle. This disease was progressive and over the following 2 years there was involvement of small joints and cervical spine too (Figure 1) along with deformities and contractures. The investigations at the time of first evaluation are given in Table 1. Radiographs in all 3 sisters showed osteoporosis and erosion of vertebrae (Figure 2).
The children were initially started on naproxen. Later, in view of rheumatoid factor positivity in eldest sister we decided to give them a trial of oral prednisolone (initially 1 mg/kg and subsequently tapered) and subcutaneous methotrexate (10 mg/m^2/week). Methotrexate was continued on long term basis. Over the next 24 months of follow-up the clinical improvement has been sustained.
Whole-exome-sequencing in all three girls has revealed mutation in *LACC1* gene [Exon 4; c.832G>C; p.(Ala278Pro), Homozygous, Autosomal recessive].
Conclusion: This case report further provides evidence to the emerging association of *LACC1* mutation with familial aggregation of JIA (1,2). Long term follow-up of these patients is necessary to determine the natural course of this intriguing clinical entity.

REFERENCES:

[1] Wakil SM, Monies DM, Abouelhoda M, Al-Tassan N, Al-Dusery H, Naim EA, et al. Association of a Mutation in *LACC1* With a Monogenic Form of Systemic Juvenile Idiopathic Arthritis: Monogenic Systemic Juvenile Idiopathic Arthritis. Arthritis & Rheumatology. 2015 Jan;67(1):288–95.
[2] Karacan I, Uğurlu S, Şahin S, Everest E, Kasapçopur Ö, Tolun A, et al. *LACC1* Gene Defects in Familial Form of Juvenile Arthritis. J Rheumatol. 2018 May;45(5):726–8.

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FRI0579 **PREDNISONE VERSUS STANDARD THERAPY IN SYDENHAM'S CHOREA: RESULTS FROM A RETROSPECTIVE STUDY**

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Background: Sydenham's chorea is a major and delayed manifestation of acute rheumatic fever [1] and is considered to be a prototype of an autoimmune disorder triggered by an infectious agent. Aside from conventional symptomatic treatment (carbamazepine, valproate, neuroleptics), the use of steroids has also been advocated, mainly in severe, drug-resistant cases or if clinically disabling side effects develop with first line therapies. However the evidence of corticosteroids efficacy is weak.
Objectives: To describe the efficacy of corticosteroids therapy versus standard therapy in children affected by Sydenham's Chorea in a cohort of Italian patients with acute rheumatic fever (ARF).
Methods: A retrospective observational study was conducted. The hospital records for all children diagnosed as having ARF between January 2007 and December 2017 in the Pediatric Rheumatology Division of the Meyer Children Hospital (Florence) and IRCCS Burlo Garofolo (Trieste) were reviewed. The diagnosis of ARF was made by pediatric rheumatologists and all the children discharged with a ICD 9 code consistent with ARF were included. For the purpose of the study only patients with Sydenham's Chorea were enrolled. Files were analyzed for demographic data, clinical and laboratory findings on admission and during the hospital stay and patients with incomplete information were excluded. Time and resolution of choreic symptoms were evaluated in consideration of presence or absence of corticosteroid therapy.
Results: Thirty patients were enrolled; 23 out of 30 (76%) had generalized chorea. 15 (50%) were treated with prednisone (2 mg/kg/day in a single administration per day for 14 days before tapering), 11 (36.6%) were not treated with medications and 4 (13.3%) received pimozide or sodium valproate. We considered together patients who did not receive any specific therapy for chorea and patients who received only symptomatic anti-chorea drugs (pimozide in 3 cases and sodium valproate in 1 case). Therefore we obtained two groups of 15 participants each: "Prednisone group" and "Standard therapy group". The time required for clinical improvement in the two groups appeared statistically different ($P = 0.002$). In "Prednisone group" the median time for improvement was 4.0 days (interquartile range: 3) whereas in "Standard therapy group" it was 16.0 days (interquartile range: 16). Furthermore, the "Prednisone group" had a median remission time of 30.0 days (interquartile range: 34) whereas "Standard therapy group" presented a median remission time of 135.0 days (interquartile range: 309) ($P < 0.001$). At least one episode of relapse occurred in 1 (6.7%) out of 15 patients in the "Prednisone group" and in 3 patients (20%) in the "Standard therapy group". However, the difference is not statistically significant ($p = 0.598$).
Conclusion: Our study shows that corticosteroid therapy is associated with a faster resolution of Sydenham's Chorea's symptoms compared to treatments considered of first line, such as: no therapy, valproate or pimozide.
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FRI0580 **ULTRASONOGRAPHY SCORE CORRELATES WITH DISEASE ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS – ENTHESITIS RELATED ARTHRITIS – A CROSS SECTIONAL OBSERVATIONAL STUDY FROM INDIA**

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Background: Enthesitis is a distinct clinical hallmark of spondyloarthropathy in children and adults. Ultrasonography (US) is a powerful tool to detect enthesitis. There are only a few studies on US detected enthesitis in Juvenile Idiopathic Arthritis - Enthesitis Related Arthritis (JIA-ERA) from India.
Objectives: To assess the presence of clinical and US detected enthesitis in JIA- ERA and to correlate with disease activity.
Methods: 51 consecutive JIA-ERA patients fulfilling the ILAR classification criteria were evaluated clinically and sonographically from October 2016 to September 2017 in a tertiary care centre from Northern India. Enthesitis was clinically assessed using the MASES (Maastricht Ankylosing Spondylitis Enthesitis Score). Additionally peripheral entheseal sites of lower limb (insertion of plantar fascia at calcaneal tuberosity, insertion of Achilles at superior pole of calcaneus, quadriceps tendon at superior pole of patella and patellar tendons proximally at inferior pole of patella and distally at anterior tibial tuberosity) were clinically and sonographically assessed for enthesitis. The clinical assessment included JADAS 27 and BASDAI for disease activity and BASFI for function. Ultrasound was performed with a multi-frequency linear-array transducer (8-13MHz) using B-mode settings of dynamic range (40-50dB); GS- frequency (11-13 MHz); GS gain (60 dB). Power Doppler (PD) mode settings used: pulsed repetition frequency (400-800 Hz); PD-gain (highest possible gain with minimum background noise). US parameters (hypo echogenicity, increased thickness of entheses, intratendinous calcification, enthesophyte and erosion(s)) were assessed according to OMERACT 2014 definitions of ultrasonography

findings of enthesitis (1). Each parameter at every site was scored as 1 if present and 0 if absent. Grading of Power Doppler signals was done as per definition by Kiris et al (2); Grade 0-no signal, Grade 1- separate dot signals or short linear signals, Grade 2- vascularity involving less than half of the enthesis, Grade 3-vascularity involving more than half of the enthesis. US enthesitis score was calculated by adding 1 point for each positive finding and the grade of PD. PD score was calculated by adding the grade of PD. Presence of clinical and US detected enthesitis was correlated with parameters of disease activity by Spearman's correlation coefficient.

Results: The mean age of patients was 14.3± 3.2 years with mean duration of disease 34.6±4.9 months. Male: Female ratio was 7.5:1. Clinical enthesitis was seen in 36 of the 51 patients (70.5%) while US detected enthesitis in all ($p<0.0001$). The mean JADAS score, BASDAI and BASFI were 17.1±10.2, 4.1 ±2.4and 37.2±27.2 respectively, indicating active disease. The US enthesitis score correlated positively with JADAS ($r = 0.3$, $P=0.03$), BASDAI ($r = 0.39$, $P=0.005$) and BASFI ($r = 0.38$, $P=0.006$). PD score correlated positively with BASFI ($r= 0.33$, P- 0.02), but did not correlate with JADAS ($r = 0.22$, $P=0.1$), BASDAI ($r= 0.24$, $P= 0.08$).

Conclusion: Ultrasound is more sensitive in detecting enthesitis in JIA-ERA than clinical assessment. The US enthesitis score correlated positively with disease activity which has implications for treatment.

REFERENCES:

[1] Terslev L, Naredo E, Iagnocco A, Balint PV, Wakefield RJ, Aegerter P, et al. Defining enthesitis in spondyloarthritis by ultrasound: results of a Delphi process and of a reliability reading exercise. Arthritis Care Res (Hoboken). May;66(5):741-8.

[2] Kiris A, Kaya A, Ozgocmen S, Kocakoc E. Assessment of enthesitis in ankylosing spondylitis by power Doppler ultrasonography. Skeletal Radiol. 2006 Jul;35(7):522-8.

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FRI0581 COMPARISON OF CLINICAL CHARACTERISTIC IN ADULTS AND CHILDREN WITH GOUT

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Background: The incidence of gout in China is increasing in adults as well as children. The clinical manifestations of juvenile gout are not well described due to the limited number of cases in the past. Delineating the features of adult and juvenile gout may help pediatric providers recognize gout more effectively.

Objectives: We aim to describe and compare the clinical characteristic of adults and children with gout.

Methods: A total of 51 juvenile gout patients (age ≤ 18 years) and 337 adult gout patients in our hospital from Jan 2016 to Dec 2018 were enrolled in the study. Clinical parameters and laboratory data of the 2 groups were analyzed.

Results: The average age of onset in children with gout was 15.0±1.9 years and the youngest patient was 8 years old. Compared to the adult group, juvenile gout patients displayed lower BMI (23.0±3.8 vs. 25.6±3.5 kg/m^2, $P<0.001$) but higher serum uric acid levels (9.98±2.65 vs. 8.09 ±2.47 mg/dL, $P<0.001$). Interestingly, systemic inflammation was less prominent in children compared to adult as illustrated by lower C-reactive protein levels (7.1±13.5 vs. 23.7±40.7 mg/L, $P=0.004$) and lower erythrocyte sedimentation rate (12.7±12.9 vs. 33.1±34.2 mm/hr, $P<0.001$). Renal function impairment was rare in children compared to adults (serum creatinine 98.73±19.04 vs 120.38±34.58 μmol/L, $P<0.001$). In terms joint manifestations, juvenile gout was associated with greater finger joint involvement (23.53% vs. 6.82%, $P<0.001$) and less knee involvement (11.76% vs. 41.84%, $P<0.001$) compared to adults. Ankle involvement was slightly more common in the pediatric group (49.02% vs. 30.56% in adults, $P=0.009$) while MTP was similarly affected (50.98% vs. 32.94%, $P=0.012$). In addition, tophi was found in four cases (7.8%) in the juvenile group compared to 113 cases in adults (33.5%), suggesting that although less common, advanced features of gout can also occur in children.

Conclusion: Juvenile gout is associated with higher serum uric acid levels and greater involvement of finger joints. Correlations with BMI and systemic inflammation were less prominent compared to gout in adults. These findings will help clinicians better recognize gout in children.

REFERENCES:

[1] Chen, S.Y. and M.L. Shen, Juvenile gout in Taiwan associated with family history and overweight. J Rheumatol, 2007. 34(11): p. 2308-11.

[2] Lu, C.C., et al., Clinical characteristics of and relationship between metabolic components and renal function among patients with early-onset juvenile tophaceous gout. J Rheumatol, 2014. 41(9): p. 1878-83.

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Other orphan diseases

FRI0582 NON-INFECTIOUS UVEITIS AS A MANIFESTATION OF THE IMMUNE RECONSTITUTION INFLAMMATORY SYNDROMEIN PATIENTS INFECTED BY HIV

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Background: Immune reconstitution inflammatory syndrome (IRIS) is a paradoxical clinical worsening of an already known condition or the new onset of an inflammatory manifestation that is presumably related with the immune reconstitution after starting highly active anti-retroviral therapy (HAART) in patients infected by the human immunodeficiency virus (HIV).

Objectives: The aim of this study is to describe the clinical characteristics, presentation and response to immunosuppressive treatment in patients with uveitis secondary to ocular IRIS in our cohort of patients infected by HIV.

Methods: Retrospective review of clinical charts of patients diagnosed with HIV and non-infectious uveitis. Data collected included: demographics, anatomic classification of the uveitis, phenotypic diagnosis of the uveitis, other systemic immune-mediated disorders (IMD), time from HIV diagnosis to uveitis, CD4 count, viral load, treatment and complications of treatment and time of follow-up.

Results: Nine-teen patients (17 males) were included in the study. The mean age at the time of HIV diagnosis was 35.4±9.6 years. The time lag between HIV diagnosis and the onset of uveitis was 9±8.9 years. Mean CD4 count was 649±292 cells/ml, while the viral load was undetectable in 13 out of 17 cases. In 2 patients, there were a worsening of a previous IMD and in 6 patients another IMD was diagnosed prior to or concurring with the uveitis diagnosis (3 cases of reactive arthritis). The most common anatomic classification of the uveitis was anterior (13 cases). The use of immunosuppressive therapies to control either the ocular syndrome or the additional IMD was necessary in 6 patients (including biologics in 4 cases) during the follow-up. Only one patient had a complication of the immunosuppressive treatment. The mean follow-up was 43.8 months (range: 0.6 -115.7).

Conclusion: Non-infectious uveitis could be the first manifestation of immune-mediated systemic disease in patients with well-controlled HIV infection. Immunosuppression appeared to be a safe therapeutic option in our cohort of patients.

REFERENCES:

[1] Shelburne SA, 3rd, Hamill RJ, Rodriguez-Barradas MC, et al. Immune reconstitution inflammatory syndrome: emergence of a unique syndrome during highly active antiretroviral therapy. Medicine (Baltimore) 2002;81 (3):213-27. [published Online First: 2002/05/09]

[2] Murdoch DM, Venter WD, Van Rie A, et al. Immune reconstitution inflammatory syndrome (IRIS): review of common infectious manifestations and treatment options. AIDS Res Ther 2007;4:9. Doi: 10.1186/1742-6405-4-9 [published Online First: 2007/05/10]

[3] Vega LE, Espinoza LR. HIV infection and its effects on the development of autoimmune disorders. Pharmacol Res 2018;129:1-9. Doi: 10.1016/j.phrs.2018.01.005 [published Online First: 2018/01/15]

[4] Sokoya T, Steel HC, Nieuwoudt M, et al. HIV as a Cause of Immune Activation and Immunosenescence. Mediators Inflamm 2017;2017:6825493. Doi: 10.1155/2017/6825493 [published Online First: 2017/12/07]

[5] Yeo TH, Yeo TK, Wong EP, et al. Immune recovery uveitis in HIV patients with cytomegalovirus retinitis in the era of HAART therapy-a 5-year study from Singapore. J Ophthalmic Inflamm Infect 2016;6(1):41. Doi: 10.1186/s12348-016-0110-3 [published Online First: 2016/11/09]

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RECUERO DIAZ: None declared, Fredeswinda Romero: None declared, Olga Sanchez Pernaute Grant/research support from: Merk Sharp Dome, Rubió, Paid instructor for: Glaxo Smith Kline, Actelion, Pfizer, Bristol Myers Squibb, Speakers bureau: Glaxo Smith Kline, Alexion, Novartis, Roche, Bristol Myers Squibb

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FRI0583 NEUROMYELITIS OPTICA OVERLAPS FREQUENTLY WITH SYSTEMIC RHEUMATIC DISEASES IN AFRICAN-AMERICANS: EXPERIENCE AT A LARGE US ACADEMIC MEDICAL CENTER

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Background: Neuromyelitis optica (NMO) and neuromyelitis optica spectrum disorders (NMOSD) are immune-mediated demyelinating disorders of the central nervous system, primarily characterized by optic neuritis and longitudinal extensive transverse myelitis. Antibodies to aquaporin-4 (AQP4-IgG) are highly specific markers of NMOSD. The coexistence of NMOSD with systemic rheumatologic autoimmune disease has been well documented, especially systemic lupus erythematosus (SLE) and Sjogren syndrome (SS) [1]. Several recent studies have demonstrated that NMOSD may disproportionately affect black patients [2,3].

Objectives: Our objective was to characterize African-Americans diagnosed with NMO at our academic medical center, and identify any associated systemic rheumatologic autoimmune diseases.

Methods: We conducted a retrospective chart review of adult African-American patients diagnosed with NMO at a single academic medical center between 2011 and 2017. The charts reviewed were identified using ICD codes for NMO, transverse myelitis and optic neuritis. The diagnosis of NMO was then confirmed as per the 2015 International Consensus Diagnostic Criteria. The diagnosis of SLE and SS were also confirmed based on existing diagnostic criteria.

Results: Of the 60 charts reviewed, 25 patients (41.7%) met criteria for NMO, and of those, 21 patients (84%) were African-American. Of the 21 African-American NMO patients, 89.5% (n=19) were AQP4-IgG positive, 95.2% were women, and 38.1% had an associated systemic rheumatologic autoimmune disease (SLE 62.5% and primary SS 37.5%). In 60% of the NMO patients with SLE, the diagnosis of NMO preceded the SLE diagnosis. Conversely, in 100% of the NMO patients with SS, the diagnosis of NMO either followed, or was made simultaneous to, the SS diagnosis. Notably, 80% of the SLE patients had primarily hematologic manifestations. ANA was positive in 78.6% of the African-American patients in whom ANA testing was performed (n=14), with anti-SSA (64.3%, n=14) and anti-SSB (50%, n=11) the next most prevalent autoantibodies. Mean age of NMO onset was 46.7 years (SD 13.6). Transverse myelitis was the most common presenting manifestation (71.4%), followed by optic neuritis (61.9%).

Conclusion: Our population had a higher mean age of onset (46.7 vs 33 years) compared with other cohorts of seropositive NMO African-Americans [2]. Additionally, African-Americans with NMO at our institution had a higher female:male distribution than has been documented[3]. Not surprisingly, SLE was the most common associated systemic rheumatic disease in our cohort, however the frequency of SLE and ANA positivity in our NMO cohort was higher than has been reported (23.8% and 78.6%, respectively) [4]. Additional larger studies are needed to further explore how NMOSD in African-Americans may differ from other populations.

REFERENCES:

[1] Iyer A, Elsone L, Appleton R, Jacob A. A review of the current literature and a guide to the early diagnosis of autoimmune disorders associated with neuromyelitis optica, Autoimmunity, 47:3, 154-161

[2] Kim SH, Mealy MA, Levy P, et al. Racial differences in neuromyelitis optica spectrum disorder. Neurology Nov 2018, 91 (22) e2089-e2099.

[3] Flanagan EP, Cabre P, Weinshenker BG, et al. Epidemiology of aquaporin-4 autoimmunity and neuromyelitis optica spectrum. Ann Neurol 2016;79:775–783.

[4] Pereira WLCJ, Reiche EMV, Kallaur AP, et al. Frequency of autoimmune disorders and autoantibodies in patients with neuromyelitis optica. Acta Neuropsychiatrica. 2017;29(3):170-178.

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FRI0584 EFFICACY AND SAFETY OF RITUXIMAB FOR INDUCTION OF REMISSION AND MAINTENANCE OF IGG4-RELATED DISEASE: EXPERIENCE FROM AN ITALIAN NATIONAL REFERRAL CENTRE

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Background: IgG4-related disease(IgG4-RD) is a systemic fibro-inflammatory disease. Treatment is based on corticosteroids(CS) but up to 50% of patients may relapse. Rituximab(RTX) has emerged as an effective treatment option[1].

Objectives: To assess the free relapse rate(FRR) in patients receiving or not maintenance RTX therapy. Secondary outcomes: time to relapse, incidence of adverse events and differences in FRR between Group 2a and 2b patients.

Patient #	Age (years)	Sex	N° of Organs involved	IgG4-RD RI	PGA	ESR (mm/1h)	CRP (mg/L)	IgG4 (mg/L)	Concomitant DMARD therapies	Previous DMARD therapies	Outcomes after RTX induction	Relapses (time to relapse)	N° of RTX infusions	RTX Adverse Events	Follow-up (months)
Group 1															
1	29	F	3(Pm,Ns, Ph)	12	90	38	25	1001	No	CTX	PR	No	1	No	32
2	47	M	2(Ly,Sg)	6	50	8	1,2	4420	No	MTX	DR	No	1	No	30
3	70	F	1(Ao)	6	70	26	3,7	850	MTX	No	DR	Yes(7)	2	No	26
4	49	M	2(Bd,Pa)	6	60	39	1,9	3360	No	No	DR	Yes(7)	2	No	26
5	52	M	4(Pm,Si,Or, Pa)	15	90	7	21	1700	No	MTX	DR	Yes(12)	2	No	18
6	52	M	3(Ly,Sg,Lu)	12	70	8	1,9	7904	MTX	No	CR	Yes(11)	2	No	18
7	80	M	3(Pa,Ly,Bd)	9	60	22	6	3620	No	MTX	DR	Yes(9)	2	No	18
Group 2															
1	53	M	5(Ly,Si,Lg, Pa,Sg)	12	80	7	0,1	5713	No	AZA	CR	0	3	No	18
2	49	F	4(Ly,Lg,Or, Ph)	15	90	22	0.3	13800	No	No	CR	0	4	No	20
3	16	F	3(Si,Or,Ly)	9	60	6	0,2	630	No	No	DR	0	7	No	48
4	28	F	4(Hy,Pm, Or,Ns)	15	90	65	5,7	2990	No	CTX	CR	0	3	Yes (Asthma)	18
5	73	F	3(Or,Ly,Ma)	12	70	17	1,2	21800	MTX	AZA	CR	0	5	Yes(Rash)	30
6	51	F	3(Lg,Or,Lu)	12	70	16	6,9	2530	No	No	DR	0	4	No	18
7	76	M	1(Bd)	6	70	31	36	470	No	No	DR	0	3	No	21

Methods: Data of IgG4-RD patients treated with RTX and followed-up for >18 months were reviewed. Patients were treated with two 1 g RTX doses 15 days apart(standard dose,SD) and then divided into: patients receiving RTX in case of relapse(Group 1) and patients receiving maintenance RTX treatment 6 monthly(Group 2). Patients in Group 2 received a first maintenance treatment RTX SD and were then further divided into patients receiving RTX SD(Group 2a) or single 1 g RTX dose(Group 2b).
Results: 14 IgG4-RD patients were included. Median number of organs involved was 3(1-5). Baseline median physician global assessment(PGA) was 70(50-90), IgG4-RD responder index(IgG4-RD RI) 12(6-12). Median eosinophil count, ESR, CRP, and serum IgG4 level were 100cells/μL(50–1.800), 19mm/h(6-64), 3.7mg/L(0.1–36) and 3.17mg/L(470–21.800) respectively. Indications for RTX were: relapse in 10/14(71%), partial response in 3/14(21%) and first-line treatment in 1(7%) patient. CS were stopped in 5 patients and reduced by month 3 in remaining patients(27.14±13.06 vs 6.43±2.45 mg daily,p=0.012). 3 patients were on concomitant methotrexate(MTX) therapy at RTX induction, MTX was stopped in all patients at month 3. At month 6 PGA, IgG4-RD RI, and serum IgG4 decreased to a median value of 10(0-50), 2(0-6), and 822 mg/L(380–7.313), respectively($p<0.001$ for all comparisons). Median eosinophil count, CRP and ESR levels did not change significantly. 8(57.1%), 5(35.7%) and 1 patient (7%) were on disease remission (DR), complete remission(CR), and partial remission(PR), respectively. Median number of RTX courses was 2(1–2) in Group 1, 3(3–7) in Group 2a, and 4(3–5) in Group 2b. Organ involvement, PGA, IgG4-RD RI, ESR, CRP, and serum IgG4 levels were not significantly different between the 2 Groups at baseline. FRR at 18 months in Group 1 was significantly lower than that in Group 2(29% vs100%,p=0.006). 5(71%) patients in Group 1 relapsed on average 9(7–12)months after RTX induction. 2(14%) patients had hypersensitivity reactions during RTX induction. 6(43%) patients, 3 in Group 1 and 3 in Group 2, experienced low-grade infections.
Conclusion: RTX is a safe and effective treatment in IgG4-RD. Both SD and single 1 g RTX dose seem effective in maintenance.

REFERENCES:

[1] CarruthersMN.Rituximab for IgG4-related disease:a prospective,open-label trial.Ann Rheum Dis.2015.

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FRI0585 EFFICACY OF CANAKINUMAB AS FIRST-LINE BIOLOGIC AGENT IN ADULT-ONSET STILL'S DISEASE

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Background: Adult-onset Still's disease (AOSD) is a rare auto-inflammatory condition characterized by fever, arthritis, skin rash, and multi-organ inflammation. The pathogenesis of AOSD is centrally mediated by the pro-inflammatory cytokine interleukin (IL)-1β; anakinra, a recombinant inhibitor of the IL-1β receptor, has thereby become the cornerstone of biologic therapy for AOSD. More recently, a new agent blocking IL-1β has become available, that is, the monoclonal antibody canakinumab.
Objectives: So far, canakinumab has been used in the treatment of AOSD following failure of multiple lines of biologic therapy, including anakinra. Here, we describe the use of canakinumab as first-line biologic agent in 6 patients with AOSD, and report the highly promising results of this treatment approach.
Methods: Six patients with severe, DMARD-refractory AOSD received canakinumab at the approved dose of 4 mg/kg once every 4 weeks following failure of conventional treatment with corticosteroids and methotrexate. Patient characteristics and response to therapy were recorded.
Results: In all patients, treatment with canakinumab led to striking and rapid clinical responses, within days of initiation. Fever and skin rash disappeared first and did not recur, followed by progressive and sustained improvement in arthritis. Inflammatory organ involvement also responded to treatment: for example, we observed resolution of pericardial inflammation in two patients, as revealed by cardiac ultrasound; another patient had hepatosplenomegaly, which also reverted to normal upon treatment. A striking reduction in serum pro-inflammatory markers C-reactive protein, erythrocyte sedimentation rate, and ferritin mirrored the efficacy on clinical manifestations. These effects amounted to a significant decrease in the modified Pouchot score for measuring disease severity (average score before canakinumab treatment: 6; after: 1.25; statistical significance of difference evaluated with Mann-Whitney: p=0.02), and allowed for tapering or discontinuation of concomitant therapy: specifically, corticosteroid treatment was completely discontinued in two patients and substantially reduced in two patients, whereas methotrexate was stopped in one patient.
Conclusion: In this study, first-line biologic therapy of AOSD with canakinumab resulted in rapid and marked efficacy, ultimately leading to full clinical remissions in all patients, and allowing for robust steroid-sparing effects. So far, canakinumab in AOSD has mostly been used as a last line of treatment following failure of multiple other agents, including anakinra. Early treatment, as described in this study, is nevertheless advisable and may reduce chances of chronic disease and permanent damage.

REFERENCES:

[1] Cavalli G, Dinarello CA: Treating rheumatological diseases and co-morbidities with interleukin-1 blocking therapies. Rheumatology (Oxford) 2015, 54 (12):2134-2144.
[2] Cavalli G, Franchini S, Aiello P, Guglielmi B, Berti A, Campochiaro C, Sabbadini MG, Baldissera E, Dagna L: Efficacy and safety of biological agents in adult-onset Still's disease. Scand J Rheumatol 2015, 44(4):309-314.

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FRI0586 THE EFFECT OF TOCILIZUMAB IN THE PREVENTION OF FAMILIAL MEDITERRANEAN FEVER ATTACKS

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Background: Familial Mediterranean Fever (FMF) is the most frequent hereditary autoinflammatory disease in the worldwide. Colchicine is the mainstay of the treatment that is used for both preventing the attacks and developing amyloidosis. In case of colchicine resistance, which constitutes almost 5% of all patients, there are some alternatives such as anti-TNF agents, IL-6 and IL-1 antagonists. These agents have also been used in patients with established amyloidosis secondary to FMF. Tocilizumab (TCZ), an IL-6 receptor antagonist, although is effective in the treatment of amyloidosis, little known about its effectiveness in the preventing of febrile attacks.
Objectives: In this study, we aimed to find out whether TCZ therapy decrease the frequency of recurrent attacks of FMF or not.
Methods: This retrospective cross-sectional study designed in a tertiary rheumatology clinic between the years 2009 and 2019. A total of 15 patients were given intravenous TCZ at a dose of 8mg/kg/month, to improve amyloidosis associated with FMF. Data of demographic and clinical characteristics of patients were obtained retrospectively from patient files.
Results: Three female and 12 male patients received TCZ for amyloidosis treatment. The mean age of patients was 42.07±14.37 years and disease duration was 25.73±10.86 years. All of the patients had biopsy results providing amyloidosis. According to international severity scoring system for FMF, all of the patients had severe disease. Demographic and clinical data were shown in Table 1. The frequency of attacks was evaluated during TCZ treatment, and it was reported that 1 patient had no response, 6 patients had decreased attack frequency and 8 patients had no attacks. Serious adverse events were seen in none of the patients.

Table 1. Demographic and clinical characteristics of the patients

	MEFV gene mutations	Treatment cycles (months)	Attacks per year before TCZ	Attacks per year after TCZ
44/ Female	M694V homozygote	96	24	5
49/Male	M694V homozygote	48	30	0
59/Male	M694V/N heterozygote	8	12	1
79/Male	M694V/M680I heterozygote	67	12	0
40/ Female	M694V homozygote	2	14	1
38/Male	M694V homozygote	3	48	3
44/Male	M694V homozygote	18	30	10
49/Male	M694V homozygote	3	36	0
34/Male	M694V homozygote	23	24	0
39/Male	MEFV-/-	33	20	0
28/Male	M694V homozygote	19	18	0
24/Male	M694V homozygote	12	30	2
27/Male	M694V homozygote	3	36	36
27/Male	M694V/M680I heterozygote	12	12	0
50/Male	M694V homozygote	12	6	0

MEFV:Mediterranean Fever, TCZ:Tocilizumab

Conclusion: Tocilizumab is found to be effective on improvement of amyloidosis. In the current analysis, we found that TCZ also decreases the frequency of recurrent attacks in patients with FMF. Besides, TCZ is well tolerated among the patients. Further and prospective studies with larger sample are needed to support these results.

REFERENCES:

[1] Yilmaz S, Cinar M, Simsek I, Erdem H, Pay S. Tocilizumab in the treatment of patients with AA amyloidosis secondary to familial Mediterranean fever. Rheumatology 2015;54:564-565

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FRI0587 IGG4-RELATED DISEASE IN ITALY: RESULTS FROM A MONOCENTRIC COHORT OF 150 PATIENTS (2013–2018)

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Background: IgG4-related disease (IgG4-RD) is a recently recognized fibro-inflammatory disease characterized by fibrotic lesions and elevated IgG4 serum level. Epidemiological and clinical data in our country have not been precisely assessed yet

Objectives: The aim of this work is to present the data from the largest monocentric Italian IgG4-RD cohort.

Methods: We conducted a retrospective analysis searching for IgG4-RD patients referred to our tertiary care centre between 2013 and 2018. Diagnosis were made according to the "Comprehensive Diagnostic Criteria 2011", and patients were clustered on the basis of a definite, probable and possible, diagnosis. Each patient underwent clinical, serological, and radiological evaluation according to the organ involvement. IgG4-RD activity was measured with IgG4-RD Responder Index (IgG4-RD RI). All the data are reported in median and interquartile range.

Results: 150 patients were included in this work (111 male, 39 female, M:F ratio 2.8:1). 75 cases received a definite IgG4-RD diagnosis, while 6 patients and 49 patients were diagnosed as *probable* and *possible* IgG4-RD, respectively. Median age at diagnosis was 60 (SD 13) years old. The most involved organ was the pancreas (66 cases; 44%), followed by lymph nodes (26 cases; 17%), biliary tree (25 cases; 17%), salivary glands (21 cases; 14%), aorta and retroperitoneum (12 cases; 8%), meninges (9 cases; 6%), nasal sinuses and nasal septum (5 cases; 3%). 18 patients (12%) had a positive history of malignancies that occurred ten years earlier or after IgG4-RD diagnosis. At baseline, IgG4 level was elevated in 92 patients (61%), while eosinophil count and IgE level were elevated in 35 (23%) and 52 (35%) patients, respectively. Circulating plasmablast were measured in 88 and elevated in 66 (1859 cell/mL, 600-3950). Median IgG4-RD RI at diagnosis was 6 (6-9). 55 patients were treated with glucocorticoids alone, whereas immunomodulator (Mycophenolate mofetil, azathioprine, cyclophosphamide) were associated in 31 cases. Rituximab was administered in 32 patients. 15 patients underwent surgical excision of the fibrotic lesion. 15 patients were candidate to a watchful waiting strategy, due to low disease burden.

Conclusion: Our study reports clinical and epidemiological data from the largest monocentric cohort of patients with IgG4-RD in Italy. Our data reflect those reported in other international cohorts of IgG4-RD patients.

REFERENCES:

[1] Della Torre E, Lanzillotta M, Doglioni C. Immunology of IgG4-related disease. Clin exp Imm.2015

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FRI0588 THE SCALE OF ACTIVITY IN IDIOPATHIC LOBULAR PANNICULITIS

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Background: Idiopathic lobular panniculitis (ILP) refers to chronic systemic connective tissue lesions (M 35.6). The disease develops with typical clinical symptoms and is characterized by alternating periods of stable condition (remission) and active manifestations (exacerbations). Assessment of the activity and identification of the disadvantageous predictors is the main task in monitoring patients with ILP, however, the "gold standard" has not been developed yet.

Objectives: to create a rating scale for the inflammatory process activity in ILP on the basis of clinical and laboratory parameters

Methods: We examined 67 patients (9 men and 58 women) with the ILP diagnosis verified in the V.A. Nasonova Research Institute of Rheumatology in 2007-2017. The age of patients ranged from 20 to 76 years, the average duration of the disease was 78.91[48;50] months. At the time of treatment at the institute only 16 patients (23,88%) were diagnosed with ILP. All the patients underwent comprehensive clinical examination and laboratory and instrumental examination of biochemical and immunological parameters, radiography or computed tomography (CT) of the chest organs, as well as pathomorphological examination of skin and subcutaneous fat biopsies from the node area.

Results: Analysis of clinical manifestations allowed to identify four forms of ILP: nodular (30 patients), plaque (10), infiltrative (15) and mesenteric (12), which had specific clinical and laboratory features. Based on the obtained data we developed a scale of the ILP activity (SA), which includes a description of the state of the 7 organ systems. The maximum score for individual systems is from 1 to 3 points depending on the number of estimated parameters. The total maximum possible score is 42 points. The score includes all types of damage since the onset of the disease (caused directly by ILP or developed as a result of therapy), while taking into account only signs that persist for 6 months. Score <5 shows inactive disease, 5-10 - low disease activity; 11-20 - moderate activity and >20 - high activity of the disease. Thus, low disease activity is characterized by the predominance in the clinical picture of limited moderately painful indurations in the absence of any significant changes in laboratory tests. At the moderate disease activity, changes in various localization with a predominance of proliferative disorders (common painful compaction of the 1st and/or 3rd stage, moderate area of damage to the trunk and limbs, subfebrile temperature, cognitive impairment, mesenteric disorders, etc.) are revealed against the background of less pronounced laboratory tests. ILP with high activity is characterized by the presence of fever and other common signs of the disease, the predominance of the 2^{nd} stage with a pronounced VAS pain intensity of the induration, the common nature of the defeat of the pancreas, involvement of the lungs, heart and gastrointestinal tract in the pathological process.

Conclusion: In fact, SA is an analysis of the organ damage, assessment of the symptoms severity, and it takes into account the development of exacerbations with the involvement of new organs in the process of the disease. The proposed ILP SA is of practical importance. Further

research and possibly search for new parameters of the ILP activity are needed.

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FRI0589 IS THERE AN OVERLAP OF ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIDES WITH IGG4-RELATED DISEASE OR NOT?

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Background: Pseudotumor orbita, pachymeningitis, periaortitis could be seen in both ANCA-associated vasculitis and IgG4-RD. Sometimes it may be difficult to differentiate these two entities. The co-occurrence/concurrence of Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) and IgG4-related disease (IgG4-RD) was recently published by a collaborative EUVAS group [1].

Objectives: Firstly, we aimed to investigate ANCA positivity of our IGG4-RD cohort. Secondly, a literature review of co-occurrence/concurrence of AAV and IgG4-RD was done.

Methods: Data of totally 62 patients with IgG4-RD in Hacettepe Vasculitis Center Database was used. Patients were diagnosed with IgG4-RD according to comprehensive diagnostic criteria [2]. Dataset of patients including demographic data, clinical characteristics, and imaging and laboratory findings of IgG4-RD was re-evaluated in terms of AAV and ANCA test.

At next step, we performed a systematic literature review of the PUBMED database covering the time period until April 2018. Relevant publications were searched using the MeSH terms "IgG4-related disease and Eosinophilic Granulomatosis with Polyangiitis", ''IgG4-related disease and Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis'' and "IgG4-related disease and Granulomatosis with Polyangiitis".

Results: Totally 29 (46.7%) of our patients had ANCA results. Out of 29 patients 15 (51.7%) were considered as probable, 10 (34.5%) as definite and 4 as possible (13.8%) for IgG4-RD. Three (10.3%) of these patients had ANCA positivity. All of these ANCA titers were in low degree positivity (MPO-ANCA 1/100, MPO-ANCA 1/32 and PR3 ANCA 1/100). These three patients didn't have any findings of vasculitis and didn't have granuloma in their biopsy. When we evaluate these three patients with regards to meeting the Ig G4- RD criteria, 1 was definite, 1 was probable and 1 was possible.

In literature review, we found 17 cases that having both features of IgG4-RD and AAV (Table). These cases were re-evaluated according to the 'Comprehensive Diagnostic Criteria for IgG4-RD'. Diagnoses of IgG4-RD were definite in 11 cases (64.7%), probable in 2 cases (11.8%) and possible in 4 cases (23.5%). ANCA were positive in 15 of 17 patients (88%). ANCA were directed against proteinase 3 (PR3-ANCA) in 6 patients and were directed against myeloperoxidase (MPO-ANCA) in 5 patients. Other four cases had both MPO-ANCA and PR3-ANCA. All PR3-ANCA positive cases have high titers of ANCA, whereas only one MPO-ANCA positive case has high titers of ANCA.

Conclusion: None of our IgG4-RD patients have any overlap with ANCA-associated vasculitis. Only in 3 patients (10.3%), ANCA positivity was detected without any histopathologic evidence. Just two patients of literature review, seemed to be full compatible with both diseases. Even though ANCA-associated vasculitis and IgG4-RD share clinical features, we think this might be as co-occurrence instead of a histopathologic link.

REFERENCES:

[1] Danlos, FX. Autoimmun Rev, 2017.
[2] Umehara, H. Mod Rheumatol, 2012.

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Table: Distribution of Demographic, Clinical, Features in Seventeen Patients at Literature



FRI0590 UVEITIS SECONDARY TO CHECKPOINT INHIBITORS

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Background: The introduction of immunotherapy (immune checkpoint inhibitors, ICI) has led to a revolution in oncological treatments. The inhibitors of CTLA4 (ipilimumab), of PD1 (pembrolizumab, nivolumab) and of the ligand of PD1 (atezolizumab, avelumab, durvalumab) regulate T activation and its effector function, being effective for the treatment of various types of cancer[1]. However, this effect leads to a series of immune-mediated adverse events, among which uveitis of autoimmune mechanism have been described in about 1% of treatments[2].

Objectives: Methods: descriptive study of retrospective review of the cases of a tertiary hospital with about 1000 treatments between the beginning of 2014 and the end of 2018.

Results: A series of 4 cases of uveitis of autoimmune origin associated with ICI is presented (see table). The series described has characteristics similar to the information previously reported in the literature[2], with an incidence of around 0.4%, according to the previously described, with frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months. The forms of presentation described before, ranges from anterior uveitis (AU) to panuveitis and often papilledema, usually bilateral, as are all those described in our series. In addition, 50% are AU (grade 2) and the other 50% panuveitis with papilledema (grade 3). In all the cases described, treatment was interrupted, a half it could be reintroduced without recurrence of uveitis. All the patients received topical treatment, the more severe systemic corticosteroids at doses of 0.5-1 mg/kg in accordance with the recommendations. The final prognosis was good, with preservation of VA in all cases, and topical and systemic treatment could be withdrawn in all patients. A patient treated with Ipilimumab presented synechiae as a complication.

	ONCO diagnosis	ONCO treatment	time	OPH diagnosis	Toxicity (G)	OPH tretament	ICI withdrawal	Prognosis	Other toxicities
♂ 79	Melanoma BRAF wt+ retroperitonealmtt	Pembrolizumab x7 Ipilimumab x2	6m 6w	Bilateral AU with synechia	2	Prednisone 1 mg/kg + Topical	Temporal	No inflammation without treatment VA Preserved Synechia	Transaminitis G2 Asthenia G2
♂ 85	Cáncer de vejiga localizado avanzado	Atelizumab x7	5m	Bilateral AU	2	Topical	Definitive	No inflammation without treatment VA Preserved	PMR G2 Thyroiditis G1 Transaminitis G1 Mucositis G1
♂ 45	Melanoma BRAF mutant (retropectoral mass)	Pembrolizumab x5	4m	Bilateral Panuveitis with synechia + papilledema	3	Prednisone 0,5 mg/kg + topical	Definitive	No inflammation without treatament VA Preserved	None
♂ 47	Melanoma BRAF wt (abdomial mass +peritoneal mtt + adrenal mtt)	Nivolumab x2 Ipilimumab x1	2m 1m	Bilateral Panuveitis with synechia + papilledema	3	Prednisone 0,5 mg/kg + topical	Nivolumab temporal Ipilimumab definitive	No inflammation without treatament VA Preserved	Rash G1 Pruritus G1 Vitíligo

Conclusion: Uveitis is an infrequent, although potentially serious, immune-mediated side effect of ICI. Early recognition, discarding other causes of uveitis, particularly the masquerade syndrome, and early intervention are key to a good prognosis. The collaboration between the oncology teams and the ocular inflammation units must be close to establish the correct diagnosis and treatment, as well as to decide individually on the reintroduction or not of the oncological treatment. The implementation of registers on the adverse effects of these drugs can help to dimension the problem more accurately.

REFERENCES:

[1] Calabrese LH, Calabrese C, Capelli, LC. Rheumatic immune-related adverse events from cancer immunotherapy. Nat Rev Rheumatol. 2018 Oct;14(10):569-579.

[2] Dalvin LA, Shields CL, Orloff M, Sato T, Shields JA. Checkpoint inhibitor immune therapy: Systemic Indications and Ophthalmic Side Effects. Retina. 2018 Jun;38(6):1063-1078.

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FRI0591 RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS ASSOCIATED WITH TREATMENT WITH IMMUNE CHECKPOINT INHIBITORS: A CASE SERIES FROM TWO REFERRAL CENTRES

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Background: Immune checkpoint inhibitors (ICI) against CTLA-4 or PD-1/PD-L1 improve the survival of patients with advanced malignancies including melanoma, lung cancer among other tumours. Because of its mechanism of action, ICI are prone to produce different immune-related adverse events (irAEs), including musculo-skeletal manifestations.
Objectives: Our aim was to describe the experience with rheumatic irAEs in two tertiary centres.
Methods: All adult patients referred to the Rheumatology department from 2015 to 2018 because of the onset of musculo-skeletal symptoms following treatment with an ICI were included. Data collected comprised demographic features as well as ICI indication and type, history of rheumatic disease, disease manifestations at irAE onset, laboratory tests, ultrasound findings and treatment. Diagnostic and treatment approach was done according clinical judgment and in a daily clinical practice setting.
Results: 20 patients were included, 50% female, with a mean age of 61,5 years (range 32-83). The indication for ICI was melanoma in 10 cases, lung cancer in 5, urothelial neoplasia in 2 and squamous skin, breast and head and neck cancer in 1 case each. Pembrolizumab was the most used ICI accounting for 9 cases (1 combined with epacadostat), 8 patients were treated with Nivolumab (4 combined with Ipilimumab), 2 wit Atezolizumab (1 combined with Ibatasertib) and 1 Ipilimumab in monotherapy.
A history of previous rheumatic disease was reported in 8 patients (1 seropositive RA, 1 Spondyloarthritis, 1 SLE, 1 gout, 1 chondrocalcinosis, 1 fibromyalgia, 1 De Quervain tendinitis, 1 hand osteoarthritis) and 1 had psoriasis.
The most frequent irAE presentation was arthritis with 8 cases (40%), arthralgia in 4 cases (20%), 1 case of myalgia, 2 presented PMR-like symptoms, 1 tenosynovitis and 2 paraesthesia (1 with associated dysesthesia).
After assessment, 7 patients were diagnosed as undifferentiated arthritis, 1 leukocytoclastic vasculitis, 1 small-vessel vasculitis, 2 psoriatic-like arthritis, 1 tenosynovitis, 2 PMR and 6 were classified as having non-inflammatory symptoms.
Antibody status was analyzed in 16 patients. Anticitrullinated-peptide antibodies, rheumatoid factor and HLA B27 were negative in all cases (except for 1 patient with seropositive RA), ANAs were positive in 4 (including 1 patient with previous SLE) but without any specificities (i.e. ENAs) and ANCA were negative in one case with small-vessel vasculitis. Ultrasound assessment was performed in 6 patients, 3 presented synovial hypertrophy with positive power Doppler (1 with tenosynovitis associated), 1 peritendinous fluid collection, 1 elbow joint effusion and 1 bilateral supraspinatus calcified tendinopathy.
Most patients were treated with glucocorticoids 12 (60%) and NSAID 6 (30%) and only 3 patients had to discontinue ICI treatment due to irAEs.
Conclusion: Our results were in line with previous studies showing that musculo-skeletal irAEs associated to ICI may present as a flare of a previous known rheumatic disease or as a de novo symptom. Most patients presented with asymmetric mono or oligoarthritis having a good response to GC and NSAID without the need of adding DMARD or withdraw of ICI therapy..
Disclosure of Interests: Sebastian C Rodriguez-García: None declared, DAVID LOBO: None declared, Raul Castellanos-Moreira Speakers bureau: MSD, Lilly, Ana Milena Millán Arciniegas: None declared, Roberto Gumucio: None declared, Ana Laiz Consultant for: Lilly, Novartis, AbbVvie, MSD, UCB and Janssen, Speakers bureau: Lilly, Novartis, Abvvie, MSD, UCB and Janssen, Virginia Ruiz-Esquide Speakers bureau: Sanofi, Lilly, MSD, Berta Magallares: None declared, Cesar Díaz-Torné: None declared, Patricia Moya: None declared, Ivan Castellví Consultant for: I received fees less than 5000USD as a consultant for Kern and Actelion, Paid instructor for: I received fees less than 2000USD as a instructor for Boehringer -Ingelheim, Novartis and Gebro, Speakers bureau: ND, Hector Corominas: None declared, Jose A. Gómez-Puerta Consultant for: Pfizer, Roche, Speakers bureau: Abbvie, BMS, Janssen, MSD, Pfizer, Roche
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FRI0592 CLINICAL CHARACTERISTICS OF OLDER AGE-ONSET BEHÇET SYNDROME PATIENTS

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Background: The usual onset of Behçet syndrome (BS) is in the 3. decade. Older age-onset defined as fulfilling the ISG criteria after 40 years of age is rare. One study from our center had reported the severity of eye disease was not different between early onset (≤ 24 years) and late onset (≥ 25 years) group. (1). While there is ambiguity in the definition of older onset, a few case series (2,3) coming mostly from ophthalmology or dermatology settings describe a similar or less severe clinical picture among late onset patients (pts) compared to early onset.
Objectives: To evaluate clinical characteristics of older onset pts and to compare them with classic onset pts.

Methods: The charts of 3335 BS pts who were registered between 2000 and 2010 were reviewed retrospectively. Pts who fulfilled ISG criteria for BS after 40 years of age were defined as older onset, while those who fulfilled the criteria before 30 as classic onset. For each older onset chart, 2 consecutively registered early onset charts were selected. Only clinical manifestations at presentation were recorded. A clinical activity index (1) was modified and calculated.
Results: There were only 134(70 M/64 F) pts with older onset BS, which gave a prevalence of 4% in the whole cohort. Age of onset was 40-44 years of age in 54 pts, 45-49 years in 47 and 50+ in the remaining 32. As controls 268(163 M/105 F) classic onset pts were selected. Demographic and clinical characteristics among older and classic onset pts are described for males and females separately, in Table. The frequency of skin manifestations, arthritis and eye disease as well as the mean clinical activity scores were significantly higher among male classic onset pts compared to older onset male pts. Interestingly, the frequency of those with positive pathergy test, vascular involvement and severe eye involvement did not seem to be different among older and classic onset male pts. On the other hand, clinical characteristics and total activity scores were similar between older and classic onset groups among females (Table). The main limitation is that the information was based solely on patient's charts and outcome information was not available.
Conclusion: Compared to classic onset pts, males tend to be less frequent in older cohort. At presentation, older onset male pts had significantly less frequent skin, joint, eye disease, and significantly lower total activity scores compared with classic onset pts. There was no difference between the classic and older onset group, among females.

Table. Clinical characteristics of older age–onset and classical-onset BS pts (Males/Females)

	Older onset males (n=70)	Classical onset males (n=163)	P	Older onset females (n=64)	Classical onset females (n=105)	P
Age at ISG criteria fulfilling, yrs	47.0 ± 6.0	24.2 ± 4.5		46.6 ± 5.7	23.1± 4.4	
Oral ulcer, n (%)	69 (99)	163 (100)	-	64 (100)	105 (100)	-
Genital ulcer, n (%)	60 (86)	137 (84)	0.845	51 (80)	90 (86)	0.307
Papulopustular lesions, n (%)	49 (70)	133 (82)	0.050	39 (61)	71 (68)	0.377
Nodular lesions, n (%)	15 (21)	76 (47)	0.0001	29 (45)	60 (57)	0.135
Arthritis, n (%)	10 (14)	45 (28)	0.028	13 (20)	25 (24)	0.597
Eye involvement, n (%)	24 (34)	88 (54)	0.006	26 (41)	41 (39)	0.839
Visual acuity: <0.1 on either or both eye	8 (33)	27 (33)	0.941	4 (15)	9 (23)	0.538
Vascular involvement, n (%)	13 (19)	27 (17)	0.710	2	0	0.142
Pathergy positivity, n (%)*	39 (56)	94 (58)	0.876	34 (53)	49 (47)	0.346
Activity score, mean ± SD	5.60 ± 3.36	6.38 ± 3.15	0.020	5.20 ± 2.21	4.79 ± 2.39	0.111

*: Pathergy test was made only in 70 older onset and 163 younger onset male pts, 64 older onset and 105 younger onset female pts.

REFERENCES:
[1] Yazici H, et al. Ann Rheum Dis.1984.
[2] Tsai J, et al. J Eur Acad Dermatol Venereol.2008.
[3] Citirik M, et al. Ophthalmologica. 2011.

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FRI0593 PATHOLOGICAL FEATURES OF LYMPH NODE IN JAPANESE PATIENTS WITH ADULT-ONSET STILL'S DISEASE

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Background: Adult-onset Still's disease (AOSD) rarely occurs in adults and no specific serological or pathological findings have ever been reported. Although multiple lymphadenopathy often develops in AOSD patients, only few reports have described their pathology so far.[1,2]
Objectives: To examine pathological features of lymph node (LN) in AOSD patients and their usefulness in diagnosis in Japan.
Methods: This is a single center, retrospective study. The subjects were 115 Japanese patients who visited our department and received LN biopsy from April 2010 to July 2018. Of these, 12 patients, in whom AOSD was suspected by clinicians at the time of biopsy, were analyzed. AOSD patients were diagnosed according to the Yamaguchi's criteria[3], except the item "excluding malignant lymphoma".
Results: The median age of the 12 cases (2 males, 10 females) was 60.5 years old (range: 18-81). Paracortical hyperplasia was shown in 7, follicular hyperplasia in 1, histiocytic necrotizing lymphadenitis (HNL) in 3, and diffuse large B cell lymphoma (DLBCL) in 1. Of 9 who fulfilled Yamaguchi's criteria, TAFRO syndrome was diagnosed in one. As for the other 8, diagnosis of AOSD was made and successfully treated as AOSD. Although 1 of the 8 had pathological features of HNL, we treated her as AOSD because her clinical feature and laboratory data were not compatible with HNL. As for the 3 who did not meet the criteria, their clinicopathological diagnosis was HNL in 2 and DLBCL in 1. We could find no associations between the clinical features and lymph node patterns in AOSD as previously reported.
Conclusion: In patient who fulfilled the criteria, most cases showed paracortical hyperplasia in LN as previously reported from outside Japan and no cases had malignant lymphoma. However, in diagnosing AOSD, LN biopsy is needed to exclude AOSD-mimicking malignant lymphoma especially in the case that does not fulfill the criteria.

REFERENCES:
[1] Kim HA, et al. Medicine (Baltimore). 2015;94:e787.
[2] Jeon YK, et al. J Clin Pathol. 2004;57:1052.
[3] Yamaguchi M, et al. J Rheumatol 1992;19:424–30.

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FRI0594 COMPARISON OF CLINICAL FEATURES BETWEEN HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS COMPLICATED WITH RHEUMATIC DISEASES OR TUMOR

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Background: Hemophagocytic lymphohistiocytosis (HLH) covers a wide spectrum of related life-threatening conditions featuring ineffective immunity characterized by an uncontrolled hyperinflammatory response, which including autosomal recessive familial HLH (FHL), familial erythrophagocytic lymphohistiocytosis, viral-associated hemophagocytic syndrome, and autoimmune-associated macrophage activation syndrome (MAS).
Objectives: Our study was to compare the difference between HLH related with rheumatic diseases or tumor.
Methods: We retrospectively reviewed the patient data with definite bone marrow hemophagocytosis in the inpatient department of the Third Affiliated Hospital of Sun Yat-sen University between 01/11/2011 to 31/05/2018. The clinical manifestations, laboratory exam and prognosis were compared between patients related with tumor and rheumatic diseases.
Results: 7 patients with rheumatic diseases and 5 patients with tumor were enrolled. In patients with rheumatic diseases, 6 with adult-onset Still's disease and 1 with SLE. In patients with tumor, 4 with lymphoma and 1 with undefined tumor. The clinical features were compared between the two types of patients as below.

Table 1. Comparing of clinical features between patients with HLH complicated with rheumatic diseases or tumor

Clinical features	Patients with rheumatic diseases (n=7)	Patients with tumor (n=5)
Age (mean)	17-66 yrs (38.7)	29-59 (47.8)
Male/Female	1/6	3/2
Fever	100%	100%
Cytopenias (≥2 blood cell lines)	85.7%	100%
Abnormal liver function tests	71.4%	100%
Hypofibrinogenemia	28.6%	100%
Hypertriglyceridemia	85.7%	80%
Hyperferritinemia	100% (4/4)	100%
Increased lactate dehydrogenase	83.3% (5/6)	80%
Lung involvement	57.1%	100%
Splenomegaly/Hepatomegaly	85.7%	75% (3/4)
Fulfill the 2004 HLH criteria	71.4%	100%
Treatment Corticosteroid	100%	100%
Cyclosporine	42.9%	0
Etoposide (VP-16)	14.3%	40%
Cyclophosphamide	14.3%	20%
Prognosis	71.4%	40%
Control during inpatient period	28.6%	60%
Dead or give up		

Conclusion: Clinical features of HLH patients complicated with tumor or rheumatic diseases were comparable in many aspects. Yet patients with tumor have more hypofibrinogenemia and lung involvement, and tend to be treated with VP-16 and Chemical therapy, and have much worse prognosis.

REFERENCES:

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FRI0595 MAY CANCER RISK BE DECREASED IN A LARGE COHORT OF CHILD AND ADULT FAMILIAL MEDITERRANEAN FEVER PATIENTS?

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Background: Recent studies suggested that the cancer incidence may be lower among FMF patients compared with healthy controls.
Objectives: We have assessed cancer risk among FMF patients with or without amyloidosis to confirm this hypothesis.
Methods: We studied FMF patients, diagnosed and followed-up in Hacettepe University hospitals. Patients were identified from the hospital registry by using the ICD-10 code for FMF. Presence of amyloidosis was also noted. Data related to cancer were collected from patient files and oncology hospital registries. We calculated age- and gender-specific standardized incidence rates according to the Turkish National Cancer Registry data at 2014.
Results: Total of 3899 FMF patients (120 patients had also amyloidosis) were included. Median age was 22 and 56% were females. Thirty-eight (0.1%) patients had cancer during the study period. Type and distribution of cancers were as follow; females: 7 breast, 5 lymphoma, 4 ovarian, 2 renal, 2 central nervous system, 2 connective tissue sarcoma, 1 lung, 1 colorectal, 1 gastric, 1 endometrium, 1 leukemia and 1 yolk sac cancer; males: 2 leukemia, 1 prostate, 1 colorectal, 1 renal, 1 pancreas, 1 lymphoma, 1 Kaposi sarcoma and 2 unclassified adenocancer. The overall cancer risk among patients with FMF was significantly lower in both males (SIR 0.42 (95% CI 0.21-0.75), p=0.002) and females (SIR 065 (95% CI 0.44-0.93), p=0.019). The overall cancer risk among patients with FMF and amyloidosis was (SIR 1.21 (95% CI 0.49-2.52), p = 0.73) without gender difference. Although the overall cancer risk seems decreased, an increased risk was found among female patients under 20 years-old (SIR 3.44 (95% CI 1.26-7.64), p = 0.003), however, there was no predominant type of cancer in this group. Detailed SIR values according to sex and age groups are given in **Table 1**.
Conclusion: Cancer incidence was significantly lower in FMF patients, confirming the results of a previous study. However, we found an increased cancer risk among female patients under 20 years-old. Further prospective studies especially in this age group are needed to comfirm this association. If so, early cancer screening may be considered in this particular patient group. Additionally, we found no increased cancer risk in FMF patients having amyloidosis. Possible underlying mechanisms need to be explained.

REFERENCES:

. SIR values for different age cut-offs in both sexes

Gender	Age	Observed/Expected Cancer Cases	SIR	95% Confidence interval	P value
Female	**<20-years**	5/1.45	3.44	1.26-7.64	0.003
	≥50-years	17/24.8	0.68	0.41-1.075	0.10
	Overall	28/43.08	0.65	0.44-0.93	0.019
Male	**<20-years**	3/1.83	1.64	0.42-4.46	0.55
	≥50-years	6/15.17	0.39	0.16-0.82	0.009
	Overall	10/23.9	0.42	0.21-0.75	0.002
Amyloidosis	**Overall**	6/4.9	1.21	0.49-2.52	0.73

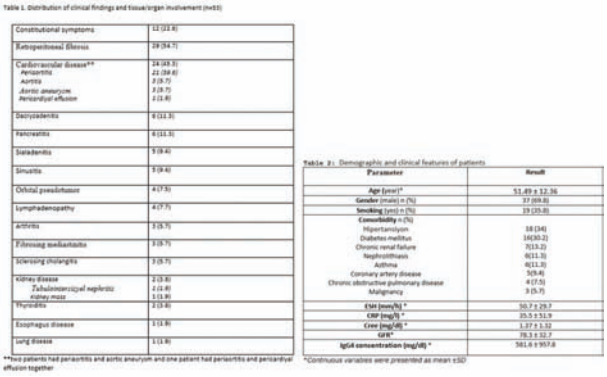
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FRI0596 AZATHIOPRINE AND GLUCOCORTICOID COMBINATION MIGHT BE A GOOD TREATMENT OPTION TO ACHIEVE REMISSION IN PATIENTS WITH IGG4-RELATED DISEASE

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Background: IgG4-related disease is a recently recognised inflammatory disease of unkown etiology, often seen in men over the age of 50 and may affect many organs and systems with elevated serum IgG4 levels and typical histopathological features.
Objectives: The aim of this study is to determine the demographic and clinical characteristics of patients with IgG4-related disease.
Methods: Patients diagnosed as having Ig-G4-related disease by their typical histopathological findings and imaging features and/or increased serum IgG4 concentrations (> 135 mg/dl) from two university hospital in Izmir were included in the study.
Results: There were 53 patients with a mean age of 51.49 yrs (69.8% male). The most common involvement was retroperitoneal fibrosis (54.7%), followed by the cardiovascular system (CVS) involvement (45.3%) (Table 1). While 22 patients had at least two organ involvement, the most common association was retroperitoneal fibrosis and CVS involvement (15 patients). Serum IgG4 levels were studied in 36 patients (67.9%) and found to be higher levels in 20 patients. (55.5%) (Table 2). In 44 patients (83%), acute phase reactants (APRs) were increased at the time of the diagnosis. There was no correlation between the extent of the disease and serum IgG4 levels and initial erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) values. 28 patients (52.8%) were diagnosed by imaging, 9 (17%) by imaging and IgG4 elevation, 5 (9.4%) by imaging and histopathology, 10 (18.9%) by imaging, histopathology and IgG4 elevation and 1 patient (1.9%) by only histopathology.

The most commonly (58.5%) used imaging method for diagnosis was computed tomography (CT). All the patients used initial glucocorticoid treatment.4 patients (7.5%) recieved only glucocorticoid,others were underwent the following treatments combined with glucocorticoid: azathioprine (AZA) (60.4%); methotrexate (mtx) (11.3%), rituximab (RTX) + AZA (9.4%), mtx + AZA (5.7%), RTX (3.8%) and infliximab (1.9%).



In the follow-up, a significant decrease in acute phase reactants was found in 62% of the patients at their last visits. While 27.3% of the patients had complete remission, 36.4% had partial remission, 20.5% had stable course, 13.6% had progression in the disease and 2.3% had recurrence. In 18 patients (64.3%) out of 28 patients who were in partial or complete remission, remission was achieved by using glucocorticoid and AZA combination treatment.

Conclusion: In conclusion, we have described a considerably large serie of patients with IgG4-related disease from Turkey. The results of the study suggested that AZA and glucocorticoid combination treatment was commonly used in Turkish patients with IgG4-related disease and it might be a good treatment option to achieve remission.

REFERENCES:

[1] Terumi Kamisawa et al; *IgG4-related disease*, Lancet 2015; 385: 1460–71

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FRI0597 INVOLVEMENT OF TWO OR MORE SETS OF LACRIMAL GLANDS AND/OR MAJOR SALIVARY GLANDS IS RELATED TO GREATER SYSTEMIC DISEASE ACTIVITY IN IGG4-RELATED DACRYOADENITIS/SIALADENITIS

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Background: IgG4-related dacryoadenitis/sialadenitis (IgG4-DS) is a major organ manifestation of IgG4-related disease (IgG4-RD) and is notable for its lack of a marked male predominance [1]. In IgG4-DS, involvement of two or more sets of lacrimal glands (LGs) and/or major salivary glands (MSGs) is regarded as a specific finding with diagnostic significance [2]. However, the influence of the presence of this finding on clinical features of IgG4-DS has not been well evaluated.

Objectives: This study aimed to clarify the influence of the involvement of $\geq$ 2 sets of LGs and/or MSGs on clinical features of IgG4-DS.

Methods: We retrospectively reviewed the medical records of 130 patients with IgG4-RD at a single center in Japan. Among them, 97 patients were diagnosed with IgG4-DS. We divided the 97 patients into Group A (n=44) with involvement of $\geq$ 2 sets of LGs and/or MSGs and Group B (n=53) with involvement of one set of LGs or MSGs or unilateral gland involvement. We compared the clinical features of Group A and B. Moreover, 33 IgG4-DS patients without extra-lacrimal/salivary gland lesions (DS-limited patients) were divided into Group a (n=14) and b (n=19) according to the presence/absence of the involvement of $\geq$ 2 sets of LGs and/or MSGs respectively, and their clinical features were also compared.

Results: The IgG4-DS patients comprised 60 men and 37 women (mean age 64.1 years). The mean follow-up period was 61.6 months, and the mean serum IgG4 level at diagnosis was 757 mg/dL. Group A had significantly more affected organs (3.5 ± 1.6 vs 2.7 ± 1.6, *P*=0.010), lower serum C3 and C4 levels (83.6 ± 29.5 vs 95.0 ± 25.2, *P*=0.018, and 16.5 ± 9.8 vs 21.4 ± 9.5, *P*=0.034, respectively), and a tendency to have higher serum IgG levels (2,509 ± 1,066 vs 2,165 ± 911, *P*=0.075) and IgG4-RD responder index (14.7 ± 6.7 vs 12.2 ± 6.5, *P*=0.050) than did Group B. In the 33 DS-limited patients, compared with Group b, Group a had no significant differences in clinical features including the proportion of patients with serum IgG4 elevation [$\geq$ upper limit of normal (ULN), 85.7% vs 78.9%, *P*=1.000; $\geq$ 2× ULN, 64.3% vs 47.4%, *P*=0.482; $\geq$ 5× ULN, 28.6% vs 21.1%, *P*=0.695].

Conclusion: Involvement of two or more sets of lacrimal glands and/or major salivary glands suggests greater systemic disease activity mainly due to involvement of more organs.

REFERENCES:

[1] Yamamoto M, et al. Everyday clinical practice in IgG4-related dacryoadenitis and/or sialadenitis: results from the SMART database. Mod Rheumatol. 2015 Mar;25(2):199-204.

[2] Masaki Y, et al. IgG4-related diseases including Mikulicz's disease and sclerosing pancreatitis: diagnostic insights. J Rheumatol. 2010 Jul;37 (7):1380-5.

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FRI0598 A SYSTEMATIC REVIEW OF THE EFFECTIVENESS AND SAFETY OF PHARMACOLOGICAL TREATMENTS IN PATIENTS WITH SYSTEMIC IDIOPATHIC JUVENILE ARTHRITIS (SJIA)

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Background: Treatment options for SJIA include canakinumab, tocilizumab (both approved by US FDA and EMA) and anakinra (approved by EMA), while anti-tumor necrosis factor inhibitors, steroids, disease-modifying anti-rheumatic drugs and non-steroidal anti-inflammatory drugs are also used.[1] A recent systematic review included only randomized controlled trials (RCTs) of biologics. We aimed to generate a more comprehensive evidence on the effectiveness and safety of treatments used in SJIA.

Objectives: To assess evidence on the effectiveness and safety of therapeutic agents for SJIA from RCTs and real-world studies.

Methods: A systematic literature review was conducted using Cochrane methodology[2] from 2000 to Jan 2018. Sources included Embase®, MEDLINE®, MEDLINE®-In Process and Cochrane library. Studies were searched for English language publications as full-text articles (2000 to Jan 2018) or conference abstracts (2015 to Jan 2018). Studies with ≤15 pts were excluded.

Results: Of the 62 included studies, 8 were RCTs and 54 were real-world studies. The interventions included in the RCTs were anakinra (ANA), canakinumab (CAN), etanercept (ETN), methotrexate (MTX) and tocilizumab (TCZ) (1 RCT each and 1 withdrawal trial for TCZ), and 2 RCTs for rilonacept (RLN); all vs. placebo (PLB). In addition to the interventions mentioned in the RCTs, real-world studies also included other interventions such as abatacept, adalimumab (ADA), infliximab (INF), non-steroidal anti-inflammatory drugs and steroids. Juvenile idiopathic arthritis - American college of rheumatology (JIA ACR)-30 was the most common composite outcome reported across studies.

In RCTs, the JIA ACR-30 (+ no fever) responses were significantly superior vs. PLB for CAN (81% vs. 10%), TCZ (85% vs. 24%), and ANA (92% vs. 50%) ($p<0.05$ for all), while other interventions (RLN and MTX) were less responsive. Additionally during the trial extension period, the inactive disease rates were 57%, 31% and 31% for TCZ, CAN and ANA respectively.

In real-world studies, the JIA-ACR 30 response rates reported for ANA, ANA or CAN (patients were on either therapy), TCZ and ETN were 50%-55%, 57%-60%, 47%-100% and 47%-73% at short-term follow-up

period (FUP, <12 months), while the corresponding response rates at long-term FUP (≥12 months) were 45%, 51%-63%, 58%-100% and 60%-100%. For ADA and ADA or ETN or INF (patients were on either therapy), while the JIA-ACR response rates at short term FUP were not reported, the response rates at long-term FUP were 100% and 78% respectively. Additionally, juvenile arthritis disease activity score (JADAS)-10 ≤ 1 scores were reported for ANA or CAN, CAN, ETN and TCZ as 52%, 48%-91%, 20% and 36% at short-term FUP. The mean changes in JADAS-71 scores at short-term FUP for ANA and TCZ were 10% and 11% respectively while the corresponding scores at long-term FUP were 13% and 14% (p<0.001).

All interventions were generally well tolerated by SJIA patients; infections, injection site reactions and macrophage activation syndrome were reported for all biologics. Other complications included gastrointestinal disorders, pharyngitis, skin disorders, increase in liver enzymes etc.

Conclusion: The current interventions especially ANA, CAN, ETN and TCZ were found to be effective and generally well tolerated in SJIA. However, the lack of head-to-head studies limits a rigorous comparison.

REFERENCES:

[1] Ringold, et al. 2013. Arthritis Rheum;65:2499-512.
[2] Higgins, et al. 2011. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0.

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FRI0599 AA AMYLOIDOSIS IN RECIPIENTS OF CADAVERIC DERIVED PITUITARY GROWTH HORMONE – POTENTIAL EFFECT OF AN AMYLOID ENHANCING FACTOR?

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Background: The development of Creutzfeldt–Jakob disease (CJD) in individuals treated with human cadaveric pituitary-derived growth hormone (c-hGH) was reported in 1985 resulting in its immediate withdrawal(1). Amyloid-β protein (Aβ) deposits have been found at autopsy in individuals previously exposed to c-hGH and misfolded Aβ peptide was recently identified in archived vials of human c-hGH; this induced Aβ pathology in an experimental model(2). The suggestion that contaminants in c-hGH could seed protein misfolding is reminiscent of the concept of amyloid enhancing factor (AEF), in which administration of tiny amounts of amyloidotic material is associated with acceleration of experimentally induced murine AA amyloidosis(3). In humans AA amyloid is a rare complication of chronic inflammation in which the amyloid fibrils are derived from Serum Amyloid A protein (SAA), a circulating component of the acute phase response.

Objectives: To seek evidence of prior exposure to c-hGH in patients with AA amyloidosis.

Methods: A database of 782 patients with AA amyloidosis seen between 1990 & 2017 was searched using: pituitary, craniopharyngioma & growth hormone. Only patients exposed to GH prior to 1985 were included.

Results: 10 cases were identified; accounting for 8% of AA of unknown etiology. 8 were female, 9 north European, median age at diagnosis of amyloid 47.9 yr with a median time since starting c-hGH of 35 yr. The indications were: 4 craniopharyngioma, resection of ependymona, nasal pharyngeal tumour & encephalocoele, 2 unexplained hypopituitarism. Chronic inflammation was assessed by serial blood tests after the diagnosis of amyloid; 1 had median SAA 131 mg/L; 4 had medians 20- 54 mg/L & the others low level inflammation, median < 20mg/L. No cause of inflammation was identified although 50% were obese. Genetic testing excluded systemic autoinflammatory disorders. 6 European patients were homozygous for SAA1.1 (66.7% compared to control frequency 29%)(4). 4 patients eventually required dialysis, 2 had renal transplants; median survival from diagnosis of amyloid was 132 mn & 3 patients have died.

Conclusion: 2,000 UK children were exposed to c-hGH; the finding of AA amyloid of uncertein etiology in these 10 cases raises the possibility that contaminants in c-hGH potentially contribute to misfolding of SAA. 80% had at least one recognised additional modest risk factor for the development of AA amyloidosis in the form of SAA1.1 homozygosity or obesity suggesting that a combination of factors may contribute to amyloidogenesis in individuals who have low levels of circulating potentially amyloidogenic protein(4).

REFERENCES:

[1] Underwood LE, Fisher DA, Frasier DS, et al. Degenerative neurologic disease in patients formerly treated with human growth hormone: Report of the Committee on Growth Hormone Use of the Lawson Wilkins Pediatric Endocrine Society, May 1985. The Journal of Pediatrics. 1985;107(1):10-2.
[2] Purro SA, Farrow MA, Lineham J, et al. Transmission of amyloid-β protein pathology from cadaveric pituitary growth hormone. Nature. 2018;564:415-9.
[3] Lundmark K, Westermark GT, Nyström S, et al. Transmissibility of systemic amyloidosis by a prion-like mechanism. Proc Natl Acad Sci U S A 2002;99(10):6979-84.
[4] Blank N, Hegenbart U, Dietrich S, et al. Obesity is a significant susceptibility factor for idiopathic AA amyloidosis. Amyloid. 2018;25(1):37-45.

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FRI0600 FIRST SINGLE-CENTERED COHORT OF CHINESE PATIENTS WITH PEDIATRIC SAPHO

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Background: The SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis) is an disease entity with chronic inflammatory osteoarticular symptoms and typical dermatological lesions. Pediatric SAPHO is regarded as equivalent of Chronic Recurrent Multifocal Osteomyelitis (CRMO) or Chronic Non-bacterial Osteomyelitis (CNO). There have already been several pediatric SAPHO cohorts about Caucasian populations. No Chinese cohorts have been reported.

Objectives: The aim of this study was to evaluate clinical features and treatment for all pediatric SAPHO patients admitted to Peking Union Medical College Hospital (PUMCH, Beijing, China)

Methods: We conducted a single-centered non-intervention retrospective study of 24 pediatric SAPHO patients who were diagnosed with Khan's modified criteria in PUMCH from April 2014 to August 2018 [1]. The demographic (sex, age, onset age, follow-up years), clinical (bone and skin symptoms), laboratory (ESR, CRP, HLA-B27, ANA, IL-6, IL-8, TNF-α), imaging (CT, MRI, bone scintigraphy), histologic (lymphocytic, granulocytic) and treatment (medications and effect) data were collected.

Results: Detailed information of 15 male and 9 female was available. The mean ± SD age at onset of bone and skin symptoms was 11.7 ± 3.8 and 14.4 ± 2.7 years, respectively. The duration of follow-up was 19.2 ± 15.2 months. 17 (71%) patients had skin manifestations (46% Severe Acne, all male; 21% Palmoplantar Pustulosis, all female; 4% psoriasis). Involvement of bone lesions varied (42% anterior chest wall, 29% mandible, 50% peripheral bones, 21% spinal bones). ESR, CRP, IL-6, IL-8, IL-10 was elevated in 88%, 96%, 50%, 71%, 70% patients, respectively. 11 did bone biopsy (6 dominantly lymphocytic, 3 granulocytic, 2 both). CT, MRI and bone scintigraphy were performed in 79%, 96%, 96% patients, respectively. A total of 6 patients have been treated with NSAIDs, 10 with bisphosphonate, 10 with TNF-α antagonist, 1 with Glucocorticoids, with a variable response. 70% patients showed complete remission after bisphosphonate or TNF-α antagonist therapy.

Table 1. Clinical characteristics of 24 pediatric SAPHO patients

Skin manifestation	17/24 (71%)
Severe acne (M/F)	11/0
PPP (M/F)	0/5
None (M/F)	3/4
Psoriasis (M/F)	0/1
Nonspecific rash (M/F)	1/0
Bone manifestation	24/24(100%)
Pain	24 (100%)
Swelling	17 (71%)
Restricted function	19 (79%)

Table 2. Effect of different treating choices for 24 pediatric SAPHO patients

Medications	Remission	Partial response	No response	Total
NSAIDs	3	3	0	6/24
Bisphosphonates	7	2	1	10/24
TNF-α antagonist	7	3	0	10/24
Glucocorticoids	0	1	0	1/24

Conclusion: This is the first Chinese cohort of pediatric SAPHO patients. Their bone lesions could be divided into 4 types, anterior chest wall, mandible, peripheral bones and spinal bones. We also provide evidence that bisphosphonate and TNF-α antagonist are useful for pediatric SAPHO treatment.

REFERENCES:

[1] Hayem G. SAPHO syndrome. Rev Prat. 2004;54(15):1635–6.

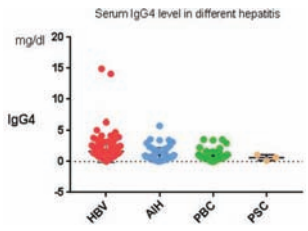
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FRI0601 SERUM IMMUNOGLOBIN G4 LEVEL IN INHEPATITIS B WAS HIGHER THAN AUTOIMMUNE LIVER DISEASE IN A CHINESE POPULATION

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Background: High serum level of Immunoglobulin G4 (IgG4) was detected in autoimmune hepatitis (AIH), but little was known in other types of hepatitis such as hepatitis B, primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC).
Objectives: The aim of this study is to evaluate the level of serum IgG4 in hepatitis B and autoimmune liver disease.
Methods: Hepatitis B and autoimmune liver disease patients were enrolled between January 1st and August 30th 2018. Diagnosis of Hepatitis B, AIH, PBC and PSC was basing on corresponding classification criteria, and established IgG4 related diseases were excluded. The levels of serum IgG4 were determined by nephelometric assay. The cut-off value of serum IgG4 was 2.01 g/L. Serum IgG4 among different liver diseases were compared.
Results: 161 HBV hepatitis and 112 autoimmune liver diseases (52 AIH, 57 PBC, 3 PSC) were enrolled in this study. The HBV hepatitis patients were younger than patients with autoimmune liver disease (44.79±12.56 vs 52.52 ± 11.16 years old). In total, 61 patients (22.34%) had elevated serum IgG4 level. IgG4 level in HBV hepatitis was significantly higher than in AIH, PBC, respectively (1.64±1.80 vs 1.11±1.16, 1.64±1.80 vs 0.96±0.87 g/L, P<0.05).



Conclusion: **High** serum IgG4 was very common in liver diseases without IgG4 related diseases especially in HBV hepatitis. Differential diagnosis should be made in patients with hepatitis accompanied with high serum IgG4.

REFERENCES:

[1] No.

Disclosure of Interests: None declared

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FRI0602 SERUM ALBUMIN PREDICTS ONCOLOGICAL OUTCOMES BUT NOT RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS FOLLOWING PD-1 INHIBITOR THERAPY

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Background: Rheumatic immune-related adverse events (irAEs) following immune checkpoint inhibitor (ICI) therapy for cancer are an increasing burden on rheumatological services but have also been associated with subsequent good oncological outcomes(1). A clinical need for biomarkers to predict rheumatic irAEs exists. High serum albumin and low lactate dehydrogenase (LDH)(2) prior to ICI therapy has been associated with subsequent good oncological outcomes, and may therefore predict rheumatic irAEs, but to the best of our knowledge this has not previously been examined.
Objectives: To determine the relationship between serum albumin and LDH of immune-related adverse events (irAEs) and oncological outcomes following treatment with the main classes of ICI therapy for cancer, programmed cell death protein 1 (PD-1) inhibitors and programmed death-ligand 1 (PD-L1) inhibitors.
Methods: We retrospectively examined all patients at a single centre who had a serum albumin performed in the institutional laboratory before treatment with a PD-1 or PD-L1 inhibitor before January 1, 2018, with follow-up until October 1, 2018. Patients with any diagnosis of a rheumatic irAE were identified. Treatment response was determined based on assessment by the treating oncologist, with favourable oncological response defined as complete or partial response. Statistical tests were performed using two-tail t-tests. Missing laboratory values were imputed using median imputation.
Results: There were 401 episodes of therapy which met criteria, of which 324 had a serum albumin level and 244 had serum LDH prior to the commencement of therapy. A rheumatic irAE was diagnosed in 26 of the 401 patients (6.5%) and a good oncological response was noted in 140 patients (34.9%). There was a statistically significant relationship between higher baseline serum albumin and favourable oncological response ($p < 0.001$), but not with the development of a rheumatic irAE (p=0.41)(Table 1). Although serum LDH levels were lower in those with favourable oncological response, this relationship was not statistically significant (p=0.16). Similarly, LDH levels were lower on average in those who subsequently developed a rheumatic irAE, however this relationship was not statistically significant (p=0.57).
Conclusion: High serum albumin was associated with good oncological outcomes following ICI therapy with a PD-1 or PD-L1, but not with rheumatic irAEs. The reason for this dissonance is not clear. Not all markers of good oncological response predict rheumatic irAEs and further study should focus on consequent implications for rheumatic irAE pathophysiology.

REFERENCES:

[1] Kostine M, Rouxel L, Barnetche T, Veillon R, Martin F, Dutriaux C, et al. Rheumatic disorders associated with immune checkpoint inhibitors in patients with cancer-clinical aspects and relationship with tumour response: a single-centre prospective cohort study. Ann Rheum Dis. 2017.
[2] Bigot F, Castanon E, Baldini C, Hollebecque A, Carmona A, Postel-Vinay S, et al. Prospective validation of a prognostic score for patients in immunotherapy phase I trials: The Gustave Roussy Immune Score (GRIm-Score). European Journal of Cancer. 2017;84:212-8.

Table 1. Albumin and LDH, and associations to oncological response and rheumatic irAE development

	Oncological non-responders	Oncological responders	p-value
Albumin (g/L)	33.4	35.2	< 0.001
LDH (units/L)	262	237	0.16
	No rheumatic irAE	**Rheumatic irAE**	**p-value**
Albumin (g/L)	34.0	34.9	0.41
LDH (units/L)	254	238	0.57

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FRI0603 SARCOIDOSIS IN A TERTIARY HOSPITAL

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Background: Sarcoidosis (S) is a systemic granulomatous disease of unknown etiology. The most frequent affectation is pulmonary, ocular and cutaneous, although sarcoidosis can damage other organs, such as the musculoskeletal system.
Objectives: To describe the clinical characteristics and the radiological pattern, in a cohort with predominant pulmonary S, as well as to establish the relationship between the angiotensin converting enzyme (ACE) levels and the S course (chronification or remission).
Methods: This is a retrospective descriptive study of patients treated in our hospital, since 2008 to 2018, with diagnosis of S. The data was obtained through the review of medical records. The delay in the diagnosis of S was defined as the difference in months between the initial diagnostic suspicion and the final diagnosis of S.
We use Chi-square tests to study the association between ACE levels and the course of the disease.
Results: Fifty-five patients (31 women) were included, with a mean age of 52 ± 12 years. The first diagnosis was: 85% S, 10% lymphoma and 4% tuberculosis. The median of months for the definitive diagnosis of S was 5.5 months.
Extrapulmonary clinical manifestations in table 1.
The ACE is increased in 38 patients (70%). Simple x-ray and high resolution tomography of chest were done in all patients. Pulmonary stage 2 was the most frequent (51%), followed by stage 3 (16%), stage 0 (14%) and stage 4 (9%).
In 90% of the patients, histological confirmation was obtained by transbronchial (47%), cutaneous (11%) or lymph node biopsy (29%).
94% of the patients have been treated with oral glucocorticoids, 52% associate immunosuppressive therapy (Methotrexate 27% and Azathioprine 14%) or biological treatment (1 patient with Adalimumab and another with Infliximab). In 54% of the patients the S had a chronic course and in 43% S remitted.
Increased levels of ACE were associated with clinical remission of the disease and normal levels with chronicity (p: 0.013).

EXTRATHORACIC CLINICAL MANIFESTATIONS	N(%)
Skin	15(27)
Neurological	4(7)
Cardiac	8(14)
Renal	2(4)
Ocular	7(13)
Monoarthrittis	3(5)
Poliarthritis	6(11)
Bilateral swelling in ankles	6(11)
Hepatosplenomegaly	8(14)

Conclusion: The results of our study resembles, in general, what has been published in the literature. In our study, elevated ACE is associated with remission of the disease, contrary to the published, in which increased levels of ACE in symptomatic patients may reflect disease activity.
Disclosure of Interests: None declared
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FRI0604 SYSTEMIC SARCOIDOSIS. STUDY OF 381 PATIENTS FROM A TERTIARY UNIVERSITY HOSPITAL IN THE NORTH OF SPAIN

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Background: Sarcoidosis is a systemic granulomatous disease characterized by the presence of non-necrotizing granulomas in different parenchyma.
Objectives: To describe demographic, clinical and analytical features in a cohort of patients with Sarcoidosis diagnosis from northern Spain during the last twenty years.
Methods: Descriptive study of 381 patients diagnosed with sarcoidosis during the period 01/01/1999 to 01/01/2019. Biopsy and/or clinical and compatible imaging tests were required for the diagnosis of sarcoidosis. Demographic parameters, clinical manifestations, complementary tests and treatment were registered. Results are expressed as mean±SD or as median and interquartile range (IQR) as appropriate.
Results: 381 patients (192 female/191 male, ratio 1:1), with a mean age 45.5±15.4 years at disease onset, and with 94.8% of Spanish nationality. 33% were smokers at diagnosis and 6.3% had tuberculosis (**Table 1**). The sarcoidosis incidence rate in our population was 3.3 cases/100000 p/year, similar to other national series[1].
Most frequent clinical manifestations were as follow: pulmonary symptoms (72.3%), general symptoms (37.3%), skin involvement (31%), joint manifestations (27.9%), ophthalmological manifestations (13.0%), digestive disorders (9.3%), neurological symptoms (6.5%), nephrological (4.7%) and cardiological involvement (1.6%) (**Table 1**). In addition, 11.5% of the patients had a Löfgren syndrome, 0.5% a Heerdfort syndrome and up to 11.5% had mediastinal adenopathy as an incidental finding in simple chest radiography.
A simple chest radiograph was performed in all patients. 83.7% presented abnormal patterns: stage I (41.4%), stage II (32%), stage III (7.6%) and stage IV (3.8%). In addition, 29.9% and 10.5% of patients presented pathological scintigraphy and PET respectively. Biopsy was performed in 81.9%, with a mediastinal approach in 43.3%. **(Table 2).**
After a median follow-up of 11.0 [6.0-17.0] years, we observed that up to 32% of patients never received treatment. In the remaining 68%, the main treatment was oral glucocorticoids with a mean dose of 43.4±19.1 mg/day. Other treatments used were conventional immunosuppressants and biological agents **(table 2).**

Table 1.

	Patients diagnosed with sarcoidosis (N=381)
DEMOGRAPHIC PARAMETERS	
Sex, n (%)	191♂/192♀ (50.1/49.9)
Age at disease onset (years), mean ± SD	45.5 ± 15.4
Current age (years), mean ± SD	59.0 ± 16.3
Follow-up, median [ICR]	11.0 [6.0-17.0]
Nationality (Spanish), n (%)	361 (94.8)
Smokers, n (%)	126 (33.1)
Asthma, n (%)	24 (6.3)
Tuberculosis, n (%)	24 (6.3)
Tumours, n (%)	23 (6.0)
CLINICAL MANIFESTATIONS	
Pulmonary symptoms, n (%)	**277 (72.3)**
- Dyspnea, n (%)	103 (26.9)
- Cough n (%)	35 (9.1)
- Pleuritic pain, n (%)	10 (2.6)
- Adenopathy, n (%)	129 (33.7)
Ocular involvement, n (%)	**50 (13.0)**
- Uveitis, n (%)	36 (9.4)
- VA, n (%)	5 (1.3)
- Exophthalmos, n (%)	2 (0.5)
- Others, n (%)	7 (1.8)
Skin involvement n (%)	**119 (31.1)**
- Erythema nodosum, n/N (%)	72 (18.8)
- Lupus pernio, n/N (%)	7 (1.8)
- Parotid gland hypertrophy, n/N (%)	7 (1.8)
- Granulomatous dermatitis, n/N (%)	33 (8.6)
Joint involvement, n (%)	**107 (27.9)**
- Arthralgia, n (%)	66 (17.2)
- Arthritis, n (%)	40(10.4)
- Sarcoidosis myopathy, n (%)	1 (0.3)
Digestive disorders, n (%)	**36 (9.3)**
- Hypertransaminasemia, n/N (%)	20 (5.2)
- Hepatic granulomas, n/N (%)	13 (3.3)
- Other granulomas, n/N (%)	3 (0.8)
Neurological symptoms, n (%)	**25 (6.5)**
- Headache, n (%)	13 (3.5)
- Meningitis, n (%)	2 (0.5)
- Neuropathy, n (%)	6 (1.5)
- Others, n (%)	4 (1.0)
Cardiological manifestations, n (%)	**6 (1.6)**
- Dilated cardiomyopathy, n (%)	4 (1.0)
- Pericarditis, n (%)	1 (0.3)
- SMVT, n (%)	1 (0.3)
Nephrological manifestations, n (%)	**18 (4.7)**
- Acute renal failure, n (%)	12 (3.1)
- Chronic kidney disease, n (%)	5 (1.3)
- Lithiasis, n (%)	1 (0.3)
Systemic symptoms, n (%)	**143 (37.3)**
- Fever, n (%)	36 (9.4)
- General syndrome, n (%)	107 (27.9)
Lymphadenopathy as incidental finding, n (%)	44 (11.5)
Löfgren syndrome, n (%)	44 (11.5)
Heerdfort syndrome, n (%)	2 (0.5)

Table 2.

	Patients diagnosed with sarcoidosis (N=381)
LABORATORY TESTS	
CRP (mg/dl), median [ICR]	0.2 [0.0-1.2]
ESR (mm/1ªh), median [RIC]	22.0 [10.0-38.0]
ACE, mean±SD	78.7 ± 46.2
Calcium, mean±SD	9.4 ± 0.9
Thrombocytosis, n (%)	9 (2.4)
Lymphopenia, n (%)	43 (11.3)
Hypercalciuria, n (%)	29 (7.6)
CD4/C8 > 3.5, n (%)	122 (32.0)
IMAGING TESTS	
Patients with abnormal radiological patterns:	**319 (83.7)**
- Stage I, n/N (%)	156 (41.4)
- Stage II, n/N (%)	122 (32)
- Stage III, n/N (%)	29 (7.6)
- Stage IV, n/N (%)	14 (3.8)
Confirmed lymphadenopathy in CT, n (%)	**300 (78.7)**
Pathological scintigraphy, n (%)	**114 (29.9)**
Pathological PET, n (%)	**40 (10.5)**
Non-caseating granulomas in biopsy, n (%)	**290 (75.7)**
- Mediastinum, n (%)	166 (43.3)
- Lung, n (%)	67 (17.5)
- Liver, n (%)	9 (2.4)
- Skin, n (%)	45 (11.7)
- Lymphadenopathy, n (%)	3 (0.8)
TREATMENT	
Not treated, n (%)	**122 (32.0)**
Glucocorticoid treatment	
- Topical treatment, n (%)	39 (10.2)
- Prednisone, n (%) / mean dose (mg/day), mean±SD	206 (54.1) / 43,4±19.1
- Bolus MTP, n (%)	15 (3.9)
Conventional immunosuppressants	
- Methotrexate, n (%) / mean dosage (mg/week), mean±SD	53 (13.9) / 15.4±5.5
- Azathioprine, n (%) / mean dosage (mg/day), mean±SD	17 (4.5) / 91.6±32.2
- Cyclophosphamide, n (%)	2 (0.5)
- Mycophenolate mofetil, n (%)	2 (0.5)
Biological agents	
- Infliximab, n (%)	14 (3.7)
- Adalimumab, n (%)	19 (5.0)
- Etanercept, n (%)	1 (0.3)
- Golimumab, n (%)	2 (0.5)
- Tocilizumab, n (%)	3 (0.8)
- Rituximab, n (%)	3 (0.8)
- Secukinumab, n (%)	1 (0.3)

Conclusion: Results obtained were similar to other national and international series, with the exception of non-predominance of female sex and the highest percentage of ocular involvement in our study. Currently, biological treatment (especially anti-TNF-alpha) is used more frequently.

REFERENCES:

[1] Mañá et al. Multidisciplinary approach and long-term follow-up in a series of 640 consecutive patients with sarcoidosis: Cohort study of a 40-year clinical experience at a tertiary referral center in Barcelona, Spain. Medicine (Baltimore). 2017 Jul;96(29):e7595.

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FRI0605 EFFECTIVENESS AND SAFETY OF OFF-LABEL USE OF TOCILIZUMAB IN AUTOIMMUNE DISEASES : A MULTICENTER STUDY IN INTERNAL MEDICINE DEPARTMENTS

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Background: Tocilizumab (TCZ) is a recombinant humanized anti-interleukin-6 receptor monoclonal antibody. There is increasing evidence of TCZ efficacy in refractory auto-immune diseases.

Objectives: To describe off-label use, efficacy and tolerance of TCZ use in Internal Medicine Departments.

Methods: This is a retrospective, descriptive and multicenter study from 9 departments of Internal Medicine. Data were reported using a standardized case report file in January 2019.

Results: Fifty one patients were included (19 men, 32 women). Mean age was 55.6 ± 17 years (range 23 - 80). TCZ was used in:

- 12 connective tissue diseases (23.5%): relapsing polychondritis (n=6), systemic sclerosis (n=3), anti-synthetase syndrome (n=1), and unclassified connective tissue disease (n=3).
- 10 vasculitis (19%): Takayasu arteritis (n=7), Cogan disease (n=1), panarteritis nodosa (n=1), unclassified vasculitis (n=1).
- 10 ophthalmologic conditions (19%): non infectious posterior uveitis (n=8), sympathetic ophtalmia (n=1), Basedow orbitopathy (n=1).
- 8 adult-onset Still's diseases (16%).
- 5 cases of polymyalgia rheumatica (10%)
- 3 miscellaneous diseases (6%): idiopathic AA amyloidosis, multicentric non HHV8 Castelmann disease, Erdheim Chester disease (1 case each).

Mean disease duration was 7.5 ± 6.4 years. In 44 cases (86%) TCZ was administered for refractory disease to corticosteroids and immunosuppressive drugs. Previous therapies included corticosteroids (83%), methotrexate (66%), TNF inhibitor drug (44%), azathioprine (20.8%), mycophenolate (12%), cyclophosphamide (8%), rituximab (10%), hydroxychloroquine (6%), anakinra in 2 patients and interferon, dapsone, etoposide, leflunomide, abatacept, salazopyrin or intra-venous immunoglobulin in 1 patient each.

TCZ was initiated as first-ligne therapy (15.5%), second-line therapy (17.5%), third-line therapy (31%), fourth-line therapy (19%), fifth-line therapy (14%), sixth-line therapy (12%) or as seventh line therapy in one case. TCZ was associated with methotrexate in 3 cases (6%). Treatment route was intravenous (96%).

At the end of the follow up, 41 patients (80%) were still using TCZ, with a mean follow up period of 22 ± 23 months (range 1-90). In these patients, daily corticosteroid use significantly decrease from 16.5 ± 18 mg to 5.7 ± 13.7 mg ($p<0.005$, using paired T test). Considering the 28 patients using TCZ since more than 6 months, short term efficacy was 93% (2 cases of loss of efficacy).

TCZ was interrupted in 10 patients (19%), because of treatment failure (n=2), loss of efficacy (n=2) or side effect (=6). Side effects were infection (2 pneumonias, zona, sinus infection), pruritus (n=1), urticaria (n=1), dyslipidemia (n=1), high blood pressure (n=2), infusion-related reaction (n=1), bullous dermatitis (n=1), acute renal failure (n=1), angioedema (n=1), mouth ulcers (n=1).

Conclusion: TCZ is used in various autoimmune diseases. TCZ allowed a significant corticosteroids reduction and short term efficacy was 93% in patients using TCZ for more than 6 months. Nevertheless TCZ was interrupted in 19% of the patients. TCZ use will probably be more common in the future to treat refractory autoimmune diseases.

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FRI0606 AUTOIMMUNE MANIFESTATIONS IN A COHORT OF PATIENTS WITH TYPE 1 DIABETES MELLITUS

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Background: Type 1 diabetes mellitus (T1D) is an organ-specific autoimmune disease characterized by the presence of circulating, islet-specific, pancreatic auto-antibodies against glutamic acid decarboxylase (GAD65) and the destruction of insulin-producing pancreatic beta cells. An increased risk of developing other serological manifestations and autoimmune diseases has been described, mainly of the thyroid (20% with antithyroid antibodies) and celiac disease (5%). In addition, it has also been described in association with Addison's disease, autoimmune polyglandular syndrome, psoriasis and other systemic autoimmune comorbidities diseases such as rheumatoid arthritis (RA), systemic juvenile idiopathic arthritis and Sjogren's syndrome. It also has been suggested that T1D might has a genetic factor, pathogenic pathways with pleiotropic effects, and cytokines such as interferon type I, among others.

Objectives: 1) Study the prevalence of autoimmune comorbidities in patients with T1D. 2) Describe the clinical-immunologic profiles of these patients.

Methods: A descriptive, retrospective study of a cohort of patients diagnosed with T1D, according to ADA (American Diabetes Association), follow-up by Endocrinology and Rheumatology Units of a 3rd level hospital from June 1975 to July 2018. Clinical and analytical-immunologic

variables were collected. Statistical analysis was was performed with SPSS.25.

Results: We included 116 patients from which 55% were women, with a mean age at diagnosis of T1D 18.7 (± 12.3 SD) years. Average age at autoimmune disease diagnosis was 38.8 (± 12.2 SD) years. Average time of evolution between onset of T1D and autoimmune comorbidity was 10.1 (± 10.6 SD) years, except one patient with autoimmune thyroiditis 10 years before T1D. Autoimmune manifestations were showed by 19/116 patients (16.4%), with the following diagnoses: autoimmune hypothyroidism: 10 patients (8.6%); autoimmune polyglandular syndrome: 3 patients (2.6%), RA in 2 patients (1.8%). As well, 1 patient with celiac disease, 1 with cutaneous lupus erythematosus (CLE), 1 with psoriasis and another one with IgG4-related orbital inflammatory disease, (0.9% respectively). Three patients developed articular manifestations (2 rheumatoid polyarthritis and 1 with limited joint mobility or cheiroarthropathy). 4/19 patients (21%) showed cutaneous lesions (2 with vitiligo, 1 CLE and 1 with psoriasis.. Hematological alterations type pernicious anemia in one patient. No visceral involvement was found. Antibodies were detected to be organ-specific: 7/17 antibodies to thyroid peroxidase (TPO) (+) and 3/17 antibodies to thyroglobulin (+) and one with anti-gliadin IgA (+). ANA (+) was detected in four patients (two fine granular pattern, one nucleolar and one homogeneous) with negative specificities and 1 patient RF (+). No Anti-CCP antibodies were detected.

Conclusion: 1) 16% of patients with T1D presented autoimmune comorbidity at 10 years after the onset of endocrinopathy. 2) Autoimmune hypothyroidism was the most prevalent autoimmune manifestation (8.6%), followed by autoimmune polyglandular syndrome and RA, similar to other studies. 3) We highlight the unusual finding of IgG4-related orbital inflammation as comorbidity of T1D. 4) The cutaneous lesions (21%) were the most common clinical manifestation in patients with T1D and autoimmunity. We emphasize the absence of visceral involvement.

REFERENCES:

[1] -Lynne et col, 2018, Associated autoimmune diseases in children and adolescents with T1D, uptodate.
[2] -Jiang P et col, 2015, Diabetes Mellitus risk factors in rheumatoid arthritis: a systematic review and meta-analysis.
[3] -Kiani AK et col, 2015, Genetic link of type 1 diabetes susceptibility loci with rheumatoid arthritis in Pakistani patients.
[4] -Zheng WY et col, 2016 Detecting shared pathways linked to rheumatoid arthritis with other autoimmune disease in a in silica analysis.

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FRI0607 IDENTIFICATION OF UNMET NEEDS RELATED TO RARE AND COMPLEX CONNECTIVE TISSUE AND MUSCULOSKELETAL DISEASES (RCTDS) ACROSS EU: THE EXPERIENCE OF THE ERN RECONNET

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Background: The European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ERN ReCONNET) is a virtual Network that aims to improve and standardize the quality of care offered to rCTDs patients in Europe, empower patients, share knowledge and expertise, enhance research, support efficient use of resources. ERN ReCONNET covers 10 rCTDs: APS, UCTD, Idiopathic Inflammatory myopathies, IgG4, MCTD, Systemic sclerosis, Relapsing Polychondritis, SLE, Sjogren and EDS.

Objectives: Identification of unmet needs in diagnosis, monitoring and management of rCTDs after literature review of existing clinical practice guidelines (CPGs).

Methods: After the review of existing CPGs, the most relevant unmet needs, both for clinicians and patients, were identified by discussion among the members of the network.

Results: A considerable number of unmet needs were identified. In particular, the lack of shared classification criteria, of evidence-based CPGs, validated tools for the assessment of treatment response and disease activity/damage are the major unmet needs especially for the rarest rCTDs. Transversal topics for all rCTDs that need to be addressed are the scarcity of EU/international randomised controlled trials, the identification of patient-reported outcomes and non-adherence to treatment, quality of life indicators, the need to develop composite disease activity scores for all rCTDs and specific (inter)national web-based registries. Patients highlighted the need of a more holistic approach to rCTDs, demanding more attention to pain, fatigue and psychological aspects related to the diseases and the promotion of an early diagnosis.

Conclusion: The identification of rCTDs unmet needs provided a very useful picture on future actions to be undertaken in order to provide a better care to patients. Many activities are ongoing towards these goals in ERN ReCONNET. These will be possible as a result of a EU collaboration among rCTDs stakeholders, the main added value of ERN ReCONNET.

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FRI0608 **ASSOCIATION BETWEEN INTERSTITIAL LUNG DISEASE AND RHEUMATIC DISEASE: IMPLICATIONS IN CLINICAL PRACTICE**

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Background: The relationship between interstitial lung disease (ILD) and rheumatic diseases is well known. Recently, a new clinical entity has been described that relates ILD with autoimmune findings, IPAF (Interstitial Pneumonia with Autoimmune Features), which allows identifying and condensing non-cataloged diseases with pulmonary and rheumatic involvement.
Objectives: Our aim is to establish which patients with ILD have a rheumatic disease, and which of them meet the IPAF criteria. We analyzed the role of nailfold capillaroscopy in these patients.
Methods: This is a prospective descriptive observational study. The observation period was 2 years (2016-2018), in a county university hospital. Patients diagnosed with ILD of unknown etiology, derived from Pneumology Service, were included. A medical history was obtained focused on autoimmune disease, rheumatological evaluation, rheumatological blood markers and nailfold capillaroscopy, in order to establish whether they had a concomitant rheumatic disease.
Results: Thirty patients with ILD were evaluated, with a mean age of 70,5 years (53 - 88). Of the 30 subjects, 12 (40%) had usual interstitial pneumonia (UIP), 11 (36.67%) had organizing pneumonia (OP) and 7 (23.33%) had nonspecific interstitial pneumonia (NSIP). Eleven (36,67%) of the 30 patients had an altered capillaroscopy, 6 of them (54,5%) had a rheumatic disease. In our sample, 5 cases meet diagnostic IPAF criteria, 4 OP and 1 UIP, three of them with altered capillaroscopy.
Conclusion: In our serie, one third of the patients were diagnosed with rheumatic disease associated with interstitial lung disease. Of the thirty evaluated patients, 36.67% had altered capillaroscopy, 54.5% presenting concomitant rheumatic disease. Following the IPAF classification criteria, we obtained 5 cases in our sample: four OP and one UIP, 3 of them with altered capillaroscopy. It is important to be aware of this association with a multidisciplinary approach for the adequate diagnosis and follow-up of these patients.

ILD	Capillaroscopy	Raynaud	Acropachy	Relevant issues	Rheumatology diagnosis
UIP	Altered (angiogenesis)	Yes	Yes	Aldolase, cANCA	Polymyalgia rheumatica
UIP	Altered (angiogenesis)	Yes	No	ANA 1/640 nucleolar	Systemic sclerosis
UIP	Altered (angiogenesis)	Yes	No	CK, aldolase, anti-Ro	Sjögren Syndrome
UIP	Altered (active pattern)	Yes	No	ANA 1/320 speckled	Systemic sclerosis
UIP	Normal	No	Yes		
UIP	Normal	No	Yes	ANA, anit-DNA, pANCA, anti-MPO	IgA nephropathy
UIP	Normal	Yes	No	Anti-PPC	IPAF
UIP	Normal	Yes	Yes	FR, anti-PPC	Rheumatoid arthritis
UIP	Normal	No	Yes		
UIP	Normal	No	Yes		
UIP	Normal	Yes	Yes	ANA, aldolase, FR, anti-PPC	Rheumatoid arthritis
UIP	Normal	Yes	No	Anti-Ro, anti-La	Sjögren Syndrome
OP	Altered (angiogenesis)	Yes	No		IPAF
OP	Altered (enlarged capillaries)	Yes	No	Anti-Ro	IPAF
OP	Altered (angiogenesis)	No	No	ANA 1/1280 hom	IPAF
OP	Normal	No	No	ANA 1/320 hom	IPAF
OP	Normal	No	No		
OP	Normal	No	No		
OP	Normal	No	No		
NSIP	Altered (angiogenesis)	No	Yes		
NSIP	Altered (Dermatomyositis)	No	No	Aldolase, anti-Ro, anti-MDA5	Dermatomyositis
NSIP	Altered (hemorrages)	No	No		
NSIP	Altered (Dermatomyositis)	No	No	CK, aldolase, anti-Jo1	Antisynthetase syndrome
NSIP	Normal	No	No		
NSIP	Normal	No	No	RF, anti-PPC	Rheumatoid arthritis
NSIP	Normal	No	No	SCLE, aRo, aLa	Sjögren Syndrome

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FRI0609 **EXPERIENCE WITH BIOLOGIC AGENTS FOR THE TREATMENT OF CARDIAC SARCOIDOSIS IN A U.S. ACADEMIC MEDICAL CENTER**

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Background: Sarcoidosis is a multisystem granulomatous disease of unclear etiology characterized histologically by non-caseating granulomas. Lungs are the most common organs affected but sarcoidosis can affect almost any organ system. While clinically manifest cardiac involvement occurs in only about 5% of patients with sarcoidosis, a significant proportion have clinically silent disease. Symptomatic cardiac involvement portends a poorer prognosis with manifestations varying from heart failure and conduction abnormalities to ventricular arrhythmias including sudden death. Immunosuppression with corticosteroids and DMARDs such as methotrexate and mycophenolate mofetil has been the mainstay of treatment despite a paucity of data. There is a subset of patients that are either non-responders to these agents or in whom the side effect profile is prohibitive for their long term use. Biologic agents, mainly TNF alpha antagonists, have been used as salvage therapies in these patients. However, the evidence regarding their efficacy and safety is limited to a few case reports. In fact, there remains much apprehension regarding the use of TNF alpha antagonists in patients with systolic heart failure due to concerns that they can exacerbate heart failure.
Objectives: To study the efficacy and safety of using biologics for the treatment of cardiac sarcoidosis.
Methods: We conducted a retrospective and prospective observational study of all adult patients with cardiac sarcoidosis treated with biologics at an academic medical center in Washington D.C, USA between 2013 and 2018.
Results: We identified 9 patients (3 men and 6 women) diagnosed with cardiac sarcoidosis at our institution. The mean age at diagnosis was 49.9 (SD 8.6). 1 patient was Caucasian and the rest (n=8) were African American. Lungs were the most common extra cardiac organ involved (n=7) followed by CNS (n=4), liver (n=4) and skin (n=3). 5 of the patients presented with systolic heart failure (EF<50%), 3 with atrial and

ventricular arrhythmias and 1 was found to have incidental abnormal myocardial uptake on PET imaging. 8 of the 9 patients had abnormal myocardial uptake on PET imaging. All but 1 patient had been initially treated with oral steroids (1 refused) and 7 of the 9 patients had also been given oral DMARDs; methotrexate (n=6), azathioprine (n=2), hydroxychloroquine (n=2) and mycophenolate mofetil (n=1). Biologics used were adalimumab (n=5), infliximab (n=3) and rituximab (n=1). The most common indication for biologics was progression of disease despite optimal doses of standard therapy, followed by intolerance or contraindication to standard therapy. 75% of the patients were noted to have marked clinical improvement with the addition of a biologic. 4 out of 9 patients had decreased myocardial uptake on PET following treatment with a biologic. One patient had no change on PET and 4 have not had repeat imaging done yet. None of the patients had worsening of left ventricular systolic function with the addition of a TNF alpha antagonist. There were no reported major infections or significant adverse events that were attributable to the use of biologics.

Conclusion: Based on our small cohort, biologics (mainly TNF alpha antagonists) appear to be safe and efficacious as salvage therapy for cardiac sarcoidosis. However, there is a need for prospective studies to further validate these findings as well as to identify the subset of patients that would benefit from early initiation of these therapies.

REFERENCES:

[1] Birnie, D. H., Nery, P. B., Ha, A. C., & Beanlands, R. S. B. (2016). Cardiac Sarcoidosis. Journal of the American College of Cardiology, 68(4), 411.

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FRI0610 CRYOPYRIN-ASSOCIATED PERIODIC SYNDROME: A SERIE OF CASES IN A ADULT´S PATIENTS COHORT WITH AUTOINFLAMMATORY SYNDROME IN A THIRD LEVEL HOSPITAL

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Background: The Cryopyrin-associated Periodic Syndrome (CAPS) or cryopyrinopathies are part of the spectrum of autoinflammatory diseases. The term cryopyrinopathy encompasses three clinical entities such as: CINCA/NOMID (chronic infantile neurologic, cutaneous and articular/neonatal onset multisystem inflammatory disease), Muckle-Wells disease and FCAS (familial cold-associated periodic syndrome). There are three different diseases that would be part of the same clinical spectrum, ranging from CINCA/NOMID (more serious) to FCAS (the less severe). It is more frequent in pediatric age although they can also be observed in adulthood. They are characterized by mutations in the NLRP3 gene and have an autosomal dominant inheritance pattern

Objectives: To describe the clinical characteristics and genetic variants of a cohort of patients in adulthood diagnosed with cryopyrinopathy and with follow-up in a 3rd level hospital

Methods: Retrospective descriptive study in adults patients with diagnosis of cryopyrinopathy since 2013 (year of introduction of genetic tests in the hospital laboratory) until now. The data was obtained from the review of medical records. All patients with mutations in NLRP3 gene and clinically compatible with this diagnosis were reviewed.

Results: Of a total of 44 patients in adulthood diagnosed with periodic fever syndromes (FMF, TRAPS, cryopyrinopathies, HIDS) and compatible genetic mutations, 7 patients (15.9%) were diagnosed with cryopyrinopathies, presenting 6 of them (13, 6%) mutations in NLRP3 gene. 1 patient was diagnosed with Muckle Wells based on clinical criteria without genetic test. 6 patients (13.6%) were women. 4 patients (9.1%) presented mutations in heterozygosis in exon 3 of NLRP3 gene (p.V198M). 1 patient presented heterozygous mutation in exon 3 of NLRP3 gene (p.R260W) and another patient presented a mutation in heterozygosis in exon 3 of the NLRP3 gene (p.S726G). The mean age at diagnosis was 38 years (IR 13-71 years). The totality of patients diagnosed with cryopyrinopathy showed elevation of acute phase reactants. 6 patients (13.6%) presented fever, joint symptoms (arthralgias and/or arthritis) and myalgias. 4 patients (9.09%) showed cutaneous involvement in the form of urticarial rash. 4 patients (9.09%) showed neurosensory deafness since childhood. 3 patients (6.8%) presented ocular involvement in form of conjunctivitis and/or uveitis. In 3 cases (6.8%), antiIL-1 (anakinra) or anti-TNF were used.

Conclusion: Cryopirinopathies are autoinflammatory diseases that occur mainly in the pediatric age, but there are also cases in adulthood. We must consider its diagnosis in those cases with periodic fever, arthralgia or arthritis, sensorineural deafness, APR elevation and urticarial rash. The genetic diagnosis will help us to confirm the diagnosis and avoid a delay in it.

Disclosure of Interests: None declared

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FRI0611 ACUTE AND LONG-TERM EFFICACY OF IL-1 INHIBITOR ANAKINRA IN IDIOPATHIC AND SECONDARY PERICARDITIS IN PATIENTS REFRACTORY OR INTOLERANT TO CONVENTIONAL THERAPY

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Background: In contrast to its use in idiopathic recurrent pericarditis (IRP), efficacy and optimal treatment duration of Anakinra are unclear in pericarditis secondary to known autoimmune or inflammatory conditions.

Objectives: a) Assess the efficacy of Anakinra in secondary and idiopathic pericarditis, refractory or intolerant to conventional therapy (CT; colchicine and corticosteroid [CS]).

b) Study the effect of extended Anakinra continuation on post-treatment relapse risk.

Methods: Retrospective chart review of 12 adults hospitalised between January 2016 and October 2018 treated with Anakinra 100mg SQ daily for pericarditis refractory or intolerant to CT (CT+A group), and 22 consecutive hospitalised patients treated with CT only (CT group).

Results: Diagnosed autoimmune or inflammatory condition was present in 83.3% (10/12) of CT+A and 40.9% (9/22) of CT group (p=0.07, Table 1). The most common etiologies in CT+A group were RA and Undifferentiated Connective Tissue/Overlap Disease (Figure 1).

Despite CT-intolerance or resistance (Figure 2), all CT+A (12/12) patients had symptom relief at discharge vs. 72.7% (16/22) in CT group (p=0.04). There was a strong trend in CT+A compared to CT group towards shorter time to symptom improvement (1.75+/-1.29 vs. 3.55+/-3.06 days; p=0.06) and symptom relief (3.75+/-1.87 vs 5.63+/-3.28 days; p=0.08). CS were tapered successfully in 71.4% (5/7) vs. 66.7% (6/9) of patients in the CT+A and CT groups (p=0.56). Anakinra was associated with a longer mean length of stay (13.0+/-16.2 vs. 8.68+/-5.07 days; p=0.25).

No recurrence during treatment was noted in CT+A group (0/12) vs. 40.9% (9/22) in CT group (p=0.009). There was a trend towards reduced post-treatment relapse risk in CT+A group [16.7% (2/12) vs. 41.7% (5/12), p=0.18]. In relapsed patients, there was no significant difference in time to relapse (1.75+/-0.34 vs 1.72+/-0.71 months, p=0.93). Within CT+A group, extended Anakinra use in 6 patients (mean: 5.58+/-6.5 months) did not reduce post-treatment relapse risk [16.7% (1/6) vs 16.7% (1/6), p>0.9]. Adverse effects were infrequent; elevated transaminases (n=1) and local injection-site reaction (n=1). Neither required permanent Anakinra discontinuation.

Table 1. Baseline Characteristics

	Anakinra plus conventional therapy % (n=12)	Conventional therapy only % (n=22)	p-value
Age (years +/- SD)	60.3+/-17.3	56.8+/-17.8	0.590
Female	66.7 (8)	50 (11)	0.349
Diagnosed autoimmune or inflammatory condition	83.3 (10)	40.9 (9)	0.074
Recurrent pericarditis (>1 episode)	33.3 (4)	27.3 (6)	0.710
Time since initial episode (months +/-SD)	49.0+/-79.9	9.21+/-11.7	0.441
Prior NSAID use	25.0 (3)	18.2 (4)	0.638
Prior Colchicine use	25.0 (3)	9.09 (2)	0.210
Prior CS use	50.0 (6)	18.2 (4)	0.051
Pericardial effusion on ECHO	75.0 (9)	81.8 (18)	0.638
Treatment during hospitalisation			
NSAID	50.0 (6)	54.5 (12)	0.799
Colchicine	58.3 (7)	63.6 (14)	0.761
CS	58.3 (7)	40.9 (9)	0.331
Risk factors for pericarditis			
PCI, cardiac surgery or chest trauma	16.7 (2)	45.5 (10)	0.093
Chest radiation	8.33 (1)	4.55 (1)	0.653

Malignancy	0 (0)	0 (0)	
Pericardial drainage	25.0 (3)	13.6 (3)	0.406
GFR<30 ml/min/1.73m^2	8.33 (1)	13.6 (3)	0.133
Family history of IRP	8.33 (1)	4.55 (1)	0.653
CRP, mg/L (mean+/-SD)	136+/-115	95.9+/-87.7	0.309
DM	8.33 (1)	27.3 (6)	0.191
HTN	25.0 (3)	63.6 (14)	0.031

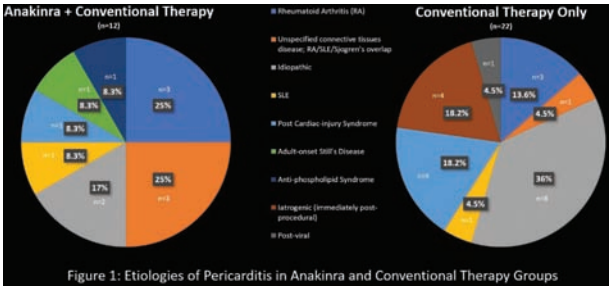


Figure 1: Etiologies of Pericarditis in Anakinra and Conventional Therapy Groups

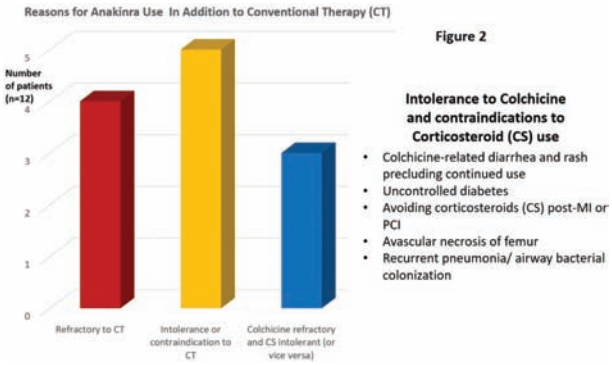


Figure 2

Intolerance to Colchicine and contraindications to Corticosteroid (CS) use

- Colchicine-related diarrhea and rash precluding continued use
- Uncontrolled diabetes
- Avoiding corticosteroids (CS) post-MI or PCI
- Avascular necrosis of femur
- Recurrent pneumonia/ airway bacterial colonization

Conclusion: In hospitalised patients with new-onset or recurrent pericarditis (secondary or idiopathic) refractory or intolerant to CT, Anakinra is associated with improved symptom relief and decreased recurrence risk. Extended continuation of Anakinra after symptom relief does not reduce post-treatment relapse risk.

Disclosure of Interests: : None declared

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FRI0612 IMMUNE-RELATED ADVERSE EVENTS ASSOCIATED WITH IMMUNOTHERAPY. LONG-TERM FOLLOW-UP OF 102 PATIENTS FROM A REFERRAL SINGLE CENTER

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Background: Immune checkpoint blockade therapy (ICBT) has shown remarkable benefit in different cancer types. Blockade of intrinsic down-regulators of immunity increases the activity of the immune system, which can lead to different immune-related adverse events (irAEs). Our aim was to assess the immune-related adverse events in patients who received anti-cytotoxic T-lymphocyte antigen 4 (CTLA-4), anti-programmed cell death 1 (PD-1) or anti-programmed cell death ligand 1 (PD-L1).

Objectives: Our aim was to assess the incidence, treatment and evolution of irAEs due to ICBT.

Methods: We set up an observational study of patients treated with Nivolumab and Pembrolizumab (anti-PD1), Atezolizumab (anti-PD-L1) and Ipilimumab (antiCTLA-4) for solid organ tumors. All these patients were followed in a single reference University Hospital from March-2015 up to December-2018. The main outcome was to determinate the incidence of irAEs.

Results: We studied 102 patients (63♂/39♀) with a mean age of 60.6 ±9.7 with lung
(n=63), melanoma (21), kidney (11), gastric (3), bladder (1), and colon cancer (n=3). Only 7 patients had a previous diagnosis of an immune-mediated disease: psoriasis (n=2), psoriatic arthritis (1), systemic lupus erythematosus
(1), spondyloarthritis (1), rheumatoid arthritis (1) and skin lupus (1).
ICTB was performed as follows: nivolumab (n=52), pembrolizumab (35), atezolizumab (10) and ipilimumab (5).
After a median of 5 [2.5-10.5] months since the ICBT onset, we observed 87
(85.3%) patients with different irAEs, summarized in **TABLE**. ICBT discontinuation was required in 39 patients. 36 patients received specific treatment (prednisone, antihistamine, levothyroxine and thiamazol), obtaining a good response in 31 cases (79.5%). ICBT was reintroduced in 28 patients (71.8%) after resolution of the adverse event, with an appropriate tolerance in all cases.

TABLE

Immune-related adverse event	Anti CTLA-4 n= 5	Anti PD1-/PD-L1 n= 97	TOTAL n=102
Gastrointestinal, n (%) *(diarrhoea, colitis, mucositis)*	1 (1.1)	38 (40)	39 (41.1)
Skin, n (%) *(rash, erythema nodosum, psoriasis, vitiligo and alopecia)*	1 (1.1)	12 (12.6)	13 (13.7)
Thyroid, n (%) *(thyroiditis)*	0 (0)	18 (18.9)	18 (18.9)
Articular, n (%) *(arthralgia, arthritis)*	0 (0)	14 (13.7)	14 (13.7)
Vasculitis, n (%) *(aortitis)*	0 (0)	1 (1.1)	1 (1.1)
LFTs alteration, n (%)	0 (0)	8 (8.4)	8 (8.4)
Nephritis, n (%)	0 (0)	6 (6.3)	6 (6.3)
TOTAL	**2 (2.1)**	**97 (97.9)**	**99 (100)**

+LFT = Liver function tests.

Gastrointestinal irAEs were the most frequent (n=39, 41.1%), with severe manifestations in 4.9% of the patients. Among these 39 patients, only 11 of them required specific treatment, with oral prednisone in all cases. The diagnosis of gastrointestinal irAEs was based on the clinical manifestations and the laboratory tests. The cutaneous most frequent irAE was rash (n=7, 6.8%), followed by vitiligo (n=2, 1.9%). 15 patients developed a rheumatological irAE (14 arthralgias/arthritis and 1 aortitis).
Patients who developed any type of irAE had a better answer to ICBT (70.1%) than those who did not (20%).

Conclusion: In our study, the majority of autoimmune side effects due to ICBT were gastrointestinal, thyroiditis and rheumatological. The develop of any irAE could be an indicator of good response to ICBT.

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FRI0613 **THERAPEUTIC STRATEGIES AND SURVIVAL IN PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES**

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Background: Recently the term "interstitial pneumonia with autoimmune features" (IPAF) has been proposed to identify patients with interstitial lung disease and autoimmune characteristics, not fulfilling the criteria for specific connective tissue diseases (CTD). Until now, only few data are available about the clinical and serological features of IPAF patients, their survival and the possible evolution in a CTD.
Objectives: Aim of the study was to investigate the therapeutic choices in IPAF patients, their efficacy and safety.
Methods: Fifty-two patients (mean age at diagnosis 65.5±11.0 years, female/male ratio 29/23) were consecutively enrolled and prospectively followed for 45±31.6 months.
Data about therapies, disease onset, serological, clinical and therapeutic features, pulmonary function tests and high-resolution computed tomography were periodically repeated. A worsening of lung function was defined as a reduction of 10% compared to baseline of forced vital capacity (FVC) and diffusion lung capacity of CO (DLCO).
Results: An immunosuppressive therapy was prescribed in 15 patients (namely cyclophosphamide in 4, mycophenolate mofetil in 6 and azathioprine in 6, respectively), while 6 patients were treated with anti-fibrotic therapies (pirfenidone or nintedanib). Thirty-three patients taken corticosteroids, associated to other drugs in 18 patients, and alone in 15. Finally, no therapies were prescribed in 16 patients. At the end of follow-up FVC remained stable in 35% of patients, worsened in 50% and increased in 15%; DLCO remained stable in 25.8% of patients, worsened in 58.1% and increased in 16.1%.
Mean survival was 94.2±8.5 months, and no differences were recorded according to the kind of therapy, while survival was significantly associated to the lung function at baseline (FVC and DLCO were confirmed to be significantly associated to death at multivariate analysis).
The treatment was generally well tolerated. In 7/15 patients treated with immunosuppressive therapy was recorded at least an adverse event, responsible for the treatment discontinuation only in 3 patients.
Conclusion: The therapeutic strategy in IPAF patients reflects the etherogeneity of the disease. Waiting for specific trial in this population, treatment is empyrical and based on the baseline features of the patients. Despite well tolerated both anti-fibrotic and immunosoppressive therapies seem to not influence the evolution of the disease.

REFERENCES:

[1] Fischer A, Antoniou KM, Brown KK, eta al. "ERS/ATS Task Force on Undifferentiated Forms of CTD-ILD". An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. Eur Respir J. 2015;46:976-87
[2] Ferri C, Manfredi A, Sebastiani M, et al. Interstitial pneumonia with autoimmune features and undifferentiated connective tissue disease: Our interdisciplinary rheumatology-pneumology experience, and review of the literature. Autoimmun Rev. 2016;15:61-70

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FRI0614 **CLINICAL AND LABORATORY FEATURES OF MACROPHAGE ACTIVATION SYNDROME IN PATIENTS WITH ADULT STILL'S DISEASE**

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Background: Adult Still's Disease (ASD) sometimes develops macrophage activation syndrome (MAS). MAS is a severe, fatal complication, however, little is known about its clinical courses and relation to initial symptoms, diagnosis and treatment.
Objectives: To clarify characteristics of MAS in patients with ASD and identify risk factors for developing MAS.
Methods: Consecutive ASD patients diagnosed with Yamaguchi's criteria in our hospital from April 2012 through September 2017 were retrospectively reviewed. Clinical symptoms, laboratory data and treatment information were collected form their charts. Patients were divided into two groups according to the complication of MAS and analyzed.
Results: Sixty five patients with ASD with available information were enrolled in the analysis. The mean age at ASD onset was 45.7 years old, and female was 81.5%. Among them, 12 patients (18.5%) developed MAS during the clinical course. Three patients developed MAS at the same time with the diagnosis of ASD, seven patients after the initiation of glucocorticoid treatment, and two patients at relapse. Five of nine who underwent bone marrow examination proved to be complicated with hemophagocytotic syndrome. The median duration from initial symptoms of ASD to fulfilment of Yamaguchi's criteria was shorter in patients with MAS than those without (10.5 days vs 21.0 days, p=0.077). Drug allergy occurred more frequently in patients with MAS (50.0% vs 22.6%, p=0.056). The maximum levels of ferritin and AST before treatment was higher in patients with MAS than those without (ferritin, 6090ng/mL vs 3434ng/mL, AST 86.5U/L vs 68.0U/L), whereas the maximum levels of CRP was lower in patients with MAS (8.9mg/dL vs 15.9 mg/dL). In nine patients who developed MAS after glucocorticoid treatment, white blood cell count decreased by almost half despite moderate to high dose of glucocorticoid, and the level of ALT increased 10-fold and ferritin increased 2-fold at MAS development. However, the levels of CRP at MAS rather decreased before treatment, suggesting the change in CRP did not reflect MAS development.
Conclusion: The incidence of MAS was 18.5% during the clinical course of ASD. Patients with MAS developed ASD more rapidly than those without. The ferritin and ALT levels predicted and reflected MAS development, whereas CRP levels was not associated with MAS.
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FRI0615 EVALUATION OF COMPLIANCE AND RELATED FACTORS IN COLCHICINE TREATMENT IN FAMILIAL MEDITERRANEAN FEVER PATIENTS

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Background: Familial Mediterranean Fever (FMF) is an autoinflammatory disease requiring long-term treatment. Increasing the compatibility with colchicine treatment in patients with FMF is the first step for preventing amyloidosis. Patients' beliefs about medicines and treatment may affect treatment adherence and treatment success.
Objectives: The aim of this study was to determine adherence to colchicine treatment and related factors in FMF patients. In addition, patients' beliefs about colchicine, which are one of the important factors affecting the treatment adherence of patients, were evaluated.
Methods: Total of 179 patients with FMF was included in this study. The demographic and clinical features and MEFV gene mutations were recorded. The treatment adherence of the patients was assessed using by Compliance Questionnaire on Rheumatology (CQR). The Beliefs About Medicines Questionnaire (BMQ-T) was used to assess patient's beliefs about colchicine. The relationship between compliance of treatment and clinical characteristics of patients were assessed.
Results: One hundred thirteen (63.1%) of the patients were male. The mean age of patients was 34.5 ± 12.7 years and mean delay in diagnosis was 6.7 ± 8.4 years. The mean dose of colchicine was 1.37 ± 0.43 mg/day and, the percentage of patients using colchicine regularly was 66.5%. Adherence to treatment was higher in patients with concomitant diseases than those without comorbidities (p = 0.028). In addition, treatment compliance was higher in married patients compared to single patients (p = 0.013). The colchicine dose used in compatible patients was higher than in non-compatible patients (p = 0.033) (Table 1). We also found that as the BMQ-T Specific Necessity scores increased, compliance with treatment increased. On the other hand, as the BMQ-T General Overuse and General Harm scores increased, non-compliance with treatment increased (Table 2).

Table 1. Relationships between socio-demographic and clinical characteristics of patients and CQR score (n =179)

Characteristics	CQR score		
	≥80% n=29	< 80% n=150	p
Age (years) median (25th–75th percentile)	37.0 (28.5-44.5)	29.0 (24.0-44.0)	0.099[a]
Gender (n,%)	15 (13.3)	98 (86.7)	0.164[b]
Male	14 (21.2)	52 (78.8)	
Female			
Marital status, (n,%)	21 (22.8)	71 (77.2)	**0.013**[b]
Married	8 (9.2)	79 (90.8)	
Single/widowed/divorced			
Comorbidities, (n,%)	12 (26.7)	33 (73.3)	**0.028**[b]
Yes	17 (12.7)	117 (87.3)	
No			
Delay of diagnosis (years) Median (25th–75th percentile)	3.0 (0.5-10.0)	3.0 (1.0-9.0)	0.920 [a]
Colchicine dose, (mg/day) Median (25th–75th percentile)	1.5 (1.25-1.75)	1.5 (1.0-1.5)	**0.033** [a]

Data represented either as the median (25th–75th percentile) or as the frequency. a: Mann-Whitney test b: Pearson Chi-Square test, CQR, Compliance Questionnaire on Rheumatology

Table 2. Beliefs about Medicines Questionnaire Scale Scores in Adherent and Nonadherent Patients.

Variable	CQR score Discontinuous			
	≥80% n=29	< 80% n=150	Z	p
BMQ-T-Specific Necessity	4.8 (4.1-5.0)	3.8 (3.35-4.25)	-5.260	**< 0.001**
BMQ-T-Specific Concerns	2.8 (2.2-3.8)	2.8 (2.4-3.6)	-0.100	0.920
BMQ-T-General Overuse	2.25 (1.75-2.63)	2.75 (2.25-3.25)	-2.936	**0.003**
BMQ-T-General Harm	1.75 (1.38-2.63)	2.38 (2.0-3.0)	-3.212	**0.001**

Z; Mann-Whitney test, Data represented as median (25th–75th percentile, CQR; Compliance Questionnaire on Rheumatology

Conclusion: In patients with FMF, it is important to evaluate the compliance with the treatment due to the importance of colchicine to prevent amyloidosis that may occur in patients without treatment. As this study shows it is also important to determine patients' beliefs about medicine in terms of their influence on patients' compliance with treatment.
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FRI0616 ANAKINRA TREATMENT IN RECURRENT PERICARDITIS: SINGLE CENTER EXPERIENCE

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Background: Recurrent pericarditis (RP), however the etiology is unknown in the majority, may be observed in autoinflammatory diseases such as familial Mediterranean fever (FMF) and tumor necrosis factor receptor-1 associated periodic syndrome (TRAPS). Colchicine has long been used to treat pericarditis related to FMF as well as patients with idiopathic recurrent pericarditis (IRP) (1). Alternative treatments have been reported for cases with colchicine resistant RP.Objectives:
Objectives: The aim is to present our data regarding anakinra treatment in recurrent pericarditis either related to FMF or idiopathic, who are resistant to colchicine.
Methods: Patients who had recieved anakinra with a diagnosis of recurrent pericarditis either idiopathic or secondary to FMF followed in our autoinflammatory disease center between 2014-2018 are evaluated retrospectively. From patients' files, demographic and clinical features, response to other treatment approaches such as NSAID, corticosteroid, colchicine, were evaluated. All patients have been genetically screened for monogenic autoinflammatory diseases (MEFV, TRAPS, MVK, NLRP3, NOD2). Patients who had at least 3 attacks were administered anakinra 100 mg/day. Therapeutic efficacy, as well as side effect profile of anakinra is also assessed.
Results: There were 5 patients (3 male and 2 female) with the diagnosis of RP, 1 was related to FMF and 4 were idiopathic. The mean age of

Table 1. Demographic features and treatment response during anakinra therapy

Patient ID #	Age	Sex	Diagnosis	Duration of pericarditis follow-up (mo)	Prior medications	Number of recurrences before anakinra	Anakinra treatment duration (mo)	Time to corticosteroid discontinuation (mo)	Number of recurrences after daily dose of anakinra
1*	23	M	IRP	129	Colchicine, NSAIDs, CS, HCQ	6	52	9	No
2	32	F	IRP	128	Colchicine, NSAIDs	7	4	NA	No
3*	40	F	IRP	21	Colchicine, CS	6	8	1	No
4	20	M	IRP	11	Colchicine, CS	3	8	2	No
5	25	M	FMF	30	Colchicine, CS	5	15	1	No

F: Female, M: Male, CS: Corticosteroid, HCQ: Hydroxychloroquine, NA: Not applicable
*Dose tapering was unsuccessful in these patients

the group was 28±8 (range 20-40). All patients diagnosed with IRP were negative for autoinflammatory genetic screening, while a MEFV variant (K695R het.) was detected in the FMF patient. Median duration of follow-up was 30 months (range 11-129). In table 1, demographic and clinical features are given. The median number of recurrence was 6 before anakinra treatment. No episode of pericarditis was observed in any of the patients after the initiation of anakinra. The response to anakinra persisted even after the dose was reduced to 100 mg/alternate day in 3 patients, however in 2, recurrence of pericarditis was observed and anakinra was escalated to initial dose. It was possible to discontinue corticosteroid treatment in all patients. Currently all patients continue anakinra treatment. No side effect including injection site reaction, has been observed by now.

Conclusion: Anakinra seems to be a safe and effective treatment approach for colchicine resistant recurrent pericarditis. However recurrence may occur during dose tapering.

REFERENCES:

[1] Adler Y, et al. Colchicine treatment for recurrent pericarditis. A decade of experience. Circulation. 1998 2;97(21):2183-5.

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FRI0617 APPLICATION OF AUTO-INFLAMMATORY DISEASE DAMAGE INDEX (ADDI) TO PATIENTS WITH FMF AND RELATED FACTORS WITH DAMAGE

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Background: Familial Mediterranean Fever (FMF) is the most frequent auto-inflammatory disease caused by MEFV gene mutations. Available reports investigated only specific components of damage such as amyloidosis. All possible organ targets of damage have not been entirely evaluated before. Such as Disease severity index which is emerged especially for FMF do not cover entire damage domains related to FMF. Recently, a new scoring system (Auto-inflammatory disease damage index) was developed and validated for autoinflammatory diseases.

Objectives: We aimed to investigate damage accrual caused by FMF and associated features with damage.

Methods: All patients recruited from FMF in Central Anatolia (FiCA) cohort, which is a duplication disabled, internal and externally controlled, cross-sectional, multicenter accessible web-based cohort. This study is comprising 970 adult patients (mean age 35.3 ±12.1 years, 61.5% female). Demographic data, FMF disease characteristics, co-morbid conditions, disease complications were meticulously questioned and laboratory features and genotype data (if available) were recruited from patient files. FMF caused damage was assessed by auto-inflammatory disease damage index (ADDI) which is recently validated. Association between damage and demographic, disease and treatment characteristics were analyzed.

Results: Proportions of FMF manifestations were fever 83.1%, peritonitis 91.5%, pleuritis 47.9%, arthritis 43.3% and skin rash 26.2%. Dominant attack types were fever in 6.2%, serositis in 65.7%, musculoskeletal in 16.8% and all types of attacks were common in rest of patients. MEFV mutations were available in 814 subjects and 75.9% of these subjects were harboring M694V mutation (42.5% homozygous for M694V). Among all 63.1% patients were well responded to colchicine and 8.8% were non-responders. Median ADDI score was 1 (min 0-max 11). Most common FMF related damages were observed in musculoskeletal, reproductive and kidney domains. Chronic musculoskeletal pain was present in 49%, joint deformity in 2.9%, infertility in 6.6%, amenorrhea in 3.9%, proteinuria in 6.9%, amyloidosis in 5.9% and renal failure in 3.7% of the patients. 411 (%42.3) of patients had no damage accrual. M694V homozygous mutation, male gender and colchicine nonresponse were found to be the independent predictors of damage.

Conclusion: M694V homozygous mutation, colchicine non-response and male gender are predictors of damage and effective therapeutic interventions must be undertaken to prevent from damage in these patients.

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FRI0618 ANALYSIS OF NEW REFERRALS TO A SPECIALIST UK ADULT AUTOINFLAMMATORY DISEASE SERVICE

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Background: Diagnosis of the systemic autoinflammatory diseases (SAIDs) requires a high index of suspicion and previous series has suggested that there are often long diagnostic delays, particularly in TRAPS and MKD.

Objectives: To look at the case mixed referred to a single adult clinic in London specialising in assessment of potential SAIDS over the course of the year of 2017.

Methods: All new referrals were accepted for clinical assessment. At the first visit patients had a full history and examination, genetic testing – varying from single gene to a 20 gene panel depending on clinical features, and laboratory testing including fortnightly blood draws for serial analysis of the hepatic acute phase response proteins, CRP and SAA over a 3 month period.

Patients with a non suggestive history, non contributory genetic testing and no evidence of inflammation accompanying symptoms were felt not to have SAIDS and referred back to their local hospitals for further management. Other cases were diagnosed based on full clinical assessment, other investigations – for example ferritin in AOSD, genetic testing results, serial monitoring of CRP and SAA and therapeutic trials, for example colchicine in presume FMF and anti IL-1 therapies in CAPS and Schnitzler's syndrome

Results: 273 new patients were referred. Median age at referral was 37.4 years, the oldest patient was 84.3 years old and 59% were female. 174 (64%) were of northern European ancestry, 68 (25%) were eastern Mediterranean, west Asian or southern European ancestry, 19 (7%) were of south or east Asian ethnicity and 4% were of African or Afro-Caribbean ancestry. 76% of referrals were from hospital specialities. The referral source was: rheumatology 38%, general practitioner 24%, dermatology 8%, immunology 8%, gastroenterology 6%, infectious diseases 3%, clinical genetics 3%, nephrology 2%, haematology 2%, gynaecology 2%, emergency department 1%, respiratory 1%, other 2%.

After work up 135 (49.5%) were felt not to have a SAID as the cause of their symptoms. Of the remaining 138 patients who did have evidence of a SAID the diagnoses made were: FMF 33%, uncharacterised SAID 26%, CAPS 9%, AOSD 8%, recurrent idiopathic pericarditis 6%, Schnitzler's Syndrome 5%, TRAPS 4%, variant PFAPA 4%, DADA2 1%, MKD 1%, CRMO 1%, Behcets 1%, Cattleman's disease 1%.

The median interval between reported symptom onset and diagnosis were as follows: 16 yrs for FMF, 28.1 yrs for CAPS, 5.0 years for recurrent idiopathic pericarditis, 4.5 yrs for Schnitzler's Syndrome, 5.7 yrs for TRAPS, 20.5 yrs for variant PFAPA, 12.5 yrs for DADA2, 17 yrs for MKD and 2 years for CRMO.

Conclusion: This series suggests that recognition and diagnosis of the SAIDS remains a challenge. More than 1/3 of referrals were from rheumatology, referrals from primary care were almost exclusively from patients with a known family history of one the inherited syndromes. The wide variety of referring specialities reflects the diverse nature of SAIDS and the importance of almost all specialities considering the possibility of SAIDS. Only just over 50% referrals had evidence of diseases falling within the recognised SAID spectrum and 26% of these have currently uncharacterised disease with non diagnostic genetic testing. Of those in whom a diagnosis could be made there are significant diagnostic delays fortunately despite late initiation of treatment no patients had evidence of systemic AA amyloidosis.

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FRI0619 INPATIENT BURDEN AND COMORBIDITIES OF SARCOIDOSIS: NATIONWIDE INPATIENT SAMPLE 2013–2014

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Background: Little is known about the inpatient burden and healthcare utilization among patients with sarcoidosis. Previous studies have focused on trends of hospitalization rate of patients with sarcoidosis over time [1] but none has investigated their inpatient prevalence, mortality and expenditures.

Objectives: The current study was conducted with the aims to shed more light on those characteristics as well as to investigate the comorbidities of sarcoidosis using the data from a large national database.

Methods: Patients with sarcoidosis were identified within the Nationwide Inpatient Sample (NIS) database of the years 2013 and 2014 using the ICD-9 diagnostic code. NIS is the largest publicly available inpatient database in the US. Data for more than seven million individual hospitalization across all-payers in the United States (US) is recorded annually in the NIS database. This is itself a 20% stratified sample of over 4,000 non-federal acute care hospitals from more than 40 states of the US and is representative of 95% of hospital discharges nationwide. Data on patient and hospital characteristics, comorbidities, total hospital costs and total hospitalization charges was collected. A propensity-matched cohort of patients without sarcoidosis from the same database was created and used as comparators for the analysis of comorbidities. Inpateint prevalence of sarcoidosis was calculated using all admissions in the NIS database as denominator. Odds ratios (OR) comapring the prevalence of comorbities between cases with sarcoidosis and propensity-matched controls without sarcoidosis were calculated.

Results: A cohort 78,055 patients with sarcoidosis was identified from the database, corresponding to an inpatient prevalence of 2.21 cases per 1,000 admissions. The most common reasons for admission among patients with sarcoidosis in this cohort were as follows; pneumonia (34.3%), respiratory failure (26.1%), cardiomyopathy (10.9%), coronary artery disease (9.2%), acute kidney injury (8.5%) and atrial fibrillation (5.5%). Analysis of comorbidities found that patients with sarcoidosis had significantly higher odds of atrial fibrillation, conduction abnormalities, aortic valvulopathy, congestive heart failure and cardiomyopathy compared to propensity-matched patients without sarcoidosis (table 1). After adjusting for confounders, patients with sarcoidosis displayed a mean additional $27,205 (p<0.01) for total hospitalization charges (the amount of money that each hospital billed for providing its service on each case) when compared to hospitalization of patients without sarcoidosis.

Conclusion: The inpatient prevalence of sarcoidosis was relatively high compared to its overall incidence. Hospitalization of patients with sarcoidosis was associated with a significantly higher total hospitalization charges. Patients with sarcoidosis have higher risk of several cardiac comorbidities.

REFERENCES:

[1] Foreman MG, et al. (2006) Hospitalization for patients with sarcoidosis: 1979-2000. Sarcoidosis Vasc Diffuse Lung Dis 23:124-129.

Table 1. Odds ratio comparing comorbidities between patients with sarcoidosis and patients without sarcoidosis

Variable	Adjusted odds ratio	95% Confidence Interval	p-value
Atrial fibrillation	1.41	1.13-1.76	<0.01
Conduction abnormalities (blocks)	2.04	1.45-2.89	<0.01
Coronary artery disease	1.10	0.94-1.29	0.26
Congestive heart failure	1.23	1.04-1.45	0.02
Cardiomyopathy	1.25	1.08-1.44	<0.01
Aortic valvulopathy	1.78	1.30-2.44	<0.01

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FRI0620 FMF PATIENTS HAVE A HIGHER PREVALENCE OF SPA-RELATED DISORDERS INCLUDING MHC-I-OPATHIES THAN CONTROLS: INSIGHTS FROM A LARGE COHORT STUDY

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Background: Familial Mediterranean fever (FMF) is a common, hereditary autoinflammatory disorder, caused by mutations in the MEFV gene encoding for pyrin. MEFV mutations have been also reported in spondyloarthritis (SpA)-associated disorders including Crohn's disease, ulcerative colitis, Behçet's disease, psoriasis and ankylosing spondylitis (AS) with the latter 3 disorders considered under the umbrella term of "MHC-I-opathies" due to population-level associations of HLA-B51, Cw0602 and HLA-B27, respectively. FMF and the SpA group of disorders share an association with disease localization to site of physical stress or microdamage with innate immune activation at such sites as a primary driver of immunopathology but this is not the case for classical autoimmune diseases where central tolerance failure is an overarching immunological concept..

Objectives: To test the hypothesis that autoinflammation in FMF may exaggerate the tendency towards adaptive immunopathology or MHC class-I associated disorders and therefore a higher prevalence of SpA-related disorders in patients with FMF.

Methods: 7,747 FMF patients and 10,080 age- and sex-matched controls in the Clalit-Health-Services medical database were identified and compared in terms of prevalence of SpA-associated disorders and also evaluated 4 classical and strong MHC class-II associated disorders, namely sarcoidosis, pernicious anaemia, pemphigus vulgaris, and myasthenia gravis to ascertain whether such associations with SpA-spectrum disease were specific or merely reflected the non-specific consequences of innate immune system activation on driving divergent types of immunity.

Results: FMF showed a strong association with MHC class I related diseases: OR 28.58 ([95%CI 6.93-117.87], p<0.0001) for Behçet's disease, OR of 10.33 ([95%CI 4.09-26.09], p<0.0001) for AS, and OR 1.67 ([95% CI 1.19-2.33], p=0.0029) for psoriasis. For weakly MHC class I linked diseases, an OR of 3.76 ([95%CI 2.48-5.69], p<0.0001) for Crohn's disease and OR of 2.64 ([95%CI 1.52-4.56], p=0.0005) for ulcerative colitis were found. No association was found between FMF and strongly MHC class II-associated including pemphigus vulgaris, sarcoidosis, pernicious anaemia and myasthenia gravis. At the Cox multivariate survival analysis, the mortality of FMF patients was higher only in Crohn's disease with an HR of 2.32 ([95%CI 1.09-4.93], p=0.0291).

Conclusion: FMF patients are associated with increased risk of SpA-related disease diagnosis including MHC-I-opathies suggesting that tissue-specific dysregulation of innate immunity share between FMF and SpA spectrum disorders may drive adaptive immune MHC class I associated conditions.

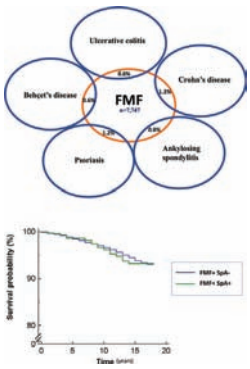


Figure 1. The proportion of FMF patients with SpA related disorders (A) and their impact on FMF patients' survival (B)

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FRI0621

ASSOCIATIONS BETWEEN ORGAN INVOLVEMENTS AND GENDER, ALLERGY, AND MALIGNANCY IN 166 PATIENTS WITH IGG4-RELATED DISEASE

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Background: Symptomatic differences between male and female patients with IgG4-related disease (IgG4-RD) have been reported [1]. Associations between IgG4-RD and allergy and malignancy have also been reported, although they are controversial.

Objectives: We previously analyzed the treatment course of IgG4-RD using a multi-center cohort [2]. In the present study, we investigated the associations between organ symptoms and gender, allergic diseases, and malignancies.

Methods: Data of 166 patients with a definitive diagnosis of IgG4-RD were retrospectively analyzed.

Results: The cohort consisted of 108 men (65%) and 58 women (35%). Most frequently, the submandibular gland (52%), pancreas (46%), lachrymal gland (43%), and lymph node (38%) were affected. Furthermore, we assessed the frequencies of female sex, allergy, and malignancy in patients with each affected organ (**Table 1**). The organs with high frequencies of women included the lachrymal gland (50%), lungs (44%), and submandibular gland (43%). Those with low frequencies of women included the thyroid gland (0%), retroperitoneum (17%), and para-aorta (19%). In addition, allergic diseases were found in 60 patients (36%) (**Fig. 1A**). The organs with high frequencies of allergy included the thyroid gland (50%), submandibular gland (47%), and lachrymal gland (40%). Those with low frequencies of allergy were the para-aorta (13%), prostate gland (30%), and retroperitoneum (31%). Malignancies were found in 23 (14%) patients (**Fig. 1B**). Organs with high frequencies of malignancy included the para-aorta (38%), prostate gland (30%), and retroperitoneum (21%). In comparison, those with low frequencies of malignancy included the thyroid gland (0%), lungs (8%), and kidney (8%).

Conclusion: Craniocervical organ involvement was associated with female sex and presence of allergic diseases, suggesting that allergy may contribute to onset of IgG4-RD in some patients. Abdominal organ involvement was associated with male sex and presence of malignancies, suggesting that malignancy may in part contribute to IgG4-RD.

REFERENCE:

[1] Wang, et al., Rheumatology, 2018. [2] Shirakashi, et al., Sci Rep, 2018.

Table 1. Frequencies of female sex, allergy, and malignancy in patients with indicated affected organ.

	Women (%)	*1	Allergy (%)	*2	Malignancy (%)	*3
Eye orbit	23	L	38	**H**	15	**H**
Lachrymal gl.	50	**H**	40	**H**	11	L
Parotid gl.	36	**H**	36	-	18	**H**
Submandibular gl.	43	**H**	47	**H**	13	L
Thyroid gl.	0	L	50	**H**	0	L
Lung	44	**H**	32	L	8	L
Pancreas	31	L	32	L	18	**H**
Bile duct	23	L	33	L	15	**H**
Kidney	40	**H**	36	-	8	L
Retroperitoneum	17	L	31	L	21	**H**
Para-aorta	19	L	13	L	38	**H**
Prostate gl.	0	L	30	L	30	**H**
Lymph node	41	**H**	38	**H**	13	L
Total	35	-	36	-	14	-

***H**, L, or "-" are marked if the frequency is higher, lower, or no change respectively, when compared to the total frequencies of female sex (35%)[1]*, allergy (36%)[2]*, and malignancy (14%)[3]*.

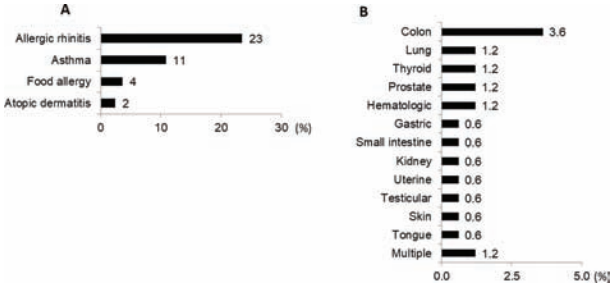


Figure 1. Frequency of allergic diseases (**A**) and malignancies (**B**) in 166 patients with IgG4-RD.

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Diagnostics and imaging procedures

FRI0622 JOINT TENDERNESS AND ULTRASOUND INFLAMMATION IN EARLY RHEUMATOID ARTHRITIS PATIENTS INCLUDED IN THE ARCTIC TRIAL

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Background: A tender joint count is part of most disease activity scores and remission criteria in rheumatoid arthritis (RA). A recent study found that tender joint count might not reflect inflammatory activity, assessed by ultrasound, in established RA (1).
Objectives: To explore if tender non-swollen joints is associated with subclinical inflammation, assessed by ultrasound, in DMARD-naïve early RA patients.
Methods: DMARD-naïve RA patients with <2 years symptom duration from first swollen joint and indication for DMARD treatment were included in the ARCTIC trial (2). For the current analyses we used data from the baseline examination, including a tender joint count assessed by Ritchie Articular Index and a 44-swollen joint count. The Ritchie Articular Index treat certain joints as a single unit (as the MCP-joints), and scoring of tenderness in joints and joint groups is graded 0-3. All patients underwent an ultrasound examination of 34 joints, with a semi-quantitative 0-3 score for power Doppler in each joint. An ultrasound atlas was available for reference (3). We predefined the wrist and the MCP 1-5 joints as joint areas of interest since they are commonly involved in RA and were assessed both clinically and by ultrasound. We selected only joints that were clinically non-swollen, and assessed the association between joint tenderness and ultrasound power Doppler signal by mixed logistic regression models with patient-specific intercept to adjust for within-patient dependencies. The analyses were repeated using generalized estimating equations for robustness. The frequency and odds ratio (OR) of ultrasound power Doppler activity (yes/no) in tender non-swollen wrists compared to non-tender non-swollen wrists were calculated. Similar analyses were performed for the MCP joints.
Results: A total of 222 patients with complete baseline data were included. 63% were female, median [SD] age 53.6 [41.2, 62.3], symptom duration 5.8 [2.9, 10.4] months, swollen joint count 9 [4, 15], joint tenderness 7 [4, 13] and power Doppler score 7 [3, 14]. Of 444 wrists, 268 were not swollen. The frequency of power Doppler signal >0 in tender non-swollen wrists were 50% (18/36), compared to 23% (53/232) in non-tender non-swollen wrists (p-value for comparison = 0.001). This corresponds to an OR of 4.32 (95% CI 1.47 to 12.65, p=0.008) for power Doppler signal if the wrist is tender but not swollen, compared to a non-tender non-swollen wrist. Similar results were found for the non-swollen MCP-joints (Table).

Table:. The frequency and odds ratio (OR) of ultrasound power Doppler (PD) activity in Ritchie positive versus Ritchie negative non-swollen wrists and MCP joints.

	PD-signal positive if Ritchie positive	PD-signal positive if Ritchie negative	OR (CI)	p-value
Non-swollen wrist, n=268	18/36 (50%)	53/232 (23%)	4.32 (1.47 to 12.65)	0.008
Non-swollen MCP joints, n=165	15/35 (43%)	28/130 (22%)	4.84 (1.31 to 17.89)	0.02

Conclusion: Ultrasound power Doppler activity was more frequent in non-swollen wrists and non-swollen MCP joints if the joints had been scored as tender or painful by Ritchie Articular Index. Our findings indicate that in early RA patients, tenderness might reflect inflammation which is not detectable clinically.

REFERENCES:

[1] Hammer HB, et al. Arthritis care & research. 2018.
[2] Haavardsholm EA, et al. BMJ. 2016;354.
[3] Hammer HB, et al. ARD. 2011;70(11).

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FRI0623 MRI-DETECTED DIGIT FLEXOR TENOSYNOVITIS IN BILATERAL PROXIMAL INTERPHALANGEAL JOINTS CONTRIBUTE TO JOINT TENDERNESS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Independent predictive value of ultrasonography-detected digit flexor tenosynovitis has been reported for rheumatoid arthritis (RA) development in patients with early arthritis, and it also was reported as an independent risk factor of flare in remission RA. However, proximal interphalangeal joints (PIPJs) were scarcely evaluated by MRI, nor recommended by RAMRIS so far.
Objectives: To explore the characteristics of MRI-detected inflammation in bilateral PIPJs in early RA patients and its clinical significance.
Methods: Early RA patients who fulfilled 2010 ACR/EULAR classification criteria with disease duration ≤1 year and DAS28-CRP≥2.6 were recruited. New methodology of 3.0T whole-body MRI with contrast-enhanced imaging was used to scan bilateral hands simultaneously. MRI tenosynovitis, synovitis and osteitis were scored referring to the 2016 updated RAMRIS. Clinical data were collected.
Results: 1) Among 75 patients recruited, the median age was 49 years old (*IQR*: 38-59) with 71% female. The median disease duration was 7 months (*IQR*: 3-12) and the mean DAS28-CRP was 5.1 (*IQR*: 4.2-6.1). Forty-four patients (59%) were treatment-naïve who had never taken any DMARDs or glucocorticoids before recruitment. Both joint tenderness and swelling were present the most frequently in PIPJ2 and PIPJ3 (48% 61% and 43% 56%, respectively, Figure 1A).2) MRI tenosynovitis, synovitis and osteitis were detected in 84%, 100% and 83% of the patients; and respectively in 21% 44%, 43% 56% and 5% 11% of various PIPJs. There were 12% 30%, 28% 40%, and 2% 8% of PIPJs without tender or swollen showing MRI tenosynovitis, synovitis and osteitis respectively. When non-dominant hands were used as self-control, the frequency of digit flexor tenosynovitis in dominant interphalangeal joint (IPJ) of thumb, PIPJ2 and PIPJ4 was 16% 18% higher than the non-dominant counterparts, indicating a potential impact of overuse on dominant tenosynovitis. 3) Tenosynovitis affects periarticular digit flexor tendon compartment and 65% 87% of tenosynovitis in PIPJs occurred together with synovitis in joint cavity and/or osteitis in subchondral bone. Among tender IPJ of thumb, 50% of them showed MRI synovitis together with digit flexor tenosynovitis, which was significantly more than those who showed MRI synovitis alone (21%, Chi-square test, $p<0.017$). Similar trend was found in tender PIPJ2 (45% vs. 26%, $p<0.01$). Generalized Estimating Equations with multivariate logistic regression showed not only MRI synovitis but also digit flexor tenosynovitis in bilateral PIPJs independently had more than twice probability of joint tenderness (both $p<0.01$, Figure 1B).

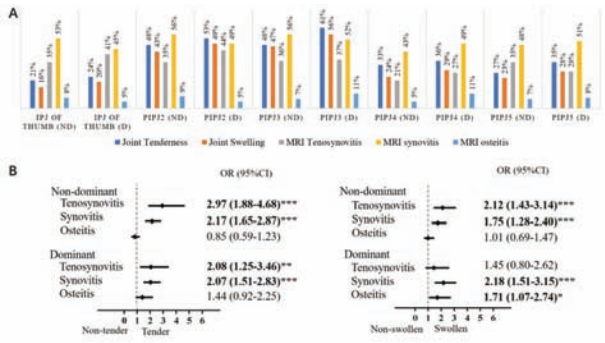


Figure 1 The prevalence and concordance between inflammation detected by MRI and physical examination in various proximal interphalangeal joints (PIPJs) of early RA patients. **A**: The prevalence of joint tenderness, joint swelling, MRI tenosynovitis, synovitis and osteitis per PIPJ. **B**: Generalized Estimating Equations with multivariate logistic regression were used to show the contribution of MRI tenosynovitis, synovitis and osteitis to joint tenderness or swelling. * p<0.05, ** p<0.01, *** p<0.001.

Conclusion: This preliminary study showed MRI-detected digit flexor tenosynovitis in bilateral PIPJs contributed to joint tenderness in early RA patients independently of synovitis which should not be ignored in clinical practice.

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FRI0624 U9: A NOVEL CLINICALLY ORIENTED ULTRASONOGRAPHIC SCALE FOR ASSESSING DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Musculoskeletal Ultrasonography (MSUS) is now a widely used tool for the monitoring of rheumatoid arthritis (RA). Although there are many proposed sets of composite scores, a fixed set of joints may not be an ideal tool to assess a disease like RA which affects many joints and tendons in different presentations.
Objectives: To assess the correlation of 3 proposed ultrasonographic composite scores with disease activity indices.
Methods: Three different composite scores were proposed by the first author, the first score (modified U8 score) which included bilateral wrists, 2nd MCP,3RD MCP and knees which of the same set of joints proposed by Yoshimi et al 2015 with a modification of scoring of each joint according to EULAR/OMERACT combined score so the range of scores (0-24). The second score (U9) was the same of the modified U8 score plus scoring the most clinically affected joint or tendon (one joint or one tendon) so the range of score (0-27). The third proposed score (8+2) was the same of the modified U8 score plus scoring the 2 most clinically affected joint or tendon (one joint and one tendon or 2 joints or 2 tendons) so the range of score (0-30). All targeted joints were evaluated by grey-scale (GS) and power Doppler (PD) ultrasound using EULAR/OMERACT combined score (0-3). Targeted tendons were scored (0-3) by either -scale (GS) and power Doppler (PD) ultrasound and the highest score was used.
One hundred and fifty four RA patients diagnosed according to ACR/EULAR criteria were recruited for the present study. A total of 154 patients with RA were included. Disease activity was assessed by clinical disease activity indices (CDAI and DAS28 ESR). Functional status was assessed by health assessment questionnaire (HAQ).
Results: In the cross-sectional cohort with 154 patients, correlation between the modified (U8) score and clinical disease activity parameters (CDAI and DAS28) was significant but modest (r=0.3, P=0.03 and r=0.4, P=0.01) respectively. The same was true for the (U 8+2 score) (r = 0.41, P= 0.0001, r=0.4, P=0.005). The 8+1 (U9 score) gave the best positive correlation with CDAI and DAS28 (r=0.7, P<0.001, r=0.6, P<0.001) respectively.
HAQ was highly correlated with U9 score (r=0.7, P<0.001) and moderately correlated with U8+2 score (r=0.3, P=0.05) and not correlated with the modified 8 score.
Conclusion: The U9 score gave the best correlation with disease activity parameters. It is simple and applicable and gives a high degree of flexibility to the sonographer according to the clinical picture.

REFERENCES:

[1] A novel 8-joint ultrasound score is useful in daily practice for rheumatoid arthritis. Modern Rheumatology 25(3).

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Disclosure of Interests: None declared
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FRI0625 ASSESSING SYNOVITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS BY ULTRASOUND – AN AGREEMENT STUDY EXPLORING THE MOST ACTIVE SIDE

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Background: Though ultrasound examination of all RA patients - if offered a very tight clinical control – may not be necessary for obtaining clinical remission (1,2), there are still patients where ultrasound may have a role in monitoring disease activity. Scoring synovitis unilaterally will by far reduce the examination time, however, no consensus exists on how to choose the side to be examined and if one side per se is always the most inflamed side.
Objectives: To assess ultrasound (US) inflammation and sensitivity to change in hands, aiming to identify if the right hand, the dominant hand, or the hand with more clinically swollen joints (SwJ) is per se the most inflamed and more sensitive to change, and hence the preferred side for unilateral scoring of synovitis by US in rheumatoid arthritis (RA) patients.
Methods: This is an agreement study exploring the impact on US scoring methods in a longitudinal study of early RA (ARCTIC trial, n=230) and established RA (ULRABIT trial, n=212) patients initiating conventional and biological Disease Modifying Anti-Rheumatic Drugs, respectively. Tender and swollen joint count for 28 joints (TJC28 and SJC28) and C-reactive protein (CRP mg/L) were obtained. Using the hands as model, bilateral MCP 1-5, PIP 2+3 and wrists were evaluated by US using a 0–3 scoring system for grey-scale (GS) and power Doppler (PD) US according to the atlas by Hammer et al. (3) GS sum score, PD sum score and global synovitis score (GLOESS) were calculated for each hand (0-30). According to our prespecified protocol a reasonable equivalence margin in this study (agreement between groups) was defined to correspond to a 95% Confidence Interval around the observed paired mean difference: -2.99 to +2.99.

Table
Ultrasound inflammatory activity in the dominant hand versus non-dominant hand, in the hand with clinically more swollen joint versus less swollen joints and the right versus left hand using different ultrasound composite scores

	Baseline			Change values from baseline to 3 months		
	GS sum score (0-30)	Doppler sum score (0-30)	GLOESS (0-30)	Δ GS sum score (0-30)	Δ Doppler sum score (0-30)	Δ GLOESS (0-30)
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Dominant Hand (n=431)						
Dominant	7.75 (7.09 to 8.40)	4.81 (4.26 to 5.35)	8.07 (7.39 to 8.75)	-3.11 (-3.65 to -2.57)	-2.57 (-3.10 to -2.04)	-3.40 (-3.90 to -2.82)
Non Dominant	7.06 (6.41 to 7.72)	4.22 (3.68 to 4.78)	7.28 (6.60 to 7.96)	-3.12 (-3.66 to -2.58)	-2.35 (-2.88 to -1.82)	-3.29 (-3.87 to -2.71)
Difference	-0.69 (-1.61 to 0.24)	-0.58 (-1.35 to 0.20)	-0.79 (-1.76 to 0.18)	0.005 (-0.76 to 0.75)	0.22 (-0.52 to 0.96)	0.11 (-0.70 to 0.92)
P-value	0.15	0.14	0.11	0.99	0.57	0.79
Clinical Hand (swollen joints) (n=314)						
Worst Clinical (more SJC)	8.51 (7.87 to 9.16)	5.37 (4.83 to 5.91)	8.83 (8.16 to 9.50)	-3.79 (-4.32 to -3.25)	-3.05 (-3.57 to -2.52)	-4.06 (-4.63 to -3.49)
Least Clinical (fewer SJC)	6.30 (5.65 to 6.94)	3.66 (3.13 to 4.20)	6.52 (5.85 to 7.19)	-2.45 (-2.96 to -1.92)	-1.87 (-2.40 to -1.35)	-2.64 (-3.21 to -2.06)
Difference	-2.21 (-3.12 to -1.30)	-1.70 (-2.47 to -0.94)	-2.31 (-3.26 to -1.36)	1.34 (0.60 to 2.08)	1.17 (0.44 to 1.91)	1.43 (0.63 to 2.22)
P-value	<.0001	<.0001	<.0001	0.0004	0.002	0.0005
Hand side (n=437)						
Right side	7.79 (7.12 to 8.44)	4.82 (4.28 to 5.37)	8.12 (7.44 to 8.80)	-3.19 (-3.73 to -2.65)	-2.64 (-3.17 to -2.11)	-3.49 (-4.07 to -2.91)
Left side	7.05 (6.37 to 7.68)	4.21 (3.6 to 4.76)	7.23 (6.55 to 7.91)	-3.05 (-3.59 to -2.51)	-2.28 (-2.81 to -1.75)	-3.21 (-3.78 to -2.63)
Difference	-0.75 1.68 – 0.18)	-0.61 1.36 – 0.16)	-0.89 1.85 – 0.08)	0.14 (-0.61 to 0.89)	0.36 (-0.38 to 1.10)	0.29 (-0.52 to 1.09)
P-value	0.11	0.12	0.07	0.71	0.34	0.49

*Analysed using a factor for the specific analysis, and trial (ARCTIC and ULRABIT, respectively) as a fixed effect, and the patient-ID was applied as a random effect

Results: 437 RA patients were included in the current analysis; 71% women, 79% anti-CCP pos, 71% RF pos, median(IQR) age 54(42-62) years, CRP 7(3-16), SJC28 5(3-26) and TJC28 6(2-28). The median (IQR) PD sum score was 3(0-7) for right hand and 2(0-5) for left hand, GS sum score was 5(2-9) for both hands, and GLOESS was 5(2-10) for right hand and 5(2-9) for left hand. The average ultrasound measured inflammation at baseline and 3 months follow-up are shown in the table. The hands with more vs fewer SwJ had more inflammation at baseline for all sum scores, all p<.0001)) and had a greater change for all sum scores at 3 months follow-up (all p<0.0005)). No such differences were found between the dominant vs non-dominant or the right vs left hands at any time points – see table.**Conclusion:** Based on this study, assessment of the dominant hand is not superior to the non-dominant hand in inflammatory activity evaluated by US. The hand with clinically more SwJ at baseline is likely to have more active inflammation according to GS, Doppler and GLOESS sum scores and exhibit a greater change, and is potentially the best choice for unilateral US scoring systems.

REFERENCES:

[1] Dale J, Stirling A, Zhang R, Purves D, Foley J, Sambrook M, et al. Targeting ultrasound remission in early rheumatoid arthritis: the results of the TaSER study, a randomised clinical trial. Ann Rheum Dis. 2016;75:1043-50.

[2] Haavardsholm EA, Aga AB, Olsen IC, Lillegraven S, Hammer HB, Uhlig T, et al. Ultrasound in management of rheumatoid arthritis: ARCTIC randomised controlled strategy trial. BMJ. 2016;354:i4205.

[3] Hammer HB, Bolton-King P, Bakkeheim V, Berg TH, Sundt E, Kongtorp AK, et al. Examination of intra and interrater reliability with a new ultrasonographic reference atlas for scoring of synovitis in patients with rheumatoid arthritis. Ann Rheum Dis. 2011;70:1995-8.

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Squibb, Roche, UCB Pharma and Pfizer
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FRI0626 DIFFICULTIES WITH MAKING A FIST IN PATIENTS WITH CLINICALLY SUSPECT ARTHRALGIA; AN EARLY PHENOMENON PREDICTIVE FOR RA THAT IS RELATED TO MRI-DETECTED TENOSYNOVITIS

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Background: Difficulties with making a fist in patients presenting with recent-onset arthralgia of small joints, in whom there is no clinically detectable arthritis, is often considered a risk factor for the development of inflammatory arthritis. The fact that rheumatologists consider difficulties with making a fist a feature of imminent Rheumatoid Arthritis (RA) is also reflected by this sign being incorporated in the EULAR definition of arthralgia suspicious for progression to RA. However, to date there is little comprehension on its predictive value and underlying cause in patients with recent-onset arthralgia.
Objectives: This study was performed to 1) determine if difficulties making a fist is indeed predictive for the development of clinical arthritis, and 2) evaluate if this sign is associated with subclinical joint inflammation, detected by magnetic resonance imaging (MRI).
Methods: 566 patients presenting with recent-onset (<1 year) arthralgia of small joints that were consecutively included in the Clinically Suspect Arthralgia (CSA) cohort were studied. At baseline the ability to completely close the fist (all fingertips touching the palm) was assessed at physical examination. Additionally, contrast-enhanced 1.5T MRI of wrist, 2^{nd}-5^{th} metacarpophalangeal (MCP) and 1^{st}-5^{th} metatarsophalangeal (MTP) joints was performed. MRIs were scored for synovitis, bone marrow edema (BME) and tenosynovitis in line with the RAMRIS. MRI-detected subclinical inflammation was considered present if it was more than observed in symptom-free controls from the general population in the same age-category (n=193). Patients were followed on the development of clinically detectable inflammatory arthritis identified at joint examination (median follow-up 19 months); none of the patients received DMARDs before the development of clinical arthritis. χ^2 tests, logistic and Cox proportional hazards regression were used as appropriate.
Results: At first presentation 12% of CSA-patients had difficulties making a fist with one or both hands. Having difficulties making a fist was predictive for development of clinical arthritis in univariable analysis (HR 2.47 (95% CI 1.46-4.19)) and in multivariable analysis (HR 2.16 (1.25-3.74) corrected for age, CRP, ACPA and MRI-detected subclinical inflammation). Patients with difficulties making a fist had significantly more often MCP tenosynovitis (flexor tenosynovitis and extensor peritendinitis combined) than patients who did not experience these problems (42% versus 16%, p<0.001). The main difference was seen in MCP flexor tenosynovitis (39% versus 10%, p<0.001). MCP flexor tenosynovitis was significantly associated with difficulties making a fist in univariable (OR 5.6 (95% CI 3.2-9.9)), and multivariable regression (OR 5.7 (3.2-10.2) corrected for extensor peritendinitis, synovitis and BME in MCP joints). Extensor peritendinitis, synovitis and BME in MCP joints were not associated with difficulties making a fist (multivariable OR 0.7 (0.2-2.1), 0.99 (0.5-2.1) and 1.6 (0.7-4.1), respectively).
Conclusion: Difficulties making a fist in patients with CSA is predictive for future inflammatory arthritis development. This sign is presumably caused by MCP flexor tenosynovitis in a significant proportion of patients.
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FRI0627 DOES ADDING AN US EXAMINATION OF SHOULDERS, TO A ROUTINE DAS-28 SCORE, IMPROVE ACCURACY OF DISEASE ACTIVITY SCORES AND DISEASE STATUS? RESULTS OF A SINGLE CENTRE PILOT STUDY

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Background: The DAS28 forms the mainstay of current RA and other chronic inflammatory arthritis (CIA) [i.e. peripheral spondyloarthritis (SpA)] management in clinical practice. DAS28 has certain limitations. Some joints especially the shoulders are difficult to evaluate correctly using this method. The shoulder is deep and highly affected by rotator cuff tendon lesions either due to degenerative or inflammatory arthritis This structural damage can produce pain and swelling. A swollen shoulder joint can be difficult to palpate by physical examination. Using a clinical approach can be inaccurate to ascertain whether shoulder involvement is actually due to true RA-derived inflammatory activity or other degenerative or structural causes.
Objectives: To investigate the added value of adding a US assessment of shoulders to DAS28 scores and on disease activity status, in patients with CIA (RA or peripheral SpA) in either disease remission or low disease states who had shoulder pain.
Methods: Patients were recruited prospectively over a 3-month period. Each patient had a standard DAS28 performed followed by a formal physical shoulder examination, of both shoulders, including testing active and passive range of movements. A complete US examination of both shoulders was carried out by a rheumatologist experienced in this technique. All patients were examined using the same real-time US machine (Esaote MyLab Twice) using a linear probe, 3-13 MHz frequency and 57% gain. The original DAS28 was recalculated (i.e. US-modified DAS28) according to the presence/absence of inflammatory findings on shoulder US.
Results: Thirty-eight patients [82% females; mean (± SD) age 60.3 (11.96) years] were included. In 33 out of 38 (87% [CI95%: 76-98%]) patients the original DAS28 was greater than the US-modified DAS28. This percentage was significantly greater than 50% ($p < 0.001$). The mean ± SD reduction of DAS28 in those patients who showed DAS28 decrease was 0.73 ± 0.39 units. Twenty-five patients (65.8%) maintained the same disease activity status with original DAS28 and US-modified

DAS28. The remaining 13 (34.2%) patients changed their status: 11 (28.9%) patients moved from low activity to remission while 2 (5.3%) patients moved from low activity to moderate activity. Figure 1 and 2 demonstrate some of the ultrasound findings observed in ourt patient group.

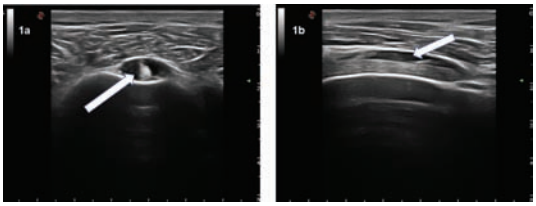


Figure 1-. Biceps tenosynovitis in a. transverse and b.longitudinal views.

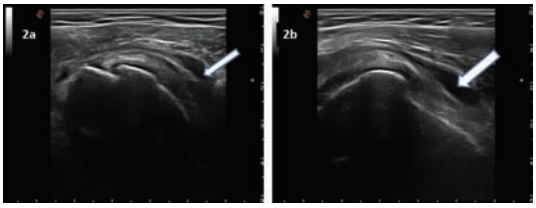


Figure 2-. Subacromial-subdeltoid (SASD) bursitis in a. transverse and b.longitudinal views.

Conclusion: This study showed that patients improved their disease activity scores and status after an US assessment of their shoulders. A low percentage increased their disease status after shoulder US which can be also important for local or systemic therapeutic decisions. Based on this study, we suggest that shoulder US can provide valuable additional information to the DAS28 when evaluating disease activity in CIA patients.

REFERENCES:

[1] Mierau M, Schoels M, Gonda G, Fuchs J, Aletaha D, Smolen JS. Assessing remission in clinical practice. Rheumatology (Oxford)2007;46: 975-9.
[2] Naredo E, Aquado P, De Miguel E, Uson J, Mayordomo L, Gijon-Banos J, Martin-Mola E. Painful shoulder: a comparison of physical examination and ultrasonagraphic findings. Ann Rheum Dis 2002; 61:132-6..
[3] Micheroli R, Kyburz D, Ciurea A, Dubs B, Bisig SP, Tamborrini G. Correlation of findings in clinical and high resolution ultrasonography examinations of the painful shoulder. J Ultrason 2015; 15: 29–44.

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FRI0628

DIAGNOSTIC VALUE OF OPTICAL SPECTRAL TRANSMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS: CORRELATIONS WITH DISEASE ACTIVITY, EPIDEMIOLOGIC AND ANTHROPOMETRIC PARAMETERS

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Background: Valid assessment of disease activity leads to improvement of long-term outcomes in patients with rheumatoid arthritis (RA) (1). Clinical disease activity assessment tools such as the Disease Activity Score 28 (DAS28) are partially subjective and do not always depict the real inflammatory burden. Ultrasound (US) and Hand-MRI are important diagnostic modalities which can nevertheless be time consuming (US, MRI), expensive (MRI) or usually performed unilaterally (MRI). Thus, further diagnostic tools are needed. Optical spectral transmission (OST) is a new modality able to assess the blood-specific absorption of light transmitted through a tissue promising quantification of inflammation in the finger and wrist joints of RA patients (commercial device: HandScan - Hemics, The Netherlands)(2).
Objectives: To examine the diagnostic value of OST in detecting inflammation in patients with RA and to evaluate for the first time its relationship with disease activity markers and various anthropometric and epidemiologic patient characteristics.
Methods: OST-Measurements were performed in 168 RA-patients and 114 healthy controls. The difference between OST in the two groups was statistically examined and subsequently controlled for the effect of possible confounding factors. Moreover, association of OST with clinical, ultrasound and serological RA activity markers was evaluated. Finally, relationship of OST with radiographic joint pathology and various anthropometric and epidemiologic parameters (BMI, hand-size, gender, age) was examined.
Results: OST was significantly higher in the patients group in comparison to the control group, even after adjustment for the effects of various confounding factors ($p_{adj}<0.001$). OST correlated in both groups significantly with gender, hand-size and Body Mass Index (*all; p<0.001*). In the patients group, OST correlated significantly with all examined disease activity markers (DAS28, ESR, counts of tender/swollen joints, VAS; all, $p_{adj}<0.05$) and with age (*p<0.001*). OST showed significant correlations with a power Doppler ultrasound-Score (*p=0.001*) and with a combined power Doppler/grey scale ultrasound-Score (*p<0.001*). Finally, receiver operating characteristic showed the best OST performance at the level of metacarpophalangeal joints level (AUC=0.75; 95%CI=0.686-0.821).
Conclusion: OST correlated with serological and clinical disease activity markers as well as with different anthropometric and epidemiological parameters of RA-patients. OST could therefore prove to be a good non-interventional complementary tool to assess RA activity next to well established diagnostic methods such as the US or MRI.

REFERENCES:

[1] Katchamart W, et al. Systematic monitoring of disease activity using an outcome measure improves outcomes in rheumatoid arthritis. J Rheumatol 2010;37:1411–1415.
[2] Onna M Van, et al. Assessment of disease activity in patients with rheumatoid arthritis using optical spectral transmission measurements, a non-invasive imaging technique. Ann Rheum Dis 2016;75:511–518.

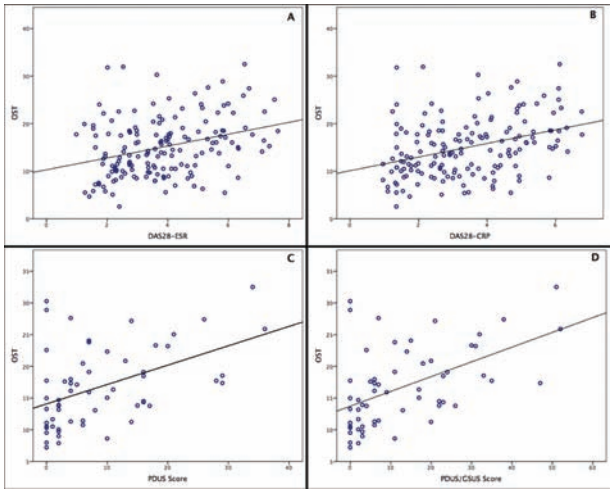


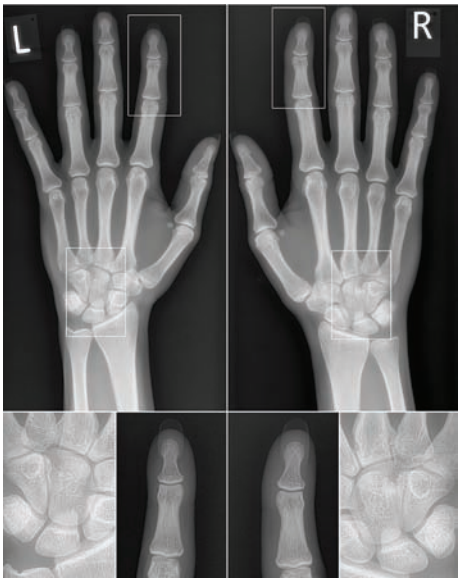
Figure 1. Correlations between optical spectral transmission (OST) and A. Disease Activity Score 28-erythrocyte sedimentation rare (DAS28-ESR) (*p<0.001*), B. DAS28-C-reactive protein (DAS28-CRP) (*p<0.001*), C. power Doppler ultrasound (PDUS) score (*p=0.001*) and D. combined power Doppler/grey scale ultrasound (PDUS/GSUS) score (*p<0.001*).

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FRI0629 **APPLICATION OF AN ADVANCED NOISE REDUCTION ALGORITHM FOR IMAGING OF HANDS IN RHEUMATIC DISEASES – EVALUATION OF IMAGE QUALITY COMPARED TO STANDARD DOSE IMAGES**

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Background: X-ray is the fundamental imaging technique in diagnosis and follow up of rheumatic diseases. As patients often require sequential X-rays, dose reduction is of great importance. New advanced noise reduction algorithms allow for a dose reduction of up to 50%.
Objectives: The aim of this study was to evaluate, whether the application of an advanced noise reduction algorithms is feasible in the context of imaging of rheumatic diseases.
Methods: A total of 298 patients were enrolled prospectively into three tiers: 80%, 64% and 50% dose reduction groups. All patients received imaging of one hand (laterality randomly assigned) with low-dose technique and of the contralateral side with standard protocol. All images were evaluated by two blinded independent readers who scored (on a scale of 1 to 5) the visualisation of bony cortex, trabeculae and joint spaces of fingers and wrist separately as well as soft tissue and overall contrast. Score values were analysed using T-tests for paired samples.
Results: Overall image quality (expressed by mean sum scores out of 40) of the 50% low-dose images was 31.52 (SD 1.94) vs. 31.66 (SD 1.82) for standard images (p=0.217). Bony contours as well as trabeculae was equally well visualized in both image sets. An image example is given in Fig. 1 (Left hand: 50%-dose image; right hand: standard-dose image). Soft tissue visualization was slightly lower for low-dose compared to standard images (mean score of 3.81 vs. 3.88; p=0.001).



Conclusion: Overall image quality of low dose images was not inferior to standard dose images. Therefore, application of low-dose technology based on advanced noise estimation algorithms in the context of imaging of rheumatic diseases is feasible.
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FRI0630 **DIAGNOSTIC UTILITY OF FLUORESCENCE OPTICAL IMAGING IN INDIVIDUALS WITH SUSPECTED ARTHRITIS – A PROBABILISTIC APPROACH**

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Background: In the arsenal of available techniques used for arthritis prediction and diagnosis[1], fluorescence optical imaging (FOI) has been proven useful in detecting clinically manifest and silent synovitis of the hands and wrists of patients with various rheumatic diseases, particularly rheumatoid arthritis (RA)[2].
Objectives: To assess the diagnostic utility of FOI in individuals with joint symptoms referred for further rheumatologic investigation, using a probabilistic approach.
Methods: Those with increased suspicion of inflammatory arthritis were referred to the rheumatology unit and clinic of Karolinska University Hospital. On acquiring informed consent and medical history, the standard clinical examination coupled with ultrasound findings of fingers, wrists and feet were assessed. Laboratory results included ESR, CRP, RF, and ACPA tests. Using the above information, a diagnostic probability assessment was completed by the responsible rheumatologist, where the probability of a) any inflammatory joint disease and b) rheumatoid/RA was given on a 5-point scale – ranging from unlikely (0-20%) to very likely (80-100%) probability. Subsequently, an FOI examination was performed. After reviewing the image reports in consensus, post-FOI diagnostic probabilities were again scored, using the same scale. If no score change in probability resulted, the rheumatologist was asked to mark whether FOI was still helpful in the diagnostic decision-making. Proportions of individuals with maximal and minimal diagnostic certainty pre- and post-test were compared using Fisher exact tests, and one-sample binomial tests for assessing the helpfulness of FOI in the absence of pre- and post-test probability score changes.
Results: Of 24 individuals screened, 21 without prior rheumatic diagnosis were included (66.7% female, 11 RF (+), 10 ACPA (+), with age average and symptom duration (SD) of 55.6 (±18.1) years and 13.9 (±15.3) months respectively). The final diagnoses were: early RA (n=17), other inflammatory joint disease (n=3), and non-inflammatory joint disease (n=1). Regarding diagnosis of any inflammatory arthritis, where the proportion of patients for whom diagnostic certainty was maximal – namely, combining <20% (lowest probability) or >80% (highest probability) of diagnostic likelihood – there was an increase from 52.4% (n=11/21) maximal certainty before FOI to 80.1% (17/21) maximal certainty after FOI (p=0.035). Regarding early RA, the maximal diagnostic certainty increased from 57.1% (12/21) to 71.4% (15/21) (p=0.002), respectively. In the event that diagnostic certainty scores didn't change pre- vs. post-test (15/21 cases, any inflammatory joint disease; 13/21 cases, early RA), the diagnosing rheumatologist indicated that FOI was still helpful in setting a final diagnosis for most cases (86.7% (13/15) p=0.007; 84.6% (11/13), p=0.022, respectively).
Conclusion: FOI significantly increased the diagnostic certainty and confidence of rheumatologists in establishing the presence and absence of inflammation in individuals suspected of inflammatory arthritis. The changes from pre- to post-test quantify the diagnostic utility of FOI in probabilistic terms.

REFERENCES:

[1] Rezaei H, Torp-Pedersen S, Af Klint E, et al. 2014 Diagnostic utility of musculoskeletal ultrasound in patients with suspected arthritis - A probabilistic approach. Arthritis Res Ther 2014;16:448. doi.101186/s13075-014-0448-6
[2] Kisten Y, Györi N, af Klint E, et al. 2015 Detection of clinically manifest and silent synovitis in the hands and wrists by fluorescence optical imaging. RMD Open 2015;1: e000106. Doi: :10.1136/rmdopen-2015-000106 https://www.ncbi.nlm.nih.gov/pubmed/26535142

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FRI0631 **MUSCLE STIFFNESS AND WEAKNESS IN RHEUMATOID ARTHRITIS – A SHEAR WAVE ELASTOGRAPHY STUDY**

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Background: Myopathy is a recognised but less investigated symptom of rheumatoid arthritis (RA) compared to other extra-articular manifestations. To date, the documentation of myopathic features in RA is poorly detailed. No studies have yet utilised a non-invasive quantitative method to define and investigate these features. Shear wave elastography (SWE), a novel ultrasound technology, can measure muscle stiffness to provide insight into the biomechanical properties of skeletal muscle.
Objectives: 1- To investigate muscle stiffness (using SWE) and strength in three cohorts of RA patients compared to healthy controls.
2- To study the association between muscle strength and stiffness in RA.
Methods: Shear wave velocity (SWV), as a measure of muscle stiffness, was evaluated in the quadriceps, hamstrings and biceps brachii in 80 RA patients from three disease activity groups newly diagnosed treatment naïve RA [n=29; mean age 56.8 ± 10.6 years], persistent active RA for at least 1 year [n=18; 60.9 ± 15.9 years] and remission RA for at least 1 year [n=33; 65.9 ± 11.6 years], and compared them to 40 healthy controls (56.8 ± 10.6 years). The participants performed various muscle tests (handgrip strength, expanded timed get up and walk test (ETGUG), chair stand and isokinetic knee extension/flexion) to assess their strength and physical performance. One-way ANOVA was used to compare SWV and muscle assessment results, and Pearson's correlation was used to evaluate the correlation between muscle stiffness and strength.
Results: Mean SWV was not significantly different amongst the RA groups or compared to the healthy controls (p>0.05). For example, the rectus femoris SWV was 1.69±0.15 m/s for healthy controls, 1.68±0.18 m/s for new RA, 1.70±0.16 m/s for active RA and 1.68±0.14 m/s for remission RA (p=0.96). The muscle assessment results are presented in table 1 and compared to healthy controls in figure 1. Overall, the active and new RA groups showed significant muscle weakness compared to healthy controls. The remission RA group did not show a significant difference except in the isokinetic knee strength (-21%; p=0.027). The correlations between SWE and the muscle assessment results were weak and insignificant (r<0.30; p>0.05).

Table 1. Muscle assessment results for all participants.

Test	Healthy controls (a)	New RA (b)	Active RA (c)	Remission RA (d)	p-value	Post hoc*
ETGUGT, Total time (sec)	16.6 (4.3)	20.7 (5.7)	21.5 (6.3)	18.2 (4.5)	**0.002**	a>b,c
Number of chair stands in 30 sec	17.0 (5.8)	12.3 (6.0)	9.5 (6.3)	14.0 (5.4)	**<0.001**	a>b,c
Handgrip strength (kg)	31.5 (13.7)	17.3 (8.1)	17.3 (8.4)	26.6 (10.9)	**<0.001**	a,d>b, c
Knee extension torque (Nm/kg)	1.29 (0.42)	1.06 (0.45)	0.93 (0.47)	1.20 (0.40)	**0.026**	a>c
Knee flexion torque (Nm/kg)	0.75 (0.27)	0.53 (0.27)	0.60 (0.29)	0.59 (0.25)	**0.006**	a>b,d
Knee extension power (W/kg)	0.75 (0.29)	0.58 (0.30)	0.52 (0.32)	0.68 (0.28)	**0.029**	a>c
Knee flexion power (W/kg)	0.47 (0.18)	0.32 (0.19)	0.34 (0.21)	0.34 (0.18)	**0.005**	a>b,d

* The signs > or < indicate that the group(s) are significantly higher or lower at 0.05 significance level compared to others.

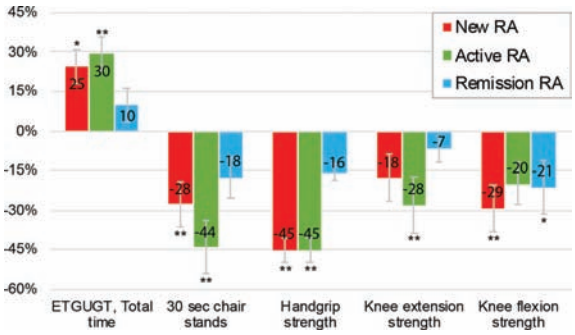


Figure 1. The difference percentages in muscle assessment results for the RA patients relative to the healthy controls.

Conclusion: Muscle stiffness, as determined using SWE, does not appear to be altered or associated with muscle weakness in RA patients. The remission RA group showed significantly better strength and physical performance compared to new untreated or persistently active RA groups. Future research should investigate the significant muscle weakness in RA in addition to developing prevention and therapeutic strategies.
Disclosure of Interests: Abdulrahman M. Alfuraih: None declared, Ai Lyn Tan: None declared, Philip O'Connor: None declared, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead,Samsung, Sandoz and Lilly, Richard Wakefield: None declared
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FRI0632 **ASSOCIATION BETWEEN ULTRASOUND DIAGNOSIS AND ANALYTICAL AND SEROLOGICAL DATA IN PATIENTS WITH SUSPECTED PRIMARY SJÖGREN SYNDROME**

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Background: Pathophysiology of primary Sjögren syndrome (SSp) is characterized by oligoclonal B-cell proliferation and ectopic lymphoid tissue formation. The association between ultrasound glandular parenchyma heterogeneity and hyperproduction of autoantibodies, which in turn represents characteristic B-cell hyperactivity of SSp, is described.
Objectives: To study the association between major salivary gland ultrasound (MSGUS) and their respective pathological grades with the analytical and serological data, and activity indexes obtained in patients with suspected SSp.
Methods: 72 patients were recruited consecutively with clinical and/or analytical suspicion of SSp from the Rheumatology outpatient consultations at the Príncipe de Asturias Hospital (2015-2018). Demographic, serological and validated activity indexes, ESSPRI and ESDAI, were collected. All of them underwent a MSGUS and their results were classified in three grades according to the *Cornec et al system*: normal (grade 0 and 1), mild (grade 2) and moderate-severe (grades 3 and 4). The final SSp diagnosis was made using both 2002 AECG and 2016 ACR/EULAR classification criteria. Data were analyzed using the software STATA. Association between MSGUS and qualitative variables was described according to the number of cases and the percentage by grades of MSGUS; the significance of the associations was tested with the Chi square test. As for the quantitative variables, the association was described with median and interval interquartile (IIQ) by grades of MSGUS and the significance of the association was verified with the non-parametric test of Kruskall-Wallis.
Results: From patients with pathological MSGUS: 51% had antiRo52, 51% antiRo60 and 36% anti-La positive; 62% hypergammaglobulinemia, 40% positive rheumatoid factor (RF), 6% and 13% C3 and C4 hypocomplementemia, respectively. Mean values were obtained: ESR 36, CRP 1.6, RF 12, ESSPRI 5.6 and ESSDAI 2. Statistically significant differences (p<0.05) were only found in antiRo52 and hypergammaglobulinemia variables in patients with normal MSGUS exam compared to those with

mild and moderate-severe pathological MSGUS exam. These data suggest that there could be differences for antiRo60, AntiLa and ESSPRI variables eventhough statistical significance was not achieved (p>0.150 in all associations explored). No differences have been found for RF, C3 and C4 hypocomplementemia, ESR, CRP and ESSDAI variables *(table1).*

Conclusion: In this series of patients, a statistically significant association was found between the positivity of anti-Ro antibodies, hypergammaglobulinemia and MSGUS, as well as its subdivision by pathological grades. No statistical significant association was found between MSGUS and positivity of antiRo60 and antiLa antibodies and ESSPRI, probably due to the small sample size. There were no differences for the rest of the variables analyzed (RF, complement, acute phase reactants and ESSDAI).

REFERENCES:

[1] Ultrasonography of salivary glands-a highly specific imaging procedure for diagnosis of Sjögren's syndrome Dirk Wernicke J Rheumatol. 2008 Feb;35 (2):285-93. Epub 2008 Jan 15

[2] . The usefulness of ultrasound in the diagnostics of Sjögren's syndrome. Fadhil Saied J Ultrason. 2013 Jun;13(53):202-11.

TABLE 1. ASSOCIATION BETWEEN MSGUS GRADES AND THE ANALYZED VARIABLES

MSGUS	NORMAL	GRADE 2 (MILD)	GRADE 3 (MODERATE-SEVERE)	p
AntiRo 52%	21	38	71	**0.004**
AntiRo 60%	32	44	62	0.150
AntiLa%	21	28	48	0.163
Hypergammaglobulinemia %	16	53	76	**0.001**
Rheumatoid factor%	47	31	52	0.460
Hypocomplementemia C3%	11	6	5	0.757
Hypocomplementemia C4%	11	10	19	0.555
ESR mean	31	34	38	0.094
CRP mean	2	1	3	0.059
RF mean	10	9	17	0.229
ESSPRI mean	5	5.6	6.3	0.349
ESSDAI mean	2	1	2	0.078

Disclosure of Interests: None declared**DOI:** 10.1136/annrheumdis-2019-eular.3614

FRI0633 POSSIBLE ADVANTAGES OF 18F-FDG PET/CT-MR IN ADULT-ONSET STILL'S DISEASE: A STUDY FROM AN ITALIAN COHORT

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Background: Adult-onset Still's disease (AOSD) is a systemic complex autoinflammatory disorder whose diagnosis is essentially clinical and necessitates the exclusion of potential mimickers. A specific diagnostic test to define the diagnosis or assess the disease activity is still not available.

Objectives: To define the advantages of PET/MR in diagnosis and therapeutic response in AOSD patients and to assess a characteristic uptake pattern of ^{18}F-FDG at PET/CT-MR images of our cohort.

Methods: 18 AOSD patients and 30 age- and sex-matched controls underwent ^{18}F-FDG PET/CT-MR between 2008 and 2018. A total of 44 PET/MR and 9 PET/CT performed at Padova University Hospital were analyzed. All AOSD patients were diagnosed according to Yamaguchi's criteria and had a regular follow-up at the Rheumatology Unit. Disease activity was evaluated using Pouchot's criteria. Uptake of affected organs was considered pathological when higher than liver uptake value. In order to analyze possible statistical differences of SUV ratios between the two groups, Mann-Whitney U-Test was applied. The variables considered were SUV ratios of spleen and bone marrow (BM). The SUV ratios were calculated between SUV of spleen-to-liver and of bone marrow-to-liver. We compared PET/MR and PET/CT of AOSD patients, evaluating possible statistical differences on SUV max ratios of bone marrow and spleen with Mann-Whitney U Test. To determine the strength and direction of the relationship between the continuous variables SUV ratios and Pouchot's score in our cohort Spearman's Rank Order Correlation Coefficient was applied.

Results: All our patients presented areas of focal ^{18}F-FDG uptake. High and homogeneous accumulation of ^{18}F-FDG was observed at PET/CT-MR in spleen, BM, lymph nodes, pharynx, salivary glands and brown adipose tissue. PET/CT-MR of patients affected presented higher SUV ratios than controls. A statistically significant difference was observed for each SUV ratio in BM. In spleen p-values of 0.014, <0.001 and 0.002 were observed for SUV min ratio, SUV max ratio and SUV mean ratio respectively. Responders to therapy showed lower uptake at PET/CT-MR images during the follow-up. The SUVratios of PET/CT and PET/MR in AOSD were not significantly different.

Conclusion: Our patients presented higher ^{18}F-FDG uptake at PET/CT-MR images compared to controls. Both PET/CT and PET/MR are not related to the disease activity expressed by Pouchot's score, however PET/CT-MR seems to be more reliable than Pouchot's score in disease activity assessment. PET/MR is more sensitive than PET/CT for the evaluation of BM in patients with low-disease activity and it is a better repeatable analysis compared to PET/CT because of less radiation dosage.

REFERENCES:

[1] Sfriso P, et al. Adult-onset Still's disease: an Italian multicentre retrospective observational study of manifestations and treatments in 245 patients. Clin Rheumatol. 2016;35(7):1683-1689.

[2] Yamashita H, et al. Clinical value of whole-body PET/CT in patients with active rheumatic diseases. Arthritis Res Ther.2014;16(5):423.

[3] Jiang L, et al. Imaging characteristics of Adult-onset Still's disease demonstrated with 18F-FDG PET/CT. Mol MedRep.2017;16(3):3683686.

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FRI0634 STANDARD REFERENCE VALUES OF METACARPAL HEAD CARTILAGE THICKNESSMEASUREMENT BY ULTRASOUND IN HEALTHY SUBJECTS

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Background: The hyaline cartilage of metacarpal head (MH) is frequently involved in patients with chronic arthtritis. Moreover, in a recent study a high correlation has been found between the anatomical and sonographic (US) measurements of hyaline cartilage[1]. However, only very few data are available on the prevalence of pathological findings and the standard reference values in healthy subjects (H).

Objectives: To determine the prevalence of the US abnormalities at metacarpal head (MH) in H, and to measure MH cartilage thickness (CT) in order to provide standard reference values.

Methods: US examinations were performed on 944 metacarpophalangeal (MCP) joints of 118 consecutive H using a MyLab Twice (Esaote Biomedica, Genoa, Italy), equipped with a high frequency probe (up to 22 MHz). H were recruited among the staff of Rheumatology Department of the "Carlo Urbani" Hospital (Jesi, Ancona, Italy), students in medicine and patients' healthy relatives. Exclusion criteria were: hand pain (VAS score >1/10) or stiffness in the previous month or hard tissue enlargement of MCP, proximal and distal interphalangeal joints.

The MH hyaline cartilage from II to V digits of both hands was scanned with the MCP joints in maximal flexion in longitudinal and transverse dorsal views, paying attention on maintaining an angle of 90° between the direction of the US beam and the cartilage surface[2]. CT was scored both semi-quantitatively (using a five-grade scoring system[3]) and quantitatively (using the mean value of longitudinal and transverse measurements of the CT). Moreover, the presence of osteophytes and bone erosions was recorded.

The association between CT and demographic data was analyzed.

Results:

Semiquantitative score: Cartilage damage was found in 21 out of 118 H (17.8%) and in 59 out of 944 MHs (6.3%): grade 1 and grade 2 in 43 (4.6%) and in 16 (1.7%), respectively. No grades 3 and 4 were detected. Osteophytes and bone erosions were respectively found in 12 (10.1%) and in 8 (6.7%) out of 118 H and in 24 (2.5%) and in 12 (1.3%) out of 944 MHs.

A slight correlation between semi-quantitative score and the presence of osteophytes was found (r=0.16, p<0.01). No association between bone erosion and cartilage thinning was found.

Quantitative assessment: A significantly thicker cartilage was found in males [0.71±0.10 mm (mean±SD)] than in females [0.68±0.12 mm, (mean ±SD)] ($p<0.01$). No significant difference was found between left and right side for each digit ($p>0.05$).
CT value of the II MH was significantly greater than the one of the other fingers ($p<0.01$). No difference was found between the CT values of III, IV and V MH ($p>0.05$).
There was a significant association between the CT value and gender ($r=0.39$; $p<0.01$), age ($r=-0.33$; $p<0.01$), height ($r=0.28$; $p=0.01$) and grade of the semiquantitative scoring system ($r=-0.19$, $p<0.01$). No correlation was found between the CT value and weight ($p=0.20$).
Conclusion: This study confirms the presence and provides data on the prevalence of US abnormalities at MH level in healthy individuals. Moreover, normal values for US CT of MH were reported.

REFERENCES:

[1] Mandl P, Supp G, Baksa G, et al. Relationship between radiographic joint space narrowing, sonographic cartilage thickness and anatomy in rheumatoid arthritis and control joints. Ann Rheum Dis. 2015;74:2022-7.
[2] Torp-Pedersen S, Bartels EM, Wilhjelm J, Bliddal H. Articular cartilage thickness measured with US is not as easy as it appears: a systematic review of measurement techniques and image interpretation. Ultraschall Med. 2011;32:54-61.
[3] Filippucci E, da Luz KR, Di Geso L, et al. Interobserver reliability of ultrasonography in the assessment of cartilage damage in rheumatoid arthritis. Ann Rheum Dis. 2010;69:1845-8.

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FRI0635 **ULTRASOUND IN THE ASSESSMENT OF TENOSYNOVITIS IN JUVENILE IDIOPATHIC ARTHRITIS: SYSTEMATIC LITERATURE REVIEW**

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Background: Tendon involvement is common in patients with juvenile idiopathic arthritis (JIA). Differentiating tenosynovitis and underlying arthritis may be challenging on the basis of clinical examination (CE) alone. In daily clinical practice, ultrasound (US) imaging with Doppler information can be more versatile as it allows a dynamic assessment of joint inflammation and can be done quickly at the bedside. US can reliably evaluate the location of inflammation and provide direct visualization when local steroid injection is considered as treatment for children with JIA.
Objectives: To present the published data concerning the US assessment of tenosynovitis and the US metric properties investigated in JIA.
Methods: A systematic literature review (SLR) was conducted comprising PubMed, Embase and the Cochrane Library (before June 2018). Search terms: "arthritis, juvenile" AND, "tenosynovitis OR tendinopathy" AND "ultrasonography" OR "Doppler" AND "diagnosis OR therapy management". Selection criteria: Original articles published in English reporting US, tenosynovitis and tendinopathy in the paediatric population (up to18 years old) with JIA. Data were extracted from manuscripts meeting the selection criteria, with particular focus on the definition used, scoring system applied and the US metric properties investigated. The quality of the studies was assessed using the same methodology developed for the SLR on paediatric synovitis [1].
Results: After selection, 11 articles were analysed. The tibialis posterior tendon group and peroneal tendons were the most commonly evaluated. Most authors applied the OMERACT definition proposed to rheumatoid arthritis (RA) [2] for evaluating paediatric tenosynovitis. Binary scoring system on both grey scale and Doppler was applied in most of studies. Doppler function was commonly included, with only five specifying the Doppler parameters that were used. Construct validity was reported in roughly 50% of articles, including the CE as the main comparator. However, some of those articles have shown that clinical evaluation underestimates tendon involvement. US reliability and responsiveness for tenosynovitis in JIA was rarely included.
Conclusion: Although US seems a promising image modality to assess tenosynovitis in JIA, this SLR emphasizes the definitions of US elementary lesions of RA are frequently used in children. Moreover, there is insufficient evidence of studies exploring the construct validity of the US-determined tenosynovitis in JIA. Further validation studies are needed for implementation in clinical practice and trials.

REFERENCES:

[1] Collado P. Arthritis Care Res 2012; 64:1011
[2] Wakefield R. J Rheumatol. 2005;32:2485

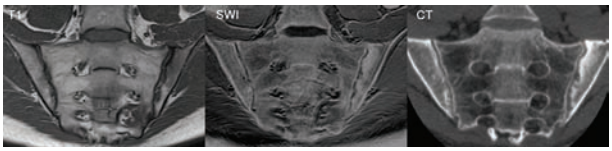
Disclosure of Interests: PAZ COLLADO: None declared, Silvia Magni-Manzoni Consultant for: Abbvie, Speakers bureau: Abbvie, MARTINA STEINER: None declared, Tracy Ting : None declared, Patricia Vega Fernandez: None declared, Clara Malattia: None declared, Ana Rodriguez: None declared, George Bruyn : None declared, Helen Keen: None declared, Lene Terslev Speakers bureau: Speakers fee from : Roche, Novartis, Pfizer, MSD, BMS, Celgene
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FRI0636 **SUSCEPTIBILITY WEIGHTED SEQUENCES IN MAGNETIC RESONANCE IMAGINGCAN CREATE COMPUTED TOMOGRAPHY-LIKE IMAGES AND IMPROVE THE ACCURACY OF STRUCTURAL LESION DETECTION OF THE SACROILIAC JOINT IN AXIAL SPONDYLOARTHRITIS**

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Background: In patients with axial spondyloarthritis (axSpA) the accurate depiction of structural lesions in magnetic resonance imaging (MRI) is impeded because MRI – while gaining signal from the bone marrow – allows only an indirect depiction of the cortical bone and sclerotic areas. Computed tomography (CT) is considered to be the gold standard as it displays the calcium-containing cortical and trabecular bone substance. However, the exhibited radiation exposure in CT limits its application in the clinical routine. Susceptibility weighted imaging (SWI) is an advanced MRI technique, that is able to visualise calcium due to its magnetic properties and allows a reconstruction of CT-like images without radiation exposure. (1)
Objectives: To investigate the diagnostic accuracy of CT-like images generated from SWI for the detection of structural lesions of the SI-joint.
Methods: Twentytwo patients with suspicion of or known axSpA were included. All patients underwent a 1.5-Tesla-MRI including T1 and SWI sequences and a low-dose CT of the sacroiliac joints. CT images were reconstructed in 4 mm oblique coronal reconstructions matching the orientation and slice thickness of the MRI. MRI and CT images were scored for erosions, sclerosis and joint space alterations applying the 24 regions method, a modification of the Berlin score. (2) Using CT as standard of reference, sensitivity (SE) and specificity (SP) values were calculated on patients' level. A score of 2 or higher in any quadrant was considered positive. The sumscores of T1 and SWI were compared to CT using Pearson's test.
Results: The mean erosion sumscore was 5.5 ± 5.5, 6.3 ± 8.2 and 5.9 ± 9.2 for T1, SWI and CT respectively. The mean sclerosis sumscore was 0.78 ± 1.5, 5.5 ± 6.5 and 6.9 ± 6.9. Five patients had joint space alterations (pseudowidening or ankylosis) in CT. Both, T1 and SWI showed an SE of 100% and a SP of 84.5% for erosions, however, the erosion sumscore corelated better for SWI (Pearson's r: 0.93) than for T1 (r: 0.64). With respect to sclerosis T1 (SE 30%, SP 100%, r 0.42) was inferior to SWI (SE 90%, SP 92%, r 0.81). It was also less

sensitive to joint space alterations (T1: SE 40%, SP 94%; SWI: SE 80%, SP 100%).
Conclusion: While T1 weighted MRI provides sufficient diagnostic accuracy for the detection of erosions, the CT-like images derived from SWI allow for a more accurate depiction of structural lesion of the SI-joint. SWI provides additional information identifying sclerosis. However, it is not suited to replace T1-weighted imaging because fatty metaplasia of the bone marrow or inside an erosion cavity cannot be detected.



REFERENCES:
[1] Bender YY, Diederichs G, Walter TC, et al. Differentiation of Osteophytes and Disc Herniations in Spinal Radiculopathy Using Susceptibility-Weighted Magnetic Resonance Imaging. Invest Radiol. 2016.
[2] Diekhoff T, Hermann KA, Greese J, et al. Comparison of MRI with radiography for detecting structural lesions of the sacroiliac joint using CT as standard of reference: results from the SIMACT study. Ann Rheum Dis. 2017.

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FRI0637 MUSCLES IN MYOSITIS PATIENTS WITH NORMAL MRI APPEARANCE HAVE HIGHER QUANTITATIVE T2 COMPARED TO THOSE IN HEALTHY CONTROLS

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Background: Myositis is an autoimmune disease which can cause a decrease in quality of life and increased mortality. Clinical presentation includes muscle weakness, myosteatosis, raised muscle enzymes and myalgia. Currently, diagnosis is reliant on subjective clinical examinations, blood tests, conventional MRI and invasive muscle biopsies. Quantitative T2 imaging offers a non-invasive measurement of muscle oedema which could help improve the understanding of muscle pathology and potentially inform diagnosis (1).
Objectives: To evaluate whether quantitative T2 MRI of muscles is sensitive enough to be able to detect differences in myositis patients compared to healthy controls, and how it compares with current radiologist scoring methods.
Methods: 19 active myositis patients (12 female, mean age 55 ± 18) diagnosed according to the Bohan and Peter myositis criteria (Mean CK 1511 ± 11291) and 19 age and gender matched healthy controls had an MRI scan of their dominant thigh. Imaging was performed using a fat-suppressed turbo-spin echo (TSE) sequence with 16 echo times, evenly spaced from 9.9ms to 153.4ms. Quantitative T2 measurements were obtained from regions of interest (ROI) drawn manually within the individual muscles that make up the quadriceps and hamstrings with no distinction made between affected and unaffected muscles. A mono-exponential fit was used to obtain an estimate of the T2 from each ROI. Two radiologists semi-quantitatively scored by consensus the muscles on a 4-point visual scale as either no oedema (0), mild oedema (1), moderate oedema (2) or severe oedema (3). In addition to MRI, all participants had knee extension and flexion measured as power and torque on an isokinetic dynamometer. Differences were assessed using independent T-tests.
Results: Quantitative T2 values were significantly higher (P=0.001) in myositis patients compared to healthy controls with mean measurements in the hamstrings (figure 1) of 47ms in patients and 40ms in healthy controls, and in the quadriceps 52ms in patients and 41ms in healthy controls, whilst muscle strength and power were significantly reduced (P=0.001). Interestingly, 8 myositis patients scored as having no oedema in the muscles by the radiologists (score = 0) still had significantly higher T2 values than 8 age and gender matched healthy controls (P=0.003 in hamstrings and P=0.001 in quadriceps) with mean T2 measurements in the hamstrings (figure 2) of 43ms in patients with no oedema and 37ms in healthy controls and in the quadriceps 43ms in patients with no oedema and 40ms in healthy controls. These results were consistent across both muscle groups and the individual muscles.
Conclusion: Quantitative T2 measurements can detect muscle differences between myositis patients and healthy control groups. They are also sensitive to differences between the muscles of myositis patients which are assessed to have no oedema by radiologist scoring, and healthy controls. This suggests that subtle systemic changes in muscle in myositis patients, which go undetected in semi-quantitative scoring, can be detected using quantitative T2 measurements. This shows the potential for T2 measurements to be a diagnostic measure in the diagnosis and management of myositis.
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REFERENCES:
[1] Maillard SM, Jones R, Owens C, Pilkington C, Woo P, Wedderburn LR, et al. Quantitative assessment of MRI T2 relaxation time of thigh muscles in juvenile dermatomyositis. Rheumatology (Oxford, England). 2004;43 (5):603-8.

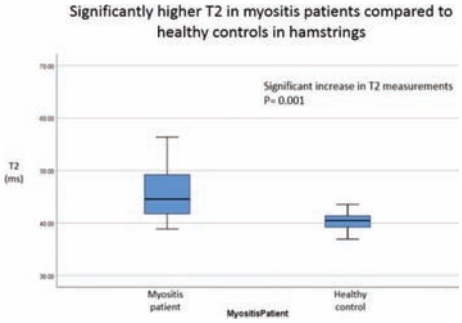


Figure 1. T2 measurements in myositis patients compared with healthy controls in the hamstrings

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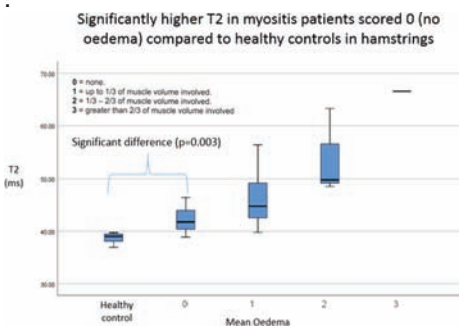


Figure 2. T2 measurements compared to semi-quantitative scores in myositis patients and healthy controls

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FRI0638 **LUMBAR SPINE BONE MASS DENSITY AS A PREDICTOR OF FRACTURES IN PATIENTS WITH COELIAC DISEASE: AN OBSERVATIONAL STUDY**

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Background: Previous studies have indicated that Lumbar spine Bone Mineral Density (BMD) could be used as an indicator to predict fractures in patients with coeliac disease (1). Patients with coeliac disease are at a higher risk of developing fragility fractures as a result of the underlying metabolic pathology. Despite previously highlighting the lumber spine BMD usefulness in predicting fractures, score systems, like the FRAX score still has not acknowledged it.Additionally recent data suggested that using a ratio of Body mass index (BMI) to BMD could increase the predictive models for fracture.
Objectives: Through a large observational study, we set out to determine the various predictors of fractures in patients with coeliac disease. Age, gender and lumber BMD were some of the factors that were considered in relation to fractures. This data was scrutinised to assess specifically the lumbar BMD's ability to predict fractures with and without using the BMI ratio.
Methods: A sample of 788 patients with coeliac disease referred for bone density estimation to a scanner in the North west of England from 2004-2010 was used to assess various predictors of fractures. Data were initially analysed using simple statistical analyses (chi-squared for categorical variables and T-test for continous variables) to compare patients who had sustained a fracture to those that had not sustained a fracture.
The data was then subject to further analysis initially using univariate and then multivariate logistic regression models. Variables analysed included Lumbar spine L1-L4 BMD, BMI/BMD ratio, gender, age at scan, family history of fractures, alcohol, smoking and rheumatoid arthritis. In order to further assess the Lumber spine BMD's vs BMI/BMD in predicting fractures, the data was further adjusted for age and gender and models compared using areas under the reciever operating characteristic (ROC) curve.
Results: Out of the 788 patients referred in the analysis period, 159 (20.2%) sustained a fracture. The mean age at the time of the scan was 55.4 (SD 14.4). A total of 576 (73.1%) were female and of those 127 (22%) had sustained a fracture. Female gender was significnatly associated with fracture ($p<0.003$). Patients with fractures were older 59.2 years (SD14) compared to 54 years (SD 14) ($p<0.001$). Using the multivariate model, it was evident that even after being adjusted for age and gender, the lumber spine BMD was a good predictor of fractures (OR 0.08 95%CI 0.02,0.3). This performed better than the ratio of BMD/BMI. AUC 0.64 vs AUC 0.62.
Conclusion: The FRAX tool should consider using lumbar spine BMD as an indicator of fragility fractures in patients with coeliac disease. We have shown using both univariate and multivariate analyses that many factors are associated with fragility fractures, but the lumber spine BMD was the best predictor. This study took the data another step further and adjusted the data for gender and age and added the ratio of BMI to BMD, but still reached a similar conclusion. Lumbar spine BMD shold be taken into consideration with more care in this group of patients.

REFERENCES:

[1] Sinha R, Bukhari M. THU0462 The Predictors of Fracture in Patients with Coeliac Disease: An Observational Study, Annals of the Rheumatic Diseases 2016;75:359.

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FRI0639 **A NOVEL SCREENING METHOD FOR HYDROXYCHLOROQUINE MACULOPATHY**

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Background: Hydroxychloroquine maculopathy is irreversible, primary prevention is done by early screening. Published data show that thinning of the retinal outer nuclear layer (ONL) is an early feature which has been described as "The flying saucer sign".
Objectives: To determine the effect of retinal outer nuclear layer thinning on the progression of hydroxychloroquine retinopathy.
Methods: We used a Heidelberg Spectralis(R) Spectral Domain Ocular Coherence Tomography (SD OCT) scanner to record the volume of the ONL in 194 eyes of 100 patients who have been on Hydroxychloroquine for 5 years or more. Volume data was analysed using the Statistical Package for Social Sciences (SPSS), we used logistic regression method to determine the probability of developing maculopathy based of the degree of reduction of the ONL volume. We correlated the loss of ONL to changes in visual fields.
Results: Mean age: 62.2 years, 20% males and 80% females. Diagnosis: 68% rheumatoid arthritis, 14% Sjogren's syndrome, 16% Systemic Lupus and 2% others. Mean duration of use was 6.3 years. Logistic regression results show strong negative correlation between the ONL volume and probability of toxicity, a reduction of 0.5 mm3 of the ONL volume carries a 51% chance of developing maculopathy ($P=0.001$), the Hosmer-Lemeshow test indicates a high significance with a high P value of 0.61. Onset and progression of visual field defects strongly correlate to loss of ONL volume of 50% or more ($P=0.000$) and age above 35 years ($P=0.0001$).
Conclusion: Outer nuclear layer volume reduction provides an accurate and objective way of predicting the development of hydroxychloroquine retinopathy, this method also helps building a cooperative relationship between ophthalmologists and rheumatologists to establish an effective screening service.

REFERENCES:

[1] I. H. Yusuf, S. Sharma, R. Luqmani and S. M. Downes, *Hydroxychloroquine retinopathy,* 2017.
[2] M. Wiącek, D. Bobrowska-Snarska, W. Lubiński, M. Brzosko and M. Modrzejewska, *What is new in recommendations on ophthalmological screening in patients treated with chloroquine and hydroxychloroquine? Update and literature review,* 2017.
[3] G. P. Smith, *High-risk category for early annual ophthalmology screening of patients receiving hydroxychloroquine,* 2017.
[4] G. Ruberto, C. Bruttini, C. Tinelli, L. Cavagna, A. Bianchi and G. Milano, "Early morpho-functional changes in patients treated with hydroxychloroquine: a prospective cohort study".
[5] J. A. Rodriguez-Padilla, T. R. Hedges, B. Monson, V. Srinivasan, M. Wojtkowski, E. Reichel, J. S. Duker, J. S. Schuman and J. G. Fujimoto, "High-speed ultra-high-resolution optical coherence tomography findings in hydroxychloroquine retinopathy," *Archives of Ophthalmology,* 2007.
[6] K. C. Iselin, P. Marti and M. Pless, "Hydroxychloroquine-Induced Retinal Toxicity," *Klinische Monatsblatter fur Augenheilkunde,* 2016.
[7] F. Babeau, T. Busetto, C. Hamel, M. Villain and V. Daien, *Adaptive optics: a tool for screening hydroxychloroquine-induced maculopathy?*, 2017.
[8] "Hydroxychloroquine and Chloroquine Retinopathy: Recommendations on Screening," 2018.

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FRI0640 **COMPARING DISEASE ACTIVITY IN THE WRIST BY REPEAT SYNOVIAL BIOPSIES, RAMRIS MAGNETIC RESONANCE SCORE AND EULAR-OMERACT ULTRASOUND SCORE: A 6-MONTH PROSPECTIVE TRIAL IN EARLY AND LONGSTANDING RHEUMATOID ARTHRITIS**

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Background: Standardized scoring systems for Rheumatoid Arthritis (RA) joint disease activity are validated in different imaging modalities and

include Larsen score for radiographs, RAMRIS for magnetic resonance imaging (MRI) and EULAR-OMERACT score for ultrasound (US). However, pairwise correlations between all three imaging modalities and their correlations with synovial histopathological assessment have not been performed.

Objectives: To investigate the relationship between histological synovitis and radiological synovitis, assessed by conventional X-ray, US and MR of the wrist radio-carpal joint.

Methods: Forty patients, 20 with treatment naive early RA (ERA) and 20 with longstanding RA (LRA), were enrolled in a 6 month prospective study. RA patients underwent US guided synovial biopsy (USGSB) of the wrist at enrollment and after 6 months. Imaging was conducted on the same hand as biopsied. MRI was performed at baseline for all, and also at 6 month for the ERA group, and scored with the RAMRIS system. Wrist X-ray was scored by Larsen score at baseline and after 6 month. Hand US examination at baseline, 3 and 6 months was scored by the EULAR-OMERACT US system. Synovial biopsy inflammation at baseline and 6 months was determined by the Krenn score, scores for CD20, CD3, CD138, CD68 staining, and classification of synovial pathotypes.

Results: In the ERA group at baseline, Krenn score was strongly correlated with both EULAR-OMERACT US combined score (r= 0.77 p<0.001) and RAMRIS MRI synovitis score (r=0.85 p<0.001), while uncorrelated at 6 months (r=0.18, p=0.38 and r=0.14, p=0.65). In the LRA group at baseline, these scores correlated strongly (r=0.83, p<0.001) to moderately (r=0.61, p=0.002), and persisted at 6 months for US score (r=0.81 p<0.001). Larsen score was not correlated with Krenn score at any point in any group. For all RA patients, change in Krenn score between baseline and 6-month biopsy, was correlated with both change in EULAR-OMERACT US combined score (r= 0.65, p<0.001) and change RAMRIS MRI synovitis score (r=0.50, p=0.03), but not to change in Larsen score. Patients with the lymphoid pathotype had higher US combined score, MRI synovitis score and Krenn-score at baseline compared to other pathotypes (all p<0.05).

Conclusion: The MRI RAMRIS synovitis score and EULAR-OMERACT US scoring system are sensitive measures of histological synovitis in LRA and ERA. After 6 months, this correlation persists in the established RA group despite effective treatment, but not in the ERA group. This suggests that ERA and LRA may have different responses to treatment intensification, possibly due to an immunological "window of opportunity" in the ERA group. Overall, significant fall in MRI/US synovitis are associated with significant fall in histological synovitis. These findings validate the use of MRI RAMRIS and EULAR-OMERACT US scores as surrogate markers of histological synovitis in established RA and early untreated RA. Synovial pathotypes have differences at baseline in degree of synovial inflammation and US and MRI imagining scores.

Disclosure of Interests: None declared

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FRI0641 THE 'SLOPE SIGN': A FEATURE OF LARGE VESSEL VASCULITIS?

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Background: Ultrasonography in large vessel vasculitis (LVV) has become popular as a non-invasive, radiation-free, point of care examination that allows assessment of entire temporal and axillary vessels. EULAR recommends ultrasound as first line imaging of giant cell arteritis (GCA) and LVV (1) and polymyalgia rheumatica (PMR).

Cranial and large vessels GCA (LV GCA) are considered the two sub types of the disease. Ultrasound in cranial GCA is well established, with the non-compressible halo of temporal arteries considered the key diagnostic finding. In LV GCA, increased intima-medial thickness (cut off >1.0 mm), is the preferred method of diagnosis.

There are other causes of thickening of arterial wall, such as atherosclerosis. Atherosclerotic US changes in US scan are localized and discrete; however, at times it may be challenging to differentiate vasculitic from atherosclerotic changes.

Objectives: We describe the 'Slope sign' as a unique additional finding in US scan of axillary arteries in LV GCA. Ultrasound scan of the axillary arteries of all these patients showed increased intima-medial thickness (IMT) > cut off value of 1.0 mm. Here we report the study of the junctional transitional region between involved and uninvolved arteries in these patients.

Methods: Images of 28 patients, with confirmed LV GCA who attended a GCA/LVV clinic at Southend Hospital between 1st September 2018 and 18th January 2019, were reviewed. They were scanned with an Esaote MyLabTwice using a LA435 linear transducer (band width 12-18 MHz). The axillary arteries were assessed in the grey scale mode in the longitudinal axis using tissue harmonic imaging. LV GCA was confirmed with an IMT of 1.0 mms or above in all patients.

Results: We observed a sloping smooth transitional zone connecting involved and uninvolved arteries (the "slope sign") in the ultrasound scan of axillary arteries in 24/28 patients with confirmed LV GCA. The remaining 4 patients did not have the transition zone imaged and therefore could not be assessed for presence of the 'slope' sign.

Table: Mean maximum and normal IMT and length of 'slope' in LV GCA patients

	Maximum (Proximal) IMT	Normal (Distal) IMT	Slope Length
Mean (SEM) mm	1.23 (0.04)	0.52 (0.03)	9.26 (0.8)

Conclusion: Presence of the 'Slope sign' in the ultrasound scan of the axillary arteries in patients with LVGCA, is a secondary confirmation alongside the abnormal IMT, of LV disease.

Biologics therapy has reduced the utility of inflammatory markers in GCA and highlighted need for imaging in disease assessment (2). The 'slope sign' may not only differentiate increased IMT of LVV from atheroma but the area under the 'slope' could potentially be used to estimate disease extent. We suggest the 'slope' sign be included in axillary artery ultrasound scan protocols for all patients with suspected GCA and also for monitoring disease activity in LVGCA.

REFERENCES:

[1] Dejaco C et al; Ann Rheum Dis 2018; 77:636-643.
[2] Coath F,et al; **Rheum (Oxford)**, https://doi.org/10.1093/rheumatology/key326

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FRI0642 USE OF MAGNETIC RESONANCE IMAGING FOR ASSESSMENT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES – A SUBANALYSIS OF THE PROMETHEUS STUDY

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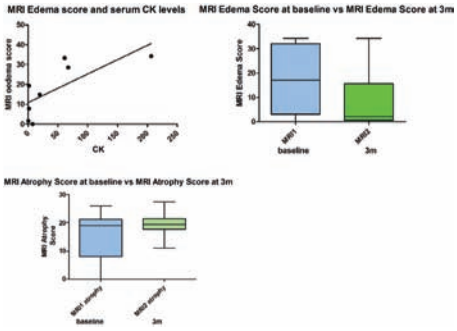
Background: Prometheus study was a prospective, randomized, assessor-blind multicenter trial, conducted to evaluate the efficacy and safety of the combination therapy with methotrexate and glucocorticoids (GC) compared to GC treatment only in patients with polymyositis (PM) and dermatomyositis (DM). Muscle MRI has been used to assess disease activity and response to treatment.

Objectives: To assess MRI findings we developed new semi-quantitative scoring method and used it for activity assessment and evaluation of treatment effect after 3 months of therapy.

Methods: In a novel semi-quantitative assessment of edema, we used scoring 0, 1, 2, and 3 according to intensity of signal in each of the 16 thigh muscles. Muscle damage was evaluated in 3 basic thigh muscle compartments and pelvic muscles using Goutallier grading (0 – 5) based on extent of fatty replacement. Both sides were assessed, an average was made for each muscle, and values were summed up in the total score. Images were scored by 2 independent evaluators and the mean was used. Manual muscle test (MMT8) and creatinkinase (CK) were measured and patient's global assessment (PGA), physician's GA (PhGA) and muscle disease activity (MDA) were recorded on visual analogue scales.

Results: Seventeen patients had MR images taken before the baseline visit, 8 had also the second MRI after 3 months of therapy. There was a significant reduction of total MRI edema score (MRI ES) after 3 months in patients with PM and DM (from the mean 17.4 points, SD 13.7 to 8.0 points, SD 12.3; p=0.025). No significant progression of fatty atrophy was observed (from 16.0 points, SD 8.8, to 19.4, SD 4.6; p=0.3). At baseline, a significant correlation between MRI ES and PGA was noted (p=0.027). There was also a borderline association of MRI ES with muscle strength evaluated by MMT 8 (p=0.053). In a subset of 8 patients with longitudinally performed two MRI evaluations we found a good correlation between

initial MRI edema score and the level of serum CK (p=0.028). However, no correlation was seen between the level of improvement in MRI ES and drop in CK or with any other clinical parameters after 3 months of treatment. The intensity of muscle edema at baseline was not predictive to improvement of any clinical parameters or CK, with a tendency to a better improvement of muscle disease activity in those who had higher MRI ES at baseline (corr. coeff. 0.445, p=0.073).



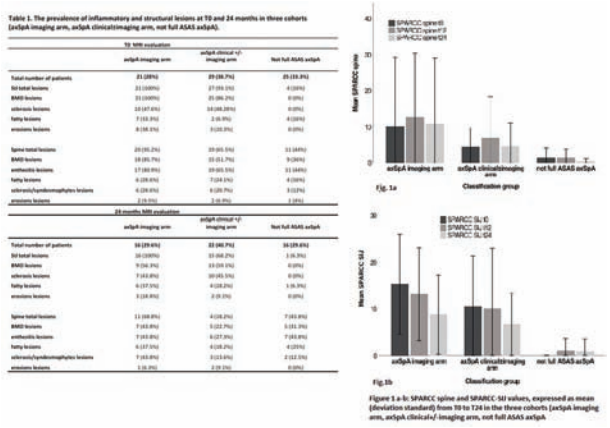
Conclusion: We proposed a new semi-quantitative scoring system for assessment of MR images in patients with PM and DM. This system was applied to record degree of muscle edema and fatty replacement in a subpopulation of patients treated in the Prometheus study. A significant reduction of MRI ES and no relevant progression of muscle atrophy and fatty replacement after 3 months of therapy was demonstrated. Initial MRI edema score correlated with some clinical and laboratory parameters (PGA, CK) but was not predictive to a degree of improvement during treatment. The results are limited by a small sample size, particularly in the subset with longitudinal MRI.**Acknowledgement:** Supported by the project (Ministry of Health, Czech Republic) for conceptual development of research organization 00023728 (Institute of Rheumatology).
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FRI0643

SPINE AND SACROILIAC JOINTS LESIONS ON MRI IN PATIENTS WITH EARLY AXIAL SPA: CORRELATION WITH CLINICAL AND DISEASE ACTIVITY INDICES IN 24-MONTHS FOLLOW UP (ITALIAN ARM OF SPACE STUDY)

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Background: Recently several studies have focused on the use of magnetic resonance imaging (MRI) that might facilitate early diagnosis and monitor the disease activity of axial spondyloarthritis (axSpA).
Objectives: Evaluate the prevalence of spine and pelvis MRI lesions in patients (pts) with low back pain (LBP) and suspected axSpA;investigate how MRI features evolve over time and relate to radiographic damage; identify the predictive factors for a more severe disease pattern with a higher probability of radiological progression.
Methods: Seventy-five pts with LBP (≥3 months, ≤2 years, onset ≤45 years) underwent a physical examination, questionnaires, laboratory tests, X-rays and MRI of the spine and sacroiliac joints (SIJ) at baseline (T0) and during a follow-up (FU) period of 24 months.Two expert rheumatologists defined axSpA diagnosis and assessed fulfilment of Assessment of SpondyloArthritis International Society ASAS criteria.Disease activity and physical functioning were assessed using: Bath Ankylosing Spondylitis Metrology Index (BASMI);Maastricht Ankylosing enthesitis Spondilities Score (MASES);Bath Ankylosing Spondylitis Disease Activity Index (BASDAI);Bath Ankylosing Spondylitis Functional Index (BASFI);Ankylosing Spondylitis disease activity score (ASDAS);Visual Analogue Scale (VAS pain);VAS night pain;VAS disease activity;Bath Ankylosing Spondylitis Patient Global Score (BASG1);BASG2;Health Assessment Questionnaire (HAQ);ESR;serum ultrasensitive CRP (hs-CRP).Spine and SIJ MRI and X-rays were scored independently by 2 readers following the SPARCC, mSASSS and score SIJ-mNY.Pts were classified in accordance ASAS criteria as:21 pts classified according to axSpA imaging arm;29 pts classified according to axSpA clinical±imaging arm;25 pts not fulfilling ASAS criteria.The Kruskal Wallis test was used to compare all indices during FU.A regression analysis was performed to identify the predictors of inflammation and radiological progression of the disease evaluated using mSASSS, score SIJ-mNY, SPARCC-SIJ and SPARCC-spine.The following independent variables were considered in this analysis:female sex,age of LBP onset,duration of LBP,presence of HLA-B27, elevated ESR/CRP, BASDAI>4, use of NSAIDs.
Results: The median LBP onset was 28.51±8.05 years, 45.3% were male, HLA-B27 was positive in 38.7% pts; 56% pts showed bone marrow edema (BME) in spine-MRI (19%,39%,33% in cervical/thoracic/lumbar region) and 61.3% pts in SIJ-MRI (respectively 58% on the right SIJ and 50% on the left SIJ).Signs of enthesitis were found in 62.7% pts (respectively 8%,58%,11% in the cervical/thoracic/lumbar spine).Eigtheen (24%) pts presented a negative BME SIJ-MRI with a positive BME spine-MRI. Predictive factors of increased radiological activity were, respectively, for a higher SPARCC-spine score, a higher use of NSAIDs and for a higher SPARCC-SIJ score, the presence of HLA-B27 and increased ESR/CRP. The prevalence of BME lesions on MRI and SPARCC-SIJ decreased during the FU period in the 2 cohorts that met the ASAS criteria for axSpA (**Table 1, Figure 1a-b**).



Conclusion: At T0 a significant prevalence of BME lesions was observed both for SIJ and the spine, with predominant involvement of thoracic district.Since positive spine-MRI images were observed in absence of sacroiliitis, we can hyphothesize that this finding could have a diagnostic significance in suspected axSpA.Further studies are warranted to assess in a more exhaustive manner the role of imaging in the monitoring of activity disease and radiological progression.**Disclosure of Interests:** None declared
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FRI0644

ANALYSIS OF CARDIOVASCULAR RISK AND CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH PSORIASIS

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Background: Psoriasis (Ps) is associated with atherosclerosis and an increased risk of cardiovascular disease (CVR). Currently, a new automated ultrasound software, based on radio frequency, called QIMT (*quantitative intima media thickness)* technology, proved to be a useful method for assessing subclinical atherosclerosis with the measurement of the intima-media thickness (IMT) in carotid arteries[1,2].
Objectives: To analyze the ultrasound results of the QIMT and Framingham score for psoriasis patients submitted to two types of treatments: methotrexate (MTX) and tumor necrosis factor inhibitor (TNF-α).
Methods: Fifty patients with psoriasis in plaques, were divided into two groups, using MTX and using TNF-α (infliximab and adalimumab). We

evaluated the measurement of abdominal circumference, blood pressure, body mass index (BMI) and presence of metabolic syndrome (SM). In addition, we evaluated cardiovascular risk with the Framingham score and IMT of the two common carotid arteries using automatic software (QIMT) and laboratory tests, including fasting glycemia and total cholesterol, fractions and triglycerides. Data were analyzed using the t-student, chi-square test and the Mann-Whitney test. For the evaluation of the CVR, univariate and multivariate logistic regression analyzes were performed. The level of significance (α) adopted was 5%, being considered statistically significant values of $p < 0.05$.

Results: Total of 50 patients in the study, 25 were on MTX (group 1) and 25 were on anti-TNF-α (group 2). Mean age was 54.8 (± 12.5) with a slight male predominance (58%). Total cholesterol, HDL, LDL and triglycerides were altered in 50%, 76%, 30% and 42% of patients, respectively. Overall, 84% of the patients had high waist circumference and 82% had a BMI above the ideal. There was a statistically significant difference ($p < 0.05$) between the groups for metabolic syndrome results (68% vs. 32%); 44% of the patients in group 1 presented Framingham score intermediate to high and 28% of group 2, and in relation to the QIMT, 56% of group 1 and 72% of group 2 showed higher than expected ($p > 0.05$). For the correlation between QIMT and Framingham Score, the Pearson (r) linear correlation coefficient found was 0.617 ($p < 0.001$), indicating a moderate to strong positive association. The cross-sectional analysis does not provide information on causality and the protective or non-protective effect of the aforementioned therapies in relation to cardiovascular risk was not evaluated.

Conclusion: The results show that patients with Ps have high rates of metabolic syndrome and subclinical atherosclerosis. There was a positive association correlating the Framingham score values with the QIMT measurement, providing evidence for the use of ultrasound in clinical practice.

REFERENCES:

[1]-Di
Geso L, Zardi EM, Afeltra A, Salaffi F, Carotti M, Gutierrez M, et al. Comparison between conventional and automated software-guided ultrasound assessment of bilateral common carotids intima-media thickness in patients with rheumatic diseases. Clinical Rheumatolgy. 2012;31:881-884.

[2] -Mendonça JA, Andrade BB, Aquino JLB, Leandro-Merhi VA, Damian GB. Spectral Doppler and automated software-guided ultrasound assessment of bilateral common carotid intima-media thickness in spondyloarthritis: is there a correlation with clinical findings? Drugs in Context. 2018;7:1-9.

Disclosure of Interests: None declared

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FRI0645 EVALUATION OF MARKETED KITS FOR MEASUREMENT OF ABP 501, THE FIRST APPROVED ADALIMUMAB BIOSIMILAR, DRUG CONCENTRATION AND ANTI-DRUG ANTIBODY LEVELS IN PATIENT SERUM

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Background: Adalimumab and its biosimilars are anti-tumour necrosis factor (TNF)- monoclonal antibodies that are approved in Europe as treatment for various autoimmune-related indications, including Crohn's disease and ulcerative colitis. Despite the clinical success of adalimumab, some patients show a diminished response after prolonged treatment. It is known that serum adalimumab trough levels are correlated with clinical response and the development of anti-adalimumab antibodies (AAA) may negatively impact trough levels. Currently, therapeutic drug monitoring (TDM) is used to measure adalimumab concentration and/or AAA allowing individualized optimization of treatment regimens. This then facilitates better clinical outcomes by avoiding delay in treatment decisions. Therefore, having a single assay that provides reliable TDM for both adalimumab and adalimumab biosimilars is important for physicians and patients. ABP 501, the first adalimumab biosimilar, is approved for the same indications as adalimumab (except those protected by regulatory exclusivity).

Objectives: The aim of this study was to evaluate the Promonitor® TDM kits for measurement of drug levels and AAA in serum samples from a selected representative subset of subjects, treated with ABP 501 or adalimumab reference product (RP) in the phase 3 study (NCT01970475).

Methods: A total of 30 subjects (15 ADA-positive; 15 ADA-negative) served as a representative subset in this evaluation. AAA positive control antibody and serum samples from subjects treated with either ABP 501 or adalimumab RP in the Phase 3 study were used to assess the suitability of the TDM (Promonitor®) kits for AAA (Promonitor® ANTI-ADL) and quantitative drug detection (Promonitor® ADL).

Results: The Promonitor®-ANTI-ADL TDM kit was able to detect a low level (10 ng/ml) of AAA positive control antibodies for ABP 501. In subjects whose serum was evaluated (18 treated with ABP 501 adalimumab biosimilar and 10 treated with adalimumab RP), the TDM kit produced 100% concordant positive or negative AAA results when compared to the assay that had been used in the phase 3 study. The quantitative drug assessment in subjects whose serum was evaluated (11 treated with ABP 501 and 9 treated with adalimumab RP) using the Promonitor® ADL TDM kit displayed a high degree of correlation (average Pearson's r = 0.987) compared with results obtained in the phase 3 study.

Conclusion: This evaluation indicates that the Promonitor® kits are suitable for use in routine detection of AAA and in quantitating serum levels of the ABP 501 adalimumab biosimilar in patients.

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Disclosure of Interests: Dan Mytych Shareholder of: Amgen, Employee of: Amgen, Marta Starcevic Manning Shareholder of: Amgen, Employee of: Amgen, Alexander Colbert Shareholder of: Amgen, Employee of: Amgen, Sarah Hoofring Shareholder of: Amgen, Employee of: Amgen, Jill Miller Shareholder of: Amgen, Employee of: Amgen, Melissa Gessner Shareholder of: Amgen, Employee of: Amgen, Vincent Chow Shareholder of: Amgen, Employee of: Amgen, Gary Fanjiang Shareholder of: Amgen, Employee of: Amgen

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FRI0646 EFFECT OF LONG-TERM MEDIUM-DOSE STEROID TREATMENT ON 18F-FDG PET/CT FINDINGS TO ASSESS VASCULAR AND MUSCULOESKELETAL INVOLVEMENT IN PATIENTSWITH POLYMYALGIA REUMATICA

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Background: Fluorine-18-fluorodeoxyglucose (^{18}F-FDG) PET/CT has been proposed as a promising tool for assessing both musculoskeletal and vascular involvement in patients with polymyalgia rheumatica (PMR). Glucocorticoids (GC) may decrease the intensity of ^{18}F-FDG uptake. Therefore, performance of PET/CT before steroid therapy is recommended. However, in many patients with PMR, large vessel vasculitis (LVV) is precisely suspected because of steroid resistance after a long-term treatment with GC [1].

Objectives: Our aim was to assess the influence of long-term medium-dose treatment on ^{18}F-FDG uptake to discern if ^{18}F FDG PET/CT could be useful to evaluate musculoskeletal and vascular involvement in patients under treatment with GC.

Methods: Single-center study of 75 patients with PMR diagnosis based on 2012 EULAR/ACR criteria. All patients underwent a PET/CT scan due to LVV suspicion based on the presence of atypical symptoms and/or persistent symptoms despite steroid therapy. We considered two groups: a) Steroid-naïve PMR patients. b) Steroid-resistant PMR patients. Both musculoskeletal and vascular ^{18}F-FDG uptake was assessed. The statistical analysis was performed with SPSS. Student´s t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher´s exact test for categorical variables as appropriate.

Results: We evaluated 75 patients, 27 men and 48 women (mean age ± SD: 68.2 ± 10.7 years). PET/CT was performed in 14 steroid-naïve PMR patients (18.7%) and 61 steroid-resistant PMR patients (81.3%). Patients under steroid treatment had received a median dose of Prednisone of 10.0 [5.0-15.0] mg/day during 9.0 [2.0-22.0] months. Vascular ^{18}F-FDG uptake was more frequently detected in steroid-naïve patients. In regard with musculoskeletal ^{18}F-FDG uptake, no statistically significant differences were seen between both groups (**TABLE**).

TABLE

	PMR patients (N=75)	Steroid-naive patients (n=14)	Steroid-resistant patients (n=61)	P#
Sex (women), n (%)	48 (64.0)	7 (50.0)	41 (67.2)	0.23
Age (years), mean ± SD	68.2 ± 10.7	65.5 ± 11.4	69.9 ± 10.5	0.29
ESR (mm/1st h), median [IQR]	41.0 [24.0-68.0]	43.5 [23.3-68.5]	41.0 [24.0-66.5]	0.92
CRP (mg/dL), median [IQR]	1.3[0.7-3.6]	1.6 [0.6-7.8]	1.3 [0.8-3.5]	0.77
F-FDG uptake				
Shoulders	45 (60.0)	9 (64.3)	36 (59.0)	0.72
Sternoclavicular joints	33 (44.0)	7 (50.0)	26 (42.6)	0.62
Hips	32 (42.7)	8 (57.1)	24 (39.3)	0.23
Cervical interspinous bursae	9 (12.0)	2 (14.3)	7 (11.5)	0.77
Lumbar interspinous bursae	29 (38.7)	4 (28.6)	25 (41.0)	0.40
Pubic symphysis	4 (5.3)	2 (14.3)	2 (3.3)	0.16
Subtrochanteric bursae	20 (26.7)	3 (21.4)	17 (27.9)	0.62
Ischial tuberosities	19 (25.3)	2 (14.3)	17 (27.9)	0.30
Knees	33 (44.0)	7 (50.0)	26 (42.6)	0.62
LVV	51 (68.0)	13 (92.9)	38 (62.3)	**0.027**

Comparisons between steroid-naïve patients and patients receiving corticosteroids

Conclusion: Vascular ^{18}F-FDG uptake detection was higher in PMR patients with LVV suspicion who had never received GC. However, PET/CT was also useful to detect vascular involvement in most of the patients under a long-term medium-dose steroid treatment.

REFERENCE:

[1] D. Prieto-Peña, I. Martínez-Rodríguez, J. Loricera, et al. Predictors of positive (18)F-FDG PET/CT-scan for large vessel vasculitis in patients with persistent polymyalgia rheumatica. Semin Arthritis Rheum; 2018): Doi: 10.1016/j.semarthrit.2018.05.007. [Epub ahead of print]

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FRI0647 COST-EFFECTIVENESS OF RHEUMATOLOGY ULTRASOUND: RETROSPECTIVE AUDIT OF THE AINTREE ULTRASOUND CLINIC

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Background: Ultrasound is useful to guide escalation of synthetic disease-modifying antirheumatic drugs (sDMARDs) and optimization of biologic DMARD therapy (bDMARDs) in inflammatory arthritis. However, there is limited published evidence of the cost effectiveness of the use of ultrasound in selecting patients for treatment tapering or escalation avoidance [1].
Objectives: To evaluate the usefulness of a Rheumatology-led Ultrasound Clinic.
Methods: Retrospective descriptive analysis of patients evaluated in the Aintree Ultrasound Clinic between January and September 2018. Our Ultrasound Clinic runs once a week and the scans are performed by expert rheumatologists (2 EFSUMB level 3, 1 advance EULAR level). Patients can be referred by specialist nurses or by other rheumatologists. Synovitis is assessed following EULAR/OMERACT guidelines.
Results: 113 patients were analysed and 10 patients were excluded (7 did not attend and 3 excluded due to not enough information available). The mean time from referral to ultrasound was 48.17 days (SD 20.21). Forty seven patients (42%) were referred by a doctor and 65 patients (58%) by a specialist nurse. Rheumatoid arthritis was the most frequent diagnosis with 74 patients (66%), other inflammatory arthritis in 23 patients (23%) and other non inflammatory conditions in 16 patients (14%). The indication for scan was to exclude subclinical inflammation (n=91, 81%), to exclude inflammatory arthritis (n=15, 13%) with not clear referral question in 7 patients (6%). The ultrasound was positive for inflammation (defined as >= power doppler OMERACT grade 2 in at least 1 joint)) in 37 patients (33%) all of whom had their treatment changed: sDMARD escalation (n=10), initiation bDMARD (n= 4), change of bDMARD(n=2) and steroid therapy (intraarticular or intramuscular injection) the same day of the scan (n= 28). Fifty eight patients were on sDMARD treatment: 14 patients had a change in treatment based on the scan (4 patients started biologic drugs, 10 patients had sDMARD escalation). There was no change of treatment in 44 patients, 7 of whom were being considered for bDMARDs before scan. Three of the 29 patients on bDMARD had a change of treatment based on the scan (2 changed to other biologic, in 1 patient another sDMARD was added). Steroids were administered the same day of the scan to 28 patients (intraarticular injection 10; intramuscular injection 18).
Conclusion: Ultrasound altered our management in most patients (n=108, 96%). Avoiding escalation to biologics in 7 patients who met clinical criteria saved an estimate of £35,000. We conclude that point of care ultrasound in patients with inflammatory arthritis is cost effective, not only in saving unnecessary escalation to high cost drugs but by prompt treatment of those with active disease.

REFERENCES: :

[1] Simpson E, Hock E, Stevenson M, Wong R, Dracup N, Wailoo A, et al. What is the added value of ultrasound joint examination for monitoring synovitis in rheumatoid arthritis and can it be used to guide treatment decisions? A systematic review and cost-effectiveness analysis. Health Technol Assess 2018;22(20).

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3124

FRI0648 USEFULNESS OF THE ULTRASOUND IN THE DECISION-MAKING PROCESS ABOUT THE USE OF BIOLOGICALS IN PATIENTS WITH RHEUMATOID ARTHRITIS – EXPERIENCE OF REAL LIFE IN A MIDDLE NCOME COUNTRY

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Background: Rheumatoid arthritis (RA) is an inflammatory autoimmune disease with a prevalence of 0.5 to 1% and the advances in pharmacological treatments offered to manage the disease have achieved many goals; however, the appearance of biologics has made the treatment of RA very costly, which has a great impact in the developing countries where accessibility to these therapies is lower. On the other hand, we now know that patients who are in clinical remission of disease activity by clinimetry in a significant percentage of cases may have the so-called subclinical activity that is found using ultrasound (US).
Objectives: To evaluate the usefulness of ultrasound within the component of evaluation of patients with moderate-severe activity of the disease before they are taken to a medical board making-decision process about the initiation or switching of biologics.
Methods: Once a rheumatologist has identified a patient RA with clinical indication for biological therapy, patient is sent, among other things, to a medical board to take a collegiate decision about beginning or switching of biologic therapy. Between 24 and 72 hours before the medical board decision, the patient undergoes an US (normally 12 joints are measured plus those clinically committed at that time), in order to determine if it presents disease activity by US which is considered negative for activity if the patient has synovitis ≤ 1 or has Power Doppler ≤ 1 in a single joint.
Results: During 12 months, 988 patients had clinical indication for using biologic based on moderate or high disease activity; they were evaluated by a multidisciplinary team to define the appropriateness of a therapy; mean DAS28 of patients was 4.81 ± 1.37; Once the patients were evaluated by US, the medical board of decisions did not in all cases decide to initiate or change a biological treatment.; the choices made by the team were: 30% initiated or re-initiated biological therapy, in 29% of cases the team decided to wait and continuing observing the patient, 22% were switched to other biologic therapies, 12% did not have indication to start biological therapy because no activity by US and in 5% the medication dose was adjusted. Thus, in a total of 41% of the patients, biological therapy was not started or changed, which is important from the point of view not only clinical but also of the health payers.

Conclusion: Basically, this study shows that in patients with clinical indication of biological therapy by RA activity, a previous evaluation and a ultrasound are necessary in order to have a more accurate approach in making decisions; ultrasound is a practical, real-life, low-cost test to define activity in RA patients. Also we avoid high costs therapies for the management of rheumatoid arthritis, therefore we contribute not only to the health outcomes of patients but the health economic aspects in the management of RA.

Disclosure of Interests: Edwin Castillo: None declared, Michael Cabrera: None declared, Diana Buitrago-Garcia: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Eva Cardozo: None declared, Ivania Ramirez: None declared, Danny Gomez: None declared, Sandra Farietta: None declared

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FRI0649 PREVALENCE OF ANCA AND ANA IN PATIENTS WITH PULMONARY TUBERCULOSIS

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Background: Tuberculosis is known to have diverse clinical presentations, some of which may mimic systemic autoimmune diseases like ANCA associated vasculitis and systemic lupus erythematous (SLE) [1]. Considering the paucity of specific biomarkers in rheumatologic practices, caution needs to be applied while interpreting ANA and ANCA results, especially in TB endemic areas. Previous studies on prevalence of autoantibodies in tuberculosis have shown contrasting results [2, 3, 4].

Objectives: To study the prevalence of ANCA subtypes and ANA in patients with bacteriologically confirmed pulmonary tuberculosis.

Methods: Patients with bacteriologically confirmed pulmonary tuberculosis were screened for recruitment. Anti-PR3, anti-MPO, anti-lactoferrin and anti-elastase ANCA subtypes were tested using enzyme-linked immunosorbent assay (ELISA). ANA was done by Indirect immunofluorescence (IIF) using Hep 2 cell lines. Patients who were positive for ANA were tested for presence for various extractable nuclear antigens using line immunoassay.

Results: Eighty nine patient were recruited in the study. Median age was 28 (range 20 – 46) years. The bacteriological confirmation was done via sputum examination in 81 (79 smear and 2 Gene Xpert) patients and bronchoalveolar lavage (BAL) fluid in 8 patients (5 smear and Gene Xpert). Out of 89, 62 patients were treatment naïve for pulmonary TB. The clinical features were fever (70%), Cough (99%), expectoration (99%), dyspnea(25%), hemoptysis(25%) and chest pain(13.5%),. The radiological features were consolidation (61%), reticulonodular opacities (50%), cavity (44%), bronchiectasis (6%) and pleural effusion (8%).Among ANCA subtypes, anti-elastase was the most common and was positive in 86 (96.62%) patients, followed by anti-PR3 seen in 7 (7.8%) patients. No sera were found positive for anti-MPO and anti-lactoferrin antibodies. Six (6.7%) patients had positive ANA (IIF).Line immunoassay in these patients was positive for SS-A/Ro-52 and U1-RNP in one patient each.

Conclusion: Anti PR3 ANCA positivity can be detected in patients with pulmonary tuberculosis and should be interpreted with caution in tuberculosis endemic areas. Anti-elastase ANCA was detected in majority of these patients and its role in differentiating tuberculosis from ANCA associated vasculitis needs further exploration.

REFERENCES:

[1] Al-Hadad I, Taha O. TB, or not TB: That is the question. Respir Med CME. 2010;3:192–4.
[2] Lima I, Oliveira RC, Cabral MS, Atta A, Marchi S, Reis E, et al. Anti-PR3 and anti-MPO antibodies are not present in sera of patients with pulmonary tuberculosis. Rheumatol Int. 2014;34:1231–4
[3] Huan G, Yang G, Xiao-yu Q, Jiancheng X, Yan-qing S, Huan G, et al. Antineutrophil cytoplasmic antibodies in Chinese patients with tuberculosis. Rev Soc Bras Med Trop. 2018;51:475–8.
[4] Elkayam O, Caspi D, Lidgi M, Segal R. Auto-antibody profiles in patients with active pulmonary tuberculosis. Int J Tuberc Lung Dis. 2007;11:306–10

Disclosure of Interests: None declared

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FRI0650 A NAILFOLD CAPILLAROSCOPY STUDY IN A COHORT OF PATIENTS WITH ANTI-PHOSPHOLIPID ANTIBODIES

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Background: Nailfold capillaroscopy (NC) is a simple and non-invasive diagnostic technique, able to investigate microvascular features. In subjects with anti-phospholipid autoantibodies (aPL) many different endothelial abnormalities have been described.

Objectives: We aimed to investigate the role of NC in aPL positive (aPL +) subjects, highlighting the main microvascular alterations, detected by NC.

Methods: We enrolled 39 patients with primary anti-phospholipids syndrome (pAPS) (32 females, mean age 43 years, mean disease duration 7 years), 47 patients with secondary anti-phospholipis syndrome (sAPS) due to Systemic Lupus Erythematosus (36 females, mean age 44 years, mean disease duration 15.5 years) and 17 aPL+ subjects without any autoimmune disease, defined as aPL carriers (16 females, mean age 42 years). All subjects underwent clinical and laboratory evaluations as well as NC with both characterization of morfological parameters and attribution of a semiquantitative score.

Results: The main NC findings were: morphological alterations (tortuous, bushy and/or ramified capillary) in 100% patients with pAPS, in 77% sAPS patients and in 88% aPL carriers; microhaemorragies in 56% pAPS patients, in 49% sAPS patients and 24% aPL carriers; enlarged hairpins in 23%, 41% and 18% subjects with pAPS, sAPS and aPL carriers respectively. In 6.3% sAPS patients, an early scleroderma pattern was detected.

A NC semiquantitative score 1 was found in 58.9% pAPS patients, in 57.4% sAPS patients and in 70.5% aPL carriers. Among those cases with abnormal NC findings, we found that a higher NC score (>2) was significantly more frequent in pAPS (21.7%) and sAPS (22.2%) patients respect to aPL carrier cases (8.3%) (p<0,005).

We also found, among the main cardiovascular risk factors, that a higher score (1) was significantly associated with the presence of diabetes mellitus in pAPS patients (p< 0,0001) and with arterial hypertension (p<0,0004) and dyslipidemia (p<0,0007) both in sAPS patients and aPL carriers.

Conclusion: Our findings show that some NC aspecific abnormalities are more frequently found in aPL positive subjects, mainly in pAPS and sAPS ones. Altough not specific, such NC features seem to be associated with the presence of vascular risk factors.

Thus NC could be regarded as a useful tool in order to evaluate microcirculation in aPL positive cases.

REFERENCES:

[1] Tavakol ME et al, Biomed Res Int 2015; 2015: 974530.
[2] Maricq HR et al, Arthritis Rheum 1980; 23: 183 – 188.
[3] Vaz JLP et al, Rheumatology 2004;43:1025–7.
[4] Sulli A, J Rheum 2000;27:1574–6.
[5] Aslanidis S, Clin Exp Rheum 2011;29:307–9.

Disclosure of Interests: massimiliano vasile: None declared, Katia Stefanantoni Consultant for: Only 1 scientific advice for Italfarmaco in 2016, Fulvia Ceccarelli: None declared, Elena Marafioti: None declared, fabrizio conti: None declared, Valeria Riccieri: None declared, Guido Valesini: None declared

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FRI0651 **THE CLINICAL IMPLICATION OF NASAL BIOPSY FOR CLASSIFYING GRANULOMATOSIS WITH POLYANGIITIS IN PATIENTS WITH RHINOSINUSITIS: A SINGLE CENTRE RETROSPECTIVE STUDY**

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Background: Granulomatosis with polyangiitis(GPA) mainly involves the upper and lower respiratory tracts and kidneys and induces necrotising vasculitis and granuloma. Nasal biopsy has been recommended in GPA-suspected patients to not only completely cure chronic rhinosinusitis, but also clearly discriminate its aetiologies.
Objectives: We investigated whether the classification of GPA could be made without nasal biopsy in immunosuppressant drug-naïve 45 patients with chronic rhinosinusitis who had previously been classified as GPA.
Methods: We retrospectively reviewed the medical records of 45 patients with GPA. Twenty-six patients exhibited chronic rhinosinusitis, among which 16 patients underwent nasal biopsy (10 with granuloma and 6 without granuloma). We applied the 2007 European Medicines Agency algorithm for the classification of GPA, the 2012 Chapel Hill Consensus Conferences Nomenclature of Vasculitis and the 2017 American College of Rheumatology/European League Against Rheumatism provisional classification criteria for GPA to them for reclassifying GPA. (Figure1)
Results: The mean age was 58.4 years and 17 patients were men. There were no differences in clinical and laboratory results between those with and without granuloma. Among 6 patients without granuloma on nasal biopsy, 3 patients with only ANCAs and chronic rhinosinusitis could be classified as GPA due to PR3-ANCA (or C-ANCA) positivity.
Among 9 patients without nasal biopsy, 3 patients with only chronic rhinosinusitis could be classified as GPA due to GPA-specific lung lesions. (Table 1) When we excluded an item of granuloma in 10 GPA patients with granuloma on nasal biopsy, 4 patients without ANCAs could be classified as GPA due to GPA-specific lung lesions and cartilaginous involvement. (Table 2)

Figure1. The algorithm for GPA patients with chronic rhinosinusitis

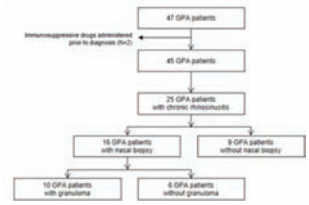


Table1 fulfilment of the 2007 EMA algorithm and the 2017 ACR/EULAR provisional criteria in 9 patients with chronic rhinosinusitis and without nasal biopsy

Patient number	PR3-ANCA or C-ANCA	MPO-ANCA or P-ANCA	GPA surrogate marker (the 2007 EMA algorithm)	Positive items (scores) (the 2017 ACR/EULAR provisional criteria)	Total score
1	Yes	No	Chronic sinusitis, Septal perforation	Sino-nasal congestion (3) Cartilaginous involvement (2), PR3-ANCA (or C-ANCA) (5), Nodule on Chest imaging (2)	12
2	Yes	No	Chronic sinusitis, Nasal crust	Sino-nasal congestion and nasal crusting (3), PR3-ANCA (or C-ANCA) (5)	8
3	No	Yes	Chronic sinusitis, Septal perforation	Sino-nasal congestion (3), Cartilaginous involvement (2), Nodule on Chest imaging (2)	7
4	Yes	No	Chronic sinusitis, Subglottic stenosis	Sino-nasal congestion (3), Cartilaginous involvement (2), PR3-ANCA (or C-ANCA) (5), Nodule on Chest imaging (2)	12
5	Yes	No	Chronic sinusitis, Otitis media	Sino-nasal congestion (3), Hearing reduction (1), PR3-ANCA (or C-ANCA) (5),	9
6	No	Yes	**Chronic sinusitis**	Sino-nasal congestion (3), **Nodule on Chest imaging (2)**	5
7	No	Yes	**Chronic sinusitis**	Sino-nasal congestion (3), **Nodule on Chest imaging (2)**	5
8	Yes	No	**Chronic sinusitis**	Sino-nasal congestion (3), PR3-ANCA (or C-ANCA) (5), **Nodule on Chest imaging (2)**	10
9	Yes	No	Chronic sinusitis, Subglottic stenosis	Sino-nasal congestion (3), Cartilaginous involvement (2), PR3-ANCA (or C-ANCA) (5)	10

Table2 Reassessment of the fulfilment of the 2007 EMA algorithm and the 2017 ACR/EULAR provisional criteria in 10 patients with chronic rhinosinusitis and granuloma on nasal biopsy by excluding granuloma on nasal biopsy

Patient number	PR3-ANCA or C-ANCA	MPO-ANCA or P-ANCA	GPA surrogate marker (the 2007 EMA algorithm)	Positive items (score) (the 2017 ACR/EULAR provisional criteria)	Total score
1	No	Yes	Chronic sinusitis, Otitis media Saddle nose	Sino-nasal congestion (3), Hearing reduction (1), Nodule on chest imaging (2)	6
2	**No**	**No**	Chronic sinusitis, Nasal crusting, Otitis media	Sino-nasal congestion (3), Hearing reduction (1), **Nodule on chest imaging (2)**	6
3	Yes	No	Chronic sinusitis, Otitis media	Sino-nasal congestion (3), Hearing reduction (1), Cartilaginous involvement (2), PR3-ANCA (or C-ANCA) (5), Nodule on chest imaging (2)	13
4	Yes	No	Chronic sinusitis, Hoarseness	Sino-nasal congestion (3), Cartilaginous involvement (2), PR3-ANCA (or C-ANCA) (5)	10
5	**No**	**No**	Chronic sinusitis, Septal perforation,	Sino-nasal congestion (3), **Cartilaginous involvement (2)**	5
6	Yes	No	Chronic sinusitis, Otitis media	Sino-nasal congestion (3), Hearing reduction (1), PR3-ANCA (or C-ANCA) (5), Nodule on chest imaging (2)	11
7	**No**	**No**	Chronic sinusitis, Septal perforation	Sino-nasal congestion (3), **Cartilaginous involvement (2)**	5
8	**No**	**No**	Chronic sinusitis	Sino-nasal congestion (3), **Nodule on chest imaging (2)**	5
9	Yes	No	Chronic sinusitis, Nasal crusting, Otitis media	Sino-nasal congestion (3), Hearing reduction (1), PR3-ANCA (or C-ANCA) (5), Nodule on chest imaging (2)	11
10	No	Yes	Chronic sinusitis, Nasal crusting	Sino-nasal congestion (3), Nodule on chest imaging (2)	5

Conclusion: Nasal biopsy is necessary and useful for classifying GPA. However, nasal biopsy could be replaced with PR3-ANCA (or C-ANCA) positivity, GPA-specific lung lesions and cartilaginous involvement in GPA suspected patients with chronic rhinosinusitis.

REFERENCES:

[1] Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013;65(1):1-11.

[2] Comarmond C, Cacoub P. Granulomatosis with polyangiitis (Wegener): clinical aspects and treatment. Autoimmun Rev. 2014;13(11):1121-5.

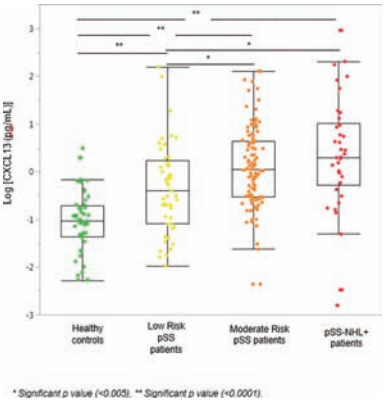
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Epidemiology, risk factors for disease or disease progression

FRI0652 **SERUM CXCL13 LEVELS ARE ASSOCIATED WITH LYMPHOMA RISK AND LYMPHOMA OCCURRENCE IN PRIMARY SJÖGREN'S SYNDROME**

Emmanuella Traianos[1], James Locke[1], Dennis Lendrem[1], Simon J. Bowman[2], Ben Hargreaves[3], Victoria Macrae[3], Jessica Tarn[1], Wan Fai Ng[1,3], UK primary Sjögren's syndrome registry study group. *[1]Newcastle University, Institute of Cellular Medicine, Newcastle upon Tyne, United Kingdom; [2]University Hospitals Birmingham, Birmingham, United Kingdom; [3]NIHR Newcastle Biomedical Research Center, Newcastle upon Tyne, United Kingdom*

Background: Primary Sjögren's syndrome (pSS) is an autoimmune disease characterized by an increased risk for non-Hodgkin lymphoma (NHL) development. Ectopic germinal center (GC) formation in the salivary gland (SG) epithelium of pSS patients is thought to be associated with high risk for pSS-associated NHL. The chemokine (C-X-C motif) ligand 13 (CXCL13) is a major chemoattractant for B cell migration into the GC, plays an important role in the organization of B cell follicles, and enhances BCR-triggered B cell activation. The increased B cell activation within ectopic GC may lead to excessive B cell proliferation and along with genetic abnormalities may drive the transition from the early clusters of GC B cells through oligoclonal and later monoclonal B cell expansion to lymphoma.
Objectives: To investigate the potential of CXCL13 as a biomarker to assess NHL risk in pSS.
Methods: Serum CXCL13 concentrations were quantified by ELISA in 48 healthy individuals, 165 pSS patients without NHL and 38 pSS patients with NHL from the United Kingdom Primary Sjögren's Syndrome Registry (UKPSSR). Among these patients, follow-up serum samples from 83 and 11 patients without and with NHL respectively were available and CXCL13 measured. PSS patients without NHL were stratified into low risk (LR), moderate risk (MR) and high risk (HR) groups according to the lymphoma risk assessment tool proposed by Fragkioudaki et al, 2016. Differences in CXCL13 levels among risk groups were analyzed using the Mann-Whitney test and differences in CXCL13 levels between initial (visit 1) and follow-up (visit 2) samples were measured by repeated measures MANOVA. Associations of CXCL13 with B cell markers were determined by Pearson correlation. Logistic regression analyses were performed to model the NHL risk against CXCL13 concentrations.
Results: At visit 1, there were 24 LR, 58 MR and 1 HR pSS patients. Because of the small sample size of the HR "group", it was excluded from further analyses. Serum CXCL13 levels were higher in all pSS groups compared to healthy controls (p <0.0001), and the levels in patients with a history of NHL were higher compared to those without (p =0.0311). Visit 1 LR patients had significantly lower CXCL13 levels than MR patients (p =0.0015) and pSS patients with NHL (p =0.0017). Serum CXCL13 levels remained stable between visit 1 and visit 2 (mean time between visits = 4 years) for all pSS groups. CXCL13 was associated with B cell markers, including Immunoglobulin G (IgG) (p = 0.0014), B-cell activating factor (p < 0.0001), beta-2 microglobulin (p < 0.0001), combined free light chains (p < 0.0001), κ light chain (p < 0.0001), λ light chain (p = 0.0002), κ-to-λ ratio (p = 0.0013), and Anti-SSA/Ro autoantibodies (p = 0.0005). Finally, serum CXCL13 levels, age, IgM, IgA, and white blood cell count were independent predictors of NHL risk score in pSS.
Conclusion: Our findings have demonstrated that serum CXCL13 levels were elevated in pSS patients with NHL and MR pSS patients compared to LR pSS patients and remained stable between visit 1 and visit 2. CXCL13 was an independent determinant of NHL risk score and could potentially be used as an additional NHL risk biomarker in pSS.



REFERENCES:

[1] Fragkioudaki S, Mavragani C, Moutsopoulos H. Predicting the risk for lymphoma development in Sjogren syndrome. Medicine. 2016;95(25): e3766.

Table 1. – NHL risk predictors for pSS patients without lymphoma at Visit 1

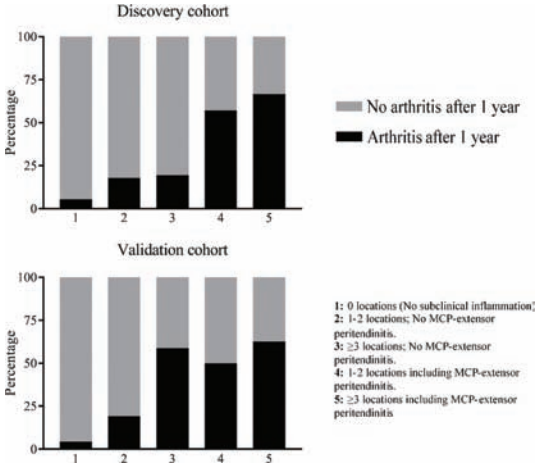
NHL Risk predictors	Likelihood ratio ChiSquare Value	Prob>ChiSq
IgA	6.6459	0.0360*
IgM	12.065	0.0024*
Disease duration	5.4365	0.0660
Age	18.546	<.0001*
Log [White blood cell count]	6.1494	0.0462*
Log [CXCL13 c(pg/mL)]	8.3463	0.0154*

Disclosure of Interests: Emmanuella Traianos: None declared, James Locke: None declared, Dennis Lendrem: None declared, Simon J. Bowman Grant/research support from: PreviouslyUCB Pharma (to University of Birmingham) and Roche, Consultant for: 2016-7: Novartis, Mitsubishi Tanabe Pharma 2017-8: AstraZeneca, MedImmune, GFK, Xtlbio, ONO Pharmaceutical 2018-9: Novartis, AstraZeneca, UCB Pharma, Ben Hargreaves: None declared, Victoria Macrae: None declared, Jessica Tarn: None declared, Wan Fai Ng: None declared
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FRI0653 IMPROVING AND VALIDATING THE PREDICTIVE ACCURACY OF MRI DETECTED SUBCLINICAL INFLAMMATION FOR RHEUMATOID ARTHRITIS DEVELOPMENT IN CLINICALLY SUSPECT ARTHRALGIA

Xanthe Matthijssen[1], Fenne Wouters[1], Debbie Boeters[1], Aleid Boer[1], Yousra Dakkak[1], Ellis Niemantsverdriet[1], Saskia Le Cessie[1], Annette van der Helm - van Mil[1,2]. *[1]Leiden University Medical Center (LUMC), Leiden, Netherlands; [2]Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands*

Background: Presence of MRI-detected subclinical joint inflammation in clinically suspect arthralgia (CSA) is predictive for progression to Rheumatoid Arthritis. Despite high negative predictive values (94%); its positive predictive value (PPV) is moderate (31%).
Objectives: We studied if, in addition to the presence of inflammation, incorporating information on severity, number and combinations of MRI-inflammatory locations improves the predictive accuracy.
Methods: In the discovery cohort, 225 CSA-patients were followed on clinical arthritis development. Contrast-enhanced 1.5T MRIs were made of unilateral MCP(2-5), wrist and MTP(1-5)-joints at baseline and scored for synovitis, tenosynovitis and bone marrow edema. Severity, number and combination of locations (joint/tendon/bone) with subclinical inflammation were determined, with symptom-free controls of similar age category as reference. Cox regression was used for predictor selection. Predictive values were determined at 1-year follow-up. Results were validated in 266 CSA-patients.
Results: In both cohorts 15% developed arthritis <1-year. The number of locations with subclinical inflammation (1-2 locations HR 2.54 (1.11-5.82); ≥3 locations HR 3.75 (1.49-9.48)) and presence of MCP-extensor peritendinitis (HR 4.38 (2.07-9.25)) were independently predictive. Severity and combinations of inflammatory lesions were not. Based on these variables, five risk categories were defined: no subclinical inflammation, 1-2/≥3 locations, with/without MCP-extensor peritendinitis. PPVs ranged 5% (lowest category; NPV 95%) - 67% (highest category). Similar findings were obtained in the validation cohort; PPVs ranged 4% (lowest category; NPV 96%) - 63% (highest category).
Conclusion: Incorporation of the number of locations with subclinical inflammation and MCP-extensor peritendinitis in MRI-evaluation improved risk stratification, yielding PPVs up to 63-67%. This promotes optimal use of MRI-data in an evidence-based way.
Disclosure of Interests: Xanthe Matthijssen: None declared, Fenne Wouters: None declared, Debbie Boeters: None declared, Aleid Boer: None declared, Yousra Dakkak: None declared, Ellis Niemantsverdriet: None declared, Saskia Le Cessie: None declared, Annette van der Helm - van Mil Grant/research support from: The research leading to these results has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (Starting grant, agreement No 714312) and from the Dutch Arthritis Foundation.
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Observed. percentage of patients that developed clinical arthritis in the first year (PPVs in black) per risk category in the discovery and validation cohorts.

FRI0654 DECREASING INCIDENCE OF CARDIOVASCULAR DISEASE IN PATIENTS WITH INCIDENT RHEUMATOID ARTHRITIS IN RECENT YEARS

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Background: There is a recognized excess burden of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) as compared to the general population. Several studies suggested reduced CVD mortality in RA in recent decades [1-3]. Longitudinal studies on trends in occurrence of CVD events in RA patients over time, and studies comparing trends in CVD events in RA vs general population are lacking.
Objectives: 1) To assess trends in incidence of CVD in patients with incident RA in 1980-2009; and 2) To compare incidence of CVD in RA patients vs non-RA subjects with RA incidence/index date in 2000-09.
Methods: The study population comprised Olmsted County, Minnesota residents with incident RA (age ≥18 years, 1987 ACR criteria met in 1980-2009) and non-RA subjects from the same underlying population with similar age, sex and calendar year of index. All subjects were followed until death, migration, or 12/31/2016. Follow-up was truncated for comparability. Incident CVD events included myocardial infarction (MI), stroke (ischemic or hemorrhagic), coronary heart disease (CHD) death and first occurrence of any of these. Patients with CVD events prior to RA incidence/index date were excluded. Cox proportional hazards models were used to compare incident CVD events by decade, adjusting for age and sex. Cumulative incidence of CVD events adjusted for death from other causes was also computed.
Results: The study included 906 patients with RA (mean age 55.9 years; 69% female). There were 201, 299 and 406 patients with incident RA in 1980-89, 1990-99 and 2000-09, respectively. During median follow-up of 10.6, 10.4 and 10.2 years per decade, CVD events occurred in 31, 38,

and 31 patients. Patients with incident RA in 2000–09 had markedly lower cumulative incidence of any CVD events than patients diagnosed in 1990s and 1980s (Figure). Hazard ratios (HR) for any CVD events demonstrated significant reduction in CVD events among patients with incident RA in 2000s compared with incident RA in 1980s (HR: 0.52; 95% confidence interval (CI): 0.32-0.86) and a reduction approaching significance compared with incident RA in 1990s (HR: 0.65; 95% CI: 0.40-1.05).
Patients with incident RA in 2000s were compared with 405 patients without RA in 2000s who experienced 30 CVD events during follow-up. Patients with incident RA in 2000s had no excess in CVD events over subjects without RA (HR: 0.88, 95% CI: 0.53-1.46). Results were similar for MI, stroke and CHD deaths when examined separately.

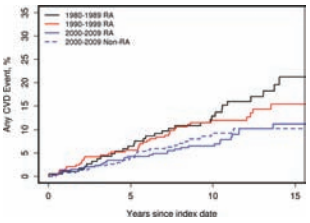


Figure. Cumulative incidence of any CVD event in RA and non-RA patients by decade of RA incidence/index.

Conclusion: Our findings show a dramatic reduction in incidence of major CVD events in RA in recent decades. The gap in CVD occurrence between RA patients and the general population may be closing. These findings may reflect increased awareness, improved primary CVD prevention and more optimal RA disease management in recent years. More studies are needed to understand the reasons and implications of these trends.

REFERENCES:

[1] Myasoedova E, et al. J Rheumatol 2017, 44(6):732-9.
[2] Kerola AM, et al. Clin Exp Rheumatol 2015, 33(3):391-8.
[3] Lacaille D, et al. Ann Rheum Dis 2017, 76(6):1057-63.

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FRI0655 THE IMPACT OF PREGNANCY ON STRUCTURAL PROGRESSION IN PREMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

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Background: Disease activity often improves during pregnancy and worsens at the postpartum period [1]. The long-term effect of pregnancy on radiographic joint damage progression among premenopausal women with RA has been barely studied.
Objectives: The aim of this study was to analyse the impact of pregnancy on radiographic progression in premenopausal women with RA.
Methods: This is an observational cohort study of RA patients included in the Swiss Clinical Quality Management in Rheumatoid Arthritis (SCQM-RA). Patients enrolled are followed-up yearly and have radiographic assessments at regular intervals. Information about female reproductive factors, such as pregnancies, breastfeeding and hormonal treatment were retrospectively retrieved using a questionnaire. For this analysis we included premenopausal women with at least two radiographic assessment and full information on reproductive factors. The primary outcome was the rate of radiographic progression (Ratingen erosion score). We analysed the radiographic progression between premenopausal women with at least one pregnancy and those with no pregnancies. Baseline time was the first radiographic assessment. We used a multilevel regression model for longitudinal data, adjusted for potential confounders, such as baseline age, disease duration, DAS-28 and treatment.
Results: Among 1966 women who were interviewed, 430 premenopausal women with sequential radiographic assessments during follow-up were analysed. Half of premenopausal women had at least one pregnancy. Women with at least one pregnancy were older than nulliparous (median of 41 vs 36 years, p<0.001) and had longer disease duration (median of 3.4 vs 2.6 years, p=0.04) (Table 1). During follow-up, the rate of radiographic progression was lower in women with pregnancies than in nulliparous women [(0.9% (95% CI: 0.0 to 1.9) vs 2.1% (95% CI: 0.9 to 3.1) over 10 years, respectively, p=0.04, Figure 1]. In a sub-analysis, the rate of radiographic progression appeared to be lower during the 13-year period after first pregnancy than after this period [(0.2% (95% CI: -0.8 to 1.3) vs 2.6% (95% CI: 1.3 to 3.9) over 13 years, respectively, p=0.003]. We found no difference in the rate of radiographic progression between women with a single pregnancy and multiparous women.
Conclusion: In premenopausal women with RA, joint damage progressed more rapidly in nulliparous women than in women with at least one pregnancy. However, we cannot make any definite causal inference, since it is well possible that women renouncing getting pregnant might be patients with more severe disease. Radiographic progression appeared to increase the longer the time since pregnancy.

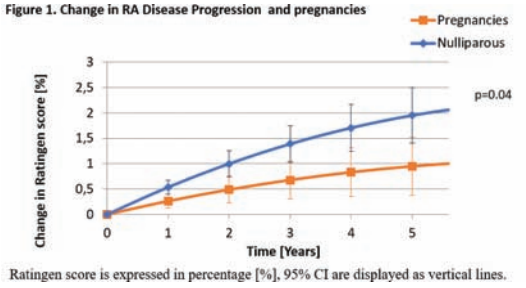
REFERENCES:

[1] Ince-Askan H, et al. J Rheumatol 2016;43 :22-5.

Table 1. Baseline characteristics of premenopausal women of SCQM cohort

General and disease characteristics	Women with pregnancies n= 213	Nulliparous women n=217
Age, years, median(IQR)	41 (36-45) *	36 (29-43)
Ever smoking, n (%)	56 (26)	66 (30)
Alcohol consumption, n (%)	129 (61)	112 (52)
Disease duration, years, median (IQR)	3.4 (0.6-8.0) *	2.6 (0.4-7.4)
Seropositive (ACPA or RF positive), n (%)	175 (82)	180 (83)
DAS 28, median(IQR)	3.6 (2.6-4.9)	3.6 (2.4-4.8)
HAQ-DI, median (IQR)	0.6 (0.3-1.3)	0.6 (0.3-1.3)
Erosion score,%, median (IQR)	1.0 (0.3-4.9)	1.4 (0.1-5.0) *
DMARD treatment, n (%)	181 (85)	186 (86)
Biologic treatment, n (%)	70 (33)	72 (33)

*p-value <0.05. DAS28: 28-joint Disease Activity Score ESR; HAQ-DI: Health Assessment Questionnaire –Disability Index; DMARD: disease-modifying antirheumatic drugs.



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FRI0656 ENVIRONMENTAL AND ATMOSPHERIC FACTORS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A REGRESSION ANALYSIS

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Background: Understanding the role of environmental exposures in the development of SLE and their association with SLE activity may help identify modifiable risk factors and potential etiological mechanisms
Objectives: We hypothesized that changes in fine particulate matter (PM2.5) concentration, ozone concentration, temperature, resultant wind, relative humidity, and barometric pressure are predictive of organ specific flares in lupus.
Methods: 1628 patients who fulfill 4 of the 11 ACR or SLICC classification criteria for SLE were included in the analysis. The data ranged from 1999 to 2017. Maximum distance between visits was 110 days with 1-month time aggregation units. Disease activity was expressed as Physician Global Estimate (PGA), taken at

every patient visit. A flare was defined as a PGA score increase of 1 point or more compared to the previous visit. Environmental and atmospheric data was obtained from the EPA, including PM2.5 and ozone concentration, temperature, residual wind, relative humidity, and barometric pressure. The average values of each factor 10 days prior to patient visit was calculated. Univariate and multivariate models were built in order to study the association of these variables with lupus disease activity. The models were adjusted for age, sex, income, racial distribution, and rural vs. urban patient residence. Multivariate logistic regression was used to identify significant determinants associated with lupus flares. Regression was performed for each organ flare outcome. Regression inference was based on generalized estimating equations (GEE) to account for the time repeated outcomes. Standard regression techniques on model building and evaluation were followed, including but not limited to performing both univariate and multivariate regressions, coefficient significance, collinearity, confounding, variable interactions and reductions in model AIC.

Results: Rash, serositis, hematologic, and joint flares were statistically significantly associated (p<0.0.5) with an increase in temperature in univariate and multivariate analysis. Renal flares were negatively associated with increases in temperature (p<0.05) in univariate and multivariate analysis.

PM2.5 concentration was significantly associated (p<0.001) with rash, joints, serositis, neurologic, pulmonary, and hematologic flares in univariate and multivariate analysis.

Ozone concentration, residual wind, and relative humidity were significantly associated with lupus flares in univariate analysis only, while barometric pressure had no associations.

Conclusion: There is a strong association between changes in PM2.5 concentration and temperature 10 days prior to patient visit and organ specific lupus activity at the visit. These data could add an important aspect to lupus trials, the outcomes of which may be affected by so far unrecognized environmental factors, and ultimately it could allow predictive modelling of lupus flares which would revolutionize the approach to treatment.

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FRI0657 METABOLIC SYNDROME PRECEDES THE ONSET OF HIP AND KNEE PAIN AND THE RISK IS NOT MODIFIED BY DIET OR CHANGES IN BMI

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Background: Excess weight and components of the metabolic syndrome have been associated with knee osteoarthritis (OA). However, the precise timing of when this risk operates in the natural history of the disease is unknown. An understanding of the sequence in which risk factors operate in OA is important for delivering effective preventative interventions.

Objectives: We examined longitudinal data from a large prospective population-based cohort to assess the association between metabolic syndrome components and the subsequent development of either knee or hip over 10 years of follow-up.

Methods: Known risk factors data were obtained at enrolment to the EPIC-Norfolk cohort between 1993 and 1997. Data were available on anthropometric variables, smoking status and lipid metabolites. Knee and hip pain were self-reported at 18 months, 3 and 10 years when respondents answered whether they had had pain in their knee or hip on most days in the preceding month. Metabolic syndrome components were defined in line with the Alberti formula. Logistic regression was used to investigate metabolic syndrome components: waist circumference (men >102cm, women >88cm), low HDL (men <1mmol/L, women <1.3mmol/L), high triglycerides (>1.7mmol/L) and their association to incident pain and any effect-modification of dietary patterns and changes in BMI over time.

Results: Amongst 20,517 respondents (age at enrolment 59.7 years (SD 9.2), 56.5% female) there were 3,886 who reported knee pain and 2,467 who reported hip pain at 18 months. By the end of follow-up there were 2619 who had developed incident knee pain and 1752 who had developed incident hip pain. In a logistic model adjusted for age and sex, significant associations were seen for incident pain for ever-smoking (knee: odds ratio 1.22, 95% CI 1.11, 1.33 p<0.001), (hip: odds ratio 1.21, 95% CI 1.08, 1.35 p=0.001) and obesity (knee: OR = 1.70 95% CI 1.51, 1.91 p<0.001), (hip: OR = 1.68 95% CI 1.47, 1.92 p<0.001). After adjustment for obesity, components of the metabolic syndrome associated with pain included waist circumference (knee: OR = 1.17 95% CI 1.03, 1.33 p=0.019), (hip: OR = 1.37 95% CI 1.17, 1.59 p<0.001) and for knee pain, low HDL (OR = 1.15 95% CI 1.05, 1.27 p=0.003) and high triglycerides (OR = 1.10 95% CI 1.00, 1.21 p=0.043). These association were not modified by dietary patterns nor changes in weight over the follow-up interval.

Conclusion: This longitudinal analysis shows that metabolic syndrome is a predictor for the future onset of hip and knee pain over an interval of 10 years and the risk is not modified by diet or subsequent weight change. These data suggest that preventative strategies need to be targeted early in the disease course, and should include a range of measures including smoking cessation and those that prevent the onset of metabolic syndrome.

Disclosure of Interests: None declared

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FRI0658 INCIDENCE AND PREVALENCE OF VACCINE PREVENTABLE INFECTIONS IN ADULT PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES (AIIRD): A SYSTEMIC LITERATURE REVIEW INFORMING THE 2019 UPDATE OF THE EULAR RECOMMENDATIONS FOR VACCINATION IN ADULT PATIENTS WITH AIIRD

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Background: Despite the well-established fact of a high burden of infections among patients with autoimmune inflammatory rheumatic diseases (AIIRD)1, little evidence is available regarding the real incidence and prevalence of vaccine preventable infections (VPI) in this population.

Objectives: To update the evidence on the incidence and prevalence rates of VPI in patients with AIIRD and compare the data to the general population when available.

Methods: A systematic literature review was performed using Medline, Embase, and Cochrane library, from October 2009 to August 2018. Search terms were defined for AIIRD and VPI. Observational studies including cohort studies for incidence rates and cross-sectional studies for prevalence rates were included, as well as systematic reviews of cohort studies and meta-analyses. The primary outcome was the incidence or prevalence of VPI in the adult AIIRD population. Meta-analysis was performed when appropriate.

Results: The search identified 3876 records, out of which 63 met the inclusion criteria. Data on the following VPI rates was retrieved and analyzed: influenza (incidence; n=4), pneumococcal disease (incidence; n=7), hepatitis B virus (HBV) (incidence and prevalence; n=10), herpes zoster (HZ) (incidence; n=29), human papilloma virus (HPV) (incidence and prevalence; n=13). For influenza, limited data pointed to an increased incidence (409.33 vs 306.12 cases per 100,000 patient-years in patients with rheumatoid arthritis (RA) vs controls, respectively) and influenza-related complications in patients with AIIRD. Data on pneumococcal disease, available mainly for patients with systemic lupus erythematosus (SLE), showed a substantially increased risk in all age groups compared to controls (incidence rate ratio (IRR) 4.7, 95% confidence interval (CI) 3.7-6.0). For HZ, an increased risk was observed across all patients with AIIRD in comparison to the general population: pooled incidence rate ratio 2.4, 95% CI 2.05-2.76, with the highest incidence rate (IR) observed in inflammatory myositis (pooled IR 35.98, 95% CI 32.33-39.64), followed by SLE (pooled IR 18.87, 95% CI 8.7-29.64), and RA (pooled IR 11.64, 95% 9.37-13.91). Studies on HPV mainly investigated the SLE population in the Latin America and Asia: HPV pooled prevalence 26%, 95% CI 17%-36% and pooled prevalence ratio 1.58, 95% CI 0.74-3.36 in comparison with the general population. In RA, limited data showed a similar prevalence of HPV in patients and controls: pooled prevalence ratio 0.72, 95% CI 0.46-1.12. For hepatitis B virus, pooled prevalence of hepatitis B surface antigen in patients with AIIRD was similar to the general population, 3%, 95% CI 1%-5%.

Conclusion: Current evidence shows an increased risk of vaccine-preventable infections in patients with AIIRD, emphasizing that prevention of infections is essential in these patients.

REFERENCES:

[1] Falagas ME, Manta KG, Betsi GI, et al. Clin Rheumatol 2007;26(5):663-70.

Disclosure of Interests: Victoria Furer: None declared, Christien Rondaan: None declared, Marloes W. Heijstek: None declared, Ulf Müller-Ladner Grant/research support from: Projekt supported by an unrestricted educational grant from Celgene GmbH., Sander van Assen: None declared, Jacob M. van Laar Grant/research support from: Genentech, Consultant for: F. Hoffmann-La Roche, Marc Bijl: None declared, Ori Elkayam: None declared

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FRI0659

REMISSION PERSISTENCE IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS UNDER BIOLOGIC TREATMENT

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Background: Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) under biologic treatment are increasingly achieving prolonged remission and tapering treatment is becoming standard practice. However, the optimal timing to start tapering remains unclear and predictors of loss of remission (LOR) are missing. Guidelines disagree on whether to wait for 6 or 12 months of sustained remission before tapering.

Objectives: To determine whether longer sustained remission (6 versus 12 months) influences subsequent LOR rates and to identify predictors of LOR.

Methods: We used the Rheumatic Diseases Portuguese Register (Reuma.pt), to identify RA, PsA and axSpA patients on stable biologic treatment in a single center and retrospectively analyze those who achieved sustained remission for at least 6 and 12 months. Survival analysis was used to characterize stability of remission and identify predictors of LOR. The Cox proportional hazards regression was stratified by diagnosis and adjusted for age, gender, smoking, baseline disease activity, type of biologic, previous switches and starting year of biologic treatment.

Results: 195 patients (100 RA, 51 PsA and 44 AxSpA) of 1078 patients (785 RA, 116 PsA, 177 axSpA) registered in Reuma.pt at a single center and treated with biologics between 1999 and 2018, had at least one remission period with a minimal duration of 6 months. This corresponded to 310 individual remission periods longer than 6 months, 232 of which (74.8%) were longer than 12 months. Median remission time (since the start of remission period) was 78.6 weeks overall vs. 99.0 weeks for patients with a minimum 12 months remission (difference in median survival: 20.4 weeks). PsA patients showed significantly longer remission periods (p<0.0001), followed by axSpA and RA. We identified active smoking (HR 1.96, p=0.008 for the total population; HR 1.53, p=0.20; HR 7.42, p=0.01, HR 0.74, p=0.79 for RA, PsA and axSpA, respectively), and infliximab use (HR 2.23, p=0.005 for the total population; HR 4.07, p<0.001, HR 3.20, p=0.36, HR 0.62, p=0.62 for RA, PsA and axSpA, respectively; subcutaneous TNF inhibitors (TNFi) used as index category) to be significantly associated with LOR. A sensitivity analysis excluding infliximab patients further suggested female gender (HR 3.21, p=0.005) and duration of disease until first biologic (HR 1.05, p=0.031) as important co-variates.

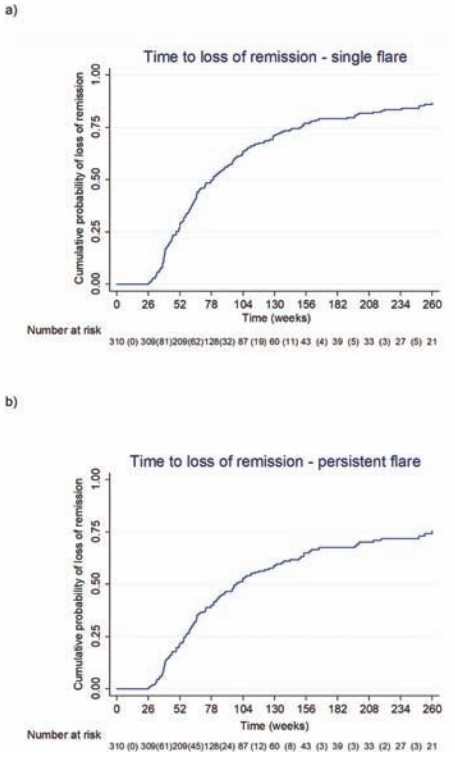


Figure 1. – time to loss of remission considering a single flare (a) vs. persistent flare (b), all patients (minimum 150 days in remission). Number of failure events indicated in parenthesis

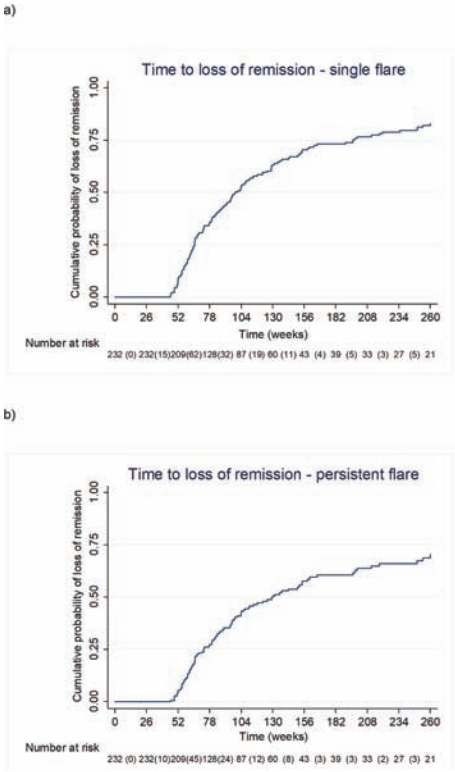


Figure 2. – time to loss of remission considering a single flare (a) vs. persistent flare (b), only patients with minimum 320 days in remission. Number of failure events indicated in parenthesis.

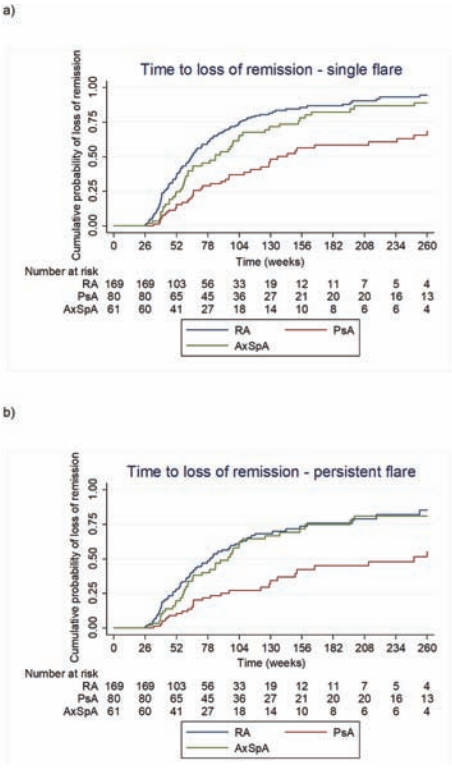


Figure 3. – time to loss of remission considering a single flare (a) vs. persistent flare (b) by diagnosis, all patients (minimum 150 days in remission).

Conclusion: 6 vs. 12 months of sustained remission did not influence the subsequent rate of LOR. Smoking, the type of TNFi, female gender and duration of disease until biologic treatment were identified as predictors of LOR.

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FRI0660 LONG- AND SHORT-TERM ASSOCIATION OF LOW-GRADE SYSTEMIC INFLAMMATION WITH CARDIOVASCULAR MORTALITY

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Background: Evidence suggests a critical role for inflammation in the pathogenesis of coronary artery/heart disease (CAD/CHD), implicating inflammatory molecules as central mediators of chronic inflammatory processes within the vascular wall. In this regard, patients with chronic inflammatory disease such as RA and SLE are at increased risk, which was attributed to the high levels of inflammatory mediators. However, less is known about the association of low-grade systemic inflammation with the cardiovascular risk.

Objectives: The aim of the present study was therefore to evaluate biomarkers representing low-grade systemic inflammation and their association with mortality in a large cohort of patients.

Methods: The Ludwigshafen Risk and Cardiovascular Health (LURIC) study included 3316 consecutive patients undergoing coronary angiography between June 1997 and May 2001 with a median follow-up of 9.9 years. Before coronary angiography fasting blood samples were collected and plasma levels of interleukin-6 (IL-6), C-reactive protein (CRP) and serum amyloid A (SAA) were measured by immunonephelometry. IL-6 and SAA polymorphisms were genotyped.

Results: During a median observation time of 9.9 years 949 deaths (30.3%) occurred, of these 597 (19.2%) died from cardiovascular events. Plasma levels of IL-6, CRP and SAA were associated with unstable CAD as well as established risk factors including type 2 diabetes, smoking, lower eGFR, lower triglycerides and lower HDL-C. In addition, IL-6 correlated with age, use of lipid lowering therapy and hypertension, SAA correlated with female gender and hypertension, and CRP correlated with female gender, lipid-lowering therapy and BMI. After adjustment for established cardiovascular risk markers and the other two inflammatory markers, SAA was found an independent risk factor for cardiovascular mortality after a short-term follow-up (1 year) with a HR of 1.41 (1.03-1.93, p=0.030), whereas IL-6 was identified as an independent risk factor for long-term follow-up (3, 5-9.9 years) with HRs of 1.21 (1.02-1.43, p=0.006), 1.22 (1.06-1.40, p=0.006) and 1.18 (1.07-1.31, p=0.001), respectively. Although 6 SNPs in the SAA gene were significantly associated with SAA plasma concentrations (none of the IL-6 SNPs associated with IL-6 levels), the genetic risk score was not associated with mortality.

Conclusion: In our large, long-term LURIC cohort study we demonstrate for the first time prospectively that plasma levels of IL-6 and SAA are not only associated with cardiovascular risk factors and the prevalence of CAD but also independently predicted cardiovascular mortality. These findings underline the importance of low-grade systemic inflammation for the cardiovascular risk and the prognostic relevance of inflammatory biomarkers, independently predicting cardiovascular mortality. Although it was not the focus of this study, our findings might suggest that even low-grade inflammation is unfavourable in chronic rheumatic disease.

Disclosure of Interests: None declared

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FRI0661 ASSOCIATIONS OF CURRENT AND CHILDHOOD SOCIOECONOMIC STATUS WITH PATIENT-REPORTED HEALTH OUTCOMES AMONG PATIENTS WITH KNEE OR HIP OSTEOARTHRITIS IN A FAMILY PRACTICE SETTING IN MEXICO CITY

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Background: The life-course approach is a useful framework to understanding socioeconomic inequalities in the prevalence and outcomes of chronic disease,[1] and in particular in osteoarthritis (OA).[2] Previous studies have measured Socioeconomic Status (SES) in 2 points of the life-course (childhood and current) and found consistent relationships between them and both prevalence and presence of worse outcomes,[2-4] but this relationship has been little explored in the Latin-American region where exposure to low SES throughout the life-course is higher than in developed countries.

Objectives: Our aim was to investigate the association of current and childhood SES with functional status, quality of life and disability among patients with knee or hip OA.

Methods: We recruited patients with self-reported doctor-diagnosed knee or hip OA in a social security family practice setting, excluding patients with other rheumatic diseases liable to causing secondary OA. We measured current SES by education, occupation type and estimated income using a validated tool;[5] and childhood SES by parental education and occupation type. We measured functional status, quality of life and disability using Spanish-language versions of the WOMAC,[6] AMICAL[7] and HAQ-DI [8] tools. We used Spearman correlations, ANOVA and multiple linear regression to test for significance, with a $p<0.05$ cutpoint.

Results: We recruited 146 patients with a mean age of 69.4 yr. 80% were female; 92%, 30% and 45% suffered from knee, hip and other joint OA, respectively, while 60% had incomes in the upper 2 quintiles of the general Mexican population. We found current income to be the best predictor of WOMAC (Spearman's ρ=-0.354, $p<0.01$), AMICAL (ρ=-0.362, $p<0.01$) and HAQ-DI scores (ρ=-0.335, $p<0.01$), and education to be correlated with all three scores as well. Occupation type was significantly associated with AMICAL and HAQ-DI but not WOMAC scores. Paternal and maternal education, and maternal occupation type, were significantly associated only with AMICAL scores.

In multiple linear regression models were income and maternal education were entered separately, after adjusting for age, sex, BMI and presence of Diabetes and Hypertension, both variables were significantly associated with WOMAC, AMICAL and HAQ-DI scores (adj $r^2$0.076-0.157, $p<0.05$). When both variables were entered into multiple linear regression models (adj r^2 0.112 and 0.110), significant associations remained between current income level and WOMAC and AMICAL scores ($p<0.01$), as well as between maternal education and AMICAL scores ($p<0.05$). Associations between both variables and HAQ-DI scores did not reach statistical significance ($p=0.07$).

Conclusion: Among patients with knee or hip OA in our setting, current SES is a significant predictor of functional status, quality of life and disability, while childhood SES – best modeled by maternal education – is a significant predictor of quality of life. More research is needed to elucidate the relationship of SES throughout the life course with outcomes among patients with OA.

REFERENCES:

[1] Ben-Shlomo Y, Kuh D. Int J of Epidemiol. 2002; 31(2): 285–293.
[2] Luong M-LN, et al. Aging Health. 2012;8(4):413-37.
[3] Baldassari AR, et al. BMC Musculoskelet Disord. 2013;14(1).
[4] Baldassari AR, et al. Arthritis Care Res. 2013;65(8):1334-42.
[5] Gutiérrez JP, et al. Salud Pública México. 2015;57(4):298.
[6] López Alonso SR, et al. Aten Primaria. 2009;41(11):613-20.
[7] Espinoza-Cuervo G, et al. Reumatología Clínica. 2014;10(14):201-274.
[8] González VM, et al. Arthritis Rheum. 1995;38(10):1429-46.

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FRI0662 ACTIVATION AND LEUKOCYTE ADHESION IS ASSOCIATED WITH VASCULAR DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Patients with inflammatory rheumatic diseases, such as rheumatoid arthritis (RA) or psoriatic arthritis (PsA), have a higher cardiovascular risk than the general population. There are data in other pathologies about the role of leukocyte adhesion on endothelial damage.
Objectives: To evaluate the relationship between leukocyte adhesion and subclinical vascular damage in patients with RA and PsA.
Methods: Observational, cross-sectional exploratory study. Patients with RA and PsA who had at least one previous vascular study were recruited in a tertiary hospital during a period of 3 months. All of them donated a sample of fresh blood. Neutrophils were isolated and perfused on a monolayer of healthy endothelial cells of the umbilical cord vein to evaluate its degree of activation, determining the leukocyte adhesion parameter. The expression of different adhesion molecules was analyzed by flow cytometry. We also gathered demographic (sex, age, BMI), clinical (disease duration, classical CV risk factors) and analytical (CRP, ESR) variables. The previous vascular study consisted of an exploration of the extracranial carotid tree with an Esaote MyLab70XVG ultrasound scanner with a linear probe (7-12mHz) and an automated program for measuring the carotid intima-media thickness (CIMT) using ("Quality intima media thickness in real-time, QIMT"), the presence of atheroma plaques as per the Mannheim consensus and the measurement of pulse wave velocity (VOP) using the Mobil or graph® device. We consider as pathological the vascular study with the presence of abnormal plaque and/or IMT (> 900µ) and/or VOP (≥ 10m/s). The statistical analysis was performed with the SPSS Statistics 22.0 program.
Results: We included 27 patients, 18 women and 9 men, with a mean age of 58.07 (SD 11.64). Eight patients were diagnosed with RA and 19 with PsA, with mean disease duration of 14 years (SD 7.14). Of these 27 patients, 15 were on biologics, 11 were treated only with DMARDs and one patient was naïve for any immunomodulatory treatment. In addition, 14 (51.9%) were taking NSAIDs and 7 (25.9%) glucocorticoids.
Regarding cardiovascular risk factors, 51.9% were exposed to tobacco, 25.9% suffered hypertension, 37% were dyslipidemic, 11% were diabetic and 11% were obese, with an average of 1.41 classic cardiovascular risk factors (SD 1.36) per patient. The previous vascular study had been considered pathological in 44.4% of the patients.
A tendency to greater leukocyte adhesion was observed in those patients with pathological IMT values (p =0.059) and in those patients who presented atheromatous plaque (p = 0.66). No significant associations were found in relation to the rest of the adhesion parameters analyzed, nor could subanalysis be performed due to the small sample size.
Conclusion: Our preliminary data suggest that an increase in leukocyte adhesion on the endothelium is involved in the mechanisms of subclinical atherosclerosis in patients with RA and PsA. Studies with a larger sample size will allow us to confirm these findings, as well as the factors implicated in their development.

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FRI0663 TREATMENT WITH BIOLOGIC DRUGS OF PREGNANT WOMEN WITH AUTOIMMUNE DISEASE, EXPERIENCE OF A REFERENCE CENTER IN HIGH RISK PREGNANCY AND AUTOIMMUNE DISEASES

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Background: Autoimmune diseases predominantly affect women of childbearing age. These women must be without clinical activity before conception, which is usually achieved thanks to immunosuppressive drugs. Also, information on new drugs does not include their possible effects on pregnancy because pregnant women are usually excluded from clinical trials.
Objectives: The aim of the study is to evaluate the safety of biological drugs (BD) in pregnant patients with different autoimmune diseases (AD).
Methods: Patients were prospectively followed in a reference Spanish center for high-risk pregnancies and AD. Follow-up was performed by a multidisciplinary team with at least one obstetrician and one expert clinician in autoimmune diseases. Females exposed to BD during the periconceptional period or during pregnancy were included in the study. Obstetric and neonatal outcomes were assessed.
Results: Between 2015 and 2018 we identified 37 exposed pregnancies in 35 women affected by different AD. At the start of pregnancy, 18 patients were taking infliximab, 11 adalimumab, 3 natalizumab, 2 rituximab, 1 etanercept y 1 tocilizumab.
The AD that required BD were Crohn's disease (20 patients, 54.1%), ulcerative colitis (7, 18.9%), rheumatoid arthritis (4, 10.8%), ankylosing spondylitis (3, 8.1%) and multiple sclerosis (3, 8.1%).
Regarding pregnancies, 5 (13.5%) had left the BD just before the pregnancy. Of these, 1 remained stable and 4 (80%) had a flare during pregnancy requiring restart of BD. Of the 32 pregnancies who took the BD during pregnancy, 8 (25%) abandoned the treatment after knowing the pregnancy, meaning that 2 of them flared; 10 (31.5%) continued with the treatment until the end of the second trimester (week 25-26) and 14 (43.7%) continued during the third trimester, 4 of them kept the drug during the entire gestation due to disease activity
In our study there was a positive correlation between preconceptional abandonment of the BD and the risk of presenting a flare (p=0.003), specially in the first and second trimesters (p=0.024). However, no relationship was found between BD and infections in the newborn (p>0.05), nor between each of the BD with the risk of infections.
Preconceptional treatment reduced the risk of flare (OR 0.545, 95%CI) and the risk of maternal complications (OR 0.5, 95%CI). Indeed, the presence of a flare during pregnancy increased the risk of maternal complications (OR 2.0, 95%CI).
Pregnancies under BD were compared to healthy controls adjusted by age finding no differences in the preterm delivery rate (p>0.05), in the induction rate of delivery (p>0.05) nor in the cesarean section rate (p>0.05).
Conclusion: In our series, the use of preconceptional BD and/or during pregnancy is not associated with an increase of maternal or fetal complications. However, fewer flares were observed. This may imply that BD can be a good tool for the treatment of women of childbearing age since control of the disease resulted in better maternal-fetal outcomes. However, more studies are needed to determine the usefulness and safety of these treatments during pregnancy.

REFERENCES:

[1] Götestam Skorpen C, et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis. 2016 May;75(5):795-810.
[2] Alijotas-Reig J, et al. Treatment with immunosuppressive and biologic drugs of pregnant women with systemic rheumatic or autoimmune disease. Med Clin (Barc). 2016 Oct 21;147(8):352-360.
[3] Bazzani C, et al. Prospectively-followed pregnancies in patients with inflammatory arthritis taking biological drugs: an Italian multicentre study. Clin Exp Rheumatol. 2015 Sep-Oct;33(5):688-93.

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FRI0664 DISEASE ACTIVITY IS THE MAJOR DISCRIMINATOR WHEN DEFINING REFRACTORY RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is characterised by the presence of a progressively destructive joint inflammation. Even in times of modern therapeutics, a subgroup of patients continues to be refractory to numerous consecutive therapeutic interventions with regards to control of inflammation and joint damage. To date, there exists no definition for refractory RA.[1]
Objectives: To explore different modifications of a definition for refractory RA.
Methods: Here we defined the base case of refractory RA as patients who had experienced ≥3 treatment courses (with at least one biological failure) over a minimum of 18 months since first treatment initiation (to avoid counting treatment courses that were given for a too short period), and the lack of reaching the treatment goal of low disease activity or remission (defined by a Clinical Disease Activity Index, CDAI, >10). We then modified our working definition based on these four variables (disease duration: 12/18/24 months; disease activity: moderate/high; number of treatment courses: ≥3/≥4; different biologic agents: ≥1/≥2).



Results: From our clinic's ongoing longitudinal data set we identified 68 refractory patients out of 688 RA outpatients. There was virtually no difference based on modifying disease duration, so we kept our working definition of a minimum disease duration of at least 18 months (n=464; 12 months: n=466; 24 months: n=453). Changing the disease activity component of the definition had a great impact on the identified refractory RA population, by requiring high instead of moderate disease activity (MDA: CDAI >10, n=129 vs. HDA: CDAI >22, n=31). In both, the MDA and the HDA group of patients, we could observe ≥60% of patients, who already experienced at least three treatment courses (MDA, n=82/129; HDA, n=21/31). Above a half in each group qualified as refractory also with the criterion of an addition fourth failed treatment course (MDA, n=64/129; HDA, n=15/31). When further stratifying patients based on the number of failed different biologic DMARDs, we could observe that regardless of the level of disease activity and number of failed treatment courses, most patients experienced at least one or even a second biologic agent (table).
Conclusion: The level of disease activity is the major discriminator when defining a population of refractory RA. The duration of treatment does not significantly impact the identification of refractory RA. The number of failed treatment courses and insufficient responses to biologic DMARDs further helps characterizing patients with refractory RA. Considerations of the impact of these different characteristics of refractory disease may well inform future criteria for refractory RA.

REFERENCES:

[1] Winthrop KL, Strand V, van der Heijde D, Mease P, Crow M, Weinblatt M, et al. The unmet need in rheumatology: Reports from the targeted therapies meeting 2017. Clin Immunol. 2017.

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FRI0665 THE ROLE OF CLINICAL JOINT INFLAMMATION AND ACUTE PHASE RESPONSE ON STRUCTURAL PROGRESSION OF PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) belongs to the group of the spondylarthropathies. It is associated with psoriasis and typically seronegative for autoantibodies. PsA disease activity can be measured using the Disease Activity in Psoriatic Arthritis (DAPSA) score which is based on both clinical (e.g., swollen joint count, SJC) and systemic (e.g., C-reactive protein, CRP) markers of inflammation. [1] However, the impact of clinical and systemic inflammation on structural progression is unclear.
Objectives: To determine the contribution of clinical and systemic inflammation on structural progression of patients with PsA.
Methods: In a secondary data analysis, we analyzed patient data from the IMPACT 2 trial of infliximab (INF) vs. placebo (PLC) in patients with established PsA (disease duration in years: INF: 7.5±7.8, PLC: 8.4±7.2). Concomitant methotrexate treatment was allowed but not mandatory in both treatment arms. [2] We obtained modified Sharp-van-der-Heijde scores from X-rays performed at baseline and after one year to compute radiographic progression. We further extracted levels of SJC and CRP and calculated time-averaged SJC (taSJC) and CRP (taCRP) values to reflect the clinical and systemic inflammation, respectively. In a multivariable binary logistic regression model, we assessed the impact of taSJC, taCRP, and their interaction, on structural progression. Next, we divided patients into different subgroups depending on their taSJC and taCRP levels into active (+) or inactive (-). We tested whether radiographic progression was different in taSJC+ vs. taSJC- and taCRP+ vs. taCRP- using the Mann-Whitney U test.
Results: 200 patients were enrolled in the IMPACT 2 trial (100 INF, 100 PLC). 151 patients were included in the analyses (76 PLC, 75 INF). Due to drop out or missing data, the remaining 49 patients were not considered for further analyses. Patients in the INF arm showed no radiographic progression (-1.16±3.96), while patients in the PLC arm showed little progression (0.74±2.98). We therefore focused on the 76 PLC patients. Despite the small overall progression, taSJC, taCRP, and their interaction were associated with radiographic progression (OR for taSJC: 1.24, CI 95%: 1.04-1.47, p=0.016; OR for taCRP: 6.08, CI 95%: 1.12-33.03, p=0.036; interaction term: p=0.097). Radiographic progression was higher in taSJC+ patients compared to taSJC- patients (1.05±3.21 and 0.56±2.30, respectively; p=0.016), as well as numerically higher without statistical significance in taCRP+ vs. taCRP- patients (1.14±3.23 and 0.05 ±2.37, respectively; p=0.532). Also, despite the limited power of subgroup analyses, there was evidence that SJC activity plays a role in CRP- patients (p=0.076), whereas CRP activity seems to be of less importance SJC- patients (p=0.643).
Conclusion: In patients with PsA, both clinical and systemic inflammation have impact on structural progression; in patients without systemic inflammation, clinical joint activity may still be considered as a risk factor for progression.

REFERENCES:

[1] Schoels M, Aletaha D, Funovits J, et al. Application of the DAREA/DAPSA score for assessment of disease activity in psoriatic arthritis. Ann Rheum Dis 2010;69:1441–7. Doi: :10.1136/ard.2009.122259
[2] Antoni C, Krueger GG, de Vlam K, et al. Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. Ann Rheum Dis 2005;64:1150–7. Doi: :10.1136/ard.2004.032268

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FRI0666 RHEUMATIC COMPLICATIONS OF IMMUNE CHECKPOINT INHIBITOR THERAPY: A CASE SERIES

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Background: Immune checkpoint inhibitor therapy reduces negative signals of T cell activation and enables tumour-specific T cells to mount a more effective response. Use of these drugs in management of malignancy has been associated with the development of auto-immune disease. There are few published studies describing immune-related adverse events affecting the musculoskeletal system.
Objectives: This study aimed to describe the spectrum of musculoskeletal presentations in patients treated with programme death (PD)-1 and/or cytotoxic T lymphocyte associated antigen (CTLA)-4 blockade.
Methods: 16 patients were identified by retrospective review of records. All patients had received treatment with monoclonal antibodies specific for PD-1, PD ligand-1 and/or CTLA4 and had been referred for rheumatology assessment of musculoskeletal complications. We assessed clinical presentation, results of blood tests for C-reactive protein (CRP), anti-nuclear antibody (ANA), rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) antibody, and response to treatment.
Results: Seven males and nine females, with mean age of 56 years were evaluated. 13 patients had melanoma, two renal cell cancer and one triple negative breast cancer. Patients presented with a spectrum of musculoskeletal symptoms. Five patients displayed features most consistent with polymyalgia rheumatica (PMR), five had peripheral spondyloarthritis (SPA) features with lower limb oligoarthritis or plantar fasciitis, four had rheumatoid arthritis (RA) features with small joint polyarthritis, one had myositis with raised creatine kinase and one had new onset of gout. Only one of 16 patients was positive for RF. All patients were seronegative for anti-CCP antibodies and ANA. One patient with RA presentation had a high CRP of 39mg/L. Five patients had a mildly elevated CRP of 5-10mg/L. Other patients did not show an acute phase response. All patients received treatment with corticosteroid with benefit. Intra-articular and soft-tissue corticosteroid injections were also effective. One of two patients with RA presentation responded to sulfasalazine, and none of two patients with RA presentation responded to methotrexate. One patient with RA presentation and one with SPA presentation responded to tumour necrosis factor (TNF)-alpha blockade.
Conclusion: Attenuating inhibitory signals of T cell activation using immune checkpoint inhibitor therapy is associated with a range of rheumatic complications, including PMR-like as well as RA- and peripheral SPA-like presentations. The majority of patients were seronegative for RF, CCP and ANA, and had low or borderline elevated CRP. All patients showed a response to prednisolone. TNF-alpha blockade was effective for RA and SPA presentations.

REFERENCES:

[1] Mitchell EL, Lau PKH, Khoo C, et al. Rheumatic immune-related adverse events secondary to anti-programme death-1 antibodies and preliminary analysis of the impact of corticosteroids on anti-tumour response: A case series. Eur J Cancer 2018; 105:88-102.
[2] Richter MD, Crowson C, Kottschade LA, et al. Rheumatic syndromes associated with immune checkpoint inhibitors: a single centre cohort of 61 patients. Arthritis Rheumatol 2018 doi:10.1002/art.40745.
[3] Mooradian MJ, Nasrallah M, Gainor JF, et al. Musculoskeletal rheumatic complications of immune checkpoint inhibitor therapy: A single center experience. Semin Arthritis Rheum 2018 Doi: :10.1016/j.semarthrit.2018.10.012.

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FRI0667 IS OBESITY A FACTOR OF POOR OUTCOME IN SPONDYLOARTHRITIS? AN ANALYSIS OF 638 PATIENTS

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Background: There are few data on obese patients with axial spondyloarthritis (axSpA).
Objectives: To explore the impact of body mass index (BMI) on personal, professional and social life of axSpA patients.
Methods: BetweenDecember 2017 and February 2018, French patients followed for axSpA by their rheumatologists or affiliated to the French patients association AFLAR, and self-reporting axSpA, participated in the European Map of Axial Spondyloarthritis (EMAS) cross-sectional patient survey[1]. Sociodemographic data (including weight and height), axSpA characteristics and disease impact on personal (social interactions, frequency of social activities) and professional life (working hours, sick leave, and disability) were collected via an online questionnaire. Patients were classified in two groups according to their BMI (obese BMI$\geq$30 kg/m^2, non-obese: BMI<30 kg/m^2) and a comparison between the two groups was conducted using chi2 or Mann-Whitney tests. There was no imputation of missing data.
Results: Data of 638 patients, mainly women 77%, median age (years) 41.5±11.1 were collected in France in 2018. Median BMI was 26.1±5.5 and 22.1% patients were obese (n=141). Median age was significantly higher in obese patients (44.1±9.9 vs 40.8±11.3; p=0.001), but there was no difference regarding gender, level of education and socio-professional categories. The obese had a longer diagnosis delay for axSPA (median 8.2±8.4 vs 6.6±8.1 years; p=0.01). They were more to report psoriasis (33.8% vs 21.9%; p=0,005) and the following comorbidities: anxiety, depression fibromyalgia, high blood pressure, hypercholesterolemia, diabetes and renal failure. Disease activity was also higher in the obese population: median BASDAI 6.5±1.5 vs 5.8±1.8 (p<0.001) and BASDAI $\geq$ 4 in 92.9% vs 84.3% (p<0.01). The same proportion of patients (61.9%) has been treated by a biologic in the two groups. The impact of axSPA on personal life was more frequently reported by the obeses: 65.2% vs 48.0% (p<0.005) had reduced the frequency of sport activities because of axSpA and 42.5% vs 28.3% (p<0.005) their sexual intercourse. There were a lower number of obeses, who had a regular physical activity (58.9% vs 68.8%; p>0.05) with a shorter mean duration of sport practice. At the opposite, no difference was observed regarding the impact of axSpA on professional life, with a similar proportion of obese and non-obese patients reporting sick leave (32.1% vs 24.9%) or disability (31.9% vs 28%). The mean number of working hours for the active people was also similar (35.5 vs 34.2 hours) in the two groups.
Conclusion: In this survey, obesity affected 22.1% of axSpA patients and was associated to a higher disease activity and a greater impact on personal life of axSpA, but not on their professional life. Obesity and its consequences have to be considered in the management of axSpA as it is already the case for psoriatic arthritis.

REFERENCES:

[1] Gossec, et al. Diagnostic Delay and Associated Factors in Axial Spondyloarthritis across Europe. Results from the European Map of Axial Spondyloarthritis Survey. Arthritis Rheumatol. 2018 Sep;70 Suppl 9:688

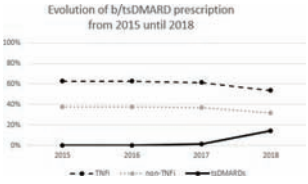
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FRI0668 FIRST DATA OF THE TARDIS-RAREGISTRY, A NATIONWIDE BELGIAN BIOLOGIC REGISTRY

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Background: The Tool for Administrative Reimbursement Drug Information Sharing (TARDIS) is an electronic platform combining data collection from patients with Rheumatoid Arthritis (RA) on biologic and synthetic targeted therapy, together with the submission of a request for reimbursement of this medication.
Objectives: To present the first data ever of the TARDIS-RA registry concerning the use of biologic and synthetic targeted therapy across Belgium.
Methods: The Belgian TARDIS-RA registry started in April 2015. All Belgian rheumatologist were obliged after a transition period to insert patient data via the online portal when prescribing. If data of a patient are entered for the first time, previous and current use of classical synthetic (cs), targeted synthetic (ts) and biologic (b) disease modifying antirheumatic drug (DMARD) therapies is registered. Afterwards, every next bDMARD or tsDMARD initiation, prolongation and discontinuation is registered electronically in the system. Other data captured are basic demographic information such as age, gender and disease duration and disease characteristics including ESR, CRP, joint counts, disease activity scores and HAQ.



Results: At 18/01/2019, information on 80 098 drug prescriptions in 13 614 patients was collected in the TARDIS-RA registry. Of these 80 098 drug prescriptions, 30 434 (38.0%) were csDMARDs and glucocorticoids, and 49 664 (62.0%) were bDMARD or tsDMARD prescriptions. This last category consisted of 30 380 (61.2%) tumour necrosis factor inhibitor (TNFi) bDMARDs, 17 104 (34.5%) non-TNFi bDMARDs and 2 170 (4.3%) tsDMARDs. Only 642 (2.3%) TNFi biosimilar prescriptions were registered. Fig1 shows the yearly evolution of bDMARD and tsDMARD prescription in Belgium from 2015 to 2018.
At first registered interaction with the rheumatologist, the 13 614 patients had a median (IQR) age of 59 (50-68) years with a median (IQR) disease duration of 9 (4-16) years; 9 666 (73.4%) were female. The clinical characteristics showed a median (IQR) DAS28CRP of 3.6 (2.1-4.8) and a median (IQR) HAQ of 1.1 (0.6-1.8). Of patients at first time registration, 37.6% could be validated as being bionaïve and 62.5% as bioexperienced.
Conclusion: Approximately 70 000 individuals in Belgium are estimated to have a RA diagnosis. Corresponding to numbers of other western European countries, 20%-25% of them would be expected to receive ts/bDMARDs. This suggests that almost the entire Belgian RA population on biologic treatment is covered by TARDIS. The registration of initiation, prolongation and discontinuation of every ts/bDMARD since 2015 combined with the simultaneous collection of demographic and clinical data, will make the TARDIS-RA registry a useful and powerful tool for the long-term drug analyses in Belgian patients with RA.
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FRI0669 DEPRESSION AND ANXIETY AND THEIR CLINICAL CORRELATES IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: In our recent systematic review, we have shown a high prevalence for depression [35% (95% CI: 29.9%-40.3%)] and anxiety [25.8% (95% CI: 19.2%-32.9%)] in Systemic Lupus Erythematosus (SLE)[1]. A better understanding of the SLE phenotypic manifestations associated with depression and anxiety may lead to enhanced early diagnosis and treatment strategies.
Objectives: To determine the overall prevalence of anxiety and depression in a cohort of SLE patients, stratified by SLE-implicated organ systems and to study their correlates.
Methods: Patients attending the Toronto Lupus Clinic from August 2017 to January 2019 were studied. Depression and Anxiety were diagnosed with Center for Epidemiological Studies-Depression Scale (CES-D; cut-off$\geq$26), BECK Depression Inventory-II (BDI-II; cut-off$\geq$18), and the BECK Anxiety Inventory (BAI; cut-off$\geq$19). Disease activity was measured with the SLEDAI-2k (SLE Disease Activity Index 2000). The SLE phenotypic manifestations were stratified based on the organ systems of cumulative 10-year SLEDAI-2K – skin, musculoskeletal (MSK), ocular, neuropsychiatric, and internal organ manifestations (including renal, pulmonary, immunologic, and hematologic). Separate univariate and multivariate logistic regression analyses (for depression [D], anxiety [A], and anxiety and depression [AD]) were performed to study the factors associated with A, D, and AD, including age at enrollment, sex, ethnicity, disease duration, inception status (enrolled in the clinic within 1 year of SLE diagnosis), fibromyalgia, and SLE phenotypic manifestations, comparing their significance to the group with neither A or D.
Results: 341 patients (89.7% female), with mean age 45.9±17.8 years were studied. The prevalence of anxiety and depression in the cohort was 34% and 27% respectively, while 21% of the total cohort was found to have both anxiety and depression. Among the 3 outcome groups (A, D, and AD), MSK system involvement has a significantly higher prevalence when compared to the group with neither A or D (p-values<0.05). Concurrently, skin system involvement was also significantly more prevalent among A, D, and AD groups, in comparison to the normal group (p-values<0.05). Patients with anxiety had significantly higher odds of skin system involvement compared to the normal group (OR=1.81; 95% CI: 1.09, 3.01). Also, patients with depression had higher odds of MSK (OR=1.94; 95% CI: 1.07, 3.50) and skin system involvement (OR=1.79; 95% CI: 1.00, 3.20) compared to the group with neither A or D. Additionally, the odds of skin system involvement was significantly higher among patients with both A and D, compared to the group with neither (OR=2.02, 95% CI: 1.05, 3.88). In all three models (A, D, and AD), employment and fibromyalgia were also significant (p-values<0.05). Age at enrolment was significant in the D and AD models (p-value<0.05), while inception patient status [inception had a mean disease duration at study visit of 12.1±11.4 years compared to non-inception 19.6±10.6 years] was significant in the D model exclusively (p-value<0.05).
Conclusion: SLE phenotypic manifestation, specifically those involving patients' skin or MSK systems, along with fibromyalgia, socio-demographic factors, and inception status were associated with anxiety or depression. Routine patient screening and evaluation, especially among patients with shorter disease duration, for these correlates may facilitate the diagnosis of these mental health disorders, and allow for more timely diagnosis and intervention strategies.

REFERENCES:

[1] Moustafa A, Hassanein M, Eder L, Wither JE, Fung W, Lambiris P, Touma Z. Prevalence and Metric of Depression and Anxiety in Lupus: A Systematic Review and Meta-Analyses [abstract]. Arthritis Rheumatol. 2016; 68 (suppl 10).

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FRI0670

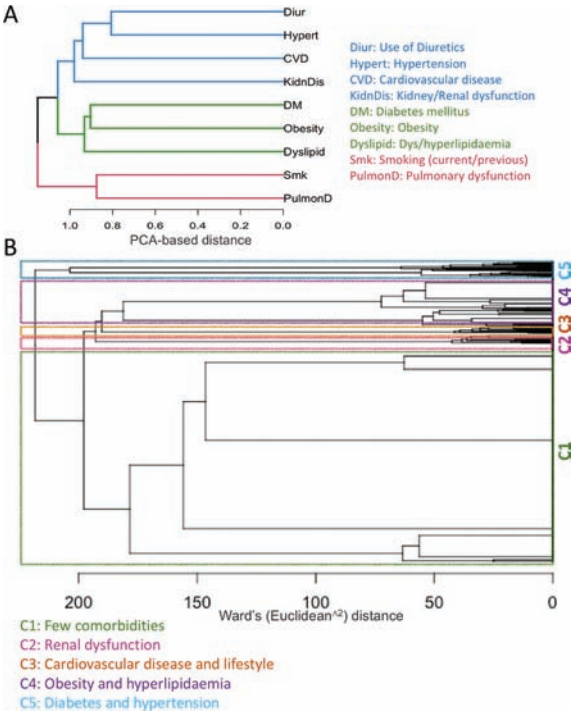
HOW DO GOUT-RELATED COMORBIDITIES AND LIFESTYLE FACTORS CLUSTER IN A LARGE HEALTH SURVEY OF THE GENERAL POPULATION? – RESULTS FROM THE MALMÖ PREVENTIVE PROJECT COHORT IN SOUTHERN SWEDEN

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Background: Several factors (comorbidities and lifestyle) have been shown to be associated or predict hyperuricemia or gout. Since these factors often are closely associated with each other, they may represent a few pathophysiological pathways rather than being individually important predictors. Identifying clusters of such factors may thus lead to a better understanding of the pathways involved in increased risk of gout. Two studies have previously indicated four to five phenotype clusters in prevalent cohorts of gout patients of European ancestry[1,2]. However, identification of clusters of gout-associated factors in the general population is lacking.

Objectives: To identify clusters of gout-related baseline comorbidities and lifestyle factors among participants in a population-based health survey.

Methods: The Malmö Preventive Project is a screening program for cardiovascular risk factors, alcohol abuse and breast cancer in Malmö, Sweden. Overall, 33,346 individuals (67% male, mean age 45.7 years at inclusion) participated. The study population was screened between 1974 and 1992. A subset of 22,057 individuals (screening period: 1975-1992) was eligible for the cluster analysis. Agglomerative hierarchical cluster analysis was performed to group similar variables and subgroup individuals with similar characteristics, using principal component and Ward's minimum variance methods in Rv3.5.2, respectively. Variables selected to cluster were obesity (BMI>30 kg/m^2), renal dysfunction (eGFR<60 mL/min/1.73m^2), diabetes mellitus (DM), hypertension, prevalent cardiovascular disease (CVD), dyslipidemia (abnormal cholesterol or triglyceride values), pulmonary dysfunction (PD, FEV_1/FVC on spirometry<0.7%), smoking and use of diuretics.



Results: Overall, 66% of the participants in the cluster analysis were males, mean age was 47 years and mean body mass index 24. Clustering of comorbidities and lifestyle factors indicated three pathways i.e. 1) mainly cardiovascular risk factors and disease, 2) variables associated with insulin resistance and 3) variables associated with PD (Fig; A).

Fig Results of cluster analysis illustrating (A) variable and (B) observation clustering

Five different clusters (C1 to C5) were identified based on clustering of observations (Fig1; B). C1 (n=16,063), mean age=46 years, characterized low rate of hypertension (14%) and PD (15%); none had obesity, kidney dysfunction, DM, CVD or dyslipidemia. C2 (n=750; mean age 51 years) had the highest proportions with gout (7.1%) and kidney dysfunction (100%), with no record of DM, CVD or use of diuretics. C3 (n=528; mean age=48 years) had the highest rates of CVD (100%) PD (22%), smoking (74%) and alcohol risk behaviour (41%). C4 (n=3673; mean age=47 years) had the highest percentage of males (75%), the highest BMI (25.91) and the greatest proportions with obesity (34%) and dyslipidemia (74%), regular smoking (65%) and alcohol risk behaviour (36%). C5 (n=1043; mean age=48 years) had by far the highest occurrence of DM (51%), frequent use of diuretics (52%), hypertension (54%) and the highest percentage of abnormal liver enzyme levels (16%).

Conclusion: Definition of clusters of comorbidities and lifestyle factors closely associated with gout, identified five separate "pathways" in this large health survey of the general population. "Pathways" relates to lifestyle, metabolism and specific comorbidity patterns. Further analyses will be performed to elucidate how these clusters predict diagnosed gout in this population.

REFERENCES:

[1] Richette P, et al. Ann Rheum Dis 2015; 74(1):142-47.
[2] Megan B, et al. Rheumatol 2018; 57(8):1358-63.

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FRI0671

SURVEY OF POTENTIAL TOXIC EXPOSURE IN PATIENTS WITH SYSTEMIC SCLEROSISIN RESCLE REGISTRY. A PRELIMINARY STUDY

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease with extremely heterogeneous clinical features and unknown etiology, although numerous studies suggest a relationship with environmental and occupational factors. So far there is little information on whether toxic substances can play a relevant role in its phenotypic expression (1).

Objectives: To analyze in a cohort of patients with SSc the proportion of patients exposed to toxic and their correlation with epidemiologic, clinical and serological data.

Methods: A survey was conducted aimed at the knowledge of the working life of patients from six centers belonging to the Spanish Scleroderma Registry (RESCLE), categorizing them in six groups: no potential exposure to toxic substances, potential exposure to silica, to hydrocarbons, to organic solvents, to mixed toxics (silica and/or hydrocarbons and/or organic solvents) and to another toxics. In all patients 87 epidemiological, clinical and analytical variables included in the registry were analyzed, carrying out a comparative study between groups.

Results: 225 SSc patients were selected. Of these, 81 patients (36%) had worked in professions with potential risk of toxic exposure, 64 women out of the 227 included (28%) and 17 men out of the 28 included (60%). The toxic agent most frequently involved was silica in 29 patients (35.8%), followed by hydrocarbons in 21 (25.9%), mixture of toxic

substances in 21 other patients (25.9%), organic solvents in 4 patients (4.9%) and other toxic in 6 cases (7.4%). Toxic exposure was associated with a lower risk of being female (OR 0.15, p <0.001), having been exposed to tobacco (OR 0.4, p 0.037) and digital ulcers (OR 0.43, p 0.016) and with a greater likelihood of hepatic involvement (OR 3.63, p 0.021), musculoskeletal involvement (OR 2.13, p 0.017) and the slow capillary pattern of Maricq (OR 1.8, p 0.063). Analyzing the exposure groups separately, patients exposed to silica had a lower probability of Raynaud's phenomenon (OR 0.25, p 0.005) and a higher probability of diagnosis at older ages (OR: 1.04, p 0.005), presence of Topoisomerase I antibody (OR 3.71, p 0.023) and slow capillary pattern of Maricq (OR 4.15, p 0.008). Patients exposed to hydrocarbons had an increased risk of liver involvement (OR 5.34, p 0.029).

Conclusion: In our cohort of 225 patients with SSc, 60% of male patients and 28% of women worked in a profession with a potential risk of toxic exposure. In this preliminary study, important differences were observed in the probability of a different phenotypic expression of the SSc according to the history of occupational exposure to toxins. Studies with a larger number of patients are needed to establish these associations in a solid way.

REFERENCES:

[1] Marie I, et al. Environmental risk factors of systemic sclerosis. Semin Immunopathol. 2015 Sep;37(5):463-73.

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FRI0672 INCIDENCE OF GIANT CELL ARTERITIS IN 6 DISTRICTS OF PARIS, FRANCE (2015–2017)

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Background: Little is known about the current incidence of giant cell arteritis (GCA) in France.

Objectives: We conducted a prospective, population-based survey over 3 years to estimate the incidence of GCA in inhabitants of Paris, France.

Methods: From January 2015 to December 2017, new GCA diagnoses in 6 districts of northeastern Paris (257,888 inhabitants ≥50 years old) were prospectively identified by 1) biannual postal mails to 1,134 general practitioners and other specialists practicing in the study area; 2) quarterly e-mail surveys among 28 hospital departments located in or close to the study area and 3) new records in the National Health Insurance System database with code M31 (other necrotizing vasculopathies) in the International Classification of Diseases, 10th revision. Clinical data of notified cases were retrieved from medical records. Retained cases lived in the study area at the time of diagnosis, fulfilled the 1990 American College of Rheumatology classification criteria and/or were ≥50 years old, with imaging or histology evidence of large-vessel inflammation and increased levels of inflammatory biomarkers. Clinical presentations with no cranial symptoms were classified as large-vessel GCA and otherwise as cranial GCA. Annual incidence rates were calculated by dividing the number of incident cases by the size of the study population and the study period (in years); 95% confidence intervals (CIs) were calculated by using the Poisson distribution. Completeness of case ascertainment was assessed by a three-source capture–recapture analysis.

Results: Among 61 retained cases (69% females; mean age: 77.1 [SD: 9.0] years), 57 (93%) were cranial GCA and 4 (7%) large-vessel GCA. GCA diagnoses were supported by temporal artery biopsy findings, imaging of the aorta and its main branches, temporal artery ultrasonography and/or aortic tissue histology in 35 (57%), 18 (30%), 7 (11%), and 1 (2%) cases, respectively. GCA incidence rate (per 100,000 inhabitants ≥ 50 years old) was estimated at 7.9 cases (95% CI: 6.0–10.1). Completeness of case ascertainment was estimated at 66% (95% CI: 52–92%).

Conclusion: Our annual incidence estimate of GCA is close to the sole published estimate for another French population established 4 decades ago [1] and adds further support to the lower incidence of GCA in non-Scandinavian versus Scandinavian populations. Large-vessel GCA cases seem a rare form of GCA as compared with cranial GCA.

REFERENCES:

[1] Barrier J, Pion P, Massari R, Peltier P, Rojouan J, Grolleau JY. [Epidemiologic approach to Horton's disease in the department of Loire-Atlantique. 110 cases in 10 years (1970-1979)].Rev Med Interne. 1982;3(1):13-20

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FRI0673 RISK OF JOINT SURGERY IN PATIENTS WITH PSORIATIC ARTHRITIS. A REGISTER-BASED TIME SERIES STUDY FROM DENMARK

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Background: The knowledge is limited about use and time trends of joint surgery among patients with psoriatic arthritis (PsA). It is also unknown whether the need for joint surgery has decreased as seen in most Rheumatoid Arthritis populations in the biologic era.

Objectives: To study time trends and cumulative incidence of joint surgery among PsA patients in Denmark from 1996 to 2017 compared to a general population cohort (GPC) in a nationwide register-based study.

Methods: The Danish National Patient Register was used to identify incident PsA patients diagnosed at a department of rheumatology or general internal medicine. We calculated the 5-year incidence rates (IR) and incidence rate ratios (IRR) of joint surgery in 4 calendar-period defined cohorts in Danish PsA patients (1996-2000; 2001-2004; 2005-2008; 2009-2012). Each patient was subsequently matched with up to 10 non-PsA GPCs.

Using the Aalen-Johansen estimator, we calculated the 5, 10 and 15-year cumulative incidences of any joint surgery and joint-sacrificing surgery (arthroplasty and arthrodesis), respectively, for all patients PsA patients diagnosed from 1996 to 2017.

Results: In total, 11 960 PsA patients (mean age 50 years; 57% female) were identified from 1996-2012. The IR of surgery was higher in each PsA calendar cohort compared with their GPC counterpart with an overall IR in PsA of 20.7 (95% CI 19.3-22.1) and GPC 9.9 (95% CI 9.6-10.2) from 1996-2012 (Table 1). Comparing PsA with GPC cohorts across calendar periods, the IRR for any joint surgery decreased slightly from 2.4 (95%CI 2.0 to 2.9) in 1996-2000 to 2.0 (95%CI 1.7 to 2.2) in 2009-2012. Among PsA patients diagnosed between 1996 and 2017, the 5, 10, and 15-year cumulative incidences of surgery were 2%, 10%, and 29%, respectively (Figure 1).

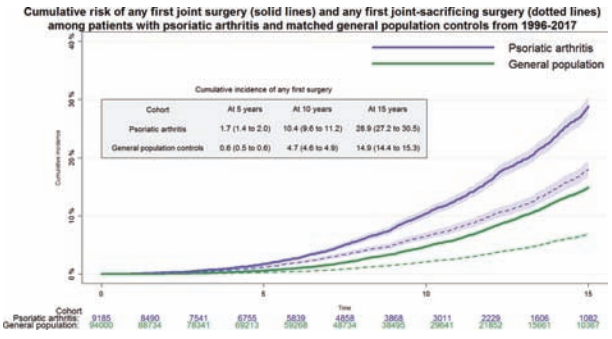


Figure 1

Conclusion: In this study, the 5-year IR of joint related surgery in PsA did not change substantially from 1996 to 2012. The IR remained about twofold higher compared with the general population. Thus, any beneficial

effect of biologics on joint damage has not translated into a clear-cut decreased need for joint sacrificing surgery as observed in several RA populations.
After 15 years of follow-up, 29% of the PsA patients had received surgery.

Table 1. Incidence of any joint surgery and joint sacrificing surgery in each calendar period and calculated incidence rate ratios

Calendar period	Any joint surgeries, n (Joint sacrificing as first surgery, n)		Person years, pyrs		Incidence rate per 1000 pyrs (95% CI)		Incidence rate ratio (95% CI) comparing PsA with GPC as reference in each calendar period
	PsA	GPC	PsA	GPC	PsA	GPC	PsA vs GPC
1996 - 2000	145 (56)	536 (180)	7966	74092	18.2 (15.4-21.4)	7.2 (6.6-7.9)	2.4 (2.0-2.9)
2001 - 2004	160 (76)	643 (198)	7572	70850	21.1 (18.0-24.7)	9.1 (8.4-9.8)	2.3 (1.9-2.7)
2005 - 2008	264 (100)	1261 (389)	12128	115197	21.7 (19.2-24.6)	11.0 (10.4-11.6)	2.0 (1.7-2.3)
2009 - 2012	316 (122)	1536 (467)	14921	143524	21.1 (18.9-23.7)	10.7 (10.2-11.3)	2.0 (1.7-2.2)

Abbreviations: n, number. CI 95%, 95% confidence interval. Ref, reference.

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FRI0674 THE ASSOCIATION BETWEEN JOINT EROSIONS PLUS AUTOANTIBODY POSITIVITY AT INITIATION OF METHOTREXATE OR BIOLOGIC THERAPY FOR RHEUMATOID ARTHRITIS AND DISEASE ACTIVITY AND DISABILITY OVER ONE YEAR

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Background: Joint erosions and autoantibody positivity (rheumatoid factor [RF], anti-cyclic citrullinated peptide antibody [anti-CCP]) predict poor outcomes in patients with rheumatoid arthritis (RA). There are limited data on the combination of these factors and clinical and patient reported outcomes over time.
Objectives: To compare the disease activity and disability over 1 year of those with poor prognostic factors at treatment initiation (methotrexate [MTX] or biologics) to those without.
Methods: Patients were recruited to 1 of 2 UK-based multi-centre prospective cohort studies: MTX-starters: Rheumatoid Arthritis Medication Study (RAMS); biologic-starters: Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS). Anti-CCP (Axis-Shield Anti-CCP test; U/ml; anti-CCP titre >5 U/ml = anti-CCP+)/RF (Beckman Coulter AU5400, RF latex assay; IU/ml; RF titre >14 IU/ml = RF+) status were determined from baseline (BL) blood samples at the co-ordinating centre; erosions (yes/no) were recorded from medical notes. Missing data resulting from anti-CCP assay failure were imputed using multiple imputation. Patients who were anti-CCP+ and/or RF+ and had erosions were classified as having poor prognosis (PP); all other patients were classified as not having poor prognosis (NPP). Patients completed the Health Assessment Questionnaire (HAQ) and the Disease Activity Score (DAS28) was calculated at BL, 6 months and 12 months. The DAS28 and HAQ scores of the prognostic groups were compared at each assessment using linear regression, adjusted for age, gender and disease duration.

Baseline characteristics of the PP and NPP patients in each cohort

Baseline characteristic	MTX-starters		Biologic-starters	
	PP	NPP	PP	NPP
N (%)	182 (15.4)	997 (84.6)	467 (40.5)	685 (59.5)
Age, years	61.5 (52, 70)	58 (48, 67)	59 (51, 67)	57 (49, 65)
Female, N (%)	116 (63.7)	647 (64.9)	344 (77.8)	516 (75.3)
Disease duration, months	16.5 (6, 86)	8 (4, 23)	132 (60, 240)	48 (24, 96)
Smoking:				
Never	68 (38.0)	390 (39.4)	146 (32.7)	233 (34.8)
Former	75 (41.9)	400 (40.4)	204 (45.7)	298 (44.5)
Current	36 (20.1)	199 (20.1)	96 (21.5)	138 (20.6)
Swollen joint count (28)	5 (2, 9)	4 (2, 9)	8 (6, 12)	8 (5, 11)
Tender joint count (28)	5 (2, 12)	6 (2, 12)	12 (9, 19)	15 (10, 20)
CRP, mg/l	7 (2, 21)	5 (2, 15)	10 (5, 25)	9 (4, 24)
DAS28	4.3 (3.4, 5.1)	4.1 (3.2, 5.1)	5.7 (5.2, 6.3)	5.8 (5.3, 6.3)
Health Assessment Questionnaire	1.00 (0.38, 1.63)	1.13 (0.50, 1.75)	1.75 (1.25, 2.13)	1.63 (1.25, 2.13)
Pain visual analogue scale	50 (29, 73)	48 (25, 70)	70 (55, 80)	69 (52, 79)
Fatigue visual analogue scale	51 (24, 75)	52 (25, 72)	73 (57, 85)	74 (55, 86)
Anti-CCP+, N (%)	139 (88.5)	405 (68.5)	193 (97.5)	226 (82.5)
Rheumatoid factor+, N (%)	170 (95.0)	489 (60.2)	410 (93.6)	367 (58.4)
Erosions, N (%)	182 (100)	46 (4.6)	467 (100)	20 (2.9)

Median (IQR) unless otherwise stated. Results from the first imputed dataset.
Anti-CCP = anti-cyclic citrullinated peptide antibody, DAS28 = Disease Activity Score (28), MTX = methotrexate, N = number, NPP = not poor prognostic group, PP = poor prognosis group

Results: In total, 1179 (PP = 182 [15.4%]) MTX-starters and 1152 (PP = 467 [40.5%]) biologic-starters were included (BL characteristics in Table). For MTX-starters, PP and NPP patients had similar DAS28, whereas for biologic-starters, PP patients had lower DAS28 compared to NPP patients after baseline (adjusted mean difference [95% CI]: MTX-starters BL = 0.1 [-0.1, 0.3]; 6 months = -0.1 [-0.3, 0.2]; 12 months = -0.1 [-0.4, 0.2]; biologic-starters BL = -0.1 [-0.2, 0.0]; 6 months = -0.2 [-0.4, 0.0]; 12 months = -0.4 [-0.6, -0.1]). HAQ scores were similar between PP and NPP patients in both cohorts (adjusted mean difference [95% CI]: MTX-starters BL = 0.08 [-0.04, 0.20]; 6 months = 0.02 [-0.11, 0.15]; 12 months = -0.03 [-0.17, 0.10]; biologic-starters BL = 0.00 [-0.09, 0.08]; 6 months = 0.00 [-0.12, 0.13]; 12 months = 0.01 [-0.14, 0.16]).
Conclusion: PP and NPP MTX-starters had similar outcomes. For biologic-starters, PP patients had lower disease activity after baseline; knowledge of these prognostic factors may have prompted more intensive assessment of PP patients after starting treatment.
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FRI0675 AUTOIMMUNE PERIPHERAL ULCERATIVE KERATITIS: ASSOCIATED ETIOLOGY, CLINICAL CHARACTERISTICS, TREATMENT AND VISUAL PROGNOSIS

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Background: Peripheral ulcerative keratitis (PUK), a rare sight-threatening condition, is an inflammatory corneal disease with an estimated incidence of 8 to 10 cases per million. PUK is characterized by the presence of an epithelial defect with progressive stromal corneal degradation and juxtalimbal thinning.
Objectives: To describe the associated etiology, demographic and clinical characteristics, treatment and visual prognosis of patients with PUK and autoimmune disease.
Methods: A retrospective, transversal, descriptive, observational cohort study was performed. The clinical file of all patients that had been diagnosed with PUK at the Inflammatory Eye Disease Clinic and who came to a follow-up appointment between January 2014 through February 2018 was evaluated. With a minimum follow-up of 6 months since PUK diagnosis.
Quantitative data was calculated in terms of means and standard deviations. Qualitative data in frequencies. Chi-square and rank sum tests were used to compare groups. Kaplan-Meier methods to estimate survival

rates according to treatment. Comparisons of survival rates between treatments were performed using log-rank tests. A *p* level of <0.05 was considered significant. Statistical analyses were performed using SPSS 24.0

Results: A total of 109 patients (155 eyes; 79.8% female; mean age 53.9 ±12.5 (23 to 81) years) were included. The frequency of the association between PUK and an autoimmune systemic disease, was 86.3% (94). The leading etiology was RA (52.3%; n=57); VAA (30.3%; n=33), being GPA the foremost recognized in this group (84.8%; 28/33). Other were SLE, PSS, JIA, and ReA.

When PUK started, RA was already diagnosed in 87.7% (50/57); 18.2% (6/33) of AAV. Mean disease evolution in RA was 15 ± 8.2 years; AAV had 3.9 ± 5.6 years (p=0.05). 29% (n=17) of RA untreated; only 4 (12.2%) AAV were immunosuppressed by the time PUK settled.

Systemic autoimmune activity, was found in 31.5% (18/57) of RA and 90.9 (30/33) of AAV. Arthralgia was foremost referred by RA (94.4%;17/18); ear–nose–throat symptoms were in AAV (86.6%; 26/30). In the latter, some degree of renal dysfunction was found in 33.3% (10/33).

PUK characteristics in RA and AAV. Moderate (34.2%) and mild (36.3%) PUK were more frequently seen in RA; whereas moderate (36.3%) and severe (33.3%) in AAV (p=0.016). RA associated PUK commonly involved the inferior corneal quadrant (54.3%), as AAV the superior one (73.8%; p < 0.01). Corneal perforation was more frequent in RA than AAV (54.5% vs 22.7%; p=0.481); although the risk of perforation associated to RA didn't show statistical significance (OR 1.14 [IC 95% 0.8 - 1.63]). Necrotizing scleritis was more commonly seen in AAV (RA n=1 vs AAV n=10.

The more frequent instated treatment in RA was oral prednisone combined with oral DMARDs (31.6%; 18/57). More aggressive therapy (MPS, CYC or Rituximab) was designated in 22.8% (n=13). On the other hand, 78.7% (26/33) of AAV were managed with the MPS-pred scheme merged with CYC (36.4%; n=12) or Methotrexate (42.4%; n=14).

Conclusion: RA and AAV are the more frequent autoimmune diseases that can manifest with PUK. In RA, the lack of arthritis could be mistaken as quiescent, and wrongly undertreated, allowing it to progress to a vasculitic stage. It may impact their life quality if complicated with corneal perforation. In AAV the PUK can be the initial sympton of the disease and is associated with a more sever ocular presentation. Routine ophthalmologic examinations might help the rheumatologist to assess RA and AAV activity and treatment.

REFERENCES:

[1.] John SL, Morgan K, Tull AB, Holt JL. Eye. 1992;6:630-6.

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FRI0676 **PREVALENCE AND UVEITIS CHARACTERISTICS OF A COHORT OF PATIENTS WITH SPONDILOARTROPATHY**

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Background: Uveitis can be a clinical manifestation of different systemic processes, known is the association of anterior uveitis in patients with spondyloarthritis (SpA)

Objectives: To describe the prevalence, characteristics and course of ocular inflammatory pathology from a cohort of patients with SpA

Methods: Retrospective descriptive study made in a cohort of 451 SpA patients according to the ASAS classification criteria in a a tertiary university hospital from Barcelona. Were selected patients who presented or had presented uveítis (defined according to the SUN[1] classification criteria) Demographic, clinical, radiological and serological data of the joint disease and characteristics of the ocular affectation were collected, as well as the treatment of both

Results: Of the 451 patients reviewed, 43 (9.53%) patients with a history of uveitis were included in the study. From the cohort, the average age at diagnosis of SPA was 37 (± 27) years and 38 (88.4%) had positive HLAB27. The most prevalent subtypes of SPA were Ankylosing Spondylitis (AS): 27 (62.8%) and Psoriatic Arthritis (APSo): 8 (18.6%). The characteristics of the sample are summarized in Table 1

The average age at the first uveitis outbreak was 45 ± 23 years. The anterior location was more prevalent (n: 39, 90.7%), unilateral (n: 35, 81.4%) and acute onset (n: 42, 97.6%)

Two of patients with anterior uveítis had other associated complications, one had macular edema and other retinal vasculitis. The treatment of uveitis was topical corticosteroids in 39 (90.6%) patients, 2 (4.6%) treatment with oral sulfasalazine. Despite the treatment, 22 (51.2%) patients presented a recurrent course. Table 2 shows the ocular clinical features

Table 1. Clinical characteristics of SpA cohort.

Sex, n% (men/women)	24/19 (55.81/44.18)
Diagnoses SpA, years ± DE	37 ± 27
Subtype SpA, n (%)	27 (62.8)
EA, n (%)	2 (4.6)
EII, n (%)	8 (18.6)
APSo, n (%)	6 (13.9)
PreRx, n (%)	
HLAB27, n (%)	38 (88,4)
Affectation SpA	25 (58.1)
Axial, n (%)	4(9,3)
Periferic, n (%)	11(25,6)
Mixed, n (%)	
Treatment SpA	14 (32)
FAMEs	5 (11.6)
Metotrexate, n (%)	2 (4.6)
Sulfasalazine, n(%)	5 (11.6)
Azatioprine, n (%)	9 (20)
Leflunomide, n (%)	17 (39.5)
ANTI- TNF	6 (13.9)
Etarnecept, n (%)	6 (13.9)
Adalimumab, n (%)	2 (4.6)
Golimumab, n (%)	1 (2.3)
Infliximab, n (%)	2 (4.6)
Certolizumab, n(%)	
Secukinumab, n (%)	
Ustekinumab, n (%)	

Table 2. Clinical characteristics of uveítis from SUN criteria.

Uveitis, n(%)	43 (9,53)
Age 1° outbreak, years ± DE	45 ± 23
Type	39 (90.7)
Anterior, n (%)	2(4.6)
Intermedite, n (%)	0
Posterior, n (%)	2(4.6)
Panuveitis, n (%)	
Unilateral, n (%)	35(81.4)
Bilateral, n (%)	8 (18.6)
Onset	42 (97.6)
Sudden, n (%)	1 (2.3)
Insidious, n (%)	38 (88.3)
Duration	5(11.6)
Limited (<=3 meses) n (%)	13 (30.2)
Persistent (>3 meses) n(%)	22(51.2)
Course	8(18.6)
Acute * n(%) Recurrent ** n (%)	
Chronic *** n (%)	
Treatment Uveitis	39 (90.6)
Corticosteroids topics, n (%)	2 (4.6)
FAME (sulfasalazine), n (%)	

* Episode sudden onset and limited duration ** Repeated episodes separated by periods of inactivity without treatment 3 months in duration ***Persistent uveitis with relapse in 3 months after discontinuing treatment

Conclusion: In our cohort of SPA, prevalence of uveitis was 10%, predominantly in HLA B27 patients and axial involvement, of which 62.8% met criteria for AD and 18.6% APSO with different degrees of axial involvement, including under systemic treatment (FAMEs/Biological). The most frequently presentation was anterior, unilateral, acute and recurrent uveitis. Being the most used treatment topical corticosteroids.

REFERENCES:

[1] Am J Ophthalmol 2005;140: 509-516
[2] Ann Rheum Dis. 2009;68:777-83

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FRI0677 IMPACT OF COMORBIDITY ON THE USE OF BIOLOGICAL AND TARGETED THERAPY IN RHEUMATIC DISEASES IN THE CLINICAL PRACTICE

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Background: Comorbid conditions often accompany rheumatic diseases and can influence the prescription of immunosuppressive therapy. Comorbidity seems to be a factor that is still underestimated in actual practice.
Objectives: To study the influence of comorbidity on the prescription of biological and targeted therapies in patients with rheumatic diseases (RD) in clinical practice.
Methods: We perform a retrospective analysis of comorbidity and prescription of biological and targeted immunosuppressors in a group of inpatients with systemic autoimmune RD in rheumatology department. From January 2018 to January 2019, 218 patients with inflammatory RD hospitalized - 146 (67,5%) women, mean age 50.6±14,6 years. Diagnoses: rheumatoid arthritis - 83 patients, spondyloarthritides – 80, systemic lupus erythematosus – 19, systemic scleroderma - 16, ANCA-associated vasculitides – 10, other conditions – 10 patients. Biologics were used in 117 (53,7%) of patients (anti-TNFs – 64 patients, rituximab – 18, tocilizumab – 16, abatacept – 8, secukinumab – 4, ustekinumab – 4, tofacitinib – 3 patients). We examined patients for comorbidities through careful examination of the history, medical records, and general therapeutic laboratory and instrumental screening. The Charlson comorbidity index calculated for every patient.
Results: 174 (79.8%) patients had at least 1 comorbid condition. The most frequent comorbidities were type2 diabetes (19,5% patients), chronic kidney disease (12,6%), cerebrovascular accidental (11,5%), ischemic heart disease and chronic heart failure (11%), chronic liver disease (7,5%). Mean Charlson index was 2,16±2,05 in total group; it was significantly lower in patients who were treated with biological and targeted therapy (1,64±1,8) than in patients who did not received this therapy (2,76±2,1), p<0,01. Biologics were prescribed in 81,8% of patients without comorbidities, in comparison with 55,3% of patients with Charlson comorbidity index 1 or 2, and 36,3% of patients with Charlson index 3 or more.
Conclusion: Comorbidity has a direct impact on the use of biological and targeted therapy in patients with rheumatic diseases in real clinical practice, limiting the ability to control the activity of the disease. It is necessary to develop a general therapeutic strategy for treating comorbid conditions in patients with rheumatic diseases.

REFERENCES:

[1] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. Journal of Chronic Diseases. 1987; 40 (5): 373–83

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FRI0678 PREVALENCE, PATIENT CHARACTERISTICS, AND TREATMENT OF GOUT AND ASYMPTOMATIC HYPERURICEMIA IN JAPAN: CROSS-SECTIONAL STUDY OF A HEALTH INSURANCE CLAIMS DATABASE

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Background: The prevalence of gout is increasing worldwide [1,2], but evidence suggests that current treatment practices do not effectively reduce serum uric acid (sUA) levels in many gout patients [3]. In Japan, urate lowering therapy (ULT) is provided to patients diagnosed with asymptomatic hyperuricemia as well as to those with gout. However, the actual treatment situation for asymptomatic hyperuricemia has not been well-documented.
Objectives: To assess the prevalence and characteristics of gout and asymptomatic hyperuricemia and the current treatment practices for these conditions in Japan.
Methods: This retrospective cross-sectional study assessed disease prevalence, patient characteristics, prescriptions, proportion of patients achieving target sUA, and incidence of gouty arthritis among 2,531,383 individuals in a database, using data from Japanese health insurance claims and medical check-ups from April 2016 to March 2017.
Results: Gout was diagnosed in 1.1% (men 1.9%, women <0.1%) of the study population and asymptomatic hyperuricemia in 2.6% (men 4.1%, women 0.4%). Hyperuricemia (sUA >7.0 mg/dL) was identified in 13.4% (men 19.6%, women 1.0%) of cases in which sUA level was measured at check-up. ULT adherence was satisfactory (median medication possession ratio [MPR] of 69.0% for febuxostat and 78.1% for allopurinol in gout, and 79.5% and 88.5%, respectively, in asymptomatic hyperuricemia), but most patients were receiving low-dose ULT. The sUA target (≤6.0 mg/dL) was achieved by less than half of patients treated with either febuxostat or allopurinol (Table). In gout patients, the incidence proportion of gouty arthritis was 47.8% and the incidence rate was 0.74 flares/person-year.
Conclusion: The prevalence of gout in our study population was low. Japanese physicians often treat gout and asymptomatic hyperuricemia with low-dose ULT, and many patients fail to reach their target sUA, suggesting gout management is suboptimal in Japan.

REFERENCES:

[1] Zhu Y, et al. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007-2008. Arthritis Rheum 2011;63(10):3136-41.
[2] Kuo CF, et al. Global epidemiology of gout: prevalence, incidence and risk factors. Nat Rev Rheumatol 2015;11(11):649-62.
[3] Roddy E, et al. Concordance of the management of chronic gout in a UK primary-care population with the EULAR gout recommendations. Ann Rheum Dis 2007;66(10):1311–5.

Table

	Gout		Asymptomatic hyperuricemia	
	Febuxostat	Allopurinol	Febuxostat	Allopurinol
N	8215	6521	16312	14220
Mean prescribed dose	18.9 mg	145.6 mg	16.5 mg	131.3 mg
Median MPR	69.0%	78.1%	79.5%	88.5%
Proportion of patients achieving target sUA (≤6.0 mg/dL)	44.7% (876/1960)	33.8% (599/1771)	47.8% (2032/4254)	35.9% (1691/4704)

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FRI0679 PREDICTORS OF DEATH IN 3693 PATIENTS WITH RHEUMATOID ARTHRITIS FOLLOWED FOR UP TO 12 YEARS IN CLINICAL PRACTICE

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Background: Patients with RA have shorter life expectancy than the background population. Severe disease, as reflected in high disease activity, comorbid conditions and functional disability have historically been associated with increased mortality (1-2). Mortality after the introduction of

biological therapies has not been investigated in detail, and little is known about the predictive value of sociodemographic and lifestyle factors.

Objectives: To investigate the predictive value of a panel of potential predictors of death in a cohort of patients with RA followed for up to 12 years during the era of biological treatments.

Methods: Outpatients with RA were recruited consecutively between July 2006 and July 2007 and followed in routine care with prospective registrations in the DANBIO registry until death or August 30th 2018, whichever occurred first. Baseline variables considered to be potential predictors were: disease activity, disease duration, IgM-rheumatoid factor (IgM-RF), radiographic status (erosive disease yes/no) and medical therapy as well as patient-reported marital status, educational level, comorbid conditions, smoking, exercise, body mass index (BMI) and health assessment questionnaire (HAQ). Vital status and date of death were extracted from the Danish National Register. A cox proportional hazards model was used to estimate the hazard ratio for death for each of the potential predictors.

Table. Age-adjusted cox proportional hazards model with death as failure.

	Hazard Ratio	95% CI		p-value
Women (vs. men)	0.53	0.44	0.63	<0.01
IgM-RF positive (vs. negative)	1.22	1.01	1.48	0.04
Baseline HAQ score (per 0.125 increase in score)	1.33	1.19	1.49	<0.01
Glucocorticoid treatment last month (vs. none)	1.50	1.28	1.75	<0.01
Weekly exercise (vs. no exercise)	0.77	0.67	0.90	<0.01
BMI <18.5 kg/m² (vs. BMI 18.5-25)	1.36	0.99	1.88	0.06
BMI >25 kg/m² (vs BMI 18.5-25)	0.94	0.80	1.09	0.42
Current smoking (vs. never)	1.85	1.51	2.26	<0.01
Former smoking (vs. never)	1.26	1.05	1.51	0.01
Married or cohabiting (vs. living alone)	0.71	0.61	0.83	<0.01
One comorbid condition (vs. none)	1.21	0.99	1.49	0.07
Two or more comorbid conditions (vs. none)	1.62	1.34	1.97	<0.01

N=3053, number of deaths=762.

Results: 3693 patients were recruited at baseline, 75% women, 77% IgM-rheumatoid factor positive, 65% with erosive disease, median (IQR) age 62 years (52-71), disease duration 7 years (3-15), DAS28 3.0 (2.2-3.9), HAQ 0.63 (0.25-1.25). 20% received a biological disease modifying anti-rheumatic drug (DMARD), 71% received a synthetic DMARD and 9% received no DMARD. The median (IQR) duration of follow-up was 11 years (9-11); 1041 patients (28%) died during follow-up. 640 patients were excluded from the regression model due to missing baseline data; these individuals were slightly (median of 3 years) older than those who entered, but with similar disease duration and disease activity. All baseline variables were statistically significant predictors in univariable analyses. Table shows hazard ratio estimates in the multivariable model, which included 3053 patients; 762 (25%) deaths. IgM-RF positivity, higher HAQ score, glucocorticoid therapy, smoking (current and former) and two or more comorbid conditions were predictors of death. Low BMI was a borderline significant predictor for death. Female sex, weekly exercise and cohabiting decreased the risk of death.

Conclusion: In a large cohort of RA patients followed for a decade in the era of biological treatments, we identified strong clinical (high HAQ, comorbidity), treatment related (glucocorticoid last month), sociodemographic and lifestyle related (male sex, living alone, smoking, physical inactivity, low BMI) risk factors for death. In the effort to prevent a poor long term outcome in patients with RA, this study provides new insight into potentially modifiable baseline variables.

REFERENCES:

[1] Mok, CC, et al. Life expectancy, standardized mortality ratios, and causes of death in six rheumatic diseases in Hong Kong, China. Arthritis Rheum 2011; 63: 1182-1189.

[2] Sokka, T, et al. Mortality in rheumatoid arthritis: 2008 update. Clin exp Rheumatol. 2008 Sep-Oct; 26 (5 suppl 51) S: 35-61.

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FRI0680 THE ASSOCIATION BETWEEN ANKYLOSING SPONDYLITIS AND UNEMPLOYMENT

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Background: Previous registry studies have noted increased rates of unemployment in patients with ankylosing spondylitis (AS)(1-2). With improved treatment options and earlier detection of AS, its was anticipated that this would no longer be true.

Objectives: The Ankylosing Spondylitis Registry of Ireland(ASRI) is a source of epidemiological data on AS patient in Ireland. The aim of this study was to examine unemployment rates in this population and possible links with disease activity, function and quality of life.

Methods: An analysis of the patient population of the ASRI with data collected from 2013 to 2017 was performed using IBM SPSS Statistics version 25. Comparison of the mean ASQoL, HAQ, BASDAI, BASFI, and BASMI score were carried out between those employed versus those unemployed. An independent two tailed t test and a Mann Whitney U test was then carried out to determine significance. Further analysis was then performed using patient age and disease duration.

Results: At the time of analysis 734 patient were enrolled in the registry. The mean age was 45 years, with 77% male and 23% female, mean duration of disease was 18 years (means: ASQoL 6.6, HAQ 0.5, BASDAI 4.0, BASFI 3.6, BASMI 3.6). Unemployment rate in the ASRI population was 23%. National unemployment during the same time period was noticeably lower with a range of 6.2% to 13.1% (3). Those patients were also noted to have higher ASQoL (9.7 versus 5.6), HAQ (0.85 versus 0.45), BASDAI (5.3 versus 3.7), and BASFI scores (5.2 versus 3.2). The difference between the means was statistically significant ($p<0.05$) across all 4 measures. However, BASMI scores were significantly lower in the unemployed (3.8 versus 3.0). No statistically significant difference was detected between genders. The distribution of age and disease duration was determined to be equal between the groups.

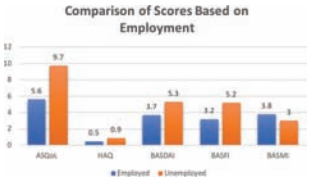


Figure 1

Conclusion: There is a higher prevalence of unemployment in the AS population as compared to the general population. Unemployed AS patients tend to have decreased quality of life, poorer levels of function, and higher levels of disease activity. Further research is needed to determine a causation between level of disease activity and employment.

REFERENCES:

[1.] Webers C, Vanhoof L, Genderen SV*, et al;* Employment perspectives of patients with ankylosing spondylitis in the biologics era; *Annals of the Rheumatic Diseases* 2017;76:157.

[2] Webers C, et al; Employment and the role of personal factors amoung patients with ankylosing spondylitis: a Dutch cross-sectional case-control study; *RMD Open* 2018. Jun27;4(1)

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FRI0681 **ASSOCIATION OF BODY COMPOSITION, PHYSICAL ACTIVITY AND PHYSICAL PERFORMANCE WITH KNEE CARTILAGE THICKNESS AND SUBCHONDRAL BONE AREA IN YOUNG ADULTS**

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Background: Body composition, physical activity and physical performance may play roles in the incidence of knee osteoarthritis. However, the effects of body composition, physical activity and physical performance on knee cartilage thickness and subchondral bone area in young adults were unknown.
Objectives: To describe associations of body composition, physical activity and physical performance with knee cartilage thickness and subchondral bone area in young adults.
Methods: Body composition, physical activity and physical performance were measured 4-5 years prior to knee magnetic resonance imaging (MRI). Cartilage thickness and subchondral bone area of patella and lateral/medial femorotibial compartment were measured quantitatively from MRI. Total knee cartilage thickness was calculated as the weighted-average according to bone area of each compartment; total knee bone area was calculated as the sum of each compartment. Associations were assessed using linear regression analysis. Age, gender, height (if fat mass or lean mass was predictor) and BMI (if physical activity or physical performance measures were predictors) were examined as potential confounders and were included in the regressions. Mediator was identified using mediation analysis (Stata's medeff command).
Results: Participants were aged 31-40 years, 48% were female (n=186). Greater lean mass, but not fat mass, was positively associated with total knee cartilage thickness (β=6.50 μm/kg, 95% confidence interval (CI): 0.86 to 12.13) and subchondral bone area (β=13.66 mm^2/kg, 95% CI: 5.73 to 21.59). Physical performance measures were positively associated with knee cartilage thickness (long jump: β=2.36 μm/cm, 95% CI 0.68 to 4.04; hand grip strength: 7.65 μm/kg, 1.53 to 13.77; physical work capacity: 1.04 μm/watt, 0.27 to 1.81) and subchondral bone area (long jump: β=4.25 mm^2/cm, 95% CI 1.01 to 7.50; hand grip strength: 19.89 mm^2/kg, 8.23 to 31.55; leg strength: 3.32 mm^2/kg. 1.25 to 5.40; physical work capacity: 3.00 mm^2/watt, 1.54 to 4.45). Mediation analysis suggested these associations were mediated by lean mass (effect mediated: 29-95%). Questionnaire based activity measures (including walking, moderate activity, vigorous activity and total activity) were not associated with total knee cartilage thickness or subchondral bone area.
Conclusion: Greater lean mass and better physical performance measures were associated with greater knee cartilage thickness and subchondral bone area in young adults, and the associations of physical performance were largely mediated by lean mass. These findings suggest lean mass may play an important role in maintaining knee joint health in young adults.

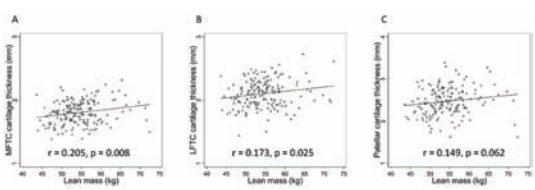


Figure. Scatter plots and linear regression lines for associations between lean mass and knee cartilage thickness (A: MFTC; B: LFTC; C: Patella).
R and P values are from models adjusted for age, gender, knee injury and height.
MFTC, medial femorotibial compartment; LFTC, lateral femorotibial compartment.

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FRI0682 **LEISHMANIASIS IN PATIENTSWITH CHRONIC INFLAMMATORY DISEASE TREATED WITH IMMUNOMODULATORS. MULTICENTER ANALYSIS**

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Background: Patients with chronic inflammatory disease in treatment with immunosuppressants have an increased risk of opportunistic infections, including leishmaniasis.
Objectives: To describe a multicenter case series of leishmaniasis in patients with chronic inflammatory diseases treated with immunosuppressants. To analyze factors related to the infection.
Methods: Observational retrospective study. We reviewed the clinical history of patients with chronic inflammatory diseases treated with immunosuppressants, who were diagnosed with leishmaniasis between 2007 and 2018. Demographic (age, sex) and clinical (type and time of evolution of the inflammatory disease, comorbidities, current treatment, leishmaniasis form) variables were collected. Immunosuppressant withdraw, subsequent reintroduction and recurrence were recorded. We analyzed differences in clinical presentation related to anti-TNFα treatment. Statistical analysis were performed using SPSS 22.0 program.
Results: 55 cases were collected. 58,2% were men and the average age was 57,2 (SD 1,9) years. Twenty-one patients had spondyloarthropathy, 17 rheumatoid arthritis, 14 inflammatory bowel disease, 1 systemic lupus erythematosus, 1 Behçet and 1 uveitis. The average duration of the disease was 11,4 (SD 1,4) years and 30,9% of patients had other causes of immunosuppression. Thirty-eight patients received treatment anti-TNFα (19 infliximab, 11 adalimumab, 5 golimumab, 2 certolizumab and 1 etanercept), 15 with DMARD (14 methotrexate, 1 leflunomide), 1 with tocilizumab and 1 with azathioprine. 27.3% patients received corticoids. 52,7% developed cutaneous form, 38,2% visceral form, 7,3% mucocutaneous form and 1 presented visceral and cutaneous involvement. Treatment was withdrawn in 37 cases and it was reintroduced in 23 cases (8 anti-TNFα). Four patients relapsed. More cases of visceral leishmaniasis were seen in patients treated with non-anti-TNFα drugs and in those treated with glucocorticoids. Most of the recurrences were associated with mucocutaneous form.
Conclusion: In our series, the majority of cases of leishmaniasis occurred in patients treated with anti-TNFα, but non-anti-TNFα patients developed more serious forms. It's important to keep in mind this infectious complication in daily clinical practice.
Disclosure of Interests: : L Montolio-Chiva: None declared, Elia Valls-Pascual: None declared, D Ybáñez-García: None declared, À Martínez-Ferrer: None declared, Marta Aguilar-Zamora: None declared, Ana V Orenes Vera: None declared, I Vázquez-Gómez: None declared, A Sendra-García: None declared, JM Paredes Arquiola: None declared, Meritxell Fernandez Matilla: None declared, L Gómez Escolar: None declared, José Miguel Senabre-Gallego: None declared, J Lluch Pons : None declared, C Campos Fernández: None declared, M Robustillo-Villarino : None declared, María Dolores García-Armario: None declared, S Antón-González: None declared, ANA URRUTICOECHEA-ARANA: None

declared, Isabel de la Morena Speakers bureau: Abbvie, Celgene, Pfzier, UCB, Ghebro, Roche, Sanofi, Janssen., J Fiter-Areste: None declared, Vega Jovani: None declared, A Martínez-Cristóbal : None declared, Lourdes Mateo: None declared, Sergi Ordoñez : None declared, D Reina-Sanz: None declared, C Vergara-Dangond: None declared, V Núñez-Monje: None declared, I Torner-Hernández: None declared, Juanjo J Alegre-Sancho: None declared

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FRI0683 **DEFINING THE GUT MICROBIOME IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS**

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Background: Although a link between gut microbiome and autoimmune diseases has been suggested, there is a gap in the understanding of the gut microbiome in ANCA-associated vasculitis (AAV).
Objectives: This study evaluated the gut microbiome in AAV (granulomatosis with polyangiitis (GPA), microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis) compared to healthy controls.
Methods: Using cross-sectional and longitudinal designs, the gut microbiome was compared among patients with i) newly-diagnosed AAV (active and remission); ii) chronic AAV (active and remission), and iii) healthy controls. Fecal samples were collected using standardized methods and analyzed by sequencing the bacterial 16S rRNA gene (V1-V2 region). Taxa with mean abundance >1% were compared using Wilcoxon rank sum test, correcting for multiple comparisons. Disease severity was assessed with the Birmingham Vasculitis Activity Score for Wegener's Granulomatosis (BVAS/WG). Effects of medications were studied using mixed effects models.
Results: 63 fecal samples were studied: 29 active AAV (15 new diagnosis/14 chronic), 20 in remission, and 14 healthy controls. Compared to controls, patients with active AAV had a different microbial composition (p=0.01). There was no statistical difference between the gut microbial composition of controls and patients in remission (p=0.16). The relative abundance of the taxa Dialister and Prevotella were different between active and remission AAV. The relative abundance of the genera Faecalibacterium and Sutterella were different between active and remission newly-diagnosed AAV (**Figure 1A**). The relative abundance of Dialister was significant in patients with high BVAS/WG compared to patients with low BVAS/WG (p<0.01) (**Figure 1B**). High BVAS/WG was associated with greater dysbiosis (**Figure 2**);. similar results were found in a multivariate linear model (p=0.02). The gut microbiome in patients with GPA on immunosuppressive agents was similar to controls (p=0.54), whereas the gut microbiome of patients with GPA not on these therapies was significantly different from controls; similar results were found with glucocorticoids and antibiotics use.
Conclusion: Active AAV is associated with an altered gut microbial composition. Patients in clinical remission have microbial composition similar to healthy controls. Immunosuppressive agents, glucocorticoids, and antibiotics may re-establish a healthy gut microbiome. Severe disease activity is associated with worsening gut dysbiosis suggesting a potential role of gut bacteria in the pathogenesis of AAV.

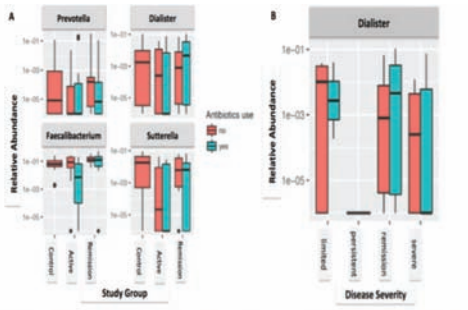


Figure 1. Bacteria with Differential Abundance Between Various Subgroups of Patients with ANCA-Associated Vasculitis (AAV). (A) Compared to patients with AAV in remission, patients with active AAV had a lower proportion of the taxa *Dialister* and *Prevotella* (p=0.02 and p=0.03, respectively and corrected for false discovery rate). Compared to patients with a new diagnosis of AAV in clinical remission, patients with a new diagnosis of active AAV had a lower proportion of the genera *Faecalibacterium* and *Sutterella* (p=0.02 and p=0.05, respectively, corrected for false discovery rate). (B) Compared to patients with less disease activity, patients with severe disease had a lower proportion of *Dialister* (p<0.01, corrected for false discovery rate).

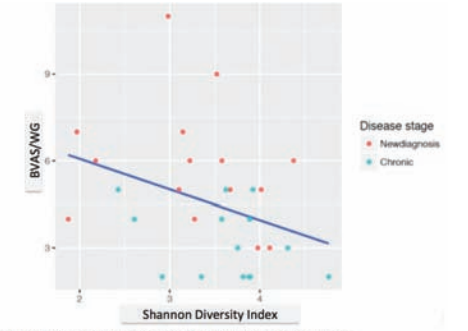


Figure 2. Scatter Plot of BVAS/WG by Shannon Diversity Index in Patients with Active AAV. High BVAS/WG correlated with a greater gut microbiome dysbiosis (lower Shannon diversity index) in patients with active AAV (Pearson coefficient= -0.35; p<0.01).

REFERENCES:

[1] Jennette J.C., et al., 2012 *revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides*. Arthritis Rheum, 2013. 65(1): p. 1-11.
[2] Merkel P.A., et al., *Identification of functional and expression polymorphisms associated with risk for anti-neutrophil cytoplasmic autoantibody-associated vasculitis*. Arthritis Rheum, 2017. 69(5): p. 1054-1066.
[3] Scher J.U., et al., *Microbiome in Inflammatory arthritis and human rheumatic disease*. Arthritis Rheum, 2016. 68: p.35-45.
[4] Scher J.U. *Intestinal dysbiosis and potential consequences of microbiome-altering antibiotic use in the pathogenesis of human rheumatic disease*. The Journal of Rheum, 2015. 42: p.355-357.
[5] Scher J.U., et al., *Decreased bacterial diversity characterizes an altered gut microbiota in psoriatic arthritis and resembles dysbiosis of inflammatory bowel disease*. Arthritis and Rheum, 2015. 67(1): p.128-139

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FRI0684 **NOVEL MAPPING FUNCTION ILLUSTRATES NONLINEARITY BETWEEN TRIAL ACR RESPONSE, DAS28 CHANGE AND EULAR RESPONSE CRITERIA**

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Background: The American College of Rheumatology (ACR) definition of improvement is a standardised, widely used outcome measure for clinical trials in rheumatoid arthritis. In routine clinical practice (and registries),

improvement is assessed by the DAS28 (Disease Activity Score 28), particularly in the UK, where it is the basis of current NICE guidance[1].
Objectives: To develop a mapping function that charts ACR20/50/70 and ACRn to ΔDAS28 and EULAR response, and determine the relationship between the response measures.
Methods: Individual patient-level data from the 428 participants randomised to the ATTRACT[2] trial were used. The proportion of participants with ACRn (ACR10-ACR90) response and the change in DAS28 (ΔDAS28) at 30 weeks from baseline were calculated and analysed analysed in participants with complete data. The cut points in ΔDAS28 that provided the equivalent proportion of participants achieving ACR10 to ACR90 at 30 weeks overall and per individual arm were searched for through tabulation. Regression models were conducted and misclassification rates calculated to test the accuracy of the mapping function. The minimum and maximum ACRn achieved per EULAR response category were also determined to establish the correlation of these two response criteria. R version 3.4.3 (2017-11-30) was used for all statistical analyses.
Results: 53%/27%/12% of all trial participants achieved ACR-ESR 20/50/70 responses, respectively. The mapping function shows that at 30 weeks a 20% improvement in ACR is equivalent to a 27.3% and 27.8% improvement from baseline in DAS28 calculated using ESR and CRP, respectively. 50% improvement in ACR is equivalent to a 45% and 46.2% improvement in DAS28-ESR and DAS28-CRP, respectively. 70% improvement in ACR is equivalent to a lower improvement in the DAS28, at 55.8% for ESR and 59.3% for CRP. Similar results were obtained when analysing the individual arms (Table 1 & Figure 1). Baseline DAS28 for all analysed groups was $\geq$ 6.0. Moderate or good EULAR responses correspond to 80% and 90% improvement in ACR, respectively, whereas the no response EULAR category showed a maximum improvement in ACR-ESR/CRP of 30%-50%, respectively (Figure 2).
Conclusion: This novel mapping function enables the comparison of trials reporting ACR20/50/70 with those reporting ΔDAS28. The results imply nonlinearity in the relationship between ACR20/50/70, ΔDAS28 and EULAR response criteria. Limitations: The mapping is dependent on the population chosen to examine it, which in this analysis comprised trial participants with very active disease.

REFERENCES: :

[1] National Institute for Health and Care Excellence (NICE), *Technology Appraisal Guidance (TA375)* 2016. 2Maini R, et al. Lancet 1999.

Table 1. Mapping between the ACR criteria and change in DAS28

	Full cohort (n=428)	Placebo arm (n=88)	IFX arm* (n=86) (3mg/kg every 8 weeks)
	ΔDAS28-ESR (%)	**ΔDAS28-ESR (%)**	**ΔDAS28-ESR (%)**
ACR-ESR criteria	**(Accuracy (%))**	**(Accuracy (%))**	**(Accuracy (%))**
20% improvement	27.3 (80)	24 (85)	29.5 (81)
50% improvement	45 (85)	39 (94)	44 (84)
70% improvement	55.8 (91)	44 (91)	57.9 (86)
	ΔDAS28-CRP (%)	**ΔDAS28-CRP (%)**	**ΔDAS28-CRP (%)**
ACR-CRP criteria	**(Accuracy (%))**	**(Accuracy (%))**	**(Accuracy (%))**
20% improvement	27.8 (83)	27 (80)	30 (82)
50% improvement	46.2 (84)	44 (92)	47.5 (84)
70% improvement	59.3 (93)	50.8 (92)	50.8 (84)

ESR (erythrocyte sedimentation rate); CRP (C-reactive protein concentration).

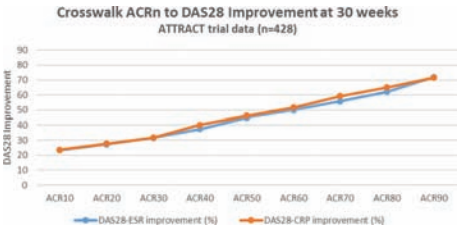


Figure 1. Mapping between ACRn (ACR10-ACR90) and DAS28 improvement at 30 weeks.

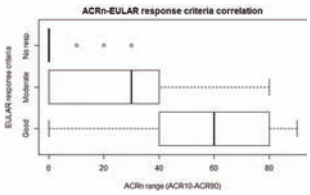


Figure 2. Correlation of the EULAR and ACR response criteria at 30 weeks.

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FRI0685

PREVALENCE OF CARDIOVASCULAR SYMPTOMS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES – A QUESTIONNAIRE BASED STUDY

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Background: Cardiovascular involvement in patients with idiopathic inflammatory myopathies (IIM) significantly worsen the prognosis and remain one of the major cause of death[1]. Although it is usually subclinical, symptomatic manifestations are not infrequent and exert considerable impact on the course of IIM[2].
Objectives: To evaluate the frequency of subjective symptoms indicating cardiovascular involvement in patients with different subtypes of IIM and assess the impact of such ailments on daily living and degree of disability.
Methods: An online questionnaire was created and distributed by means of online support groups to English-speaking patients with IIM. Responders were asked to answer 40 questions concerning subtype and duration of disease, cardiac and musculoskeletal symptoms as well as to fill the Short 2-page Health Assessment Questionnaire (HAQ). Responses of patients with dermatomyositis (DM), polymyositis (PM), inclusion body myositis (IBM) and overlapping syndrome (OS) were analysed statistically.
Results: Questionnaire was completed by 377 responders, among which 38,78% had IBM, 34,07% DM, 16,62% PM and 10,53% OS. Dyspnoea at rest affected at least a few times a month 48,33% patients with PM, 43,09% with DM, 28,95% with OS but only 20,71% with IBM (PM vs OS p=0,057, IBM vs DM p<0,001, IBM vs PM p<0,001). Dyspnoea during daily activities was declared by 55,26%-60,98% of patients with OS, PM and DM, but only 37,14% with IBM (IBM vs OS p=0,04, IBM vs DM p<0,001, IBM vs PM p=0,003). Dyspnoea at exercise was more prevalent in PM and DM groups (respectively 80% and 86,18% vs 71,05% and 52,14% in OS and IBM; DM vs OS p=0,03, IBM vs OS p=0,04, IBM vs DM p<0,001, IBM vs PM p<0,001). Chest pain was noted mostly by participants with DM, OS and PM as in 38,33%-45,53% of them it occurred at least a few times a month, while it affected only 1/5 of responders with IBM (IBM vs OS p=0,002, IBM vs DM p<0,001). Only 37,14% of patients with IBM experienced palpitations while it was declared by 51,67%-63,16% of participants with PM, DM, OS (IBM vs OS p=0,004, IBM vs DM p<0,001, IBM vs PM p=0,056). In contrary to bradycardia, a feeling of too fast heart rate was common, mostly in patients with DM. Ankle oedema and dry cough occurred in respectively 43,90-60% and 43,33-52,03% of participants. Degree of disability, assessed with HAQ was significantly higher in IBM patients. Regardless of myositis subtype dyspnoea during daily activities hindered reaching, dressing and gripping (respectively p=0,015, p=0,03, p<0,01 if comparing patients with and without dyspnoea). Arising, walking and maintaining hygiene was less troublesome for participants with exertional dyspnoea, chest pain, palpitations or tachycardia as compared to patients without those symptoms.
Conclusion: Symptomatic cardiovascular involvement is frequent in patients with IIM. Patients with IBM are less affected by cardiac symptoms yet present the highest degree of disability. Most of cardiac symptoms do not aggravate disability.

REFERENCES:

[1] Diederichsen LP, Cardiovascular involvement in myositis, Curr Opin Rheumatol. 2017 Nov;29(6):598-603

[2] Diederichsen, LP, et al., Cardiac Abnormalities in Adult Patients With Polymyositis or Dermatomyositis as Assessed by Noninvasive Modalities, Arthritis Care Res (Hoboken). 2016 Jul;68(7):1012-20

Disclosure of Interests: None declared
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FRI0686 RELATIONSHIP BETWEEN VITAMIN D SUPPLEMENTATION AND MUSCULAR STRENGTH IN ELDEST POPULATION. A SISTEMATIC REVIEW

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Background: Sarcopenia is the loss of skeletal muscle mass, strength and function that occurs as a consequence of aging. This condition result in physical disability, which limits the capacity to walk, increases the risk of falls and osteoporotic fractures. Several studies suggested an inverse relation between 25OHD serum levels, muscular strength and physical performance in the eldest.
Objectives: To evaluate if vitamin D supplementation in patients > 50 years improves muscle mass, strength and performance in older patients.
Methods: We performed a systematic review through Medline, Cochrane Library, and EMBASE. Inclusion criteria: 1) patients > 50 years old, 2) receiving treatment with vitamin D 3) muscle mass and muscle strength measurements 4) systematic reviews (SR) 5) randomized clinical trials (RCT) 6) Papers written in English or Spanish.
Results: Five studies were included (4 SR and 1 RCT), n patients ranged from 121 to 5615. Patients mean age oscillated between 58-88 years, receiving variable vitamin D dose. Follow-up period fluctuated from 6 to 12 months.

Author	N° clinical studies-patients	Results
Beaudart 2014 SR	N=30(CS) n=5.615	Significant increment in patients with 25OHD < 30nmol/L and > 65 years. Muscular strength SMD 0.17 (P=0.02)
Muir 2011 SR	N=13(CS) n=2.268	Significant improvement with vitamin D supplementation in: 1-Postural balance reduction DME -0.20 (IC95% -0.39 a -0.01,P=0.04, I2 = 0%) 2-Reduction in time to finish the test TUG -0.19 (IC95% -0.35 a -0.02, P =0.03, I2 = 0%)
Beaudart 2017 SR	N=2 (CS) n=121	No additional effect of vitamin D, except for TUG (n=1)
Stockton 2011 SR	N=17(CS) n=5.072	Patients with serum 25(OH)D <25 nmol/L caused significant improvement in hip muscular strength with vit D supplementation (DME 3.52, IC95% 2.18, 4.85).(n=2)
Cangussu 2015 RCT	N=160	Significant increment in vitamin D group. Muscular strength (chair test) 25.3% (p <0.0001)

CS= Clinical studies, SR=Systematic reviews, RCT=Randomized clinical trials, SMD=Standardized mean difference, TUG= Time UP and Go.

Conclusion: • Vitamin D supplementation in patients > 65 years with inadequate 25OHD serum levels, improve muscular strength.
• There were no benefits in muscle mass or muscular performance.

REFERENCES:

[1] Beaudart C, Dawson A, Shaw S C, Harvey N H, Kanjis J A, Binkley N, et al. Nutrition and Physical activity in the prevention and treatment of sarcopenia.: systematic review. Osteopor Int 2017; 28: 1817-1833.
[2] Cangussu LM, Nahas-Neto J, Orsatti CL, Bueloni-Dias FN, Nahas EAP. Effect of Vitamin D supplementation alone on muscle function in postmenopausal women: a randomized double-blind, placebo-controlled clinical trial. Osteopor Int 2015; 26:2413-2421.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.4396

FRI0687 NEUROMYELITIS SPECTRUM DISORDERS ASSOCIATED WITH AUTOIMMUNE DISEASES: DIFFERENCES IN CLINICAL CHARACTERISTICS AND MRI FINDINGS

Milena Rodriguez Alvarez[1], Manjeet Bhamra[1], Vinodkumar Velayudhan[1], Fernando. Cuascut[2], Latoya Freeman[1], Su Yien Zhaz[3], Joshy Pathiparampil[1], Naureen Kabani[1], Kristaq Koci[1], Alexandra Kreps[1], Justin Levinson[4], Sophia Francis[1], Steve Xie[1], Helen Valsamis[1], Abhimanyu Amarnani[1], David Ozeri[5], Samir Alkabie[1], Yaacov. Anziska[1], Isabel Mcfarlane[1]. *[1]SUNY Downstate Medical Center, Medicine, BROOKLYN, United States of America*; *[2]Baylor University Medical Center, Neurology, Dallas, United States of America*; *[3]Samaritan Medical Center, Watertown, United States of America*; *[4]Temple University Hospital, Philadelphia, United States of America*; *[5]Sheba Medical Center, Tel Aviv, Israel*

Background: Neuromyelitis Optica Spectrum disorders (NMOSD) is a rare autoimmune disease characterized by optic neuritis (ON) and/or longitudinal extensive transverse myelitis (LETM). It is commonly associated with other autoimmune diseases (OAD). Recent reports suggested racial differences in clinical phenotype and presentation of NMOSD. However, data on Black population is scarce.
Objectives: We aim to characterize, in our largely Black population, the clinical, laboratory and radiologic features of patients with NMOSD and OAD. We also aim to ascertain differences in clinical presentation between NMOSD patients with and without OAD.
Methods: In a retrospective analysis, patients $\geq$ 18 years of age with a confirmed diagnosis of NMOSD as per the International Panel for NMOSD Diagnosis Criteria, seen at 2 NYC urban hospitals from 1/2005 to 4/2017 were identified. Demographic, clinical, and laboratory data were extracted together with expanded disability status scales (EDDS) and imaging studies. Brain magnetic resonance imaging (MRI) was reviewed by a neuro-radiologist who applied the NMOSD Radiological criteria to identify typical findings of the disease.
Results: Forty-one patients fulfilled NMOSD criteria. 85.4% were women with a mean age of 44.7±2.03 years. 82.9% of the patients were Black and 34.1% (14/41) had an associated OAD. Systemic lupus erythematosus (SLE) was the most common OAD present prior to NMOSD diagnosis, followed by thyroid disease and Sjogren's syndrome. Aquaporin 4 immunoglobulin G (AQP4IgG) was positive in 82.9% of the entire cohort and in 76.9% (10/13) of patients with NMOSD and OAD. Hypertension (33.3% vs. 15.3%), and cardiovascular disease (13.3% vs. 4%) were more frequent in NMOSD with OAD, compared with the NMOSD only group. On initial presentation of the NMOSD only group, visual changes (40% vs. 28.5%) and ON (38.4% vs. 20%)were predominant. In the intial presentation of NMOSD with OAD group, sensory loss (78.5% vs. 57.7%), acute myelitis (40% vs. 23.1%), and elevated C reactive protein (CRP) (20.85±11.2 vs. 3.2±1.85mg/d/L) were more freuent. Disability scores (EDDS) were 5.5 for each group. Brain MRI revealed lesions affecting corpus callosum in a marble pattern, (21.4% vs. 13.6%), the hemispheres in a spindle like pattern(33%vs 22.7%), the dorsal medulla (50% vs. 39.1%), the area postrema (38.5% vs. 27.3%) and the pons (21.4% vs. 13.4) for NMOSD with OAD and without respectively. LETM with predilection for the thoracic region was (66.7% vs 54.5%), cord edema (69.2% vs. 40.9%) and gadolinium enhancement (69.2% vs. 59.1%) for NMOSD with OAD and NMOSD only patients respectively.
Conclusion: AQP4IgG-positivity was observed in most of the cases in our predominantly Black NMOSD population. Over a third of the NMOSD patients had OAD. SLE was the most commonly reported. NMOSD with OAD patients tended to present with sensory loss, acute myelitis, and elevated CRP, while in NMOSD without OAD presented more with visual changes and ON. The NMOSD with OAD group had more MRI lesions involving corpus callosum, hemispheres, brainstem and LETM, compared to those with NMOSD only group.

REFERENCES:

[1] Katz S I. NMOSD. Multiple Sclerosis and Other Demyelinating Diseases p. 864896. June 2016, Vol.22, No.3. Doi: 10.1212/CON.0000000000000337

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FRI0688 **PREDICTORS OF EROSION AND JOINT SPACE NARROWING PROGRESSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

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Background: Joint damage in rheumatoid arthritis (RA) includes erosions and joint space narrowing (JSN). Predictors of these processes, and the underlying mechanisms, require further study[1].
Objectives: To investigate the relation between patient characteristics at RA diagnosis and progression of erosions and JSN, over 5 years.
Methods: Consecutive early RA patients (symptom duration <12 months), recruited 1995-2005 from a defined area, managed according to usual care with no pre-specified treatment protocol, were followed through 5 years. Radiographs of hands and feet were scored in chronological order by a trained reader according to the modified Sharp-van der Heijde score (SHS), including separate erosion- and JSN scores. The relations between baseline variables and progression of erosion- and JSN scores over 5 years (log transformed), were assessed using linear regression.
Results: 233 early RA patients where included. Radiographs at baseline and 5 years were available for 162 patients. Results on predictors of rapid radiographic progression of the total SHS have been reported previously[2]. The median (interquartile) progression of erosion and JSN scores were 4 (0-8) and 8 (1-16), respectively. RF and anti-CPP predicted progression of erosions and JSN over 5 years, with stronger associations for erosions (**Table 1**). Baseline erosion- and JSN scores each predicted progression of JSN, while baseline JSN did not predict progression of erosions. In crude analyses, higher disease activity, CRP and ESR were associated with progression of both erosions and JSN, while statistically more robust for the former. Smoking and high levels of Cartilage Oligomeric Matrix Protein (COMP) (>12 U/L) were both associated with progression of erosions ((B= 0.12, p= 0.016) and (B= 0.12, p= 0.02) respectively) but not JSN, in adjusted analyses (**Table 1**). Overweight or obesity (BMI >25kg/m^2) was associated with less progression of JSN (B= -0.14, p= 0.018, adjusted for RF, age and baseline JSN score).

Table 1. Baseline predictors of progression of erosion and JSN scores (log transformed) from baseline to 5 years in linear regression

	Erosion score				JSN score			
Baseline characteristics	**Crude**		**Adjusted for RF and baseline erosion score**		**Crude**		**Adjusted for RF, age and baseline JSN score**	
	B	p	B	p	B	p	B	p
Age (per SD)	0.02	0.39	0.02	0.45	0.06	0.051	NA	NA
Overweight or obese vs. normal BMI[a]	-0.05	0.34	-0.03	0.62	-0.14	0.03	-0.14	0.018
Ever vs. never smokers	0.16	0.004	0.12	0.016	0.05	0.49	0.06	0.33
RF positivity	0.23	<0.001	NA	NA	0.18	0.004	NA	NA
Anti-CCP positivity	0.23	<0.001	0.13	0.02	0.17	0.008	0.09	0.18
COMP >12 U/L	0.10	0.08	0.12	0.02	0.08	0.24	0.08	0.23
Erosion score (per SD)	0.07	0.006	NA	NA	0.12	<0.001	0.08	0.02
JSN score (per SD)	0.04	0.12	-0.01	0.69	0.11	<0.001	NA	NA
High vs. moderate DAS28[b]	0.17	0.003	0.12	0.03	0.14	0.04	0.12	0.054
ESR (per SD)	0.11	<0.001	0.08	0.002	0.09	0.003	0.06	0.04
CRP >9 mg/l (median)[c]	0.15	0.003	0.09	0.08	0.13	0.03	0.07	0.26

NA, not applicable; vs, versus.
[a] Overweight or obese >25 kg/m^2; normal 18.5 – 24.99 kg/m^2.
[b] High >5.1; moderate >3.2 to ≤5.1.

Conclusion: RF, anti-CCP and markers of inflammation and disease activity predicted progression of erosions and JSN, in particular erosions. Development of erosions may predate cartilage damage leading to JSN. Smoking and high baseline levels of COMP predicted progression of erosions, but not JSN. Overweight and obesity may be associated with mechanisms that protect from JSN.

REFERENCES:

[1] Smolen et al, Ann Rheum Dis. 2009;68:1535-40.2 Rydell et al, Arthritis Res Ther. 2018;20:82.

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FRI0689 **EFFECT OF AIR POLLUTION EXPOSURE ON DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS**

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Background: Environmental exposure (e.g. tobacco smoking, pollution) has been accepted to contribute in autoimmune diseases. Air pollution has been described to be a risk factor for developing rheumatoid arthritis (RA). Currently, RA disease remission is considered an achievable target in a significant proportion of patients. Nevertheless, diseases flares, that significantly contributes to damage progression and disability, remain unpredictable. Thus, factors able to potentially interfere on disease activity should be considered and assessed.
Objectives: The aim of our study is to evaluate the influence of particulate matter (PM) on disease activity and general health (GH) in patients with RA.
Methods: Consecutive patients with RA (ACR/EULAR Criteria 2010) resident in Lombardy (Italy) were enrolled. In each patient Disease Activity Score on 28 joints (DAS28), Simple Disease Activity Index (SDAI) and patients' GH were assessed. Daily PM concentrations, estimated by Regional Environmental Protection Agency at municipality resolution, were used to assign short-term exposure from day of visit back to 14 days. Continuous variables are expressed as mean±SD. Categorical variables are presented as absolute numbers and frequencies. Multivariable linear regression models were performed to identify the day of PM10 and PM2.5 independently associated with DAS28, GH and SDAI indices, adjusting for the variables significant at the univariate analysis. GH was log transformed to achieve normality of residuals. β coefficients were reported for 10 µg/m3 increments of PM concentrations. All statistical analyses were performed using SAS 9.4.
Results: 258 patients (age at visit 57.4±13.5 years, disease duration 16.2 ±12.1, female 80.2%, rheumatoid factor and/or anti-citrullinated peptide antibodies positivity 60.5%, smokers 15.5%, radiographic damage 41.5%) were enrolled in the study. Multivariable linear regression models were adjusted for radiographic damage, disease duration and age. Increases of PM2.5 and PM10 exposure (9 day before the visit) were significantly associated with worsening of DAS28, SDAI and GH (table below). PM concentrations in days other than 9 days before were significantly associated with disease activity and GH.

	PM Exposure	β x 10	SE	95% CI		P-value
DAS28	PM_{10} Day -9	0,10	0,05	0,00	0,19	0,041
	$PM_{2.5}$ Day -9	0,11	0,06	0,00	0,23	0,048
SDAI	PM_{10} Day -9	0,80	0,39	0,02	1,57	0,043
	$PM_{2.5}$ Day -9	0,95	0,48	0,00	1,90	0,049
GH	PM_{10} Day -9	0,11	0,04	0,03	0,18	0,004
	$PM_{2.5}$ Day -9	0,14	0,05	0,06	0,23	0,002

Conclusion: In our cohort, PM10 and PM2.5 exposure seems to influence RA disease activity with a lag period that can last until 9 days before the visit. Nevertheless, the association between day-to-day PM changes and disease activity do not confirm causation. Further studied are required to evaluate the influence of air pollution on RA activity.

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FRI0690

WOMEN WITH RHEUMATOIDARTHRITIS HAVE HIGHER LIFETIME PROFESSIONAL AND NON-PROFESSIONAL EXPOSURE TO SILICA DUST COMPARED TO FRENCH GENERAL POPULATION

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Background: Occupational exposure to silica dust is associated with increased risk of developing ACPA positive Rheumatoid arthritis (RA). Little is known about non-occupational exposure, as there are no available tools to assess it in clinical practice.

The Dust Exposure Life-Course Questionnaire (DELCQ), developed within the SILICOSIS project, a European Research Council Advanced Grant, provides clinical research with a tool derived from social sciences. The DELCQ allows to quantify both occupational and non-occupational (e.g. body care; hobbies such as DIY, woodworking, stone cutting, etc..) exposure to silica and some other inorganic particles during the whole lifetime.

In the DELCQ, the identification of sources of exposure is grounded on an extensive list of products and activities summed up by the International Agency on Research on Cancer and on a wide overview of the literature addressing silica exposure and silica-related (or suspected-to-be-related) diseases.

Objectives: To explore occupational and non-occupational silica exposure in a series of consecutive RA patients and the association of quantified silica dust exposure with major disease features (ACPA positivity) or outcomes (erosive disease).

Methods: The DELCQ was administered to 97 consecutive RA patients (77F, 20M, mean age 59.1+/- 13.3 yrs.,75 ACPA positives, 66 with erosive disease) attending the rheumatology department of Avicenne Hospital (Bobigny, FRANCE). The DELCQ scores of patients were compared to those of 388 controls, matched for sex, age and smoking status, from a 2739-subject national cohort, representative of the general French population (ELIPSSilice). Within RA subjects, the association of the scores with ACPA positivity and with erosive disease was assessed after adjustment for tobacco use.

Results: RA patients had higher median scores of occupational (10 [0, 17] vs. 0 [0, 4]) exposure vs. controls ($p<0.0001$). Median occupational exposure was higher in both men and women compared to controls matched by age, sex and tobacco use (23.5 [18, 34.5] vs. 2.5 [0, 12] for men and 7 [3, 14] vs. 0 [0, 5] for women, $p<0.0001$ for both). Non-occupational median exposure was significantly higher only in women with RA (15 [9, 21] vs. 12 [5, 21], $p< 0.05$). Male vs. female RA patients had higher median occupational scores of exposure ($p<0.001$), while non-occupational exposure was not significantly different. After adjusting for smoking (smokers>5 pack/y vs. nonsmokers or smokers <5 pack/y), neither professional of non-professional scores were associated with erosive disease, despite a strong negative interaction with tobacco use.

Conclusion: Women with RA have higher professional and nonprofessional lifetime exposure to silica dust compared to age, and sex-matched subjects from the French general population. In this series, constituted mainly of non-smoking women, exposure to silica may be a relevant environmental factor for the development of RA. Higher occupational exposure in RA is confirmed in men with RA. Neither occupational nor non-occupational exposure was associated with ACPA positivity or erosive disease, likely due to the high prevalence these features in the patient series.

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FRI0691

DISCREPANCY BETWEEN THE EFFICACY OF BIOLOGICAL DMARDS BASED ON RANDOMIZED CONTROLLED TRIALS AND THE EFFICACY OF BIOLOGICAL DMARDS IN REAL-WORLD SETTINGS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A STUDY USING THE IORRA COHORT

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Background: Randomized controlled trials (RCTs), which are currently considered to provide the highest level of evidence, include patients with high disease activity and exclude those with comorbidities often seen in the real world. With the increasing recognition of the importance of real-world evidence, attention is being paid to discrepancies between RCT-based evidence and the patient population in routine clinical practice; however, few reports assessing these gaps in the context of rheumatoid arthritis (RA) are available.

Objectives: We investigated the discrepancy between the efficacy of biological DMARDs (bDMARDs) in RCTs and the effectivenessof bDMARDs in routine clinical practice in patients with RA based on the IORRA cohort.

Methods: The effectiveness of bDMARDs (etanercept [ETN; n=33], golimumab [GLM; n=20], certolizumab [CZP; n=17], abatacept [ABT-subcutaneous injection {sc}; n=14], and tocilizumab [TCZ-sc; n=24]) in RA patients who newly initiated bDMARD therapy in our hospital in 2016 was compared with the efficacy reported in phase 2 or 3 trials (8 total RCTs: ETN, 1; GLM, 2; CZP, 2; ABT, 1; TCZ, 2) during the RCT's observational periods. Effectiveness was evaluated by percentages of patients achieving ACR20, ACR50, and ACR70 and clinical remission based on DAS28 remission criteria using the IORRA cohort database. We also compared treatment responses between IORRA eligible and non-eligible patients in the MATSURI study, a phase 2 trial that evaluated TCZ-sc efficacy and safety and had relatively lenient inclusion criteria, since some RA patients in the IORRA cohort belonged to both the eligible and non-eligible groups.

Results: In 7 RCTs (excepting the MATSURI study), very few patients fulfilled the IORRA inclusion criteria (Table). The ACR achievement rates were higher among patients in RCTs, while remission rates were higher among IORRA patients (Table). The average DAS28 at baseline in the RCTs group was significantly higher than that in the IORRA group (Table). In the MATSURI study, 13 of 24 patients who newly initiated TCZ-sc met the inclusion criteria in the IORRA. Although the percentages of patients achieving ACR20, ACR50, and ACR70 and clinical remission among eligible patients were similar to those of patients in the MATSURI study, those of non-eligible patients were lower than those of MATSURI patients (Table). This indicates better effectiveness in eligible patients than in non-eligible patients.

Conclusion: Although RA patients in RCTs experienced a better ACR achievement rate than those in routine practice, clinical remission was difficult to achieve. This might be due to the difference in disease activity at the time of bDMARD introduction, suggesting that it is necessary to interpret the efficacy of RCTs based on differences in patient background.

REFERENCES:

Table

RCT										IORRA cohort								
study name	drug	ITT population (n)	FAS population (n)	period	DAS28 at baseline	ACR 20*	ACR 50*	ACR 70*	DAS28 remission*		ITT population (n)	FAS population (n)	who fulfilled inclusion criteria of each RCT	DAS28 at baseline	ACR 20*	ACR 50*	ACR 70*	DAS28 remission*
MATSURI	TCZ	32	32	24 weeks	5.4±1.0	83.0%	83.0%	50.0%	83.0%	TCZ								
										eligible case**	13	10	13	5.0±1.1	70.0%	50.0%	40.0%	80.0%
										non-eligible case***	11	8		3.9±0.7	12.5%	12.5%	0.0%	62.5%
MUSASHI	TCZ	173	159	24 weeks	6.1±0.9	79.2%	63.5%	37.1%	49.7%	TCZ		24	18	2	4.5±1.1	44.4%	33.3%	22.2%	72.2%
Phase III study	ABT	59	57	24 weeks	5.6±0.8	91.5%	66.1%	37.1%	49.7%	ABT		14	12	0	3.5±1.1	25.0%	25.0%	25.0%	66.7%
GO-MONO	GLM	316	308	24	5.8±1.1	46.5%	27.7%	16.6%	17.2%	GLM		21	17	0	4.0±0.9	29.4%	23.5%	23.5%	43.8%
GO-FORTH		209	201	weeks	5.5±1.2	70.9%	41.9%	34.9%	34.9%					0					
HIKARI	CZP	110	82	24	6.1±0.9	63.8%	46.0%	25.9%	16.4%	CZP		17	12	2	4.1±1.3	33.3%	25.0%	8.3%	45.4%
J-RAPID		82	66	weeks	6.2±0.8	73.2%	54.9%	29.3%	17.1%					0					
A Phase3 trial	ETN	182	151	52 weeks	5.8±1.0	78.6%	62.1%	36.3%	34.1%	ETN		33	20	2	3.9±1.7	40.0%	30.0%	10.0%	70.0%

RCT: randomized control trial, ITT: Intension-to-Treat, FAS: Full Analysis Set, n: number of the patients, TCZ:tocilizumab; ABT:abatacept; GLM:golimumab; CZP:certolizumab, ETN:etanercept
* percentages of the patients achieving ACR20, ACR50, and ACR70 and clinical remission based on DAS28
** patients who fulfilled inclusion criteria of MATSURI study in the IORRA
*** patients who did not fulfill inclusion criteria of MATSURI study in the IORRA

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FRI0692

34. REHABILITATION HUMAN PAPILLOMA VIRUSSCREENING AND CHRONIC INFLAMMATORY ARTHRITIS: AN AUDIT

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Background: Patients with autoimmune diseases suffer from an immunosuppressive state related to a pro-inflammatory environment and therapies received. Immunosuppression is a known risk factor for developing virus-associated cancers, including at uterine cervix (1,2). One of the major risk and prognostic factors for cervical neoplasm is missing the screening and early detection programs of human papilloma virus (HPV) (3). This screening is recommended for immunosuppressed women to be performed annually between 21 and 65 years of age (4).

Objectives: To audit the degree of adherence to HPV-cervical cancer screening of patients with chronic arthritis in the rheumatology unit of a tertiary center.

Methods: A descriptive, cross-sectional study was performed. The medical records of adult, female patients, with clinical diagnosis of rheumatoid arthritis (RA) and psoriatic arthritis (PsA), being followed in rheumatology clinics were reviewed. Assistance to screening clinics and cervical cytology and HPV-PCR results were revised to determine if patients had followed the screening program. Type of screening, number of visits and findings were also collected. A descriptive analysis is presented, with an estimate of the 95% confidence interval (95%CI) for the primary study variable.

Results: 233 medical histories (144 AR, 89 PsA) from patients with a median age of 55 years (p25-75 18-60) were included. Information related to the performance of cervical screening was found in the clinical records of 137 patients (58.8%, 95% CI 52.4-64.9%). Regarding the type of arthritis, the prevalence of performing cervical screening in RA and PsA was 60.4% and 56.2%, respectively, while rates of women attending the program at least twice were 45.1% for RA and 37.1% for PAs. In relation of screening findings, HPV infection was detected in 8 patients (5.8%), cervical dysplasia in 6 (4.4%), while no case of invasive cancer was detected.

Conclusion: Autoimmune and inflammatory diseases, along with the treatment employed, are associated with an increased risk of cervical HPV infection. Despite this, information regarding HPV cervical screening was collected in only half of patients. Both patients and their treating rheumatologists must be aware of this risk and adhere to cervical screening programs to achieve an early diagnosis and management.

REFERENCES:

[1] JAMA.2006;296:2823. 2) Int J Cancer.2013;132:1429. 3) Int J Cancer.2012;130:937. 4) Rev.Esp.Patol.2014;47(1):1-43.

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Rehabilitation

FRI0693 **RESILIENCE TRAITS IN A LARGE COHORT OF PATIENTS WITH ANKYLOSING SPONDYLITIS (AS), RHEUMATOID ARTHRITIS (RA) AND FIBROMYALGIA (FM)**

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Background: The study of resilient traits (RT) including self-compassion, self-forgiveness, forgiveness of others, and gratitude has garnered the attention of investigators involved in health and healthcare research (1, 2). Little is known about such RT in patients with AS, RA, and FM.
Objectives: To examine patient group differences in levels and mental and physical health correlates of self-compassion, self-forgiveness, forgiveness of others, and gratitude.
Methods: We conducted an online survey with patients attending the Gastein Healing Galleries in Bad Gastein, Austria. In this health facility, approximately 12,000 patients suffering from different diseases are treated annually. Of those, 6,465 patients were invited by email to participate anonymously. Socio-demographics and health-related variables including depression, pain, and current health status were measured in all respondents. Also measures of self-compassion, self-forgiveness, forgiveness of others, and gratitude were administered in a subset of participants.
Results: In total 2,017 patients responded (=31%) of which a subset of 562 patients with AS (44%), FM (38%), and RA (18%) completed measures of RT. Sex ratio (male/female) was 52%/48%, mean age 57 (SD=11) and level of education was: Elementary School 28%, Junior High School 22%, High School 20%, College 13%, and University 17%. Across patient groups, no differences emerged in levels of self-forgiveness, forgiveness of others, or gratitude (ps>.30), although FM patients reported lower levels of self-compassion compared to patients with AS and RA (p<.05). Self-compassion, self-forgiveness, forgiveness of others, and gratitude were related to depression in all three patient groups, but gratitude was the only RT that was related to depression, pain, and health across all three patient groups.
Conclusion: We found that only self-compassion varied across patient groups, with FM patients reporting lower levels. All RT were consistently related to depression across the three patient groups, but gratitude was also related consistently across groups to both pain and health. RT may well vary according to patient diagnoses with some traits offering more support and resilience-building to the patient than other traits. An important key for treatment support and management may be to identify which traits are most useful to encourage the development of resilience and health in specific patient groups.

REFERENCES:

[1] Sirois, F. M., Molnar, D. S., & Hirsch, J. K. (2015). Self-compassion, stress, and coping in the context of chronic illness. Self and Identity, 14(3), 334-347.
[2] Liu L, Xu X, Xu N, Wang L. Disease activity, resilience and health-related quality of life in Chinese patients with rheumatoid arthritis: a multi-center, cross-sectional study. Health Qual Life Outcomes. 2017 Jul 24;15(1):149.

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FRI0694 **SELF-REPORTED SLEEPING PROBLEMS AND FATIGUE IN LARGE COHORT OF PATIENTS WITH ANKYLOSING SPONDYLITIS (AS), RHEUMATOID ARTHRITIS (RA) AND FIBROMYALGIA (FM)**

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Background: Sleep problems and fatigue are very common in rheumatic diseases and painful conditions. There is mounting evidence that sleep problems and fatigue have reciprocal influences on musculoskeletal pain, mood, and overall well-being of patients with rheumatic disorders. In addition, sleeping problems are a risk factor for developing chronic widespread pain.
Objectives: To assess and compare sleep problems and fatigue in a cohort of patients with AS, RA and FM.
Methods: We conducted an online survey with patients regularly attending the Gastein Healing Galleries in Bad Gastein, Austria. In this health facility appr. 12,000 patients with a variety of disease are being treated annually. Of those, 6,465 patients were invited by email to fill out the survey anonymously. Sociodemographics and disease related variables (e. g. pain, depression) were assessed, including current health status, three items concerning sleep quality, duration of sleep problems, and the number of nights affected by sleep problems, and four items from the Multidimensional Fatigue Inventory (general fatigue subscale) concerning feeling fit, tired, rested, and tiring easily.
Results: In total 2,017 patients responded (=31%) of which a subset of 784 respondents indicated a diagnosis of AS (43%), RA (40%), or FM (17%). Their mean age (SD) was 58 years (11) and 53% were male. Level of education was: Elementary School 30%, Junior High School 22%, High School 20%, College 13%, and University 15%. Only 17% of AS, 20% of RA and 12% of FM patients indicated that their sleep quality is not affected. In 51.6% of AS, 47.2% of RA and 64% of FM patients the duration of the sleeping problem persists more than one year. Examining levels of sleep problems and fatigue across these three groups revealed significant variation (p<.001). Regarding sleep problems, FM patients showed significantly higher levels of problems than AS (p<.001) and RA patients (p<.001), and the latter two groups do not significantly differ. FM patients reported significantly higher levels of fatigue than AS (p<.001) and RA patients (p<.001), and AS patients had significantly higher levels of fatigue than RA patients (p<.001). Fatigue and sleep problems were correlated in expected directions with depression, pain, and health. However, while there was little variability in the magnitude of the associations between fatigue and sleep problems with depression and pain, there was considerable variation in the association of fatigue and sleep problems with health. AS patients showed a small and non-significant association, whereas, RA patients showed a larger association (r≈.20) and FM patients showed the largest association (r≈.5).
Conclusion: We found sleep problems and fatigue to be common, chronic and elevated in AS, RA and FM, but not equally so across diagnostic categories. FM patients showed the greatest problems with sleep and fatigue. Furthermore, it appears that fatigue and sleep problems may have the most important connection to health for FM patients. To conclude, it is important to address sleep problems and fatigue in routine clinical assessment and management of patients with AS, RA and FM.

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FRI0695 **NEURAL MANUAL MOBILIZATION VS ROBOTIC ASSISTED MOBILIZATION TO REDUCE PAIN HYPERSENSITIVITY IN HANDOSTEOARTHRITIS: A RANDOMISED CONTROLLED PILOT TRIAL**

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Background: Recent studies suggest that osteoarthritis (OA) is a mixed pain state and that in some patients' central nervous system factors can play an important role.

Objectives: In this study, we showed some preliminary dataon the effectiveness of neural manual mobilization vs robotic assisted mobilization, on reduce pain sensitivity in subjects with dominant hand OA.
Methods: A pilot randomized controlled trial was conducted. 50 patients (50 to 90 years old) with a diagnosis of dominant hand OA were randomized into two groups of 25 participants. The experimental group received an intervention of neurodynamic mobilization of median, radial and ulnar nerves plus exercise, the control one received a robotic assisted passive mobilization treatment (Gloreha Workstation, Idrogenet srl, Brescia, Italy) plus exercise. Both groups received 12 treatment sessions over 4 weeks. Pressure pain thresholds (PPTs) were assessed bilaterally over the Radial, Median and Ulnar nerves, first Carpometacarpal (CMC) joint, Hamate bone and in the C5-C6 zygapophyseal joint. Intensity of pain (Visual analogue scale, VAS), Quick-DASH scale, grip and pinch strength were also measured bilaterally. Patients were assessed at beginning, at the end of therapy and after a period of 1 and 3 months.
Results: In comparison with pre-treatment values, the experimental treatment increased the PPTs in the first CMC joint, radial and median nerves ($P < 0.05$) and this effect was maintained until the 2nd Follow up session in the dominant hand. No significant changes in PPT at the hamate bone and ulnar nerve during treatment were found. No significant interaction for pain intensity (VAS) of hand while executing a grip strength, over the last 24 hours and over the last week also was found. Similarly, grip and pinch of the dominant hand did not increase after treatment.
Conclusion: Neurodynamic mobilization by sliding technique decreases pain in the hand joints in patients with hand OA, suggesting alternative therapies to surgery or to the use of analgesic. This research suggests alternative therapies to surgery or the use of analgesic therapy.

REFERENCES:

[1] Kroon FPB, Carmona L, Schoones JW, Kloppenburg M. Efficacy and safety of non-pharmacological, pharmacological and surgical treatment for hand osteoarthritis: a systematic literature review informing the 2018 update of the EULAR recommendations for the management of hand osteoarthritis. RMD open 2018; 4(2): e000734.
[2] Villafane JH, Valdes K, Pedersini P, Berjano P. Osteoarthritis: a call for research on central pain mechanism and personalized prevention strategies. Clinical rheumatology 2018.
[3] Villafane JH, Bishop MD, Fernandez-de-Las-Penas C, Langford D. Radial nerve mobilisation had bilateral sensory effects in people with thumb carpometacarpal osteoarthritis: a randomised trial. Journal of physiotherapy 2013; 59(1): 25-30.
[4] Villafane JH, Silva GB, Bishop MD, Fernandez-Carnero J. Radial nerve mobilization decreases pain sensitivity and improves motor performance in patients with thumb carpometacarpal osteoarthritis: a randomized controlled trial. Archives of physical medicine and rehabilitation 2012; 93(3): 396-403.
[5] Villafane JH, Cleland JA, Fernandez-de-Las-Penas C. The effectiveness of a manual therapy and exercise protocol in patients with thumb carpometacarpal osteoarthritis: a randomized controlled trial. The Journal of orthopaedic and sports physical therapy 2013; 43(4): 204-13.

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FRI0696 **THE NEXT STEP; MOVING TOWARDS A MORE PHYSICALLY ACTIVE RHEUMATOLOGY POPULATION**

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Background: For individuals with rheumatic diseases, it is important to be sufficiently physically active. Several standardized exercise programs have been developed for patients with rheumatic diseases, that have proven to be effective in increasing physical activity level for a short period of time or only in a selection of the patients. A more personalized approach based on shared-decision making to tailor the intervention on personal physical activity goals could increase compliance to improve and sustain the physical activity level in patients with rheumatic diseases.
Objectives: Primary, this study will examine whether a personalized physical activity program is effective to increase and sustain the level of physical activity in patients with a rheumatic disease. Secondary, this study will examine whether this program also results in a reduction in pain and fatigue.
Methods: A before after study will be performed among patients of the rheumatology outpatient clinic of Bernhoven in the Netherlands who do not meet the international physical activity recommendations[1] and who are motivated to improve their physical activity level. Physical activity will be measured with an activity tracker (steps/week) and as secondary outcomes the VAS pain and VAS fatigue will be measured over time. Measurements will take place before and 1, 3, 6 and 12 months after inclusion. Each participant starts the programme with an intake by a physiotherapist to identify motives and barriers for being physically active. Additionally, motivational interviewing and shared decision-making are used to tailor the intervention on personal physical activity goals. Participants will perform an individualized program, but they will also be a member of a group of 5-15 participants who will start at the same time. This group will meet three times a year to get feedback about their goals and physical activity level. Besides that, they can share experiences, questions, remarks and ideas with each other and with the physiotherapists involved in this study.
Results: Since February 2018, 49 patients are included in the physical activity program with a mean (±sd) age of 53 ± 12 years and a median (IQR) disease duration of 2 (1-6) years. The majority of the participants is female (71%) and most frequently diagnoses are rheumatoid arthritis, spondyloarthropathy and fibromyalgia. At baseline mean ±sd daily steps is 8469±4170, mean VAS pain is 43±23 and mean VAS fatigue is 53±25. Results after 1, 3 and 6 months after baseline will be presented at EULAR. The inclusion of newly participants is still ongoing.
Conclusion: Despite it is too early to make a statement about the effectiveness of a personalized physical activity program, there are signs that participants became more physically active. During group meetings patients told they spent more time being physically active; they took more frequently their bike or went outside for a walk. This study will be continued giving the patients of the rheumatology outpatient clinic a personalized opportunity to become more physically active.

REFERENCES:

[1] JM. Weijers, SAA. Rongen-van Dartel, PLCM. van Riel. Exercise participation has increased in patients with Rheumatoid Arthritis: A cross-sectional comparison between two Dutch RA cohorts. Mediterr J Rheumatol. 2018;29(4):199-206.

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HPR Epidemiology and public health (including prevention)

FRI0697-HPR **CONSUMPTION OF DAIRY PRODUCTS AND RISK OF RHEUMATOID ARTHRITIS AMONG WOMEN: A POPULATION-BASED PROSPECTIVE COHORT STUDY**

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Background: Conflicting results have been reported regarding the association between consumption of milk and dairy products and the risk for development of rheumatoid arthritis (RA).
Objectives: The aim of this study was to investigate the association between consumption of milk and dairy products and the development of RA in a large population-based cohort of women.
Methods: In a prospective cohort study 35,600 women aged 48-83 years, from the Swedish Mammography Cohort (SMC), were followed between 2003 and 2015. Consumption of dairy products was assessed in 1997 at a mean age of mean age of 61.5 years (SD 9.1 years) with a 96-item self-administered questionnaire. The risk (hazard ratio; HR) of RA development associated with consumption of dairy products was estimated using Cox proportional hazard regression models with adjustment for age, alcohol intake, smoking, energy intake, meat and fish consumption.
Results: During the follow-up of 12 years, 368 individuals were identified with a new diagnosis of RA. Comparing high consumption with low consumption of dairy products, no association between consumption of dairy

products and the development of RA was observed: HR for the fully adjusted model=1.12 (95% CI: 0.78-1.59 (Table 1). Also when evaluating milk and cheese consumption separately, no association with the risk of RA was observed: HR for the highest milk consumption=1.10 (95% CI: 0.82-1.44) and highest cheese consumption HR=1.20 (95% CI: 0.81-1.79), compared with low consumption (fully adjusted models, table 1).
Conclusion: In this large population-based cohort study, consumption of dairy products was not associated with risk to develop RA.

FRI0697HPR Table 1. Relative risk of developing rheumatoid arthritis during follow-up (2003-14) of women in the Swedish Mammography Cohort by consumption of dairy products in 1997.

	N of cases	N of person years	HR, adjusted for age	HR,fully adjusted model*
Total dairy				
<=3 servings/week	73	77148	1 (Ref)	1 (Ref)
3-4.5 servings/week	103	105043	1.00 (0.75-1.35)	1.05 (0.78-1.43)
4.5-6 servings/week	76	83777	0.93 (0.68-1.28)	1.01 (0.72-1.43)
>6 servings/week	111	115333	1.00 (0.74-1.33)	1.12 (0.78-1.59)
Milk				
<=0.5 servings/week	113	118630	1 (Ref)	1 (Ref)
0.5-1 serving/week	67	62227	1.16 (0.86-1.57)	1.17 (0.86-1.58)
1-2 serving/week	95	104788	1.01 (0.77-1.33)	1.03 (0.78-1.35)
>2 serving/week	85	89145	1.09 (0.82-1.44)	1.10 (0.82-1.48)
Cheese				
<=1 servings/week	81	84818	1 (Ref)	1 (Ref)
1-2 serving/week	119	124044	1.03 (0.77-1.36)	1.06 (0.80-1.41)
2-4 serving/week	106	108849	1.04 (0.78-1.39)	1.12 (0.82-1.51)
>4 serving/week	47	45405	1.08 (0.75-1.54)	1.20 (0.81-1.79)

*Adjusted for age, alcohol intake, smoking, energy intake, meat and fish consumption

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HPR Interventions (educational, physical, social and psychological)

FRI0698-HPR A RANDOMISED CONTROLLED CLINICAL TRIAL COMPARING THE EFFECTIVENESS OF 6 AND 12 WEEKS OF A SHOULDER SPECIFIC EXERCISE PROGRAMME FOR PATIENTS WITH ROTATOR CUFF RELATED SHOULDER PAIN

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Background: Research has shown loaded exercise to be beneficial for patients with rotator cuff related shoulder pain in terms of improving shoulder function, self-reported disability and pain[1,2]. The optimal duration for which these patients should complete a loaded exercise programme to achieve beneficial effects remains unclear.
Objectives: The purpose of this study is to determine if 6 weeks of a supervised shoulder specific exercise programme is as effective as 12 weeks of the same programme, for improving shoulder function, self-reported disability and pain, in patients with rotator cuff related shoulder pain.
Methods: In this randomised controlled single-blinded study patients with a history of lateral upper arm pain with MRI confirmation of rotator cuff pathology or positive testing on a cluster of clinical rotator cuff tests were included. Patients with a recent history of shoulder surgery or a shoulder fracture were excluded. Participants were randomly assigned to complete either 6 weeks (short group) or 12 weeks (long group) of the exercise programme. Both groups performed the same specific set of loaded exercises daily at home and attended 6 clinic-based group exercise sessions[2]. Participants were assessed at 6 weeks, 3 and 6 months. Shoulder function was assessed using the Constant-Murley (CM) score. Disability was assessed using the QuickDash and the Shoulder Pain and Disability Index (SPADI). Pain was assessed using a visual analogue scale. Group comparisons were made using univariate generalised linear models.
Results: 85 patients were included in this study as per Table 1.

FRI0698HPR Table 1.

Group	Short (n = 45)	Long (n = 40)
Background variables		
Sex (male/female)	24/21	21/19
Age in years median (SD)	57 (15)	57 (14)
Duration of symptoms (median months)	19	24

Within each group shoulder function, self-reported disability and pain improved significantly at 3 months (p < .05). Comparisons at 3 months showed the long group had significantly lower pain scores (p = .02). At 3 months there was no significant difference between the two groups in the CM score (p = .415), SPADI score (p = .053) and QuickDash score (p = .245). However, at 6 months, the long group had significantly greater changes in both the CM score (p = .007) and the SPADI score (p = .002).
Conclusion: In the management of patients with rotator cuff related shoulder pain the findings of this study indicate that a 12 week exercise programme results in better outcomes for pain at 3 months and self-disability and shoulder function at 6 months.

REFERENCES:

[1] Littlewood C, et al. Exercise for rotator cuff tendinopathy: A systematic review. Physiotherapy. 2012; 98(2), 101 - 109.
[2] Holmgren T, et al. Effect of specific exercise strategy on need for surgery in patients with subacromial impingement syndrome: randomised controlled study. Br J Sports Med. 2014; 48(19), 1456-1457.

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FRI0699-HPR DEVELOPMENT OF DELPHI-BASED RECOMMENDATIONS FOR THE MANAGEMENT OF CARDIOVASCULAR COMORBIDITIES IN PATIENTS WITH PSORIATIC ARTHRITIS AND MODERATE-TO-SEVERE PSORIASIS: STUDY PROTOCOL

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Background: Psoriasis (PSO) and Psoriatic Arthritis, (PsA) particularly moderate to severe disease (MS-PSO), are inflammatory systemic

conditions that are associated with a high risk of cardiovascular (CV) complications further beyond the increased prevalence of classical risk factors in this population. Consequently, the early identification of patients with MS-PSO and PsA who may benefit from primary CV prevention is essential. However, medical providers do not routinely screen or counsel their patients for CV risk factors or comorbidities. In addition, paucity of robust clinical data complicates the implementation of management protocols for primary CV prevention in MS-PSO and PsA.

Objectives: To generate expert-based recommendations on the management of CV comorbidities in patients with MS-PSO and PsA through the application of the Delphi technique.

Methods: The development of Delphi-based recommendations included four steps: (1) systematic literature review to explore current information and clinical recommendations on management of CV comorbidities in patients with PsO and PsA; (2) two subsequent meetings with project coordinators (n = 3) and scientific advisors (n = 7) from different medical specialties (rheumatology, dermatology, endocrinology, internal medicine, pneumology, rehabilitation, psychiatry and primary care) to examine the results of the review and decide which statements should be included in the final version of the questionnaire; (3) a two-round Delphi questionnaire aimed at specialists in rheumatology and dermatology to assess the degree of consensus on the different points raised; (4) finally, a face-to-face meeting with the project coordinators and scientific advisors to discuss and ratify the results of the Delphi process.

Results: As a result of the literature review and the assessment and approval of scientific advisors, the final version of the Delphi survey contains 52 statements grouped into 35 questions. The questionnaire is divided into 3 topic sections: (1) identification, diagnosis and referral of MS-PSO and/or PsA patients with CV comorbidities (n = 12 statements); (2) management and treatment of CV comorbidities associated with MS-PSO and/or PsA (n = 36); (3) influence of MS-PSO and/or PsA treatments on CV comorbidities and vice versa (n = 4).

Conclusion: This Delphi-based study may fill an important gap in the evidence by providing relevant information on the management of CV comorbidities in patients with MS-PSO and/or PsA.

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FRI0700-HPR LESSONS LEARNED FROM PILOT IMPLEMENTATION OF PHYSICAL ACTIVITY RECOMMENDATIONS IN AXSPA EXERCISE GROUP THERAPY – LESS MAY BE MORE

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Background: The Ankylosing Spondylitis Association of Switzerland (SVMB) offers 68 exercise groups (EG) for people with axial Spondyloarthritis (axSpA). Participants exercise weekly with focus on strength and flexibility supervised by a physiotherapist (PT). Given the EULAR physical activity (PA) recommendations [1] and recent research [2, 3], the SVMB aims to further develop the concept of their EG by introducing: a) exercises in all dimensions, cardiorespiratory fitness, muscle strength, flexibility and neuromotor performance, according to the general PA recommendations [4]; b) individual exercise-coaching (three sessions in first six months) by the group PT, specifically trained in communication and action planning skills to support individual exercising, and c) bi-annual fitness-assessments for all exercise dimensions.

Objectives: To evaluate the new EG concept among the participating people with axSpA and PTs across four pilot groups.

Methods: After six months, a survey on the perception and satisfaction towards the new EG concept was sent to 30 people with axSpA, who rated the questions on a 0-10 numeric rating scale (0=not satisfied, 10=very satisfied). Semi-structured telephone-interviews were conducted with the PTs to explore their experiences with the new GE concept.

Results:

People with axSpA: The survey's response rate was 83% (25/30); of these, 15 (62%) participants were satisfied with the concept (mean 6.7 ±2.23) and 20 (80%) with the exercise-coaching (mean 7.7±2.92). 22 (88%) individuals defined a training goal and 15 (60%) achieved it. The exercise diary was used by 16 (64%) participants, five reported app-based. Reasons for not using the diary were the daily effort and problems with correctly allocating activities to exercise dimensions. A minority (n=7, 28%) reported to use a technical device for cardiovascular exercising. 17 (68%) were satisfied with the fitness-assessment (mean 7.5±1.78). *PTs* perceived the exercise-coaching as very useful for supporting individualised exercising. However, they emphasised that the frequency of the sessions should be flexibly based on the participant's individual training goal and motivation. The PTs perceived controversial reactions to the fitness-assessments: increased but also decreased motivation towards exercising.

Conclusion: Exercise-coaching and fitness-assessments were generally appreciated; however, the frequency was perceived as too high. The GE concept will be adapted accordingly to improve feasibility for national implementation: the exercise-coachings will be reduced to two in the first six months, the first one compulsory for all participants, then bi-annually, according to individual needs and training goals. The fitness-assessments will take place annually instead of bi-annually. There is a need for easy-to-use exercise diaries, covering all exercise dimensions.

REFERENCES:

[1] Rausch AK, et al. Ann Rheum Dis 2018; 9(77):1251-1260.
[2] Sveaas SH, et al. Br J Sports Med 2017;51:1065-1072
[3] Rausch AK, et al. RMD open, accepted
[4] Garber CE, et al. Med Sci Sports Exerc 2011;43:1334–59.

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FRI0701-HPR EFFICACY OF INTERMITTENT AEROBIC EXERCISE ON SLEEP EFFICIENCY IN PATIENTS WITH RHEUMATOID ARTHRITIS. A RANDOMIZED CONTROLLED TRIAL

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Background: Insomnia is seen in >60% of patients with rheumatoid arthritis (RA). While cross-sectional studies have shown a positive association between regular physical activity and good sleep, there is a lack of knowledge on the effect of physical activity on insomnia in patients with RA.

Objectives: To examine the efficacy of intermittent aerobic exercise on sleep efficiency as well as the effect on fatigue and depressive symptoms.

Methods: 38 patients with RA were randomly assigned to either intermittent aerobic exercise training; 3 session/week for 6 weeks; intervention group (n=17) or usual care (controls group n=21). The primary outcome was change in polysomnography (PSG) assessed sleep efficiency while secondary outcomes included sleep (Pittsburgh Sleep Quality Index), fatigue (Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional Questionnaire) and depression (The Center for Epidemiological Studies-Depression).
Results: Sleep efficiency improved significantly in the intervention group from baseline 0.84 (95% CI 0.80-0.87) to end of the intervention 0.88 (95% CI 0.84-0.92) p=0.03, while for the control group the mean change was not significant. No between-group difference in change was observed. Fatigue was significantly reduced in the intervention group compared to the control group -16.0 (95%CI -25.1 - -7,04), including physical fatigue -4.99 (95%CI -7.25 - -2.74), cognitive fatigue -2.43 (95%CI -4.22 - -0.63) and living with fatigue -2.50 (95%CI -4.45- -0.54).

	Baseline		Post-intervention		Within-group change			Between-group difference		
	Estimate	95%CI	Estimate	95%CI	Estimate	95%CI	P-value	Estimate	95%CI	P-value
Sleep efficiency (PSG)										
IG	0.84	0.80-0.87	0.88	0.84-0.92	0.04	0.00-0.07	**0.03**			
CG	0.88	0.84-0.91	0.88	0.85-0.92	0.01	-0.03-0.04	0.77	0.04	-0.02-0.08	0.16
Global PSQI score										
IG	7.40	5.57-9.23	6.72	5.01-8.42	-0.68	-2.40-1.03	0.41			
CG	7.31	5.55-9.06	7.48	5.83-9.12	0.17	-1.52-1.86	0.83	-0.85	-3.27-1.56	0.46
Physical fatigue										
IG	14.27	11.5-16.9	10.8	8.20-13.5	-3.38	-5.03- -1.74	0.0002			
CG	10.95	8.53-13.3	12.5	10.1-15.0	1.60	0.06-3.15	0.04	-4.99	-7.25- -2.74	**0.0001**
Living with fatigue										
IG	5.88	4.27-7.49	3.11	1.50-4.72	-2.76	-4.17- -1.35	0.0003			
CG	4.47	3.02-5.92	4.21	2.69-5.73	-0.26	-1.61- -1.08	0.69	-2.50	-4.45- -0.54	**0.01**
Cognitive fatigue										
IG	5.41	3.92-6.89	3.58	2.10-5.07	-1.82	-3.11- -0.53	0.007			
CG	4.14	2.80-5.48	4.74	3.24-6.15	0.60	-0.63-1.84	0.32	-2.43	-4.22- -0.63	**0.009**
Emotional fatigue										
IG	3.29	2.18-4.39	2.0	0.89-3.10	-1.29	-2.20- -0.38	0.006			
CG	2.52	1.53-3.51	2.3	1.25.3.33	-0.22	-1.09-0.64	0.59	-1.06	-2.32-0.19	0.09
Depression										
IG	13.7	10.0-17.4	10.7	7.2-14.3	-2.99	-6.83-0.85	0.12			
CG	8.6	5.2-12.1	12.4	8.5-16.2	3.75	-0.38-7.90	0.07	-6.75	-12.4- -1.1	**0.02**

IG=intervention group; CG=control group

Conclusion: An intermittent aerobic exercise intervention presented no statistically significant effect on sleep efficiency in patients with RA compared with usual care. However, significant between-group differences were seen in subjectively reported fatigue including physical fatigue and cognitive fatigue and on depressive symptoms.

REFERENCES:

[1] Loppenthin K, Esbensen BA, Jennum P, et al. Effect of intermittent aerobic exercise on sleep quality and sleep disturbances in patients with rheumatoid arthritis - design of a randomized controlled trial. BMC musculoskeletal disorders 2014

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FRI0702-HPR NON PHARMACOLOGICAL MANAGEMENT OF FIBROMYALGIA: A SYSTEMATIC REVIEW OF SYSTEMATIC REVIEWS

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Background: Despite the number of guidelines and available therapies, many individuals with fibromyalgia (FM) still experience significant pain and a reduced quality of life. Patient heterogeneity and clinical uncertainty can lead to delays in selecting the most appropriate management strategy. There are more than 300,000 publications surrounding the management of FM, thus affecting clinicians' ability to make informed decisions. The systematic review of randomised controlled trials is the gold standard in evaluating an intervention. However, the increase in systematic reviews (SRs) has led to some questions regarding their quality. Therefore there is a need to synthesise the evidence with an overview of SRs.
Objectives: To evaluate the quality of the current evidence from SRs on the effects of non-pharmacological interventions for the management of FM.
Methods: A systematic search of seven databases (1990-2018) was completed to identify SRs reporting the effects of non-pharmacological interventions on the primary outcomes of pain, function and quality of life (QoL). Data was extracted according to the PICO framework in addition to intervention prescription where appropriate. Methodological quality was assessed using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR-2) instrument (Shea et al 2017).
Results: Twenty-six SRs with 243 primary studies met the inclusion criteria. Reviews were classified into 6 categories (1) land-based exercise; (2) water-based exercise; (3) mind-body; (4) electrotherapy; (5) manual therapy and (6) complementary and alternative medicine (CAM). Quality of the included SRs were variable with many interventions scoring low to critically low. High quality evidence was found to support the use of land-based exercise and mind-body therapies for the improvement of pain, function and QoL (Table). In particular aerobic exercise with or without strength training and mind-body therapies demonstrated the best outcome.
Conclusion: With the exception of land-based exercise and mind-body exercise, the quality of evidence for the non-pharmacological management of FM is mostly poor, with more than half of the included reviews scoring low or critically low on the AMSTAR-2 instrument. Improved reporting of outcome data and stricter methodological quality will allow stronger recommendations in the future.

REFERENCES:

[1] Shea, B.J., et al., *AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.* bmj, 2017. **358**: p. j4008 0959-8138.

Table: Quality of reviews surrounding interventions on FM

	Results*	Quality of evidence
Land-based exercise (3)	Pain$^+$/function$^+$/QoL$^+$	High
Water-based exercise (5)	Pain$^+$/function$^+$	Moderate
Mind-body therapies (4)	Pain$^+$/QoL$^+$	High
Electrotherapies (8)	Pain$^+$/QoL$^+$	Low
Manual therapy (3)	Pain$^+$	Critically Low
CAM (3)	Pain$^+$	Low

* + = positive effects, ? = no or unclear results

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FRI0703-HPR INVESTIGATION OF THE EFFECTIVENESS OF AEROBIC EXERCISE TRAINING IN INDIVIDUALS WITH ANKYLOSING SPONDYLITIS: RANDOMIZED CONTROLLED STUDY

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Background: Aerobic capacity is a measure of the functional capacity of the oxygen system and the cardiopulmonary system. In Ankylosing spondylitis(AS) patients, aerobic capacity is lower than healthy peers, and this is due to inflammation, muscle atrophy and peripheral muscle weakness, fatigue, low physical activity level, negatively affected respiratory function, peripheral arthritis, decreasing chest expansion and respiratory muscle strength.
Objectives: The aim of the study was to investigate the effects of aerobic exercise training on functional status and aerobic capacity in individuals with AS.
Methods: Twenty-eight voluntary individuals diagnosed with AS according to Modifie New York Criteria who applied to Pamukkale University Department of Internal Medicine, Department of Rheumatology were included in the study. Individuals were randomly divided into two groups, as there would be aerobic exercise training (n=17; mean age=46.58 ±11.94years) and supervised exercises group (n=11; mean age=42.54 ±8.75years). All assessments were done before and after the training.

After the demographic characteristics and disease related data of the individuals were recorded; for the functional status, the Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI) were used. Six-minute walk test(6MWT) was used for the assessment of aerobic capacity. Group I was attended 40 min aerobic exercises sessions (5-min warm up, 30-min treadmil, 5-min cool down), plus supervised spinal mobilite exercises and Group II was attended only supervised spinal mobilite exercises per day, 3 times a week, for 12 weeks. Data were analysed Wilcoxan and Mann Whitney U Test.

Results: After training aerobic exercise group, BASMI (p=.021), BASDAI (p=.002) and 6MWT(p=.036) results were statistically significant, while the difference was not significant in BASFI (p=.068). It was observed that there was no significant difference in the after training period in the supervised exercises group. BASDAI, in group aerobic exercise group had improved more significantly when compared to supervised exercises group.

Conclusion: As a result of the study, it was noted that when aerobic exercise training applied together with the supervised exercises in ankylosing spondylitis patients, effectiveness on mainly disease activity, spinal mobility and aerobic capacity was increased. Key words: Ankylosing spondylitis, aerobic exercise training, supervised exercised.

REFERENCES:

[1] Pulmonary System Lımıtatıons To Endurance Exercıse Performance In Humans. Exp Physiol. 2012;97(3):311–318.

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FRI0704-HPR THE EFFECTS OF CLINICAL PILATES TRAINING IN PATIENTS WITH FIBROMYALGIA: A RANDOMIZED CONTROLLED TRIAL

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Background: Fibromiyalgia (FM) is a chronic condition characterized by widespread pain, sleep disorders, fatigue and reduced quality of life. Exercise is commonly recommended in the approach of people with FM. Researches support some forms of exercises reduce fibromyalgia symptoms and improve quality of life. Pilates recently has become popular form of exercise which focused core strenghening, posture and coordination of breathing with movement. Studies showed that clinical pilates can be used to provide improvements in patients with FM. However there is no study which compared clinical pilates-based supervised exercises and group exercises on FM patients in literature.

Objectives: The first aim of the study was to investigate the effects of clinical pilates training, secondly to compare the effects of supervised exercises and group exercises training on disease activity, functional status, anxiety, quality of life and biopsychosocial status in individuals with FM.

Methods: 42 voluntary women diagnosed with FM according to 2010 American College of Rheumatology Criteria in the age range of 35-65, who applied to Pamukkale University Department of Internal Medicine, Department of Rheumatology were included in the study. Individuals were randomly divided into two groups, as there would be supervised exercises (Group I, n=16, mean age 55,93±8,03) and group exercises (Group II, n=26, mean age 47,80±5,87). All participants attended 60-min exercises sessions (10-min warm up, 40-min clinical pilates exercises, 10-min cool down) per day, 2 times a week, for 6 weeks. The training was applied by same physiotherapist who received clinical pilates certificate by an experienced Pilates instructor and physiotherapist. After the demographic characteristics and disease related data of the individuals were recorded; disease activity were assessed with the Fibromyalgia Impact Questionnaire (FIQ), functional status with Health Assessment Questionnaire (HAQ), anxiety with Beck Anxiety Inventory (BAI), quality of life with Short Form 36 (SF-36) scale and biopsychosocial status with the Cognitive Exercise Therapy Approach Scale (BETY). All outcomes were assessed just before and 6 weeks after training. The data were statistically evaluated by the Wilcoxon test and Mann-Whitney Test.

Results: There were no significant differences in baseline demographics between the Group I and Group II (p>0.05). After 6 weeks, showed for both groups a statistically significant improvement in FIQ,SF-36 (physical and mental component) and BETY also Group II showed a statistically significant improvement in HAQ and BAI (p<0.05). When both group were compared, a significant difference was observed in FIQ (p<0.05) in Group II, whereas no statiscal differences were found in other outcomes (p>0.05)

Conclusion: This study showed that clinical pilates training which were applied 6 weeks, resulted in improvement on disease activity, functional status, anxiety, quality of life and biopsychosocial status in individuals with FM. Besides group exercises training provides social interaction so we suggest clinical pilates as an effective and safe method for people with FM.

REFERENCES:

[1] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristic of fibromyalgia in the general population. Arthritis Rheum 1995;38:19-28
[2] Busch, Angela J., et al. Exercise therapy for fibromyalgia. Current pain and headache reports 2011;15:358.
[3] Burke, Shauna M., et al. Group versus individual approach? A meta-analysis of the effectiveness of interventions to promote physical activity. Sport and Exercise Psychology Review, 2006, 2.1: 19-35.

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FRI0705-HPR THE RELATIONSHIP BETWEEN SELF-REPORTED PAIN EXPERIENCE AND FUNCTIONALITY IN PATIENTS WİTH JUVENILE SCLERODERMA

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Background: Juvenile scleroderma (JS) is a rarely seen chronic connective tissue disorder characterized by inflammation and fibrosis of the skin. Pain and functionality is a widely neglected symptom in patients with JS, even though it may be common and have a significant impact on the quality of life. Clinical trials and small treatment studies suggest that pain is significant in scleroderma, but few data speak of the frequency or presence and experience of pain and the relationship between self-reported pain and functionality.

Objectives: This study aimed to determine whether the presence of pain (based on physical conditions and participants' report) and self-reported pain experience in children with JS differ from same gender population controls.

Methods: 30 patients (26 girls, 4 boys) with JS between the ages of 6-18 years and 30 healthy controls (20 girls, 10 boys) with similar age and gender were included in our study. The follow-up form was prepared considering the relevant parameters such associo-demographic status of JS disease.Self-reported presence and experience of pain were assessed in rest, during a physical activity and after or during an exercise. Children rated their pain severity on a six-item Wong-Baker Pain Scale (WBS:0-10) from none to worst. The location, spread and character of the pain were asked (flammable, sinking, squeezing, restlessness, tingling, throbbing, tingling, electric shock etc.). Children completed their functional abilitiy status with "Childhood Health Assessment Questionnaire (CHAQ)" and "Jebson Taylor Hand Function Test (JTHFT)".

Results: The mean age of the JS group was 14.06 ± 3.24 years (86% female, 14% male; while the%53 localized scleroderma,%47 SSc).Compared with controls, more JS participants, who indicated pain and comprehended self-reporting scales, reported higher pain affect and intensity pain and/or discomfort with activity and with exercise (p<0.05, 47% vs p<0.05, 57%), but fewer JS participants reported pain at the test (p<0.05, 3.3%). 40% of the patients described the character of the pain as sneezing, 7% had throbbing, 7% had tingling, 3% had flammable, and 3% had a smear. The rest of 40% population had no pain. There was a significant correlation between pain at rest and CHAQ-Total scores (r=0.576; p=0.001). There was no significant relationship between pain during activity or exercise and JTHFT and CHAQ-Total (p> 0.05).

Conclusion: In our study, only a significant relationship was found between pain at rest and functionality. These findings indicate that pain is common in JS and that pain is significant determinants of physical

functioning and social adjustment, two important components of health-related quality of life. Increased attention to effective management of pain in pediatric scleroderma will likely lead to improved functioning and quality of life.

REFERENCES:

[1] Rocha, L. F., Marangoni, R. G., Sampaio-Barros, P. D., Levy-Neto, M., Yoshinari, N. H., Bonfa, E.,. .. & Kowalski, S. C. Cross-cultural adaptation and validation of the Brazilian version of the Scleroderma Health Assessment Questionnaire (SHAQ). Clinical rheumatology. 2014; 33(5):699-706.
[2] Wong DL., Baker CM. Pain in children: comparison of assessment scales. Pediatr Nurs. 1988; 14(1):9-17

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FRI0706-HPR COMPARISON OF IMPACT OF VERUM AND PLACEBO THUMB BASE ORTHOSES ON SKIN SURFACE TEMPERATURE AND PRESSURE : A PROOF OF CONCEPT STUDY

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Background: Basal thumb osteoarthritis (OA) can cause significant pain and cause a decline in hand function (Litwic et al 2013). Guidelines for treatment of symptomatic basal thumb OA supports a conservative approach, including splinting to support the carpometacarpal joint (CMCJ) and reduce the painful movements of the thumb joint during functional tasks (Zhang et al 2000). Lack of legitimate placebo thumb splint has been a barrier to research to distinguish the specific mechanism of the perceived therapeutic effect of wearing thumb splints. Despite this, splinting of the basal thumb joint remains a common intervention for pain. This research contributed to a national CRN portfolio adopted study examining the clinical effectiveness and efficacy of basal thumb splints for people with basal thumb OA.
Objectives: In the present study, the efficacy of two novel placebo splint designs are examined in comparison to widely used verum thumb splint and no splint for the effect at skin surface interface whilst performing a functional task
Methods: This proof of concept study used a single blind, cross-over design that assessed the effect of wearing different splint conditions on the skin surface interface during a functional hand task.
17 healthy participants (male n=8; female n=9) who met the inclusion criteria were recruited to take part in the study. Skin surface temperature (°C) and pressure exerted at the skin surface interface was recorded during performance of a standardised hand function task, the nine-hole peg test (9HPT) for four splint conditions i) verum splint (Promedics NC79562), ii) placebo lycra splint (P1); iii) placebo lycra splint "lite" (P2) and iv) no splint. Data were recorded and analysed by one rater using MatLab and SPSS software.
Results: It was observed from the mean rank that the verum splint condition caused the greatest pressures compared to all other splint conditions. Post hoc analysis revealed there was no difference in pressure exerted over the CMCJ between the no splint condition and P1 (Z= -1.577, p=0.115) and P2 (Z= -0.365, p=0.715). The verum splint caused a significant increase in pressure over the CMCJ in comparison to all other test conditions (Z= -3.516, p<0.0005).
ANOVA showed a significant effect of splint design on temp ($F(3,16)= 22.96$, $p<0.05$). Post hoc analysis revealed that the verum splint produced a significantly higher skin surface temperature (32.67°C ±1.10°C) than P1 (31.75°C ±1.10°C, p<0.0005), P2 (31.85°C ±1.11°C, p=0.001) and no splint (31.06°C ±1.24°C, p<0.0005) conditions. No differences in skin temperature was shown between placebo designs (p=1.00).
Conclusion: This study is the first to characterise the effect of different thumb splint designs on the skin surface temperature and the mechanical loading force local to the CMCJ.
This study further informs the specific effect of thumb splints at the joint interface. Identifying that new placebo splint designs do not provide additional support to the thumb joint is a novel supplement to research surrounding thumb splinting intervention and can support the use of these devices as placebo splint conditions in future trials.

REFERENCES:

[1] Litwic A, et al. Epidemiology and burden of osteoarthritis. British medical bulletin. 2013 Jan 20;105(1):185-99
[2] Zhang W, et al. EULAR evidence based recommendations for the management of hand OA: report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Annals of the rheumatic diseases. 2007 Mar 1;66(3):377-88

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FRI0707-HPR IS A TAILORED DELIVERY OF NORDIC WALKING ACCEPTABLE FOR PEOPLE WITH INFLAMMATORY RHEUMATIC DISEASE?

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Background: People with inflammatory rheumatic diseases find it more difficult to stay physically active. Although interventions delivered in a clinical setting lead to short-term benefits, sustaining physical activity is challenging. Nordic Walking is a whole-body physical activity that involves walking with poles. It has been shown to be beneficial in long-term conditions but not specifically for inflammatory rheumatic diseases.
Objectives: To establish the acceptability of a tailored Nordic Walking intervention in this population as preparation for a full efficacy trial.
Methods: The intervention was developed collaboratively with patient research partners and involves a 30-minute training session followed by 10 one hour sessions of Nordic Walking over 10 weeks. Twelve people received the intervention between May and July 2018 and 12 more from September to November 2018. The intervention differed from standard Nordic Walking in several ways; initial training was provided in small groups of 2 to 3 by an instructor and a rheumatology physiotherapist. Flexible routes enabled participants to self-select their pace and distance. Routes radiated from, and circled back to, a central base with seats and drinking water.
Participants completed a Short Form (36) Health Survey (the RAND) at baseline and post-intervention and took part in a focus group or interview.
Results: Eighteen females and six males; mean age 60 years (range 35-82) were recruited from rheumatology clinics in the Southwest of England. All participants had a diagnosis of an inflammatory rheumatic disease including rheumatoid arthritis, psoriatic arthritis, axial spondyloarthropathy, connective tissue disease and systemic vasculitis. SF-36 data suggested a trend towards improvements and qualitative data provided insights into why the intervention was acceptable. All 24 participants enjoyed being active outdoors and reported benefits such as 'walking taller', 'better posture', 'better balance' and 'improved well-being'.
Results reveal how important the adaptations with this tailored delivery of Nordic Walking were to participants. They found it reassuring that rheumatology specialists had contributed to the design of the intervention and that delivery was supported by a physiotherapist. Learning Nordic Walking in small groups alongside people with similar conditions was popular and meant that participants could walk at their own pace, engage with peers and felt supported. Participants said they would not join a non-specialised Nordic Walking group. Several participants subsequently purchased their own Nordic Walking poles and have arranged to meet independently to continue, indicating the potential for sustainability.
Conclusion: This tailored delivery of Nordic Walking has the potential to offer acceptable, beneficial and sustainable physical activity for patients with inflammatory rheumatic diseases. Further research is now needed to investigate the long-term impact in a full efficacy trial.

REFERENCES:

[1] Breyer M-K, Breyer-Kohansal R, et al. (2010) "Nordic Walking improves daily physical activities in COPD: A Randomised Controlled Trial" Respiratory Research; 11, 112
[2] Hutton I, GambleG, et al. (2010) "What is Associated with being Active in Arthritis? Analysis from the Obstacles to Action Study" Intern Med Journal; 40, 512-20
[3] O'Donovan R and Kennedy N (2015) "Four legs instead of two – Perspectives on a Nordic Walking-Based Programme Among People with Arthritis" Disability and Rehabilitation; 37:18, 1635-1642

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FRI0708-HPR PROGNOSTIC FACTORS ASSOCIATED WITH AN EARLY RESPONSE TO PHYSIOTHERAPY TREATMENT IN PATIENTS WITH CHRONIC NONSPECIFIC NECK PAIN: AN EXPLORATORY PROGNOSTIC MODEL

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Background: Chronic nonspecific neck pain (CNP) is a common health problem worldwide. Previous studies identified sociodemographic and clinical factors associated with successful outcomes in patients at discharge of physiotherapy treatment. However, the prognostic factors associated with an early response to physiotherapy treatment in patients with CNP are unclear. This knowledge may allow to identify a profile of patients with higher odds of improvement at the beginning of treatment, supporting clinical decision-making considering benefits versus non-benefits at short-term.
Objectives: This study aimed to identify prognostic factors associated with an early successful response to Physiotherapy treatment in patients with CNP. The successful response was defined as a reduction on disability of ≥30% after 3-weeks of physiotherapy treatment.
Methods: A prospective cohort study was conducted on 52 patients with CNP lasting ≥3 months, undergoing a physiotherapy treatment programme of mobilisation and exercise (coordination, strength, endurance). Patients were assessed at baseline, and then 3-weeks later. Participants were categorised as having a successful outcome if they scored a difference in their disability above the Minimal Clinical Important Difference (MCID) of the Neck Disability Index (NDI). Logistic regression analysis (backward stepwise conditional method) was used to identify the associations between baseline prognostic factors and outcome. Socio-demographic and clinical characteristics of CNP were included as potential prognostic factors.
Results: A total of 51 participants completed the intervention. At 3-weeks post-treatment, 75% (38/51) of the participants achieved a successful response to physiotherapy treatment. In the final multivariate model (Omnibus Tests p<0.001), an early successful response to Physiotherapy treatment was significantly associated with the disability score (OR 1.16 – CI 95% 1.02-1.32), and pain intensity (OR 1.81 – CI 95% 1.03-3.20) at the baseline. This model improves the classification ability from 74.5 to 86.3%, explaining 50.6% of the outcome, with good predictive ability of sensibility (94.5%) and modest specificity (61.5%). The area under the ROC curve for disability score (0.8; 95% CI: 0.6-0.9) and pain intensity (0.7; 95% CI: 0.5-0.9) indicated good and acceptable discriminatory ability, respectively. After 3-weeks of mobilisation and exercise, the patients with scores ≥12 on NDI and ≥7 on Numeric Pain Rating Scale at baseline have increased odds of achieving an early response to treatment in the presence of both variables (+LR=1.71 95% CI: 0.84-3.50) or one variable (+LR=1.45 95% CI: 0.69-3.04).
Conclusion: This study suggests that patients with medium to high levels of disability and high levels of pain at the baseline, treated with a physiotherapy programme of mobilisation and exercise, are more likely to experience an early reduction on their disability score. References:
Disclosure of Interests: Lucia Domingues: None declared, Eduardo B. Cruz: None declared, Fernando Pimentel dos Santos Grant/research support from: From Abbvie and Novartis, Speakers bureau: Abbvie, Novartis, Pfizer, Biogen, Jaime Branco: None declared
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FRI0709-HPR EFFECTS OF LAND- AND WATER-BASED EXERCISE INTERVENTIONS ON PAIN IN PEOPLE WITH FIBROMYALGIA: A PRELIMINARY REPORT FROM THE AL-ÁNDALUS RANDOMISED CONTROLLED TRIAL

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Background: Non-pharmacological approaches are the mainstay of treatment in fibromyalgia. The current recommendations of the European League Against Rheumatism (EULAR) for the management of fibromyalgia highlight that exercise is the only therapy with a 'strong' evidence [1]. Exercise has been typically implemented on either land- or water-based settings. However, it is unclear whether to perform exercise in different settings has different effects on pain; this knowledge might help to maximise the beneficial effects that exercise has in fibromyalgia [2]
Objectives: To compare the effects of two exercise interventions (land- and water-based training) on pain in people with fibromyalgia.
Methods: From 272 initially randomized, a total of 151 participants (50.6 ±7.6 years old, 98% women) completed all the assessments and attended to at least 70% of the programme; 48, 42 and 61 participants pertained to the land-based exercise, water-based exercise, and usual care (control) groups, respectively. The intervention groups trained 3 non-consecutive days/week (45-60 minutes per session) for 24 weeks. Each session included aerobic exercises, muscular strengthening and stretching for all the major muscle groups. Pain was measured by the 0-100 mm visual analogue scale (VAS) from the Fibromyalgia Impact Questionnaire (FIQ). Catastrophizing and self-efficacy pain-related cognitions were assessed by the Pain Catastrophizing Scale (PCS total score) and pain management subscale (PSE) of the Chronic Pain Self-efficacy Scale (CPSS), respectively. We calculated an algometer score based on the sum of pain thresholds (kg/cm2) of the 18 tender pints according to the 1990 American College of Rheumatology fibromyalgia diagnostic criteria. Participants were evaluated at baseline (pre-test), at the end of the 24-week intervention (post-test) and after a 12-week detraining period (re-test).
The groups were comparable in sociodemographic and clinical characteristics; they only differ on age, which was included as a covariate along with baseline levels of pain.
Results: Adjusting for Bonferroni, most of the between-group comparisons of pain changes over time were not significant. As exceptions, in comparison to the control group, participants in the land-based exercise group lowered catastrophizing and improved algometer score at the post-tests; mean difference (95% interval confidence) [MD(95% CI)] = -4.0 (-7.5 to -0.5) and 6.2 (2.0 to 10.5), respectively. These differences became non-significant at the re-test.
Conclusion: These preliminary results suggest that a 24-week land-based exercise intervention had beneficial effects by reducing pain catastrophizing and increasing algometer score in people with fibromyalgia. However, these benefits were unsustained after the detraining period. In compassion to the control group, a water-based exercise intervention did not show any effect on pain. Although our finding suggest that a land-based exercise intervention may have short-term beneficial effects on pain, these findings must be considered as preliminary until more robust analyses are performed.

REFERENCES:

[1] Macfarlane GJ, et al. Ann Rheum Dis 2017;76:318–28. Doi: :10.1136/annrheumdis-2016-209724
[2] Carbonell-Baeza A, et al. BMC Musculoskelet Disord 2012;13:18. Doi:10.1186/1471-2474-13-18

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FRI0710-HPR **EFFECTIVENESS OF EXERCISE IN THE MANAGEMENT OF FATIGUE AND SLEEP QUALITY IN FIBROMYALGIA: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: Non-pharmacological interventions are the mainstay of treatment for fibromyalgia, however, current evidence-based guidelines report that the only therapy supported by 'strong for' evidence is exercise intervention for pain in fibromyalgia [1]. While increased fatigue and poor sleep quality are among the most burdensome symptoms in fibromyalgia, there remains limited evidence for the effectiveness of exercise in the management of these symptoms [2,3]
Objectives: To determine the effectiveness of exercise in the management of fatigue and sleep quality in fibromyalgia.
Methods: A systematic search was conducted using PubMed and Web of Science in October 2018 (Prospero Registration No. CRD42018118005). Eligible studies were randomised controlled trials (RCT) including adults with fibromyalgia (population), who received exercise (intervention) compared to usual care (comparator). Outcomes of interest were fatigue and/or sleep quality. No restrictions were applied for language nor for publication date. Random effects meta-analyses were conducted. The Cochrane Collaboration's tool was used for assessing risk of bias in the included studies. The quality of evidence was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework.
Results: Twenty RCTs were included, 17 included measures of fatigue (n=1003) and 12 measures of sleep quality (n=731). In comparison to usual care, exercise had beneficial effects on fatigue (Figure 1, P<0.001) but not on sleep quality (Figure 2, P=0.06). The most beneficial interventions for fatigue and improving sleep quality, were those in which fatigue was the primary outcome and those based on body-mind interventions, respectively (both, P<0.001). A moderate risk of bias was present in most of the included studies.
Conclusion: According to the GRADE framework, this review provides low-to-moderate quality evidence that exercise is moderately effective for improving fatigue, and moderate evidence of no/meaningless effects of exercise to improve sleep quality. Further high quality RCTs are required to determine the effectiveness of exercise on fatigue, and in particular, sleep quality in fibromyalgia

REFERENCES:

[1] Macfarlane GJ, et al. Ann Rheum Dis 2017;76:318–28. Doi:10.1136/annrheumdis-2016-209724
[2] Bidonde J, *et al. Cochrane Database Syst Rev* 2017;**2017**. Jun 21;6: CD012700 doi:10.1002/14651858.CD012700
[3] Busch AJ, *et al. Cochrane database Syst Rev* 2013;:CD010884. doi:10.1002/14651858.CD010884

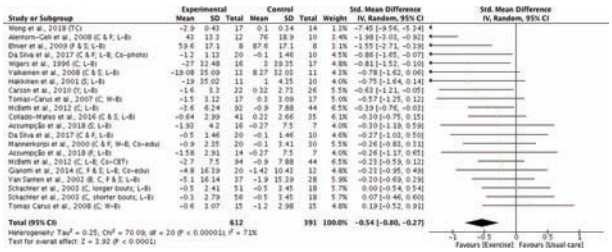


Figure 1. Pooled effects of randomised controlled trials analysing the effectiveness of physical exercise on reducing fatigue in people with fibromyalgia.

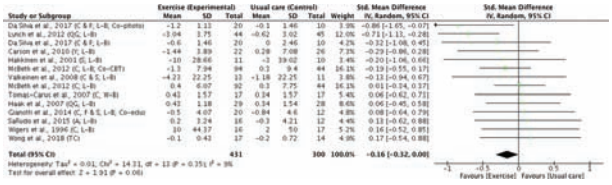


Figure 2. Pooled effects of randomised controlled trials analysing the effectiveness of physical exercise on enhancing sleep quality in people with fibromyalgia.

Analyses were conducted using a random effects model. CI, Confidence Interval; df, degrees of freedom; Std, Standardised; SD, Standard Deviation; IV, Inverse Variance; Co-, Co-intervention (Photo, phototherapy; edu, education); C, Cardiorespiratory exercise; F, flexibility exercise; S, Strength training; TC, Tai Chi; QG, Quigong; Y, Yoga; L- and W-B, land- and water-based exercise, respectively.

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Disclosure of Interests: None declared
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FRI0711-HPR **PATIENT PERSPECTIVES ON HOW TO IMPROVE MEDICATION EDUCATION**

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Background: EULAR recommends that people with inflammatory arthritis should have access to and be offered patient education throughout the course of their disease (1). The content and delivery of patient education should be individually tailored (2). Patients should be educated on their medication and know its purpose, mode of action, possible side effects and monitoring guidelines (3). Improving patients' ability to make informed choices and to use medication effectively and safely should result in significant benefits for the health service and improve patient well-being (4). Our institute's yearly Consumer Quality Index (CQI) revealed that our current medication education needs improvement.
Objectives: To improve medication education from the patient perspective.
Methods: A representative cross-sectional sample of 100 rheumatoid arthritis patients was invited to complete a specially designed questionnaire, based on the Satisfaction with Information about Medicines Scale (SIMS) questionnaire (5). All caregivers at our Rheumatology unit (rheumatologists, trainees, rheumatology nurses) participated in single-blinded structured observational sessions of their regular patient consultation with the patient's consent. Data was collected on the type and content of medication information that was given during the consultation. Local ethical approval was obtained and patient confidentiality was assured.
Results: At present 40 (40%) patients returned the questionnaire. Overall, patients are satisfied with the medication education provided (average overall satisfaction score of 7.4 (0-10). However patients experienced insufficient education on the following topics;
- whether the medication has influence on sex life
- the risk of having side effects
- how to act when side effects occur
- possible interaction with concomitant medication
- whether the medication can cause drowsiness

Between December 2018 and January 2019 caregivers at our unit (4 rheumatologists, 2 trainees, 1 nurse) participated in multiple single-blinded observational sessions. In 100% of observed consultations medication information was provided. However, most caregivers did not address the topic of side effects during their consultation. Furthermore, in all cases caregivers failed to document in the electronic patient file which information was provided.
Conclusion: Rheumatoid arthritis patients express overall satisfaction with medication education but experience an unmet need for information on possible medication effects on their sex life, medication side effects and on interaction with concomitant medication. Further analysis of the questionnaires will be performed and a plan of improvement will be implemented to meet the patients need for more and better education on medication. Patient medication education will be implemented in a continuous cycle of improvement.

REFERENCES:

[1] Zanghi HA, Ndosi M, Adams J, et al. (2015) EULAR recommendations for patients education for people with inflammatory arthritis.

[2] Daïen Cl, Hua C, Come B, et al. (2016) Pharmacologic and non-pharmacologic therapies in early arthritis: results of a systamatic literature informing the 2016 update of the EULAR recommendations for the management of early arthritis. *RMD open 2016*

[3] An Bord Altranais. (2003). Guidance to Nurses and Midwives on Medication Management. An Bord Altranais.

[4] Dublin.Roycroft-Malone J., Latter S., Yerrell P. and Shaw D. (2000). Nursing and medication education. Nursing Standard. 14. (50) 35-39.

[5] Horne R, Hankins M, Jenkins R. The Satisfaction with Information about Medicine Scale (SIMS): a new mesurement tool for audit and research. Qual Health Care. 2001;10:135-140

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FRI0712-HPR EFFICACY OF GRADED ACTIVITY WITH AND WITHOUT DAILY-MONITORED-WALKING ON SELECTED CLINICAL ATTRIBUTES OF PATIENTS WITH CONCOMITANT LOW-BACK PAIN AND TYPE-2 DIABETES

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Background: Graded Activity (GA) is efficacious in managing clinical attributes of patients with Low-Back Pain (LBP) in the general population [1,2]. It is unknown whether GA is efficacious in managing these clinical attributes in patients with concomitant LBP and Type-2 Diabetes (T2D) or additional daily-monitored-walking as a form of physical activity will be required.
Objectives: The objectives of this study were to investigating the effects of GA with and without daily-monitored-walking, and also to compare the efficacy of the two treatment modes on selected clinical attributes of patients with concomitant LBP and T2DM.
Methods: A single-blind controlled trial involving 58 patients (mean age: 48.3±9.4 years, 64.7% females) with concomitant LBP and T2D who received treatment twice weekly for twelve weeks was conducted. Participants were randomized into GA or GA with daily-monitored-walking (GAMW) groups. Pain Intensity (PI), Back Extensors Endurance (BEE), Abdominal Muscular Endurance (AME) and Glycaemic Control (GC) was assessed using Visual Analogue Scale, Biering-Sorensen test, flexor endurance test and HBA1c analyser respectively at baseline, 4th, 8th and 12th week. Data were analysed using repeated measures ANOVA, medians, Mann-Whitney U and Unpaired t-tests at $\alpha = 0.05$.
Results: At baseline, treatment groups were not significantly different in their physical and clinical characteristics. There were within-group significant differences on PI, AME and BEE in each of GA and GAMW groups across the time points of the study. Within group difference on GC was significant for GAMW (6.3±0.9%, 5.7±0.7%) but not GA (6.3±0.9%, 6.3 ±0.9%) groups. There were no significant difference between the effects of GA and GAMW on PI at week 4 (Median=-0.78, IQR=0.06; Median=-0.78, IQR=0.08), week 8 (Median=-1.72, IQR=0.06; Median=-1.71, IQR=0.18) and week 12 (Median=-1.46, IQR=0.10; Median=-1.53, IQR=0.18) of the study. Further there was no significant difference between the effects of GA and GAMW on AME at weeks 4 (6.64±0.15; 6.65±0.09), 8 (7.01±0.16; 7.03±0.1) and 12 (5.16±0.05; 5.19±0.09) of the study. Graded activity with daily-monitored-walking had higher improvements than GA alone on BEE (7.34±0.1, 7.25±0.1) at week 8, but not at week 4 (2.37±0.08; 2.36±0.1) or 12 (4.5±0.06; 4.53±0.08) of the study. The GAMW participants also had significant improvement on glycaemic control than GA participants (-0.5±0.2%, -0.6±0.5%) at week 12. Graded activity relieves back symptoms via the development of a sense of control over pain, elimination of pain avoidance as well as by improving overall physical fitness/function [3].
Conclusion: Graded activity with daily-monitored-walking produced positive effects on GC and yielded better improvement on BEE.

REFERENCES:

[1] Lindstrom, I., Ohlund, C., Eek, C., Wallin, L., Peterson, L., Fordyce, W.E. and Nachemson, A.L. 1992a.The effect of graded activity on patients with subacute low back pain: a randomized prospective clinical study with an operant-conditioning behavioural approach. Phys Ther. 72:279-293.

[2] Macedo LG, Latimer J, Maher CG, Hodges PW, McAuley JH, Nicholas MK, Tonin L, Stanton CJ, Stanton TR, Stafford R. Effect of motor control exercises versus graded activity in patients with chronic nonspecific low back pain: a randomized controlled trial. Phys Ther. 2012; 92:363–377.

[3] Bello AI, Quartey JNA, Lartey M. Efficacy of Behavioural Graded Activity Compared with Conventional Exercise Therapy in Chronic Nonspecific Low Back Pain: Implication for Direct Health Care Cost. Ghana Med J. 2015; 49:173-180.

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FRI0713-HPR COMPARISON OF BIOPSYCHOSOCIAL STATUS OF PATIENTS WITH ANKYLOSING SPONDYLITIS WITH AND WITHOUT ANTI-TNF TREATMENT

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Background: It is known that anti-TNF therapy is given to patients with persistently high disease activity despite conventional treatments according to the ASAS recommendations (1). Although biopsychosocial symptoms were well known, biopsychosocial assessments are insufficient in the literature.
Objectives: The aim of this study was to compare the biopsychosocial status between patients with AS who were decided to be treated with anti-TNF treatment and patients with AS who did not receive any anti-TNF treatment. Also, it was aimed to investigate the effectiveness of 3 months anti-TNF treatment on biopsychosocial status.
Methods: 74 AS patients who are decided to receive anti-TNF treatment and 38 AS patients, who didn't, were included in the study. Socio-demographic informations of patients were collected. The mean age of the patients (n = 112) was 41,9±19,8 years. Health Assessment Questionnaire (HAQ) was used to assess functional status and daily living activities. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression levels. Biopsychosocial status of the patients was evaluated by the BETY-Biopsychosocial Questionnaire (BETY-BQ) (2,3). The same evaluations were repeated after 3 months in 36 patients using anti-TNF.
Results: A statistically significant difference was observed in BETY-BQ, HADS anxiety and HAQ scores, when the groups were compared. There was no statistically significant difference in HADS depression scores (Table 1). The difference after 3 months of anti-TNF treatment was significant in all parameters (Table 2).

FRI0713HPR Table 1. Difference between the patients who decided to receive anti-TNF and who did not.

	Anti-TNF Decided Group (n=74)	Non-receiving Anti-TNF Group (n=38)	p-value*
HAQ	14,33±10,1	5,46±10,7	**,000**
HADS - Anxiety	10,24±5,0	7,58±5,0	**,011**
HADS - Depression	8,38±4,3	6,45±4,3	,053
BETY-BQ	59,32±24,1	46,74±25,8	**,032**

*Mann-Whitney U

FRI0713HPR Table 2. First and 'After 3 months' measurements in patients who received anti-TNF treatment.

N=36	1st measurement	'After 3 months' measurement	p-value*
HAQ	14,99±11,1	5,36±10,6	**,000**
HADS - Anxiety	10,33±5,3	7,72±4,7	**,001**
HADS - Depression	8,89±4,7	5,78±4,7	**,000**
BETY-BQ	59,33±25,1	44,28±23,2	**,000**

* Wilcoxon Test

Conclusion: It was observed that the patients who were decided to be received anti-TNF treatment had worse functionality, anxiety, and biopsychosocial status than the patients who did not receive anti-TNF treatment. Anti-TNF treatment was found to be effective in three months period in terms of these biopsychosocial symptoms that the patients had.

REFERENCES:

[1] Braun Jv, Van Den Berg R, Baraliakos X, Boehm H, Burgos-Vargas R, Collantes-Estevez E, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Annals of the rheumatic diseases. 2011;70(6):896-904.

[2] Ünal E, Arin G, Karaca Nb, Kiraz S, Akdoğan A, Kalyoncu U, et al. Romatizmalı hastalar için bir yaşam kalitesi ölçeğinin geliştirilmesi: madde havuzunun oluşturulması. Journal of Exercise Therapy and Rehabilitation. 2017;4(2):67-75.
[3] Kisacik P, Unal E, Akman U, Yapali G, Karabulut E, Akdogan A. Investigating the effects of a multidimensional exercise program on symptoms and antiinflammatory status in female patients with ankylosing spondylitis. Complementary therapies in clinical practice. 2016;22:38-43.

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FRI0714-HPR A PILOT NURSE-LED TELEPHONE TRIAGE LINE OF PATIENTS WITH RHEUMATOLOGIC RARE DISEASES IN A TERTIARY CENTER

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Background: The general rheumatology outpatient clinics are facing an increasing workload. The patients already in evidence with rare or complex inflammatory diseases, such as inflammatory myopathies, systemic lupus erythematosus, mixed connective tissue diseases, systemic sclerosis, Sjogren's syndrome, relapsing polychondritis, systemic vasculitides and other collagen-vascular diseases are being scheduled for outpatient or hospital assessment at the current visit. However the patients may need earlier appointments, given the possibility of flares or other issues.
Objectives: To assess the role of a nurse-led telephonic triage line in patients with rare rheumatologic diseases.
Methods: The nurses accepting to be enrolled in the programme answered the phone for the patients already in the department's and their follow-up with rare or complex inflammatory rheumatic diseases. A 2-hours training programme with attending physicians was completed. Respecting confidentiality agreement regulations, the calls were registered with the nume, diagnosis and phone number on a standard form. The calls reasons were recorded: appointments scheduling, medical issues or others. The alarming symptomes and signs requiring doctor advice or earlier appointments were checked on a short form: aggravating dyspnea, dysphagia, weakness or Raynaud's phenomenon, ulcerations, etc. Other issues, such as lumbar pain, joint pain, nausea, heartburn, etc requiring counselling, were registered as well.
Results: Over 2 months, 280 calls from patients with rare rheumatologic diseases were received, out of which 171 (61%) were for scheduling or changing appointments. The rest were for medical advice regarding minor ailments, medication side effects, regular blood tests or other investigations performed after the last visit, issues regarding travelling etc. The triage nurses referred the patients to Emergency in 2 cases (0.7%), to the General Practitioner in 28 cases (10%) or planned an early appointment to the attending rheumatologist for medical issues in 20 cases (7.3%), briefed the attending physician in 94 cases (33%) and offered counselling in the other cases (49%), which included: medication side effects, analyses to be repeated, diet and promoting self-care.
Conclusion: Telephonic calls, managed by experienced nurses, documented by standardized forms, are valuable additional tools in the management of rare inflammatory diseases. The pilot phone triage procedure improve patient's access to healthcare services. Periodic specialty training regarding rheumatologic emergency and communication skills increase the quality of this approach in rare diseases.

REFERENCES:

[1] Thwaites C, Ryan S, Hassel A, Rheumatology (Oxford) 2008; 47(4):522-5, Doi: 10.1093/rheumatology/ken041
[2] Fereira RO, Marques A, Cruz Mendes AMO, da Silva JA, Acta Reumatol Portuguesa 2015; 40:163-8.

Disclosure of Interests: None declared
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FRI0715-HPR FACTORS WHICH IMPACT COMPLETION AND NON-COMPLETION OF PHYSICAL ACTIVITY INTERVENTIONS FOR PEOPLE WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory condition which results in pain, fatigue, joint stiffness and an increased risk of cardiovascular issues. Physical activity (PA) has been proven to help reduce the severity of these symptoms and the risk of cardiovascular disease [1]. However, recent literature has shown that people with rheumatoid arthritis do not meet PA guidelines [2]. The systematic review aims to determine the factors which affect the completion rates of adults with RA in PA interventions.
Objectives: 1) Review the effect of the frequency, intensity, time and type of exercise (FITT principle) on participation rates. 2) Review the reasons for dropping out of an intervention and consider how this can be avoided in planning future interventions. 3) Examine the effect of behaviour change techniques used on completion rates.4) Explore the effect of adverse outcomes on completion rates.
Methods: A systematic review of the literature was carried out in February 2018. Inclusion criteria were: detailed intervention information, completion rates reported, published between 1998-2018 and published in English. Included papers were assessed using the Cochrane risk of bias tool by two assessors. The relevant data was then extracted, compared and conclusions were drawn.
Results: Nine studies with varying levels of quality were included in this review. Reasons for not completing an intervention could be divided into modifiable and non-modifiable factors; modifiable factors include the FITT principle, the behaviour change component and controlling for adverse outcomes. Non-modifiable factors included the environment, illness/flare-up and accidents. The results found that when people with RA had an individualised PA program that started at a low-moderate intensity they had higher participation rates than those who followed a generalised program, with no behaviour change component. Altering the intervention in response to patient's pain levels improved completion rates of the intervention.
Conclusion: When designing PA programs for people with RA, the EULAR PA guidelines for people who have inflammatory arthritis [3] should be followed. However, it should be noted that engagement and participation in PA interventions is increased when the intervention is of low impact PA and starts at a low-moderate intensity. Individualising the activity to the person and applying behaviour change techniques have also been found to improve participation.

REFERENCES:

[1] Kerschan-Schindl, K. and MacHold, K. (2011) 'Rehabilitation von Patienten mit rheumatoider Arthritis', *Physikalische Medizin Rehabilitationsmedizin Kurortmedizin*, 21(6), pp. 297–310. doi: 10.4061/2011/681640.
[2] Larkin, L. and Kennedy, N. (2014) 'Correlates of Physical Activity in Adults with Rheumatoid Arthritis: A Systematic Review', *Journal of Physical Activity and Health*, 11(6), pp. 1248–1261. Doi: 10.1123/jpah.2012-0194.
[3] Rausch Osthoff, A. K. et al. (2018) '2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis', Annals of the Rheumatic Diseases, 77(9), pp. 1251–1260. Doi: 10.1136/annrheumdis-2018-213585.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.2811

FRI0716-HPR FACTORS WHICH IMPACT COMPLETION AND NON-COMPLETION OF PHYSICAL ACTIVITY INTERVENTIONS FOR PEOPLE WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory condition which results in pain, fatigue, joint stiffness and an increased risk of cardiovascular issues. Physical activity (PA) has been proven to help reduce the severity of these symptoms and the risk of cardiovascular disease [1]. However, recent literature has shown that people with rheumatoid arthritis do not meet PA guidelines [2]. The systematic review aims to determine the factors which affect the completion rates of adults with RA in PA interventions.
Objectives: 1) Review the effect of the frequency, intensity, time and type of exercise (FITT principle) on participation rates. 2) Review the

reasons for dropping out of an intervention and consider how this can be avoided in planning future interventions. 3) Examine the effect of behaviour change techniques used on completion rates.4) Explore the effect of adverse outcomes on completion rates.

Methods: A systematic review of the literature was carried out in February 2018. Inclusion criteria were: detailed intervention information, completion rates reported, published between 1998-2018 and published in English. Included papers were assessed using the Cochrane risk of bias tool by two assessors. The relevant data was then extracted, compared and conclusions were drawn.

Results: Nine studies with varying levels of quality were included in this review. Reasons for not completing an intervention could be divided into modifiable and non-modifiable factors; modifiable factors include the FITT principle, the behaviour change component and controlling for adverse outcomes. Non-modifiable factors included the environment, illness/flare-up and accidents. The results found that when people with RA had an individualised PA program that started at a low-moderate intensity they had higher participation rates than those who followed a generalised program, with no behaviour change component. Altering the intervention in response to patient's pain levels improved completion rates of the intervention.

Conclusion: When designing PA programs for people with RA, the EULAR PA guidelines for people who have inflammatory arthritis [3] should be followed. However, it should be noted that engagement and participation in PA interventions is increased when the intervention is of low impact PA and starts at a low-moderate intensity. Individualising the activity to the person and applying behaviour change techniques have also been found to improve participation.

REFERENCES:

[1] Kerschan-Schindl, K. and MacHold, K. (2011) 'Rehabilitation von Patienten mit rheumatoider Arthritis', *Physikalische Medizin Rehabilitationsmedizin Kurortmedizin*, 21(6), pp. 297–310. Doi: 10.4061/2011/681640.

[2] Larkin, L. and Kennedy, N. (2014) 'Correlates of Physical Activity in Adults with Rheumatoid Arthritis: A Systematic Review', *Journal of Physical Activity and Health*, 11(6), pp. 1248–1261. Doi: 10.1123/jpah.2012-0194.

[3] Rausch Osthoff, A. K. et al. (2018) '2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis', Annals of the Rheumatic Diseases, 77(9), pp. 1251–1260. Doi: 10.1136/annrheumdis-2018-213585.

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FRI0717-HPR A COMPARISON OF THE EFFECTIVENESS OF CORE STABILIZATION EXERCISE AND COMBINED EXERCISE ON PAIN, FATIGUE, SLEEP PROBLEM AND HEALTH STATUS IN WOMEN WITH FIBROMYALGIA

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Background: Fibromyalgia (FM) is a syndrome characterized mainly by chronic widespread pain, fatigue, sleep disorders and decrease in health status. Exercise, one of the non-pharmacological approach, has favorable effects on clinic findings in FM, but studies investigating which types of the exercise are more effective in FM are limited.

Objectives: This study aimed to compare the effectiveness of core stabilization exercise (CSE) and combined exercise (CE) on pain, fatigue, sleep problem and health status in women with FM.

Methods: A total of 34 women with FM were included, allocated into the CSE (n:18, age: 43.05±9.23 years, body mass index (BMI): 27.25±5.23 kg/m^2) and the CE (n:16, age: 38.43±9.55 years, BMI: 25.62±3.68 kg/m^2) groups. Both the CSE and the CE programs were carried out 2 days a week for 6 weeks under the supervision of a physiotherapist. Pain, fatigue and sleep problems with Visual Analog Scale and health status with Fibromyalgia Impact Questionnaire were evaluated at baseline and after 6-weeks program.

Results: Physical characteristics of the groups were similar (p_{age}=0.162, p_{bmi}=0.313). After the program, it was found that pain (p=0.001; p=0.014), fatigue (p=0,002; p=0.011), and sleep problem (p=0.007; p=0.039) decreased, health status (p=0.001; p=0.001) improved in both the CE and the CSE groups, respectively. Moreover, sleep problem decreased in the CE group in comparison to the CSE group (p=0.038); but pain (p=0.240), fatigue (p=0.178), and health status (p=0.098) did not differ between groups.

Conclusion: In this study, it was observed that both the CSE and the CE programs were effective in decreasing pain, fatigue, sleep problem and improving health status of women with FM. In addition, the study suggested that the CE was superior in decreasing sleep problem in comparison to the CSE in women with FM. In clinics, both the CSE and the CE programs may be preferred to improve the symptoms of FM; however, the CE should be taken into account for the sleep problems in FM.

REFERENCES:

[1] Busch, A. J., Webber, S. C., Brachaniec, M., Bidonde, J., Dal Bello-Haas, V., Danyliw, A. D., .. & Schachter, C. L. (2011). Exercise therapy for fibromyalgia. Current pain and headache reports, 15(5), 358.

[2] Sosa-Reina, M. D., Nunez-Nagy, S., Gallego-Izquierdo, T., Pecos-Martín, D., Monserrat, J., & Álvarez-Mon, M. (2017). Effectiveness of therapeutic exercise in fibromyalgia syndrome: a systematic review and meta-analysis of randomized clinical trials. BioMed research international, 2017.

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FRI0718-HPR THE EFFECT OF THE BIOPSYCHOSOCIAL EXERCISE PROGRAM ON PAIN COPING SKILL AND FATIGUE IN RHEUMATIC DISEASES

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Background: Although the trend towards biopsychosocial approaches is increasing today, studies on psychosocial effects of exercise are limited in the literature. There is a need for framed exercise programs to assess the clinical effectiveness of biopsychosocial approaches. The reason why biopsychosocial programs are important may be due to multidimensional features of symptoms such as pain, fatigue.

Objectives: The purpose of this study is to investigate the effectiveness of the biopsychosocial exercise program on pain coping skill and fatigue in rheumatic patients.

Methods: Ninety-one patients with the rheumatic disease were included in this study. The patients were divided into two groups based on a prospective cohort (BETY group, n = 56; and control group, n = 35). BETY is a biopsychosocial exercise approach (1). It was performed in a period of one hour, 3 times a week for 12 weeks and included clinical pilates exercises, dance therapy-authentic movement and pain management information. The control group did not take any exercise treatment. The BETY-Biopsychosocial Questionnaire (BETY-BQ) was used to evaluate the pain coping skill and fatigue as well as assessing whole biopsychosocial status of individuals (2). The answers were given to the 5th question (I don't know how to control my pain.) and the 11th question (I feel tired.) of the BETY-BQ were recorded as a 5-point Likert at ranging from 'yes, always' to 'no, never. Also, the total score of BETY-BQ was recorded. Demographic data were given as mean ± standard deviation (X ± SD), and answers given to the questionnaire were expressed in frequency tables.

Results: The mean ages of BETY group and control group were 49.63 ± 11 and 39.74 ± 10 years and body mass indexes were 26.93 ± 3 kg/m2 and 26,54 ± 4 kg/m2, respectively. The frequency of answers to the 5th and 11th question and the total score of the BETY-BQ on the first assessment (pre-treatment) and the second assessment (post-treatment) were shown in Table 1.

FRI0718HPR Table 1. Comparison of assessment results

	BETY exercise group			Control Group		
	Pre-treatment	Post-treatment	p	Pre-treatment	Post-treatment	p
BETY-BQ (0-120)	54.60±27	38.55±25	**<0,001**	56.51±24	53.63±28	0.221
5th question						
Yes always (%)	24.1	7.4	**<0,001**	28.6	28.6	0.734
Yes often (%)	7.4	3.7		20	14.3	
Yes sometimes (%)	25.9	22.2		8.6	17.1	
Yes rarely (%)	25.9	20.4		17.1	8.6	
No never (%)	16.7	46.3		25.7	31.4	

11th question						
Yes always (%)	33.3	14.8	**<0,001**	51.4	42.9	0.198
Yes often (%)	25.9	18.5		25.7	22.9	
Yes sometimes (%)	25.9	37		11.4	20	
Yes rarely (%)	9.3	20.4		5.7	8.6	
No never (%)	5.6	9.3		5.7	5.7	

Conclusion: It was concluded that BETY as a biopsychosocial exercise approach is effective in reducing fatigue and improving the pain coping skill as well as the biopsychosocial status of rheumatic patients. BETY should be kept in mind for further studies in terms of biopsychosocial aspects of pain coping, fatigue, etc.

REFERENCES:

[1] Kisacik, Pinar, et al. "Investigating the effects of a multidimensional exercise program on symptoms and antiinflammatory status in female patients with ankylosing spondylitis." Complementary therapies in clinical practice 22 (2016): 38-43.

[2] ÜNAL, Edibe, et al. "Romatizmalı hastalar için bir yaşam kalitesi ölçeğinin geliştirilmesi: madde havuzunun oluşturulması." *Journal of Exercise Therapy and Rehabilitation* 4.2 (2017): 67-75.

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FRI0719-HPR AN EVALUATION OF A FIBROMYALGIA EXERCISE PROGRAMME DELIVERED IN THE UNITED KINGDOM NATIONAL HEALTH SERVICE

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Background: Fibromyalgia (FM) is a complex long-term condition affecting up to 5.4% of the UK population[1]. It is associated with chronic widespread pain, fatigue, stiffness, sleep problems, memory and concentration difficulties, and irritable bowel syndrome[2]. FM guidelines recommend exercise as a core treatment for the management of FM symptoms[3]. Evidence shows exercise interventions are effective for people with FM, reducing pain and improving function and muscle strength[4].
Objectives: This study aimed to evaluate the effectiveness of introducing a FM exercise group programme within a United Kingdom National Health Service hospital setting.
Methods: A pre and post evaluation was conducted. People with FM attending a rheumatology therapy department were invited to take part in a FM group exercise programme (60 minutes, once per week, seven weeks). To improve adherence, the exercise programmes were individualised based upon patients' preferences for aerobic or resistance exercise or both. Pre and post Revised Fibromyalgia Impact Questionnaire (FIQR), self-efficacy scale and sit-to-stand in 30 seconds outcome data were collected. Data were analysed using parametric paired samples t-tests and standardised effect size (Cohen's d).
Results: A total of n=20 patients completed the exercise programme (n=3 non-completers had higher baseline FIQR scores). Of the 20 completers the mean age was 49.9 years; n=19 were women; n=2 had a concomitant diagnosis of Joint Hypermobility Syndrome and n=1 had Inflammatory Arthritis. The results demonstrated statistically significant improvements across all outcome measures. There were large standardised effect sizes: self-efficacy d=0.93 (95% Confidence Interval (CI) 1.56, 0.26), FIQR d=-1.00 (-0.32, -1.64), sit to stand in 30 seconds d=0.76 (0.07, 0.75).
Conclusion: An exercise programme for patients affect by FM can be successfully delivered in a hospital setting. Those who completed the programme saw large improvements in pain, self-efficacy and sit to stand. However, further research is needed to confirm the findings of this uncontrolled study.

REFERENCES:

[1] Weir PT, Harlan GA, Nkoy FL, Jones SS, Hegmann KT, Gren LH, Lyon JL. The incidence of fibromyalgia and its associated comorbidities: a population-based retrospective cohort study based on International Classification of Diseases, 9th Revision codes. JCR: Journal of Clinical Rheumatology. 2006 Jun 1;12(3):124-8.

[2] Bennett RM. Clinical manifestations and diagnosis of fibromyalgia. Rheumatic Disease Clinics of North America. 2009 May 31;35(2):215-32.

[3] Macfarlane GJ, Kronisch C, Dean LE, Atzeni F, Häuser W, Fluß E, Choy E, Kosek E, Amris K, Branco J, Dincer F. EULAR revised recommendations for the management of fibromyalgia. Annals of the rheumatic diseases. 2016 Jul 4:annrheumdis-2016.

[4] Busch AJ, Webber SC, Richards RS, Bidonde J, Schachter CL, Schafer LA, Danyliw A, Sawant A, Dal Bello Haas V, Rader T, Overend TJ. Resistance exercise training for fibromyalgia. Cochrane database of systematic reviews. 2013(12).

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FRI0720-HPR DEVELOPMENT AND VALIDATION OF A SELF-ADMINISTRATED QUESTIONNAIRE MEASURING ESSENTIAL KNOWLEDGE FOR PATIENTS WITH RHEUMATOID ARTHRITIS: THE RHEUMATOID ARTHRITIS ASSESSMENT KNOWLEDGE QUESTIONNAIRE (RAKE)

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Background: Improving knowledge and skills is recommended for patients with rheumatoid arthritis (RA) to enhance self-management. Measuring knowledge is also part of the educative approach. However, the available Knowledge questionnaires (KQs) (ref 1,2) needed to be updated according to recent recommendations for RA management and the patients' needs (ref 3).
Objectives: To develop and a validate a new KQ in RA.
Methods: 4 steps. Step1. Selection of knowledge considered essential for patients with RA through Delphi rounds by a working group of rheumatologists, health professionals (HPs) and patients leading to a list of consensual items (ref3). Step2. Two rheumatologists and a rheumatology nurse constructed the first version of the KQ, each question of the KQ referring to a selected item on the list. The formulation was then amended by the working group. A new version was elaborated during a face-to-face meeting of 3 HPs and one patient. Step 3. The KQ was submitted to ten patients for cognitive debriefing, comments were analysed and a the final version was elabored. Step 4. Multicentric validation in 11 rheumatology departments: acceptability was measured by the rates of missing data per item, reproducibility and sensitivity to change were assessed respectively by test/retest at a 2 weeks interval (Lin's concordance correlation coefficient) and by testing the KQ before and after patient education sessions. The sample size estimation and statistical analyses were conducted according to COSMIN recommendations, especially concerning thresholds of metrological indexes.
Results: Step1 obtained 45 knowledge items, 32 considered essential and 13 considered useful, selected respectively by more than 2/3 and more than 50% of participants to the Delphi rounds, leading to the RAKE: a 45-items questionnaire, with a 32-items short form. The RAKE contains 6 knowledge domains: disease knowledge (10 items), pharmacological treatment (14), non -pharmacological treatment (7), comorbidities (1), self-care for pain and fatigue (5), adaptative skills to psychosocial and professional issues and health care system (8). The validation included 130 patients, 108 (83%) women, mean age 56.4±12.10 years, median disease duration 9 years [4; 23]. The missing data rate per item was <0,05. The RAKE's internal validity (Kuder-Richardson) was 0.90. Reproducibility (in 72 patients) was 0.86 [0.80; 0.92]. Sensitivity to change was measured in 54 patients. A statistically significant difference in total knowledge score was observed between the two assessment times: 30.1±7.4 vs. 37.7±5.7 (p<0.001), representing an effect size >1.1 [0.7; 1.6]. The RAKE's

external validity was confirmed by correlation with the RAID score of 0.16 (p=0.08).
Conclusion: This study enabled the development and the validation of the RAKE, a Knowledge questionnaire for patients with RA, with a good acceptability, reproducibility and sensitivity to change. This KQ will be helpful to assess the process of knowledge acquisition in patient education approaches.

REFERENCES:

[1] Hill and al., Br J Rheumatol. 1991,30 :45-9. Lineker and al., J Rheumatol. 1997, 24(4):647-53. Beauvais C, et al. ARD 2015; 74, suppl 2.

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FRI0721-HPR EFFECTIVENESS OF NON-PHARMACOLOGICAL AND NON-SURGICAL INTERVENTIONS ON THE IMPACT OF RHEUMATOID ARTHRITIS: AN OVERVIEW OF REVIEWS

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Background: Impact of disease persists in many patients with rheumatoid arthritis (RA) even after inflammatory remission is achieved, requiring the need for adjunctive interventions targeting the uncontrolled domains of disease impact. Several systematic reviews have addressed nonpharmacologic interventions, but there is still uncertainty due to scarce or conflicting results or significant methodological flaws.
Objectives: To determine the effectiveness of non-pharmacological and non-surgical interventions upon the impact of RA.
Methods: A comprehensive search strategy for 13 databases and grey literature was developed. This review included quantitative systematic reviews that examined the effectiveness of non-pharmacological and non-surgical interventions of any form, duration, frequency and intensity, alone or in combination with other interventions designed to reduce the impact of disease in adult patients with RA. The outcomes were pain, functional disability, fatigue, emotional well-being, sleep, coping, physical well-being and global impact of disease. Critical appraisal and data extraction were performed independently by two reviewers and summarized using a narrative synthesis approach.
Results: Eight systematic reviews were included (Figure 1), with a total of 91 RCT's and nine observational studies (6740 participants). Four systematic reviews examined the effects of multicomponent or single exercise/physical activity interventions, two examined the effects of hydrotherapy/balneotherapy, two evaluated the effects of psychosocial interventions and one assessed the effects of custom orthoses for the foot and ankle. Multicomponent or single exercise/physical activity interventions, psychosocial interventions and custom orthoses appeared to be effective in improving pain and functional disability. Fatigue also improved with the implementation of multicomponent or single exercise/physical activity interventions and psychosocial interventions. Only exercise/physical activity interventions appeared to be the effective in improving the global impact of disease. None of the included systematic reviews reported on emotional well-being, sleep, coping or physical well-being as an outcome measure. Other types of interventions were not sufficiently studied and their effectiveness is not yet established.

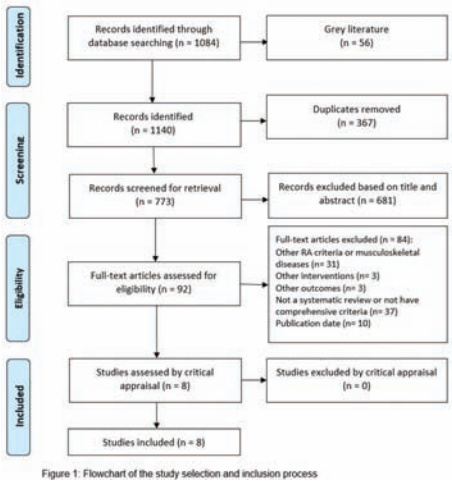


Figure 1: Flowchart of the study selection and inclusion process

Conclusion: Only multicomponent or single exercise/physical activity interventions, psychosocial interventions and custom orthoses seems to be capable of reducing the impact of rheumatoid arthritis. Future evidence should be created and synthesized in the fields identified as knowledge gaps, namely emotional well-being, sleep, coping and physical well-being. Further investigation should be encouraged on the effects of interventions that have not been assessed at all or sufficiently to established their effectiveness, so that robust decisions and recommendations can be made.
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FRI0722-HPR THE INVESTIGATION OF THE RELATIONSHIP BETWEEN PSYCHOSOCIAL AND FUNCTIONAL STATUS OF CHILDREN WITH JIA

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Background: JIA is the most common rheumatic disease in children and may result in significant morbidity with joint deformity, growth disorder, and persistence of active arthritis to adulthood (1). According to the model of biopsychosocial pain, emotions affect the degree of functional impairment (2).
Objectives: The aim of this study is to investigate the relatıonshıp between the psychosocial and functional status of children with juvenile idiopathic arthritis (JIA).
Methods: 382 children with JIA were included in the study. Individuals were assessed with the Juvenile Arthritis Biopsychosocial Questionnaire (JAB-Q) (3) and Children Health Assessment Questionaire (CHAQ) was applied for functional status (4).
Results: The mean age of the subjects included in the study (n = 386) was 12.48 ± 3.81 years. The median value of the JAB-Q functional status was 2 (min: 0 max: 34), psychosocial status was 10 (min: 0 max: 38). And the median value of the CHAQ was 0,25 (min: 0 max: 3). Correlation coefficients and statistical significance were calculated by using Pearson's test. There was a low positive correlation between BETY-BQ functional status and BETY-BQ psychosocial status ($r = 0.347$, $p < 0.001$), a low positive correlation between CHAQ and BETY-BQ psychosocial status ($r = 0.395$, $p < 0.001$). There was a good positive correlation between BETY-BQ functional status and CHAQ ($r = 0.678$, $p < 0.001$) (Table 1).

FRI0722HPR Table 1. Comparison of JAB-Q Psychosocial, JAB-Q Function and CHAQ scores of children with JIA

		BETY-BQ Psychosocial	BETY-BQ Function	CHAQ
BETY-BQ Psychosocial	r	1	0,347**	0.395**
p		0.000	0.000	
BETY-BQ Function	r	0,346**	1	0.678**
	p	0.000		0.000
CHAQ	r	0.395**	0.678**	1
	p	0.000	0.000	

Conclusion: The psychosocial status of children is not affected by functional status. Psychosocial status may be affected by different variables. It was concluded that children should be encouraged to participate in social activities independently their functional problems. Further studies are needed to examine the other variables' effects on psychosocial status in children with JIA.

REFERENCES:

[1] Kahn, P. Juvenile idiopathic arthritis: current and future therapies. Bulletin of the NYU hospital for joint diseases, 2009, 67(3), 291-291.
[2] Gatchel R, Peng Y, Peters M, Fuchs P, Turk D. The biopsychosocial approach to chronic pain: Scientific advances and future directions, Psychological Bulletin, 2007, vol.1334 (pg.581-624)
[3] Unal, Edibe, et al. "A new biopsychosocial and clinical questionnaire to assess juvenile idiopathic arthritis: JAB-Q." Rheumatology international 2018: 1-8.
[4] Singh G, Athreya BH, Fries JF, Goldsmith DP. Measurement of health status in children with juvenile rheumatoid arthritis. Arthritis Rheum 1994;37:1761–9.

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FRI0723-HPR A MIXED METHOD STUDY TO EXPLORE THE FEASIBILITY AND PATIENT SATISFACTION OF TWO DIFFERENT EXERCISE PROGRAMS IN SYSTEMIC SCLEROSISASSOCIATED MICROSTOMIA

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Background: Systemic sclerosis (SSc) is a severe autoimmune disease and fibrotic cutaneous involvement of hands and face is a typical characteristic. Oral involvement with reduced oral aperture is frequent and associated with impaired food intake, oral hygiene and secondary dental problems. Several studies have shown that stretching (placing the thumbs in opposite corners of the mouth hand, pulling outward) and oral augmentation (tongue depressors between the back molars) exercises can increase oral aperture but is often hampered by low adherence rates.
Objectives: The aim of this descriptive explorative mixed method study was to explore feasibility, patient satisfaction and effectiveness of two exercise programs, Therabite and orofacial exercises, in systemic sclerosis associated microstomia.
Methods: We included adult patients suffering from systemic sclerosis (fulfilling the ACR/EULAR 2013 criteria) and microstomia (maximal oral aperture <40mm). We discerned two groups: Group A exercised with a passive jaw motion device (Therabite®), and Group B performed mouth-stretching exercises. Patients were expected to exercise for 10 minutes, 3 times/day for 3 months. Patients were contacted 4 times by telephone to address encountered problems and completed an exercise diary to document the adherence rate. Patients were evaluated at baseline, 3 months (period without intervention), 6 months (after 3 months of intervention) and at 9 months (post-intervention visit). At time point 6 months, semi-structured one to one interviews were conducted. Interviews were recorded, transcribed verbatim and systematically analyzed using Qualitative Analysis Guide of Leuven.
Results: We included 6 women and 3 men, with a median age of 60 years (range 40-75) and a median disease duration of 8 years (range 3-22). At time point 6 months, all patients in group A (n=4) and 4 patients in group B (n=5) improved with a median of 9mm (range 2-10) and 7mm (range 4-11), respectively. One patient had a decrease of 2mm. The compliance, measured as the ratio of executed exercises relative to the planned number of exercises ranged between 63.7% and 98,9% in group A and between 48.5% and 97,4% in group B. Details are shown in Table 1. In the follow-up period, we documented maintenance of the observed increase in oral aperture in those patients that continued exercising daily. In all others, maximal oral aperture declined again. All 9 patients attended the interview. Three main themes emerged from the data: drivers, challenges and perceived improvement. Patients highlighted several drivers to perform the exercises at home, such as the motivation to improve current disability cause by microstomia. Furthermore, they equally highlighted several challenges regarding feasibility, such as the struggle to exercise multiple times a day. Most of the patients were hoping that they could keep their improvement. They were willing to continue practicing if necessary, but with a lower frequency.
Conclusion: This study suggests that both types of intervention can improve maximal oral aperture. The adherence to therapy was higher than expected but none of the patients considered it feasible to continue practicing 3 times/day in the long-term resulting in a decline of improvement post intervention. This is the first study to report the feasibility of the exercises for the patients and can be very useful for health professionals giving guidance. Future studies are needed in order to define exercise programs that are feasible and can be sustained in the long term.
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Table 1: Evolution in maximal oral aperture for both intervention groups

Intervention group	Participant number	Evolution between M3 and M6	Evolution between M6 and M9	Adherence rate between M3 and M6
A	1	+9 mm	-3 mm	95.2%
	2	+2 mm	-2 mm	85.7%
	3	+9 mm	-3 mm	98.9%
	4	+10 mm	+4 mm	63.7%
B	1	+11 mm	-2 mm	97.4%
	2	+10 mm	+2 mm	48.6%
	3	+4 mm	-2 mm	68.3%
	4	+7 mm	+1 mm	93.8%
	5	-2 mm	+2 mm	48.5%

M: month; M3: start intervention; M6: end of intervention; M9: post-intervention.

FRI0724-HPR THE EFFECTIVENESS OF TAI CHI CHUAN IN OSTEOARTHRITIS OF THE KNEE: A SYSTEMATIC REVIEW

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Background: Osteoarthritis (OA) is the most prevalent joint disease in the elderly. The signs and symptoms are degeneration of joint surface, pain, stiffness, swelling and decrease in physical function. Knee OA is the most common joint disease and more prevalent among older adults. Tai Chi Chuan is a safe exercise modality of Chinese origin, which may be a potentially in reducing symptoms.
Objectives: The aim of systematic review was to identify the effects of Tai Chi Chuan in the elderly with knee osteoarthritis.
Methods: This systematic review was registered in Prospero (CRD42018098699). MEDLINE, EMBASE, PEDro, Cochrane, Scopus, Scielo, Lilacs and Web of Science, were screened between May 2008 to May 2018 in English, Spanish, Portuguese and Mandarin language. Randomized controlled trials (RCTs) comparing Tai Chi to control conditions were included. Two authors independently assessed risk of bias using the risk of bias tool recommended by Jadad index. Outcome measures included were pain, stiffness, muscular strength, functionality and quality of life.
Results: In the search we founded 161 studies, MEDLINE (29), Pedro (58), Web of Science (17), Embase (29), Cochrane (6), Scopus (18), Manual search (4). Eight articles were included and seven showed the effectiveness of Tai Chi Chuan, being higher to the interventions of the control groups, consisting of self-care educational activities, or strengthening and endurance exercises of knee flexors and extensors. Only one study, that patients received a lower limb resistance training program, presented better results in pain, stiffness and physical function scores. Tai Chi Chuan was not associated with adverse events.
Conclusion: Tai Chi Chuan was effective in improving pain, stiffness and physical function of sleep quality, in addition to increased speed and step length during gait, and strength gain of knee extensor muscles in elderly patients with knee OA. This systematic review found moderate

evidence for short-term improvement of pain, physical function and stiffness in patients with knee AO. More high quality RCTs are urgently needed to confirm these results.

REFERENCES:

[1] Michael Wortley,Songning Zhang, Maxime Paquette, Erin Byrd, Lucas Baumgartner, Gary Klipple, John Krusenklaus, Larry Brown. Effects of resistance and Tai Ji training on mobility and symptoms in knee osteoarthritis patients. Journal of Sport and Health Science. 2013; 2: 209- 214.

[2] Zhu Q, Huang L, Wu X, Wang L, Zhang Y, Fang M, Liu Y.Effects of Tai Ji Quan training on gait kinematics in older Chinese women with knee osteoarthritis: A randomized controlled trial. Journal of Sport and Health Science. 2016; 5: 297-303.

[3] Pereira MM, Oliveira RJ, Silva MAF, Souza LHR, Vianna LG. Effects of Tai Chi Chuan on knee extensor muscle strength and balance in elderly women. Rev Bras Fisioter. 2008; 12: 121-6.

[4] Lü J1, Huang L1, Wu X1, Fu W1, Liu Y2. Effect of Tai Ji Quan training on self-reported sleep quality in elderly Chinese women with knee osteoarthritis: a randomized controlled trail. Sleep Med. 2017; 33:70-75.

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FRI0725-HPR A TAILOR-MADE EXERCISE PROGRAM DESIGNED FOR IMPROVING CARDIORESPIRATORY FITNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INCREASED CARDIOVASCULAR RISK

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Background: Rheumatoid arthritis (RA) is associated with low levels of cardiorespiratory fitness (CRF), especially in patients with RA and cardiovascular (CV) risk. The optimization of management of CV risk in patients with RA is an important aim in the treatment, including also exercise, particularly in patients with RA with a high CV risk, defined as a 10-year CV risk of 20% or higher. However, exercise to improve CRF in these patients is challenging since professionals should take multiple factors into account, such as comorbid conditions related to CV risk. It is unknown which intensity of exercise improves CRF and is safe for patients with RA and CV risk.

Objectives: To design a tailor-made exercise therapy program to improve CRF for RA patients with CV risk >20%.

Methods: To design a tailor-made exercise therapy program, patients and experts' opinions were collected, and a systematic literature search on exercise programs in RA and CV risk factors was performed. The ACSM guidelines were also used to gain insight into frequency, intensity, type and progression of the exercises. In addition, a cardiology rehabilitation team and an arthritis rehabilitation team were consulted during the development of the program. The designed program was partly based on cardiac rehabilitation protocols and especially the way the training load was increased, taking into account the joint load. Finally, the developed exercise program was discussed and approved by an expert panel of patients, rheumatologists, a cardiologist, physical therapists and researchers in rheumatology. The designed program was tested on 10 patients in which the feasibility and safety was tested.

Results: Intensity of exercises was based on the results from the baseline exercise tests showing that on average the VO_2max was under the standard. The maximum Heart Rate (HR max), which was on average (mean, SD) 140.6 (10.9) beats per minute, was used to determine the individually performed intensity of exercises. The duration of the program was 12 weeks. Patients had two training sessions per week with a duration of one hour each. To guarantee safety, the training load was progressively increased, and the tolerability was assessed at every training. Exercises consisted of aerobic and muscle strength exercises. The first four weeks patients trained 30 minutes (which were spread over three exercises) on 65% of the HR max which was gradually increased until 75% of the HR max in the sixth week. From the fifth week three exercises to improve muscle strength were added to the program. From the seventh week interval training started, with a peak of 85% of the HR max and a rest of 65% of the HR max. The program also included motivational interviewing because one of the main reasons for a high CV risk is the inactivity during daily life. All patients were motived to perform 30 minutes of moderate exercises every day at home.

Conclusion: A tailor-made exercise program to improve cardiorespiratory fitness in patients with RA and CV risk is developed, based on the opinion and experience of patients and health professionals and supported by a literature review and guidelines. A progressively increase in intensity of the exercise program, based on the individual maximum HR, is tolerable and safe and might increase cardiorespiratory fitness in patients with RA and CV risk.

REFERENCES:

[1] Metsios, et al. Rheumatology 2015 Dec;54(12):2215-20.

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FRI0726-HPR DOES ART THERAPY MAKE A DIFFERENCE IN THE MANAGEMENT OF CHILDREN AND YOUNG PEOPLE WITH RHEUMATIC DISEASES: A MULTI-SITE SERVICE REVIEW TO EXPLORE THE IMPACT OF ART THERAPY IN TWO TERTIARY PAEDIATRIC RHEUMATOLOGY SERVICES IN SCOTLAND

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Background: Art therapy interventions in various medical settings are known to contribute to the mental health and wellbeing of patients. In paediatric rheumatology there is a well documented unmet need for psychological support for children and families coping with chronic disease and its treatment. The role that art therapy could have in this provision is unknown and there is no evidence-based research to help understand its potential contribution. The Teapot Trust is a Scottish charity working with paediatric rheumatology services offering art therapy to children and young people with rheumatic diseases.

Objectives: This project aimed to evaluate the service provided by art therapists in two tertiary paediatric rheumatology units in Scotland. The objective was to better understand which patients were referred for art therapy; why they were referred; levels of engagement and acceptability of therapy and benefit resulting in improved outcome.

Methods: A retrospective review was conducted of referrals received in the period 2012-2018 to art therapy from paediatric rheumatology services. A mixed method approach was used for gathering quantitative, secondary and qualitative data. Quantitative data was collected by collating numerical and demographic information from referral forms; art therapist service databases; and patient medical records. Secondary and qualitative data has been gathered from pre-existing service information; the use of outcome measurement tools; end of therapy evaluations; end of therapy reports and patient feedback forms.

Results: The demographics of children seen were as expected in a paediatric rheumatology service with the majority being females with juvenile idiopathic arthritis and on treatment with methotrexate. Peak age of referral was between 7 and 12 years. The majority of referrals were for help with coping either with their diagnosis or the emotional impact. Patient reported outcomes show significant improvements for patients in their social and emotional wellbeing. This review highlighted the limitations

of art therapists using a variety of validated and non-validated outcome measures making it difficult to objectively evaluate outcomes.

Data ↓ Service→	Edinburgh	Glasgow	Combined
Total referrals*	34*	65**	34% Edinburgh / 66% Glasgow
Age bands*	0-6: 12%, 7-12: 50%, 13-18: 38%	0-6: 6%, 7-12: 75%, 13-18: 19%	0-6: 8%, 7-12: 67%, 13-18: 25%
Gender*	M: 15%, F: 85%	M: 17%, F: 83%	M: 16%, F: 84%
Reason for referral**	Coping with treatment: 16% Coping with diagnosis: 17% Coping with pain: 5% Coping with emotional impact: 62%	Coping with treatment: 22% Coping with diagnosis: 10% Coping with pain:7% Coping with emotional impact: 61%	Coping with treatment: 19% Coping with diagnosis: 13% Coping with pain:6% Coping with emotional impact: 62%
Diagnosis**	JIA: 50 %, Other: 50%	JIA: 50%, Other 50%	JIA: 50%, Other: 50%
Medication**	Methotrexate: 82% Other: 18%	Methotrexate: 82%, Other: 18%	Methotrexate: 82%, Other: 18%
Patient uptake**	88%	62%	75%
CAN/DNA**	12%	38%	25%
Sessions offered**	Average 20	Average 8 sessions	Average 14 sessions
Patients per week**	Average 8	Average 4	Average 10 patients per week
Waiting times**	1-2 weeks	8-12 weeks	Average 8 weeks waiting times
Clinical hours**	56%	56%	56%
Non-clinical hours**	44%	44%	44%
Outcome measures used**	PEDS QL: 60%, Other: 40%	PEDS QL: 60% Other: 40%	PEDS QL: 60% Other: 40%
Patient reported outcomes**	Increased confidence 34% Feeling calmer/less anxious 18% Better able to share feelings 33% Experience of fun in hospital 15%	Increased confidence 33% Feeling calmer/less anxious 17% Better able to share feelings 33% Experience of fun in hospital 17%	Increased confidence 34% Feeling calmer/less anxious 17% Better able to share feelings 33% Experience of fun in hospital 16%

* Complete sample ** Cross sample *Data collection period 2014-18 **Data collection period 2012-18

Conclusion: This retrospective multi-site service review demonstrated that art therapy was well used by clinicians as an appropriate psychological support for children and young people with rheumatic diseases. Engagement with the service was good and feedback positive. The review highlighted the challenge of objectively assessing outcomes, with the need to use validated and standardised assessment tools to collect this systematically going forward. A standardised service evaluation framework will be developed to facilitate future service reviews and is hoped that this represents a first step in developing evidence-based research to investigate the impact and benefit of art therapy in supporting children and young people in paediatric rheumatology.

Disclosure of Interests: None declared

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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

FRI0726B-HPR INVESTIGATION OF PHYSICAL ACTIVITY LEVELS OF PATIENTS WITH BEHCET'S DISEASE

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Background: Behcet's disease (BD), which is followed by a chronic course with attacks, is a significant cause of morbidity and mortality due to skin and mucosal lesions, joint involvement and eye involvement which can cause vision loss. It disrupts the physical and mental health of the individual as well as the disability of the physical functions and can affect the quality of life negatively (1, 2). There is strong evidence for the benefits of Physical activity (PA) on improvements on disease activity, activities and participation; however, people with rheumatic and musculoskeletal diseases (RMDs) are in general less active compared with healthy controls (3-5).

Objectives: The aim of the study was to evaluate PA in patients with BD and also to compare status of PA with healthy controls.

Methods: 67 patients (female=49, male=18) with BD and 66 healthy peers (female=43, male=23) were enrolled in the study. The subjects were recruited in a rheumatology clinic. They were diagnosed with BD by a rheumatologist based on the clinical diagnostic criteria. PA was evaluated with International Physical Activity Questionnaire-Short Form (IPAQ-SF) in all participants. Metabolic Equivalent (MET) values were calculated due to IPAQ-SF. In addition, the pain and fatigue status of patients with BD was asked.

Results: The mean age of the patients was 42.95±10.60 years. The mean disease duration was 14.14±9.13 years. The means of physical activity MET scores were 699.74±508.09 and 2006.75±1162.16 in patients with BD and healthy peers, respectively. It was found that the means of PA MET scores in BD was significantly decreased comparing with healthy peers ($p<0.001$). While 53.7% of patients with BD had low levels of PA and 46.3% had moderate levels of PA, 9.1% of healthy subjects had low level of PA, 47% of them had moderate levels of PA and 43.9% high levels of PA ($p<0.001$). 86.6% of patients with BD reported pain, 73.1% of them also reported fatigue.

Conclusion: This study is the first study to evaluate PA in patients with BD. The level of PA was significantly lower in patients with BD compared to their healthy peers. Decreased PA may be associated with pain and fatigue frequently seen in patients with BD. In future studies, it is recommended to investigate the factors affecting PA in patients with BD.

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REFERENCES:

[1] Uguz F, Dursun R, Kaya N, Cilli AS. Behçet hastalarında ruhsal belirtiler ve yaşam kalitesi. Anadolu Psikiyatri Dergisi 2006;7:133-139.

[2] Cingu AK, Onal S, Urgancioglu M, Tugal-Tutkun I. Comparison of presenting features and three-year disease course in Turkish patients with Behcet uveitis who presented in the early 1990s and the early 2000s. Ocul Immunol Inflamm 2012;20:423-8.

[3] Hernández-Hernández V, Ferraz-Amaro I, Díaz-González F. Influence of disease activity on the physical activity of rheumatoid arthritis patients. Rheumatology 2014;53:722–31.

[4] Swinnen TW, Scheers T, Lefevre J, et al. PA assessment in patients with axial spondyloarthritis compared to healthy controls: a technology-based approach. PLoS One 2014;9:e85309.

[5] de Groot IB, Bussmann JB, Stam HJ, et al. Actual everyday PA in patients with end-stage hip or knee osteoarthritis compared with healthy controls. Osteoarthritis Cartilage 2008;16:436–42.

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HPR PATIENTS' PERSPECTIVES, FUNCTIONING AND HEALTH (DESCRIPTIVE: QUALITATIVE OR QUANTITATIVE)

FRI0727-HPR PREDICTORS OF FUNCTIONAL CAPACITY AT 24 MONTHS FOLLOW-UP IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in childhood and it causes short and long-term disability. Periodic assessment of functional capacity is important to determine the presence or absence of physical disability.

Objectives: To identify predictive factors of absence of functional disability after 24 months follow-up in a cohort of children with JIA treated at a tertiary referral hospital.

Methods: Longitudinal, retrospective, analytical, and observational study. Patients who met the following criteria were included in the study between 2013 and 2016:1 to 16 years old, diagnosis of JIA according to the International League of Associations for Rheumatology (ILAR); recently initiated (3 months) care at our clinic, complete C-HAQ (Childhood Health Assessment Questionnaire) records throughout the follow-up period. Patients were treated according to current guidelines for pharmacological and physical therapy. Functional capacity was assessed according to the C-HAQ every 3 months. For the analysis, the C-HAQ scores were divided into 3 categories: 0 - 0.49 (absence of disability), 0.5 - 1.5 (mild to moderate disability), and 1.51 - 3 (severe disability). Univariate comparisons were made to determine the relationship between different variables with the dependent variable "absence of functional disability at 24 months of follow-up". Independent variables included: disease activity, functional capacity, and treatment-related outcome measures. Those with p values <0.05 were included in a multiple logistic regression analysis. The model was adjusted for basal functional capacity and inflammatory activity at 24 months. Items with a p value <0.05 were considered significant. Adjusted odds ratios (adjOR) and 95% confidence intervals (95% CI) are reported as a measure of association. The precision of the model was analyzed through the Area under the Curve (AUC).

Results: Of a total of 148 patients, 122 met the inclusion criteria. Median age: 7.4 years (1-16), 69 female (56.6%). Most patients had Polyarticular (44 patients, 36.1%) or Oligoarticular (33 patients, 27%) JIA. At the beginning of the study, 36 patients (29.5%) did not show functional disability; 70 (57.4%) exhibited mild-moderate disability and 16 (13.1%) severe disability. At 24 months, 73 patients (59.84%) had no disability, 37 (30.33%) moderate/mild disability, and 12 (9.84%) severe disability. In the multiple logistic regression model, performing regular physical therapy (PT) (adjOR 6.83 [95% CI 2.26 - 20.61], p = 0.001), starting PT within 12 months after diagnosis (adjOR 5.45 [95% CI 1.83 to 16.18], p = 0.002), baseline pain Visual Analogue Scale (pVAS, 0-10) less than 3 (adjOR 4.55 [95% CI 1.58 to 13.12], p = 0.005) and adherence to pharmacological treatment (adjOR 15.23 [95% CI 1.86 to 124.8], p = 0.011) were independent factors for not presenting functional disability at 24 months. The area under the model curve was 0.92 (95% CI 0.88 to 0.97).
Conclusion: The findings of this study reinforce the need of early and regular PT and medical treatment in children with JIA, in order to maintain or improve functional capacity over time.These results are not only statistically significant but clinically relevant since they reflect impact in functional skills in this population. Further studies are needed to confirm these outcomes in larger cohorts with longer follow – up.

REFERENCES:

[1] Magni-Manzoni S, Pistorio A. A longitudinal analysis of physical functional disability over the course of juvenile idiopathic arthritis Rheum Dis 2008; 67:1159–1164.i:10.1136/ard.2007.078121
[2] Ravelli A, Martini A. Early predictors of outcome in juvenile idiopathic arthritis. ClinExpRheumatol 2003;21(Suppl 31):S89–93.

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FRI0728-HPR PERCEPTIONS OF PHYSICAL ACTIVITY IN INDIVIDUALS WITH RA – A QUALITATIVE THEMATIC SYNTHESIS

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Background: The effects of physical activity (PA) in rheumatoid arthritis (RA) are well documented and PA is besides pharmacological interventions considered a cornerstone in the treatment. Despite this, many individuals with RA does not reach recommended levels of PA. To highlight aspects involved in supporting a positive PA behavior it is important to understand the patients' perceptions of the phenomenon. Several qualitative studies have been conducted throughout the years, describing perceptions on physical activity in RA.
Objectives: The aim of this study is to review and synthesize the qualitative literature on physical activity in rheumatoid arthritis.
Methods: A purposive search in electronic databases (MEDLINE, CINAHL and Pedro) using combinations of terms such as "qualitative methods, qualitative study, interviews, physical activity, exercise and rheumatoid arthritis", from inception to July 2018 was carried out. Title/abstract and full- text screening were conducted independently by 2 researchers. Further, back-tracking of reference list of retrieved articles was made, and contacts were taken with known experts in the field. Studies were eligible if they qualitatively explored perceptions of different aspects of PA in individuals with RA. Eligible articles were appraised using the McMaster Critical review form. All relevant data were extracted from eligible articles and analyzed inductively using thematic analysis.
Results: 11 primary studies met the inclusion criteria. Studies were conducted in Denmark, Ireland, New Zealand, Sweden, United Kingdom and the United States of America. The sample includes 170 individuals with rheumatoid arthritis (129 women, 41 men, aged 21-83).
Across the studies, preliminary themes were found: worries and fear (increasing symptoms, worsen the disease, safety), awareness of PA (knowledge, information, discussion), social support (competence, guidance, demands, joy), effects on health (retain independence, decrease symptoms, coping with the disease), body awareness (adaptation, pacing, listen to the body, self-efficacy) and determination (motivation, focus, goals, priorities, responsibility). A preliminary thematic map, interpreting the continuous interrelation between the themes and the disease itself was described.
Conclusion: It is important that the promotion of PA in individuals with RA is in line with individual challenges and resources, in order to enhance adoption and maintenance of PA behavior. In RA, the disease seems to pervade all aspects related to the individuals' perception of physical activity. Strategies to enhance this behavior should therefore include minimizing negative perceived consequences of physical activity by raising both cognitive and physical awareness. Another strategy could be focusing on finding proper social support either within health care or preferably outside of health care but with a sense of affinity. Finally, strengthening the individual's ability to use self-regulation strategies to overcome barriers should be emphasized.

REFERENCES:

[1] Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. BMC Medical Research Methodology. 2008;8:45. Doi: 10.1186/1471-2288-8-45
[2] Walsh D, Downe S. Meta-synthesis method for qualitative research: a literature review. Journal of Advanced Nursing. 2005;50(2):204-211.

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FRI0729-HPR LIVING EVERY-DAY LIFE IN THE SHADOW OF PAIN OR LIVE EVERY-DAY LIFE WITH THE PAIN IN THE SHADOW – A CONSTANT BALANCING

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Background: Approximately 10% of the population report chronic widespread pain (CWP), the condition is more common in women than in men. Long-term pain is a public health problem. For most women, the pain interferes with many aspects of every-day life and implies large consequences. Thus, knowledge about how to facilitate life for these women is important.
Objectives: To explore women's experiences of how CWP influence their daily life
Methods: The study has a latent qualitative content analysis design [1]. Individual interviews were conducted in 19 women 45-67 of age, who had reported CWP in a survey 2016. CWP was defined according to the 1990 ACR criteria for fibromyalgia. Pain that had lasted for more than three months, during the last 12 months, was considered chronic. A latent qualitative content analysis was used to analyze the main questions "Can you describe your experiences of living with CWP?" and "How do the CWP influence your life today?" The interviews were recorded, transcribed verbatim and coded into eight subcategories and three categories; represent the manifest content, and a latent theme exploring the interpreted content of women's experiences of how CWP influence their every-day life.
Results: The interviewed women expressed a life with CWP as "Living every-day life in the shadow of pain or live every-day life with the pain in the shadow" including three categories; the experience of alienation, limitations and plasticity. 1) The experiences of alienation appeared in the subcategories; suspicion and loneliness. Suspicion meant a feeling of not be taken seriously by healthcare and authorities and loneliness meant not being able to participate in social contexts. 2) The experiences of limitations in daily life includes the subcategories; barriers, stress, and dependence of other people. Barriers meant that fatigue limits the activities in every-day life, stress that constitutes limitations in life and dependence on other people' support. 3) The experiences of plasticity referred to the subcategories resignation, adjustment and resistance. Resignation meant refraining from activities that could affect the pain, such as gardening, walking and dancing. Adjustment were manifested by making the best of the situation, and resistance meant to resist letting the pain set the terms, to give the pain a fight.
Conclusion: Women with CWP have to deal with their physical, mental, social and spiritual environment in every-day life. They express a constant balancing in their life between mastering the pain in order to continue living as normal, and allowing the pain to set the terms, i.e. living every-day life in the shadow of pain or live every-day life with the pain in the shadow. Healthcare professionals may consider supporting the patients in finding their individual counterweight to manage life in order to reach better treatment outcome.

REFERENCES:
[1] Graneheim UH, Lindgren BM and Lundman B. Methodological challenges in qualitative content analysis: A discussion paper. Nurse education today. 2017; 56: 29-34.

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FRI0730-HPR **CAROTID ATHEROSCLEROSIS AND CARDIOVASCULAR RISK FACTORS IN FEMALES WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: Pts with systemic lupus erythematosus (SLE) have an increased risk for cardiovascular diseases (CVD) that cannot be explained by traditional risk factors only. Its relevant to search novel cardiovascular risk markers in those pts.
Objectives: We aimed to evaluate carotid atherosclerosis presence in females with SLE and its relationship with traditional and nontraditional cardiovascular risk factors.
Methods: 52 females with low-activity SLE (the median age – 48.2 [41.8; 52.9] years, the median duration of SLE 89.4 [68.9; 101.5] month) without verificated coronary artery disease were enrolled. Control group included 30 pts without SLE compared by risk factors profile. The cardiovascular risk was calculated using SCORE. The total cholesterol (TC), lipoproteins, triglycerides (TG) were measured in the blood. Carotid ultrasound, endothelial-dependent flow mediated vasodilatation (EDVD) by D. Celermajer method were performed. In all pts was calculated body mass index (BMI) and measured blood pressure (BP). All pts received steroid therapy.
Results: High levels of TC, LDL and TG were in 55.8%, 61.5% and 25% of pts with SLE (the median levels 5.9 [5.2; 6.4] mmol/l, 4.1 [3.7; 4.6] mmol/l and 1.8 [1.3; 2.4] mmol/l respectively). The obesity and hypertension were estimated in 51.9% and 63.5% respectively (median BMI – 31.6 [28.4; 33.2] kg/m^2, median systolic BP – 154,2 [138.4; 162.3] mm Hg, median diastolic BP – 90.2 [82.4; 93.7] mm Hg). EDVD was impaired in 32.6% pts with SLE and 16.7% control pts ($p<0.05$). Carotid atherosclerosis was established in 41 (78.8%) pts with SLE and 48 (54%) control group pts ($p<0.05$). The majority of pts with SLE have stable carotid atherosclerotic plaques - 32 (61.5%), unstable plaques - 6 (11.5%) pts, in control group – 10 (33.3%) and 2 (6.7%) pts respectively. In the same time the median cardiovascular level matched by SCORE was 2.1 [1.5; 2.9]% in females with SLE, in control group - 1.8 [1.3; 2.5]% ($p>0.05$). The presence of carotid atherosclerotic plaques in females with low-activity SLE was associated with endothelial dysfunction (OR=2.5, p=0.002), obesity (OR=1.5, p=0.004), duration of steroid therapy (OR=2.8, p=0.0005).
Conclusion: Females with low-activity SLE and moderate cardiovascular risk level are characterized by high frequency of carotid atherosclerosis. The carotid ultrasound may be useful additional tool for the evaluating of cardiovascular risk in these patients.
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Adaptive immunity (T cells and B cells) in rheumatic diseases

SAT0001 FOSL-2 IS A REPRESSOR OF FOXP3 EXPRESSION DURING TREG DEVELOPMENT AND CONTROLS AUTOIMMUNITY

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Background: Fos like 2 (Fosl-2) is a transcription factor belonging to the AP-1 transcription complex. We have recently described a Fosl-2 transgenic (tg) mouse model which develops a multi-organ inflammatory and autoimmune phenotype. In these mice, we have characterized a decrease in regulatory T cells (Tregs), which preceded the activation of T cells and the development of inflammation.
Objectives: To analyze how Fosl-2 reduces the Treg population and triggers autoimmunity in Fosl-2 tg mice.
Methods: We used previously generated Fosl-2 tg overexpressing and Fosl-2 T cell specific knock out (Fosl-2 ko) mice. For mixed bone marrow transfer experiments, lethally irradiated recipients received a one to one mix of Fosl-2 tg (CD45.2) and wt (CD45.1) bone marrow to create Fosl-2 tg-wt chimera. We addressed the contribution of Tregs to the inflammatory phenotype by co-transferring Fosl-2 tg CD4 T cells and wt Tregs to $Rag2^{-/-}$ recipients. Treg and T cell populations were analyzed by flow cytometry and inflammation was addressed by CD45 staining on paraffin-embedded sections. RNA-sequencing was used to compare wt, Fosl-2 tg and Fosl-2 ko CD4 T cells after 24 hours of stimulation with anti-CD3 (2µg/ml) and anti-CD28 (2µg/ml).
Results: We first addressed whether Fosl-2 affected Tregs in a cell intrinsic way using mixed bone marrow experiments. In these animals, the CD45.2 Fosl-2 tg CD4 T cells showed a much lower proportion of Tregs compared to the CD45.1 wt population, both in the spleen (0.73%±0.15 vs 31.6%±3.6, P=0.062) and thymus (1.3%±1.04 vs 3.23%±0.78, P=0.001). This demonstrates that Fosl-2 overexpression represses Treg development in a cell intrinsic way.
In T cell transfer experiments, $Rag2^{-/-}$ mice receiving 10^6 Fosl-2 tg CD4 cells developed lung inflammation 5 weeks after transfer, confirming that T cells are inducers of inflammation in Fosl-2 tg mice. Moreover, co-transfer of either $3*10^5$ or 10^6 wt Treg cells resulted in a dose dependent reduction of inflammation. These data indicated that the decrease in the Treg population in Fosl-2 tg mice is responsible for the induction of inflammation.
We then analysed Fosl-2 transcriptional targets in T cells by RNA-seq. Using a fold change > 1.5 and False Discovery Rate (FDR) of 0.05, we identified 191 differentially expressed genes in both Fosl-2 tg and Fosl-2 ko cells compared to wt. Interestingly, one of the top target genes of Fosl-2 was FoxP3. This unbiased approach thus revealed that FoxP3 expression is repressed by Fosl-2, with a 6.5 fold reduction in Fosl-2 tg cells and a 2.5 fold increase in Fosl-2 ko cells. This effect was confirmed on the protein level with a reduction in FoxP3 induction in Fosl-2 tg cells treated with TGFβ. The repression of Treg development observed in Fosl-2 tg mice could thus be explained by a direct transcriptional control of FoxP3 expression. Additionally, we found that Fosl-2 repressed a set of genes important for Tregs and other T helper cells. This included Nr4a2, a transcription factor involved in Treg development, IRF8 and Eomes, two genes involved in the polarization of Th1 and Th17 cells, or Ccl1 a chemokine important for Treg homeostasis.
Conclusion: Fosl-2 is involved in the control of FoxP3 expression in T cells. Through this, overexpression of Fosl-2 represses Treg development and induces a Treg dependent autoimmune phenotype in mice. This mechanism could thus be involved in the pathogenesis of autoimmune diseases and might represent a therapeutic target to modulate the Treg population.
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SAT0002 DIFFERENTIAL RECONSTITUTION OF B-CELL SUBSETS IN SYSTEMIC SCLEROSIS PATIENTS AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Autologous hematopoietic stem cell transplantation (AHSCT) is nowadays a clinical reality as an effective and safe approach to treat systemic sclerosis patients' refractory to conventional therapy using immune suppressive drugs, although its immune mechanisms are still not completely understood[1,2,3].
Objectives: To evaluate the reconstitution of B-cell subsets in SSc patients following AHSCT.
Methods: Peripheral blood samples were harvested from twenty-four SSc patients before transplantation and at 30, 60, 120, 180 and 360 days post-AHSCT. The immunophenotyping, regulatory B-cell IL-10 production and suppressive assays were assessed by flow cytometry.
Results: Compared to baseline, naïve B-cells ($CD19+CD27^-IgD^-$) significantly decreased in frequency and absolute counts at 30 days post-AHSCT, followed by an increase at 360 days. There was a transient decrease of non-class-switched memory-B-cell ($CD19^+CD27^+IgD^+$) frequency at 30 days, followed by an increase at 360 days. In addition, mature class-switched memory-B-cells ($CD19^+CD27^+IgD^-$) and plasma cell ($CD19^+CD27^{high}IgD^-$) decreased ($P<0.05$) respectively at 60 and 360 days post-AHSCT, while the frequency of double-negative B-cell ($CD19+CD27^-IgD^-$) increased at 30 days post-AHSCT. The subset $CD20^+CD43^+CD27^+CD69^-$ (human B1-cell) showed higher percentage at 30 days, followed by a decrease at 360 days. The regulatory B cell $CD19^+CD24^{hi}CD38^{hi}$ (transitional B-cell subset) significantly increased at 360 days, while $CD19^+CD24^{hi}CD27^+$ Breg (B10 subset) decrease transiently from 30 to 180 days post-AHSCT. The frequency of $CD19^+PD1^+$ B-cells transiently increased at 30 days. The frequency of IL-10-producing regulatory B-cells $CD19+CD24^{hi}CD38^{hi}$ and $CD19+CD24^{hi}CD27^+$ increased post-transplantation. After AHSCT the regulatory B-cell $CD19+CD24^{hi}CD38^{hi}$ recover their ability to suppress cytokine production by Th1 CD4+ T-cell in vitro.
Conclusion: Following transplantation, SSc patients displayed increased naive-B-cells values and decreased memory B-cells, which might contribute to self-tolerance reestablishment, disease remission and clinical improvement on these patients. SSc patients showed increases of Breg numbers after AHSCT as well as an increase of IL-10 production, suggesting improvements in immunoregulatory mechanisms.

REFERENCES

[1] Burt, et al. Lancet 2013:381(9872):1116–24.
[2] van Laar, et al. JAMA 2014;311(24):2490–8.
[3] Sullivan, et al. N Engl J Med 2018;378:35–47.

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SAT0003 PIM1 REGULATES CD4+ T CELL EFFECTOR FUNCTION IN EARLY RHEUMATOID ARTHRITIS AND HAS POTENTIAL FOR USE AS A NOVEL, MEASURABLE THERAPEUTIC TARGET

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Background: We previously showed PIM1, among other STAT3-target genes, to be strikingly upregulated in circulating CD4+ T cells of treatment-naïve 'early' rheumatoid arthritis (eRA) patients[1,2]. PIM1 has a recognised role in T cell development, has been implicated in the pathogenesis of autoimmunity[3], and is the target of specific inhibitors in clinical development in oncology; for example PIM1 was recently identified as a promising target in triple-negative breast tumours[4].
Objectives: We sought to understand the relevance of dysregulated PIM1 gene transcription for T-cell pathobiology during disease initiation and to determine the effects of its inhibition on T cell function. We hypothesised that, amongst a readily-identifiable, high PIM1 expressing subgroup of eRA patients, PIM1 overexpression in CD4+ T cells is a targetable early event in pathogenesis that lies downstream of STAT3-mediated IL-6 signalling.
Methods: Peripheral blood was obtained from consenting treatment-naïve arthritis patients or healthy donors and highly pure CD4+ T cells were isolated. PIM1 knock-down (SMARTpool siRNA, Dharmacon) or protein inhibition (small molecule inhibitors; PIM1-selective TCS-PIM-1 1, Tocris and panPIM AZD1208) was undertaken. Flow cytometric analysis was then used to assess activation and proliferation following CD3/CD28-mediated stimulation.
Results: In eRA, *ex vivo* CD4+ T cells exhibited an activated, hyper-proliferative phenotype compared with those isolated from healthy donors. Significantly higher PIM1 mRNA expression in CD4+ T cells was seen using PrimeFlow (flow cytometry) compared to that of other inflammatory arthritidies. Both PIM1 knock-down, PIM1-specific and panPIM inhibition decreased the activation and proliferation of stimulated eRA (Figure 1A) and healthy donor CD4+ T cells. Moreover, in eRA, PIM1 and panPIM inhibition increased FoxP3 expression (Figure 1B) and increased the proportion of regulatory T cells (Figure 1C).

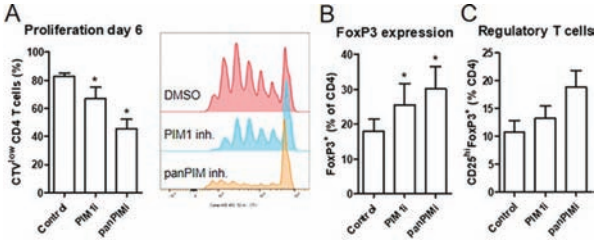


Figure 1. Early RA CD4+ T cell (A) proliferation is significantly decreased by either a PIM1-selective or a panPIM small molecule inhibitor, whereas (B) FoxP3 expression and (C) the proportion of regulatory T cells is increased.

Conclusion: Taken together, these data implicate PIM1 as prominent among genes whose induction may "pre-programme" CD4+ T cells to function aberrantly in disease. Conceivably, targeting PIM1 may prove an attractive approach to regulating aberrant CD4+ T cell effector function in an identifiable sub-population of early RA patients that exhibit high CD4+ T cell PIM1 expression in their peripheral blood.

REFERENCES

[1] Pratt AG et al, Ann Rheum Dis 2012; 71(8) 1374-81
[2] Anderson AE et al, Rheumatology 2018 (in press)
[3] Li Z, et al. J Biol Chem 2014; 289(39):26872-81
[4] Horiuchi D, et al. Nature Medicine 22(11):1321-9

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SAT0004 EVALUATION OF AUTOPHAGY IN INFILTRATING AND CIRCULATING LYMPHOCYTES FROM PATIENTS WITH SJOGREN'S SYNDROME

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Background: Autophagy is a lysosome mediated catabolic process that promotes cell survival during stress conditions. Aberrant regulation of autophagy is involved in the pathogenesis of a widening spectrum of autoimmune disorders: in particular, activation of autophagy pathway is implicated in aberrant survival of activated T cells. We recently demonstrated that autophagy is up-regulated in CD4+ T lymphocytes from patients with Sjogren's Syndrome (SS) both in peripheral blood and tissue. Moreover, aberrant autophagy correlates with systemic disease activity. Little is known on the role of autophagy in B cells homeostasis in SS.
Objectives: To investigate the activation of the autophagy pathway in lymphocytes infiltrating salivary gland in SS and peripheral blood from patients with SS.
Methods: Frozen SS minor salivary glands (MSG) from 20 patients were sectioned and evaluated with immunohistochemistry (IHC) by staining for CD3+, CD20+, and CD21+. MSG sections, sequential to IHC, were stained by Cresyl Violet and microdissected (Laser Capture Microdissection) in order to isolate and collect small infiltrates, large CD21- infiltrates, and large CD21+ infiltrates (GC-like structures). Microdissected GC from frozen human tonsils were used as control. The expression of autophagy genes Atg5 and MAP1LC3II (expressed as 2^deltaCT normalized to GADPH) was determined by qPCR on microdissected tissue.
For studies on peripheral blood, 19 SS patients and 11 healthy controls were enrolled, and autophagy, expressed as the ratio between Mean Fluorescence Intensity and the isotopic control (rMFI), was evaluated by Cyto-ID® Autophagy detection kit in T lymphocytes (CD4+ and CD8+) and B lymphocytes (CD19+) using a FACSCalibur cytometer.
Results: Expression of the autophagy genes Atg5 and MAP1LC3 was significantly higher in the GCs from SS salivary glands compared to control tonsils ($p<0.0001$ and $p=0.0013$, respectively). In the salivary glands of SS patients, progressively higher expression levels of both Atg5 and MAP1LC3 mirrored the organization and severity of the inflammatory infiltrates (small vs. large CD21+ infiltrates $p=0.0005$ and $p<0.0001$ respectively).
Immunophenotyping studies revealed activation of the autophagy pathway in both circulating CD19+ and CD4+ lymphocytes from SS ($p=0.04$ and $p=0.03$ compared to HC); conversely, no pathway activation was detected in CD8+ cells. Of note, in patients with SS activation of autophagy was most marked in circulating CD19+ B cells compared the other subsets [(CD19+ vs CD4+ ($p<0.0001$); CD19+ vs CD8+ ($p= 0.001$)].
Conclusion: Our findings revealed that the autophagy pathway is aberrantly activated in lymphocytes infiltrating salivary glands of SS patients. Of note, progressively higher expression levels of autophagy genes mirrored the severity and extension of inflammatory infiltrates. Immunophenotyping studies revealed that activation of autophagy is preeminent in B cells. Thus, activation of autophagy emerges as a feature of both infiltrating and circulating SS lymphocytes, and as mechanism possibly implicated in the activation and survival o f autoreactive cells.
Disclosure of Interests: Serena Colafrancesco: None declared, Antonina Minniti: None declared, Roberta Priori: None declared, Marta Vomero: None declared, cristiana barbati: None declared, Francesca Arienzo: None

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SAT0005 DETECTION OF HIGHLY EXPANDED T CELL CLONES IN THE PERIPHERAL BLOOD OF AT RISK INDIVIDUALS FOR RHEUMATOID ARTHRITIS BEFORE THE CLINICAL ONSET OF THE DISEASE

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Background: Rheumatoid arthritis (RA) is an autoimmune disease with unknown etiopathogenesis. Systemic autoimmunity precedes clinical disease onset, and current evidence suggests that the immune onset of RA takes place outside of the joints several years before clinical manifestations. Expanded T cell clones can be found in the synovial tissue of established RA patients. The mechanisms by which systemic immune abnormalities progress to joint-specific autoimmunity are not yet understood.

Objectives: To examine if expanded T cell clone signatures can be detected in the peripheral blood before the development of clinical RA.

Methods: Next-generation sequencing of the T Cell Receptor β (TCRβ) CDR3 repertoire was performed on genomic DNA isolated from blood samples of individuals genetically at risk for RA, namely first-degree relatives of RA patients (RA-FDR) at different pre-clinical phases of disease development (SCREEN-RA cohort), and of matched RA patients used as a control group (SCQM cohort). All individuals were matched for age and sex, and categorized into four groups (n=20/group): **Group 1**: "healthy" asymptomatic RA-FDR without autoantibodies or symptoms associated with possible RA. **Group 2:** Asymptomatic RA-FDR with evidence of 'systemic autoimmunity associated with RA' defined by high levels of anti-citrullinated peptide antibodies (ACPA; 3x≥ ULN). **Group 3:** RA-FDR having presented undifferentiated arthritis (n=8) or having developed classifiable RA after inclusion (n=12). **Group 4:** patients with established RA of less than 3 years duration. T cell clones were identified by their unique TCRβ CDR3 sequence. Clones with a frequency over 0.5% were considered to be highly expanded clones (HEC). Both absolute number and frequency of productive T cell clones was compared between the 4 groups using mixed effect regression models to account for matching.

Results: As expected, the large majority of clones in the peripheral blood were detected at very low frequency (<0.1%) in all groups (Figure 1A). Interestingly, expanded clones (>0.1% of total TCR analysed) tended to occur more frequently in later preclinical phases and established disease. A significant difference among groups was observed for highly expanded clones (HEC) (p=0.001). Specifically, the absolute number of HEC was significantly higher in RA patients (group 4; mean 4.65, p=0.003) and tended to be higher in symptomatic RA-FDR (group 3; mean 3.4, p=0.07) compared to "healthy" RA-FDR (group 1; mean 1.55) (Figure 1B). A trend towards a higher frequency of the top 50 expanded clones was also observed in symptomatic RA-FDR (group 3; mean 0.17%) compared to "healthy" RA-FDR (group 1; mean 0.11%). At risk individuals defined by the presence of high ACPA levels (group 2) did not differ from "healthy" RA-FDR in terms of absolute number and frequency of clones.

Conclusion: For the first time, highly expanded T cell clones were detected in the peripheral blood of at risk individuals before the clinical onset of RA, in particular in the later pre-clinical phases of RA development. Tracking these dominant T cell clones in longitudinal analyses and elucidating their role might help to better understand the earliest pathogenic events in RA.

REFERENCE

[1] Catrina AI et al. Nat Rev Rheumatol. 2017;13(2):79-86; Klarenbeek PL et al. Ann Rheum Dis. 2012;71(6):1088-93

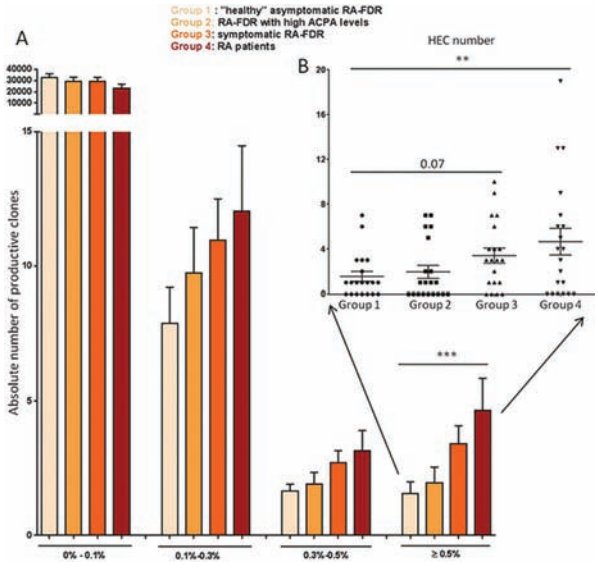


Figure 1. Absolute number of productive TCR clones by clonal size. (A) Bars show mean and standard error of the mean (mixed effect regression model). (B) Each dot represents the HEC number observed for 1 individual (mixed effect regression model).

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SAT0006 T-CELL IMMUNOGLOBULIN AND MUCIN DOMAIN 3 (TIM-3) IS INCREASED IN ACTIVE RHEUMATOID ARTHRITIS AND ASSOCIATED WITH CLINICAL DISEASE ACTIVITY AND RADIOGRAPHIC PROGRESSION

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Background: Co-inhibitory receptors are important for the regulation of inflammation in autoimmune diseases. Among these, T-cell Immunoglobulin and mucin domain-3 (Tim-3) has recently gained attention, as it is expressed on exhausted T cells co-expressing PD-1 (1).

Objectives: To investigate Tim-3's role in rheumatoid arthritis (RA).

Methods: Early RA (eRA) patients were randomized to conventional methotrexate (MTX) treatment + placebo or MTX + adalimumab (ADA) (2). Plasma were analysed by ELISA at baseline (n=98) and after 3 and 12 months of treatment. Clinical follow up including 28-joint Disease Activity Score with CRP (DAS28CRP) and Total Sharp Score (TSS) were available. Intrasubject differences in sTim-3 between baseline and 3 months were assessed by parametric paired t tests and compared with plasma from HV (n=44) by parametric unpaired t tests. Spearman correlation and Mann-Whitney test were used to investigate relations between sTim-3 and clinical follow up. From chronic RA (cRA) patients (n=17) plasma and synovial fluid were analysed by ELISA and peripheral blood mononuclear cells (PBMC) and synovial fluid mononuclear cells (SFMC)

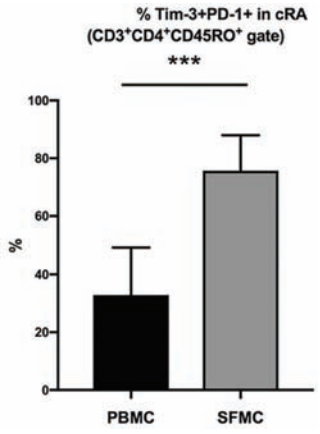
(n=8) were analysed by flow cytometry. Intrasubject differences were assessed by paired parametric t tests, and comparison with PBMC from HV (n=6) by unpaired parametric t test. Parametric data are reported as mean differences (MD) [95%CI]. P values < 0.05 were considered significant.

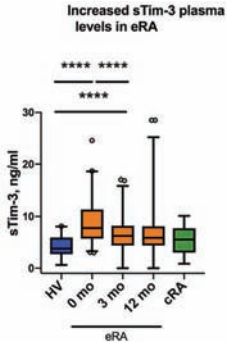
Results: Among memory prone T cells ($CD3^+CD4^+CD45RO^+$) in SFMC, the percentage of $Tim\text{-}3^+$ cells were increased compared with similar gated PBMC from patients (MD 17.4%, [10.7;24.1], p<0.005) and HV (MD 12.9%, [4.1;21.8], p=0.007). In the joint, more of these $Tim\text{-}3^+$ cells co-expressed PD-1 compared with similar gated PBMC (MD 42.8%, [27.8;57.9], p<0.005) (Figure 1). On average, sTim-3 plasma levels were higher in eRA compared with HV (MD 4.6 ng/ml, [3.3;5.9], p<0.005) (Figure 2). In eRA, baseline sTim-3 levels correlated with DAS28CRP (rho=0.28, p=0.005). eRA patients with TSS progression within 24 months of treatment decreased more in plasma sTim-3 during 3 months of treatment compared with patients without TSS progression ($median^{+progression}$: -1.4 ng/ml, $median^{-progression}$: -0.5 ng/ml (U=849.5), p=0.048). The decrease in plasma sTim-3 was not influenced by treatment ($median^{MTX+Placebo}$:-0.9 ng/ml, $median^{MTX+ADA}$: -1.2 ng/ml (U=1015), p=0.4). In SF, sTim-3 levels were increased compared with plasma (MD 37.4 ng/ml, [26.3;48.4], p<0.0001).

Conclusion: Tim-3 expression is upregulated in memory prone T cells in RA joints and the majority co-express PD-1. Levels of sTim-3 are increased in SF. In eRA, baseline sTim-3 plasma levels are elevated and correlate with DAS28CRP. Decrease of sTim-3 during treatment associates with future radiographic progression. We suggest, that Tim-3 expression and sTim-3 plasma and SF levels reflect ongoing immune response, thus immune regulation in RA. These data indicate that maintenance of sTim-3 plasma levels during treatment is favourable, consistent with Tim-3 being a co-inhibitory receptor.

REFERENCE

[1] Ana C. et al. Immunity 2016;44:989-1004**,** 2 Hørslev-Petersen K, et al. Ann Rheum Dis 2014;73:654-661.





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SAT0007

THE SUPPRESSIVE ACTIVITY OF PERIPHERAL BLOOD TREG REPRESENTS IMMUNOLOGICAL REMISSION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) patients with sustained remission may have relapsed disease after DMARDs tapering. Many predictors such as multibiomarker disease activity, ultrasound and MRI for detecting subclinical synovitis have some role to be prognostic tools. However, their values are limit.[1, 2] The number of Foxp3+ Treg may indicate immunological status in some situation, but is controversial.[3] The Treg function may represent the different stages of RA

Objectives: This study aimed to determine the suppressive activity of Foxp3+ Treg from peripheral blood (PB) of RA patients with clinical remission compare with active RA.

Methods: In this cross-sectional study, blood samples were collected from RA patients with sustained clinical remission for at least 6 months and from active RA patients. The Treg and autologous conventional T cell were isolated from PB of the patients by using FACS sorting. Then the isolated cells were evaluated suppressive activity by co-culture suppression assay.

Results: The Treg of patients with sustained clinical remission (for more than six months) showed higher suppressive activity compared to Treg from active RA patients [57.24% versus 23.67%, p < 0.0001, 95% CI; 20.88-44.01(showed in figure 1A)]. Moreover, the suppressive activity correlated with the degree of disease activity. When we analyzed in patients with DAS28 score < 2.6 (remission), >2.6-3.2 (low DAS), >3.2-5.1 (moderate DAS) and >5.1 (high DAS), the suppressive activity of Treg dependently decreased to the degree of disease activity [57.97%, 39.15%, 23.01%, and 17.07%, respectively (showed in figure 1B)].

Conclusion: This suppressive activity of Treg may indicate immunological remission in RA patients with clinical remission, especially in patients who candidate for DMARDs reduction.

REFERENCES

[1] Schett G, Emery P, Tanaka Y, et al. Tapering biologic and conventional DMARD therapy in rheumatoid arthritis: current evidence and future directions. Annals of the Rheumatic Diseases. 2016;75(8):1428

[2] Hirata S, Dirven L, Shen Y, et al. A multi-biomarker score measures rheumatoid arthritis disease activity in the BeSt study. Rheumatology. 2013;52 (7):1202-1207.

[3] Kleinewietfeld M, Hafler DA. The plasticity of human Treg and Th17 cells and its role in autoimmunity. Seminars in Immunology. 2013;25(4):305-12.

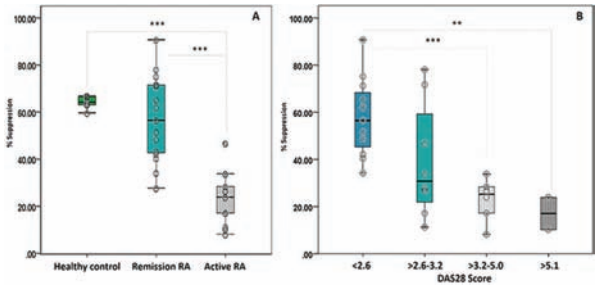


Figure 1. Suppressive activity of Treg in different stages of RA patients. The suppressive activity of Treg was measured by 3 days co-culture suppression assay. (A) Suppressive activity of Treg in healthy control (n=7), clinical remission (n=14) and active RA (n=13). (B) Suppressive activity of Treg in patients with various DAS28 score: DAS28 <2.6 (remission),

>2.6-3.2 (low DAS), >3.2-5.0 (moderate DAS), and >5.1 (high DAS), respectively. ***p*<0.01, ****p*<0.0001 (Independent t-test and Kruskal Wallis test)

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SAT0008 IL-23 DRIVES PATHOGENIC TH17 CELLS THROUGH EPIGENETIC REGULATION BY STAT3 IN SLE PATIENTS

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by loss of self-tolerance and by broad immune dysregulation, which result in overproduction of autoantibody and cause severe inflammation in various organs(1). Although amplified mature Th17 cells are thought to be vital role in the development and progression of SLE, mechanism underlying their pathogenicity remain widely elusive in human(2).
Objectives: To elucidate the mechanism of pathogenic Th17 cells expansion, we probe the phenotype of Th17 cells in lupus patients and underlying epigenetic modification mediated by cytokine-induced signal transducer and activators of transcription (STAT) family factors in vitro.
Methods: Human naive CD4+ T cells were cultured by Th17 polarizing condition (TGF-β, IL-6, and IL-1β) for 5 days in vitro. To examine the role of specific cytokine in maturation of Th17 cells, we added various cytokines including IL-23 at the later time point (72hr). Expression of characteristic markers of pathogenic Th17 cell and STATs phosphorylation (p-STATs) were analyzed by flow cytometry and qPCR. The effect of baricitinib which is JAK1/JAK2 inhibitor on maturation of Th17 cell was investigated. Histone modifications were assessed by chromatin immunoprecipitation(ChIP)-PCR. To define the signals mediated by cytokine required for expansion of Th17 cell in SLE, Th17 phenotype and pSTATs were analyzed from blood samples of lupus patients by multi-color flow cytometry.
Results: In vitro, re-stimulation of Th17 cells with IL-23 markedly induced the characteristic markers of pathogenic Th17 cells such as RORγt and IL-17. IL-23 overwhelmingly activates the p-STAT3, not p-STAT4 for development of mature Th17 cells. IL-23-induced p-STAT3 was inhibited by baricitinib. In addition, proliferation of Th17 cells was suppressed by baricitinib in concentrate dependent manner. The loci of RORγt at STAT binding sites were marked by bivalent histone modifications. After IL-23 stimulation, STAT3 exclusively bound on RORγt gene loci supplemented by activating H3K4me3 and repressing H3K27me3 modifications. In memory Th17 cells, high proportion of IL-23R expression and STAT3/4 activation were identified from SLE patients compare with healthy individuals. Moreover, p-STAT3 was hypersensitively activated by IL-23 stimulation in memory Th17 cell only from lupus patients but not from healthy controls.
Conclusion: This study proves that IL-23 serves as a pivotal factor that drives expansion of pathogenic Th17 cells. IL-23-mediated STAT3 alter histone modification, resulting in inflammatory function of pathogenic Th17 cell that are characteristically expanded in patients with SLE. These findings could be one of the underlying mechanisms of pathogenesis of SLE and helpful evidence toward novel therapeutic targets for SLE.

REFERENCE

[1] Tsokos GC. Systemic lupus erythematosus. N Engl J Med. 2011;365 (22):2110-21. (2) Ma, J., et al., The imbalance between regulatory and IL-17-secreting CD4+ T cells in lupus patients. Clinical rheumatology, 2010. 29(11): p. 1251-1258.

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SAT0009 THE EFFECT OF FCGR3A POLYMORPHISM ON THE INITIAL DEPTH OF B-CELL DEPLETION BY RITUXIMAB, FUNCTIONAL NK-CELL MEDIATED KILLING AND CLINICAL RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Antibody-dependent cellular-mediated cytotoxicity (ADCC) is an important effector mechanism that contributes to the depletion of therapeutic antibody-opsonised cells *in vivo*. Rituximab (RTX) is an anti-CD20 antibody with a native IgG1 Fc, which crosslinks Fc receptors (FcγRs) expressed on immune effector cells. NK cells, which express FcγRIIIa, are believed to play an important role with less well-characterised contribution from monocytes/macrophages and neutrophils. A genetic variant in *FCGR3A* (158V) with an increased affinity for IgG1 has been reported to correlate with clinical response to RTX in RA[1]. Data in SLE are limited as the *FCGR* genetic locus is characterised by structural variation making genotyping challenging.
Objectives: To assess the effect of *FCGR3A*-F158V polymorphism on (i) the initial depth of B-cell depletion by RTX; (ii) its functional effect on NK cell-mediated killing (iii) clinical response and (iv) 10-year RTX retention for the treatment of SLE.
Methods: A prospective longitudinal study was conducted in RTX-treated SLE patients in Leeds. B-cells were measured at baseline and 6 weeks using highly sensitive flow cytometry. Complete depletion was defined as total B-cell count<0.0001 x 10^9/L. A major clinical response (MCR) was defined as improvement of all active BILAG-2004 domains to grade C/better and no A/B flare at 6 months. We measured qualitative polymorphism for *FCGR3A* using a multiplex ligation-dependent probe amplification as previously described[2]. Median expression of FcγRIIIa on NK cells (CD3-CD56+CD16+) and NK cell degranulation (CD107a) in the presence of RTX-coated Raji cells (B-lineage cell line) were assessed using flow cytometry.
Results: 85 SLE patients with at least 2 x BILAG B were studied [Female: 82(96%); mean age (SD): 40(14) years; 60/85(71%) on concomitant DMARDs; ANA positive: 100%]. In cycle 1 RTX, 64/85(75%) achieved BILAG response [major=36%; partial=39%]. Both complete depletion and MCR were associated with carriage of the *FCGR3A*-158V allele (158FV or 158VV), OR 2.73 (95% CI 1.13-6.58) and 3.06 (95% CI 1.19-7.58) vs 158FF, respectively.
Patients who had complete B-cell depletion post-RTX had higher level of FcγRIIIa on NK cells vs incomplete depletion; p=0.006. Comparing patients with *FCGR3A*-158V allele carriage vs FF genotype, there was a trend to higher expression of CD3-CD56+CD16+ in the former p=0.073. Moreover, degranulation as defined by ratio between%CD107a+NK cell in the presence of Raji cells + RTX and%CD107a+NK cell in Raji cells only, was higher in the V allele carriers vs FF genotype; p=0.024.
Over 10-year follow-up, 27/85 (31.8%) had stopped RTX [primary inefficacy=7; secondary inefficacy=8; HACA=10; death=2]. *FCGR3A*-158FF genotype was associated with increased risk of RTX discontinuation; OR 2.36 (95% CI 1.08–5.18) after adjusting for age and DMARDs.
Conclusion: An ADCC-enhancing FcγRIIIa variant was associated with initial complete B-cell depletion and MCR in RTX-treated SLE patients. This was supported by functional data on NK cell-mediated cytotoxicity and 10 year outcomes. These results elucidate one mechanism of resistance to rituximab in SLE and may guide development of more effective B-cell targeted strategies. With further validation, this polymorphism may be used to stratify SLE patients for therapy.

REFERENCES

[1] Ruyssen-Witrand A et al. ARD 2012
[2] Nagelkerke S et al. Genes and Immunity 2015

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SAT0010 FUNCTIONAL BIOMARKER DEVELOPMENT FOR CELL-BASED THERAPY IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is an autoimmune disease in which early treatment prevents joint damage. Autoantibodies such as rheumatoid factors (RF) and anti-citrullinated peptide antibodies (APCA) define a subset of RA patients at the highest risk for damage. Reduction of RA disease activity is associated with improvement in function(s) of regulatory T cells (Treg) and attenuated responses of pro-inflammatory T effector cells (Teff). Human Mesenchymal Stem Cells (hMSC) isolated from bone marrow and culture-expanded have strong immunomodulatory properties; we hypothesize that therapeutic use of hMSCs may skew the immune system to resemble its pre-RA state. Lack of available biologic correlates measured early-on that indicate response to treatment limits efficacy assessment of cell-based therapy. Use of clinical response criterion requires large numbers of patients and may be impractical in early stage clinical trials. This work was performed in anticipation of conducting a Phase I safety trial of cell-based therapy in early RA.
Objectives: We set out to develop functional assay(s) as biomarkers of response that would indicate early-on that hMSC were or were not modulating immune function in a manner that could potentially predict potency and efficacy in RA patients.
Methods: Sero-positive female patients with active early RA (RAPID 3 avg 5.7/10 (high severity)) and healthy donor age and sex-matched controls were enrolled. Second passage bone marrow hMSCs were obtained from healthy donors < 30 y.o. (Case Comprehensive Cancer Center Hematopoietic Biorepository and Cellular Therapy Core). Peripheral blood CD4+ T cells were stimulated by cross-linking CD2/CD3/CD28 for 5 days. CD4+ T-cell proliferation rates were measured, and suppression indices calculated by comparing proliferation indices of CD4+ T-cells cultured with and without hMSC-conditioned medium.
Results: hMSC-related suppression 32.2 ±7.8 (mean +/- SE) percent in RA CD4+ T-cells compared to 45.7± 8.9 percent for healthy donors CD4 + T-cells. We demonstrated that soluble products from hMSCs can inhibit proliferative responses of CD4+ T cells from patients with active RA though the studies were not powered to detect differences between RA and healthy donors. With limited number of early RA patients, correlation between level of MSC-related suppression and antibody status were not possible. That being said, the data trend appears promising.
Conclusion: Our ex vivo experiments demonstrated that MSCs may be suppressive in RA as well as in healthy donors. To our knowledge, this study is the first demonstration of the potential for using ex vivo suppression assays to predict response to cell-based therapy in early RA. Such assays might be performed to predict the efficacy of selected hMSCs to treat RA.
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SAT0011 TRANSCRIPTOMICS UNVEILS UNIQUE BIOLOGICAL PROFILE OF TERTIARY LYMPHOID STRUCTURES GERMINAL CENTERS

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Background: The development of the B cell repertoire is regulated by the process of affinity maturation occurring within the inner part of the B cell follicles [germinal centers (GCs)] within secondary lymphoid organs (SLOs). In autoimmunity, this process might occur within aberrant aggregates of lymphocytes in target organs, such as the ectopic lymphoid structures (ELS) found in the salivary glands of patients with Sjogren's Syndrome (SS) (1). The phonotypical and functional features supporting ELS which may sustain the development of autoimmune diseases have not been identified. Moreover, functional proof that ELS contribute to the development of autoimmunity independently from SLOs has not been provided.
Objectives: To characterise the transcriptome profile of human ELS isolated from SS salivary glands in comparison with SLOs.
Methods: Frozen minor salivary gland biopsies were obtained from SS patients and selected for presence of GCs+ ELS. Human tonsils were obtained by volunteers undergoing tonsillectomy for clinical need and used as SLO control. In order to detect GCs, all samples were stained for CD21, bcl6, CD20 and CD3. Sequential sections, were stained by Cresyl Violet and GCs (*CD21+ infiltrates*) from both salivary glands and tonsil were selectively microdissected (Laser Capture Microdissection). Salivary gland *small infiltrates* and *large CD21- infiltrates* were microdissected too. RNA was isolated and transcribed. RNA sequencing studies were performed using ClonTech SMARTseq v4 kit. Changes and differences in the expression of specific genes of interest were confirmed with targeted PCR studies.
Results: Transcriptomics analyses revealed that GCs from ELS and SLO exhibit markedly different gene expression profiles. Of note, sequencing unveiled that GCs from ELS are characterized by an aberrant cell-proliferation profile with downregulation of BCL6 and AID, the enzymes responsible for B cell affinity maturation (both $p<0.0001$). Also in ELS, progressive upregulation of CD21 transcript mirrored increases in infiltrate size and organization (being lowest in *small infiltrates* and progressively higher in *large CD21- infiltrates* and *CD21+ infiltrates,* $p=0.002$). Similar data were obtained for AID, whose expression was significantly higher in *large CD21+ infiltrates* compared to *small infiltrates* ($p=0.0006$). A cytokine signature was identified in ELS GCs based on the expression of TNF, INFγ, BAFF, APRIL, CXCL12, CXCL13, FAS, and FASL, all of which were upregulated compared to GCs from tonsils.
Conclusion: Our studies reveal that GCs forming in ELS exhibit marked transcriptional differences from classic GCs observed in SLOs. Main features characterizing ELS include lower levels of Bcl6 and AID, aberrant apoptosis, and a pathogenic inflammatory cytokine signature. Despite similarities in the anatomical organization and appearance of GCs in ELS and SLO, critical transcriptional differences emerge, which are likely functionally implicated in impaired regulation of the B cell cycle and survival of autoreactive B cell clones, ultimately leading to the development of autoimmune disease.

REFERENCE

[1] Barone F. et al. PNAS 2015.

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SAT0012 DETECTION OF CIRCULATING PR3-SPECIFIC B CELLS IN PATIENTS WITH ACTIVE ANCA-ASSOCIATED VASCULITIS

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Background: We recently reported that, in a small number of subjects, the proportion of proteinase 3 (PR3)-specific B cells was higher in patients with PR3-ANCA-associated vasculitis (AAV) compared to healthy controls (HCs).
Objectives: The objectives of this work were to replicate our previous findings on a larger number of subjects, including myeloperoxidase (MPO)-AAV patients as disease controls, and to study the association of PR3-specific B cell proportions with clinical and biological features in patients with PR3-AAV.
Methods: We analyzed frozen PBMCs from 166 patients who participated in the RAVE trial, including 113 patients with PR3-AAV and 53 patients with MPO-AAV, as well as 27 HCs. We measured the proportion of PR3-specific B cells and subsets among PBMCs using a multi-color flow cytometry panel including CD19, IgD, CD27, CD38, CD24, and a biotinylated PR3 revealed by fluorescent streptavidin. In parallel, one million PBMCs from each sample were cultivated in vitro for 12 days and stimulated by CpG, BAFF, and IL-21. PR3-ANCAs were quantified in the culture supernatants and in the serum.
Results: The mean (SD) proportion of PR3-specific B cells was higher in patients with PR3-AAV compared to patients with MPO-AAV and to HCs: 2.78% (2.64) vs 1.97% (1.2) vs 1.24% (0.49) respectively, p<0.001 for each comparison. We observed a shift towards a more mature phenotype of these PR3-specific B cells in patients with PR3-AAV compared to MPO-AAV and HCs, as represented by a higher proportion of PR3-specific B cells among the switched memory (IgD neg, CD27 pos) B-cell subset, respectively 2.20% (1.99) vs 1.3% (0.72) vs 0.71% (0.40), p<0.001. In patients with PR3-AAV, we did not observe any associations between PR3-specific B cell proportion and age, sex, new diagnosis vs relapsing disease, or disease activity (BVAS/WG). Serum PR3-ANCA levels were significantly correlated with in-vitro PR3-ANCA secretion (Spearman r=0.44, p<0.001). The ratio of PR3-specific B cells in the switched memory/naïve B cell subsets showed a low correlation with serum PR3-ANCA levels (r=0.20, p=0.04), but not with in-vitro PR3-ANCA secretion.
Conclusion: The proportion of circulating PR3-specific B cells is higher in patients with PR3-AAV than in patients with MPO-AAV and HCs, and importantly, their repartition is shifted towards a memory phenotype. Further studies are ongoing to characterize the dynamics of the PR3-specific B cells after therapy, and to understand the differences of these autoreactive B cells between patients with PR3-AAV and HCs.

REFERENCE

[1] Cornec D, Berti A, Hummel A, Peikert T, Pers JO, Specks U. Identification and phenotyping of circulating autoreactive proteinase 3-specific B cells in patients with PR3-ANCA associated vasculitis and healthy controls. J Autoimmun. 2017 Nov;84:122-131.

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SAT0013 CHANGES AND SIGNIFICANCE OF CD4+CD25+FOXP3 +TREG CELLS IN THE PERIPHERAL BLOOD OF PATIENTS WITH AUTOIMMUNE DISEASES

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Background: In recent years, studies have found that the maintenance of immune tolerance of Treg cells palys a pivotal role in the occurrence and development of AID, and that the mutual regulation and dynamic equilibrium between Treg cell and other T lymphocyte plays a significant role in maintaining the immune hemostasis within the body.Therefore, the present research proposes to explore the status of the absolute numbers of Treg cells among various AID patients and correlation with disease activity using a large sample.
Objectives: To determine $CD4^+CD25^+Foxp3^+$T regulatory (Treg) cell levels in peripheral blood (PB) of patients with autoimmune diseases (AID) and age- and sex-matched healthy controls, and to explore the correlation between the levels of peripheral Treg cells and clinical parameters in AID.
Methods: A total of 1561 AID patients, and 196 age- and sex-matched healthy controls were enrolled. The absolute numbers of $CD4^+CD25^+Foxp3^+$Treg and other T subsets [total T, $CD4^+$T, $CD8^+$T, T helper 1 (Th1), T helper 2 (Th2), and T helper 17 (Th17) cells] in PB were measured by Flow Cytometer (FCM). Erythrocyte sedimentation rate (ESR) was analyzed by the Westergren method. Serum concentrations of C-reactive protein (CRP) were measured by monoclonal immunoassay.
Results: (1) The absolute numbers of Treg cells in PB of patients with AID [22.90 (18.31, 36.47)] were significantly lower than those of healthy controls [30.24 (21.85, 41.34); $p<0.05$), which was also seen in rheumatoid arthritis (RA), Sjogren's syndrome (SS), systemic lupus erythematosus (SLE), systemic vasculitis (SV), idiopathic inflammatory myopathy (IIM) and other diseases. The levels of $CD4^+$T, Th1/Treg, and Th2/Treg in PB of AID patients were higher than those of healthy controls. **(2)** The absolute numbers of most T cell subsets in PB of most AIDs were lower than those of healthy controls, but the Treg cells were greatly decreased, so the ratio of Treg to other T lymphocyte subsets were higher than those of healthy controls. **(3)** The levels of inflammatory indicators were inversrly associated with numbers of Tregs, total T, $CD4^+$T, $CD8^+$T, Th1 and Th1/Treg cells.
Conclusion: In AID, the absolute numbers or function of $CD4^+CD25^+Foxp3^+$Treg cells were decreased, so it cannot effectively maintain immune tolerance or inhibit inflammatory response, which may be one of the important mechanisms of disease. Treatment promoting $CD4^+CD25^+Foxp3^+$Treg cell function may become a new strategy for AID therapy.

REFERENCES

[1] Tao JH, Cheng M, Tang JP, et al. Foxp3, Regulatory T Cell, and Autoimmune Diseases [J]. Inflammation. 2017;40(1):328-339.
[2] Dall'Era M, Pauli ML, Remedios K, et al. Autoimmunity Centers of Excellence. Adoptive Regulatory T Cell Therapy in a Patient with Systemic Lupus Erythematosus [J]. Arthritis Rheumatol. 2018 Oct 1.
[3] Yokoyama Y, Iwasaki T, Kitano S, et al. IL-2-Anti-IL-2 Monoclonal Antibody Immune Complexes Inhibit Collagen-Induced Arthritis by Augmenting Regulatory T Cell Functions [J]. J Immunol. 2018;201(7):1899-1906.
[4] Zhang SX, Ma XW, Li YF, et al. The Proportion of Regulatory T Cells in Patients with Systemic Lupus Erythematosus: A Meta-Analysis [J]. J Immunol Res. 2018;2018:7103219.
[5] Moulton VR, Suarez-Feuyo A, Meidan E, et al. Pathogenesis of human systemic lupus erythematosus: a cellular perspective [J]. Trends Mol Med. 2017,23(7):615-635.
[6] Zhao Z, Zhang X, Su L, et al. Fine tuning subsets of CD4(+) T cells by low-dosage of IL-2 and a new therapeutic strategy for autoimmune diseases [J]. Int Immunopharmacol. 2018,56:269-276.

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SAT0014 DECREASED CIRCULATING CD19 +CD24HICD38HIREGULATORY B CELLS IN ACPA POSITIVE RHEUMATOID ARTHRITIS: EFFECT OF IL-6 RECEPTOR BLOCKADE

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Background: CD19+CD24^{hi}CD38^{hi} B cells have a regulatory capacity and their frequency is altered in the peripheral blood of patients with various autoimmune conditions, including RA.
Objectives: To determine the frequency of circulating CD19+CD24^{hi}CD38^{hi} regulatory B cells (cBreg) in ACPA+ vs ACPA- patients with RA, and its possible modification by IL-6R blockade.
Methods: Peripheral blood was drawn from ACPA+ (n= 37) or ACPA- (n=19) RA patients treated with conventional synthetic DMARDs (csDMARDs), and from ACPA+ (n=31) or ACPA- (n=12) RA patients treated with tocilizumab; in additon one age and gender-matched healthy control was studied alongside with each patient (n= 99). After isolation by Ficoll-Hypaque gradient, PBMCs were stained with antibodies to CD3, CD4, CD19, CD24, and CD38, and examined by flow cytometry.
Results: A decreased frequency of cBreg cells was observed in ACPA+ but not ACPA- RA patients treated with csDMARDs. Interestingly, the frequency of cBreg cells showed a significant negative correlation with ACPA titers ($r = -0.44$, $p = 0.021$). In contrast, no correlation was found between the frequency of cBreg cells and either RF titres or disease activity as determined by the DAS28 score. However, not only in ACPA- but also in ACPA+ patients receiving tocilizumab, the percentage of cBreg cells was not different from that observed in HC. Four ACPA+ patients treated with csDMARDs who initiated tocilizumab, demonstrated a significant elevation of their cBreg frequency at 12 months.
Conclusion: A decreased frequency of cBreg cells is apparent in ACPA+ but not ACPA- RA patients receiving csDMARDs, that is related with ACPA titres but not with RF titres or disease activity. In contrast, in ACPA+ patients treated with tocilizumab, the frequency of CD19 +CD24^{hi}CD38^{hi} B cells is comparable to that observed in HC, suggesting that IL-6R blockade is able to modify the altered Breg cell balance.

REFERENCE

[1] Flores-Borja F, et al. Sci Transl Med. 2013;5:173ra23.

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SAT0015 TREATMENT WITH ABATACEPT BUT NOT WITH TNF BLOCKERS, IS ASSOCIATED WITH A REDUCTION OF CONSTITUTIVELY ELEVATED CIRCULATING FOLLICULAR HELPER T CELLS IN RHEUMATOID ARTHRITIS

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Background: Circulating CD4 T cells that express CXCR5 together with PD-1 and/or ICOS are considered as counterparts of bona fide Tfh cells and function as B cell helpers. In addition, circulating CD4+CXCR5+ T cells can be subdivided into three subpopulations: CXCR5+CXCR3+CCR6- (Tfh-Th1), CXCR5+CXCR3-CCR6+ (Tfh-Th17) and CXCR5+CXCR3-CCR6- (Tfh-Th2). Only Tfh-Th17 and Tfh-Th2 but not Thf-Th1 cells seem to provide B cell help. Altered frequencies of circulating Tfh cells (cTfh) and of cTfh cell subpopulations have been associated with autoimmune conditions. We previously described that patients with RA treated with conventional synthetic DMARDs (csDMARDs), demonstrate constitutively altered frequencies of cTfh and cTfh cell subpopulations that are observed not only in patients with an active disease but also in patients who are in remission.
Objectives: To determine if treatment with biological agents (TNF blockers or abatacept) is able to modify the constitutively altered cTfh and cTfh subpopulation numbers, observed in RA patients receiving csDMARDs
Methods: Peripheral blood was drawn from RA patients receiving csDMARDS (n=22), TNF blockers (n=21: 10 infliximab, 6 etanercept, 3 certolizumab, 2 adalimumab), or abatacept (n=17). For each patient, an age and gender-matched healthy control was also studied (n=60). cTfh and plasmablast frequencies were determined by flow cytometry of freshly isolated PBMCs.
Results: As described, RA patients receiving csDMARDs demonstrated, whether they had an active or inactive disease, an increased frequency of CD4+CXCR5+PD-1^{hi} and CD4+CXCR5+ PD-1^{hi}ICOS+ T cells, together with an increased frequency of circulating plasmablasts. In addition, the frequency of Tfh-Th1 cells was significantly decreased and the frequency of Tfh-Th17 and Tfh-Th2 cells were significantly increased as compared with HC; subsequently, the ratio (Tfh-Th17+Tfh-Th2)/Tfh-Th1 was increased in RA: that is, RA patients demonstrated a higher proportion of Tfh cell subsets bearing a phenotype associated with B cell helping capacity. Interestingly, these alterations were also observed in RA patients treated with TNF blockers, whether they had an active or inactive disease. In contrast, in patients receiving abatacept, the frequencies of cTfh, cTfh cell subpopulations and plasmablasts, were not different from those observed in HC.
Conclusion: Patients with RA receiving csDMARDs or TNF blockers demonstrated a constitutively increased frequency of cTfh cells and an over-representation of cTfh subsets bearing a B cell helper phenotype, suggesting that altered germinal center dynamics play a role in RA pathogenesis. Remarkably, in RA patients treated with abatacept these frequencies and ratio were not altered, indicating that costimulation blockade is able to revert the increased generation of Tfh cells in RA; conversely, TNF neutralization does not seem to affect the generation or recirculation of cTfh.

REFERENCE

[1] Simpson N et al, Arthritis Rheum 2010; Craft J, Nat Rev Rheumatol 2012; Morita R, et al., Immunity 2011; Arroyo-Villa I, et al., Arthritis Res Ther 2014.

Disclosure of Interests: Paula Fortea-Gordo: None declared, Laura Nuño: None declared, Alejandro Villalva: None declared, Maria-Jose Santos-Bornez: None declared, Diana Peiteado: None declared, Irene Monjo: None declared, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Maria-Eugenia Miranda-Carus Grant/research support from: Roche Pharma, BMS
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SAT0016 RHEUMATOID ARTHRITIS PATIENTS DISPLAY B-CELL DYSREGULATION ALREADY IN THE NAÏVE REPERTOIRE

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Background: Seropositive rheumatoid arthritis (RA) is associated with autoreactivity to citrullinated proteins and rheumatoid factor activity. The adaptive immune system and B cells are postulated to be central in RA pathogenesis, yet possible B-cell dysregulations have not been extensively studied. Here, we use exploratory mass cytometry and next generation sequencing to study overall B cell repertoire shifts in RA patients compared to healthy individuals.
Objectives: We hypothesized that there are an underlying B cells repertoire distortion in RA that may be an important key to understanding the autoimmune pathogenesis.
Methods: B cells enriched from PBMCs from nine ACPA pos., seven ACPA neg. RA patients, and six matched heathy controls were phenotyped with mass cytometry (CyTOF) using a 35-marker panel. Single cell data from all samples were pooled clustered via flowSOM in R to identify distinct cell populations, and visualized with tSNE. Cell numbers in each cluster/population were calculated to identify over-representation in patient groups or controls. ANOVA was performed to account for confounding

factors such as age, sex and cell preparation date and differential expression of markers between groups was calculated via t-test. In parallel, PBMC B cell receptor (BCR) repertoires were investigated in 13 ACPA pos. RA patients and six age-matched healthy donors using the Illumina MiSeq platform and PCR multiplex amplicon libraries with a molecular barcode strategy to generate full variable region coverage. Sequences were filtered using pRESTO, annotated by IMGT and Change-O, finally generating 587 000 unique V-regions. Total serum IgM levels were screened by sandwich ELISA in 157 population controls, 193 ACPA pos., and 50 ACPA neg. RA patients. Variable gene frequency was analyzed by Chi-square with Yates correction and serum IgM levels with Kruskal-Wallis test.

Results: Several B-cell phenotypes were found to be significantly different in ACPA pos. RA compared to controls including an increase in HLA-DR across subsets, CD11c in IgA memory and CD22 expression in clusters of mature naïve IgM positive B cells. Moreover, we could see lower circulating cell counts in ACPA pos. RA in IgG memory ($p=0.01$) and trends for elevation in an CXCR5/CCR6 high transitional B cell cluster ($p=0.06$), with parallel lower number of transitional B cells with lower CCR6 expression ($p=0.06$). Notably, ACPA neg. RA generally had an intermediate phenotype between healthy controls and ACPA pos. RA. Several significant shifts in the RA BCR repertoire could be observed, including an expected higher frequency of VH N-linked glycosylation in highly mutated BCR ($p<0.0001$). Yet, the most striking difference was a significantly higher frequency of VH with low somatic hypermutation (SHM) levels in RA-derived B cells (<5 mutations, $p<0.0001$ 14.7% vs 8,7). This was seen in all sequences, both IgM and class-switched, but was especially prominent in IgG1 rearrangements (9.6% vs 18.8% low mutation, $p<0.0001$ OR=2.2 CI:2.0-2.35). In line with an IgM and low mutation profile in RA, we also observed that both ACPA pos. ($p<0.0001$) and ACPA neg. ($p<0.001$) RA patients have a significant increase in total IgM levels compared to controls (1.4 ± 0.7; 1.3 ± 0.7;1.0 ± 0.6 mg/ml, respectively).

Conclusion: Previous studies have shown that anti-citrulline autoreactivity in RA is primarily originates from memory B cells and characterized by high somatic mutations and N-glycosylation sites. However, here the largest B cell distortions in ACPA positive RA are observed in the naïve B cell population that have not undergone germinal center responses. These differences could reflect baseline shifts and elevated natural autoreactivity as an underlying mechanism in RA pathogenesis.

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SAT0017 COMPARISON OF IMMUNOREGULATORY WITH CONVENTIONAL DMARDS THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by joint synovitis that ultimately leads to joint destruction and loss of function. Conventional therapy or standard medical treatment of RA involves the disease-modifying antirheumatic drugs (DMARDs). Because DMARDs act nonspecifically on the patient's immune cells, it can weaken the body's ability to fight infections. We previously reported that imbalance of effector and regulatory T cells (Tregs) that should be an important cause of RA. Therefore, we developed an immunomodulatory therapy for restoring the reduced Treg cells is the main direction for the treatment of RA. [1]

Objectives: To compare the effects of new immunoregulatory therapy and conventional DMARDs therapy on disease remission and immune homeostasis in RA patients, and to investigate the efficacy of immunoregulatory therapy in the reconstruction of immune tolerance.

Methods: The study included 184 patients with RA (meeting the diagnostic classification criteria for RA revised by ACR in 1987).According to the therapeutic regimen they have received, there were assigned to the immunoregulatory (144 patients, Sirolimus capsule, 0.5mg twice a week and Tretinoin tablets, 10mg once a day, for 12 weeks) and conventional DMARDs group (40 cases,Leflunomide tablets, 10 mg once a day for 12 weeks). Other drugs are similar between the two groups. The absolute numbers of Th17 and Treg cells in peripheral blood were measured by Flow Cytometer (FCM).

Results: 1. There was no statistically significant difference in DAS28 score ($P>0.05$) between the two groups. 2. In the immunomodulatory group, there were statistical differences in the number of Treg as compared with normal controls ($P<0.05$). After immunoregulatory therapy, the absolute number of Treg cells was increased, leading to ratio of Th17/Treg decreased (Table1, Figure1). 3. Conventional DMARDs therapy reduced, significantly the number of Treg cells ($P<0.05$), leading to a increase in the ratio of Th17/Tregs (Table 1, Figure 2).

Conclusion: The results of this study show that the remission rates of immunomodulation group and conventional DMARDS group were 37.39% and 36.00%, respectively. There was no significant difference between the two groups. But as for the effects on their immune cells, immunomodulatory therapy can increase the level of Treg cells compared with conventional DMARDs. It also shows that immunomodulatory therapy may play an important role in restoring immune tolerance in patients with RA, which may help us find new ideas for treating RA. However, we need to enlarge the sample size and extend the treatment time to observe the long-term efficacy of the immunomodulatory therapy in the population.

REFERENCE

[1] Benson R A, Patakas A, Mcqueenie R, et al. Arthritis in space and time – To boldly go![J]. Febs Letters, 2011, 585(23):3640-3648.

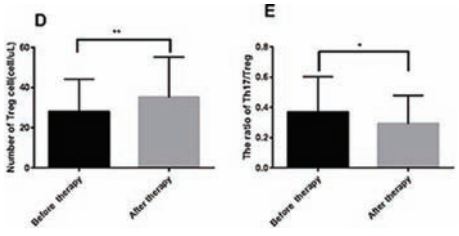


Figure 1. The number of Treg cells and the ratio of Th17/Treg before and after immunomodulatory therapy.

Table 1. The number of Th17 and Treg cell (cell/ul), ratio of Th17/Treg in immunomodulatory therapy and Traditional DMARDs therapy.

Immune Cells	Immunomodulatory n=144		Traditional DMARDs n=40		P value A vs B	P value C vs D
	Before therapy (A)	After therapy (B)	Before therapy (C)	After therapy (D)		
Th17	8.6453 (4.673,11.000)	9.2359 (4.440,12.570)	7.4693 (4.300,10.850)	9.8622 (4.045,8.100)	0.086	0.512
Treg	27.9202 (15.900,36.270)	31.9208 (22.90,39.7775)	38.6240 (31.190,43.120)	30.2330 (24.150,37.380)	0.021	0.001
Th17/Treg	0.3669 (0.199,0.490)	0.2907 (0.172,0.341)	0.2343 (0.127,0.347)	0.3581 (0.202,0.515)	0.020	0.024

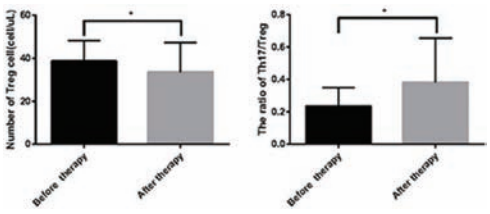


Figure 2. The number of Treg cells and the ratio of Th17/Treg before and after conventional DMARDs therapy.

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SAT0018 THE STUDY OF CD4+T CELL SUBSETS IN RECURRENT POLYCHONDRITIS

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Background: Relapsing polychondritis (RP) is an rare inflammatory disease of unknown causes, characterized by recurrent inflammation in cartilaginous tissues of the whole body[1]. The histologic features of the chondritis include loss of basophilic staining of the cartilage matrix, perichondrial inflammation, cartilage destruction with replacement by fibrous tissue, and perivascular cellular infiltration with plasma cells and lymphocytes. Additional clinical features of the disease include ocular inflammation, vasculitis, audiovestibular dysfunction, myocarditis, cardiac valvular insufficiency, and nonerosive inflammatory arthritis. Many studies have shown that the imbalance of helper T cell 17(Th17) and regulatory T cell (Treg) is involved in the pathogenesis of autoimmune diseases such as SLE and RA. But little is known about the roles of peripheral immune cell subsets peripheral in RP patients. Up to now, just few studies focus on this issue.
Objectives: We aimed to analyse the distribution and phenotype of CD4 +T cell subsets in the peripheral blood of patients with RP.
Methods: The proportion and absolute counts of circulating immune cells were assessed in 14 patients diagnosed as RP and 14 healthy controls. CD4+T cell subsets were also analysed in 9 untreated RP patients and 9 healthy volunteers by flow cytometry. All statistical analyses were performed with SPSS v. 22.0. Continuous variables were reported as median. For all study variables, comparison among controls and RP subjects was based on the non-parametric Wilcoxon Mann-Whitney exact test. For all analyses, we used two-sided tests, with p-values <0.05 denoting statistical significance.
Results: Proportion and absolute counts of Treg cells were significantly reduced in RP patients in comparison with controls (proportion, 3.61% vs. 5.24%, p<0.001; absolute counts, 27.36/μl vs. 46.56/μl,p<0.001). But there were no significant difference between the percentage and number of Th17, Th1 or Th2 cells in patients with RP and healthy controls. Thus, the ratio of Th17/Treg increased in RP patients (0.25 vs. 0.14, p<0.001), as did the ratio of Th2/Treg (0.28 vs. 0.22, p<0.001) and Th1/Treg(2.75 vs. 1.92, p=0.019)(Figue 1). Similarly, the proportion and absolute counts of Treg cells in untreated RP patients were significantly lower than that in healthy controls (proportion, 3.78% vs. 5.66%, p=0.008; absolute counts, 32.24/μl vs. 50.76/μl, p<0.001).And the ratio of Th17/Treg slso increased in untreated RP patients (0.25 vs. 0.15, p=0.003), as did the ratio of Th1/Treg (2.35 vs. 1.88, p=0.014)(Figue 2).
Conclusion: Our data suggested that the immune-inflammation in RP patients may be related to the depletion of Treg cells and the imbalance of Th17 or Th1 or Th2 and Treg cells.Reduction of peripheral Treg cells may exacerbate the disease progression by not being inhibited Th cells.

REFERENCE

[1] Kingdon J, Roscamp J, Sangle S, et al. Relapsing polychondritis: a clinical review for rheumatologists[J]. Rheumatology, 2017, 57(9): 1525-1532.

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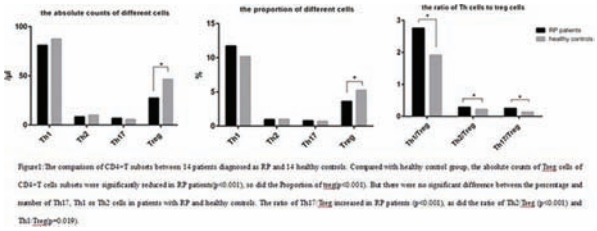


Figure1:The comparison of CD4+T subsets between 14 patients diagnosed as RP and 14 healthy controls. Compared with healthy control group, the absolute counts of Treg cells of CD4+T cells subsets were significantly reduced in RP patients(p<0.001), so did the Proportion of Treg(p<0.001). But there were no significant difference between the percentage and number of Th17, Th1 or Th2 cells in patients with RP and healthy controls. The ratio of Th17/Treg increased in RP patients (p<0.001), as did the ratio of Th2/Treg (p<0.001) and Th1/Treg(p=0.019).

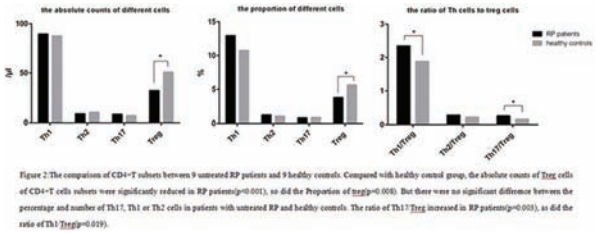


Figure 2:The comparison of CD4+T subsets between 9 untreated RP patients and 9 healthy controls. Compared with healthy control group, the absolute counts of Treg cells of CD4+T cells subsets were significantly reduced in RP patients(p<0.001), so did the Proportion of Treg(p=0.004). But there were no significant difference between the percentage and number of Th17, Th1 or Th2 cells in patients with untreated RP and healthy controls. The ratio of Th17/Treg increased in RP patients(p=0.003), as did the ratio of Th1/Treg(p=0.019).

SAT0019 CONDITIONED MEDIUM FROM ADIPOSE MESENCHYMAL STEM CELL EXERT IMMUNOSUPPRESSIVE EFFECT ON TH17/TREG AXIS IN RHEUMATOID ARTHRITIS IN VITRO

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Background: Emerging data have demonstrated that mesenchymal stem cells (MSC) are well endowed with a broad repertoire of immunosuppressive tools and they could modulate the immune response on several levels via production of a plethora of soluble factors and contact-dependent mechanisms. For these reasons, mesenchymal stem cells-based protocols were spotlighted as promising multiple-hit treatment candidates for therapeutic intervention in a multitude of autoimmune diseases and debilitating conditions such as rheumatoid arthritis (RA).
Objectives: In line with aforementioned and taking in mind the current shift in Th1/Th2 paradigm suggesting a key role of Th17/Treg axis dysregulations in RA pathogenesis, we aimed to appraise the immunoregulatory effects of secretory factors produced by adipose-derived MSC (AT-MSC) on Th17 and Tregs subsets and also pro-inflammatory cytokines production in patients with RA.
Methods: The study encompasses 17 patients matching the ACR/EULAR 2010 criteria for RA. AT-MSC were isolated and cultured according to well-established protocols. Peripheral blood mononuclear cells (PBMCs) isolated from RA patients' samples were cultured in AT-MSC conditioned media and in control media. Flow cytometry was used for detection of Th17 and Treg markers (of CD3, CD4, CD161, CD196 and CD25 and intracellular expression of FoxP3). ELISA was performed for testing the cytokines produced by PBMC (TGF-β1, TNF-α, IL-17A, IL-21).
Results: We found significant elevation in percentage of $CD4^+CD25^+FoxP3^+$Treg cell in the pool of PBMC cultured with AT-MSC as opposed to control medium, 4.22 ± 2% (mean ± SD) vs. 6.04 ± 3.6% (p = 0.001). Paired sample analysis of Th17 cells percentage values from all $CD4^+$ in PBMC cultured with control media (mean ± SD) 10.13 ± 3.88% in contrast to Th17 percentage in PBMC cultured with AT-MSC supernatants 8.98 ± 3.58% showed significant decrease in Th17 numbers (p = 0.02) under the influence of AT-MSC secretory factors. Cultivation of RA patient`s PBMCs with AT-MSC supernatants led to significant up-regulation of TGF-β1 levels, (median [IQR]) 8.318 ng/ml (6.327 – 11.686 ng/ml) vs. 6.227 ng/ml; (1.681 – 10.148 ng/ml) (p = 0.013) and decrease in levels of TNF-α, IL-17A, and IL-21 respectively: 5 pg/ml (1.75 – 11.65 pg/ml) vs. 1 pg/ml (0.7 – 1.9 pg/ml) (p = 0.001); 4.2 pg/ml (3.1 – 6.1pg/ml) vs. 2.3 pg/ml (0.75 – 5.42 pg/ml) (p = 0.017); 75.1 ± 35.95 pg/ml vs. 52.09 ± 30.8 pg/ml (p = 0.022). The reduction in IL-17 levels positively correlated with the decrease of TNF-α (r = 0.921, p = 0.001).
Conclusion: Our study unambiguously demonstrated that secretory factors produced by AT-MSC exert an immunoregulatory effect on Th17 and Treg cells and also could inhibit major effector cytokine pathways: TNF-α, IL-17, IL-21 production in RA *in vitro*. The study of mechanisms of immunoregulation induced by MSCs provide us better insight into the pathogenesis of rheumatoid arthritis and could be a potential therapeutic approach.

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SAT0020 BLOOD RNA SEQUENCING REVEALS IMMUNOLOGICAL PROCESSES ASSOCIATED WITH THE RESPONSE TO ABATACEPT IN RHEUMATOID ARTHRITIS

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Background: Abatacept (CTLA4-Ig) is an approved biological therapy for the treatment of rheumatoid arthritis (RA). Similar to other biological agents, most patients (60%) respond significantly to this therapy. To date, however, the biological mechanisms underlying the lack of efficacy for this drug are unknown.

Objectives: The objectives of the present study were to characterize the biological processes underlying the lack of efficacy of abatacept and to evaluate the blood transcriptome as a valid source for drug response prediction.

Methods: A total of n=57 patients diagnosed with RA were recruited for this study from 16 rheumatology departments in Spain. All patients were >18 years old and, had >6 months of disease evolution. The primary clinical response to abatacept was defined at week 12 using the EULAR criteria. Good and moderate responders were aggregated into a single response group, and compared to the no response group of patients. Blood RNA was collected from all patients at baseline. From a subgroup of patients (n=31), blood RNA was also obtained at weeks 12, 24 and 48 of treatment with abatacept. Gene expression levels were determined using paired-end RNA-seq (Illumina). Differential gene expression, association to biological processes, longitudinal association analysis and building of the multigenic predictor were performed using the R software and the specialized Bioconductor libraries. The the prediction accuracy was evaluated using the ROC AUC.

Results: From the 57 patients treated with abatacept, n=10 (17.5%) were good EULAR responders, n=24 (42%) moderate EULAR responders and n=23 (40.5%) non-responders at week 12 of therapy. Biological process analysis identified two significantly distinct biological profiles between responders and non-responders. In responders, we found an association to pathways associated with the effector phase of T cells (e.g. interleukin-15 and 2 signalling, $P < 0.05$). Non-responder patients showed instead a strong association to biological processes associated with antigen presentation and activation of T cells ($P < 0.005$). Using the baseline gene expression profiles, we built a multigenic predictor of response to abatacept with an AUC = 75%. In the longitudinal cohort, patients were stratified based on reaching an inactive state (i.e. DAS28 < 3.2). Using this endpoint measure, the longitudinal analysis of the 4 time points corroborated the association of response with antigen presentation ($P < 0.01$).

Conclusion: The analysis of blood RNA profiles of RA patients has enabled the identification of specific biological processes associated with the lack of response to abatacept. Also, we demonstrate that blood expression profiles can be predictive of the response to the drug at week 12 of therapy.

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SAT0021 ELEVATED NUMBERS OF C-TYPE LECTIN CD161 POSITIVE PR3-SPECIFIC T-CELLS IN GPA

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Background: Various alterations of the peripheral T-cell compartment have been reported in granulomatosis with polyangiitis (GPA) such as elevated populations of CD4+CD8+ double-positive and CD4+CD161+ and CD28- single-positive effector memory T-cells (T_{EM}) within the total CD3+ T-cell population (1). Analysis of antigen-specific T-cell subpopulations shows, that PR3-specific T-cells display Th2-type, Th17 and Th22 cytokine profiles in GPA (2). Moreover, concomitant cellular CMV- and Epstein Barr virus (EBV)-infection has been found to be associated with the expansion of CD28- T_{EM} in GPA (1,2). Notably, C-type lectin CD161 +CD8+ T-cells displaying a polyfunctional memory profile directed against several common viruses have been reported. Furthermore, CD161+ T-cells are involved in the pathogenesis of early stage autoimmune hepatitis (3). CD161 expression on proteinase 3 (PR3)-specific T-cells in comparison to other antigen-specific T-cells has not been described in GPA as yet.

Objectives: To determine the amount of C-type lectin CD161 on antigen-specific CD8+ single-positive and CD4+CD8+ double positive T-cells in patients with GPA

Methods: In this study, we analyzed the expression of CD161 and CD28 on circulating antigen-specific CD8+ single-positive and CD4+CD8+ double positive T-cells in HLA-A2 positive patients with GPA (n=21) and healthy controls (n=21) using flow cytometry. Antigen-specific T cells were detected using peptide/MHC class 1 dextramers containing major peptide epitopes for PR3, Epstein Barr virus (EBV) BMLF1, and Cytomegalovirus (CMV) pp65 (aa 196-177, aa 280-288, and aa 495-504, respectively).

Results: Patients with GPA showed a higher frequency of circulating CD8 + single-positive and CD4+CD8+double-positive PR3-specific T-cells with increased expressions of CD161 compared to HC. Compared to EBV- or CMV-specific T-cells, there was an increased expression of CD161 on PR3-specific T-cells in GPA. In contrast to HC and EBV- or CMV-specific T-cells, the percentage of CD28+ T-cells was expanded within the PR3-specific CD8+ T-cell subset in GPA.

Conclusion: These findings suggest a potential role of CD161 as an additional TCR-independent co-stimulatory receptor on PR3-specific T-cells in GPA. The role of these cells in the pathophysiology and as a potential therapeutic target remains be further investigated.

REFERENCES

[1] Kerstein A, et al., Environmental factors and inflammation-driven alteration of the total peripheral T-cell compartment in granulomatosis with polyangiitis; J Autoimmun. 2017 Mar;78-79-91

[2] Lamprecht P, et al., Pathogenetic and clinical aspects of anti-neutrophil cytoplasmatic autoantibody associated vasculitis. Front. Immunol. 2018; 9:680

[3] Renand A, et al. Immune alterations in patinents with type 1 autoimmune hepatitis persist upon standard immunosuppressive treatment. Hepatol Commun. 2018 Aug 6;2(8):868-981

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SAT0022 THE SUBPOPULATION FEATURES OF DENDRITIC CELLS AS A POTENTIAL BIOMARKER OF EARLY RHEUMATOID ARTHRITIS

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Background: Dendritic cells (DCs) are professional antigen-presenting cells (APCs), which play important role in immune responses. DCs are a heterogeneous population and can be divided into groups: myeloid (mDCs) and plasmacytoid (pDCs). Furthemore, DCs are important in rheumatoid arthritis (RA) pathogenesis through antigen presentation and activation autoreactive T-lymphocytes. As established the different subpopulation DCs can promote different immune reactions. That's why, it may be possible to consider them as a potential target for the development of new target of the immunopathological disorders therapy.
Objectives: To investigate the subpopulations of peripheral blood DCs (myeloid and plasmacytoid) in patients with early RA as a predictor of responsibility to disease-modifying antirheumatic drugs (DMARDs) treatment.
Methods: Forty nine patients with early RA (duration of the disease up to 12 months) were included in the study. All patients fullfield ACR/EULAR criteria (2010) and received methotrexate, leflunomide, sulfasalazine or their combination. Forty three patients with osteoarthritis (OA) used as a control group. Analysis of the content of the B-lymphocytes, myeloid and plasmacytoid DCs, labeled by antibodies against surface markers, was carried out by flow cytometry. B-lymphocytes, subtypes of peripheral blood DCs were characterized by the following phenotypes: myeloid DCs (CD3-CD14-CD19-HLA-DR + CD11c + CD123-), plasmacytoid DCs (CD3-CD14-CD19-HLA-DR + CD11c-CD123 +), B-lymphocytes (CD19 +). Analysis were performed before treatment and after 3 and 6 months.
Results: Patients with early RA are characterized by significant evaluation of the population of plasmacytoid DCs in comparison of patients with moderate stages of rheumatoid arthritis and osteoarthritis (3.8 vs2.1 vs 1, p=0.0042). Furthermore, the difference was found in the number of cells with the phenotype B-lymphocytes: 7.95 * 106/l vs. 3.6* 106/l, respectively (p = 0.014). No significant differences were observed in the number of myeloid DCs. After 6 month of observation we detected reducing amount of plasmacytoid DCs (3.8 before treatment and 2.1 in 6 month, p=0.002) and B-cells that correlated with activity of disease.
Conclusion: The data obtained indicated that plasmacytoid DCs are predominant in patients with inflammatory arthritis especially in early RA and correlate with activity of disease that can use as a predictor of good response on DMARDs treatment.
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SAT0023 THE DIFFERENTIAL PRODUCTION OF REACTIVE OXYGEN SPECIES IN T CELL SUBSETS IN PERIPHERAL BLOOD OF RHEUMATOID ARTHRITIS PATIENTS

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Background: T cells play a regulatory role in rheumatoid arthritis (RA) through inducing the homeostasis maintenance and self-tolerance [1]. Specially, the production and the oxidation mechanism of reactive oxygen species (ROS) were out of balance.
Objectives: The aim of the study was to compare ROS productions in T cell subset, which are helper T (TH) cell, cytotoxic T (TC) cell, T helper 17 (TH17) cell and regulatory T (Treg) cell in peripheral blood mononuclear cells (PBMC) of RA patients with RA activity.
Methods: Blood samples were collected from 30 RA patients and 10 healthy adult volunteers under IRB approval. RA activity was divided according to clinical parameter DAS28 [2]. PBMC cells were obtained from the whole blood using lymphocyte separation medium density gradient centrifugation. For separation between the live and dead cell populations, PBMC was stained with Live/Dead stain dye. After PBS washing, cells were incubated with antibodies for CD3, CD4, CD8, and CD25. Following fixation and permeabilization, and further stained with antibodies for FoxP3 and IL-17A. For ROS staining, CellRox and MitoSox were used.
Results: The frequency of TH cell was increased and that of TC cell was decreased in the peripheral blood of RA patients. TH17 and Treg cell population were significantly increased more than about 2-3 folds in active and inactive RA than healthy control. When the whole of cellular ROS production was measured, only Treg cell population was significantly increased in RA than control. Although ROS level was steadily increased with RA activity, there was a slight decline in severe RA compared to moderate and low RA. This difference is lager in mitochondrial specific ROS than total cellular ROS. The mitochondrial complex inhibitor reduced Treg cell frequency in PBMC from RA patients.
Conclusion: Treg is the most sensitive to ROS production among T cell subsets in RA. These findings provide a novel approach to regulate Treg function in RA through mitochondrial metabolism related ROS production.

REFERENCES

[1] Szekanecz, Z., et al., New insights in synovial angiogenesis. Joint Bone Spine, 2010. 77(1): p. 13-9.
[2] Prevoo, M.L., et al., Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum, 1995. 38(1): p. 44-8.

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SAT0024 TRANSCRIPTOMIC PROFILING OF THE MICROENVIRONMENT DRIVEN RE-SHAPING OF PATHOGENIC CIRCULATORY AND SYNOVIAL HLA-DR+ CD4 T SUBSETS IN ACTIVE JUVENILE IDIOPATHIC ARTHRITIC PATIENTS

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Background: We have previously identified two pathogenic circulatory CD4 subsets in both Teff $(CPLs)_1$ and Treg $(iaTreg)^2$ compartments of JIA patients that are HLA-DR^+, antigen experienced, pro-inflammatory, correlating positively with disease activity and possessing strong synovial TCR sequence coverage. Despite being two functionally discordant T cell subsets (Teff/Treg), their immuno-phenotype and association with clinical fate suggests that these subsets may originate from a common precursor.
Objectives: We seek to understand how the microenvironment could potentially influence and drive these subsets (CPLs/iaTregs) towards their pathological state. In an attempt to elucidate the common pathological gene drivers, we decided to perform next-generation RNA sequencing on sorted CPLs/iaTregs and conventional Teff/Treg counterparts in both circulation and synovium.
Methods: CPLs were sorted as $CD3^+$ $CD4^+$ $CD14^-$ $HLADR^+$ CD25/CD127 Teff gate, and iaTregs were sorted as $CD3^+$ $CD4^+$ $CD14^-$ $HLADR^+$ $CD25^{hi}/CD127^{low}$ Treg gate with FACs Aria II from n=16 active JIA PBMCs, n=8 paired JIA SFMCs, and n=8 healthy paediatric PBMCs. As a comparative control, similar $HLADR^-$ counterparts were respectively sorted from the same patients. Sorted cells were lysed and extracted for RNA, and cDNA conversion/amplification were then carried out using SMART-seq v4. Libraries are prepared and multiplexed using Nextera XT DNA library preparation kit, and ran on the Illumina HiSeq High output platform.
Results: Comparative differential gene expression (DEG) analysis within the circulatory compartment indicate transcriptomic convergence between CPLs/iaTreg and divergence away from conventional Teff/Treg pools. Circulatory CPLs/iaTregs exhibit (a) common pathway dysregulation in T cell signalling (IFN-g, PD1, CD28 costimulation), (b) restriction in TCR oligoclonality and (c) common transcription factor drivers (SPL1 and E2F1) within the gene regulatory network, suggesting a common driving source acting on these two disparate compartments.
To understand how this convergence originate, we compared CPLs/iaTreg and conventional Teff/Treg subsets from (a) healthy circulatory PBMCs, (b) JIA circulatory PBMCs and (c) paired JIA synovium. There was a gradual increase in transcriptomic convergence between Teff/CPLs, Treg/iaTreg and CPLs/iaTreg across the spatial/disease continuum, that is paralleled by an antigenic convergence in shared TCR clonotypes in CPLs/

iaTreg. In particular synovium CPLs/iaTreg reveal 7 common dysregulated pathways; MHC II antigen presentation, T cell costimulation, IFNg pathway, apoptosis, viral response, bacteria response and chemotaxis.
Conclusion: Overall the data indicate immune-phenotypic convergence between CPLs/iaTregs, that is strengthen across disease/spatial states. These findings underscore a potential mechanistic role of the inflammatory microenvironment in shaping two functionally dichotomic populations, relevant to disease pathogenies and progression.

REFERENCES

[1] Spreafico R, et al. A circulating reservoir of pathogenic-like CD4+ T cells shares a genetic and phenotypic signature with the inflamed synovial micro-environment. Ann Rheum Dis 75, 459-465 (2016).
[2] Rossetti M, et al. TCR repertoire sequencing identifies synovial Treg cell clonotypes in the bloodstream during active inflammation in human arthritis. Ann Rheum Dis 76, 435-441 (2017).

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SAT0025 THE EFFECT OF DIMETHYL FUMARATE ON PLASMABLAST DIFFERENTIATION TRANSCRIPTIONAL PROGRAMMES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Dimethyl fumarate (DMF), is an immunomodulatory drug approved for the treatment of Multiple Sclerosis (MS) and Psoriasis. The exact mechanism of action of DMF is not entirely known. Anti-inflammatory and immunomodulatory effects have been observed, including the upregulation of NRF-2, the inhibition of TIGAR and the block of the E2 ubiquitin-conjugating enzyme UBEL3. Further evidence from MS patients suggests a modulation on B cell activation. Although beneficial effects of DMF have been observed in animal models of lupus nephritis and limited cases human cutaneous lupus, the effect of DMF on B cell maturation transcriptional programmes in systemic Lupus Erythematosus (SLE) has not been fully investigated.
Objectives: To examine the effect of DMF on SLE plasmablast differentiation and identify the transcriptomic changes in cultured SLE B cells after DMF administration.
Methods: B cells were isolated from the peripheral blood of SLE patients (n=15) by negative magnetic sorting. B cell differentiation toward plasmablasts was induced in-vitro by stimulation with TLR-7 agonist Resiquimod, CD40L, IL-2, IL-10 and IL-15 for 5 days in the presence of DMF 25 uM or vehicle, added 24h after plating. IgG and IgM production were quantified in the supernatant by ELISA. In-vitro differentiated B cells were immunophenotyped by 10-colour flow cytometry in order to identify Naïve ($CD27^-IgD^+$), Memory ($CD27^+IgD^-$), IgD^+ Memory ($CD27^+IgD^+$), Double Negative (DN) ($CD27^-IgD^-$) B cells, pre-plasmablasts (pre-PBs) ($CD27^+$, CD20low, $CD38^-$) and plasmablasts (PBs) ($CD27^+$, $CD20^{low}$, $CD38^+$). Naïve B cells and PBs from 3 patients were isolated by fluorescence-activated cell sorting and underwent to RNA-sequencing followed by pathway analysis.
Results: DMF administered from day 2 led to a relative increase in the percentage of Naïve B cells (p=0.002) and a substantial reduction in Memory B cells (p=0.005), while the proportion of DN cells and IgD^+ Memory B cells were not altered. DMF reduced the percentage of PBs (p=0.003), in contrast, the percentage of pre-PBs was significantly increased (p=0.006). Consistently, IgG and IgM secretion were significantly reduced (p<0.001). DMF treatment induced significant transcriptional changes in both PBs and Naïve B cells, with 269 and 652 genes modulated in PBs and Naïve B cells, respectively (Paj <0.05). Pathway analysis highlighted the downregulation of a number of pathways: detoxification of reactive oxygen species, transcriptional regulation of cell cycle inhibitor p21, mitophagy and Pink/Parkin Mediated mitophagy, interleukin-12 signalling, TP53 and p53 regulation, PERK mediated endoplasmic unfolded protein response, and NF-kB mediated cell survival. Conversely, pathways related to epigenetic regulation, RUNX1 signalling, Rho and GTPase signalling were upregulated.
Conclusion: Our results show that Dimethyl Fumarate exerts a significant inhibition on SLE plasmablast differentiation and antibody production. The transcriptomic analysis allowed to dissect B cell transcriptional programmes activated in the context of autoimmune B cell differentiation in SLE. The transcriptional perturbations induced by DMF highlighted some of the gene expression pathways necessary for plasmablast differentiation and survival. In addition, these data provide new insight into DMF pharmacodynamics and may support the repositioning of DMF in the treatment of SLE.
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SAT0026 IMPACT OF TOCILIZUMAB ON IMMUNE PHENOTYPES IN PATIENTS WITH LARGE VESSEL VASCULITIS

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Background: The pathogenesis of large vessel vasculitis (LVV) such as Takayasu arteritis (TAK) and giant cell arteritis (GCA) consists of the immune abnormalities including the interaction between vascular dendritic cells, macrophages and T cells. It is reported that genetic polymorphisms in the immune-modulating cytokine genes such as *IL6* and *IL12B* are associated with LVV. However, little is known about pathological immune cell subsets targeted by immunosuppressants and/or molecular-target therapy such as IL-6 blockade.
Objectives: The aim of this study was to assess the relationship between the phenotype of peripheral immune cells with clinical manifestations and responsiveness to the treatment in patients with LVV.
Methods: Peripheral blood mononuclear cells were obtained from 22 patients with active LVV (TAK 7, GCA 15) and 19 healthy donors (HD). All patients were treated with high dose glucocorticoid (GC). The study included the patients treated with immunosuppressive agents such as azathioprine and methotrexate (n=8) or with anti-IL-6 receptor antibody tocilizumab (n=7). The blood samples were taken at baseline and week 24 after treatment. The peripheral immune cell subset was defined based on comprehensive 8-color flow cytometric analysis for human immune system termed "the Human Immunology Project" by NIH and FOCIS [(1)], and the correlation with clinical characteristics and responsiveness to the therapies were evaluated.
Results: The proportion of $CD3^+CD4^+CXCR3^-CCR6^+CD38^+HLA\text{-}DR^+$ activated Th17 cells and $CD3^+CD4^+CXCR5^+ICOS^+CD38^+$ activated Tfh cells in patients with TAK and that of activated Th17 cells and $CD19^+CD20^+CD27^-IgD^-$ double negative effector B cells in patients with GCA were significantly higher compared with HD. At baseline, the frequency of activated Tfh cells showed positive correlation and that of $CD4^+CCR4^+CD25^+CD127^{low}$ T regulatory (Treg) cells showed negative correlation with disease activity scores such as Indian Takayasu Activity Index (ITAS)2010 [(2)] and ITAS.A (CRP) in both TAK and GCA. The immunosuppressive therapy improved the disease activity in all patients. The frequency of activated Tfh cells was reduced by 24-week treatment with high dose GC and immunosuppressants in TAK and GCA. However, the frequency of Th17 cells was not changed by those treatments. Of note, tocilizumab decreased the proportion of activated Th17 cells and increased the proportion of Treg cells in both TAK and GCA.
Conclusion: The results indicated that the abnormal T cell differentiation correlated with disease activity of LVV. Although Tfh cell activation was improved, Th17 cell activation was not changed by the conventional immunosuppressive agents. By contrast, tocilizumab reduced Th17 cells and increased Treg cells, indicating that IL-6 blockade may correct the impaired balance of Th17 and Treg cells in patients with LVV.

REFERENCES
[1] Maecker HT, et al. Standardizing immunophenotyping for the Human Immunology Project. Nat Rev Immunol 2012; 12: 191-200.
[2] Misra R, et al. Development and initial validation of the Indian Takayasu Clinical Activity Score (ITAS2010). Rheumatology (Oxford). 2013; 52: 1795-801.

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SAT0027 CIRCULATING CD3+CD31+CXCR4+ T CELLS IN RHEUMATOID ARTHRITIS PATIENTS: CORRELATION WITH RETINAL MICROVASCULAR DAMAGE AND POTENTIAL EFFECT OF ABATACEPT THERAPY

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Background: T-cells play a role in pathogenesis of rheumatoid arthritis (RA) and in its cardiovascular (CV) comorbidities [1]. CD3+CD31+CXCR4 +T-cells may be involved in damaged endothelium repair [2]. The percentage of these cells in the peripheral blood was reported to be lower in RA than in healthy controls, as an effect of disease activity rather than of traditional CV risk factors [3]. Abatacept (ABA), a T-cell co-stimulation blocker, is approved for the treatment of RA. In addition to its effect on disease activity, it may have a CV protective action [4].
Objectives: To evaluate CD3+CD31+CXCR4+T-cells in a cohort of RA patients in correlation with disease activity, CV parameters, and the potential effect of ABA therapy.
Methods: Thirty-one RA patients (median[10^{th}-90^{th}percentile] age=60[40-70] years, baseline C-reactive protein (CRP)-DAS28=4[3-5.4], body mass index (BMI)=21[17.3-28.6] kg/m^2, rheumatoid factor (RF) positive:55%, anti-citrullinated peptide autoantibodies (ACPA) positive:77%) were enrolled. Thirteen patients were evaluated before and after 6 months of ABA therapy. Among them, in 5 patients without known CV risk factors (history of arterial hypertension, diabetes, hypercholesterolemia, previous CV events and smoking), a morphological evaluation of retinal arterioles was performed by adaptive optics, a validated technique quantifying microvascular damage [5]. The response to treatment was evaluated with the EULAR response criteria. Phenotypic analysis of peripheral blood T lymphocytes was made by flow-cytometry.
Results: At baseline, no correlation was found between relative CD3 +CD31+CXCR4+T-cell number and age, BMI, CRP DAS28, RF and ACPA titer. However, a negative correlation was observed with retinal wall thickness (Figure1). After ABA therapy (n=13), no significant differences were found between good-moderate responders (n=10) and non-responders (n=3), but the two groups seemed to show an opposite trend (T0 vs T6; from 23.8[4-45.4] to 11.9[5-38.7] and from 20.4[15.4-32.3] to 27.4[17.8-41]% of CD3+ cells, respectively). All 5 patients without known CV risk, evaluated also with adaptive optics, had a good EULAR response. A trend for reduction of CD3+CD31+CXCR4+T-cells after ABA therapy was also observed (19[7.9-45.6] vs 12.4[4.6-26.1]% of CD3+), as well as of the retinal wall thickness (14.4[12.9-16.2] vs 14.2[11.7-14.9] μm). A significant reduction of retinal wall cross-sectional area was observed (5123.3[4027.8-6145.5] vs 4852.3[3554.9-5788.2] μm^2;p=0.04).
Conclusion: In a subgroup of patients without known CV risk factors, CD3+CD31+CXCR4+T-cell number was inversely related to the possible presence of subclinical CV involvement, as evaluated by retinal microvascular damage. This improved after ABA therapy. These findings may suggest a possible value of CD3+CD31+CXCR4+T-cell number in the evaluation of microvascular damage, and a possible beneficial effect of ABA on the microcirculation in RA patients.

REFERENCE
[1] Dessein PH, J Rheumatol 2005. [2] Hur J, Circulation 2007. [3] Rodriguez Carrio J, ARD 2015. [4] Kallikourdis M, Nat Commun 2017. [5] De Ciuceis, J Hypertens 2018.

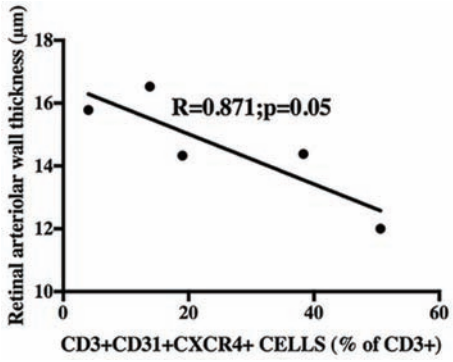


Figure 1.

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SAT0028 PERIPHERAL BLOOD REGULATORY T-LYMPHOCYTES OF PATIENTS WITH RHEUMATOID ARTHRITIS BEFORE AND AFTER ALFACALCIDOL THERAPY

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Background: The identification of regulatory T cells (Treg) changed the Th1/Th2 dihotomy response in the pathogenesis of autoimmune diseases. Treg suppresses various autoreactive responses and maintain auto-tolerance in the immune system. The vitamin D receptor is widely expressed in immune cells, including monocytes, macrophages, dendritic cells, NK cells, and T and B lymphocytes, and plays an important role in the regulation of the immune system, and in the modulation of immunologically mediated diseases. Alfacalcidol, a synthetic analogue of hormone D, used in the prevention and treatment of osteoporosis, but the last results indicate its potential therapeutic effects in autoimmune diseases.
Objectives: Assess the presence of regulatory T cells in patients with active rheumatoid arthritis (RA)patients before and after 12 weeks of 2 mcg of alfacalcidol administration daily, and in healthy controls.
Methods: The study included 16 patients with RA, both sexes, with active disease (DAS 28 (SE)> 3.2, despite therapy with LMTBs for at least a month and 20 healthy volunteers (the same distribution of sex and age) - a control group of healthy subjects. In addition to their regular LMTB therapy, patients with RA received daily alfacalcidol (2mcg/day) for 12 weeks. Phenotypic characterization of peripheral blood lymphocytes was performed by direct and indirect immunofluorescence technique using the BD FACS Aria III flow cytofluorimeter. Descriptive and analytical statistics were used in data analysis.
Results: A small percentage of activated Treg cells (HLA-DR + compared to total T-reg lymphocytes) in the peripheral blood of patients with active RA was detected in the Treg lymphocytes in relation to the control group of healthy subjects, which is close to the statistical significance level (4.76% versus 6.5% = 0.07). In contrast, the percentage of total Treg cells (Treg versus total CD4 +) was slightly higher in patients compared

to a healthy control group (7.6% versus 5.85%, p = 0.129). After a 12-week treatment with alfacalcidol in patients with RA, an increase in the percentage of activated Treg cells (HLA-DR + relative to total T-reg lymphocytes) was observed in relation to the values detected at the beginning of the study, up to the level recorded in the group of healthy controls 6.13% vs. 4.76%, p = 0.219).

Conclusion: It is believed that functional blockade of Treg cells plays the most important role in RA immunopathogenesis, most likely due to inhibition of their function by proinflammatory cytokines, due to an increase in the number of activated effector T cells, or perhaps due to the fact that some completely differentiated T reg cells can be very unstable. Our results are in favor of the potential immunomodulatory effect of alfacalcidol in autoimune Th1/Th17-mediated diseases.

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SAT0029 THE IMMUNE-PATHOGENIC CHARACTERISTICS OF AUTOREACTIVE B CELLS AGAINST CITRULLINATED ANTIGENS IN RHEUMATOID ARTHRITIS

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Background: Autoreactive B cells are critical mediators of autoimmune pathology. At present, little is known about the functional and phenotypic characteristics of these cells in human autoimmune disease. Rheumatoid arthritis (RA), a common autoimmune disease, is characterized by the presence of disease-specific anti-citrullinated protein antibodies (ACPA). Different lines of evidence indicate that CD20+ B cells, and in particular the citrullinated antigen-specific, ACPA-expressing subset, are critically involved in disease pathogenesis.

Objectives: To delineate the molecular make-up of ACPA-expressing B cells and to define their pathogenic effector functions.

Methods: Protective tetanus toxoid (TT)-specific and autoreactive ACPA-expressing B cells were identified and analyzed directly ex-vivo from individual RA patients and from ACPA-positive individuals at-risk for developing disease. Both antigen-specific cell populations were enumerated and phenotypically characterized by flow cytometry. In addition, ACPA-expressing B cells were isolated and functionally analyzed in B cell culture systems.

Results: In contrast to TT-specific B cells from the same patients, ACPA-expressing B cells were larger in size and strongly expressed CD19, HLA-DR, CD80, CD86 and the proliferation marker Ki-67, while down-regulating CD32. This activated phenotype was less pronounced in ACPA-positive 'at-risk' arthralgia patients. Furthermore, ACPA-expressing B cells in blood of RA patients secreted elevated levels of pro-inflammatory cytokines, in particular IL-8, upon stimulation and did so spontaneously as differentiated plasmablasts/-cells in synovial fluid. Notably, ACPA-expressing B cell-derived IL-8 induced neutrophil migration in vitro.

Conclusion: Our findings provide first evidence that ACPA-expressing B cells are well equipped to activate T cells, actively differentiate into IL-8 producing plasmablasts and, hence, could attract neutrophils to the rheumatoid joint. These findings define important phenotypic and functional characteristics of autoreactive B cells in a prototypic human autoimmune disease. They point to a direct pathogenic role of ACPA-expressing B cells in the inflammatory disease process underlying RA and favour approaches that aim at their antigen-specific depletion.

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SAT0030 CITRULLINE-REACTIVE B CELLS ARE PRESENT IN INFLAMED GINGIVAL TISSUE AND DISPLAY CROSS-REACTIVITY BETWEEN BACTERIAL AND HUMAN ANTIGENS

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Background: Antibodies targeting citrullinated proteins (ACPA) are highly specific for rheumatoid arthritis (RA). However, the etiology and molecular basis for ACPA production is still unclear. Based on an epidemiological association between RA and periodontitis (PD), and the unique ability of the oral pathogen *P.gingivalis* (*Pg*) to express a PAD enzyme that can citrullinate both bacterial and human proteins, it has been hypothesised that the ACPA response may be triggered in the gum mucosa in response to *Pg*.

Objectives: The main purpose of this study was to investigate if citrulline-reactive B cells reside in inflamed gingival tissue, and to examine ACPA cross-reactivity between citrullinated bacterial and human epitopes on a monoclonal level.

Methods: Using a single-cell antibody cloning approach, 55 recombinant monoclonal antibodies (mAbs) were generated from gingival tissue (GT) CD19+ B cells (n=1 ACPA+ RA/PD patient). Citrulline reactivity was determined using the anti-CCP2 kit (EuroDiagnostica AB), and in-house peptide ELISAs (including a citrullinated peptide derived from *Pg* PAD (CPP3) and citrullinated peptides derived from human α-enolase, fibrinogen, vimentin, fillaggrin and histone 4). Reactivity against CCP2 and CPP3 was also investigated in: 19 mAbs from bronchoalveolar lavage (BAL) CD19+ B cells (n=2 ACPA+ RA patients); 29 mAbs from bone marrow (BM) plasma cells (n=4 ACPA+ RA patients); 142 mAbs from synovial fluid (SF) plasma cells (n=5 ACPA+ RA patients); and 36 mAbs from peripheral blood memory/plasma cells (n=4 ACPA+ RA patients). Predicted germline versions were produced for two of the mAbs.

Results: Among 55 GT mAbs, 14 unique clones (25%) were reactive to the bacterial CPP3-peptide. We also detected CPP3-reactive mAbs from BAL (n=9/19), BM (n=3/29), SF (n=1/142) and peripheral blood (n=1/36). Interestingly, 11 out of 28 (39%) CPP3-reactive clones also bound citrullinated peptides derived from human proteins. Notably, three of these clones were positive in the clinical anti-CCP2 test, and when converted back to the predicted germline sequence, these clones became CCP2 negative, while maintaining reactivity against the bacterial CPP3 peptide.

Conclusion: Our data show that B cells reactive with a citrullinated peptide derived from *Pg* PAD are present in gingival tissue, lungs, bone marrow, blood and the inflamed joint of ACPA+ RA patients. Moreover, the finding that a number of these clones are cross-reactive with citrullinated peptides derived from human proteins as well as the gold standard CCP2 test suggests mechanisms of molecular mimicry in the generation of ACPA. Importantly, the germline versions of these ACPA were *Pg*-reactive but not autoreactive, supporting the hypothesis of a bacterial origin for this ACPA response.

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SAT0031 **VITAMIN B3 (NAM) SUPPRESSES T CELL ACTIVATION IN AND PRODUCTION OF PRO-INFLAMMATORY CYTOKINES IN VITRO IN A DOSE DEPENDENT MANNER INDICATING THERAPEUTIC POTENTIAL FOR THE TREATMENT OF JIA**

Lotte Nijhuis[1], Renee van de Wetering[1], Isabelle Houtzager[1], Arief Lalmohamed[2], Sebastian Vastert[3], Jurg van Loosdregt[1]. [1]*University Medical Center Utrecht, Laboratory of Translational Immunology, Utrecht, Netherlands*; [2]*University Medical Center Utrecht, Clinical pharmacy, Utrecht, Netherlands*; [3]*University Medical Center Utrecht, Pediatric Rheumatology and Immunology, Utrecht, Netherlands*

Background: Impaired immunological tolerance in Juvenile Idiopathic Arthritis (JIA) is the result of a disturbed balance between regulatory T-cells (Tregs) and effector T-cells (Teffs). Restoring this balance by either enhancing the suppressive function of Tregs or inhibiting activity of pro-inflammatory Teffs seems a promising therapeutic strategy. We have previously demonstrated that high concentrations of Vitamin B3 (VitB3), also known as nicotinamide (NAM), lead to an increase in FOXP3 positive cells *in vitro*, via suppression of the deacetylase SIRT1. Because the transcription factor FOXP3 is essential for Treg function, this approach could promote immunological tolerance. We now aim to translate these laboratory findings into clinical practice and envision a role for VitB3 as a novel therapeutic strategy for patients with JIA. However, while VitB3 has promising effects on Tregs, the effect of VitB3 on Teff cells, the other side of the scale, is still unexplored.
Objectives: To investigate the effect of VitB3/SIRT1 inhibition on proliferation, activation, cytokine production and TCR signaling of Teff cells.
Methods: T-cells were isolated from the blood of healthy controls and JIA patients, as well as from the synovial fluid from JIA patients. Cells were stimulated with aCD3/aCD28 and cultured in the presence of increasing concentrations of VitB3 (0-9mM) for 1-4 days. Proliferation and expression of activation makers in primary T cells were determined using flow cytometry. Cytokine production was determined by qPCR, Luminex and flow cytometry. ERK phosphorylation was measured by flow cytometry and Western blot. ERK phosphorylation and GFP expression were also determined by flow cytometry using a murine NFAT-GFP reporter celline.
Results: *In vitro* VitB3 treatment of JIA patient CD4+ Teff-cells significantly decreased the production of the pro-inflammatory cytokines IL-2 and IFNy measured both on mRNA and protein level. Correspondingly, surface activation markers were downregulated after VitB3 incubation, and ERK phosphorylation was decreased. Furthermore, proliferation of both CD4+ and CD8+ T-cells was inhibited with VitB3 treatment in a dose dependent manner. Murine reporter cells showed similar results. Experimental outcomes were verified using another SIRT1 inhibitor; EX-527.
Conclusion: In addition to the previously demonstrated increase of Treg numbers and functioning, this data demonstrates that VitB3 treatment also inhibits proliferation and activation of Teff cells *in vitro*. VitB3 treatment could therefore modulate the immunological balance by both increasing tolerance and suppressing immune activation. We envision that VitB3 treatment as an adjuvant therapy has the potential to benefit JIA patients and potentially patients with other autoimmune diseases. To assess the clinical relevance of these findings, we are currently in the preparation of a phase III clinical trial.
Disclosure of Interests: None declared
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SAT0032 **ACTIVATION OF TH LYMPHOCYTES ALTERS THE PATTERN EXPRESSION AND CELLULAR LOCATION OF VIP RECEPTORS IN HEALTHY DONORS AND EARLY ARTHRITIS PATIENTS**

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Background: $CD4^+$ T helper (Th) cells are decisive in the struggle against pathogens and in the maintenance of immune homeostasis. Their activation and differentiation can take many forms and generate immune memory in which the extracellular environment plays a critical role in both homeostatic and pathological states. VIP is one of the best-studied neuropeptides with anti-inflammatory and immunomodulatory actions in normal and pathological conditions (1,2,3). There are evidences that VIP may have therapeutic effects for human Rheumatoid arthritis and might be used as a prognostic marker for this disease (3,4). However, there are no deepen studies related to the expression pattern, cellular location, signalling pathways and functionality of its receptors ($VPAC_1$ and $VPAC_2$) during the activation of Th cells. Further in-depth studies of their behavior can contribute to the design of new therapies based on their activation and/or blockade.
Objectives: To describe the expression pattern, cellular location and functional role of VIP receptors, $VPAC_1$ and $VPAC_2$, during the activation of human memory Th cells in healthy conditions and in early arthritis (EA).
Methods: Human memory Th cells were isolated from healthy donors (HD) and EA patients. Two experimental conditions, resting state and *in vitro* activation, were used. Cells were activated (anti-CD3/CD28) and cultured in presence or absence of VIP or specific VPAC receptors agonists. Cellular location of VPAC receptors was examined by western-blot and confocal microscopy, and their mRNA levels were analyzed by semi-qPCR. Cytokines, transcription factors and cell markers related to pathogenic profile of Th cells were analyzed by semi-qPCR, ELISA and flow cytometry. To study the signalling pathways, pull-down assays (Rap1), western-blot (CREB) and ELISA (cAMP) were performed. Expression of different chemokines were analyzed by flow cytometry whereas cell migration assays were performed using transwell membranes.
Results: The protein expression pattern of $VPAC_1$ did not change with the activation of Th lymphocytes, whereas $VPAC_2$ was up-regulated. In resting cells, $VPAC_1$ receptor was located on the plasma membrane and nucleus, while it only appeared in the nucleus in activated cells. $VPAC_2$ was always found in plasma membrane location. VIP receptors signalled through a PKA-dependent pathway in both conditions, and also through a PKA-independent pathway in activated cells. VIP receptors agonists decreased the pathogenic profile during the activation of Th lymphocytes. Similar results were observed in Th lymphocytes from EA patients.
Conclusion: VIP is an important immunomodulator of $CD4^+$ T cells in normal and pathological conditions. Our data revealed a change in the expression pattern and cellular location of its receptors (VPAC) during the activation of these cells, giving a wider range of possibilities to dissect its cellular and molecular mechanisms, that would provide new therapies or targets as activity markers in inflammatory/autoinmune diseases.

REFERENCES

[1] Gomariz RP, et al., Ann NY Acad Sci USA. 2006; 1070: 51-74
[2] Jimeno R, et al. J Leuk Biol. 2015; 98(2): 257-269.
[3] Villanueva-Romero R, et al. J Immunol Res. 2018; 6043710.
[4] Martínez C, et al. Plos One. 2014; 9(1): e85248

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SAT0033 **TCR REPERTOIRE PROFILING OF SYNOVIAL FLUID OF HLA-B*27+ AND HLA-B*27- PATIENTS WITH PSORIATIC ARTHRITIS**

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Background: Diagnosis of psoriatic arthritis (PsA) is primarily based on clinical phenotype because of the diversity of the associated features [1]. The heterogeneity likely implies different mechanisms of the disease progression or initiation. Certain HLA alleles have been shown as risk factors for different spondyloarthropathies (SpAs), implying role of T cells in the pathogenesis. The most prominent association have been shown for HLA-B*27 allele with ankylosing spondylitis (AS), giving raise to the arthritogenic peptide theory of the disease initiation. Recently, using deep TCR profiling, new data supporting potential role of CD8+ T cells in AS have been published by our group and others [2,3]. Despite heterogeneous phenotype 24% of patients from combined cohort of AS and PsA fulfill both CASPAR and modified new-york criteria [4]. Also there is known tendency for axial disease in HLA-B*27+ PsA patients
Objectives: Here we for the first time applied deep TCR profiling to study T cell repertoire of inflamed joints of patients with PsA, to characterise the similarity in clonal composition between patients in presence and absence of HLA-B*27

Methods: We collected paired PB and SF samples from HLA-B*27+ (n=5) and HLA-B*27- (n=7) patients. All patients fulfilled the CASPAR criteria. TCR beta profiling for total P/SFMC samples and T cell subsets was performed using high throughput sequencing of 5'-RACE double-barcoded TCR beta cDNA libraries following by repertoire reconstruction with molecular barcode-based error correction [5]
Results: Clonal diversity in SF was largely restricted compared to PB, with significant enrichment of mostly expanded SF clonotypes compared to PB, suggesting antigen-driven migration and expansion of the T cells into inflamed site. Major clonal expansions of SF were private for each patient, yet SF shared significantly more clonotypes than PB independently from HLA-B*27 status. Most important, in CD8+ subsets from PB and SF we identified the previously described AS-associated T-cell clonotypes. These clonotypes were detected in SF of all HLA-B*27+ patients but not in samples from HLA-B*27- patients, suggesting the HLA-B*27 restriction of the TCR beta motif. The clonotypes were enriched in SF compared to PB, representing up to 1.6% of CD8+ SF T cells. All HLA-B*27+ patients had several variants of the TCR beta clonotypes in SF, suggesting the selection of the TCRs during disease development
Conclusion: Our results further support the supposed role of the CD8+ T cells in SpAs and suggest that similarity of clinical phenotype between AS and HLA-B*27+ PsA patients could be associated with autoimmune response to similar antigens, represented by HLA-B*27 molecule

REFERENCES

[1] Veale D. J. and Fearon U. (2018) 'The pathogenesis of psoriatic arthritis', Lancet (London, England). Elsevier Ltd, 391(10136), pp.2273–84
[2] Faham M. et al. (2016) 'Discovery of T-Cell Receptor Beta Motifs Specific to HLA-B27 + Ankylosing Spondylitis by Deep Repertoire Sequence Analysis', Arthritis & Rheumatology, 11(10), pp.300–8
[3] Komech E. A. et al. (2018) 'CD8+ T cells with characteristic T cell receptor beta motif are detected in blood and expanded in synovial fluid of ankylosing spondylitis patients', Rheumatology (Oxford), 57(6), pp.1097–104
[4] Jadon D. R. et al. (2017) 'Axial Disease in Psoriatic Arthritis study: Defining the clinical and radiographic phenotype of psoriatic spondyloarthritis', Annals of the Rheumatic Diseases, 76(4), pp.701–7
[5] Zvyagin I.V. et al. (2017) 'Tracking T-cell immune reconstitution after TCRαβ/CD19-depleted hematopoietic cells transplantation in children', Leukemia, 31(5), pp.1145-53

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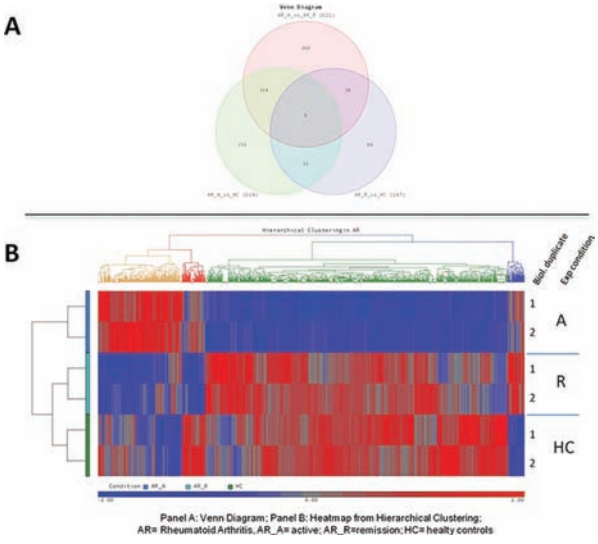
Rheumatoid arthritis – etiology, pathogenesis and animal models

SAT0035

IS PHARMACOLOGICAL CLINICAL REMISSION SYNONYMOUS WITH BIOLOGICAL INACTIVE DISEASE? DIFFERENTIAL GENE EXPRESSION ANALYSIS IN RHEUMATOID ARTHRITISAND HEALTY CONTROLS

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Background: Remission is an important goal of therapy in rheumatoid arthritis (RA), but data on molecular players of clinical remission and effective disease inactivation are scarce. Gene expression profiling analysis is useful to elucidate the pathogenic mechanisms of diseases, and differential gene expression analysis between diverse disease conditions produces gene signatures characteristic of the state or disease being studied.
Objectives: Our aim was to compare the transcriptional profiles of patients with clinically active versus inactive (remission state) RA, and healthy controls (HCs).
Methods: From a cohort of around 1000 patients affected by RA according to ACR-EULAR 2010 criteria, we first selected 20 patients with active disease state (without biologic treatment ongoing) (A) and 20 patients with >1-year remission induced by TNFα antagonism (Etanercept) (R), as assessed by DAS28(PCR) scores, and from 20 HCs matching for age and gender ratio. Both RA groups were not on corticosteroid treatment. RNA from peripheral blood was extracted and, following quality analysis by Agilent Bioanalyzer, each condition has been profiled using RNAs pools in biological duplicates by distinct Affymetrix Human GeneChip HTA 2.0, for a total of 6 arrays. Data analysis was performed using the commercial software Partek Genomics Suite, V 6.6. To identify a transcript as differentially expressed, a value of fold change 1.5 and *p-value* 0.05 has been set.
Results: The Venn diagram shows all comparative groups (A vs R, A vs HC, R vs HC) with their relative amount of transcripts differentially expressed, generated using abovementioned parameters, and the relationship between sets (fig1, panel A). Using the list of transcripts differentially expressed in at least one of the aforementioned comparison, a hierarchical clustering was carried out to view the intra-condition expression profile. Here, we have identified (arbitrarily) 4 clusters of transcripts with analogous transcriptional profile and to each of them a color code has been assigned (Heatmap in Fig1, panel B). For these clusters and for all lists of transcripts differentially expressed founded by our comparative study, we carried out the Gene Set Enrichment Analysis by Gene Ontology (GO), in order to identify how molecular functions, cellular components or biological processes occurs more frequently than expected in a reference list of transcripts.
Conclusion: Considering the amount of differentially expressed transcripts and the hierarchical clustering analysis, is evident that the drug-induced remission (R) is more similar with HCs condition, while active disease state (A) has a different profile; however "similar" profile does not mean "identical". In fact, the Gene Set Enrichment Analysis Score showed us that mRNA transcripts dysregulated in the R condition vs HCs, are involved in several biological processes regarding the immune system, response to stimulus, biological regulation, locomotion and others. Our next step will be to validate, by Real Time PCR in a large cohort of patients, the most interesting dysregulated genes covering biological functions eventually sustaining disease activity.



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SAT0036 **IMPACT OF RHEUMATOID ARTHRITIS IN LIVER DAMAGE. INVOLVEMENT OF ANTI-CITRULLINATED PROTEIN ANTIBODIES**

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Background: Liver damage in rheumatoid arthritis (RA) is most common in the form of asymptomatic abnormal liver biopsies. It is difficult to differentiate between hepatic manifestations of the primary disease and potential hepatotoxicity of the therapies. Inflammation, oxidative stress, apoptosis and loss of lipid droplets are involved in the hepatic fibrogenesis

Objectives: 1)To analyze the impact of RA in the liver function and 2)To evaluate the direct effect of anti-citrullinated protein antibodies (ACPAs) in the liver fibrosis.

Methods: 150 RA patients and 100 healthy donors (HD) were included. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), phosphatase alkaline (ALP), albumin and levels of autoantibodies and inflammatory markers were evaluated in serum. **In vitro studies:** Hep G2 cells were treated with IgG-ACPAs isolated from RA patients. Molecules involved in lipid metabolism, insulin resistance, oxidative stress and inflammation were analyzed by RT-PCR and Western blot. Activation of intracellular pathways involved in fibrogenesis were analyzed. Lipid accumulation was evaluated by fluorescence microscopy. **Mouse model:** 20 CB57J/BL mice were used; 5 mice were used as non-diseased group, and 15 were used in CIA modelling. Liver samples were collected. Genes involved in insulin signal, lipid accumulation, macrophage infiltration and polarization and inflammation were evaluated. Activation of intracellular pathways related to fibrogenesis were analyzed. Immunohistochemistry was used to evaluate the percentage of fibrotic cells.

Results: Within the normal range of hepatic enzymes, the percentage of RA patients with levels of AST, ALT and ALP above the mean was significantly higher compared to HD. In contrast, percentage of RA patients displaying levels of albumin bellow the mean was significantly elevated compared to HD. Differences remained significant after adjusting for potential confounders (treatment). Moreover, high levels of AST and ALT were associated with ACPAs and inflammatory markers. IgG-ACPAs induced the expression of inflammatory and oxidative stress markers and decreased genes involved in insulin signal and lipid accumulation in Hep G2 cells. In addition, lipid content decreased after IgG-ACPAs treatment. The phosphorylation of intracellular pathways involved in fibrogenesis was modulated by Ig-ACPAs.The induction of arthritis in mice elevated inflammatory cytokines and markers of macrophages presence and polarization state M1 and reduced genes related to lipid droplets in the liver. Phosphorylation of ERK and mTOR was increased in the liver of CIA mice. Additionally, the percentage of cells positive for α-smoth muscle antibody was increased in the liver of CIA mice.

Conclusion: (1) RA patients displayed a subclinical alteration of the hepatic enzymes levels associated with levels of autoantibodies ACPAs, which may suggest that RA is associated with an abnormal liver function induced by autoantibodies. (2) ACPAs may induce alterations in hepatic cells, increasing inflammation and oxidative stress, reducing lipid accumulation and activating intracellular pathways, processes closely involved in fibrogenesis. (3) In a CIA mice, arthritis induced inflammation, infiltration of macrophages, reduction of genes involved in lipid accumulation and activation of intracellular pathways involved in fibrogenesis

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SAT0037 **INCREASED CARDIOMETABOLIC RISK FACTORS ARE RELATED TO THE ABNORMAL ADIPOCYTOKINE PROFILE AND AUTOIMMUNITY IN RHEUMATOID ARTHRITIS. MODULATION BY TNFALPHA AND IL6R INHIBITORS**

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by excess morbidity and mortality from cardiovascular disease. In addition, metabolic alterations have been observed in these patients, which significantly contributes to the cardiovascular risk burden. Thus, the identification of therapies able to mitigate the cardiometabolic alterations in RA is essential. In addition, numerous studies suggest that cardiometabolic risks are mediated through adipocytokines. However, this relationship is not completely defined in RA.

Objectives: 1) To evaluate the relationship among cardiometabolic risk factors and the levels of adipocytokines and autoantibodies in RA patients. 2) To analyze the effects anti-TNFα and anti-IL6 therapies on the cardiometabolic alterations.

Methods: 1.- A cross-sectional study including 100 RA patients and 50 age-matched healthy donors was carried out. Different parameters related to the cardiometabolic risk were analyzed, including: lipid profile, atherogenic index, ratio ApoB/ApoA, insulin resistance (IR), obesity, hypertension, and the SCORE. Levels of adipocytokines (TNFα, IL6, IL1β, visfatin, adiponectin, leptin and resistin) were evaluated in serum. Carotid intima media thickness (CIMT) was evaluated as atherosclerosis marker. 2.-A prospective study in 15 RA patients before and after 3 months of anti-TNFα therapy and 15 RA patients before and after 3 months of treatment with tocilizumab (TCZ) was performed. All the parameters evaluated in the cross-sectional cohort were tested in this prospective study.

Results: RA patients had elevated levels of leptin/adiponectin ratio, visfatin, resistin and inflammatory markers in serum. Our cohort of RA patients displayed increased rates of cardiometabolic risk factors, such as insulin resistance, hypertension, SCORE, pathologic CIMT, atherogenic index and ratio apoB/apoA. The alteration in the levels of adipocytokines were closely related to the autoimmunity, disease activity and clinical inflammatory markers. Of note, visfatin and C3 complement levels were determinant for IR, high levels of SCORE, increased parameters of CVD risk defined by apoB/apoA ratio and pathologic CIMT.

Both biological therapies reduced clinical inflammatory markers and disease activity after 3 months of treatment. Anti-TNFα therapy modulated the cytoadipokine profile, reducing serum levels of IL-6, IL-1β, resistin and visfatin, decreasing IR.

After treatment with tocilizumab, serum levels of C3 complement, IL-1β and resistin were reduced.

Conclusion: 1) Altered adipocytokine profile is closely related to the increased cardiometabolic risk factors associated with RA, where autoimmunity and systemic inflammation play a key role. 2) Anti-TNFα and anti-IL6R therapies, administered for 3 months, could have beneficial effects in the reduction of cardiometabolic risk factors in RA.

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SAT0038 SEMAPHORINS: FROM ANGIOGENESIS TO INFLAMMATION IN RHEUMATOID ARTHRITIS

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Background: Synovial neoangiogenesis is an early and crucial event to promote the development of the hyperplasic proliferative pathologic synovium in rheumatoid arthritis (RA). A recent microarray analysis of Endothelial cells (ECs) issued from patients with RA and matched controls has revealed a differential expression of semaphorin family in RA ECs, which is known to contribute to angiogenesis and autoimmunity/ inflammation.
Objectives: Our aim was to study the potential implication of semaphorins in RA pathogenesis.
Methods: mRNA levels of class 3 and 4 Semaphorins (SEMA) SEMA3A, SEMA3E, SEMA4A and SEMA4E, as well as their receptors PlexinD1 (PLXND1) and Neuropillin-1 (NRP1), were measured by real-time quantitative PCR in RA (n = 15) and control (n = 15) ECs. Protein expression of these 4 semaphorins and their receptors was evaluated in ECs of 10 RA patients and controls by western blot, and in the synovial tissue of 10 RA patients and 5 controls by immunohistochemistry and immunofluorescence. Serum concentrations of these 4 semaphorins were measured by sandwich ELISA in a cohort of 130 patients with RA (85% women, mean age: 58 ± 12 years and mean disease duration: 11 ± 12 years) and 30 age- (56 ± 10 years) and sex- (82% women) matched controls.
Results: SEMA4A, SEMA3E and their receptors PLXND1 and NRP1 mRNA (Real time quantitative PCR) and protein (western blot analyses) levels were found to be markedly increased in RA ECs compared to control ECs. The expression of SEMA4A, SEMA3A, SEMA3E, PLXND1 and NRP1 was strikingly increased in the synovial tissue of patients with RA. Confocal microscopy with double labeling for CD31 confirmed the prominent endothelial expression of these class 3 and 4 semaphorins and their receptors. SEMA3A serum levels were significantly lower in RA compared to controls (13.93±5.69 vs. 18.29±6.69 ng/mL, P<0.001). Levels of SEMA3E (1.21±0.884 vs. 0.78±0.80 ng/mL, P=0.041), SEMA4A (65922 ±27109 vs. 53189±25808 pg/ml, P=0.010) and SEMA4D (3.59±3.39 vs. 1.90±3.95 ng/mL, P=0.012) were significantly increased in patients with RA compared to controls. In patients with RA, SEMA3A, SEMA4A and SEMA 4D correlated with CRP levels (r=-0.36, P<0.001, r=0.39, P<0.001 and r=-0.31, P=0.001, respectively). SEMA4A and 4D correlated with the Disease Activity Score (DAS)-28, (r=0.27, P=0.006 and r=-0.23, P=0.020, respectively). SEMA3A, SEMA4A and SEMA4D also correlated with the Global OMERACT-EULAR Synovitis Score, reflecting the intensity of synovial vascularization measured by power Doppler ultrasound (r=-0.22, P=0.023, r=0.21, P=0.030 and r=-0.242, P=0.013, respectively). In addition SEMA4A and SEMA3E correlated with serum levels of the angiogenic markers Tie-2, angiopoietin, Interleukin-8 and soluble Vascular Cell Adhesion Molecule.
Conclusion: Gene expression profiling of ECs identified semaphorins as potential biomarkers and therapeutic candidates in RA. Class 3 and 4 semaphorins are overexpressed in ECs, synovial vessels and the serum of patients with RA. They also correlated with validated markers of inflammation and angiogenesis. Thus, semaphorins might be novel and appealing EC-derived inflammatory and proangiogenic targets in RA.
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SAT0039 ZAP-70 CONTROLS AUTOIMMUNE ARTHRITIS VIA REGULATION OF APOPTOSIS THROUGH BCL-2, BIM AND CBL IN T CELLS

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Background: The recombinant human G1(rhG1)-induced mouse arthritis (GIA) model resembles human rheumatoid arthritis in many aspects[1]. Similarly, to RA, GIA is also a T cell dependent disease: T cell activation and apoptosis has been shown to regulate arthritis severity[2]. ZAP-70 kinase is a key molecule of T cell receptor signaling, in its absence T cell differentiation and activation is seriously hindered[3]. In preliminary experiments, we found that partial ZAP-70 deficiency (in ZAP-70$^{+/-}$ heterozygous mice) ameliorated autoimmune arthritis in the GIA model, supported by both *in vivo* (decreased severity and milder arthritis) and *in vitro* tests (decreased T cell proliferation, IL-4 and IL-6 production).
Objectives: In the present work we wanted to test the hypothesis that the observed changes in GIA in partial ZAP-70 deficient mice are due to complex alterations in T cell apoptosis.
Methods: T cells were isolated from healthy and arthritic BALB/c and ZAP-70 heterozygous (ZAP-70$^{+/-}$) knockout mice, then stimulated *in vitro* for 72 hours with anti-CD3/anti-CD28-coated beads. After stimulation, cells were lysed and the homogenates were subjected to Western-bloting using antibodies against activated Caspases-3,-8, and -9, respectively, and other apoptotic markers (cytochromeC), and some important regulator molecules (Bcl-2, Bim and Cbl).
Results: Overall, as expected, we have seen decreased tyrosine phosphorylation in the T cells of arthritic ZAP-70$^{+/-}$ mice compared to the controls. The levels of cleaved (activated) Caspase-8 and -9 were comparable in ZAP-70$^{+/-}$ samples to the controls, however, we detected elevated levels in case of Caspase-3. There was slightly lower Cytochrome C release and Bcl-2 and Bim levels in the activated T cells of ZAP-70$^{+/-}$ mice. Importantly, there was markedly less Cbl-b in the T cells of arthritic ZAP-70$^{+/-}$ mice.
Conclusion: Our results show the complex changes in the apoptotic pathways of activated T cells caused by the partial deficiency of ZAP-70. Impaired T cell activation through the T cell receptor complex, as shown by decreased phosphorylation, accompanied by slightly increased apoptosis sensitivity of T cells (stronger Caspase-3 signal) might explain the less severe arthritis seen in ZAP-70$^{+/-}$ mice. Furthermore, based on these results Cbl-b (a negative regulator of T cell activation) might serve as an important early molecule interacting with ZAP-70 and thus fine regulate T cell activation and apoptosis in autoimmune arthritis.

REFERENCES

[1] Glant TT, Radacs M, Nagyeri G, Olasz K, Laszlo A, Boldizsar F, Hegyi A, Finnegan A, Mikecz K. Arthritis Rheum. 63(5):1312-21., 2011
[2] Hanyecz A, Olasz K, Tarjanyi O, Nemeth P, Mikecz K, Glant TT, Boldizsar F. Biomed Res Int. 2014:942148., 2014
[3] Kadlecek TA, van Oers NSC, Lefrancois L, Olson S, Finlay D, Chu DH, Connolly K, Killeen N, Weiss A. J Immunol. 161:4688-4694; 1998

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SAT0040 PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA COACTIVATOR-1B FACILITATES PSEUDOPODIA FORMATION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS VIA ACTIVATING RHO GTPASES

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Background: Fibroblast-like synoviocytes (FLS) play critical roles on joint inflammation and destruction of cartilage and bone in rheumatoid arthritis (RA) due to their aggressive behavior including increased migration. The Rho family of small GTPases are the master regulators of actin cytoskeleton remodeling which leads to pseudopodia formation and migration. Peroxisome proliferator-activated receptor-gamma coactivator-1 (PGC-1) β is a transcriptional regulator which plays important roles on regulating multiple signaling pathways. Our previous study revealed that elevated PGC-1β in RA-FLS promoted their migration and invasion. However, the underlying mechanism remains elusive.
Objectives: To investigate the role of PGC-1β on regulating pseudopodia formation of RA-FLS and its underlying mechanism.
Methods: Synovial tissues were obtained from six patients with active RA and FLS were isolated and cultured in vitro. RA-FLS were transfected with a lentivirus vector for PGC-1β knockdown or over-expression, and transfected with same lentivirus vectors marked Lv-sh-GFP or Lv-GFP as negative controls. The change of cytoskeleton was stained with fluorescent phalloidin to visualize polymerized actin in lentivirus transfected RA-FLS. The mRNA expression of RhoA, Rac1, and Cdc42 was measured

by qPCR. Their activity was measured using a Rac1, RhoA or Cdc42 Pulldown & G-Lisa Activation Assay Kit.
Results: 1) PGC-1β knockdown inhibited lamellipodia and filopodia formations of RA-FLS compared with Lv-sh-GFP transfection group (cells with lamellipodia: 24% ± 7% vs. 40% ± 5%, *P*=0.035; cells with filopodia: 34% ± 9% vs. 49% ± 4%, *P*=0.041), while PGC-1β over-expression promoted lamellipodia and filopodia formations of RA-FLS compared with Lv-GFP transfection group (cells with lamellipodia: 50% ± 4% vs. 34% ± 6%, *P*=0.040; cells with filopodia: 67% ± 7% vs. 52% ± 6%, *P*=0.045, Figure 1A).
2) PGC-1β knockdown or over-expression did not affect the mRNA expression of Rac1, RhoA or Cdc42 (all *P*>0.05, Figure 1B). However, PGC-1β knockdown suppressed the activity of Rac1, RhoA and Cdc42 (Pulldown assays: 65%~78% reduction; G-LISA assays: 28%~53% reduction, all *P*<0.05), while PGC-1β over-expression significantly increased their activity (Pulldown assays: 1.55~1.72 folds; G-LISA assays: 1.43~1.68 folds, all *P*<0.05, Figure 1C, D).
Conclusion: Our findings revealed that elevated PGC-1β in RA-FLS promoted pseudopodia formation by activating Rho family proteins which imply a novel target on regulating RA-FLS migration.

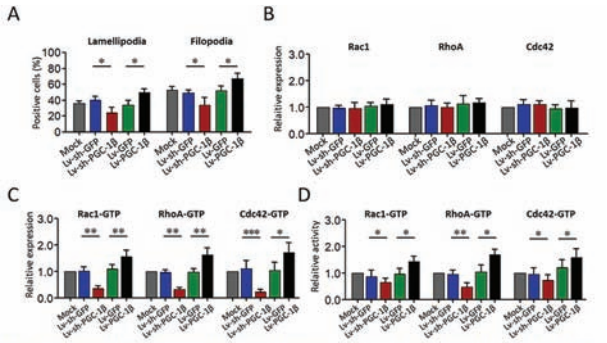


Figure 1 Effects of PGC-1β on pseudopodia formation and the activity of Rho GTPases in RA-FLS. RA-FLS were transfected with lentivirus for PGC-1β knockdown or over-expression. **(A)** Comparison of lamellipodia and filopodia formations by F-actin staining in RA-FLS. **(B)** The mRNA expression of Rac1, RhoA and Cdc42 was measured by qPCR. **(C)** The activity of Rac1, RhoA and Cdc42 was measured by Pulldown assays. **(D)** The activity of Rac1, RhoA and Cdc42 was measured by G- LISA assays. Data were representative as means ± SD, **P*<0.05, ***P*<0.01, ****P*<0.001.

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SAT0041 GENOTYPE OF THE RHEUMATOID ARTHRITISSEVERITY LOCUS, RS26232, IS ASSOCIATED WITH INVASIVENESS OF RASFS IN VITRO

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Background: The single nucleotide variant rs26232 has been associated with both the susceptibility to, and severity of, rheumatoid arthritis (RA). There is an allele dose response between rs26232 and radiological damage, with the minor, T, allele being protective against disease severity. Rs26232 is situated in the first intron of C5orf30, which is a negative regulator of tissue damage and inflammation in RA.
Objectives: The objective of this study is to elucidate the mechanism by which rs26232 may mediate disease severity. We also aimed to determine the genotype-phenotype association of rs26232 in rheumatoid arthritis synovial fibroblasts (RASF).
Methods: RASF were derived from knee biopsies of RA patients taken at arthroscopy (n=33). RASFs were used between passages 3-8. Matrigel-coated Boyden transwell chambers were used to measure invasion. Wound healing (scratch assays) were used to measure migration, whereas proliferation was measured via crystal violet staining of fixed RASF. Intracellular cytokine staining and cell surface markers were measured via flow cytometry. Secreted cytokines were measured in the supernatant of RASF using ELISA. Rs26232 genotype was determined by PCR genotyping assay with allelic discrimination analysis. Anticitrullinated protein antibody (ACPA) status was measured for each participant. Quantitative real-time PCR was used to measure gene expression. Mann-Whitney U test was used to compare two independent groups, Kruskal-Wallis test was used to compare groups of greater than two.
Results: 49% (n=16) of our RASF cohort where homozygous for the major allele CC, 42% (n=14) were heterozygous CT, 9% (n=3) were TT. Rs26232 is associated with invasion of RASFs with the CC genotype being more invasive than the CT genotype (p=0.021). RASFs with the CC genotype had increased ICAM1 and VEGF cell surface expression compared to CT genotype (p=0.001, p=0.05 respectively). MCP1/CCL2 was decreased in CC compared to CT (p=0.013). No association was found between rs26232 genotype and migration, proliferation, or expression of MMP3, TIMP3, IP10 or MIP1a.
rs26232 is located in the first intron of C5orf30. There was no differential expression of total C5orf30 or with any of the 3 individual transcript variants in rs26232 genotype groups. In silico analysis of the region in which rs26232 is located on chromosome 5 identified a DNase Hypersensitivity cluster. Furthermore, mining of the Genotype-Tissue Expression (GTEX) expression quantitative trait loci (eQTL) database revealed a cluster of genes located upstream on chromosome 5 (102,850,000-103,150,000) associated with rs26232. This region upstream from rs26232 contains 4 genes (EIF3KF1, PPIP5K2, PAM and GIN1), of which three are eQTLs of rs26232. In silico analysis revealed that the 3 eQTLs (EIF3KF1, PPiP5K2 and PAM) also contain the active enhancer mark H3K27Ac, whereas GIN1 does not.
Conclusion: The CC genotype of rs26232 is associated with both increased invasiveness of RASFs and increased adhesion markers compared to CT genotype. Rs26232 does not mediate its affect via its nearest gene, *C5orf30*. Rather, in silico analysis predicts rs26232 may function as a distal regulator of *EIF3KF1*, *PPIP5K2* and *PAM*. Future work will test the hypothesis that rs26232 genotype phenotype association is mediated by EIF3KF1, PPIP5K2 and PAM.
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SAT0042 TWO POPULATIONS OF PD-1HICD4 T CELLS WITH DISTINCT B CELL HELPING CAPACITY, ARE ELEVATED IN THE PERIPHERAL BLOOD OF PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: A novel population of B helper cells, phenotypically CD4 +CXCR5-PD-1^{hi}, has been described in the synovial tissues and peripheral blood of seropositive RA patients with an established disease, and termed 'peripheral helper' (Tph) cells. Contrary to CD4+CXCR5+PD-1^{hi} follicular helper T (Tfh) cells, Tph cells are not located in lymphoid organs but accumulate in inflamed tissues. The frequency and kinetics of circulating Tph cells have not been examined in patients with early, untreated RA.
Objectives: To study the frequency of circulating Tph (cTph) cells, and also of circulating Tfh cell counterparts (cTfh), in patients with early RA (eRA).
Methods: Peripheral blood was drawn from DMARD-naïve early RA patients (2010 ACR criteria) with a disease duration < 24 weeks (n=48). For each patient, an age and gender-matched healthy control was also studied (HC, n=48). After isolation by Ficoll-Hypaque gradient, freshly isolated PBMCs were stained with antibodies to CD3, CD4, CXCR5, ICOS, PD-1 and CCR2, and examined by flow cytometry. Autologous cocultures of naïve or memory B cells were established with CXCR5 (+) or (-) memory CD4 T cells.
Results: Seropositive (RF+ and/or ACPA+, n=31) but not seronegative eRA patients (n=17), demonstrated increased frequencies and absolute numbers of cTph and cTfh cells. cTph but not cTfh cells expressed CCR2. Those eRA patients who experienced a significant clinical improvement at 12 months, demonstrated a marked reduction of their cTph whereas their cTfh cell numbers remained unchanged; at the same time, rheumatoid factor titres decreased significantly but ACPA (anti-citrullinated peptide antibodies) titres did not vary. Both CXCR5+ and CXCR5-CD4+ T cells were able to induce maturation of memory B cells, whereas only CXCR5+CD4+ T cells could differentiate naïve B cells.
Conclusion: Two populations of PD-1^{hi}CD4 T cells with distinct phenotype and B cell helping capacity, are increased in the peripheral blood of

seropositive eRA patients. Whereas cTph are related with disease activity, cTfh cells seem to be constitutively elevated.

REFERENCE

[1] Rao DA, et al. Nature 2017

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SAT0043 ANALYSIS OF THE ROLE OF RORΓT+FOXP3+ (TR17) IN THE REGULATION OF AUTOIMMUNE ARTHRITIS

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Background: RORγt$^+$Foxp3$^+$ regulatory T (Treg) cells, designated as Tr17 is one of the new subset of Treg cells, having the potential to regulate the development of experimental autoimmune encephalomyelitis (EAE) thorough a specific repression of Th17 mediated inflammation (1). The function of Tr17 remain unclear in the development of other autoimmune diseases such as collagen induced arthritis (CIA).
Objectives: To clarify the role of RORγt$^+$Foxp3$^+$ (Tr17) cells in the development CIA.
Methods: 1) Lymphocytes in draining lymph node (LN) were harvested from C57BL/6 mice on 10 days after immunization of type II collagen (CII) emulsified with complete Freund's adjuvant. The expression of RORγt in Foxp3$^+$Treg cells was analyzed by flow cytometry and compared them with lymphocytes of non-immunized mice. 2) At 10 days after CII immunization, C-C chemokine receptor type 6 (CCR6), CD25, cytotoxic T-lymphocyte antigen 4 (CTLA-4), and glucocorticoid-induced TNF-receptor (GITR) expression on Tr17, RORγt$^-$Treg cells, and RORγt$^+$non-Treg cells in LN were analyzed by flow cytometry. 3) Lymphocytes were harvested from Foxp3$^{IRES\text{-}gfp}$ reporter mice on 10 days after first CII immunization. CD4$^+$GFP$^+$ Treg and CD4$^+$GFP$^-$ T cells were isolated and stimulated with anti-CD3 monoclonal antibody (mAb) and anti-CD28 mAb *in vitro*. The expression of IL-10 and IL-17 in RORγt$^+$GFP$^+$ Tr17 cells was analyzed by flow cytometry and compared with that in RORγt$^-$GFP$^+$ cells or RORγt$^+$GFP$^-$ cells. 4) After the induction of CIA, lymphocytes in inflamed ankle joints and LN were harvested from C57BL/6 mice. The expression of RORγt in both Foxp3$^+$Treg cells and Foxp3$^-$ non-Treg cells were analyzed by flow cytometry. 5) Foxp3^{cre}RORγt$^{fl/fl}$ (conditional knock out; cKO) mice which deficit Tr17 cells were immunized with CII on days 0 and 21. Incidence and severity of CIA were analyzed and compered with Foxp3^{wt}RORγt$^{fl/fl}$ (control) mice. 6) At 10 days post first CII immunization. Lymphocytes from control mice and cKO mice were cultured with or without 100 μg/mL of denatured CII for 72 h. IL-17 and IFNγ levels in supernatants measured by ELISA.
Results: 1) Tr17 cells in draining lymph nodes were significantly increased in CII-immunized mice compared with non-immunized mice. 2) CCR6, CD25, CTLA-4, and GITR expression was elevated on Tr17 cells compared with RORγt$^-$Treg cells and Th17 cells. 3) IL-10 producing cells were significantly increased in Tr17 cells compared with RORγt$^-$Treg cells (12.57 +/- 1.135, $p < 0.001$). On the other hand, IL-17 producing cells was tended to be decreased in Tr17 cells in spite of the high expression of RORγt compared with RORγt$^+$Th17 cells (2.376 +/- 0.231, $p = 0.176$). 4) Tr17 cells and RORγt$^+$non-Treg cells were increased and Foxp3$^+$Treg cells were decreased in inflamed ankle joints compared with LN after the induction of CIA. 5) CIA tended to be exacerbated in cKO mice compared with control mice. 6) Production of IL-17 tended to be higher in cKO mice than in control mice.
Conclusion: Tr17 cells were increased in the course of CIA and infiltrated into inflamed joints. Moreover, Tr17 cells had the potential to regulate the development of CIA thorough the high expression of suppressive molecules such as IL-10 and CTLA-4.

REFERENCE

[1] Byong-Seok K. et al. Generation of RORγt$^+$ Antigen-Specific T Regulatory 17 Cells from Foxp3$^+$ Precursors in Autoimmunity. Cell Reports. 2017. 21, 195-207

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SAT0044 HIGH THERAPEUTIC EFFICACY OF ORAL RAS INHIBITORS IN COLLAGEN INDUCED ARTHRITIS: INHIBITION OF RELEVANT MAP-KINASES AND THE CONSEQUENT INDUCTION OF AUTOREACTIVE PATHOGENIC T CELLS AND AUTOANTIBODIES

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Background: The Ras family of GTPases plays an important role in signaling nodes downstream to T cell antigen receptor (TCR) and CD28, potentially lowering the threshold for TCR activation by autoantigens [1]. Somatic mutation in NRAS or KRAS may cause a rare autoimmune disorder coupled with abnormal expansion of lymphocytes. T cells from Rheumatoid Arthritis (RA) patients show excessive activation of Ras/MEK/ERK pathway. The small molecule Farnesylthiosalicylic acid (FTS) interferes with the interaction between RasGTPases and their prenyl-binding chaperones to inhibit proper plasma membrane localization and effective downstream signaling. Previous studies in the Lewis rat adjuvant induced arthritis show that FTS attenuates arthritis development and that the inhibition of pathogenic Th17-type cells is a central mechanism of action of this compound [2].
Objectives: To further study the therapeutic efficacy and molecular mechanisms that mediate the immunomodulatory effects of FTS in DBA/1 mouse collagen type-II induced arthritis (CIA) the pre-clinical model.
Methods: Arthritis was induced in 8-10 week old male DBA/1 mice by immunization with collagen type-II (CII) and complete Freund's adjuvant. Animals were treated semi-prophylactically with daily oral FTS (100 mg/kg); weekly i.p. injection of MTX (0.5 mg/kg); or daily 0.5% CMC vehicle solution (control treatment). Arthritis severity was graded daily by a validated clinical score (0-16 scale), starting at disease onset till study termination. In addition, multiple relevant immunological and molecular biomarkers were analyzed.
Results: We found that the clinical scores of mice in the FTS and MTX arms was significantly reduced (by ~80%, area under curve) compared to the control arm. Accordingly, FTS therapy significantly reduced joint pathology scores for inflammation, pannus formation, bone resorption, and cartilage damage. FTS also significantly inhibited the production of pathogenic anti-CII autoantibodies, anti–citrullinated peptide antibodies, and notably the de-sialylation of these autoantibodies as compared to control mice (Figure 1). The analysis of the effect of FTS on the T cell response to CII immunization, revealed strong attenuation of IL-22, IL-17, IL-9, GM-CSF, TNF, and IFN-gamma producing pro-inflammatory CD4+ Th cells. Importantly, we found that in vitro FTS treatment during TCR-stimulation (anti-CD3/CD28 mAbs) significantly inhibited the ensuing phosphorylation of multiple critical MAP kinases such as Erk, Akt, p38, and mTOR.
Conclusion: We determined in the preclinical CIA model that FTS, a first-in-class oral Ras-GTPases inhibitor, is a potent immune modulator, via the inhibition of TCR/CD28/Ras-dependent activation of critical MAPKs, consequently attenuating the generation of pro-inflammatory autoreactive T cells.

REFERENCES

[1] Singh K, et al. (2012) K-RAS GTPase- and B-RAF kinase-mediated T-cell tolerance defects in rheumatoid arthritis. Proc Natl Acad Sci USA 109(25): E1629-1637.
[2] Zayoud M, et al. (2017) Ras Signaling Inhibitors Attenuate Disease in Adjuvant-Induced Arthritis via Targeting Pathogenic Antigen-Specific Th17-Type Cells. Frontiers in immunology 8:799.

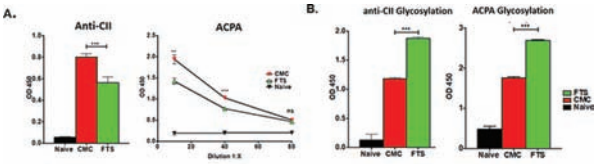


Figure 1: FTS therapy reduces the levels of pathogenic autoantibody and alters glycosylation of autoantibodies.

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SAT0045 A NOVEL SMALL MOLECULE, MBS2133, MODULATES OSTEOCLAST PRE-CURSOR METABOLISM TO INHIBIT OSTEOCLAST DIFFERENTIATION: AN ALTERNATIVE THERAPY FOR OSTEOLYTIC PATHOLOGY IN RA

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with substantial local and systemic bone loss. Despite the availability of several treatment options many patients do not reach low disease activity. Furthermore, current therapeutics generally target inflammation rather than erosive pathology. Thus, there remains a need for new therapies that can target both aspects of the disease. Prior studies have shown that biphenylcarboxylic acid small molecule derivatives not only inhibit murine osteoclastogenesis but also attenuate inflammation and bone destruction in murine models of RA[1,2].
Objectives: To evaluate a novel small molecule derivative, MBS2133, on human osteoblastogenesis, osteoclastogenesis and cellular function, and to investigate the *in vitro* mechanism-of-action.
Methods: Osteoblasts were derived from human mesenchymal stem cells. Cells were differentiated in the presence or absence of MBS2133 and mineralization assessed by Alizarin Red staining. Human $CD14^+$ blood monocytes were differentiated into osteoclasts (OCs) with M-CSF and RANK-L, in the presence or absence of MBS2133, and/or metabolites. Mature OCs were stained with tartrate-resistant acid phosphatase (TRAP) and quantified by light microscopy. Osteolytic activity was assessed on mineral-coated surfaces. Western blot analysis was used to assess downstream signalling pathways. Changes in the metabolic profile of pre-osteoclasts following 4h exposure to MBS2133 was carried out by liquid chromatography mass spectrometry.
Results: MBS2133 had no effect on the differentiation and function of primary human osteoblasts. In comparison, exposure of RANK-L stimulated $CD14^+$ monocytes to MBS2133 significantly reduced OC differentiation and osteolytic activity of mature OCs. Notably, exposure of pre-OCs to MBS2133 for 2h at initiation of osteoclastogenesis, was sufficient to significantly reduce subsequent OC differentiation. Evaluation of treated pre-osteoclasts revealed that RANKL-mediated phosphorylation of p38 was reduced. Metabolomic analysis of pre-osteoclasts revealed that MBS2133 induced a substantial reduction in a range of metabolites associated with glycolysis, oxidative phosphorylation and fatty acid oxidation pathway. Notably, L-carnitine, which facilitates the transportation of fatty acids to the mitochondrial matrix and enables processing and entry into tricarboxylic acid (TCA) cycle for further energy production, was significantly reduced. *In vitro* supplementation of L-carnitine inhibited the ability of the compound to switch off OC differentiation and osteolytic activity.
Conclusion: The results of this study demonstrate that MBS2133 specifically modulates the metabolome of myeloid cells, which has a substantial impact on their ability to differentiate into mature osteoclasts. These findings highlight the importance of modulating the glycolysis/oxidative phosphorylation axis in osteoclastogenesis and suggest that targeting the metabolic state of pre-osteoclasts could offer a new therapeutic approach to treat bone resorption in rheumatic diseases.

REFERENCES

[1] Greig IR, et al. Development and Characterization of Biphenylsulfonamides as Novel Inhibitors of Bone Resorption. J.Med.Chem. 2006;49:7487–7492
[2] Coste E, et al. Identification of small molecule inhibitors of RANKL and TNF signalling as anti-inflammatory and antiresorptive agents in mice. AnnRheumDis 2015;74:220–6.

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SAT0046 ARE SENSE OF SOCIAL SUPPORT AND LOW DECISION LATITUDE AT WORK LINKED TO RISK OF RHEUMATOID ARTHRITIS, AND IF SO, HOW DO THEY RELATE TO OTHER RISK FACTORS? RESULTS FROM THE SWEDISH EIRA STUDY

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Background: The role of psycho-social factors in the development of rheumatoid arthritis (RA) is debated.
Objectives: We investigated whether psychosocial stress measured as low sense of social support, and low decision latitude at work, were linked to risk of RA, and whether they related to known lifestyle risk factors for RA.
Methods: The Swedish population-based EIRA study included incident RA cases (N=3724) and controls (N=5937), matched for age, sex and residential area. Responders filled in questionnaires regarding self-reported social support, decision latitude at work and life-style-factors.
The distribution of answers among controls were used to define exposure, thus for social support, those in the lowest quartile of social support were considered exposed to low social support and similarly for decision latitude, those in the lowest quartile were considered exposed to low decision latitude at work.
Using logistic regression, we first evaluated whether exposures associated with RA risk, considering potential confounding of established risk factors. Then, we investigated whether the frequency of those factors differed between individuals reporting low social support or low decision latitude at work or not, among cases and controls.
Results: There were 898 cases with low social support and 285 cases with low decision latitude at work (latter only available in first part of EIRA).
Low social support was not associated with RA risk in unadjusted analyses (OR= 1.05, 95%CI=0.95-1.15). Low decision latitude at work did associate with a higher RA risk in the unadjusted analyses (OR=1.52, 95% CI=1.20-1.94), but this association was no longer significant after further adjustment for smoking, obesity and university degree (adjusted OR=1.24, 95% CI=0.93-1.63). Associations between those life-style risk factors and RA were confirmed (no university degree, OR=1.50; smoking OR=1.71; obesity OR=1.15).
Next, we evaluated whether low social support or low decision latitude at work differed by previously established risk factors. Cases with RA reporting low sense of social support were more often men (OR=1.60, 95% CI=1.40-1.83), current smokers (OR=1.46, 95%CI=1.26-1.70), obese (OR=1.29, 95%CI=1.09-1.54), physically inactive (OR=2.78, 95%CI=1.98-3.90) and without a university-degree (OR=2.04, 95%CI=1.77-2.36); with similar pattern among the controls. For working-conditions, cases reporting low decision latitude at work were also more often current smokers (OR=2.05, 95%CI=1.33-3.16) and with no university degree (OR=8.23, 95%CI=5.13-13.22), but less often male (OR = 0.40, 95%CI=0.26-0.60). Again, the pattern was similar among controls. RF/ACPA-positivity did not associate with low social support or low decision latitude.
Conclusion: Neither low social support nor low decision latitude at work were associated with an increased risk of RA after adjustment for other known lifestyle risk factors for RA. An initial crude association between

low decision latitude at work and risk for RA was explained by differences in smoking and educational level. However, both low social support and low decision latitude at work associate strongly with known, and here validated, risk factors for RA (smoking, obesity, no university degree) with similar pattern among both cases and controls.

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SAT0047 PRIMARY LYMPHOID TISSUE FROM RHEUMATOID ARTHRITIS PATIENTS HARBOUR CITRULLINE SPECIFIC PLASMA CELLS

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Background: Anti-citrullinated protein antibodies (ACPA) are specific markers with pathological effects in rheumatoid arthritis (RA). ACPA-specific B-cells have been identified in synovial joint fluid and peripheral blood. An increased concentration of ACPA is found in synovial fluid and lung tissue compared to blood suggest local production, partly confirmed by detection ACPA synovial plasma blasts, but primary lymphoid tissue have not previously been examined.

Objectives: In this study we investigated the plasma cell repertoire in the bone marrow and occurrence of autoantibody producing plasma cells.

Methods: For this study we developed a method to collected and process bone marrow samples from proximal femur in RA patients undergoing hip joint replacement. Bone marrow samples were processed and mononuclear cells were obtained by Ficoll separation. CD138+ plasma cells were single cell sorted by flow cytometry. Paired heavy and light chains were PCR amplified, sequenced, and analyzed by V-Quest and IgBLAST towards the **IMGT** database to annotate variable gene usage. To enrich for ACPA, sequences were selected based on high somatic hypermutations number and Fab N-glycosylation sites. Selected sequences were cloned and expressed as IgG in Expi293 cells. Monoclonal antibody reactivity to citrullinated and arginine form of vimentin, enolase, fibrinogen, histone, tenascin C peptides; carbamylated and malondialdehyde-acetaldehyde bovine serum albumin, and tetanus toxoid antigens were examined by ELISA. Included patients were clinical examined and donating peripheral blood samples.

Results: After method development and quality analysis we were able to include five bone marrow samples in this study. The five included RA patients, median age 74 (range 66-82) years, had in median 20 (range 4-44) years of destructive disease, all were RF positive, four were females and anti-CCP2-positive, and all except one were treated with anti-rheumatic drugs.

Overall, from the processed bone marrow, 465 paired heavy-light IgG plasma cell sequences were obtained, in total 368 (range 20-194) from ACPA positive patients and 97 from the ACPA negative patient. We observed statistically significant changes in heavy chain variable gene usage with lower VH-1 and higher VH-3 frequency in sequences from ACPA positive RA patients compared to sequences from the ACPA negative RA patient. We also found statistically significant increase in VH N-glycosylation in sequences from the ACPA positive RA patients (22.6% ACPA positive vs 12.4% ACPA negative; p=0.03) but no difference in mutation numbers. From obtained sequences, 34 interesting clones were selected for monoclonal antibody-expression. Among the 34 clones we found two citrulline specific reactive clones (reactivity towards CCP2, citrullinated vimentin and fibrinogen peptides) and one malondialdehyde-acetaldehyde (MAA) reactive clone, originating from three different APCA positive patients with the most longstanding disease. None of these clones had reactivity towards control antigens such as arginine versions of peptides.

Conclusion: Plasma cells producing ACPA are present in primary lymphoid tissue from RA patients. Further studies of difference in characteristics, IgG gene usage and N-glycosylation, between ACPA-positive and ACPA-negative patients are needed.

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SAT0048 ANTI-FRACTALKINE MONOCLONAL ANTIBODY AMELIORATE JOINT DESTRUCTION AND SYNOVIUM THROUGH SUPPRESSION OF OSTEOCLAST PRECURSOR MIGRATION AND INDUCTION OF SYNOVIAL CELL DEATH IN COLLAGEN-INDUCED ARTHRITIS MODEL

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Background: In the Phase 1/2 clinical study, E6011, a novel humanized anti-fractalkine (FKN) mAb demonstrated a promising efficacy in active RA patients who were inadequately controlled by MTX and/or TNF-α inhibitors (NCT 02196558)[1].In RA joint tissue, increased expression of fractalkine (FKN) and abundant infiltration of CX3CR1-positive cells were observed[2]. FKN is expressed on endothelial cells and fibroblast-like synoviocytes in synovium and also expressed on osteoblasts. CX3CR1 is expressed on monocytes/macrophages and osteoclast precursors (OCPs). Therefore, FKN-CX3CR1 interaction could play pivotal roles in migration, differentiation and activation of those cells. However, the precise mechanism(s) of FKN-CX3CR1 axis in RA, especially on joint destruction remains to be elucidated.

Objectives: To elucidate the roles of FKN-CX3CR1 axis in cartilage destruction, bone damage and proliferated synovial cells by using anti-mouse FKN mAb (anti-mFKN mAb).

Methods: For the induction of CIA, mice were immunized with bovine type II collagen. Anti-mFKN mAb was injected twice a week. The clinical arthritis score was monitored, and joint destruction was evaluated by soft x-ray and histology. The mRNA expression levels were assessed by quantitative RT-PCR. Blood parameters were measured using ELISA. In in vitro, effect of immobilized FKN on RANK ligand (RANKL)-induced osteoclast differentiation was examined. In in vivo, bone marrow-derived OCPs were fluorescein-labeled and transferred to CIA mice to evaluate the migration of OCPs into synovium. Inhibitory effect of anti-mFKN mAb, etanercept or tofacitinib against OCP migration was assessed. To examine the effect of anti-mFKN mAb against proliferated synovial cells, propidium iodide (PI) was injected to anti-mFKN mAb-treated CIA mice to detect the synovial cell death.

Results: Anti-mFKN mAb significantly reduced the arthritis and soft x-ray scores in both prophylactic and therapeutic treatment. Anti-mFKN mAb histologically improved synovitis, cartilage destruction and bone damage, with marked reduction of osteoclast numbers. Plasma levels of COMP and MMP-3 were also decreased. Interestingly, anti-mFKN mAb significantly suppressed Tnf and Il6 mRNA expression in the affected joints. In in vitro, RANKL-induced osteoclast differentiation was enhanced by immobilized FKN, and anti-mFKN mAb suppressed FKN-dependent osteoclast formation. In in vivo, anti-mFKN mAb strongly inhibited the migration of OCPs into the proliferated synovial cells of mice with CIA, whereas etanercept or tofacitinib had no significantly effect. Importantly, synovial cell death was abundantly found in proliferated synovial cells of mice with CIA after the anti-mFKN mAb treatment[3].

Conclusion: Anti-mFKN mAb remarkably ameliorated the joint destruction with the marked reduction of osteoclasts by the inhibition of both OCP survival and OCP migration in inflamed joint tissues. In addition, anti-mFKN mAb immediately induced synovial cell death in the proliferated synovial cells, suggesting the direct inhibitory effect in the synovitis. These results strongly indicate that inhibition of FKN-CX3CR1 axis by a humanized anti-FKN mAb, E6011, is an attractive and affected joints-selective therapeutic strategy for the treatment of both inflammatory synovitis, cartilage destruction and bone damage in RA patients.

REFERENCES

[1] Tanaka Y, et al., Mod Rheumatol (2018) 28, 58-65

[2] Nanki T, et al., Arthritis Rheum (2002) 46, 2878-83
[3] Hoshino K, et al., Arthritis Rheumatol (2018) Aug 6 [Epub ahead of print]

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SAT0049 INFECTION WITH CITRULLINATING PORPHYROMONAS GINGIVALIS CAN INDUCE AUTOIMMUNITY TO HUMAN RIBOSOMAL PROTEINS AND TNF ALPHA TREATMENT NONRESPONSE

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Background: Porphyromonas gingivalis (P g.) is involved in triggering self-reactive immune responses when cirtullinating bacterial or human proteins. However, first evidence to link anti-ribosomal T and B cells responses to rheumatoid arthritis (RA) has been published but the mechanism and its influence on therapy is not clear (1). Infection based autoimmunity induced by citrullination of human proteins with P g. peptidyl arginine deiminase from RA patient (RA-PPAD) and crossreactivity binding induced by P g. was investigated using patient sera, affinity purified RA patient antibodies and monoclonal antibodies to cit-RA-PPAD.
Objectives: Antibodies to RA-PPAD isolated from an RA patients (RA-PPAD) was first time linked to target specific citrullinated ribosomal proteins and therapy.
Methods: Screening of RA sera was conducted on 37.830 unique human proteins on protein marcoarrays (http://www.engine-gmbh.de) with 30 RA sera. The autoantibody response to 840 different proteins was recorded and bioinformatically evaluated. Protein arrays were citrullinated with human peptidyl arginine deiminase PAD 2, 4, rabbit PAD and RA-PPAD from P.g. Sera and affinity purified antibodies were used to detect reactivity to 840 autoantigens and 15aa CCP peptide form RA-PPAD. Sera from TBA treated sera anti-TNF (adalimumab, etanercept, certolizumab) treatment were tested with the cit-PPAD-peptide of 15aa (CPP).
Results: A human protein macroarray consisting of 840 indentified autoantigens from RA patients was modified by human PAD2 and PAD4, rabbit PAD, and RA-PPAD form P g. Using cit specific monoclonal antibodies we identified the ribosomal proteins (RP), RPL18a, RPS27a, modified by PAD2, RPL18a and MRPS11 modifies by PAD4, and RPL7L1 modified by rabbit PAD specifically targeted. In addition 6 RA patient sera and 3 osteoarthritis (OA) control sera were used to identify the citrullinated RA-PPAD specific modified autoantigens not targeted when modified by human PAD2 or PAD4 or rabbit PAD. We identified the RA-PPAD citrullinated ribosomal Proteins RPL3, RPL21, RPS24, RPL9, RPL15, RPS24, RPS3a, MRPL28 specifically targeted by RA patients. This identifies ribosomal proteins as major specific RA-PPAD citrullination targets. Moreover, affinity purified antibodies bound to native and citrullinated RA-PPAD from 6 RA patient sera and 3 OA patient sera were tested for crossreactvity on citrullinated human proteinarray. Antibodies to citrullinated ribosomal proteins MRPS11, RPL21, RPS3a, RPL18a, RPS27a, MRPL28 were detected in the RA group but not in the OA control group. High antibody titre against the cit-PPAD-peptide of 15aa (CPP) derived from the autocitrullination site (R63) of RA-PPAD correlates with TNFα-inhibitor (TBA) non-response (n=61). DMARD patients refractory to different treatment regimes (n=61), receiving anti-TNF (adalimumab, etanercept, certolizumab), do not respond when maintaining high α-CPP IgG level.
Conclusion: Failure of *Porphyromonas gingivalis* clearance in RA patients leads to infection induced enzymatic mimicry based autoreactivity targeting evolutionary conserved human ribosomal proteins. Autoimmunity to ubiquitous self-antigens may trigger localized tissue damage in RA.TBA non-response leads to the suggestion to clear Porphyromonas gingivalis infection before α-TNF treatment.

REFERENCE

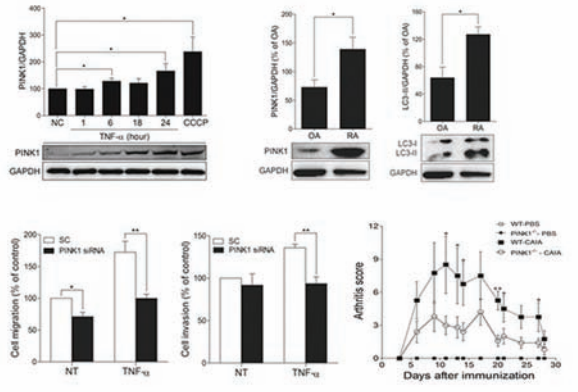
[1] :Ito, Y. et al. Detection of T cell responses to a ubiquitous cellular protein in autoimmune disease. Science 346, 363–368 (2014)

Disclosure of Interests: Madeleine Jenning: None declared, Bianka Marklein: None declared, Ute Nonhoff: None declared, Zoltan Konthur: None declared, Gerd Rüdiger Burmester Consultant for: Roche, Sanofi-Genzyme, Speakers bureau: Roche, Sanofi-Genzyme, Karl Skriner: None declared
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SAT0050 TNF-A INDUCES MITOPHAGY FORMATION IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLAST AND INHIBITION OF MITOPHAGY AMELIORATES SYNOVITIS IN COLLAGEN ANTIBODY-INDUCED ARTHRITIS

sang youn jung. *Bundang CHA medical Center, Department of Rheumatology, Seongnam, Gyeonggi-do, Korea, Rep. of (South Korea)*

Background: Rheumatoid arthritis (RA) is a systemic and chronic autoimmune disease that primarily targets synovial membranes. Mitophagy is a selective form of autophagy which removes damaged mitochondria. When mitochondria become damaged, PINK1 (PTEN-induced putative kinase 1) is accumulated on the outer membrane of damaged mitochondria and induces mitophagy. The study of mitophagy in lung fibrosis and parkinson's diseases has recently been described. However, the role of mitophagy in RA has not been reported yet.
Objectives: The aim of this study was to determine the roles of mitophagy in rheumatoid arthritis synovial fibroblast (RASF) and collagen antibody-induced arthritis (CAIA) mice model.
Methods: We studied the mitophagy marker, PINK1, in RASF treated with TNF-a by western blotting and immunofluorescence. Arthritis was induced in PINK1 knockout mice by intraperitoneal (i.p.) injection of anti-type II collagen antibody cocktail, followed by i.p injection of lipopolysaccharide. The severity of rheumatoid arthritis was histopathologically assessed
Results: PINK1 expression and damaged mitochondria increased in RASF treated with TNF-α. TNF-α produced Intracellular ROS in RASF and mitophagy was regulated by ROS. PINK1 knockdown RASF decreased migration and invasion function. Histopathological examination revealed that the paws from PINK1-knockout mice showed markedly reduced swelling and inflammation compared with those of wild type mice
Conclusion: Taken together, the results suggest that regulation of PINK1 expression in RA may represent potential therapeutic and diagnostic targets for RA



REFERENCES

[1] Huber LC, Distler O, Tarner I, Gay RE, Gay S, Pap T. Synovial fibroblasts: key players in rheumatoid arthritis. Rheumatology (Oxford). 2006;45 (6):669-75.

[2] Choy EH, Panayi GS. Cytokine pathways and joint inflammation in rheumatoid arthritis. The New England journal of medicine. 2001;344(12):907-16.
[3] McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. The New England journal of medicine. 2011;365(23):2205-19.
[4] Connor AM, Mahomed N, Gandhi R, Keystone EC, Berger SA. TNFalpha modulates protein degradation pathways in rheumatoid arthritis synovial fibroblasts. Arthritis research & therapy. 2012;14(2):R62.
[5] Rinaldi N, Schwarz-Eywill M, Weis D, Leppelmann-Jansen P, Lukoschek M, Keilholz U, et al. Increased expression of integrins on fibroblast-like synoviocytes from rheumatoid arthritis in vitro correlates with enhanced binding to extracellular matrix proteins. Annals of the rheumatic diseases. 1997;56(1):45-51.
[6] Bueno M, Lai YC, Romero Y, Brands J, St Croix CM, Kamga C, et al. PINK1 deficiency impairs mitochondrial homeostasis and promotes lung fibrosis. The Journal of clinical investigation. 2015;125(2):521-38.
[7] Ding WX, Yin XM. Mitophagy: mechanisms, pathophysiological roles, and analysis. Biological chemistry. 2012;393(7):547-64.

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SAT0051 BARICITINIB IMPROVES JOINT MOBILITY AFTER INJURY IN A RODENT FORCED-AMBULATION MODEL

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Background: Movement-evoked pain and impaired joint mobility are common comorbidities in inflammatory diseases such as Rheumatoid Arthritis (RA) and Osteoarthritis. The Janus kinase (JAK) pathway has been implicated in both inflammation and chronic pain. Clinical data suggests that baricitinib, a selective JAK 1/2 inhibitor, can robustly and rapidly alleviate pain in RA.[1]Utilizing a rodent forced-ambulation model, we have previously shown attenuation of gait deficits with analgesics such as opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and an anti-NGF (Nerve Growth Factor) antibody.[2] However, in this same model a fusion protein blocker of TNFα (tumor necrosis factor alpha) signaling failed to demonstrate efficacy though inflammation was decreased. The present work investigated the potential of baricitinib, recently approved for treatment of RA, to reduce inflammagen-induced joint pain and gait impairment in this model of joint inflammation mediated pain.
Objectives: To determine if JAK 1/2 pathway inhibition is effective in treating inflammagen-induced joint pain and gait impairment.
Methods: Unilateral joint injury was induced in female Sprague Dawley rats (Harlan, Indianapolis, IN, USA) by unilateral intra-articular injection of 20 µg Complete Freund's Adjuvant (CFA). Using the GaitScan (CleverSys Inc., Reston, VA) treadmill system, a composite gait score comprising of range of motion, normalized stance distance, stance/swing ratio, and paw print size was evaluated over 3 days post-injection.[2] Rats were treated with vehicle, positive control (40 mg/kg Tramadol), or clinically relevant (based on plasma levels) increasing doses of baricitinib (1, 3, or 10 mg/kg p.o., 2-hrs prior to each test, q.d.). Dorsal root ganglion (DRG) were harvested post-gait evaluation and Total STAT3 (Cell Signaling, #4904) and phospho-STAT3 (Y705) (Cell Signaling, #9131) protein levels were examined via immunoblotting. The p-values were derived from repeated measures ANOVAs.
Results: In rat DRG homogenates, baricitinib significantly decreased phospho-STAT3 (Y705) protein levels in a dose-dependent manner ($p<0.01$) with a significant effect after a 3 mg/kg dose and a maximal response after a 10 mg/kg in both the ipsilateral (right) and contralateral (left) sides. Total STAT3 protein levels remained unchanged. Similarly, treatment with baricitinib significantly improved composite gait score at the 10 mg/kg dose ($p<0.05$) by Day 3.
Conclusion: These data indicate that treatment with baricitinib attenuates CFA-induced joint deficits, a surrogate measure of joint pain. This effect correlated with the pharmacodynamic inhibition of JAK-STAT signaling in DRGs. These data support a role for JAK-STAT signaling in pain signaling and provide an opportunity to investigate the potential mechanism of action of baricitinib in joint pain.

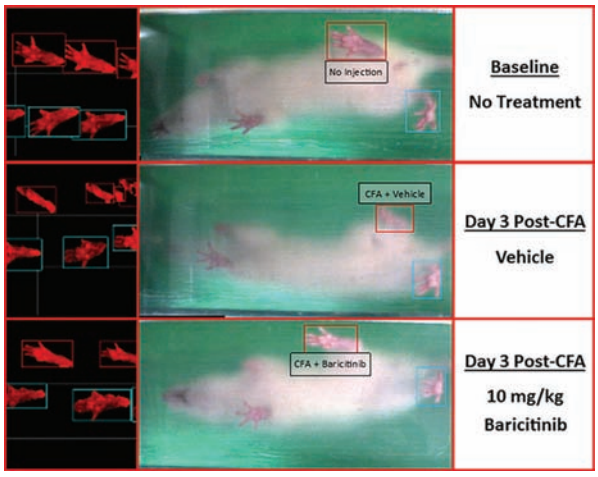


Figure 1. Representative still images from video recordings of animals during gait analysis at baseline (Top Panel), 3 Days post-CFA and vehicle treatment (Middle Panel) and 3 Days post-CFA with 10 mg/kg daily baricitinib treatment (Bottom panel). The ventral image of the rat illustrates the same part of the gait cycle (ipsilateral stance phase initiation) across treatment groups to highlight impairment in the CFA-injected limb (Red Box) vs Baseline and apparent improvement following 10 mg/kg baricitinib treatment. The panels on the left provide examples of software-detected paw prints for each treatment group which show that CFA + vehicle treatment produced a small, closed-toed paw print (Middle) which appears restored to near baseline levels following baricitinib treatment (Bottom).

REFERENCES

[1] Keystone. Ann Rheum Dis. 2017;76(11):1853-1861.
[2] Adams. Osteoarthritis Cartilage. 2016;24(11):1928-1939.

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SAT0052 PHOTODYNAMIC THERAPY TARGETING ACTIVATED FIBROBLASTS INDUCES SYNOVIAL CELL DEATH IN EXPERIMENTAL ARTHRITIS

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Background: Activated synovial fibroblasts (SF) contribute to rheumatoid arthritis (RA) by producing a multitude of cytokines, chemokines and proteases thus aggravating disease. Activated SF can be distinguished from quiescent fibroblasts by their expression of fibroblast activation protein (FAP). Selective depletion of FAP+ SF in inflamed joints could decrease their contribution to the arthritis process and thus constitute a viable treatment option. Further focussing of the treatment to only those areas affected by the disease can be accomplished by applying targeted photodynamic therapy (tPDT). In tPDT a light sensitive molecule, a photosensitizer (PS), is conjugated to a targeting moiety. Upon activation by light this construct produces reactive oxygen species, killing the targeted cells.
Objectives: To this end we developed and tested a therapy that selectively depletes activated SF by targeting FAP on these cells with an

antibody, 28H1, to which the PS, IRDye700DX, for tPDT is attached. Here we investigated the feasibility of using FAP-tPDT to induce cell death in murine arthritic synovium ex vivo.

Methods: After conjugation of the IDRye700DX to 28H1 (28H1-700DX), binding and specificity of the conjugate was determined. Subsequently, tPDT efficiency in vitro was established using a 3T3 fibroblast cell line stably transfected with FAP. Biodistribution using an [^{111}In] In-DTPA-28H1 conjugate with and without IRDye700DX was performed in healthy C57BL/6N mice as well as in C57BL/6N mice with antigen induced arthritis (AIA). Finally, the potential of FAP-tPDT to induce targeted cell death in the synovial lining was determined by treating knee joints from mice with AIA ex vivo.

Results: Conjugation of IRDye700DX to the antibody did not negatively influence the immunoreactive fraction or binding capacity of the conjugate (94.7% for 28H1-700DX). 28H1-700DX was able to efficiently induce FAP-specific cell death in vitro. At 17.6 J/cm^2 radiant exposure, 89.24% ± 3.67% of fibroblasts died in the group incubated with antibody compared to control incubated with buffer only ($p<0.001$). Biodistribution of the compound with the PS showed increased accumulation in the liver compared to the antibody without PS (31.46 ± 5.49% injected dose per gram tissue (%ID/g) versus 5.32 ± 1.17 %ID/g for the antibody with or without PS, respectively ($p<0.001$)). However, despite this increased clearance to the liver, accumulation in the inflamed joints was increased in the group injected with the antibody-PS construct (1.61 ± 0.08 %ID versus 1.13 ±0.06 %ID for the antibody with or without PS ($p<0.001$)). Interestingly, ex vivo FAP-tPDT of knee joints of arthritic mice caused significant photo-bleaching of the PS (19.69 ± 2.02% fluorescent signal remaining versus 96.00 ± 25.98% compared to the unexposed control at baseline, $p=0.047$). Furthermore FAP-tPDT induced marked apoptosis as was indicated by an increased staining of the markers caspase-3 and yH2AX evident in the synovium of treated knee joints.

Conclusion: Here we demonstrated the feasibility of conjugating a PS to an antibody targeting FAP on activated SF without negatively impacting the binding capacity thereof. Furthermore we showed that this construct can then be used to deliver cell specific cytotoxicity through tPDT both in vitro and ex vivo in a mouse model of arthritis. This approach may have therapeutic potential in the treatment of RA.

Disclosure of Interests: Daphne Dorst: None declared, Mark Rijpkema: None declared, Mijke Buitinga: None declared, Peter Laverman: None declared, Marti Boss: None declared, Christian Klein Employee of: Roche pharmaceutics, Anne Freimoser-Grundschober Employee of: Roche pharmaceutics, Birgitte Walgreen: None declared, Peter van der Kraan: None declared, Martin Gotthardt: None declared, Marije Koenders: None declared

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SAT0053 GLYCOSYLATION IN MAMMALS PROTECTS CITRULLINATED CHEMOKINES FROM PARTIAL DEGRADATION

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Background: Citrullination is a posttranslational modification of specific proteins by peptidylarginine deiminase (PAD) activities. Nowadays citrullination is recognized as a hallmark of rheutamoid arthritis and other autoimmune diseases. In our recent study we have shown a presence of citrullinated chemokines epithelial-derived monocyte chemotactic protein-1 (MCP-1/CCL2), macrophage inflammatory protein-1α (MIP-1α/CCL3) and neutrophil-activating peptide 78 (ENA-78/CXCL5) in biological fluids collected from patients suffering from rheumatoid arthritis (RA) versus non-autoimmune arthritis diseases and demonstrated citrullinated ENA-78/CXCL5 as an efficient macrophage chemoattractant in a contrast with non-citrullinated ENA-78/CXCL5. In our current work we found that citrullinated *in vitro* bacterially produced chemokines cannot be efficiently used as the standards in modified enzyme linked immunosorbent assay (ELISA) assays designed to detect citrullinated chemokines.

Objectives: In our work we aimed generate a procedure for preparation of stable citrullinated chemokines suitable for research aplications and to validate a *hypothesis that posttranslational modifications occurring in mammalian cells that can stabilize chemokines can also protect citrullinated chemokines from quick degradation*.

Methods: MCP-1/CCL2 and MIP-1α/CCL3 were cloned from total RNA isolated from synovial fibroblasts obtained from RA patient. Both bacterially-produced and mammalian cells-produced recombinant human chemokines were citrullinated by commercial rabbit PAD2. Success in citrullination was confirmed with Western blotting and mass-spectrometry. Citrullinated chemokine concentrations were measured by modified sandwich ELISA assays.

Results: Both commercially available and self-made bacterially produced chemokines MCP-1/CCL2, MIP-1α/CCL3 and ENA-78/CXCL5 undergo quick partial degradation upon their *in vitro* citrullination by PAD2 and cannot be detected with either Western blotting or mass-spectrometry. At the same time mammalian cells-produced properly glycosylated MCP-1/CCL2, MIP-1α/CCL3 and ENA-78/CXCL5 can be efficiently citrullinated and successfully used as the standards in modified ELISA assays as well as in bioassays.

Conclusion: Glycosylation that is lucking in bacterially-produced proteins but occurs in mammalian cells stabilizes citrullinated chemokines thus protecting them from quickly ongoing partial degradation.

BioEthics Committee Approval: All human subject samples were collected after approval by the Institutional Review Board of the Academic Medical Center/University of Amsterdam, Amsterdam, The Netherlands (Protocol MEC 07/079 #10.17.0708) and provision of informed consent by the patients.

REFERENCE

[1] Yoshida K., Korchynskyi O., Tak P.-P., Isozaki T., Ruth J.H., Campbell P. L., Baeten D.L., Gerlag D.M., Amin M.A., and. Koch A.E. (2014) *Arthritis and Rheumat* 66, No 10, P.2716-2727.

Disclosure of Interests: None declared

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SAT0054 INVESTIGATING MECHANISMS OF AUTOANTIBODY INDUCED PAIN, BONE LOSS AND ARTHRITIS DEVELOPMENT

Akilan Krishnamurthy[1], Yogan Kisten[1], Katalin Sandor[2], Alexandra Circiumaru[1], Gustaf Wigerblad[1], Peter Damberg[3], Koji Sakurabas[1], Heidi Wähämaa[3], Patrik Jarvolli[4], Juan Jimenez Jimenez Andrade[5], Vivianne Malmström[1], Lars Klareskog[1], Camilla Svensson[2], Bence Réthi[1], Anca Catrina[1]. [1]*Karolinska Institutet, Rheumatology unit, Medicine, stockholm, Sweden*; [2]*Karolinska Institutet, Physiology and Pharmacology, stockholm, Sweden*; [3]*Karolinska Institutet, Karolinska Experimental Research and Imaging Centre (KERIC), stockholm, Sweden*; [4]*Karolinska Institutet, stockholm, Sweden*; [5]*Universidad Autónoma de Tamaulipas, Reynosa, Tamaulipas, Mexico*

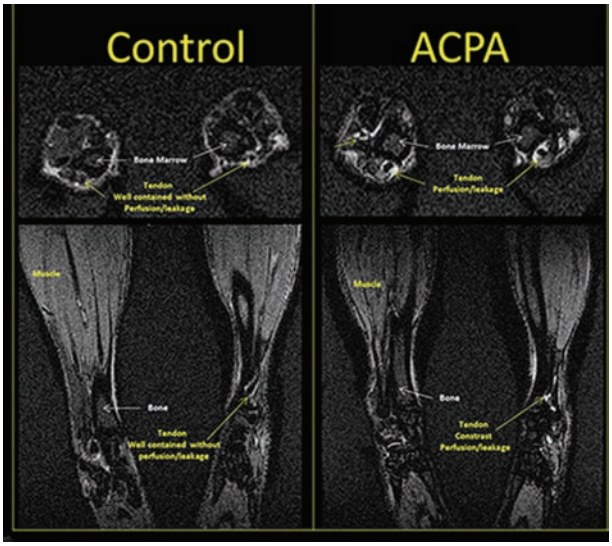
Background: In rheumatoid arthritis (RA), autoantibodies against citrullinated proteins (ACPAs) have been reported to be associated with bone loss, pain and tenosynovitis prior to disease onset.

Objectives: We aimed to investigate if transfer of human ACPAs into mice could reproduce these clinical observations.

Methods: Monoclonal ACPA (1325:04C03 and 1325:01B09) and control (1362:01E02) antibodies (mAbs) were generated from synovial plasma or memory B cells of RA patients. 2mg of combination of monoclonal ACPAs or control antibody were injected in BALB/c female mice (12-16 Weeks) with or without a consecutive intra-articular injection of LPS after 8 days. Pain-like behavior was monitored by measuring mechanical hypersensitivity using von Frey filaments every 3 days and estimation by up-down Dixon method. Bone mineral density was measured by micro-CT. Using specially designed mobilization casts, dedicated mouse MRI coils, and gadolinium enhanced contrast medium, the hind limbs of these mice were scanned and evaluated for any signs of soft tissue joint inflammation. Blinded to ACPA and controls, the MRI images were scored for the presence of synovial thickening, effusion and tendon inflammatory changes by 3 readers in consensus.

Results: ACPAs (1325:04C03 and 1325:01B09) induced significantly more pronounced pain-like behavior (lasting for at least 4 weeks) and reduction of the trabecular bone thickness in the hind limbs, whereas no such effect was seen with the control mabs generated in the same way as the monoclonal ACPAs. While no macroscopic sign of joint inflammation could be detected, preliminary MRI data shows that sub-clinical joint inflammation (such as tenosynovitis) in mice injected with ACPAs but not those injected with control mAb. Intra-articular LPS injection resulted in significantly increased prolonged mechanical hypersensitivity in mice initially receiving sub-optimal doses of monoclonal ACPA as compared to those receiving control mAb. This was associated with higher levels of sub-clinical inflammation (as shown by MRI scans) in ACPA injected mice.

Conclusion: We show that ACPA induces pain-like behavior, bone loss and sub-clinical inflammation in mice, a model that mimics the pre-clinical state of ACPA positive RA.



REFERENCES

[1] Harre, U. et al. J Clin Invest (2012)
[2] Krishnamurthy, A. et al. Ann Rheum Dis (2016)
[3] Wigerblad, G. et al. Ann Rheum Dis (2016)
[4] KleyerA, Seminars in Arthritis and Rheumatism (2016)

Disclosure of Interests: Akilan Krishnamurthy: None declared, Yogan Kisten: None declared, Katalin Sandor: None declared, Alexandra Circiumaru: None declared, Gustaf Wigerblad: None declared, Peter Damberg: None declared, Koji Sakurabas: None declared, Heidi Wähämaa: None declared, Patrik Jarvolli: None declared, Juan Jimenez Jimenez Andrade: None declared, Vivianne Malmström: None declared, Lars Klareskog Grant/research support from: Yes, but not for the presented study., Camilla Svensson: None declared, Bence Réthi: None declared, Anca Catrina Grant/research support from: Yes, but not for the presented study.
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SAT0055

JOINT SPECIFIC TNF RESPONSE OF SYNOVIAL FIBROBLASTS IN RHEUMATOID ARTHRITIS

Raphael Micheroli[1], Amanda Mcgovern[2], Kerstin Klein[1], Xiangyu Ge[2], Paul Martin[2], Oliver Distler[1], Mojca Frank-Bertoncelj[1], Stephen Eyre[2], Caroline Ospelt[1]. [1]*Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland;* [2]*Arthritis Research UK Centre for Genetics and Genomics, School of Biological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, United Kingdom*

Background: Synovial fibroblasts (SF) in rheumatoid arthritis (RA) play a major role in chronic inflammation and joint destruction. We showed previously that their epigenetic and transcriptional profile as well as their function vary significantly between different joints. However, it is unknown whether there is a joint-specific inflammatory response of SF.
Objectives: To compare transcriptional changes between SF from hand, shoulder and knee joints after stimulation with the pro-inflammatory cytokine TNF.
Methods: We cultured SF from synovial tissues of hand (metacarpophalangeal and proximal interphalangeal joint), shoulder and knee joints of RA patients. After stimulation of the SF with 10 ng/ul TNF for 24h (n=2 for each joint location), RNA was sequenced on the Illumina HiSeq4000 platform. We analyzed differential gene expression with R v3.5.2 and CuffDiff and DESeq2 packages.
Results: As shown in Figure 1, principal component analysis showed evident separation of joint locations and condition (unstimulated vs TNF stimulated). In a sample-to-sample distance matrix, hand samples (TNF stimulated and unstimulated) grouped apart from shoulder and knee samples (Figure 2).
Of the regulated genes, 26% appeared in all three joint locations and 56% overlapped between knee and shoulder, but only 30% overlapped between hand and shoulder and between hand and knee SF. Similarly, also enriched pathways differed particularly between hands and the more proximal joints.
'Defense response' ($p=8.11\times10^{-23}$) and 'cytokine activity' ($p=1.27\times10^{-21}$) were the most significantly enriched gene ontology terms for genes regulated in TNF stimulated hand SF. These processes were less prominently enriched in stimulated knee ($1.58x10^{-15}$ and $8.84x\ 10^{-08}$) and shoulder SF ($2.02x10^{-11}$ and $3.20x10^{-07}$), where 'cell cycle' ($p=2.26\times10^{-30}$ in knee and $p=2.18\times10^{-32}$ in shoulder), and 'DNA packaging complex' ($p=4.63\times10^{-49}$ in knee and $p=8.91\times10^{-36}$ in shoulder) were the most significantly enriched gene ontology terms. These processes were not significantly enriched in stimulated hand SF.
Conclusion: SF from different joints in RA react differently to TNF stimulation. In particular hand SF reacted different to TNF stimulation than shoulder and knee SF, which appeared more similar. These qualitative and quantitative differences of the inflammatory response might translate into joint-specific pathotypes of synovitis with distinct therapeutic responses and disease outcomes.

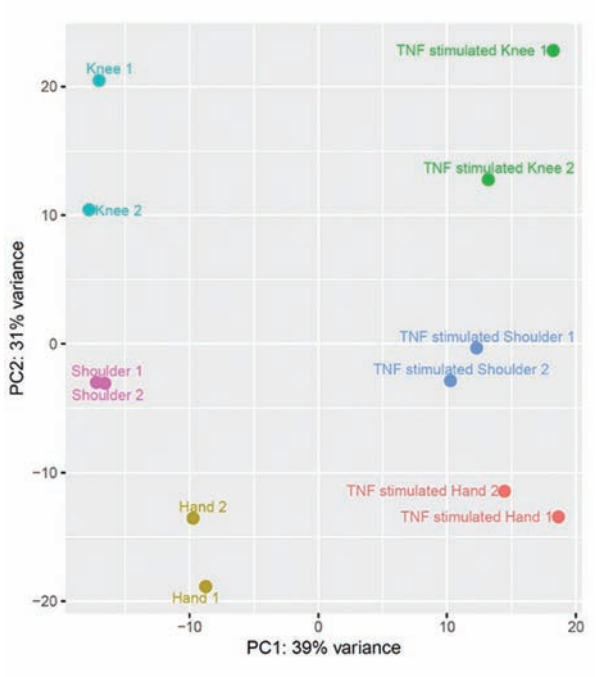


Figure 1. Principal component analysis of TNF stimulated and unstimulated synovial fibroblasts

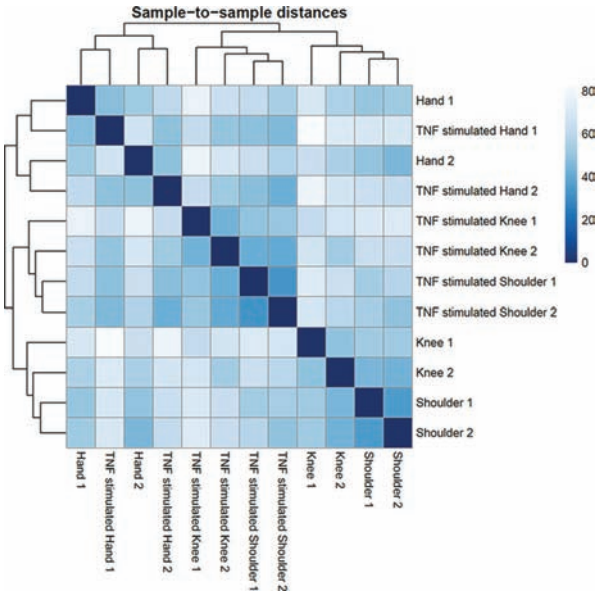


Figure 2. Sample-to-sample distance matrix of TNF stimulated and unstimulated synovial fibroblasts

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Disclosure of Interests: Raphael Micheroli: None declared, Amanda McGovern: None declared, Kerstin Klein: None declared, Xiangyu Ge: None declared, Paul Martin: None declared, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Mojca Frank-Bertoncelj : None declared, Stephen Eyre: None declared, Caroline Ospelt: None declared
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SAT0056 TAS5315, A NOVEL BRUTON'S TYROSINE KINASE INHIBITOR, DEMONSTRATES POTENT EFFICACY AGAINST BONE DESTRUCTION IN AN ANIMAL MODEL FOR RHEUMATOID ARTHRITIS

Naruto Noma, Fumihito Hosoi, Satoru Iguchi, Ryusuke Kaneko, Yohei Yoshiga, Yasunobu Arima, Daichi Akasaka, Kenji Tanaka, Akihiro Saito, Teruhiro Utsugi, Koichi Ikizawa. *TAIHO PHARMACEUTICAL CO., LTD., Tsukuba, Japan*

Background: Bone erosions and cartilage damages are a pathological hallmark of rheumatoid arthritis (RA) and are associated with poor functional outcome[1]. Aberrant activations of osteoclasts induced by receptor activator of nuclear factor κB ligand (RANKL)[2] are involved in the bone erosions of RA. It has also been recently shown that under chronic inflammatory conditions such as RA, inflammatory cytokines in joints induce pathological osteoclast differentiation and cause excessive bone resorption independent of RANKL-RANK signaling[3]. The Bruton's tyrosine kinase (BTK) signaling pathway plays a pivotal role in inflammatory response and bone resorption[4]. Thus, targeting BTK may be efficacious against not only inflammation but also bone erosion by regulating activation of effector cells such as B cells, macrophages and osteoclasts in RA. We have already shown the inhibitory effects of TAS5315 on RANKL-dependent osteoclast activation. However, it remained uncertain whether TAS5315 inhibits osteoclast activation induced by inflammatory cytokines.
Objectives: In this study, we evaluated the effects of TAS5315 on osteoclast activation induced by inflammatory cytokines (*in vitro*) and the infiltration of tartrate-resistant acid phosphatase (TRAP)-positive osteoclasts in the joint of a mouse CIA model.
Methods: *In vitro* biochemical assay was performed using available kinase assay panels. The BioMAP® Diversity PLUS panels were used to determine the profile of TAS5315 in primary human cell systems. The effects of TAS5315 on osteoclasts were assessed by examining osteoclast-mediated bone resorption. TAS5315 was orally administrated once a day in an established mouse CIA model. TRAP-positive osteoclasts were counted manually. Bone mineral density (BMD) and bone erosion were assessed using micro-CT analysis. The mechanical properties of the tibia were evaluated by a compression test of proximal metaphysis using a material-testing machine.
Results: TAS5315 selectively inhibited the enzyme activity of BTK and had less off target inhibition against other kinases. In BioMAP® systems, TAS5315 decreased the production of IgG and the expression of cytokines (TNF-α, IL-6, IL-17A). TAS5315 also inhibited osteoclast-mediated bone resorption induced by inflammatory cytokines. On the other hand, anti-RANKL antibody did not inhibit bone resorption induced by inflammatory cytokines. Futhermore, in the mouse CIA model, TAS5315 significantly ameliorated paw swelling and pathological changes. TAS5315 significantly decreased the infiltration of TRAP-positive osteoclasts in the joint and also showed improvement of BMD and bone erosion by time-dependent micro-CT analysis. In vehicle-treated mice, the mechanical strength of tibia was decreased compared with normal mice. TAS5315-treated mice recovered the decreased parameters of the mechanical strength compared with vehicle-treated mice.
These data suggests that TAS5315 improves bone erosion in murine model for RA through direct inhibition of osteoclast activation induced by inflammatory cytokines as well as RANKL.
Conclusion: Our study demonstrates that TAS5315 would be an attractive RA therapeutic drug that could improve bone destruction as well as inflammation.

REFERENCE

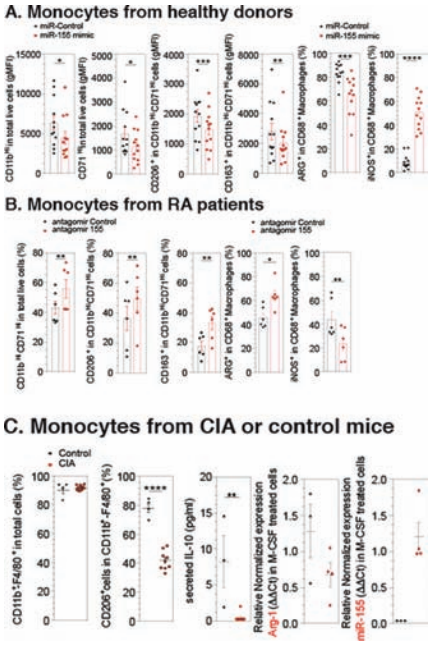
[1] Nat Rev Rheumatol. 2012;8,656-64. 2: Nat Rev Rheumatol. 2015;11,189-94. 3: Arthritis Rheumatol. 2016;68,2889-2900. 4: Drug Discov Today. 2014;19,1200-4.

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SAT0057 INCREASED MICRORNA-155 IS ASSOCIATED WITH A SPECIFIC DEFECT OF ANTI-INFLAMMATORY M2 MACROPHAGES POLARIZATION BOTH IN HUMAN RHEUMATOID ARTHRITIS AND IN COLLAGEN-INDUCED-ARTHRITIS MICE

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Background: Monocytes/macrophages are key players in the pathogenesis of Rheumatoid arthritis (RA). Monocytes can differentiate into pro-inflammatory macrophages (M1-like) or into anti-inflammatory. macrophages (M2-like) We previously found a defect of monocytes polarization into M2-like macrophages, in RA patients and not in healthy donors (HD) or in patients with other inflammatory diseases (such as connective tissue diseases or spondyloarthritis), and a propensity for preferential maturation towards M1-like pro-inflammatory macrophages that could contribute to synovial inflammation.
MiR-155 expression has been shown elevated in RA synovial macrophages and in blood monocytes. MiR-155 inhibits mRNA of 2 important proteins involved in programming of M2 macrophages (SOCS-1 and C/EBP-β).
Objectives: We assessed if miR-155 could play a role in the defect of monocytes polarization into M2-like macrophages both in human RA and in a mouse model of collagen-induced-arthritis (CIA) mice.
Methods: Monocytes were isolated from PBMCs for HD and RA by negative selection. Purified monocytes were transfected using **AMAXA technologies** with miR-155 mimic (for HD) or antagomiR155 (for RA) or controls miRs. Then monocytes were incubated in the presence of human serum (SAB) (M2-like) for 6 days. Expressions of total macrophages markers (**CD11b** and **CD71**), M2-like macrophage markers (**CD163**, **CD206** and **Arg-1**), M1-like macrophage marker (**iNOS**) were evaluated by flow cytometry, ELISA or immunofluorescence.



DBA/1 mice were immunized by intradermal injection at day-0 and at day-21 with a grade chick type II collagen and complexe Freund's adjuvant. Monitoring of arthritis indices was done from day-25 to day-35. At day-35, monocytes were isolated from bone marrow by negative selection. To generate MDMs, purified monocytes were incubated 6 days in the presence of M-CSF+IL-4 (M2-like). Expressions of total macrophages markers (**CD11b** and **F4/80**), M2-like macrophage polarization markers (**CD206**, **IL-10** and **Arg-1**) were evaluated by flow cytometry, ELISA or qPCR.

Results: Overexpression of miR-155 in HD monocytes significantly decreased the gMFI of the pan-macrophages markers, CD11b and CD71, but also the M2-like markers, CD206 and CD163 after 6 days of culture with human SAB. Likewise, we demonstrated a significant reduction of Arg-1 expression and increase in iNOS expression in M2-like macrophages after miR-155 transfection of HD monocytes **(Fig. 1A).**

Conversely, *ex vivo* silencing of miR-155 with antagomir in RA monocytes restored the defect of M2-like phenotype macrophages by increasing the percentage of pan-macrophages markers, CD11b and CD71 and M2-like macrophages markers CD206 and CD163 after a 6-day culture in human SAB. Moreover, miR-155 antagomir increased significantly the Arg-1 expression and reduced iNOS expression in M2-like macrophages **(Fig. 1B).**

The defect of monocytes capacity of differentiation into M2-like phenotype was also found in in CIA mice as compared to controls, with a decreased expression of CD206, IL-10 secretion and Arginase-1 expression **(Fig. 1C).** MiR155 was also involved in this defect in mice: its expression level was the same in M1-like macrophages between controls and CIA mice, whereas it was increased in M2-like CIA macrophages compared to controls mice **(Fig. 1C).**

Conclusion: MiR155 plays a key role in the specific defect of anti-inflammatory M2 macrophages polarization found both in human rheumatoid arthritis and in CIA mice. MiR155 could represent a new therapeutic target in RA that can be tested in the mouse model of CIA.

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SAT0058 DEFICIENT DNA DAMAGE RESPONSE AND REPAIR IN ACTIVE RHEUMATOID ARTHRITIS AND THE EFFECT OF TREATMENT

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Background: Increased endogenous DNA damage poses a serious threat to cell health, since it may lead to mutagenesis, genomic instability and cellular apoptosis. DNA damage accumulation in immune cells occurs in patients with chronic inflammatory diseases, however; little is known on the types and prevalence of endogenous DNA damage in patients with Rheumatoid arthritis (RA).

Objectives: To study DNA damage response and repair network in patients with active RA and to test the hypothesis that anti-rheumatic treatment influences this network.

Methods: Peripheral blood mononuclear cells were isolated from 15 patients with active RA and 65 apparently healthy controls; 8 patients were re-examined after 12-week treatment. Endogenous DNA damage was determined using alkaline comet assay. Specific markers for single-strand DNA breaks (SSBs; RPA32) and double-strand DNA breaks (DSBs; γH2Ax, 53BP1) were measured using western-blot. Formation of DNA damage was assessed by oxidative stress and abasic DNA sites measurements. Chromatin organization and the two subpathways of the fundamental nucleotide excision repair mechanism, namely, transcription-coupled repair (TCR) and global genome repair (GGR), were assessed along the N-ras gene.

Results: A 3-fold increase of endogenous DNA damage levels (Olive Tail Moment reflecting both SSBs and DSBs) was evident in active RA [mean±SD; 12.8±7.5 versus 4.5±2.4, $p<0.001$), as well as induction of RPA32, γH2Ax and 53BP1, higher oxidative stress levels and increased abasic sites, compared to controls. While TCR capacity was preserved, GGR capacity was deficient in all active RA patients. Moreover, a more condensed chromatin structure was found in active RA compared to controls. Following treatment, chromatin structure loosened, GGR capacity was restored, oxidative stress and abasic sites decreased and levels of endogenous DNA damage reached control values in all patients.

Conclusion: Deregulated chromatin organization, deficient DNA repair capacity and augmented formation of DNA damage contribute to the accumulation of endogenous DNA damage in patients with active RA and are reversible after treatment. Additional studies to better understand the negative impact of DNA endogenous damage accumulation may create new therapeutic opportunities for patients with RA.

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SAT0059 APOLIPOPROTEIN B DERIVED PEPTIDES INHIBIT PRODUCTION OF PRO-INFLAMMATORY CYTOKINES IN PBMC OF RHEUMATOID ARTHRITIS (RA) PATIENTS AND IMPROVE ARTHRITIS IN ANIMAL MODEL OF RA

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Background: Alpha-enolase (ENO1) is a multifunctional glycolytic enzyme. The cell-surface expression of ENO1 is increased in monocytes isolated from peripheral blood mononuclear cells (PBMCs) of RA patients. In previous experiments, we reported apolipoprotein B (apoB) to be as a novel ligand of cell surface expressed ENO1 and to enhance chronic inflammation in RA (1).

Objectives: This study was performed to evaluate agonistic or antagonistic function of peptide sequences within apoB, which modulated severity of arthritis in K/BxN serum transfer arthritis mouse model.

Methods: Peptides binding to ENO1 were evaluated by peptide microarray. Peptides were designed to have twelve amino acids lengths with ten amino acids overlap. Levels of pro-inflammatory cytokines produced by PBMCs were measured after treatment with peptides in RA patients and healthy controls (HCs). To evaluate the antagonistic function of peptides, RA PBMCs pre-treated with peptides were stimulated with apoB and pro-inflammatory cytokines were measured in culture supernatant. Peptides were injected in K/BxN serum transfer mice and we measured the thickness of ankles and arthritis score to determine whether peptides could reduce arthritis severity.

Results: Among eighty five peptides from apoB, five peptides exhibited strong binding to ENO1. Two peptides increased production of pro-inflammatory cytokines, IL-1β, IL-6 and TNF-α, but three peptides did not change levels of pro-inflammatory cytokines in RA and HC PBMCs. However the three peptides reduced production of pro-inflammatory cytokines in RA PBMCs stimulated with apoB. These three peptides were named IP (inhibitory peptide)1, IP2 and IP3. IPs were injected after induction of the arthritis in K/BxN serum transfer mice in vivo. Ankle thickness and arthritis scores were substantially reduced in IPs treated group than control group, and synovial inflammation, bone erosion and cartilage damage of arthritis were less severe in the IPs-treated groups. Especially, IP2 showed the most significant effect.

Conclusion: The apoB derived peptides interacting with ENO1 could have novel therapeutic effect in RA.

REFERENCE

[1] Lee, J. Y., et al. (2018). "Apolipoprotein B binds to enolase-1 and aggravates inflammation in rheumatoid arthritis." Ann Rheum Dis 77(10): 1480-1489

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SAT0060 CHOLESTEROL SEQUESTERING IN MACROPHAGES CONTRIBUTES TO THE LIPID PARADOX IN CHRONIC ARTHRITIS

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Background: Patients with active rheumatoid arthritis (RA) have increased cardiovascular mortality, paradoxically associated with reduced circulating lipid levels (1-3). Several disease-modifying antirheumatic drugs (DMARDs), such as the JAK inhibitor tofacitinib, ameliorate disease activity along with an increase in serum lipids (4, 5). We previously demonstrated *in vitro* that tofacitinib favored cholesterol efflux from macrophages through an ABCA1-dependent mechanism (6). Furthermore, tofacitinib-treated chronic arthritic rabbits showed increased circulating lipids and decreased lipid accumulation within the synovium (6).
Objectives: Our aim was to explore *in vivo* whether inflammation impedes cholesterol efflux from macrophages, and whether tofacitinib restores macrophage cholesterol release during chronic arthritis. For that purpose, we assessed the ability of intraperitoneally-injected ^{3}H-cholesterol labelled macrophages to efflux cholesterol to circulating lipoproteins in collagen-induced arthritis (CIA) mice treated with tofacitinib or placebo, as compared to healthy controls.
Methods: DBA/1J mice were randomly assigned to healthy controls (Control, n = 9), CIA (CIA, n = 6) and CIA mice receiving 50 mg/kg/day tofacitinib, orally, for three consecutive days, starting on day 39 after CIA induction and coinciding with disease peak (CIA+TOFA, n = 6). The day after, ^{3}H-cholesterol labeled RAW264.7 macrophages were intraperitoneally injected into mice and tracer appearance was monitored in plasma lipoprotein subfractions, synovium, liver, bile and feces.
Results: The CIA group showed higher C-Reactive protein levels (CRP, *µg/ml*; Control: 10.90±0.49, CIA: 13.86±1.05, p=0.03 *vs.* Control) and lower circulating ^{3}H-cholesterol levels (*% of injected disintegrations per minute (dpm)/ml;* Control: 1.29±0.11, CIA: 0.92±0.11, p=0.04 *vs.* Control). Both serum CRP and ^{3}H-cholesterol –particularly the HDL fraction– were restored to baseline after the treatment with the JAK inhibitor (CIA +TOFA: 10.97±0.67 *µg/ml* and 1.37±0.20 *% of injected dpm/ml*, respectively, p=0.05 *vs.* CIA). Concomitantly, we observed an upward trend in ^{3}H-cholesterol accumulation within the synovium of CIA animals as compared to controls, which tended to normalize with the treatment.
Conclusion: Systemic inflammation induces cholesterol sequestering within macrophages *in vivo* by acting on cholesterol efflux transporters (6). Tofacitinib favors cholesterol release to plasma lipoproteins, hence increasing circulating cholesterol. This is not only due to a decrease in inflammation –an effect very likely shared with some other biologic DMARDs–, but also to a direct mechanism on ABCA1 transporters that favors cholesterol efflux. To our knowledge, this is the first report suggesting that cholesterol dynamics in the macrophage may contribute to the overall circulating cholesterol levels, especially considering that this phenomenon may occur in other cell types, such as adipocytes.

REFERENCES

[1] Johnsson H. et al. Ann Rheum Dis. 2013;73:1495–9.
[2] Myasoedova E. et al. Ann Rheum Dis. 2012;70:482–7.
[3] Choy E, Sattar N. Ann Rheum Dis. 2009;68:460–9.
[4] Charles-Schoeman C. et al. Semin Arthritis Rheum. 2016;46:71–80.
[5] Robertson J. et al. Nat Rev Rheumatol. 2013;9:513–23.
[6] Pérez-Baos S. et al. Br J Pharmacol. 2017;174:3018–31.

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SAT0061 IMPORTANT ROLE OF CD11C+ CELLSIN INFLAMMATORY ARTHRITIS

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Background: Dendritic cells (DCs) are important antigen presenting cells (APCs) and therefore they play an important role in bridging the innate and the adaptive immune response. DCs can be divided in different subsets with specific functions. As powerful APCs, DCs are thought to play an important role in the induction of autoimmune diseases such as rheumatoid arthritis. However, the active role of DCs in joint inflammation is not known yet.
Objectives: Investigation of the role of DCs cells in joint inflammation and destruction.
Methods: We analyzed histological sections of K/BxN serum transfer arthritis as well as hTNFtg arthritis for the presence of CD11c+ cells by immunohistochemistry. We used CD11c-diphteria toxin receptor (DTR) transgenic mice. K/BxN serum transfer arthritis was induced, and mice were given either DT or PBS or in wt and BARF3 deficient mice. In addition CD11c DTR mice were crossed into hTNFtg animals and also received either DT or PBS. The severity of arthritis was determined clinically and histologically.
Results: Both CD8+CD11c+ and CD11b+CD11c+, can be found in synovial tissue in TNF driven arthritis. Upon depletion of CD11c+ cells clinical signs of K/BxN serum transfer arthritis were significantly reduced. Histological analysis found reduced synovial inflammation after the depletion of CD11c+ cells in K/BxN arthritis. In addition, local bone destruction and the number of osteoclasts was also significantly reduced. In addition to K/BxN arthritis, we found that also in TNF-driven arthritis depletion of CD11c+ cells led to a striking reduction of synovial inflammation and a complete depletion of osteoclasts.
Conclusion: These data show that in addition to initiating an adaptive immune response, CD11c+ dendritic cells, are also involved in innate effector mechanisms of inflammatory arthritis. Especially CD11b+CD11c+ and monocyte derived inflammatory seem to play a role in inflammatory arthritis, suggesting that they could be an important therapeutic target.
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SAT0062 STRATIFIED MEDICINE FOR RHEUMATOID ARTHRITIS: PREDICTING RESPONSE TO BIOLOGIC THERAPY USING IMMUNE CELL SIGNATURES

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Background: Treatment selection of biologic therapy for patients with rheumatoid arthritis (RA) is currently a trial and error process, with approximately 40% failing to respond well to the first biologic. The lack of biomarkers to predict treatment response leads to further pain, joint damage, patient anxiety and is cost ineffective for those who are non-responders.
Objectives: We aim to identify immune signatures from a pre-treatment blood test to inform the choice of treatment strategies for stratified medicine.
Methods: RA patients with active disease (DAS28 > 5.1) who failed to respond to conventional DMARDs and were due to commence biologic treatment were included in the BRAGGSS cohort. Peripheral blood mononuclear cells (PBMCs) taken before the initiation of biologic treatment were available for 300 patients (good (60%), moderate (25%), and non-

responders (15%) to various biologics (anti-TNFs (68%), Rituximab (16%), Tocilizumab (13%), Abatacept (3%)). PBMCs were left unstimulated or stimulated (anti-CD3/CD28 beads or 10 ng/mL LPS) and stained with three flow cytometry panels including specific surface, intracellular and intranuclear markers to deeply characterise the function of several subsets of monocytes, NK cells, T cells and B cells (e.g. disease-associated cell populations such as PD-1^{hi}CXCR5^{-} peripheral T helpers (Rao DA *Nature* 2017), CD27^{-}HLA-DR^{+} effector CD4^{+} T cells (Fonseka CY *Sci Transl Med* 2018) and cytotoxic PD-1^{+}CXCR5^{-} CD8^{+} T cell subsets, $T_{bet}$$^{+}$CD11c^{+} autoimmune-associated B cells, CD14^{+}IL1β^{+} pro-inflammatory monocytes (Zhang F *BioRxiv* 2018)). Hypothesis-free clustering algorithms were also used for data analysis to identify unreported cell populations. Statistical association testing was preformed using mixed effects ordinal (EULAR response) or linear (DAS28 or its components) regression models.

Results: Preliminary interim analysis identified associations between pan-biologic non-response and spontaneous expression of pro-inflammatory cytokines (Th1, Th17 lineage) by CD4^{+} T cells ($p<0.003$). Good response to all biologic drugs was independently associated with the number of CD56^{dim}CD16^{+} NK cells ($p<0.001$). Good response to anti-TNFs was associated with TNFα, IFNγ and perforin producing CD4^{+} T cells after *in vitro* stimulation with anti-CD3/CD28 ($p<0.02$).

Conclusion: Ongoing work involves the replication of these results. The identification of immune cell types associated with response to a particular class of biologic drugs (e.g. anti-TNFs, but not other classes) might inform the choice of first line biologic drugs based on individual patients' immune profiles (stratification to treatment response categories). Cells or cytokines generally associated with non-response to all biologics could represent new therapeutic targets, at least in some patients groups.

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SAT0063 ASSOCIATION OF SMOKING WITH TRIPLE CONCORDANT SEROPOSITIVITY IN RA PATIENTS, AND WITH RHEUMATOID FACTOR IN THE REMAINING PATIENTS

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Background: The contribution of cigarette smoking to the risk of rheumatoid arthritis (RA) is larger for seropositive than for seronegative patients. Current pathogenic models explain this difference via the production of anti-citrullinated protein antibodies (ACPA) induced by protein citrullination in the lungs as a consequence of smoking. However, there are inconsistent results with this model including the van Wesemael *et al.* report, which found an association of smoking with the concurrent presence of ACPA, rheumatoid factor (RF) and anti-carbamylated protein antibodies (ACarPA), rather than with ACPA.

Objectives: We aimed to explore the relationship between smoking and the presence of FR, ACPA and ACarPA and their combinations in patients with RA.

Methods: Six cohorts with 2253 RA patients were obtained to replicate the van Wesemael *et al.* results. After replication, they were combined with the three cohorts from that study comprising 2238 patients to a total of 4491 patients. The results from the different cohorts were combined by fixed-effects meta-analysis. Most analyses involved comparisons between two levels of smoking exposure, never and ever smokers, considering the RF^{-}/ACPA^{-}/ACarP^{-}patients as the reference.

Results: Analysis of the replication set confirmed the predominant association of smoking with the concurrent presence of the three RA autoantibodies (OR = 1.99, P = 2.5 x 10^{-8}), whereas the patients with one or two antibodies were not different from the patients without antibodies (OR = 1.22, p = 0.4 and OR = 1.22, p = 0.3, respectively). The combined meta-analysis with all the cohorts clarified the dominant association of smoking with the triple concordant seropositivity (OR = 2.00, p = 4.4 x 10^{-16}). In contrast, there was no association with the patient bearing one autoantibody (OR = 1.12, p = 0.4), and an in-between association with the concurrent presence of two antibodies (OR = 1.26, p = 0.009). Moreover, the association with the presence of three antibodies was significantly larger than with two antibodies (OR = 1.54, p = 1.4 x 10^{-6}), whereas the association with the presence of two antibodies was not larger than with one autoantibody (OR = 1.11, p = 0.3). In the patients remaining after exclusion of the triple seropositive, the smokers were exclusively associated with the RF^{+} (OR = 1.28, p = 0.03 and OR = 1.30, p = 0.004 in the double and single positive patients, respectively). This association was independent of the reference, either the triple seronegative (OR = 1.29, p = 0.001) or all the RF^{-}patients (OR = 1.32, p = 0.0002).

Conclusion: Smoking increases RA susceptibility by promoting pathways leading to the concurrent presence of the three RA autoantibodies and, in its defect, to the production of RF. These actions are not covered by current pathogenic models and suggest that smoking accelerates epitope spreading.

REFERENCE

[1] van Wesemael, et al. Arthritis Res Ther. 2016;18:285.

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SAT0064 EXPANSION OF CD16+ MONOCYTE SUBSETS AND ACE EXPRESSION ARE ASSOCIATED WITH ARTERIAL THICKENING AND VASCULAR FUNCTION IN VERY EARLY RHEUMATOID ARTHRITIS

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Background: monocytes are largely recognized as drivers of the atherosclerosis development, the leading determinant of cardiovascular (CV) morbidity in rheumatoid arthritis (RA). Far from being a unique population, functionally and phenotypically subpopulations can be distinguished, although their relevance to CV disease is uncertain. Recently, the expression of angiotensin-converting enzyme (ACE) expression has been

described, with some heterogeneity being observed across monocyte subsets. However, although previously linked to blood pressure control, the significance of ACE expression on monocytes remains obscure.
Objectives: to evaluate whether monocyte subsets and ACE expression were associated with surrogates of CV subclinical disease in very early RA patients.
Methods: patients were recruited upon early referral to the rheumatology department. All patients were untreated at the time of sampling. The frequency of classical (CD14+CD16-), intermediate (CD14+CD16+) and non-classical (CD14lowCD16+) monocyte subpopulations and ACE expression were assessed by flow cytometry in peripheral blood. Plaque occurrence, cIMT and stiffness parameters were analyzed by Doppler ultrasound in internal carotid, middle cerebral and basilar arteries.
Results: 53 patients were recruited, 47 fulfilling 2010 ACR/EULAR classification criteria for RA (36 women, 26 FR+ and 26 ACPA+) and 6 fulfilling criteria for Clinically Suspect Arthralgia (CSA) (6 women, 3 RF+ and 2 ACPA+). Non-classical and intermediate monocytes were positively associated with cIMT (r=0.413, p=0.005 and r=0.353, p=0.018, respectively), as well as with pulsatility (r=0.332, p=0.026 and r=0.323, p=0.030) and resistivity indices (r=0.286, p=0.050 and r=0.277, p=0.045) at the left internal carotid artery. Expansion of CD16+ monocytes was not associated with disease activity, measured as DAS28 or SDAI (all p>0.050), but frequency of intermediate monocytes paralleled duration of the symptoms (r=0.324, p=0.020).
ACE expression was higher in CD16+ monocyte subsets than in their classical counterparts. ACE expression was not associated with blood pressure, individual traditional CV risk factors, body mass index nor with mSCORE (all p>0.050). ACE expression on intermediate and classical monocytes was correlated with cIMT (r=0.382, p=0.010 and r=0.349, p=0.019, respectively). Moreover, ACE expression in all monocyte subsets was strongly associated with resistivity and pulsatility indices at the internal carotid artery (all p<0.010).
Conclusion: the expansion of CD16+ monocyte subsets and the ACE expression are associated with arterial wall thickening and vascular functionality in treatment-naïve RA patients, hence suggesting a very early role for monocyte traits in this scenario.
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SAT0065 WNT5A INCREASES RHEUMATOID SYNOVIOCYTE MIGRATION THROUGH RYK RECEPTOR AND RHO-ROCK PATHWAY

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Background: Fibroblast-like synoviocytes (FLS) are pivotal in inflammation and joint damage of rheumatoid arthritis (RA). These cells acquire an aggressive and invasive phenotype and secrete inflammatory mediators, metalloproteases and cathepsins that perpetuate inflammation and lead to cartilage and bone damage. Given the importance of FLS in the pathogenesis of RA, there is a growing interest in developing new therapies aimed to revert their aggressive phenotype. To this end, a better knowledgement of molecular mechanisms involved in FLS behavior is needed. Recently, the role of non-canonical Wnt pathway has been highlighted in several processes as migration, invasion and inflammatory responses. The non-canonical Wnt signaling pathway included the planar cell polarity (PCP), with the activation of Rho and Rac GTPases, and the Wnt/Ca2+ pathways. We have previously demonstrated that Wnt5a contributes to the aggressive phenotype of FLS by increasing their migration and invasion ability, and by stimulating the inflammatory response.
Objectives: To analyse the molecular mechanisms involved in the enhancing effects of non-canonical Wnt5a pathway on the aggressive phenotype of rheumatoid synoviocytes.
Methods: The expression of receptors of non-canonical Wnt5a pathway was assessed in FLS from six RA patients by real-time PCR. Expression of these receptors was suppressed by siRNA transfection (Dharmacon) and the antibody (anti-RYK, Abgent). Pharmacological inhibitors were used to identify the signaling pathways. Thus, an inhibitor of ROCK pathway (Y-27632, Selleckchem) was used and a calcium chelator (BAPTA-AM, Enzo) for the inhibition of the PKC pathway. The expression of MAPKs was analyzed by western blot. Migration after stimulation with recombinant Wnt5a protein was analyzed by the wound healing assay using Ibidi inserts. The occupation area was determined by Image J software.
Results: We analyzed the expression of Wnt5a receptors, FZD1, FZD2, FZD4, FZD5, FZD7, ROR1, ROR2 and RYK of RA FLS. Although all receptors were expressed in theses cells, whereas ROR2 was weakly expressed, RYK showed the highest expression. Migration assays after receptor suppression by siRNA transfection or blocking antibodies showed the involvement of RYK on Wnt5a signaling in RA FLS. In effect, Wnt5a-induced migration was reduced by more than 25% in FLS treated with the anti-RYK antibody. In addition, Wnt5a-induced migration in FLS treated with ROCK inhibitor (Y-27632) was 32% lower than in FLS not treated. No change in spontaneous migration was observed in FLS treated with Y-27632. However, the treatment with the calcium chelator, BAPTA-AM, did not show any differential effect between the spontaneous or the Wnt5a-induced migration. In addition, we found the activation of MAP kinases, ERK and P38, as well as, AKT and GSK3β in FLS treated with rWnt5a. Nevertheless rWnt5a did not activate JNK. These effects were reversed after treatment with the ROCK inhibitor or after blocking the RYK receptor.
Conclusion: These results indicate that Wnt5a contributes to the aggressive phenotype of RA FLS by binding to RYK receptor, through Rho-ROCK pathway and the activation of MAPKs, ERK and P38, as well as the activation of AKT and GSK3β.
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SAT0066 DEFICIENCY OF TRANSCRIPTIONAL FACTOR T-BET ACCELERATES THE DEVELOPMENT OF COLLAGEN-INDUCED ARTHRITIS BY INDUCING T HELPER TYPE 17 DIFFERENTIATION

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Background: The transcriptional factor T-bet is required for Th-1 differentiation and important for regulating Th-17 differentiation, which plays a critical role in the development of collagen-induced arthritis (CIA). Previous studies reported that overexpression of T-bet suppresses Th-17 differentiation via inhibition of retinoic acid-related orphan receptor (ROR) γt and aryl hydrocarbon receptor (AhR) (1, 2). However, the function of T-bet in the development of CIA remains largely unknown.
Objectives: To clarify the role of T-bet on the pathogenesis of CIA.
Methods: 1) T-bet knockout (T-bet$^{-/-}$) mice (C57BL/6, B6 background) were generated as previously described (3). T-bet$^{-/-}$ mice were immunized with CII with CFA, and the incidence and severity of CIA was assessed. 2) Anti-CII antibodies in the sera from T-bet$^{-/-}$ mice on day 60 after the first immunization were measured. 3) Lymph node cells from B6 or T-bet$^{-/-}$ mice immunized with CII were analyzed by flow cytometry using antibodies specific for CD3, CD4, CD8, CD11b, CD11c, CD19, Gr1 and NK1.1. 4) The lymph node cells described above were cultured in the CII containing medium, then the cytokine production was assayed by ELISA.
Results: 1) CIA developed in the T-bet$^{-/-}$ mice was more severe than that of B6 wild-type mice and the incidence of arthritis was around 1.5-fold higher. 2) The levels of total IgG, IgG1, IgG2b, IgG3 antibodies against native chicken CII were significantly higher in T-bet$^{-/-}$ mice. However, IgG2a antibody production was significantly lower in T-bet$^{-/-}$ mice compared to B6 mice. 3) The number of CD4+ T (CD3+CD4+), CD8+ T (CD3+CD8+), B (CD19+), dendritic cells (CD11c+), macrophage (CD11c-CD11b+Gr1-), neutrophil (CD11c-CD11b+Gr1+), NK cell (CD3-NK1.1+) in the lymph node was not different but the number of NKT (CD3+NK1.1+) cells was significantly decreased in T-bet$^{-/-}$ mice.
4) The level of IL-17 and IL-22 in the culture supernatant was significantly higher in T-bet$^{-/-}$ mice, whereas that of IFNγ was comparable in the two groups.
Conclusion: CIA was significantly severe in T-bet$^{-/-}$ mice. The mechanisms of severe arthritis might be mediated through the up-regulation of IL-17 and IL-22 by Th-17 differentiation in the T-bet deficient and IFNγ independent manner or the decrease of NKT cells.

REFERENCES

[1] Kondo Y, et al. Overexpression of T-bet gene regulates murine autoimmune arthritis. Arthritis Rheum 2012;64:162-72.

[2] Yokosawa M, et al. T-bet over-expression regulates aryl hydrocarbon receptor-mediated T helper type 17 differentiation through an interferon g-independent pathway. Clin Exp Immunol 2016;188:22–35.
[3] Szabo, et al. Distinct effects of T-bet in TH1 lineage commitment and IFNg production in CD4 an CD8 T cells. Science. 2002;295:338-42.

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SAT0067 SECRETORY ANTIBODIES TO CITRULLINATED PEPTIDES IN PLASMA AND SALIVA FROM RHEUMATOID ARTHRITIS PATIENTS AND THEIR UNAFFECTED FAMILY MEMBERS

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Background: Mucosal involvement in early phases of rheumatoid arthritis (RA) pathophysiology has emerged as an attractive hypothesis, supported by several findings. Elevated levels of antibodies against citrullinated peptides/proteins (ACPA) can be found during a long pre-symptomatic period, preceding manifest arthritis. Secretory antibodies are produced at mucosal surfaces, but can also be detected in the circulation. Secretory ACPA in plasma has been demonstrated in patients with RA (1). First-degree relatives (FDRs) of patients with RA can be regarded as potential pre-RA patients or at-risk individuals. In a previous study, a higher prevalence of ACPA was found in FDRs than in healthy controls (2), with IgA-ACPA being more common than IgG-ACPA.
We hypothesized that formation of secretory ACPA is an early step in RA development, preceding the occurrence of regular non-secretory ACPA, and consequently secretory ACPA would be prevalent in a large proportion of FDRs.
Objectives: To evaluate secretory ACPA in plasma and saliva from patients with RA and FDRs.
Methods: We analyzed secretory antibodies to 2nd generation cyclic citrullinated peptides (anti-CCP) in plasma from 194 patients with RA and 191 FDRs unaffected by RA and salivary samples from 25 RA patients, 21 first-degree relatives and 11 controls.
In plasma, cutoff for secretory ACPA was set at the 99th percentile of healthy blood donors. In saliva, a positive test was defined as a difference between optical density values for IgA anti-CCP and IgA anti-cyclic arginine peptide (delta OD value) >2 SD above the mean delta OD value of the controls.
Mann-Whitney U test was used for continuous variables and Pearson Chi-square for categorical variables.
Results: Secretory ACPA occurred in 37 (19.1%) of RA patients but only in 2 (1%) of FDRs (table 1). Salivary IgA ACPA was found in 3/25 (12%) of patients with RA, but not in any of the 21 FDRs. 27% of FDRs were positive for regular non-secretory IgA ACPA in plasma, and out of them, only 2 individuals (5%) were positive for secretory ACPA in plasma. Among FDRs negative for regular ACPAs, no one was positive for secretory ACPA. Secretory ACPA had the highest PPV for identifying patients, while IgG ACPA had the highest negative predictive value (table 2).

Table 1. Demographic and laboratory characteristics of the study participants

	FDRs (n=191)	RA patients (n=194)	P value
Age (years), median (IQR)	60 (26)	66 (18.3)	<0.001
Female n (%)	111 (58.1)	136 (70.1)	0.014
Shared epitope, n (%)	83 (53.9)	116 (71.2)	0.001
Smoker ever, n (%)	81 (47.9)	109 (58.0)	0.057
IgG ACPA+, n (%)	34 (21.7)	140 (85.9)	<0.001
IgA ACPA+, n (%)	42 (26.8)	118 (72.4)	<0.001
IgM ACPA+, n (%)	35 (22.3)	74 (45.4)	<0.001
Secretory ACPA+, n (%)	2 (1)	37 (19.1)	<0.001
IgM RF+, n (%)	22 (14)	121 (74.2)	<0.001
IgA RF+, n (%)	35 (22.3)	123 (75.5)	<0.001

Table 2. Performance of circulating antibodies to identify patients with RA vs first-degree relatives

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Secretory ACPA+, n (%)	19.1	99.0	94.9	54.6
IgG ACPA+, n (%)	72.2	82.2	80.5	74.4
IgA ACPA+, n (%)	60.8	78.0	73.8	66.2
IgM ACPA+, n (%)	38.1	81.7	67.9	56.5
IgM RF+, n (%)	62.4	88.5	84.6	69.8
IgA RF+, n (%)	63.4	81.7	77.8	68.7

Conclusion: Secretory ACPA in plasma and saliva was rare in FDRs. Circulating secretory ACPA had the highest PPV of the RA-related antibodies tested to identify RA in these families. This implies that mucosal production of ACPA is not common in an at-risk population, but may be important in the transition from increased risk to actual RA disease.

REFERENCES

[1] Roos K, et al. Arthritis Res Ther. 2016;18(1):119.
[2] Young KA, et al. Arthritis Rheum. 2013;65(8):1995-2004.

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SAT0068 CIRCADIAN RHYTHMS OF IMMUNE SYSTEM IN HEALTHY INDIVIDUALS AND PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Chronobiological aspects play an important role in rheumatoid arthritis (RA), with major symptoms such as joint pain and stiffness follow a day-night-cycle that peak in the early morning. The circadian behavior of symptoms has been attributed to the rhythmic expression of cytokines and hormones[1,2]. Animal models of autoimmune inflammation demonstrated that immune cells, which belong to the vast producers of such cytokines, circulate in a circadian manner and that the circadian rhythm of circulating immune cell is different in health and disease[3]. Moreover, coordinating timing of glucocorticoid therapy (chronotheraphy) results in a greater reduction of morning stiffness and pain compared with the same glucocorticoid dose taken in the morning[4].
Objectives: Here, we aim to analyse the circadian rhythms of circulating immune cell populations in the periphery of healthy individuals and RA patients in order to optimize treatment strategies.
Methods: We performed a 24-hours study involving 14 eligible RA patients and 12 healthy individuals to monitor the dynamic occurrence of diverse immune cells in the periphery. A week prior to study day, the biological rhythms were synchronized by scheduled activities and food intakes. On the study day, blood was drawn every 2 hours throughout 24 hours using peripheral venous catheter. The participants were provided with regular meal, allowed to eat snacks ad libitum and carry passive activities. Blood samples were subsequently analyzed by flow cytometry using TruCount Beads to count absolute cell numbers. RNA from CD14$^+$ monocytes was analyzed by real-time PCR to monitor the circadian clock genes expression.
Results: We investigated major immune populations and found chronobiological differences in NK T cells, NK cells, CD8 T cells, CD4 T cells and regulatory T cells (Tregs) of healthy individuals and patients with RA. In RA Tregs showed a lag phase of 5 hours, while CD8 and CD4 T cells showed a mild reduction of the amplitude. NK T cells and NK cells did not circulate in a circadian manner in healthy individuals, but they exhibited circadian pattern in RA. In addition, the qPCR data also indicated a disrupted circadian rhythm on RNA level. Among ten clock genes that were examined, *REVERBα*, *PER1*, and *PER3* showed altered expression in RA patients. The expression of *REVERBα* was suppressed by 50% and the rhythm of *PER1* was diminished in RA patient.

Furthermore, the rhythm of *PER3* was present exclusively in RA patients, but not in healthy participants.
Conclusion: Taken together, we conclude that the circadian rhythms of immune cells in RA patients are different from that in healthy individuals. The alteration can be observed on both cellular and RNA level. We postulate that the alterations in circadian rhythms may contribute to disease manifestations and may have impact for optimizing diagnosis and therapy in RA. Further analysis is required to expand the data set. It is also of interest to investigate the functionality of circadian clock genes in immune cells.

REFERENCES

[1] Cutolo M, et al. Ann. Rheum. Dis. 67, 905–8 (2008).
[2] Straub RH, et al. Arthritis Rheum. 56, 399–408 (2007).
[3] Druzd D, et al. Immunity. 46(1),120-132 (2017).
[4] Buttgereit, et al. Lancet. 371: 205–14 (2008).

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SAT0069 **PROTECTIVE EFFECT OF PROTOCATECHUIC ACID RICH FRACTION OF TRIANTHEMA PORTULACASTRUM AGAINST COLLAGEN INDUCED RHEUMATOID ARTHRITIS VIA GUT MICROBIOTA MODULATION**

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Background: Rheumatoid arthritis, a chronic inflammatory joint disease affects people all over the world. Trianthema portulacastrum (TP) has been traditionally utilized for the treatment of rheumatism.
Objectives: The current study was envisaged to evaluate the effect of protocatechuic acid rich fraction of TP on type II collagen induced rheumatoid arthritis, inflammation and microbial population of gut by using rodent model.
Methods: Hydroethanolic extract of TP was fractionated with three different solvents (ethyl acetate, chloroform and n-butanol) and quantitatively analyzed with HPLC-DAD method which revealed n-butanol fraction of TP (BFTP) is rich in protocatechuic acid along with other phenolic compounds. Animals were randomly divided into five groups. Four groups were injected with bovine type-II collagen (BTC-II; 100μg) in Freund's complete adjuvant (0.1 ml) intradermally. On day 21, animals were again treated with BTC-II along with booster incomplete Freund's adjuvant injection. After 24 hrs, animal groups were administered intraperitoneally with their respective drug treatment, i.e., vehicle, BFTP (100, 200 and 400 mg/kg b.w.) and methotrexate (3 mg/kg b.w.), respectively once in a day for next 21 days. At the end of experiment serum level of pro-inflammatory cytokines was determined, and gut microbioata was analyzed by using Illumina HiSeq.
Results: Results revealed BFTP preadministered group exhibited significantly reduced level of paw swelling and arthritis score as compared to vehicle group. Inflammatory markers (IL-1β, IL-6, IL-7, IL-23 and TNF-α) of rheumatoid arthritis were also significantly alleviated by BFTP. Histological studies of mice ankle soft tissue also support the protective effect of BFTP. Additionally, BFTP repair altered gut microbial communities by reducing relative loads of inflammatory microbes such as Mucispirillum, Helicobacter and Lachnospiraceae.
Conclusion: The results conclude that BFTP possess beneficial anti-inflammatory response in arthritic model and can be used as a potential anti-arthritic agent for the management of arthiritis.
Disclosure of Interests: None declared
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Rheumatoid arthritis – prognosis, predictors and outcome

SAT0070 **PROTEOMIC SPECTRUM PROFILE IN INFLAMMATORY AND DEGENERATIVE ARTHRITIS**

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Background: The identification and quantification of protein biomarkers present in tissues and body fluids is a new area of interest in the clinical management of rheumatic diseases. Proteomics may identify novel biomarker(s) which assist in understanding the pathogenesis of rheumatic disorders with diagnostic and prognostic implications. In addition, proteomic techniques in RA may be helpful to identify newer autoantibodies and inflammatory acute phase proteins.
Yet, the integration of potential biomarkers resulting from rheumatic proteomics analyses in differential diagnosis of rheumatologic disorders is not yet fully established and so several studies are needed to confirm the efficacy of these approaches.
Objectives: The purpose of this study was to use Matrix Assisted Laser Desorption Ionization – Time of Flight – Mass Spectrometry (MALDI-TOF-MS) to identify differentially expressed disease-related and condition-specific peptide in serum of patients with Rheumatoid arthritis (RA) and osteoarthritis (OA).
Methods: Hundred participants were divided into three groups as following: RA group (35 patients with Rheumatoid arthritis representing patients with inflammatory arthritis); OA group (35 patients with Osteoarthritis representing patients with non-inflammatory arthritis); healthy control group (30 healthy volunteers). All participants were subjected to full history taking; clinical examination; and clinical Assessment of disease activity in RA patients using Disease activity score 28 (DAS-28); routine laboratory investigations; Acute phase reactants; serological tests; plain x-ray of affected joints, as well as serum proteomic profile using Magnetic beads (MB) separation and (MALDI – TOF – MS)**.[1]** Using the spectral data from the three groups, three different classification models for the three groups were generated using GA, SNN and QC algorithms. The GA model showed the best sensitivity and specificity in the three trials (RA versus control, OA versus control, and RA versus OA).
Results: In comparing RA versus control group; the results revealed 101 peaks that discriminated the RA from the control group; 53 were significant (PWKW p>0.05) and 48 nonsignificant. Three peaks (14;25;62) were significant and 2 were nonsignificant (43;53).
Regarding OA versus control group; 95 peaks were identified that discriminated the OA from the control group; 38 were significant (PWKW p>0.05) and 57 nonsignificant. Three peaks (18;3;14) were significant and peak 75 and 23 were nonsignificant.
Finally the RA group was discriminated from the OA group, the trial showed 113 peaks 73 were significant (PWKW p>0.05) and 40 nonsignificant. Five peaks were integrated (75:7767.82 40:2953.29 41:2991.59 48:4054.75 68:6434.51), and all integrated peaks were significant. The integrated peaks showed that all peaks were downregulated except peak 40 was upregulated.
Conclusion: Data obtained from proteomic analysis allow differentiation between RA, OA, and healthy subjects. Because of its simplicity and accuracy, (MALDI–TOF–MS) is a promising method for identifying differentially expressed inflammatory versus degenerative disease-related peptide.

REFERENCE

[1] Lorenz P, Ruschpler P, Koczan D, Stiehl P, Thiesen HJ. From transcriptome to proteome: differentially expressed proteins identified in synovial tissue of patients suffering from rheumatoid arthritis and osteoarthritis by

an initial screen with a panel of 791 antibodies. Proteomics 2003; 3(6): 991–1002.

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SAT0071 ANALYSIS OF CHRONOLOGICAL CHANGES IN JAPANESE VERSION OF HEALTH ASSESSMENT QUESTIONNAIRE SCORE AND FACTORS ASSOCIATED WITH J-HAQ REMISSION AT 5 YEARS AFTER DISEASE ONSET IN PATIENTS WITH RHEUMATOID ARTHRITIS USING THE IORRA COHORT

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Background: Recent advances in rheumatoid arthritis (RA) treatment including the introduction of biologics have greatly affected treatment strategies for RA, achieving remission as a realistic treatment target. However, few reports have been concerned chronological changes in long-term physical dysfunction among large numbers of RA patients in daily practice.
Objectives: To evaluate chronological changes in Japanese version of Health Assessment Questionnaire score (J-HAQ) score and J-HAQ remission rates at 5 years after RA onset using the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort.
Methods: RA patients who developed RA between 2000 and 2010 and who first visited our hospital during the year of RA onset were divided into two groups: 1) former onset group (RA onset between 2000 and 2005) and 2) recent onset group (RA onset between 2006 and 2010). J-HAQ scores and J-HAQ remission rates at baseline and at 5 years after onset were investigated for each group, and factors associated with J-HAQ remission after 5 years were assessed by logistic regression analysis. Methotrexate (MTX), corticosteroid (steroid) and biologic DMARDs user (bDMARDs) was defined as the patients if they were used each medication during the observation period.
Results: The former onset group and recent onset group included 357 and 291 RA patients, respectively. For the former onset group, the average J-HAQ score/J-HAQ remission rate at baseline and 5 years after the onset were 0.659/54.6% and 0.430/71.4%, respectively. The recent onset group showed significant improvements relative to the former onset group in J-HAQ score/J-HAQ remission rates at baseline and 5 years of 0.705/52.2% and 0.316/78.4%, respectively (p=0.011/0.044). The percentage of MTX and bDMARDs users was significantly higher in the recent onset group (former vs. recent onset group; MTX: 70.9% vs. 86.6% [p<0.0001]; bDMARDs: 5.3% vs. 23.0% [p <0.0001]). Significant factors associated with achieving J-HAQ remission at 5 years after RA onset were: patients in the recent onset group (p<0.001), male (p<0.001), younger (p<0.001), lower J-HAQ score (p<0.001) at baseline, and non-steroid user (p<0.001).
Conclusion: In daily practice, J-HAQ scores for RA patients remarkably improved with recent advances in RA treatment strategies. To achieve J-HAQ remission at 5 years of RA onset, beginning treatment in the early disease stage is needed to prevent deterioration of J-HAQ and treatments that avoid steroid use appear to be important.
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SAT0072 EVALUATION OF RHEUMATOID ARTHRITIS TREATMENTS AND JOINT OUTCOMES IN RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: RA-associated interstitial lung disease (RA-ILD) is an extra-articular manifestation of RA and is one of the leading causes of death in patients (pts) with RA.[1] Previous studies have indicated that clinical factors such as age, sex, smoking and autoantibody positivity are strongly associated with RA-ILD.[2] There is also evidence of active RA being related to increased risk for clinically apparent ILD.[3] However, there are limited data on how pts with RA-ILD are managed for their joint conditions and joint outcomes.
Objectives: To evaluate RA treatment patterns in pts with subclinical and clinical RA-ILD compared with pts with RA without ILD, and to assess joint disease activity at baseline and change in disease activity by treatment in all cohorts.
Methods: Data from adult pts with RA enrolled in a longitudinal sequential RA registry were analysed. Pts in the registry were evaluated annually by a rheumatologist for disease activity and treatment, and semi-annually on multiple clinical patient-reported outcomes (PROs) and resource utilisation parameters. Pts with chest computed tomography (CT) scans performed to evaluate clinical indications for ILD and with blood samples were included in this analysis. Pts with chest CT scans that were indeterminate for ILD were excluded from the study. Pts were then divided into two mutually exclusive groups: non-ILD RA pts and RA-ILD pts. RA-ILD pts were further divided into subclinical and clinically evident ILD. Date of chest CT scan was considered the index date. The two cohorts were compared using descriptive statistics to summarise baseline differences in demographics, disease activity measures, serostatus and treatments. Kruskal–Wallis test for continuous variables and chi-square test for categorical variables were performed, with two-sided significance level of 0.05. Multivariable linear regression was used to evaluate change from baseline to 12 months in joint disease activity for pts with available data at baseline and follow-up.

Table 1. Baseline characteristics and treatments by RA-ILD groups

	No ILD (n=29)	ILD (n=46)	Subclinical ILD (n=29)	Clinically evident ILD (n=17)
Age, years, mean (SD)	53.0 (12.2)	66.9 (9.5)*	68.3 (9.6)*	64.6 (9.1)*
Duration of RA, years, mean (SD)	16.9 (11.6)	23.0 (13.3)*	24.4 (14.4)*	20.6 (11.0)
Female, n (%)	28 (96.6)	36 (78.3)*	23 (79.3)	13 (76.5)
History of smoking, n (%)	12 (41.4)	29 (63.0)	20 (69.0)	9 (52.9)
RF positive, n (%)	n=27 18 (66.7)	39 (84.8)	24 (82.8)	15 (88.2)
RF titre, IU/mL, mean (SD)	n=27 105.0 (177.9)	338.7 (618.0)*	423.2 (759.3)*	194.7 (174.1)*
ACPA positive, n (%)	15 (51.7)	40 (87.0)*	26 (89.7)*	14 (82.4)*
ACPA titre, IU/mL, mean (SD)	87.1 (130.0)	212.8 (191.9)*	183.7 (149.3)*	262.6 (245.7)*
CDAI score, mean (SD)	n=21 21.1 (15.6)	n=39 26.3 (14.5)	n=25 26.3 (14.6)	n=14 26.4 (14.9)
mHAQ score, mean (SD)	n=27 0.4 (0.4)	n=43 0.6 (0.5)	n=27 0.5 (0.5)	n=16 0.6 (0.5)
Previous TNFi bDMARD, n (%)	2 (6.9)	7 (15.2)	2 (6.9)	5 (29.4)
Current TNFi bDMARD, n (%)	12 (41.4)	16 (34.8)	10 (34.5)	6 (35.3)
Previous non-TNFi, n (%)	0 (0.0)	3 (6.5)	0 (0.0)	3 (17.6)*
Current non-TNFi, n (%)	3 (10.3)	5 (10.9)	2 (6.9)	3 (17.6)
Previous steroids, n (%)	16 (55.2)	31 (67.4)	19 (65.5)	12 (70.6)
Current steroids, n (%)	6 (20.7)	22 (47.8)*	13 (44.8)*	9 (52.9)*
Previous MTX, n (%)	3 (10.3)	5 (10.9)	4 (13.8)	1 (5.9)
Current MTX, n (%)	7 (24.1)	17 (37.0)	14 (48.3)	3 (17.6)

*p<0.05 vs no ILD

ACPA=anti-citrullinated protein antibody; bDMARD=biologic DMARD; ILD=interstitial lung disease; mHAQ=modified HAQ; TNFi=TNF inhibitor

Results: 75 pts with chest CT scans were included in the analysis. Of these, 38.7% (n=29) were non-ILD RA and 61.3% (n=46) had some manifestation of RA-ILD. Of the RA-ILD cohort, 63.0% (n=29) and 37.0% (n=17) were classified as subclinical and clinically evident RA-ILD, respectively. At the time of chest CT scan, RA-ILD (vs non-ILD RA) pts were older with longer disease duration, a greater proportion were male and had higher anti-citrullinated protein antibody and RF titres (Table 1). In terms of RA treatments, a significantly greater proportion of RA-ILD (vs non-ILD RA) pts were on corticosteroids (CS; 47.8% vs 20.7%) and a significantly greater proportion of clinically evident RA-ILD (vs non-ILD RA) were on non-TNF inhibitor (TNFi) biologics. RA-ILD (vs non-ILD RA) pts had numerically higher joint disease activity and modified HAQ score at baseline (Table 1). However, the change in joint disease activity and PROs in RA-ILD pts was numerically greater vs non-ILD RA pts. In a multivariable analysis, RA-ILD status did not impact change in joint disease activity, but baseline joint disease activity was significantly associated with reduction in joint disease activity at 12 months (Table 2).
Conclusion: RA-ILD pts compared with non-ILD RA pts in clinical practice are more likely to be managed with CS therapy and non-TNFi bDMARDs. The improvement in joint disease activity was similar between RA-ILD and non-ILD RA pts. The analysis was limited by small sample size; further studies with larger pt numbers are required to confirm the findings.

Table 2. Multivariable analysis of change in disease activity (CDAI)

Parameter	Estimate	95% CI
Intercept	0.8	(–12.5, 14.0)
No ILD (vs ILD)	–3.9	(–12.8, 5.1)
RA duration, years	–0.1	(–0.5, 0.3)
Baseline CDAI score*	0.4	(0.0, 0.7)
No CS (vs CS)	–3.6	(–13.5, 6.2)

*p<0.05 vs no ILD
CS=corticosteroids; ILD=interstitial lung disease

REFERENCES

[1] Doyle JT, et al. Am J Respir Crit Care Med 2015;191:1403–12.
[2] Sparks JA, et al. *Arthritis Care Res (Hoboken)* 2016;68:753–62.
[3] Sparks JA, et al. *Arthritis Rheumatol* 2018; 70(suppl 10):abstract 884.

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SAT0073 STAT3/STAT5 BALANCE AS A BIOMARKER IN RA: CTLA4-IG AND T CELL DIFFERENTIATION THROUGH STAT SIGNALING

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Background: Regulatory T cells (Treg) play suppressive functions and are modulated by Abatacept (CTLA4-Ig). Limited data are available on CTLA4-Ig effect on Treg population in Rheumatoid Arthritis (RA).
Objectives: The aim of the study was to analyze if STAT3/STAT5 expression in CD4+ T cells in peripheral blood (PB) of RA patients at baseline predicts response to Abatacept treatment (after 12 months follow-up).
Methods: Early RA (ERA) and long-standing RA (LS-RA) patients with conventional DMARDs insufficient response were enrolled in this observational, investigative, monocentric, non-randomized, no profit study, and treated with CTLA4-Ig in combination with methotrexate. Each enrolled RA patients underwent peripheral blood sampling and CD4+ cells isolation using magnetic micro-beads at baseline and after 6-12 months follow-up. Flow cytometric analysis (FACS) for CD4 positive cells phenotype was performed to assess T-regulatory cells (Treg) as CD4+/CD25+/CD127- and CD4+/CD25+/Foxp3+, respectively. STAT3/STAT5 gene expression on CD4+ cells was performed by RT-PCR for each enrolled patient at every time-point follow-up. Low disease activity (LDA) and disease remission (DAS) achievement were assessed at 6 and 12 months follow-up (FU), respectively.
Results: A total of 35 patients were enrolled in the study (16 ERA and 19 LS-RA, respectively). At baseline, ERA and LS-RA did not differ based on clinical parameters. Eight (22.9%) withdrew from the study because of treatment failure (n=6), severe infection (n=1) and death (n=1). LDA or DAS remission within twelve months follow-up were achieved in 28/34 (82.4%) and 16/34 (47.1%) patients, respectively, without any significant difference among ERA and LS-RA. There were no significant differences in the demographic and clinical characteristics of RA patients at study based on LDA or DAS remission status achievement within 12 months FU, even stratifying patients based on disease duration. FACS analysis showed CD4+/CD25+/CD127- and CD4+/CD25+/Foxp3+ cells decrease during CTLA4-Ig treatment (p=0.01 and p=0.02, respectively after 12 months FU), despite disease duration. RT-PCR revealed that PB CD4+ cells of RA patients achieving LDA, but not DAS remission, after CTLA4-Ig treatment have significantly lower endogenous expression of STAT3 and STAT5 compared to RA patients not achieving this outcome (p=0.03 and p<0.001, respectively). Moreover, baseline STAT3/STAT5 ratio in PB CD4+ cells of RA patients directly correlates with Treg cells percentages (CD4+/CD25+/CD127- cells (%): R=0.518, p=0.03; CD4+/CD25+/Foxp3+ cells (%): R=0.549, p=0.02, respectively). Finally, baseline STAT3/STAT5 expression ratio on CD4+ cells > 0.93 (obtained by ROC analysis: AUC:0.754+/-0.100; Sensitivity 75.0%, Specificity: 80.0%) arose as baseline predictor factor of LDA achievement in RA patients treated with CTLA4-Ig [OR(95%CIs): 12.0 (1.98-72.89)].
Conclusion: STAT3/STAT5 expression ratio in T cells at baseline identify RA patients better responding to CTLA4-Ig, which decreases Treg cells.
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SAT0074 DAS-28 DISEASE ACTIVITY DEFINES THE TNFR1/2 CO-EXPRESSION PROFILE IN RHEUMATOID ARTHRITIS PATIENTS

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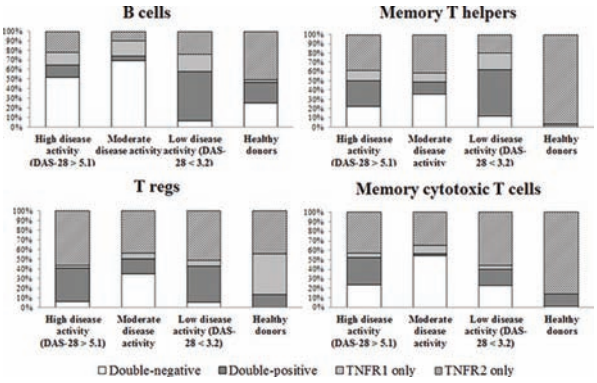
Background: TNF-alpha act as main proinflamantory cytokine in rheumatoid arthritis (RA) immune processes. However, TNF-alpha activity and functions may be regulate not only by soluble receptors (which act as decoys) but also by number, density, and co-expression of its membrane-bound receptors type 1 and 2 (TNFR1 and TNFR2).
Objectives: To analyze the TNFR1\2 co-expression profile in RA patient with different disease activity in comparison to healthy donors (HD).
Methods: PBMC were analyzed from 46 HD and 64 patients with RA using flow cytometry. Patients were divided according to the DAS-28 index into groups with high (n=22, 34.4%), moderate (n=30, 46.9%) and low (n=12, 18.8%) disease activity. Co-expression of TNFR1/2 was evaluated as percentage of cell with different receptors. Number of receptors of each type per cell was counted using QuantiBrite PE beads (BD, USA). The following populations were analyzed: total monocyte pool; common pool of B lymphocytes; common pool of T lymphocytes; cytotoxic T cells (CD8+), T helper cells (CD4+), activated (CD25+) cells among CD8+ and CD4+, T memory (CD45R0+) and naïve T cells

(CD45RA+) among cytotoxic and T helper cells; T regulatory cells (CD4 +CD25highCD127low); B1 cells (CD45+CD19+CD5+).

Results: We found that analyzed cell populations differ significantly in the co-expression of type 1 and 2 receptors for TNFα both between each other and compared to healthy donors. The most pronounced differences between groups of patients in the expression profile were shown for B cells, T reg and memory cells (figure).

The total proportion of cells with at least one type of receptors was significantly decreased as compared with HD (in the case of B cells, T-helper memory cells) or increased (in the case of naive cytotoxic T cells, naïve T helper cells, monocytes, T regs). This indicator may reflect the overall sensitivity of the cells of the subpopulation to the effects of cytokine. This mechanism may reflect the ability of the cells to react on certain TNF-alpha concentration or anti-cytokine therapy.

Conclusion: The profile of TNFR1\2 co-expression is changed in RA compared to heath. RA disease activity is associated with the changes in the amount and co-expression of type 1 and type 2 receptors for TNF-alpha on the surface of immunocompetent cells.



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SAT0075 FACTORS ASSOCIATED TO DEVELOPING CVD AND STROKE IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS- A BARFOT COHORT STUDY

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Background: Patients with rheumatoid arthritis (RA) have a higher risk of cardiovascular diseases (CVD) and stroke. More knowledge about associated factors is needed since it could have implications on different treatment strategies

Objectives: To study factors associated to CVD and stroke development in patients with established RA.

Methods: A questionnaire was sent twice to patients with established RA in the BARFOT cohort, in 2010 (n=1525) and in 2017 (n=1046) with a response rate of 73% and 68% respectively. 950 patients responded to both questionnaires. All patients fulfilled the ACR criteria for classification of RA and had a disease duration at inclusion (1992 to 2006) of ≤12 months. The patients reported body mass index, smoking habits, tender (TJC) and swollen joint count (SJC, 28-joints), pain intensity (NRS) and physical function (HAQ), health related QoL (EQ5D), and medical treatment (DMARD, corticosteroids and NSAID). Possible factors associated with developing CVD or stroke at the questionnaire in 2017 or not (dependent variable) was studied by using a logistic regression analysis.

Results: Twenty-two patients (3%) developed CVD and 55 (6%) patients stroke over the seven years between the two questionnaires. Patients that developed CVD were older and to a higher rate men. They also more often, 40% vs. 11%, p=0.001, reported treatment with corticosteroids at both questionnaires. In a multivariate regression analysis age, OR (95% CI) 1.071 (1.015-1.129), male gender 7.459 (2.664-20.883) and reporting treatment with corticosteroids at both questionnaires 4.473 (1.525-13.117) were associated to CVD. Patients that developed stroke were older and more often not treated with any DMARD, 30% vs. 18%, p=0.069. There were no other significant differences between the groups. In a multivariate regression analysis age, OR (95% CI) 1.081 (1.047-1.117) and reporting treatment with conventional DMARD 0.510 (0.259-1.004) were associated to stroke at the second questionnaire. There were no associations between reported use of NSAIDs and development of CVD or stroke in this study.

Conclusion: Knowledge about factors associated to cardiovascular disease is important when treating patients with established RA. Long-term treatment with corticosteroids seems to increase the risk to develop CVD. Treatment with DMARDs, especially conventional DMARDs, seems to decrease the risk to develop stroke. There were no association between developing CVD or stroke and NSAIDs in this study.

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SAT0076 EARLY REMISSION IS ESSENTIAL TO PREDICT LONGTERM REMISSION. CLINICAL RESULTS OF THE BELGIAN CAP48 RA COHORT

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Background: Early therapeutic intervention is crucial for patients with early rheumatoid arthritis (ERA). The goal of remission is achievable in a proportion of ERA patients.

Objectives: To evaluate the rate of patients in remission at 6 months and to correlate the 3 year remission rate. To identify baseline characteristics differences between patients achieving remission or not, and to report the best remission composite criteria to be used in daily care.

Methods: The Belgian CAP48 cohort supported by the French speaking radiotelevision (RTBF) is a unique prospective observational study of patients less than 50 years old with a recent diagnosis of ERA. All patients are naïve to DMARDs therapy and were recruited in different rheumatologic centers in Brussels and Wallonia. At baseline and every 6 months, demographic, specific clinical evaluation, questionnaires and laboratory were completed and treatment was adapted according each physician decision.

Results: 207 RA patients from 16 centers were analysed (162 F, 45 M, mean age 36.0 years, 27.8% with baseline erosion, 62.3% with ACPA, 59.9% with FR, mean HAQ 1.9, mean DAS28-CRP 4.54, mean SDAI 24.9 and mean CDAI 23.4) history) and a group of 106 patients followed up to 36 months. Clinical results are summarized in this Table.

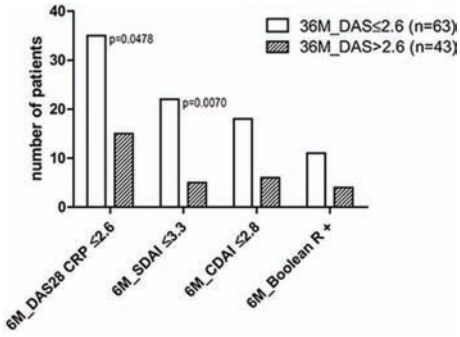
	DAS28-CRP mean	SDAI mean	CDAI mean	Remission (DAS28-CRP /SDAI/CDAI/Boolean) %	HAQ mean
Baseline n=207	4.54 (1.15)	24.9	23.4		1.09
Months 6 n=207	2.83 (1.21)	10.3	9.7	49.3/29.0/25.1/21.7	0.61
Months 36 n=106	2.47 (1.11)	8.5	7.5	59.4/39.6/34.9/31.1	0.52

Correlation between early 6 months response and long-term remission at 36 moths was performed in 106 patients: 63 patients achieved DAS28-CRP remission at 36 months *versus* 43 patients.

DAS28-CRP and SDAI composite remission criteria observed at 6 months could predict long-term remission observed at 36 months (Figure); with DAS28-CRP, SDAI and CDAI mean values statistically different ($p < 0.01$, test-t) between two group.

At baseline, the following parameters are similar in two groups “long term remission” and “no long term remission”, respectively: age (34.3 vs 33.8 yrs); Female (76.2 vs 72.1%); smoker (24.1 vs 34.2%); ACPA positive (66.7 vs 62.8%); mean DAS28-CRP (4.4 vs 4.7); mean HAQ (1.0 vs 1.2); baseline X-ray erosion (21.7 vs 39.5%).

The time for diagnosis and treatment initiation is statistically shorter in "long term remission" group compared to the "no remission group" (mean of 1.4 months vs 3.4 months; p=0.042).
Additionally, global remission (DAS28-CRP<2,6, HAQ<0,5 and no X-ray progression) was observed in 41.5% of the long term remission group. The majority of these patients (79%) are treated with Methotrexate.
Conclusion: Early and long term remission is an achievable goal in our observational CAP 48 study cohort. Early diagnosis is critical in standard of care. At 6 months, DAS28-CRP and SDAI were the best remission criteria to predict long term remission.



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SAT0077 IMPACT OF THE COMBINED PRESENCE OF EROSIONS AND ACPA ON 6 AND 12 MONTHS CLINICAL OUTCOMES OF RHEUMATOID ARTHRITIS : RESULTS FROM THE METEOR REGISTRY

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Background: Despite efforts to predict treatment response, treatment of rheumatoid arthritis (RA) patients remains mostly a case of trial and error. Presence of erosions and ACPA are often considered poor prognostic factors based on their association with radiographic damage progression, but with the introduction of treat-to-target ever fewer patients develop significant radiographic damage. Therefore research into prognostic factors should focus on clinical outcomes.
Objectives: To investigate in newly diagnosed RA patients if presence of erosions and/or ACPA are associated with functional ability, disease activity and treatment survival during the first year of treatment in daily practice.
Methods: Newly diagnosed patients with a clinical diagnosis of RA, ≥3 months follow-up and available data on ACPA, erosions and medication were identified in the international, observational METEOR registry (n patients=4623). Timing and frequency of follow-up visits were according to daily practice. We focused at results after a maximum follow-up duration of 6 months or of 1 year from baseline. Associations between the presence of erosions and/or ACPA (4 groups) with the change of DAS and HAQ over time were assessed using linear mixed models.
Time to treatment change during the first year of follow-up was compared between the ACPA/erosions groups using multiple failure-times Cox regression. Treatment change was defined as a change in type of treatment. A change in medication dose or tapering was not considered a treatment change.
Missing data were imputed using multiple chained equations (40 cycles) and models were adjusted for the potential confounders age, gender, smoking, symptom duration, BMI, initial medication and country. In case of statistically significant effect modification (p<0.20) by country, medication group (csDMARD monotherapy, csDMARD combination therapy, csDMARD + glucocorticoid and other) or symptom duration group (<1 year, 1-2 years, 2-5 years and >5 years), results were stratified.
Results: Baseline characteristics and follow-up duration of each ACPA/erosions group are shown in table 1. Baseline DAS and HAQ were slightly higher in erosions+ patients. Follow-up duration was similar between the 4 groups. We found statistically significant differences in DAS and HAQ change over time between the 4 groups, both after maximum follow-up durations of 6 months and of 1 year (table 1), but differences were small and not clinically relevant.
Patients who were erosions-/ACPA- were less likely to switch treatment [HR (95% CI) 0.79 (0.69; 0.90)] compared to a reference group of erosions-/ACPA+ patients. Patients who were erosions+/ACPA- [HR (95% CI) 0.92 (0.79; 1.08)] or erosions+/ACPA+ [HR (95% CI) 1.01 (0.92; 1.10)] were not statistically significantly different from the reference group in their likelihood to switch treatment. No effect modification was found by country, medication or symptom duration.
Conclusion: In this analysis of worldwide real life data, we found statistically significant, but no clinically relevant differences in treatment response to initial DMARD therapies as measured by DAS and HAQ in ACPA-/erosions-, ACPA-/erosions+, ACPA+/erosions- and ACPA+/erosions+ RA patients. However, ACPA-/erosions- patients were less likely to switch treatment. Thus, in newly diagnosed RA patients who are treated according to modern treatment strategies, the (combined presence of) ACPA and erosions was no risk factor for worse disease activity or physical functioning, although ACPA-/erosions- patients had fewer treatment changes.

Table 1. Baseline characteristics and follow-up duration of each ACPA/erosions group.

		ACPA negative		ACPA positive	
		Erosions negative n=701	Erosions positive n=344	Erosions negative n=1585	Erosions positive n=1993
Female (%)		83.0	83.4	81.4	84.9
RF (% positive)		31.0	33.5	93.0	95.3
Smoking (%)	Never	81.2	88.6	85.3	91.6
	Current	7.3	4.7	9.3	5.2
	Stopped	11.6	6.7	5.4	3.2
Age (years) *mean (SD)*		51 (16)	50 (14)	48 (13)	49 (12)
BMI *mean (SD)*		27.7 (6.0)	27.0 (6.0)	25.9 (5.9)	25.7 (5.7)
Symptom duration (months) *median (IQR)*		12 (4-36)	36 (12; 72)	18 (6-48)	48 (19; 108)
HAQ *mean (SD)*		0.98 (0.61)	1.1 (0.6)	0.88 (0.59)	1.1 (0.6)
DAS *mean (SD)*		3.5 (0.93)	4.0 (1.0)	3.6 (0.97)	4.0 (0.95)
ESR *mean (SD)*		47.5 (32.8)	60.1 (37.8)	65.5 (36.0)	72.8 (36.0)
Initial treatment (%)	csDMARD mono	51.8	42.2	55.5	29.1
	csDMARD combi	14.3	17.4	17.9	22.6
	csDMARD + GC	27.5	37.2	23.9	45.1
	Other	6.43	3.2	2.7	3.2
Follow-up duration (months) *median (IQR)*		9.2 (6.0; 10.6)	8.8 (6.0; 10.7)	9.0 (6.2; 10.6)	9.3 (6.7; 10.6)

Based on non-imputed data. ACPA = anti-citrullinated protein antibodies, RF = rheumatoid factor, BMI = body mass index, HAQ = health assessment questionnaire, DAS = disease activity score, ESR = erythrocyte sedimentation rate, mono = monotherapy, combi = combination therapy, GC = glucocorticoid.

Table 2. Associations between the presence of erosions and/or ACPA on the change of DAS and HAQ over time (n=4623).*

	6 months p-value†	12 months p-value†	6 months B(95% CI)	12 months B(95% CI)
	Interactions with time		Stratified analyses: evolution over time (months)	
DAS				
Ero- ACPA-	0.481	0.551	-0.24 (-0.27; -0.22)	-0.11 (-0.12; -0.10)
Ero+ ACPA-	0.001	<0.001	-0.30 (-0.34; -0.26)	-0.14 (-0.16; -0.12)
Ero- ACPA+	*Ref*	*Ref*	-0.24 (-0.25; -0.22)	-0.11 (-0.11; -0.099)
Ero+ ACPA+	<0.001	<0.001	-0.30 (-0.32; -0.29)	-0.12 (-0.13; -0.12)
HAQ				
Ero- ACPA-	0.035	0.121	-0.081 (-0.096; -0.065)	-0.034 (-0.040; -0.027)
Ero+ ACPA-	0.072	0.034	-0.084 (-0.10; -0.064)	-0.038 (-0.047; -0.029)
Ero- ACPA+	*Ref*	*Ref*	-0.062 (-0.072; -0.053)	-0.027 (-0.031; -0.023)
Ero+ ACPA+	<0.001	0.047	-0.086 (-0.095; -0.078)	-0.033 (-0.037; -0.029)

*Results stem from multivariable linear mixed models analyses with random intercept and slope and exchangeable covariance matrix, adjusted for age, gender, smoking, symptom duration, BMI, initial medication and country. Regression coefficients represent the units of change in the outcome per unit of time, in this case, per month. Missing data were imputed using multiple chained equations (40 cycles).
†P-values are only shown for the interaction between erosions/ACPA and time in months. In the presence of a statistically significant interaction, results are stratified by gender and the evolution of DAS and HAQ over time is shown for the erosions/ACPA groups separately.

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SAT0078 MAJOR CHANGES IN THERAPY PRODUCE SIGNIFICANT CLINICAL IMPROVEMENT ACROSS A BROAD RANGE OF CLINICAL DISEASE ACTIVITY IN US VETERANS WITH RHEUMATOID ARTHRITIS

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Background: Our recent work showed that 41% of patients with moderate/severe rheumatoid arthritis (RA) by Disease Activity Score for 28 joint count (DAS28) did not have changes in RA therapy as recommended by current guidelines (1). Reasons identified for the decision not to escalate therapy was provider's opinion that RA disease was adequately controlled despite moderate/severe disease activity by DAS28, and that changes in therapy may not produce significant improvements in disease activity (1).

Objectives: 1) Compare short-term differences in ACR20 response between patients with and without a major therapeutic change (MTC) over a range of disease activity; 2) Determine whether ACR20 responses vary by disease activity measures (DAMs) used to assess disease activity (i.e., DAS28, Clinical Disease Activity Index [CDAI], Routine Assessment of Patient Index Data 3 [RAPID3]).

Methods: Each clinic visit for US Veterans enrolled in the VA Rheumatoid Arthritis (VARA) registry was evaluated if the visit had: 1) a complete set of DAMs (DAS28, CDAI, RAPID3) recorded; 2) two other visits with all DAMs during the preceding 18 months separated by at least 60 days and one visit with all DAMs between 60 and 180 days following the visit date; 3) clinical data available for 18 months prior to visit date; and 4) $\geq$6 tender and $\geq$6 swollen joints at visit date. Each patient was assessed for MTC within 1 week before and 30 days after visit date. MTC was defined as any of the following: 1) initiation of new biologic or nonbiologic disease-modifying antirheumatic drug (DMARD) or prednisone (as new agent or after 90-day gap during baseline); 2) escalation of DMARD dose by $\geq$25%; or 3) increase in monthly average prednisone dose by 25%; and/or 4) injection of 2 or more joints with corticosteroids. Clinical improvement was defined as an ACR20 response comparing each eligible visit DAM to the first follow-up visit DAM observed between 60 and 180 days of the eligible visit date. ACR20 response was compared between eligible visits with and without a MTC and stratified by quartiles of disease activity by each DAM. The Generalized Estimating Equations (GEE) model was fitted using the exchangeable working covariance structure to account for clustering of visits within patients. Models for each DAM were adjusted for age, disease duration, race, seropositive status, comorbidities, disease stability, and recent medication changes in the observations period prior to the visit date.

Results: There were 383 patients (92% were male, mean age was 62.9 years, mean disease duration was 12.5 years, 83% tested positive for rheumatoid factor, and 79% positive for anti-cyclic citrullinated peptide antibodies) who contributed 1,193 eligible visits. Visits with a MTC had a higher rate of ACR20 response in comparison to visits without a MTC at all levels of disease activity. A MTC at a visit with the highest disease activity (quartile 4) consistently had the largest proportion of follow-up visits with an ACR20 response. The overall effect for MTC was statistically significant across all 3 DAMs. Across quartiles, the MTC group consistently had a higher proportion of follow-up visits with ACR20 response compared to the group without a MTC. Risk Ratios from the adjusted analysis are presented in the table.

Conclusion: All patients with active RA have a significant potential to benefit with a MTC. This potential for improvement was seen across all degrees of disease activity and with all three DAMs.

ACR 20 response with or without major therapeutic change (MTC)			
DAMs, quartiles (Q)	**With MTC**	**Without MTC**	**Risk Ratio**
DAS28			
Overall effect	34% (29%, 39%)	22% (18%, 28%)	1.52 (1.23, 1.88)
Q1: 2.35–4.87	25% (17%, 33%)	15% (10%, 22%)	1.60 (0.98, 2.54)
Q2: 4.88–5.60	33% (24%, 43%)	20% (14%, 28%)	1.65 (1.07, 2.56)
Q3: 5.61–6.29	30% (23%, 39%)	23% (16%, 30%)	1.31 (0.89, 1.95)
Q4: 6.30–8.76	47% (40%, 57%)	30% (22%, 41%)	1.55 (1.12, 2.38)
CDAI			
Overall effect	35% (31%, 40%)	23% (19%, 31%)	1.52 (1.19, 1.89)
Q1: 14.7–26.6	31% (22%, 41%)	15% (10%, 21%)	2.10 (1.28, 3.35)
Q2: 26.7–32.9	27% (20%, 35%)	21% (15%, 31%)	1.25 (0.84, 1.95)
Q3: 33.0–41.7	41% (33%, 49%)	30% (23%, 39%)	1.34 (1.02, 1.87)
Q4: 41.9–71.0	42% (34%, 52%)	26% (18%, 39%)	1.60 (1.10, 2.52)
RAPID3			
Overall effect	34% (29%, 38%)	21% (17%, 26%)	1.59 (1.28, 2.00)
Q1: 0.33–3.61	22% (14%, 31%)	18% (12%, 25%)	1.23 (0.69, 1.91)
Q2: 3.62–4.99	39% (31%, 49%)	21% (15%, 28%)	1.86 (1.32, 2.70)
Q3: 5.00–6.28	31% (23%, 39%)	20% (13%, 29%)	1.53 (0.92, 2.46)
Q4: 6.31–9.55	42% (35%, 51%)	25% (17%, 34%)	1.68 (1.19, 2.62)

Data presented with 95% confidence intervals.

REFERENCE

[1] Stever, et al. Utility of administrative and clinical data to predict major change in medical treatment in US Veterans enrolled in the Veterans Affairs Rheumatoid Arthritis (VARA) registry. Clin Exp Rheumatol; 2018 Epub ahead of print.

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SAT0079 PREDICTING PATIENTS WITH HIGH PAIN & PSYCHOLOGICAL SYMPTOMS (P&PS) IN EARLY RHEUMATOID ARTHRITIS USING LATENT CLASS ANALYSIS. RESULTS FROM THE TACERA, A LONGITUDINAL COHORT

Lewis Carpenter, Katie Bechman, Andrew Cope, Elena Nikiphorou, James Galloway, Sam Norton, On behalf of all the researchers of the Towards A Cure for Early Rheumatoid Arthritis (TACERA) working group . *King's College London, London, United Kingdom*

Background: Despite advances in the treatment of rheumatoid arthritis (RA), pain and psychological symptoms remain a burden for many patients. The precise relationship between inflammation and patient reported symptoms, such as pain, fatigue and mental health in the disease is unclear. However, evidence suggests that over time there may be discordance between inflammation and patient reported outcomes, such that some patients with low inflammation will experience persistent symptoms. It is hypothesised that three distinct patient sub-groups exist; low inflammation/low symptoms, low inflammation/high symptoms, and high inflammation/high symptoms.

Objectives: To identify sub-groups of patients with respect to inflammatory markers and levels of P&PS over time.

Methods: Demographic, clinical and laboratory data were recorded at baseline (pre-treatment), 6, 12, and 18-months from 239 early RA patients recruited to the Towards A Cure for Early Rheumatoid Arthritis (TACERA) cohort. Individual components of the DAS28 (tender joints, swollen joints, ESR, CRP and patient global) at post-treatment assessments, along with patient reported visual analogue scales for pain, fatigue and the SF-36 Mental Component Score (MCS) were used to identify sub-groups using longitudinal latent class analysis (LCA). Logistic regression models identified variables associated with class membership at 6, 12 and 18-months follow-up.

Results: LCA indicated two rather than the hypothesised three sub-groups; low inflammation/low symptoms and low inflammation/high symptoms. This was likely because ESR and CRP were well controlled by 6-months and maintained by 18-months for the majority of individuals. There were 86 (36%) 59 (35%) and 41 (39%) classified as having high symptoms at 6, 12 and 18-months. 78% of patients initially in the low symptom group remained in the low symptom group between 6 and 18-

months. Rheumatoid Factor (RF) positivity and higher baseline fatigue were associated with high symptoms at 6months; decreasing ESR from 6 to 12-months was associated high symptoms at 12months, and having high symptoms at 12-months, along with reduced Swollen Joint Count (SJC), CRP and MCS from month 12 to 18 was associated with high symptoms at 18-months.

Conclusion: Tight treatment control resulted in controlled Inflammation by 6-months, resulting in just two main patient sub-groups; those with low and high P&PS. Over one-third of patients experienced high pain and psychological symptoms. Membership of the high symptom group was associated with RF positivity but was mainly driven by prior symptom experience. Whilst inflammatory control remains a primary target, other treatments targeting pain, fatigue and mental health must be considered to reduce the burden of disease.

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SAT0080 COMPARISON OF INFLAMMATORY CYTOKINES LEVELS IN RHEUMATOID ARTHRITIS WITH CAROTID PLAQUE; CASE-CONTROL STUDY

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Background: There is a 50% increase in cardiovascular mortality in RA compared to controls. Chronic inflammation causes endothelial dysfunction and accelerated atherosclerosis. Key molecular pathways in this process are dependent on cytokines like TNF-α, IL-1, IL-6, among others, which are shared with RA. Increased disease activity could contribute to atherosclerosis. Carotid ultrasound (US) has recently been recommended as a screening tool for early detection of subclinical atherosclerosis.

Objectives: To compare different cytokines between Mexican-mestizo RA-subjects with/without carotid plaque (CP).

Methods: An observational cross-sectional trial was designed. Inclusion criteria: age between 40-75 years old, fulfillment of the 2010 ACR/EULAR classification criteria, and detection of a CP during a carotid US. Subjects with a prior diagnosis of cardiovascular disease or a poor US window were excluded. RA subjects were matched to controls (RA patients without CP) by age and cardiovascular (CV) comorbidities. Every subject had a carotid US performed; reviewed by two board-certified radiologists. Cytokines measured were IL-1, IL-6, TNF-α, VCAM-1, ICAM-1 and MMP-9, using an ELISA reader (Glomax E9032). Descriptive analysis was done with frequencies (%), median (q25-q75), and comparisons between groups with Chi square test and Mann U Whitney's test.

Results: 71 subjects were included, 95.8% were females, with a median age of 58 years (54-65). Levels of cytokines in Table 1. Comparisons between groups are in Table 2. Groups were well balanced, with no differences in CV comorbidities (p>0.05). No significant differences among cytokine levels regarding CP were found. Subjects in remission (n=12, 33%) had a lower prevalence of CP (p<0.05, OR: 0.3; 95% CI: 0.1-0.9) and a lower median IL-1 level than those with higher disease activity (p<0.05). No significant differences were found among any other of the compared cytokines.

Table 1. Cytokines levels

	Median(q25-q75)
IL1, pg/ml	8.1 (6.6-9.6)
TNF-a, pg/ml	76 (61-101)
IL6, pg/ml	4.4 (4.1-4.8)
ICAM, ng/ml	91 (61-141)
VCAM, ng/ml	56.5 (41.3-65.1)
MMP9, pg/ml	811 (721-931)

Table 2. Clinical characteristics.

Variable	CP (n= 37)	No CP (n=34)	*p*
Age, years median (q25-q75)	59.2 (54.8-66.1)	57.7 (53-61.2)	NS
Female, n (%)	35 (94.6)	33 (97.1)	NS
Dyslipidemia, n (%)	7 (18.9)	6 (17.6)	NS
T2DM, n (%)	10 (27)	7 (20.6)	NS
Hypertension, n (%)	12 (32.4)	10 (29.4)	NS
BMI, median (q25-q75)	29 (26.5-31.1)	27.9 (24.6-33.2)	NS
Disease duration, media ± SD	12.4 ± 9.9	10.6 ± 9	NS
DAS28 CRP, median (q25-q75)	2.9(1.5-3.9)	2.39 (1.8-3.1)	NS
MTX n, (%)	17 (45.9)	22 (64.7)	NS
Prednisone, n (%)	27 (73)	24 (70.6)	NS
IL-1 pg/ml, median (q25-q75)	8.7 (6.7-10.1)	7.9 (6.1-9.3)	NS
TNF-a pg/ml, median (q25-q75)	76 (61-101)	76 (61-96)	NS
IL-6 pg/ml, median (q25-q75)	4.4 (4.1-4.9)	4.4 (3.9-4.8)	NS
ICAM ng/ml, median (q25-q75)	91 (61-118.5)	83.5 (61-217.2)	NS
VCAM ng/ml, median (q25-q75)	58.1 (42.1-64.8)	54.3 (35.1-65.9)	NS
MMP9 pg/ml, median (q25-q75)	811 (711-938.5)	821 (724.7-931)	NS
Remission (DAS 28-CRP<2.6), n (%)	12 (33.3)	20 (58.8)	**0.032**

Conclusion: In our cohort subjects in remission had a lower prevalence of CP (OR= 0.3, 0.1-0.9). No difference was found between cytokines regarding CP. Subjects with active disease had a higher level of IL-1 than subjects in remission. To our best knowledge, this is the first study to evaluate levels of cytokines in Mexican RA-subjects.

REFERENCES

[1] López R, et al. Cardiovascular risk assessment in patients with rheumatoid arthritis. Autoimmun Rev 2016.

[2] Pasceri V, et al. A tale of two diseases: Atherosclerosis and rheumatoid arthritis Circulation 1999.

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SAT0081 BOTH OVERFAT AND MYOPENIA ARE ASSOCIATED WITH PHYSICAL DYSFUNCTION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Comprehensive disease control has been recommended by EULAR guidelines for rheumatoid arthritis (RA) which includes simultaneous achievement of stringent control of the signs and symptoms of inflammation, the absence of radiographic progression and normal physical function. Identifying those patients at high risk of disability at a sufficiently early stage of their disease course presents a major challenge. The associations of body mass index (BMI) and body composition (BC) with physical activity function in RA patients still obscure.

Objectives: To investigate the characteristics of BC and BMI in RA patients and their association with physical activity function.

Methods: Consecutive RA patients were recruited and clinical data including disease activity, function and radiographic assessment were collected. BC was assessed by bioelectric impedance analysis. Overfat was defined by body fat percentage (BF%) as ≥25% for men and ≥35% for women. Myopenia was defined by appendicular skeletal muscle mass index (ASMI) ≤7.0kg/m^2 in men and ≤5.7kg/m^2 in women. Subjects were categorized by BMI as underweight (BMI<18.5 kg/m^2), normal weight (18.5 kg/m^2≤BMI<24 kg/m^2), overweight (24 kg/m^2≤BMI<28 kg/m^2) and obese (BMI≥28 kg/m^2) according to Chinese criteria. Physical dysfunction was defined by HAQ-DI≥0.5.

Results: There were 516 RA patients (mean age 49.8±12.9 years old with 83% women) recruited, and 37% with physical dysfunction. Compared with those with normal physical function, RA patients with physical dysfunction

were older with longer disease duration, and had higher disease activity indicators including timing of morning stiffness, 28TJC, 28SJC, PtGA, PrGA, PainVAS, ESR, CRP, DAS28-CRP, SDAI and CDAI, as well as higher radiographic assessment including mTSS, JSN subscore and JE subscore (all *P*<0.05). As for BMI and BC, RA patients with physical dysfunction had higher BF% (mean 31.05% vs. 29.02%, *P*=0.007) and prevalence of overfat (44% vs. 27%, *P*<0.001), lower ASMI (mean 5.73 vs. 6.11, *P*<0.001) and higher prevalence of myopenia (55% vs. 38%, *P*<0.001) than those with normal physical function, while no difference in BMI between two groups. After adjustment confounding factors, multivariate logistic regression analysis showed overfat (*OR*=2.990, 95%*CI*: 1.695-5.274) and myopenia (*OR*=1.960, 95%*CI*: 1.191-3.225) were positively associated with physical dysfunction respectively. Further compared with patients with normal fat, patients with overfat had significantly higher rates of dysfunction of all eight physical activities including dressing, rising, eating, walking, hygiene, reaching, griping and activities respectively (all P<0.01), with the highest rate 57.5% in eating dysfunction and the lowest rate 38.6% in dressing dysfunction. Comparisons between patients with and without myopenia showed similar results with the highest rate 52.4% in eating dysfunction and the lowest rate 37.7% in rising dysfunction in those with myopenia.

Conclusion: Overfat and myopenia are present in near half RA patients with physical dysfunction which are associated with dysfunction of all eight physical activities especially eating.

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SAT0082 ASSOCIATIONS OF BASELINE CLINICAL AND BIOMARKER FACTORS WITH SYMPTOMS AND FUTURE DEVELOPMENT OF CLINICALLY-APPARENT RHEUMATOID ARTHRITIS IN AN ACPA POSITIVE COHORT

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Background: Subjects who are in the preclinical rheumatoid arthritis (RA) state can be identified through serum elevations of circulating RA-related autoantibodies, including rheumatoid factor (RF) and antibodies to citrullinated protein antigens (ACPA), prior to the clinical appearance of inflammatory arthritis (IA) and RA. Studying Preclinical RA may identify factors and pathways in disease development, and help to identify therapeutic targets for prevention. Furthermore, trials in ACPA+ subjects have been completed or are underway with the primary goal to prevent future IA/RA. However, relatively few individuals have been studied through the evolution of the Preclinical ACPA+ state to Classified RA. As such there are still many gaps in the understanding of the clinical and immunologic evolution from Preclinical to Classified RA.

Objectives: The study objective is to identify the clinical, environmental and immunologic factors/pathways that are associated with incident IA/RA development in individuals with serum ACPA elevations.

Methods: We created a cohort of 86 ACPA+ subjects who at their baseline study visit did not have a historical or examination (66/68 count) evidence of IA/RA. ACPA+ was defined as a serum elevation of anti-CCP3 (IgG, Inova) on $\geq$2 occasions above the established cut-off ($\geq$20 units). These subjects were recruited over 18 months through community health-fair screening, ACPA testing of first-degree relatives of patients with RA, and rheumatology clinics. Clinical, environmental and biomarker factors, including RF IgA and IgM [Inova] and high-sensitivity C-reactive protein [hsCRP], were assessed at the baseline visit. Herein we present interim analyses of baseline visits on the whole ACPA+ cohort and longitudinal follow-up on a subset of subjects, with a specific focus on factors that are associated with baseline symptoms and subsequent incident IA/RA.

Results: At baseline, the 86 ACPA+ subjects were a mean age of 58, 66% female, 82% were Caucasian, and 40% self-reported no joint pain, morning stiffness or fatigue. hsCRP positivity (>3 mg/L) was associated with increased rates of self-reported fatigue of >0 on VAS (20% vs. 41%, p=0.04). Ever smoking was associated with increased rates of self-reported morning joint stiffness (18% vs 50%, p≤0.01). In addition, in analyses of longitudinal follow-up data available to date, 10/86 subjects (12%) developed IA classified as RA (2010) a median of 293 days after baseline visit. At baseline, individuals with incident RA exhibited a higher BMI compared to those who did not (27 vs. 32, p=0.03). In addition, positivity for hsCRP and RF, and higher median anti-CCP3 levels, were present in those who developed incident IA/RA although not statistically significant.

Conclusion: Within this new cohort of prospectively followed ACPA+ individuals, smoking and an elevated hsCRP are associated with clinical symptoms of stiffness and fatigue, respectively. The relationship of stiffness and smoking suggests this factor is related to early joint symptoms, and the association of high BMI with incident RA may indicate this is a modifiable risk factor for RA (de Hair 2013). This prospective study will continue, with further study of the factors/pathways that may influence well-being in ACPA+ individuals as well as may influence predictive of or causally linked to the future IA/RA.

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SAT0083 PREVALENCE OF FRAILTY AND ITS ASSOCIATED FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL ANALYSIS

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Background: The concept of frailty is a recent issue in the rheumatologic field, by now, the prevalence of frailty among individuals with rheumatoid arthritis (RA) has not been extensively examined and few studies on frailty in RA adults have been conducted. Moreover, the relationship between frailty and sociodemographic or disease characteristics in RA are unknown.

Objectives: The aims of the present research were to assess the prevalence of frailty and its potential associated factors in adult patients with RA.

Methods: Consecutive RA patients and healthy controls were assessed according the Survey of Health, Ageing and Retirement in Europe Frailty Instrument (SHARE-FI) (1), and classified as frail, pre-frail or non-frail. Patients underwent to a clinimetric assessment in order to establish disease activity (Simple Disease Activity Index [SDAI]), function (Health Assessment Questionnaires Disability Index [HAQ-DI]), comorbidities (modified Rheumatic Disease Comorbidity Index [mRDCI])(2), and radiographic damage (Simple Erosion Narrowing Score [SENS]). Chi-square, analysis of variance (ANOVA), and multinomial logistic regression analyses were used to test the prognostic value of frailty for the outcomes of interest.

Results: 210 consecutive RA patients were included (72 male, 138 female) and the mean age was 60.4 years. The study group was composed by 100 healthy controls (63 females and 47 males). The mean age was 59.1. According to SHARE-FI criteria, 35 RA patients (16.6%) were categorized as frail, 68 (32.4%) as pre-frail, and 107 (51%) as non-frail, while 8 control subjects were categorized as frail, (8%), 17 as pre-frail (17%), and 75 as non-frail (75%) (chi-squared 12.8; p=0.0016). The results from logistic regression analysis revealed that age (odd ratio [OR] = 1.12, 95% confidence interval [CI] = 1.07-1.17; P <0.0001), comorbidities (OR = 1.51, 95% CI = 1.01-2.27; P = 0.0446), and high disease activity (OR = 1.10, 95% CI = 1.04-1.16; P = 0.0006) were independently associated with frailty in RA patients (Fig 1).

Conclusion: Frailty or pre-frailty are common in RA. The SHARE-FI may be a specific tool for the screening of frailty in RA and may summarize

the results of a comprehensive RA assessment providing a marker of deficits accumulation. Future studies will need to examine longitudinal relationships between frailty and health outcomes in RA.

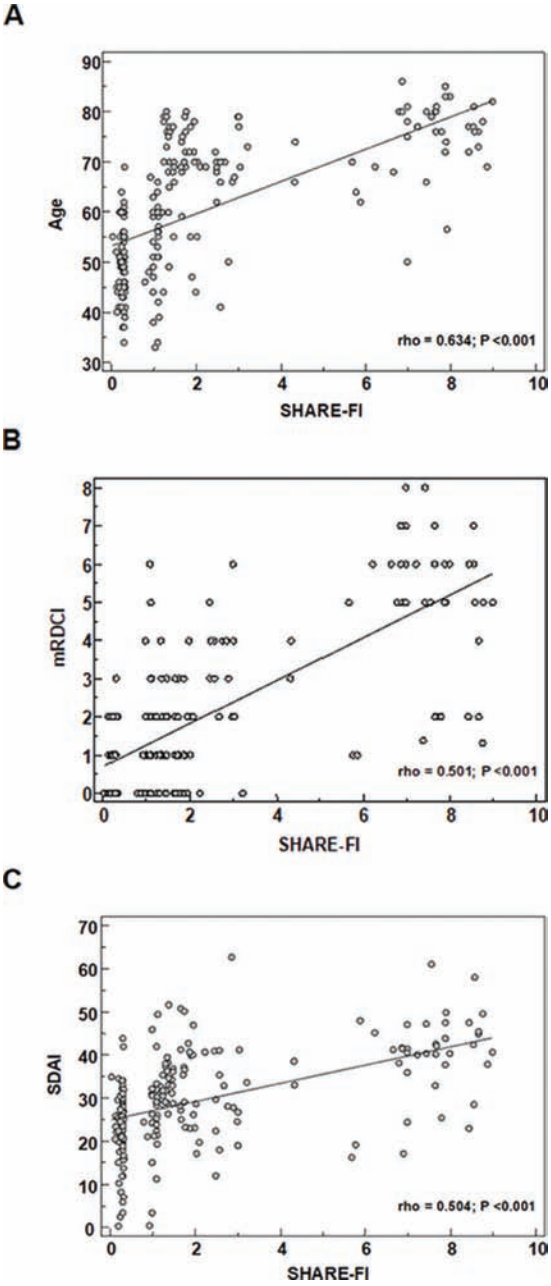


Figure 1. Correlations (Spearman's rho) between Survey of Health, Ageing and Retirement in Europe Frailty Instrument (SHARE-FI) and age (**A**), modified Rheumatic Disease Comorbidity Index (mRDCI) (**B**), and Simplified Disease Activity Index (SDAI) (**C**).

REFERENCES

[1] Romero-Ortuno R, Walsh CD, Lawlor BA, et al. A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). BMC Geriatr 2010;10:57

[2] Iannone F, Salaffi F, Fornaro M, Di Carlo M, Gentileschi S, Cantarini L, Lopalco G. Influence of baseline modified Rheumatic Disease Comorbidity Index (mRDCI) on drug survival and effectiveness of biological treatment in patients affected with Rheumatoid arthritis, Spondyloarthritis and Psoriatic arthritis in real-world settings. Eur J Clin Invest. 2018;48(11):e13013.

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SAT0084

IDENTIFICATION OF POOR PROGNOSTIC JOINT LOCATIONS IN AN EARLY, RAPIDLY PROGRESSING RA COHORT: A POST HOC ANALYSIS OF THE AGREE STUDY

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Background: Early RA patients (pts) often present with different areas of joint involvement, but limited data exist to identify which specific joint locations may be indicative of greater disease severity[1].
Objectives: This analysis investigated the baseline (BL) prevalence of swelling and erosions in individual joint locations and their possible association with disease characteristics and prognostic factors in a unique cohort of early erosive RA patients using the AGREE study population.
Methods: In this post-hoc analysis of the Phase III AGREE study where methotrexate (MTX) naïve RF and/or ACPA seropositive pts with early (≤2 years [yrs]) erosive RA were treated with abatacept (ABA) plus MTX (n=256) or MTX (n=253)[2], prevalence of BL swollen joint status (present, absent) was analysed for 6 large and 14 small joint locations: respectively wrists, elbows, shoulders, jaw, knees, ankles and MCP1-5, PIP2-5 and MTP1-5. Similarly, prevalence of BL erosive joint status was analysed for wrist, MCP1-5, PIP2-5 and MTP1-5. The association between BL disease characteristics and BL swelling or erosions was investigated for the individual joints.
Results: In this cohort of early, seropositive erosive RA (n=509), BL swelling was most frequently observed in the wrist (91.90%) and MCP2 joint (90.1%), whereas BL erosion was most frequently observed in the MTP5 joint (43.5%) (Table 1). BL swelling in the knee, jaw, wrist and elbow was highly associated (p<0.001) with higher tender and swollen joint counts, higher DAS28 (CRP) and higher SDAI and CDAI. As expected, patients with BL presence of erosions had a higher total Genant-modified Sharp score (TSS) whatever the joint location. Overall, men seem more prone for erosions, and this is seen in all joint locations, except for the wrist. Moreover, in this already highly seropositive cohort, patients with BL erosions were more ACPA, but not RF, positive for all evaluated joints of the feet. BL swelling does not seem to be associated with erosive status, neither in the individual joint nor in the TSS, except for the MCP2 joint (erosion positivity was 21% and 4% and TSS was 7.4 [9.5] and 4.7 [5.6] in swollen and non-swollen MCP2 joints respectively).
Conclusion: In this cohort of early, seropositive erosive RA, swelling in the knee, jaw, wrist and elbow seems to be associated with the poorest prognosis, whereas BL MCP2 swelling seems to be associated with joint damage. While the data require further validation, a difference in joint location presentation may identify patients for an intensive treatment or a personalized treatment approach.

Table 1. Prevalence BL swelling and erosion positivity by joint location in the total AGREE cohort (n=509)

Large joint	Swelling
Wrist	91.90%
Ankle	79.20%
Knee	68.40%
Elbow	48.10%
Shoulder	33.80%
Jaw	8.80%

Small joint	Swelling	Erosion
MCP1	75.80%	27.60%
MCP2	90.10%	19.50%
MCP3	84.40%	18.60%
MCP4	52.50%	5.90%
MCP5	50.70%	9.10%
MTP1	40.60%	24.30%
MTP2	48.90%	19.70%
MTP3	50.30%	25%
MTP4	39.40%	17.30%
MTP5	31.30%	43.50%

REFERENCES

[1] Bergstra SA, et al. RMD Open 2017;3:e000568.
[2] Westhovens, et al. Ann Rheum Dis 2009;68:1870–7.

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SAT0085

A MATRIX RISK MODEL FOR PREDICTING 5-YEAR RADIOGRAPHIC PROGRESSION IN A COHORT OF EARLY RHEUMATOID ARTHRITIS TREATED ACCORDING TO T2T STRATEGY

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Background: In the treatment strategy of early rheumatoid arthritis (ERA) it is of pivotal importance to detect those patients who are at risk of radiographic progression (RP) in order to avoid decline in both functional capacity and quality of life.
Objectives: To identify baseline predictive factors for 5-year RP in an observational cohort of ERA treated according to treat-to-target (T2T) strategy, and to create a matrix risk model including the strongest predictors.
Methods: A total of 212 ERA patients with less than 12 months of disease duration (mean age 52.8±13.9 years, 75% female, 74.5% seropositive) and with available radiographs at 5 years of follow-up (FU), were enrolled in the study. ERA patients fulfilled the 2010 ACR criteria for RA and were followed according to the T2T strategy. At baseline, and every three months, the ACR/EULAR core data set variables were recorded. At baseline and every year, hand and foot radiographs were examined according to modified Total Sharp score (mTSS). At each visit, clinical improvement and remission were evaluated according to EULAR criteria. The achievement of Comprehensive Disease Control (CDC) (28-joint Disease Activity Score using C reactive protein <2.6, Health Assessment Questionnaire <0.5 and change from baseline in mTSS ≤0.5) was assessed every year of FU.
Results: Fifty-six ERA patients (26.4%) had erosions on hand and foot radiographs performed at baseline.
At 5 years of FU additional 56 subjects (26.4%) developed RP. ERA patients showing RP were in higher percentage ACPA positive (78.6%) and erosive at baseline (41.1%) compared to subjects not manifesting RP (65.4% ACPA positive, p=0.07; 21.2% erosive at baseline, *p=0.004*, respectively). Moreover, radiographic progressors had a VERA disease (disease duration less than three months) with lower frequency (21.4%) compared to non progressors (34.6%, p=0.07). CDC was achieved at twelve months of FU more frequently by non progressors (52.6%) compared to patients developing RP (30.4%, *p=0.004*). There were no differences regarding age, disease duration, BMI and smoking habit. Comparing the treatments between the two groups, we found similar frequencies of conventional and biotechnological drugs.
In logistic regression analysis, the variables predictive of 5-year RP were ACPA positivity [OR (95%CI): 2.51 (1.12-5.63)], presence of erosions at baseline [OR (95%CI): 2.42 (1.16-5.06)] and not reaching CDC at the twelfth month of FU [OR (95%CI): 2.38 (1.18-4.76)]. Combining the coexistence of erosions at baseline and ACPA positivity (registered in 35 subjects, 16.5%o of the total cohort), the risk of RP increased [OR (95%CI): 3.50 (1.55-7.88)].
Dividing patients according to autoantibody positivity, the independent variables associated to RP were the presence of erosions at baseline [OR (95%CI): 2.91 (1.28-6.63)] and not having a VERA disease [OR (95%CI): 2.86 (1.06-7.69)]. In seronegative subjects predictive factors of RP were not identified.
Using the parameters showing the strongest association with RP, three-parameter risk matrix was created, showing the proportion of ERA patients with RP in each box (Figure 1).
The higher proportion of RP was showed in ACPA positive patients, regardless of all the other baseline predictors.
Conclusion: In our cohort the predictive factors of 5-year RP were ACPA positivity, presence of erosions at baseline and not achieving CDC at 12th of FU. Although CDC is the advisable treatment goal, the radiological damage is not fully prevented in case of ACPA positivity.

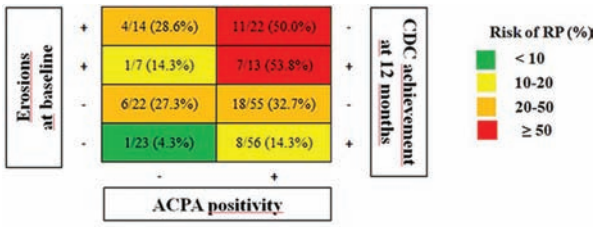


Figure 1. Three-parameters risk matrix showing the proportion of ERA patients with RP.

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SAT0086

EVALUATION OF MEDICATION PERSISTENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH NON-TNFI DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

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Background: Persistence to prescribed biologic (b)DMARDs, such as TNF inhibitors (TNFi), in patients (pts) with RA has been suboptimal, with rates ranging from 30–80%. There are limited data on the persistence of non-TNFi bDMARDs and targeted synthetic DMARDs, such as tofacitinib (TOF).
Objectives: To compare medication persistence in pts with RA treated with different non-TNFi DMARD treatment options including abatacept (ABA), TOF and tocilizumab (TOC), and to evaluate characteristics (e.g. demographics, comorbidities, baseline treatments) of these pts.
Methods: Pts (≥18 years) from the Truven MarketScan™ administrative claims database with RA (≥2 claims for RA identified with International Classification of Diseases [ICD]-9 or ICD-10) being treated with a non-TNFi DMARD from Jan 2006 to Sep 2017 were included. The date of the first claim of a drug of interest on or after diagnosis of RA was considered the index date. Pts were required to have at least 6 months of continuous enrolment prior to the index date (baseline). Pts with claims of other bDMARDs at the index date were excluded from the study. Persistence was defined as the number of days from the index date to the first switch or discontinuation of the index date DMARD, or end of the study period, or end of enrolment, whichever came first. Pts were stratified by prior TNFi use (TNFi-naïve or TNFi-experienced) and by prior corticosteroid (CS) use. Pairwise comparison of persistence between the non-TNFi DMARDs was performed, with ABA as the reference using Kruskal–Wallis test. A p value of <0.05 was considered statistically significant.
Results: A total of 30,556 pts satisfied the inclusion and exclusion criteria, of which 20,410, 5048 and 5098 were initially treated with ABA, TOF and TOC, respectively. Overall, the ages of therapy initiation for the ABA and TOF cohorts were comparable, while the TOC cohort was slightly younger. The majority (80%) of the study population was female. The proportion of pts with prior CS use was lower in the ABA cohort vs the other cohorts. Overall, the comorbidity index between treatment cohorts was similar; however, there were some differences in types of comorbidities at baseline (Table 1). The ABA cohort tended to have a lower proportion of pts with chronic obstructive pulmonary disease/asthma, pulmonary nodule, dyslipidaemia and osteoarthritis, while the proportions of pts with heart failure, ischemic heart disease and lupus were higher relative to other cohorts (Table 1). Overall, mean (SD) time on therapy for pts in the ABA cohort was longer compared with pts in the TOF (338 [418] vs 257 [288] days) and the TOC cohorts (338 [418] vs 294 [345] days). Similar differences were observed when further stratified by pts' prior use of TNF and CS (Table 2).
Conclusion: Based on the analysis of a large US claims database, pts with RA who were prescribed abatacept had higher persistency with therapy compared with other non-TNFi DMARDs such as TOF and TOC, regardless of prior use of TNFi and CS. Further analysis of medication persistence adjusting for pt characteristics is warranted.

Table 1. Baseline characteristics by cohort

	ABA (n=20,410)	TOF (n=5048)	TOC (n=5098)
Age, years, mean (SD)	55.4 (12.6)	55.1 (11.7)	54.2 (13.1)*
Female, n (%)	16,784 (82.2)	4123 (81.7)	4107 (80.6)*
TNF-experienced, n (%)	10,171 (49.8)	2431 (48.2)*	2895 (56.8)*
CS use, n (%)	12,167 (59.6)	3379 (66.9)*	3148 (61.7)*
CCI score, mean (SD)	1.4 (1.0)	1.4 (0.9)	1.4 (1.0)
COPD/asthma	282 (1.4)	123 (2.4)*	103 (2.0)*
Pneumonia	661 (3.2)	131 (2.6)*	158 (3.1)
Pulmonary nodule	437 (2.1)	182 (3.6)*	185 (3.6)*
Heart failure	623 (3.1)	107 (2.1)*	132 (2.6)
Dyslipidaemia	3185 (15.6)	926 (18.3)*	951 (18.7)*
Ischaemic heart disease	1448 (7.1)	324 (6.4)	307 (6.0)*
Osteoarthritis	5623 (27.6)	1648 (32.6)*	1594 (31.3)*
Lupus	929 (4.6)	148 (2.9)*	169 (3.3)*
Infections	9347 (45.8)	2196 (43.5)*	2300 (45.1)

*p<0.05 vs ABA
ABA=abatacept; CCI=Charlson Comorbidity Index; COPD=chronic obstructive pulmonary disease; CS=corticosteroid; TOC=tocilizumab; TOF=tofacitinib

Table 2. Persistence by cohorts: overall and stratified by prior TNF and CS use

	ABA	TOF	TOC
Overall	n=20,410 337.9 (416.8) 191	n=5046 257.3 (288.0)* 151	n=5098 294.0 (345.1)* 168
TNF-naïve	n=10,239 328.1 (409.7) 179	n=2616 252.9 (285.3)* 146	n=2203 276.7 (341.2)* 148
TNF-experienced	n=10,171 347.7 (423.7) 201	n=2430 262.1 (290.9)* 159	n=2895 307.2 (347.6)* 178
CS-naïve	n=8243 333.0 (415.1) 186	n=1668 263.4 (289.6)* 160	n=1950 288.7 (335.8)* 165
CS-experienced	n=12,167 341.1 (418) 194	n=3378 254.3 (287.3)* 148	n=3148 297.3 (350.8)* 169

Values are expressed as mean (SD) median, in days reported
*p<0.05 vs ABA
ABA=abatacept; CS=corticosteroid; TOC=tocilizumab; TOF=tofacitinib

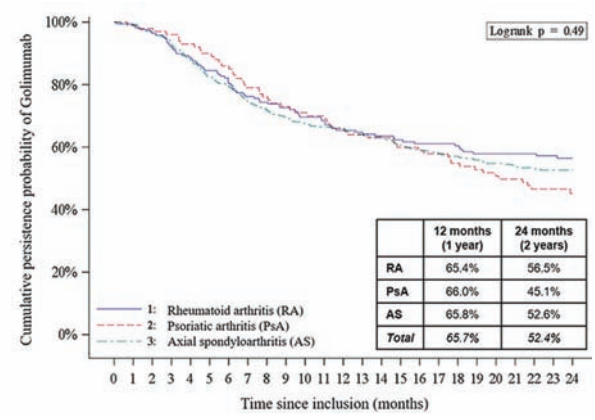
Disclosure of Interests: Leticia Ferri Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Evo Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Sonie Lama Employee of: Bristol-Myers Squibb, Aarti Rao Consultant for: Bristol-Myers Squibb
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SAT0087

REAL-LIFE GOLIMUMAB PERSISTENCE IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: FINAL RESULTS OF THE GO-PRACTICE STUDY

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Background: Golimumab (**GLM**) is the fifth, most recent anti-TNFα to be indicated in the treatment of chronic inflammatory rheumatic diseases. GO-PRACTICE aimed to assess GLM use in real-life clinical practice, in patients with rheumatoid arthritis (**RA**), psoriatic arthritis (**PsA**), and axial spondyloarthritis (**AS**).
Objectives: Primary objective was to assess the persistence of GLM over 2 years after initial prescription. Cumulative persistence probabilities were estimated with the Kaplan-Meier method. Secondary objectives included evaluations of: 1) clinical disease activity from inclusion to 2 years (with **DAS28** for RA and PsA; **ASDAS** for AS); 2) change in patient reported evaluations of pain (**VAS** [0-100]), disease activity (**RAPID3** for RA and PsA; **BASDAI** for AS), functional ability (**HAQ)** and quality of life (**EQ-5D** and **SF-12**); 3) GLM clinical safety.
Methods: Observational, prospective, multicenter French study. Patients ≥18 years with RA, PsA and AS were included consecutively, following GLM initiation and were followed-up for 2 years. Data were collected at baseline (**BL**), year 1 and year 2.
Results: 770 patients selected from January 2015 to March 2016 at 134 sites, of which 754 included in the analysis. Mean age was 46 years and 61% were female. Most had AS (63%), followed by RA (23%) and PsA (14%). Mean duration of rheumatic disease was 7.6 years and 37% had previously received biologics; the proportion of patients who received 1, 2, 3 and ≥4 biologics were 18%, 11%, 6% and 2%, respectively. Most patients were prescribed 50mg GLM monthly (97%). Concomitant treatments included disease-modifying anti-rheumatic drugs (38%), corticosteroids (19%) and NSAIDs/analgesics (71%).
Persistence of GLM at 2 years was 52.4% (56.5%, 45.1% and 52.6% for RA, PsA and AS respectively), and in the AS group was higher for biologics naïve than biologics pretreated patients (59.2% vs. 42.7%, *P*<.01). Disease activity showed clinically significant improvements from BL to 2 years in persisting patients. For RA, mean DAS28-CRP from 4.3±1.1 to 2.3±0.8 (*P*<.0001), mean RAPID3 from 4.5±1.8 to 1.8±1.7 (*P*<.0001). For PsA, mean DAS28-CRP from 3.9±1.0 to 2.0±0.8 (*P*<.0001), mean RAPID3 from 5.3±1.4 to 2.8±2.2 (*P*<.0001). For AS, mean ASDAS-CRP from 3.2±0.8 to 1.7±1.0 (*P*<.0001), mean BASDAI from 5.5±1.6 to 2.8 ±1.9, (*P*<.0001). Pain, HAQ, EQ-5D and SF-12 also improved significantly over 2 years.
During the study, 67 (8.9%) patients discontinued GLM due to intolerance or adverse event (**AE**); reported AEs were consistent with GLM's known safety profile. Post-hoc multivariate analyses with sociodemographic and medical history variables showed that for GLM discontinuation over the 2 years, gastrointestinal disease was a risk factor in RA patients [HR 3.9, CI95% (2.0-7.6)] and being female was a risk factor in AS patients [HR 1.9, CI95% (1.4-2.6)]. GLM was re-prescribed for 338 (93.4%) of 362 patients who persisted on GLM at 2 years.
Conclusion: GLM persistence in real-life is satisfactory at 2 years and accompanied by clinical improvements in RA, PsA and AS patients.



	12 months (1 year)	24 months (2 years)
RA	65.4%	56.5%
PsA	66.0%	45.1%
AS	65.8%	52.6%
Total	*65.7%*	*52.4%*

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SAT0088 COMPARISON OF THE INITIAL DIAGNOSTIC FINDINGS AND ONSET FACTORS OF RHEUMATOID ARTHRITIS (RA) IN ELDERLY ONSET RA AND ADULT ONSET RA BY MULTICENTER COHORT – ARE THERE ANY DIFFERENCES OF ONSET FACTORS? –

Keiko Funahashi[1], Tsukasa Matsubara[2], Esuke Shono[3], Motohiro Oribe[4], Keisuke Hashimoto[5], Akira Sagawa[6], Tamami Yoshitama[7], Takeshi Mitsuka[8], Tomohiko Yoshida[9], Atsuko Imai[10], Nobuaki Miyake[11], Kazuyasu Ushio[12], Izumihara Tomomaro[13], Tsuru Tomomi[14], Yosuke Nishioka[15], Shigeto Kiyokawa[16], Norihiro Nishimoto[17]. *[1]Matsubara Mayflower Hospital, Clinical research, Kato, Japan*; *[2]Matsubara Mayflower Hospital, Rheumatology, Kato, Japan*; *[3]Shono Rheumatisum clinic, Fukuoka, Japan*; *[4]Oribe Rheumatology clinic, Oita, Japan*; *[5]Hashimoto Rheumatology clinic, Kobe, Japan*; *[6]Sagawa Akira Rheumatic clinic, Sapporo, Japan*; *[7]Yoshitama rheumatology clinic, Kirishima, Japan*; *[8]Mitsuka clinic, Narashino, Japan*; *[9]Yoshida clinic, Setagaya-ku, Japan*; *[10]Ichibancho Rheumatology clinic, Matsuyama, Japan*; *[11]Miyake clinic, Shizuoka, Japan*; *[12]Ushio clinic, Osaka, Japan*; *[13]Izumihara rheumatology clinic, Kagoshima, Japan*; *[14]PS clinic, Fukuoka, Japan*; *[15]Nishioka memorial central clinic, Shima, Japan*; *[16]Fujimori clinic, Hachioji, Japan*; *[17]Osaka Rheumatology clinic, Osaka, Japan*

Background: In recent years, it has been reported that elderly onset RA (EORA) is a pathology different from that adult RA (AORA) [1)]. It has been reported that RA is due to genetic background, and many other factors. However it is not clear whether EORA and AORA share onset factors.

Objectives: We compared the initial diagnostic finding of EORA and AORA patients who were diagnosed by RA specialist at their own hospital. We also compared the presence or absence of the onset factors between EORA and AORA.

Methods: 1185 patients at 18 facilities who were initially diagnosed with RA were included. EORA (n=398) was defined by disease onset at over 60 years and AORA (n=732) was defined by disease onset from16 to 59 years. We compared blood examination, clinical findings, presence of bone erosion, gender, age, and background factors pre-onset (family history, history of smoking/operation, presence of periodontal disease/gynecological diseases/digestive system diseases) between EORA and AORA. Clinical findings were analyzed with Mann-Whitney U-test and frequency of pre-onset history were analyzed by 2 × 2 Chi square test.

Results: The average age of EORA and AORA were 72 years and 54 years old. The ratio of female was 75% in EORA, but 84% in AORA, a significant difference (P<0.01). The average values of CRP (ug/ml) were 2.0 in EORA, but it is 1.3 in AORA, significantly lower (P<0.001). Also ESR (mm/h) and MMP-3 (ng/ml) of EORA were 46 and 83, whereas those of AORA were 36 and 29 significant as CRP. On the other hand, TJC, SJC, PaGA and PhGA were not significantly different.

We also compared the prevalence of onset factors between EORA and AORA. There was no clinical significant difference in smoking history and gynecological conditions. The presence rate of stress and family history in AORA were 71% and 38%, whereas that in EORA was 54% and 26%, significantly lower (P<0.001). On the other hand, the presence rate of history of gastrointestinal disease, periodontal disease and operation history in AORA were 43%, 36% and 40%, but those in EORA were 49%, 46% and 52%, significantly higher(P<0.01).

As in previous reports[2)], the ratio of men and the inflammation values in EORA were significantly higher, but there was no difference in SJC, PaGA, and PhGA. This study verified in Japanese EORA as the other reports. There were differences in the presence rate of onset factors between the two groups, while EORA had many external factors such as surgical history, whereas AORA had genetic factors and stress in their backgrounds. Regarding the presence of bone erosion, it was caused by the period from the appearance of the symptoms until the diagnosis and was unrelated to age at onset.

Conclusion: This study suggests that the onset of EORA is more likely to be attributed to external factors than genetic factors.

REFERENCES

[1] G.Bajocchi et.al, Clin Exp Rheumatol 2000; 18(suppl.20), S49-50
[2] Dejaco.C et.al., Arthitis Care & Res 2013; 65, 304-308

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SAT0089 SAFETY AND EFFICACY OF LY3337641, A BRUTON'S TYROSINE KINASE INHIBITOR IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, 2-PART PHASE 2 STUDY

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Background: LY3337641 is an irreversible covalent inhibitor of Bruton's tyrosine kinase (BTK), a key signaling molecule in the B-cell-receptor and Fc-receptor pathways and mediator of B-cell– and myeloid-cell–dependent inflammatory arthritis.[1,2] RA-JUVENATE was a multicenter, randomized, double-blind, placebo-controlled, 2-part Phase 2 trial with long-term extension (LTE) in adult patients (pts) with rheumatoid arthritis (RA).

Objectives: The objective of this analysis is to present the primary results from Part B of the study.

Methods: In Part A, 36 pts with at least mildly active RA were randomized 1:1:1:1 to receive oral LY3337641 5, 10, or 30 mg or placebo (PBO) once daily (QD) for 4 weeks (wks) with the primary objective of safety and tolerability. There were no safety signals to preclude moving to Part B; pts in Part A were not eligible to participate in Part B. In Part B, 250 pts with active moderate to severe RA were randomized 1:1:1:1 receive oral LY3337641 5 (N=63), 10 (N=62), or 30 mg (N=63) or PBO (N=62) QD for 12 wks. The primary endpoint of Part B was the proportion of pts achieving $\geq$20% improvement in American College of Rheumatology criteria (ACR20) at Wk 12. A logistic regression model was used to compare each LY3337641 dose to PBO for primary and secondary endpoints. Nonresponder imputation was used to impute missing data. After an interim analysis showed a low likelihood of demonstrating significant efficacy at the conclusion of the trial, the sponsor discontinued Part B of the study, including the LTE. Efficacy results (except analysis of low disease activity and remission) included pts who completed through Wk 12 at the time of study discontinuation; safety was results included all pts who received $\geq$1 dose of study drug.

Results: Of the 250 pts (mean age 51.0 years; 86.4% female; mean disease duration 11.2 years) randomized in Part B, 189 (75.6%) completed 12 weeks and 180 entered the LTE (72.0%); 61 discontinued study treatment in Part B.. The most common reasons for discontinuation were study terminated by sponsor (27 [10.8%]), withdrawal by subject (8 [3.2%]), adverse event (8 [3.2%]), and lack of efficacy (4 [1.6%]). There was no statistically significant difference in the ACR20 response between any treatment group of LY3337641 and PBO at Wk 12 (p>0.05 for all comparisons; Table); a high placebo rate was noted, but no underlying reason was identified in post hoc analyses. There were 5 serious adverse events: 2 in PBO pts (joint dislocation and cholecystitis acute) and 3 in 30-mg pts (foot fracture, multiple injuries, and venous thrombosis). There was 1 death (30-mg pt, multiple injuries after 4-story fall down elevator shaft). There were no safety findings that precluded continuation of the study.

Conclusion: Although there were no safety findings that precluded continuation of the study, the study sponsor determined that the observed benefit-risk profile of LY3337641 in the study did not warrant its continuation.

Table. Efficacy and safety outcomes at Week 12

	Placebo (N=62)	LY3337641 5-mg (N=63)	LY3337641 10-mg (N=62)	LY3337641 30-mg (N=63)
Efficacy, n (%)				
ACR	n=54	n=56	n=52	n=55
ACR20[a]	26 (48.1)	31 (55.4)	23 (44.2)	28 (50.9)
ACR50[a]	15 (27.8)	14 (25.0)	8 (15.4)	16 (29.1)
ACR70[a]	9 (16.7)	5 (8.9)	1 (1.9)	9 (16.4)
DAS28-CRP	n=62	n=63	n=62	n=63
Low disease activity[b]	15 (24.2)	18 (28.6)	11 (17.7)	16 (25.4)
Remission[b]	11 (17.7)	11 (17.5)	4 (6.5)	14 (22.2)
	n=44	n=49	n=47	n=43
Change from baseline, observed, mean (SD)[a]	-1.6 (1.4)	-1.6 (1.2)	-1.2 (1.1)	-1.8 (1.5)
Safety, n (%)[c]				
Treatment emergent adverse events	31 (50.0)	22 (34.9)	37 (59.7)	34 (54.0)
Serious adverse events	2 (3.2)	0	0	3 (4.8)
Deaths	0	0	0	1 (1.6)
Adverse events leading to discontinuation	2 (3.2)	1 (1.6)	3 (4.8)	3 (4.8)

ACR=American College of Rheumatology; ACR20/50/70=20%/50%/70% improvement according to the criteria of the ACR; DAS28-CRP=Disease Activity Score for 28 joints based on C-reactive protein.
[a]Includes patients who completed through Week 12 at time of study discontinuation by sponsor.
[b]Includes all patients who received study drug.

REFERENCES

[1] Di Paolo JA, et al. Nat Chem Biol. 2011;7:41-50
[2] Chakravarty SD, et al. Clin Immunol. 2013;148:66-78.

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SAT0090 GUT MICROBIOTA COMPOSITION IS CONTINGENT WITH DISEASE PHASES IN RHEUMATOID ARTHRITIS

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Background: Increasing evidences suggest that alterations in the gut microbiota may contribute to the pathogenesis and influence the clinical outcome of Rheumatoid arthritis (RA).
Objectives: To characterize the gut microbiota composition in RA patients in different disease phases contingently to therapeutic regimens.
Methods: Forty-four RA patients (7 naïve to treatment, 13 MTX-IR and 24 in sustained clinical and ultrasound remission under conventional and bDMARD combination therapy, respectively) (age 55.2±11.4 years, 79.5% female and 59.1% positive for ACPA and/or RF) and 20 age/sex matched healthy controls (HC) were enrolled in the study. At study entry, RA specific data set were collected and dietary habits were recorded using the 14-items Mediterranean Diet Adherence Screener (MeDAS) questionnaire. DNA was extracted from stool samples of each patient, amplified and 16S rRNA gene V3–V4 region was sequenced using an Illumina MiSeq™ platform. For downstream sequence analysis, a combination of software packages QIIME (v1.9.1) and VSEARCH (v1.1) was used and a biological observation matrix (BIOM) at different taxonomic levels (from phylum to genus) was produced. The BIOM was analysed using the Web-based program MicrobiomeAnalyst. Statistical analyses were performed using the R phyloseq software package. Differences in the relative abundance of individual bacterial taxa between a priori defined groups were assessed by LEfSe analysis.
Results: Microbiota composition analysis showed that RA patients had a decrease in the gut microbial species richness compared to HC ($p<0.01$). In particular, the principal coordinate analysis (PCoa) visualization of Uni-Frac distances and analysis of group similarities (ANOSIM) showed that faecal microbiota composition differs between RA and HC ($p<0.01$) confirmed by the LEfSe analysis showing that RA microbiota is enriched of *Bacteroidetes* and *Proteobacteria*, whereas HC were enriched of *Verrucomicrobia* and *Firmicutes*. Considering the RA cohort, no significant differences in microbiota composition were found stratifying patients based on autoantibody profile, disease duration and BMI category. However, considering the disease phase, RA patients with active disease (DAS>3.7) showed significant differences in α-diversity compared to RA patients in LDA or in sustained clinical and ultrasound remission ($p=0.01$) with a relative abundance of *Haemophilus parainfluenzae* in high disease activity patients ($p<0.01$). A slightly higher α-diversity in RA patients with the highest adherence to Mediterranean diet ($p=0.10$).
Conclusion: Despite limited sample size, this study strengthen the concept of significant microbiota differences in RA, contingently with disease phases, compared to HC. The evaluation of microbiota composition in the patients follow-up according to response to therapies is ongoing.
Disclosure of Interests: Elisa Gremese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Francesco Cianci: None declared, Stefano Alivernini Speakers bureau: BMS, Giulia Menchinelli: None declared, Anna Laura Fedele: None declared, Barbara Tolusso: None declared, Brunella Posteraro: None declared, Maurizio Sanguinetti: None declared
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SAT0091 INCREASED FREQUENCY AND DEFECTIVE SUPPRESIVE CAPACITY OF CD4+CD25+FOXP3+ TREG CELLS IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Conflicting evidence exists regarding the proportion and function of $CD4^+CD25^+Foxp3^+$ Treg Cells in the peripheral blood (PB) of patients with rheumatoid arthritis (RA)[1-6].
Objectives: The aim of our study was to determine whether Treg cells are defective in Chinese RA patients.
Methods: Levels of $CD4^+CD25^+Foxp3^+$ Treg cells in the peripheral blood of 224 patients with RA and 38 healthy controls were detected by flow cytometry. The expression of CTLA-4, GITR,Helios and ICOS was also evaluated in order to gain insight into the regulatory function of Treg cells. The production of IFN-γ, IL17 and IL10 cytokines by Treg cells was also evaluated. Clinical parameters, including DAS28_ESR, the levels of serum Anti-CCP, IgG and IgM were tested. Correlations with Treg cells were systematically analyzed.
Results: Compared to the healthy controls, active RA patients had significantly higher frequency of $CD4^+CD25^+Foxp3^+$ Treg cells ($P < 0.01$). Furthermore, the $CD4^+CD25^+Foxp3^+$ Treg cells expressed lower CTLA4 ($P < 0.01$) and produced higher IL17 ($P < 0.05$) and lower IL10 ($P < 0.05$) in RA patients compared with healthy controls in vitro stimulation assay. We also found the proportions of $CD4^+CD25^+Foxp3^+$ Treg cells were significantly higher in Anti-CCP $^+$patients compared Anti-CCP$^-$patients ($P < 0.01$). The frequency of $CD4^+CD25^+Foxp3^+$ Treg cells in RA patients was positively correlated with DAS28_ESR($r = 0.135$, $P = 0.043$), the levels of serum Anti-CCP($r = 0.239$,$P < 0.001$),IgG($r = 0.239$, $P < 0.001$) and IgM($r = 0.168$, $P = 0.015$).
Conclusion: We showed higher frequency of $CD4^+CD25^+Foxp3^+$ Treg cells in PB of RA patients, of which the suppressive capacity was defective.

REFERENCES

[1] Vitales-Noyola M, Layseca-Espinosa E, Baranda L, et al. Analysis of Sodium Chloride Intake and Treg/Th17 Lymphocytes in Healthy Individuals and Patients with Rheumatoid Arthritis or Systemic Lupus Erythematosus. *Journal of immunology research* 2018; 2018: 9627806.

[2] Han GM, O'Neil-Andersen NJ, Zurier RB, et al. CD4+CD25high T cell numbers are enriched in the peripheral blood of patients with rheumatoid arthritis. Cellular immunology 2008; 253: 92-101.
[3] van Amelsfort JM, Jacobs KM, Bijlsma JW, et al. CD4(+)CD25(+) regulatory T cells in rheumatoid arthritis: differences in the presence, phenotype, and function between peripheral blood and synovial fluid. Arthritis and rheumatism 2004; 50: 2775-2785.
[4] Furuzawa-Carballeda J, Lima G, Jakez-Ocampo J, et al. Indoleamine 2,3-dioxygenase-expressing peripheral cells in rheumatoid arthritis and systemic lupus erythematosus: a cross-sectional study. European journal of clinical investigation 2011; 41: 1037-1046.
[5] Kailashiya V, Singh U, Rana R, et al. Regulatory T Cells and Their Association with Serum Markers and Symptoms in Systemic Lupus Erythematosus and Rheumatoid Arthritis. Immunol Invest 2018: 1-15.
[6] Naciute M, Maciunaite G, Mieliauskaite D, et al. Increased Numbers of CD4(+)CD25(+) and CD8(+)CD25(+) T-Cells in Peripheral Blood of Patients with Rheumatoid Arthritis with Parvovirus B19 Infection. In vivo 2017; 31: 181-185.

Table 1. Demographic and clinical characteristics of the study subjects

	Treg cell frequency and phenotype assays							Functional assays	
			Disease activity		Treatment				
	Healthy controls	All patients	Remission (DAS28-ESR <2.6)	Active disease (DAS28-ESR ≥2.6)	Untreated	DMARDs	TNF inhibitors	Healthy controls	RA
No of blood donors	20	224	81	143	35	148	41	7	10
Sex, no. female/male	15/5	188/36	63/18	125/18	33/2	123/25	32/9	6/1	9/1
Age, years Mean ±SEM	45.05±15.15	45.05±14.66	44.11± 15.53	46.50± 14.10	42.10 ± 15.86	46.85± 13.99	43.29 ± 16.01	39 .00± 11.09	51.50 ± 12.50
disease duration, months Mean ±SEM	-	76.20±83.88	57.69±66.16	86.96±91.69	62± 95.63	75.25± 81.90	96.81± 81.78	-	81.67±102.39
ESR, mm/hour Mean ±SEM	-	26.54±22.21	13.10± 7.5	34.15 ±24.11	27.89± 17.40	25.84± 22.86	27.02± 25.70	-	44.70± 30.50
CRP, mg/liter Mean ±SEM	-	18.54±16.43	4.70± 5.20	14.16± 19.62	10.91± 17.91	18.51 ± 15.24	18.41± 18.90	-	30.70± 31.05
DAS28-ESR, Mean ±SEM	-	3.57 ±1.76	1.97±0.49	4.49±1.50	4.33 ± 1.71	3.55± 1.85	3.08 ± 1.63	-	5.16± 1.60
Anti-CCP,IU/ml positivity	-	75.7%	44.7%	79.9%	61.8%	78.3%	74.4%	-	70%
RF,IU/ml positivity	-	62.3%	46.9%	71.6%	52.9%	66.3%	76.9%	-	80%

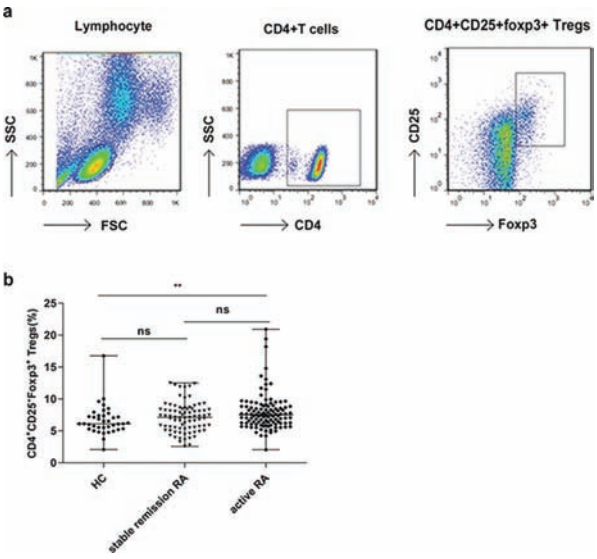


Fig1. Flow cytometry analysis of $CD4^+CD25^+Foxp3^+$ Treg cells in healthy controls(HC), stable remission RA patients and active RA patients

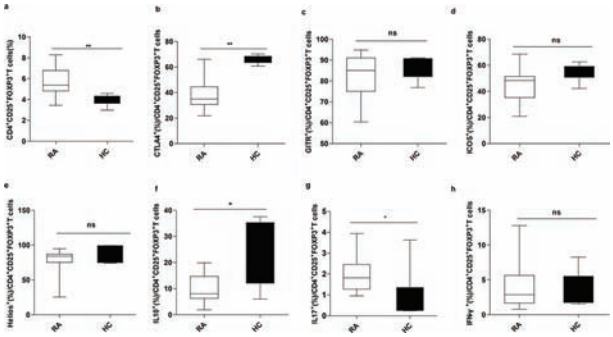


Fig2. Function analysis of $CD4^+CD25^+Foxp3^+$ Treg cells in RA and healthy controls.

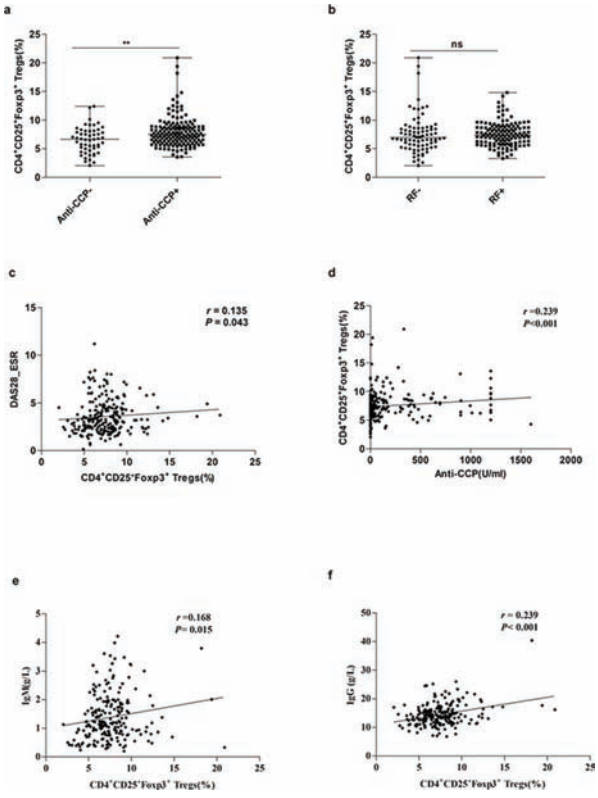


Fig 3. Correlation analysis of $CD4^+CD25^+Foxp3^+$ Treg cells with clinical data.

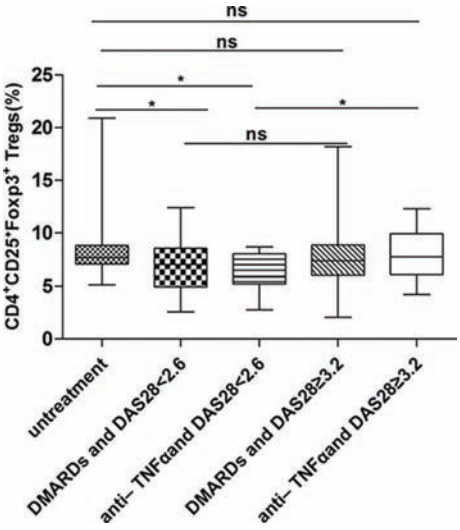


Fig4. The proportion of $CD4^+CD25^+Foxp3^+$ Treg cells in treated RA patients under different treatment regimes.

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SAT0092 **LOW SERUM LEVEL OF VITAMIN D AT TIME OF DIAGNOSIS IS ASSOCIATED WITH HIGHER ONE-YEAR REMISSION RATE IN PATIENTS WITH NEWLY DIAGNOSED RA, TREATED AGGRESSIVELY DURING FOLLOW-UP: POST-HOC ANALYSES OF THE CIMESTRA TRIAL**

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Background: Vitamin D is often low in Rheumatoid Arthritis(RA), and immunomodulatory properties of vitamin D might be associated with disease-course in RA.(1)
Objectives: To evaluate association between baseline vitamin D metabolites and one-year remission, in newly diagnosed, treatment-naïve RA patients, aggressively treated during follow-up.
Methods: The CIMESTRA-cohort comprises 160 newly diagnosed RA patients, treated aiming at remission with methotrexate and intraarticular steroid, further randomized 1:1 to ciclosporine or placebo-ciclosporine.(2) A total of 158 patients had vitamin D metabolites measured at time of diagnosis. Dietary vitamin D supplementation was recommended in accordance with the national guidelines. Serum vitamin D_{total} (sum of $25OHD_2$ and $25OHD_3$) and $1,25(OH)_2D$ at time of diagnoses were measured by LC-MS/MS or RIA. D_{total} were dichotomized at 50 nmol/l, and $1,25(OH)_2D$ categorized in tertiles. Primary outcome was remission (DAS28-CRP ≤ 2.6) after one year. Associations were calculated using logistic regression, presented as Odds Ratios with 95% Confidence Intervals (95%CIs). Adjustment of analyses included sex, age, symptom duration prior to diagnosis, DAS28-CRP and season of diagnosis.
Results: In univariate analyses, neither D_{total} nor $1,25(OH)_2D$ at time of diagnosis predicted remission at year one. In adjusted analysis, D_{total} < 50 nmol/l at time of diagnosis showed better odds for achieving one-year remission, compared to sufficient D_{total}; OR 2.56, 95%CI (1.11; 5.90) p = 0.03. $1,25(OH)_2D$ was not associated to remission.
Conclusion: Low D_{total} at time of diagnosis is associated to increased odds for achieving remission at year one in early, treatment naïve RA patients, treated aggressively during follow-up.

REFERENCES

[1] Jeffery LE, et al. Vitamin D in rheumatoid arthritis-towards clinical application. NatRevRheumatol. 2015.
[2] Hetland ML, et al. Combination treatment with methotrexate, cyclosporine, and intraarticular betamethasone compared with methotrexate and intraarticular betamethasone in early active rheumatoid arthritis: an investigator-initiated, multicenter, randomized, double-blind, parallel-group, placebo-controlled study. Arthritis Rheum. 2006;54:1401-9.

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SAT0093 **THE ASSESSMENT OF THE SYNOVIAL VASCULARIZATIONWITH POWER DOPPLER ULTRASONOGRAPHY AND ITS CORRELATION WITH THE SYSTEMIC INDICATORS OF INFLAMMATION AND WITH THE DISEASE ACTIVITY**

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Background: Rheumatoid arthritis (RA) is an autoimmune disease with the predominant synovial inflammation. The disease activity and inflammatory markers in the serum indicate an active stage of the disease with a risk of joint destruction. As the synovial hypervascularity is considered a proof of an active inflammation, its assessment with different scoring methods in Power Doppler ultrasonography (PDUS) is being discussed.
Objectives: We investigated correlation of synovial vascularization (assessed in PDUS) with inflammatory markers and disease activity. We compared two methods for the evaluation of synovial vascularization : quantative and semi-quantitative.
Methods: We studied 50 RA patients, mean age of 58 years, predominantly female (F/M ratio 3:1), mean disease duration span of 9,5 years. Data on: age, sex, patient global assessment of pain measured by a 100-mm visual analog scale (VAS) were obtained. The disease activity state was defined by DAS28 score (score in 28 joints) and simplified disease activity index (SDAI). Of the laboratory tests: erythrocyte sedimentation rate (ESR), serum C-reactive protein level (CRP), the presence of rheumatoid factor(RF) and anti–cyclic citrullinated peptide antibodies (ACPA) were performed. In ultrasound, the examination of the synovial vascularity, as a symptom of inflammation, was scored in PDUS, utilizing the validated scoring system, grade 0 – lack of flow, 1 – one to two vessels visible within the synovium, 2 – numerous vessels occupying up to 50% of the thickened synovium, 3 – numerous vessels occupying over 50% of the synovium volume. The second quantitatively scale was also used, with the color fraction index (CFI), defined as the ratio of the

number of color pixels to all the pixels in a selected range of interest (ROI). The study was approved by the proper ethics committee. Statistical analysis: differences between groups were analyzed using U Mann-Whitney test (continuous variables). Correlations between quantative variables were assessed with the Spearman correlation coefficient. Statistical significance was set at $p<0.05$.

Results: DAS-28: mean 6.0 (SD=0.9); median 6.1 (IQR: 5.5 - 6.6); SDAI: mean 61.1 (SD=38.3); median 51.3 (36.8 - 76.4). No correlation was found between CFI and age, platelet count, CRP, RF, ACPA, DAS28 and SDAI as well as with the disease duration. But there was a strong positive correlation between CFI and PDUS results, rho = 0.71; $p < 0.05$. As expected, DAS28 and SDAI strongly correlated with inflammatory markers (ESR, CRP). The results showed, that CFI between 2-8 % ia an equivalent of PDUS grade 1, CFI 8-50% of PDUS grade 2 and CFI > 50% of PDUS grade 3.

Conclusion: i)although PDUS is a method used to assess synovial inflammation, through the determination of the synovial vascularization, its results, regardless of the scoring system employed, do not correlate with the systemic inflammation indicators, such as ESR and CRP or with the disease activity – which needs further explanation, ii)the approximate equivalence of CFI and of PDUS scoring system is as follows: CFI > 50% - PDUS grade 3, CFI 8-50% - PDUs grade 2, CFI< 8% - PDUS 1, which confirms previously published research.

REFERENCE

[1] Jindal S, et al. Gray Scale and Power Doppler Ultrasonographic Findings in the Assessment of Disease Activity and Their Correlation with Disease Activity Parameters in Rheumatoid Arthritis", Curr Rheumatol Rev (2018) 14: 153. 2. Schmidt WA, et al. Grading of ultrasound Doppler signals in synovitis: does it need an update? Rheumatology (Oxford). 2015;54 (10):1897-903.

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SAT0094

UNITED STATES RHEUMATOLOGY PRACTICE-BASED REAL-WORLD EVIDENCE OF METHOTREXATE UTILIZATION AND RESPONSE TO THERAPY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH INTRAVENOUS GOLIMUMAB

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Background: AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis) is an ongoing Phase 4 comparator study designed to provide a real-world assessment of intravenous golimumab (GLM) and intravenous infliximab (IFX) in patients (pts) with rheumatoid arthritis (RA). The primary objective of AWARE is to assess the incidence of infusion reactions, the concomitant use of methotrexate (MTX) is also reported. The FDA approved label for GLM states that it is indicated for the treatment of patients with moderately to severely active RA in combination with MTX; however prospectively obtained real world evidence based data on the rate of GLM use without MTX has not been reported.

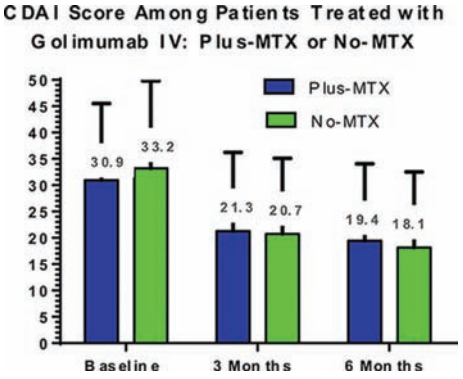
Objectives: Here we compare patient demographics, disease characteristics, response to therapy and discontinuation of GLM treated patients with and without concomitant MTX from an interim analysis (IA) of the AWARE study.

Methods: AWARE is a prospective, noninterventional, observational, multicenter 3-year study conducted in the US. RA pts (1,200 adults) were enrolled at the time of initiating treatment with GLM or IFX. All treatment decisions including MTX utilization are made at the discretion of the treating rheumatologist. Imputations of CDAI data were not performed at this IA. Data shown are mean ± standard deviation.

Results: 678 GLM pts were enrolled; of these 487 (71.8%) were GLM Plus-MTX and 191 (28.2%) were GLM No-MTX. Demographics are shown in the table. Response to therapy was assessed with CDAIs and shown in the figure below. Overall, 92.6% of GLM Plus-MTX and 91.5% of GLM No-MTX pts had a baseline (BL) categorical CDAI disease activity of moderate or high, and 7.4% of GLM Plus-MTX and 8.5% of GLM No-MTX pts had a BL categorical CDAI disease activity of low or remission. Discontinuation from the study during the period of this IA was similar between the GLM Plus-MTX (173/487; 35.5%) and GLM No-MTX (64/191; 33.5%). 7.9% of GLM No-MTX pts reported leflunomide use.

	GLM Plus-MTX	GLM No-MTX
Number of Patients	487	191
Age (years)	61.7 ± 12.85	58.7 ± 14.55
Sex (% Female)	87.1%	81.7%
Disease Duration (yr)	9.0 ± 9.67	9.6 ± 10.74
Baseline CDAI	30.9 ± 14.58	33.2 ± 16.61
Race		
White	86.2%	87.4%
African American	8.6%	8.4%
Other	5.1%	4.2%
Weight (kg)	83.6 ± 24.55	84.0 ± 22.21
BMI (kg/m^2)	31.0 ± 8.45	30.8 ± 7.89

Conclusion: At BL 28.2% of pts on GLM did not report concomitant MTX use. The demographics of the GLM Plus-MTX pts did not differ remarkably from GLM No-MTX pts. The reported early response to treatment, assessed by CDAI score after 3 months and 6 months was similar in the GLM Plus-MTX and GLM No-MTX groups. These preliminary IA data suggest that in a real-world rheumatology practice setting, use of GLM with or without concomitant MTX led to similar CDAI scores at 3 and 6 months in RA pts with predominantly moderate to high BL CDAI disease category.



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SAT0095

MEDICATION NECESSITY AND CONCERN BELIEFS ARE DISTINCT, INTERACTIVE PREDICTORS OF TREATMENT ADHERENCE IN RHEUMATOID ARTHRITIS

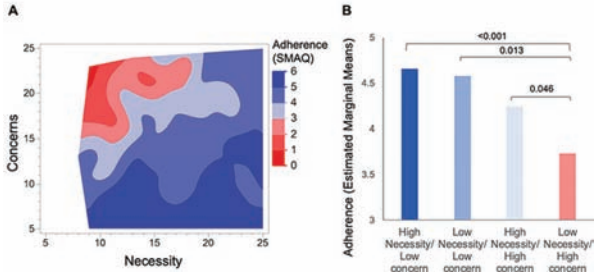
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Background: Medication adherence is instrumental for the successful management of rheumatoid arthritis (RA) to a goal of remission. Awareness of medication necessity and concerns regarding its use influence adherence and respectively foster or undermine the achievement of treatment goals.

Objectives: We explored the unique and interactive roles of patient beliefs about the necessity of RA medications and concerns about them in predicting adherence to prescribed treatments.

Methods: We evaluated 316 patients with established RA from a single center. Beliefs about the necessity of RA medications and concerns regarding their use were evaluated with the Beliefs about Medicines Questionnaire-Specific (BMQ) Necessity and Concerns scales (range 5-25). Self-reported rheumatoid arthritis treatment adherence was assessed using the Simplified Medication Adherence Questionnaire (SMAQ, range 0-6). Multivariable linear regression evaluated the effects of necessity, concerns and their interactions with adherence. A latent profile analysis (LPA) subsequently classified patients in groups according to patterns of necessity and concerns; adherence scores were then compared across latent groups using ANCOVA.
Results: Full adherence (SMAQ score 6/6) was reported by 101 (32%) patients. Necessity and concerns had independent and opposing contributions to adherence (β=0.21 and β=-0.28 respectively, p<0.001 and figure 1a) even after adjustments for age, gender and disease duration. An interaction between necessity and concerns with adherence was also observed (p=0.009); post-hoc simple-slope tests showed that necessity predicted adherence with increasing concerns. Johnson-Neyman technique revealed that while concerns were significantly associated with adherence across the entire range of necessity scores, necessity was significantly related to adherence only at BMQ Concerns scores $\geq$13. LPA revealed four latent patient groups: Low necessity/Low concerns (indifferent, n=33), Low necessity/High concerns (skeptical, n=70), High necessity/High concerns (ambivalent, n=92) and High necessity/Low concerns (accepting, n=121). Adherence varied across groups even after adjusting for between-group differences (p=0.002, Figure 1b); adherence was highest in the accepting group and lowest in the skeptical group.
Conclusion: The relationship between necessity and concern beliefs regarding RA medications significantly influences adherence behavior and may further direct physicians to effectively target their education efforts. A message aimed at reducing concerns might be more effective in the ambivalent subgroup, whereas emphasizing medication necessity may be more fruitful in the skeptical group.

Figure 1. Interaction between Necessity and concerns on medication adherence in RA



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SAT0096 CORRELATION OF GROWTH FACTORS WITH RHEUMATOID ARTHRITIS CLINICAL COURSE INDICATORS

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Background: The evaluation of early destruction markers in rheumatoid arthritis (RA) is of significant clinical importance for improving the patient`s life quality. One of the immunological markers of RA early diagnosis and of severe disease is antibodies to cyclic citrullinated peptide (ACCP). Instrumental methods for early diagnosis of RA include the ultrasound of joints. Vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF) can stimulate the processes of angiogenesis and proliferation, which in turn can increase the infiltration and hyperplasia of synovia, the growth of pannus mass and contribute to the development of bone and cartilage erosions.
Objectives: to establish the correlation of growth factor indicators with markers of the destructive course of rheumatoid arthritis.
Methods: 194 patients with a diagnosis of RA were examined, among the examined patients women prevailed - 86.6%, the age was 47.7 ± 10.22 years. Positive by the presence of ACCP (> 20 U/ml) was 76.8%, and negative - 23.2%. The ELISA in the serum was determined by the concentration of CRP and TNF-α (Vector-Best, Russia), antibodies to cyclic citrulinated peptide (ACCP) (Euroimmun, Germany), VEGF and FGF (BCM Diagnostic, Canada). Ultrasound of the joints was performed by the device "ESAOTE MyLAB40" (Netherlands, 2011) with a linear sensor of 7.5 L 70 (frequency 7.5 MHz), semi-quantitative evaluation of indicators was used: effusion into the joint space (JS), synovial thickness, vascularization of the synovial membrane (SM), the presence of pannus and bone-cartilage erosion.
Results: Direct correlations with CRP and ACCP levels (p = 0.02; p = 0.01, respectively), TNFα and DAS28 (p <0.001) were established during analysis of the correlation links between VEGF and RA clinical course indicators. Analysis of the correlation of VEGF and ultrasound indices of the joints in the examined patients RA established strong direct links with the JS effusion parameters and the SM vascularization assessment (p <0.001, in all cases), and a direct interaction of weak force with the indicator of pannus (p = 0.04) was found. Regression analysis of the dependence of the variability of the SM vascularization assessment on the level of VEGF in the blood showed a sufficient value of the coefficient of determination (0.57), and the data of the normalized index DW = 2.09 reliably indicate the absence of autocorrelation (0.06).
Direct correlations with Rö stage (p <0.001) and the rate of CRP (p = 0.02) were established during analysis of correlation links of FGF with the RA clinical course. Analysis of the correlation of FGF and ultrasound indices of the joints in the examined RA patients established strong direct correlations with the indicators of the thickness of SM, pannus, and bone-cartilage erosion (p <0.001, in all cases), the direct correlation of weak force (p = 0.04) was with the SM vascularization assessment index. Regression analysis of the dependence of the variability of the SM thickness indicator on the FGF blood level showed a sufficient value of the multiple correlation R^2 = 0.47. Also showed a regression analysis of the dependence of the variability of pannus and bone and cartilage erosion indices on the FGF blood level (R2 = 0.51; R2 = 0.46, respectively), which evidences the regression line approximation to the observed data.
Conclusion: According to the correlations of VEGF, FGF levels with CRP, ACCP, assessment of synovial vascularization and bone-cartilage erosions - the high levels of VEGF, FGF in the blood can be used as markers of severe destructive course of RA and of the high rate of disease progression, which requires the early aggressive basic therapy of RA with the use of genetically engineered biologic drugs prescription.
Disclosure of Interests: None declared
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SAT0097 ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND SUBSEQUENT CHANGES IN DISEASE ACTIVITY IN PEOPLE LIVING WITH RHEUMATOID ARTHRITIS

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Background: Various studies have found that rheumatoid arthritis (RA) patients perform less physical activity than the general population, likely due to joint pain and impaired physical function. However, recent studies suggest that physical activity may have a beneficial effect on inflammation and could therefore contribute to reducing RA disease activity. A greater understanding of the relationship between physical activity levels and RA disease activity would be valuable for physical activity counselling of RA patients.
Objectives: The aim of this study was to evaluate the association between baseline physical activity levels and subsequent changes in measures of disease activity in patients with RA using self-reported data.
Methods: We conducted a longitudinal study using 2015-2017 data from an annual survey administered to an RA cohort derived from a population-based cohort for BC originally assembled using physician billing data and a previously validated algorithm. Subjects were grouped into three levels (Low, Medium and High) of physical activity (PA) at the baseline year (2015) according to the specifications of the International Physical Activity Questionnaire. We examined whether physical activity at baseline was associated with a change over time in RA disease activity outcomes

from 2015 to 2017. We fitted linear mixed models for Rheumatoid Arthritis Disease Activity Index (RADAI), Fatigue visual analog scale (VAS), and Pain VAS scores separately without/with adjusting for age, sex, sociodemographic factors, body mass index, RA duration, physical function (Modified Health Assessment Questionnaire [mHAQ]), smoking, depression and other comorbidities at baseline. Models include the outcome at three years (2015-2017) as the dependent variables, an indicator variable representing the year of measurement (2015-17), PA level at baseline, their interactions, and baseline characteristics as covariates. Models include random effects for subjects to account for correlations among within-subject repeated measures. Missing values were imputed using multiple imputation methods. The analyses were conducted using R 3.5.

Results: Of the 169 patients who responded to the 2015 survey, 29.6%, 42.0%, and 28.4% had low, medium, and high levels of PA in 2015, respectively. There were no significant differences in RADAI (p=0.67), Fatigue (p=0.78), and Pain (p=0.98) at baseline (Figure 1). The low PA group experienced significant worsening of disease activity outcomes over time, including yearly increases of 0.31 in RADAI (p=0.007), 0.41 in Fatigue (p=0.007), and 0.43 in Pain (p=0.007). Those in the medium and high PA groups at baseline experienced either a decrease or no change in their disease activity outcomes over time. The interaction terms for PA level and year show that the low PA group had significantly different time trends for RADAI, Fatigue, and Pain compared to the medium and high PA groups (all p values <0.05). The results remain robust after adjusting for age, sex, and other covariates.

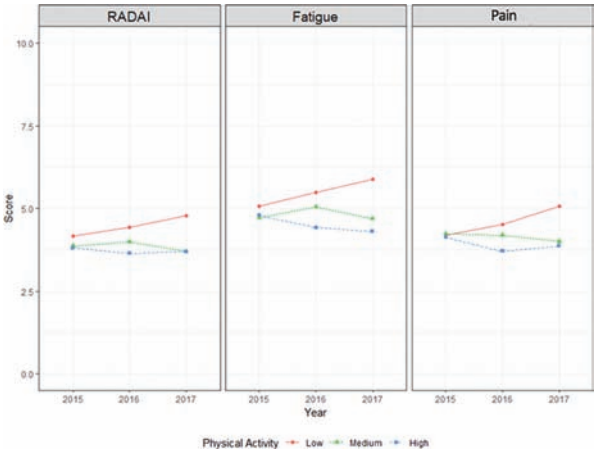


Figure 1. Time Trends for Mean RADAI, Fatigue, and Pain by Baseline Physical Activity Level

Table 1. Linear Mixed Model without/with Adjusting for Baseline Characteristics

Model	RADAI		Fatigue		Pain	
Covariates	Coef. [95% CI]	p	Coef. [95% CI]	p	Coef. [95% CI]	p
A. Unadjusted Linear Mixed Model						
Physical Activity (PA)						
Low	ref		ref		ref	
Medium	-0.24 [-0.99, 0.52]	0.542	-0.24 [-1.26, 0.77]	0.638	0.08 [-0.87, 1.04]	0.865
High	-0.39 [-1.22, 0.44]	0.357	-0.33 [-1.44, 0.78]	0.558	-0.13[-1.17, 0.92]	0.811
Year (Low PA Group)	0.31 [0.07, 0.54]	0.012	0.41 [0.1, 0.72]	0.009	0.43 [0.11, 0.75]	0.009
Physical Activity#Year						
Medium#Year*	-0.36 [-0.67,-0.05]	0.025	-0.44 [-0.84,-0.03]	0.036	-0.5 [-0.92,-0.08]	0.021
High#Year**	-0.35 [-0.69,-0.01]	0.048	-0.68 [-1.12,-0.24]	0.003	-0.54 [-1.01,-0.08]	0.021
B. Adjusted Linear Mixed Model						
Physical Activity (PA)						
Low	ref		ref		ref	
Medium	0.54 [-0.22, 1.29]	0.162	0.25 [-0.55, 1.06]	0.537	0.54 [-0.22, 1.29]	0.162
High	0.94 [0.11, 1.77]	0.027	0.74 [-0.15, 1.63]	0.105	0.94 [0.11, 1.77]	0.027
Year (Low PA Group)	0.44 [0.12, 0.77]	0.007	0.43 [0.12, 0.74]	0.007	0.44 [0.12, 0.77]	0.007
Physical Activity#Year						
Medium#Year*	-0.51 [-0.94,-0.08]	0.019	-0.46 [-0.86,-0.05]	0.028	-0.51 [-0.94,-0.08]	0.019
High#Year**	-0.56 [-1.03, -0.1]	0.017	-0.7 [-1.14, -0.26]	0.002	-0.56 [-1.03, -0.1]	0.017

* The difference in trends for RA disease activity outcomes between the Medium and Low PA groups.
** The difference in trends for RA disease activity outcomes between High and Low PA groups.

Conclusion: Across RADAI, Fatigue VAS, and Pain VAS scores, RA patients with a low PA level demonstrated a significant increase in disease activity over the span of three years. The trends for both the high and medium PA groups differ significantly from that of the low PA group, showing small, overall decreases in disease activity over time. These results add to the accumulating evidence that physical activity may reduce disease activity and is an essential aspect of RA management.

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SAT0098 ANTIBODIES AGAINST CITRULLINATED ANTIGENS ARE ASSOCIATED WITH TREATMENT RESPONSE IN ACPA-NEGATIVE RHEUMATOID ARTHRITIS PATIENTS

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Background: RA patients who are ACPA-positive ($ACPA^+$) are known to have worse prognosis. Less is known regarding predictors of treatment outcomes in ACPA-negative ($ACPA^-$) patients.

Objectives: We investigated whether autoantibodies captured on a custom array were associated with response to therapy in $ACPA^-$ RA patients.

Methods: RA patients were recruited to either the Biologics in RA Genetics and Genomics Study Syndicate (BRAGGSS, starting adalimumab, established disease) or the RA Medication Study (RAMS, starting methotrexate, early disease). Serum samples were collected at pre-treatment and 3/6 months in BRAGGSS/RAMS, respectively. Treatment groups were pooled for analysis. ACPA was measured using a commercially available ELISA (Axis-Shield Diagnostics Ltd, Dundee, UK). Pre-treatment RA and healthy blood donor control (HC) serum samples were incubated on a bead-based assay (Luminex FlexMap 3D) containing 376 human protein antigens associated with autoimmune disease (39 in citrullinated (cit) form) to detect autoantibodies. Median fluorescence intensity (MFI) values were calculated for each autoantibody for RA and HC, then normalised and log2-transformed. The 95th percentile for each autoantibody in HC was used to determine whether an RA sample was positive/negative for that autoantibody. Proteins with <10% frequency in RA patients were excluded from analysis. Linear regression was used to determine autoantibodies differing in MFI between RA and HC; p-values were adjusted using the Benjamini-Hochberg correction. Significant autoantibodies (adjusted p<0.05) were tested for associations with treatment outcomes in RA patients only using: (i) linear regression for improvement in DAS28; (ii) logistic regression for good/poor vs all EULAR response. All regression was adjusted for age, gender, disease duration and baseline DAS28. Subanalysis was carried out in a subset of $ACPA^-$patients.

Results: 168 patients with RA were included in analysis (mean age 59.6 years, mean disease duration 14.3 years, 126 (75%) female patients, 90 (53.6%) $ACPA^+$ patients). 34 autoantibodies were differentially expressed in RA patients, only one of which (TNF ligand superfamily member 13, TNFSF13) was lower than in HC. 29/34 autoantigens were in cit-form. In multivariate models of all differentially expressed autoantibodies, heterogeneous nuclear ribonucleoprotein A1 (HNRNPA1) was significantly associated with EULAR response (coefficient (coef) 0.7, 95% CI 0.1-1.3), and cit-vimentin (VIM) was significantly associated with poor EULAR response (OR_{adj} 4.2, 95% CI 1.1-18.3) and reduced odds of good EULAR response (OR_{adj} 0.2, 95% CI 0.1-0.8). ACPA remained the best predictor of treatment response. In a subanalysis of the 78 $ACPA^-$patients, cit-cleavage and polyadenylation specificity factor subunit 6 (CPSF6) was significantly associated with worse DAS28 (coef (-1.8), 95% CI (-3.6)-(-0.1)). cit-DnaJ homolog subfamily B member 1 (DNAJB1) was significantly associated with DAS28 improvement (coef 2.2, 95% CI 0.6-3.8). No autoantibody was associated with EULAR response.

Conclusion: A subset of $ACPA^-$patients have ACPA fine specificities not seen by a commercial assay. Larger ACPA profiling may provide additional information on treatment response. This requires validation with larger sample sizes and replication in an independent cohort.

REFERENCE

[1] Ann Rheum Dis 2013;72:844. 2. Arthritis Res Ther 2016;18:235.

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SAT0099 **THE RELATIONSHIP OF RHEUMATOLOGY ATTITUDES INDEX WITH OUTCOME MEASURES OF RHEUMATOID ARTHRITIS IN AN ASIAN PATIENT POPULATION**

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Background: The Rheumatology Attitudes Index (RAI) is a questionnaire comprising of fifteen questions that assesses a patient's beliefs and perception of helplessness and the ability to control rheumatoid arthritis (RA). However, the relationship between RAI and patient demographics, disease activity and functional status is inadequately explored.
Objectives: We analysed the association of RAI with educational level, Physician's Global Assessment of Activity (DGA), Patient's Global Assessment of Activity (PGA), Disease Activity Score (DAS 28), and Health Assessment Questionnaire (HAQ). We also investigated if RAI is sensitive to change over a six-month period in comparison with DGA, PGA, DAS28 and HAQ.
Methods: All patients from Tan Tock Seng Hospital, a tertiary hospital in Singapore, who fulfilled the 1987 ACR criteria for RA, and completed the self-administered RAI questionnaire twice over six months were included. We analysed the DAS28, DGA, PGA and HAQ. Repeated measure ANOVA was used to analyse the association between RAI and educational level. Spearman correlation was used to study the association between RAI and the parameters DAS 28, HAQ, DGA and PGA, both cross-sectionally and longitudinally. We used SPSS version 19.0 (IBM Corp, Armonk, NY). P-value <0.05 was considered statistically significant. All the tests were two sided.
Results: There were 501 patients suitable for study. The mean age of disease onset was 43 years and mean disease duration was 15 years. The majority were Chinese (83.4%), married (68.5%) and most (79.4%) received fewer than 10 years of education. About half (50.7%) of the participants suffered from hypertension, 13.6% diabetes mellitus, 61.5% hyperlipidaemia, 20.8% renal disease, 21.6% liver disease and 16.6% thyroid disorder. Patients with <10 years education have higher RAI scores ($p<0.001$) compared to those with $\geq$ 10 years of education. Cross-sectionally, weak positive correlation was found between RAI and DAS 28 ($r = 0.225$, $p<0.001$), DGA ($r= 0.107$, $p=0.017$) and PGA ($r= 0.283$, $p<0.001$). On the other hand, there was moderate positive correlation between RAI and HAQ ($r=0.440$, $p<0.001$). Weak positive correlation was found between the change in RAI compared with changes in DAS 28 ($r= 0.114$, $p=0.011$), HAQ ($r= 0.249$, $p<0.001$), DGA ($r= 0.163$, $p< 0.001$) and PGA ($r= 0.155$, $p=0.001$).
Conclusion: Higher RAI scores denoting greater perceived helplessness were associated with higher RA activity, HAQ, PGA and DGA. RAI was responsive to change over a six-month period compared with these four parameters. High RAI score was also associated with lower educational level. Higher RAI scores reflects higher disease activity and worse functional status in a cross-sectional cohort and for the same patient longitudinally.

REFERENCE

[1] Stein MJ, et al. Factor structure of the Arthritis Helplessness Index. J Rheumatol 1988 15(3): 427-32

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SAT0100 **IN THE ABSENCE OF GUIDELINES, HOW ARE RHEUMATOLOGISTS MANAGING ANTI-CCP POSITIVE PATIENTS WITHOUT CLINICAL SYNOVITIS?**

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Background: The emphasis on early referral and treatment of rheumatoid arthritis (RA) means rheumatologists are now seeing patients earlier in the natural history of RA. Despite clear guidelines for the management of early arthritis, there are no guidelines on how to manage anti-CCP positive (CCP+) patients with symptoms but no clinical synovitis who are at-risk of developing RA. Given the frequent use of ultrasound (US) in early arthritis clinics, we hypothesised that imaging is being used by rheumatologists to guide the management of these at-risk patients.
Objectives: To survey national practice to identify, in the absence of any guidelines, how CCP+ patients without clinical synovitis are being managed by rheumatologists in the UK and specifically to investigate how imaging is being used to guide management in the 'pre-arthritis' phase of RA.
Methods: Anonymous questionnaires were completed by rheumatologists at a national rheumatology meeting focused on recent advances in rheumatology (Revolutions in Rheumatology 2018, London, UK) and at regional general rheumatology meetings in Yorkshire, UK.
Results: Questionnaires were returned from 47 consultant rheumatologists working in 39 different UK hospitals. 44/47 (94%) rheumatologists reported they are referred CCP+ patients who have musculoskeletal (MSK) symptoms but no clinical synovitis in their routine clinical practice. Of these, 32/44 (73%) were referred $\geq$5 patients per year. In CCP+ patients with 'inflammatory symptoms' but no clinical synovitis, 36/44 (82%) would request an US scan to help guide management and 2/44 (5%) would request an MRI scan. All respondents would follow these patients regularly and 5/44 (11%) would consider a clinical trial. In CCP+ patients with 'non-inflammatory' symptoms and no clinical synovitis, 18/44 (41%) would request an US scan, 13/44 (30%) would observe in clinic and 12/44 (27%) would discharge back to primary care. When specifically asked about use of high-resolution imaging in CCP+ patients without clinical synovitis, 40/44 (91%) reported they used imaging, with most (37/40, 93%) using US. In patients where power Doppler (PD) signal is present on US in at least one joint, most (55%) would start disease-modifying anti-rheumatic drug (DMARD) treatment (figure 1) and 16% would treat according to RA guidelines. In patients with US tenosynovitis but no US synovitis, most (73%) would treat with either corticosteroids alone (48%) or a DMARD (48%). In contrast, in patients with no US synovitis or US tenosynovitis, 23/37 (62%) would observe without therapy while 12/37 (32%) would discharge the patient (figure 1).
Conclusion: UK rheumatologists are routinely referred CCP+ patients in the pre-arthritis phase of RA and often treat these patients with synthetic DMARDs, guided by US findings. Whether this pragmatic approach is an appropriate one needs to be tested in clinical trials with RA prevention as the ultimate ambition. Guidance on management of these patients would clearly be helpful.

Management	Ultrasound findings		
	Power Doppler signal in ≥ 1 joint: n (%)	Tenosynovitis only: n(%)	No synovitis or tenosynovitis: n(%)
Treat according to RA guidelines	6 (16)	0 (0)	0 (0)
MTX monotherapy	8 (21)	3 (8)	0 (0)
MTX or HCQ monotherapy	2 (5)	0 (0)	0 (0)
HCQ monotherapy	11 (29)	10 (27)	2 (5)
Corticosteroids only	6 (16)	13 (35)	0 (0)
Observe in clinic (no treatment)	1 (3)	8 (21)	23 (62)
Discharge from clinic (no treatment)	0 (0)	0 (0)	12 (32)
Consider for clinical trial	3 (8)	3 (8)	0 (0)

Figure 1: The management of anti-CCP positive patients without clinical synovitis according to ultrasound findings as reported in a survey of consultant rheumatologists in the UK. RA, rheumatoid arthritis; MTX, methotrexate; HCQ, hydroxychloroquine.

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SAT0101

INTRAHOSPITAL MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: OBSERVATIONAL STUDY AT THE NATIONAL LEVEL OVER A 17-YEAR PERIOD (TREND-AR STUDY)

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Background: There have been important changes in the management of RA in the last 20 years, such as T2T strategy or new biologic agents. The potential impact of these therapeutic strategies on important objectives such as intrahospital mortality due to different causes is not known.
Objectives: To analyze the incidence and tendency of mortality by different causes (global, cardiovascular, infectious, neoplasm, and others) in patients with RA, in Spain, during the period 1999-2015.
Methods: Retrospective cohort study based on the exploitation of the database that collects a minimum basic set of data (MBDS) of all income in patients with RA. Period: 1999 to 2015. We analyzed cases of intrahospital death and the main diagnosis of these cases. The causes of death were identified by the presence of the corresponding ICD 9 codes in the main diagnostic fields. The causes of death in the hospital, global, by sex and in periods 1999-2001, 2003-2006, 2007-2010 and 2011-2015 are described. The results are expressed in absolute numbers and in proportion to the total number of deaths.
Results: There was a total of 338,343 hospital admissions in patients with RA during the 17 years of the study period, corresponding to a total of 176,097 patients (117,985 women and 58,112 men). There was a total of 18,641 hospital exitus (5.5% of the incomes). 63.4% were women. The mean age was 76.4 (SD 10.1) (in females of 77.2 (SD 10.2) and in men of 75.1 (SD 9.9) p <.001). The mean of Charlson index was 3.2 (SD 2.4). The mean age was increased linearly from 73.5 (1999-2002) to 78.23 (2011-215). The following table shows the causes of death grouped by sex and period:

% of deaths (both sexes)	Periods (both sexes)				
Row tags	1999-2002	2003-2006	2007-2010	2011-2015	Total general
Cardiovascular (non infectious)	22.81%	24.36%	24.12%	24.16%	24.00%
Infections	18.51%	19.11%	20.20%	21.32%	20.16%
Respiratory (non infectious)	13.27%	14.38%	16.80%	15.86%	15.43%
Neoplasms	11.54%	11.87%	12.59%	13.43%	12.62%
Digestive (non infectious)	9.88%	9.41%	8.05%	7.82%	8.50%
Difficult classification	7.32%	6.74%	4.86%	3.57%	5.10%
External cause	4.64%	4.63%	4.09%	4.44%	4.41%
Nefrologic (non infectious)	3.47%	2.74%	2.26%	2.33%	2.56%
Extraricular RA	3.21%	2.35%	2.03%	1.82%	2.18%
Hematologic (not neoplasic)	2.30%	1.59%	1.97%	1.93%	1.92%
Neurologicas (non infectious)	1.09%	1.05%	1.14%	1.62%	1.30%
Endocrine	1.32%	1.20%	1.26%	1.08%	1.19%
Skin	0.64%	0.58%	0.63%	0.63%	0.62%

Conclusion: The main causes of intrahospital mortality in patients with RA in Spain were cardiovascular (24%), infections (20%), respiratory-non-infectious (15%) and neoplasms (12%). The average age of death increased 5 years in the study period. The deaths from infections, respiratory and neoplasms have increased, while those of digestive origin and AR extrarticular have decreased.
Disclosure of Interests: None declared
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SAT0102

ASSOCIATION BETWEEN BASELINE HAEMOGLOBIN LEVELS AND RADIOGRAPHIC JOINT DAMAGE PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB OR STANDARD OF CARE

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Background: In patients with active rheumatoid arthritis (RA), haemoglobin (Hb) levels have been inversely associated with radiographic progression of structural joint damage.[1-3]. In two randomized 52-week (wk) studies, baricitinib (BARI), a selective JAK1/JAK2 inhibitor, reduced radiographic progression in patients with moderate to severe active RA who had received no/minimal prior methotrexate (MTX; RA- BEGIN)[4] or had inadequate response to MTX (RA-BEAM).[5]
Objectives: To assess the association between baseline Hb levels and structural damage progression and to study the effect of BARI 4-mg once daily on structural damage progression at 52 wks based on baseline Hb levels.
Methods: Data from the modified intention-to-treat (mITT) populations of RA-BEGIN (MTX=210; BARI 4-mg=159; BARI 4-mg + MTX=215 patients) and RA-BEAM (placebo [PBO]=488, adalimumab [ADA]=328, BARI 4-mg=487 patients) were included for analysis. Structural damage progression was defined as change from baseline (CFB) greater than the smallest detectable change (SDC) in the modified total Sharp score (mTSS) at wk 52. In RA-BEGIN SDC was 1.4 and in RA-BEAM SDC was 1.5. Missing mTSS data at wk 52 were imputed using linear extrapolation based on baseline data and the most recent radiographic data prior to the missed radiograph. Observed proportions of patients with CFB in mTSS >SDC at wk 52 were calculated for low (males:<13.0g/dL, females:<12.0g/dL) or normal baseline Hb for each treatment arm from both studies. Multivariate logistic regression (MLR) was used to study the association of baseline Hb with structural joint damage at 52 wks. The MLR included treatment, baseline Hb (g/dL), baseline hsCRP (Normal ≤3mg/L; Elevated >3mg/L), baseline CDAI, baseline HAQ-DI, BMI, smoking status (Yes/No), geographical area and joint erosion status at baseline (Yes/No in RA-BEGIN; ≥3/1 or 2 + seropositivity in RA-BEAM). Thirty-nine patients from RA-BEGIN (MTX=18; BARI 4-mg=5; BARI 4-mg + MTX=16) and 68 patients from RA-BEAM (PBO=36; ADA=18; BARI 4-mg=14) with missing baseline/post-baseline radiographic data were excluded from MLR analyses; in addition, 7 and 19 patients from RA-BEGIN and RA-BEAM with missing data for the covariates of the MLR were excluded. All analyses were post-hoc.
Results: Overall, RA-BEGIN and RA-BEAM patients with higher baseline Hb were less likely to show CFB in mTSS >SDC (RA-BEGIN: adjusted odds ratio [OR]=0.72, p=0.001; RA-BEAM: adjusted OR=0.76, p<0.001) at 52 wks, independent of other factors included in the MLR model. In RA-BEGIN (Figure A), CFB in mTSS >SDC was less frequent in patients with low baseline Hb who received BARI alone or BARI + MTX versus those on MTX alone; in patients with normal baseline Hb, the difference between treatments was less pronounced. In RA-BEAM (Figure B), CFB in mTSS >SDC was less frequent in patients with both low or normal baseline Hb for patients receiving BARI or ADA versus PBO.
Conclusion: In patients with RA, lower baseline Hb levels were associated with increased structural damage progression. Treatment with BARI 4-mg reduced structural progression, irrespective of patient baseline Hb status; structural progression at 52 wks was more pronounced in patients with low baseline Hb receiving MTX alone (RA-BEGIN) or PBO and background MTX (RA-BEAM).

REFERENCE

[1] Möller B et al. *Arthritis Care Res* (Hoboken). 2018;70(6):861-8; 2Möller B et al. Ann Rheum Dis. 2014;73(4):691-6; 3Westhovens R et al. Ann Rheum Dis 2016;75:237-8; 4Fleischmann R et al. *Arthritis Rheumatol*. 2017;69(3):506-17; 5Taylor PC et al. *N Engl J Med* 2017;376:652-62

Figure. Observed proportions of patients with change from baseline in mTSS >SDC at week 52 based on baseline haemoglobin levels. ADA, adalimumab; BARI, baricitinib; CFB, change from baseline; Hb, haemoglobin; IR, inadequate response; mTSS, modified total Sharp score; MTX, methotrexate; PBO, placebo; SDC, smallest detectable change.

Figure A. **RA-BEGIN** (no/minimal previous MTX; N=545)

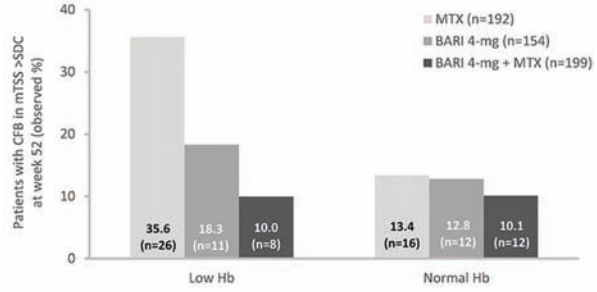
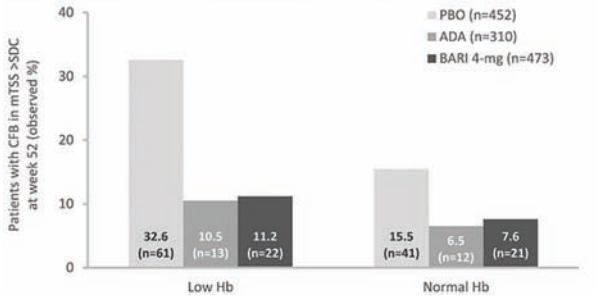


Figure B. RA-BEAM (MTX IR, on background MTX; N=1235)



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SAT0103 LONGITUDINAL PRE-DISEASE TO DISEASE SERUM SAMPLES IDENTIFY BIOMARKERS THAT ARE UPREGULATED PRIOR TO THE DIAGNOSIS OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) patients have autoantibodies reactive against several citrullinated peptides that develop 10-15 years before the clinical onset of disease. However, there is a more limited understanding of serological biomarkers of disease progression, specifically those that are upregulated in patients 6-18 months before the clinical diagnosis of RA.
Objectives: Identification of biomarkers that could classify patients 6-18 months before the clinical diagnosis of RA.
Methods: We identified 500 subjects with RA, 500 with Reactive Arthritis (ReA) (based on ICD9-CM code) as well as 250 age, gender and time-matched healthy control subjects from the Defense Medical Surveillance System (DMSS). For each subject, up to four serum samples were obtained from the Department of Defense (DoD) serum repository, 3 pre-disease diagnosis points and one immediately prior to or around disease diagnosis. A discovery subset of these serum samples was assessed for soluble PD-1 (sPD-1), as well as 497 protein analytes measured by SomaLogic SOMAscan proteomic platform.
Results: Serum levels of sPD-1 increased over time from pre-diagnosis to RA but trended to decrease over time in ReA subjects and healthy controls. A composite score of 24 SOMAscan analytes associated with recently diagnosed RA increased in serum 6-8 months before RA diagnosis and, to a lesser extent, before ReA diagnosis. IFN-inducible chemokines CXCL9 (MIG), CXCL10 (IP-10), CXCL12 (I-TAC), and CXCL13 (BLC) increased over time preceding RA but not ReA diagnosis. Acute phase proteins (CRP, SAA, haptoglobin) and MMP-3 increased before diagnosis in serum samples from both RA and ReA patients. These protein analytes represent potential new biomarkers of early RA.
Conclusion: Samples from the US DoD serum repository have identified novel biomarkers (sPD-1 and IFN-inducible chemokines) of early RA that are elevated within 8 months of disease diagnosis. These protein analytes may afford the opportunity to develop novel biomarker(s) for diagnosis and disease progression to early RA. An understanding of the role of these proteins could provide increased insight into RA pathogenesis prior to disease diagnosis.
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SAT0104 INITIAL EVIDENCE FOR THE NEED OF A DUAL TREAT-TO-TARGET STRATEGY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The treat-to-target (T2T) strategy has been established as a key concept in the management of patients with rheumatoid arthritis (RA) aiming to achieve remission or at least low disease activity [1]. However, it might be more important for patients to set individual treatment goals which are related to their specific life context. For this reason, Ferreira at al [2] recently proposed a dual T2T strategy including both biological remission and individual patient reported symptom remission. It is currently unclear how achieving biological remission and individual patient treatment goals overlap and whether patients who reach the T2T target also reach their individual treatment goals.
Objectives: To explore if achieving T2T biological remission and individual patient treatment goals overlap in RA patients with initially low, moderate, or high disease activity (LDA, MDA, HDA).
Methods: We recruited a consecutive convenience sample of patients with RA diagnosed according to ACR/EULAR criteria and with LDA, MDA, or HDA into this observational longitudinal study. Disease activity was measured with the Clinical Disease Activity Index (CDAI) and the individual patient goals were assessed with the Goal Attainment Scale (GAS) at baseline and after three to five months. The number and proportion of patients who reach the T2T target, but not their individual goals and vice versa were calculated.
Results: We enrolled 162 patients in the study (131 [80.9%] women, median age 59.0, IQR= 49-71). 101 patients (62%) had a follow up visit with no missing data after three months. Of these, 48 (47.6%) patients had LDA, 43 (42.6%) had MDA, and 10 (9.9%) had HDA at baseline. 62 patients (61.4%) reached remission (14.7%) or stayed in LDA (46.1%), and 66 patients (65.3%) achieved their individual goal(s) (Table 1). 18 (17.8%) patients did not achieve their individual treatment goals, even if T2T was successful and 22 (21.8%) patients achieved their individual goals despite not reaching remission or LDA.
Conclusion: Our results indicate that most patients achieving T2T attain their individual treatment goals but a respectable part of T2T outcomes

had to be supplemented by the individual patient reported treatment goals.

REFERENCES

[1] Smolen JS, Landewe R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 2017; 76(6): 960-977.

[2] Ferreira RJO, Ndosi M, de Wit M, et al. Dual target strategy: a proposal to mitigate the risk of overtreatment and enhance patient satisfaction in rheumatoid arthritis. Ann Rheum Dis 2018; [Epub ahead of print 22 Aug 2018].

Table 1. Comparison of achieved T2T and individual patient goals

		T2T achieved, n (%)		
		Yes	No	Overall
Patient goal(s) achieved, n (%)	Yes	44 (43.6)	22 (21.8)	66 (65.3)
	No	18 (17.8)	17 (16.8)	35 (34.7)
Overall		62 (61.4)	39 (38.6)	101 (100.0)

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SAT0105 HAND DISABILITY IN RHEUMATOID ARTHRITIS: AN ENGINEERED GLOVE FOR THE COMPUTERISED QUANTIFICATION OF THE DAMAGE

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Background: Tenderness, swelling and loss of motility of the joints are the main determinants of the disability function (DF) of Rheumatoid Arthritis (RA) patients (RApts)[1]. The evaluation of DF is performed by Patient Reported Outcomes (PROs), like Health Assessment Questionnaire (HAQ)[2]. The lack of objective evaluation of DF is one of the most important "unmet needs" in RA. The Hand Test System (HTS, ETT) is an engineered glove, nowadays applied for neuroscience studies to evaluate hands motility with interesting perspectives of use in other clinical research fields[3-4].

Objectives: To quantify the DF of RApts by the analysis of speed and right execution of fingers opposition movement in both hands, evaluated by HTS. To verify the correspondence with the HAQ.

Methods: In this pilot study 14 consecutives RApts (3 males, 11 females, age 61 ± 11,5 years, mean duration of disease 11,21 ± 5,07 years), classified according to 2010 ACR/EULAR criteria[5], and 13 healthy controls (HC – 7 males, 6 females, age 50 ± 15 years) were enrolled from the RA clinic. After consent, all participants undergone HTS test that recognizes the touches between the finger tips during the opposition movements of the hands in standard sequences of movements, after dressed the glove. A multiple finger evaluation (MFE) and a single finger evaluation (SFE) were performed using a dedicated software that provided the physician the following quantitative parameters: Touch Duration (TD), Inter Tapping Interval (ITI) and Movement Rate (MR). Average time for hand 2 minutes. RApts compiled the HAQ and a tender and swollen joint count of the hands was performed. Continue variables were summarized as mean and standard deviation (SD) or median and interquartile range (IQR), discrete variables were summarized with count and percentage. Variables with skewed distribution was converted to natural logarithm. T-test was used to compare log glove parameters between groups. Pearson's r and p value were used to report the correlation between log-converted glove parameters and HAQ score.

Results: In MFE, glove parameters TD and ITI were significantly higher in RApts (TD 257.34 ± 123.93 ms, ITI 377.8 ± 211.35 ms) than HC (TD 172.25 ± 59.36 ms, ITI 177.98 ± 78.53 ms) ($p = 0.004$ and $p < 0.001$) and MR was significantly lower in RApts (1.51 ± 0.47 Hz) compared to HC (2.87 ± 0.9 Hz) ($p < 0.001$). TD of RApts had a significant correlation with the total score of the HAQ (Pearson $r = 0.79$, $p = 0.001$). In SFE non-active fingers (NAF, not swollen and not tender) of RApts seemed to perform slightly better than a clinically active finger (AF) but significantly worse than average HC finger (ANOVA, $p < 0.001$).

Conclusion: HTS is a new easy and totally safe tool that seems to quantify in an objective manner the hand DF in RApts. The significant correlation found with HAQ underlines the value and veracity of self-assessment tools in clinical practice. Further studies are ongoing with larger number of RApts to validate its application to monitor the improvement or the worsening of RA in order to optimize pharmacological treatments. The study is now extended in other Rheumatic and Musculoskeletal Diseases.

REFERENCE

[1] Hakkinen A, et al. Ann Rheum Dis. 2005; 64:59–63. 2 Fries J, et al. Arthritis Rheum. 1980; 23:137–45. 3 Bonzano L, et al. Eur J Neurol. 2019;26 (1):162-167. 4 Signori A, et al. PLoS One. 2017 Oct 18;12(10): e0186524. 5 Aletaha D, et al. Ann Rheum Dis. 2010;69(9):1580-8.

Disclosure of Interests: None declared

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SAT0106 NOVEL SUBCLASS OF INTRAVASCULAR NON-CLASSICAL SYNOVIAL MONOCYTES ARE CRITICAL FOR RHEUMATOID ARTHRITIS

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Background: There are at least three populations of circulating monocytes; classical, intermediate and non-classical. We demonstrated that circulating non-classical monocytes are required for the effector phase of arthritis and spontaneous models of arthritis in mice. While the vast majority of studies on monocytes have focused those in circulation, very little is known about the monocytes in the synovium.

Objectives: The aim of this study was to examine the heterogeneity of tissue monocytes with those circulation and determine their involvement in inflammation.

Methods: Female 8-10-week-old NR4A1$^{-/-}$, CX3CR1$^{ERCre.zsGFP}$, and C57Bl/6 mice were used in all studies. CX3CR1$^{ERCre.zsGFP}$ were utilized for cell tracking studies and joint shielded bone marrow chimeras via administration of tamoxifen (tam). Intravascular monocytes were identified using fluorescent anti CD45 antibody before perfusion. STIA was induced via I.V. KBxN sera. Monocyte populations were quantified by flow cytometry and FACS sorted for RNA-sequencing (RNA seq). Nonclassical tissue monocytes were identified CD45^{+}CD11b^{+}Ly6G^{-}TIM4^{-}CD64^{-}Ly6c^{lo} and subdivided into intravascular (CD45-labeled, CD43^{+}), trans-vascular (CD45-labeled CD43^{-}) and extravascular (no CD45-label). Human synovium was obtained from ultrasound guided synovial biopsies and CD45+ cells were FAC-Sorted for single cell RNA seq.

Results: NR4A1$^{-/-}$ mice exhibit a 95% reduction in circulating Ly6c^{lo} monocytes but retain Ly6c^{lo} cells in the joint and develop STIA. The transcriptional profiling of bulk populations of Ly6c^{lo} cells in the synovium are distinct from those circulating in the blood. We then identified three populations of Ly6C^{lo} monocytes in the joint; extra-vascular, trans-vascular cells, and intra-vascular cells using 18 color flow cytometry. Lineage tracing studies reveal that the origin of extra-vascular and trans-vascular synovial monocytes are from the embryo while the intravascular monocytes are derived post-natally. The intravascular monocytes are depleted with clodronate loaded liposomes while the extravascular and trans-vascular remain unaffected. Moreover, the intravascular monocytes rapidly expand during the first 1hour of STIA, increasing by 30x in population size. RA patients also display similar populations of non-classical monocytes using single cell RNA seq

Conclusion: We have identified and described three previously uncharacterized populations of non-classical monocytes cells in the joint, an intravascular adherent, a trans-vascular population and an extra-vascular

population. These cells have distinct origins and phenotype from both tissue resident macrophages and circulating non-classical monocytes. Further, the findings presented here strongly suggest intravascular are a key effector cells in inflammatory arthritis.

Disclosure of Interests: None declared

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SAT0107 BIOMARKERS OF CLINICAL RELAPSE AND RADIOLOGICAL PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITISIN REMISSION. OBSERVATIONAL STUDY OF 5 YEARS OF FOLLOW-UP

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Background: Patients with Rheumatoid Arthritis (RA) in remission will present flares during the evolution of the disease.Definitive biomarkers have not been identified to predict flares and radiographic progression (RP) in this kind of patients

Objectives: To search biomarkers of clinical relapse and RP in patients with RA in clinical remission

Methods: RA patients in clinical remission (DAS28-ESR<2.6 for>6 months) were selected.Clinical,epidemiological and serological data were analyzed. MRI of dominant hand,ultrasound assessment of knees and hands and serum levels of inflammation and angiogenesis biomarkers were evaluated at 0 and 48 weeks.Synovial biopsy was performed in patients with subclinical synovitis.Patients were follow-up for 5 years.Radiological data were collected.Clinical relapse was defined as the loss of remission status involving a therapeutic intervention.RP was defined as the change in the Sharp van der Heijde (SvH) index at 5 years >10.47 [SDD (minimum detectable change)].

Results: 60 patients in DAS28 remission. 1/3 also met remission criteria for SDAI(33.3%),CDAI(31.6%) and ACR(35%).78% were women,mean age 53 years. 82% were ACPA+.26% were taking oral prednisone,76% DMARDs and 45% biological therapies.48% met criteria for subclinical synovitis(UdAS:SH>2+PD)[1].

After 5 years of follow-up, 44(73%), 11(18%), 9(15%) and 10(17%) patients remained in remission according to DAS28,SDAI, DAI and ACR criteria,respectively.

29 patients (48%) had flares at any time during the 5 years. In the multivariate analysis, the variables that were related to clinical relapse were the BMI (OR 1.6 CI 95% 1.1-2.3), bone edema at baseline (OR 1.2,CI 95% 1-1.5), PD signal at 48w (OR 9.2,CI 95% 1.2-66.7) and the change in levels of CXCL16 (OR 1.04 CI 95% 0.9-1) and ESR (OR 3.6,CI 95% 1.1-12.2) between the first and latest evaluation (Rate). In the subgroup of 23 patients undergoing synovial biopsy, the number of mast cells was higher in those patients (n=10) who flared (p=0.02).

20 patients (33%) changed DMARDs or biological therapy. In the logistic regression analysis, BMI (OR 1.3 CI 95% 1-1.6), biological therapy (OR 17.8 CI 95% 2-167.1),progression of erosions measured by MRI (OR 1.1, CI 95% 1-1.3) and the rate of progression of calprotectin levels during the first year (OR 4.4,CI 95% 1.1-17.2) were the main factors that predicted the change in baseline therapy after 5 years of follow-up.

Finally, only 6 patients (10%) had RP according to the SvH index and 7 (12%) had erosion progression.This small number of "progressors" did not allowed more exhaustive analysis of factors predicting RP.However,the number of macrophages and T cells at sinovial tissue (ST) was much higher in patients with RP.Likewise,the first-year rate of bone edema was significantly higher in patients suffering structural progression (p=0.04).

Conclusion: 27% of RA patients lost clinical remission (DAS28) after 5 years of follow-up.BMI,baseline bone edema,PD signal at 12m and first-year rate of CXCL16 and VSG levels were predictors of joint flares. Baseline BMI, use of biological therapy,MRI erosions and calprotectin levels predicted the change of baseline therapy for RA. Only 10% of patients had RP along the study.Sinovial mast cells were associated with disease flares. Macrophages and T cells in ST were higher in patients with RP in an exploratory analysis.

REFERENCE

[1] Ramirez J, Ruiz-Esquide V, Pomes I, Celis R, Cuervo A, Hernandez MV, et al. Patients with rheumatoid arthritis in clinical remission and ultrasound-defined active synovitis exhibit higher disease activity and increased serum levels of angiogenic biomarkers. Arthritis Res Ther. 2014;16:R5.

Disclosure of Interests: Julio Ramirez: None declared, Andrea Cuervo: None declared, Raquel Celis: None declared, Raul Castellanos-Moreira Speakers bureau: MSD, Lilly, Sebastian C Rodriguez-García: None declared, Virginia Ruiz-Esquide: None declared, José Gomez Puerta Speakers bureau: BMS, Pfizer, Amgen, Raimón Sanmartí Speakers bureau: PFIZER, SANOFI, LILLY, MSD, UCB, NOVARTIS, JANSSEN, Juan D. Cañete: None declared

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SAT0108 CHARACTERISTICS OF MULTIRESISTANT PATIENTS TO BIOLOGICAL TREATMENTS IN RHEUMATOID ARTHRITIS, AND ASSOCIATED FACTORS : AN OBSERVATIONAL AND RETROSPECTIVE STUDY IN 385 PATIENTS

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Background: Despite a wide range of biological treatments (bDMARDs) in the management of rheumatoid arthritis (RA), some patients fail in different lines of treatment. Currently, there is no consensual definition of multiresistance to bDMARDs in RA.

Objectives: The aim of our study was to describe the characteristics of « multiresistant » patients and to establish associated factors with multiresistance to bDMARDs in RA.

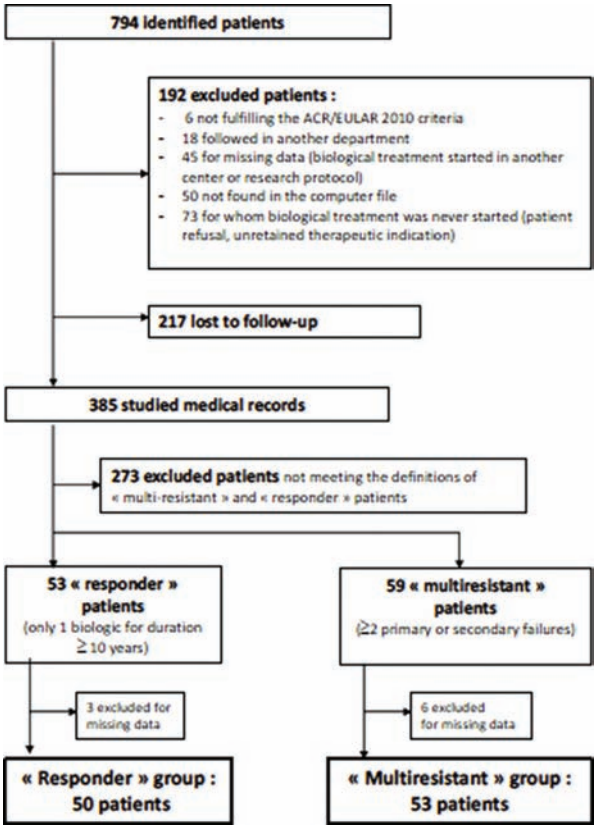
Methods: In this observational and retrospective study were identified patients with RA admitted for administration of a bDMARD at Rouen University Hospital (France) between January 2007 and July 2017 (sources : diagnostic coding using International Classification of Diseases 10th revision and traceability of intra-hospital pharmacy). In the absence of a consensual definition, multiresistance to bDMARD was defined in this study by failure, primary and/or secondary, to at least 2 bDMARDs. The clinical and paraclinical characteristics of these patients at the initiation of the first bDMARD were collected using data from their standardized monitoring, then compared to those of patients who received a single bDMARD effective for 10 years or more, constituting the "responder" group.

Results: We identified 794 patients: 385 constituted our active RA file under bDMARD, 192 patients excluded for different reasons (6 patients not fulfilling the ACR/EULAR 2010 criteria, 18 followed in another department, 45 for missing data at bDMARD's initiation, 50 not found in computerized file, 73 for whom the expected bDMARD was never started) and 217 lost to follow-up. Among our active RA file under bDMARD (385 patients), 53 were « multiresistant » (at least 2 bDMARDs failed), and 50 patients received a single and effective bDMARD for 10 years or more, after excluding some patients for missing data (Figure 1). The mean age of « multiresistant » patients at initiation of bDMARD was 50.3 years (±13.2 years), and the sex ratio was 2.8 women/1 man. They presented erosive RA (77.4%), rheumatoid factor and anti-citrullinated peptide antibodies positive (73.6%), highly active (median number of tender and swollen joints 8/28, median visual analog scale disease activity 70/100, median C-reactive protein (CRP) 21 mg/L, mean Disease Activity Score 28 CRP mean 5.36±1.28), and with high functional impact (Health Questionnaire Median Assessment: 1,500/3). The age of disease onset was significantly later in « multiresistant » patients than in « responder » patients (43±14.2 years versus 37.9±10.7 years, p = 0.042). No demographic, anamnestic, clinical and paraclinical characteristics differed significantly between « multiresistant » and « responder » patients.

Conclusion: It is an original work, counting in the literature as a single similar study [1], with nevertheless significant methodological differences. There is no consensual definition of multiresistance to bDMARD in RA, and its mechanisms remain misunderstood. Identifying predictive factors would make it possible to early identified patients with a refractory profile, in order to adapt the therapeutic strategy. Multidrug resistance in RA remains one of the challenges in the management of this pathology.

REFERENCE

[1] Kearsley-Fleet L, Davies R, De Cock D, Watson KD, Lunt M, Buch MH, et al. Biologic refractory disease in rheumatoid arthritis: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. Ann Rheum Dis Epub ahead of print : 8 July 2018



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SAT0109

SMOKING CESSATION IN PATIENTS WITH RA IS ASSOCIATED WITH REDUCED CVD EVENT RATES AND IMPROVED LIPID PROFILES AND PREDICTS LOWER RA DISEASE ACTIVITY

Ida Kristiane Roelsgaard[1], Eirik Ikdahl[2], Silvia Rollefstad[2], Grunde Wibetoe[2], Bente Appel Esbensen[1], George D. Kitas[3,4], Piet van Riel[5], Sherine Gabriel[6], Tore K. Kvien[7], Karen Douglas[8], Solveig Wallberg Jonsson[9], Solbritt Rantapaa Dahlqvist[9], George Karpouzas[10], Patrick Dessein[11,12], Linda Tsang[12], Hani El-Gabalawy[13], Carol Hitchon[13], Virginia Dr. Pascual[14], Irazu Contreras-Yáñez[14], Petros Sfikakis[15], Miguel A. González-Gay[16], Cynthia S. Crowson[6], Anne Grete Semb[2]. *[1]Rigshospitalet, Center for Rheumatology and Spine Diseases, Copenhagen Center for Arthritis Research (COPECARE), Glostrup, Denmark*; *[2]Diakonhjemmet Hospital, Preventive Cardio-Rheuma Clinic, Department of Rheumatology, Oslo, Norway*; *[3]Dudley Group NHS Foundation Trust, West Midlands, United Kingdom[4]University of Birmingham, School of Sport, Exercise and Rehabilitation, Birmingham, United Kingdom[5]Radboud University Medical Center, Radboud Institute for Health Sciences, IQ healthcare, Nijmegen, Netherlands*; *[6]Mayo Clinic, Department of Medicine, Division of Rheumatology, Rochester, MN, United States of America*; *[7]Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway*; *[8]Dudley Group NHS Foundation Trust, West Midlands, United Kingdom[9]Umeå University, Department of Public Health and Clinical Medicine, Rheumatology, Umeå, Sweden*; *[10]Division of Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, United States of America*; *[11]Vrije Universiteit Brussel, Brussel, Belgium*; *[12]Universitair Ziekenhuis Brussel, Brussel, Belgium*; *[13]University of Manitoba, Winnipeg, MB, Canada*; *[14]Instituto Nactional de Ciencias Médicas y Nutrición Salvador Zubirán, México City, Mexico*; *[15]National and Kapodistrian University of Athens, First Department of Propedeutic Internal Medicine, Athens, Greece*; *[16]Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Universidad de Cantabria, Santander, Spain*

Background: Smoking is a major risk factor for development of both cardiovascular disease (CVD) and rheumatoid arthritis (RA) and causes an attenuated response to antirheumatic treatment.
Objectives: The aim of this study was to compare disease activity and CVD risk factors across smoking status in RA patients. Further to evaluate the impact of smoking cessation on risk of future CVD events in these patients.
Methods: RA disease characteristics, CVD risk factors and relevant medication were recorded in patients from 10 countries (Norway, UK, Netherlands, USA, Sweden, Greece, South Africa, Spain, Canada and Mexico). Information on CVD events were collected after a median follow-up of 3.54 years (inter-quartile range 2.51 – 6.06). Adjusted analysis of variance, logistic regression and COX proportional hazards analyses with time to event as response variable were applied to compare RA disease activity (measured by DAS28), CVD risk factors and CVD event rates across current, former and never smokers.
Results: Among the 3311 included RA patients (1012 former, 887 current and 1412 never smokers), 235 experienced a CVD event(s) during follow-up. At enrollment into the study current smokers were more likely to have moderate/high disease activity compared to former and never smokers (p<0.001 for both) (Figure 1). There was a gradient of worsening CVD risk factor profiles (lipoproteins and blood pressure) from never smokers, via former smokers, to current smokers. Furthermore, after 3.54 years of follow up former and never smokers had significantly lower CVD event rates compared to current smokers (hazard ratio (95% confidence interval): 0.70 (0.51, 0.95), p=0.02 and 0.48, (0.34, 0.69), p<0.001, respectively) (figure 2). The CVD event rates for former and never smokers were comparable.
Conclusion: We show for the first time that smoking cessation in RA patients was associated with lower disease activity, improved lipid profiles and was a predictor of reduced rates of CVD events.

Figure 1. Disease activity across smoking status

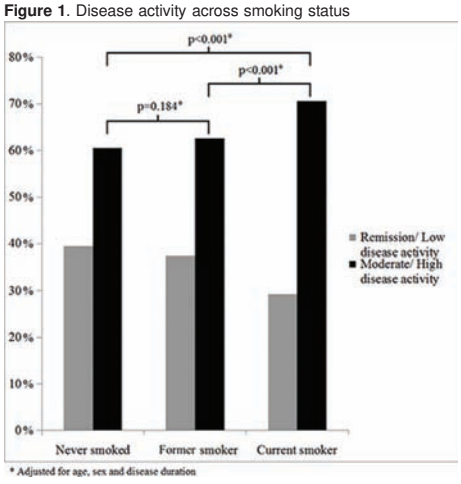
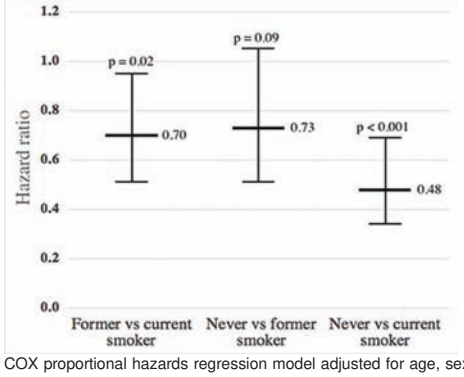


Figure 2. Risk of future CVD event across smoking status in RA patients



COX proportional hazards regression model adjusted for age, sex, statin and antihypertensive use. HR; hazard ratio, 95% CI: 95% confidence interval.

Disclosure of Interests: Ida Kristiane Roelsgaard: None declared, Eirik Ikdahl: None declared, Silvia Rollefstad: None declared, Grunde Wibetoe: None declared, Bente Appel Esbensen Speakers bureau: For Pfizer, George D Kitas Speakers bureau: GDK has received honoraria for lectures, participation in advisory boards and/or hospitality by Roche, Abbvie, Pfizer, Novartis, UCB, BMS, GSK and received grant support from Lilly., Piet van Riel: None declared, Sherine Gabriel: None declared, Tore K. Kvien Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB., Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB, Karen Douglas: None declared,

Solveig Wallberg Jonsson: None declared, Solbritt Rantapaa Dahlqvist: None declared, George Karpouzas Grant/research support from: Pfizer, Consultant for: Sanofi-Genzyme-Regeneron, Janssen, Roche-Genentech, Pfizer, Speakers bureau: BMS, Sanofi-Genzyme-Regeneron, Janssen, Roche-Genentech, Patrick Dessein: None declared, Linda Tsang: None declared, Hani El-Gabalawy: None declared, Carol Hitchon: None declared, Virginia Dr. Pascual: None declared, Irazu Contreras-Yáñez : None declared, Petros Sfikakis: None declared, Miguel A González-Gay Grant/research support from: Prof. MA Gonzalez-Gay received grants/ research supports from Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker´s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Cynthia S. Crowson: None declared, Anne Grete Semb: None declared

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SAT0110 HIGH SERUM LONG-CHAIN OMEGA-3 FATTY ACIDS ARE ASSOCIATED WITH 6-MONTHLOWER DISEASE ACTIVITY IN EARLY RA: RESULTS FROM THE ESPOIR COHORT

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Background: Dietary long-chain polyunsaturated fatty acids (PUFAs) of the n3 and n6 families are involved in immune homeostasis and can contribute to modulate inflammatory processes. Dietary intake of n3PUFA (by either supplementation or fish consumption) has been inversely associated with RA incidence in different populations. Some evidence suggests that, in subject at high risk of developing rheumatoid arthritis (RA), high erythrocyte membrane content in long-chain n3-PUFA is associated with lower ACPA prevalence and progression to RA. While long-chain n6PUFA are considered mainly proinflammatory, some, like gamma-linolenic acid (GLA), are endowed with anti-inflammatory activity, and the erythrocyte content in n6 linoleic acid was inversely associated with the development of RA in a nested-case control study. No study hitherto evaluated the longitudinal association between individual PUFA profile and disease activity in early RA.

Objectives: To characterize serum profiles of PUFA and to determine their association with baseline variables and with 6-month disease activity in a cohort of patients with early RA.

Methods: Serum PUFAs were quantified by gas chromatography-mass spectrometry (GC/MS) in 594 patients with early RA at the time of recruitment in the French Etude et Suivi des POlyarthrites Indifférenciées Récentes (ESPOIR) cohort. Principal component analysis on 19 serum fatty acids with 14 to 22 carbon atoms allowed to determine 3 orthogonal patterns of baseline serum PUFA. Pattern 1 included high proportions of short-chain fatty acids, pattern 2 was high in n3 long-chain PUFA (EPA et DHA), pattern 3 was rich in n6 long-chain fatty acids (among which, GLA had the highest concentration). Patients were stratified in tertiles according to how much the fitted into each pattern, with tertile 1 meaning lowest and tertile 3 highest fitting into the pattern. The association of PUFA patterns with baseline variables was tested in univariate analysis. The association with 6-month disease activity (with high disease activity defined as DAS28>5.1) was tested in multivariable analysis after adjustment on baseline CRP, corticosteroid and/or NSAIDs use, socioeconomic status, ACPA and RF positivity, traditional and biologic DMARDs treatment between 0 and 6 months after inclusion.

Results: In baseline univariate analysis, pattern 1 was associated with high BMI, active smoking and with non-Caucasian origin. Profile 2 was associated with higher socioeconomic status and inversely associated with DAS28 and CRP. Profile 3 was associated with ACPA positivity and higher baseline CRP. In multivariate analysis, fitting into pattern 2 and 3 was associated with lower odds of having active disease after 6 months (OR for tertile 3 vs. tertile 1: 0.49 (95% CI 0.25 to 0.97, p<0.05) for pattern 2 and 0.51 (0.28 to 0.95) for pattern 3, respectively).

Conclusion: In a cohort of early RA patients, we could identify a high serum long-chain n3PUFA profile associated with low disease activity between 0 and 6 months of follow-up in the cohort. This is consistent with a presumed immunomodulatory action of n3PUFA. Despite the baseline association with disease severity features, like ACPA positivity and high CRP, a high serum long-chain n6PUFA profile is also associated with 6-month lower disease activity, possibly due to the presence of high concentrations of GLA in this profile.

Disclosure of Interests: Johanna Sigaux Speakers bureau: celgene, Camille de Brauer Buscail: None declared, Chantal Julia: None declared, Rene Marc Flipo: None declared, Alain Cantagrel: None declared, Bernard Bannwarth: None declared, Francois Laporte: None declared, marie-Christophe Boissier Grant/ research support from: Pfizer MSD, Speakers bureau: Pfizer Lilly Biogen, Luca Semerano Grant/research support from: pfizer, Speakers bureau: pfizer, roche, msd.

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SAT0111 RED CELL DISTRIBUTION WIDTH IS A MARKER OF EARLY RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITIS

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Background: Red blood cell distribution width (RDW) has recently emerged as a possible surrogate biomarker of inflammation. Its potential role as prognostic biomarker has not been evaluated yet in Rheumatoid Arthritis (RA).

Objectives: The following study aims to evaluate the potential prognostic role of RDW in the prediction of early response to methotrexate (MTX).

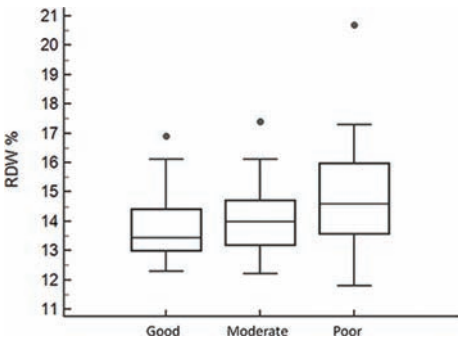
Methods: We performed a retrospective analysis of clinical records of patients affected by RA, according to ACR/Eular classification Criteria. The baseline RDW was recorded and correlated with disease activity scores and inflammatory markers. The response to treatment was evaluated at the 3-months follow-up visit according to Eular response criteria.

Results: We selected 88 patients (58 females, 65.9%), with a median age of 62 [52-69] years. 61 patients were positive for Rheumatoid Factor (RF) and/or anticitrullinated antibodies – anti-CCP (69.3%). The median DAS28 for Erythrocyte sedimentation rate (DAS28ESR) at the diagnosis was 4.16 [3.33-5.00] while the median RDW was 14.0 [13.1-14.9]%. The baseline RDW was directly associated to CRP (ρ= 0.250; p=0.02), but not with ESR (p=0.32) or DAS28ESR (p=0.40).

All the patients received methotrexate (MTX) at a median dose of 10 [10-15] mg/week, 79 (89.8%) also received prednisone (median dose 5 [5-10] mg/day) and 20 hydroxychloroquine in addition to MTX. A significant trend towards a larger RDW was reported from patients with a good Eular response at three months (13.5 [13.0-14.4]%) to those with a moderate response (14.0 [13.2-14.7]%) and finally to those with a poor response (14.6 [13.6-16.0]%; p=0.004). At logistic regression, RDW (p=0.02), but not CRP or ESR (p=0.70 and p=0.37 respectively), was a predictor of a good Eular response.

Moreover, in a further logistic regression model, baseline RDW (p=0.03) and baseline DAS28ESR (p=0.0009) were the only predictors of a good Eular response at three months, while age, gender, MTX and prednisone dosage and seropositivity did not fit the model.

After the treatment RDW significantly increases (14.7 [14.0-15.7]%) and the variation of RDW from baseline is inversely related to the variation of DAS28ESR (ρ= -0.263; p=0.02). The increase of RDW is significantly higher in patients with a good Eular response, with a trend towards a smaller increase in case of moderate and poor response (0.95 [0.35-1.35]% vs. 0.65 [0.1-1.9]% vs. 0.2 [-0.62-0.77]%; p=0.015).



Conclusion: RDW is a promising predictor of early response to MTX in RA; in this context, it performs better than classical inflammatory markers. Moreover, RDW significantly increases after MTX initiation, proportionately to response to treatment, suggesting a potential role for RDW as a marker of MTX effectiveness.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7044

SAT0112 NO DIFFERENCE IN TREATMENT CONTINUATION OF DIFFERENT BIOLOGICS IN ELDERLY PATIENTS > 70 YEARS COMPARED TO YOUNGER PATIENTS ≤ 65 YEARS

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Background: Due to demographic changes an increasing number of persons reach an age above 70 years. Therefore, the adequate therapy of elderly patients with rheumatoid arthritis (RA) is an increasingly important topic.
Objectives: To compare treatment continuation of several biologic DMARDs in patients ≤ 65 with elderly patients > 70 years, stratified by onset of disease (young onset (<65 years) and late onset (≥65 years)) and by seropositivity.
Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. For the current analysis patients who were enrolled with a biologic DMARD between 01/2007 and 04/2018 were included. Kaplan Meier methods were applied to analyse treatment continuation.
Results: Among the 9,819 RA patients included in the analysis, 7,972 were ≤ 65 years old and 1,847 were older than 70 years (among them 180 patients above 80 years). Among the patients ≤ 65 years, 28% received a csDMARDs and 72% a bDMARD, while among the patients above 70 years, 35% received a csDMARDs and 65% a biological. Elderly patients with a young disease onset (YORA) were more frequently women and more frequently seropositive, on average had a higher number of prior treatment failures, a worse physical function and were more likely to have joint erosions than elderly patients with late onset (LORA) (Table 1). On all bDMARD treatments investigated, elderly RA patients showed the same treatment continuation as seen in younger patients. While neither the age of the patients nor the age at disease onset changed the continuation of biologics, patients being seronegative had a significantly lower continuation with rituximab and abatacept treatment, irrespective of age (Figure 1).

Tables and Figures

Table 1. Baseline characteristics of patients, stratified by age and disease onset.

Parameter	≤ 65 years	> 70 years, LORA	> 70 years, YORA
N	7972	1009	838
Age in years	51.6 (9.5)	76.4 (3.9)	74.3 (2.9)
% female	74.7%	72.7%	79.4%
Disease duration in years	8.6 (7.8)	4.4 (3.4)	20.4 (10.4)
Number of prior therapy failures	2.1 (1.1)	1.7 (0.9)	2.5 (1.2)
ESR	27.2 (21.3)	34.6 (24.5)	33.9 (23.6)
CRP	13.4 (20)	15.3 (20.5)	16.4 (23.4)
DAS28	4.8 (1.3)	5 (1.3)	5.2 (1.3)
Number of comorbidities	1.8 (1.9)	3.4 (2.6)	3.7 (2.5)
% of patients with >3 comorbidities	26.9%	55.5%	62.4%
% of patients with no comorbidities	28.1%	4.6%	4.2%
Seropositive patients (RF/ACPA)	72.4%	69.1%	81.3%
% of full physical function	67.5 (22.4)	60.3 (24.4)	55.4 (23.4)
Glucocorticoid dose in mg/d	6 (6.2)	6.1 (4.5)	5.6 (4.4)
% of patients with joint erosions	47.9%	46.2%	76%

Where not otherwise indicated, numbers are given in the format 'mean (standard deviation)'.

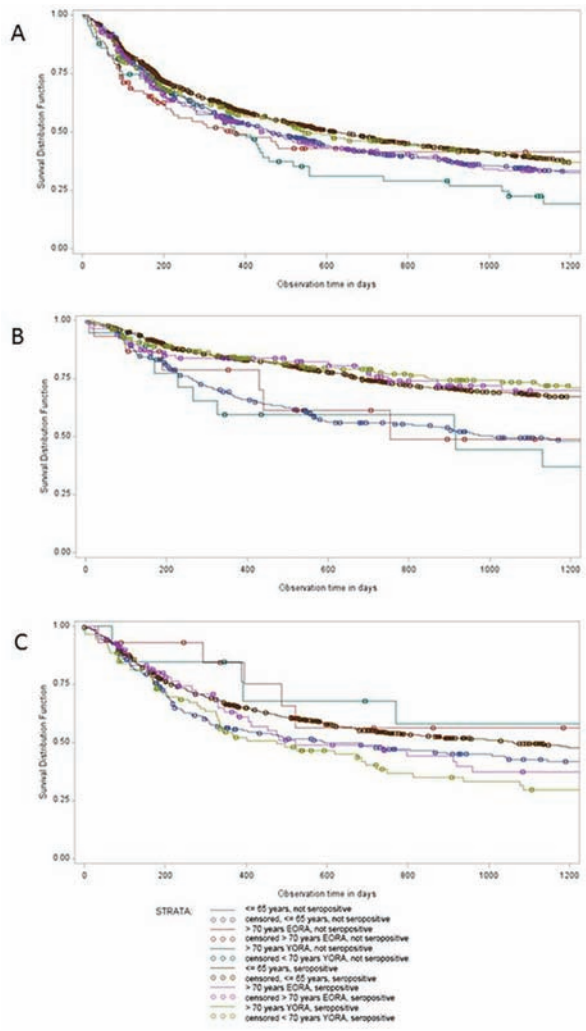


Figure 1. Treatment continuity in (A) TNF inhibitors, (B) abatacept and rituximab, (C) tocilizumab

Conclusion: These results suggest that bDMARD treatment may be used for elderly patients with the same effectiveness as in younger patients.
Acknowledgement: RABBIT is supported by a joint, unconditional grant from AbbVie, Bristol-Myers Squibb, Celltrion, Hexal, Lilly, MSD Sharp & Dohme, Pfizer, Roche, Samsung Bioepis, Sanofi-Aventis and UCB.
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SAT0113 LIMITING FACTORS OF REACHING ACR/EULAR BOOLEAN REMISSION IN EARLY RA PATIENTS TREATED ACCORDING TO CURRENT GUIDELINES

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Background: Abrogation of inflammation is important to prevent irreversible joint damage and maximize health-related quality of life in early RA patients. The ACR/EULAR Boolean remission criteria have the most stringent remission definition.(1) It has been reported that patient global assessment (PGA) is the variable most commonly scored above the cut-off in patients who almost fulfill the ACR/EULAR Boolean remission criteria.(2)
Objectives: To assess which components of the ACR/EULAR Boolean criteria that most often limit attainment of remission in modernly treated

early RA, and quantify the extent of subclinical inflammation in these patients.

Methods: DMARD-naïve early RA patients included in the treat-to-target ARCTIC trial were followed by a strict tight control regime aiming for DAS remission and no swollen joints, with an additional target of ultrasound remission in half of the patients.(3) Examination of all patients included 44SJC, Ritchie articular index (RAI), laboratory tests, patient reported outcomes included physical function (PROMIS), ultrasound (US) of 32 joints and magnetic resonance imaging (MRI) of the dominant hand and wrist (scored according to RAMRIS). Patients with complete clinical data at the 2-year follow-up visit were included in the current analyses. We assessed the proportion of patients fulfilling ACR/EULAR Boolean remission (based on 44 joints) and the proportion of patients fulfilling three out of four remission criteria, and in such cases, which were the limiting factors. We compared physical function and imaging inflammation (assessed by US power Doppler score, US grey scale score, MRI synovitis and bone marrow edema) in patients reaching complete ACR/EULAR Boolean remission to patients not reaching ACR/EULAR Boolean remission due to the most often limiting factors. Chi2 test and Wilcoxon rank sum test were used for the comparisons.

Results: Of the 203 patients included, 62% were females, mean (SD) age was 52 (13) years, and 81% were ACPA positive. ACR/EULAR Boolean remission was achieved by 112 of 203 patients after 24 months (55%), while 49 (24%) fulfilled three of the four remission criteria. Among these 49 patients, the major limiting factor for not reaching remission was PGA (n=29, 59%), with tender joints as the second most common limiting factor (n=11, 22%) (Figure). In patients not achieving remission due to PGA, the median [IQR] PGA value was 3.1 [2, 4.4]. Subclinical inflammation measured by ultrasound and MRI was not significantly different for patients in ACR/EULAR Boolean remission compared to patients not fulfilling these criteria due to PGA and/or tender joints (Table), but the latter reported more subjective symptoms such as fatigue and impaired physical function.

Figure: The proportion of patients with failure to fulfill the ACR/EULAR Boolean remission criteria due to one of the four components; tender joint count >1 or SJC44 >1 or CRP>1 mg/dl or PGA>1. N=49.

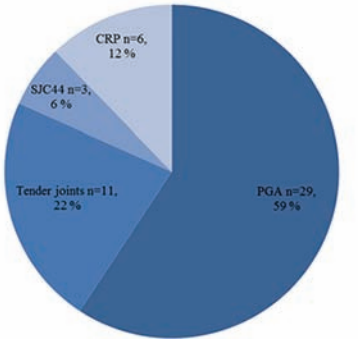


Table: Characteristic of patients in ACR/EULAR Boolean remission (N=112) and patients with SJC44≤1 & CRP≤1 (N=61) after two years of treat-to-target. Variables are median [IQR] unless otherwise stated. P-values <0.05 in bold.

	ACR/EULAR Boolean remission	SJC44≤1 + CRP≤1 + PGA >1 and/or tender joints >1	P-value for difference
Age	53.6 [41.1, 63.4]	53.3 [43, 61.2]	0.77
Female, n (%)	65 (58.0)	44 (72.1)	0.07
ACPA, n (%)	88 (78.6)	53 (86.9)	0.18
RF, n (%)	74 (66.1)	43 (70.5)	0.55
PROMIS physical function t-score	62.5 [50.0, 62.5]	45.3 [40.2, 50.0]	**<0.001**
Fatigue VAS (0-100)	3.5 [1.0, 12.0]	34.0 [17.0, 50.0]	**<0.001**
Physician's global (0-10)	0.2 [0.1, 0.8]	0.8 [0.4, 1.2]	**<0.001**
Ultrasound power Doppler score (0-96)	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.75
Ultrasound Grey Scale score (0-96)	3.0 [1.0, 5.5]	3.0 [0.0, 6.0]	0.69
MRI RAMRIS synovitis (0-39)	5.4 [3.7, 7.1]	5.0 [3.8, 6.2]	0.68
MRI RAMRIS bone marrow edema (0-105)	1.0 [0.0, 3.2]	1.8 [0.0, 3.2]	0.21

Conclusion: PGA and tender joints are the variables most often limiting patients from achieving ACR/EULAR Boolean remission, also in a treat-to-target setting with high remission rates. The level of subclinical inflammation is not elevated in these patients compared to patients in ACR/EULAR Boolean remission. Further research is still needed to assess which clinical remission criterion is best suited to guide treatment.

REFERENCES

[1] Felson DT, et al. ARD. 2011;70(3).
[2] Studenic P, et al. ARD. 2012;71(10).
[3] Haavardsholm EA, et al. BMJ. 2016;354.

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SAT0114 INCREASED PREVALENCE AND SEVERITY OF CORONARY ARTERY DISEASE IN PATIENTS WITH CHEST PAIN AND SEROPOSITIVE RHEUMATOID ARTHRITIS: AN ANALYSIS FROM A LARGE-SCALE POPULATION COHORT REFERRED FOR CARDIAC COMPUTED TOMOGRAPHY

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Background: Inflammation plays a central role in the development of atherosclerosis and inflammatory disease might promote progression of CAD.

Objectives: To examine the impact of the most frequent systemic inflammatory disease, rheumatoid arthritis (RA), on the prevalence and severity of coronary artery disease (CAD) in patients referred for rule out of CAD by cardiac computed tomography (CCT).

Methods: In total, 39,534 patients from a mandatory national CCT database were included. Patients with a validated RA diagnosis were subgrouped based on serology, treatment with biological disease-modifying anti-rheumatic drugs (DMARDs), and the need for flare treatment with intraarticular and intramuskular glucocorticoid injections (GCIs). Outcomes were coronary artery calcium score (CACS) > 0 and CACS > 400. Differences in prevalences were assessed by odds ratios (OR). Outcomes were adjusted for cardiovascular risk factors and comorbidities.

Results: A total of 337 (0.9%) patients with RA were identified. OR for having CACS > 0 was 1.17 (0.91-1.50) for overall RA and 1.33 (1.00-1.77) for seropositive RA. Patients who had received ≥1 GCI in the period 3 years prior to the CCT had an OR of 1.49 (0.99-2.27) for having CACS > 0. The OR for having CACS > 400 was 1.31 (0.95-1.81) for overall RA and 1.49 (1.04-2.12) for seropositive RA. OR for having CACS > 400 was 1.43 (0.99-2.07) for RA patients treated with conventional synthetic DMARDs, but 1.01 (0.51-1.99) for patients treated with biological DMARDs.

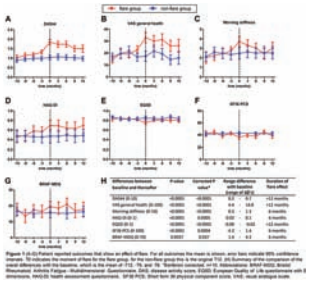
Conclusion: Coronary artery calcifications are more frequent in RA patients being seropositive or needing flare treatment. The occurrence of severe calcification is more frequent in seropositive RA patients and in RA patients not escalated to biological DMARDs. These findings support the hypothesis that systemic inflammation accelerates the atherosclerotic process leading to increased coronary artery calcium, which may explain the increased risk of cardiovascular events among RA patients.

Disclosure of Interests: None declared
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SAT0115 FLARING OF RHEUMATOID ARTHRITIS DUE TO TAPERING OF DMARDS: HOW DOES IT AFFECT PATIENTS' WELL-BEING? A STUDY ON PATIENT REPORTED OUTCOMES

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Background: Previous studies have shown that it is possible to taper DMARDs in RA patients with an inactive disease, but this is accompanied with a higher chance of disease flares. Current recommendations advise to taper DMARDs from a clinical viewpoint. However, data on the feasibility of tapering DMARDs from a patient's perspective are sparse.
Objectives: To determine the impact of flare after DMARD-tapering on patients quantifying the changes in patient relevant domains e.g. functional ability, fatigue, quality of life, and worker productivity, and to explore the duration of the effect.
Methods: Data were used from all 113 patients that flared after tapering DMARDs in the TARA study, a multicenter randomised controlled trial in which patients in sustained remission (DAS<2.4&SJC<1) tapered either their csDMARDs or TNF-inhibitor per protocol. For the current analysis, we compared the following secondary outcomes before and after flare over time; DAS44, functional ability (HAQ-DI), fatigue (BRAF-MDQ), quality of life (EQ-5D and SF36), anxiety and depression (HADS), morning stiffness, VAS general health, and worker productivity. Follow-up started three months before flare, at the moment of flare, and every 3 months thereafter. These were compared to baseline values, calculated by taking the average of 12, 9 and 6 months before flare. We used Linear Mixed Models (LMMs) with a random intercept and an autoregressive covariance matrix to determine an overall effect of flare. We adjusted for multiple testing with a Bonferroni correction. For determining the duration of the effect of a flare, we tested if the separate time points differed from the baseline with the same model. For the worker productivity we used descriptive statistics.
Results: In total, 113 patients experienced a flare. Patients who had a flare had a less stable course of the outcomes over time, compared with patients without flare (Figure 1A-G). When comparing all time points to baseline, statistical significant differences were found for DAS44 (p<0.0001), VAS general health (p<0.0001), morning stiffness (p<0.0001), HAQ-DI (p=0.0002), EQ-5D (p<0.0001), BRAF-MDQ (p=0.04), and the SF36 physical component scale (p=0.0004) (Figure 1A-H). The duration of these effects was more than 12 months for the DAS44, morning stiffness, and VAS general health. For the HAQ-DI, EQ5D, BRAF-MDQ, and SF36 PCS the duration of the effect of a flare was 6 months (Figure 1H). The effect sizes, expresses as differences with baseline, are indicated in Figure 1H and were rather small for most outcomes. The number of patients with payed work and unemployment were not affected by flare. The amount of sick leave increased from 1 to 1.3 days per month in the 6 months after flare and productivity decreased 1 point on a 0-10 scale in the 3 months after flare.
Conclusion: Having a flare does affect patient reported outcomes. It affects DAS44, VAS general health, morning stiffness, functional ability, quality of life, and fatigue. This effect lasted for more than 6 months. Although we only found minor differences with baseline on group level, on the individual patient level this can still be of great importance.



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SAT0116 DYNAMIC PREDICTION OF FLARES IN RHEUMATOID ARTHRITIS USING JOINT MODELLING AND MACHINE LEARNING: SIMULATION OF CLINICAL IMPACT WHEN USED AS DECISION AID IN A DISEASE ACTIVITY GUIDED DOSE REDUCTION STRATEGY

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Background: Most rheumatoid arthritis (RA) patients on a (b)iological DMARD achieve and maintain remission or low disease activity. Then, tapering the drug is safe and cost-effective[1], but with increased risk of short lived flares and joint damage progression. We developed so-called dynamic prediction models, using joint-modelling (JM) and machine learning (ML) respectively to predict an individual patients' risk of flaring. These models can make short-term (e.g. 3 month) predictions repeatedly at every clinic visit, based on routine care data, i.e. the longitudinal course of the patients' disease activity and medication, demographic and disease characteristics.[2]
Objectives: To externally validate the JM and ML model and evaluate the clinical impact on flare occurrence and bDMARD use, when using predictions as decision aid for tapering bDMARDs in a protocolised disease activity guided tapering strategy.
Methods: For external validation, an RCT comparing protocolised dose reduction (stepwise increase injection interval, until flare or discontinuation, n=121) with usual care (n=59) was used.[1]
Both models were applied to the trial data and AUC-ROC and calibration were assessed. To simulate our dose-reduction strategy, first, we defined optimal cut-offs for predictions using Youden's index as well as a cut-off at higher/lower predicted risks. Thereafter we applied them to the dose reduction arm of the trial. Assumptions were that 1) no further tapering was performed when the cut-off was reached without any flares occurring over time in the simulation and 2) when in the trial a flare occurred for which the bDMARD dose was increased to a value higher than when tapering was stopped in simulation, this flare occurred and the higher dose was used in simulation as well.
Results: AUC-ROC's in external validation were, as expected, somewhat lower than in the development cohort: 0.76 (95%CI 0.71–0.85) and 0.73 (0.72–0.74) versus 0.78/0.79 for JM/ML respectively, but still satisfactory. Calibration was better for ML, resulting in different cut-offs for the models. Results show that about 40% and 50% of flares can be prevented respectively and that the majority (66% and 76%) of the dose reduction can be maintained using the optimal cut-offs in our prediction aided dose reduction strategy over 18 months. Table 1 shows the proportion of full dose used, mean number of flares per patient, and percentage of patients experiencing a flare for several cut-offs as well as in the disease activity guided dose reduction strategy (in bold). As context values are also shown for usual care (trial control arm; in italic).

Strategy	Prop. full bDMARD dose (95%CI)	Mean # flares (95%CI)*	% pat. Flaring (95%CI)*
Usual care arm	*0.89 (0.85-0.93)*	*0.34 (0.22-0.46)*	*25 (18-33)*
Tapering arm	**0.50 (0.45-0.55)**	**1.42 (1.24-1.61)**	**80 (73-87)**
Simulation tapering JM (optimal)	0.62 (0.58-0.66)	0.81 (0.62-1.00)	49 (40-58)
Simulation tapering JM (< risk score)	0.68 (0.64-0.72)	0.66 (0.48-0.84)	39 (30-48)
Simulation tapering ML** (optimal)	0.67 (0.64-0.70)	0.67 (0.49-0.85)	41 (32-50)
Simulation tapering ML** (> risk score)	0.57 (0.53-0.61)	1.12 (0.92-1.31)	64 (55-73)

* Flare based on van der Maas et al. Ann Rheum Dis. 2011;72:1800-5; **Refitted without variable selection; <> cut-off at lower/higher flare risk then optimal cut-off; higher/lower cut-off for JM/ML did not lead to meaningful reductions in flares / savings in bDMARD use

Conclusion: Both models proved to be externally valid. Using them to aid decisions on biological dose reduction has the potential to reduce the occurrence of flares significantly while largely retaining the reduction in dose as obtained by a disease activity guided dose reduction strategy.

This finding, and its cost-effectiveness, should be validated in a clinical study.

REFERENCES

[1] Kievit W., et al.. Ann Rheum Dis 2016, 75:1939-1944
[2] Vodencarevic A., et al.. DATA 2018: 187-192

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SAT0117 THE IMPACT OF DIFFERENT CRITERIA SETS ON EARLY REMISSION AND IDENTIFYING ITS PREDICTORS IN RHEUMATOID ARTHRITIS: RESULTS FROM AN OBSERVATIONAL COHORT (2009–2018)

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Background: Currently, with increased awareness of early diagnosis and intervention and the identified association of early remission with a better clinical outcome in patients with rheumatoid arthritis (RA), shorter time to remission appears to be a more attractive goal. There are several studies reported the prevalence of early remission, no study so far has demonstrated the issue in Chinese population. Moreover, further investigative studies need to be performed due to limited and conflicting predictors of early remission in previous studies.

Objectives: To assess rates of early remission and investigate the concordance across different remission definitions, and to identify predictors of early remission in Chinese patients with RA.

Methods: For this study, clinical records were retrospectively reviewed for RA patients at rheumatologic clinic in Peking University First Hospital from 2009 to 2018. Disease activity and remission were determined according to DAS28-ESR, CDAI, SDAI, and Boolean criteria. Early remission was defined as time to remission ≤ 6 months. A secondary definition evaluated early remission as ≤ 3 months. Logistic-regression analyses were performed to identify determinants of early remission.

Results: 869 consecutive patients contributing 8,640 clinic visits were studied. Early remission rates were respectively 42.0% (DAS28-ESR), 25.0% (CDAI), 29.4% (SDAI), and 26.1% (Boolean). Notably, patients achieving remission within 6 months more frequently attained sustained remission by contrast to those not achieving early remission (68.7-75.1% vs. 31.2-33.1%, P<0.0001). Further logistic-regression analyses revealed male (OR=1.42-1.74, p<0.05), early RA (OR=1.64-2.22, p<0.05), as well as initial hydroxycloroquine treatment (OR=1.41-1.81, p<0.05) were independently associated higher probability of early remission, as demonstrated by nearly all definitions, while a higher baseline disease activity (DAS28-ESR, CDAI, and SDAI) lowered the possibility of early remission in corresponding remission indices. However, the significant associations of treatment-naïve, serological features with early remission were not confirmed.

Conclusion: Early remission was strongly associated with sustained remission, however infrequently achievable in real-life practice. Male, early RA, a low baseline disease activity, and initial hydroxycloroquine treatment were stable independent predictors of early remission.

Disclosure of Interests: None declared

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SAT0118 PRETREATMENT PREDICTION OF INDIVIDUAL OUTCOME OF RHEUMATOID ARTHRITIS PATIENTTO INFLIXIMAB THERAPY USING SERUM BIOMARKERS AND CLINICAL DATA

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Background: Infliximab (IFX), is a most effective b-DMRD, and results in a 60% remission rate on average in rheumatoid arthritis (RA) patients. The remaining 40% of patients undergo other biologics treatments that follow a 'treat-to-target method' until they achieve remission. Predicting in advance that a patient cannot achieve clinical remission with IFX, would allow doctors to start such patients on treat-to-target treatments sooner. Unfortunately, no reliable method has yet been found to predict patient-response.

Objectives: We tried to establish a prediction method using the serum of individual patient with RA related biomarkers present in varying amounts before they underwent IFX.

Methods: This study uses an observational retrospective study with 85 patients. 22 clinical data were used as explanation variables, such as, disease duration, combination of c-DMRDs, DAS 28-ESR, and day 0 laboratory data. 84 biomarkers in patients' pretreatment serum were measured using Multi-Plex Human Cytokine Chemokine beads array. DAS-28-ESR after 24 weeks was used as an objective variable. Patients administered IFX with regular method were divided into two groups: complete remission (DAS 28-ESR<2.6) and non-remission (DAS 28-ESR 2.6) at 24 weeks. The log–transformed value of all parameters were used for the statistical analysis. We used the least absolute shrinkage and selection operator (Lasso) approach to select combination markers that were most predictive of remission. In the process of multi-marker prognostic model building, to avoid over fitting, leave-one-out cross validation (LOOCV) was used to evaluate the performance of the multi-marker model.

The receiver operating characteristic (ROC) analysis was used to evaluate the ability of the models to predict the 24-week outcome of patients. The area under the ROC curve is the product of the cross validation procedure.

Results: We selected a combination from 104 markers. 3 to 5 combinations were most predictive of remission with 1.405 Cohen's d and at 0.85 AUC, 0.826 PPV, 0.882 NPV, and 0.689 ACC. On the contrary, using 22 clinical parameters, AUC, PPV, NPV and ACC were 0.726, 0.713, 0.649 and 0.673, respectively.

Conclusion: Using the pre-treatment serum, we were able to predict with high accuracy patients who would achieve remission. Our method is stable and economical; therefore, it may be applicable as a way of identifying individual patients who are resistant to IFX therapy, so as to avoid treating them with IFX in the first place. The next step is to confirm these results in larger scale retrospective and prospective studies. The first highly accurate method identified for predicting remission and non-remission in individual RA patients who are targeted for IFX treatment.

REFERENCE

[1] Uno K, Yoshizaki K, et all. Pretreatment Prediction of Individual Rheumatoid Arthritis Patients' Response to Anti-Cytokine Therapy Using Serum Cytokine/Chemokine/Soluble Receptor Biomarkers. PLoS One. 2015 Jul 15;10(7): e0132055.

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Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Abbivie GK, Nipponkayaku Co.Ltd, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Taiho Pharmaceutical Co. Ltd., Chugai Pharmaceutical Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., GlaxoSmithKline K.K., UCB Japan Co. Ltd., Consultant for: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Asahi Kasei Medical K.K., AbbVie GK, Daiichi Sankyo Co., Ltd., Bristol Myers Squibb, and Nipponkayaku Co. Ltd., Speakers bureau: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Speakers bureau: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Astellas Pharma Inc, Diaichi Sankyo Co. Ltd., Eisai Co. Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co. Ltd., Novartis Pharma K.K., Keisuke Izumi Grant/research support from: Asahi Kasei Pharma, Speakers bureau: Asahi Kasei Pharma Corp, Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Eli Lilly Japan K.K., Mitsubishi Tanabe Pharma Co., Mitsuhiro Iwahashi: None declared, Hitoshi Fujimiya: None declared

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SAT0119

CREATE RISK PREDICTION MODELING AND DRUG WITHDRAW ROAD MAP THROUGH PATTERN EXTRACTION AND DATA MINING: A MASTER ALGORITHM DEVELOPMENT FROM THE SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: Combination therapy with DMARDs for treating RA is standard of care. However, certain rates of adverse events (AEs) are unavoidable. The stigmas are how to predict the risk and how to define drug withdraw sequence if AEs persist for optimal risk reductions. The decisions made are always empirically.

Objectives: To develop a risk prediction model and an algorithm for drug withdraw sequence based on data mining from the SSDM.

Methods: SSDM is an interactive mobile disease management tool, including two application systems (APPs) for both the doctors and the patients. The patients can input medical records (including medication and laboratory test results) and perform self-evaluation (DAS28, HAQ) via App. The data synchronizes to mobiles of authorized rheumatologists through cloud and advices could be delivered. In previous studies, we demonstrated that patients could master SSDM after training.

In order to develop a prediction model and the master algorithm, abnormal white blood cell counts (WBC) and alanine aminotransferase (ALT) elevation were targeted. Data was collected, extracted, validated, and Bayesian networking, data mining, modeling were performed. WBC under 4k/ml is defined as leukocytopenia (LP), over 10k/ml as infection predisposing (IP), and ALT > 40 U/L as ALT elevation.

Results: From Jun 2014 to Jan 2019, 44,533 RA patients from 587 centers registered in SSDM. 135 different drugs and 882 combination therapies are identified. LP happens at 317 and IP at 286, ALT at 322 cases in 641 treatment regiments. Among them, MTX based regiments are 257 types, and the risk ratio (RR) are profiled as prediction model by comparing each AE rate of combination regiment with that of MTX monotherapy (Fig 1). The RR ranges from 0.28 to 6.28. The highest risk combination of prednisone (Pred), leflunomide (LEF), methotrexate (MTX), hydroxychloroquine (HCQ) and Celecoxib is selected (RR=6.28) to develop a master algorithm. Figure 2 shows Bayesian network, in which, quartet correlaties with 31 different regiments. Based on Bayesian method, the probabilities of LP, IP and ALT are plotted through 64 modeling, and the algorithm for drug withdraws strategies is generated. Drug withdrawing sequence for LP is HCQ, then Cel, then LEF, then Pre, the risks of LP are reduced by 41%, 22% 36% and 15%, respectively. For IP, withdraw sequence is Pred, then LEF, then Cel, then HCQ, the risks of IP are reduced by 45%, 28%, 23% and 4%, respectively, For ALT, withdraw sequence is MTX, then Pred, LEF, then Cel, the risks of ALT are reduced by 48%, 8%, 7%and 6%.

Conclusion: Through patterns extraction, data mining, modeling, and Bayesian networking, a risk prediction model and a master algorithm for drug withdraw strategy in reduction of AEs are developed, which are expendable and replicatablei. Via continuing data inputs and machine leaning, an artificial intelligent system in assisting clinical forecast and decision-making may be achieved with SSDM.

Fig.1 AE rate of combination regiment with that of MTX monotherapy.

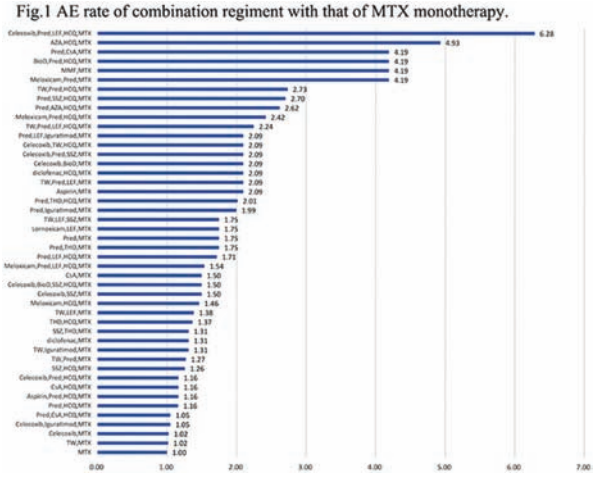


Figure 1

Figure 2. Bayesian network and date processing: Patients number (black as blow) and the rate of LP, IP and ALT elevation in 31 regiments.

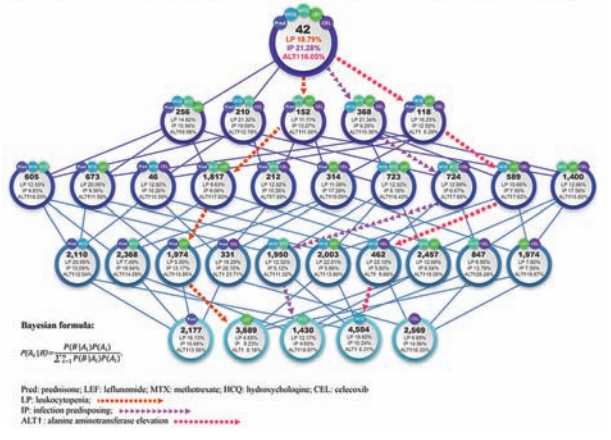


Figure 2

Disclosure of Interests: None declared

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Rheumatoid arthritis – biological DMARDs

SAT0120 COMPARATIVE EFFECTIVENESS OF TOFACITINIB AND TNF INHIBITORS SINCE 2014. IMPACT OF COMBINATION WITH METHOTREXATE

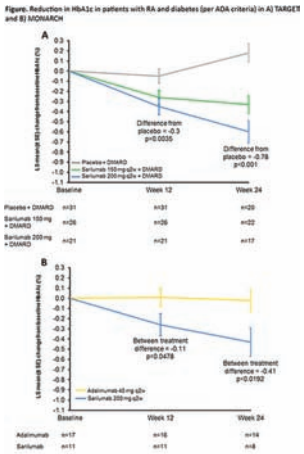
Denis Choquette[1], Louis Bessette[2], Loïc Choquette Sauvageau[1], Isabelle Ferdinand[1], Paul Haraoui[1], Frédéric Massicotte[1], Jean-Pierre Pelletier[1], Jean-Pierre Raynauld[1], Marie-Anaïs Rémillard[1], Diane Sauvageau[1], Édith Villeneuve[1], Louis Coupal[1]. [1]*Institut de Recherche en Rhumatologie de Montréal (IRRM), Rhumatology, Montréal, Canada*; [2]*Centre de l'Ostéoporose et de Rhumatologie de Québec (CORQ), Québec, Canada*

Background: Tofacitinib (TOFA), a targeted synthetic DMARD, has been approved for the treatment of rheumatoid arthritis (RA) in Canada since April 2014. This oral agent preferentially inhibits signalling by cytokine receptors associated with JAK1 and JAK3 subunits. It is also indicated for the treatment of PsA and UC since October 2018. Clinical experience with this molecule has been increasing, and questions relating to its efficacy and long-term safety are of interest. Data collection through RHUMADATA®, a Quebec based clinical database and registry, allows comparison of newer options with more traditional agents such as tumor necrosis factor inhibitors (TNFi).
Objectives: The current analysis compares TOFA to TNFi used with and without methotrexate (MTX) among patients with RA.
Methods: Data collected since January 1, 2014 (when TOFA became available in Canada) at the *Institut de Recherche en Rhumatologie de Montréal* (IRRM) and the *Centre de l'Ostéoporose et de Rhumatologie de Québec* (CORQ) was extracted from Rhumadata® on January 7, 2019. Patients initiated on TOFA or a TNFi (adalimumab, certolizumab, etanercept, golimumab, infliximab) without or with MTX were selected. Data include baseline characteristics (socio-demographic variables, concomitant and past medication, comorbidities and the Charlson comorbidity index (CCI)), variables measured over time (lab results, patient and physician-reported outcomes, and disease activity measures) and persistence data (treatment duration, reason for cessation). The groups were compared to identify potential confounder, and persistence data were analyzed using Kaplan-Meier and Cox methods.
Results: A total of 480 patients were prescribed TOFA (n=162) or a TNFi (n=318) since January 1, 2014. Of those, 57% (n=92) and 70% (n=224) were treated with MTX in the TOFA and TNFi group respectively and mean disease duration was 12.1 (standard deviation=11.0) and 7.2 (8.1) years. TOFA and TNFi represent the first treatment following csDMARD-IR for 33%(TOFA) and 62%(TNFi). In the TOFA group, 84% were women, 15% were smokers and the mean age at treatment initiation was 57.7 (11.5) years. In the TNFi group, 77% were women, 12% were smokers and the mean age at treatment initiation was 54.2 (13.7) years. At treatment initiation, patient global, pain and fatigue assessments, made on a visual analogue scale ranging from 1 to 10, were 5.6 (2.5), 5.9 (2.7) and 5.7 (2.9) in the TOFA group and 5.0 (2.9), 5.5 (3.0) and 5.1 (3.1) in the TNFi group. Baseline disease activity was assessed as moderate or high/severe in 85.9% and 76.7% of TOFA (?) patients (DAS28(4)-ESR criteria). Among the 56 (35%) TOFA and 146 (46%) TNFi patients ceasing therapy, reasons for cessation were "inefficacy" (TOFA: 64% vs TNFi: 56%) and "adverse events" (TOFA: 16% vs TNFi: 11%). Patients remaining on TOFA and TNFi therapy at last follow-up had an average treatment duration of 1.7 (1.1) and 2.7 (1.5) years and no difference in retention was observed between TOFA and TNFi treated patients (log-rank p=0.41). Patients treated with a TNFi in combination with MTX had better treatment retention than those treated without MTX (log-rank p=0.04) while patients treated with TOFA+/-MTX had similar retention (log-rank p=0.96). These results remain unchanged when adjusted for gender, age at treatment initiation, disease duration, and comorbidities.
Conclusion: In our real-world data registry, treatment with TNFi and TOFA yielded similar retention over time. Subjects treated with TNFi and MTX remained on treatment longer than those treated without MTX while subjects treated with tofacitinib with or without MTX had similar retention.
Disclosure of Interests: Denis Choquette Grant/research support from: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Consultant for: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Speakers bureau: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Louis Bessette Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant for: AbbVie, Celgene, Eli Lilly, Novartis, Pfizer Inc, Loïc Choquette Sauvageau: None declared, Isabelle Ferdinand Consultant for: AbbVie, Amgen, Novartis, Pfizer, Speakers bureau: Amgen, Pfizer, Paul Haraoui Grant/research support from: Abbvie, Amgen, Pfizer, UCB, Consultant for: Abbvie, Amgen, Lilly, Pfizer, Sandoz, UCB, Speakers bureau: Pfizer, Frédéric Massicotte Consultant for: AbbVie, Pfizer, Janssen, Eli Lilly, Speakers bureau: Janssen, Jean-Pierre Pelletier Shareholder of: Shareholder in ArthroLab Inc., Grant/research support from: Study funded by TRB Chemedica SA, Consultant for: TRB Chemedica SA, Jean-Pierre Raynauld Consultant for: ArthroLab Inc., Marie-Anaïs Rémillard Consultant for: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Paid instructor for: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Speakers bureau: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Diane Sauvageau: None declared, Édith Villeneuve Consultant for: AbbVie, UCB, Celgene, Roche, Pfizer, Amgen, BMS, Sanofi-Genzyme, Paid instructor for: AbbVie, Speakers bureau: AbbVie, Pfizer, BMS, Roche, Louis Coupal: None declared
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SAT0121 EFFECT OF SARILUMAB ON GLYCOSYLATED HEMOGLOBIN IN PATIENTS WITH RHEUMATOID ARTHRITIS AND DIABETES

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Background: Sarilumab is a human mAb blocking the IL-6Rα, approved for adult patients with moderately to severely active RA. The incidence of Type 2 diabetes is increased in patients with RA, and elevated IL-6 may be an independent risk factor.
Objectives: We conducted a post hoc analysis into the effect of sarilumab treatment on glycosylated hemoglobin (HbA1c) levels.
Methods: TARGET (NCT01709578) was a 24-week study of sarilumab 150/200 mg q2w vs placebo (all +csDMARD) in TNFi-inadequate response/intolerant (IR/INT) patients. MONARCH (NCT02332590) was a 24-week monotherapy study of sarilumab 200 mg q2w vs adalimumab 40 mg q2w in MTX-IR/INT, bDMARD-naïve patients. There were 78/546 (14.3%) and 28/369 (7.6%) diabetic patients per ADA criteria (baseline fasting glucose ≥7 mmol/L or baseline HbA1c ≥6.5%) in TARGET and MONARCH, respectively.
Results: In patients with RA and diabetes, the decrease in HbA1c at Week 24 was greater in sarilumab-treated groups than placebo (TARGET; in combination with csDMARDs) or adalimumab (MONARCH; monotherapy) groups (Figure). There was no interaction between change in HbA1c and corticosteroid use nor were changes in HbA1c correlated with changes in CRP, DAS28-CRP, or hemoglobin level. Among sarilumab-treated patients, those with baseline IL-6 >37.5 pg/mL (>3× upper limit of normal) had greater reductions in HbA1c (least squares mean change -0.27) than those with baseline IL-6 levels ≤37.5 pg/mL (least squares mean change -0.11). Sarilumab safety profile was similar in diabetic vs non-diabetic patients with RA.



Conclusion: Patients with RA and diabetes treated with sarilumab had greater improvements in HbA1c than those treated with adalimumab or placebo. With monotherapy, differences between sarilumab and

adalimumab were more pronounced among patients with higher baseline serum IL-6 levels.

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SAT0122 COMPARISON OF REAL-WORLD PERSISTENCE OF SUBCUTANEOUSLY ADMINISTERED BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG (DMARD) THERAPIES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS (RA) SWITCHING FROM ANOTHER BIOLOGIC

Jennie H. Best, Lenore Tominna, Ibrahim Abbass. *Genentech, Inc., South San Francisco, United States of America*

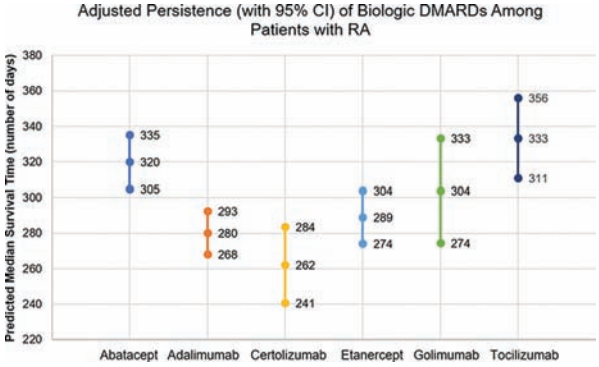
Background: The EULAR and ACR clinical guidelines recommend switching to a different disease-modifying antirheumatic drug (DMARD) when biologic-treated patients experience treatment failure or toxicity. Lack of efficacy and adverse events are among the most commonly reported reasons for switching biologic therapies. Limited information is available regarding biologic therapy persistence across subcutaneously administered (SC) biologic agents in the real-world setting, as well as for comparative information on biologic persistence for SC biologics among patients with rheumatoid arthritis (RA) who are not naive to biologic treatment.

Objectives: To compare persistence of SC biologic DMARDs (bDMARDs) in patients with RA as subsequent-line therapy following a failure of first line bDMARDs.

Methods: US administrative claims data were used to create a longitudinal cohort of adult patients with RA initiating SC biologic between 1/1/2012 and 6/30/2017 (initiation date = index). Patients were required to have failed 1st bDMARD to enter study (but could later switch therapy) and to have 6 and at least 3 months of continuous enrollment pre- and post-index (date of prescription for bDMARD). Those with other autoimmune conditions were excluded from the study. Outcomes were biologic persistence, defined as number of days between initiation date and last supplied day of last fill. Parametric survival models with exponential distribution with robust variance estimator were used to compare outcomes for tocilizumab versus other biologics, adjusting for differences in baseline characteristics, accounting for correlation among different bDMARD episodes.

Results: There were 10,301 patients with 12,704 bDMARD episodes: abatacept (n=2,988), adalimumab (n=3,599), certolizumab (n=982), etanercept (n=2,760), golimumab (n=745), or tocilizumab (n=1,630). Mean age was 51.0-53.3. Mean [SD] Elixhauser comorbidity scores were significantly higher ($p<0.001$) for tocilizumab (2.8 [2.3]) compared to abatacept (2.5 [2.2]), adalimumab (2.5 [2.1]), certolizumab (2.4 [2.0]), etanercept (2.4 [2.0]), or golimumab (2.4 [2.2]). Adjusted median days (95% CI) of persistence were: abatacept 320 (305, 335); adalimumab 280 (268, 293); certolizumab 262 (241, 284); etanercept 289 (274, 304); golimumab 304 (274, 333); and tocilizumab 333 (311, 356). Tocilizumab had significantly ($p < 0.05$) higher persistence compared to adalimumab, certolizumab, and etanercept (**Figure 1**).. Of patients who were observed for 12 months, 45% of patients initiated tocilizumab bi-weekly and 55% initiated weekly. Of the 347 patients initiating bi-weekly tocilizumab, 33% switched to weekly over 12-month follow up; the mean time to switch was 177 days. After 12 months of follow-up, approximately 68% of patients finished on weekly dosing and 32% on biweekly dosing.

Conclusion: Among patients with RA who previously used ≥1 other biologic, tocilizumab-treated patients had similar or statistically significantly better biologic persistence compared with other biologics.



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Disclosure of Interests: Jennie H. Best Employee of: Genentech, Inc., Lenore Tominna Employee of: Genentech, Inc., Ibrahim Abbass Employee of: Genentech, Inc.

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SAT0123 RISK FOR TUBERCULOSIS DURING TREATMENT WITH BIOLOGICAL THERAPY: IS IT TIME FOR REVIEWING SCREENING PROTOCOL? – RESULTS FROM BRAZILIAN REGISTRY OF BIOLOGICAL THERAPIES IN RHEUMATIC DISEASES (BIOBADABRASIL)

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Background: As Brazil is accountable for 33% of the tuberculosis (TB) burden in Americas, with an annual incidence of 33.5/100,000 in 2017[1], the occurrence of tuberculosis infection in patients with rheumatic diseases in use of biological therapy is a recurrent concern.

Objectives: To assess incident TB among patients with rheumatic disease in use of biological therapy in a country with high incidence of TB.

Methods: BiobadaBrasil is a multicentric prospective cohort study involving patients with rheumatic diseases who started the first biologic or a synthetic disease modifying anti-rheumatic drug (DMARD)[6]. This analysis includes patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) recruited from Jan 2009 to Aug 2018 and followed-up for one or multiple courses of treatment until censoring or incident TB. The primary outcome was the incidence of tuberculosis (in any organ site). The history of exposure to tuberculosis, chest Rx, screening and treatment for latent tuberculosis infection (LBTI), and use of prophylactic isoniazid were evaluated before each course of treatment. Multivariate Cox proportional hazards models (with DMARDs included as time-varying covariates) were used to estimate hazard ratios (HR) and 95% confidence intervals (CI); analyses were performed with the Survival package of R.

Results: Sample: 2858 patients (female =70,2%; RA = 72%, AS=20%, and PsA = 8%). A total of 31 (1.1%) patients developed tuberculosis during treatment. One patient on abatacept and one on tocilizumab developed TB while all the others were on TNF-inhibitors(29). The median (interquartile range) exposure to the current DAMRD course was 11.1 (5.9-20) months. TB patients did not significantly differ from others regarding disease duration, sex or age. Almost half (n=14,45%) of TB patients did not present evidence of previous exposure or any screening positive test for TB; 9 (29%) TB patients had received adequate LTBI treatment (isoniazid) recently or in the past. Furthermore, 8(26%) had incomplete/inconsistent screening. The overall incidence of TB was 1.9/1000 patients/year, and was not significantly different among the diseases (1.63 for RA, 2.06, for AS, and 3.79/1000/year for PsA). In univariate analysis, exposure to anti-TNF monoclonal antibodies (HR 3.1, 95%CI 1.18-8.15, P=0.02) and presence of any marker of previous contact with TB (positive history of TB, known contact with TB, positive TST, or abnormal chest X-ray: HR 4.2 (2.1-8.5, $p<0,001$) were positively associated with the risk of TB. Including simultaneously these variables in the Cox model, they were independent risk factor for TB ($p<0.05$).

Conclusion: Monoclonal anti-TNF antibodies and previous exposure/diagnosis of TB are independent risk factors for developing TB in Brazil. TB

cases occurred both early and lately during treatment courses, suggesting LTBI screening failures, treatment non-adherence or re-exposure. Current application and content of the protocol for screening and treatment of LTBI needs to be reviewed.

REFERENCES

[1] WHO TB report 2018.https://www.who.int/tb/publications/global_report/en/
[2] Rev Bras Reumatol Engl Ed. 2017;57 Suppl 2:477-483. doi: 10.1016/j.rbre.2017.05.005.

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SAT0124 MOLECULAR CHARACTERIZATION OF THE SERUM PROFILE ASSOCIATED TO THE INCREASED CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS PATIENTS. EFFECTS OF BIOLOGICAL DRUGS.

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Background:
Objectives: 1- To characterize the serum molecular profile associated to the increased cardiovascular (CV) risk in Rheumatoid Arthritis (RA) patients. 2- To evaluate the *in vivo* and *in vitro* effects of biological drugs on the reestablishment of this altered molecular profile.
Methods: Serum samples of 280 RA patients and 100 healthy donors (HD) were studied. miRNomes were identified using next-generation sequencing miRNA assay (HTG EdgeSeq technology). The inflammatory profile, Netosis-derived products, and circulating biomolecules related to oxidative stress were quantified using commercial kits. The Cardiovascular Risk SCORE for RA patients was calculated following EULAR recommendations. Carotid intima-media thickness (CIMT) was evaluated as early atherosclerosis marker. The in vivo effects of biologic drugs such as Infliximab (IFX), Tocilizumab (TCZ) and Rituximab (RTX) were evaluated before and after 6 months of therapy in 45, 20 and 25 RA patients, respectively. Serum from RA patients with high and low CV risk scores -either before and after IFX, TCZ and RTX therapies-, were further added to HUVECs, monocytes, and neutrophils purified from HD, and activity profiles were evaluated.
Results: The miRNA whole transcriptome assay identified 104 circulating miRNAs altered in RA patients. Functional classification (IPA) established their involvement in inflammatory response, as well as in immunological and hematological diseases. Circulating biomolecules related to inflammation -interleukins, chemokines, adhesion molecules-, Netosis -cell-free nucleosomes, elastase and DNA- and oxidative stress -lipoperoxides, nitrated proteins, and total antioxidant capacity- were also found coordinately altered in the serum of RA patients. Multivariate analyses showed that levels of a number of those altered biomolecules and circulating microRNAs were predictors of a high Cardiovascular Risk SCORE and the presence of a pathologic CIMT in RA patients.
The in vivo treatments with IFX, TCZ and RTX for six months reduced disease activity and induced the re-establishment of normal levels in those altered biomolecules in RA patients. Mechanistic *in vitro* studies showed increased pro-inflammatory profiles of leukocytes subsets and HUVECSs after treatment with serum from high CV risk score-RA patients. These profiles were reversed by incubation with serum from those patients after biologic drugs treatment.
Conclusion: 1. Specific mediators of inflammation, oxidative damage and Netosis, along with the microRNAs modulating their expression, coordinately contribute to the higher CV risk score present in RA patients. 2. Biologic drugs such as IFX, TCZ and RTX, restore the normal levels of these altered biomolecules, reducing the CV risk in RA patients.
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SAT0125 LONG-TERM SAFETY WITH SARILUMAB PLUS CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS AND SARILUMAB MONOTHERAPY IN RHEUMATOID ARTHRITIS: AN INTEGRATED ANALYSIS WITH 9,000 PATIENT-YEARS OF FOLLOW-UP

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Background: Sarilumab, a human IL-6R blocker approved for the treatment of RA, has shown efficacy as monotherapy and in combination with csDMARDs in Phase 3 trials.
Objectives: We assessed long-term safety from the sarilumab clinical development program in adult patients with RA who received subcutaneous (SC) sarilumab in eight clinical trials and their open-label extensions: MOBILITY (NCT01061736), TARGET (NCT01709578), ASCERTAIN (NCT01768572), EASY (NCT02057250), COMPARE (NCT01764997), ACT11575 (NCT01217814), MONARCH (NCT02332590), ONE (NCT02121210), and the open-label extension EXTEND (NCT01146652).
Methods: Data (cut-off Jan 15, 2018) were pooled from patients on sarilumab+csDMARD (N=2887) or sarilumab monotherapy (N=471). Patients had received sarilumab 200 mg or 150 mg q2w SC, except for 151 patients from MOBILITY Part A who received 100 mg qw, 150 mg qw, or 100 mg q2w. Treatment-emergent (TE) adverse events (AEs), AEs of special interest (AESIs), and discontinuations were assessed.

Results: Demographics were similar between combination and monotherapy pools (mean age 52 years; 81–83% female), and 38.7% and 8.5% of patients had received prior bDMARDs. Cumulative drug exposure was 7,985.5 and 798.7 patient-years (PY), with maximum duration 7.3 and 3.5 years. Exposure-adjusted rates of TEAEs, serious AEs, and TEAEs leading to discontinuations were similar (Table). Infections were the most common AESI. Rates of serious infection were 3.7 and 1.0/100 PY for combination and monotherapy, respectively, and were not associated with decreased absolute neutrophil counts (ANCs). Incidences of ALT >3× upper limit of normal and ANC <1.0 giga/L were 10.3% and 12.7% for combination, respectively, and 5.5% and 14.9% for monotherapy. Rates of confirmed GI perforation for combination and monotherapy were 0.1 and 0/100 PY. Analyzing data by 6-month intervals showed no increase in rate over time for serious infections, malignancy, major adverse cardiac events, or ANC <1.0 giga/L.

	Sarilumab+csDMARD (N=2887)	Sarilumab monotherapy (N=471)
Safety overview: n/Y_{EE} (IR/100 PY)[a]		
TEAEs	2489/1726 (144.2)	386/254 (151.8)
Serious TEAEs	685/7270 (9.4)	52/770 (6.7)
TEAEs leading to death	31/8187 (0.4)	5/812 (0.6)
TEAEs leading to discontinuation	705/8061 (8.7)	53/805 (6.6)
AESI: number of events (IR/100 PY)[b]	**PY=8187.7**	**PY=812.4**
Infections	4451 (54.4)	446 (54.9)
Serious infections	301 (3.7)	8 (1.0)
Opportunistic infections	76 (0.9)	6 (0.7)
Herpes zoster[c]	53 (0.6)	4 (0.5)
Tuberculosis[c]	4 (0.0)	1 (0.1)
Leukopenia[d]	1482 (18.1)	244 (30.0)
Thrombocytopenia[d]	147 (1.8)	8 (1.0)
Hepatic disorders	726 (8.9)	58 (7.1)
Confirmed GI perforations[e]	9 (0.1)	0
Elevation in lipids[d]	498 (6.1)	18 (2.2)
Major adverse cardiovascular events[f]	45 (0.5)	2 (0.2)
Hypersensitivity	444 (5.4)	48 (5.9)
Anaphylaxis	0	0
Injection site reactions	1934 (23.6)	279 (34.3)
Malignancy	56 (0.7)	5 (0.6)
Malignancy excluding NMSC	38 (0.5)	4 (0.5)
Lupus-like syndrome	5 (0.1)	0
Demyelinating disorders	0	1 (0.1)

n. number of patients; Y_{EE}, cumulative years at risk of first event; IR, incidence rate; GI, gastrointestinal; NMSC, non-melanoma skin cancer; PY, patient-years. [a]Exposure period is cumulative time at risk of first event; [b]AESI were investigator reported; exposure period is cumulative total TEAE period; [c]herpes zoster was reported as an opportunistic infection per protocol requirement; all cases of tuberculosis were reported as opportunistic infections; [d]individual events were reported and laboratory abnormalities were not necessarily persistent; [e]3 upper, 6 lower; [f]MACE includes cardiovascular death, myocardial infarction, stroke, hospitalization for either unstable angina and/or transient ischemic attack.

Conclusion: The long-term safety profile of sarilumab, either as monotherapy (observed for >3.5 years) or with csDMARD (observed for >7 years), remains stable and consistent with the anticipated profile of an IL-6R blocker.

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SAT0126

A PHASE 2 STUDY OF E6011, AN ANTI-FRACTALKINE MONOCLONAL ANTIBODY, IN PATIENTS WITH RHEUMATOID ARTHRITIS INADEQUATELY RESPONDING TO BIOLOGICS

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Background: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. We have conducted clinical trials of E6011, a novel humanized anti-FKN monoclonal antibody, for patients with rheumatoid arthritis (RA) in Japan[1]. This is the first report of a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group comparison study of E6011 in RA patients inadequately responding to biologics (NCT02960490).

Objectives: To evaluate efficacy and safety of E6011 compared with placebo.

Methods: During the 24-week double-blind period, patients with moderately to severely active RA of inadequate response to biologics were randomly assigned to E6011 400 mg or placebo groups at a 1:1 ratio. Patients who continued the study beyond Week 12 were further allocated to E6011 200 mg or 400 mg at a 1:1 ratio within the initially assigned group. Patients received either E6011 400 mg or placebo at Weeks 0, 1, 2, and every 2 weeks subsequently until Week 10 and then E6011 200 mg or 400 mg every 2 weeks between Weeks 12 and 22 in a double-blind manner. This abstract reports the results from the first 12-week placebo controlled period.

Results: A total of 64 subjects (33 in the placebo group and 31 in the E6011 400 mg group) received study drug. Of the 64 subjects, 55 completed and 9 discontinued study treatment prematurely during the 12-week placebo controlled double-blind period. The ACR20 response rate at Week 12 (non-responder imputation), the primary endpoint, was 27.3% (9/33 subjects) in the placebo group and 22.6% (7/31 subjects) in the E6011 group. ACR50 and ACR70 response rate at Week 12 were 3.0%, 0% in the placebo group and 9.7%, 3.2% in the E6011 group, respectively. Numerically greater improvement from baseline was found for some parameters of the ACR components in the E6011 group, however, no statistically significant differences were found in any of the ACR components between the placebo and E6011 groups. From the exploratory PK exposure analysis, there was a tendency that the effect of E6011 became clearer in the subjects who achieved higher serum trough E6011 concentration. Adverse events that occurred in at least 2 subjects in the E6011 group were stomatitis, injection site erythema, nasopharyngitis, and blood creatine phosphokinase increased. As a results, E6011 was well tolerated with no notable safety concerns at doses of 400 mg when administered subcutaneously for 12 weeks.

Conclusion: E6011 400 mg was well tolerated but did not show clear efficacy at Week 12 compared with placebo in RA patients with inadequately responding to biologics. Further investigation to seek an optimal clinical dose and evaluation period of E6011 are warranted.

REFERENCE

[1] Tanaka Y, et al., Mod Rheumatol (2018) 28, 58-65

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SAT0127 LONG-TERM OUTCOME OF CHILDREN BORN TO MOTHERS WITH CHRONIC ARTHRITIS AND EXPOSED TO TNF-INHIBITORS DURING PREGNANCY: A CASE-CONTROL STUDY

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Background: Treatment with tumor necrosis factors inhibitors (TNFi) during pregnancy may be required in order to control maternal disease which itself can be a threat for maternal-fetal well-being and pregnancy outcome. Information about the follow-up of in utero exposed offspring is limited

Objectives: The aim of this study was to compare the health and developmental conditions of children born to mothers with chronic arthritis who were exposed *in utero* to TNFi with those of unexposed children born to patients with the same age at conception and disease.

Methods: An *ad-hoc created* questionnaire was used to collect data on birth and growth parameters, breastfeeding, weaning, developmental milestones, vaccinations and illnesses.

Results: 122 live births in 97 women with chronic arthritis (65 RA and 32 SpA) were observed: 59 pregnancies were exposed to TNFi at the time of conception and 63 pregnancies were TNFi-naïve. In 57/59 (97%) pregnancies, TNFi was discontinued at positive pregnancy index. In 2/59 (3%) pregnancies TNFi was mantained throughout pregnancy due to active disease at conception. TNFi was restarted in 16/57 pregnancies (28%) (10 ETA, 5 CTZ, 1 ADA) during the 2nd-3rd trimester due to moderate-severe flare (median exposure 22 weeks; discontinuation of TNFi between 32-39 gestational weeks). In second group, TNFi (1 ETA, 1 CTZ) was introduced in 2/63 (3%) pregnancies during the 2nd trimester due to a severe flare. 16 in 16/63 (25%) pregnancies were managed with an increase of prednisone (max 10mg/day). To investigate the long-term follow-up of children exposed in utero to TNFi, 61 children exposed to TNFi at conception or during 2nd-3rd trimester (median age 29 months) and 61 unexposed children (median age 49 months) were compared. No significant differences in growth parameters and developmental milestones were observed. No excess nor particular pattern of congenital defects/malformations were observed. In both groups, vaccinations were performed according to the national schedule (no live vaccines in the first year of life) without relevant complications (Figure 1).

Conclusion: TNFi may be required in patients that experienced flare during pregnancy and they are effective in controlling maternal disease and ensures a good pregnancy outcome without complications for the health and growth of exposed children.

Table 1. Long-term follow up of children

	Pregnancies *exposed* to TNFi (n=61)		*P value*	Pregnancies *unexposed* to TNFi (n=61)	*P value*
	TNFi until positive pregnancy index (n=41)	TNFi during the 2nd-3rd trimester (n=20)			
Age at interview, mths	32(10-86)	29(7-153)		49(7-169)	
Children growth					
Weight					
-at 6 mths, g	7250(7000-7600)	7550(6959-8178)	0.95	8000(7250-8245)	**0.01**
-at 12 mths, g	9350(8950-9850)	9975(9360-10838)	0.09	9600(8948-10673)	0.61
-at 24 mths, g	13000(11780-13625)	11250(10775-12825)	0.16	12680(11275-13510)	0.98
Length					
-at 6 mths, cm	67(65-68)	66(65-68)	0.95	68(65-70)	0.06
-at 12 mths, cm	75(74-77)	77(74-79)	0.29	76(73-78)	0.18
-at 24 mths, cm				90(86-92)	0.15
Head circumference					
-at 6 mths, cm	43(42-44)	44(42-44)	0.61	43(42-44)	0.45
-at 12 mths, cm	46(45-47)	47(45-49)	0.31	46(45-47)	0.96
Age at seated position, mths	6(6-7)	6(6-7)	0.41	6(6-7)	0.38
Age at walking, mths	12(11-13)	13(11-15)	0.17	13(11-14)	0.32
Age at speaking (simple sentences), mths	20(15-24)	19(12-24)	0.77	24(14-24)	0.52
Reactions to vaccinations (performed according to the vaccination schedule for childhood)	1 rash post measles vaccines	1 post MPR (measles, mumps, and rubella): fever, rash and conjunctivitis		1 allergic reaction to PCV (Pneumococcal Conjugate Vaccine)	
Pathological conditions during the first year of life	1 hand foot and mouth disease 1 cardiac murmur 1 cryptorchidism surgery 1 anal fissure	1oral mucocele 1 atopic dermatitis 1 meningitis 1 pyelonephritis		1 hydrocephalus and testicular hydrocele 1 atopic dermatitis 1 inguinal hernia 1 lactose intolerance	
Pathological conditions after the first year of life	1 autism spectrum disorder	1 amblyopia		1 language disorder 1 recurrent otitis	

All data are expressed as median (IQR)

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SAT0128 A PHASE 4 TRIAL ASSESSING THE IMPACT OF RESIDUAL INFLAMMATION AND CLINICAL CHARACTERISTICS ON THE OUTCOME OF DOSE TAPERING OF ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE IN STABLE CLINICAL REMISSION

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Background: For rheumatoid arthritis (RA) pts in stable clinical remission (SCR) on bDMARDs, EULAR and ACR recommend to consider tapering

the dose of bDMARD.[1,2] However, there are limited data indicating which factors, if any, are prognostic of flares after tapering. Moreover, association between underlying inflammation and disease flare following tapering remains unclear.

Objectives: Investigate association between residual disease activity at double-blind(db) bl detected by MRI and occurrence of flares in SCR RA pts randomized to an adalimumab (ADA) dose tapering regimen controlled by ADA withdrawal (w/d).

Methods: Pts in SCR (DAS28[ESR or CRP] <2.6) for at least 6 mos and at screening (DAS28[ESR] <2.6) on ADA 40 mg eow were enrolled in this phase 4, randomized, db, parallel group study. Following 4-wksof open-label lead-in (OL-LI) during which SCR was confirmed, pts were randomized 5:1 to taper (ADA 40 mg q3w) and w/d arms for 36 wks. Pts experiencing flare (defined as either DAS28[ESR] >2.6 and DAS28 [ESR] increase >0.6 from bl or DAS28[ESR] increase ≥1.2 from bl, irrespective of absolute DAS28[ESR]) received rescue OL ADA 40 mg eow for up to 16 wks. The primary endpoint was the association between bl hand and wrist synovitis and bone marrow edema (BME) RAMRIS scores and their composite with flare occurrence. Secondary endpoints were association between pt and disease characteristics and occurrence of flare, time to and occurrence/severity of flares, maintenance of remission, and time to and regain of clinical remission following flare. Logistic regression, descriptive statistics (counts and proportions with 95% CI) and Kaplan-Meier estimates are provided. Last observation carried forward was used for missing data. Treatment-emergent adverse events were monitored.

Results: Of 146 pts who entered the OL-LI period, 122 were in SCR at wks 0 and 4 and were randomized to taper (n=102) or w/d (n=20) arm. Pts were female (75%) with ~13 yrs of active disease, received ADA for >5 yrs (~2 yrs in SCR). Bl disease activity measures were low (DAS28[ESR]: 1.7; composite synovitis and BME RAMRIS score: 4.0), and >85% pts were in CDAI and/or SDAI remission. In the taper and w/d arms, 37 (36%) and 9 (45%) pts experienced flare, respectively. Time to flare was 18.0/13.3 wks (Q1 for taper/withdrawal arm). At wks 12/24/36, flare rates were 13.1/27.4/34.9% in the taper arm and 10.0/35.0/40.0% in the w/d arm. Neither of the bl RAMRIS scores nor their composite was associated with flare occurrence in the taper arm (**Table**). Only bl HAQ-DI was associated with flare occurrence. Through 16 wks of OL rescue with ADA 40 mg eow, 38% and 50% of pts in the taper and w/d arms, respectively, regained clinical remission; approximately 85% in both arms were in clinical remission by DAS28(ESR) <2.6 at week 40. No new serious risks or safety signals were identified.

Conclusion: A relatively low flare rate was observed among this established RA population in longstanding SCR who tapered or withdrew ADA. Baseline HAQ-DI, but not MRI inflammation, was found to be associated with flare occurrence, which may be reflective of the very low bl MRI inflammation scores in this sustained remission cohort.

REFERENCES

[1] Smolen, et al. Ann Rheum Dis, 2017;76:1113-36.
[2] Singh, et al. *Arthritis Rheumatol*, 2016;68:1-26.

Baseline Parameters and Occurrence of Flare Among Subjects in the Tapering Arm

	Odds Ratio (95% CI)	*P*-value
Baseline synovitis RAMRIS score (n = 102)	0.99 (0.82, 1.20)	0.94
Baseline BME RAMRIS score (n = 102)	0.96 (0.82, 1.12)	0.59
Baseline composite synovitis and BME RAMRIS score (n = 102)	0.98 (0.89 , 1.08)	0.69
Smoking status (current vs non-current) (n=101)	2.00 (0.74, 5.39)	0.17
Baseline co-morbidities (yes vs no) (n=102)	3.96 (0.84, 18.79)	0.08
Baseline anti-citrullinated peptide antibody status (positive vs negative) (n=101)	1.06 (0.42, 2.71)	0.90
Baseline rheumatoid factor status (positive vs negative) (n=101)	1.14 (0.50, 2.58)	0.75
Baseline disease duration (years) (n = 102)	1.04 (1.00, 1.08)	0.06
Previous treatment with bdmards(excluding adalimumab) (yes vs no) (n=102)	1.41 (0.57, 3.51)	0.46
Previous treatment with csdmards and bdmards(excluding adalimumab) (yes vs no) (n=102)	1.54 (0.61, 3.87)	0.36
Baseline duration of adalimumab therapy (years)(n = 102)	1.07 (0.95, 1.21)	0.26
Baseline remission duration (years) (n=85)	1.07 (0.87, 1.32)	0.51
Baseline DAS28(ESR) (n = 102)	0.60 (0.29, 1.21)	0.15
Baseline CRP (mg/l) (n = 102)	1.01 (0.99, 1.03)	0.40
Baseline HAQ-DI (n = 102)	1.34 (1.01 , 1.77)	0.04*

bDMARDs: biological disease modifying anti-rheumatic drugs; csDMARDs: conventional synthetic disease modifying anti-rheumatic drugs; DAS28(ESR): 28-joint disease activity score based on erythrocyte sedimentation rate; CRP: C-reactive protein; HAQ-DI,: health assessment questionnaire disability index; RAMRIS: RA-MRI scoring; BME: bone marrow edema; *Statistically significant at 0.05 levels

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SAT0129

DISEASE FLARES DURING PREGNANCY IN RHEUMATOID ARTHRITIS: WHAT IS THE IMPACT OF STOPPING BDMARDS AT THE BEGINNING OF PREGNANCY?

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Background: During pregnancy, patients with rheumatoid arthritis (RA) can experience flares, which might influence pregnancy ouctomes.

Objectives: To assess disease course during pregnancy and identify possible risk factors of disease flares in RA.

Methods: Data on RA patients prospectively-followed in a pregnancy clinic were retrospectively analyzed before conception and during each trimester. Clinical characteristics, disease activity (DAS28-CRP3), medication use, and pregnancy outcomes were analyzed. Flare was defined by an increase of DAS28-CRP3 greater than 0.6.

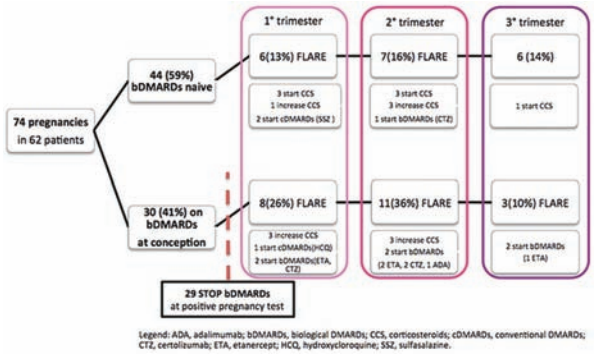
Results: Among 85 RA-pregnancies (mean age 34, SD 4,8; median disease duration 97 months, IQR 31-156) in 66 patients enrolled between 2010 and 2018, 8 pregnancies ended with early miscarriages, 1 with intrauterine fetal death and 2 were voluntary interrupted (1 for MTX exposure and 1 for encephalocele). The remaining seventy-four pregnancies in 62 patients were analyzed. Before conception, 52(71%) were in remission, 13(18%) in low disease activity and 8(11%) with moderate disease activity. Flares occurred in 29/74 (39%) patients during pregnancy (14/1° trimester,18 2° trimester,9 3° trimester). Flares occured more frequently in patients with a previous use of more than one conventional DMARDs (cDMARDs)(p 0,28) and a higher disease activity before conception (0,025) and in the 1°trimester (p 0,08). At conception, 30 (41%) patients were on biological DMARDs (bDMARDs) (16 ETA, 8 CTZ, 3 GOL, 2 ADA) and 16% with an active disease. 29 discontinued the treatment at positive pregnancy test and 8(27%) reintroduced bDMARDs because a flare during 1° (1 CTZ, 1 ETA), 2°(1 ADA, 2CTZ, 2 ETA) and 3° trimester (1 ETA) (Figure 1). 20/30(66%) experienced at least one flare during pregnancy.Forty-four (59%) patients were bDMARDs naive at conception (47% CCS, 41% HCQ, 16% SSZ, 2,3% MTX, 4,5% CyA), 6(7%) with an active disease. 16/44(36%) patients experienced at least one flare during pregnancy, 3 more than one flare (Figure 1). Seventeen live births were accompanied by complications (7 preterm deliveries, 2 very preterm deliveries, 6 premature rupture of membranes and 2 newborns small for gestational age). 60% of preterm births occurred in patients with a flare during pregnancy.

Conclusion: In a cohort of prospectively-followed RA-pregnancies 39% of patients experienced at least one flare during pregnancy. A higher frequency was observed in patients on bDMARDs at conception after stopping the drug at positive pregnancy test. This suggests that patients with a more aggressive disease, as those on bDMARDs, require continuing treatment beyond conception. Counselling of patients on preconception treat-to-target management may help to achieve lower disease activity, especially in patients with a more severe disease (active disease or previous use of more than one cDMARDs). This may result in better pregnancy outcomes.

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SAT0130 ANTI-CITRULLINATED PEPTIDE ANTI-BODIES TITERS DECREASE AFTER RITUXIMAB BUT NOT AFTER ABATACEPT OR TNF BLOCKERS TREATMENT: A REAL-LIFE ANALYSIS

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Background: There is an increasing body of evidence suggesting a direct pathophysiological role of ACPA in Rheumatoid Arthritis (RA). Therefore, on the top of clinical, biological and imaging remission, one target could be immunological remission, defined as the normalization of the ACPA titers after therapy. In this sense, data related to the capacity of different biologics to normalize ACPA are contradictory.
Objectives: To evaluate the changes in ACPA titers before and after treatment with different biologics.
Methods: RA patients treated with biologics were identified via the hospital's pharmacy and/or the Electronic Medical Record of the patients; thereafter, for each patient, ACPA titers before/after treatment were retrieved from the department of biology. To be included, patients had to be diagnosed with RA, to have received a biologic (either abatacept IV or SC, TNF-inhibitors(TNFi) (Infliximab iv and Etanercept SC), or Rituximab IV) and to have at least two dosages of ACPA (at least one before and one after biologic treatment). ACPA titers were compared before and after treatment in each of the treatment groups. A mixed model analysis including an interaction between the drug and time was also performed.
Results: Among the 328 selected RA patients 92 patients (female: 84%, mean age: 62 years) had enough biological data to be included for the analysis: 36 patients had received rituximab, 21 abatacept, 35 TNFi. Mean (Standard deviation) ACPA levels in the whole group before treatment was 924.8 (1164.6) UI/L. ACPA titers (summarized in figure 1) decreased significantly after Rituximab (from 1287 (1322) to 301(387) UI/L; p<0.005) but not after Abatacept (from 857(1166) to 1352(1241) UI/L) or TNF blockers (from 593(881) to 1116(1398) UI/L). Modelisation of ACPA titers over follow-up (mixed models) revealed a significant interaction between drug and time, suggesting a drug effect of such variation (Figure)

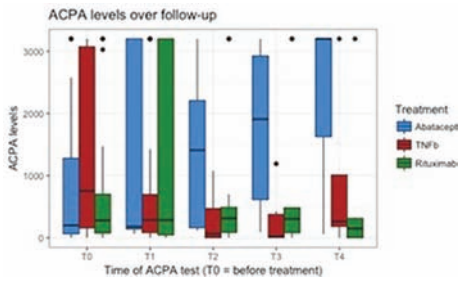


Figure 1. Changes in the ACPA titers after biologics treatment in RA where T0 = before biologic; T1 to T4 = timepoints after biologic

Conclusion: In this real-life study, ACPA titers decrease slightly only after Rituximab therapy. These data suggest that there is potentially a huge unmet need in RA if the target is to achieve an immunological remission.**Disclosure of Interests:** Stéphane Hilliquin: None declared, Loriane Gutermann: None declared, Claire Goulvestre: None declared, Jerome Avouac: None declared, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Anna Moltó: None declared
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SAT0131 SAFETY AND EFFECTIVENESS OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (BDMARDS) IN OLDER ADULTS WITH RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY

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Background: Rheumatoid arthritis is common among older adults and biological disease-modifying antirheumatic drugs (bDMARDs) are effective in treating this population. However, older patients reportedly experience more adverse events (AEs) with effectiveness being either equivalent or worse than younger patients.
Objectives: Our primary objective was to compare the AEs associated with the use of bDMARDs and their relative effectiveness in three age groups: Group 1 (75+), Group 2 (65-74 years) and Group 3 (55-64 years) patients. We explored if sex, disease activity, baseline functional impairment, and the type of bDMARDs used differed across the three age groups as a secondary objective.
Methods: A retrospective cohort study of adults 55+ with RA seen between Jan 1, 2007 and July 31, 2009 was performed utilizing the RAPPORT (Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics) database housed in Edmonton, Alberta, Canada. Baseline characteristics (age, sex, DAS28 score, HAQ score, types of bDMARDs used), drug effectiveness (based on DAS28 score) and associated AEs were compared across the three age groups. Descriptive statistics (Mean, SD, percentages) were used. An intention to treat analysis with chi-square testing for categorical variables and t testing for continuous ones were used to test for the significance of differences found.
Results: A total of 333 patients met our entry criteria (69.4% female, 30.6% male) with 52, 125 and 156 from groups 1, 2 and 3 respectively. Group 1 patients had a significantly higher mean HAQ score (2.16) compared to the younger groups (P<0.0.5), and a mean DAS28 (6.52) score significantly higher than the 55-64 group (P<0.05). Group 1 patients were also more likely to experience AEs (p<0.05), which were more likely to be infectious (p<0.05), life threatening/severe (p<0.05), cause discontinuation of treatment (p<0.05) and multiple (p<0.05) compared to the two younger groups. We also interestingly found the remission rate to be significantly higher in Group 1 patients compared to Group 2 (p<0.05). Etanercept was the most commonly used drug among all age groups. Rituximab and abatacept were much less frequently used. Rate of AEs and therapy effectiveness did not differ significantly by sex across the three age groups.
Conclusion: Older adults aged 75+ treated with bDMARDs for RA are at a significantly higher risk of AEs, which should be included in the treatment discussion. The higher remission rate in those 75+ compared to those 65-74, which has not been reported previously, warrants further study.

REFERENCES

[1] Dalal D, Duran J, Brar T, Alqadi R, Halladay C, Lakhani A, Rudolph J. Efficacy and safety of biological agents in the older rheumatoid arthritis patients compared to Young: A systematic review and meta-analysis. Seminars in Arthritis and Rheumatism. 2018 Jul 31. pii: S0049-0172(18) 30162-8 [Epub ahead of print].
[2] . Sugihara T, Harigai M. Targeting Low Disease Activity in Elderly-Onset Rheumatoid Arthritis: Current and Future Roles of Biological Disease-Modifying Antirheumatic Drugs. Drugs & Aging. 2016; 33(2): 97-107.
[3] . Filippini M, Bazzani C, Favalli E, et al. Efficacy and Safety of Anti-Tumour Necrosis Factor in Elderly Patients with Rheumatoid Arthritis: An

Observational Study. Clinical Reviews in Allergy & Immunology. 2009; 38 (2-3): 90-96.

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SAT0132 LONG-TERM SAFETY, IMMUNOGENICITY AND EFFICACY IN RANDOMIZED, DOUBLE-BLIND, AND OPEN-LABEL EXTENSION STUDIES COMPARING FKB327, AN ADALIMUMAB BIOSIMILAR, WITH THE ADALIMUMAB REFERENCE PRODUCT IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: FKB327 is a biosimilar of adalimumab reference product (RP). Studies with adalimumab biosimilars have shown no increase in safety signals or immunogenicity versus RPs studied at 52 weeks.
Objectives: To study the long-term safety, immunogenicity and efficacy of FKB327 compared with Adalimumab RP in a randomized double blind (DB) phase 3 study in patients (pts) with active rheumatoid arthritis (RA) inadequately controlled with methotrexate (MTX) and in a subsequent randomized, open-label extension (OLE) study with treatment switching assessed long-term safety, efficacy, PK, and immunogenicity.
Methods: Pts aged ≥18 years with moderate-to-severe, active RA (2010 ACR/EULAR criteria) for ≥3 months and receiving a stable dose of MTX were randomized 1:1 to FKB327 or RP (40 mg subcutaneously [SQ]) every other week with MTX. In the OLE study, pts who completed the DB study with clinical response and no serious adverse events (AEs) were rerandomized in a 2:1 ratio to FKB327 or RP. All pts received FKB327 through week 76 (Period 2). The primary end point was safety; the secondary end point was efficacy. Pooled data for up to 2 years were analyzed to assess long-term safety. Incidence rates of treatment-emergent AEs were adjusted by overall exposure to enable safety comparison of FKB327 and RP.
Results: Of 728 pts in the DB study, 645 were enrolled in the OLE; of those, 572 and 515 pts completed periods 1 and 2, respectively. Safety results from the pooled data were comparable between treatment sequences. Mean serum drug concentrations appeared to be in steady–state in all treatment sequences in Period 1 and comparable among sequences in Period 2. The proportion of pts with positive antidrug antibody (ADA) status in Period 1 was comparable between treatment sequences, and the majority of patients with positive ADA status had neutralizing activity. The mean proportion of patients achieving an ACR20 response remained stable between studies and was similar for all treatment sequences.

Table. Summary of Efficacy & Safety End Points at Week 30 (Period 2): Full Analysis Set

	F-F-F N = 216	F-H-F N = 108	H-F-F N = 108	H-H-F N=213
ACR20 response rate				
n	185	98	92	189
Responders, n (%)	154 (83.2)	82 (83.7)	79 (85.9)	158 (83.6)
95% CI	77.1-88.3	74.8-90.4	77.0-92.3	77.5, 88.6
ACR50 response rate				
n	185	98	92	189
Responders (%)	112 (60.5)	57 (58.2)	50 (54.3)	113 (59.8)
95% CI	53.1-67.6	47.8-68.1	43.6-64.8	52.4, 66.8
DAS28-CRP response rate				
n	183	99	92	189
Mean (SD)	3.04 (1.237)	3.28 (1.385)	3.20 (1.247)	3.13 (1.239)
Range	1.2-7.1	1.2-7.1	1.3-6.3	1.2, 7.4
ADA status				
Total	187	100	93	190
Positive	97 (51.9)	61 (61.0)	42 (45.2)	98 (51.6)

ACR indicates American College of Rheumatology; ADA, antidrug antibody; CI, confidence interval; DAS28, Disease Activity Score-28 with C-reactive protein; F, FKB327; H, adalimumab; SD, standard deviation.

Conclusion: The safety, immunogenicity, and efficacy of FKB327 were maintained over long-term treatment and after switching between the biosimilar and RP.
Disclosure of Interests: Rieke Alten Grant/research support from: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, Mark C. Genovese Grant/research support from: Sanofi/Genzyme, Genentech/Roche, RPharm, Consultant for: Sanofi/Genzyme, Genentech/Roche, RPharm, Yasumasa Arai Employee of: I am an employee of Fujifilm Kyowa Kirin Biologics., Rafael Muniz Shareholder of: Employee of Mylan, Consultant for: Employee of Mylan, Employee of: Employee of Mylan, Herbert Kellner Grant/research support from: Roche, Consultant for: Roche

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SAT0133 TREATMENT PATTERNS, PERSISTENCE, AND DURABILITY IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (BDMARDS)

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Background: EULAR and ACR recommend bDMARDs, as monotherapy or in combination with methotrexate, in patients whose rheumatoid arthritis (RA) remains active despite methotrexate use.[1] Treatment options for bDMARD inadequate response (IR) patients vary. Understanding the real-world treatment patterns and treatment duration in bDMARD IR patients may help identify the most suitable next treatment.
Objectives: We studied treatment patterns, treatment persistence, and treatment durability in bDMARD IR patients who switched to another treatment regimen.
Methods: In US health plan claims data, this study selected adult RA bDMARD patients: those with ≥2 RA diagnoses ≥30 days apart, who newly initiated a bDMARD (1/1/2012 - 3/31/2017; baseline) and then switched to another bDMARD or JAKi (index date, ID). All patients had continuous ≥1-year enrollment before and after ID. Patient characteristics were evaluated at baseline; treatment patterns, persistence, and durability (duration) were evaluated during pre- and post-index periods. Kaplan-Meier curves were used to evaluate treatment persistence.
Results: Among 105,039 patients who were initiated on bDMARDs, 19,085 (18%) demonstrated IR; among those, 4,656 met all the selection criteria: median age 54 years, 22% male, 17% from Northeast, 26% Midwest, 42% South, 15% West.
At baseline, 26% used tumor necrosis factor inhibitors (TNFi) monotherapy and 64% used TNFi in combination with conventional synthetic DMARD (csDMARD). Baseline median treatment duration was 8.3 months overall, including 5.8 months for monotherapy and 9.4 months for combination therapy.
Upon switch, 46% of patients used monotherapy (28% TNFi, 11% other bDMARD, 7% janus kinase inhibitors [JAKi]), and 54% used bDMARD in combination with csDMARD (37% TNFi + csDMARD, 12% other bDMARD

Table. Post-switch treatment patterns, duration, and 12-month persistence.

	Patient allocation	Median treatment duration (months)	12-month persistence
All patients (N=4,656)	100%	9.5	48%
Index monotherapy (N=2,149)*	46%	5.8	33%
TNFi (N=1,305)**	28%	5.1	31%
other bDMARDs (N=521)**	11%	6.9	35%
JAKi (N=323)**	7%	6.7	41%
Index combination therapy (N=2,507)*	54%	13.1	60%
csDMARD + TNFi (N=1,740)***	37%	12.3	57%
csDMARD + other bDMARDs (N=569)***	12%	15.1	69%
csDMARD + JAKi (N=198)***	4%	14.3	67%

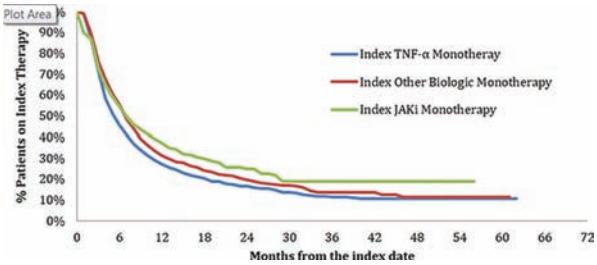
* P<0.0001 (treatment duration); P<0.0001 (persistence);
** P=0.0840 (treatment duration); P=0.0022 (persistence);
*** P=0.1582 (treatment duration); P=0.0615 (persistence).

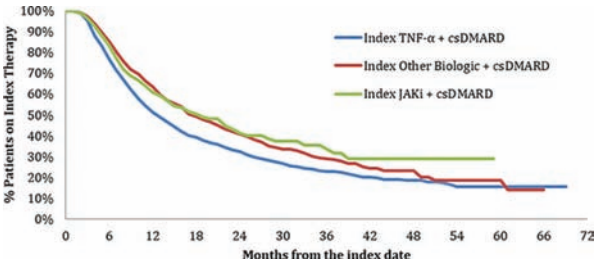
+ csDMARD, 4% JAKi + csDMARD). Median treatment duration was longer for combination therapy than monotherapy (13.1 vs. 5.8 months, p<0.001). TNFi showed a trend towards shortest treatment duration and lowest 12-month treatment persistence among monotherapies and combination therapies. (Table) JAKi showed best treatment persistence among monotherapies (Figure 1; p-value=0.0004) and combination therapies (Figures 2; p-value<0.0001).

Conclusion: In biologic DMARD IR patients, the first bDMARD treatment lasted, on average, for 8.3 months before switch. Post-switch, TNFi showed a trend towards the shortest durability and JAKi showed the longest durability. The data suggest substantial unmet need in bDMARD patients. A well-tolerated effective therapy, with potent clinical efficacy and improved treatment durability may benefit this patient population.

REFERENCE

[1] Singh J.A., et al. Arthritis & Rheumatology. 2016; 68(1):1-26.





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SAT0134

COMPARING REAL-WORLD RETENTION RATES IN A MATCHED COHORT OF RHEUMATOID ARTHRITIS PATIENTS WHO EITHER REMAINED ON THE ETANERCEPT ORIGINATOR OR SWITCHED TO A BIOSIMILAR

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Background: In Germany, the first etanercept biosimilar was licensed in 2016. In contrast to other European countries there is no uniform recommendation for the prescription of biosimilars.

Objectives: To compare treatment survival between patients who were switched from the etanercept originator to the etanercept biosimilar SB4 and patients who stayed on the originator treatment.

Methods: We used data of rheumatoid arthritis patients observed in the prospective, longitudinal RABBIT (***R***heumatoid ***A***rthritis: O***b***servation of ***bi***ologic ***t***herapy) cohort until November 2018 who were treated with the etanercept originator (oETA) for at least six months. Patients who thereafter were switched to the biosimilar SB4 (bsETA) were matched (1:n) to patients who stayed on the original treatment using prescription time distribution matching [1] to control for survival bias. Matching criteria were sex, time of switch or corresponding duration of originator treatment in non-switchers and age as well as DAS28 at the time of switching or corresponding time point in non-switchers. The retention rates over one year were analyzed using Kaplan-Meier curves.

Results: Overall, 1,751 patients fulfilled the inclusion criteria of whom 113 were switched to bsETA. Of these, 102 switchers could be matched to 598 patients who remained on oETA. In both groups, 78% of the patients were female, mean age was about 59 years, DAS28 was 3.2 and physical function as well as numbers of prior biologics were similar. Patients who remained on oETA were more often rheumatoid factor positive (71% vs. 63%), had more erosions (56% vs. 47%) and had more frequently three or more comorbidities (34% vs. 28%) than those who were switched to bsETA. The most common reason for switching was costs (79%). After one year, 35% of the patients in both groups had stopped the respective treatment (oETA, n=210, bsETA, n=36). The main reasons for withdrawal were loss of efficacy (oETA: 57%, bsETA: 36%) and adverse events (oETA: 20%, bsETA: 42%). In both groups about the same portion of the adverse events that led to treatment discontinuation were serious events (24% vs. 27%). Kaplan-Meier curves showed similar retention rates over 12 months for bsETA and oETA (figure). Nine bsETA patients were switched back to oETA.

Conclusion: Retention rates of etanercept treated RA patients who were either switched to the biosimilar SB4 or who stayed on the originator are comparable. Only few patients switched back to the originator.

REFERENCE

[1] Zhou Z, Rahme E, Abrahamowicz M, Pilote L. Survival bias associated with time-to-treatment initiation in drug effectiveness evaluation: a comparison of methods. Am J Epidemiol. 2005 Nov 15; 162(10):1016-1023.

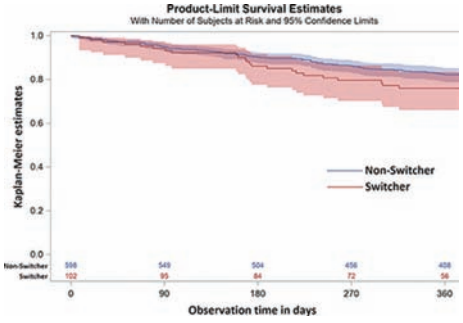


Figure. Treatment continuation in etanercept patients who were either switched to the biosimilar SB4 or stayed on the originator.

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SAT0135

MAINTAINING REMISSION IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS WHILE TAPERING ETANERCEPT: AN INSIGHT IN THE TAPERA TRIAL

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Background: EULAR 2016 recommendations for the management of Rheumatoid Arthritis (RA) suggest to consider tapering of biological Disease-Modifying Antirheumatic Drugs (bDMARDs) in patients in sustained remission. More insight on the effect of tapering strategies is needed in daily practice.

Objectives: To investigate maintaining disease control after spacing dosages of etanercept 50mg from weekly to every other week (EOW) in a pragmatic randomized controlled trial (RCT).

Methods: Patients with RA who were in remission according to the disease activity score 28 (DAS28) remission criteria for at least 6 months and treated with etanercept 50mg weekly for at least a year were included in the one-year non-blinded multicentre TapERA (Tapering Etanercept in RA) RCT (EudraCTnumber 2012-004631-22). Patients were 1:1 randomly assigned to continue etanercept 50mg weekly or to taper to 50mg EOW. Patients who lost remission (DAS28 C-Reactive Protein (CRP) $\geq$ 2.6) received nonsteroidal anti-inflammatory drugs and if needed were re-escalated to etanercept weekly. If remission was still not reached, treatment had to be adapted, at the discretion of the treating rheumatologist. The outcomes were proportion of patients in DAS28 remission at 6 and 12 months, proportion in sustained remission and proportion regaining remission after reintroducing weekly etanercept (intention to treat analysis). Missing components of DAS28 were imputed using expectation maximization.

Results: In total, 69 patients (69.6% female) with a mean ± standard deviation (SD) age of 55.7 ± 11.3 years and a mean ± SD disease duration of 14.7 ± 8.0 years were included. The weekly and EOW group consisted of 35 and 34 patients respectively. At the month 6 visit 77.1% patients of the weekly and 76.5% of the EOW group were in remission (p=0.947) and 68.6% and 58.8% respectively maintained remission on every visit (p=0.400) (Table 1).

Three (8.6%) patients of the weekly and 11 (32.4%) of the EOW group required a treatment adaptation, which was statistically significantly different (p=0.014). There was no difference between the weekly and EOW group in the mean ± SD DAS28 CRP at the first time of losing remission in patients flaring, namely 3.1 ± 0.6 and 3.1 ± 0.5 respectively (p=0.957).

Eleven patients were re-escalated to a weekly treatment after a mean ± SD duration of 4.5 ± 3.1 months. Of these, 54.5% (6/11) regained remission after a mean ± SD duration of 4.7 ± 1.7 months. Of the 5 patients not regaining remission, 1 switched to a weekly regimen on the last trial visit, 1 required switching to another bDMARD and 3 patients had no additional treatment changes (mean ± SD DAS28 CRP at month 12: 3.4 ± 0.2). Two patients of the EOW group restarted weekly etanercept while still being in remission.

Table 1: Proportion of patients of the weekly and EOW group in remission and LDA

	Weekly group (n=35)	EOW group (n=34)	p-value
Remission at M6 n(%)	27 (77.1)	26 (76.5)	0.947
LDA at M6 n(%)	29 (82.9)	30 (88.2)	0.526
Sustained remission M6 n(%)	24 (68.6)	20 (58.8)	0.400
Sustained LDA M6 n(%)	29 (82.9)	26 (76.5)	0.510
Remission at M12 n(%)	30 (85.7)	24 (70.6)	0.128
LDA at M12 n(%)	33 (94.3)	28 (82.4)	0.122
Sustained remission M12 n(%)	21 (60.0)	15 (44.1)	0.187
Sustained LDA M12 n(%)	25 (71.4)	24 (70.6)	0.939
Patients with treatment adaptation due to efficacy loss n(%)	3 (8.6)	11 (32.4)	0.014

Treatment adaptation is defined in the weekly and EOW group as intensifying DMARD therapy and re-escalation to weekly respectively; EOW *every other week*, M *month*, LDA *low disease activity (DAS28 CRP ≤ 3.2)*

Conclusion: Approximately half of the EOW group was in sustained remission after 1 year and two thirds remained on their reassigned treatment. Furthermore, one in two patients were able to regain remission after reintroducing etanercept weekly. Therefore tapering of etanercept to EOW seems a feasible strategy in patients with RA in sustained remission, potentially leading to a beneficial cost-saving and safety profile.

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SAT0136

CONSISTENCY WITH INTERNATIONAL GUIDELINES REGARDING MOTHERS WITH RHEUMATOLOGIC DISEASES EXPOSED TO TUMOUR NECROSIS FACTOR INHIBITORS (TNFI) DURING THE ANTE- AND POSTNATAL PERIODS AND CHANGE OVER TIME

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Background: Many women with rheumatologic diseases require ongoing treatment with TNFi during pregnancy to maintain remission or low disease activity. Until recently, there has been a paucity of published evidence regarding the safe use of these medications during the ante- and postnatal periods to guide clinical practice.

Objectives: To observe compliance with current guidelines for TNFi therapy in Australian women with rheumatologic diseases during the ante- and postnatal periods and change over time.

Methods: All Australian women with rheumatologic diseases, exposed to biologics (bDMARDs) and targeted synthetic disease modifying antirheumatic drugs (tsDMARDs) during the preconception, antenatal and/or postpartum periods were eligible to participate in the Pregnancy Exposed to Biological (PEB) study. Commencing in 2015, recruitment was via invitation from patient's treating rheumatologists, community groups, and social media. Following self-referral to the study, retrospective data was collected, including rheumatologic condition and management recommendations made by health professionals.

Results: Preliminary data is available for 37 infants born to 29 mothers from Feb 2009-Dec 2018. Of these, 32 women received TNFi. We assessed 3 outcomes – TNFi continuation during pregnancy, TNFi continuation during lactation and vaccination practice in infants exposed to TNFi. Women exposed to non-TNFi bDMARDs and tsDMARDs were excluded from this abstract, as these are not recommended for use during the perinatal period (2).

Specialist Society Guidelines from the British Society of Rheumatology and the British Health Professional in Rheumatology were published in 2016 regarding the safety of TNFi during pregnancy (2). Prior to guideline publication, 67% (n=16/24) of the women in PEB ceased their TNFi pre-conception. Of those in PEB who became pregnant subsequent to guideline publication, only 25% (n=2/8) ceased TNFi pre-conception. Overall, 40.6% (n=13/32) women received a TNFi during the antenatal period consistent with guidelines, which improved from 33.3% (n=8/24) pre-publication, to 62.5% (n=5/8) post publication.

84.4% (n=27/32) women exposed to TNFi breastfed their infants. Prior to availability of evidence regarding the safety of TNFi during lactation, 79.2% (n=19/24) of infants were breastfed. After publication, 100% (n=8/8) infants exposed to TNFi were breastfed.

In total, 96.9% (n=31/32) of the infants exposed to TNFi in PEB were vaccinated. Rotavirus vaccine should have been delayed in 43.8% (n=14/32) infants, but was not. 9.4% (n=3/32) infants had live vaccines deferred until only 3 months; 3.1% (n=1/32) infants had live vaccines unnecessarily delayed. Only 3.1% (n=1/32) infants had live vaccines appropriately delayed until 7 months. Compliance with vaccination recommendations increased from 43.5% (n=10/24) pre-publication to 62.5% (n=5/8) post publication of guidelines.

Conclusion: Preliminary data from PEB suggests that there has been a shift in practice following the publication of Specialist Society Guidelines, with increasing numbers of women continuing TNFi therapy during pregnancy and the postpartum period, in keeping with current evidence. Compliance with vaccination recommendations could be improved to be more consistent with published international guidelines.

REFERENCE

[1] Flint J, et al. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding-Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford). 2016;55 (9):1693-7.

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SAT0137

PATIENTS (PTS) SWITCHED TO SARILUMAB FROM ADALIMUMAB ACHIEVE CLINICALLY IMPORTANT IMPROVEMENTS IN RA DISEASE ACTIVITY: RESULTS FROM MONARCH TRIAL OPEN-LABEL EXTENSION (OLE)

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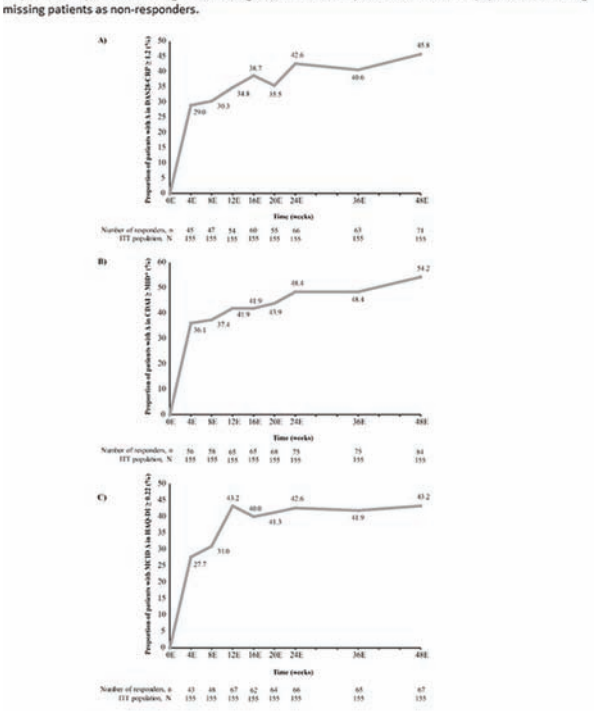
Background: In MONARCH (NCT02332590), sarilumab monotherapy (200 mg subcutaneously [SC] every 2 weeks [q2w]) demonstrated superiority to adalimumab monotherapy (40 mg SC q2w) in DAS28-ESR, ACR20/50/70 response, HAQ-DI, and CDAI in pts with RA and inadequate response/intolerance to methotrexate.

Objectives: To assess long-term safety/efficacy in RA pts continuing sarilumab or switching from adalimumab to sarilumab monotherapy in the ongoing OLE of MONARCH.

Methods: Pts completing MONARCH were eligible for the OLE, in which they received sarilumab 200 mg SC q2w. Efficacy and safety data were reported up to OLE Wk 48 and March 2017, respectively. Responder rates were based on the intent-to-treat population. Continuous efficacy endpoints were based on the observed population.

Results: Of 369 pts enrolled in MONARCH, 320 (87%) entered OLE (switch: n=155; continuation: n=165). By safety data cut-off, pt attrition was similar in switch (24; 15.5%) and continuation groups (22; 13.3%), as were treatment-emergent adverse events (AEs) (switch: 76.1%, 267.4/100 PY; continuation: 70.9%, 230.2/100 PY) and infections (switch: 41.9%; continuation: 35.8%). For DAS28-ESR and CDAI endpoints, >40% of switch pts achieved a minimally important difference (MID) improvement from OLE baseline by OLE Wk 12, increasing to >50% by OLE Wk 48. Additionally, >40% of switch pts achieved a MID in DAS28-CRP and a minimally clinically important difference (MCID) in HAQ-DI from OLE baseline to OLE Wk 48 (Fig). Of pts achieving CDAI ≤10 from baseline OLE to Wk 24 of the OLE, 70.7% (switch group) and 83.5% (continuation group) achieved sustained response at OLE Wks 36 and 48. In the randomized controlled phase, response rates were higher in sarilumab-treated than adalimumab-treated pts, hence fewer pts in the continuation group achieved additional MID during OLE (data not shown). AEs of special interest are reported (Table). Two deaths occurred in the switch group (malignancy; cerebrovascular accident) versus one in the continuation group (subarachnoid hemorrhage). No GI-related AEs (ulcerations/perforations/diverticulitis) were observed.

Figure. Proportions of switch patients (A) achieving MID in DAS28-CRP (≥1.2 change from OLE entry), (B) reporting improvements from OLE entry ≥MID in CDAI,* and (C) reporting improvements from OLE entry ≥MCID in HAQ-DI.
Proportions of patients meeting or exceeding these levels are reported for the full ITT population, counting missing patients as non-responders.



Baseline = Week 0E; Week numbers with E afterwards refer to the number of weeks since entry into the OLE.
*For CDAI, the definitions of MID were: MID=12 if baseline CDAI >22; MID=6 if baseline CDAI=10–22; MID=1 if baseline CDAI <10.

Table. AEs of special interest

	ADA/SAR (N=155) n (%)	SAR/SAR (N=165) n (%)	ADA/SAR (PY=165.7) n_E (n_E/100 PY)	SAR/SAR (PY=182.4) n_E (n_E/100 PY)
Infections	65 (41.9)	59 (35.8)	110 (66.4)	97 (53.2)
Serious infections	3 (1.9)	0	3 (1.8)	0
Opportunistic infections	3 (1.9)	1 (0.6)	3 (1.8)	1 (0.5)
Tuberculosis	1 (0.6)	0	1 (0.6)	0
Leukopenia	21 (13.5)	22 (13.3)	46 (27.8)	56 (30.7)
Thrombocytopenia	3 (1.9)	1 (0.6)	5 (3.0)	1 (0.5)
Hepatic disorders	10 (6.5)	13 (7.9)	15 (9.1)	20 (11.0)
GI ulcerations/diverticulitis/potential GI perforations	0	0	0	0
Elevation in lipids	4 (2.6)	6 (3.6)	4 (2.4)	7 (3.8)
Hypersensitivity	8 (5.2)	7 (4.2)	16 (9.7)	8 (4.4)
Anaphylaxis	0	0	0	0
Injection-site reactions	14 (9.0)	17 (10.3)	66 (39.8)	101 (55.4)
Malignancy	3 (1.9)	0	4 (2.4)	0
Lupus-like syndrome	0	0	0	0
Demyelinating disorders	0	0	0	0

n_E, number of events; PY, patient-years; ADA, adalimumab; SAR, sarilumab

Conclusion: Pts switched from adalimumab to sarilumab experienced clinically meaningful improvements in signs and symptoms of RA. Safety observations in OLE were generally consistent with those in MONARCH.

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SAT0138

PREDICTORS OF CLINICAL EFFICACY OF ABATACEPT IN RHEUMATOID ARTHRITIS: DATA FROM A LARGE OBSERVATIONAL STUDY

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Background: Abatacept (ABA) is a biologic DMARD (bDMARD) used to treat rheumatoid arthritis (RA) since 2006. There are limited data on real life efficacy of ABA, and on predictors for ABA treatment response.
Objectives: Objectives: To compare the effectiveness of ABA in the treatment of RA between bionaïve patients and patients with previous bDMARDs and to investigate predictors of clinical response to ABA.
Methods: In an observational cohort study, based on data from a large national quality register database, patients with RA diagnosis who initiated treatment with ABA between April 2006 and November 2017 were included. LUNDEX corrected response was defined as the fractions remaining on the drug and achieving the outcome among all who initiated treatment (1). Clinical response at 6 and 12 months was evaluated by means of LUNDEX corrected EULAR (L-EULAR) Good Response and LUNDEX corrected HAQ response (change of $\geq$0.3 from baseline) (L-HAQ). Predictors for clinical response were investigated using logistic regression, with significance based backwards selection of variables for the final multivariate model. The study was supported by an unrestricted grant from Bristol Myers-Squibb.
Results: 2716 RA patients were included in the study. More patients in the bionaïve population achieved L-EULAR Good Response and L-HAQ response at 6 and 12 months than bDMARDs experienced patients (Fig. 1a and 1b). Male sex, no previous bDMARD exposure and a low HAQ score were independent predictors of L-EULAR Good Response at 6 and 12 months (Table 1). Lack of previous bDMARD exposure also predicted L-HAQ response at 6 and 12 months. There was a positive associations between baseline HAQ and L-HAQ response at 6 months (multivariate adjusted odds ratio 1.73; 95% CI 1.46-2.05).
Conclusion: In patients with RA, response rates for treatment with abatacept were substantially higher in bionaïve patients than in those with previous bDMARD experience. Male sex also predicted LUNDEX corrected EULAR good response to abatacept. Patients with extensive disability, measured by HAQ, were less likely to remain on treatment and achieve a EULAR Good Response, but more likely to have significant HAQ improvement.

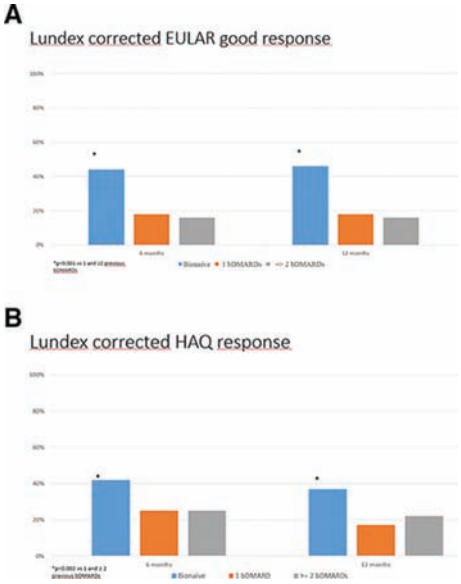
REFERENCE

[1] Kristensen, et al. Arthritis Rheum. 2006;54(2):600-6.

Table 1. Significant predictors of Lundex EULAR good response. Bivariate and adjusted analysis. Odds ratios (95% CI).

	6 months		12 months	
Predictors	Bivariate	Multivariate	Bivariate	Multivariate
Male sex	2.11 (1.41-3.13)	2.28 (1.45-3.57)	2.46 (1.71-3.54)	2.14 (1.44-3.19)
Bionaive (Reference: $\geq$2 bDMARDs)	4.00 (2.60-6.15)	3.59 (2.25-5.72)	4.45 (2.95-6.71)	4.29 (2.77-6.65)
Current Methotrexate	*	**	1.46 (1.04-2.06)	**
HAQ score (per SD)	0.64 (0.52-0.77)	0.75 (0.61-0.93)	0.65 (0.54-0.78)	0.74 (0.61-0.90)
Disease duration (per SD)	0.79 (0.65-0.96)	**	0.72 (0.59-0.87)	**
Age (per SD)	0.76 (0.65-0.91)	0.79 (0.65-0.96)	*	**
Current Glucocorticoids	0.59 (0.42-0.83)	0.59 (0.40-0.86)	*	**
Intravenous ABA (Reference: Subcutaneous)	0.53 (0.38-0.75)	**	0.70 (0.51-0.98)	**

*= not significant for this outcome
**= not included in the final model.



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SAT0139

A MULTICENTRE, RANDOMISED, DOUBLE-BLIND, PARALLEL ACTIVE-CONTROLLED CLINICAL TRIAL COMPARING PHARMACOKINETICS, PHARMACODYNAMICS, SAFETY AND EXPLORATORY EFFICACY BETWEEN HLX01 AND EUROPE-SOURCED RITUXIMAB AS A NEW INDICATION IN CHINESE MODERATE TO SEVERE PATIENTS WITH RHEUMATOID ARTHRITIS

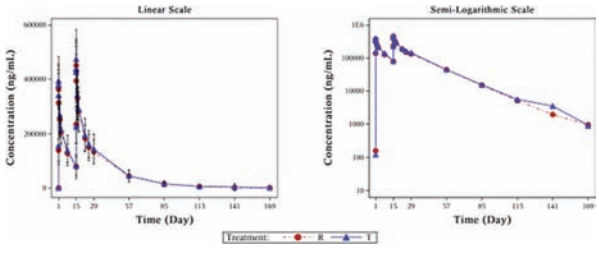
Xiaofeng Zeng[1], Yongfu Wang[2], Zhenyu Jiang[3], Zhuoli Zhang[4], Lan He[5], Xiao Zhang[6], Xin Lu[7], Xiumei Liu[8], Jian Xu[9], Cibo Huang[10], Rui Liu[11], Xiaoxia Zuo[12], Baozeng Zhao[13], Wenting Qiu[13], Katherine Chai[13], Xinjun Guo[13], Xin Zhang[13], Eugene Liu[13], Alvin Luk[13], Weidong Jiang[13], Scott Liu[13], Pei Hu[1], Xia Chen[14]. [1]*Peking Union Medical College Hospital, Beijing, China*; [2]*The First Affiliated Hospital of BaoTou Medical College, Inner Mongolia University of Science and Technology, Baotou, China*; [3]*The First Hospital of Jilin University, Changchun, China*; [4]*Peking University First Hospital, Beijing, China*; [5]*The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China*; [6]*Guandong Provincial People's Hospital, Guangzhou, China*; [7]*China-Japan Friendship Hospital, Beijing, China*; [8]*The First Hospital of Shanxi Medical University, Taiyuan, China*; [9]*The First Affiliated Hospital of Kunming Medical University, Kunming, China*; [10]*Beijing Hospital, Beijing, China*; [11]*Peking University Third Hospital, Beijing, China*; [12]*Xiangya Hospital Central South University, Changsha, China*; [13]*Shanghai Henlius Biotech Inc., Shanghai, China*; [14]*Beijing Tian Tan hospital, Capital Medical University, Beijing, China*

Background: Biologic products, such as rituximab and adalimumab, have revolutionized the treatment for chronic inflammatory disorders, providing an option to patients who were non-responsive to conventional systemic therapies. In China, rituximab is only approved for the treatment of certain haematologic malignancies. At present, there are several approved biosimilar drugs in Europe but none in China. HLX01, a China-manufactured proposed rituximab biosimilar, was first developed for patients with non-Hodgkin's lymphoma later as a new drug for the treatment for autoimmune diseases. Currently, HLX01's biosimilar NDA for the treatment of non-Hodgkin's lymphoma is being reviewed by authorities in China.

Objectives: Evaluation of clinical PK, safety and exploratory efficacy in RA patients to support the development of HLX01 for the treatment of autoimmune disease

Methods: We conducted a multi-centre, randomised, double-blind, parallel active-controlled clinical trial to compare the PK, PD safety and exploratory efficacy (ACR20 and DAS28-CRP) between HLX01 and Europe sourced rituximab (EU-RTX) as two-1000 mg intravenous infusions (Days 1 and 15) in moderately to severely active RA patients who have had inadequate response to treatment with disease-modifying antirheumatic drugs (DMARDs). The PK equivalence was achieved if 90% confidence intervals (CIs) for the test-to-reference ratios of area under the curve from time zero to infinity ($AUC_{(0\text{-}inf)}$) and maximum observed concentration (C_{max}) fall within the pre-defined 80-125% equivalence margin.

Results: In the study, a total of 196 patients randomised at 1:1 ratio to HLX01 and EU-RTX and 179 subjects (88 in HLX01 group; 91 subjects in EU-RTX group) were included in the PK pre-protocol set (PPS). The 90% confidence intervals (CI) for the ratio of geometric means for the pairwise comparisons of the primary PK endpoint $AUC_{(0\text{-}inf)}$ (Figure 1), as well as $AUC_{(0\text{-}14d)}$, $AUC_{(0\text{-}t,1)}$, $AUC_{(15d\text{-}t)}$, $C_{max,1}$, $C_{max,2}$, C_{min} were within the pre-specified limits of 80-125% (Table 1). Based on the ACR20 and DAS28-CRP results at week 24, HLX01 group and EU-RTX group are similar. In addition to the efficacy similarity, there was also no statistical difference in safety and immunogenicity between the two treatment groups.



PK parameters (Unit)	Geometric mean and its ratio					90%CI (%)	Inter-individual variation (%)	Power (%)
	n	HLX01 (T)	n	MabThera (R)	Ratio (%)			
Primary PK variables								
$AUC_{(0\text{-}inf)}$ (μg*h/mL)	88	200753.720	91	192435.090	104.32	96.49, 112.80	32.39	98.49
Secondary PK variables								
$C_{max,1}$ (μg/mL)	88	404.81	91	388.18	104.28	99.54, 109.25	18.99	>99.9
$C_{max,2}$ (μg/mL)	88	480.35	91	464.57	103.40	98.33, 108.72	20.52	>99.9
C_{min} (μg/mL)	88	75.09	91	71.38	105.20	95.09, 116.38	42.62	87.62
$AUC_{(0\text{-}14d)}$ # (μg*h/mL)	87	50488.920	91	48072.250	105.03	99.60, 110.75	21.64	>99.9
$AUC_{(0\text{-}t,1)}$ (μg*h/mL)	88	50722.070	91	48223.080	105.18	99.74, 110.92	21.75	>99.9
$AUC_{(15d\text{-}t)}$ (μg*h/mL)	88	146631.600	91	141854.640	103.37	93.52, 114.25	42.23	92.56

Note: T=1000 mg HLX01 (Shanghai Henlius Biotech, Inc.); R=1000 mg MabThera (Roche Pharma (Schweiz) Ltd.); #Parameter $AUC_{(0\text{-}14d)}$ of subjects 017022 in study drug group could not be calculated, thus a total of 87 subjects in HLX01 group were included in the statistical analysis of this parameter .

Conclusion: We report successful demonstration of similarity in PK, safety and initial efficacy between first China-manufactured biosimilar of rituximab, HLX01, and Europe-sourced rituximab in patients with moderately to severely active rheumatoid arthritis. These results support the Phase 3 confirmatory clinical trial for the development of HLX01 for the treatment of rheumatoid arthritis.

Disclosure of Interests: Xiaofeng Zeng: None declared, Yongfu Wang: None declared, Zhenyu Jiang: None declared, Zhuoli Zhang: None declared, Lan He: None declared, Xiao Zhang: None declared, Xin Lu: None declared, Xiumei Liu: None declared, Jian Xu: None declared, Cibo Huang: None declared, Rui Liu: None declared, Xiaoxia Zuo: None declared, Baozeng Zhao Employee of: Employee of Shanghai Henlius Biotech Inc., Wenting Qiu Employee of: Employee of Shanghai Henlius Biotech Inc., Katherine Chai Employee of: I am an employee of Shanghai Henlius, Xinjun Guo Employee of: Employee of Shanghai Henlius Biotech Inc., Xin Zhang Employee of: I am an employee of Shanghai Henlius Biotech,Inc., Eugene Liu Employee of: I am an employee of Shanghai Henlius Biotech,Inc., Alvin Luk Employee of: I am an employee of Shanghai Henlius Biotech,Inc., Weidong Jiang Shareholder of: I am the co-founder of Shanghai Henlius Biotech,Inc., Employee of: I am an employee of Shanghai Henlius Biotech,Inc., Scott Liu Shareholder of: I am the CEO of Shanghai Henlius Biotech,Inc., Employee of: I am an employee of Shanghai Henlius Biotech,Inc., Pei Hu: None declared, Xia Chen: None declared

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SAT0140

COMPARATIVE EFFECTIVENESS OF TOFACITINIB AND NON-TNF AGENTS SINCE 2014. IMPACT OF COMBINATION WITH METHOTREXATE

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Background: Tofacitinib (TOFA), a targeted synthetic DMARD, has been approved for the treatment of rheumatoid arthritis (RA) in Canada since April 2014. This oral agent preferentially inhibits signalling by cytokine receptors associated with JAK1 and JAK3 subunits. It is now indicated for the treatment of psoriatic arthritis (PsA) and ulcerative colitis (UC) since October 2018. Clinical experience with this molecule has been increasing, and questions relating to its efficacy and long-term safety are of interest. Data collection through RHUMADATA®, a Quebec based clinical database and registry, allows comparison of various advanced treatment options including TOFA and non-TNFi biologic agents (i.e., agents with other modes of action - OMA) such as fusion proteins (abatacept), and IL-6 (sarilumab, tocilizumab) and CD20 inhibitors (rituximab).

Objectives: This analysis compares TOFA and OMAs used with and without methotrexate (MTX).

Methods: Data collected since January 1, 2014 (since TOFA became available in Canada) at the *Institut de Recherche en Rhumatologie de Montréal* (IRRM) and the *Centre de l'Ostéoporose et de Rhumatologie de Québec* (CORQ) was extracted from the Rhumadata® on January 7,

2019. The selected patients had initiated therapy with either TOFA or OMA (either without or in combination with MTX). The collected data include baseline characteristics (socio-demographic variables, concomitant and past medication, comorbidities and the Charlson comorbidity index (CCI)), variables measured over time (laboratory test results, patient and physician-reported outcomes, and disease activity measures such as CDAI and DAS28(4)-ESR) and persistence data (treatment duration, reason for cessation). The groups were compared to identify potential confounder, and persistence data were analyzed using Kaplan-Meier and proportional hazard methods.

Results: A total of 483 patients were initiated on TOFA (n=162) or an OMA (n=321) since January 1, 2014. Of those, 57% (n=92) and 59% (n=191) were treated with MTX in the TOFA and OMA group respectively. These represent the first treatment following csDMARD inadequate response for 33%(TOFA) and 29%(OMA) of these patients. These patients had a mean disease duration of 12.1 (standard deviation=11.0) and 11.1 (10.3) years. In the TOFA group, 84% were women, 15% were smokers, and the mean age at treatment initiation was 57.7 (11.5). In the OMA group, 75% were women, 18% were smokers, and the mean age at treatment initiation was 57.3 (12.0) years. Patient global, pain and fatigue assessments, made on a visual analogue scale ranging from 1 to 10, were 5.6 (2.5), 5.9 (2.7) and 5.7 (2.9) in the TOFA group and 5.7 (2.5), 6.1 (2.7) and 6.0 (2.8) in the OMA group. Disease activity was assessed as moderate or high/severe in 85.9% and 88.3% of patients (DAS28(4)-ESR criteria). Among the 56 (35%) TOFA and 149 (46%) OMA patients ceasing therapy, reasons for cessation were "inefficacy" (TOFA: 64% vs OMA: 59%) and "adverse events" (TOFA: 16% vs TNFi: 17%). Patients remaining on TOFA and OMA therapy at last follow-up had an average treatment duration of 1.7 (1.1) and 2.6 (1.4) years. No difference in retention was observed between TOFA and OMA treated patients (log-rank p=0.6138). Patients treated with an OMA+/-MTX had similar retention (log-rank p=0.2640) as did patients treated with TOFA+/-MTX (log-rank p=0.9553). These results remain unchanged when we adjust for age at treatment initiation, gender, disease duration, and comorbidities (CCI) using Cox models.

Conclusion: OMA and TOFA have similar retention as do subjects treated with OMA or TOFA with or without MTX.

DISCLOSURE OF INTERESTS

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SAT0141 FREQUENCY AND REASONS FOR SWITCHING BACK TO BIOLOGIC ORIGINATOR FOLLOWING INITIAL SWITCH TO BIOLOGIC BIOSIMILAR

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Background: Since February 2015, a number of biosimilar drugs have been introduced for treatment of rheumatoid arthritis (RA) in the UK. Biosimilars are required to have no clinically meaningful differences in efficacy or safety from the originator product. There are clear cost-saving implications when switching patients to a biosimilar; however, the longer term implications of switching have yet to be studied.

Objectives: To describe the frequency of switching back to biologic-originator (BIO-O) in patients who initially switch from BIO-O to biologic biosimilar (BIO-B), focussing on etanercept (ETA) and infliximab (INF).

Methods: The study population comprised RA subjects recruited to BSRBR-RA to 30/11/2018 who had switched from BIO-O to BIO-B (INF and ETA) and had completed at least one further study follow-up following switch. Baseline characteristics at point of switch and the proportion of patients who were recorded as switching back to BIO-O or discontinuing BIO completely following switch with reasons are described.

Results: Nine hundred and sixty six patients were included (760 switching from ETA-O; 206 switching from INF-O). After a median follow-up of 22.5 months post-switch, the majority of patients remained on BIO-B (ETA-B = 619 (81%), INF-B =166 (81%)). Seven percent of patients switched back to originator, with a majority following reports of ineffectiveness or feeling generally unwell (Table). Eleven percent stopped BIO completely, with a majority stopping for serious adverse events such as malignancy or infection. Similar results were seen for both ETA and INF. Six ETA and 3 INF reported injection or infusion related reactions following switch (0.9% overall) leading to switch back (4 ETA) or biologic discontinuation (2 ETA/3 INF).

Conclusion: Data from this study show that the majority of patients who switched from BIO-O to BIO-B remain on the biosimilar over the short term. A small proportion of patients have switched back to the originator drug with the majority doing so for reports of ineffectiveness rather than safety concerns. Hypersensitivity reactions, such as infusion reactions were rare reasons to stop either drug completely or switch back to originator.

Table 1

	Patients Switching from O to B	
N	966	
Etanercept	760 (79)	
Infliximab	206 (21)	
Age, years	66 (56-72)	
% Female	75	
Disease duration, years	20 (13-28)	
DAS28 score	3.2 (2.2-4.2)	
Time on BIO-O before switch years	11 (3-13)	
Follow-up time after switch, months	22.5 (16-25)	
Patients switching back or stopping biologic	**BIO-B to BIO-O Switch back**	**Stop all BIO**
N	71	104
Time to switch back or stop, months	5 (3-8)	7 (4-12)
Ineffectiveness	38	24
Adverse event	18	56
Drug hypersensitivity/infusion reaction	4	5
Infection	0	12
Malignancy	0	14
Generally unwell	8	2
Other AE*	2	20
AE unknown	4	3
Patient decision	2	1
Remission	0	4
Unknown	13	19

All values are median (IQR) or n(%). **Other adverse events include those that are unique events per patient*

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SAT0142 DIFFERENCES IN PATIENT CHARACTERISTICS AND PATTERNS OF TREATMENT BY DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARD) IN BDMARD NAIVE VERSUS EXPERIENCED PATIENTS

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Background: For RA patients (pts), EULAR and ACR recommend various DMARDs. Available treatments have short durability and low persistency. Understanding differences between patients who initiate DMARDs as

biologic naive vs experienced may help clinicians tailor treatment decisions to pts needs.

Objectives: This study aimed to compare DMARD initiation events in biologic naïve vs experienced pts.

Methods: In the Corrona registry (as of 2/28/2018), we selected DMARD initiation events (with at least one 6-month follow up) and stratified them on whether the initiator was biologic naive or experienced. We compared pts baseline characteristics (demographic, clinical, treatment) between strata. We used Kaplan-Meier curves to describe time to discontinuation and log rank test to assess differences in persistence.

Results: For 48,246 RA pts, 10,347 DMARD initiations (index date, baseline; on 11/2012 or thereafter) in 6,858 adults were identified. Within initiations, 38% (n=3,931) occurred in bDMARD naïve pts. Females comprised 76% (naive) vs 80% (experienced). Despite comparable age and retirement status (Table), the bDMARD experienced initiators had RA for longer (mean: 12.6 vs 5.4), were more likely to be disabled (19.6% vs 11.0%), had marginally higher CDAI scores (mean: 19.1 vs 17.6), were more likely to discontinue index treatment due to elevated CDAI (15.5% vs 10.9%), and had a shorter treatment duration (mean: 13.8 vs 15.1 months) than bDMARD naïve initiators. Persistency was higher in the bDMARD naïve than in experienced initiators (Figure)

Conclusion: The marked difference in RA duration and pts disability status, despite comparable age, confirms prior reports that bDMARD experienced pts do not respond as well to therapy as bDMARD naïve pts. The increased CDAI scores and shortened durability of response suggests that there is still a need for new efficacious and well-tolerated RA therapy.

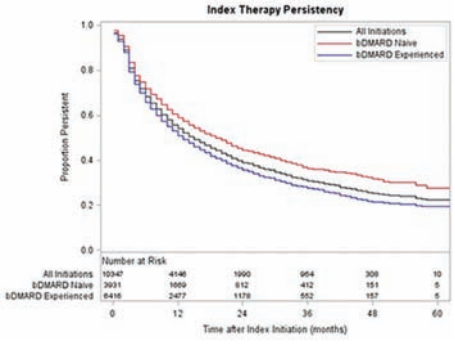
Table. Patient and treatment characteristics

Characteristics	All initiations		bDMARD Naïve		bDMARD Experienced		p-value
	N=10,347	100%	N=3931	38%	N=6416	62%	
Demographics							
Female	8154	78.8	2992	76.1	5162	80.5	< 0.0001
Age (years), mean (SD)	58.9	12.7	58.9	13.3	58.9	12.4	0.8
Disabled	1688	16.3	433	11.0	1255	19.6	< 0.0001
Retired	3012	29.1	1220	31.0	1792	27.9	
RA Duration (years), mean (SD)	9.9	9.9	5.4	7.9	12.6	10.1	< 0.0001
CDAI, mean (SD)	18.5	13.8	17.6	14.1	19.1	13.7	< 0.0001
Therapy allocation (n, %)							
Monotherapy	3366	32.5	1496	38.1	1870	29.1	< 0.0001
Combination therapy	6981	867.5	2435	61.9	4546	70.9	
Index treatment duration (months), mean (SD)	14.3	13.4	15.1	13.8	13.8	13.1	< 0.0001
Reasons for discontinuation of index therapy (n, %)							
One or more reasons	4916		1624		3292		
Safety[a]	925	15.4	376	18.5	549	13.8	< 0.0001
Efficacy[b]	1446	24.1	383	18.8	1063	26.8	< 0.0001
CDAI>10[c]	1421	25.8	427	10.9	994	15.5	< 0.0001

a Safety: serious side effect, minor side effect, fear of future side effect, toxicity, lymphoma/malignancy, and infection.

b Efficacy: inadequate initial response, failure to maintain initial response, and lack of efficacy.

c Patients are counted as discontinuing due to high disease activity (CDAI>10) if no discontinuation reason is reported and CDAI>10 at time of discontinuation.



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SAT0143 SAFETY AND EFFECTIVENESS OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Elderly population with rheumatoid arthritis (RA) is increasing. However, these patients are frequently excluded from clinical trials and data on effectiveness and safety of biologic Disease-Modifying Antirheumatic Drug (bDMARD) is scarce.

Objectives: To assess the persistence of 1st bDMARD and the effectiveness and safety of bDMARD among elderly (≥65 years).

Methods: Prospective multicenter cohort-study of RA patients starting a 1st bDMARD registered at Reuma.pt. Demographic and disease characteristics, comorbidities, medications, disease activity at baseline and follow up (3, 6 and 12 months) and adverse events (AE) were compared between elderly and adult (<65 years) patients. Treatment persistence was estimated using Kaplan-Meier analysis. Effectiveness was measured as EULAR crude response rates, LUNDEX corrected, and adjusted for baseline characteristics.

Results: 2400 patients were included, of which 486 aged ≥65 years (table 1). Crude median persistence in bDMARD was 19.7 months (95% CI 14-25) in adults and 14.5 (95%CI 3-26) in elderly patients (log rank test, p=0.46) (figure 1). EULAR response (crude and LUNDEX corrected) was similar in the two groups at 3 and 6 months (figure 2). After adjustment for baseline characteristics, response rate was inferior in elderly at 12 months (p=0.01). There were 697 AE reported. Except for infections, more common in elderly patients (p=0.03), the rates of severe AE, opportunistic infection, allergic reactions, cancer or hospitalizations were similar in the two groups, as well as the time to 1st AE occurrence (figure 2).

Conclusion: Our findings showed that persistence of 1st bDMARD was similar in adults and elderly RA patients. Though elderly had more severe disease and comorbidities at baseline, bDMARD treatment was equally effective and safe in the short term. However, it is necessary to consider the greater risk of infection in elderly when prescribing a biologic.

	Total	Adults	Elderly	P value
Female - N (%) N=2400	2038 (85)	1630 (85.2)	408 (84)	
Disease duration till 1st bDMARD in years - N (%) N=2074	10.3 (3.7-14.5)	7.4 (4-14)	9.6 (4-18)	<0.01
RF and/or anti-CCP positive - N (%) N=2400	1693 (70.5)	1350 (70.5)	343 (71)	
Erosive disease - N (%) N= 1639	1213 (74)	947 (73)	266 (79)	
Extraarticular manifestations - N (%) N=2400	482 (20)	383 (20)	99 (20.4)	
Hypertension - N (%) N=1769	530 (30)	381 (27)	149 (43)	<0.01
Dyslipidemia - N (%) N= 1769	141 (8)	107 (7,5)	34 (10)	
BMI - median ± IQR N=1210	27 (24-30)	26 (24-30)	27 (23-30)	
Diabetes - N (%) N= 1769	148 (8.4)	98 (7)	50 (14.3)	<0.01
Cardiovascular disease – N (%) N=1769	134 (8)	107 (7.5)	24 (10)	<0.01
DAS 28-ESR - mean ± SD N=1295	5.6 ± 1,3	5.5 ± 1.3	5.7 ± 1.3	0.02
CDAI - mean ± SD N=1069	29 ± 13	28 ± 13	31 ± 15	0.03
SDAI - mean ± SD N=1023	31 ± 14	30 ± 13	33 ± 16	0.01
HAQ-DI - mean ± SD N=1090	1.5± 0.6	1.4 ± 0.6	1 ± 0.7	<0.01

Table 1 - Baseline characteristics. N: number; IQR: interquartile range; SD: standard deviation; RF: Rheumatoid factor; CCP: Cyclic Citrullinated Peptide; BMI: Body Mass Index DAS: disease activity score, CDAI -clinical disease activity Index, SDAI – simple disease activity index, HAQ-DI health assessment questionnaire-disability index. When p value>0,05 no value is presented.

Table 1. Baseline characteristics. N: number; IQR: interquartile range; SD: standard deviation; RF: Rheumatoid factor; CCP: Cyclic Citrullinated Peptide; BMI: Body Mass Index DAS: disease activity score, CDAI -clinical disease activity Index, SDAI – simple disease activity index, HAQ-DI health assessment questionnaire-disability index. When p value>0,05 no value is presented.

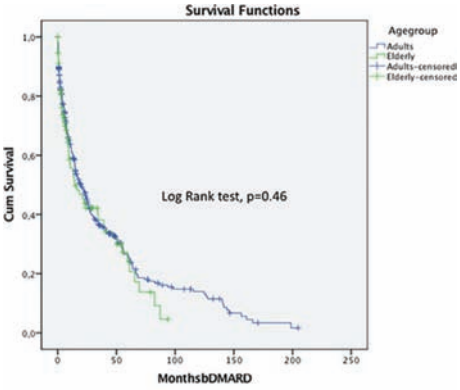


Figure 1 – Persistence in 1st bDMARD (months) for elderly and adults

Efficacy and safety	Total	Adults	Eldery	P value
EULAR response at 3 month (Lundex corrected) %	77.8 (51)	78.4 (51)	75 (51)	
EULAR response at 6 month (Lundex corrected) %	80.6 (50)	81.7 (52)	76 (45.2)	
EULAR response at 12 month (Lundex corrected) %	81.5 (35.6)	83.8 (37)	71.5 (29.3)	0,01
N patients with AE during 1st bDMAR	409	319	90	
AE infection –N (%) N=407	237 (58,2)	176 (55,3)	61 (68,5)	0,03
AE opportunist infection – N (%) N=408	30 (7,4)	21 (6,6)	9 (10)	
AE allergic reaction – N (%) N=407	71 (17,4)	59 (18,6)	12 (13,5)	
Severe AEs– N (%) N=391	82 (21)	64 (21)	18 (20,9)	
Hospitalization– N(%) N=407	56 (13,8)	42 (13,2)	14 (15,7)	
bDMARD suspention due to AE – N (%) N=407	171 (42)	130 (40,9)	41 (46,1)	
bDMARD reintrodution after AE– N (%) N=211	61 (28,8)	48 (30)	13 (25,5)	

Figure 2 – Efficacy and safety. AE: adverse event. When p value>0,05 no value is presented.

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SAT0144 UNDERSTANDING THE LONG-TERM OUTCOME OF RITUXIMAB – IMPLICATIONS FOR MANAGEMENT

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Background: In patients with rheumatoid arthritis (RA), rituximab (RTX) is often prescribed after loss of response to TNF inhibitors; however, little is known about the long-term outcome of patients receiving treatment with RTX. Previous work [1,2] has shown that aiming for "complete B-cell depletion with clinical response" (CD-R) leads to an optimal management of the disease but unfortunately not all patients maintain this status. Whether CD-R can be regained with RTX retreatment remains unclear.
Objectives: To assess the outcome of RA patients treated with consecutive cycles of RTX, focusing on those who achieved complete B-cell depletion with clinical response.
Methods: A prospective 12 year observational study was conducted in RA patients who were treated with RTX in Leeds. Consecutive cycles of RTX consisting of 2 infusions of 1000mg were administered either on clinical relapse or a 6-monthly basis. B-cells were measured using highly sensitivity flow cytometry at 0 and 2 weeks post-RTX. Complete depletion (CD) was defined by total B-cell count $<0.0001x10^{9}/L$ at week 2. Clinical response was defined by EULAR response criteria and CD-R was seen as the optimal outcome.
Results: 755 patients participated in the study of which 723 had complete data (see fig.1). The mean (range) number of RTX cycles administered was 3.8 (1-14). 76% (549/723) of patients reached CD-R at some stage during therapy while 24% (174/723) never did. The latter patients had a shorter period of RTX treatment vs CD-R with an OR of 7.98 after adjusting for age, gender, prior therapy with TNF-I and concomitant DMARDs (95% CI 5.86-10.86); p<0.001 (see fig.2). 84% of those who were retreated with RTX recovered CD-R (77% of them did it in the following cycle). Half of the patients that reached CD-R maintained it in prospective cycles but 47% lost it subsequently. A third of the patients that lost either clinical response or B-cell depletion were switched to other medication without receiving further cycles. Overall, at the end of the study, 55% of all patients treated with RTX (400/723) remained in CD-R.
Conclusion: Most patients treated with RTX will achieve CD-R, but approximately half of them will lose this optimal status at some point. In patients who achieve CD-R but subsequently lose it, retreatment with RTX appears to be an effective strategy since 80% of them will regain it and will maintain long-term treatment with therapy

REFERENCES

[1] Md Yusof, et al. EULAR 2016
[2] Garcia-Montoya, et al. EULAR 2018

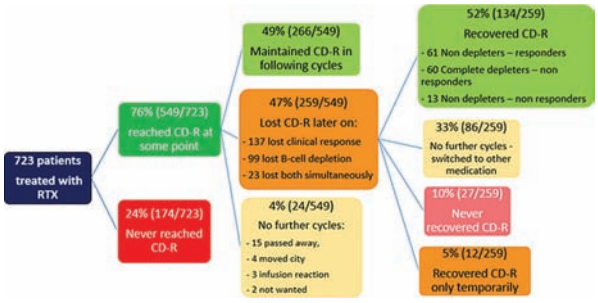


Figure 1

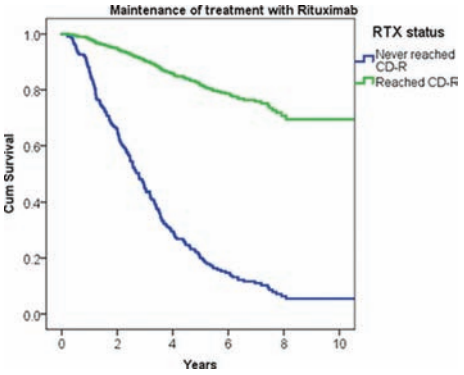


Figure 2

Acknowledgement: Shouvik Dass Maya Buch Sarah Bingham
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SAT0145 ON TAPERING THERAPY FOR RA PATIENTS IN CLINICAL REMISSION; FLARE ON CS-DMARDS IS PREDICTED BY CLINICAL PARAMETERS AND ULTRASOUND, WHEREAS T-CELL ABNORMALITIES ARE PREDICTIVE FOR B-DMARD TAPERING

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Background: Tapering of disease-modifying therapy (DMARDs) is recommended by EULAR/ACR for rheumatoid arthritis (RA) patients who achieve sustained remission on stable therapy(1,2). However, there is no guidance on how to manage this in clinical practice.
Objectives: We aimed to assess flare over 12 months in RA patients in sustained remission who were offered structured tapering of either conventional synthetic (cs) or biologic (b) DMARDs.
Methods: RA patients (ACR/EULAR 2010) prospectively attending a remission clinic were recruited when fulfilling the criteria of stable remission as defined by 3-variable DAS28CRP<2.6 for ≥6 months (stable therapy & no corticosteroids). Patients were offered tapering according to a structured protocol (Figure 1). For patients receiving combination cs/b-DMARDs, only the b-DMARD was tapered. Clinical, ultrasound (US) + immunological (T-cell subsets: naïve, Treg (both age-corrected) and

inflammation related cells, IRC) data were collected. Flare over a period of 12 months was assessed using several definitions in order to evaluate their relevance for clinical outcomes. Associations with baseline characteristics were assessed using univariate statistics (Mann-Whitney-U and Chi-square). No correction for multiple testing was attempted.

Results: 98 patients (cs-DMARDs n=66, b-DMARDs n=32) accepted tapering and achieved at least 12 months follow-up. In the cs-DMARD group 55% were female; the median age was 64 years and median remission duration 25 months. For b-DMARDs 63% were female; the median age was 61 years and median remission duration 28 months. There was great heterogeneity in terms of flare rate according to the definitions used (Figure 2). Flare on tapering b-DMARDs was more commonly observed (29-70%) compared to cs-DMARDs (24-52%). Demographics were not associated with flare by any definition (except longer disease duration for cs-DMARD patients who lost Boolean remission status). Clinical (notably seropositivity) and US measures were associated with flare for cs-DMARDs. Reduced Treg and higher IRC's at baseline were associated with flare in patients tapering b-DMARDs.

Conclusion: Flare rate varied with the definition used and was more common when tapering b-DMARDs compared to cs-DMARDs. Flare was predicted in the latter patients by clinical and US (including seropositivity) findings, whereas T-cell abnormalities predicted flare in b-DMARD patients. These results will help formulate further tapering strategies.

REFERENCES

[1] Smolen JS, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017.

[2] Singh JA, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis & rheumatology (Hoboken, NJ). 2016.

Figure 1. Tapering Protocol

Order*	Drug	Baseline Dose	Taper 1	Taper 2	Taper 3	Taper 4	Taper 5
1	Hydroxychloroquine	400mg od	200mg od	stop	-	-	-
2	Sulfasalazine	1.5g bd	1g bd	1.5g od	500mg bd	500mg od	stop
3	Methotrexate	25mg/ week	15mg/ week	7.5mg/ week	no change	stop	-
N/A	Etanercept	50mg/ week	25mg/ week	25mg/ every other week	25mg/ every 4 weeks	stop	-
N/A	Adalimumab	40mg/ every other week	40mg/ every 4 weeks	40mg/ every 8 weeks	40mg/ every 16 weeks	stop	-
N/A	Infliximab	Variable	Halve dose	Double time interval	Double time interval	stop	-
N/A	Certrolizumab	200mg/ every other week	200mg/ every 4 weeks	200mg/ every 8 weeks	200mg/ every 16 weeks	stop	-
N/A	Golimumab	Variable	Every month	Every 2 months	Every 4 months	stop	-

NB: Patients were seen 3-monthly. If they remain in remission, they proceed to the next taper unless there is a significant clinical reason not to taper at the time of assessment (as per standard care). * Order of cs-DMARD therapy tapered if on dual/triple therapy

Figure 2. Rate of flare according to different definitions and associations with baseline characteristics

Flare Definition	csDMARD (n=66) Hydroxychloroquine n=13, Sulfasalazine n=4, Methotrexate n=49. (On monotherapy n=43, Combination therapy n=23)	bDMARD (n=32) Etanercept n=17. Adalimumab /Infliximab/ Certolizumab/Golimumab n=15
Physician Judgement (Increase in therapy +/- prescription of corticosteroid):	47% flare Higher total PD (p=0.005) RF positive (p=0.010) Higher total GS (p=0.012) ACPA positive (p=0.041)	50% flare Reduced Treg (p=<0.0001)
DAS28 flare (Increase in 3vDAS by ≥1.2)	24% flare RF positive (p=0.007) Higher total PD (p=0.018)	29% flare Reduced Treg (p=0.001)
Loss of remission (3vDAS28 ≥2.4)	38% flare Higher TJC28 (p<0.0001) Higher total PD (p=0.003) Higher CRP (p=0.008) RF positive (p=0.009)	44% flare Reduced Treg (p=0.001) Increased IRC (p=0.008)
Loss of LDA (3vDAS28 >3.2)	27% flare Higher TJC28 (p<0.0001) Higher CRP (p=0.01)	37% flare Reduced Treg (0.004) Increased IRC (p=0.006) RF positive (p=0.014)
Loss of Boolean remission* (TJC, SJC & CRP all ≥1)	52% flare Longer disease duration (p=0.005) Higher CRP (p=0.002)	70% flare No associations

* Considering only patients who were in Boolean remission at baseline; 46 for DMARDs and 30 for biologics. Patient global health assessment omitted due to missing data.

Abbreviations: Rheumatoid Factor (RF), Anti-Citrullinated Protein Antibodies (ACPA), Power Doppler Synovitis (PDS), Grey Scale Synovial Hypertrophy (GS), Tender/Swollen Joint Counts (TJC28/SJC28), Age-corrected T-regulatory cells (Treg), Inflammatory Related Cells (IRC).

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SAT0146

COMPARING DRUG SURVIVAL FOR BIOSIMILAR SB4 ETANERCEPT IN RHEUMATOID ARTHRITIS BOTH ETANERCEPT NAÏVE AND NON-MEDICAL SWITCH PATIENTS WITH ETANERCEPT REFERENCE DRUG IN A NORWEGIAN OUT-PATIENT CLINIC. PRELIMINARY RESULTS FROM A MULTI-CENTER STUDY

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Background: In Norway encouraged by the health authorities non-medical switch from reference drug to biosimilar drug has been performed in most patients on biologic reference drugs with biosimilar drugs available, including etanercept. There is a need for real life data understanding the effect of biosimilar drugs when these drugs are introduced in clinical practice.

Objectives: To explore drug survival for biosimilar SB4 etanercept in RA patients, both etanercept naïve and non-medical switch patients, and compare with the etanercept reference drug.

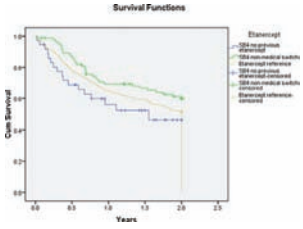
Methods: Preliminary 2 years drug survival data from one center in a 5 center study in Norway exploring drug survival for etanercept reference drug and biosimilar etanercept SB4 is presented. At this outpatient clinic RA patients as part of standard clinical care has been monitored systematically since 2003. Drug survival for SB4 etanercept, both the etanercept naïve and the non-medical SB4 switch group, was compared with patients treated with the etanercept reference drug in the period 2003-2018. Baseline demographic, clinical and treatment data were retrieved and analyzed. Kaplan-Meier survival curves were used to explore 2 years drug survival. Survival differences between groups were tested using Breslow statistics.

Results: At the outpatient clinic the number of RA patients treated with etanercept reference drug was 356, the number of patients treated with SB4 with no previous etanercept was 36 and the patients with a non-medical switch from reference etanercept to etanercept SB4 was 84. In the table below baseline demographics and disease measures are shown for the etanercept reference group, the non-medical SB4 switch group and the SB4 naïve to etanercept group. Data in table are presented as percentage for group variables and as mean with standard deviation (SD) for continuous variables.

	Etanercept reference (n=356)	SB4 non-medical switch (n=84)	SB4 etanercept naïve (n=36)
Age, years	63.7 (15.4)	62.2 (11.6)	58.1 (15.3)
Females	71.1%	69.0%	77.8%
Disease duration, years	12.6 (10.3)	18.3 (11.2)	8.5 (8.4)
Anti-CCP positive	75.4%	75.0%	73.7%
DAS28	4.9 (1.4)	2.8 (1.3)	4.0 (1.4)
ESR mm/hr	29.5 (21.5)	17.6 (13.7)	29.2 (26.3)
CRP mg/l	20.3 (23.1)	5.0 (6.5)	13.7 (16.7)
Pain (VAS 0-100)	53.1 (27.0)	30.2 (25.3)	46.5 (20.5)
Fatigue (VAS 0-100)	53.4 (30.6)	34.4 (33.4)	44.7 (27.6)
MHAQ	0.78 (0.56)	0.51 (0.61)	0.71 (0.44)

Mean (95%CI) drug survival for the non-medical SB4 switch group was1.53 (1.38-1.68) years, for the SB4 group with no previous etanercept 1.23 (0.95-1.51) years and for etanercept reference group 1.38 (1.31-1.46) years. A statistically significant difference (p<0.02) was found between the groups except between etanercept reference group and the etanercept SB4 group without prior etanercept (p=0.23). The percentage of RA patients starting with etanercept as first biologic drug was for etanercept reference 64.6% and for biosimilar etanercept SB4 36.1%.

In the figure below Kaplan-Meier drug survival curves are shown.



Conclusion: To the best of our knowledge this is the first data showing that drug survival of an etanercept biosimilar drug after a non-medical

switch is higher than a historical cohort of etanercept reference drug. This is expected, since it is a selected group of etanercept responders. The interpretation of the results should be cautious, since only few patients are included in this first analysis. A larger number of patients from other participating out-patient clinics is planned to be included.

Disclosure of Interests: Glenn Haugeberg Grant/research support from: For this study grant from Biogen, Consultant for: Medical Advisory boards for several companies, Paid instructor for: I have been paid for giving lectures for pharmaceutical companies and their employees, Speakers bureau: I have been paid for giving lectures in meetings organized by pharmaceutical companies, Bjørg Tilde Svanes Fevang: None declared, Gunnstein Bakland: None declared, Erik Rødevand: None declared, Andreas Diamantopoulos: None declared

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SAT0147 EFFECTS OF BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUG TREATMENT ON PHYSICAL ACTIVITY, MUSCLE POWER, AGILITY AND INHIBITION OF FALL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: It has been demonstrated that biological DMARDs (bDMARDs) treatment rapidly improved sign and symptom in patients with rheumatoid arthritis (RA). Those were evaluated using composite measures or biomarkers in daily clinical practice or clinical studies. Although rapid improvement of composite measures or biomarkers is important in the treatment of RA, primary important goal of treatment is improvement of long term health-related quality of life (HR-QOL) [1]. HR-QOL is based on physical function such as muscle power and agility.

Objectives: This study investigated the efficacy of bDMARDs on physical function and fall risk in patients with RA.

Methods: Periodic evaluation of physical function by the staffs in rehabilitation center in our institute has been performed in addition to routine rheumatology evaluation (SDAI, biomarkers, mHAQ) in RA patient initiated their first bDMARDs treatment from Oct. 2015 to Feb. 2018. 47 cases was registered in total. Evaluation of physical function included evaluation of muscle power (grasping power [GP] and knee extension power [KEP]), agility (Time up and go test [TUG] and 10m walking time [10mW]) and questionnaire using mHAQ, portable fall risk index [2] and the 25-question geriatric locomotive function scale (locomo25) [3] at baseline (initiation of bDMARDs), 1month, 3months, 6months and 12months. Disease activity of RA (SDAI, CRPMMP-3) was evaluated at same time point. Although 26 cases have passed one year from initiation of bDMARDs treatment, 9 cases dropped out from evaluation of physical function due to stopping of bDMARDs treatment or patient's hope not to e evaluated on physical function or major joint surgery performed in patient which was influence physical function. Results of early 17 cases who completed evaluation at 12 months were investigated in this study.

Results: Baseline patients characteristics was as follow (n=17): mean age 59.1 years old, RA duration 13.7 years, Mean SDAI 19.6, mean CRP 1.9mg/dl. Used bDMARDs were tocilizumab in 5 cases, golimumab in 4 cases, etanercept in 3 cases, abatacept in 3 case, certolizumab in one case and infliximab-biosimilar in one case. Date is presents as mean values at baseline-1-3-6-12 months below. SDAI and CRP were significantly improved on and after one month (SDAI: 19.6-9.6-5.8-5.7-5.5, CRP [mg/dl]: 1.9-0.3-0.3-0.3-0.8). GP and knee extension power significantly improved on and after one months except KEP at 3 months (GP [kg]: 12.3-14.1-15.9-16.9-17.4, KEP [N/kg] 2.6-3.1-3.1-3.4-3.5). TUG at 10mW significantly improved on and after one months except TUC at 3months and 10mW at 3 months (TUG [s]: 9.3-8.0-8.2-7.3-7.4, 10mW[s]: 8.3-7.7-7.5-6.9-6.8). MHAQ significantly improved on and from 6 months (0.46-0.33-0.19-0.20-0.12). Locomo25 significantly improved on and from 1 month (31.7-20.6-18.5-16.7-15.0). Portable fall risk index significantly improved at only 12 months (8.8-8.6-7.8-7.8-6.8).

Fig1. Mean values and p-value by bDMARDs Treatment in RA Patients

	Baseline	1 month	3 months	6months	12months
SDAI	19.6 (Cont.)	9.6 (<0.01)	5.8 (<0.01)	5.7 (<0.01)	5.5 (<0.01)
CRP (mg/dl)	1.9 (Cont.)	0.3 (<0.01)	0.3 (<0.01)	0.3 (<0.01)	0.8 (<0.01)
Grasping Power (kg)	12.3 (Cont.)	14.1 (0.049)	15.9 (0.01)	16.9 (<0.01)	17.4 (<0.01)
KEP (N/kg)	2.6 (Cont.)	3.1 (0.02)	3.1 (0.21)	3.4 (<0.01)	3.5 (<0.01)
TUG (second)	9.3 (Cont.)	8.0 (0.03)	8.2 (0.055)	7.3 (0.01)	7.4 (0.02)
10mW (second)	8.3 (Cont.)	7.7 (0.02)	7.5 (0.14)	6.9 (<0.01)	6.8 (<0.01)
mHAQ	0.46 (Cont.)	0.33 (0.12)	0.19 (0.02)	0.20 (<0.01)	0.13 (<0.01)
locomo25	31.7 (Cont.)	20.6 (0.03)	18.5 (<0.01)	16.7 (<0.01)	15.0 (<0.01)
Fall risk index	8.8 (Cont.)	8.6 (0.83)	7.8 (0.16)	7.8 (0.12)	6.8 (<0.01)

Data is expressed as mean (p-value). P-value was caluculated using Wilcoxon signed-rank test between baseline and each month.
SDAI: simplified disease activity index, KEP: knee extention power, TUG: timed up and go test, 10mW: 10m walking time, mHAQ: modified health assessment questionnaire

Conclusion: Signs and symptoms of RA were rapidly improved after the initiation of bDMARDs treatment and improvement of physical function was also rapidly improved. The changes from baseline and one month were more drastic in composite measure or biomarker of inflammation than that in muscle power and agility in respect with p-values. Inhibition of fall were achieved 12 months after bDMARDs initiation. These results suggested that physiotherapy might play an important role in RA patients treated with bDMARDs to gain more rapid improvement of physical function.

REFERENCES

[1] Smolen JS, et al. Ann Rheum Dis 2016.
[2] Toba K, et al. Jpn J Geriat 2005.
[3] Seichi A at al. J Orthop Sci 2012.

Disclosure of Interests: None declared

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SAT0148 IMMUNOGLOBULIN A LEVELS IN ADDITION TO RHEUMATOID FACTOR PREDICTS REMISSION ACHIEVEMENT WITH ABATACEPT IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Biological disease modifying antirheumatic drugs (bDMARDs) now play an important role of clinical practice for patients with rheumatoid arthritis (RA). Abatacept (ABT) has a biologic agent that has an unique mechanism of action suppressing T lymphocyte activation. Although many prediction studies about therapeutic responses to bDMARDs for RA have been conducted to date [1], few studies has focused on ABT.

Objectives: The aim of this study was to identify predictive clinical biomarkers for remission achievement with ABT in RA patients.

Methods: We retrospectively reviewed consecutive patients with RA who started ABT from 2010 through 2018 in Keio University Hospital. We defined early ABT use as the initiation of ABT within two years from diagnosis without radiographic progression in hand X rays, and stratified the patients into the early ABT users and the late ABT users. Baseline characteristics were compared between patients who achieved CDAI remission achievement at 6 months and those who did not in both groups.

Results: One hundred and seven RA patients who were treated with ABT with baseline information available were enrolled in the study. Among them, 15 patients were classified into the early ABT users and 92 were the late ABT users, and the remission rates at 6 months were 40% and 24%, respectively. In the early ABT users, patients who achieved CDAI remission at 6 months showed significantly higher IgA levels than those who did not achieve remission (390 mg/dL vs 279 mg/dL, P=0.04, respectively). The difference in IgA disappeared in the late ABT users (332 mg/dL vs 313 mg/dL, P=0.60, respectively). Principal component analysis revealed that in the early ABT users, patients who

achieved remission and those who did not could be clearly separated by the levels of IgA, IgG, rheumatoid factor, and albumin (Figure), whereas those baseline characteristics were mostly overlapped in the late ABT users (cut-off value for predicting remission with sensitivity and specificity in the early ABT users; IgA 342 mg/dL with 83% and 100%, IgG 1880 mg/dL with 50% and 100%, rheumatoid factor 152 IU/mL with 50% and 100%, albumin 3.7 g/dL with 88% and 67%, respectively). The area under the curves of receiver operating characteristic curves to predict remission were 0.833 of IgA and 0.778 of rheumatoid factor titer.
Conclusion: We identified serum IgA titer was the novel predictive factor for response of ABT.

REFERENCE

[1] Wijbrandts CA, Tak PP. Prediction of Response to Targeted Treatment in Rheumatoid Arthritis. Mayo Clin Proc. 2017;92:1129-1143.

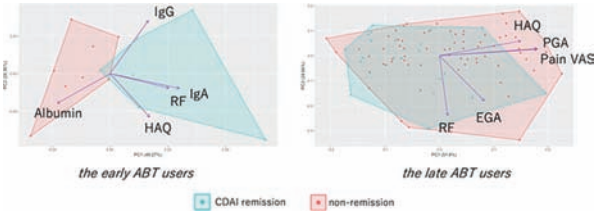


Figure. Principal component analysis by clinical parameters.RF; rheumatoid factor, HAQ; health assessment questionnaire, EGA; evaluator's global disease activity, PGA; patient global assessment, VAS; visual analog scale

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SAT0149 EVALUATION OF A PROSPECTIVE COHORT EVENT MONITORING MODEL FOR PATIENT-REPORTED ADVERSE DRUG REACTIONSATTRIBUTED TO BIOLOGICAL DMARDS: VALIDITY OF THE PATIENT-REPORTED INFORMATION AND REPRESENTATIVENESS OF THE PARTICIPANTS

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Background: To gain knowledge on the prevalence, course and treatment of adverse drug reactions (ADRs) attributed to biological DMARDs (bDMARDs) and the experienced impact of ADRs on patients, an ADR-focused online questionnaire system was developed by Netherlands Pharmacovigilance Centre Lareb (*Dutch Biologic Monitor*). 898 consecutive patients of eight centers who used a bDMARD indicated for an inflammatory rheumatic disease were followed between 1 January 2017 and 31 December 2018.
Objectives: Validation of the quality of the patient-reported information in the *Dutch Biologic Monitor* and evaluation of the representativeness of the participants in relation to the source populations.
Methods: Patients of 18 years and older who used a bDMARD indicated for an inflammatory rheumatic disease were included by the participating hospitals. The patient-reported medical information (bDMARD, indication and concomitant DMARDs) of 479 patients with a rheumatic disease (Reade, Amsterdam: *N*=174; Sint Maartenskliniek, Nijmegen: *N*=305) was verified by comparing the patient-reported parameters to the patient's electronic health record using percentage agreement and/or Cohen's kappa. Representativeness was tested in 550 patients with an inflammatory rheumatic disease (Reade, Amsterdam: *N*=192; Sint Maartenskliniek, Nijmegen: *N*=358) by comparing their grouped age, grouped gender and prescribed bDMARD to the source populations of the respective hospitals using Mann-Whitney U test, Chi-Square Goodness-of-Fit and Fisher's exact test with Monte Carlo simulation.
Results: 95.8% of the tested rheumatic disease patients correctly reported their bDMARD (active substance and brand name). Furthermore, agreement between patients and the electronic health record was strong for the reported indications (90.4% agreement, κ = 0.832) and moderate for the concomitant therapy (79.7% agreement; κ=0.725). The subpopulations were representative for their source populations based on grouped gender (38.4% vs. 38.8% male, $\chi 2(df=1, N=550)=0.038$; $p>0.05$) and bDMARD use (both $p>0.05$). Grouped median age was not representative (58.0 vs. 56.0 years; $U=962872$; $p=0.04$), since the male participants were older (58.5 vs. 55 years; $p=0.001$).
Conclusion: So far, the *Dutch Biologic Monitor* seems to be a valid tool to obtain knowledge on ADRs attributed to bDMARDs, since the reported medical information corresponded to the patients' electronic health records and the participants generally represented their source populations regarding grouped gender and prescribed bDMARD.
Disclosure of Interests: Leanne Kosse: None declared, Naomi Jessurun: None declared, Renske Hebing: None declared, Victor Huiskes: None declared, Karin Spijkers: None declared, Michael Nurmohamed Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB
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SAT0150

EFFICACY OF TOCILIZUMAB FOR SUPPRESSING RADIOGRAPHIC PROGRESSION OF CERVICAL LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARISON WITH METHOTREXATE; THREE YEARS OF FOLLOW-UP ~A MULTICENTER REGISTRY STUDY ~

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Background: Cervical lesions are known to occur at high frequency as a complication of rheumatoid arthritis (RA). Treatment with biological agents are more clinically effective than the DMARDs that were in use previously, in particular, with their efficacy in suppressing joint destruction having been emphasized. We reported the efficacy of infliximab, anti-tumor necrosis factor antibodies for suppressing the radiographic progression of RA cervical lesions at ACR2009, EULAR2010, 11, 12, 13, 14, 16 and 18. However there is still few studies of efficacy of against RA cervical lesions of Tocilizumab (TCZ), anti-interleukin 6 receptor antibody.

Objectives: To evaluate the efficacy of TCZ for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 3 years.

Methods: We used TCZ or MTX for treating Japanese patients with active RA who fulfilled the ACR criteria in 1987. The final study cohort of each 50 and 75 patients received continuous TCZ and MTX treatment for at least 3 years. For evaluation of cervical lesions, the atlanto-dental interval (ADI), the space available for the spinal cord (SAC), and the Ranawat value were measured by plain lateral radiographs in the flexion position, at initiation and Year 1,2 and 3.

Results: In the patients receiving TCZ (n=50) and MTX (n =75), the number of female were each 38(76%) and 52(69%) cases(p=0.416). The mean age was 58.7 ± 13.0 and 63.6 ± 11.0 years old (p=0.046); disease duration was 7.7 ± 7.8 and 8.0 ± 9.5 years (p=0.247) and the mean dose of MTX was 9.2 ± 3.6 and 8.2 ± 2.9 mg/w (p=0.146). Clinical findings related to RA were as follows; CRP 4.2± 3.4 and 1.7± 2.3 mg/dl(p<0.001); ESR 55.0± 24.0 and 31.9 ± 21.8mm/h(p<0.001); MMP3 401 ± 311 and 223 ± 350ng/ml(p<0.001); the number of RF-positive 40 (80%) and 60(80%) cases(p=0.999); DAS28-ESR 5.45 ± 0.98 and 4.30 ± 1.38 (p<0.001); ADI 2.9 ± 1.7 and 2.6 ± 1.6mm(p=0.335); SAC 18.9 ± 2.7 and 20.8 ± 2.5mm(p<0.001) and Ranawat value 15.2 ± 1.6 and 16.0 ± 1.5mm (p=0.008).

The respective changes in cervical lesion parameters after 3 years were as follows: ADI: 0.46 ± 0.79 and 0.71 ± 0.80 mm (p = 0.044); SAC: −0.34 ± 0.63 and −0.63 ± 0.82 mm (p = 0.027); and Ranawat value: −0.32 ± 0.59 and −0.44 ± 0.66 mm (p = 0.295) between TCZ and MTX patients (Fig.1).

The numbers of patients who did not showed progression in ADI, SAC and Ranawat value were each 34(68%) vs 37(49%) cases(p=0.039); 37 (74%) vs 40(53%) cases(p=0.020) and 37(74%) vs 49(65%) cases (p=0.306) after 3 years. Also the number who was able to suppress progression in all three parameters were each 34 cases (68%) receiving TCZ and 37 cases (49%) receiving MTX (p=0.039) after 3 years (Fig.2).

Conclusion: This study suggested that TCZ treatment can be used to suppress the progression of RA cervical lesions more than MTX treatment.

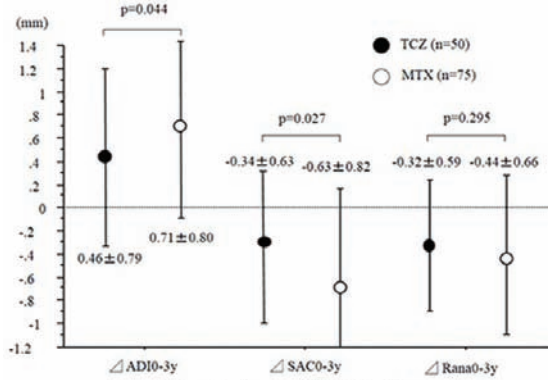


Figure 1 : Respective changes in ADI, SAC and Ranawat value from Year 0 to Year 3 between TCZ and MTX patients

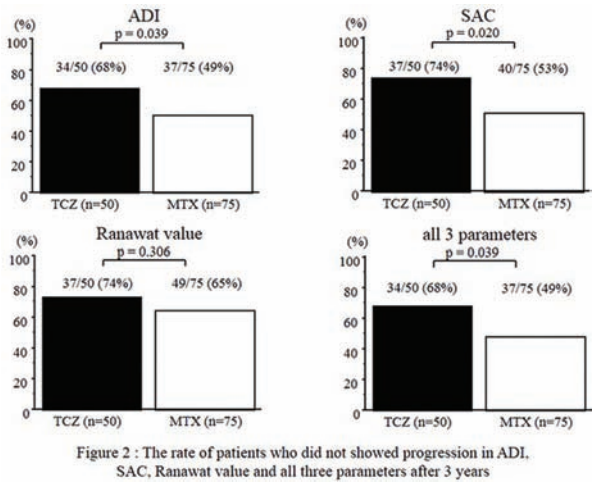


Figure 2 : The rate of patients who did not showed progression in ADI, SAC, Ranawat value and all three parameters after 3 years

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SAT0151

TIME TO INITIATION OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN THE FRENCH COHORT ESPOIR

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Background: Access to biologic Disease-Modifying Anti-Rheumatic Drugs (DMARDs) of early rheumatoid arthritis (RA) patients is highly variable across countries and may depend on patient characteristics, disease expression, physicians behaviors as well as care organization in the patient region of living.

Objectives: 1) To assess the time to initiation of bDMARDs in the French cohort ESPOIR, and 2) To assess the factors associated with the timing of bDMARD initiation.

Methods: In this national multicenter cohort, 813 adult patients with suspected or confirmed early RA were included between December 2002 and March 2005, and followed up during 10 years. In the present analysis, we considered only patients who were fulfilling the ACR-EULAR 2010 criteria for RA at baseline. The primary outcome was the time to initiation of a biologic DMARD, in months, since diagnosis. It was assessed by Cox model based survival analysis with time dependent covariates; the threshold used for p-value was 0.05. Predictors colinearity was then assessed by adapted tests. All statistical analysis were done with R version 3.5.1.

Results: Among the 658 patients fulfilling the ACR-EULAR 2010 criteria for RA (77% women, 52% smokers at baseline, mean-aged 48 at diagnosis, with positive RF in 46.6%, positive ACPA in 43% and polyarticular presentation at baseline in 54.5%), 178 patients (31%, CI 95%= [27%;34.7%]) initiated a biologic DMARD during the 10-year follow-up (Figure 1). Variables associated with an earlier bDMARD initiation in the bivariate analysis were: 1) at baseline: younger age (p = 0.0016), younger age of first joint pain (0.0014), younger age of first joint swelling (0.0014), 2) during the follow up: joint pain (p < 0.0001), high HAQ (p <

0.0001) and DAS28 (p < 0.0001), radiologic progression (p < 0.0001), positive RF (p < 0.0001), positive ACPA (p < 0.0001), elevated ESR (p < 0.0001) and CRP (p < 0.0001). In multivariate analysis, DAS28 (p < 0.0001), radiologic progression (p < 0.0001) and positive ACPA (p=0.000176) were significantly associated with an earlier initiation of a biologic DMARD, whereas an older age of first joint pain was a protective factor (p < 0.0001) (Table 1).

Conclusion: In this study, less than one third of the ESPOIR cohort patients initiated a bDMARD over the 10-year follow-up. RA poor prognostic factors were associated with earlier initiation as expected.

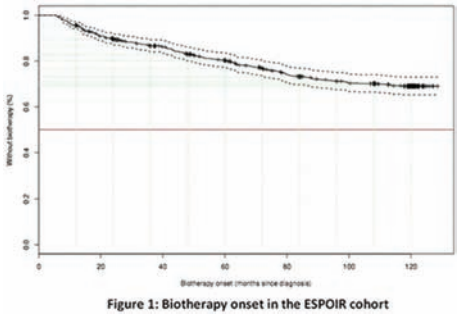


Figure 1: Biotherapy onset in the ESPOIR cohort

Table 1. Results of the multivariate analysis

Covariates	Hazard-ratios [95% CI]	p-value
Age of 1st joint pain	0.97 [0.96 ; 0.98]	< 0.0001
DAS28	2.04 [1.84 ; 2.26]	< 0.0001
Structural damage on X-rays	2.30 [1.64 ; 3.22]	< 0.0001
Positive ACPA	2.01 [1.40 ; 2.89]	0.000176

Disclosure of Interests: Joanna KEDRA: None declared, Benjamin Granger: None declared, Stephanie Emilie: None declared, Cecile Gaujoux-Viala Consultant for: Speaking and/or consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Merck-Serono, Medac, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi and UCB Pharma., Speakers bureau: Speaking and/or consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Merck-Serono, Medac, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi and UCB Pharma., Anne-Christine Rat: None declared, Bernard Combe Consultant for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB, Bruno Fautrel Grant/research support from: AbbVie, Lilly, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, Sanofi-Aventis, Sanofi Genzyme, SOBI, UCB

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SAT0152 PREVALENCE AND SUCCESS OF 'TRY AND SEE' SUBCUTANEOUS BIOLOGIC DMARD DOSE REDUCTION IN ROUTINE CARE AND COST SAVING IMPLICATIONS

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Background: Biologic disease modifying anti-rheumatic drugs (bDMARD) are widely used in rheumatologic practice. Subcutaneous bDMARDs are licenced in a fixed dose for all indications (RA, PsA, AS) yet therapeutic drug monitoring (TDM) of TNF inhibitors (TNFi) reveals a wide range of serum drug concentrations (1). EULAR recommendations (2) state that 'one can consider tapering bDMARDs' if a patient is in persistent remission (usually by lengthening the interval between subcutaneous injections), and in trials up to 80% sustain remission after tapering over 39 weeks (3). In routine care bDMARD dose reduction is usually initiated on a 'try and see' basis, in the absence of guidelines.

Objectives: To assess the prevalence and success of subcutaneous bDMARD dose reduction in routine care, per disease indication and bDMARD class, and the cost saving implications.

Methods: Dose interval information was collected prospectively in patients on subcutaneous bDMARDs with RA, PsA and AS attending for routine review at St George's University Hospitals NHS Foundation Trust from October – November 2018. Department practice is that bDMARD dose reduction is discussed (but not mandated) with patients in sustained remission on a 'try and see' basis, without TDM.

Results: Data on 88 patients (female 46) were collected, RA 39, PsA 36, AS 13, mean age 50 years (range 24-78), TNFi n=75, other bDMARDs n=13. The dose interval was per licence in 79.5%, less frequent in 18% and more frequent in 2.5%. In those taking a bDMARD less frequently than per licence, the dose interval was increased by a mean 2.15 x licenced interval (range 1.14 – 6 x); in RA 1.88x, PsA 2.12x and AS 2.64x. Dose reduction had been attempted in 32%, but failed due to loss of efficacy in 43% of these (13.6% of entire cohort), including 50% with RA, 46% PsA and 20% AS. In those attempting a dose reduction, there was no difference in the% sustaining this for Etanercept 57% (8/14) and Adalimumab 50% (5/10) but lower for all TNFi (54%, 13/24) treated patients compared to other bDMARDs (75%, 3/4). Dose reduction had not been attempted at any stage in 66% (RA 72%, PsA 61%, AS 62%). Cost savings from 16 patients with sustained dose reduction over 3 years in this cohort were £97,653, extrapolated to 18% of the entire population (n~1500) on subcutaneous bDMARDs at our Trust makes £1.65 million saving over 3 years.

Conclusion: 'Try and see' dose reduction of subcutaneous bDMARDs has been attempted in one third of patients in routine care, with more success in AS where 80% sustained a lower dose at a mean 2.64 x licenced interval, compared to 50% of RA and 54% PsA patients at 1.88 and 2.12 x licenced interval respectively. Guidelines, possibly based on TDM, are needed to optimise current practice which falls short of the success of dose reduction in clinical trials (3). Even with a 'try and see' approach failing in 43% of attempts, the cost savings are very substantial to the healthcare economy.

REFERENCES

[1] Merel J l'Ami, et al. Ann Rheum Dis 2018; 77: 484-7
[2] Smolen JS, et al. Ann Rheum Dis 2017; 76: 960-77
[3] Emery P, et al. N Engl J Med 2014; 371: 1781-92

Disclosure of Interests: Jatin Mistry: None declared, Catherine Smith: None declared, Malama Sumbwanyambe: None declared, Margaret Sibley: None declared, Patrick KIELY Paid instructor for: Amgen, Gilead, BMS, Speakers bureau: Abbvie, BMS, UCB, Lilly, Pfizer

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SAT0153 1,25(OH)2D AND IL-6 BLOCKADE SYNERGISTICALLY REGULATES RHEUMATOID ARTHRITIS VIA SUPPRESSION OF TH17 AND OSTEOCLASTOGENESIS

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Background: Immune cells express vitamin (vit) D receptor and vit D is known as a potent immune-modulator.

Objectives: Based on negative association of serum vit D level with rheumatoid arthritis (RA) disease activity on previous studies, we aimed to evaluate the role of the vit D in treatment response in RA patients on anti-IL-6 receptor antibody – tocilizumab.

Methods: RA patients on tocilizumab were enrolled, and data were collected retrospectively. Disease activity (disease activity score (DAS) 28), serum 25(OH)D level, modified Sharp's score of hand x-ray at the time of tocilizumab initiation and follow up were analyzed. Peripheral blood mononuclear cells (PBMCs) were differentiated into Th17 or osteoclast in the presence or absence of various concentrations of tocilizumab and/or $1,25(OH)_2D$. Proportion of Th17 was analyzed by FACS.

Results: Among 98 RA patients on tocilizumab, 34 (34.7%) patients had sufficient serum 25(OH)D level ($\geq$30ng/mL) when tocilizumab was initiated. On 24 weeks, DAS 28 reduction was greater (64.6 ± 15.5% vs. 52.7 ± 20.7%, P=0.004) and more patients achieved low disease activity (91.2% vs. 70.3%, P=0.018) or remission (82.4% vs. 57.8%, P=0.014) in vit D sufficient group. On 48 weeks, DAS28 reduction and proportion of patients with remission was greater in vit D sufficient group as well. However, there was no significant difference in hand & wrist erosion progression. In vitro, tocilizumab and active vit D $1,25(OH)_2D$ treatment synergistically suppressed Th17 differentiation and osteoclastogenesis from PBMC.

Conclusion: RA patients being treated with IL-6 blocker show better response when they have sufficient serum vit D level. Active vit D

seems to suppress Th17 and osteoclasts differentiation in RA patients in synergy with tocilizumab.

REFERENCE

[1] Bellan M. Role of Vitamin D in Rheumatoid Arthritis. Adv Exp Med Biol. 2017;996:155-168

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SAT0154 STABILIZATION OF RHEUMATOID ARTHRITIS ASSOCIATED INTERSTITIAL LUNG DISEASEBY RITUXIMAB: A SINGLE CENTER EXPERIENCE WITH LONG-TERM FOLLOW-UP

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Background: Interstitial lung disease (ILD) is the most significant pulmonary manifestation of Rheumatoid Arthritis (RA)[1], contributing to decreased quality of life, progressive chronic disability and high utilization of healthcare resources. Treatment is challenging with mixed results from different biologics while Rituximab (RTX) has the most encouraging data based on retrospective observational studies. [2]
Objectives: To evaluate the efficacy and safety of RTX in patients with RA-ILD in the context of daily practice.
Methods: Observational retrospective study (2009-2019) of patients with a diagnosis of RA-ILD from a cohort of RTX-treated RA patients in the University Hospital of Heraklion. ILD was diagnosed by HRCT and monitored by means of pulmonary function tests (PFTs), HRCT and 6-minute walking test (6MWT, clinically important difference>50 m). RTX was used at standard dose (1 gr x2/6 months). ILD progression was defined by any of: decrease of pre-RTX forced vital capacity (FVC) >10%, or diffusion capacity of carbon monoxide (DLCO) >15% predicted score, or death from progressive ILD. Improvement was defined by any of: increase of pre-RTX FVC >10% or DLCO >15% predicted. All other patients were classified as having stable disease. RA activity was assessed by DAS28 (ESR).

TABLE

	Baseline	End of follow-up
6MWT, n (%)		
– Stable		10/12(83%)
– Improvement		0/12(0%)
– Worsening		2/12(17%)
FVC, n (%)		
– Stable		10/13(76%)
– Improvement		1/13(7.7%)
– Worsening		2/13(15.3%)
DLCO, n (%)		
– Stable		10/13(76%)
– Improvement		1/13(7.7%)
– Worsening		2/13(15.3%)
HRCT, n (%)		
– Stable		13/16(81%)
– Improvement		1/16(6.25%)
– Worsening		2/16(12.75%)
DAS 28 (ESR) (median (IQR)	5.05(2-6.9)	2.99(2.9-5.5)

Results: Of 247 RA patients treated with RTX, 16 (11 women, 5 men) had RA-ILD (prevalence 6.5%). 12/16 (75%) had radiographic pattern of UIP and 4/16 (25%) had NSIP. 9/16 (56%) were positive for ACPA and/or RF. The median (IQR) age at RTX initiation was 66 (54-77) years, ILD duration prior to RTX was 5.2 (1-15) years. Number of prior biologics was 1 ± 4 and 11/16 (69%) have been treated with concomitant DMARDs. 1/16 (6.25%) had previously received Cyclophosphamide. Concomitant COPD was present in 3/16 (19%) of the patients. Follow-up while on RTX was 37 (6-136) months. The overall dose of RTX was 13 (2-40) g. Following RTX treatment, new-onset ILD was diagnosed in 3/247 patients (incidence=1.2%). During follow-up, data for ILD were available for 13/16 patients. Post-RTX, 10/13(76%) showed stabilization, 1/13 (7.7%) had improvement, while 2/13(15.3%) had progression of RA-ILD. 1/16(6.25%) switched to Cyclophosphamide. During follow-up period, 6 admissions were recorded due to infections (4 for community-acquired pneumonia and 2 for hospital-acquired pneumonia) and 1/16(6.25%) patient died after progression of ILD.
Conclusion: In this cohort of RA-ILD, the majority of patients treated with RTX showed stabilization of lung disease, while RA improved significantly, over a prolonged follow-up period. RTX appears to be an acceptable and safe therapeutic choice for patients with RA-ILD. Nevertheless, randomized studies are warranted to prove any clinical effectiveness of RTX in RA-ILD.

REFERENCES

[1] P.Spagnolo, et al. Arthritis & Rheumatology 2018 Oct; 70(10):1544-1554.
[2] Md Yuzaiful Md Yusof, et al. Rheumatology 2017; 56:1348-1357

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SAT0155 THE PRESENCE OF ANTI-NUCLEAR ANTIBODIES BEFORE ANTI-TNF THERAPY IS A RISK FACTOR FOR THE APPEARANCE OF ANTI-DRUG ANTIBODIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: TNF inhibitors (TNFi) revolutionized the treatment of rheumatoid arthritis (RA), but have often developed anti-drug antibodies (ADrA) and also induced other autoimmune pathology[1, 2].
Objectives: To determine whether presence of anti-nuclear antibodies (ANA) predict the development of ADrA and clinical efficacy in RA patients treated with TNFi, infliximab (IFX) or adalimumab (ADA).
Methods: A total of 92 RA patients, 38 cases treated with IFX and 54 cases with ADA, were prospectively enrolled. Observation period of IFX-treated group was 3 years, and that of ADA-treated group was 1 years. ANA were measured before and serially during the therapy. ANA were measured by indirect fluorescent assay using a Computer-aided microscope system with HEp20-10 cells. The concentrations of anti-IFX antibodies (HACA) and anti-ADA antibodies (AAA) were measured by radioimmunoassay at Sanquin Diagnostic Services, Netherlands. Clinical response to therapy was judged by EULAR response criteria based on Disease Activity Score (DAS) 28-CRP.
Results: Thirteen (34.2%) of 38 patients in IFX group and 18 (33.3%) of 54 patients in ADA group became positive for HACA and AAA, respectively, during the treatment. All of the ADrA-positive patients were ANA-positive before the therapy. In contrast, none became ADrA-positive after treatment in 15 RA patients negative for ANA before therapy (6 cases in IFX group and 9 cases in ADA group), and the positive rate for ADrA was significantly different between ANA-positive and negative patients (p=0.0018). In addition, the positive rate for HACA was significantly higher in patients positive for ANA titers of $\geq$640 (p=0.034), but that for AAA was not related to ANA titers. Next, ANA became positive in 4 of 6 ANA-negative patients and ANA titers increased in 21 of 32 ANA-positive patients after IFX treatment. HACA positive rate was significantly higher in patients with ANA titers of $\geq$640 after IFX treatment (p=0.0045). ANA titers of patients in ADA group were mostly unchanging after treatment, and were not related to the appearance of AAA.

Continuance rete of TNFi (IFX and ADA) treatment was significantly lower in ADrA-positive patients than in those negative (p=0.0066 and p=0.0127, respectively). In IFX group, patients with ANA titers of ≥160 before treatment and those with ANA titers of ≥ 320 after treatment positive showed worse EULAR treatment response (p=0.037 and p=0.033, respectively). In ADA group, 7 of 9 ANA-negative patients before treatment showed moderate or good EULAR response, but positive ANA both before and after treatment was not connected with to the clinical response.
Conclusion: The presence of ANA before IFX or ADA is a risk factor for the appearance of ADrA, while ADrA did not appeared in any patient negative for ANA before treatment. ANA of high titers before and after IFX treatment predicted existence of ADrA and possibly leading to the treatment failure.

REFERENCES

[1] Kalden JR, Shulze-Koops: Nat Rev Rheumatol, 2017, 13: 707-18.
[2] Takase K, et al: Ann Rheum Dis, 2014, 73: 1695-99.

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SAT0156 METHOTREXATE DISCONTINUATION AND DOSE DECREASES AFTER THERAPY WITH TOCILIZUMAB: RESULTS FROM THE CORRONA RHEUMATOID ARTHRITIS REGISTRY

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Background: Methotrexate (MTX) is frequently prescribed with biologic disease-modifying antirheumatic drugs. Evidence has shown that tocilizumab (TCZ) monotherapy is effective in the treatment of patients with rheumatoid arthritis (RA).[1,2] Similar outcomes have been shown in patients responding to TCZ combination therapy who discontinued MTX or remained on combination therapy.[3]
Objectives: To examine MTX discontinuation and dose decreases in patients with RA initiating TCZ and to describe disease activity outcomes in a real-world setting.
Methods: TCZ-naïve patients enrolled in the Corrona RA Registry who initiated TCZ and had a 6-month follow-up visit without discontinuation of TCZ were included. Patients were grouped by MTX dose at the time of TCZ initiation (≤ 10 mg, > 10 to ≤ 15 mg, > 15 to ≤ 20 mg, > 20 mg). The primary outcome was the proportion of patients with changes in MTX use at 6 months. Changes in disease activity (Clinical Disease Activity Index [CDAI]) and patient-reported outcomes (PROs) over the follow-up period are described.
Results: Of 444 eligible patients, 82.7% were female, and 83.7% were white, with a mean (SD) disease duration of 11.6 (9.3) years and a baseline CDAI score of 24.0 (15.4). The mean (SD) MTX dose at baseline was 17.7 (5.8) mg. Overall, a total of 139 patients (31.3%) discontinued or decreased MTX at 6 months (overall mean [SD] dose change, −3.0 [7.5] mg); across baseline MTX dose groups, the proportion of patients who discontinued or decreased MTX at 6 months ranged from 28.2% to 38.2%. Improvements in CDAI scores and PROs were observed at 6 months in all baseline MTX dose groups and in patients who discontinued, decreased, maintained, or increased MTX doses at 6 months (**Table 1**). Similar patterns and results were observed at 12 months (not shown).
Conclusion: A considerable proportion of patients initiating TCZ were able to discontinue or decrease the dose of MTX after TCZ initiation. Patients who were able to discontinue or decrease MTX experienced similar improvements in disease activity and functionality. Discontinuing or decreasing MTX may be an effective treatment strategy for patients initiating TCZ combination therapy.

Table 1. Change in Disease Activity and PROs* at 6 Months in Patients With RA

	All Patients (N = 444)	Discontinued MTX (n = 72)	Decreased MTX Dose (n = 67)	No Change in MTX Dose (n = 269)	Increased MTX Dose (n = 36)
CDAI	−7.8 (14.3)	−5.5 (13.1)	−7.1 (13.6)	−8.4 (14.7)	−9.8 (15.2)
DAS28	−1.2 (1.7)	−1.0 (1.7)	−1.1 (1.5)	−1.3 (1.6)	−0.9 (2.4)
Tender joint count	−3.2 (7.9)	−1.3 (7.1)	−1.8 (7.5)	−3.8 (8.1)	−4.2 (7.6)
Swollen joint count	−2.6 (5.6)	−2.2 (5.2)	−2.2 (5.1)	−2.7 (5.8)	−3.1 (6.1)
Physician global assessment	−13.1 (23.1)	−13.3 (23.4)	−17.0 (20.7)	−11.8 (23.4)	−16.2 (24.0)
Patient global assessment	−7.6 (25.9)	−6.4 (25.9)	−13.5 (28.5)	−6.4 (25.0)	−7.3 (26.4)
mHAQ	−0.1 (0.4)	−0.1 (0.4)	−0.1 (0.4)	0 (0.4)	−0.2 (0.5)
Patient pain	−7.3 (24.4)	−6.2 (23.7)	−8.2 (24.8)	−7.0 (24.3)	−10.8 (26.2)
Patient fatigue	−6.3 (26.6)	−7.3 (26.5)	−8.6 (30.7)	−5.0 (26.3)	−10.3 (20.2)
Morning stiffness present, n (%)	−29 (7.1)	−6 (9.4)	−5 (8.2)	−17 (6.8)	−1 (3.0)
Morning stiffness time, h	−0.1 (3.7)	−0.7 (2.8)	0 (2.1)	−0.1 (3.8)	0.3 (6.1)

CDAI, Clinical Disease Activity Index; DAS28, Disease Activity Score in 28 joints; mHAQ, modified Health Assessment Questionnaire; MTX, methotrexate; PRO, patient-reported outcome; RA, rheumatoid arthritis.
* Changes in disease activity and PRO measures are presented as mean (SD) unless otherwise indicated.

REFERENCES

[1] Bykerk VP, et al. Clin Rheumatol. 2015;34(3):563-571.
[2] Jones G, et al. Ann Rheum Dis. 2010;69(1):88-96.
[3] Kremer J, et al. *Arthritis Rheumatol*. 2018;70(8):1200-1208.

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SAT0157 REAL-WORLD EVALUATION OF PERSISTENCE WITH EARLY-LINE ABATACEPT VERSUS TUMOR NECROSIS FACTOR-INHIBITORS FOR RHEUMATOID ARTHRITIS COMPLICATED BY POOR PROGNOSTIC FACTORS

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Background: Abatacept reduces signs and symptoms, inhibits the progression of structural damage, and improves physical function in adult patients with moderately to severely active rheumatoid arthritis (RA). Real-world data on its use as an early-line biologic agent are limited.
Objectives: To assess 12-month treatment persistence in early-line abatacept versus tumor necrosis factor inhibitor (TNFi) treated patients with RA complicated by poor prognostic factors.
Methods: We performed a multicenter retrospective medical record review of adult RA patients with poor prognostic factors treated at 5 United States clinics located in the West, Midwest, and Southeast. Patients were treated with abatacept or TNFi as the first biologic treatment at the clinic (defined as early line). Poor prognostic factors included positive anti-cyclic citrullinated peptide antibodies, positive rheumatoid factor antibodies, increased C-reactive protein levels, elevated erythrocyte sedimentation rate levels, or presence of joint erosions. TNFis included adalimumab, etanercept, infliximab (and their biosimilars), certolizumab pegol, or golimumab. Data were collected from biologic treatment initiation (between 8/9/11 and 11/14/16) for ≥1 year. Patients with Crohn's disease, ankylosing spondylitis, ulcerative colitis, psoriatic arthritis, or anal fistula were excluded. Demographic, disease, and treatment information (start, stop, reason for discontinuation) was abstracted. Treatment persistence (continuation of index treatment with gap ≤60 days) at 12 months and time to discontinuation were reported. Multivariate logistic and Cox regressions were used to compare 12-month persistence and overall discontinuation rate between abatacept and TNFi, controlling for demographic and clinical characteristics (age, sex, Charlson comorbidity index, RA duration), baseline utilization, and clinic.
Results: Data on 209 patients (88 abatacept, 121 TNFi) were collected. Abatacept patients were older than TNFi patients (64.36 vs. 57.23 years, p<0.001). There were no significant differences in either gender (79.55% vs. 72.73% female, p=0.257) or duration of treatment at the clinic (5.79 vs. 5.10 years, p=0.226) in the abatacept and TNFi cohorts. Median time to discontinuation was 1,672 days for abatacept vs. 612 days for TNFi (p=0.002). At 12 months, 86.36% of abatacept patients were persistent

vs. 65.29% of TNFi patients (p<0.001). In the Cox model, rate of discontinuation was 77% higher in TNFi patients (Hazard Ratio 1.767, 95% Confidence Interval (CI) 1.113-2.806, p=0.0158). In the logistic regression, the odds of TNFi patients being persistent at 12 months was 52% lower than abatacept patients, although this difference was not statistically significant (Odds Ratio 0.485, 95% CI 0.208-1.133, p=0.0947). Reasons for discontinuation of index treatment differed between cohorts, including discontinuation due to disease progression (27.78% vs. 53.85%), insurance coverage (19.44% vs. 12.82%), and adverse events of medication (2.78% vs. 11.54%) in abatacept and TNFi patients, respectively (p<0.001).

Conclusion: In a real-world setting, RA patients with poor prognostic factors are significantly less likely to discontinue abatacept compared with TNFi. This difference may be explained by the lower proportion of patients discontinuing abatacept due to disease progression or adverse events related to medication.

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SAT0158 FACTORS ASSOCIATED TO PERSISTENCE OF TREATMENT WITH GOLIMUMAB IN THE BIOBADASER REGISTRY, WITH UP TO 6 YEARS OF FOLLOW-UP

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Background: Survival, or persistence in treatment with a biological drug can be considered an indirect measure of efficacy, safety and tolerability

Objectives: We assessed the probability of persistence (survival) of treatment with golimumab in patients with rheumatic diseases and the factors associated to persistence with up to 6 years of follow-up.

Methods: BIOBADASER is the Spanish registry of biological drugs of the Spanish Society of Rheumatology and the Spanish Medicines Agency. A data-base analysis was done in December 2018 on all the patients aged 18 years or more who had initiated golimumab for one of the approved indications (rheumatoid arthritis [RA], axial spondyloarthritis [SpA] or psoriatic arthritis [PsA]). The probability of persistence was calculated with a Kaplan-Meier test. Factors related to persistence were analyzed with a Cox-regression model.

Results: 581 patients were included (165 [28.4%] RA, 249 [42.9%] axial SpA and 167 [28.7%] PsA), mean age 51 [12] years, 53% women). Median duration of disease at the onset of golimumab was 8.0 (3.0-14.7) years. Golimumab was prescribed as first biological drug in 37.9% of the patients, as second in 32.1% and as third or further in 30.0%. Concomitant medications at golimumab initiation included steroids (28.2%), methotrexate (MTX) (35.5%), sulphasalazine (7.2%) and leflunomide (13.9%). The probability of persistence of treatment with golimumab since treatment initiation was 74.3% at year 1 (95% CI 70.3 – 77.8), 63.5% at year 2 (59.0 – 67.6), 60.5% at year 3 (55.9 – 65.8), 54.5% (49.1 – 59.7) at year 4 and 5, and 52.1% (44.9 – 57.7) at year 6. Persistence was higher when golimumab was used as first biological agent (p log-rank <0.001) and for the treatment of axial SpA or PsA compared to RA (p log-rank <0.001). As first biological drug the probability of persistence was 82.8% (year 1) and 66.5% at year 4. At year 5, survival rates (all lines of therapy) were 59.7%, 63.4% and 37.3% for axial SpA, PsA and RA respectively. Cox-regression analysis (table) showed that the probability of persistence in treatment with golimumab therapy was higher in first vs second or third biological line patients (Hazard Ratio [HR] for discontinuation: 1.78 for second and 2.41 for third or further line versus first line), in SpA and PsA patients (HR discontinuation of RA patients: 1.94 versus PsA), and lower in women (HR: 1.62), in those needing steroids (HR: 1.47) or DMARDs different to MTX (HR: 2.17). Patients treated with MTX had higher but non-significant persistence rate (HR discontinuation 0.79, table).

Conclusion: The probability of persistence (survival) on therapy with golimumab was high up to 6 years of follow-up and was higher in patients treated with golimumab as first biological drug or for PsA and SpA, and lower in those needing steroids, DMARDs different to MTX and in women.

Table. Cox-regression analysis. HR for discontinuation of golimumab

	Hazard Ratio	95% Confidence interval	p
Gender (women vs men)	1.62	(1.17-2.25)	0.004
Age at golimumab initiation	1.00	(0.99-1.02)	0.516
Smoking habit (smoker vs non-smoker)	1.32	(0.94-1.85)	0.107
Smoking habit (past smoker vs non-smoker)	1.10	(0.69-1.77)	0.686
Overweight (vs normal)	1.29	(0.87-1.92)	0.200
Obesity (vs normal)	1.17	(0.77-1.77)	0.467
Second vs first biological drug	1.78	(1.24-2.55)	0.002
Third vs first biological drug	2.41	(1.69-3.43)	<0.001
RA vs PsA	1.94	(1.33-2.82)	<0.001
Axial SpA vs PsA	1.22	(0.83-1.79)	0.321
Methotrexate	0.79	(0.58-1.07)	0.122
Steroids	1.47	(1.07-2.02)	0.017
Other DMARD	2.17	(1.23-3.83)	0.008

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SAT0159 CHANGING PATTERN OF THE USE OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS

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Background: During the last 15 years, the comprehensive understanding of the safety, effectiveness, expanding access, and availability of new biologic disease-modifying antirheumatic drugs (bDMARDs) has likely contributed to the pattern of use of these compounds in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS).

Objectives: To assess changes in the baseline characteristics of patients who underwent biological therapy from 2007 to 2018 in a real world setting.

Methods: Data were obtained from BIOBADASER, the Spanish registry of biologics. Recorded data is obtained from routine clinical practice. Patients diagnosed with RA, PsA and AS and who started biological treatment from 2007 to 2018 were included. Sociodemographic and clinical variables, as well as first bDMARD used, were stratified by the starting year period (2007-2009; 2010-2012; 2013-2015; 2016-2018) and compared using Anova and Chi-square tests.
Results: 6943 patients (2827 RA patients, 1274 PsA and 1261 AS) were included in this analysis (Table 1). Patient age at the beginning of the first biologic was significantly higher during the period 2016-2018 than in 2007-2009 (48.3 vs 50.6). Disease duration until the use of biologics decreased from 8.6 to 8.1 years. In RA patients, disease activity, as assessed by DAS28 at the start of the biological treatment, was significantly higher in the 2007-2009 period than in the last period analyzed (5.1 vs 4.7). The use of TNF inhibitor as a first option also changed significantly (94.6% vs 58.5%). Regarding comorbidities, the number of rheumatic patients treated with biologics and a past history of cancer (1.8% vs 3.7%), ischemic heart disease (1.8% vs 3.1%), hypercholesterolemia (13.6% vs 26.1%), or hypertension (21.7% vs 23.7%) has increased significantly.
Conclusion: Our data show that during the last decade the pattern of use of biologics in patients with rheumatic diseases has changed. Nowadays these compounds are used in older patients, with shorter disease duration, with lower disease activity in RA, and with more comorbidities.

Table 1. Patient characteristics at the start of biological treatment. Pattern of use.

Variable	Period of time				p
	2007-2009	2010-2012	2012-2015	2016-2018	
Patients included	2243	1240	371	3089	
Sex (women) (%)	1361 (60.7)	770 (62.1)	213 (57.4)	1858 (60.1)	0.393
Mean age (SD)*	48.3 (15.5)	48.9 (15.5)	46.6 (18.2)	50.6 (14.6)	<0.001
Disease duration (SD)*	8.6 (9.0)	8.5 (12.7)	7.2 (8.9)	8.1 (8.2)	0,075
TNF-inhibitor as first biologic (%)	94.6	76.4	79.8	58.5	<0.001
RA (%)	94.1	61.3	62.8	37.7	<0.001
AS (%)	100	98.5	100	87.7	<0.001
PsA (%)	99.7	97.2	100	71.1	<0.001
DAS28 (only in RA)*	5.1 (1.6)	4.7 (1.6)	4.2 (2.0)	4.7 (1.4)	<0.001
Comorbidities, n (%)					
Cancer	40 (1.8)	21 (1.7)	4 (1.1)	113 (3.7)	<0.001
Ischemic cardiopathy	41 (1.8)	21 (1.7)	9 (2.4)	97 (3.1)	0,005
Hypercholesterolemia	305 (13.6)	185 (14.9)	53 (14.3)	805 (26.1)	<0.001
Hypertension	486 (21.7)	244 (19.7)	57 (15.4)	733 (23.7)	<0.001
Smoker	376 (16.8)	177 (14.3)	55 (14.8)	650 (21.0)	<0.001

***At the beginning of first biologics.**
*At the beginning of first biologics.

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SAT0160 PREFERENCES OF EUROPEAN RHEUMATOLOGISTS ON THE DISCONTINUATION OF BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The introduction of biologic disease-modifying antirheumatic drugs (bDMARDs) revolutionized the treatment of rheumatoid arthritis (RA) and made remission (REM) or low disease activity (LDA) a realistic goal for most patients. It was shown that the discontinuation of bDMARDs in patients in REM or LDA is feasible (1,2) and that the physician's opinion plays an important part in the decision to discontinue (3). However, there is no reliable way of identifying patients who would benefit from bDMARD discontinuation after reaching REM or LDA.
Objectives: To identify the preference of rheumatologists regarding different parameters while discontinuing a bDMARD in their patients.
Methods: A systematic literature review was conducted with the aim of identifying predictors of successful bDMARD discontinuation in RA patients in REM or LDA. These predictors were then adapted into general parameters and sorted into different categories: patient demographics (n=6), disease activity (n=6), patient reported outcomes (n=6), treatment related parameters (n=5), laboratory parameters (n=6) and imaging parameter (n=5). Those parameters were reviewed by an expert panel and then distributed to rheumatologists in Europe. Rheumatologists were asked to state whether they find the presented parameter important to support their decision to discontinue bDMARD therapy or not. They also had the opportunity to state parameters they consider important.
Results: 313 rheumatologists from 29 different European countries responded. Most of the participants have been practicing for 10 to 20 years and see 10 to 25 RA patients per week. The majority of the parameters were considered important by the participants, with 19 out of the 34 presented parameters being considered important by $\geq$ 70%. The most commonly considered parameters were (percentage of participants who considered the parameter important): Time in REM or LDA (99%), c-reactive protein (96%), swollen joint count (93%), concomitant conventional synthetic DMARD therapy (93%) and disease activity score – 28 joints (90%). The least commonly considered parameters were: simplified disease activity score (48%), gray scale positivity (47%), rheumatoid factor (41%), smoking status (35%), gender (13%), interleukin-6 (9%) and shared epitope (8%). An overview of responses is given in ***figure 1***. and ***figure 2***.. The most frequently mentioned parameter in the comments was the patient's opinion on discontinuation (n=28).

Figure 1. Opinion on presented parameters

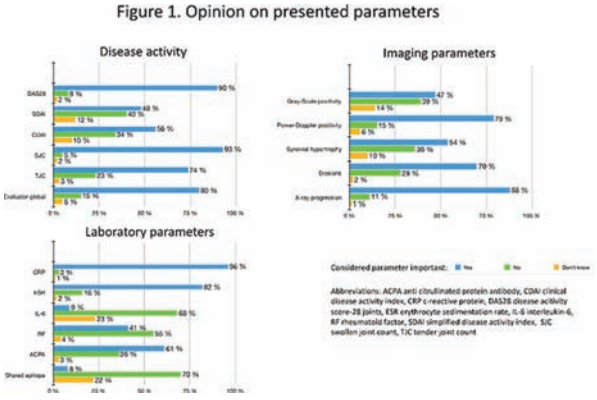
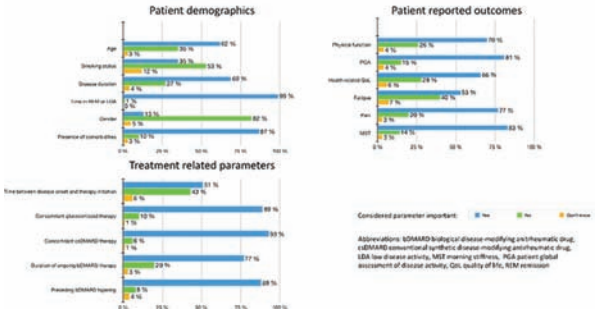


Figure 2. Opinion on presented parameters



Conclusion: Rheumatologists appear to be very diligent in the things they consider when discontinuing bDMARDs in their patients. 19 of the 34 parameters have been considered important by $\geq$ 70% of participants. This might be because the presented parameters were based on predictors of successful discontinuation. This data gives insight into the current state of bDMARD discontinuation and can be used in further research to help identifying patients who would benefit from bDMARD discontinuation.

REFERENCES

[1] van den Broek M, Klarenbeek NB, Dirven L, van Schaardenburg D, Hulsmans HM, Kerstens PJ, et al. Discontinuation of infliximab and potential predictors of persistent low disease activity in patients with early rheumatoid arthritis and disease activity score-steered therapy: subanalysis of the BeSt study. Annals of the rheumatic diseases. 2011;70(8):1389-94.

[2] Tanaka Y, Yamanaka H, Ishiguro N, Miyasaka N, Kawana K, Kimura J, et al. Low disease activity for up to 3 years after adalimumab discontinuation in patients with early rheumatoid arthritis: 2-year results of the HOPEFUL-3 Study. Arthritis Res Ther. 2017;19(1):56.

[3] Strand V, Miller P, Williams SA, Saunders K, Grant S, Kremer J. Discontinuation of Biologic Therapy in Rheumatoid Arthritis: Analysis from the Corrona RA Registry. Rheumatol Ther. 2017;4(2):489-502.

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SAT0161 SUSTAINED MODERATE DISEASE ACTIVITY (SMDA) IN RHEUMATOID ARTHRITIS PATIENTS ON BIOLOGIC THERAPIES IS ASSOCIATED WITH 5 YEARS FUNCTIONAL LIMITATION AND SERIOUS ADVERSE EVENTSDEVELOPMENT; EVIDENCE TO SUPPORT TREAT-TO-TARGET APPROACH FOR PATIENTS IN SMDA AND ESPECIALLY THOSE IN HIGH SMDA

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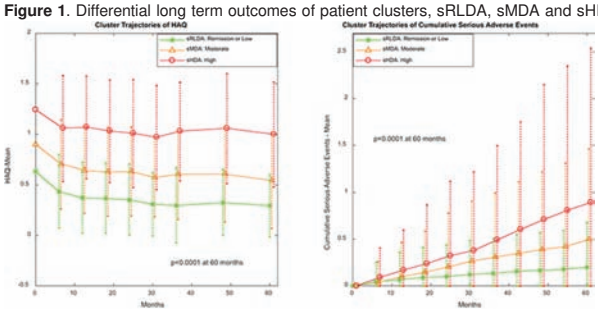
Background: Registry data have shown that treatment with biologic disease modifying antirheumatic drugs (bDMARDs) induces remission or low disease activity in up-to 50% of Rheumatoid Arthritis (RA) patients, yet 30-50% of patients remain in moderate disease activity (MDA) with limited data on their long-term prognosis [1].

Objectives: To assess the long-term outcome of RA patients with sustained MDA on bDMARDs, in clinical practice.

Methods: We analyzed data from the Hellenic Registry of Biologic Therapies. Disease activity, function, treatments of patients starting a bDMARD are recorded prospectively every 3-6 months. Herein, we included patients with at least 5 years of follow-up, irrespective of treatment switches. If DAS28-ESR was at the same disease activity range for at least 50% of the follow-up time, patients were assigned to one of 3 main groups: sustained remission or low disease activity (sRLDA) with DAS≤3.2, sustained moderate disease activity (sMDA) with 3.2<DAS≤5.1 and sustained high disease activity (sHDA) with DAS>5.1. Patients in sMDA were further divided into subgroups *low* and *high sMDA* (50% of follow-up has DAS lower or greater than 4.2 respectively). Function at 5 years based on Health Assessment Questionnaire (HAQ) was the primary outcome, while cumulative serious adverse events (SAEs) and bDMARDs switches were also analyzed.

Results: Out of 527 patients with available data, 90 (17%), 295 (56%) and 142 (27%) were assigned to sRLDA, sMDA and sHDA groups respectively. At baseline, sMDA patients were older, more often women, had received more csDMARDs and had higher DAS, HAQ and EuroQol status compared to sRLDA group. During follow-up, sMDA patients had more bDMARDs switches as compared to sRLDA (mean ±sd: 1.82 ±1.03 vs 1.26 ±0.53, p<0.0001). Notably, patients in sMDA had significant improvement in HAQ at 5 years compared to baseline (p<0.0001), yet they presented significantly higher HAQ compared to sRLDA group (mean ±sd: 0.55 ±0.47 vs 0.30 ±0.31, p<0.0001). Trajectories of longitudinal HAQ for groups sRLDA, sMDA and sHDA, were clearly differentiated during treatment course (Figure 1). Clusters sRLDA, sMDA and sHDA also displayed differential 5 years outcomes (p<0.0001) regarding SAEs (Figure 1). Interestingly, within sMDA patients, the *low sMDA* patient subgroup had better long-term outcome (p<0.05) concerning both HAQ at 5 years and cumulative SAEs as compared to patients in *high sMDA* subgroup

Figure 1. Differential long term outcomes of patient clusters, sRLDA, sMDA and sHDA



Conclusion: In clinical practice 56% of RA patients on bDMARDs have sustained MDA in spite of bDMARDs switches, presenting 5 years worse functional status and more SAEs compared to patients in sRLDA. These data support the treat-to-target approach for patients in sMDA and especially those with high sMDA.

REFERENCE

[1] I. Flouri, et al., Comparative effectiveness and survival of infliximab, adalimumab, and etanercept for rheumatoid arthritis patients in the Hellenic Registry of Biologics: Low rates of remission and 5-year drug survival. Seminars in arthritis and rheumatism 43 (2014).

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SAT0162 A POOLED ANALYSIS OF 1-YEAR CLINICAL OUTCOMES AMONG 6-MONTH RESPONDERS AND NON-RESPONDERS FROM THREE RANDOMISED CONTROLLED STUDIES OF TNF INHIBITOR BIOSIMILARS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: SB4, SB2, and SB5 are biosimilars of etanercept, infliximab, and adalimumab. Phase III randomised, double-blind studies were conducted to compare efficacy and safety between biosimilars and reference products.

Objectives: Assess and compare 1-year outcomes among 6-month responders and non-responders.

Methods: Patients who had 6-month data from each phase III study were pooled and categorised, based on their disease status at 6 months (week 24 for etanercept and adalimumab and week 30 for infliximab) and 1 year (week 52 for etanercept and adalimumab and week 54 for infliximab).

Responders included patients who achieved an ACR20 response or low disease activity (including remission) by DAS28, SDAI, or CDAI at 6 months. Those who did not or dropped out were considered non-responders.

Primary outcome was the proportion of responders who maintained responses from 6 months to 1 year or non-responders at 6 months who achieved responses at 1 year.

Results: Data from 1461 patients were included in the analysis. For all treatments combined, 81.1% of ACR20 responders, 69.6%, 77.8%, and 77.0% of responders with DAS28, SDAI, and CDAI low disease activity (LDA) at 6 months maintained their responses at 1 year, and 33.9%, 18.8%, 26.7%, and 24.9% of 6-month non-responders achieved responses at 1 year, respectively. The proportions of patients maintaining or achieving an ACR20 response or DAS28, SDAI, and CDAI LDA at 1 year were similar across different treatment groups (Table 1).

Conclusion: A pooled analysis of TNF inhibitor biosimilars and reference products showed that about 20-30% of responders lost their response, while about 20-30% gained it. Thus, the overall stability of disease fluctuation in our 1-year phase III studies is a consequence of a similar success and failure rate. The validity of these data can be seen by the similarities in these outcomes between different types of TNF-inhibitors and similarity between biosimilars and respective reference products.

REFERENCES

[1] Emery, et al. Rheumatology. 2017 Dec;56(12):2093-2101.
[2] Smolen, et al. Ann Rheum Dis. 2018 Feb;77(2):234-240.
[3] Weinblatt, et al. Arthritis Rheumatol. 2018 Jan;70(1):40-48.

Table 1. Proportion of responders at 1 year based on 6-month clinical outcomes

Group	ACR20 responders* at 1 year (n/n', %)		DAS28 responders at 1 year (n/n',%)		SDAI responders at 1 year (n/n',%)		CDAI responders at 1 year (n/n',%)	
	Responder at 6 month	Non-responder at 6 month	Responder at 6 month	Non-responder at 6 month	Responder at 6 month	Non-responder at 6 month	Responder at 6 month	Non-responder at 6 month
All Tx Combined	850/1048 (81.1%)	140/413 (33.9%)	302/434 (69.6%)	193/1027 (18.8%)	509/654 (77.8%)	215/804 (26.7%)	489/635 (77.0%)	206/826 (24.9%)
BS Combined	465/564 (82.4%)	85/231 (36.8%)	177/241 (73.4%)	118/554 (21.3%)	287/359 (79.9%)	112/433 (25.9%)	275/350 (78.6%)	114/445 (25.6%)
RP Combined	385/484 (79.5%)	55/182 (30.2%)	125/193 (64.8%)	75/473 (15.9%)	222/295 (75.3%)	103/371 (27.8%)	214/285 (75.1%)	92/381 (24.1%)
SB4+ETN	359/433 (82.9%)	46/126 (36.5%)	121/175 (69.1%)	73/384 (19.0%)	219/270 (81.1%)	77/289 (26.6%)	207/255 (81.2%)	73/304 (24.0%)
SB2+INF	252/334 (75.4%)	49/184 (26.6%)	83/133 (62.4%)	51/385 (13.2%)	157/217 (72.4%)	59/300 (19.7%)	156/218 (71.6%)	54/300 (18.0%)
SB5+ADA	239/281 (85.1%)	45/103 (43.7%)	98/126 (77.8%)	69/258 (26.7%)	133/167 (79.6%)	79/215 (36.7%)	126/162 (77.8%)	79/222 (35.6%)
SB4	183/220 (83.2%)	27/67 (40.3%)	67/93 (72.0%)	41/194 (21.1%)	118/145 (81.4%)	36/142 (25.4%)	111/137 (81.0%)	39/150 (26.0%)
ETN	176/213 (82.6%)	19/59 (32.2%)	54/82 (65.9%)	32/190 (16.8%)	101/125 (80.8%)	41/147 (27.9%)	95/118 (81.4%)	34/154 (22.1%)
SB2	123/161 (76.4%)	24/92 (26.1%)	44/65 (67.7%)	28/188 (14.9%)	80/108 (74.1%)	25/144 (17.4%)	79/108 (73.1%)	25/145 (17.2%)
INF	129/173 (74.6%)	25/92 (27.2%)	39/68 (57.4%)	23/197 (11.7%)	77/109 (70.6%)	34/156 (21.8%)	77/110 (70.0%)	29/155 (18.7%)
SB5	159/183 (86.9%)	34/72 (47.2%)	66/83 (79.5%)	49/172 (28.5%)	89/108 (84.0%)	51/147 (34.7%)	85/105 (81.0%)	50/150 (33.3%)
ADA	80/98 (81.6%)	11/31 (35.5%)	32/43 (74.4%)	20/66 (23.3%)	44/61 (72.1%)	28/68 (41.2%)	41/57 (71.9%)	29/72 (40.3%)

ACR, American college of rheumatology; ADA, reference product adalimumab; BS, biosimilars; CDAI, Clinical Disease Activity Index scores; DAS28, disease activity score based on 28-joint count; ETN, reference product etanercept; INF, reference product infliximab; RP, reference products; SDAI, Simplified Disease Activity Index scores; Tx, treatments
*Responders included patients who achieved an ACR20 response or low disease activity (including remission) by DAS28, SDAI, or CDAI.

Disclosure of Interests: Josef S. Smolen Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Michael E. Weinblatt Shareholder of: Stock option: CanFite, Lycera, Scipher, Inmedix, Grant/research support from: Crescendo Bioscience, Bristol Myers Squibb, Sanofi, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, CanFite, Corrona, Crescendo, GlaxoSmithKline, Gilead, Horizon, Lilly, Lycera, Merck, Novartis, Pfizer, Roche, Samsung, Scipher, Set Point, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead,Samsung, Sandoz and Lilly, Jung-Yoon Choe: None declared, Jonathan Kay Grant/research support from: Gilead Sciences, Pfizer, UCB Pharma, Consultant for: AbbVie, Boehringer Ingelheim GmbH, Celltrion Healthcare, Merck Sharp & Dohme Corp., Novartis Pharmaceuticals, Pfizer, Samsung Bioepis, Sandoz, UCB Pharma, Jieun Lee Employee of: Samsung Bioepis, Gihyun Myung Employee of: Samsung Bioepis, Hyoryeong Seo Employee of: Samsung Bioepis, Jeehoon Ghil Employee of: Samsung Bioepis
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SAT0163 LOW CARDIOVASCULAR EVENT RATE DURING TOCILIZUMAB TREATMENT IN THE NON-INTERVENTIONAL STUDY ICHIBAN

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Background: Rheumatoid arthritis (RA) patients (pts) have a 1.5 to 2-fold increased risk for cardiovascular (CV) events and CV mortality [1]. Traditional risk factors as well as underlying disease, including therapy with glucocorticoids (GC) contribute to the increased CV risk. Typical risk factors include age, male sex, hypertension, adiposity, and diabetes mellitus [2].

Objectives: The exploratory post-hoc analysis of the non-interventional study (NIS) ICHIBAN (NCT 01194401, final dataset) investigated the CV risk of RA pts during intravenous tocilizumab (TCZ) treatment over 2 years.

Methods: Data of 3164 pts (total) who received at least one dose of TCZ were available. Analysis focuses on the CV events myocardial infarction (MI), coronary heart disease (CHD), and stroke. The incidence of respective treatment-emergent adverse events (TEAEs) (according to MedDRA preferred term) and/or AEs of special interest (AESIs, recorded by the investigator) was evaluated. The following risk factors (at baseline [BL]) were analysed: sex, age, smoking status, RA duration, DAS28, CDAI, seropositivity, CRP, comorbidities, previous therapies, concomitant therapies, and combinations thereof.

Results: At BL, pts were more frequently female (74.8%), on average 55.5 years old, had a mean BMI of 26.9 kg/m2, and mean RA duration of 9.7 years. 72% of pts suffered from comorbidities (37% hypertension, 17% osteoporosis, 10% diabetes mellitus).The majority (66.4%) was pre-treated with TNF inhibitors, while 30.0% received csDMARDs only. Co-medication was csDMARDs in 50.7% of pts and GC in 80.6%.

Overall, 46.6% of pts experienced at least 1 TEAE. The rate of pts who experienced a CV event was 0.8% for MI, 0.4% for CHD, and 0.6% for stroke (Table 1).

Table 1 Treatment-emergent adverse events (TEAEs) during TCZ treatment

	Total (n = 3164)
AEs	
• No. of patients with AE, % (n)	46.6 (1474)
• Rate of AEs per 100 patient years	108.4
SAEs	
• No. of patients with SAE, % (n)	14.9 (472)
• Rate of SAEs per 100 patient years	23.9
Fatal	
• No. of patients with fatal event, % (n)	0.6 (19)
• Rate of fatal events per 100 patient years	0.9
Myocardial infarction	
• No. of patients with MI, % (n)	0.8 (26)
• Rate of MIs per 100 patient years	0.8
Coronary heart disease	
• No. of patients with CHD, % (n)	0.4 (14)
• Rate of CHDs per 100 patient years	0.5
Stroke	
• No. of patients with stroke, % (n)	0.6 (18)
• Rate of strokes per 100 patient years	0.6

For patients with typical risk factors a higher rate of CV events was observed: male pts, pts of higher age, pts who were anti-CCP negative, and pts who suffered from diabetes mellitus, coronary heart disease (only for CHD), asthma, and renal insufficiency (see Table 2 for details; exploratory p-values are given).

Interestingly, no differences were observed between subgroups of smoking status, RA duration, DAS28, CDAI, CRP, previous therapies, concomitant therapies, and combinations thereof (data not shown).

Table 2 Observed occurrence of cardiovascular events (TEAEs) in different subgroups (based on pts with respective TEAE)

Risk factor (at BL)	Myocardial infarction	Coronary heart disease	Stroke
Sex, % (n)			
• Male (n = 797)	1.4 (11)	0.8 (6)	0.9 (7)
• Female (n = 2367)	0.6 (15)	0.3 (8)	0.5 (11)
• p value	0.0435	0.1270	0.1794
Age groups, % (n)			
• < 50 years (n = 924)	0.4 (4)	0.2 (2)	0.3 (3)
• 50 – 65 years (n = 1496)	0.9 (13)	0.4 (6)	0.7 (10)
• > 65 years (n = 744)	1.2 (9)	0.8 (6)	0.7 (95)
• p value	0.2068	0.2042	0.5328
Seropositivity, % (n)			
• Anti-CCP positive (n = 983)	0.9 (9)	0.3 (3)	0.2 (2)
• Anti-CCP negative (n = 203)	2.0 (4)	0.5 (1)	2.0 (4)
• p value	0.2547	0.5286	0.0094
Diabetes mellitus, % (n)			
• With (n = 314)	2.5 (8)	1.9 (6)	1.3 (4)
• Without (n = 2844)	0.6 (18)	0.3 (8)	0.5 (14)
• p value	0.0004	<0.0001	0.0900
Coronary heart disease, % (n)			
• With (n = 140)	0.7 (1)	3.6 (5)	0.0 (0)
• Without (n = 3018)	0.8 (25)	0.3 (9)	0.6 (18)
• p value	1.0000	<0.0001	1.0000
Asthma, % (n)			
• With (n = 111)	1.8 (2)	0.9 (1)	0.9 (1)
• Without (n = 3047)	0.8 (24)	0.4 (13)	0.6 (17)
• p value	0.2318	0.3947	0.4758
Renal insufficiency, % (n)			
• With (n = 90)	2.2 (2)	2.2 (2)	3.3 (3)
• Without (n = 3068)	0.8 (24)	0.4 (12)	0.5 (15)
• p value	0.1684	0.0585	0.0134

*Percentages refer to the number of pts with remission data available
TEAE: Treatment-emergent adverse event
P values from Chi-Square test. In case Chi-Square test was not valid, Fisher's exact test was used

Conclusion: In the NIS ICHIBAN, with its long-lasting patient population, the rate of CV events during TCZ treatment was comparable to former

investigations [1, 3, 4]. In pts with the typical risk characteristics at BL, i. e. male sex, higher age, diabetes mellitus, and CHD, higher rates of CV events were observed. In addition, increased rates were also found in anti-CCP negative pts and in pts with asthma or renal insufficiency

REFERENCES

[1] Pujades-Rodriguez M, et al. PLoS ONE 11(3): doi:10.1371/journal. pone.0151245.
[2] Löwel H, et al. Robert Koch Institut. Heft 33.
[3] Mohan S, et al. ACR2017-550.
[4] Giles JT, et al. ACR2016-969.

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SAT0164

COMPARISON OF THE RETENTION RATE OF EACH BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUG GROUP ACCORDING TO THE STATUS AND CONCENTRATION OF ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY AND RHEUMATOID FACTOR: DOUBLE CENTERCLINICAL STUDY

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Background: Although biological disease-modifying antirheumatic drugs (bDMARDs) have markedly improved the clinical course for patients with rheumatoid arthritis (RA), there are no reliable predictors of treatment response in individual patients. The drug retention rate in observational studies can be considered as a composite measure and index of drug effectiveness[1)].
Objectives: The aim of this study was to investigate potential predictors for bDMARDs by clarifying and comparing the retention ratio of bDMARDs according to the status and concentration of anti-cyclic citrullinated peptide antibody (anti-CCP), rheumatoid factor (RF), and antinuclear antibody (ANA).
Methods: We included consecutive RA patients from Mitsui Memorial Hospital and Kawakita General Hospital (both in Tokyo) who received bDMARD treatment between April 2018 and August 2018. We obtained data on the administered bDMARDs and the reason for discontinuation for each patient, and collected patient information, including the status of RF and ANA, at the initiation of each bDMARD, as well as the baseline status and concentration of anti-CCP. We categorized infliximab, etanercept, adalimumab, golimumab, and certolizumab pegol as TNF inhibitors (TNFi), and compared the TNFi group with the tocilizumab (TCZ) group and abatacept (ABT) group in terms of patient characteristics and retention rate. Statistical analysis of the group comparison was performed using one way ANOVA and Kruskal-Wallis tests, and categorical data were assessed by Fisher's exact test. The retention ratio was compared using the Kaplan-Meier generalized Wilcoxon test.
Results: This study included 214 patients (male 34, female 180, mean age 66.8) and 305 bDMARD cases were analyzed. The TNFi group included 160 cases, and the TCZ group and ABT group comprised 66 and 79 cases, respectively. Overall, the ABT group had the highest retention rate compared with the TNFi and TCZ groups, and the persistency rate of the ABT group at 60 months was 66.1%. Reasons for discontinuation of bDMARDs were insufficient efficacy (63.0%) and adverse events (29.4%). There was no significant difference regarding to the retention rate between anti-CCP negative and -positive patients or between RF-negative and -positive patients in each bDMARD group. After stratifying all patients according to anti-CCP status and concentration, among the three bDMARD groups, the ABT group (n=70) had the highest retention rate ($p<0.05$) in the anti-CCP-positive category, whereas the TCZ group (n=12) had the highest retention rate ($p=0.27$) in the anti-CCP-negative category. Regarding the concentration of anti-CCP, in the $\geq$ 100 U/ml category, the ABT group (n=42) had the highest retention rate ($p<0.05$), but such differences were not found in the 4.4 - <100 U/ml category. The persistency rates of the ABT group in the $\geq$ 100 U/ml category at 60 months was 73.4%. Moreover, the ABT group (n=59) had the highest retention rate ($p<0.05$) in the RF-positive category, whereas the TCZ group (n=20) had the highest retention rate in the RF-negative category ($p=0.15$). The persistency rate of the ABT group in the RF-positive category at 60 months was 68.3%. There were no significant differences in the retention rate among the three bDMARD groups in the ANA-negative or -positive categories.
Conclusion: The status and concentration of anti-CCP, and the status of RF were found to be useful predictors for bDMARD efficacy in patients with RA.

REFERENCE

[1] Ebina K, et al. Drug retention and discontinuation reasons between seven biologics in patients with rheumatoid arthritis – The ANSWER cohort study-. PLoS ONE 2018;13:e0194130

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SAT0165

PERSPECTIVES OF WOMEN WITH CHRONIC RHEUMATIC DISEASES ON THEIR JOURNEY TO MOTHERHOOD: COMPARISON OF SURVEYS FROM ASIA-PACIFIC AND EUROPE

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Background: The onset and diagnosis of chronic rheumatic disease (CRD) in women often overlap with their peak reproductive years. A previous survey[1] reported fears and misconceptions amongst women with CRD in Germany, France, UK, Italy and Spain (EU5) on their journey to motherhood.
Objectives: To explore the perspectives of women with CRD in Asia-Pacific (APAC) regarding disease management and pregnancy, and the support they receive compared with patients in Europe.
Methods: Women of childbearing age (18−45 years) with self-reported moderate to severe CRD (rheumatoid arthritis [RA], psoriatic arthritis [PsA], axial spondyloarthritis [axSpA]/ankylosing spondylitis [AS]) from Australia (AUS), Japan (JPN) and Hong Kong/Taiwan (HK/TW) completed a 20-min online survey (Sep−Nov 2018), similar to the previous EU5 survey.[1] Participants had been pregnant in the past 2–5 years.
Results: 210 APAC participants had CRD (RA: n=122, PsA: n=48, axSpA/AS: n=40); 306 EU5 participants had CRD. Most APAC patients had moderate CRD (77%; severe: 23%). In their most recent pregnancy, 40% of the women were actively trying to get pregnant, 40% were neutral and 20% were either not thinking about a pregnancy or were actively trying to avoid it. Prior to pregnancy, more women consulted rheumatologists (62%) vs primary care physicians (26%) or OB/GYNs (20%; multiple responses were possible). Pregnancy planning was first discussed with a healthcare professional (HCP) at diagnosis (33%), at treatment initiation

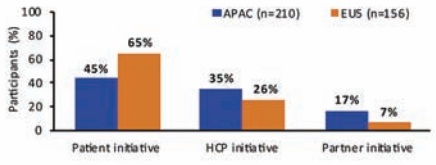
(32%) or during a regular visit (30%). Similar to EU5, discussions on family planning with HCPs in APAC were most often initiated by patients (Figure A). APAC and EU5 patients delayed pregnancy for similar reasons including: fear of passing on health issues to their child, not feeling physically healthy enough to carry a child to term, not being emotionally ready to become a parent (Figure B). Antepartum, 55% of women reported disease improvement, 27% stable disease and 18% worsening disease activity. Compared with EU5, APAC women were less likely to have a treatment plan aligned between HCPs (APAC: 50%; EU5: 65%). The most frequently reported reasons for cessation of medications in pregnancy were 'worried about the treatment harming the foetus' (HK/TW: 68%; JPN: 59%; EU5: 54%) and 'switched to a safer treatment' (AUS: 52%). Similar to EU5, most women in APAC discussed breastfeeding with an HCP (>85%). However, whether women felt they had to decide between treatment and breastfeeding postpartum varied (HK/TW: 79%; EU5: 69%; JPN: 66%; AUS: 43%). Compared with EU5, fewer women in APAC felt they had all the information they needed on the impact of rheumatic disease and treatment on pregnancy and health (APAC: 34%; EU5: 56%).

Conclusion: Fears and misconceptions about family planning, pregnancy and breastfeeding are common amongst women with CRD in APAC and Europe. In APAC, there may be a greater need for patient access to consistent and accurate information. Pregnancy planning with input from both physicians and obstetricians could alleviate patient concerns and minimise delays to pregnancy or treatment interruption.

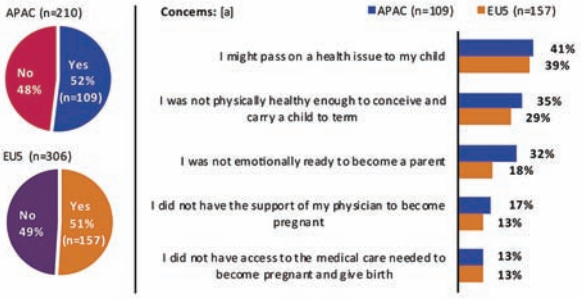
REFERENCE

[1] Tincani A. ARD 2018;77(Suppl):A866.

Figure: A) Patients consulting a healthcare professional before pregnancy were most likely to take the initiative in raising the subject of pregnancy



B) Women of childbearing age with CRD had concerns that delayed their decision to become a mother



[a] Multiple answers were possible. APAC: Asia-Pacific (Australia, Japan, Hong Kong and Taiwan); CRD: chronic rheumatic disease; EU5: Europe (Germany, France, UK, Italy and Spain); HCP: healthcare professional.

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Alexion – Meeting presentation aHUS and pregnancy June 2018
Autoimmune disease in pregnancy Nov 2018 UCB $550 pending, Azusa Sameshima: None declared, Yu-Jih Su: None declared, Carine Saadoun Employee of: UCB Pharma, Priscilla C Wong: None declared

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SAT0166

GOLIMUMAB AS FIRST, SECOND OR AT LEAST THIRD BIOLOGIC AGENT IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA), PSORIATIC ARTHRITIS (PSA) OR ANKYLOSING SPONDYLITIS (AS) – POST HOC ANALYSIS OF A NON-INTERVENTIONAL STUDY IN GERMANY

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Background: Golimumab (GLM) has demonstrated efficacy in RA, PsA, and AS in several randomized clinical trials with biologic-naïve patients. Data from real world practice comparing biologic naïve and experienced patients are lacking.

Objectives: The aim of this post hoc analysis is to assess effectiveness of GLM used as first, second, or at least third biologic agent in RA, PsA and AS in a real-life setting.

Methods: Post hoc analysis of the non-interventional, prospective, 24-month GO-NICE study with RA, PsA and AS patients (pts.) starting GLM 50mg SC once monthly in a real practice setting in Germany, details were shown earlier (1,2). Endpoint measures DAS28-ESR, PsARC, and BASDAI are shown as observed.

Results: In 1458 pts. with RA, PsA or AS GLM was administered as first (n=305, 286, 292, resp.), second (n=104, 136, 130 resp.), or at least third biologic agent (n=64, 79, 58 resp.). Biologic argents in previous treatments included Adalimumab (348), Etanercept (287), Infliximab (139), Tocilizumab (27), Rituximab (15), Certolizumab (14), or Abatacept (n=12). 43.0, 30.8, 39.1% of pts. with RA, 53.1, 38.2, 34.2% with PsA, and 53.8, 49.2, 41.4% with AS completed the study until month 24.

RA pts: (n=473) RF was positive in 76.9%, 70.2%, and 59.4%, ACPA + in 76.2%, 78.4%, 59.0%, and disease duration was 9.7, 10.1, 14.3 years, in pts. with GLM use as 1st, 2nd, at least 3rd line respectively.
DAS28 score at BL was 5.0, 4.9, 5.1 in first, second, and at least third line use of GLM, respectively and dropped significantly in all groups (table). After 3 months of treatment 27.5%, 19.5%, 14.5% of pts. were in remission (<2.6), after 24 months 45.3%, 50.0% or 33.3%, respectively.

PsA pts: (n=501) Disease duration was 12.4, 13.7, 13.8 yrs, in pts. with GLM use as 1st, 2nd, at least 3rd line respectively. PsARC response was achieved in 76.4%, 51.0% and 50.0% in first, second, and at least third line use of GLM, respectively at 24 months.

AS pts: (n=483) HLAB27-positive in 81.2%, 80.8%, and 74.1%, in pts. with GLM use as 1st, 2nd, at least 3rd line respectively. At BL 162 pts. had extra articular manifestations, most commonly iritis, enthesitis, IBD, and dactylitis (in 31.2%, 35.9%, and 43%, pts. respectively. Pts. with at least 2 previous bDMARDs had higher BASDAI at BL than pts. with GLM use in 1st or 2nd line: 5.7 vs. 5.0, and 4.9. After 24 months of treatment the mean BASDAI scores decreased significantly (p<0.001 vs. BL) to 2.1, 2.9, 2.9 in 1st, 2nd, and at least 3rd line use of GLM, respectively.
Overall safety findings were comparable to those reported in controlled trials and no new safety signals were detected.

RA DAS28-ESR	1st line (bDMARD-naïve)	2nd line	3rd line (at least)
Month (mo) 0, BL mean DAS28 [SD]	n=303 5.0 ± 1.3	n=104 4.9 ± 1.3	n=64 5.1 ± 1.5
mo 24: mean DAS28 [SD] p vs. BL	n=128 2.9 ±1.3 <.0001	n=32 2.9 ± 1.3 <.0001	n=24 3.4 ± 1.5 <.0001
PsA PsARC	1st line (bDMARD-naïve)	2nd line	3rd line (at least)
visit 1 mo 0, BL	n=286	n=136	n=79
mo 24: PsARC. response n (%)	n=113 76.4%	n=25 51.0%	n=12 50.0%
AS BASDAI	1st line (bDMARD-naïve)	2nd line	3rd line (at least)
mo 0, BL mean BASDAI [SD]	n=290 5.0 ± 2.0	n=130 4.9 ± 2.0	n=58 5.7 ± 2.0
mo 24: mean BASDAI [SD] p vs. BL	n=157 2.1 ±1.8 <.0001	n=64 2.9 ± 2.4 <.0001	n=24 2.9 ± 2.0 <.0001

Conclusion: In this non-interventional study of pts. with RA, PsA and AS, golimumab therapy was effective, with better outcomes achieved in biologic-naïve pts. Significant improvement of DAS and BASDAI was also achieved with GLM use in second line. Third line use of GLM results in less benefit.

REFERENCES
[1] K. Krüger, et al. BMJ Open 2018
[2] K. Krüger, et al. Rheumatology International 39 (1) 2019

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SAT0167 INCREASED HIGH MOLECULAR WEIGHT ADIPONECTIN AND LEAN MASS DURING TOCILIZUMAB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS. A 12 MONTHMULTICENTER STUDY

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Background: Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular (CV) diseases. TNFa blockade in RA patients has been associated with weight gain, increase in fat mass and variations in serum adipokines. Adiponectin (Adp), a protein produced by adipocytes, plays a beneficial role in insulin sensitivity and CV disease prevention, especially its high molecular weight (HMW) isoform.
Objectives: To analyse the changes in serum adipokines and especially Adp (total and HMW) and body composition during TCZ therapy in RA.
Methods: Multicenter open-label study. All patients enrolled had active RA (2010 ACR/EULAR criteria and DAS28$\geq$ 3.2) with previous inadequate response to a csDMARDs and/or bDMARDs. They all were TCZ naïve and received TCZ IV. Patients were evaluated at baseline,1,3,6 and 12 months. Clinical assessment included body mass index (BMI), waist circumference, DAS28 and HAQ scores. Laboratory parameters of inflammation (ESR, CRP, IL-6), lipid parameters (total chol., LDL and HDL chol., triglycerides), metabolic parameters (glycemia, insulin), serum Adp (total and HMW), leptin, resistin, and ghrelin were measured at each time point. Body composition (lean mass, fat mass,% of fat, fat in the android and gynoid regions) was evaluated at baseline, 6, and 12 months (DEXA, Lunar GE). Our primary criteria was the changes in Adp (total and HMW) at 6 months.
Results: 107 patients (78 F; mean age ± SD: 56.6 yr ± 13.5; disease duration: 9.9 yr ± 8.1; previous bDMARD: 64.5%; corticosteroids: 69%; concomitant csDMARD: 72.8%) were included. 97 were still on treatment at month 6 and 77 completed the study. Most of the patients (95%) received TCZ 8 mg/kg by infusion. Patients were responding to TCZ with a significant DAS28 decrease between baseline and months 6 and 12 ($p<0.0001$). HAQ, ESR, and CRP levels significantly decreased along the study ($p<0.0001$). BMI and abdominal circumference significantly increased at month 6 and 12, as well as lean mass ($p=0.0097$ at month 6 and 0.021 at month 12). Fat mas,% of fat and android fat did not change over the study. Total chol and LDL chol increased while glycaemia and insulin remained stable. Both total and HMW Adp increased from baseline to month 6 and month 12 (total Adp: baseline vs month 6: $p=0.055$; HMW Adp: baseline vs month 6: $p=0.02$, baseline vs month 12: $p=0.057$). Serum leptin, resistin and ghrelin did not change during the follow-up.
Conclusion: These variations in Adp during TCZ treatment may have a positive impact on the CV risk of RA patients and may contribute to the protective role of TCZ against the CV burden in RA.
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SAT0168 IMPACT OF AGE ON THE APPEARANCE OF ADVERSE EVENTSAT THE BEGINNING OF BIOLOGICAL TREATMENT: DATA FROM THE BIOBADASER 3.0 REGISTRY

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Background: Currents medical advances are allowing patients with chronic arthritis to live to advanced ages. Although the risks of biological therapies in elderly patients have been previously evaluated, data are scarce since they are mainly derived from clinical trials, in which elderly populations are often underrepresented or event excluded (patients up to 75 years old). In addition, comparisons between such studies are difficult in the absence of a consensus in defining the groups' age.
Objectives: To evaluate the impact of age on the appearance of adverse events (AE) in patients with rheumatic diseases (rheumatoid arthritis -RA-, ankylosing spondylitis -AS- and psoriatic arthritis -PsA) at the start of biological treatment.
Methods: Multicenter prospective study in a real-world setting. Information was obtained from BIOBADASER, a national safety registry of patients with rheumatic diseases treated with biologics or targeted synthetic disease modifying anti-rheumatic drugs. For this analysis, all patients included in this registry since 2000 and diagnosed with RA, AS or PsA were included, and classified into four categories according to age at initiation of biologic treatment: young (< 25 years-old), adults (25-64 years-old), elderly (65-75 years-old) and very elderly (> 75 years-old). Data collected included: 1) patient's data 2) data on treatment and 3) data on AE. Proportions, means and standard deviations were used to describe the population. Poisson regression model was carried out to explore factors associated with the appearance of AEs. Crude and adjusted incidence rate ratios (IRRs) were calculated.
Results: A total of 2531 patients were included: 1154 RA (45.59%), 680 PsA (26.87%), and 697 AS (27.54%). Age groups: there were 64 young patients (2.52%), 2166 adults (85.57%), 243 elderly adults (9.6%), and 58 very elderly adults (2.29%). Comorbidities increased with age, while smoking rates decreased. Methotrexate use was similar in all age groups (53.99% in the total sample), but corticosteroid treatment increased with age (young 27.7%, adults 47%, elderly adults 64.36% and the very elderly 70.21%). 77.87% received anti-TNF treatment, and 22.13% other biological drugs. Poisson regression model showed an increased probability of suffering a first adverse event with increasing age regardless of the

disease (IRR for AS: 1.04 (0.87-1.26); IRR for PsA: 1.08 (0.92-1.28)). Other factors associated with higher IRR were sex (being woman), type of biological treatment (TNF inhibitors), concomitant therapy (methotrexate), smoking, comorbidities (Charlson Index) and time of evolution of rheumatic disease. No differences were found between pathologies.

Table. Results of the Poisson regression model. Factors associated with risk of incidence of a first adverse event since biological therapy initiation.

	CRUDE IRR (IC95%)	P	ADJUSTED IRR (IC95%)	P
AGE AT THE BEGINNING OF BIOLOGICAL TREATMENT (REF. ADULTS)				
YOUNG	0.78 (0.55-1.11)	0,175	1.04 (0.71-1.53)	0,829
ELDERLY ADULTS	1.61 (1.36-1.91)	<0.001	1.47 (1.20-1.80)	<0.001
ELDERLY	1.99 (1.44-2.76)	<0.001	1.90 (1.32-2.75)	0,001
WOMEN	1.32 (1.19-1.47)	<0.001	1.41 (1.23-1.61)	<0.001
TNF INHIBITOR	0.84 (0.74-0.96)	0,009	0.67 (0.57-0.79)	<0.001
DIAGNOSIS (REF RA)				
AS	0.80 (0.70-0.91)	0,001	1.04 (0.87-1.26)	0,651
PSA	0.97 (0.86-1.10)	0,642	1.08 (0.92-1.28)	0,327
CORTICOIDS	1.31 (1.18-1.47)	<0.001	1.10 (0.96-1.26)	0,186
METHOTREXATE	1.42 (1.27-1.59)	<0.001	1.35 (1.19-1.54)	<0.001
OTHER DMARDS	1.16 (1.04-1.30)	0,009	1.16 (1.01-1.32)	0,038
SMOKING (REF. NO)				
SMOKER	1.16 (1.02-1.32)	0,028	1.19 (1.02-1.39)	0,029
FORMER SMOKER	1.61 (1.32-1.97)	<0.001	1.59 (1.23-2.07)	<0.001
COPD	1.37 (0.97-1.94)	0,072	1.12 (0.76-1.66)	0,571
DIABETES	1.31 (1.07-1.59)	0,008	1.30 (1.02-1.65)	0,034
CHARLSON INDEX	1.15 (1.08-1.21)	<0.001	1.10 (1.02-1.19)	0,009
TIME OF EVOLUTION OF DISEASE	1.01 (1.00-1.01)	0,074	1.01 (1.00-1.02)	0,021

Conclusion: A mix of clinical and patient factors seem to explain the appearance of a first AE after biological therapy initiation, with age being one of those explanatory variables.

REFERENCE

[1] Ishchenko A, Lories RJ. Safety and Efficacy of Biological Disease-Modifying Antirheumatic Drugs in Older Rheumatoid Arthritis Patients: Staying the Distance. Drugs Aging 2016; 33:387–398

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SAT0169 RISK OF SERIOUS INFECTIONS IN OFFSPRING ACCORDING TO TNFI SUBTYPES

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Background: TNFi subtypes have differential trans-placental passage; infliximab and adalimumab (both monoclonal immunoglobulins) have the highest transfer, reaching higher fetal than maternal blood levels, while certolizumab (a pegylated Fab fragment) and etanercept (a fusion protein) display the lowest passage (less than 0.25% and 4-7% respectively). Thus, some TNFi subtypes could cause immunosuppression in the offspring. However, to date, there is no data on the risk of serious infections according to TNFi subtypes.
Objectives: We evaluated serious infections in a large group of children born to mothers with chronic inflammatory diseases who used TNFi during pregnancy. Our comparators were unexposed offspring born to affected and unaffected mothers. We determined if the risk of serious infections differed according to TNFi subtypes.
Methods: We identified all women with ≥1 hospitalization for delivery after a diagnosis of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriasis (PsO), psoriatic arthritis (PsA), or inflammatory bowel diseases (IBD), and a randomly selected group of unaffected mothers, matched ≥4:1 for age, year of delivery, and state of residence, using MarketScan database (2011-2016). Only women continuously enrolled within MarketScan for ≥12 months prior to delivery and with available child linkage were included. We defined TNFi exposure based on ≥1 filled prescription and/or infusion procedure code during pregnancy and/or the preconception period. We further refined TNFi exposure based on potential for high (infliximab, adalimumab, golimumab) versus low (certolizumab, etanercept) placental transfer. We ascertained serious infections in the offspring based on ≥1 hospitalization with infection as a primary diagnosis, in the first year of life. We performed multivariate analyses, adjusting for maternal demographics, disease type, co-morbidities, pregnancy complications, and drugs (corticosteroids, DMARDs, non-TNFi biologics).
Results: We identified 16,490 offspring of mothers with RA (4,142), AS (381), PsO/PsA(5,743), and IBD (6,731), as well as 164,553 children born to unaffected matched mothers. Among offspring whose mothers had inflammatory diseases, 1,611 (9.8%) were exposed to TNFi during pregnancy, 338 (2.0%) were unexposed during pregnancy but exposed in the preconception period, and 14,541 (88.2%) were unexposed both during the pregnancy and preconception periods. The percent of serious infections in offspring of inflammatory disease mothers with no TNFi exposure (2.1%; 95% CI 1.9, 2.3) was similar to those with TNFi exposure (2.3%; 95% CI 1.6, 3.0), while the percent of serious infections in children born to unaffected mothers was 1.6% (95% CI 1.6, 1.7). In offspring exposed to TNFi with high placental transfer, the percent of serious infections was 2.3% (95% CI 1.6, 3.3), while for TNFi with low transfer, it was 1.7% (95% CI 1.0, 3.1).
In multivariate analyses, we did not observe an increased risk of serious infections in TNFi exposed offspring versus unexposed offspring of mothers with inflammatory diseases (OR 1.0; 95% CI 0.7, 1.5). Results were similar when we restricted TNFi exposure to the third trimester (OR 1.1; 95% CI 0.7, 1.7). In multivariate analyses of children exposed to TNFi with high versus low placental transfer, our point estimate was consistent with increased risk, but the confidence interval was wide, including the null value (OR 1.43; 95% CI 0.66, 3.08).
Conclusion: When we compared the risk of serious infections in offspring exposed to TNFi with high versus low placental transfer, we observed a potential trend for an increased risk, although the confidence interval was wide and included the null value. Our findings stress the need to further study this issue.
Disclosure of Interests: None declared
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SAT0170 A NOVEL FORMULATION OF CT-P13 FOR SUBCUTANEOUS ADMINISTRATION: 30 WEEK RESULTS FROM A PART 2 OF PHASE I/III RANDOMIZED CONTROLLED TRIAL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: CT-P13 subcutaneous (SC) formulation showed comparable efficacy and safety with CT-P13 intravenous (IV) formulation in rheumatoid arthritis (RA)[1] and Crohn's disease[2] preliminary studies (Part 1).
Objectives: The purpose of this study was to demonstrate non-inferiority (NI) of efficacy and compare safety profiles of CT-P13 SC to CT-P13 IV in RA patients over 30 weeks of Part 2.
Methods: In this randomized, controlled, double blinded, phase I/III study, RA patients received CT-P13 IV 3 mg/kg at Weeks 0 and 2 and were randomized at Week 6 to receive CT-P13 SC 120 mg every 2 weeks or CT-P13 IV 3 mg/kg every 8 weeks. From Week 30, all patients received CT-P13 SC 120 mg every 2 weeks. The primary efficacy endpoint, change of DAS28 (C-reactive protein [CRP]) from baseline to Week 22,

was analyzed by using an analysis of covariance (ANCOVA). Non-inferiority is to be concluded if the lower bound of the 95% CI for the treatment difference in the change of DAS28 (CRP) from baseline to Week 22 is greater than the pre-specified NI margin of -0.6.

Results: A total of 362 patients were enrolled, of whom 348 were randomly assigned at Week 6 into 2 treatment arms in a 1:1 ratio (169 and 179 patients in SC 120 mg and IV 3 mg/kg arms, respectively). The mean change of DAS28 (CRP) from baseline to Week 22 was similar between the arms. The lower limit of two-sided 95% CI (0.03) was greater than the pre-specified NI margin (-0.6) which indicated NI of SC 120 mg compared to IV 3 mg/kg (Table 1). Additional efficacy including ACR responses were similar between two treatment arms up to Week 22 with slightly higher response rate trend observed in SC 120 mg arm at Week 30 (Figure 1). The safety profiles which occurred after study drug administration at Week 6 in SC 120 mg arm were generally comparable to IV 3 mg/kg arm. All of injection site reactions were grade 1 or 2 in intensity. Majority of administration-related reactions (ARRs) were grade 1 or 2 in intensity except 1 patient in IV 3 mg/kg arm who experienced grade 3 ARR and was withdrawn from the study due to this event (Table 2).

Table 1. Analysis of Change (decrease) from Baseline of DAS28 (CRP) at Week 22 (ANCOVA)

Treatment	n	DAS28 (CRP) decrease Least Square Mean (Standard Error)	Estimate of Treatment Difference	95% CI of Treatment Difference
SC 120 mg	164	2.22 (0.221)	0.28	(0.03, 0.53)
IV 3 mg/kg	171	1.95 (0.209)		

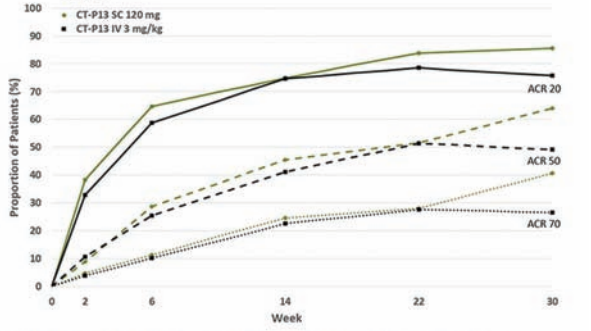
Note. Country, Week 2 serum CRP concentration (≤0.6 mg/dL vs >0.6 mg/dL), and Week 6 body weight (≤100 kg vs >100 kg) were considered as covariates.

Table 2. Summary of Safety Results up to from Weeks 6 to 30

		SC 120 mg (N=170)	IV 3 mg/kg (N=178)
Safety, n (%)	Treatment-emergent AEs	62 (36.5)	76 (42.7)
	Administration-related reactions	1 (0.6)	8 (4.5)
	Injection site reactions	11 (6.5)	4 (2.2)
	Infections	34 (20.0)	32 (18.0)

Note. One patient in IV 3 mg/kg arm was analyzed as SC 120 mg arm in Safety Population as receiving CT-P13 SC at Week 14.

Figure 1. The proportion of patients Achieving Clinical Response according to the ACR Criteria up to Week 30



Note. Results at Week 2 and Week 6 were obtained following IV infusion in the Dose-Loading Phase.

Conclusion: The study demonstrated NI of efficacy for CT-P13 SC to the CT-P13 IV. Also, CT-P13 SC showed similar efficacy and safety profiles to CT-P13 IV up to Week 30. CT-P13 SC could provide a favorable benefit to patients with an alternative convenient way of administration.

REFERENCES

[1] Westhovens R, et al. Annals of the Rheumatic Diseases 2018;77(-):315 (suppl2)

[2] Schreiber, S, et al. Gastroenterology 2018;154(6):S-1371

Disclosure of Interests: Rene Westhovens Grant/research support from: Bristol-Myers Squibb, Consultant for: Celltrion, Galapagos-Gilead, Piotr Wiland Speakers bureau: Novartis, Pfizer, Abbvie, Gedeon-Richter, Lilly, Roche and Sandoz, Marek Zawadzki Grant/research support from: Celltrion, Inc., Delina Ivanova Grant/research support from: Celltrion, Inc, PPD, Quintiles, Egis Pharmaceuticals, and Pfizer., Alfredo Berrocal Grant/research support from: Celltrion, Inc., Elias Chalouhi Grant/research support from: Celltrion, Inc., Éva Balázs Grant/research support from: Celltrion, Inc., Consultant for: Merck and Amgen, Sergii Shevchuk: None declared, Larisa Eliseeva Grant/research support from: Celltrion, Inc., Mykola Stanislavchuk Grant/research support from: AstraZeneca, Celltrion, Galapagos, Genentech, GlaxoSmithKline, Human Genome, Lilly, MedImmune, Pfizer, Roche and UCB, Roman Yatsyshyn Grant/research support from: Celltrion, Inc., SangJoon Lee Shareholder of: Celltrion, Inc., Employee of: Celltrion, Inc., JeeHye Suh Employee of: Celltrion, Inc., SeulGi Lee Employee of: Celltrion, Inc., Yunah Kim Employee of: Celltrion, Inc., DaeHyun Yoo Grant/research support from: Celltrion, Inc., Consultant for: Celltrion, Inc.

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SAT0171

A RETROSPECTIVE ANALYSIS OF LONG TERM SAFETY UP TO FIVE YEARS OF INFLIXIMAB BIOSIMILAR CT-P13 IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

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Background: Long term safety and efficacy of anti-TNF inhibitors in rheumatic diseases is an important aspect of patient treatment. CT-P13 is the first infliximab biosimilar approved by EMA and FDA and has demonstrated comparable efficacy and safety with reference infliximab in rheumatoid arthritis (RA)[1,2] and ankylosing spondylitis (AS)[3,4]. However, long term data of infliximab biosimilar to date has been limited to two years[5,6].

Objectives: To demonstrate drug survival and long term safety and efficacy of CT-P13 up to 5 years in patients with RA or AS, including patients who switched from reference infliximab to CT-P13.

Methods: Long term data was retrospectively collected from medical records of patients with RA and AS treated with CT-P13 at least once between September 2012 and December 2017 in five referral hospitals in Korea. Patients included both those who were infliximab-treatment naïve at the start of CT-P13 treatment (naïve patient) and those who switched from reference infliximab to CT-P13 (switched patient). Primary endpoints were safety and drug survival up to 5 years analyzed by Kaplan-Meier curve.

Results: Data from 491 patients (154 RA and 337 AS) were collected and analyzed, including 19 and 118 switched patients with RA and AS, respectively. Median disease duration was 64.7 months (range: 4.7 to 265.9 months) for patients with RA and 56.3 months (range: 3.0 to 216.7 months) for patients with AS. The median duration of CT-P13 treatment was 46.8 weeks (range: 0 to 250.6 weeks) and 94.1 weeks (range: 0 to 246.0 weeks) for patients with RA and AS, respectively. The probability of survival at year 5 for patients with RA was 0.42 and 0.53 respectively for naïve and switched patients. The probability of survival at year 5 for patients with AS was 0.64 and 0.72 respectively for naïve and switched patients. Median DAS28-ESR score decreased from 5.80 at baseline to 2.73 at year 5 and median DAS28-CRP score decreased from 5.14 at baseline to 1.29 at year 4 for patients with RA. Median BASDAI score decreased from 6.60 at baseline to 3.00 at year 5 for patients with AS. The most common reason for discontinuation for both patients with RA and AS was lack of efficacy. 31.8% of patients with RA and 29.4% of patients with AS experienced at least one adverse event and the most frequently observed type of adverse event was upper respiratory tract infection for 3.90% in patients with RA and 4.15% in patients with AS.

Conclusion: This is the longest evidence to date of safety and efficacy of infliximab biosimilar CT-P13 treatment in patients with RA or AS. Five year analysis of medical records showed that long term treatment with CT-P13 was safe and efficacious based on drug survival, disease activity measurements, and adverse events. Drug survival was similar between patients who were naïve at the start of CT-P13 treatment and switched from reference to CT-P13.

REFERENCES

[1] Yoo DH, et al. Ann Rheum Dis. 2013;72(10):1613-20.

[2] Yoo DH, et al. Arthritis Res Ther. 2016;18:82.
[3] Park W, et al. Ann Rheum Dis. 2013;72(10):1605-12.
[4] Park, et al. Arthritis Res Ther. 2016;18:25.
[5] Yoo DH, et al. Ann Rheum Dis. 2017;76(2):355-363.
[6] Park W, et al. Ann Rheum Dis. 2017;76(2):346-354.

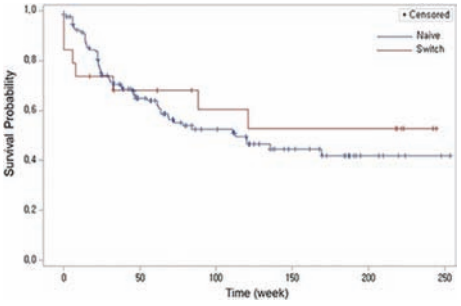


Figure 1. Drug survival probability of patients with RA treated with CT-P13

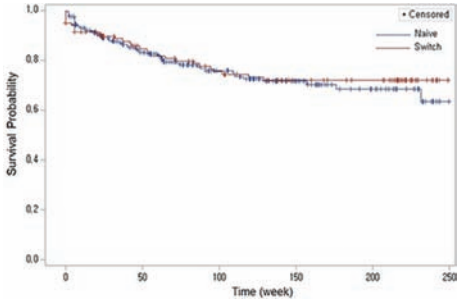


Figure 2. Drug survival probability of patients with AS treated with CT-P13

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SLE, Sjögren's and APS – clinical aspects (other than treatment)

SAT0172

ANTIBODIES TO BOTH RO52 AND RO60 DEFINE A SUBSET OF SJÖGREN'S MOST SUITABLE FOR CLINICAL TRIALS OF AGENTS TARGETING LYMPHOPROLIFERATIONS

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Background: Anti-SSA antibodies comprise reactivity to two distinct proteins, Ro52 and Ro60, encoded by separate genes and found on separate ribonucleoprotein particles. Specific testing for Ro52 and Ro60 antibodies is now clinically available, yet the phenotypic correlates of Ro52 and Ro60 reactivity profiles have not been well defined.
Objectives: To determine the phenotypic correlates of antibody reactivity to Ro52 alone, Ro52 + Ro60, and Ro60 alone in patients being evaluated for Sjögren`s syndrome (SS).
Methods: We initially studied 840 patients seen at the Hopkins Sjögren`s Syndrome Center with suspected or established SS. Each had serum tested for antibodies to recombinant Ro52 (Inova Quanta Lite ELISA) and Ro60 (**IVTT im***munoprecipitation*). We then validated our findings in a second cohort consisting of 194 patients, each with testing for antibodies to recombinant anti-Ro52 and anti-Ro60 by a chemiluminescent assay (Inova Bioflash). Statistical analyses were performed using JMP pro 13. The Chi-square or Fisher exact test was used to compare the groups.
Results: The discovery cohort of 840 patients included 751 (89%) women, with a mean age of 58.5±13.5 years. 371 (44%) patients met the ACR/EULAR classification criteria. There were 311 with anti-Ro52 +Ro60, 108 with anti-Ro60 alone, 95 with anti-Ro52 alone, and 326 with neither antibody. The 311 patients with anti-Ro52+Ro60 reactivity had a distinctive phenotype, with a markedly increased prevalence of ANA≥ 1:320, RF, IgG≥1560 mg/dL, and SS-B positivity ($p<0.008$ for all inter-group comparisons) and an increased prevalence of focus score ≥1 and hypoechoic lesions on parotid gland ultrasonography which trended toward statistical significance. These differences were also validated in the second cohort, with the exception of focus score and parotid gland hypoechoic lesions, possibly as a result of smaller group numbers.The Ro52 and Ro60 alone groups were equivalent to each other in their phenotypic associations, except for RF, which was higher in the Ro52 alone group. Measures of lacrimal and salivary gland function and the prevalences of extraglandular manifestations did not show consistent differences between the groups or the two cohorts.
Conclusion: Testing anti-Ro52 and anti-Ro60 in patients with suspected or established SS identifies a unique subset, namely those with both Ro52 and Ro60 antibodies, distinguished by a much higher prevalence of B-cell activation markers and glandular inflammation as measured by focus score and hypoechoic lesions. This subset may be most suitable for inclusion in clinical trials where the therapeutic agent targets glandular lymphoproliferation.

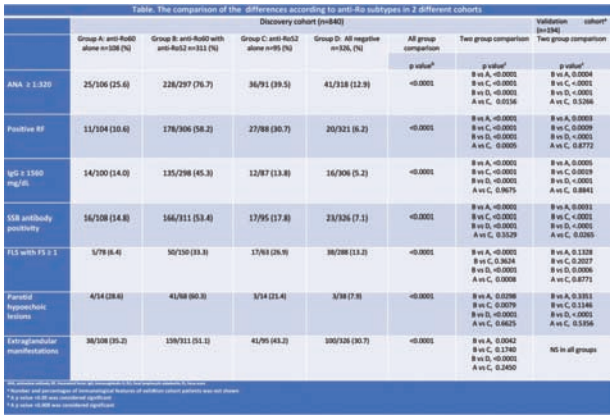


Table. The comparison of the differences according to anti-Ro subtypes in 2 different cohorts

	Discovery cohort (n=840)						Validation cohort* (n=194)
	Group A: anti-Ro60 alone n=108 (%)	Group B: anti-Ro60 with anti-Ro52 n=311 (%)	Group C: anti-Ro52 alone n=95 (%)	Group D: All negative n=326, (%)	All group comparison	Two group comparison	Two group comparison
					p value†	p value‡	p value‡
ANA ≥ 1:320	25/106 (25.6)	228/297 (76.7)	36/91 (39.5)	41/318 (12.9)	<0.0001	B vs A, <0.0001 B vs C, <0.0001 B vs D, <0.0001 A vs C, 0.0156	B vs A, 0.0004 B vs C, <.0001 B vs D, <.0001 A vs C, 0.5266
Positive RF	11/104 (10.6)	178/306 (58.2)	27/88 (30.7)	20/321 (6.2)	<0.0001	B vs A, <0.0001 B vs C, <0.0001 B vs D, <0.0001 A vs C, 0.0005	B vs A, 0.0003 B vs C, 0.0009 B vs D, <.0001 A vs C, 0.8772
IgG ≥ 1560 mg/dL	14/100 (14.0)	135/298 (45.3)	12/87 (13.8)	16/306 (5.2)	<0.0001	B vs A, <0.0001 B vs C, <0.0001 B vs D, <0.0001 A vs C, 0.9675	B vs A, 0.0005 B vs C, 0.0019 B vs D, <.0001 A vs C, 0.8441
SSB antibody positivity	16/108 (14.8)	166/311 (53.4)	17/95 (17.8)	23/326 (7.1)	<0.0001	B vs A, <0.0001 B vs C, <0.0001 B vs D, <0.0001 A vs C, 0.3529	B vs A, 0.0031 B vs C, <.0001 B vs D, <.0001 A vs C, 0.0265
FLS with FS ≥ 1	5/78 (6.4)	50/150 (33.3)	17/63 (26.9)	38/288 (13.2)	<0.0001	B vs A, <0.0001 B vs C, 0.3624 B vs D, <0.0001 A vs C, 0.0008	B vs A, 0.1328 B vs C, 0.2027 B vs D, 0.0006 A vs C, 0.8771
Parotid hypoechoic lesions	4/14 (28.6)	41/68 (60.3)	3/14 (21.4)	3/38 (7.9)	<0.0001	B vs A, 0.0298 B vs C, 0.0079 B vs D, <0.0001 A vs C, 0.6625	B vs A, 0.3351 B vs C, 0.1146 B vs D, <.0001 A vs C, 0.5356
Extraglandular manifestations	38/108 (35.2)	159/311 (51.1)	41/95 (43.2)	100/326 (30.7)	<0.0001	B vs A, 0.0042 B vs C, 0.1740 B vs D, <0.0001 A vs C, 0.2450	NS in all groups

*Number and percentage of immunological features of validation cohort patients was not shown
†A p value <0.05 was considered significant
‡A p value <0.008 was considered significant

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SAT0173

RENAL GALLIUM SCAN CORRELATED WITH INFLAMMATION IN RENAL HISTOLOGY OF PATIENTS WITH LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is the leading cause of mortality in lupus patients. But there is only one image assessment method, the histopathology through invasive renal biopsy.
Objectives: This study aimed to investigate the clinical value of the non-invasive image assessment method: renal gallium scan, in renal histological parameters of LN in a cohort of one single tertiary referral center.
Methods: Between 2006 and 2018, a hospital-based observational study was conducted to enroll 266 biopsy-proved and 40 repeated-biopsied LN patients who underwent renal gallium scan before biopsy. The classification and scoring of LN were assessed according to the International

Society of Nephrology/Renal Pathology Society. A delayed 48-hour gallium scan was performed and interpreted by visual and semiquantitative methods. The renal histological results were compared with gallium scan parameters.

Results: Out of 266 participants, 189 (71%) were proliferative LN. Baseline gallium left kidney/spine (K/S) ratio was significantly higher in class IV LN as compared to class III or class V (median [inter-quartile range, IQR]: 1.14 [1.0-1.3], 0.97 [0.9-1.1], 1.035 [0.9-1.2], respectively, $p<0.001$). Patients with higher daily urine protein, renal activity index, endocapillary proliferation and interstitial inflammation tended to exhibit higher gallium uptake by regression analysis. Besides, changes of gallium uptake ratio between 2 biopsies were positively correlated with daily urine protein change ($r=0.699$, $p<0.001$), change of activity index ($r=0.339$, $p=0.033$), endocapillary proliferation ($r=0.380$, $p=0.027$) and neutrophils infiltration ($r=0.405$, $p=0.018$) in renal pathology findings.

Table1. (N=266)

	Class I&II (n=7)	III (n=43)	IV (n=146)	V (n=70)	*P* value
Age	42.0 (33.0-43.0)	31.0 (26.0-40.0)	32.0 (25.0-41.0)	31.0 (26.0-40.3)	0.572
Gender					0.577
F	7 (100.0%)	36 (83.7%)	118 (80.8%)	59 (84.3%)	
M	0 (0.0%)	7 (16.3%)	28 (19.2%)	11 (15.7%)	
Lab data					
Daily urine protein	0.7 (0.1-1.8)	1.9 (1.0-2.5)	3.7 (2.1-5.6)	2.1 (0.9-6.3)	**<0.001****
Creatine	0.7 (0.5-0.8)	0.8 (0.6-1.2)	1.4 (0.9-2.8)	0.8 (0.7-1.1)	**<0.001****
eGFR	97.5 (91.0-139.2)	88.3 (65.6-125.6)	48.5 (22.3-79.0)	88.2 (60.8-117.6)	**<0.001****
dsDNAAb	248.7 (166.5-477.0)	169.0 (64.7-347.7)	265.4 (125.5-464.1)	126.0 (33.3-286.9)	**<0.001****
C3	78.2 (71.3-90.5)	76.4 (63.7-93.2)	54.6 (40.7-67.0)	67.9 (47.9-97.0)	**<0.001****
C4	15.1 (4.1-20.9)	14.4 (10.4-22.2)	10.6 (6.7-18.0)	12.5 (7.2-23.5)	**0.048***
SLEDAI	18.5 --	14.0 (10.0-14.0)	14.0 (8.0-20.0)	8.0 (5.5-10.8)	**0.025***
Renal pathology					
ActivityIndex	0 (0-1)	3 (1-4)	8 (5.0-10.3)	0 (0-2)	**<0.001****
Cellular crescent	0 (0-0)	0 (0-0)	2 (0-2)	0 (0-0)	**<0.001****
Necrosis/ Karyorrhexis	0 (0-0)	2 (0-2)	2 (0-2)	0 (0-0)	**<0.001****
Endocapillary proliferation	0 (0-0)	1 (0-1)	2 (2-3)	0 (0-1)	**<0.001****
Hyaline thrombus/wire loop	0 (0-0)	0 (0-0)	1 (0-2)	0 (0-0)	**<0.001****
Neutrophils infiltration	0 (0-0)	0 (0-0)	0 (0-1)	0 (0-0)	**<0.001****
Interstitial inflammation	0 (0-1)	0 (0-1)	1 (0-2)	0 (0-1)	**<0.001****
Chronicity Index	0 (0-1)	2 (0-3)	1 (0-4)	1 (0-2)	**0.036***
Glomerular stenosis	0 (0-0)	1 (0-1)	1 (0-2)	0 (0-1)	**0.001****
Tubular atrophy	0 (0-0)	1 (0-1)	0 (0-1)	0 (0-1)	0.094
Interstitial fibrosis	0 (0-1)	1 (0-1)	0 (0-1)	0 (0-1)	0.405
Fibrous crescent	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0.066
Tubulointerstitial nephritis	1 (14.3%)	17 (39.5%)	83 (56.8%)	22 (31.9%)	**0.001****
Atherosclerosis	1 (14.3%)	9 (20.9%)	32 (21.9%)	8 (11.8%)	0.343
L't/c's ratio	0.9 (0.8-1.2)	1.0 (0.9-1.1)	1.1 (1.0-1.3)	1.0 (0.9-1.2)	**<0.001****
R't/c's ratio	1.0 (0.9-1.4)	1.0 (0.9-1.2)	1.2 (1.1-1.4)	1.1 (1.0-1.2)	**<0.001****
Gallium visual grading					**<0.001****
0-1&1&1-2	4 (57.1%)	19 (44.2%)	26 (17.8%)	18 (25.7%)	
2	1 (14.3%)	17 (39.5%)	42 (28.8%)	33 (47.1%)	
2-3	0 (0.0%)	6 (14.0%)	38 (26.0%)	10 (14.3%)	
3	2 (28.6%)	1 (2.3%)	40 (27.4%)	9 (12.9%)	

Chi-square test. †Kruskal-wallis test. *P <0.05, **P <0.01

Table2. LK ratio spine (Multivariate1 Adjust R^2=0.219; Multivariate2 Adjust R^2=0.217; Multivariate3 Adjust R^2=0.225)

	Univariate			Multivariate1			Multivariate2			Multivariate3†		
	B	95%CI	*P* value	B	95%CI	*P* value	B	95%CI	*P* value	B	95%CI	*P* value
Age	-0.002	(-0.005, 0.000)	0.079									
Gender												
F	Reference	Reference										
M	0.004	(-0.076, 0.084)	0.925									
Lab data												
Daily urine protein	0.023	(0.016, 0.031)	**<0.001****	0.020	(0.012, 0.027)	**<0.001****	0.019	(0.011, 0.026)	**<0.001****	0.018	(0.011, 0.026)	**<0.001****
Creatine	0.016	(-0.002, 0.035)	0.088									
eGFR	-0.001	(-0.001, 0.000)	**0.016***	0.000	(-0.001, 0.001)	0.965	0.000	(-0.001, 0.001)	0.757			
dsDNAAb	0.000	(0.000, 0.000)	0.113									
C3	-0.001	(-0.002, 0.000)	**0.019***	0.001	(-0.001, 0.002)	0.370	0.001	(-0.001, 0.002)	0.257			
C4	-0.001	(-0.004, 0.001)	0.375									
SLEDAI	-0.005	(-0.020, 0.009)	0.448									
Renal pathology												
ActivityIndex	0.021	(0.015, 0.027)	**<0.001****	0.018	(0.010, 0.026)	**<0.001****						
Cellular crescent	0.043	(0.022, 0.065)	**<0.001****				0.000	(-0.029, 0.030)	0.995			
Necrosis/ Karyorrhexis	0.030	(0.017, 0.055)	**<0.001****				0.017	(-0.007, 0.040)	0.167			
Endocapillary proliferation	0.073	(0.048, 0.098)	**<0.001****				0.029	(-0.010, 0.069)	0.144	0.039	(0.011, 0.068)	**0.007****
Hyaline thrombus/wire loo	0.083	(0.049, 0.117)	**<0.001****				0.019	(-0.025, 0.064)	0.396			
Neutrophils infiltration	0.101	(0.053, 0.149)	**<0.001****				0.008	(-0.048, 0.065)	0.768			
Interstitial inflammation	0.091	(0.057, 0.125)	**<0.001****				0.051	(0.011, 0.091)	**0.013***	0.053	(0.016, 0.090)	**0.005****
Chronicity Index	-0.002	(-0.014, 0.009)	0.700									
Glomerular stenosis	-0.015	(-0.047, 0.017)	0.358									
Tubular atrophy	-0.010	(-0.045, 0.026)	0.592									
Interstitial fibrosis	-0.002	(-0.038, 0.034)	0.899									
Fibrous crescent	0.025	(-0.002, 0.143)	0.672									
Tubulointerstitial nephritis	0.020	(-0.041, 0.081)	0.519									
Atherosclerosis	-0.024	(-0.101, 0.054)	0.547									
Gallium visual grading												
0-1&1&1-2	Reference	Reference										
2	0.175	(0.134, 0.217)	**<0.001****									
2-3	0.343	(0.295, 0.390)	**<0.001****									
3	0.416	(0.368, 0.464)	**<0.001****									

Linear regression.†Stepwise. *P<0.05 **P<0.01

Conclusion: Higher renal gallium uptake predicts higher active inflammation in LN. Changes of gallium uptake ratio were correlated with changes histopathological parameters and daily urine protein. Renal gallium scan appeals to be a valuable non-invasive tool in assessing activities of LN.

REFERENCES

[1] Tsai, S. C., Hsieh, T. Y., Huang, P. W., & Lin, W. Y. (2016). Absolute quantitative evaluation of 67Ga scintigraphy in lupus nephritis. Clinical nuclear medicine, 41(6), 442-446.

[2] Lin, W. Y., Hsieh, J. F., Tsai, S. C., Lan, J. L., Cheng, K. Y., & Wang, S. J. (2000). Semi-quantitative evaluation of gallium-67 scintigraphy in lupus nephritis. European journal of nuclear medicine, 27(11), 1626-1631.

[3] Nomura, S., Watanabe, Y., Otsuka, N., & Osawa, G. (1996). Gallium 67 scintigraphy as a predictor of renal prognosis in primary immunoglobulin A nephropathy. American journal of kidney diseases, 27(2), 204-208.

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SAT0174

CHARACTERISTICS AND TREATMENTS OF PATIENTS WITH SJÖGREN'S SYNDROME IN A REAL-WORLD SETTING

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Background: Sjögren's syndrome (SS) is one of the most common autoimmune diseases. Main symptoms include dry eyes and mouth, followed by difficulty swallowing and serious systemic manifestations including neurological, pulmonary and musculoskeletal effects.[1] However, SS is not homogeneous; it affects patients in different ways, with varying symptoms and severity. Identifying discrete patient types and understanding their commonalities and differences is integral to enhancing disease knowledge, identifying areas of unmet need, defining the size of the affected population and determining appropriate treatment approach.

Objectives: Using data gathered by the SS Foundation through a survey of over 3000 patients with SS, analyses were performed to: 1) describe patient characteristics and treatment in a real-world setting and 2) categorise patients based on baseline characteristics.

Methods: The analytical approach used clustering techniques to synthesise the mixed-data–type survey in two separate analyses. Data were filtered to include patients 40–65 years of age. Analyses were performed firstly to identify relationships between features—related to demographic, disease state, treatments, etc—and secondly to identify clusters of patients. A Bayesian network model was used to evaluate feature correlations and the probability of a specific survey answer given one or many preliminary conditions. With respect to patient clustering, the model used was based on Gower distance and Partitioning Around Medoids, which each can include both numerical and categorical data.

Results: We evaluated comorbidities, symptoms and treatment to identify traits that differed most significantly among patient types. Four discrete patient clusters were identified (disease severity measured by median EULAR SS Patient Reported Index score[2]; Table 1):

- 1. Recent: Most recently diagnosed, least severe disease manifestation
- 2. Slower progressing: Longest time since diagnosis, second–lowest disease severity
- 3. Second–second: Second in time since of diagnosis, second in disease severity
- 4. Most severe: Most severe disease manifestations and comorbidities

The most differentiating comorbidities across all clusters included gastroesophageal reflux disease, fibromyalgia and Raynaud's syndrome (Table 2). The symptoms that impacted patients' lives the most and that were differentiating across clusters were brain fog, fatigue and forgetfulness. The treatments that were most contrasting were oral comfort agents, followed by DMARDS and secretagogues (Figure 1). The patient cluster definitions above suggest some contradictions, because not all significant cluster characteristics progressively worsened with increasing disease severity.

Conclusion: These analyses show differences in disease characteristics and treatment across patient clusters; however, more work is required to validate these clusters.

REFERENCES
[1] Ienopoli S, et al. Oral and Maxillofac Surg Clin North Am 2014;26:91-9.
[2] Seror R, et al. Ann Rheum Dis 2011;70:968-72.

Table 1. Most significant patient features

	Recent	Slower progressing	Second-second	Most severe
Patients, n	154	243	184	132
Female, %	92	95	95	92
Age, years (median)	57	57	59	59
Years since diagnosis (median)	5	9	6	8
ESSPRI score (median)	4	5.3	6	6.5
Dryness (median)	6	6	7	7
Fatigue (median)	5	6	7	7
Pain (median)	2	4	5	6
Total hospitalisation (ER/UCC/hospital), %	14	17	22	27
HCP (median)	3	4	4	5
Total spending (mean $US)	1708	3020	3823	5550
Prescriptions, n (median)	2	2	3	5
OTC medications, n (median)	3	3	4	5
Awarded social security disability, %	2%	8%	9%	16%

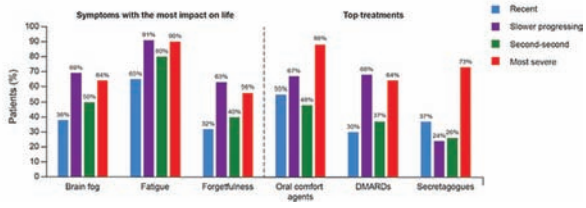
ER=emergency room; ESSPRI=EULAR SS Patient Reported Index; HCP=healthcare provider; OTC=over the counter; UCC=urgent care centre

Table 2. Top comorbidities that differentiate clusters

Comorbidity, %	Recent	Slower progressing	Second-second	Most severe
GERD	21	45	45	53
Pneumonia or bronchitis	8	12	10	18
Leucopoenia	8	16	11	16
Anaemia	11	17	10	17
Fibromyalgia	10	27	38	43
Hypertension	18	22	21	24
Sinusitis	14	31	38	49
Mixed connective tissue disease	4	13	12	14
Irritable bowel syndrome	14	32	33	35
Raynaud's disease	24	35	35	40

GERD=gastroesophageal reflux disease

Figure 1. Top three symptoms and treatments that differed most significantly among clusters



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SAT0175 ULTRA-HIGH-FREQUENCY ULTRASOUND OF LABIAL SALIVARY GLANDS HIGHLY CORRELATES WITH HISTOPATHOLOGY IN PRIMARY SJÖGREN'S SYNDROME

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Background: In the last few decades many studies have investigated the role of major salivary glands ultrasound (SGUS) in the diagnostic work-up of patients with suspected primary Sjögren's syndrome (pSS). Recent development of ultra-high-resolution ultrasound systems (UHFUS), with frequencies as high as 70 MHz and capability resolution as fine as 30 μm, has permit new diagnostic applications to a variety of superficial targets including labial salivary glands (LSGs). To date, however, no information are available regarding the use of UHFUS for the study of LSGs in humans.
Objectives: To evaluate the feasibility and the diagnostic accuracy of UHFUS of LSGs in patients with suspected SS and to assess the correlations between LSG histopathology, UHFUS and SGUS.
Methods: Consecutive patients with clinically suspected pSS were included in this study. All patients underwent a complete diagnostic work-up including conventional SGUS and LSG biopsy. The same expert pathologist calculated for all the samples the focus score (FS), number of foci and evaluated the presence of ectopic germinal centers (GCs). UHFUS of LSG was performed by specialized radiologists scanning first the central compartment of the inferior lip, and then both peripheral compartments. The following parameters were evaluated: distribution of the glands, parenchymal inhomogeneity (score 0-3, from normal to evident), fibrosis and eco color-Doppler vascular pattern and grade of vascular intensity.
Results: We included 32 patients with suspected pSS. At the end of the work-up, pSS diagnosis was confirmed in 12/32 (37.5%) cases. No differences between pSS patients and no-SS sicca controls were observed in UHFUS findings related to LSG distribution and eco color-Doppler vascular parameters. By contrast, pSS patients presented statistically significant differences in peripheral UHFUS inhomogeneity (p=0.006), and a higher degree of fibrosis (p=0.01). Considering a score $\geq$2 in parenchymal inhomogeneity as suggestive for pSS, UHFUS appeared less specific than conventional SGUS (UHFUS Sp=70% vs SGUS Sp=95%) but more sensitive (UHFUS Se=83.3% vs SGUS Se = 58.3%). In addition, when we investigated the relationship between UHFUS, SGUS and LSG histopathology we found that the correlation coefficients between UHFUS inhomogeneity and LSG FS (UHFUS r=0.706** *vs* SGUS r=0.393*), number of foci (UHFUS r=0.712** *vs* SGUS r=0.445*), and number of ectopic GCs (UHFUS r=0.525** *vs* SGUS r=0.141), were significantly higher than those observed with conventional SGUS.
Conclusion: the application of UHFUS to the study of LSG in pSS appeared feasible and sensitive. Because of the anatomical details obtained with this technique and its stronger correlation with LSG histopathology, UHFUS might offer unique advantages over the existing major salivary gland imaging modalities in pSS assessment.
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SAT0176 MACROPHAGE ACTIVATION SYNDROME IN MONOGENIC LUPUS: A RARE COMPLICATION OF A RARE DISEASE

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Background: Macrophage activation syndrome (MAS) is one of the most severe, potentially life-threatening complication of childhood rheumatic diseases, especially SoJIA and J-SLE. MAS in the course of J-SLE has a high mortality rate (8%-22%) [1]; however, it is difficult to differentiate from the SLE flare itself.

Objectives: This case report is presented to emphasize that the deterioration of certain clinical and laboratory findings of an SLE patient should alert the physician for development of MAS.
Methods: We reported a monogenic lupus patient with MAS clinic with acute pancreatitis, who had c1qA gene mutation.
Results: A 9-year-old male was first referred with photosensitivity and erythematous crusted lesions on his extremities and face while he was 2 years old. ANA was positive (1/1000 dilution) and skin biopsy from lesions was compatible with subacute lupus. Steroid, metotrexate and hydroxychloroquine were administrated. Patient's male identity and atypical age for lupus was further evaluated with "whole exome sequencing" method. Complement c1qA gene mutation was detected. Monthly fresh frozen plasma and IVIG treatments were added, which able to control the disease to some extent.
He had acute gastroenteritis and fever, leading to activation of skin and oral mucosa lesions with on bilateral parotitis in his last visit (Figure-A). His body temperature was 39.9 °C. USG confirmed the parotitis. Regarding infectious gastroenteritis, IVIG and plasma with broad-spectrum antibiotics were administrated. Despite treatment, high fever persisted. He had hypotension, irritability, and hepatosplenomegaly with abdominal tenderness on physical examination. Abdomen CT was compatible with acute pancreatitis (Figure-B), and he had high amylase and lipase levels. Despite IV hydration with intense therapy, developing pancytopenia, hypoalbuminemia, increase in hepatic enzymes, decrease in fibrinogen and ESR with elevated CRP and ferritin levels were alerts for MAS. Bone marrow aspiration demonstrated hemophagocytosis (Figure-C). Pulse high dose IV methyl prednisolone treatment was started. Clinical and laboratory findings, particularly ferritin level, improved in the third day of treatment. Steroids were gradually reduced while cyclosporine was added. He is under remission with low dose steroid, cyclosporine-A and regular plasma infusions per 3 weeks.

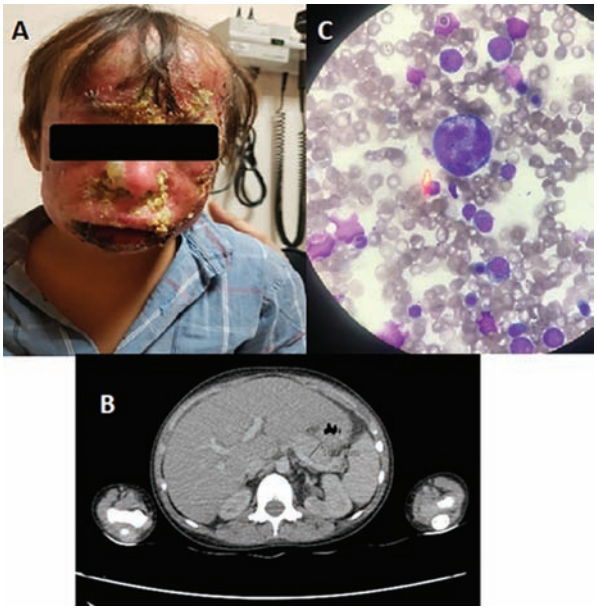


Figure. **A**. Bullous and crusted lesions on face and around oral mucosa. **B.** Shortening of the pancreas tail in CT. **C.** Hemophagocytic cells in the bone marrow.

Conclusion: MAS is rarely seen in course of monogenic J-SLE, but may be serious. It is the first juvenile monogenic lupus case with MAS in the English literature, to best of our knowledge. It is important to distinguish this mortal clinical condition from the flare of disease and appropriate treatment should be started as soon as possible.

REFERENCE

[1] Atteritano M, David A, Bagnato G, et.al. Hemophagocytic syndrome in rheumatic patients. A systematic review. Eur Rev Med Pharmacol Sci. 2012 Oct; 16(10):1414-24.

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SAT0177

CLINICAL AND EPIDEMIOLOGICAL RELEVANCE OF ALLERGY IN SYSTEMIC LUPUS ERYTHEMATOSUS: AN OBSERVATIONAL STUDY

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Background: Altered innate and adaptive immune response is a hallmark of the pathogenesis of systemic lupus erythematosus (SLE). Autoimmune manifestations are a major cause of morbidity and damage accrual and constitute the main target of treatment in patients with SLE. Exposure to medications for purposes of immune suppression or treatment of complications might also synergise with an aberrant immune response and facilitate infections as well as hypersensitivity to non-harmful antigens. Epidemiological data about allergy in SLE are scanty.
Objectives: To describe clinical and epidemiological features of allergy and asthma in SLE.
Methods: One-hundred-thirty-five patients with SLE (classified according to the American College of Rheumatology, ACR, 1990 revised criteria) were enrolled. Retrospective data collection included autoimmune manifestations during the course of SLE and history of asthma. In addition, we recorded timing, clinical features, culprit(s) of the first three hypersensitivity reactions (HyR, together with concomitant infections, SLEDAI-2K and prednisone dose at time of each reaction. Damage accrual was quantitated by employing the SLE International Collaborating Clinics/ACR damage index (SDI).
Results: A history of one or more HyR was found in 40.7% of patients. Immediate-type HyR were most significantly represented (83.6% of cases) and four cases were anaphylaxis (lifelong incidence rate of 67.04/105 persons-years). Respiratory allergy (allergic rhinitis or asthma) occurred in 19 patients (34.5%). Twenty-one out of 55 (38.3%) patients with allergy had $\geq$2 manifestations, five (9.1%) had $\geq$3 manifestations. Drugs were the most frequent culprits, accounting for 81.8% of HyR. Early-onset SLE (before the age of 21) associated with a higher risk of becoming allergic during SLE course compared with late-onset SLE (LR=8.01; p=0.005; HR=2.28, 95%CI=1.27-4.11). Patients with allergy onset after SLE (52.7% of cases) developed a second HyR more frequently and earlier (LR=11.49; p=0.001; HR=5.19, 95%CI=1.87-14.42). SLE with vasculitic manifestations also was a risk factor for developing HyR (LR=4.00; p=0.045; HR=2.13, 95%CI=1.00-4.55). Patients with allergy post-lupus had a SLEDAI-2K>4 and a prednisone dose>5mg/day in 51.7%, 41.7%, 50% of cases and in 37.9%, 50% and 50% of cases at first, second and third HyR respectively. Concomitant infections were detected in 20.7, 25% and 0% of cases respectively. Patients with $\geq$2 HyR had faster damage accrual compared to patients with $\leq$1 manifestations (median SDI/year=0.04, IQR=0.00-0.11 vs 0.00, IQR=0.00-0.06; p = 0.048).
Conclusion: Patients with SLE have a high prevalence of allergy, which might contribute to its protean phenotype SLE deflects allergy incidence trajectories towards an increased risk. Allergy, in turn, associates with increased SLE activity, medication burden and infectious complications and might affect the risk of long-term damage accrual.

REFERENCES

[1] Sequeira JF, et al., Lupus, 1993
[2] Hsiao YP, et al., Int. J. Environ. Res. Public Health 2014
[3] Goldman JA, et al., Arthritis Rheum 1976
[4] Pope J, et al. J Rheumatol, 2002
[5] Morton S, et al. Ann Rheum Dis, 1998
[6] Danza A et al, Lupus, 2013
[7] Touma Z, et al., Curr Opin Rheumatol, 2013
[8] Sin E, et al., Autoimmun Reviews, 2016
[9] Wozniacka A, et al., Mediators Inflamm, 2003

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SAT0178 **THE EFFICACY AND SAFETY OF ANTI-PNEUMOCOCCAL VACCINATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: Systemic lupus erythematosus (SLE) is a complex, multi-factorial chronic systemic autoimmune disease, characterized by a clinically relevant heterogeneity, affecting women more commonly than men. It has an estimated prevalence of 20 to 150 cases per 100,000 persons. The immune system dysregulation in SLE patients is associated with a higher risk of infections, including pneumococcal pneumonia. Anti-pneumococcal vaccines represent a valuable and effective preventative tool to mitigate and counteract pneumococcal pneumonia. However, the efficacy and safety of anti-pneumococcal immunization in SLE patients is both controversial and not completely agreed upon. Indeed, several epidemiological studies investigating the anti-pneumococcal vaccine safety and efficacy in patients suffering from SLE have reported short-term immunogenicity with elevated anti-pneumococcal antibody titres but inconsistent long-term findings, with some studies finding poor responses, mainly for long-term immune protection.
Objectives: We conducted a systematic review and meta-analysis to better understand the efficacy and safety of pneumococcal vaccination administered to SLE patients.
Methods: A comprehensive literature search in accordance with the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) guidelines was performed. We mined also the gray literature and searched also for unpublished studies, presented at congresses either as oral communications or posters. We were able to identify 18 studies. All studies were designed as longitudinal investigations, 2, in particular, were of high quality, being randomized, double-blind trials. Four studies had control groups.
Results: Total sample size included 601 participants. Vaccine immunogenicity in terms of subjects with protective antibody titers ranged from 36% to 97.6%. According to our systematic review and meta-analysis, high erythrocyte sedimentation rate (ESR), older age, earlier SLE onset, high disease activity, and immunosuppressive therapy were found to be statistically significant predictors of poor immunogenicity, although belimumab was found to have no significant impact. With regard to safety, no serious adverse events were found, with up to one third of cases reporting mild/low-grade complaints.
Conclusion: Due to the high risk of pneumococcal infection in SLE patients and given the safety and, at least partial, effectiveness, according to our systematic review and meta-analysis, in such patients, preventive strategies mainly by immunization, are required in all age groups and, in those needing immunosuppressive therapy, immunization should be given prior the initiation of the treatment.
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SAT0179 **CHANGE IN IMMUNOLOGICAL PARAMETERS DURING FOLLOW-UP OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: DATA FROM THE FRENCH ASSESS COHORT**

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Background: Primary Sjögren's Syndrome (pSS) is associated with a biological panel of B-cell activity markers such as hypergammaglobulinemia, rheumatoid factor (RF), decreased C3/C4 complement, cryoglobulinemia, and an increase in β2-microglobulin, used to calculate the biological domain of The EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). In 80% of patients, anti-nuclear autoantibodies, especially anti-Ro/SSA and anti-La/SSB, are also observed. The change in these biological tests during follow-up of pSS patients has been poorly investigated.
Objectives: The objectives of our study were to assess the change in immunological parameters during the follow-up of pSS and to analyse the association with the clinical evolution.
Methods: We analysed data from the French prospective multicenter ASSESS cohort, including 395 patients with pSS. Clinical and biological data were collected at the baseline, then annually. Patients were included if at least two biological assessments and concomitant ClinESSDAI activity scores were available, based on standardized clinical evaluations of the patients. Anova, Wilcoxon and Chi-square tests were used to analyse the relationship between the clinical evolution and immunological profile. A p-value≤0.05 was considered as statistically significant.
Results: 362 of 395 patients had required data to allow their inclusion. The mean number of visits was 5.5. In 81.7% of patients, the biological status did not change throughout the 5-year follow-up (Table 1). The clinical evolution was not related to the immunological changes observed between the previous two visits (p=0.30). There was no significant difference between the number of abnormal immunological markers and the ClinESSDAI activity score (p=0.437) at the same visit. Disease activity according to the ClinESSDAI score remained stable in 257 patients (out of 351 with available data) during follow-up. 175 patients (49.8%) were in remission and 82 (23.3%) had an active disease. The number of abnormal biological markers at baseline was associated with subsequent clinical evolution: detection of ≥5 B-cell activity markers at baseline was a bad prognostic marker, (present in 12.4% of patients having persistent disease activity, versus 3.6% among patients with clinical favourable outcome) (p=0.04).
Conclusion: The biological profile of pSS patients is usually stable over time, especially if the initial assessment is negative, but a higher immunological activity profile might be a bad prognostic factor. Changes in biological parameters do not predict the subsequent clinical course. In conclusion, it is not relevant to systematically repeat the complete immunological screening in pSS patients.

Table 1: Immunological variations during the follow-up of patients from the ASSESS cohort

Immunological markers	Number of patients with positive marker at baseline, n (%)	Change during follow –up (n %)	
		Negative to positive	Positive to negative
Rheumatoid factor	37/63 (58.7)	12 (19.0)	2 (3.1)
Cryoglobulinemia	58/323 (17.9)	24 (7.4)	24 (7.4)
Hypergammaglobulinemia	109/337 (32.3)	5 (1.5)	32 (9.5)
Hypogammaglobulinemia	2/337 (0.6)	3 (0.9)	0 (0.0)
β2-microglobuline ≥ 2.3mg/L	12/25 (48.0)	3 (9.0)	2 (8.0)
C3 Complement ≤0,80mg/L	11/87 (12.6)	10 (11.5)	1 (1.1)
C4 Complement ≤0,15mg/L	12/85 (6.4)	7 (8.2)	1 (1.1)
ANA ≥1/80UI/L	151/203 (74.4)	27 (13.3)	9 (4.4)
Anti-SSA positivity	110/189 (58.2)	10 (5.3)	2 (1.0)
Anti-SSB positivity	69/179 (38.5)	7 (3.9)	13 (7.2)
Monoclonal gammapathy	37/254 (3.9)	45 (17.7)	16 (6.3)

n : number, % : percentage, ANA : antinuclear antibodies

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SAT0180 EVALUATION OF FRAILTY IN SJ GREN'S SYNDROME: CREATION OF A FRAILTY INDEX

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Background: Frailty is a condition characterized by the reduction of the individual's homeostatic reserves, leading to an increased vulnerability to stressors and an increased risk of unfavourable events. The aging of the population and the consequent need to implement new paradigms of care and assistance, have given this tool a growing interest in many medical disciplines[1]. In rheumatology, however, the interest is still limited[2]. The Frailty Index (FI), developed on an arithmetical model of deficit accumulation, is an accurate tool for assessing frailty, providing an estimate of the biological aging.
Objectives: Creation of a FI to be used in clinical practice in patients with Sjögren's syndrome (SS) and evaluation of the correlations with patient's age, duration of illness, activity and disease damage at baseline and in the following 5 years.
Methods: The FI is composed by a checklist of non-predefined variables (deficits) constituted by symptoms, signs, diseases, disabilities, and laboratory findings. The deficits must meet these criteria: age-related; associated with negative outcomes; multidimensional (referring to different domains of the health status); present in at least 1%, but not more than 80% of the sample. To each variable is assigned the value of 0 (= no deficit) or 1 (= deficit). The FI is the ratio between deficits presented by the individual and the total number of deficits considered, thus providing a measure of frailty ranging between 0 (no frailty) and 1 (maximum of frailty)[3]. A FI was developed for patients with SS consisting of 43 items (17 comorbidities, 14 signs and symptoms, 5 disabilities and 7 laboratory findings). Statistical analysis was performed with Spearman's test for correlation assessment, the Mann Whitney test for comparing non-parametric variables was used.
Results: FI was administered to a first small group of 30 female consecutive patients recruited as outpatients at the clinic dedicated to SS. The average age was 57.2 yrs, mean age at diagnosis 52.7 yrs and average disease duration 4.7 yrs. At the time of completing the FI, the average disease activity (ESSDAI) was 3.4, the mean value of the damage (SjSDDI) 1.6 and the average score of FI equal to 0.21. A statistically significant correlation between FI and age has been reported (p = 0.017). No significant correlations between frailty and duration, activity and disease damage have been highlighted at the moment.
Conclusion: For the first time a FI was developed for patients with SS consisting of 43 items. The data shows a relationship between age andFI. The correlation is statistically significant, similarly to what is reported in the literature for other conditions. This confirms that FI is indeed an objective marker of aging and even though the sample population is young (average age = 57.2 years), FI maintains its main properties. This tool can be used to assess the health status of patients, making it possible to identify those at greater risk of trajectories or unfavourable outcomes. It is currently being administered the FI to patients with SS whose clinical course will be evaluated in the next 5 years (complications, mortality, hospitalization, institutionalization and disability).

REFERENCES

[1] Canevelli M, et al, Promoting the Assessment of Frailty in the Clinical Approach to Cognitive Disorders, Front. Aging Neurosc 2017
[2] Rockwood MR, et al, FI to Measure Health Status in People with SSc, J Rheum 2014
[3] Searle SD, et al, A standard procedure for creating a FI, BMC Geriatrics 2008

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SAT0181 CONTRACEPTIVE COUNSELING AND USE AMONG WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT RISK FOR UNPLANNED PREGNANCY

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease that primarily affects women of reproductive age. Disease activity and medication use can complicate pregnancies in SLE, due to the disease itself and/or exposure to teratogenic medications. Therefore, these patients should be counseled and are candidates for highly effective contraceptive methods.
Objectives: To examine contraceptive counseling and use among SLE patients attending our Rheumatology Department.
Methods: Cross-sectional study in which women aged 15-50 followed in our Rheumatology Centre with SLE diagnosis completed a researcher-administered survey. Premenopausal women who were sexually active were considered at risk of pregnancy. We compared self-reported rates of contraceptive counseling and use, stratified by treatment with teratogenic medications, and by history of thrombosis or antiphospholipid antibodies (aPL). The statistical analysis was performed using SPSS 23.0, and $p<0.05$ was taken to indicate statistical significance.
Results: 95 women were interviewed, of these, 60 were considered to be at risk for unplanned pregnancy. Their median age was 36 years (range 17-48), and median disease duration 9.9 years (range 0.25-37.0). 85% were aware of the complications associated with pregnancy in their medical condition and 73.3% had received contraceptive counseling. Fifty-six patients (93.3%) reported consistent contraceptive use. Younger patients were more likely to have received contraceptive counseling (35.0 [17-46] years versus 42.5 [20-48] years, p=0.021). Counseling was more frequently reported by patients with higher educational level (p=0.026). Those who were counseled were using more effective contraceptives and in logistic regression contraceptive counseling was a predictor of highly effective contraception use (OR=13.1, p<0.0001).
Women using teratogenic medications or with a history of thrombosis were no more likely to have received contraceptive counseling or to use more effective contraceptives. Those with positive aPL were using more effective contraceptives (p=0.024). In our model, having a high school degree and positive lupus anticoagulant predicted contraceptive counseling (OR=12.6, p=0.041; OR=3.1, p=0.02, respectively).
Conclusion: This study highlights the importance of contraceptive counseling in SLE patients at risk for unplanned pregnancy. A multidisciplinary team including rheumatologists, gynecologists and family phsycians is needed to improve the education and provision of adequate contraceptive counseling to these women.

REFERENCES

[1] Bundhun PK, Soogund MZ, Huang F. Impact of systemic lupus erythematosus on maternal and fetal outcomes following pregnancy: a meta-analysis of studies published between years 2001-2016. J Autoimmun. 2017;79:17-27.
[2] Yazdany J, et al. Contraceptive counseling and use among women with systemic lupus erythematosus: a gap in health care quality?.Arthritis Care Res (Hoboken). 2011;63:358-65.

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SAT0182 DYSLIPIDEMIA, HYPERTENSION, LUPUS NEPHRITIS AND HIGHER PREDNISONE USAGE CONTRIBUTE TO EVOLUTION OF CAROTID INTIMA-MEDIA THICKNESS IN MILD SYSTEMIC LUPUS ERYTHEMATOSUS: A 7-YEAR FOLLOW-UP STUDY

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Background: In SLE accelerated progression of carotid plaque and contribution of inflammatory factors for premature vascular changes have been reported. Effect of classical risk factors on progression of carotid intima-

media thickness (cIMT) in patients with SLE in comparison with population controls is not clear.
Objectives: To examine in SLE and population controls (1)prevalence of risk factors overtime; (2)evolution of cIMT; (3)risk factors promoting cIMT evolution.
Methods: The study sample originated from the SLEVIC cohort (SLE vascular impact cohort study) which included consecutive patients with SLE and age and sex matched population controls. Seven years after inclusion all participants were asked to take part in the follow-up investigation. The standardized data collection and carotid ultrasound were performed at two assessments, 7 years apart. Effect of risk factors on cIMT overtime was examined with linear mixed models adjusted for age, sex and traditional CV risk factors.
Results: A total of 77 patients with SLE (68% of original cohort), 87% females, at inclusion mean age 47 years, disease duration 11.4 years, SLEDAI 3.0, SLICC/ACR 1.1, and 74 controls (61% of original cohort), 89% females, mean age 51years, completed 7-years follow-up.
At inclusion, patients with SLE were younger and had lower levels of LDL than controls but were more likely to have hypertension and higher levels of triglycerides (TG). Between the assessments both groups were measured with an increase in blood pressure, levels of total cholesterol (TC), LDL, but at follow-up the patients still had lower TC, LDL and HDL levels and higher TG than controls. At both assessments, patients used more frequent antihypertensive and aspirin than controls, p<0.001.
The mean cIMT increased statistically significant in patients and controls, average absolute progression of 0.009 mm/year in patients and 0.011 mm/year in controls, p<0.001 for change in both groups, with no intergroup difference, p=0.867 age- and sex-adjusted.
In multivariate analysis, the patients showed a statistically significant association between mean cIMT overtime and higher systolic blood pressure, lower levels of HDL, higher TC/HDL- and LDL/HDL-ratio, higher triglycerides, dyslipidemia and detection with (any) carotid plaque at inclusion. In the control group, lower levels of HDL, history of dyslipidemia and finding with bilateral plaque at inclusion were associated with cIMT overtime. At follow-up, hypertension and blood lipid measures in patients (with exception for TG) and HDL in controls were still significantly associated with cIMT overtime. Of all, the strongest association was shown for HDL in both patients and controls. Effect of other cardiometabolic risk factors at inclusion and cumulative risks were not significant after adjustment for age and sex.
In the patients, history of nephritis at inclusion and follow-up, and a higher average dose of prednisone used since diagnosis, but not other treatments, were associated with cIMT overtime.
Conclusion: We observed similar progression of cIMT over 7 years in patients with long-standing mild well-controlled SLE disease and population controls. Our findings suggest importance of recognition with dyslipidemia and hypertension, and support recommendation to limit use of corticosteroids in patients with SLE as a part of CV risk management. The factors protecting or promoting atherosclerotic progression should be further explored.
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SAT0183 LUPUS NEPHRITIS: A RETROSPECTIVE LONGITUDINAL STUDY LOOKING FOR CHRONIC RENAL DISEASE ASSOCIATED FACTORS, FROM THREE SOUTH-EUROPEAN COHORTS OF PATIENTS IN FOLLOW-UP SINCE 2000

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Background: Renal involvement in systemic lupus erythematosus (SLE) is the most frequent severe manifestation and carries a bad prognosis.
Objectives: To analyze the outcome of lupus nephritis (LN) in terms of chronic kidney disease development (CKD).
Methods: Design: multicentre restrospective observational study. Patients: SLE patients (ACR97) with biopsy proven LN attending to three South European Rheumatology departments. Variables: demographics, SLE related variables, including global activity (SLEDAI-2K), renal flares, therapies, ACR response criteria and CKD. Statistical analysis: descriptive bivariate and multivariate analysis exploring factors associated to CKD.
Results: Seventy-six patients with biopsy-proven LN were included, 90,7% female; mean age: 33 years; mean disease: duration 14 years; mean follow-up time (since LN diagnosis): 8,5 years. LN class III, IV and V were present in 22%, 75% and 3% of the cases, respectively. At LN diagnosis 68 (89%) patients had a severe renal flare. Forty-one (56.1%) and 49 (64.4%) had HTA and nephrotic syndrome, respectively. The mean 24h proteinuria levels at LN diagnosis was 4,6g. Mean SLEDAI-2K at the time of flare was 20.3, with 69 (65.7%) patients having an extrarenal flare.
The treatments used to induce remission were: glucocorticoids (100%): pulses M-prednisolone in 49 (64%) and oral prednisone (mean starting dose): 43 mg/day (±20.6); intravenous cyclophosphamide in 42 (55%) patients; mycophenolate mofetil (MMF) in 21 (27%) patients; calcineurin inhibitors in 5 (11%) patients; rituximab in 4 (5.2%) patients; and oral cyclophosphamide in 4 (5,2%) patients. Forty-eight (63%) patients were receiving hydroxychloroquine. MMF was the immunosuppressant (IS) more frequently used (52%) as maintenance therapy.
At 3, 6 and 12th months, the mean proteinuria was 2.3g/24h, 1.53g/24h, 1.1g/24h, respectively (p< 0.001). Fifty-five (77,5%) of patients achieved complete response and 61 (84.7%) presented complete or partial response. Median time to renal remission: 12.5 months (6,17.5). In 32 patients (42%) it was possible to discontinue IS. Sixteen (21.9%) patients developed CKD, 4 (5.3%) needing dialysis and 1 (0.76%) renal transplantation. Serious infection was recorded in 23 (34.8%) patients. Five (6.6%) patients died (2 cardiovascular cause).
In the bivariate study, the following variables were significantly associated with CKD: male sex, hypertension, ACEI drugs, severe infection after LN, temporal dyalisis, non ACR renal response, non use of hydroxychloroquine, time to achieve 10mg/day of prednisone, previous creatinine to LN, maximum creatinine at LN, hyperlipidemia at 3 months of LN, active urinary sediment at 12 months, creatinine at 6 and 12 months, proteinuria at 6 and 12 months.
In the logistic regression model, using genetic algorithms, we found that proteinuria at 6 months was significantly associated with CKD (OR:2.95; 95%CI 1.19,9.29, p= 0.03). Hypertension and male sex were marginally associated (p=0.06, both).
Conclusion: A considerable percentage of LN patients developed renal chronic failure (21,9%). A high percentage of ACR response was achieved using medium dose (40mg) of glucocorticoids for induction. A significative reduction of proteinuria was achieved at 3 months, but proteinuria at 6 months was the only factor finally associated with CKD.
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SAT0184 ASSOCIATION OF SERUM AND URINE LEVELS OF TWEAK, MCP-1 AND NGAL WITH DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: TWEAK, MCP-1 and NGAL, mediators in pathogenesis of systemic lupus erythematosus (SLE), are proinflammatory cytokines/chemokines that are thought as potential biomarkers reflecting disease activity (1).
Objectives: In this study, we aimed to investigate the association of serum (s) and urine (u) levels of TWEAK, MCP-1 and NGAL with disease activity in both renal and non-renal SLE.
Methods: Thirty active patients with SLE (15 renal and 15 non-renal) were recruited. Thirty-one inactive patients with SLE (16 renal and 15

non-renal), 14 patients with ANCA-associated vasculitis (AAV) all of whom had active renal involvement and 20 healthy volunteers were selected as control groups. Serum and urine levels of TWEAK, MCP-1 and NGAL were tested using ELISA.

Results: Sixty-one SLE patients, 51 (83.6%) of whom were female, with a median disease duration of 83 (23.5-135) months and a median age of 35 (27-47.5) were included in the study. Serum and urine levels of TWEAK and NGAL were significantly higher in the active SLE group compared with the inactive SLE (n=31) group (sTWEAK: p=0.005; uTWEAK: p=0.026; sNGAL: p<0.001; uNGAL: p=0.002); whilst no significant differences regarding serum and urine MCP-1 levels were observed (p=0.189 and p=0.106). uTWEAK (p=0.237), sMCP-1 (p=0.141), uMCP-1 (p=0.206), sNGAL (p=0.419) and uNGAL (p=0.443) levels did not differ between patients with active LN and non-renal active SLE; yet levels of sTWEAK were higher in patients with active LN (p=0.006). There were no differences between active LN and renal active AAV. Levels of all biomarkers were correlated with SLEDAI (sTWEAK: p=0.001; uTWEAK: p=0.006; sMCP-1: p=0.049; uMCP-1: p=0.014; sNGAL: p<0.001; uNGAL: p=0.002).

Conclusion: sTWEAK, uTWEAK, sNGAL and uNGAL are significant biomarkers showing disease activity in SLE. However, our results implicate that these biomarkers may not be specific for SLE, and can be elevated in patients with active renal involvement of AAV. sTWEAK may be of use for discriminating active nephritis from non-renal active disease in SLE. Further studies are awaited to confirm these results (This study was funded by Istanbul University with the project number TTU-2017-24738 and Turkish Society for Rheumatology).

REFERENCE

[1] Mok CC. Biomarkers for lupus nephritis: a critical appraisal. J Biomed Biotechnol. 2010;2010:638413.

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SAT0185 THE EFFECTS OF DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS ON COGNITIVE FUNCTION

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Background: Cognitive dysfunction (CD) affects up to 90% of systemic lupus erythematosus (SLE) patients and significantly impacts patient quality of life. The cause is multifaceted with many factors common across chronic diseases. It is thus difficult to ascertain the direct impact active disease in SLE has upon immediate cognitive function.

Objectives: The aim of this study was to investigate the effects of active disease in SLE on CD. We compared cognitive measures in SLE patients with stable disease activity (SLE-S) to those with active disease (SLE-F).

Methods: 34 SLE-S and 24 SLE-F were recruited, all meeting 1997 ACR criteria. Active disease was defined as BILAG A or B with a change in treatment. Stable disease was defined as SLEDAI-2K ≤4. Overall 14/24 SLE-F patients were assessed again at 2nd visit (v1 vs v2) when their disease activity had reduced. CD was measured using tests from a computerized battery of tests (CANTAB®). fMRI was used to examine neuronal responses to a working memory and attention task (n-back) and a facial emotional processing task (FERT). Analysis compared the SLE-S and SLE-F groups as well as a within group comparison for v1 vs v2. fMRI data were analysed using SPM12. All other data were analysed using SPSS 22.

Results: There were no differences between the SLE-S and SLE-F groups or between v1 and v2 on demographic and clinical measures except disease activity. The SLE-F group scored higher than the SLE-S group on the MADRS depression scale (p=0.003) but no other significant differences in psychiatric symptoms were observed. There were no significant differences on the CANTAB® for either comparison (table 1). The fMRI showed a SLE-S vs SLE-F difference in n-back related response in the medial prefrontal cortex (p=0.012; figure 1). No v1 vs v2 differences were found, nor for either comparison for the FERT.

Table 1. Baseline characteristics, SLE-S vs SLE-F

	Variable		SLE-F (n=24)	SLE-S (n=34)	p-value
			Mean (S.D.), Median (LQ, UQ) or n (%)		
Demographic and clinical	Age (years)		36 (12)	39 (11)	0.330
	Age at diagnosis (years)		26 (9)	28 (11)	0.537
	BILAG total score*		12 (9, 16)	1 (0, 2)	**<0.001**
	Oral corticosteroids (y/n)		15 (63)	12 (35)	0.061
	Current immunosuppressant use		18 (75)	14 (41)	**0.016**
	Current antimalarial use		18 (75)	19 (58)	0.261
	Biologic medication		4 (17)	3 (9)	0.432
Depression & anxiety	MADRS	8 (4, 12)	4 (1, 8)	**0.003**	
	HADS – A	6 (5, 10)	6 (3, 10)	0.713	
CANTAB®	Visual memory	28 (17, 75)	28 (19, 63)	0.897	
	Attention	18 (15, 22)	13 (12, 20)	0.063	
	Emotion processing	62 (10)	62 (9)	0.727	
	Executive function	1.3 (1.3, 1.6)	1.4 (1.3, 1.7)	0.981	

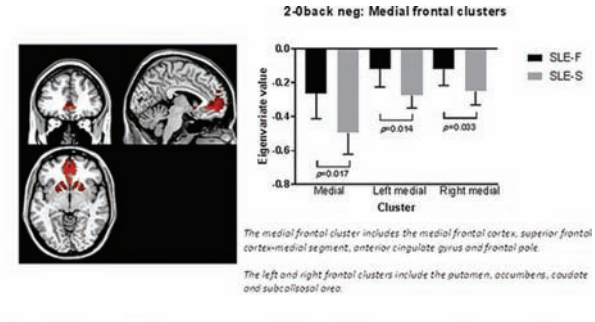


Figure 1 Differences in BOLD response between the SLE-S and SLE-F groups during the n-back (working memory task), 2-0back condition, negative main effect.

Conclusion: In a cohort well matched on confounding factors these results suggest that active disease does not impair cognitive function. However, the differences in the medial frontal cluster during the working memory task may indicate the use of compensatory mechanisms to maintain cognitive function as has been found elsewhere. Alternatively, as this is a default mode network region, often implicated in self-reflective processes it may be that CD is more directly associated with differences in mood. As such when treating SLE patients with self-reported CD it is important to consider factors other than disease activity.

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SAT0186 **Ω MORTALITY IN CHILDREN WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS IN AN ARGENTINE PEDIATRIC CENTRE.**

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Background: Juvenile systemic lupus erythematosus (JSLE) is a complex multisystemic autoimmune disease, often causing irreversible damage, reduced quality of life and life expectancy. Data on causes of death and time trends in infant lupus mortality are limited.
Objectives: The aim of this study was to determine mortality in a pediatric cohort.
Methods: This retrospective study included patients with childhood onset lupus (fulfilling ACR 1997) who were diagnosed at the Paediatric centre in Santa Fe Argentine, Alassia Children Hospital from 1991 to 2018 and had 15 years of age at presentation.
Results: This study includes 54 JSLE children (F:M=12,5 :1) with a mean age of onset lupus 12 years (range 4-15 years). During a mean follow-up in our centre of 3 years (range 12m–10 years), 12 patients (24%) was died; 5 during the follow-up in our centre and 7 in adult centre,4 lost to follow-up.
The average age of death was16 years (range 10-29 years) and the average since diagnose time was 17 months (range 3m-15 years).
The principal system involved was renal (100%). 10 patients with diffuse proliferative lupus nephritis (WHO class IV), 2 membranous lupus nephritis (WHO class V), 5 patients (41.6%) with hematological disorders (2 pancytopenia, 2 leukopenia,1 Macrophage Activation Syndrome). 3 patients had thrombosis. 5 patients (41.6%) with neurological involvement (4 psychosis, 1 depression). One patient with liver dysfunction. There one death related to renal biopsy.
The principal cause of mortality was active disease and infection. Meningococcal meningitis, Klebsiella peritonitis, Pneumococcal cellulitis of the neck, peritonitis and 1 patient with disseminated tuberculosis.
11 patients (91,6%) had received intravenous steroids as pulses and Cyclophosphamide pulse therapy, azathioprine or mycophenolate mofetil, hydroxychloroquine immunoglobulins. In some patients peritoned dialysis and ventilation. 8 patients (66%) with bad socioeconomic environment. Four patients (33%) with poor adherence to treatment.
Conclusion: In this single-center study, childhood onset lupus was associated with a mortality of 24%. With higher frequency of aggressive renal disease and higher requirement for steroids and immunosuppressive drugs. Pediatric care should consider transition to adult's centers and ensure continuity of treatment.

REFERENCE

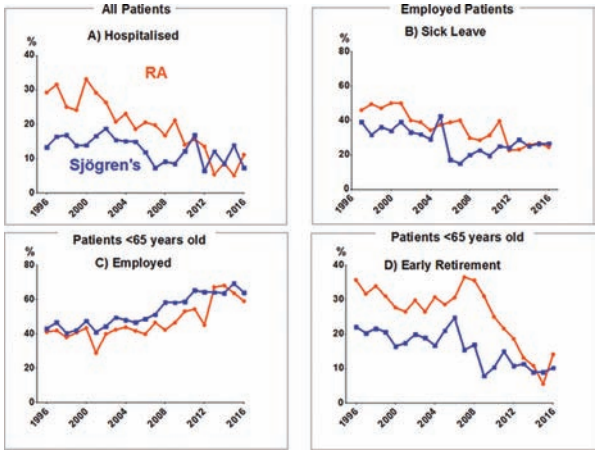
[1] Childhood systemic lupus erythematosus in Latin America. The GLADEL experience in 230 children. February 2008 Lupus 17(6):596-604 DOI: 10.1177/0961203307088006

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Disclosure of Interests: None declared
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SAT0187 **TRENDS IN EMPLOYMENT AND HOSPITALIZATION IN PATIENTS WITH SJÖGREN'S SYNDROME 1993–2016: RESULTS FROM THE GERMAN NATIONAL DATABASE**

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Background: During the last 20 years, employment rates increased substantially in the German population and also in patients with arthritis [1]. Whether patients with primary Sjögren's syndrome (pSS) also show this trend is less clear in the absence of new treatment options.
Objectives: To assess trends in treatment and outcomes in patients pSS, focusing on employment, hospitalization and medical treatment in the past two decades.
Methods: From 1996 to 2016, ~300 patients with pSS were documented annually in the National Database of the German Collaborative Arthritis Centres. Data on treatment, physician assessment of disease activity, patient-reported outcomes, hospitalization and employment were collected and compared to patients with rheumatoid arthritis (RA), matched 1:1 for age, sex and disease duration for each calendar year.
Results: Patients with pSS (>90% female, age ~44 years at disease onset, disease duration ~10 years) were more frequently assessed to be in low disease activity in 2016 (93%) than in 1996 (62%, p<0.01). Treatment with antimalarials increased (31% to 50%, p<0.01) and less patients were on glucocorticoids (50% to 34%, p<0.01); Less than 5% were treated with biologics in 2016. The percentage of employed patients (<65 years) increased by 21 percentage points (43% to 64%, p<0.001), exceeding the increase observed for RA patients (+15 percentage points). In 2016, significantly less patients compared to 1996 were on early retirement (22% and 10%, p=0.01), hospitalized/year (13 and 7%, p=0.08) or on temporary sick leave (27% compared to 39%, p=0.09). This trend is comparable to RA patients.



Conclusion: Overall, similar trends were observed for RA and pSS cohorts despite minor changes in pSS therapy. Work participation has improved significantly over two decades in pSS. A greater perception of pSS without systemic manifestations may have caused a shift towards less severely affected patient cohorts today.

REFERENCE

[1] Mau W, Listing J, Huscher D, Zeidler H, Zink A. Employment across chronic inflammatory rheumatic diseases and comparison with the general population. J Rheumatol. 2005;32(4):721-8

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Disclosure of Interests: Johanna Callhoff: None declared, Katja Thiele: None declared, Thomas Dörner Grant/research support from: Eli Lilly, Janssen, Roche, UCB Pharma, Consultant for: Eli Lilly, Janssen, Roche, UCB Pharma, Speakers bureau: Eli Lilly, Janssen, Angela Zink Speakers bureau: Speakers fees from AbbVie, Janssen, Pfizer, Roche, Sanofi, Jörg Henes: None declared, Jutta Richter Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Katinka Albrecht: None declared
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SAT0188 **WHOLE BLOOD VERSUS SERUM HYDROXYCHLOROQUINE LEVELS FOR DRUG MONITORING OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: PRELIMINARY RESULTS OF A PHARMACOLOGICAL STUDY**

Benoit Blanchet[1], Moez Jallouli[1], Marie Allard[1], Pascale Ghillani Dalbin[2], Lionel Galicier[3], Véronique Le Guern[1], Noel Zahr[2], Claire Goulvestre[1], Zahir Amoura[2], Jean-Charles Piette[2], Noemie Jourde-Chiche[4], Nathalie Costedoat-Chalumeau[1], Group PLUS. [1]*Cochin Hospital, Paris, France*; [2]*Pitié Salpêtrière Hospital, Paris, France*; [3]*Saint Louis Hospital, Paris, France*; [4]*Aix-Marseille Univ, C2VN, INSERM, INRA, AP-HM Centre de Néphrologie, Marseille, France*

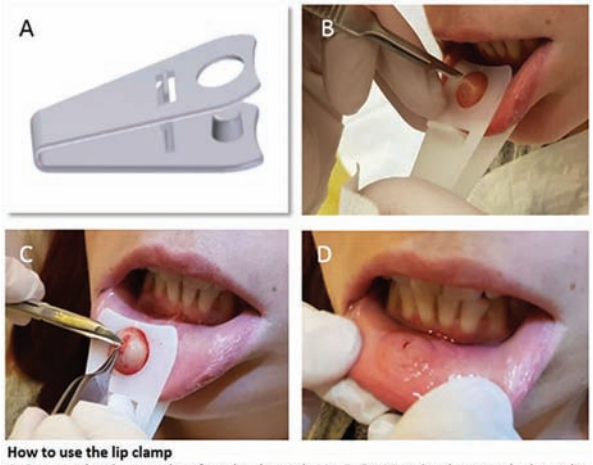
Background: In order to assess the pharmacokinetic/pharmacodynamic relationship of hydroxychloroquine (HCQ) in patients with systemic lupus erythematosus (SLE), HCQ levels have been measured in whole blood as well as in serum but both methods have never been compared. In addition, cut offs for non-adherence (classically 200ng/ml but also 100 ng/mL) have been established only in whole blood.

Objectives: The aims of this study were (1) to compare these two pharmacological approaches, and (2) since it would be very interesting to retrospectively assess severe non-adherence in clinical trials or in large cohort of patients in which only serum samples are usually available, to determine if serum HCQ level cut offs could be established for identification of severe non-adherent patients.
Methods: The HCQ and desethylchloroquine (DCQ) levels were measured in serum and whole blood from 573 SLE patients. The risk factors for active SLE (SLEDAI score >4) were identified using multiple logistic regression. HCQ serum level was also measured in 51 non-adherent patients (whole blood HCQ level <200 ng/mL).
Results: The mean HCQ and DCQ levels were 916 ± 449 and 116 ± 55 ng/mL in whole blood, respectively; and 469 ± 223 and 63 ± 31 ng/mL in serum, respectively. The mean ratio of serum/whole blood level for HCQ and DCQ were 0.53 ± 0.15 and 0.57 ± 0.21, respectively. A strong positive correlation was found between serum and whole blood levels of HCQ (rho=0.837 [CI95% 0.810-0.860], p<0.0001), and DCQ (rho=0.771 [CI95% 0.736-0.802], p<0.0001). In the multivariate analysis, only corticosteroids (p=0.044), immunosuppressant (p=0.027), HCQ whole blood level (p=0.023) and hemoglobin (p=0.009) were identified as an independent risk factor of active SLE but serum HCQ level was not.
Given the mean ratio of serum/whole blood level for HCQ was 0.53, we extrapolated that serum HCQ level cut offs of 106 and 53 ng/mL would correspond to the previously used cut-off of 200 and 100 ng/mL of HCQ in whole blood.
Using HCQ serum level cut off of 106 ng/mL, 43 of 51 patients (84%) with blood HCQ levels <200 ng/mL would also have been considered as non-adherent. The positive and negative predictive value of HCQ serum level < 106 ng/ml to detect non-adherence were 96.6% and 63.6%, respectively.
Of these 51 patients, 25 patients (49%) exhibited HCQ whole blood concentration below 100 ng/mL. Using HCQ serum level cut off of 53 ng/mL, 23 of 25 patients (92%) with HCQ whole blood level<100 ng/mL, would also have been considered as non-adherent. The positive and negative predictive value of HCQ serum level < 53 ng/ml to detect non-adherence were 82.1% and 90.9%.
Conclusion: Our data support the use of whole blood rather than serum as the matrix for drug monitoring of HCQ levels in SLE patients. However, when whole blood is not available, our results support the use of HCQ serum level to assess non-adherence with a cut off of 106 ng/mL corresponding to 200 ng/ml in whole blood.
Disclosure of Interests: None declared
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SAT0189 A NOVEL DEVICE FOR RAPID MINOR SALIVARY GLAND BIOPSY IN SUSPECTED SJÖGREN'S SYNDROME

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Background: Labial minor salivary glands (MSG) biopsies are a frequently performed diagnostic procedure for Sjögren's syndrome. MSG biopsy usually requires additional assistance e.g. to provide lower lip protrusion and to apply pressure on the lip during the procedure. The latter is done to foster protrusion of salivary glands and therefore to reduce the incision depth and potential nerve damage. We recently developed a new single-use device for MSG by 3D-printing in form of a lip clamp with a stamp on the lower arm to reduce invasiveness and to facilitate the intervention.
Objectives: To assess practicability and to describe the technical application of this device for MSG biopsies in the rheumatology department.
Methods: Retrospective study of MSG biopsies performed with the use of a dedicated lip clamp. For each MSG biopsy, we recorded if any assistance was needed during the procedure, occurrence of any complication, if salivary glands were obtained and if the quality of the salivary gland tissue sample was adequate for histologic analysis.
Results: 12 MSG biopsies performed on 12 patients with suspected Sjögren's syndrome were included in the study. MSG biopsies were performed between August 2018 and January 2019. Using the lip clamp, the physician was able to perform all the biopsies without assistance. No complication occurred with a follow-up of 1 week for each patient. Salivary glands tissue samples were obtained in 11/12 of the patients using 1 incision. For 1 patient, a second incision had to be performed on the contralateral side of the lip during the same intervention because no glands were found on the first attempt. Quality of all the samples was adequate for histologic analysis. We did not observe an increase in procedure time compared to routine MSG biopsy procedure.
Conclusion: The use of a single-use lip clamp facilitates MSG biopsy without needing assistance and potentially reduces invasiveness and collateral damage. Quality of the tissue samples obtained was adequate for histological analysis.



How to use the lip clamp
A: Prepare the clamp and perform local anesthesia. **B:** Position the clamp on the lower lip with the recess of the clamp facing up, at 0.5-1 cm off the midline. **C:** Perform a 5 mm vertical superficial incision. Due to the pressure from below, a minor salivary gland appears. Seize it with forceps and cut it with scissors or scalpel. **D:** Open and remove the clamp. No stiches are required.

Disclosure of Interests: Alexandre Dumusc: None declared, Bettina Bannert: None declared, Diana Dan: None declared, Thomas Huegle Grant/research support from: AbbVie, Lilly, Novartis and Pfizer, Speakers bureau: AbbVie, Lilly, Novartis and Pfizer
DOI: 10.1136/annrheumdis-2019-eular.5974

SAT0190 LYMPHOMA IN PRIMARY SJÖGREN'S SYNDROME: A RETROSPECTIVE CLINICAL STUDY WITH PATIENTS FROM THE UPA (UDINE, PISA, ATHENS) GROUP

Andreas Goules[1], Chiara Baldini[2], Saviana Gandolfo[3], Aristea Papageorgiou[4], Dimitris Ziogas[4], Francesco Ferro[2], Valentina Donati[2], Cathryn Scott[3], Salvatore De Vita[3], Michael Voulgarelis[4], Athanasios Tzioufas[5]. *[1]Athens School of Medicine, National and Kapodistrian University of Athens, Athens, Greece., Pathophysiology, Athens, Greece; [2]University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy; [3]University of Udine, Department of Medical and Biological Sciences, Rheumatology Clinic, Udine, Italy; [4]Athens School of Medicine, National and Kapodistrian University of Athens, Athens, Greece., Pathophysiology, Athens, Greece; [5]Athens School of Medicine, National and Kapodistrian University of Athens, Athens, Greece., Pahtophysiology, Athens, Greece*

Background: Lymphoma development in Sjögren's syndrome has significant impact on morbidity and mortality of the disease.
Objectives: To describe and compare clinical, serological and histological features of patients with primary Sjögren's syndrome (pSS) associated non-Hodgkin's lymphomas (NHLs) in 3 cohorts, from Greece (1) and Italy (2).
Methods: 140 consecutive pSS patients with NHLs who fulfilled the 2002 AECG criteria for Sjögren's were included in the study. Patients were recruited from 3 centers (Udine, Pisa, Athens, cohort named UPA), two from Italy (Udine and Pisa University Hospitals with a total of 63 cases, named cohort UP) and one from Greece (University of Athens with 77 cases, named cohort A). Age at NHL onset, NHL subtype and distribution, SS disease duration until lymphoma development, serum anti-SSA/SSB antibodies and rheumatoid factor, history of salivary gland enlargement, cryoglobulinemia with or without vasculitis and C4 hypocomplementemia before the onset of NHL were recorded and compared.
Results: The Greek cohort (A) had a median age at lymphoma diagnosis 58 years (range: 28-90 years) and the (UP) cohort a median age at diagnosis of lymphoma 55.6 years (range: 25-77 years). The median time from SS to lymphoma diagnosis was 65.8 months (range: 0-456 months) vs 48 months (range: 0-276 months) for (A) and (UP) cohort respectively. The commonest histologic subtypes such as, MALT (mucosa associated lymphoid tissue), diffuse large B cell (DLBC) and nodal or splenic marginal zone (MZ) lymphomas were observed in similar frequencies between

the 2 cohorts. The proportion of pSS NHLs patients with MALT lymphomas and >1 involved sites was significantly higher in cohort (A) compared to (UP) cohort [25/51, (49%) vs 5/40 (12.5%%), p=0,0003)] while extranodal localization of DLBC lymphomas was less frequent in Greek compared to Italian patients [2/12 (16.7%) and 4/10 (40%) respectively]. No significant differences were observed regarding anti-Ro/SSA, anti-La/SSB, rheumatoid factors (RF) or history of parotid gland enlargement. Interestingly, no significant difference was also observed in the frequencies of serum cryoglobulinemia (without vasculitis) and C4 hypocomplementemia. Importantly, cryoglobulinemic skin vasculitis was significantly more frequent in cohort (A) than in cohort (UP) [33/77 (42,9%) vs 12/63 (19,0%) p=0,0027] as well as bone marrow involvement by lymphoma [21/77 (27.2%) vs 4/63 (6.3%) respectively, p=0,0015].

Conclusion: The similar lymphoma histologic subtypes, coupled with the differences in the frequency of cryoglobulinemic skin vasculitis and bone marrow involvement by lymphoma between Greek and Italian patients, suggest potential diversities in genetic background, environmental factors, disease progression and pathologic pathways in different cohorts, offering novel perspectives to study the biology of SS associated lymphomagenesis.

Disclosure of Interests: Andreas Goules: None declared, Chiara Baldini: None declared, Saviana Gandolfo: None declared, Aristea Papageorgiou: None declared, Dimitris Ziogas: None declared, Francesco Ferro: None declared, Valentina Donati: None declared, Cathryn Scott: None declared, Salvatore De Vita Grant/research support from: Roche, Pfizer, Abbvie, Novartis, BMS, MSD, Celgene, Janssen, Consultant for: Roche, Michael Voulgarelis: None declared, Athanasios Tzioufas Grant/research support from: ABBVIE, PFIZER, AMGEN, NOVARTIS, GSK

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SAT0191 LOW SOCIOECONOMIC STATUS AND HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Socioeconomic factors have been considered as possible confounding factors in the attribution of greater damage accrual in Afro-Caribbean and Hispanic patients with Systemic lupus erythematosus (SLE). Patients with SLE often experience long-term morbidity that can adversely affect their health-related quality of life (HRQoL)[1]

Objectives: To analyze the relation between socioeconomic status, damage accrual and HRQoL

Methods: Analytic study in a cohort of SLE patients that were closely monitored in an autoimmunity program in Colombia. We stratified patients with damage (SDI $\geq$1) and no damage (SDI <1) and according to socioeconomic status as a surrogate value for economic income with dichotomization in low and medium/high income. We performed a non-parametric analysis of related simples of Wilcoxon in each of the dimensions of quality of life in EuroQoL 5d

Results: We analyzed 400 Colombian patients. Baseline median age was 49 years (15 IQR) with median age at diagnosis and disease duration of 37 years (17 IQR) and 9 years (13 IQR) respectively. There were 94% female patients and 17.3% late onset SLE. Most frequent clinical manifestations were hematological (82.8%), mucocutaneous (75.3%) and nephritis (33.8%). Only 4.5% had neurological involvement. The mean SLEDAI were 1.18 and 0.65 at first and second measurement respectively, in the first measurement 97.1% of the patients had a SLEDAI ≤4. The mean SDI was 0.7275 at first measurement and 0.985 at the second measurement. When comparing the intervention in patients with SDI$\geq$1 there was a significative improvement in the Quotidian Activities, Pain/Discomfort, Anxiety/Depression domains, independent of economic income. In patients with medium-high income there was also a significative improvement in the mobility and personal care domains. In the no-damage groups there was only a positive impact in the Anxiety/Depression domain in a statistically significant manner, and the medium-high income subgroup had improvement in the Pain/Discomfort domain. We didn't find other statistically differences in the other domains. Low economic income seems to exert a negative influence in the different HRQoL domains with independence regarding treatment strategy, specially in patients with no damage accrual. In patients with higher income and damage accrual the opposite seems to appear, which could be related with a better ability or resources to cope with the consequences of the disease

Conclusion: In Colombian patients with SLE, socioeconomic status (as a reflection of income) might be related with HRQoL. This relationship could be influenced by damage accrual

REFERENCE

[1] Panopalis P, Petri M, Manzi S, Isenberg DA, Gordon C, Senecal JL, et al, and the Tri-Nation Study Group. The systemic lupus erythematosus Tri-Nation study: cumulative indirect costs. Arthritis Rheum 2007;57:64–70

Disclosure of Interests: None declared

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	Damage present						Damage absent					
	Low incoming			Mid -high incoming			Low incoming			Mid -high incoming		
	Initial (%)	Final (%)	p Value †	Initial (%)	Final (%)	p Value †	Initial (%)	Final (%)	p Value †	Initial (%)	Final (%)	p Value †
Mobility	51	55	**0,4**	56,6	72,3	**0,004**	54,3	60,3	**0,35**	59,2	68	**0,13**
1	48	45		42,2	27,7		44,8	37,9		40,8	32	
2	1	0		1,2	0		0,9	1,7		0	0	
3												
Personal Care	72	76	**0,35**	73,5	84,3	**0,016**	72,4	76,7	**0,5**	78,8	79,8	**0,85**
1	27,1	23		24,1	15,7		26,7	21,6		21,2	20,2	
2	1	0		2,4	0		0,9	1,7		0	0	
3												
Quotidian	51,5	67	**0,005**	59,8	73,2	**0,03**	60,3	62,9	**0,7**	65	68,9	**0,5**
Activities	44,3	33		36,6	25,6		38,8	31,9		34	30,1	
1	4,1	0		3,7	1,2		0,9	5,2		1	1	
2												
3												
Pain/Discomfort	34	38,1	**0,008**	30,1	44,6	**0,003**	37,9	30,2	**0,5**	23,1	40,4	**0,002**
1	39,2	53,6		50,6	49,4		41,4	52,6		53,8	47,1	
2	26,8	8,2		19,3	6		20,7	17,2		23,1	12,5	
3												
Anxiety/	51	70,8	**0,001**	61	79,3	**0,001**	51,3	66,4	**0,01**	53,9	73,5	**0,001**
Depression	32,3	22		26,8	18,3		35,4	27,4		32,4	23,5	
1	16,7	7,2		12,2	2,4		13,3	6,2		13,7	2,9	
2												
3												

† Wilcoxon test

SAT0192 MYOSITIS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: DATA FROM A FRENCH NATIONWIDE SURVEY

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Background: Myositis is recognized as a manifestation of primary Sjögren's syndrome (pSS). Grading muscle involvement using the EULAR Sjögren Syndrome Disease Activity index (ESSDAI) does not require biopsy-proven active myositis or extensive immunological investigations. However, several studies have reported that a high proportion of pSS-associated myositis is either inclusion body myositis (IBM) or an overlap with idiopathic inflammatory myopathies.
Objectives: The objective of our study was to investigate the nature of inflammatory muscle involvement in a large sample of patients with pSS and concurrent myositis.
Methods: We conducted a French nation-wide survey among reference centers known for their experience in the field of systemic auto-immune diseases. Patients with physician-based diagnosis of pSS and inflammatory muscle involvement were included. They were categorized and subsequently described and compared according to the identification of an associated condition likely to explain inflammatory muscle involvement.
Results: 60 cases of myositis in patients with pSS were identified. Patients were mostly female (52/60) and pSS classification criteria were met in 43/60. Muscle biopsy was performed in 50/60 patients and showed inflammatory lesions in 80% of cases. An associated condition likely to explain myositis was identified in 31 patients: typical dermatomyositis rash (n=8), MCTD-specific antibodies (n=11), myositis specific antibodies (n=10), and systemic lupus erythematosus, scleroderma or ANCA associated vasculitis specific antibodies in favor of an overlap syndrome (n=7). Among the 29 patients without associated condition likely to explain myositis, 17 had a biopsy proven inflammatory muscle disease, showing histopathologic features consistent with IBM in 5 cases. 4 of the 5 patients with IBM histological features received corticosteroids and/or other immunosuppressive agents to treat muscle disease. Worsening of muscular involvement despite treatment was reported in these 4 patients. Comparative analysis showed a lower ESSDAI (p = 0.001) among patients without identified associated condition likely to explain myositis.
Conclusion: In most cases of concurrent pSS and myositis, inflammatory muscle involvement is explained by a context of overlap syndrome or has a histological pattern consistent with IBM. Extensive immunological investigations and muscle biopsy appear to be necessary in pSS patients with suspected inflammatory muscle involvement, in order to avoid misclassification and/or overtreatment.
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SAT0193 THE USE OF A SYMPTOM CHECKLIST TO RECOGNISE PATIENTS WITH COMORBID FIBROMYALGIA ON A BACKGROUND OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Fibromyalgia (FM) and systemic lupus erythematosus (SLE) are both characterised by non-specific symptoms such as pain and fatigue. To make diagnosis even more challenging, fibromyalgia is overrepresented in the SLE population.
Objectives: To identify which symptoms can discriminate between patients with comorbid FM and patients without comorbid FM in the SLE population, using a routinely distributed questionnaire.
Methods: Patients with SLE (n=88) completed a Multi-Dimensional Health Assessment Questionnaire (MDHAQ) [1] and the 2011 FM Criteria questionnaire [2]. FM status was determined using the 2016 modification of the 2010/2011 FM criteria [3]. The MDHAQ contains a 60-item symptom checklist section, giving a score of 0-60. Patients with complete data were analysed for specific symptoms that were discriminating for FM using student's t test with Bonferroni correction.
Results: SLE patients with FM reported a higher prevalence of positive responses for every symptom except for 'dark or bloody stools' and 'burning in sexual organs'. Nineteen symptoms demonstrated a significant difference between those with and without FM. The most discriminating symptoms were muscle pain, swelling (of hands, ankles and in other joints), back pain, neck pain, problems with thinking and dry mouth (all $p<0.0001$). Grouping the above 8 symptoms, a cut-off of ≥ 4 gave a sensitivity of 91% and specificity of 88%, correctly classifying 89% of patients when compared to FM criteria. Overall, patients with FM reported a mean total of 23.6 items on the symptom checklist, compared to 8.09 for patients without FM.
Conclusion: The symptom checklist section of the MDHAQ can provide clues that help discriminate between SLE patients with and without FM. Clinicians can find valuable information in the specific symptoms experienced by the patient, as well as the overall number of symptoms. Grouping the discriminatory symptoms together in the questionnaire may assist clinicians to consider the diagnosis of FM more easily in patients with SLE.

REFERENCES

[1] Pincus, T., Y. Yazici, and M. Bergman, *Development of a multi-dimensional health assessment questionnaire (MDHAQ) for the infrastructure of standard clinical care.* Clinical & Experimental Rheumatology, 2005. **23**(5 Suppl 39): p. S19-28.
[2] Wolfe, F., et al., *Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia.* J Rheumatol, 2011. 38(6): p. 1113-22.
[3] Wolfe, F., et al. 2016 *Revisions to the 2010/2011 fibromyalgia diagnostic criteria.* in *Seminars in arthritis and rheumatism.* 2016. Elsevier.

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SAT0194 EVALUATION OF PSYCHOMETRIC PROPERTIES OF THE PATIENT-REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM (PROMIS) PHYSICAL FUNCTION 10-ITEM SHORT FORM IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: While the PROMIS (Patient-Reported Outcomes Measurement Information System) physical function short form 10a (PF10a) is both practical and acceptable for implementation in routine clinical practice, its psychometric properties have not been evaluated in Systemic Lupus Erythematosus (SLE).
Objectives: The objectives of our study were to examine the validity and responsiveness of PF10a in SLE among a racially/ethnically diverse clinic population and develop estimates of the minimally important difference (MID).

Methods: Data were derived from electronic health records for all SLE patients seen in a university-based rheumatology clinic between 2013 and 2018. We evaluated the PF10a's floor and ceiling effects among different racial/ethnic groups. Construct validity was assessed by examining Spearman's correlation coefficients between the PF10a and other patient-reported (pain (scale 0-10) and pain visual analogue scale (VAS) (scale 0-100)), physician-reported (SLE disease activity index (SLEDAI)) and laboratory (erythrocyte sedimentation rate (ESR)) measures. Known-group validity was assessed by evaluating effect size (Cohen's d) between categories of pain (no pain vs. moderate-severe pain). We used standardized response means to examine the responsiveness of the PF10a to longitudinal changes in pain and SLEDAI. MID was estimated using distribution based and anchor-based methods.
Results: We included 612 patients in cross-sectional analyses of validity and 462 patients in longitudinal analyses of responsiveness. Mean age was 40.5±14.6, 87% were female and 32% Caucasian. The PF10a had ceiling effects above the commonly accepted criteria of 15% among Caucasian (23%), Asian (23%) and Other (17%) race/ethnicities, and no floor effects. Construct validity analyses showed strong correlations (ρ=0.66, p<0.05) with pain VAS, moderate correlations (ρ=0.58, p<0.05) with pain, and weak correlations with ESR (ρ=0.25, p<0.05) and SLEDAI (ρ=0.16, NS). Known-group validity analyses showed large differences among pain groups (Cohen's d=1.49, p<0.05). The PF10a was responsive to improvements in pain (SRM=0.5) and SLEDAI (0.49), but less so to deteriorations in pain (SRM=-0.42) or SLEDAI (SRM=-0.24). Distribution-based MIDs were +8 for improvement and -7 for deterioration. Anchor-based MIDs were +2 for improvement, -3 for deterioration with pain as anchor and +5 for improvement, -5 for deterioration with SLEDAI as anchor.
Conclusion: Although the PF10a showed some ceiling effects, it had good validity in this young racially/ethnically diverse sample with SLE. The PF10a was responsive to improvements in pain and disease activity. The anchor-based MIDs appear to be similar to those reported for PF10a in rheumatoid arthritis(1). This information supports the use of the PF10a in SLE and provides important information to facilitate interpretation of scores.

REFERENCE

[1] Wahl E, Gross A, Chernitsky V, Trupin L, Gensler LS, Chaganti K, et al. Validity and Responsiveness of a 10-Item Patient-Reported Measure of Physical Function, PROMIS PF-10a, in a Rheumatoid Arthritis Clinic Population. Arthritis care & research. 2016.

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SAT0195 SYSTEMIC DISEASES ASSOCIATED WITH AUTOIMMUNE LIVER DISEASES

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Background: Autoimmune liver diseases are considered as a group of hepatobiliary injuries mediated by abnormal immunity in subjects with genetic predisposition. It mainly includes autoimmune hepatitis, primary biliary cholangitis,primary sclerosing cholangitis and overlap syndrome. They are oftently associated with different manifestations of autoimmune systemic diseases such as systemic lupus erythematosus, CREST syndrome ….
Objectives: The aim of this study was to evaluate the prevalence and the characteristics of systemic diseases associated with autoimmune hepatopathies
Methods: We carried out a retrospective study from January 1996 to December 2018 including all patients with autoimmune liver diseases followed in our department: 64primary biliary cholangitis (PBC), 22 autoimmune hepatitis (AIH), 23 overlap syndrome (OS), 15 primary sclerosing cholangitis (PSC).
Results: One hundred and twenty four patients were included in our study : 107 women and 17 men with an average age of 55 years [18-87 years]. An immunological disorder was found in 58 cases (48%): [28 PBC/12 AIH/12 OS/6 PSC] with a female predominance (Sex ratio (Men/Women) = 0.09). Systemic diseases included respectively: Sjögren's syndrome in 20 cases, systemic lupus erythematosus in 7 cases, rheumatoid arthritis in 5 cases, CREST syndrome in 11 cases and autoimmune thyroiditis in 2 cases. The discovery of autoimmune disorder was in most cases concomitant to the diagnosis of the autoimmune liver disease (67%). Our study showed biological assessment perturbation in 20 cases with positivity of : anti-centromere antibodies (11 cases), anti-SSA antibodies (5 cases), anti-cardiolipin antibodies (4 cases) and rheumatoid factor (5 cases)
Conclusion: Our study shows a strong prevalence of systemic disease during autoimmune hepatopathies. A systematic screening for clinical and biological immune manifestations are highly recommended in those patients.
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SAT0196 RENAL FLARE IN CLASS V LUPUS NEPHRITIS: INCREASED RISK IN PATIENTS WITH TUBULOINTERSTITIAL LESIONS

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Background: Lupus nephritis leads to considerable morbidity and mortality in patients with systemic lupus erythematosus. Although membranous lupus nephritis has a better renal prognosis than proliferative lupus nephritis, progression to end-stage renal disease does occur. Renal flare is an independent predictor of renal prognosis in membranous lupus nephritis.
Objectives: To investigate the risk factors of renal flare in patients with membranous lupus nephritis.
Methods: Biopsy-proven pure membranous lupus nephritis patients diagnosed between January 1997 and September 2017 were studied. We assessed and compared the clinical and pathological parameters between patients who experienced renal flare and those who did not. To identify risk factors of renal flare, multivariable Cox proportional hazard regression analysis with stepwise backward elimination was performed.
Results: Out of the 53 patients with pure membranous lupus nephritis, 17 patients (32.1%) experienced renal flare during a median follow-up of 121.5 months (range, 44.4 – 196.9). Patients who experienced renal flare had significantly higher proportion of tubulointerstitial inflammation at baseline (76.5% vs. 36.1%, p = 0.006) and tubular atrophy/interstitial fibrosis (70.6% vs. 27.8%, p = 0.003). In multivariable Cox proportional hazard regression analysis, presence of tubulointerstitial inflammation (adjusted hazard ratio (HR) 5.532, 95% confidence interval (CI) 1.722 – 17.776, p = 0.004) and tubular atrophy/interstitial fibrosis (adjusted HR 4.328, 95% CI 1.450 – 12.916, p = 0.009) at baseline were significantly associated with increased risk of renal flare.
Conclusion: Presence of tubulointerstitial inflammation and tubular atrophy/interstitial fibrosis is associated with increased risk of renal flare in patients with membranous lupus nephritis. Closer monitoring of membranous lupus nephritis patients with tubulointerstitial lesions could lead to earlier treatments and better outcomes.

Table. Multivariable Cox proportional hazard regression analysis evaluating risk factors of renal flare in membranous lupus nephritis

	Adjusted HR	95% CI	P value
Urine WBC ≥ 3-5/HPF	0.854	0.193 – 3.774	0.835
Lupus anticoagulant	1.118	0.039 – 4.040	0.865
Activity index (glomerular component)†	1.218	0.621 – 2.387	0.567
Chronicity index (glomerular component)*	1.135	0.752 – 1.712	0.547
Tubulointerstitial inflammation	5.532	1.722 – 17.776	**0.004**
Tubular atrophy/Interstitial fibrosis	4.328	1.450 – 12.916	**0.009**

Variables with P value less than 0.1 in the univariable analysis were selected for inclusion in the multivariable analysis.
†Glomerular component of activity index, rather than total activity index, to avoid multicollinearity with tubulointerstitial inflammation
*Glomerular component of chronicity index, rather than total chronicity index, to avoid multicollinearity with tubular atrophy/interstitial fibrosis

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SAT0197 INCIDENCE AND OUTCOME OF NON-TYPHOID SALMONELLA BACTEREMIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN COMPARISON WITH RHEUMATOID ARTHRITISAND PRIMARY SJÖGREN'S SYNDROME

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Background: Non-typhoid Salmonella (NTS) infection is an important problem in patients with systemic lupus erythematosus (SLE) [1, 2]. However, less is known about the incidence rate (IR) for NTS bacteremia.
Objectives: To evaluate the IR of NTS bacteremia in patients with SLE, in comparison to rheumatoid arthritis (RA) and primary Sjögren's syndrome (SjS), and by comparison with other Gram-negative bacilli (GNB) bacteremia including Escherichia coli (E. coli) and Pseudomonas aeruginosa (PsA). Furthermore, to access the survival outcome after NTS bacteremia.
Methods: In this single-center retrospective cohort study, we analyzed the registry of catastrophic illnesses database for patients fulfilled the criteria of SLE, RA, and SjS in National Taiwan University Hospital. The patients aged over 20 years, with adequate follow-up during January 1, 2008 to December 31, 2017 were included. Only new episodes of positive blood cultures during the observation period were taken into analysis. Cox proportional hazards regression model was applied for calculating the incidence rate ratio (IRR) of bacteremia between different diseases, and the hazard ratio (HR) of mortality.
Results: This study included 5953 patients. NTS bacteremia happened in 33 cases, among which 27 (81.8%) were group D1 and 4 (12.1%) were group B Salmonella. The baseline characteristics, IR of each GNB bacteremia, and the IRR adjusted for age, sex, diabetes mellitus (DM) as well as chronic kidney disease (CKD) are shown in Table 1. Compared to patients with RA, the IRR for NTS bacteremia was highest in SLE. The IRR for E. coli bacteremia in patients with SLE also increased in comparison with RA, although not as high as for NTS bacteremia. When compared to SjS, patients with SLE still had an elevated IRR of 3.52 (95% CI: 1.29–9.63, p=0.014) for NTS bacteremia. In SLE patients, DM increased the IR for NTS bacteremia (IRR: 4.43, 95% CI: 1.71–11.43, p=0.002; adjusted for age and sex).
In the 33 cases with NTS bacteremia [male: 21.2%; age: 49.0 (37.9–64.2) years], the median observation time to event was 11.1 (IQR, 3.0–38.1) months. No recurrent bacteremia was found. There were 14 (42.4%) deaths, and 7 (21.2%) died within 60 days after NTS bacteremia. The median time to all-cause mortality was 54 (IQR, 17–153) days. In survival analysis, an abnormal body mass index (BMI, normal $\geq$18.5 and <24) at the onset of bacteremia had a crude HR of 6.20 (95% CI: 1.64–23.52, p=0.007). The diagnosis of SLE, age, gender, DM, CKD, levels of C-reactive protein and white blood cell count did not significantly increase HR.

Table 1

Diagnosis	SLE n=2057	SjS n=1532	RA n=2364
Age (y) [median (IQR)]	40.0 (30.2–52.5)	56.3 (47.4–64.3)	56.7 (47.7–66.4)
Male gender (%)	11.3	9.1	18.3
Observation time (y) [median (IQR)]	3.22 (0.81–7.34)	1.75 (0.46–4.2)	2.77 (0.66–6.96)
NTS bacteremia (n)	26	5	2
IR per 1000 PY (95% CI)	3.10 (2.05–4.44)	1.18 (0.42–2.54)	0.22 (0.04–0.67)
Adjusted IRR (95% CI)	19.02 (4.35–83.24)**	5.72 (1.08–30.17)*	Reference
E. coli bacteremia (n)	61	15	34
IR per 1000 PY (95% CI)	7.26 (5.59–9.24)	3.54 (2.03–5.64)	3.71 (2.60–5.11)
Adjusted IRR (95% CI)	2.63 (1.67–4.16)**	0.83 (0.45–1.54)	Reference
PsA bacteremia (n)	14	4	5
IR per 1000 PY (95% CI)	1.66 (0.93–2.68)	0.94 (0.29–2.19)	0.54 (0.19–1.17)
Adjusted IRR (95% CI)	3.03 (0.98–9.35)	1.80 (0.47–6.94)	Reference

y, years; PY, person-years; *, p<0.05; **, p<0.001

Conclusion: Among the GNB bacteremia, patients with SLE were especially susceptible to NTS bacteremia when compared to RA and SjS. DM was a risk factor. The mortality rate after NTS bacteremia was high, and an abnormal BMI may predict it.

REFERENCES

[1] Green L, Vinker S. Recurrent salmonella sepsis with different species in a systemic lupus erythematosus patient. Clin Rheumatol. 1996 Jan; 15 (1):72-74.
[2] Huang CF, Chen PL, Liu MF, Lee CC, Lee NY, Chang CM, et al. Nontyphoidal Salmonella bacteremia in patients with connective tissue diseases. J Microbiol Immunol Infect. 2012 Oct; 45(5):350-355.

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SAT0198 PERIPHERAL NERVOUS SYSTEM INVOLVEMENT IN PRIMARY SJOGREN'S SYNDROME – UNCOMMON OR UNDERESTIMATED PROBLEM?

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Background: Systemic manifestations are common in primary Sjögren's syndrome (pSS) and play a major role in the prognosis. Neurological complications may affect both the peripheral (PNS) and central nervous system (CNS). The incidence varies from several to several dozen percent. The course of the disease and the severity of the symptoms may be mild and self-limiting or progressive, leading to permanent neurological deficits. It is worth remembering that the symptoms of nervous system involvement may precede the onset of symptoms of dryness, and diagnosis of pSS may be delayed after a certain duration of neurological symptoms.
Objectives: The aim of the study was to determine the prevalence of PNS involvement among symptomatic and asymptomatic patients with the diagnosis of pSS in our University Clinical Centre.
Methods: We studied a consecutive group of fifty unselected patients aged from 33 to 74 years (mean 55.8 years). All patients fulfilled the criteria for the diagnosis of pSS. Additional connective tissue diseases and diabetes were the exclusion criteria. Disease activity was evaluated according to the EULAR Sjögren's syndrome disease activity index (ESSDAI). All patients underwent clinical neurological examination and nerve conduction studies (NCS) of nine peripheral nerves. For the classification of polyneuropathies the ESTEEM (European Standardized Telematic tool to Evaluate Electrodiagnostic Methods) guidelines were used. Clinical examination and nerve conduction study were performed and evaluated by one certified neurologist.
Results: Of our 50 patients, 48 were female with a mean (±SD) age 53.6±10.5 years and mean disease duration 7.9±5.3 years. Two were male with mean age 43.7±25.8 years and mean disease duration 5.7±0.6 years. The mean age at diagnosis was 50.4±14 years. 23 (46%) patients fulfilled the criteria for the diagnosis of neuropathy. The most common PNS manifestation was sensorimotor neuropathy 11/23 (47%), mononeuropathy was present in 6/23 (26%) patients, pure axonal sensory neuropathy was present in 1/23 (4.3%) patient, axonal motor neuropathy in 1/23 (4.3%), SFN in 1/23 (4.3%) and cranial nerve involvement was present in 4/23 (17.4%) (one of the patients had both cranial and sensorimotor neuropathy). Neurological symptoms preceded the diagnosis of pSS in 8 (35%) of 23 PNS+ patients. The frequency of following symptoms and extraglandular manifestations was significantly higher in PNS+ compared to PNS- patients: salivary gland enlargement (74% vs 44% p<0,05), respiratory tract involvement (65% vs 37% p<0,05) and lymphadenopathy (61% vs 19% p<0,05). The mean ESSDAI in patients with and without neurological involvement was 7±6,82 and 4,7±4,58 respectively (p=0.245). In this subgroup the use of cyclophosphamide, due to extraglandular manifestations, was increased (p<0,05).
Conclusion: We found that PNS involvement is a common extraglandular manifestation of pSS (46% in our group). Sensorimotor neuropathies were most frequent. Involvement of the PNS seems frequent but remains underestimated. NCS is a non-invasive test which might be useful at diagnosis and follow-up. Guidelines for the diagnosis and treatment of peripheral neuropathies in patients with pSS are needed.

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SAT0199

POLYAUTOIMMUNITY IN SYSTEMIC LUPUS ERYTHEMATOSUS. DATA FROM A LARGE SPANISH COHORT: SPANISH SOCIETY OF RHEUMATOLOGY REGISTRY OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (RELESSER).

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Background:

Objectives: Estimate the frequency of the association of SLE with other autoimmune diseases in a large Spanish cohort of patients with systemic lupus erythematosus (SLE).

Methods:

Design: RELESSER is a nationwide multicentre, hospital-based registry of SLE patients. This is a cross-sectional study. **Patients**: Unselected consecutive adult patients with SLE, classified according to the ACR 1997 criteria. **Main outcome:** Polyautoimmunity was defined as patients who fulfilled criteria for SLE and other autoimmune disease: autoimmune thyroiditis, rheumatoid arthritis, systemic sclerosis or inflammatory myopathy and mixed connective tissue disease. Multiple autoimmune syndrome (MAS) was defined as patients who meet SLE criteria and at least two other autoimmune diseases. **Statistical analysis:** Descriptive. Multiple logistic regression analysis to investigate the possible risk factors for polyautoimmunity in patients with SLE.

Results: From 3679 (91.4%) patients included in the registry, 501 (13.6%) had Polyautoimmunity. The characteristics are showed in Table. The most frequent polyautoimmunity types associated with SLE were: autoimmune thyroiditis (7.5%), other connective tissue disorders (7.1%). Other autoimmune diseases not considered within the scope of Polyautoimmunity was 12.8% for Sjögren's syndrome and 12.7% for antiphospholipid syndrome. A family history of SLE was 12.4% and MAS in 10.2%. The multivariate analysis identified age (odds ratio [95% CI], 1.01 [1.00-1.02]), sex (3.00 [1.48-6.04]), Raynaud's phenomenon (1.79 [1.34-2.39]), pulmonary fibrosis (2.88 [1.32-6.30]), Ro-La autoantibodies (1.68 [1.20-2.36]), antiRNP (1.79 [1.32-2.42]) and treatment with methotrexate (1.54 [1.08-2.18]) or with antimalarials (0.57 [0.41-0.78]) as factors associated with polyautoimmunity.

Conclusion: SLE patients associated poliautoimmunity in 14%, MAS in 2%. More studies are needed to better understand the increase of polyautoimmunity in these patients.

Variable	polyautoimmunity, (n=501)
Sex (female), n (%)	473 (94.4)
Age >50 years, n (%)	134 (15.4)
Raynaud's phenomenon, n(%)	226 (45.8)
Lupus Nephritis, n (%)	131 (26.5)
Pulmonary fibrosis, n (%)	25 (5.0)
ANA+, n (%)	497 (99.0)
Anti-RNP, n (%)	164 (34.1)
Methotrexate, n (%)	120 (24.7)
Hydroxychloroquine, n (%)	369 (76.7)

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SAT0200

UNUSUAL SYSTEMIC LUPUS ERYTHEMATOSUS/ SJOEGREN'S SYNDROME PHENOTYPE IN A PATIENT WITH A TNFAIP3 GENE MUTATION

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Background: Mono-allelic mutation in tumor necrosis factor alpha induced protein 3 (*TNFAIP3*) has been found to cause haploinsufficiency of A20 protein, the cause of an early-onset auto inflammatory disease resembling Behcets's disease (BD). Single nucleotide polymorphism in *TNFAIP3* may also contribute to susceptibility to systemic lupus erythematosus (SLE). Several mutations in *TNFA1P3* have been shown to be disease-causing, including a single case with heterozygous mutation in the *TNFAIP3* gene for c.811C>T; p.(arg271*) with a BD-like phenotype.

Objectives: To report the case of a child with heterozygous mutation *TNFAIP3* (c.811C>T; p.(arg271*) with an unusual SLE/SS (Sjoegren syndrome) phenotype, thus expanding the phenotype associated with this mutation; and describe the disease course and treatment

Methods: Clinical details were retrospectively collated using routine clinical records. The molecular cause of the phenotype was investigated using a targeted gene next generation sequencing (NGS) panel (the vasculitis and inflammation panel, VIP). Confirmation of findings detected by NGS were confirmed using conventional Sanger sequencing in the index case and subsequently in the parents.

Results: A 4yr old Caucasian female presented with a 2-year history of photosensitive malar rash, mouth ulcers, hair loss, arthralgia, livedo reticularis, cervical lymphadenopathy and hepatosplenomegaly. Laboratory tests revealed anemia, raised inflammatory markers and hypocomplementemia; RF, ANA and anti Ro positivity, raised C1q antibodies and low C1Q level. 7 out of 11 classification criteria for SLE were met and treatment with hydroxychloroquine was commenced.

Subsequently she developed blepharitis, acute anterior uveitis, chilblains and discoid skin lesions. Azathioprine and oral steroids were added.

Due to young age at disease onset, NGS screening was performed and revealed heterozygous mutation in *TNFAIP3* c.811C>T; p.(Arg271*). Screening of both parents revealed the same mutation in the mother, who is asymptomatic. The child further developed Raynaud's and underwent renal biopsy for intermittent proteinuria which revealed ISN/RPS Class III and V lupus nephritis. Azathioprine was switched to mycophenolate mofetil. One year later her skin symptoms continue to improve, uveitis is in remission and her renal function is normal. Prednisolone was tapered off.

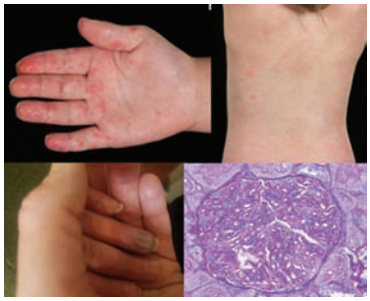


Figure:. chilblain and discoid skin lesions, Raynaud's and histopathological changes from a renal biopsy consistent with glomerulonephritis

Conclusion: We further expand the phenotype associated with mutation in the *TNFAIP3*; the c.811C>T; p.(arg271*) variant previously described as the cause of a BD-like-phenotype, in our case caused an auto immune disease with severe SLE/SS phenotype. This variant also demonstrated variable penetrance in our pedigree, since the mother harbours the same variant but remains asymptomatic. Thus, the genetic cause of monogenic lupus continues to expand, and the distinction between autoinflammatory and autoimmune disease is less clear-cut than first thought.

REFERENCES:

[1] Aeschlimann, F. A., & Laxer, R. M. (2018). Haploinsufficiency of A20 and other paediatric inflammatory disorders with mucosal involvement. Curr Opin Rheumatol, 30(5), 506-513.

[2] Liu, X., Qin, H., Wu, J., & Xu, J. (2018). Association of *TNFAIP3* and TNIP1 polymorphisms with systemic lupus erythematosus risk: A meta-analysis. Gene, 668, 155-165.

[3] Zhou, Q., Wang, H., Schwartz, D. M., Stoffels, M., Park, Y. H., Zhang, Y., . . . Aksentijevich, I. (2016). Loss-of-function mutations in *TNFAIP3* leading to A20 haploinsufficiency cause an early-onset autoinflammatory disease. Nat Genet, 48(1), 67-73.

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SAT0201 CARDIOVASCULAR EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): THE ROLE OF TRADITIONAL CARDIOVASCULAR RISK AND SLE-RELATED FACTORS

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Background: Patients with SLE may have an increased risk of cardiovascular (CV) events due to the contribution of disease-related factors.

Objectives: to determine the prognostic role of traditional CV risk factors and SLE-related factors in the assessment of the risk of CV events development in a cohort of patients affected by SLE.

Methods: Two hundred and sixty two consecutive SLE patients (age 42.9 ± 14.5 years, 89% female, disease duration 11.5 ± 8.2 years) have been evaluated, 240 (92%) with articular, 226 (86%) with cutaneous, 167 (64%) with hematological, 61 (23%) with serositis involvement respectively and 86 (33%) with lupus nephritis (LN) and 105 (40%) with neuropsychiatric SLE (NPSLE). The follow-up data were collected and information on traditional CV risk factors (age, sex, diabetes, smoking, arterial hypertension, dyslipidemia), disease-specific parameters (SLEDAI-2K, chronic steroid therapy, current antimalarial and other immunosuppressive therapy) and autoantibody profile (ANA, anti-SSa/Ro, anti-SSb/La, IgA and IgM Rheumatoid factor (RF), complement reduction, anticardiolipin (ACLA), anti-beta2glicoprotein 1 (antiβ2GP1), lupus anticoagulant (LAC)) were analyzed for each patient. As CV manifestations, acute cardiac and cerebrovascular ischemic events and chronic ischemic heart disease were considered.

Results: Twenty-seven SLE patients (10.3%) experienced CV events during the follow-up period with a significantly higher rate of male sex (24% in males vs 8.6% in females, p=0.01) among the considered demographical parameters. Among those patients, 10 (37%) presented cerebrovascular accidents, 6 (22%) acute cardiac ischemic events, 7 (26%) chronic ischemic heart disease and 4 (15%) both cardiac and cerebrovascular events during the follow up period. In particular, SLE patients who experienced CV events during the follow up were older at disease onset than patients who did not experience CV events during the follow-up (42.2 ± 19.4 vs 29.8 ± 13.1 years, p<0.001). Considering the traditional CV-related risk factors, among the SLE cohort, patients who experienced CV events during the follow-up were more likely having concomitant dyslipidemia (p=0.03), diabetes mellitus (p=0.01) and arterial hypertension (p<0.001) compared to SLE patients who did not experience CV events. Considering the disease-related parameters, no significant association between CV events development and ANA, anti-SSa/Ro, anti-SSB/La positivity and complement reduction was found (p>0.05) despite SLE patients who experienced CV events during the follow-up were more likely with concomitant neurological involvement (p=0.002) and ongoing chronic corticosteroid therapy (p=0.03) compared to SLE patients who did not experience CV events.

Finally, considering the antiphospholipid antibodies (aPL) profile, SLE patients who experienced CV events during the follow-up were more likely positive for antiβ2GP1 (p <0.0001), ACLA (p<0.0001) and LAC (p <0.0001) compared to SLE patients who did not experience CV events. In addition, multivariate analysis revealed that, aPL positivity arose as an independent risk factor associated with CV events development in SLE patients contingently to the number of aPL positivities (single aPL positivity, OR 4.52 (0.97-21.18); double aPL positivity, OR 23.95 (4.39-130.76); triple APL positivity, OR 34.01 (7.64-151.40)).

Conclusion: in SLE patients, aPL positivity significantly increases the risk of CV events development regardless to the traditional CV risk factors contingently to the number of aPL positivities.

Variable	polyautoimmunity, (n=501)
Sex (female), n (%)	473 (94.4)
Age >50 years, n (%)	134 (15.4)
Raynaud's phenomenon, n(%)	226 (45.8)
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Pulmonary fibrosis, n (%)	25 (5.0)
ANA+, n (%)	497 (99.0)
Anti-RNP, n (%)	164 (34.1)
Methotrexate, n (%)	120 (24.7)
Hydroxychloroquine, n (%)	369 (76.7)

REFERENCE

[1] Boulos D, Koelmeyer RL, Morand EF and Hoi AY, Lupus Science & Medicine, 2017

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SAT0202 EVALUATION OF LEFT ATRIAL MYOCARDIAL DEFORMATION AS MARKER OF SUBCLINICAL DAMAGE IN PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The left ventricle diastolic dysfunction (LVDD) may be the only manifestation of cardiac involvement in patients with systemic lupus erythematosus (SLE), preceding systolic dysfunction. The myocardial deformation of left atrium (LA) through the evaluation of LA global longitudinal strain (LALS) may be useful in assessing diastolic function since the lower the LALS the worse is the diastolic function.

Objectives: The main objective of this study was to evaluate the LA function through myocardial deformation by strain and strain rate derived from speckle tracking echocardiography in patient with SLE without any cardiovascular symptoms and compare with Control Group (CG). To compare LA strain of patients with active, inactive SLE disease and control group and determinate the independent factors associated with depressed LALS.

Methods: A cross sectional study was performed. Fifty patient that fulfilled 2012 SLICC classification criteria for SLE were included and they were compared with fifty age- and gender -matched healthy subjects as control group. Myocardial deformation was measured by transthoracic

echocardiogram, performed by a board-certified echocardiographer, to investigate the LALS, the strain of the three phases of the LA cycle and the strain rate. SLE disease activity was defined as a Mexican version of the Systemic Lupus Erythematosus Disease Activity Index (Mex-SLEDAI) ≥9 and SLE-related organ damage as SLICC/ACR damage Index (SDI) ≥1. Descriptive statistics with mean and standard deviation or median and Interquartile range were calculated and categoric variables were expressed as proportions. Chi-squared test was done to compare categoric variables; quantitative variables were compared with student´s t test. ANNOVA test was used to evaluated differences among multiple groups. A univariate linear regression analysis was performed to determinate de independent factors associated with LAGLS less than thirty five percent.

Results: 90% of patients were females and their mean age was 34 (±12) years old. 16% of patients had positive antiphospholipid antibodies. The mean MEX-SLEDAI was 8.7 (±5) and the mean SDI was 0.7 (±0.3). The mean of disease duration was 6 years. The patients with SLE had greater diastolic disfunction evaluated with conventional echocardiography compared with CG (E/e´Ratio of 7.9 (±2.6) vs 6.4 (±1.8), p=0.001) (left atrial volume index (LAVI) of 26.1 mL/m2 (±8.8) vs 20.7mL/m2 (±4.4), p<0.001). SLE patients had significant impaired of LALS compared with CG (41.6% vs 50.5%; p=0.02). As well in the 3 phases of the LA cycle. Also, the LALS was significantly lesser in patients with active disease than inactive and CS (36.3% (25.3-54.3) vs 43% (35.2-52.6) vs 50.5% (41.7-70.6)). The positivity of antiphospholipid antibodies, lupus nephritis, glucocorticoids use, and the presence of disease activity were significant independent factors for depressed LALS in the univariate analysis.

Conclusion: SLE patients have lower myocardial deformation of the LA, which is expressed as a lower diastolic function correlating with early subclinical myocardial damage.

REFERENCES

[1] Dai M, Li KL, Qian DJ, Lu J, Zou YH, Cao YX, et al. Evaluation of left atrial function by speckle tracking echocardiography in patients with systemic lupus erythematosus. Lupus.2016;25(5):496-504

[2] Li K, Wang R, Dai M, Lu J, Zou Y, Yang X. Evaluation of Left Atrial Function by Real-time 3-D Echocardiography in Patients with Systemic Lupus Erythematosus. The Journal of Rheumatology.2015;42(2):196-201.

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SAT0203

THE CORRELATION BETWEEN THE SERUM 1,25(OH) 2D3 LEVEL AND CLINICAL DATA OF PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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Background: The role of vitamin D in regulating immune function in autoimmune diseases has been extensively studied. While there is less research on vitamin D in Sjogren's syndrome. This study will explain the relationship between vitamin D and Sjogren's syndrome.

Objectives: To explore the relationship between the serum $1,25(OH)_2D_3$ level and the changes of disease activity in patients with Primary Sjogren's Syndrome (PSS) [1], and to explore whether supplementation of VD could be a potential therapy for the treatment of PSS.

Methods: PSS patients (n=60, according to the 2002 International Classification (Diagnostic) Standard for Sjogren's Syndrome) were enrolled and health individuals were normal controls. Laboratory examinations were analyzed including that serum levels of 1,25-dihydroxycholecalciferol [$1,25(OH)_2D_3$], lymphocytes and CD4+T cell subsets by flow cytometry, urine pH value, ALT, AST, BUN, Cr, IgG, C3, C4, ESR, CRP, serum levels of $1,25(OH)_2D_3$. Physical examination data include Salivary flow rate, secretion of tears, breakup time of tear film (BUT), and labial glands biopsy. Patient's disease activity was accord to ESSDAI (EULAR SS disease activity index, 2010) classification.

Results: Compared with that in normal controls, the levels of serum VD in patients with PSS was decrease significantly, Z= -7.367, P <0.001(Figure 1). Spearman correlation analysis and comparison with the collected indexes, showed that VD was significantly correlated with secretion of tears (r=-0.455, p<0.002), IgG (R=-0.581, p<0.000), B cell absolute count (R=-0.474, p=0.002), B cell percent (R=-0.391, p=0.005), Th1 absolute count (R=0.318, p=0.023), Th17 absolute count (r=0.297, p=0.034), Th17

Table 2. Correlation between the serum 1,25(OH)2D3 level and clinical data

the serum 1,25(OH)2D3 level	BMI r	BMI P	disease duration r	disease duration P	ESSDAI r	ESSDAI P	base salivary flow rate r	base salivary flow rate P	stimulant salivary flow rate r	stimulant salivary flow rate P
-.196	.300	-.113	.416	-.123	.037	-.077	.621	-.049	.756	

the serum 1,25(OH) 2D3 level	WBC r	WBC P	RBC r	RBC P	HB r	HB P	PLT r	PLT P	LY r	LY P
-.558	.684	-.240	.089	-.189	.189	-.170	.230	-.148	.301	

the serum 1,25(OH)2D3 level	neutrophile granulocyte r	neutrophile granulocyte P	urine pH value r	urine pH value P*	ESR r	ESR P	ALT r	ALT P	AST r	AST P
-.003	.985	.335	.013	-.111	.432	.132	.344	.001	.996	

the serum 1,25 (OH)2D3 level	BUN r	BUN P	Cr r	Cr P	C3 r	C3 P	C4 r	C4 P	CRP r	CRP P
-.081	.556	.120	.382	-.148	.381	.202	.224	.000	.998	

the serum 1,25(OH)2D3 level	T cell ($CD3^+CD19^-$) r	T cell ($CD3^+CD19^-$) P	T cells% r	T cells% P	B cell ($CD3^-CD19^+$) r	B cell ($CD3^-CD19^+$) P*	B cell% r	B cell% P**	Th cell ($CD3^+CD4^+$) r	Th cell ($CD3^+CD4^+$) P	Th cell% r	Th cell% P
.034	.810	.242	.088	-.276	.046	-.391	.005	-.035	.809	-.092	.523	

the serum 1,25(OH)2D3 level	Ts cell ($CD3^+CD8^+$) r	Ts cell ($CD3^+CD8^+$) P	Ts cell% r	Ts cell% P**	NK cell ($CD3^-/CD16^+CD56^+$) r	NK cell ($CD3^-/CD16^+CD56^+$) P	Th1 cells r	Th1 cells P*	Th2 cells r	Th2 cells P	Th17 cells r	Th17 cells P*
.239	.091	.372	.007	.121	.388	.318	.023	.029	.842	.297	.034	

the serum 1,25(OH) 2D3 level	Treg cells r	Treg cells P	Th1 cell% r	Th1 cell% P*	Th2 cell% r	Th2 cell% P	Th17 cell% r	Th17 cell% P	Treg cell% r	Treg cell% P
-.274	.052	.282	.045	-.058	.685	.263	.059	-.170	.227	

the serum 1,25(OH)2D3 level	Th1/Th2 r	Th1/Th2 P**	Th17/Treg r	Th17/Treg P**
.382	.004	.385	.004	

*P<005, ** P<0. 01, *** P<0. 001

percent (r=0.282, p=0.007), ration of Th1/Th2(r=0.385, p=0.004) and ration of Th17/Tregs(r=0.385, p=0.004) (Table 2).
Conclusion: The level of serum VD in PSS patients was significantly lower than that in normal controls, which was negatively correlated to secretion of tears, IgG, the absolute number of B, Th1, and Th17, the percentage of B and Th17, and radios of Th1/Th2 and Th17/Tregs. Raising serum VD levels by supplementation of VD, may be a potential Therapy for Sjogren's syndrome.

REFERENCES

[1] Garcia-Carrasco M, Jimenez-Herrera EA, Galvez-Romero JL, de Lara LV, Mendoza-Pinto C, Etchegaray-Morales I, et al. Vitamin D and Sjogren syndrome. Autoimmun Rev. 2017;16(6):587-93.

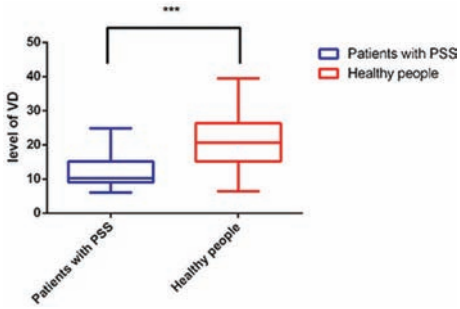


Figure 1. Comparison of VD levels(ng/ml) between patients with PSS and healthy people

Results are given as median (P_{25},P_{75}), ***patients with PSS*** 10.2 0 (9.00,15.11), ***healthy people*** 20.71(15.16,26.41) Z=-7.37 P<0.001
Disclosure of Interests: None declared
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SAT0204 LUPUS LOW-DISEASE ACTIVITY STATE VS SLE RESPONDER INDEX IN A "REAL-LIFE" SETTING

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Background: Systemic lupus erythematosus (SLE) is a chronic multi-organ autoimmune disease characterised by a heterogeneous pathogenic background and by protean clinical manifestations. Recent efforts in identifying novel agents for therapeutic interventions have led to disappointing results and designing a reliable way to assess drug efficacy and verify the achievement of remission, has become itself a major challenge. The SLE responder index (SRI) is a composite tool developed and validated in clinical trials to define in patients with active disease an acceptable response to investigational agents. The role of SRI outside clinical trials has not been defined. The lupus low disease activity state (LLDAS) has been originally validated in a cohort-based setting and it focuses on the achievement of fixed conditions rather than variations from baseline. A formal comparison of these tools outside clinical trials has not been performed.
Objectives: To prospectively assess the performance of SRI and LLDAS in a "real world" observational setting.
Methods: One hundred-thirty-one consecutive patients SLE were subdivided into two groups based on the need or not to escalate their immune suppressive treatment. Clinimetrics including Physician Global Assessment scale (PGA), SLE Disease Activity Index 2000 (SLEDAI-2K) and British Isles Lupus Assessment Group index (BILAG) 2004 version were measured at baseline and at six and 12 months, together with laboratory data and treatment changes. LLDAS and SRI were calculated at each time point.
Results: LLDAS achievement correlated with treatment de-escalation over 12 months (χ2=5.2, p=0.034, OR=4.1 with 95%CI=1.2-14.4), whereas SRI-4 achievement did not. LLDAS responses were more frequent in patients with lower basal SLEDAI-2K (i.e SLEDAI-2K<6; χ2=21.5, p<0.001, RR=8.4 with 95%CI=3.2-25.0), while SRI-4 responses were more prevalent among patients with higher basal SLEDAI-2K and/or severe renal activity at baseline (χ2=5.9, p=0.025, RR=10.8 with 95%CI=1.1-103.1). Positive anti-DNA antibodies associated with non-achievement of LLDAS at any time point. Serositis was associated with lack of LLDAS at baseline, but did not affect LLDAS achievement at 12 months. Normalising complement levels anticipated the achievement of LLDAS and SRI-4.
Conclusion: LLDAS is a valuable tool for assessing response to treatment in the daily rheumatology practice. SRI might be less informative, at least in patients with low basal SLEDAI.

REFERENCES

[1] Franklyn K, et al. Ann Rheum Dis. 2016
[2] Luijten KM, et al. Autoimmunity reviews. 2012
[3] Piga M, et al. Arthritis Res Ther. 2017

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SAT0205 A CYTOKINE "SCAR SIGNATURE" CHARACTERIZES PATIENTS WITH FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND SJOGREN'S SYNDROME

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Background: Fatigue is highly prevalent in systemic lupus erythematosus patients (SLE) and primary Sjoegren's syndrome (pSS) and represents one of its unmet needs.[1] Its pathogenesis is multifactorial, with the activity of the underlying disease exerting a prominent role, along with psychological factors and co-morbid conditions. Previous studies evaluating fatigue and cytokines in patients with SLE and pSS have yielded inconclusive results.
Objectives: We aimed to evaluate patient-reported outcome measures reflecting fatigue and their correlation to serum cytokines in patients with SLE and pSS and healthy volunteers (HV). A panel of circulating cytokines, chemokines and growth factors was compared between groups, correlated to the level of fatigue and within SLE and pSS to global disease activity. The objective was to identify cytokines reflecting the degree of fatigue, which could be exploited as biomarkers and therapeutic targets.
Methods: We performed a cross-sectional study on subjects included in the Swiss SLE Cohort Study (SSCS). All subjects were evaluated clinically and had a serum sample taken. Fatigue was assessed by FAS (Fatigue Assessment Scale) and by the vitality subscale (VT) of the Medical Outcomes Study 36-Items Short Form Healthy Survey. Clinical activity in SLE and pSS patients was determined by a 4-point Likert-scale Physician's Global Assessment (PGA). SLE activity was assessed with the SLE Disease Activity Index score with the Safety of Estrogens in SLE National Assessment modification (SELENA-SLEDAI). Serum cytokines were assessed by multiplex bead array analysis (ProcartaPlex, Thermofischer Scientific, USA). P values were adjusted for multiple comparisons.
Results: Fifty-six patients with SLE, 18 with pSS and 18 healthy volunteers (HV) were included between November 2015 and June 2016. There were no significant differences between groups regarding to age, gender and body mass index (BMI). FAS and VT correlated strongly (Spearman's rho -0.87, p<0.01). FAS was significantly higher in patients than in healthy individuals (median FAS 23 [16-31], 28[20.5-35], 17 [15-27] in SLE, pSS and HV respectively; p=0.02). Patients with SLE and pSS displayed higher serum levels of interferon (IFN)-gamma (median [IQR] 10.29 [4.94-15.25] pg/mL in SLE, 9.64 [6.25-13.86] pg/mL, undetectable in HV; p <0.01). Interleukin (IL)-10 also was only detected in pSS and SLE. Hepatocyte growth factor (HGF) was more expressed in patients than in controls (p= 0.01). The levels of most other cytokines (IFN-alpha, IL-1 alpha, IL-2, IL-4, IL-6, IL-17, IL-21 and IL-23) were not detectable. Only HGF displayed a significant correlation with FAS (P Pearson 0.29, p< 0.01).
Conclusion: Patients with SLE and pSS display a molecular pattern of chronic inflammatory conditions, with higher serum levels of IFN-gamma, IL-10 and HGF. The latter two are both involved in regeneration and tissue repair ("scar signature")[2]. HGF levels correlated independently with

the degree of fatigue. More studies are needed to understand the role of this pleiotropic growth factor in self-perceived fatigue in SLE and pSS.

REFERENCES

[1] Chaigne B, Chizzolini C, Perneger T, Trendelenburg M, Huynh-Do U, Dayer E, Stoll T, von Kempis J, Ribi C, Swiss Systemic Lupus Erythematosus Cohort Study G: Impact of disease activity on health-related quality of life in systemic lupus erythematosus - a cross-sectional analysis of the Swiss Systemic Lupus Erythematosus Cohort Study (SSCS). BMC Immunol 2017, 18(1):17.

[2] Fukushima T, Uchiyama S, Tanaka H, Kataoka H: Hepatocyte Growth Factor Activator: A Proteinase Linking Tissue Injury with Repair. Int J Mol Sci 2018, 19(11).

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SAT0206 FACTORS ASSOCIATED WITH HYDROXYCHLOROQUINE USE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH END STAGE RENAL DISEASE

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Background: Hydroxychloroquine (HCQ) use in SLE has been associated with a lower risk of end-organ damage, SLE flares, and thrombosis, with potential mortality benefit among SLE with end stage renal disease (ESRD)[1, 2, 3]. However, fewer than 30% of SLE continue HCQ after ESRD onset[3]. On the other hand, there is an increased risk of HCQ toxicity among SLE-ESRD[4]. It has not been studied what factors are associated with HCQ use after ESRD. Understanding these factors may inform future studies assessing the safety and efficacy of HCQ in SLE-ESRD and address the "confounding by-indication" bias (i.e. different treatments are intentionally chosen for patients with different prognoses) when analyzing retrospective data regarding HCQ use in SLE patients with ESRD.
Objectives: To determine the factors associated with HCQ use among SLE patients with ESRD.
Methods: We performed a retrospective chart review of SLE patients with ESRD at a single tertiary care center between 2010-2017. All included patients met ACR and/or SLICC criteria for SLE and had at least one visit with rheumatology, nephrology, or primary care, before and after the development of ESRD. SLE-related symptoms, serologic markers of disease activity, and rheumatology visits were identified, both pre- and post-ESRD onset. Transplanted patients were excluded at the time of their first renal transplant.
Results: A total of 69 patients were included, 58 had pre-ESRD data. Of these patients, 33/58 (57%) were taking HCQ prior to ESRD onset. Following the diagnosis of ESRD, 40/69 (58%) were prescribed HCQ within six months after ESRD onset. Of these, six discontinued HCQ by the last documented visit, and one patient initiated HCQ six months after ESRD onset (prescribed by a rheumatologist). At the last documented visit, 35/69 patients (51%) had an active HCQ prescription. Patients taking HCQ were younger, more likely to be followed by a rheumatologist, had a higher frequency of documented arthritis, higher frequency of corticosteroid use and immunosuppressive medication use (Table 1). A history of oral ulcers, cytopenias, and elevated levels of dsDNA at any point (either pre or post-ESRD onset) was not significantly associated with HCQ use at the last visit.
Conclusion: HCQ is more likely to be continued among patients with signs of persistently active SLE. HCQ was more likely to be prescribed by a rheumatologist and was associated with the presence of arthritis. Limited systemic evaluation and documentation by the different providers may have resulted in under-reporting of some of the SLE symptoms. However, these findings reflect the "real-world" experience with HCQ use after ESRD in a large tertiary care center.

Table 1. Factors associated with HCQ use at the last visit post-ESRD*

	HCQ+ last ESRD visit N=35	HCQ- last ESRD visit N=34	p-value
Age at ESRD onset, median (IQR)	33 (26, 46)	46 (29, 53)	**0.05**
Time from ESRD onset to the last visit, months, median (IQR)	40 (21, 72)	59 (11, 99)	0.3
Women, n(%)	29 (83)	28 (82)	0.95
Arthritis, n(%)	7 (20)	0	**0.01**
Rash, n(%)	2 (6)	1 (3)	0.61
Oral ulcers, n(%)	1 (3)	0	0.33
Alopecia, n(%)	1 (3)	2 (6)	0.52
Serositis, n(%)	2 (6)	3 (10)	0.59
Cytopenia, n(%)	27 (82)	26 (79)	0.75
Low complement, n(%)	16 (50)	19 (58)	0.54
Elevated dsDNA, n(%)	12 (39)	10 (31)	0.54
Corticosteroid use, n(%)	31 (89)	23 (72)	**0.08**
Immunosuppressive use, n(%)	25 (71)	14 (42)	**0.02**
Rheum visit post ESRD at least once, n(%)	29 (85)	20 (59)	**0.02**

*Symptoms and medications recorded as "ever" after ESRD onset

REFERENCES

[1] Jung H, et al. Arthritis and rheumatism. 2010;62(3):863-8.
[2] Ruiz-Irastorza G, et al. Annals of the rheumatic diseases. 2010;69(1):20-8.
[3] Broder A, et al. The Journal of rheumatology. 2011;38(11):2382-9.
[4] Bertsias GK, et al. Annals of the rheumatic diseases. 2012;71(11):1771-82.

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SAT0207 DEVELOPMENT OF QUESTIONNAIRES TO ASSESS HEALTHCARE UTILIZATION AND ACCESS IN PATIENTSWITH PRIMARY SJÖGREN'S SYNDROME AT THE DIAGNOSIS AND DURING THE DISEASE COURSE

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Background: The geographic variation in healthcare spending, utilization and quality, across and within countries is well documented.
Objectives: In this study, we develop and validate a tool to collect comparable information in Europe to establish practice profiles in the diagnosis, management and treatment of patients with Primary Sjögren's Syndrome (pSS).
Methods: Two questionnaires, one to newly diagnosed patients and one for patients at their follow-up visits, have been developed and validated through a pilot survey. The questionnaires aim to assess the pSS patients' experience and satisfaction with the primary care and specialist services received. The questionnaires consist of 30 items and collect patient-reported data on: type and intensity of treatments and services received, costs, patients' satisfaction, patients' overall health, and socio-demographic characteristics. A narrative-based medicine section is also included to explore patients' journey to pSS diagnosis. The questionnaires are administered to a sample of pSS patients attending >20 clinical centers within the European Horizon2020 project "HarmonicSS". Additionally, a short questionnaire is administered to the specialists of the clinical centers to collect data on their organization.
Results: Preliminary results of pilot survey based on questionnaires administered to 164 pSS patients (157 F: 7 M, mean (SD) age = 60 (12.2) years) from 5 clinical centers have been analyzed. The majority of the respondents had a primary or secondary school (59%). Both the total number of specialists involved in the care other than the rheumatologist and the number of treatments received in the last 12 months before the interview varies among patients and across centers ($p<0.001$). Although, as expected, the most frequently involved specialists were the ophthalmologist (90%) followed by the gynecologist and the dentist. Additionally, patients with lower education have attended on average less specialists than those with a high school or university degree ($p<0.001$). Findings from the survey to clinicians also show significant geographic variations in the organization of the care to pSS in the participating centres and in the level of integration among different professionals and care settings. On average, 4 professionals (i.e. clinicians and nurses) per centre are involved in care of pSS patients although with significant differences among centre (min=1, max=10) also in the mix of the staff. In 80% of the centres clinicians use written documentation to exchange patients' information, followed by periodic meetings with colleagues (56%) and phone calls with the family doctor (37%). In 54% of the centres the newly diagnosed patients are provided with information pamphlet and

patients health education is performed in 35% of the center through periodic individual meetings.
Conclusion: Preliminary results confirm that the questionnaire is a valid tool to assess and compare patterns of care for pSS patients in terms of access and utilization of treatments and services across and within providers. Once available the questionnaires from all the centres, patient-reported data linked with information from clinical records will allow to measure the patients journey more comprehensively along the care pathway and to identify best practices in terms of the level of perceived quality and the way the care is delivered and, moreover, opportunities for increasing value for patients.
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SAT0208 TEN-YEAR OVERALL SURVIVAL AND STANDARIZED MORTALITY RATIO IN THE LARGEST SINGLE CENTER COHORT OF PATIENTS WITH PRIMARY SJOGREN'S ASSOCIATED LYMPHOMAS

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Background: The development of non-Hodgkin's Lymphoma (NHL) in Sjögren's syndrome (SS) contributes to an inferior survival compared to SS patients without lymphoma.
Objectives: To record the long-term outcomes of SS patients with and without NHLs with 10-year survival curves and standardized mortality ratio (SMR) for first time in the literature.
Methods: In order to estimate the effect of NHL development in SS outcome, we expanded the follow-up time of the previously published cohort of SS-associated NHL cases and we retrospectively compared them with age- and sex-matched SS patients without NHL from our center. As outcome end-points, overall and event-free survivals (OS and EFS, respectively) were used. An event was defined as disease relapse or progression, histological transformation or death. Ten-year survival plots and SMR compared to General Greek population were calculated. The impact of rituximab in the outcome of SS associated NHL treated patients was also studied.
Results: From a total of 712 consecutive SS patients who fulfill the 2002 AECG classification criteria for Sjögren's, 77 were diagnosed with NHL. The prevalence of MALT and DLBC lymphoma in the total SS cohort was 7.1% and 1,7% respectively. The median follow-up time from SS diagnosis was 16.67 years (range: 4.00-38.91 years) corresponding to a total of 1283.71 person-years for SS-associated NHL patients and 17.92 years (range: 2.00-34.00 years) with a total of 1380 person-years for SS patients without NHL. The median time from SS to lymphoma diagnosis was 5.5 years (range: 0-38 years) and the median follow-up time after lymphoma diagnosis was 8.2 years (range: 0.1-26.2 years) months. During follow-up, 15 patients from the SS-NHL group died, 11 of whom due to lymphoma-related causes, while only 2 patients died in the control group (one due to advanced ovarian cancer and one due to cardiac arrest) (p=0.0013). Patients with SS associated NHL displayed a significantly higher risk of death (HR=5.95, 95%CI: 1.66 - 21.38, log-rank test, p=0.0006) compared to their counterparts without lymphoma. The corresponding age-adjusted SMR of SS with and without NHLs versus the general Greek population was 7.94 (95%CI 6.82-9.06) and 1.06 (95%CI - 0.06-2.18) respectively. In addition, 18 patients with SS-associated NHL (23.38%) experienced lymphoma relapse or progression and 2 (2.6%) lymphoma transformation; The vast majority of recorded events (27 of 29 events) were observed within the first ten years from NHL diagnosis and DLBCL was associated with the worst outcome; The 10-year EFS% and OS% for DLBC was 22.22% and 48.61% respectively while for MALTL were 68.15% and 82.03%, respectively. Interestingly, the introduction of rituximab in the anti-lymphoma chemotherapeutic regimens didn't offer any long-term survival benefit.
Conclusion: Herein, we present the longest, to our knowledge, follow-up time of patients with SS-associated NHL; The majority of events that determine the morbidity and mortality of SS-NHL patients have already occurred within the first ten years from NHL diagnosis. In individuals with SS, the evolution of NHL was found to have a detrimental effect in patients' survival. Among them, DLBCL patients experienced the worst outcome.
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SAT0209 A SIMPLIFIED APPROACH FOR SLE PATIENTS TO REPORT DISEASE ACTIVITY USING A REVISED VERSION OF THE SWEDISH SYSTEMIC LUPUS ACTIVITY QUESTIONNAIRE

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Background: The Systemic Lupus Activity Questionnaire (SLAQ) is a validated questionnaire, which captures patients' assessments of SLE-related symptoms and disease activity (1). However, it is extensive and in a recent study we found that some questions were difficult to answer, added little information, or had poor correlation with physicians' assessments (2). Thus, herein we revised the Swedish version of the questionnaire (SWE-SLAQr), building on previous results and we also asked patients for input. Our aim was to get an improved and shorter version, to support clinical work and online registries. The original SLAQ includes 26 items, while SWE-SLAQr includes 20 items.
Objectives: We compared patients' assessments of SLE disease activity, as reported in the SWE-SLAQr, with physicians' assessments using SLE activity measure (SLAM) and SLE disease activity index (SLEDAI-2K). In addition, we evaluated the performance of the symptom items of SWE-SLAQr as compared to the corresponding items in SLAM.
Methods: Patients filled out SWE-SLAQr prior to physicians' assessments. Correlations between SWE-SLAQr-total, sub-scales (Symptom score, Patients global) and SLAM-excluding the 7 laboratory items (SLAM-nolab), SLAM and SLEDAI-2K as well as between the corresponding items in SLAQ and SLAM, were evaluated using Spearman's ρ.
Results: We included 101 patients, 85% women, median age 43 (IQR 22) years, disease duration 14 (IQR 15) years. Patients reported more symptoms than recorded by doctors. Correlations between patients' and physicians' assessments were for SLAM-nolab: SWE-SLAQr total, ρ=0.674, Symptom score, ρ=0.670, and Patients global, ρ=0.667, as expected the correlations were lower for SLAM: SWE-SLAQr total, ρ=0.472, Symptom score, ρ=0.467, and Patients global, ρ=0.501. No correlations were found between patients' and physicians' assessments when using SLEDAI-2K (ρ<0.09 for all). Of symptom items fatigue (ρ=0.741), alopecia (ρ=0.695) and weight loss (0.517) showed highest degree of correlation. Notably, symptoms of dyspnea/pleuritic chest pain had no correlation between patients' and physicians´ assessments (ρ=0.152, p=0.130).
Conclusion: We conclude that SWE-SLAQr performed equally well as SLAQ (2), demonstrating that it can be used to monitor disease activity. We encourage further use of SWE-SLAQr and recommend its implementation in clinical care, we believe it is especially well suited to support digital and telephone contacts. However further attention is needed to evaluate the discrepancy between physicians' and patients' evaluation of thoracic pain/symptoms.

Table. Characteristics of participants

	Median	IQR
SWE-SLAQr total (0-37)	8	3.5-13
Symptom score (0-19)	9	4-13.5
Patients global (0-10)	4	1-7
SLAM	4	2-8
SLAM nolab	3	1-6
SLEDAI-2K	2	2-5.5

REFERENCES

[1] Karlson EW, et al. *Validation of a Systemic Lupus Activity Questionnaire (SLAQ) for population studies*. Lupus. 2003.

[2] Pettersson S, et al. *A comparison of patients' and physicians' assessments of disease activity using the Swedish version of the Systemic Lupus Activity Questionnair*e. Scand J Rheumatol. 2017.

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SAT0210 THE ANTI-RO52 PREVALENCE IN THE SJÖGREN'S SYNDROME PICTURE: A SINGLE CENTER CROSS SECTIONAL STUDY

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Background: Sjögren syndrome (SjS) is an autoimmune disorder characterized by inflammation and destruction of exocrine glands. The presence of autoantibodies (AA) against the Ro52/TRIM21, an RNP complex binding to the stem-loop structure of human cytoplasmic RNA, might be relevant in the SjS pathogeny. It has been suggested that distinguishing between antibody reactivity against Ro60 and Ro52/TRIM21 could be helpful in terms of evaluating clinical course, features and even pre-symptomatic stages of the disease (1).

Objectives: To evaluate the prevalence of anti-Ro52/TRIM21 antibodies in a cohort of patients diagnosed with primary SjS.

Methods: In this cross-sectional study we evaluated 179 patients with primary SjS according to the ACR classification criteria who had been admitted between December 2008 and December 2018 to our outpatient clinic. All patients had ANA titers higher than 1:320 (2) in at least two positive determinations for any pattern. ANA, anti-Ro52/TRIM21, anti-Ro60, anti-La and rheumatoid factor (RF) were tested by immunoblot (Euroimmun, Lübeck, Germany).

Results: In our cohort the median age at diagnosis was 57 years (range: 20- 85 years) with a clear dominance of females (n=160, 89%). the most frequently reported ANA patterns were speckled (93%), while only few patients had a homogeneous (6%) pattern. 177/179 were positive for anti-Ro52/TRIM21 (98%), 159/179 (88%) for anti-Ro60, 127/179 for anti-La (79%) and 94/179 (52%) showed RF reactivity. 76/179 (42%) patients showed all four reactivities (anti-Ro52/TRIM21, anti-Ro60, anti-La and RF). Out of these 76 patients, 11 (6%) patients exhibited Raynaud's syndrome, 25 (13%) exhibited arthritis/arthralgia, 31 (17%) had hypergammaglobulinemia, 13 (7%) had hypocomplementemia and 26% had elevated free kappa/lambda chains, as typical clinical and laboratory features described in SjS.

Conclusion: Our results showed that anti-Ro52/TRIM21 but not anti-Ro60 is present in virtually all patients with SjS and had the most prevalent antibody reactivity. This finding needs to be considered in the current classification criteria of SjS (2), which include the presence of anti-Ro60, rather than anti-Ro52/TRIM21. Also, including the anti-Ro52/TRIM21 measurement in larger cohorts and longitudinal studies would also help us in improving the knowledge of its pathogenic role and to define of more focused diagnostic/therapeutic strategies.

REFERENCES

[1] Menendez A, Gomez J, Escanlar E, Caminal-Montero L, Mozo L. Clinical associations of anti-SSA/Ro60 and anti-Ro52/TRIM21 antibodies: Diagnostic utility of their separate detection. Autoimmunity. 2013; 46(1):32–9.

[2] Shiboski SC, Shiboski CH, Criswell L, et al. American College of Rheumatology classification criteria for Sjögren's syndrome: a data-driven, expert consensus approach in the Sjögren's International Collaborative Clinical Alliance cohort. Arthritis Care Res (Hoboken) 2012;64(4):475-87.

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SAT0211 LYMPHOPENIA WITH SYSTEMIC LUPUS ERYTHEMATOSUS: LYMPHOCYTE SUBSETS OF PATHOPHYSIOLOGICAL FEATURES

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease involving multiple systems. It is mainly characterized by abnormal activation of T and B lymphocytes and the production of a large number of autoantibodies. Blood system involvement is a common clinical manifestation. The occurrence of lymphopenia is very common, easy to merge infection and primary immunodeficiency[1-3].

Objectives: To study the distribution characteristics of peripheral blood lymphocyte cell subsets in patients with newly diagnosed SLE and to explore the possible mechanism of lymphocyte reduction.

Methods: Sixty-six female patients with initial SLE. The diagnosis was consistent with the 1997 revised American College of Rheumatology (ACR) SLE classification criteria, and no glucocorticoids and immunosuppressive agents were used. According to the absolute value lymphocytes with SLE, 40 patients were divided into lymphopenia group(LA)(LY< 1.0×10^9/L), and 26 patients were normal lymphocytes group(LN). 30 female healthy controls. The absolute numbers of lymphocyte cell subsets and T subsets (total T, $CD4^+$T, $CD8^+$T, T helper 1 (Th1), T helper 2 (Th2), T helper 17 (Th17) and $CD4^+CD25^+Foxp3^+$T regulatory (Treg) cells) in peripheral blood were measured by Flow Cytometer (FCM).

Results: In the lymphopenia group, the absolute counts of T cell subsets and NK cells were significantly reduced, but the percentage of B cells and Th1 cells and the ratio of Th1/Th2 cells were significantly increased (Figure 1). The absolute number of CD4+ T cells and CD8+ T cells was significantly positively correlated with C3 levels(Figure 2).

Conclusion: Decresed T cell subsets and NK cells may be key pathophysiological features, as risk factor for development of severe infections and primary immunodeficiency in patients lymphopenia with SLE. Meanwhile, decreased CD4+ T cells and CD8+ T cells and increased B cells may cause auto- antibodies production leading to lymphopenia with SLE. Further studies are needed to assess profound lymphopenia and require specific management.

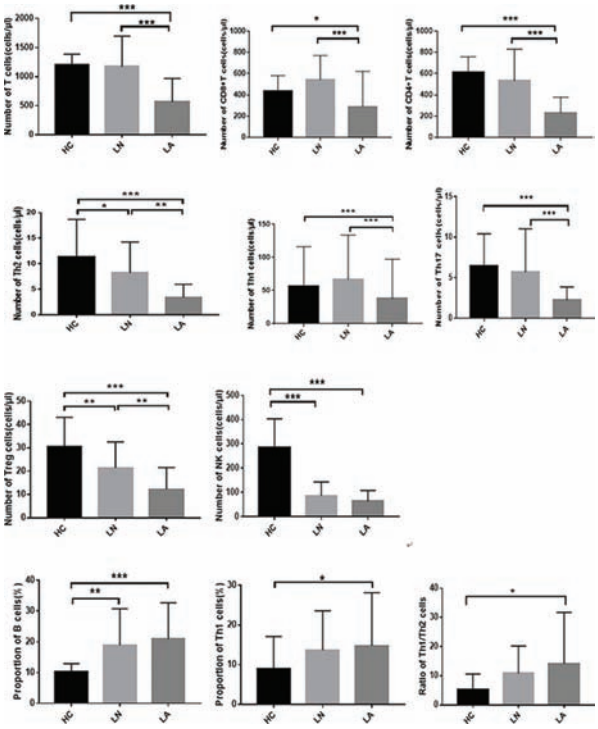


Figure 1. Absolute number and percentage of peripheral T cells, T-cells subsets, B cells and NK cells of patients with HC, LN and LA. One-Way ANOA analysis was used to compare HC and LN and LA with SLE(*p<0.5, **p<0.01, ***p<0.001). HC, healthy control; LN, lymphocyte normal; LA, lymphopenia.

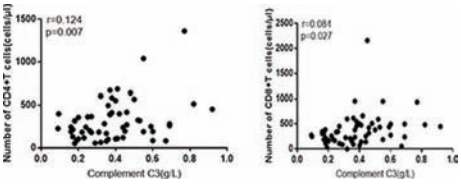


Figure 2:. Correlation of the absolute number of peripheral CD4+T cells and of CD8+T cells with the serum levels of complement C3.

REFERENCES

[1] MartinM, GuffroyA, ArgemiX,eta1.Systemic lupus erythematosus and lymphopenia: Clinical and pathophysiological features[J].Rev Med Interne. 2017 Sep;38(9):603-613.

[2] Chen D, Li H, Xie J,etal. Herpes zoster in patients with systemic lupus erythematosus: Clinical features, complications and risk factors[J]. Exp Ther Med. 2017 Dec;14(6):6222-6228.

[3] Merayo-Chalico J, Gómez-Martín D, Piñeirúa-Menéndez A,etal. Lymphopenia as risk factor for development of severe infections in patients with systemic lupus erythematosus: a case-control study[J]. QJM. 2013 May;106 (5):451-7.

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SAT0212 ASSOCIATION BETWEEN SELF-EFFICACY AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Self-efficacy for managing chronic conditions assesses the confidence a person has on the ability of successfully perform specific tasks related to a chronic condition in several different situations. Self-efficacy is considered one of the most important modifiable factors in educational interventions that enhance Systemic Lupus Erythematosus (SLE) patients' mental health status. Low disease self-efficacy is associated with SLE morbidity.[1]
Objectives: To determine the association of several domains of self-efficacy for managing chronic conditions and health-related quality of life (HRQoL) in SLE patients.
Methods: We evaluated patients with SLE from a single center cohort between October 2018 and January 2019. Using a standard protocol, we evaluated demographic characteristics, clinical manifestations and treatment. Self-efficacy was measured with the Spanish version of the Self-Efficacy for Managing Chronic Disease Scale (PROMIS Short Form v1.0) which include six domains: general self-efficacy, managing emotions, managing symptoms, managing daily activities, managing social interactions, managing medications and treatment. A score of 50 is the average for the US general populations with a standard deviation of 10 (such values are not available for Peruvian or Latin American populations). HRQoL was measured with the LupusQoL, disease activity was ascertained with the Systemic Lupus Erythematosus Disease Activity Index – 2K (SLEDAI-2K), and damage with the Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) damage index (SDI). The associations between self-efficacy (six domains) and each domain of LupusQoL were examined using linear regression models, adjusted by gender, age at diagnosis, socioeconomic status, educational level, SLEDAI-2K, SDI, prednisone daily dose, and antimalarial and immunosuppressant use.
Results: A total of 60 patients fit the inclusion criteria. Of them, 54 (90.0%) were female, their mean (SD) age at diagnosis was 37.3 (13.4) years, disease duration was 9.2 (7.2) years. The HRQoL domains most affected were the following: burden to others, intimate relationships, and body image. Self-efficacy was lower than the expected for the general population ranging between 43.1 and 48.6. The six domains of self-efficacy were positively associated with the majority of the domains of HRQoL, as depicted in Table 1.
Conclusion: Low disease self-efficacy in the management of SLE negatively correlated with HRQoL. The impact of the improvement of self-efficacy in the HRQoL should be evaluated prospectively.

Table 1. Association between several domains of self-efficacy for managing of Systemic Lupus Erythematosus and the health-related quality of life. Multivariable analyses.

Self-Efficacy Domains		HR-QoL Domains: Physical health	Pain	Planning	Intimate relationship	Burden to others	Emotional health	Body image	Fatigue
General self-efficacy 4a	B (SE)	1.15 (0.26)	1.33 (0.32)	1.08 (0.33)	0.75 (0.38)	1.18 (0.31)	1.40 (0.32)	1.26 (0.32)	1.50 (0.29)
	p	<0.001	<0.001	0.001	0.049	<0.001	<0.001	<0.001	<0.001
Self-Efficacy for Managing emotions 8a	B (SE)	1.82 (0.29)	2.06 (0.36)	2.04 (0.36)	1.41 (0.43)	1.93 (0.35)	2.36 (0.34)	1.75 (0.40)	2.05 (0.35)
	p	<0.001	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001
Self-Efficacy for Managing symptoms 8a	B (SE)	1.27 (0.32)	1.54 (0.38)	1.21 (0.40)	1.04 (0.44)	1.47 (0.37)	1.55 (0.39)	1.64 (0.37)	1.44 (0.37)
	p	<0.001	<0.001	0.002	0.020	<0.001	0.001	<0.001	<0.001
Self-Efficacy for Managing daily Activities 8a	B (SE)	2.20 (0.26)	2.43 (0.34)	2.08 (0.37)	1.41 (0.45)	1.89 (0.37)	2.13 (0.38)	1.92 (0.40)	2.47 (0.31)
	p	<0.001	<0.001	<0.001	0.002	<0.001	<0.001	<0.001	<0.001
Self-Efficacy for Managing social Interactions 8a	B (SE)	1.18 (0.36)	1.44 (0.43)	1.42 (0.43)	0.95 (0.49)	1.82 (0.39)	2.03 (0.40)	2.04 (0.41)	1.33 (0.42)
	p	0.001	0.001	0.001	0.052	<0.001	<0.001	<0.001	0.002
Self-Efficacy for Managing medications and Treatments 8a	B (SE)	0.47 (0.36)	0.65 (0.42)	0.39 (0.43)	0.24 (0.43)	0.90 (0.40)	1.21 (0.41)	1.53 (0.41)	0.97 (0.40)
	p	0.189	0.123	0.355	0.578	0.024	0.003	<0.001	0.015

SE standard error

REFERENCE

[1] Mazzoni D, et al. Health-related quality of life in systemic lupus erythematosus: a longitudinal study on the impact of problematic support and self-efficacy. Lupus. 2017 Feb; 26(2):125-131.

Disclosure of Interests: None declared
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SAT0213 PREGNANCY AND UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE: OUTCOME AND RISK OF FLARE IN 100 PREGNANCIES

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Background: Undifferentiated connective tissue disease (UCTD) is a group of systemic autoimmune conditions which do not fulfil the criteria for a definite connective tissue disease (CTD). The interaction between pregnancy and UCTD is still poorly studied and scarcely recognized.
Objectives: The purpose of this study was to evaluate the risk of disease flares or differentiation into a well-defined CTD and also the risk of adverse outcome in pregnancy in patients with UCTD.
Methods: A total of 100 pregnancies in 81 UCTD followed at a single center were included in this analysis. From the time the pregnancy was detected, each patient was evaluated every 4 – 6 weeks and the diagnosis was re-evaluated at each observation; the follow-up was considered completed after the last visit during puerperium. At each visit, patients were assessed by a rheumatologist and by a gynecologist.
Results: Eleven pregnancies (11%) ended with abortion in the first trimester and the remaining 89 (89%) ended with a live birth. Twelve patients (12%) flared during pregnancy or puerperium and three (3%) had major flares and evolved to systemic lupus erythematosus (SLE) with renal involvement. Obstetric complications were observed in twenty-nine out of the 89 successful pregnancy (33%), including two cases (2%) of preeclampsia. We found a significant association between anti-dsDNA antibodies positivity at baseline and disease flare ($p<0.01$), while disease activity at the beginning of pregnancy was associated with flare ($p<0.01$) and also with cumulative obstetric complications ($p<0.05$).
Conclusion: The impact of pregnancy appears to be less serious in UCTD than in other CTDs, however disease flares and obstetric complications can represent a clinical challenge; disease clinical and serological activity seem important determinants of pregnancy outcomes. Thus, a pre-pregnancy counselling and planning as well as a close monitoring during pregnancy is warranted.
Disclosure of Interests: : Dina Zucchi: None declared, Chiara Tani: None declared, Elena Elefante: None declared, Linda Carli: None declared, Alice Parma: None declared, Francesca Anna Letizia Strigini: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB

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Vasculitis

SAT0214 CLINICAL FEATURES OF ANEURYSMAL BEHÇET DISEASE

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Background: Arterial aneurysmatic lesions are one of the unique features of Behçet's disease (BD). However, it is difficult to determine which BD patients will develop an aneurysm.
Objectives: In this study, we aimed to determine the differences between BD patients with and without an arterial aneurysm.
Methods: Data of the 23 BD patients with an arterial aneurysm was published as an abstract in 2013 (1). We retrospectively reviewed the medical records of 441 patients with BD according to International Study Group (ISG) criteria between January 2013 and June 2018. Totally, we determined 45 BD patients with an arterial aneurysm. Six patients with isolated carotid and/or cranial arterial aneurysms who were followed by other clinics excluded from the analysis. Overall, 39 BD patients with an extracranial and extra carotidal aneurysm included in the study. Data regarding demographic features, clinical, laboratory and vascular imaging findings were collected.
Results: A total of 39 BD patients (Male: 76.9%) with an arterial aneurysm were analyzed in this study. Mean age, mean age of diagnosis and a median follow-up of patients were 40.9±11.0 years, 29.7±7.7 and 71.8 (2-186) months, respectively. The mean age at the onset of the arterial aneurysm was 36.1±11.5 years. The median time lag between the onset of BD and detection of an aneurysm was 63.6 (0-482) months. The prevalence of male patients in BD with aneurysms, without aneurysms and only mucocutaneous were 76.9%, 52.3%, and 34.3%, respectively. Comparison of BD patients with and without an aneurysm shown in table 1. In multivariate analysis, having a venous thrombosis was the sole risk factor for the development of arterial aneurysm (OR 10.53, 95% CI 1.53-72.71) (Table). Distribution of aneurysms was shown in the figure. At the first diagnosis, a median number of the aneurysm was 1 (1-4), the median diameter of an aneurysm was 39 mm (10-80) and 16 (41%) patients had more than one aneurysm. Type of the firstly detected aneurysm was as follows; 38.5% saccular, 17.9% fusiform, 15.4% pseudoaneurysm and 2.6% dissecting aneurysms. Aneurysm type was not known in 25.6% of patients. The first diagnostic finding was an aneurysmal symptom in the 25% of BD patients.
Conclusion: Aneurysm was the diagnostic symptom in 25% of BD patients with an aneurysms. The median time lag between the onset of BD and detection of an aneurysm was almost 5 years. In aneurysmal BD, there is male sex dominance and having venous thrombosis is the most important risk factor. Although pulmonary arteries have an important role in the BD course, the involvement of the aorta and iliac arteries can be seen frequently.

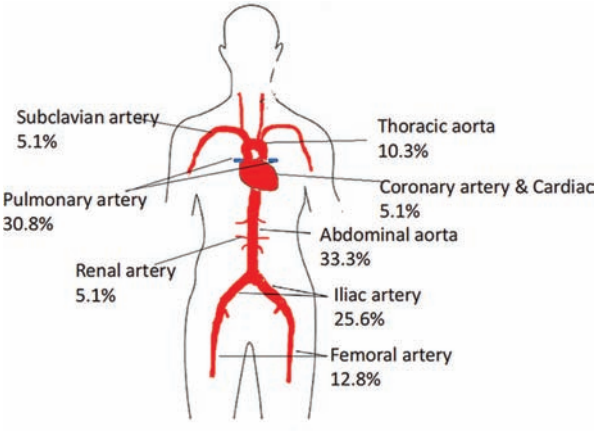


Figure.. Distribution of aneurysms

REFERENCES
[1] Kalyoncu U, et al. Ann Rheum Dis 2013;72 (abs)

Table.. Clinical features of Behçet disease patients with and without arterial aneurysm

	BD with arterial aneurysm, n=39	BD without arterial aneurysm, n=396	p
Age (mean±SD, year)	40.9±11.0	41.0±11.8	0.971
Age at diagnosis (mean ±SD, year)	29.7±7.7	29.2±9.1	0.504
Male	76.9	52.3	**0.003**
Smoke,%	36.7	48.0	0.235
Oral ulcers,%	100	99.7	1
Genital ulcers,%	80.6	74.5	0.425
Pathergy,%	34.5	44.8	0.303
Erythema nodosum,%	33.3	44.3	0.20
Papulopustular lesions,%	47.2	54.9	0.374
Ocular involvement,%	28.2	51.2	**0.006**
Arthritis,%	27.8	28.8	0.9
Gastrointestinal involvement,%	7.7	4.6	0.423
Neurologic involvement,%	5.1	18.7	**0.033**
Fever,%	24.3	NA	NA
Venous thrombosis,%	51.3	20.1	**<0.001**

BD: Behçet disease, NA: Non available

Disclosure of Interests: Berkan Armagan: None declared, Ertuğrul Çağri Bölek: None declared, Alper Sari: None declared, Gözde Kübra Yardimci: None declared, Bayram Farisoğullari: None declared, Emre Bilgin: None declared, Fatma Gonca Eldem: None declared, Levent Kiliç: None declared, Omer Karadag: None declared, Bora Peynircioğlu: None declared, Barbaros Erhan Çil: None declared, Metin Demircin: None declared, Ali Akdoğan: None declared, Şule Apraş Bilgen: None declared, Ali İhsan Ertenli: None declared, Sedat Kiraz: None declared, Umut Kalyoncu Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim
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SAT0215 APREMILAST IN REFRACTORY ORAL AND/OR GENITAL ULCERS IN BEHÇET'S DISEASE. MULTICENTER STUDY OF 49 CASES IN CLINICAL PRACTICE

Belén Atienza-Mateo, José Luis Martín-Varillas, J. Loricera, Vanesa Calvo-Río, Jenaro Graña, Gerard Espinosa, Clara Moriano, Trinidad Pérez-Sandoval, Manuel Martín-Martínez, Elvira Diez Alvarez, María Dolores García-Armario, Esperanza Martínez, Ivan Castellví, Patricia Moya, Francisca Sivera, Jaime Calvo, Isabel de la Morena, Francisco Ortiz-Sanjuán, José Andrés Román-Ivorra, Ana Pérez Gómez, Sergi Heredia, Alejandro Olive, Águeda Prior-Español, Carolina Díez, Juanjo J. Alegre-Sancho, D Ybáñez-García, Ángels Martínez-Ferrer, J. Narváez, Ignasi Figueras, Ana Isabel Turrión, Susana Romero-Yuste, Pilar Trénor, Soledad Ojeda, Santos Castañeda, Monica Calderón-Goercke, D. Prieto-Peña, Iñigo González-Mazón, Lara Sánchez Bilbao, Miguel Á. González-Gay, Ricardo Blanco. *Reference hospitals, Rheumatology and Dermatology, Spain*

Background: Oral and/or genital aphthous ulcers are the most common symptoms of Behçet´s disease (BD), and are often refractory to conventional treatment. The inhibitor of phosphodiesterase-4 Apremilast (APR) has demonstrated efficacy in the treatment of this manifestations.
Objectives: To assess the efficacy and safety of APR in BD patients with oral and/or genital ulcers refractory to conventional treatment.
Methods: National multicenter open-label study on 49 BD patients treated with APR at maintained standard dose of 30 mg twice daily, with the initial 5-day titration schedule in 38 cases. The main outcome was achievement of oral and/or genital ulcers remission.
Results: We included 49 patients (35 women/14 men), mean age of 44.5 ±13.4 years. Before APR, all patients had received several systemic conventional and/or biological drugs: oral corticosteroids (n=45), colchicine (n=48), NSAIDs (n=21), methotrexate (n=27), azathioprine (n=23), cyclosporine (n=9), dapsone (n=6), adalimumab (n=12), infliximab (n=8), tocilizumab (n=3), etanercept (n=3), sulfasalazine (n=2), cyclophosphamide (n=2) and/or others (pentoxifylline, thalidomide, mycophenolate mofetil, hydroxychloroquine, golimumab, 1 each). The main clinical symptoms for starting APR were oral (n=18) and genital (n=2) aphthous ulcers or both (n=29). After a mean follow-up of 8.3±6.8 months, most of the patients experienced main clinical improvement and prednisone dose was reduced or discontinued (TABLE). In this period of time, 31 patients developed any side-effect, most of them transitory: nausea (n=12), diarrhea (n=11),

dyspepsia (n=9), abdominal pain (n=7), headache (n=5), loss of appetite (n=4), weight loss (n=3), halitosis (n=1), dry mouth (n=1), palpitations (n=1) and/or depression (n=1). Six patients had to reduce the dose to 30 mg/day. APR was discontinued in 11 patients due to: not obtaining the expected improvement (n=5), intense gastrointestinal adverse effects (n=3), desire of pregnancy (n=1), persistent erythema nodosum (n=1) and development of neurological involvement (n=1).

Conclusion: Our data show a rapid and maintained improvement with APR in patients with mucocutaneous ulcers of BD refractory to several systemic drugs, including biologic therapy.

REFERENCES:

[1] Davatchi F, et al. The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. J Eur Acad Dermatology Venereol. 2014;28(3):338–47.

[2] Gulen Hatemi, et al. Apremilast for Behçet's Syndrome — A Phase 2, Placebo-Controlled Study. N Engl J Med 2015; 372:1510-1518.

TABLE. Evolution of main symptoms and reduction prednisone dose with apremilast therapy.

	Basal	Week 1-2 n= 47	Week 4 n= 43	Month 3 n= 37	Month 6 n= 28	Month 12 n= 12	Month 18 n=4	Month 24 n=2
Outcome of oral and/or genital ulcers n, (%)								
Complete resolution		18 (38.3)	30 (69.8)	31 (83.8)	20 (71.4)	6 (50)	3 (75)	2 (100)
Partial resolution		24 (51.1)	10 (23.2)	2 (5.4)	7 (25)	6 (50)	1 (25)	0
No response		5 (10.6)	3 (7)	4 (10.8)	1 (3.6)	0	0	0
Dose of prednisone (mg/day), median [IQR]	10 [5-15]	10 [5-15]	10 [5-12.5]*	5 [3-7.5]*	5 [2.5-10]*	2.5 [2.5-5]	2.5 [2.5-2.5]	0 [0-0]*

*p<0.05
n=available data.

Disclosure of Interests: Belén Atienza-Mateo: None declared, José Luis Martín-Varillas: None declared, J. Loricera: None declared, Vanesa Calvo-Río: None declared, Jenaro Graña: None declared, Gerard Espinosa: None declared, Clara Moriano: None declared, Trinidad Pérez-Sandoval: None declared, Manuel Martín-Martínez: None declared, Elvira Diez Alvarez: None declared, María Dolores García-Armario: None declared, Esperanza Martínez: None declared, Ivan Castellví Consultant for: I received fees less than 5000USD as a consultant for Kern and Actelion, Paid instructor for: I received fees less than 2000USD as a instructor for Boehringer -Ingelheim, Novartis and Gebro, Speakers bureau: ND, Patricia Moya: None declared, Francisca Sivera: None declared, Jaime Calvo Consultant for: Bristol-Myers Squibb, Janssen, Celgene, Sanofi Genzyme, Speakers bureau: Bristol-Myers Squibb, Isabel de la Morena Speakers bureau: Abbvie, Celgene, Pfzier, UCB, Ghebro, Roche, Sanofi, Janssen., Francisco Ortiz-Sanjuán: None declared, José Andrés Román-Ivorra: None declared, Ana Pérez Gómez: None declared, Sergi Heredia: None declared, Alejandro Olive: None declared, Águeda Prior-Español: None declared, Carolina Díez: None declared, Juanjo J Alegre-Sancho: None declared, D Ybáñez-García: None declared, Ángels Martínez-Ferrer: None declared, J. Narváez Consultant for: Bristol-Myers Squibb, Ignasi Figueras: None declared, Ana Isabel Turrión : None declared, Susana Romero-Yuste: None declared, Pilar Trénor: None declared, Soledad Ojeda Grant/research support from: AMGEN, Speakers bureau: AMGEN, Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Monica Calderón-Goercke: None declared, D. Prieto-Peña: None declared, Iñigo González-Mazón: None declared, Lara Sánchez Bilbao: None declared, Miguel Á. González-Gay: None declared, Ricardo Blanco: None declared

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SAT0216 PATIENT PERCEPTIONS OF PHYSICAL ACTIVITY AFTER A DIAGNOSIS OF GIANT CELL ARTERITIS: A SECONDARY ANALYSIS OF MULTINATIONAL QUALITATIVE DATA

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Background: Giant cell arteritis (GCA) is the most common vasculitis in the UK, with an incidence of 220 cases/million in adults over 50 years of age. The physical symptoms as well as the side effects of glucocorticoids may impact patients' ability to exercise. Maintaining physical activity (PA) has been shown to be beneficial to disease activity in other inflammatory conditions, and is also a specific priority for GCA patients.

Objectives: To explore patient perceptions of physical activity in GCA.

Methods: Multinational qualitative study, using interviews with 36 patients from the UK (25) and Australia (11), all of whom had a definitive diagnosis from imaging or biopsy. Interviews were recorded, transcribed, and analysed using inductive thematic analysis. This is secondary analysis of data collected to explore health-related quality of life in people with GCA.

Results: 84 individual themes were reported by patients, each of which fell broadly into two overarching themes: barriers to and facilitators of physical activity. Within each theme, four subthemes were identified. In terms of barriers, these were: negative physical symptoms (including visual loss, fatigue, weakness, pain and stiffness), lack of physical capability (including poor stamina, confidence and mobility), negative perceptions around PA, and negative reinforcement (i.e. new physical symptoms following PA). Facilitators of physical activity were also grouped into four subthemes: external facilitators (including motivation from healthcare professionals and support groups), access to appropriate facilities, personal strategies (including pacing and goal-setting) and personal facilitators (including internal motivation to improve symptoms, and positive reinforcement from PA).

Conclusion: There are a variety of barriers to physical activity in GCA patients, including patients being fearful of exercise. In other inflammatory conditions, patients report improved symptoms following physical activity as well as wider benefits to general wellbeing and cardiovascular health. Education, motivational interviewing, and personalised strategies may be beneficial components of an intervention to support physical activity in patients with GCA.

REFERENCES

[1] Hellmann DB, Uhlfelder ML, Stone JH, Jenckes MC, Cid MC, Guillevin L, et al. Domains of health-related quality of life important to patients with giant cell arteritis. Arthritis Care Res 2003;49(6):819-25

[2] Perandini LA, de Sa-Pinto AL, Roschel H, Benatti FB, Lima FR. Bonfa E & Gualano B. Exercise as a therapeutic tool to counteract inflammation and clinical symptoms in autoimmune rheumatic diseases. Autoimmun Rev 2012;12(2)218-24

[3] Smeeth L, Cook C & Hall AJ. Incidence of diagnosed polymyalgia rheumatic and temporal arteritis in the United Kingdom, 1990-2001. Ann Rheum Dis 2006;65(8):1093-98

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SAT0217 EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: CLINICAL PREDICTORS OF LONG-TERM ASTHMA SEVERITY

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Background: Bronchial asthma in Eosinophilic Granulomatosis with Polyangiitis (EGPA) patients is commonly present before, at and after the diagnosis of vasculitis, often requiring high doses of oral corticosteroid (OCS) to be controlled.

Objectives: We aimed to better characterize long-term asthma in EGPA and to identify predictors of long-term asthma severity.

Methods: Retrospective cohort study of anti-neutrophil cytoplasmic antibodies associated vasculitis patients who fulfilled standardized criteria for EGPA (American College of Rheumatology 1990 and/or Lanham criteria and/or Chapel Hill Consensus Conference 2012) that were followed in a single referral center from 1990-2017. Baseline and 3 (±1) years of follow-up clinical, laboratory and pulmonary function data were analyzed. The definition from American Thoracic Society Workshop was used to identify patients with severe/uncontrolled asthma. Severe rhinosinusitis was defined as rhinosinusitis that needed sinus surgery to control nasal polyps and/or reduce symptoms ($\geq$1 surgery).

Results: One-hundred-eighty-seven patients with EGPA were identified, from which 89 patients with documented asthma assessment at baseline and after 3 years from diagnosis were included. Severe/uncontrolled asthma was observed in 42.7% of patients at diagnosis and was associated with a previous history of respiratory allergy ($p<0.01$), higher serum total IgE levels ($p<0.05$), and increased use of high dose inhaled corticosteroids (ICS) ($p<0.05$) and OCS ($p<0.001$) for respiratory symptoms the year before the diagnosis of EGPA. Improvement or worsening of asthma during follow-up was experienced by 22.4% patients, with no discriminative baseline features that allowed their distinction. Severe/uncontrolled asthma was present in 40.5% of patients at 3 years, and was associated with increased airway resistance on pulmonary function testing ($p<0.05$). Long-term PFT did not improve during long-term follow-up regardless of ICS and OCS therapy (both FEV1/FVC and FEV1, $p>0.05$). Using multivariate binary logistic regressions, severe rhinosinusitis, pulmonary infiltrates, overweight and severe/uncontrolled asthma at vasculitis diagnosis independently predicted severe/uncontrolled asthma at the 3-year endpoint (Table below).

Table. Multiple binary logistic regressions of baseline variables associated with severe/uncontrolled asthma at 3 (±1) years of follow-up

Variables	Odds Ratio	95% Confidence of Interval	p value
Severe/uncontrolled asthma	10.64	3.43-39.08	**<0.001**
Pulmonary infiltrates	5.16	1.43-21.85	**0.011**
Severe rhinosinusitis	3.57	1.07-13.55	**0.038**
Overweight (BMI≥25 kg/m^2)	3.41	1.05-12.90	**0.041**

Conclusion: In this large cohort of patients with EGPA, long-term severe/uncontrolled asthma is frequent, and patients affected display a higher proportion of bronchial obstruction and have more severe airway resistance. Overall, pulmonary function does not improve during the follow-up regardless of ICS and OCS therapy. Finally, long-term severe/uncontrolled asthma is associated with baseline pulmonary and ENT manifestations, but not with vasculitic features.

REFERENCES

[1] Cottin V, et al. Respiratory manifestations of eosinophilic granulomatosis with polyangiitis (Churg-Strauss). The European respiratory journal. 2016;48(5):1429-41.

[2] Berti A, et al. Severe/uncontrolled asthma and overall survival in atopic patients with eosinophilic granulomatosis with polyangiitis. Respiratory medicine. 2018;142:66-72.

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SAT0218 PATIENTS' JOURNEY THROUGH GIANT CELL ARTERITIS: A QUALITATIVE STUDY

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Background: Giant cell arteritis (GCA) is the most common form of vasculitis. Diagnosis is difficult due to multiple presenting symptoms: headache, jaw and limb claudication, myalgia and visual impairment. Access to care may be delayed because often multiple providers are involved in the diagnosis of GCA and disease management. Treatment with high-dose glucocorticoids (GCs) can relieve symptoms and prevent vision loss, but GC-related adverse events are common; GCA often relapses once GCs are tapered.
Objectives: To understand the GCA patient care pathway and unmet needs in GCA through in-depth patient interviews.
Methods: US patients with GCA were recruited through outreach to physicians and The Vasculitis Foundation, which used email newsletters and social media to recruit ≈ 50% of participating patients. Extensive individual interviews with patients were conducted by qualitative researchers by phone or in person and explored patients' perspectives and experiences from the onset of GCA symptoms to diagnosis and disease management. Patients were asked open-ended questions and encouraged to share their stories to provide additional insights into the patient journey and their individual perspectives. The qualitative data collected were analyzed using human-centered design methodology, including patient typologies (personas: optimist, fearful, stoic or despondent), forced temporal zoom (journey maps), forced semantic zoom (stakeholder system mapping) and affinity mapping for pattern recognition of unmet needs.
Results: A total of 28 patients were interviewed; 23 (82%) were women and mean age was 69 years (Table). The number of patients in each persona category is shown in the Table. Stoic and optimist personas had medium to high levels of self-advocacy and a positive/engaged attitude about their condition, while fearful and despondent personas had low levels of self-advocacy with disengaged/negative attitudes toward their condition. Patients often ascribed their milder GCA symptoms to causes such as stress and did not consult a physician until they developed moderate to severe symptoms, such as persistent headache, jaw pain or visual disturbances. Patients with existing inflammatory disorders were less likely to share symptoms of GCA unless the symptoms substantially worsened. In most cases, physicians diagnosed GCA based on abnormal erythrocyte sedimentation rate, often followed by a temporal artery biopsy. After diagnosis of GCA, all patients received GCs with little information on the chronicity of GCA. Few patients were offered treatment alternatives to GCs. Overall, patients managed their GCA independently, with moderate support from friends or family, and sought to balance relief of GCA symptoms with the adverse effects of GCs. Patients concentrated on tapering and discontinuing GCs, with less concern about relapse. Furthermore, patients who were most uncomfortable with the adverse effects of GCs often waited until their GCA symptoms became debilitating before telling their physician. Almost all patients reported searching for a support group after the diagnosis.
Conclusion: Patients with GCA experience adverse effects from GCs and remain focused on reducing their GC dose. For those with inflammatory comorbidities, diagnosis of GCA is another burden in a debilitating journey that results in a sense of disempowerment and resignation toward their condition and paucity of therapeutic options. Patients with GCA want a clearer understanding of treatment options and need access to support groups. Patients' attitudes and self-advocacy vary depending on their personas; recognizing these personas may help HCPs coordinate patient care. Increased awareness of GCA among patients and HCPs may accelerate the path to diagnosis and treatment, and emerging therapies may help reduce GC burden.

Table. Demographics of Patients With GCA Who Participated in Interviews and Personas Based on Analysis of Qualitative Interview Data

	Patients N = 28
Age, mean, years	69
Women, n (%)	23 (82)
Interview type, n (%)	
Phone	15 (54)
In person	13 (46)
US region, n (%)	
Midwest	10 (36)
Northeast	6 (21)
South	5 (18)
Mid-Atlantic	4 (14)
West	3 (11)
Persona, n (%)*	
Optimist	9 (32)
Despondent	9 (32)
Fearful	8 (29)
Stoic	6 (21)

* Some interviewees fit into multiple personas.

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SAT0219

EFFICACY AND SAFETY OF TOCILIZUMAB IN GIANT CELL ARTERITIS INDEPENDENTLY OF THE INICIAL PREDNISONE DOSE

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Background: Tocilizumab (TCZ) has been approved for the treatment of Giant Cell Arteritis (GCA). It showed to be effective to induce remission, prevent relapses and decrease the cumulative prednisone dose. However, the glucocorticoids are the mainstay in the acute treatment of GCA.
Objectives: Our aim was to compare the efficacy and safety of the initial dose of prednisone at the onset of TCZ treatment.
Methods: Retrospective, multicenter study on 134 patients with GCA in treatment with TCZ. We compared two subgroups of patients according to the initial dose of prednisone at TCZ onset. Clinical efficacy, analytical improvement and safety was studied.
Results: We studied 134 patients (101 w/33 m) and made a comparative study between 2 groups: a) TCZ and ≤ 15 mg of prednisone; 68 (50.7%) cases, and b) TCZ and > 15 mg of prednisone, 66 (49,3%) patients. It is summarized in **TABLE 1**. It was no statistical significance according to age, sex and evolution time of disease. In the group receiving > 15 mg of prednisone, the patients presented more visual involvement (p<0.001) at TCZ onset. In terms of prolonged remission and relapses no significant difference was seen between both groups. The risk of presenting adverse effects (11.8% vs 36.4%) and severe infections (4.4% vs 19.7%) was related with the prednisone dose, being more frequent in the group with > 15 mg of prednisone (p=0.001 and p=0.006, respectively). **TABLE 2** summarizes the infections of our patients.
Conclusion: According with our results, we can conclude that TCZ is equally effective; in terms of prolonged remission and relapses, with doses ≤ 15 mg of prednisone at treatment onset. Being the most important data, the higher risk to develop adverse effects, as well as infections with higher doses of prednisone.

TABLE 1

	PREDNISONE ≤ 15 mg (n=68)	PREDNISONE > 15 mg (n=66)	p
ACUTE PHASE REACTANTS			
ESR, mm/1st hour, mean (SD)	38.6 ± 30.5	34.5 ± 32.2	0.500
CRP, mg/dL mean (SD)	3.3 ± 6.8	2.6 ± 3.2	0.603
Hemoglobin, g/dL, mean (SD)	11.5 ± 0.64	13.2 ± 1.5	0.104
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	9.8 ± 3.7	34.8 ± 14.3	**<0.001**
EFFICACY AND SAFETY AFTER TCZ			
Prolonged remission n (%)			
Month 6	37 (69.8)	21 (44.7)	**0.018**
Month 12	27 (73)	19 (59.4)	0.232
Month 24	19 (82.6)	8 (47.1)	0.018
Relapses n (%)			
Month 1	3 (4.5)	1 (1.6)	0.620
Month3	3 (4.9)	4 (6.6)	1.000
Month 6	2 (3.8)	3 (6.4)	0.664
Month 12	3 (8.1)	6 (18.8)	0.285
Month 24	2 (8.7)	5 (29.4)	0.113
SIDE EFFECTS, n (%)			
Relevant adverse events	8 (11.8)	24 (36.4)	**0.001**
Serious infections	3 (4.4)	13 (19.7)	**0.006**

TABLE 2

	PREDNISONE ≤ 15 mg (n=68)	PREDNISONE > 15 mg (n=66)
SERIOUS INFECTIONS, n (%)		
Cytomegalovirus (bilateral pneumonia)	-	1 (1.5)
Endocarditis	-	1 (1.5)
Facial Herpes Zoster Infection †	-	2 (3.0)
Bacterial Infective Bursitis †	-	1 (1.5)
Severe Infectious Cellulitis †	-	1 (1.5)
Infectious Meningitis	-	1 (1.5)
Infected ulcer †	-	1 (1.5)
Infected Necrotizing ulcer	-	1 (1.5)
Pneumonia	2 (2.9)	1 (1.5)
Recurrent urinary infection and sepsis †		2 (3.0)
Urinary sepsis	1 (1.5)	1 (1.5)
Anal abscess ‡		1 (1.5)

REFERENCES

[1] Proven A. Glucocorticoid therapy in giant cell arteritis: duration and adverse outcomes. Arthritis Rheum. 2003; 49:703-8.
[2] Calderón-Goercke M. Tocilizumab in giant cell arteritis. Observational, open-label multicenter study of 134 patients in clinical practice. Semin Arthritis Rheum. 2019 Jan 5. pii: S0049-0172(18)30571-7. doi: 10.1016/j.semarthrit.2019.01.003. [Epub ahead of print]

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SAT0220 USE OF TOCILIZUMAB IN AORTITIS. A MULTICENTER STUDY OF 79 PATIENTS

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Background: Aortitis can be idiopathic or associated with other conditions. It is frequently refractory to conventional immunosuppressive therapy. Tocilizumab (TCZ), an anti-IL-6 receptor antibody seems to be effective and safe.
Objectives: Our aim was to assess the efficacy and safety of TCZ at short and long follow-up in a series of patients with Aortitis.
Methods: Retrospective, multicenter study of 79 patients diagnosed of inflammatory aortitis based on imaging techniques (PET/CT, CT angiography and/or MR angiography).
Results: We study 79 patients (61 w/ 18 m). 59 (74.7%) cases were Aortitis secondary to Giant Cell Arteritis (GCA), while 20 (25.3%) were idiopathic. The mean age was 71±8.5 years vs 64.2±7.1 years, respectively (p=0.001). At time of disease diagnosis more than a half of patients (59.5%) presented as main symptom polymyalgia rheumatica (PMR). Aortitis was diagnosed with PET/CT (71 patients), angioRMN (12 patients) and angioCT (8 patients). Prior to TCZ treatment, 61 (77.2%) patients had received conventional immunosuppressive drugs, 59 (74.7%) of them received MTX. After 24 months of treatment with TCZ, more than 75% of patients reached a prolonged remission in both groups (p=0.527), with only 4% of relapses after the same follow-up period (p=1.000). 40 (50.6%) patients had a control image technique (PET/CT) throughout follow up. 4 (3 secondary to GCA and 1 idiopathic) patients reached a complete improvement in uptake after one year of treatment.
Conclusion: Our results show that idiopathic aortitis occurs in younger patients compared with aortitis secondary to GCA. TCZ proved to be effective in both pathologies, allowing clinical and analytical improvement, as well as a reduction of corticoid dose, without increasing the risk of relapse. However, the improvement in imaging techniques seems to be slower.

REFERENCE

[1] Loricera J, Blanco R, Castañeda S, Humbría A, Ortego-Centeno N, Narváez J, et al. Tocilizumab in refractory aortitis: study on 16 patients and literature review. Clin Exp Rheumatol. 2014; 32:79-89.

TABLE

	Idiopathic aortitis (n=20)	Aortitis secondary to GCA (n=59)	p
EFFICACY OF TCZ			
Prolonged remission, n (%)			
Month 6	5 (41.7)	23 (45.1)	0.830
Month 12	5 (45.5)	14 (41.2)	0.803
Month 24	3 (75)	18 (85.7)	0.527
Relapses, n (%)			
Month 1	2 (15.4)	1 (3.3)	0.213
Month 3	2 (16.7)	5 (10.4)	0.546
Month 6	1 (9.1)	8 (16.3)	0.544
Month 12	1 (9.1)	4 (11.8)	1.000
Month 24	0	1 (4.8)	1.000

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SAT0221 OFF-LABEL USE OF BIOLOGICAL THERAPIES IN RELAPSING AND/OR REFRACTORY POLYARTERITIS NODOSA

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Background: Polyarteritis nodosa (PAN) is a rare systemic necrotizing vasculitis of medium- and small-sized arteries, not associated with anti-neutrophil cytoplasmic antibodies (ANCA). Conventional treatments include glucocorticoids (GCs) for non-severe disease and a combination of GCs and immunosuppressive agents for severe disease. Nevertheless, some patients have refractory and/or relapsing disease.
Objectives: We examined the use of off-label biological therapy for relapsing/refractory PAN.
Methods: This retrospective European collaborative study included patients with PAN meeting ACR criteria and/or Chapel Hill Consensus Conference 2012 definitions. Treatment efficacy and safety are recorded. Remission was defined as the absence of vasculitis manifestations (BVAS = 0) with a prednisone dose ≤5 mg/day. Partial response was defined as a BVAS = 0 with a prednisone dose between 6 and 10 mg/day.
Results: Fifty-one patients (24 men, 27 women; median age 51 years) were included. Eighteen (35%) patients received TNF-alpha blockers, 16 (31%) received rituximab (RTX), 9 (18%) tocilizumab (TCZ), and 8 (16%) other biologics (including alemtuzumab in 3, anakinra in 2, interferon-alpha in 2 and abatacept in one). Previous treatments were: GCs in all cases, including methylprednisolone infusions (72%) and oral GCs (92%), cyclophosphamide (61%), azathioprine (53%), methotrexate (45%) and mycophenolate mofetil (47%). At inclusion, median BVAS was 5 (range 0-18), including 5 (2-12) in the TNF-alpha blockers group, 5 (2-12) in the RTX group and 4 (0-6) in the TCZ group.
After median follow-up of 34.4 months (IQR 21.5-59.5), remissions, partial responses and treatment failure, respectively, were noted in 41%, 6% and 53% for TNF-alpha blockers recipients, 25%, 12% and 63% for RTX recipients, and 57%, 0% and 43% for TCZ recipients. No remission was noted in patients treated with anakinra, alemtuzumab and abatacept.
Median BVAS dropped to 3 at 6 months, 0 at 12 months and 0 at last follow-up in the TNF-alpha blockers group, to 3.5, 0 and 2 in the RTX group, respectively, and 0, 0 and 0 in the TCZ group. A GC-sparing effect seemed more important with TNF-alpha blockers and TCZ. Median GCs dose decreased from the baseline 15 mg/day to 10 at 6 months, 5 at 12 months and 5 at last follow-up in the TNF-alpha blockers group, from 15 mg/day to 10 at 6 months, 5 at 12 months and 10 at last follow-up in the RTX group, and from 15 mg/day to 7 at 6 months, 5 at 12 months and 5 at last follow-up in the TCZ group.
Four (22%) patients stopped TNF-alpha blockers because of allergic reaction in one and refractory disease in 3. Six (38%) stopped RTX because of refractory disease. Finally, 4 (44%) stopped TCZ because of adverse

events in 2 (testicular abscess and worsening renal failure) and refractory disease in 2.

Conclusion: The results of this study suggest that TNF-alpha blockers and TCZ may achieve higher rates of remission and GC-sparing in relapsing and/or refractory PAN than other biologics. Our data warrant further study to confirm or not these findings.

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SAT0222 COOPERATION OF T FOLLICULAR HELPER CELLS AND B CELLS IN TERTIARY LYMPHOID STRUCTURES IN TAKAYASU ARTERITIS

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Background: Takayasu's arteritis (TA) and giant cell arteritis (GCA), the two most common types of large vessel vasculitis (LVV), are characterized by an arterial inflammatory granulomatous infiltrate mainly located in the media and the adventitia. However, distinct histological features of the immune response are poorly known.

Objectives: To investigate distinct pathological mechanisms of the immune response in patients with GCA and TA.

Methods: We performed comparative immunohistochemistry analysis of aorta of GCA and TA patients. We performed microarray gene analysis of purified CD4+ T cells of TA and GCA patients. Reverse transcriptase PCR, flow cytometry analysis and cell culture were used to investigate T and B cells subpopulations in 54 patients with TA, 52 with GCA and 60 controls.

Results: We found higher proportion of tertiary lymphoid structures composed of CXCR5+, CD4+, PD-1+ and CD-20+ cells in inflammatory aortic lesions in TA as compared to GCA. We demonstrated increased proportion of aortic B cells in TA.

We next evaluated differentiation of circulating CD4+ T cells in both diseases. Among sixty-seven genes differentially expressed in CD4+ T cells of TA compared to GCA patients, we identified a specific "T follicular helper" (Tfh) signature in TA patients. We also found a specific Tfh 17 signature in TA patients. Flow cytometry analysis confirmed increased circulating Tfh, defined as CXCR5+ CD4+ T cells, in TA patients as compared to GCA and healthy donors (HD) [median of 15.4 (10;30.8)% versus 5.3 (1.4; 12.2)% and 9.7 (5.6; 12.5)% ($p<0.0001$ and $p=0.0001$)] in TA, GCA and HD, respectively. Among Tfh subpopulations, Tfh-17, CXCR5+ CCR6+ CXCR3- CD4+, cells were specifically increased in TA.

Functionally, CXCR5+ CD4+ T cells of TA patients helped B cells to differentiate into memory cells, to proliferate and to secrete type G immunoglobulins.

We sequenced the TCR repertoire α/β in CD3+CD4+CXCR5- and CD3 +CD4+CXCR5+ cells, in aortic and blood samples from 2 patients. In both patients, we identified oligoclonal profile of TCR repertoire only for aortic CXCR5+ cells, suggesting antigenic selection of CXCR5+ CD4+ T cells.

Conclusion: We provide evidence of the presence of tertiary lymphoid structures composed of Tfh and B cells in TA aorta. We identified a specific Tfh signature in circulating CD4+ T cells that distinguishes TA and GCA patients. The key cooperation of Tfh and B cells in TA and the oligoclonal repertoire of CXCR5+ CD4+ T cells strongly suggest the role of antigenic trigger.

Disclosure of Interests: : Anne-Claire DESBOIS Speakers bureau: SOBI en 2015, Anna Maciejewski-Duval: None declared, Paul Régnier: None declared, Valentin QUINIOU: None declared, Cloé Comarmond: None declared, Hélène Vallet: None declared, Patrick Bruneval: None declared, Pierre Fouret: None declared, Michele Rosenzwajg: None declared, David Klatzmann: None declared, Fabien Koskas: None declared, Marlène Garrido: None declared, Guillaume Darrasse-Jèze: None declared, Patrice cacoub Consultant for: d'Abbvie, Astra Zeneca, Bayer, Boehringer Ingelheim, Gilead, Glaxo Smith Kline, Janssen, Merck Sharp Dohme, Pfizer, Roche, Servier, and Vifor., Speakers bureau: d'Abbvie, Astra Zeneca, Bayer, Boehringer Ingelheim, Gilead, Glaxo Smith Kline, Janssen, Merck Sharp Dohme, Pfizer, Roche, Servier, and Vifor., David Saadoun Grant/ research support from: Roche, Abbvie, Consultant for: Janssen, Celgene, Abbvie, Roche

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SAT0223 FACTORS ASSOCIATED WITH DAMAGE PROGRESSION IN BEHÇET'S SYNDROME UVEITIS

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Background: Uveitis in Behçet's syndrome (BS) follows a recurrent disease course with inflammatory exacerbations causing damage in the uvea, retina and optic nerve even with treatment. Frequent attacks and posterior involvement are considered as predictors of poor visual outcome.

Objectives: The aim of this study is to delineate the predictors of damage in more detail using a standard screening method among a group of BS patients with long term regular follow-up.

Methods: Patients with uveitis who were registered in our multidisciplinary BS clinic between 1990 and 2008 were screened. Among these, 50 patients who were followed for at least 10 years, who were regularly seen in our clinic at least once in every 4 months, who did not have > Grade 2 damage at baseline, and who represented different levels of damage severity during the last visit (between Grade 0 and 5) were selected. The damage severity was graded according to a validated damage grading instrument (5=worst) specifically developed for BS uveitis (Ozyazgan et al. in preparation). One patient was later excluded because it was realized that he did not fulfill these criteria. A standard form was used for retrieving data on demographics, baseline and final visual acuities, number and localization (anterior/posterior/panuveitis) of attacks during follow-up, presence of retinal infiltration, retinal hemorrhage and hypopyon uveitis. Candidate factors for damage progression were compared between patients who had a progression in damage score and those who did not.

Results: 98 eyes of 49 patients (M:F 35:14, mean age at baseline 27±8 years, mean follow-up duration 20.9±5.5 years, mean number of visits 76.5±35.2) were evaluated. The mean visual acuity was 0.02±0.08 at baseline and 0.47±0.52 at the final visit. The mean number of attacks was 13.2±9.4. Damage grades at baseline were Grade 0 in 79, Grade 1 in 16 and Grade 2 in 3 eyes. Damage grades at final visit were Grade 0 in 15, Grade 1 in 21, Grade 2 in 32, Grade 3 in 12, Grade 4 in 10 and Grade 5 in 8 eyes. There was damage progression in 81/98 eyes at the final visit. Isolated anterior uveitis attacks were not associated with progression of damage (2.5±2.9 vs 2.8±5.5, $p=0.7$). Parameters that were significantly more frequent among patients with damage progression were: number of attacks (14.5±10.8 vs 23.3±12.3; $p=0.008$), number of posterior attacks (0.4±1.2 vs 6.5±4.9, $p<0.001$), number of panuveitis attacks (0.8 ±1.3 vs 6.6±5.0, $p<0.001$), number of attacks with severe vitrous opacity preventing examination of the retina (0 vs 3.2±3.8, $p<0.001$), retinal infiltration (0.2±0.4 vs 1.4±1.9, $p<0.001$) and retinal hemorrhages in the arcuate region (0.1±0.2 vs 0.7±1.4, $p<0.001$), and the number of hypopyon attacks (0.2±1.0 vs 0.9±1.3, $p=0.019$)

Conclusion: This study confirmed that the anterior uveitis attacks are not associated with progressive damage in BS, whereas posterior and panuveitis attacks, attacks causing severe vitreous opacity, retinal infiltrates and hemorrhage in the arcuate region and hypopyon attacks are important predictors of damage. Patients showing these features should be treated more aggressively.

REFERENCE

[1] Ozyazgan, Yilmaz, et al. "Ocular involvement of Behçet's syndrome: a comprehensive review." Clinical reviews in allergy & immunology 49.3 (2015): 298-306.

Disclosure of Interests: Yilmaz Ozyazgan Speakers bureau: ABBVIE, Didar Ucar: None declared, Mustafa Erdogan: None declared, Yesim Ozguler: None declared, Gulen Hatemi Consultant for: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Sebahattin Yurdakul: None declared, Vedat Hamuryudan Consultant for: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Izzet Fresko: None declared, Melike Melikoglu: None declared, Emire Seyahi: None declared, Serdal Ugurlu: None declared, Hasan Yazici: None declared

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SAT0224 PRESENTATION, MANAGEMENT AND OUTCOME OF ANCA ASSOCIATED VASCULITIDES IN ITALY: A 20-YEAR FOLLOW-UP STUDY

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Background: ANCA associated vasculitis (AAV) are systemic diseases with a wide spectrum of clinical presentation and organ involvement.
Objectives: To analyze presentation, management and 5 years-outcomes of AAV patients diagnosed between 2000 and 2018 in the monocentric cohort of Padova Vasculitis Center.
Methods: We retrospectively collected all AAV patients diagnosed between 2000 and 2018 and followed in the Vasculitis Center of Padova University. We focused on demographic and clinical features at baseline, first line immunosuppressive (IS) treatment, 6 months mortality, 5 years-relapse rate and survival rate and. In the analysis, we kept separate eosinophilic granulomatosis with polyangiitis (EGPA) from granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).
Results: We identified 171 patients (F/M 93/78) with AAV diagnosed since 2000 (61 between 2000-2010 and 110 between 2011-2018,% of increased in diagnosis rate +183%): 82 (48%) were GPA, 28 (16%) MPA and 61 (36%) EGPA. The patients were mostly Caucasian (98%), with a mean age at diagnosis of 58.4±16.1 years, slightly younger if diagnosed in the second decade (2010-2018) than in first decade (2000-2010) (59.5 ±16.6 years vs 61.6±14.7 years, p=0.049). ANCA were tested in 163 patients: 23% ANCA negative, 37% cANCA/PR3, 39% pANCA/MPO and 1% double positive.
GPA/MPA patients were mostly ANCA positive at diagnosis (96/110 patients), in particular we counted 12 (15%) GPA-ANCA negative patients, 55 (68%) GPA-PR3, 13 (16%) GPA-MPO, 1 GPA with double positivity while MPA resulted only ANCA positive, 22 (82%) MPA-MPO and 5 (19%) MPA-PR3. In EGPA group, only 28/54 presented with ANCA positivity, all p-ANCA/MPO specificity.
Disease severity at diagnosis was assessed only in GPA/MPA patients: 12/101 limited disease, 34 early systemic, 29 generalized and 26 severe. In particular, GPA/MPA more frequently presented with systemic symptoms (76%), ENT and lung involvement (respectively 62% and 66%). Renal vasculitis was reported in 65% of patients with a mean eGFR of 50.2±39.8 ml/min. Moreover, we registered 17 alveolar haemorrhages, 4 cardiac involvement and 3 gastrointestinal (GI) disease.
EGPA patients, instead, presented more frequently with ENT (85%) and lung involvement (96%) (mostly uncontrolled asthma and pulmonary infiltrates). 31 (54%) EGPA presented nerve involvement (4 with CNS involvement) and 9 (16%) with cardiac involvement. Interestingly, no renal or GI vasculitis was reported.
The first line IS treatment administered was: cyclophosphamide (CYC) in 66 (38%), rituximab (RTX) in 14 (8%), azathioprine (AZA) in 27 (16%), methotrexate (MTX) in 25 (14%) and mycophenolate (MMF) in only 5 (3%).
Mortality rate at 6 months in all cohort resulted of 1.2% (2 event), while the 5-years survival calculated with Kaplan Meier method was 94.3% (8 events). All deaths occurred in the GPA/MPA group. A relapse occurred in 36% of patients, with a significant higher frequency in GPA/MPA than in EGPA (46.3% vs 17%, p=0.017).
Conclusion: Our cohort is characterized by significant higher rate of AAV diagnosis in the last decade and this could reflect the increasing incidence and prevalence reported in literature[1]. Interestingly, GPA diagnosis, especially with cANCA/PR3 specificity, was prevalent in our cohort despite some authors reported an higher prevalence of MPA in Mediterrean area[1-2]. Finally, EGPA confirmed a better outcome at last follow up than GPA and MPA, but we noted that no renal and GI involvement was observed in our EGPA patients.

REFERENCE

[1] Berti A, Dejaco C. Update on the epidemiology, risk factors, and outcomes of systemic vasculitides. Best Pract Res Clin Rheumatol. 2018;32(2):271-294.
[2] Romero-Gómez C, et al. Epidemiological study of primary systemic vasculitides among adults in southern Spain and review of the main epidemiological studies. Clin Exp Rheumatol. 2015;33(2 Suppl 89):S-11-8

Disclosure of Interests: None declared

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SAT0225 TARGETED SERUM METABOLIC PROFILE IN PATIENTS WITH TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) is a chronic inflammatory arteritis that mainly affects aorta and, its major branches. Often the course is unpredictable and it remains a challenge to assess disease activity despite the availability of acute phase reactants and imaging modalities [1]. Management heavily relies on physician global assessment. Analysis of serum metabolites using nuclear magnetic resonance spectroscopy is a promising exploratory approach towards identifying new biomarkers in TAK which may cast some light on disease pathogenesis and disease activity.
Objectives: Aim of the study was to evaluate the performance of serum amino acids as determinants of disease activity in TAK.
Methods: Patients with TAK fulfilling ACR 1990 criteria were enrolled and disease activity assessed using ITAS2010 and ITAS-A[2]. Samples were analysed using 1D 1H 800 MHz Nuclear magnetic resonance spectrometer equipped with a Cryoprobe (at 300 K). The spectra were processed and the concentration of amino acids were measured with respect to internal reference metabolite formate assuming its concentration 10 μM in commercial software program CHENOMX (www.chenomx.com) and the resulted normalized values were compared using Tukey's multiple comparison test and diagnostic potential was evaluated using receiver operating characteristic (ROC) curve analysis.
Results: 45 active TAK patients with ITAS-A $\geq$ 4 and 53 inactive TA patients with median age 27 years [IQR, 22-35 and IQR, 23-37 years respectively] were enrolled. Female to male (F:M) ratio was 3.5:1 and 4.9:1 and median duration of illness 5 [IQR, 2-9 years] and 3 [IQR, 1-6 years] years in active and inactive group respectively. Majority had class V disease. 43 individuals served as health control(HC) with mean age 30 years and F:M ratio of 4.3:1. Serum levels of Phenylalanine (Phe), Tyrosine (Tyr), Histidine (His), Valine (Val) and Alanine (Ala) were found to be decreased in TAK patients suggesting augmented utilization in the immune-metabolic pathways mainly to replenish the energy demand and self-repair mechanism under conditions of inflammation and oxidative stress. An analysis of amino acids ratio revealed significantly higher His/Tyr, Ala/Tyr and Val/Tyr ratio in HC when compared to active TAK patients. Ratio were lower in active TAK when compared to inactive TAK patients but only Val/Tyr ratio was significant (AUROC, 0.64 and p, 0.01). Ratio served as a gradient with lowest value in active disease and gradually increasing and moving towards HC as disease was getting controlled

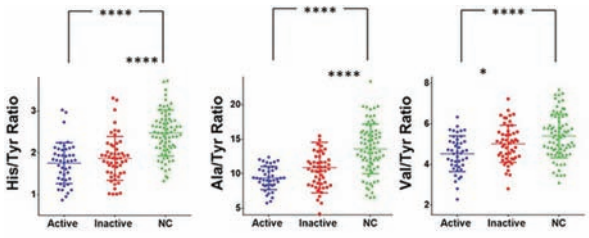


Figure 1: Comparison of various amino acid ratio in active and inactive TAK patient with respect to healthy control. Ratio served as a gradient with lowest in active disease and gradually moving towards HC as disease was getting controlled.
*significant p value; Ala, alanine; His, Histidine; NC, Normal healthy control; Tyr, tyrosine; Val, Valine

Conclusion: The present targeted NMR based metabolomics study demonstrated that the serum metabolic profiles of amino acid may help guide therapy and ratio of Val/Tyr can differentiate active from inactive patients. However, future studies on large patient cohorts are required to establish its clinical utility.

REFERENCES

[1] Nakagomi D, Jayne D. Outcome assessment in Takayasu arteritis. Rheumatol. (United Kingdom) 2016;55:1159–71.
[2] Misra R, Danda D, Rajappa SM, Ghosh A, Gupta R, Mahendranath KM, et al. Development and initial validation of the Indian Takayasu Clinical Activity Score (ITAS2010). Rheumatol. (United Kingdom) 2013;52:1795–801.

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SAT0226 INFLIXIMAB FOR THE TREATMENT OF REFRACTORY POLYARTERITIS NODOSA

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Background: Polyarteritis Nodosa (PAN) is a necrotizing vasculitis predominantly affecting medium and small size arteries (1). Cyclophosphamide, a drug with narrow therapeutic range and poor safety profile, constitutes the treatment of choice for PAN vasculitis with major organ involvement. (2)
Objectives: To describe our clinical experience in treating refractory PAN with infliximab (a TNF inhibitor), a drug with good tolerability and better safety profile than cyclophosphamide.
Methods: Twenty-six PAN patients were admitted to our rheumatology unit between 2006 and 2017, of whom 9 patients, with severe and refractory disease, were treated with infliximab after failure of standard treatment.
We describe herein the patients' characteristics, clinical manifestations, severity and response to infliximab treatment and review the current literature.
Results: Complete remission was defined as the absence of features of active disease and withdrawal of prednisone therapy. Significant improvement was defined as clinical improvement and prednisone dose reduction of at least 50% or a 50% reduction in immune modulatory medications other than prednisone.
After 4 months of treatment, 8/9 (89%) patients achieved significant improvement, with two of them achieving complete remission.
Conclusion: We suggest anti TNF agents, and in particular infliximab, are relatively safe and efficacious treatment options in refractory PAN
A randomized controlled trial should be done in order to objectively evaluate infliximab in PAN.

REFERENCES

[1] Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013; 65:1-11.
[2] De Virgilio A, Greco A, Magliulo G, Gallo A, Ruoppolo G, Conte M, Martellucci S, de Vincentiis M. Polyarteritis nodosa: A contemporary overview. Autoimmun Rev. 2016; 15:564-70.

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SAT0227 MYOCARDIAL FIBROSIS IS ASSOCIATED WITH ANCA STATUS, ORGAN INVOLVEMENT AND DISEASE SEVERITY IN PATIENTSWITH GRANULOMATOSIS WITH POLYANGIITIS

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Background: Granulomatosis with polyangiitis (GPA) is a systemic vasculitis with an increased burden of cardiovascular (CV) events compared to the general population, but the prevalence of primary cardiac involvement in this disease is unknown.
Objectives: The objective of this prospective study was to describe with cardiac magnetic resonance (CMR) the myocardial abnormalities associated with GPA and their correlations with disease characteristics.
Methods: Twenty-six patients with GPA and no prior CV disease (CVD) or diabetes mellitus underwent contrast-enhanced CMR, including late gadolinium-enhancement (LGE), T1 mapping for native T1 and extra-cellular volume (ECV) quantification for assessment of myocardial fibrosis and tissue tagging for assessment of left ventricular (LV) function. Characteristics of disease, treatments and CV risk factors were collected; disease relapse was defined as reappearance or worsening of vasculitis symptoms requiring an increase of the current treatment or introduction of additional immunosuppressive medication. Twenty-five healthy volunteers (HV) with comparable age, sex, BMI and arterial blood pressure served as controls.
Results: Patients with GPA (median age 58 years, disease duration 8 years, BVAS 2; females 46%, PR3 ANCA 58%) had similar cardiovascular risk profile to HV. A focal, non-ischemic LGE pattern of fibrosis was detected in 24% of patients and no controls (p=0.010; Table 1). Patients with myocardial LGE were more frequently PR3 ANCA negative (93% vs 7%, p=0.007), and they presented more frequently with involvement of the lower respiratory tract (75% vs 25%, p=0.097) and skin (63% vs 38%, p=0.087). Values of LGE-related fibrotic mass were higher in patients presenting with renal involvement (p=0.036). Native T1 and ECV were higher in patients with GPA than HV (Table 1); ECV was higher in those with relapsing disease, and native T1 was inversely associated with PR3 ANCA (β=-0.664, p=0.001). Peak systolic strain was slightly reduced in GPA than controls (Table 1); LV ejection function (LVEF) was inversely correlated with disease duration (β=-0.454, p=0.026).

Table 1. CMR measures†

LV volumes and mass			
LV end diastolic volume index, mL/m^2	69 (61, 84)	79 (70, 89)	0.105
LV end systolic volume index, mL/m^2	28 (23, 37)	32 (28, 39)	0.122
LV mass index, g/m^2	37 (42, 47)	50 (42, 56)	0.014
LV mass/LV end diastolic volume, g/mL	0.59 (0.48, 0.66)	0.59 (0.54, 0.66)	0.486
LV function			
LV ejection fraction,%	59 (56, 63)	58 (53, 62)	0.351
LV peak systolic strain			
Base	-0.19 (-0.21, -0.16)	-0.21 (-0.22, -0.19)	0.017
Mid	-0.21 (-0.23, -0.20)	-0.22 (-0.23, -0.20)	0.298
Apex	-0.21 (-0.23, -0.16)	-0.23 (-0.25, -0.20)	0.101
Torsion, deg	12.3 (9.2, 14.5)	13.8 (11.6, 16.0)	0.086
Peak twist	14.1 (9.0, 15.7)	14.1 (11.7, 17.7)	0.222
Myocardial tissue characterization			
Native T1 (ms)	1225 (1199, 1255)	1203 (1185, 1233)	0.006
Extracellular volume,%	25.0 (23.3, 27.2)	23.6 (20.5, 25.1)	0.009
LGE, n (%)	6/25 (24)	0/25 (0)	0.010
LGE scar tissue, g	1.25 (0.81, 2.63)	0 (0, 0)	NA

†*Continuous data are presented as median (interquartile range).*

Conclusion: Patients with GPA had significant myocardial abnormalities on CMR compared to HV. ANCA status, systemic organ involvement and disease severity were associated with CMR markers of myocardial fibrosis. CMR could be a useful tool for identification and future risk stratification of myocardial involvement of GPA.
Disclosure of Interests: : Alessandro Giollo: None declared, Raluca-Bianca Dumitru: None declared, Peter Swoboda: None declared, Sven Plein : None declared, John Greenwood: None declared, Maya Buch Grant/ research support from: Pfizer LTD, UCB, Consultant for: AbbVie, Eli Lilly, EMD Serono, Pfizer Ltd., Sanofi, Jacqueline Andrews: None declared
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SAT0228 LEUKOCYTE DYNAMICS IN GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA PATIENTS BEFORE, DURING AND AFTER TREATMENT

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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are inflammatory diseases requiring long-term treatment with

glucocorticoids. Currently, only limited data on dynamics of peripheral leukocytes and leukocyte subset composition before, during and after treatment is available.

Objectives: To gain insight into the dynamics of leukocytes during the entire disease course and to determine whether patients in treatment-free remission resemble healthy controls.

Methods: Newly-diagnosed, treatment-naive GCA (N=42) and PMR (N=31) patients were prospectively followed for up to 7 years. Absolute numbers of leukocyte subpopulation, both myeloid (neutrophils, monocytes) and lymphoid (CD4 and CD8 T-cells, B-cells and NK-cells) were measured at fixed time points. Laboratory inflammation markers (CRP, ESR, platelets and haemoglobin) were assessed as well. Values were compared with age-matched healthy controls (N=51) and infection controls (N=13). A stable treatment-free remission group for at least 6 months was defined.

Results: Neutrophil and monocyte numbers were higher in baseline GCA and PMR patients compared to healthy controls, whilst NK-cell numbers were reduced. In baseline GCA patients, CRP correlated positively with monocyte numbers. In baseline PMR patients, B-cell numbers were lowered and B-cell and NK-cell numbers correlated negatively with CRP. During glucocorticoid treatment, fluctuations in numbers of all leukocyte subsets were observed but neutrophil and monocyte numbers remained elevated and NK-cells numbers remained lowered during the entire treatment period (fig. 1). CRP and ESR were reduced by GC treatment and only moderately elevated during relapses. GCA patients in treatment-free remission still had elevated neutrophil and monocyte numbers. In addition, ESR and platelet numbers, were elevated whilst haemoglobin was lowered. PMR patients in treatment-free remission still had elevated monocytes while NK-cell and CD8+ T-cell numbers were decreased. Inflammatory markers and haemoglobin was normal.

Conclusion: In baseline GCA and PMR patients a shift towards the myeloid lineage is observed. This myeloid bias persisted in spite of GC treatment and also in treatment-free remission, suggesting a long-term effect of inflammation (an inflammatory imprint) on the peripheral blood compartment. Only GCA patients showed persistently elevated inflammatory markers; whether this reflects ongoing subclinical disease remains to be investigated.

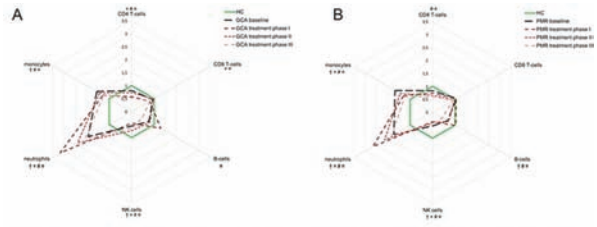


Figure 1. Dynamics in leukocyte subset numbers during follow-up in GCA (A)and PMR (B) patients. Numbers at baseline (GCA n=42, PMR n=31), treatment phase I (GCA n=38, 69 samples; PMR n=25, 54 samples), phase II (GCA n=32, 43 samples; PMR n=23, 33 samples) and phase III (GCA n=29, 65 samples; PMR n=19, 56 samples) are expressed as median fold-change compared to healthy controls (n=51). †: sign difference between HC and baseline, ×: sign difference between HC and treatment phase I, #: significant differences between HC and phase II and ¤: significant differences between HC and phase III (Mann-Whitney U test, P<0.05).

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SAT0229 INTESTINAL PERMEABILITY IN IGA-VASCULITIS IN ADULTS

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Background: Primary IgA-vasculitis and inflammatory bowel diseases (IBD) share many clinical signs, such as abdominal syndrome, skin purpura and IgA-nephropathy. It may indicate a common pathogenetic background for both pathological conditions. One of the hypotheses to explain a common IgA abnormalities and clinical similarities between two conditions is rupture of intestinal barrier resulting in defective antigen exclusion at mucosal level and increased antigen absorption into systemic circulation. While increased intestinal permeability has been well established in IBD there are few reports addressing this issue in IgA-vasculitis.

Objectives: Evaluation of small intestinal permeability in IgA-vasculitis. We have also looked for correlation between this parameter and clinical activity of the disease.

Methods: Intestinal permeability was assessed in 34 adult patients having primary IgA-vasculitis. EULAR/PRINTO/PRES criteria [1] were used for making of diagnosis after thorough laboratory and instrumental screening aiming to exclude a secondary nature of disease, including upper and lower endoscopy. Skin purpura was present in all patients being mandatory diagnostic criterion. Arthritis/arthralgia were seen in 20 patients (58%). There were no patients with evident abdominal damage just before and during investigation, although 15 (44%) patients had transient abdominal pain in the history. Mild to moderate signs of renal involvement (hematuria and/or proteinuria) were seen in 16 (47%) patients without renal impairment.

We have evaluated the gut permeability using ovalbumin (OVA) which has been measured in serum 3 hours after fasting oral intake of the two raw chicken eggs. The level of OVA in serum was measured using bivalent solid-phase immune-enzyme assay ("Sandwich-ELISA"). An increase of OVA in serum above 4 ng/ml was considered as the evidence of increased intestinal permeability.

Results: Totally, intestinal permeability to OVA was found to be increased in 20 of 34 patients (59%). In seventeen of twenty patients (85%) with increased intestinal permeability there were clinical sings of disease activity (skin purpura and/or arthritis and/or urinary abnormalities).

To find out which pattern of clinical activity is best associated with increased intestinal permeability we have separately analyzed the level of OVA in patients with skin purpura, arthritis and urinary abnormalities correspondingly during remission and exacerbation of the process.

Statistically significant difference ($p<0,05$) of OVA level was found only in patients selected on the basis of skin purpura activity: at the moment of clinically evident skin purpura the median OVA level was much higher (50 ng/ml) than during periods with no skin purpura (5 ng/ml).

The difference between the rate of increased intestinal permeability in patients with and without abdominal syndrome in the history was not statistically significant ($p=0.87$).

Conclusion: Results of our study may indicate a subclinical abdominal involvement in considerable part of patients with IgA-vasculitis, characterized with transient episodes of increased intestinal permeability. This phenomenon is chronologically related to disease activity, particularly to flare-up of the skin purpura. It could be speculated that this transient increase of intestinal permeability may result from mucosal inflammation which needs to be clarified in further investigations.

REFERENCE

[1] Ozen Set al., EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. Ann Rheum Dis. 2010 May;69(5):798-806.

Disclosure of Interests: None declared

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SAT0230 GIANT CELL ARTERITIS WITH INTRACRANIAL VASCULITIS: A CASE SERIES

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Background: Giant cell arteritis (GCA) is a large vessel vasculitis that primarily affects the aorta and its branches. Extracranial branches of the carotid artery are frequently affected; however, intracranial involvement in GCA is rare [1].

Objectives: To determine the clinical features and outcome of patients with intracranial giant cell arteritis (IC-GCA).

Methods: A retrospective medical record review was performed to identify all patients with IC-GCA from 1/1996 through 5/2018. Demographic, clinical, laboratory, radiographic, and treatment data at baseline and subsequent follow-up visits were collected. Data was summarized using descriptive statistics.

Results: The study cohort included 9 patients with IC-GCA (78% male, mean [±SD] age 72.1 [±7.9] years). 8 of 9 patients had positive temporal artery biopsies. One patient with negative biopsy had evidence of large-vessel GCA on thoracic CT angiography.

The mean time from onset of GCA to intracranial involvement was 17 months (±38). All patients had neurologic symptoms, 33% (n:3) had a stroke and 22% (n:2) had a transient ischemic attack.
IC-GCA was diagnosed by cranial imaging in 8 patients and by autopsy in one. Cranial imaging modalities used included magnetic resonance angiography (n=8), CT angiography (n=2) and cerebral angiography (n=2). Intracranial vasculitis most commonly affected the internal carotid artery 78% (N=7) followed by the, vertebral artery 56% (n=5), posterior cerebral artery 56% (n=5), middle cerebral artery 44% (n=4), anterior cerebral artery 33% (n=3) and posterior inferior cerebral artery 11% (n=1). Stenosis was present in 89%, occlusion in 33%, dilatation in 11%, and wall thickening in 11%.
All patients received glucocorticoids. For treatment of intracranial disease, additional agents included: cyclophosphamide (67%), Tocilizumab (22%). Despite treatment, outcomes for patients with IC-GCA were poor. Five of nine patients died during a mean length of follow-up of 2.4 months.
Conclusion: Although rare, IC-GCA is associated with significant morbidity and mortality. It occurs predominantly in men, presenting with ischemic cerebrovascular events. Current treatment strategies appear to be of limited efficacy for IC-GCA.

REFERENCE

[1] Salvarani C, Giannini C, Miller DV, Hunder G. Giant cell arteritis: Involvement of intracranial arteries. Arthritis Rheum. 2006;55(6):985-9.

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SAT0231 AGE AND THE CLINICAL FEATURES OF ADULT IGA VASCULITIS

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Background: IgA vasculitis (IgAV) is a common vasculitis of adult population, yet the disease in adults is still poorly defined.
Objectives: The aim of our study was to evaluate the potential influence of age on the presentation of adult IgAV.
Methods: We analyzed medical records of adult, histologically proven IgAV cases, diagnosed and followed at our secondary/tertiary rheumatology center between January 2010 and December 2018. We stratified IgAV cases into four groups, based on the patient age at presentation (18-39, 40-59, 60-79 and ≥80 years). The clinical features were compared between the groups.
Results: During the 108-month observation period we identified 265 new IgAV cases (60.0% males, median (IQR) age 64 (45–77) years). Skin, joint, gastrointestinal tract (GIT) and renal involvement developed in 265, 103 (38.9%), 80 (30.2%), and 118 (44.5%) cases, respectively. Younger adults (≤40 years) more frequently reported an infection prior to IgAV, and developed arthritis or GIT involvement. Severe renal involvement was less common under the age of 40 years. The incidence of skin limited IgAV and of necrotic purpura increased with patient age. Follow-up data were available for 189 patients. During a median (IQR) follow-up of 12 (6–24) months, 29 (15.3%) patients relapsed. Relapsing disease was more frequent in younger adults (≤40 years), compared to older ones. Data on age related variations in the clinical presentation of IgAV are presented in Table 1.
Conclusion: We found subtle age related differences in the presentation and during follow up of adult IgAV.
Disclosure of Interests: : None declared
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Table 1. Age and clinical features of adult IgAV

Clinical characteristics	*Age interval*			
Age (years)	18-39	40-59	60-79	≥80
Number of cases	49	69	96	51
Male gender (%)	63.3	68.1	62.5	41.2
Prior infection (%)	57.1	36.2	28.1	21.6
Generalized purpura (%)	49.0	52.2	50.0	45.1
Skin necroses (%)	14.3	43.5	55.2	62.7
Skin limited IgAV	16.3	18.8	35.4	41.2
Joint involvement (%)	63.3	49.3	30.2	17.6
Arthritis (%)	28.6	14.5	14.6	2.0
GIT involvement (%)	42.9	34.8	21.9	27.5
Severe GIT involv. (%)	14.3	7.2	7.3	2.0
Renal involvement (%)	36.7	43.5	50.0	43.1
Severe renal involv. (%)	2.0	15.9	14.6	11.8
Elevated serum IgA	22.6	45.6	56.5	48.6
Relapses (% and number)	25.0 (9/36)	13.2 (7/53)	18.6 (13/70)	0 (0/30)

Legend: Generalized purpura: purpura extending above the waistline; GIT: gastrointestinal tract; severe GIT involvement: bloody diarrhea or ileus or bowel perforation; severe renal involvement: nephritic syndrome with acute renal failure or nephrotic syndrome;

SAT0232 DISTRIBUTION OF MACROPHAGE SUBSETS IN TEMPORAL ARTERY BIOPSIES OF PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a granulomatous vasculitis characterized by recruitment of T-cells and monocytes to the vessel wall. Upon recruitment, monocytes are activated and differentiate into macrophages. These lesional macrophages take on different phenotypes depending on cues from the microenvironment. These macrophages are known to produce pro-inflammatory cytokines, chemokines, matrix-metalloproteinases (MMPs), and growth factors contributing to amplification of the inflammatory response, vessel wall injury and remodeling. However, current knowledge regarding macrophage subsets in GCA lesions is limited.
Objectives: To examine the distribution of macrophage subsets in GCA lesions.
Methods: Immunohistochemistry was performed on consecutive sections of paraffin-embedded temporal arteries of biopsy-confirmed GCA patients (n = 11) with antibodies to selected markers of inflammation and tissue remodeling (Table 1). Positive cells were scored in three layers of the vessel wall (adventitia, media-intima, inner-intima) using a semi-quantitative scoring system. Expression by macrophages was confirmed by double staining with the macrophage transcription factor PU.1.

Table 1. Immunohistochemistry panel. AB019

Pro-inflammatory	Tissue remodeling
IL-6	CD206 (MR)
IL-1β	IL-10
IL-12	FR-β
IL-23	MMP-12
CD64	MMP-9
	MMP-2

Results: The pro-inflammatory marker CD64 and pro-inflammatory cytokines (IL-12, IL-23 and IL-1β) were strongly expressed by macrophages throughout the vessel wall, most prominently in the adventitia. However, subsets of these CD64+ macrophages also showed concomitant expression of the tissue remodelling markers CD206 and FR-β in specific compartments of the lesions. More specifically, CD206+ macrophages were mainly found along the media borders which co-localized with positive MMP-9 staining. Interestingly, FR-β positivity was also found in the inner-intima of TABs with a high degree of intimal hyperplasia. FR-β expression was significantly higher in the inner-intima region in TABs with

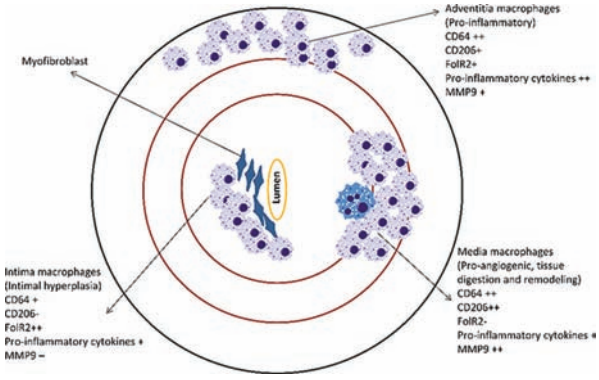


Figure 1. Spatial distribution of macrophage subsets in temporal artery of GCA affected vessel.

massive intimal hyperplasia compared to TABs with mild intimal hyperplasia (p = 0.01).

Conclusion: Based on the expression of markers of inflammation and tissue remodeling, different subsets of infiltrating macrophages can be distinguished. Macrophages in vascular lesions of GCA patients display a distinct spatial distribution pattern within the inflamed vessel wall (Figure 1). Adventitial macrophages express highest level of pro-inflammatory cytokines indicating pro-inflammatory functions of these macrophages. Co-localization of CD206 and MMP-9 along media borders indicates a role for CD206+ macrophages in collagen digestion and angiogenesis. Additionally, the association of increased numbers of FR-β+ macrophages with extensive intimal hyperplasia suggests that FR-β+ macrophages promote myofibroblast proliferation.

REFERENCE

[1] Watanabe R, Maeda T, Zhang H, Berry GJ, Zeisbrich M, Brockett R, Greenstein AE, Tian L, Goronzy JJ, Weyand CM. MMP (Matrix Metalloprotease)-9-Producing Monocytes Enable T Cells to Invade the Vessel Wall and Cause Vasculitis. Circ Res. 2018 Aug 31;123(6):700-715.

Disclosure of Interests: William Febry Jiemy: None declared, Yannick van Sleen: None declared, Annemieke Boots Grant/research support from: grant from MSD in 2010-2015, Consultant for: I was a consultant for Grunenthal Germany 2016-2017, Employee of: I was an employee of Organon, Shering-Plough and MSD from 1991-2011, Riemer Slart: None declared, Peter Heeringa: None declared, Elisabeth Brouwer Speakers bureau: Dr. Brouwer as an employee of the UMCG received speaker fees and consulting fees from Roche which were paid to the UMCG

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SAT0233 VALIDATION OF A NOVEL DISEASE CLASSIFICATION IN HACETTEPE TAKAYASU ARTERITIS COHORT

Ertuğrul Çağri Bölek, Selcan Demir, Alper Sari, Ummusen Kaya Akca, Levent Kiliç, Ali Akdoğan, Sedat Kiraz, Omer Karadag, Seza Özen, Hacettepe University Vasculitis Center (HUVAC). *Hacettepe University Vasculitis Center, Ankara, Turkey*

Background: Takayasu Arteritis (TAK) is a rare idiopathic granulomatous large vessel vasculitis and it is a clinically heterogenous disease. Various classifications and subsets which based on distribution of arterial lesions were defined in the literature in order to exhibit and predict different disease courses.

Objectives: We aimed to validate a new disease subsets developed by Goel et al in our TAK series (1).

Methods: We retrospectively evaluated the medical records of 164 TAK patients followed at Department of Rheumatology and Department of Pediatric Rheumatology in Hacettepe University, Ankara, Turkey between August 2005 and October 2018. The pediatric-onset (< 18 years of age at disease diagnosis) and adult-onset patients fulfilled the Ankara 2008 and the American College of Rheumatology (ACR) 1990 criteria for TAK, respectively. All patients were assigned to three clusters (Cluster 1: Abdominal Predominant, Cluster 2: Aortic Arch Predominant, Cluster 3: Focal Disease) using a decision tree defined in the original study (1). Demographics, clinical and laboratory features, treatment regimens were compared between in three groups.

Results: There were forty-two (25.6%), sixty-three (38.4%) and fifty-nine (36%) patients in Cluster 1, 2 and 3, respectively. Demographic and clinical data was summarized in Table-1. Cluster 1 included approximately half of patients (45.8%) with pediatric-onset TAK (p= 0.048). Baseline acute phase reactants (Erithrocyte Sedimentation Rate:ESR and C-reactive protein:CRP) and age at disease diagnosis were slightly lower in Cluster 1, however none of them did not reach statistical significance (p= 0.94, p=0.99 and 0.56, respectively). In contrast, cerebrovascular accident rates were slightly higher in Cluster 2 (p=0.24). Although anti-TNF biological agents were more frequently used for treatment in Cluster 1 (p=0.004), cyclophosphamide and/or overall biological agents usage was similar in three groups (p=0.15).

Conclusion: Decision tree which defined by Goel et al. was applied to our single center pediatric and adult TAK cohort. In contrast to original validation cohorts, there was no difference among three clusters of our cohort except pediatric-onset disease and anti-TNF usage. Dissimilarities among the cohorts in terms of new classification system may be caused either number of patients or ethnic/regional differences.

REFERENCE

[1] Goel R, Gribbons KB, Maksimowicz-McKinnon K, Hoffman GS, Kumar S, Joseph G, et al., editors. Discovery and Validation of Novel Disease Subsets in 806 Patients with Takayasu's Arteritis across Four International Cohorts. ARTHRITIS & RHEUMATOLOGY; 2018: WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA.

Table 1. Demographics and Clinical Features of TAK Disease Clusters

	Cluster 1 (n=42) (Abdominal Predominant)	Cluster 2 (Aortic Arch Predominant) (n=63)	Cluster 3 (Focal Disease) (n=59)	p
Female, n (%)	37 (88.1)	58 (90.1)	53 (89.8)	0.791
Age at TA diagnosis, years, Mean ± SD	29.3 ± 15.5	32.0 ± 13.7	32.6 ± 13.8	0.56
Pediatric-Onset (< 18 years of age at disease diagnosis)	11 (26.1)	7 (11.1)	6 (10.2)	**0.048**
Median disease duration, years (IQR)	4.5 (5.1)	5.2 (6.8)	4.9 (6.9)	0.83
Median ESR at TA diagnosis, mm/h (IQR)	48.5 (59)	53.0 (59.0)	62.0 (49.0)	0.94
Median CRP at TA diagnosis, mg/dL (IQR)	2.4 (10)	3.8 (9.0)	3.6 (8)	0.99
Hypertension (HT) , n (%)	18 (42.9)	17 (27)	15 (25.4)	0.13
Serebrovasculary Accident (SVA) , n (%)	3 (7.1)	11 (17.5)	6 (10.2)	0.24
Death, n (%)	3 (7.1)	2 (3.2)	2 (3.4)	0.56
Methotrexate, n (%)	22 (52.4)	38 (60.3)	34 (57.6)	0.72
Azathiopurine, n (%)	16 (38.1)	18 (28.6)	19 (32.2)	0.59
Leflunomide, n (%)	4 (9.5)	5 (7.9)	2 (3.4)	0.42
Cyclophosphamide, n (%)	19 (45.2)	27 (42.9)	18 (30.5)	0.24
Interleukin-6 blockage, n (%)	9 (21.4)	14 (22.2)	10 (16.9)	0.75
TNF-α inhibitors, n (%)	13 (31.0)	7 (11.1)	5 (8.5)	**0.004**
Cyclophosphamide and/or biologics, n (%)	27 (64.3)	37 (58.7)	27 (45.8)	0.15
Endovascular intervention*,n (%)	8 (19)	3 (4.8)	7 (11.9)	0.069
Vascular surgery*, n (%)	4 (9.5)	10 (15.9)	4 (6.8)	0.26

Disclosure of Interests: Ertuğrul Çağri Bölek: None declared, Selcan Demir: None declared, Alper Sari: None declared, Ummusen Kaya Akca: None declared, Levent Kiliç: None declared, Ali Akdoğan: None declared, Sedat Kiraz: None declared, Omer Karadag: None declared, Seza Özen Consultant for: Seza Ozen is receiving consultancy fees from Novartis, Speakers bureau: Roche

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SAT0234 RNA SEQUENCING IDENTIFIES AN IGA VASCULITIS ASSOCIATED SERUM MICRORNA SIGNATURE, DISCRIMINATING PATIENTS WITH IGA VASCULITIS FROM AGE- AND SEX-MATCHED HEALTHY SUBJECTS

Alojzija Hocevar[1], [1,2]Katja Lakota, Thomas Grentzinger[3], Alexis Sarazin[3], Neža Brezovec[1], Tadeja Kuret[1,4], Oliver Distler[5], Sasa Cucnik[1,4], Olivier Voinnet[3], Snežna Sodin-Šemrl[1,2], Matija Tomšič[1,6], Mojca Frank-Bertoncelj[5]. *[1]University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia*; *[2]University of Primorska, FAMNIT, Koper, Slovenia*; *[3]Swiss Federal Institute of Technology (ETH Zurich), Zurich, Switzerland*; *[4]University of Ljubljana, Faculty of Pharmacy, Ljubljana, Slovenia*; *[5]University Hospital Zurich, Center of Experimental Rheumatology, Department of Rheumatology, Schlieren, Switzerland*; *[6]University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia*

Background: Immunoglobulin A vasculitis (IgAV) is a small vessel vasculitis with IgA deposits in the vessel wall, manifesting with skin purpura, arthralgia/arthritis, gastrointestinal (GI) and renal complications. Altered serum miRNA signatures can reflect disease-specific pathology, which makes serum miRNAs promising disease biomarkers. We have recently reported that miRNA expression is changed in the affected skin of IgAV patients. The profile of serum miRNAs in IgAV, however, remains unknown.

Objectives: To determine the serum miRNA signatures in adult patients with IgAV as compared with healthy controls (HC) and explore *in silico* their gene targets and pathways.

Methods: Small RNA were isolated from sera of IgAV patients with high disease activity (sera collected at the time of diagnosis) and from the age- and sex-matched HC (n=6 each). Small RNA libraries were sequenced with Illumina technology and reads were mapped onto human genome (GRCh38). One IgAV sample was omitted from analysis due to too low number of recovered miRNA reads. Unsupervised clustering was based on the expression of 150 miRNAs with the highest variance across samples. The miRror platform was used to predict gene targets of differentially expressed (DE) miRNAs with log2 fold change $\geq |1|$ and $p_{adj} < 0.01$. The STRING protein networks platform was used for pathway enrichment analysis of these genes.

Results: Unsupervised clustering of serum miRNA reads clearly distinguished between IgAV patients and HC (Figure 1). Among 1918 annotated miRNA (miRBase), 446 miRNAs were detected in serum samples and 88 miRNAs were identified as DE between IgAV patients and HC (log2 fold change $\geq |1|$, $p_{adj} < 0.05$). Specifically, 28 miRNAs were elevated in the serum of IgAV patients (e.g. miRNA-22, -146a, -185, -320a/

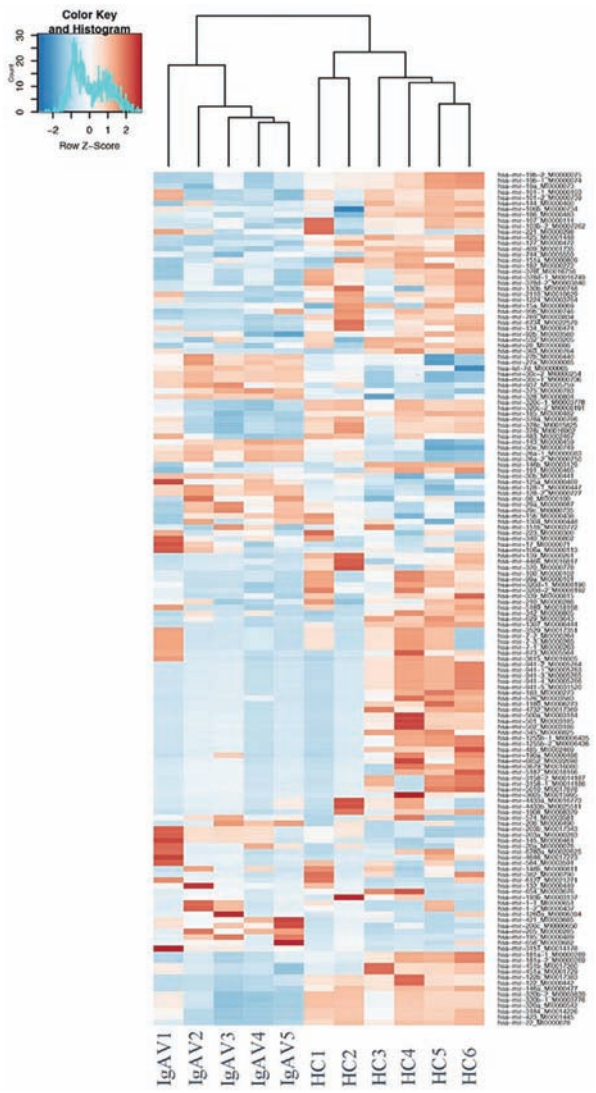


Figure 1. Heatmap based clustering analysis of serum miRNA expression

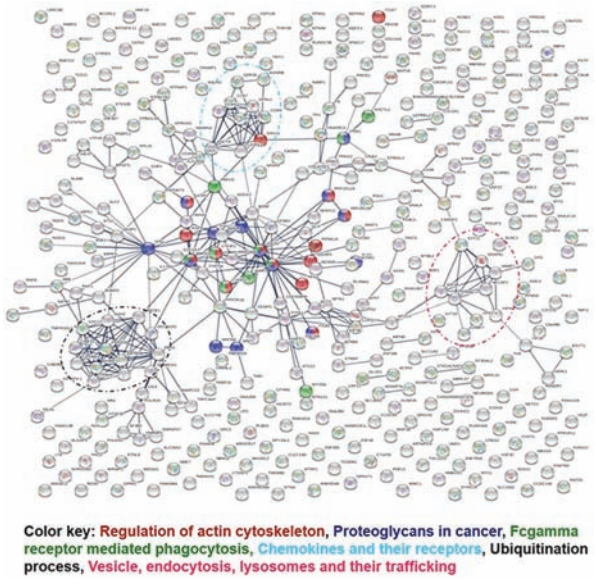


Figure 2. STRING Protein networks of gene targets of DE miRNAs

b/c, -378a, -423, -3184; $p_{adj} < 10^{-10}$), whereas 60 miRNAs were decreased (e.g. miRNA-128, -937, -30c, -328, -26a, $p_{adj} < 0.005$), thereby representing the IgAV-associated serum miRNA signature. The miRror platform identified 426 protein-coding genes as targets of the 54 DE miRNAs (log2 fold change $\geq |1|$, $p_{adj} < 0.01$). As analyzed by STRING, these miRNA target genes were enriched in distinct molecular networks and biological pathways, including "Phosphoproteins (FDR $7.4*10^{-5}$), "Alternative splicing" (FDR $2.8*10^{-4}$), "Regulation of actin cytoskeleton" (FDR 0.008), "Proteoglycans in cancer" (FDR 0.009) and "Fcgamma receptor dependent phagocytosis" (FDR 0.01) (Figure 2). Additionally, miRNA gene targets formed three distinct molecular clusters, specifically "Chemokines and their receptors", "Ubiquitination process" and "Vesicle, endocytosis, lysosomes and their trafficking" (Figure 2). This suggests that the altered miRNAs in IgAV regulate diverse cellular functions, reflecting or contributing to the key aspects of disease pathogenesis.

Conclusion: Here we report for the first time an IgAV-associated serum miRNA signature. The altered miRNAs clearly discriminate IgAV patients from HC, and might play a key role in the pathogenesis of IgAV. Our study sets the basis for the identification of novel, serum-based disease biomarkers in vasculitis.

Disclosure of Interests: ALOJZIJA HOCEVAR: None declared, Katja Lakota: None declared, Thomas Grentzinger: None declared, Alexis Sarazin: None declared, Neža Brezovec: None declared, Tadeja Kuret: None declared, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders, Sasa Cucnik: None declared, Olivier Voinnet: None declared, Snežna Sodin-Šemrl: None declared, Matija Tomšič: None declared, Mojca Frank-Bertoncelj : None declared

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SAT0235 BIOLOGICAL THERAPYIN NEUROBEHÇET. MULTICENTER STUDY OF 29 PATIENTS

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Background: Behçet's disease (BD) is a variable vessel vasculitis and typically presents with mucocutaneous involvement. However, any organ can be affected, being the neurological affectation (neurobehçet, NB) one of the most serious manifestations.

Objectives: Our aim was to assess the efficacy and safety of biological therapy as treatment of NB.

Methods: We set up a multicenter observational study of 29 patients with NB on treatment with biological therapy (BT). NB diagnosis was made by neuroimaging, CSF analysis and/or suggestive clinical signs of central and/or peripheral nervous system involvement, excluding infectious causes or more prevalent pathology. Results are expressed as mean±SD or as median and interquartile range (IQR) as appropriate.

Results: 29 patients (15♂/14♀) with an average age of 39.6 ± 10.5 years. HLA-B51 was positive in 48.3% of the patients. **Table** shows the non-neurological manifestations. Regarding the neurological manifestations, 23 patients (79.3%) had parenchymal involvement (hemiparesis (n=6),

brainstem involvement (n=1), encephalopathy (n = 4), optic neuropathy (n=3), dysphasia (n=1), polyneuropathy (n=6), cognitive impairment (n=4), and non-steroidal psychosis (n=1), while the remaining 6 patients (20.7%) presented aseptic meningitis as a non-parenchymal affectation (**Table**).

Prior to BT, patients had received the following treatment: oral prednisone (n=27), methylprednisolone bolus (n=9), CsA (n=8), AZA (n=16), MTX (n=14) and mycophenolate (n=2).

After a median of 31 [10-60] months since the beginning of the neurological symptoms, the following BT was initiated: infliximab (IFX)(n=17), adalimumab (ADA)(n=7), tocilizumab (TCZ) (n=2), golimumab (GOL) (n=2) and Etanercept (ETN) (n=1). A first switch to ADA was necessary in 8 patients with IFX due to primary failure. In addition, 2 of them needed a second switch to TCZ, getting a partial response. The BT was discontinued in 5 patients, 2 of them for obtaining clinical remission and the remaining 3 for inefficacy.

After a median follow-up of 5.4±4.6 years, complete response was obtained in 15 patients, partial response in 11 and no response in the remaining 3. We observed an anaphylactic reaction and psoriasis induced by IFX, without other serious adverse events (**Table**).

Conclusion: BT, especially anti-TNF, seems effective and safe for treatment in NB.

Table.

Demographical parameter	
- Patients, n	29
- Sex, n (%)	15$_{M}$/14$_{F}$ (51.7/48.3)
- Age, year (mean±SD)	39.6±10.5
- HLA-B51 +	14 (48.3)
Non Neurological manifestation	
- Oral ulcers	28 (96.6)
- Genital ulcers	23 (79.3)
- Uveitis	16 (55.2)
- Skin lesions	20 (69)
- Arthritis	6 (20.7)
- Arthralgia	19 (65.6)
- Venous/arterial thrombosis	7 (24.1)/3 (10.3)
Neurological manifestation	
Parenchymal Disease, n (%)	23 (79.3)
- Hemiparesis	6 (20.7)
- brainstem syndrome	1 (3.4)
- encephalopathy	4 (13.8)
- optic neuropathy	2 (6.8)
- dysphasia	1 (3.4)
- polyneuropathy	6 (20.7)
- cognitive dysfunction	4 (13.8)
- psychosis	1 (3.4)
Non-parenchymal Disease (aseptic meningitis), n (%)	6 (20.7)
Time from diagnosis to BT onset, months (median[IQR])	31 [10-60]
Previous immunosuppressants	
- Oral corticoids	27 (93.1)
- Bolus MTP	9 (31)
- Azathioprine	16 (55.2)
- Methotrexate	14 (48.3)
- Cyclosporine	8 (27.6)
- Mycophenolate	2 (6.9)
First Biological therapy	
- Infliximab	17 (58.6)
- Adalimumab	7 (24.1)
- Tocilizumab	2 (6.9)
- Golimumab	2 (6.9)
- Etanercept	1 (3.4)
Follow-up, months (median[IQR])	22 [18.5-74]
- 1st/2nd Switch, n (%)	8 (27.6) / 2 (6.9)
- Discontinued (inefficacy)	3 (10.3)
- Severe adverse events	0 (0)

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SAT0236 RELATIONSHIP BETWEEN RITUXIMAB CONCENTRATION AND AUTOANTIBODY LEVELS IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS

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Background: Rituximab is approved in patients with anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV). Antibodies to proteinase 3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA) decrease with therapy (1) and may therefore be used as biomarkers.

Objectives: To investigate the relationship between rituximab concentration and ANCA levels in AAV patients.

Methods: 92 AAV patients from the RAVE trial (rituximab for ANCA-associated vasculitis) were assessed. Both MPO-ANCA, and PR3-ANCA antibody levels were used as biomarkers. ANCA levels were measured at baseline, at months 1, 2, 4, 6, 9, 18, and every 6 months until the second rituximab cycle if any, using ELISA supplied by Euroimmun. A semi-mechanistic model including a deep compartment which was sensitive to rituximab and a feedback mechanism, and a blood compartment were tested to describe the concentration-ANCA autoantibodies relationship. A population modeling approach using sequential methods was used for model building. Influence of sex, body surface area (BSA), BVAS/WG score, newly diagnosed status, major renal involvement at baseline, and relapse were investigated as covariates on pharmacodynamics parameters.

Results: A two compartment model including feedback mechanism from the circulating ANCA well described the concentration autoantibody relationship. The mean (interindividual standard deviation) estimated rituximab IC50, assessing potency, in patients with MPO-ANCA and PR3-ANCA were 21.9 mg/l (28%) and 11.2 mg/l (48.6%), respectively. Moreover, among patients with PR3-ANCA, rituximab IC50 was higher in patients with major renal involvement at baseline ($p=2.47 \times 10^{-2}$) and newly diagnosed status ($p=6.42 \times 10^{-5}$) than in others.

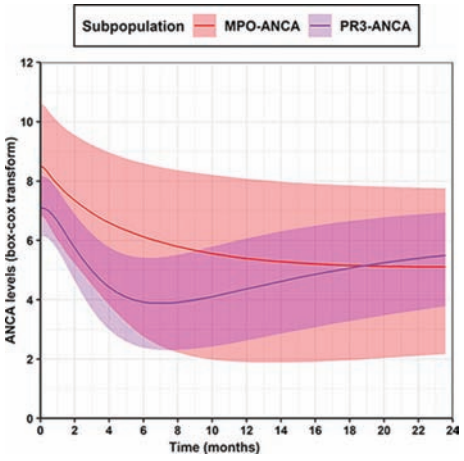


Figure 1. Simulations of ANCA-time profile in patients with MPO-ANCA (red line) and PR3-ANCA (purple line), using typical pharmacodynamic parameters. The central curve are the median dynamics of ANCA and the shadow are 90% prediction intervals.

Conclusion: A two compartments model including feedback mechanism from the circulating ANCA well described concentration-ANCA levels relationship. The potency of rituximab was higher in patients with PR3-ANCA than in patients with MPO-ANCA.

REFERENCE

[1] Fussner LA, et al. Factors Determining the Clinical Utility of Serial Measurements of Antineutrophil Cytoplasmic Antibodies Targeting Proteinase 3. Arthritis Rheumatol. 2016;68:1700-10.

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SAT0237 MYOCARDIAL FDG-PET/CT FINDINGS IN CHILDREN WITH TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) is a chronic large-vessel vasculitis affecting the aorta and its major branches[1)]. In Japan, ^{18}F-fluorodeoxyglucose positron emission tomography with computed tomography (FDG-PET/CT) was approved since April 2018. Recently, usefulness of FDG-PET/CT to diagnose TAK or assess disease activity has been reported[2)]. However, the findings in children with TAK except for vascular lesions remain unknown.
Objectives: We aimed to retrospectively analyse the FDG-PET/CT findings in children with TAK except for vascular lesions.
Methods: This is a single-center retrospective observational study. We evaluated 9 children with TAK and compared them with 10 children with other rheumatic disease (systemic juvenile idiopathic arthritis; 5, polyarticular juvenile idiopathic arthritis; 1, juvenile dermatomyositis; 1, Crohn's disease; 2, Kikuchi's disease; 1) (control group). All children underwent FDG-PET/CT before the treatment. We compared the two groups for the age at performed FDG-PET/CT, sex, duration of onset to performed FDG-PET/CT, FDG-PET/CT findings. Binary data were analyzed by Fisher's exact test.
Results: Median age of the performed FDG-PET/CT was 13.9 (range; 11.1-14.9) years old in TAK children and 5.4 (1.4-12.4) years old in control group. Both groups include 6 females. Median duration of onset to performed FDG-PET/CT was 1 (range; 0-12) months in TAK children and 0 (0-12) months in control group. FDG accumulation in bone marrow was observed in 7 TAK patients (78%) and in 7 (70%) of control group. Moreover, FDG accumulation in spleen was observed in 7 TAK patients (78%) and in 10 (100%) of control group. These findings were common in both groups. On the other hand, FDG accumulation in left ventricular myocardium was observed in 8 TAK patients (89%) but in 3 (30%) of control group (p=0.02). Six TAK children received follow-up FDG-PET/CT. Myocardium FDG accumulation was continued in 3 children but resolved in 2. TAK children with persistent accumulation in myocardium had ascending aorta dilation later.
Conclusion: FDG accumulation in left ventricular myocardium would be a characteristic finding in children with TAK, and possibly related to later ascending aorta dilation.

REFERENCES

[1] Jennette JC, Falk RJ, Bacon PA, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013; 65: 1-11
[2] Danve A, O'Dell J. The Role of 18F Fluorodeoxyglucose Positron Emission Tomography Scanning in the Diagnosis and Management of Systemic Vasculitis. Int J Rheum Dis 2015; 18: 714-24

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SAT0238 SHORTTERM PROGNOSIS OF A PROSPECTIVELY FOLLOWED COHORT OF UNSELECTED ADULT IGA VASCULITIS PATIENTS – A SINGLE RHEUMATOLOGY CENTRE EXPERIENCE

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Background: The acute phase of adult IgA vasculitis (IgAV) is well characterized. Data of even short-term prognosis of adult IgAV is scarce, mostly retrospective and usually limited to patients with significant renal disease.
Objectives: Our aim was to examine the short-term prognosis in a cohort of unselected adult IgAV cases.
Methods: We analysed medical records of newly diagnosed, histologically proven cases of IgAV at our department of rheumatology between 1 January 2010 and 31 May 2018, that were followed until 30 November 2018.
Results: During the 101-month observational period we identified 245 IgAV cases. The clinical characteristics at presentation and the initial treatment are shown in Table 1. During the acute phase of the disease four patients died (3 due to active vasculitis, 1 due to generalized CMV infection and heart failure). During the follow-up period 23 patients died, all deaths were unrelated to IgAV. 28 patients were lost to follow-up. The clinical characteristics of the remaining 190 patients who were followed for a median 12.7 (IQR 6.9–24.5) months at follow-up are shown in Table 2.

Table 1. The clinical characteristics at presentation and initial treatment of IgAV

% male	58.8		
Median age (IQR), years	64.7 (45.6–77.3)		
Purpura, # (%)	245 (100)		
necrotic, # (%)	114 (46.5)		
generalized, # (%)	121 (49.4)		
Joint involvement, # (%)	98 (40.0)		
GI tract involvement, # (%)	74 (30.2)		
severe GI, # (%)	18 (7.3)		
Renal involvement, # (%)	110 (44.9)		
severe, # (%)	29 (11.8)	Treatment, # (%)	190 (77.6)
median BVAS-3 (IQR)	8 (3–15)	local GC, # (%)	29 (11.8)
Newly diagnosed malignancy, # (%)	3 (1.2%)	systemic GC, # (%)	172 (70.2)
		cyclophosphamide, # (%)	24 (9.8)
		IVIG, # (%)	7 (2.9)

Legend: # - number of patients; IQR – interquartile range; GI - gastrointestinal tract; severe GI tract involvement - bloody diarrhoea or ileus or surgical intervention; severe renal involvement - acute renal failure or nephrotic syndrome; BVAS-3 - Birmingham vasculitis activity score; GC – glucocorticoids; IVIG – intravenous immunoglobulin; Malignancy – concurrently diagnosed malignancy.

Table 2. Clinical characteristics at last follow-up visit

	Pts. No (%)
Relapse	30 (15.8)
one; two; more than three	21 (11.1);5 (2.6);4 (2.1)
skin limited	22 (11.6)
skin+renal; skin+GI; renal	3 (1.6);1 (0.5); 3 (1.6)
Urinary abnormalities	79 (41.6)
microhematuria	68 (35.8)
proteinuria - <1g/day; ≥1g/day	20 (10.5); 7 (3.7)
Renal function worsening	22 (11.6)

Conclusion: Contrary to the experience in children, IgAV in adults does not seem to be a benign disease even in the short-term. Admittedly, it is impossible to conclude whether this is due to the nature of the adult IgAV or because adults have more comorbidities than children.
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SAT0239 PREDICTION OF LONG-TERM EVOLUTIONARY PROFILES IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (CHURG–STRAUSS) BASED ON BASELINE AND FOLLOW-UP CHARACTERISTICS

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss) is a small-vessel necrotizing vasculitis characterized by blood and tissue eosinophilia and asthma. Glucocorticoids (GCs) control the disease, but GC-dependence is frequent. Evolving concepts distinguish vasculitis-related symptoms from asthma and/or ENT manifestations. That distinction has become even more important since the development of B-cell and eosinophil-targeted therapies.

Objectives: This study aimed to describe and identify characteristics predicting long-term EGPA outcomes.

Methods: We set up a multicenter European cohort that included 636 EGPA patients. Based on recent consensus, we distinguished 4 EGPA-evolutionary profiles: GC-dependent asthma and/or ENT manifestations (requiring prednisone >7.5 mg/d), ≥1 vasculitis relapse(s) (excluding asthma and/or ENT flares), both phenotypes, and complete remission (no GC-dependent asthma/ENT signs, no vasculitis relapse and prednisone <5 mg/d at last follow-up). Baseline and follow-up characteristics predicting those outcomes were analyzed.

Results: After median follow-up of 63 (IQR 30-110) months, 35.8% had GC-dependent asthma and/or ENT manifestations, 12.9% had ≥1 vasculitis relapse(s), 14.3% had both phenotypes, 14.6% were in complete remission, 14.4% were in partial remission and 7.8% had not reach remission.

Patients with GC-dependent asthma/ENT manifestations were younger at diagnosis (p<0.0001), had more frequent GC-treated asthma before overt EGPA (p=0.002), had more ENT manifestations (p=0.01) and less frequent MPO-ANCA (p<0.0001). Their daily GC dose was higher at every time point (p<0.0001), and they had more frequent active asthma at last follow-up (p<0.0001).

Patients with vasculitis relapse(s) had more frequently neurological manifestations at diagnosis (p=0.002) and MPO-ANCA positivity (p<0.0001), and less frequently pulmonary infiltrates (p=0.031). Median time from diagnosis-to-1st vasculitis relapse was 25 (11–60) months. During follow-up, their daily GC dose was lower than those with GC-dependent asthma/ENT manifestations, but similar to those in complete remission. At last follow-up, neurological sequelae tended to be more frequent (p=0.06).

Finally, patients in complete remission were older (p<0.0001), had more fever (p=0.03), less GC-treated asthma (p=0.002) and ENT manifestations at diagnosis (p=0.01), lower daily GC dose during follow-up (p<0.0001), lower eosinophils count at 6 months (p=0.002) and less frequent sequelae (p=0.003).

Conclusion: EGPA seems to evolve toward distinct phenotypic profiles, which could be identified using baseline and follow-up characteristics. Early identification of those profiles could allow guided choices of the best therapeutic option.

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SAT0240 DEVELOPMENT AND PRELIMINARY VALIDATION OF THE BEHÇET'S SYNDROME OVERALL DAMAGE INDEX (BODI)

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Background: Irreversible organ damage is considered a core outcome by the OMERACT working group. However, no specific tools are currently available to detect and measure damage accrual in Behçet's syndrome (BS).

Objectives: To develop and preliminarily validate the **B**ehçet's syndrome **O**verall **D**amage **I**ndex (BODI). NCT03803462.

Methods: A preliminary version of the instrument (p-BODI) was developed by reviewing pre-existing tools [e.g. Vasculitis damage index (VDI)] and through an extensive literature review. p-BODI was then reviewed and implemented by a multi-rounds Delphi process, involving an international and multidisciplinary (5 rheumatologists, 4 internist, 1 ophthalmologist, 1 neurologist) panel of experts in BS management and a patients' delegate. A group of clinicians (CG), not involved in the BODI development, was asked to independently score a set of clinical vignettes, in order to test the instrument reliability, after a training process consisting of a user manual and a video-tutorial. Then, Cohen's K and Intra-class correlation coefficient (ICC) between assessors and gold standard were calculated. Afterwards, BODI validation was conducted according to the OMERACT Filter 2.0 in a multicenter BS cohort.

Results: Starting from a list of 120 candidate items, the final version of BODI consisted of 4 overarching principles, 30 items and 12 sub-items (each of them scores one point) grouped in 8 domains (figure).

In terms of reliability, the mean K coefficient was 0.84 (95%CI 0.78 to 0.90) and the ICC was 0.88 (95%CI 0.80-0.95).

Validation cohort consisted of 228 BS patients (49.1% males), with a median (IQR) age and disease duration of 46.9 (35.5-55.0) and 11.7 (5.8-20.7) years, respectively. Overall, prevalence of any BODI damage (BODI ≥1) was 56.1% with a median score of 1.0 (0-2.0). In regard of construct validity, BODI score significantly correlated with VDI (Spearman's rho 0.693, p<0.001). Besides, BODI score did not correlate with BDCAF (rho-0.016, p=0.807), contrary to VDI (rho 0.141, p=0.034). Such results support the validity of BODI, unlike VDI, in discriminating damage from current disease activity in BS. On multiple regression analysis, factors independently associated to higher BODI damage score were male gender (β coefficient 0.143; p = 0.014), longer disease duration (β0.221; p < 0.001), past major organ involvement (β 0.377; p < 0.001) and required use of anti-TNFα inhibitors (β 0.222; p < 0.001).

Full agreement among the CG was reached in judging BODI as a credible, comprehensive, easy to use, timesaving and acceptable instrument.

Conclusion: BODI is the first tool specifically developed to assess damage in BS. Preliminary data encourage further validation of BODI in more extended and multi-ethnic BS cohorts before being applied in clinical practice and as a therapeutic outcome.

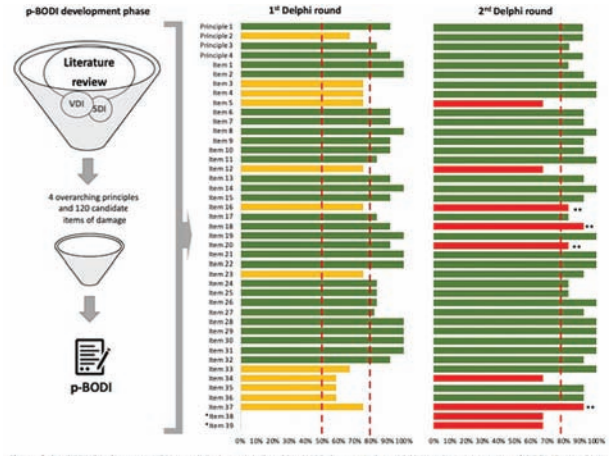


Chart of the BODI development. VDI: vasculitis damage index; SDI: SLICC damage index; p-BODI: preliminary version of BODI. Overarching principals and items of damage with respective definition were classified as approved ( ), approved conditionally to rephrase ( ) or rejected ( ), according to the pre-set levels of agreement (- - - - -) between members of the expert panel. * items proposed by experts; ** items rejected after validation process. Sub-items are included in the main items definition.

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SAT0241 HEALED TEMPORAL ARTERITIS. ANALYSIS OF PATIENTS REFERRED TO RHEUMATOLOGY WITH A DIAGNOSIS OF TEMPORAL ARTERITIS

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Background: The diagnosis of giant cell arteritis (GCA), or temporal arteritis (TA), is a clinical one. Temporal artery biopsy is usually obtained to strengthen support for treatment. Unfortunately a biopsy does not always confirm the diagnosis; results can be reported as active, healed, or negative even in patients with all other features of giant cell arteritis. Histopathologic features suggestive of resolving inflammation are evident in healed TA, but these are non-specific and can also be seen in other conditions that are unlikely to benefit from prolonged steroid treatment. It is not clear if a pathological diagnosis of healed TA helps to support treatment which may be associated with significant toxicity.
Objectives: We analyzed clinical features of patients with "healed" TA and compared them to patients with active and negative biopsies with the goal of identifying any features that may aid treatment decisions.
Methods: Retrospective analysis of 49 patients with established TA diagnosis, seen at a rheumatology practice in Houston, Texas from 8/2007 to 12/2018. Fifty seven percent were referred by Ophthalmology, the rest by other specialties. Patients were divided into 3 groups based on biopsy: Active, Healed, and Negative. Clinical features analyzed at the time of presentation were gender, age of onset, fulfillment of the American College of Rheumatology (ACR) 1990 criteria for the classification of Giant Cell Arteritis and the 2016 revised ACR criteria for early diagnosis of Giant Cell Arteritis (rACR), and the presence of vision abnormalities, headache, temporal artery tenderness/induration, jaw claudication, fever, anemia, sedimentation rate at onset, and flares during follow up.
Descriptive data was reported as means ± standard deviation for continuous variables and as proportions for categorical variables; analyzed with ANOVA and chi squared, respectively. Post hoc analysis with Bonferroni corrections and Fisher's exact tests were used. All analyses were performed on Stata version 15 (StataCorp LP, College Station, TX, USA). A p-value of ≤ 0.05 was considered statistically significant.
Results: Thirty-two (65%) of the 49 patients were female and 17 (35%) were male. Biopsy reports showed active disease in 14 (28.5%), healed in 31 (63.3%) and negative in 4 (8.2%) patients. Average age was 72.7 years ±6.3, 73.0 ±9.1, 61.25 ±1.3 years in these 3 groups, respectively (p value 0.008). The Active versus Healed groups were statistically different with respect to age (p 0.028), those meeting ACR and rACR criteria (p 0.029 and p 0.002), and the incidence of jaw claudication: 8 active (57.1%) versus 5 healed (16.1%) patients (p 0.05). There was no statistically significant difference in ophthalmologic manifestations, headache, temporal artery palpation, fever, anemia, and flares. In addition, 90% of patients reported side effects from steroids.
Conclusion: The percent of healed TA was 63.3%, higher than in other studies. Patients with healed TA were less likely to fulfill ACR and rACR criteria for giant cell arteritis. Further studies are needed to identify the subset of patients with healed TA who would have a clear benefit from high dose steroids, that would outweigh the treatment side effects. At the end of the day, the diagnosis of TA remains a clinical one and early involvement of Rheumatology may help avoid unnecessary biopsies and treatment. Ultrasound, MRA, and PET-CT scan may be able to fill the gap when biopsy fails to confirm the diagnosis.
Disclosure of Interests: None declared
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SAT0242 SENSITIVITY OF TEMPORAL ARTERY BIOPSY IN GIANT CELL ARTERITIS: SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS OF CLINICAL DATA

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Background: The role of temporal artery biopsy (TAB) as a reference test for the diagnosis of giant cell arteritis (GCA) is currently questioned by the use of non-invasive imaging techniques such as temporal artery ultrasonography (TA-US). Although TAB is highly specific, a subset of patients with a clinical diagnosis of GCA does not show the characteristic histopathological signs. The lack of knowledge of the proportion of GCA cases with positive findings on TAB hampers comparisons of the sensitivity of TAB and imaging tests for diagnosing GCA.
Objectives: We performed a systematic literature review and meta-analysis to estimate the sensitivity of TAB in GCA and to identify factors that may influence the estimate.
Methods: We searched MEDLINE via PubMed, EMBASE and CENTRAL databases for articles reporting TAB in GCA that were published from 1990 to 2017, with no language restriction. Eligibility criteria included studies with $\geq$30 GCA cases fulfilling the original or modified 1990 ACR classification criteria for GCA. From eligible publications, two independent researchers extracted the main methodological, geographic, demographic, and clinical characteristics and the number of TAB-positive cases among all cases with interpretable results for TAB. By meta-analysis, we computed the pooled proportion of TAB-positive GCA cases by using a random-effects model with a binomial-normal distribution and assessed heterogeneity by the I^2 statistic. Subgroup and meta-regression analyses were used to examine the effect of 16 covariates (e.g., geographic, demographic, clinical and study descriptors) on TAB positivity.
Results: Among 3820 screened publications, 32 independent studies (3092 GCA patients in total) were used for the analysis. The pooled proportion of TAB positivity was estimated at 77.3% (95% confidence interval 71.8–81.9%), with high between-study heterogeneity (I^2=90%). Subgroup analysis suggested a potential influence of year of publication (Table). This result was confirmed by univariate (P=0.0008) and multivariate meta-regression (P=0.0004). No other analyzed covariate significantly influenced the sensitivity of TAB in GCA.
Conclusion: The 77% estimated sensitivity of TAB in GCA indicates that it is not inferior to that of TA-US (1). The decline in TAB-positive GCA cases over time could reflect an increasing propensity of clinicians to accept GCA diagnosis in the absence of proof by TAB. The unexplained high between-study heterogeneity could also result from differences in TAB sampling, processing or interpretation.

REFERENCE

[1] Duftner C, Dejaco C, Sepriano A, et al. Imaging in diagnosis, outcome prediction and monitoring of large vessel vasculitis: a systematic literature review and meta-analysis informing the EULAR recommendations. RMD Open. 2018;4:e000612.

Table. Proportion of TAB-positive GCA stratified by the main covariates.

Study and pt. characteristics		No. of studies (pt.)	Positive TAB (%) (95% CI)	I^2 (%)
Mean age at diagnosis	<72.7 yrs	10 (961)	81.2 (71.1–88.4)	91
≥72.7 yrs	11 (1067)	74.8 (65.1–82.6)	91	
Females	<71% of pt.	12 (1156)	78.3 (67.0–86.5)	94
	≥71% of pt.	11 (1319)	81.6 (73.9–87.4)	88
Polymyalgia rheumatica	<42% of pt.	7 (629)	70.6 (59.4–79.9)	87
	≥42% of pt.	7 (1024)	79.2 (66.2–88.0)	94
Ophthalmological signs	<21% of pt.	6 (893)	81.8 (66.2–91.2)	95
	≥21% of pt.	7 (606)	72.2 (60.4–81.6)	87
Large-vessel	<25% of pt.	2 (373)	63.0 (50.6–73.8)	78
involvement	≥25% of pt.	2 (203)	61.1 (54.2–67.5)	0
Study purpose	Diagnostic	3 (153)	88.8 (68.5–96.7)	75
	Other	29 (2939)	76.0 (70.4–80.9)	90
Study type	Retrospective	24 (2688)	75.5 (69.3–80.8)	91
	Prospective	8 (404)	83.1 (70.6–90.9)	86
Year of publication	<2012	16 (1806)	84.4 (77.1–89.6)	92
	≥2012	16 (1286)	68.4 (63.4–72.9)	69

Pt : patients

Disclosure of Interests: Emma Rubenstein: None declared, Carla Maldini: None declared, Solange GONZALEZ-CHIAPPE: None declared, Sylvie Chevret: None declared, Alfred Mahr Consultant for: Chugai Pharma France, Speakers bureau: Roche SAS Chugai Pharma France
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SAT0243 EFFECTS OF TOFACITINIB SUPPRESSED PULMONARY VASCULAR REMODELING OF ALLERGIC VASCULITIS IN A MURINE MODEL

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Background: We reported allergic granulomatous vasculitis with eosinophil infiltration in an asthma model of C57BL/6 sensitized with ovalbumin (OVA). TGF-btea and IL-6 are thought to play an important role in fibroblasts proliferation and is critical to vascular remodeling in vasculitis. Tofacitinib inhibits vascular endothelial cells proliferation and canalization.
Objectives: To elucidate the role of tofacitinib in vascular remodeling of allergic granulomatous vasculitis, we examined the effects of tofacitinib on the vasculitis of the murine model.
Methods: C57BL/6 mice (6-8 weeks) were sensitized with ovalbumin (OVA) and alum. The positive controls (n=9) were exposed to aerosolized OVA daily for 7 days. The other group of mice (tofacitinib treated mice (n=9)) were administered with tofacitinib (100mg/kg intraperitoneal administration) in parallel with daily exposure to aerosolized OVA for 7 days. On 7th day, bronchoalveolar lavage (BALF) was performed and the lungs were excised for pathological analysis. Cytokines in BALF were measured.
Results: The total cell number and the number of. Eosinophils in BALF on the 7th day were decreased significantly in the tofacitinib-treated mice compared with those of the control-positive mice. The blood eosinophil counts in the positive control increased after OVA inhalation. The blood eosinophil counts in the tofacitinib treated mice were lower on the than those in the positive control.

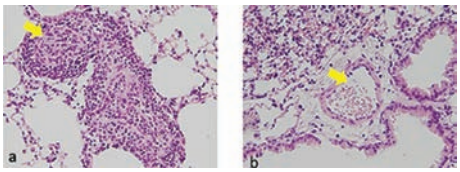


Figure 1. a. Positive control: Totally occluded pulmonary artery by intraluminal myofibroblasts in the OVA-sensitized mice with exposure to OVA in 7th day. (HE staining) b. Tofacitinib: Intraluminal myofibroblast accumulation was not observed in the OVA-sensitized mice with exposure to OVA and treated with tofacitinib in 7th day. (HE staining).

The concentrations of IL-4, IL-5, IL-6 and TGF-beta in BAL fluids reduced significantly in the tofacitinib treated group. The pathological scores reduced significantly in the tofacitinib treated group compared to the positive control group. Intra luminal infiltration and proliferation of Ki67 positive myofibroblasts, IL-6 positive cell and α-SMA positive cells in pulmonary arteries were reduced dramatically in the tofacitinib treated group compared to the positive control group.
Conclusion: Tofacitinib suppressed pulmonary vascular remodeling in a murine model of allergic vasculitis with eosinophil infiltration. Tofacitinib is a hopeful therapeutic drug for Eosinophilic granulomatosis with polyangiitis.
Disclosure of Interests: None declared
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SAT0244 EXPANDING SPECTRUM OF ADENOSINE DEAMINASE 2 (DADA2) MANIFESTATIONS: EXPERIENCE 13 PATIENTS FROM INDIA

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Background: Deficiency of adenosine deaminase 2 (DADA2) is a recently described hereditary autoinflammatory disease with limited published literature [1-5]. There are no previous case series published from Asia.
Objectives: To describe the clinical features and treatment responses of patients diagnosed with DADA2 from India.
Methods: Patients diagnosed with DADA2 at 4 different centres in India were included. Details of clinical features, laboratory investigations, ADA2 activity, genetic analysis of CECR1 gene, therapy received and outcomes were noted.
Results: A total of 13 patients (12 Indians and one Syrian) were diagnosed with DADA2 between April 2017 and January 2019. The median age was 22 years (range: 7-39 years) and 8 (61.5%) patients were males. The diagnosis was made at a median duration of 30 months (range: 1-360 months) from the onset of first symptom. Figure 1 shows the various clinical manifestations. One patient had unknown manifestation of bad obstetric history mimicking APLA syndrome. ESR (median: 49.5 mm/hr; range: 15-130 mm/hr) was raised in all except one patient who was in remission at the time of diagnosis. CRP value was available in 11 patients and was elevated in all (median: 51.4 mg/L; range: 17.6-140 mg/L). Immunoglobulin levels assessed in 4 patients were normal. Neuroimaging done in nine patients showed infarcts in 5, bleed in 3, multiple aneurysms and features of PRES in one patient each. Abdominal microaneurysms were noted in 5 patients. Arterial occlusion of peripheral limb vessels was noted in 2 patients. ADA2 activity was assessed in 9 patients and all had nearly undetectable activity. CECR1 gene mutation analysis was available in 9 patients: 8 patients were homozygous for p.(Gly47Arg) missense mutation at exon 2 of CECR1 gene while one patient displayed compound heterozygosity for two novel mutations, P.(Leu188Val) in exon 4 and C.753+2 T>A in intron 4 of CECR1 gene. Eight patients were started on anti-TNF drugs (adalimumab in 7 and etanercept in 1). One patient required higher doses of adalimumab (40mg followed by 120mg at week 1 and 80mg at week 2) for severe gastrointestinal involvement but later died due to disseminated herpes infection. Rest of the seven patients started on anti-TNF drugs achieved disease control. Our patients had CNS, eye and GI manifestations lower than those reported by Zhou et al[1] but higher than those reported by Nanthapisal et al[2] and Navon Elkan et al[4]

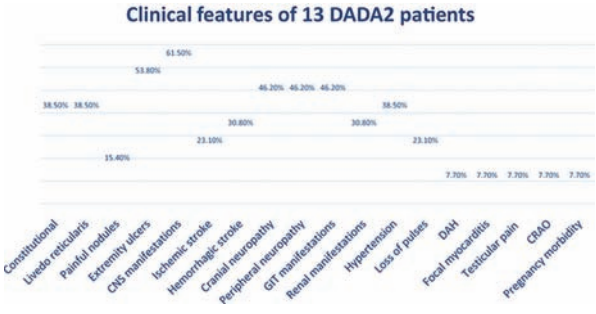


Figure 1. Clinical manifestations noted in our cohort of 13 patients with DADA2.

Conclusion: The spectrum of clinical presentations in Indian patients is different from those reported in previous cohorts. Anti TNF therapy was effective in majority.

REFERENCES

[1] Zhou Q, Yang D, Ombrello AK, et al. Early onset stroke and vasculopathy associated with mutations in ADA2. N Engl J Med. 2014; 370: 911–920.
[2] Nanthapisal S, Murphy C, Omoyinmi E, et al. Deficiency of adenosine deaminase Type 2: a description of phenotype and genotype in fifteen cases. Arthritis Rheumatol. 2016; 68: 2314–2322.
[3] Caorsi R, Penco F, Grossi A, et al. ADA2 deficiency (DADA2) as an unrecognised cause of early onset polyarteritis nodosa and stroke: a multicentre national study. Ann Rheum Dis. 2017; 76: 1648–1656.
[4] Navon Elkan P, Pierce SB, Segel R, et al. Mutant adenosine deaminase 2 in a polyarteritis nodosa vasculopathy. N Engl J Med. 2014; 370: 921-31.
[5] Sharma A, Naidu GSRSNK, Chattopadhyay A, et al. Novel CECR1 gene mutations causing deficiency of adenosine deaminase 2, mimicking antiphospholipid syndrome. Rheumatology. 2019; 58: 181-2.

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SAT0245 CHOROIDAL EVALUATION IN PATIENTS WITH CHILDHOOD POLYARTERITIS NODOSA (PAN) ANDADENOSINE DEAMINASE-2 DEFICIENCY (DADA-2)

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Background: Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis affecting small or medium arteries with a negative ANCA serology and no evidence of glomerulonephritis.
Objectives: The aim of this study was to evaluate the choroid with optical coherence tomography (OCT) in children with polyarteritis nodosa (PAN) and adenosine deaminase-2 deficiency (DADA-2).
Methods: The study included all PAN and DADA-2 patients (n=15), examined between June 2017 and September 2018, and an age and gender-matched control group (n=15). After ocular examination, choroidal images taken with sd-OCT (Heidelberg Spectralis) were evaluated with regard to choroidal thickness (ChT) at five points (750 and 1500 microns from the center of the fovea both in the temporal, nasal quadrant and under the fovea), total subfoveal choroidal area (TCA), luminal area (LA), stromal area (SA) and choroidal vascularity index (CVI).
Results: None of the patients had active ocular complaints or findings. The mean (±SD) age was 8.4 ± 3.69 years. ChT at 3 points, TCA, LA, and SA were found to be higher in patients with PAN and DADA-2. The CVI values were similar in both groups. No correlations were found between the OCT findings, activity score index (PVAS) and the biochemical parameters (Erythrocyte sedimentation rate, leukocyte, C-Reactive Protein).
Conclusion: The results of this study showed that the choroid was thicker in patients with PAN and DADA-2 than in the control group, suggesting that PAN and DADA-2 may affect the choroid. Ophthalmologic evaluation is important in PAN and DADA-2 patients, even in the absence of relevant complaints.

REFERENCES

[1] Ozen S, Anton J, Arisoy N, et al. Juvenile polyarteritis: results of a multicenter survey of 110 children. J Pediatr. 2004;145(4):517-522.
[2] Kur J, Newman EA, Chan-Ling T. Cellular and physiological mechanisms underlying blood flow regulation in the retina and choroid in health and disease. Prog Retin Eye Res. 2012;31(5):377-406.

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SAT0246 USING BONE MINERAL DENSITY VERSUS THE RATIO OF BODY MASS INDEX TO BONE MINERAL DENSITY TO PREDICT FRACTURE RISK IN POLYMYALGIA RHEUMATICA

Khojasta Talash, Marwan Bukhari. *Royal Lancaster Infirmary, Lancaster, United Kingdom*

Background: Polymyalgia Rheumatica (PMR) is the commonest inflammatory rheumatic condition that affects the elderly population and treatment with long-term corticosteroids is common[1]. Whilst steroid treatment is beneficial in managing symptoms, it has many side effects including increasing the risk of osteoporosis and hence fractures[2]. There has been recent research that suggests using the ratio of BMD to Body Mass Index (BMI) is a better marker of predicting fracture risk in obese patients than BMD alone[3].
Objectives: Our research set out to find out whether BMD alone or the ratio of BMI to BMD is a better predictor of fracture risk in patients with PMR.
Methods: Data were used from a cohort of PMR patients referred for DEXA scan to a District General Hospital between June 2004 and October 2010. The following were recorded: age, sex, whether a fracture was sustained, whether they had had steroid therapy at any point, BMI, BMD at L1-L4, BMD at femoral neck (left and right) and BMD at hip (left and right). Logistic regression models were fitted using fracture as the dependent variable. The independent variables for the first set of logistic regression models were BMD at each level and for the second set BMI: BMD ratio at the same levels. Data were adjusted for sex and age at scan. Logistic models were compared using area under the ROC curves (AUC).
Results: 714 patients were used in the study, of whom 532 (75%) were female. Mean age was 70.5 (SD 8.84) with age range 45.8 to 96.5 years. 703 (98%) were recorded to have had steroid therapy at any point. Mean BMI was 28.2 kg/cm^2 (SD 5.24). 156 (22%) had sustained a fracture. Odds ratios and AUC values for each level were as shown in the table. The fit of the models using the BMD alone was superior to the fit of the models using the ratio as the AUC values were greater for BMD alone.

Table 1. – Odds ratios (age- and sex-adjusted) and AUC values

Level	Odds Ratio and CI (BMD)	AUC (BMD)	Odds Ratio and CI (BMI:BMD)	AUC (BMI:BMD)
L1	0.192 (0.0656, 0.560)	0.6789	1.04 (1.01, 1.07)	0.6621
L2	0.138 (0.0529, 0.358)	0.6977	1.06 (1.03, 1.09)	0.6777
L3	0.192 (0.0795, 0.463)	0.6881	1.06 (1.03, 1.09)	0.6730
L4	0.243 (0.108, 0.544)	0.6837	1.05 (1.02, 1.09)	0.6731
L1 to L4	0.150 (0.0560, 0.400)	0.6837	1.06 (1.03, 1.09)	0.6737
L FEMORAL NECK	0.103 (0.0219, 0.492)	0.6727	1.04 (1.01, 1.06)	0.6576
R FEMORAL NECK	0.0785 (0.0143, 0.430)	0.6837	1.05 (1.02, 1.08)	0.6750
L TOTAL	0.0980 (0.0233, 0.412)	0.6824	1.06 (1.03, 1.10)	0.6777
R TOTAL	0.0623 (0.0136, 0.285)	0.6917	1.07 (1.04, 1.11)	0.6821

Conclusion: This study identifies that the BMI:BMD ratio does not provide better indication of fracture risk than BMD alone in our cohort of patients with PMR. We have previously shown that the same is true for patients with rheumatoid arthritis. A limitation of this study is not stratifying by steroid use.
Further work will be done to study the role of the ratio in predicting fracture risk in patients with other conditions.

REFERENCES

[1] Milchert, M., & Brzosko, M. (2017). Diagnosis of polymyalgia rheumatica usually means a favourable outcome for your patient'. Indian journal of medical research, 145(5), 593-600.
[2] Michet, C.J., & Matteson, E.L. (2008). Polymyalgia rheumatica. *BMJ (Clinical research ed.)*, 336(7647), 765-9.
[3] Tucker, M., (2018, May 18). *Simple Ratio May Predict Fracture Risk in Obese Patients*. Retrieved from https://www.medscape.com/viewarticle/896882

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SAT0247 FEMALE SEX AND AGE AT DIAGNOSIS ARE ASSOCIATED WITH A DECREASED POSSIBILITY OF DRUG DISCONTINUATION IN GIANT CELL ARTERITIS: DATA FROM A MULTICENTER PROSPECTIVE COHORT OF 177 PATIENTS

Tsalapaki Christina[1], Argyro Lazarini[1], Maria Tektonidou[2], Petros Sfikakis[2], Vasiliki Dania[3], Kyriaki Boki[3], Evripidis Kaltsonoudis[4], Paraskevi V. Voulgari[4], Gerasimos Evangelatos[5], Alexios Iliopoulos[5], Evangelos Theotikos[6], Antonia Elezoglou[6], Charalampos Papagoras[7], Theodoros Dimitroulas[8], Alexandros Garyfallos[8], Dimitrios Boumpas[9], Georgios Vosvotekas[10], Dimitrios Vassilopoulos[1]. *[1]Joint Rheumatology Program,Clinical Immunology-Rheumatology Unit, 2nd Department of Medicine and Laboratory, University of Athens, School of Medicine, Athens, Greece*; *[2]Joint Rheumatology Program,First Department of Propedeutic Internal Medicine, University of Athens, School of Medicine, Athens, Greece*; *[3]Sismanoglio Hospital, Rheumatology Unit, Athens, Greece*; *[4]Rheumatology Clinic, University of Ioannina, Ioannina, Greece*; *[5]NIMTS Hospital, Rheumatology Unit, Athens, Greece*; *[6]Asklipiion General Hospital, Rheumatology Unit, Athens, Greece*; *[7]Democritus University of Thrace, Rheumatology Clinic, Thrace, Greece*; *[8]Aristotle University, 4th Department of Medicine, Thessaloniki, Greece*; *[9]Joint Rheumatology Program,4th Department of Medicine, Attikon Hospital, University of Athens, School of Medicine, Athens, Greece*; *[10]Private Practice, Thessaloniki, Greece*

Background: Giant cell arteritis (GCA) usually requires long-term therapy with corticosteroids and/or Disease Modifying Anti-rheumatic Drugs (DMARDs) but the exact factors that are associated with drug discontinuation in these patients have not been well defined.
Objectives: To evaluate the baseline or on-treatment factors that influence drug survival in GCA.
Methods: Data were derived from an ongoing, multicenter, prospective cohort study of patients with GCA. During the 1st phase of the study, data regarding demographic and clinical characteristics at baseline, type of treatment, adverse events of therapy and co-morbidities were retrospectively collected and analyzed. Predictors of drug discontinuation were examined by univariate and multivariate logistic regression analyses.
Results: One hundred and seventy seven patients were included in the study; 70% (n=120) were women with a mean age at diagnosis of 74 ± 8.4 years. Diagnosis was established by temporal artery biopsy in 127 patients (72%), ultrasound of temporal arteries in 37 patients (21%) and large vessel imaging in 10 patients (6%). At diagnosis, the median ESR and CPR were 103 mm/h and 63 mg/L, respectively. All patients were treated initially with pos corticosteroids (median daily starting dose: 41 mg), while 12 (7%) of patients received pulse steroids. At the 1st patient evaluation (median follow-up from diagnosis: 3 years), the median daily steroid dose was 5 mg, while in 34% (n= 62) and 8% (n= 14) of patients a synthetic or biologic DMARD had been added, respectively. During that period, 24% (n=43) of patients had discontinued corticosteroids and 18% (n=32) all treatments. By univariate analysis, DMARD use was associated with a higher possibility for corticosteroid discontinuation (OR=2.3, p=0.017) but by multivariate logistic regression analysis only female sex (OR=0.49, p=0.07) and age at diagnosis (OR=0.94, p=0.01) were associated with a decreased risk for corticosteroid discontinuation. Similar results were found for discontinuation of all drugs [female sex (OR=0.4, p=0.05) and age at diagnosis (OR=0.9, p=0.046)].
Conclusion: In this large GCA cohort, only one out of four patients managed to discontinue corticosteroids and 20% all treatments ~3 years after diagnosis. Multivariate analysis revealed only female sex and age at diagnosis as independent factors for treatment discontinuation.
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Disclosure of Interests:
None declared
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SAT0248 CLINICAL OUTCOMES OF PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB IN REAL-WORLD CLINICAL PRACTICE

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Background: Previously, the GiACTA study demonstrated the superiority of subcutaneous (SC) tocilizumab (TCZ) plus prednisone vs prednisone alone in achieving sustained glucocorticoid (GC)-free remission in patients with giant cell arteritis (GCA).[1]
Objectives: To evaluate the effectiveness and safety of SC and intravenous TCZ in real-world clinical practice.
Methods: We performed a retrospective analysis of GCA patients treated with TCZ at a single center (MGH) between 2010-2018. Annual relapse rate, time to disease relapse, number of relapses, prednisone use, and adverse events (AE) before and after TCZ initiation were assessed. Disease relapse was defined as the re-appearance of clinical manifestations of GCA (e.g., cranial symptoms) that required treatment modification.
Results: A total of 60 GCA patients were included in the analysis. **Table 1** depicts the baseline characteristics and the treatments received by this cohort. The median (IQR) disease duration before TCZ use was 0.6 (0.2-1.6) years. Fifty-eight patients (96.7%) received concomitant prednisone (mean [SD] dose: 30 [18.3] mg daily) at the time of TCZ initiation. Patients received TCZ for a median (IQR) period of 0.5 (0.3-1.4) years. Before TCZ treatment, 43 patients (71.7%) had ≥1 relapse (median [IQR] time to relapse 0.5 [0.3-0.7] years). After TCZ initiation, 18 patients (30.0%) had ≥1 relapse (estimated median [IQR] time to relapse 2.1 [0.6-2.3] years). The annual rate of relapse was lower on TCZ than while off TCZ (RR=0.40 [95% CI, 0.25-0.63]; *P*=0.0001) (**Table 2**). Twenty-seven patients (46.6%) successfully tapered off prednisone during TCZ treatment. The incidence of AEs and serious AEs (SAE) was similar before and after TCZ initiation (**Table 2**). During TCZ treatment, however, 38 of 81 AEs were considered related or possibly related to prednisone. An AE led to TCZ discontinuation in 5 patients. No deaths occurred during the study period.
Conclusion: In this retrospective analysis, TCZ improved clinical outcomes in patients with GCA as indicated by a reduced incidence of relapses and by the ability to discontinue prednisone. The occurrence of AEs and SAEs (many due to GC) did not differ substantially while patients were on or off TCZ. These real-world findings support the previously reported efficacy and safety profile of TCZ in patients with GCA.

REFERENCE

[1] Stone JH, et al. N Engl J Med. 2017;377(4):317-328.

Table 1.. Patient baseline characteristics and treatments

	Total Patients (N = 60)
Age, mean (SD)	69.4 (9.4)
Female sex, n (%)	43 (71.7)
Caucasian ethnicity, n (%)	53 (88.3)
Clinical manifestations at disease onset	
Headache, n (%)	47 (78.3)
Scalp tenderness, n (%)	26 (43.3)
Jaw claudication, n (%)	31 (51.7)
Amaurosis fugax, n (%)	11 (18.3)
Transient blurry vision, n (%)	18 (30.0)
Diplopia, n (%)	2 (3.3)
PMR symptoms, n (%)	32 (53.3)
ESR (mm/hr), mean (SD)	72.6 (33.6)
CRP (mg/L), mean (SD)	76.1 (72.6)
Positive TA biopsy, n (%)	26 (43.3)
Prednisone dose (mg/day) at disease onset, mean (SD)	54 (19.0)
Use of other immunosuppressants before TCZ initiation, n (%)*	15 (25)
Duration of disease before TCZ initiation (years), median (IQR)	0.6 (0.2-1.6)
Prednisone dose (mg/day) at TCZ initiation, mean (SD)	30 (18.3)
Received TCZ IV, n (%)†	22 (37.3)
Received TCZ SC, n (%)†	43 (72.9)
Duration of TCZ treatment (years), mean (SD)	0.9 (1.0)
Duration of TCZ treatment (years), median (IQR)	0.5 (0.3-1.4)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IV, intravenous; PMR, polymyalgia rheumatica; SC, subcutaneous; TA, temporal artery; TCZ, tocilizumab.

Table 2. Clinical outcomes and adverse events

	Off TCZ (N = 60)	On TCZ (N = 60)
Follow-up time, median (IQR), years	0.60 (0.20-1.57)	0.59 (0.32-1.50)
Patients with ≥ 1 relapse, n (%)	43 (71.7)	18 (30.0)
1 relapse	19 (31.7)	11 (18.3)
2 relapses	11 (18.3)	3 (5.0)
3 relapses	4 (6.7)	3 (5.0)
≥ 4 relapses	9 (15.0)	1 (1.7)
Time to relapse, median (IQR), years	0.5 (0.3-0.7)	2.1 (0.6-2.6)
Annual relapse rate (95% CI), events per year*	1.43 (0.95-2.13)	0.57 (0.33-0.98)
Patients with ≥ 1 AE, n (%)	29 (48.3)	32 (53.3)
AEs attributed to GC†	52 / 59 (88.1)	38 / 81 (46.9)
AEs attributed to TCZ†	NA	27 / 81 (33.3)
AEs attributed to GC or TCZ†	52 / 59 (88.1)	53 / 81 (65.4)
Patients with ≥ 1 SAE, n (%)	6 (10.0)	6 (10.0)
SAEs attributed to GC	7 / 8 (87.5)	4 / 9 (44.4)
SAEs attributed to TCZ	NA	3 / 9 (33.3)
SAEs attributed to GC or TCZ	7 / 8 (87.5)	6 / 9 (66.7)

AE, adverse event; CI, confidence interval; GC, glucocorticoids; IQR, interquartile range; NA, not applicable; SAE, serious AE; TCZ, tocilizumab.
* Rates are estimated from a Poisson regression model with ongoing treatment (TCZ and GC combinations), age, smoking history, new or relapsing GCA as covariates, and random patient effect.
† Multiple occurrences of AEs are included. Denominators are all AEs or SAEs.

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SAT0249 IGA VASCULITIS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE. A RETROSPECTIVE STUDY

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Background: Leukocytoclastic vasculitis has been reported in patients with inflammatory bowel disease (IBD) but cases of IgA vasculitis (IgAV) in IBD are considered rare.
Objectives: The purpose of this study was to describe the baseline characteristics and outcome of a series of patients with IBD and IgAV.
Methods: Biopsy-proven IgAV-patients with prior history of IBD were identified retrospectively at Mayo Clinic, Rochester, MN. Data were abstracted from direct medical chart review. Each IBD-IgAV case was matched to two controls with IgAV but without IBD history based on age, sex and baseline renal function at time of IgAV onset.
Results: A total of 9 patients were included in the study group (6 male, 3 female). Crohn's disease (CD) and Ulcerative Colitis (UC) were present in 7 and 2 patients, respectively. The mean length of time between IBD diagnosis and onset of IgAV was 17.3±19.9 years. For patients on biologic treatment for IBD, the mean length of time between initiation of biologic and onset of IgAV was 3.3±3.8 years (range 0-12 years). Active IBD at IgAV-onset was present in 56% (5/9) of patients.
Tumor necrosis factor inhibitors (TNFi) were the most frequent biologics used for IBD (8, 89%); infliximab was the most common (7, 78%). At IgAV-onset, only 5 patients were on treatment with TNFi; two subsequently discontinued, two switched to another TNFi (adalimumab), and one patient continued. At last follow-up, two of three patients that remained on TNFi had full resolution of IgAV despite ongoing TNFi use.
Comparison of baseline characteristics between cases with IBD-IgAV and matched non-IBD IgAV controls is demonstrated in Table 1. No differences were seen in regards to development of end-stage renal disease, resolution of hematuria and/or proteinuria, time to complete IgAV response or first IgAV relapse.
Conclusion: Baseline characteristics and outcomes of patients with IBD-IgAV are similar to those with IgAV without IBD. Development of IgAV is not limited to patients with clinically active IBD. Whether use of TNFi is related to the pathogenesis of IgAV in some patients with IBD remains unclear. Further research into the pathophysiologic connection between IBD and IgAV is needed.

REFERENCES

[1] Saint Marcoux B, De Bandt M. Vasculitides induced by TNFalpha antagonists: a study in 39 patients in France. Joint, bone, spine : revue du rhumatisme. 2006;73(6):710-3.
[2] Sy A, Khalidi N, Dehghan N, Barra L, Carette S, Cuthbertson D, et al. Vasculitis in patients with inflammatory bowel diseases: A study of 32 patients and systematic review of the literature. Seminars in arthritis and rheumatism. 2016;45(4):475-82.
[3] Ko JS, Uberti G, Napekoski K, Patil DT, Billings SD. Cutaneous manifestations in inflammatory bowel disease: a single institutional study of non-neoplastic biopsies over 13 years. Journal of cutaneous pathology. 2016;43 (11):946-55.
[4] Ozen S, Pistorio A, Iusan SM, Bakkaloglu A, Herlin T, Brik R, et al. EULAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. Ann Rheum Dis. 2010;69(5):798-806.
[5] Laresche C, Locatelli F, Biver-Dalle C, Nachury M, Heyd B, Koch S, et al. Severe Henoch-Schonlein purpura complicating infliximab therapy for ulcerative colitis. Cutis. 2017;99(1):E20-e2.

Table 1: Baseline characteristics of patients with inflammatory bowel disease and immunoglobulin-A vasculitis compared to patients with IgAV without inflammatory bowel disease

Characteristic	IBD-IgAV (n=9)	Non-IBD IgAV (n=18)	*p*-value
Age at IgAV diagnosis, years*	40.8±17.5	40.7±17.4	0.96
Male sex	6 (67%)	12 (67%)	1.00
Length of follow-up, years*	1.3±2.6	1.1±1.2	---
Creatinine, mg/dL*	1.0±0.4	0.9±0.3	0.59
eGFR (ml/min/1.73m²)*	91.4±31.6	96.4±22.9	0.72
C-reactive protein, mg/L*	23.3±12.2	27.0±27.4	0.62
Renal involvement	7 (78%)	10 (56%)	0.26
Microscopic hematuria	5 (56%)	7 (39%)	0.41
Proteinuria	7 (78%)	8 (44%)	0.10
Palpable purpura	9 (100%)	18 (100%)	1.00
Abdominal Ischemic symptoms	3 (33%)	2 (11%)	0.161
Disease status at IgAV diagnosis			
Active IBD	5 (56%)	-	-
TNF-α inhibitor at diagnosis	2/5 (40%)	-	-
o Ever TNF-α inhibitor	5/5 (100%)	-	-
Inactive IBD	4 (44%)	-	-
TNF-α inhibitor at diagnosis	3/4 (75%)	-	-
o Ever TNF-α inhibitor	3/4 (75%)	-	-

IBD, inflammatory bowel disease; IgAV, immunoglobulin-A vasculitis; eGFR, estimated glomerular filtration rate; TNF-α, tumor necrosis factor-α inhibitor.
*Mean ± standard deviation

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SAT0250 MUSCLE INVOLVEMENT REVEALED BY 18F-PET-CT IN POLYMYALGIA REUMATICA

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Background: Imaging techniques in polymyalgia reumatica (PMR) have revealed mainly bursitis, tenosynovitis, capsulitis and enthesitis. This is also the case for 18F-FDG-PET-CT. This technique, which has shown its interest in the diagnosis of PMR, allows an assessment of the metabolic activity of the entire musculoskeletal system and in particular of muscle structures.
Objectives: The objective of this work was to evaluate muscle damage using 18F-FDG-PET-CT in PMR.
Methods: This is a retrospective study including patients with PMR (ACR/EULAR 2012 criteria) seen in our department, who had an 18F-FDG PET-CT examination between September 2012 and November 2018. A control group consisting of subjects without rheumatological manifestations who had such an examination as part of neoplastic research or neoplastic disease control was also evaluated. PET evaluation included 17 sites suggestive of PMR, as previously reported [1], leading to a global PET score ranging from 0 to 51. Muscle hypermetabolism areas were similarly rated according to the same Goerres classification [2](0 = no uptake; 1 = slight uptake, less than liver; 2 = uptake like liver; 3 = uptake higher than liver). Muscle activity sites have been identified. A comparison of PMR patients with and without muscle involvement was performed using the Mann Whitney or Fisher's exact test.

Results: 134 cases were reviewed, concerning 80 PMR (mean age 67.9) and 54 "controls" (mean age 68.1). Overall, PET muscle damage was observed in 27 cases (34%) in PMR and 6 cases (11%) in controls (p=0.004). The damage is bi or multi-focal in 16/27 cases. The affected sites are: thighs and ischium-leg (n = 10), spinal (11), piriform/buttocks (7), pectoral (5), large serrated (4), subspinatus/subscapular (3), deltoid (1), trapezius (1). Fasciitis was found in 4 cases. As expected, PMR patients exhibited higher TEP scores than controls (p<0.001). In PMR patients, PET muscle involvement was associated with higher ESR values (p<0.05), but not with age, CRP or global PMR PET score.
Conclusion: Muscle involvement assessed by 18F-Fluorodeoxyglucose PET-CT is frequent in PMR (1/3), located at usual sites of symptoms of the disease, without association with age, CRP levels or global PET score for PMR. Muscle should be carefully evaluated during PET in cases of PMR; these pictures may be a new diagnosis feature of the disease.

REFERENCES

[1] Sondag.M, et al. Rheumatology 2016;55(8):1452-7.
[2] Goerres GW, et al. Clin Nucl Med 2006;31:386-90.

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SAT0251 SEX- AND AGE-RELATED DIFFERENCES IN CLINICAL MANIFESTATIONS OF BEHÇET'S DISEASE IN A LARGE COHORT OF CHINA PATIENTS

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Background: Behçet's disease (BD) is a systemic vasculitis with multiple symptoms such as recurrent oral and/or genital ulceration, skin lesions, ocular lesions, and other systems affection. Studies have been conducted to reveal sex- and age-related differences in clinical characteristics of BD in several countries[1-5], but up to now sex and age influence for Chinese BD patients is very limited.
Objectives: This study aimed to investigate the clinical phenotypes of BD concerning gender and age in China.
Methods: We retrospectively reviewed the medical records of BD patients followed up in the Departments of Rheumatology, Peking Union Medical College Hospital (PUMCH) between March 2014 and January 2019. Demographics, clinical features at onset and during follow-up were obtained from a review of medical records.
Results: A total of 489 BD patients were included in our database: 286 males (58.49%) and 203 females (41.51%) (Sex ratio M/F was 1.41), with a median age of 34 years (interquartile range: 28-44 years). Recurrent oral ulceration was the most common manifestation (96.32%), followed by genital ulceration (71.17%), skin lesions (57.67%), vascular lesions (25.36%), and ocular involvement (24.13%). Gastrointestinal (GI) involvement (15.13%), positive pathergy test (14.11%), and neurological involvement (5.93%) were less frequently observed. The comparative study between males and females revealed that ocular lesions (28.67% vs 17.73%, P=0.005), vascular lesions (31.47% vs 16.75%, P< 0.001) and positive pathergy test (17.83% vs 8.37%, P=0.002) were more common in male, while genital ulceration was more common in female (64.34% vs 80.79%, P<0.001). Regarding age difference, ocular lesions (P=0.017) were more frequently observed in younger patients, while vascular lesions(P=0.024) and GI symptoms(P=0.010) were more common in older patients. Gender differences of these manifestations were more prominent in certain age groups among 20-50 years old than other groups.
Conclusion: These analyses support that the clinical features of Chinese BD were different depending on sex and age.

REFERENCES

[1] Bonitsis, NG. et al. *Gender-specific differences in Adamantiades-Behçet's disease manifestations: an analysis of the German registry and meta-analysis of data from the literature*. Rheumatology 2015. 54, 121.
[2] Ishido, T. et al. Clinical manifestations of Behçet's disease depending on sex and age: results from Japanese nationwide registration. Rheumatology 2017. 56,1918-1927.
[3] Ugurlu, N. et al. *The natural course and factors affecting severity of Behçet's disease: a single-center cohort of 368 patients*. Rheumatol Int 2015. 35, 2103-7.
[4] Khabbazi A, et al. *Demographic and clinical features of Behcet's disease in Azerbaijan*. Int J Rheum Dis 2014. 21,1114-1119.
[5] Hamzaoui, A. et al. *Comparison of clinical features of Behcet disease according to age in a Tunisian cohort*. Acta Med Iran 2014,52,748.

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Scleroderma, myositis and related syndromes

SAT0252 AN EVALUATION OF THREE DIFFERENT METHODS TO EVALUATE SKIN IMPAIRMENT IN SYSTEMIC SCLEROSIS PATIENTS

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Background: One of the characteristics of systemic sclerosis (SSc) is an increase in dermal thickness (DT) (1-3). Although the standard method to evaluate the extent of skin involvement is the modified Rodnan skin score (mRSS) (3,4), high frequency ultrasounds (US) and the plicometer skin test (Plicometry) (5-8) are now being used in SSc patients.
Objectives: The aim of this study was to determine any correlations between mRSS, US and Plicometry during the evaluation of skin impairment in SSc patients.
Methods: A total of 63 SSc patients (mean age 64±13SD years, mean SSc duration 7±6 years) and 63 healthy subjects (HS) (mean age 64 ±12SD years) were enrolled.
The three methods (mRSS, US and Plicometry) were used to evaluate skin impairment in the seventeen areas of the skin usually evaluated by mRSS (face, fingers, dorsum of hands, forearms, arms, chest, abdomen, thighs, legs and feet) and the total score was calculated, as previously reported (1,3,4,8). Intra-rater reliability of the three techniques was assessed by having the same rater performing 2 consecutive measurements at each skin site. Statistical evaluation was performed by non-parametric tests.
Results: A significant positive correlation was observed between the three methods used to evaluate DT in the SSc patients (mRSS vs US r=0.64, p<0.0001; mRSS vs Plicometry r=0.97, p<0.0001; US vs Plicometry r=0.55, p<0.0001). Conversely, there was no correlation between these parameters in the CNT group (p>0.05). The intraclass correlation coefficients for mRSS was 0.95, 0.97 for US and 0.96 for Plicometry. Data collection for mRSS took almost 10 minutes, 15 minutes for Plicometry and 20 minutes for US.
Conclusion: This study demonstrates a significant relationship between mRSS, US and Plicometry in the DT evaluation of SSc patients. The SSc patients had statistically significantly higher values than HS when the 3 techniques were used to evaluate the seventeen skin areas.

REFERENCES:

[1] Cutolo M, et al. Best Pract Res Clin Rheumatol. 2016;30:670-687.
[2] Ruaro B, et al. Arthritis Rheumatol 2015; 67 (suppl 10).
[3] Clements P, et al. J Rheumatol 1995;22:1281-5.
[4] CzirjákL, et al. Ann Rheum Dis. 2007; 66: 966-9.
[5] Hesselstrand R, et al. Rheumatology 2008;47:84-7.
[6] Kaloudi O, et al. Ann Rheum Dis. 2010;69:1140-3.
[7] Ruaro B, et al. Microvasc Res. 2018;115:28-33.
[8] Parodi MN, et al. Br J Rheumatol. 1997;36:244-50.

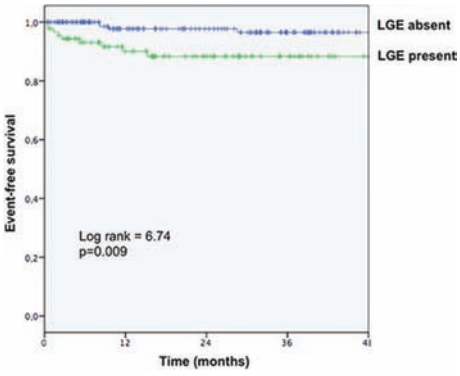
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SAT0253 **PROGNOSTIC VALUE OF CARDIAC MAGNETIC RESONANCE IN SYSTEMIC SCLEROSIS**

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Background: Cardiac involvement is frequent in patients with systemic sclerosis (SSc). It is often subclinical, but significantly affects the prognosis of the disease. Cardiovascular magnetic resonance (CMR) is the non-invasive gold standard to quantify biventricular functional parameters and to perform a myocardial tissue characterization.
Objectives: To evaluate the prognostic value of CMR for cardiac events in SSc.
Methods: Two hundred and seventy-three SSc patients with a thorough clinical assessment underwent a CMR exam using a 1.5 T GE scanner. We quantified biventricular function parameter by SSFP cine images, oedema by STIR T2 images, and macroscopic fibrosis by late gadolinium enhancement (LGE) technique. Patients were followed-up and cardiac events were recorded as new onset of pulmonary arterial hypertension (PAH), new onset of heart failure (HF), or at least sustained ventricular tachycardia.
Results: Mean follow-up was 23.9 ± 17.0 months. During the follow-up a total of 14 events occurred (3 new onset PAH, 5 new onset HF, 6 ventricular tachycardia). CMR predictors of cardiac events by univariate analysis were left and right ventricular ejection fractions, indexed left and right atrial areas, and LGE (see Table). Myocardial fibrosis by LGE was the only independent predictor at multivariate analysis (hazard ratio 3.175; 95% C.I. 1.021-9.870, see Figure).

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Left Ventricular Ejection Fraction	0.904 (0.843 – 0.969)	**0.004**	0.935 (0.868 – 1.007)	0.075
Indexed Left Atrial Area	1.244 (1.002 – 1.546)	**0.048**		
Right Ventricular Ejection Fraction	0.926 (0.884 – 0.969)	**0.001**	0.958 (0.904 – 1.014)	0.139
Indexed Right Atrial Area	1.384 (1.059 – 1.809)	**0.017**		
Right Ventricular End-Diastolic Mass	1.039 (0.991 – 1.091)	0.115		
Right Ventricular End-Systolic Mass	1.036 (0.988 – 1.086)	0.148		
T2 ratio	0.247 (0.019 – 3.251)	0.288		
Late Gadolinium Enhancement	3.871 (1.289 – 11.623)	**0.016**	3.175 (1.021-9.870)	**0.046**



Conclusion: Cardiac magnetic resonance anatomical and functional parameters of both the left and right heart have significant prognostic value in patients with SSc.
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SAT0254 **VASODILATOR THERAPY IN THE LONG TERM PREVENTION OF MYOCARDIAL MANIFESTATIONS IN SYSTEMIC SCLEROSIS (SSC): RESULTS FROM DESSCIPHER INCEPTION COHORT STUDY**

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Background: Calcium channel blockers (CCB) and angiotensin converting enzyme inhibitors (ACEinh) are known to improve in the short term, cardiac perfusion and function in patients with SSc (Parks JL et al. Rheum Dis Clin North Am 2014). No study has been carried out so far to investigate the long-term effectiveness of these drugs.
Objectives: To address this topic and other aspects of the management of SSc, the DeSScipher (To decipher the optimal treatment of SSc) project was submitted to and financed by the European Community (FP7-HEALTH n°305495).
Methods: From Dec.1, 2012 to Nov. 30, 2015, 512 SSc patients who, as inclusion criterion, had no significant gut or lung or kidney involvement, were treated for 0.5-4 years (median 2.31) with either (n= 359: group 1) vasodilator treatment (i.e. CCB, or ACE-inh or Angiotensin II receptor blockers [AgIIrb] or a combination of them i.e. CCB plus either ACEinh or AgIIrb) or (n= 153:group 2) no vasodilator therapy. The 296 patients of the 2 groups, who had been assessed at baseline and along the follow-up for conduction blocks (CB), ventricular arrhythmias (VA), pacemaker implantation (PMI), left ventricular ejection fraction (LVEF) < 55%) and congestive heart failure (CHF), and sudden cardiac death (SCD) during follow-up, were investigated for the cumulative incidence rate (IR) of all these events. The IR of single manifestations were calculated in the patients investigated for each of them. Cox regression analysis was carried out in the 296 patients with no missing value to identify independent predictors of the occurrence of any myocardial manifestation.
Results: During 1164 patient-years follow-up,6/508 were implanted a PM,10/506 developed a LVEF<55%, 2/492 a CHF,11/325 a VA, 36/305 a CB, none underwent a SCD, any of these manifestations intervening in 59 out of the 296 investigated for all the manifestations. The IR of PMI and VA was greater in group 2 patients as compared with group 1 (1.3 vs 0.2x100 pts/year; p=0.02) and (2.7 vs 1.1x100 pts/year; p=0.077). In stepwise Cox regression analysis, male gender (HR 2.44, 95%CI 1.3-4.6; p=0.005), age at enrollment (HR 2.97, 95%CI 1.7-5.2; p=0.0002) and vasodilator therapy (HR 0.41, 95%CI 0.2-0.7; p=0.002) were independent positive and respectively, negative predictors of new onset cardiac manifestations.
Conclusion: Long term vasodilator therapy is likely to have a preventative role on the occurrence of myocardial manifestations of SSc.
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SAT0255 EVALUATION OF THE CARDIOVASCULAR INVOLVEMENT OF SYSTEMIC SCLEROSIS USING NON-INVASIVE CARDIAC IMAGING TECHNIQUES

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Background: Systemic sclerosis (SSc) is a systemic disease that may affect many organs; among them, cardiac involvement. The prevalence of cardiac involvement in SSc varies depending on the sensitivity of the methods used for its detection. Indirect evidence suggests that subclinical cardiac involvement may eventually occur in the vast majority of patients with SSc. Early detection and monitoring of myocardial involvement are integral to SSc management, as cardiovascular involvement is known to be a poor prognostic indicator when present

Objectives: To describe myocardial perfusion abnormalities and potentially associated coronary arteries lesions using non-invasive imaging techniques in a group of patients with SSc and suggestive symptoms of myocardial involvement (symptomatic) in comparison with a control group of patients with SSc without cardiac symptoms

Methods: A retrospective observational study was performed including a total of 61 patients diagnosed with SSc, 52 symptomatic, with dyspnea and/or chest pain (57.98 ± 12.3 years, 45 women) and 9 asymptomatic controls (50.2±15.21 years, 8 women).

All patients underwent a post-stress (treadmill or pharmacological) myocardic perfusion gated-SPECT, a cold-induced stress SPECT, that were compared to a rest SPECT (to assess ischemia and/or necrosis), as well as a cardiac CT-angiography (to asses significant coronary arteries lesions, considering stenosis of more than 50%)

Results: Twenty-one out of the 52 symptomatic patients (50%) showed myocardial perfusion defects in the stress-rest SPECT: 13 (25%) showed ischemia, 13 (25%) fibrosis/necrosis, and 5 (9.6%) ischemia and necrosis. In the cold-induced SPECT, 17 patients (32.7%) had myocardial perfusion abnormalities: 10 (19.2%) showed ischemia, 13 (25%) fibrosis/necrosis and 6 (11.5%) ischemia and necrosis.

In the other hand, of the 9 asymptomatic patients only 1 (11%) had ischemia and necrosis in the stress-rest SPECT, being only positive for necrosis in the cold-induced SPECT images.

In the cardiac CT-angiography, 7/52 patients (13.4%) showed significant coronary lesions, 4 (57.2%) of them with perfusion defects in the SPECT images, and 3 (42.8%) without significant perfusion alterations

Of the 9 asymptomatic patients, 1 (11%) had significant coronary lesions, being the same patient who presented perfusion defects in myocardial SPECT images

Conclusion: The gated-SPECT is a sensitive tool for detecting myocardial perfusion alterations, normally with no associated significant coronary lesions, suggesting microvascular abnormalities. In this cohort, myocardial perfusion abnormalities were detected in 50% of symptomatic patients, whereas in only 11% of non-symptomatic patients

REFERENCES

[1] Fernández-Codina A, Simeón-Aznar CP2, Pinal-Fernandez I, Rodríguez-Palomares J, Pizzi MN, Hidalgo CE, Guillén-Del Castillo A, Prado-Galbarro FJ, Sarria-Santamera A, Fonollosa-Plà V, Vilardell-Tarrés M. **Cardiac involvement in systemic sclerosis: differences between clinical subsets and influence on survival**. Rheumatol Int. 2017 Jan;37(1):75-84. doi: 10.1007/s00296-015-3382-2. Epub 2015 Oct 25.

[2] Rangarajan V, Matiasz R, Freed BH. Cardiac complications of systemic sclerosis and management: recent progress. Curr Opin Rheumatol. 2017 Nov;29(6):574-584. doi: 10.1097/BOR.

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SAT0256 EFFICACY AND SAFETY OF ANTIFIBROTIC THERAPY IN DIFFUSE INTERSTITIAL PULMONARY DISEASE ASSOCIATED WITH SYSTEMIC AUTOIMMUNE DISEASES

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Objectives: Assess the efficacy and safety of antifibrotic agents (pirfenidone and nintedanib) in refractory diffuse interstitial lung disease (DILD) associated with systemic autoimmune diseases (SAD).

Methods: Open observational study in patients with active symptomatic DILD-SAD (evidence of clinical and functional impairment) despite treatment with glucocorticoids (GC) and immunosuppressant therapy.

Results: We included 13 patients (8 women) with a mean age (± SD) of 55 ± 12 years (range, 27-71). The baseline SAD were: eighth systemic sclerosis, one rheumatoid arthritis, one ankylosing spondylitis, one microscopic polyangiitis with pulmonary fibrosis and one interstitial lung disease with autoimmune characteristics (IPAF). Mean time from diagnosis to initiation of antifibrotic therapy was 3 ± 8.2 years (IQR 25-75%: 1.6-9.5). The histopathological patterns found were: seven cases (54%) of usual interstitial pneumonia (UIP), three (23%) nonspecific interstitial pneumonia (NSIP), two cases (15%) combined pattern of pulmonary fibrosis plus emphysema (CPFE), and one (8%) non-classifiable pulmonary fibrosis (without histospecific radiological pattern).

In addition to GC, the previous therapy tested for DIDL was mycophenolate mofetil (MMF) in 77% of the patients, cyclophosphamide (8 intravenous boluses) in 46%, and rituximab (RTX) in 54% (the number of RTX cycles administered were 4 ± 3.3; range, 1-9). Despite this, during the year prior to start the antifibrotic drugs, all patients presented a worsening in the values of % pFVC (-8.77%) and% pDLCO (-12.41%).

Five (38%) patients received pirfenidone at doses of 3 tablets/8 hours (2403 mg/day) and eight (62%) nintedanib (5 at a dose of 150 mg/ 12 hours and 3 at a dose of 100 mg/ 12 hours).

Antifibrotic therapy was administered in combination with MMF (1.5-2 g/ day) in 10 patients (77%) and with rituximab in 3 (23%), in addition to GC at doses between 5 and 20 mg/ prednisone per day. The mean

	Pre-treatment (mean ± SD)	Post-treatment (mean ± SD)	Delta (mean)	p
%pFVC	67.9 ± 15.6	74.2 ± 13.9	+ 5.13	NS
%pTLC	66 ± 10.8	77 ± 15.55	+ 4.86	NS
%pDLCO	37.8 ± 7.22	44 ± 7.32	+ 4.42	NS
Walking (meters)	409 ± 52	415 ± 103	+ 7.57	NS

The response in the Pulmonary function testing (PFT) in these 9 patients categorized according to the definitions of the American Thoracic Society was as follows: A)% pFVC: stabilization in 5 cases and improvement in 4; B)% pDLCO: stabilization in 7 cases and improvement in 3.

duration of follow-up was 15 months (range 3-59). At the end of the follow-up period, 10 of the 13 patients (77%) were still in treatment. In 2 patients (15%) the therapy failed, requiring lung transplantation in 1 case (after 7 months of therapy), while an autologous hematopoietic stem cell transplant was conducted in the other patient (after 13 months of antifibrotic). In one patient (8%) the treatment was discontinued due to adverse effects.

When quantifying the degree of response in patients who continued treatment, only 9 of the 10 patients were included in the analysis, since 1 had only 3 months of therapy. In these 9 patients there was an improvement of% pFVC (mean: +5.13; SD: 8.38) and% pDLCO (+4.42; SD: 5.06). The evolution of the efficacy variables analyzed is shown in the table.

The response in the Pulmonary function testing (PFT) in these 9 patients categorized according to the definitions of the American Thoracic Society was as follows: A)% pFVC: stabilization in 5 cases and improvement in 4; B)% pDLCO: stabilization in 7 cases and improvement in 3.

The frequency of adverse effects was 31% (4/13), but only the treatment was withdrawn in 1 patient (8%). Three patients presented digestive discomfort that forced to reduce the dose of the antifibrotic. One patient developed a toxic hepatitis due to nintedanib after 4 months of treatment that forced the withdrawal of the drug, replacing it 1 month ago with pifernidone. None of the patients died during the follow-up period.

Conclusion: Our data provides evidence of the safety and tolerability of both pirfenidone and nintedanib in patients with DIDL-SAD refractory to GC and immunosuppressant therapy.

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SAT0257 THE SIGNIFICANCE ON THE TRANSITION THROUGH DIFFERENT PATTERNS OF NAILFOLD MICROVASCULAR DAMAGE ON THE COURSE OF SYSTEMIC SCLEROSIS

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Objective: To investigate the timing of transition through different patterns of nailfold microvascular damage in systemic sclerosis (SSc) patients and to determine the significance of this transition.

Methods: In the period January 2012 to December 2017, 400 SSc patients were followed up by nailfold videocapillaroscopy (NVC) the same operator (SPD) every 6 months. Demographic, clinical and laboratory data were recorded. The capillaroscopic findings were classsified as normal, nonspecific or scleroderma pattern ("early", "active", or "late").The evolution on the NVC pattern over time was monitored and recorded.

Results: The transition of microvascular damage through different NVC patterns of microangiopathy was seen in 53/400 (13.25%) SSc patients. At the baseline 11/53 (21%) patients had the non-specific changes, the early pattern had 25/53 (47%) patients, and the active pattern had 17/53 (32%) SSc patients. The mean ± SD time of progression from one to another NVC patterns was 27.68 ± 35.11 months. Improvement of the NVC patterns was found in 15/53 (28%) patients and deterioration in the remaining 38 (72%) patients. The mean time of progression from non-specific to early pattern (in 10 patients) and non-specific to active pattern (in 1 patient) was 14.5 ± 9.73 vs. 12 months, respectively. Time of changed from early to nonspecific (in 7 patients), early to active (in 17 patients) and early to late pattern (in 1 patient) was 30.85 ± 22.56 vs 22.29 ± 16.61 vs 24 months, respectively. Time of changed from active to early (in 8 patients) and active to late pattern (in 9 patients), was 26.25 ± 11.1 vs 18.00 ± 13.97 months, respectively. Progression of non-specific to early or active NVC pattern was related with limited form of SSc (91%), diffuse hand swelling (54%), arthralgia/arthirtis (45%) and involvement of lungs (48%). Also, progression of early to active NVC pattern was related with limited form of SSc (64%), sclerodactyly (48%) and involvement of lungs (48%). In contrast, progression of active to late NVC pattern was related with diffuse form of SSc (53%), digital ulcerations (35%) and more frequent involvement of lungs (65%). These differences in the frequency of involvement of certain organs were not statistically significant.

Conclusion: These results demonstrate dynamic transition of microvascular damage through different NVC patterns of microangiopathy in about 13% of SSc patients. Patients with rapid progression from the early to active, as well as active to the late NVC patterns (<2 years) should be monitored closely, because they are at risk of further significant damage to the internal organs.

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SAT0258 SEXUAL HEALTH IMPAIRMENT IN WOMEN WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease that may affect all aspects of life including sexual function.

Objectives: To assess sexual function, pelvic floor function and sexual quality of life women with SSc compared to age-/sex-matched healthy controls (HC). To subanalyze sexual function in sexually active individuals.

Methods: In total 47 women with SSc (mean age: 50.5, disease duration: 5.6 years, lcSSc/dcSSc: 27/20, mRSS: 12.7, ESSG activity index: 2.5), who fulfilled the ACR/EULAR 2013 criteria, and 47 healthy women (mean age: 50.5) filled in 11 well-established and validated questionnaires assessing sexual function, pelvic floor function, quality of life, fatigue, physical activity and depression. Data are presented as mean±SEM.

Results: Compared to HC, patients with SSc had significantly higher prevalence and greater severity of sexual impairment (FSFI, BISF-W), pelvic floor dysfunction (PISQ-12, PFIQ7), and worse sexual quality of life (SQol-F) (table 1). There were no significant differences in sexual function between limited and diffuse SSc. Even sexually active SSc patients reported significantly greater sexual health impairment compared to sexually active HC. Sexual health impairment in SSc was associated with dis-

Table 1.

Questionnaire: score range	SSc (n=47)	HC (n=47)	p-value	SSc SA (n=29)	HC SA (n=29)	p-value
FSFI :2(worst)-36 (best)	14.7 ±1.6	25.7 ±1.6	p<0.0001	20.6±1.7	28.5±1,4	p<0.0001
BISF-W:-16(worst)-75(best)	16.6 ±2.5	31.0 ±2.6	p=0.0002	25.7±2.8	34.9±2.3	p=0.0143
SQoL-F: 0(worst)-100(best)	53.5 ±3.7	79.9 ±3.1	p<0.0001	58.0±5.0	84.5±2.6	p<0.0001
PISQ–12: 0(best)-48(worst)	14.6 ±0.9	8.4±0.6	p<0.0001	13.6±1.0	7.9±0.7	p<0.0001
PFIQ7: 0(best)-300 (worst)	29.0 ±6.2	7.9±2.0	p=0.0075	15.5±5.0	9.3±2.8	ns

Abbreviations: FSFI: Female Sexual Function Index; BISF-W: Brief Index of Sexual Function for Women; SQoL-F: Sexual Quality of Life Questionnaire; PISQ–12: Pelvic Organ Prolapse/ Urinary Incontinence Sexual Questionnaire short form; PFIQ7: Pelvic Floor Distress Inventory Questionnaire, SA: sexually active; ns:not significant

Table 2.

Parameter: score range	Correlated parameters	r	p-value
FIS (fatigue):	FSFI (sexual function)	-0.446	p=0.0016
0(best)-160(worst)	BISF-W (sexual function)	-0.445	p=0.0016
MAF (fatigue): 1(best)-50(worst)	SQol-F (sexual quality of life)	-0.415	p=0.0050
BDI-II (depression):	FSFI	-0.485	p=0.0005
0(best)-63(worst)	BISF-W	-0.483	p=0.0005
	SQoL-F	-0.375	p=0.0119
	PIFQ-7 (pelvic floor function)	0.445	p=0.0017
HAP (physical activity):	FSFI	0.412	p=0.0040
0(worst)-94(best)	BISF-W	0.398	p=0.0055
SHAQ (scleroderma health status):	FSFI	-0.557	p<0.0001
0(best)-100(worst)	BISF-W	-0.505	p=0.0002
	PIFQ-7	0.429	p=0.0025
ESSG activity index: 0(best)-10 (worst)	PISQ-12 (pelvic floor function)	0,322	p=0.0400
Disease duration	PIFQ-7	0.361	p=0.0124

Abbreviations: FIS: Fatigue Impact Scale; MAF: Multidimensional Assessment of Fatigue; BDI-II: Beck's Depression Inventory II; HAP: Human Activity Profile; SHAQ: Scleroderma Health Assessment Questionnaire; ESSG: European Scleroderma Study Group

ease activity/duration, health status, physical activity, fatigue and depression (table 2).

Conclusion: Women with SSc reported significantly impaired sexual function, sexual quality of life and pelvic floor function than age-matched HC. Worse scores in SSc were associated with disease activity/duration/health status, physical activity, fatigue, and depression.

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SAT0259 PREDICTIVE FACTORS FOR TREATMENT RELATED MORTALITY AND MAJOR ADVERSE EVENTS AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR SYSTEMIC SCLEROSIS: RESULTS OF A LONG TERM FOLLOW-UP MULTICENTRE STUDY

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Background: Autologous hematopoietic stem cell transplantation (HSCT) has shown superior efficacy to cyclophosphamide pulse therapy in systemic sclerosis (SSc) but its application is hampered by high treatment related mortality (TRM). To date factors, other than smoking, predicting TRM are unknown.

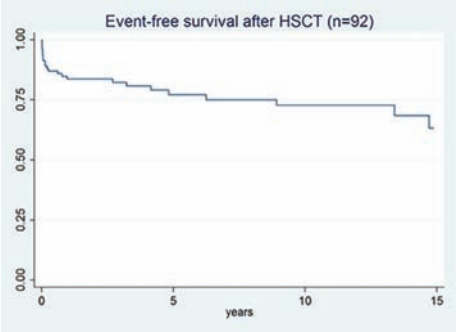
Objectives: To describe event-free survival and TRM after HSCT and to evaluate the predictive value of baseline characteristics. Event-free survival was defined as the absence of mortality or major organ failure (i.e. cardiac failure (left ventricular ejection fraction (LVEF) < 30%, respiratory failure (resting PaO2 < 8kPa/60 mm Hg or PaCO2 > 6,7 kPa or chronic oxygen supplementation), or renal failure requiring dialysis.

Methods: All patients who started with the procedure of HSCT for SSc in the Netherlands between 1.1.1998 and 31.12.2016 were included. Except in 4 patients, eligibility criteria and procedures of the ASTIS trial were used (1). A Kaplan-Meier event-free survival curve was constructed. All deceased patients were discussed in a consensus meeting, to determine the cause of death as TRM, progression of SSc or other. The univariate association of TRM and event-free survival with baseline characteristics (gender, age, disease duration, smoking ever, FVC, DLCO, LVEF) was examined by Cox regression analysis.

Results: 92 patients were included, including 4 patients with limited cutaneous subtype who were treated because of interstitial lung disease. The median (IQR) follow-up time was 4.5 (2.3 – 12.3) years. Twenty patients died during the observation period of whom 10 (10.8%, 9 males) in the first year because of TRM. Twelve patients (13.1%) developed major organ failure (6 lung, 3 kidney and 3 heart) of whom 8 died during the observation period. Event-free survival after five and ten years was 68% (40/59 patients) and 59% (30/51), respectively. TRM was significantly associated with male gender (HR (95% CI): 8.7 (1.1 -68.9), but not with smoking; events were associated with male gender, older age and LVEF <50% at baseline (HR: 4.08 (1.5 – 11.0); 1.1 (1.0-1.1) and 4.7 (1.1-20.6), respectively).

Table 1:. demographic and disease related factors

Male/female	49/43
LcSSc/DcSSc	4/88
Age at HSCT mean (SD) (year)	46.8 (10.3)
Disease duration at HSCT mean (SD)(year)	2.4 (2.4) median 1.6
mRSS mean (SD)	26 (10.1)
Antibodies: ANA, ATA, Anti-RNAP positive	88/92; 34/92; 1/92
Ever smoker	54/84
FVC as% pred. mean (SD)	84.9 (22.7)
DLCO as% pred mean (SD)	55.1 (16.2)
LVEF < 50% (by echo)	3/92



Conclusion: In this national cohort study of HCST in patients with SSc and poor prognosis we observed a median event-free survival of 4.3 years. TRM was 10,8% and major events occurred in 13%. TRM was correlated to male gender. Low LVEF, male gender and older age were correlated with major events.

REFERENCES

[1] van Laar JM, Farge D, Sont JK, et al. Autologous hematopoietic stem cell transplantation vs intravenous pulse cyclophosphamide in diffuse cutaneous systemic sclerosis: a randomized clinical trial. JAMA. 2014;311 (24):2490-8.

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SAT0260 MUSCULAR INVOLVEMENT OF THE LOWER LIMBS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: A MRI EVALUATION

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Background: Since many years, muscular magnetic resonance imaging (MRI) has been used in the diagnosis and follow-up of patients with idiopathic inflammatory myopathies (IIM), but the clinical significance and the pattern of the muscular alterations (edema, fatty infiltration and atrophy) in different subsets of the disease are still not well defined.

Objectives: The aims of this study were to analyse possible differences in the involved muscles between dermatomyositis (DM) and polymyositis (PM); the correlations between the pattern of muscular involvement in different subsets of the disease and disease parameters in a monocentric cohort of patients.

Methods: We retrospectively collected data from 85 patients with poly and dermatomyositis (EULAR/ACR criteria) who performed pelvic and tights muscle MRI from January 2010 to December 2018: 27 had DM and 58 PM, mean age 58.6±13.4 years, mean disease duration of 45±73 months. The images in 22 muscles for the presence of muscular edema, fatty infiltrates and atrophy were assessed by a dedicated radiologist. Moreover, data about serum creatine kinase (CK) and manual muscle

test 8 (MMT8) were collected. Data were reported as median±interquartile range; non-parametric tests were used for the analysis.
Results: Sixty-three patients presented muscular edema in at least one muscle. Patients with muscular edema had higher CK levels (1506±1976 vs 235±224 p<0.001) lower disease duration (9.5±47.0 vs 19.8±97.2 p=0.031). and lower MMT8 (63.6±11.2 vs 69.8±10.7 p=0.031).
Forty-eight patients presented fatty infiltrates that were more frequent in older patients (63.1±11-3 vs 52.8±13.7 p=0.01) and in those with longer disease duration (39.1±95.4 vs 9.5±12.5 p=0.024). CK levels and MMT8 were not different in patients with or without muscular fatty infiltrates. With the multivariate analysis the disease duration represents the only independent factor for the presence of muscular fatty infiltrates (p=0.05).
Muscular atrophy was present in 17 patients but it was not correlated to age and disease duration. CK and MMT8 were not different in presence/ absence of fatty infiltrates or muscular atrophy.
Edema and atrophy were not different between poly- and dermatomyositis. The fatty infiltrate was more present in the posterior compartment of the tights (biceps femoris and semitendinosus muscle) in patients with PM compared to DM (68.2% vs 29.6% p=0.046).
Conclusion: The alterations identified with MRI in our cohort changed according to the disease duration and the age of the patients. In particular, fatty infiltration was more frequent in patients with longer disease duration, but was not associated to CK levels and muscular weakness. Moreover, fatty infiltration was prevalent in the posterior compartment of the tights in PM patients.
Muscular MRI is widely used in the diagnosis and follow-up but the clinical meanings of the different alterations still need to be investigated.
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SAT0261 CHARACTERISTICS ASSOCIATED TO SCLERODERMAL RENAL CRISIS, AND INCIDENCE VARIATION OVER TIME IN THE RESCLE REGISTRY

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Background: Scleroderma Renal Crisis (SRC) is a serious complication of Systemic Sclerosis (SSc). Nowadays, it seems that there is a reduction in its prevalence and mortality[1].
Objectives: To evaluate the characteristics of patients with SRC in a large cohort of SSc pacients. To investigate predictors of SRC, and epidemiologic differences over time.
Methods: 1933 patients were collected in ongoing registry of Spanish SSc pacients – RESCLE. We did descriptive study and epidemiologic analysis.
Results: Out of 1933 SSc, 43 (2.2%) developed SRC. Univariate analysis showed significant differences of SRC vs. non-SRC cases: SSc subtypes: diffuse cutaneous SSc (dcSSc), 72% vs. 19%; limited cutaneous SSc (lcSSc), 26% vs. 61%. Demographics: Female gender, 77% vs. 89%; time from SSc onset to SSc diagnosis, 3.0±8.0 vs. 6.6±9.5 years; arterial hypertension (HT), 56% vs. 32%. 1st manifestation: Raynaud's phenomenon (RP), 68% vs. 82%. Clinical manifestations: RP, 88% vs. 96%; digital ulcers, 70% vs. 38%; arthritis, 45% vs. 20%; myositis, 30% vs. 13%; joint contractures, 45% vs. 18%; intestinal involvement, 24% vs. 11%; malabsorption, 24% vs. 7%; interstitial lung disease 58% vs. 41%; pulmonary HT, 56% vs. 29%; pericardial effusion, 28% vs. 7.4%; pericarditis, 24% vs. 8.3%; ischemic cardiopathy, 31% vs. 12%; diastolic dysfunction, 67% vs. 34%. Capillaroscopy: active pattern 77% vs. 33%. Immunological data: anti-Topoisomerase I, 39% vs. 20%; anti-centromere, 15% vs. 49%; anti-RNApol III, 45% vs. 11%. Prognosis: Overall mortality, 56% vs. 18%; SSc-related mortality, 83% vs. 49%. Survival at 5, 10, 20, and 30 years was 73% vs. 96%, 56% vs. 92%, 28% vs. 80%, and 28% vs. 67%, respectively. Treatment: ACEI use, 35% vs. 14%, corticoid use, 51% vs. 25%. Multivariate analysis: dsSSc subtype, RR 22.68 (5.81-88.51) p<0.001; intestinal malabsorption, RR 7.35 (2.55-21.18) p<0.001, and active capillaroscopy pattern RR 7.26 (1.61-32.7) p<0.010. Prevalence of SRC (P) in dcSSc subtype 7.8%, and in lcSSc subtype 0.9%. P over decades: P-80's, 3.8%; P-90's, 2.7%; P-00's: 2.3% and P-10's: 0.9%, achieving statistical significance in the last decade RR: 0.33 (0.13-0.85) p=0.014.
Conclusion: In RESCLE cohort, SRC predominated in dcSSc patients, and it was associated to intestinal malabsorption, and an active pattern by capillaroscopy. SRC showed a very poor prognosis. Finally, we evidenced a decreasing prevalence of SRC over time in our cohort.

REFERENCE

[1] Turk M, et al. The Frequency of Scleroderma Renal Crisis over Time: A Metaanalysis. J Rheumatol 2016; 43: 1350.

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SAT0262 MODIFIED ACR COMPOSITE RESPONSE INDEX IN SYSTEMIC SCLEROSIS SCORE SHOWS SENSITIVITY AND EXTERNAL VALIDATION TO MEASURE MAGNITUDE OF RESPONSE AT 12 MONTHS IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

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Background: The Composite Response Index in Systemic Sclerosis (CRISS) is a 2-step process for the probability of improvement of patients with diffuse cutaneous systemic sclerosis (dcSSc) ranging from 0.0 (no improvement) to 1.0 (1). The limitation of probability is that it does not measure magnitude of response and it cannot be negative, hence reflecting worsening.
Objectives: Here we aimed to test the performance of CRISS numerator normalised by baseline values to assess% change at 12 months in an observational cohort.
Methods: Consecutive dcSSc patients were included in the study at a single centre. Clinical data were collected at baseline and 12 months and CRISS calculated using the published formula. To explore the quantitative value of the numerator, each of the 5 domains was corrected for their baseline value (e.g (12 months baseline)/baseline = Delta%) while keeping their original relative weight in the formula. The weighted sum was then divided by the number of domains. The modified CRISS (mCRS) was then compared with the original CRISS score and with another composite score validated in randomized controlled trials, the Global Ranked Composite Score (GRCS) (2). Death and organ failure were also included and assigned the worst negative values. Spearman's test was used for Prism 7 correlation analysis. $P < 0.05$ was considered significant.
Results: Thirty-three dcSSc patients were enrolled. Twenty-one patients had a CRISS = 0%. Twelve patients had a positive CRISS ranging from 1% to 77%. 18/21 patients with CRISS = 0% showed a negative mCRS (negative response = worsening) ranging from -9% to -2500%. 10/12 with positive CRISS showed a corresponding positive mCRS ranging from 1% to 22%. mCRS had a significant correlation with CRISS ($r = 0.5$, $p = 0.003$) and GRCS ($r = 0.7$, $p < 0.0001$) despite the low number of patients enrolled.
Conclusion: Normalization by baseline data within CRISS numerator offers a quantitative score to assess magnitude of response, considering the 5 domains and their relative weight within the original CRISS. The mCRS

measures magnitude of response rather than probability of response and includes the possibility of measuring worsening of disease. Application of the simple formula to the results of RCTs adopting CRISS as explorative efficacy objective will determine the validity of mCRS in offering quantitative assessment of response in SSc.

REFERENCE

[1] Khanna D, Berrocal VJ, Giannini EH, et al. The American College of Rheumatology Provisional Composite Response Index for Clinical Trials in Early Diffuse Cutaneous Systemic Sclerosis. Arthritis Rheumatol 2016;68:299-311.
[2] Sullivan KM, Goldmuntz EA, Keyes-Elstein L, et al. Myeloablative Autologous Stem-Cell Transplantation for Severe Scleroderma. N Engl J Med 2018; 378:35-47.

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SAT0263 MALIGNANT CONDITIONS IN SYSTEMIC SCLEROSIS PATIENTS, SINGLE CENTER EXPIRIENCE

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Background: Internal organ complications (interstitial lung disease [ILD], pulmonary hypertension [PAH], renal crisis [SRC], gastrointestinal involvement [GIT], etc.) have significant influence on scleroderma (SSc) patients' morbidity and mortality; malignancy could contribute to SSc outcome.
Objectives: We aim to assess the incidence of malignancy, clinical and laboratory factors associated with this complication.
Methods: We identified 43 patients with biopsy and/or imaging confirmed malignant conditions (SSc-C); additionally, case-control study was performed with identifying SSc patients without cancer (All-NC, N=86) divided into two subgroups: matching age (Age-NC, N-43) and matching disease duration (DD-NC, N=43).
Results: Since 2004, 424 SSc patients were assessed at our center (340 EUSTAR registry participants); 43 (10.1%) SSc-C patients (7 males [16.3%]; age [years, standard deviation, SD] 68.1[12.7]; age at SSc onset 52.9[14.9]; age at 1st cancer diagnosis 54.2[12.7]; smoking 12 [27.9] had various types of tumors: breast 9; lung 8; neck & head 8 (brain-3, thyroid-3, parotis-1, laryngs-1); genito-urinary 8 (prostate-1, ovary-3, utery-4; GIT 6 (stomach 2, pancreas 2, colon 2); hematologic 3 (lymphoma 2, myeloma 1); skin 3; pheochromocytoma 1, carcinoid 2; sarcoma 1. Thirteen patients (30.2%) developed cancer three years before or after SSc onset; 7 patients had cancer long before SSc; 6 patients had two cancers. Comparison between SSc-C patients and subgroups Age-NC, DD-NC and All-NC patient's subgroup did not reveal any difference in term of disease subset, presence of antibodies to topoisomerase, centromere, RNA polymerase, and clinical features (digital ulcers, ILD, GIT & heart involvement, PAH, myositis, polyautoimmunity); there were no cases of SRC in SSc-C patients compared to 8 (9.3%) patients in All-NC patients. Twenty-six (60.5%) SSc-C patients died compared to 16 (37.2) in Age-NC (P<0.08), DD-NC (P<0.001), All-NC (P<0.001). SSc related death was reported in 22.1% of All-NC patients and 16.3% of SSc-C (P=NS); 19 patients dead from cancer (73.1%). There were no differences between cancer and non-cancer patients in term of treatment with methotrexate, mycofenolate, azathioprine, cyclophosphamide, calcium blockers and iloprost; 24.3% SSc-C patients were treated with bosentan compared to 44.5% (P,0.015).
Conclusion: Malignancy is an often and variable scleroderma complication; it could preclude SSc or appeared during SSc course. Patients with malignancy had higher mortality rate and mostly dead from cancer. There no cases of tumor in those patients who developed SRC. Patients treated with bosentan has less incidence of tumor. Prompt screening for cancer should be consider as a reasonable approach in caring SSc patients; early diagnosis and treatment of tumor may improve SSc patients' survival.

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SAT0264 GAZE PATTERN ANALYSIS IN THE ASSESSMENT OF DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: The assessment of chronic wounds such as digital ulcers (DUs) in systemic sclerosis relies heavily on visual aspects. However, inter-rater variability in the assessment and definition of digital ulcers is low and there are no evidence-based data concerning the visual assessment of digital ulcers[a].
Objectives: We analysed gaze pattern data in order to evaluate differences in the visual assessment of digital ulcers in systemic sclerosis patients.
Methods: We analysed gaze pattern data from 36 subjects: 9 expert medical professionals (EMP), 8 non-expert medical professionals (NEMP), 9 medical graduates (MG) and 10 lay persons (novices). Assessment was done using a mobile eye-tracking device that tracks eye movements of subjects. Twenty pictures from digital ulcers of SSc patients were presented to each subject, 30 seconds each and characteristics of gaze pattern data were analysed. The analysis comprised the scan path, the dwell times (for areas of interest, AOI), fixation counts and the entry time for each picture and subject. Areas of interest were defined as the wound ground, wound margin, wound surroundings and distracting and non-relevant parts of the pictures. The visual assessment of the digital ulcers was accompanied by questions for each subject about their assessment of the DUs, the expected healing of the ulcer, the medical treatment of the patient.
Results: Most significant differences were found between novices and medically educated groups (expert medical professionals, non-expert medical professionals, medical graduates - EMP, NEMP, MG). Dwell times in the wound area for novices differed statistically significant from all medically educated groups (1.76s-3.1s less). Above all, novices had lower dwell times in wound margin and wound surrounding and spent more time in areas with other distracting features of the picture and white space (up to 1.92s longer). Correspondingly, they had less fixation points and longer overall scan paths in wound areas. Similar gaze pattern data were observed for medically educated groups, however NEMP had a statistically significantly lower dwell time in the wound area than EMP. Questionnaire responses were compared to an expert opinion (gold standard) and EMP had significantly more correct answers on prognosis and treatment than MG for wound assessment, but not better than NEMP.
However, treatment and prognosis were best in the EMP group with statistical difference to the NEMP and MG group.
Conclusion: For the first time, we provide evidence-based data on the visual assessment of digital ulcers in SSc. These data will be useful for the development of a structured educational programme for young physicians, rheumatology trainees and medical graduates. A key finding is that the visual assessment of digital ulcers should increasingly emphasize the importance of pathologic changes in the wound margin and surrounding area of the wound. Hence a structured approach should focus on all areas of the wound while discarding distracting visual information. An adequate terminology should be used alongside.

REFERENCE

[1] Hughes M et al., J Scleroderma Relat Disord. 2018 Jun 1;3(2):170-174.

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SAT0265

DETERMINANTS OF RENAL RESISTIVE INDEX (RRI) AT RENAL ARTERY DOPPLER ULTRASOUND IN SYSTEMIC SCLEROSIS (SSC): MORE THAN GENERAL POPULATION FACTORS

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Background: RRI can be measured on renal artery Doppler ultrasound, showing the difficulty blood flow encounters distally from where it is measured. RRI can be determined by vascular and interstitial renal features: studies on the general population showed arterial hypertension, arteriosclerosis, low-grade inflammation, diabetes mellitus, hyperuricaemia as possible causes of renal vasculopathy or tubular-interstitial nephropathy, thus determining altered RRI values. Studies on SSc have shown increased RRI values, associated with nailfold-videocapillaroscopy pattern and history of digital ulcers.
Objectives: to identify determinants of RRI in SSc patients.
Methods: SSc patients fulfilling the 2013 ACR/EULAR criteria were enrolled from two SSc-care units. Data regarding SSc clinical manifestations, instrumental and laboratory evaluation for renal, cardiac and cardiovascular involvement were collected. RRI was measured at least once in each patient. Linear regression analysis was carried out to determine predictors for baseline RRI and change in RRI in time (ΔRRI).
Results: 380 patients [aged 57 (46-68) years, 12% males] were enrolled in the study. On univariate analysis, both general population determinants (age, arterial hypertension, diabetes mellitus, hyper-lipidaemia and hyper-uricaemia) and SSc specific features [time from Raynaud's phenomenon onset, ACA positivity, scleroderma renal crisis history, estimates systolic pulmonary arterial pressure on Echo (sPAP), presence of dyspnea,%DLCO and presence of lower intestinal symptoms] predicted RRI values, with only age and sPAP being significant independent predictors at baseline. Follow-up RRI, available for 230 patients, showed that none of the general population determinants was predictive for ΔRRI, while presence of telangectasias, baseline FVC, use of Sildenafil, change in sPAP and new diagnosis of PAH were predictive at univariate regression. Among them, only presence of baseline telangectasias was an independent predictor of ΔRRI at multivariate regression analysis.
Conclusion: Data show that among general population determinants, age is the only predictive factor for RRI in SSc patients. However, also sPAP (for RRI) and telangectasias could be predicitive for ΔRRI. Therefore, the use of specific age-adjusted cut-offs (table 1) are recommended when assessing SSc patients.
Data show that among general population determinants, age is the only predictive factor for RRI in SSc patients. However, also sPAP (for RRI) and telangectasias could be predicitive for ΔRRI. Therefore, the use of specific age-adjusted cut-offs (table 1) are recommended when assessing SSc patients.

Table 1. Age-adjusted cut-offs for Renal Resistive Index (RRI) in Systemic sclerosis patients.

Age (years)	Age-SSc adjusted Pathologic RRI
1st quartile ≤ 49 y	≥0.68
2nd quartile 50-59 y	≥0.70
3rd quartile 60-69 y	≥0.75
4th quartile ≥70 y	≥0.78

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SAT0266

DIGITAL ULCER (DU) AND VENTRICULAR ARRHYTHMIAS PREDICT THE LATE GADOLINIUM ENHANCEMENT (LGE) IN CARDIAC MAGNETIC RESONANCE (CMR) IN SYSTEMIC SCLEROSIS (SSC): PROPOSAL OF CANDIDATE RED FLAGS FOR EARLY REFERRAL

Cosimo Bruni[1], Luna Gargani[2], Alessia Pepe[3], Antonella Meloni[3], Daniele De Marchi[3], Giancarlo Todiere[3], Gennaro D'angelo[2], Alberto Moggi Pignone[1], Serena Guiducci[1], Marco Matucci-Cerinic[1]. *[1]Careggi University Hospital, Firenze, Italy*; *[2]CNR IFC Istituto di Fisiologia Clinica, Pisa, Italy*; *[3]Fondazione Toscana "Gabriele Monasterio", Pisa, Italy*

Background: in SSc, cardiac involvement either primary or secondary, is frequently subclinical. In myocardial diseases, CMR is considered the non-invasive gold standard to diagnose myocardial tissue involvement and LGE has a significant impact on prognosis.
Objectives: to identify the predictors of the presence of LGE in SSc patients.
Methods: patients fulfilling the 2013 ACR/EULAR classification criteria were assessed with CMR (1.5 T GE scanner) when clinically indicated. Data on demographics, clinical SSc features, laboratory and instrumental tests for cardio-pulmonary, microvascular and renal involvements were recorded at the time of CMR evaluation. Binary regression analysis was performed with SPSS version 20.0.
Results: 317 SSc patients (284 women, mean age 52±14) were enrolled in the study. LGE-CMR was present in 32.9% and Myocardial edema (ME-CMR) in 6.1% of patients. On univariate regression analysis,%DLco values, NYHA functional class, history of DU (hDU), TAPSE and couples of ventricular premature beats (VPBc) were predictors of LGE-CMR or ME-CMR. At multivariate analysis,TAPSE (OR 0.832, 95% CI 0,727-0,951, p=0.007), hDU (OR 3.893, 95% CI 1.614-9.387, p=0.002) and VPBc (OR 4.238, 95%CI 0.959-18.738, p=0.057) were independent predictors for LGE-CMR. Presence of pericardial effusion was the only predictor for ME-CMR (OR 3.379, 95% CI 1.018-12.988, p=0.047).
Conclusion: DU history, ventricular ectopic beats on 24 hours ECG, TAPSE impairment and pericardial effusion on echocardiography may predict myocardial LGE. More studies are necessary to further verify and validate these "red flags" to refer the patients to CMR.
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SAT0267

SERUM ANTI-HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN ANTIBODY CHARACTERIZES SYSTEMIC SCLEROSIS WITH ANTI CENTROMERE ANTIBODY AND SEVERE RAYNAUD'S PHENOMENON WITH DIGITAL ULCERS

Natasa Isailovic[1], [1,2]Angela Ceribelli, Carolina Gorlino[1], Elena Generali[1], Maria De Santis[1], Marta Caprioli[1], Giacomo Maria Guidelli[1], Piercarlo Sarzi-Puttini[2,3], Minoru Satoh[4], Carlo Selmi[1,3]. *[1]Humanitas Clinical and Research Hospital, Rheumatology and Clinical Immunology, Rozzano (MI), Italy*; *[2]Luigi Sacco University Hospital, Rheumatology, Milan, Italy*; *[3]University of Milan, Milan, Italy*; *[4]University of Occupational and Environmental Health, Clinical Nursing, School of Health Sciences, Kitakyushu, Japan*

Background: Systemic Sclerosis (SSc) is characterized by the presence of serum autoantibodies (autoAbs) which may be crucial in the diagnosis, prediction of organ involvement, follow-up, and treatment choices. However, SSc sera can be negative for autoAbs identified using commercially available tests, and several new and rare autoAbs have been identified in the last decade with immunoprecipitation (IP) techniques. We recently reported a new IP pattern corresponding to anti-heterogeneous nuclar ribonucleoprotein (hnRNP) antibodies in a cohort of SSc patients.
Objectives: To analyze the IP pattern of anti-hnRNP antibodies in SSc sera and determine their clinical and laboratory correlations.
Methods: We investigated sera from 63 consecutive patients with SSc attending our Unit between 2014 and 2018, using protein-IP of ^{35}S-methionine-labeled K562 cell extract followed by SDS-PAGE and autoradiography, and IP-Western Blot for hnRNP-L and C1+C2 following

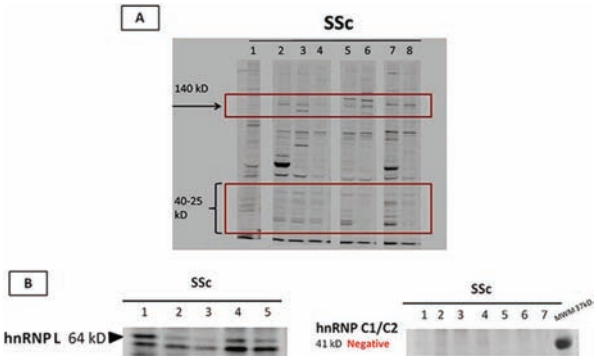
established protocols. Clinical charts were used to analyze clinical and laboratory data for possible statistical correlations, performed by Prism (GraphPad Software 4.0, Fisher exact test) with statistical significance set at p values <0.05.

Results: We identified a new protein-IP pattern characterized by a set of several proteins of 140/40-25kD in 8/63 (13%) SSc sera (Figure panel A). This IP pattern corresponds to the hnRNP complex which is composed of several proteins and RNAs involved in RNA processing and splicing. These proteins have molecular weights ranging between 32 and 45kD as the set of proteins we identified in our experiments. To define the 140/40-25kD pattern identified in 8 SSc cases, we performed IP-WB using two anti-hnRNP antibodies selected by the molecular weight of the target antigen. We tested anti-hnRNP C1+C2 and anti-hnRNP L monoclonal antibodies in these 8 samples after preparation by crosslinking of IgG to PAS beads and protein-IP protocol, followed by WB (Figure panel B). Results show that 5/8 SSc anti-140/40-25kD samples are positive for hnRNP L, while no reactivity was observed with hnRNP C1+C2 monoclonal antibody. We further observed that anti- hnRNP antibodies are significantly associated with serum ACApositivity (p=0.008), severe Raynaud's phenomenon with digital ulcers requiring IV prostacyclin (75%, 6/8 vs 7/54 ACA+, 13%; p=0.0006), and esophageal involvement in 4 cases.

Conclusion: We identified anti-hnRNP antibodies as new target antigen of a subset of SSc patients with ACA positivity and severe peripheral vascular involvement. Additional analysis is necessary to study the several components of anti-hnRNP antibodies, and longitudinal data will provide evidence on the predictive value of this biomarker.

REFERENCE

[1] Ceribelli A, et al. J Rheumatol. 2010 Oct;37(10):2071-5



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SAT0268

CLINICAL FEATURES OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH KOREAN IDIOPATHIC INFLAMMATORY MYOPATHIES ACCORDING TO THE AUTOANTIBODY PROFILE

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Background: Myositis-specific and myositis-associated autoantibodies (MSA and MAA) have been used for more detailed classification and prediction of clinical course of idiopathic inflammatory myopathies (IIM). Interstitial lung disease (ILD) is known to be complicated with approximately 50% of IIM patients, having poor prognosis.

Objectives: The aim of this study is to investigate clinical features of ILD in Korean adult patients with IIM according to the autoantibody profile including MSA and MAA.

Methods: We conducted a multicenter cohort study including 108 adult patients (age≥18 years) who have been diagnosed as IIM by ENMC criteria MSA and MAA were screened with Immunoblot assay using Euroline strip (EUROIMMUN, Germany). Clinical information including the time of developing ILD and imaging findings of chest CT was reviewed using by medical record.

Results: ILD was found in about half (52.8%, 57 of 108) of enrolled patients and closely associated with the presence of anti-ARS Abs, anti-MDA5 and anti-Ro52. Among 43 patients, Anti-ARS Abs were most common (46.5%) and included anti-Jo-1 (23.3%), -OJ (2.3%), -EJ (9.3%), -PL7 (14%), and -PL12 (7%) (Figure 1). To analyze the correlation of autoantibodies with pattern of ILD onset, we stratified the 43 patients into three groups: into ILD-preceding (7/43, 16.3%), simultaneous (31/43, 72.1%) and myopathy-preceding (6/43, 14%). In the ILD-preceding group, anti-ARS antibodies were frequent. ILD preceded myopathy by 19.5 months on average. The imaging pattern of ILD in the ILD-preceding group were Cryptogenic Organizing Pneumonia (COP) 6, Nonspecific Interstitial Pneumonia (NSIP) 1 and no *Usual interstitial pneumonia* (*UIP*). A half of patient in ILD-preceding group had Raynaud`s phenomenon, and one patient had mechanic hand. On the other hand, in myopathy-preceding group, 30% of patients (2/6) were UIP and a half of patients had pulmonary function which required treatment (DLCO <65%).

Conclusion: In our study, ILDs were accompanied by over half of the cases of IIM and most of them had autoantibodies. There are characteristic clinical features by onset time of ILD, so paying attention to them will help early diagnosis and prognosis prediction of ILDs.

Figure 1. Prevalence of MSA/MAA in IIM patinets with ILD (N=43)

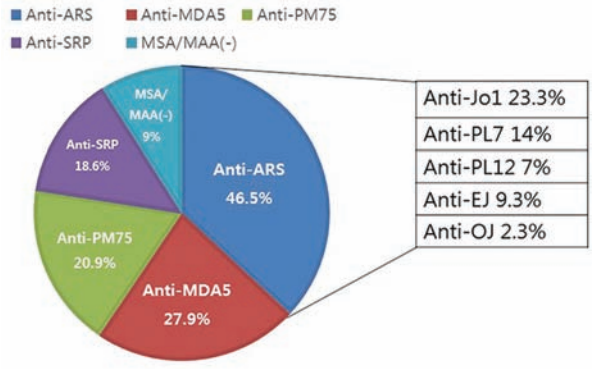


Table 1. Clinical features and autoantibody profile of IIM-ILD patients

	IIM-ILD (n=43)
Age (years)*	55.6±12.0
Gender (F:M)	33 : 10
Smoking Hx	5 (11.6)
Raynaud phenomenon	9 (20.9)
Time of ILD onset	
ILD preceding	7 (16.3)
Concomitant with myositis	31 (72.1)
myositis preceding	6 (14.0)
HRCT Findings	
NSIP	19 (44.2)
UIP	6 (14.0)
COP	18 (41.9)
Pulmonary function test	
FEV1/FVC, %	85.0±13.7
DLCO, %	64.8±23.2
DLCO <65%	**16 (37.2)**

	IIM-ILD (n=43)
Myositis-Specific Autoantibodies (MSA)	
Anti-ARS	**20 (46.5)**
Anti Jo-1	10 (23.3)
OJ,EJ,PL7,PL12	11 (25.6)
Anti-SRP	8 (18.6)
Anti-MDA5	**12 (27.9)**
Anti-Mi2	4 (9.3)
Anti TIF1-r	1 (2.3)
Anti-SAE	1 (2.3)
Myositis-Associated Autoantibodies (MAAs)	
Anti-Ro52	26 (60.5)
Anti-Ku	1 (2.3)

REFERENCE

[1] Yoshifuji H. Clin Med Insights Circ Respir Pulm Med. 2016 Apr 3;9 (Suppl 1):141-6.

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SAT0269 THE IMPACT OF SMOKING ON NAILFOLD MICROANGIOPATHY AND AUTOANTIBODY STATUS IN MALE AND FEMALE PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Smoking is a risk factor for primary Raynaud's phenomenon and, in patients with systemic sclerosis (SSc), has detrimental effects on the intensity of peripheral microangiopathy[(1)]. Two studies on SSc observed a lower prevalence of anti-topoisomerase I antibodies (ATA) in ever-smokers compared to never smokers[(2,3)], but little is known about how the effect of smoking on autoantibody status differs in male and female patients.

Objectives: The aim of our study was to evaluate, in a cohort of SSc patients, the influence of smoking on nailfold videocapillaroscopy (NVC) patterns and autoantibody positivity, comparing findings between men and women.

Methods: We included 361 adult patients (279 women and 82 men) with SSc. At baseline NVC was performed and microvascular damage was qualitatively assessed based on normal findings, aspecific/secondary pattern, or distinct "early", "active", or "late" scleroderma patterns. Information about smoking status was collected, but data regarding duration and intensity were not available for all individuals, so patients were categorized as never smokers or ever smokers. The presence of SSc-specific ATA, anti-centromere (ACA), and anti-RNA polymerase III (ARA) antibodies was investigated at baseline. Chi-square was used to compare proportions and significance level was set at 0.05.

Results: No significant difference was observed in the qualitative assessment of microangiopathy between ever smokers and never smokers, nor in autoantibody positivity. Scleroderma patterns early, active, and late, were respectively present in 12%, 44% and 21% of ever-smokers, and 9%, 48%, and 29% of never-smokers. Equal proportions of NVC patterns were found also in the gender-based sub-cohorts. Regarding autoantibodies, 27% of women who never smoked were ATA positive compared to 11% of ever smokers ($p<0.001$), while the opposite trend was observed in men, although not reaching statistical significance possibly due to the relatively small size of the male cohort.

Conclusion: In our large cohort of SSc patients, microangiopathy was not influenced by smoking status in male or female patients. The prevalence of ATA was, albeit not significantly, lower in ever smokers. Our finding is in accordance with previous studies[(2,3)], but it is worth noting that this disparity is largely contributed by the statistically significant higher frequency of ATA positivity in women who never smoked, compared to ever smokers.

Table 1. microangiopathy pattern and autoantibody positivity in ever smokers and never smokers in all SSc patients and in gender-based sub-cohorts. ATA: anti-topoisomerase I, ACA: anti-centromere, ARA: anti-RNA polymerase III, NVC: nailfold videocapillaroscopy.

	All SSc patients			Men			Women		
	Ever smokers	Never smokers	p-value	Ever smokers	Never smokers	p-value	Ever smokers	Never smokers	p-value
n (%)	208 (58)	153 (42)		62 (76)	20 (24)		146 (52)	133 (48)	
NVC Pattern									
scleroderma early, n (%)	26 (12)	14 (9)	*ns*	5 (8)	0	*ns*	21 (14)	14 (10)	*ns*
scleroderma active, n (%)	91 (44)	73 (48)	*ns*	24 (39)	11 (55)	*ns*	67 (46)	62 (47)	*ns*
scleroderma late, n (%)	44 (21)	45 (29)	*ns*	13 (21)	5 (25)	*ns*	31 (21)	40 (30)	*ns*
normal, n (%)	4 (2)	0	*ns*	2 (3)	0	*ns*	2 (1)	0	*ns*
aspecific/secondary, n (%)	43 (21)	21 (14)	*ns*	15 (24)	3 (15)	*ns*	20 (14)	14 (10)	*ns*
Autoantibodies									
ATA, n (%)	41 (20)	40 (26)	*ns*	25 (40)	4 (20)	*ns*	16 (11)	36 (27)	***<0.001***
ACA, n (%)	90 (43)	66 (43)	*ns*	10 (16)	6 (30)	*ns*	80 (55)	60 (45)	*ns*
ARA, n (%)	11 (5)	5 (3)	*ns*	2 (3)	0	*ns*	9 (6)	5 (4)	*ns*

REFERENCES

[1] Hudson M, et al. Cigarette smoking in patients with systemic sclerosis. Arthritis Rheum 2011 Jan;63(1):230-8

[2] Chaudhary P, et al. Cigarette smoking is not a risk factor for systemic sclerosis. Arthritis Rheum 2011 Oct;63(10):3098-102

[3] Jaeger VK et al. Brief Report: Smoking in Systemic Sclerosis: A Longitudinal European Scleroderma Trials and Research Group Study. Arthritis Rheumatol 2018 Nov;70(11):1829-1834

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SAT0270 COMPREHENSIVE ICF CORE SET AND ICF-BASED QUESTIONNAIRE ASSESSING ACTIVITIES AND PARTICIPATION IN PATIENTS WITH SYSTEMIC SCLEROSIS: THE SCISCIF STUDY

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Background: Recent guidelines regarding systemic sclerosis (SSc) emphasized the need of measuring functioning along with organ-specific measures, pointing out the importance of patient-reported outcome measures (1). The International Classification of Functioning, Disability and Health (ICF) endorsed by the WHO in 2001 set a unified language covering all dimensions of human functioning, including body structures, body functions, activities and participation and environmental factors.

Objectives: To develop a comprehensive ICF core set for SSc and to conceive a patient-centered ICF-based questionnaire assessing activities and participation in patients with SSc.

Methods: The development of the ICF comprehensive core set followed 2 steps (2). In the first step, meaningful concepts related to SSc were collected using data source triangulation from patients (N=18), experts (N=10) and literature (N=174 articles). In the second step, concepts were linked to the best-matching ICF categories by 2 independent reviewers according to prespecified linking rules (3). Finally, patient-reported activities and participation categories of the comprehensive ICF core set were translated into understandable questions

Results: After linking concepts to ICF codes, 151 ICF categories were collected from focus groups, 22 from experts and 82 from literature. After fusion of the sources and removal of duplicates, the comprehensive ICF core set included 165 categories: 1 at the first level, 158 at the second level, 6 at the third level, with 50 categories on body functions, 15 on body structures, 53 on activities and participation and 47 on environmental factors. Patient-reported ICF categories on activities

Conclusion: We developed a comprehensive ICF core set that offers a conceptual framework for SSc patients' care and health policy. Using a patient-centered approach, we conceived a patient-centered ICF-based questionnaire, the Cochin Scleroderma ICF-65 questionnaire, assessing activities and participation in patients with SSc.

REFERENCES

[1] Merkel PA, Clements PJ, Reveille JD, Suarez-Almazor ME, Valentini G, Furst DE, et al. Current status of outcome measure development for clinical trials in systemic sclerosis. Report from OMERACT 6. J Rheumatol. 2003;30(7):1630-47.

[2] Selb M, Escorpizo R, Kostanjsek N, Stucki G, Ustun B, Cieza A. A guide on how to develop an International Classification of Functioning, Disability and Health Core Set. Eur J Phys Rehabil Med. 2015;51(1):105-17.

[3] Cieza A, Geyh S, Chatterji S, Kostanjsek N, Ustun B, Stucki G. ICF linking rules: an update based on lessons learned. J Rehabil Med. 2005;37 (4):212-8.

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SAT0271 RELATIONSHIP BETWEEN ANTI-MDA5 ANTIBODIES AND CANCER: RETROSPECTIVE ANALYSIS OF AN INTERNATIONAL AND MULTIDISCIPLINARY COHORT

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Background: Myositis specific antibodies play a central role in the assessment of idiopathic inflammatory myopathies (IIMs) as their presence may indicate specific disease subsets/manifestations or cancer risk. At present, anti-MDA5 antibodies have been associated with the occurrence of rapidly progressive interstitial lung disease (RP-ILD), a life-threatening condition, generally refractory to treatment.
Objectives: To describe the relationship between malignancy and anti-MDA5 antibodies in IIMs.
Methods: Patients with anti-MDA5+ IIMs and a history of cancer were included in this study. Data were retrospectively collected. Because of the lack of RP-ILD shared definitions, we defined RP-ILD as an admission to the Intensive Care Unit (ICU) for IIMs related respiratory insufficiency.
Results: In our cohort (n=133, 67% females) we identified 17 patients (13%) with a history of cancer (8 males [47%], 9 females [53%]; median age at IIMs onset 62 years [IQR 53-67], at cancer diagnosis 56 years [IQR 51-66]). All but 1 patient had solid tumours, 5 (29%) had breast cancer. In 9 patients (53%) cancer diagnosis ranged ± 3 years from IIMs onset; in 3 patients the delay exceeded 120 months. Three patients (18%) developed RP-ILD respectively 82, 66 and 0 months after the diagnosis of cancer. Four (24%) patients died respectively 0 (neoplasia), 0 (RP-ILD in ICU, diagnosis of cancer after an autopsy), 7 (neoplasia) and 66 (infection after RP-ILD in ICU) months after cancer diagnosis. The 13 surviving patients had a median rheumatological follow-up of 47 months (IQR 19-84) and an oncological follow-up of 57 months (IQR 10-130). Interestingly, in the overall cohort 66% of patients without cancer (76 out of 116) had less than 3 years of follow-up. Of the 22 RP-ILD patients without neoplasia 14 died, 11 during ICU admission. In the latter patients, we could not rule out an occult neoplasia due to the emergency of the situation. Only one patient, with a 18 month history of IIMs before ICU admission, underwent autopsy and was reported negative for cancer.

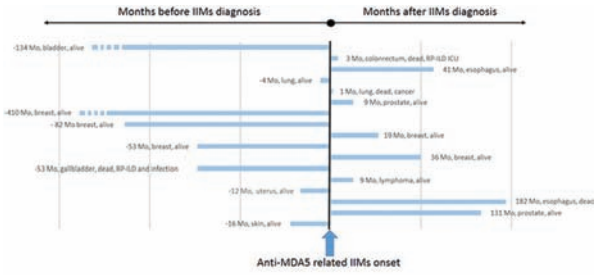


Figure 1: temporal relationship between anti-MDA5 related IIMs and cancer diagnosis, comprehensive of neoplasia site and outcome; legend: IIMs, Idiopathic Inflammatory Myopathies; Mo= months

Conclusion: This is the first study addressed to tackle the relationship between cancer and anti-MDA5+ IIMs. Although in some cases no clear relationship between IIMs and cancer can be proved because of the time gap, in others the timing of occurrence of cancer and IIMs was very close, suggesting a link between these manifestations. Finally, we emphasize the importance of an accurate neoplasm screening in anti-MDA5+ RP-ILD, because treatment refractoriness could suggest the paraneoplastic nature of the manifestation.

REFERENCES

[1] Barsotti S, et al. Rheumatol Int 2014
[2] Lu X, et al. PLoS One 2014

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SAT0272 RITUXIMAB SIGNIFICANTLY DIMINISHES CD86+ B CELLS IN SYSTEMIC SCLEROSIS

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Background: Rituximab (RTX) is a monoclonal antibody that targets the CD20 surface marker. This results in a reduction of $CD20^+$ immune cell populations, foremost B cells. B cell depletion via RTX was found to be beneficial for patients suffering from systemic sclerosis (SSc), leading to an improvement of skin fibrosis and autoimmunity (1,2). However, little is known about the influence of RTX on specific B subsets in SSc.
Objectives: The purpose of this study was to further characterize the effect of RTX on B cell populations in patients with SSc.
Methods: Peripheral blood samples from 37 patients suffering from SSc (mean age: 54 years ± 1.64 SEM, female ratio: 0.78) and 10 age-matched healthy participants were drawn over a sampling period of 2 years. 20 SSc patients in this study group were at the time under RTX treatment and the modified Rodnan Skin score (mRSS) was measured before and after treatment start. The percentage of $CD19^{+/-}$, $CD20^{+/-}$ lymphatic cells and $CD19^+CD20^+$ B cells co-expressing either CD5, CD24, CD27 or CD86 on their surface was done by staining freshly isolated PBMCs. A quantitative flow cytometric bead-based assay (QuantiBRITE PE kit from Becton Dickinson) was used for the estimation of CD19 antibodies bound per cell. All cytometric measurements were performed using a standardized BD LSRFortessa platform.
Results: RTX induced a significant decrease in mRSS from 19.7 ± 2.8 to 8.1 ± 1.7 (mean ± SEM; $p<0.000$). In addition, $CD19^-CD20^+$ cells were significantly diminished as a result of the treatment. Thus, the frequency of $CD19^-CD20^+$ cells in the non-treatment group was 1.3% ± 0.3% compared to 0.7% ± 0.2% ($p = 0.048$). Within the B cell population 33.3% ± 3.8% were positive for CD86, a checkpoint molecule for the activation of T cells during an immune response. RTX treatment significantly decreased this B cell population to 11.2% ± 4.7% ($p = 0.039$). Quantification of the number of CD19 molecules on the surface of $CD19^+CD20^+$ B cells revealed a significantly lower number in SSc patients compared to healthy participants. The mean ± SE of molecules per cell was 6862 ± 625 and 7449 ± 569, respectively ($p \leq 0.001$).
Conclusion: RTX treatment in SSc might not only be effective by reducing B cells but also by down regulation of the CD86 B cell surface marker on B cells. This would indicate that B cells under RTX treatment are less capable of activating T cells.

REFERENCES

[1] Lafyatis R, Kissin E, York M, Farina G, Viger K, Fritzler MJ, et al. B Cell Depletion With Rituximab in Patients With Diffuse Cutaneous Systemic Sclerosis. 2009;60(2):578–83.

[2] Jordan S, Distler JHW, Maurer B, Huscher D, Laar JM Van, Allanore Y, et al. Effects and safety of rituximab in systemic sclerosiss: an analysis from the European Scleroderma Trial and Research (EUSTAR) group. 2014;1–7.

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SAT0273 PREDICTIVE VALUE OF THE REVISED EUROPEAN SCLERODERMA TRIALS AND RESEARCH GROUP ACTIVITY INDEX (EUSTAR-AI)

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Background: Disease activity as measured by the European Scleroderma Study Group Activity Index (EScSG-AI) (1) has been recently found to predict the development of damage over time in an early systemic sclerosis (SSc) cohort (2). The European Scleroderma Trials and Research Group Task Force for the Development of Revised Activity Criteria for SSc recently succeeded in identifying a preliminarily revised activity index (EUSTAR-AI) that had a greater construct validity than the EScSG-AI i.e. performing better in identifying patients with active disease (3).

Objectives: To assess in patients with SSc the predictive value of the EUSTAR-AI for disease severity accrual.

Methods: SSc patients from the EUSTAR database with a disease duration from the onset of the first non-Raynaud sign/symptom≤5 years were first extracted. Patients were considered for the study if they presented the following features: a)availability of items included in the EUSTAR-AI, in the EScSG-AI and in the Medsger severity scale at baseline and yearly for 2 consecutive years; b)availability of vital status at the last observation; c) availability of other disease features known to predict disease progression (male sex, clinical and serological subset).

To capture the disease activity variations over time, we calculated the EUSTAR-AI and EScSG-AI adjusted mean (area under the curve over time divided by time interval). Disease progression was based on the Medsger severity scale and included accrual of a $\Delta \geq 1$ summed severity score and of a $\Delta \geq 1$ severity in each organ systems at the 2 year follow-up visit compared with the initial visit. To explore specific determinants of disease progression, logistic regression analysis was carried out.

Results: A total of 549 patients satisfied the entry criteria. At univariate logistic regression analysis (among sex, age, clinical and serological subset, EScSG-AI and EUSTAR-AI adjusted mean and baseline severity score), EScSG-AI adjusted mean (OR 1.41 95%CI 1.20-1.67), antiScl70 antibody positivity (OR 1.72 95%CI 1.20-2.47), diffuse subset (OR:1.46 95%CI 1.01-2.10) and EUSTAR-AI adjusted mean (OR 1.41 95%CI 1.23-1.61) predicted disease severity accrual. Multivariate analysis revealed that the EUSTAR-AI adjusted mean was the best predictor of disease progression (Table1). Moreover, at multivariate analysis the EUSTAR-AI adjusted mean also predicted severity accrual of lung (OR 1.32), heart (OR 1.40), skin (OR 1.48) and peripheral vascular disease (OR 1.45).

Conclusion: The adjusted mean EUSTAR-AI has a distinct predictive value for disease progression and development of severe organ involvement in SSc and works better than EScSG-AI.

Table 1.. Predictive features of severity progression by multivariate regression analysis

Predictive factors	OR (IC 95%)	severity deterioration	p- value
Adjusted mean EUSTAR-AI	1.41 (1.23-1.61)	Δ summed severity score ≥ 1	<0,0001
Adjusted mean EUSTAR-AI	1.32 (1.14-1.54)	Δ lung severity score ≥ 1	0,0002
Adjusted mean EUSTAR - AI age	1.40 (1.15-1.70) 1.03 (1.01-1.05)	Δ heart severity score ≥ 1	0,0005 0,0223
Adjusted mean EUSTAR-AI age	1.48 (1.21-1.82) 0.97 (0.95-0.99)	Δ Skin severity score ≥ 1	0,0002 0,0359
Adjusted mean EUSTAR-AI	1.45 (1.24-1.70)	Δ Peripheral Vascular severity score ≥ 1	<0,0001

REFERENCES

[1] Valentini G, et al. Ann Rheum Dis 2001;60:592-8.
[2] Nevskaya T, et al. Rheumatology (Oxford). 2017;56:1111-1122.
[3] Valentini G, et al. Ann Rheum Dis. 2017;76:270-276.

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SAT0274 THE EFFECT OF RITUXIMAB ON LUNG FUNCTION AND SKIN SCORE IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE. LONG-TERM OBSERVATION

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Background: There is a large clinical experience about the efficiency of rituximab (RTX) for the treatment of systemic sclerosis (SSc). There are several studies showing the decrease in skin induration and interstitial fibrosis in the lungs as the effect of therapy. However, there are not many long-term observations.

Objectives: To describe the efficacy of RTX on lung function and skin score in patients with systemic sclerosis-associated interstitial lung disease, in long-term follow-up.

Methods: This study included 71 patients (pts) with SSc. Data were collected prospectively. The mean follow-up period was 42 mo (12-72). Mean age was 46 years (17-66), female-59 (83%), diffuse cutaneous subset of the disease had 42 (59%), Scl-70 positivity-73% of pts. Duration of the disease was 5,6±4,4 yrs. All pts received concomitant treatment with low dose prednisolone and 45% - with immunosupressants. The following indicators were evaluated: forced vital capacity,% predicted (FVC), diffusing capacity for carbon monoxide,% predicted (DLCO) and Rodnan skin score (mRss) over a periods of 12-18 months (point 1), 24-30 months (point 2), 36-42 months (point 3), 48-54 months (point 4) and 60-72 months (point 5) after the start of therapy. The results are presented in the form of mean values, delta, median, upper and lower quartile.

Results: In point 1 (n=71) the cumulative mean dose of RTX was 1,43 ±0,6 gr. The mRss decreased from 11,3±9,6 to 8±6,6 (p = 0,000007). FVC increased from 77,4±19,9 to 82,6±20,7% (p=0.0001). DLCO remained stable (from 47,0±18,5 to 47,23±16,7%). In point 2 (n=55) the cumulative mean dose of RTX was 2,97±0,8 gr. ΔmRss – 5,4 (median 3; 25th% 0; 75th% 10). ΔFVC – 7,5% (median 8,2; 25th% -1,1; 75th% 14,4). ΔDLCO – 0,21% (median -0,2; 25th% -6,2; 75th% 6,6). In point 3 (n=36) the cumulative mean dose of RTX was 3,45±1,3 gr. ΔmRss – 5,1 (median 3,5; 25th% 0; 75th% 9). ΔFVC – 9,3% (median 7,7; 25th% 1,45; 75th% 15,3). ΔDLCO – 3,4% (median 3,6; 25th% 2,45; 75th% 7,76), p=0,02. In point 4 (n=24) the cumulative mean dose of RTX was 3,96±1,1 gr. ΔmRss – 5,3 (median 3; 25th% 0; 75th% 10). ΔFVC – 12,2% (median 7,9; 25th% 1,1; 75th% 24,2). ΔDLCO – 3,9% (median 0,45; 25th% -0,95; 75th% 6,8). In point 5 (n=17) the cumulative mean dose of RTX was 5,15±1,7 gr. It should be noted that this group included patients with initially the lowest DLCO (below 40%). ΔmRss – 7,3 (median 5; 25th% 1; 75th% 14). ΔFVC – 13,2% (median 11; 25th% 8,7; 75th% 23,4). ΔDLCO – 5,9% (median 1,6; 25th% -4,8; 75th% 13,8).
Conclusion: The results of this study confirm the data on the positive effect of RTX in patients with SSc (decrease of skin induration, increase of FVC, stabilization of DLCO). The decrease of skin score is accompanied by the improvement of lung function indicators. In our study, there was a significant increase of DLCO associated with long-term treatment (over 36 mo) and a cumulative dose of RTX over 3,45±1,3 gr. Patients with initially lower DLCO can achieve a significant improvement by the 60th month of RTX therapy. Our work shows that patients with SSc-associated interstitial lung disease are required long-term treatment with RTX (at least 3-5 years) to achieve an obvious improvement of the lung function.

REFERENCE

[1] Jordan S, Distler JH, Maurer B, Huscher D, van Laar JM, Allanore Y. et al; EUSTAR Rituximab study group. Effects and safety of rituximab in systemic sclerosis: an analysis from the European Scleroderma Trial and Research (EUSTAR) group. Ann Rheum Dis 2015;74(6):1188–94.

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SAT0275 PERFORMANCE OF THE ANTISYNTHETASE ANTIBODIES AND THEIR INDIRECT IMMUNOFLUORESCENCE PATTERNS IN THE ANTISYNTHETASE SYNDROME DIAGNOSIS

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Background: The antisynthetase syndromes (ASSD) are characterized by the presence of anti-aminoacyl transfer RNA synthetase (ARS) autoantibodies; which difficult the binding of amino acids to the transfer RNA during the protein synthesis. ARS can be detected by indirect immunofluorescence (IIF), and can be identified by immunoblot assay and ELISA (Enzyme-Linked ImmunoSorbent Assay) and immunoblotting. The main clinical features of the ASSD are myositis, arthritis, interstitial lung disease, Raynaud's phenomenon, mechanic hands, and fever. Two ASSD diagnosis criteria have been developed; those proposed by Connors, and the stricter criteria proposed by Solomon (1, 2).
Objectives: To evaluate the performance of the ARS and their IIF patterns in the ASSD diagnosis.
Methods: We performed an observational retrospective study in one center during the period 06/2008-06/2018. We searched all the myositis immunoblots (Euroimmun assay) requested by the Rheumatologists under suspicion of ASSD or myositis. We assessed: 1) the rate of cases with positive ARS; 2) the rate of cases with Connor´s or Solomon´s diagnosis criteria fulfillment; and 3) their relation with the IIF patterns (Hep-2 cells; $\geq$1/80) evaluated by an expert in autoimmune tests.
Results: A total of 140 myositis immunoblots were searched. Twenty-seven cases (19.3%) presented positive ARS: anti-Jo1 (n=13), anti-PL-12 (n=7), anti-PL-7 (n=1), anti-EJ (n=2), and anti-OJ (n=4). Twenty-five of these (17.9%) fulfilled Connors´ criteria, and 15 (10.7%) additionally met Solomon´s criteria. Thus, the fulfillment of Connor´s and Solomon´s criteria in patients with a positive ARS was of 92.6% and 55.5%, respectively.
All cases (100%) with positive ARS presented positive immunofluorescence: 19 (70.4%) showed a cytoplasmic pattern (10 of them with an associated nuclear pattern) and 8 cases (29.6%) presented only a nuclear pattern. On the other hand, 99 of the 113 cases (87.6%) with negative ARS presented positive IIF: 29 (25.7%) showed a cytoplasmic pattern (21 of them with an associated nuclear pattern) and 42 cases (37.2%) presented only a nuclear pattern.
Correlating the ARS positivity, IIF pattern and the diagnosis criteria fulfillment:
- 13 of 15 cases (86.6%) with positive ARS and Solomon´s criteria fulfillment presented a cytoplasmic pattern; and 2 of 15 cases (13.3%) presented only a nuclear pattern.
- 13 of 19 cases (68.4%) with positive ARS and cytoplasmic pattern fulfilled Solomon´s criteria; and 6 only fulfilled those from Connors´.
Conclusion: One-fifth of the immunoblots requested by Rheumatologists presented positive ARS; almost all these cases fulfilled Connor´s criteria, and more than a half fulfilled the stricter Solomon´s criteria. All patients with positive ARS, and a high rate of those without ARS, presented positive IIF. The presence of a cytoplasmic pattern was considerably higher in patients with ARS positivity and in those that met Solomon´s criteria.
Thus, our results suggests that in patients evaluated by a Rheumatologist, with clinical suspicion of ASSD or myositis and with ARS positivity, the probability of fulfilling Solomon´s criteria is higher when the IIF presents a cytoplasmic pattern than when only a nuclear pattern is observed. Nevertheless, presenting only a nuclear pattern does not exclude the detection of ARS in the myositis immunoblot and the fulfillment of Solomon´s criteria.

REFERENCES

[1] Solomon J, et al. Jornal brasileiro de pneumologia. 2011;37(1):100-9.
[2] Connors GR, et al. Chest. 2010;138(6):1464-74.

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SAT0276 STUDY OF THE EPIDEMIOLOGICAL, CLINICAL AND ANALYTICAL CHARACTERISTICS IN PATIENTS WITH SYSTEMIC SCLEROSIS AND CANCER IN VALL D'HEBRON HOSPITAL

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Background: Scleroderma or systemic sclerosis (SSc) is a systemic, chronic autoimmune disease characterized by great clinical heterogeneity. In recent years, studies have proven that there is a relationship between SSc and neoplasia.
SSc is associated with an increased risk of certain types of cancer, particularly lung, liver, hematological, non-melanoma skin and urothelial cancer. Despite this increasement, the relative risk of developing cancer is still low in these patients. In the literature, neoplasms have been described in 3-11% of patients with SSc.
Objectives: Our objective is to analyze the epidemiological, clinical and analytical characteristics previously described as possibly linked to the development of a cancer in patients with systemic sclerosis (SSc) in the Vall d'Hebron Hospital cohort.
Methods: We analyzed 583 patients in the Vall d'Hebron Hospital cohort of SSc. The inclusion criteria were age > 18 years and the diagnosis of SSc limited, diffuse and SSc sine scleroderma. The different variables were analyzed by univariate statistical analysis with SPSS v21.

VARIABLE	NEOPLASIA (n=94)	NO NEOPLASIA (n=427)	p
General Characteristics			
SEX (M/F)	8/86 (9/91%)	51/376 (12/88%)	0.73
AGE >65Y AT DIAGNOSIS	24 (26%)	102 (24%)	0.34
MORTALITY	34 (36%)	119 (28%)	0.10
SMOKERS	6 (6%)	36 (8%)	0.50
SUBTYPE (LIMITED /DIFFUSE /SINE)	65/16/13 (70/16/14%)	282/94/51 (66/22/12%)	0.54
CAPILLAROSCOPY PATTERN (SLOW /ACTIVE)	**57/6 (60/6%)**	**236/68 (55/16%)**	**0.04/ 0.02**
Clinical manifestation			
RAYNAUD'S PHENOMENON	88 (93%)	415 (97%)	0.08
SKIN ULCERS	38 (40%)	214 (50%)	0.08
TELANGIECTASIAS	70 (74%)	325 (76%)	0.73
CALCINOSIS CUTIS	22 (23%)	91 (21%)	0.65
ESOPHAGEAL INVOLVEMENT (PATOLOGICAL MANOMETRY)	57 (61%)	292 (68%)	0.36
ARTHRALGIA	44 (47%)	236 (55%)	0.13
ARTHRITIS	17 (18%)	81 (19%)	0.84
PULMONARY HYPERTENSION	43 (46%)	184 (43%)	0.63
ILD	25 (27%)	103 (24%)	0.72
CARDIAC AFFECTION	58 (62%)	285 (67%)	0.38
Immunology pattern			
AC SCL70 (ATA I)	11 (12%)	88 (21%)	0.02
ACA +	37 (39%)	139 (33%)	0.18
ANTI- RNA POL III +	7 (7%)	25 (6%)	0.65
ANTI PM/SCL +	**9 (10%)**	**18 (4%)**	**0.04**
Treatment			
CYCLOPHOSPHAMIDE	9 (10%)	36 (8%)	0.72
AZATHIOPRINE	**6 (6%)**	**88 (21%)**	**0.000 06**
MYCOPHENOLATE	10 (11%)	61 (14%)	0.35
METHOTREXATE	0 (0%)	23 (5%)	0.68
ANTIPLATELET	40 (43%)	231 (54%)	0.09
ACEIs	32 (34%)	125 (29%)	0.36
ARBs	**20 (21%)**	**54 (12%)**	**0.03**
CCBs	**57 (60%)**	**304 (71%)**	**0.04**
CORTICOIDS	40 (42%)	172 (40%)	0.95
PROSTAGLANDINS	4 (4%)	37 (9%)	0.15

TYPES OF CANCER	(n=94)	%
BREAST CANCER	22	24%
HEMATOLOGIC MALIGNANCIES	21	23%
LUNG CANCER	13	14%
NON MELANOMA SKIN CANCER	6	6%
MELANOMA	2	2%
COLON CANCER	5	5%
ENDOMETRIAL CANCER	5	5%
GASTROESOPHAGEAL CANCER	4	4%
THYROID CANCER	4	4%
UROTHELIAL CANCER	2	2%
OVARIAN CANCER	1	1%
OTHERS	9	10%

Results: We included 521 patients with diagnosis from January 1985 to August 2016. 88.7% were women, with an average age of 53. 94 patients were diagnosed with neoplasia. The analyzed variables and their statistical significance and the types of cancer developed by our cohort patients are shown in *Fig 1*.

Conclusion: In the analyzed cohort, a slow pattern in capillaroscopy, positivity for Pm/Scl and the use of ARBs is associated with the development of neoplasia in patients with SSc. It has an inverse association the positivity of Scl70 (ATA I), the active pattern in capillaroscopy and the use of azathioprine and CCBs. In our cohort 94 patients with SSc have developed cancer. The most prevalent types of cancer were breast cancer, hematologic malignancies and lung cancer, as shown in the literature.

REFERENCES

[1] Onishi A, Sugiyama D, Kumagai S, Morinobu A. Cancer incidence in systemic sclerosis: meta-analysis of population-based cohort studies. Arthritis Rheum 2013; 65: 1913–21.

[2] Bernal-Bello D, de Tena JG, Guillén-del Castillo A, et al. Novel risk factors related to cancer in scleroderma. Autoimmun Rev 2017.

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SAT0277 THE 100 MOST INFLUENTIAL PUBLICATIONS IN SYSTEMIC SCLEROSIS: A BIBLIOMETRIC STUDY

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Background: In recent years, a large volume of important clinical and scientific papers about systemic sclerosis can be found in the most influential journals. Bibliometric analysis is a statistical method that enables researchers to analyze citation patterns and highlight characteristics of highly cited scholarly work. It has been infrequently utilized in Rheumatology[1,2]. Prior studies have not addressed the bibliometric literature gap in the field of systemic sclerosis.

Objectives: This study aims to identify the 100 most cited papers in systemic sclerosis and to describe their characteristics.

Methods: We sought to assess the characteristics of the top 100 most referenced citations in systemic sclerosis. We searched the Scopus and Web of Science databases to identify all articles relating to 'Scleroderma', 'limited' or 'diffuse Systemic Sclerosis' and 'CREST syndrome'. Articles were arranged in descending order of citations and were scrutinized by two independent reviewers. Selected articles were analyzed with respect to number of citations, publication year, journal characteristics, research type, focus area, authors and countries of authors of publications.

Results: Retrieved articles were published mostly in rheumatology journals (*n*=42*)* with impact factors ranging between 3.47 and 12.35 in these journals, followed by journals in general medicine, pulmonology, and experimental biomedical research. Journals with the highest number of top-cited articles included *Arthritis and Rheumatism* (*n*=25), followed by the *The New England Journal of Medicine* (*n*=9) and *Annals of the Rheumatic Diseases* (*n*=8). Studies conducted in USA, UK, and Italy that were published in high-impact journals had the highest citation count. Temporal analysis indicated that the majority of top-cited articles were published between 1998 and 2014 (*n*=65). The most productive 5-year time period was between 2000 and 2005 when 23 of the 100 most cited publications were produced. Among retrieved citations, guidelines and recommendations comprised 5% of all articles, narrative reviews 21%, randomized clinical trials 12%, observational studies 35%, non- randomized clinical studies (basic and translational research) 24%, case series 1%, and meta-analyses 2%. Our analysis shows that articles defining the classification criteria of Systemic Sclerosis were among the most cited work followed by those describing the pathophysiology of the disease. Other highly cited areas included cellular and molecular mechanisms of fibrosis (with special emphasis on the role of TGF-β) and Randomized Controlled Trials for Bosentan and Epoprostenol in the treatment of pulmonary hypertension. Regarding individual organ manifestations, Pulmonary and Cardiac complications (pulmonary hypertension, lung disease, myocardial effects) (*n*=21) were of highest interest, while other articles focusing on Cutaneous (ulcers, skin changes, Raynaud's phenomenon) (*n*=16), Renal (renal crises) (*n*=3) and Gastrointestinal complications (dysmotility) (*n*=1) were cited to a lesser extent. Interestingly, articles primarily describing hematopoietic stem cell transplant as a viable treatment option did not feature on this list.

Conclusion: Our study provides the first bibliometric overview of the most highly cited scientific papers on systemic sclerosis. These findings provide useful insights into trends of published work and may serve as a useful guide to researchers in this field.

REFERENCES

[1] Cheng T, Zhang G. Worldwide research productivity in the field of rheumatology from 1996 to 2010: a bibliometric analysis. Rheumatology 2013, 52 (9): 1630-1634.

[2] Tetik-Aydogdu Y, Aydogdu O, Sari Z. AB1275 Research contribution to the journal of annals of the rheumatic diseases from 2012 to 2016: a bibliometric analysis. Annals of the Rheumatic Diseases 2018, 77(Suppl 2): 1731.

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SAT0278 STUDY OF QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS- A CROSS-SECTIONAL STUDY

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Background: There has been no study on quality of life (QoL) in patients with systemic sclerosis (SSc) in India.

Objectives: 1) To determine the difference in QoL in patients with SSc compared to general population. 2) To determine the difference in QoL in subsets of patients with SSc between a) Limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc); b) SSc with and without interstitial lung disease (ILD) c) SSc with disease duration of ≤ 5 yrs and > 5 yrs.

3) To find out the contributing factors to impaired QoL with the help of a newly developed patient reported questionnaire.

Methods: In this cross-sectional study, all consecutive adult patients with SSc, satisfying 2013 ACR/EULAR classification criteria, attending a tertiary rheumatology clinic in Western India from January 2016 to March 2017 were compared to age and sex-matched controls. A new questionnaire [Indian Systemic Sclerosis QoL questionnaire (Indian SyS-QoL)] was developed to identify the contributing factors to impaired QoL with feedback from 15 SSc patients and 11 rheumatologists. This questionnaire had 10 factors and each was scored by individual patients between 0-3 (0-no impact; 3-severe impact on QoL in previous month). Demographic data, clinical profile and relevant investigations were recorded. Patients filled Medical Outcomes Trust Short Form 36 version 2 (SF-36v2) questionnaire, Indian SyS-QoL questionnaire and Indian Health Assessment Questionnaire –(Indian HAQ).

Results: 94 SSc patients (7 males; 87 females) were compared to 100 age and sex-matched controls. QoL was significantly impaired in patients with SSc compared to healthy controls in all 8 domains of SF-36 ($p<0.001$), the finding similar to other studies (Table 1). There was no statistically significant difference in mean scores in any domain between patients with dcSSc [56 patients (59.6%)] and lcSSc [38 patients (40.4%)]; between patients with disease duration ≤5 yrs [43 patients (45.7%)] and >5 years [51 patients (54.3%)] and in those with ILD [56 patients (59.6%)] and without ILD [38 patients (40.4%)]. Two most important factors responsible for poor QoL based on Indian SyS-QoL questionnaire score (mean±SD) were 'feeling of dependency on family' (1.4±1.3) and 'cost of treatment'(1.3±1.2)(Fig 1).

Table 1:. SF-36 Scores in SSc patients among different studies:

	Present study	Frantz et al	Georges et al	Danieli et al	Cossutta et al
N	94	1902	89	76	95
SF-36v2 domain	mean±SD	mean±SD	mean±SD	median (Range)	mean±SD
Physical function	55.2±25.4	52.7±28.3	50±31	57.5 (35-80)	61.3±25.1
Role physical	53.2±32.0	35.6±40.6	40±42	50 (0-100)	39±40.3
Role emotional	62.5±30.9	54.1±44.0	46±44	66.6 (0-100)	49.1±41.2
Energy/vitality	45.7±22.9	36.1±22.0	39±22	50 (35-60)	50.3±19.7
Mental health	55.7±23.0	61.0±20.5	-	56 (38-68)	55.7±21.2
Social function	60.5±33.9	56.8±26.2	58±28	87.5 (56.2-100)	66.5±23.2
Pain	58.4±31.2	50.8±25.5	47±28	61 (41-76.5)	50.2±25.6
General health	40.3±23.6	35.7±18.4	41±22	35 (23.7-45)	40.0±20.8

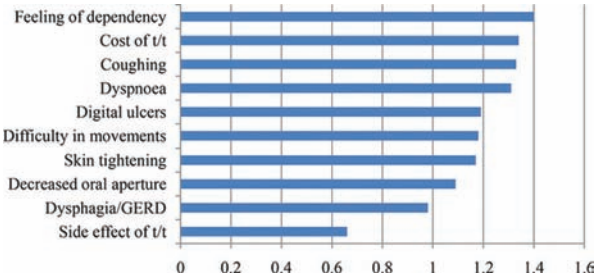


Figure 1:. Factors contributing to impaired QoL in descending order of Indian SyS-QoL mean scores:

Conclusion: This maiden study from India showed that QoL was significantly affected in patients with SSc compared to the general population; but there was no significant difference in QoL in patients with different subsets of SSc; disease duration ≤ 5 yrs and > 5 yrs, and presence or absence of ILD. The new graded scale devised to assess the impact of SSc on QoL using a simple patient-reported questionnaire showed 'Feeling of dependency' and 'cost of treatment' as the 2 most important factors affecting QoL in Indian patients with SSc. This would help direct more resources to support the patients both mentally and financially.

REFERENCES

[1] Hudson M, et al. Arthritis Rheum. 2009;61(8):1112–20.
[2] Steen VD, Medsger TA. Arthritis Rheum. 1997;40(11):1984–91.

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SAT0279

MULTICENTER DOUBLE-BLIND, PROOF-OF-CONCEPT, RANDOMIZED PLACEBO-CONTROLLED TRIAL OF RIOCIGUAT IN SYSTEMIC SCLEROSIS-ASSOCIATED DIGITAL ULCERS (RESCUE)

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Background: The soluble guanylate cyclase stimulator riociguat (RIO) is a vasodilator and has antifibrotic effects in animal models and efficacy in patients with pulmonary arterial hypertension associated with connective tissue diseases.

Objectives: We present results from a randomized placebo-controlled trial (NCT02915835), which evaluated the efficacy and safety of RIO in patients with systemic sclerosis-associated digital ulcers (SSc-DU).

Methods: Eligible subjects (with active or painful indeterminate DUs) were randomized in 1:1 ratio to either placebo (PLA, n = 8) or RIO (n = 9) in individualized doses (maximum of 2.5 mg three time daily) during an 8-week titration period, followed by an 8-week stable dosing period. PDE5 inhibitors were not allowed. The primary end point was the change from baseline to week 16 in net ulcer burden (NUB), analyzed using an ANCOVA model, accounting for baseline NUB. Other outcome measures included change from baseline to week 16 in the Raynaud's Condition Score (RCS), RP attack number, symptom severity during RP attack, patient global assessment, and proportion of subjects with treatment-emergent adverse events (AEs). Eleven plasma biomarkers were measured by ELISA and changes were tested using ANCOVA, after testing for normality.

Results: We randomized 17 participants with SSc-DUs between January 2017 and March 2018. Baseline characteristics were comparable between treatment groups, except participants randomized to PLA were older (mean 61 vs. 43 yrs) and had longer disease duration (mean 17.5 vs. 7.1 yrs). At baseline, the mean (SD) NUB was 2.5 (2.0) in the PLA and 2.4 (1.4) in the RIO. No significant difference was observed between RIO and PLA in change from baseline to 16 weeks in NUB [p=0.70; Table]. No significant treatment effect was observed in the secondary outcome measures. All 17 participants reported ≥1 adverse event, with the vast majority being mild or moderate. There were 4 SAEs, 3 in RIO (worsening DU, NSTEMI, and non-Hodgkin's lymphoma) and 1 in PLA (digital ischemia; none of SAE's were related to the study medication). Statistically significant elevation of cGMP was observed at 16 weeks [p=0.05]; no other biomarkers showed statistically significant changes.

Conclusion: In participants with SSc-DU, treatment with RIO did not reduce the number of NUB compared with PLA. The safety profile of RIO was similar to that previously reported. There is evidence of target engagement. The negative results may reflect small number of patients, low number of NUB at baseline, moderate-to-severe vasculopathy with long term disease, and difficulty to recruit patients in the era of widespread use of PDE5 inhibitors.

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	Placebo (N=8)	Riociguat (N=9)	Treatment Difference (95% CI)	p-value
Net Ulcer Burden, mean*#	-0.98	-1.22	-0.24 (-1.46 to 0.99)	0.70
Patient assessment, mean*#				
Severity of RP (0-10)	-1.41	-3.47	-2.06 (-4.63 to 0.51)	0.11
Severity of DU (0-10)	-4.00	-4.63	-0.63 (-3.68 to 2.41)	0.66
Pain during RP attack (0-100)	-7.01	-0.30	6.71 (-14.01 to 27.43)	0.49
Numbness during RP attack, mean (SD) (0-100)	-15.44	-19.73	-4.28 (-33.44 to 24.87)	0.75
Tingling during RP attack, mean (SD) (0-100)	-7.49	1.18	8.67 (-13.75 to 31.09)	0.41
Raynaud's Condition Score, mean (SD) (0-10)	-0.82	-1.15	-0.33 (-2.60 to 1.94)	0.76
Number of Raynaud's attacks per day, mean	-0.96	-1.24	-0.28 (-1.36 to 0.79)	0.57
Plasma Biomarkers, mean*				
cGMP nM	41.2	198.5	157.3 (3.1 to 311.5)	0.046
*A higher number denotes worse symptoms				

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Cumberland Pharmaceuticals, Tracy Frech: None declared, Pei-Suen Tsou: None declared
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SAT0280 ESOPHAGEAL DYSMOTILITY AND PULMONARY DISEASE IN PATIENTS WITH SCLERODERMA: A RETROSPECTIVE STUDY

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Background: Systemic sclerosis (SSc) is a connective tissue disease with pulmonary involvement seen in 75% of patients and esophageal involvement in 90% of the patients. Pulmonary disease has overtaken renal disease as the leading cause of death (1). There is conflicting evidence about the association between esophageal dysmotility and lung involvement (Interstitial Lung Disease (ILD) and Pulmonary Artery Hypertension (PAH)).
Objectives: Our aim was to evaluate the relationship between esophageal dysmotility and lung disease by correlating the results of Echocardiogram and Pulmonary Function Test (PFT) with Esophageal Transit Study (ETT).
Methods: Charts of SSc patients fulfilling 2013 ACR/EULAR classification criteria seen in Rheumatology clinic from 2004 to 2015 were reviewed. Patient demographics, ETT result, FVC and DLCO data from PFT as well as pulmonary pressures from echocardiogram were collected at baseline, years 1, 3, 5 and 10. Patients were divided based on their initial ETT findings into normal and abnormal ETT groups. Using logistic regression models, we compared elevated PASP with ETT status at baseline, and years 3 and 5. Linear mixed effects model was used to adjust for covariates (disease subtype, smoking, obesity, use of immunomodulator) when analyzing PFT outcome with time period and ETT status
Results: 130 patients were identified with either Limited Cutaneous SSc (109) or Diffuse Cutaneous SSc (21) with a mean age of 52.65 years ± 12.59. ETT was normal in 67(52%) and abnormal in 63(48%) patients. Number of patients with abnormal PASP was not statistically different between the two groups (p values 0.104, 0.178, 0.653 at baseline, years 3 and 5 respectively). Likewise, the odds ratio for abnormal PASP was 2.75 in patients with abnormal ETT compared to normal ETT, but the results were not statistically significant (p: 0.428), and the odds ratio did not vary with time (p: 0.731). Sample size was too small to conduct separate longitudinal analysis for adjusted models. The mean DLCo was statistically worse in abnormal ETT patients [p value <0.0001 and 0.0004 for unadjusted and adjusted models] as were the progression rates per year for DLCo at -1.95 (p-value: 0.023) and -2.25 (p-value: 0.019) for unadjusted and adjusted models respectively. The Mean FVC was not statistically different between the two groups, although it's progression rate per year was statistically worse only in the adjusted model (p value: 0.018).
Conclusion: Esophageal dysmotility was associated with increased pulmonary involvement in the form of abnormal DLCo with worsening progression rates per year. Interestingly, neither PASP nor FVC were statistically different even though progression rate for FVC was worse in adjusted models. We postulate that the small sample size for Echo and differences in the factors determining DLCo vs. FVC and PASP explains the disparity in the results. Larger prospective trials are needed to investigate if there is a causal relationship between esophageal dysfunction and pulmonary involvement.

REFERENCE

[1] Mathai, S. C., Hummers, L. K. (2009), Survival in pulmonary hypertension associated with the scleroderma spectrum of diseases: Impact of interstitial lung disease. Arthritis & Rheumatism, 60: 569-577. doi:10.1002/art.24267

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SAT0281 RELATIONSHIP BETWEEN AUTOANTIBODIES AND CYTOKINE PROFILES IN PATIENTS WITH MYOSITIS

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Background: By autoantibodies, myositis is recently classified into subgroups with distinctive clinical features. Cytokines play critical roles in the development of the clinical features. However, it is not fully unknown whether myositis subgroups defined by autoantibodies have unique cytokine profiles.
Objectives: To clarify the relationship between cytokine profiles and autoantibodies in myositis.
Methods: Subjects were myositis patients who admitted Dokkyo Medical University and whose serum before starting therapy were available. Serum cytokine levels (IL-1a, 1b, 2, 4,5, 6, 10,12, 13,15,17, 23,IFN-g, TNF-a, IFN-a, b,IP-10 and MCP-1) in sera from the patients and controls were measured using Q-Plex™ Multiplex Arrays. Demographic and clinical data were obtained by reviewing medical record retrospectively.
Results: Subjects were 45 myositis patients with male/female; 22/23 and 59.4 years of mean age. Amyopathic dermatomyositis (ADM), classical DM and polymyositis (PM) were 21, 11 and12 cases, respectively. Autoantibodies were anti-MDA5+ in 21, anti-ARS+ in18 and anti-TIF1g+ in 5 cases. ILD and malignancy was complicated in 39 and 5 cases, respectively.
Serum cytokine levels were measured. As shown in Fig.1, IP-10 levels were increased in all types of myositis patients, but not in controls. In ant-MDA5 Ab + myositis, IL-6, IL-10, IL-15, TNF-a, IFN-a and MCP-1 levels were increased. In anti-ARS Ab+ cases, IFN-b levels were elevated as well as TNF-a and MCP-1.
Through the correlation analysis between cytokine levels, cytokine groups were identified (Fig.2). In anti-MDA5 Ab+ cases, 2 cytokine groups were identified; one includes IFN-a, IL-15, TNF-a and IL-10, and the other involved IL-6, MCP-1. Both groups connected with IP-10. In In anti-ARS

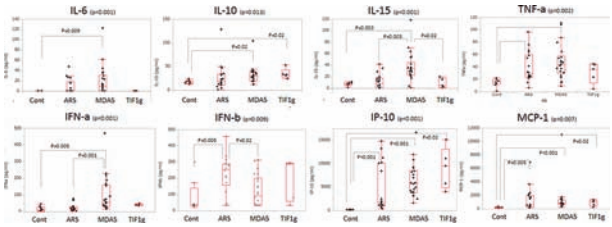


Figure 1. Serum cytokine levels in myositis

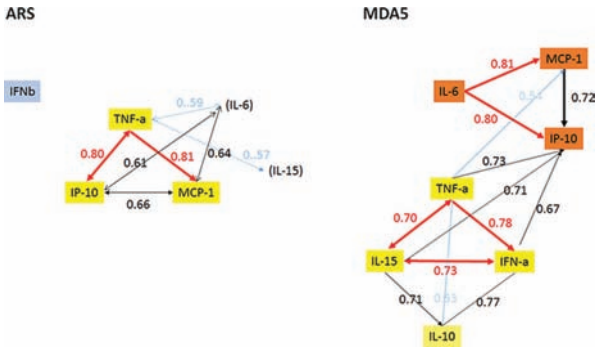


Figure 2. Cytokine networks in a-ARS ab+ and a-MDA5 ab+ myositis

Ab+ cases, 2 groups were found; one included TNF-a, MCP-1and IP-10, and the other had IFN-b as a sole component.
Conclusion: Cytokine profiles differ among subgroups in myositis. In anti-DDA5+ myositis, IL-15 and IFN-a with strong correlation and IL-6 were characteristic cytokines, while IFN-b was a unique one in anti-ARS+ myositis
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SAT0282 EFFICACY AND SAFETY OF ORAL PROSTACYCLIN RECEPTOR AGONIST SELEXIPAG IN PATIENTS WITH SYSTEMIC SCLEROSIS -ASSOCIATED PULMONARY ARTERIAL HYPERTENSIONIN DAILY CLINICAL PRACTICE, A CASE SERIES

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Background: Pulmonary arterial hypertension (PAH) is a frequent complication in systemic sclerosis (SSc) and a major cause of death despite the available treatments (1). Until the availability of the oral prostacyclin receptor agonist selexipag in 2016, parenteral medication targeting the prostacyclin pathway was often not feasible for patients with SSc -PAH due to practical barriers. Selexipag added to background therapy improves prognosis of PAH in the published pivotal trial (2). However, to date information on results of SSc-PAH patients treated with any combination of targeted therapies including selexipag in daily clinical practice are lacking.
Objectives: Evaluation of the efficacy and safety of selexipag in SSc-PAH patients in a real life case series.
Methods: All patients with SSc associated PAH (WHO group 1) diagnosed by right heart catheterization who started with selexipag between 09-2016 and 06-2018 from two PAH expert centres were included. Data on demographics, concurrent medication, functional class, 6 minute walking distance and NT-pro-BNP level were recorded at baseline and during follow-up. Every 12 weeks we recorded the opinion of the treating expert team, resulting in a conclusion “improvement”, “stabilization” or “deterioration”. Additionally treatment effect was assessed according to the abbreviated risk assessment described by Boucly (3). Side effects and adverse events were registered and evaluated.
Results: We included 13 SSc-PAH patients, all classified as limited cutaneous SSc. Ten patients were female. Median age was 68 years (IQR 58-75), median SSc disease duration 7.4 years (IQR 4.7-13.5) and median PAH duration 4 years (IQR 2.5-7.5). All patients were on double background therapy. At baseline 1 patient had two low risk criteria, 1 patient had one low risk criterion, the other patients had no low risk criteria. Two patients discontinued selexipag within 4 weeks due to side effects. The eleven patients reaching maintenance dosage had a median follow up of 48 weeks (IQR 24-72). At the end of follow up, 2/11 patients improved, 4/11 stabilized, and 5/11 deteriorated as evaluated by their expert team. Two of these deteriorated patients died due to right ventricular failure and gastro-intestinal bleeding respectively. Of the patients deteriorating, 3 initially stabilized for a period of 24 to 60 weeks. None of the patients achieved 3 low risk criteria, three patients achieved 1 low risk criterion. No unknown side effects were reported.
Conclusion: Adding selexipag to double background therapy in a high risk cohort stabilized symptoms in the majority of these patients with an acceptable safety profile. Sustained improvement of PAH symptoms is reached in only a minority of our SSc-PAH patients. Further research examining multiple target therapy, including selexipag, in patients with early SSc-associated PAH is warranted.

REFERENCES

[1] Lefevre G, et al. Survival and prognostic factors in systemic sclerosis-associated pulmonary hypertension: a systematic review and meta-analysis. Arthritis Rheum. 2013;65(9):2412-23.
[2] Sitbon O, et al. Selexipag for the Treatment of Pulmonary Arterial Hypertension. N Engl J Med. 2015;373(26):2522-33.
[3] Boucly A, et al. Risk assessment, prognosis and guideline implementation in pulmonary arterial hypertension. Eur Respir J. 2017;50(2).

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SAT0283 CLINICAL AND SEROLOGICAL FEATURES OF SYSTEMIC SCLEROSIS IN ITALIAN AND EGYPTIAN PATIENTS

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Background: Clinical and serological variations exist in the severity of Systemic Sclerosis (SSc) patients, according to different geographic areas.
Objectives: To evaluate clinical and serological features in 2 cohorts of Italian and Egyptian SSc patients and to identify factors associated with Interstitial lung disease (ILD), a leading cause of mortality, by using multivariate logistic regression analysis.
Methods: An Italian center and 3 Egyptian centers participated in SSc patient recruitment in 2017. The cross-sectional demographic, clinical, and laboratory data were collected and defined according to severity score and activity index, previously developed [1, 2]. The database included 152 consecutive Italian patients, 135 women (88.8%) and 17 men (11.2%) and 197 consecutive Egyptian SSc patients, 177 women (89.8%) and 20 men (10.2%), all of whom fulfilled the classification criteria proposed by LeRoy and Medsger [3].
Results: We found that Egyptians SSc patients were younger (41.18±12.5 vs 58.59±12.6 yrs), had an earlier onset of the first non Raynaud’s Phenomenon symptom (7.28±5.89 vs 14.99±11.11) and a more severe Modified Rodnan Skin Score (MRSS>14) (79.27% vs 13.6%). A greater percentage of Egyptian patients presented the active form of the disease (53.3% vs 15.5%) and had a Pulmonary Arterial Pressure (PAPs) estimated by echocardiography $\geq$40mmHg (37.5% vs 10.6%), than Italian patients. Furthermore, Egyptian patients affected from the limited form of the disease (lcSSc), presented a higher MRSS (67.2% vs 2.6%), higher PAPs levels (34.5% vs 9.2%), an active form (41.7% vs 7.8%) and history of past/current ulcers (62.2% vs 30.6%) than Italian lcSSc patients. Severity score was higher in Egyptian patients than in the Italians (General: 22.9% vs 6.2%,Peripheral vascular: 48.2% vs 23.9%, skin: 19.8% vs 3.6%, joint/tendon: 19.9% vs 8.5%, muscle: 8.1% vs 2.6%, lung: 41.1% vs 25.3%, heart: 11.2% vs 4.1%). Kidney involvement was more severe in the diffuse cutaneous form (dcSSc) of the disease in Egyptians patients than Italians (2% vs 0.4%). In the multivariate analysis, PAPs $\geq$40mmHg (OR: 2.622, 95%CI:1.031-6.660, p=0.043), past/current ulcers (OR:3.450, 95%CI:1.265-9.409, p=0.016), presence of anticentromere (ACA) (OR:3.846, 95%CI:1.488-9.940, p=0.005) and anti-topoisomerasi I (SCL70) (OR:5.012, 95%CI:1.740-14.441, p=0.003) antibodies and heart involvement (OR:3.018, 95%CI:1.448-6.288, p=0.003) were associated with ILD in the Egyptian database, suggesting a potential role as predictive biomarkers. Advanced age (OR:1.036, 95%CI:1.009-1.063, p=0.008), dcSSc (OR:4.726, 95%CI:2.021-11.049, p=0.001) and joint involvement (OR:1.695, 95%CI:1.094-2.627, p=0.018) were independently associated with ILD in the Italian patients.
Conclusion: This cross-sectional study analyzed the demographic, clinical and laboratoristic variations in Egyptians and Italian patients and their association with ILD, suggesting possible differences to be further investigated in adequately powered studies.

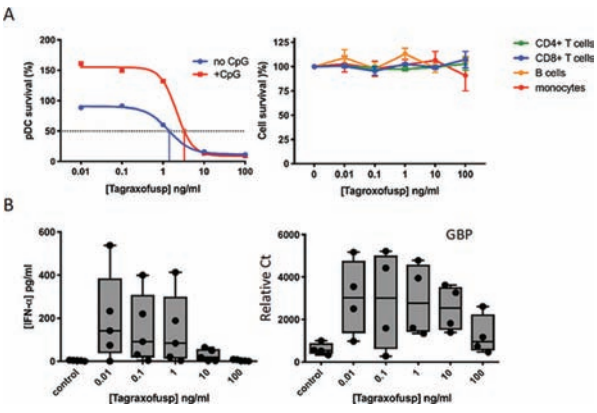
REFERENCES
[1] Valentini, et al. Ann Rheum Dis 2001
[2] Medsger TA Clin Exp 2003
[3] LeRoy EC, et al. J Rheumatol. 1988 Feb

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SAT0284 CD123+ PLASMACYTOID DENDRITIC CELLS (PDCS) FROM SYSTEMIC SCLEROSISPATIENTS ARE SUSCEPTIBLE TO THE CYTOTOXIC ACTIVITY OF TAGRAXOFUSP, A CD123-TARGETED THERAPY

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Background: Tagraxofusp is a novel targeted therapy directed to the interleukin-3 receptor (CD123). Tagraxofusp is comprised of human IL-3 recombinantly fused to a truncated diphtheria toxin (DT) payload engineered such that IL-3 replaces the native DT receptor-binding domain. In this way, the IL-3 domain of tagraxofusp directs the cytotoxic DT payload to cells expressing CD123. Upon internalization, tagraxofusp irreversibly inhibits protein synthesis and induces apoptosis of the target cell.
Tagraxofusp was recently approved by the FDA for the treatment of patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN), a malignancy derived from the plasmacytoid dendritic cell (pDC) precursor. pDCs are immune cells that express CD123, secrete IFN-α, and play a role in inflammation and disease pathogenesis observed in systemic sclerosis (SSc) patients[1,2]. Therapeutic depletion of pDCs or attenuation of pDC function may represent a novel approach to treating SSc patients.
Objectives: To assess the ability of tagraxofusp to selectively deplete pDCs from SSc patients *ex vivo*.
Methods: Patients fulfilled the 2013 ACR/EULAR classification criteria for SSc[3]. PBMCs from either SSc patients or healthy volunteers (HV) were prepared using Ficoll-Paque density gradient from fresh blood. pDCs were isolated from PBMCs as previously described and used to enrich the frequency of pDCs in an additional draw of PBMCs[4]. pDC-enriched PBMCs (3-6% pDCs) were cultured at $2x10^5$ cells per well in the presence or absence of CpG-274 (0.5 μM) to activate pDCs and then incubated with tagraxofusp (0.01-100 ng/ml, 0.17 pM-1.7 nM) at 37°C, 5% CO_2, and 95% humidity. After 24 h of culture, pDC survival was assessed by flow cytometry (CD14-, CD3- BDCA4+ CD123+), and supernatants were collected for cytokine quantification by a multiplexed Luminex assay. Changes in gene expression were measured by PCR on 10 μg cDNA, and calculated based on relative threshold cycle and expression of a ubiquitin housekeeping gene.
Results: Tagraxofusp was cytotoxic towards pDCs from both HV (n=5) and SSc donors (n=5) to a similar extent. The ED_{50} of tagraxofusp in pDCs from HV and SSc was 4.3 and 3.2 ng/ml (74.4 and 55.4 pM), respectively; no effect was observed on B or T cells across the tagraxofusp dose range tested (Fig.1A). Tagraxofusp-mediated pDC depletion was further accompanied by a 68-fold reduction in secreted IFN-α and a 3-fold downregulation of GBP, a type 1 IFN-induced gene (Fig. 1B).
Conclusion: Tagraxofusp is a novel CD123-targeted therapy that is cytotoxic towards pDCs from SSc patients. These data present a novel approach of targeting pDCs in the treatment of SSc, and a clinical trial is under design.



REFERENCES
[1] Ah Kioon MD, Tripodo C, Fernandez D, et al. Plasmacytoid dendritic cells promote systemic sclerosis with a key role for TLR8. Sci Transl Med. 2018 Jan 10;10(423).
[2] van Bon L, Affandi AJ, Broen J, et al. Proteome-wide analysis and CXCL4 as a biomarker in systemic sclerosis. N Engl J Med. 2014 Jan 30;370 (5):433-43.
[3] van den Hoogen F, Khanna D, Fransen J, et al. 2013 classification criteria for systemic sclerosis: An American College of Rheumatology/European League against rheumatism collaborative initiative. Ann Rheum Dis. 2013 Nov;72(11):1747-55.
[4] Guiducci C, Ott G, Chan JH, et al. Properties regulating the nature of the plasmacytoid dendritic cell response to Toll-like receptor 9 activation. J Exp Med. 2006 Aug 7;203(8):1999-2008.

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, Marie Dominique Ah Kioon Grant/research support from: stemline, Franck Barrat Grant/research support from: stemline, Christopher Brooks Shareholder of: Stemline stock, Grant/research support from: stemline, Employee of: stemline
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SAT0285 EVALUATION OF CHRONIC PAIN IN PATIENTS WITH SYSTEMIC SCLEROSIS COMPARED TO THOSE WITH CHRONIC HEADACHE AND RHEUMATOID ARTHRITIS

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Background: Systemic Sclerosis (SSc) is a chronic systemic disease frequently leading to disability and low quality of life. Chronic pain (CP), due to severe disease complications and internal organs involvement, is often underestimated. Based on available data around a 60-70% of patient with SSc suffer of chronic pain but we still lacking of fine tools to better evaluate it and follow up patients
Objectives: Evaluate pain in SSc patients, in terms of its intensity, sensory and affective components, the interference with physical and social activities, impact on quality of life and correlation with main SSc clinical manifestations.
Methods: From January 2013 to January 2018 we retrospectively evaluated 98 patients with a diagnosis of SSc [F/M=87/11; Limited/Diffuse SSc 63/35 anti-Scl70/ACA/ANA nucleolar positivity 45/39/14; mean age 55,6 ± 12,6 DS; mean disease duration 9,9 ± 7,6 DS] according to 2013 ACR/EULAR criteria; 47 patients with a diagnosis of chronic headache (CH) as defined by the International Classification for Headache Disorders, Third Edition beta version (ICHD-3 beta) criteria [F/M 37/10; mean age 52,6 ± 14,2 DS; mean disease duration: 7 ±2 yrs DS] and 46 patients with Rheumatoid Arthritis [F/M 36/10, mean age 61±13, mean disease duration 10±2 yrs, DS]. All patients fulfilled self-complying questionnaires for the evaluation of pain and quality of life: Visual Analogic Scale (VAS), Numeric Rating Scale (NRS), Short Form-McGill Pain Questionnaire (SF-MPQ), Brief Pain Inventory Score (BPI) e Health Assessment Questionnaire (HAQ).

Results: SSc patients started to suffer of CP in younger ages compared to AR/CH cohort but patients suffering of CH have higher mean scores in all questionnaires compared to AR/SSc. CH patients, have higher mean score in SFMPQ-sensory and affectory. Hundred percent (100%) of AR patients suffered of chronic pain. They, generally, had higher scores than SSc patients with a prevalence of the affectory component. The 83.9% (67/75 pts) of SSc patients experienced chronic pain [SF-MPQ PRI: 6.25±8.34DS; SF-MPQ PPI: 1.69±1.34DS; BPI-fattore1: 13.37 ±11.26DS; VAS: 40.7±29.6DS; NRS: 4.08±2.98DS] and in a great majority (84%) that pain interfered with their working activities and social lifes. Fortyeight percent of SSc patients had digital ulcers and 41.3% had musculoskeletal involvement. Pain used to correlate with both of them [p=0.004; p=0.041]. In patients with DUs, affectory component of pain overuled on the sensory one

Conclusion: SSc patients frequently experience chronic pain and particularly those who have a history of active DUs and musculoskeletal involvement. By the way, it seems that the BPI questionnaire could be more suitable than VAS or NRS in assessing DUs' pain. Furthermore it provides useful information on the impact of CP on social life and work impairment. Otherwise, SF_MPQ allows clinicians to better discriminate affective or sensory components of pain.

REFERENCES

[1] The impact of systemic sclerosis on health-related quality of life assessed by SF-36: A systematic review and meta-analysis. Li L, et al.; Int J Rheum Dis. 2018 Nov;21(11):1884-1893.

Disclosure of Interests: Luca Magnani: None declared, Federica Lumetti: None declared, Emanuele Cocchiara: None declared, Amelia Spinella: None declared, CArlo Baraldi: None declared, Luigialberto Pini: None declared, Lanfranco Pellesi: None declared, Gianluigi Baiocchi: None declared, Carlo Salvarani Grant/research support from: Roche, Consultant for: Eli Lilly and Company, Roche, Abbvie, Dilia Giuggioli: None declared
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SAT0286 EVALUATION OF SWALLOWING ALTERATIONS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Dysphagia represents a frequent and disabling symptom in patients with Idiopathic Inflammatory Myopathies (IIMs) and it has been recently included in the new ACR/EULAR classification criteria for IIMs. Despite the clinical relevance, dysphagia assessment in IIMs is not currently standardized and evaluation tools are highly variable between different centers. Functional Endoscopic Evaluation of Swallowing (FESS) is an exam that allows, by using nasal endoscopy, the direct evaluation of anatomic structures and swallowing abilities in different swallowing phase. In fact, FESS could help the identification of different problems leading to dysphagia occurrence and to related dysphagia problems. Thanks to these characteristics, FESS for ENT specialists is the gold standard technique for evaluating swallowing functions. However, no studies so far have investigated the role of FESS in the assessment of IIMs and we are completely lacking a semeiotic description of FESS findings in these patients.

Objectives: To provide the first semeiotic description of swallowing alterations evidenced by FEES in a cohort of IIMs patients.

Methods: We retrospectively reviewed the FEES findings of IIMs patients performed at our hospital.

Results: We enrolled 19 patients with a diagnosis of IIMs (10 patients were positive for a myositis specific antibody), of these 16 (84%) reported symptomatic dysphagia. We divided patients into 3 groups based on levels of peripheral muscle strength. Six patients (32%) had no clinical sign of active muscle disease (MRC scale 5, median CK 51 mU/ml, IQR 35-235), 5 patients (26%) had a mild reduction in muscle strength (MRC scale 4, median CK 76, IQR 54-220) and 8 patients (42%) showed a moderate-severe reduction in muscle strength (MRC scale ≤3, media CK 1440, IQR 628-6180). The 67% of patients without muscle disease activity showed an impairment in the oral phase of swallowing for solids and the 33% for fluids; 33% had a reduction in the activation of the pharyngeal phase of swallowing for both fluids and solids; only 17% of patients showed any sign of penetration, aspiration or pharyngeal residue for both solids and fluids. In the group of patients with moderate muscle activity, 80% of patients showed impairment in the oral phase of swallowing for solids and 40% for fluids; 60% had a reduction in the activation of the pharyngeal phase of swallowing for solids while 40% for fluids; 40% of patients showed signs of penetration, aspiration or pharyngeal residue for both solids and fluids. Finally, in the group of patients with severe muscle disease activity, 88% of patients showed an impairment in the oral phase of swallowing for solids and 50% for fluids; 63% had a reduction in the activation of the pharyngeal phase of swallowing for solids while 50% for fluids; 75% of patients showed signs of penetration, aspiration or pharyngeal residue for both solids and fluids. The 15% of all patients (3 cases, 1 from each group of muscle activity) showed a dysfunction in the upper esophageal sphincter. Of note, 3 patients (15%; 1 with moderate and 2 with severe muscle disease activity) required nutrition through nasogastric tube.

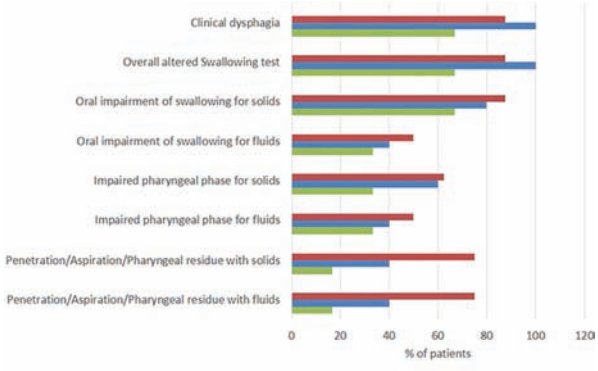


Figure 1: swallowing alteration for solids and fluids in patients divided by muscle disease activity: no signs of muscle disease activity (green), moderate muscle disease activity (blue) and severe muscle disease activity (red).

Conclusion: We showed that FESS study identified swallowing dysfunctions in both the oral and pharyngeal phases of swallowing. Swallowing dysfunctions were more prevalent in patients with greater muscle involvement; however, alterations were not rare also in patients with no clinical signs of muscle activity and, in particular, in the few patients without reported symptoms of dysphagia. FEES appears as a useful tool for the evaluation of dysphagia in IIMs.

REFERENCE

[1] Brady S, Otolaryngol Clin North Am. 2013 Dec;46(6):1009-22

Disclosure of Interests: Emiliano Marasco: None declared, Giulia Bertino: None declared, Ludovico De Stefano: None declared, Lorenzo Volpiano: None declared, Pietro Canzi: None declared, Marco Benazzo: None declared, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Lorenzo Cavagna: None declared
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SAT0287 SERUM CYTOKINE PROFILE IDENTIFIES PATHOMECHANISM AND EFFICIENT BIOMARKERS OF DISEASE ACTIVITY AND PROGNOSIS IN INTERSTITIAL PNEUMONIA COMBINED WITH POLYMYOSITIS/ DERMATOMYOSITIS

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Background: Polymyositis (PM) and dermatomyositis (DM) are idiopathic inflammatory myopathies that mainly involve the muscles, skin, lungs, and heart. PM/DM are frequently complicated by interstitial lung disease (ILD) that causes increased mortality. Anti-aminoacyl tRNA synthetase (ARS) antibody and anti-melanoma differentiation-associated gene 5 (MDA5) antibody are associated with complications of ILD. Anti-ARS antibody-positive PM/DM-ILD responds well to immunosuppressive therapy and has a good short-term prognosis but a high rate of relapse over the long term. In contrast, anti-MDA5 antibody-positive PM/DM-ILD responds poorly to immunosuppressive therapy, and its prognosis is poor. Recently, a number of cytokines have been implicated in the pathomechanism and

outcome of PM/DM-ILD. High levels of serum IL-6, IL-8, IL-10, IL-18, CCL2, CXCL10, TNF-α, and IFN-α were detected in PM/DM-ILD cases, suggesting the pathological involvement of activated macrophages, type 1 T helper (Th1) cells, and neutrophils (ref 1, 2). However, investigation of the pathomechanism using serum cytokines remains insufficient in PM/DM-ILD. We hypothesised that multiple inflammatory cytokine pathways related to the above inflammatory cells would be involved in the pathomechanism of PM/DM-ILD.

Objectives: We measured serum cytokine levels before and during treatment of patients with PM/DM-ILD and examined the associated pathomechanism.

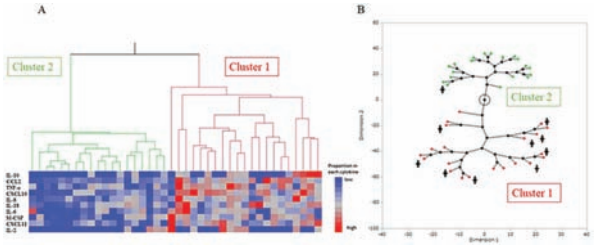
Methods: Serum cytokines were collected from 40 PM/DM-ILD patients. Principal components analysis (PCA) and cluster analysis were used to classify patients into subgroups. We compared cytokine profile of the survivors and dead patients as well as anti-MDA5 antibody-associated ILD and anti-ARS antibody-associated ILD. We also examined the association of various cytokines with disease activity indicators and prognosis of ILD.

Results: PCA revealed that the diversity of cytokines was driven by three groups: (1) neutrophilic and M1-macrophage-driven cytokines, (2) Th1 cell-driven and M2-macrophage-induced cytokines, and (3) M2-macrophage-driven cytokine. Based on cluster analysis, patients were classified into two subgroups according to the cytokine levels of all groups (Figure A). Ninety percent of patients who died of ILD were included in clusters with high cytokine levels (Figure B). Serum cytokine levels of all groups were significantly higher in the anti-MDA5 antibody-positive patients than in the anti-ARS antibody-positive patients. Factors of poor prognosis in PM/DM-ILD correlated significantly with serum cytokine levels of groups 1 and 2. Among the 3 groups, serum cytokine levels of group 1 were significantly higher initially and at 2 and 4 weeks in the death group.

Conclusion: These findings suggest that the activation of monocytes, macrophages, and Th1 cells, and neutrophils plays a role in the pathomechanism. Group 1 cytokines could be efficient biomarkers for predicting prognosis of PM/DM-ILD.

REFERENCES

[1] Gono T, et al. *Rheumatology (Oxford)* 2014;53:2196–203
[2] Oda K, et al. Sci Rep 2017;7:1635.



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SAT0288 A SYSTEMATIC REVIEW OF SYSTEMIC SCLEROSIS CLINICAL TRIALS SINCE 2005. LACK OF EARLY DISEASE TARGETING, CONFUSION RELATED TO DISEASE DURATION DEFINITION AND LOW LEVEL OF INCORPORATION OF THE NEW CLASSIFICATION CRITERIA

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Background: It is still unknown whether treatment in very early systemic sclerosis (SSc) can affect long term outcomes.

Objectives: To systematically review clinical trials in SSc during the last 14 years aiming at answering the following questions: 1) how many clinical trials in SSc have targeted early disease and whether treatment of patients with early disease leads to better clinical outcomes, 2) how is disease duration defined in SSc clinical trials and whether data on duration since Raynaud's onset are provided and 3) whether the new 2013 ACR/EULAR SSc criteria have been incorporated in clinical trials throughout the last 5 years.

Methods: A search in published studies indexed in MEDLINE was performed from Jan-2005 to Dec-2018. The *Clinical Trial* filter was activated and the terms "systemic sclerosis treatment" used. Studies were included if they evaluated adult patients with systemic sclerosis, concerned systemic treatments, presented data for clinical endpoints assessing fibrosis and were prospective in design.

Results: Seventy-three studies with a total number of 3078 patients met the inclusion criteria and were subjected to data extraction. The total weighted mean disease duration (adjusted to the number of patients in each study) was 38.55 months which is more than 3 years, the usual threshold for defining early disease. Baseline total weighted mean MRSS was 21.54 indicating that most patients had full blown fibrotic disease. Only 24 studies (32.9%) recruited early (<36 months disease duration) cohorts, with only 4 studies among them concerning very early disease (<18 months disease duration). We next focused on studies that did not specifically target early disease (n=49) and explored whether disease duration associated with clinical outcomes. We identified such an analysis only in 13 studies. In 8/13 studies there was no difference regarding outcomes according to disease duration. Nevertheless, in 4/13 studies investigators reported better outcomes in patients with shorter disease duration with only one study showing the opposite. Significant heterogeneity was found regarding disease duration definition. Four separate definitions were identified: 1) "From first non-Raynaud's symptom" (49.3%), 2) "From disease diagnosis" (11%), 3) "From skin thickening onset" (5.5%), 4) "From first symptom" (11%). The remaining studies (23.3%) presented no clear definition in their manuscript for disease duration in their cohorts. The stratification of the studies according to year of publication showed a tendency for greater consistency regarding the definition used in recent years since most studies published from 2015 and onwards use the definition "From first non-Raynaud's symptom". Data regarding the duration since Raynaud's onset were available only in 9 studies (12.3%). A separate analysis of all articles published from 2014 until 2018 was performed to explore the incorporation of the new 2013 ACR/EULAR criteria. Only 6 studies (25%) incorporating the new criteria were identified.

Conclusion: 1) The majority of patients recruited in clinical trials throughout the last 14 years do not have early disease, 2) Only one third of the studies were specifically designed to target early disease, 3) The question of whether early implementation of therapy may lead to better clinical outcomes cannot be definitely answered based on existing data, 4) there is confusion related to disease duration definition across SSc clinical trials but an obvious trend towards improvement was evident throughout the last few years and 5) there is still a very low level of incorporation of the new classification criteria in SSc trials.

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SAT0289 THE ROLE OF CAPILLAROSCOPY IN THE EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis is a multisystem autoimmune disease characterized by fibrosis of the skin and internal organs and vascular damage. The diagnosis is usually made in the late stages, when irreversible damage has already occured. Recently, we have established new criteria to detect early cases of the disease. Performing capillaroscopy and its findings are crucial in the diagnosis of early systemic Sclerosis or "prescleroderma" and there may be changes seen in capillaries of patients without skin manifestations.

Objectives: To analyze the nailfold capillaroscopy findings in patients with anti-centromere or anti-topoisomerase antibodies and evaluate their usefulness for the diagnosis of systemic sclerosis.

Methods: Of a total of 255 capillaroscopy performed in our Rheumatology department, those patients with positive anti-centromere or anti-topoisomerase were selected. In all cases, capillaroscopy was performed in eight fingers, always by the same observer. The following findings were considered pathological or scleroderma pattern: Local or global capillary loss (> 20%), hemorrhages: two or more in at least two fingers and enlarged capillaries: two or more capillary with double or more caliber in at least two different fingers.

Statistical analysis was performed with SPSS 19.0 program.

Results: The study included 69 patients: 5 (7.2%) males and 64 (92.8%) women, 14 (20.3%) smokers, 47 (68.1%) non-smokers and 8 (11.6%) quitters. The characteristics of the patients included in the study were as follows: 20 patients (30%) were previously diagnosed of systemic sclerosis (19 limited and one diffuse), of which 4 patients had concomitant primary biliary cirrhosis Syndrome (Reynolds), 1 patient with

primary biliary cirrhosis and positive anti-centomere without the presence of Raynaud, one patient diagnosed with Sjögren's syndrome with positive anti-centromere without presence of Raynaud, 26 patients with suspected early systemic sclerosis and 21 patients with disease-specific autoantibodies in the absence of Raynaud. Nailfold capillaroscopy was normal in 32 patients (46.4%) and pathological (scleroderma pattern) in 37 patients (53.6%); we detected limited enlarged capillaries in 26.2%, generalized enlarged capillaries also in 26.2%, giant capillaries in 37.7%, local loss of capillaries in 27.9%, global loss of capillaries in 8.2%, hemorragies in small claims in 29.5% and abundant hemorrhagies in 9.8%. All patients previously diagnosed of systemic sclerosis had a pathological capillaroscopy except one. However, no changes were observed in capillaroscopy in patients who had only disease-specific autoantibodies in the absence of Raynaud's phenomenon. While, the 26 patients who were referred for suspected systemic sclerosis (at least with the presence of Raynaud and autoantibodies) in 18 (69.9%) of these scleroderma pattern was observed with subsequent diagnosis of early systemic sclerosis or "prescleroderma".

Conclusion: Nailfod capillaroscopy is a useful and inexpensive tool for the diagnosis of systemic sclerosis. The scleroderma pattern is very specific of this disease and we can make an early diagnosis even in patients who only have autoantibodies and Raynaud's phenomenon, without the presence of other severe manifestations. We have also observed that the absence of Raynaud's phenomenon is associated with a normal result on capillaroscopy.

REFERENCE

[1] Nailfold digital capillaroscopic findings in patients with diffuse and limited cutaneous systemic sclerosis. Saeedeh Shenavandeh, Mahyar Yousefipour Haghighi, Mohammad Ali Nazarinia. Reumatologia 2017; 55, 1: 15–23

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SAT0290

TRADITIONAL AND DISEASE-RELATED RISK FACTORS FOR ARTERIAL AND VENOUS THROMBOTIC EVENTS (TE) IN IDIOPATHIC INFLAMMATORY MYOPATHIES (IIM)

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Background: Thromboembolic cardiovascular diseases (CVD), affecting both arterial and venous sides, are one of the leading causes of death in patients with Idiopathic Inflammatory Myopathies (IIM), with highest peak of mortality within the first year after diagnosis (1).

Objectives: To assess the prevalence of traditional and disease-related risk factors for arterial and venous thrombotic events (TE) in patients with IIM by comparing those reporting TE (cases) with those without history of TE (comparators). To compare clinical characteristics, autoantibody profile inclusive antiphospholipid antibodies (aPL) and serum levels of adhesion molecules (VCAM, ICAM and e-selectin) between cases and comparators as well as between cases reporting arterial vs venous TE.

Methods: Using national and international registries, and medical charts, we identified 58 cases and 195 comparators with IIM followed at Karolinska University Hospital between 1993 and 2014. Information on gender, age at the time of diagnosis, IIM subgroup, presence of interstitial lung disease (ILD), myositis specific antibodies (MSAs), was retrospectively collected. Information on traditional risk factors for arterial and venous TE (essential hypertension, diabetes, dyslipidemia, smoking, malignancy) was retrieved for both groups. Serum levels of aPL and adhesion molecules were analyzed in stored sera from the time of diagnosis in both groups, before TE in cases and in 40 age and gender matched heathy controls (HC).

Results: One out of 5 IIM patients (22,92%) had suffered from at least one TE, which was observed especially during the first 5 years after diagnosis. Myocardial infarction was the most frequent TE, followed by pulmonary embolism and deep venous thrombosis. In the multivariate analysis, male gender and older age were independent risk factors for TE. Essential hypertension had statistically significant higher prevalence in cases than comparators. Arterial TE was more common in polymyositis, while venous TE occurred more frequently in patients with dermatomyositis, history of malignancy and in those with MSAs. At time of IIM diagnosis, the prevalence of aPL was 6% with no difference between cases and comparators. Significantly higher levels of VCAM and ICAM were obtained in IIM patients compared to HC (Fig.1 and Fig.2). ICAM levels were found significantly higher in comparators than cases (Fig.2). Lower levels of e-selectin were associated with higher odds of developing TE, especially in males and older patients, with no difference between arterial and venous TE (Fig.3).

Conclusion: A high risk of arterial and venous TE should be taken into account in patients with IIM, particularly close to time of diagnosis, with extra attention in male patients and older individuals. Preventive measures should be considered especially in patients with concomitant essential hypertension and malignancy. Lower serum levels of e-selectin might predict TE in IIM patients but the mechanism for this risk factor is not known.

REFERENCE

[1] Dobloug GC, Svensson J, Lundberg IE, Holmqvist M. Mortality in idiopathic inflammatory myopathy: results from a Swedish nationwide population-based cohort study. Ann Rheum Dis. 2018;77(1):40-7.

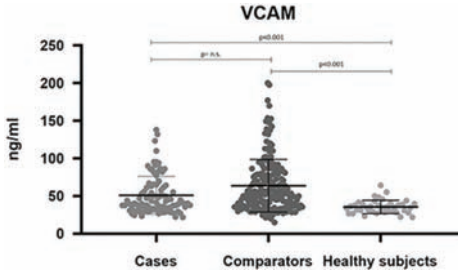


Figure 1

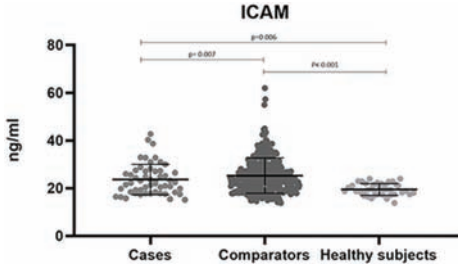


Figure 2

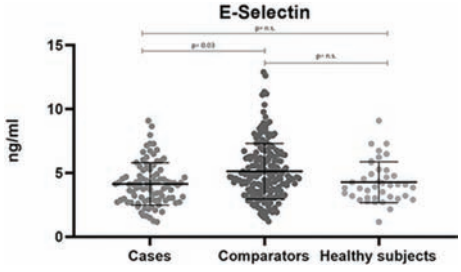


Figure 3

Disclosure of Interests: Antonella Notarnicola: None declared, Simone Barsotti: None declared, Linnea Näsman: None declared, Quan Tang: None declared, Marie Holmqvist: None declared, Ingrid E. Lundberg Grant/research support from: Dr. Lundberg has received honoraria from Bristol Myers Squibb and MedImmune and is currently receiving a research grant from Bristol Myers Squibb and from Astra Zeneca., Consultant for: She is a scientific advisor for Bristol Myers Squibb, and aTyr, Aleksandra Antovic: None declared
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SAT0291 PULMONARY INVOLVEMENT AND FUNCTIONAL LIMITATION IN SYSTEMIC SCLEROSIS

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Background: Pulmonary involvement is the main cause of death in Systemic Sclerosis patients (SS). However, there is little information whether its presence is capable of affecting the functional capacity of patients and if this influences the quality of life perceived by them.
Objectives: To determine whether the presence of pulmonary involvement in patients with SS (Interstitial Lung Disease and or Pulmonary Arterial Hypertension) is related to greater functional disability.
Methods: Observational and cross-sectional study, with a prospectively performed protocol, of patients diagnosed of SS according to ACR/EULAR 2013 criteria. Demographic, clinical, analytical, activity (EUSTAR index), severity (Medsger scale and modified Rodnan index), health perception (SF36) and disability (HAQ and Cochin test) variables were collected. Moreover, Videocapillaroscopy (VCL) and Respiratory Function Test were made. All the patients had pulmonary TCMD and echocardiography in order to describe pulmonary features.
Results: 42 patients were included (95.4% women), with an average age of 59.2 (S.D 12.9) years. The median of years from diagnosis was 4, and 6 from the first not Raynaud symptom. Out of them, 20 were SS limited, 20 patients SS diffuse; and 2 patients SS sine scleroderma. Pulmonary hypertension (HTP) was found in 11.9% of patients, as well as EPID in 33.3% (UIP 16.7%, NSIP 14.3%, bronchiolitis 2.3%). Analyzing the subgroup of patients with EPID, we can highlight higher score of HAQ, Cochin and activity index EUSTAR, with less influence in Rodnan index and without differences in SF36.

	ILD patients	Non-ILD patients	PAH patients	Non-PAH patients
HAQ (median)	0.75	0.44	1.25	0.5
EUSTAR activity index (median)	6	4	6.3	4
Cochin (median)	10.5	5	5	5
SF36 (median)	0.52	0.52	0.42	0.44
Rodnan (median)	3	2.5	4	3
Medsger Severity (median)	4	4	5	4
PAH (%)	7.1	14.2	20	35.1
Centromeric nuclear ANA pattern (%)	7	71	40	51.3
Homogeneous nuclear ANA pattern (%)	36	14	20	24.3
Anti-centromere (%)	7	71	40	51
Anti-Scl70 (%)	36	7	20	16
Anti-RNApolymeraseIII (%)	14	7	20	8.1
Reduction in DLCO (%)	71	53	80	56.8
Reduction in FVC (%)	21	14	40	13.5
Sclerodermiform pattern en VCL (%)	78,6	85,7	100	81.1

Regarding the subset of patients with PAH, we found higher score on HAQ, EUSTAR activity index, index Rodnan, Medsger gravity scale and the SF36, than in non-PAH patients, with no differences in Cochin test.
Conclusion: We can highlight the presence of greater functional limitation that is especially reflected in rates of disability (HAQ and Cochin), as well as a increased activity of disease and a lower self-perception of health in patients with Systemic Sclerosis pulmonary involvement.
Disclosure of Interests: None declared
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SAT0292 SELF-ADMINISTERED VERSUS INTERVIEW BASED INTERNATIONAL CONSENSUS CRITERIA FOR THE DIAGNOSIS OF RAYNAUD'S PHENOMENON QUESTIONNAIRE – A SINGLE CENTRE EXPERIENCE

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Background: International Consensus Criteria for diagnosing Raynaud's Phenomenon (RP) have been proposed recently (1). These criteria are based on the three-step conditional approach (i.e. a screening question, assessment of colour changes and an item of disease score calculation). It is unclear whether differences exist between the self-administered and interview-based way of questionnaire fulfilment.
Objectives: We aimed in our study to evaluate the two approaches in patients with suspected RP.
Methods: This cross-sectional study was conducted at our secondary/tertiary rheumatology centre between 1 October 2018 and 31 December 2018. Each patient referred for the video capillaroscopy was asked to complete the RP questionnaire on the day of the referral. The same questionnaire was applied as an interview by the rheumatologist before the video capillaroscopy. Differences in answers and level of individual agreement on individual three items, as well as the result of the questionnaire, between the two ways of questionnaire completion were assessed with Fisher exact test and Kappa coefficient, respectively.
Results: During the 3-month period we included 84 consecutive patients (88.1% female, median age (IQR) 49.5 (41.9–56.5) years). Results of answers to each item, final outcome of the questionnaire and the level of individual agreement for each item are presented in Table 1.

Table 1.. Answers to Raynaud's phenomenon International Consensus Criteria questionnaire according to mode of administration

	Self-administered	Interview based	p-value**	Measure of individual agreement– Kappa coefficient (95% CI)
	Yes, N (%)	Yes, N (%)		
Item 1. Are your fingers unusually sensitive to cold?	79 (94.0%)	78 (92.9%)	1	0.514 (0.101–0.927)
Item 2. Occurrence of biphasic colour change during the vasospastic episodes (white and blue)	40 (47.6%)	42 (50.0%)	0.877	0.762 (0.623–0.900)
Item 3. RP disease score	53(63.1%)	67 (79.8%)	0.026	0.549 (0.330–0.747)
Presence of RP according to RPICq	31 (36.9%)	36 (42.9%)	0.529	0.777 (0.640–0.915)

*RP – Raynaud's phenomenon; **RPICq** - International Consensus Criteria for the Diagnosis of Raynaud's Phenomenon questionnaire, ** Fisher-exact test

Conclusion: Overall, there was a substantial level of agreement between self-administered and interview-based application of International Consensus Criteria for the Diagnosis of Raynaud's Phenomenon questionnaire. However, we observed that the patients were inclined to score the severity of their RP lower than the physicians.

REFERENCE

[1] Maverakis E, Patel F, Kronenberg DG, Chung L, Fiorentino D, Allanore Y, et al. International consensus criteria for the diagnosis of Raynaud's phenomenon. J Autoimmun 2014;**48–**49:60–5.

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SAT0293 SPECIFIC ALTERATIONS OF NAILFOLD CAPILLARIES MIGHT ANTICIPATE THE APPEARANCE OF THE EARLY CAPILLAROSCOPIC SCLERODERMA-PATTERN IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Non-specific abnormalities (i.e. capillary enlargements) are usually found at the nailfold videocapillaroscopy (NVC) analysis in patients affected by primary Raynaud's phenomenon (PRP). We have previously demonstrated that capillary diameter is an independent predictor for development of systemic sclerosis (SSc) associated secondary Raynaud's Phenomenon (SRP), so that progression to SRP is unlikely for subjects affected by RP when average nailfold capillary diameter is under 30 μm [1]. However, until now these findings have not been clearly classified in a defined pattern able to really predict the evolution to a scleroderma-pattern.
Objectives: This pilot study aimed to identify in a cohort of SSc patients a "very early" NVC pattern at high risk of evolution in the already defined NVC scleroderma-patterns.

Methods: We selected the NVCs of 273 patients affected by SSc (according to 2013 ACR criteria) who presented one of the validated NVC scleroderma patterns (81 with "Early" pattern, 84 with "Active" pattern, 92 with "Late" pattern, 16 with "scleroderma-like" pattern) (2). Among the 273 SSc patient with an established NVC scleroderma-pattern, a number of 54 subjects who had previously NVC analyses performed before the development of the scleroderma-pattern were enrolled. Time of evolution was calculated, and a detailed pilot study of capillaroscopic characteristics was random executed on 10 of those patients. The analysis included the number and the limbs diameters (arterial, venous, and apical) of capillaries with a diameter over 30 μm, together with the total number of capillaries and microhemorrhages, in 16 images per subject.
Results: All the 54 patients (100%) showed enlarged capillaries with an average diameter over 30 μm in their previous NVC. At the follow up, thirty-one patients (57%) developed an "Early" scleroderma pattern in the following 3 years, 6 patients (11%) developed an "Active" pattern in 4 years, 3 patients (6%) evolved in "Late" NVC pattern in 5 years, whereas 14 patients (26%) developed a "scleroderma-like pattern" in 4 years. The average time of evolution in a scleroderma-pattern was 4 years. The detailed pilot morphological analysis conducted on 10 patients revealed an average total number of capillaries of 8.6/mm at last non-specific NVC analysis; among these 2.66 (31%) capillaries showed a diameter over 30 μm. The mean value diameter of the most dilated capillary was 35.74 μm (arterial limb 33.34 μm, apical limb 43.94 μm, venous limb 30 μm); the mean value for microhemorrhages was 0.6/mm. The mean number of capillaries reduced from 8.6±0.8 to 6.9±2.2/mm (p=0.01) during follow-up (4 years).
Conclusion: Present detailed pilot study demonstrates that SSc patients showed a significant increase of nailfold capillary diameter over 30 μm before development of a validated NVC scleroderma-pattern at follow up. Even if this is an independent predictor for development of SSc as previously demonstrated, the data could help in intercepting patients with RP at higher risk of evolution in a validated SSc NVC pattern.

REFERENCE

[1] Trombetta AC, et al. J Rheumatol. 2016;43:599-606. 2. Cutolo M, et al. J Rheumatol 2000;27:155-60.

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SAT0294 ANALYSIS OF POLIAUTOIMMUNITY IN THE DIFFERENT SUBSETS OF SCLERODERMA

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Background: Coexistence of different connective tissue diseases based on their common autoimmune base is a feasible circumstance, which is known as poliautoimmunity (PAI).
Objectives: Evaluation of the occurrence of PAI in systemic sclerosis (SSc) according to subtypes in the patients included in the Spanish SSc Registry (RESCLE). Causes of death were also analyzed.
Methods: A nationwide, cross-sectional study was carried out. All participating centers had obtained local ethics committee approval.
Results: PAI was present in 46% out of 1911 patients, of whom, 33% had more than one association. Most of these patients were women (93%, p<0.001), with no significant differences regarding first manifestation: Raynaud's phenomenon, puffy hands, arthralgia or skin sclerosis. Isolated SSc was more frequent in all subsets (table 1). Sjogren's syndrome was by far the most frequent associated disorder, with a RR of 1376 (table 2). Causes of death (SSc-related or not) did not significantly differ whether PAI was present or not.

Table 1.. Prevalence of PAI according to subsets.

	Isolated SSc	PAI	P-VALUE
lcSSc	588 (57%)	554 (63%)	0.008
dcSSc	210 (20%)	188 (21%)	0.611
ssSSc	121 (12%)	85 (9.7%)	0.160
earlySSc	28 (2.7%)	16 (1.8%)	0.222
preSSc	85 (8.2%)	36 (4.1%)	<0.001

Table 2.. Prevalence of the different associated autoimmune disorders.

	TOTAL	lcSSc	dcSSc	sineSSC	earlySSC	preSSc
Sjögren's síndrome	475 (25%)	317 (28%)	106 (27%)	34 (17%)	6 (14%)	12 (9.9%)
Thyroid autoimmune disorder	268 (14%)	173 (15%)	36 (9.0%)	35 (17%)	8 (18%)	16 (13%)
Primary biliary colangitis	88 (4.6%)	61 (5.3%)	5 (1.3%)	17 (8.3%)	0 (0.00%)	5 (4.1%)
Sclerosing colangitis	6 (0.31%)	4 (0.35%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.7%)
Autoimmune hepatitis	20 (1.0%)	17 (1.5%)	2 (0.50%)	0 (0.00%)	0 (0.00%)	1 (0.83%)
Systemic lupus erythematosus	11 (0.58%)	7 (0.61%)	1 (0.25%)	3 (1.5%)	0 (0.00%)	0 (0.00%)
Antiphospholipid syndrome	16 (0.84%)	8 (0.70%)	5 (1.3%)	2 (0.97%)	1 (2.3%)	0 (0.00%)
Inflammatory myopathy	99 (5.2%)	45 (3.9%)	47 (12%)	6 (2.9%)	1 (2.3%)	0 (0.00%)
Rheumatoid arthritis	6 (0.31%)	4 (0.35%)	2 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Conclusion: A rather higher prevalence than reported was observed, although distribution of the associated disorders was similar. No remarkable differences were found regarding SSc subsets, either PAI prevalence, initial manifestations or causes of death.
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SAT0295 ABSTRACT WITHDRAWN

SAT0296 FAST TRACK ALGORITHM: HOW TO DIFFERENTIATE A SCLERODERMA PATTERN FROM A NON-SCLERODERMA PATTERN

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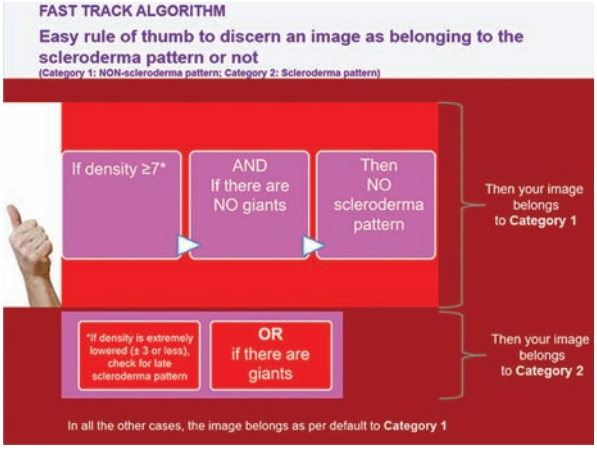
Background: The European League Against Rheumatism Study Group on Microcirculation in Rheumatic Diseases is a non-profit international network of expert centres. Its main research focus is to investigate the

morphology and function of the microcirculation with different non-invasive techniques such as nailfold videocapillaroscopy (NVC). NVC is of paramount importance for the differential diagnosis of primary and secondary Raynaud's phenomenon [1], and is part of the 2013 ACR/EULAR classification criteria for systemic sclerosis. As there is a wide variety of non-scleroderma patterns, the categorisation of capillaroscopic images as non-scleroderma patterns may be a challenge to the capillaroscopist.

Objectives: This study was designed to propose a simple fast track algorithm to differentiate scleroderma patterns from non-scleroderma patterns and to assess its interobserver reliability.

Methods: During the 8th EULAR course on capillaroscopy held in Genoa, September 2018, a lecture on teaching the fast tract algorithm to categorise an image as non-scleroderma (category 1) or scleroderma pattern (category 2) (see figure) was given to all attendees (from 43 different countries): 6 experts, 68 novices, 53 moderately experienced (< 5 years of experience with capillaroscopy) and 14 experienced physicians (> 5 years of experience with capillaroscopy). Immediately after training, an examination was performed on 30 images. Classification of the images was defined by the presenter (VS) as the gold standard. Interobserver reliability was assessed by the calculation of kappa coefficients and proportion of agreement versus the gold standard.

Results: The light kappa was 1 for the independent experts (n=6) and 0.92 for the attendees (n=135). When comparing with the gold standard, an equal mean kappa of 0.96 (95%CI 0.95 – 0.98) was found for both independent experts and attendees. Analyses according to the reported level of experience on capillaroscopy revealed a mean index of reliability of 0.98 (95%CI 0.96 – 0.99) for novices, 0.96 (95%CI 0.93 – 0.99) for moderately experienced raters and 0.93 (95%CI 0.85 – 1.01) for experienced raters.



Conclusion: For the first time a fast track algorithm has been developed that was trainable within an hour to non-experienced capillaroscopists and has an excellent reliability to discern a non-scleroderma from a scleroderma pattern by medical doctors with varying levels of expertise in capillaroscopy.

REFERENCE

[1] Koenig M, et al. Arthritis Rheum. 2008;58(12):3902-12.

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SAT0297 DISTINCT CLINICAL PROFILES OF CHINESE AND SWEDISH IDIOPATHIC INFLAMMATORY MYOPATHY PATIENTS WITH ANTI-MELANOMA DIFFERENTIATION ASSOCIATED GENE 5 (MDA5) ANTIBODY

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Background: Anti-melanoma differentiation-associated gene 5 antibody (anti-MDA5 Ab) is one of the most clinically important myositis specific antibodies. It has been found to be associated with severe cutaneous and pulmonary complications. Nonetheless, there appears to be geographical variations in the prevalence and phenotypic presentation of the antibody [1]. We conducted the first comparative study of two ethnogeographically different idiopathic inflammatory myopathy (IIM) cohorts focusing on anti-MDA5 Ab, using standardized classification criteria, antibody detection methods and clinical features assessment.

Objectives: The objectives of the study were to compare the prevalence of the anti-MDA5 Ab and its associated clinical features between Chinese IIM patients in Hong Kong and Caucasian patients in Sweden.

Methods: This multicenter retrospective cohort study was conducted on IIM patients followed up in the rheumatology clinic or admitted to the rheumatology wards of the participating hospitals in Hong Kong and Sweden with anti-MDA5 Ab tested between September 2015 and August 2018. The diagnosis of IIM was based on the 2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria with definite or probable cases being included. Demographics and clinical features were collected by reviewing the medical records. A commercial line blot immunoassay kit (EUROIMMUN) was used to detect the anti-MDA5 autoantibodies.

Results: Altogether, 409 patients with IIM (Sweden: 206, Hong Kong: 203) were recruited. The Swedish patients were generally older (mean age 58.1 vs 51.5 years, p<0.001) at diagnosis, and more of them were male (41.4% vs 23.2%, p<0.001). Subgroups of patients were: dermatomyositis 42.9%, polymyositis 39.3%, inclusion body myositis 15.7% and clinically amyopathic dermatomyositis 2.1% in the Swedish cohort, and 39.4%, 39.4%, 0% and 21.2% respectively in the Chinese cohort. Anti-MDA5 Ab was found in 11.8% of the Chinese and 5.83% of the Swedish patients (p=0.032). The Hong Kong Chinese patients were found to have significantly more ILD (52.7% vs 34.7%) and RPILD (9.41% v 3.65%), while the Swedish patients had more dysphagia (55.3% vs 29.7%) and cardiac involvement (14.0% vs 5.3%). Anti-MDA5 Ab was associated with male gender, younger age at diagnosis, amyopathy, refractory rash, ILD and RPILD in the Swedish patients. The same associations were found in the Chinese patients except the young age at diagnosis. Besides, in the Chinese cohort, the antibody was also positively associated with skin ulceration, vasculitis and hoarseness, but negatively associated with cancer, dysphagia and other connective tissue diseases. When comparing only patients with anti-MDA5 Ab, Chinese patients were significantly older at diagnosis (mean age 47.9 vs 36.4 years, p=0.001), more likely to be amyopathic (79.2% vs 18.2%, p=0.002) and had more vasculitic skin changes (65.2% vs 0%, p<0.001) than the Swedish patients. They also had a tendency towards developing more skin ulcers (45.8% vs 18.2%, p=0.15) and less dysphagia (8.33% vs 36.4%, p=0.063).

Conclusion: The distinct clinical profiles identified in the Chinese and Swedish IIM patients with anti-MDA5 Ab could depend on different genetic or environmental factors, and may enhance our knowledge about

the clinical utility of the antibody and help deciphering the pathogenesis of this complex disease.

REFERENCE

[1] So H, Ip R, Wong V, Yip R. Analysis of anti-melanoma differentiation-associated gene 5 antibody in Hong Kong Chinese patients with idiopathic inflammatory myopathies: diagnostic utility and clinical correlations. Int J Rheum Dis 2018;21(5):1076-1081.

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SAT0298 DIAGNOSIS OF SYSTEMIC SCLEROSIS: HOW AND WHEN

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Background: Systemic sclerosis (SSc) is a heterogeneous disease regarding its clinical expression, evolution and forms of presentation. In spite of the lack of a disease modifying therapy, there are effective treatment options to control complications such as pulmonary arterial hypertension (PAH), interstitial lung disease (ILD) or digital ulcers (DU). Early diagnosis is crucial and allows the physician to start these treatments as soon as possible. To know how and when we diagnose SSc and its clinical manifestations will help us to detect potential improvement areas.
Objectives: To study the main clinical manifestations that lead to diagnosis of SSc, the delay of the diagnosis after the beginning of the first symptom, and to analyze the role of the different clinical features in the diagnosis.
Methods: A retrospective and descriptive study was conducted, which included patients with SSc from our Rheumatology Department. Clinical data and specific autoantibodies profile (ACA, Scl-70, RNP) were recorded, paying special attention to the clinical manifestations that led to diagnosis. We classified them in eight categories: secondary Raynaud's phenomenon (SRP), digital ischemia or DU, musculoskeletal symptoms, skin induration, ILD, PAH, specific autoantibodies detection, and others. The date of starting of Raynaud's phenomenon (RP), of the first non-Raynaud symptom and the date when the diagnosis was established were registered. Analysis were conducted using STATA.
Results: The sample included 149 patients with SSc, meeting the 2013 ACR/EULAR criteria. RP appeared several years prior to the diagnosis (median of 3 years, IQR 0-8), and typically before the first non-Raynaud symptom. 141 out of 149 patients (94,6%) presented RP prior to the diagnosis. However, SRP was the manifestation that led to diagnosis in only 42/149 patients (41,6%), followed by skin induration (18,1%) and DU (12,7%). Surprisingly, 30/149 patients (20,1%) were diagnosed after the appearance of severe complications such as DU, ILD or PHA. Most patients started symptoms related to SSc several years before diagnosis (details in Table 1). 40/48 patients (83%) that were diagnosed due to SRP, presented abnormalities in nailfold capillaroscopy as well as specific autoantibodies (Table 2). Presenting telangiectasia, calcinosis, ILD or PAH was not associated with an early diagnosis, nor was ACA, Scl-70 or RNP positivity.
Conclusion: An early approach of RP with capillaroscopy and specific autoantibodies would avoid delays to SSc diagnosis, allowing a close follow-up and an early treatment if necessary. SSc must always be considered as a differential diagnosis in patients with DU, ILD or PAH. An adequate *referral of patients from primary care physicians* to rheumatologists, and a multidisciplinary approach with Vascular Surgery, Pneumology and Cardiology Units would advance the diagnosis of this complex and potentially severe disease.

Table 1.

CLINICAL MANIFESTATION THAT LEADS TO DIAGNOSIS	PACIENTS *n (%)*	YEARS FROM FIRST SYMPTOM TO DIAGNOSIS *median (IQR)*	YEARS FROM RAYNAUD'S PHENOMENON TO DIAGNOSIS *median (IQR)*
Secondary Raynaud's Phenomenon	62 (41,6)	3 (1-10)	3 (1-9)
Skin induration	27 (18,1)	1 (0-4)	1 (0-4)
Digital Ischemia/UD	19 (12,7)	2 (0-12)	2 (0-12)
Musculoskeletal symptoms	18 (12,1)	3 (0-6)	3,5 (0-6)
ILD	8 (5,3)	2,5 (1-4)	3 (0-4)
Specific autoantibodies	6 (4)	5,5 (4-9)	3 (0-9)
Others	6 (4)	5,5 (0-10)	5,5, (0-10)
PAH	3 (2)	35 (20-35)	35 (20-35)

Table 2.

PACIENTES WITH SECONDARY RAYNAUD'S PHENOMENON	*n (%)*
With abnormal capillaroscopy	48/59 (81)
…and only ACA+	36 (75)
…and only anti Scl-70+	3 (6,2)
…and only anti-RNP+	2 (4,1)
… and ACA+ and/or Scl70+ and/or anti-RNP+	40 (83,3)
… without autoantibodies	8 (16,6)

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SAT0299 PREVALENCE OF PERIPHERAL EOSINOPHILIA AND CLINICAL ASSOCIATIONS IN THAI SYSTEMIC SCLEROSIS PATIENTS

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Background: Eosinophilia has been reported in systemic sclerosis (SSc) and localized scleroderma, so it might be part of the immune response in the pathogenesis of the disease.
Objectives: To determine the prevalence and clinical associations with peripheral eosinophilia in Thai SSc patients.
Methods: A cross-sectional study was conducted among Thai adult SSc patients, followed up at the Scleroderma Clinic, Khon Kaen University, Thailand, between November 1, 2016 and November 30, 2017. We excluded patients who had clinical overlap with other connective tissue disease, coexisting with localized scleroderma, eosinophilic fasciitis, or eosinophilia myalgia syndrome, and other diseases that cause eosinophilia. Peripheral eosinophilia is defined when total eosinophil count (TEC) is greater than 500 cells/mm^3. Clinical, laboratory tests for tissue parasite, cytokines, and others for evaluation the cause of eosinophilia were done on the study date.
Results: A total of 185 SSc patients were enrolled. Fifty-seven cases (10.1%) were peripheral eosinophilia of which 21 had the causes of eosinophilia identified by laboratory without clinical symptoms (viz., 9 adrenal insufficiency, 2 tuberculosis, and 10 parasitic infection). The total prevalence of the unknown causes of peripheral eosinophilia in SSc was 21.9% (95%CI 15.9-29.1) (36 of 164 cases). Five of the patients had TEC above 1500 cells/mm^3. Of the 164 SSc patients, the majority (70.6%) had diffuse cutaneous SSc, and the female to male ratio was 2.3:1. The respective median age and median duration of the disease was 57.0 years (IQR 52.2-63.9) and 6.5 years (IQR 2.9-10.5). According to a multivariate analysis, being male and duration of disease increasing

every year were significantly associated with peripheral eosinophilia in SSc patients (OR 3.46 (95%CI 1.11-10.73) and 1.16 (95%CI 1.03-1.30), respectively), while Raynaud's phenomenon had a significantly negative correlation with peripheral eosinophilia in SSc (OR 0.27: 95%CI 0.09-0.84). Other parameters—such as SSc subset, severity of skin tightness, serology, cytokines (transforming growth factor-β, interleukin-5)—were not correlated with peripheral eosinophilia.

Conclusion: Peripheral eosinophilia of unknown cause can be detected 1 in 5 SSc patients. The factors associated with peripheral eosinophilia are longer disease duration and being male while vasculopathy has a negative association.

REFERENCES

[1] Falanga V, Medsger TA. Frequency, levels, and significance of blood eosinophilia in systemic sclerosis, localized scleroderma, and eosinophilic fasciitis. J Am Acad Dermatol. 1987 Oct;17(4):648–56.
[2] Giordano M, Ara M, Valentini G, Chianese U, Bencivenga T. Presence of eosinophilia in progressive systemic sclerosis and localized scleroderma. Arch Dermatol Res. 1981;271(4):411–7.
[3] Tefferi A, Patnaik MM, Pardanani A. Eosinophilia: secondary, clonal and idiopathic. Br J Haematol. 2006 Jun;133(5):468–92.
[4] Mejia R, Nutman TB. Evaluation and differential diagnosis of marked, persistent eosinophilia. Semin Hematol. 2012 Apr;49(2):149–59.
[5] Kargili A, Bavbek N, Kaya A, Koşar A, Karaaslan Y. Eosinophilia in rheumatologic diseases: a prospective study of 1000 cases. Rheumatol Int. 2004 Nov;24(6):321–4.
[6] Gustafsson R, Fredens K, Nettelbladt O, Hällgren R. Eosinophil activation in systemic sclerosis. Arthritis Rheum. 1991 Apr;34(4):414–22.

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SAT0300 ABSTRACT WITHDRAWN

SAT0301 THE USE OF 16 GRIPS TEST TO EVALUATE HAND IMPAIRMENT IN SYSTEMIC SCLEROSIS (SSC): PRELIMINARY TO CONSTRUCTION OF PERSONALIZED DEVICES

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Background: Systemic sclerosis (SSc) is a progressive connective tissue disease of unknown etiology characterized by autoimmune response and changes in the microvascular system. Although skin fibrosis represents the primary element of this disease, patients may present muscular and/or joint damage. Hand impairment is a major cause of morbidity and disability in about 90% of SSc patients. The ADL difficulties are similar to those of patients with rheumatoid arthritis but SSc patients use a low number of assistive device. In our center an interdisciplinary research unit composed of rheumatologists, rehabilitators, occupational therapists, and design engineers, with the directly involvement of the SSc patients within the design team, are developing a design method to prototype ergonomic assistive device personalized for hands.

Objectives: Evaluate through the 16 grip test which were the most difficult grips for SSc patients in order to understand what particular changes we need to focus on more rehabilitative attention. Determine what ADL can be linked to difficult grips to understand how to work on it. Give advice and design appropriate customized ergonomic aids.

Methods: 92 patients (79 females and 13 males) with SSc followed by our tertiary Universitary based Rheumatologic Center have been specifically evaluated by Hand Rehabilitation Service. The average age of patients was 56y. The 16 grip test was used to evaluate patients. It includes 16 different pattern of grip divided into power grip and precision pinch - Moreover it tests basically two different grip and pinch modalities: static prehension and dynamic prehension. The score for each grip goes from 0 to 4 (0=impossible,1=realized with high difficulty, 2=medium difficulty, 3= low difficulty, 4=normal).

Results: 30 patients (32%) had no grip problem, 9 only on the left and 5 on the right hand; 4 patients presented grip difficulty in both hands with a reduction> 25%. 31 had difficulty in 2 or more grip pattern. The most interested grips are the monodigital and pluridigital pressure, the tip to tip pinch, the extension grip in both sexes; the teno-digital in males and the digito-palmar in females. Over 60% of the grips were normal; in particular in our patients only few deficiencies in the power and in the static prehension grips were reported. The most interested patterns of grips are in the group of precision handling related to the use of the pads; the extension grip to the difficulty in opening the first commissure.

Conclusion: Over 60% of the grips were normal.; in particular in our patients only few deficiencies in the power grips and in the static prehension grips were reported. The most interested patterns of grips are in the group of precision handling related to the use of the fingertips; the extension grip to the difficulty in opening the first commissure. The problems of hand impairment are restricted to a subset of patients around 10-15%. From these results we can obtain useful data to construct our personalized devices for SSc hands.

REFERENCES

[1] A Co-Design Method for the Additive Manufacturing of Customised Assistive Devices for Hand Pathologies. F Gherardini, MT Mascia, V Bettelli, F Leali. JIDPS Pre-press, pp. 1-18, 2018

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SAT0302 SINGLE-PORT THORACOSCOPIC SYMPATHICOTOMY IS VERY EFFECTIVE FOR TREATMENT RESISTANT RAYNAUD'S PHENOMENON: A ONE MONTH FOLLOW-UP

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Background: In some patients, Raynaud's Phenomenon (RP) symptoms prove resistant to conventional vasodilatory treatment. Thoracic sympathectomy is shown to be effective as treatment of RP, but is associated with surgical burden. During this procedure, the sympathetic nerve traversing to the upper extremity is dissected, subsequently leading to vasodilatation. In our centre, single-port thoracoscopic sympathicotomy (SPTS) has been developed, a minimally invasive technique, extensively limiting surgical burden. [1]

Objectives: To evaluate SPTS feasibility and efficacy after one month in patients with treatment resistant RP.

Methods: In this study RP patients were their own controls, as they received an unilaterally left sided sympathicotomy. The effects of the SPTS was assessed at baseline and one month after the procedure. Perfusion of the hand was assessed using a cooling and recovery procedure, and laser speckle contrast analysis (LASCA) at room temperature of 23 degrees Celsius. The number and duration of RP attacks was reported over a two week period prior to reassessment by standard questionnaire.

Results: Eight patients were included in the study, 6 male/2 female, with a median (IQR) age of 45.2 (30.2–55.3) years, body mass index of 23.9 (23.4–26.8) kg/m², and RP duration of 7.0 (2.5–14.3) years. Five patients suffered from primary RP, and three patients had RP secondary to connective tissue disease (CTD) [mixed CTD (n=2) and limited cutaneous systemic sclerosis (n=1)]. All patients were very satisfied with the results and the number of attacks in the left hand decreased (p=0.018). After surgery an unilateral improvement in left hand perfusion was observed

during the cooling and recovery procedure (p=0.008, figure 1), and in the fingertips with LASCA (p=0.023). No serious adverse events occurred.

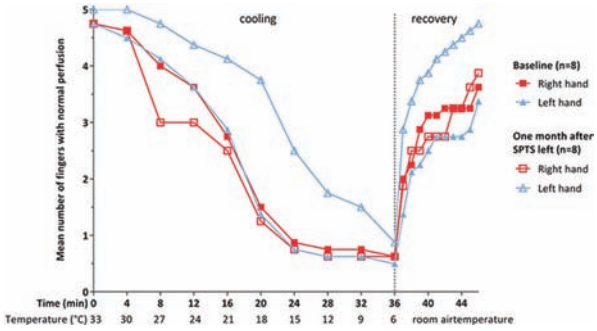


Figure 1.. Mean number of fingers per hand with normal perfusion during a cooling and recovery procedure before and after left-sided SPTS

Conclusion: SPTS, a minimally invasive technique, appears to be feasible and effective in improving hand perfusion in patients with RP after one month. Although these results are promising, long-term efficacy needs to be established and therefore follow-up is on-going.

REFERENCE

[1] Kuijpers M, Klinkenberg TJ, Bouma W, DeJongste MJ, Mariani MA. Single-port one-stage bilateral thoracoscopic sympathicotomy for severe hyperhidrosis: prospective analysis of a standardized approach. J Cardiothorac Surg 2013;8:216-8090-8-216.

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SAT0303 DESIGN OF PHASE 3 STUDY OF LENABASUM FOR THE TREATMENT OF DERMATOMYOSITIS

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Background: To date, there has not been a Phase 3 study evaluating efficacy and safety of a new chemical entity solely in subjects with dermatomyositis (DM). There is no precedence for design of such a pivotal study, including selection of patients or efficacy outcomes.
Objectives: Develop a Phase 3 study design for testing efficacy and safety of lenabasum in DM that would be acceptable to experts and for registration purposes.
Methods: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses. Lenabasum had acceptable safety and tolerability and improved multiple physician-reported and patient-reported efficacy outcomes in a 16-week double-blinded, randomized, placebo-controlled Phase 2 trial in DM subjects with refractory, skin-predominant involvement, as well as in the open-label extension of that study. The Phase 3 trial design was based on Phase 2 data, input from a steering committee of experts in DM clinical trials, and recommendations made by regulatory authorities in the US, EU, Sweden, and Japan.
Results: A global, double-blind, randomized, interventional design was chosen to provide an unbiased assessment of the efficacy, safety and tolerability of lenabasum 20 mg bid and 5 mg bid compared to placebo in the treatment of DM. A 52-week treatment duration was selected to provide safety and efficacy data adequate to support chronic treatment. Subjects with DM were classified by Peter and Bohan criteria or the 2017 EULAR/ACR classification criteria for DM (both amyopathic DM and classic DM). Subjects will be required to have active disease, as assessed by an expert and based on a range of muscle, skin, and other disease manifestations. Subjects must be on stable doses of current DM treatments with any background immunosuppressive medications allowed except prednisone $\geq$ 20 mg per day or equivalent. This inclusivity allows testing of efficacy and safety of lenabasum in the setting of current treatment practice and reduces risk of disease flare early in the study. The primary efficacy outcome is change from baseline in 2016 ACR/EULAR Total Improvement Score (TIS) for DM and polymyositis. This composite outcome has six domains that broadly capture improvement in disease activity, is relevant to the range of manifestations in DM, and is applicable to the assessment of efficacy in the target patient population. Secondary efficacy outcomes were chosen to assess how the subject functions (Short Form – 36 physical functioning domain), major organ involvement (MMT-8, CDASI activity score, and a new Investigator Global Assessment scale of skin activity designed specifically for this study), and lung function (FVC). Change in oral corticosteroid dose also will be captured.
Conclusion: To our knowledge, this is the first Phase 3 study in DM with a new molecular entity. As such, agreement with experts and regulatory authorities on design represents a step forward in the development pathway of new treatments for DM.
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Corbus—design of clinical trial in DM
23 and me—ad hoc consulting
Admiryx—ad hoc consulting
Janssen—SAB for PSOLAR database
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SAT0304 RELATIONSHIP BETWEEN INTERLEUKIN-23 AND GASTROINTESTINAL INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Growing evidence suggests that T-cell proliferation and cytokine secretion play an important role in the pathogenesis of systemic sclerosis (SSc). Gut involvement is the leading cause of morbidity in patients with SSc. In this study we evaluated interleukin-23 (IL-23) protein expression profiles and investigated its association with gastrointestinal involvement in SSc patients.

Objectives: To evaluate IL-23 expression profiles and to explore association between IL-23 and gastrointestinal involvement in SSc patients.
Methods: Study included 31 SSc patients. The expression level of IL-23 mRNA was determined by qRT-PCR method and Enzyme-Linked Immunosorbent Assay (ELISA) was used for analysis of IL-23 serum protein level. We used UCLA GIT 2.0 questionnaire to assess gastrointestinal (GIT) involvement in SSc patients.
Results: We found a positive correlation between disease duration and expression levels of IL-23mRNA ($r = 0.49$, $p<0.05$). Nine SSc patients with high IL-23 levels (cut off point 6.8 pg/ml) had significantly higher UCLA GIT 2.0 score, compared to 22 SSc patients with normal IL-23 levels ($p<0.05$). Serum level of IL-23 positively correlated with total GIT score ($r = 0.35$, $p<0.05$) and distension scale score ($r= 0.5$, $p<0.05$).
Conclusion: High IL-23 serum levels significantly correlated with gastrointestinal involvement (higher UCLA GIT 2.0 score) in patients with SSc.

REFERENCES

[1] Komura K, Fujimoto M, Hasegawa M, Hara T, Muroi E, et al. (2008) Increased serum interleukin 23 in patients with systemic sclerosis. J Rheumatol: 35; 120.
[2] Savarino E, Furnari M, De Bortoli N, Martinucci I, Bodini G, Ghio M, et al. (2014). Gastrointestinal involvement in systemic sclerosis. Presse Med 43: e279-91.
[3] Khanna D, Hays RD, Maranian P, Seibold JR, Impens A, Mayes MD, et al. (2009) Reliability and validity of the University of California, Los Angeles scleroderma clinical trial consortium gastrointestinal tract instrument. Arthritis Rheum; 61: 1257-63.
[4] Zekovic A, Damjanov N (2017) Validation of Serbian version of UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument in 104 patients with systemic sclerosis. Rheumatol Int;37(5):735-741.

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Spondyloarthritis - clinical aspects (other than treatment)

SAT0305

ASSOCIATION OF SKIN PSORIASIS WITH CLINICAL AND RADIOGRAPHIC CHARACTERISTICS IN AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

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Background: Overlap between psoriasis and axial spondyloarthritis (axSpA) is common, as psoriasis occurs in approximately 10% of patients with axSpA. It has been noted that such an association may result in a particular phenotype of the disease, which has not been extensively investigated so far.
Objectives: To analyze the association between skin psoriasis and clinical and radiographic characteristics of axSpA.
Methods: Altogether 210 patients with definite axSpA (115 with radiographic and 95 with non-radiographic axSpA) from the German Spondyloarthritis Inception Cohort (GESPIC) were included in the current study. Information on the presence of psoriasis, clinical features, parameters of disease activity, and treatment were collected at baseline and every 6 months thereafter. Radiographs of sacroiliac joints and spine were obtained at baseline and after 2 years of follow-up and were scored by two trained readers according to the conventional grading system of the modified New York criteria (grade 0 to 4 per joint) and mSASSS (score 0-72). Group comparison was performed using Mann-Whitney U-Test for continuous variables and Fisher exact test for binary variables. A logistic regression model was constructed to assess the association of the psoriasis with radiographic progression in the sacroiliac joints and in the spine.
Results: Overall, 28 patients (13.3%) with axSpA had skin psoriasis. Patients with psoriasis were less frequently HLA-B27 positive in comparison with patients with no skin symptoms (57.1% and 82,9% respectively, p=0.004), had more frequently a history of peripheral arthritis (57.1% and 31.9%, p= 0.01), had higher disease activity (BASDAI baseline 5.0 ± 2.2 and 3.8 ± 2.1, respectively, p=0.01) and worse physical function (BASFI at baseline 3.8 ± 2.3 and 2.8 ± 2.3, respectively, p=0.02) (***Table 1***). They were also more frequently treated with DMARDs (57.1% and 24.7%, respectively, p=0.001). Baseline radiographic characteristics were comparable between the groups. There was no statistically significant difference in rates of radiographic spinal progression and progression of radiographic sacroiliitis in patients with vs. without psoriasis (***Table 2***). In the multivariable logistic regression analysis, adjusted for the smoking status, sex, NSAID intake, presence of syndesmophytes at baseline and time-averaged ASDAS, skin psoriasis showed no significant association with radiographic spinal progression (OR 2.93, 95% CI 0.81 to 10.58) nor with progression of radiographic sacroiliitis by at least 1 grade (OR 1.98, 95% CI 0.72 to 5.43)
Conclusion: Presence of skin psoriasis in patients with axSpA was associated with HLA-B27 negativity, peripheral arthritis, higher disease activity and worse functional status, but had no significant impact on radiographic characteristics of the disease.

REFERENCES:

none

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Table 1. Demographic, clinical and radiographic characteristics of axSpA patients with and without psoriasis.

Parameter (n (%) or mean±SD)	Psoriasis (n=28)	No psoriasis (n=182)	P*
Clinical characteristics and demographics			
Male sex	12 (42.9%)	95 (52.2%)	0.419
Age, years	39.1 ± 10.7	37.0 ± 10.5	0.278
Age at symptom onset, years	33.9 ± 11.4	33.0 ± 10.8	0.63
Diagnostic delay, years	3.2 ± 2.1	2.6 ± 2.4	0.08
HLA-B27 positivity	16 (57.1%)	150 (82.9%)	**0.004**
Smoking, BL	6 (21.4%)	65 (35.7%)	0.20
Inflammatory back pain, BL	25 (89.3%)	153 (84.1%)	0.58
Family history of SpA	15 (53.6%)	63 (34.6%)	0.06
Peripheral arthritis at BL	7 (25%)	24 (13.2%)	0.15
Peripheral arthritis ever	16 (57.1%)	58 (31.9%)	**0.01**
Enthesitis at BL	8 (28.6%)	38 (20.9%)	0.34
Inflammatory bowel disease, ever	1 (3.6%)	3 (1.6%)	0.44
Uveitis, ever	6 (21.4%)	36 (19.8%)	0.80
Disease activity			
BASDAI, BL	5.0 ± 2.2	3.8 ± 2.1	**0.01**
CRP mg/l, BL	10.1 ± 13.1	9.7 ± 15.6	0.84
Functional status			
BASFI, BL	3.8 ± 2.3	2.8 ± 2.3	**0.02**
BASMI, BL	2.1 ± 1.5	1.7 ± 1.7	0.07
Radiographic characteristics			
Fulfillment of the mNY criteria, BL	17 (60.7%)	98 (53.8%)	0.55
Sacroiliitis sum score, BL	4.1 ± 2.2	4.1 ± 2.0	0.95
Asymmetric sacroiliitis, BL (difference in by ≥1 sacroiliitis grade between the sides)	2 (7.1%)	17 (9.3%)	1.00
Mean mSASSS, BL	7.4 ± 12.1	3.8 ± 7.5	0.25
At least 1 syndesmophyte, BL	9 (32.1%)	55 (30.2%)	0.84
Treatment			
NSAID intake, BL	17 (60.7%)	123 (67.6%)	0.52
NSAID Index over 2 years of follow-up	43.6 ± 30.9	31.6 ± 27.1	0.06
DMARD intake, BL	16 (57.1%)	45 (24.7%)	**0.001**
TNFi intake over 2 years of follow-up	6 (21.4%)	16 (8.8%)	0.08
CS intake, BL	3 (10.7%)	9 (4.9%)	0.20

* Mann-Whitney U-Test for continuous variables, Fisher exact test for binary variables.

BL – baseline; HLA-B27 - Human leukocyte antigen B27; SpA – spondyloarthritis; BASDAI – Bath Ankylosing Spondylitis Disease Activity Index; CRP - C-reactive protein; BASFI – Bath Ankylosing Spondylitis Functional Index; BASMI – Bath Ankylosing Spondylitis Metrology Index; mNY Criteria – modified New York Criteria for Ankylosing Spondylitis, 1984; mSASSS - modified Stoke Ankylosing Spondylitis Spine Score; NSAID – non-steroid anti-inflammatory drugs, DMARD – disease-modifying anti-rheumatic drugs; TNFi – tumour necrosis factor α inhibitors; CS – corticosteroids.

Table 2. Association of skin psoriasis with radiographic progression in axial spondyloarthritis after 2 years of follow-up.

Outcome	Psoriasis (n=28)	No psoriasis (n=185)	p*
Spine			
mSASSS change	1.52 ± 4.02	0.61 ± 1.95	0.55
Progression of mSASSS by ≥2 points	6 (21.4%)	24 (13.2%)	0.25
New syndesmophytes or progression of syndesmophytes	7 (25.0%)	26 (14.3%)	0.16
Sacroiliac joints			
Change of the sacroiliitis sum score	0.18 ± 0.63	0.12 ± 0.87	0.71
Progression of sacroiliitis by at least 1 grade in opinion of both readers	3 (10.7%)	23 (12.6%)	1.00

* Mann-Whitney U-Test for continuous variables, Fisher Exact test for binary variables.

mSASSS - modified Stoke Ankylosing Spondylitis Spine Score.

Rudwaleit Consultant for: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma, Consultant for: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma, Denis Poddubnyy Grant/research support from: AbbVie, Merck Sharp & Dohme, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, UCB Pharma

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SAT0306 COMPARISON OF MEN AND WOMEN WITH AXIAL SPONDYLOARTHRITIS IN THE US-BASED CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

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Background: Axial spondyloarthritis (AxSpA) is a chronic inflammatory rheumatic disease that primarily affects the axial skeleton and frequently affects the peripheral joints and entheses. AxSpA encompasses ankylosing spondylitis and nonradiographic AxSpA. Sex differences have been described for patient reported outcomes (PROs) in SpA; however, more research is needed to better understand the overall clinical burden of AxSpA in women, particularly in the United States.

Objectives: To compare the patient demographics, clinical characteristics, treatment profiles, disease activity, quality of life, and work productivity between men and women with AxSpA in the US-based Corrona PsA/SpA Registry.

Methods: This study included patients aged ≥ 18 years with AxSpA enrolled in the Corrona PsA/SpA Registry between March 2013 and November 2018. Patients who were concurrently diagnosed with PsA were excluded. Patient demographics, clinical characteristics, treatment profiles, disease activity, quality of life, and work productivity were characterized for all patients with AxSpA at enrollment and were compared between men and women using *t* tests or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher's exact tests for categorical variables.

Results: Of 498 patients with AxSpA who were included in the study, 307 (61.6%) were male and 191 (38.4%) were female. Compared with men, women were less likely to work full time, were more likely to be normal weight/underweight, had a shorter disease duration, and were more likely to have depression, fibromyalgia, and prior csDMARD and prednisone use (**Table 1**; all $P < 0.05$). At enrollment, women with AxSpA had a shorter occiput-to-wall distance, but also had worse disease activity compared with men, as reflected by higher BASDAI and BASFI scores, higher enthesitis and tender/swollen joint counts, worse pain and fatigue, worse physical function (HAQ-S) and health state today (EQ VAS), and more severe work and activity impairment (**Table 2**; all $P < 0.05$).

Conclusion: In this US registry of patients with AxSpA, women had an increased overall burden of disease compared with men, including higher patient reported symptoms, higher disease activity, and greater work productivity impairment. Women also had lower scores for spinal mobility with increased signs of peripheral arthritis (eg, higher tender/swollen joint and enthesitis counts), suggesting that conventional definitions of AxSpA centered around axial symptoms may not be representative of the female population with disease. Improved awareness of sex differences in presentation of AxSpA may aid physicians in earlier identification and improved management of the disease.

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Table 1. Demographic and Clinical Characteristics and Treatment Profiles in Men and Women With AxSpA at Enrollment

Characteristic	Patients With AxSpA		*P* Value
	Men (N = 307)	Women (N = 191)	
Age, mean (SD) [n], years	47.3 (13.9) [305]	47.7 (13.5) [190]	0.75
Race, n (%)	n = 302	n = 186	0.08
White	276 (91.4)	172 (92.5)	
Black	3 (1.0)	6 (3.2)	
Other	23 (7.6)	8 (4.3)	
Work status, n (%)	n = 306	n = 190	< 0.01
Full time	190 (62.1)	102 (53.7)	
Part time	11 (3.6)	20 (10.5)	
Disabled	49 (16.0)	24 (12.6)	
Retired	38 (12.4)	22 (11.6)	
Other	18 (5.9)	22 (11.6)	
BMI, mean (SD) [n], kg/m²	29.8 (6.0) [297]	30.0 (8.5) [189]	0.32
BMI (in kg/m²) categories, n (%)	n = 297	n = 189	0.04
Normal/underweight (< 25)	64 (21.5)	60 (31.7)	
Overweight (25 to < 30)	102 (34.3)	54 (28.6)	
Obese (≥ 30)	131 (44.1)	75 (39.7)	
Symptom duration, mean (SD) [n], years	17.6 (12.3) [296]	15.7 (11.6) [184]	0.09
Disease duration, mean (SD) [n], years	10.3 (10.8) [301]	8.2 (9.9) [188]	0.02
HLA-B27 positive test result, n (%)	224 (73.0)	124 (64.9)	0.06
Select comorbidities, n (%)			
Depression	37 (12.1)	49 (25.7)	< 0.01
Fibromyalgia	3 (1.0)	20 (10.5)	< 0.01
Ulcerative colitis	9 (2.9)	13 (6.8)	0.04
Anxiety	7 (2.3)	10 (5.2)	0.08
Prior biologic use, n (%)	89 (29.0)	63 (33.0)	0.35
Number of prior biologics, n (%)			0.62
0	218 (71.0)	128 (67.0)	
1	57 (18.6)	39 (20.4)	
≥ 2	32 (10.4)	24 (12.6)	
Prior csDMARD use, n (%)	41 (13.4)	42 (22.0)	0.01
Prior prednisone use, n (%)	27 (8.8)	30 (15.7)	0.02

AxSpA, axial spondyloarthritis; BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug.

Table 2. Disease Activity, Quality of Life, and Work Productivity in Men and Women With AxSpA at Enrollment

Characteristic	Patients With AxSpA		*P* Value
	Men (N = 307)	Women (N = 191)	
ASDAS, mean (SD) [n]	2.6 (1.2) [179]	2.8 (0.9) [123]	0.07
BASDAI (0-10), mean (SD) [n]	4.2 (2.5) [294]	4.9 (2.3) [187]	< 0.01
BASFI (0-10), mean (SD) [n]	3.4 (2.8) [295]	4.1 (2.7) [185]	< 0.01
Lateral lumbar flexion (average of left and right), mean (SD) [n], cm	24.1 (20.1) [276]	23.4 (19.0) [170]	0.76
Occiput to wall, mean (SD) [n], cm	5.8 (7.7) [277]	2.7 (5.0) [172]	< 0.01
Enthesitis, n (%)	62 (20.2)	71 (37.2)	< 0.01
SPARCC Enthesitis Index (1-16)	3.2 (2.4) [62]	4.8 (3.2) [71]	< 0.01
Dactylitis, n (%)	9 (2.9)	3 (1.6)	0.39
Dactylitis count (1-20)	3.4 (3.5) [9]	1.3 (0.6) [3]	0.37
Tender joint count (0-68), mean (SD) [n]	1.8 (4.7) [299]	5.1 (9.6) [190]	< 0.01
Swollen joint count (0-66), mean (SD) [n]	0.6 (2.5) [299]	0.9 (2.2) [190]	0.01
Physician global assessment, mean (SD) [n]	25.7 (23.4) [295]	30.8 (22.2) [188]	< 0.01
Patient pain (VAS 0-100), mean (SD) [n]	45.3 (30.5) [293]	51.6 (27.8) [172]	0.03
Patient fatigue (VAS 0-100), mean (SD) [n]	45.4 (29.1) [306]	53.9 (27.4) [191]	< 0.01
Morning stiffness, n (%)	n = 299	n = 190	0.10
< 30 minutes	88 (29.4)	43 (22.6)	
≥ 30 minutes	211 (70.6)	147 (77.4)	
Patient global assessment (VAS 0-100), mean (SD) [n]	52.2 (32.5) [102]	52.5 (33.1) [41]	0.82
HAQ-S (0-3), mean (SD) [n]	0.59 (0.62) [258]	0.82 (0.65) [131]	< 0.01
EQ VAS (0-100), mean (SD) [n]	66.2 (22.2) [298]	61.1 (22.4) [189]	< 0.01
WPAI domains, mean (SD) [n]			
Current employment, n/m (%)	206/304 (67.8)	121/189 (64.0)	0.39
% Work time missed	6.7 (18.4) [190]	7.3 (17.4) [109]	0.33
% Impairment while working	24.9 (23.8) [199]	35.4 (28.5) [113]	< 0.01
% Overall work impairment	28.4 (27.1) [184]	36.4 (28.6) [105]	0.03
% Activity impairment	36.1 (29.7) [299]	45.9 (30.0) [188]	< 0.01

ASDAS, Ankylosing Spondylitis Disease Activity Score; AxSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Functional Index; EQ VAS, EuroQol visual analogue scale; HAQ-S, Health Assessment Questionnaire for the Spondyloarthropathies; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment questionnaire.

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SAT0307 LONG-TERM ASSOCIATION BETWEEN DISEASE ACTIVITY MEASURED BY ASDAS AND PHYSICAL FUNCTION IN A LARGE EARLY AXIAL SPONDYLOARTHRITIS COHORT

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Background: The Ankylosing Spondylitis Disease Activity Score (ASDAS) has been progressively replacing the Bath Ankylosing Spondylitis Disease Activity Score (BASDAI) as the main disease activity measure to assess patients with axial spondyloarthritis (axSpA), both in the research context as well as in clinical practice. However, further evidence is needed to show its meaningfulness regarding the longitudinal relationship with physical function.

Objectives: To study the long-term association between disease activity and physical function in axSpA.

Methods: DESIR is a prospective observational cohort of patients with recent onset (<3 years) inflammatory back pain, suggestive of axSpA. We analysed data collected during the first five years of follow-up and selected patients with a definite diagnosis of axSpA according to the treating rheumatologist. Physical function was assessed using the Ankylosing Spondylitis Health Assessment Questionnaire (HAQ-AS). Disease activity was measured using the ASDAS C-reactive protein (ASDAS-CRP) and BASDAI. In a first step, associations between HAQ-AS (dependent variable) and disease activity (defined by ASDAS or BASDAI), clinical and demographic variables were tested in univariable models. Multivariable models were then built adjusting for potential confounding factors found to be significant in the univariable analysis.

In a second step, additional multivariable analysis was conducted using the Chi-square Automatic Interaction Detector (CHAID) method, with HAQ-AS as dependent variable. The following independent variables were tested: ASDAS/BASDAI, enthesitis score, arthritis, employment status, gender, symptom duration, body mass index (BMI), HLA-B27 status, treatment with non-steroidal anti-inflammatory drugs (NSAID), conventional disease modifying anti-rheumatic drugs (cDMARD) and TNF-blockers. The final model fixed as criteria: 70 parent nodes and 20 child nodes to create new generations in the decision tree.

Results: Data from 644 patients and 4944 visits were analysed. There was a significant independent association between HAQ-AS and gender, employment status, peripheral arthritis, ASDAS-CRP/BASDAI, enthesitis, NSAID and anti-TNF treatment (Table 1). The decision tree revealed ASDAS as the first variable with discriminative power on HAQ-AS, according to the following cut points: 1.3, 2.2 and 2.4. In addition, for ASDAS values above 3.5 the model yield a higher number of explanatory variables setting different patients' profiles regarding their functional status, namely: gender, anti-TNF and NSAID treatment. Notably, the ASDAS cut-offs that separated different patient profiles largely mimicked the cut-offs previously defined for ASDAS disease activity states (inactive, low, high and very high disease activity). According to this hierarchical model, gender, anti-TNF treatment and enthesitis score were the next variables explaining HAQ-AS variation, followed by employment status and NSAID treatment.

Conclusion: We have shown that disease activity contributes longitudinally to physical function and that it is hierarchically superior to any other variables or disease domains. Previously defined ASDAS-CRP disease activity categories identified different patient profiles on the hierarchical analysis.

REFERENCE

None.

Table 1. GEE models for HAQ-AS (dependent variable) in axSpA

Characteristics	Univariable analysis, OR (95% CI)	Multivariable analysis taking ASDAS-CRP into account, adjOR (95% CI)	Multivariable analysis taking BASDAI into account, adjOR (95% CI)**
Age, years	1.00 (1-00-1.05)	NA	NA
Male gender	0.73 (0.68-0.78)	0.82 (0.78-0.86)	0.84 (0.80-0.88)
BMI, Kg/m2	1.01 (1.00-1.01)	*	*
HLA-B27 positive	0.84 (0.78-0.90)	*	*
Symptoms duration, years	0.98 (0.98-0.99)	*	*
Currently employed	0.95 (0.91-0.99)	0.95 (0.91-98)	0.95 (0.91-0.98)
Current smoker	1.01 (0.98-1.05)	NA	NA
Peripheral arthritis	1.21 (1.13-1.30)	1.10 (1.04-1.16)	1.09 (1.03-1.16)
ASDAS-CRP	1.26 (1.24-1.29)	1.25 (1.23-1.27)	NA
BASDAI	1.01 (1.01-1.01)	NA	1.01 (1.01-1.01)
Enthesitis score (0 to 39)	1.02 (1.02-1.03)	1.01 (1.01-1.02)	1.01 (1.01-1.01)
Modified NY criteria	0.95 (0.89-1.01)	NA	NA
MRI sacroiliitis	1.01 (0.96-1.07)	NA	NA
mSASSS score	0.99 (0.98-1.01)	NA	NA
NSAIDs (last 6 months)	1.13 (1.09-1.16)	1.03 (1.01-1.06)	1.03 (1.01-1.06)
cDMARDs (last 6 months)	1.09 (1.03-1.14)	*	*
TNF-blocker (last 6 months)	0.92 (0.88-.96)	1.07 (1.03-1.11)	1.04 (1.01-1.08)

* Not selected for this model; NA – not applicable; ** Model adjusted with the cofactors considered significant in the proposed multivariable model for ASDAS (previous column)

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SAT0308 CLUSTER-BASED SPONDYLOARTHRITIS PHENOTYPES DEFINED AT BASELINE ARE PREDICTIVE OF 5-YEAR SEVERITY OUTCOME IN THE DESIR COHORT

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Background: The course of axial spondyloarthritis (SpA) is heterogeneous, varying from mild to severe and remains to be better defined. DESIR is a French cohort of early undifferentiated axial SpA that are longitudinally followed-up, offering such opportunity. We recently performed a cluster analysis in the DESIR cohort, according to baseline characteristics and identified 2 clusters: one characterized by an isolated axial disorder (A for axial) and one by additional high frequency of peripheral

manifestations (B for both)[1]. Those cluster-based SpA phenotypes could correspond to different levels of disease severity.

Objectives: To assess whether cluster-based SpA phenotypes defined at baseline are conserved over time and might predict disease outcome at follow-up.

Methods: We analysed longitudinal data from the 586 patients who completed all follow-up visits until 5-year (mo 6, 12, 18, 24, 36, 48 and 60) out of the 679 patients included in the DESIR cohort used to define clusters at baseline. We performed a linear mixed-effect analysis for quantitative variables (using lme4 R package) and a generalized linear mixed-effect analysis for qualitative variables (using glmer R package) with cluster and follow-up visits as fixed effects and subjects as random effect. *P*-values were obtained by likelihood ratio tests of the full model with cluster against the model without cluster as fixed effects.

Results: Over the time, both clusters continued to show sustainable consistent differences characterized by higher frequency of peripheral involvement, higher disease activity, worse patient-reported outcome, higher frequency of conventional DMARDs and TNF blockers usage in cluster B, and higher frequency of radiographic and MRI sacroiliitis at 2 and 5 years in cluster A (Table).

Variable*	Fixed effect estimate ± standard error**	P-value
BASDAI	7.28 ± 1.08	3×10^{-7}
ASDAS-CRP	0.22 ± 0.06	1.3×10^{-4}
HAQ	0.20 ± 0.03	4.4×10^{-8}
Presence of at least one synovitis	0.95 ± 0.21	1.5×10^{-7}
Swollen joint count	0.09 ± 0.03	0.001
Enthesitis clinical score (MASES)	1.81 ± 0.34	1.3×10^{-7}
TNF blocker-usage	1.81 ± 0.54	5.2×10^{-8}
Conventional DMARDs usage	2.00 ± 0.38	4.9×10^{-16}
Radiographic sacroiliitis	-0.92 ± 0.62	0.002
MRI sacroiliitis	-0.76 ± 0.23	5.4×10^{-5}

* All the variables have been recorded at all the follow-up visits except radiographic and MRI sacroiliitis which have been evaluated at inclusion, 2 and 5 years.

** Cluster B compared to cluster A

Table – Significant results of the linear mixed effect and generalized linear mixed-effect analysis.

Conclusion: Cluster-based SpA phenotypes defined at baseline in the DESIR cohort were predictive of severity outcome after 5 years. Patients from cluster A were more prone to develop sacroiliitis despite lower disease activity over the time, whereas those from cluster B had poorer clinical outcome and higher need for conventional DMARDs and TNF blockers.

REFERENCE

[1] Costantino F, Aegerter P, Dougados M, Breban M, D'Agostino M-A. Two Phenotypes Are Identified by Cluster Analysis in Early Inflammatory Back Pain Suggestive of Spondyloarthritis: Results From the DESIR Cohort. Arthritis & Rheumatology (Hoboken, NJ). 2016;68(7):1660–8.

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SAT0309 CLINICAL, IMAGING AND BIOLOGIC FEATURES OF SPONDYLOARTHRITIS IN AN AT-RISK POPULATION: DATA FROM THE PRE-SPA COHORT

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Background: Diagnosis in axial spondyloarthritis (axSpA) is challenging and often delayed by several years, resulting in a delay in treatment. Previously we reported presence of spondyloarthritis (SpA) features and imaging abnormalities in first-degree relatives (FDRs) of HLA-B27 axSpA patients, who are at risk of developing axSpA [1]. Follow up of these at risk individuals could help to identify clinical signs, imaging abnormalities or biomarkers that are predictive of development of axSpA.

Objectives: To investigate imaging, biologic and/or clinical signs of SpA at baseline and after 1 year follow up, as well as development of clinicallly manifest axSpA after 1 year follow up in at risk individuals.

Methods: The Pre-SpA cohort[1] is a prospective inception cohort in which FDRs of HLA-B27 positive axSpA patients are included and followed for 5 years. The main exclusion criteria were: a diagnosis of SpA at baseline and back pain with a previous non-rheumatic diagnosis, such as spinal disc herniation. Clinical and biologic characteristics were collected at baseline and after 1 year. Imaging was performed at baseline including MRI of the sacroiliac joints (SIJ) and X-rays of the cervical and lumbar spine and SIJ. MRIs were scored according to the ASAS definition for a positive MRI by two readers. X-rays were scored according to the modified New York (mNY) criteria for ankylosing spondylitis by two readers.

Results: In the current study we report the characteristics of 201 participants at baseline and 123 participants after one year of follow-up. 126 (62.7%) participants reported back pain, of which 39(19.4%) fulfilled criteria for inflammatory back pain. Median [IQR] VAS total back pain (0-100mm) was 11 (0-28). Six (2.9%) were previously diagnosed with arthritis by a physician, nine(4.4%) with enthesitis and one(0.5%) with dactylitis. In none of these participants a diagnosis of SpA was made. Seven participants were previously diagnosed with an extra-articular manifestation possibly related to SpA: four with psoriasis and three with anterior uveitis. Three (1.5%) participants fulfilled the mNY criteria for sacroiliitis on radiography. Ten (5%) participants had bone marrow edema on MRI of the SIJ suggestive of SpA. Fifty-six (27.8%) participants would have fulfilled ASAS classification criteria for axSpA if they would have had a clinical diagnosis of axSpA. After one year patient-reported disease activity variables remained stable; median [IQR] VAS total back pain (0-100mm) was still low: 4[0-24]. During one year of follow-up, in total seven participants developed symptoms and were clinically diagnosed with axSpA.

Conclusion: Imaging signs and clinical signs of SpA are present in a substantial proportion of seemingly healthy FDRs of HLA-B27 positive AxSpA patients. Twelve (6.0%) participants had imaging suggestive of SpA, but a clinical diagnosis of axSpA was still rare after one year of follow up (5.7%). Future follow-up will increase numbers of individuals diagnosed with axSpA and help us identify early symptoms and signs of SpA in this at risk population.

REFERENCE

[1] Turina MC, et al., Arthritis Rheumatol. 2016Oct;68(10):2444-55

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SAT0310 IDENTIFICATION OF FACTORS ASSOCIATED WITH MAGNETIC RESONANCE IMAGES CHANGES SUGGESTIVE OF AXIAL SPONDYLOARTHRITIS IN THE AXIAL SKELETON OF INDIVIDUALS <45 YEARS – EVALUATION OF DATA FROM A LARGE COMMUNITY STUDY

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Background: Active (bone marrow edema, BME) and structural (fatty lesions, FL) lesions in the spinal and the sacroiliac joints (SIJ), as assessed by magnetic resonance imaging (MRI), have been described in patients with axial spondyloarthritis (axSpA) but may also occur in non-axSpA patients and healthy individuals (1,2).
Objectives: Identify factors associated with the occurrence of BME and FL in spinal- and SIJ-MRIs in the population-based Study of Health in Pomerania (SHIP).
Methods: All available spinal- (sagittal T1/T2 sequences) and SIJ- (semi-coronal STIR sequences) MRIs were evaluated by two trained readers blinded to clinical data. BME (SIJ and spine) and FL (spine) suggestive of axSpA were recorded. Disagreements were resolved by consensus. BME was quantified using Berlin MRI scores. Clinical information was available for age (increase per decade), sex, smoking (ever vs. never), prevalence of spinal pain (NRS≥4/10 in last 3 months), CRP, HLA-B27 status and body mass index (BMI) categories (WHO definition of under- (cat. 1), normal (cat. 2) or overweight (cat. 3)). Associations between clinical factors and MRI lesions were analyzed (a) by modeling of number and size of lesions using negative binomial count regression and (b) for presence/absence of lesions using univariate logistic regression.
Results: MRIs of 793 volunteers, 392 male (49.4%), 45 CRP-positive (5.7%), 67 HLA-B27+ (8.4%), 497 smokers (62.7%) were evaluated. BME lesions were found in 136 SIJ-MRIs (17.2%) and in 218 (27.5%) spinal MRIs, while FL were found in 645 spinal MRIs (81.3%).
A higher number and larger sized SIJ BME lesions were associated (exp (β), 95% CI) with HLA-B27 (2.8, 1.5-4.9), spinal pain (1.7, 1.2-2.6), and higher BMI (cat. 1 vs 3, 1.7, 1.0-3.0). In the spine, higher number and larger sized BME were associated with age (1.5, 1.2-2.0), while FL were associated with higher BMI, (cat. 1 to cat. 3 (1.9, 1.5-2.2), age (1.6, 1.5-1.8) and male sex (1.4, 1.2-1.6).
Presence (odds ratio, 95% CI) of spinal BME (1.3, 1.0-1.7) and/or FL (1.7, 1.3-2.3) was associated with age, while FL alone were associated with a higher BMI (cat. 1 to cat.3, 3.3, 1.8-6.1).
In total, 22 subjects (16.2%) had large (>33% of surface involvement) and 114 small (≤33% of surface involvement) SIJ-BME lesions. Large SIJ-BME lesions were found in 4.5% HLA-B27-positive vs. 2.6% HLA-B27-negative subjects (p=0.40).
Out of 187 quadrants with BME lesions in SIJ, the majority (n=66, 35.3%) was located in the upper sacral quadrant. Most SIJ lesions (n=156, 83.4%) were small. Out of 362 spinal segments with BME, the majority n=152, 42%) was located in the lower (T7/8-T11/12) thoracic spine. Most spinal lesions (n=329, 90.9%) were small.
Conclusion: In this large population-based study, higher numbers of large SIJ-BME lesions were significantly associated with HLA-B27, back pain and BMI. In some contrast, spinal BME and FL were associated with older age, male sex and BMI but not HLA-B27. The association for HLA B27 was only shown on the quadrant but not on the patient level. These findings are in accordance with previously published hypotheses that question the specificity of sacroiliitis and spondylitis in axSpA (3).

REFERENCES

[1] Weber U et al, Arthritis Rheumatol 2018
[2] De Winter J et al, Arthritis Rheumatol 2018
[3] Braun J et al, Rheumatology 2018

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SAT0311 DIAGNOSTIC UTILITY OF INDIVIDUAL INFLAMMATORY BACK PAIN PARAMETERS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: A recent study in German chronic back pain (CBP) patients (pts) with a suspicion of axial spondyloarthritis (axSpA) report on the performance of, among others, the ASAS inflammatory back pain (IBP) criteria and the individual IBP parameters. Pts were diagnosed by a rheumatologist blinded for all clinical features but IBP and by a rheumatologist with all diagnostic tests available as in daily practice (reference standard). Data show high sensitivity but low specificity of the ASAS IBP

1a	Be-Giant cohort axSpA N=205	SPACE cohort axSpA N=307	SPACE cohort No axSpA N=354
IBP (ASAS definition), n (%)	172 (83.9)	228 (74.3)	177 (50.0)
Age at onset <40 years	197 (96.1)	277 (90.2)	312 (88.1)
Insidious onset	185 (90.2)	261 (85.0)	298 (84.2)
Improvement with exercise	181 (88.3)	252 (82.1)	228 (64.4)
No improvement with rest	172 (83.9)	264 (86.0)	269 (76.0)
Pain at night	162 (79.0)	172 (56.0)	131 (37.0)
No. of IBP parameters present, n (%)			
0	0	1 (0.3)	0
1	1 (0.5)	5 (1.6)	7 (2.0)
2	7 (3.4)	22 (7.2)	56 (15.8)
3	25 (12.2)	51 (16.6)	114 (32.2)
4	53 (25.9)	116 (37.8)	108 (30.5)
5	119 (58.1)	112 (36.5)	69 (19.5)

1b	Sensitivity (confidence interval)		Specificity (confidence interval)	LR+	
	Be-Giant cohort	SPACE cohort		Be-Giant cohort	SPACE cohort
IBP (ASAS definition)	83.9% (78.0-88.5)	74.3% (68.9-79.0)	50.0% (44.7-55.3)	1.7	1.5
Age at onset <40 years	96.1% (92.2-98.2)	90.2% (86.2-93.2)	11.9% (8.8-15.8)	1.1	1.0
Insidious onset	90.2% (85.1-93.8)	85.0% (80.4-88.7)	15.8% (12.3-20.1)	1.1	1.0
Improvement with exercise	88.3% (82.9-92.2)	82.1% (77.2-86.1)	35.6% (30.6-40.9)	1.4	1.3
No improvement with rest	83.9% (78.0-88.5)	86.0% (81.5-89.6)	24.0% (19.7-28.9)	1.1	1.1
Pain at night	79.0% (72.7-84.3)	56.0% (50.3-61.6)	63.0% (57.7-68.0)	2.1	1.5

Figure. Performance of individ ual parameters of the ASAS IBP criteria

criteria and individual IBP parameters(1). Performance of IBP in other countries is less studied.
Objectives: What is the diagnostic utility of IBP and the individual IBPpar according to the ASAS IBP criteria in several rheumatology settings in West- and Northern-Europe?
Methods: Data of the multicentre, observational Be-Giant and SPondyloArthritis Cause Early (SPACE) cohorts were used. The Be-Giant cohort included ≥18 years old, newly diagnosed axSpA pts who were diagnosed by a rheumatologist and fulfilled the ASAS axSpA criteria. SPACE cohort included pts, ≥16 years, with (almost) daily CBP for ≥3 months and ≤2 years, with a symptom onset <45 years. In SPACE, axSpA pts were diagnosed by a rheumatologist (plus a level of confidence of ≥7 on a 0–10 scale). All other pts in SPACE were labelled as 'no axSpA'. Pts underwent a diagnostic workup according to the protocol of the corresponding cohort, including data on the individual parameters of the ASAS IBP criteria. Sensitivity, specificity and positive likelihood ratios (LR+) were calculated using the axSpA pts from each cohort separately and the "no axSpA" pts as control group.
Results: IBPpar data was available in 661 pts (SPACE) and 228 pts (Be-Giant); 36.0% and 49.6% were male, mean age 30.8±8.2 and 34.7 ±9.7 years, respectively. The figure shows a majority of axSpA pts with >2 IBPpar, but this is also seen in the no axSpA pts. IBPpar show high sensitivity but very low specificity with 'pain at night' as exception with a slightly better specificity. LR+ were, in both cohorts, much lower (figure) than the LR+ of 3.1 for IBP previously reported as diagnostic estimate in routine practice.
Conclusion: IBP and the individual IBPpar. are commonly seen in patients with and without an axSpA diagnosis. Our data confirm results from Germany, showing that the diagnostic utility of IBP in a rheumatology setting is lower than previously assumed with a (very) low specificity and LR+. It seems the distinctive impact of IBP is expressed when physicians refer their patient to the rheumatologist.

REFERENCE

[1] Poddubnyy D, et al. RMD Open 2018;4:e000825

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SAT0312

GENDER CONTRASTS IN PATIENT REPORTED OUTCOMES DON'T ALTER THE DISEASE ACTIVITY SCORE IN AXIAL SPONDYLOARTHRITIS PATIENTS

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Background: Disease activity in axial spondyloarthritis (axSpA) is often quantified by the Axial Spondyloarthritis Disease Activity Score (ASDAS), a composite index which combines 4 patient reported outcome (PRO) parameters and C-reactive protein (CRP) as an acute phase reactant. ASDAS commonly acts as a target in treat-to-target approaches in axSpA patients.
Objectives: To identify the impact of gender on ASDAS in newly diagnosed axSpA patients and to determine whether possible differences are PRO- or CRP-driven.
Methods: Patients originate from the Be-Giant cohort, a Belgian observational registry of newly diagnosed axSpA patients (expert opinion). Included patients fulfill the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA and are anti-TNF naïve prior to inclusion. An extensive patient description was performed at baseline, including PRO and laboratory investigations with CRP (mg/L). ASDAS was calculated for each patient and subdivided in a PRO-component (ASDAS-PRO) and a CRP-component (ASDAS-CRP) (1).
Results: By January 2019, 291 axSpA patients were included (138 male, 153 female). At baseline, ASDAS could be calculated in 262 patients. ASDAS-PRO was significantly higher in women compared to men (1,66 vs. 1,48, p = 0,04), while ASDAS-CRP did not differ significantly (0,90 for both genders, p = 0,96). No significant difference was found between the total ASDAS of women and men (2,54 vs. 2,38, p = 0,09) (Figure 1). When categorizing the score into 4 disease activity states (2), 60,8% (76/125) of men show high or very high disease activity (ASDAS > 2.1) at baseline compared to 67,2% (92/137) of women (p = 0,35).
Concerning the 5 ASDAS components, the discrimination between male and female axSpA patients was most pronounced for *patient global* scores (Figure 2). Men reported a baseline patient global score of 4,3 (95% CI 3,8 – 4,8), compared to a score of 5,1 (95% CI 4,7 – 5,6) in women (p = 0,01).
Conclusion: Female axSpA patients report a significantly higher *patient global* score compared to men. This contributes to a significantly higher ASDAS-PRO in women. However, neither the ASDAS itself nor the ASDAS disease activity categories are significantly affected by gender contrasts in PRO.

REFERENCES

[1] Lukas C, Landewe R, Sieper J, Dougados M, Davis J, Braun J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Annals of the rheumatic diseases. 2009;68(1):18-24.
[2] Machado PM, Landewe R, Heijde DV. Ankylosing Spondylitis Disease Activity Score (ASDAS): 2018 update of the nomenclature for disease activity states. Annals of the rheumatic diseases. 2018;77(10):1539-40.

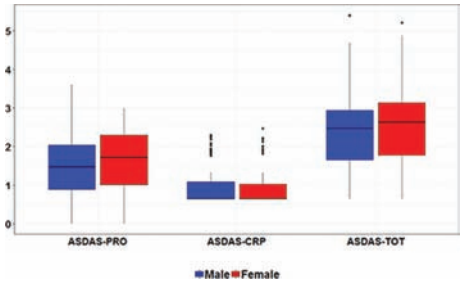


Figure 1. Total ASDAS score (ASDAS-TOT), subdivided in a PRO-component (ASDAS-PRO) and a CRP-component (ASDAS-CRP) in male and female axSpA patients.

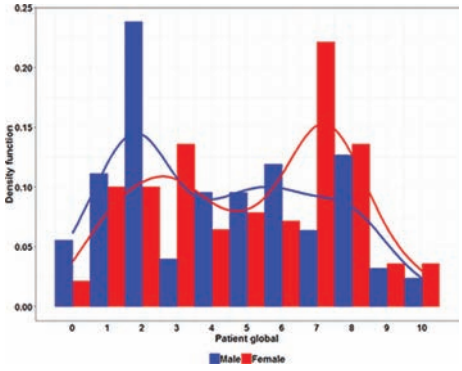


Figure 2. Patient global score in male and female axSpA patients.

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SAT0313

ILEAL BUT NOT COLONIC INFLAMMATION IS LINKED TO FATTY LESIONS ON MRI OF THE SACROILIAC JOINTS IN SPONDYLOARTHRITIS PATIENTS

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Background: Gut and joint inflammation in spondyloarthritis (SpA) are closely intertwined. About 50% of axial SpA patients display microscopic signs of inflammation in ileum and/or colon, a risk factor to develop Crohn's disease over time. It is currently not known if presence of microscopic gut inflammation in new onset SpA is associated with more structural lesions on magnetic resonance imaging of the sacroiliac joints (MRI-SIJ) and whether these lesions relate to the localization of gut inflammation.

Objectives: To assess whether structural lesions on MRI-SIJ (A) are associated with microscopic gut inflammation in SpA patients and (B) are preferably related to colon or ileum inflammation in case of gut involvement.

Methods: We analyzed baseline information from the Be-Giant cohort, a registry of SpA patients fulfilling the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axial or peripheral SpA. MRI-SIJ was scored by 3 readers, blinded for subject characteristics. Six consecutive slices were assessed for structural lesions: sclerosis, erosions, fatty lesions and (partial) ankylosis. MRI sum scores were analyzed as 2 out of 3 (median) scores. Colon and ileum biopsies were evaluated for microscopic signs of inflammation. The effect of gut inflammation (colon and/or ileum) on MRI-SIJ lesions was investigated by generalized linear models (GLM), adjusted for age and gender and stratified for the SpA phenotype.

Results: By January 2019, baseline data were available on 105 patients (95 axial and 10 peripheral SpA). Gut inflammation was present in 35 patients (17 ileum, 8 colon, 10 both). Table 1 shows the slope (β_1) of the GLMs for erosions, fatty lesions, sclerosis and (partial) ankylosis and the p-value for the SpA phenotype as an interaction term. Erosions, sclerosis, nor ankylosis show a significant association with gut inflammation in general. If present, colon inflammation has no significant relationship with each individual structural lesion. In contrast, presence of ileum inflammation was associated with an increase in the number of fatty lesions by 0,68 (95%CI 0,04 – 1,38). All results are independent of the SpA phenotype (p > 0,05).

Conclusion: Ileal but not colonic inflammatory gut lesions are linked to more fatty lesions on MRI-SIJ in newly diagnosed SpA patients. Baseline microscopic gut inflammation was not associated with erosions, sclerosis nor ankylosis. These data support the concept that microscopic gut inflammation, especially ileal inflammation, is associated with more severe axial inflammation in SpA.

Table 1. *Association between MRI–SIJ structural lesions and gut inflammation in SpA patients.*

Structural lesion	Gut inflammation	β_1	95% CI	p-value	p-value interaction term*
	Colon and/or ileum	0,02	(-0,39 – 0,45)	0,92	0,53
Erosions	Colon	-0,08	(-0,56 – 0,45)	0,75	0,50
	Ileum	-0,01	(-0,47 – 0,46)	0,94	0,66
	Colon and/or ileum	0,38	(-0,23 – 1,04)	0,22	0,61
Fatty lesions	Colon	-0,54	(-1,28 – 0,30)	0,16	0,94
	Ileum	**0,68**	**(0,04 – 1,38)**	**0,04**	0,88
	Colon and/or ileum	-0,19	(-0,60 – 0,23)	0,35	0,81
Sclerosis	Colon	0,05	(-0,45 – 0,60)	0,84	0,60
	Ileum	-0,27	(-0,68 – 0,17)	0,22	0,62
(Partial)	Colon and/or ileum	-0,38	(-1,14 – 0,44)	0,35	0,41
Ankylosis	Colon	-0,40	(-1,33 – 0,76)	0,45	0,60
	Ileum	-0,24	(-1,05 – 0,68)	0,58	0,40

**SpA subtype (axial versus peripheral SpA) as an interaction term.*

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SAT0314

IMPLEMENTATION OF AN ASSESSMENT CHECKLIST FOR PATIENTS WITH SPONDYLOARTHRITIS IN DAILY PRACTICE

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Background: Nowadays, despite international and national guidelines on the evaluation and management of spondyloarthritis (SpA), several studies have depicted a sub-optimal assessment of these diseases.

Objectives: To analyze the feasibility and changes in the collection of clinical measures after the implementation in daily practice of a checklist designed for an optimal evaluation and monitoring of patients with SpA, including psoriatic arthritis (PsA).

Methods: An observational prospective study was performed. The feasibility of the assessment checklist (paper/on-line format) for patients with SpA was tested (time to complete the checklist, simplicity, amenity clarity, usefulness). Through a medical files review, changes in the number of the checklist variables collected were analyzed previous to the implementation of the checklist and 6 months later. A descriptive and bivariate analysis was performed.

Results: A total 6 hospitals and 11 rheumatologists participated. The median time to checklist completion was 15 (12-20) minutes, and the mean scores for the rest of variables of the feasibility test were in general positives, 6.9±1.1 (simplicity) and 6.9±0.8 (amenity), to 7.5±1.2 (clarity) and 7.5±1.4 (usefulness). A total of 83 and 68 medical files pre-implementation and post-implementation were reviewed respectively. Patient's features were similar. Mean age at diagnosis was 42.3±1.6 and 40.3±1.3 years respectively. In both study samples around a half of patients were men, and axial SpA and PsA were equally distributed as well (40.2% and 44.8% pre- and post-implementation (47.6% and 47.8%). We observed a significant increase in the collection of many of the checklist variables after the implementation. The record of BASDAI increased from 46.2% to 73.1% (p=0.001), physical activity from 48.2% to 88.2% (p<0.0001), physician global (VAS) from 28.0% to 73.5% (p<0.0001), patient global (VAS) from 48.8% to 85.3% (p<0.0001), morning stiffness from 62.8% to 84.8% (p=0.003), ASDAS (in axial SpA) from 12.2% to 32.8% (p=0.002), BASFI from 43.7% to 65.7% (p=0.008), or DAS28 (in PSA) from 24.7% to 46.3% (p=0.006). The record of extra-articular symptoms and signs and all of the comorbidities but for osteoporosis and peptic ulcer significantly improved too. The percentage of change ranged from 20% (extra-articular symptoms and signs or arterial hypertension) to 30% (diabetes mellitus, hyperlipidemia, gout/hyperuricemia and renal failure. Other checklist variables increased but not significantly. However, some of them like the HLA-B27 or work status were already recorded (before the implementation of the checklist) in the 82.3% and 95.2% of medical files respectively. Changes were observed irrespectively of SpA classification.

Conclusion: The implementation of an assessment checklist in daily practice is feasible and improve the assessment of SpA patients.

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SAT0315

STRUCTURAL DAMAGE PROGRESSION OVER 4 YEARS OF SECUKINUMAB TREATMENT IN ANKYLOSING SPONDYLITIS: POST-HOC ANALYSIS OF MEASURE-1 TRIAL USING A LONGITUDINAL BAYESIAN MIXTURE MODEL

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Background: Ankylosing spondylitis (AS) is an inflammatory disease resulting in progressive disability due to structural damage in the spine. The identification of predictors of progression would allow treating physicians to personalize treatments but requires an approach accounting for a relatively short follow-up of clinical studies, large between-patient variability, and low sensitivity of X-ray images which generate intra-patient variability when repeated measurements are taken.

Objectives: 1) To identify patient characteristics predicting faster structural damage progression. 2) To quantify the progression over four years of secukinumab treatment, depending on dose/exposure.

Methods: Data came from the phase 3 randomized placebo-controlled trial MEASURE 1 (NCT01358175)[1] in which patients were treated with secukinumab (intravenous loading of 10 mg/kg at weeks 0, 2, and 4, followed by secukinumab subcutaneously at a dose of either 75 mg or 150 mg every 4 weeks) over 208 weeks. Only patients treated with secukinumab with at least two assessments of structural damage were included. We explored the effect of multiple baseline demographic traits, disease stage, severity, bone cartilage biomarkers as well as prior and current treatment on change in modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) using a longitudinal Bayesian mixture model with random effects, which accounted simultaneously for the probability of progression, magnitude of progression and inter-patient variability. Posterior predictive check was performed.

Results: Out of 249 patients randomized to secukinumab, 167 had their structural damage assessed at least twice. These patients contributed in total 409 assessments of change in structural damage between weeks 0, 52, 104 and 208.

Of the factors tested, a higher baseline BASMI score was associated with faster progression rate in a statistically significant way (+0.60 in mSASSS/year for each additional standard deviation of baseline BASMI (SD=1.74), 95% interval 0.03 to 1.14). Trends were also detected for association between faster mSASSS progression and younger age, prior exposure to TNFα inhibitor, HLA-B27 positivity, and higher osteocalcin levels. Increased exposure to secukinumab was associated with slower structural damage progression (-0.23 in mSASSS/year for each additional standard deviation in exposure, 95% interval -0.58 to 0.10). Model estimation suggested that secukinumab 150 mg was associated with a yearly progression of -0.2 (95% interval -1.2 to 0.8) in the first two years of treatment and 0.1 mSASSS (95% interval -0.8 to 1.0) in the third and fourth year of treatment. Analogously, secukinumab 75mg (currently not approved for clinical use) was associated with a progression of -0.2 mSASSS/year (95% interval -1.3 to 0.9) in the first two years of treatment and 0.5 mSASSS/year (95% interval -0.5 to 1.6) in the third and fourth year of treatment.

Conclusion: Potential predictors of structural progression suggested by the model were higher baseline BASMI, younger age, prior exposure to TNFα inhibitor, HLA-B27 positivity, and higher osteocalcin at baseline, although only baseline BASMI showed statistical significance. Further analyses using larger, deeper and real-world data are needed to confirm these findings and to estimate progression rates in AS patients in daily practice.

REFERENCE

[1] Baeten D, Sieper J, Braun J, et al. Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis. N Engl J Med. 2015;373(26):2534-2548.

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SAT0316

EARLY RECOGNITION OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS BY USING A PRACTICAL REFERRAL SYSTEM – EVALUATION OF THE RECENTLY PROPOSED 2-STEP STRATEGY

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Background: Early recognition of axial spondyloarthritis (axSpA) in primary care (PC) is difficult due to the high prevalence of low back pain resulting in a major delay for a diagnosis of axSpA. Recently we proposed a 2-step referral strategy (1) which concentrates on patients ≤45 years with chronic back pain who are to be referred to a rheumatologist if fulfilling 2 of 3 features: buttock pain, improvement by movement, psoriasis (Step 1), or, in case of ≤1 feature, positive testing for HLA-B27 (Step 2).

Objectives: To prospectively evaluate this 2-step referral strategy in PC.

Methods: Consecutive patients ≤45 years who presented in PC to general practitioners or orthopedic surgeons working in PC with back pain lasting ≥2 months who had not been diagnosed before received questionnaires (Q1) relevant for the referral process. Thereafter, the PC physician asked the same questions in a separate questionnaire (Q2), including the decision on HLA-B27 testing. All patients were then referred to two experienced rheumatologists in a tertiary center who performed a complete workup including clinical, laboratory and imaging with radiographs and magnetic resonance imaging (MRI) examinations before their final diagnosis of axSpA or non-SpA (Q3).

Results: A total of 320 patients (mean age 35.9±10.3 years) was recruited. The proposed referral strategy (prS) was fulfilled by 127 patients in Q1 (39.7%), 160 in Q2 (50%), 102 by both, Q1 and Q2 (31.9%), and 83 with either Q1 or Q2 (25.9%). Overall, 47 patients were diagnosed with axSpA by the rheumatologist at Q3 (14.7%), 66% of which were male, mean age 34.7±10.1 years, 70.2% HLA-B27 positive, mean CRP 0.8±1.4mg/dl, mean ASDAS 3.2±0.8, mean BASDAI 5.1±2.0. Of these, 37 patients had fulfilled the prS in Q1 or Q2 (78.7%), and 31 in both Q1 and Q2 (66%), respectively. In the latter, the HLA-B27 prevalence was significantly higher (27/31, 87.1%) as compared to patients diagnosed with axSpA at Q3 but who did not fulfill the prS in Q1 and Q2 (5/16, 31.3%) ($p<0.001$).

The sensitivity and specificity of the prS was 78.7% and 69.2% in Q1, 78.7% and 62.2% in Q2, and in both, Q1 and Q2, 66% and 74%, respectively.

AxSpA patients correctly identified by the prS in Q1 and Q2, were significantly more frequently positive for HLA-B27 and CRP and fulfilled more frequently the ASAS definition of inflammatory back pain in Q3.

Conclusion: This study confirms the feasibility a simple referral strategy using a combination of clinical features for identifying axSpA patients in PC without laboratory and imaging examinations. This strategy performed already well at the early patient and PC physician level just based on a symptom-based questionnaire.

REFERENCE

[1] Braun A et al, ARD 2011

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SAT0317 INCIDENCE OF EXTRA-ARTICULAR MANIFESTATIONS IN ANKYLOSING SPONDYLITIS, PSORIATIC ARTHRITIS AND UNDIFFERENTIATED SPONDYLOARTHRITIS – RESULTS FROM A NATIONAL REGISTER-BASED COHORT STUDY

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Background: Spondyloarthritis (SpA), including ankylosing spondylitis (AS), psoriatic arthritis (PsA) and undifferentiated SpA (uSpA), are all to varying degrees associated with extra-articular manifestations (EAMs).
Objectives: To estimate incidence rates (IRs) for EAMs (anterior uveitis, inflammatory bowel disease (IBD) and psoriasis) in patients with AS, PsA and uSpA, respectively.
Methods: In this nationwide cohort study, three separate cohorts of patients aged 18 to 69 years with AS (n=8517, 68% men, mean age 47 ±13 years), PsA (n=22667, 46% men, mean age 49±12 years) and uSpA (n=10245, 44% men, mean age 42±13 years) were identified 2001-2015 in the Swedish National Patient Register (NPR). The follow-up began 1 January 2006, or six month after the date of the first SpA diagnosis thereafter in previously undiagnosed cases, and ended at the first date of EAM, death, emigration or 31 December 2016, respectively. Both the SpA diagnoses and EAMs were identified according to specified ICD codes. Number of outcomes, person-years at risk and IRs with 95% CI were calculated for each EAM and stratified by sex and age-intervals. Patients with a prior EAM in NPR before start of follow-up were excluded from that specific analysis.
Results: The IRs for each EAM are presented in Table 1. The overall highest IRs were noted for anterior uveitis in patients with AS (14.4 (13.2-15.5) per 1000 person-years at risk). Patients with PsA had considerably lower IRs for anterior uveitis (1.7 (1.5-1.9) per 1000 person-years at risk) and slightly lower IRs for IBD than patients with AS and uSpA. The IRs for anterior uveitis were significantly higher in men than in women in both AS and uSpA.
Conclusion: IRs for EAMs clearly differed between the SpA subtypes, and especially for anterior uveitis where the IRs were by far highest in patients with AS and uSpA compared to patients with PsA.
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Table 1.

	AS		PsA		uSpA	
	Prior EAM n (%)	IRs (95% CI)	Prior EAM n (%)	IRs (95% CI)	Prior EAM n (%)	IRs (95% CI)
ANTERIOR UVEITIS						
All	**1852 (22)**	**14.4 (13.2-15.5)**	**356 (1.6)**	**1.7 (1.5-1.9)**	**1498 (15)**	**7.7 (6.9-8.5)**
Men	1315 (23)	15.8 (14.3-17.3)	177 (1.7)	1.7 (1.4-2.0)	771 (17)	10.1 (8.8-11.5)
Women	537 (20)	11.2 (9.4-13.1)	179 (1.5)	1.8 (1.5-2.1)	727 (13)	6.0 (5.1-6.9)
IBD						
All	**615 (7.2)**	**2.8 (2.4-3.3)**	**504 (2.2)**	**1.1 (0.9-1.3)**	**632 (6.2)**	**2.5 (2.1-2.9)**
Men	403 (7.0)	2.6 (2.0-3.1)	192 (1.8)	1.0 (0.8-1.2)	268 (5.9)	2.6 (2.0-3.2)
Women	212 (7.7)	3.4 (2.5-4.3)	312 (2.6)	1.2 (1.0-1.4)	364 (6.4)	2.4 (1.8-2.9)
PSORIASIS						
All	**264 (3.1)**	**5.6 (5.0-6.3)**	*NA*	*NA*	**405 (4.0)**	**7.7 (7.0-8.4)**
Men	171 (3.0)	5.4 (4.7-6.2)	*NA*	*NA*	199 (4.4)	6.9 (5.9-8.0)
Women	93 (3.4)	6.1 (4.9-7.3)	*NA*	*NA*	206 (3.6)	8.3 (7.3-9.3)

The IRs are presented as number of EAMs per 1000 person-years at risk. NA, not applicable.

SAT0318 PREVALENCE AND PREDICTORS OF DEPRESSION AMONG PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS IN A CANADIAN REAL WORLD OBSERVATIONAL COHORT: RESULTS FROM THE COMPLETE STUDIES

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Background: Ankylosing pondylitis (AS) and psoriatic arthritis (PsA) are chronic inflammatory diseases known to cause physical, emotional, social and psychological impairment. However, few data are available on comorbidities such as depression and the factors associated with depression.
Objectives: To evaluate the prevalence of depression and to identify sociodemographic and disease-related factors associated with depression among PsA and AS patients.
Methods: Patients eligible for the COMPLETE studies are anti-TNFα naïve adults with active AS or PsA requiring change in their treatment regimen. In this analysis, patients enrolled between Jul/2011 - Nov/2017, treated with adalimumab or non-biologic DMARDs were included. Depression was defined as Beck's Depression Inventory (BDI) ≥20 and/or patients treated with an antidepressant/anxiolytic at baseline (before treatment modification). Associated symptoms of depression were assessed with the BDI considering% of patients with a score of 2 or 3 (moderate to severe symptoms). Univariate and multivariate logistic regression were used to identify sociodemographic and disease-related predictors associated with depression at baseline. In addition, the correlation of the BDI score and the following parameters at baseline was assessed with the Pearson coefficient (r): age, disease duration, PsA disease specific parameters (28-tender [TJC] and swollen joint count [SJC], patient global assessment [PtGA], physician global assessment [MDGA]), and AS disease specific parameters (BASDAI, BASFI, morning stiffness, and number of extra-articular manifestations [EAMs]).
Results: A total of 492 AS and 333 PsA patients were included. Mean (SD) age was 42.7 (13.2) and 51.5 (12.2) years for AS and PsA, respectively, and disease duration was 5.4 (9.1) and 14.7 (13.7) years. The prevalence of baseline depression was 24.6% for AS and 25.5% for PsA. The most commonly reported symptoms of associated with depression, were loss of energy (33.2% and 26.2%), changes in sleeping

pattern (41.3% and 34.9%), fatigue (35.3% and 28.6%), and loss of interest in sex (21.7% and 21.9%), for AS and PsA, respectively.
In univariate analysis (Table 1), female gender (OR=1.73), unemployment due to disability (OR=3.06) or other reasons (OR=2.38), increased BASDAI (OR=1.40), increased BASFI (OR=1.33), and increased morning stiffness (OR=1.01) were significantly associated [all P<0.001 except gender (P=0.009)] with baseline depression among AS patients. For PsA, significantly associated parameters included female sex (OR=2.35; P=0.001), unemployment due to disability (OR=3.57; P<0.001), increased TJC (OR=1.05; P=0.009), increased PtGA (OR=1.03; P<0.001) and increased morning stiffness (OR=1.01; P=0.010). Weak correlations (P<0.05) were observed between the BDI score and BASFI (r=0.425), BASDAI (r=0.375), morning stiffness (r=0.285), and number of EAMs (r=0.114) for AS; and TJC (r=0.155), MDGA (r=0.132), and PtGA (r=0.451) for PsA.
In multivariate regression analysis for AS, higher BASFI (OR=1.32; P<0.001), female sex (OR=1.89; P=0.007) and being unemployed due to other reasons (OR=1.91; P=0.017); and, for PsA, lower baseline disease duration (OR=0.97; P=0.018), and higher PtGA (OR=1.04; P<0.001) were identified as significant independent predictors of baseline depression.
Conclusion: Depression in AS and PsA patients was common in this real-world cohort. Female sex, unemployment, and higher disease activity for AS, and shorter disease duration along with higher PtGA for PsA were significant independent predictors of depression.
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SAT0319 OBESITY AND ASSOCIATED FACTORS IN NORWEGIAN AXIAL SPONDYLOARTHRITIS PATIENTS. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITISSURVEY

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Background: Obesity increases the risk of developing chronic inflammatory diseases, including axial spondyloarthritis (axSpA)[1,2]. Information about how obesity correlates with disease activity in axSpA patients is limited.
Objectives: The objective of this survey was to investigate the association between body mass index (BMI) and patient reported disease activity in Norwegian axSpA patients.
Methods: The European Map of Axial Spondyloarthritis (EMAS), conducted from July 2017 to February 2018, was a cross-sectional on-line survey of 2,846 unselected patients with self-reported axSpA from 13 European countries (Austria, Belgium, France, Germany, Italy, Netherlands, Norway, Russia, Slovenia, Spain, Sweden, Switzerland, and the UK). Participants were recruited through an on-line panel and patient organizations. This analysis is based on data from the 509 Norwegian respondents. Sociodemographic variables (age, gender, BMI, comorbidity), and disease related variables (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (0-10), self-reported spinal stiffness (3-12) and General Health Questionnaire (0-12) (GHQ-12)) were reported.
Results: Out of the 509 Norwegian participants with axSpA, 69.7% (N:355) were women. The mean age was 48±12 years, mean disease duration was 5.3±2.0 years, 82.3% were HLA-B27 positive, and 55.2% (N:281) were university educated. In total, 35% (N:180) of the participants were normal/underweight (BMI < 25) and 65% (N:329) were overweight/obese (BMI >25). The mean (sd) disease activity, as measured by BASDAI (0-10), was 5.3±2.0. Overweight/obese patients reported significantly higher disease activity (BASDAI 5.5±1.9) compared to normal weight patients (BASDAI 5.0± 2.1). Moreover, being overweight/obese was associated with a significantly higher degree of spinal stiffness, number of comorbidities and a numerically, but not significantly, higher GHQ-12 score. There was no significant differences in alcohol consumption, smoking, or prevalence of inflammatory bowel disease (Crohn's disease or ulcerative colitis).
Conclusion: Norwegian overweight/obese axSpA patients from the EMAS survey report significantly higher disease activity, spinal stiffness and number of comorbidities. The results highlight the serious impact of overweight and obesity on the health status of axSpA patients. Therefore, obesity should be considered as a preventable risk factor and within the disease management of axSpA.

REFERENCES

[1] Maas, et al. Obesity Is Common in Axial Spondyloarthritis and Is Associated with Poor Clinical Outcome. The Journal of Rheumatology 2016; 43 (2) 383-387.
[2] Shan, et al. Impact of obesity on the efficacy of different biologic agents in inflammatory diseases: A systematic review and meta-analysis. Joint Bone Spine. 2018, in press.

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SAT0320 FREQUENCY AND CHARACTERISTICS OF INFLAMMATORY BOWEL DISEASE IN SPONDYLOARTHRITIS WITH BIOLOGICAL THERAPY. STUDY OF 270 PATIENTS FROM THE SAME CENTER

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Background: Inflammatory bowel disease (IBD) is an extra-articular manifestation that can appear in spondyloarthritis (SpA), as well as uveitis and psoriasis. Its prevalence is 5-10%, although subclinical intestinal inflammation has been found in up to 60%. Biological therapy (BT) can be the treatment for IBD or produce it paradoxically. Fecal calprotectin (FC) is an intestinal inflammation marker, useful for early diagnosis and monitoring disease activity.
Objectives: To describe the frequency and characteristics of IBD in SpA with BT.
Methods: Descriptive and retrospective study (January 2003-January 2019) of patients with SpA that develop IBD in a single center. Epidemiological variables, type of SpA, presence of IBD and its characteristics, levels of FC, presence of BT at IBD onset and treatment received were registered.
For the analysis, frequencies and percentages were used in qualitative variables and mean±standard deviation (SD) in quantitative. Statistical analysis was performed with IBM SPSS v.23.
Results: We studied 270 patients with SpA, 70.4% male with a mean age of 39.9±12 years. The subtypes of SpA were: ankylosing spondylitis (AS) (n=133; 49.3%), psoriatic arthritis (PsA) (n=116; 43%), undifferentiated SpA (n=16; 5.9%), SpA non-Rx axial (n=3; 1.1%) and reactive arthritis (n=2; 0.7%).
IBD was observed in 25 patients (9.26%), 80% male. At the time of IBD onset, they had a mean age of 39.12±9.8 years, the mean ESR was 31.15±24mm1^{a}h, CRP 2.7±2mg/dL and BASDAI 4.6. 16 patients had AS, 6 PsA and 3 undifferentiated SpA. TABLE 1.
Regarding Spa diagnosis, IBD appeared after in 15 patients with an average time of development of 8.39±8 years, before in 7 and was simultaneous in 3. The subtypes of IBD were: Crohn's disease (CD) in 13 patients, ulcerative colitis (UC) in 9 and indeterminate colitis (IC) in 3. The FC was > 200µg/g in 17 patients (68%), normal (<50µg/g) in 1 and between 50-200µg/g in 7. The incidence rate adjusted for follow-up of the 25 cases was 7.7 cases/1000 patients-year.
At the time of the IBD onset, 6 patients were with BT: Etanercept (ETN) (n=2), Infliximab (IFX) (n=1), Adalimumab (ADA) (n=1), Secukinumab (SCK) (n=1) and Ustekinumab (UST) (n=1). The BT had been initiated the previous 12 months in 5 of them. The incidence rate adjusted for follow-up of the 6 cases of IBD after BT was 1.83 cases/1000 patient-years. TABLE 2.
The treatment of the 25 patients with IBD was mesalazine (n=15), oral corticoid (n=5), methotrexate (n=7) and BT in all cases. The BT was:

ADA (n=11; 44%), IFX (n=6; 24%), UST (n=3; 12%), golimumab (n=3; 12%), SCK (n=1; 4%) and vedolizumab (n=1; 4%). The indication was intestinal in 4 patients, joint in 8 and both in 13.
The clinical and analytical evolution in all patients was satisfactory, with a mean ESR of 11.6±9mm1ªh, CRP 0.6±0.3mg/dL and BASDAI 2 in the last control, after an average time of evolution of 12.5±9.3 years.
Conclusion: In this series, IBD was observed in 9.26% of patients with SpA of which 64% were AS. The most frequent form was CD and it was diagnosed after SpA in 60% of the cases. 6 patients were with BT at the time of IBD onset. High FC (> 200µg/g) was observed in the majority of patients.
Therefore, we recommend assessing the presence of digestive manifestations (abdominal pain, weight loss or diarrhea) in patients with SpA due to their possible association with IBD. The FC is a useful tool in these patients.

TABLE 1. CHARACTERISTICS OF IBD IN SpA SUBTYPES

	AS (n=16, 64%)	PsA (n=6, 24%)	uSpa (n=3, 12%)	TOTAL= 25
MEN/WOMEN	14/2	4/2	2/1	20/5 (80%/20%)
AGE AT IBD DX (average in years)	37.56	45.8	34	39.12
HLA B27+ (n, patients)	13	1	1	15 (60%)
CD/UC/IC (n, patients)	9/6/1	2/2/2	2/1/0	13/9/3 (52%/36%/12%)
ESR (average in mm1ª h)	30.07	39.75	21.5	31.15
CPR (average in mg/dL)	2.44	3.08	3.42	2.7
FC (average in µg/g) (24 patients with levels> 50 included)	369.2	409.67	1009	459.29
BEFORE / SIMUL / AFTER (IBD in relation to SpA DX)	6/2/8	0/0/6	1/1/1	7/3/15 (28%/12%/60%)
BT AT IBD DX (n, patients)	3	2	1	6 (24%)
BT	ETN (n=1), IFX (n=1), SCK (n=1)	ADA (n=1), UST (n=1)	ETN (n=1)	ETN (n=2), IFX (n=1), ADA (n=1), SCK (n=1), UST (n=1)

IBD: inflammatory bowel disease, AS: ankylosing spondylitis, PsA: psoriatic arthritis, uSpA: undifferentiated spondyloarthritis, CD: Crohn's disease, UC: ulcerative colitis, IC: indeterminate colitis, ESR: erythrocyte sedimentation rate, CPR: C-reactive protein, FC: fecal calprotectin, BEFORE/SIMUL/AFTER: before the diagnosis of SpA/ simultaneously/after, DX: diagnosis, BT: biological therapy, ETN: etanercept, ADA: adalimumab, IFX: infliximab, SCK: secukinumab, UST: ustekinumab

TABLE 2. BT IN 270 PATIENTS WITH SpA.

	Patients (n)	IBD development after BT (n)	IBD development after BT (%)
ETN	57	2	3.50%
ADA	98	1	1.02%
IFX	36	1	2.78%
SCK	22	1	4.54%
UST	15	1	6.67%
CZP	25	0	0 %
GLM	15	0	0 %
VDZ	2	0	0 %
TOTAL	270	6	2.22%

BT: biological therapy, IBD: inflammatory bowel disease, ETN: etanercept, ADA: adalimumab, IFX: infliximab, SCK: secukinumab, UST: ustekinumab, CZP: certolizumab, GLM: golimumab, VDZ: vedolizumab

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SAT0321 CARDIOVASCULAR EVENTS IN SPONDYLOARTHRITIS : A META-ANALYSIS

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Background: Several studies have demonstrated the possibility of increased risk of cardiovascular disease in patients with inflammatory arthritis such as anklyosing spondylitis and rheumatoid arthritis. In recent years, studies using population -based cohort and insurance claim data have been actively conducted.
Objectives: To compare risks for cardiovascular disease including myocardial infarction (MI), ischemic heart disease (IHD), stroke and mortality of spondyloarthritis compared to general population using large-scale data.
Methods: A systematic search was performed in MEDLINE, EMBASE with additional manual searches for studies associated with spondyloarthritis published between January 1997 and October 2018. All search screening and data collection were performed independently by two reviewers. We calculated the incidences of MI, IHD, stroke and mortality in a meta-analysis of proportion and determined risk ration (RR) by Mante-Haenszel method.
Results: We identified total 495 articles and 16 articles met criteria for meta-analysis including 13 anklyosing spondylitis (AS) studies, 3 psoriatic arthritis (PsA) studies and 1 undifferentiated spondyloarthritis study. The articles were based on large-scale data such as national population cohort or insurance claim data. A meta-analysis result showed a significant increase in the risk of MI (RR= 1.38; 95% CI 1.18 to 1.61), and stroke (RR= 2.04; 95% CI 1.11 to 3.78) in spondyloarthritis patients compared to general population. However, mortality related with cardiovascular disease (RR=1.19; 95% CI 0.96 to 1.48) and total mortality (RR= 1.31; 95% CI 0.8 to 2.15) results did not show significant increases in spondyloarthritis patients.
Conclusion: Our meta-anaylsis results showed that the the risk of MI and stroke significantly increased although mortality associated with cardiovasular (CV) disease and overall mortality did not increase in spondyloarthritis compared to general population. These findings support the reduction of inflammation as well as the management of traditional cardiovascular disease risk factors may reduce CV risk in patients with spondyloarthritis.

REFERENCES

[1] Szabo SM, Levy AR, Rao SR, et al. Increased risk of cardiovascular and cerebrovascular diseases in individuals with ankylosing spondylitis: a population-based study. Arthritis Rheum 2011; 62: 3294-304.
[2] Park CJ, Choi YJ, Kim JG, et al. Association of acute myocardial infarction with ankylosing spondylitis: a nationwide longitudinal cohor study. Journal of Clinical Neuroscience 2018; 56: 34–37.
[3] Bengtsson, K, Forsblad-d'Elia H, Lie E, et al. Are ankylosing spondylitis, psoriatic arthritis and undifferentiated spondyloarthritis associated with an increased risk of cardiovascular events? A prospective nationwide population-based cohort study. Arthritis Res Ther 2017; 19:102.

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SAT0322 AXSPA PATIENTS WITH SYMPTOM ONSET <30 YEARS HAVE MORE STRUCTURAL LESIONS ON MRI OF THE SACROILIAC JOINTS WHEN FULFILLING THE MODIFIED NEW YORK CRITERIA

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Background: The modified New York criteria (mNY) combine clinical symptoms with radiographic sacroiliitis on conventional pelvic radiographs (X-SI) classifying radiographic axial SpA patients (r-axSpA). AxSpA is known to typically start in the third era of life but there is a diagnostic delay of ±7 years. As the mNY criteria classify the most typical and severe expression of axSpA it is suggested that the mNY criteria are less useful in younger patients.
Objectives: To explore the diagnostic utility of the mNY criteria in newly diagnosed axSpA patients with a symptom onset <30 years. In addition, describe the extent of lesions on MRI of the sacroiliac joints (MRI-SI) in mNY positive (mNY+) patients with a symptom onset <30 years.
Methods: This study involved newly diagnosed axSpA patients, age ≥18 years, from a Belgian (Be-Giant) cohort. Patients underwent diagnostic tests involving clinical examination, lab tests, and imaging assessment containing an X-SI and an MRI-SI. mNY criteria was assessed on X-SI. MRI-SI reads contained the assessment of inflammatory lesions according to the Spondyloarthritis Research Consortium of Canada (SPARCC) scoring method and erosions, fatty lesions (FL), sclerosis, ankylosis using an adapted method of the SPARCC. Also, the ASAS definition of a positive MRI-SI was evaluated. T1-weighted and STIR images were viewed simultaneously. X-SI and MRI-SI were evaluated independently by 3 trained readers who were also blinded for clinical features. Imaging scores (X-SI grading according to the mNY criteria and mNY fulfillment, and MRI-SI lesion scores) were calculated as 2 out of 3 reader scores.
Results: In the 173 patients with available X-SI, the average age at symptom onset was 27.4 years old. In 114/173 (65.9%) patients, the symptom onset was below 30 years. Of those, 11 (9.6%) patients fulfilled the mNY criteria. Seven of the 11 (63.6%) patients that were mNY+ were male, which was slightly lower than in the mNY- patients (n=55; 53.4%). The presence of HLA-B27 was comparable between mNY+ and mNY- patients; 8 (72.7%) patients and 82 (79.6%) patients, respectively.
Average X-SI grading in mNY+ patients was 4.7±1.3 (on a scale from 0-8) and in mNY negative (mNY-) patients (n=103) the average X-SI grading was 1.1±1.1.When looking at the MRI-SI assessment, 8/11 mNY+

patients (72.7%) and 60/103 mNY- patients (58.3%) had a positive MRI-SI (ASAS definition).
The table shows the mean scores for MRI-SI lesions. In erosions, fatty lesions and ankylosis, either partial or complete ankylosis, there was a statistically significant difference (p<0.05) between mNY+ and mNY- patients.

Table:. Average MRI-SI lesion scores in axSpA patients with a symptom onset of <30 years fulfilling and not fulfilling the modified New York criteria.

MRI lesions	mNY+ (n=11)	mNY- (n=103)	P-value
Inflammatory lesions (SPARCC score)*	8.9 (±6.0)	7.3 (±7.2)	0.341
Erosions*	7.6 (±4.4)	3.5 (±4.2)	0.003
Fatty lesions*	6.6 (±8.3)	1.8 (±4. 6)	0.005
Sclerosis*	1.1 (±2.0)	0.9 (±2.6)	0.237
(Partial) Ankylosis*	7.6 (±11.5)	0.8 (±3.2)	0.030

*mean (±SD)

Conclusion: Patients with newly diagnosed axSpA and a symptom onset before 30 years infrequently fulfill the mNY criteria. A statistically significant difference in the presence of MRI-SI structural lesions was reported between mNY+ and mNY- patients. AxSpA patients with an early symptom onset have more erosions, fatty lesions and ankylosis on MRI when fulfilling the mNY criteria.
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SAT0323 HEPATOCYTE GROWTH FACTOR IS A PREDICTOR OF DEVELOPMENT OF NEW SYNDESMOPHYTES IN MEN WITH ANKYLOSING SPONDYLITIS. A FIVE YEAR PROSPECTIVE STUDY

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Background: Patients with ankylosing spondylitis (AS) have an increased risk of spinal new bone formation characterized by the development of syndesmophytes. Knowledge of predictors for development of syndesmophytes is limited. Hepatocyte growth factor (HGF) has regulatory effects on a variety of cells in many different organs. HGF signaling can affect both osteoclast and osteoblast lineages and has been shown to promote osteogenesis. Cross-sectional association between increased HGF and increased modified Stoke Ankylosing Spine Score (mSASSS) has previously been shown [1], whereas knowledge of HGF as a predictor for new bone formation is lacking.
Objectives: To study serum HGF as a predictor for development of new syndesmophytes in patients with AS followed for five years.
Methods: Serum levels of HGF was analyzed using ELISA in patients with AS (modified NY-criteria) and in healthy controls (HC) at baseline. Spinal lateral radiographs were obtained at baseline and at the 5-year follow-up and assessed for development of new syndesmophytes using mSASSS. Univariate and multivariable logistic regression analyses were used to assess predictors for development of $\geq$ 1 new syndesmophyte.
Results: Serum HGF and radiographs at baseline and follow-up were available for 163 patients, 88 men and 75 women, baseline mean age 50±12 years. AS patients had higher serum HGF than HC (n=80), p=0.050. In the AS group, 36 patients (22%) developed $\geq$ 1 syndesmophyte, 27 men and 9 women. In the total AS group, neither did baseline serum HGF differ between those who developed $\geq$ 1 new syndesmophyte and those who did not progress, nor did it predict development of $\geq$ 1 new syndesmophyte in the univariate analysis, p=0.25. Interestingly, men who developed $\geq$1 new syndesmophyte had higher serum HGF than the non-progressors (1706±454 vs 1420±338 pg/mL, p=0.001) and increased serum HGF at baseline predicted development of $\geq$ 1 syndesmophyte (OR per 1 SD HGF 2.39, 95% CI 1.31 to 4.36) in the univariate analysis. Serum HGF did not predict new syndesmophytes in women, p=0.13. Multivariable analysis for men including age, smoking, baseline syndesmophyte and serum HGF showed high HGF (OR per 1SD 1.90, 95% CI 1.01 to 3.59) and $\geq$1 baseline syndesmophyte (OR 3.48, 95% CI 1.09 to 11.07) to independently predict development of $\geq$ 1 new syndesmophyte. If baseline CRP was included in the multivariable model, serum HGF and baseline syndesmophytes remained the significant predictors.
Conclusion: High baseline serum HGF was shown to independently predict the development of at least one new syndesmophyte over five years in men with AS.

REFERENCE

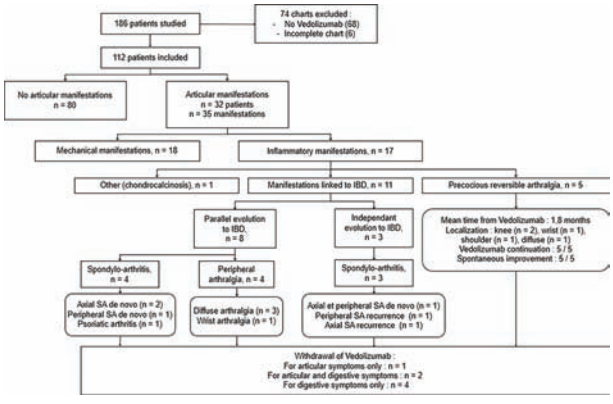
[1] Torres L, Klingberg E, Nurkkala M, Carlsten H, Forsblad-d'Elia H. Hepatocyte growth factor is a potential biomarker for osteoproliferation and osteoporosis in ankylosing spondylitis. Osteoporos Int 2018.

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SAT0324 ARTICULAR MANIFESTATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH VEDOLIZUMAB

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Background: Vedolizumab (VDZ) is a humanized IgG1 monoclonal antibody anti-$\alpha4\beta7$ integrin agent used in inflammatory bowel disease (IBD). It has been incriminated in occurrence of articular manifestations but, as it is given in most cases after anti-TNFÎ± therapy, it is not known if these articular manifestations are linked to IBD-associated arthritis and unmasked by withdrawal of anti-TNFÎ± or are more directly linked to VDZ.
Objectives: The purpose of this study is to describe articular manifestations occurring in patients treated by vedolizumab, and to highlight risk factors for inflammatory manifestations.
Methods: In this retrospective monocentric study, we collected all the cases of incident articular manifestations occurring in the follow-up of the patients treated by VDZ for IBD.
Results: Between February 2013 and June 2017, 112 patients were treated withvedolizumab (56 women, age 39.9 ± 16 years, disease duration = 9.1 ± 7.8 years). IBD cases were distributed into59 (52.7%) Ulcerative Colitis (UC), 49 (43.8%) Crohn's disease (CD), and 4 (3.6%) Undetermined Colitis. Fourpatients (3.6%) had a history of spondyloarthritis and 13 (11.6%) of peripheral arthralgia associated with IBD. 102 (91.1%) patients previously received anti-TNFα. At initiation of vedolizumab, 55 (49.1%) received an associated DMARD (azathioprine in 19.6%, purinethol in 11.6%, methotrexate in 7.1%).



After a mean follow up duration of 11.4 ± 8.6 months, 32 (28.6%) patients presented 35 types of articular manifestations, mechanical (n = 18) (mostly osteoarthritis and tendinitis)or inflammatory (n = 17). Inflammatory articular manifestations were: early reversible arthralgia mostly occurring during perfusion (n = 5), manifestations linked to IBD (n = 11, axial spondyloarthritis, n = 3, peripheral spondyloarthritis, n = 3,

peripheral and axial spondyloarthritis, n = 1, peripheral inflammatory arthralgia, n = 4) with parallel evolution to intestinal symptoms (n = 8) or with independent evolution (n = 3). One patient had chondrocalcinosis (n = 1) (cf figure).

Among the 11 patients with articular manifestations linked to IBD, 10 were previously treated with anti-TNFα. The only predictive factor for inflammatory manifestation was a history of previous inflammatory articular manifestation, present in43.8% (n = 7/16) of patients with inflammatory articular manifestation versus in 12.5% (n = 10/80) of patients without articular manifestation, p = 0.007.

Vedolizumab was stopped in 7 patients (6.3%), due to articular symptoms (n = 1), to digestive symptoms (n = 4) or both (n = 2).

Conclusion: Articular manifestations occurred in almost 30% of patients treated with vedolizumab. Half of them were inflammatory (15%), including 5% of early reversible arthralgia during perfusion. We observed 11 manifestations linked to IBD, including 7 spondyloarthritis, potentially unmasked by withdrawal of anti-TNFα. Indeed, the only predictive factor of inflammatory arthritis was history of previous articular inflammatory manifestation. However, awithdrawal of vedolizumab because of inflammatory arthritis was necessary in only 0.9% of all patients.

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SAT0325 REDUCED STRAIN AND INCREASED STIFFNESS OF COMMON CAROTID ARTERIES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is associated with an increased risk of cardiovascular disease (CVD) which also contributes to the increased mortality observed in AS. It is therefore important to develop non-invasive, accurate methods for early detection of atherosclerotic vascular changes. Studies, in other populations, have demonstrated associations between arterial stiffness and atherosclerotic burden and incident cardiovascular events. The arterial stiffness can be examined by ultrasound providing the β stiffness index that evaluates mechanical deformation properties. Technological advancements in ultrasound have developed a method assessing strain, using speckle tracking technique, which measures deformation mechanics in more dimensions. The speckle tracking method assessing arterial wall motion might permit earlier detection of subclinical CVD.

Objectives: To study, for the first time, bilateral common carotid arterial (CCA) circumferential strain and β stiffness index in patients with AS and 1) compare the results with age and sex-matched controls and 2) explore relationships between circumferential strain and β stiffness index with disease activity, physical function and traditional risk factors for CVD in patients with AS.

Methods: A cohort of 149 patients with AS from Northern Sweden (Modif NY, mean age 55.3±11.2 years, 102(68.5%) men, 146(98%) HLAB27) were assessed with spinal radiographs for mSASSS, clinical examination and BASMI, BASFI, ASDAS-CRP and BASDAI. Forty-six patients with AS (50.4±8.7 years, 31(67%) men) and 46 age- and sex-matched controls (49.8±9.2 years, 31(67%) men) with no known hypertension, diabetes or previous CV events were compared. Bilateral CCA ultrasound was carried out on all patients and controls. The circumferential systolic strain was measured and the β stiffness index was calculated. To analyze factors associated with strain and β stiffness index univariate and standard multivariable linear regression analyses were used. Variables with a univariate *p*-value ≤ 0.1 were considered for the multivariable models. For dichotomous variables, yes was coded 1 and no was coded 0.

Results: The mean strain was significantly lower in AS patients compared with controls, 7.9±2.6% vs 10.3±1.9%, p<0.001 and the mean β stiffness index was significantly higher in AS compared to controls, 13.1±1.6 mmHg/mm vs 12.3±1.3 mmHg/mm, p=0.018.

Conclusion: Both CCA strain and β stiffness index differed significantly between AS patients and controls indicating a worse subclinical arterial status in AS. The CCA strain was associated with several AS related variables while the β stiffness index with age and smoking indicating that the methods complement each other in the assessment of distensability of arteries in patients with AS.

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Table.. Multivariable linear regression analysis in 149 patients with AS

Mean CCA circumferential strain,%			**Mean β stiffness index, mmHg/mm**		
Covariates	**β**	***p*-value**	**Covariates**	**β**	***p*-value**
Age, years	**-0.22**	**0.021**	**Age, years**	**0.29**	**0.008**
Anterior uveitis, Y/N	**-0.17**	**0.021**	Peripheral arthritis, Y/N	0.077	0.35
cs and/or bDMARD, Y/N	**-0.15**	**0.036**	Hypertensive disease, Y/N	0.066	0.43
BASFI, score	0.033	0.69	BASMI, score	0.12	0.32
BASMI, score	-0.008	0.93	Syndesmophyte, Y/N	-0.039	0.69
ESR, mm/h	**-0.30**	**<0.001**	**Pack years, smokers, n**	**0.16**	**0.059**
Cholesterol, mmol/L	-0.021	0.79	Pulse pressure, mmHg	-0.002	0.98
HDL, mmol/L	-0.094	0.22	Heart rate, bpm	0.13	0.12
Systolic blood pressure, mmHg	-0.025	0.81			
Diastolic blood pressure, mmHg	-0.121	0.22			
Heart rate, bpm	-0.16	**0.038**			
Adjusted R^2 0.31			**Adjusted R^2 0.22**		

SAT0326 PLANS FOR MOTHERHOOD ARE CHANGED AFTER DIAGNOSING ANKYLOSIS SPONDYLITIS (AS). AS FEMALE PATIENTS' ATTITUDE TO THE USE OF AS MEDICATIONS DURING PREGNANCY PLANNING AND CONCEPTION

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Background: Plans for motherhood are changed after diagnosing ankylosis spondylitis (AS). AS female patients' attitude to the use of AS medications during pregnancy planning and conception.

Objectives: To describe the impact of diagnosing AS on woman's plans to have children, and patients' attitude to continuing AS therapy while planning pregnancy or after definite conception.

Methods: 302 AS female patients participated in the survey conducted from May to November 2018. Patient's mean age was 32.4±6.0 years, average AS duration from onset of symptoms was 10.2±7.4 years. 224 (74.2%) respondents had higher education, 68 (22.5%) – vocational college education and 10 (3.3%) – secondary education. Totally 492 pregnancies were reported in 214 (70.9%) respondents, including 278 pregnancies before AS onset, while 214 occurred with underlying AS.

Results: 206 women (68,2%) have changed their attitude to potential pregnancy occurring during AS:

– 12 (5.8%) were firmly set to terminate an unplanned pregnancy;

– 21 (10.2%) were giving up on pregnancy because they already have children born before AS onset;

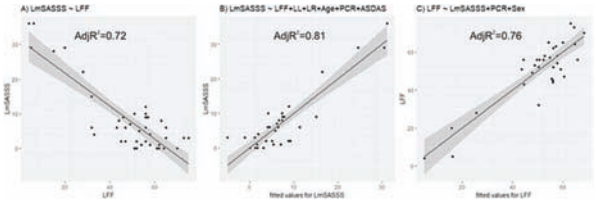
– 9 (4.4%) were against getting pregnant, although they yet haven't had children;

– 164 (79.6%) accepted potential pregnancy, although recognizing they would experience continuous emotional discomfort and fear for their own health and health of the unborn child.

– 42 (13%) women were distinctly against getting pregnant in case they have AS.

There was a weak inverse correlation between AS duration and changing patients' attitude to pregnancy (R=-0.14, p<0.05).

150 (49.7%) respondents discussed pregnancy planning with a rheumatologist. Women with university degree were more likely to consult a rheumatologist before trying for a baby compared to subjects with vocational college and secondary education (55.5%, 35.3% and 40%, respectively; p=0.02). 53 (35.3%) patients failed to receive a comprehensive answer to their questions related to AS and pregnancy mutual influence, the probability of AS inheritance by a child, safety of AS therapy at conception



and during pregnancy; moreover, in 4 cases AS was interpreted as contraindication to pregnancy.

107 (35.4%) respondents believe that AS medications should be discontinued during pregnancy planning and conception, 75 (24.8%) subjects accepted possible use of AS therapy during this period, while 120 (39.8%) didn't know the answer. 15.2% of respondents were ready to continue on NSAIDs, 20 (6.6%) – on glucocorticoids and sulfasalazine, and 21 (7%) – on biological drugs (GEBD). Of those who are ready to continue on AS medications at conception, 46 women (61.3%) consulted pregnancy planning with a rheumatologist. Respondents with higher education were slightly more likely to continue on AS therapy at conception (29%) compared to women with vocational college education (11.8%). Age, AS duration, or marital status had no influence on patients' attitude to AS therapy during pregnancy planning and conception.

Conclusion: The majority of surveyed female patients changed their attitude to pregnancy after establishing AS diagnosis, although only 13% of them were ready to avoid pregnancy due to AS. No more than 50% of respondents were consulted a rheumatologist before planning pregnancy, and up to one third of them were not receive all expected answers to their questions and recommendations. Only 1/4 of participants accept the idea of continuing AS therapy during pregnancy planning and conception.

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SAT0327 SEGMENTAL RELATIONSHIP BETWEEN MOBILITY, STRUCTURAL DAMAGE AND DISEASE ACTIVITY IN AXIAL SPONDYLOARTHRITIS

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Background: Axial Spondyloarthritis (axSpA) is characterised by progressive loss of spinal mobility, due to inflammation and structural damage. Conventional mobility tests have been used alongside radiographic structural damage and disease activity scores in order to explore the overall relationship between spinal mobility, structural damage and disease activity. This has rarely been done at the segmental level e.g. at the level of the lumbar spine only. The ViMove inertial motion sensor-based system allows segmental spinal mobility to be directly measured, namely at the lumbar spine level.

Objectives: To analyse the relationship between mobility, structural damage and disease activity in the lumbar spine of patients with axSpA.

Methods: Lumbar spinal mobility was measured using the the ViMove system with a pair of sensors located at L1 and the sacrum. Lumbar ROM in the three planes (anterior flexion - LFF, extension - LFE, lateral flexion – LL, and rotation - LR) was measured. Radiographs were obtained to calculate the lumbar part of the mSASSS (LmSASSS). Other outcome measures were: BASMI, Schober and lateral flexion (measured with a tape), BASDAI and ASDAS-CRP. Subgroups of patients with high and low levels of lumbar structural damage were defined, by dichotomising the population based on the median LmSASSS (5.5). Pearson correlations between measures, Student T tests for significant differences between groups and linear regression analysis, to analyse relationship between structural damage and mobility, were obtained.

Results: 44 axSpA patients were recruited from the COSPAR cohort of the Reina Sofia University Hospital (39% females, age 43±12 years, disease duration 17±14 years, BMI 26±3). All mobility measurements (except for LFE) in the severe damage group were significantly reduced compared to the group with less damage (p<0.001). BASDAI and ASDAS were not significantly different between these groups. LmSASSS correlated (p<0.001) with all mobility measures obtained by IMU system and conventional metrology, especially with LFF, but not with activity indexes. Only a weak relation between BASDAI and LFE was found (p<0.05). A linear regression for analysing relationship between LmSASSS and LFF including as variables: age, sex, evolution time, BMI, PCR, ASDAS, LFF, LFE, LL, LR and LmSASSS was done. LmSASSS linear regression using only LFF obtained an adjusted R^2 of 0.72 (Figure-A). Introducing the rest of variables, the most significant for LmSASSS was LFF (p<0.001) and the other mobility measures (LL, LR with p<0.05) and age, PCR and ASDAS (p<0.01) with an adjusted R2 of 0.81(Figure-B). For LFF, LmSASSS was the most significant (p<0.001), with Sex (p<0.01) and PCR (p<0.05) included, obtaining an adjusted R2 of 0.76 (Figure-C). Differences between models and fitted values (RMSE) were 3.8 units for LmSASSS and 7.7° for LFF.

Conclusion: Other studies have shown a relationship between mobility, structural damage and disease activity using a more global assessment. Our study focuses on the analysis of structural damage and mobility in the lumbar vertebrae, and our results suggest that structural damage is the dominant factor determining spinal mobility in this region (especially lumbar frontal flexion). Further studies are needed combining these results with MRI.

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SAT0328 PATIENT-REPORTED ATTITUDES TOWARDS AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE EMAS SURVEY

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Background: Understanding patient disease-related attitudes plays an important role in effective management of axial spondyloarthritis (axSpA). Nevertheless, the patient perspective remains insufficiently explored.

Objectives: To describe patients' axSpA-related fears and hopes and their associations with sociodemographic, disease outcomes and psychological distress.

Methods: The European Map of Axial Spondyloarthritis (EMAS), conducted from July 2017 to February 2018, was a cross-sectional on-line survey of unselected patients with self-reported axSpA from Austria, Belgium, France, Germany, Italy, Netherlands, Norway, Russia, Slovenia, Spain, Sweden, Switzerland, and the UK. Participants were recruited through an online panel and patient organizations. Participant's axSpA-related fears and hopes were freely expressed through open-ended questions (except in France where multiple-choice items were used). Thematic analysis, using the French categories and data-driven codes, was performed and frequencies of specific fears and hopes were subsequently calculated. Associations between disease-related fears and hopes with sociodemographic characteristics, disease outcomes (BASDAI, self-reported spinal stiffness and functional limitation), and psychological distress (General Health Questionnaire, GHQ-12; with a cut-off point of ≥3) were

	N	Flexion	Extension	Lateral	Rotation	LmSASSS	BASMI	ASDAS	BASDAI
Total	44	48.8(17.4)	10.5(13.4)	42.7(17.0)	24.8(8.8)	8.0(9.7)	3.0(1.9)	1.9(1.1)	3.7(2.0)
Low	22	57.2(10.0)	12.7(16.9)	49.4(10.1)	27.9(7.6)	1.8(1.5)	2.3(1.4)	1.8(1.2)	3.6(1.9)
High	22	39.6(19.7)	7.7(9.1)	35.1(20.0)	21.1(8.4)	14.2(10.5)	3.9(2.1)	2.2(1.0)	3.7(2.1)

Table 1. Association between patients' fears and sociodemographic and disease outcomes (N: 2166)

Areas of concern		Age (years)	Gender (Male)	Educational Level (University)	Marital Status (Married)	BASDAI (0-10)	Stiffness index (3-12)	Global Limitation (0-54)	GHQ-12 (0-12)
Disease progression	Yes	42.4±11.6	25.9%	47.4%	64.0%	5.7±1.8	8.6±2.3	17.7±12.0	4.5±4.0
	No	44.0±13.1	41.3%	54.0%	68.3%	5.3±2.1	7.3±2.4	12.3±11.2	5.4±4.0
(mean ± SD or %)	p-value	**0.016***	**<0.001***	**<0.001***	**0.010***	**<0.001***	**<0.001***	**<0.001***	**<0.001***
Suffering pain	Yes	41.7±11.5	21.9%	48.8%	64.3%	6.0±1.7	8.8±2.2	18.6±12.4	5.9±4.1
	No	44.2±13.1	42.2%	53.0%	67.9%	5.2±2.1	7.3±2.4	12.3±10.9	4.3±3.9
(mean ± SD or %)	p-value	**<0.001***	**<0.001***	**<0.001***	0.105	**<0.001***	**<0.001***	**<0.001***	**<0.001***
Stiffness	Yes	42.1±12.3	20.9%	47.5%	65.4%	5.9±1.7	9.1±2.0	18.8±12.2	5.8±4.1
	No	43.7±12.7	39.5%	52.7%	67.1%	5.3±2.0	7.5±2.4	13.1±11.4	4.5±4.0
(mean ± SD or %)	p-value	**0.021***	**<0.001***	**0.007**	0.372	**<0.001***	**<0.001***	**<0.001***	**<0.001***
Loss of mobility	Yes	42.2±11.4	23.9%	50.2%	65.0%	5.9±1.8	8.9 ± 2.2	18.6±12.6	5.8±4.1
	No	43.9±13.1	41.1%	52.3%	67.6%	5.2±2.0	7.3±2.4	12.3±10.8	4.3±4.0
(mean ± SD or %)	p-value	**0.010***	**<0.001***	**0.002***	0.281	**<0.001***	**<0.001***	**<0.001***	**<0.001***
Loss of independence/ disability	Yes	42.0±11.2	22.4%	49.7%	63.8%	6.0±1.7	8.8±2.2	19.7±12.2	6.2±4.0
	No	43.9±13.1	41.1%	52.4%	68.0%	5.2±2.1	7.4±2.4	12.1±10.9	4.2±3.9
(mean ± SD or %)	p-value	**0.005***	**<0.001***	**<0.001***	**0.036***	**<0.001***	**<0.001***	**<0.001***	**<0.001***
Social isolation (friends, family)	Yes	40.2±10.3	17.8%	49.7%	56.9%	6.2±1.6	9.3±2.0	21.3±12.0	7.2±4.0
	No	43.9±12.9	38.8%	52.0%	68.4%	5.3±2.0	7.6±2.4	13.1±11.3	4.4±3.9
(mean ± SD or %)	p-value	**<0.001***	**<0.001***	**0.031***	**<0.001***	**<0.001***	**<0.001***	**<0.001***	**<0.001***
Loss of job/ inability to work	Yes	39.8±9.6	20.6%	50.6%	61.7%	5.9±1.8	8.8±2.1	18.1±11.6	6.2±4.0
	No	44.6±13.3	41.0%	52.0%	68.5%	5.3±2.1	7.5±2.5	13.0±11.5	4.3±3.9
(mean ± SD or %)	p-value	**<0.001***	**<0.001***	**<0.001***	**0.005***	**<0.001***	**<0.001***	**<0.001***	**<0.001***
Complications during a pregnancy/infertility	Yes	30.1±5.8	2.6%	66.7%	50.9%	5.4±2.0	8.3±2.6	20.4±12.6	5.9±3.8
	No	44.1±12.5	37.7%	50.8%	67.7%	5.4±2.0	7.8±2.4	13.9±11.6	4.7±4.1
(mean ± SD or %)	p-value	**<0.001***	**<0.001***	**<0.001***	**<0.001***	0.747	**0.017***	**<0.001***	**0.001***
Impact of the disease on my everyday activities	Yes	41.0±11.2	18.1%	49.3%	64.6%	5.9±1.7	8.9±2.2	19.2±11.8	6.2±4.0
	No	44.2±13.0	41.8%	52.5%	67.5%	5.3±2.1	7.4±2.4	12.6±11.3	4.3±3.9
(mean ± SD or %)	p-value	**<0.001***	**<0.001***	**0.007***	0.172	**<0.001***	**<0.001***	**<0.001***	**<0.001***

*Chi-square and Mann-Whitney to test possible associations between variables.

Table 2. Association between patients' hopes and sociodemographic and disease outcomes (N: 2166)

Areas of concern		Age (years)	Gender (Male)	Educational Level (University)	Marital Status (Married)	BASDAI (0-10)	Stiffness index (3-12)	Global Limitation (0-54)	GHQ-12 (0-12)
To stop disease progression	Yes	43.1±12.1	27.0%	53.6%	63.8%	5.5±2.0	8.3±2.4	16.2±12.1	5.4±4.1
	No	43.6±12.9	40.2%	50.8%	68.3%	5.4±2.0	7.6±2.4	13.3±11.5	4.5±4.0
(mean ± SD or %)	p-value	0.486	**<0.001***	0.198	0.145	0.429	**<0.001***	**<0.001***	**<0.001***
To be treated/ cured	Yes	41.0±11.7	31.2%	53.5%	65.9%	5.6±2.0	8.4±2.5	16.5±11.9	5.4±4.0
	No	44.0±12.8	37.0%	51.2%	67.0%	5.4±2.0	7.7±2.4	13.7±11.6	4.6±4.0
(mean ± SD or %)	p-value	**0.000***	**0.026***	**0.008***	**0.005***	**0.008***	**<0.001***	**<0.001***	**<0.001***
To eliminate pain	Yes	43.0±11.7	24.2%	50.2%	65.1%	5.9±1.8	8.7±2.2	18.3±11.9	5.4±4.0
	No	43.6±13.0	41.2%	52.3%	67.6%	5.2±2.1	7.4±2.4	12.4±11.2	4.5±4.0
(mean ± SD or %)	p-value	0.537	**<0.001***	0.291	0.127	**<0.001***	**<0.001***	**<0.001***	**<0.001***
To improve my quality of life	Yes	42.0±11.7	21.2%	50.1%	64.6%	5.9±1.7	9.0±2.1	18.7±11.6	5.6±4.1
	No	43.8±12.9	40.2%	52.1%	67.5%	5.3±2.1	7.5±2.4	12.9±11.5	4.6±4.0
(mean ± SD or %)	p-value	**0.008***	**<0.001***	**0.001***	0.201	**<0.001***	**<0.001***	**<0.001***	**<0.001***
To live without constraints/ limitations	Yes	42.6±11.7	21.4%	48.9%	64.6%	5.8±1.9	8.9±2.2	18.5±12.1	5.7±4.1
	No	43.6±12.9	39.6%	52.4%	67.5%	5.4±2.0	7.5±2.4	13.2±11.4	4.6±4.0
(mean ± SD or %)	p-value	0.212	**<0.001***	0.202	0.301	**<0.001***	**<0.001***	**<0.001***	**<0.001***
For an effective treatment (mean ± SD or %)	Yes	42.9±11.6	21.8%	52.0%	65.3%	5.7±1.9	8.7±2.2	17.8±11.8	5.7±4.0
	No	43.6±13.0	40.7%	51.5%	67.3%	5.3±2.0	7.5±2.4	13.0±11.5	4.5±4.0
	p-value	0.445	**<0.001***	**<0.001***	0.156	**<0.001***	**<0.001***	**<0.001***	**<0.001***
To improve mobility	Yes	43.2±12.0	24.3%	51.4%	64.7%	5.8±1.8	8.9±2.2	18.3±12.0	5.7±4.1
	No	43.5±12.8	38.6%	51.7%	67.3%	5.4±2.0	7.5±2.4	13.3±11.5	4.6±4.0
(mean ± SD or %)	p-value	0.753	**<0.001***	0.240	0.508	**0.001***	**<0.001***	**<0.001***	**<0.001***
To exercise	Yes	42.2±11.9	20.3%	51.9%	62.0%	5.7±1.8	8.9±2.2	17.3±11.7	5.6±4.0
(mean ± SD or %)	No	43.6±12.8	39.1%	51.6%	67.8%	5.4±2.0	7.6±2.4	13.6±11.7	4.6±4.0
	p-value	0.059	**<0.001***	0.362	**0.044***	**0.007***	**<0.001***	**<0.001***	**<0.001***

* Chi-square and Mann-Whitney to test possible associations between variables.

explored through mean and contingency analysis and significance was confirmed by Mann-Whitney and Kruskal-Wallis tests.

Results: 2846 axSpA patients participated in EMAS: mean age was 43.9 ±12.3 years, 61.3% were female and 48.1% university-educated. Mean disease duration was 17.2±12.4 years, disease activity (BASDAI) 5.5±2.0 and psychological distress (GHQ-12) 5.0±4.1. The most frequent reported fears were fear of disease progression (32.9%), suffering pain (30.5%), and loss of mobility (30.0%). Accordingly, the most frequent hopes were to halt disease progression (32.5%), eliminate pain (30.7%), and access effective treatment (23.3%). Female patients and those with lower educational level more frequently expressed disease-related fears, while married patients less frequently reported fears. Patients with poorer disease outcomes and higher psychological distress more frequently reported disease-related fears.

Conclusion: Higher physical and psychological burden was significantly associated with expressing fears relating to axSpA. Defining the concerns that are important for patients needs to be considered in order to improve patient-physician communication and shared decision-making with regard to treatment options and goals.

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SAT0329 IMPACT OF AXIAL SPONDYOARTHRITIS (AXSPA) ON SOCIAL AND FAMILY LIFE: RESULTS OF THE EMAS SURVEY OF 638 PATIENTS IN 2018

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Background: Axial Spondyloarthritis (axSpA) has an impact on daily life, but data in the biologics era are scarce.

Objectives: To assess the patient-reported impact of axSpA on social and family life.

Methods: Between December 2017 and February 2018, patients followed for axSpA by their rheumatologists or affiliated to the French patients association AFLAR, and self-reporting axSpA, participated in the European Map of Axial Spondyloarthritis (EMAS) cross-sectional patient survey in France1. Socio-demographics and disease characteristics were collected and the impact of axSpA on personal life was evaluated through a questionnaire established by an international committee on social interactions (better/worse), frequency of social activities (less or more frequent), patient fears and the impact of flares on 10 aspects of daily life evaluated as no/low to moderate/severe. No imputation of missing data was performed and the analyses were descriptive.

Results: Data from 638 persons, mean age 41.5±11.1 years, 77% women, mean disease duration 6.9±8.2 years, 19.1% on biologics, were analyzed. The disease (axSpA) was often active (mean BASDAI: 5.9 ±1.7). Social interactions were reported as worse or much worse since axSpA: with friends (43%), work colleagues (39%), spouse (35%) and family (31%). AxSpA had also an impact on the frequency of social and sport activities, which were «much less frequent than before» for sport (52%), travels (38%), sexual intercourse (31%) and cultural outings (29%). A moderate to severe impact of disease flares was reported on walking in the street (53%), intimate relations (49%) and personal hygiene (35%). Regarding fears linked to the disease, 71% of participants feared being unable to do their daily tasks and loosing autonomy and 42% feared social isolation.

Conclusion: More than half of patients with axSpA in France described a negative impact of axSpA on their family and social life, in a context of fears for the future. These data are important to take into account for shared decision-making.

REFERENCE

[1] Gossec L, et al. Diagnostic Delay and Associated Factors in Axial Spondyloarthritis across Europe. Results from the European Map of Axial Spondyloarthritis Survey. Arthritis Rheumatol. 2018 Sep;70 Suppl 9:688

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SAT0330 VALUE OF DIAPHRAGMATIC ASSESSMENT IN RELATION TO PULMONARY FUNCTIONS AND DISEASE ACTIVITY IN AXIAL SPONDYLOARTHROPATHIES: PRELIMINARY REPORT

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Background: Axial Spondyloarthropathies (SpA) are chronic, systemic, inflammatory diseases which affect the axial skeleton, limit chest mobility and cause serious impairments in pulmonary functions.
Objectives: In this cross-sectional study, as a new approach; diaphragm thickness is assessed by ultrasound in patients with axial SpA to determine possible relationships with pulmonary functions and disease activity.
Methods: 49 axial SpA patients enrolled in the study were assessed by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology index (BASMI), Erythrocyte Sedimentation Rate (ESR), serum C-Reactive Protein levels (CRP) and chest expansion (cm). 15 patients with lung diseases other than axial SpA pulmonary involvement, neuromuscular diseases, scoliosis and congenital chest deformity were excluded. Dynamic pulmonary function tests (PFT) and 6 min walk (6MW) tests were done and physical activity levels were evaluated by short form International Physical Activity Questionnaire (IPAQ). Diaphragm thickness was measured at end expiration (dtFRC) and deep inspiration (total lung capacity (dtTLC)). Thickness ratio (dtr: dtTLC/dtFRC) and thickness change (dtc: dtTLC-dtFRC) were calculated.
Results: The descriptive data of the patients are presented in Table 1. Patients had a moderate disease activity and all the patients were category 1 (inactivity) according to IPAQ. Mean value of dtr and PFT seem to be within normal range according to population studies and dtr was significantly correlated with dynamic pulmonary function tests, yet negatively correlated with ESR (r: -0.466, p: 0.006). There was insignificant negative correlation with age, disease duration, BASDAI, BASFI, and BASMI.
Conclusion: To the best of our knowledge, this is the first study evaluating the relation between diaphragm thickness and pulmonary functions with disease activity. Even though, there was no limitation in PFT and expected values were obtained in dtr, the negative correlation with ESR makes us think about the possible effect of disease activity on dtr. With these preliminary results, it is early to conclude, but dtr assessment may be complementary to PFT and early measures to improve diaphragm function with specific exercises should be implemented in patients with axial SpA.

Table 1. Baseline descriptive data characteristics of patients

Age[a] (y)	46±10.7
Female (n,%)	26 (76.5)
Male (n,%)	8 (23.5)
Disease duration- month[b]	60 (3-300)
	Female Male
dtFRC [a] (cm)	0.17±0.4 0.18 ±0.3
dtTLC [a] (cm)	0.34±0.9 0.43±011
dtr [a]	1.9±0.3 2.42±0.35
BASFI[b]	4.7 (0-8.5)
BASMI[b]	1 (0-9)
BASDAI[b]	4.5 (0.4-8.4)
MASES[b]	3.5 (0-13)
6 MWT[a] (m)	438±105
VCMax[a]	3.2±0.8 (95.09%N)
FEV1[a]	2.5±0.6 (93.6%N)
PEF[a]	6.0±1.6 (87.4%N)

REFERENCE

[1] Carrillo-Esper R, Pérez-Calatayud ÁA, Arch-Tirado E, Díaz-Carrillo MA, Garrido-Aguirre E4, Tapia-Velazco R, Peña-Pérez CA, Espinoza-de Los Monteros I, Meza-Márquez JM, Flores-Rivera OI, Zepeda-Mendoza AD, de la Torre-León T. Standardization of Sonographic Diaphragm Thickness Evaluations in Healthy Volunteers Respir Care 2016;61(7):920-4

a: mean± SD, b: median (min-max), MASES: Maastrich Ankylosing Spondylitis Enthesitis Score, VC: Vital Capacity, FEV: Forced Expiratory Volume, PEF: Peak Expiratory Flow, N: Normal

Disclosure of Interests: None declared
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SAT0331 THE DIAGNOSTIC UTILITY OF THE DETECTION OF EROSIONS IN SACROILIAC JOINTS IN PATIENTS WITH EARLY SPONDYLOARTHRITIS

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Background: In the light of new therapeutic strategies, it has become essential to detect spondyloarthritis (SpA) in its earliest stages in order to initiate treatment as early as possible. Magnetic resonance imaging (MRI), with its ability to detect active lesions, is usually considered as a key tool for early recognition of sacroiliitis. However, a growing number of studies reported the lack of specificity of bone marrow edema (BME) leading sometimes to a false "positive MRI" of sacroiliac joints (SIJ). In addition, many recent studies have pointed out the utility of detecting structural lesions, especially erosions, reported as the earliest structural change on SIJ in the course of sacroiliitis.
Objectives: We aimed to assess the reliability of early recognition of erosions in patients with suspected SpA.
Methods: Consecutive patients, aged 16 and over, consulting from February 2014 to February 2017 for symptoms suggestive of SpA (inflammatory back pain, enthesitis or dactylitis…) were enrolled in this cohort. They were referred for computed tomography (CT) and MRI of the SIJ. The CT and MR images were reviewed for the presence of erosions by 2 musculoskeletal radiologists blinded to clinical findings. After a follow-up of 2 years, 2 experienced rheumatologists confirmed or excluded the diagnosis of SpA. Diagnostic utility of erosions for diagnosis of SpA was determined by calculating sensitivity, specificity, positive and negative likelihood ratio with final clinical diagnosis made by rheumatologists as golden standard.
Results: Fifty-four patients were included, 13 men and 41 women. The mean age was 39 years [17-71]. The mean duration of symptoms was 75 months (6 years). Cervical, thoracic, lumbar and buttock pain were noted respectively in 46.3%, 37%, 87%, and 57.4% of the studied patients. Morning stiffness was noted in 55.5% of patients. The prevalence of HLA–B27 was 23.4%. After a follow-up of 2 years, the referring rheumatologists made a diagnosis of SpA in 77.8% of patients, whereas SpA was excluded in 22.2%. Among the 42 patients classified as having a confirmed SpA, erosions were detected on SIJ by CT in 64.3% (n=27) and by MRI in (n=18) 42.85% of patients. Among the 12 patients in whom Spa was excluded, erosions were detected on SIJ by CT in 25% (n=3) of patients and were not detected by MRI in any patient. Sensitivity, specificity, positive and negative likelihood ratio of erosions detected by CT were respectively estimated at 64.3%, 75%, 90% and 37.5%. Those of erosions detected by MRI were estimated at 42.9%, 100%, 100%, 33.33%. A statistically significant association was observed between erosions and rheumatologists' diagnosis of SpA (p= 0.05 for CT and p= 0.012 for MRI). The likehood ratio was estimated respectively for CT and MRI at 3.8 and 7.6.
Conclusion: In our study, detection of erosions showed a high specificity for recognition of sacroiliitis, especially when detected by MRI. This study highlights the utility of structural SIJ lesions, particularly erosions, to reduce the number of false positives.
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SAT0332 GENDER DIFFERENCES IN DISEASE STATUS, QUALITY OF LIFE AND TREATMENT PATTERNS AMONG AXIAL SPONDYLOARTHRITIS PATIENTS: FINDINGS FROM A GLOBAL SURVEY

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Background: Axial spondyloarthritis **(**AxSpA) is a chronic inflammatory disease of the axial skeleton associated with impaired health-related quality of life (HRQoL) and disability.[1-2] Gender differences in clinical and quality of life (QoL) measures have been demonstrated in axSpA (ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA), but not well quantified in a real-world clinical setting.
Objectives: To compare the clinical characteristics, QoL and treatment patterns of male and female AS and nr-axSpA patients from a multinational survey.
Methods: Data from a cross-sectional, multi-national survey conducted in Australia, Canada, France, Germany, Italy, Japan, Spain, United Kingdom and the United States were analyzed. Demographics, disease status and medication use were reported by the physician, while work disability and QoL measures were reported by the patient. Gender comparison analyses were conducted for AS and nr-axSpA subgroups.
Results: Data from 432 physicians (407 rheumatologists, 13 orthopedists, 12 internists) 2,300 AS patients (male: 1,673[72.74%]; female: 627 [27.26%]), and 2,099 nr-axSpA patients (male: 1,146 [54.60%]; female: 953 [45.40%]) were included in this analysis. Male AS and nr-axSpA patients were more likely to be younger (AS: p=0.0141; nr-axSpA: p=0.1327), smokers (AS: p<0.0001; nr-axSpA: p<0.0001), have full-time employment (AS: p<0.0001; nr-axSpA: p<0.0001), and currently be in remission (AS: p<0.0001; nr-axSpA: p=0.0001) when compared to female AS and nr-axSpA patients. Male AS patients were more likely to be prescribed biologic treatment when compared to female AS patients (p=0.0070); however, rates of biologic use between male and female nr-axSpA patients were comparable (p=0.2148). Male AS and nr-axSpA patients also had lower Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores than female patients (AS: p<0.0001; nr-axSpA: p<0.0001). In addition, female AS and nr-axSpA patients were more likely to report worse QoL and more activity impairment, as assessed by the Ankylosing Spondylitis Quality of Life (ASQoL) (AS: p<0.0001; nr-axSpA: p=0.0001), Assessment of SpondyloArthritis international Society Health Index (ASAS HI) (AS: p<0.0001; nr-axSpA: p<0.0001), and Work Productivity and Activity Impairment (WPAI) (AS: p=0.0006; nr-axSpA: p=0.0002).
Conclusion: Male AS patients were more likely to be prescribed biologics when compared to female AS patients, despite females experiencing worse QoL and greater activity impairment. This study highlights an unmet need among female patients for more appropriate treatment approaches.

REFERENCES

[1] Boonen A, et al. Ann Rheum Dis 2010
[2] Kotsis K, et al. Expert Rev Pharmacoeconomic Outcomes Res. 2014

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SAT0333 THE DIFFERENCES OF CLINICAL MANIFESTATIONS BETWEEN FAMILIAL AND SPORADIC ANKYLOSING SPONDYLITIS PATIENTS

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease which could lead to pain, functionally limitation and even less life expectancy. Morning stiffness often occur in the patients. Familial aggregation has been found due to genetic susceptiblity of the disease. There are certain difference in the patients with or without familal AS. For example. familial AS patients were reported to show a lower frequency of oligoarthritis [1].
Objectives: Our study was to investigate the difference of morning stiffness in the patients with familial AS or sporadic AS.
Methods: Study participants were recruited from Department of Rheumatology in theThird Affiliated Hospital of Sun Yat-sen University. Each patient was assessed by at least two qualified rheumatologists, and the diagnosis was made according to 1984 Modified New York Classification Criteria for AS. Through detailed family history, AS patients with 2 or more patients in his/her family who firstly went to our clinic were included as a possible proband. Then the probands broughtthe affected relatives to our clinic for further examination. Or three rheumatologists and two nurses drove to the places where a possible proband's family member lived. Baseline assessments were completed by trained by using identical questionnaires including demographic information (age, gender), disease related characteristics (back pain, morning stiffness, peripheral arthritis, uveitis, etc.), Bath
Ankylosing Spondylitis Disease Activity Index (BASDAI), and Bath Ankylosing Spondylitis Functional Index (BASFI). The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis. The difference between familial and sporadic AS patients were examined by using Independent T test or M-U test.
Results: Of all the 264 AS patients, 175 (66.3%) were males and 89 (33.7%) were female patients.
Mean age was 31.0±9.5 years, and disease duration was 7.3±6.7 years. Mean age of disease onset was 23.4±8.5 years. There was no difference between familial and sporadic AS patients in the aspects of age, sex, age of onset and disease duration. However, age of onset of male familial AS patients was significantly lower than that of female patients (21.9 ±8.4 VS 26.3±8.2,p=0.004), while no such sex difference was detected in sporadic patients (22.6±8.1 VS 25.3±8.6,p=0.08). Familial patients were inclined to have hip joint involvement, compared with sporadic patients (58.6% VS 9.6, p<0.01). 186 (70.5%) patients suffered from morning stiffness with medial time of 61.6 minutes. Degree of morning stiffness was 3.5±3.0. Sporadic patients had more morning stiffness than familial patients (p=0.007). There was no difference in the presentation of peripheral arthritis (p>0.05). Mean BASDAI score was 3.6±2.0, and mean BASFI score was 1.4±1.8. The BASDAI score was slightly higher in sporadic group (p=0.027).
Conclusion: Familial AS patients had more hip joint involvement, less morning stiffness and an earlier disease onset, especially in male patients, compared with sporadic patients.

REFERENCE

[1] Kim, H.W., et al., Phenotype difference between familial and sporadic ankylosing spondylitis in Korean patients. J Korean Med Sci, 2014. 29(6): p. 782-7.

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SAT0334 DOES DEPRESSION PREDICT FUTURE DISEASE STATUS AND IMPROVEMENTS IN DISEASE PARAMETERS? RESULTS FROM THE COMPLETE STUDIES, A CANADIAN REAL WORLD OBSERVATIONAL COHORT

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Background: Depression is a common comorbidity in rheumatic diseases such as Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS), whereby it is associated with increased disease activity, decreased functionality, and lower persistence with treatment.
Objectives: The objective of this analysis was to assess if baseline depression in Canadian patients with PsA or AS predicts future disease status and improvement in disease parameters.
Methods: COMPLETE is a Canadian observational cohort of anti-TNFα naïve adults with PsA and AS, who require a change in their treatment. Separate analyses were performed for each disease group. Depression was defined as BDI score ≥20 (or use of anti-depressants and/or anxiolytic medication). Multivariate logistic regression was used to assess the

baseline predictors of achievement of low disease activity (LDA) in BASDAI (<4) and BASFI (<4) for patients with AS; or DAPSA LDA (≤13), DAS28 LDA (<3.2), DAPSA remission (≤4), DAS28 remission (<2.6) and BSA <3% for patients with PsA. The maximum improvement (highest change from baseline at either 6 or 12 months) in BASDAI, BASFI, DAPSA, DAS28 was assessed for using multivariate linear regression and the least square means (LSMs). The maximum improvement in HAQ-DI and SF-12 physical component scale (PCS) and mental component scale (MCS) were also assessed among PsA patients.

Results: A total of 492 patients with AS and 333 with PsA had BDI assessments (or criteria for depression) at baseline and were included in the analysis; mean (SD) age was 42.7 (13.2) and 51.5 (12.2) years, respectively. Patients with AS were mostly male (54.1%) and initiated adalimumab treatment (70.9%) with mean (SD) disease duration of 5.4 (9.1) years; for PsA, sex was evenly distributed (female 50.5%), 66.4% initiated treatment with adalimumab and mean (SD) disease duration was 14.7 (13.7) years. The prevalence of depression at baseline was 24.6% and 25.5% in patients with AS and PsA, respectively.

Upon adjusting for potential confounders, presence of depression in patients with AS was associated with significantly lower odds of achieving BASDAI LDA (OR: 0.51, p=0.021) and BASFI LDA (OR: 0.52, p=0.045) during treatment. In these analyses, positive HLA B27 status was also identified as a significant positive predictor of either outcome ($OR_{BASDAI\ LDA}$: 1.91, p=0.016; $OR_{BASFI\ LDA}$: 1.98, p=0.029), while older age was identified as a negative predictor of BASFI LDA achievement (OR: 0.98, p=0.044). Similarly, patients with depression experienced significantly lower improvements in BASDAI (LSM: -1.72 vs. -2.44; p=0.007), and BASFI scores (-1.46 vs. -2.02; p=0.029) compared to those without depression.

Among patients with PsA, presence of depression appeared to be associated with lower odds of achieving DAPSA remission (OR: 0.35, p=0.070). No association was observed between presence of depression and DAPSA LDA, DAS28 LDA or remission, and BSA<3%. In terms of disease improvement, significant lower improvement in DAPSA score (LSM: -11.00 vs. -14.66; p=0.047) and SF-12 MCS (LSM: -3.01 vs. 4.36; p=0.007) were observed among patients with depression.

Conclusion: A significant proportion of AS and PsA patients suffer from depression. Baseline depression seems to negatively affect treatment outcomes in both AS and PsA patients. Whether this is due to differences in the assessment of patient-reported outcomes or due to physiological differences remains to be confirmed.

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SAT0335 CLINICAL COURSE OF ANKYLOSING SPONDYLITIS (AS) IN PREGNANCY: INTERIM DATA FROM PROSPECTIVE STUDY

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Objectives: To study the dynamics of clinical signs, AS activity and patients' functional status during gestation.

Methods: 19 pregnant females with confirmed AS based on modified NY criteria (1984) were included. Patients' mean age was 32,2±1,1y., mean age at AS onset was 22,6±3,1 y., mean disease duration was 147±20,7 months. Control visits were scheduled at 10-11, 20-21 and 31-32 weeks of pregnancy. BASDAI and ASDAS-CRP calculators were used to assess AS activity, while patients' functional status was assessed using BASFI and BASMI scores, and MASES score was used for evaluation of enthesitis.

Results: Pregnancy outcomes included 18 full-term births at 37,6±1,1 weeks of gestation, and a non-developing pregnancy at 18 weeks in one case. Newborns' weight – 3518±67 g.

Inflammatory low back pain at conception was reported by 78,9% of participants with mean pain intensity 2,2±0,4 scores by NRS. Pain during pregnancy was observed in 95% of all patients, its' intensity increased by the II trimester (4,6±0,7) and persisted at the same level in the III trimester (p<0,05 between conception and II & III trimesters). Patients reported changing pain patterns by the III trimester: 55,5% noticed pain improvement at rest, and 61,1% indicated exacerbation of pain after physical exercise. Enthesitis rates and intensity were also increasing in the course pregnancy: MASES score was higher in the III trimester (2,3 ±0,5) vs I trimester (0,4±0,22, p<0,05). Meanwhile the rates of AS others non-axial and non-skeletal manifestations were not changing during gestation.

BASDAI score was increasing from the moment of conception (1,7±0,3) until the II trimester (3,3±0,5, p<0,05), staying thereafter at the same level in the III trimester. Multivariate regression revealed BASDAI score (R^2=0,7) and low back pain (R^2=0,9) at conception, as well as biological therapy at 3 months prior to conception (R^2=0,7) as orchestrated predictors of relevant BASDAI score in III trimester. During all pregnancy the BASDAI score was predetermined by assemblage of low back pain intensity (β=0,6), fatigue (β=0,6), and enthesitis-associated pain (β=0,3). Increasing fatigue (by 68,5%), and low back pain (by 24,1%) generated BASDAI score increment by the end of the I trimester. While during the II trimester further increase in BASDAI score was provided by exacerbation of enthesitis (30,7% increment), and back pain (27% increment). ASDAS-CRP score was relatively stable with some trend to increase in the II trimester (2,3±0,3) as compared to baseline at conception (1,7 ±0,2). CRP also showed some increase in the II the trimester (9,7±2,9 mg/ml) vs I trimester (6,7±2,4 mg/ml, p>0,05).

BASMI score insignificantly changed during all 3 trimesters (1,3±0,9; 1,8 ±0,2; 2,1±0,3 – in I, II and III trimesters, correspondingly). BASFI score showed increase by the III trimester (3,9±0,7) as compared to I trimester (1,4±0,3, p<0,05). Score increase in the III trimester was due to increased AS activity interfering with habitual physical performance, and also due to pregnancy (forward bend, questions 1,2,4).

Conclusion: AS clinical activity increases by the II trimester of pregnancy and persists at moderate and high levels afterwards during all gestation period. AS activity at conception can predetermine AS activity during all pregnancy. 50% of pregnant patients are likely to experience low back pain in the III trimester due to increasing pressure of a growing fetus on the spine. Functional disability increases with progress in pregnancy, being caused in the III trimester by both – AS activity and pregnancy per se.

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SAT0336 CLINICAL DIAGNOSES OF AXIAL SPONDYLOARTHRITIS SHOW A HIGH OVERALL CONCORDANCE WITH CLASSIFICATION CRITERIA FULFILMENT, BUT ARE LESS CONSISTENT FOR DIFFERENTIATION BETWEEN SUBTYPES IN ESTABLISHED AXIAL DISEASE: RESULTS FROM THE SPARTAKUS COHORT

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Background: The ASAS axial SpondyloArthritis (axSpA) criteria encompass radiographic (r-axSpA) and non-radiographic (nr-axSpA) disease to enable classification early, while the modified New York criteria (mNY) for Ankylosing Spondylitis (AS) require radiographic sacroiliitis. Studies of agreement between clinical diagnoses of axSpA and classification criteria are sparse, especially for nr-axSpA.

Objectives: To study the concordance between clinical axSpA diagnoses and classification criteria fulfilment (mNY and ASAS axSpA) in a population-based cohort of established axSpA, and to compare demographics and outcomes between radiographic axSpA and nr-axSpA.

Methods: Patients with clinical diagnoses (ICD-10) of AS (M45.9) or undifferentiated spondyloarthritis (USpA; M46.0, M46.1, M46.8, M46.9),

followed at Skåne University Hospital, and living in a defined area of southern Sweden were assessed in a cross-sectional study. USpA patients had to report back pain ≥3 months before age 45, by telephone screening, to be eligible. To enable classification, included patients underwent clinical assessments, a classification questionnaire, blood testing (including HLA-B27), and scoring of plain X-rays and MRI scans of the sacroiliac joints by an experienced radiologist.

Results: Out of 233 patients with clinical AS or axial USpA, 198 (85%) fulfilled either mNY or ASAS axSpA classification criteria, while 35 (15%) met neither criteria set. Among 118 patients with a clinical AS diagnosis, 103 fulfilled ASAS axSpA criteria and 84 mNY criteria (positive predictive value [PPV] of clinical AS diagnosis for fulfilling mNY criteria was 71% and for ASAS r-axSpA 69%). For 115 patients with a clinical USpA diagnosis, 89 fulfilled ASAS axSpA criteria, while a higher number was classified as AS (n=48) than nr-axSpA (n=36; PPV of clinical USpA diagnosis for fulfilling nr-axSpA criteria was 31%) (**Figure**).

Comparing characteristics between patients classified as radiographic axSpA (AS [mNY] and/or ASAS r-axSpA) vs. ASAS nr-axSpA, few differences were observed; the former were older, more often men, had longer disease duration and worse spinal mobility (**Table**).

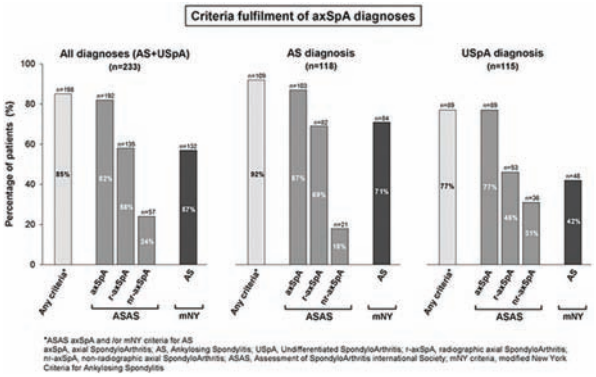


Table. Clinical characteristics and outcome measures

	Radiographic axSpA[a]	nr-axSpA	Radiographic SpA vs. nr-axSpA	No axSpA
	n=141	n=57	*p-value**	n=35
Age, years	54 (14)	45 (12)	≤0.001	49 (12)
Male sex, n (%)	88 (62)	18 (32)	≤0.001	10 (29)
Symptom duration, years	29 (14)	19 (11)	≤0.001	20 (13)[†]
HLA-B27 positive, n (%)	115 (84)	48 (84)	0.83	4 (11)[†§]
ASDAS-CRP	1.9 (1.0)	1.9 (0.9)	0.94	2.0 (1.0)
BASDAI	3.1 (2.3)	3.2 (2.1)	0.77	3.9 (2.4)
BASFI	2.3 (2.4)	2.1 (2.1)	0.51	2.8 (2.3)
BASMI	3.4 (1.8)	2.3 (1.1)	≤0.001	2.7 (1.0)[†]

Mean (SD) unless indicated. Missing data 0-14%

*Statistical comparisons by Student's t-test or Chi-Square test

[a]ASAS r-axSpA and mNY together.

[†]statistically significant difference (p<0.05) radiographic axSpA vs. no axSpA and [§]nr-axSpA vs. no axSpA.

Conclusion: The overall concordance between clinical diagnoses and fulfilment of axSpA classification criteria was good, with >4/5 meeting any criteria. For disease subtypes, however, the agreement was substantially weaker, and a large group of patients with USpA in this established cohort fulfilled the mNY criteria for AS. The results indicate that in studies aiming to compare radiographic and non-radiographic axSpA, classification according to defined classification criteria is important.

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SAT0337 MORE THAN 30% PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS PRESENT WITH PERIPHERAL ARTHRITIS: INCIDENCE AND FACTORS ASSOCIATED DURING 5 YEARS OF FOLLOW-UP OF THE DESIR COHORT

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Background: Peripheral arthritis is the most frequent peripheral manifestation in Spondyloarthritis (SpA). However, there is a lack of knowledge about its prevalence and incidence over time in recent axial SpA (axSpA). Objectives: a) To describe the prevalence and incidence of peripheral arthritis during 5 years of follow-up on the DESIR cohort; b) to describe the time of onset regarding axial symptoms; c) to evaluate factors associated with their appearance; d) to evaluate the impact of this symptom on treatment, Patient Reported Outcomes (PROs) and sick leave during 5 years of follow-up.

Methods: Data from the early axSpA patients from the DESIR cohort (first 5 years of follow-up) were analysed. The prevalence and the incidence of peripheral arthritis at each study visit were calculated. A Kaplan-Meier curve was performed to evaluate the time of onset of this manifestation regarding the axial symptoms onset. Univariate and multivariate logistic regressions were performed to evaluate baseline factors associated to the development of the arthritis. We compared the use of drugs between patients with and without arthritis by Chi-square test, and finally we evaluate the impact of this symptom on PROs (BASDAI, BASFI and SF36-questionnaire) and on days of sick leave after 5 years of follow-up through the use of a mixed model with random effects (patients).

Results: Out of the 708 patients included in the analysis, 255 (36.0%) showed at least one episode of arthritis (151 before the inclusion visit, and 104 during the follow-up), with a time-person rate of 3.7 cases per 100 person-year. Regarding axial symptoms, 20.4%, 13.70% and 65.9% patients suffered the first episode of arthritis before, concomitantly and after axial symptoms onset, respectively. Multivariate analysis showed that baseline factors associated to the development of arthritis are age ≥33 years (OR 1.60, 95%CI 1.12-2.27), non-smokers (OR 1.58, 95%CI 1.10-2.27), HLAB27 negative (OR 1.47, 95%CI 1.04-2.08), CRP >6mg/dl (OR 1.99, 95%CI 1.35-2.92), no history of uveitis (OR 2.03, 95%CI 1.07-3.84), dactylitis (OR 8.50, 95%CI 4.96-14.60) and enthesitis (OR 2.00, 95%CI 1.41-2.84). Concerning the use of drugs, patients with arthritis showed a significant greater use of TNF blockers (49.4% vs. 29.1%, p<0.001), csDMARDs (40.4% vs. 13.9%, p<0.001), oral corticosteroids (37.6% vs. 22.1%, p<0.001) and ≥1 intraarticular corticosteroids (31.0% vs. 6.8%, p<0.001), in comparison with patients without history of arthritis. We did not found differences concerning NSAIDs, intramuscular and intravenous corticosteroids. Finally, the mixed model showed that, after 5 years of follow-up, patients with arthritis had higher levels on BASDAI (40.5±22.6 vs. 34.3±20.7, p<0.001) and BASFI (27.9±23.2 vs. 22.5±21.0, p=0.001), poorer quality of life (SF36-mental component 42.7±11.7 vs. 44.0±11.0, p=0.003; SF-36 physical component 40.9±9.7 vs. 43.1±0.2, p<0.001) and higher number of days of sick leave (18.0±57.5 vs. 12.8±47.2, p=0.024).

Conclusion: In recent axSpA, 36% of patients reported peripheral arthritis at any time of the disease, and this appeared more frequently after axial symptoms onset. This symptom is more prevalent among patients with HLAB27 negative, non-smokers, with high CRP and with other peripheral manifestations. Arthritis were associated with a greater use of bDMARDs, csDMARDs and corticosteroids, and had an impact on function, quality of life and days of sick leave.

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SAT0338 DELAYED DIAGNOSIS OF ANKYLOSING SPONDYLITIS: RESULTS FROM A SURVEY OF 1690 US PHYSICIANS FROM 10 SPECIALTIES

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Background: There is a significant delay in the diagnosis of ankylosing spondylitis (AS) in the United States. Several studies have estimated that

the time between symptom onset and physician diagnosis is 5-7 years. Diagnosis delay is attributed to nonspecific presentation of chronic back pain, requiring clinical experience to recognize early AS.

Objectives: To identify obstacles to early diagnosis of AS by assessing the knowledge of nonrheumatology health care providers (HCPs) on inflammatory back pain (IBP) and possible barriers to referral to a rheumatologist.

Methods: Survey content was first conceptualized based on concept elicitation interviews with HCPs, and questionnaires were developed by the study investigators to identify clinical characteristics, symptom presentation, and diagnostic measures that lead an HCP to suspect IBP and their perspectives on the referral process. The survey was then cognitively tested with HCPs from 10 specialties (family medicine, internal medicine, dermatology, gastroenterology, ophthalmology, orthopedics, chiropractic, pain management, physical therapy, and physiatry), revised, and finalized. HCPs from these 10 specialties were invited to participate in the cross-sectional web-based survey hosted by Survey Sampling International between June 27 and July 20, 2018. HCPs who were currently licensed, actively practicing in the US, and had referred a patient with suspected IBP (except ophthalmology) or referred a patient with uveitis/iritis (ophthalmology only) within the past 12 months were eligible to participate. Descriptive statistics were used to analyze the data.

Results: Of 2395 HCPs screened, 1690 were eligible and included in our study. Overall, HCPs saw a median of 100 patients with chronic back pain within the past 12 months of the survey. Regarding criteria leading to suspicion of IBP, 61% of HCPs indicated morning stiffness > 30 minutes, 29% sleep disturbance due to back pain, 28% pain that improves with activity, and 16% alternating buttock pain. Among HCPs who would order diagnostic blood work, ≈ 90% selected C-reactive protein, erythrocyte sedimentation rate, antinuclear antibody (ANA), and rheumatoid factor (RF), while 76% selected HLA-B27 (**Figure 1**).. Most HCPs suspected underlying conditions of rheumatoid arthritis (RA; 94%), AS (90%), and psoriatic arthritis (81%) as related to IBP. Almost 40% of HCPs would treat patients with suspected IBP themselves; of these, ≈ 80% would recommend nonsteroidal anti-inflammatory drugs and physical therapy (**Figure 2**).. Regarding referrals, 57% of HCPs would refer patients with suspected IBP to another physician, but only 13% would refer immediately; 49% would perform further evaluations, 24% would wait until initial treatment response, 11% would monitor patient for some time, and 3% would consult with another physician before referring. Upon referral, 90% of HCPs estimated a wait time of up to 2 months for their patient to see another specialist. Of 1670 HCPs queried, 80% indicated that the specialist's expertise in treating autoimmune disease is the most important factor influencing their referral.

Conclusion: Most HCPs did not recognize IBP criteria in patients with chronic back pain. As most considered RA to be the underlying condition, ANA and RF were ordered as diagnostic workup. Many HCPs opted to treat and monitor patients with suspected IBP before referral, and most reported a wait time of up to 2 months for their patients to see a specialist.

Figure 1. Diagnostic blood tests health care providers elected to order or recommend when suspecting inflammatory back pain

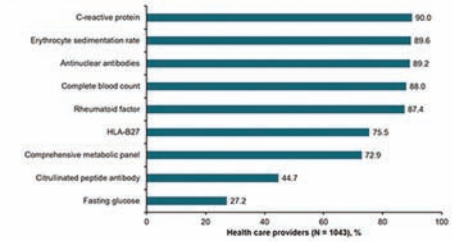
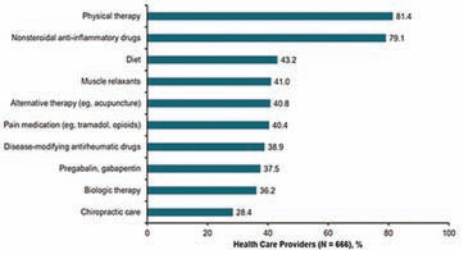


Figure 2. Treatment recommendations by health care providers who opted to treat patients with suspected inflammatory back pain themselves



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SAT0339 WHAT IS THE IMPACT OF IMAGING ON DIAGNOSTIC ASCERTAINMENT OF PATIENTS PRESENTING WITH UNDIAGNOSED BACK PAIN AND WHAT IS THE IMPACT OF CENTRAL EVALUATION? DATA FROM THE SCREENING IN AXIAL SPONDYLOARTHRITIS IN PSORIASIS, IRITIS, AND COLITIS (SASPIC) COHORT

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Background: Although MRI of the sacroiliac joints (SIJ) is the most sensitive imaging modality for early diagnosis of axial spondyloarthritis (axSpA) it is costly and not readily available. Therefore, clinicians still rely primarily on radiography. The relative degree to which radiography and MRI changes diagnostic ascertainment of axSpA in patients presenting with undiagnosed back pain has not been formally studied.

Objectives: We aimed to assess the relative impact of radiography and MRI evaluation on diagnostic ascertainment of axial SpA in patients presenting with undiagnosed back pain to rheumatologists, and the impact of central evaluation.

Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at early detection of axial SpA. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation is ordered per rheumatologist decision. The rheumatologist determines the presence or absence of axial SpA at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. The eCRF, radiographs, and MRI scans were also assessed centrally.

Results: The SASPIC cohort comprises 246 patients (52.4% male, mean age 34.5 years, mean symptom duration 7.3 years, mean back pain duration 7.1 years, B27+ 36.2%) referred with AAU (29.7%), psoriasis

Table 1

Stage of global assessment	Data source	axSpA YES	axSpA YES with confidence >7	NOT axSpA	axSpA NO with confidence <-4
1. N = 246	**Clinical**	169 (**68.7%**)	50 (20.3%)	77 (31.3%)	40 (16.3%)
2. N = 246	**Clinical plus radiography**	141 (**57.3%**)	66 (26.8%)	105 (42.7%)	78 (31.7%)
Patients who had MRI					
1. N = 149	**Clinical**	107 (**71.8%**)	23 (15.4%)	42 (28.2%)	19 (12.8%)
2. N = 149	**Clinical plus radiography**	94 (**63.1%**)	30 (20.1%)	55 (36.9%)	38 (25.5%)
3. N = 149	**Clinical plus radiography plus MRI**	70 (**47.0%**)	44 (29.5%)	79 (53.0%)	70 (47.0%)

Table 2

Stage of global assessment	Data source	axSpA YES, number (%)	axSpA NO, number (%)
2. N = 246	Clinical plus radiography	141 (57.3%)	105 (42.7%)
2. N = 246	Clinical plus radiography after central reader assessment	79 (32.1%)	167 (67.9%)
3. N = 149	Clinical plus radiography plus MRI	70 (47.0%)	79 (53.0%)
3. N = 149	Clinical plus radiography plus MRI after central reader assessment	45 (30.2%)	104 (69.8%)

(18.7%), Crohn's colitis (31.3%), ulcerative colitis (20.3%). MRI was conducted in 149 patients. The number of patients diagnosed with axSpA by the local rheumatologist decreased after radiography and then decreased further after MRI while confidence in the diagnosis progressively increased (Table 1). After central evaluation of all patient data, the number of patients diagnosed with axSpA decreased substantially compared to assessment by local readers (Table 2).

Conclusion: In a setting of undiagnosed back pain and higher risk for axial SpA, imaging is primarily helpful in ruling out SpA and reducing false positives. Despite this, central evaluation raises concerns regarding ascertainment of false positive SpA in routine practice.

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SAT0340

CHARACTERIZATION OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS BY PRESENCE OF ENTHESITIS: DATA FROM THE CORRONA PSORIATIC ARTHRITIS/ SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

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Background: Enthesitis is a common extra-axial manifestation in patients with axial spondyloarthritis (AxSpA)[1,2]; however, not much is known about the prevalence of enthesitis in AxSpA and its impact on disease burden in US real-world settings.

Objectives: This study describes characteristics of patients with AxSpA who had enthesitis vs patients without enthesitis.

Methods: This study included patients aged $\geq$ 18 years with AxSpA enrolled in the Corrona PsA/SpA Registry between March 2013 and August 2018. Enthesitis at enrollment was assessed via the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index. Patient demographics, clinical characteristics, treatment profiles, disease activity, quality of life, and work productivity were compared between patients with and without enthesitis using *t* tests or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher's exact tests for categorical variables.

Results: Of 477 patients with AxSpA, 121 (25.4%) had enthesitis. Symptom and disease duration were similar between patients with and without enthesitis. In patients with enthesitis, a higher proportion were female, were more likely to have non-radiographic AxSpA and a history of depression, serious infections, and fibromyalgia vs those without enthesitis (all $P < 0.05$; **Table 1**). Current treatment with biologics or conventional synthetic disease-modifying antirheumatic drug (csDMARD) monotherapy was similar regardless of presence of enthesitis; however, patients with enthesitis were more likely to have prior csDMARD and biologic use, as well as current methotrexate use. Patients with enthesitis had worse disease activity (ASDAS, BASDAI, and BASFI scores; tender and swollen joint counts; physician global assessment; and DAPSA and cDAPSA scores), spinal mobility measures, quality of life (pain, fatigue, HAQ scores, and EQ VAS scores), and greater work impairment than patients without enthesitis (all $P < 0.05$; **Table 2**).

Conclusion: Among patients with AxSpA in this US real-world study, the presence of enthesitis was associated with worse disease activity and quality of life compared to patients without enthesitis.

Table 1. Demographic and Clinical Characteristics and Treatment Profiles in Patients With AxSpA Stratified by Presence of Enthesitis at Enrollment

Characteristic	No Enthesitis (N = 356)	With Enthesitis (N = 121)	*P* Value
Non-radiographic AxSpA, n (%)	56 (15.7)	34 (28.1)	< 0.01
Age, mean (SD) [n], years	47.3 (14.1) [351]	47.3 (13.1) [120]	0.99
Female, n/m (%)	112/351 (31.9)	61/121 (50.4)	< 0.01
White, n/m (%)	319/344 (92.7)	105/119 (88.2)	0.16
Work status, n (%)	n = 351	n = 121	0.30
Full time	214 (61.0)	69 (57.0)	
Part time	22 (6.3)	7 (5.8)	
Disabled	42 (12.0)	24 (19.8)	
Retired	44 (12.5)	12 (9.9)	
Other	29 (8.3)	9 (7.4)	
BMI, mean (SD) [n], kg/m^2	29.8 (6.8) [345]	29.9 (6.9) [120]	0.83
Symptom duration, mean (SD) [n], years	16.8 (11.8) [340]	17.3 (13.1) [118]	0.67
Disease duration, mean (SD) [n], years	10.2 (10.7) [347]	8.2 (10.3) [120]	0.09
Comorbidities, n (%)			
Cardiovascular disease	140 (39.3)	56 (46.3)	0.18
Hypertension	109 (30.6)	37 (30.6)	0.99
Depression	53 (14.9)	29 (24.0)	0.02
Hyperlipidemia	52 (14.6)	21 (17.4)	0.47
Uveitis	40 (11.2)	13 (10.7)	0.88
Metabolic syndrome	27 (7.6)	9 (7.4)	0.96
Diabetes mellitus	20 (5.6)	11 (9.1)	0.18
Psoriasis	22 (6.2)	7 (5.8)	0.88
Serious infections	16 (4.5)	12 (9.9)	0.03
Fibromyalgia	11 (3.1)	11 (9.1)	0.01
Ulcerative colitis	18 (5.1)	3 (2.5)	0.31
Any cancer (excluding NMSC)	16 (4.5)	5 (4.1)	0.87
Crohn disease	14 (3.9)	6 (5.0)	0.63
Prior csDMARD use, n (%)	47 (13.2)	30 (24.8)	< 0.01
Prior biologic use, n (%)	97 (27.2)	47 (38.8)	0.02
Number of prior biologics, n (%)			0.01
0	259 (72.8)	74 (61.2)	
1	68 (19.1)	26 (21.5)	
≥ 2	29 (8.1)	21 (17.4)	
Current biologic use, n (%)	237 (66.6)	84 (69.4)	0.56
Current csDMARD use only (no biologics or tsDMARDs), n (%)	30 (8.4)	12 (9.9)	0.62
Methotrexate (any), n (%)	37 (10.4)	21 (17.4)	0.04

AxSpA, axial spondyloarthritis; BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; NMSC, nonmelanoma skin cancer; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.

Table 2. Disease Activity, Quality of Life, and Work Productivity in Patients With AxSpA Stratified by Presence of Enthesitis at Enrollment

Characteristic	No Enthesitis (N = 356)	With Enthesitis (N = 121)	*P* Value
ASDAS, mean (SD) [n]	2.5 (1.2) [212]	2.9 (0.9) [79]	< 0.01
BASDAI (0-10), mean (SD) [n]	4.1 (2.4) [340]	5.3 (2.2) [118]	< 0.01
BASFI (0-10), mean (SD) [n]	3.3 (2.7) [338]	4.5 (2.8) [119]	< 0.01
Lateral lumbar flexion (average of left and right), mean (SD) [n], cm	21.5 (18.8) [308]	28.1 (21.1) [116]	0.01
Enthesitis, n (%)	—	121 (100.0)	—
SPARCC Enthesitis Index (1-16), mean (SD) [n]	—	3.9 (2.9) [121]	—
Dactylitis, n (%)	7 (2.0)	4 (3.3)	0.40
Dactylitis count (1-20), mean (SD) [n]	3.6 (3.9) [7]	2.0 (2.0) [4]	0.35
Tender joint count (0-68), mean (SD) [n]	1.3 (4.2) [347]	8.2 (10.8) [121]	< 0.01
Swollen joint count (0-66), mean (SD) [n]	0.5 (2.0) [347]	1.3 (3.3) [121]	< 0.01
DAPSA, mean (SD) [n]	15.6 (8.3) [54]	28.6 (21.1) [12]	0.02
DAPSA group, n (%)	n = 54	n = 12	0.03
Remission	2 (3.7)	1 (8.3)	
Low	25 (46.3)	2 (16.7)	
Moderate	21 (38.9)	4 (33.3)	
High	6 (11.1)	5 (41.7)	
cDAPSA, mean (SD) [n]	12.5 (7.9) [109]	22.1 (18.1) [21]	0.02
Physician global assessment, mean (SD) [n]	23.5 (21.9) [345]	36.6 (21.9) [117]	< 0.01
Physician global assessment of psoriasis, mean (SD) [n]	0.5 (1.0) [70]	0.1 (0.5) [38]	0.03
Patient pain (VAS 0-100), mean (SD) [n]	43.5 (29.5) [331]	57.5 (26.7) [111]	< 0.01
Patient fatigue (VAS 0-100), mean (SD) [n]	45 (28.6) [353]	56.5 (27.5) [121]	< 0.01
Morning stiffness, n (%)	318 (89.3)	117 (96.7)	0.72
< 30 minutes	71 (22.3)	28 (23.9)	
≥ 30 minutes	247 (77.7)	89 (76.1)	
Patient global assessment (VAS 0-100), mean (SD) [n]	54.1 (32.9) [115]	49.8 (29.7) [24]	0.56
HAQ-DI (0-3), mean (SD) [n]	0.6 (0.6) [299]	0.9 (0.7) [89]	< 0.01
EQ VAS (0-100), mean (SD) [n]	66.4 (22.0) [344]	59.7 (22.7) [120]	< 0.01
WPAI domains, mean (SD) [n]			
Current employment, n/m (%)	241/351 (68.7)	75/119 (63.0)	0.26
% Work time missed	5.8 (16.8) [218]	9.0 (18.8) [71]	0.06
% Impairment while working	25.3 (24.4) [230]	38.3 (27.4) [71]	< 0.01
% Overall work impairment	27.6 (26.6) [210]	41.4 (29) [69]	< 0.01
% Activity impairment	35.6 (29.3) [343]	49.8 (29.5) [121]	< 0.01

ASDAS, Ankylosing Spondylitis Disease Activity Score; AxSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; cDAPSA, Clinical Disease Activity Index for Psoriatic Arthritis; DAPSA, Disease Activity Index for Psoriatic Arthritis; EQ VAS, EuroQol visual analogue scale; HAQ-DI, Health Assessment Questionnaire Disability Index; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment Questionnaire.

REFERENCES
[1] Nadon V, et al. Clin Exp Rheumatol. 2018 Dec 19 [Epub ahead of print].
[2] de Winter JJ, et al. Arthritis Res Ther. 2016;18(1):196.

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SAT0341 THE PREVALENCE OF RENAL FAILUREIN A PROSPECTIVE AXIAL SPONDYLOARTHRITIS COHORT AND POSSIBLE ASSOCIATED FACTORS

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Background: Extra-articular manifestations and comorbidities are significant complications in the evolution of patients with spondyloarthritis (SpA). The presence of renal failure (RF) is a multifactorial comorbidity that has been shown to be associated with this disease, and its prevalence has been reported around 5% (COMOSPA[1]). There are no prevalence studies in our environment.
Objectives: To determine the prevalence and possible factors associated with RF in patients with axial spondyloarthritis (axSpA).
Methods: Data was retrieved from a prospective database designed for the monitoring of patients with SpA from a large teaching hospital. We only included patients with axSpA. Demographic and clinical data were recorded, as well as possible risk factors associated with RF: arterial hypertension (AHT), smoking status, Diabetes (DM), Dyslipidemia (DL), NSAIDs use and renal function from last test available (we considered RF when eGFR<60 mL/min).
Continuous data were compared with Student t-test if the variables presented normal distribution (previous Shapiro-Wilk test) or Mann Whitney U test otherwise. Chi-square or Fisher test was performed if the variable was categorical.
Results: 339 patients were included. 73.2% were male with a mean age of 56.68 (±14.8) years and a mean age of onset of 32.0 (±11.4) years. The mean disease duration was 32.8 (±11.4) years. 83.7% were HLAB27+. The clinical variables for the whole cohort were: BASDAI 3.56 (±2.13), BASFI 3.74 (±2.65), CRP 5.61 (±6.92) and ESR 2.28 (±0.89). The following risk factors were registered: smokers 58.3%, AHT 33.3%, DL 31.3% and NSAID use of 34.6%. 27.4% of patients were receiving biologic therapy.
41 patients (12.1%) presented RF criteria. Comparison between two groups is shown in table 1. A statistically significant association with RF was found in age, sex, AHT, DL, no use of NSAIDs, higher BASFI and ASDAS indexes as well as ESR value.
Conclusion: There is a substantial prevalence of RF in patients with axSpA in our cohort. We should maximise our awareness of RF in old patients, those suffering from AHT and DLP, as well as subjects with high BASFI, ASDAS and ESR values.

REFERENCE
[1] Couderc, et al: *Renal impairment in SpA*; The Journal of Rheumatology 2018; 45:6

Table 1. Comparative analysis of patients with RF and recorded variables

Variables	RF (n=41)	No RF (n=298)	P-value
Age, mean (SD)	71.12 ± 7.8	54.64 ±14.52	<0.0001*
Male	87.8%	71.1%	0.024*
Arterial hypertension	82.9%	26.5%	<0.0001*
Dyslipidemia	46.3%	29.2%	0.026*
Diabetes Mellitus	19.5%	9.7%	0.103
BMI, mean (SD)	28.45 ± 5.72	26.36 ± 4.39	0.065
Smokers	69.7%	56.9%	0.159
HLA B27(+)	80%	84.2%	0.5
axSpA phenotype	100%	91.6%	0.056
- **AS**	0%	8.4%	
- **non-Rx SpA**			
Disease duration, mean (SD)	34.83 ± 13.71	22.84 ± 15.35	<0.0001*
Age at diagnosis, median (IQR)	33 ± 22	30 ± 16	0.138
NSAID (>25%)	22%	36.4%	0.003*
Biologic	24.4%	27.9%	0.641
BASDAI	4.005 ± 2.1	3.5 ± 2.13	0.156
BASFI	5.2 ± 2.56	3.5 ± 2.61	<0.0001*
ASDAS-CRP	2.57 ± 0.87	2.22 ± 0.92	0.04*
ASDAS-ESR	2.66 ± 0.9	2.23 ± 0.87	0.01*
CRP, median (IQR)	3.8 ± 6.65	3.0 ± 5.65	0.052
ESR, median (IQR)	15 ± 23.3	8 ± 13	0.008*

*p<0.05

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SAT0342 RISK FACTORS FOR ARTHROPATHY IN ULCERTIVE COLITISPATIENTS AFTER TOTAL COLECTOMY; A RETROSPECTIVE, A SINGLE CENTER STUDY

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Background: Ulcertive colitis (UC) is associated with a variety of extraintestinal manifestations (EIMs) that may have negative effects on performance status and quality of life. EIMs frequently affect musculoskeltal systems (peripheral and axial arthropathies), skin, hepatobiliary tract and eyes[1,2]. Previous studies showed that peripheral and axial arthropathies were seen 4-23% patients with UC and they tend to have peripheral rather than axial arthropathies[3]. UC is generally thought to become in remission when patients undergo total colectomy. However, in clinical practice, patients often suffered from arthropathy which is thought as EIMs even after total colectomy. The distribution and risk factors for the occurrence of peripheral and axial arthropathies among UC patients after total colectomy have not been investigated yet.
Objectives: In this study, we aimed to clarify frequency and distribution of arthropathy and to investigate risk factors for developing arthropathy among UC patients after colectomy.
Methods: In this retrospective, single center, observational study, we investigated the backgrounds and risk factors for arthropathy using patients underwent total colectomy from January 2007 to February 2016 in Mie University. As backgrounds, age, sex, presence and distribution of arthropathy, other EIMs, and duration after colectomy, clinical activity (mild/moderate/severe), Matts classification (grade 1+2 vs 3+4), presence of massive hemorrhage and toxic megacolon, previous therapies for UC were collected from electronic medical records. Arthropathy was defined as joint pain or swelling without definite cause which was improved by using glucocorticoid. Background factors were described as median (IQR) for continuous variables or as percentage (%) for categorical variables and difference was analyzed by Wilcoxon for continuous variables and by chi-square for categorical variables. Factors with p-value < 0.1 in univariate analyses were included in multivariate logistic regression analysis for risk of developing arthropathy.
Results: We enrolled 219 patients (female; 40.2% and median age at operation; 38.0 [27.0, 53.0] years). Among them, 40 (18.3%) patients had arthropathy, peripheral type in 23 (57.5%), axial type in 3 (7.5%), mixed type in 14 (35.0%). Duration from operation to onset of arthropathy was 0.7 [0.4, 1.2] years. The risk factors for developing arthropathy by univariate analyses were Matts classicification (grade 3+4 vs 1+2) ($p < 0.05$), follow up periods ($p < 0.001$), presence of other EIMs ($p < 0.001$), ileal pouchitis ($p < 0.01$), but previous treatment of biologics was not significant ($p = 0.84$). Table 1 showed the risk factors for developing arthropathy by multivariate logistic regression analysis using age, sex,

Matts classicification, follow up period, presence of other EIMs and ileal pouchitis. Follow up period [OR 1.17 (95% CI 1.03-1.33, p < 0.05)], Matts classicification [OR 2.61 (95% CI 1.19-5.74, p < 0.05)] and ileal pouchitis [OR 2.65 (95% CI 1.16-6.07, p < 0.05)] were significantly associated with an increased risk of developing arthropathy of UC patients after colectomy.

Table 1. The risk factors for developing arthropathy in patients with ulcerative colitis after underwent colectomy by multi variate logistic regression analysis.

	Odd ratio	95% CI	p value
Age at operation, years	1.02	0.99, 1.04	NS
Sex (female vs male)	1.81	0.84, 3.91	NS
Follow-up period, years	1.17	1.03, 1.33	<0.05
Matts Classification (grade 3+4 vs 1+2)	2.61	1.19, 5.74	<0.05
Ileal pouchitis	2.65	1.16, 6.07	<0.05
Extraintestinal manifestations	2.74	0.85, 8.87	NS

Conclusion: About one fifth patients with UC who underwent colectomy developed arthropathy presenting predominantly peripheral type. Long follow up period, High disease activity by endoscopic classification, and ileal pouchitis were risk factors of developing arthropathy in UC patients after total colectomy. The frequency and risk factors for developing arthropathy even after colectomy was demonstrated in this study for the first time.

REFERENCES

[1] Paraskevi VV, et al. Ann Gastroenterol. 2011; 24: 173-80.
[2] Orchard TR, et al. Gut. 1998; 42: 387–91.
[3] Das KM, et al. Dig Dis Sci 1999;44:1–13.

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SAT0343

BURDEN OF DISEASE AT TREATMENT INITIATION AMONG BIOLOGIC-NAÏVE PATIENTS WITH OLIGOARTICULAR VERSUS POLYARTICULAR PSORIATIC ARTHRITIS IN THE CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS REGISTRY

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Background: Oligoarticular PsA accounts for ≈50% of PsA worldwide, but only a paucity of data describes disease burden among patients with this subtype. The Corrona PsA/SpA Registry, a prospective, US-based, observational cohort study, collects real-world data on characteristics and treatment of PsA patients, including those with oligoarthritis.
Objectives: To characterize demographics, clinical characteristics and patient-reported outcomes (PROs) at treatment initiation in biologic-naïve patients with oligoarticular (≤4 swollen and ≤4 tender joints) vs. polyarticular (>4 swollen or >4 tender joints) PsA.
Methods: Biologic-naïve patients ≥18 years of age diagnosed with PsA and enrolled in the registry who initiated apremilast, biologics and/or csDMARDs for PsA from March 2013–December 2018 were included. Data on patient demographics, disease activity, treatment history, comorbidities and PROs were analyzed at treatment initiation; comparisons between oligoarticular and polyarticular PsA patients were performed using *t*-tests or Wilcoxon rank-sum tests for continuous variables and chi-square tests or Fisher's exact tests for categorical variables, as appropriate.
Results: 330 biologic-naïve PsA patients initiating apremilast, biologics and/or csDMARDs were included (oligoarthritis: n=149; polyarthritis: n=181). Demographics and clinical characteristics were mostly similar for patients with oligoarthritis and polyarthritis, including mean age (51.6 vs. 54.3 years; *P*=0.068), proportion of females (51.0% vs. 59.7%; *P*=0.117), mean disease duration (3.0 vs. 3.1 years; *P*=0.789) and prior use of csDMARDs (13.4% vs. 21.0%; *P*=0.072). History of comorbidities was similar between the 2 groups, but the proportion of patients with fibromyalgia was higher in the polyarthritis group (2.0% vs. 8.8%; *P*=0.008; Table 1). Patients with oligoarthritis had lower disease activity at treatment initiation vs. those with polyarthritis based on SJC (0-66) and TJC (0-68), nail psoriasis VAS score, cDAPSA score, presence of enthesitis, SPARCC enthesitis score, presence of dactylitis and dactylitis count. More patients with oligoarthritis were classified with minimal disease activity vs. patients with polyarthritis (Table 2). Mean Pain VAS (42.6 vs. 59.8), Fatigue VAS (41.9 vs. 55.3), Patient's Global Assessment of Disease Activity VAS (38.6 vs. 47.7) and HAQ-DI (0.7 vs. 1.0) scores were significantly lower and the proportion of patients with HAQ-DI score <0.5 was significantly greater for patients with oligoarthritis vs. polyarthritis (39.7% vs. 20.1%) (all *P*≤0.001). Presence of inflammatory back pain (8.7% vs. 10.5%; *P*=0.588) and mean psoriasis-involved body surface area (8.0% vs. 6.8%; *P*=0.276) were similar in the 2 groups.
Conclusion: This Corrona PsA/SpA Registry analysis showed similar overall disease burden and comorbidity burden in biologic-naïve patients with oligoarthritis and polyarthritis. However, patients with oligoarthritis vs. polyarthritis had lower scores on disease activity and PRO measures at treatment initiation.

Table 1. History of Comorbid Conditions Among Biologic-Naïve Patients With Oligoarticular vs. Polyarticular PsA*,†

History of Comorbidity, n (%)	Oligoarthritis n=149	Polyarthritis n=181	*P* Value
Cancer (any except NMSC)	15 (10.1)	19 (10.5)	0.898
Cardiovascular disease	17 (11.4)	23 (12.7)	0.719
Depression	20 (13.4)	36 (19.9)	0.119
Diabetes mellitus	20 (13.4)	33 (18.2)	0.236
Fibromyalgia	3 (2.0)	16 (8.8)	0.008
Hyperlipidemia	26 (17.4)	38 (21.0)	0.418
Hypertension	48 (32.2)	74 (40.9)	0.104
Metabolic syndrome	19 (12.8)	33 (18.2)	0.174
Nail psoriasis	65 (43.6)	97 (53.6)	0.071
Psoriasis	121 (81.2)	150 (82.9)	0.694

*Oligoarticular PsA (≤4 swollen and ≤4 tender joints) vs. polyarticular PsA (>4 swollen or >4 tender joints). †Includes patients initiated on apremilast, biologics and/or csDMARDs. NMSC=non-melanoma skin cancer.

Table 2. Disease Characteristics of Biologic-Naïve Patients With Oligoarticular vs. Polyarticular PsA*,†

Disease Characteristic	Oligoarthritis n=149	Polyarthritis n=181	*P* Value
Swollen joint count (0-66), mean (SD)	1.3 (1.5)	6.2 (5.3)	<0.001
Tender joint count (0-68), mean (SD)	1.6 (1.5)	13.9 (12.7)	<0.001
Nail psoriasis VAS, mean (SD)	11.4 (23.6)	15.7 (24.6)	0.037
cDAPSA score, mean (SD)	10.9 (5.6)	31.1 (15.8)	<0.001
High (>27) cDAPSA, n (%)	0 (0.0)	91 (52.0)	<0.001
Presence of enthesitis, n (%)	37 (24.8)	84 (46.4)	<0.001
SPARCC enthesitis score, mean (SD)	2.1 (1.3)	4.4 (3.4)	<0.001
Presence of dactylitis, n (%)	25 (16.8)	54 (29.8)	0.006
Dactylitis count, mean (SD)	1.9 (1.6)	2.4 (1.7)	0.060
Minimal disease activity, n (%)	40 (29.6)	6 (3.6)	<0.001

*Oligoarticular PsA (≤4 swollen and ≤4 tender joints) vs. polyarticular PsA (>4 swollen or >4 tender joints). †Includes patients initiated on apremilast, biologics and/or csDMARDs. SPARCC=Spondyloarthritis Research Consortium of Canada.

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SAT0344 **STRUCTURAL RADIOLOGICAL DAMAGE MSASSS SCORE: ASSOCIATION WITH THE PRESENCE OF SUBCLINICAL CAROTID ATHEROMATOSIS IN PATIENTS WITH AXIAL SPONDYLARTHROPATHY**

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Background: Axial spondyloarthropathies (SpA) are associated with an increase in cardiovascular morbidity and mortality, showing an increase of 20% to 40% in the risk of cardiovascular events compared to the general population and constituting the main cause of death. The presence of subclinical atheromatosis, in the form of carotid plaques, is more frequent in patients with SpA than in healthy controls. Axial structural radiological damage in SpA is a consequence of the inflammatory activity of the disease.
Objectives: To analyze whether axial radiological damage by mSASSS (Modified Stoke Ankylosing Spondylitis Spine Score) is related to cardiovascular risk factors or the presence of subclinical atheromatosis in patients with SpA.
Methods: 195 patients diagnosed with SpA according to ASAS criteria without previous history of cardiovascular events or diabetes were assessed. The clinical characteristics, cardiovascular comorbidity, risk profile by Systematic Coronary Risk Evaluation (SCORE) and axial radiological damage (mSASSS score) were analyzed. The presence of plaques and intima-media thickness (cIMT) was determined by carotid ultrasound. The relationship between mSASSS and subclinical atheromatosis was analyzed by multivariate regression analysis.
Results: 36% of patients with SpA showed presence of carotid plaque and a cIMT of 0.651 ± 0.121 mm. *log* mSASSS disclosed a positive univariate relationship with age (beta coefficient 0.07 [95% CI 0.06-0.08], p = 0.000) and classic cardiovascular risk factors such as abdominal waist, hypertension (0.73 [95% CI 0.31-1.16], p = 0.001), smoking (0.33 [IC95% 0.08-0.59], p = 0.010), SCORE (0.33 [IC95% 0.24-0.42], p = 0.000) and levels of C-reactive protein, glucose and C-peptide. Similarly mSASSS showed a positive relationship with the BASFI (0.18 [IC95% 0.11-0.26], p = 0.000) and BASMI (0.31 [IC95% 0.23-0.38], p = 0.000) scores, but not with ASDAS-CRP or BASDAI. The presence of carotid plaque (0.51 [95% CI 0.09-0.93], p = 0.018) and a higher cIMT (4.1 [IC95% 2.4-5.7], p = 0.000) were also significantly and positively related to a higher mSASSS. When these analyzes were performed in a multivariate phasion adjusting for age and sex, the relationships of *log* mSASSS with cardiovascular risk factors were lost, although the relationship of the former with BASFI, BASMI and SCORE remained statistically significant. With regard to subclinical atheromatosis, the relationship between log mSASSS and cIMT was not significant after the multivariate analysis; however, the presence of plaque showed an almost significant relationship after adjustment for age, sex and cardiovascular risk factors (0.34 [95% CI -0.42-0.73], p=0.081).
Conclusion: Axial radiological damage through mSASSS is independently related to cardiovascular risk SCORE. A tendency to an independently significant relationship with the presence of carotid plaque was observed.
Disclosure of Interests: None declared
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SAT0345 **PREGNANCY RATES AND OUTCOMES IN EARLY AXIAL SPONDYLOARTHRITIS: ANALYSIS OF THE DESIR COHORT**

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Background: Only scarce data is available on regarding pregnancy rates and pregnancy outcomes in early axial Spondyloarthritis (axSpA).
Objectives: a) to estimate the probability of achieving a clinical pregnancy over time and its associated factors in early axSpA, b) to estimate the probability of presenting an unfavorable pregnancy outcome over time and its associated factors in this population.
Methods: Observational prospective French cohort (DESIR) with 6y of follow-up, including 381 of TNFi-naïve women with early axSpA. Study visits were scheduled every 6 months in the first two years of follow up then yearly up to 6 years. Data on pregnancy were collected both retrospectively (before cohort inclusion) and prospectively (since inclusion) up to 6 years of follow up. Baseline characteristics of nulligravidae and uni/multigravidae patients where compared. The probability of achieving at least one pregnancy over time was estimated (Kaplan Meier). Associated factors were estimated by multivariable Frailty Shared Models and mixed models taking into account the correlation between several pregnancies from the same women. The probability to present an unfavorable pregnancy outcome over time (i.e. a miscarriage or pre-term delivery or an elective termination of pregnancy) was estimated only during the prospective period (Kaplan Meier) since associated factors were collected also prospectively. Associated factors to an unfavourable pregnancy outcome were estimated by multivariable Frailty Shared Models and mixted models.
Results: Of the 381 women included in the analysis, 276 (72.4%) and 105 (27.6%) women were respectively multigravidae and nulligravidae at the end of the 6y follow-up. Multigravidae women were significantly older (37.2±8.0 vs 27.6±7.1, p<0.01), less educated (56.7% vs 71.2% university studies, p=0.01), reported higher fatigue levels (6.3±2.1 vs 5.7±2.4, p=0.02), higher BASDAI (4.9±1.9 vs 4.4±1.9, p=0.03), and higher BASFI (3.6±2.4 vs 2.8±2.2, p=0.003) scores at baseline. The probability to have at least one pregnancy throughout life was 61.8% [55.1-67.5]. The mean age at the first pregnancy was 27.3 years old.
One hundred and twenty-four pregnancies occurred during follow-up. The probability to have at least one clinical pregnancy during this period was 28.5% [0.2-0.3]. Lack of TNFi use in the 6 months preceding the pregnancy outcome (HR=2.0 [95%IC 1.1-3.3], p=0.01) and a CRP$\geq$ 6mg/L (HR=1.7[95%IC 1.2-2.5], p= 0.01) were found to be associated with a pregnancy over follow-up.
Among the 80 pregnancies occurring after inclusion with data available on the outcome, 60 (75%) presented a full-term delivery while 12 (15.0%) presented an unfavorable pregnancy outcome (6 (7.5%) and 6 (7.5%) had a miscarriage or a pre-term delivery, respectively), 2(2.5%) had a voluntary interruption of pregnancy and 6 (7.5%) were pregnancies still ongoing at the end of follow-up. Only NSAID use (HR=2.5[95%IC 1.1-5.0], p=0.02) within 6 months of delivery were associated with an unfavorable outcome. TNFi use during pregnancy (6 patients) was not associated with an unfavorable outcome (HR= 2[95%IC 0.8-5.0], p=0.10).
Conclusion: More than 70% patients within this early axSpA had at least one pregnancy. A favorable pregnancy outcome (i.e. full-term delivery) was observed in 75% of patients, which is comparable to the general population data. Patients who achieved a pregnancy were more likely to have stopped their TNFi 6 months prior to the pregnancy outcome and increased their CRP, probably reflecting clinical practice from 10 years ago, when recommendation was to withdraw TNFi before pregnancy. NSAID use within 6 months of delivery was independently associated with an unfavorable pregnancy outcome, while TNFi use was not.
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SAT0346 **EARLY RECOGNITION OF AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH ACUTE ANTERIOR UVEITIS: COMPARISON OF TWO REFERRAL STRATEGIES**

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Background: Diagnostic delay in axial spondyloarthritis (axSpA) remains with 5 to 9 years very high. Extraarticular manifestations like acute anterior uveitis might occur as first manifestations. Up to 40% of patients with acute anterior uveitis have an undiagnosed SpA. Recently, the Dublin Uveitis Evaluation tool (DUET) was proposed as a SpA screening

instrument for ophthalmologists [1]. At the same time, the ASAS referral tool [2] can also be used on the level of ophthalmologists.

Objectives: The objective of the study was to compare the performance of the DUET and the ASAS referral tools for recognition of SpA in patients with acute anterior uveitis.

Methods: A total of 100 consecutive patients with acute anterior uveitis of an ophthalmology clinic were included, 87 had completed a standardized rheumatological examination (including MRI of sacroiliac joints) allowing for a definite conclusion on the presence/absence of SpA. The sensitivity, the specificity and the positive predictive value of both referral tools were calculated.

Results: Out of the 87 patients with acute anterior uveitis 54 (62%) were diagnosed with SpA (51 with axSpA, one with peripheral SpA, one with reactive arthritis and one with psoriatic arthritis), in 36 cases the diagnosis was made for the first time. The performance of both referral tools is presented in table. The ASAS referral tool showed higher sensitivity (that was especially evident in the previously undiagnosed population) but somehow lower specificity compared to the DUET. The positive predictive value was comparable for both tools indicating that approximately 2 patients with uveitis should be referred in order to diagnose one case of SpA.

In our study, MRI scans were performed on all patients including those without back pain. We thereby diagnosed axial spondyloarthritis in 5 patients, even though they did not fulfill the ASAS classification criteria as they never reported back pain (1 patients) or their back pain did not start prior to the age of 45 years (4 patients).

Table. Test performance of two referral tools in all patients and only patients without a diagnosed spondyloarthritis (SpA): Dublin Uveitis Evaluation Tool (DUET) versus an adaption of the Assessment of SpondyloArthritis International Society referral tool (ASAS).

	ASAS, n/N (%)	DUET, n/N (%)	ASAS, patients without a known diagnosis of SpA, n/N (%)	DUET, patients without a known diagnosis of SpA, n/N (%)
Sensitivity	48/54 (88.9%)	45/54 (83.3%)	31/35(86.1%)	27/35(75.0%)
Specificity	8/33 (24.2%)	13/33 (39.4%)	8/31(25.8%)	12/32(41.9%)
Positive predictive value	48/73 (65.8%)	45/65 (69.2%)	31/54(57.4%)	27/45(60.0%)

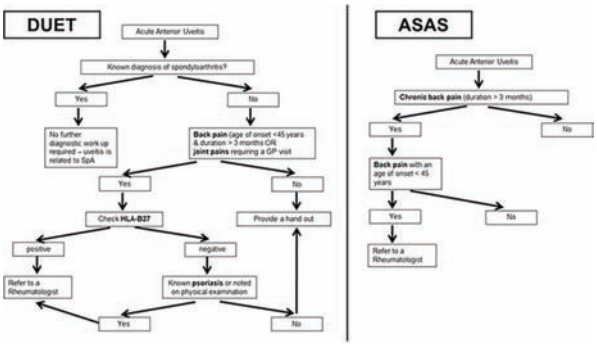


Figure. DUET and ASAS referral tool, modified after [1,2].

Conclusion: We revealed a high prevalence of undiagnosed SpA in patients with acute anterior uveitis. As anticipated, the more complex DUET including also psoriasis and HLA-B27 positivity showed higher specificity for recognition than the ASAS referral tool. However, the ASAS tool has a higher sensitivity (especially in undiagnosed population) and a better feasibility (purely clinical tool, does not include HLA-B27 testing and evaluation of psoriasis by an ophthalmologist).

REFERENCES

[1] Haroon M, et al. Ann Rheum Dis 2015;74:1990-5.
[2] Poddubnyy D, et al. Ann Rheum Dis 2015;74:1483-7.

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SAT0347

COMORBID CONDITIONS ARE ASSOCIATED WITH HIGHER DISEASE ACTIVITY AND WORSE FUNCTIONAL STATUS IN AXIAL SPONDYLOARTHRITIS: A POPULATION-BASED ANALYSIS OF INSURANCE CLAIMS LINKED TO PATIENT SURVEY DATA

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Background: Data on the prevalence of comorbidities and their association with disease activity and functional status in axial spondyloarthritis (axSpA) are scarce.

Objectives: The aim of this study was to investigate the prevalence of comorbid conditions and to analyse their association with disease activity and functional status in a population-based cohort of patients with axSpA.

Methods: A stratified random sample of subjects with a diagnosis of axSpA (ICD-10 M45) was drawn from health insurance data in Germany and received a questionnaire on disease-related, demographic and socioeconomic parameters. A sex- and age-matched control cohort without axSpA was drawn from the claims data. Information on comorbidities, drug prescriptions and non-pharmacological treatment was retrieved from claims data and linked to the questionnaire data for axSpA. Multivariable linear regression models were used to determine the association of comorbidities (defined by Elixhauser coding algorithms excluding rheumatic diseases) with disease activity and functional status.

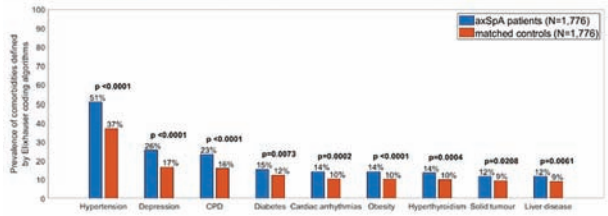
Results: A total of 1,776 patients with axSpA were included in the analyses; mean age was 56.1 years and 46.4% were female. The most prevalent comorbid conditions were hypertension (50.9%), depression (25.5%), and chronic pulmonary disease (23.4%) (Figure 1). The prevalence of the majority of comorbidities was higher in axSpA as compared to controls. In the multivariable linear regression analyses, the number of comorbidities was significantly associated with both BASDAI and BASFI: each comorbidity was associated with BASDAI increase by 0.12 and BASFI increase by 0.10 points independently of other factors including treatment (Table 1).

Table 1. Impact of comorbidity on disease activity (BASDAI) and functional impairment (BASFI) in patients with axial spondyloarthritis (N=1,776): Results from multivariable linear regression models.

	Reference	BASDAI β (95% CI)	BASFI β (95% CI)
Elixhauser Index*	per unit	0.12 (0.07, 0.17)	0.10 (0.04, 0.17)
Number of pharmaceuticals**	per unit	-	0.03 (0.01, 0.06)
Age	per 10 years	0.11 (0.04, 0.19)	0.51 (0.42, 0.60)
Sex, female	male	0.55 (0.37, 0.73)	-0.02 (-0.24, 0.21)
Uveitis, present	not present	-0.42 (-0.74, -0.09)	-
In rheumatological care	no	0.29 (0.09, 0.50)	0.60 (0.37, 0.82)
Body mass index, kg/m²	per unit	0.02 (0.00, 0.04)	0.07 (0.05, 0.10)
Lack of exercise	no	-	0.62 (0.37, 0.88)
Smoking (current)	no	0.28 (0.05, 0.52)	0.54 (0.28, 0.80)
Suffering from stress	no	0.76 (0.57, 0.95)	0.23 (0.01, 0.46)
NSAIDs	no	0.43 (0.24, 0.62)	-
bDMARDs	no	-0.37 (-0.63, -0.11)	-
Non-opioid analgesics	no	0.34 (0.12, 0.56)	0.43 (0.15, 0.71)
Opioids	no	1.02 (0.76, 1.27)	1.64 (1.32, 1.97)
Steroids	no	0.26 (0.02, 0.49)	-
Physical therapy	no	0.31 (0.13, 0.50)	0.37 (0.15, 0.59)

*excluding rheumatic diseases; **except axSpA-related medication.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; bDMARDs, biological disease-modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs.

Figure 1 Comorbidities defined by Elixhauser coding algorithms in patients with axial spondyloarthritis (N=1,776) and matched controls (N=1,776).*



**excluding rheumatic diseases. AxSpA, axial spondyloarthritis; CPD, chronic pulmonary disease.*

Conclusion: Comorbid conditions are common in axSpA patients and are independently associated with higher disease activity and higher level of functional impairment. Higher disease activity and a higher level of functional disability might be indicators of a severe disease resulting in the development of comorbid conditions.

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SAT0348 HOW FREQUENT IS NEUROPATHIC PAIN COMPONENT IN PATIENTS WITH SPONDYLOARTHRITIS?

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Background: Criteria to define inflammatory back pain in Spondyloarthritis (SA) are multiple. Although neuropathic pain component was known to be part of disease symptoms, it has been rarely assessed.

Objectives: The aim of this study was to determine the prevalence of the neuropathic pain component in SA patients and secondarily, to detect correlation with the disease duration, activity scores and functional impairment.

Methods: A cross-sectional study including patients with radiographic axial SA defined by ASAS criteria was conducted. Patients were questioned about their neuropathic pain using painDETECT questionnaire and Douleur Neuropathique en 4 Questions (DN4) interview. Further information about disease characteristics, activity (BASDAI, $ASDAS_{CRP}$) and functional (BASFI) scores were assessed the same day.

Statistical analysis, was performed by Khi^2-test for qualitative variables and Student-test for quantitative variables. A p value ≤0.05 was considered significant.

Results: Forty patients were included. The average age was about 41 years old (±12.9) and the sex ratio was 12.3 (H/F). The mean disease duration was 10.7±6.9 years. Most of patients suffered from back pain and the visual analogic scale pain scale was about 3.78±2.5. The mean BASDAI score was 2.75±2.3 and the mean $ASDAS_{CRP}$ was 2.24±1.07. The average BASFI score was 2.57±2.5. Neuropathic pain component was noted only in 7.5% of patients by DN4 interview (≥4/10) and in 10% of patients by pain DETECT questionnaire.

As expected, patients with DN4≥4 were correlated to the visual analogic scale pain (p=0.04) and female gender (p=0.07). But no relation was found with the type of SA or the disease activity or the functional scores.

Conclusion: Neuropathic pain component was noted only in 10% of SA in our work. Positive correlation was found with visual analogic scale pain and female gender. Larger studies are needed to assess this type of pain since therapeutic strategy may be affected.

Disclosure of Interests: None declared

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SAT0349 HIGHER DISEASE ACTIVITY IS ASSOCIATED WITH MORE SPINAL RADIOGRAPHIC PROGRESSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Alexandre Sepriano[1], Sofia Ramiro[1], Stephanie Wichuk[2], Praveena Chiowchanwisawakit[3], Terrie Maccosham[2], Joel Paschke[4], Désirée van der Heijde[1],Robert B.M. Landewé[5], Walter P. Maksymowych[2,4]. *[1]LUMC, Leiden, Netherlands*; *[2]University of Alberta, Edmonton, Canada*; *[3]Mahidol University, Bangkok, Thailand*; *[4]CARE Arthritis, Edmonton, Canada*; *[5]ARC, Amsterdam, Netherlands*

Background: The association between disease activity and spinal radiographic progression in radiographic axial spondyloarthritis (r-axSpA) has been previously shown in a cohort of patients (pts) not being treated with TNF inhibitors (TNFi).[1]

Objectives: To test the possible association between disease activity and spinal radiographic progression in r-axSpA in a real-life cohort, also including patients treated with TNFi.

Methods: Pts with axial spondyloarthritis (axSpA) fulfilling the modified New York criteria (mNY) were included in this prospective, observational cohort (ALBERTA FORCAST). Clinical and imaging data were collected at baseline and every 2 years up to 10 years of follow-up. Radiographs of the spine were independently scored by 2 central readers and one adjudicator (if disagreement), with known chronological order but blinded to clinical data, using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). To be included, pts had to have ≥ one 2-year interval with data on mSASSS from ≥1 reader available as well as complete data on ASDAS and TNFi exposure at the start of the interval. The association between ASDAS at the start of the interval (t) and mSASSS 2 years later (t+1) was tested in two types of longitudinal GEE models: i. multilevel (2 readers) model with the individual reader scores as outcome (2-level models); ii. Using as outcome averaged scores between readers (1-level models). Both type of models were adjusted for mSASSS at t (autoregression) and for a set of potential confounders defined a priori on clinical grounds (Figure).

Results: In total, 314 pts (442 intervals) were included [74% males, mean symptom duration 17.8 (SD 11.7) years, 83% HLA-B27 positive and 7% previously treated with ≥1 TNFi]. At baseline the mean ASDAS was 2.7 (1.3) and the mean mSASSS 13.8 (18.9). During follow-up 213 (68%) pts received treatment with TNFi in ≥1 visit. Overall, the average 2-year progression was 1.33 (2.68) mSASSS-units per 2-year interval. In the 2-level multivariable model, 1 ASDAS-unit increase at t was associated with an increase of 0.25 mSASSS-units at t+1 [β (95% CI): 0.25 (95%CI 0.10; 0.41)] (Figure). Results were similar using the averaged mSASSS as the outcome [β (95% CI): 0.25 (0.08; 0.43)].

Conclusion: These data add to previous evidence by showing that a higher ASDAS is associated with higher spinal radiographic progression in pts with r-axSpA independent of prior treatment with TNFi.

REFERENCE

[1] Ramiro S, et al. Ann Rheum Dis 2014;73:1455–61.

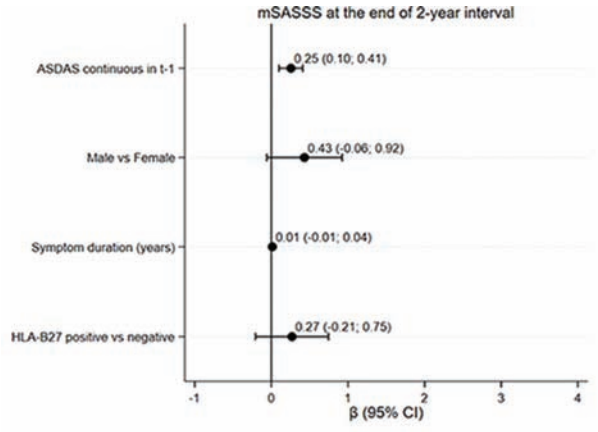


Figure. Longitudinal effect of ASDAS at the start of the interval on mSASSS 2 years later in a multilevel, multivariable linear GEE model with autoregression [N=313; model also adjusted for mSASSS at t-1 ('autoregressor'), Number of TNFi before baseline (continuous) and TNFi at t-1 (yes vs no)].

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Pfizer, Sanofi, Stephanie Wichuk: None declared, Praveena Chiowchanwisawakit: None declared, Terrie MacCosham: None declared, Joel Paschke: None declared, Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Robert B.M. Landewé: None declared, Walter P. Maksymowych Grant/research support from: Abbvie, Novartis, Pfizer, Consultant for: Abbvie, Boehringer, Celgene, Galapagos, Lilly, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Boehringer, Celgene, Galapagos, Lilly, Novartis, Pfizer, UCB

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SAT0350 THE IMPACT OF FIBROMYALGIA ON SLEEP DISTURBANCE AND QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Sleep disturbance is a very frequent symptom in patients with diseases associated with pain syndrome [1, 2]. Prevalence of sleep disorders in ankylosing spondylitis (AS) patients varies in a range of 35% to 90% [2]. One of the most common comorbid condition in patients with AS is fibromyalgia (FM), that can significantly worsen quality of life and sleep quality in patients with AS.

Objectives: The aim of this study was to evaluate the impact of FM comorbidity on sleep disturbance and quality of life in patients with AS.

Methods: One hundred and nineteen patients with AS according to modified New York criteria (mean age (M±SD) 42.23±11.5 years; 21 women and 98 men) were enrolled in the study. FM was diagnosed based on the 1990 American College of Rheumatology classification criteria. All patients were asked to complete self-report questionnaires, including the Pittsburgh Sleep Quality Index (PSQI) and Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) to assess sleep disturbance and quality of life.

Results: Of the AS patients, 23 (19.3%) met the criteria for FM. The patients were divided into two groups in terms of having or not having FM. Groups were representative for age and disease duration. Patients with AS and concomitant FM showed significantly increased frequency of sleep disturbance according to the PSQI. Only 26 patients with AS (27%) scored <5 and indicated as "good sleepers", whereas all patients with AS and concomitant FM has poor sleep quality. In group with AS patients mean scores (M±SD) of PSQI were 7.52±3.96 and in group with AS+FM - 11.04±3.5 (P< 0,01). Table 1 shows detailed information on the sleep quality of patients with and without FM.

Table 1. *Sleep Disturbances in patients with Ankylosing Spondylitis and Concomitant Fibromyalgia according to Pittsburgh Sleep Quality Index (sleep component scores)*

Component	AS with FM (n=23)	AS without FM (n=96)	P
	(M ± SD)	(M ± SD)	
Sleep quality	1.78±0.74	1.49±0.74	< 0,05
Sleep latency (time to fall asleep)	2.00±0.85	1.31±1.03	< 0,05
Sleep duration (hours of sleep)	1.61±1.08	1.16±1.02	< 0,05
Sleep efficiency (percentage of time asleep while in bed)	1.83±1.19	0.85±1.15	< 0,05
Sleep disturbances	1.87±0.46	1.32±0.55	< 0,05
Use of sleep medication	0.30±0.70	0.15±0.53	NS
Daytime dysfunction	1.65±0.93	1.23±0.91	< 0,05

In general, for each of the component scores, patients with AS scored lower than patients with AS+FM, with statistically significantly less severe sleep problems on all domains except for use of sleep medication.

Patients with AS and concomitant FM showed poorer quality of life according to ASQoL compared to patients with alone AS (13.8±2.35 vs. 8.6±4.01; p< 0,01).

Conclusion: Sleep disturbance is a frequent condition in patients with AS. Our study results demonstrate the significant impact of FM comorbidity on sleep disturbance and quality of life in patients with AS.

REFERENCES

[1] Bigatti, S. M., Hernandez, A. M., Cronan, T. A., & Rand, K. L. (2008). Sleep disturbances in fibromyalgia syndrome: relationship to pain and depression. Arthritis Care & Research: Official Journal of the American College of Rheumatology, 59(7), 961-967.

[2] Leverment, S., Clarke, E., Wadeley, A. et al. (2017) Prevalence and factors associated with disturbed sleep in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a systematic review *Rheumatol Int*, 37: 257 https://doi.org/10.1007/s00296-016-3589-x

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SAT0351 IBIS-Q (IBD IDENTIFICATION OF SPONDYLOARTHRYTIS QUESTIONNAIRE): A NEW TOOL TO DETECT SPONDYLOARTHRITIS IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Background: Extra-intestinal manifestations (EIM) are frequent in IBD with peripheral and axial spondyloarthritis (SpA) being the commonest EIM, being reported in up to 23% of subjects.. Early detection of SpA is clinically relevant to drive the therapeutic management including the right treatment at the right time to prevent disability and improve the quality of life. In the literature there are few validated Rheumatology referral models for SpA for gastroenterological use

Objectives: The aim of this study was to develop a questionnaire to identify peripheral and axial SpA in a cohort of IBD patients (setting: IBD Unit of Sacro Cuore-Negrar Hospital Verona in a rheumatological-gastroenterology clinic).

Methods: During a preliminary meeting a group of experts in SpA-IBD (6 rheumatologists and 4 gastroenterologists) generated a list of 42 items thought to cover all possible SpA manifestations including spinal, articular and entheseal involvement. Consecutive patients referred to the IBD Unit were then enrolled from January to May 2018 without excluding patients affected by EIM. Rheumatologic assessment was performed in the same day by a Rheumatologist blinded to the medical story and to the questionnaire results in order to collect data about the 66 swollen joint count (SJC) and 68 TJC, MASEI, LEI, presence of ASAS criteria for axial and peripheral SpA, presence of diagnostic criteria for fibromyalgia (FM) and non-specific low back pain (NSLB) pain mainly due to OA). If the patient presented a tender/swollen entheses, a US exam completed the clinical examination. The patient completed BASDAI and BASFI questionnaires in the same day. Factorial analysis to identify the main factors; ROC curves for sensibility/specificity; Youden index for cut-off were performed.

Table 1

1. Have you had pain in your heels?
2. Have you ever had back pain lasting at least 3 months that was not injury related?
3. Have you ever had a swollen wrist without having any trauma?
4. Have you ever had a swollen knee without having any trauma?
5. Do you wake up at night and walk because of low back pain?
6. In the morning is your back stiff for more than 30 minutes?
7. Have you ever had a stiff neck for some weeks or months?
8. Have you ever had a pain in your thigh which goes down to your knee and not beyond?
9. Is it difficult to pick things up from the floor without flexing your knees?
10. Have you ever had a swollen finger like a "saugage" for some days?
11. Do you find it difficult to walk because of foot pain?
12. Do you feel pain when people shake your hand?
13. Have you ever had swollen and painful hands?
14. Have you ever had swollen and painful feet?

Results: A final 38-items questionnaire was tested in 210 patients (excluding 17 patients for presence of other rheumatic diseases and 12 for incomplete evaluation). The psychometric analysis of the questionnaire was done on data of 181 patients. 58 patients of the enrolled patients met the ASAS criteria for SpA (13 axial, 5 both axial and peripheral 40 peripheral). The SpA prevalence in our cohort was 32% with 10 new cases detected by the questionnaire (5.5%: 7 peripheral and 3 axial). Through the psychometric and factorial analysis, we selected 14-items to

include in the final questionnaire (named IBIS-Q; Table 1) having a sensitivity 84.4% and specificity 80% to detect SpA (AUC 0.8803 with CI 95% 0.8305- 0.9301). We propose as cut-off of 4 positive questions of the IBIS-Q for SpA patient identification

Conclusion: IBIS-Q seems to be a useful and simple tool to use in our IBD clinic for the detection of SpA, with a good statistical performance. Further studies are needed to validate this questionnaire

Disclosure of Interests: Ilaria Tinazzi: None declared, Angela Variol: None declared, Antonio Marchetta: None declared, Andrea Geccherle: None declared, Pierluigi Macchioni: None declared, Dennis McGonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB

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SAT0352 THE FREQUENCY OF OCULAR MANIFESTATIONS IN PATIENTS WITH ADULT VS. CHILDHOOD SPONDYLOARTHRITIS

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Background: Adult spondyloarthritis (SpA) is characterized by abnormal bone overgrowth and inflammatory erosive osteopenia in the spine. SpA may be associated with psoriasis and psoriatic arthritis (PsA), inflammatory bowel disease, reactive arthritis, enthesitis, and ocular features such as acute anterior iritis, and chronic uveitis. Juvenile SpA onsets in children under 16 years old and may present with more peripheral enthesopathies and arthritis than adult SpA.

Objectives: This meta-analysis investigated the frequency and type of ocular involvement in childhood and adult SpA. The difference in frequency between childhood and adult SpA was also investigated.

Methods: Medline, Web of Science and Cochrane databases were searched to September, 2018 to identify publications related to spondyloarthropathy (SpA), and ankylosing spondylitis (AS) with ocular conditions (OC) (conjunctivitis, keratoconjunctivitis sicca, xeropthalmia, uveitis, eye hemorrhage, optic neuritis, papilledema, orbital disease, retinal artery/vein occlusion, macular edema, retinitis, chorioretinitis, scleritis, iridocyclitits, choroid hemorrhage, blindness and amaurosis fugax). The rates of OC were extracted and random effects models estimated their frequency. Heterogeneity was evaluated using I^2. Inclusion criteria were studies in SpA of either children or adults that included a frequency of OC. Differences in frequencies of OC between childhood and adult disease were compared using chi squared tests.

Results: The search process identified 3164 articles, of which 41 were eligible for inclusion. A pooled random effects model showed the prevalence of uveitis was 24% [20%-27%] in adult AS (23 studies, N= 11943 patients), 10% [7%-14%] in adult PsA (9 studies, N=1817), and 17% [10%-24%] in undifferentiated adult SpA (9 studies, 6568 patients). In juveniles with AS, the prevalence of uveitis was 27% [16%-39%] (8 studies, 927 patients). In child onset PsA, uveitis occurred in 16% [10%-21%] (5 studies, N=498), and in juvenile undifferentiated SpA, uveitis had a frequency of 7% [1%-12%] (2 studies, N=1531). The differences in frequency of uveitis in adults vs. child onset SpA spectrum diseases were not significantly different between AS and JAS (p=0.891), PsA and JPsA (p=0.732) and between SpA and JSpA.

Conclusion: This meta-analysis compares the frequency of ocular involvement in seronegative spectrum diseases in adults and children where it appears that the frequency of uveitis is not statistically different in adult vs. child onset SpA and the subsets.

REFERENCES

[1] Reveille JD, Weisman MH. The epidemiology of back pain, axial spondyloarthritis and HLA-B27 in the United States. Am J Med Sci 2013;345:431-6.

[2] Smith JA. Update on ankylosing spondylitis: current concepts in pathogenesis. Curr Allergy Asthma Rep 2015;15:489.

[3] Stolwijk C, Essers I, van Tubergen A, Boonen A, Bazelier MT, De Bruin ML, et al. The epidemiology of extra-articular manifestations in ankylosing spondylitis: a population-based matched cohort study. Annals of the Rheumatic Diseases 2015;74:1373-8.

[4] Lin Y-C, Liang T-H, Chen W-S, Lin H-Y. Differences between juvenile-onset ankylosing spondylitis and adult-onset ankylosing spondylitis. J Chin Med Assoc 2009;72:573-80.

[5] Cantini F, Nannini C, Cassarà E, Kaloudi O, Niccoli L. Uveitis in Spondyloarthritis: An Overview. J Rheumatol Suppl 2015;93:27-9.

Disclosure of Interests: Matthew Turk: None declared, Jacqueline Hayworth: None declared, Tatiana Nevskaya: None declared, Janet Pope Consultant for: Eli Lilly and Company

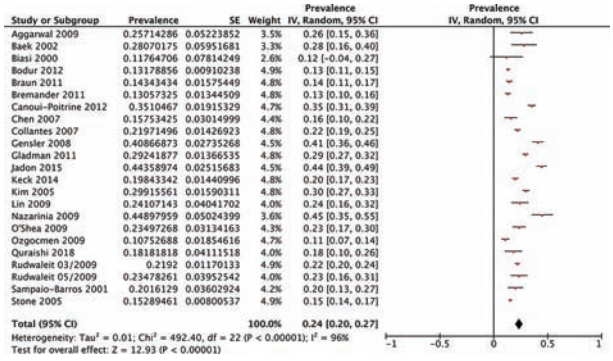


Figure 1. The frequency of ocular manifestations in adults with ankylosing spondylitis

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SAT0353 HIGH PREVALENCE OF NEWLY DIAGNOSED AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH ACUTE ANTERIOR UVEITISAND CHRONIC BACK PAIN – PRELIMINARY RESULTS OF THE SP-EYE STUDY

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Background: One third of the axial spondyloarthritis (axSpA) patients suffers from acute anterior uveitis (AAU). Correspondently, AAU can be the first sign of axSpA and previous studies described undetected axSpA in up to 40% of the patients with noninfectious AAU.

Objectives: To study whether referral of all patients with AAU and chronic back pain results in a high prevalence of newly diagnosed axSpA patients.

Table 1. Patient characteristics at referral.

	Overall (N=50)	**Definite AxSpA** (N=13)	**Suspicion of early axSpA** (N=21)	**No suspicion of axSpA** (N=16)
Age	42 (±13)	44 (±15)	38 (±9)	45 (±15)
Gender, men	26 (52)	10 (77)	11 (52)	5 (31)
Back pain duration, *years*	15 (5-27)	14 (5-27)	9 (4-24)	21 (15-32)
Inflammatory back pain	21 (42)	9 (70)	9 (43)	3 (19)
>1 anterior uveitis	26 (52)	9 (69)	12 (57)	5 (31)
HLA-B27 positive	27 (54)	11 (85)	12 (57)	4 (25)
SpA features (ASAS)	3 (±1)	4 (±1)	3 (±1)	2 (±1)
SI joint abnormality	16 (32)	9 (69)	6 (29)	1 (6)
Sacroiliitis, mNY criteria	9 (18)	7 (54)	2 (10)	0 (0)
BASMI	2.4 (±2.4)	4.2 (±4.0)	1.6 (±0.7)	2.0 (±1.3)
BASDAI	3 (2-5)	2 (2-4)	3 (2-5)	3 (2-5)
ASDAS-CRP ≥2.1	21 (42)	6 (46)	10 (48)	5 (31)

Legend: Numbers are depicted as mean (±SD), median (Q1-Q3) or number of patients (%).

Methods: A prospective ongoing observational study was started in April 2017, including all patients with noninfectious AAU and a history of back pain (≥3 months, started < age of 45 years), referred from six Ophthalmology clinics to the Rheumatology Outpatient Clinic of the VU medical center. Patients with a known systemic disease associated with AAU were excluded. Patient characteristics, laboratory (HLA-B27, C-reactive

protein) and patient reported parameters (e.g. BASDAI, ASDAS) were collected. X-rays were evaluated according to the modified New York (mNY) criteria for sacroiliitis. The clinical axSpA diagnosis was made by the rheumatologist. Patients were either diagnosed with 'definite SpA', 'suspicion of SpA' or 'no suspicion of SpA', based on the clinical assessment. Patients with 'definite SpA' were classified into radiographic or non-radiographic axSpA according to the ASAS criteria. Patients were treated according to standard care guidelines.

Results: Between April 2017 and October 2018, 65 patients were referred to the Rheumatology clinic, of whom 50 (mean age 42 years; 48% female; median back pain duration 15 years) met all inclusion criteria. AxSpA was diagnosed in 13 patients (26%), of whom seven fulfilled the criteria for radiographic and six for non-radiographic axSpA (table 1). Another 21 patients (42%) were considered clinically suspicious for early axSpA, of whom four had SI joint abnormalities and two even fulfilled the mNY criteria for sacroiliitis. Forty-two% of all patients had a high disease activity score (ASDAS≥2.1). Patients diagnosed with axSpA were significantly more often male and HLA-B27 positive, had more SpA features and a higher BASMI score. In 25 patients treatment was started, mostly with nonsteroidal anti-inflammatory drugs. Two patients received a tumor necrosis factor inhibitor shortly after diagnosis.

Conclusion: In this study, 26% of the patients referred with noninfectious AAU and chronic back pain (≥3 months, started < age of 45 years) were newly diagnosed with axSpA. Furthermore, another 40% required further follow up because of a suspicion for beginning axSpA. These results stress the importance of systematic referral of AAU patients with chronic back pain from the ophthalmologist to the rheumatologist, to improve early recognition of axSpA.

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SAT0354 CARDIVASCULAR RISK IN YOUNG PATIENTS WITH LOW AXIAL SPONDYLOARTHRITIS ACTIVITY: PROMISING SCORING TOOLS

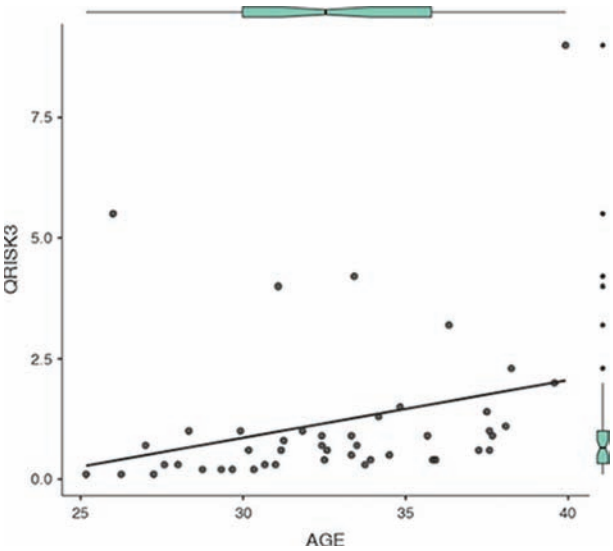
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Background: Patients (pts) with axial spondyloarthritis (axSpA) have increased cardiovascular morbidity and mortality, compared to the general population. However, assessment of cardiovascular risk (CVR) in axSpA is complicated, as in age < 40 years conventional CVR scales (SCORE, ets.) are not recommended, as conventional risk factors do not completely determine an increased CVR. The QRESEARCH Cardiovascular Risk Algorithm (QRISK) is the only scale of measuring probability of major cardiovascular events in pts aged 25 to 40.

Objectives: To measure CVR in young pts with low activity of axSpA, and to evaluate the interrelation between CVR, measured with QRISK and gene predisposition.

Methods: The study included 46 pts 25-40 years old with axSpA (ASAS criteria 2009), achieved inactive disease on TNF-α inhibitors. AxSpA activity was measured with ASDAS and BASDAI. CVR was calculated with the modified QRISK (QRISK3) (https://qrisk.org/three/). All parameters of QRISK3 were collected: smoking and diabetes statuses, angina or heart attack in a 1st degree relative <60, chronic kidney disease (3-5 stage), atrial fibrillation, blood pressure, migraines, rheumatoid arthritis, systemic lupus erythematosus, severe mental illness, atypical antipsychotic medication, regular steroid tablets usage, erectile dysfunction, cholesterol/HDL ratio, systolic blood pressure, Standard deviation (SD) of at least two most recent systolic blood pressure readings (mmHg), height (cm), weight (kg). Gene polymorphisms to main cytokines of axSpA and atherosclerosis pathogenesis were measure (IL17A-197, IL17F7 His/Arg, IL17F-11139 c/g, TNF-863, TNF-308, TNF-238, IL1B-31, IL4-590, IL6-174, IL10-1082, IL10-592, VEGF-2578, VEGF936, MMP2-1306, MMP3-5A6A, MMP9-1562). To identify the relationship between genetic factors and clinical characteristics an exploratory factor analysis was performed.

Results: Mean age ± SD of included pts was 32.5±3.87 years (26% of pts aged 25 – 30, 28.3% – 30-35, 28.3% – 35-40 years), 36 (78.3%) patient were male, symptoms duration 8.71±4.72 years, duration of TNF-α inhibitor treatment 3.1±2.4 years, ASDAS 1.95±1.23, BASDAI 1.4±0.8. All three age groups were comparable (p≥0.05). Out of the 46 pts 25 – 40 years old 34 (75.6%) had a low CVR and 11 (23,9%) had increased CVR (fig.1). Average QRISK3 score of all the patients was 1.18±1.64%. In the 25-30 year old age QRISK3 was 1.51±0.25%, in pts 30-35years old – 1.09±0.6%, in 35-40 years old–2.31±1.0% (p<0.05 for the inter-group difference).



All patients with increased CVR had a direct associations with homozygous in CC allele IL17F-11139 gene, heterozygous in GA allele of TNF-308 and heterozygous in CG allele IL6-174. Negative associations were found between CVR and heterozygosity in His/Arg and homozygous in His/His of IL17F7, homozygosity in GG allele TNF-308, homozygosity in CC IL6-174, table 1. Interrelation of CVR with another gene polymorphisms was not significant (data are not present).

Table 1. Interrelation of QRISK 3 and Gene polymorphisms - exploratory factor analysis with 'varimax' rotation.

QRISK 3	IL17F-11139 CC	IL17F-11139 CG	IL17F7 His/His	IL17F7 His/Arg	IL17F7 Arg/Arg	IL6-174 CC	IL6-174 CG	TNF-308 GA	TNF-308 GG
0,458	0,830	- 0,830	-0,824	0,809	-	-0,564	0,545	0,935	-0,935

Conclusion: A quarter of young axSpA pts had an increased 10-year probability of cardiovascular events. Gene polymorphisms in IL-6, IL17F, and TNF-α locuses are strongly associated with increased CVR. QRISK3 and gene polymorphisms could be promising tools in CVR assessment in axSpA.

Further larger studies are needed for evaluation of CVR factors in axSpA.

REFERENCE

[1] Julia Hippisley-Cox, et al. BMJ 2017; 357 doi: https://doi.org/10.1136/bmj.j2099.

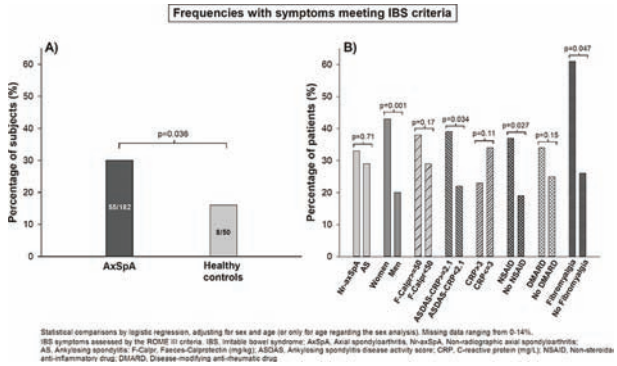
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SAT0355 **IRRITABLE BOWEL SYNDROME SYMPTOMS IN AXIAL SPONDYLOARTHRITIS AND HEALTHY CONTROLS, AND THEIR RELATION TO DISEASE CHARACTERISTICS – IS IT AN OVERLOOKED COMORBIDITY?**

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Background: While inflammatory bowel disease (IBD) is a well-known comorbidity in axial spondyloarthritis (axSpA), little is known about the prevalence, drivers and impact of irritable bowel syndrome (IBS). In the general population, the IBS prevalence has been estimated to ~11%.[1]
Objectives: To compare the frequency of gut symptoms meeting IBS criteria between axSpA patients and controls, and to examine how such symptoms relate to disease characteristics.
Methods: Consecutive axSpA patients were examined and classified as non-radiographic axial SpA (nr-axSpA; ASAS criteria; n=63) or ankylosing spondylitis (AS; modified New York criteria; n=119), excluding cases with known IBD. Proportions reporting gut symptoms meeting the ROME III IBS criteria were compared between axSpA patients and sex and age matched controls (without rheumatic disease or IBD; n=50) by logistic regression.[2] Within the axSpA group, separate logistic regression models were also applied to examine whether the presence of IBS symptoms differed according to disease subtype (nr-axSpA/AS), sex, disease activity, level of systemic and gut inflammation, NSAID and DMARD use, and comorbid fibromyalgia (according to the 1990 fibromyalgia criteria).[3] Finally, we analysed associations between the presence of IBS symptoms and standard patient-reported axSpA outcomes and evaluator´s VAS global assessment of disease activity. All analyses were sex and age adjusted.
Results: Symptoms meeting IBS criteria were significantly more common among axSpA patients (30%) than controls (16%; OR 2.5 [95%CI 1.1-5.7]; **Figure 1A**). Within the axSpA group, no difference was observed between nr-axSpA and AS (**Figure 1B**). Furthermore, no associations were observed with markers of systemic or gut inflammation, whereas the presence of IBS symptoms was significantly more frequent among patients with higher disease activity (OR 2.2 [95%CI 1.1-4.5] for ASDAS-CRP ≥2.1 vs. <2.1), in females (OR 3.0 [1.5-5.8] vs. men), among NSAID users (OR 2.3 [1.1-4.6] vs. non-users), and in patients fulfilling fibromyalgia criteria (OR 3.0 [1.0-8.6] vs. not); **Figure 1B**). All patient-reported outcomes, but not evaluator´s VAS global, were significantly worse in patients reporting IBS symptoms (**Table**).



	No IBS symtoms n=127	IBS symptoms n=55	p-value *
VAS global (mm)	30 (25)	44 (25)	0.010
VAS pain (mm)	30 (26)	43 (26)	0.020
VAS fatigue (mm)	32 (27)	50 (27)	0.001
EQ-5D utility †	0.75 (0.22)	0.61 (0.30)	0.004
BASFI	1.8 (2.2)	2.9 (2.2)	0.016
BASDAI	2.6 (2.1)	4.3 (2.1)	<0.001
Evaluator´s VAS global (mm)	16 (14)	19 (14)	0.569

Values are mean (SD). * Adjusted for sex and age by ANCOVA. † UK preference set. Missing data ranging from 3-9%.

Conclusion: In axSpA patients without an IBD diagnosis, gut symptoms meeting IBS criteria were twice as common as in healthy controls. While IBS symptoms do not appear to be driven by subclinical gut inflammation or systemic inflammation, the associations with criteria-assessed fibromyalgia, female sex, and worse levels of patient-reported outcomes indicate a link to central pain sensitization, although side effects of NSAIDs may also play a role.

REFERENCES

[1] Lovell RM, et al. Clin Gastroenterol Hepatol. 2012;10:712-21.
[2] Drossman DA. Gastroenterology. 2006;130:1377-90.
[3] Wolfe F, et al. Arthritis Rheum. 1990;33:160-72.

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SAT0356 **DACTYLITIS IN EARLY SPONDYLOARTHRITIS. DATA FROM THE DESIR COHORT**

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Background: Dactylitis is a particular feature shared across the several phenotypical forms of spondyloarthritis (SpA), part of the classification criteria. There are only few data available about impact of dactylitis in early stage of SpA, and factors associated with the presence/history of dactylitis.
Objectives: To study, at baseline and after 5 years in the DESIR cohort, the presence/history of dactylitis in an attempt to evaluate frequency of dactylitis in SpA and to look at the factors associated with presence of dactylitis.
Methods: DESIR is a prospective observational cohort of patients with recent onset (less than 3 years) inflammatory back pain, beginning before 50 years, suggestive of axial SpA, All available factors in the database (clinical, biological, imaging and medico economic) were compared between patients with and without past or present dactylitis at baseline (for categorical variables : odds-ratio +/- 95% CI and chi-square/Fisher tests, for continuous variables : unpaired t-tests/Mann-Whitney), by uni and then multivariate analysis(logistic regression). Significance: p less than 0.05.
Results: At baseline, 708 patients were analyzed. 97 had a past history or a concomitant dactylitis [prevalence 13.7% (CI 95% : 11.6 – 16.2)]. Dactylitis occurred before axial symptoms in 41.3% and before any other symptom in 14.1% of the cases. By univariate analysis, dactylitis was significantly associated with history of arthritis, enthesitis, psoriasis, with elevated CRP and ESR, enthesitic and arthritis scores, BASDAI, ASDAS,BASFI, SF-36, HAQ, ASQoL, shorter disease duration, systemic and local steroids use, and with lower structural damage (sacro iliac, spine). Table shows the result of the multivariate analysis at baseline.

item	OR	CI 95%
Arthritis history or presence	2.9	[11.2 – 30.9]
csDMARD use during the past 6 months	5.2	[2.9 – 9.1]
Calcaneal enthesitis history or presence	6.7	[3.0 – 14.7]
BASDAI > median	1.08	[1.05 – 1.11]
BASFI > median	1.04	[1.02 – 1.06]
SF36 phys <median	0.92	[0.87 – 0.97]
Systemic steroids during the past 6 months	5.49	[2.93 – 10.28]
Sacro iliac erosion (MRI central reading)	0.02	[0.004 – 0.13]
mSASSS (central reading)	0.37	[0.21 – 0.66]

After 5 years, 138 cases were recorded in 480 patients with complete follow-up : prevalence 28.75% [CI 95% 24.75-32.75], with estimated incidence of 1.7/100 patient-years. At 5 years, dactylitis was significantly associated (multivariate analysis) with : Achilles enthesitis (OR : 3.3), history of psoriasis (OR: 3.9), cumulative number of ASAS criteria (OR: 7.2), modified New York criteria fulfillment (OR: 0.35), DMARD use (OR: 2.7) and elevated CRP (OR:0.9).

Conclusion: In the DESIR cohort of patients suspected for early SpA, history of dactylitis is present in 13.7% of the cases at baseline and an estimated incidence of 1.7/100 p-y over 5 years. It is an early feature associated with peripheral involvement, and associated with more burden of the disease, more frequent use of DMARDs and steroids, but with less structural damage.

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SAT0357 PREVALENCE OF RADIOGRAPHIC ENTHESEAL LESIONS AT THE HIP AND PELVIC REGION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Enthesitis is one of the features of ankylosing spondylitis (AS). High prevalence of structural and inflammatory ultrasound lesions of peripheral entheses are found in AS patients. Furthermore, plain radiographs provide good imaging of peripheral enthesopathy at well-defined skeletal sites1. There are several entheseal sites at the pelvis and hip region, but little is known about the presence of structural entheseal anomalies at these sites in AS.

Objectives: Our aim was to investigate the prevalence of radiographic entheseal lesions at the hip and pelvic region in patients with AS.

Methods: The present analysis was performed in 214 patients from the Groningen Leeuwarden Axial SpA (GLAS) cohort study, who were included between November 2004 and December 2010 and had available anteroposterior (AP) pelvis radiographs at baseline. All patients fulfilled the modified New York criteria for AS. Radiographs were scored by two trained readers blinded for patient characteristics and treatment. Anomalies with absolute agreement were reported. The entheseal sites scored were: trochanter major, trochanter minor, os ischium, crista iliaca, both left and right side and symphysis pubis. The following 3 anomalies were scored: cortical irregularities/erosions, calcifications and enthesophytes.

Results: Of the 214 patients, 148 (69%) were male, mean age was 42.5 ± 11.6, 171 (80%) were HLA-B27 positive and median symptom duration was 16 years (IQR 8-24). Reader agreement on the entheseal lesions was moderate to excellent with Cohen's kappa's between 0.474 and 0.882. 122 patients (51%) showed enthesopathy with 309 lesions in total. The most prevalent lesions were irregularities/erosions (n=220; 71%), followed by enthesophytes (n=71; 23%) and calcifications (n=16; 5%). Most lesions were found at the os ischii (n=168; 54%), followed by the tuberculum majus (n=42; 14%), crista iliaca (n=40; 13%), tuberculum minus (n=30; 10%) and symphysis pubis (n=29; 9%).

Conclusion: In this cohort of established AS patients, a high prevalence of radiographic entheseal lesions at the hip and pelvic region was found. Irregularities and erosions were most frequently found, especially at os ischium. These new findings concerning structural entheseal lesions at the pelvis and hip region contributes to the knowledge of entheseal involvement in AS.

REFERENCES

[1] Voudouris KP, Sidiropoulos P, Vounotripidis P, Arvanitakis M. Enthesial fibrocartilage – bone interaction: a radiographic study of selected sites of nonsynovial peripheral enthesopathy. J Musculoskelet Neuronal Interact. 2003 Mar;3(1):89-100.

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SAT0358 EROSION MIGHT INCREASE PROBABILITY OF POSITIVE AXIAL SPONDYLOARTHRITIS (SPA) DIAGNOSIS IN PATIENTS WITH EARLY INFLAMMATORY BACK PAIN(IBP). A PROSPECTIVE 3.5 YEAR FOLLOW UP OF 133 PATIENTS

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Objectives: To analyse sensitivity, specificity and predictive values of inflammatory back pain (IBP), positive HLA B27 antigen, increased C-reactive protein (CRP), clinical features (CF) such as peripheral arthritis, dactylitis, psoriasis, uveitis, inflammatory bowel disease and enthesitis, familial history (FH) of SPA and assess probabilities to develop SPA. To evaluate the impact of chronic (T1) MRI lesions in early diagnosis of SPA

Methods: We prospectively collected and followed up 133 patients referred to our department with suspicion of SPA from September 2014 to March 2018. Data such as IBP, HLA B27 antigen, increased CRP, CF, FH and sacroiliac X-rays were collected for each patient. STIR and T1 MRI imaging were separately and independently evaluated by a rheumatologist and two radiologists. In case of disagreement, agreement between two readers was regarded as conclusive. MRI STIR sacroiliac joints (SI) images were assessed in a semi-qualitative way as follows: 1) strongly positive MRI imaging(SPMRI): patients with at least 2 highly specific bone marrow oedema(BME) lesions, easily classifiable as SPA. 2) Weakly positive MRI imaging (WPMRI): patients with at least 2 tiny BME lesions, suggestive, but not easily classifiable as SPA. 3) Clearly negative MRI imaging: patients without any of those features. T1 SI MRI images were assessed for erosion, fat metaplasia, backfill and sclerosis in a qualitative way as positive, if there were 1 or more than one, or negative, if there were none of those lesions.

Results: The average age in our study was 38.9 years. 47(35.3%) patients received diagnosis axial SPA. Radiographic sacroiliitis had 8 (17%). Sensitivity (St), specificity (Sf) and predictive positive values (PPV) were found as follows for each item (p<0.001): IBP: 83% St, 81.4% Sf, 71%PPV, positive HLA B27: 49% St, 80% Sf, 57.5% PPV, increased CRP: 40.4% St, 93% Sf, 76% PPV, and CF: 36.2% St, 91% Sf, 68%PPV. Multivariate logistic regression binary analysis applied to the group of patients with non-radiographic SPA showed Odds Ratios for positive diagnosis, 64.8 for IBP (p=0.000), 9.4 for increased CRP (p=0.005) and 11.9 for CF (p=0.006). For the total group of patients the Odds Ratios were as follows: 49.2 for IBP

(p=0.000), 10.3 for increased CRP (p=0.002) and 11.3 for CF (p=0.002). STIR MRI imaging assessment proved acceptable sensitivity (79%), excellent specificity (94%), and high PPV (88%) for SPMRI (p<0.001). WPMRI displayed better sensitivity (87%) nonetheless, specificity (67%) and PPV decreased (59%) (p<0.001). T1 MRI examination showed reasonable sensitivity (72%) excellent specificity (97%) and high PPV (85%) for erosion (p<0.001). Sensitivity for backfill was lower (32%), but specificity (100%) and PPV (100%) were excellent (p<0.001). Association, erosion and SPMRI pointed out a highly strong specificity (100%) and PPV (100%), however decreased sensitivity (51%) (p<0.001). Association, erosion and WPMRI significantly increased specificity (98%) and PPV (94%), although slightly decreased sensibility (64%)(p<0.001). Inter-observer agreement was higher for STIR MRI performance 0.70(95%CI0.59; 0.80), and lower for T1 0.47 (95% CI 0.35; 0.59).

Conclusion: At the onset, IBP, increased CRP, CF and IBD might be good indicators for selecting patients with a higher likelihood of positive diagnosis. Strongly positive SI MRI imaging is highly specific, brings acceptable sensibility and may be an excellent tool for early diagnosis of SPA. Weakly positive MRI STIR imaging might be helpful to detect patients with early SPA but lacks specificity. Early detection of erosion adds additional value to the STIR MRI reading, enhancing the specificity and increasing the probability of positive SPA diagnosis

Disclosure of Interests: None declared

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SAT0359 **THE AGREEMENT BETWEEN CT AND BONE SCINTIGRAPHY IN DETECTING OSTEOARTICULAR LESIONS IN SAPHO SYNDROME**

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Background: Computed tomography (CT) and ^{99m}Tc-MDP bone scintigraphy are commonly used to detect osteoarticular lesions and the typical bull's head sign of the anterior chest in the diagnosis of Sapho syndrome [1,2]. Since bone scintigraphy visualizes high radioactive uptake which basically indicates inflammatory lesions, and CT demonstrates the structural lesions in bones and joints, the findings of the two modalities usually do not correspond with each other [3,4]. However, little is known about the agreement between CT and bone scintigraphy on the findings of osteoarticular lesions in the patients of Sapho syndromes.

Objectives: To determine the agreement between CT and bone scintigraphy on the findings of osteoarticular lesions in Sapho syndrome.

Methods: A total of 68 patients who met the standard criteria of Sapho syndrome proposed by Kahn and Khan [5] with simultaneous (the interval <1 month) whole spinal CT scan and bone scintigraphy were recruited in Peking Union Medical College from 2015 to 2016. Every CT or scintigraphy result was evaluated by at least two specialists independently and blindly. CT scan and scintigraphy results of all patients were evaluated for whether the following osteoarticular structures were involved: the clavicle, sternoclavicular joints, sternocostal joints, sacroiliac joints and all vertebra. The respective involvement frequencies and the kappa value of agreement were calculated.

Results: Involved vertebra on the CT scan present as corner lesions or endplate lesions. Involved joints on the CT scan present as narrowed articular spaces or damaged articular facets. CT scan is more sensitive to detect the involvement of vertebra and sternocostal joints, but less sensitive for sternoclavicular and sacroiliac lesions than bone scintigraphy. Kappa value was calculated to assess the agreement between CT and bone scintigraphy (Table. 1). It ranges from 0.103 to 0.593 over different structures, indicating a slight to moderate agreement between the two tests.

Table 1. Agreement analysis between CT and bone scintigraphy

Structures/ Locations	Involvement frequency on CT	Involvement frequency on bone scintigraphy	Measure of agreement, κ value	P value	
Cervical vertebra	14/68	2/68	0.209	0.055	
Thoracic vertebra	29/68	15/68	0.103	0.343	
Lumbar vertebra	33/68	19/68	0.464	0.001	
Sacral vertebra	20/68	3/68	0.199	0.006	
Sternal angle	27/68	24/68	0.593	<	0.001
Clavicle	3/68	4/68	0.248	0.039	
Left sternoclavicular joint	27/68	36/68	0.274	0.019	
Right sternoclavicular joint	26/68	40/68	0.209	0.06	
Left sternocostal joint	40/68	6/68	0.024	0.683	
Right sternocostal joint	39/68	8/68	0.075	0.283	
Left sacroiliac joint	8/68	14/68	0.145	0.208	
Right sacroiliac joint	9/68	18/66	0.415	<	0.001

The two tests have comparable detection rates for the involvement of sternal angle with a highest kappa value (0.593). But there are huge differences at other structures with extremely low kappa value, which suggests the routine bone scintigraphy for diagnosis cannot replace a CT scan in terms of evaluating osteoarticular lesions.

Conclusion: The agreement between CT and bone scintigraphy was poor, indicating an importance of implementing routine CT tests in Sapho syndrome.

REFERENCES

[1] Sugimoto H, Tamura K, Fujii T. The SAPHO syndrome: defining the radiologic spectrum of diseases comprising the syndrome. EurRadiol 1998;8:800–6.
[2] Salles M, Olive A, Perez-Andres R, Holgado S, Mateo L, Riera E, et al. The SAPHO syndrome: a clinical and imaging study. ClinRheumatol 2011;30:245–9.
[3] Akisue T, Yamamoto T, Marui T, et al. Lumbar spondylodiscitis in SAPHO syndrome: multimodality imaging findings. J Rheumatol 2002;29 (5):1100–1.
[4] Depasquale R, Kumar N, Lalam RK, et al. SAPHO: What radiologists should know. ClinRadiol 2012;67(3):195–206.
[5] Kahn MF, Khan MA. The SAPHO syndrome. BaillieresClinRheumatol 1994; 8:333-62.

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Psoriatic arthritis

SAT0360 **REMISSION IN PSORIATIC ARTHRITIS: DEFINITION AND PREDICTORS**

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Background: No validated definition of remission exists for psoriatic arthritis (PsA) to date. We previously identified 17.6% of our patients as

Table 1. Weibull regression model for first remission, adjusted by gender and disease duration

Covariate	Multivariable full model		Multivariable reduced model	
HR 95% CI	p-value	HR 95% CI	p-value	
Age	1.02 (0.94, 1,11)	0.53		
Age at Diagnosis of PsA	0.98 (0.90, 1.07	0.7048		
BMI	0.97 (0.93, 1.00)	0.0824	0.96 (0.92, 0.99)	0.02
Axial	0.85 (0.85, 1.99)	0.2276		
NSAIDs	0.71 (0.46, 1.10)	0.1224		
DMARDs	1.14 (0.74, 1.75)	0.5592		
Biologics	1.69 (1.11, 2.57)	0.0150	1.73 (1.15, 2.61)	0.009
Diabetes	0.57 (0.24, 1.34)	0.1984		
Infection	1.60 (1.00, 2.56)	0.0518		
Depression/Anxiety	0.60 (0.31, 1.16)	0.1302		
Elevated ESR	0.68 (0.41, 1.13)	0.1400		
Gender (male vs female)	1.10 (0.72, 1.68)	0.6696	1.10 (0.73, 1.67)	0.64
Disease Duration	0.95 (0.87, 1.04)	0.2967	0.97 (0.95, 1.00)	0.05

CI – confidence interval; BMI-Body Mass Index; NSAIDs- nonsteroidal anti-inflammatory drugs; DMARDs- disease modifying anti-rheumatic drugs; ESR- erythrocyte sedimentation rate

having remission (no actively inflamed joints for 12 months). However, we did not take into account the other domains of the disease.

Objectives: We aimed to test the concept of remission as the absence of disease manifestations in PsA, determine the frequency of remission in our PsA cohort, and identify predictors for remission.

Methods: PsA patients followed between 2000 and 2015 were included. Patients are assessed at 6- to 12-month intervals according to a standard protocol, which includes the information necessary for minimal disease activity (MDA) assessment. Remission was defined as a visit that patients had no tender or swollen joints, no inflammatory back pain, no tender entheseal sites, minimal skin involvement with BSA<1%, patient pain on visual analog scale (VAS) score of <15, patient global disease activity VAS score of <20, Health Assessment Questionnaire (HAQ) score <0.5. We used imputation to determine remission status for each patient and did a sensitivity analysis including only visits with all information available. We fit a Weibull regression model with interval/right censored and left truncated data adjusted for sex and disease duration at baseline. Both multivariable full model and reduced model with Hazard Ratio (HR), 95% confidence interval (CI) estimates, and p-value are provided in Table1.

Results: 985 patients (57% males, mean age 47.4 yrs Table) were included. Using imputation 175 (18.2%) patients had remission at least once and 107 (10.9%) achieved sustained remission. In the sensitivity analysis, 109 (10.9%) patients achieved remission at least once, and 48 (4.9%) sustained remission for 2 consecutive visits. Using baseline variables with imputation, only BMI was significant and lowered the chance of remission. In the sensitivity analysis no baseline variables were significant. Using a model with time varying covariates higher BMI lowered the chance of remission, while use of biologics increases the chance of remission. Similar results were obtained with the sensitivity analysis. Only biologics predicted sustained remission.

Conclusion: We defined remission as a state of no clinical activity. Remission occurred in 18% of patients with PsA at least once and was sustained in 11%. High BMI reduced and use of biologic agents increased the chance of sustained remission.

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SAT0361 CARDIOVASCULAR RISK FACTORS AND COMORBIDITIES IN PATIENTS WITH PSA, RA AND THE GENERAL POPULATION

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Background: Patients with psoriatic arthritis (PsA) have previously been reported to have increased cardiovascular morbidity and mortality compared to psoriasis, rheumatoid arthritis (RA) and the general population (GP). Obesity has been linked to an increased risk of developing PsA and to be higher in patients with PsA compared to those with psoriasis, RA and GP. Furthermore, obese patients with PsA are more likely to have high disease activity and a reduced response to treatment. Few studies have reported on life style data in combination with traditional cardiovascular risk factors in patients with PsA compared to GP and RA in the same setting.

Objectives: We aimed to assess cardiovascular risk factors in patients with PsA compared to age- and sex matched RA and GP subjects.

Methods: We performed a cross-sectional study in the Western Sweden Health Care Region (WSHCR). All Individuals who were ≥18 and had at least one ICD-10 diagnosis for PsA (ICD-10 codes M073) or RA (ICD 10 codes M059 and M060), at a visit at any of three rheumatology clinics in the WSHCR during a two-year period (Jan 2015 through Feb 2017) were identified. From these we randomly selected PsA patients (n=1200) and RA patients (n=1246), with equal sex distribution and they were sent a postal questionnaire. Data for non-responders were limited to age and sex.

The questionnaire included questions on demographics, comorbidities, smoking, alcohol consumption, physical activity, medications and disease specific entities. The National public health survey from 2015, "Health on equal terms", which was sent to randomly selected citizens in Sweden aged 16-84, was used as a sex- and aged matched reference population with five controls matched per RA and PsA case. Obesity was defined according to WHO standards as BMI ≥30. Daily smoking, alcohol consumption (≥5 standard drinks of alcohol per week) and physical activity (≥3 hours per week) were also analyzed.

Results: Response rates were n=687 (57.3%) for PsA and n=742 (59.6%) for RA. After age- and sex matching there were 432 individuals with PsA, 431 with RA and 4314 matched subjects from the general population left for analyses. Mean age was 61.1 (SD 12.0) years and 42% males in all three groups. Patients with PsA were more frequently obese, compared to both GP (p<0.001) and RA (p=0.012). Smoking was more prevalent in RA and PsA than in GP. In addition, hypertension was more common in PsA compared to RA (p=0.044) and GP (p<0.001). Diabetes was also more prevalent in PsA than in GP (p=0.007), as was hyperlipidemia (p=0.039). Patients with PsA drank more often ≥5 standard drinks of alcohol per week than patients with RA did (p=0.046).

Conclusion: In PsA, obesity and comorbidities related to CVD were increased above what was seen for both RA compared to the GP. This highlights the need to address these partly modifiable factors in particular for patients with PsA

Disclosure of Interests: Anton Landgren: None declared, Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lily and Janssen, Mats Dehlin: None declared, Ulrika Bergsten: None declared, Eva Klingberg Grant/research support from: Unrestricted grant from Roche, Consultant for: Novartis, Speakers bureau: Speakers fee from Lilly

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Table 1. characteristics of PsA, RA and GP subjects

	PsA, n=432	RA, n=431	GP, n=4314	p-value (PsA vs RA)	p-value (RA vs GP)	p-value (PsA vs GP)
BMI, mean (std)	27.4 (4.8)	26.3 (4.6)	26.4 (4.3)	0.001	0.705	<0.001
BMI≥30, n(%)	98 (22.7)	69 (16.0)	739 (17.1)	0.012	0.555	<0.001
Daily smoker, n(%)	37 (8.6)	55 (12.8)	N/A	0.046	N/A	N/A
≥5 standard drinks of alcohol per week, n(%)	92 (21.3)	69 (16.0)	N/A	0.046	N/A	N/A
Physical activity ≥3 hours per week, n(%)	224 (51.9)	205 (47.6)	2354 (54.6)	0.208	0.005	0.289
Diabetes, n(%)	52 (12.0)	42 (9.7)	356 (8.3)	0.167	0.301	0.007
Myocardial infarction, n(%)	28 (6.5)	25 (5.8)	N/A	0.501	N/A	N/A
Stroke, n(%)	16 (3.7)	15 (3.5)	N/A	0.675	N/A	N/A
Gout, n(%)	25 (5.8)	19 (4.4)	N/A	0.199	N/A	N/A
Kidney disease, n(%)	9 (2.1)	11 (2.6)	N/A	0.814	N/A	N/A
Hypertension, n(%)	195 (45.1)	170 (39.4)	1350 (31.3)	0.044	<0.001	<0.001
Hyperlipidemia, n(%)	94 (21.8)	70 (16.2)	N/A	0.039	N/A	N/A

SAT0362 DEPRESSIVE SYMPTOMS ARE ASSOCIATED WITH A GREATER CARDIOVASCULAR RISK IN PATIENTS WITH PSORIATIC ARTHRITIS.

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Background: Cardiovascular (CV) events are the leading cause of death in patients with psoriatic arthritis (PsA) but current cardiovascular risk prevention strategies in these subjects appear to be inadequate. The prevalence of depressive symptoms, even in the absence of a diagnosed depressive disorder, is greater in patients with PsA than in the general population.

Objectives: The objective of the study is to evaluate the association between CV risk factors and depressive symptoms in a cohort of patients with PsA.

Methods: We enrolled consecutive patients with PsA (CASPAR criteria) without a diagnosis of major depression or history of major CV events. The presence of significant depressive symptoms was defined by the Hospital Anxiety and Depression Scale (HADS) for scores â‰¥ 8. The subjects were characterized by disease phenotype, duration and activity (according to the DAPSA index) and immunosuppressive, antihypertensive, glucose-, urate- and lipid-lowering therapy. In order to assess the prevalence of traditional CV risk factors, patients were characterized by BMI, waist and hip circumference, blood pressure (BP), smoking habits, physical activity and familiarity for myocardial infarction, lipid, glucose and serum urate. The predicted risk of CV events was calculated by the Framingham Risk Score (FRS), Atherosclerotic Cardiovascular Disease (ASCVD) score and Systematic COronary Risk Evaluation (HeartSCORE) risk charts.

Results: One-hundred patients with PsA were enrolled (males 47.0%, mean age 54.9±12.5 years, duration of illness 9.1±10.6 years) of which 20.6% were in remission, 43.3% in low disease activity, 28.8% in moderate disease activity and 10.3% in high disease activity according to DAPSA; 38% had significant depressive symptoms according to the HADS questionnaire. Patients without depressive symptoms had a higher mean age (57.8±12.3vs52.1±12.4 years, p=0.002) compared to patients with significant depressive symptoms but were comparable according to M:F ratio, duration and domains of psoriatic disease, PASI, DAPSA and immunosuppressive therapy. The presence of depressive symptoms was associated with a higher prevalence of obesity (34.2%vs9.7%, p=0.002) and â€œat riskâ€ abdominal circumference (84.2%vs61.3%, p=0.015) and hip/waist ratio (81.6%vs50.0%, p=0.002). Moreover, these patients had more frequently a history of active or previous smoking (63.2% vs.40.3%, p=0.027) but did not differ according to lifestyle, BP, antihypertensive therapy or familiarity with myocardial infarction compared to patients without depressive symptoms. With regard to the metabolic profile, patients with and without depressive symptoms did not differ in terms of exposure to lipid- and glucose-lowering drugs and fasting glucose values. However, patients with depressive symptoms had increased atherogenic risk index more frequently (76.3%vs54.8%, p=0.046) and greater LDL/HDL ratio (2.6±1.2vs2.1±0.7, p=0.017) and serum triglycerides values (135.1±53.7 mg/dl vs 108.8±58.6 mg/dl, p=0.046). The estimated risk of cardiovascular events at 10 years for traditional risk factors was greater for patients with depressive symptoms (FRS 16.8 ±12.3vs10.4 ± 6.0, p=0.003; HeartSCORE 1.9±1.5vs1.1±1.0, p=0.011; ASCVD 11.7±8.8vs7.8±8.4, p=0.05).

Conclusion: The presence of depressive symptoms is associated with a higher incidence of modifiable CV risk factors and a higher predicted risk of CV events in patients with PsA. Systematic research of depressive symptoms in patients with PsA could contribute to the correct assessment of CV risk, helping to implement more effective prevention strategies.

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SAT0363 ENTHESITIS BUT NOT DACTYLITIS CONTRIBUTES TO BURDEN OF DISEASE IN PSA PATIENTS: DATA FROM THE BEPAS REAL LIFE COHORT

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Background: Psoriatic arthritis (PsA) significantly impacts physical function and quality of life. Limited data are available to specifically evaluate the impact of the different disease domains such as arthritis, axial involvement, skin disease, enthesitis and dactylitis. The BEPAS cohort, a prospective daily life cohort of PsA patients allows to study the impact of enthesitis and dactylitis on disease activity, disability and quality of life in PsA patients.

Objectives: 1) to measure the impact of enthesitis and dactylitis on health-related quality of life in PsA patients in Belgium.

Methods: At the inclusion visit, a cross-sectional analysis of dactylitis and enthesitis was performed among 462 patients from the BEPAS cohort and impact of enthesitis and/or dactylitis was studied. Patients were evaluated for the demographics, clinical disease manifestations, disability, disease global assessment and inflammatory markers at inclusion. Differences of tested variables between patients with and without dactylitis and/or enthesitis were evaluated by T-test or Chi –square testing.

Results: 462 patients (273 males and 189 females) with a mean disease duration of 8.53 years (SD: 9.25yrs) were recruited in 17 BEPAS centers from December 2012 to July 2014. 111 patients had enthesitis and 63 patients had dactylitis at inclusion. 17 patients had both enthesitis and dactylitis. Results are summarized in the table below:

Conclusion: Enthesitis has a larger impact on Quality of Life and Health Status than dactylitis in PsA. Patients with enthesitis and dactylitis have higher joint scores but not higher markers of systemic inflammation than those without.

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Disclosure of Interests: Kurt de Vlam Consultant for: Pfizer Inc, Consultant for: Johnson & Johnson, Rik Lories Consultant for: Abbvie, Celgene, Eli-Lilly, Janssen, Merck, Novartis, Pfizer, UCB, Serge Steinfeld: None declared, Filip van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCB., Adrien Nzeusseu Toukap: None declared, Hermine Leroi Employee of: HL is a employee of MSD Belgium

	Enthesitis (n=111)	No Enthesitis (n=351)	Dactylitis (n=63)	No Dactylitis (n=399)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Disease duration	7.97 (8.87)	8.71 (9.37)	**5.12 (6.35)**	**9.07 (9.53)***
BMI	27.89 (4.94)	27.30 (4.95)	27.35 (4.97)	27.47 (4.94)
TJ78	**7.71 (10.34)**	**23.49)§**	**8.57 (11.99)**	**3.36 (5.89)§**
SJ76	**2.94(4.40)**	**1.86 (4.51)***	**6.33 (7.42)**	**1.45 (3.41)§**
BSA	**5.11 (13.22)**	**2.85 (6.67)***	3.18 (5.74)	3.44 (9.20)
CRP	4.88 (6.06)	6.17 (11.14)	6.04 (6.16)	5.82 (10.64)
PTGAVAS	**47.04 (19.88)**	**32.92 (23.49)§**	**42.54 (26.78)**	**35.33 (22.63)***
PGAVAS	**34.88 (21.23)**	**21.28 (20.12)§**	**39.2 (23.63)**	**22.16 (19.79)§**
DAS28CRP	**3.42 (1.14)**	**2.66 (1.06)§**	**3.55 (1.39)**	**2.73 (1.03)§**
DAPSA/DAREA	**24.11(15.66)**	**17.27 (16.66)***	**19.03 (16.65)**	**17.17(15.39)§**
MDA	**9/111 (8%)**	**164/349 (47%)§**	**10/63 (16%)**	**163/397 (41%)§**
HAQ	**0.93(0.60)**	**0.65 (0.63)§**	0.82 (0.69)	0.70 (0.62)
HAQ score status (<0,3)	**16/111 (14%)**	**135/359 (38%)§**	19/62 (30%)	132/399 (33%)
PSAQOL	**8.20(5.25)**	**5.17(5.27)§**	**7.24(6.46)**	**5.70(5.22)***
SF36 phys funct	**51.56(25.85)**	**65.39(27.13)§**	57.84(31.56)	62.69(26.73
SF36 role-physical	**44.15(27.28)**	**59.70(29.86)§**	51.81(33.90)	56.62(29.31)
SF36 role-emotional	**57.63(31.98)**	**72.22(25.33)§**	65.18(35.37)	69.30(30.40)
SF36 vitality	**40.51(19.03)**	**54.58(21.91)§**	50.06(24.70)	51.37(21.67)
SF36 mental health	**53.56(21.53)**	**66.41(20.73)§**	62.06(24.17)	63.51(21.22)
SF36 social funct	**60.69(25.16)**	**72.41(25.33)§**	65.72(26.19)	70.18(25.66)
SF36 bodily pain	**38.70(19.59**	**54.00(23.92)§**	45.19(24.07)	51.12(23.75)
SF36 general health	**40.42(18.33)**	**50.14(21.10)§**	48.72(21.68)	47.69(20.76)
SF36 Phys Comp Sum	**35.88(8.64)**	**41.32(10.42)§**	38.14(10.25)	40.33(10.27
SF36 Ment Comp Sum	**39.49(12.80)**	**46.44(12.77)§**	43.60(14.71)	45.00(12.84)

*p<0.05, §p<0.001

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SAT0364

EFFECT OF ACHIEVING DAPSA-LDA ON THE PROGRESSION OF BONE EROSION AND ENTHESIOPHYTES IN PATIENTS WITH PSORIATIC ARTHRITIS: A LONGITUDINAL HR-PQCT STUDY

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Background: Psoriatic arthritis (PsA) is characterized by structural bone damage with bone erosions and enthesiophytes. Whether achieving low disease activity (LDA) according to Disease Activity in PSoriatic **Arthritis (**DAPSA-LDA) limits progression of structural bone damage, as assessed by high resolution-peripheral quantitative computed tomography (HR-pQCT), is uncertain.
Objectives: To investigate the progression of structural bone abnormalities at the metacarpal head in patients with PsA over a 5-year period.
Methods: HR-pQCT examination was were performed in 60 PsA patients at baseline and after 5 years. Baseline-indexed image registration and slice matching were performed to acquire precisely matched baseline and follow-up volumes of interest (VOI) at the 2nd and 3rd metacarpal heads (MCH2 & 3). A semi-automated method was used to calculate bone erosion and enthesiophyte volume [1]. Erosion and enthesiophyte progression was defined as change exceeding the smallest detectable change (SDC). The primary objective of this study was to investigate the degree of bone erosion and enthesiophyte progression in PsA patients receiving routine care. Secondary objectives were to compare changes in bone erosion and enthesiophyte volume between patients who 1) received (TNFi group) or did not receive TNF inhibitor (non-TNFi group); 2) achieved or did not achieve sustained DAPSA-LDA(sDAPSA-LDA) at both baseline and 5-year.
Results: A total of 108 bone erosions and 99 enthesiophytes were detected at baseline. Three new bone erosions and no new enthesiophytes were evident at 5 years. Mean (±SD) individual bone erosion (4.23±4.15 mm^3) and enthesiophyte (3.39±2.30 mm^3) volume at baseline increased significantly (0.58±1.50 mm^3, p<0.001 for bone erosion; 0.47 ±0.76 mm^3, p<0.001 for enthesiophyte volume) over a 5-year period despite disease modifying anti-rheumatic drug being used in 88.3% of patients (Figure 1). The total bone erosion (7.83±7.41 mm^3) and enthesiophyte volume (5.59±5.46 mm^3) per patient also increased by 1.07±2.16 mm^3 (p<0.001) and 0.78±1.11 mm^3 (p= 0.001) respectively. 14 patients received TNFi throughout the 5-year period. Comparable changes in bone erosion and enthesiophyte volume were found between the TNFi and the non-TNFi groups. After 5 years, 26 (43%) patients achieved sDAPSA-LDA. Less erosion progression (12/51 [23.5%] vs 25/60 [41.7%], P=0.047) was observed those who did rather than did not achieve sDAPSA-LDA. Similarly, enthesiophyte volume change (0.28±0.67 vs 0.61±0.80 mm^3; P=0.048) and total enthesiophyte volume change (0.42±0.69 vs 1.05±1.29 mm^3; P=0.019) were lower in those who did rather than did not achieve sDAPSA-LDA.
Conclusion: Once DAPSA-LDA is achieved, it should be maintained for a long period so as to minimize progression of structural bone damage in patients with PsA.

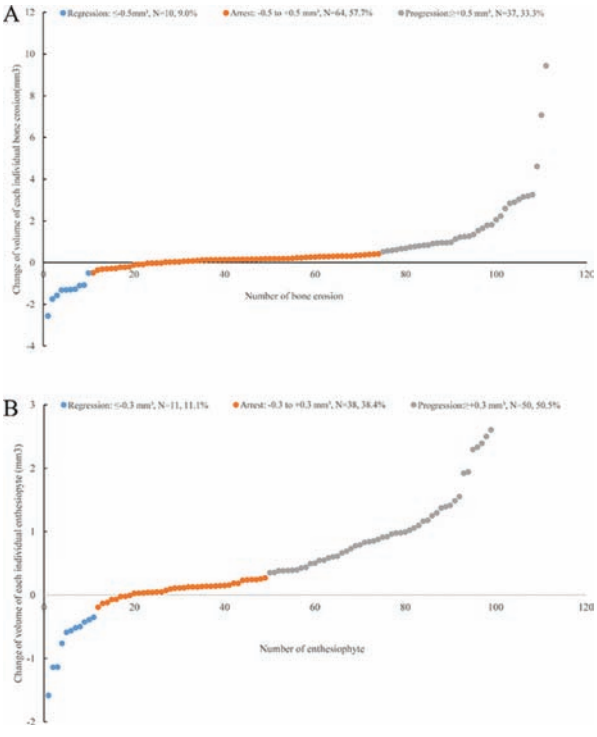


Figure 1. Probability plot of each individual bone erosion and enthesiophyte

REFERENCE

[1] EULAR 2018 (OP0132) & ACR 2018 (865)

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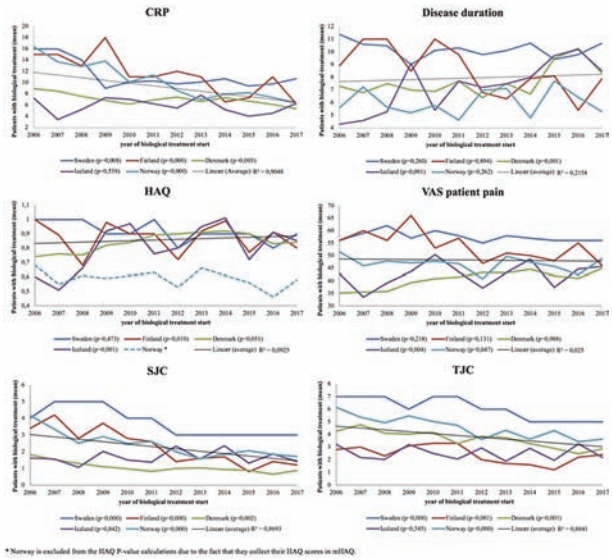
SAT0365

SECULAR CHANGES IN PSORIATIC ARTHRITIS PATIENTS STARTING FIRST COURSE OF BIOLOGIC THERAPIES – INFLAMMATORY HALLMARKS OF LESSER PROMINENCE: A NORDIC POPULATION-BASED COHORT STUDY

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disorder associated with skin and joint manifestations, several extra-articular symptoms, various comorbidities, and disability[1,2]. The emergence of tumour necrosis factor inhibitor (TNFi) therapy has dramatically changed the course of disease. Additional TNFi therapies (certolizumab pegol and golimumab) have been marketed, and recently ustekinumab has become available for PsA.
Objectives: To assess the use of biological agents (bDMARDs) in PsA from 2006-2017, using data from the Nordic Rheumatology registers.
Methods: Based on data from the registers DANBIO, ICEBIO, NOR-DMARD, ROB-FIN, and SRQ, PsA patients initiating bDMARDs or biosimilars, as a first or subsequent biological therapy were identified. Adalimumab, etanercept and infliximab were grouped as *1st generation therapies*; certolizumab pegol, golimumab were grouped as *2nd generation therapies* and biosimilar treatments were grouped. Treatments with ustekinumab were also identified. Pearson correlation tests were calculated and p>0.05 were considered significant. $R^2 \approx 1$ showed a strong correlation between the baseline characteristics.
Results: A total of 18,089 treatment initiations were identified (DANBIO 4,361, ICEBIO 449, NOR-DMARD 1,948, ROB-FIN 1,069, SRQ 10,262). 53.68% of the patients were female. Overall, 6,198 patients initiated *1st generation therapies*, 1,447 *2nd generation therapies*, 1,353 biosimilars and 52 ustekinumab, as their first course of bDMARDs. Initiations of second or subsequent bDMARDs were 4,560, 1,630, 2,176 and 376 patients, respectively. The total of first course bDMARD initiators increased significantly from 2006-2017 (p<0.001), similar to patients switching therapy (p<0.001). Ustekinumab was primarily used as a second or subsequent bDMARD. The figure shows the secular trends of baseline characteristics collected from the Nordic countries with the subcategories of CRP, disease duration, HAQ score, VAS patient pain, swollen joint count and tender joint count from 2006-2017. All five countries showed trends of decreasing CRP, SJC and TJC values over time. Other parameters only showed slight or no correlation.

Figure: *biological treatment initiators by baseline characteristics from 2006-2017*



*Norway is excluded from the HAQ P-value calculations due to the fact that they collect their HAQ scores in mHAQ.

Conclusion: Across the Nordic countries the prescription pattern for biological therapies for PsA has changed significantly over time. The decreasing levels of both CRP scores and SJC suggest that PsA patients who initiate bDMARD treatment have changed towards a less active inflammatory phenotype from 2006-2017. Collaboration across registers will allow for robust assessment of the uptake of newer biological therapies. Overall the number of prescribed therapies increased during the observational period, indicating a previously unmet need for biological therapies in the Nordic population.

REFERENCES

[1] Ballegaard C, Kristensen L. E, et al. Impact of comorbidities on tumour necrosis factor inhibitor therapy in psoriatic arthritis: a population-based cohort study. Arthritis. 2018;70(4):592-599.

[2] Kristensen L. E, Jørgensen T. S, et al, Societal costs and patients' experience of health inequities before and after diagnosis of psoriatic arthritis: a Danish cohort study. Ann Rheum Dis. 2017;(76):1495-1501.

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SAT0366 GENDER DIFFERENCES IN PSORIATIC ARTHRITIS – IMPACT ON TUMOR NECROSIS FACTOR INHIBITORS PERSISTENCE AND RESPONSE

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Background: The impact of gender on tumor necrosis factor inhibitors (TNFi) effectiveness has been poorly studied in Psoriatic Arthritis (PsA) patients.

Table 1. Baseline characteristics of PsA patients from Reuma.pt, treated with a 1st TNFi, according to gender.

Characteristics		Population (n=750)	Female (n=377)	Male (n=373)	p-value
Age at 1st TNFi, years (mean ± sd)		47.6 ± 11.6	48.5 ± 11.7	46.7 ± 11.5	0.030†
Obese (BMI>30Kg/m^2), n (%)		104 (25.2%)	64 (30.9%)	40 (19.5%)	0.008†
Clinical subtype, n (%),	Symmetric polyarthritis	401 (60.6%)	228 (68.9%)	173 (52.3%)	<0.001†
	Arthritis distal interphalangeal joins	29 (4.4%)	9 (2.7%)	20 (6.0%)	
	Asymmetric oligoarthritis	95 (14.3%)	49 (14.8%)	46 (13.9%)	
	Mutilating arthritis	9 (1.4%)	3 (0.9%)	6 (1.8%)	
	Predominant axial	128 (19.3%)	42 (12.7%)	86 (26.0%)	
Years since diagnoses until 1st TNFi (mean ± sd)		6.6 ± 6.8	7.1 ± 7.0	6.0 ± 6.6	0.033†
Swollen joints (mean ± sd)		5.3 ± 5.5	6.2 ± 6.3	4.4 ± 4.4	<0.001†
Tender joints (mean ± sd)		9.7 ± 9.6	11.9 ± 10.4	7.3 ± 8.1	<0.001†
ESR mm/1st h (mean ± sd)		31.8 ± 25.3	35.8 ± 26.0	27.1 ± 23.8	<0.001†
MASES (mean + sd)		2.0 ±3.2	3.0 ± 3.9	1.1 ± 2.1	<0.001†
DAS28 (mean + sd)		4.9 ± 1.4	5.2 ± 1.3	4.5 ± 1.4	<0.001†
DAPSA (mean ± sd)		29.9 ± 15.4	32.5 ± 16.5	26.7 ± 13.3	0.001†
HAQ-DI (mean ± sd)		1.13 ± 0.68	1.34 ± 0.66	0.90 ± 0.63	<0.001†
Concomitant csDMARDs, n (%)		505 (67.6%)	276 (73.6%)	229 (61.6%)	<0.001†
Concomitant corticosteroids, n (%)		253 (33.9%)	157 (41.9%)	96 (25.8%)	<0.001†

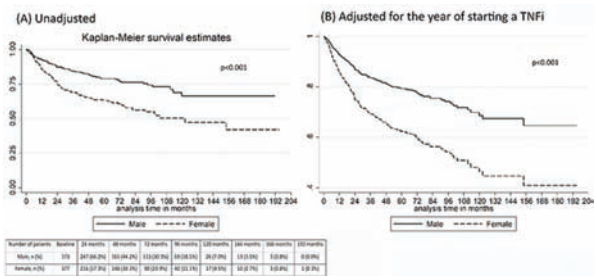


Figure 1. First-line TNFi persistence of PsA patients from Reuma.pt, according to gender and adjusted for the year of staring a TNFi.

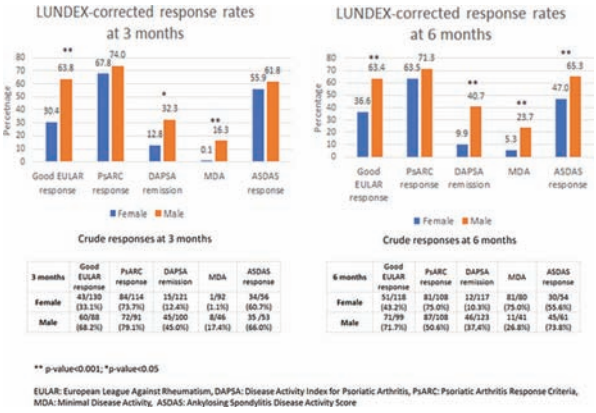


Figure 2. First-line TNFi LUNDEX-corrected responses of PsA patients from Reuma.pt, according to gender.

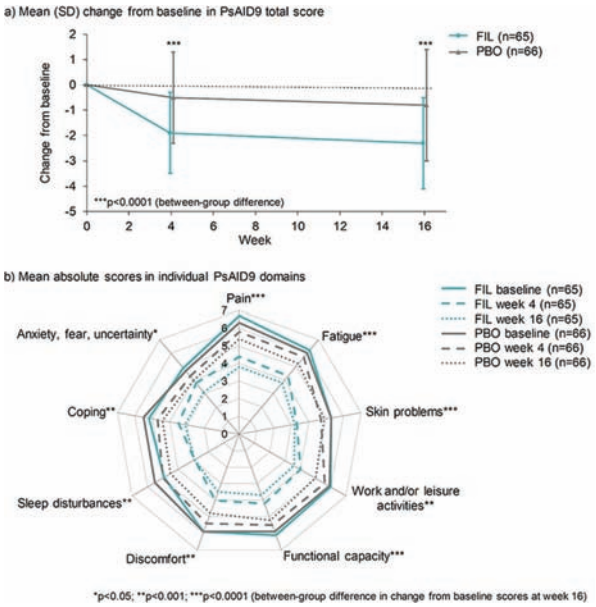
Objectives: To study gender differences in persistence and response of 1st TNFi in PsA patients.
Methods: PsA patients prospectively followed at the Rheumatic Diseases Portuguese Registry (Reuma.pt), treated with a 1st TNFi, between 2001 and 2016. Drug retention assessed by Kaplan-Meier survival analysis and Cox models, adjusted for the year of starting a TNFi. Response rates measured by EULAR response, DAPSA remission, MDA and ASDAS response, applying LUNDEX method, were compared between genders. Baseline predictors of discontinuation and response were identified (Cox and logistic regression models).
Results: 750 PsA patients, mean age 47.6 (± 11.6) years and 50.3% (n=377) females. PsA females showed significantly different baseline PsA disease characteristics in comparison with males and had more severe peripheral disease activity (Table 1). The overall TNFi survival rate for females was also significantly lower when compared with males (Figure 1). Additionally, females experienced lower rates of response at 3 and 6 months (Figure 2). Female gender was further identified as an independent predictor factor of worse persistence and showed a lower chance of good EULAR response.
Conclusion: PsA females from Reuma.pt have distinct PsA features and worse persistence and response to a 1st TNFi in comparison with males. This might be related to gender dependent inflammatory pathways and was independent of baseline disease activity.
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SAT0367

PSAID9 IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS TREATED WITH FILGOTINIB VS PLACEBO: RESULTS FROM EQUATOR, A RANDOMIZED, PHASE 2 STUDY

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Background: Filgotinib (FIL) is an oral, selective Janus kinase 1 inhibitor that, compared with placebo (PBO), significantly improved patient-reported outcomes in active psoriatic arthritis (PsA) in the phase 2 EQUATOR randomized controlled trial (RCT; NCT03101670) [1]. PsA Impact of Disease (PsAID) is a validated, EULAR-developed, PsA-specific questionnaire for measurement of health–related quality of life (HRQoL) [2]. PsAID is less complex than generic HRQoL tools, such as the 36–Item Short Form Survey (SF–36). To our knowledge, this is the first RCT reporting efficacy results using PsAID9.
Objectives: To determine the effect of FIL vs PBO on PsAID9 in participants of EQUATOR.
Methods: EQUATOR was a multicenter, double-blind study in which patients were randomized 1:1 to FIL 200 mg or PBO once daily for 16 weeks [1]. HRQoL was assessed at weeks 4 and 16 with PsAID9 (total and individual domain scores [each scored 0–10]) and, for comparison, with the Physical Component Summary (PCS) and Mental Component Summary (MCS) of SF-36. Higher PsAID scores correspond to greater impact of PsA [2]. Analysis of covariance was used to compare outcomes between groups.
Results: There were 131 participants in EQUATOR (FIL: n=65; PBO: n=66). Mean (standard deviation [SD]) age was 49 (12.2) and 50 (10.9) years and mean (SD) baseline PsAID9 scores were 5.8 (1.6) and 5.7 (2.0) for FIL and PBO, respectively. Effects of FIL on PsAID9 and SF-36 scores were observed as early as week 4. FIL significantly improved PsAID9 total scores vs PBO; at week 16, PsAID9 total scores were 3.5 (2.0) for FIL and 4.9 (2.2) for PBO. Mean change (SD) from baseline at week 16 was –2.3 (1.8) vs
–0.8 (2.2), respectively (**Figure 1a**); least-squares (LS) mean of group difference (95% confidence interval) was –1.48 (–2.12, –0.84), p<0.0001. At week 16, significant improvements were observed in all nine individual



PsAID9 domains for FIL vs PBO, including pain (p<0.0001; **Figure 1b**). A significant improvement in SF–36 PCS, but not in MCS, with FIL vs PBO was observed. The mean change (SD) from baseline in PCS at week 16 was 7.4 (6.6) vs 2.4 (6.6) for FIL vs PBO, respectively (LS mean of group difference 4.67 [2.58, 6.76], p<0.0001).

Conclusion: Compared with PBO, FIL significantly improved disease impact in patients with active PsA, as measured by the PsA-specific PsAID9 total score and individual domain scores. Significant improvement in SF-36 PCS score was also seen with FIL.

REFERENCE

[1] Mease P, et al. Lancet 2018;392:2367–77. 2. Orbai AM, et al. J Rheumatol 2018;doi: 10.3899/jrheum.181077.

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SAT0368 GO-DACT: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLED PROOF-OF-CONCEPT TRIAL OF GOLIMUMAB PLUS METHOTREXATE (MTX) VERSUS MTX MONOTHERAPY, IN IMPROVING DACTYLITIS, IN MTX NAÏVE PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) dactylitis is associated with an increased risk of erosions and higher disease activity. Dactylitis treatment strategies are however controversial due to the absence of evidence from randomized controlled trials studying dactylitis as a primary outcome.

Objectives: To assess the efficacy of golimumab plus MTX versus placebo plus MTX for active dactylitis in PsA patients, in a phase 3b trial.

Methods: GO-DACT was a proof-of-concept multicentric, investigator-initiated randomized, double-blind, placebo-controlled, parallel-design trial, conducted in 13 Portuguese Rheumatology Centers. PsA patients, naïve for MTX and biologic disease modifying anti-rheumatic drugs (bDMARDs), with active dactylitis, were randomly allocated to either golimumab in combination with MTX or MTX monotherapy. The primary endpoint was the change from baseline in the dactylitis severity score (DSS) assessed at week 24. Key secondary endpoints included DSS response and the magnetic resonance imaging (MRI) dactylitis score, as well as composite indexes of PsA activity.

Results: 44 patients were centrally randomized, 21 to golimumab plus MTX and 23 to placebo plus MTX, for 24 weeks, and 1 patient from each arm dropped out. Due to favorable results on a planned interim analysis recruitment was halted. The median MTX dose in the golimumab plus MTX group was 15mg/week and in the MTX monotherapy group 20mg/week. The median baseline DSS was 6 in each arm. Patients treated with golimumab plus MTX experienced significantly greater improvements in the DSS at week 24 (median change of 5) as compared to the MTX group (median change of 2) (p=0.026). At week 24, 12 (60.0%) patients treated with golimumab plus MTX and 4 (18.2%) with MTX, achieved the DSS70 response (p<0.05). Significant differences were also observed in the median changes from baseline to week 24 in MRI dactylitis score, Disease Activity Score 28 (DAS28), Disease Activity Index for PsA (DAPSA), PsA Disease Activity Score (PASDAS) and Target Nail Psoriasis Severity Index (tNAPSI), favoring the golimumab and MTX association arm. Likewise, higher proportions of patients treated with golimumab plus MTX achieved DSS50 responses and the American College of Rheumatology 20/50 responses, at week 24. There were no new safety issues for golimumab during this trial.

Conclusion: GO-DACT suggests additional benefits from the combination of golimumab and MTX as first-line bDMARD therapy versus MTX monotherapy, in the treatment algorithm of PsA active dactylitis.

REFERENCE

Not applicable

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SAT0369 SECUKINUMAB IMPROVES GRAPPA-OMERACT CORE DOMAINS OF PSORIATIC ARTHRITIS REGARDLESS OF PREVIOUS EXPOSURE TO A TNF INHIBITOR

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Background: Secukinumab, a fully human interleukin 17 (IL-17A) monoclonal antibody, has demonstrated efficacy in psoriatic arthritis (PsA) in phase 3 clinical trials.[1–4] The PsA core domain set, updated by the

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and endorsed by Outcome Measures in Rheumatology (OMERACT), aims to improve and standardize the assessment of PsA outcomes.[5]

Objectives: To report the efficacy of secukinumab vs placebo across individual PsA core domains at week 16 in patients naive to tumor necrosis factor (TNF) inhibitors or who were inadequate responders (TNF-IR), using pooled data from 4 phase 3 FUTURE studies.

Methods: Patients with active PsA participated in the phase 3 FUTURE 2, 3, 4, and 5 trials.[1–4] Data were pooled for secukinumab 150 mg (load vs. no load), 300 mg, or placebo at the end of the 16-week double-blind period. Efficacy was assessed using multiple clinical and laboratory measures to evaluate the updated GRAPPA-OMERACT PsA core domain set for disease activity, pain, function, and quality of life (Table 1).

Results: A total of 2049 patients were included (1436 TNF naive and 613 TNF-IR). Baseline demographics and disease characteristics were broadly similar in all treatment groups. Efficacy results for the core inner circle domains are shown in Table 1.

Table 1. Pooled Efficacy Results Across GRAPPA-OMERACT PsA Core Domains by TNF Inhibitor Status

		Improvement in Patients With PsA at Week 16 in FUTURE Trials							
		Secukinumab 300 mg n = 461		Secukinumab 150 mg n = 572		Secukinumab 150 mg, no load n = 335		Placebo n = 681	
	TNF inhibitor status	Naive	TNF-IR	Naive	TNF-IR	Naive	TNF-IR	Naive	TNF-IR
PsA Core Domains	Measures and Improvement Definitions, % (n/m)								
Musculoskeletal disease activity	SJC66, ≥ 50% improvement	73.7 (233/316)	57.9 (84/145)	64.7 (258/399)	56.1 (97/173)	65.2 (159/244)	44.0 (40/91)	42.8 (204/477)	31.4 (64/204)
	SJC66 resolution	41.5 (131/316)	18.6[a] (27/145)	29.3 (117/399)	22.0 (38/173)	25.0 (61/244)	18.7[a] (17/91)	16.8 (80/477)	12.3 (25/204)
	TJC68, ≥ 50% improvement	67.1 (212/316)	49.7 (72/145)	56.9 (227/399)	47.4 (82/173)	58.6 (143/244)	44.0 (40/91)	32.5 (155/477)	22.1 (45/204)
	TJC68 resolution	24.4 (77/316)	9.0[a] (13/145)	15.8 (63/399)	11.6 (20/173)	9.4[a] (23/244)	9.9[a] (9/91)	5.7 (27/477)	5.9 (12/204)
	LEI resolution	56.9 (111/195)	44.9 (40/89)	46.4 (115/248)	40.5 (51/126)	44.8 (60/134)	32.8[a] (20/61)	32.3 (94/291)	22.1 (31/140)
	LDI resolution	63.2 (74/117)	49.1 (28/57)	48.0 (60/125)	49.2 (31/63)	45.0 (50/111)	40.0[a] (12/30)	32.9 (55/167)	26.6 (17/64)
Skin disease activity	PASI 75	69.6 (103/148)	72.7 (48/66)	58.8 (130/221)	52.9 (45/85)	57.9 (77/133)	47.4 (18/38)	10.8 (26/241)	9.4 (8/85)
	IGA mod 2011 0/1	51.4 (76/148)	54.5 (36/66)	44.3 (98/221)	31.8 (27/85)	33.1 (44/133)	28.9 (11/38)	8.3 (20/241)	5.9 (5/85)
Pain	PsA pain VAS, ≥ 3-point improvement[b]	72.2 (228/316)	58.6 (85/145)	72.4 (289/399)	65.9 (114/173)	72.1 (176/244)	58.2 (53/91)	51.8 (247/477)	41.2 (84/204)
Patient global	PGA, mean change from BL (n)[b,c]	−21.11 (305)	−19.64 (135)	−17.38 (383)	−16.08 (162)	−17.84 (237)	−13.48 (82)	−7.46 (446)	−5.13 (171)
Physical function	HAQ-DI, MCID = 0.3	60.4 (191/316)	49.7 (71/143)	49.4 (197/399)	48.8 (84/172)	54.9 (134/244)	41.8 (38/91)	36.3 (173/476)	26.0 (53/204)
HRQOL	SF-36 PCS, MCID ≥ 2.5	68.4 (216/316)	60.7 (88/145)	61.9 (247/399)	53.8 (93/173)	65.6 (160/244)	50.5 (46/91)	45.3 (216/477)	34.3 (70/204)
	SF-36 MCS, MCID ≥ 2.5	49.4 (156/316)	46.2[a] (67/145)	51.1 (204/399)	47.4 (82/173)	51.2 (125/244)	45.1[a] (41/91)	42.1 (201/477)	36.3 (74/204)
Fatigue	FACIT-Fatigue, mean change from BL (n)[b,c]	6.07 (305)	6.67 (137)	5.36 (383)	5.13 (163)	5.67 (237)	4.78 (82)	2.01 (450)	1.21 (171)
Systemic inflammation	Elevated CRP (> 10 mg/L) resolution	78.6 (55/70)	62.2 (28/45)	67.1 (57/85)	51.8 (29/56)	79.6 (39/49)	44.8 (13/29)	38.3 (44/115)	21.2 (11/52)

BL, baseline; CRP, C-reactive protein; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; HRQOL, health-related quality of life; IGA, Investigator's Global Assessment; IR, inadequate responder; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; MCID, minimal clinically important difference; MCS, mental component summary; PASI 75, 75% reduction in the Psoriasis Area and Severity Index; PCS, physical component summary; PGA, Patient Global Assessment; PsA, psoriatic arthritis; SJC66, swollen joint count based on 66 joints; TJC68, tender joint count based on 68 joints; TNF, tumor necrosis factor; VAS, 100-mm visual analog scale.
All *P* values vs placebo were $P < .05$ except where indicated. All *P* values were for hypothesis generation. No adjustment was made for multiple comparisons. [a] P = not significant. [b] No MCID has been defined in PsA. [c] Least-squares mean change from BL; n is the number of patients with measures at both BL and week 16 visit.

Conclusion: Secukinumab demonstrated efficacy compared with placebo across GRAPPA-OMERACT PsA core domains in the phase 3 clinical trials program, regardless of prior TNF inhibitor use.

REFERENCE

[1] McInnes IB, et al. *Rheumatology*. 2017;56:1993-2003; 2. Nash P, et al. *Arthritis Res Ther.* 2018;20:47; 3. Kivitz A, et al. PANLAR 2018 [abstract 364]; 4. Mease PJ, et al. Ann Rheum Dis. 2018;77:890-897; 5. Orbai AM, et al. Ann Rheum Dis. 2017;76:673-680.

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SAT0370 IMBALANCE OF TH17 AND REGULATORY T CELLS IN PATIENTS WITH PSORIATIC ARTHRITIS AND RE-BALANCE BY LOW-DOSE IL-2

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Background: Psoriatic arthritis (PsA) is an T lymphocytes-mediated inflammatory condition [1]. Although regulatory T cells (Tregs) isolated from blood and psoriatic skin have been showed a functional deficiency in suppressing effector T-cells in PsA[2], absolute quantitative status of peripheral Treg or Th17 cells is still unclear. On the other hand, recent studies have revealed that low-dose IL-2 alleviate**s** some of autoimmune disease activity by upregulating Treg cells [3, 4], which is expected to control the development of PsA.

Objectives: To assess the absolute numbers of peripheral lymphocyte subpopulations and the efficacy and safety of low-dose IL-2 therapy in PsA patients.

Methods: Total 95 PsA patients and 106 age-and sex-matched healthy controls were recruited. Of them, 22 cases received the treatment of low-dose IL-2 at 0.5 million IU per day for 5 days subcutaneously. The absolute numbers of lymphocyte subgroups and $CD4^+T$ subsets in peripheral blood were measured by flow cytometry. The clinical manifestations and laboratory indicators as well as the levels of peripheral lymphocyte and $CD4^+T$ subsets were compared before and after the treatment.

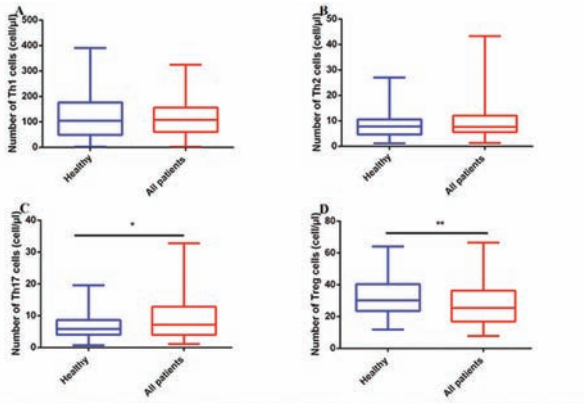


Figure 1: Comparison of absolute numbers of peripheral $CD4^+T$ cell subsets between PsA patients (n=95) and health controls (n=106). The level of Th17 was significantly increased while that of Tregs reduced in patients with PsA. Data were calculated and compared with Mann-Whitney *U* test. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$.

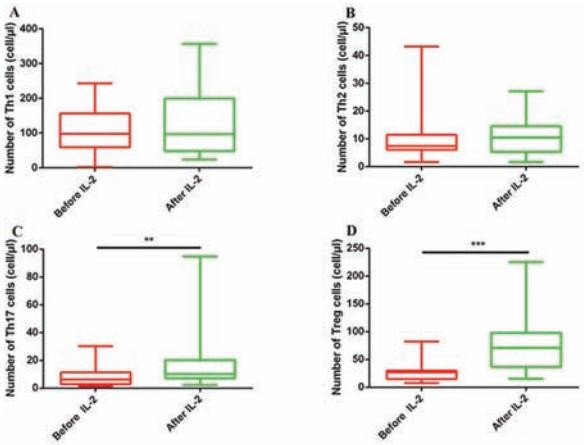


Figure 2: Comparative analysis the changes of $CD4^+T$ cell subsets in patients with PsA between pre- and post-treatment (n=22). Low-dose IL-2 markedly raised the absolute numbers of Treg and moderately increased the level of Th17 cells in PsA patients. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$.

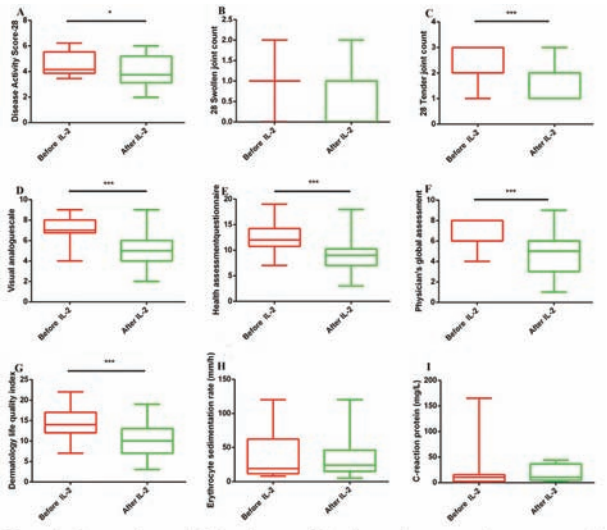


Figure 3: Comparative analysis the changes of PsA signs and symptoms between pre- and post-treatment (n=22). Data were presented as median(range) and calculated and compared with Mann-Whitney *U* test.(A-I) show that low-dose IL-2 treatment provided a significant decrease in 28 tender joint count, DAS28-ESR index, VAS index, PHGA index, DLQI index and HAQ index. $*P < 0.05$, $***P < 0.001$.

Results: Notably, the absolute numbers of lymphocyte subpopulations in peripheral blood such as NK, $CD4^+T$, Th17 and Tregs in PsA patients were lower than those of healthy controls ($P<0.05$). The absolute number of Treg was significantly and negatively correlated with the levels of disease indicators, including DAS28, the number of tender joints, visual analogue scale, physician's global assessment, dermatology life quality index, and health assessment questionnaire ($P<0.05$). After low-dose IL-2 treatment, compared with the baselines, there was a significant increase in the absolute numbers of NK ($P<0.05$), $CD4^+T$ ($P<0.01$), Th17 ($P<0.01$) and Treg cells ($P<0.001$). Interestingly, IL-2 markedly raised the level of Tregs in PsA patients even higher than that of healthy donors ($P<0.001$), leading to re-balance of Th17 and Tregs. Further, low-dose IL-2 treatment rapid reduced the disease activity such as DAS28, the number of tender joints, visual analogue scale, physician's global assessment, dermatology life quality index, and health assessment questionnaire ($P<0.05$).

Conclusion: Patients with PsA had an imbalance between pro- and anti-inflammatory cells, particularly the reduction of the absolute number of Tregs. Low-dose IL-2 combination treatments restored the decreased number of Treg cells and lowered disease activity indicators of these patients without over-treatment and evaluable side effect. Further studies are needed to evaluate the long-term immunoregulatory ability of IL-2 treatment.

REFERENCES

[1] Gossec L, Coates LC, de Wit M, *et al.* Management of psoriatic arthritis in 2016: a comparison of EULAR and GRAPPA recommendations[J]. Nature reviews Rheumatology, 2016, 12(12):743-750.doi:10.1038/nrrheum.2016.183.

[2] Szentpetery A, Heffernan E, Gogarty M, *et al.* Abatacept reduces synovial regulatory T-cell expression in patients with psoriatic arthritis[J]. Arthritis research & therapy, 2017, 19(1):158.doi:10.1186/s13075-017-1364-3.

[3] Jeffery HC, Jeffery LE, Lutz P, *et al.* Low-dose interleukin-2 promotes STAT-5 phosphorylation, Treg survival and CTLA-4-dependent function in autoimmune liver diseases[J]. Clinical and experimental immunology, 2017, 188(3):394-411.doi:10.1111/cei.12940.

[4] Miao M, Hao Z, Guo Y, *et al.* Short-term and low-dose IL-2 therapy restores the Th17/Treg balance in the peripheral blood of patients with primary Sjogren's syndrome[J]. Annals of the rheumatic diseases, 2018, 77 (12):1838-1840.doi:10.1136/annrheumdis-2018-213036.

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SAT0371

CARDIOVASCULAR IMPACT OF HYPERURICEMIA IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Inflammatory joint diseases (IJD) such as psoriatic arthritis (PsA) have an increased risk of cardiovascular disease (CVD) since inflammation plays a pivotal role in the pathogenesis of coronary artery disease (CAD), heart failure (HF) and atrial fibrillation (Afib)[1]. Ischemic heart disease and HF are the main causes of the increased and premature mortality among patients with IJD[2].

Additionally, patients with PsA have a prevalence of hyperuricemia (HUC) of 32%, 3 times greater as compared with the general population, which may be related to increased cell turnover as well as the release of pro-inflammatory cytokines and tumor necrosis factor[3].

Prolonged exposure to high levels of uric acid (UA) has been shown to result in oxidative stress causing endothelial dysfunction, ionic channel changes, atrial and ventricular remodeling[4]. There is experimental evidence indicating that uric acid stimulates renin-angiotensin-aldosterone system (RAAS), and it is associated with an increase in cardiac tissue xanthine oxidase activity, all of which induce cardiomyocyte hypertrophy, myocardial oxidative stress, interstitial fibrosis and impaired diastolic relaxation[5].

Objectives: The aim of this study is to assess the correlation of HUC and the clinical expression of CVD in patients with PsA.

Methods: This is a retrospective cohort study using the 2016 National Inpatient Sample (NIS) of adults diagnosed with PsA based on ICD-10 codes, to detect the prevalence of cardiovascular (CV) conditions such as CAD, Afib, and HF with preserved ejection fraction (HFpEF) in patients with concomitant HUC or gout versus age matched controls. Chi square was used for point prevalence and multivariate linear regression adjusted for age, gender, race, CAD, diabetes mellitus, HTN, hyperlipidemia (HLD), smoking, chronic kidney disease (CKD) and Charlson comorbidity index for prevalence odds ratio (POR). We used STATA-15 for statistical analysis.

Results: We identified 37,315 patients with PsA, of whom 2,165 had concomitant HUC or gout (5.80%). Mean age was 61 years, 57% were females. Our results showed that PsA with concomitant HUC or gout compared to PsA without HUC or gout was associated with a higher rate of Afib (17.8% vs 6.1%, $p < 0.001$), CAD (35.1% vs 19.4%, $p < 0.001$) and HFpEF (7.2% vs 3.1%, $p < 0.001$). Furthermore, patients with PsA and HUC/gout appeared to have more risk of developing Afib (POR 1.79; 95%-CI 1.31-2.45; $p < 0.001$) and HFpEF (POR 1.56; 95%-CI 1.08-2.26; p=0.018), compared to patients with normal uric acid after multivariate-adjustment for risk factors. No statistical difference in CAD was identified between the two groups (POR 1.21; 95%-CI 0.94-1.55; p=0.131) after multivariate linear regression adjustment for confounders.

Conclusion: This study showed that HUC is independently associated with CVD, mainly with Afib and HFpEF in patients with PsA. It remains to be seen if a treat to target approach with normalization of UA in patients with PsA will result in improved CV outcomes. We believe that our findings merit further investigation and that this study adds weight to the hypothesis of UA as a potential risk factor for CVD. Prospective studies are needed to establish the role of serum uric acid level as a biomarker or predictor for CVD, including CAD, Afib and HFpEF in patients with PsA.

REFERENCES

[1] Manolis AS, et al. International Reviews of Immunology. 2018; 20:1-22.
[2] Braun J, et al. Dtsch Arztebl Int. 2017; 114(12):197-203.
[3] AlJohani R, et al. The Journal of Rheumatology. 2018; 45(2):213-217.
[4] Gonzalez-Juanatey C, et al. Arthritis & Rheumatism. 2007; 57(2):287-293.
[5] Yu M, et al. Journal of Hypertension. 2010; 28(6):1234-1242.

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SAT0372 CHANGE OF SUBCLINICAL ATHEROSCLEROSIS AFTER FIVE YEARS ANTI-TNF TREATMENTS IN PSORIATIC ARTHRITIS

Abdulsamet Erden[1], Uğur Canpolat[2], Oğuz Abdullah Uyaroğlu[3], Cem Çöteli[2], Levent Kiliç[1], Ali Akdoğan[1], Umut Kalyoncu[1], Omer Karadag[1], Ali İhsan Ertenli[1], Sedat Kiraz[1], Kudret Aytemir[2], Şule Apraş Bilgen[1]. *[1]Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey; [2]Hacettepe University Faculty of Medicine, Department of Cardiology, Ankara, Turkey; [3]Hacettepe University Faculty of Medicine, Department of Internal Medicine, Ankara, Turkey*

Background: Although cardiovascular (CV) diseases are very common in inflammatory arthritis like psoriatic arthritis (PsA), long-term impact of medication on CV outcomes is lacking.
Objectives: The aim of our study was to evaluate the long-term effects of anti-TNF-a drugs on subclinical atherosclerosis assessed by the flow-mediated dilatation (FMD) and carotid intima media thickness (IMT).
Methods: A total of 30 patients with PsA according to classification of psoriatic arthritis (CASPAR) criteria1 and 28 healthy controls were enrolled in this cross-sectional study between June 2011-July 2012. 22 out of 30 PsA patients completed the study. Demographic data (sex, age), PsA and psoriasis duration, joint pattern (monoarthritis, oligoarthritis or polyarthritis) and other PsA involvements (nail, enthesis, dactilytis) were noted. Tender joint count, swollen joint count and disease activity score (DAS)-28 were used for joint activity assessment. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were used for acute phase reactants. Sex and age matched healthy controls were selected as the control group for this study. Flow mediated dilatation (FMD) from brachial artery and carotid intima media thickness (IMT) were measured by an experienced cardiologist both at initial and 5-year follow-up visits.
Results: Psoriasis duration of PsA patients was 180±114 months. PsA disease duration was 108±33 months. The mean duration between two evaluations was 62±9 months. At first evaluation, 14 (63.6%) patients had peripheral joint, 1 (4.5%) patient had axial, and 7 (31.8%) patients had both peripheral and axial involvement among patients. Dactilytis in 6 (27.3%), enthesis in 7 (31.8%) and nail in 12 (54.5%) patients were other clinical involvements. FMD% was lower in PsA patients than healthy controls [9.3±3.9 vs 12.9±1.8, p<0.001] and carotid IMT was more obvious in PsA patients than healthy controls [0.64±0.17 vs 0.54 ±0.09, p=0.017] (Figure). All PsA patients used anti-TNF alpha treatment during the follow-up period. 68.1% of the PsA patients were in remission during the control. At 5-year follow-up visits, there was no CV event in study groups. However, FMD% was lower in PsA patients than healthy controls [7.6±4.8 vs 12.9±1.8, p<0.001] and carotid IMT was also similar between PsA patients and healthy controls [0.61±0.33 vs 0.54±0.09, p=0.306]. After 5-year follow-up visits, there was no statistically significant difference in FMD% compared to baseline [p = 0.254]. ΔFMD% was found to be moderately correlated with the ΔBASDAI (r= -0.45).
Conclusion: Our results showed that there was a significant impact of anti-TNF-a drugs on progression of subclinical atherosclerosis at the vascular wall level, but no impact on the endothelial dysfunction. Further large-scale randomized studies are needed to confirm our findings.

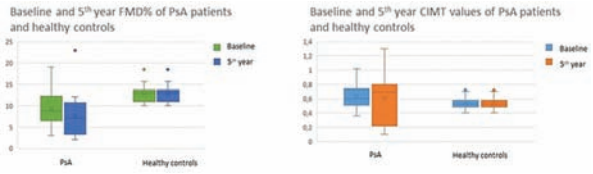


Figure.

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SAT0373 EFFECT OF FILGOTINIB ON PATIENT-REPORTED OUTCOMES IN ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM EQUATOR, A RANDOMIZED, PHASE 2 STUDY

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Background: Filgotinib (FIL) is an oral, selective Janus kinase 1 inhibitor under clinical investigation in a number of inflammatory diseases. FIL significantly improved multiple disease domains vs placebo (PBO) in patients with active psoriatic arthritis (PsA) in the multicenter, double-blind, phase 2 EQUATOR trial (NCT03101670) [1].
Objectives: To evaluate the effect of FIL vs PBO on patient reported outcomes (PROs) in EQUATOR and the extent to which effects on composite disease endpoints translate to clinically relevant improvements for patients.
Methods: Patients were randomized 1:1 to FIL 200 mg or PBO once daily for 16 weeks [1]. Patient's Global Assessment of Disease Activity (PtGADA), pain intensity (visual analog scale), Pruritus Numerical Rating Scale (NRS), Health Assessment Questionnaire Disability Index (HAQ-DI), 36-Item Short Form Survey (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS), and Functional Assessment of Chronic Illness Therapy-Fatigue scale (FACIT-F) were assessed at week 16. Analysis of covariance was used to compare changes from baseline in outcomes between groups. Proportions of patients achieving normative PRO scores or minimal clinically important differences (MCIDs) were compared using Cochran-Mantel-Haenszel tests [2, 3].
Results: FIL significantly improved multiple PROs vs PBO at week 16 (Table). Proportions of patients reaching normative PRO values for FACIT-F and SF-36 PCS (≥40 or 50, respectively), and achieving MCIDs in HAQ-DI and SF 36 PCS, were significantly greater for FIL vs PBO (Table). Significant improvement in 6/8 SF 36 domains was observed at week 16 with FIL vs PBO (Fig a). Improvement in most individual FACIT F items was also observed (Fig b).
Conclusion: In EQUATOR, FIL-treated patients with active PsA reported greater and clinically meaningful improvements in most PROs at week 16 vs PBO, mirroring improvements previously reported with FIL in disease activity measures [1].

Table

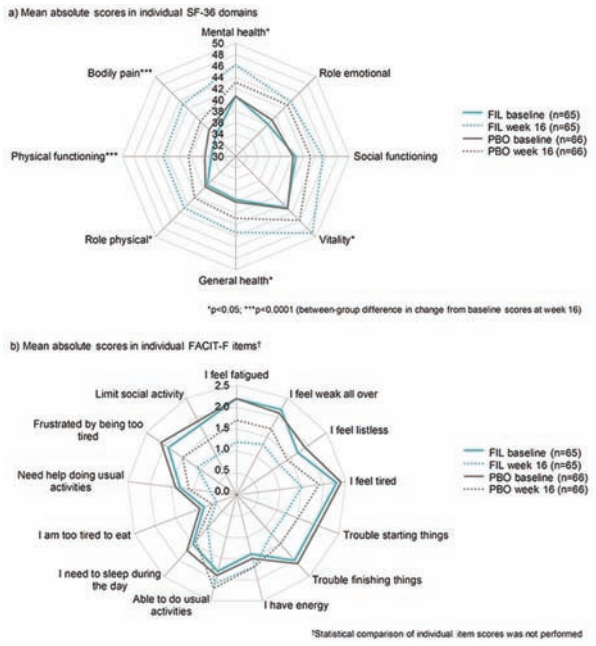
Table

Week 16		FIL (n=65)	PBO (n=66)	Treatment difference (95% CI)	p
Mean change from baseline					
PtGADA (mm)		−27.2 (22.1)	−13.5 (25.8)	−15.2[a] (−22.3, −8.1)	<0.0001
Pain (mm)		−31.6 (21.3)	−11.1 (29.7)	−18.9[a] (−26.7, −11.1)	<0.0001
Pruritus NRS		−2.5 (2.1)	−0.6 (2.2)	−2.2[a] (−3.1, −1.4)	<0.0001
HAQ-DI		−0.6 (0.5)	−0.3 (0.5)	−0.3[a] (−0.4, −0.1)	0.0009
SF-36 PCS		7.4 (6.6)	2.4 (6.6)	4.7[a] (2.6, 6.8)	<0.0001
SF-36 MCS		4.3 (8.3)	3.2 (9.2)	1.2[a] (−1.7, 4.0)	0.4128
FACIT-F		8.2 (7.3)	5.5 (8.1)	3.2[a] (0.8, 5.5)	0.0086
Response rate, n/N (%)					
HAQ-DI	MCID ≥0.35	41/63 (65)	26/62 (42)	23.2[b] (5.7, 38.8)	0.0085
SF-36 PCS	Score ≥50	11/64 (17)	4/63 (6)	10.9[b] (−0.7, 22.5)	0.0471
	MCID ≥2.5	49/65 (75)	26/66 (39)	36.0[b] (19.2, 50.0)	<0.0001
SF-36 MCS	Score ≥50	13/46 (28)	14/47 (30)	−1.5[b] (−19.4, 16.6)	0.9879
	MCID ≥2.5	32/65 (49)	40/66 (61)	−11.4[b] (−27.4, 5.5)	0.2607
FACIT-F	Score ≥40	18/58 (31)	7/57 (12)	18.7[b] (3.6, 33.0)	0.0105
	MCID ≥4	43/65 (66)	37/66 (56)	10.1[b] (−6.5, 25.9)	0.1921

[a]Least-squares mean. [b]Arithmetic mean.
CI, confidence interval

REFERENCES

[1] Mease P, et al. Lancet 2018;392:2367–77.
[2] Mease P, et al. J Rheumatol 2011;38:2461–5.



[3] Genovese M, et al. Arthritis Res Ther 2018;20:57.

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SAT0374 IXEKIZUMAB, WITH OR WITHOUT CONCOMITANT METHOTREXATE, IMPROVES THE SIGNS AND SYMPTOMS OF PSA FOR UP TO 52 WEEKS OF TREATMENT

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Background: Ixekizumab (IXE) is a high affinity monoclonal antibody selectively targeting interleukin (IL)-17A. It was previously demonstrated that IXE, with or without concomitant methotrexate (MTX), was superior to placebo (PBO) in improving the signs and symptoms of patients with psoriatic arthritis (PsA) for up to 24 weeks[1,2].

Objectives: To evaluate the efficacy of IXE, with or without continuous concomitant MTX, for up to 52 weeks of treatment in patients with active PsA.

Methods: Patients with active PsA who were biologic naïve (SPIRIT-P1, NCT01695239) *or* had prior inadequate response or intolerance to tumour necrosis factor inhibitors (SPIRIT-P2; NCT02349295) were randomised to PBO (N=224), 80 mg IXE every 4 weeks (IXEQ4W, N=229) or every 2 weeks (IXEQ2W, N=226), after a 160 mg starting dose. In this post-hoc analysis, efficacy was assessed up to Week 52 for the following two subgroups: (i) patients who were treated with IXE as monotherapy i.e. no concomitant conventional disease-modifying anti-rheumatic drugs and (ii) patients who received constant dose of MTX from Weeks 0 to 52. Patients who had MTX dose change were excluded. Efficacy outcome measurements included American College of Rheumatology (ACR) 20/50/70 responses, minimal disease activity (MDA), and disease activity in psoriatic arthritis (DAPSA) low disease activity (LDA) (score ≤ 14). Patients who discontinued from treatment before Week 52 were included in the analysis. Missing values were imputed using non-responder imputation. All analyses were done post-hoc.

Results: Among patients randomised to IXE at Week 0, 177 (38.9%) patients were treated with IXE monotherapy while 183 (40.2%) patients received constant dose of MTX up to Week 52. The average MTX dose was 15.7 mg/week and 16.0 mg/week for IXEQ4W and IXEQ2W, respectively. Week 52 results are presented in Table 1. At Week 52, similar results were observed between the two groups of patients for the different disease activity measures (ACR, MDA, and DAPSA LDA) and there was also a trend for a numerical higher proportion of patients achieving ACR responses with IXE monotherapy compared to patients with concomitant MTX use. Over time (Weeks 0-52), ACR 20, 50, and 70 response rates increased from baseline and were largely similar between the two subgroups (data not shown).

Conclusion: In this post-hoc analysis, IXE treatment showed sustained efficacy in patients with PsA up to one year of treatment, with or without concomitant MTX therapy.

REFERENCES

[1] Nash P, et al. RMD Open. 2018;4(2):e000692.
[2] Coates LC, et al. RMD Open. 2017;3(2):e000567.

Table 1. Efficacy Outcomes at Week 52

	IXEQ4W N=229		IXEQ2W N=226	
Concomitant Medication:	None (n=95)	MTX (n=85)	None (n=82)	MTX (n=98)
ACR 20	66.3%	55.3%	63.4%	55.1%
ACR 50	48.4%	38.8%	48.8%	38.8%
ACR 70	35.8%	27.1%	35.4%	23.5%
DAPSA LDA*	52.6%	52.9%	54.9%	41.2%
MDA	38.9%	35.3%	36.6%	22.7%

* score ≤ 14

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So Young Park Employee of: Eli Lilly and Company, Matthew Hufford Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB

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SAT0375 MILD COGNITIVE IMPAIRMENTIN PSORIATIC ARTHRITIS: PREVALENCE AND ASSOCIATED FACTORS

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Background: A growing body of data demonstrated that systemic inflammation is a predisposing condition for developing cognitive impairment. Different studies highlighted that psoriasis (PsO), a multisystem chronic inflammatory disorder, is associated with cognitive impairment. No data are available regarding psoriatic arthritis (PsA).

Objectives: To assess the prevalence and the factors associated with mild cognitive impairment (MCI) in patiens suffering from PsA.

Methods: Consecutive PsA patients, classified as suffering from PsA with the ClASsification criteria for Psoriatic ARthritis (CASPAR), were enrolled in this study. For each patient were collected the sociodemographic data (age, gender, years of school attendance, years of articular disease duration, years of cutaneous disease duration, treatment), the values of C-reactive protein (CRP) and the following clinical variables: 68 tender joint count (TJC), 66 swollen joint count (TJC), the Leeds Enthesitis Index (LEI), the dactylitis digit count, the Psoriasis Area and Severity Index (PASI), 10 cm numerical rating scale (NRS) for pain and for assessment of disease activity (PaGA), the Dermatology Life Quality Index (DLQI), the 12-item Psoriatic Arthritis Impact of Disease (PsAID-12), the Health Assessment Questionnaire (HAQ), and the Self-administered Comorbidity Questionnaire (SCQ). Cognitive impairment was assessed through the Montreal Cognitive Assessment (MoCA). The exclusion criteria were represented by the presence of: age older than 70 years, major depressive disorder, dementia, Parkinson's disease, active skin disease other than PsO, concomitant inflammatory joint conditions (such as gout or calcium pyrophosphate deposition), and comorbid fibromyalgia.

Results: The study involved 96 PsA patients, with a mean age of 52.8 years. Twenty (20.8%) patients were suffering from PsA sine PsO. The mean articular disease duration was 9.9 years, and the mean cutaneous disease duration was 14.9 years. The mean Disease Activity index for Psoriatic Arthritis (DAPSA) was 11.8, and the mean PASI was 0.95. MCI (defined as a MoCA score <26/30) was detected in 47 (48.9%) patients, with a mean value of MoCA of 25.1±3.1. Short-term memory was the most affected domain (mean value 2.6 on 0-5 point scale). The variables under investigation significantly correlated with a worsening cognitive performance (Spearman's Rho) were functional capacity (MoCA vs HAQ, r_s = -0.227, p = 0.026) and fatigue (MoCA vs PsAID item 2, r_s = -0.222, p = 0.029).

Conclusion: MCI is present in a significant proportion of PsA patients, and is present in a relative young age. MCI occurrence is associated with the presence of a worse functional capacity and a greater fatigue. Short-term memory is the more frequently affected domain. Although not predominantly of rheumatological interest, the MCI presence should be carried out in all patients with PsA.

REFERENCES

[1] Gisondi P, Sala F, Alessandrini F, et al. Mild cognitive impairment in patients with moderate to severe chronic plaque psoriasis. Dermatology. 2014;228(1):78-85.

[2] Colgecen E, Celikbilek A, Keskin DT. Cognitive Impairment in Patients with Psoriasis: A Cross-Sectional Study Using the Montreal Cognitive Assessment. Am J Clin Dermatol. 2016;17(4):413-9.

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SAT0376 MAKING THE NEXT STEPS IN PSORIATIC ARTHRITIS MANAGEMENT: DOMAIN DRIVEN, TREAT-TO-TARGET, TAILORED MANAGEMENT APPROACH

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Background: The diverse clinical picture of psoriatic arthritis (PsA) suggests the need to identify suitable therapies to address the different combinations of clinical manifestations and comorbidities. The current treatment paradigms recommend early diagnosis and treatment, and a strategic, target orientated approach, aiming at a low disease activity status. The introduction of new treatment modalities highlighted the need for guidelines to prioritize these options for doctors and patients

Objectives: To develop an evidence-based recommendation for the management and treatment of PsA. The management paradigm should cover all domains of psoriatic disease and provide a stepwise tailored treatment options giving clear advice on treatment from the initial diagnosis, including inclusion/exclusion criteria for treatment, monitoring requirements and how to quantify response to treatment.

Methods: A Steering Committee formulated a set of overarching principles for the management of PsA based on evidence derived from a systematic literature review. These were subsequently discussed, amended and voted on by a Task Force of 20 rheumatologists, dermatologists and patient research partners. Using the nominal group technique and Delphi method, 7domains were identified (peripheral arthritis, axial disease, enthesitis, dactylitis, skin and nails as well as comorbidities including uveitis). A multidisciplinary, evidence- and consensus-based treatment recommendations for PsA were developed for each of the domains based on three consensus discussions. A set of recommendations for a sequential DMARD/biologic treatment algorithm for patients with PsA was also set.

Results: literature review provided evidence regarding an optimised domain specific, treat-to- target approach to management. The guidelines addressed both drug and non-drug interventions. 20-statements regarding diagnosis, disease activity scoring, US/MRI scanning, and drug therapy were generated. Percentage of positive votes ranged between 86-100%; whereas mean±SD level of agreement was 9.6+0.3. The main treatment outcome is to achieve remission status or at least low disease activity state, which should be based on a shared decision with parents/patients. Treatment should be adapted according to disease activity. Treatment should be also adapted if the remission state got lost.

Conclusion: Although no clear correlation exists between joint inflammation and the skin in every patient, the skin and joint aspects of the disease often must be treated simultaneously. Treatment recommendations for the cardinal physical manifestations of PsA were developed based on a literature review and consensus between rheumatologists, dermatologists and patients. It is anticipated that periodic updates will take place using this framework as new data become available.

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SAT0377

DIFFERENCES IN CLINICAL CHARACTERISTICS, QUALITY OF LIFE, DISABILITY, AND WORK PRODUCTIVITY IN PSORIATIC ARTHRITIS PATIENTS BY GENDER: FINDINGS FROM A CROSS-SECTIONAL SURVEY IN THE US AND EUROPE

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Background: Psoriatic arthritis (PsA) prevalence is equal in men and women, though gender may play a role in driving mechanisms of PsA leading to differences in manifestations of clinical disease (1).
Objectives: Assess key differences in clinical characteristics, disability, quality of life, and work productivity by gender in real-world practice.
Methods: Cross-sectional survey of rheumatologists and dermatologists and their patients in France, Germany, Italy, Spain, UK, and US. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Data were analyzed by gender. Demographic characteristics, treatment use, and clinical characteristics (Tender Joint Count [TJC], Swollen Joint Count [SJC], Body Surface Area [BSA] psoriasis) were reported by physicians, while quality of life (EQ5D and PsAID12), disability (HAQ-DI), and work productivity (WPAI) were reported by patients. Men and women were compared using parametric tests and non-parametric tests where appropriate.
Results: Data were collected for 2270 patients (595 US, 1675 Europe). Demographic characteristics, time from first symptoms to diagnosis, biologic treatment, and clinical characteristics were comparable between women and men (Table 1). More women reported worse quality of life, disability, and work activity impairment than men (Table 2).

Table 1. Demographic and clinical characteristics in women and men [mean (SD) or n (%)]

	Women	Men	P value
n (%)	1047 (46.1)	1223 (53.9)	-
Age, years	48.3 (13.7)	48.8 (12.8)	0.42
Working full time*, n (%)	206 (49.4)	350 (68.6)	<0.01
Charlson Comorbidity Index score	1.10 (0.51)	1.15 (0.58)	<0.01
Time from first symptoms to diagnosis, years	1.48 (3.53) 4.87 (6.15)	1.14 (2.48) 4.95 (5.79)	0.76 0.42
PsA duration, years			
Currently receiving biologic treatment, n (%)	557 (53.2)	674 (55.1)	0.38
BSA psoriasis involvement, mean%	5.5 (8.4)	5.5 (8.1)	0.87
Swollen Joint Count	3.2 (7.0)	3.5 (6.9)	0.39
Tender Joint Count	4.1 (5.2)	4.5 (8.0)	0.03
Enthesitis, n (%)	59 (5.6)	72 (5.9)	0.86
Dactylitis, n (%)	79 (7.5)	75 (6.1)	0.21

*Outside the home

Table 2. Quality of life, disability, and work productivity in women and men [mean (SD)]

	Women	Men	P value
EQ5D utility score	0.80 (0.18)	0.82 (0.17)	0.02
HAQ-DI score	0.56 (0.60)	0.41 (0.52)	<0.01
PsAID12 score	2.66 (2.07)	2.27 (1.98)	<0.01
WPAI percentage of activity impairment	27.9 (22.0) 4.0 (14.0)	24.6 (22.4) 5.8 (19.2)	<0.01 0.62
WPAI percentage of work time missed			

Conclusion: In women and men with similar PsA disease activity and treatment rates, women experienced worse quality of life, greater disability, and greater work impairment, despite a lower burden of comorbidities.

REFERENCE

[1] Billi AC, Kahlenberg JM, Gudjonsson JE. Sex bias in autoimmunity. Curr Opin Rheumatol. 2019 Jan;31(1):53–61.

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SAT0378

DRIVERSOF DISCORDANCE IN PSORIATIC ARTHRITIS WHEN ANALYZING THE LINK BETWEEN PATIENT-PERCEIVED GOOD STATUS AND THE DISEASE ACTIVITY IN PSORIATIC ARTHRITIS (DAPSA) COMPOSITE SCORE: AN ANALYSIS OF 436 PATIENTS FROM THE INTERNATIONAL REFLAP OBSERVATIONAL STUDY

Laure Gossec, Maarten de Wit, Laura C. Coates, Umut Kalyoncu, Emmanuelle Dernis, Adeline Ruyssen-Witrand, Ying Ying Leung, Rossana Scrivo, Juan D. Cañete, Penelope Palominos, Sandra Tälli, Uta Kiltz, Martin Soubrier, Lihi Eder, Ana-Maria Orbai, Josef S. Smolen. *RFlP study group, PARIS, France*

Background: In Psoriatic arthritis (PsA), the objective of treatment is remission or low disease which can be defined using the Disease Activity in PSoriatic Arthritis (DAPSA) (ref1). We previously showed DAPSA was associated to patient-perceived good status (i.e., self-assessed remission or low disease, yes/no) (ref2). However, some discordance was noted between patient-perceived status and the composite score. This discordance may be linked to demographic elements (such as age, gender or country), disease activity components (such as skin involvement which is not assessed in DAPSA) or patient-reported outcomes (such as fatigue or depressive affects). A better understanding of this discordance would be helpful in the context of shared decision-making.
Objectives: To explore the drivers of discordance between patient-perceived remission or low disease and DAPSA-defined remission or low disease.
Methods: This is an analysis of the first visit of ReFlap (NCT03119805, ref2), an observational study in 14 countries of consecutive adult patients with definite PsA >2 years of disease duration. Discordance in assessment of remission/low disease status was defined as a disagreement between a specific patient question (are you in remission or low disease, yes/no) and DAPSA-defined remission/low disease (i.e., score <=14, yes/no). Potential drivers of this discordance were analysed through univariable then stepwise multivariable logistic regression. Variables analysed were demographic (age, gender, disease duration, gross domestic product of country of origin), disease-related (joint counts, psoriasis BSA, enthesitis, CRP) and patient-reported outcomes (pain, fatigue, depressive affect and anxiety). There was no imputation of missing data.
Results: Among 436 patients, mean age 52.3 (SD 12.5) years, mean disease duration 10.1 (8.1) years, 218 (50.8%) male; 259 (63.5%) were taking a conventional DMARD and 247 (60.5%) a biologic. Disease activity was moderate: 36.1% had no current psoriasis skin lesions and mean swollen joint count was 2.2 (7.1). Remission or low disease was frequent both using the patient question (N=286, 65.6%) and using DAPSA (N=246, 56.4%). Discordance between patient-reported status and DAPSA

concerned 112 (25.7%) patients, of whom 76 (17.4% of 436) self-reporting REM/LDA, and 36 (8.3% of 436) reporting not being in REM/LDA. When exploring drivers of this discordance in univariate analyses, tender joint count, CRP, pain, fatigue and depression were significant. The multivariate analysis found CRP, pain and depression to be independent drivers of discordance (Table).

Table. Factors associated to discordance between DAPSA-defined remission or low disease, and patient-defined remission or low disease, in multivariable regression.

Characteristic	Value in discordant patients, mean (SD)	Value in concordant patients, mean (SD)	Odds ratio (95% CI)
Model 1			
CRP, mg/l	2.8 (9.1)	1.1 (3.1)	1.06 (1.01, 1.12)
Pain (0-10)	4.9 (2.3)	3.9 (2.9)	1.14 (1.05, 1.23)
Model 2 without pain			
CRP, mg/l	2.8 (9.1)	1.1 (3.1)	1.06 (1.01, 1.12)
Depression (0-10)	2.8 (3.2)	2.1 (2.8)	1.08 (1.01, 1.16)

Conclusion: Remission or low disease appears to be an attainable outcome in PsA. Patients widely self-reported themselves as being in a similar status as the status indicated by the DAPSA score. Discordance in assessment concerned 25.7% patients and was mainly related to CRP (driving higher DAPSA), pain and fatigue (driving patient assessments). When faced with discordance in assessment, the health professional should assess these elements carefully.

REFERENCE

[1] Schoels MM, et al. Ann Rheum Dis. 2016;75(5):811-8. 2. Gorlier C, et al. Ann Rheum Dis. 2019;78(2):201-208.

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SAT0379

SUBCUTANEOUS VERSUS ORAL METHOTREXATE IN ACHIEVING MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS. CLINICAL PRACTICE: RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PSART) DATA

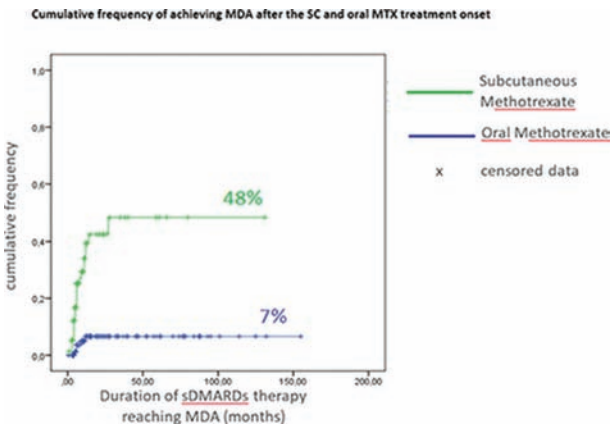
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Background: The aim of psoriatic arthritis (PsA) therapy is to achieve minimal disease activity (MDA) or clinical remission. Methotrexate (MTX) is the first-line treatment; however, the extent of the disease-modifying effect of MTX on PsA is a matter of debate. It has been shown that the MTX treatment achieves MDA in 6 months in <20% of patients (pts) (1). It has been demonstrated that parenterally administered MTX results in rapid and complete absorption, higher serum levels, and less variable exposure than the oral dosing (2). Clinical practice data on the results of the use of MTX for treating PsA are contradictory.

Objectives: To show the efficacy of MTX in PsA pts in clinical practice and to compare the effectiveness of oral and subcutaneous (SC) MTX treatments.

Methods: 256 pts out of RU-PsART received synthetic disease-modifying antirheumatic drugs (sDMARDs), of whom 182 (71.1%) pts (M/F–68/114) received MTX, and were included in the study according to CASPAR criteria. Their median age 42 [Min 19-Max 73] years (yrs). Pts underwent standard clinical examination of PsA activity at the baseline and the follow-up visits. All pts were biological-naïve. They all were treated with MTX monotherapy: 80 received SC and 102 oral MTX. The main purpose was to determine the cumulative frequency of achieving MDA after the MTX therapy onset. MDA is defined as: the presence of at least 5 out of the following 7 domains: tender joint count ≤1, swollen joint count (SJC) ≤1, Psoriasis Area Severity Index (PASI) ≤1 or body surface area ≤3%, tender entheseal points ≤1, Health Assessment Questionnaire score ≤0.5, patient global disease activity measured by Visual Analogue Scale (VAS) score ≤20, and patient pain VAS ≤15. Medians and quartiles [Me (Q25; Q75)], [Min; Max], ORs with 95% CI, Breslow, Long Rank, Tarone-Ware tests were performed. Cumulative frequency was computed using the Kaplan-Meier method. All CI >1, p <0.05 were considered to indicate statistical significance.

Results: Only 16.5% of all 182 pts treated with MTX, both orally and SC, achieved MDA. In the SC MTX group 25 pts (31%) achieved MDA, while 55 (69%) did not achieve it. In the oral MTX group 5 pts (5%) achieved MDA, while 97 (95%) did not achieve it. SC MTX treated pts significantly more often achieved MDA compared with those orally treated OR 8.8 [3.2 – 24.3]. Cumulative frequency of achieving MDA in 27 months from the treatment onset was 48% for SC administration, and 7% for the oral one (p<0.05). MTX median dose in SC administered pts who achieved MDA was 17 mg/weekly (wk), and 15 mg/wk in the group of pts who did not achieve MDA. Among orally administered pts who both achieved and did not achieve MDA the MTX dose was 15 mg/wk.



Conclusion: In clinical practice, the sDMARD given to the majority of pts is MTX, but its use achieves the recommended treatment target of MDA only in 16.5% of pts. The SC MTX treatment significantly, up to 30%, improves the achievement of MDA. The use of SC MTX could be a therapy optimized option in clinical practice.

REFERENCES

[1] B.J. Sheane, et al. J Rheumatol. 2016;43(9):1718-23.
[2] G.A. Vena et el. Ther Clin Risk Manag. 2018;14:105-16.

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SAT0380 FIBROMYALGIA IS THE STRONGEST NEGATIVE PREDICTOR FOR THE ACHIEVEMENT OF EITHER REMISSION AND MINIMAL DISEASE ACTIVITY IN NAIVE PSORIATIC ARTHRITIS PATIENTS STARTING BIOLOGIC DRUGS

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Background: There is evidence that fibromyalgia (FM) can increase the burden of disease in patients affected with psoriatic arthritis (PsA) and interfere with the assessment of clinical disease activity, but studies focusing the impact of FM on long-term clinical outcomes are lacking.
Objectives: We aimed at evaluating the impact of FM on the achievement of clinical remission or minimal disease activity (MDA) in naïve PSA patients on treatment with a first biologic drug in real life settings.
Methods: We retrospectively assessed PsA patients, fulfilling CASPAR criteria, from 1st January 2010 through 30th June 2017, starting a first biologic drug or apremilast. At baseline and at each visit thereafter, DAPSA, PASI, MDA, ASDAS-CRP, and HAQ were evaluated. Rate of patients achieving DAPSA based low disease activity (LDA) was assessed at 3 months, and MDA or DAPSA-remission at 12 months. LOCF method was carried out for those patients who did not reach 12 months follow-up or discontinue the treatment before 12 months. The persistence on the first treatment was evaluated by Kaplan-Mayer survival curves. Estimated hazard ratios (HRs) of discontinuing therapy or achieving remission or MDA at last observation were assessed by a multivariate stepwise backward Cox regression model, adjusting for patient demographics (gender, age, BMI, comorbidities) and disease characteristics (co-therapy with MTX or glucocorticoids, DAPSA).
Results: Upon excluding pure axial PsA without peripheral involvement, 238 patients (126 female) with mean age 51 years (95% CI, 40-59), BMI 26 (95% CI, 23-30), disease duration 24 (95% CI, 10-60) months were analyzed. At baseline, 120 had polyarticular involvement ($\geq$ 5 joints), 118 had oligoarticular pattern, and 64 had concomitant spine involvement. One hundred-fifteen begun a treatment with anti-TNF-receptor, n.106 with anti-TNF-mAb, n.9 with ustekinumab, n.6 with apremilast, and n.2 with secukinumab. FM was diagnosed, according to both 1990 and 2019 ACR classification criteria, in 58 (female 74%) patients. Crude drug survival rate was significantly lower in FM-PsA patients (50%) (mean survival time (MST, 95% CI) 32 (25-38) months than in PsA patients without FM (74%) MST 42 (38-45) months (log rank=15.6, p=0.0001) (Figure 1a). This large difference was also seen estimating drug survival by ineffectiveness, FM-PsA 58.6% (MST 35 (28-42) months) vs PsA 82% (MST 45 (42-48) months) (log rank=18.5, p=0.0001) (Figure 1b), but not by adverse events (data not shown). LDA at 3 months was reached by 78% of PsA patients and by 21% of FM-PsA patients (p=0.0001). At 12 months, MDA was achieved by 62% of PsA and only by 2% (1 out of 58) of FM-PsA (p=0.0001), and likewise remission was seen in 47% of PsA and in 2% of FM-PsA p=0.0001) Figure 2. FM was the only independent factor associated to drug discontinuation (HR 2.5, 1.6-4.1 (95% CI), or to the achievement of either MDA (HR 0.23, 0.1-0.5 (95% CI) and clinical remission (HR 0.26, 0.1-0.6 (95% CI), with the first biologic drug within the time span of the study.

Conclusion: Our findings clearly demonstrate the FM has a striking negative impact on clinical outcomes in PsA, as early as 3 months of treatment. Clinicians should be aware that treating PsA patients with comorbid FM is demanding, and appropriate patient shared strategies should be adopted in these settings.

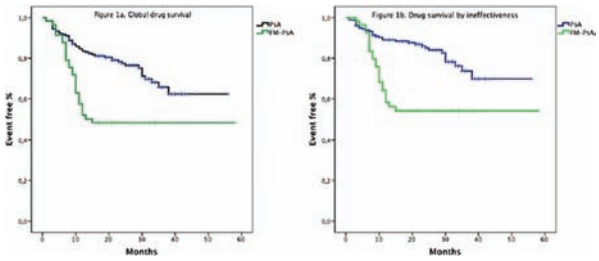


Figure 1. Kaplan-Mayer curves of crude drug survival (left) and by ineffectiveness in PsA patients with or without fibromyalgia.

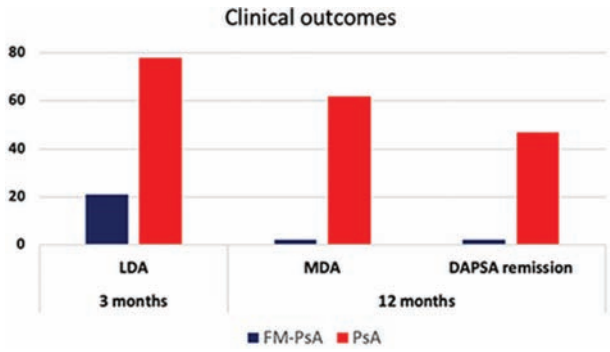


Figure 2.. Percentage of PsA patients with or without fibromyalgia achieving LDA-DAPSA at 3 months, and MDA or DAPSA-remission at 12 months.

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SAT0381 MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS PREDICTS LOW IMPACT OF DISEASE

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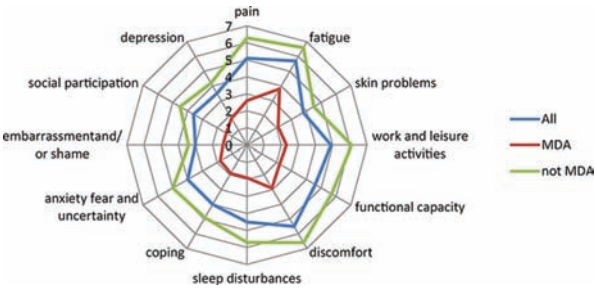
Background: Psoriatic arthritis (PsA) is the commonest form of inflammatory spondyloarthropathy with prevalence of 0.19% in UK. Patients suffering from PsA often have significant impact on daily life due to articular, non-articular and psychological symptoms. Minimal disease activity is an increasingly used target of therapy in both clinical trials and clinical practice.
Objectives: We aimed to assess relationships between physician and patient reported outcomes in routine clinical practice.
Methods: We performed a retrospective analysis of routinely collected patient reported and physician reported outcomes. We obtained clinical information of patients with PsA attending clinic from March 2018 to December 2018. Data was gathered from clinical letters (swollen and tender joint count, Leeds enthesitis index, Body surface area psoriasis), laboratory results (ESR, CRP) and questionnaire responses (HAQ, global assessments and PSAID12). Data were analysed using SPSS25. Logistic regression was used to assess patient reported outcomes which were associated with achieving MDA.
Results: Data were available for 205 patient visits. Presence of MDA could be evaluated at 187 patient visits (MDA n=60, Not MDA n=127).

All components of PSAID12 were associated with MDA achievement on univariate logistic regression but only pain remained an independent variable on multiple logistic regression. Disease duration, age and sex were not associated with achievement of MDA.

Patients in MDA had significantly lower PSAID12 then those not in MDA (mean 2.1 ± SD 1.9 vs. 5.8 ±1.9. We also looked at individual components of PSAID (Figure1, mean values for numerical rating scales). Patients in MDA continue to report pain and discomfort despite good clinical outcomes, albeit far lower than patients not in MDA.

PSAID12 of less than 4 is considered a good outcome. All components of MDA assessment were associated with low PSAID12 on univariate analysis, but only pain VAS and HAQ remained independent predictors on multiple regression analysis.

Patients with active but not severe arthritis (SJ or TJ 2-3) continued to have high PSAID (one way ANOVA p<0.001), driven by other psoriatic disease manifestations including skin and enthesitis.



Conclusion:

- MDA is a relevant treatment target in psoriatic arthritis, with markedly lower PSAID12 in patients in MDA
- Patients with even low numbers of tender or swollen joints continue to have significant impact of disease, supporting the use of a multidimensional treatment target.
- Pain and fatigue are dominant symptoms in patients with psoriatic arthritis, even in those in MDA

REFERENCES

[1] Ann Rheum Dis. 2014 Jun;73(6):1012-9. doi: 10.1136/annrheumdis-2014-205207

[2] RMD Open. 2017 Jul 18;3(1):e000415. doi: 10.1136/rmdopen-2016-000415. eCollection 2017

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SAT0382 THE RISK FACTORS RELATED TO MENTAL HEALTH PROBLEMS IN PATIENTS WITH PSORIATIC ARTHRITIS IN A LARGE MULTICENTER STUDY; DATA FROM TLAR-NETWORK

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Background: Psoriatic arthritis (PsA) can lead to significant mental burden affecting several aspects of life in majority of patients. Mental health problems, such as depression and anxiety may result in poor treatment adherence and difficulty in coping with disease burden.

Objectives: The aim of this study is to determine the risk factors associated with clinically significant depression and anxiety in patients with PsA.

Methods: The data from 1128 patients with PsA who met CASPAR classification criteria enrolled by Turkish League Against Rheumatism (TLAR)-Network derived from 25 investigating centers. All of the patients underwent clinical, radiological and also laboratory assessment by using standardized protocol. The associations between psychological variables and clinical parameters were assessed by univariate and multivariate analyses.

Results: Of the 1128 patients with PsA (the mean age 46.9 ±12.2,%64 F), 574 (%50.9) had high risk for depression (HADS-D score $\geq$7) and 270 (%23.9) for anxiety (HADS-A score $\geq$10). By univariate analysis, the highest odds ratio (OR) associated with both depression and anxiety were SF36-MCS<50 (OR 6.9, [95%CI:5.3–9]; OR 9, [95%CI:6.5–12.6], respectively. The lowest OR associated with depression belong to PASI total score (OR 1.1, [95%CI:1–1.1]), while the lowest OR associated with anxiety belong to BASMI (OR 1.2, [95%CI:1.1–1.3]). Multivariate logistic regression analysis of potential risk factors for mental health revealed that BASFI (OR 1.9, [95%CI:1.3–2.9], BASDAI (OR 1.6, [95%CI: 1.2–2.3]), BASRI (OR 1.1, [95%CI: 1–1.2]), SF36 MCS<50 (OR 4.7,[95%CI: 3.3–6.8) and unemployed (OR 1.4, [95%CI: 1–1.9]) were factors that influence the risk of depression whereas the BASDAI (OR 1.6, [95%CI: 1–2.4]), SF36 MCS<50 (OR 6, [95%CI: 4–9.2]), BASMI (OR 1.2, [95%CI: 1.1–1.3]) and FIRST≥5 (OR 3, [95%CI: 2–4.5]) were factors that influence the risk of anxiety.

Conclusion: This large nationwide database indicated that higher disease activity, functional disability, fibromyalgia (FMS), poor health related quality of life as well as structural damage were estimated as the important risk factors for mental disorders in PsA.

Disclosure of Interests: : Gamze Kiliç: None declared, Kemal Nas: None declared, Erkan Kilic: None declared, ibrahim tekeoğlu: None declared, Betul Sargin: None declared, Sevtap Acer Kasman: None declared, Hakan Alkan: None declared, Nilay Sahin: None declared, Gizem Cengiz: None declared, Nihan Cuzdan: None declared, Ilknur Albayrak Gezer: None declared, Dilek Keskin: None declared, Cevriye Mülkoğlu: None declared, Hatice Resorlu: None declared, Şebnem Ataman: None declared, Ajda Bal: None declared, Mehmet Tuncay Duruöz Grant/research support from: Abvie, Speakers bureau: Novartis, AMGEN, Abdi İbrahim, İlko, Okan Kucukakkas: None declared, Ozan Volkan Yurdakul: None declared, Meltem Alkan Melikoglu: None declared, Yildiray Aydin: None declared, Figen Ayhan: None declared, Hatice Bodur: None declared, Mustafa Calis: None declared, Erhan Capkin: None declared, Gul Devrimsel: None declared, SAMI HIZMETLI: None declared, Ayhan Kamanli: None declared, Kevser Gok: None declared, Yasar Keskin: None declared, Hilal Kocabas: None declared, Oznur Kutluk: None declared, Nesrin Şen: None declared, Omer Faruk Sendur: None declared, Murat Toprak: None declared, Sena Tolu: None declared, Tiraje Tuncer: None declared:

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SAT0383 COMPARISON OF THE EFFICACY AND SAFETY OF TOFACITINIB AND APREMILAST IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Young Ho Lee, Gwan Gyu Song. *Korea University, Rheumatology, Seoul, Korea, Rep. of (South Korea)*

Background: The therapeutic options for psoriatic arthritis (PsA) include conventional disease-modifying antirheumatic drugs and biologics. However, an unmet need exists for PsA therapies owing to drug intolerance, non-responsiveness, and therapeutic resistance. Therefore, there is a need for additional treatment options with novel mechanisms of action. Tofacitinib is an orally administered JAK inhibitor and apremilast is a novel oral phosphodiesterase 4 inhibitor that regulates inflammatory mediators.

Objectives: The aim of this study is to assess the relative efficacy and safety of tofacitinib and apremilast at different doses in patients with active PsA.

Methods: We conducted a Bayesian network meta-analysis to combine evidence from randomized controlled trials (RCTs) for examination of the efficacy and safety of tofacitinib 10 mg, tofacitinib 5 mg, apremilast 30 mg, and apremilast 20 mg in PsA.

Results: Eight RCTs including 3,086 patients met the inclusion criteria. There were 10 pairwise comparisons including 6 direct comparisons of 5 interventions. All the interventions achieved a significant American College of Rheumatology 20 (ACR20) response compared with placebo. Tofacitinib 10 mg and apremilast 30 mg were among the most effective treatments for active PsA, followed by tofacitinib 5 mg, and apremilast 20 mg. The

ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that tofacitinib 10 mg had the highest probability of being the best treatment in terms of the ACR20 response rate (SUCRA = 0.785), followed by apremilast 30 mg (SUCRA = 0.670), tofacitinib 5 mg (SUCRA = 0.596), apremilast 20 mg (SUCRA = 0.448), and placebo (SUCRA = 0.001). No significant differences were observed in the incidence of serious adverse events after treatment with tofacitinib 10 mg, apremilast 30 mg, tofacitinib 5 mg, apremilast 20 mg, or placebo.
Conclusion: In active PsA patients, tofacitinib 10 mg and apremilast 30 mg were the most efficacious interventions and were not associated with a significant risk of serious adverse events.

REFERENCES

[1] Mease P, Hall S, FitzGerald O, et al. (2017) Tofacitinib or Adalimumab versus Placebo for Psoriatic Arthritis. N Engl J Med 377:1537-1550
[2] Gladman D, Rigby W, Azevedo VF, et al. (2017) Tofacitinib for Psoriatic Arthritis in Patients with an Inadequate Response to TNF Inhibitors. N Engl J Med 377:1525-1536
[3] Schafer P (2012) Apremilast mechanism of action and application to psoriasis and psoriatic arthritis. Biochemical pharmacology 83:1583-1590

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SAT0384 COMPARATIVE ANALYSIS OF FREQUENCY AND TIMING OF MINIMAL DISEASE ACTIVITY (MDA) ATTAINMENT IN EARLY AND LONG-TERM PSORIATIC ARTHRITIS (PSA) PATIENTS (PTS) AFTER BIOLOGICAL (B) DMARDS TREATMENT INITIATION IN CLINICAL PRACTICE: RUSSIAN PSA REGISTRY (RU-PSART) DATA

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Background: MDA is a treatment target of PsA. There is limited data about the frequency and the time of MDA achievement by the use of bDMARD therapy in early and long-term PsA in clinical practice. RU-PsART collected data from 25 rheumatology clinics in the Russian Federation.
Objectives: to investigate the cumulative frequency and timing of MDA attainment in early and long-term PsA after starting bDMARDs in clinical practice.
Methods: 140 (M/F–77/63) bDMARD-naive PsA pts according to CASPAR criteria were included in the RU-PsART, after signing consent participation forms; median (Me) age 42 [Min 19-Max 73] years (yrs). All patients were divided into two groups based on PsA duration at the time of bDMARDs initiation: early PsA≤2 yrs (67pts) and long-term PsA>2 yrs (73pts). All pts underwent standard clinical examinations of PsA and psoriasis activity and were treated with the following bDMARDs: Infliximab (26pts), Etanercept (20pts), Adalimumab (37pts), Ustekinumab (33pts), Golimumab (19pts), Sekukinumab (4pts), Certolizumab pegol (1pts). MDA was defined as ≥ 5 of the following criteria: tender joint count ≤1, swollen joint count ≤1, PASI≤1 or BSA≤3, patient pain global assessment VAS≤15, patient´s global disease activity VAS≤20, HAQ≤0,5, enthesitis count ≤1. The cumulative frequency and the time of MDA attainment were calculated in both groups. Kaplan-Meier cumulative analysis, Me (CI95%), Min-Max,%, Breslow, Tarone-Ware, Log Rank tests were performed. All CI>1, p<0.05, were considered to indicate statistical significance.
Results: MDA has been achieved after bDMARDs initiation in 33 out of 67 (49%) pts with early PsA and in 23 out of 73 (32%) pts with long-term PsA. The Me time of MDA achievement was significantly shorter in early PsA in comparison to long-term PsA pts: 21 (CI 95%:13.1-28.9) months and 58 (CI95%:0-118.1) months of bDMARD therapy accordingly (p<0.05 for all tests) (Fig.1).
Conclusion: Comparative analysis has shown that cumulative frequency of MDA achievement after bDMARDs initiation was significantly higher (49% vs 32%) and faster (21 vs 58 months) in early PsA than in long-term PsA. That confirms the benefit of bDMARD therapy initiation at the early stage of PsA.

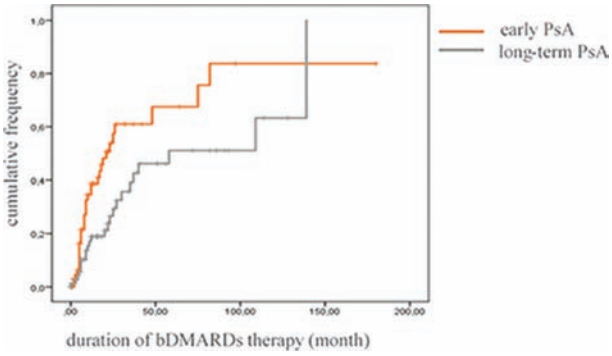


Figure 1. Cumulative frequency and time of MDA achievement after starting bDMARDs in early and long-term PsA.

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SAT0385 ASSOCIATION OF SUBCLINICAL MYOCARDIAL DEFORMATION AND DISEASE ACTIVITY IN PSORIATIC ARTHRITIS

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Background: Subclinical impaired myocardial deformation is common in patients with PsA, even with no clinical evidence for CV disease (1). Recent evidence supports the link between the extent of inflammation and CV risk in patients with PsA (2). Elevated levels of inflammatory biomarkers and high activity of joint inflammation were associated with a higher burden of atherosclerosis (2). It is suggested that patients with active disease may have an impaired myocardial deformation (3). But it is unclear if the patients with higher activity of PsA have higher grade of myocardial impairment than the patients without activity of inflammatory rheumatic disease. Speckle-tracking echocardiography (STE), an angle-independent technique, was proposed as a reliable and sensitive method for assessment of subclinical myocardial dysfunction (4).
Objectives: The aim of the study was to assess if there is an association of disease activity of PsA assessed by DAPSA with grade od myocardial impairment measured by Speckle-tracking echocardiography (STE).
Methods: 48 PsA patients (28 females, 20 males) who fulfilled Caspar criteria, with no clinically evident CV disease or concomitant diseases, were included in the study. Patients who had classic CV risk factors or had experienced CV or cerebrovascular events were excluded. Upon clinical and laboratory evaluation, all subjects underwent conventional echocardiography and 2-dimensional speckle tracking echocardiography (STE).
Results: The results of STE analysis showed that patients with higher DAPSA result have average global longitudinal strain AM ± SD -19.44 ± 2.98%. Significant correlation was determined between PsA patients with higher DAPSA result and lower values of the variable GLS (R=0,368; p=0.0036).
Conclusion: Subclinical impaired myocardial deformation measured by STE was more common in PsA patients with higher disease activity, even in absence of traditional CV risk factors. Global longitudinal strain was associated with the status of PsA disease activity.

REFERENCES

[1] Yilmazer B, Sahin T, Cefle A. Impaired myocardial deformation in psoriatic arthritis patients assessment by speckle tracking echocardiography. Acta Reumatol Port. 2016 Apr-Jun;41(2):131-7.

[2] Eder L, Thavaneswaran A, Chandran V, Cook R, Gladman DD. Increased burden of inflammation over time is associated with the extent of atherosclerotic plaques in patients with psoriatic arthritis. Ann Rheum Dis. 2015 Oct;74(10):1830-5.
[3] Shang Q, Tam LS, Sanderson JE, Lee AP, Li EK, Yu CM. Impaired left ventricular apical rotation is associated with disease activity of psoriatic arthritis. J Rheumatol. 2014 Apr;41(4):706-13.
[4] Blessberger H, Binder T. NON-invasive imaging: Two dimensional speckle tracking echocardiography: basic principles. Heart. 2010 May;96(9):716-22.

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SAT0386 PREVALENCE OF SUBCLINICAL CARDIOVASCULAR DISEASE IN PSORIATIC ARTHRITIS: A MULTICENTRIC STUDY

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Background: There are scarce data regarding subclinical vascular disease in psoriatic arthritis (PsA)(1). Similarly to rheumatoid arthritis, the real CVR could also be underestimated by clinical risk charts (2).
Objectives: To study the prevalence of subclinical vascular atheromatosis in patients with PsA; to analyze the association of carotid plaques with PsA characteristics; to identify which patients with intermediate or high clinical risk would be worthwhile to undergo carotid ultrasound to detect plaque.
Methods: Descriptive, transversal and multicentric study, of patients with clinical diagnose of PsA followed in 4 Spanish hospitals. Demographic data, classic CVR factors and clinical characteristics were recorded. The probability of a 10 years fatal cardiovascular event was calculated by SCORE charts adapted for Spain (3), and afterwards a systematic bilateral common carotid ultrasound (4) was conducted. The intima-media thickness of the carotid wall and the presence of atheroma plaque were registered. Patient's characteristics were described using descriptive analysis techniques. For univariate comparisons we used Chi2 and Anova. Multivariate analyses were conducted by logistic regression. The probability of plaque according to the age and the presence of CVR factors was calculated for patients with clinical intermediate or high risk by means of logistic regression. The study was approved by the Hospital General Universitario de Elda Ethic Committee (RCV-PS-MC/26/02/2016).
Results: 309 patients were included. The characteristics of the sample and the prevalence of CVR factors are depicted in Table 1. Patients were stratified by SCORE as follows: low risk 41 patients (13.3%), intermediate 182 (58.9%), high 75 (24.3%) and very high 11 (3.6%) patients. Plaque criteria by ultrasound was found in 95 patients (30.7%), who were reclassified as very high risk. Final distribution after carotid ultrasound showed a decrease in all groups (12%, 43.7% and 14.2% in low, intermediate and high risk, respectively) with a consequent increase in the very high risk group (30.1%). In the univariate study, plaque was associated with age (p<0.001), diabetes (p=0.004), hypertension (p=0.001), hyperuricemia (p=0.01) and dyslipidaemia (p<0.001); any association with PsA characteristics wasn't found. In the multivariate analyses, plaque was associated with age >55 years (OR 2.84; IC 1.54-5.55), and with the number of classical CVR factors (OR 1.49; IC 1.13-1.97). In the presence of 3 or more risk factors, the probability of having plaque was 57.2% in patients with clinical intermediate risk and 61.8% in patients with high risk, and raised with increasing presence of CVR factors (Table 2).
Conclusion: Subclinical vascular disease is present in almost a third of the patients with PsA. SCORE tables may prove inaccurate for estimating the real CVR, and carotid ultrasound would be advisable in patients with intermediate or high risk who present any classical CVR factor.

Table 1.. Clinical characteristics

Sex	Women 149 (48.2%), Men 160 (51.8%)
Age	54.8 (SD 12.5), median 55
Type of PsA	Axial: 94 (30.4%) Only axial: 18 (5.8%)
	Peripheral: 290 (93.9%) Only peripheral: 215 (69.6%)
	Axial and peripheral: 76 (24.6%)
Treatment	NSAIDs 31 (10%)
	cDIMARDs 124 (40.1%)
	bDIMARDs 151 (48.8%)
	Others (Aza, cyclosporin) 2 (0.6%)
PsA duration	125.1 months (SD 110.5)

Hypertension	89 (28.8%)
DM	45 (14.6%)
Dyslipidaemia	82 (26.5%)
Previous CV events	12 (3.9%)
BMI ≥30	110 (35.6%)
Tobacco	73 (23.6%)
Hyperuricemia	50 (16.2%)
Presence of CVR factors	
0 factors	107 (34.6%)
1 factor	108 (35%)
2 factors	60 (19.4%)
≥3 factors	34 (11%)

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SAT0387 CONSISTENT EFFICACY IN PATIENT SUBGROUPS ACROSS BASELINE DEMOGRAPHICS AND DISEASE CHARACTERISTICS: RESULTS FROM A PHASE 2 STUDY OF GUSELKUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Guselkumab (GUS) is a monoclonal antibody targeting interleukin-23 that has demonstrated efficacy in a phase 2 trial of psoriatic arthritis (PsA).[1]
Objectives: Here subgroup analyses were conducted to evaluate the consistency of efficacy on the primary endpoint, ACR20 response.
Methods: In this randomized, double-blind, placebo-controlled, Phase-2 trial, pts with active PsA (≥3 tender, ≥3 swollen joints, C-reactive protein ≥3 mg/L, ≥3% body surface area [BSA] of plaque psoriasis) despite current or previous treatment with standard-of-care therapies were randomized 2:1 to subcutaneous GUS 100 mg (n=100) or placebo (PBO, n=49) at Wk0, Wk4, and every 8 wks (q8w) through Wk44. At Wk16, pts with <5% improvement in both swollen and tender joints could escape early to open-label ustekinumab. Pts continuing PBO crossed-over to receive GUS 100mg at Wk 24, 28 then q8w through Wk44. The primary analysis was performed in a modified Intent-to-Treat (mITT) population which include all randomized subjects who received at least 1 administration of study agent based on their assigned treatment regardless actual treatment received. Pts who met treatment failure criteria, escaped early, or had missing data at Wk24 were considered non-responders for ACR20 at Wk24. Pre-planned subgroup analyses by demographic and disease characteristics at baseline and PsA medication use were performed, using the same data handling rules as in the primary analysis.
Results: At Wk24, 58/100 (58·0%) of pts in the GUS vs 9/49 (18.4%) in the PBO group achieved an ACR20 response (p<0·001). Efficacy was consistently observed in subgroups defined by demographics (gender, age, weight, region), disease characteristics at baseline (disease duration, PsA subtypes, tender/swollen joint counts, HAQ-DI, CRP, presence of dactylitis or enthesitis, PASI, and BSA) or PsA medication use (prior use of DMARDs or anti-TNFs, concomitant use of MTX, oral corticosteroids, or NSAIDs) (Table). The treatment effect was statistically significant in the majority of subgroups with the lower bound of the 95% confidence interval of the difference between GUS and PBO exceeding 0 in favor of GUS. There are a few exceptions where small sample sizes of the subgroups limited the interpretation. All enrolled subjects were white; therefore, the effect of guselkumab in other racial groups could not be assessed. Among GUS-treated pts, pts with enthesitis, dactylitis, PASI ≥12, BSA >10%, tender joint count ≤10 or swollen joint count ≤10 appeared to have numerically higher ACR20 response rate than those corresponding subgroups defined otherwise, although the sample size is small and the data should be interpreted with caution.

Table. Number of Patients Achieving ACR-20 Response at Week 24 by Treatment Group in Subgroups of Patients Defined by Baseline Demographic/Disease Characteristics and PsA Medication Use

		Placebo n/N (%)	Guselkumab n/N (%)	Difference (95% CI)
All Patients		9/49 (18.4)	58/100 (58.0)	39.6 (25.2, 54.1)
Gender	Male	5/24 (20.8)	29/52 (55.8)	33.8 (12.6, 54.9)
	Female	4/25 (16.0)	29/48 (60.4)	43.2 (22.8, 63.7)
Age (yrs)	<65	9/47 (19.1)	48/89 (53.9)	34.7 (19.6, 49.9)
	≥65	0/2 (0)	10/11 (90.9)	90.9 (73.9, 100.0)
Weight (kg)	≤90	8/31 (25.8)	38/67 (56.7)	31.2 (11.9, 50.5)
	>90	1/18 (5.6)	20/33 (60.6)	55.2 (35.7, 74.7)
Geographic Region				
USA, Canada, Spain, or Germany		2/11 (18.2)	9/19 (47.4)	29.9 (0.0, 59.7)
Poland, Russia, or Romania		7/38 (18.4)	49/81 (60.5)	42.4 (26.2, 58.5)
PsA duration (yrs)	<1	1/10 (10.0)	10/15 (66.7)	56.7 (26.4, 86.9)
	1 to <3	5/10 (50.0)	16/25 (64.0)	16.7 (−19.6, 52.9)
	≥3	3/29 (10.3)	32/60 (53.3)	43.0 (26.4, 59.6)
PsA Subtype				
Arthritis Mutilans		0/3 (0)	0	
Asymmetric Peripheral Arthritis		2/14 (14.3)	18/26 (69.2)	52.3 (25.4, 79.2)
Dip Joint Involvement		3/7 (42.9)	8/17 (47.1)	-2.9 (-49.5, 43.6)
Polyarticular Arthritis with Absence of Rheumatoid Nodules		3/20 (15.0)	19/39 (48.7)	32.1 (9.1, 55.0)
Spondylitis with Peripheral Arthritis		1/5 (20.0)	13/18 (72.2)	48.8 (7.0, 90.5)
# Swollen joints	<5	0/7 (0)	4/10 (40.0)	40.0 (9.6, 70.4)
	5-10	5/25 (20.0)	28/44 (63.6)	43.1 (22.0, 64.2)
	>10	4/17 (23.5)	26/46 (56.5)	32.1 (7.6, 56.6)
# Tender joints	<5	0/1 (0)	1/2 (50.0)	50.0 (−19.3, 100.0)
	5-10	0/11 (0)	13/20 (65.0)	66.6 (46.5, 86.8)
	>10	9/37 (24.3)	44/78 (56.4)	32.1 (14.7, 49.6)
CRP	<1	5/28 (17.9)	29/53 (54.7)	36.5 (16.9, 56.1)
	≥1	4/21 (19.0)	29/47 (61.7)	41.9 (20.1, 63.6)
HAQ-DI	<1	1/10 (10.0)	11/19 (57.9)	46.8 (16.5, 77.0)
	≥1	8/39 (20.5)	47/81 (58.0)	37.5 (21.0, 53.9)
PASI Score	<12	6/31 (19.4)	30/60 (50.0)	30.9 (12.2, 49.6)
	12-20	0/9 (0)	12/17 (70.6)	72.4 (52.7, 92.2)
	>20	2/8 (25.0)	15/21 (71.4)	43.4 (6.9, 80.0)
Psoriatic BSA (%)	3-10	6/29 (20.7)	24/43 (55.8)	34.9 (14.0, 55.9)
	10-20	1/6 (16.7)	17/30 (56.7)	40.5 (5.5, 75.5)
	>20	2/14 (14.3)	17/27 (63.0)	48.1 (22.3, 73.9)
Enthesitis	Yes	5/31 (16.1)	46/76 (60.5)	43.9 (27.1, 60.8)
	No	4/18 (22.2)	12/24 (50.0)	26.7 (−0.2, 53.5)
Dactylitis	Yes	6/23 (26.1)	36/58 (62.1)	35.8 (14.1, 57.5)
	No	3/26 (11.5)	22/42 (52.4)	40.8 (21.5, 60.2)
Prior PsA Med use:				
Anti-TNF	Yes	0/4 (0)	6/9 (66.7)	66.7 (35.9, 97.5)
	No	9/45 (20.0)	52/91 (57.1)	37.1 (21.7, 52.6)
DMARD	0	2/8 (25.0)	4/10 (40.0)	15.0 (−27.7, 57.7)
	1	5/33 (15.2)	43/71 (60.6)	45.4 (28.8, 62.0)
	≥2	2/8 (25.0)	11/19 (57.9)	30.6 (−7.2, 68.3)
Baseline PsA Med use:				
MTX	Yes	5/19 (26.3)	27/47 (57.4)	30.0 (5.8, 54.2)
	No	4/30 (13.3)	31/53 (58.5)	44.4 (26.5, 62.2)
Corticosteroid (oral)	Yes	2/8 (25.0)	10/12 (83.3)	61.3 (27.3, 95.4)
	No	7/41 (17.1)	48/88 (54.5)	37.5 (22.0, 52.9)
NSAID	Yes	7/36 (19.4)	42/70 (60.0)	40.6 (23.5, 57.8)
	No	2/13 (15.4)	16/30 (53.3)	38.3 (12.0, 64.6)

ACR-20 = 20% improvement in American College of Rheumatology criteria; BSA = Body Surface Area; CI = confidence interval; CRP = C-Reactive Protein; HAQ-DI = Health Assessment Questionnaire–Disability Index; MTX = methotrexate; Med=medication; NSAID = non-steroidal anti-inflammatory drug; PASI = Psoriasis Area and Severity Index; PsA = psoriatic arthritis; TNF = tumor necrosis factor.
95% CI's were calculated based on Wald statistics.

Conclusion: In this phase 2 trial of patients with PsA, GUS demonstrated efficacy consistently across subgroups of pts according to baseline demographics, disease characteristics, and PsA-medication use. The relationship between baseline characteristics and clinical outcome will be further explored in phase 3 studies with a larger PsA population.

REFERENCE

[1] Deodhar A, et al. Lancet 2018;391: 2213–24.

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SAT0388

CHARACTERIZATION OF PATIENTS WITH PSORIATIC ARTHRITIS AND NAIL PSORIASIS: DATA FROM THE CORRONA PSORIATIC ARTHRITIS/ SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

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Background: Nail disease is an important feature of PsA and may even precede the disease by many years.[1] Nail psoriasis is considered one of the 6 disease domains of PsA[2]; however, there have been limited real-world studies that have examined characteristics of patients with PsA and nail psoriasis, particularly in the United States.

Objectives: To characterize the disease activity, quality of life, and work productivity of patients with PsA with and without nail psoriasis in the US-based Corrona PsA/SpA Registry.

Methods: This study included all patients in the Corrona PsA/SpA registry enrolled between March 2013 and October 2018 with a diagnosis of PsA who had non-missing data on physician-reported nail psoriasis. Patients were stratified by presence vs absence of nail psoriasis at the time of enrollment, defined as a non-zero response on the nail psoriasis visual analog scale (VAS) of 0–100. Descriptive analyses of patient demographics, disease activity, quality of life, and work productivity were assessed at enrollment and compared between nail psoriasis groups using *t*-tests or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher's exact tests for categorical variables.

Results: A total of 2841 patients with PsA met the inclusion criteria, including 1152 patients (40.5%) with nail psoriasis and 1689 patients (59.5%) without nail psoriasis at enrollment. Patients with and without nail psoriasis were similar in terms of demographic and clinical characteristics; however, patients with nail psoriasis were slightly younger (53.1 vs 54.4 years) and more likely to be male (51.9% vs 44.1%) and have a higher history of depression (17.8% vs 13.3%) compared with patients without nail psoriasis (all $P < 0.05$). Patients with nail psoriasis had more severe psoriasis and PsA disease activity, as reflected by statistically significantly higher percentage of affected body surface area (BSA), higher tender and swollen joint counts, decreased likelihood of being in minimal disease activity, worse mean Disease Activity in Psoriatic Arthritis (DAPSA) and Psoriatic Arthritis Disease Activity Score (PASDAS) values, and increased likelihood of having enthesitis and dactylitis at enrollment compared with patients without nail psoriasis (**Table 1**; all $P < 0.05$). Patients with nail psoriasis had worse self-reported physical function (HAQ-DI), pain, fatigue, EQ-5D scores, and work and activity impairment compared with patients without nail psoriasis (**Table 2**; all $P < 0.05$).

Conclusion: PsA patients with nail psoriasis at the time of registry enrollment had worse disease activity, quality of life, and work productivity compared with those patients without nail involvement. These findings emphasize the importance of identification and management of nail disease in patients with PsA.

REFERENCES

[1] Gladman DD, et al. Ann Rheum Dis. 2005;64(suppl 2):ii14-7.
[2] Coates LC, et al. *Arthritis Rheumatol.* 2016;68(5):1060-71.

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Table 1. Disease Activity Among Patients With PsA at Enrollment Stratified by Presence of Nail Psoriasis

Characteristic*	With Nail PsO (N = 1152)	Without Nail PsO (N = 1689)	*P* Value†
Nail PsO (VAS 0–100)	18.9 (22.5) [1152]	0 [1689]	—
Tender joint count (0-68)	6.0 (9.9) [1127]	3.5 (7.1) [1639]	< 0.01
Swollen joint count (0-66)	2.4 (4.4) [1125]	1.7 (3.5) [1639]	< 0.01
MDA, n/m (%)‡	359/1027 (35.0)	716/1503 (47.6)	< 0.01
DAPSA	18.1 (15.7) [643]	13.4 (12.4) [994]	< 0.01
DAPSA group, n (%)	n = 643	n = 994	< 0.01
Remission	90 (14.0)	232 (23.3)	
Low	231 (35.9)	402 (40.4)	
Moderate	195 (30.3)	247 (24.8)	
High	127 (19.8)	113 (11.4)	
PASDAS	3.8 (1.6) [619]	3.3 (1.5) [972]	< 0.01
PASDAS group, n (%)	n = 619	n = 972	< 0.01
Inactive	215 (34.7)	465 (47.8)	
Moderate	132 (21.3)	227 (23.4)	
Active	228 (36.8)	239 (24.6)	
Very active	44 (7.1)	41 (4.2)	
Enthesitis, n/m (%)	319/1152 (27.7)	287/1689 (17.0)	< 0.01
SPARCC Enthesitis Index (1-16)	3.8 (2.9) [319]	3.5 (2.8) [287]	0.14
Dactylitis, n/m (%)	140/1152 (12.2)	125/1689 (7.4)	< 0.01
Dactylitis count (1-20)	2.4 (2.3) [140]	2.2 (1.8) [125]	0.50
BSA, % affected	7.9 (14.8) [1125]	3.5 (7.6) [1636]	< 0.01
BSA (categorical), n (%)	n = 1125	n = 1636	< 0.01
No disease (0%)	201 (17.9)	583 (35.6)	
Mild disease (> 0% to ≤ 3%)	469 (41.7)	680 (41.6)	
Moderate disease (> 3% to ≤ 10%)	258 (22.9)	254 (15.5)	
Severe disease (> 10%)	197 (17.5)	119 (7.3)	

BSA, body surface area; DAPSA, Disease Activity in Psoriatic Arthritis; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PsO, psoriasis; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale.
* All values were calculated based on available data and are presented as "mean (SD) [n]" unless otherwise stated.
† *t*-test or Wilcoxon rank-sum test for continuous variables and χ^2 or Fisher's exact test for categorical variables.
‡ MDA is defined as 'yes' if a patient met at least 5 of the 7 following categories: tender joint count ≤ 1, swollen joint count ≤ 1, body surface area ≤ 3%, patient pain VAS ≤ 15, patient global activity visual analogue scale ≤ 20, health assessment questionnaire ≤ 0.5, and tender entheseal points ≤ 1.

Table 2. Patient-Reported Outcome Measures Among Patients With PsA at Enrollment Stratified by Presence of Nail Psoriasis

Characteristic*	With Nail PsO (N = 1152)	Without Nail PsO (N = 1689)	*P* Value†
Patient pain (VAS 0-100)	41.7 (30.1) [1081]	36.1 (29.1) [1603]	< 0.01
Patient-reported fatigue (VAS 0-100)	43.9 (29.4) [1135]	39.0 (29.6) [1661]	< 0.01
Patient global assessment of arthritis (VAS 0-100)	41.8 (29.5) [1132]	38.0 (30.1) [1663]	< 0.01
Patient global assessment of arthritis and psoriasis (VAS 0-100)	41.6 (29.0) [1130]	37.4 (30.0) [1659]	< 0.01
Morning stiffness	n = 1118	n = 1644	< 0.01
< 30 minutes	380 (34.0)	600 (36.5)	
≥ 30 minutes	738 (66.0)	1044 (63.5)	
HAQ (0-3)	0.7 (0.7) [1087]	0.6 (0.6) [1613]	< 0.01
EQ-5D (0-1)	0.7 (0.2) [1080]	0.8 (0.2) [1600]	< 0.01
EQ VAS (0-100)	68.6 (21.4) [1127]	72.1 (21.1) [1663]	< 0.01
WPAI domains			
Current employment, n/m (%)	678/1109 (61.1)	1003/1636 (61.3)	0.93
% Work time missed	5.9 (16.9) [575]	4.6 (14.9) [868]	0.26
% Impairment while working	20.3 (23.8) [605]	18.1 (23.1) [929]	0.02
% Overall work impairment	23.2 (26.1) [540]	20.5 (25.3) [839]	0.02
% Activity impairment	32.5 (30.2) [1026]	26.6 (28.0) [1543]	< 0.01

EQ-5D, EuroQol 5 Dimensions questionnaire; HAQ-DI, Health Assessment Questionnaire Disability Index; MDA, minimal disease activity; PsO, psoriasis; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment questionnaire.
* All values were calculated based on available data and are presented as "mean (SD) [n]" unless otherwise stated.
† *t*-test or Wilcoxon rank-sum test for continuous variables and χ^2 or Fisher's exact test for categorical variables.

None declared, Blessing Dube Employee of: B. Dube is an employee of Corrona, LLC., Meghan Glynn Employee of: M. Glynn is an employee of Corrona, LLC., Alexis Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer Inc, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda
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SAT0389

INHIBITIONOF RADIOGRAPHIC PROGRESSION WAS ACHIEVED WITH INTRAVENOUS GOLIMUMAB IN ACTIVE PSA PATIENTS REGARDLESS OF CHANGES IN COMPOSITE INDICES OF DISEASE ACTIVITY IN A PHASE III TRIAL

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Background: GO-VIBRANT is a Phase 3 trial of intravenous (IV) golimumab (GLM), an anti-tumor necrosis factor alpha (TNFα) monoclonal antibody, in adult patients (pts) with active psoriatic arthritis (PsA).
Objectives: To assess if changes in Disease Activity in PsA (DAPSA), PsA Activity Score (PASDAS), Minimal Disease Activity (MDA), Very Low Disease Activity (VLDA), and Clinical Disease Activity Index (CDAI) measures correlate with X-ray progression.
Methods: In this multicenter, randomized, double-blind, placebo (PBO)-controlled trial, 480 bionaïve PsA pts with active disease (≥5 swollen & ≥5 tender joints, C-reactive protein ≥0.6mg/dL, active plaque psoriasis or documented history despite treatment w/csDMARDs &/or NSAIDs) received IV GLM 2mg/kg (N=241) at Wks0/4 then q8wks or PBO (N=239) at Wks0/4/12/20 with crossover to GLM at Wk24. In a post-hoc analysis, association of disease activity measures DAPSA, PASDAS, MDA, VLDA, & CDAI with X-ray progression was examined. Total modified van der Heijde-Sharp (vdH-S) score assessed X-ray progression at Wks 0/24/52. Last observation carried forward imputation was used for partially missing data & non-responder imputation for missing data. Nominal p-values are reported without multiplicity adjustment.
Results: Mean changes from baseline in vdH-S scores were lower with GLM than PBO at Wk24 (-0.36 vs 1.95, respectively, p<0.001) and at Wk52 after crossover from PBO to GLM arm (-0.49 vs 0.76). Changes in all disease activity measures appeared to correlate with X-ray progression (Table). GLM-treated pts had less X-ray progression regardless of disease activity measure. GLM treated pts in remission or with low disease activity tended to have less X-ray progression at Wk52 vs pts with moderate or high disease activity (mean change in vdH-S: DAPSA remission or low disease activity -0.88, moderate activity -0.48, high disease activity 0.41). Similar patterns were seen with PASDAS and CDAI (Table). Irrespective of level of disease activity, GLM-treated pts from Wk 0-52 tended to have less X-ray progression vs PBO-treated pts who switched to GLM at Wk24 (mean change in vdH-S 0-52 wk GLM vs PBO→GLM: DAPSA remission or low disease activity -0.88 vs 1.49, moderate activity -0.48 vs 1.38, high disease activity 0.41 vs 1.27).
Interestingly, pts treated with GLM who did not achieve MDA or VLDA by Wk52 also tended to have less X-ray progression vs PBO pts (mean change no MDA GLM 0.03 vs PBO 1.50; p=0.0011 and mean change no VLDA GLM -0.30 vs PBO 1.45; p<0.0001).
Conclusion: In this analysis, all disease activity measures generally correlated with X-ray progression from baseline to Wk24 and to Wk52. Higher disease activity was associated with increased X-ray progression. GLM–treated pts not achieving MDA & VLDA at Wk52 tended to have less X-ray progression vs PBO→GLM pts. GLM's ability to inhibit X-ray progression, despite pts not being in clinical remission or low disease activity, illustrates an example of "disconnect" between clinical outcomes & X-ray progression seen in other studies.
Disclosure of Interests: Philip J Mease Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Consultant for: AbbVie, Amgen, BMS, Galapagos, Gilead Sciences,

Table. Mean change from baseline (SD) in total modified vdH-S score stratified by CDAI, DAPSA, PASDAS, MDA, and VLDA in PsA patients from GO-VIBRANT

	Baseline to Wk24		Baseline to Wk52	
	PBO	GLM 2 mg/kg	PBO→GLM 2[a]	GLM 2 mg/kg
DAPSA				
Remission–low disease activity (≤14), n	10	107	105	119
Mean change (SD)	-0.05±2.14	-0.64±1.66	1.49±4.96	-0.88±2.34
p-value		0.4422		<0.001
Moderate disease activity (>14–28), n	37	59	66	64
Mean change (SD)	0.29±1.81	-0.32±1.54	1.38±4.16	-0.48±1.82
p-value		0.0268		0.0025
Active disease activity (>28), n	190	71	66	54
Mean change (SD)	1.77±3.56	0.21±1.97	1.27±4.36	0.41±3.30
p-value		0.0007		0.2598
PASDAS				
Inactive disease activity (≤3.2), n	12	101	114	118
Mean change (SD)	-0.17±2.136	-0.64±1.729	1.53±4.850	-1.01±2.384
p-value		0.4305		<0.0001
Moderate disease activity (>3.2 & <5.4), n	85	109	83	83
Mean change (SD)	0.73±1.926	-0.16±1.750	1.14±3.727	-0.20±1.965
p-value		0.0003		0.0055
High disease activity (≥5.4), n	125	22	19	17
Mean change (SD)	2.29±4.107	0.47±1.891	3.81±7.052	0.54±3.066
p-value		0.0290		0.1122
MDA				
Yes, n	11	78	80	101
Mean change (SD)	0.91±2.49	-0.83±1.78	1.19±3.86	-1.16±2.46
p-value		0.0232		<0.0001
No, n	226	159	157	136
Mean change (SD)	1.49±3.39	-0.05±1.70	1.50±4.90	0.03±2.44
p-value		<0.0001		0.0011
VLDA				
Yes, n	1	16	24	35
Mean change (SD)	0	-0.91±1.04	0.91±3.32	-1.49±2.22
p-value		0.3749		0.0041
No, n	236	221	213	202
Mean change (SD)	1.47±3.36	-0.26±1.80	1.45±4.69	-0.30±2.52
p-value		<0.0001		<0.0001
CDAI				
Remission (≤2.8), n	5	43	58	63
Mean change (SD)	-0.60±1.34	-0.80±1.76	1.52±5.55	-1.06±2.41
p-value[b]		0.9170		0.0003
Low disease activity (>2.8 & ≤10), n	28	98	78	92
Mean change (SD)	0.77±2.01	-0.41±1.43	1.21±3.59	-0.81±2.12
p-value		0.0011		<0.0001
Moderate disease activity (>10 & ≤22), n	67	66	64	69
Mean change (SD)	0.88±2.73	-0.10±2.04	1.32±4.25	0.20±2.82
p-value		0.0429		0.0905
High disease activity (>22), n	137	30	37	13
Mean change (SD)	1.96±3.79	0.30±1.95	1.75±5.34	1.11±2.65
p-value		0.0079		0.8144

CDAI=Clinical Disease Activity Index; DAPSA=Disease Activity in Psoriatic Arthritis score; GLM=golimumab; MDA=Minimal Disease Activity; PBO=placebo; PASDAS=Psoriatic Arthritis Activity Score; PsA=active psoriatic arthritis; SD=standard deviation; vdH-S=van der Heijde-Sharp; VLDA=Very Low Disease Activity
[a]PBO pts crossed over to IV GLM 2 mg/kg at Wk24.
[b]P-value is based on ANOVA w/ Van der Waerden rank test

Inc., Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer and UCB, M Elaine Husni Grant/research support from: Janssen, Shelly Kafka Shareholder of: J&J, Employee of: J&J, Soumya D Chakravarty Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson, Diane D Harrison Employee of: Janssen Research & Development, LLC, Kim Hung Lo Employee of: Janssen Research & Development, LLC, Stephen Xu Employee of: Employee of Janssen Research & Development, LLC, Elizabeth C Hsia Employee of: Employee of Janssen Research & Development, LLC, Arthur Kavanaugh Grant/research support from: UCB Pharma

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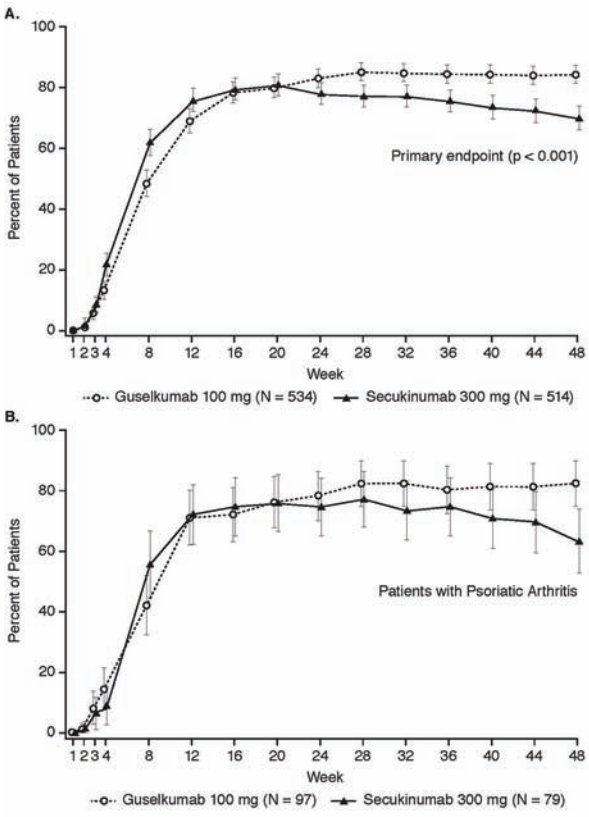
SAT0390

GUSELKUMAB WAS MORE EFFECTIVE THAN SECUKINUMAB IN PATIENTS WITH PLAQUE PSORIASIS AND THE SUBSET OF PATIENTS WITH SELF-REPORTED PSORIATIC ARTHRITIS IN THE RANDOMIZED, DOUBLE-BLIND, HEAD-TO-HEAD COMPARISON STUDY ECLIPSE OVER 1 YEAR

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Background: Guselkumab (GUS, an antibody against IL-23) and secukinumab (SEC, an antibody against IL-17A) are both approved for the treatment of psoriasis (PsO). Up to 30% of patients with PsO may have psoriatic arthritis (PsA).
Objectives: The ECLIPSE study compared efficacy and safety of GUS vs SEC in patients with plaque PsO. Post hoc analyses examined outcomes in the subgroup of patients with self-reported psoriatic arthritis (PsA).
Methods: ECLIPSE was a randomized, double-blind trial of adults with moderate-to-severe plaque PsO who received GUS 100 mg at Weeks 0, 4, then every 8 weeks, or SEC 300 mg at Weeks 0, 1, 2, 3, and 4, then every 4 weeks, both through Week 44. The primary endpoint was the proportion of patients achieving ≥90% improvement compared to baseline in the Psoriasis Area and Severity Index (PASI) score at Week 48. Cochran-Mantel Haenszel chi-square testing stratified by investigator was used to compare treatment-group responses.
Results: Overall, treatment groups [GUS (n=534), SEC (n=514)] were comparable at baseline: weight 89kg, 24% body surface area PsO, and Investigator Global Assessment (IGA) moderate (76%) or severe (24%). These characteristics were similar to those of subgroups with self-reported PsA [GUS (n=97), SEC (n=79)]. In the overall population, the primary endpoint of PASI 90 response at Week 48 was achieved by 84.5% of GUS vs 70.0% of SEC patients (treatment difference 14.2 [95% CI=9.6%,18.8%], P<0.001). Among patients with PsA, the primary endpoint of PASI 90 response at Week 48 was achieved by 82.5% of GUS vs 63.3% of SEC patients (treatment difference 19.2% [95% CI=5.0%, 33.4%]). Beyond week 20, in both the overall study population and the PsA subpopulation, GUS-treated patients maintained the PASI 90 response while SEC-treated patients had a reduction in response through week 48 (Figure). In the overall population, results of the first major secondary endpoint (proportion of patients with a PASI 75 response at both Week 12 and 48) showed non-inferiority of GUS vs SEC (GUS-84.6% vs SEC-80.2% of patients, p<0.001), but superiority was not demonstrated (p=0.062). Adverse events observed in the overall population and PsA subgroup were generally consistent with the established safety profiles for GUS and SEC.
Conclusion: In the subset of patients with self-reported PsA in the ECLIPSE study, GUS demonstrated better maintenance of response and higher efficacy at approximately one year compared with SEC in the treatment of moderate to severe plaque PsO. These findings were consistent with those for the overall study population of patients with plaque PsO. AEs observed were generally consistent with the established safety profiles for GUS and SEC.
Disclosure of Interests: Joseph F Merola Grant/research support from: Janssen, Shu Li Employee of: Janssen Research & Development, LLC, Ming-Chun Hsu Employee of: Janssen Research & Development, LLC, Chetan Karyekar Shareholder of: J&J, Employee of: Janssen Scientific

Figure. Proportion of Patients Achieving PASI 90 Response (95% CI)



A. Total ECLIPSE population of patients with moderate to severe plaque psoriasis.
B. Subgroup of patients with Psoriatic Arthritis.
Non-responder imputation was used for missing data.
CI=Confidence interval, PASI 90=90% improvement in the Psoriasis Area and Severity Index (PASI).

Affairs, LLC, Abbott, BMS, Novartis, Susan Flavin Employee of: Janssen Research & Development, LLC, Bruce Randazzo Employee of: Janssen Research & Development, LLC, Laura C Coates Grant/research support from: AbbVie, Celgene, Lilly, Novartis and Pfizer, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead Sciences Inc., Janssen, Lilly, Novartis, Pfizer, Prothena Corp and UCB

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SAT0391

REMISSION AND DRUG RETENTION RATES OF SECUKINUMAB IN 1549 PATIENTS WITH PSORIATIC ARTHRITIS TREATED IN ROUTINE CARE – POOLED DATA FROM THE OBSERVATIONAL EUROSPA RESEARCH COLLABORATION NETWORK

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Background: There is a lack of data on exposure, treatment outcomes and retention rates of secukinumab in patients with psoriatic arthritis (PsA) treated in routine care.

Objectives: Primary objective: To assess the proportion of PsA patients in remission after 6 months of secukinumab treatment across Europe. Secondary objectives: To compare baseline clinical and demographic characteristics, 6-month crude and LUNDEX adjusted remission rates, 6-month retention rates and median time to secukinumab withdrawal (due to loss of efficacy/adverse events) between bDMARD naïve and non-naïve patients as well as across the participating European registries.

Methods: PsA patients starting secukinumab in routine care and followed for at least 6 months were included from 12 European registries within the European Spondyloarthritis Research Collaboration (EuroSpA). Independent t-test, Mann-Whitney U test, ANOVA, Kruskal-Wallis and Chi-square test were used for group comparisons as appropriate, and Kaplan-Meier plots with log rank test for comparison of secukinumab drug survival.

Results: A total of 1549 PsA patients starting secukinumab were included (Table). 6-month remission and retention rates were significantly different between the registries (Table). Biologic DMARD (bDMARD) naïve compared with non-naïve patients had significantly higher 6-month remission rates and a trend towards better 6-month retention rates (Table, Figure 1a-b).

Conclusion: This study of >1500 patients in 12 European countries provides real-world data on the effectiveness of secukinumab in patients with PsA, adding evidence to existing RCTs. A majority of the patients had long disease duration and was previous bDMARD users. DAS28CRP, SDAI and DAPSA28 remission at 6 months were achieved by 35%, 12% and 12%, respectively. The overall retention rate was 86%, with significant differences across the registries. bDMARD naïve compared with non-naïve patients had significantly better 6-month remission rates and a trend towards better secukinumab retention rates.

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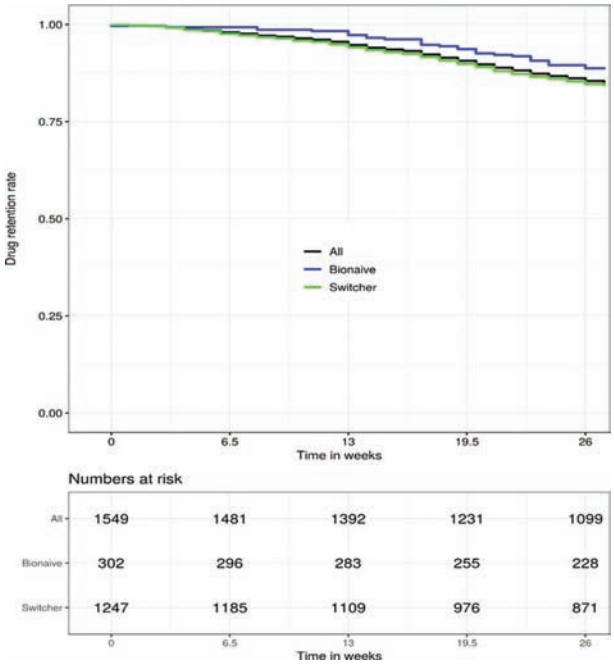


Figure 1. **a** Overall 6-month secukinumab retention rate in EuroSpA as well as compared between bDMARD naïve and non-naïve patients (Kaplan-Meier, log rank test; p=0.07)

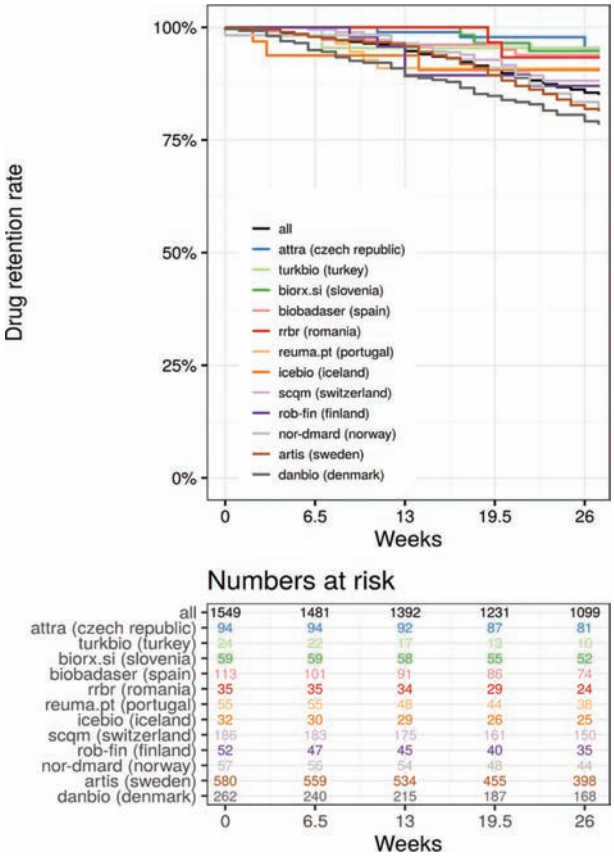


Figure 1. **b** 6-month secukinumab retention rates overall and compared across the different registries in the EuroSpA collaboration (Kaplan-Meier, log rank test; p<0.001)

Pooled data from all registries	All patients (n=1549)	bDMARD naive patients (n=302)	Previous bDMARD users (n=1247)	p*
Age (years), mean (SD)	52 (11)	50 (12)	52 (11)	0.005
Male, n/total (%)	42%	47%	40%	0.03
Disease duration (years), mean (SD)	9 (8)	7 (7)	10 (8)	<0.001
Current smokers, %	18%	17%	18%	0.97
Baseline CRP (mg/L), median (IQR)	5 (2-13)	8 (2-22)	5 (2-11)	<0.001
Baseline ESR (mm/h), median (IQR)	17 (7-33)	22 (10-42)	15 (7-30)	<0.001
Baseline SJC (0-28), median (IQR)	2 (0-4)	2 (0-5)	1 (0-4)	0.002
Baseline TJC (0-28), median (IQR)	4 (1-9)	5 (1-10)	4 (1-9)	0.41
Baseline Pain (0-10), median (IQR)	7 (5-8)	6 (5-8)	7 (5-8)	0.14
6-month DAS28 remission rate (<2.6), % (95%CI)	35% (32-38%)	52% (44-61%)	32% (28-35%)	<0.001
6-month SDAI remission rate (≤3.3), % (95%CI)	12% (9-15%)	23% (16-31%)	9% (6-11%)	<0.001
6-month DAPSA28 remission rate (≤4), % (95%CI)	12% (10-14%)	22% (14-29%)	11% (8-13%)	0.001
6-month secukinumab retention rate, % (95%CI)	86% (84-87%)	89% (85-93%)	85% (83-87%)	0.07
LUNDEX adj. 6-month DAS28 remission rate, % (95%CI)	25% (23-27%)	39% (32-46%)	22% (20-24%)	<0.001
LUNDEX adj. 6-month SDAI remission rate, % (95%CI)	9% (6-11%)	17% (11-23%)	6% (4-8%)	<0.001
LUNDEX adj. 6-month DAPSA28 remission rate, % (95%CI)	9% (7-10%)	17% (11-22%)	8% (6-9%)	0.004
Time to secukinumab withdrawal due to loss of efficacy or adverse events before 6 months, median (IQR) weeks , n of events	17 (10-21), n=203	18 (14-23), n=31	16 (9-21), n=172	0.09
Mean (95%CI) drug retention time, weeks (censored by 26 weeks)	24.5 (24.3-24.7)	25.0 (24.6-25.4)	24.4 (24.1-24.6)	0.07
*Comparison between bDMARD naive and non-naive patients				

According to registry	ARTIS n=480	ATTRA n=84	BIOBADASER n=113	BioRx.is n=69	DANBIO n=262	ICEBIO n=32	NOR-DMARD n=67	REUMAPT n=68	ROB-FIN n=82	RRBR n=38	SCQM n=188	TURKBIO n=24	p*
Age (years) mean (SD)	53 (12)	51 (10)	50 (11)	54 (10)	51 (12)	55 (14)	54 (11)	51 (11)	52 (11)	51 (13)	52(11)	48(12)	0.07
Male, n/total (%)	39%	54%	42%	41%	42%	25%	32%	42%	38%	43%	52%	33%	0.04
Disease duration (years),mean(SD)	8(7)	11(8)	8(7)	11(8)	9(8)	15(11)	13(10)	9(9)	13(9)	6(7)	9(7)	11(10)	<0.001
Current smokers, %	15%	16%	25%	22%	26%	22%	28%	17%	15%	3%	10%	25%	0.04
BL CRP (mg/L), median (IQR)	5 (2-11)	13 (4-27)	2 (1-5)	5 (1-14)	4 (2-12)	3 (1-5)	4 (2-11)	5 (3-17)	4 (1-8)	24 (16-40)	4 (1-8)	6 (3-14)	<0.001
BL ESR (mm/h), median (IQR)	14 (6-27)	28 (13-0)	17 (8-34)	20 (10-40)	-	-	21 (9-34)	20 (10-31)	-	47 (36-70)	12 (6-22)	-	<0.001
BL SJC (0-28), median (IQR)	2(0-4)	4(1-7)	3(0-3)	4(3-7)	1(0-4)	1(1-3)	0(0-2)	4(1-7)	0(0-2)	6(3-9)	1(0-3)	0(0-2)	<0.001
BL TJC (0-28), median (IQR)	5(2-9)	8(4-14)	3(1-7)	4(2-8)	3(1-9)	3(2-5)	3(1-6)	4(2-12)	1(0-4)	12(7-18)	3 (1-8)	0(0-2)	<0.001
BL Pain (0-10), median (IQR)	7(5-8)	7(5-8)	-	7(5-8)	7(5-9)	7(5-8)	6(3-8)	7(4-8)	5(3-8)	-	6 (3-7)	5(3-7)	<0.001
6-month DAS28CRP <2.6, %	39%	40%	50%	47%	30%	25%	57%	46%	38%	50%	52%	**	0.001
6-month SDAI ≤3.3, %	7%	18%	-	15%	11%	0%	10%	15%	17%	**	23%	**	0.13
6-month DAPSA28 ≤4, %	8%	20%	-	12%	11%	0%	14%	15%	24%	-	38%	**	<0.001
6-month secukinumab retention rate, % (95%CI)	82% (79-85%)	95% (91-100%)	94% (89-99%)	95% (88-100%)	79% (74-85%)	91% (81-100%)	83% (74-94%)	91% (84-99%)	87% (78-97%)	97% (85-100%)	95% (91-100%)	95% (87-100%)	<0.001
LUNDEX adj. 6-month DAS28 <2.6, %	22 %	38%	53%	47%	26%	25%	47%	42%	33%	47%	48%	**	<0.001
LUNDEX adj. 6-month SDAI≤3.3, %	6%	17%	-	14%	9%	0%	8%	14%	15%	**	19%	**	0.11
LUNDEX adj. 6-month DAPSA ≤4, %	6%	19%	-	11%	9%	0%	12%	14%	21%	-	31%	**	<0.001
Median (IQR) weeks to secukinumab withdrawal, n events	18 (13-22) n=84	**	**	**	13 (8-19) n=40	**	**	**	**	**	17 (12-21) n=21	**	0.01
*Comparison across the registries; **Less than 10 observations; BL, baseline; - not available													

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SAT0392

IMPLEMENTING THE PSORIATIC ARTHRITIS DISEASE ACTIVITY SCORE (PASDAS) IN ROUTINE CLINICAL PRACTICE: (IM)POSSIBLE?

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease, with involvement of at least five health domains: peripheral joint disease, enthesitis, dactylitis, axial involvement, and skin and nail psoriasis. Because of the heterogeneity of the disease, assessment of disease activity is challenging. One of the many single or composite outcome measures that has been developed is the Psoriatic Arthritis Disease Activity Score (PASDAS). The PASDAS is a comprehensive measure that takes arthritis (66/68 joint score), dactylitis, enthesitis, CRP, physician disease activity VAS score and patient-reported outcomes into account[1]. Furthermore, it is a continuous outcome measure in contrast to the Minimal Disease Activity criteria (MDA), facilitating the longitudinal follow-up of disease activity. The PASDAS also has better parametric distribution and discriminative capacity compared to other outcome measures such as the Disease Activity for PSoriatic Arthritis score (DAPSA). However, feasibility of PASDAS use in routine clinical care has been questioned due to its complexity. It requires a CRP and filled-out SF36 form at time of assessment, does not include a formal skin assessment, is difficult to calculate and is time consuming for both patient and physician.

Objectives: To implement PASDAS measurements and skin assessments in routine clinical care for all 1300 PsA patients treated at our centre.

Methods: The implementation consisted of the following stages: 1) assessment of patients' acceptability of measurement burden; 2) implementation of mathematical calculations of the PASDAS in our electronic health record; 3) PASDAS and skin assessment training of rheumatology nurses and rheumatologists; and 4) (logistic) adjustments to the outpatient visit.

Results: Our patient partners preferred comprehensive clinical assessment of skin and joints above a limited assessment (such as the DAS28-CRP), although the latter would be less time consuming. For this reason, and to comply with international guidelines, we decided to also add assessment of skin disease, by using the Body Surface Area (BSA) and Physician Global Assessment score (PGA). Furthermore, research demonstrated that for the PASDAS calculation the physical component score (PCS) of the SF36 could be substituted by the SF12-PCS[2]. As the SF12 is more concise, minimizing patient burden, we chose to implement the SF12 instead of the SF36. The SF12-PCS, together with the other separate component scores and corresponding mathematical calculation of the PASDAS, was implemented in our electronic health record. Lastly, we set-up a three phase consultation that consists of laboratory tests and consultation with a rheumatology nurse who performs the physical measurements before each visit with the physician.

Conclusion: Standardized and routine measurement of the PASDAS and skin involvement at each outpatient visit of all our PsA patients before consultation with the treating rheumatologist was successfully implemented, underscoring the feasibility of this approach. In addition to improving clinical care, routine outcome measurements can be used for a variety of clinical studies.

REFERENCES

[1] Helliwell, P.S., et al., The development of candidate composite disease activity and responder indices for psoriatic arthritis (GRACE Project). Ann of the Rheum Dis. 2013 Jun;72(6):986-91.

[2] Helliwell, P.S, et al., Modification of the Psoriatic Arthritis Disease Activity Score (PASDAS). Ann Rheum Dis. 2018 Mar;77(3):467-468.

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SAT0393 EFFECTIVENESS AND SAFETY OF INFLIXIMAB, GOLIMUMAB AND USTEKINUMAB IN PSORIATIC ARTHRITIS PATIENTS FROM A PROSPECTIVE OBSERVATIONAL REGISTRY

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Background: Long-term registries are essential to evaluate new therapies in a patient population that differs from clinical trials and usually varies over time.

Objectives: To describe the profile of psoriatic arthritis (PsA) patients selected for treatment with infliximab (IFX), golimumab (GLM) or ustekinumab (UST) treatment in Canadian routine care and to describe the long-term real-world effectiveness and safety of these agents.

Methods: 462 PsA patients treated with IFX, GLM or UST were enrolled into the Biologic Treatment Registry Across Canada (BioTRAC) registry between 2006-2015, 2010-2017 and 2014-2017, respectively. Study visits occurred at baseline and every 6 months thereafter. Effectiveness was assessed with changes in TJC28, SJC28, skin, enthesitis, dactylitis, pain, HAQ, acute phase reactants. Safety was evaluated with the incidence of adverse events (AEs) and drug survival rates.

Results: Of the 111 IFX-, 281 GLM- and 70 UST-treated patients, the proportion of males were 52.3%, 46.3% and 37.1%, the mean age was 48.4, 52.8 and 53.1 years and the mean disease duration was 5.8, 6.1 and 5.7 years, respectively. Most patients were bio-naive (85.6%, 77.9% and 55.7% for IFX, GLM and UST, respectively (p<0.001). A reduction in mean baseline duration of morning stiffness was observed in the IFX cohort (from 69.8 to 42.6 to 23 min in 2006-2008 to 2009-2012 to 2013-2015; p=0.003). Most other baseline disease parameters remained similar over time in all three cohorts. However, UST-treated patients had lower mean baseline DAS28 CRP (3.4 vs 3.9; p=0.0031), SJC (3.8 vs 5.3; p=0.0046) and higher PASI (4.8 vs 2.2; p=0.0061) compared to patients treated with GLM.

Treatment with IFX, GLM and UST was associated with significant improvements in all disease parameters over time (P<0.001) from baseline up to 84, 84 and 40 months, respectively with similar efficacy between agents. The only exception was the proportion of patients in minimal disease activity at 12, 24 and 36 months which reached 40.7%, 50.0% and 55% in IFX-patients; 64.7%, 68.8% and 78.9% in GLM-patients and 58.8%, 60.0% and 83.3% in UST-patients (p=0.004 and p<0.001 vs IFX).

AEs were reported for 74.8%, 69.8% and 52.9% (138, 114 and 115 events/100 PYs) and SAEs for 19.8%, 8.5% and 5.7% (8.8, 19.6 and 28.6 events/100 PYs) covering 325, 567 and 87 years of exposure for IFX-, GLM- and UST-treated patients, respectively. One, one and no death occurred IFX-, GLM- and UST-treated patients, respectively. The proportion of patients who discontinued treatment were 63.1%, 50.9% and 50.0% over a mean exposure of 2.9, 1.9 and 1.2 years to IFX, GLM and UST, respectively.

Conclusion: Differences in baseline characteristics between patients treated with an anti-TNF over an anti-IL12/23 agent suggest that the level of joint to skin involvement might be driving physician choice when the time comes to choose a biologic agent. IFX, GLM and UST treatment significantly reduced disease activity and improved functionality in a similar fashion and were well tolerated in patients with PsA.

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SAT0394 POSSIBLE POTENTIAL INTERACTIONS BETWEEN OBESITY, QUALITY OF LIFE, PSYCHOLOGICAL STATUS AND CLINICAL PARAMETERS IN PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA), a chronic rheumatic disease associated with reduced quality of life. Obesity is an important clinical problem which may interfere with loss of functioning and quality of life. Obesity is usually an overlooked entity in patients with PsA. Several studies were invastigated prevalence and the impact of obesity on disease activity in patients with PsA, however relationship between psychological status and quality of life have not been evaluated comparatively.

Objectives: To assess the impact of obesity on quality of life, psychological status and clinical parameters in patients with PsA.

Methods: Patients with PsA were recruited who met CASPAR classification criteria enrolled by Turkish League Against Rheumatism-NETWORK (TLAR-NETWORK) derived from 24 different centers of our country. Patients with BMI $\geq$30 kg/m^2 were considered obese. Differences among patients with or without obesity were assessed.VAS fatigue, psychological status and health related quality of life measures [SF-36; HAQ; Psoriatic arthritis quality of life (PsAQoL); Hospital Anxiety and Depresson Scale], FACIT-Fatigue, DAS28, BASDAI, BASFI, BASMI, Maastrich Ankylosing Spondylitis Enthesitis *Score* (MASES) and Psoriasis area severity index (PASI) scores were compered between this groups.

Results: A total 1130 patients with PsA (36.0% male, 64.0% female) included in this study. In this cohort 37.6% obese and 62.4% non-obese. The presence of peripheral arthritis, enthesitis, dactylitis, uveitis and spine involvement, PASI scores as well as MASES scores were quite similar between patients with and without obesity. Obese patients had significantly higher scores in VAS fatigue and disease activity, poorer QoL and physical functions compared to non-obese patients (p<0.05). Obese patients had high risk for anxiety and depression (p <0.05).

Conclusion: Obesity associated with the risk of depression and anxiety, fatigue, poorer QoL and higher disease activity.These findings suggest that obesity should be considered while assessing patients with PsA.

REFERENCES

[1] Li W,Han J,Qureshi AA.Obesity and risk of incident psoriatic arthritis in US women.Ann Rheum Dis.2012Aug;71(8):1267-72.

[2] Klingberg E,Bilberg A,Björkman S, et al.Weight loss improves disease activity in patients with psoriatic arthritis and obesity:an interventional study.Arthritis Res Ther.2019Jan11;21(1):17

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SAT0395

RESPONSIVENESS AND CLINICAL TRIAL DISCRIMINATION OF SWOLLEN AND TENDER JOINT COUNTS FOR THE MEASUREMENT OF MSK DISEASE ACTIVITY IN PSORIATIC ARTHRITIS

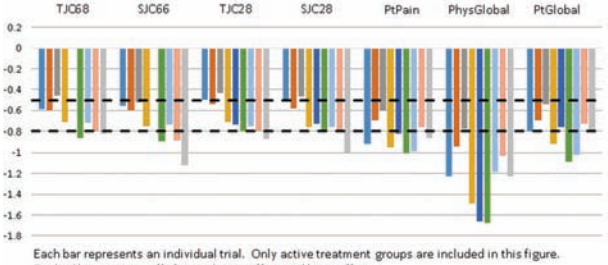
Ali Duarte-Garcia[1], Lihi Eder[2], Niti Goel[3], Maarten de Wit[4], Dafna D. Gladman[5], Oliver Fitzgerald[6], Philip J. Mease[7], Ying Ying Leung[8], Ana-Maria Orbai[9], Bev Shea[10], Vibeke Strand[11], Philip Helliwell[12], Alisa Stephens-Shields[13], William Tillett[14], Laura C. Coates[15], Alexis Ogdie[13], GRAPPA-OMERACT Psoriatic Arthritis Working Group. *[1]Mayo Clinic, Rochester, MN, United States of America*; *[2]Women's College, University of Toronto, Toronto, ON, Canada*; *[3]Patient Research Partner, Durham, NC, United States of America*; *[4]Patient Research Partner, Amsterdam, Netherlands*; *[5]Toronto Western, University of Toronto, Toronto, ON, Canada*; *[6]7St Vincent's University Hospital and Conway Institute for Biomolecular Research, University College, Dublin, Ireland*; *[7]Swedish Medical Center/ Providence-St. Joseph's Health and University of Washington, Seattle, WA, United States of America*; *[8]Singapore General Hospital, Singapore, Singapore*; *[9]Johns Hopkins University, Baltimore, MD, United States of America*; *[10]University of Ottawa, Ottawa, Canada*; *[11]Stanford University, Palo Alto, United States of America*; *[12]University of Leeds, Leeds, United Kingdom*; *[13]University of Pennsylvania, Philadelphia, PA, United States of America*; *[14]Royal National Hospital for Rheumatic Diseases and the University of Bath, Bath, United Kingdom*; *[15]University of Oxford, Oxford, United Kingdom*

Background: While tender and swollen joint counts (TJC and SJC) are key instruments for the assessment of peripheral arthritis in PsA, little is known about the psychometric properties of TJC and SJC in randomized controlled trials (RCTs) and how these properties differ among patient subgroups. [1]

Objectives: To assess the responsiveness and discrimination of TJC and SJC in PsA using RCT datasets and evaluate subgroups of patients with early vs. established disease and 3 or less vs 4 or more active joints.

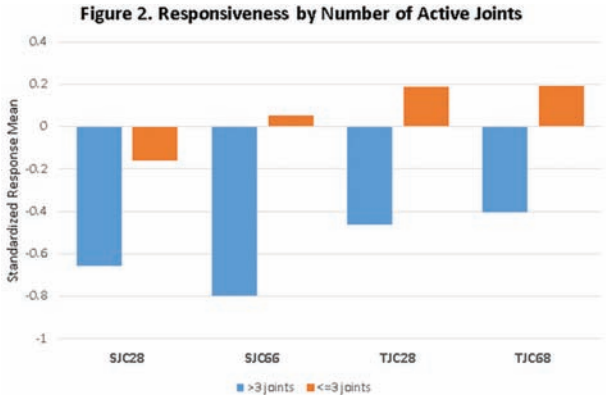
Methods: Patient-level data from 8 phase III RCTs and the TIght COntrol of Psoriatic Arthritis (TICOPA) trial were analyzed[2]. The standardized response mean (SRM, mean difference between baseline and follow up divided by the standard deviation (SD) of the mean difference) and standardized mean differences (SMD, mean difference in the treated group minus the mean difference in the placebo group divided by the pooled SD for the change) were used to address responsiveness and discrimination respectively. TJC28, SJC28, TJC68, and SJC66 were the primary measures of interest but physician and patient global assessments (PhGA and PtGA) and pain were included for comparison. SRMs were calculated in subgroups of patients with less than 3 (TJC68/SJC66 ≤ 3) or more than 3 (TJC68/SJC66) active joints as well as early (< 2 years) and established (≥2 years) disease.

Figure 1. SRM among treated patients by trial



Each bar represents an individual trial. Only active treatment groups are included in this figure. Dashed lines are cut offs for moderate effect and large effect.

Figure 2. Responsiveness by Number of Active Joints



Results: In traditional phase III RCTs, TJC and SJC were responsive and had good clinical trial discrimination. SRMs were similar and ranged from -0.8 to -0.4 ('moderate' responsiveness) (Figure 1). SMDs were similar among SJC28 and SJC66 and likewise between TJC28 and TJC68 but mostly within the small effect range (-0.2 to -0.5; not shown). PhGA and PtGA had higher SMDs than the joint counts. SRMs were substantially lower for joint counts (and also PtGA) among the low compared with the higher joint count groups (Figure 2). There were no substantial differences in SRMs between patients with early and established disease.

Conclusion: Joint counts are responsive to change and have reasonable discrimination in RCTs among patients higher disease activity at baseline. However, joint counts may not be ideal outcome measures in oligoarticular disease and have lower responsiveness and discrimination in this subgroup.

REFERENCES

[1] Duarte-Garcia et al. J Rheumatol 2019 *In Press.*
[2] Coates et al. Lancet 2016

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SAT0396 IMPROVEMENT IN THE SIGNS AND SYMPTOMS OF PSORIATIC ARTHRITIS WITH IXEKIZUMAB COMPARED TO PLACEBO IN PATIENT SUBGROUPS DEFINED BY BASELINE DISEASE CHARACTERISTICS

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Background: Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets interleukin-17A, was superior to placebo (PBO) in two randomized Phase 3 studies in patients (pts) with active psoriatic arthritis (PsA).[1,2]
Objectives: To assess the consistency of response of IXE across subgroups of pts defined by specific baseline disease characteristics.
Methods: Data were analyzed from an integrated database of 2 randomized, double-blind, Phase 3 studies in pts who were either biologic Disease Modifying Anti-Rheumatic Drug (bDMARD)-naïve (SPIRIT-P1) or who had prior inadequate response or intolerance to TNF inhibitors (SPIRIT-P2). Analyses included pts randomly assigned to the approved dosing regimen of IXE (80 mg IXE every 4 wks [IXE Q4W] with a starting dose of 160 mg IXE) or to PBO through Wk 24. Efficacy was measured as the percentage of pts achieving ≥20%, 50%, or 70% improvement from baseline in the American College of Rheumatology criteria (ACR20/50/70) or minimal disease activity (MDA) in subgroups of pts defined by baseline presence of enthesitis, dactylitis, psoriasis body surface area (BSA) involvement (<3% or ≥3%), and c-reactive protein (CRP >6 or ≤6 mg/L). Missing data were imputed by nonresponder imputation.
Results: Clinical response rates at Wk 24 in each subgroup are summarized (Table). Significantly ($p<0.05$) more patients achieved ACR20, ACR50, ACR70, and MDA with IXE compared to placebo across patient subgroups defined by presence of enthesitis, presence of dactylitis, percentage of psoriasis BSA involvement, and by CRP levels at baseline.
Conclusion: At Wk 24, IXE was superior to placebo for the treatment of PsA signs and symptoms regardless of baseline presence of dactylitis or enthesitis, BSA involvement, or CRP levels.

REFERENCES

[1] Mease, et al. Ann Rheum Dis. 2017
[2] Nash, et al. Lancet. 2017

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SAT0397 DESCRIPTIVE COMPARISONS OF THE IMPACT OF APREMILAST AND METHOTREXATE MONOTHERAPY ON PATIENTS WITH OLIGOARTICULAR PSORIATIC ARTHRITIS IN THE CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS REGISTRY

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Background: Therapeutic effectiveness has rarely been studied in a subpopulation of patients with oligoarticular PsA.
Objectives: To examine baseline characteristics and 6-month clinical assessments of PsA patients with oligoarthritis (≤4 swollen joints) who initiated apremilast (APR) or methotrexate (MTX) monotherapy in the Corrona PsA/SpA Registry, a prospective, US-based, observational cohort study. Patients initiating bDMARD monotherapy were also examined as a point of reference.
Methods: Patients ≥18 years of age with PsA and oligoarthritis in the registry who initiated APR, MTX or a bDMARD (reference group) monotherapy and had a 6-month follow-up visit between June 2014 and March 2018 were included. Descriptive statistics were calculated for patients' clinical characteristics and disease assessments at treatment initiation and at the 6-month follow-up visit.
Results: The analysis included 150 patients initiating therapy (APR: n=34; MTX: n=15; bDMARD: n=101). Among APR and MTX initiators, 79% and 20% received at least 1 prior bDMARD, respectively. APR initiators, compared with MTX initiators, were younger (mean [SD]: 55.7 [12.6] vs. 61.5 [16.6] years), had longer disease duration (mean [SD]: 8.0 [6.7] vs. 5.4 [7.8] years), and had higher levels of disease activity

Clinical responses at Week 24 in subgroups defined by baseline disease characteristics (NRI)

	ACR20		ACR50		ACR70		MDA	
	PBO (N=224)	IXE Q4W (N=229)	PBO (N=224)	IXE Q4W (N=229)	PBO (N=224)	IXE Q4W (N=229)	PBO (N=224)	IXE Q4W (N=229)
Enthesitis Present	29/142 (20)	88/159 (55)†	12/142 (9)	58/159 (37)†	2/142 (1)	31/159 (20)†	6/142 (4)	41/159 (26)†
Enthesitis Absent	26/81 (32)	39/70 (56)‡	10/81 (12)	28/70 (40)†	4/81 (5)	21/70 (30)†	14/81 (17)	25/70 (36)*
Dactylitis Present	12/59 (20)	55/92 (60)†	6/59 (10)	38/92 (41)†	2/59 (3)	24/92 (26)†	5/59 (9)	33/92 (36)†
Dactylitis Absent	43/164 (26)	72/137 (53)†	16/164 (10)	48/137 (35)†	4/164 (2)	28/137 (20)†	15/164 (9)	33/137 (24)†
BSA <3%	20/85 (24)	44/80 (55)†	8/85 (9)	29/80 (36)†	2/85 (2)	17/80 (21)†	6/85 (7)	21/80 (26)‡
BSA ≥3%	35/134 (26)	77/141 (55)†	14/134 (10)	55/141 (39)†	4/134 (3)	34/141 (24)†	13/134 (10)	42/141 (30)†
CRP ≤6 mg/L	29/100 (29)	45/97 (46)*	11/100 (11)	31/97 (32)†	2/100 (2)	16/97 (17)†	11/100 (11)	25/97 (26)‡
CRP >6 mg/L	26/122 (21)	80/129 (62)†	11/122 (9)	54/129 (42)†	4/122 (3)	36/129 (28)†	9/122 (7)	41/129 (32)†

Data are provided as n/Ns (%) where n=number of responders and Ns=number of patients in each subgroup p-values from Fisher's exact test; *=p<0.05, ‡=p<0.01, †=p<0.001
ACR20/50/70 = ≥20%, 50%, or 70% improvement from baseline in the American College of Rheumatology criteria; BSA = body surface area; CRP = c-reactive protein; IXE Q4W = 80 mg IXE every 4 weeks; MDA = minimal disease activity; PBO = placebo

at baseline, including greater skin involvement (mean body surface area affected [SD]: 7.1% [17.6%] vs. 4.8% [9.4%]), swollen joint count (mean [SD]: 1.5 [1.5] vs. 1.0 [1.1]) and Clinical Disease Activity for Psoriatic Arthritis (cDAPSA) moderate and high disease activity (50% [APR] vs. 27% [MTX]; mean score [SD]: 14.0 [8.5] vs. 11.5 [4.9]). APR initiators also had greater disease impairments at baseline, represented by numerically higher scores on patient-reported outcome (PRO) measures, including the Health Assessment Questionnaire-Disability Index (HAQ-DI; mean [SD]: 1.0 [0.7] vs. 0.5 [0.4]), Patient's Global Assessment of Disease Activity–Psoriasis (PtGA-PsO; mean [SD]: 47.1 [29.4] vs. 28.4 [16.6]); Patient's Global Assessment of Disease Activity–Psoriatic Arthritis (PtGA-PsA; mean [SD]: 47.1 [29.8] vs. 32.5 [26.3]), fatigue (mean [SD]: 55.9 [30.0] vs. 37.8 [31.9]) and overall pain (mean [SD]: 50.5 [31.1] vs. 46.7 [26.5]). Taken together, results suggest that APR initiators had more refractory oligoarthritis compared with MTX initiators. Clinical assessments at the 6-month follow-up indicate that patients who initiated APR experienced numerically higher improvements in disease activity and various PRO measures compared with MTX, as well as achievement of ≤1 swollen joint, HAQ-DI minimal clinically important difference and cDAPSA remission or low disease activity (Table). Of note, results associated with bDMARDs were more comparable to that of APR.

Conclusion: In this analysis of the Corrona PsA/SpA Registry, APR monotherapy was more often used in patients with refractory oligoarthritis compared with MTX monotherapy. Despite this, the APR treatment group experienced numerically greater improvements in disease activity measures. Improvements observed with APR treatment in patients with long-standing disease and refractory oligoarthritis were comparable to that of bDMARDs.

Clinical Disease Assessments of Corrona PsA/SpA Registry Patients With Oligoarthritis at the 6-Month Visit

Disease Characteristics	APR n=34	MTX n=15	bDMARD n=101
Swollen joint count (0-66)	n=34	n=15	n=101
Mean (SD) change	−0.4 (1.2)	0.1 (0.4)	0.2 (1.4)
Achieved swollen joint count (0-66) ≤1*	n=17	n=4	n=26
n (%)	7 (41.2)	0 (0.0)	4 (15.4)
cDAPSA (0-154)	n=32	n=11	n=96
Mean (SD) change	−1.5 (5.8)	−0.2 (1.9)	−0.1 (6.8)
cDAPSA category[§], n (%)	n=17	n=3	n=36
Remission (≤4)	1 (5.9)	0 (0.0)	2 (5.6)
Low disease activity (>4–≤13)	4 (23.5)	0 (0.0)	6 (16.7)
PtGA-PsO (VAS 0-100 mm)	n=34	n=11	n=97
Mean (SD) change	−2.3 (22.1)	1.7 (10.1)	−2.0 (27.4)
PtGA-PsA (VAS 0-100 mm)	n=34	n=13	n=97
Mean (SD) change	−0.2 (23.8)	2.5 (13.9)	0.4 (25.0)
Patient-reported fatigue (VAS 0-100 mm)	n=33	n=15	n=100
Mean (SD) change	−1.4 (15.7)	0.3 (30.2)	−0.3 (20.1)
Patient-reported overall pain (VAS 0-100 mm)	n=32	n=14	n=99
Mean (SD) change	0.2 (26.3)	−0.1 (15.6)	0.1 (20.4)
Achieved HAQ-DI MCID (≥0.35 point decrease)	n=34	n=14	n=100
n (%)	4 (11.8)	1 (7.1)	8 (8.0)

*Assessed among patients with >1 swollen joint at initiation. [§]Assessed among patients who did not meet criteria for either cDAPSA remission or low disease activity at the time of treatment initiation. Change at 6 months was calculated as the 6-month visit value minus the baseline value. MCID=minimal clinically important difference; VAS=visual analog scale.

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SAT0398

EVALUATION OF THE PREDICTIVITY OF THE THERAPEUTIC RESPONSE ACCORDING TO THE PRESENCE OF METABOLIC COMORBILITIES IN PATIENTS WITH PSORIASIC ARTHRITIS ON BIOTECHNOLOGY THERAPY: OBSERVATIONAL RETROSPECTIVE STUDY

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Background Psoriatic Arthritis (PsA) is a systemic chronic inflammatory disease, which leads to an increased oxidative stress and to endothelial alterations, with increased cardiovascular and metabolic risks. These conditions explain the high prevalence of myocardial infarction, cerebrovascular accidents, diabetes mellitus, obesity, steatohepatitis, alterations of lipid set and an increased prevalence of metabolic syndrome in patients with PsA. The results of other studies suggest that these comorbidities could negatively influence the disease activity and the therapy response in patients with PsA.

Objectives The aim of the study is to evaluate a population of patients with PsA treated with biological drugs (bDMARDs) and the achievement of MDA during the observation.

Methods Ninety-eight patients with PsA treatd by DMARDs from January 2016 to January 2018 were enrolled. Data were collected for 24 months of treatment, related to the check-ups performed every three months. Demographic characteristics, cardiovascular risk factors and cardio-metabolic comorbidities, disease joint involvement at baseline and the assumed therapy were analyzed. The association with the presence of MDA at 0 months and 24 months was evaluated for each of these parameters. Age and gender of patients, duration of illness and smoking habits were taken into consideration. Cardio-vascular risk factors and cardio-metabolic comorbidities selected at baseline were arterial hypertension, diabetes, obesity, hepatic steatosis, hypercholesterolemia, hypertriglyceridaemia, hyperuricaemia, cardiac disorders (myocardial infarction and atrial fibrillation) and cerebro-vascular accidents (stroke and TIA). The population was subdivided according to oligoarticular or polyarticular involvement of the disease present at baseline. As far as the therapy carried out is concerned, the patients were classified according to the class of bDMARDs (anti-TNF-α and not anti-TNF-α), the treatment line at the beginning of the observation (first line or second line and subsequent), the number of switches at 12 and 24 months and simultaneous therapy with relative average dose of drugs (methotrexate and glucocorticoids).

Results Male sex was more associated with the condition of MDA, both at baseline ($p = 0.01$) and at 24 months ($p = 0.04$). A statistically significant association between the presence of cerebro-vascular accidents (stroke and TIA) and the disease status was found at baseline: amongst patients with such comorbidity, 75% were not found in MDA at time 0 ($p = 0.03$). The same result was not found in relation to MDA after 24 months. No other cardio-metabolic comorbidity was associated with a worse outcome. There was no association with a better outcome for any of the two classes of biological drugs considered (anti-TNF-α and not anti-TNF-α). Polyarticular involvement was associated with a worse disease status, both at baseline ($p = 0.01$) and after 24 months of therapy ($p = 0.04$).

Conclusion In the current study, the polyarticular form of PsA present at baseline was the most associated feature (OR 0.44) with a worse outcome in a population of patients with cardio-metabolic comorbidities on bDMARDs. Cerebro-vascular accidents appeared as the only morbid condition associated with a worse state of disease at the beginning of the observation, but this correlation disappears after 24 months. This result can be justified by the immunosuppressive treatment, which decreases the risks related to the inflammatory condition characteristic of PsA.

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SAT0399 EFFECT OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS ON BONE STRUCTURE AND STRENGTH IN PSORIATIC ARTHRITIS PATIENTS

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Background: In contrast to rheumatoid arthritis, little is known about the effect of disease modifying anti-rheumatic drugs (DMARDs) on bone structure and bone biomechanics in psoriatic arthritis (PsA).
Objectives: To address whether the use of methotrexate (MTX) and biological DMARDs (bDMARDs) impacts bone structure and biomechanical properties in PsA patients.
Methods: Cross-sectional study in PsA patients receiving no DMARDs, MTX or bDMARDs. Volumetric bone densities (vBMD), microstructural parameters and biomechanical properties (stiffness/failure load) were determined by high-resolution peripheral quantitative computed tomography (HR-pQCT) and micro-finite element analysis. Bone parameters were compared between PsA patients with no DMARDs and those receiving any DMARDs, MTX or bDMARDs, respectively.
Results: 165 PsA patients were analyzed, 79 received no DMARDs, 86 received DMARDs, of them 52 bDMARDs (TNF, IL-17- or IL-12/23 inhibitors) and 34 MTX. Groups were balanced for age, sex, comorbidities, functional index and bone-active therapy, while disease duration was longest in the bDMARDs group (7.8±7.4 years), followed by the MTX group (4.6±7.4) and the no-DMARD group (2.9±5.2). No difference in bone parameters was found between the no-DMARD group and the MTX group. In contrast, the bDMARDs group revealed significantly higher total (p=0.001) and trabecular vBMD (p=0.005) as well as failure load (p=0.012) and stiffness (p=0.012). In regression models age and bDMARDs influenced total vBMD, while age, sex and bDMARDs influenced failure load and stiffness.
Conclusion: Despite longer disease duration bDMARDs treated PsA patients benefit from higher bone mass and better bone strength than PsA patients receiving MTX or no DMARDs. These data support the concept of better control of PsA-related bone disease by bDMARDs.
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SAT0400 REAL-WORLD SWITCH RATES AMONG BIOLOGIC-NAIVE PSORIATIC ARTHRITIS PATIENTS INITIATING APREMILAST, TUMOR NECROSIS FACTOR INHIBITORS OR INTERLEUKIN INHIBITORS

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Background: Psoriatic arthritis (PsA), an inflammatory arthritis, manifests in joints and surrounding tendons and ligaments.[1] As PsA progresses, patients may switch from 1 therapy to another, discontinue medication or use agents in combination. Previous real-world studies have demonstrated that treatment persistence and adherence rates for biologic-naïve PsA patients initiating apremilast or biologics (ie, tumor necrosis factor [TNF] and interleukin [IL] inhibitors) are not different.[2,3] Treatment switching is common among PsA patients.
Objectives: This study compares the rate of treatment switching among adult patients initiating treatment with apremilast, TNF inhibitor or IL inhibitors.
Methods: Adult patients with PsA were identified if they newly initiated treatment with apremilast, a TNF inhibitor (adalimumab, certolizumab, etanercept, golimumab, infliximab) or an IL inhibitor (ixekizumab, secukinumab, ustekinumab) between January 1, 2015, and December 31, 2016, and had a minimum of 12 months pre-index and post-index continuous enrollment in the Truven Health (now IBM Watson) MarketScan® Commercial and Medicare Supplemental Database. Propensity score matching, based on available demographic and clinical characteristics, up to 1:2, was utilized between apremilast and biologic patients. Switch was defined as a claim for a new PsA treatment after initiation of the index medication. Days to switch was defined as the number of days between the index date and date of switch. Adherence was assessed utilizing the proportion of days covered (PDC). Outcomes were assessed every 3 months, up to 24 months. *T*-test, Wilcoxon rank-sum test and chi-squared test were used to evaluate differences between cohorts for continuous and categorical variables, as appropriate.
Results: 471 biologic-naive PsA patients initiating apremilast were matched to 890 biologic-naive PsA patients initiating biologics (TNF: n=804; IL: n=86). Patient characteristics were similar between the 3 cohorts (mean age: 50 years; Charlson Comorbidity Index: 0.58 [apremilast], 0.55 [TNF] and 0.56 [IL]). There was a greater proportion of females in the apremilast vs IL cohorts (55% vs 42%; *P*=0.0249) and a lower proportion of patients with prior PsA systemic treatment (59% vs 79%; *P*=0.0046). In the TNF cohort, 64% patients received adalimumab, 29% etanercept, 4% infliximab, 2% certolizumab and 1% golimumab. In the IL cohort, 78% of patients received ustekinumab, 21% secukinumab and 1% ixekizumab. At 12 months, significantly fewer patients initiating apremilast switched treatment compared with those initiating TNF inhibitors (15.5% vs 26.6%; *P*<0.0001), while no significant differences were observed for apremilast vs IL patients (15.5% vs 14%; *P*=0.714). Similar switching trends were observed at 24 months for patients initiating apremilast vs TNF (25.0% vs 36.5%; *P*=0.0109) or those initiating apremilast vs IL (25.0% vs 26.7%; *P*=0.8465). Among those switching by 12 months, mean days to switch was similar between apremilast and TNF patients (199 vs 200 days; *P*=0.9759) and apremilast and IL patients (199 vs 227 days; *P*=0.3602). Patients initiating apremilast had a similar treatment adherence rate as patients initiating a TNF inhibitor (PDC: 0.81 vs 0.84; *P*=0.0749) and a higher treatment adherence rate than patients initiating an IL inhibitor (0.81 vs 0.76; *P*=0.0071).
Conclusion: Biologic-naive PsA patients initiating apremilast demonstrated lower switch rates vs biologic-naive PsA patients initiating TNF inhibitors in a large US administrative claims database. No difference in rates of switching was observed between apremilast and IL patients.

REFERENCE

[1] Stankler L. Clin Exp Dermatol. 1981;6:303-6. 2. Wu JJ. Poster presented at: ISPOR 2018. 3. Curtis JR. Poster presented at: ISPOR Europe 2018.

Disclosure of Interests: David Kaplan Consultant for: Celgene Corporation, Speakers bureau: Celgene Corporation. Abbvie, Pfizer, Brian Ung Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, Corey Pelletier Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, Chuka Udeze Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, Marc Tian Shareholder of: Celgene Corporation, Employee of: Celgene Corporation
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SAT0401 USE OF AND RESPONSE TO METHOTREXATE IN EARLY PSORIATIC ARTHRITIS: RESULTS FROM THE REAL WORLD COHORT, DEPAR STUDY

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Background: Methotrexate (MTX) is the preferred drug of most rheumatologists for treating psoriatic arthritis (PsA). Despite its widespread use in

clinical practice, scientific evidence of methotrexate on the different manifestations of psoriatic disease is limited. Specifically, data of MTX use in usual care and in early PsA patients are lacking.
Objectives: To describe the response to MTX for patients with PsA and an oligoarthritis or polyarthritis phenotype in usual care in the first year after diagnosis, and its impact on different aspects of the disease, including patients not achieving minimal disease activity (MDA) despite continuous exposure to MTX
Methods: Data collected in the Dutch southwest Early Psoriatic Arthritis cohort (DEPAR) study were used. Patients with a new diagnosis of PsA who have not started disease-modifying antirheumatic drugs (DMARDs) for PsA were eligible to participate. In this analysis, only patients with a phenotype at time of diagnosis of oligoarthritis or polyarthritis (resp. 2-4 joints involved or 5 or more joints, as defined by the rheumatologist), and at least one year follow up were included. Research nurses collected clinical data and data on medication use every three months in the first year after diagnosis. The following outcomes were used to evaluate disease activity: MDA, EULAR active disease (at least one tender and swollen joint), disease activity index for PsA low disease activity (DAPSA-LDA: DAPSA≤14), and disease activity score 28 low disease activity (DAS28-LDA: DAS28≤3.2). Disease activity at six months of patients who started MTX within six months after diagnosis and have continued using MTX until one year after diagnosis was analyzed.
Results: In April 2018, 219 patients had a phenotype of oligoarthritis (n=134, 61%) or polyarthritis (n=85, 39%) at time of diagnosis, and at least one year follow up. In 183 (84%) patients, MTX monotherapy was started within six months after diagnosis. Within the first year, 23 of these used MTX intermittently, 25 switched to a different DMARD, and 45 started a different DMARD while remaining on MTX therapy. The remaining 90 patients used MTX monotherapy throughout the first year and of these we assessed disease activity at 6 months after diagnosis. At 6 months, 38 patients out of these 90 were not in MDA despite continuous MTX treatment, while 44 achieved MDA. Major differences amongst the two groups included tender joint count, physical function, evaluation of pain and global disease activity and impact on health-related quality of life scores (Table 1). Conversely, 18% of all patients started MTX monotherapy were in sustained MDA at one year while continuing MTX monotherapy.
Conclusion: The majority of patients with a new diagnosis of PsA with a phenotype of oligoarthritis or polyarthritis started MTX within a year after diagnosis. MTX is maintained as monotherapy in half of these patients, with 18% of them achieving sustained MDA using MTX monotherapy at one year. Interestingly, approximately half of the patients who had continued methotrexate monotherapy were not achieving MDA after six months and they report higher impact of disease on clinical and patient reported outcomes, suggesting need to consider improvement of therapy for these patients.

Table 1. Disease activity and health-related quality of life at six months after diagnosis, of patients on MTX monotherapy in the first year after diagnosis

	No MDA at 6 months (n=38)	MDA at 6 months (n=44)
Swollen joint count	0 (0-1)	0 (0-0.5)
Swollen joint count > 1	8 (21)	3 (7)
Tender joint count	2 (0-4)	0 (0-0.5)
Tender joint count > 1	21 (55)	3 (7)
Leeds enthesitis index	0 (0-2)	0 (0-0)
Leeds enthesitis index > 1	10 (26)	1 (2)
PASI > 1	22 (58)	15 (34)
VAS Pain > 15	36 (95)	10 (23)
VAS Global > 20	35 (92)	7 (16)
HAQ > 0.5	27 (71)	7 (16)
PsAID-12	3.8 ± 2.2	1.0 ± 1.0
PsAQoL	7.6 ± 4.9	1.2 ± 2.0
Short Form 36		
Physical functioning	56 ± 18	86 ± 12
Physical role functioning	44 ± 22	82 ± 19
Bodily pain	49 ± 14	75 ± 14
General health	49 ± 16	69 ± 14
Vitality	49 ± 19	72 ± 17
Social functioning	68 ± 22	93 ± 12
Emotional role functioning	64 ± 27	91 ± 15
Mental health	71 ± 19	84 ± 12
Physical component scale	37 ± 5.1	49 ± 5.2
Mental component scale	46 ± 10	55 ± 6.8

Data shown as n (%), median (interquartile range) or mean ± standard deviation
MDA: minimal disease activity; MTX: methotrexate; PASI: psoriasis area and severity index; VAS: visual analogue scale; HAQ: health assessment questionnaire; PsAID: psoriatic arthritis impact of disease; PsAQoL: psoriatic arthritis specific quality of life

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Crystal diseases, metabolic bone diseases other than osteoporosis

SAT0402

SEL-212 PHASE 2 CLINICAL STUDY IN SYMPTOMATIC GOUT PATIENTS: IMMTOR TOLEROGENIC NANOPARTICLES COMBINED WITH PEGADRICASE MITIGATES IMMUNOGENICITY AND ENABLES SUSTAINED REDUCTION OF SERUM URIC ACID LEVELS, LOW RATE OF GOUT FLARES AND MONTHLY DOSING

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Background: Pegylated uricases are promising therapies for the treatment of severe chronic gout, but are limited by their immunogenicity. We have previously shown that ImmTOR tolerogenic nanoparticles (formerly known as SVP-Rapamycin) encapsulating rapamycin co-administered with pegadricase prevented the formation of anti-drug antibodies (ADAs) in a dose-dependent manner. A prior Phase 1b study of SEL-212, a novel combination product candidate consisting of pegadricase and ImmTOR, demonstrated sustained control of serum uric acid (SUA) for at least 30 days after a single dose. Here we provide data from a recently completed Phase 2 multidose clinical trial.
Objectives: To assess data on the safety, tolerability, and effects on SUA, ADAs, and gout flares of five monthly doses of SEL-212 in symptomatic gout patients treated with 0.1 or 0.15 mg/kg ImmTOR in combination with 0.2 mg/kg pegadricase.
Methods: Patients with symptomatic gout (≥1 tophus, gout flare within 6 months, and/or gouty arthropathy) and elevated SUA (≥6 mg/dL) were enrolled in SEL-212 treatment cohorts. Patients reported here received up to five monthly doses of SEL-212 (0.2 mg/kg pegadricase combined with 0.1 or 0.15 mg/kg ImmTOR). Safety, tolerability, SUA, and ADAs were monitored, and clinical data were collected.
Results: As of 17 Dec 2018, 152 patients had been dosed in the Phase 2 study. All evaluable patients receiving 0.1 or 0.15 mg/kg ImmTOR administered with 0.2 mg/kg pegadricase who achieved three months of SUA control maintained SUA control in months four and five of combination treatment. Approximately 66% of evaluable patients maintained SUA levels below 6 mg/dL at week 20 after five monthly doses of SEL-212. The sustained reduction of SUA correlated with low or no ADAs. SEL-212 was generally well tolerated and associated with a low rate of gout flare rates. Only 35% of patients treated with five doses of 0.1-0.15 mg/kg ImmTOR, and 29% of all current patients in the SEL-212 Phase 2 trial, experienced gout flares after initiation during the first month of treatment with continued reduction of gout flare rates over months two through five. This low rate of gout flares appears to be in contrast with higher incidence of gout flares reported in clinical trials involving other urate lowering therapies.
Conclusion: SEL-212 has been well-tolerated, showing substantially reduced immunogenicity, sustained control of SUA, and low rate of gout flares with repeated monthly dosing. SEL-212 has a favorable product profile to address the unmet need of patients with severe, chronic gout

including low immunogenicity allowing continued dosing, lower reported flare rates and convenient monthly dosing.

Disclosure of Interests: Stephen Smolinski Shareholder of: Selecta Biosciences, Inc., Employee of: Selecta Biosciences, Inc., Alan Kivitz Shareholder of: Novartis, Consultant for: Abbvie, Janssen, Pfizer, UCB, Genzyme, Sanofi, Regeneron, Boehringer Ingelheim, Sun Pharma Advanced Research, Flexion., Paid instructor for: Celgene, Horizon, Merck, Novartis, Pfizer, Genzyme, Sanofi, Regeneron, Speakers bureau: Celgene, Horizon, Merck and Genetech, Flexion, Wesley DeHaan Shareholder of: Selecta Biosciences, Inc., Employee of: Selecta Biosciences, Inc., Lloyd Johnston Shareholder of: Selecta Biosciences, Inc., Employee of: Selecta Biosciences, Inc., Rehan Azeem Shareholder of: Selecta Biosciences, Inc., Employee of: Selecta Biosciences, Inc., Kei Kishimoto Shareholder of: Selecta Biosciences, Inc., Employee of: Selecta Biosciences, Inc.

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SAT0403 SEX DIFFERENCES ARE PRESENT IN CLINICAL CHARACTERISTICS, BUT NOT IN RESPONSE TO DIFFERENT URATE LOWERING THERAPIES IN PATIENTS WITH GOUT

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Background: Clinical characteristics of gout differ between women and men[1]. Little however is known about the association between these differences and response to treatment. As women seem to have lower mean uric acid excretion compared to men[2,3], response to uricosuric agents might be better compared to xanthine oxidase inhibitors.

Objectives: To identify sex differences in clinical characteristics and response to urate lowering therapy (ULT) in patients with gout and in women difference in response to allopurinol or benzbromarone.

Methods: Patients with clinical diagnosis of gout, a first outpatient visit between January 2010 and March 2018 and a follow-up of at least 6 months were included in a retrospective cohort study, with ongoing recruitment, conducted in two rheumatology centres in the Netherlands. From this cohort, patients who started ULT were selected. Clinical characteristics and treatment outcomes of allopurinol and benzbromarone were compared between women and men, including drug survival (corrected for age and renal function) and cumulative incidence of achieving target serum uric acid (<0.36 mmol/l). In women, difference in cumulative incidence of achieving target serum uric acid while using allopurinol or benzbromarone was compared.

Results: From a total of 519 (105 women/414 men) patients, 513 (104 women/409 men) and 74 (18 women/56 men) patients were included in the allopurinol and/or benzbromarone group, respectively. Clinical characteristics are described in Table 1. Drug survival was similar for women and men for allopurinol (hazard ratio 1.08; 95% confidence interval (CI) 0.71-1.64) as well as for benzbromarone (hazard ratio 0.66; 95% CI 0.26-1.66) (Figure 1a and b). Cumulative incidences of achieving target serum uric acid were 66% (69/104) and 73% (300/409) after allopurinol and 83% (15/18) and 82% (46/56) after benzbromarone for women and men, respectively. Comparison in women between response to allopurinol and benzbromarone was not statistically significant (p = 0.15).

Conclusion: Clinical characteristics of gout differ between women and men, confirming previous studies, with women being older, having more comorbidities and using diuretics more often.

Although women have shown to be more uric acid under secretors compared to men, this does not seem to result in a difference in response to a xanthine oxidase inhibitor or an uricosuric agent.

Table 1. Clinical characteristics

	Women (n =105)	Men (n = 414)	p-value*
Age (years), median (IQR)	73.9 (54.3-71.6)	62.9 (54.3-71.6)	<0.01
Current alcohol use, n (%)	34 (45)	275 (79)	<0.01
Comorbidities, n (%)	71 (68)	200 (48)	<0.01
Hypertension	41 (39)	76 (18)	<0.01
Renal impairment	36 (34)	80 (19)	<0.01
Diabetes mellitus			
Diuretics use, n (%)	67 (64)	137 (33)	<0.01
Joint involvement, n (%)	14 (13)	68 (17)	0.38
Monoarthritis	64 (62)	220 (62)	
Oligoarthritis	26 (25)	120 (29)	
Polyarthritis			
History or presence of tophi, n (%)	39 (37)	94 (23)	<0.01
Crystal proven gout, n (%)	89 (85)	348 (89)	0.86
Baseline serum uric acid (mmol/L), mean (SD)	0.44 (0.13) (n=93)	0.43 (0.12) (n=360)	0.73

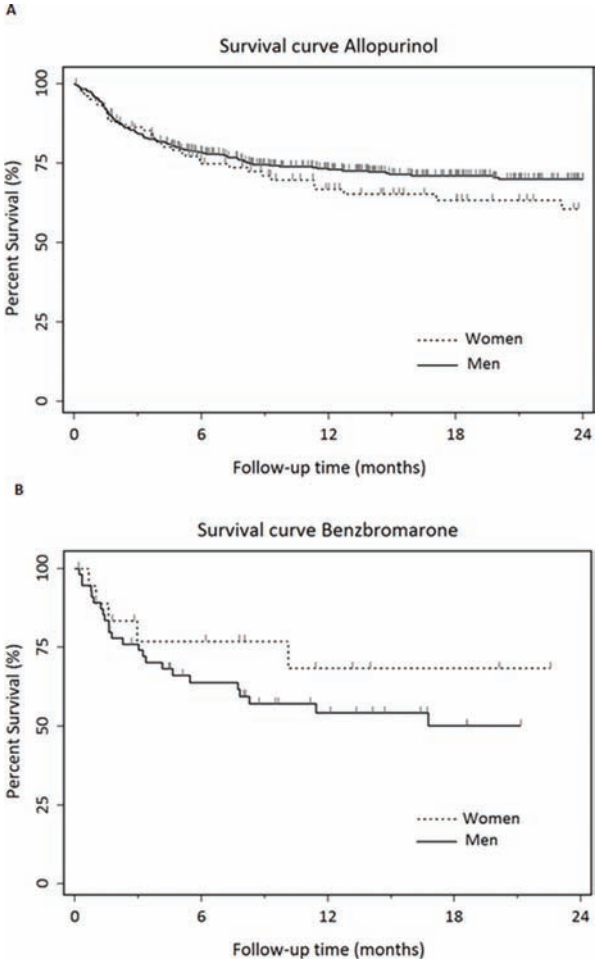
IQR = inter quartile range

* P-values for categorical variables were calculated by chi-square analysis, for continuous variables the appropriate (non)parametric analysis was used based on Gaussian distribution.

REFERENCES

[1] Harrold LR, et al. Ann Rheum Dis. 2006 Oct;65(10):1368-72.
[2] Park YB, et al. Clin Rheumatol 2000;19(2):142-6.
[3] te Kampe R. et al. Ann Rheum Dis.2018;77: Suppl A1637

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SAT0404 PRETREATMENT AND CO-ADMINISTRATION WITH METHOTREXATE IMPROVED DURABILITY OF PEGLOTICASE RESPONSE: A PROSPECTIVE, OBSERVATIONAL, PROOF-OF-CONCEPT, CASE SERIES

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Background: Pegloticase is a recombinant DNA-produced porcine-like uricase enzyme, which metabolizes relatively insoluble urate to highly soluble allantoin. It is used in the treatment of refractory gout which has

failed maximal medical management, typically with xanthine oxidase inhibitors (XOI). Studies have shown a complete responder rate of 42% when defined as repeat serum uric acid (sUA) levels <6.0 mg/dL for >80% of the time during months 3 and 6 of treatment. Patients that do not maintain a low uric acid while on pegloticase therapy are presumed to have developed anti-drug antibodies (ADA) which rapidly clear the pegloticase molecule. As is routinely utilized in the treatment of other rheumatologic diseases, coadministration of immunomodulatory medications, such as methotrexate, could potentially temper the development of these ADAs (as defined by maintenance of sUA response) in patients treated with pegloticase for refractory gouty arthropathy.

Objectives: The aim of the current case series was to identify and clinically evaluate patients in a real-world practice setting in order to investigate the utility of adding methotrexate to a pegloticase regimen to increase the durability of response.

Methods: In this prospective, proof-of-concept, observational case series, 10 sequential patients with refractory tophaceous gouty arthropathy being started on treatment with pegloticase 8 mg every two weeks (as per the label) were identified from 3 separate infusion centers. No inclusion/exclusion criteria were implemented or prescreening performed. Methotrexate (MTX) 15 mg orally once weekly and folic acid 1 mg orally once daily was started one month prior to the initial administration of pegloticase and continued throughout pegloticase treatment. Any infusion pre-medications, which were consistent with standard practices, were administered per the individual physician's discretion as well as management of any gout flares which occurred during the treatment course. As per standard of care, sUA was measured every two weeks, prior to each subsequent infusion. At the completion of pegloticase treatment for all patients, the number and percentage of patients able to maintain an sUA at goal <6.0 mg/dL was recorded.

Results: Ten patients ranging in age from 35-80 were identified, from 3 separate infusion centers. There were 143 total pegloticase infusions performed within the observation period. All 10 patients received at least 10 infusions (5 months), 9 patients at least 12 infusions (6 months), 5 patients at least 16 infusions (8 months), 2 patients at least 18 infusions (9 months), and 1 patient received 19 infusions. All 10 patients completed a full course of pegloticase treatment. All patients stayed on MTX 15 mg/week. There were no dose adjustments. 100% of patients were responders as defined by >80% of sUA levels being maintained at goal <6.0 mg/dL during the observation period. None of the 10 patients stopped pegloticase therapy due to increased sUA or loss of response and there were no infusion reactions in any of the 143 infusions or safety concerns identified. Gout flares did occur, primarily following the initial infusion, with less severity/prevalence with subsequent infusions. No patients discontinued treatment because of flares.

Conclusion: In this proof-of-concept case series of 10 sequential patients, pretreatment and co-administration of methotrexate 15 mg orally once weekly and folic acid 1 mg orally once daily with pegloticase resulted in a 100% maintenance of pegloticase sUA response with no infusion reactions. Although additional studies would be needed to corroborate these results, these data support a potential paradigm shift in treatment of refractory gout with pegloticase.

REFERENCE

[1] Sundy JS, et al. JAMA. 2011;306:711

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Disclosure of Interests: John Botson Shareholder of: Publicly traded stock: Horizon, Johnson and Johnson, Pfizer, Rigel, Consultant for: Celgene, Eli Lilly, Genentech, Horizon, Mallinckrodt, Novartis, Pfizer, Speakers bureau: Celgene, Eli Lilly, Horizon, Mallinckrodt, Novartis, Pfizer, Jeff Peterson Consultant for: Celgene, Genentech, Horizon, Lilly, Novartis, Regeneron (2017-2018), Speakers bureau: Abbvie, Horizon, Lilly, Novartis (2017-2018)

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SAT0405 GOUT AND HYPERURICEMIA IN THE US: PREVALENCE AND TRENDS

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Background: While the prevalence of gout and hyperuricemia is believed to be increasing worldwide, there is little population-based data in the US after 2008. We evaluated the prevalence of gout and hyperuricemia in the US National Health and Nutrition Examination survey (NHANES) from 2007-08 to 2015-16, and compared these to previously published estimates to study whether the time-trends continue to show an increase in these rates.

Objectives: To study the prevalence of gout and hyperuricemia in the US population from 2007-08 to 2015-16.

Methods: We studied adults 20 years and older from the National Health and Nutrition Examination Survey (NHANES), beginning with the continuous NHANES 2-year survey cycles from 2007-08 to 2015-2016. The samples in each cycle were selected using a stratified, multistage, clustered probability sampling design. Persons with gout were identified from the home interview question "Has a doctor or other health professional ever told you that you had gout?" Hyperuricemia was defined as a serum urate level of greater than 6.8 mg/dl (supersaturation levels at physiological temperatures and pH), with alternate definitions of greater than 6.0 mg/dl (defined as the treat-to-target level in some treatment guidelines)(1). All statistical analyses were performed with appropriate survey procedures in SAS v9.4 (SAS Institute Inc., Cary, NC). Survey design variables and weight variables were used to account for the complexity of the NHANES survey design with stratification and clustering. Age-adjusted rates were calculated using 2010 US population numbers (direct standardization).

Results: In 2015-16, the overall prevalence of gout among US adults was 3.9%, corresponding to a total affected population of 9.2 million US adults. Gout was significantly more prevalent in men (5.2%) compared to women (2.7%), and the prevalence increased with age. Hyperuricemia (above 6.8 mg/dl) was seen in 14.6% of US population (estimated 32.5 million individuals), and was much more common in men (24.7%) compared to women (5.2%). The alternative definition of hyperuricemia (more than 6.0 mg/dl) was seen in 29.9% of individuals (estimated 66.6 million adults). Both hyperuricemia and gout were less prevalent in Mexican-Americans compared to Whites and African-Americans. No significant trends were identified in the age-adjusted prevalence of gout and hyperuricemia. Statistical comparisons between 2007-08 and 2015-16 age-adjusted rates were not significant.

Conclusion: While the age-adjusted prevalence of gout and hyperuricemia has remained unchanged in the most recent decade from 2007-08 to 2015-16, the estimated total number of persons with self-reported gout has gone up from 8.3 million to 9.2 million, reflecting the growth and increased aging of the US population. The age-adjusted prevalence of hyperuricemia has declined slightly but the total number of affected individuals is virtually identical (32.5 million in 2015-16 compared to 32.1 million in 2007-08). While the stabilization of gout and hyperuricemia prevalence rates is encouraging, our study highlights the still considerable burden of gout and hyperuricemia in the increasingly aging US population.

REFERENCE

[1] Ruoff G, Edwards NL. Overview of Serum Uric Acid Treatment Targets in Gout: Why Less Than 6 mg/dL? Postgraduate medicine. Sep 2016;128 (7):706-715.

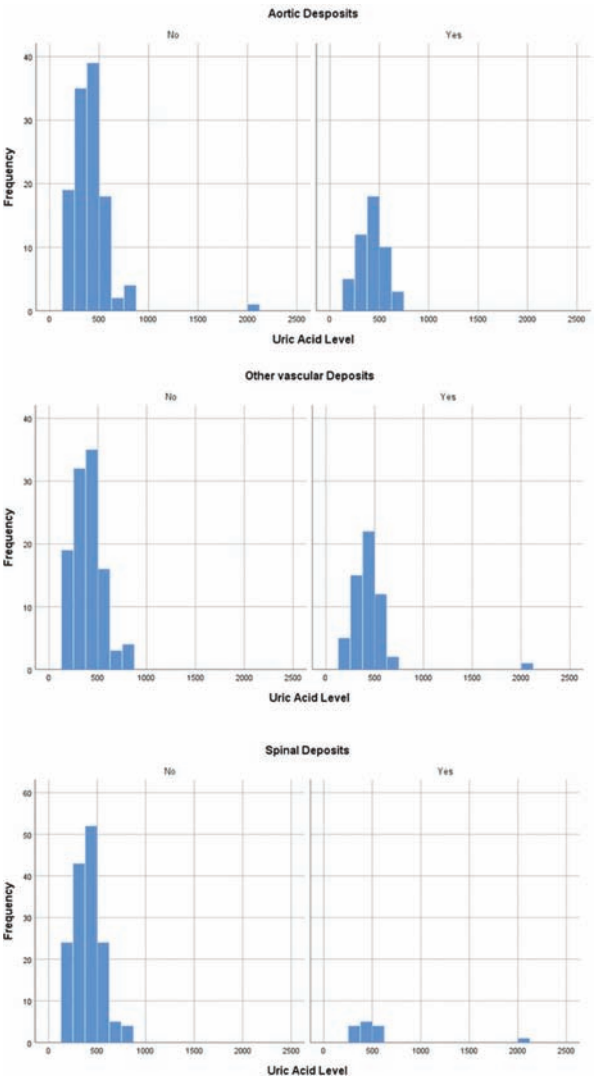
Disclosure of Interests: Gurkirpal Singh Shareholder of: Merck, Pfizer, Grant/research support from: Horizon, Acorda, UCB, Consultant for: Horizon, Acorda, Sancilio, Unipharm, Bharathi Lingala: None declared, Alka Mithal: None declared

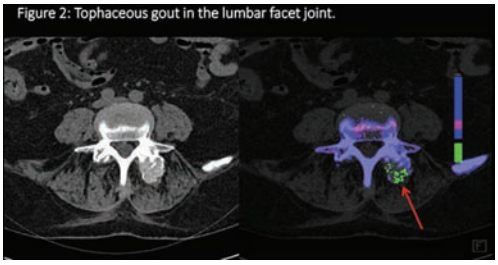
DOI: 10.1136/annrheumdis-2019-eular.4438

SAT0406 COMPUTED TOMOGRAPHIC MAPPING OF SPINAL AND VASCULAR URATE DEPOSITION IN THE ABDOMEN WITH CORRELATION TO URIC ACID LEVEL

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Background: Gout is characterized by accumulation of monosodium urate (MSU) in joints and soft tissues. Gout prevalence is about 1-5% in the western world, predominantly in elderly men. Accurate diagnosis of gout is paramount in managing disease progression and guiding treatment. A meta-analysis in 2018 showed that Dual-Energy CT (DECT) has high sensitivity, specificity and diagnostic accuracy in MSU detection. MSU





deposition outside 'classic' extremities has been scarcely investigated yet may be a potential indicator of tophus burden and impending clinical deterioration.

Objectives: 1. Anatomical mapping of gout deposition in the abdomen (vessels, solid organs and lumbosacral spine).

2. Determine correlation between uric acid level and vascular, solid organ and spinal MSU deposition.

Methods: Retrospective analysis of all DECT abdomen and pelvis scans done in our institution (from January 2007 to July 2018). The inclusion criteria were: males > 50 years with high or normal uric acid level. All cases were then assessed by 2 radiologists with extensive experience in DECT for MSU deposits. Validated dual-energy gout analysis software was used.

Results: 235 DECT cases met the inclusion criteria. Medical Record document review showed no diagnosis of gout in any patient in the sample. By the time this abstract was submitted, 166 cases were reviewed. The analyzed sample (n = 166), showed MSU deposits (1 or more deposits) in the abdominal aorta (n = 48/166; 28.92%), abdominal vessels other than aorta (n = 57/166; 34. 34%) and lumbosacral spine (n = 15/166; 9.04%). No deposits were detected in the solid abdominal organs (n = 0/166; 0%). There was a statistically significant positive correlation between uric acid level and spinal deposits (r= 0.22, P= 0.004). No significant correlation between uric acid level and aortic (P= 0.86) or vascular deposits (P= 0.19). Regression analysis showed uric acid levels can't significantly predict the presence of aortic, vascular or spinal deposits.

Conclusion: Computed tomographic mapping of MSU deposits was positive in the abdominal aorta, other abdominal vessels and lumbosacral spine in patients with normal or high uric acid levels who were asymptomatic for gout. Uric acid level was positively correlated with spinal gout, but not with aortic or vascular gout. Interestingly, uric acid levels can't significantly predict the presence of aortic, vascular or spinal gout. Larger sample size, wider variation in uric acid levels are still needed.

REFERENCES

[1] Yu, Z., Mao, T., Xu, Y., Li, T., Wang, Y., Gao, F., & Sun, W. (2018). Diagnostic accuracy of dual-energy CT in gout: a systematic review and meta-analysis. Skeletal radiology, 1-7.

[2] Barazani, S. H., Chi, W., Pyzik, R., Jacobi, A., O'Donnell, T., Fayad, Z.,. .. & Ali, Y. (2018). Detection of Uric Acid Crystals in the Vasculature of Patients With Gout Using Dual-Energy Computed Tomography. Circulation, 138(Suppl_1), A11821-A11821.

[3] Gamala, M., Linn-Rasker, S. P., Nix, M., Heggelman, B. G. F., van Laar, J. M., Pasker-de Jong, P. C. M.,. .. & Klaasen, R. (2018). Gouty arthritis: decision-making following dual-energy CT scan in clinical practice, a retrospective analysis. Clinical rheumatology, 1-6.

[4] Chew, N., & Cho, J. (2018). Dual-energy CT for the diagnosis of sacroiliac and spinal gout. Joint Bone Spine.

Table 1. correlation Analysis.

	Uric Acid Levels	
	Correlation coefficient	*P value*
Aortic Deposits	-0.013	0.86
Vascular Deposits	0.101	0.198
Spine	0.223	0.004

Table 2. Regression analysis

	Uric Acid Levels	
	Regression coefficient	*P value*
Aortic Deposits	0.00	0.86
Vascular Deposits	0.001	0.226
Spine	0.003	0.053

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SAT0407

GOUT PATIENTS ARE GETTING MORE POSITIVE ABOUT THEIR MEDICINES WHILE TREATED TO TARGET: DATA FROM THE NOR-GOUT STUDY

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Background: Low adherence to medication is a concern in gout where urate lowering therapy (ULT) is indicated to prevent disease severity and

comorbidities. Not believing in medication may impact on the success of achieving these treatment goals.

Objectives: To study which factors were associated to and predictive of beliefs about medicines during one year in patients with a recent gout attack and a need for ULT.

Methods: Baseline data from a prospective observational study were used in patients with crystal-proven gout after a recent gout flare and insufficiently treated serum urate (sUA) level (>360 μmol/L/>6 mg/dl). In these patients a treat-to-target approach was planned to meet the treatment target (sUA <360 μmol/L, or <300 μmol/L if clinical tophi). Assessments included demographic and clinical data, baseline serum urate levels, medication, comorbidities, physical function (HAQ), and SF-36 mental (MCS) and physical component summary scores.

The Beliefs in Medicines Questionnaire (BMQ)(1) queries patient beliefs about medicines on four subscales (necessity and concerns specific for the patient, generally on overuse and harm). Respondents indicated their degree of agreement with each individual statement about medicines on a 5-point Likert scale, (1=strongly disagree to 5=strongly agree). Scores within the four subscales were summed (ranges 5-25 for necessity and concern, 4-20 for overuse and harm). Calculation of the difference between necessity and concern shows the relative importance of patients' view on taking medication, and was grouped as high and low relative to the median.

Using multivariate analysis with logistic regression, baseline variables were explored as predictors of high beliefs in the relative importance of medication after 12 months.

Results: 202 patients were included at baseline, 94.1% men, 90.3% caucasian, mean (SD) age 56.6 (14.2) years, disease duration 8.0 (7.7) years). Mean sUA level was 494 (SD 86.8) μmol/L at baseline, body mass index 28.9 (4.6) kg/m2, and physical function (HAQ) 0.36 (0.57). 18.8% (n=28) had tophi, and 30.4% (n=55) were previous users of allopurinol.

During the first year the beliefs in necessity of medication and the perceived importance of medication increased, while the concerns decreased (Table).

Table: Beliefs in Medicines questionnaire (BMQ) subscales. *=p<0.05, **=p<0.01vs. baseline

Month (n)	0 (195)	3 (158)	6 (144)	12 (126)
Necessity (SD)	17.1 (4.5)	18.2 (3.4)*	18.4 (3.4)**	18.5 (3.3)**
Concern (SD)	13.7 (4.8)	13.3 (4.5)	13.3 (4.6)*	13,1 (4.6)**
Nec – Conc (SD)	3.4 (6.2)	4.9 (5.4)*	5.1 (5.5)**	5.4 (5.5)**
Overuse (SD)	10.6 (2.8)	10.8 (2.5)	10.6 (2.8)	10.6 (2.7)
Harmful (SD)	9.4 (2.4)	9.5 (2.5)	9.6 (2.5)	9.2 (2.7)

Bivariate comparisons studying demographic, medication and clinical variables did not show consistent cross-sectional associations with beliefs in the importance of medication. However, after 12 months, bivariate comparisons revealed statistically significant differences in mental health (SF36 MCS), physical function (HAQ) and self-efficacy for symptom control.

In logistic regression analyses, adjusting for age,gender, BMI and comorbidites, prediction of high beliefs in the relative importance of medication after 12 months were independently associated with baseline self-efficacy for symptom control (OR 1.04 per unit, 95% CI 1.01-1.06).

Conclusion: During one year of treat-to-target strategy in patients with gout, perceived necessity of medication and higher importance of medication increases. Self-efficacy for symptom control at baseline was an independent predictor of high beliefs in importance of medication after 12 months. These findings support that patients increase their perception of the necessity of beliefs in medication during a treat-to-target approach with ULT.

REFERENCE

[1] Horne R, et al. Psychology & Health, 1999. 14(1): 1–24.

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SAT0408 BODY FAT MEDIATES THE CORRELATION BETWEEN FRUCTOSE-CONTAINING BEVERAGES CONSUMPTION AND SERUM URIC ACID IN MALE GOUT PATIENTS

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Background: Fructose-containing beverages (FCB) consumption has been recognized as a promoter of hyperuricemia and gout in recent years. FCB consumption also contributes to the development of obesity which is an important risk factor of gout. However, data about the associations among FCB consumption, obesity and the level of serum uric acid (sUA) is limited.

Objectives: To investigate the associations among FCB consumption, obesity and sUA level in gout patients.

Methods: Consecutive gout patients who fulfilled the 2016 ACR/EULAR classification criteria were recruited. Demographic information, clinical characteristics and comorbidities of gout were collected. A 10-items food frequency questionnaire was developed which included alcohol, red meat, animal offal, seafood, hotpot, slow-cooking soup, FCB, tea, coffee and milk/milk products. Patients were asked to report the average consumption frequency over the one year prior to the first gout attack. Body composition was assessed by bioelectric impedance analysis and overfat was defined by body fat percentage (BF%) as $\geq$25% for men and $\geq$35% for women.

Results: 1) Among 331 recruited gout patients, 96.1% were male, so only male patients were further analyzed. The median age of male patients was 37.5 (30, 49) years and median sUA was 9.5 (7.8, 10.5) mg/dl with 18.9% presented tophi. The mean BF% was 25.6±6.2% and 54.7% male patients were overfat. The prevalence of hypertension, diabetes, dyslipidemia, metabolic syndrome and fatty liver were 34.6%, 8.5%, 62.9%, 44.3% and 46.9% respectively. 2) There were no significant difference of food intake frequency between overfat patients and normal fat patients. Spearman correlation analysis results showed that FCB consumption was positively correlated with BF% (r=0.176, P=0.002), while milk/milk products consumption was negatively correlated with BF% (r=-0.117, P=0.038). After adjusted by age, duration, family history, eGFR, hypertension, diabetes mellitus, dyslipidemia, metabolic syndrome, fatty liver and the other nine dietary factors, multivariable linear regression showed that FCB consumption was positively correlated with BF% (compared with <1 time/w, 3-4 times/w: coefficient β=2.4619, 95%CI 0.3580~4.5657, P=0.022; 4 times/w: coefficient β=2.6696, 95%CI 0.8266~4.5726, P=0.0049), and BF% was positively correlated with sUA (coefficient β=0.0784, 95%CI 0.0328~0.1239, P<0.001). However, FCB consumption was not correlated with sUA after adjusted by above confounders and BF% (P=0.079). 3) Further mediation analysis were performed to evaluate whether BF% mediated the correlation between FCB consumption and sUA. After adjusted by the confounding factors mentioned above, the total effect of FCB consumption on sUA was significant (compared with <1 time/w, >4 times/w: coefficient β=0.8813, 95%CI 0.1457~1.6169, P=0.019). BF% produced indirect effect on the correlation between FCB consumption and sUA (compared with <1 time/w, >4 times/w: indirect effect coefficient β=0.2115, 95%CI 0.0453~0.4032).

Figure 1 Linear regression analysis of the correlation between food intake frequency and BF% and sUA in male gout patients

Food intake frequency	All patients (n=318)	Correlation with BF%[1]				Correlation with sUA[2]			
		Coefficient β	LLCI	ULCI	P	Coefficient β	LLCI	ULCI	P
Alcohol									
None	141(44.3)	0.0	NA	NA	NA	0.0	NA	NA	NA
1-28g/d	89(28)	-1.0446	-2.5604	0.4711	0.1760	-0.3685	-0.9298	0.2429	0.2498
29-84g/d	39(12.3)	0.2762	-1.8168	2.3692	0.7953	0.2723	-0.5348	1.0793	0.5072
>84g/d	49(15.4)	0.7476	-1.3134	2.8086	0.4758	0.3847	-0.4607	1.1301	0.4082
Red meat									
0-100g/d	102(32.1)	0.0	NA	NA	NA	0.0	NA	NA	NA
101-200g/d	149(46.9)	-0.9870	-2.4907	0.5567	0.2126	-0.2361	-0.8253	0.3530	0.4307
201-300g/d	52(16.4)	-0.6439	-2.5878	1.3000	0.5149	0.3158	-.4343	1.0659	0.4079
>300g/d	15(4.7)	0.9134	-2.2809	4.1076	0.5740	0.1041	-1.1282	1.3364	0.8680
Animal offal									
<1 time/w	227(71.4)	0.0	NA	NA	NA	0.0	NA	NA	NA
1-2 times/w	65(20.4)	0.5580	-1.2227	2.3388	0.5378	-0.5776	-1.2646	0.1095	0.0991
3-4 times/w	15(4.7)	-0.8508	-3.9278	2.2261	0.5867	-0.7524	-1.9394	0.4346	0.2131
>4 times/w	11(3.5)	-2.5660	-6.1948	1.0628	0.1650	10.1541	-0.2499	2.5581	0.1068
Seafood									
<1 time/w	215(67.6)	0.0	NA	NA	NA	0.0	NA	NA	NA
1-2 times/w	59(18.6)	0.7836	-0.9244	2.4915	0.3672	-0.1298	-0.7893	0.5297	0.6987
3-4 times/w	25(7.9)	-0.9334	-3.3759	1.5091	0.4525	-0.0335	-0.9762	0.9092	0.9443
>4 times/w	19(6)	-2.5593	-5.3741	0.2555	0.0746	-0.1390	-1.2305	0.9525	0.8023
Hotpot									
<1 time/w	287(90.3)	0.0	NA	NA	NA	0.0	NA	NA	NA
1-2 times/w	23(7.2)	0.7567	-1.7281	3.2415	0.5493	-0.1055	-1.0642	.8532	0.8286
3-4 times/w	4(1.3)	-1.0259	-6.7562	4.7043	0.7248	0.1551	-2.0547	2.3650	0.8902
>4 times/w	4(1.3)	-1.0445	-6.9190	4.8299	0.7266	-0.0671	-2.3326	2.1983	0.9535
Slow-cooking soup									
<1 time/w	129(40.6)	0.0	NA	NA	NA	0.0	NA	NA	NA
1-2 times/w	99(31.1)	-0.1611	-1.6797	1.3576	0.8348	-0.3682	-0.9538	0.2174	0.2169
3-4 times/w	52(16.4)	-1.1055	-3.0452	0.8342	0.2628	-0.1888	-0.9383	0.5608	0.6205
>4 times/w	38(11.9)	0.7027	-1.4212	2.8265	0.5154	-0.3409	-1.1604	.4786	0.4135
Fructose containing beverages									
<1 time/w	168(52.8)	0.0	NA	NA	NA	0.0	NA	NA	NA
1-2 times/w	44(13.8)	1.4198	-0.5328	3.3725	0.1534	0.0239	-0.7318	0.7795	0.9504
3-4 times/w	41(12.9)	2.4619	0.3580	4.5657	0.0220	-0.0888	-0.9077	0.7301	0.8311
>4 times/w	65(20.4)	2.6996	0.8266	4.5726	0.0049	0.6698	-.0628	1.4023	0.0730
Tea									
<1 time/w	147(46.2)	0.0	NA	NA	NA	0.0	NA	NA	NA
1-2 times/w	34(10.7)	-0.5431	-2.7650	1.6789	0.6308	0.0261	-0.8309	0.8832	0.9522
3-4 times/w	14(4.4)	0.9783	-2.2133	4.1700	.5467	-0.1891	-1.4205	1.0423	0.7626
>4 times/w	123(38.7)	-0.1466	-1.5924	1.2992	.8375	0.2479	-0.2942	0.7900	0.3688
Coffee									
<1 time/w	293(92.1)	0.0	NA	NA	NA	0.0	NA	NA	NA
1-2 times/w	15(4.7)	-1.9200	-4.9623	1.1223	.2152	-0.9499	-2.1262	0.2264	0.1130
3-4 times/w	1(0.3)	0.7034	-10.4653	11.8761	.9012	10.1822	-3.1249	5.4894	0.5894
>4 times/w	9(2.8)	-1.6474	-5.7000	2.4052	.4243	0.2745	-1.2899	1.8388	0.7301
Milk and milk products									
<1 time/w	173(54.4)	0.0	NA	NA	NA	0.0	NA	NA	NA
1-2 times/w	95(29.9)	-0.5368	-1.9924	0.9188	.4685	0.3462	-0.2155	0.9080	0.2260
3-4 times/w	27(8.5)	-1.7837	-4.1081	0.5407	.1320	-0.2811	-1.1810	0.6188	0.5391
>4 times/w	23(7.2)	0.0540	-2.4738	2.5819	.9665	0.0890	-0.8857	1.0636	0.8575

Multivariate[1], adjusted for potential confounding factors including age, duration of gout, family history, eGFR, comorbidities [including hypertension (yes/no), diabetes mellitus (yes/no), dyslipidemia (yes/no), metabolic syndrome (yes/no), and fatty liver (yes/no)] and the other dietary factors.
Multivariate[2], adjusted for the confounding factors mentioned above and BF%.
LLCI, lower limit of confidence interval; ULCI, upper limit of confidence interval; NA, not applicable; time/w, the frequency of dietary intake per week; BF%, body fat percentage; sUA, serum uric acid.

Conclusion: Our data show that body fat mediates the correlation between FCB consumption and sUA in male gout patients, which imply the importance of body composition assessment.

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SAT0409 P2X7R PROMOTE THE ATTACK OF ACUTE GOUTY ARTHRITIS IN RATS FROM CLINICAL TO PATHOLOGY

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Background: ATP may be the second causative signal for the onset of gout, which acts on P2X7R to regulate the development of acute gouty arthritis (1 . P2X7R is the most relevant to the inflammatory response in the P2X family and is also an ATP-gated cation channel (2

Objectives: The aim of this study was to activate P2X7R signaling pathway through changes in extracellular ATP concentrations, leading to the development of acute gouty arthritis and the production of pro-inflammatory.

Methods: 120 male Sprague-Dawley rats were randomly divided into 3 groups: After establishment of acute gouty arthritis model, rats were given P2X7R agonist ATP, P2X7R inhibitor BBG and PBS, respectively. The clinical manifestations of the ankle joints were evaluated at 6h, 12h, 24h, 48h and 72h before the rats were sacrificed, and rat ankle synovial slices for H&E staining. IL-1β, IL-6 and TNF- in the serum of rats were detected by ELISA kits.

Results: 1. P2X7R regulates the development of acute gouty arthritis: At 12h, the clinical scores of ATP group were significantly higher than those of BBG group and control group (P=0.001,0.042), and the control group was higher than BBG group (P=0.034); At 12h and 24h, the swelling index of ATP group was the most obvious than other two groups (P=0.000, 0.001; P=0.000, 0.003), followed by control group (P=0.009, 0.001); Furthermore, there was a large infiltration of inflammatory cells in the synovial tissue of the right ankle joint of rats, at 12h, and 24h, the infiltration of mononuclear cell in ATP group was significantly higher than that in BBG group and control group (P=0.000, 0.007; P=0.000, 0.001); The neutrophils infiltration in ATP group was the highest among the three groups at 24h (P=0.001, 0.04), and the control group was higher than BBG group (P=0.04). **2. P2X7R regulates pro-inflammatory cytokines production:** At 24h, the level of IL-1β in ATP group was significantly higher than BBG group and control group (P=0.001, 0.003); At 6h, 12h and 24h, higher level of IL-6 in ATP group compared with BBG group and control group (P=0.004, 0.04; P=0.000, 0.002; P=0.001, 0.012); The level of TNF- was obviously higher in ATP group than in BBG group and control group at 6h and 24h (P=0.007, 0.011; P=0.001, 0.018), and BBG group was lower than control group, but without statistically significant (P>0.05).

Conclusion: Activation of P2X7R can significantly promote the attack of acute gouty arthritis and the production of IL-1β, IL-6 and TNF- , suggesting that P2X7R affects the development of acute gouty arthritis and regulates the secretion of pro-inflammatory cytokines.

REFERENCE

[1] Tao JH, Zhang Y, Li XP. P2X7R: a potential key regulator of acute gouty arthritis. Semin Arthritis Rheum, 2013, 43(3): 376-380. (2) Hechler B, Gachet C. Purinergic receptors in thrombosis and inflammation[J]. Arterioscler Thromb Vasc Biol, 2015, 35:2307-2315

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SAT0410 RADIOGRAPHIC EROSION SCORE IMPROVED WITH TARGETED URATE-LOWERING THERAPY IN A PROSPECTIVE GOUT VIETNAMESE COHORT

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Background Urate deposition in joints of patients with neglected gout leads to destructive arthropathy, with subchondral bone erosion, bone construction, and late joint space narrowing. Gouty erosions are believed to improve under urate lowering drugs (ULDs), but their course has been little studied. We therefore performed a systematic prospective study of a Vietnamese cohort started on allopurinol at inclusion.

Objectives To characterize radiographic outcome of gouty erosions under serum urtae-targeted ULD

Methods Included patients had crystal-proven gout, eGFR > 60 ml/min and were not taking ULDs at inclusion. Allopurinol was progressively increased to reach EULAR- recommended uricemia targets and patients were prospectively followed-up, in particular with sequential hand and foot antero-posterior radiographs and MTP and knee ultrasound (US) scans. Joint erosions were scored according to a validated index1, double contour thickness was evaluated by a 4 point-score. One index tophus per patient (hand or foot) was measured by US scan.

Results 100 patients (99M) with a mean age of 45.9 + 9.9 years, and median gout duration of 8 years (range 0-33) were included. 91 had clinical tophi. Mean baseline uricemia was 492 µmol/L. Median final allopurinol dose was 520 mg/day. 71 patients had evidence of urate arthropathy at baseline, 68 of the feet and 23 of the hands (all but 3 with foot involvement). 1st MTPs were predominantly involved (44 and 35 patients on the right and left sides respectively). Urate arthropathy at baseline correlated with gout duration (p=0.01), clinical tophi (p=0.0007), maximum double contour thickness and index tophus US measurement (p=0.03) by univariate analysis and with clinical tophi by multivariable analysis (p=0.03). Uricemia target <300 µmol/L was obtained in 63.6, 67.8, 70.6, and 61.0 % of patients at 3, 6, 12 and 24 months respectively. Median radiological follow-up was 12 months (range 3-49). Mean radiological erosion score1 was 12.1 at baseline (n=71), with a decrease of -0.7 at 6 months (n=38,

p=0.004), -1.4 at 12 months (n=47, p<0.0001) and -4.2 at 24 months (n=14, p=0.001). Complete radiographic erosion healing was observed in only one foot joint in which a small baseline erosion disappeared on M33 radiograph. Erosion score decrease correlated with decrease of double contours at 12 months (rho=0.45, p=0.001) and with mean SUA between M3 and M12 (rho=0,59, p=0,03). A total of 41 joints (hand and foot DIPs, foot II-V PIPs) could not be scored due to score specifications. Prominent diaphysis erosions were seen in 6 patients and were not allowed scoring despite improvement. Bone construction and reappearance of bone contours were striking features of improved radiographs that were not measured by the score. Ankylose of a toe joint was observed in 4 patients. Shrinking of 3 toes developed during dissolution of massive joint space/subchondral bone urate deposits.

Conclusion Urate-lowering improved gouty erosion score, in correlation with decrease of uricemia and urate crystal load. However, complete erosion recovery was seldom observed during a median follow-up of 12 months. Increased bone production and massive urate dissolution under ULD occasionally led to 2 undescribed features of gouty arthropathy: joint ankylose and shrinking of involved toes respectively

REFERENCES

[1]Dalbeth
et al, Arthritis Care Res 2007;57:1067-73.

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SAT0411

COMORBIDITY PATTERNS IN GOUT USING THE US GENERAL POPULATION – CLUSTER ANALYSIS OF THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2007-2016

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Background: Gout is associated with many metabolic and cardiorenal comorbidities. Several previous studies investigated the comorbidity patterns by cluster analysis; however, no such study has been based on the entire general population. As such, the generalizability, which is essential to these pattern analyses, remains unknown.

Objectives: We used cluster analysis on a large, representative general population sample of the United States to identify discrete phenotype patterns comorbidities observed in gout patients.

Methods: We used data from 8,607,137 participants in the 2007-2016 National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of adults in the United States. Diagnosis of gout was based on survey of physician- or health professional-diagnosed gout. We used cluster analysis to identify subgroups among participants with gout with distinct comorbidity subgroups based on 9 variables: obesity, hypertension, diabetes, hypercholesterolemia, hypertriglyceridemia, coronary heart disease (CHD), heart failure (HF), chronic kidney disease (CKD), and liver disease.

Results: Cluster analysis identified 5 different subgroups (C1-C5) (Table 2). C1 had the highest proportion of patients with CKD (97%). C2 consisted of patients with gout but few other comorbidities. All patients in C3 had diabetes, but no HF, CHD, or CKD. C4 consisted primarily of patients with liver disease (85%), with high prevalences of lipid abnormalities and obesity. C5 had the highest proportion of patients with CHD and HF.

Conclusion: These findings from a nationally representative data of US adults indicate that gout comorbidities have 5 distinctive phenotypic patterns. These subgroups may have implications in pathogenesis of gout and/or for personalized care in the management of gout and comorbidities.

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Table 1. Characteristics of Patients with Gout (n = 8607137)

Characteristics	Overall (n = 8607137)
Demographics	
Age, years (SD)	61.4 (0.6)
Body Mass Index, kg/m^2 (SD)	32.0 (0.3)
Comorbidities	
Obesity (%)	4586268 (53)
Hypertension (%)	6280529 (73)
Diabetes (%)	2991109 (35)
Dyslipidemia (%)	5328364 (62)
Hypercholesterolemia (%)	5200179 (60)
Hypertriglyceridemia (%)	500382 (6)
Metabolic Syndrome (%)	4295088 (50)
Coronary Heart Disease (%)	1026990 (12)
Heart Failure (%)	976066 (11)
Cerebrovascular Disease (%)	731253 (9)
Chronic Kidney Disease (%)	1747506 (20)
Nephrolithiasis (%)	1333749 (16)
Liver Disease (%)	1559172 (18)
Malignancy (%)	1866732 (22)

Table 2. Clustering of Patients with Gout Based on Comorbidities

Characteristics	C1 (n = 1257504)	C2 (n = 3455594)	C3 (n = 1199819)	C4 (n = 1430528)	C5 (n = 1263692)
Demographics					
Age (Years)	68.9 (0.9)	58.5 (0.8)	62.2 (1.0)	56.2 (1.2)	66.9 (0.9)
Male gender (%)	831369 (66%)	2342105 (67%)	868002 (72%)	986610 (69%)	815468 (64%)
Body Mass Index (kg/m^2)	31.6 (0.5)	30.7 (0.3)	34.5 (0.9)	33.1 (0.8)	32.2 (0.6)
Comorbidities					
Obesity	644864 (51%)	1634488 (47%)	841074 (70%)	857774 (60%)	608068 (48%)
Hypertension	990667 (79%)	2098496 (61%)	919843 (77%)	1169545 (82%)	1101979 (87%)
Diabetes	519609 (41%)	0 (0%)	1199819 (100%)	562870 (39%)	708811 (56%)
Hypercholesterolemia	766072 (61%)	1880096 (54%)	767170 (64%)	1003052 (70%)	783789 (62%)
Hypertriglyceridemia	6584 (0.5%)	9440 (0.3%)	54026 (5%)	411456 (29%)	18876 (2%)
Coronary Heart Disease	20621 (2%)	0 (0%)	0 (0%)	66088 (5%)	940281 (74%)
Heart Failure	219615 (18%)	2434 (0.1%)	0 (0.0%)	12845 (0.9%)	741172 (59%)
Chronic Kidney Disease	1217813 (97%)	0 (0.0%)	0 (0.0%)	210085 (15%)	319608 (25%)
Liver Disease	9216 (0.7%)	80403 (2%)	33896 (3%)	1216843 (85%)	218814 (17%)

SAT0412 DOES THERAPEUTIC EDUCATION IMPROVE GOUT MANAGEMENT: THE EXPERIENCE OF LARIBOISIERE UNIVERSITY HOSPITAL PARIS-FRANCE

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Background: Gout is a frequent and curable arthritis affecting 0.9% of adults in France. Its management remains suboptimal and less than one third of patients have efficient urate-lowering treatment (ULT). However, when individualized information were given and patients engaged in their care a treat-to-target strategy permits to achieve serum urate level (SU) at target (SU < 360 µmol/L) in more than 95% of patients.
Therapeutic education sessions (TES) may improve patient knowledges, gout flare and ULT management.
Objectives: To assess the percentage of patients achieving SU target at 1 year after a TES.
Methods: TES was set up in the department since January 2014. Patients willing to participate to TES responded to a questionnaire and were interviewed with a nurse assessing their knowledges, believes and gout representations. Each TES included 5 to 8 patients and was conducted according to participants' needs. We retrospectively included all patients who had attended one TES between 1stJanuary 2014 and 31thDecember 2017 and who had at least one visit between 9 and 15 months later.
TES patients were matched in 1:1 with no-TES patients regarding age, sex and referent practitioner.
For all patients were collected: demographics, disease duration, SU, treatments and comorbidities (type 2 diabetes, chronic kidney disease, hypertension, and cardiovascular diseases).
Results: Overall, 54 TES patients were included and matched with 54 non-TES patients. Patients' characteristics (demographics, disease duration, SU, treatments and comorbidities) were similar at baseline except for the body mass index (BMI) and the follow-up. BMI was higher (31.0 ± 5.7 vs 28.4 ± 5.0 kg/m², p=0.03) and the final visit shorter (11 ± 3.6 vs 14.4 ± 4.8 months, p=0,001) in no-TES patients than in TES patients, respectively.
At final visit, 36 TES patients (67%) and 34 no-TES patients (63%) reached the SU target (< 360 µmol/L) (p=0.84) (Table 1). Moreover, 22 (41%) TES patients and 18 (33%) no-TES patients had a final SU < 300 µmol/L (p=0.43). There were no differences between groups (TES vs no-TES patients respectively) for: final SU (342 µmol/l ± 94 vs 338 ± 71, p=0.84), ULT (89% vs 96%, p=0.16), ULT dosage and hyperuricemic therapy (15% vs 11%, p=0.77).

Table 1. Patient's characteristics for gout at the end of the follow-up

	Baseline		End of follow-up		p value
	TES	No-TES	TES	No-TES	
Patient with serum urate < 360 µmol/L, n (%)	0 (0%)	0 (0%)	36 (67%)	34 (63%)	0,84
Patient with serum urate < 300 µmol/L, n (%)	0 (0%)	0 (0%)	22 (41%)	18 (33%)	0,43
Serum urate concentration (µmol/L), mean (SD)	533 (105)	528 (97)	342 (94)	338 (71)	0,84
Taking ULT	21 (39%)	19 (35%)	48 (89%)	48 (96%)	0,16
Allopurinol, n (%)	16 (30%5)	12 (22%)	22 (41%)	22 (44%)	0,89
Febuxostat, n (%)	5 (9%)	7 (13%)	26 (48%)	26 (52%)	0,84
ULT dose					
Allopurinol (mg/day), mean (SD)	196 (169)	183 (41)	284 (102)	241 (76)	0,22
Febuxostat (mg/day), mean (SD)	100 (30)	86 (10)	92 (26)	83 (13)	0,32
Taking hyperuricemia therapy, n (%)	13 (24%)	16 (30%)	8 (15%)	6 (11%)	0,77
Aspirine, n (%)	6 (11%)	8 (15%)	2 (4%)	2 (4%)	1
Thiazide diuretics, n (%)	5 (9%)	7 (13%)	6 (11%)	3 (6%)	0,49
Furosemide, n (%)	6 (11%)	7 (13%)	2 (4%)	2 (4%)	1

ULT = urate-lowering therapy

Conclusion: The percentage of patients achieving SU target after one single TES was high compare to literature data. However, it was not different from usual care achieved in our department, a tertiary care center expert in gout management. The diffusion of our *savoir-faire* and the TES will improve gout management.

REFERENCE

[1] Doherty M, Jenkins W, Richardson H, Sarmanova A, Abhishek A, Ashton D, et al. Efficacy and cost-effectiveness of nurse-led care involving education and engagement of patients and a treat-to-target urate-lowering strategy versus usual care for gout: a randomised controlled trial. The Lancet. 2018;392(10156):1403–1412.

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SAT0413 SIZE MATTERS – EXTENT OF MONOSODIUM URATE DEPOSITS BUT NOT SERUM URATE LEVEL PREDICTS COMPLETE RESOLUTION OF MONOSODIUM URATE CRYSTAL DEPOSITS IN PATIENTS WITH GOUT

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Background: Gout is based on the deposition of monosodium urate (MSU) crystals. While it is well established that life-style intervention and/or conventional urate lowering therapy can lead to a decrease in serum urate levels, the impact of such interventions to resolve already existing MSU deposits is very limited.
Objectives: In this study we wanted to determine if and to what extent MSU deposits resolve if patients follow structured life-style intervention or continuously conventional urate lowering therapy.
Methods: Subjects with diagnosis of gout and the presence of MSU deposits in the feet in baseline dual energy CT (DECT) scan, received either life-style intervention only (N=24) or additional conventional urate lowering therapy (allopurinol: N=29, febuxostat: N=22, benzbromarone N=2) for a mean period of 18 months before receiving a follow-up DECT examination. MSU deposits were quantified by volumetric measurement and semi quantitative scoring at baseline and follow up.
Results: Serum uric acid (SUA) level decreased from 7.2±1.7 to 6.7 ±1.7mg/dl with life-style intervention; from 7.0±1.5 to 5.5±1.8mg/dl with allopurinol and from7.8±3.0 to 5.1 ± 2.5mg/dl with febuxostat. MSU volume significantly decreased in patients undergoing life-style intervention (baseline: 0,07cm3 ± 0,09; follow up: 0,05 ± 0,15cm3; p=0.007), treatment with allopurinol (0,11 ± 0.15 cm3 to follow up: 0.02 ± 0,04 cm3, p<0.001) or febuxostat (MSU volume baseline: 0.99 ± 2.8 to follow up: 0.64 ± 2.09; p=0.001). With respect to conversion from a DECT+ into a DECT- state, baseline MSU deposit burden, but not baseline SUA level or decrease in SUA level, was associated with reaching a DECT- state.

Thus patients with smaller deposits were more likely to completely resolve the deposits.
Conclusion: We show that both life-style intervention and conventional urate lowering drug therapy reduce the volume of monosodium urate deposits. The size of MSU deposits, but not serum urate level, was the main factor that influenced complete resolution of deposits. This finding reemphasizes that the burden of deposits essentially defines the likelihood and time for complete resolution of gout.

REFERENCES

[1] Manger B, Lell M, Wacker J, Schett G, Rech J. Detection of periarticular urate deposits with dual energy CT in patients with acute gouty arthritis. Ann Rheum Dis. 2012;71(3):470-2.
[2] Bongartz T, Glazebrook KN, Kavros SJ, Murthy NS, Merry SP, Franz WB, 3rd, et al. Dual-energy CT for the diagnosis of gout: an accuracy and diagnostic yield study. Ann Rheum Dis. 2015;74(6):1072-7.
[3] Bayat S, Aati O, Rech J, Sapsford M, Cavallaro A, Lell M, et al. Development of a Dual-Energy Computed Tomography Scoring System for Measurement of Urate Deposition in Gout. Arthritis Care Res (Hoboken). 2016;68(6):769-75.

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SAT0414 CLINICAL PRESENTATION OF PAGET DISEASE OF BONE: IS IT CHANGING? A RETROSPECTIVE ANALYSIS ON 368 PATIENTS

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Background: In the last few years, it has been reported a secular change of Paget disease of bone (PDB), expressed as a reduction of prevalence[1] and severity, assessed by disease extent[2].
Objectives: To retrospectively evaluate the baseline clinical and demographic characteristics of a contemporary cohort of patients affected by PDB, compared with a cohort of a previous decade[3].
Methods: Data were retrospectively extracted from a monocentric registry, which included PDB patients at their first evaluation in a tertiary rheumatology Center between January 2000 and September 2018. Descriptive data of baseline characteristics included demographics, presenting manifestation and diagnostic procedures (diagnosed by chance or by investigations requested for specific clinical manifestations), extent of PDB, and biochemical data. Patients were divided into two groups according to the year of first evaluation: group 1 before July 2007, group 2 after July 2007. Comparisons between the two groups were performed by T test and chi-square test; logistic regression was used to analyze the association between disease extent and other collected variables.
Results: The overall population included 368 patients (males (M) 57.6%, mean age at diagnosis [± standard deviation, SD] 62.0±12.4 yrs). Diagnosis was made by chance in 43.8% cases, 54.3% patients had symptoms at disease onset; 49.5% was monostotic, mean serum alkaline phosphatase at presentation (sALP) was 198.5±167.5 UI/L.
Group 1 included 217 patients (M 56.2%, mean age at diagnosis 61.0 ±11.6 yrs, 6.5% family history of PDB; 45.6% diagnosed by chance, 51.2% had symptoms at disease onset, mean sALP 218.9±11,7, 43.3% monostotic). Group 2 included 151 subjects (M 59.6%, mean age at diagnosis 64.3±11.1 yrs, 7.3% family history of PDB; 41.1% diagnosed by chance, 62.9% had symptoms at disease onset, mean sALP 162.7 ±14,2,58.3% monostotic).
Poliostotic disease was significantly higher in Group 1 vs Group 2 (p=0.007), and the odd to have a poliostotic disease was higher in Group 1 [OR 1.82 (IC 1.2-2.8), p<0,005]. sALP was significantly higher in Group 1 vs Group 2 (218,9±11,7 vs 162,7±14,2; p=0,003). No differences were found in sex, age at diagnosis, presence of family history of PDB between patients diagnosed incidentally or by symptoms.
Conclusion: Our data confirm the reduction of clinical severity, assessed by the proportion of skeleton involved, and the decrease of biochemical markers over time. The reduction of the disease extent is consistent with a serological biomarker of the disease, such as mean sALP levels.

REFERENCES

[1] Michou L, et al. JBS 2016;83: 650–655.
[2] Tan A, Ralston SH. Calcif Tissue Int 2014;95:385–392.
[3] Varenna M, et al. J Rheum 2010;37:155-160.

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SAT0415 HIGH BODY FAT OF TRUNK IS POSITIVELY CORRELATED WITH SERUM URIC ACID IN MALE GOUT PATIENTS

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Background: Obesity is an important risk factor of gout which is defined by body mass index (BMI). However, BMI has been challenged for the limitation of failure to differentiate comprising tissues of the body. More accurate body composition (BC) has been frequently recommended to assess metabolic status.
Objectives: To investigate the characteristics of BC in gout patients and its clinical significance.
Methods: Consecutive gout patients who fulfilled the 2016 ACR/EULAR classification criteria were recruited between June 2017 and December 2018. BC was assessed by bioelectric impedance analysis including body fat percentage (BF%), the mass and distribution of muscle and fat in trunk and appendicular extremities. Demographic information, clinical characteristics and comorbidities were collected. Overfat was defined by BF% $\geq$25% for male and $\geq$35% for female.
Results: Among 362 recruited gout patients, 96.1% were male and the median age was 38 (30, 50) years, mean serum uric acid (sUA) was 9.2±2.2mg/dl, 18.0% presented tophi. The mean BF% was 25.8±6.4% with 53.6% overfat. Male gout patients with overfat (53.7%) showed more affecting joints, higher sUA and higher prevalence of comorbidities than those without overfat (P<0.05, Figure 1). Their BF%, trunk BF% and limb BF% were positively correlated with count of affecting joints, sUA, hypertension, metabolic syndrome and fatty liver in Spearman correlation analysis, respectively (r=0.133~0.424, all P<0.05). The male patients with overfat also presented higher BMI and waist circumstance (WC), higher trunk/limb BF% ratio (P<0.05, Figure 1). Their BF%, trunk BF% and limb BF% were also positively correlated with BMI and WC, respectively (r=0.604~0.755, all P<0.05). After adjustment for age, duration, family history, eGFR, hypertension, diabetes mellitus, dyslipidemia, metabolic syndrome, fatty liver, coronary heart diseases, urolithiasis, BMI and WC, multivariable linear regression showed that BF% (β=0.072, 95%*CI*

0.012~0.132, P=0.018) and trunk BF% (β=0.152, 95%*CI* 0.043~0.261, *P*=0.007), but not limb BF%, were positively correlated with sUA.

Figure 1 Clinical characteristics and body composition of gout patients

Characteristics	All patients (n=362)	Grouped by gender			Male patients grouped by overfat		
		Male (n=348)	Female (n=14)	P	Overfat (n=187)	Non-overfat (n=161)	P
Age, years	38(30, 52)	38(30, 50)	66(59, 72)	<0.001	38(30, 51)	37(30, 50)	0.969
Duration, years	3(2, 7)	3(2, 7)	3(1, 6)	0.423	4(2, 7)	3(1, 6)	0.163
Count of affecting joints	3(2, 6)	3(2, 6)	3(1, 5)	0.494	4(2, 6)	2(2, 5)	0.002
Family history, n(%)	130(35.9)	124(35.6)	6(42.9)	0.581	74(39.6)	50(31.1)	0.098
Tophi, n (%)	65(18.0)	64(18.4)	1(7.1)	0.472	36(19.3)	28(17.4)	0.655
Serum uric acid , mg/dl	9.2±2.2	9.2±2.2	9.2±2.5	0.957	9.6±2.1	8.7±2.2	<0.001
eGFR, ml/min-1/1.73m-2	83.8±17.0	84.3±16.9	70.4±11.7	0.002	85.1±18.2	83.5±15.3	0.395
Urolithiasis, n (%)	88(24.3)	85(24.4)	3(21.4)	0.795	49(26.2)	36(22.4)	0.405
Hypertension, n (%)	133(36.7)	124(35.6)	9(64.3)	0.029	83(44.4)	41(25.5)	<0.001
Diabetes mellitus, n (%)	36(9.9)	33(9.5)	3(21.4)	0.313	23(12.3)	10(6.2)	0.053
Dyslipidemia, n (%)	228(63.0)	218(62.6)	10(71.4)	0.504	131(70.1)	87(54.0)	0.002
Body mass index , kg/m2	25.5±3.6	25.5±3.6	25.7±3.1	0.882	27.4±3.3	23.3±2.6	<0.001
Obesity, n (%)	79(21.8)	77(22.1)	2(2.5)	0.392	73(39.0)	4(2.5)	<0.001
Waist circumstance, cm	90.8±9.4	90.8±9.5	89.3±7.4	0.551	95.9±8.3	85.0±7.2	<0.001
Metabolic syndrome, n (%)	165(45.6)	158(45.4)	7(50.0)	0.735	114(61.0)	44(27.3)	<0.001
Fatty liver, n (%)	172(47.5)	165(47.4)	7(50.0)	0.849	108(57.8)	57(35.4)	<0.001
Coronary heart disease, n (%)	8(2.2)	6(1.7)	2(14.3)	0.027	1(0.5)	5(3.1)	0.100
BF%, %	25.8±6.4	25.5±6.2	35.0±5.0	<0.001	30.1±3.8	20.1±3.7	<0.001
Overfat, n (%)	194(53.6)	187(53.7)	7(50.0)	0.783	187 (100)	0 (0)	<0.001
Trunk BF%, %	13.3±3.7	13.1±3.6	17.9±2.8	<0.001	15.8±1.9	10.1±2.4	<0.001
Limb BF%, %	11.0±3.7	10.7±2.8	18.1±10.2	0.017	12.7±2.1	8.4±1.5	<0.001
Trunk/Limb BF% ratio	1.22±0.15	1.22±0.14	1.10±0.24	0.003	1.25±0.11	1.19±0.17	<0.001

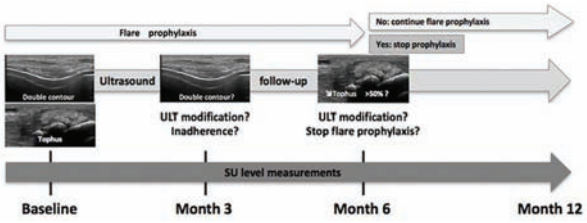
eGFR: estimated glomerular filtration rate; BF%: body fat percentage; ASMI: appendicular skeletal muscle index.

Conclusion: The characteristics of fat distribution in male gout patients is more in trunk and trunk BF% is positively correlated with sUA.
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SAT0416 ULTRASOUND EVALUATION IN FOLLOW-UP OF URATE-LOWERING THERAPY IN GOUT PHASE 2 (USEFUL-2): DURATION OF FLARE PROPHYLAXIS

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Background: Recent studies showed that ultrasonography (US) could be useful for managing urate-lowering therapy (ULT) in gouty patients. In the first phase of the present study (USEFUL-1), we suggested that US was an accurate tool to follow monosodium urate (MSU) crystal dissolution under efficient ULT.
For gout flare after starting ULT, prophylaxis is recommended during the first 6 months of ULT. The duration of gout flare prophylaxis over the 6 months is consensual with a grade B recommendation. However, little is known about the probability of relapse according to the urate load modification.
Objectives: To determine whether a modification of US features of MSU crystal deposition is associated with reduced number of flares after stopping gout flare prophylaxis.
Methods: We performed a 1-year multicentre prospective study including patients with proven gout and US features of gout. The first phase of the study was a 6-month US follow-up after starting (ULT) with gout flare prophylaxis. After 6 months of ULT, gout flare prophylaxis was stopped, followed by a clinical follow-up (month [M] 6 to 12). Outcomes were the proportion of patients with relapse between M6 and M12 according to the modification of US features of gout and determining a threshold decrease in tophus size according to the probability of relapse.
Results: We included 79 patients with gout (mean [± SD] age 61.8 ± 14 years, 91% males, disease duration 6.3 ± 6.1 years). Among the 49 completers at M12, 23 (47%) experienced relapse. Decrease in tophus size $\geq$ 50% at M6 was more frequent without than with relapse (54% *vs* 26%, P= 0.049). On ROC curve analysis, a threshold decrease of 50.8% in tophus size had the best sensitivity/specificity ratio to predict relapse. Probability of relapse was increased for patients with a decrease in tophus size <50% between baseline and M6 (OR 3.35 [95% confidence interval 0.98; 11.44]).
Conclusion: A high reduction in US tophus size is associated with low probability of relapse after stopping gout prophylaxis. US follow-up may be useful for managing ULT and gout flare prophylaxis.



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SAT0417 HOW EFFECTIVE IS GOUT EDUCATION PROGRAMME TO IMPROVE GOUT KNOWLEDGE AMONG PRIMARY CARE DOCTORS?

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Background: Gout is a potentially curable disease with simple pharmacological treatment, although its management remained suboptimal.[1, 2] A disconnection between primary care doctors who treat gout most frequently, and rheumatologists who lead the development of gout management guidelines, is one of the challenges in managing gout in primary care.[3] A concerted effort is needed to improve the quality of care of patients with gout and this includes physician education.[4]
Objectives: To determine the effectiveness of gout educational programme in improving gout knowledge among primary care doctors.
Methods: A gout education programme consisted of five 20-minute presentations on gout (challenges in gout, principles of gout management, treat to target, disease burden and gout diet) and a session on case discussion of two gout cases was conducted for primary care doctors. Participants were invited to complete the same set of questions distributed before (pre-test) and after (post-test) the programme. A set of 10 true/false multiple choice questions (MCQ) based on a clinical scenario of a patient with gout was constructed and vetted by two rheumatologists. Comparison between the pre-test and post-test scores were analysed using paired t-test.
Results: Forty-four primary care doctors who attended gout educational programme, answered pre-test and post-tests and the scores are shown in Table 1. The scores for recall questions were higher than application questions.The mean scores for recall questions in post-test were significantly higher compared to pre-test (4.35±0.73 vs 3.51±0.47, p<0.01) but not significant for application questions (2.91±0.71 vs 2.79±0.62, p=0.56). Less than half of participants obtained correct answers for 13 out of 50 options in the pre-test mainly in questions 2, 3, 4, 6 and 7. (Table 1)

Table 1. The pre-test and post-test mean scores for all participants of gout education programme.

Question no	Question type	Areas of knowledge tested	Mean scores, n=30			p-value
			Post-test	Pre-test	Difference	
1	Application	Features of gout for diagnosis	3.47 ±0.97	3.53 ±1.11	-0.07±1.02	0.72
2	Application	Interpretation of investigation	2.73 ±0.79	2.3 ±1.12	0.433±0.73	<0.01
3	Application	Treatment of acute gout	1.97 ±0.85	2.27 ±0.74	-0.30±1.01	0.14
4	Application	Treatment of stable gout	3.47 ±1.22	3.07 ±1.05	0.40±1.52	0.16
5	Recall	Indication of urate lowering therapy	4.87 ±0.34	3.87 ±0.97	0.47±0.90	<0.01
6	Recall	Allopurinol mechanism	3.17 ±0.99	2.77 ±0.94	0.40±1.19	0.08
7	Recall	Allopurinol dose initiation	5.00 ±0.00	3.53 ±1.14	1.47±1.14	<0.01
8	Recall	Allopurinol side effects	4.97 ±0.18	4.1 ±0.89	0.87±0.9	<0.01
9	Recall	Non-pharmacological management	4.00 ±0.46	3.6 ±1.10	0.4±1.25	0.09
10	Recall	Medication which can aggravate gout	4.07 ±0.74	3.23 ±1.46	0.833±1.51	<0.01

Conclusion: Gout educational programme for primary care doctors was effective in improving recall knowledge but not in application knowledge. Some specific areas of deficiency in gout knowledge identified were features of gout and management of acute and stable gout.

REFERENCES

[1] Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis 2017; 76: 29–42.
[2] Abhishek A, Doherty M, Education and non-pharmacological approaches for gout. Rheumatology, 57(suppl_1), 2018; i51-58.
[3] Dalbeth N. Management of gout in primary care: challenges and potential solutions. Rheumatology. 2013; 52(1): 1549-1550
[4] JA Singh. Quality of Life and Quality of Care for patients with Gout. Curr Rheumatol Rep, 2009; 11(2): 154-160

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SAT0418 ASSOCIATION BETWEEN ANEMIA AND HYPERURICEMIA: KOREAN NATIONAL HEALTH AND NUTRITION SURVEY 2016

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Background: Hyperuricemia and anemia may be related in terms of sharing comorbidities such as chronic kidney disease and cardiovascular disease. However, to our knowledge, no studies have been conducted on the relationship between two conditions. For the association of gout and anemia, there was a previous cohort study showing that patients with anemia had a 2-fold higher risk of gout compared to patients without anemia. And the risk of gout was significantly higher after adjusting for serum urate levels and kidney function. However, there is a lack of data on the relationship between anemia and hyperuricemia.
Objectives: The purpose of this study was to investigate the association between hyperuricemia and anemia using data from Korean National Health and Nutrition Examination Survey (KNHANES VII; 2016), which is representative of the Korean population.
Methods: The present study included 5887 participants aged $\geq$ 19 years from KNHANES VII. Logistic regression was used to examine the association between anemia and hyperuricemia. Subgroup analysis was performed to confirm whether the association between two conditions varies according to participant characteristics.
Results: In an adjusted model that corrected for body mass index, smoking, drinking, physical activity, income, and education levels, hyperuricemia was 1.4 times more than that those without anemia (HR 1.41, 95% CI 1.01-1.98). The association of anemia with hyperuricemia was not seen under 65 years of age (HR 2.68, 95% CI 1.60-4.48). In addition, this association was not clear in women, but was significant in men (HR 2.62, 95% CI 1.47-4.70). In the results of subgroup analysis according to comorbidities, the association of anemia with hyperuricemia was significant only in subgroups with chronic kidney disease, diabetes, hypertension, metabolic syndrome, and cardiovascular diseases. There was no association between anemia and hyperuricemia in obese subjects, but hyperuricemia risk was higher in non-obese subjects with anemia compared to those who did not have anemia.
Conclusion: In a Korean representative sample, the risk of hyperuricemia was higher for anemia. The association of anemia with hyperuricemia was more pronounced in subjects with older age, male population, and other comorbid conditions.
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SAT0419 HAS THE INTRODUCTION OF A PRIMARY CARE GOUT GUIDELINE RESULTED IN SERUM URIC ACID (SUA) TARGETS BEING ACHIEVED?

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Background: Gout is the most common inflammatory arthritis thought to affect 2.4% of the UK population. A local primary care audit in 2012 suggested suboptimal gout management. In an attempt to improve gout management we introduced a local guideline which was supported by an increase in gout education to our local primary care physicians.
Objectives: To assess the impact of a local primary care gout guideline (introduced in 2015) by comparing pre-guideline audit data (2012) to post guidelines audit data (2019). To identify if the introduction of this guideline translated into a reduction in secondary care referrals for advice on gout management.
Methods: Retrospective analysis of primary care data covering all patients with active diagnosis of gout since 2015 in a large primary care medical group (list size of 30,000 patients). This data was then compared to the results of a previous audit carried out prior to introduction of guideline (2012). As well as assessing primary care data, we carried out a secondary care audit pre and post guideline introduction.
Results: Out of a population list of 30,000 patients, 650 (2.1%) cases were coded as gout. 521 (80%) were male and 129(20%) were female. 429(66%) were on ULT. 407 (94.8%) were on Allopurinol. 21(4.8%) were on Febuxostat and only 1 patient on sulfinpyrazone.
Of those on Allopurinol, 24 (5.9%) had no documented monitoring of sUA levels. Out of the remaining 383 (94.1%), 179 (46.7%) achieved target sUA of <360, compared to 16.7% in the previous audit. 204 (53.3%) had not achieve the target SUA levels. 178 (46.4%) patients had had their sUA levels checked in the last year compared to 23.5% in the previous audit. 107 (28%) had SUA levels checked in last 3 years compared to 40% in the previous audit. SUA levels were not checked in the last 3 years in 98(25.6%) compared to 36.4% in the past.
Of those on febuxostat, 14 (67%) achieved target sUA levels. 7 (33%) did not achieve target sUA levels. 10 (47%) patients had their sUA levels checked in the last year. 7(33%) had their sUA levels checked within the last 3 years and 4 (20%) had not had their sUA levels checked within the last 3 years.
No patient was prescribed more than 300mg allopurinol daily by their primary care physician despite the recommended dose being up to 900mg daily.
We found a 70% reduction in the number of referrals to secondary care for gout management over the same period of time.
Conclusion: The introduction of a local primary care gout guideline and associated education appears to have improved the number of patients achieving target serum uric acid levels as well as leading to a reduction in secondary care referrals for gout.

REFERENCES
[1] http://www.lancsmmg.nhs.uk/download/guidelines/Gout-Prescribing-Guidance-Version-1.2-FOR-WEBSITE.pdf
[2] https://academic.oup.com/rheumatology/article/56/7/e1/3855179

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SAT0420 IS THERE LIFE TO GOUT TREATMENT AFTER RHEUMATOLOGY IS OUT OF THE EQUATION?

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Background: Previous studies show a low persistence rate to urate-lowering therapy (ULT), in patients diagnosed with gout, after being discharged back to primary care from Rheumatology consultations.
Objectives: To assess persistence and adherence to ULT in patients with gout, previously evaluated in specialized care, who have been discharged from Rheumatology consultations to their primary care physician.
Methods: A transverse study of patients with gout included in an inception cohort and followed in a tertiary care centre. Patients were selected according to their status of "discharge", in case they had been referred back to their primary care centre from specialized care, or "loss", in case they had stopped coming to Rheumatology consultations.
Data, including active prescription of ULT, time since suspension of ULT (if applicable), last serum uric acid (sUA) levels and time for that determination, were procured by electronic history. General data of patients and follow-up were obtained from the database of such cohort.
Patients lacking data or deceased were dismissed from the study.
Results: A total of 518 patients, classified either as "discharge" or "loss", with available data accessed by electronic history, followed in specialized consultations during an average time of 52 months (36, 18-72) were studied. Average time since their last visit to Rheumatology services was 90 months (76, 36-132). 88% of them had, at least, one determination of sUA; 80% within the last 12 months, with no differences between the patients with or without active treatment. 376 patients (72.6%) out of 518 had an active prescription of ULT, 338 of them ordered by primary care and 38 by specialized care.
Patients lost during follow-up showed a lower rate of ULT prescription and a higher requirement of specialized attention after than those who were discharged from Rheumatology.

	Loss (172)	Discharge (346)	P
Follow-up (number of months)	31±34	64±49	<0.001
Time since follow-up (number of months)	113±72	80±55	<0.001
Prescription (%)	64	73	<0.001
sUA w/o prescription (mg/dl)	7.44±2,02	7.07±1,33	0.231
sUA <6 mg/dl w/o prescription (%)	18	29	0.275
sUA w/prescription (mg/dl)	6.26±2.09	5.66±1,59	0.010
sUa <6 mg/dl w/ prescription (%)	55	58	0.764
Adherence (% average TPM)	76±30	85±24	0.007
Adherence (% TPM >80%)	64	79	0.003
Need of specialized care after (%)	11	6	<0,001

Conclusion: Patients discharged from Rheumatology consultations maintain good persistence to long-term treatment with ULT, higher than those who were lost during consultation follow-up. Nevertheless, persistence and adherence in the latter group show a higher rate than the ones obtained in patients being followed by primary care, which does not exclude a beneficial influence of the previous assistance provided by Rheumatology services.

REFERENCES
[1] Aung T, Myung G, FitzGerald JD. Treatment approaches and adherence to urate-lowering therapy for patients with gout. Patient Prefer Adherence. 2017;11:795-800. Published 2017 Apr 19. doi:10.2147/PPA.S97927
[2] Perez-Ruiz F, Desideri G. Improving adherence to gout therapy: an expert review. Ther Clin Risk Manag. 2018;14:793-802. Published 2018 May 3. doi:10.2147/TCRM.S162956
[3] Scheepers L, van Onna M, Stehouwer C, et al. Medication adherence among patients with gout: A systematic review and meta-analysis. Semin Arthritis Rheum. 2018 Apr;47(5):689-702. doi: 10.1016/j.semarthrit.2017.09.007. Epub 2017 Oct 7.
[4] Yin R, Li L, Zhang G, et al. Rate of adherence to urate-lowering therapy among patients with gout: a systematic review and meta-analysis. BMJ Open. 2018;8(4):e017542. Published 2018 Apr 10. doi:10.1136/bmjopen-2017-017542

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SAT0421 LONG-TERM URATE-LOWERING THERAPY: IS IT 'ALL LIFELONG' NECESSARY?

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Background: It has been published that 13% of gout patients remain in a situation of normouricemia after the suspension of urate-lowering therapy (ULT) and, consequently, would not require lifelong treatment. Prospective and specialized follow-up in a tertiary care centre may have favored these positive outcomes, which have not been replicated afterwards.
Objectives: To assess the percentage of patients diagnosed with gout, previously followed in Rheumatology consultations, in situation of normouricemia once ULT is suspended.
Methods: A transverse study of patients with gout included in an inception cohort and followed in a tertiary care centre. Selected patients were no longer followed by specialized attention.
Data, including active prescription of ULT, time since suspension of ULT (if applicable), last serum uric acid (sUA) levels and time for that determination, were procured by electronic history. General data of patients and follow-up were obtained from the database of such cohort.
Results: One hundred and forty-two (27.4%) out of 518 patients, with available data accessed by electronic history, lacked prescription of ULT, with an average time since its interruption of 65 months (58, 28-120) and sUA average levels of 7.2±1.7 mg/dl. Nevertheless, 19.2% of these patients showed sUA levels <6 mg/dl, against 61% and 63% of patients with active ULT prescription followed by primary care and specialized care, respectively.
Considering a higher target level of uric acid in the long run and taking into account that these patients had already received treatment for an average mean of 50 months, either in patients with active ULT prescription or patients without it (p=0.35), 41.7% of patients without ULT showed sUA levels <6.8 mg/dl vs. 77% of those with an active ULT prescription (both primary and specialized care).
Patients without ULT, showing sUA levels <6 mg/dl or <6.8 mg/dl also showed lower sUA levels during previous follow-up in Rheumatology consultations than those with sUA levels out of target (4.9mg/dl vs. 5.2mg/dl, p<0.01 and 5.0mg/dl vs. 5.3mg/dl). Likewise, among patients with sUA levels <6mg/dl during follow-up, 25.3% showed sUA levels <6mg/dl vs. 0% of those with sUA levels >6mg/dl during follow-up (p<0.01).
Conclusion: Between 20% and 40% of patients without a prescription of ULT, previously followed by Rheumatology, showed sUA levels <6mg/dl and <6.8mg/dl, respectively.
Patients with sUA levels below target during follow-up show a higher rate of sUA levels in target once ULT is suspended.

REFERENCES

[1] Perez Ruiz F, Sanchez-Piedra CA, Sanchez-Costa JT, et al. Improvement in Diagnosis and Treat-to-Target Management of Hyperuricemia in Gout: Results from the GEMA-2 Transversal Study on Practice. *Rheumatol Ther*. 2017;5(1):243-253.

[2] Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Annals of the Rheumatic Diseases 2017;76:29-42.

[3] Yin R, Li L, Zhang G, et al. Rate of adherence to urate-lowering therapy among patients with gout: a systematic review and meta-analysis. BMJ Open. 2018;8(4):e017542. Published 2018 Apr 10. doi:10.1136/bmjopen-2017-017542

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SAT0422 URATE VOLUME AND DISTRIBUTION BY DUAL ENERGY CT: CLINICAL AND RADIOLOGICAL CORRELATION IN GOUT PATIENTS

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Background: Dual-energy CT (DECT) has shown tremendous potential as a novel non-invasive method of urate detection in patients with gout.

Objectives: Our aim was to determine the concordance between urate volume and distribution measured on DECT with clinical presentation among patients with gout.

Methods: We conducted a retrospective descriptive study of patients with gout who were referred by a rheumatologist for gout DECT scans between January 2008 and February 2018. At our institution, routine DECT scans for gout consist of four sets of images with limbs scanned in pairs: the hands/wrists, elbows, knees and ankles/feet. We obtained volumetric measurements for all four anatomical regions, and assessed the concordance with clinical presentation as retrieved from patient electronic health record.

Results: A total of 182 patients were included in this study; 96 patients (80.2% male, age range: 27-90, mean age: 62) had urate deposits on DECT scans. Among urate-positive patients, the mean total volume of deposits was 2.45 cm^3 (hands/wrists: 0.17 cm^3, 7%; elbows: 0.62 cm^3, 25%; knees: 0.70 cm^3, 28%; ankles/feet: 0.96 cm^3, 39%). The average number of urate-positive joints was 2.5, higher than that of clinically symptomatic joints (1.9). Discordance between DECT results and clinical symptoms were seen more often in elbows (46 urate-positive vs. 22 symptomatic) and knees (68 vs. 43), compared with hands/wrists (31 vs. 30) and ankles/feet (90 vs. 87). Only in 25 (26.0%) patients, the distribution of symptomatic joints fully matched the distribution of urate deposits. In 6 patients (6.3%), there was no overlap between these two distribution patterns.

Conclusion: On DECT scans, most urate deposits in gout patients occur in the ankles/feet, followed by knees, elbows, and hands/wrists. DECT scans can reveal urate deposit in asymptomatic joints, especially in elbows and knees. Assessing the concordance of urate distribution with clinical presentation in all limb joints in gout patients, our results can help understand the pathophysiology of urate deposition in gout, and guide the development of DECT protocols for the screening, assessment and follow-up management of gout patients.

REFERENCE

[1] Nicolaou S, Liang T, Murphy DT, Korzan JR, Ouellette H, Munk P. Dual-energy CT: a promising new technique for assessment of the musculoskeletal system. AJR Am J Roentgenol. 2012; 199:S78-86.

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SAT0423 WHERE SHOULD WE EXAMINE FOR URIC ACID DEPOSITS? RESULTS FROM THE NOR-GOUT ULTRASOUND STUDY

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Background: Ultrasound (US) has received an increasing attention in detecting uric monosodium urate (MSU) deposits, and US is included in the ACR/EULAR classification criteria for gout. OMERACT has developed definitions for US elementary lesions in gout including double contour (DC) sign (deposits of crystals on the surface of cartilage), tophus (larger hypo-echoic aggregation of crystals, usually well delineated) and aggregates (small hyper-echoic deposits).

Objectives: The present objective was to explore by US the most frequent locations of MSU deposits.

Methods: Baseline data from a prospective observational study were used where patients with crystal-proven gout who presented after a recent gout flare were included (202 patients (mean (SD) age 56.6 (14.2) years, disease duration 8.0 (7.7) years, 94.1% men), all with insufficiently treated serum uric acid level (>360 μmol/L/>6 mg/dl). We performed an extensive assessment with US (GE E9 machine, grey scale 15MHz) for semi-quantitative scoring of MSU deposits (0=none, 1=possible/small, 2=moderate, 3=major) using OMERACT definitions for DC, tophi and aggregates. The following locations were examined bilaterally; radiocarpal, MCP 2 and MTP 1 joints, triceps and quadriceps insertions, patellar (proximal and distal) and Achilles tendons as well as distal femur (maximal flexed knee) and talar cartilage. Sum scores for each crystal deposit were calculated and correlations were performed by use of Spearman rho, comparisons by paired samples test, and frequencies of deposits were calculated as percentages.

Results: The baseline mean (SD) serum uric acid level was 494 (87) μmol/L. Table 1 shows uric acid deposits to be correlated with kidney function and disease duration. Table 2 includes frequencies with at least moderate US scores ($\geq$2) in the different joint and tendon localisations and shows DC primarily to be found in MTP1, followed by talar and femoral cartilage. Tophi and aggregates were primarily found in MTP1, followed by distal patellar and triceps tendons. There were no major differences between right and left side. In 25 patients (12.5%) DC was seen on femoral or talar cartilage but with no depositions in the MTP1 joint.

Conclusion: Uric acid deposits were associated with reduced kidney function as well as disease duration. When gout is suspected the present study suggests US examinations of MTP1, distal patellar and triceps tendons as well as talar and femoral cartilage to be the most important sites to examine for presence of MSU deposits.

Table

	Disease duration	Uric acid µmol/L	Creatinine µmol/L	Creatinine µmol/L
Sum score DC	0.35**	0.30**	0.26**	-0.27**
Sum score tophi	0.27**	0.13	0.27**	-0.37**
Sum score aggregates	0.16*	0.05	0.22*	-0.36**
Sum score DC, tophi and aggregates	0.29**	0.16*	0.29**	-0.40**

Table 2. Percentages of patients with different forms of ultrasound detected uric acid deposits

	Double contour		Tophus		Aggregates	
	Right	Left	Right	Left	Right	Left
Wrist	1.5	0.5	7.0	8.5	6.0	7.0
MCP 2	2.0	1.0	5.0	2.5	4.0	3.0
Distal femur cartilage	16.9	16.9	NA	NA	NA	NA
Talar cartilage	15.4	16.9	NA	NA	NA	NA
MTP 1	36.0	35.8	44.0	45.5	51.5	50.3
Triceps	NA	NA	15.0	12.5	32.8	31.8
Quadriceps	NA	NA	5.5	8.0	10.1	15.9
Proximal patellar tendon	NA	NA	5.0	7.0	9.5	13.4
Distal patellar tendon	NA	NA	19.5	15.0	42.5	37.3
Achilles	NA	NA	9.5	8.0	12.1	6.0

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SAT0424 PHENOTYPE OF PATIENTS WITH EARLY ONSET GOUT

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Background: Gout is a frequent inflammatory arthritis in men after 45 years old. In this common (CG) form, gout is associated with comorbidities (CMs) including metabolic syndrome, hypertension, type 2 diabetes (T2D), obesity, chronic kidney disease and cardiovascular (CV) diseases. In contrast, very few data are available for early onset gout (EOG), defined as first flare before 30 years old.
Objectives: The aim of this study was to compare gout characteristics and CMs between EOG and CG.
Methods: We retrospectively included all gout patients (pts) with ineffective ULT who were referred to our department between 2014 and 2018, and who had at least one visit between 9 and 15 months after first visit. At baseline, ineffective ULT was defined by a serum urate level (SUL) above target (> 360 µmol/L). Demographic characteristics, gout history and CMs, treatments were systematically recorded.
Results: Among 213 pts, 39 (18.3%) had experienced a first gout flare before 30 years old. Pts and gout characteristics are summarized in table 1. Mean age of first flare in EOG was 24.8 (± 5.5) years. Familial history of gout was more frequent in EOG than in CG (60.6 vs 24.6%). First flare involved the 1st metatarsophalangeal joint in 70% of EOG pts. EOG pts had more severe gout than CG pts: longer disease duration (p<0.0001), more flares in the last 12 months (p<0.0001), more tophi (p=0.005) and higher febuxostat (FBX) dosage (p=0.02) to achieve SUL target.
Pts with CG had more CMs than EOG pts: CV diseases, hypertension, T2D, dyslipidemia and kidney transplantation. Non-alcoholic fatty liver disease was more frequent in EOG than CG (61.1 vs 24.1%).
At final visit, 62.8 and 67.9% of EOG and CG patients, respectively, achieved SUL target (p=0.56). Proportion of pts taken ULT was similar in both groups as well as proportion of pts treated with allopurinol or FBX.

Table 1. Patient characteristics between early onset and common gout

Variables	Early onset gout (N=39)	Common gout (N=174)	p
Age at inclusion (years), (mean ± SD)	40.2 (12.2)	62.2 (11.8)	**<0.0001**
Sex (male)	38 (97.4%)	145 (83.3%)	**0.02**
BMI (kg/m^2), (mean ± SD)	29.6 (5.8)	28.9 (4.9)	0.49
Family history (n,%)	20 (60.6%)	30 (24.6%)	**<0.0001**
Age at first flare (years), mean ± SD)	24.8 (6.2)	55.4 (12.6)	**<0.0001**
Disease duration (years) (mean ± SD)	15.4 (12.6)	6.9 (7.6)	**<0.0001**
Tophi (n,%)	24 (61.5%)	58 (36.9%)	**0.005**
Urate arthropathy (n,%)	21 (65.6%)	61 (49.6%)	0.11
Number of flares last 12 months (mean ± SD)	4.7 (2.9)	3.0 (2.82)	**0.009**
eGFR (ml/min/1.73), (mean ± SD)	91.7 (33.4)	63.4 (24.5)	**<0.0001**
Baseline SUL (µmol/l) (mean ± SD)	495.9 (147.4)	521.1 (109.1)	0.23
CV diseases (n,%)	0	21 (13.2%)	**0.02**
HT (n,%)	9 (23.7%)	107 (64.8%)	**<0.0001**
Type 2 diabetes (n,%)	3 (7.9%)	41 (25.3%)	**0.02**
NAFLD (n,%)	11(61.1%)	14 (24.1%)	**0.003**
Dyslipidemia (n,%)	13 (33.3%)	70 (45.5%)	0.17
Chronic kidney disease stage 3-5 (n, %)	8 (25.8%)	58 (40.6%)	0.12
Final SUL (µmol/l) (mean ± SD)	360.7 (135.5)	336.6 (109.9)	0.26
SUL at target (<360 µmol/l) (n,%)	22 (62.8%)	110 (67.9%)	0.56
ULT final (n,%)	36 (92.3%)	148 (92.5)	0.97

BMI : body mass index; eGFR : estimated glomerular filtration rate; NAFLD : non-alcoholic fatty liver disease; SUL : serum urate level; ULT : urate-lowering therapy

Conclusion: In conclusion, EOG is more severe and EOG pts have less CMs. Moreover, EOG has a higher inheritability trait than CG patients suggesting different pathological mechanisms.
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SAT0425 CLINICAL CHARACTERISTICS AND RISK FACTORS OF ULCERATION OVER TOPHI IN PATIENTS WITH GOUT

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Background: With increasing prevalence of gout world-wide, ulceration associated with tophaceous gout is becoming increasingly common in recent years. Investigation of the clinical characteristics and risk factors will allow us to better understand the fact of ulceration over tophi and improve the management for such challenge problem.
Objectives: To describe clinical characteristics of ulceration over tophi in patients with gout and determine risk factors associated with ulceration.
Methods: Patients presenting with tophi or ulceration(s) over tophi were prospectively recruited and their clinical characteristics were recorded. Comparison of clinical characteristics and risk factors for ulceration were analyzed between groups.

Results: A total of 105 patients were enrolled. 33 patients with ulcerations were older, with prolonged duration with gout and tophi, a higher rate of obesity, greater number of tophi, lower level of GFR, and higher level of serum creatinine, ESR and CRP. The mean duration of ulceration was 1.63 ± 2.32 months. The ulcerations mainly located in ankle (34.21%) and MTP (39.47%), with a mean size of 32.37 × 22.76 mm. The majority of ulcerations were categorized as stage I (42.4%) and stage II (51.5%). In univariate regression analysis, age, glucocorticoid abuse, gout duration, tophi duration, tophi number and GFR were associated with ulceration. In the multivariable model, significant differences were demonstrated in glucocorticoid abuse, tophi duration, tophi number.
Conclusion: Gout patients with ulceration(s) over tophi present several different aspects of clinical characteristics compared with those without ulceration. Glucocorticoid abuse, prolonged duration with tophi and greater number of tophi are risk factors for ulceration over tophi. Avoiding indiscriminate use of glucocorticoid needs to be emphasized, and prevention of tophi formation via initiate effective urate-lowering therapy is highly recommended in patients with gout.

REFERENCES

[1] Lam G, Ross FL, Chiu ES. Nonhealing Ulcers in Patients with Tophaceous Gout: A Systematic Review. Adv Skin Wound Care. May 2017;30(5):230-237.

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SAT0426

TOPHI, THE PREDICTIVE FACTOR OF ARTERIAL STIFFNESS IN PATIENTSWITH GOUT AND HYPERURICEMIA

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Background: Gout is the most common form of inflammatory arthritis and its prevalence is increasing in recent decades. Many studies have reported that gout and hyperuricemia are associated with an increase in all-cause mortality and cardiovascular mortality. Increased arterial stiffness is an independent marker of cardiovascular diseases and risk predictors. Many studies have shown a significant correlation between uric acid levels and arterial stiffness. Augmentation Index (AI) is an indirect measure of arterial stiffness. Tophi is formed when gout is left untreated for a long time.
Objectives: The aim of this study is to determine whether the presence of tophi could predict an increase in arterial stiffness.
Methods: Between June 2017 and June 2018, augmentation index was measured using SphygmoCor for patients who visited Jeju National University Hospital in South Korea with gout or hyperuricemia. Medical records, laboratory and AI data were retrospectively analyzed.
Results: One hundred twenty two patients participated in the study and AI was measured. Most (96.7%) of the patients were male. At the time of the examination, 99 patients (81.1%) were treated with uric acid lowering agent and the mean duration of the disease was 6.9 years. When the patients were divided into two groups according to the presence or absence of Tophi, the average age (60.2±11.6 vs 53.4±13.2, p=0.023) of the patients with Tophi was significantly higher, duration of disease (13.0 ±6.5 vs 5.4±5.4, p=0.000) was longer and the AI (28.7±7.8 vs 20.7±10.4, p=0.001) was higher. When multiple linear regression analysis was performed to exclude the effects of other variables (DM, HTN, hyperlipidemia, age, BMI, total cholesterol, creatinine), tophi was a predictor of high AI (b = 5.478; 95% CI, 0.343-10.613; p=0.037). Multiple logistic regression analysis was performed to determine the predictors of tophi. The duration of disease and AI @ 75 values were significantly predictive of the presence of tophi (Odds ratio 1.113; 95% CI, 1.024-1.209; p=0.012)
Conclusion: This study suggests that the presence of tophi is an independent predictor of increased arterial stiffness in patients with gout and hyperuricemia.



Figure 1. Multiple ulcerations over tophi in one patient

Table 1. Clinical parameters in gout patients with ulceration and without ulceration

*Variable	Total (n= 105)	Ulceration (n = 33)	Non-ulceration (n = 72)	*P* value
Age, years	54.2 ± 14.9	61.1 ± 16.0	51.1 ± 14.9	0.002
Male, n (%)	102 (97.1%)	32 (97.0%)	70 (97.2%)	0.943
BMI, kg/m^2	24.2 ± 3.6	23.7 ± 3.5	24.4 ± 3.7	0.335
Smoking history, n (%)	45 (42.9%)	17 (51.5%)	28 (38.9%)	0.225
History of alcohol intake, n (%)	33 (31.4%)	11 (15.3%)	22 (30.6%)	0.776
Diet control, n (%)	77 (73.3%)	23 (69.7%)	54 (75.0%)	0.568
Glucocorticoid abuse, n (%)	40 (38.1%)	22 (68.8%)	18 (25.0%)	< 0.001
Gout duration, years	10.9 ± 6.2	12.5 ± 7.9	10.2 ± 5.2	0.208
Tophi duration, years	4.4 ± 3.1	6.6 ± 3.7	3.4 ± 2.1	< 0.001
Tophi number, n	5.2 ± 4.1	7.6 ± 4.9	4.1 ± 3.1	0.003
Hypertension, n (%)	49 (46.7%)	17 (51.5%)	32 (44.4%)	0.500
Diabetes, n (%)	21 (20.0%)	11 (33.3%)	10 (13.9%)	0.021
Cardiovascular disease, n (%)	9 (8.6%)	4 (12.1%)	5 (6.9%)	0.614
Urinary calculus, n (%)	37 (35.2%)	12 (36.4%)	25 (34.7%)	0.870
Serum creatinine, μmol/L	109.1 ± 55.0	122.9 ± 62.1	102.7 ± 50.0	0.003
Serum uric acid, μmol/L	624.0 ±130.7	650.6 ± 117.6	611.8 ± 135.3	0.159
ESR, mm/h	59.2 ± 39.4	79.9 ± 37.5	49.7 ± 36.7	< 0.001
CRP, mg/L	44.7 ± 47.1	53.8 ± 39.9	40.7 ± 49.8	0.005
GFR, ml/min/1.73 m^2	61.2 ± 30.0	51.1 ± 31.1	65.8 ± 28.6	0.001

n, number.
+ refers to number of the patients.

Table 2. Ulceration characteristics in 33 patients with gout including 38 ulcerations

Variable	Results
Ulceration duration, month	1.63 ± 2.32
Ulceration location	
Ankle, n (%)	13 (34.21%)
MTP, n (%)	15 (39.47%)
Knee, n (%)	1 (2.63%)
MCP, n (%)	5 (13.16%)
PIP, n (%)	2 (5.26%)
Hip, n (%)	1 (2.63%)
Elbow, n (%)	1 (2.63%)
Ulceration size, mm	
Length	32.37 ± 16.10
Width	22.76 ± 15.28
Ulceration stage, n (%)	
I	14 (42.4%)
II	17 (51.5%)
III	2 (0.61%)
IV	0

n, number.

REFERENCES

[1] Choi HK, Mount DB, Reginato AM. Pathogenesis of gout. Ann Intern Med 2005;143:499-516.

[2] Kuo C-F, Grainge MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. Nature Reviews Rheumatology 2015;11:649.
[3] Mehta T, Nuccio E, McFann K, Madero M, Sarnak MJ, Jalal D. Association of Uric Acid With Vascular Stiffness in the Framingham Heart Study. Am J Hypertens 2015;28:877-83.

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SAT0427 RISK OF MALIGNANCIES IN PATIENTS WITH GOUT: A POPULATION-BASED COHORT STUDY

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Background: Gout is a chronic disease characterized by deposition of monosodium urate crystals. Comorbidities including hypertension, chronic kidney disease, obesity, diabetes and cardiovascular diseases are common in patients with gout. In contrast to these well-known comorbidities, little is known about the risk of malignancies in patients with gout.
Objectives: To investigate the risk of malignancies in patients with gout, compared with general population.
Methods: We conducted a retrospective cohort study using Korean National Health Insurance Service-Medical check-up Cohort Database, which composed of qualified individuals as of 2002 in the age of 40-79 in 2002-2003 who received general medical check-up (Approximately 510,000). We enrolled patients newly diagnosed with gout, based on the diagnostic code and relevant medication history, who were between 40 and 65 years of age at the time of diagnosis between 2003 and 2007 (we washed out first year for newly detected cases). The gout patients (case group) were matched by 1:2 propensity score matching using confounding variables (age, sex, income group, region of residence, smoking status, alcohol intake, exercise habit, comorbidities including diabetes mellitus, hypertension and dyslipidemia, body mass index, blood pressure, serum glucose level, total cholesterol, and hemoglobin) and survival analysis was performed to estimate the risk of malignancy.
Results: A total of 4991 cases and 419992 controls were identified. The prevalence of Gout was 4991 (1.17%, male 4093 (82.01%); female 898 (17.99%)). During a mean follow-up of 12 years, malignancy was newly diagnosed in 30262 patients (7.12% of the total cohort). Gout was associated with increased risk of malignancy in the multivariable Cox proportional hazard regression analysis before propensity score matching (hazard ratio (HR) 1.248, 95% confidence interval (CI) 1.130-1.379, p<0.001), as well as after matching (HR 1.369, 95% CI 1.209-1.549, p<0.001).
Conclusion: A total of 4991 cases and 419992 controls were identified. The prevalence of Gout was 4991 (1.17%, male 4093 (82.01%); female 898 (17.99%)). During a mean follow-up of 12 years, malignancy was newly diagnosed in 30262 patients (7.12% of the total cohort). Gout was associated with increased risk of malignancy in the multivariable Cox proportional hazard regression analysis before propensity score matching (hazard ratio (HR) 1.248, 95% confidence interval (CI) 1.130-1.379, p<0.001), as well as after matching (HR 1.369, 95% CI 1.209-1.549, p<0.001).

REFERENCES

Not applicable

Table. Estimation of risk of malignancy using Cox proportional hazard regression analysis

	Before propensity score matching Cox			After propensity score matching Cox		
	HR	95% CI	P	HR	95% CI	P
Gout	1.248	1.130-1.379	<0.001	1.369	1.209-1.549	<0.001

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SAT0428 ANALYSIS OF THE PREVALENCE AND TIMING OF GOUT CO-MORBIDITY IN PATIENTS UNDERGOING KIDNEY TRANSPLANT

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Background: Patients receiving kidney transplants are at increased risk for the development of hyperuricemia and gout compared to the general population, which is generally attributed to the frequent use of calcineurin inhibitors (cyclosporine and tacrolimus). However, the precise proportion of renal transplant patients that develop gout and the time period post-transplant in which this occurs is less established.
Objectives: To analyze a large, mixed-insurance, US population database to determine gout prevalence in the renal transplant population.
Methods: A retrospective review of Humana Healthcare claims data (private and Medicare) from 2007 to 2017 was undertaken to identify kidney transplant patients with at least 6 months in plan prior to transplant and at least 6 months in plan post-transplant. Diagnosis of gout ($\geq$1 gout ICD 10/ICD 9 code) was evaluated in relationship to the time of kidney transplant.
Results: The database contained 6,082 patients with a kidney transplant and at least 6 months in plan both pre and post-transplant. Of the 6,082 kidney transplant patients, 1,505 (25%) had a gout diagnosis: 908 (15% of transplant patients) with gout before and after transplant and 597 (10% of transplant patients) with a gout code only after transplant. In patients developing gout post-transplant, the mean time between transplant and gout diagnosis was 1.79 ± 1.85 years.
Conclusion: As expected, gout was a common comorbidity in renal transplant patients. 15% of the patients receiving renal transplants had gout prior to the transplant, and another 10% developed new-onset gout a mean of 1.79 years after receiving a renal transplant. This retrospective analysis demonstrates that kidney transplant patients commonly suffer from gout both before and after their transplant. In addition to more research on this topic, an increased focus on screening and treatment of gout in the renal transplant population may be warranted.

REFERENCES

[1] Abbott K.C., Kimmel P.L., Dharnidharka V., et al. Transplantation. 2005; 80:1383-1391
[2] Zhu Y., Pandya B.J., Choi H.K. Arthritis & Rheumatism. 2011; 63 (10):3136-3141

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SAT0429 COMORBIDITIES IN AN EARLY DIAGNOSED COHORT OF UNCONTROLLED VERSUS CONTROLLED GOUT: ANALYSIS OF A LARGE US PAYER DATABASE

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Background: Gout is a widely prevalent progressive systemic inflammatory arthritis. The pathogenic cause of gout is elevated serum uric acid or hyperuricemia, and appropriate treatment of gout involves reduction of uric acid levels to a minimum goal of less than 6 mg/dL. Patients who do not achieve uric acid goals are generally described as uncontrolled gout patients and tend to do worse in terms of clinical outcomes such as occurrence of flares and persistence/worsening of tophi. Gout patients often suffer from specific comorbidities, though whether uncontrolled gout patients have a different comorbidity profile is unclear.
Objectives: The objectives of this evaluation were to compare the comorbidities and hospitalizations in uncontrolled versus controlled gout patients from a large de-identified US payer database.
Methods: A retrospective review of Humana Healthcare data from 2007 to 2016 in private pay and Medicare patients was performed to identify

patients with at least 1 gout ICD 10/ICD 9 diagnosis code (N=539,802) and 90 days of continuous urate-lowering therapy within 1 year of diagnosis. Two cohorts of patients were categorized according to their sUA levels ($\geq$ 1 test) after at least 90 days of gout therapy: sUA<6.0 mg/dL (controlled) and sUA $\geq$8 mg/dL (uncontrolled).

Results: The controlled gout group (sUA<6 mg/dL) included 5,473 patients and the uncontrolled gout group (sUA$\geq$8 mg/dL) had 1,358 patients. The two groups were comparable in terms of demographic features. Chronic kidney disease (CKD) was a common comorbidity overall in this gout population with higher prevalence in the uncontrolled gout cohort (49.4% of uncontrolled vs. 32.4% of controlled population; OR 2.04; 95% CI of 1.808 to 2.301, p<0.001). The most frequent hospitalization codes were similar between the uncontrolled and controlled patients with the exception of congestive heart and acute kidney failure. 20% of uncontrolled patients were hospitalized for congestive heart failure vs. 7% in controlled (OR 3.16, 95% CI: 2.674 to 3.739, p<0.001), and 20% of uncontrolled patients were hospitalized for acute kidney failure vs. 8% in controlled (OR 2.95, 95% CI: 2.497 to 3.480, p<0.001).

Conclusion: Gout patients frequently suffer from cardiovascular and renal diseases. This large retrospective analysis suggests that when divided based on uric acid levels attained, uncontrolled gout patients are more likely to suffer from CKD and also more likely to be hospitalized for acute renal failure than controlled gout patients. Whether hyperuricemia in uncontrolled gout causes the development of specific cardiovascular and renal comorbidities, or if specific cardiovascular and renal diseases lead to hyperuricemia and uncontrolled gout is not fully established.

REFERENCES

[1] Neogi T. NEJM. 2011; 364:443-52
[2] Khanna D., FitzGerald J.D., et al. Arthritis Care Res. 2012; 64(10):1431-1446
[3] Fels E., Sundy J.S., et al. *Curr Opin Rheum*. 2008; 20:198-202
[4] 4. Kuo C.F., Grainge M.J., et al. *Clin and Epidem Res.* 2014; 0:1-8
[5] Khanna P., et al. Health and Quality of Life Outcomes. 2012; 10:117

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SAT0430 IMPACT OF GOUT ON ALL-CAUSE MORTALITY AMONG MEDICARE BENEFICIARIES WITH A HISTORY OF KIDNEY TRANSPLANTATION: A RETROSPECTIVE COHORT STUDY

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Background: Gout is a frequent comorbidity among kidney transplant recipients. A recent analysis estimated that 13% of kidney transplant receipients had an active diagnosis of gout. The clinical impact of comorbid gout in this population is not well understood, including if gout as a co-morbidity associates with higher mortality rates among kidney transplant recipients.

Objectives: This retrospective patient claims analysis was performed to determine whether an association between gout and mortality exists in the prevalent kidney transplant population.

Methods: A retrospective study using administrative claims from the Medicare fee-for-service (FFS) Limited Data Set (LDS) was conducted. Multivariable Cox proportional hazards regression assessed the relationship between gout and all-cause mortality. Given the ambiguity of the causal relationship between gout and comorbidities that make up the Charlson Comorbidity Index (CCI), three analyses were conducted assuming: 1) gout and certain comorbid conditions are associated by way of a common pathogenetic root, 2) gout is a precursor for developing these comorbid conditions, and 3) these conditions modify the effect of gout on mortality.

Results: Gout was associated with higher unadjusted risk of all-cause mortality (hazard ratio, HR: 1.44, 95% CI: 1.27-1.63). After adjusting for baseline demographics and time from transplantation, the HR risk with gout was attenuated but still statistically significant (HR: 1.16, 95% CI: 1.02-1.32). Further adjustment for baseline CCI found gout was not a significant risk factor (HR: 1.03, 95% CI: 0.90-1.17). Stratified models show gout among baseline CCI=0 score was associated with a 3.5-fold increased risk of all-cause mortality (HR: 3.48, 95% CI: 1.27-9.57).

Conclusion: The presence of gout was not an independent predictor of all-cause mortality among Medicare beneficiaries with a history of kidney transplantation. That gout in a subset of beneficiaries without baseline comorbidities was a predictor may suggest that gout serves as an early indicator of declining health in the larger prevalent kidney transplant population. Further research is needed to understand the relationship of gout and mortality in the kidney transplant population.

REFERENCES

[1] Abbott KC, et al. Transplantation. 2005; 80(10):1383-1391.
[2] Hernández-Molina G, et al. Transplantation. 2008; 86(11):1543-1547.
[3] Brigham MD, et al. *Arthritis Rheumatol*. 2018; 70 (suppl 10).

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SAT0431 RED GINSENG EXTRACTS SUPPRESS MONOSODIUM URATE CRYSTAL INDUCED NLRP3 ACTIVATION

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Background: It is well known that red ginseng extracts (RGE) has anti-inflammatory properties.

Objectives: We aimed to investigate if RGE could suppress monosodium urate crystal (MSU) - induced NLRP3 activation and thus could be a potential therapeutic for gout.

Methods: Acute air-pouch model was used to investigate *in vivo* effect on acute gouty inflammation of RGE in mice. Human monocyte cell line –THP-1- was stimulated with MSU in the presence of RGE and expression of NLRP3, ASC, caspase-1, IL-1β was measured by PCR, immunoblotting and ELISA. Twenty four gout patients in intercritical period were randomized either to red ginseng tablet or placebo receiving group in a double-blind manner. After 3months of taking red ginseng tablets (RGT)/placebo, expression of NLRP3 and inflammatory cytokines of peripheral blood mononuclear cell was addressed by PCR.

Results: RGE sufficiently inhibited acute gouty inflammation in air-pouch mouse model, represented by reduced number of white blood cells in air pouch lavage fluid. *In vitro*, RGE dose-dependently suppressed MSU-induced IL-1 β production of THP-1 cells. RGE did not affect NLRP3 or pro IL-1 β expression. However, ASC oligomerization was inhibited and suppreseed NLRP3 inflammasome assembly. Patients taking RGT for 3 months showed significantly reduced NLRP3 expression compared to baseline, which was not observed in the control group.

Conclusion: RGE successfully suppressed MSU-induced acute inflammation in mouse model. Also, RGT reduced NLRP3 expression in intercritical gout patients. These results suggest that red ginseng can be implicated as a therapeutic agent for gout.

REFERENCES

[1] Martinon F, Petrilli V, Mayor A, Tardivel A, Tschopp J. Gout-associated uric acid crystals activate the NALP3 inflammasome. Nature. 2006;440 (7081):237-41.

[2] 2 Kingsbury SR, Conaghan PG, McDermott MF. The role of the NLRP3 inflammasome in gout. Journal of inflammation research. 2011;4:39-49.

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SAT0432 GOUTY ARTHRITIS AND DRUG-INDUCED LIVER INJURY AFTER THE TREATMENT WITH NSAIDS

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Background: In order to relieve the pain during acute gout attacks, most patients take high doses of nonsteroidal anti-inflammatory drugs (NSAIDs), which can provoke the hepatotoxicity, or DILI (drug-induced liver injury).
Objectives: To define the timing of DILI formation after the treatment with NSAIDs and its severity in patients with gouty arthritis (GA).
Methods: 738 patients with GA from our database who meet the criteria of the ACR (1977) were included into the study. NSAIDs-induced liver damage is known to be mainly hepatocellular. The dynamic ALT concentration in blood before the start of NSAIDs and during the treatment has been assessed. Hepatocellular toxicity was determined according to the DILI classification criteria based on the blood ALT level increased > 2 times to the upper limit of norm (42 U/l for men and 35 U/l for women). Inclusion criteria for the study group (n = 88) were: normal ALT before the treatment with NSAIDs, its increase during the treatment and return to the norm after the treatment.
Exclusion criterion was chronic hepatitis of any etiology. The comparison group (n = 650) consisted of patients with normal blood ALT level throughout the treatment.
Results: Among 738 patients with GA, 11.9% (n = 88) developed the hepatotoxicity following the NSAIDs therapy. No significant differences in age (54 (44-59.5) and 57 (52-63) years; p> 0.05) and gender (men 93.3% and 87.6%; p > 0.5) between the study and comparison groups were found. In the study group, the duration of NSAIDs administration was 10 (6–14) days, which did not differ from that in the comparison group — 9.5 (7–12) days (p> 0.05).
In patients with DILI, the elevated ALT was observed as follows: 2-3 times in 74 patients (84.1%); 3 to 5 times in 10 (11.4%); more than 5 times in 4 patients (4.5%). So, minimal cytolysis was presented more frequently than more severe forms (p < 0.05).
In the subgroup with the ALT concentration 3-5 times (n = 10), 6 patients received Diclofenac in high doses, 2 patients were treated with Nimesulide, 1 patient with Etodolac and 1 with Dexalgin during the observation period.
The elevation of ALT concentration 5 times was observed in 3 patients taking Diclofenac i/m and Nimesulide per os, simultaneously, and in 1 patient taking Diclofenac in high doses.
Patients with DILI were taking the following medications: Diclofenac 48.9% (n = 43); Nimesulide 18.2% (n = 16); Meloxicam 5.7% (n = 5), the combination of NSAIDs 20.5% (n = 18) without statistical differences (p > 0.05).
The number of patients who abused alcohol in DILI and control groups did not differ significantly — 53.4% and 48.2%, respectively (p>0.05).
Conclusion: In patients with GA, the hepatocellular DILI was observed in 11.9% cases after the treatment with NSAIDs during 10 days (from 6 to 14 days). Among patients with DILI, 84.1% (n = 74) had NSAIDs-induced hepatitis with minimal cytolysis. Mild cytolysis was seen in 10 (11.4%), moderate in 4 patients (4.5%). In our study, no severe or fatal DILI has been noted. No significant differences for particular drugs in the hepatotoxicity incidence have been found (p > 0.05).
Disclosure of Interests: None declared
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SAT0433 AN ANALYSIS OF PRESCRIPTION RECORDS OF GOUT PATIENTS IN EUROPE: EVIDENCE OF SUBOPTIMAL MANAGEMENT AND CLINICAL INERTIA

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Background: Urate-lowering therapy (ULT) should be prescribed to people with recurrent gout flares and tophi, and offered to people with first-onset gout. Despite effective drugs, gout flares are common. Reasons for this include lack of prescription of ULT, under-dosing of ULT by physicians (clinical inertia), and poor adherence to ULT.
Objectives: To ascertain the quality of gout care delivered by general practitioners (GPs), prescribing patterns for ULT were analysed in 4 western European countries.
Methods: Data for this retrospective study were obtained from IQVIA's Real-World Data Longitudinal Prescription databases of GPs from France, Italy, Spain and United Kingdom (UK). The databases contain anonymised patient prescription records, including demographics, dispensing details (pharmacy, prescription date), and medication (name, dose, therapy duration). Data for patients with gout with or w/o ULT were analysed from July 2015 to June 2016.
Results: Crude prevalence of gout was 0.7% (UK) to 1.1% (France, Italy, and Spain) [Table 1]. Only about half (France, Italy, UK) to 2/3 (Spain) of diagnosed patients were on ULT. Between 19.9% (France) and 56.4% (Spain) of people on ULT had serum urate (sUA) measurements recorded within the year. Only 26.6% (Italy) to 45.6% (France) of patients with a recorded sUA level were at target (<6.0 mg/dL). The most common 1st-line treatment was allopurinol (ALLO), almost always at a dose ≤300 mg/d. Febuxostat (FBX) was prescribed as a 1st-line alternative in France and Italy. Switch to 2nd-line ULT, such as FBX, was uncommon, especially in Spain and UK. Uricosurics in monotherapy were not used. Average time on ULT ranged from 57.3% (Italy) to 72.6% (France) of the assessment year. At least one comorbidity (CM) was present in >78% of patients, the most common being hypertension, dyslipidemia, diabetes, chronic kidney disease, and obesity.
Conclusion: In the study period, management of patients with gout in 4 EU countries was suboptimal. Nearly half of diagnosed patients were not prescribed ULT. sUA levels were not being monitored regularly and mean sUA levels were above target. ALLO as the most common 1st-line ULT was generally prescribed at sub-therapeutic doses. Initiation of 2nd-line therapy was infrequent indicating a status quo and/or other reasons and medication adherence was poor indicating low patient self-management

and/or low monitoring by GPs. Early treatment was not being initiated despite a high prevalence of CMs. Efforts must be undertaken to improve gout management, avoid clinical inertia, and reduce the individual and societal burden of gout.

Table 1. Prescribing information for patients with a diagnosis of gout who were receiving anti-gout treatment
(M04A chronic therapy; *based upon 2016 statistics).

	France	Italy	Spain	UK
Total diagnosed patients, n	736,352	642,063	523,592	441,505
Crude prevalence* (%)	1.1	1.1	1.1	0.7
Treated patients, n (%)	397,689 (54.0)	311,688 (48.5)	365,030 (69.7)	244,899 (55.5)
sUA measurement recorded in the year (%)	19.9	56.4	39.5	40.3
Mean sUA, mg/dL	6.5	8.1	6.7	6.5
Achieved sUA goal (among patients with sUA measurement recorded in the year) (%)				
<6.0 mg/dL	45.6	26.6	37.9	41.9
≥6.0 – <9.0 mg/dL	44.4	47.8	47.2	50.3
≥9.0 mg/dL	9.9	25.6	14.8	7.7
Treatment (%)				
Allopurinol	57.4	6.5	23.4	23.0
<300mg	15.7	43.9	15.3	13.2
300mg	0.5	0.1	0.1	2.8
>300mg				
Febuxostat	28.2	14.2	1.0	2.0
Second-line treatment (%)	15.9	13.4	1.9	4.3
Average days on treatment, n	265	209	218	247
Comorbidities present (%)	86.1	93.6	96.8	78.8

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SAT0434 A TRANSIENT DECREASE IN SERUM URATE CHANGES THE CLINICAL TRAJECTORY OF SUBJECTS WITH ADVANCED GOUT

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Background: The standard approach to monitor subjects with gout is to measure serum urate. The assumption is that the signs and symptoms of disease will improve if serum urate is maintained below the target level of 6 mg/dL. However, there has been little emphasis on whether lowering urate transiently would have a prolonged impact on the clinical manifestations of advanced gout.
Objectives: Assess the clinical benefit in patients with advanced gout who had transient lowering of serum urate resulting from treatment with pegloticase, a pegylated recombinant uricase.
Methods: A post hoc analysis was carried out using the results from two randomized controlled trials (RCTs) of 6 months duration to assess the efficacy of treatment with 8 mg of pegloticase every 2 weeks (q2w)[1]. Serum urate was measured before each infusion and the serum urate area under the curve (AUC) was calculated as described[2] for the first and second three-month periods of time in the RCTs. The following clinical outcomes were assessed: gout flares, tophus reduction, patient global assessment (PtGA), tender and swollen joints (TJC and SJC), pain measured with a 100-mm visual analog scale (VAS) and a variety of patient reported outcomes (36-Item Short Form Health Survey [SF-36] Physical Component Score [PCS] and Arthritis-Specific Health Index Score [ASHIS]).
Results: The analysis included 85 subjects treated with q2w pegloticase and 43 patients who received placebo. Of the 85 pegloticase-treated subjects, 49 had only a transient decrease in serum urate owing to the development of anti-pegloticase antibodies. The mean length of time these subjects experienced a serum urate <6 mg/dL was approximately 6 weeks[3]. Despite the transient reduction in serum urate, the serum urate AUC for the first and second 3 months of the RCTs was significantly (p=0.008) decreased compared to placebo-treated subjects. However, it was significantly (p<0.0001) less reduced compared with those with persistent urate lowering throughout the 6 month RCTs (Table 1). Results for both the subjects with persistent and transient lowering of serum urate to <6 mg/dL indicated significant reduction in tophi and improvements from baseline in PtGA, TJC, SJC, pain, and ASHIS after 6 months of the RCT. No significant improvements were observed in the patients who received placebo.

Table 1 Serum Urate Area Under the Curve in Subjects Treated with Pegloticase or Placebo

	Mean (± SD) Serum Urate Area Under the Curve (mg/dL·hr)	
Treatment	**Month 0-3**	**Month 3-6**
Placebo	21,093.0±3,990.1	16,665.8±3,462.0
Transient Responders	14,361.2±8,517.3	14,373.1±9,218.2
Persistent Responders	2,540.1±2,132.8	338.9±1,137.9

Transient responders versus placebo, first 3 months, p<0.0001, second 3 months, p=0.008
Persistent responders versus placebo for months 0-3 and months 3-6, p<0.0001
Persistent responders versus transient responders for months 0-3 and months 3-6, p<0.0001

Conclusion: A transient reduction in serum urate resulting from pegloticase therapy can result in significant clinical benefit lasting through the 6 months of the RCTs. These results suggest that transient lowering of urate can alter the trajectory of the clinical manifestations of advanced gout. Moreover, estimates of serum urate AUC may be more helpful in assessing the impact of urate lowering therapy than individual measurements of serum urate.

REFERENCES

[1] Sundy, JS, et al. JAMA. 2011; 306:711
[2] Mandell, BF, et al. *Arthritis Research Ther.* 2018; 20:286
[3] Lipsky, PE, et al. Arthritis Res Ther. 2014; 16:R60

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SAT0435 MANAGEMENT OF ADVANCED GOUT: A CLAIMS-BASED ANALYSIS FROM THE UNITED STATES

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Background: Gout is one of the most common inflammatory arthropathies. Despite available urate lowering therapies (ULT), many patients progress to chronic or advanced gout, characterized by the development of tophi, chronic inflammatory arthritis, and other manifestations resulting from persistent urate deposition. While numerous guidelines exist for the management of gout, there is little information on the frequency of their implementation, especially in patients with advanced gout.
Objectives: To evaluate the real-world practice patterns in patients diagnosed with advanced gout using a large administrative claims database from the United States.

Methods: We carried out a retrospective analysis of the Symphony Integrated Dataverse to identify patients with advanced gout over an approximately 6-year period from October 2012 to August 2018. Patients were identified as having advanced gout if they were >18 years of age and had at least two medical claims for the diagnosis of gout on different days, separated by at least 3 months. Patients with advanced gout were identified and stratified based on their diagnosis as either chronic gout (ICD-9 274.02, 274.03, ICD-10 M1A.x) or tophaceous gout (ICD-9 274.03, 274.81, 274.82, ICD-10 M1A.xxx1). A third category designated "uncontrolled gout" was clinically defined as any patient with at least three primary diagnoses of idiopathic gout (ICD-10 M10.0x, M1A.0x) along with at least three urate tests (CPT 84550, 84560). Percent and frequency of urate testing, rheumatology specialist visits, and administration of ULT (allopurinol, febuxostat, probenecid, and lesinurad) were evaluated for each diagnostic group.

Results: We identified 191,097 advanced gout patients, including 177,610 (93%) with chronic gout, 31,475 (16.5%) with tophaceous gout, and 20,943 (11%) with uncontrolled gout. 35,992(18.8%) were coded in more than 1 diagnostic category. The median age was 67 (range: 19-80), 24.7% were female and 75.3% male, with an average of 5.4 years of claims history in the database. As shown in Tables 1 and 2, despite the diagnosis of advanced gout, urate testing, rheumatology consults, and ULT were inconsistent. Urate testing was definitional for uncontrolled gout patients, but was done in less than 65% of patients with the diagnosis of chronic or tophaceous gout and then less than once per year. Similarly, less than 60% of subjects with advanced gout received care by a rheumatologist and less than 80% received ULT and for less than 50% of the year.

Table 1. Percentage of patients with urate testing, rheumatologist visits, and urate lowering therapy

Population	N	Urate testing (% of patients)	Rheumatologist visit (% of patients)	ULT+ (% of patients)
Chronic Gout	177,610	61.72%	34.32%	76.54%
Tophaceous Gout	31,475	63.74%	57.86%	76.98%
Uncontrolled Gout	20,943	100.00%*	59.57%	81.32%

+Urate lowering therapies
*Definitional

Table 2. Frequency of urate testing, rheumatologist visits, and urate lowering therapy in advanced gout

Population	N	Mean urate tests/ year	Mean rheumatologist visits/year	Mean ULT+ prescriptions per patient	Mean days with active ULT+ prescriptions/year
Chronic Gout	177,610	0.73	2.00	7.5	160.27
Tophaceous Gout	31,475	0.98	3.72	9	160.14
Uncontrolled Gout	20,943	2.25*	4.18	7.1	169.36

+Urate lowering therapies
*Definitional

Conclusion: The subset of patients with advanced gout, identified either as chronic, tophaceous or uncontrolled, received suboptimal care compared to current guidelines. As this group of advanced gout patients is the most affected by urate deposition, added attention should be paid to optimizing their care.

Disclosure of Interests: N. Lawrence Edwards Consultant for: Horizon Pharma, Astra Zeneca, Selecta Biosciences, Naomi Schlesinger Consultant for: Astra Zeneca, Novartis, Horizon Pharma, Sanders Clark : None declared, Theresa Arndt: None declared, Peter Lipsky Consultant for: Consulting fees from Horizon Pharma

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SAT0436 CROWNED-DENS SYNDROME: A RECENT CASE SERIES IN A SINGLE CENTRE IN THE UNITED KINGDOM

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Background: The crowned dens syndrome is a rare presentation of Calcium pyrophosphate deposition disease. It is characterised by severe acute or recurrent neck pain associated with headache, fever and elevated inflammatory markers. CT usually demonstrates calcium pyrophosphate crystal deposition in the suspensory ligaments adjacent to the atlanto-axial joint. We are reporting a series of four patients presenting with sudden onset of neck pain and raised inflammatory makers over a 9 month period.

Objectives: To raise awareness of crowned-dens syndrome, its clinical presentation, radiographic findings and management.

Methods: Four patients' electronic patient records including history, clinical findings and treatment were reviewed. Imaging was discussed at a rheumatology/radiology multi-disciplinary meeting.

Results: Four patients (2 female, 2 male) aged between 64 and 86 years presented with severe neck pain and stiffness. In all cases the onset of symptoms was less than a week prior to presentation and was associated with greatly restricted mobility. 2 patients had associated headache, arthralgia and myalgia. All patients had normal tone, power, reflexes and sensation on neurological examination. There was no pyrexia. Inflammatory markers were markedly raised with CRP ranging from 90-343 mg/L at presentation (Table 1). One patient had a neutrophilia. CT scan of the head was performed in each case and showed no evidence of subarachnoid haemorrhage, space occupying lesion or meningeal enhancement. PET-CT scan in all patients showed intense uptake around the atlanto-axial joint as well as calcification of the ligaments. All patients were commenced on a reducing regime of prednisolone starting at 40mg daily, tapering to 0mg over 6 weeks. Symptoms and inflammatory markers reduced on induction of steroids. Two patients suffered a relapse on reducing steroids and required further higher doses of steroid.

Table 1. Patient demographics

Patient	Age (Years)	Gender	CRP on presentation (mg/ L)	ESR on presentation (mm/ Hr)
1	64	Male	90	77
2	74	Male	247	-
3	81	Female	133	120
4	86	Female	343	112

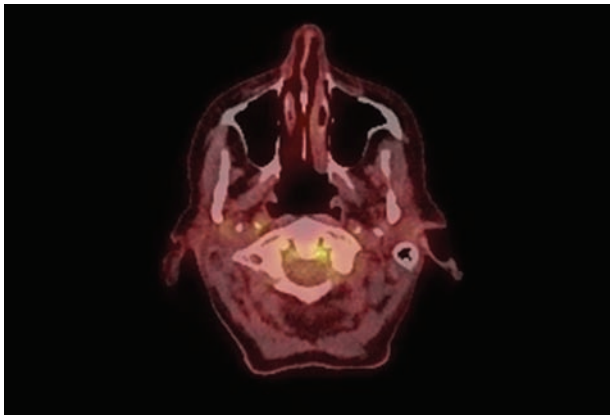


Figure 1. Image from PET-CT scan of Patient 4 showing increased tracer uptake around the odontoid peg (arrow)

Conclusion: Patients presenting with acute neck pain, headache and raised inflammatory markers require evaluation for an infective aetiology. Pyrophosphate disease of the atlanto-axial joint however, appears to be an increasingly recognised cause of this presentation. Awareness by acute physicians, rheumatologists and radiology colleagues is important, as the condition can be misdiagnosed as Giant Cell Arteritis, Polymyalgia Rheumatica or meningitis; in order to avoid unnecessary investigations and delay in initiating the appropriate treatment. The condition is steroid responsive.

REFERENCES

[1] Heck A, Nolan N, Rojas-Moreno C, **Crowned Dens Syndrome: Calcium Pyrophosphate Deposition Disease Masquerading as Osteomyelitis**. J Rheumatol. 2018 Oct;45(10):1422-1423

[2] Ledingham D, Cappelen-Smith C, Cordato D, Crowned dens syndrome. Pract Neurol. 2018 Feb;18(1):57-59
[3] Tagami S, Inokuchi R, Awaji K, Maehara H, Yamaguchi Y, Nakajima S, **Crowned dens syndrome and interspinous ligament inflammation due to calcium pyrophosphate deposition in an elderly man**. Spine J. 2016 Jul;16(7):e453-4

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SAT0437 **ABSTRACT WITHDRAWN**

SAT0438 **TO SCREEN OR "WAIT AND SEE" – CAN HLA GENE TESTING PREVENT ALLOPURINOL RELATED SEVERE CUTANEOUS ADVERSE REACTION? AND WHO ARE AT RISK?**

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Background: Allopurinol is one of the most common causes of drug-induced severe cutaneous adverse reaction (SCAR). HLA-B*58:01 gene positivity is shown to be the strongest risk factor. However, local data on HLA-B*58:01 test and allopurinol-related SCAR is scanty. Moreover, there is no consensus on routine checking of HLA-B*58:01 before starting allopurinol in Hong Kong and this test is performed according to physicians' clinical judgement.
Objectives: This study review the use of HLA-B*58:01 in daily practice, included the clinical characteristics and its implications in patients who developed allopurinol allergy in a tertiary internal medicine and rheumatology referral center.
Methods: This is a retrospective study of patients who had HLA-B*58:01 checked in Queen Elizabeth Hospital from January 2008 to December 2017. Patients' demographic data, clinical characteristics, laboratory findings, gene profile, drug allergy records were retrieved from Clinical Data Analysis and Reporting System and outcomes were reviewed.
Results: Within 10 years, 432 patients had HLA-B*58:01 checked - 23% (N=99) were positive (Figure 1). Among patients who were HLA-B*58:01 positive, 86% had clinical and/or crystal proven gout and 68% were male (M:F=67:32). Gene testing was performed as screening in 58% (57/99) and after skin reaction in 42% (42/99). Alternative urate lowering therapy was considered for patients who screened positive for HLA-B*58:01 and none developed SCAR (Febuxostat 16 patients, probenecid 3 patients). For those who reported skin reaction after allopurinol, 50% had minor rash while 50% (each 21 patients) developed SCAR. In SCAR-group, 52% was male, 76% were chronic kidney disease (CKD) ≥stage 3 and/or age ≥60years, with mean age 71.2+/-14.2 and mean estimated glomerular filtration rate 57.1+/-30.7 mL/min/1.73m² (Figure 2 and table 1). The mean time interval to SCAR was 44.8+/-52.1 days and the mean starting dose of allopurinol was 154.6+/-90.7 mg/day. SCAR was associated with substantial morbidity and mortality: 71% (15/21) required steroid and/or intravenous gammaglobulin in addition to supportive care and 17% (4/21) died in the same admission due to sepsis including pneumonia. For patients who were tested negative for HLA-B*58:01, although 12% reported skin reaction, these were self-limiting and all recovered after allopurinol was stopped. Renal impairment was less pronounced in this group, yet 38% were CKD ≥stage 3.
Conclusion: In our cohort, HLA-B*58:01 can identify most of the high risk patients who prompt to develop SCAR. Thus in routine practice, clinicians should consider screening HLA-B*58:01, especially in patients with CKD ≥stage 3 or age ≥60year, before starting allopurinol, and consider alternatives if positive, to prevent allopurinol-related SCAR.

REFERENCES

[1] Richette P, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2017;76(1):29-42.
[2] Wang YH, et al. The Medication Risk of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Asians: The Major Drug Causality and Comparison With the US FDA Label. Clin Pharmacol Ther. 2018.
[3] Khanna D, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. Arthritis Care Res (Hoboken). 2012;64(10):1431-46.
[4] 4. Stamp LK, Barclay ML. How to prevent allopurinol hypersensitivity reactions? Rheumatology (Oxford). 2018;57(suppl_1):i35-i41.

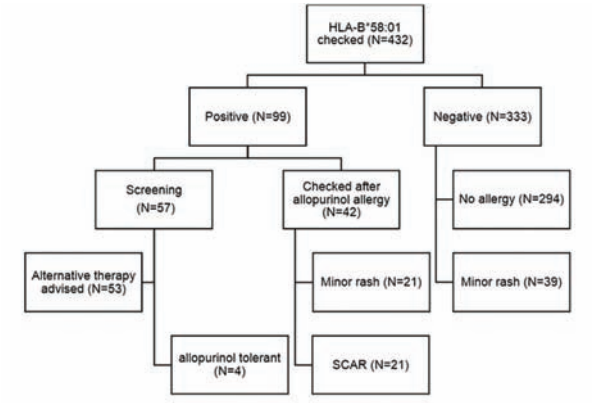


Figure 1. Total 432 patients had HLA-B*58:01 checked in 10 years period (January 2008 – December 2017). 99 patients were tested positive. Forty-two of these patients had the gene checked after development of allopurinol allergy. 21 of them had minor rash while 21 of them presented as SCAR. In HLA-B*58:01 negative patients, only 12% produced self-limiting rash and all recovered after allopurinol stopped.

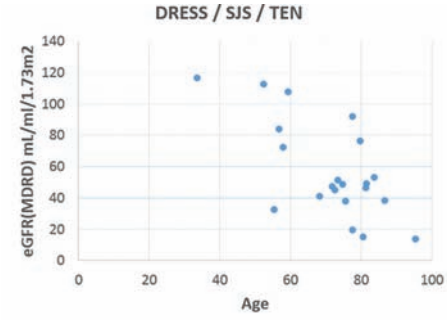


Figure 2: Relationship between eGFR and age in patients who developed allopurinol-induced SJS / TEN / DRESS (N=21).

Table 1. Summary of patients with allopurinol-induced SCAR (N=21), 76% (16 patients) were CKD ≥stage 3 and/or age≥60 years.

Sex	Age	Indication of ULT	eGFR	Days to allergy	Allopurinol starting dose	Outcome	Treatment
F	79.6	gout	76.4	5	200mg/day	Died	IVIg, steroid
F	86.6	gout	38.5	3	*unknown*	recovered	Steroid
M	56.7	hyperuricemia	84.1	22	*unknown*	recovered	Steroid
M	55.3	gout	32.3	50	100mg/day	recovered	Steroid
M	83.6	gout	52.9	52	*unknown*	Died	Supportive
M	95.3	gout	13.7	237	50mg/day	Died	IVIg, steroid
F	77.4	gout	19.6	119	100mg/day	recovered	Supportive
M	72.6	gout	45.1	7	*unknown*	recovered	Steroid
M	73.3	gout	51.4	30	*unknown*	recovered	IVIg, steroid
F	74.9	gout	48.6	39	*unknown*	recovered	Supportive
M	75.5	gout	38.2	38	200mg/day	Died	IVIg
M	77.4	chemotherapy	91.9	18	300mg/day	recovered	Supportive
M	33.5	gout	116.6	22	*unknown*	recovered	Steroid
F	52.2	chemotherapy	112.5	35	*unknown*	recovered	Steroid
F	71.7	gout	47.3	12	*unknown*	recovered	IVIg, steroid
F	80.6	hyperuricemia	15.1	37	*unknown*	recovered	Steroid
F	68.2	gout	40.8	28	100mg/day	recovered	Steroid
M	59.3	gout	107.6	*unknown*	*unknown*	recovered	Supportive
M	81.2	gout	46	67	200mg/day	recovered	IVIg
F	81.4	gout	49	50	50mg/day	recovered	Supportive
F	57.9	gout	72.9	20	300mg/day	recovered	Steroid

Abbreviation: *eGFR = estimated glomerular filtration rate (mL/min/1.73m²). ULT = urate lowering therapy. IVIg = intravenous immunoglobulin*

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SAT0439 RENOPROTECTIVE EFFECT OF URATE LOWERING THERAPY IN GOUTY PATIENTS WITH MODERATE CHRONIC KIDNEY DISEASE

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Background: Approximately 25% of gouty patients suffer from chronic kidney disease (CKD). High serum uric acid (sUA) levels have been related to estimated glomerular filtration-rate (eGFR) imbalance. Beneficial effect of treatment with xanthine oxidase inhibitors (XOI), mostly allopurinol, has already been proved in patients with CKD and asymptomatic hyperuricemia. Although several studies have described the efficacy and renal safety of treatment with XOI in gout, few authors have analyzed its effect on GFR in gouty patients with moderate CKD.
Objectives: To assess the effect of XOI therapy in gouty patients with moderate CKD, in terms of eGFR changes.
Methods: In this multicenter, retrospective study, we included patients from 4 centers diagnosed with gout (EULAR/ACR criteria) and stage-3 CKD according to Cockroft-Gault formula (eGFR 30-59 ml/min/m^2) who received XOI (febuxostat and allopurinol) with a follow-up for 6 and 12 months. We used clinical records to collect patient features (age, sex, body mass index, sUA, hypertension (HTA), diabetes mellitus (DM), dyslipidemia (DL), cardiovascular events), treatments (lipid-lowering drugs, antihypertensives, antidiabetics, antiplatelet therapy, NSAIDs, urate lowering treatments and colchicine) and gout history (duration of disease, tophi presence, clinical and ultrasonographic (US) pattern (monoarticular, oligoarticular, polyarticular).
Statistical analysis: descriptive analysis of variables. Mixed effects model lineal regression Differences were considered significant $p<0.05$.
Results: 52 patients with gout and stage-3 CKD were identified. We obtained complete 6 and 12-months follow-up from 37 patients (33 males and 4 females). Mean age was 74.11±6.96 years, 32.4% DM, 83.78% HTA, 56% DL, 40% tophaceous gout, Clinical and US pattern (37.8% polyarticular, 37.8 oligoarticular and 24.3% monoarticular). Febuxostat 19 patients, Allopurinol 18. Mean baseline sUA was 8.63±1.33 mg/dl, and baseline eGFR was 47.77±8.45 ml/min/m^2. To assess the effects of considered variables over eGFR a linear mixed model was adjusted using *nlme R-package*. Within the adjusted model we obtained significant differences in eGFR between baseline and 6 months (p=0.0081), and between baseline and 12-months (p=0.0028). sUA decreased significantly between baseline and 6 (p=0.0181) and 12 months (p=0.0188).
Conclusion: Reduction of sUA levels in gouty patients with XOI entitles an improvement of eGFR in stage-3 CKD. These findings suggest that the response to urate lowering therapy take place in the first 6 months, leading to an improvement in eGFR in this period. From 6 months to 1 year, sUA levels are stabilized and so is eGFR.

REFERENCES

[1] Tanaka K, Nakayama M, Kanno M, et al. Renoprotective effects of febuxostat in hyperuricemic patientswith chronic kidney disease: a parallel-group, randomized, controlled trial. Clin Exp Neprhol 2015
[2] Juge PA, Truchetet ME, Pillebout E, et al. Efficacy and safety of febuxostat in 73 gouty patients with stage 4/5 chronic kidney disease. A retrospective study of 10 centers. Joint Bone Spine (2016)

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SAT0440 DOES MONOSODIUM URATE DEPOSITION IN GOUT PATIENTS ALTER THE BIOCHEMICAL PROPERTIES OF MENISCAL FIBROCARTILAGE AND HYALINE CARTILAGE? A DUAL-ENERGY COMPUTED TOMOGRAPHY STUDY

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Background: Dual-energy computed tomography (DECT) is increasingly used in gout to assess monosodium urate (MSU) crystal deposition in soft tissues. In contrast to ultrasound (US) with its typical double-contour (DC) sign, DECT seems unable to identify MSU deposition deep within joints, where flares occur. DECT has recently shown its potential for discriminating between the various crystal types owing to their biochemical signature.
Objectives: We aimed to assess whether DECT attenuation properties differed between knees of gout patients with and without deep articular MSU deposition characterized by the DC sign on US; more specifically if MSU deposition altered the electron density (ρe) of various knee structures.
Methods: Consecutive patients with gout were included in this cross-sectional study and their knee MSU burden was assessed using combined DECT and US. Knees were assigned to either DC+ or DC- groups depending on the presence/absence of the DC sign on US. Regions of interest (ROI) were drawn in the following knee zones on a specific coronal DECT image: hyaline cartilage of the patellofemoral and medial and lateral tibiofemoral joint spaces, as well as medial and lateral menisci. Regions of interest that exhibited chondrocalcinosis were excluded. Five DECT parameters were obtained: CT numbers (HU) at 80 and 140 kV, dual-energy index (DEI), electron density (ρe), and effective atomic number (Zeff). Knee zones were compared between groups using mixed linear models.
Results: A total of 115 patients were included. Gout duration was 9.8 ±9.0 years, mean serum urate was 7.3±2.3 mg/dL and 48 (41.7%) patients were under urate lowering therapy. Out of a total 230 knees, 46 (20%) were assigned to the DC+ group. Menisci from DC+ and DC- patients had a mean (± standard deviation) Zeff of 7.5±0.2 and 7.6±0.2 (p=0.49), mean ρe of 77±14 and 73±13 (p=0.15) and mean DEI of -0.0003±0.0036 and 0.0001±0.0042 (p=1), respectively. Hyaline cartilage from DC+ and DC- patients had a mean Zeff of 7.6±0.2 and 7.7±0.2 (p=0.49), mean ρe of 65±21 and 60±18 (p=0.17) and mean DEI of 0.0020±0.0049 and 0.0025±0.0043 (p=1), respectively. No differences were noted between groups in the patellofemoral joint space.
Conclusion: There is an expected increased electron density (ρe) in meniscal fibrocartilage and hyaline cartilage of gout patients with MSU deposition, even though DECT measures do not reach statistical significance. Particular attention will be given to patients with high MSU burden (large DC signs on US).
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SAT0441 SKIN ADVERSE EVENTS WITH FEBUXOSTAT IN GOUT PATIENTSWITH PREVIOUS SKIN REACTIONS TO ALLOPURINOL. A MULTICENTRE DESCRIPTIVE STUDY

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Background: Allopurinol is first-line urate-lowering drug (ULD) for patients with gout. However, around 10% of them refer adverse events, often at skin, which can be severe. Febuxostat is a non-purine selective xanthine oxidase inhibitor, often a therapeutic alternative in this setting, though data regarding safety in those patients with previous cutaneous adverse reactions (CAR) to allopurinol is still limited. Some cases and small

retrospective series have reported skin adverse events under both allopurinol and febuxostat.
Objectives: To assess the cutaneous safety of febuxostat when used in patients with previous skin reactions to allopurinol.
Methods: A multicentre retrospective, descriptive study performed in seven Rheumatology units around Spain. Crystal-proven gout patients with previous CAR to allopurinol and treatment with febuxostat were selected. Demographic (age, gender), clinical (skin events, liver disease, concomitant thiazides) and laboratory variables (serum urate (SU), glomerular filtration rate) were collected. The primary study variable was the rate of patients developing CAR also with febuxostat. A descriptive analysis with estimation of 95% confidence interval (95%CI) is presented.
Results: Sixty-seven gout patients with prior allopurinol-related CAR treated with febuxostat were enrolled. Their average age was 68.1 years (SD±14.8), being 49 males (73.1%). Thirteen of them were under thiazide treatment (19.4%) and average glomerular filtration rate was 66.1 ml/min (±24.3) when allopurinol was started, at a median dose of allopurinol of 100 mg/day (IQR 50-300) and mean SU of 8.9 mg/dl (±1.7). The reported CAR under allopurinol were nonspecific in 55 (82.1%), maculopapular rash in 9 (13.4%), and Stevens-Johnson's syndrome in 3 (4.5%).. Out of 67 patients, 10 developed CAR with febuxostat (14.9%; 95%CI 8.3-25.3%): nonspecific in 8 cases, one case of maculopapular rash and other of Stevens-Johnson's syndrome. Median (IQR) glomerular filtration rate, starting dose of febuxostat and SU level were 69.5 (42-87.8), 80 mg/day (40-80) and 8.2 mg/dl (7.15-9.14), respectively.
Benzbromarone was initiated in all 10 patients with CAR to both allopurinol and febuxostat, and only one developed a nonspecific rash.
Conclusion: In this multicentre study, around 15% of patients with prior allopurinol-related CARs also developed them with febuxostat. Further prospective and intervention studies are needed to confirm these results, though caution is recommended when using febuxostat in this subgroup of patients.
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SAT0442 CALCIUM PYROPHOSPHATE CRYSTAL ARTHRITIS DURING HOSPITALIZATIONS: A PROSPECTIVE, CRYSTAL-PROVEN CASE SERIES

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Background: Despite having passed more than fifty years after its initial description, essential questions for calcium pyrophosphate (CPP) crystal disease, such as clinical spectrum, diagnosis or management schemes, remain unsolved. Acute flares often occurred during hospitalizations. Scant reports have addressed this common setting for CPP crystal disease, and whether these patients behave similarly to ambulatory cases is unknown.
Objectives: The aim of this work was to describe in a prospective way a crystal-proven case series of patients developing acute CPP crystal arthritis during hospitalizations for another conditions.
Methods: An observational, cross sectional descriptive study was conducted in two Spanish centers from November 2013 to December 2018. A prospective convenience sampling was employed to select patients with crystal-proven CPP acute arthritis seen during hospital admissions. Demographic, clinical and CPP-related variables were collected, and X-rays (pelvis, knees, hands, affected joint when different) and laboratory tests (to rule out associated metabolic conditions) were systematically requested. A descriptive analysis is presented.
Results: 90 episodes of acute CPP arthritis in 87 patients were seen in the study period, with an average age of 81.8 years (SD 7.7), 50.6% of them men. Approximately 26% of patients reported prior episodes of arthritis, most of them (68.4%) as outpatients. Only three patients were on preventive treatment for CPP arthritis (two on colchicine and one on low dose glucocorticoids). Regarding the acute CPP arthritis during admissions, they were predominantly monoarticular (81.0%) and the main involved joints were knee (46.0%), wrist (13.8%) and ankles (6.9%). The reasons for admission were diverse, with a mean of 7.7 days (SD 9.1) from admission to flare. About X-rays, 23.8% showed no chondrocalcinosis (CC) in the evaluated joints [61/80]. In 57.1% of patients there was chondrocalcinosis in the affected joint [44/77] and regarding usual joints: 74.3% in knees [55/74], 51.5% in triangular carpal ligament [34/66], 25.4% in metacarpo-phalangeal joints [17/67], 20% in pubic symphysis [14/70] and 17.6% in coxofemoral joints [12/68]. A secondary form of osteoarthritis was only seen in 10 patients (12.5%). About associated metabolic diseases, one case of primary hyperparathyroidism-related hypercalcemia and five cases of hypomagnesemia at the time of the flare were detected. In all six patients with a polyarticular presentation, laboratory tests for rheumatoid factor and ACPA were negative.
Conclusion: From the findings of this prospective, crystal-proven series of CPP crystal arthritis in an intrahospital setting, we can remark:

- 1. The low numbers of previous ambulatory flares may suggest a different clinical entity of CPP disease.
- 2. Radiological CC was absent in around a quarter of patients despite a extensive assessment, so synovial fluid analysis remains essential for diagnosis.
- 3. The rarity of associated metabolic diseases seen runs against ruling out secondary causes of CPP disease in this setting.

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SAT0443 RECONCILIATION OF URATE LOWERING THERAPIES DURING HOSPITALIZATION AND THE IMPACT OF RHEUMATOLOGIC CONSULTATION ON MANAGEMENT OF INPATIENT GOUT FLARES

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Background: Hospitalizations complicated by gout flares have an impact on patient care. Delayed diagnosis and suboptimal management can lead to prolonged discomfort, impair chronic outcomes of the disease and lengthen the hospitalization [(1)]. Patients on urate lowering therapy (ULT) are frequently admitted to the hospital for unrelated causes but there is variability in inpatient medication management of the urate lowering agent and acute management of the flare.
Objectives: In this descriptive study, we analyse the variability of reconciliation of ULT on admission and discharge and the impact of rheumatology consultation on acute and chronic management of gout.
Methods: Patients- above the age of 18- admitted to our tertiary care hospital from 01/01/2010 to 01/01/2016 with an ICD-9 or an ICD-10 diagnosis of gout were reviewed. The first 200 patients underwent a retrospective chart review as a pilot study for an ongoing project. We reviewed patient demographics, laboratory testing, and co-morbid conditions; medications on admission and discharge, incidence of gout flare-diagnosis and management during hospitalization, rheumatology consultation and discharge plan for these patients.
Results: Of the 200 patients reviewed, 2.69 admissions per person. We further described the patients who had a gout flare during hospitalization (n =54, 27%). 66% of these patients were males, mean age 69.8 years and BMI 31.78kg/m^2. A majority of patients had hypertension, renal disease, and dyslipidemia (Table 1).
70% of the patients were on chronic medications for gout (Table 2). 29.6% of these patients were continued on these agents upon admission and only 64.8% of these patient was eventually discharged on these drugs.
Rheumatology consulted for 68.5% of the patients. Arthrocentesis was more frequently performed when rheumatology was consulted (70% vs.17.6%; p<0.001). Rheumatology consultation did not decrease length of stay in the hospital. 78.5% of the patients managed by primary team were discharged on a ULT or colchicine compared to 100% in the group managed by rheumatology consult team (100% vs 78.5%; p<0.0431). Outpatient rheumatology follow up was documented in discharge papers for 62% of the patients managed with rheumatology consult compared to 11.7% in the comparison group. (62% vs 11.7%; p<0.002).
Conclusion: Rheumatology consultation improved adherence to guidelines in diagnosis and management of gout flare and improved the discharge planning and follow up.

REFERENCES

[1] Robinson PC, Kempe S, et al. Epidemiology of inpatient gout in Australia and New Zealand: temporal trends, comorbidities and gout flare site. Int J Rheum Dis. 2016 Jul 26. doi: 10.1111/1756-185X.12941.

TABLE 1

BASELINE DEMOGRAPHICS	TOTAL PATIENTS (n=200)	PATIENTS WITH A GOUT FLARE (n=54)	RHEUMATOLOGY CONSULT (n=37)	PRIMARY TEAM (n=17)
Age (years)	70.99 ± 12.33	69.89 ± 11.28	70.62 ± 11.94	68.29 ± 9.82
RACE N(%) African-American/ Caucasian/Others	164(82)/30 (15)/6(3)	49(90.8)/3(5.5)/2 (3.7)	32(86.4)/3(8)/2(5.4)	17(100)/0/0
BMI (kg/m^2)	31.39 ± 9.21	31.79 ± 8.83	31.71 ± 7.75	31.94 ± 10.88
Hypertension	177(88.5)	48 (88.9)	32 (84)	16 (94)
Diabetes mellitus	84 (42)	25 (46)	18 (48.6)	7 (41)
Renal dysfunction	139 (69.5)	43 (79.6)	29 (78)	14 (41)
Cardiovascular disease	119 (59.5)	25 (46.3)	17 (46)	8 (47)

TABLE 2

	TOTAL PATIENTS (n=200)	PATIENTS WITH A GOUT FLARE (n=54)	RHEUMATOLOGY CONSULT (n=37)	PRIMARY TEAM (n=17)
No of patient on chronic Gout medications N (%)	169 (84.5)	38 (70)	24 (64.8)	14 (82)
Allopurinol/Febuxostat	139 (69.5)/2 (1)	23 (42.6)/2 (3.7)	15 (40.5) 2 (5.4)	7 (41.2)/0
Colchicine	50 (25)	25 (46.3)	15 (40.5)	9 (52.9)
Combination of drugs	22 (11)	12 (22.2)	8 (18.9)	2 (11.7)
Inpatient Continuation of medication	117 (58.5)	16 (29.6)	10 (27)	6 (82)
Medications on discharge	153 (76.5)	35 (64.8)	24(64.8)	11 (78.5)
Length of Hospitalization (days)	5.00 ± 4.83	5.06 ± 2.56	4.73 ± 2.34	5.81 ± 2.99
Rheumatology follow up: N (%)	35 (17.5)	25 (46.3)	23 (62)	2 (11.7)

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SAT0444 DETECTION OF CLINICAL FORMS AND RISK FACTORS OF CPPD DEPENDING ON AGE

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Background: CPPD is more often diagnosed in elderly and old age. The age peculiarities of the disease are not studied well.

Objectives: to assess clinical forms of CPPD, impact of risk factors and concomitant diseases depending on age.

Methods: the study included 113 patients (59 women and 54 men) with verified diagnosis of CPPD (according to McCarty criteria); all had calcium pyrophosphate dehydrate depositions in synovial fluid. The mean age was 60.2±11.8 years. Roentgenography of knee joints was conducted in anteroposterior and lateral views, of hands – in frontal view. The patients were divided into two groups: <55 years – 38 patients, with the mean age of 46.7±7.1 years; and >55 years – 75 patients, with the mean age of 65.5±7.8 years.

The study compared clinical characteristics according to the classification (presence of acute or chronic arthritis, osteoarthritis (OA) with CPP crystals, VAS pain assessment, presence of chondrocalcinosis of hands and knees according to roentgenography images, presence in past history of injuries and familial chondrocalcinosis, and presence of hypomagnesemia, hyperparathyroidism); presence of concomitant diseases (rheumatoid arthritis (RA), gout, chronic kidney disease (CKD) (over stage 3 GFR <60 mL/min/1.73m^2 using the MDRD formula), reception of diuretics.

Results: chronic arthritis was detected more often in the patients >55 years (63 pts (84%) as against the patients <55 years (13 pts (34%)) (p=0.001). On the contrary, acute arthritis was registered more often in the patients <55 years (in 10 pts (26%) than in the patients >55 years (in 4 pts (5%) (p=0.014), as well as OA with CPP crystals – in 15 pts (40%) <55 years and in 8 pts (11%) >55 years (p=0.003). The mean VAS in the group >55 years was 51±20 mm and in the group <55 years - 40±20 mm. During the past year, reception of NSAIDs or colchicine due to painful joints was significantly more often needed by the patients >55 years - 68 pts (91%) than the patients <55 years – 29 pts (76%) (p=0.005). Familial chondrocalcinosis was registered equally often in the patients <55 years - 6 pts (16%) and in the patients >55 years – 2 (3%) (p=0.46).

According to the roentgenography images, knee chondrocalcinosis was significantly more often registered in the patients >55 years – 49 pts (65%) than in the patients <55 years – 14 pts (37%) (p=0.001). According to the hands roentgenography, chondrocalcinosis was detected equally often in the patients <55 years – 21 pts (55%) and in the patients >55 years – 36 pts (48%).

Hyperparathyroidism was almost equally often detected in the patients >55 years – in 8 pts (11%) and in the patients <55 years – 6 pts (16%) (p=0.48), as well as its combination with gout in 20 pts (27%) and 8 pts (21%) respectively (p=0.44); hypomagnesemia was registered in 1 patient (3%) <55 years, and its combination with rheumatoid arthritis was not registered in the patients <55 years, whilst in the patients >55 years it was detected in 5 pts (7%) (p=0.09). Presence of CKD was detected in 2 pts (6%) <55 years and in 10 pts (13%) >55 years (p=0.2). Its combination with OA was registered significantly more often in the patients >55 – in 59 pts (79%) than in the patients <55 years - 9 pts (24%) (p=0.005).

Diuretics were more often received by the patients >55 years – 27 pts (36%) than by the patients <55 years - 5 pts (13%) (p=0.006).

There were no significant differences detected in the presence of joint injuries in past history – in 22 pts (58%) <55 years and in 35 pts (47%) >55 years.

Conclusion: Prevalence of CPPD in young people may be underestimated; the frequency of detection of factors associated with CPPD in different age groups is identical, excluding OA, which is more often diagnosed in patients >55 years. The patients with CPPD >55 years are more often diagnosed with chronic form of arthritis, they more often need to receive NSAIDs and colchicine and more often are diagnosed with chondrocalcinosis of the knee.

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SAT0445 ADEQUATE URATE LOWERING THERAPY FOR GOUT IS RARE IN CLINICAL PRACTICE BUT PRESERVES RENAL FUNCTION WHEN EFFECTED

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Background: Optimal urate lowering therapy (ULT) as defined by most guidelines requires monitoring of serum urate (SU) and titration of the medication dose to achieve a target level of SU. In Sweden, allopurinol is the most widely used ULT and most patients with gout are managed in primary care. As a first step towards implementation of gout treatment guidelines in the Swedish region of Dalarna, we undertook a register study to assess how allopurinol is prescribed and to what extent monitoring of SU takes place.

Objectives: To determine the proportion of patients with gout that receive a) ULT and b) adequate ULT and to determine to what extent SU is monitored. A secondary aim was to explore the effects of adequate ULT on SU and estimated glomerular filtration rate (eGFR) over time.

Methods: Data was retrieved from the electronic healthcare record database of the region. The database holds records of all diagnoses at visits to physicians, prescriptions made in primary care as well as results of laboratory tests. We searched the database from 1997-2012 for individuals with a first diagnosis of gout during 2000-2012 and retrieved data for all prescriptions of allopurinol for the identified patients. Results and dates of SU and creatinine measurements after gout diagnosis were retrieved. MDRD eGFR was calculated from s-creatinine, sex and the age of the patient at the time of measurement. The value nearest in time before initiation of ULT was defined as the baseline measurement for both urate and creatinine. Duration of therapy was defined as number of days from first to last prescription adding 365 days (the usual period for which chronic medication is prescribed in Sweden). The mean daily dose of allopurinol was estimated from prescription data.

Adequate ULT was defined as a mean daily dose of at least 300 mg of allopurinol and a duration of therapy of at least 2 years. Patients that had received adequate ULT were matched using propensity score on the basis of baseline eGFR and length of follow-up time to patients that received non-adequate ULT. Change from baseline in SU and eGFR was calculated and compared between groups.

Results: We identified 5433 patients with an incident gout diagnosis during 2000-2012 (and no gout diagnosis or prescription for ULT during 1997-1999).

Of these, 2393 (44%) received at least one prescription for allopurinol. SU was measured at some time point after initiation of ULT in 58% of patients. Adequate ULT as defined above was prescribed for 154 patients (3%), of these, 112 (73%) had a SU measurement at some time point after initiation of therapy and 35 (23%) had such a measurement done within 6 weeks of starting treatment.

Matched controls could be identified for 109 of the patients with adequate ULT. Mean urate and eGFR at the start of therapy and end of follow up for the group with adequate ULT treatment and the controls are shown in table 1.

Table 1. Values are mean (SD) or n (%)

	Adequate ULT, n=109	Matched controls, n=109	p-value
Age	66 (14)	68 (13)	0.19
Female, n (%)	25 (23)	38 (35)	0.05
Allopurinol daily dose in mg	359 (61)	119 (63)	<0.0001
Baseline s-urate, µmol/L	511 (111)	509 (100)	0.91
Baseline eGFR, ml/min	66 (21)	66 (21)	0.84
Length of follow-up, years	4.2 (3.5)	5.2 (3.9)	0.05
Δ s-urate, (baseline compared to last available value)	-168 (153)	-78 (125)	<0.0001
Δ e-GFR (baseline compared to last available value)	-1 (15)	-5 (16)	0.039
Last eGFR worse than baseline measurement, n (%)	50 (46)	67 (61)	0.021

Conclusion: ULT was prescribed to less than half of the patients identified. Adequate ULT was rare in clinical practice during the time period studied. Urate monitoring occurred in less than half of ULT-treated patients. The patients with adequate ULT achieved greater lowering of serum urate than matched controls and were more likely to maintain unchanged renal function over time.

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SAT0446 GOUT IN THE US: SIGNIFICANT ASSOCIATIONS WITH CARDIOVASCULAR AND RENAL DISEASE HOSPITALIZATIONS

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Background: Gout is a disorder of uric acid metabolism and often presents as acute severe joint pain. Previous work from our group suggests that all-cause hospitalizations in patients with gout in the United States (US) have significantly increased by 410% in the last 22 years, almost hundred-fold of the 4.8% increase in US population all-cause hospitalization rate in the same time-period. The current study focused on identifying potential reasons for the excess hospitalizations.

Objectives: To compare the primary reasons for hospitalizations in patients with gout to those in age-matched patients without gout in the US in 2016.

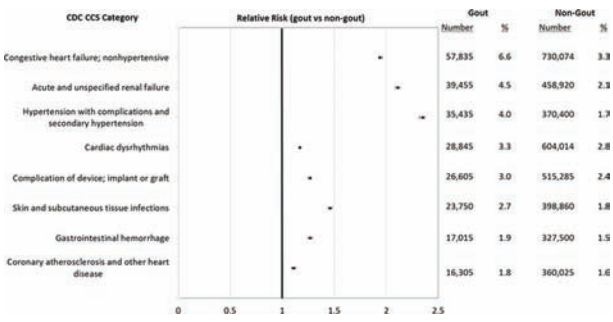
Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in the NIS in 2016 among patients 40 years or older with a primary or secondary diagnosis of gout and compared them to total all-cause hospitalizations in patients without a gout diagnosis in the same age group during the same period. Over 69,800 ICD 10 diagnoses codes were collapsed into a smaller number of clinically meaningful categories, consistent with the Centers for Disease Control (CDC) Clinical Classification Software. The top 15 primary causes for hospitalization were evaluated and compared between the two cohorts.

Results: In 2016, there were 892,379 all-cause hospitalizations in the US in patients with gout with 14,135 (1.6%) of these for a primary diagnosis of gout. The primary diagnoses for 878,244 hospitalizations in patients with gout were compared with those in 21.9 million hospitalizations in the general US population without gout. The most common primary cause of hospitalizations in both cohorts was septicemia (7.8% in gout vs. 7.4% in general population). Significant differences were seen in several other categories. For example, acute renal failure was twice as frequent among gout patients (39,455 hospitalizations, 4.5%) compared to the general population (458,920 hospitalizations, 2.1%) (Relative Risk (RR) 2.11, 95% CI 2.08 – 2.13, p<0.0001). Hospitalizations for "hypertensive complications and secondary hypertension" were also higher (35,435, 4.0% in gout vs 370,400, 1.7% in general population, RR 2.35, 95% CI 2.32 – 2.37, p<0.0001). Hospitalizations from gastrointestinal bleeding were 30% more common in gout patients, perhaps associated with concomitant NSAID treatments (Figure).

Conclusion: Among patients with gout, a far greater proportion of serious hospitalizations are related to renal and cardiovascular complications as compared to age-matched general population. This calls for an increased awareness and management of serious co-morbid conditions in patients with gout.

REFERENCES

[1] Singh G, Mithal A, Mithal A. NOT JUST A SWOLLEN BIG TOE: INCREASING ALL-CAUSE HOSPITALIZATIONS IN PATIENTS WITH GOUT IN THE UNITED STATES: 1993–2014: Presented at EULAR Congress 2017



Figure

Primary reasons for comorbid hospitalizations more common in patients with gout compared with age-matched patients without gout, classified by Centers for Disease Control Clinical Classification Software (CDC CCS).

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SAT0447 MANAGEMENT OF GOUT: AN AUDIT IN PRIMARY CARE GENERAL PRACTICE IN LEICESTERSHIRE, UNITED KINGDOM

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Background: Both acute and long-term management of gout in primary care in UK is reportedly suboptimal[1], with patients rarely being offered lifestyle advice or urate Lowering Therapy (ULT). Further, ULT is often not titrated according to the patient's serum uric acid (sUA) levels, so that they fail to achieve target sUA levels.

Objectives: To audit and evaluate the management of gout in patients in a primary care setting against the current guidelines treat to target guidelines set by the British Society of Rheumatology (BSR)[2].

Methods: Audit criteria were derived from the latest BSR gout guideline (Hui et al; 2017). A randomised sample of adult patients with a read code for the diagnosis of gout from Jan 2006-Jan 2018 was chosen from six large general practices in Leicestershire County of the United Kingdom. The data collected included demographics, provision of patient information, management of acute attacks and prophylactic treatment, screening of appropriate co-morbidities, dosing of urate-lowering therapy (ULT) and titration of doses against measurement of uric acid levels.
Results: Data was obtained for 861 patients The mean age was 60 years and 91% were male, 21.5% were recorded as being provided with written information about gout and 60.5% of patients were treated with NSAIDs and COXIBs for acute attacks of gout. When colchicine was prescribed to patients, 71% had no dose recorded in their clinical records. 323 (37.5%) of patients were prescribed a ULT and the recorded starting dose of allopurinol was 100mg daily for 73.8%. Titration of subsequent allopurinol doses was recorded in only 21% of patients. 539 patients (62.6%) had no record of a serum urate level check after starting ULT.
Conclusion: Clinical records indicate that the management of gout by UK General Practitioners in Primary Care is suboptimal in concordance with the BSR guidelines. It was clear that general practices did not employ the treat to target strategy. There is a clear need for increased GP awareness and adherence to the BSR guidelines in order to optimise deficient areas of care, particularly in patient education, initiation and titration of ULT and monitoring of serum urate levels in gout patients. Appropriate patient recording templates are needed so that key information is captured during a patient consultation in order to enable medicines optimisation for those with gout. Most aspects of gout management in primary care did not concord well with published BSR guidelines.

REFERENCES

[1] Kuo, C., Grainge, M.J., Mallen, C., Zhang, W. and Doherty, M. (2014) Rising burden of gout in the UK but continuing suboptimal management: a nationwide population study. Annals of the Rheumatic Diseases, [online] 74(4) pp.661-667.
[2] Hui, M., Carr, A., Cameron, S., Davenport, G., Doherty, M., Forrester, H., Jenkins, W., Jordan, K., Mallen, C., Mcdonald, T., Nuki, G., Pywell, A., Zhang, W. and Roddy, E. (2017) The British Society for Rheumatology Guideline for the Management of Gout. Rheumatology, [online] 56 (7) pp. e1-e20.

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SAT0448 ATP IS THE SECOND KEY SIGNAL OF GOUT FLARE BESIDES MSU

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Background: Gout is an inflammatory disease associated with hyperuricemia and characterized by recurrent arthritis. In previous study, MSU which generated by hyperuricemia was recognized by the toll-like receptor and NOD receptor of the intrinsic immune system, then activated the NALP3 **inflammasome to induce the secretion of IL-1**beta, **causing gout**. However, this mechanism cannot explain why most patients with hyperuricemia do not have gout attacks in clinical practice, suggesting that there may be other pathogenic signals in the flare of gout. Our team previously found that P2X7R might play a key regulatory role in the pathogenesis of gout [1].What's more, single nucleotide polymorphisms associated with P2X7R function regulate the onset of gouty arthritis[2], suggesting that ATP, as the ligand of P2X7R, may be a second key signal in addition to MSU to stimulate gout attack.
Objectives: To understand whether ATP act as a key factor in gout development besides MSU.
Methods: The rat hyperuricemia model was prepared by intraperitoneal injection of the uratase inhibitor oxazinic acid. Followed by ATP injection into the tail vein to observe the incidence of arthritis and compared with the Coderre's method-established gouty arthritis [3].
Results: Forty hyperuricemia rats were prepared and 0.5ml ATP (10mM) solution was injected into the tail vein of the rat respectively, about 95% (38 rats) developed spontaneous arthritis. This type of spontaneous arthritis is very different from the Coderre's method in the following aspects: (1) The onset time of spontaneous arthritis is faster. The time of joint swelling in spontaneous arthritis peaked at 6**.0**±2**.0** hours after ATP injection, while it took 2 to 3 days for arthritis caused by local injection of MSU to reach its peak. (2) The affected joints were different: The Coderre's method joints swelling only at the MSU injection site. Spontaneous arthritis can involve multiple joints, in which 71% have one joint affected, 21% have two joints affected and 8% with three or more than three joints affected by redness and swelling. (3) Distinct histopathologic characteristic: In Coderre's method, lymphocytes caused by local injection account for about 60%, with fewer neutrophils; In spontaneous arthritis, neutrophils account for more than 90% and lymphocytes are less. (4) Different sources of MSU: there is local MSU in spontaneous arthritis, which is associated with hyperuricemia; the local presence of MSU in Coderre's arthritis was artificially injected.
Conclusion: The spontaneous arthritis due to the synergistic effect of ATP and MSU is consistent with the characteristics of human gout arthritis, suggesting that ATP is the key second signal besides MSU to stimulate gout attack.

REFERENCES

[1] Tao JH, Zhang Y, Li XP. P2X7R: A potential key regulator of acute gouty arthritis. Semin Arthritis Rheum. 2013; 43(3): 376-380.
[2] Tao JH, Cheng M, Tang JP, et al. Single nucleotide polymorphisms associated with P2X7R function regulate the onset of gouty arthritis. PLoS One. 2017 Aug 10;12(8):e0181685.
[3] CoderreTJ, Wall PD.Ankle joint urate arthritis (AJUA) in rats: An alternative animal model of arthritis to that produced by Freund's adjuvant. Pain. 1987; 28(3):379-93.

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SAT0449 EFFECT OF CHOLESTEROL AND TRIGLYCERIDE ON THE FREQUENCY OF GOUT ATTACKS

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Background: Gout is an autoinflammatory disease characterized by hyperuricemia and recurrent arthritis. ATP and MSU synergistically activate NALP3 inflammasome to induce the secretion of IL-1β, leading to the onset of gouty arthritis, and P2X7R plays a key role in gout[1,2]. This mechanism above can explain the clinical phenomenon that some patients with hyperuricemia never suffer gouty arthritis, however, it cannot explain why the frequency of gout attacks increases as the course prolongs. Cholesterol or triglyceride can activate the innate immune and induce inflammatory response. It is speculated that Cholesterol and triglyceride levels can increase with the duration of gout, and they may reduce the threshold of gout attacks.
Objectives: To demonstrate the effect of elevated cholesterol and triglyceride on the onset of gout.
Methods: A cohort study was performed to observe the difference of arthritis episodes between the high cholesterol group and the normal, the high triglyceride group and the normal in gout patients. The frequency of gout attacks was compared using statistical methods of independent sample test and paired sample test between the two groups.
Results: A cohort study was performed to observe the difference of arthritis episodes between the high cholesterol group and the normal, the high triglyceride group and the normal in gout patients. The frequency of gout attacks was compared using statistical methods of independent sample test and paired sample test between the two groups.
RESULTS: A total of 68 patients with gout were observed. Among them, 21 were in normal cholesterol group, 13 in elevated group, 21 in normal triglyceride group and 13 in elevated group. The results of the independent sample test between the two groups are as follows: (1) The frequency of gout attacks between the normal cholesterol group and the elevated group is statistically significant within three months, six months and one year (0.81±0.60 vs 1.77±0.83, Z=-3.200, *P*=0.001; 1.14±0.73 vs 3.15±2.15, Z=-3.430, *P*=0.001; 1.43±0.81 vs 4.77±3.44, Z=-3.199, *P*=0.001). (2) The frequency of gout attacks between the normal triglyceride group and the elevated group is statistically significant within three months, six months and one year (0.81±0.60 vs 1.54±0.97, Z=-2.359, *P*=0.018; 1.14±0.73 vs 2.38±1.66, Z=-2.417, *P*=0.016; 1.43±0.81 vs 3.54 ±2.50, Z=-3.005, *P*=0.003). The results of the paired sample test between

the two groups are as follows: (1) 6 pairs of normal cholesterol group and elevated group were screened according to age, course and uric acid level. There is significant difference in the frequency of gout attacks between the two groups within six months and one year (1.17±0.75 vs 2.83±2.23, Z=-2.060, *P*=0.039; 1.33±0.82 vs 4.17±3.43, Z=-2.032, *P*=0.042). (2) 11 pairs of normal triglyceride group and elevated group were screened as above. There is significant difference in the frequency of gout attacks between the two groups within one year (1.45±0.82 vs 3.45±2.58; Z=-2.328, *P*=0.020).

Conclusion: Cholesterol and triglyceride levels can affect the frequency of gout attacks. The phenomenon mentioned in background can be explained by the increase of cholesterol and triglyceride levels as the course prolongs.

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REFERENCES

[1] Tao JH, et al. P2X7R: A potential key regulator of acute gouty arthritis. Semin Arthritis Rheum. 2013; 43(3): 376-380.
[2] Tao JH, et al. Single nucleotide polymorphisms associated with P2X7R function regulate the onset of gouty arthritis. PLoS One. 2017 Aug 10;12 (8):e0181685.

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SAT0450 SENSITIVITY OF DUAL-ENERGY CT SCANNING, ULTRASOUND, AND X-RAY FOR CRYSTAL-PROVEN PSEUDOGOUT

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Background: Advanced imaging modalities such as ultrasound (US) and dual-energy CT (DECT) can help diagnose crystalline arthritis. DECT is highly sensitive and specific in gout and has not been well studied in pseudogout.

Objectives: To compare the sensitivity of DECT, US, and x-ray (XR) in pseudogout.

Methods: We prospectively enrolled patients with crystal-proven pseudogout at a tertiary care center, 3/2018-11/2018. We searched the electronic medical record for synovial fluid crystal lab orders and reviewed the record to identify candidates. Eligible patients were 18 years old with acute monoarthritis, joint aspiration, and synovial fluid calcium pyrophosphate (CPP) crystals on polarized microscopy. Patients with both monosodium urate and CPP crystals were excluded. Subjects provided informed consent and underwent DECT, US, and XR of the aspirated joint and standardized joint (right wrist). All images were interpreted by a musculoskeletal radiologist and a rheumatologist trained in US; consensus was reached on each image. DECT images were post-processed using Siemens Syngo.via software, applying color-coded overlay indicating volume and location of CPP deposits. We considered two volume thresholds (cm^3) for a positive DECT scan. Imaging abnormalities defining a positive scan were: color-coded changes consistent with CPP (DECT); hyperechoic deposits in hyaline-, fibro-cartilage, or tendon (US); and chondrocalcinosis in hyaline- or fibro-cartilage (XR). We calculated sensitivity and 95% confidence interval (CI) of positive scans in the aspirated joint and prevalence (95% CI) in the standardized joint.

Results: Ten of 27 eligible patients enrolled. Mean (SD) age was 73 (9.7) years; 40% were female. Eight knees and two wrists were aspirated a mean (SD) of 17 (9) days before enrollment. Six subjects received intra-articular steroids before enrollment. Imaging results are shown in Table 1. In the aspirated joint, sensitivity (95% CI) was 90% (71-100%) for DECT volume >0.40 cm^3, and 100% (100-100%) for DECT volume >0.01 cm^3; 100% (100-100%) for US; and 70% (42-98%) for XR. In the standardized joint, DECT was positive in 20% (0-45%) for volume >0.40 cm^3, and 90% (71-100%) for volume >0.01 cm^3. XR chondrocalcinosis was present in 30% (2-58%) and US was positive in 80% (55-100%) of wrists.

Conclusion: DECT and US had high sensitivity for pseudogout using synovial fluid CPP crystals as the gold standard. Larger studies testing DECT sensitivity and specificity in pseudogout vs. other arthritis and establishing a volume threshold are needed.

REFERENCES

none

Table 1. Presence and location of imaging abnormalities in 10 pseudogout subjects

	Aspirated joint			Standardized joint (right wrist)		
Subject	DECT color–coded changes (cm^3)	US hyperechoic deposits	XR chondro–calcinosis	DECT color–coded changes (cm^3)	US hyperechoic deposits	XR chondro–calcinosis
1	PF, PSFC, M, TF, (0.48)	M	M	IC, IP1, MCP3, RC, TFCC (0.07)	TFCC	TFCC
2	ICN, M (0.73)	FC, M	M	CMC1 (0.08)	TFCC	none
3	ICN, M, PF, TF (2.85)	FC	ICN, M, PF	CMC1, CMC3, IC, IP1, MCP2, RC, TFCC (0.51)	TFCC	not done
4	ICN, M, PF, PSFC, Pop, Q (1.05)	FC	M	IC (0.10)	none	none
5	M, PSFC, Q (0.50)	FC	M, PF	IC, TFCC (0.04)	TFCC	none
6	M, PF (0.67)	FC	none	CMC1, IC (0.03)	TFCC	CMC1
7	M, PF, PSFC (1.33)	FC, M	M, PF	none (0.01)	TFCC	none
8*	IC (0.02)	IC, TFCC	none	IC (0.02)	IC, TFCC	none
9	M (0.45)	M	none	IC (0.05)	TFCC	none
10	CMC1, IC, MCP1–5, TFCC (0.82)	TFCC	IC, MCP1–2, RC, TFCC	CMC1, IC, MCP1–5, TFCC (0.84)	none	IC, MCP1–4, TFCC

*Right wrist was the aspirated and standardized joint. CMC: carpometacarpal. FC: femoral cartilage. ICN: intercondylar notch. IP: interphalangeal. M: meniscus. MCP: metacarpophalangeal. PF: patellofemoral. Pop: popliteus tendon insertion. PSFC: posterior superior femoral condyle. Q: quadriceps tendon. RC: radiocarpal. TF: tibiofibular. TFCC: triangular fibrocartilage complex.

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SAT0451 GOUT FLARES BECOME INFREQUENT DURING A TREAT-TO-TARGET STRATEGY OVER ONE YEAR: DATA FROM THE NOR-GOUT STUDY

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Background: Urate lowering therapy (ULT) is expected to prevent new gout flares. Treat-to-target ULT is however often not performed, and we need more evidence on how often patient become flare- free during ULT.

Objectives: Urate lowering therapy (ULT) is expected to prevent new gout flares. Treat-to-target ULT is however often not performed, and we need more evidence on how often patient become flare- free during ULT.

Methods: In a prospective observational study, patients with crystal-proven gout with a recent gout attack and insufficiently treated serum urate (sUA) level (>360 μmol/L/>6 mg/dl) were included. They received ULT with drug escalation during monthly follow-up until the target sUA level was met (sUA <360 μmol/L, or <300 μmol/L if clinical tophi). Assessment in this ongoing data collection included demographic and clinical variables, serum urate levels, previous medication with allopurinol, colchicine and NSAIDs, co-morbidities, and health related quality of life (SF-36). Flares during the last six months of one year with "treat-to-target" were recorded. Bivariate analyses and logistic regression analyses examined factors associated with and prediction (odds ratio with 95% confidence intervals) of a flare-free period during months 6-12.

Results: 202 patients were included, and 140 completed a 12-month-follow-up: 94.0% males, 90.3% Caucasian, mean (SD) age 56.7 (14.1) years, disease duration 8.0 (7.7) years), sUA level 494 (87) µmol/L, eGFR 78.0 (18.8) ml/min. 58.6% had college education, 76.9% were married/cohabiting, 18.3% had tophi.

Allopurinol had at baseline previously been used by 30.0% (54/180), colchicine by 51.8% (100/193) and NSAID by 78.6% (154/196).

70.0% (98/140) of the patients were flare-free between 6 and 12 months, and among patients with flares only 10.2% (4/39) were not at treatment target. 80.9% (106/131) were at treatment target at month 12 (sUA<360 or 300µmol/l).

A number of variables at baseline were bivariately ($p<0.05$) related to a flare-free outcome: male gender, low BMI, no previous use of colchicine or NSAIDs, better physical function summary score (SF-36), low level joint pain during strongest attack ever, and high number (>5) of previous gout attacks.

In multivariate logistic regression analyses, also adjusting for age, and gender in the final model, a lower BMI (OR 0.90 per unit, 95% CI 0.83-0.99), low baseline serum urate (OR 0.99 per unit, 95% CI 0.99-1.00) and no previous use of colchicine (OR 4.0, 95% CI 1.6-10.2) predicted a flare-free period between months 6 and 12. When substituted for colchicine, also lack of NSAID use (OR 6.9, 95%CI 1.8-26.1) was a predictor of a flare-free period during this period.

Conclusion: Most patients (70%) did not experience flares during the second half of the first treat-to-target year during ULT. High baseline level of sUA, and high BMI decreased the chance of a flare free period, as did experience with colchicine or NSAID.

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SAT0452

VITAMIN D INSUFFICIENCY AND DEFICIENCY ARE ASSOCIATED WITH A HIGHER LEVEL OF SERUM URIC ACID: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Several studies have revealed a relationship between vitamin D status and a number of non-skeletal health conditions such as insulin resistance, metabolic syndrome, cardiovascular diseases, inflammatory diseases, infection and malignancy. The interaction between serum uric acid and vitamin D has also been observed. A study found that uric acid can suppress 1-alpha-hydroxylase in vitro and in vivo, leading to the reduction in the conversion of the storage form of 25-hydroxyvitamin D into the active form of 1,25-dihydroxyvitamin D [1]. In fact, several epidemiological studies have suggested that patients with vitamin D insufficiency and deficiency tend to have a higher level of serum uric acid compared to those with adequate vitamin D level although the results were inconsistent across the studies.

Objectives: To compare serum uric level between individuals with normal vitamin D level versus patients with vitamin D deficiency and vitamin D insufficiency.

Methods: A systematic review was conducted using MEDLINE and EMBASE database from inception to October 2018 to identify all studies that compared the level of serum uric acid between individuals with normal vitamin D level and patients with vitamin D insufficiency/deficiency. Eligible studies must be cohort or cross-sectional studies that consisted of two groups of adult participants, one with normal level of vitamin D (vitamin D level >30 ng/ml) and one with vitamin D insufficiency (vitamin D level 20-30 ng/ml) or vitamin D deficiency (vitamin D level of <20 ng/ml). Mean serum uric acid level and standard deviation of participants in each group were extracted from each study to calculate mean difference (MD) between the groups. Pooled MD was then calculated by combining MDs of each study using random-effects model.

Results: A total of seven cross-sectional studies were eligible for the meta-analyses. Individuals with normal vitamin D level had a significantly lower serum uric acid level than patients with vitamin D insufficiency with the pooled MD of -0.33 mg/dL (95% CI, -0.61, -0.04) (figure 1) and also had a significantly lower serum uric acid level than patients with vitamin D deficiency with the pooled MD of -0.45 mg/dL (95% CI, -0.82, -0.08) (figure 2). The statistical heterogeneity was high with the I^2 of 78% and 89%, respectively. Funnel plots of both meta-analyses were fairly symmetric which did not suggest the presence of publication bias.

Conclusion: Both patients with vitamin D insufficiency and patients with vitamin D deficiency had a significantly higher level of serum uric acid compared to individuals with normal vitamin D level.

REFERENCES

[1] Chen W, et al. (2014) Uric acid suppresses 1 alpha hydroxylase in vitro and in vivo. Metabolism. 63, 150-60.

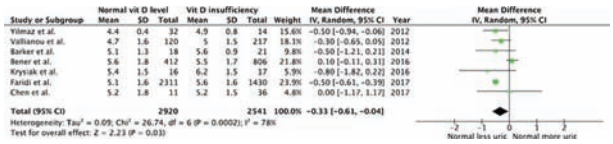
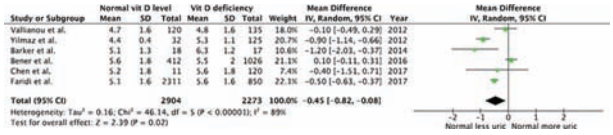


Figure 1. Forest plot of the meta-analysis of vitamin D insufficiency versus normal vitamin D level



. Forest plot of the meta-analysis of vitamin D deficiency versus normal vitamin D level

Disclosure of Interests: None declared

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Infection-related rheumatic diseases

SAT0453

JOINT MANIFESTATIONS OF WHIPPLE'S DISEASE: CLINICAL AND RADIOLOGICAL PRESENTATION OF 19 PATIENTS

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Background: Whipple's disease (WD) is a rare chronic systemic bacterial infection caused by *Tropheryma whipplei*. It affects middle-aged men with diarrhea, weight loss, fever and joint manifestations. It usually develops as oligoarthritis or polyarthritis of large joints. WD may mimic chronic inflammatory rheumatisms. Some studies and case reports show that immunosuppressive treatment can worsen WD[1].

Objectives: Clinical and radiological (radiograph, ultrasound (US), MRI) presentation of joint manifestations of WD.

Methods: This retrospective monocentric observational study was led in Strasbourg University Hospital, Reference Center for Rare Diseases and included patients with WD diagnosed between 2006 and 2017. Patients were included if they had joint manifestations, positive *T.whipplei* polymerase chain reaction in stools or/and saliva, positive *T.whipplei* polymerase chain reaction on duodenal biopsy and/or positive periodic acid-Schiff performed on duodenal biopsy and good evolution with antibiotics.

Results: Nineteen patients including fifteen men were included. The median age at diagnosis was 57. The median time from first symptoms to diagnosis was 60 months. Before the diagnosis of WD, 13 patients had immunosuppressive therapy.

Clinical presentation was: 11 polyarthritis, 3 oligoarthritis, 1 monoarthritis and 4 inflammatory polyarthralgia including 3 with axial pain. Wrists (15/19), ankles (11/19) and knees (10/19) were the most affected. The metacarpophalangeal joints were affected in 8 patients. Eight patients had diarrhoea and weight loss.

C-reactive protein median was 45 mg/l.
Feet and hands radiographies were performed for seventeen patients. Five patients had carpitis and two patients had tarsitis. Two patients had unilateral sacroiliitis.
Hand and wrist US were performed for twelve patients. Ten patients had joint damage. We found 7 radiocarpal and intercarpal synovitis, including 5 with a positive power Doppler (PD) signal, in 5 patients. US showed one distal radio-ulnar synovitis with no PD signal. Four patients had metacarpophalangeal synovitis including 3 with a positive PD signal. Proximal inter-phalangeal synovitis with no PD signal was found for one patient. There was no involvement of distal interphalangeal joint. Four patients had unilateral tenosynovitis including 2 with a positive PD signal.
Feet US were done for ten patients. US showed joint damage for six patients. Three patients had metatarsophalangeal synovitis including one with a positive PD signal. Ankle synovitis with no PD signal was found for two patients. US showed one tarsal synovitis with a positive PD signal. Two patients had tenosynovitis including one with a positive PD signal.
US showed joint abnormalities in 6 patients with normal X-rays.
Hands joints MRI were performed for three patients. Carpitis was found for one patient. One patient had radio-ulnar synovitis with tenosynovitis. One patient had radio-ulnar synovitis with metacarpophalangeal synovitis.
Six patients had one or two erosions on feet or hands: 2 on radiographs, 3 on US and 3 on MRI (including one shown by US).
Conclusion: Clinical and radiological (radiograph and US) joints manifestation in WD affect large joints. However, small joints can also be affected. Axial involvement is rare. WD can affect both joints and tendons. Erosions are rare and never exceed 2 per patient in our series. US can show joint damage whereas radiograph is normal. US should be systematic for patient with WD in order to improve knowledge about this disease and to distinguish it from autoimmune arthritis.

REFERENCES

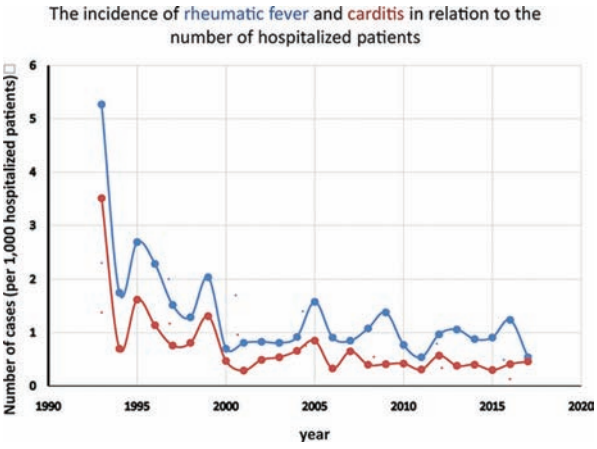
[1] - Meunier M, Puechal X, Hoppé E, Soubrier M, Dieudé P, Berthelot JM, et al. Rheumatic and musculoskeletal features of Whipple disease: a report of 29 cases. J Rheumatol. déc 2013;40(12):2061-6.

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SAT0454 RHEUMATIC FEVERIN A TERTIARY MEDICAL CENTER – 25 YEARS OF FOLLOW-UP

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Background: Rheumatic Fever (RF) occurs after a pharyngeal infection caused by group A-B-hemolytic streptococci, and is often classified as a connective tissue disease. RF mostly affect children and it's diagnosis is determined using the Jones criteria.



Its principal clinical significance is causing carditis at the acute phase of the disease, and valvular impairment, leading to a significant hemodynamic disturbance, as a late sequela.
Despite being a completely preventable disease, Rheumatic fever continues to be the most common cause of acquired heart disease among children in developing countries. In developed countries, a sharp decline in ARF was seen in the last decades.
Objectives: To examine the number of cases of Rheumatic fever in Schneider Children's medical center, and to find whether it has declined during the years of its existence. In addition, to characterize the patient population during that period, determine the clinical characteristics of ARF, It's risk factors and asses the course of the disease and it's treatment. In addition, we will address the relapse rates, with an emphasis on cardiac relapses, with a correlation to preventive treatment.
Methods: A retrospective cohort study was conducted, by collecting data from medical records of patients with rheumatic fever who were admitted to the Schneider Medical Center from 1993 to 2017. A database was built based on these medical records in order to assess the incidence of rheumatic fever and rheumatic heart disease, and the relapse rates, by use of descriptive and survival analysis.
Results: A 402 cases with relevant diagnostic codes were examined during the follow-up period, of which 307 patients met the inclusion criteria. During the acute phase,197of the patients (64%)presented with arthritis, 159 patients (52%) with carditis, 47 patients (15%) with chorea, 16 patients(5.2%) with erythema marginatum, and 2 patients (0.7%) with subcutaneous nodules. Carditis was found in higher rates among Jewish patients than among Arabs. 31 patients (19.5%) developed severe carditis, 21 patients (13.2%) of whom developed heart failure signs, 5 were hospitalized in intensive care, and one died. There was a decrease in incidence of rheumatic fever and rheumatic heart disease during the study period. Thirty-two patients (12% of all patients with rheumatic fever) developed a relapse of the disease and 11 of whom (4 percent of all patients) developed a cardiac relapse.
Median follow-up time was 49 months, and relapse rate was 13.9% after 5 years of follow-up. 15% of the patients who received oral prophylaxis experienced relapse, compared to 9% of those who received intramuscular injection therapy.
The rate of recurrence among all patients with rheumatic fever was 2.8% after 2 years of follow-up, and about 7% after 8 years of follow-up. 10 (90.9%) of the 11 patients with cardiac recurrence were present with carditis during the initial disease, with 7 of them (63.6% of patients with cardiac recurrence) having isolated carditis and 3 of them had a combined involvement of arthritis and carditis (27.3% of Cardiac relapses). Only in one case (9.1% of patients with cardiac recurrence) was an isolated occurrence of arthritis in the initial presentation.
It was found that chorea is more common among females.
Conclusion: Despite the reduction in incidence of rheumatic fever and rheumatic heart disease during the study period, the disease remains a significant cause of general and cardiac morbidity among children despite being completely preventable, therefore, It should remain in the mind of every doctor, pediatricians in particular.
Disclosure of Interests: None declared
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SAT0455 A QUALITY IMPROVEMENT INTERVENTION TO INCREASE INFLUENZA AND PNEUMOCOCCAL VACCINATION RATES IN IMMUNOSUPPRESSED INFLAMMATORY ARTHRITIS PATIENTS

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Background: Disease-related immune dysfunction and medications cause immunosuppression in inflammatory arthritis (IA)(1). EULAR and Centers for Disease Control (CDC) recommend influenza and 23-valent pneumococcal polysaccharide (PPSV23) vaccination. Previous studies show suboptimal coverage.
Objectives: To increase influenza (annual) and PPSV23 (5 yearly) vaccination in immunosuppressed IA patients through a multifaceted quality improvement intervention.
Methods: Between April and September 2017, IA patients completed an anonymous paper 23 question worksheet recording demographics, medical history, medications, vaccination knowledge, status and barriers. All patients on oral steroids, bDMARDs or immunosuppressant cDMARDs were included.

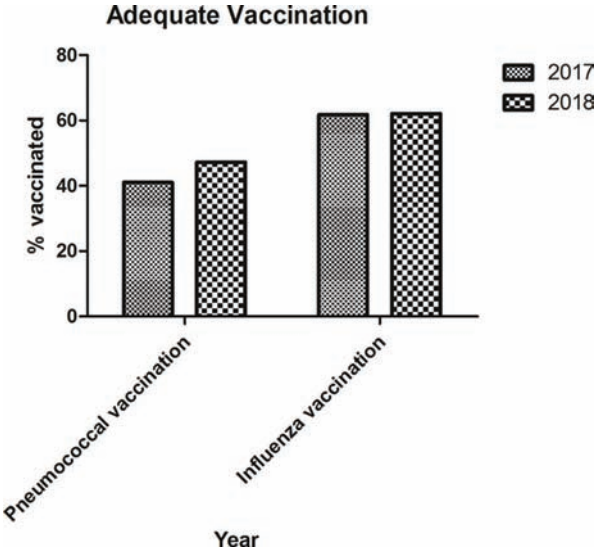
Simultaneously, we introduced staff education sessions, point-of-care paper "Arthritis and Infection Worksheets" and "Vaccination Advice Letters". In 2018, the clinic was re-assessed.

Results: 163 patients met inclusion criteria in 2017 and 262 in 2018. Patients were typical of an IA clinic (74% women, 45.4%≥60 years old, 72.7% had RA, 61.1% on cDMARDs, 53.6% on methotrexate, 46.6% on bDMARDs, 23.1% on cDMARD plus bDMARD).

In 2017, 104 (65.4%) knew of the increased infectious risk of IA. In 2018, 168 (65.6%) were aware. Awareness of infection risk with medications increased from 111 (69.8%) to 172 (66.9%).

Table 1 shows vaccination rates. PPSV23 rates increased from 41.0% to 47.2% (P value=0.29. Pearson Chi squared), and influenza from 61.8% to 62.1% (P value=0.95, Pearson Chi squared).

Table 1. Vaccination Rates



Vaccination awareness was higher for influenza (Table 2). Most patients were informed of requirements and vaccinated by general practitioners (GPs), with <5% of patients vaccinated in hospital. In 2017, the most common reason for non-vaccination was lack of awareness. This decreased post intervention. 70% of patients had smart phone access. 78% were willing to use this for vaccination reminders.

Table 2. Vaccination awareness, provision and reasons for non-compliance

	Influenza		PPSV23	
	2017	2018	2017	2018
Aware required	128 (80.0%)	212 (81.9%)	60 (38.0%)	118 (46.8%)
Aware of frequency	133 (99.3%)	219 (99.1%)	59 (75.6%)	98 (65.8%)
Source of awareness	92 (73.0%)	146 (71.2%)	49 (75.4%)	87 (70.2%)
GP	29 (23.0%)	44 (21.5%)	15 (23.1%)	27 (21.8%)
Hospital	0	12 (5.9%)	0	8 (6.5%)
Clinical Nurse Specialist	0	8 (3.9%)	0	1 (0.8%)
Public Health/Ward Nurse	6 (4.8%)	9 (4.4%)	1 (1.5%)	1 (0.8%)
Radio	5 (4.0%)	6 (2.9%)	0	0
Television				
Site of last vaccine	93 (78.8%)	149 (77.2%)	53(89.8%)	98 (90.7%)
GP	7 (5.9%)	14 (7.3%)	0	0
Work	6 (5.1%)	3 (6.7%)	0	1 (0.9%)
Pharmacy	6 (5.1%)	10 (5.2%)	1 (1.7%)	3 (2.8%)
Public Health Nurse	4 (3.4%)	5 (2.6%)	3 (5.1%)	4 (3.7%)
Hospital	2 (1.7%)	2 (1.0%)	2 (3.4%)	3 (2.8%)
Other				
Non-compliance reasons	18 (36.7%)	26 (34.2%)	69 (82.1%)	94 (76.4%)
Unaware	12 (24.5%)	18 (23.7%)	7 (8.3%)	10 (8.1%)
Fear of side effects	6 (12.2%)	10 (13.2%)	0	1 (0.8%)
Too busy	2 (4.1%)	2 (2.6%)	0 (0%)	1 (0.8%)
Cost	13 (26.5%)	22 (28.9%)	8 (9.5%)	17 (13.8%)
Other				

Conclusion: This study shows suboptimal vaccination awareness and uptake. Our interventions increased PPSV23 and influenza vaccination rates. There is debate about who is responsible for vaccinations. Guidelines advocate specialists sharing responsibility with GPs. 57% of rheumatologists considered GPs responsible (2). Perhaps, we should take a more active approach.

REFERENCES

[1] Doran MF, Crowson CS, Pond GR, O'Fallon WM, Gabriel SE. Frequency of infection in patients with rheumatoid arthritis compared with controls: a population-based study. Arthritis & Rheumatism. 2002;46(9):2287-93

[2] McCarthy EM, Azeez MA, Fitzpatrick FM, Donnelly S. Knowledge, attitudes, and clinical practice of rheumatologists in vaccination of the at-risk rheumatology patient population. JCR: Journal of Clinical Rheumatology. 2012;18(5):237-41

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SAT0456

SERO-REACTIVITY TO GALACTOSE-ALPHA-1,3-GALACTOSE AND CLINICAL PRESENTATIONS OF PATIENTS SEEN IN A RHEUMATOLOGY OUTPATIENT PRACTICE

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Background: Analphylactic reactions to cetuximab, a monoclonal antibody used in cancer therapy, were recognized in 2007 as a regional complication related to recognition of a protein epitope by IgE. This protein epitope was defined as galactose-alpha-1,3-galactose (alpha-gal), which is found in non-primate mammalian tissue. Reactivity to this epitope was also found to occur after meat consumption with manifestations including anaphylaxis, urticaria, or angioedema. Further study showed that reactivity was induced by tick bites from the Lone Star tick. Similar cases of reaction to red meat have been described in Australia in 2006, and more recently in Japan and various European countries. In our Rheumatology practices where patients often raise concerns about possible tick-borne illnesses, we have observed patients presenting with symptoms related to consumption of mammalian meat, but generally less severe, and with IgE reactivity to alpha-gal.

Objectives: We have characterized the range of presenting symptoms in our alpha-gal positive patients, and their response to dietary modification.

Methods: Patients referred to this Rheumatology practice who had known exposure or risk factors for tick exposure were tested for IgE antibodies against galactose-alpha-1,3-galactose (alpha-gal) using a standardized test administered by Viacor-IBT, and also tested for typical Rheumatologic markers, as indicated by their symptoms. Alph-gal IgE levels varied from 0.38 to >100 kU/L (normal <0.35 kU/L).

Results: 147 patients were identified as positive for alpha-gal, and were recommended to avoid mammalian meat. Followup testing and evaluation was achieved in 38 patients, along with documentation of symptoms for improvement or persistence.

Clinical manifestations, laboratory findings, and reasons for referral in symptomatic alpha-gal positive patients were diverse. Dermatologic manifestations occurred in 9 including urticarial vasculitis, serpiginous urticarial rash, purpuric rash, psoriasiform rash, nummular eczema, and subcutaneous nodules.

Arthritic manifestations varied and included monoarthritis (one patient, with negative Lyme PCR of fluid), oligoarthritis in 2 patients, inflammatory polyarthritis in 10 who did not meet criteria for a diagnosis of RA, and polyarthralgia in 22. 15 patients were diagnosed with Rheumatoid Arthritis, and 13 with Spondyloarthritis.

28 patients were referred with positive ANA tests. 25 were felt to be false positive ANAs who did not meet criteria for any connective tissue disease. Anticardiolipin antibodies were present in 4 patients.

Surprisingly only 11 patients had a history of severe reaction to mammalian meat, and only one had been previously diagnosed with mammalian meat allergy

Of the 38 patients seen in followup, 10 reported symptom improvement with mammalian meat restriction.

Conclusion: Alpha-gal reactivity from tick bites is more common than Lyme disease or other tick-borne disease in our catchment area. The patients rarely recall distinct exposure to a Lone Start tick.

Manifestations are protean, and do not correlate with alpha-gal IgE level. Some patients are shown to improve with restriction of dietary mammalian meat. Somewhat surprisingly, other patients prefer to tolerate intermittent mild symptoms to maintain current dietary patterns.

In areas where Lone Star ticks are present, and in patients with risk factors for tick exposure, alpha gal IgE reactivity should be considered and tested for as part of a "tick panel" in patients who present with symptoms of potential rheumatologic diseases.

REFERENCES

[1] Chung C, Mirakhur B, etal. 2008. NEJM 358:1109. Cetuximab-Induced Anaphylaxis and IgE Specific for Galactose-α-1,3-Galactose

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SAT0457 PATTERNS AND CONSEQUENCES OF POST-CHIKUNGUNYA ARTHRITIS – A LONGITUDINAL STUDY IN A TERTIARY CARE HOSPITAL IN BANGLADESH

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Background: Chikungunya fever (CF), is a viral illness, characterized by 3–7 days of high fever, headache, rash, myalgia, and severe arthralgias/arthritis, the hallmark of the disease.[1] There is evidence that links Chikungunya infection (CHIKV) with development of unspecific Post-Viral Arthritis, Rheumatoid Arthritis, Seronegative Spondylitis and other non-inflammatory musculoskeletal complaints like persistent arthralgia.[2]
Objectives: To identify the clinical patterns and consequences of Post-Chikungunya arthritis.
Methods: This longitudinal study was carried out during a major out-break of CHIKV infection in Dhaka, Bangladesh, among 142 patients (CHIKV IgM and/or IgG positive) who were followed-up for the next one year. Their clinical, laboratory, radiographic and ultrasonographic features were evaluated. Functional status was assessed by validated Bengali version of Health Assessment Questionnaire (HAQ).
Results: The mean age of the patient's was 43.12 ±10.94 where 50.7% were male and 81.7% were urban resident. At presentation (D1),95.1% patients were Chikungunya IgM positive where as 20.4% were IgG positive. Polyarthritis was noted among 69.7% patients. Symmetrical joint involvement and joint swelling were present in 84.5% in 47.2% patients respectively. The mean HAQ score was 1.34±0.72. After 3 months (D90) follow up, 40.8% patients reported Chronic Chikungunya arthritis where 6.9% had Rheumatoid Arthritis, 3.4% had Spondyloarthropathy and 89.6% were Undifferentiated arthritis. Among the Chronic Chikungunya arthritis patients, 5.2% were Anti-CCP positive, 1.7% were Rheumatoid factor positive, 3.4% were HLA-B27 positive and 3.4% had X-Ray findings of bilateral Sacroiliitis. Patients were treated with NSAID (100.0%) and steroid (10.0%) initially. Chronic arthritis was treated with Sulfasalazine (12.0%), Methotrexate (7.0%) and *Tofacitinib* (3.4%).
Conclusion: This study demonstrated that chronic arthritis was a frequent complication of acute Chikungunya infection where majority had undifferentiated arthritis.

REFERENCES

[1] Brighton SW, Prozesky OW, de la Harpe AL (1983) Chikungunya virus infection — a retrospective study of 107 cases. S Afr Med J 63,313-5.
[2] Yaseen HM, Simon F, Deparis X, Marimoutou C (2014) Identification of initial severity determinants to predict arthritis after chikungunya infection in a cohort of French gendarmes. BMC musculoskeletal disorders 15,249.

Table 1. Clinical presentation of the patients at onset (n=142)

Characteristics of joint involvement at onset	n (%)
Monoarthritis	7(4.9)
Oligoarthritis	36(25.4)
Polyarthritis 99(69.7)	
Symmetrical joint involvement	120(84.5)
Joint swelling	67(47.2)
Morning stiffness	116(81.7)
Skin involvement	90(63.4)
Erythematous rash 24(16.9)	
Erythematous rash and itching	66(46.5)
Myalgia 46(32.4)	
Ultra-sonographic findings	(n=**32)**
Tenosynovitis	22(68.8)
Synovial hypertrophy	11(34.4)
Tendinitis	8(25.0)
Median nerve involvement (CTS)	4(12.5)
Joint effusion	3(9.4)

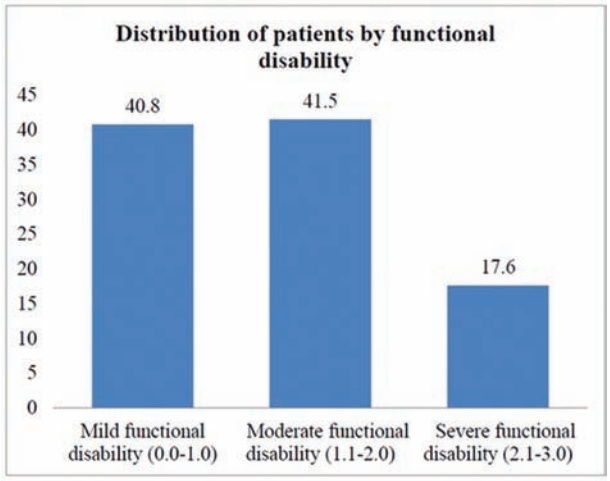


Figure 1: Distribution of patients by functional disability using HAQ

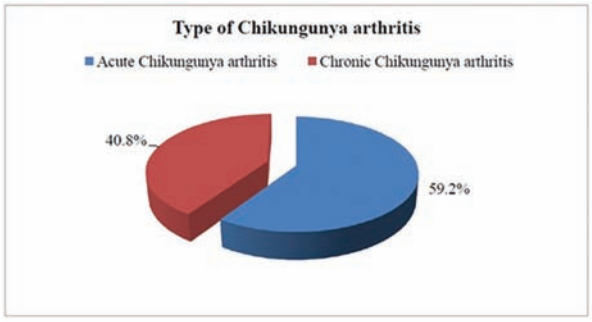


Figure 2: Type of Chikungunya arthritis

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SAT0458 EVALUATION OF DISABILITY IN THE COLOMBIA CHIKUNGUNYA EPIDEMIC WITHIN A COLOMBIAN COPCORD STUDY

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Background: During the 2014-2015 a Chikungunya virus (CHIKV) epidemic reached Colombia. Concurrently, the Community Oriented Program for the Control of Rheumatic Diseases (COPCORD) was being developed in Colombia to establish rheumatic diseases prevalence. Since CHIKV generates rheumatic manifestations, the presence of CHIKV infection was included.
Objectives: Based on the population entered in this program this study was developed with the aim to describe the disability of CHIKV infection through four questionnaires (HAQ-DI, EQ-5D, EQ-5D VAS and VAS for pain).
Methods: World Health Organization (WHO) criteria for CHIKV diagnosis and ELISA IgG and IgM serology were performed to identify CHIKV infection. Four groups of patients were defined: true positives (WHO + and + serology), true negatives (WHO - and - serology), false positives (WHO + and - serology), false negatives (WHO - and + serology). Three scores of disability and one of pain were applied to evaluate disability. A descriptive analysis was made using the media and standard deviation for continuous variables and percentage for the categorical variables, the Odds ratio was calculated with a confidence interval of 95% and a p< 0.05% for statistical significance
Results: From 548 patients with clinical suspicion of CHIKV infection, 295 were positive for CHIKV IgG and/or CHIKV IgM. Functionality evaluated by HAQ-DI showed a media of 0.17 (SD±0.45), with highest score after 7 weeks since the beginning of symptoms and the lowest in patients

with CHIKV IgM positive. In the EQ-5D (Figure 1), between 72% and 92% of patients didn't report problems on the mobility, self-care, usual activities, anxiety and depression dimensions. In contrast pain and discomfort dimensions were affected from moderate to extreme (44.7% and 8.6%). There weren't significant differences between true positives, true false, false negative within all the variables, except on the anxiety and depression dimensions where the false positives had a higher significant score in comparison to the other groups (n: 10, 38.5%; p=0.00; OR:4.17, IC:1.8-9.57). In the EQ-5D-VAS, media for VAS was 75.56 (SD±21.18) where the highest scores of VAS were found on the false negatives. In pain VAS, false positives as well as the duration greater than 7 weeks where associated with several pain (n: 10, 2.9%; OR: 0.2; IC 1.25–6.33 y n: 27, 21.3%; p=0.018; OR 2.02, IC: 1.12-3.66 respectively).
Conclusion: In general, the disability of CHIKV infected patients was mild to moderate, finding the most affected dimensions to be pain, discomfort, anxiety and depression. The false positives and the population with anxiety and depression are related with higher score of disability.

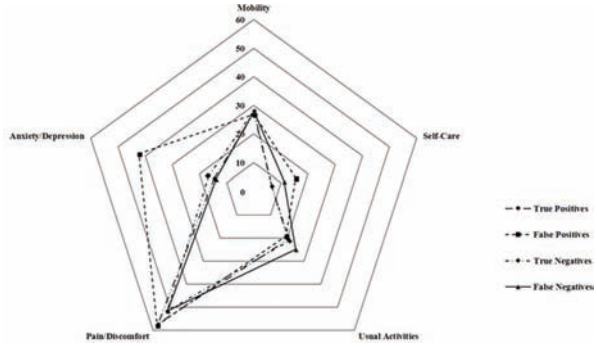


Figure 1. EuroQol-5D in patients with CHIKV infection from the Colombian COPCORD cohort.

Disclosure of Interests: None declared
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SAT0459 DIAGNOSIS AND MANAGEMENT OF ACUTE HOT JOINTS AT A TERTIARY RHEUMATOLOGY CENTRE OVER A 7-MONTH PERIOD

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Background: The acute hot joint presentation is common in clinical practice, often due to crystal arthritis or non-inflammatory conditions. The most serious diagnosis is septic arthritis (SA), which can destroy cartilage within days, and therefore must be promptly diagnosed or excluded. The mortality rate for SA is 7-15%, despite antibiotic use [1]. Crystal arthropathies and SA are difficult to distinguish clinically, requiring arthrocentesis and synovial fluid (SF) analysis, in keeping with national guidelines.
Objectives: 1. Quantify number of acute hot joint presentations to our hospital over 7 months, including incidence of SA and crystal arthropathy.
2. Determine clinical features and outcomes (including morbidity/mortality) in SA.
3. Compare clinician diagnosis with laboratory diagnosis (gold-standard diagnostic test; crystal microscopy and culture).
4. Determine the correlation between WCC and crystal arthropathy or SA.
Methods: We retrospectively analysed laboratory diagnostic data and electronic clinical records, for patients presenting to a tertiary rheumatology centre in Northwest England with an acute hot joint, February-August 2018. For crystal arthropathy and SA, sensitivity, specificity, likelihood ratios, and accuracy of diagnosis were calculated for clinician diagnosis when compared to laboratory diagnosis, using the statistical software 'R'. WCCs were used to create receiver operating curves (ROCs), with area under the curve and predicted diagnostic threshold for SA and crystal arthropathy. In cases of SA, organism, serum inflammatory markers, and outcomes were recorded.
Results: 137 patients were included. The most common site of arthrocentesis was the knee (n=108). There were 53 clinician-confirmed cases of crystal arthropathy. Compared to laboratory crystal microscopy, this yielded a sensitivity of 91.7%, specificity 80.2%, diagnostic accuracy 83.2%. There were 10 cases of native joint SA (plus 2 prosthetic and 1 case of osteomyelitis). SF cultures were positive in 80% of cases, all of which grew *Staphylococcus aureus*. 50% had commenced antimicrobials prior to arthrocentesis. 8 cases were treated successfully (5 prolonged admission due to underlying rheumatological disease); the 2 culture-negative cases had significant morbidity, with persistent symptoms. For SA, mean serum C-reactive protein at presentation was 152; serum WCC was 12. Clinician diagnosis, compared to culture results, yielded a sensitivity of 100%, specificity 98.4%, diagnostic accuracy 98.5%. Figure 1 shows mean SF WCC by diagnosis; highest value was SA (WCC=136293). ROC analysis of WCC yielded potential diagnostic threshold of 36450 for SA (AUC=0.7) and 10000 for crystal arthropathy (AUC=0.7) in our cohort.
Conclusion: The acute hot joint continues to be a common presentation in the acute medical setting. SA has considerable morbidity associated with it, especially in the presence of co-existing rheumatological disease. Our results confirm the importance of prompt arthrocentesis, prior to commencement of antimicrobials. SF WCC may also be utilised as a rapid diagnostic marker, especially differentiating between inflammatory and non-inflammatory causes of a hot joint, when taken with clinical assessment.

REFERENCES

[1] Margaretten ME, et al. Does this adult patient have septic arthritis? JAMA. 2007 Apr;297(13):1478–88.

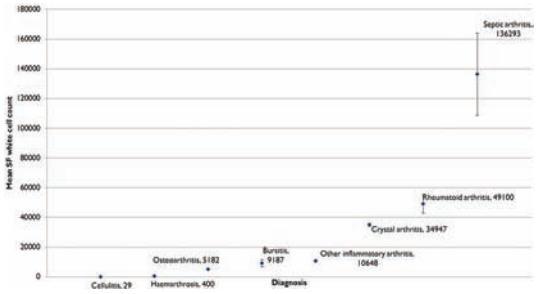


Figure 1

Disclosure of Interests: Mrinalini Dey: None declared, Pankaj Lal: None declared, Robert N. Thompson : None declared, Nicola Goodson Grant/ research support from: Research support grant from Novartis, Speakers bureau: Paid speaker UCB
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SAT0460 HCV-RELATED MIXED CRYOGLOBULINAEMIA IN THE DIRECT-ANTIVIRAL AGENTS ERA: IS THERE ADVANTAGE IN SEQUENTIAL THERAPY WITH RITUXIMAB?

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Background: Mixed Cryoglobuminaemia(MC) is a small vessel vasculitis characterized by the presence of a monoclonal rheumatoid factor(RF) and polyclonal immunoglobulins that precipitate at cold temperature, with a large spectrum of clinical manifestations. MC is strongly associated with hepatitis C(HCV) infection>90%. The new direct–acting antivirals(DAA) against HCV, which can eradicate the virus in >95% of patients, are supposed to have benefits on clinical manifestations of MC, nonetheless the amount of data is still limited. Patients with severe vasculitis may require anti-CD20 agent Rituximab(RTX) over DAA. However, despite the strong rationale, the advantage of dual therapy is still debated and the optimal therapeutic schedule unknown.
Objectives: To investigate the impact of DAA treatment on clinical manifestations and biochemical parameters of disease activity in HCV-related MC patients who reached complete viral eradication, and if pre-treatment with RTX was able to define a subset of patients with a different outcome.
Methods: Data was collected from 31 patients with MC, mean age 68 yrs, female 80%, mean disease duration 10 yrs who were treated with

DAA and reached complete viral eradication, at 3 time points: before starting DAA (pre-DDA), after completing DAA (post-DAA), 52 weeks after completing DAA (52w). Additionally, a population of 9 patients with the same disease (mean age 65 yrs, female 77%, mean disease duration 9 yrs) but treated with one or more cycles of RTX prior receiving DAA, was analysed at the same timepoints and additionally before starting RTX(pre-RTX). At each time point clinical data (presence/absence of purpura, neuropathic manifestations, arthralgia, fatigue, nephritis) and biochemical parameters (% cryoglobulins, C3, C4 and RF) were recorded. The change in clinical and biochemical parameters at different timepoints were evaluated.

Results: Among patients treated with DAA only, the prevalence of clinical manifestations before starting treatment was the following: purpura 31%, neuropathic manifestations 52%,arthralgia 28%,fatigue 14%, nephritis 3%. We observed a significant reduction in purpura after treatment (pre-DDA vs post-DAA=31% vs 13%,p=0.044) that persisted at 52w (pre-DAA vs 52w=31% vs 0%,p=0.004%). This in parallel with a significant reduction in the level of cryoglobulins (pre-DAA vs 52w=3.99±5.28 vs 1.6 ±1.7, p=0.029 and pre-DAA vs 52w=3.99 ± 5.28 vs 0.92 ± 1.75,p=0.008). Among patients pre-treated with RTX, the prevalence of clinical manifestations before starting RTX was: purpura 78%, neuropathic manifestations 100%,arthralgia 44%,fatigue 50%,nephritis 22%;and before starting DAA was: purpura 22%,neuropathic manifestations 100%,arthralgia 0%,fatigue 0%,nephritis 0%. A significant reduction in the rate of purpura (pre-RTX vs pre-DAA=78% vs 22%, p=0.009%) and arthralgia (44% vs 0%, p=0.012%) after RTX treatment was observed, but no difference in any clinical parameter when comparing pre-RTX with post-DAA and 52w. No significant change in any of the serological parameter was observed.

Conclusion: DAA treatment is associated with rapid and sustained decrease in the level of cryoglobulins and related clinical improvement, specifically purpura. Patients who had been pre-treated with RTX showed clinical improvement in terms of purpura and arthralgia, albeit transient; subsequent treatment with DAA did not result in any immediate or long term additional clinical benefit.

REFERENCES

[1] Mazzaro C. Clin Exp Rheum 2017.

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SAT0461 VERTEBRAL OSTEOMYELITIS IN THE IMMUNOSUPPRESSED PATIENTS

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Background: Vertebral Osteomyelitis (VO) is an infectious disease that could involve intervertebral space (discitis). Its incidence is raising for several reasons, such as the increasing number of patients on immunosuppressive therapy. The treatment includes long term antibiotic, that should be initiated after biopsy (if possible) and sometimes, further surgery is needed[1].

Objectives: To analyze the influence on prognosis of detection of OV in immunosuppressed (IS) patients.

Methods: Single center retrospective observational study including IS adult patients diagnosed of VO based on the combination of clinical presentation with either a definitive bacteriologic diagnosis or pathological and/or imaging studies from January 2010 to January 2019. Demographic features, concurrent diseases, clinical history (length of pain and fever prior to admission), laboratory findings, microbiological diagnosis and radiological data were compiled. We considered as IS patients those who had rheumatic or inflammatory bowel disease undertaking immunomodulatory drugs, solid organ transplantation receptors, patients with an active malignancy or Human Immunodeficiency Virus (HIV) infected. Clinical and radiological history of lumbar stenosis or disc herniation was considered as prior spine pathology. Surgical infections were excluded. We considered deaths attributive to PVO those which were directly caused by the infectious picture and/or its complications during the next year after diagnosis.

Results: Eighteen of 122 patients with VO (21.96%) were IS. Basal demographic and clinical features are exposed in table 1. Detailed data about the cause of the IS is provided separately in table 2. Duration of pain prior to diagnosis had a median of 30 days (15.5, 55). C reactive protein showed a median value of 65.2mg/L (19.32, 153.9) and Erythrocyte Sedimentation Rate mean value was 80.57mm/H (31.75). MRI was the imaging technique most often used for diagnosis (83.33%), followed by CT-scan(16.67%). The region most frequently affected was lumbosacral spine (44.44), then dorsal (33.33%) and finally cervical (22.22%). Some abscess (epidural or paravertebral) was detected in 16 patients (88.89%) close to non-IS patients (90.38%). Worst data concerning vertebral destruction was observed (66.67% in IS group against 49.04 in non-IS, p=0.3) and cord compression (61.11% versus 26.92% respectively, p=0.05). Fifteen patients underwent CT guided biopsy (83.33%) with prior antibiotic exposure in 11 of them. Median exposure was 4.5 days (3, 8.75). Delay from admission to procedure had a median value of 6 days (3.5, 9). Culture was positive in 53.33% of cases. In 10 patients, the picture was attributed to Gram+ (55.56%), in other 2 cases Gram- (11.11) and 1 case of tuberculosis (5.56). In 5 cases (27.78%) final pathogen was unknown. Four patients (22.22%) required further surgery and 2 patients (11.11) died, similar than non-IS group, 11.54%.

Conclusion: In general terms, data about imaging is worse in IS patients and higher proportion of cervical spine involvement was also noted. Although, early intervention (diagnosis, punction guided biopsy and treatment) seems to be protective against a bad outcome, since IS patients showed similar prognosis (further surgical procedures and death) than non IS patients. To sum up, new onset back pain in a IS patient, should be thoroughly studied so as to consider a VO as soon as possible.

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SAT0462 INTEREST OF FOLLOW-UP IMAGING EXAMINATIONS IN PATIENTS WITH PYOGENIC VERTEBRAL OSTEOMYELITIS: A RETROSPECTIVE STUDY

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Background: Systematic follow-up imaging in patients with pyogenic vertebral osteomyelitis (PVO) is widespread. However, it is discussed, and there is no recommendation.

Objectives: Evaluate the interest of follow-up imaging examinations in patients with pyogenic vertebral osteomyelitis

Methods: We conducted a retrospective cohort analysis of patients with PVO who had both baseline and follow-up imaging results available in a French university hospital during the period of 2010-2018. We have classified the follow-up images into two groups, improvement/stability and deterioration, compared with the baseline findings. For each patient, we compared their imaging follow-up to their clinical-biological condition assessed at the same time.

Results: We have collected 80 patients. The median age was 71 years [32-89], 46 men, 13 patients had a history of spinal surgery. The most frequently reported germ was methicillin-sensitive staphylococci and the level of spinal involvement was predominantly lumbar. A Computerized Tomography (CT) was performed in 64% and a Magnetic Resonance Imaging (MRI) in 85% at the time of diagnosis. We identified 89 follow-up images, 58 MRIs, 31 CTs. The median delay of realisation was 85 days [11-364]. Soft tissue infiltration was observed in 50 patients compared to 26 on follow-up images but 3 were new. Similarly, 24% of the initial images had epiduritis compared to 16% during follow-up, 3% had appeared secondarily. There were 12% initial erosions described compared to 25% at follow-up. Of the 33 patients with clinical and biological recovery, 67% of follow-up images were classified as improving/stable and 33% as worsening (new abscesses (n=3), extension of soft tissue infiltration (n=2) and/or epiduritis (n=2) or appearance of new locations (n=2)). Among the 37 patients considered as unhealed, 87% of follow-up images were classified as improving/stable and 13% as worsening (new abscesses (n=1), extension of soft tissue infiltration (n=1) and/or epiduritis (n=1) or appearance of new locations (n=1)).

Conclusion: Our study showed that there was no correlation between the clinical condition of patients and their follow-up imaging in the context of PVO. Clinical and biological evaluation seems sufficient to determine whether or not the patient is cured. Many images are made during the follow-up with a questionable cost/effectiveness ratio. A standard radiograph may be sufficient to provide a basic structural condition at the end of antibiotic therapy.
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SAT0463 BRUCELLAR SPONDYLODISCITIS: CLINICAL, RADIOLOGICAL AND THERAPEUTIC FEATURES

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Background: Brucellosis is an endemic disease around the Mediterranean and especially in Tunisia and Brucellar spondylodiscitis is the most common osteoarticular localization.
Objectives: The aim of our study is to study the,clinical, radiological and therapeutic characteristics of Brucellar spondylodiscitis.
Methods: This is a retrospective descriptive study, conducted over 20 years (1999-2019) at a Rheumatology Department. We collected cases of Brucellar spondylodiscitis. We studied the clinical, radiological features and therapeutics outcomes.
Results: We included 23 patients, 15 men and 8 women, with a mean age of 53.21 years [31,79].
Contact with livestock or consumption of raw milk was noted in 16 cases. The diagnosis time was, on average, 3.8 months [1,9]. Spine pain was present in all cases, with lumbar seat in 16 cases and was inflammatory in 20 cases. At the examination, 19 patients had a limitation of spinal mobility and 4 had neurological abnormalities. A motor deficit with a horsetail syndrome was objectified in one case. We noted a biological inflammatory syndrome in 19 cases. Wright's serology was positive in 21 cases. Standard radiographs showed disc narrowing in 10 cases. 21 patients had spinal magnetic resonance imaging showing the abnormalities of the disc and adjacent vertebrae. We found abscess in four patients and epiduritis associated with the abscess in six patients. MRI showed spinal compression in 2 patients. Disco-vertebral biopsy was performed in 11 cases and helped to make the diagnosis in 3 cases. The patients had received antibiotic therapy with a combination of doxycylin and rifampicin with a mean total duration of 4.9 months [2.12]. Evolution was favorable in 19 cases. Complications were mainly neurological (n=3)or related to the toxicity of the treatment(n=3).
Conclusion: Brucellar spondylodiscitis can be serious because of the neurological complications that it can cause. At the slightest diagnostic doubt, we should perform an MRI. And antibiotic treatment must be urgent and well-adapted with careful monitoring of patients.
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SAT0464 HEPATITIC SAFETY OF ANTI-TUBERCULOUS TREATMENT IN SPONDYLODISCITIS

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Background: Tunisia is considered as a country with high tuberculosis endemicity. The anti-tuberculous treatment is quite long and binding and requires close hepatic monitoring.
Objectives: The purpose of this study was to highlight the hepatitic safety of anti-tuberculous treatment in tuberculous spondylodiscitis.
Methods: This is a retrospective descriptive study, over 20 years (1999-2019) collating cases of tuberculous spondylodiscitis in a rheumatology department. We studied the epidemiological, clinical, radiological and therapeutic aspects.
Results: Our study included 62 patients, 35 women and 27 men. Mean age was 56 years [16-86]. The diagnosis delay averaged 5.59 months [0.23-24]. Tuberculous contact was noted in 11.3% of the cases. Neurological abnormalities were noted in 16,1% of cases with spine compression in 3,22%. The tuberculin skin test was positive in 29 cases and the Koch bacillus investigations in the sputum and the urine were positive in only 3 patients. Magnetic resonance imaging was performed in 71% of the patients, and mainly showed images of disc destruction with images of abscess, epiduritis and epidural extension. Infectious spondylodiscitis affected the lumbar spine in 66.1% of the cases, the dorsal spine in 14.51% of the cases and the cervical spine in 6.55% of the cases. It was bi-staged in 19.35% of the cases and bifocal in 17.74% of the cases.
Disco-vertebral biopsy was performed for 72.5% of patients and helped to make the diagnosis in 33.87% of the cases. All patients have received anti-tuberculosis treatment based on rifampicin, pyrazinamide, ethambutol and Isoniazid for an average duration of 2.8 months. Following the initial 4-drug regimen, most patients continued to receive a two-drug regimen with RMP and INH for a mean duration of nine months. Hepatotoxicity was seen in 13% : 11.4% of the patients had a history of cholestasis due to TB treatment, Only 2% of the patients had cytolysis. We nedded then to modify the treatment in 3,22%, and switch to triple anti-TB therapy based on Isoniazid, Rifampicin and ethambutol with a favorable evolution. No cases of hepatic insufficiency were noted.
Conclusion: In our study, we note 8 cases of hepatotoxicity. The diagnosis of tuberculous spondylodiscitis requires urgent treatment with anti-tuberculosis antibiotics. However, it should be kept in mind that this treatment can lead to severe and life-threatening hepatotoxicity. Thus a rigorous monitoring of the treatment will be required.
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SAT0465 VALUE OF SERUM PROCALCITONIN FOR THE DIAGNOSIS OF BACTERIAL SEPTIC ARTHRITIS IN DAILY PRACTICE IN RHEUMATOLOGY

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Background: Septic arthritis is a diagnostic and therapeutic emergency because of a high morbidity and mortality. Nevertheless, the etiologic diagnosis is often difficult.
Objectives: The aim of our study was to determine if serum procalcitonin was a discriminatory biomarker in case of arthritis of undetermined etiology.
Methods: Patients were separated in 5 groups: gouty arthritis, calcium pyrophosphate deposition arthritis, osteoarthritis or post-traumatic arthritis ("mechanical" arthritis), chronic inflammatory rheumatic arthritis, and septic arthritis. Levels of serum with blood cells, C-Reactive Protein and procalcitonin were measured.
Results: 98 patients were included: 18 in the "gout" group, 26 in the "calcium pyrophosphate deposition arthritis" group, 16 in the "mechanical" group, 18 in the "chronic inflammatory rheumatic" group and 20 in the "sepsis" group. The area under the receiver operating characteristic curve of with blood cells, C-Reactive Protein and procalcitonin levels to diagnose a septic arthritis were 0.69 (IC95% 0.55-0.83), 0.82 (IC95% 0.73-0.91), and 0.87 (IC95% 0.76-0.98) respectively. For a cut-off of 0.5 ng/ml, procalcitonin sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio were 65%, 91%, 65%, 91%, 7.2 and 0.4, respectively. Serum C-Reactive Protein and procalcitonin levels were correlated, were not different in "sepsis" or "gout" groups and were higher in non-septic arthritis with poly-arthritis than with mono-arthritis ($p<0.05$).
Conclusion: Serum procalcitonin is a useful biomarker in arthritis management with diagnosis performances higher than those of other biomarkers (with blood cells, C-Reactive Protein).
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SAT0466 PNEUMOCOCCAL CELLULITIS AND FASCIITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW

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Background: Streptococcus pneumoniae (SPN) is an encapsulated gram-positive bacterium that can be found in the nasopharynx as part of the normal flora. However, is the most common cause of community-acquired pneumonia in adults and can also cause invasive diseases such as bacteremia, meningitis, and otitis media. Pneumococcal cellulitis and fasciitis

are uncommon. Several factors are associated with a predisposition to infections in patients with Systemic Lupus Erythematosus (SLE).
Objectives: To describe and analyze all documented cases of cellulitis or fasciitis caused by SPN in SLE patients.
Methods: In the framework of the study of a 24-years-old woman that during the SLE onset presented left tight cellulitis and fasciitis caused by SPN, a systematic review was conducted (until September 2018). The search included terms to identify any SPN infection in SLE patients and all those articles that reported cellulitis or fasciitis were selected (Table 1).

Table 1. flow chart.

Search: "Lupus Erythematosus, Systemic"[Mesh] AND "Streptococcus pneumoniae"[Mesh]) OR "Pneumococcal Infections"[Mesh] (filter "humans", "english", "spanish").
Total searched articles: 313
- Medline 72, Embase 241, Cochrane 0.
- Duplicated 23.
- Excluded by: title 248, abstract 21, text 13.
- Selected: 8
Manual included articles: 1.

Results: A total of 313 articles were obtained. Eight of them (1-8) and 1 article identified in a manual search (9) described a total of 15 cases presenting SLE and cellulitis or necrotizing fasciitis caused by SPN; our case is the 16th described.
Documented infections (n=16):

- – Cellulitis (n=8): neck, face or chest (n=5, 62.5%); extremities (foot or hand) (n=2, 25%); breast (n=1, 12.5%).
- – Fasciitis (n=8): neck, face ot chest (n=5, 62.5%); tights (n=3, 37.5%).

Description of the documented cases:

- – Demographic characteristics (n=13): female sex (n=11, 85%); <30 years of age at the moment of the infection (n=11, 85%).
- – Time of SLE evolution at the moment of the infection (n=9): ≤ 1 month (n=3, 33.3%); ≤ 3 years (n=3, 33.3%); ≤ 8 years (n=3, 33.3%).
- – Associated conditions (n=12): previous high doses of prednisone (n=5, 45%); recent respiratory sympthoms (n=4, 33.3%); renal insufficiency (n=2, 16.6%); previous SPN infections (n=1, 8.3%); recent surgery in the affected área (n=1, 8.3%).
- – Microbiological diagnosis (n=12): blood cultures (n=11, 91.6%); other cultures (n=5, 41.6%).
- – Treatment (n=12): beta–lactams (n=12, 100%); intensive care support (n=6, 50%); surgical debridment (n=5, 41%).
- – Outcome (n=15): death (n=3, 20%); reccurrent SPN infections (n=2, 13.3%).

Conclusion:

- – Pneumococcal cellulitis and fasciitis in SLE were predominantly presented in young women and in a high rate of cases during the disease onset.
- – Almost half of the cases were previously treated with high doses of steroids. Nevertheless, no other potential predictors of pneumococcal cellulitis or fasciitis were identified; in addition, only one patient presented a previous surgery in the affected anatomical area, previous trauma were not described in any case, and a low number of cases reported associated respiratory symptoms. This supports the importance of the intrinsic immune dysregulation in SLE patients.
- – Pneumococcal cellulitis and fasciitis in SLE patients present poor prognosis, requiring intensive care support and surgical debridement in a high rate of cases, and presenting a fatal outcome in a fifth of them.

REFERENCES

[1] DiNubile; 1991.
[2] Hill; 1997.
[3] Isik; 2007.
[4] McDonald; 1993.
[5] Page; 2003.
[6] Patel; 1994.
[7] Sabio; 2006.
[8] Sánchez; 2016.
[9] Kamran; 2008.

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SAT0467 CROSS-SECTIONAL SCREENING STUDY FOR MYCOBACTERIUM LEPRAE DNA AND ANTIBODIES IN PATIENTS UNDER IMMUNOBIOLOGICAL TREATMENT

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Background: Leprosy is an endemic disease, highly dependent of the involved proinflammatory response. Immunobiological drugs improved the treatment for autoimmune diseases, but it larger use also brought the need for screening infectious diseases. There are some case reports about leprosy and immunobiological drugs, although the real risk of leprosy in those patients is unknown.
Objectives: To access the risk of leprosy by clinical and complementary evaluation in immunobiological treated patients living in endemic region.
Methods: We conducted a cross-sectional screening study and consecutively included patients with autoimmune diseases attending Dermatology and Rheumatology ambulatory. Patients were tested for serology (anti-PGL1) and conventional polymerase chain reaction (PCR) targeting *Mycobacterium leprae* DNA.
Results: 311 patients were included: 96 on immunobiological drugs, 94 on conventional immunosuppressive drug (mostly metothrexate), 69 on non-immunosuppressive treatment, and 52 controls with no autoimmune disease or immunosuppressive treatment. Two patients of immunobiological group were diagnosed with multibacillary leprosy. The PCR for *M. leprae* was positive in more 5 subjects (1 control, 1 on MTX and 3 on immunobiologicals). The anti-PGL1 test was performed in 284 patients, and was positive in 64, 15 with a high index (above 2).
Conclusion: Immunological status is critical for leprosy control and the findings of possible subclinical infection with *M. leprae* suggest that leprosy screening should be considered in patients treated with immunosuppressive drugs.

REFERENCES

[1] FRADE MAC, et al. Unexpectedly high leprosy seroprevalence detected using a random surveillance strategy in midwestern Brazil: A comparison of ELISA and a rapid diagnostic test. PLoS neglected tropical diseases, v. 11, n. 2, p. e0005375, 23 fev. 2017.
[2] ANTONIO JR, et al. Biological agents: investigation into leprosy and other infectious disease before indication. An Bras Dermatol 2013; 88:23-5
[3] LLUCH P, et al. Development of leprosy in a patient with rheumatoid arthritis during treatment with etanercept: a case report. Semin Arthritis Rheum 201242:127-30

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SAT0468 **INFECTIOUS SPONDYLODISCITIS IN A SPANISH REGIONAL HOSPITAL BETWEEN 2000 AND 2018: 66 CASES**

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Background: Spondylodiscitis have a large spectrum of clinical manifestations. The early diagnosis and treatment of this condition are essential to give the patient the best chance of a good outcome.
Objectives: To analyze the clinical characteristics, most frequent diagnostic methods and different treatments used in spondylodiscitis (SD) in our sanitary area.
Methods: Descriptive and retrospective study of patients with the diagnose of infectious SD (clinical or microbiological) from 2000 to 2018. In each case we studied the presence of underlying diseases, an episode of infection in the previous 6 months, way of presentation, location, diagnostic methods, treatment and evolution, comparing among different etiologies.
Results: 66 patients were diagnosed of spondylodiscitis. 44 men (24-90 years: mean 71.7). 62 were pyogenic, 3 tuberculous (TBC) SD, and 1 candida. The patients with TBC were younger (mean age: 45.3; $p<0.05$). An underlying disease was observed in 51 patients, specially Diabetes Mellitus (DM) (31% of SD). 4 patients were Rheumatoid Arthritis patients. A previous episode of bacteriemia or a primary source of infection was identify in a 34.8% of the cases, obtaining a microbiological isolation in 50/66 (75.7%) SD (46 bacterial, 3 TBC and 1 Candida). The most frequent pathogens were Gram +(G+) (51% of the total SD) being S. aureus and S epidermidis responsible of 23/66 cases (34.8%). In the 94% of SD caused by G+, hemocultures positive were obtained, in comparison to a 55% of SD caused by G- (p=0.016).
The most frequent presentation symptoms were: lumbar pain (90%), fever (53%) and neurological deficit (19%). Leucocytosis was present in only a third of the SD, observing an increase of ESR and CRP in the pyogen etiology (p no significative for low number of patients in SD group caused by TBC) and lower levels of hemoglobin, cholesterol and albumin. Lumbar area was affected in the 75.7% of SD (77% in G+ and 50% in G-). In a 13.6% of patients, more than one intersomatic space was affected, being visible the presence of an abscess in 47/66 cases (71.2%). It was necessary surgical treatment in 10/47 (21.2%). 5 patients died due to pathology related to SD (7.5%), without any correlation with a risk factor and other 5 presented a relapse in the subsequent months.
Conclusion: - The bacterial SD are the predominant group, being DM the most frequent risk factor.
- The incidence of SD due to TBC and fungi is scarce in our environment, being absent the Brucella etiology.
- The G+ SD usually have a previous associated bacteriemia.
- The majority of the patients had pain in the presentation, but only half of them had associated fever.
- The most frequent location of SD was lumbar.
- We established a 7.5% of mortality rate in our sanitary area.

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SAT0469 **THE IMPACT OF CHIKUNGUNYA VIRUS INFECTION ON QUALITY OF LIFE, FUNCTIONAL STATUS AND WORK ABILITY**

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Background: Chikungunya virus (CHIKV) is a reemergent arbovirus from the Alphavirus genus transmitted by Aedes species mosquitoes. The main feature of CHIKV disease is severe polyarthralgia, which is reported in more than 90% of cases. Musculoskeletal symptoms may persist in the subacute (> 3 weeks) and chronic (> 12 weeks) phases, causing critical physical impairment and significantly impacting the quality of life of patients.
Objectives: To assess the impact of CHIKV on pain, functional status, work ability and health-related quality of life (HRQoL) in the subacute and chronic phases of the disease.
Methods: Patients with a diagnosis of CHIKV disease (confirmed by PCR or serology) with persistent musculoskeletal symptoms after 4 weeks were referred to the Rheumatology outpatient clinic and followed up from April 2018 to January 2019. Evaluation questionnaires of pain (visual analogue scale – VAS), disability (Health Assessment Questionanaire – HAQ), HRQOL (Short-form 12 – SF-12) and work ability (Work Productivy and Activity Impairment-WPAI) were applied. The assessments were divided into 3 stages according to the time of disease: subacute from 4 to 12 weeks, chronic from 12 to 24 weeks and chronic with more than 24 weeks.
Results: Of the 69 patients analyzed, 76.81% were women, mean age 49.78 ± 14.24 years, 49.27% had some comorbidity (such as hypertension and diabetes), 26 were obese and 37.68% presented a previous musculoskeletal condition. Fifty-eight patients initiated follow-up in the subacute phase, in which the average pain was 6.84±1.9, mean HAQ of 1.59±0.57, mean Physical Health Composite Scale Score (PCS) of 26.81 ±14.3 and Mental Health Composite Scale Score (MCS) of 36.77±15.9. Of the 58 patients, 35 were employed and of these, 54.25% were absent from work during the previous week. Women presented lower scores in the mental component of SF-12 (p=0.0215) and the presence of comorbidity was related to higher values reported in the pain VAS (p = 0.026). In the chronic phase of 12-24 weeks, 50 patients were evaluated, with mean pain 5.27 ± 2.22, HAQ 1.16 ± 0.61, PCS of 38.82±17.26 and MCF 43.72±17.13). Thirty-two patients were employed, of which 25% were absent the antecedent week. During this stage, women presented lower values of MCS (p = 0.0245) and the presence of obesity was related to higher values in HAQ (p=0.0157). Finally, in the evaluation of the chronic phase after 24 weeks of evolution, we included 25 patients with the mean of pain 5.64 ± 2.3, HAQ 1.11 ± 0.49, PCS 36.72±19 and MCS 41.56±17.74. Fifteen of the 25 patients were employed and 33% were absent from work the previous week. There was no significant difference between the groups evaluated after 6 months of evolution.
Conclusion: In this study, we demonstrated that the impact of chikungunya persists after 1 month of evolution in a large number of patients. The incapacity for work caused by the disease, represented by persistent rates of absenteeism at work in an economically active age group, further aggravates the magnitude of the problem.

REFERENCES

[1] Couturier, E., Guillemin, F., Mura, et.al. Impaired quality of life after chikungunya virus infection: a 2-year follow-up study. Rheumatology. 2012 Jul; 51(7), 1315–22.
[2] Soumahoro, M.-K., Gérardin, P., Boëlle, P.-Y. Et al. Impact of Chikungunya Virus Infection on Health Status and Quality of Life: A Retrospective Cohort Study. PLoS ONE. 2009 Nov; 4(11), e7800.

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SAT0470 **RISK OF HOSPITAL ADMISSION DUE TO INFECTION IN PATIENTS UNDERGOING TREATMENT WITH BIOLOGICAL THERAPY: CASE-CONTROL STUDY**

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Objectives: To know risk of admission due to infection in patients treated with biological drugs (DMARDb).
Methods: Case-control study, in patients admitted for infection, treated with DMARDb, from 2000-2018. As a control group, patients included, in treatment with conventional synthetic DMARDs (DMARDcs).
General data (age, gender), disease (diagnosis, time evolution, DMARDb, time in DMARDb, DMARDcs); and infection (time in DMARDb to infection, location of infection, more than one admission).
Results: Of 364 patients, 48 (13%) admitted for infection: 32 (9%) treated with DMARDb, 16 (4%) with DMARDcs alone. When comparing patients admitted vs who do not, RA predominates and no differences in the treatment with DMARDb and/or DMARDcs, corticosteroids, type of DMARD or the infection.

Of 275 patients with DMARDb, 41 admissions for infection in 32 patients (11.6%); more than once. 20 (62.5%), were women, with mean age 69.2 ±2.12 years, mean time evolution 24.5±22.6 years. Diagnosis was RA: 22 (69%) patients, ankylosing spondylitis: 7 (22%), psoriatic arthritis: 3 (9%). Concomitant with DMARDcs in 81% and 26% corticosteroid (mean dose: 4.6±2.6 mg). The diagnosis of 41 admitted was: Pneumonia: 9 (41%), non-pneumonic respiratory infection: 5 (24%), septic arthritis: 8 (24%), urinary infection-pyelonephritis urinary o sepsis: 8 (22%), influenza A: 3 (7%), abscess, gastroenteritis and leishmaniasis in 2 (5%) each, osteomyelitis and varicella in 1 (2%) each.

The DMARDb at admission were: anti-TNF: 34 (83%) patients (adalimumab: 19/46%, etanercept: 7/17%, infliximab: 4/10%, golimumab and certolizumab: 2/5% each), tocilizumab: 4 (10%), abatacept: 2 (5%).

When comparing patients admitted for infection, patients with DMARDb has higher number of admissions (41 (67%) vs 20 (33%), p <0.01), and lower percentage of DMARDcs (23/72%) vs 16 (100%). p=0.02) and corticosteroids (14/34% vs 10/50%). p <0.001), at similar doses (4.7±2.6 vs 4.5±2.6 mg, p = 0.7). The incidence of admission for infection are indicated in table.

Conclusion: 1. The prevalence of admission due to infection in DMARDb is 9% and 4% in DMARDs in monotherapy. 2. Admission predominates in RA, with a long evolution, with biological therapy. 2. The most frequent infections were respiratory origin, followed by sepsis or bacteremia and septic arthritis.

	DMARDb	DMARDcs	DMARDb +DMARDcs
Admission general incidence for infection	1.92 (0.88-3.58)	0.95 (0.6-1.42)	2.6 (1.55-4.05)
Admission incidence for infection in RA	4.1 (1.47-8.82)	1.16 (0.72-1.75)	2.64 (1.37-4.53)
Mean time (years) to admission due to infection[1]	7.77 (4.17-11.36)	19.17 (13.83-24.52)	6.15 (4.06-8.23)
Mean time (years) until admission for infection, in RA	9.05 (3.58-14.53)	17.95 (12.99-22.9)[2]	6.6 (3.93-9.26)

[1]p<0.001.
[2]p<0.001, DMARDb vs DMARDcs

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SAT0471 HIGH-RESOLUTION MELTING CURVE ANALYSIS: A RAPID AND PRAGMATIC APPROACH FOR SCREENING OF MULTIDRUG RESISTANT OSTEOARTICULAR TUBERCULOSIS (OATB)

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Background: Emergence of MDR in extrapulmonary tuberculosis (EPTB) is a major concern in endemic areas. Timely diagnosis and screening of multidrug resistance in patients of Osteoarticular Tuberculosis (OATB) is a challenge.

Objectives: To evaluate the rpoB gene real time PCR (RT PCR) in synovial fluid/pus samples and its comparison with MPB64 and IS6110 RT PCR for diagnosis of OATB.

Methods: Real time PCR using IS6110, MPB64 and *rpo*B genes was carried out in 150 cases of OATB and in100 non TB control group. Out of these, 20 OATB cases were culture confirmed and 130 were clinically suspected cases. Phenotypic susceptibility testing for culture isolates was performed by standard proportion method.DNA extracted from samples of the culture confirmed cases and the suspected OATB cases confirmed by RT PCR were subjected to *rpo*B and *kat*G HRM analysis for screening of MDR.

Results: The sensitivity of *rpo*B RT PCR, MPB64 RT PCR and IS6110 RT PCR was 86.5%, 86.5% and 76.5% respectively. All RT PCR were negative in the control group thus the specificity was 100%. HRM analysis detected rifampicin resistance in 10 cases of which, 8 (80%) were MDR while 2 (20%) had isolated rifampicin resistance. Of the 13 cases of isoniazid resistance detected by HRM analysis, 8(61.5%) were MDR while 5(38.46%) were isolated isoniazid resistant. HRM analysis detected an additional 4 MDR cases directly from the samples which were negative by culture. Subsequently, results of HRM analysis were confirmed by *rpo*B sequencing and mutation were observed at codon 531 (60%); 533 (16%); 516 (12%) and 526 (12%). *kat*G sequencing revealed mutation at codon 315(100%). There was 100% concordance in the results of phenotypic DST, sequencing results and HRM analysis.

Conclusion: *rpo*B and *kat*G HRM analysis is a promising method in reliable and rapid screening of drug resistance in OATB cases in 90 minutes.

Disclosure of Interests: None declared

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SAT0472 THE CONTRIBUTION OF MRI IN THE DIAGNOSIS OF INFECTIOUS SPONDYLODISCITIS

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Background: Infectious spondylodiscitis is a diagnostic and therapeutic emergency, and if there is any doubt, an MRI should be performed to support the diagnosis.

Objectives: The aim of our study is to highlight the role of MRI in the diagnosis of infectious spondylodiscitis.

Methods: This is a 20-year retrospective study (1999-2019) performed at a rheumatology department, collecting cases of infectious spondylodiscitis. We have identified the epidemiological, clinical, and radiological characteristics.

Results: Our study included 106 patients, 57 men and 49 women. The average age was 55 [16; 86]. Mean disease duration averaged 4.54 months [0.23; 24]. All patients had spinal pain: lumbar in 65.09% of cases, dorsal in 17% of cases and cervical in 6% of cases. Standard X-rays showed abnormalities suggestive of spondylodiscitis in 88.67% of cases. Magnetic resonance imaging was then performed in 76.41% patients and was pathological in all cases. The abnormalities found were paravertebral abscess in 23.58% of cases, epiduritis in 10.37% of cases and association of abscess and epiduritis in 32.07% of cases. The rest of the abnormalities noted were vertebral osteolysis (8.49%), spinal cord compression (9.43%) abnormalities of the intervertebral disc with narrowing and/or signal modification (4%). The abnormalities were monofocal in 82.07% of cases and bifocal in 13.2% of cases. 78.57% of bifocal lesions were objectified in tuberculous spondylodiscitis. 82.07% of the spinal injuries were single-stage and 15.09% were bi-staged. 75% of these were of tuberculous origin. There were 2.83% of spondylodiscites up to 3 stages and all were tuberculous.

Conclusion: MRI is a great diagnostic aid during infectious spondylodiscitis. It also allows to orient towards the etiological diagnosis.

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SAT0473 MUSCULOSKELETAL STIFFNESS IN CHIKUNGUNYA DISEASE: DISTINCT FROM PAIN AND RELEVANT TO QUALITY OF LIFE

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Background: Musculoskeletal stiffness is reported to be frequent following chikungunya infection and can persist for many months after infection. However, stiffness severity and its impact is not well characterised in this disease. A stiffness patient reported outcome instrument has been developed for use in rheumatoid arthritis.

Objectives: Our objective was to assess the use of this questionnaire and importance of musculoskeletal stiffness in a cohort of chikungunya

patients with chronic joint symptoms in the Atlántico Department of Colombia.

Methods: Sixty-seven patients with chronic arthralgia and 15 patients without arthralgia were followed up a mean of 40 months after chikungunya infection. The patients came from a larger cohort of 500 patients previously followed up 20 months after infection. Those consenting to a 40-month in-person follow-up were included here. Tender joint counts, a pain intensity visual analogue scale (VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI) and the EuroQol overall health VAS (EQ-VAS) were completed. A 21-item musculoskeletal stiffness questionnaire (MSQ) was completed and summarized as percentage scores for overall stiffness and its components: stiffness severity, physical impact and psychosocial impact.

Results: The 82 patients (12 male and 70 female) had a mean age 51 ±14 years. Forty-two out of sixty-seven patients with arthralgia and 3/15 patients without arthralgia reported musculoskeletal stiffness. Stiffness in those patients had a median severity of 28% (IQR 0-42). An impact of their stiffness on physical activities was reported by 39/45 patients (87%) and psychosocial impact by 32/45 patients (71%). Overall MSQ score was a median of 16% (IQR 0-34). Mean tender joint count in patients reporting arthralgia was 6.2±7.1, mean pain intensity 65±20 out of 100, mean HAQ-DI = 0.54±0.52, and a mean EQ-VAS = 68±62 out of 100.

Overall stiffness scores were poorly correlated with tender joint counts (r^2=0.17) and pain intensity (r^2=0.22). Stiffness scores were more strongly associated with the HAQ-DI (r^2=0.52) and EQ-VAS overall health VAS scores (r^2=0.46), whereas tender joint counts were not: r^2=0.22 for HAQ-DI and r^2=0.21 for EQ-VAS.

Conclusion: Musculoskeletal stiffness following chikungunya infection is distinct from the persistent arthralgia usually reported. It does not necessarily occur in the same patients and is poorly correlated with joint pain severity. Stiffness, as measured by this questionnaire, may be more strongly associated than arthralgia with overall health and disability indices in patients with chikungunya disease. The MSQ is a potentially useful instrument for assessing symptoms in chronic chikungunya disease.

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SAT0474 AUTOIMMUNE MANIFESTATIONS OF VISCERAL LEISHMANIASIS IN CHINESE PATIENTS

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Background: Visceral leishmaniasis (VL), caused by the protozoan Leishmania species, is the most severe form of leishmaniasis. The parasite migrates to the internal organs such as the liver, spleen, and bone marrow, and if left untreated, will almost always cause the host to die [1]. Due to polyclonal B cells activation, VL may present signs and symptoms resembling those of rheumatic diseases, especially systemic lupus erythematosus (SLE) [2-4]. This can sometimes lead to mis-diagnosis and treatment of corticosteroids.

Objectives: To analyze 27 Chinese VL patients retrospectively and focused on their autoimmune findings that could help clinicians to differentiate VL from SLE.

Methods: 27 in-hospitalized VL patients in our hospital from 2006 to 2015 were analyzed. VL was diagnosed by the presence of high titers of anti-leishmania antibodies in the blood or by demonstration of intracellular parasites on bone marrow aspiration. All patients were negative for hepatitis B, hepatitis C and human immunodeficiency viruses. Autoimmune antibodies were detected. Levels of serum globulins, complement C3, C4 and RF were evaluated. Coagulation parameters, including prothrombin time (PT) and activated partial thromboplastin time (APTT) were also tested.

Results: The basic characteristics and laboratory findings of the 27 patients were summarized in Table 1. All patients had hepatosplenomegaly. 38.9% had positive ANA, but the titer was no more than 1:320. None of the patients had positive anti-Sm antibody and only 1 had anti-dsDNA antibody. 89.5% had increased IgG level and none had decreased C3 or C4.

All patients were cured with sodium stibogluconate, and ANA titers decreased after treatment.

Conclusion: VL may mimic symptoms of SLE due to polyclonal activation of B cells. However, hepatosplenomegaly is a common symptom seen in VL but not so common in SLE. Furthermore, VL patients don't have typical autoantibodies of SLE, their ANA titer are normal to low and they tend to have normal complements, which could help clinicians to differentiate these two diseases.

Table 1. Basic characteristics and clinical manifestations of VL patients

Sex (Femal/Male)	4/23
Age (median, range)	37 (9-59)
Disease duration (months) (median, range)	1 (0.17-24)
Anti- leishmania antibodies positive	27
Parasites positive in bone marrow	24
Fever	25
Hepatosplenomegaly	27
Weight loss	14
Anemia	26
Leucocytopenia	23
Thrombocytopenia	20
Prolonged APTT	12/21
Prolonged PT	12/21
Positive ANA	7/18

REFERENCES

[1] Martins-Melo FR, Lima Mda S, Ramos ANAN Jr., and, et al. Mortality and case fatality due to visceral leishmaniasis in Brazil: a nationwide analysis of epidemiology, trends and s patial patterns. PLoSOne. 2014; 9: e93770.

[2] Ozlem Guzel Tunccan, Abdurrahman Tufan, Gülçin Telli, et al. Visceral Leishmaniasis Mimicking Autoimmune Hepatitis, Primary Biliary Cirrhosis, and Systemic Lupus Erythematosus Overlap. Korean J Parasitol. 2012; 50 (2): 133–6

[3] Voulgarelis M, Voulgari PV, Serelis J, et al. Visceral leishmaniasis mimicking systemic lupus erythematosus. J Clin Rheumatol. 2010;16(4): 203-4.

[4] Drosos AA, Skopouli FN. Visceral leishmaniasis resembling systemic lupus erythematosus. Clin Rheumatol. 2003; 22(6):452-5.

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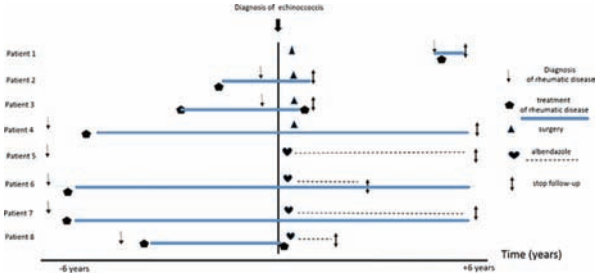
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SAT0475 ECHINOCOCCOSIS AND AUTO-IMMUNE INFLAMMATORY ARTHRITIS; REPORT OF 8 CASES AND REVIEW OF THE LITERATURE

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Background: The prevalence of Echinococcosis in Western Europe and Switzerland has been rising in the past 20 years: >30 cases per year have been reported since 2005 (1). A few case reports (2) and some experimental animal studies (3) have suggested that the immunosuppression linked to inflammatory arthritis and their treatments could favor the development and the growth of parasitic lesions. On the other hand, a recent French study (4) has a shown that the prevalence of Echinococcosis in arthritis patients was close to the normal population. The characteristics of the parasitic disease were quite similar whether inflammatory arthritis was present or not

Objectives: To evaluate the yearly recent incidence of this disease among patients with inflammatory arthritis in Switzerland and to search



for any interaction between arthritis, the treatment of arthritis and development and evolution of the echinococcosis.
Methods: We collected all the cases with the diagnosis of echinococcosis among the patients regularly followed and treated for inflammatory arthritis in three different tertiary rheumatology centers of Westen Switzerland (1.7 million inhabitants, 5000 arthritis pts).
Results: Between 2012 and 2018, 8 cases of echinococcosis (1.3 case/year/5000pts) could be found. The estimated yearly incidence among this arthritis population appears therefore to be significantly higher ($p<0.0001$) than the one reported in the general population in Switzerland (30/8000000 inhabitants). Figure summarized the relation between the parasitic and the inflammatory disease. Different types of inflammatory arthritis were implicated. Previous and ongoing arthritis treatments comprised also different types of biologics. In 6/8 cases, the parasitic disease was asymptomatic and limited to a single organ, a proportion much higher than what is usually found in the general population. In 2 of them, the discovery was very close in time to the diagnosis of arthritis and treatment initiation (<6 months). 4 pts could be treated by surgery alone. 6 continued their treatments for arthritis. No evidence of relapses after surgery (4 pts) or progression under albendazole (4 pts, median follow-up: 44 months) was found.
Conclusion: The incidence of echinococcosis in autoimmune arthritis appears to be higher than in general population but remains very low. Outcome seems not to be affected by inflammatory arthritis and their treatments but the long-time effects of the combination between arthritis treatments and albendazole need to be further evaluated.

REFERENCES

1:. Vuiton DA, et al. :Veterinary parasitology (2013), 110-20
2:. Weiner SM et al; Rheumatol Int (2011),1399–1400
[3] : Armuda-Fernandez MT, et al.; Parasitology (2016), 1252–1260.
[4] : Gauchet A, et al.; Clinical Infectious Diseases (2014),1095–104

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Paediatric rheumatology

SAT0476 JUVENILE IDIOPATHIC ARTHRITIS IN SINGAPORE: A 10-YEAR CLINICAL EXPERIENCE

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Background: Juvenile Idiopathic Arthritis (JIA) is the commonest inflammatory arthritis of childhood worldwide.
Objectives: To describe the incidence, clinical characteristics and experience with JIA in Singapore over a 10-year period.
Methods: A prospective study was conducted in KK Women's & Children's Hospital and National University Hospital, Singapore from Jan 2009-Dec 2018. JIA was defined and classified according to ILAR criteria[1]. Demographics and clinical information were collected for every patient diagnosed with JIA.
Results: 379 children were diagnosed with JIA (60.2% male, 71.2% Chinese). Average estimated incidence was 5.8 per 100000/yr. Clinical characteristics and treatment used are summarized in Table 1.
Table 1. *Median (IQR). Rest expressed in n (%).

	Overall	Systemic	Oligo-articular	Polyarticular (RF -)	Polyarticular (RF +)	Psoriatic	ERA	Undifferentiated
N (%)	379 (100)	32 (8.4)	133 (35.1)	47 (12.4)	13 (3.4)	10 (2.6)	137 (36.1)	7 (1.8)
Onset age, yr*	10.4 (6.6-13.3)	6.6 (4.5-10.1)	8.5 (5.1-12.1)	7.9 (3.5-12.8)	9.9 (7.1-13.5)	13.3 (6.2-14.3)	12.2 (10.0-14.3)	9.7 (6.2-13.5)
Diagnosis age, yr*	10.9 (7.1-14.0)	6.4 (4.1-10.2)	9.0 (6.0-13.4)	8.6 (3.7-13.3)	10.2 (7.4-13.7)	13.8 (10.7-15.3)	12.6 (10.7-14.7)	11.2 (9.2-15.1)
Lag time, mth*	2.9 (1.0 – 7.4)	0.7 (0.3-1.2)	3.1 (1.1-7.6)	3.0 (1.6-9.8)	2.6 (2.1-4.6)	5.0 (1.2-12.4)	3.6 (1.2-8.1)	8.3 (1.6-36.5)
ANA *(n = 253)* Positive	124 (32.9)	11 (34.4)	50 (40.3)	23 (48.9)	5 (38.5)	8 (80.0)	27 (20.0)	0 (0.0)
RF *(n = 374)* Positive	23 (6.1)	5 (17.2)	2 (1.5)	0 (0.0)	13 (100.0)	0 (0.0)	2 (1.5)	1 (14.3)
HLA-B27 *(n = 368)* Positive	112 (30.4)	0 (0.0)	4 (3.1)	2 (4.3)	0 (0.0)	0 (0.0)	104 (75.9)	2 (28.6)
Uveitis diagnosed	11 (2.9)	0 (0.0)	6 (4.5)	1 (2.1)	0 (0.0)	0 (0.0)	4 (2.9)	0 (0.0)
DMARD use	257 (67.8)	21 (65.6)	47 (35.3)	40 (85.1)	13 (100.0)	10 (100.0)	121 (88.3)	5 (71.4)
Biologic use	145 (38.3)	17 (53.1)	17 (12.8)	17 (36.2)	9 (69.2)	3 (30.0)	79 (57.7)	3 (42.9)

Disease modifying anti-rheumatic drugs (DMARD) were used in 67.8%, and younger age of diagnosis ($p=0.002$), longer lag time ($p=0.004$), males ($p=0.018$) and ERA ($p=0.043$) predicted their use. 38.3% required biologics, and males ($p=0.047$), longer lag time ($p=0.037$) and HLA-B27 positivity ($p=0.030$) were associated with their use. Uveitis incidence was 2.9%; 54.5% had oligoarthritis, 36.4% ERA, 9.1% polyarthritis (RF-). Younger age at JIA diagnosis was associated with uveitis ($p=0.030$).
Conclusion: ERA is the commonest subtype of JIA in our cohort, explaining the male predominance and higher HLA-B27 positivity as compared to the West[2]. Longer lag time was associated with DMARD and biologic use, likely due to more severe disease at presentation. HLA-B27 association with biologic use may predict ineffectiveness of DMARD. Uveitis incidence was low as compared to Western literature that cites a prevalence of 11-30%[3,4]. Young age at diagnosis is a risk factor for uveitis. Interestingly, ANA-positivity and female gender were not associated with uveitis cases.

REFERENCES

[1] Petty RE, et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004 Feb;31(2):390-2.
[2] Žuber Z, et al. Prevalence of HLA-B27 antigen in patients with juvenile idiopathic arthritis. Reumatologia. 2015;53(3):125-30.
[3] Angeles-Han ST, et al. Characteristics of a cohort of children with Juvenile Idiopathic Arthritis and JIA-associated Uveitis. Pediatr Rheumatol Online J. 2015;13(1):19.
[4] Clarke SL, et al. Juvenile idiopathic arthritis-associated uveitis. Pediatr Rheumatol Online J. 2016;14:27.

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SAT0477 QUALITY OF LIFE IN SUBJECTS WITH PRE-PUBERTAL ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) can be a severe disease, especially when diagnosed in childhood. Onset prior to puberty (Tanner stage II) is rare, and less is known about the impact SLE has on this pediatric subpopulation. We assessed clinical and quality of life (QOL) measures in a prepubertal SLE onset cohort to better globally understand the burden of this disease in this group.

Objectives: To assess quality of life measures in pre-pubertal subjects with SLE and examine the correlation with clinical manifestations.
Methods: In a prospective, multicenter (10 Childhood Arthritis and Rheumatology Research Alliance sites), observational study, subjects with pre-pubertal onset of SLE were enrolled. Subjects either were still in Tanner I or no later than Tanner stage II at enrollment. QOL measures were collected in addition to comprehensive medical history, physical examination findings, laboratory assessments, SLEDAI-2K scores, and SLICC/ACR Damage Index. QOL measures were obtained by PedsQL™ 4.0 Core and PedsQL™ 3.0 Rheumatology Module surveys completed by the child at the enrollment visit. QOL means were compared with disease manifestations by t tests.
Results: QOL data was available for 42 subjects (31 females, 11 males). At enrollment, the mean age of diagnosis was 9.9 years, with a mean disease duration of 1.2 years. Males were older at diagnosis than females (10.9 vs 9.5 years, p=0.023) with no difference in enrollment disease duration. The mean SLEDAI-2K score was 7 (range 0-18). Disease activity and individual SLE manifestations did not vary by gender. Laboratory markers of activity were present more frequently on the SLEDAI-2K than clinical exam findings, of which rash (24%), alopecia (12%) and arthritis (12%) were the most common. Seven subjects had disease damage reported on the SLICC/ACR DI.

PedsQL™ Measure	% Affected	Mean Score
PedsQL™ 4.0 Core	86%	83.8
Physical Health	67%	85.4
Emotional Functioning	69%	85.0
Social Functioning	52%	88.3
School Functioning	79%	76.4
PedsQL™ 3.0 Rheumatology Module	81%	86.2
Pain and Hurt	55%	82.6
Daily Activities	24%	95.7
Treatment	60%	86.5
Worry	40%	84.1
Communications	45%	82.1

School functioning domain had the worst QOL measure with the greatest number of children impacted (Table). Active arthritis was associated with lower mean scores in Physical Health (p=0.007), PedsQL Core total (p=0.048), Pain and Hurt (p=0.002), Daily Activities (p=0.003), Treatment (p=0.002), Worry (p=0.036), and PedsQL Rheumatology total (p=0.001). There was no association with QOL measures for rash, alopecia, or laboratory markers. Disease damage on SLICC/ACR DI was associated with greater impact on the Worry domain (mean 64.3 vs 88.1, p=0.23).
Conclusion: Children with pre-pubertal SLE onset report significant impacts on QOL regarding school. The disease manifestation affecting the most QOL domains was arthritis, whereas skin manifestations, while common, did not demonstrate an impact on QOL. This is the first study to specifically address quality of life for children who develop SLE prior to pubertal development.

REFERENCES

[1] Varni JW, Seid M, Smith Knight T, et al. The PedsQL in pediatric rheumatology: reliability, validity, and responsiveness of the Pediatric Quality of Life Inventory Generic Core Scales and Rheumatology Module. Arthritis Rheum 2002;46:714–25.

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SAT0478 AFTER 24 MONTHS OBSERVATION PERIOD THE PATIENTS RELATED OUTCOMES IMPROVE SIGNIFICANTLY IN THE JUVENILE SCLERODERMA INCEPTIONS COHORT. WWW.JUVENILE-SCLERODERMA.COM

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Background: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in a 1 000 000 children(1). Currently there is nearly no data published about the course of jSSc patients with standardized assessment. We report our date from Juvenile Scleroderma Inception cohort (JSSIC) with a follow up of 24 months.
Objectives: to evaluate the organ involvement and patient reported outcomes (PRO) during the first 24 months in the JSIC
Methods: The JSSIC is a prospective multicenter registry of patients with jSSc, who fulfill the adult classification criteria(2), and presented the first non-Raynaud symptom before 16 years of age and were younger then 18 years at the time of inclusion in the JSSIC. Patients who were followed at least 24 months in the JSSIC, were evaluated.
Results: 52 patients were followed at least 24 months in the registry. 77% were female and 77% had diffuse subtype. 19% had overlap features. Mean disease duration at time of inclusion was 3.2 years. Mean age of at Raynaud's onset was 8.8 years and the first non-Raynaud's symptom 9.4 years. 85% received DMARDs at the time of inclusion and 96% after 24 months. 88% of the patients were ANA positive, 35% anti-Scl70 positive and 3% anticentromere positive. The mean modified skin score decreased from 14.3 to 12.6. The frequency of Raynaud´s stayed around 87%. The frequency of the nail-fold capillary changes increased from 56% to 63%, but the frequency of active ulcerations stayed stable around 21%. The number of patients with FVC <80% decreased from 39% to 34% (p=0.734). The number of patients with pulmonary hypertension assessed by ultrasound increased from 4% to 8% (p=0.652). No patient developed systemic hypertension or renal crisis. Urinary sedimentary changes decreased from 8% to 4%. Gastrointestinal involvement decreased from 33% to 29% (p=0.829). Number of joints with decreased range increased from 46% to 63% (p=0.076). Total muscle weakness decreased from 8% to 3% (p=0.237) and elevated CK from 22% to 9% (p=0.033) too.
Several PROs improved significantly. Patient global disease activity (VAS 0-100) changed from 46 to 29 (p=0.002), patient global disease damage (VAS 0-100) from 46 to 28 (p=0.02) and patient Raynaud activity VAS 0-100) from 27 to 14 (p=0.009) as physician global disease activity (VAS 0-100) from 43 to 29 (p=0.021) and physician global disease damage from 46 to 28 (P=0.01).
Conclusion: Over the 24 months observation period patient and physician related outcomes improved significantly. Regarding organ involvement there was an increase in patients of pulmonary hypertension and joint contractures.

REFERENCES

[1] Beukelman T, Xie F, Foeldvari I. Assessing the prevalence of juvenile systemic sclerosis in childhood using administrative claims data from the United States. Journal of Scleroderma and Related Disorders. 2018;3 (2):189-90.
[2] van den Hoogen F, Khanna D, Fransen J, Johnson SR, Baron M, Tyndall A, et al. 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism collaborative initiative. Arthritis Rheum. 2013;65(11):2737-47.

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SAT0479 UPDATE FROM THE JUVENILE SCLERODERMA INCEPTION COHORT. WWW.JUVENILE-SCLERODERMA.COM

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Background: Juvenile systemic scleroderma (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. There are limited data regarding the clinical presentation of jSSc. The Juvenile Systemic Scleroderma Inception Cohort (JSSIC) is a multinational registry that prospectively collects information regarding patients with this disease in a standardized manner.

Objectives: Evaluation of the jSSc patients at the time of inclusion in the JSSIC.

Methods: Patients were included in the JSSIC if they fulfilled the adult classification criteria, if they presented the first non Raynaud symptom before 16 years old and if they were younger than 18 years of age at the time of inclusion. Patients' characteristics at time of inclusion were evaluated.

Results: Currently, the cohort includes 120 patients, being 89% Caucasian and 80% female. The majority had diffuse subtype (74%) and 18% had overlap features. The mean age of onset of Raynaud phenomenon was 9.7 years in the diffuse subtype (djSSc) and
10.7 years in the limited subtype (ljSSc). The mean age of non-Raynaud's symptoms was 10.0 years in the djSSc and 11.4 years in the ljSSc (p=0.041). Mean disease duration at time of inclusion was 3.4 years in the djSSc and 2.4 years in the ljSSc group.
Mean Modified Rodnan skin score was 17.5 in the djSSc and 7.3 in the ljSSc (p=0.002). Gottron papulae were significantly more common in the djSSc compared to ljSSc group (29% vs 6%, respectively) (p=0.011). History of ulceration was significantly more common in the djSSc than in the ljSSc group (57% vs 30%, respectively) (p=0.004). FVC<80% occurred in 31% in the djSSc and 24% in the ljSSc group (p=0.55). Pulmonary hypertension assessed by echocardiogram occurred around 7% in both groups. No systemic hypertension or renal crisis was reported. Gastrointestinal involvement occurred in 39% in the djSSc and in 26% in the ljSSc (p=0.176). Number of joints with decreased range of motion was observed in approximately half of patients in both groups. Muscle weakness with joint contractures was present in 18% in the djSSc and 38% in the ljSSc group (p=0.271). Tendon friction rub was present in 11% in djSSc and 4% in the ljSSc group. djSSc patients had significantly worse scores for physician global disease activity (VAS 0-100) (41vs 30) (p=0.020) and for physician global disease damage (VAS 0-100) (37 vs 18) (p=0.001). Patient judgment of disease activity and damage was similar in both subtypes. ANA positivity was 88% in both groups. Anti-Scl70 was positive in 33% in djSSc and 37% in the ljSSc group. Anticentromere positivity occurred in 3% in the djSSc and 10% in the ljSSc group. ESR was elevated in 30% in djSSc compared to 18% in the ljSSc group. DMARDs were used in 86% of the patients.

Conclusion: In this large cohort of jSSc patients there were surprisingly not many significant differences between djSSc and ljSSc. According to the physician global scores the djSSc patients have a significantly more severe disease.

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SAT0480 CHRONIC KIDNEY DISEASE IN PATIENTS WITH JUVENILE SYSTEMIC LUPUS ERYTHYMATOSUS: EVIDENCE FROM A SINGLE CENTRE

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Background: Estimated 10- 20% of all patients with systemic lupus erythematosus (SLE) develop clinical disease before the age of 18 years and are therefore classified as juvenile-onset SLE (JSLE). JSLE is characterised by a higher prevalence of lupus nephritis, compared to adult- onset SLE (1). Chronic kidney disease (CKD) refers to a state of irreversible kidney damage and/or reduction of kidney function that is associated with progressive loss of function over time. Lupus nephritis does not always lead to CKD. However, when it does it is associated with increased morbidity and mortality (2).

Objectives: We aimed to identify clinical and laboratory predictors of CKD development in JSLE patients by comparing the baseline characteristics of JSLE patients with and without CKD to ascertain if there are any significant differences between the two groups.

Methods: This is a single-centre retrospective study, who included patients reviewed in our young adult and adolescent clinics. All data were analyzed descriptively. Mann- Whitney U or Chi- square test were performed to compare the characteristics between the patients with and without CKD. We used the Pearson's (r) or Kendall's τ (tau) correlation to examine if there is any association between the CKD and the baseline characteristics.

Results: We identified 44 JSLE patients, out of which 17 (39%) fulfilled the diagnostic criteria for CKD at their last clinical review. The stages of CKD varied from 2 to 5. All patients with CKD also had lupus nephritis, while 5/44 patients (11%) had lupus nephritis without CKD. The baseline characteristics are detailed in the table below. There were statistical significant differences in the treatments used for patients with and without CKD. As expected, the highest dsDNA levels were higher in patients with CKD (p= 0.03). There was also a positive moderate correlation (ρ= 0.32) between raised levels of dsDNA and the development of CKD (p= 0.008). We also found a negative moderate correlation (τ= -0.439) between the presence of RF and CKD (p= 0.04).

Conclusion: Acknowledging the limitations posed by this small study, we identified a negative moderate correlation between the presence of RF and CKD, which has also been reported in the literature before (3). We cannot conclude that RF exerts a protective effect against renal disease in SLE, because of the many confounders that might account for a decreased RF in JSLE. Further research using a large JSLE cohort enabling multivariate logistic regression is recommended. DsDNA antibody levels are a measure of disease activity in lupus nephritis and therefore this might explain why patients who developed CKD were noted to have higher anti-dsDNA levels, in comparison with the patients who did not develop CKD.

REFERENCES

[1] Ambrose N, et al. Differences in disease phenotype and severity in SLE across age groups. Lupus. 2016;25(14):1542-50.
[2] Hagelberg S, et al. Longterm followup of childhood lupus nephritis. J Rheumatol. 2002;29(12):2635-42.
[3] Helin H, et al. Rheumatoid factor in rheumatoid arthritis associated renal disease and in lupus nephritis. Ann Rheum Dis. 1986;45(6):508-11.

Table: Baseline characteristics of JSLE patients in the Arthritis UK Centre for Adolescent Rheumatology

	CKD	Without CKD	p
Number of patients, n (%)	17 (39%)	27 (61%)	
Female, n (%)	14 (80%)	23 (85.2%)	p= 0.47
Age at diagnosis, years	12 (10- 11)	12 (11- 15)	p= 0.62
Disease duration, years	12 (8- 14)	12 (7- 13)	p= 0.78
Highest dsDNA	215 (34- 644)	32 (6.8- 104)	p= 0.03*
SLEDAI at last assessment	2 (0- 4)	0 (0- 2)	p= 0.33
Arthritis, n (%)	13 (76%)	16 (59%)	p= 0.24
Rituximab, number of courses	1.5 (0- 2.3)	0 (0- 1)	p= 0.04*
Mycophenolate Mofetil, months	44 (21- 96)	17 (0- 70)	p= 0.04*
Steroids, months	48 (37- 82)	25 (11- 50)	p= 0.03*

Numbers are medians (interquartile ranges) unless otherwise stated. *p< 0.05 is significant

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SAT0481 DIAGNOSIS AND INITIAL MANAGEMENT OF JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS IN THE UK AND IRELAND

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Background: The incidence of Juvenile-onset Systemic Lupus Erythematosus (JSLE) in the UK is not well described. Furthermore, we do not know how children and young people initially present and when and where they access care. Previous work has described significant variation in time to diagnosis for UK patients[1].
Objectives: To describe how patients with JSLE currently present, are diagnosed and managed across the UK.
Methods: Data was collected over 13 months on all children (aged <18 years) in the UK and Ireland with a new diagnosis of JSLE (meeting either American College of Rheumatology classification criteria (ACR-1997) or Systemic Lupus International Collaborating Clinics classification criteria (SLICC-2012)). Data was collected monthly from all UK and Ireland paediatricians using British Paediatric Surveillance Unit (BPSU) methodology[2] and from relevant adult clinicians using a parallel reporting system. Anonymised patient data was collected by the clinician and sent to the study team. Patient consent was not required following Ethical and Confidentiality Advisory Group approval.
Results: 102 cases were reported from Sept 2017–Oct 18. 65 cases were excluded (duplicate cases, diagnosis date outside study period, case definition not met, clinical data pending) and 37 included.
All patients met SLICC-2012 and 35 patients met ACR-1997. Of the two patients meeting SLICC-2012 but not ACR-1997, one had lupus nephritis on renal biopsy and positive ANA, and the other met the SLICC-2012 hypocomplementaemia criterion.
Of the 35 patients meeting ACR-1997, median age at diagnosis was 12.8 years (interquartile range (IQR) 11.8–14.7 years) with female:male gender of 4.8:1 respectively. 24/35 (69%) were non-Caucasian. Median time from symptom onset to diagnosis was 2 months (IQR 1–6 months). The longest delay was 106 months (patient initially diagnosed with Henoch Schnolein Purpura). 9/35 (26%) of patients experienced a delay in diagnosis measured by at least one of: established organ damage due to JSLE at diagnosis (5 patients), review by $\geq$1 paediatric sub-specialist prior JSLE diagnosis (3 patients) or patient not referred despite medical review (6 patients).
The diagnosis was made by or in conjunction with paediatric rheumatology in 21/35 (60%) patients. 4/35 (11%) patients were diagnosed solely by paediatric nephrology, 2/35 (6%) by adult rheumatology, 7/35 (20%) by general paediatrics and 1/35 (3%) by the paediatric infectious diseases team. Of the 12/35 (34%) patients where diagnosis did not involve a rheumatologist 10 were referred to either adult or paediatric rheumatology and 2 patients were managed solely by paediatric nephrology.
31/35 (89%) patients were treated with oral and/or IV steroids and 33/35 (94%) with hydroxychloroquine. Other treatments used were: mycophenolate mofetil (17/35, 49%); rituximab (8/35, 23%); azathioprine (6/35, 17%); methotrexate (5/35, 14%); cyclophosphamide (3/35, 9%); ofatumumab (1/35, 3%); IV immunoglobulin (1/35, 3%); plasmapheresis (1/35, 3%). No patients died within one month of diagnosis.
Conclusion: Diagnosis of JSLE involved paediatric rheumatology in 60% of cases. Median time to diagnosis from symptom onset is two months but there is significant variation; future work will focus on factors influencing this. Analysis of final data (2 year incidence data) will facilitate estimation of current UK incidence rate and description of factors affecting time to diagnosis.

REFERENCES

[1] Smith EMD, Foster HE, Gray WK, Taylor-Robinson D and Beresford MW. Predictors of access to care in juvenile systemic lupus erythematosus: evidence from the UK JSLE Cohort Study. Rheumatology 2014;53:557-61
[2] RCPCH. British Paediatric Surveillance Unit. http://www.rcpch.ac.uk/bpsu (accessed 17th January 2019)

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SAT0482 TREAT-TO-TARGET STUDY FOR IMPROVED OUTCOME IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

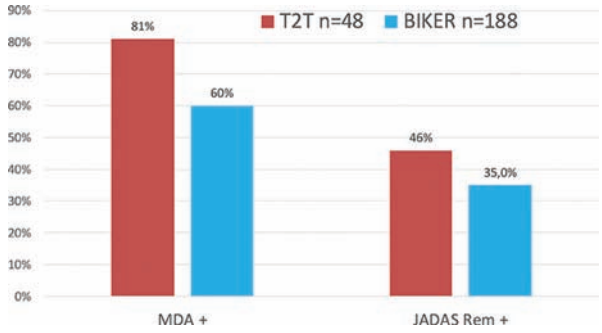
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Background: Evidence suggests that early effective treatment is important to minimize the burden of Juvenile idiopathic arthritis (JIA). We hypothesize that a guided treat to target (T2T) approach as recommended by the German Society for Pediatric Rheumatology (1) is superior to routine care in polyarticular JIA (pJIA) in terms of reaching minimal disease activity and remission after 12 months of treatment.
Objectives: To assess the clinical benefit in subjects with pJIA treated in compliance with national recommendations measured by rates of patients reaching JADAS remission ($\leq$ 1), JADAS minimal disease activity (MDA) ($\leq$3.8), JADAS acceptable disease status ($\leq$ 5.4).
Methods: After informed consent, patients with early (disease duration $\leq$ 12 months) and active (JADAS10 > 5.4) pJIA were enrolled. Initially, all patients received methotrexate (MTX). Targets for treatment were defined by the level of improvement and are progressively more rigourous with ongoing treatment. Failure to meet a defined target required treatment modification of specified intervals. The choice of biologic was made by shared decision between the investigator and the patient/parent and not influenced by the protocol. Minimal treatment target defined as recognizable improvement of disease activity (2) was demanded after 3 months, JADAS acceptable disease status at month 6, JADAS MDA at month 9 and JADAS-remission at month 12. T2T Patients were 1:4 matched to a pJIA cohort with unguided therapy documented by the BIKER-registry.
Results: Altogether 62 patients (16 males, 26%) with non-systemic JIA (48/9 RF negative/positive polyarthritis, 3 extended Oligoarthritis, 1 ERA, 1PsA) were included (mean age 9.4+/-4.8 years, disease duration 0.5+/-0.6 years). At month 3; 49 (79%) patients showed JADAS improvement. In 13 (21%) treatment with a biologic was started. At month 6, 45/56 (80%) reached JADAS acceptable disease. In 6 (11%) a biologic agent was started. At month 9, 41/48 (85%) reached JADAS acceptable disease and 38/48 (79%) reached JADAS-MDA. In 4 (10.8%) a biologic was started and two patient switched biologics.
So far, 52 patients completed 12 months of observation. 4 patients did not start a biologic although mandatory according to protocol and were excluded. JADAS MDA was reached by 39/48 (81%) and JADAS remission was reached by 22/48 (46%). Compared to the matched control cohort, upon T2T guidance significant more patients reached JADAS MDA (81% vs. 60%; odds 2.9[1.3-6.3]; 0=0.006) and more patients reached JADAS remission (46% vs. 34%; odds 1.6[0.8-3.0]; p=0.15). During the first 12 months of treatment, the T2T approach lead to a significant increase of use of biologics (46% vs. 21%; odds 3.2[1.7-6.3]; p=0.0004).

	Baseline n=62	Month 3 n=62	Month 6 n=56	Month 9 n=52	Month 12n=48
JADAS mean +/-SD	19.2+/-4.9	7.8+/-5.7	4.3+/-4.8	3.2+/-4.5	2,6+/-2,8
JADAS- minimal response	n.a.	79%	89%	96%	96%
JADAS acceptable disease ($\leq$5.4)	0,0%	37%	80%	85%	83%
JADAS MDA ($\leq$3.8)	0,0%	34%	73%	79%	82%
JADAS Remission ($\leq$1)	0,0%	15%	30%	44%	46%
MTX only	100%	65%	62%	50%	48%
Biologics +MTX	0%	31%	33%	37%	29%
Biologics only	0%	3%	5%	13%	19%
2nd biologic	0%	0%	0,0%	4%	4%

Conclusion: These data indicate that a T2T concept is feasible and superior. A high rate of patients reached JADAS MDA and JADAS

remission after 12 months of treatment. Interestingly, about half of patients did not need to be treated with a biologic to reach predefined T2T (2). Thus, the early treatment escalation seems advantageous indicating a window of opportunity to successfully treat polyarticular JIA.



REFERENCES
[1] Horneff G, et al. Pediatr Rheumatol Online J. 2017; 15:78
[2] Horneff G et Becker I. Rheumatology. 2014;53:1229-34.

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Disclosure of Interests: Gerd Horneff: None declared, Joachim Peitz: None declared, Ivan Foeldvari Consultant for: Chugai, Novartis, Ralf Trauzeddel: None declared, Toni Hospach Speakers bureau: Chugai, Roche, Novartis, Tilmann Kallinich Grant/research support from: Novartis, Speakers bureau: Sobi, Roche, Novartis, CLB, Frank Weller-Heinemann: None declared, Ariane Klein: None declared, Kirsten Minden: None declared
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SAT0483 COMPARISON OF THE CLINICAL DIAGNOSTIC CRITERIA AND RESULTS OF THE NEXT GENERATION SEQUENCE GENE PANEL IN PATIENTS WITH PERIODIC FEVER

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Background: Autoinflammatory diseases (AID) are a group of hereditary diseases characterised by inflammation periods accompanied with clinical findings such as fever, skin rash, lymphadenopathy, abdominal pain, musculoskeletal symptoms, and with sign of inflammation in the blood. Each disease has own typical clinical findings and they are associated with mutations in specific genes such as in MEFV gene in familial Mediterranean fever (FMF), MVK gene in mevolonate kinase deficiency (MKD), TNFRSF1A gene in TRAPS and NLRP3 gene in cryopyrin associated periodic fever syndrome (CAPS). There are also patients exhibit the incomplete phenotype of a disease or overlap signs of more than one AID. The diagnosis of these patients have difficult and may not be possible by a single target gene analysis. Screening of the periodic fever syndrome (PFS) genetic panel including various AID genes may be beneficial to define the atypical cases.
Objectives: The aim of this study was to compare the phenotypic diagnoses to the genotypic results obtained from the PFS genetic panel, which studied in patients with phenotypic findings of AIDs except the FMF, such as MKD, TRAPS and CAPS.
Methods: This is a prospective study and conducted between June 2016 and December 2018. Patients who met "The Eurofever clinical diagnostic/classification criteria"* for MKD, TRAPS and CAPS were included in the study. Next-generation sequencing (NGS) analysis was performed including 8 genes (MEFV, MVK, NLRP3, NLRP12, TNFRSF1A, TNFRSF11A, LPIN2 and PSTPIP1) in 37 patients with phenotypic findings of MKD, TRAPS or CAPS. The patients phenotypic preliminary diagnoses and genotypic results were compared.
Results: Thirty seven patient included in the study who met the clinical diagnostic criteria for MKD, TRAPS or CAPS. As a result of clinical signs; 19 patients were diagnosed with MKD, 10 were TRAPS and 8 were CAPS.
In the PFS genetic screening panel of 19 patients with phenotypic diagnosis of MKD; disease causing mutation was found in 8 patients in MVK gene, in 3 patients in MEFV gene, in 2 patients in NLRP12 gene and in 1 patient in TNFRSF1A gene. No pathogenic mutation was shown in 3 patients and genetic variants of uncertain significance (VUS) in different genes were shown in two patient.
In the result of PFS panel of 10 patients with phenotypic diagnosis of TRAPS; disease causing mutation was found in 5 patients in MEFV gene and in 2 patients in TRAPS gene. No pathogenic mutation was identified in 3 patients.
In 8 patients who were diagnosed phenotypically as CAPS; disease causing mutation was found in 3 patients in NLRP3 gene, in 2 patients in NLRP12 and in one patient in MEFV. No mutation was detected in remaining two patient.
The final diagnosis was made by both phenotypic and genotypic data. In 37 patients (phenotypically 19 MKD, 10 TRAPS, 8 CAPS), respectively; 8 had MKD, 9 had FMF, 3 had CAPS, 3 had TRAPS, 4 had FCAS2 and 10 had undifferentiated PFS.
Conclusion: In our study, we have shown that clinical diagnostic criteria may not always be sufficient to establish the correct diagnosis. In case of clinical suspicion or in the presence of more than one autoinflammatory disease findings, NGS analysis may help to determined the diagnosis.
Acknowledgement: We are grateful to all participating children and their families. Ethics committee approval was received from the Institutional Review Board of Umraniye Training and Research Hospital. All the participants and their legal guardians were informed, and their written consent was obtained. Disclosure of Interest: None Declared
Disclosure of Interests: None declared
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SAT0484 QUALITY OF LIFE IN JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED UVEITIS: DO WE NEED A NEW ASSESSMENT QUESTIONNAIRE?

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Background: Uveitis, the most common extra-articular manifestation in juvenile idiopathic arthritis (JIA), occurs in 10-20% of patients. Although prognosis of uveitis within JIA (JIA-U) improved, complications still cause severe impairment of visual function in 25-33% of children that affects their psychophysical and psychosocial development and quality of life (QoL).
Objectives: To study the QoL and it's dimensions in children suffering from JIA-U as well as to investigate is there any difference in childhood's and parent's perception of disease between the group of children with JIA-U and children with JIA without uveitis.
Methods: The study included 42 children with JIA and their parents. Patients were divided into two groups. The first consisted of 21 children with JIA-U and the second of 21 children with JIA and no uveitis. Both groups of patients and their parents filled the Juvenile Arthritis Multidimensional Assessment Report questionnaire (JAMAR) for monitoring and assessing the health status of children with JIA. The variables used to test differences were: QoL, functional ability, pain level, disease activity estimation, and current emotional state of the child. The significance of differences between groups of children and parents was verified by the independent-samples t-test. The Pearson correlation coefficient was used for measurement of the strength of the linear relationship between variables.
Results: There were no statistically significant differences in the JIA-U group and the control group in either of the examined variables. Although there is a tendency of higher scores in children with JIA-U, which indicates their worse functioning, higher pain intensity and worse current emotional state, these differences were not statistically significant. Two groups did not differ significantly in the assessment of their own overall functional ability, which was associated with experienced pain intensity. Stronger pain intensity was associated with dysfunction (r = 0.642, p

<0.01) while a lower level of QoL was associated with more intense pain (r = 0.542, p <0.01) and poor current emotional state (r = 0.401, p <0.05). The activity of the disease in children was not significantly related to any determinant of the QoL. In contrast to children, parents of children with JIA-U estimated current emotional state of their children significantly worse (t = 2.05, p <0.05) and the overall level of functioning significantly lower than parents whose children did not have uveitis (t = 2.03, p <0.05).

Conclusion: Since children with JIA evaluated the QoL equally well, whether they had uveitis or not, we can conclude that they are psychologically well adapted to their health status and cope well with different levels of pain. Unlike children with uveitis, their parents evaluated the current emotional state and overall functionality significantly worse compared to parents of children who did not have uveitis. These results support a need for the development of new uveitis specific questionnaires that will enable us better identification of patient's requirements. It is necessary to implement a holistic and multidisciplinary approach to assess the emotional functioning of the children and their families, and to devise appropriate psychosocial interventions for continuing support for ill children and their families.

REFERENCES

[1] Filocamo G, Consolaro A, Schiappapietra B, et al. A new approach to clinical care of juvenile idiopathic arthritis: the Juvenile Arthritis Multidimensional Assessment Report. J Rheumatol. 2011;38:938-53.

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SAT0485 THE FIRST 18 MONTHS OF A PEDIATRIC RHEUMATOLOGY SERVICE AT A TERTIARY REFERRAL HOSPITAL IN KENYA

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Background: Pediatric rheumatic diseases impart a significant disease burden upon children and their families with the potential to cause diminished quality of life and significant direct and indirect costs [1-3]. Determination of the burden of disease is a prerequisite to improving access to care and optimizing use of the healthcare ecosystem for the well-being of these patients [4-5].

Objectives: We thus set out to describe what clinical cases were referred to the Pediatric Rheumatology Service at Aga Khan University Hospital Nairobi, Kenya (AKUHN) for the first 18 months since its establishment.

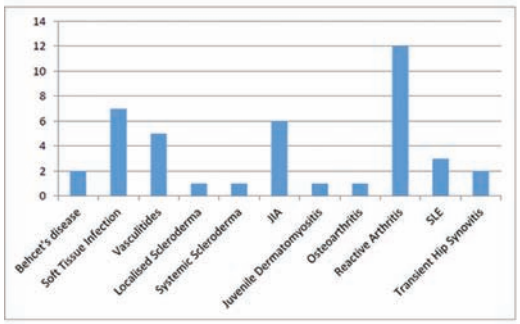
Methods: A prospective chart review of all patients referred to the pediatric rheumatology service at AKUHN was undertaken from October 2016 to March 2018. Patients were followed up for at least 3 months to determine the course of their disease. Data on bio-demographics and diagnosis was extracted from medical records of these patients and documented in a standard study tool. Frequencies were calculated for each disease category and sub-category.

Results: A total of 113 patients attended the pediatric rheumatology service of which 61.06% (69 of 113) were female and 53.15% (59 of 113) were aged above 10 years. Most patients attending the service were Kenyan accounting for 95.58% (108 of 113). Among the Kenyan patients seen, 77.88% (88 of 113) were from the capital, Nairobi. Out-patients accounted for 84.96% (96 of 113) of the patients compared to 15.04% (17 of 113) who were seen as in-patients. Inflammatory musculoskeletal conditions accounted for 36.3% of all cases (41 of 113) compared to 52.2% (59 of 113) of non-inflammatory musculoskeletal conditions.

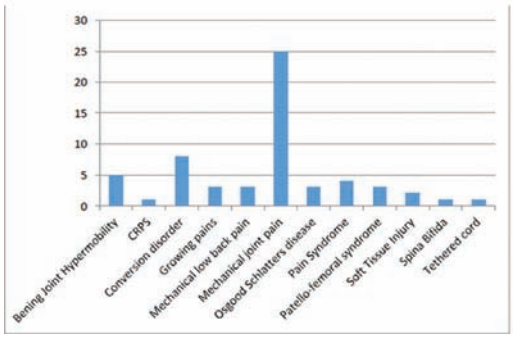
Among the inflammatory conditions diagnosed, reactive arthritis accounted for 29.3% (12 of 41), juvenile idiopathic arthritis (JIA) accounted for 14.6% (6 of 41) and vasculitis accounted for 12.2% (5 of 41) of the cases as demonstrated in graph 1. The non-inflammatory musculoskeletal conditions included mechanical joint pain 42.4% (25 of 59), conversion disorder 13.6% (8of 59), benign joint hypermobility 8.5% (5 of 59) among others as illustrated in graph 1. The other medical conditions diagnosed at the pediatric rheumatology service were two cases of acute lymphoblastic leukemia and one case of neurofibromatosis, serum sickness, sturge weber syndrome, diabetes, eczema, epidermolysis bullosa and a case of suspected griscelli syndrome. There were four patients lost to follow up; two children with prolonged fever and two others with unexplained painless unilateral limb swelling. There were three mortalities; two lupus patients and the systemic scleroderma patient, all of whom succumbed to sepsis.

Conclusion: Non inflammatory mechanical musculoskeletal complaints are the commonest complaints noted at AKUHN pediatric rheumatology clinic. The three commonest inflammatory musculoskeletal conditions are reactive arthritis, JIA and vasculitis. Sepsis was the main cause of mortality among the pediatric rheumatology patients. Further studies are required to better describe the burden and natural history of these diseases in Kenya and Sub-Sahara Africa at large.

Graph 1: Distribution of inflammatory cases reviewed at AKUHN's Pediatric Rheumatology Service



Graph 2: Distribution of non-inflammatory cases reviewed at AKUHN's Pediatric Rheumatology Service



REFERENCES

[1] Moorthy LN, Peterson MG, Hassett AL, Lehman TJ. Burden of childhood onset arthritis. Pediatr Rheumatol Online J. 2010;8:20.
[2] Minden K, Niewerth M, Listing J, et al. The economic burden of juvenile idiopathic arthritis-results from the German paediatric rheumatologic database. Clin Exp Rheumatol. 2009;27(5):863–9.
[3] Bernatsky S, Duffy C, Malleson P, Feldman DE, St Pierre Y, Clarke AE. Economic impact of juvenile idiopathic arthritis. Arthritis Rheum. 2007;57 (1):44–8.
[4] WHO Scientific Group on the Burden of Musculoskeletal Conditions at the Start of the New Millenium. The burden of musculoskeletal conditions at the start of the new millenium. World Health Organ Tech Rep Ser. 2003; 919(i-x):1–218.
[5] Scott C, Webb K. Pediatric rheumatology in sub-Saharan Africa. Rheumatology (Oxford). 2014;53(8):1357–8.

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SAT0486 SERIOUS ADVERSE EVENTS OF TOCILIZUMAB IN CHILDREN WITH RHEUMATIC DISEASES – A REAL-WORLD EXPERIENCE

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Background: Tocilizumab (TCZ) is a humanized monoclonal antibody that blocks interleukin 6. In children, TCZ has been approved for the

treatment of systemic-onset and polyarticular course juvenile idiopathic arthritis (JIA), and is used off-label in other treatment refractory inflammatory diseases. Real-world data regarding tolerance of TCZ in children are scarce.

Objectives: To assess the incidence rate and type of serious adverse events in children treated with TCZ.

Methods: A single-center retrospective review of all consecutive patients receiving TCZ in the pediatric rheumatology division from 01/2007 to 12/2018 was performed. Inclusion criteria were a diagnosis of inflammatory rheumatic disease and treatment with at least one dose of TCZ. Patients with missing data were excluded. Serious adverse events (SAE) were defined as a life-threatening event and/or an event requiring hospital admission, leading to permanent disability or treatment discontinuation.

Results: A total of 70 children (39 females) were included. Thirty children had systemic JIA, 25 polyarticular course JIA, 14 systemic inflammatory disorders such as autoinflammatory syndromes and one patient severe refractory idiopathic uveitis. Median age at diagnosis was 4.2 years (IQR 2.0 – 7.3). The majority of children had received prednisone (n=56), and/or at least one biologic agent (n=63) prior to TCZ initiation. At TCZ start, children had a median age of 8.9 years (IQR 4.9 – 12.3) and disease duration of 3.2 years (IQR 0.9 – 7.4). TCZ was initiated at a 2-weekly interval in 44 children, 26 children received TCZ every 4 weeks. Fifty-eight children received concomitantly another immunosuppressive agent (prednisone (n=47) and/or methotrexate (n=20) and/or various other drugs (n=5)). A median of 26 TCZ doses were given per child (IQR 7 – 48), TCZ exposure was 146.8 patient years. Twenty-two SAE were observed in 18 (26%) children (SAE 14.9/100 patient years): 8 severe infusion reactions, 7 serious infections, 3 cutaneous reactions (toxic reaction, cutaneous vasculitis, scleroderma-like skin thickening with fasciitis), two macrophage activation syndromes, and one abnormal hepatic function and severe dizziness each. Infusion reactions occurred most frequently during the first few infusions (median during 4th infusion, IQR 3 – 5). All patients with infusion reactions had either systemic JIA (n=4) or another autoinflammatory disease (n=4). At time of infusion reaction, all children (8/8) had active disease, 7/8 had a concomitant treatment with prednisone and 2/8 additionally with cyclosporine.

At last follow up, 35 (50%) children were still on TCZ, the other 35 had discontinued TCZ: 4 for remission, 13 because of inefficacy, 12 because of side effects, 3 because of both inefficacy and side effects, and 3 for other reasons. No death occurred during TCZ treatment; two patients with systemic inflammatory disease, in whom TCZ had been inefficient, died from uncontrollable disease 13 and 15 months after TCZ discontinuation, respectively.

Conclusion: In this cohort, serious adverse events were observed in a quarter of children with half of them having severe infusion reactions. Higher incidence rates of severe infusion reactions were observed in children with systemic JIA or autoinflammatory diseases. Ongoing careful monitoring of patients treated with TCZ, especially those with important systemic inflammation is required.

Disclosure of Interests: Florence Aeschlimann: None declared, Andreas Wörner: None declared, Richard Mouy Consultant for: Honoraries received by Roche for Tocilizumab trial in children, Carine Wouters Grant/research support from: Grant/research support to Istituto Gaslini from GlaxoSmithKline immune-inflammation: unrestricted grant to study Blau syndrome; Roche: unrestricted rese

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SAT0487 THE OUTCOMES OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) IN CHILDREN MANAGED WITH CURRENT TREATMENTS: THE SINGAPORE EXPERIENCE

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Background: JIA remains one of the most common rheumatic diseases afflicted children in SE Asia1. Despite the improvement in our treatment, outcomes of children treated with current therapy are unknown.

Objectives: To describe the clinical outcomes of children with JIA in a large, single center cohort in Singapore

Methods: Children diagnosed with JIA with a minimum follow-up of 6 month duration were recruited from our registry, from 1997 to 2015, at KK Women's and Children's Hospital, Singapore. Kaplan-Meier survival analyses were used to estimate the probability of ever attaining inactive disease (ID), remission with (CRM) or off (CR) medication according to modified Wallace criteria2. Revised Steinbroker functional classification was used to assess functional status of JIA patients at their last follow-up visit. Non-parametric descriptive statistics including median (IQR) were used to described data.

Results: In a cohort of 251 children (62% male and 71% Chinese; 35% ERA, 34% oligoarthritis and 12% RF-negative polyarthritis were among the most common JIA subtypes encountered locally), 43% used biologics and 65% used methotrexate. Median follow-up was 35 months (IQR 13 – 70). Of all subtypes, 89%, 71% and 21% achieved ID, CRM and CR at least once during the course of follow-up, respectively. Over 85 – 100% of all JIA children could experience ID, including RF-positive polyarthritis (Fig. 1, 2). The probabilities of attaining ID within 1 and 5 years were 30 - 81% and 80 - 100%. The probabilities of attaining remission within 1 and 5 years were 10-59% and 67-100% across JIA subtypes. All of our psoriatic arthritis and systemic onset JIA reached remission on medication within 3 and 5 years, respectively. Only 33.6% of children could totally stop their medication at 1 year, but 19.3 – 87.0% could do so at 5 years. However, none of the RF-positive polyarthritis and undifferentiated JIA children had CR during the course of their diseases. Functional classes were achieved in 96%, 4%, 0.4% and 0% for class I – IV, respectively.

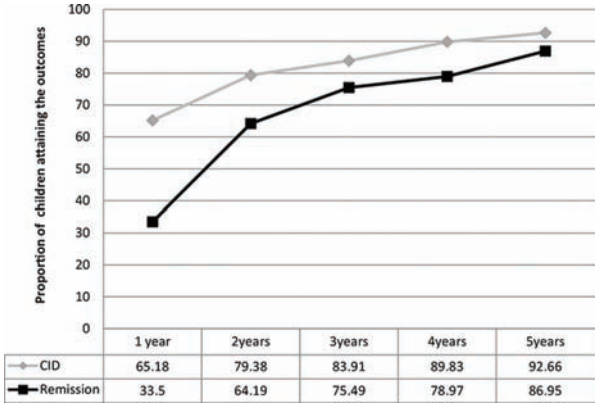


Fig 1. Cumulative proportion of children attaining clinical inactive disease and clinical remission on medication

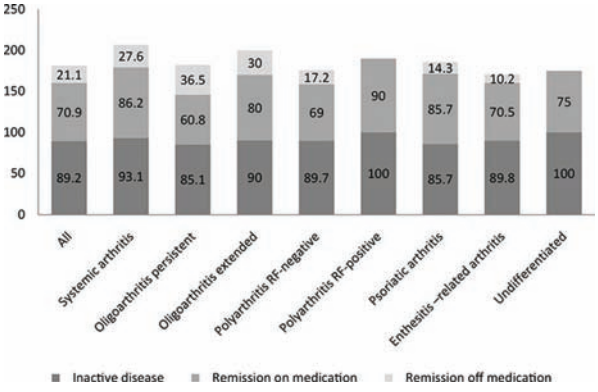


Fig 2. Proportion of children achieving at least one time of clinical inactive disease and remission in each JIA category during the follow-up period.

Conclusion: Majority of children with JIA managed by our current therapy attained inactive disease in 2 years. Despite significant improvement in JIA therapy, most of them remained on medications to maintain their inactive disease status. Only 20% were able to totally withdraw treatment. Almost all of our JIA children had no disability.

REFERENCES

[1] Arkachaisri T, Tang SP, Daengsuwan T, Phongsamart G, Vilaiyuk S, Charuvanij S, et al. Paediatric rheumatology clinic population in Southeast Asia: are we different? Rheumatology. 2017 Mar 1;56(3):390-8. PubMed PMID: 27994096.

[2] Guzman J, Oen K, Tucker LB, Huber AM, Shiff N, Boire G, et al. The outcomes of juvenile idiopathic arthritis in children managed with

contemporary treatments: results from the ReACCh-Out cohort. Annals of the rheumatic diseases. 2015 Oct;74(10):1854-60. PubMed PMID: 24842571.

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SAT0488 THE FRENCH PAEDIATRIC COHORT OF CASTLEMAN DISEASE

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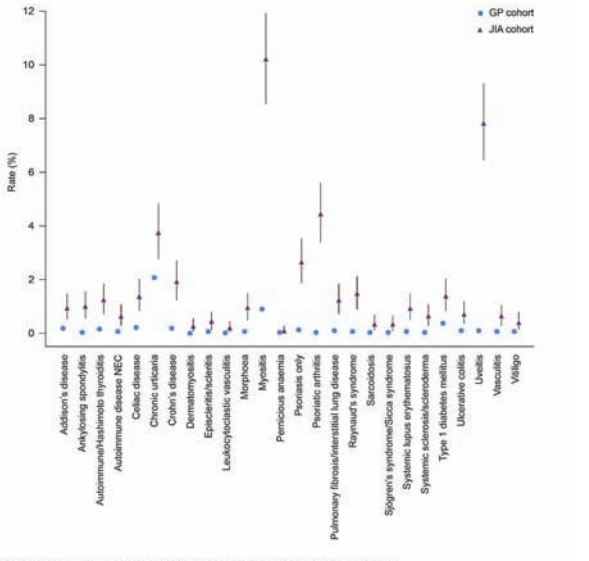
Background: Castleman disease (CD) is a very rare non-malignant lymphoproliferation of undetermined origin. CD diagnosis is difficult and often delayed because of insidious onset, low awareness and clinical heterogeneity. Two major disease phenotypes can be distinguished: unicentric CD (UCD) and multicentric CD (MCD). Diagnosis confirmation is based on histopathological findings on an involved lymph node.
Objectives: We attempted to survey all cases of paediatric CD identified in France so far, in order to set up a national registry aimed to improve CD early recognition, treatment and follow-up, within the context of a new reference centre (http://www.castleman.fr).
Methods: In 2016, we e-mailed a questionnaire to members of the French paediatric immunohaematology society, the French paediatric rheumatology society and the French Reference Centre for Castleman Disease to retrospectively collect cases of paediatric CD (first symptoms before age 18 years). Anatomopathological confirmation was mandatory.
Results: We identified 23 patients (12 girls and 11 boys) diagnosed with UCD (n=17) and MCD (n=6) between 1994 and 2018 in 14 centres. The average age at first symptoms was 11.5 years for UCD and 8.3 years for MCD. The mean diagnosis delay was 8.2 months for UCD and 5.2 years for MCD. In UCD, the initial symptoms were: isolated lymph nodes (n = 10) or lymph node associated with other symptoms (n = 7), fever was present in 3 patients. Patients with MCD presented with fever (n=5), abdominal lymph nodes (n=5), failure to thrive (n=3), hepatomegaly and/or splenomegaly (n=3), arthralgia (n=2), abdominal pain (n=2), fatigue (n=2), facial oedema (n=1), isolated lymphadenopathy (n=1), trunk rash (n=1), vascular hepatopathy with oesophageal varicose veins (n=1), diarrhea (n=1) or cholestasis (n=1). One patient had a Duchenne muscular dystrophy. No patients had HIV or HHV8 infection.
In MCD cases, one patient with recurrent fevers, had a heterozygous mutation in *MEFV* gene and another had a homozygous mutation in *TNFRSF1A* gene (P75L). A UCD patient experienced fever episodes and pericarditis two years after surgery. Genetic tests revealed one heterozygous mutation in *IL10RA* gene (V406L) and one in *IL36RN* gene (S113L). Nevertheless, our patient did not have any psoriasis or inflammatory bowel disease.
Treatment of UCD was mainly surgical resection, steroids, and radiotherapy. Treatments of MCD were tocilizumab, rituximab, anakinra, steroids, chemotherapy and splenectomy. Overall survival after an average of 6 years of follow-up, was 100% for both unicentric and multicentric forms.
Conclusion: Paediatric CD seems still underdiagnosed with a significant diagnosis delay specially for the MCD but new international criteria will help in future. In UCD, surgery is the main treatment. New drugs are used specially for the MCD, but more studies need to be conduct in children. The global survey is better in children than adults.
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SAT0489 PREVALENCE OF AUTOIMMUNE DISEASES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is one of at least 80 different types of autoimmune diseases, and is the most common paediatric rheumatic disease. After cancer and heart disease, autoimmune diseases are the most common type of disease in the US. The estimated prevalence of autoimmune diseases is 3.2% and 5.9% in the US[1] and Europe,[2] respectively, with a corresponding increase in mortality.[3] Many autoimmune diseases share a common pathogenic mechanism. There are few published studies quantifying the occurrence of other autoimmune diseases in patients with JIA.
Objectives: To estimate and compare the prevalence of 38 co-existing autoimmune diseases in patients with JIA and in a general paediatric population.
Methods: This was a retrospective cohort study conducted using registry data from the Cincinnati Children's Hospital Medical Center (CCHMC; Cincinnati, OH, USA) from Jan 2010 to Oct 2018. Patients <21 years old who had at least one clinic visit at the CCHMC were included in the general patient (GP) cohort, excluding pts with JIA. The JIA cohort consisted of patients <21 years old who had one of the International Classification of Diseases (ICD)-9 or ICD-10 diagnosis codes for JIA. No exclusion criteria were applied. Cases for each of 38 autoimmune conditions (AICs) were identified using ICD9/10 codes.
Comparisons were made between the JIA and the GP cohorts for each of the 38 AICs in crude prevalence (reported as X cases per patient-year) for each year up to the end of the study period. A Bayesian Poisson regression model was used for estimating and comparing prevalence rates for the JIA and GP cohorts at the end of study period. The rate and corresponding 95% confidence limits of the two cohorts on their prevalence rates are reported.
Results: There were 2,026 and 41,572 patients included in the JIA and GP cohorts, respectively. Out of 38 AICs, 26 showed significantly higher prevalence in the JIA cohort compared with the GP cohort (Figure). Of the 38 ICD9/10 codes assessed, 14 (36.8%) showed a more than 20-fold greater prevalence in the JIA cohort than in the GP cohort. There

Figure. Significant results from Bayesian Poisson analyses on point prevalence comparisons: JIA cohort vs GP cohort



GP=general patient; JIA=juvenile idiopathic arthritis; NEC=not elsewhere classified

were statistically significant differences in 26 conditions (Figure), with the most striking differences comparing the GP cohort with the JIA cohort in ankylosing spondylitis (0.001% vs 0.98%), psoriatic arthritis (0.01% vs 4.44%), systemic sclerosis/scleroderma (0.004% vs 0.6%), uveitis (0.07% vs 7.82%) and sarcoidosis (0.003% vs 0.3%). Only alopecia areata was more frequent in the GP cohort than in patients with JIA (4.5% vs 0.2%).

Conclusion: Patients with JIA have more pronounced autoimmunity prevalence than the general paediatric population, especially for ankylosing spondylitis, psoriatic arthritis, uveitis, systemic sclerosis/scleroderma and sarcoidosis.

REFERENCES

[1] Eaton WW, et al. J Autoimmun 2007;29:1–9.
[2] Jacobson DL, et al. Clin Immunol Immunopathol
[3] American Autoimmune Related Disease Association. Autoimmune statistics. 2016. https://www.aarda.org/news-information/statistics/. Accessed 7 July 2016.

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SAT0490 IL-1 BLOCKADE IN PEDIATRIC RECURRENT PERICARDITIS: A MULTICENTRIC RETROSPECTIVE STUDY ON THE ITALIAN COHORT

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Background: Acute pericarditis is an inflammatory condition causing the occurrence of pericardial effusion. In a third of patients, the disease is recurrent. Most of the cases are idiopathic or occur after a pericardial procedure. First line treatment of idiopathic pericarditis consists in NSAIDs and colchicine; glucocorticoids represent the second line treatment in resistant or intolerant cases. The use of different biologics and immunosoppressant has been reported, with variable responses. A recent clinical trial has enlightened the effectiveness of anakinra in patients with colchicine-resistant recurrent pericarditis.

Objectives: To describe the clinical characteristics and response to treatment in a cohort of paediatric patients with recurrent pericarditis treated with IL inhibitors.

Methods: Pediatric patients with recurrent pericarditis followed at 19 Italian centers of paediatric rheumatology or cardiology and treated with IL1 inhibitors were included in the study. Demographic, clinical and response to treatment data were retrospectively collected.

Results: 55 patients were included in the study. The mean age at onset of the first episode of pericarditis was 12.53 years. The mean number of relapses of pericarditis before the beginning of treatment with IL1 inhibitors was of 3.4. 53 out of 55 patients had previously received treatment with NSAIDS and 44 colchicine. 44 patients received steroidal treatment: 2 of them displayed a steroidal-resistance and 39 steroidal-dependence with reoccurrence of the symptoms following any attempt to reduce or withdraw this treatment.

Anakinra (mean dosage of 1.67 mg/kg/day) was used as first Il-1 inhibitor in 54 of the 55 patients, Canakinumab (150 mg every 4 weeks) in one. 53 out of 54 patients treated with anakinra displayed a complete clinical response to treatment within a mean of 2 days: NSAIDs, glucocorticoids and colchicine were withdraw in 25 out of 26, 31 out of 35 and 15 out of 32 patients respectively. 50 of 54 patients displayed a complete response; among these, three were switched to Canakinumab, 17 patients continued treatment at the same dosage while in 30 patients a reduction of treatment was attempted. 12 patients presented, during anakinra tapering, a disease flare, promptly resolved after an increasing of the dosage. The remaining 18 patients did not present any flare despite the reduction of the drug. Anakinra was withdrawn in 16 patients, with recurrence of the symptoms in 11 (9 restarted anakinra, 2 were treated with glucocorticoids and colchicine, with good response).

5 patients were treated with Canakinumab: 1 as first anti-IL1 drug, 4 were switched from anakinra (two for poor compliance, one for side effects and one for incomplete control of the disease). 2 out of five patients had a complete control of the diseases, 2 patients discontinued the treatment because of inefficacy and 1 patient required low dose of glucocorticoids to control the disease.

At last follow-up 34 patients were on anakinra, 7 on anakinra and colchicine, 2 on canakinumab, 1 on canakinumab plus colchicine and NSAIDs. In 9 patients all treatments were withdrawn for complete control of the disease.

Conclusion: This study confirm the effectiveness of IL-1 blockade in paediatric patients with recurrent pericarditis. However, most of the patients require prolonged treatment to maintain clinical remission. Moreover, in our cohort of patients the rate of response was higher for anakinra then for canakinumab, suggesting a possible role of IL1α in the pathogenesis of this condition.

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SAT0491 METABOLIC DISORDERS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: The urgency of identifying metabolic disorders causing the formation and complication of rheumatic diseases is associated with the difficulties of early and differential diagnosis, and often unfavorable outcomes with a high incidence of patient disability.

Objectives: The purpose of the study is to study the lipid, lipoprotein spectrum of blood serum, lipid peroxidation and antioxidant protection in children with juvenile idiopathic arthritis (JIA).

Methods: On the state of lipid metabolism was evaluated by the study content of total lipids, total cholesterol, triglycerides, lipoprotein spectrum of blood serum apolipoprotein atherosclerotic and antiatherogenic lipoproteins (apoB, apoA, apoE), activity of lipoprotein lipase, primary and secondary products of lipid peroxidation (LPO) and the content of antioxidant ability of water - and fat-soluble antioxidants.

Results: 147 children with juvenile idiopathic arthritis (JIA) aged from 2 to 17 years were examined. The control group consisted of 50 healthy children. In children with JIA, a significant increase in the content of triglycerides, total cholesterol ($p<0.001$) and a decrease in cholesterol-HDL levels ($p<0.05$) in comparison with the same indicators in the control group was established. The mean concentrations of cholesterol-HDL significantly decreased with an increase in the degree of disease activity: 1.15 [0.98; 1.3] mmol/l with minimal activity, 1.02 [0.87; 1.17] mmol/l with moderate activity and 0.94 [0.78; 1.01] mmol/l with a high activity of the disease.

Lipoprotein lipase is a key enzyme in lipid metabolism, ensuring the hydrolysis of plasma triglycerides found in chylomicrons and very low density lipoproteins. An increase in the catalytic activity of lipoprotein lipase leads to a decrease in the level of TG and an increase in the level of HDL in the blood. According to the results of the survey in children with JIA, the concentration of lipoprotein lipase was 13.9 [7.1; 25.3] µg/l, with obesity 27.5 [9.9; 47.8] µg/l. A direct relationship was established between its content in blood serum and the concentration of LDL (rs=0.37; p<0.05) and the inverse with the level of LDL (rs = –0.4; p<0.05). There was a significant difference (p<0.05) by gender: the level of lipoprotein lipase in the blood serum in girls was 25.8 [16.7 - 54.4] µg/l, in boys - 15.6 [7.8 - 29,0] µg/l. A correlation was also established between the level of lipoprotein lipase and body mass index (rs = 0.35; p<0.05).

According to the results of the study, a significant (p<0.05) increase in the level of primary (DK233) and secondary (DK278 and MDA) LPO products in the blood serum of children with JIA was found in comparison with the control group. During the correlation analysis, a positive correlation was established between the levels of DK233, DK278 in serum and ESR (rs = 0.587, p<0.01). The results obtained indicate the intensification of lipid peroxidation processes. A significant (p<0.05–0.01) decrease in the content of water-soluble (ACW) and fat-soluble (ACL) antioxidant capacity of substances in the blood serum of children with JIA was found when compared with similar indicators in the control group. During the correlation analysis, a negative correlation was established between the level of CRP and the content of ACL in serum (rs = -0.346, p<0.05), between the content of ACW and CRP in serum (rs = -0.54, p<0, 01).

Conclusion: It can be concluded that the activation of lipid peroxidation and the failure of the antioxidant system play a significant role in the development and progression of JIA in the examined children, as well as in the formation of atherogenic disorders by the lipid peroxidation mechanism. In addition, children with JIA have abnormalities in the lipid spectrum, acquiring an atherogenic orientation, which, together with hemostasiological changes, can be regarded as a risk factor for atherothrombosis.

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SAT0492 GASTROINTESTINAL MANIFESTATIONS IN CHILDHOOD BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is an idiopathic, chronic, inflammatory systemic vasculitis characterized by recurrent oral and genital aphthous ulcers, skin lesions, and ocular involvement. It can also affect multiple visceral organ and system such as heart, lung, blood vessels, gastrointestinal (GI) system, and central nervous system (1). The etiology of the disease is still unknown. New diagnostic criteria for pediatric Behçet's patients have been established In 2015, and its largely based on clinical findings (2). Although the GI manifestations are not take part in to the diagnostic criteria, it can be emerge in great deal of patients and associated with significant morbidity and mortality. The most common GI symptoms in BD are abdominal pain, nausea, diarrhea and GI bleeding in, respectively. Also, the most common reported site of intestinal involvement was ileocecal. The literature data related to GI involvement of BD are frequently concern adult patients and pediatric studies are limited.

Objectives: We analyzed the GI manifestations and its endoscopic findings in children diagnosed with BD.

Methods: We retrospectively reviewed the clinical records of 64 patients who fulfilled the international pediatric classification criteria for BD from December 2015 to December 2018. Endoscopic examination results of 13 patients were also collected and analyzed.

Results: Of the 64 children with BD, 37 were male and 27 were female, and sex ratio (male/female) was 1.37/1. The mean age of our patients was 9.49±4.10 and 11.52±3.50; at onset of symptoms and at the time of diagnosis, respectively. Assessment of our 64 patients revealed that the prevalence of GI symptoms is 60% (39/64). The most frequent GI symptoms were abdominal pain in 56% (36/64), chronic diarrhea in 18% (12/64), nausea/vomiting in 11% (7/64), chronic constipation in 12% (8/64), and regurgitation or heartburn in 7% (5/64). Upper GI endoscopy was performed in 7 patients and colonoscopy in 6. All of the patients who underwent the endoscopy or colonoscopy, had findings support the GI inflammation. The endoscopic findings shown in the patients are; gastric inflammation in 100% (7/7), oesophageal inflammation in 57% (4/7), duodenal inflammation in 42% (3/7), colonic erythema and inflammation in 83% (5/6), polyps in 50% (3/6), ulceration in 66% (4/6), and hemorrhoids in 16% (1/6). Upper GI ulceration was not observed. Pathology specimens were taken in 7 upper endoscopies and 6 colonoscopies within our patients. The findings of pathology specimens were vascular congestion and inflammation in 100% (7/7) of upper GI biopsies and 83% (5/6) of colonic biopsies, cryptitis in 66% (4/6) of colonic biopsies. Acute colitis in pathology specimens was shown in 83% (5/6) of the patients. Three of the patients with colitis had punch ulcers, and these patients were evaluated as BD-associated colitis. The other two patients were diagnosed and treated as Crohn's colitis accompanying BD.

Conclusion: The GI system is one of the most frequently affected organ by the BD. It may cause the inflammation and ulceration in the GI tract. Inflammatory bowel diseases can also cause GI inflammation similar to BD. In patients with symptoms of GI inflammation, upper and lower GI endoscopic examination and pathological analysis may be helpful in determine the underlying etiology.

REFERENCES

[1] - Sakane T, Takeno M, Suzuki N, Inaba G. Behçet's disease. N Engl J Med 1999;341:1284-91

[2] - Koné-Paut I, Shahram F, Darce-Bello M, Cantarini L, Cimaz R, Gattorno M et al, PEDBD group. Consensus classification criteria for paediatric Behçet's disease from a prospective observational cohort: PEDBD. Ann Rheum Dis. 2016;75:958-64.

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SAT0493 THE CHALLENGE OF TREATİNG PULMONARY VASCULITIS IN BEHÇET'S DISEASE: TWO PEDIATRIC CASES

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Background: Behçet's Disease (BD) is a multisystemic autoinflammatory disease and the most severe complication of BD is pulmonary artery involvement (PAI). Data regarding treatment and outcomes of pediatric patients with PAI is very limited.

Objectives: Herein, we report two pediatric patients with BD presenting with PAI and treated successfully with aggressive immunosuppressive treatment.

Methods: Demographic data, clinical manifestations, laboratory and radiological findings, and treatments of patients were documented from patient charts retrospectively.

Results:

Case 1: A 15-year-old boy was admitted with abdominal pain and fever. An abdominal Doppler ultrasonography (USG) showed stenosis of vena cava inferior (VCI) with a thrombus. Transthoracic echocardiography (TTE) detected that the thrombus extended from VCI to the right atrium. When he started to have hemoptysis, he was referred to our hospital. TTE showed a mass in RV. The computed chest and abdominal tomography angiography (CTA) showed bilateral aneurysmatic dilatation with thrombi in the pulmonary arteries and thrombosis in vena hepatica. The pathergy test was negative and the HLA B5 was negative. According to the ICBD, the patient had been diagnosed as BD due to genital ulcers and vascular involvement. He was given pulse methylprednisolone (MP) 500 mg 3 days along and followed by oral prednisolone 1 mg/kg/day, intravenous cyclophosphamide at a dose of 15 mg/kg every 3 weeks for a total of 6 cycles, and Interferon-α2a (IFN-α2a) 3 times a week. Within one month, hemoptysis and fever disappeared, and CRP values normalized. After a three-month treatment, TTE and CTA revealed that thrombi shrank significantly. The dosage of prednisolone was tapered gradually and stopped 2 years later. Immunosuppressive treatment was continued with adalimumab. The patient has been followed in remission for nearly 6 years.

Case 2: A fifteen-year-old boy was referred to our hospital for the evaluation of fever for over 4 months and a thrombus in his right ventricle. He had a medical history with cough, fever, intermittent hemoptysis and weight loss for the past 3 months. Physical examination revealed acne-like rashes over face and back, oral ulcers. A CTA confirmed the

thrombus in RV and showed bilateral multiple aneurysms along the pulmonary artery and its branches. According to ICBD, the patient was diagnosed with BD due to having aphthous ulcers, pseudofolliculitis, and vascular involvement. Iv MP (500 mg/day) for 3 days was followed by oral prednisolone 1 mg/kg/day, which was subsequently tapered. Iv cyclophosphamide at a dose of 500 mg was also given every 3 weeks for a total of 6 cycles, followed by oral azathioprine (AZA). Concomitant subcutaneous IFN-α2a was given two times per week for 6 months. Within two weeks, cough and fever disappeared, CRP values normalized. After 1 year the pulmonary artery aneurysm disappeared and cardiac thrombosis resolved. We have been following the patient with AZA for four years without recurrence.

Conclusion: We present two pediatric patients with pulmonary involvement of BD. PAI is a life-threatening condition and should be managed with more aggressive medical therapy. Early diagnosis and aggressive immunosuppressive treatment are very important in PAI. We strengthened our treatment with IFN-α2a. There is no data in the literature regarding the use of IFN-α-2a in PAI treatment along with low dose cyclophosphamide. There were no mortality or recurrences within the 6 and 4 years follow up period. An aggressive immunosuppressive therapy leads to better prognosis in this most dreadful complication of BD.

REFERENCES

[1] Ozen S, Bilginer Y, Besbas N, Ayaz NA, Bakkaloglu A. Behcet disease: treatment of vascular involvement in children. Eur J Pediatr. 2010;169 (4):427-30.

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SAT0494 HOME MONITORING OF INACTIVE DISEASE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: PREDICTIVE VALUE OF EQ-5D-5L-Y

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Background: In recent years, juvenile idiopathic arthritis (JIA) research has shifted towards treat-to-target therapy based on clinical assessments and patient-reported outcomes (1). A well-known measurement of quality of life is the EQ-5D-5L (2). Herewith, we report preliminary results of a retrospective study using the child-friendly 'EQ-5D-5L-Y' with an E-health application (Reuma2GO) to monitor children with JIA in an outpatient setting.

Objectives: To assess the relationship between dimensions of the health-related quality of life 'EQ-5D-5L-Y' questionnaire and conventional assessments for children with JIA, including the Juvenile Arthritis Multidimensional Assessment Report (JAMAR) and active joint count (AJC), and to investigate the potential of the EQ-5D-5L-Y as instrument for outpatient management.

Methods: The study was designed as monocentric retrospective cohort study. Data from October 2017 to January 2019 were available for 70 patients with JIA. The relationships between individual dimensions of the EQ-5D-5L-Y, JAMAR and several clinical assessments were investigated. Furthermore, dimensions of the EQ-5D-5L-Y were investigated as possible predictors for binary disease activity using AJC > 0 as reference standard for active disease.

Results: Seventy patients with JIA completed 115 EQ-5D-5L-Y and JAMAR questionnaires within two weeks before a clinical visit. Moderate to high correlations were found between the EQ-5D-5L-Y and JAMAR. Moreover, the best possible EQ-5D-5L-Y score, with and without health-related visual analogue scale (EQ-VAS), demonstrated high sensitivity (81.1%) and negative predictive value (84.8%) for active disease (Table 1). The few patients who were incorrectly classified as having inactive disease (false-negatives) did not have their medication changed at the clinical visit and experienced little to no impact of disease activity on their quality of life, as indicated by the JAMAR questionnaire.

Table 1. Predictive value of EQ-5D-5L-Y dimensions for active disease using AJC > 0 as reference standard.

Cut-off for 'Active Disease'	Accuracy (%, CI)	Sensitivity	Specificity	PPV	NPV
EQ-5D Mobility > 1	74.8% (65.8-82.4)	59.5%	82.1%	61.1%	81.0%
EQ-5D Self-Care > 1	76.5% (67.7-83.9)	35.1%	96.2%	81.2%	75.8%
EQ-5D Usual Activities > 1	67.8% (58.5-76.2)	73.0%	65.4%	50.0%	83.6%
EQ-5D Pain/Discomfort > 1	62.6% (53.1-71.5)	62.2%	62.8%	44.2%	77.8%
EQ-5D Anxiety/Depression > 1	73.9% (64.9-81.7)	51.4%	84.6%	61.3%	78.6%
EQ-5D EQ-VAS <85	60.0% (50.4-69.0)	64.9%	57.7%	42.1%	77.6%
EQ-5D Total Score > 5	60.0% (50.4-69.0)	81.1%	50.0%	43.5%	84.8%
EQ-5D Score > 5 & EQ-VAS <85	52.2% (42.7-61.6)	83.8%	37.2%	38.8%	82.9%

PPV: positive predictive value; NPV: negative predictive value.

Conclusion: These results demonstrate the discriminatory value of the EQ-5D-5L-Y between active and inactive disease in our cohort of patients with JIA. High negative predictive value was found for the total EQ-5D-5L-Y score, with and without EQ-VAS. In conclusion, the EQ-5D-5L-Y could be a valuable instrument for monitoring children with JIA in an outpatient setting which could aid physicians with deciding whether a clinical visit is necessary or not.

REFERENCES

[1] Filocamo G, et al. A new approach to clinical care of juvenile idiopathic arthritis: The juvenile arthritis multidimensional assessment report. J Rheumatol 2011;38:938–953.
[2] Janssen MF, et al. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. Qual Life Res 2013;22:1717–1727.

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SAT0495 PHENOTYPE OF PATIENTS WITH JUVENILE DERMATOMYOSITIS ASSOCIATED WITH ANTI-FACTOR H AUTO-ANTIBODY : A SEVERITY FACTOR?

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Background: Juvenile Dermatomyositis (JDM) is a rare, autoimmune and highly heterogeneous paediatric-onset myopathy, characterized by skin and muscles inflammation. Development of vasculopathy is associated with the severe extra-muscular manifestations of JDM, and portends a poor prognosis. Impaired function of JDM vasculature includes immune complex and complement deposition.

Objectives: The aim of our study is to describe the clinical and paraclinical phenotype of patients with anti-factor H autoantibody (Ab) associated with JDM and overlap myositis.

Methods: Patients with a diagnosis of JDM or overlap myositis and presence of anti-FH auto-antibody, followed in two Parisian tertiary centers over the last twelve years, were retrospectively selected. Besides demographic data, clinical features (cutaneous lesions, severity of muscle involvement, extra-muscular manifestations), treatment options and their outcome were retrieved for each patient. Biological data and presence of myositis-specific autoantibodies were collected, muscle MRI were examined, and data from muscle biopsies were assessed using a validated score tool when available.

Results: Eleven female patients were included in the study, with a median age at diagnosis of 8.8 years [2.8 – 13.1], and a median follow-

up of 3 years [1 – 11.7]. Apart typical cutaneo-muscular presentation, seven developed calcinosis, and six presented with subcutaneous oedema (of which 5 were anti-NXP2 positive). Median CMAS was 24/52 [1 – 47], and median MMT was 52/80 [2 -76]. Gastro-intestinal involvement was found in 10 patients (91%), 4 presented a pulmonary impairment, and 3 girls had psychiatric symptoms. Six patients had a severe form (54%), one of them led to death (after 2.8 years of evolution).
MSA were found in 9 patients (anti-NXP2 = 1, anti-fibrillarine = 2, anti-MDA5 = 1 and anti-TIF1gamma = 1). IFN-signature was positive in 9 patients. Complement exploration was normal in all patients, and median positive rate of Anti-Factor H Ab was 260 UA/L [115 – 2800]. Muscle biopsy was performed in all patients but one with a median total score severity of 20. All patients received corticosteroids, and one to six other lines of treatment to achieve remission, obtained in 8 patients, with a median time to remission of 2 years [0.5; 4.8]. Use of plasmapheresis/immunoadsorption and/or Ruxolitinib was necessary in 3 of them (27%).
Conclusion: Presence of anti-factor H auto-antibodies in JDM or overlap myositis patients seems associated with more frequent gastro-intestinal involvement, and a more severe phenotype, requiring more aggressive treatment.

REFERENCES

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SAT0496 THE FREQUENCY OF JOINT HYPERMOBILITY IN TURKISH SCHOOLCHILDREN: EFFECTS TO PHYSICAL ACTIVITY, BALANCE, PAIN AND QUALITY OF LIFE

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Background: Recent studies have focused on the joint hypermobility (JH) to show the association with musculoskeletal pain, functional disability, motor development and psychological distress (1). In contrast, in some publications, the negative effects of JH in childhood were not observed (2).
Objectives: The aim of this study was mainly to determine the frequency of JH in Turkish schoolchildren and to investigate whether relationship between JH and pain, physical activity level and the balance. In addition, the study aimed whether JH has an impact on the quality of life.
Methods: This cross-sectional school-based study evaluated 737 children (52.5% girls) from 8 to 14 years of age, and the data were collected in 2018 in the city of Denizli, Turkey. Firstly, each of the participants was individual assessed by a clinician on the Flamingo Balance Test for stability and Beighton for the diagnosis of JH. According to Beighton, children who scored $\geq$5 were accepted as hypermobile. Secondly, all participants completed the self-reported measures for the screening of physical activity level and quality of life. The Physical Activity Questionnaire (PAQ) and the Pediatric Quality of Life Inventory (PedsQL) tests were used to determine the level of physical activity and the quality of life. Also, pain severity was quantified by the Visual Analogue Scale (VAS) that is ranging from no pain (score: 0 mm) to worst pain (score: 100 mm) in the last month.
Results: The prevalence of JH in schoolchildren was 19.7% in Turkish population (Table 1). The mean pain severity was 1.29±2.024 in all children. Significant differences were found between hipermobile and non-hipermobile groups in social and school functioning ($p<0.05$), but no significant differences were found in pain, physical activity level ($p>0.05$) (Table 2). Beighton score was not significant correlated with pain severity, physical activity, quality of life and balance in childhood (p=0.515, p=0.986, p=0.512, p=0.362 respectively).
Conclusion: As a result, the existence of hypermobility in children had an impact on school and social functions. However, it has been observed that hypermobility does not have a negative effect on these children's pain, balance, physical activity level, and physical and emotional functions.

REFERENCES

[1] Scheper MC, Engelbert RH, Rameckers EA, Verbunt J, Remvig L, Juul-Kristensen B. Children with generalised joint hypermobility and musculoskeletal complaints: state of the art on diagnostics, clinical characteristics, and treatment. Biomed Res Int. 2013;2013:121054. doi: 10.1155/2013/121054.

[2] Leone V, Tornese G, Zerial M, et al. Joint hypermobility and its relationship to musculoskeletal pain in schoolchildren: a cross-sectional study. Archives of Disease in Childhood 2009;94: 627-632.

Table 1. Demografic findings of 737 Turkish Schoolchildren

Age		11.47 ± 1.304 (8-14)
Sex	**Female**	387 (52.5%)
	Male	350 (47,5%)
Beighton Score		2.75 ± 2.191 (0-9)
BS = 5		46 (6.3%)
BS = 6		53 (7.2%)
BS = 7		24 (3.3%)
BS = 8		15 (2.0%)
BS = 9		7 (1.0%)
Hypermobility	**Positive**	145 (19.7%)
	Negative	592 (80.2%)
Pain severity		1.29 ± 2.024 (0-10)

Table 2. Comparison of the results of children with and without hypermobility

	With Hypermobility (n= 145)	**Without Hypermobility (n=592)**	**P**
Age (year)	11,13 ± 1,35	11,55 ± 1,28	**0.000**
Weight (kg)	42,42 ± 11,85	45,58 ± 12,3	**0.004**
Height (cm)	148,8 ± 10,7	151,76 ± 10,19	**0.002**
Beighton Score	6,2 ± 1,14	1,9 ± 1,42	**0.000**
Pain severity (During Motion)	1,04 ± 1,8	1,35 ± 2,07	0.148
Pain severity (During Rest)	0,91 ± 1,86	1,16 ± 1,9	0.063
Balance	28,13 ± 9,44	30,04 ± 9,45	0.062
PAQ Score	27,13 ± 7	26,18 ± 7,4	0.102
PedsQL 4.0			
Physical functioning	85 ± 12,74	96,21 ± 331,71	0.068
Emotional functioning	77,05 ± 18,18	75,37 ± 20,04	0.533
Social functioning	91,67 ± 13,1	90,44 ± 29,14	**0.049**
School functioning	83,72 ± 13,71	80,32 ± 16,09	**0.030**

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SAT0497 CLINICAL PICTURE OF 7 PAPA PATIENTS FOLLOWED IN A SINGLE PEDIATRIC RHEUMATOLOGIC CENTER

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Background: Pyogenic sterile arthritis, pyoderma and acne (PAPA) syndrome is an autosomal dominant inflammatory disorder caused by mutations in the *PSTPIP1* gene primarily affecting joints and skin. The E250K mutation cause the hyperzincaemia/hypercalprotectinemia syndrome termed *PSTPIP1*-associated-related proteinemia inflammatory (PAMI) syndrome in which a bone marrow involvement is reported
Objectives: To describe the clinical presentation of 7 PAPA patients followed at a single pediatric rheumatology center
Methods: For each patient clinical and laboratory data were collected from medical charts. *PSTPIP1* was sequenced through Sanger Sequencing or targeted resequencing using a customized panel, and analyzed with the NextSeq® platform (Illumina)
Results: We describe 7 patients from 4 unrelated families with the E250K mutation in a mother and 2 siblings, the A230T variant in a father and his son and the R405C and D266N respectively in the last 2 unrelated patients. Disease onset occurred within the 7th year of life in all patients. Patients 3 and 4 (table) presented since the 1st year of life recurrent episodes of fever without any cutaneous or articular symptoms. In both patients inflammatory markers were elevated during fever episodes, but persistently negative during wellbeing not requiring any therapy. The variants described in these patients were not previously reported. However their pathogenic role is supported by the detection of markedly high serum calprotectin levels (>10.000 microg/ml). The predominant feature of patients 1 and 2 was articular involvement with recurrent episodes of arthritis associated to acne. Patient 1 was initially treated

with prednisone with good clinical response but relapse of arthritis at discontinuation followed by the development of a sterile muscle abscess. An anti-TNF drug was started in both patients with complete clinical response. Patient 5 reported severe acne and psoriasis, and recurrent episodes of sterile arthritis. She presented a persistent elevation of acute phase reactants with severe anemia and leukopenia not resolving after splenectomy. His son (pts 6) presented with recurrent episodes of sterile arthritis, hepato-splenomegaly, anemia and neutropenia. Zinc and calprotectin serum levels resulted respectively 728 micromol/l and 2600 microg/ml. IL-1 inhibition determined a complete normalization of inflammatory parameters with no effects on anemia and neutropenia. In patient 6 zinchemia decreased to almost normal value after 4 months of therapy. Patient 7 presented at the age of 4 years a sterile lymphnode abscess. She also presented with splenomegaly and neutropenia with persistent elevation of acute phase reactants. Anakinra was proposed but not administered for poor compliance

Conclusion: The clinical picture of patients carrying *PSTPIP1* mutation may be heterogeneous. In our cohort TNF-inhibitors were successfully used in PAPA patients preventing new arthritis episodes and resolving cutaneous manifestation where present. In 2 patients the clinical picture was mild not requiring continuous treatment. One PAMI patient had a good response to IL-1 inhibition, which however, had no effect on hematological manifestations

Pts	Mutation	Clinical features	Laboratory features	Therapy
1	A230T	Recurrent fever, acne, cutaneous abscesses, arthritis	↑CRP, ESR, SAA	Anti-TNF
2	A230T	Acne, arthritis	↑CRP, ESR, SAA	Anti-TNF
3	R405C	Recurrent fever	↑CRP, ESR, SAA, zincaemia	/
4	D266N	Recurrent fever	↑CRP, ESR, SAA, zincaemia	/
5	E250K	Acne, psoriasis, arthritis, hepatosplenomegaly	↑CRP, ESR, SAA, zincaemia calprotectinemia	/
6	E250K	arthritis, hepatosplenomegaly	↑CRP, ESR, SAA, zincaemia calprotectinemia	Anti IL-1
7	E250K	Limphnode absess, hepatosplenomegaly	↑CRP, ESR, SAA	/

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SAT0498 THE IMPACT OF OVERWEIGHT ON THE OUTCOME OF JUVENILE IDIOPATHIC ARTHRITIS

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Background: Overweight and obesity are considered to have a negative impact on Rheumatoid Arthritis in adults and there is less information regarding the correlation in juvenile idiopathic arthritis(JIA).

Objectives: To assess the effect of overweight on the activity of JIA as well as the stability and ability to achieve a remission using the cJADAS-10 score.

Methods: This is a longitudinal retrospective study design. We collected data of 164 patients suffering from JIA from three consecutive visits. Treatment was conducted between 2012 and 2015 at our centre in accordance to current guidelines. Remission was defined by cJADAS10 score ≤0,5 in Oligoarthritis and ≤0,7 in Polyarthritis. Patients were categorized by weight-for-age percentiles as heavily underweight (less than 3rd percentile) underweight (4th up to 10th percentile) healthy (11th up to 90th percentile) overweight (91th up to 96th percentile) and obese (97th up to 100th percentile). We compared the cJADAS10 of normal-weighted children with the cJADAS10 of the overweight and the obese patients, respectively.

Results: Of all patients, 13 were "underweight" (7,9%), 109 were defined as "normal weight" (66,5%) and 42 patients were categorized as "overweight" (25,6%) of which 16 children (9,8%) were "obese". 95 (57.9%) reached a remission during follow-up visits. Overweight was associated with higher disease activity compared to healthy weight children at the first visit (mean 9,5 vs. 8,5) and a wider range of the cJADAS10 score (0-22 vs.0-20,5). Results from the 3-months-follow-up revealed an overall good response to the prescribed medication. At 6-months-follow-up, overweight children couldn't stabilize the improvement since cJADAS10 range rises while it stays stable in healthy weight children. At the same time, while interpreting the disease activity of "overweight" and "obese" children separately, obese children show significantly less disease activity than overweight children, especially at the 3- and 6-months-follow-ups.

Conclusion: Overweight seems to have a negative influence on the disease activity and remission of JIA patients but it is most likely not the only influencing factor since obese patients show a better result regarding the cJADAS10 score than overweight patients. In the future, factors like socioeconomic status, BMI of the parents or physical activity level of the patient should be included in the evaluation. Also, the 7 subtypes of JIA should be analyzed individually since they show heterogeneous etiology, phenotype and prognosis.

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SAT0499 ORAL MICROBIOME IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITISIN RELATION TO DISEASE STATUS, TEMPOROMANDIBULAR JOINT ARTHRITIS AND MEDICATION: A NORWEGIAN 2-YEAR PROSPECTIVE STUDY

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children, with an annual incidence of 1-2 per 1000 children. The temporomandibular joint (TMJ) is involved in 40-70%. The human microbiome might be a potential contributing factor to the development of JIA.

Objectives: To describe the oral salivary microbiome in children with JIA and relate this to disease activity, TMJ arthritis, and systemic medications.

Methods: 93 children; JIA (n=59), Healthy (n=34) were recruited. Demographics, disease activity, presence of TMJ-arthritis and type of medication was collected in this Norwegian prospective study (www.norjia.com). 116 saliva samples were analyzed using Next Generation Sequencing, V1-V3 region of the 16S rRNA gene, coupled with BLASTn-based, species-level taxonomy assignment algorithm. Downstream bioinformatics analysis was performed with QIIME and LEfSe.

Results: Mean age for healthy group (n=34; 27 females) is 12.3 ±3.0 years while for the JIA group (n=59; 43 females) the mean age is 12.6 ±2.7 years. A total of 541 bacterial species belonging to 111 genus and 10 phyla were identified, with Prevotella, Streptococcus, Actinomyces, Rothia Haemophilus and Veillonella accounting for the bulk of the average microbiome. There were no significant difference between JIA and healthy subjects in species richness and alpha diversity. However, differential abundance analysis revealed genera TM7-G1, Solobacterium and Mogibacterium to be associated with JIA, while Haemophilus and Lactococcus to be overabundant in healthy subjects.

Conclusion: It seems that taxa associated with chronic inflammation were found to be enriched in the saliva of JIA patients.

REFERENCES

[1] Frid P, Nordal E, Bovis F, Giancane G, Larheim TA, Rygg M, et al. Temporomandibular Joint Involvement in Association With Quality of Life, Disability, and High Disease Activity in Juvenile Idiopathic Arthritis. Arthritis Care Res (Hoboken). 2017;69:677-86.

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SAT0500 JUVENILE RECURRENT PAROTITIS: A RARE MANIFESTATION OF RHEUMATIC IMMUNE-MEDIATED DISEASES

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Background: Juvenile recurrent parotitis (JRP) is the second most common childhood disease of the salivary glands after mumps and mainly affects children between the ages of 3 and 6. There is a male predilection, often with spontaneous resolution at puberty. However, in some cases, it can be the first manifestation of a rheumatic immune-mediated disease.
Objectives: To analyze the clinical, laboratory and imaging profile of children with JRP and investigate the prevalence of rheumatic immune-mediated diseases in these patients.
Methods: Retrospective study from 2008 to 2018 including all cases of recurrent parotitis with juvenile onset at our center. Parameters evaluated included gender, age, laterality, number of recurrences, symptoms of presentation, associated conditions, imaging details, blood tests, treatment, outcome and follow-up.
Results: 40 patients were identified over a 10-year period, with a female to male ratio of 5:3; 62.5% females. The youngest child was nine months old and the eldest was 16 years old with median age at presentation of 5 years. The median (min-max) follow-up period was 3 (0.04-33) years. 29 children (72.5%) only ever reported unilateral symptoms, while the rest had both glands affected, although not usually at the same time. Pain and swelling were the most common presenting symptoms, seen in all cases. Fever in 15 (37.5%) and whitish discharge from Stenson's duct in one (2.5%). 14 (35%) had palpaple cervical lymphadenopathy and 4 (10%) had dental caries. The average reported frequency was 1.25 episodes per year, with a range of 0.43-5 episodes. Numbers of recurrences were in range of one to 15 with average of 3 times. Younger age at first episode didn't increase the likelihood of recurrences in our sample (p=0.123). Sonography was performed in 34 cases as primary investigation. Reports showed multiple hypoechoic lesions with enlarged intraglandular lymph nodes and enlarged gland. MRI was performed in 10, CT in 4, scintigraphy in 2 and biopsy of minor salivary glands in 1. The median level of C-reactive protein and erythrocyte sedimentation rate was 4 (range 0.2-55.5 mg/l, n=30) and 7 (0.5-76 mm in 1st hour, n=20), respectively. The median blood leukocyte count 8.13 x 10^9/L (range 3.73-25.4 x $l0^9$/L, n = 36). 20 (50%) patients had serum immunoglobulins measured, 6 of them having hypergammaglobulinaemia. One patient had a marginally low serum Immunoglobulin A (50; normal variation 55-210). Antibody screening was performed in 18 patients (45%), with 10 with positivity for antinuclear antibodies, 3 anti-SSA, 2 anti-SSB, 2 anti-RNP and 2 rheumatoid factor. One of the children had sialolithiasis in the parotid gland and other had an abcess with microaerophilic streptococcus isolated in culture of pus. Among all patients, 5 (12.5%) had a final diagnosis of a rheumatic immuno-mediated disease: 3 with primary Sjögren Syndrome (SS) and 2 with mixed connective tissue disease. An idiopathic etiology was determined in 33 (82.5%). These were treated with analgesics and nonsteroidal antiinflammatory drugs with complete resolution of symptoms and the previous ones with immunossupressants/ immunomodulators.
Conclusion: The clinical, laboratory and imaging profile of our sample is in accord with the literature, except for sex predilection. Although recurrent juvenile parotitis is more common, primary juvenile SS should be considered. A high suspicion is crutial mainly because of a lower incidence of xerostomy and xerophthalmia in this population.

REFERENCES

[1] De Luca R, et al. Juvenile Recurrent Parotitis: Could be a Primary Pediatric Sjogren Syndrome? SM Otolaryngol. 2017; 1(3): 1013.

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SAT0501 THE IMPACT OF MORNING STIFFNESS ON THE DEFINITION OF INACTIVE DISEASE IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. Morning stiffness is a major symptom of JIA, and is usually associated with active disease. The 2004 preliminary criteria for inactive disease (ID) in JIA did not include the assessment of morning stiffness, whereas the 2011 revision of the criteria has allowed the presence of morning stiffness (MS) lasting ≤ 15 minutes. MS was included in 2011 revision based on the consideration that MS of a short duration (i.e., ≤ 15 minutes) can represent residua of previously active disease without current active disease. However, it is unclear whether the disease status of children with ID who have or do not have morning stiffness is comparable.
Objectives: To compare the disease status of children with JIA who met the 2004 and 2011 revised criteria for ID in relation to the presence or absence morning stiffness.
Methods: A database of 1208 Italian children included in 2 multicenter studies (1,2) who underwent a total of 3380 visits was examined to identify all visits in which the patients fulfilled the 2004 or 2011 criteria for ID. In case a patient met the ID criteria in more than 1 visit, only the first visit was retained. For each visit with ID, the duration of morning stiffness was categorized as ≤ 15 min or > 15 min. Clinical assessments included demographic features and parent-reported outcomes
Results: A total of 668 visits in which patients met the criteria for ID were identified. Absence of morning stiffness was reported in 564 (84.4%) visits, whereas in 104 visits (15.5%) there was morning stiffness. Among the visits with morning stiffness, in 55 (8.2%) duration was ≤15 min, and in 49 (7.3%) duration was > 15 min. The table shows the comparison of disease duration and parent-reported outcomes between patients with absence or presence of morning stiffness.

	Patients meeting 2004 ID criteria			
	Patients meeting 2011 ID criteria			
	No MS N = 564	MS ≤ 15 min N = 55	MS > 15 min N = 49	p-value
Median [IQR] disease duration	2.2 [0.6, 6.3]	2.0 [0.8, 4.0]	3.4 [0.4, 7.3]	0.859
JAFS total score > 0	107 (19.0)	24 (43.6)	38 (77.6)	< 0.001
PRQL PhS > 1 SD*	61 (10.9)	22 (40.7)	38 (79.2)	< 0.001
PRQL PsS > 1 SD*	32 (5.8)	9 (17.0)	16 (33.3)	< 0.001
VAS DA>0	170 (30.1)	44(80.0)	43(87.8)	< 0.001
VAS well-being > 0	211 (37.4)	42 (76.4)	44 (89.8)	
VAS pain>0	140 (24.8) 484	39 (70.9) 31	35 (71.4) 20	< 0.001
Remission	(87.5)	(59.6)	(41.7)	<0.001

MS: morning stiffness; IQR: interquartile range, *above the mean of healthy children (2)
Conclusion: Among patient**s** who met the 2011 criteria for ID, those with morning stiffness ≤15 min had worse parent-reported outcomes than those without morning stiffness. This finding suggests that parents may not perceive their child's disease state as true remission when lower degrees of morning stiffness are present. Notably, a sizeable proportion (7,3%) of children meeting the 2004 ID criteria had morning stiffness lasting > 15 min. The removal of the criterion "Duration of morning stiffness of ≤ 15 minutes" to "Absence of morning stiffness" in the definition for ID should be considered.

REFERENCES

[1] Filocamo, et al. A new approach to clinical care of juvenile idiopathic arthritis: the Juvenile Arthritis Multidimensional Assessment Report. J Reumatol 2011

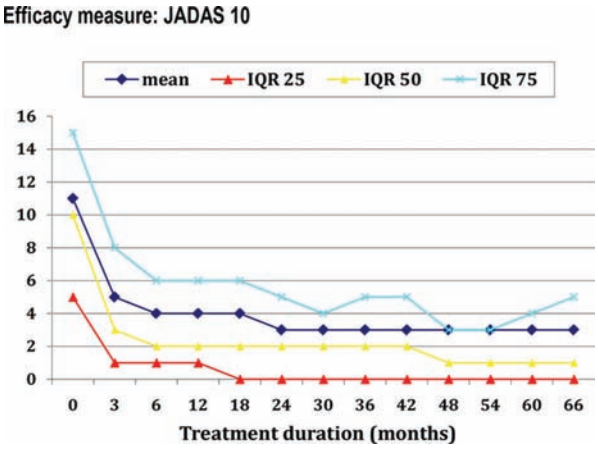
[2] Verazza, et al. Disease status, reasons for discontinuation and adverse events in 1038 Italian children with juvenile idiopathic arthritis treated with etanercept. PROJ 2016

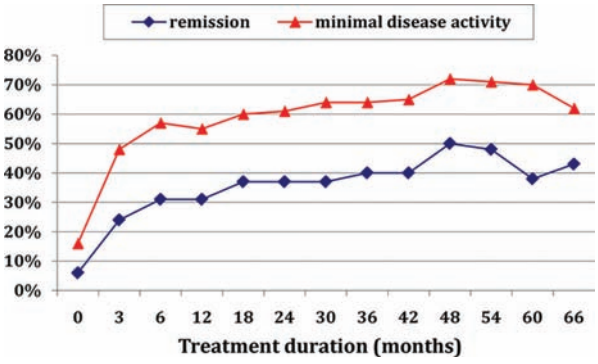
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SAT0502 EFFICACY AND SAFETY OF ADALIMUMAB IN JUVENILE IDIOPATHIC ARTHRITIS – 10 YEAR EXPERIENCE USING DATA OF THE BIKER REGISTRY

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Background: Since 2008, Adalimumab is approved for polyarticular juvenile idiopathic arthritis (JIA) and approval has been extended to other JIA categories and for uveitis.
Objectives: To evaluate efficacy and safety of Adalimumab in clinical practice in JIA patients in comparison to a biologic-naïve JIA cohort using the German Biologics registry (BiKeR).
Methods: Baseline demographics and disease activity parameters have been documented. Efficacy was determined using the JADAS10. Safety assessments were based on adverse events (AE) reports processed according to MedDRA.
Results: Until October 1, 2018, 951 JIA patients treated with Adalimumab were registered in BiKeR, representing 1519 patient-years (PY) of exposure. The total observation time (from date of first dose until last follow-up, censored, if another biologic was started) was calculated with 1709 PY.
At baseline, the cohort treated with Adalimumab had experienced disease with a disease duration of 5.4+/-3.9 years (mean+/-SD). 849 patients (89.3%) were pretreated with methotrexate, 525 (54.2%) with Etanercept. Concomitantly, 584 (61.4%) received methotrexate, 529 (55.6%) NSAIDs and 255 (26.8%) systemic corticosteroids. In the control cohort, 1517 biologic naive JIA patients started methotrexate.
Upon treatment, the median (IQR1-3) JADAS10 score decreased from 9.8 (4.7-15.5) at baseline to 3.9 (0.9-9.7) at the last follow-up. With respect to patients with ongoing treatment, approximately 43% achieved a JADAS defined minimal disease activity while 25% reached a JADAS defined remission at last follow-up.
904 AE have been observed during exposure or up to 90 days follow-up (58.4/100 exposure years (EY) [95% CI 54.7-62.3]). 66 qualified as serious AE (SAE) (4.3/100 EY [3.3-5.4]). These figures were compared to 1294 AE reported in the control cohort (34.8/year [32.9-36.8]) and 52 SAE (1.4/100 EY [1.1-1.8]).
Adverse events of special interest were serious/medically important infection (n=33), opportunistic infection (n=6, all H. zoster), malignancy (n=2), anaphylaxis/hypersensitivities (n=3), thrombotic disorders (n=2), autoimmune diseases (n=91, including 12 cases with psoriasis and 53 reports of uveitis), bleeding (n=3), cytopenias (n=4), pregnancies (n=2). Macrophage activation syndrome, demyelination, cardiac or cerebral infarction, or death were not observed. However, 2 malignancies were reported in patients who had ever been exposed to Adalimumab before. Both events were judged as unrelated.
A total of 449 patients (48.5%) discontinued Adalimumab, 188 (19.8%) due to lack of efficacy, 111 (11.7%) due to remission and 78 (8.2%) because of intolerance.
Conclusion: The current analysis adds to the established safety profile of Adalimumab and demonstrates that the rate of SAEs was comparable and consistent with the overall AE profile in paediatric patients. As expected, infections were the most frequent SAE. Uveitis, as well as psoriasis, are likely associated with JIA. Of notice, only one patient developed a chronic inflammatory bowel disease. No new safety signals specific to the paediatric population were identified in this large cohort of JIA patients.





REFERENCES

[1] Klein A, Becker I, Minden K, Foeldvari I, Haas JP, Horneff G. Adalimumab versus adalimumab and methotrexate for the treatment of juvenile idiopathic arthritis: long-term data from the German BIKER registry. Scand J Rheumatol. 2018 Nov 9:1-10.

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SAT0503 DEVELOPMENT OF MALIGNANCIES IN JIA PATIENTS EXPOSED TO BIOLOGIC AGENTS:A SINGLE CENTRE RETROSPECTIVE STUDY

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Background: Over the last two decades, the usage of biological agents in the treatment of Juvenile Idiopathic Arthritis (JIA) has been a successful and promising approach in controlling the disease activity and preventing chronic sequelaes. However, since Food and Drug Administration (FDA) has drawn attention to the possible association between the use of biological agents and the development of malignancy in 2008, there are ongoing concerns about the long-term safety data and side effect profile of the drugs with the contradictory study results.
Objectives: We aimed to present preliminary data on the incidence of malignancy in patients with JIA treated with biological agents versus the general population rates in Turkey.

Methods: A retrospective single-center hospital-based cohort study was performed to analyse cancer occurrence among JIA patients treated with biologic agents over the observation period between January 2004 and January 2018. The medical patient records were reviewed to obtain information about the clinical follow-up. As reference data for direct standardization; age, sex and calendar-year-specific incidence rates from Turkish cancer registry were used. The standardized incidence ratio (SIR, ratio of cancers observed to expected) was generated, with 95% confidence intervals.

Results: The study sample consisted of 504 JIA patients, who had been started their first biologic treatment between 2004 and 2018. Mean age was 17.1 years (SD 5.6) with 56% of female proportion. The mean disease duration was 10,3±5.1 years. Median time from baseline to start of the first biological was 17,5 (IQR:43) months. Mean age of initiation of biologic treatment was 9,8 ± 4,2 years. Etanercept was most commonly preferred drug to initiate as first-line biologic treatment (n=361,72%). 172 (34.1%) patients in the cohort required a switch to a second biologic agent. Main reason for switching to another biologic agent was due to lack of response (16.6%). Median duration of biologic use was 35 (IQR:41) months. One cancer occurred within observation period, compared with 0.095 expected (SIR:10.53, 95% CI 0.526 to 51.91). The patient was 18-year-old male, who had previously received etanercept and tocilizumab up until diagnosis of the hematological malignancy.

Conclusion: In our JIA cohort, patients treated with biologic agents appeared to have an increased rate of incident malignancy compared to children of the same sex and age group in the general population in Turkey. However, before mentioning a clear causal relationship, other potential contributing factors such as inflammatory process of the underlying disease itself and the use of concomitant immunosuppressants should be taken into consideration. Additional long-term studies with larger populations are needed to be able to draw definite conclusions.

REFERENCES

[1] Barth S, Schlichtiger J, Hartmann B, Bisdorff B, Michels H, Radon K, Hügle B, Walsh L, Haas JP. Incidence of malignancies in patients with juvenile idiopathic arthritis: A retrospective single-center cohort study in Germany. Mod Rheumatol. 2017 Jan;27(1):60-65.

[2] Mannion ML, Beukelman T. Risk of malignancy associated with biologic agents in pediatric rheumatic disease. Curr Opin Rheumatol. 2014 Sep;26 (5):538-42.

[3] **.** Turkish public health institution, Cancer Statistics of Turkey, 2016, https://hsgm.saglik.gov.tr/tr/kanser

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SAT0504 IGG4 RELATED DISEASE IN CHILDREN: A SINGLE CENTRE EXPERIENCE FROM NORTH-WEST INDIA

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Background: Immunoglobulin G4 related disease (IgG4RD) is a mutisystemic diorder characterized by elevated serum IgG4 levels and infiltration of IgG4 positive plasma cells accompanied by fibrosis. It is mostly considered a disease of adults and elderly people. There is paucity of literature on pediatric IgGRD. A recent systematic review has found only 25 pediatric cases.

Objectives: To report broad patterns of organ involvement in IgG4RD in children and also to create awareness among treating pediatricians about this new entity.

Methods: The study is based on a review of the hospital records of children with IgG4RD at tertiary centre from North-West India. Diagnosis was based on clinical features, IgG4 levels and characteristic histopathology findings.

Results: Six patients had IgG4RD. **Pt-1**; 10-year-old boy presented with fever for 3 months and significant hepatomegaly. Investigations showed anemia, thrombocytopenia, elevated erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). Ultrasonography (USG) revealed a hepatic mass (10x5x6 cm) that was confirmed on computed tomography. Liver biopsy showed increased plasma cells (>50 IgG4 positive plasma cells/HPF) and storiform fibrosis suggestive of IgG4 related hepatic mass. Serum IgG4 level was 420 mg/dl (N: 6-28). **Pt-2**; 12-year-old girl presented with an abdominal lump. Upper gastrointestinal endoscopy showed an intragastric mass with exophytic component. Histopathology of abdominal mass was consistent with IgG4RD. Serum IgG4 level was >170 mg/dl (N: 6-28). **Pt-3**; 21-year-old male symptomatic since age of 14 years with recurrent erythematous swellings over dorsum of the left hand, forearm and chest. Investigations showed anemia, elevated ESR, CRP, and hypergammaglobulinemia. IgG4 levels were 211 mg/dl (N: 7-57). Histopathology from left hand showed lymphoplasmacytic infiltrates, storiform fibrosis, obliterative phlebitis and increased IgG4 plasma cells (>50/HPF). **Pt-4**; 18-year-old girl presented with fever and weight loss. She had anemia, thrombocytosis, elevated ESR and CRP. USG abdomen showed omental thickening. Serum IgG4 level was 215 mg/dl (N: 7-57). Peritoneal and omental biopsy showed fibrosing stage of IgG4RD. **Pt-5**; 7-year-old girl presented with fever, oliguria, and anasarca. Investigations revealed anemia, elevated CRP, ESR, deranged renal functions and nephrotic proteinuria. Renal biopsy showed plasma cell infiltrate, storiform fibrosis, and 10-16 IgG4 plasma cells/HPF; consistent with IgG4 related tubulointerstitial nephritis. Serum IgG4 was 68 mg/dl (N: 7-26). **Pt-6**; 14-year-old, boy presented with painful protrusion of right eye for 8 months. MRI orbit showed bulky and enhancing extra-ocular muscles of the right eye with lacrimal gland involvement. Serum IgG4 was 119 mg/dl (N: 7-26). Histopathology of mass showed extensive fibrosis, obliterative phlebitis and lymphoplasmacytic cells infiltrate with IgG4 plasma cells >30/HPF, consistent with IgG4RD. All patients showed good clinical response to oral prednisolone (1-2 mg/kg/day and subsequently tapered). Four patients required maintenance therapy with azathioprine.

Conclusion: We report 6 cases of pediatric IgG4RD with varied organ involvement and clinical manifestations. Some of the cases presented as space-occupying lesions that can sometimes be confused with neoplastic lesions. It is important to suspect these disorders early and start immunosuppressive therapy promptly to halt end-organ damage due to fibrosis.

REFERENCES

[1] Karim F, Loeffen J, Bramer W, et al. IgG4-related disease: a systematic review of this unrecognized disease in pediatrics. Pediatr Rheumatol Online J. 2016;14(1):18

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SAT0505 LONG-TERM FOLLOW-UP IN KAWASAKI SYNDROME: EVIDENCE FROM RETROSPECTIVE MONOCENTRIC DATA IN REAL LIFE

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Background: Kawasaki syndrome (KS) is a severe medium size vasculitis with predilection for coronary arteries, mainly affecting young children. The identification of risk factors for coronary artery lesions (CAL) is the aim of the scientific society in order to early detect patients who need a more aggressive therapy.

Objectives: To report clinical data of a monocentric cohort of children with KS over a long-term follow-up.

Methods: A monocentric retrospective study between Feb 1982 and Aug 2018, involving children with KS diagnosis followed at the Rheumatology and Cardiology Unit of A. Meyer Children's Hospital. According to cardiac involvement, patients (pts) have been stratified in subject with absence of CAL (no-CAL) and presence of CAL. This latter has been divided in coronary ectasia (CE) and presence of coronary aneurism (CAn). Data analysis was conducted performing a descriptive analysis and assessing risk factors for CAL with analysis of variance (Tukey, LSD and Bonferroni test) and correlation test (Spearman rho test, Chi-square test). Each pt, regardless coronary involvement, underwent a scheduled cardiologic follow-up after 6-8 weeks (6 months, 1 year and ergometric test at 8 years old). Pts with CAL received additionally cardiac evaluations on clinical need. Pts with a follow-up of less than 1 year were excluded from follow-up analyses.

Results: Data from 361 pts (219 M, 142 F, aged 1 month-24 years and 5 months) have been reported. Median age of disease onset was 2 years and 1 month; 90% of pts developed the disease < 5 yrs. Disease onset at < 6 months was in 32 patients (8.9%), at < 1 year in 94 (26%). Full clinical data were available in 267 pts. Beside fever,

polymorphic rash was in 244 pts (91.4%), conjunctivitis in 229 (85.8%), mucositis in 224 (83.9%), extremities abnormalities in 196 (73.4%) and lymphadenopathies in 165 (61.8%). The average duration of fever was 7 days (range 1-25 days). CAL were detected in 73 pts (20.2%): 58 (16%) had CE, 15 (4.15%) had CAn. Median long-term follow-up was 10 years and 2 months (range 1years – 36 years). The variance analysis in the different groups of CAL showed a significative difference as regard age at disease onset (F= 2.77, p= 0.025), duration of fever (F=16.32, p<0.0001), CRP value (F=6.94, p=0.001) and day of first administration of IVIG (F=7.963 p<0.0001) (Table). A significant correlation between CAL and disease onset at <6 months (ρ=0.137, p=0.009), the need to administer 2 IVIG doses (ρ=0.305, p< 0.001), and male (ρ=-0.109, p=0.038) has been highlighted.

At the last follow-up, in the group of no-CAL (261 pts), cardiological visit, ECG, echocardiography and ergometric test (performed 177/261 pts) were normal in all pts. At the last available follow-up, 53 pts with CE had normal cardiological visit, ECG, echocardiography and ergometric test (performed 39/53 pts). Conversely, all 13 pts with CAn showed a normal cardiological visit, whilst ECG was abnormal in 1 patient (7.69%) and echocardiography showed persistent CAn in 8 (61.53%). Ergometric test was performed in 9/13 pts showing abnormal results in one pt (11.11%).

	No-CAL	CE	CAn
N pts	288	58	15
Median age at disease onset	2 y 1 m	2 y 5 m	5 m
Median duration of fever (days)	7	8	11
Average value of CRP (mg/dl)	6.81	8.38	14.15
Day of first dose of IVIG	8	7	11

Conclusion: Our long-term follow-up in a large, even monocentric, cohort reports possible risk factor of CAL according to current literature. Our long-term follow-up assesses, in real life, the benign course of KS in children without CAL after 6-8 weeks from onset. According to recent guidelines, stopping cardiologic assessment in no risk pts results economically advantageous, timesaving and able to reduce emotional discomfort in children and their families.

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SAT0506

KAWASAKI DISEASE AND CARDIOVASCULAR OUTCOMES IN THE LAST 25 YEARS. STUDY OF 55 PATIENTS FROM A REFERAL HOSPITAL IN THE NORTH OF SPAIN

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Background: Kawasaki disease (KD) or "mucocutaneous lymph node syndrome" is a systemic vasculitis in children that involve medium-sized vessels with predilection for coronary arteries. Due to the high probability of cardiovascular complications, an early diagnosis and treatment is required.

Objectives: A) To describe demographic, clinical and analytical features in a cohort of patients with KD diagnosis from northern Spain. B) To assess the rate of long-term cardiovascular outcomes.

Methods: We set up an observational study of patients with KD in a University Hospital between Jan-94 and Dec-18. Classic classification criteria were used for diagnosis[1]. Diagnosis of aneurysms was made by serial echocardiography and/or coronary-CT. Results are expressed as mean±SD or as median and interquartile range (IQR) as appropriate.

Results: 55 patients (28 women/27 men), with a mean age at diagnosis of 3.6±2.8 years. 60% presented a previous infection prior to diagnosis, most of them viral infection (**table 1**). At diagnosis, 43 patients were classified as complete KD (78.2%), presenting fever >5 days (98.2%), maculopapular rash (98.2%), oral mucosal involvement (89.1%), hands and feet edema (74.5%), conjunctival hyperemia (85.5%) and cervical adenopathy (50.9%). Analytically, there was an increase in acute phase reactants, presence of leucocytosis and thrombocytosis. All patients presented a monophasic disease course with a mean duration of symptoms of 12.6±4.9 days (**table 2**). In 8 patients (14.5%) coronary aneurysms were demonstrated and pericarditis/myocarditis was observed in 2. However, after a follow-up of 13.9±7.0 months, only 1 of them maintained coronary involvement. 98.2% received intravenous immunoglobulin (IGIV) according to international recommendations (2 g/kg). All patients received anti-inflammatory doses of acetylsalicylic acid at diagnosis and subsequently antiplatelet doses. 2 required endovenous corticosteroid, and in 1, an anti-TNF drug (infliximab) was needed (**table 2**). The incidence rate of KD in our cohort was 0.37 cases/100,000/year, 8-10 times lower than other national series[2]. However, mean age at onset, presence of previous viral infections and aneurysms development, were similar to countries with higher prevalence[3].

Conclusion: Although the incidence of KD in our population is lower than other territories, it is still the most frequent cause of acquired heart disease in childhood. Early recognition and treatment with IVIG improve prognosis leading to a decrease in the rate of long-term cardiovascular outcomes.

Table 1.

	Patients with KD (N=55)
Baseline data	
Age at diagnosis, mean±SD	3.57 ± 2.78
Sex (*female/male*), n (%)	28/27 (50.9/49.1)
Nationality (*Spanish*), n (%)	52 (94.5)
Follow-up (*months*), mean±SD	107.1 ± 75.7
Pregnancy and Birth	
Pregnancy (*to term*), n (%)	48 (87.3)
Weeks of pregnancy, mean±SD	39.3 ± 1.76
Infection during pregnancy, n (%)	2 (3.6)
Birth weight (*grams*), mean±SD	2935.8 ± 1223.7
Birth height (*cm*), mean±SD	50.0 ± 2.26
Predisposing factors	
Previous infections, n (%)	33 (60.0)
- Respiratory tract, n (%)	17 (30.9)
- Skin, n (%)	6 (10.9)
- Gastrointestinal, n (%)	11 (20.0)
Concomitant diseases, n (%)	22 (40.7)
- Asthma, n (%)	9 (16.4)
- Atopy, n (%)	9 (16.4)
- Others, n (%)	6 (10.9)
Family background of autoimmune disease, n (%)	1 (1.8)

Table 2.

	Patients with KD (N=55)
Kawasaki Disease	
Kawasaki criteria (*complete/incomplete*), n (%)	43/12 (78.2/21.8)
Fever, n (%)	54 (98.2)
Involvement of skin, n (%)	54 (98.2)
Involvement of oral mucosal, n (%)	49 (89.1)
Cervical adenopathy, n (%)	28 (50.9)
Hand or feet edema, n (%)	41 (74.5)
Conjunctival hyperemia, n (%)	47 (85.5)
Arthritis, n (%)	1 (1.8)
Gastrointestinal symptoms, n (%)	16 (20.1)
- Diarrhoea, n (%)	6 (10.9)
- Vomits, n (%)	8 (14.5)
- Abdominal pain, n (%)	4 (7.3)
Aseptic meningitis, n (%)	2 (3.6)
Pleural effusion, n (%)	1 (1.8)
Duration of symptoms (*days*), mean±SD	12.6 ± 4.9
Monophasic course, n (%)	55 (100.0)
Cardiovascular outcomes	
Acute manifestations (*pericarditis/myocarditis*), n (%)	2 (3.6)
Aneurysms, n (%)	8 (14.5)
Heart attack, n (%)	0 (0)
Sudden death, n (%)	0 (0)
Laboratory tests	
CRP (*mg/dL*), mean±SD	11.7 ± 8.3
ESR (*mm/h*), median [IQR]	82.0 [51.3 - 107.5]
Thrombocytosis, n (%)	32 (59.3)
Platelet (*× 10⁷/L*), median [IQR]	525 [346 - 878]
Treatment	
Immunoglobulin, n (%)	52 (98.2)
Acetylsalicylic acid, n (%)	55 (100.0)
Clopidogrel, n (%)	3 (5.5)
LMWH, n (%)	0 (0.0)
Corticoids, n (%)	2 (3.6)
Biological therapy (IFX), n (%)	1 (1.8)

REFERENCES

[1] Wood LE. Expert Rev Cardiovasc Ther.2007;5:553-61.
[2] Sánchez-Manubens J. Clin Exp Rheumatol 2016;34 (Suppl. S139-S144).
[3] Rowley AH, et al. Front Pediatr. 2018 Dec 11;6:374.

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SAT0507 EVALUATION OF THE NEW CLASSIFICATION CRITERIA FOR PFAPA SYNDROME

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Background: Modified Marshall criteria used for PFAPA syndrome have never been validated and are little used by the experts because the symptoms of monogenic fevers often overlap with PFAPA ones. A new set of classification criteria based on an international survey and a consensus conference in Genoa was developed in 2018.
Objectives: Evaluate the performance of the new criteria in a real-life setting
Methods: This is a multicentric, prospective and descriptive cohort study, through the recurrent fever module of the JIRcohorte platform. 417 patients diagnosed with PFAPA (187), monogenic fever syndromes (167) or unclassified recurrent fever syndrome (UPF=63) from Swiss and French centers were enrolled in the study. The new classification criteria were applied to this cohort and we calculated their performance. We then analyzed which of the criteria performed the less well.
Results: One hundred fourteen from 187 (61%) PFAPA patients met the new criteria, as well as 20/230 non-PFAPA patients (FMF: 3, MKD: 4, UPF: 13); 73 PFAPA patients did not meet the criteria. We calculated a specificity of 91.3% and a sensitivity of 60.9%. The least satisfied criterion among PFAPA patients not meeting the criteria was “absence of skin rash”. By removing this criterion, the sensitivity improved (81.2%), but the specificity decreased slightly to 86%.
Conclusion: Genoa 2017 classification criteria for PFAPA syndrome showed a good specificity but an insufficient sensitivity. Excluding the less satisfied criterion, the set reaches a sensitivity and specificity around 80% which could be a fair compromise for PFAPA classification criteria. Our study highlights the difficulty in establishing classification criteria due to the lack of gold standard for PFAPA diagnosis.

REFERENCES

[1] Vanoni F, Federici S, Antón J, Barron K, Brogan P, De Benedetti F, Dedeoglu F, Demirkaya E, Hentgen V, Kallinich T, Laxer R, Russo R, Toplak N, Uziel Y, Martini A, Ruperto N, Gattorno M, Hofer M. An international Delphi survey for the definition of the variables for the development of new classification criteria for Periodic Fever Aphthous stomatitis Pharyngitis Cervical Adenitis (PFAPA). Pediatr Rheumatol Online J. 2018, 16(1):27.

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SAT0508 AN INTERNATIONAL SURVEY ON APPROACHES TOWARDS IMMUNISATION IN CHILDREN WITH RHEUMATIC DISEASES: A REPORT OF THE PRES VACCINATIONS WORKING GROUP

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Background: Data on immunisation practices in Paediatric Rheumatology are scarce. EULAR recommendations for vaccination in paediatric patients with rheumatic disease (RD) were published in 2011. In some countries national recommendations for vaccination of immunocompromised patients are available.
Objectives: To ascertain the opinion and current practices of paediatric rheumatologists with regards to immunisation of children with rheumatic diseases (RD), and to establish their confidence to immunise the patients with RD on immunosuppressive medication with live vaccines in light of the evidence available.
Methods: An online survey of practices and opinions towards immunisations with a focus on immunisation of the immunocompromised child with RD was distributed to paediatric rheumatologists across the globe. Responses were collected via SurveyMonkey and descriptive analysis was performed. Responses were anonymous with the exception of identification of the country and length of practice.
Results: 289 responses were received from 53 countries in Europe, North and South America, Australia and Asia. 35% of the respondents had over 15 years of practice in Paediatric Rheumatology, while 42% had 5 - 15 years.
57% responded that all immunisations or at least part of them are given in their paediatric rheumatology unit, and 60% that the vaccinations are mandatory in their country. 93% of respondents support the immunisation of paediatric patients with RD, 6.9% responded that they are either not supportive/not sure/support only vaccinations with inactivated vaccines. 53% reported that national recommendations for immunisations of immunosuppresed child are available but not specific to Paediatric Rheumatology. 41% of respondents inform their practice on immunisation of patients with RD based exclusively on the EULAR recommendations, 37.5% based on national guidelines, 8.5% on local guidelines and 10% on combinations of the above. 48% of clinicians would postpone vaccinations in all cases if disease is active.
In terms of immunisations with live vaccines of patients with JIA on immunosuppresive treatment, 41% of respondents would recommend the first dose of MMR or Varicella vaccines to patients with stable disease on Prednisolone < 1 mg/kg/day (maximum 20 mg) for less than 1 month or higher dose up to 2 mg/kg/day for less than 14 days, 14% would also recommend these vaccines if the above steroid dose was given in combination with Methotrexate (MTX) < 15mg/kg/week, 30% would recommend these vaccines if the patient was on MTX monotherapy. Comparable percentages reported confidence to also recommend booster doses of the two vaccines for the above drug combinations (45%, 15.7%, 37%, respectively), whilst up 10% of respondents would recommend them to patients on anti-TNF agent alone, and up to 7% for other biologics. For patients with SLE and quiescent disease on similar medications as above, 41%, 15%, 31%, respectively, of clinicians reported confidence to recommend MMR or Varicella booster doses.
48% of the respondents identified the reluctance of other health professionals involved in the process of immunisations as the main reason hampering the vaccination of paediatric patients with RD, whilst 22% indicated parental refusal or hesitancy.
Conclusion: There is variation in practice and opinions worldwide with regards to immunisations in paediatric patients with RD, and this likely reflects the discrepancies between national guidelines for immunisation of immunosuppressed child and also national policies. More studies are required, but there is an increasing vote of confidence towards immunisation of patients on lower grade immunosuppression with MMR or varicella vaccines

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SAT0509 BODY MASS INDEX AND DISEASE ACTIVITY IN PORTUGUESE AND BRAZILIAN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS: RESULTS FROM RHEUMATIC DISEASES PORTUGUESE REGISTER – REUMA.PT

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Background: The influence of body mass index (BMI) on Juvenile Idiopathic Arthritis (JIA) disease activity is poorly understood. In adults with Rheumatoid Arthritis, obesity has been associated with higher disease activity, while in JIA patients, a previous study has failed to find any association.
Objectives: To investigate the relationship between BMI and JIA disease activity.
Methods: This is an international, multicenter, observational, cross-sectional study. JIA patients (according to ILAR criteria) aged ≤ 18 years, registered at Reuma.pt in Portugal and Brazil were included. Data was analysed upon records from the first registered visit. Age- and sex-specific BMI percentiles (P) were calculated based on WHO growth standard charts and categorized into underweight (P<3), normal weight (3≤P≤85), overweight (85<P≤97) and obesity (P>97). Disease activity was assessed by Juvenile Arthritis Disease Activity Score (JADAS-27). Univariate linear regression was used to examine the association of JADAS-27 with BMI categories. Two multivariate regression models were performed a) adjusting for age, gender, race, country, disease duration and JIA category (model 1); b) adjusting for those covariates plus use of DMARDs (model 2).
Results: 255 patients included, mean age 10.1±4.7 years, mean disease duration 6.3±4.9 years; 62% female; 85% Caucasian. Thirty-two percent were persistent oligoarticular, 9% extended oligoarticular, 34% polyarticular RF+, 6% systemic, 13% enthesitis-related arthritis, 5% psoriatic arthritis and 1% undifferentiated arthritis. The prevalence of underweight, normal weight, overweight and obesity was 7.5%, 65.9%, 15.7% and 11%, respectively. In the univariate linear regression, underweight was significantly associated with higher JADAS-27, compared to normal weight (B=-9.563, *p*<0.001), overweight (B=-10.661, *p*<0.001) and obesity (B=-7.422, *p*=0.004). Lower age (B=-0.299, p=0.012), shorter disease duration (B=-0.396, p=0.001), black race (B=6.852, p=0.033), RF+ polyarthritis (B=7.101, p<0.001), living in Brazil (B=5.357, p=0.002) and the absence of DMARD therapy (B=4.831, p<0.001) were also associated with higher JADAS-27.
In the model 1 of multivariate analysis, the same variables, except the country, remained significantly associated with higher disease activity. When DMARD therapy was added to the model (model 2), RF+ polyarthritis (B=4.447, *p*=0.001) and living in Brazil (B=4.728, *p*=0.013) were associated with higher JADAS-27. Patients with normal weight (B=-9.964, *p*<0.001), overweight (B=-10.316, *p*<0.001) and obesity (B=-9.502, *p*=0.001) had significantly lower activity disease, compared to underweight patients, as well as those under DMARD therapy (B=-4.858, *p*<0.001).
Conclusion: Despite the lack of adjustment for corticosteroids use, there seems to be an independent association between underweight and higher disease activity in JIA patients. Importantly, these results suggest that active disease can impair child's weight gain. Further studies are needed to confirm these findings and understand the underlying mechanisms of this association.
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Table 1. Relationship between JADAS-27 (dependent variable) and demographic and clinical characteristics of JIA patients.

	Univariate analysis			Multivariate analysis					
				Model 1			Model 2		
	B	95% CI	*p*-value	B	95% CI	*p*-value	B	95% CI	*p*-value
Age, years	-0.299	[-0.532 – (-0.066)]	**0.012**	-0.378	[-0.613-(-0.143)]	**0.002**			
Disease duration, years	-0.396	[-0.625-(-0.167)]	**0.001**	-0.245	[-0.465-(-0.024)]	**0.030**			
Gender (female)	0.104	[-2.173 – 2.382]	**0.928**						
Country (Portugal)	-5.357	[-8.675- (-2.038)]	**0.002**				-4.728	[-8.427-(-1.030)]	**0.013**
Ethnicity									
White european*									
White non-european	-0.620	[-8.549- 7.308]	**0.878**						
Black	6.852	[0.545 – 13.159]	**0.033**	5.967	[0.225-11.708]	**0.042**			
Biracial	-5.985	[-14.831-2.860]	**0.184**						
Romani	8.240	[-9.340-25.819]	**0.357**						
Asiatic	-0.860	[-11.053-9.332]	**0.868**						
JIA subtype									
Persistent oligoarthritis*									
Extending oligoarthritis	-1.408	[-5.365 – (2.548)]	**0.484**						
RF-positive polyarthritis	7.101	[4.557-9.644]	**<0.001**	5.471	[3.303-7.640]	**<0.001**	4.447	[1.968-6.925]	**0.001**
Systemic-onset	2.853	[-1.785- 7.490]	**0.227**						
Enthesitis-related arthritis	2.226	[-1.139 – 5.851]	**0.202**						
Psoriatic arthritis	2.856	[-2.078-7.789]	**0.255**						
Undifferentiated arthritis	8.833	[-3.049-20.714]	**0.144**						
BMI									
Underweight*									
Normal weight	-9.563	[-13.664 – (-5.462)]	**<0.001**	-9.706	[13.678-(-5.735)]	**<0.001**	-9.964	[-14.364 – (-5.565)]	**<0.001**
Overweight	-10.661	[-15.382 – (-5.940)]	**<0.001**	-10.382	[-14.949-(-5.816)]	**<0.001**	-10.316	[-15.540- (-5.902)]	**<0.001**
Obesity	-7.422	[-12.458 – (-2.386)]	**0.004**	-7.819	[-12.660-(-2.978)]	**0.002**	-9.502	[-14.912-(-4.092)]	**0.001**
cDMARD use	-3.414	[-6.055-(-0.773)]	**0.012**					-	
bDMARD use	-2.660	[-6.227-0.906]	**0.143**					-	
Any DMARD use	-4.831	[2.168-7.493]	**<0.001**				-4.858	[-7.319- (-2.396)]	**<0.001**

*Reference group

SAT0510 NON-BACTERIAL OSTEITIS IN CHILDREN: PROGNOSTIC FACTORS

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Background: The incidence of non-bacterial osteitis (NBO), a rare autoinflammatory disease in childhood, has increased over the past few years. Early diagnosis and treatment, as well as an adequate follow-up, are necessary to prevent sequelae and complications. However, prognostic factors of the disease are unknown.
Objectives: To establish the prognostic factors of NBO.
Methods: A retrospective study of NBO, according to Jansson criteria, in children (<14 years) at a tertiary hospital from 2009 to 2018. Descriptive statistics were performed to examine clinical features, diagnoses, treatments and progress of the disease. Furthermore, bivariate analysis was performed in order to investigate factors involved in the remission of the disease (with/out treatment), the number of relapses and sequelae. We considered p<0,1 as *significance level due to the small sample size*.
Results: We reviewed 15 cases. Table shows the descriptive data. The likelihood of remission was found to be associated with the presence of X-ray findings apart from sclerosis/lysis, (80% vs 40%, *p 0.07*), a high white blood cell count (mm3) (11988.7 ± 3004.9 vs 8915.7 ± 3310.3, p 0.08) and ESR (mm) (58.3 ± 36.3 vs 26.8 ± 17.4, *p 0.05*) at diagnosis

Table. Descriptive analysis

EPIDEMIOLOGIC DATA	
Sex (female), n (%)	13 (86.7)
Age (years), mean (±SD)	9,5 (±1,7)
Delayed diagnosis (months), median (IQR)	3 (2-6)
Clinical presentation, n (%)	
Pain	15 (100)
Limited movemen	13 (86,7)
Swelling	9 (60)
No. of lesions, median (IQR)	2 (1-5)
Bone lesion sites (n= 43), n (%)	
Clavicles	8 (53,3)
Hip	7 (46,7)
Others	20 (26,7)
BIOLOGICAL TESTS	
Blood test	
White blood cells (mm3), mean (±SD)	10554,7 (±3424,8)
CRP (mg/L) at diagnosis, median (IQR)	9,2 (4,9-18,1)
ESR (mm) at diagnosis, mean (±SD)	43,7 (±32,5)
MRI (n=14), findings, n (%)	
Edema	12 (85,7)
Lysis and/or cortical disruption	5 (35,7)
Periosteal reaction	3 (21,4)
Bone biopsy (n=12); histopathology, n (%)	
Fibrosis	9 (75)
Inflammation	8 (66,7)
TREATMENT	
Antibiotics, n (%)	8 (53,3)
Duration (days), mean (±SD)	50,5 (±15,9)
NSAIDs, n (%)	14 (93,3)
Duration (days), median (IQR)	72 (19,5-219,5)
Corticoids, n (%)	9 (60)
Duration (days), median (IQR)	110 (60-195)
Methotrexate, n (%)	2 (13,3)
Duration (days), median (IQR)	547,5 (365-547,5)
Pamidronate, n (%)	8 (53,3)
No. of cycles, mean (±SD)	7,8 (±6,9)
Zoledronate, n (%)	4 (26,7)
No. of cycles, median (IQR)	3 (2,3-3)
TNF inhibitors, n (%)	3 (20)
Duration (days), median (IQR)	880 (300-880)
OUTCOME	
No. of relapses, median (IQR)	2 (0-6)
Follow-up time (years), mean (±SD)	4,5 (±2,8)
Current status, n (%)	
Remission without treatment	8 (53.3)
Remission with treatment	7 (46.7)
Sequelae, n (%)	
Localized deformation	2 (13.3)

and a longer duration of disease (months) (5.7 ± 1.6 vs 3.1 ± 3.2, *p 0.06*). In addition, fewer relapses were found among patients with peroneal involvement [0 (0-0) vs 5 (1-6.7), *p 0.05*], a high white blood cell count at diagnosis (r -0.569, *p 0.02*) and those who were not treated with pamidronate [0 (0-5) vs 5 (1.2-6.7), *p 0.07*]. Finally, the lack of sequelae was related to the administration of pamidronate (100% vs 57.1%, *p 0.07*), younger age at diagnosis (years) (9.08 ± 1.4 vs 11 ± 2, *p 0.07*) and lesser CRP level at diagnosis (mg/L) [2.9 (2.9-2.9) vs 3.8 (2.9-3.8), *p 0.005*].

Conclusion: Advanced cases of NBO, without radiological signs of sclerosis or lysis, were more likely to achieve remission. Elevation of acute phase reactants was related to a better response to treatment and a lower relapse rates, but with a greater probability of sequelae. As described in the literature, bisphosphonates achieve higher rates of clinical and radiological remission. In our study, they are also associated with a lower relapse rates and the lack of sequelae. The last is the main reason to be considered the first treatment choice in NBO.

REFERENCES

[1] Schnabel A, Range U, Hahn G, Berner R, Hedrich CM. Treatment Response and Longterm Outcomes in Children with Chronic Nonbacterial Osteomyelitis. J Rheumatol. 2017; 44: 1058-1065

[2] Roderick MR, Sen ES, Ramanan AV. Chronic recurrent multifocal osteomyelitis in children and adults: current understanding and areas for development. Rheumatology. 2018; 57:41-48

[3] Zhao Y, Wu EY, Oliver MS, Cooper AM, Basiaga ML, Vora SS, et al. Consensus treatment plans for chronic nonbacterial osteomyelitis refractory to nonsteroidal anti-inflammatory drugs and/or with active spinal lesions. Arthritis Care Res (Hoboken). 2018; 70(8):1228-1237.

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SAT0511 CANAKINUMAB IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: CLINICAL INACTIVE DISEASE RATE AND SAFETY IN ITALIAN PATIENTS

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Background: Systemic juvenile idiopathic arthritis (sJIA) is a polygenic autoinflammatory disease. The innate immune mechanisms play a central role with overproduction of inflammatory cytokines. The increased knowledge on the role of these cytokines has provided a change in the natural history of the disease with the introduction of the targeted treatments. Remarkable results has been observed with canakinumab, an anti-interleukin-1β monoclonal antibody, in two clinical trials but little information are available in real life.

Objectives: To evaluate clinical inactive disease rate and safety of canakinumab in Italian patients with sJIA.

Methods: We have collected retrospectively clinical and laboratory data of patients with sJIA treated with canakinumab in 9 Italian Pediatric Rheumatology centers. Clinically inactive disease (CID) at 6 months was defined according to Wallace criteria. We analyzed the effect of canakinumab on fever, rash, number of actives joints, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and physician's global assessment of disease activity score.

Results: Forty seven patients (26 F) were included in the analyses. The median age (range) at the diagnosis and at the beginning of treatment with canakinumab was 7.6 (1-14.7) and 10.2 (1.7-22.2) years, respectively. Twenty seven patients (57.4%) had been previously treated with other biologic agents (18 with anakinra, 1 with tocilizumab, 6 with both and 2 with etanercept), withdrawn for inefficacy in 15/27 (55.5%). Thirty patients (63.8%) were receiving concomitant treatment with glucocorticoids at the median dose (range) of 0.69 (0.02-2.75) mg/kg/die. Thirtynine out of 47 patients had > 6 months of follow-up. Among these 39 patients, 27 (69.2%) achieved CID at 6 months and 5/27 (18.5%) were still on glucocorticoids. Of the 30 patients who received concomitant glucocorticoids at baseline, 24 achieved 6 months of follow-up and 12 (50%) of these were able to withdraw glucocorticoids. Minor adverse events were reported in 5/30 (16.6%) patients: upper respiratory tract infections in 4 and transient injection site reaction in 1. No cases of macrophage activation syndrome was reported.

Conclusion: Our results provide initial real world evidence of the efficacy of treatment with canakinumab in patients with sJIA. In our study the percentage of patients who reached CID at 6 months is slightly higher (69.2%) than reported at the end (from 3 months to one year) of the 2 published randomized trials (60%). No serious adverse events were recorded in our population.

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SAT0512 LONG-TERM FOLLOW-UP OF CARDIOVASCULAR OUTCOMES IN KAWASAKI DISEASE. OBSERVATIONAL STUDY FROM A SINGLE CENTER

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Background: Kawasaki disease (KD) is an acute systemic vasculitis of unknown aetiology which can lead to coronary aneurysm (CA) formation in 15-20% of patients. Long-term rates of adverse cardiac events are not well-known.

Objectives: a) to compare demographic, clinical and laboratory features of patients who developed coronary aneurysm with patients who did not. b) to assess long-term cardiovascular outcomes in the subgroup of patients who developed cardiac aneurysms.

Methods: Single center study of 55 patients with KD who were diagnosed between 1994-2009. KD diagnosis was based on the classic classification criteria[1]. We considered two groups: a) patients who presented CA at diagnosis. b) patients who did not present CA. Statistical analysis was performed with SPSS. Student´s t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher´s exact test for categorical variables as appropriate.

Results: Out of 55 patients with KD, 8 patients (3 men/5 women) presented CA at diagnosis. Differences between the two groups mentioned above are shown in **TABLE 1**. Mean age at diagnosis was lower in patients who presented CA (1.74 vs 3.88 years; p=0.044). The duration of symptoms was longer in patients with CA (14.0 vs 12.0 days; p=0.015), however there were no qualitative differences in the symptomatology. Regarding laboratory markers, C- reactive protein (CRP) levels were significantly higher in patients who developed CA (17.0 vs 10.8 mg/dL; p=0.047). There was also a tendency to higher levels of erythrocyte sedimentation rate (ERS) and higher platelet count. All patients received intravenous immunoglobulin (IVIG) and antiplatelet agents at the time of

TABLE 1

	Kawasaki Disease (N =55)		
	Aneurysms (n= 8)	No aneurysms (n= 47)	P
Demographic data			
Age (*años*), mean ± DS	1.74 ± 0.94	3.88 ± 2.88	0.044
Sex (women), n (%)	3 (37.5)	25 (53.2)	0.47
Pregnancy and birth			
Pregnancy (*full-term*), n (%)	7 (87.5)	41 (87.2)	0.47
Weight at birth (*g*), mean ± DS	3127.5 ± 1287.9	2903.2 ± 1223.9	0.64
Length at birth (*cm*), mean ± DS	50.6 ± 1.7	49.9 ± 2.3	0.54
Risk factors			
Previous infections, n (%)	3 (37.5)	30 (63.8)	0.24
- Respiratory tract, n (%)	1 (12.5)	16 (34.0)	0.22
- Skin, n (%)	0 (0.0)	6 (12.8)	0.28
- Gastrointestinal, n (%)	2 (25.0)	9 (19.1)	0.70
Concomitant diseases, n (%)	1 (12.5)	21 (44.7)	0.13
- Asthma, n (%)	1 (12.5)	8 (10.0)	0.75
- Atopy, n (%)	1 (12.5)	8 (17.0)	0.75
Diagnosis and clinical manifestations			
Kawasaki criteria (*complete*), n (%)	6 (75.0)	37 (78.7)	0.99
Fever, n (%)	8 (100.0)	46 (97.9)	0.99
Skin affection, n (%)	8 (100.0)	46 (97.9)	0.99
Mucosal involvement, n (%)	7 (87.5)	42 (89.4)	0.88
Cervical lymphadenopathy, n (%)	4 (50.0)	24 (51.1)	0.96
Swollen hands and/or feet, n (%)	5 (62.5)	36 (76.6)	0.40
Bilateral conjunctival injection, n (%)	6 (75.0)	41 (87.2)	0.36
Gastrointestinal manifestations			
- Diarrhea, n (%)	1 (12.5)	5 (10.6)	0.88
- Nausea, n (%)	1 (12.5)	7 (14.9)	0.99
- Abdominal pain, n (%)	0 (0.0)	4 (8.5)	0.39
Meningitis, n (%)	0 (0.0)	2 (4.3)	0.99
Pleural effusion, n (%)	0 (0.0)	1 (2.1)	0.99
Duration of symptoms (*days*), median [IQR]	14.0 [11.0-20.0]	12.0 [9.0-14.0]	0.015
Laboratory markers			
CRP (*mg/dL*), mean ± DS	17.0 ± 8.2	10.8 ± 8.0	0.047
ESR (*mm/1ª hora*), median [IQR]	105.0 [62.0-131.0]	76.0 [48.0-98.0]	0.072
Thrombocytosis, n (%)	6 (85.7)	26 (55.3)	0.22
Platelet count (*× 10^9/L*), median [IQR]	900.0 [603.0-961.0]	503.0 [339.0-744.0]	0.54
Treatment			
Immunoglobulins, n (%)	8 (100.0)	47 (100.0)	0.99
AAS, n (%)	8 (100.0)	47 (100.0)	0.99
Glucocorticoids, n (%)	1 (12.5)	1 (2.1)	0.27
Clopidogrel, n (%)	2 (25.0)	1 (2.1)	0.05
Infliximab, n (%)	1 (12.5)	0 (0.0)	0.15

diagnosis. Some of the patients with CA required glucocorticoids and anti-TNF agents. **TABLE 2** shows the characteristics of the 8 patients with CA who were followed-up for a mean of 13.7 ± 7.8 years. The mean size of the aneurysms was 5.6 ± 2.3 mm. Left coronary artery was the most common location (n=5). In two patients, cardiac arrhytmia was described. Five patients underwent ergometry tests being negative for ischemia in all of them. Coronary tomography was performed in other two patients observing persistence of CA in just one of the patients after 131 months of follow-up.

Conclusion: In our cohort, patients with KD who presented CA at the time of diagnosis were younger, had a longer duration of symptoms and higher levels of CRP. All patients received early treatment with IVIG and antiplatelet agents. At long-term follow up, persistent coronary affection was reported in just one of the patients. No severe cardiovascular outcomes were shown.

TABLE 2

	Sex/ Age at diagnosis (months)	Follow-up (months)	Kawasaki (complete/ incomplete)	CRP (mg/dL)	Duration of symptoms (days)	Aneurysm size (mm)	Aneurysm Location (coronary artery)	Treatment	Persistent aneurysm (yes/no)	Resolution time (months)	Arrythmia	Ergometry	Coronary tomography
1	Man/ 25	266	Complete	1.3	15	7	Left	IVIG + AAS	no	-	no	normal	-
2	Man/ 29	221	Uncomplete	17.3	11	4,7	Left	IVIG + AAS	no	12	VES	normal	-
3	Man/32	388	Complete	27.3	10	7	Right	IVIG + AAS	no	12	-	-	-
4	Woman/33	165	Complete	28.2	11	10	Left	IVIG + AAS + Dipiridamol	no	31	no	normal	normal
5	Woman/9	165	Complete	13.9	21	3	Left	IVIG + AAS	no	2	no	normal	-
6	Man/22	131	Complete	18.5	11	3	Left	IVIG + AAS	yes	-	no	normal	persistent aneurysm
7	Woman/8	38	Uncomplete	11.8	13	5	Right	IVIG + AAS + Clopidogrel	no	2	no	-	-
8	Man/5	41	Complete	18.0	30	5	Right	IVIG + AAS + Clopidogrel + Glucocorticoids + etx	no	36	LBBB	-	-

AAS: Acetylsalicylic acid; **CRP:** C- reactive protein; **IVIG:** Intravenous immunoglobulins; **LBBB:** left bundle branch block; **VES:** ventricular extrasystole.

REFERENCES

[1] Wood LE, et al. Expert Rev Cardiovasc Ther. 2007; 5: 553-61

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SAT0513 THERAPEUTIC APPROACH IN JUVENILE IDIOPATHIC ARTHRITIS: EMPHASIZING PAIN MEDICATION AND NEWLY INITIATED DISEASE MODIFYING ANTIRHEUMATIC DRUGS

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Background: Pain relief remains an important aspect in treating patients with juvenile idiopathic arthritis (JIA) despite of the new advanced therapeutic options. Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended providing symptomatic relief in JIA[1]. There is evidence of increased opioid use in adults with rheumatoid arthritis[2], the use of opioids in children with JIA is poorly studied.

Objectives: Aim of the study was to describe patterns in using of pain medication and newly initiated antirheumatic drugs in outpatients with JIA.

Methods: Data on 1507 patients (<16 years) with newly diagnosed JIA from 1 Jan 2010 to 31 Dec 2014 were collected from the register of the Finnish Social Insurance Institution. The index day was the date when reimbursement for JIA medication was admitted. The study period included 12 months pre- and post-index date. All patients were without disease modifying antirheumatic drugs (DMARDs) before the index day. For each patient three age-, gender- and residence-matched controls (altogether 4511) were identified from the National Centre for Population. Drug purchases were assessed in 3-month periods. Co-morbidities were evaluated.

Results: 20-fold more JIA patients purchased NSAIDs, 10-fold more paracetamol, and 10-fold more opioids (mostly tramadol and codeine) compared to controls. 648 patients (43%) purchased NSAIDs during 0-3 months before and after the index day, and 165 patients (11%) 10-12 months after the index day.

28 patients (2%) purchased opioids 12 months before the index-day, and 14 patients (1%) 12 months after. Paracetamol was purchased by 83 patients (5.1%) and by 59 patients (3.9%), respectively.

Methotrexate (n = 1361 (90.3%)) was most commonly prescribed conventional DMARD, followed by prednisolone (n = 368 (24.4%)), hydroxychlorine (n = 194 (12.9%)), sulfasalazine (n = 107 (1.8%)), and biological DMARDs (n = 41 (2.7%)). 26 patients (1.7%) were without antirheumatic treatment at 3-months after index-day.

JIA patients had significantly more comorbidities and traumas ($p<0.001$), and more surgical procedures ($p<0.001$) compared to controls.

Conclusion: Purchases of pain medication reduced after DMARDs were started. Only small proportion of JIA patients purchased opioids, despite of having more traumas and surgical procedures.

REFERENCES

[1] Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: Initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res 2011; 63:465-482.

[2] Zamora-Legoff JA, Achenbach SJ, Crowson CS, Krause ML, Davis JM,3rd, Matteson EL. Opioid use in patients with rheumatoid arthritis 2005-2014: A population-based comparative study. Clin Rheumatol 2016;35:1137-1144.

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SAT0514 **MIRAJE: A TRANSVERSAL THERAPEUTIC EDUCATION PROGRAM FOR CHILDREN AND ADOLESCENTS WITH CHRONIC INFLAMMATORY RHEUMATISM**

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Background: Therapeutic patient education (TPE) is now recommended in the health care pathway of patients with chronic inflammatory rheumatism (CIR) but few pediatric programs are currently available. MIRAJE is a program for children and adolescents with CIR. It has been developed within a French health network (RESRIP (Réseau Rhumatismes Inflammatoires Pédiatriques)) to improve patient care for paediatric patients with CIR living in the Ile de France region.

The originality of the program was to design cross-cutting TPE using common issues to different pathologies: the experience of chronic illness, the management of daily life, inflammatory attacks, long-term treatments, physical activity.

Objectives: Assessment of acquisition of coping, self-care and safety skills.

Methods: After signing a written consent, an educational assessment is conducted in an individual interview with the patients and/or parents (for children under 6 years old), by a member of the multidisciplinary team. Five group sessions and one self-injection session are offered to patients. During the collective sessions, patients and parents are reappointed according to 4 groups: the group of parents, that of adolescents (12-18 years), that of children (6-11 years) and that of toddlers (<6 years). To investigate the cognitive and behavioral impact of TPE on our patients and/or parents, we selected patients aged over 6 years who completed TPE program. A pre-post comparison was performed using a skill/knowledge questionnaire, based on three educational objectives: adaptation (8 skills), self-care (5 skills) and safety (1 skill), before and after the intervention.

Results: We present the results of the first year of implementation of our TPE program (2017). Nineteen children and 20 parents attended at least one group session. Ten participants (6 children aged 6 to 17 and 4 parents) completed the TPE program. The diseases covered were juvenile idiopathic arthritis (7), systemic lupus (2) and mevalonate kinase deficiency (1). All participants improved their knowledge and skills following TPE with greatest improvement in management of inflammatory attacks (self-care) (10 patients after TPE versus 1 at initial assessment), chronic fatigue (6 versus 1) and in development of physical activity (8 versus 2) (adaptation). Otherwise, all 10 participants acquired self-care skills (4.1 versus 1.4 average skills per patient at initial assessment), 9 acquired coping skills (6.8 versus 2.6 skills) and 8 security skills. Regarding self-injection workshop, most patients (4/5) have acquired skills in subcutaneous self-injection.

Conclusion: MIRAJE is the first French cross-cutting TPE program for children suffering from CIR and their parents. Although the number of participants having benefited from a full TPE program is relatively low, the first results are very encouraging. Indeed, TPE has allowed improving knowledge and skills for most children and parents.

TPE allows a better acceptance of the disease and fosters patient's empowerment in daily management. We plan to expand our program to more patients with various RICs.

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SAT0515 **GROWTH AND DEVELOPMENT OF PATIENTS WITH POLYARTICULAR-COURSE JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH SUBCUTANEOUS ABATACEPT**

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Background: Efficacy of SC abatacept (ABA) in patients (pts) with polyarticular-course juvenile idiopathic arthritis (pJIA) was shown in a 2-year, open-label, Phase III international study (NCT01844518).[1] Restricted growth and delayed puberty are associated with pJIA;[2] however, the effect of ABA on growth and development is unknown.

Objectives: To investigate the effect of ABA on height, BMI and Tanner staging, and to assess the impact of BMI on ABA efficacy in pts with pJIA.

Methods: Patients with pJIA were grouped into two age cohorts (2–5 and 6–17 years [yrs]) and received weight-tiered SC ABA (10 to <25 kg [50 mg], 25 to <50 kg [87.5 mg], ≥50 kg [125 mg]) weekly for 4 months (mths). JIA-ACR30 criteria responders at 4 mths could receive SC ABA for another 20 mths.[1] Standardised height and BMI were obtained by z-score calculation with age adjustment using World Health Organization Child Growth Standards (2007); mean changes from baseline (BL) in z-scores were assessed over time to Day (D) 645. Efficacy was assessed by age cohort using linear regression (BL standardised BMI as a continuous variable) and by logistic regression with BL standardised BMI (z-score) classed as low (≤−2), normal (>−2 to ≤1), overweight (>1 to ≤2) and obese (>2) (intent-to-treat, non-responder imputation for missing efficacy data). In the 6–17-yr cohort, Tanner staging was recorded at BL and at discontinuation or completion of study.

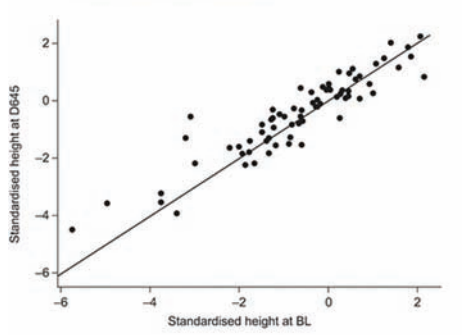
Results: Data for standardised height and BMI are presented. In 6–17-yr-old pts with BL Tanner stage ≤3 (n=100), BL mean (SD) height was −0.53 (1.53); at D645, mean (95% CI) change was 0.20 (0.06, 0.34; Figure 1). In 6–17-yr-old pts with a BL height ≤−1 (n=42), BL mean (SD) height was −2.10 (1.01) and mean (95% CI) change at D645 was 0.49 (0.23, 0.76). In 2–5-yr-old pts, BL mean (SD) height was 0.07 (1.37); at D645, mean (95% CI) change was 0.13 (−0.09, 0.36). In 13 pts aged 6–17 yrs of the lowest height (Tanner stage ≤3 and BL height ≤−2), mean (SD) height increased from −3.28 (1.10) at BL to −2.59 (1.31) by D645.

At BL, mean (SD) BMI was 0.20 (1.33) in the 6–17-yr cohort (n=173) and 0.25 (1.57) in the 2–5-yr cohort (n=46); at D645, mean (95% CI) change in BMI was 0.02 (−0.13, 0.16; Figure 2) and 0.17 (−0.08, 0.42), respectively. Overall, no relationship was seen between change from BL in Juvenile Arthritis Disease Activity Score 71 (JADAS71) and BL BMI in either age cohort. The proportions (odds ratio [OR]; 95% CI of OR) of obese pts aged 6–17 yrs achieving JIA-ACR30 (0.15; 0.04, 0.55), JIA-ACR50 (0.18; 0.05, 0.63), JIA-ACR70 (0.17; 0.04, 0.67) and JADAS71 minimal disease activity (0.27; 0.07, 1.03) at Day 645 were significantly lower compared with pts with a normal BMI, but the sample size in the obese category was low (n=12); this effect was not seen in overweight pts (n=37).

In female pts (n=92), shifts in Tanner stages from BL to D645 were as expected; male sexual maturation was difficult to assess due to the small sample size (n=20).

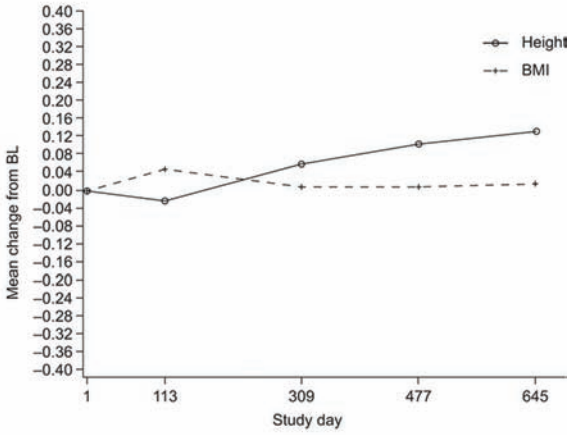
Conclusion: Abatacept improves growth and development in pts with pJIA. Early therapeutic intervention with abatacept may help reduce growth restrictions in pts with pJIA. BMI may impact the efficacy response, resulting in lower efficacy in obese, but not in overweight, pts with pJIA versus pts with normal BMI.

Figure 1. Standardised baseline height versus standardised height at D645 in pts aged 6–17 yrs with Tanner stage ≤3



BL=baseline; D=day; pt=patient; yr=year

Figure 2. Standardised height and BMI over the study period in pts aged 6–17 yrs



Height (n)	173	161	147	140	125
BMI (n)	173	161	147	140	125

BL=baseline; pt=patient; yr=year

REFERENCES

[1] Brunner HI, et al. *Arthritis Rheumatol* 2018;70:1144–54.
[2] Umławska W, et al. Arch Med Sci 2010;6:19–23.

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I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:
AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.
The money received for these activities are directly transferred to the Gaslini Institute's bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Daniel J Lovell Consultant for: Consulting fees and/or honoraria from Astra Zeneca, Wyeth Pharma, Amgen, Abbott, Pfizer, F. Hoffmann-La Roche, Novartis, UBC, Takeda, GSK, Boehringer, and Celgene

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SAT0516 CLINICAL FEATURE OF ACUTE RHEUMATIC FEVER AND POST-STREPTOCOCCAL REACTIVE ARTHRITIS

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Background: Acute Rheumatic Fever (ARF) and Post-streptococcal reactive arthritis (PSRA) are well known as post-streptococcal syndromes with arthritis in children. ARF have been declining in developed nations and it is generally thought to be a disease of the past. Despite decreasing incidence, focal outbreaks have been reported in developed nations. Despite its importance, ARF and PSRA epidemiology has not been reviewed recently.
Objectives: The aims of this study were to assess ARF and PSRA incidence between 2010 and 2018 in Japan.
Methods: This retrospective Study examined ARF and PSRA incidence in 2010-2018, using medical record included in a total of 108 hospitals.
Results: From a total of 63 hospitals (58% response rate), 34 cases of ARF and 32 cases of PSRA were reported.
The mean age of ARF was 8.0 years (3-15 years), and female/male ratio was 13/21. Manifestations including; carditis, 26 (78.8%); arthritis, 26

(78.8%); Erythema marginatum in 7 (21.2%); Sydenham chorea, 4 (12.1%); Subcutaneous nodules, 2 (6.1%), respectively. And minor criteria were; fever, 27 (81.8%); first degree heart block, 7 (21.2%); elevated inflammatory markers (ESR, CRP), 30 (90.9%). ARF patients were treated with antimicrobial agent therapy 33 (100%); NSAIDs 24 (72.7%); and glucocorticoids therapy 15 (45.4%). All ARF patients were prescribed with antimicrobial agent prophylaxis.

On the other hand, the mean age of PSRA was 8.0 years (3-14 years), and female/male ratio was 17/14. Three patients (9.4%) had monoarthritis, 15 patients (46.9%) had oligoarthritis, and 14 patients (43.6%) had polyarthritis. Two patients had arthritis and enthesitis. And fever in 24 (75.0%) and Elevated inflammatory markers in 29 (90.6%). PSRA patients were treated with antimicrobial agent therapy 25 (78.1%); NSAIDs 27 (84.4%); and glucocorticoids therapy 3 (9.4%). During the follow up, there was no patient with carditis. 18 (56.3%) patients with PSRA were prescribed with antimicrobial agent prophylaxis.

Conclusion: In this study, ARF is rare in the Japanese pediatric population, but ARF has not yet disappeared. We observed high incidence of arthritis, carditis and erythema marginatum. No PSRA case was complicated with carditis. General pediatrician need to have updated information about ARF and PSRA even in industrialized countries.

REFERENCES

[1] Sato S, Uejima Y, Suganuma E, et al. A retrospective study: Acute rheumatic fever and post-streptococcal reactive arthritis in Japan. Allergol Int. 2017;66(4):617-620.

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SAT0517 MANAGEMENT OF RISK OF VARICELLA INFECTION IN IMMUNOCOMPROMISED CHILDREN: WHAT IS THE EVIDENCE?

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Background: Varicella-naive children on methotrexate are at risk of severe infection if they encounter varicella. Current guidance advises that children on low-dose methotrexate can safely receive live vaccines[1], but management of children on higher doses or combination immunosuppression is challenging as there is no consensus about their management. Acyclovir and varicella-zoster immune globulin (VZIG) are commonly used as post-exposure prophylaxis (PEP).

Objectives: Assess the evidence for use of acyclovir and/or VZIG as PEP in the management of varicella exposure in susceptible children taking methotrexate.

Methods: A literature search using PubMed, the Cochrane Library and EMBASE was conducted from November to December 2017, using the terms methotrexate, immunocompromised, varicella, child, prophylaxis, acyclovir, VZIG and their variations. Only full papers, in English language, studying children were analysed (63 abstracts read for relevance, 28 papers obtained, 11 papers included).

Results: There have been no randomised controlled trials (RCTs) analysing the effectiveness of acyclovir and/or VZIG as PEP in immunocompromised children. The studies that do exist (see table for key publications) are small and uncontrolled and have largely been carried out in oncology rather than rheumatology patients. While they suggest that acyclovir and VZIG are effective at reducing historical infection rates of >70%[1], a significant proportion of recipients still get varicella.

Conclusion: There is only level 3 evidence for the use of acyclovir and/or VZIG as PEP in susceptible children on methotrexate. The literature indicates acyclovir is more effective, but this is a grade 3 recommendation only. A RCT to compare the effectiveness and acceptability of VZIG and acyclovir is needed, however the difficulty of randomising a cohort of similarly immunocompromised patients should not be underestimated.

REFERENCES

[1] Public Health England (2017). Contraindications and special considerations: the green book, chapter 6. *Immunisation against infectious disease*.

[2] Evans, et al. (1980*). HUMAN ANTI-CHICKENPOX IMMUNOGLOBULIN IN THE PREVENTION OF CHICKENPOX*. The Lancet 315(8164):354-356.

[3] Zaia, et al. (1983). Evaluation of Varicella-Zoster Immune Globulin: Protection of Immunosuppressed Children after Household Exposure to Varicella. The Journal of Infectious Diseases 147(4):737-743.

[4] Shinjoh, et al. (2009). Varicella zoster exposure on paediatric wards between 2000 and 2007: safe and effective post-exposure prophylaxis with oral aciclovir. Journal of Hospital Infection 72(2):163-168.

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SAT0518 READINESS FOR TRANSITION – CROATIAN VERSION AND PILOT EVALUATION OF THE TRANSITION READINESS ASSESSMENT QUESTIONNAIRE (TRAQ) IN RHEUMATOLOGIC PATIENTS

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Background: Rheumatic diseases of childhood extend to adulthood as an active disease in 30-70% of patients, which is the reason for requiring transition of rheumatologic care into adulthood. Transition should be individualized based on patient's readiness, and good transition readiness analysis tools should be available at the time of transition.

Objectives: As systematic review of the available assessment tools for transitional readiness in adolescents with chronic diseases has shown that only the Transition Readiness Assessment Questionnaire (TRAQ) has proven reliability in its key measurement components[1], we have decided to use the TRAQ[2] in pediatric rhematology patients.

Methods: English version of TRAQ was translated to Croatian, afterwards a back-translation to English was done. Due to difference in the insurance policy in Croatia (health care is free for children under 18 years of age), question 9 was modified into: "Are you aware of the fact that after 18 years of age you have to start paying for the additional health insurance?"

A pilot study was performed in order to validate translated TRAQ by applying questionnaire to pediatric rheumatology patients at the time of transition.

Results: A total of 41 patients at the median age of 18.25 years (range 17.8-21.1 years) were enrolled, 28 female and 13 male patients. Most of

Authors	No. of Patients & VZV Status	Cause of Immunosuppression	Treatment	Outcomes
Evans et al (1980)[2]	102 immunosuppressed children, 80 of whom were known to be seronegative for VZ IgG antibodies	Variable	Zoster immune globulin (ZIG) as a single dose - up to 1 year, 100 mg; 1-5 years, 250 mg; 6-10 years, 500 mg; 11-14 years, 750 mg; 15-16 years, 1000 mg	24/80 became infected; 17 with symptoms
Zaia et al (1983)[3]	164 immunocompromised children	Variable 131: malignancy 30: other immunosuppressive treatment 3: primary immunodeficiency	81 given VZIG 83 given ZIG Dose: 1.25 ml/10 kg (max dose, 6.25 ml), given within 96 hours of exposure	VZIG: 49/81 became infected ZIG: 57/83 became infected Varicella pneumonia occurred in 3 cases in each group
Shinjoh et al (2009)[4]	65 immunocompromised children (some with a history of varicella); 76 immunocompetent children; 11 immunocompetent controls	Variable	Oral acyclovir (10 mg/kg/dose; 400 mg max dose; 4 times daily). Minimum of 7 days treatment, starting from 7 days after exposure	2/65 immunocompromised children developed varicella. 1/76 immunocompetent children developed varicella. 2/11 controls developed varicella

the patients had juvenile idiopathic arthritis (28 patients, 68.3%), 7 (17.1%) had mixed connective tissue disease, 3 (7.4%) had Raynaud's syndrome and there was one patient (2.4%) with each of the following diagnosis: SLE, fibromyalgia, and polyarteritis nodosa. The mean follow up time before the transition was 5.3 years (3 months - 14 years).

In general, the TRAQ was well understood and was completed in a short time by the study participants. No major difficulties were observed and all the patients were able to read and answer the questionnaire.

Average score for each of the subparts of TRAQ was: managing medication 4.29 (range 2.25-5.0), appointment keeping 3.82 (1.43-5.0), tracking health issues 3.63 (1.67-5.0), talking with providers 4.68 (2.0-5.0), managing daily activities 4.39 (3.0-5.0) with overall score 4.05 (2.50-5.0), showing good overall readiness of our patients for transition. Readiness for transition in our group of patients is likely due to the age of transitioning over 18 years and good preparing for transition done by the team in the months preceding transition.

Conclusion: The Croatian version of the Transition Readiness Assessment Questionnaire was validated in the population of transitional patients with chronic rheumatic diseases. It has proven to be easily applied and well understood, and its results showed adequate readiness for transition among our patients. According to our 7-year experience and 81% of follow up visits in adult rheumatology among transitioned patients in previous years, we believe that these results are correct.

We shall continue following these patients through adult rheumatology visits and in few years' time we shall verify whether they continue regular follow ups and prove to have been ready for transition as TRAQ has suggested.

REFERENCES

[1] Zhang LF, Ho JS, Kennedy SE. A systematic review of the psy-chometric properties of transition readiness assessment tools in adolescents with chronic disease. BMC Pediatr. 2014;14:4.

[2] Sawicki GS, Lukens-Bull K, Yin X, Demars N, Huang IC, Livingood W, Reiss J, Wood D. Measuring the transition readiness of youth with special-healthcare needs: validation of the TRAQ -Transition ReadinessAssessment Questionnaire. J Pediatr Psychol. 2011; 36:160–171.

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SAT0519 CLINICAL CHARACTERISTICS, TREATMENT AND OUTCOMES OF ENTHESITIS-RELATED ARTHRITIS IN TAIWAN

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Background: Juvenile idiopathic arthritis (JIA) has been categorized into seven different subtypes according to International League of Associations for Rheumatology system (ILAR) criteria [1]. Enthesitis-related arthritis (ERA) has represented the largest subtype in Taiwanese cohort study [2].

Objectives: The aim was to compare the clinical characteristics, treatments and outcomes of ERA in one of tertiary medical center in Taiwan to other subtypes of JIA. Further, to determine patients' characteristics and risk factors help to predict the development of active and non-active treatment outcomes in ERA.

Methods: Retrospective review of patients diagnosed with JIA between March 1993 and December 2018 at a pediatric rheumatology clinic in National Taiwan University Hospital (NTUH), Taipei, Taiwan were enrolled. The outcome assessments were based on Wallace criteria to categorize patient into active and non-active (inactive, remission on medication and remission off medication) group.

Results: One hundred and eighty-three patients were included for 8 years mean follow up duration. Distribution of JIA subtypes in Figure 1 shown ERA was the single largest category of JIA (39.89%) in Taiwan. The demographic details of ERA patients in Table 1 revealed: male predominant (86%), late onset age (11.1±3.2 yrs), majority with HLA-B27 positive (92%), sacroiliac join or lumbosacral involvement (16%) and anterior uveitis (10%). Category specific outcomes in Table 2 showed ERA and extensive oligoarthritis were less likely to achieve non-active treatment response compared to persistent oligoarthritis. Among risk factors contributed to poorer treatment response in ERA were any clinical signs of sacroiliitis with P value of significant (0.0057).

Table 1. ERA patients and disease characteristic, n=73

Characteristics	N (%)
Demographic characteristics	
Male sex	63 (86)
Age at onset, mean ±SD years	11.1±3.2
Age at follow-up visit, mean ±SD years	17.6±5.4
Disease duration at follow-up visit, mean ±SD years	6.5±5.0
Disease characteristic	
Enthesitis and arthritis	71 (97)
Presence of HLA-B27 antigen	67 (92)
Presence of or a history pf sacroiliac joint tenderness and/or inflammatory lumbosacral pain	12 (16)
Onset of arthritis in a male> 6y/o	68 (93)
Acute (symptomatic) anterior uveitis	7 (10)
History of AS/ERA/sacroilitis with IBD, Reiter's syndrome, or acute anterior uveitis in 1st degree relative	8 (11)

Table 2. JIA category-specific outcomes

	ERA n=73	Persistent Oligo n=33	Extensive Oligo n=22	Polyarticular RF(+) n=9	Polyarticular RF(-) n=19	Systemic n= 25
Active	46 (63)	14 (42)	15 (68)	7 (78)	10 (53)	14 (56)
Non-active	24 (33)	18 (55)	5 (23)	2 (22)	8 (42)	8 (32)
Inactive	13 (18)	2 (6)	3 (14)	2 (22)	3 (16)	0 (0)
Clinical remission on medication	5 (7)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)
Clinical remission off medication	6 (8)	15 (46)	2 (9)	0 (0)	5 (26)	8 (32)
Loss follow up	3 (4)	1 (3)	2 (9)	0 (0)	0 (0)	2 (8)
Expire	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	1 (4)
Active/Non-active (P)	46/24 (**0.036)	14/18 (————)	15/5 (** 0.027)	7/2 (0.071)	10/8 (0.422)	14/8 (0.151)

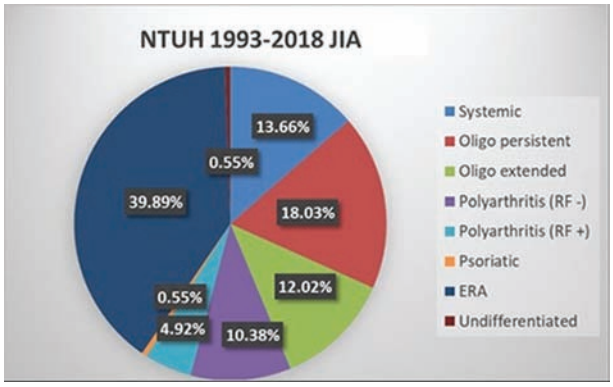


Figure 1. Distribution (%) of JIA subtypes in 183 Taiwanese children from NTUH between year 1993~2018

*Comparison to Persistent Oligoarthritis. **P<0.05 with significant

Conclusion: ERA has represented the most common subtype of JIA in Taiwanese cohort study and has poorer treatment responses when compared to other JIA subtypes. To identify risk factors that contributing to poorer ERA treatment response might help more aggressive therapeutic strategy and improve outcome of ERA.

REFERENCES

[1] Ravelli, A. and A. Martini, Juvenile idiopathic arthritis. The Lancet, 2007. 369(9563): p. 767-778.

[2] Shen, C.C., et al., Clinical features of children with juvenile idiopathic arthritis using the ILAR classification criteria: a community-based cohort study in Taiwan. J Microbiol Immunol Infect, 2013. 46(4): p. 288-94.

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SAT0520 **DEFINING OUTCOME MEASURES IN JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS BY A SYSTEMATIC REVIEW ANALYSIS. DO WE NEED A CONSENSUS?**

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Background: Juvenile Idiopathic Arthritis associated Uveitis (JIA-U) represents its most frequent extra-articular manifestation and the main cause of childhood uveitis in in developed countries. The broad variety of outcome measures utilized makes the comparison of the disease course, risk for complications, impairment in visual function, and responses to treatment quite difficult.
Objectives: Our aim was to define related and unified outcome measures in JIA-U.
Methods: A systematic review between January 2000 and December 2018 was performed to identify studies investigating outcome measures used in JIA-U
Results: The initial search identified 8252 articles of which 29 were potentially eligible. Eighteen eligible articles remained in the analysis. A total of 27 studies, including 2 RCTs, were included. Among these studies 12 outcome measures for JIA-U use have been identified (grade of cells in the AC, grade of flare in the AC, VA, amblyopia, structural complications, use and sparing of oral corticosteroids and immunosuppressive drugs, surgery requirement, biomarkers, bilateral disease, JIA persistence, quality of life assessments, uveitis subtype). As regards primary outcome measures, 44% among studies included one or more variables related to disease activity (i.e. grade of flare, grade of cells); 56% included visual function performance (i.e. visual acuity); 68% (17/25) included one or more variables of disease-associated tissue damage or complications (i.e. cataract, amblyopia); 24% included disease features (i.e. bilateral disease; uveitis subtype); 44% included laboratory features (i.e. biomarkers); 8% included JIA features (i.e. persistence of disease); 12% included quality of life (i.e. EYE-Q); 44% included management (i.e. use and sparing of oral corticosteroids and other immunosuppressive drugs; surgery requirement).
Conclusion: Our systematic review surveys the heterogeneity around outcome measures related to JIA-U in children, even in RCTs. It does not provide the solution to overcome the heterogeneity in uveitis studies, but it does provide an estimate of the scale of the problems and provides data to inform this important debate; highlighting the requirement to obtain a new consensus regarding a common approach to identify suitable and efficient outcome measures in JIA-U.

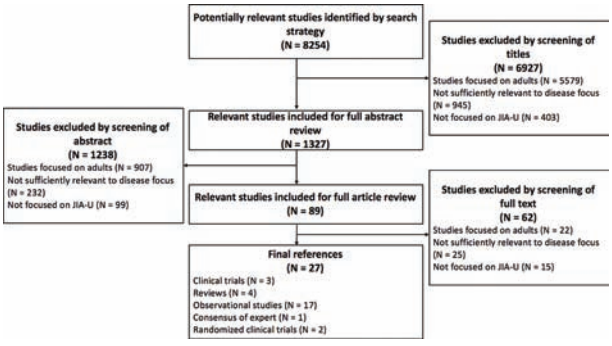


Figure 1. Study selection process flow diagram of literature research.

Legend. N= number of identified studies.

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SAT0521 **RISK FACTORS FOR THE OCCURRENCE OF UVEITIS IN THE PATIENTS WITH OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS**

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Background: Oligoarticular (oligo) onset juvenile idiopathic arthritis (JIA) is defined as 4 or fewer affected joints within 6 mo of disease onset. This JIA subtype typically involves large joints. Patients who develop arthritis in 4 joints after the first 6 mo are considered to have extended oligo JIA, and have a worse prognosis. Chronic uveitis is a common and serious comorbid condition of juvenile idiopathic arthritis, with insidious presentation and potential to cause blindness. Knowledge of clinical associations will improve risk stratification.
Objectives: We aim to analyzed identification of the incidence of oligo articular JIA-associated uveitis and its risk factors is essential to optimize early detection.
Methods: We enrolled 185 patients who were diagnosed with oligo JIA and seen at our clinic. Visual acuity was recorded in logMAR. LogMAR is the logarithmic representation of visual acuity. Visual impairment was stratified by severity as logMAR >0.3 (worse than 6/12) or $\geq$ 1.0 (6/60 or worse).
Results: A total of 185 oligo JIA patients were included in this study (61.6% female, 65.9% ANA positive). 32 of all patients (72.2%) developed uveitis within follow-up. The median age (IQR) at diagnosis was 89 (42-131.5) months, median follow-up of 24.5 (10-29) months. At disease onset, 12% of all patients were examined small joint arthritis (defined as involvement of any of the metatarsophalangeal or proximal or distal interphalangeal joints of the foot, or metacarpophalangeal or proximal or distal interphalangeal joints of the hand). 7 out of 35 (20%) patients with oligo onset JIA involving only small joints developed extended arthritis (>4 joints), compared to 15 out of 150 (10%) of patients with only large joint oligo onset JIA [p<0.01]. 10 of 32 patients with uveitis had small joints involvement (p<0.01)
Of these, 18 (56%) patients developed uveitis after enrollment while 14 (44%) patients had uveitis before first JIA symptoms. 58.8% of patients (n=8) developed uveitis with in first two years of JIA while 41.2 patients had uveitis developed up to 2 years. Uveitis was associated with positive ANA (p<0.001) and small joint involvement. In contrast, young age (< 7 years) at oligo JIA diagnosis, female sex, extended oligo JIA and used systemic steroid were not finding associated with uveitis. Of the 57 affected eyes, posterior synechiae (n=20) was the predominant complication on presentation. During the follow-up period new complications were seen in 11 eyes (13%). Posterior synechiea (6 eyes, 7,5%) was the most frequent complication observed followed by cataract (3 eyes, 3,%) and glaucoma (2 eyes, 2,5%). At the presentation, 8 patients (25%) had visual acuity loss to > 0.3 LogMAR (6/12) and to $\geq$1.0 LogMAR (6/60). However, 3 (0.09%) patients had visual acuity loss end of the follow up time. Biologically were used in 75% of JIA patients while 8 (25%) children with JIA did not require any biologic treatment. Systemic and topical steroids treatment were gradually tapered and discontinued in all patients after initiation of biologics. In JIA associated uveitis patients, biologic therapy was used in 24/32 (75%) at the follow up time (infliximab in 9, adalimumab in eleven, and tocilizumab in one patient) and 9 children (37.5%) required $\geq$2 biologics over the follow up period.
Conclusion: The patients with oligo JIA who had present antinuclear antibodies, and small joint involvement should be particularly close observation.

REFERENCES

[1] Rheumatology (Oxford). 2018 Dec 26. doi: 10.1093/rheumatology/key406
[2] Reumatologia. 2018;56(3):149-154. doi: 10.5114/reum.2018.76902

Disclosure of Interests: None declared
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SAT0522 COMPARISON OF CHILDREN CARRYING E148Q VARIANT WITH CHILDREN CARRYING HOMOZYGOUS PATHOGENIC VARIANTS

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Background: Familial Mediterranean fever (FMF) is the most frequent autoinflammatory disease. Nearly 300 *MEFV* variants had been reported and recorded in INFEVERS database. The most common disease-associated variants are mapped on exon 2 and 10 of chromosome 16. Although *E148Q* variant is the most common one among carriers, its role as a disease causing mutation is still debate (1).
Objectives: The aim of our study was to evaluate and compare the demographic data, clinical features and severity scores of patients carrying only *E148Q* variant with the patients homozygous for pathogenic MEFV mutations (*M694V, M694I, M680I, V726A*). One of our objective was to test and compare these two groups for the diagnostic utility of 2 adults and 1 pediatric FMF diagnostic criteria (Tel Hashomer, Livneh and Pediatric) (2-4).
Methods: The medical records of 1685 children diagnosed and followed up as FMF were reviewed retrospectively. The demographic, clinical and genetic data of children carrying only *E148Q* variant (either heterozygous or homozygous carriers) (group 1) and children with pathogenic homozygous mutations (*M694V, M694I, M680I, V726A*) (group 2) were collected. All patients were evaluated for three diagnostic criteria.
Results: Children with *E148Q* variant were 128 and children with pathogenic homozygous variants were 429. Male to female ratio was 1.13 in group 1 and 1.15 in group 2 ($p>0.05$). The mean age of patients in group 1 was 12.1±4.7, in group was 2 14±5.9 ($p<0.001$). The mean age of symptom onset was 5.4±4.1 in group 1, 4.3±3.6 in group 2 ($p=0.01$. Consanguinity was significantly higher in group 2 (29% *vs* 53%, $p<0.01$). In group 1 17.9% had a sibling with FMF, while in group 2 27% had a sibling with FMF ($p=0.03$). Clinical features like pleuritis, synovitis, recurrent fever, erysipelas-like erythema and monoarthrtis were significantly more common in group 2 than group 1(31.7% *vs* 9.3%; $p<0.001$, 55.9% *vs* 32%; $p<0.001$, 86.9% *vs* 78.9%; $p<0.03$, 31.2% *vs* 7%; $p<0.001$, 51.7% *vs* 28.1%; $p<0.001$, respectively). Incomplete attacks were significantly more common in group 1 than group 2 (16.4% *vs* 7.4%; $p<0.005$). Moderate and severe PRAS scores were significantly higher in group 2 (93.9% *vs* 71.9%; $p<0.001$). Laboratory values like C-reactive protein, erythrocyte sedimentation rate, serum amyloid A were found significantly higher in group 2 than group 1. (3.6±6.3 *vs* 0.8±1.2; $p<0.001$, 13±10 *vs* 7.3±6; $p<0.001$, 6.9±22.5 *vs* 2.9±2.2; $p=0.007$, respectively). The percentage of children diagnosed according two Tel Hashomer and pediatric criteria was significantly higher in group 2 than group 1 (88.5% *vs* 77.3%; $p=0.002$, 95.3% *vs* 84.3%; $p<0.001$, respectively). But both groups show similar diagnostic utility according to Livneh criteria.
Conclusion: Although children carrying *E148Q* variants meet the three validated diagnostic criteria of FMF. They had milder course of disease than children homozygous for pathogenic *MEFV* variants both clinically and in laboratory means.

REFERENCES

[1] Touitou I (2001) The spectrum of Familial Mediterranean Fever (FMF) mutations. Eur J Hum Genet 9, 473–83
[2] Sohar E, Gafni J, Pras M, Heller H (1967) Familial Mediterranean fever. A survey of 470 cases and review of the literature. The American journal of medicine 43:227-253
[3] Livneh A, Langevitz P, Zemer D, Zaks N, Kees S, Lidar T, Migdal A, Padeh S, Pras M (1997) Criteria for the diagnosis of familial Mediterranean fever. Arthritis and rheumatism 40:1879-1885.
[4] Yalcinkaya F, Ozen S, Ozcakar ZB, Aktay N, Cakar N, Duzova A, Kasapcopur O, Elhan AH, Doganay B, Ekim M, Kara N, Uncu N, Bakkaloglu A (2009) A new set of criteria for the diagnosis of familial Mediterranean fever in childhood. Rheumatology (Oxford, England) 48:395-398.

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SAT0523 EVALUATION OF COEXISTING DISEASES IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is most common periodic fever syndrome in childhood. It is characterized by fever attacks, abdominal pain lasting between 6 - 72 hours, serositis and erysipelas like erythema. Since FMF is inherited in autosomal recessive manner, it has higher frequency in populations that have higher rate of consanguineous marriages. As it is a lifelong chronic disorder, it is important to understand its clinical course for preventive medicine. Despite the higher incidence of variety of disorders shown studies among adult FMF patient, there is not enough data from pediatric populations.
Objectives: The objective of the study is to evaluate the comorbid disorders in a large pediatric familial Mediterranean fever cohort.
Methods: Six hundred and eighty-six children with FMF were interviewed by the same investigator between October 2018 and January 2019 in our pediatric rheumatology department. Demographic features and MEFV gene mutations were recorded from patients' charts. Patients and/or their parents were asked about characteristics of their fever episodes, presence of arthralgia, arthritis, abdominal pain, chest pain in the course of fever attack and coexistence of any other disease confirmed by a physician.
Results: Female-male ratio of our cohort was 0,85. Mean age of the patients was 12,8 ± 7,4 years. Mean age of patients at disease onset and at the time of diagnosis was 4,38 ± 3,46 years and 6,55 ± 3,67 years, respectively. Sixty-five and a half percent of patients had family history of FMF. Consanguineous marriage rate was 29,8%. Most common MEFV mutations were: M694V homozygotes (18,8%), M694V heterozygotes (17,7%), R202Q heterozygotes (13,1%), R202Q homozygotes (5,5%) and V726A heterozygotes (4,9%), respectively. Resistance to colchicine treatment was present in 43 (6,2%) patients. Number of patients that underwent tonsillectomy were 9 (1,3%) and number of patients that had appendectomy was 11 (1,6%). Detected coexisting diseases are listed in **Table 1**.

. Detected coexisting diseases in patients group.

	n(%)
Juvenile Idiopathic Arthritis	40(5,8)
• Systemic	4 (0,5)
• Oligoarticular	17(2,4)
• Polyarticular	5(0,7)
• Enthesitis Related Arthritis	1(0,1)
• Juvenile Spondylitis	13(1,8)
Asthma/Reactive Airway Disease	26(3,7)
Henoch Schonlein Purpura	18(2,6)
Uveitis	10(1,4)
Inflammatory bowel disease	9(1,3)
Periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis (PFAPA)	7(1)
Acute Rheumatic Fever	7(1)
Migraine	7(1)
Allergic Rhinitis	6(0,8)

Conclusion: In this study, we have reported increased frequency of juvenile idiopathic arthritis, asthma- reactive airway disease, Henoch Schonlein purpura, uveitis, inflammatory bowel disease, PFAPA syndrome and acute rheumatic fever in a large pediatric FMF cohort. Those findings consistent with data from literature. It is important to be alert about these diseases that may develop in patients with FMF for preventing them from the potential morbidities.

REFERENCES

[1] Barut K, Sahin S, Adrovic A, et al. (2018). Familial Mediterranean fever in childhood: a single-center experience. Rheumatology international, 38(1), 67-74.
[2] Beser ÖF, Kasapçopur Ö, Çokugras F Ç, et al. (2013). Association of inflammatory bowel disease with familial Mediterranean fever in Turkish

children. Journal of pediatric gastroenterology and nutrition, 56(5), 498-502.
[3] Barut K, Sahin S, Kasapcopur O. (2016). Pediatric vasculitis. Current opinion in rheumatology, 28(1), 29-38.
[4] Pehlivan E, Adrovic A, Sahin S, et al. (2018). PFAPA Syndrome in a Population with Endemic Familial Mediterranean Fever. The Journal of pediatrics, 192, 253-255.

Disclosure of Interests: None declared
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SAT0524 THE ROLE OF MEFV GENE SEQUENCING ON PREDICTING THE RISK AND DISEASE SEVERITY OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Genetically susceptibility was essential in pathogenesis of systemic juvenile idiopathic arthritis (SJIA).
Objectives: To find out whether *MEFV* mutations contributed to the occurrence of SJIA and study the association of *MEFV* mutations with systemic juvenile idiopathic arthritis (SJIA) patients' disease severity.
Methods: SJIA children diagnosed based on the ILAR criteria[1] and followed up for at least 6 months between January 2011 and July 2018 were enrolled. Meta-analysis was performed to evaluate the contribution of *MEFV* mutations to SJIA susceptibility. All included children were divided into three groups by presence and number of *MEFV* mutations, namely, those without *MEFV* mutation, the one mutation group, and those with more than one mutation. Demographic and clinical characteristics, as well as disease severity were compared among these groups. Disease severity was evaluated with the following three items, i.e., average duration of use of each drug, the proportion of disease activity duration and relative relapse rate. Kaplan-Meier curves and log rank test were used to estimate the probability of the first relapse.
Results: Eighty-nine patients met the ILAR criteria, among which 55 patients were eligible for further analysis. The *MEFV* mutations of our subjects primarily existed in exons 2 and 3. No significant difference were found in frequency of each mutation between SJIA children and healthy controls. Meta-analysis demonstrated that M694V was a risk factor for SJIA (pooled OR: 7.13, 95% CI: 3.01-16.89). Comparing with the one mutation group, biologics were used more frequently in those without or with more than one mutation in *MEFV* (p=0.017). Moreover, the proportion of disease activity duration was significantly lower in the one mutation group than the other two groups (p=0.028 and 0.002 respectively).
Conclusion: The mutation M694V in *MEFV* contributed to occurrence of SJIA. SJIA patients carrying one heterozygous mutation in *MEFV* tend to be less severe, which might be attributed to E148Q.

REFERENCES

[1] Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International league of associations for rheumatology classification of juvenile idiopathic arthritis: Second revision, Edmonton, 2001. J Rheumatol. 2004;31(2):390-2.

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SAT0524B THE HETEROGENEITY OF JUVENILE PSORIATIC ARTHRITIS: EVIDENCE FROM A LARGE MULTINATIONAL COHORT

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Background: Despite being considered as a distinct diagnostic category in the current ILAR classification criteria, Juvenile Psoriasic Arthritis (JPsA) is known to be a heterogeneous clinical entity, with growing evidence suggesting at least two age-based distinct subgroups(1)
Objectives: To identify and characterize subgroups of patients classified as JPsA according to the ILAR criteria and their possible differences in outcomes.
Methods: Cross-sectional data from patients enrolled in The EPidemiology, treatment and Outcome of Childhood Arthritis (EPOCA) study and classified as JPsA according to ILAR criteria (n=308) were analyzed. Latent class analysis (LCA) was used to identify subgroups of subjects with similar profiles ILAR criteria for JPsA (presence at onset of psoriasis, dactylitis, nail changes, first-degree relative with psoriasis) and age of arthritis onset. Multinomial logistic regression (three-step method) was performed to explore differences across the obtained classes in clinical-laboratoristic features at onset and outcomes measures collected at visit, namely JADAS scores, VAS-measured Pain, Overall Well-Being (PGA) Pediatric Rheumatology Quality of Life Scale (PRQL). In patients with disease duration more than 2 years (n=233), the relation with Articular and Extraarticular Juvenile Arthritis Damage Index (JADI) was also assessed.
Results: LCA revealed 5 classes: 1) late-onset patients with psoriasis, characterized by higher frequency of axial involvement at visit (n = 121); 2) early-onset patients with psoriasis, more likely to be ANA-positive (n = 66); 3) young females with dactylitis at onset and family history of psoriasis, more likely to present with symmetric joint involvement (n = 62); 4) subjects with nail changes and family history of psoriasis(n=34); 5) patients exhibiting dactylitis and nail changes at onset, mostly males, with higher rates of HLA-B27 positivity, small joint involvement and enthesitis at visit (n = 25). Class 1 is associated with higher scores of JADAS10, pain, PGA and JQ; these group also shows higher JADI-A than Class 3. Extraarticular damage is worst for Class 2 subjects.
Conclusion: The data driven clustering approach revealed several subgroups, confirming the heterogeneity of JPSA in a multinational cohort. Later-onset subjects with psoriasis have more aggressive disease, being clearly distinct from early-onset ANA-positive patients with psoriasis. The results suggest the need to revise the current classification in order to identify groups that may benefit from different therapeutic choices.

REFERENCES

[1] Stoll ML, Nigrovic PA. Clin Dev Immunol. 2006;13(2–4):377–80.

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Diagnostics and imaging procedures

SAT0525 IMMUNOSCINTIGRAPHY OF SACROILIAC JOINTS SHOWS VERY GOOD AGREEMENT WITH INFLAMMATION ON MRI IN AXIAL SPONDYLOARTHRITIS PATIENTS

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Background: Currently MRI is the preferred imaging method to detect bone marrow edema (BME), the hallmark of sacroiliitis. MRI plays an important role in the early diagnosis of axial Spondyloarthritis (axSpA). Biological disease-modifying anti-rheumatic treatment has revolutionized the therapeutic armamentarium of axSpA. With drugs targeting TNFα, 50% of axSpA patients achieve a clinically important response. Therefore, we hypothesized that if we would be able to demonstrate in vivo expression of TNFα in sacroiliac joints by scintigraphy with 99mTc-radiolabeled certolizumab pegol (99mTc-CZP), this might lead to more 'evidence-based biological therapy'.

Objectives: To investigate the agreement between BME on MRI-SIJ and tracer uptake on immunoscintigraphy with 99mTc- CZP in the same location in patients with axSpA.

Methods: CZP was conjugated with S-HYNIC and subsequently radiolabeled with approximately 740 MBq Tc99m and injected intravenously. Static images with single photon emission tomography (SPECT)/computed tomography (CT) of SIJ were acquired 4-6h post injection. Uptake of the tracer was scored semi-quantitatively, per quadrant of the SIJ: 0=no uptake, 1=faint uptake or 2=clear uptake. BME on MRI was scored per quadrant over 6 slices as absent or present, providing a maximum score of 6 per quadrant. Agreement between MRI-SIJ and immunoscintigraphy was calculated (kappa; percentage agreement) for all quadrants separately. To calculate the agreement a cut-off of $\geq$1 was used for MRI scores as well as immunoscintigraphy scores. In addition, depth and intensity of BME lesions on MRI-SIJ (as defined in the Spondyloarthritis Research Consortium of Canada (SPARCC) method) were assessed per slice per SIJ.

Results: 7 axSpA patients (mean age 36±5.7 years) had both MRI-SIJ and immunoscintigraphy available. The mean score for BME lesions seen on MRI was 12.9±13.2 and 4.86±5.4 for tracer uptake observed on the immunoscintigraphy. In 2 out of the 7 patients there was no BME on MRI and in the same 2 patients there was no tracer uptake seen on scintigraphy. In table 1 kappa coefficients and percentage agreement for every quadrant are shown. The mean and median of agreement for all quadrants was k=0.80 and k=0.86, respectively. Clear tracer uptake (score 2) was correlated to deep BME lesions on MRI-SIJ (extending over the depth of at least 1cm from the articular surface); the observed Spearman's rho correlations were 0.986 (p<0.00) and 0.956 (p<0.00) for left and right SIJs, respectively. Regarding intensity, no significant correlation with clear tracer uptake was found. Interestingly, in one additional patient with complete ankylosis of the SIJs on radiographs no tracer uptake could be detected, suggesting that in vivo detection of TNF does not correlate with bone formation.

Table 1. Agreement on presence of BME on MRI-SIJ in a quadrant and tracer uptake on the immunoscintigraphy in that same quadrant.

Location of the SIJ quadrant	Kappa (CI)	Percentage agreement
Right upper iliac quadrant (RQ1)	0.720 (0.21-1)	85.7%
Right upper sacral quadrant (RQ2)	0.696 (0.14-1)	85.7%
Right lower sacral quadrant (RQ3)	0.417 (0-1)	71.4%
Right lower iliac quadrant (RQ4)	1 (1-1)	100%
Left upper iliac quadrant (LQ1)	1 (1-1)	100%
Left upper sacral quadrant (LQ2)	0.588 (0-1)	85.7%
Left lower sacral quadrant (LQ3)	1 (1-1)	100%
Left lower iliac quadrant (LQ4)	1 (1-1)	100%

Conclusion: Inflammation on MRI-SIJ can be detected with immunoscintigraphy with 99mTc-CZP. The immunoscintigraphy showed good correlation with BME lesions on MRI in patients with axSpA. Deep lesions, considered specific for axSpA, showed an almost perfect correlation.

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SAT0526 THE COURSE OF ABERRANT FINDINGS ON MRI OF THE SACROILIAC JOINTS OVER 6 MONTHS IN POSTPARTUM WOMEN

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Background: Sacroiliac bone marrow oedema (BME) on magnetic resonance imaging (MRI) can have different causes. Besides spondyloarthritis (SpA), other more rare causes as stress fractures, mechanical stress, infections or malignancies can be identified. There are limited data regarding the specificity of MRI lesions in a non-SpA population. Pregnancy and vaginal delivery might induce the presence of inflammatory and/or structural MRI lesions by mechanical stress.

Objectives: To assess aberrant findings on MRI features of the sacroiliac joints (SIJ) in postpartum women and describe the course after a 6 month time period.

Methods: Twenty-five women underwent an MRI of the SIJ within 10 days after childbirth; delivery by caesarean section was excluded. The scan was repeated after 6 months. One subject was lost to follow-up. Three trained readers systematically scored inflammatory and structural SpA-like lesions (not reported here) and qualitatively described other aberrant findings. Both time points were scored on T1-weighted and short tau inversion recovery (STIR) MRI images. Readers were blinded for time sequence and clinical and demographic information on the subjects.

Results: In 16 out of 25 (64%) subjects there were aberrant MRI findings at baseline. Thirteen out of 25 (52%) showed BME at the symphysis pubis on the baseline MRI (fig. 1). After 6 months, 6 out of 24 (25%) subjects still showed BME; in 1 subject BME of the symphysis pubis was increased at 6 months. Two out of 25 (8%) displayed a sacral fracture on the baseline MRI. Both these fractures were asymptomatic and resolved completely after 6 months (fig. 2). One out of 25 subjects (4%) showed degenerative disc disease at level L5-S1 in the form of Modic type 2; vertebral and endplate related replacement of bone marrow with fat deposition. As expected, the presence of Modic type 2 did not decrease at follow-up. No other aberrant findings were seen.

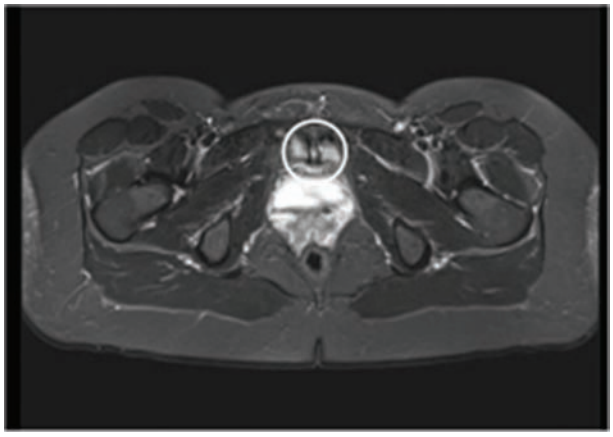


Figure 1. BME of the symphysis pubis on STIR sequence.

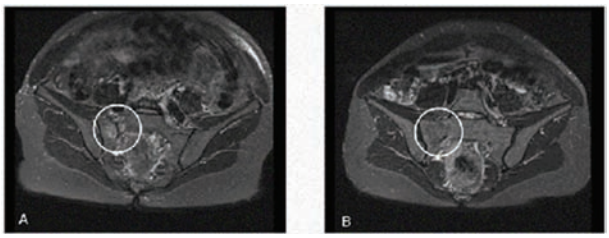


Figure 2. STIR image of sacral fracture at baseline (**A**) and after 6 months (***B***).

Conclusion: Aberrant findings, like sacral fractures and degenerative disc disease, are observed when assessing MRI-SIJ of postpartum women for SpA-like lesions. BME at the symphysis pubis was often seen shortly after birth and half of those lesions persisted at follow-up after 6 months.
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SAT0527 DOPPLER IN ENTHESES: A POTENTIAL USEFUL OUTCOME IN ACTIVE SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS

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Background: The assessment of activity in spondyloarthritis (SpA) and psoriatic arthritis (PsA) involves several domains, including entheses. Clinical enthesitis has shown low sensitivity, specificity and reliability. The inclusion of ultrasound (US) could be an objective outcome in the assessment of the disease.
Objectives: To assess the prevalence of peripheral US enthesitis using an US score, at patient level, among active SpA and PsA patients.
Methods: A cross-sectional study in patients with SpA and PsA active disease (defined as patients proposed to start or switch biological therapy according to physician criteria and in agreement with clinical guidelines) was undertaken. Basal assessment included clinical features, physical examination and laboratory tests. Patients underwent bilateral US examination of peripheral entheses according to the MAdrid Sonographic Enthesitis Index (MASEI). MASEI and OMERACT enthesitis Power Doppler (PD) definitions were checked. Each enthesis was scanned in both the longitudinal and transverse planes, and 5 second videos were recorded for reliability. An inter-reader analysis by three readers was performed. For statistical analysis Mann-Whitney U test, Kruskal-Wallis test and intraclass correlation coefficients (ICCs) were used.
Results: 36 patients were included, of whom 19(52.8%) were ankylosing spondylitis (AS) patients, 10(27.8%) PsA, and 7(19.4%) non radiographic axial spondyloarthritis (nr-axSpA). Mean age was 49.8±13.1 years and 18 (50%) were females. Mean DAS28 (3.5±1.3), ASDAS (3.7±0.9), BASDAI (5.7±2.2) and CRP values (11.5±12.6) reflect moderate-high disease activity. Demographic and clinical baseline characteristics are shown in Table 1. Mean global MASEI score was 28.1(±9.1) and 30 patients (83.3%) scored ≥18 (proposed cut-off point to diagnose SpA). Abnormal US findings consistent with at least one enthesis showing PD signal (whether using MASEI or OMERACT PD definition) were observed in 29(80.6%) of patients while two or more PD in entheses were observed in 21(58.3%) patients (PD MASEI definition) or 18(50%) patients (PD OMERACT definition), without significant variation among the different SpA subtypes. The inter-reader reliability among the three readers was high (mean ICC of 0.85). Table 2 shows the ICC of every reader pair.
Conclusion: Presence of PD enthesitis is found in 80% of patients with active SpA and PsA. This finding is independent of SpA subtype and support the usefulness of PD US in the assessment of enthesitis.

Table 1. Baseline characteristics of active SpA patients

		Total n= 36	AS n=19 (52.8%)	PsA n=10 (27.8%)	nr-axSpA n=7 (19.4%)	p
Age		49.8±13	50.3±14.5	51.1±12.9	46.3±9.9	0.7
Sex	Female	18 (50%)	9 (47.4%)	5 (50%)	4 (57.1%)	0.9
CRP (mg/L)		11.5 ±12.6	13.7±11.4	11±17	6.8±9.1	0.4
DAS28 n= 22		3.5±1.3	3.1±1.1	4±1.4	3.2±1.4	0.4
ASDAS n= 17		3.7±0.9	3.7±1	4.1±0.6	3.5±0.6	0.5
BASDAI n=24		5.7±2.2	5.3±2.5	5.4±0.8	7.1±1	0.2
MASEI score ≥18		30 (83.3%)	18 (94.7%)	7(70%)	5(71.4%)	0.2
Mean number of enthesis with PD OMERACT		1.7±1.3	1.7±1.3	1.7±1.3	1.6±1.7	0.9
Mean number of enthesis with PD MASEI		1.8±1.4	1.9±1.4	1.8±1.2	1.7±1.7	0.9
PD OMERACT	≥1	29 (80.6%)	15 (78.9%)	9 (90%)	5(71.4%)	0.8
	≥2	18 (50%)	11 (57.9%)	4 (40%)	3 (42.9%)	0.6
PD MASEI	≥1	29 (80.6%)	15 (78.9%)	9 (90%)	5(71.4%)	0.8
	≥2	21 (58.3%)	12 (63.2%)	5 (50%)	4 (57.1%)	0.8

Table 2. Inter-reader reliability

	Reader 1	Reader 2	Reader 3
ICC reader 1		0.784 (95% CI 0.58 to 0.89)	0.909 (95% CI 0.82 to 0.95)
ICC reader 2	0.784 (95% CI 0.58 to 0.89)		0.855 (95% CI 0.72 to 0.93)
ICC reader 3	0.909 (95% CI 0.82 to 0.95)	0.855 (95% CI 0.72 to 0.93)	

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SAT0528 DETECTION OF FACET JOINT ANKYLOSIS ON WHOLE SPINE LOW-DOSE CT IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: DATA FROM THE SENSITIVE IMAGING OF AXIAL SPONDYLOARTHRITIS (SIAS) COHORT

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Background: In radiographic axial spondyloarthritis (r-axSpA), whole spine low-dose CT (ldCT) is superior in detecting syndesmophytes to conventional radiography (CR), which is limited to the lumbar and cervical spine. As facet joints are difficult to visualize on CR, CT has been used to study facet joint ankylosis in r-axSpA in parts of the spine. However, facet joints in the whole spine have never been studied.
Objectives: To assess visibility and interreader reliability of facet joint ankylosis as detected by whole spine ldCT and to describe the prevalence of facet joint ankylosis in patients with r-axSpA.
Methods: In an observational cohort, 60 r-axSpA patients with 1-18 syndesmophytes on CR and at least one inflammatory lesion on spinal MRI, underwent ldCT (approximately 4 mSV) of the whole spine. Images were assessed independently by two trained readers and left and right C2-C3 to L5-S1 facet joints were scored as ankylosis present (1) or absent (0). The percentages of missing joint scores per reader were calculated.

		Reader 1		Reader 2	
	C1	Left	Right	Left	Right
Cervical	C2- C3	1.7%	1.7%	3.3%	1.7%
	C3 - C4	1.7%	1.7%	6.7%	5.0%
	C4 - C5	6.7%	6.7%	11.7%	11.7%
	C5 - C6	8.3%	8.3%	18.3%	18.3%
	C6 - C7	18.3%	18.3%	45.0%	45.0%
	C7 - T1	18.3%	18.3%	51.7%	51.7%
Thoracic	T1 - T2	15.0%	15.0%	33.3%	33.3%
	T2 - T3	8.3%	8.3%	10.0%	10.0%
	T3 - T4	6.7%	6.7%	5.0%	5.0%
	T4 - T5	1.7%	1.7%	1.7%	1.7%
	T5 - T6	1.7%	1.7%	1.7%	1.7%
	T6 - T7	1.7%	1.7%	0.0%	0.0%
	T7 - T8	0.0%	0.0%	0.0%	0.0%
	T8 - T9	0.0%	0.0%	0.0%	0.0%
	T9 - T10	0.0%	0.0%	0.0%	0.0%
	T10 - T11	0.0%	0.0%	0.0%	0.0%
	T11 - T12	0.0%	0.0%	0.0%	0.0%
	T12 - L1	1.7%	1.7%	1.7%	1.7%
Lumbar	L1 - L2	1.7%	1.7%	1.7%	1.7%
	L2 - L3	3.3%	1.7%	1.7%	1.7%
	L3 - L4	0.0%	0.0%	0.0%	0.0%
	L4 - L5	0.0%	0.0%	0.0%	0.0%
	L5 - S1	1.7%	0.0%	0.0%	0.0%

Figure: Percentages of missing scores per reader on ldCT of facet joint ankylosis, for the left and right joint. Colors reflect the amount of missings, ranging from green (no missings) to red (largest percentage of missings)

Ankylosis scores were summed per patient for the whole spine and per segment and presented as mean scores per reader. Interreader reliability was assessed by calculating intraclass correlation coefficients (ICCs), two-way average, absolute agreement.

Results: 60 r-axSpA patients were analyzed (mean age 47.7 years, 85% male, 80% HLA-B27+). Reader 1 had between 0% and 18.3% missings per joint, reader 2 had between 0% and 51.7% missings per joint (figure). Most missings occurred in the cervicothoracic junction for both readers and mostly at both left and right facet joints of the same level. Means (SD) of sum-scores for the whole spine and cervical, thoracic and lumbar segments for both readers as well as ICCs are presented in the Table. The lowest ICC was found in the cervical segment. After excluding facet joints with more than 15% missings (C5-C6 to T1-T2), ICCs were 0.93, 0.84 and 0.91 for the whole spine and cervical and thoracic segments, respectively. A striking finding is that while patients with >18 syndesmophytes were excluded from our study, very high scores of ankylosis were reported, suggesting that facet joint ankylosis may occur without syndesmophytes at the same level.

Conclusion: In patients with r-axSpA and at least one syndesmophyte, facet joint ankylosis was detected in all spinal segments. Facet joints around the cervicothoracic junction were difficult to score in a relatively high percentage of patients. The interreader reliability of the remaining levels was good to excellent. These results show that ldCT can be used to study facet joint ankylosis in axSpA in all segments of the spine except the cervicothoracic junction.

Table: Facet joint ankylosis scores per reader and interreader reliability

	Reader 1 mean (SD) *range*	Reader 2 mean (SD) *range*	ICC (95% CI)
Total - whole spine *max score 46*	9.3 (11.9) 0 - 42	10.6 (12.2) 0 - 45	0.92 (0.87-0.95)
Cervical *max score 12*	2.3 (3.9) 0 - 12	2.0 (3.4) 0 - 12	0.74 (0.56-0.84)
Thoracic *max score 24*	5.9 (7.8) 0 - 24	6.8 (8.1) 0 - 24	0.91 (0.85-0.95)
Lumbar *max score 10*	1.0 (2.5) 0 - 10	1.8 (3.1) 0 - 10	0.81 (0.67-0.89)
Total excluding C5-T2 *max score 38*	7.3 (10) 0 - 34	9.4 (10.9) 0 - 37	0.93 (0.87-0.96)
Cervical excluding C5-T1 *max score 6*	0.9 (1.8) 0 - 6	1.1 (2) 0 - 6	0.84 (0.73-0.90)
Thoracic excluding T1-T2 *max score 22*	5.4 (7.4) 0 - 22	6.5 (7.6) 0 - 22	0.91 (0.85-0.95)

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SAT0529

TWO-YEAR PROGRESSION OF FACET JOINT ANKYLOSIS ON WHOLE SPINE LOW-DOSE CT IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: DATA FROM THE SENSITIVE IMAGING OF AXIAL SPONDYLOARTHRITIS (SIAS) COHORT

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Background: Facet joints are difficult to visualize on conventional radiography (CR). As an alternative, CT has been used to study facet joint ankylosis in radiographic axial spondyloarthritis (r-axSpA) in parts of the spine. In the SIAS study we have shown that, with the exception of the cervicothoracic junction, which is difficult to visualize, low-dose CT (ldCT) can be used to study facet joint ankylosis in the whole spine.

Objectives: To study facet joint ankylosis progression in the whole spine over two years in patients with r-axSpA.

Methods: In an observational cohort, r-axSpA patients who had between 1-18 syndesmophytes on CR and $\geq$1 inflammatory lesion on spinal MRI underwent ldCT of the whole spine (approximately 4 mSV) with a repeated ldCT after two years. Paired ldCTs were assessed by two trained readers independently blinded to chronology. Left and right C2-C3 to L5-S1 facet joints were scored as ankylosis present (1) or absent (0). Change scores, intraclass correlation coefficients (ICCs) (two-way average, absolute agreement) and smallest detectable change (SDC) were calculated for the whole spine and per segment. Joints C2-C3 to L5-S1 were included in the analysis, with the exception of the facet joints between C5-T2, which were excluded in all patients due to high levels of missing joint scores as previously reported. For change score calculations, segments of individual patients with >25% missings were excluded. Remaining missings were imputed with the segment change score mean. Total scores were calculated using only patients with no excluded segments.

Results: Baseline and 2-year follow up ldCT were available in 53 axSpA patients (mean age 48.3, 85% male, 79% HLA-B27+). For reader 1, 17%, 5.7% and 3.8% of segments were excluded from the cervical, thoracic and lumbar spine for change score analysis, respectively, and 20.7% of patients were excluded for the whole spine change score analysis. For reader 2 the percentages were 15.1%, 1.9%,1.9% and 17%, respectively. Therefore, the numbers of patients differed per reader and segment. Mean scores for baseline and follow-up, mean change scores,

SDCs and ICCs are presented in Table 1. ICCs for mean status scores are good to excellent, with the lowest ICCs occurring in the cervical segment. ICCs for change scores vary greatly, the lowest ICCs being in the lumbar segment, the highest in the cervical segment. The proportion of patients with change larger than 0, larger than the positive SDC and larger than the negative SDC are given in Table 2 per reader and for consensus between readers. The largest percentages of change are seen in the thoracic segment.

Conclusion: Reliability of facet joint ankylosis progression was good in the whole spine but poor in the lumbar segment where little progression was seen. Over two years, a fair number of patients had progression of facet joint ankylosis with most progression occurring in the thoracic spine. These results show that using whole spine ldCT, progression of facet joint ankylosis can be studied in r-axSpA patients.

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Table 1: Facet joint ankylosis prevalence, interreader reliability and progression in patients with r-axSpA with at least one syndesmophyte

	Reader 1 mean (SD) *range*	Reader 2 mean (SD) *range*	ICC (95% CI)	SDC
Whole spine excluding C5-T2 *max score 38*				
Baseline	6.9 (9.5) 0 - 34	9.2 (10.3) 0 - 32	0.93 (0.87-0.96)	
Follow-up	7.8 (9.7) 0 - 34	10.3 (10.9) 0 - 34	0.91 (0.82-0.95)	
Change score	0.8 (2.4) -8.4 - 6	0.9 (2.1) -4.2 - 6.3	0.75 (0.53-0.87)	2
Cervical excluding C5-T1 *max score 6*				
Baseline	0.8 (1.7) 0 - 6	1.1 (1.9) 0 - 6	0.84 (0.73-0.90)	
Follow-up	0.7 (1.6) 0 - 6	1.2 (1.9) 0 - 6	0.72 (0.52-0.84)	
Change score	0.0 (0.4) -2 - 1	0.0 (0.4) -2- 1.2	0.91 (0.83-0.95)	0.2
Thoracic excluding T1-T2 *max score 22*				
Baseline	5.1 (7.1) 0 - 22	6.4 (7.4) 0 - 22	0.91 (0.85-0.95)	
Follow-up	6.0 (7.2) 0 - 22	7.3 (7.9) 0 - 22	0.90 (0.82-0.94)	
Change score	0.9 (2.5) -8.8 - 7	0.9 (2.3) -4.4 - 11	0.56 (0.21-0.75)	2.7
Lumbar *max score 10*				
Baseline	1.0 (2.4) 0 - 10	1.6 (2.9) 0 - 10	0.81 (0.67-0.89)	
Follow-up	1.1 (2.5) 0 - 10	1.8 (3) 0 - 10	0.85 (0.73-0.92)	
Change score	0.0 (0.8) -2 - 3	0.2 (0.9) -2 - 5	0.10 (-0.58-0.48)	1.1

Baseline and follow-up: N=52 (reader 1), N=53 (reader 2); whole spine change score: N=42 (reader 1), N=44 (reader 2), N=38 (ICC); cervical segment change score: N=44 (reader 1), N=45 (reader 2), N=40 (ICC); thoracic segment change score: N=50 (reader 1), N=52 (reader 2), N=50 (ICC); lumbar segment change score: N=51 (reader 1), N=52 (reader2), N=51 (ICC)

Table 2: Number of radiographic axSpA patients with progression of facet joint ankylosis during 2-year follow

	SDC	Reader 1 N(%)	Reader 2 N(%)	Consensus N(%)
Whole spine	2			
Change >SDC positive		12 (28.6%)	11 (25%)	6 (15.8%)
Change >SDC negative		1 (2.4%)	3 (6.8%)	1 (2.6%)
Change >0		13 (30.1%)	15 (34.1%)	6 (15.8%)
Cervical segment	0.2			
Change >SDC positive		2 (4.5%)	3 (6.6%)	1 (2.5%)
Change >SDC negative		1 (2.3%)	1 (2.2%)	1 (2.5%)
Change >0		2 (4.5%)	3 (6.6%)	1 (2.5%)
Thoracic segment	2.7			
Change >SDC positive		9 (18%)	8 (15.4%)	3 (6%)
Change >SDC negative		1 (2%)	2 (3.8%)	1 (2%)
Change >0		15 (30%)	15 (28.8%)	5 (10%)
Lumbar segment	1.1			
Change >SDC positive		3 (5.9%)	4 (7.7%)	2 (3.9%)
Change >SDC negative		3 (5.9%)	1 (1.9%)	1 (2%)
Change >0		3 (5.9%)	6 (11.5%)	2 (3.9%)

Whole spine: N=42 (reader1), N=44 (reader 2), N=38 (consensus);
cervical segment: N=44 (reader 1), N=45 (reader 2), N=40 (consensus);
thoracic segment: N=50 (reader 1), N=52 (reader 2), N=50 (consensus);
lumbar segment: N=51 (reader 1), N=52 (reader 2), N=51 (consensus)

SAT0530

SPSAMRIS: A TIME AND RESOURCE SAVING ALTERNATIVE FOR DETECTION AND MONITORING OF DISEASE-RELATED JOINT CHANGES?

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Background: Standardized imaging scores in MRI are barley used in daily clinical practice whereby the high expenditure (in terms of time and staff) is often given as a reason.

Objectives: To develop and evaluate a simplified version of the OMERACT Psoriatic Arthritis Magnetic Resonance Imaging Score (PsAMRIS).

Methods: 19 patients with PsA according to CASPAR classification criteria with inadequate methotrexate response received anti-TNF treatment and were assessed by 3T MRI of the clinically dominant hand at baseline and after 6 months. Scoring was according to PsAMRIS. Items were reduced based on standard response mean (SRM) resulting in sPsAMRIS, which was compared to PsAMRIS by calculation of the total SRM and relative efficiency (RE) after bootstrapping.

Results: PsAMRIS subscore of MCP3, 4, and PIP4 resulted in the highest SRM (-0.07 each) and were therefore included in sPsAMRIS. sPsAMRIS had higher SRM compared to PsAMRIS (-0.13 vs. -0.02) and a higher RE (29.46). PsAMRIS and sPsAMRIS highly correlated at baseline ($r = 0.75$; $p < 0.01$) and follow-up ($r = 0.64$; $p = 0.01$). Evaluation time was reduced from 471 to 142 seconds at baseline and from 478 to 133 seconds at follow-up ($p < 0.001$).

Conclusion: The abbreviated MRI scoring system for PsA-related changes in hands, sPsAMRIS, showed a strong correlation with the well-evaluated PsAMRIS. Hence, sPsAMRIS can be considered as a time and resource saving alternative for semi-quantitative evaluation and monitoring of PsA related joint-pathology.

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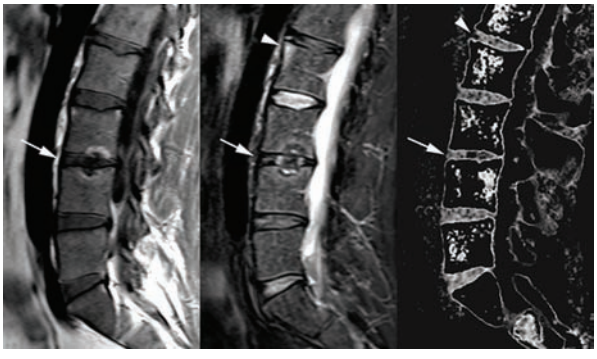
Disclosure of Interests: Philipp Sewerin: None declared, Daniel Abrar: None declared, Ralph Brinks: None declared, Stefan Vordenbäumen: None declared, Alexander Lautwein: None declared, Matthias Schneider Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Speakers bureau: Chugai, Benedikt Ostendorf: None declared, Christoph Schleich: None declared
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SAT0531

COLLAGEN IMAGING USING DUAL-ENERGY COMPUTED TOMOGRAPHY CAN DETECT SOFT-TISSUE INVOLVEMENT OF THE INTERVERTEBRAL DISC IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Based on the unique physical properties of collagen, dual-energy computed tomography (DECT) is able to detect pathological changes in fibrous structures. This has been demonstrated for the Achilles tendon (1) and traumatic disc injury in elderly patients (2).
Objectives: The purpose of this study was to assess the diagnostic potential of DECT collagen imaging for the detection of intervertebral disc involvement in patients with axial spondyloarthritis (axSpA) in correlation with osseous lesions in MRI.
Methods: Sixteen patients with suspicion of or known axSpA and back pain were included. All patients underwent a 1.5-Tesla-MRI including T1 and STIR sequences and an ultra-low-dose DECT of the spine using two sequential helical acquisitions. DECT images were reconstructed in 120 kV-equivalent standard CT images and collagen maps with 1.0 mm slice thickness in sagittal reconstructions. MRI and CT images (D1 to S1) were scored for transdiscal ankylosis, Andersson lesions, syndesmophytes, spondylitis anterior and fatty corner lesions (when applicable) as well as for degenerative findings. DECT images were scored for a loss of collagen density affecting the nucleus pulposus or the anulus fibrosus. Sensitivity (SE) and specificity (SP) values were calculated. All analyses were performed on the level of the disco vertebral units.
Results: Twelve male and four female patients with a mean age of 46.6 ± 11.6 years were included. Eleven were finally diagnosed with axSpA, 3 with degenerative spine disease and 2 with diffuse idiopathic skeletal hyperostosis (DISH). MRI detected 73 lesions in 274 discovertebral units (61 SpA related, 12 degenerative; 26 affecting the disc and 35 affecting the vertebral corner) and CT 68, whereas DECT identified pathologically decreased collagen content in 60 discs (35 in the nucleus and 25 in the anulus). DECT showed high diagnostic accuracy when compared to SpA-related and degenerative changes (MRI and CT combined; SE: 67%; SP 99.5%) and for SpA-lesions only (SE 72%; SP 94.2%), however, was less susceptible for degeneration (SE 60%; SP 81.9%). When comparing disc lesions in SpA as detected by MRI (transdiscal ankylosis and Andersson lesions) with nucleus-pulposus changes in DECT, it showed an SE of 88.5% and an SP of 95.1%. However, the diagnostic accuracy was inferior when comparing anterior spondylitis and fatty corner lesions in MRI with anulus fibrosus changes in DECT (SE 51.4% and SP 97%), although the SE was markedly higher for active inflammatory corner lesion (92.3%) than for fatty marrow lesions (23.3%). The mean radiation exposure was 8.1 ± 3.4 mSv.
Conclusion: DECT is able to demonstrate soft-tissue involvement of the disc, especially for transdiscal ankylosis, Andersson lesions and active anterior spondylitis. This can be achieved with considerably low radiation exposure. While measuring the collagen density, it provides additional information to conventional CT and MR images. Thus, it has high potential to develop into a useful tool to further enhance our understanding of pathologic soft-tissue changes in axSpA patients outside the bone and bone marrow.



REFERENCES
[1] Mallinson PI, Stevens C, Reisinger C, Nicolaou S, Munk PL, Ouellette H. Achilles tendinopathy and partial tear diagnosis using dual-energy computed tomography collagen material decomposition application. J Comput Assist Tomogr.
[2] Pumberger M, Fuchs M, Engelhard N, et al. Disk injury in patients with vertebral fractures-a prospective diagnostic accuracy study using dual-energy computed tomography. Eur Radiol. 2019.

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SAT0532

MRI DETECTS SUBCLINICAL PLANTAR FASCIA AND ACHILLES TENDON ENTHESITIS IN PATIENTS WITH PSORIATIC ARTHRITIS, PSORIASIS AND ANKYLOSING SPONDYLITIS

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Background: Enthesitis is thought to be a key feature driving the development of spondyloarthritis, although head-to-head studies in patients with psoriasis (Pso) versus psoriatic arthritis (PsA) are scarce. In PsA and ankylosing spondylitis (AS) patients the plantar fascia and Achilles tendon are among the entheseal structures most frequently affected clinically. MRI allows for objective detection of enthesitis in patients with rheumatic diseases.
Objectives: To assess the frequency of MRI-detected enthesitis at the plantar fascia and Achilles tendon in Pso, PsA and AS patients.
Methods: The cross-sectional observational 'EXTEND-UP' study* included patients with Pso (diagnosed by a dermatologist, PsA excluded by rheumatologist), PsA (fulfilling CASPAR criteria) and AS (fulfilling ASAS criteria). With the exception of two PsA patients, no study participants received DMARDs. Study participants were included regardless of the presence/absence of clinically-suspect enthesitis (nail blanching pressure on enthesis). Clinicians were blinded to the MRI-scan results. 3 Tesla MRI-scans of both ankles were performed and evaluated by one observer with over four years of experience in musculoskeletal MRIs, who was blinded to diagnosis and clinical examination. MRI-defined enthesitis was scored following the OMERACT MRI definitions for PsA.
Results: This study evaluated a total of 79 ankles from 13 Pso patients, 15 PsA patients and 12 AS patients. The MRI-scan of one ankle was not assessable for enthesitis because of suboptimal fat suppression. Overall, MRI-defined enthesitis either at the plantar fascia and/or Achilles tendon was detected in 30% (9/30) of PsA ankles, compared to 8% (2/26) of Pso ankles ($p<0.05$, Fisher's exact test). Specifically, MRI-detected enthesitis at the plantar fascia(s) occurred in 0% (0/13) of Pso patients, 20% (3/15) of PsA patients and 8% (1/12) of AS patients. MRI-detected enthesitis at the Achilles tendon(s) occurred in 8% (1/13) of Pso patients, 33% (5/15) of PsA patients and 0% (0/12) of AS patients. Agreement between clinically-suspect versus MRI-detected enthesitis was moderate ($\kappa = 0.41$) regarding plantar fascia enthesitis (table 1). There was a poor concordance ($\kappa = 0.12$) between clinically-suspect versus MRI-detected Achilles tendon enthesitis, where 8 out of 9 Achilles tendons that were judged as normal in physical examination, did show inflammation on MRI (table 1).
Conclusion: This study shows a substantial incidence of MRI-detected plantar fascia and Achilles tendon enthesitis in PsA, occurring more frequently compared to PsO. The clear discrepancy between clinically-suspect enthesitis and MRI-defined enthesitis, even at prototypical sites, warrants caution before using clinical evaluation of enthesitis as part of clinical decision-making or trial outcome measures.

Table 1. MRI-detected enthesitis versus clinical examination

	Plantar fascia MRI		
Clinical examination for enthesitis	No enthesitis (n = 74)	Enthesitis (n = 5)	κ-value
Normal, no (%)	72 (97)	3 (60)	0.41
Clinically suspect, no (%)	2 (3)	2 (40)	
	Achilles tendon MRI		
Clinical examination for enthesitis	No enthesitis (n = 70)	Enthesitis (n = 9)	κ-value
Normal, no (%)	68 (97)	8 (89)	0.12
Clinically suspect, no (%)	2 (3)	1 (11)	

*=This investigator-initiated study was funded by Janssen Inc.

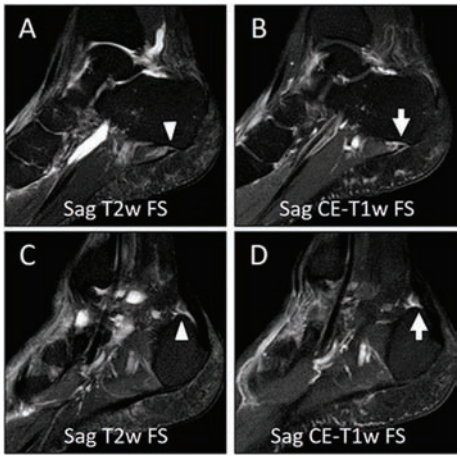


Figure 1. Plantar fascia (A & B) and Achilles tendon (C & D) with increased T2 signal reflecting edema (arrowhead) and contrast enhancement (arrow) around the entheses.

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SAT0533 MRI ASSESSMENT OF HIP JOINTS INVOLVEMENT IN EARLY AXIAL SPONDYLOARTHRITIS PATIENTS

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Background: Based on available data from epidemiological studies in Russia different degree of hip involvement was found in 46% of ankylosing spondylitis (AS) patients, but only 7% of all cases resulted in total hip replacement procedures.
Objectives: To compare the ultrasound (US) manifestations of hip arthritis (coxitis) with the results of magnetic resonance imaging (MRI) of the hip joints (HJ) in patients with early axial spondyloarthritis (AxSpa).
Methods: We examined 39 patients (mean age 28 ± 5.92 years) with a diagnosis of AxSpa (ASAS criteria 2009), with prescription inflammatory back pain no more than 5 years; age <45 years with US of coxitis. The median duration of the disease was 21 [3-60] months. BASDAI 4.0 ± 2.0, BASFI 2.0 [0.4; 3.5]. All patients underwent clinical, radiological, ultrasound, and MRI scans of HJ. For ultrasound coxitis was considered an increase in cervical-capsular distance (CCD) more than 7 mm. Coxitis is found in 27 men and 12 women. The CCD median was 7.5 [7.0; 8.2] mm.
Results: All patients in addition to ultrasound signs of coxitis had MRI signs of inflammation of the HJ. Pain in the HJ was determined in 33 (85%) patients. The relationship between the level of pain and the amount of effusion in HJ was not detected. RCC significantly correlated with laboratory parameters of disease activity, such as ESR (r = 0.34) p <0.05 and CRP (r = 0.3), p <0.05. X-ray examination revealed radiological changes in 7 patients (BASRI hip II-III). The following inflammatory changes (IC) were identified in the study population using MRI: synovitis was established in 36 (92%) patients, bone marrow edema (BME) – in 1 (3%), and combination of synovitis with BME was observed in 2 patients (5%).
Conclusion: Ultrasound allows you to detect changes in H in the early stages of the disease. It is possible to use ultrasound as a screening method to determine the presence of synovitis in the TBS. MRI HJ with AxSpa, allows to determine whether the patient has inflammatory changes, including in the absence of radiological changes in these joints. In 15% of cases, coxitis is asymptomatic at early stages, which requires a thorough examination of patients with AxSpa. In addition to clinical and radiological examination, all patients were subjected to MRI with T1 and STIR modes.
Disclosure of Interests: : Ekaterina Agafonova: None declared, Tatiana Dubinina: None declared, Daria Rumiantceva: None declared, Anastasiya Demina: None declared, Shandor Erdes Consultant for: Development of studies concepts., Speakers bureau: Educational meetings organized or supported by companies.
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SAT0534 MAGNETIC RESONANCE IMAGING MARKERS IMPROVE THE PREDICTION MODEL FOR TOTAL KNEE REPLACEMENT OVER 13 YEARS IN OLDER ADULTS

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Background: Quantitative and semi-quantitative measurement of structural changes on MRI have been widely adopted in knee osteoarthritis (OA) research. However, few long-term studies describe the independent association of these structural factors and total knee replacement (TKR) in older adults.
Objectives: To describe whether cartilage defects, bone marrow lesions (BMLs), effusion-synovitis, and meniscal pathologies at baseline are associated with TKR over 13 years and to estimate the additive effect of these measures for risk prediction of TKR.
Methods: 1082 participants (mean age 62.8 years, 50% female) were randomly recruited from Tasmania and followed over 13.3 years. A 1.5T MRI scan of the right knee was acquired at baseline (n=930). Cartilage defects (grade 0-4), BMLs (grade 0-3), effusion-synovitis (grade 0-3), meniscal tears (grade 0-3) and meniscal extrusion (grade 0-2) was scored at baseline using T1-weighted and T2-weighted MRI. WOMAC knee pain was recorded from questionnaires and radiographic OA (ROA) was assessed by OARSI scale. The incidence of primary (first-time) TKR was determined by data linkage to the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR). Log binomial regression were used to estimate the risk of TKR associated with baseline MRI measures, adjusting for age, sex, BMI, ROA, and pain. Receiver operating characteristic (ROC) analyses were used and area under the curves (AUCs) were compared.
Results: After adjustment for age, sex, BMI, and ROA status, baseline cartilage defects (grade 2, RR=6.71; grade 3, RR=11.17; grade 4, RR=13.2; all p<0.01) were consistently and significantly associated with TKR over 13 years. These associations remained significant after further adjustment for other MRI pathologies. BMLs (grade 1, RR=2.74; grade 2, RR=2.64; grade 3 RR=4.01, all p<0.05 except grade 2), grade 3 effusion-synovitis (RR=2.74, p<0.05) and suprapatellar effusion-synovitis area were associated with TKR over 13 years. However, these associations of BMLs and effusion-synovitis with TKR were largely dependent on cartilage defects. Those who had TKR all had a meniscal tear at baseline, with 96% of them having a grade 3 tear.
Compared to the baseline model with age, sex and BMI (area under the ROC curve [AUC = 0.62]), Model 1 with the addition of ROA and WOMAC pain performed better (AUC =0.77). Addition of cartilage defects to Model 1 resulted in a significant increase of AUC to 0.84. However, addition of BMLs and effusion-synovitis to the model 1 resulted in a non-significant small increase in AUC (0.78 and 0.76) only. The combination of all MRI pathologies to Model 1 resulted in a significant increase of AUC to 0.82.
Conclusion: Baseline knee MRI structural pathology markers can predict TKR over the long-term, suggesting that MRI structural markers are good predictors of rapid knee OA progression in the general population.

Semiquantitative MRI measures such as cartilage defects significantly improve the model performance for prediction of TKR over 13 years, and hence could be utilized in prediction/decision making of TKR.

Base model – Age, sex, BMI
Model 1 – Base model + WOMAC + knee ROA
Model 2 – Model 1 + Cartilage defects
Model 3 – Model 1 + BMLs
Model 4 – Model 1 + Effusion Synovitis
Model 5 – Model 1 + Cartilage defects + BMLs + Effusion Synovitis

Combined model for comparison.

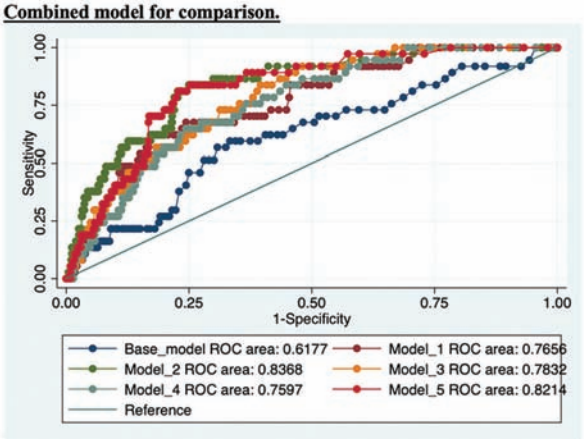


Figure 1. ROC (receiver operating characteristic) curves of prediction models using combinations of semi-quantitative MRI measurements.

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SAT0535 ANTI-CARBAMYLATED ANTIBODIES IN DISCRIMINATION BETWEEN RHEUMATOID ARTHRITISAND CHRONIC HEPATITIS C INDUCED ARTHROPATHY PATIENTS

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Background: Rheumatoid arthritis (RA) is an autoimmune disease presenting by chronic joint inflammation. Early diagnosis and therapy of RA are crucial for avoiding joint damage and functional disability.
HCV related arthropathy (HCVrA) is one of the RA mimics that is detected in around 52.2% of HCV patients.(1) The discrimination between HCVrA and RA is a challenge especially in early onset RA because of their similar manifestations. Detection of certain serologic markers in sera of arthritis patients could be helpful to differentiate between both types of arthritis. Besides RF and ACPA, anti-Carbamylated Protein (anti-CarP) antibodies were described for their role in early identification of RA, as they can be found in up to 45% of early RA patients. Moreover, they can be detected in ACPA-negative RA patients.(2)
Objectives: To determine the role of anti-CarP antibodies in the differentiation between RA and HCVrA.
Methods: This study was carried out on 4 groups:
Group I:20 patients with chronic HCV infection, **group II :20** Patients with HCVrA, **group III :20** Patients with RA fulfilling the 2010 (ACR/EULAR) classification criteria and **group IV: 20** Patients with both chronic HCV infection and RA.
All patients were subjected to detailed history taking and musculoskeletal examination. Routine laboratory investigations were done for all patients in addition to ESR,CRP, RF, ACPA and anti-CarP antibodies. Plain X ray hands and feet were performed to all patients with arthritis.

Results: • Morning stiffness, joint erosions in plain X-rays, inflammatory markers, ACPA and anti-CarP antibodies were significant differentiating points between RA and HCVrA ($p<0.001$, $p<0.001$, $p=0.008$, $p<0.001$ and $p<0.001$, respectively), while the differences between RA and HCVrA groups regarding symmetry of joint symptoms and level of RF were not significant ($p=0.507$, $p=0.110$, respectively).

Table: Comparison between groups II and III according to serological markers

	Group II (HCVrA)	Group III (RA)	p
RF (IU/ml)			
Mean ± SD.	56.76 ± 110.77	126.86 ±197.42	0.110
Median	17.30	44.50	
ACPA (IU/ml)			
Mean ± SD.	3.52 ± 4.67	257.27 ± 206.05	<0.001*
Median	2.82	215.0	
Anti-CarP (U/ml)			
Mean ± SD.	36.79 ± 12.72	50.92 ± 14.38	<0.001*
Median	33.80	46.24	

- Anti-CarP antibodies were detected in the sera of 12.5% of HCV patients (10% with and 15% without articular symptoms) in comparison to 75% of RA patients. The difference between the two groups was statistically significant ($p<0.001$).

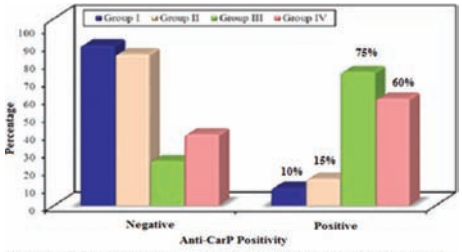


Figure (1): Comparison between studied groups according to anti-CarP Positivity

- ACPA were detected at low titers in 15% of HCV patients (with and without articular involvement).
- There was a significant positive correlation between RF and anti–CarP antibodies (r= 0.386) and between ACPA and anti–CarP antibodies in the total sample studied (r =0.393).

Conclusion: The presence of anti-CarP antibodies together with clinical features could discriminate RA patients from HCVrA patients. The detection of ACPA and anti-CarP antibodies in few HCV patients should be interpreted with caution.
Simaltaneous detection of both anti-CCP and ani-CarP antibodies could be of great value in differentiating RA from other mimicking conditions like HCVrA.

REFERENCES

[1] Cacoub P. et al. Medicine 2000;79(1):47-56.
[2] Shi J, et al. Proc Natl Acad Sci 2011;108(42):17372-7.

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SAT0536 DIAGNOSTIC UTILITY OF POSITRON EMISSION TOMOGRAPHY FOR THE EVALUATION OF PATIENTS WITH INFLAMMATION OF UNKNOWN ORIGIN

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Background: Underlying causes of inflammation cannot be established sometimes, despite meticulous medical history and physical examination, laboratory tests including cultures, immunologic and serologic tests and widely used radiologic procedures such as plain x-rays, echocardiography, ultrasonography and computed tomography. Rheumatologists quite oftenly face with these patients which is termed as inflammation of unknown

origin (UIO). Differential diagnosis of UIO is diverse and investigation of such cases are challenging and time consuming.
Objectives: to assess diagnostic utility of PET CT in the diagnosis of patients with UIO
Methods: Study comprised 68 (36 male, mean age 58.7±14.8, range 19-87 years) adult IUO subjects without a previous diagnosis of an inflammatory or malignant disease. Patients were screened with PET CT after 8 hours fasting, if a specific diagnosis could not be established with comprehensive evaluation including; meticulous history and physical examination, pertinent microbiologic cultures, brucella agglutination, Mantoux test, serum protein electrophoresis, echocardiography, plain x-rays, computed tomography of thorax and abdomen/pelvis.
Results: Final diagnosis were established in follow up were inflammatory diseases in 37 (54.4%), malignant disorders in 16 (23.5%) and infections in 5 (7.4%), whereas a final diagnosis cannot be made in 10 (14.7%). PET CT aided diagnosis in 40 (58.8%) patients but was ineffective in 28 (41.2%). All three PET CT positive subjects with a final diagnosis of infection had tuberculosis (tb). On of two PET negative subjects had EBV and one other also had tb. PET CT was positive in 24 of 37 (64.9%) subjects with a final diagnosis of inflammatory rheumatic disease. Final inflammatory diseases were large vessel vasculitis 15, polymyalgia rheumatica 5, seronegative arthritis 4, and other rare miscellaneous diseases, such as small vessel vasculitis, inflammatory myositis, polychondritis, sarcoidosis and IgG4 related disease. PET was positive in 11 of 15 (73.3%) large vessel vasculitis patients and 2 of 5 (40%) PMR patients. Because of small number of miscellaneous rheumatic diseases, diagnostic value of PET cannot be evaluated in these.
Conclusion: Investigation of underlying etiology of UIO is time and effort consuming. PET CT may help to identify final diagnosis more quickly by directing an obscure inflammatory site. PET CT may also have advantages like reducing number of unnecessary biopsies, diagnostic time, anxiety, work loss, morbidity and mortality

REFERENCES

[1] Kan Y, Wang W, Liu J, Yang J, Wang Z. Contribution of 18F-FDG PET/CT in a case-mix of fever of unknown origin and inflammation of unknown origin: a meta-analysis. Acta Radiologica. 2018:0284185118799512.

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SAT0537 THE REMS TECHNIQUE IS NOT AFFECTED BY ARTHROSIS ARTIFACT, WHICH CAN HINDER THE DENSITOMETRIC RECOGNITION OF OSTEOPOROSIS

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Background: the measurement of bone mineral density (BMD) with dual-energy X-ray absorptiometry (DXA) is the current "gold standard" for diagnosing and monitoring osteoporosis, any errors in demographic information, improper patient positioning, incorrect scan analysis or interpretation can lead to erroneous results and decisions [1]. Moreover, a common condition represented by osteoarthritis, by modifying the joint soft tissues composition, can alter the values of BMD [2].
In patients affected by discarthrosis, in fact, osteoporotic T-score values at femoral neck (FN) can be associated with normal or osteopenic T-score values of the lumbar spine (LS), the latter influenced by the presence of osteophytes and/or subchondral bone sclerosis.
Objectives: To evaluate the predictive value of an innoative densitometric technique, the Radiofrequency Echographic Multi Spectrometry (REMS) [3], in detecting bone fragility in patients affected by osteoarthritis.
Methods: The T-score values of 35 postmenopausal women with clinical and/or radiological signs of osteoarthritis (mean age 71 years, average BMI 24,2) obtained by DXA at lumbar spine and femoral neck were compared with those obtained by REMS technique performed in the same anatomical sites.
Results: In all the subjects, LS T-score resulted significantly higher than the FN one according to DXA measurement. However, REMS outcomes in both the sites were significantly lower than the corresponding DXA measurement (significant difference between DXA and REMS T-score for both LS ($p = 0.006$) and FN ($p = 0.010$), and spinal REMS T-scores resulted more similar to femural REMS (average REMS T-score LS: -2.6 ± 1,6 vs T-score FN: -2.4 ± 0, 6) and to femural DXA values.
Conclusion: These preliminary data suggest that REMS technique, which has been shown to have high sensitivity, specificity and accuracy when compared with DXA in diagnosing and monitoring osteoporosis [3], is not affected by the presence of alterated soft tissues composition. it would therefore be particularly useful for the evaluation of bone fragility in subjects at risk of osteoarthritis.

REFERENCES

[1] Watts NB. Ost Intern 2004;15(11):847–854;
[2] Blake GM, Fogelman I. J Bone Min Res 2008; doi: 10.1359/JBMR.0711;
[3] Di Paola M, et al. Ost Int 2018; doi:10.1007/s00198-018-4686-3.

Disclosure of Interests: None declared
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SAT0538 THE LEVEL OF AGREEMENT BETWEEN CLINICAL EXAMINATION AND ULTRASONOGRAPHY IN EARLY ARTHRITIS

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Background: Over the past decades, Early Arthritis Clinics (EAC) have been created to identify early arthritis and institute appropriate treatment as soon as possible. In Rheumatoid Arthritis (RA) many studies show that ultrasonography (US) is superior to clinical exam for the detection of synovitis and has good correlation with clinical findings and markers of inflammation and can be used to improve the certainty of a diagnosis of RA.[1]. However, few studies address the agreement between the US with the clinical examination in patients with early arthritis.
Objectives: To evaluate the agreement between clinical examination and US findings of metacarpophalangeal and proximal interphalangeal joints of patients with early arthritis
Methods: Patients from the EAC of our department with suspect arthralgia were included. Patients were submitted to clinical evaluation by a rheumatologist to identify tender and swollen joints. They were then submitted to an US examination of metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints, by an experienced sonographer oblivious of the previous examination. Each joint was scored for the presence of synovial hypertrophy (SH) and Power Doppler (PD) signal. Based on OMERACT guidance, we defined synovitis as: $\geq$ grade 1 grey scale synovitis (hypoechoic SH regardless of the presence of effusion) and $\leq$ grade 1 power-Doppler. The diagnostic value of clinical evaluation was assessed through sensitivity, specificity, Negative predictive value (NPV) and Positive predictive value (PPV), assuming the US synovitis as gold standard. Clinical arthritis was defined by joint swelling. Cohen's kappa coefficient was used to analyse concordance between joint swelling appreciated by clinical exam and HS, PD and the presence of US synovitis. Kappa values < 0 were considered poor, 0-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 good and 0.81-1.00 excellent.[2] Statistical significance was defined as $p<0.05$. Statistical analysis was performed using IBM SPSS Statistics, version 21.0.
Results: 77 consecutive patients were included (53.2% female) with a mean age of 53.8±19.1 years. We evaluated 770 MCP and 770 PIP joints. The sensitivity and specificity of clinical examination in relation to US synovitis was respectively 71% and 60% for MCP and 54.5% and 43.9% for PIP. The NPV and PPV for MCP were 87.8% and 33.3% respectively, and for PIP were 85.3% and 13.9%. The level of agreement between joint swelling and HS, PD and the presence of synovitis is show on Table 1.

Table 1-. Level of agreement between clinical exam and US synovitis

	joint swelling and US synovitis§ (kappa)		
	Synovial hypertrophy	Power Doppler signal	Synovitis §
MCP	0,32 *	0,33 *	0,32 *
PIP	0,11 *	0,08 *	0,11 *
All joints	0,21 *	0,19 *	0,21 *
	joint tenderness and US synovitis§		
MCP	0,17 *	0,22 *	0,20 *
PIP	0,17 *	0,12 *	0,17 *
All joints	0,16 *	0, 16 *	0, 16 *
	joint tender and swelling and US synovitis§		
MCP	0,29 *	0,28 *	0,29 *
PIP	0,11 *	0,07 ‡	0,11 *
All joints	0, 19 *	0, 17 *	0, 19 *

§ Defined as ≥ grade 1 grey scale synovitis and ≤ grade 1 power-Doppler.
* p<0,001; ‡p=0,006

Conclusion: The clinical evaluation of MCP showed a better performance than clinical evaluation of PIP. The high NPV of clinical examination makes its suitable to be used to rule out MCP and PIP involvement in patients with early arthritis. The performance of the two assessment strategies on the same day may increase agreement and diagnostic certainty.

REFERENCES

[1] - Colebatch AN, et al. EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. Annals of the Rheumatic Diseases 2013;72:804-814.
[2] - McHugh. Interrater reliability: the kappa statistic. Biochem Med (Zagreb). 2012;22(3):276-82.

Disclosure of Interests: None declared
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SAT0539 DUAL ENERGY CT FINDINGS IN GOUT WITH RAPID KILOVOLTAGE-SWITCHING SOURCE WITH GEMSTONE SPECTRAL IMAGING

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Background: The gold standard for diagnosis of gout is the demonstration of monosodium urate(MSU) crystals in the synovial fluid or in tophi. However, joint aspiration is seldom performed and most patients do not have visible tophi. Dual energy CT(DECT) has been shown capable of detecting MSU crystals with high precision in many studies but the vast majority of these studies were performed using CT scanners with two X-ray tubes(dual source) while the performance of other technical CT solutions are much less investigated.
Objectives: In the present study we wanted to investigate the performance of DECT with rapid kilovoltage-switching source with Gemstone Spectral Imaging(GSI) to identify MSU crystals and validate these results against severity of gout disease.
Methods: Patients with incident/prevalent gout who had been examined with DECT GSI scanning of the feet at Sahlgrenska University Hospital, Sweden between 2015 and 2018 were identified. Their medical records were examined for gout disease characteristics (onset of disease, tophi, erosive disease), comorbidities, medication, body mass index(BMI), serum urate, and renal function. Their DECT GSI images were examined by two radiologists in two consensus readings. Urate deposits in MTP1, MTP 2-5, ankle/midfoot joints and tendons were scored semiquantatively in both feet in the following manner: 0=no deposit, 1=dots, 2=single deposit and 3=more than 1 deposit, thus generating a maximum total score of 24 for both feet and a maximum score of 6 per location) Presence of artefacts in nail and skin as well as beam hardening and noise were also identified.
Results: We identified a total of 55 patients, mean age 58 years (SD=15), with a clinical diagnosis of incident or prevalent gout who all fulfilled the 2015 ACR/EULAR classification criteria for gout. Mean disease duration was 7 years (SD=7). A minority of patients (40%) were on urate lowering treatment(ULT) at time of DECT(table1). The majority of patients had increased urate (>360 µmol/L), irrespective of ULT(table 1). Urate deposits were found in the feet of all patients, most commonly seen in the MTP-joints but also present in ankle/midfoot joints and tendons(table 1). The total urate deposit score was significantly higher in the presence of clinically identified tophi(Wilcoxon Mann-Whitney, p=0.0005) and correlated strongly to disease duration(Spearman corr. coefficient 0.64, p<.0001) while no association or correlation was seen to age, sex, erosive disease, urate levels, BMI, diuretic or ULT use or renal function. The majority of patients displayed nail artefacts while skin artefacts only were seen in 31% (table 1). Beam hardening was only found in one patient and noise was not seen at all(table 1).

Table 1,. gout disease characteristics, urate deposit scores and presence of artefacts, * at time of DECT examination

	Total, n=55
Age, mean years (SD)	58 (15)
Men, n (%)	43 (78)
Disease duration, mean years (SD)	7 (7)
Tophus, n (%)	7(13)
Erosive disease, n (%)	36 (65)
ULT at deCT, n (%)	22 (40)
Urate* w ULT, µmol/L, mean (SD), n=22	405 (114)
Urate*) w/o ULT, µmol/L, mean (SD), n=33	491 (137)
All joints and tendons, mean score (SD)	14.0 (5.5)
MTP1, n positive (%), score (SD)	55 (100) 4.0 (1.5)
MTP 2-5, n positive (%), mean score (SD)	55 (100) 3.9 (1.7)
Ankle/midfoot, n positive (%), mean score (SD)	53 (96) 3.6 (1.8)
Tendons, n positive (%), mean score (SD)	41 (75) 2.5 (2.3)
Nailartefact, n positive (%)	40 (73)
Skinartefact, n positive (%)	17 (31)
Beam hardening, n positive (%)	1 (1.8)
Noise, n positive (%)	0

Conclusion: The DECT GSI technique performs well in detection of urate deposits and these correlate to clinical gout characteristics in the same manner as previously shown with DECT dual source technique.
Disclosure of Interests: : Elin Svensson: None declared, Ylva Aurell: None declared, Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lily and Janssen, Anton Landgren: None declared, Valgerdur Sigurdardottir: None declared, Mats Dehlin: None declared
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SAT0540 CLINICAL AND ULTRASONOGRAPHIC ASSESSMENT OF STERNOCLAVICULAR JOINT IN PATIENTS WITH RA

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Background: The sternoclavicular (SC) joint is a real diarthrodial joint that can be affected during the route of RA; but, its scientific implications appear to remain underestimated through the rheumatology network, (1) ultrasound (US) is right extensively common imaging approach in each clinical exercise and in rheumatology studies to visualize joints and tender tissues. To date, there is a regular frame of evidence assisting its validity, reliability, and feasibility inside the evaluation of persistent inflammatory arthritis and its higher sensitivity than scientific exam in the analysis of synovitis, enthesitis, and tenosynovitis in these patients (2).
Objectives: To describe the prevalence of sternoclavicular (SC) joint involvement and the relationship between clinical and ultrasound (US) findings in patients with rheumatoid arthritis.
Methods: 120 subjects with age range from 20 to 50 years were recruited from Physical Medicine, Rheumatology and Rehabilitation department of Sayed Galal and Al-Hussein Al-Azhar University Hospitals, during the period from April 2018 to October 2018.
All the patients were informed about the study and signed an informed consent.
S**ubjects were divided into two groups:** Group A: 60 patient known as RA fulfilling ACR criteria for classification of rheumatoid arthritis (1987) (3). Group B: 60 normal control subjects.
All subjects have been clinically evaluated and t blinded US examinations of the SC joint were performed bilaterally in both groups. The presence of gray-scale synovitis, erosions, and intraarticular power Doppler (PD) was recorded.
Results: A total of 240 SC joints were evaluated: 120 from patients with RA and 120 from healthy controls. In the RA group, 21 joints (17.5%) were found to be clinically involved (pain/swelling), in contrast to only 6

(5%) in the control group (P = 0.002). In the RA group, US abnormalities were recorded in 62 SC joints (51%) compared with 3 (2.5%) in the healthy control group (P = 0.0001), comprising synovitis in 28 (23.3%) versus 3 (2.5%);(P <0.001), erosions in 27 (22.5%) versus none (P <0.001), and intraarticular PD in 7 (5.8%) versus none (P = 0.031). Furthermore, a correlation between the presence of US synovitis (P < 0.001) and intraarticular PD (P < 0.0001) with a higher Disease Activity Score in 28 joints (DAS28) was found.

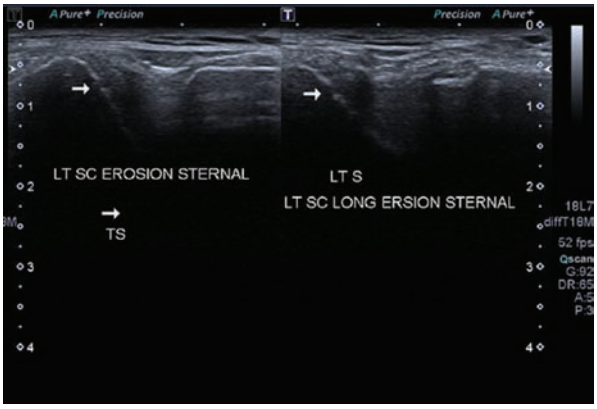


Figure (1) showing erosions of clavicular head of sternoclavicular joint.

Conclusion: US is extra sensitive than medical examination for detecting SC joint involvement in RA. The correlation amongst US synovitis, intraarticular PD, and the DAS28 show that SC joints actively participate within the systemic inflammatory manner of RA. The precise position of US within the assessment of the SC joint in sufferers with RA is but to be mounted firmly in the rheumatologic examination.

REFERENCES

[1] - Rodríguez-Henríquez, P., Solano, C., Peña, A., León-Hernández, S., et al. (2013). Sternoclavicular joint involvement in rheumatoid arthritis: clinical and ultrasound findings of a neglected joint. Arthritis care & research, 65 (7), 1177-1182.
[2] - Filippucci, E., Annamaria, I., Meenagh, G., Riente, L., Delle Sedie, A., Bombardieri, S.,. .. & Grassi, W. (2006). Ultrasound imaging for the rheumatologist II. Ultrasonography of the hand and wrist. Clinical and experimental rheumatology, 24(2), 118-122.
[3] — Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315–24.

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SAT0541 MULTIDRUG TRANSPORTERS OF PERIPHERAL LYMPHOCYTES SERVE AS BIOMARKERS TO BDMARD RESPONSE IN RHEUMATOID ARTHRITIS (RA)

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Background: Multidrug resistance transporters (MDR-ABC transporters, namely MDR1, MRP1 and BCRP) play essential role in the homeostasis of a variety of endogenous molecules, proinflammatory mediators among them [1]. When the regulation of this phenomenon is disturbed, cell migration, proliferation and inflammatory processes are over activated which finally results in the pathogenesis of RA. Moreover, enhanced function of MDR proteins leads to multidrug resistance [2].
Objectives: In our multicenter, multinational clinical trial we aimed to assess the predictive value of flow cytometry-based multidrug resistance activity measurement of the previously mentioned MDR proteins for bDMARD response in RA in $CD3^+$ and $CD19^+$ lymphocytes before and as well as 4 to 6 and 12 weeks after initiation of bDMARD therapy.
Methods: Peripheral blood samples were collected from 27 bDMARD responders and 12 non-responder RA patients at the indicated time points. Multidrug activity factors (MAFs) were measured from $CD3^+$ and $CD19^+$ lymphocytes by using SOLVO MDQ Kit™. Cut-off values were determined by using ROC curve analysis.
Results: Before starting bDMARD therapy, MAF_C and MAF_{MDR1} values of $CD3^+$ cells were higher in non-responders as compared with responders. Six weeks after starting therapy, the same pattern was detected in case of MAF_c, MAF_{MDR1} and MAF_{MRP1} in both investigated cell types. ROC analysis revealed that when MAF_C value is higher than 21.3 in $CD3^+$ cells before starting bDMRAD therapy are likely to be non-responders. At later time points, MAF_C values above 20.3 and MAF_{MRP1} above 6.0 and MAF_{MDR1} values above 13.9 in $CD3^+$ cells also predict unfavourable treatment response. Of note, these cut-off values are all below the respective reference ranges in healthy individuals established in our earlier study [3].
Conclusion: Importantly, little is known about the relation of MDR activities and therapeutic success to bDMARDs. Proinflammatory mediators and cytokines may serve as an interface between pharmacological activity of bDMARDS and MDR transporters [4-6].

REFERENCES

[1] Fletcher, J.I., et al., *ABC transporters in cancer: more than just drug efflux pumps*. Nat Rev Cancer, 2010. 10(2): p. 147-56.
[2] Marki-Zay, J., et al., *MDR-ABC transporters: biomarkers in rheumatoid arthritis*. Clin Exp Rheumatol, 2013. 31(5): p. 779-87.
[3] Szeremy, P., et al., *Determination of reference values of MDR-ABC transporter activities in CD3+ lymphocytes of healthy volunteers using a flow cytometry based method*. Cytometry B Clin Cytom, 2018.
[4] Garcia-Carrasco, M., et al., *P-glycoprotein in autoimmune rheumatic diseases*. Autoimmun Rev, 2015. 14(7): p. 594-600.
[5] Ghandadi, M. and A. Sahebkar, *Interleukin-6: A Critical Cytokine in Cancer Multidrug Resistance*. Curr Pharm Des, 2016. 22(5): p. 518-26.
[6] Ronaldson, P.T., T. Ashraf, and R. Bendayan, *Regulation of multidrug resistance protein 1 by tumor necrosis factor alpha in cultured glial cells: involvement of nuclear factor-kappaB and c-Jun N-terminal kinase signaling pathways*. Mol Pharmacol, 2010. 77(4): p. 644-59.

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SAT0542 DETECTION OF SUBCLINICAL LV MYOCARDIAL DYSFUNCTION IN RHEUMATOID ARTHRITIS PATIENTS BY SPECKLE TRACKING

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Background: Patients with rheumatoid arthritis (RA) have shorter life expectancy and their risk of cardiovascular (CV) death is more than 50% higher than the rest of the population.
Early myocardial dysfunction may be detectable more precisely and sooner using speckle tracking echocardiography.
Objectives: This study was designed to assess myocardial (LV) systolic function by STE (speckletracking
Echocardiography) strain imaging in patients with RA without known CVD and to correlate the findings with characters of the disease.
Methods: Cross-sectional observational study enrolled 60 patients with RA (mean age 46.22 ± 8.14 years) without known CVD, and 20 healthy controls.
All subjects underwent a standard echocardiographic examination as well as the speckle tracking assessment of left ventricle strains.
Results: Speckle-tracking assessment of LV systolic function revealed decreased GLS among the patients group (-16.80% vs. -22.35%, P<0.001). There was a negative correlation between the duration of RA and the GLS (r = - 0.301). Receiver operating characteristics (ROC) curve was used to define the best cut off value of GLS which was -20, with sensitivity of 76.7%, specificity of 80%, positive predictive value of 92%, negative predictive value of 63% with diagnostic accuracy of 83.9%.
Conclusion: The speckletracking method for myocardial strain analysis showed unambiguously systolic impairment of longitudinal strain parameters. So, patients with RA should undergo a full comprehensive echocardiographic study for assessment of LV systolic function.

REFERENCES

[1] SHARMA A, KAUSHIK R, KAUSHIK RM, KAKKAR R: Echocardiographic evaluation of diastolic dysfunction in rheumatoid arthritis– a case–control study. Mod Rheumatol 25: 552- 557, 2015.

[2] KARPOUZAS GA, MALPESO J, CHOI TY, LI D, MUNOZ S, et al.: Prevalence, extent and composition of coronary plaque in patients with rheumatoid arthritis without symptoms or prior diagnosis of coronary artery disease. Ann Rheum Dis 73: 1797-1804, 2014.

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SAT0543 AUTOMATIC DETECTION OF HAND JOINT REGION, ANKYLOSIS AND SUBLUXATION IN RADIOGRAPHIC IMAGES USING DEEP LEARNING: DEVELOPMENT OF ARTIFICIAL INTELLIGENCE-BASED RADIOGRAPHIC EVALUATION SYSTEM FOR BONE DESTRUCTION

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Background: Artificial intelligence (AI) techniques including deep learning have been rapidly evolving and have yielded appreciable benefits in many fields in recent years. In rheumatology field, however, these techniques have not been used often.
Objectives: In an early phase of development of an AI-based automatic radiographic evaluating system for bone destruction, we aimed to develop learning-based models to automatically detect hand joint region, ankylosis and subluxation in radiographic images.
Methods: A total of 130 radiographic image sets of both hands were randomly obtained from rheumatoid arthritis patients who had visited our division at Keio University Hospital in 2015. Well-trained rheumatologists determined the boundaries of regions of MP and PIP/IP joints and evaluated the presence of ankylosis and subluxation of each joint in radiographs. These evaluations of hand joints were performed using our developed annotation software tool [1].
In learning phase, joint images were randomly divided into five sets for 5-fold cross validation. As deep learning models, we utilized Single Shot Multibox Detector (SSD) method [2] with ensemble learning for detecting ankylosis and subluxation of MP and PIP/IP joint regions.
Results: Our model showed 100% detection rate of MP and PIP/IP joint regions. As a performance of detecting hand joint ankylosis and subluxation, our model presented precision values of 0.85 and 0.73, recall values of 0.94 and 0.79, and F-measure values of 0.90 and 0.76, respectively.
Conclusion: Deep learning-based models to automatically detect hand joint region, ankylosis and subluxation in radiographic images were developed with relatively small samples, which suggests that the predictive performance may increase by collecting more training dataset. Next, we are elaborating a plan for a deep learning-based evaluating system for erosion and joint space narrowing.

REFERENCES

[1] Izumi K, Hashimoto M, Suzuki K, Endoh T, Doi K, Iwai Y, Jinzaki M, Ko S, Takeuchi T. Detecting Hand Joint Ankylosis in Radiographic Images Using Deep Learning: A Step in Developing Automatic Radiographic Scoring System for Bone Destruction. *Arthritis Rheumatol* 2018;70(suppl 10).
[2] Liu W, Anguelov D, Erhan D, Szegedy C, Reed S, Fu CY, Berg AC. SSD: single shot multibox detector. *European Conference on Computer Vision (ECCV)* 2016.

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SAT0544 CORONARY PLAQUE PROGRESSION IN RHEUMATOID ARTHRITIS: ROLE OF INFLAMMATION, CARDIAC RISK FACTORS, MEDICATIONS AND IMPACT ON EVENT RISK

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Background: Patients with Rheumatoid Arthritis (RA) exhibit higher prevalence, burden and different composition of occult coronary plaque compared with age and gender-matched controls. Moreover, plaque burden on coronary computed tomography angiography (CCTA) predicted long-term cardiovascular events (CVE) in RA beyond cardiac risk factors or scores.
Objectives: To evaluate change in coronary plaque burden and composition, predictors thereof and its impact on CVE risk in RA.
Methods: One hundred-one participants with a baseline CCTA underwent a follow-up evaluation in 83±3.6 months. Plaque load was reported as segment involvement score (SIS-number of segments with plaque); segment stenosis score (SSS- cumulative stenosis over all evaluable segments) and total plaque score (TPS- collective plaque amount over all segments). Plaque composition was defined as non-calcified (NCP), mixed (MP) or calcified (CP). Coronary artery calcium (CAC) was quantified by the Agatston method. Robust logistic regression models evaluated predictors of increased plaque burden compared to non-progression.

Independent predictors entered as continuous variables included age, time-averaged c-reactive protein (CRP), cumulative prednisone dose, bDMARD exposure (years), and statin exposure (years). Gender, hypertension, dyslipidemia, diabetes, and presence of IgA anti-beta2-glycoprotein1 antibodies (a-b2GPI-IgA) constituted dichotomous independent variables. Cox proportional hazards models assessed the role of SIS, SSS, TPS and CAC progression on incident CVE risk 14±2.7 months later, after adjustment for cardiac risk scores, or baseline plaque load.

Results: Total plaque burden increased in 42% of patients; progression was predicted by older age, higher cumulative inflammation (TA-CRP) and higher total prednisone dose (table 1).

Longer exposure to bDMARDs and statins was linked to lower risk of NCP progression (all $p<0.05$). MP change was predicted by a-b2GPI-IgA presence, whereas CP progressors were older, more obese, hypertensive and with higher cumulative inflammation compared to non-progressors ($p<0.05$). CAC increase correlated with older age, hypertension, obesity, higher inflammation and a-b2GPI-IgA presence (Table 1). Both total plaque and CAC progression predicted CVE independently of baseline burden and cardiac risk scores (all $p\leq0.014$).

Conclusion: Change in coronary atherosclerosis burden and consistency was differentially impacted by Inflammation, cardiac risk factors, a-b2PI-IgA presence and medications such as prednisone, biologics and statins and independently predicted cardiovascular events in RA.

Table 1. Coronary plaque progression in RA: Role of Inflammation, risk factors and medications

Model	Predictors	OR (95% CI)
SIS Total	Age	1.09 (1.04-1.15)***
	time-averaged CRP	2.04 (1.33-3.13)***
SSS Total	Age	1.07 (1.02-1.12)**
	time-averaged CRP	1.83 (1.20-2.77)**
TPS Total	Age	1.08 (1.03-1.14)**
	Cumulative prednisone dose	1.01 (1.00-1.02)*
	Time-averaged CRP	1.66 (1.02-2.71)*
CAC	Age	1.14 (1.05-1.23)***
	Hypertension	4.98 (1.46-16.94)**
	Waist-to-height ratio	1.10 (1.02-1.17)**
	a-b2GPI IgA (+)	4.67 (1.22-17.94)*
	Time-averaged CRP	1.68 (1.00-2.84)¶

¶p<0.1, *p<0.05, **p<0.01, ***p<0.001

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SAT0545 A COMPARATIVE STUDY OF NAILFOLD CAPILLAROSCOPIC CHANGES IN IDIOPATHIC INTERSTITIAL PNEUMONIA WITH IDIOPATHIC INTERSTITIAL PNEUMONIA AUTOIMMUNE FEATURES

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Background: Lung involvement especially interstitial lung disease (ILD), can be the first manifestation of an underlying connective tissue disorder (CTD). About 25% of ILD occurs in the context of an "undifferentiated" CTDs, characterized by signs and symptoms that are not specific for any of the described CTD entities, now known as IPAF. Nailfold capillaroscopy (NFC) is an important tool, which helps us in early recognition of microvascular changes in patients with ILD

Objectives: To study the various patterns on Nailfold Capillaroscopy in patients of Interstitial Pneumonia with autoimmune features (IPAF) and compare them with those having Idiopathic Interstitial Pneumonia (IIP).

Methods: The study population consisted of 50 patients each of IIP and IPAF who fulfilled ERS/JRS/ALAT 2011 revised diagnostic criteria for IIP and ERS/ATS classification criteria for Interstitial pneumonia with autoimmune features respectively. The study also included 50 age and sex matched controls, having normal respiratory examination clinically, normal CXR and normal PFTs. All patients underwent NFC at room temperature and the following parameters were recorded: capillary density, presence of megacapillaries, tortousity, avascular areas, disarrangement and neoangiogenesis.

Results: Our study consisted of 23 (46%) female patients and 27 (54%) male patients for IPAF group and 19 (38%) female patients and 31 (62%) male patients for IIP group. The mean capillary density was significantly reduced in IPAF group and also had presence of abnormal capillary morphologic patterns (microhemorrhages, neoangiogenesis and megacapillaries).

Conclusion: This single centre study found that Nailfold Capillaroscopy (NFC) is an important adjunct to differentiate between patients of IPAF and IIP demonstrating a higher frequencies of abnormalities (microhemorrhages, megacapillaries and reduced capillary density) among patients with IPAF.

REFERENCES

[1] Harari S, Caminati A. Update on diffuse parenchymal lung disease. Eur Respir Rev 2010;19:97-108.
[2] Morgenthau AS, Padilla ML. Spectrum of Fibrosing Diffuse Parenchymal Lung Disease. Mount Sinai J Medicine 2009;76:2-23.
[3] Singh S, et al. Interstitial Lung disease in India. Results of a prospective Registry. Am J Respir Crit Care Med 2017; 195-196.
[4] Fischer A, du Bois R. Interstitial lung disease in connective tissue disorders. Lancet 2012; 380: 689–698.
[5] Tzelepis GE, Toya SP, Moutsopoulos HM. Occult connective tissue diseases mimicking idiopathic interstitial pneumonias. Eur Respir J 2008; 31: 11–20.

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SAT0546 IL-17A IS UPREGULATED IN SYSTEMIC SCLEROSIS PATIENTS WITH MIXED ANA IMMUNOFLUORESCENT PATTERN AND MORE THAN ONE POSITIVE ANTINUCLEAR ANTIBODY IN THE SERUM

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Background: Systemic sclerosis (SSc, scleroderma) is a rare systemic connective tissue disease characterized by deposition of connective tissue in the skin and internal organs, microvascular impairment and shift in cellular and humoral immune response. More than 95% of the patients produce antinuclear autoantibodies (ANA) years before the first clinical manifestations of SSc. The majority of SSc patients have positive ANA at a high-titre of dilution and nucleolar immunofluorescent staining pattern. The indirect immunofluorescent assay (IFA) on HEp-2 cells is the reference method for ANA screening. According to the International consensus on antinuclear antibody patterns (ICAP) the most relevant and usual patterns ANA patterns have been assigned an alphanumeric code from anti-cell (AC)-1 to AC-28 and are organized into a classification tree.

Objectives: The aim of the present study is to investigate whether there is a significant correlation between the AC-pattern and the specific autoantibodies in the serum of SSc patients on the one hand, and the percentage of Tregs, Th17 cells and the serum levels of their corresponding cytokines - IL-6, IL-10, TGF-β, IL-17A on the other hand.

Methods: We enrolled 31 patients who fulfilled the 2013 ACR/EULAR Classification Criteria for SSc at mean age of 47±3 were recruited in the study: 17 with diffuse SSc and 14 patients with localized SSc, respectively. IFA on HEp-2 cells was performed to screen the patients' sera for ANA and to determine the AC staining pattern. Immunoblot method was used to evaluate the specific ANA in patients' sera. We performed flow cytometric analysis of Th17 and Tregs' percentage in the peripheral blood of the patients. The serum levels of IL-6, IL-10, TGF-β and IL-17A were detected by ELISA.

Results: All patients 'sera were ANA positive at high titer of dilution (above 1:1280). We detected increased IL-17A levels in the serum of patients with AC-3 IFA pattern versus patients positive for AC-29 (18.7 [3.95-99.67] *vs* 2.5[0.35-8.45], p=0.045). Moreover, IL-17A levels were elevated in the sera with AC-4 IFA pattern when compared to AC-29 (15.6 [4.4-28.9] *vs* 2.5[0.35-8.45], p=0.033). When opposing patients 'sera, positive for only one ANA, with "simple" AC-IFA pattern, to sera with mixed AC pattern (positive for more than one ANA on immunoblot) we found: increased levels of IL-17A (13.7 [10.2 – 67.2] *vs* 3.9 [0.4 – 11.6], p = 0.01) and IL-10 (4.4 [2.2 – 5.8] *vs* 1.5 [0.3 – 3.2], p = 0.043) in the

sera with mixed AC pattern. Regarding the Tregs and Th17 cells, we identified a reduced percentage of the CD25negTregs at a marginal trend toward significance in the patients with mixed AC pattern versus the group with simple AC pattern (5.9 [3.2 – 10.6] *vs* 11.2 [6.1 – 14.3], p = 0.06).

Conclusion: Although the pathogenetic contribution of ANA in SSc remains unclear, ANA play an important role in the differential diagnosis, risk stratification and assessment of disease activity in SSc. Further research is warranted to clarify the interconnection between the disregulated Th17/Tregs axis and the production of high-high-titer specific ANA in SSc. In the future rheumatologists could benefit from ANA in order to apply the most accurate therapeutic strategy for each patient.

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SAT0547 ULTRASONOGRAPHIC FOLLOW UP OF ENTHESOPHYTE GROWTH IN A CONSECUTIVE SERIES OF IBD PATIENTS

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Background: Previous studies have found an interconnection between inflammatory intestinal diseases (IBD), particularly Crohn disease (CD) and Ulcerative Colitis (UC), and spondyloarthritis.

Objectives: We prospectively **evaluate** the pattern and predictive factors of enthesophyte growth in a cohort of patients with IBD.

Methods: A total of 68 IBD consecutive patients (31 CD, 36 UC, 1 ID, M/F 37/31, mean age 40.2 ± 13.2 years, mean disease duration 107.5 ±129 months) were enrolled. Rheumatological examination included 66 peripheral joint count, MASES and Leeds entheseal indexes, BASDAI, BASFI and evaluation of spine mobility. US examination was done at baseline and at 24 months using an Esaote MyLabClass, 18-6 MHz linear multifrequence transducer both in B-mode and PD-mode. The following sites were blindly evaluated bilaterally: lateral epicondyle of the humerus, distal quadricipital insertion at the patella, superior and inferior pole of the patella, Achilles tendon insertion, and plantar aponeurosis insertion. Quadriceps, patellar, Achille and plantar fascia entheses were scored according to the 0-36 Glasgow Ultrasound Enthesitis Scoring System (GUESS) and power Doppler (PD). The presence of enthesophyte were scored dichotomously as present (=1) or absent (=0) for each site and summed up to generate the ARE score (ARES). Enthesophytes was also scored semiquantitatively in a 0-3 scale (0 = absent, 1 = minimal, 2 = discrete, 3 = massive) for each site and summed up to generate RES score (RESS).

Results: Eighteen patients showed no increase of the RESS, 13 pts had 1 point increase, 12 pts less than 4 and 25 pts more than 4 points increase of the RESS at the end of follow-up. Baseline factors associated with RESS progression were age > 50 years, male sex, BMI > 25, CRP > 0.50 mg/dl, and alcohol consumption. As far as the number of sites involved only 8 patients showed no increase of ARES, while 25 pts had ARES increased more than 4. Baseline factors predicting ARES increase were pre-existing presence of enthesophytes at quadriceps tendon insertion at superior patellar pole, age > 50 y, male sex, and alcohol consumption. Progression of ARES and RESS was not associated with type of IBD, use of corticosteroid, biological agents or immunosuppressive drugs nor with the concomitant presence of cutaneous psoriasis, smoke habit, diabetes, dyslipidemia.

Conclusion: US examination of selected entheseal area demontrates the increase of number and size of enthesophytes during a 2 years follow-up of IBD patients. Alcohol consumption and the presence at baseline of enthesophytes are the most important predictive factors for RESS and ARES progression respectively.

Disclosure of Interests: None declared
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SAT0548 TRACKING RESIDUAL INFLAMMATION USING ULTRASONOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL REMISSION

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Background: With current treatment strategies, achieving a state of remission has become a realistic goal in rheumatoid arthritis (RA). Several composite scores and indices are available to assess remission based on clinical and biological parameters. None of the European League Against Rheumatism or American College of Rheumatology current recommendations include ultrasonography (US) findings as a parameter to define whether or not a patient is in remission.

Objectives: Describe and compare clinical and ultrasonographic findings in RA patients in clinical remission.

Methods: We included RA patients who were in clinical remission by the Disease Activity Score (DAS28<2,6) for at least three months. B mode and Power Doppler (PD) US examination were performed by an experienced rheumatologist, blinded to clinical data. Twenty-two joints of both hands (wrists, metacarpo-phalangeal (MCP) and proximal interphalangeal joints (PIP)) were assessed. A binary score (absence or presence) of synovial hypertrophy/effusion (SH) and power Doppler (PD) signals was applied for each joint. The sonographic Remission was defined by the absence of PD signals.

Results: Thirty patients were recruited (25 female and 5 male). The mean age of our population was 48 ± 8,98 years-old. All patients were in remission according to DAS28. The mean DAS28 was 2,03 ± 0,40 ranged from 1,13 to 2,6. Average length of remission was 16 months [3-72 months].

On clinical examination, nine swollen joints were identified, represented by wrists in all cases.

On B mode, synovial hypertrophy was detected in 80% of patients. Among the 660 joints examined, synovitis was identified in 89 cases. A wrist synovitis was detected in 55% of cases (33 out of 60 wrists studied) making it the most affected joint, followed by the second and third PIP in 14 and 12 cases out of 60 studied, respectively [Table 1].

PD signal, as a sign of active disease, was observed in 78% of patients and detected in 43% of the total wrists examined (26/60) [Table 1].

Among the swollen joints found on clinical examination, only one had no synovial hypertrophy in B mode. However, subclinical synovitis was detected in 81 joints (12% of total joints) with predilection for PIP joints (47% of subclinical synovitis). In PD mode and among subclinical synovitis, PD signals were found in 38 joints (47%).

Thus, the sensitivity of the clinical examination to identify swollen joints compared to US was 9%, its specificity of 99%, its PPV of 89% and its VPN of 88%.

Conclusion: Subclinical joint inflammation detected by US might explain the structural deterioration in RA patients despite clinical remission. Our findings support the use of US for the accurate evaluation of disease status before concluding to remission or otherwise to adjust treatment.

REFERENCES

[1] Karimzadeh H, Karami M, Bazgir N, Karimifar M, Yadegarfar G, Mohammadzadeh Z. Ultrasonographic findings of rheumatoid arthritis patients who are in clinical remission. J Res Med Sci. 2018;23:38. Published 2018 Apr 26.

[2] E Naredo, L Valor,I De la Torre,J Martínez-Barrio, M Hinojosa F Aramburu et al,Ultrasound Joint Inflammation in Rheumatoid Arthritis in Clinical Remission: How Many and Which Joints Should Be Assessed?.Rheumatoid Arthritis Vol65, Issue4 Apr 2013: 512-517

Table 1. Clinical and Ultrasonographic synovitis distribution in B mode and PD mode

Examined joint	Wrist	MCP1	MCP2	MCP3	MCP4	MCP5	IP1	PIP2	PIP3	PIP4	PIP5
Swollen joints	9	0	0	0	0	0	0	0	0	0	0
Synovial hypertrophy	33	1	5	4	3	4	1	14	12	9	2
Active synovitis on PD	26	1	5	2	1	1	0	4	3	2	0

Disclosure of Interests: None declared
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SAT0549 SARCOPENIA IN RHEUMATOID ARTHRITIS FEMALE PATIENTS: RELATIONSHIP BETWEEN WHOLE BODY AND TRABECULAR BONE SCORE

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Background: Rheumatoid arthritis (RA) is associated with muscle loss, osteoporosis and an increased risk of fractures. Sarcopenia is a syndrome in which muscle mass loss is linked to functional loss.Trabecular Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) that provides an indirect measurement of bone axial microarchitecture and allows to get information about bone quality [1-3].
Objectives: The aims of this study were to examine associations between bone mineral density, bone quality, fat mass and lean mass in the whole body in female patients with RA and healthy controls (CNT).
Methods: 55 female patients (mean age 58±12 years) affected by RA and 55 CNT (mean age 52±16 years) were enrolled. Bone Mineral Density (BMD, g/cm ^{2}) of the lumbar spine (L1-L4) and whole body expressed by Relative skeletal mass index (RSMI) was analyzed using a DXA scan (GE, Lunar Prodigy). Lumbar spine TBS was derived for each spine DXA examination using the TBS index (TBS iNsight Medimaps).For all subject was calculate the Body Mass Index (BMI, kg/m^2). According to the anthropometric equation [4], sarcopenia was defined as RSMI<5.5 kg/m^2 on women.
Results: The mean BMD±SD compared by RA and CNT was 0.894 ±0.127 g/cm^2 vs 1.298±0.672 g/cm^2 at the lumbar spine and 0.694±0.842 g/cm^2 vs 1.132±0.998 g/cm^2 on total hip, respectively, all p<0.001. The mean of BMI and RSMI value in RA patients was lower, 26.1 ± 3.92 kg/m^2 and 5.94 ± 0.42 kg/m^2 respectively, compared by CNT (23.7± 2.98 kg/m^2 and 6.92±0.71 kg/m^2). Nineteen RA women (35%) presented sarcopenia. Most of RA patients (80%) had bone loss that was significantly lower when compared with control group (p<0.001). Lumbar spine TBS was found significantly lower in RA patients compared with CNT (0.868±0.227 vs 1.482±0.113,p<0.001, respectively). There was not significant correlation between BMI kg/m^2 and RSMI kg/m^2 values. There was a positive correlation between the TBS and RSMI values in RA patients (p=0.002).
Conclusion: This study show that sarcopenia is frequent in RA patients, mostly on those classified as normal or overweight according to BMI. Therefore TBS and BMD values, as demonstrated could have a key role in a bone-muscle feedback in chronic systemic inflammatory rheumatic diseases, such as RA.

REFERENCES

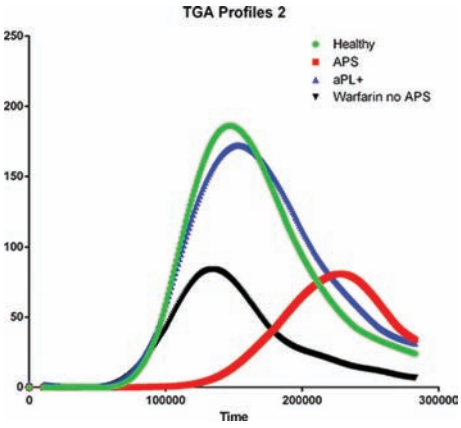
[1] Cutolo M et al. Autoimmun Rev 2011:12;84-7 2. Ruaro B, Casabella A, et al. Rheumatology (Oxford). 2018;57:1548-1554. 3.Ruaro B, Casabella A, et al. Rheumatology (Oxford). 2018;57:1548-1554 4. Baumgartner RN et al., J Epidemiol. 147:755–763

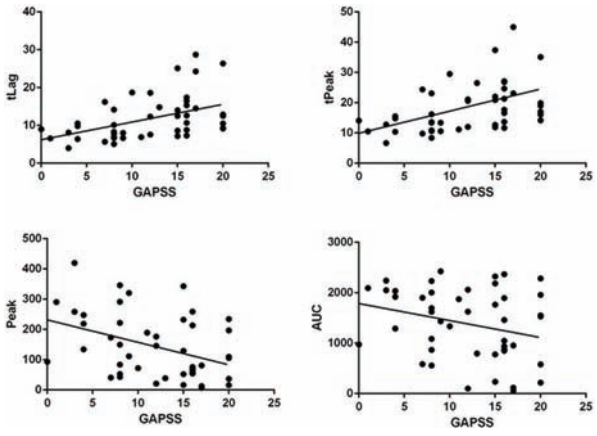
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SAT0550 THROMBIN GENERATION ASSAY AND GLOBAL ANTIPHOSPHOLIPID SCORE (GAPSS) FOR RISK STRATIFICATION IN ANTIPHOSPHOLIPID SYNDROME

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Background: Thrombin generation assay (TGA) is a simple and reproducible technique, that could potentially be used in coagulation laboratories, that measures the concentration of generated thrombin after plasma recalcification. The clinical usefulness of TGAs in assessing thrombotic risk has been a matter of growing interest, however, it has not been applied on a large scale to a large cohort of patients with antiphospholipid syndrome (APS).
Objectives: The aim of our study was to assess the potential use of TGA in monitoring the pro-coagulant state in APS patients and its role in predicting the relative risk score in developing APS clinical manifestations, by comparing its parameters to the validated global antiphospholipid score (GAPSS).
Methods: After chart-reviewing all APS patients that presented at San Giovanni Bosco Hospital in the last 5 years, we enrolled 4 groups of patients for the sake of this study, matched for age and sex. Clinical and laboratory characteristics were retrospectively collected.
Inclusion criteria were as follows:
Group A) Fulfilled the diagnosis of Thrombotic APS defined as per Sidney criteria [1]: 60.
Group B) Patients with aPL positivity, but with no clinical manifestations of APS defined as per Sidney criteria [1]: 30.
Group C) Patients treated with Warfarin (target INR 2-3), negative for aPL and other autoimmune conditions: 60.
Group D) Healthy Controls: 60.
Results: Figure 1 resumes the representative TGA profiles between groups.
Healthy controls and patients with aPL positivity, but no APS clinical manifestations, had similar TGA profiles [mean tLag (min) 9.6 ±2.9 v.s. 8.6 ±3.2; mean tPeak (min) 16.2 ±4.7 v.s. 13.7 ±5.8; mean Peak (nM) 209.2 ±103.8 v.s. 265.4 ±106.2; mean AUC (nM) 2023 ±489.2 v.s. 2057.1 ±571.8, respectively].
When analyzing the TGA profile curve of the patient with APS compared with healthy controls and aPL positive patients with no clinical manifestations of APS, we observed a statistically significant higher tLag (13.3 ±5.9 min; p= 0.003; p= 0.008, respectively) and tPeak (21.3 ±9.2 min; p= 0.006; p= 0.014, respectively) with lower Peak (99.1 ±71.8 nM; p< 0.001; p= 0.005, respectively) and AUC (1150.5 ±637.4 nM; p< 0.001; p= 0.004, respectively).
Furthermore, also when analyzing the TGA profile of APS patients compared to patients treated with warfarin and no APS, APS patients had significant higher tLag (13.3 ±5.9 min v.s. 8.2 ±2.1; p< 0.001), tPeak (21.3 ±9.2 min v.s 13 ±2.8; p< 0.001), Peak (99.1 ±71.8 nM v.s. 62.3 ±21.5; p= 0.018) and AUC (1150.5 ±637.4 nM v.s. 605 ±148.8; p< 0.001).
When analyzing a correlation model between GAPSS and TGA parameters, we observed a statistically significant correlation for tLag (Pearson





0.444; p= 0.002), tPeak (Pearson 0.464; p= 0.001) and Peak (Pearson -0.382; p= 0.008). AUC showed no statistical significant correlation (Pearson -0.255; p= 0.083).
Correlation analysis between GAPSS and TGA parameters is resumed in Figure 2.
When stratifying the patients for clinical manifestations, patients with a more aggressive clinical profile, who experienced both arterial and venous thrombosis, when compared with patients who had an history of either arterial or venous thrombosis, had significant different levels of GAPSS (mean GAPSS 17.5 ± 2.1 v.s. 12.4± 5.5, respectively; p= 0.001) and had a significant higher tLag (16.5 ± 7.4 v.s. 11.9± 4.5, respectively; p= 0.048) and tPeak (27.4 ± 13.5 v.s. 19± 6.3, respectively; p= 0.027).
Conclusion: TGA might represent a valuable tool to stratify the risk of developing clinical manifestations in APS patients.

REFERENCES

[1] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost [Internet]. 2006 Feb

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SAT0551 INCIDENTAL FINDINGS OF TEMPOROMANDIBULAR JOINT DISORDERS ON STANDARD BRAIN MRIS: A CROSS-SECTIONAL STUDY

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Background: The temporomandibular joints (TMJ) changes is quite often ignored as a differential diagnosis in the evaluation of patients with suspicion on rheumatic and musculoskeletal disease such as temporal arteritis, fibromyalgia, rheumatoid arthritis. To understand whether TMJ changes have to be included in routine workup of patient's evaluation with the suspect to rheumatic disease, we assessed the prevalence of TMG changes incidental findings in standard brain MRI scan. In our experience, numerous incidental findings are found on a standard brain MRI scan, especially the elderly. A literature search revealed that no studies have reported the prevalence of these findings and their clinical relevance.
Objectives: To evaluate the prevalence of incidental TMJ findings on standard brain magnetic resonance imaging scans and assess if these findings are associated with symptoms.
Methods: Our sample comprised 65 males (47.1%) and 75 females (52.9%), mean age 54.75±17.45 (range: 18-87). Data collected from each TMJ included articular displacement, articular effusion, condyle flattering, condyle erosions, capsule enhancement, and bone marrow edema. Dichotomous data as to TMJ-related symptoms such as headaches, earaches, dizziness, clicking or grating sound, pain or soreness of the joint, limited mouth opening, locking of the jaw, facial muscle pain, unexplained teeth pain, neck pain or stiffness and difficulty swallowing, were acquired during telephone interviews.
Results: The most frequent finding was disc displacement (39.9% on the right side and 47.8% on the left), followed by condyle flattering (33.3% on the right side and 44.2% on the left). All findings, except bone marrow edema, were significantly more frequent on the left side than the right (Table 1). Significant associations were found between incidental findings in the TMJ and earaches (odds ratio 2.759, P=0.043), dizziness (odds ratio 2.325, P=0.031), a clicking or grating sound (odds ratio 6.492, P=0.002) and facial muscle pain (odds ratio 11.255, P=0.003) (Table 2).
Conclusion: Incidental findings of TMJ degenerative features were commonly found on standard brain magnetic resonance imaging. The high frequency of the findings and strong association with facial pain requires performing TMJ assessment in all patients who undergo medical inquiry for suspected rheumatic and musculoskeletal disease.

Table I: Frequencies of incidental findings in TMJs on standard brain MRI (n=138).

Variables	Right	Left	Comparison*
Disc displacement	N=55 (39.9%)	N=66 (47.8%)	**Z=-1.98, P=0.048**
Articular effusion	N=5 (3.6%)	N=13 (9.4%)	**Z=-2.14, P=0.033**
Condyle flattering	N=46 (33.3%)	N=61 (44.2%)	**Z=-2.89, P=0.004**
Condyle erosion	N=13 (9.4%)	N=24 (17.4%)	**Z=-2.20, P=0.028**
Capsule enhancement	N=4 (2.9%)	13 (9.4%)	**Z=-2.50, P=0.013**
Bone marrow edema	N=11 (8%)	N=16 (11.6%)	Z=-1.51, P=0.132

*Results of Wilcoxon Signed Ranks test; Significant differences (p<0.05) are marked in bold.

Table 2. Association between clinical TMJ-related symptoms and TMJ- incidental findings on standard brain MRI *

Symptoms	B	p-value	Odds ratio
Headache	0.475	0.220	1.607
Earaches, stuffiness or ringing	**1.015**	**0.043**	**2.759**
Dizziness, lightheadedness	**0.844**	**0.031**	**2.325**
A clicking or grating sound	**1.871**	**0.002**	**6.492**
Pain or soreness of the TMJ	0.753	0.424	2.123
Pain in facial muscles (cheeks)	**2.421**	**0.003**	**11.255**
Unexplained teeth pain	1.736	0.169	5.676
Neck pain or stiffness	0.602	0.147	1.826
Difficulty swallowing (sore throat)	1.559	0.057	4.752

*Results of logistic regression analysis (d.f.=1) with the symptom as a dependent variable and TMJ- incidental findings, age, and sex as independent predictors. A significant association (p<0.05) is marked in bold.

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SAT0552 PAEDIATRIC NON-INFECTIOUS DACRYOADENITIS: THE GOSH EXPERIENCE

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Background: Dacryoadenitis is an inflammatory enlargement of the lacrimal gland and the most common orbital inflammatory condition in the paediatric population, although only 6 to 17% of orbital inflammatory disorders occur in children (1-4). Dacryoadenitis may be idiopathic or associated with infections or inflammatory diseases. Systematic inflammatory disorders are more typically associated with chronic than acute dacryoadenitis (3).
We describe the largest paediatric cohort of biopsy proven non-infectious dacryoadenitis (4,5).
Objectives:
1. To describe lacrimal gland biopsy results
2. To report associated clinical, laboratory features and treatment

Methods: We identified 72 children who had lacrimal gland biopsy at GOSH between 25/09/2000 and 12/04/2018 using two key-words: "lacrimal" and "dacryoadenitis". We excluded patients with infectious dacryoadenitis, benign tumors or malignancy. We retrospectively reviewed the medical notes, laboratory and histopathology results.
Results: Twenty six patients had non-infectious dacryoadenitis with or without soft tissue involvement. All cases manifested as upper lid swelling. 19 (73.1%) patients had unilateral involvement. 12 (46.2%) patients were male. Mean age at time of biopsy was 10.5 years and median 13 years (range 1 – 17.7).
Four patients had GPA (granulomatous polyangiitis), 4 patients sarcoidosis, 1 patient IgG4-related disease, 1 patient Sjögren with secondary antiphospholipid syndrome and 16 patients non-specific chronic inflammation (NSCI). 2/4 patients with sarcoidosis had extra-ocular involvement. One patient with sarcoidosis had NOD2 mutation without Blau phenotype. One patient with GPA had extra-ocular involvement.
4/13 children tested had raised ACE including 2 sarcoidosis and 2 NSCI. 7/17 had raised amylase (2 sarcoidosis, 1 Sjögren, 4 NSCI). 7/20 had

raised ESR (1 Sjögren, 5 NSCI and 1GPA with renal involvement). 3/16 had raised IgG (IgG4 disease, GPA with renal involvement and NSCI).
13 (50%) patients received systemic steroids. 11 (42.3%) patients received DMARDS (MMF, Methotrexate, Azathioprine and Hydroxychloroquine). 4 (15.4%) patients received a biologic: 3/4 rituximab (2 GPA and one IgG4-related disease) and one patient with NSCI received anti-TNF. 6 (23.1%) patients underwent orbitotomy. Patients still on follow-up had good response to treatment and did not experience any local complication.
One patient with NSCI developed auto-immune thyroiditis and polymyositis.
Conclusion: Most of the patients in our retrospective cohort study had NSCI and may be idiopathic. Few patients had a specific diagnosis on biopsy allowing targeted treatment.
Patients with non-infectious dacryoadenitis may benefit from tissue biopsy to exclude infection and malignancy and streamline management. Ongoing monitoring is important for patients with NSCI to identify underlying inflammatory diseases at an early stage.

REFERENCES

[1] Belanger C, et al. Inflammatory Disorders of the Orbit in Childhood: A Case Series. Am J Ophthalmol. 2010 Oct;150(4):460-3
[2] Spindle J, Tang SX, Davies B, Wladis EJ, Piozzi E, Pellegrini M, Lally SE, Shields C, Shinder R. Pediatric Idiopathic Orbital Inflammation: Clinical Features of 30 Cases. Ophthalmic Plast Reconstr Surg. 2016 Jul-Aug;32 (4):270-4
[3] Andrew NH, Kearney D, Sladden N, McKelvie P, Wu A, Sun MT, McNab A, Selva D. Idiopathic Dacryoadenitis: Clinical Features, Histopathology, and Treatment Outcomes. Am J Ophthalmol. 2016 Mar;163:148-153
[4] Luemsamran P, Rootman J, White VA, Nassiri N, Heran MKS. The role of biopsy in lacrimal gland inflammation: A clinicopathologic study. Orbit. 2017 Dec;36(6):411-418
[5] Boulter EL, Eleftheriou D, Sebire NJ, Edelsten C, Brogan PA. Inflammatory lesions of the orbit: a single paediatric rheumatology centre experience. Rheumatology 2012. 51(6):1070–1075

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SAT0553 HIGH FEASIBILITY AND ACCEPTANCE OF A MUSCULOSKELETAL ULTRASOUND PROGRAM TO IMPROVE DMARDS ADHERENCE IN RHEUMATOID ARTHRITIS

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Background: Disease modifying anti-rheumatic drugs (DMARDs) non-adherence is a widespread issue in rheumatoid arthritis (RA) which needs to be urgently addressed as it can lead to suboptimal therapy with poor disease outcomes. The subsequent need for more aggressive therapy, treatment of disease related complications and increased consultations can translate into increased healthcare utilization and costs.
Objectives: To describe the feasibility and patient's acceptance of a Musculoskeletal Ultrasound Program (MUSP) developed to improve DMARDs adherence in RA patients who are non-compliant to their conventional DMARDs (Methotrexate, Leflunomide, Sulfasalazine and/or Hydroxychloroquine) therapy.
Methods: The MUSP is a standardized approach (i.e. each patient given the same standardized intervention) which synergises (1) the patients' direct visualization of their joint pathologies (inflammation and/or erosions) using real-time ultrasonography and (2) a Rheumatologist's simultaneous reinforcement of the need for medication adherence, thereby improving patient's understanding of their joint disease and motivating them to adhere to their DMARDs therapy. Joints utilized to demonstrate joint pathologies real-time were clinically affected ones. In the event that a specific joint pathology is not demonstrable on ultrasonography, the subject will be shown a representative picture of an ultrasound lesion corresponding to that specific joint pathology. Patient acceptability was assessed using questionnaire administered by an interviewer who is not the Rheumatologist conducting the MUSP. Categorical variables were reported using frequency counts and percentages, while continuous variables using mean and standard deviation (SD).
Results: 62 RA patients (baseline characteristics: majority Chinese, 40/62 (64.5%); 55/62 (88.7%) female; mean (SD) age, 49.2 (12.0), mean (SD) DAS28, 3.27 (1.39); mean (SD) disease duration, 6.1 (5.4) years) completed the MUSP. The mean (SD) time taken to complete the MUSP was 9.2 (4.6) minutes. All patients had at least one joint pathology demonstrable to them on real-time ultrasonography. Specifically, 62/62 (100%), 14/62(22.6%) and 25/62 (40.3%) had demonstrable synovial hypertrophy, power Doppler synovial vascularity and bone erosions, respectively. Figure 1 shows the frequency distribution of the joint sites utilized to demonstrate joint pathologies real-time using ultrasonography. The majority of patients reported that the MUSP had moderately or very much improved their understanding of their underlying joint condition (i.e. 44/62 (71.0%) patients) and the importance of regularly taking their RA medication (i.e. 49/62 (79.0%) patients) (figure 2). Most patients (i.e. 56/62 (90.3%) patients) will also recommend the MUSP to another RA patient.
Conclusion: Our results demonstrated high feasibility and acceptance of a MUSP developed to improve DMARDs adherence in RA patients. Further studies are required to establish the clinical impact and cost-effectiveness of the MUSP in this population.

Figure 1. Frequency distribution of the joint sites utilized to demonstrate joint pathologies real-time

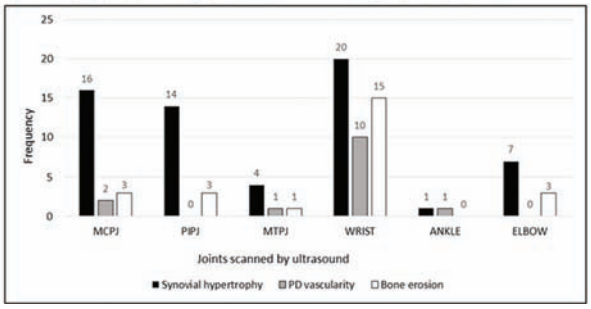
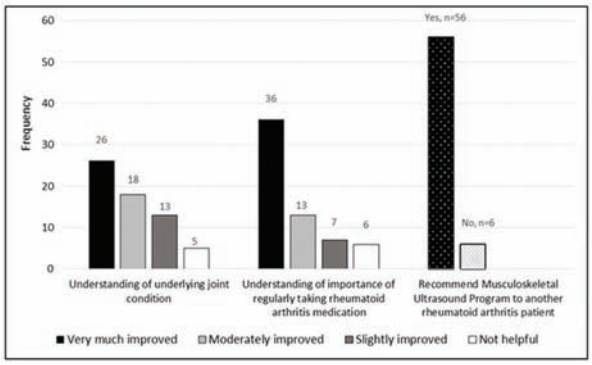


Figure 2. Musculoskeletal Ultrasound Program and its impact on patients' understanding



REFERENCES

[1] Harrold LR, Andrade SE. Medication adherence of patients with selected rheumatic conditions: a systematic review of the literature. Semin Arthritis Rheum. 2009; 38(5):396-402.

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SAT0554 CLINICAL FEATURES ANALYSIS OF 50 MESENTERIC PANNICULITIS CASES DIAGNOSED BY COMPUTERIZED TOMOGRAPHIC SCANNING

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Background: Mesenteric panniculitis (MP) is a chronic idiopathic inflammatory disease that occurs in mesenteric adipose tissue,which lacks of specific diagnostic methods.

Objectives: To retrospectively summarize 50 cases of patients with mesenteric panniculitis(MP diagnosed by CT to improve the clinicians' understanding of the disease.
Methods: The patients with MP diagnosed by abdominal CT were collected from the hospital of Shanxi Medical University from January 2013 to May 2017. The demographic characteristics, clinical features, auxiliary examination, treatment and prognosis were analyzed and summarized.
Results: The proportion of men and women was1:0.92, the age of onset was 25 ~ 85 years old, the average age was (59.1±14.0) years old. Most of the patients presented with abdominal pain, fever, hematuria, and lymphadenopathy.22 cases with tumor, the most common type is lymphoma, 16 cases with abdominal surgery history. There were no special laboratory tests, no patients had mesenteric pathologic biopsy. 6 cases had abdominal CT review, 1 case of who used hormone treatment showed the lesion was significantly absorbed, the remaining 5 cases no significant changes.
Conclusion: MP is common in the elderly, the clinical manifestations are diverse, easy to merge tumor, lymphoma more common, abdominal CT is its most important diagnostic means, when found MP, should pay attention to whether the merger with malignant tumors.

REFERENCES

[1] Bashir MS, Abbott CR.Mesenteric lipodystrophy[J]. J Clin Pathol, 1993, 46 (9):872-874.
[2] Ehrenpreis ED, Roginsky G, Gore RM. Clinical significance of mesenteric panniculitis-like abnormalities on abdominal computerized tomography in patients with malignant neoplasms[J].World J Gastroenterol, 2016, 22 (48):10601-10608.
[3] Protin-Catteau L, Thiéfin G, Barbe C, et al. Mesenteric panniculitis: review of consecutive abdominal MDCT examinations with a matched-pair analysis[J]. Acta Radiol,2016, 57(12):1-7.
[4] Scheer F, Spunar P, Wiggermann P, et al. Mesenteric Panniculitis (MP) in CT - A Predictor of Malignancy?[J]. Rofo, 2016, 188(10):926-932.
[5] Mahmoud Rezk Abdelwahed, Hussein, Saad Rezk, Abdelwahed. Mesenteric panniculitis: an update[J]. Expert Rev Gastroenterol Hepatol, 2015, 9 (1):67-78.
[6] Emory TS, Monihan JM, Carr NJ, et al. Sclerosing mesenteritis, mesenteric panniculitis and mesenteric lipodystrophy: a single entity?[J]. Am J Surg Pathol, 1997, 21(4):392-398.
[7] Van PN, van Bommel EF, Elgersma OE, et al. Mesenteric panniculitis: prevalence, clinicoradiological presentation and 5-year follow-up[J]. Br J Radiol, 2014, 87(1044):20140451.

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Public health, health services research, and health economics

SAT0555 LOSS TO FOLLOW-UP IN REGISTRIES OF RHEUMATIC PATIENTS TREATED WITH BIOLOGICS: A POTENTIALLY VALUABLE HIDDEN REAL-WORLD DATA THAT IS BEING OVERLOOKED?

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Background: The information associated with loss to follow-up (LFU) patients (Pts) may affect a real-world data evaluation of the use of biologics (Bio) that is not being adequately captured in registries.
Objectives: To identify the reasons for LFU in rheumatic patients treated with biologics in our center.
Methods: We identified all Pts treated with Bio in our center who had no registered visits in Reuma.pt for more than 6 months. We retrieved baseline information from Reuma.pt and from the hospital electronic clinical record. We then performed a telephonic interview to characterize the reasons for LFU up at our day care unit. For Pts unable to be contacted by telephone a letter of invitation to an appointment at the hospital was sent.
Results: From a total of 790 Pts registered in Reuma.pt at our centre with active Bio therapy (BioTx) 227 did not have any information registered in last 6 months. Of this, 36 Pts were on BioTx prescribed by other Department (Dermatology, GEA) and maintain follow-up in these departments. 102 Pts had suspended BioTx by medical indication, and this information was registered in the hospital electronic clinical records but not updated in Reuma.pt. For 89 Pts (47%) no information could be retrieved from either the hospital electronic clinical record or Reuma.pt and we classified these Pts as true LFU. Reasons of LFU were: being followed in other Rheumatology centres (n=28; 31.4%), death (n=26; 29.2%), adverse effects (AE) (n=11; 12.4%), other (n=5, 5.6%) and clinical remission (n=4; 4.5%). 15 Pts (16.9%) could not reach us by telephone or attend the appointment.
28 of these LFU Pts were being followed up in another Rheumatology center. The most frequent reasons for this change were: 15 (16.9%) decided to move the follow-up to a newly created and closer Rheumatology Department; 6 (6.7%) moved to another city; 5 patients (5.6%) had administrative problems related to our Department/Hospital and 2 (2.3%) patients referred socio-economic reasons that were interfering with travelling.
26 of the LFU Pts died, at a mean age of 66.3 years. The mean disease duration was 14.3 years and 20 Pts (76.9%) had RA. The mean duration of Bio was 5.9 years and 53.8% were under anti-TNF therapy, 16% under Anti-CD20 therapy and 12% under interleukin-6R inhibitors. Cause of death was identified in only 3 patients: 1 had a myocardial infarction, 2 had surgery complications. None of these Pts was on BioTx at the moment of death.
11 Pts of the LFU had stopped BioTx and abandoned follow-up by their own decision after suffering AE attributed by the patient to the use of Bio. 6 patients (6.7%) had infections: cutaneous (n=3, 3.4%) or urinary tract related (n=3, 3.4%); with need of hospital admission in 2 of the cases (2.2%). The remaining Pts stopped the drug because of cutaneous reactions (n=5. 5.62%).
4 Pts of the LFU were in remission and decided to stop the drug and the medical follow up. All of them believed that the disease was inactive without the need of medical drugs.
Conclusion: Identifying LFU Pts and clarifying the reason for the loss of data in a register contributes to a better knowledge on strategies to discontinue Bio in stable Pts, to a better pharmacovigilance of adverse effects and to more efficiency in data capture by registries. The authors of this study are now making additional efforts to contact the 15 still missing Pts and obtaining access to death certificates in order to further clarify the cause of death of 23 Pts.

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SAT0556 EVALUATING RESEARCH PARTICIPANT EXPERIENCE IN A RHEUMATOID ARTHRITIS OBSERVATIONAL STUDY

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Background: Patient and public involvement (PPI) in research is increasingly common (1), but the experience of research participants is rarely evaluated, missing opportunities to gain insights for improving future studies. (2) Observational studies are often used to study natural progression and treatment response in chronic diseases like rheumatoid arthritis (RA).
Objectives: We aimed to pilot a participant experience questionnaire in an observational study of RA patients, to gain feedback on the study and evaluate the questionnaire as a feedback tool.
Methods: The Rheumatoid Arthritis Medication Study (RAMS) is a large UK prospective observational study of patients with RA or undifferentiated polyarthritis starting methotrexate (MTX) for the first time. Participants were recruited prior to initiation of MTX and followed-up at 3, 6 and 12 months. At visits, disease activity is measured and participants complete a study questionnaire including patient reported outcomes. Participants also complete a weekly diary about their MTX use. (3)
A subset of RAMS participants were given a feedback questionnaire at their final visit. The questionnaire was designed by researchers and study coordinators with feedback from patients. Questions addressed the value of participation, study conduct and priorities for future research.
Multiple-choice question responses were summarised and key themes were identified in the free-text responses.

	Frequency (%)						
	Strongly Agree	Agree	Neither agree nor disagree	Strongly disagree	Disagree	N/A	Missing
It is worthwhile to take part in this study	132 (66)	57 (28)	12 (6)	0 (0)	0 (0)	0 (0)	0 (0)
I have the opportunity to ask questions about the study	87 (43)	94 (47)	15 (7)	1 (0)	3 (1)	1 (0)	0 (0)
It is easy to communicate with the study staff	119 (59)	60 (30)	16 (8)	1 (0)	2 (1)	3 (1)	0 (0)
The number of appointments for this study is about right	88 (44)	91 (45)	17 (8)	1 (0)	2 (1)	2 (1)	0 (0)
The total length of the study is about right	78 (39)	94 (47)	24 (12)	2 (1)	2 (1)	1 (0)	0 (0)
The amount of paperwork I have to complete is about right	74 (37)	101 (50)	21 (10)	3 (1)	2 (1)	0 (0)	0 (0)
How likely would you be to recommend the study to friends and family eligible to take part?	96 (48)	84 (42)	12 (6)	4 (2)	2 (1)	2 (1)	1 (0)

Results: 201 of 357 (56%) patients eligible to receive the questionnaire completed it. Multiple-choice questions had 100% completion and responses are presented in Table 1. 189 (94%) participants agreed that participating in RAMS was worthwhile and 180 (90%) would recommend participation to eligible friends and family. The most frequent theme in recommending the study was the desire to "help people" (47%) and most respondents (57%) did not know what future research they would like carried out or did not answer.
Conclusion: The majority of RAMS participants were happy to share their experience of participation and had positive views. Many had altruistic reasons for taking part. Multiple-choice questions had high completion rates and free-text fields were less completed. More details on participant research priorities may be gained by offering options to select from. Future investigation of participant experience should also consider those lost to follow-up, participants who choose to withdraw, and potential participants who did not enrol.

REFERENCES

[1] INVOLVE. Approaches to Public Involvement: NIHR; [http://www.invo.org.uk/posttyperesource/approaches-to-public-involvement/]
[2] Planner C, Bower P. Trials need participants but not their feedback? A scoping review of measures of participant experience of taking part in trials. School for Primary Care Research - 2017 Showcase Blavatnik School of Government; Oxford: NIHR; 2017
[3] Sergeant JC, Hyrich KL, Anderson J, et al. OP0013 Prediction of Non-Response To Methotrexate Therapy in The Rheumatoid Arthritis Medication Study (RAMS). Annals of the Rheumatic Diseases2016. p. 57-8

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SAT0557 OUTPATIENT READMISSION IN RHEUMATOLOGY: A MACHINE LEARNING PREDICTIVE MODEL OF PATIENT'S RETURN TO THE CLINIC

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Background: Readmissions can be defined as the return of a patient to a healthcare setting after a discharged. Attention has been mainly focused on readmissions following inpatient hospitalizations. In the outpatient setting, readmissions have been far less studied. Premature outpatient discharges can have negative impacts at multiple levels, as they may prolong disability, and increase the chance of disease chronification, the demands to the immediate patient's support system, and healthcare resources utilization. As the first step in preventing outpatient readmission, the assessment of the individual patient's risk could be useful to help identify those subjects at greatest risk, so, in a further step we could focus the delivery of an intervention in those patients to reduce their risk.
Objectives: To develop and validate a machine learning predictive model based on Random Forest, to estimate the risk of readmission in an outpatient rheumatology clinic after discharge (outpatient readmission).
Methods: Patients stored in a departmental electronic health record from April 1st, 2007 to November 30th, 2016, and followed-up until November 30th, 2017, were included in this study. Only readmissions taking place between 3 and 12 months after discharge were analyzed. Discharge episodes were split into training, validation and test datasets. Clinical and demographic variables, including diagnoses, treatments, quality of life, and comorbidities, were used as predictors. Models were developed using Random Forest in the training dataset, though the combination of several tuning parameters. Models that maximized the area under the receiver operating characteristic curve (ROC-AUC) in the validation set were assessed in the test set. The model with the highest AUC-ROC in the test dataset was considered as the best final model.
Results: 17,473 patients (18,117 discharges episodes) were analyzed and 1,960 (10.8%) discharges episodes were classified as outpatient readmissions. 48,654 models were finally developed. The best final model showed an AUC-ROC of 0.674 a sensitivity of 0.330 and a specificity of 0.867. The most relevant variables in the model were the number of diagnoses given at discharge, follow-up duration, age, number of previous discharges, previous corticosteroids use and disability.
Conclusion: We have developed a predictive model for outpatient readmission in a rheumatology setting. Clinical, demographical characteristics as well as medication and disability were the most important predictors.
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SAT0558 IDENTIFYING HEATH LITERACY PROFILES OF RA AND SPA PATIENTS USING THE HEALTH LITERACY QUESTIONNAIRE

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Background: Delivery of rheumatological care is suggested to be compromised by patient health literacy. Prevalence of problematic health literacy in the Netherlands is estimated to be as high as 36%. *"Health literacy represents the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health"* (Nutbeam, 1998). A deeper understanding of diverse health literacy profiles of patients attending rheumatology clinics could facilitate development of interventions tailored to patients' needs, in order to improve health outcomes and reduce inequities.
Objectives: To identify health literacy strengths and weaknesses among patients with Spondyloarthritis (SpA) and Rheumatoid Arthritis (RA) attending a rheumatology clinic, and identify typical 'health literacy profiles' based on these strengths and weaknesses.
Methods: Consecutive RA and SpA patients attending the outpatient clinic at Maastricht UMC+, the Netherlands, were invited to participate. Health literacy was assessed using the Health Literacy Questionnaire (HLQ), which includes nine dimensions (Figure 1). Socio-demographics and health-related characteristics were also collected. Hierarchical cluster analysis following Ward's method identified clusters based on HLQ scale scores. This method groups subjects into a predefined number of clusters, based on smallest differences to the mean of all scales, creating minimal variance within each cluster, and maximum variance between clusters. Three researchers jointly examined twenty cluster solutions for meaningfulness by interpreting HLQ scales and patient characteristics. Meaningful clusters are translated into health literacy profiles using HLQ patterns and demographic data. A patient representative confirmed the identified profiles.
Results: In total, 133 patients with RA and 106 with SpA completed the questionnaire. Of these, 61% (n=146) were female, mean age was 61.6 (±13.3), 27% (n=65) lived alone, 11% (n=26) did not speak Dutch at

home, 28% (n=68) were employed, and 22% and 50% had received low and medium education, respectively. Figure 1 displays identified health literacy profiles and scale scores, with greener values representing strengths and red scores representing weaknesses. Overall, the pattern indicates RA and SpA patients have similar profiles, but some represent a clear majority of SpA or RA patients and could be considered disease-specific. For example, cluster 10 includes patients who typically feel comfortable in their relationship with their doctor (scales 1 and 6), and are rather confident in managing their health and getting the information they need (scale 3 and 7). However, they struggle in understanding health information (scale 9), and lack the social support needed to make health decisions and maintain good health (scale 4). This profile appeared restricted to RA patients.

Conclusion: This study identified potential typical health literacy profiles in patients with inflammatory arthritis in our clinic. Profiles reflected distinctive strengths and weaknesses on the nine health literacy dimensions. Some profiles appeared to be condition-specific, which warrants further investigation. Identified profiles will feed into co-design workshops with patients, professionals and other stakeholders, in order to develop interventions to tailor the care to patients' needs.

	Cluster number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Total
	Number of patients in cluster (n)	13	14	15	1	11	5	20	69	30	4	12	17	13	6	5	4	239
Scales part 1: range 1-4 (strongly disagree – strongly agree)	1: Healthcare provider support	3,92	3,84	3,75	3,75	3,32	3,00	3,15	3,08	2,85	3,31	2,98	3,04	2,63	2,96	2,90	2,81	3,16
	2: Having sufficient information	3,90	3,38	3,08	3,75	3,16	2,90	3,00	2,99	2,79	2,81	2,96	2,84	2,46	2,58	1,85	2,94	2,97
	3: Actively managing health	3,63	3,30	2,96	1,00	3,00	2,70	2,64	2,95	2,70	3,20	2,95	2,75	2,77	2,13	2,56	2,85	2,89
	4: Social support for health	3,57	2,60	3,59	3,60	3,29	2,56	2,91	2,99	2,77	2,10	2,58	2,73	2,75	2,97	1,80	2,95	2,92
	5: Critical appraisal of information	3,34	2,99	2,56	1,60	3,05	2,32	2,61	2,90	2,25	2,80	2,80	2,52	2,54	1,80	2,28	2,50	2,69
	6: Actively engaging with providers	4,60	4,34	4,61	5,00	4,79	4,76	4,13	3,98	3,89	3,75	3,43	3,75	2,97	3,30	2,56	1,60	3,94
Scales part 2: range 1-5 (always difficult – always easy)	7: Navigating the health system	4,32	4,15	4,07	4,33	4,56	4,70	4,13	3,73	3,69	3,79	3,29	3,11	2,94	2,61	2,20	2,13	3,70
	8: Finding health information	4,34	4,01	3,97	4,60	4,73	4,60	4,31	3,90	3,79	3,55	3,08	3,54	3,20	2,00	2,12	1,60	3,78
	9: Understanding health information	4,48	4,17	4,40	3,80	4,85	4,64	4,48	3,92	3,97	2,80	3,65	3,35	3,34	2,20	2,49	2,05	3,90
Patient diagnosis	% RA in cluster	46,2	85,7	33,3	100	63,6	20,0	60,0	50,7	56,7	100	91,7	52,9	38,5	33,3	60,0	75,0	55,6
	% SpA in cluster	53,8	14,3	66,7	0	36,4	80,0	40,0	49,3	43,3	0	8,3	47,1	61,5	66,7	40,0	25,0	44,4

Figure 1: Heat map of identified patient health literacy profiles based on cluster analysis. *Red values indicate low scores or high difficulty; yellow to green scores indicate medium to low difficulty. Scales one to five scores range from 1 to 4, scales six to nine range from 1 to 5.*

REFERENCES

[1] Nutbeam D. (1998). Health promotion glossary. Health Promotion International, 13, 349–364.

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SAT0559 IMPACT OF BLOCK SWITCH TO BIOSIMILAR ETANERCEPT IN PRACTICE – AN EXPERIENCE FROM ONE TERTIARY RHEUMATOLOGY DEPARTMENT

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Background: Biosimilars of biotechnological agents represent an important opportunity to increase accessibility to these medications. Clinicians still maintain reservations regarding the similarity of their efficacy and safety in practice.
Objectives: To evaluate the clinical consequences of a non-medical switch of etanercept (ETN) original to biosimilar in a clinical practice setting.
Methods: The study included all patients aged 18+ treated in a Tertiary Rheumatology Department with original ETN who were switched to his biosimilar following a decison by the hospital administration, accepted by rheumatologists. Patients were informed of the switch prior to its occurrence, in simple terms underlining the similarity in terms of regulatory issues and scientific evidence. Disease activity, adverse events and adaptation to the drug delivery system were evaluated at each visit. Disease activity at baseline (time of switch), 3 and 6 months after was compared using Paired samples T-test or Wilcoxon test as adequate. A $p \leq 0.05$ was considered statistically significant. Continuous variables are presented as means and categorical variables as proportions.
Results: From 98 patients treated with original ETN in our department, 89 were switched to his biosimilar. The remaining ones maintained the treatment with the reference biological product for several reasons. Eight patients were excluded from this analysis due to poor adherence to treatment (n=4) and early interruption of treatment [n=4: due to surgery (n=1), respiratory infection (n=1), suspected allergic reaction to biosimilar (n=1) and own initiative (n=1)]. Of the remaining 81 patients (58% female, mean age 56.2±12.1 years), 38.3% had RA, 40.7% SpA, 18.5% PsA and 2.5% JIA. Disease activity was stable over the follow up in patients with RA, PsA and SpA as no statistically significant differences were observed in acute phase reactants, patient or physician global assessment between the three time points. Minor adverse events were reported by 2 patients (pain and local cutaneous reaction), 2 reported sense of disease exacerbation in the first three months that was not confirmed by clinical and analytical evaluation and 2 patients reported minor infections. Good adaptation to the drug delivery instrument was reported by 93.8% of patients (n=76).
Conclusion: The switch from ETN to his biosimilar in this group of patients followed in routine care did not affect the overall efficacy and safety of treatment. We did not observe a significant impact of nocebo effect.

Table 1. Acute phase reactants, disease activity, joint count, patient and physician global assessment through follow-up.

	Baseline	3 Months after switch	6 Months after switch
ESR (mm/h) ϕ	8.00(12)	8.00(11.75)	10.50 (11.50)
CRP (mg/dL) ϕ	0.20(0.47)	0.31(0.51)	0.29 (0.38)
DAS-28-ESR ϕ*	2.07(0.97)	2.17(0.95)	2.39 (1.08)
Tender joint-28 §	0.43(0.108)	0.43(0.09)	0.94 (0.26)
Swollen joint-28 §	0.22 (0.078)	0.49(0.11)	0.92 (0.36)
PtGA (0-100) §	38.22(3.41)	40.24(3.19)	42.50 (3.57)
PhGA (0-100) ϕ	10.00(17.00)	5.00(20.00)	10.00(10.00)

CRP- C-Reactive Protein; ESR- Erythrocyte Sedimentation Rate; PhGA physician global assessment; PtGA- patient global assessment; ϕ median (Interquartile range); § mean (Standard deviation). *Only for RA and PsA patients (n=46). DAS-28-ESR and PtGA were compared using T-test; the remaining ones were compared using Wilcoxon test. None of the differences between time-points was statistically significant by paired tests.

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SAT0560 A QUALITATIVE STUDY EVALUATING NEAR-PATIENT TOOLS INCLUDING A MOBILE APPLICATION FOR EARLIER RA REFERRAL; POTENTIAL TO REDUCE CHRONIC DISEASE BURDEN

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Background: Rheumatoid arthritis (RA) is a chronic, debilitative autoimmune disease. Patients who are treated with disease modifying therapy within 6-12 weeks of symptom onset have better outcomes which leads to a reduced economic burden of disease.[1] Technology that enables near-patient blood testing coupled with digital health applications may increase the proportion of patients treated within this window.
Objectives: This study aimed to assess the perceived unmet need for early treatment amongst clinicians and patients as well as their perceptions of a near-patient blood test and digital health mobile application.
Methods: 74 participants, approximately half from each of Canada (n=18) and the US (n=20) participated in a combination of in-depth interviews and surveys for 40-50 minutes. 38 of the 74 subjects, consisted of 16 rheumatologists, 14 primary care physicians (PCPs) and 8 RA patients. To supplement the patient study-sample, 36 additional patients completed an online survey of quantitative and open-ended questions focused on diagnosis and perspectives of a described near-patient blood test and mobile application. Rheumatologists who were in full-time practice and PCPs who see at least 15 RA patients a month were included. Patients were between 18 and 60 years old, had an RA diagnosis and experience using apps for health management.
Results: Almost all Rheumatologists and PCPs indicated that the time between symptom onset and treatment initiation (currently 6-18 months) could be improved and agreed that difficulty diagnosing is still one of the biggest unmet needs. Referrals to a Rheumatologist range from 6 weeks to 3 months. Patients indicated that it took 8 months to 2 years before treatment initiation. Most Rheumatologists said the longest delay is due to inconclusive PCP clinical exams and blood work, leading to repeated visits before patients are referred. Most clinicians and patients welcomed new tools with 33% of patients willing to pay for the near-patient blood test and mobile application. Clinicians had few concerns about a near-patient blood test and indicated that it should be available in the clinic, not the pharmacy. Patients reported the appeal of an easy to use near-

patient blood test that could have meant an earlier diagnosis over a traditional laboratory blood test.
Conclusion: RA is difficult for PCPs to identify for early referral and treatment within 6-12 weeks of symptom onset. The clinicians and patients we surveyed reported positive perspectives regarding near-patient blood tests and mobile applications and welcome their use to assist with earlier referral and treatment. With the emergence of innovative near-patient technologies, opportunities exist to intervene earlier and potentially reduce the social and economic burden of chronic diseases.
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REFERENCES

[1] Nell VP, Machold KP, Eberl G, et al. Benefit of very early referral and very early therapy with disease-modifying anti-rheumatic drugs in patients with early rheumatoid arthritis. Rheumatology (Oxford)2004;43:906–14.10.1093/rheumatology/keh199

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SAT0561 DIAGNOSTIC ACCURACY OF GOUT IN ELECTRONIC HEALTH RECORDS AND THE ROLE OF RHEUMATOLOGY ELECTRONIC CONSULTS

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Background: Gout is the most prevalent inflammatory arthritis globally. Despite treatment advances, it still has a significant effect on quality of life and healthcare costs. There have been inconsistent studies on administrative coding as an accurate marker of true diagnosis. Although gout can be solely managed by primary care physicians (PCPs), complex cases often require rheumatology consultation. The wait time for an initial rheumatology clinic visit ranges from 38 days to 47 weeks. However, electronic consults (e-consults) allow for swift two-way communication between PCPs and rheumatologists (pre-consult exchange) to facilitate coordination of care among providers.
Objectives: To determine the accuracy of gout diagnosis based on ICD 9 and 10 coding, and the differences in gout outcomes based on PCP management, e-consult or rheumatology clinic visits at two Veterans Affairs Medical Centers.
Methods: A retrospective cohort study was created from 2009-2014 including 101 e-consult patients and a control group of 176 patients. In the e-consult group, 78 patients were ICD 9 or 10 coded for gout; in the control group, 116 were ICD 9 or 10 coded for gout. A blinded abstractor determined the accuracy of gout coding based on chart review and EULAR criteria.
A second random sample of 183 gout patients from 2009-2014 was identified and stratified to 3 modes of management: PCP only (48), e-consult (68), and rheumatology clinic visit (67). Data was reviewed for 24 months following initial gout diagnosis or e-consult. Management was evaluated based on frequency of flares and related ED visits, creatinine clearance, and serum uric acid levels (sUA).
Results: The sensitivity and specificity of ICD coding for accurate gout diagnosis was 94% and 79% in the control (PPV 88%, NPV 90%). For e-consult patients, the sensitivity and specificity was 100% and 70% (PPV 87%, NPV 100%). E-consult patients were more accurately diagnosed with gout by PCPs than in the control group (p=0.03).
83% of e-consults were resolved electronically and 17% were converted to rheumatology clinic visits. The mean wait time for e-consult recommendations was 1.8 days. The mean clinic visit wait after pre-consult exchange was 22.9 days compared to an average of 43.1 days for direct rheumatology clinic consults. Both e-consult and rheumatology clinic patients had more gout flares and related ED visits at diagnosis compared to PCP care; however, at 12 months, both groups had significantly fewer gout-related ED visits, decreased sUA, and improved creatinine clearance (p<0.05).
Conclusion: VA databases are an accurate source of gout patients based on ICD coding. When viewing e-consults, rheumatologists can rely on accurate PCP gout diagnoses, confidently answer clinical questions, and triage more efficiently. E-consult serves as an effective alternative in managing gout with shorter wait times for recommendations and appointments while still reimbursing physicians at a reasonable rate. Therefore, complex gout management can be enhanced by e-consults to improve clinical outcomes, decrease gaps in care and optimize healthcare resources.

REFERENCES

[1] Zhang W, et al. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2006;65(10):1312-24.
[2] Widdifield J, et al. Wait times to rheumatology care for patients with rheumatic diseases: a data linkage study of primary care electronic medical records and administrative data. CMAJ Open. 2016;4(2):E205-12

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SAT0562 BURDEN OF RHEUMATIC DISEASE AMONG KOREAN WOMEN IN CHILDBEARING YEARS BASED ON THE NATIONAL HEALTH INSURANCE SERVICE

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Background: Many rheumatic diseases (RDs) predominantly affect women in their reproductive years, and have a significant impact on childbearing, but its burden remains incompletely understood.
Objectives: The study aimed to identify the prevalence and incidence of RDs among Korean women in childbearing years, and the effect of the diseases on prevalence of comorbidities, medication use, and pregnancy rate.
Methods: From National Health Insurance Service data during 2009-2016, we identified 9,217,139 women aged between 20-44 years. Among these women, we estimated the prevalence and incidence of RDs including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and ankylosing spondylitis (AS). Prevalence of chronic diseases such as cancer (Ca), hypertension (HT), hyperlipidemia (HLD), and diabetes mellitus (DM) was compared in women with or without RDs. The prescription prevalence of medications including NSAIDs and corticosteroids were compared according to the presence of RDs. We also investigated pregnancy rate in women with rheumatic or chronic diseases, and control subjects without rheumatic or chronic diseases.
Results: Overall prevalence of RDs was 56.3 per 100,000 20-44 aged females, and overall incidence was 7.68 cases per 100,000 person-years. Women with RDs had increased risk for overall chronic diseases (OR 3.0), and for Ca (OR 1.3), HT (OR 1.4), HLD (OR 2.9), and DM (OR 2.8), respectively (p<0.0001). The prescription of NSAIDs and steroids was significantly more frequent in women with RDs than those without (81.62% vs 21.79% in NSAIDs, 77.83% vs 4.28% in steroids, p<0.0001). Pregnancy rate was significantly lower in women with RDs compared with the controls (15.92% vs 19.30%, p<0.001). Among women with RDs, women with RA were less likely to become pregnant (OR 0.80, p<0.0001), whereas women with SLE and AS showed no significant difference in pregnancy rate compared with the normal controls.
Conclusion: RDs are a significant burden for women in childbearing years causing increased co-morbidities and medication use and causing reduced pregnancy rate.

REFERENCES

[1] Sung YK, Cho SK, Choi CB, Bae SC. Prevalence and incidence of rheumatoid arthritis in South Korea.
Rheumatol Int 2013;33:1525-32.
[2] Sammaritano LR. Pregnancy in rheumatic disease patients. J Clin Rheumatol 2013;19:259-66.
[3] Castaneda S, Nurmohamed MT, Gonzalez-Gay MA. Cardiovascular disease in inflammatory rheumatic diseases. Best Pract Res Clin Rheumatol 2016;30:851-69.

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SAT0563 **WHAT CAN WE LEARN FROM NEW MUSCULOSKELETAL EXTENDED SCOPE PRACTITIONER REFERRALS TO RHEUMATOLOGY SECONDARY CARE? A PROSPECTIVE SERVICE EVALUATION**

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Background: Common non-inflammatory musculoskeletal (MSK) problems are increasingly referred in the UK from primary care to extended scope practitioners (ESPs) that are not doctors. A new local ESP service has been established. Primary care is directed to refer inflammatory problems to secondary care, and non-inflammatory cases to the ESP service, with onward referral to rheumatology if required. There is limited data to show how these services perform, and where they can be improved.
Objectives: The objective is to understand and learn lessons of the patient journey through ESP services, with a view to supporting service design, evaluation, and training needs analysis for ESP and primary care practitioners.
Methods: This is a prospective service evaluation, reviewing patients referred by ESPs to our service seen by a single consultant, over a 42-month period (5/15 –10/18). Patient data was collected prospectively, including age, gender, key clinic-pathologic ESP findings, ESP suspected diagnosis, and the secondary care diagnosis. The ESP suspected diagnosis was recorded in 14 categories, derived from a previous published service evaluation. Our Electronic Patient Record (EPR) was used to check the source data and complete any missing data, and record any secondary care follow up. We excluded any ESP referrals that did not attend, or where missing data could not be found in the EPR.
Results: ESP referrals made up 47/1390 (4%) of new patients seen. The average age was 54 (SD 16.9), 38 (81%) were female and 21 (45%) had a history of depression. The main referral concern was 'small joint inflammatory arthritis' (20/47, 42%), with 2/20 (10%) confirmed diagnoses requiring follow up (rheumatoid and undifferentiated inflammatory arthritis). The main secondary care diagnosis was osteoarthritis (10/47, 21%), followed by fibromyalgia (9/47, 19%). The majority of ESP referrals ultimately had non-inflammatory problems with only 7/47 (15%) referrals receiving a secondary care diagnosis that was an inflammatory condition. ESPs were most likely to suspect and correctly identify crystal arthritis, correctly suspecting 2/2 cases (100%). They were incorrect for all referrals where they suspected large joint inflammation arthritis (4), polymyalgia rheumatica (1), axial spondyloarthropathy (4) and connective tissue disease (1). We did find unusual non-inflammatory conditions e.g. a glomus tumour (1). This data was used to design a bespoke ESP training session to 20 ESPs, delivered in December 2018. This included raw data, pitfalls in ESP assessments, chronic pain assessment, and investigations, returning universally positive evaluations.
Conclusion: This service evaluation provides empirical data to support our understanding of the primary care- ESP- rheumatology interface. We have identified areas for training and service improvements, and implemented new training. Our data support the current inflammatory referral pathways (only 1/47 ESP referrals for new rheumatoid arthritis). This data may help rheumatologists to triage ESP referrals, and data from future research in this area could be used to develop quality metrics for primary care, ESP, and rheumatology practitioners.
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SAT0564 **EFFICACY OF ETANERCEPT OVER A PERIOD OF 12 MONTHS IN THE ROUTINE TREATMENT OF PATIENTS WITH RA, AXSPA, PSA OR PSO: FINAL RESULTS OF A GERMAN NON-INTERVENTIONAL, PROSPECTIVE, MULTI-CENTER STUDY (ADEQUATE)**

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Background: For patients with chronic autoimmune diseases such as rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), psoriatic arthritis (PsA) or plaque psoriasis (Pso), the treat-to-target concept requires attaining remission or at least low disease activity and is defined by the corresponding guidelines. The achievement of these targets affects radiological progression and functional measures. If treat-to-target has not been achieved after 3 months, current treatment could either be continued with an expected increased response over time or could be switched to another treatment option.
Objectives: The primary goal of this non-interventional study was to determine the proportion of patients achieving the treat-to-target criteria with Etanercept at month 3, 6 and 12 in a real-life setting. Secondly, the proportion of patients achieving the treat-to-target criteria at month 6, even if it has not yet been fully attained until month 3, was determined.
Methods: Into this German non-interventional, prospective, multi-center cohort study, adult patients with confirmed diagnosis of RA, axSpA, PsA or Pso without prior Etanercept treatment were included. Planned recruitment number was 2,100 patients: 1,200 RA patients, and 300 patients each with axSpA, PsA or Pso. Criteria for remission and minimal clinical efficacy were defined according to recommendations of the respective treatment guidelines and the study protocol. The analyses were based on the number of patients completing the respective study period (3, 6 and 12 months).
Results: Overall, 1,465 patients were included (treated set), i.e. 901 females (61.5%) and 564 males (38.5%); patients' mean ± SD age was 54.9 ± 14.5 years. Patients' median disease duration ranged across the rheumatic indications from 3.4 years in PsA to 5.5 years in RA, and was markedly longer in Pso (median: 15.3 years). At week 12, the proportion of patients reached remission was 24.4% in RA, 19.0% in axSpA, 38.3% in PsA and 7.1% in Pso. Further increases were seen up to week 24 in RA (30.6%), PsA (50.7%) and Pso (18.6%), while axSpA rates remained similar (18.4%). In all indications, these proportions continued to increase from week 24 up to week 52 (RA: 37.3%, axSpA: 23.4%, PsA: 54.0%, Pso: 31.8%). Considering low disease activity as target, the proportion of patients achieving that goal at week 12, were 39.4% patients for RA, 38.6% for axSpA, 50.0% for PsA and 34.3% for Pso, while further increases were noted up to week 24 in all indications (RA: 45.2%, axSpA: 45.4%, PsA: 60.3%, Pso: 50.8%). During the observational period, a total of 702 patients (47.9%) experienced at least one treatment emergent Adverse Event (TEAE). However, serious drug-related AEs were only reported in 41 patients (2.8%).
Conclusion: A considerable proportion of patients attained the target of remission or low disease activity at week 12 under daily routine practice conditions, proving a reliable positive therapeutic effect of Etanercept in a real life setting. These percentages further increased up to week 24 except for axSpA patients. With regard to the safety profile of Etanercept, the incidence numbers and types of AEs were in an expected range and in-line with documented safety profile according to the SmPC.
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SAT0565 COST EVOLUTION OF BIOLOGICAL AGENTS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN A TERTIARY HOSPITAL INFLUENTIAL FACTORS IN PRICE

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Background: The availability of biological therapy has changed the approach to treating rheumatoid arthritis. Spending on biological agents has risen due to the drugs' high cost and the increased prevalence of rheumatoid arthritis.

Objectives: To evaluate the annual cost-per-patient and cost for each biological drug for in patients with rheumatoid arthritis from 2009 to 2017, and to calculate factors that affect at treatment cost, such as optimized therapies by monitoring drug serum levels, the use of biosimilars-TNF inhibitors, and discounts or negotiated rebates in biologicals acquired by pharmacy department.

Methods: Retrospective, observational study in a Spanish tertiary hospital. Main outcome: Annual cost-per-patient and per drug. Influential factors that affected the costs and demographic parameters and disease activity were also analyzed.

Results: A total of 320, 270, and 389 patients were treated in 2009, 2013, and 2017, respectively. Annual cost-per-patient decreased: € 10,798 in 2009, € 7491 in 2013 to € 7116 in 2017. The introduction of new drugs drives economic competition leading to *total savings per drug*, with discounts reaching 24.6%, 15.5%, 11.5%, 17.8%, 17.9% and 21.1% for original infliximab, etanercept, adalimumab, certolizumab, golimumab and tocilizumab respectively, while rebates for biosimilar-infliximab reached 43.1% in 2017. Patients with optimized therapies reached 35.2% in 2017, which lead in cost savings of € 1,288,535, in addition to savings from official discounts and rebates of € 458,535 and savings from optimized therapies of € 830,000 in 2017.

Percentage of patients with optimized regimes for the study period increased from 4.6% in 2009, 51.5% in 2013 to 35.2% in 2017. Disease activity was lower annualy in the patient group with the optimized regimes *versus* the group without optimized regimes (p<0,001). Biological drugs more optimized were infliximab, adalimumab etanercept, and tocilizumab reaching 57.1%, 55.3%, 39.8%, and 32.0%, patients respectively, in 2017.

Conclusion: The cost of biological treatments declined after official discounts, negotiated rebates, and optimized therapies, leading to a significant decrease in the annual cost per patient. The greatest contribution to economic savings in biological therapy according to our study was biological therapy optimization.

REFERENCES

[1] González-Fernández M, Villamañán E, Jiménez-Nácher I, Moreno F, Plasencia C, Gaya F, et al. Cost evolution of biological agents for the treatment of spondyloarthritis in a tertiary hospital: influential factors in price. Int Jour Clin Phar 2018; 40:1528-1538. DOI:10.1007/s11096-018-0703-z

[2] Plasencia C, Pascual-Salcedo D, García-Carazo S, Lojo L, Nuño L, Villalba A, et al. The immunogenicity the first anti-TNF therapy determines the outcome of switching to a second anti-TNF therapy in spondyloarthritis patients. Arthritis Res Ther. 2013; 15(4):R79.

3.. Pascual-Salcedo D, Plasencia C, Jurado T, Valle LG del, Sabina P, Diego C, et al. Dose-Tapering Of TNF Inhibitors in Daily Rheumatology Practice Enables the Maintenance of Clinical Efficacy While Improving Cost-Effectiveness. J Pharmacovigil 2015;3(4).

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SAT0566 LIVING WITH CHRONIC INFLAMMATORY AUTOIMMUNE DISEASE IN BRAZIL: THE PATIENT'S PERSPECTIVE

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Background: The patient's journey is a complex phenomenon. It includes all the stages, perceptions, and experiences that the patient goes through since the identification of the first symptoms of a given disease. Therefore, it is crucial to understand this journey as it may help to optimize the patient's quality of life, especially for those who live with chronic inflammatory autoimmune diseases such as Rheumatoid Arthritis (RA), Psoriatic Arthritis (APs) and Axial Spondyloarthritis (axSpA).

Objectives: The aim of this study was to understand the journey of people living with rheumatic disease in Brazil and its impact on several different areas of the patient's life, including family planning, use of medications, and access to health care services and professionals.

Methods: The data were extracted from an exploratory, descriptive and quantitative research, with primary data collection. It was performed between May 09, 2018 and August 01, 2018. The survey had 58 questions and it was available online for public participation through the GRUPARJ PETRÓPOLIS website.

Results: The survey was accessed by 1223 participants. The proportion of patients with RA, PsA, and axSpA were 70.97%, 17.42% and 11.61%, respectively. Most participants were female (87.64%) and 59.21% of all attendees were between 18 and 54 years old. Only 38.72% of the participants declared that they were working, while 32.34% admitted to being retired or on sick leave. About 60% of the attendees have taken more than a year to visit a rheumatologist and 48.08% received their diagnose after at least one year of the first symptoms. Nevertheless, once they started to visit a rheumatologist, more than two thirds do not have difficulty to schedule a visit with this specialist. In addition, participants are satisfied with the health care they receive and feel well informed about their treatment. At least half of the attendees used synthetic disease-modifying antirheumatic drugs to control their disease, 41.73% also used corticoids and 33.87% are on biologic drugs. Nevertheless, 37.24% and 17.35% of the participants classified their disease activity as moderate or high, respectively, thus not achieving the target of treatment from their own perspective. This may affect the patient´s quality of life as reflected in the percentage of respondents suffering from emotional problems (46.62%) as well as in the proportion of patients having some or many difficulties to do daily activities. This scenario is impacted by the fact that more than half of the participants do not have access to another health care provider other than the rheumatologist to help manage their condition. This survey has also delved on the topic of family planning. Whit regards family planning, 50% of the women indicated an unplanned pregnancy (n=142). Moreover, 48.59% (n=69) of these women had never discussed with their rheumatologist about the desire to be pregnant. Furthermore only 13.38% (n=19) affirmed that their treatment during pregnancy was discussed between the rheumatologist and the gynecologist/obstetrician.

Conclusion: Although most of the participants in this survey indicated a good level of satisfaction with the health care they receive, data also indicate opportunities for improving the patient's quality of life. Patients are satisfied with the access to the rheumatologist, drug treatment as well as the information they receive on physician's appointments. This work illustrates the complexity of these chronic inflammatory autoimmune disease and the importance of multidisciplinary treatment to manage it to impact positively the patient journey.

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SAT0567 SIX MONTHS OF RESULTS OF A MULTIDISCIPLINARY FRACTURE LIAISON PREVENTION UNIT IN THE SOUTH OF SPAIN

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Background: As part of the IOF recommendations and the "Capture the fracture" program a Multidisciplinary and focussed on Primary Medicine Fracture Liaison Prevention Unit (FLS) was created in May of 2018 in the Hospital Universitario Virgen Macarena, in Seville, Spain. In previous reprts, the rate of osteoporosis treatment prescription after the fragility fracture was as low as 20%, with a poor communication between the medical specialties involved in the attention of this patients.
Objectives: To improve the medical attention and treatment of patients with a FF. To create a multidisciplinary FLS with the collaboration of Primary Care Medicine, Internal Medicine, traumatology, Emergency Room, Rheumatology, Rehabilitation Service and the Medicine Department of the Seville University.
Design: A prospective, observational study in the setting of usual clinical practice and with approval of the local ethics committee.
The Multidisciplinary FLS started to work at may, 2018 connecting primary care with medical specialties. The FLS has 3 weekly consultations (11 first visits, 4 second visits and email consultation, each day) attended by 2 internal medicine physicians, one Rheumatologist and one nurse. All the medical specialties involved in the attention of patients with FF can refer patients and the inclusion criteria is the history of a FF in the past 18 months. In a single medical visit, the doctor and the nurse make a clinical history, assesses the risk of FF according to FRAX, the risk of falls (J.H. Downton scale), they evaluate malnutrition (Mini Nutritional Assessment Elderly) and sarcopenia (hands dynamometry and Short Physical Performance Battery). Complete blood count and blood and urine biochemistry in order to evaluate secondary causes of osteoporosis and vertebrae radiographs are done. A treatment plan agreed and discussed with the patient is started. The plan advice on diet and exercises, drugs, and a written report and medical prescription. And a phone follow-up is programmed. The data are entered and stored in a database (OpenClinica) in real time.
Results: From May to October of 2018, 170 patients have been included; 135 (89%) women. The mean (standard deviation) age was 73 ± 11.8 years old; 25% of them with ages between 83 to 94 years. The patients were referred from Perioperative Internal Medicine (46%), Traumatology and orthopedic surgery (37%), Rheumatology (6%), Primary Medicine (5%) and others medical areas (6%). The anatomical sites of the FF were hip (58%), vertebrae (22%), distal radius (13%), humerus (4%) and other sites (7%). The prescribed treatment was alendronate (66%), denosumab (18%), teriparatide (10%), risedronate acid (4%) and calcium and/or vitamin D supplementation in 98% of the patients. The compliance was measured by phone call in 42 patients that completed six months after the first evaluation, and it was good in 100%.
Conclusion: The multidisciplinary FLS activity increased the rate of evaluation of risk and prescription of treatment at 100% with rates of compliance at six months of 100%. The FLS allows the creation of fluid reference circuits and improves the patient care.

REFERENCES

[1] Walters S, et al. Clinical Interventions in Aging 2017:12 117–127

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SAT0568 THE IMPACT OF ARTHRITIS ON UTILIZATION OF MENTAL HEALTH TREATMENT FOR COMORBID MENTAL DISORDERS: FINDINGS FROM A NATIONALLY REPRESENTATIVE MENTAL HEALTH SURVEY

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Background: Individuals with arthritis experience an increased prevalence and incidence of mood and anxiety disorders, however, it is unclear if they are receiving adequate treatment for their comorbid mental disorders.
Objectives: To conduct a population-based evaluation of the association between arthritis and utilization of mental health treatments among individuals with comorbid mental disorders.
Methods: We used nationally representative data from the 2012 Canadian Community Health Survey – Mental Health (CCHS-MH) to draw a sample of 1,810 participants with depression, anxiety, or bipolar disorder. Depression, anxiety, and bipolar disorder (bipolar I, bipolar II, or hypomania) were defined by a series of screening questions in the CCHS-MH derived from the World Health Organization version of the Composite International Diagnostic Interview. The explanatory variable was self-reported doctor-diagnosed arthritis and included all rheumatic diseases. The outcome of interest was utilization of mental health treatments in the previous 12 months, including: 1) medications; 2) professional services (e.g. physician, psychiatrist, nurse); or 3) non-professional services (e.g. family, self-help group, internet). Multivariable binomial logistic regression was used to evaluate whether utilization of mental health treatment differs among those with and without arthritis, adjusting for the confounding effects of age, sex, race/ethnicity, and household income.
Results: A total of 447 (20.5%) participants from our study sample reported having arthritis (66.9% female). Utilization of mental health treatments in the previous 12 months was reported by 82.4% individuals with arthritis and 79.5% without arthritis. The most common treatment utilized by those with arthritis was professional services (66.5%), followed by medication (61.8%) and non-professional services (51.5%). Participants without arthritis most often received mental health treatment in the form of non-professional services (67.3%), followed by professional services (58.1%) and medication (45.6%). The point estimate of the adjusted analysis suggested a positive association between arthritis and utilization of at least one type mental health treatment (odds ratio [OR] 1.41, 95% confidence interval [CI] 0.85, 2.34), though not statistically significant. In the sub-analysis, the ORs for the association between arthritis and specific mental health treatments were increased for medications (OR 1.30, 95% CI 0.86, 1.99) and for professional services (OR 1.27, 95% CI 0.83, 1.93), but decreased for non-professional services (OR 0.81, 95% CI 0.52, 1.27).
Conclusion: These nationally representative data show that a high proportion of individuals with arthritis seek treatment for their comorbid mental disorders. Findings of this study may also suggest a positive association between having arthritis and seeking care for comorbid mental disorders, which may be explained by an already established connection with the health care system to manage arthritis. Opportunities to improve mental health treatment among those with arthritis include optimizing access to non-professional services.
Disclosure of Interests: None declared
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SAT0569 CHANGING TRENDS AND PRESCRIBING PATTERNS IN OPIOID-TREATED PRIMARY CARE PATIENTS WITH NON-CANCER PAIN

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Background: The opioid epidemic in the U.S. has led to similar concerns about prescribed opioids in countries within Europe. In new users, the rate of escalation to more potent opioids is likely to contribute to long-term prescriptions, which in turn may be associated with opioid dependency, addiction and overdose. The scale of such escalation however is unclear in the U.K for non-cancer pain.

Objectives: We sought to: (i) describe trends of prescribed opioids for non-cancer pain in the UK primary care setting over a 10-year period (ii) assess the sequential transition of opioid strength from index date over a 2-year period.
Methods: We conducted a retrospective observational study over a 10-year period from 1/1/2006 to 31/12/2015 using the Clinical Practice Research Datalink (CPRD). CPRD collects de-identified patient data from a network of GP practices across the UK. New users of opioids, 18 years or over, without cancer in the 2 years prior to index date were included. The number of prescriptions for each drug were calculated by each calendar year accounting for the number of eligible patients registered in CPRD for that year. Sunburst plots were created to evaluate the sequential transition of opioids over time. A 4-state hidden Markov model was used to estimate the transition probability for individuals escalating to more potent opioids over a 2 year period. States were defined as (i) no drug (ii) weak opioid (codeine, dihydrocodeine) (iii) moderate opioid (tramadol) (iii) strong opioid (all others in CPRD). Methadone prescriptions were excluded for the purposes of this analysis.
Results: 1,026,955 opioid users were included: mean age (SD) was 55 (18) years; 58% being female. New users of opioids were most commonly prescribed codeine (n=723,102; 70.8%), followed by dihydrocodeine (n=179,831; 17.6%), tramadol (n=93,338, 9.1%) with n=24,808 (2.4%) strong opioid prescriptions. The rate of prescribing strong opioids/10,000 population increased 12 fold from 2006-2013, followed by a gradual decline till 2015 (Figure 1). This trend was most marked with certain opioids: morphine, oxycodone, buprenorphine and fentanyl (28.5 prescriptions per 10,000 population to a peak of 353.0 prescriptions per 10,000 population in 2013 and 303.1 prescriptions per 10,000 population in 2015). Using sunburst plots, of the new users prescribed weak opioids as their first prescription at index date, 5.5% transitioned to moderate opioids, 4.1% to strong opioids over 2 years (Figure 2). Transition probability of moving from weak to strong opioid at a given time point over 2 years was 0.001, whilst staying on a strong opioid (if first prescription at index date) was 0.97.

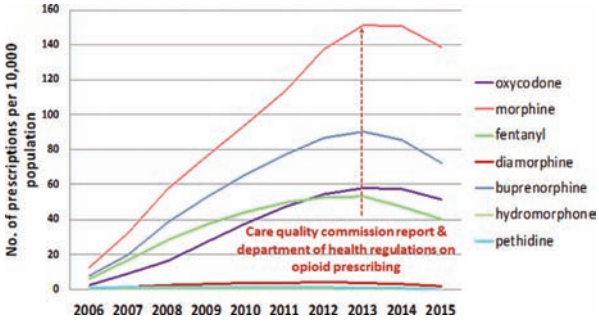


Figure 1. Strong opioid prescribing trends over 10 years

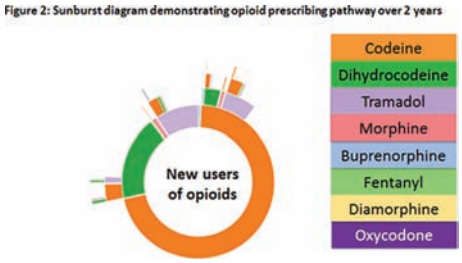


Figure 2

Conclusion: Strong opioid prescribing increased till 2013-14 gradually decreasing following UK initiatives to improve monitoring and use of controlled drugs. Although less potent codeine prescriptions made up the majority of first prescriptions, the transition probability of staying on a strong opioid at 2 years remained high if prescribed first as a new user.
Disclosure of Interests: None declared
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SAT0570

GAPS IN PATIENT SAFETY PERFORMANCE IN PATIENTS WITH IMMUNOSUPPRESSIVE THERAPY: RESULTS OF SCREENING FOR INFECTIONS AND VACCINATION STATUS IN A LARGE REAL-LIFE COHORT

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Background: Patients with chronic inflammatory rheumatic diseases (CIRD) are known to have an increased risk of infections compared to the general population. Therefore, prevention of infections by vaccination strategies is mandatory.
Objectives: To evaluate the vaccination status in patients with CIRD.
Methods: Consecutive patients with CIRD were prospectively recruited. Disease characteristics, vaccination status and screening for latent tuberculosis infection (LTBI) and hepatitis B (hepB) were analyzed. Antibodies against measles and hepB were measured. The vaccination status was assessed by a predefined vaccination score (range 0-26): 3 points for a complete vaccination, 2 points for a basic immunization and 1 point for an incomplete vaccination status for tetanus, diphtheria, poliomyelitis or pertussis. For hepB, pneumococcal, influenza, meningococcal, measles, rubella and varicella 2 points were given for a complete vaccination status and 1 point for an incomplete vaccination status. Finally, patients were categorized into 3 immunization states: low (0-6), moderate (7-13), good (14-20) and high (21-26).
Results: A total of 975 patients with CIRD were included (table 1). All patients on bDMARDs (n=499) were screened for LTBI, and 469 also for hepB (94%). Only 16 patients with LTBI received prophylaxis with isoniazid (3.2%) and only 16 patients with hepatitis B received prophylaxis with lamivudine (3.4%). The mean anti-HBs titer was 251.1±258.1 IU/l. Protective measles specific IgG-antibodies were found in 901 patients (92.4%). No more than 30% of patients had undergone pneumococcal vaccination and less than 20% were protected against hepB and influenza. Although 629 patients had been educated about vaccination strategies (64.5%), only 540 patients could show a vaccination certificate (55.4%). The mean vaccination score was 12.8±4.9 with 5.3% of patients categorized having a low, 24.3% a moderate, 26.1% a good and 1.8% a high score.
Conclusion: Screening for tuberculosis and hepatitis is successfully implemented in clinical routine in Germany but many patients are not sufficiently vaccinated against pneumococci, hepatitis B, influenza and measles. Our vaccination strategy is based on cooperation with GPs. However, this strategy did not seem to work. The overall rate of successful vaccination was low to moderate although patients received professional information about vaccine strategies.
All values are given in mean (SD) otherwise indicated
*Physical function was assessed with HQA except in axSpA patients in whom the BASFI was used.

Table 1. Patients characteristics of our cohort

	RA (n=424)	axSpA (n=145)	PsA (n=132)	SLE (n=41)	Other diseases (n=233)
Age, years	60,7 (13,4)	43,7 (12,4)	51,3 (12,7)	48,4 (17,6)	56,1 (16,9)
Gender, male, n (%)	137 (32,3)	95 (65,5)	55 (41,7)	4 (9,8)	64 (27,5)
Current use of bDMARDs, n (%)	163 (38,4)	103 (71,0)	76 (57,6)	9 (22,0)	59 (25,3)
Physical function*	1,30 (0,76)	4,0 (2,55)	1,28 (0,68)	1,12 (0,67)	1,03 (0,69)
CRP (mg/dl), median (IQR)	0,3 (0,1-0,7)	0,2 (0,1-0,6)	0,2 (0,1-0,7)	0,2 (0,0-0,4)	0,3 (0,1-0,6)
Vaccination card available	230 (54,2)	76 (52,4)	66 (50,0)	28 (68,3)	140 (60,1)
Received information about vaccination	273 (64,4)	101 (69,7)	81 (61,4)	28 (68,3)	146 (62,7)
Complete pneumococcal vaccination status	129 (30,4)	33 (22,8)	26 (19,7)	12 (29,3)	66 (28,3)
Complete influenza vaccination status	85 (20,0)	(11,7)	20 (15,2)	8 (19,5)	50 (21,5)
Complete hepatitis B vaccination status	36 (8,5)	26 (17,9)	13 (9,8)	10 (24,4)	37 (15,9)

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SAT0571 IDENTIFYING DETERMINANTS OF PRESENTEEISM IN WORKERS WITH INFLAMMATORY ARTHRITIS

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Background: Work disability (WD) and presenteeism (decreased at-work productivity) are often caused by arthritis, leading to major impact on individuals' quality of life and cost to society.
Objectives: Our study objective was to identify the determinants of presenteeism in workers with inflammatory arthritis.
Methods: Baseline data from the randomized controlled trial of an employment intervention, the Making-it-Work^{TM}program, were used. Participants were recruited from British Columbia, Alberta and Ontario. Inclusion criteria: diagnosis of inflammatory arthritis, currently employed, age 18-59, and having concerns about arthritis affecting ability to work. The primary outcome, presenteism, was assessed using the% impaired while at work subscale of the Work Productivity and Activity Impairment scale for Specific Health Problem (WPAI-SHP). First, the association between potential explanatory variables and WPAI was assessed in bivariate analyses. Variables evaluated included: 1) *sociodemographic variables:* age, gender, ethnicity, marital status, education, children under age 19; 2) *disease variables*: IA diagnosis, disease duration, number of limiting comorbidities, global assessment of disease activity (VAS), joint pain (VAS), Disease activity [Rheumatoid Arthritis Disease Activity Index (RADAI)], physical function (HAQ II), Fatigue [VAS, Global Fatigue Index from the Multidimensional Assesment of Fatigue (MAF)], Sleep quality [Insomnia Severity Index (ISI), Depression (Patient Health Questionnaire – PHQ-9); 3) *work variables*: physical demand, job autonomy, difficulty commuting to/from work, job spillover, job strain, psycho-social work characteristics [Job Content Questionnaire (JCQ) decision latitude, physical and psychological job demands, social support at work], self-employment, family support of decision to work, importance of working. Variables correlated with WPAI-SHP at $p \leq 0.20$ were selected for inclusion in the multivariable linear regression analysis, using stepwise selection with alpha of 0.15.
Results: The sample included 565 participants [49% with RA, 17% PsA, 14% SLE, 20% AS] with median (IQR) arthritis duration of 7(3-15) years; mean (SD) age 45.6 (10) years; 43% were 50 years or older; 78% were females; 76% had completed post secondary education; 17% were self-employed. Multivariable linear regression analyses revealed that age < 30 (vs.age 30-49, p=0.067; vs. age ≥ 50, p=0.266), having more fatigue (GFI-MAF) (p<0.001), job strain (p=0.011), job spill over (p=0.002), disease activity (RADAI) (p<0.001), poor family support for working (p=0.049), poor physical function (HAQ II) (p=0.077) and commuting difficulty (p=0.081) were associated with greater impairment in work productivity.
Conclusion: This study identified important sociodemographic, disease and work-related factors associated with reduced productivity at work in people with inflammatotry arthritis. These results provide useful information to health professionals counselling patients on dealing with employment issues.

Table: Multivariable linear regression modeling determinants of presenteeism

VARIABLE	ESTIMATE	P-VALUE	95%CI
Fatigue (MAF-GFI)	0.74	<0.001	(0.54, 0.95)
Job Spillover	3.79	0.002	(1.46, 6.13)
RADAI	2.06	<0.001	(0.96, 3.17)
Job Strain	2.91	0.011	(0.67, 5.15)
Commuting Difficulty	1.12	0.081	(-0.14, 2.38)
Family support (higher = worse)	1.29	0.049	(0.01, 2.57)
Physical function (HAQII) (higher =worse)	3.91	0.077	(-0.42, 8.23)
Age 30-49	-4.78	0.067	(-9.89, 0.34)
Age≥ 50	-2.96	0.266	(-8.19, 2.26)
Age<30	0.00	.	.
Model R-square: 0.516, F-statistic: 61.14			

REFERENCES

[1] Carruthers, **et al**.
[2] "Employment and arthritis: making it work" a randomized controlled trial evaluating an online program to help people with inflammatory arthritis maintain employment (study protocol). *BMC Medical Informatics and Decision Making* 2014 **14**:59

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SAT0572 ANTINUCLEAR ANTIBODIES IN PRIMARY CARE SETTING: IS IT WORTH IT?

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Background: Antinuclear antibodies (ANA) are the most frequently used screening tests for connective tissue diseases. However, their diagnostic value depends on the pre-test probability of such conditions.
Objectives: To evaluate the usefulness, clinical correlates and associated direct costs of ANA testing in the primary care setting in an Early Arthritis Clinic (EAC) referral cohort.
Methods: A retrospective study of consecutive patients referred to the EAC between 2011 and 2018 was conducted. Referral is based on the fulfillment of specific criteria: presence of arthritis or clinically suspected arthralgia beginning in the previous 12 months, plus suggestive laboratorial abnormalities (rheumatoid factor, C-reactive protein or erythrocyte sedimentation rate). Many general practitioners also performed ANA testing (ANA-GP) and all patients underwent ANA testing, per protocol, in EAC (ANA-EAC). All patients having these 2 separated ANA results were included in the analysis. ANA-EAC titters and pattern were assessed by indirect immunofluorescence (Hep2, positive=titter≥1:160). Direct associated costs of ANA-GP were calculated, based on the mean charge of 3 different local labs. Positive (PVV) and negative predictive values (NPV) of ANA-GP for the diagnosis of inflammatory rheumatic disease, ANA-related rheumatic disease (ARD) and for the presence of ANA-EAC were determined.
Results: 207 patients were referred to the EAC Clinic during this period (64.3% female, aged 53.9 ± 18.2 years-old). Fifty eight percent of these patients (n=120) had their ANA previously determined in primary care setting. Of these, only 9.2% of cases (n=11) were positive, this being one of the main reasons for referral. Only 73% percent of positive (n=8) and 24% of negative ANA-GP were confirmed as such in our lab. Of the 8 patients testing positive in both settings, 2 had no rheumatic disease, 2 had an ARD and 4 had another type of inflammatory rheumatic disease.

ANA-GP PPV and NPV were: i) 18.2% and 92.7% (LR 2.44) for ARD,; ii) 63.6% and 27.5% (LR 0.74) for inflammatory rheumatic disease and 72.7% and 23.9% (LR 0.124) for a positive ANA-EAC result. The referral criteria with the highest PPV for the diagnosis of inflammatory rheumatic disease were: positive rheumatoid factor (76.2%), high erythrocyte sedimentation rate (71.6%) and clinical signs of arthritis (70.8%). The direct cost associated with duplicate ANA testing was estimated in 2.160€ .

Conclusion: ANA testing in the primary care setting had a poor predictive value in this cohort, which can be explained by its application in patients with low pretest probabilities for ARD. Although the direct costs may not seem impressive, we speculate the real cost to be much higher since ANA test rarely is requested solo but, instead, along with a lot of other autoantibodies in a "trawl fishing" attempt to diagnosis. ANA evaluations are not recommended for the study of putative arthritis cases in primary care and local campaigns should be promoted in order to improve referral quality avoiding unnecessary, costly and lengthy lab tests as ANA.

Disclosure of Interests: None declared

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SAT0573 HEALTHCARE RESOURCE UTILISATION AMONG PATIENTS DIAGNOSED WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE IN ENGLAND

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Background: Systemic sclerosis-associated interstitial lung disease (SSc-ILD) places a substantial burden on patients and on healthcare services. Despite this, assessments of healthcare resource utilisation and costs incurred during the management of SSc-ILD are limited.

Objectives: To assess healthcare resource utilisation and costs among patients with SSc-ILD compared with SSc overall and patients with SSc and other organ involvement (SSc-OOI).

Methods: This was a population-based cohort study. Routinely collected healthcare data were extracted from medical records (dated 1 January 2005 to 31 March 2016) in the Clinical Practice Research Datalink (CPRD) and the Hospital Episode Statistics (HES) databases. Patients with SSc, with or without ILD and/or OOI, were identified from primary and secondary care records in combination with modified European League Against Rheumatism (EULAR) classification criteria. Patients were included in the OOI sub-cohort if their SSc affected cardiac, gastrointestinal, renal or oral function. Eligible patients were aged at least 18 years at first diagnosis, were diagnosed within the study period, and had at least 12 months of available data in CPRD/HES before and after diagnosis. All-cause healthcare resource utilisation (inpatient stays; A&E attendances; outpatient visits; general practitioner visits) and costs among patients with SSc, SSc-ILD and SSc-OOI were calculated to 2016 GBP. Medication costs were not included. Predictors of total healthcare costs were estimated using a multivariate generalised linear model, with a gamma distribution and log link function to allow for non-normal distributed costs. Comorbid diseases were categorised using the Charlson Comorbidity Index.

Results: Of 675 patients with SSc, 127 (19%) had ILD and 477 (71%) had OOI; a subset of 103 (15%) patients had both ILD and OOI. The remaining 174 patients (26%) had SSc without ILD or OOI. Median (interquartile range) annual healthcare costs per patient were: £2,601 (£962–6,885) in SSc; £3,449 (£1,271–8,717) in SSc-OOI; £5,899 (£2,986–13,905) in SSc-ILD; £6,375 (£3,046–15,041) in SSc-ILD-OOI. Patients with SSc-ILD (with or without OOI) had the highest rates of inpatient stays, outpatient visits, A&E attendances, and general practitioner visits per person-year. Inpatient stays alone accounted for >60% of the total healthcare costs among SSc patients with ILD (median cost >£3,600 per patient per year). Each patient with SSc-ILD had, on average, 10 outpatient visits per year, at a total yearly median cost of >£840. In comparison, patients with SSc-OOI averaged 7 outpatient visits at a total yearly median cost of £615. Characteristics significantly associated with higher yearly healthcare costs among SSc patients were: older age at diagnosis, diagnosis of anaemia, and number of comorbid diseases.

Conclusion: The annual healthcare cost for a patient with SSc-ILD is substantial (£2,986–13,905), with inpatient stays the major cause of costs, and is much higher than for patients with SSc-OOI (without ILD). Healthcare costs are also higher among older SSc patients and those with more comorbidities. These results quantify the economic burden of SSc-ILD in a real-world setting, which will be useful when evaluating the cost-effectiveness of new treatment options for SSc-ILD. There is an unmet need for effective therapies for SSc-ILD.

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Disclosure of Interests: Alicia Gayle Employee of: Employee of Boehringer Ingelheim, Nils Schoof Employee of: Employee of Boehringer Ingelheim, Margarida Alves Employee of: Employee of Boehringer Ingelheim, Deborah Clarke Employee of: Employee of Boehringer Ingelheim, Christina Raabe Employee of: Employee of Boehringer Ingelheim, Prithwiraj Das Employee of: Employee of Boehringer Ingelheim, Toby Maher Grant/research support from: Received funds from BI advisory board participation and conference travel. Received research funding and/or consulting fees or other remuneration from GSK, UCB, AstraZeneca, Roche, Bayer, Biogen Idec, Cipla, Prometic, and Sanumed. Toby Maher has, via his institution, received industry-academic funding from GlaxoSmithKline R&D and UCB., Consultant for: Toby Maher has received consultancy or speakers fees from Apellis, AstraZeneca, Bayer, Biogen Idec, Boehringer Ingelheim, Galapagos, GlaxoSmithKline R&D, Indalo, Pliant, ProMetic, Roche, Samumed and UCB; and has received consultancy fees from Galecto.

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SAT0574 A SYSTEMATIC LITERATURE REVIEW OF HEALTHCARE BURDEN IN PATIENTS WITH BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is a chronic, multisystem, inflammatory disorder primarily characterized by recurrent oral ulcers (OU) and other key features, such as genital ulcers, skin lesions and articular and ocular inflammation. The prevalence of BD is typically reported as higher in Silk Road countries (e.g., Turkey, Jordan); however, it has increased in developed countries (e.g. Europe), likely due to migration. Given the diagnoses across geographic regions, we sought to understand the prevalence of BD manifestations, related symptoms and the impact on comorbidities, treatments, and quality of life (QoL).

Objectives: To understand the clinical and humanistic burden among patients (pts) with BD based on a systematic literature review (SLR).

Methods: An SLR was performed to identify real-world BD studies reporting symptom, comorbidities, treatments or QoL. Articles and conference abstracts indexed in Embase/MEDLINE describing pts with BD and published from Jan 1, 2003–May 1, 2018 were included. An independent reviewer extracted, reviewed and analyzed the data and another performed standard quality check. Studies with <10 pts and those only including pts with ocular, neurologic, or vascular involvement were excluded. For categorical outcomes, the number (#) of studies, median, interquartile range (IQR) and/or min-max range of prevalence are reported; for continuous outcomes, the # of comparisons with significance ($P \leq 0.05$) are reported.

Results: A total of 2656 citations were identified, of which 66 citations (55 manuscripts; 11 abstracts) describing >21,000 pts with BD were reviewed.

The most common manifestation was OU, with 19 of 27 studies reporting 100% prevalence (IQR: 84%-100%). One study reported an average of 12.7 OU per patient per year; in another study, OU were the only manifestation currently or previously experienced by all pts. Frequently reported symptoms included fatigue/sleep-related issues (7; 70%), pain (4; 59%), and headache (5; 58%); skin lesions were also common (19; 58%). Several comorbidities, e.g. emotional issues (4; 24%–44%), fibromyalgia (4; 8%–24%), hearing loss (3; 10%–59%), etc. were significantly

increased in pts with BD vs healthy controls. Most pts reported using colchicine (20; 52%) and/or corticosteroids (21; 41%), with fewer reporting use of immunosuppressants, such as azathioprine (7; 15%) and anti-TNF biologics (6; 6%).

Compared to healthy controls, pts with BD had significantly worse QoL overall (5/6), as well as in specific domains, such as symptom severity (1/2), physical functioning (13/13), sleep (4/5), fatigue (4/7), pain (8/8), cognition (2/3), mental health (29/40), and social functioning (6/6). Two studies reported significant impairments in QoL associated with OU, including oral health (e.g., plaques) as well as overall QoL. Pts with BD had similar (11/19) or significantly worse (5/19) QoL vs. other chronic inflammatory conditions (e.g., rheumatoid arthritis).

Conclusion: Patients with BD experience an increased symptom, comorbidity, and QoL burden vs. healthy controls, and their QoL is comparable or worse than patients with other chronic inflammatory conditions. Findings suggest oral ulcers are highly prevalent and can directly contribute to poor QoL, reflecting the need to improve oral ulcer management. Further research is needed to better understand the impact of treatment on oral ulcer occurrence, associated pain, QoL and healthcare burden.

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SAT0575 RACIAL DIFFERENCES IN PRESCRIPTION PATTERNS OF DISEASE MODIFYING ANTI-RHEUMATIC DRUGS, NARCOTICS AND GLUCOCORTICOIDS AMONG MIDDLE-AGED PATIENTS WITH DISABILITY AND RHEUMATOID ARTHRITIS

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Background: Many patients with rheumatoid arthritis (RA) become disabled. While racial/ethnic differences in RA treatment have been described in RA patients without disability, less is known about racial/ethnic differences in RA treatment among middle-aged individuals with RA receiving disability benefits.

Objectives: To determine if racial/ethnic differences exist in the prescription patterns of conventional synthetic (CS) and biologic (B) disease modifying anti-rheumatic drug medications (DMARD), glucocorticoids, and opioids.

Methods: We conducted cross-sectional analyses in the calendar year 2014 using Medicare and Medicaid claims data of individuals receiving Social Security Disability Income (SSDI). To be included, patients had to be continuously enrolled over one year, aged <65 years, eligible for both Medicare and Medicaid, and have RA, defined as: 1) two RA diagnoses (ICD9-714.xx) by a rheumatologist between 7 to 365 days apart; OR 2) one RA diagnoses by a rheumatologist and at least 1 prescription for a DMARD. We examined the proportion of patients with CS-DMARD, B-DMARD, glucocorticoid (>7.5 mg prednisone daily for >30 days), or opioid (either a prescription for opioids with 3 refills or at least one 90 day supply) prescriptions in each year by race/ethnicity. Generalized estimating equation (GEE) models was used to report adjusted differences in prescription rates for Blacks, Hispanics, and Other using Whites as the reference group, adjusting for age, gender, and medical comorbidities.

Results: The were 9,265 patients in 2014 out of which 60% were White, 21% were Black, 15% were Hispanic, and 5% were Other race. The proportion of female patients by race/ethnicity was >75% for each group. Hispanics had a 6.6% point higher rate of B-DMARD prescriptions and a 10.7% point lower rate of opioid prescriptions compared to Whites. Blacks had a 3.4% point higher rate of glucocorticoid prescriptions, and a 3.3% point lower rate of opioids prescriptions compared to Whites.

Conclusion: We observed racial differences in arthritis-related treatment patterns, among disabled RA patients, with Blacks receiving less biologic treatment and Whites receiving more opioids. Hispanics received the highest prescription rates of biologics and the Other race received lowest prescription rates of opioids among the three racial/ethnic groups. Further studies are needed to examine the reasons for such differences.

Table: Adjusted differences (95% CI) in rates of prescription for CS-DMARD, B-DMARD, glucocorticoids or opioids among Blacks, Hispanics, and Other compared to Whites*

2014				
	Black	**Hispanic**	**Other**	**White Adjusted Reference Percentage (95% CI)**
CS-DMARD	**4.3 (1.8, 6.8)**	2.4 (-0.5, 5.2)	2.2 (-2.6, 6.9)	61.9% (60.5 – 63.4)
Any B-DMARD	-4.6 (-7.2, 2.0)	**6.6 (3.7, 9.5)**	**5.9 (1.0, 10.7)**	53.7% (52.1 – 55.2)
Any SQ B-DMARD	**-5.2 (-7.7, -2.7)**	1.5 (-1.3, 4.3)	4.4 (-0.3, 9.1)	36.0% (34.5 – 37.5)
Any IV B-DMARD	0.3 (-1.8, 2.3)	**6.8 (4.5, 9.2)**	3 (-0.9, 6.9)	17.3% (16.1 – 24.1)
Glucocorticoids	**3.4 (1.7, 5.2)**	-0.2 (-2.2, 1.8)	0.4 (-2.9, 3.7)	13.5% (12.5 – 14.6)
Opioids	**-3.3 (-5.8, -0.8)**	**-10.7 (-13.5, -7.9)**	**-16.4 (-21.1, -11.7)**	64.1% (62.7 – 65.6)

*Adjusted for age, sex and Charlson comorbidity index. CS-DMARD = conventional synthetic disease modifying anti-rheumatic drug; B-DMARD = biologic disease modifying anti-rheumatic drug; SQ = subcutaneous

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SAT0576 ETANERCEPT BIOSIMILAR SWITCH: CAN IT BE SUCCESSFUL WITHOUT CLINIC REVIEW?

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Background: Since the introduction of anti-TNF biosimilars in routine clinical practice, there has been a drive to implement the switch program for all biosimilars at the point of availability. Etanercept biosimilar (SB4) was granted marketing authorisation by the EMA in January 2016. Our Trust was one of the leading centres to switch all patients within one year of the drug's availability. The aim of the non-medical switch was to obtain significant savings for the NHS whilst achieving similar clinical outcomes.

Objectives: We report patient experience after a year of completing the switch program.

Methods: A list of all patients prescribed etanercept was extracted through our database. The original strategy included a 'switch' letter sent to all patients including SB4 information sheet. Patients were given the opportunity to contact nurse helpline for information or if disease control worsened/adverse effects developed. We reviewed all relevant records and collected data on any adverse events and disease outcome on either side of the switch.

Results: 84 patients were prescribed reference etanercept. 41 (49%) had RA, 17 (20%) had PsA, 18 (21%) had AS and remaining eight had JIA. One person declined the transfer to the biosimilar and one patient with JIA was on 37.5mg weekly dose which was unavailable. 82 agreed to the switch that was completed by March 2017. Median age of switchers was 59.6 (range 14-74 years). 25 (30%) were men and remaining 59 (75%) were women.

76 patients remain on SB4 biosimilar a year after switch. Seven patients described concerns within the first five months of switching. One was found to have concurrent severe Vit D deficiency which upon correcting allowed him to continue with the biosimilar. Six patients had side effects with corresponding worsening of respective disease activity scores. Four returned to the originator with resolution of adverse effects and disease control was regained. Two continued to have uncontrolled disease and were moved to alternative mode of action.

Conclusion: Overall patient experience following etanercept biosimilar switch has been positive. 90% continue with SB4 originator a year later with no adverse outcomes. All were happy to switch after receiving a

Table. Patient characteristics of switch related adverse events

Age	Gender	Ethnicity	Diagnosis/ date	Etanercept initiation	Pre-switch Disease score	Switch date	Post-switch Disease score	Switch Back date	Final Disease Score
41	F	Asian	RA/Feb 06	Feb 10	DAS 2.6	Jul 17	DAS 3.5	Dec 17	DAS2.0 (Apr 18)
70	F	Asian	RA/Aug 07	May 11	DAS 2.2	May 17	DAS 3.3	Dec 17	DAS 2.4 (Feb 18)
55	F	White	AS/Apr 09	Oct 09	BASDAI 1.6 Spinal VAS 0	Feb 17	BASDAI 4 Spinal VAS 4	Sev Vit D def treated	BASDAI 3.2 Spinal VAS 1 SB4 continued
38	M	White	AS/Dec 10	Jul 13	BASDAI 3 Spinal VAS 3	May 17	BASDAI 4 Spinal VAS 4	Aug 17	BASDAI 3 Spinal VAS 0 (Aug 17)
24	F	White	JIA/Feb 97	Jun 10	TJ 0, SJ 0	Feb 18	TJ 3, SJ 3	Jul 18	TJ 0, SJ 0 (Sep 18)
63	M	White	RA/Mar 00	Apr 06	DAS 2.2	May 17	DAS 5.2	Mar 18	DAS 5.3 (Aug 18)
46	F	White	RA/Jan 07	Jun 10	DAS 2.6	Apr 17	DAS 6.2	Jan 18	DAS 5.2 (Jun 18)

letter and having the opportunity to contact if necessary. This made the process quite smooth, easy to administer and avoided costs associated with face-to-face review. Substantial annual cost savings of nearly £100,000 were achieved once the switch process completed. Only six patients (7%) encountered adverse effects, two of whom had uncontrolled diease despite switching back to the originator. We support the routine switching from originator to biosimilar etanercept in view of good patient experience and disease outcomes. This can be achieved with minimal contact in a cost-efficient manner.

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SAT0577 ABSENTEEISM OF PATIENTS WITH RA AND AS IN SLOVENIA: TREND ANALYSIS BASED ON NATIONAL LEVEL DATA BETWEEN 2001 AND 2016

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Background: Indirect costs due to absenteeism of rheumatoid arthritis (RA) and ankylosing spondylitis (AS) in Slovenia have not been thoroughly researched despite availability of national administrative data on sick leave and evidence from other countries on their sizable burden [1, 2].

Objectives: To compare absenteeism trends in Slovenia in the 2001-2016 period between three age cohorts of RA and AS patients given that age is an important determinant of sick leave [3].

Methods: Retrospective population data on sick leave from the Slovenian National Institute of Public Health was collected. Total annual number of days on sick leave was used as an indicator of absenteeism. Patients were classified into three age cohorts (20-39 years, 40-54 years and 55-69 years). Changes in absenteeism during the 16-year period were estimated using a linear trend function.

Results: In the 2001-2016 period, patients with RA spent 448.828 days on sick leave. For AS patients the number of sick days was 92.990. Patients aged 40-54 accounted for 66.6% of all sick days of RA patients, while the shares for patients aged 20-39 and 55-69 were 16.6% and 16.8%, respectively. Estimated linear trend reveals a statistically significant reduction of sick days in RA patients from all age cohorts throughout the observed period. RA patients aged 20-39 experienced a decrease of 483.7 days spent on sick leave annually on average (p=0.000; R2=0.849). Patients aged 40-54 experienced a higher average annual decrease of 952.3 days (p=0.000, R2=0.74). RA patients aged 55-69 experienced an average annual increase of 250.3 days spent on sick leave in the 2001-2016 period (p=0.001; R2=0.567).

Sick days of AS patients aged 40-54 represented 64.4% of all sick days of AS patients. For AS patients aged 20-39 this share was 25.0%, and 10.6% for those aged 55-69. Estimated linear trend shows that, on average, patients with AS aged 20-39 and 40-54 experienced an 11.4 and 5.9 decrease of sick days, respectively, whereas the patients with AS aged 55-69 experienced an average annual increase of 19.4 days spent on sick leave in the observed period. However, none of the linear trends were statistically significant for AS patients.

Conclusion: Results indicate that RA patients aged 20-39 and 40-54 experienced a significant average annual decrease in days spent on sick leave during the 2001-2016 period. This suggests a general decline in economic burden due to absenteeism in patients with RA, which could be attributed to innovative treatments, improved disease management practices and other organizational and process changes in treating RA. Yet, the results do not show any statistically significant changes in days spent on sick leave for AS patients, regardless of age. This implies that factors other than age should be investigated to explain changes in absenteeism for AS patients. Future studies should focus on other potential associations and causal mechanisms of changes in days spent on sick leave in AS and RA patients.

REFERENCES

[1] Malinowski KP, Kawalec P. 2015. The Indirect Costs of Ankylosing Spondylitis: A Systematic Review and Meta-analysis. Expert Rev Pharmacoecon Outcomes Res, 15(2): 285-300

[2] Verstappen SMM. 2015. Rheumatoid Arthritis and Work: The Impact of Rheumatoid Arthritis on Absenteeism and Presenteeism. Best Pract Res Clin Rheumatol, 29(3): 495-511

[3] Bouville G, Dello Russo S, Truxillo D. 2018. The moderating role of age in the job characteristics–absenteeism relationship: A matter of occupational context? J Occup Organ Psychol, 91(1): 57-83

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SAT0578 TOWARDS EUROPEAN HARMONISATION OF HEALT CARE FOR PATIENTS WITH RARE IMMUNE DISORDERS: ERN RITA RESULT FROM THE REGISTRIES SURVEY

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Background: Rare Immunodeficiency, AutoInflammatory and AutoImmune Disease (RITA) network is a European Research Network that brings together the leading centres for rare immune disorders (RID).

Objectives: To know the state of the art about diseases registries and research networks in Europe regarding patients with RID.

Methods: On April 2018 an on-line survey was sent to all 126 RITA members, of whom 45 are healthcare providers and 8 patients/family organizations. All data were collected and analysed using Excel program.

Results: Ninety RITA members (71%) replied. Collectively, 27 members are coordinating 25 registries, 53 members are participating in 38 registries, and 27 members knew the existence of 16 registries without participating. Only two members are not involved in any registries. Data about 53 different registries were collected across 14 European countries. Almost 50% of registries collect data on autoimmune disorders, while

others are dedicated to primary immunodeficiencies and autoinflammatory diseases (respectively 15 registries, 28%, and 12 registries, 23%). Fifteen registries (28%) enrolled patients with a single specific disorder: in particular, three registries are devoted to systemic lupus erythematosus, two registries to Kawasaki disease or Behcet disease, and single registry to juvenile dermatomyositis, juvenile systemic sclerosis, juvenile idiopathic arthritis (JIA)-related uveitis, systemic JIA, Blau syndrome, sarcoidosis, Guillain-Barre syndrome, and myasthenia gravis. More than 55000 patients with RID are enrolled. The majority of registries (36; 68%) enrol only patients from national territories. Among the internationals, six collect data on autoimmune disorders (Pharmachild, BrainWorks, EuroMyositis, EULAR web library, UKIVAS registry and JIR cohort), five on primary immunodeficiencies (ESID, EBMT, SCETIDE, PCID and HLH registry), and three are devoted to autoinflammatory diseases (Eurofever, Infevers, and ImmunAID), despite also ESID registry and JIR cohort collect data on autoinflammatory diseases. Data usually collected in these registries are demography, diagnosis, clinical manifestations, laboratory tests and treatment, while genetic and imaging data are less frequently reported (respectively in 38% and 9% of registries). A treatment safety profile is reported in 29 registries (55%). Collectively, fifteen biobanks are counted.

Conclusion: The survey highlighted the pivotal role of national and international organizations in Europe to collect and organize clinical data on immune diseases, allowing the rapidly growing knowledge on these rare disorders, creating research networks and providing significant numbers of data to support new discoveries in the field. RITA network could improve the coordination of these numerous entities, supporting initiatives of collaboration. As a first attempt, the present survey revealed that the collection of key parameters about patient safety, as well as outcome data and quality of life measures should be improved among the registries of RITA network.

REFERENCES

[1] Beukelman T, Anink J, Duffy C, et al. A survey of national and multinational registries and cohort studies in juvenile idiopathic arthritis: challenges and opportunities. Pediatric Rheumatology 2017;15(1):31.

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SAT0579 AN ELECTRONIC MDHAQ (MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE) GIVES SIMILAR RESULTS TO A PAPER VERSION

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Background: A self-report multi-dimensional health assessment questionnaire (MDHAQ) is used in many routine care rheumatology settings as a pragmatic tool to recognize efficacy and adverse events. The MDHAQ is informative in all rheumatic diseases in which it has been studied. An electronic version of the MDHAQ (eMDHAQ) could offer several advantages, including completion at home rather than in the waiting area and completion from any site between visits to report possible change in status and/or adverse events of a medication. Furthermore, the 4-page, "new patient" eMDHAQ can allow a patient to store a full medical history at a password-protected, secure website. Reports of the patient history can be available for an electronic medical record (EMR) without dictation or typing by the doctor, although interaction with the EMR vendor is required, which often has proven difficult. Implementation of eMDHAQ software requires documentation that eMDHAQ responses are similar to those on a paper MDHAQ.

Objectives: To compare scores on an eMDHAQ vs paper version of MDHAQ.

Methods: All patients with all diagnoses complete a paper MDHAQ at all visits in the waiting area as part of routine clinical care in one setting. Consecutive patients completed MDHAQ in paper and in an iPad at the same visit. The MDHAQ includes 0-10 scores for physical function, pain and patient global visual analog scales (VAS), compiled into 0-30 RAPID3, as well as a 0–48 self-report painful joint count, and 0–60 symptom checklist. For this study, at the conclusion of the visit, the rheumatologist asked a patient if she/he would volunteer to complete an eMDHAQ on an iPad indicating no problem if a patient declined for any reason. Patients who agreed to participate completed the an eMDHAQ, with identical content to the paper MDHAQ. The patient also completed a 3-query questionnaire, with 2 VAS concerning the value of the MDHAQ to the patient or the doctor (0= no value, 10= great value), and a query of her/his preference for the eMDHAQ vs paper MDHAQ or no preference. Test-retest reliability was examined by intraclass correlation coefficients (ICC).

Results: 65 patients completed the study. The ICC for physical function, patient global VAS, and RAPID3 was >0.9 indicating excellent reliability between the electronic and paper versions, while the ICC for pain, self-report painful joint count, and symptom checklist was $\geq$0.75, indicating good reliability. Differences between the 2 versions were within variation on the paper questionnaire. The mean rating for the value of MDHAQ was 8.85/10 to the patient, and 8.88/10 to the doctor. Among the 65 patients, 43 (66%) indicated a preference for the eMDHAQ, 7 (11%) for the paper MDHAQ, and 15 (23%) indicated no preference.

Table. Mean (SD) for paper versus I-pad format for MDHAQ in 65 patients

	Paper	I-Pad	Diff. (95%CI)	ICC (95%CI)
Physical Function (0-10)	2.0 (1.7)	2.0 (1.7)	0.04 (-0.6, 0.6)	0.96 (0.94, 0.98)
Pain (0-10)	5.3 (3.2)	5.1 (3.1)	0.3 (-0.8, 1.4)	0.87 (0.80, 0.92)
Patient global (0-10)	4.8 (2.8)	4.5 (2.8)	0.3 (-0.7, 1.3)	0.94 (0.90, 0.96)
RAPID3 (0-30)	12.1 (7.1)	11.4 (7.2)	0.7 (-1.7, 3.2)	0.93 (0.88, 0.95)
Symptom checklist (0-60)	9.9 (8.5)	10.8 (9.5)	-0.9 (-4.1, 2.2)	0.75 (0.62, 0.84)
RADAI-48 (0-48)	9.9 (8.9)	11.4 (10.7)	-1.4 (-7.9, 1.9)	0.81 (0.71, 0.88)

Conclusion: An eMDHAQ appears to have similar performance compared to a paper MDHAQ version. A high percentage of patients prefer the digital version to paper, although about 20% of patients are likely to require a paper MDHAQ. An eMDHAQ offers remote completion at home, before and/or between visits, to report issues concerning efficacy and/or adverse events. Expanded eMDHAQ software can allow a doctor to develop flowsheets and a database for all patients, a full patient medical history, and interfacing with any electronic medical record (EMR), although that requires interaction with the EMR vendor, which often is difficult. The eMDHAQ appears useful independent of the EMR.

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SAT0580 HEALTHCARE BURDEN AND COST OF ILLNESS OF GIANT CELL ARTERITIS IN THE ITALIAN REGION OF FRIULI VENEZIA GIULIA: A 17-YEAR INTEGRATIVE ANALYSIS OF DIGITAL ADMINISTRATIVE DATABASES

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Background: Giant cell arteritis (GCA) is the most common systemic vasculitis in persons aged 50 and above (1). Data on incidence and prevalence of GCA are welcomed. Further information is also needed on the healthcare burden and resource consumption. The use of multiple digital databases with the integration of clinical data from a formalized network of specialists is needed.

Objectives: To estimate incidence, prevalence and costs of GCA by an integrative analysis of multiple administrative databases of the healthcare system of the Italian Region of Friuli Venezia Giulia (about 1,2 millions of inhabitants), cooperating with the existing local Rheumatology Network.

Methods: A 17-year retrospective study was conducted through the following administrative health regional digital databases of the Friuli Venezia

Giulia Region: the Database of Regional Potential health Care Beneficiaries, the Hospital Discharge Database, the Ambulatory Care Database, the Pharmaceutical Prescription Database, the Emergency Department Database, the Mortality Database, the Anatomical Pathology Database, the Database of Exemptions from Medical Charges, and the Regional Rare Disease Registry. All the databases were integrated at the individual patient level using a univocal stochastic key.

Results: From 2001 to 2017, 208 patients with GCA were registered. The crude identification rate of patients identified with GCA until 2017 in the population ≥45 years of age was 3.8/100,000 person-years (95%CI: 2.5-5.5). The maximum incidence rate was observed in the age group 70-74 years. The prevalence of GCA in the population ≥45 years of age as of December 31st, 2017 was 27.2/100,000 (95%CI 23-5-31.4).

The mean medical observation was 4.5±3.6 years per patient, totaling 940.8 years of observation.

192 patients had at least one ambulatory specialist visit, resulting in a total of 3182 specialist visits (338 per 100 patient-years). The most frequent medical specialties involved were Rheumatology (N=610, 19.2%), Internal Medicine (N=564, 17.7%), Ophthalmology (N=292, 9.2%), and Orthopedics (N=191, 6%).

108 (52%) patients had at least one hospitalization, resulting in 287 hospitalizations (30 per 100 patient-years). Circulatory Cardiovascular diseases were the most common discharge diagnoses, followed by musculoskeletal conditions.

199 subjects were prescribed medications for a total of 9588 prescriptions (1019 per 100 patient-years). Notably, an immunosuppressive drug, usually methotrexate, was prescribed in more than half of the patients. Cardiovascular medications were prescribed to 154 (74%) patients; bisphosphonates or other anti-osteoporotic drugs to 123 patients (59%). The average annual direct cost of GCA was 2374 Euros per patient-year (61 for outpatient visits, 1661 for hospitalizations, 312 for prescribed medications and 340 for medications directly dispensed by the hospital pharmacies). The overall estimated direct healthcare cost for 940.8 patient-years was 2,234,070 Euros.

Conclusion: Novel epidemiologic data in GCA are reported after a very long-term observation, and by integrating data from multiple databases with clinical data from a Regional network of specialists (Rheumatology being the major contributor to disease clinical follow-up).

Cost of illness is high in GCA. Both the diseases itself and cardiovascular manifestations, and, possibly, the complications of glucocorticoids, may contribute the to the healthcare burden of GCA. Despite a high use of immunosuppressors in our Region, new drugs (2) and novel treatment strategies are required.

REFERENCES

[1] Buttgereit F, et al. JAMA. 2016;315:2442-58
[2] Stone JH, et al. N Engl J Med. 2017;377:317-328

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SAT0581 POOR HEALTH-RELATED QUALITY OF LIFE (HRQOL) AND FATIGUE ARE ASSOCIATED WITH A HIGHER WORK PRODUCTIVITY IMPAIRMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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Background: Because most patients with SLE are in their productive-age years, the ability to maintain a gainful employment is fundamental for both, the patient and society at large. It is thus quite important to determine the work and non-work factors that are associated with work productivity impairment in these patients.

Objectives: To determine the factors associated with absenteeism (percentage of the time missed from scheduled work-time over the preceding 7 days, due to SLE), presenteeism (percentage of time from scheduled work-time where productivity was impaired while patient was at work, over the preceding 7 days, due to SLE) and overall work impairment (combination of absenteeism and presenteeism) in patients with SLE.

Methods: A total of 133 consecutive (1997 American College of Rheumatology (ACR) criteria) working patients with SLE were assessed between October 2017 and December 2018, using a standardized data collection form. Sociodemographic, disease and work-related variables were collected. Disease activity was ascertained with the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI); disease damage with the Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI); health-related quality of life was assessed with the LupusQoL and fatigue with the FACIT-Fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue). Work Productivity and Activity Impairment (WPAI) was assessed with the respective questionnaire; absenteeism and presenteeism due to overall health and symptoms during the past 7 days were scored. Linear regression models were performed to determine the factors associated with absenteeism, presenteeism and overall work impairment. Potential factors included were age at diagnosis, gender, socioeconomic status, educational level, SLEDAI, SDI, FACIT- Fatigue and the components of the LupusQoL.

Results: The mean age at diagnosis was 32.2 years (11.8); 121 (91.7%) were female. Nearly all patients were Mestizo. Mean years of education was 14.1 (2.6). The mean disease duration was 11.9 (7.5) years. Mean SLEDAI was 2.9 (4.0), and mean SDI was 1 (1.4). The mean percent of time for absenteeism was 5.0 (12.9), it was 28.5 (26.4) for presenteeism, and it was 31.3 (27.2) for overall work impairment. In the multiple regression analysis, factors associated with absenteeism were disease duration (B=-0.34; SE=0.12; p=0.007); pain (B=-0.14; SE=0.06; p=0.046); intimate relationship (B=-0.07; SE=0.03; p=0.046) and emotional health (B=0.16; SE=0.06; p=0.006), with presenteeism were physical health (B=-0.43; SE=0.14; p=0.002) and FACIT (B=-0.87; SE=0.30; p=0.005) and with overall work impairment were pain (B=-0.40; SE=0.11; p=0.001) and FACIT-Fatigue (B=-0.74; SE=0.28; p=0.010).

Conclusion: A poor HRQoL and higher levels of fatigue were associated with a higher percentage of absenteeism, presenteeism and overall work impairment in SLE patients. Addressing the factors related to HRQoL and Fatigue may have significant impact on work performance among SLE patients.

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SAT0582 THE LATIN AMERICAN RHEUMATOLOGIST SURVEY: LARS STUDY

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Background: Currently, Latin America does not have detailed information of rheumatologists in the region based on: education, working conditions, productivity, distribution of time between work activities and job satisfaction.

Objectives: The purpose of this survey was to provide more information on the rheumatology community in Latin America

Methods: A digital survey was created using the Google Forms platform, it was approved and endorsed by the scientific committee of PANLAR and later sent to the different rheumatology associations of the region. The data was analyzed in the statistical programSPSS v.23:

Results: 456 surveys of rheumatologists from 23 countries were received. The majority were females (54%). The mean age was 47.18 ± 11.79 [25-78] years, with a majority of mixed race 58%. 63% are married, 23% are single, 8% are divorced, 5% in free union and 2% are widowed. The mean number of children was 2 [0-7]. Birthplaces included Argentina (27%), Brazil (18%). The setting of the professional practice after obtaining the title of specialists was: public hospital (35%), private (25%), private/teaching in a university hospital (12%), public/teaching in a university hospital (14%), and industry (1%). The main place of work was in public/government hospitals by 30% followed by private practice 31%, private hospital 23%, university hospital 15% and nonprofit organizations 1%. The average of weekly working hours was 39.12 ± 27.53. 89% of the sample practices adult rheumatology, 17% pediatric rheumatology, 2% immunology

and 3% another specialty. 30% had an early arthritis care center at their workplace, 71% had an infusion unit, 17% had ultrasound, 23% had a densitometer, 17% had a resonator and 9% had X-rays, however, most work in collaboration. 30% have training in ultrasound and 9% are in training period, 75% have training in reading densitometry and 2% in training period, 54% have training in resonance reading and 11% in training period. The average satisfaction with practice as a rheumatologist was 5/7, career options/professional growth 4/7, geographic location 5/7, income 4/7, job security 4/7, colleagues and co-workers 5/7. 33% had an annual compensation of <19,000 US dollars. Only 58% have malpractice insurance and 87% have medical insurance. 40% present at least one clinical comorbidity.

Conclusion: The majority of rheumatologists in the region who responded were female and feel satisfied with their clinical practice. This survey shows a low level of income for the region, however, more data should be obtained. This is the first study of its kind in Latin America, being an initiative for similar projects.

Disclosure of Interests: None declared

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SAT0583 DEVELOPMENT AND TESTING OF A SMARTPHONE APPLICATION TO SELF-MONITOR DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Several mobile applications (apps) exist to monitor symptoms of rheumatoid arthritis (RA), but high-quality apps are lacking.[1] We developed an app with patients, following the Medical Research Council guidance for developing and evaluating complex interventions.[2] The app facilitates telemonitoring through a weekly MDHAQ/RAPID3[3] questionnaire and has been integrated with the local electronic medical record.

Objectives: To evaluate the users' satisfaction, usability and engagement of the application, as a first and preparatory step toward the ultimate goal of telemonitoring and self-initiated care.

Methods: In a first, one month, pilot study 42 RA patients used the app. User's satisfaction was measured using an 11-point Likert scale. Usability was measured using the three concepts of the Technology Acceptance Model (TAM).[4] According to TAM, perceived usefulness (PU), perceived ease of use (PEOU), (behavioral) intention to use (ITU) predict how and when a product will be used. The PU and PEOU were measured using the system usability scale (0-100). A score of 68, or higher, indicates sufficient system usability.[5] The ITU was measured on a 11-point Likert scale. Engagement was measured by the percentage of patients completing all weekly questionnaires. General feedback was collected and implemented.

In a second, one month, pilot study, the improved app was evaluated in 24 RA patients using 5 themes derived from the Mobile App Rating Score[6]: "engagement", "functionality'', "aesthetics'', "information'' and "subjective quality.'' Participants rated the questions on a 5 - point Likert scale. All responses were categorized into three categories: negative (1-2), neutral (3) and positive (4-5). Afterwards, nine participants (three users, three dropout users, and three non-users) agreed to participate in a semi-structured interview to get feedback on the App.

Results: In the first study, the ReumaMeter scored an overall median score of 8.0 (interquartile range (IQR) 7.0-9.0), a mean system usability score of 76 (SD 14.8) and participants intended to keep using the ReumaMeter in the future (median 7.0, IQR 5.0-9.0). Engagement decreased to 61% in week 4. During the second study, the number of positive responses for each category was at least twice as high as the number of negative responses (Figure 1). Feedback that emerged during the interviews matched these responses. In addition, several participants stated that app usage declined due to low disease activity.

Conclusion: The participants' overall feedback was positive in terms of users' satisfaction and usability. Engagement dropped, which may be due to lack of internal triggers to measure disease activity when patients are in remission. To assess the overall impact of the app on RA patient care, a randomized controlled trial is planned.

REFERENCES

[1] Grainger R, et al. JMIR Mhealth Uhealth. 2017. 2:e7.
[2] Craig P., et al. BMJ. 2008. doi:10.1136/bmj.a1655
[3] Pincus, T.et.al. The Journal of Rheumatology. 2008. 35,2136-37.
[4] Davis, F.D. MIS Quarterly. 1989. 13(3):319-339.
[5] Bangor, A. International Journal of Human-Computer Intervction. 2008. 24 (6) 574-594.
[6] Stoyanov, S.R., et al. JMIR Mhealth Uhealth, 2015. 3(1): p. e27.

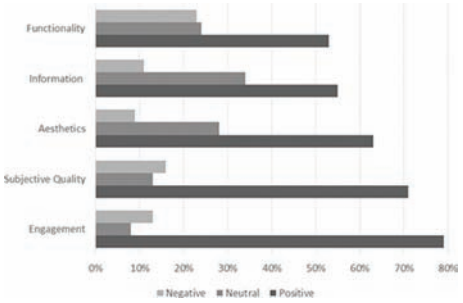


Figure 1. Qualitative results of app-evaluation - 79% of participants responding

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SAT0584 POORER OUTCOMES AND HIGHER HEALTHCARE UTILIZATION AFTER TOTAL HIP ARTHROPLASTY IN PATIENTS WITH LUPUS

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Background: Hip osteonecrosis and hip osteoarthritis are common causes of severe hip disease in lupus (1), both treated successfully with a total hip arthroplasty (THA). A recent systematic review of arthroplasty outcomes reported that the risk of overall complications post-THA was higher than in patients with lupus compared to those without lupus (2). However, no analyses were provided for specific outcomes such as infection, revision or associated health care utilization.

Objectives: To assess the risk of specific post-THA outcomes, i.e., infection, transfusion, revision and mortality and associated health care utilization, associated with lupus.

Methods: We used the 1998-2014 U.S. National Inpatient Sample data. Multivariable-adjusted separate Cox proportional hazard regression models assessed the association of lupus with post-operative complications (infection, transfusion, THA revision and mortality) and health care utilization outcomes (total hospital charges, discharge to inpatient facility, length of hospital stay) post-THA, adjusting for demographics, underlying diagnosis, comorbidity, insurance payer, and hospital characteristics, using hazard ratios (HR) and 95% confidence intervals (CI).

Results: Among 4,116,485 primary THA hospitalizations, 22,557 (0.5%) were in lupus patients. Patients with lupus were younger, more likely to be female, African-American or Hispanic and, have higher comorbidity, Medicaid insurance payer, lower income, or living in the South. In multivariable-adjusted analyses, lupus was associated with a significantly higher risk of infection, transfusion, hospital charges above the median

($37,658) and discharge to inpatient facility, with respective HRs of 1.95 (95% CI, 1.28, 2.97), 1.34 (95% CI, 1.25, 1.43), 1.21 (95% CI, 1.01, 1.44) and 1.38 (95% CI, 1.30, 1.47). Lupus was not significantly associated with the risk of revision, mortality or hospital stay above the median (>3 days), the HRs were 1.10 (95% CI, 0.68, 1.78) and 0.95 (95% CI, 0.61, 1.47) and 1.06 (95% CI, 0.99, 1.13).

Conclusion: Lupus was associated with a higher risk of infection and transfusion and higher hospital charges post-primary THA. Insight into modifiable factors associated with these outcomes may improve outcomes in lupus patients undergoing THA.

REFERENCES

[1] Mertelsmann-Voss C, Lyman S, Pan TJ, Goodman S, Figgie MP, Mandl LA. Arthroplasty rates are increased among US patients with systemic lupus erythematosus: 1991-2005. J Rheumatol 2014;41:867-74.

[2] Kennedy JW, Khan W. Total Hip Arthroplasty in Systemic Lupus Erythematosus: A Systematic Review. Int J Rheumatol 2015;2015:475489.

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SAT0585 COMPARISON OF KNEE OSTEOARTHRITIS TREATMENT PATTERNS BY RHEUMATOLOGISTS VS. OTHER PROVIDERS IN A U.S. ADMINISTRATIVE CLAIMS DATABASE

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Background: Knee osteoarthritis (OA) is a painful, disabling condition with increasing prevalence.

Objectives: To compare characteristics and treatment patterns of patients newly diagnosed with knee OA by rheumatologists (RH) to those diagnosed by general practitioners (GP) and those diagnosed by orthopedic surgeons (OS).

Methods: U.S. administrative claims data from 2011-2018 (IBM Watson Health MarketScan® Research Database) was used to perform an observational cohort study. Inclusion criteria included ≥18 years and ≥1 claim with ICD9 lower-leg OA diagnosis prior to October 2015, followed by a confirmatory ICD10 knee OA diagnosis *or* ≥1 claim with an ICD10 knee OA diagnosis. Index date was the earliest claim/diagnosis date preceded by ≥2 years of prior continuous enrollment without these diagnoses. Demographic characteristics and diagnosing physician specialty were assessed on index date, whereas comorbid conditions and treatment patterns were observed during the variable post-index follow-up period. A two-sample t-test or a two-sample proportion test, where appropriate, was used to perform comparisons in GP vs RH and OS vs RH ($P<0.05$ considered statistically significant).

Results: 488,510 knee OA patients met inclusion criteria of which 76% (371,219) had physician type of interest noted on initial diagnosis claim. RH-diagnosed knee OA accounted for 3.2% (15,517), while GP and OS for 20.2% (98,911) and 47.6% (232,567), respectively. The average age of patients diagnosed by RH and OS was less than those GP-diagnosed (RH, 58.9; GP, 63.4; OS, 58.9; RH vs GP, $P<0.001$; RH vs OS, P=0.91). There were more female patients in the RH- than GP- or OS-diagnosed group(s) (RH, 75.6%; GP, 58.4%; OS, 58.9%; RH vs GP, P<0.001; RH vs OS, $P<0.001$). The RH-diagnosed group had significantly higher comorbidity burdens, as summarized by Deyo-Charlson Comorbidity Index (CCI) (RH, 1.53; GP, 1.40; OS, 1.01; RH vs GP, P<0.001; RH vs OS, $P<0.001$). The proportion of comorbid rheumatoid arthritis (RA) diagnoses was about 10-fold higher in RH-diagnosed patients, potentially indicating knee OA as an ancillary diagnosis noted on clinic visits for these patients (RH, 29.7%; GP, 3.8%; OS, 2.7%; RH vs GP, $P<0.001$; RH vs OS, $P<0.001$). RH-diagnosed patients received fewer total knee replacements (TKRs) (RH, 5.7%; GP, 9.3%; OS, 14.3%; RH vs GP, $P<0.001$; RH vs OS, $P<0.001$) and time to TKR initiation was significantly longer than GP- or OS-diagnosed patients (RH, 596.1 days; GP, 448.2 days; OS; 399.9 days; RH vs GP, $P<0.001$; RH vs OS, $P<0.001$). More RH-diagnosed patients received corticosteroids (CS) and hyaluronic acid (HA) with shorter initiation times than GP-diagnosed patients but OS diagnosed patients utilized HA and CS the most with the shortest initiation times; CS use: (RH, 73.0%, 109.6 days; GP, 62.3%, 122.5 days; OS, 74.3%, 84.7 days; RH vs GP, $P<0.001$; RH vs OS, $P<0.001$), HA use: (RH,15.8%, 227.5 days; GP, 14.3%, 236.8 days; OS, 23.2%, 198.7 days; RH vs GP, $P<0.001$; RH vs OS, $P<0.001$). Furthermore, RH-diagnosed patients received more NSAIDS (RH, 58.1%; GP, 51.4%; OS, 53.9%; RH vs GP, $P<0.001$; RH vs OS, $P<0.001$) and opioids with >30-day supply (RH, 27.3%; GP, 23.5%; OS, 19.8%; RH vs GP, $P<0.001$; RH vs OS, $P<0.001$) than GP- or OS-diagnosed patients.

Conclusion: This descriptive claims analysis suggested that rheumatologists saw a considerable number of knee OA patients, with different characteristics to other providers, particularly females and those with co-occurring RA. Rheumatologist-diagnosed patients received the least number of TKRs, which may represent a higher CCI patient population not suitable for surgery. However, rheumatologists prescribed pharmaceutical therapies more than general practitioners. Further research into treatment patterns and characteristics of knee OA patients treated by rheumatologists is warranted.

Disclosure of Interests: : Angela Bedenbaugh Shareholder of: shares, Employee of: employee, Machaon Bonafede: None declared, Joanne Wu: None declared, Elizabeth Marchlewicz: None declared, Vinson Lee Consultant for: Samumed, LLC, Jeyanesh Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC

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SAT0586 THE INFLUENCE OF THE NEW PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENTS IN AXIAL SPONDYLOARTHRITIS ON WORK PARTICIPATION: A SYSTEMATIC REVIEW

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Background: The concept of spondyloarthritis (SpA) comprises several chronic inflammatory joint diseases. SpA patients can be distinguished as patients with predominantly peripheral SpA (pSpA) or with predominantly axial SpA (axSpA) according to their clinical presentation. AxSpA primarily affects the axial skeleton and the sacroiliac joints. Within axSpA patients, a subdivision based on the radiographic changes of the sacroiliac joints can be made: radiographic axSpA, which corresponds to ankylosing spondylitis (AS), and non-radiographic axSpA (nr-axSpA). SpA occurs typically in young and professionally active patients. Since 2000, important improvements have been made in the management of SpA, both on a pharmacological (introduction of biological disease-modifying antirheumatic drugs (bDMARD)) and a non-pharmacological (holistic approach) level. As a result of early diagnosis followed by adequate treatment, the majority of patients achieve a state of clinical remission allowing them to function without significant problems. However, many of these persons still experience problems such as exclusion clauses, additional premiums and even contract refusals when contracting private insurances because mostly risk assessments are solely based on historical data.

Objectives: The aim of this systematic literature review was to investigate whether the work participation in patients with axSpA has significantly improved since the introduction of the bDMARD and the non-pharmacological treatment modalities. This would provide arguments for a more accurate and updated risk assessment of the expected personal and economic incapacity of axSpA patients by private insurance companies.

Methods: A systematic literature review from January 1997 until November 2017 was performed using Pubmed, Embase and Web of Science. Different search terms were used in each database: absenteeism, presenteeism, employment, sick leave, work disability and work participation. All studies assessing one of the search terms were analysed.

Results: In total, 33 studies out of 603 retrieved citations were included. Overall, the results were highly heterogeneous because of the different study designs and different use of definitions regarding work outcomes. Patients with AS were significantly confronted with restrictions on work participation compared to the general population before the availability of bDMARD. In addition, our literature review showed that, since the introduction of the bDMARD and other non-pharmacological treatments, there is no evident improvement in work disability in AS patients. In contrast, a significant improvement could be observed on absenteeism, presenteeism and work productivity. Only 6 studies included patients with nr-axSpA. In most of these studies a positive tendency towards work productivity was detected. In addition, contextual factors such as the type of job, support from employers and colleagues, adjustments in workplace,

and personal behaviour were identified as important factors for work participation in these patients.
Conclusion: Most of the patients included in the selected studies had longstanding AS with significant structural damage. The great heterogeneity between the studies in patient populations, study design and evaluation methods impeded the formation of a uniform conclusion. However, since the introduction of the new treatment modalities, a positive tendency in work productivity in AS and nr-axSpA patients could be observed. More observational, cross-sectional and prospective studies are needed - especially in nr-axSpA patients - to evaluate the effect of both pharmacological and non-pharmacological treatment on the work outcome in SpA patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7090

Epidemiology, risk factors for disease or disease progression

SAT0587 THE ART OF IMPUTING MISSING DATA OF DISEASE AND FUNCTION ACTIVITY IN RHEUMATOID ARTHRITISREGISTRIES

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Background: Large observational studies become more common in rheumatoid arthritis (RA). Disease registers [1] allow to analyse the effectiveness and safety of RA treatments in real-world populations, but observational studies suffer from missing data. To minimise bias, it has been shown that imputing missing data is superior to the use of complete case analysis [2]. Although some imputation methods have been studied in clinical trials of rheumatic diseases [3] and in small registers [4], the various imputation techniques have never been systematically compared in large registers.
Objectives: To compare the effects of available imputation methods on the estimated values and on RA remission rate for missing disease activity measures in large registers.
Methods: We used 1000 patients with complete data for disease activity (Disease Activity Score (DAS28) and Clinical Disease Activity Index (CDAI)) at baseline (treatment initiation), 6, 12, and 24 months after initiation of abatacept or a tumor-necrosis factor inhibitor (TNFi) from an existing register collaboration (PANABA).
Simulation procedure: Values were deleted randomly and imputed with three types of imputation methods: (1) methods imputing forward in time, such as Last Observation Carried Forward (LOCF) or Linear Forward Extrapolation (LFE); (2) methods considering data both forward and backward in time, such as Nearest Available Observation (NAO), Linear Extrapolation (LE) or Polynomial Extrapolation (PE); and (3) methods using computer-intensive multi-individual imputations, such as Linear Mixed Effects cubic regression (LME3) and Multiple Imputation by Chained Equation (MICE).
We conducted a simulation study by performing this procedure 1000 time and computing the mean difference between the true and the imputed values, and between the true remission rate (CDAI and DAS28) and the imputed ones.
Results: Results are summarised in Fig. 1. At baseline, all methods underestimated the true values by at least 20%. Despite this, LME3 and MICE were able to provide estimates of baseline remission rates with less than 3% of error. For follow-up data, missingness at 6, 12, or 24 months, NAO, LE and PE led to relative bias of the mean values ≤15%, and almost unbiased remission rate. LOCF and LFE respectively over and under-estimated the mean imputed values up to 20%, leading respectively to a non-negligible under and over-estimation of the remission rate. Although LME3 and MICE had low bias in estimating the mean values, they narrowed the distribution of the imputed values and thus strongly underestimated remission rate

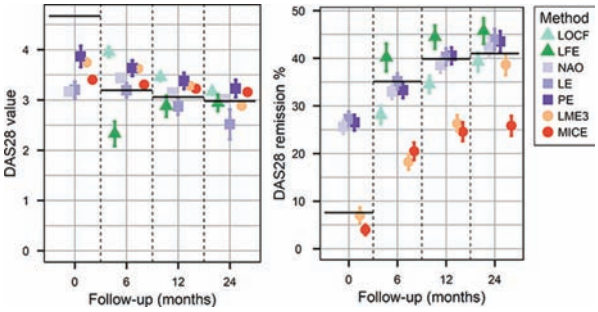


Fig. 1: Mean imputed DAS28 and DAS28 remission rate. Plain lines are the true values.

Conclusion: When imputing disease activity in rheumatoid arthritis register data, researchers should prefer Linear Mixed Effects cubic regression (LME3) for baseline and nearest available observation (NAO) for follow-up data.

REFERENCES

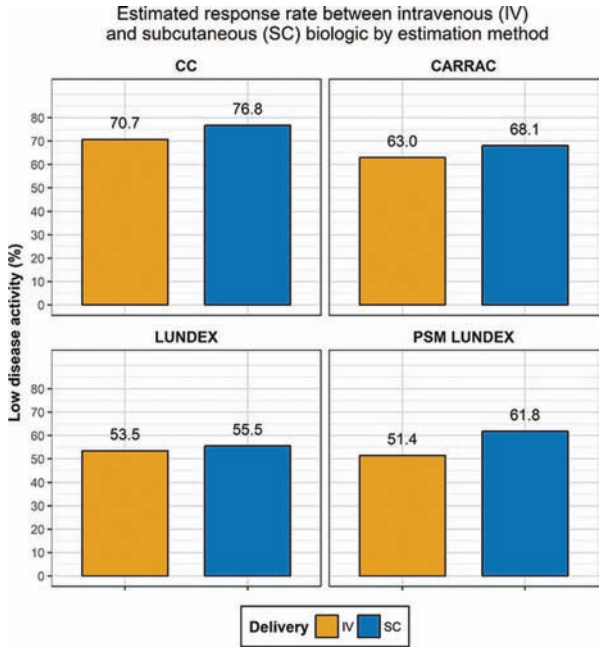
[1] Finckh A, Courvoisier D. Joint Bone Spine 2018;85:271–4. doi:10.1016/j.jbspin.2017.12.005
[2] van der Heijden GJMG, T. Donders AR, Stijnen T, et al. Journal of Clinical Epidemiology 2006;59:1102–9. doi:10.1016/j.jclinepi.2006.01.015
[3] van der Heijde D, Fleischmann R, Wollenhaupt J, et al. Ann Rheum Dis 2014;73:233–7. doi:10.1136/annrheumdis-2013-203697
[4] Descalzo MÁ, Garcia VV, González-Alvaro I, et al. *Rheumatology (Oxford)* 2013;52:331–6. doi:10.1093/rheumatology/kes245

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SAT0588 COMPARATIVE EFFECTIVENESS RESEARCH IN OBSERVATIONAL SETTINGS: EVALUATING TWO NEW METHODS TO ANALYSE RESPONSE RATES

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Background: Researchers typically report the proportion of patients reaching a defined clinical threshold (e.g. EULAR response, low disease activity (LDA) rates) after a set time. Comparing response rates (%rr) in observational settings is hampered by two major threats. 1. Confounding: Patient, disease, and treatment characteristics often differ for each drug. 2. Attrition bias: Assessing%rr after a set time excludes patients who discontinued their treatment, which may overestimate drug effectiveness. Currently, no proposed method accounts for both confounding and attrition.



Objectives: To propose two new methods (3 and 4) to adequately compare%rr in patients with different baseline characteristics, while accounting for attrition and compare them to established methods (1 and 2).
Methods: 1. Complete case (CC)
%rr is computed as the percentage of responders on total patients still on treatment at the given time point.
2. LUNDEX[1]:
CC%rr is corrected for attrition by multiplying it by the Kaplan Meier estimates of the survival (SKM), thus considering all patients not on treatment as non-responders, irrespective of the reason for drug discontinuation.
3. PSM LUNDEX: Propensity Score (PS) Matching LUNDEX
Step A: Select patients in both exposure groups using propensity score matching
Step B: Use the LUNDEX to compute the%rr.
4. CARRAC: Confounder-Adjusted Response Rate with Attrition Correction by reason for drug discontinuation
Step A: Compute estimates of drug survival for the main reasons of drug discontinuation (e.g., ineffectiveness, adverse events, remission, other reasons).
Step B: Estimate%rr using random effect IPD meta-analysis with estimates for each reason of drug discontinuation.
Step C: Combine%rr estimates using weights of step A.
The methods will be illustrated using CDAI LDA (≤10) rates in data from a collaboration of registries[2].
Results: We used 3448 patients treated by a biologic, either intravenously (IV: n=2414) or subcutaneously (SC: n=1034). Before matching, the population differed in terms of body mass index, function (Health Assessment Questionnaire, HAQ), concomitant treatments and erythrocyte sedimentation rate (ESR). Adjustment was done using these potential confounders. For PSM LUNDEX, PS matching was done on a 1:1 basis, yielding 561 patients in each group with similar characteristics.
Estimated%rr differed by more than 20%, depending on the method used (Figure). Compared to CC%rr, both PSM LUNDEX and LUNDEX methods yielded much lower%rr, while the CARRAC method estimated%rr was in between these estimates.
Compared to CC analysis, differences in%rr between the SC and IV groups were smaller for the LUNDEX methods, larger for PSM LUNDEX, and close to CC for the CARRAC method (Figure).
Conclusion: Both LUNDEX methods certainly underestimates the true response rates by considering all patients stopping treatment as non-responders, while complete case method certainly overestimates the%rr by considering patients stopping as having a similar%rr to patients continuing treatment. As expected, the CARRAC method, which accounts for attrition by reason for drug discontinuation, obtained%rr estimates in between complete-case and LUNDEX corrections. Simulation studies are needed to assess the most accurate estimation method.

REFERENCES

[1] Kristensen, et al. 2006 A&R
[2] Lauper, et al. 2018 RMD Open

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SAT0589 A VALIDATED TEXT-MINING ALGORITHM TO EXTRACT RA MEDICATION CONTAINED IN FORMAT-FREE FIELDS OF EMRS

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Background: Rapidly expanding collections of Electronic Medical Records (EMR) form a valuable resource for clinical research. Besides entries with a standardized format, EMRs often also contain free text fields intended for noting specifications of the treatment policy. While these free text fields contain essential information, their free nature makes them hard to parse, as they often contain typos or acronyms. As a result, data extraction from EMR is often performed manually, or is performed while excluding the format-free fields.
Objectives: To develop and validate a text-mining approach to extract medication prescribed for Rheumatoid Arthritis as contained in format-free fields of an EMR.
Methods: The EMR dataset consisted of 2,771 patients that visited the rheumatology outpatient clinic of the Leiden University Medical Centre between 2007 and 2018, resulting in a total of 45,012 EMR entries. We randomly selected 15% and 7,5% of the entries to create a training and test set, with 5,992 and 2,993 entries respectively, which were manually annotated by a trained rheumatologist. The training set was used to design the algorithm, whereas the test set was used as an independent validation of the algorithm's performance of identifying each of the DMARDs and biologicals routinely prescribed for treating RA.
Using methods derived from Natural Language Processing, we developed an algorithm that consecutively performs three tasks: 1. Text pre-formatting 2. Acronym recognition and 3. Typo correction. Text pre-formatting consisted of several simple operations to deal with the most prevalent textual artifacts, including separation of special characters, numbers and punctuation sticking to words.
Ten independent clinicians compiled lists of acronyms for each of the drug routinely prescribed to treat RA. Lastly, for typo correction, we employed the Damerau Levenshtein [1] (DL) distance that determines the similarity between two words by counting the number of single character operations (remove, add, move or replace) required to transform one word into another. Using the training set, we computed for each drug DL distances between all words in the free fields of the EMRs and a particular drug name or its acronym. Using the annotations created in the training set we then determined the DL distance optimally distinguishing between a typo and two similar words with a different meaning.
Results: Fifteen medications for the treatment of RA were present in our sample (see Figure 1). In total, medication was present in 1,789 out of the 2,993 entries. The median DL cutoff for typos was 2 with a standard deviation of 0.96.
The overall accuracy of our drug-identification-algorithm was very good per medication in general (0.97) and the individual test characteristics were high: sensitivity=0.98, specificity=0.95, PPV=0.98 and NPV=0.95. Also on an individual drug-level the performance was high: accuracy>=0.99, sensitivity>=0.89 and specificity>=0.99, NPV>=0.99 and

PPV>=0.90 for all medication except golimumab, which had a low prevalence in our dataset.

Conclusion: We developed and validated an algorithm enabling a highly accurate automated extraction of RA medication from format-free fields of Electronic Medical Records.

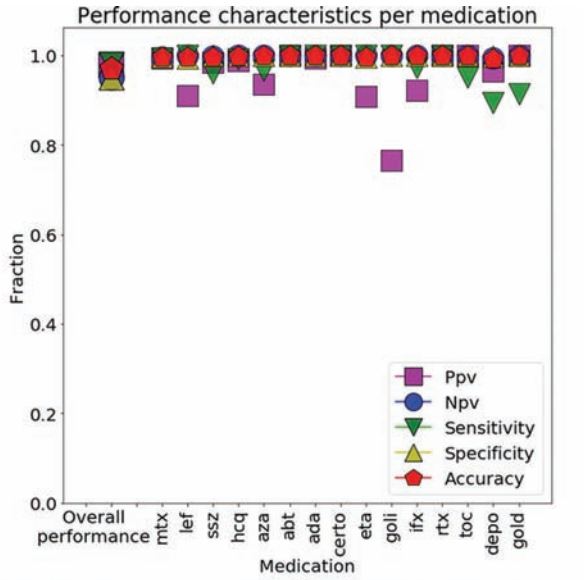


Figure 1: Performance characteristics for the extraction of medication in general and for each medication individually. With the fraction on the Y-axis and the different medications on the X-axis. Where mtx=methotrexate, lef=leflunomide, ssz=sulfasalazine, hcq=hydroxychloroquine, aza=azathioprine, abt=abatacept, ada=adalimumab, certo=certolizumab, eta=etanercept, goli=golimumab, ifx=infliximab, rtx=rituximab, toc=tocilizumab and depo=depomedrol.

REFERENCES

[1] Damerau, Fred J. (March 1964), "A technique for computer detection and correction of spelling errors", Communications of the ACM, ACM, 7 (3): 171–176, doi:10.1145/363958.363994

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SAT0590

AUTOMATED DIAGNOSIS EXTRACTION FROM ELECTRONIC MEDICAL RECORDS WITH MACHINE LEARNINGCLASSIFIERS

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Background: While Electronic Medical Records (EMR) constitute a rich resource for research into various diseases, their unstructured format often poses practical challenges. For instance, retrieval of the records belonging to all patients with a particular outcome is often accomplished with naïve methods such as exact word matching. A more advanced alternative is to employ methods of Machine Learning (ML) for text classification. Rather than requiring a set of rules, an ML-model extracts these rules by itself given sufficient example records with known annotations.

Objectives: To build a reliable classifier with machine learning techniques that can identify Rheumatoid Arthritis (RA) cases in provided EMR entries.

Methods: Data was acquired from the HiX-EMR database consisting of 2,771 patients that visited the rheumatology outpatient clinic of the Leiden University Medical Centre between 2007 and 2018. This database featured a total of 38,216 entries. The first visit entry (if available) was selected per patient for annotation, resulting in a total of 1,361 entries. The annotated sample was then randomly split into an equally sized training and test set. Both sets were preprocessed and then classified with the following methods: Exact word-matching, Naive Bayes (NB), Decision Tree, Gradient Boosting (GB), Neural Networks and Support Vector Machines (SVM), see table 1 for more information. Classification of the naïve word-matching model was based on the presence of the Dutch RA-defining terms 'Reumatoïde Artritis' and 'RA'. Default Scikit-learn implementations [1] were used to create the ML-models.

Finally, the performance of the models was evaluated with a receiver operating characteristic (ROC) curve analysis via the pROC R-package [2]. The Delong test was used to assess the 95% confidence intervals (CI) and to determine the difference in performance between the word-matching method and the ML-models.

Table 1: Overview of the different characteristics for each classifying method.

Classifying Method	*Probabilistic*	*Multi-class*	*Description*
Exact word-matching	-	+	Utilizes a list of words a.k.a. textual patterns to classify the data
NB	+	+	Simple probabilistic model that treats every feature independently
Neural Networks	-	+	Utilizes multiple 'hidden' layers with weighted connections in between to form a 'response'
GB	+	+	Composition of multiple weak learners (decision trees in this case)
Decision Tree	-	+	Builds a flowchart-like structure and classifies based on multiple binary decisions
SVM	-	+	Defines the most optimal boundary (hyperplane) between classes

Note: Probabilistic = model returns probabilities, Multiclass= model can be applied to data with multiple classes, Description= classifying approach of model.

Results: The exact word-matching approach resulted in an area under the curve (AUC) of 0.76 (CI: 0.7265-0.7783), see figure. Likewise, the ML-models resulted in relatively high AUC-scores (CI) as well: NB =0.83 (0.80-0.86), SVM=0.91 (0.89-0.93), Neural Networks=0.92 (0.90-0.94) and the GB-method with a 0.94 (0.92-0.96). The Decision Tree showed the worst performance with an AUC-ROC of only 0.51 (0.49-0.56). In comparison to the exact word-matching ROC-curve, all the ML-models showed a significant difference: Decision Tree (p<2.2e-16), NB (p= 0.004), Neural Networks (p<2.2e-16), GB (p<2.2e-16) and the SVM (p=4.0e-16).

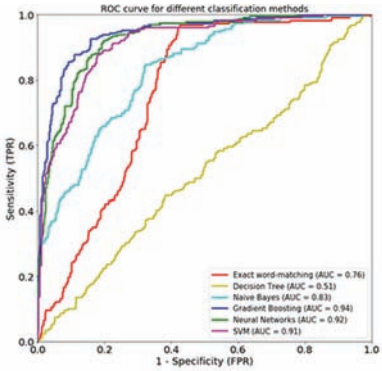


Figure 1: ROC-curve applied on both the ML-methods and the naïve exact word-matching method

Conclusion: The Gradient Boosting, Neural Networks, SVM and Naïve Bayes models all showcased a significantly better performance than a naïve exact word matching, which establishes these ML-methods as an efficient approach for data extraction from EMR.

REFERENCES

[1] Pedregosa, F. et al. JMLR (2011) 12: 2825-2830
[2] Robin, X. et al. BMC Bioinformatics. (2011) 12: 77

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SAT0591 A CLINICAL TOOL FOR AUTOMATED PREDICTION OF HIP AND MAJOR OSTEOPOROTIC FRACTURES USING ELECTRONIC MEDICAL RECORDS DATA: THE EPIC STUDY

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Background: With increasing availability of patient data in healthcare, there is an unprecedented opportunity for prediction tools that can be automatically implemented in electronic medical records system.
Objectives: We aimed to develop and validate a fracture prediction tool that leverages patient data as routinely available in primary care computerized records.
Methods: We conducted a population-based cohort study. Data was extracted from all subjects registered in the SIDIAP database on 1/1/2012, with data for 1+ years, and aged 50 years or older on that date. SIDIAP contains primary care records linked to pharmacy dispensations for >6 million people, equivalent to >80% of the population of Catalonia. Participants were followed up until the earliest of death, transfer out/migration, or end of 2017.
Two models were developed to predict hip fracture (main outcome) and major osteoporotic (hip, clinical vertebral, wrist/forearm, and proximal humerus) fracture risk over 5 years.
Potential predictors were pre-specified based on previous literature and combined in Cox models to derive prediction tools. Internal validation was performed using c-statistic for discrimination, and observed vs predicted plots for calibration. Multiple imputation with chained equations was used to minimize the impact of missing data on body mass index, smoking, and alcohol drinking. Bootstrapping methods were used to select key predictors to be combined in the final resulting models.
Results: A total of 1.76 million people (9.76 million person-years) were included, 50.7% women, of average age 65.4 years old. A 10.1% and 7.4% were lost to follow-up over 5 years due to mortality and migration respectively.
Fracture rates were 3.57/1,000 person-years [95%CI 3.53-3.60] for hip and 11.61 [11.54-11.68] for major fracture. Key predictors of increased fracture risk included age, female gender, history of falls or previous fractures, specific medication/s use (insulin, GnRH inhibitors, anticonvulsants, sedatives, SSRI, antipsychotics), and a history of diabetes mellitus (type 1>type 2), cerebrovascular disease, ischemic heart disease, COPD and anorexia nervosa. Variables associated with lower fracture risk included use of statins, thiazidic diuretics, and overweight/obesity.
Combined, these resulted in a c-statistic of 84.9% for hip and 72.9% for major fracture. Calibration was excellent for both outcomes.
Conclusion: We have developed and validated a clinical prediction tool for 5-year hip and major osteoporotic fracture risks. The algorithm has excellent performance and can be installed in electronic primary care records systems for automated risk calculations at the population level. More research is needed on the transportability and external validity of this prediction tool.
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SAT0592 THE IMPACT OF ORAL GLUCOCORTICOIDS ON THE DEVELOPMENT OF CATARACTS AND GLAUCOMA IN INCIDENT RHEUMATOID ARTHRITIS PATIENTS

Rachel Black[1,2,3,4], Susan Lester[2,3], [1,2]Catherine Hill[3], [4,5]Will Dixon[6]. *[1]Royal Adelaide Hospital, Rheumatology Unit, Adelaide, Australia*; *[2]The Queen Elizabeth Hospital, Rheumatology Unit, Adelaide, Australia*; *[3]The University of Adelaide, Adelaide, Australia*; *[4]University of Manchester, Arthritis Research UK Centre for Epidemiology, Manchester, United Kingdom*; *[5]University of Manchester, Health eResearch Centre, Farr Institute for Health Informatics Research, Manchester, United Kingdom*; *[6]University of Manchester, NIHR Manchester Biomedical Research Centre, Manchester, United Kingdom*

Background: Cataracts and glaucoma are recognised glucocorticoid (GC) adverse effects. However, the impact of GC use, dose and timing on the development of cataracts and glaucoma has not been well quantified.
Objectives: 1. To determine the association between GC use and dose and the development of cataract and glaucoma in patients with incident RA, 2. To determine the lag effect of GC dose.
Methods: Data were used from the Clinical Practice Research Datalink (CPRD), a large UK primary care database derived from an electronic medical record (Jan 1992- Dec 2017). RA patients were identified using a validated algorithm and only incident patients were included. Parametric log-logistic survival models were used to assess the impact of GC use, dose (prednisolone daily dose equivalent) and lagged dose (at 1, 3, 6 months, 1 & 2 years). A square root transformation of dose was used for the cataract models. Smoking, gender and uveitis were included as covariates in the model and age was used as the timescale. Comorbidities on the causal pathway, such as diabetes and hypertension, were not included. Results were reported as odds ratios (OR) for the cumulative incidence.
Results: There were 22607 patients with incident RA (median age 66, IQR 37-84, 68% female), of which 241 had cataracts and 164 had glaucoma on or before baseline. Median duration of follow up was 8.7 years (IQR 1.8-19.8) and 39% were ever GC users during follow up. The incidence rate, per 1000 patient-years was 12.3 (95% CI 11.8, 12.9) for cataracts and 3.1 (95% CI 2.8, 3.4) for glaucoma, and increased with age. Uveitis was an important predictor for both cataracts and glaucoma, and cataracts were more frequent in females. GC use and GC dose were associated with both cataracts and glaucoma (Table 1). In the multivariable lagged dose analysis, GC dose at 1-year prior had the greatest effect size for cataracts (OR 1.26, 95% CI 1.12, 1.42), whereas GC dose at 3-months prior had the greatest effect size for glaucoma (OR 1.06, 95% 1.01, 1.11).

Table 1

CATARACTS		GLAUCOMA	
GC	Adjusted OR (95% CI)	GC	Adjusted OR (95% CI)
GC +/-	2.28 (1.90, 2.73)	GC +/-	1.63 (1.22, 2.16)
√GC dose	1.42 (1.31, 1.53)	GC dose	1.07 (1.03, 1.11)

Conclusion: The quantification of the risk associated with GCs and the development of cataract and glaucoma is of clinical utility in daily practice. EULAR guidelines recommend patients are informed of the risks and benefits of GC treatment prior to commencement, however the risk of these potential adverse effects had not previously been quantified. This information will allow patients to make better-informed treatment choices in conjunction with their treating doctor.
Disclosure of Interests: None declared
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SAT0593 INCIDENCE OF RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND SPONDYLOARTHRITIS AND THEIR ASSOCIATED COMORBIDITIES IN A BELGIAN GP REGISTRY

Sofia Pazmino[1], Veerle Stouten[1], Patrick Verschueren[1,2], Pavlos Mamouris[3], Rene Westhovens[1,2], Kurt de Vlam[1,2], Delphine Bertrand[1], Kristien Van der Elst[2], Bert Vaes[3], Diederik De Cock[1]. *[1]KU Leuven, Skeletal Biology and Engineering Research Centre, Leuven, Belgium*; *[2]University Hospitals Leuven, Rheumatology, Leuven, Belgium*; *[3]KU Leuven, Department of Public Health and Primary Care, Leuven, Belgium*

Background: Rheumatoid arthritis (RA), psoriatic arthritis (PSA) and spondyloarthritis (SPA) are the most common inflammatory rheumatic diseases

and all of them are associated with a high burden of comorbidities. Incidence of these diseases and of their comorbidities are unknown in Belgium.

Objectives: To determine incidences of disease and comorbidities in patient populations of RA, PSA and SPA in a General Practitioners (GP) setting.

Methods: Data were obtained from Intego over a 13-year time interval from 1999 to 2012. Intego is a Flemish GP-based morbidity registration network hosted at the Academic Center for General Practice of KU Leuven, covering 2% of the Flemish general population, Patients classified under the International Classification of Primary Care codes L88 (rheumatoid/seropositive arthritis) and L99 (musculoskeletal disease other) were selected for this study. Experienced rheumatologists verified if the keywords mapped to these codes corresponded to a diagnosis of RA/SPA/PSA. The entry date of these diagnoses in Intego was considered "baseline". Yearly disease incidence and comorbidity incidence over 3 years are presented. The following comorbidities with high impact on outcomes like disability, costs, hospitalization and death were considered: lung disease, cardiovascular disease including myocardial infarction, stroke or other heart condition, hypertension, fracture of the spine/hip/leg, depression, diabetes mellitus, digestive disease including ulcers and stomach disorders and malignancies [1].

Results: Over a 13-year period, 817, 258 and 190 patients were included with a diagnosis of RA, SPA or PSA, respectively. The average incidence of RA was 0.47, of SPA 0.15 and of PSA 0.11 per 1000 person years. Fig1 gives the yearly incidence per disease.

The RA cohort had a mean(SD) age of 57.7(17.2) with 68% being women. The SPA cohort had a mean(SD) age of 40.6(15.1) with 50% being women. The PSA cohort had a mean(SD) age of 47(13.2) with 48% being women.

The comorbidity with the highest prevalence (23%) and incidence (29.6/1000 person years) in RA was hypertension. In the SPA cohort, digestive disease was most common at baseline (14%) and during follow-up (21.0/1000 person years). PSA patients presented most frequently with depression at baseline (18%) and during follow-up (9.8/1000 person years). RA patients presented with a higher number of incident cases of diabetes (17.7/1000 person years) compared to SPA or PSA patients. (See table 1)

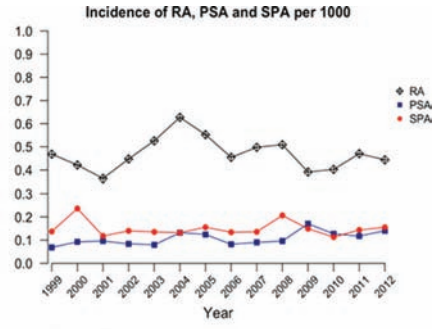


Fig1: Yearly incidence per disease per 1000

Table 1: Comorbidities at baseline and incidence rate after a 3-year follow up period

	RA n=817		SPA n=258		PSA n=190	
	Comorbidities BL or before n (%)	Incidence comorbidities n (CI)	Comorbidities BL or before n (%)	Incidence comorbidities n (CI)	Comorbidities BL or before n (%)	Incidence comorbidities n (CI)
Lung Disease	112(14%)	30(16.16)	18(7%)	5(7.86)	23(12%)	4(9.25)
Cardiovascular disease	133(16%)	43(24.09)	12(5%)	4(6.14)	17(9%)	10(23.01)
Hypertension	187(23%)	48(29.62)	18(7%)	5(7.85)	28(15%)	6(14.39)
Fracture	45(6%)	20(9.66)	5(2%)	6(8.93)	11(6%)	3(6.48)
Depression	98(12%)	14(7.26)	19(7%)	4(6.25)	35(18%)	4(9.82)
Diabetes mellitus	81(10%)	34(17.7)	8(3%)	2(3.00)	11(6%)	4(8.73)
Digestive disease	131(16%)	28(15.59)	36(14%)	12(20.96)	31(16%)	4(9.9)
Malignancies	23(3%)	21(11.72)	4(2%)	3(4.43)	11(6%)	7(15.94)

n = number, BL = baseline, CI = crude incidence rate per 1000 calculated as the number of new cases divided by the total persons years of persons at risk (not having comorbidity at baseline) with a maximum of 3 years of follow-up per person.

Conclusion: The incidence of RA appears to remain stable while incidence of PSA - and to a lower extent SPA - seem to increase over a 13-year interval. A control cohort will be formed to improve comparability of comorbidity presence, yet from these preliminary results we can determine that an important subpopulation of patients with rheumatic diseases already presents with significant comorbidities at baseline, or during 3-year follow-up. This study highlights the growing issue of multimorbidity in patients with musculoskeletal diseases and the importance of a holistic approach to manage these patients.

REFERENCES

[1] England BR, Sayles H, Mikuls TR, Johnson DS, Michaud K. Validation of the rheumatic disease comorbidity index. Arthritis Care Res (Hoboken) 2015;67(6):865-72.

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SAT0594

ADVERSE AUTOIMMUNE EVENTS IN CANCER PATIENTSTREATED WITH IMMUNOTHERAPY. ANALYSIS OF CASES BETWEEN 2011 AND 2018

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Background: Immunotherapy has revolutionized the treatment of cancer. The use of checkpoints inhibitors aimed at stimulating the immune system to mediate regression of established malignant tumors has shown a noticeably increase in the last decade. However, immunotherapy has been associated with side effects novel to cancer patients such as immune-related adverse events (IAEs) that can affect any organ or system, either during the course of immunotherapy or once the treatment was completed.

Objectives: To survey the occurrence and type of AAEs in 190 cancer patients treated with immunotherapy between 2011 and 2018.

Methods: We surveyed the occurrence of IAEs in cancer patients who received immunotherapy in the Oncology Service at 'Virgen del Rocío' University Hospital (Seville, Spain) between 2011-2018. The types of cancer present in the patients analysed included: non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), melanoma, kidney cancer, bladder cancer and others. The checkpoints inhibitors analysed included Ipilimumab (CTLA-4), Nivolumab (PD-1), Pembrolizumab (PD-1) and Atezolizumab (PD-L1). The nature of IAEs (rheumatic/non-rheumatic), the magnitude of complaint (mild/moderate/severe) and the outcome of patients depending on IAEs management was analysed. Finally, we used a multivariate analysis in search for patterns in IAE occurrence depending on cancer type, patient and treatment factors.

Results: A total of 190 patients were collected, 143 men and 47 women having NSCLC (51.1%), melanoma (25.3%), kidney cancer (6.8%), bladder cancer (5.3%), SCLC (2.1%) and others. They received immunotherapy with Atezolizumab (15.8%), Ipilimumab (4.7%), Nivolumab (61.1%) and Pembrolizumab (18.4%). Overall, 28 patients (14%) developed an AAE secondary to immunotherapy. Four of them involved rheumatic diseases (1 seronegative polyarthritis, 1 inflammatory myopathy and 2 rheumatic polymyalgia), whereas other non-rheumatic diseases were observed: 13 endocrine (12 thyroiditis and 1 DM type I debut with ketoacidosis), 5 pulmonary (pneumonitis), 3 dermatological (2 atopic dermatitis and 1 psoriasis), 2 digestive (colitis and autoimmune pancreatitis) and 1 neurological (hypophysitis). The drug that showed the highest occurrence of IAEs was Nivolumab (30%). In these patients, IAEs were associated with a median number of cycles of 7 (Q_1 = 4, Q_3 = 17.7, non-parametric data, Shapiro-Wilk test, p <0.0001). Mild adverse events occurred in 60% of patients

with IAEs, for which immunotherapy was not suppressed. However, the medication was suppressed in the remaining 40% of the cases. Exceptionally, one patient underwent a severe IAE (pneumonitis) that resulted in death. In terms of the occurrence of IAEs, there was no difference between sexes (men 6.3%, women 6.4%). The rheumatic IAEs responded well to treatment with corticosteroids without further biological treatments or DMARDs.

Conclusion: Immunotherapy is changing the typology of side effects in cancer patients, including IAEs. The cases analysed showed a relatively small number of rheumatic events that were easily solved with corticosteroids (nor the immunotherapy treatment was suppressed or immunosuppressive treatment was necessary). The study highlights the benefits of involving multidisciplinary medical teams to manage oncologic patients treated with immunotherapy towards the early detection and treatment of IAEs.

REFERENCES

[1] Michael A. Postow, M.D., Robert Sidlow, M.D., and Matthew D. Hellmann, M.D. Immune-Related Adverse Events Associated with Immune Checkpoint BlockadeN Engl J Med 2018; 378:158-168. DOI: 10.1056/NEJMra1703481

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SAT0595

DIRECT COMPARISON OF CERTOLIZUMAB PEGOL, ABATACEPT AND BIOSIMILAR INFLIXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED IN ROUTINE CARE. OBSERVATIONAL DATA FROM THE DANISH DANBIO REGISTRY ANALYZED LIKE A RANDOMIZED CLINICAL TRIAL

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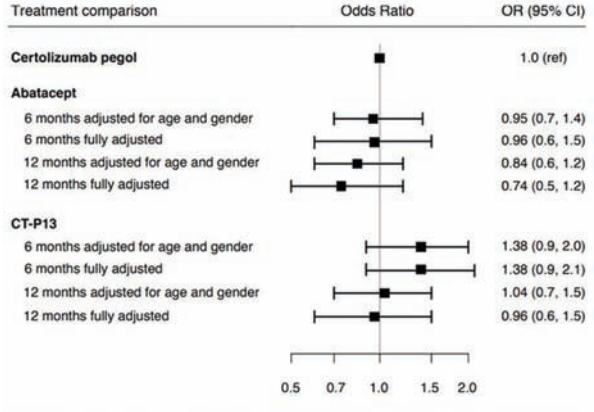
Background: Nationwide Danish guidelines regarding RA patients (pts) initiating bDMARDs are issued approximately annually. For bio-naïve pts on concomitant methotrexate (MTX) the recommended drugs (year, recommended compliance) were: certolizumab pegol(CTZ)(2013-2014, 80%)/abatacept(ABA)(2014-2015, 80%)/biosimilar infliximab(CT-P13)(2015-2016, 50%). We hypothesized that the guidelines could be perceived as a surrogate randomization tool where calendar-time rather than patient-specific factors defined choice of bDMARD.

Objectives: To assess compliance to guidelines (justifying the assumption of surrogate randomization) and compare effectiveness of CTZ/ABA/CT-P13 in Danish RA patients treated according to guidelines.

Methods: Observational cohort study analyzed like a randomized clinical trial (RCT, intention-to-treat). RA patients were identified in DANBIO. Compliance in each calendar period was defined as number of pts adherent to guideline/numbers of all bio-naïve pts initiating bDMARD +MTX. Outcomes were DAS28-remission-rates (at 6 and 12-months) and one-year retention rates, compared across treatments (confounder-adjusted multivariable logistic and Cox regression analyses).

Results: Compliance to guidelines was 70%/65%/59%, and 776 patients were included (CTZ/ABA/CT-P13: 336/215/225). Baseline characteristics were similar across drugs. DAS28 remission-rates after 6 and 12 months were: 37%/34%/44% and 37%/33%/36%, respectively. Adjusted odd ratios for achieving DAS28 remission were at 6 months: 0.96(95% CI: 0.6;1.5) for ABA and 1.38(0.9;2.1) for CT-P13; 12 months: 0.74(0.5;1.2) and 0.96 (0.6;1.5), CTZ reference drug(figure). The adjusted hazard ratios for withdrawal were 1.16(95% CI: 0.84;1.60) for ABA and 0.83 for CT-P13 (0.59;1.17)(table).

Figure. Confounder-adjusted odds ratios (OR) for achieving DAS28 remission at 6 and 12 months. Results of logistic regression analyses.



Fully adjusted: adjusted for baseline age, gender, DAS28, HAQ, smoking and CCI. Patients with missing DAS28 or HAQ data excluded. Abbreviations: DAS28: Disease activity score of 28 joints, HAQ: Health assessment questionnaire, CCI: Charlson comorbidity index.

Table. RA patients starting first bDMARD according to Danish national guidelines during the three calendar periods. Baseline characteristics and adjusted hazard ratios (HR) for withdrawal during the first year of treatment (Cox regression analyses).

	Certolizumab pegol N=336	Abatacept N=215	CT-P13 N=225
Calendar time periods for guideline	Jan 2013 - July 2014	July 2014-July 2015	July 2015-July2016
Expected compliance to guideline	80%	80%	50%
Actual compliance to guideline	70%	65%	59%
Age, years	57 (48-65)	57 (48-65)	59 (50-66)
Female	71%	72%	68%
Hazard ratio for withdrawing from treatment			
0-90 days			
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Adjusted for age and gender	1.0 (ref)	0.78 (0.45 to 1.36)	0.63 (0.35 to 1.13)
Fully adjusted*	1.0 (ref)	0.70 (0.39 to 1.27)	0.58 (0.33 to 1.10)
91-365 days			
Adjusted for age and gender	1.0 (ref)	1.15 (0.85 to 1.56)	0.74 (0.53 to 1.04)
Fully adjusted*	1.0 (ref)	1.16 (0.84 to 1.60)	0.83 (0.59 to 1.17)

Variables are median (IQR) unless otherwise mentioned. *age, gender, DAS28, HAQ, smoking, CCI Abbreviations: CCI: Charlson Comorbidity Index: CI: confidence intervals, DAS28: Disease Activity Score of 28 joints, HAQ: Health assessment questionnaire

Conclusion: Compliance to guidelines was high. Direct comparison showed that remission and retention rates were highest for CT-P13, intermediate for certolizumab and lowest for abatacept. Results should, however, be interpreted with caution due to wide CIs and risk of residual confounding.

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SAT0596

RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS AND A LOW-INTERMEDIATE Á PRIORI RISK OF CORONARY ARTERY DISEASE AFTER INITIAL CT-BASED DIAGNOSIS AND TREATMENT A REGISTRY-BASED FOLLOW-UP STUDY USING DATA FROM THE WESTERN DENMARK HEART REGISTRY

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Background: Rheumatoid arthritis (RA) is a known risk factor for developing coronary artery disease (CAD). The influence of RA on the prognosis after initial diagnosis and treatment of CAD is however largely unknown.
Objectives: To examined the risk of major cardiovascular events among RA and non-RA patients with chest pain referred to cardiac computed tomography (CCT).
Methods: This was a follow-up study, using data from the Western Denmark Heart Registry[1]. Information on RA diagnosis and co-variates were identified through nationwide administrative registers. The primary outcome was a combined outcome including, myocardial infarction, ischemic or uspecified stroke, coronary artery bypass grafting, percutaneus coronary intervention, *and all-cause mortality. In the studied region, RA-f*lares are controlled through escalation of disease modifying drugs and intra-articular or intramuscular glucocorticoid injections (GCI). Hence, the number of times a patient had received GCIs 3 years prior to the CCT were used as a surrogate marker of *disease activity*. Analyses were performed for overall RA and the serological subtypes: 'seropositive RA'(ICD-10: M05) and 'other RA'(ICD-10: M06).
Median time until events or censoring was 3.5 years (min/max: 0.0: 9.2). Cox proportional hazard models were used to examine the association between RA/non-RA patients and outcomes.
Results: Among 42,257 patients, referred between 2008 and 2016, we identified 358 (0.8%) with RA. An increased risk was seen in RA compared to non-RA (adjusted hazard ratio (HR) 1.35 (95% CI: 0.93; 1;96)). An additional risk was found among patients who had received flare treatment more than once prior to CCT (adjusted HR 1.80 (95% CI: 1.08; 3.00)), and in patients with sero-positive RA (adjusted HR: 1.42 (95% CI: 0.93; 2.16)).
Conclusion: In patients with low-intermediate a priori risk of CAD, we found an association between RA and the combined primary outcome, supporting that RA per se, but in particular sero-positive and active RA, increase the risk of cardiovascular events even after initial CAD diagnosis and treatment.

REFERENCES

[1] Nielsen LH, et al. The Western Denmark cardiac Computed Tomography Registry: a review and validation study. Clinical epidemiology 2014, Dec 31; 53-64

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SAT0597

RISK OF HEART FAILURE FOLLOWING EXPOSURE TO NON-TNFI COMPARED TO TNFI BIOLOGICS IN US PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Biologic disease modifying drugs including TNF-inhibitors (TNFi) and non-TNFi agents have become cornerstone of rheumatoid arthritis (RA) management. Case reports on new-onset heart failure (HF) following TNFi initiation led to an FDA black box warning released in October 2001. Subsequent observational studies have shown no association or even a protective effect of TNFi for HF, but the black box warning is still in place. There is a lack of knowledge regarding the risk of HF following exposure to the newer non-TNFi biologics.
Objectives: We aimed to assess the risk of incident HF following exposure to non-TNFi compared to TNFi biologics.
Methods: Using US claims data from Truven MarketScan (2004-2016), we conducted a cohort study of RA patients who initiated a 'TNFi' (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab), or 'non-TNFi' biologic or targeted synthetic DMARD (abatacept, anakinra, tocilizumab, tofacitinib). Patients were excluded if they were <18 years old, had previous HF, an implantable cardiologic device, or a loop-diuretics prescription. Patients were followed from the day after treatment initiation until the earliest event of the following: death, insurance disenrollment, treatment switching or discontinuation. The primary outcome of incident HF was defined based on primary inpatient diagnosis. Cox proportional hazards regression compared risk of HF among new users of non-TNFi compared to TNFi. To control for confounding, we used multivariable adjustment as well as propensity score (PS) adjustment by decile with trimming.
Results: A total of 13,290 non-TNFi patients were included, primarily consisting of abatacept (65%), tocilizumab (17%), and tofacitinib (15%). For the TNFi group, we identified 67,892 patients, primarily consisting of etanercept (42%), adalimumab (37%), and infliximab (15%). More patients treated with non-TNFi were female, older, had higher proportion of comorbidities and number of rheumatologist visits; but lower proportion of NSAID/Coxib use, Table 1. The crude hazard ratio (HR) of HF after initiating a non-TNFi was 1.28 (95%CI 0.75-2.18) versus TNFi. After confounding adjustment in a multivariable model, the HR was attenuated to 1.08 (95%CI 0.57-2.05). The PS adjusted analysis showed consistent results (Table 2).
Conclusion: In this large US-based cohort of 81,182 RA patients, we found no difference in the risk of incident HF after initiation of non-TNFi biologic or targeted synthetic DMARD versus TNFi.

Table 1. Patient characteristics in 1 year prior to treatment initiation.

	Non-TNFi, n (%)	TNFi, n (%)
Number of patients, n	13,290	67,892
Females	10,907 (82.1)	51,066 (75.2)
Age, mean (SD)	53.3 (12.6)	51.6 (12.7)
Diabetes	1,852 (13.9)	8,481 (12.5)
Hyperlipidemia	3,982 (30.0)	18,304 (27.0)
Hypertension	6,831 (51.4)	30,951 (45.6)
Myocardial infarction	60 (0.5)	222 (0.3)
Renal dysfunction	464 (3.5)	1,601 (2.4)
Stroke or TIA	228 (1.7)	884 (1.3)
Oral steroids	9,504 (71.5)	46,322 (68.2)
NSAIDs or coxibs	6,066 (45.6)	37,023 (54.5)
Number of rheumatology visits, mean (SD)	13.8 (19.9)	9.4 (14.4)

Table 2,. Risk of HF in non-TNFi versus TNFi initiators.

	Number of patients	Number of person-years	Number of events	Incidence rate 1,000 person-years	Crude HR (95% CI)	Fully adj. HR (95% CI)	PS adj. HR (95% CI)
Non-TNFi	13,284	14,821	16	1.08	1.28 (0.75-2.18)	1.08 (0.57-2.05)	0.98 (0.51-1.88)
TNFi	67,860	102,425	89	0.87		Ref.	

Covariates included in adjusted and PS models: year of cohort entry, age, gender, region, comorbidities, prior drug-use, and health utilization.
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SAT0598

RHEUMATIC IMMUNE RELATED ADVERSE EVENTS ASSOCIATED WITH CANCER IMMUNOTHERAPY: A NATIONWIDE MULTI-CENTER CANADIAN COHORT FROM THE CANADIAN RESEARCH GROUP OF RHEUMATOLOGY IN IMMUNO-ONCOLOGY (CANRIO)

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Background: Immune checkpoint inhibitors (ICI) have revolutionized cancer therapy by harnessing the immune system to fight cancer. As the indications for ICI continue to expand, their success in advanced stage malignancies is tempered by the development of autoimmune toxicities, referred to as immune-related adverse events (irAE). Rheumatic irAE (Rh-irAE), particularly arthralgias and arthritis are common and optimal management remains unknown.

Objectives: The Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO) is an emerging network of Canadian rheumatologists with an interest in Rh-irAE secondary to ICI. We describe the clinical presentation and management of Rh-irAE associated with ICI in patients seen at 9 CanRIO sites.

Methods: Patients presenting with rheumatic symptoms associated with ICI therapy between 2013 and January 2019 at participating CanRIO sites were identified. Cases were stratified based on the presence or absence of pre-existing autoimmune disease (PAD). Standardized data were extracted by chart review. The data were pooled and analyzed descriptively.

Results: 118 patients without PAD who developed 140 Rh-irAE were identified, 59% were male with a mean age of 62 years. Common indications for ICI were melanoma (n=57, 48.3%), lung (n=30, 25.4%), and genitourinary cancer (n=19, 16.1%). ICI included nivolumab (n=30, 25.6%), pembrolizumab (n=38, 32.5%), ipilimumab (n=1, 0.9%), durvalumab (n=3, 2.6%), atezolizumab (n=4, 3.4%) or combination therapy (n=29, 24.8%). Common Rh-irAE included symmetric polyarthritis (n=45, 32%), arthralgias/myalgias or acute flare of osteoarthritis (n=20, 14.3%), polymyalgia rheumatica-like presentation (n=17, 12%), tenosynovitis/enthesitis (n=17, 12%), sicca syndrome (n=11, 7.9%) and myositis (n=9, 6.4%). 20 patients with PAD were identified, 70% of whom were in remission prior to starting ICI. 50% (n=10) had flares, 15% (n=3) developed a new Rh-IrAE and 20% (n=4) developed O-irAE.

53% experienced at least one other non-rheumatic irAE (O-irAE) (n=63). Mean time from first ICI exposure to onset of Rh-irAE was 6.8 months. In 65% ICI was held or discontinued (n=77). Despite this, 68.6% (n=81) had favorable tumor response, while 12% (n=14) had tumor progression. There were no deaths related to Rh-irAE.

The majority of patients without PAD had partial or complete response to mono or combination therapy with oral prednisone (n=77; maximum dose 60 mg/d), nonsteroidal anti-inflammatories (NSAID; n=52), intra-articular corticosteroids (n=29), hydroxychloroquine (n=26), methotrexate (n=17), or tumor necrosis factor alpha inhibitors (n=9).

Conclusion: This is the largest multi-centered cohort of Rh-irAE described to date. Seronegative inflammatory polyarthritis was the most common Rh-IrAE although a broad range of conditions were identified. The most common first-line treatment was systemic corticosteroids followed by NSAID and intra-articular steroid injections. Prednisone was effective, however higher doses were required. Disease-modifying antirheumatic drugs (DMARD) and biologic therapy were well tolerated and effective, with hydroxychloroquine being the most commonly used DMARD. Despite moderate to high doses of immunosuppression, the majority of patients had favorable tumor responses.

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SAT0599

EXPLORING HETEROGENEITY IN RHEUMATOID ARTHRITIS: OUTCOMES UP TO 4 YEARS OF FOLLOW-UP IN PATIENT CLUSTERS IDENTIFIED BY DATA-DRIVEN ANALYSIS OF THE BRASS REGISTRY

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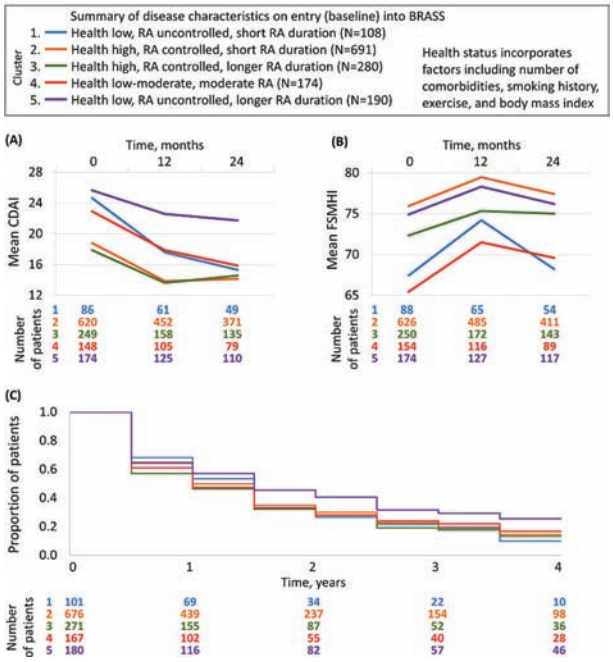
Background: Patients with rheumatoid arthritis (RA) may share characteristics that relate to their future outcomes.

Objectives: To investigate clinical outcomes over a 4-year follow-up period in objectively identified RA patient clusters derived empirically via a data-driven approach using the BRASS registry.

Methods: Patient clusters were identified by principal components (PC) and cluster analysis of demographic, socio-economic, health and disease characteristics of patients on entry (baseline) into the BRASS registry. Patients in BRASS are followed in the clinic at least annually and are sent questionnaires at 6-month intervals. Mean score was calculated at 12- and 24-months follow-up as observed for Clinical Disease Activity Index (CDAI), Disease Activity Score 28-joint count C-reactive protein (DAS28-CRP), BRASS self-administered Rheumatoid Arthritis Disease Activity Index (RADAI), swollen and tender joint count (SJC and TJC), Multidimensional Health Assessment Questionnaire (MDHAQ), and Functional Status Mental Health Index (FSMHI). Time to first infection and to first RA medication change over 4 years was analysed via Kaplan-Meier curves.

Results: PC analysis of variables among 1443 patients recorded at entry into BRASS identified 41 PCs that capture the fundamental characteristics involved in RA. These PCs informed the identification of 5 novel patient clusters. Cluster 1 patients ("health low, RA uncontrolled, shorter RA duration") exhibited the greatest reduction in TJC. Cluster 2 patients ("health high, RA controlled, shorter RA duration") remained free of infection longer than other clusters. Cluster 3 patients ("health high, RA

Figure. (A) mean Clinical Disease Activity Index (CDAI), (B) mean Functional Status Mental Health Index (FSMHI), (C) time to first change in baseline conventional synthetic or biological disease-modifying antirheumatic drug in five objectively identified patient cluster phenotypes



controlled, longer RA duration") sustained the lowest mean SJC throughout follow-up. Cluster 4 patients ("health low–moderate, moderate RA") exhibited the greatest improvement in mental health (FSMHI; Figure). Cluster 5 patients ("health low, RA uncontrolled, longer RA duration") exhibited the highest CDAI scores (Figure) and maintained baseline line of therapy the longest.

Conclusion: Five patient clusters identified by data-driven PC analysis of the BRASS registry exhibited distinct patterns of clinical outcome and management over a 4-year follow-up period. The clinical outcomes data suggest the clusters represent clinically meaningful categories of RA and illustrate the potential of data-driven patient profiling as a tool to support personalized medicine in RA. Validation in an independent dataset is ongoing.

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SAT0600 COMPARATIVE CARDIOVASCULAR SAFETY OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) AMONG INDIVIDUALS WITH OSTEOARTHRITIS; FINDINGS FROM PROVINCIAL PRESCRIPTION CLAIM RECORDS IN BRITISH COLUMBIA, CANADA

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Background: Osteoarthritis (OA) has been reported as an independent risk factor for cardiovascular diseases (CVD) (1). Furthermore, mediating role of NSAIDs in the observed OA-CVD association has also been noted (2). Thus, a substantial proportion of the total risk of CVD among OA patients compared to non-OA controls was attributable to NSAID use (2). This is particularly worrisome as there is no cure for OA and NSAIDs are the mainstay of treatment in controlling the primary symptoms of pain and inflammation among OA patients. However, only a handful of observational studies evaluated the risk of a specific NSAID among OA patients for a specific CVD event such as myocardial infarction (MI) (3). The overall cardiovascular safety of NSAIDs used in treating OA in the real-world therefore remains unknown.

Objectives: To evaluate the comparative safety of various NSAIDs against CVD when treating patients with OA.

Methods: We used linked health administrative data (HAD) of a previously assembled, population-based cohort of 720,055 British Columbians from Canada. We identified individuals with OA who received at least one NSAID prescription from January 1996 to December 2013. Eligible study subjects were at least 20 years old, did not have CVD and had not received an NSAID prescription within the last 90 days from their OA diagnosis date. We defined composite CVD outcome from hospital discharge abstract database, payment information file of Medical Services Plan and vital statistics deaths data file using ICD-9 or ICD-10 codes. We created an NSAID exposure variable in a time-dependent fashion in which individuals were considered at risk for the duration of NSAID prescriptions. We used time-dependent Cox regression analysis to estimate CVD risk associated with NSAID use overall as well as four unique groups of NSAIDs, i.e., coxibs, naproxen, ibuprofen and other conventional NSAIDs.

Results: Our cohort included 3,806 OA individuals. There were 1,147 CVD events. After adjusting for age, sex, SES, COPD, diabetes, hypertension, hyperlipidemia, peptic ulcer disease and Romano comorbidity score, the hazard ratio (HR) and 95% confidence interval (CI) from the time-dependent Cox regression model was 1.48 (1.27, 1.73). When exposure to different groups of NSAID was compared with unexposed person-time, CVD risk were similar among coxibs and naproxen followed by other conventional NSAIDs and ibuprofen, adjusted HR (95% CI) were 1.58 (1.24, 2.00), 1.58 (1.11, 2.24), 1.39 (1.10, 1.75) and 1.36 (0.75, 2.47), respectively.

Conclusion: Our study is the first retrospective cohort study using BC HAD that looked at the overall CVD risk of NSAID use in treating OA in a real-world setting. After modelling exposure to NSAIDs as time-dependent, we found that exposure to NSAIDs substantially increased overall CVD risk compared to non-exposed periods. We also found that coxibs and naproxen may increase CVD risk more than conventional NSAIDs including ibuprofen.

REFERENCES

[1] Wang H, Bai J, He B, Hu X, Liu D. Osteoarthritis and the risk of cardiovascular disease: a meta-analysis of observational studies. Sci Rep [Internet]. 2016 Dec [cited 2017 Sep 6];6(1). Available from: http://www.nature.com/articles/srep39672

[2] Atiquzzaman M, Kopec J, Karim ME, Wong H, Anis A. OP0190 The role of nsaids in the association between osteoarthritis and cardiovascular diseases: a population-based cohort study. Ann Rheum Dis. 2018 Jun 1;77 (Suppl 2):144–144.

[3] Cunnington M, Webb D, Qizilbash N, Blum D, Mander A, Funk MJ, et al. Risk of ischaemic cardiovascular events from selective cyclooxygenase-2 inhibitors in osteoarthritis. Pharmacoepidemiol Drug Saf. 2008 Jun 1;17 (6):601–8.

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SAT0601 MORTALITY RATE IN PATIENTS TREATED WITH BIOLOGICS: DATA FROM THE ROMANIAN REGISTRY OF RHEUMATIC DISEASES

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Background: Rheumatoid arthritis (RA) is associated with increased mortality, with longitudinal studies averaging a standardised mortality ratio of

1.5 (95%CI 1.2 to 1.8) for RA patients compared to the general population [1]. In contrast, information on mortality in ankylosing spondylitis (AS) is scarce, whereas there are conflicting reports of the mortality risk among patients with psoriatic arthritis (PsA), but it is accepted that patients with PsA do not have a significantly elevated risk of mortality [2].

Objectives: To estimate the Mortality Rate in RA, SA and PsA for patients (pts) treated with biologics in Romania.

Methods: Data were gathered from the Romanian Registry of Rheumatic Diseases (RRBR), which comprises all patients treated with biologics in Romania for RA, AS and PsA. We have studied demographic data, disease duration, exposure to biologics in person-years (PY), and all-cause mortality until 01.01.2018.

Results: The cohort included 9577 pts (35596.83 PY) as following: 5224 RA pts (18676.75PY), 3469 AS pts (12680.63PY) and 884 PsA pts (4212.45PY). The mean age of the cohort was 54.86 yrs (62.87 yrs for RA, 45.54 yrs for AS, 56.18 yrs for PsA); 3196 pts (33.37%) were men: 79 (1.5%) RA pts, 2681 (77.28%) AS pts and 436 (49.3%) PsA pts. Mean disease duration for the cohort was 16.46 yrs for RA, 11.46 yrs for AS and 10.99 yrs for PsA. The number of all-cause deaths was 89 (74 deaths in RA, 11 in AS and 4 in PsA group). The mortality rate for the entire cohort was 0.25/100PY, and the rate varied across the diseases: 0.39/100PY in RA pts, 0.08/100PY in AS pts and 0.09/100PY in PsA. Infections were the major mortality cause in RA (0.09/100PY) and AS (0.04/100PY). Cardiovascular fatal events occurred in 0.06/100PY in RA population, significantly higher than 0.007/100PY in AS pts. Rate of solid neoplasm death in RA cohort was 0.04/100PY, compared to 0.007/100PY in AS; non-Hodgkin lymphoma was recorded only in RA pts (0.005/100PY). All deaths reported in PsA cohort (4 deaths) were of unknown cause.

Conclusion: This is the first report on mortality rate in biological treated patients in Romania. These data support data from the literature, showing that RA patients have a higher mortality risk compared to AS and PsA.

REFERENCES

[1] Dadoun S, Zeboulon Ktorza N, et al. Mortality in rheumatoid arthritis over the last fifty years: systematic review and meta-analysis. Joint Bone Spine. 2013:80(1):29-33

[2] Ogdie A, Haynes K, Troxel AB, et al. Risk of mortality in patients with psoriatic arthritis, rheumatoid arthritis and psoriasis: a longitudinal cohort study. Ann Rheum Dis. 2012;73(1):149-53.

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SAT0602 SHOULD ALL PATIENTS WITH ANTI-CENTROMERE ANTIBODIES BE REFERRED FOR A RHEUMATOLOGY ASSESSMENT?

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Background: Anti-centromere antibodies (ACA) are commonly associated with systemic sclerosis (SSc). The presence of ACAs in patients with SSc is known to increase the likelihood of developing Pulmonary Hypertension, which has a high mortality rate. ACAs are also seen in patients with other connective tissue diseases (CTD) and can sometimes be identified after testing for antinuclear antibodies in patients who have not reported any rheumatological symptoms. It is possible that connective tissue diseases are being under diagnosed due to a lack of awareness by physicians of the clinical significance of ACAs.

Objectives: To investigate whether patients with ACAs are being appropriately referred to the Rheumatology service.

Methods: All patients who were positive for ACAs in Southend university hospital between April 2016 and October 2018 were included in this single centre retrospective observational study. We identified patients' demographics, diagnosis, ANA titre, additional diagnosis and immunosuppressive therapy. We also captured their monitoring with pulmonary function testing and echocardiography.

Results: A total of 75 patients were identified with ACAs. The average age was 65 years, 61 females, 14 Male. Fifty-six patients were referred to rheumatology team and were found to have the following diagnosis, LcSSc (21), Sjogren's syndrome (SS) (10), undifferentiated connective tissue disease (UCTD) (6), Rheumatoid arthritis (RA) (5), ANCA associated vasculitis (AAV) (3), Raynaud's phenomenon (3), Lupus (2), Antiphospholipid syndrome (APS) (1), Primary biliary cirrhosis with Sjogren's syndrome (SS) (1), Juvenile idiopathic arthritis (1), Antisynthetase syndrome (AS) (1), Autoimmune hepatitis (1) and osteoarthritis (1). Of those 33 patients had a routine screening with an Echocardiogram and 26 had pulmonary function tests. One patient with LcSSc developed pulmonary hypertension. The remaining 19 patients were not referred and did not have the adequate screening for pulmonary hypertension. ANA titre was 1:80 in one patient, 1:320 for 4 patients, unknown for three and 1:640 for the remaining 67. 11 patients were treated with Hydroxchloroquine (4 SS, 4 UCTD, 1 lupus, 1 APS and 1 Lc SSc), 5 on Methotrexate (4 RA and 1 AS), 2 on MMF and steroid (AAV).

Conclusion: Nearly all patients with ACAs that were seen in the Rheumatology clinic had an autoimmune rheumatic disease. However, we found that 25% of people with ACAs were not referred to the Rheumatology service. The reasons for this are unclear. It is possible that patients did not report symptoms that would have prompted a referral. Some of the CTDs in which ACAs are typically found (LcSSc and SS) are associated with symptoms that can be mild and might not be reported by the patients or general physicians do not associate them with rheumatological disorders (e.g. sicca symptoms, gastro-oesophageal reflux and Raynaud's phenomenon). Early diagnosis might enable earlier treatment and prevent complications from these diseases. General physicians should therefore be made aware of these antibodies and the disorders that they can be associated with.

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SAT0603 SENSITIVITY TO PHENYLTHIOCARBAMIDE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Sensitivity to phenylthiocarbamide (PTC) as the ability to taste this bitter compound is a genetic marker ranked alongside eye color and blood groups [1,2]. Almost 90 years have passed since the first publication of A.L. Fox on the relationship of the "chemical constitution" and sensitivity to PTC [3] and 35 years later J. Stepan et al. (1965) analyzed the sensitivity to PTK in patients with joint diseases. According to the literature [4,5] sensitivity to PTK is associated with the peculiarities of clinical manifestation and the course of these diseases.

Objectives: To estimate the sensitivity to PTC in RA patients and its influence on the prognosis of the disease.

Methods: The physiological parameter of sensitivity to PTC was determined by H. Harris et al. [6]. The total number of dilution thresholds was 15 (PTC_{0-14}). Patients were considered as non-tasters (not able to taste PTC) in the case of PTC_{0-4} sensitivity thresholds and as tasters in the case of PTC_{5-14} sensitivity thresholds. Sensitivity to PTC was assessed in 140 RA patients, 110 women and 30 men, at Minsk clinical hospital №9 and we used the data on the PTC sensitivity of the mixed population of Minsk as a control [7].

Results: The frequencies of tasters (PTC+) and non-tasters (PTC-), as well as allele frequencies (T and t) of the PTC sensitivity gene among RA patients and controls are presented in the table.

Group	n	Phenotypes				Allele frequencies		σ
		PTC– (0-4)		PTC+ (5-14)				
		n	%	n	%	T	t	
RA, ♀	110	32	29.1	78	70.9	0.4606	0.5394	0.0257
RA, ♂	30	10	33.3	20	66.7	0.4226	0.5774	0.0527
RA, ♀ + ♂	140	42	30.0	98	70.0	0.4523	0.5477	0.0231
Control, ♀	130	40	30.77	90	69.23	0.4453	0.5547	0.0365
Control, ♂	119	41	34.45	78	65.55	0.4130	0.5870	0.0371
Control, ♀+♂	249	81	32.53	168	67.47	0.4296	0.5804	0.0261

There were no significant differences between general groups of PTC tasters and non-tasters among RA patients and the controls (two-way Fisher exact test, two-way FET, p> 0.1) while the sensitivity threshold of PTC_0 was revealed 2 times less in RA patients than in the control group - 10.7% and 22.1%, respectively (two-way FET, p=0,0057). Operating characteristics of PTC_0 are the following: OR=0.43 CI_{95} 0.23-0.78, LR^+=0.49 CI_{95}0.28-0.81, LR^-=1.15 CI_{95} 1.05-1.23, that means that a taste threshold of PTC_0 decreases the chances of RA by 2.0 times.

Seronegative RA was significantly more common in non-tasters vs tasters men (two-way FET, p=0,0236) and significantly more common in non-tasters men vs non-tasters women (two-way FET, p=0,0031). RA patients-tasters (PTC+) had significantly more severe functional disorders (functional class 3) vs non-tasters (PTC-) (two-way FET, p=0,0003) and more

advanced stages of RA (3-4 stages by O. Steinbrocker) (two-way FET, p=0,0024) with the same duration of RA.
Conclusion: The taste threshold of PTC_0 decreased the chances of RA by 2.0 times and non-sensitivity to PTC was associated with seronegative RA, especially in men, and more benign course of the disease.

REFERENCES

[1] Bartoshuk L.M.//Chem. Senses. 2000; 25: 447-460.
[2] Guo S.-W., Reed D. R. Ann. Hum. Biol. 2001; 28(2): 111–142.
[3] Fox A.L.//Science News Letter. 1931; 9: 249.
[4] Stepan J. et al.//Acta Rheumatol. Scand. 1965; 11(4): 258-265.
[5] Ondrasík M. et al.//Fysiatr. Revmatol. Vestn. 1972; 50(4): 183-191.
[6] Harris H., Kalmus H.//Ann. Eugen. Lond. 1949; 15(1): 24-31.
[7] Salivon I.I. et al. (1976): Essays on Anthropology of Belarus. Science and technic, Minsk; 272p.

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SAT0604 ANALYSIS OF INFECTIOUS SPONDYLODISCITIS: 20-YEARS DATA: EPIDEMIOLOGY, CLINICAL FEATURES, DIAGNOSIS AND TREATMENT

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Background: Infectious spondylodiscitis is defined as an infectious disease involving intervertebral disks and adja- cent vertebral bodies. It is rare and difficult to diagnose due to its non-specific clinical features.
Objectives: To study the clinical, microbiological, radiological, therapeutic and evolving of infectious spondylodiscitis.
Methods: Retrospective monocentric study including patients diagnosed as spondylodiscitis and hospitalized in our department between January 1999 and December 2018. The diagnosis was based on clinical, biological, radiological and bacteriological data.
Results: We included 107 patients. There were 58 men (54.2%) and 49 women (45.8%) with a mean age of 55 years [16–86]. Predisposing factors were found in 59 patients (55.1%): This was diabetes in 21.49% of cases, history of cancer in 2.8% of cases, hepatic disease in 5.6% of cases, a long-term corticosteroid in 1.8% of cases, recent spinal surgery in 0.93% of cases, visceral surgery in 3.73% of cases, extra-articular history of tuberculosis in 2.8% of cases and consumption of unpasteurized milk in 25.23% of cases.
The approximate time from onset of symptoms to diagnosis was from 0.23 to 24 months (median 3 months). Back pain was the most common symptom. Impaired general condition was observed in 71% of cases, fever in 35.5% of cases and night sweats in 42.9% of cases. Radiculalgia was found in 42.9% of cases. A neurological deficit was noted in 16.82% of cases: motor deficit in 1.8% of cases, spinal cord compression in 1.8% of cases and Cauda equina *syndrome in 2.8% of cases*.
The inflammatory syndrome was found in 90.6% of cases.
The lumbar spine was most affected (54.2%), followed by the dorsal spine (29.9%) and the cervical spine (8.4%). The spondylitis was multifocal in 19.6% and multi-stage in 15.8% of cases.
Radiographs of the spine were abnormal in 83.1% of cases.
CT and Spinal MRI was performed respectively in 60% and 78.8% of cases and showed paravertebral abscess in 63.5%, epiduratis in 54.2%, spinal cord compression 9.3% and vertebral ostelysis in 8.4% of cases.
The causative microorganism was identified in 51 cases (47.66%): brucella in 21 patients, mycobacterium tuberculosis in 16 patient, and pyogenic germs in 12 patients.
All of them received initially adapted antibiotics. Surgical treatment was performed in 8 patients.
Most of the patients showed good response (71.9%). Disturbance of liver function due to treatment occurred in 8 cases with good subsequent evolution. Neurological complication occurred in 11 cases and sepsis occurred in 4 cases. And 4 patients were dead.
Conclusion: The microbiological diagnosis of infectious spondylodiscitis is often difficult to establish and the disease requires prolonged antibiotic treatment. Early diagnosis is needed to avoid neurological complications associated with poorer long-term outcomes.
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SAT0605 BODY MASS INDEX AND SYSTEMIC CORTICOSTEROID USE AS INDICATORS OF DISEASE BURDEN AND THEIR INFLUENCE ON THE SAFETY PROFILE OF CERTOLIZUMAB PEGOL ACROSS INDICATIONS

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Background: Certolizumab pegol (CZP) is an anti-TNF drug approved for rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), psoriatic arthritis (PsA), psoriasis (PSO) and Crohn's disease (CD). Older age, comorbidity burden and corticosteroid (CS) use have been linked to increased risk of serious infectious events (SIEs) in CZP-treated patients (pts) with RA.[1] However, the impact of overall disease burden on the risk of serious adverse events (SAEs) has not been fully examined for other CZP indications. High body mass index (BMI) has been associated with systemic inflammation and greater comorbidity risk.[2,3] Greater disease burden in these pts may lead to increased CS use – a known risk factor for SAEs.[1]
Objectives: To examine the contribution of BMI and CS use to the risk of SIEs, malignancies and major adverse cardiovascular events (MACE) in CZP-treated pts across indications.
Methods: Safety data were pooled across 49 CZP clinical trials (27 RA, 1 axSpA, 1 PsA, 5 PSO, 15 CD). SAEs of potential concern were medically reviewed by an external expert committee using predefined case rules. Incidence rates (IR) were calculated per 100 pt–years (PY). Multivariate Cox modeling was used to estimate relative risk (hazard ratio [HR]) of time to first SIE, malignancy or MACE by baseline BMI (<18.5, 18.5–<25, 25–<30, ≥30 kg/m^2) and CS use (yes, no). The model was adjusted for baseline age, sex, disease duration, methotrexate (MTX) use, prior anti-TNF drug use, and CZP indication.
Results: Across indications, 11,317 pts received CZP (21,695 PY total exposure; max: 7.8 years [yrs]; exposure for RA: 13,542 PY; axSpA: 978 PY; PsA: 1,316 PY; PSO: 1,481 PY; CD: 4,378 PY). Mean BMI was 27.8 kg/m^2 in RA, 27.6 kg/m^2 in axSpA, 29.8 kg/m^2 in PsA, 30.1 kg/m^2 in PSO, and 24.0 kg/m^2 in CD. Overall, 4,132 pts (37%) took CS at baseline, more so in RA (46%) and axSpA (51%). Across indications, IRs were 0.82/100 PY for all malignancies (IR for malignancies excluding non-melanoma skin cancer [NMSC] was 0.66/100 PY), 0.47/100 PY for

Table: Cox proportional hazards models of time to first SAE of interest

Covariate		SIEs		Malignancies		MACE	
		HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
Indication	RA	Ref.		–		Ref.	
	axSpA	0.64 (0.38–1.10)	0.1053	–		0.27 (0.04–1.99)	0.2001
	PsA	0.59 (0.38–0.93)	0.0216	–		1.11 (0.50–2.47)	0.8035
	PSO	0.48 (0.30–0.79)	0.0038	–		0.44 (0.15–1.25)	0.1211
	CD	2.22 (1.69–2.91)	<.0001	–		0.38 (0.15–0.98)	0.0457
Sex	Male	Ref.		–		Ref.	
	Female	1.15 (0.97–1.35)	0.1112	–		0.54 (0.35–0.82)	0.0036
Age (yrs)	<45	Ref.		Ref.		Ref.	
	45–<65	0.92 (0.77–1.09)	0.3245	4.32 (2.68–7.00)	<.0001	4.61 (2.05–10.39)	0.0002
	≥65	1.68 (1.33–2.12)	<.0001	11.41 (6.80–19.13)	<.0001	13.40 (5.73–31.34)	<.0001
Disease duration (yrs)	<1	Ref.		Ref.		–	
	1–<5	1.10 (0.87–1.39)	0.4494	0.69 (0.45–1.06)	0.0883	–	
	5–<10	1.23 (0.96–1.56)	0.1038	0.60 (0.38–0.95)	0.0297	–	
	≥10	1.36 (1.07–1.73)	0.0133	0.61 (0.39–0.95)	0.0290	–	
CS use + BMI (kg/m^2)	No + <18.5	1.01 (0.66–1.55)	0.9765	–		–	
	No + 18.5–<25	Ref.		–		–	
	No + 25–<30	0.91 (0.71–1.16)	0.4415	–		–	
	No + ≥30	1.04 (0.80–1.34)	0.7702	–		–	
	Yes + <18.5	0.99 (0.58–1.68)	0.9636	–		–	
	Yes + 18.5–<25	1.34 (1.08–1.68)	0.0091	–		–	
	Yes + 25–<30	1.07 (0.82–1.41)	0.6101	–		–	
	Yes + ≥30	1.72 (1.33–2.22)	<.0001	–		–	
BMI (kg/m^2)	<18.5	–		–		1.93 (0.67–5.51)	0.2226
	18.5–<25	–		–		Ref.	
	25–<30	–		–		0.97 (0.57–1.64)	0.9008
	≥30	–		–		1.74 (1.06–2.84)	0.0284
CS use	No	–		–		Ref.	
	Yes	–		–		1.30 (0.87–1.94)	0.2092
Concomitant MTX use	No	Ref.		Ref.		–	
	Yes	1.19 (0.93–1.50)	0.1629	0.72 (0.53–0.99)	0.0405	–	
Prior anti-TNF use	No	Ref.		Ref.		–	
	Yes	1.20 (1.00–1.44)	0.0558	1.46 (0.98–2.18)	0.0605	–	

The above variables result from a stepwise selection procedure with p>0.25 for entry and retention into the model. A covariate was defined as a risk factor if p≤0.05. All p values are nominal and should be interpreted in an exploratory manner. axSpA: axial spondyloarthritis; BMI: body mass index; CD: Crohn's disease; CI: confidence interval; CS: corticosteroid; HR: hazard ratio; MACE: major adverse cardiovascular events; MTX: methotrexate; PsA: psoriatic arthritis; PSO: psoriasis; RA: rheumatoid arthritis; Ref.: reference category used as denominator in the hazard ratio calculations; SIE: serious infectious event; yrs: years.

MACE, and 3.62/100 PY for SIEs. According to the Cox model, age ≥45 yrs, disease duration <1 yr (compared with ≥5 yrs), and no MTX use were risk factors for malignancies (including NMSCs); BMI and CS use did not have a detectable impact (**Table**). MACE risk was higher in RA and PsA; BMI ≥30 kg/m^2 was a risk factor for MACE, in addition to age ≥45 yrs and male sex (**Table**). Compared with RA, SIE risk was higher in CD and lower in PSO and PsA; key risk factors included age ≥65 yrs, disease duration ≥10 yrs and CS use. Without CS use, BMI did not impact SIE risk, but among CS users, SIE risk was higher for obese pts (**Table**).

Conclusion: In CZP-treated pts across indications, malignancy risk was not influenced by BMI or CS use. As expected, obesity and CS use increased the risk of MACE. The SIE risk associated with CS use was compounded in obese pts, which may reflect the contribution of comorbidities, disease activity or other factors not examined here.

REFERENCES

[1] Curtis J. Arthritis Res Ther 2017;19:276; 2. Pérez de Heredia F. Proc Nutr Soc 2012;71:332–8; 3. Harpsøe M. Int J Epidemiol 2014;43:843–55.

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SAT0606

RISK OF MAJOR AUTOIMMUNE DISEASES IN PATIENTS WITH FEMALE BREAST CANCER: A NATIONWIDE, POPULATION-BASED COHORT STUDY

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Background: Prior studies showed that breast cancer patients had an increased spontaneous expression of CTLA-4 on T lymphocytes in breast tissue and peripheral blood mononuclear cells, leading to impaired T cell activation. We hypothesized that breast cancer patients may have a decreased risk of autoimmune diseases. However, the incidences of autoimmune disease in breast cancer are still unclear.

Objectives: To investigate the risk of major autoimmune diseases including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Sjögren's syndrome (SS), polymyositis (PM)/dermatomyositis (DM) in female breast cancer patients.

Methods: We identified all newly-diagnosed female breast cancer patients during 2007–2013 using the 1997–2013 Taiwanese national health insurance database as the incident female breast cancer cohort. We randomly selected non-breast cancer female controls matching female breast cancers patients for age and the year of index date from one million representative population as the comparison cohort. We estimated the risks of SLE, RA, SS and PM/DM in female breast cancer patients compared with the comparison cohort using Cox regression analysis adjusting for age, Charlson comorbidity index, hormone therapy and chemotherapy.

Results: A total of 54,311 female breast cancer patients and 217,244 matched non-breast cancer female individuals were included. The mean ± SD age was 53.6±12.7 years in both groups. After adjusting for potential confounders, female breast cancer patient had a lower risk of developing SLE (hazard ratio [HR], 0.04; 95% confidence interval [CI], 0.01–0.24), RA (HR, 0.03; 95% CI, 0.02–0.04) and SS (HR, 0.21; 95% CI, 0.09–0.48) than the comparison cohort. However, the risk of PM/DM was not significantly different between female breast cancer group and the comparison group (HR, 0.37; 95% CI, 0.08–1.80).

Table 1. Incidence rates and risks of SLE, RA, SS and PM/DM in female breast cancer compared with matched non-breast cancer individuals

	SLE	RA	SS	PM/DM
Non-breast cancer (n=217,244)				
Event (%)	82 (0.04)	348 (0.16)	312 (0.14)	14 (0.006)
Person-years	816,360	815,557	815,713	816,581
IR,/10^5 years	10.0	42.7	38.2	1.7
Breast cancer (n = 54,311)				
Event (%)	4 (0.01)	33 (0.06)	35 (0.06)	4 (0.01)
Person-years	170,627	170,560	170,561	170,627
IR,/10^5 years	2.3	19.3	20.5	2.3
Breast cancer patients compared with non-breast cancer individuals				
IRR (95% CI)	0.23 (0.09–0.64)	0.45 (0.32–0.65)	0.54 (0.38–0.76)	1.37 (0.45–4.15)
HR# (95% CI)				
Crude	0.23 (0.08–0.62)	0.45 (0.32–0.64)	0.55 (0.39–0.78)	1.35 (0.44–4.10)
Adjusted*	0.04 (0.01–0.24)	0.03 (0.02–0.04)	0.21 (0.09–0.48)	0.37 (0.08–1.80)

SS: Sjogren's Syndrome; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus.
#Using Cox proportional hazard regression model
*Adjusted variables included age, Charlson comorbidity index, hormone therapy and chemotherapy.
Female breast cancer patients had a decreased risk of developing SLE, RA and SS, but not PM/DM.

Conclusion: Female breast cancer patients had a decreased risk of developing SLE, RA and SS, but not PM/DM.

REFERENCES

[1] Mao H, Zhang L, Yang Y, Zuo W, Bi Y, Gao W, et al. New insights of CTLA-4 into its biological function in breast cancer. Curr Cancer Drug Targets. 2010;10:728-36.

[2] Khalife E, Khodadadi A, Talaeizadeh A, Rahimian L, Nemati M, Jafarzadeh A. Overexpression of Regulatory T Cell-Related Markers (FOXP3, CTLA-4 and GITR) by Peripheral Blood Mononuclear Cells from Patients with Breast Cancer. Asian Pac J Cancer Prev. 2018;19:3019-25.

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SAT0607 INCIDENCE AND SEVERITY OF FRAGILITY FRACTURES IN FRANCE

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Background: Certain fragility fractures (for example of the hip and femur) in the elderly are considered major since they are associated with increased mortality and morbidity.[1]
Objectives: To describe the characteristics of adults aged ≥50 years in France experiencing fragility fractures according to the site of fracture.
Methods: A postal questionnaire was sent to 15,000 individuals aged ≥50 years in order to identify and characterise subjects with a history of fragility fracture. Subjects were asked whether they had experienced a fracture in the previous 3 years and, if so, how many. Fractures were classified according to site into major (shoulder, vertebrae, pelvis, hip or femur and ≥3 ribs) or minor (other sites).[1]
Results: Of the 13,914 subjects returning the questionnaire, 425 (3%) reported ≥1 fragility fracture. The fracture history rate in the previous year was 1.4% [95%CI: 1.2–1.6]; this rate was higher in women (2.0%) than in men (0.7%) and increased with age. 147 subjects reported major fractures and 287 subjects minor fractures. Most fractures (82.4%) resulted from falling over. The most frequent major fracture sites were the humerus (10.6% of all fractures), vertebra (8.1%) and hip (7.1%). The most frequent minor fracture sites were the forearm/wrist (24.7%) and ankle (17.7%). 25 subjects reported >1 fractures and were excluded from further analyses. Subjects with a history of major fractures were older (p<0.01) than those with minor fractures (72.6±11.3 vs. 67.1±10.6 years; p<0.01). Distribution of gender, body mass index and comorbidities did not differ between prior fracture types. Current obesity was, however, associated with a higher rate of previous fracture of the lower limb. Subjects with a history of major fractures reported a significantly greater loss in height since the age of 20 (p<0.01) than those with a history of minor fractures (-3.38±2.35 vs. -2.75±2.02 cm). Subjects who reported lifetime corticosteroid use for ≥3 months more frequently reported major fractures than minor fractures (odds ratio: 1.90 [1.13;3.18]), as did post-menopausal women (odds ratio: 4.64[1.06;20.43]) and women using oestrogen-based hormone replacement therapy (odds ratio: 1.86 [1.06;3.29]). Parental fracture history, a history of falls, excess alcohol consumption or active smoking, and use of drugs that may increase risk of falls (antidepressants, antiepileptic drugs) were not associated with the type of fracture.
Conclusion: Extrapolated to the total French population, >340,000 people aged ≥50 years would be expected to experience a fragility fracture each year. One third of these fractures are major. Characteristics found to be associated with the severity of the prior fracture were older age, corticosteroid use, post-menopausal status and use of oestrogens. Limitations of the study include retrospective data collection, risk of recall bias, lack of ascertainment of fracture history and failure to capture subjects in residential care or who had died since the fracture.

REFERENCES

[1] Bliuc, et al. JAMA 2009; 301:513-21.

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SAT0608 THE PREVALENCE OF RHEUMATOID ARTHRITIS IN CHILE, A STUDY PERFORMED AS PART OF THE NATIONAL SURVEY HEALTH (ENS 2016-17)

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Background: Genetic and environmental backgrounds influence the development of rheumatoid arthritis (RA) and its frequency has regional variations. In Latin America epidemiologic data are scarce.
Objectives: We aimed to determine the prevalence of RA in Chile as part of the National Health Survey (ENS, Encuesta Nacional de Salud).
Methods: ENS was a cross-sectional household survey with a stratified multistage probability sample of 6,233 participants performed between August 2016 and March 2017. A screening instrument for RA was applied to a random sample of 3,700 subjects >30 years old.[1, 2] Positive screening was defined by at least one of the following: (i) 2 swollen joints for at least 4 consecutive weeks (past or present) and/or (ii) a diagnosis of arthritis in the past. Individuals with positive screening had Rheumatoid Factor, Anti-citrullinated protein antibodies, and C-reactive protein measured and clinical examination was performed by a rheumatologist. Self-report of doctor-diagnosed RA was also performed.
Results: The screening questionnaire was applied to 2,998 subjects. Seven hundred and thirty-eight (22.1%) had a positive screening. Among the subjects with a positive screening 493 (66%) had consulted a rheumatologist. Thirty-one subjects had RA according to the ACR/EULAR 2010 classification criteria, which corresponds to 0.6% (95%CI 0.3, 1.2). Three point three per cent reported having RA. Prevalence was higher in women and in high SES.
Conclusion: According to this national population-based study RA prevalence in Chile is 0.6% (0.3, 1.2). This is similar to the prevalence previously reported in developed countries, which is noteworthy given the differences in sociodemographic characteristics which exist compared to Chile. Self-reporting leads to an important overestimation of RA. Our study suggests there is a higher risk of RA in subjects with high SES in this region.

REFERENCES

[1] MacGregor AJ, Riste LK, Hazes JMW, Silman AJ. Low prevalence of rheumatoid arthritis in Black Caribbeans compared with Whites in inner city Manchester. Ann Rheum Dis 1994;53:293–7
[2] Carmona L, et al. The prevalence of rheumatoid arthritis in the general population of Spain. Rheumatology (Oxford). 2002;41(1):88-95.

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SAT0609 **WOMEN WITH METABOLIC SYNDROME AND GENERAL OBESITY ARE AT HIGHER RISK FOR SIGNIFICANT HYPERURICEMIA THAN MEN: RESULTS FROM THE 2016 KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY**

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Background: Hyperuricemia is emerging as a potential biomarker and a predictor for metabolic syndrome (MetS) and its related complications.
Objectives: We aimed this study to investigate the risk factors of hyperuricemia, particularly, the association of hyperuricemia with MetS and general obesity.
Methods: We performed multivariate logistic regression analyses using the 2016 Korea National Health and Nutrition Examination Survey (KNHANES) data collected in a representative sample of Korean adults. Hyperuricemia was defined by serum uric acid level $\geq$7.0 mg/dl for men and $\geq$6.0 mg/dl for women. General obesity was based on body mass index (BMI) $\geq$25 kg/m^2.
Results: Among a total of 5,591 Korean adult participants, 685 (12.3%) individuals were classified as having hyperuricemia. Hyperuricemia was significantly associated with MetS in men (Odd ratio (OR): 1.74, 95% CI: 1.29-2.34) and women (OR: 2.47, 95% CI: 1.55-3.93) after adjustments for age, sex, smoking, alcohol, exercise, BMI and estimated glomerular filtration rate (eGFR). General obesity was also independently related to hyperuricemia in both sex (OR: 1.70, 95% CI: 1.31-2.19 in men, OR: 3.73, 95% CI: 2.57-5.41 in women). Among the components of MetS, elevated blood pressure, elevated triglyceride and reduced HDL-cholesterol in men, and increased waist circumference, hyperglycemia, elevated triglyceride in women were risk factors for hyperuricemia. In subgroup analyses, the presence of concomitant MetS and general obesity posed strikingly higher risk for hyperuricemia among women (OR: 7.24, 95% CI: 4.56-11.50 in women, versus, OR: 2.90, 95% CI: 2.12-3.96 in men) when compared to individuals free of neither conditions (OR: 1.00, referent). In addition, the risk of hyperuricemia has increased up to 6-fold by the presence of MetS and general obesity among young adults aged less than 40 years old.
Conclusion: Hyperuricemia was independently associated with MetS and general obesity, regardless of sex. These increases in risk of hyperuricemia were more prominent in women. Among women, those who had both MetS and general obesity were at nearly 7-fold increased risk for hyperuricemia compared to those without both conditions. It may be considered to incorporate hyperuricemia as one of the components of MetS.

REFERENCES

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SAT0610 **THE DELPHI METHOD IN RHEUMATOLOGY RESEARCH: ARE WE DOING WELL?**

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Background: Delphi method is an iterative process, designed to combine the opinion of a group of experts within a consensus. It is a structured methodology to systematically collect expert judgments about a problem, process the information and finally build a general group agreement[1]. It has 4 defining characteristics: iterative, anonymous process, generates feedback and generates a consensus[2].
Objectives: To evaluate the methodology and application of the Delphi method in rheumatology research.
Methods: Search of the literature was performed in the MEDLINE, EMBASE, Clinical key and Scielo databases. MESH terms "Delphi Technique", "Rheumatology" and "Consensus" were used, finding 404 articles. A total of the abstracts of these studies was read, discarding duplicates, articles of consensus methodology different from the Delphi technique and articles from studies of other specialties. The consultation was held on 30-10-18.
Results: 109 articles were found. Journal with highest number of publications was Clinical Rheumatology (30 articles), followed by Journal of Rheumatology (11 articles). Rheumatoid arthritis was the first rheumatic diseases studied in 21.1% (n=23), followed by psoriatic arthritis in 11% (n=12). Only 16.5% (n=18) of the studies met the 4 characteristics of the Delphi method, 31.2% (n=34) met 3 characteristics, 18.3% (n=20) met 2 characteristics and 33.9% (n=37) meets only one of the defining characteristics of the method. Feedback was made in 43.1% (n=47) of the studies. Process was iterative in 64.2% (n=70) of papers. The coordinating group of the exercise was only reported in 27.5% (n=30), with an average of 8 (± 3.14) coordinators for each study. The group of experts was reported in 93.6% (n=102) of the studies, with a median of 28 (interquartile range: 54) experts per study. In 30.4% (n = 45) of the studies, the way in which communication with the group of experts was established was not reported. The modification of the Delphi technique was declared in 14.9% (n = 22) of the studies, however, in 18 of these studies it is not explained which was the modification of the technique; in 4 studies, the modification consisted of holding a face-to-face meeting of the group of experts after the consultation rounds; one of the studies clarifies having made a "RAND/UCLA" method without explaining in more detail what this method consists of. To refer to the modified versions of the method, terms such as "informal Delphi" or "Delphi like study" are coined, without further considerations or clarifications to what these mean
Conclusion: Use of Delphi technique in rheumatology has not been carried out following the original methodology in most of the evaluated works, which puts at risk the validity of the results of these studies. Propening for the correct use of the technique, will improve the validity of the results obtained with this type of qualitative research. It is necessary to establish and validate minimum compliance criteria, so that an expert consensus exercise through the Delphi method achieves its purpose in a valid way. This context allows to open a line of methodological research in evaluation of the application of the Delphi methodology in the health area.

REFERENCES

[1] Dalkey N, Helmer O. An experimental application of the Delphi method to the use of experts. Manage Sci. 1963;9:458–68.
[2] Ono R, Wedemeyer DJ. Assessing the validity of the Delphi technique. Futures. Pergamon; 1994;26:289–304

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SAT0611 **PREVALENCE OF HYPOTHYROIDISM WITH THERAPEUTIC INDICATION IN PATIENTS WITH RHEUMATOLOGICAL DISEASES**

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Background: Hypothyroidism is known as a common complication of rheumatological diseases(RD). Thyroid hormone supplementation is important not only in clinical hypothyroidism but subclinical one for cardiovascular events in the future[1]. But the data about prevalence of hypothyroidism requiring treatment and it's changes with follow up in patients with RD is limited.
Objectives: To reveal the prevalence and risk factors of hypothyroidism, especially which requires thyroid hormone supplementation, in patients with RD and compare it with that of general population.
Methods: We retrospectively reviewed charts of RD patients and healthy controls in preventive medicine center, at St. Luke's International Hospital from January 2004 to July 2018. We investigated basic demographics, underlying diseases, blood tests including thyroid functions and treatment with thyroid hormones. We compared the number of hypothyroidism requiring treatment (Thyroid stimulating hormone: TSH 10 μU/mL or physician started treatment) and it's changes in follow up using univariate analysis and Kaplan–Meier method with log rank test. Cox proportional hazard model was performed for evaluating the risk of hypothyroidism which needs treatments in all patient and only RD patients.
Results: 2307 RD patients and 78251 controls without past medical history of hypotyroidism with therapeutic indications are included. Newly-detected hypothyroidisms requiring treatments are significantly frequent in

RD patients (6.9%vs2.0%, P<0.001) (table.1). Kaplan–Meier method and Cox's proportional hazards model revealed having RD and high baseline TSH (4.5 μU/mL) are strongly associated with hypothyroidism requiring treatments (adjusted hazard ratio: HR = 4.39; 95%CI 3.35-5.75, and 25.9; 95%CI 23.4-28.6, respectively) (Figure 1).

Table 1. Comparison of RD patients and control

	RD patients (n = 2307)	Control (n = 78251)	p. value
Age(yr)	53.7 (16.3)	46.1 (11.9)	<0.001
FEMALE (%)	1826 (79.2)	38632 (49.4)	<0.001
BMI	22.7 (3.9)	22.4 (3.3)	0.03
Hb (g/dl)	12.1 (1.6)	13.9 (1.4)	<0.001
MCV (fl)	88.9 (5.7)	91.0 (4.9)	<0.001
Cre (mg/dl)	0.61 (0.29)	0.73 (0.21)	<0.001
L-CHO (mg/dl)	107.2 (29.1)	115 (30.2)	<0.001
RF positive (%)	961 (41.7)	6734 (8.6)	<0.001
Hypothyroidism requiring treatment (%)	**159 (6.9)**	**1573 (2.0)**	**<0.001**
Times of TSH check	2 [1-75]	5 [1-28]	<0.001
Duration of TSH follow up (days)	258.00 [0-4999]	1992.00 [1-5230]	<0.001
Baseline TSH Level(μU/mL)	1.76 [0.01-110.8]	1.74 [0-735.7]	0.137
4.5 (%)	170 (7.4)	4051 (5.2)	<0.001
10 (%)	22 (1.0)	365 (0.5)	0.003
TSH in follow up			
4.5 (%)	378 (16.4)	11099 (14.2)	0.003
10 (%)	85 (3.7)	1228 (1.6)	<0.001
Supplementation Treatment (%)	129 (5.6)	718 (0.9)	<0.001

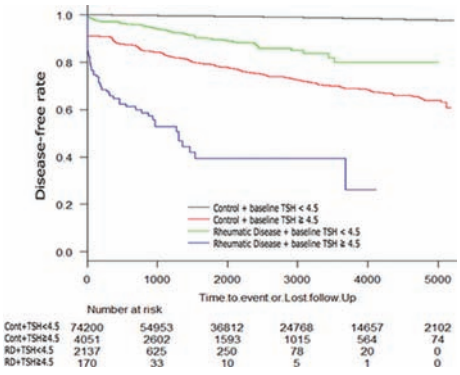


Figure 1. Relationship between hypothyroidism requiring treatment, RD and baseline TSH

When focus on RD patients, patients with older age, ANA (Anti-nuclear antibody) 80, higher Cre and TSH, and baseline positive anti-thyroid peloxydase(TPO-Ab) or anti-thyrogloburin antibodies(Tg-Ab) have higher risk of hypothyroidism requiring treatment after adjusting confounders in Cox's proportional hazards model (Table.2).

Table 2. Multivariate analysis in RD patients

	Adjusted HR [95%CI]	p value
Age	1.01 [1.00-1.03]	0.047
ANA 80	1.91 [1.19-3.06]	<0.001
Cre	1.78 [1.13-2.80]	0.013
Baseline TSH	1.12 [1.10-1.15]	<0.001
Baseline TPO-Ab or Tg-Ab	2.21 [1.25-3.93]	<0.01

Conclusion: Hypothyroidism with therapeutic indication is more frequent in RD patients, even if screening TSH is within normal range. We encourage active routine measurement of thyroid function tests in patients with RD, especially with above risk factors.

REFERENCES

[1] Nicolas Rodondi, et al. Subclinical Hypothyroidism and the Risk of Coronary Heart Disease and Mortality: JAMA. 2010;304(12):1365-1374.

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SAT0612 FREQUENCY OF POLYAUTOIMMUNITY IN A TERTIARY HOSPITAL

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Background: Polyautoimmunity (PAI) is the presence of more than one Autoimmune Disease (AID) in one patient. PAI have been reported in different AIDs as systemic lupus erythematosus (SLE) (33-45%), rheumatoid arthritis (RA) (13-23%), systemic sclerosis (SSc) (10-43%) or Sjögren Syndrome (SS) (32-52%). On the other hand, Multiple Autoimmune Syndrome (MAS) where three or more AIDs coexisting in one patient has been reported.
Objectives: To determine PAI frequency in the context of AIDs reported in a tertiary hospital.
Methods: Cross-sectional observational study with systematic revision of patients' electronic clinical records with AIDs (from 2014 to 2018). We selected those patients who had two or more diagnosis of AIDs. Demographic, clinical and immunological data were collected.
Results: Of 1854 patients with AIDs, 96 (5.17%) had PAI. Mean age was 56±15 years and 93.75% were female. 7 patients from the 96 (0.4%) also had MAS.
The mean age at diagnosis of the first AID was 39.03±15.93 years and mean age at diagnosis of the second AID was 48.16±15.04 years. A mean difference of 9.17±10.18 years between first and second AIDs debut was observed.
The most frequent AIDs registered are shown in table 1.

RHEUMATIC AUTOINMUNE DISEASES	TOTAL CASES	POLYAUTOIMMUNITY CASES	FREQUENCY (%)
APS	70	23	32.86
SS	154	42	27.27
SLE	261	41	15.71
SSc	88	5	5.68
RA	926	46	4.97
Vasculitis	83	4	4.82
Psa	371	7	1.89
NON RHEUMATIC AUTOINMUNE DISEASES		**POLYAUTOIMMUNITY CASES**	
IBD		12	
AHyp		9	
CD		7	
DM-1		2	
AHep		1	

Antiphospholipid syndrome (APS), Sjögren syndrome (SS), Systemic lupus erythematosus (SLE), Systemic sclerosis (SSc), Rheumatoid arthritis (RA), Psoriasic arthritis (PsA), Inflammatory bowel disease (IBD), Autoimmune hypothyroidism (AHyp), Celiac disease (CD), Diabetes mellitus type 1 (DM-1), Autoimmune hepatitis (AHep).
The most frequent PAI cases registered were RA-SS (N=23), SLE-APS (N=17), SLE-SS (N=11), AR-IBD (N=7), RA-SLE (N=5), RA-CD (N=5), SS-SSc (N=4) and PsA-IBD (N=4).
In the total group of 1854 patients with AIDs, SLE with PAI was present in 41 (2.21%) patients, SS with PAI in 42 (2.26%), RA with PAI in 46 (2.48%) and APS with PAI in 23 (1.2%). Moreover, SS was present in the 4.21% of SLE patients and in the 2.48% of RA patients. In contrast, APS was present in the 6.51% of SLE patients, being de of 7.64 (17.62) years the difference between the onset of the first AID and the second AID.
In the MAS group an AHyp-SLE-APS in 2 patients was observed, as well as 1 patient with SLE-SS-Aps, 1 with SS-RA-APS, 1 with RA-vasculitis-AHyp and 1 with SS-Ahyp-Ahep.
Conclusion: A 5.17% frequency of patients with PAI in our group of AID patients was observed, mostly women. APS, SS and SLE respectively were the diseases that most PAI showed. The most frequent association of AID diseases in PAI cases were RA-SS, APS-SLE and SS-SLE. We

found a rather lower frequency compared with those published in the literature, possibly due to the putative bias of retrospective studies and the geographical differences of PAI patients.
Disclosure of Interests: None declared
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SAT0613 CHANGING TREATMENTS AND OUTCOMES FOR JUVENILE IDIOPATHIC ARTHRITIS: INITIAL FINDINGS FROM A NEW CANADIAN INCEPTION COHORT

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Background: Treatments for juvenile idiopathic arthritis (JIA) are changing rapidly. Healthcare providers and families require up-to-date knowledge of current treatment practices and expected outcomes to inform their decisions.
Objectives: To assess changes in treatment practices and outcomes for children in a new Canadian inception cohort diagnosed with JIA in 2017-2018, compared to children in the Research in Arthritis in Canadian Children emphasizing Outcomes cohort (ReACCh-Out) diagnosed in 2005-2010 [1].
Methods: A new investigator-driven Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) JIA Registry was started in February 2017 to prospectively collect information on children enrolled within 3 months of JIA diagnosis. Information about disease activity, treatments, outcomes and adverse events is collected at all clinic visits. Registry data were extracted in October 2018 and clinical characteristics at presentation, use of anti-rheumatic medications, attainment of inactive disease, cJADAS10 scores and adverse events were described. Selected findings were compared to those observed in the ReACCh-Out cohort. The proportion of patients (cumulative incidence) receiving various treatments and their outcomes were estimated with Kaplan Meier survival methods.
Results: A total of 166 patients enrolled a median of 6 weeks after diagnosis at 10 centres were included. Median age at diagnosis was 9 years (IQR 3, 13), 61% were female and 51% had oligoarthritis. At enrolment, subjects had a median of 2 active joints (IQR 1, 3), a Physician Global Assessment of 3 (1.5, 4) and a Parent Global Assessment of 1 (0, 3). The median cJADAS10 score was 6.5 (4, 10). Table 1 compares baseline characteristics and the cumulative incidence of medication use and inactive disease at one year after diagnosis with those observed in the ReACCh-Out cohort, diagnosed on average 10 years earlier. Figure 1 shows the Kaplan Meier curves for attainment of inactive disease.
Conclusion: In Canada, treatments for newly diagnosed patients with JIA have intensified in the last 10 years, and 35% will now start their first biologic within 1 year of diagnosis. Short-term outcomes have improved, 81% of current patients now attaining inactive disease within one year of diagnosis. Funding: The Arthritis Society, Canada.

REFERENCES

[1] Guzman J, Oen K, Tucker LB, et al. The outcomes of juvenile idiopathic arthritis in children managed with contemporary treatments: results from the ReACCh-Out cohort. Ann Rheum Dis.2015;74:1854-60

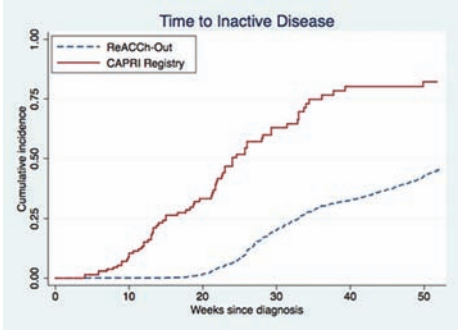


Figure 1. Time to inactive disease across Canada in the new CAPRI cohort (2017-2018) and the ReACCh-Out cohort (2005-2010)

Table 1:

Characteristic	Previously reported ReACCh-Out findings[1]	New CAPRI JIA registry
BASELINE CHARATERISTICS:		
Age at diagnosis, median (25th, 75th centiles)	9 (4, 13)	9 (3, 13)
Female sex,%	64	61
JIA categories,%:	38	51
Oligoarthritis	21	14
RF-negative polyarthritis	14	16
Enthesitis related arthritis	7	5
Systemic arthritis	6	5
Psoriatic arthritis	4	3
RF-positive polyarthritis	10	5
Undifferentiated		
Active joint count at enrolment	3 (1, 7)	2 (1, 3)
PGA at enrolment	3 (1.7, 5.2)	3 (1.4, 4.0)
CUMULATIVE INCIDENCE 1y AFTER DIAGNOSIS:		
Started a NSAID,% (95% CI)	>88	96 (90-99)
Received a joint injection	37	59 (49-69)
Started a first DMARD	48	70 (58-81)
Started a biologic medication	5	35 (21-55)
Started systemic corticosteroids	20	25 (18-35)
Attained inactive disease	45	81 (71-90)
cJADAS10 ≤1	–	64 (52-76)
cJADAS10 ≤2.5	–	79 (68-88)
Had at least one adverse event	–	48 (34-65)

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SAT0614 DOES DRUG EFFECTIVENESS OF 2ND AND 3RD TNF INHIBITORS IN PATIENTS WITH PSORIATIC ARTHRITIS DEPEND ON THE REASON FOR WITHDRAWAL FROM THE PREVIOUS TREATMENT? – RESULTS FROM THE EUROSPA RESEARCH COLLABORATION

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[1]EuroSpA Research Collaboration, On behalf of the DANBIO (Denmark), ARTIS (Sweden), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), biorx.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RRBR (Romania), ARC (Netherlands), BSRBR-AS (United Kingdom), GISEA (Italy), Denmark

Background: Tumour necrosis factor inhibitors (TNFi) are efficacious in patients with psoriatic arthritis (PsA), but some patients switch to a different TNFi because of adverse events (AE) or lack of effect (LOE). The EuroSpA Collaboration has previously demonstrated a 1-year retention rate of 77% and 6 months LUNDEX adjusted 28-joint count Disease Activity Score (DAS28) remission rates of 45%[1] in patients with PsA initiating the first TNFi treatment. Little is known about the effectiveness of switching to a second and third TNFi in patients with PsA.
Objectives: Firstly, to investigate retention and remission rates at 6, 12 and 24 months in patients with PsA initiating the 2nd and 3rd TNFi in clinical practice across Europe. Secondly, to investigate whether the outcomes are associated with the reason for withdrawal (AE or LOE) from the previous TNFi-treatment.
Methods: Prospectively collected data on PsA patients in routine care from 12 European registries were pooled. Kaplan-Meier estimation was used to investigate TNFi retention rates. LUNDEX adjusted[2] remission rates were calculated for DAS28<2.6 and 28 joint Disease Activity index

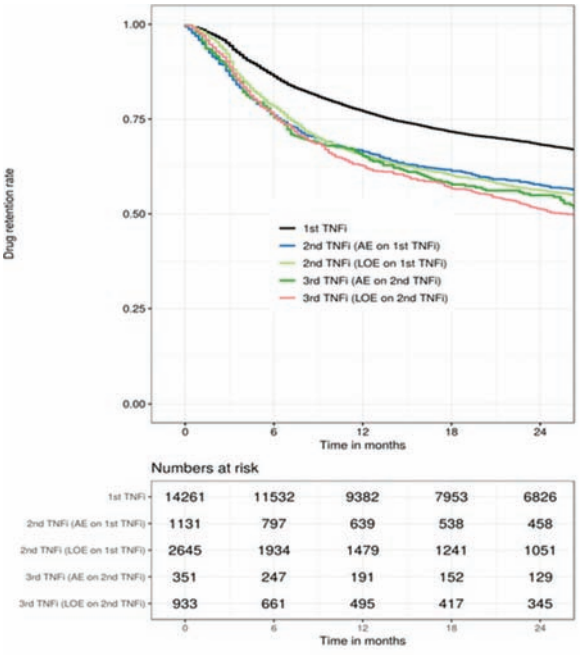


Figure: Kaplan-Meier curves (top) showing drug retention rates up to 24 months for 1st TNFi*, for 2nd (AE or LOE on 1st TNFi) and 3rd TNFi (AE or LOE on 2nd TNFi). The table (bottom) shows the number of patients who were still being treated at the corresponding time points
*previously reported

Table: Baseline characteristics, retention and remission rates of PsA patients initiating 2nd and 3rd TNFi overall and stratified by reason for withdrawal from the previous TNFi (AE or LOE).

	2nd TNFi (n=4971)*		3rd TNFi (n=1768)**	
	Baseline characteristics			
Age, years	50(41-58)		51(42-59)	
Male	42%		38%	
Concomitant/prior csDMARD	54% / 82%		53% / 86%	
Disease duration, years	5(2-11)		7(4-13)	
First TNFi drug **Infliximab/ Etanercept / Adalimumab / Certolizumab / Golimumab**	12% / 38% / 34% / 4% / 13%		18% / 28% / 29% / 5% / 20%	
DAS28	4(3.1-4.9)		4.1(3.2-5)	
DAPSA28	24.6(15.2-37)		25.3(16.3-38.6)	
	Retention rates			
6 months (95% CI)	80% (78-81%)		78 % (76-80%)	
12 months (95% CI)	69% (67-70%)		66 % (64-68%)	
24 months (95% CI)	60% (59-61%)		56 % (53-58%)	
	Initiating 2nd TNFi because of AE on 1st TNFi	**Initiating 2nd TNFi because of LOE on 1st TNFi**	**Initiating 3rd TNFi because of AE on 1st TNFi**	**Initiating 3rd TNFi because of LOE on 1st TNFi**
6 months (95% CI)	76% (73-79%)	78% (77-80%)	75% (71-80%)	76% (73-79%)
12 months (95% CI)	66% (64-69%)	65% (64-67%)	65% (60-71%)	63% (59-66%)
24 months (95% CI)	58% (55-61)	56% (54-58%)	55% (50-61%)	51% (48-55%)
	Remission rates			
	LUNDEX adjusted ***		**LUNDEX adjusted *****	
DAS28 remission at 6 / 12 / 24 months	35% / 29% / 23%		27% / 22% / 18%	
DAPSA28 remission at 6 / 12 / 24 months	14% / 11% / 9%		10% / 9% / 7%	
	Initiating 2nd TNFi because of AE on 1st TNFi	**Initiating 2nd TNFi because of LOE on 1st TNFi**	**Initiating 3rd TNFi because of AE on 1st TNFi**	**Initiating 3rd TNFi because of LOE on 1st TNFi**
	LUNDEX adjusted ***			
DAS28 remission at 6 / 12 / 24 months	34% / 30% / 23%	31% / 26% / 20%	26% / 25% / 21%	26% / 20% / 18%
DAPSA28 remission at 6 / 12 / 24 months	13% / 10% / 10%	11% / 9% / 8%	9% / 7% / 9%	9% / 8% / 6%

for Psoriatic Arthritis (DAPSA28) ≤4. Group comparisons were performed by Chi-square test.

Results: A total of 4971 patients initiating their 2nd TNFi and 1768 patients initiating their 3rd TNFi were included. Baseline characteristics are shown in the Table.

The overall retention rates for 2nd and 3rd TNFi at 12 months were 69% (67-70%) and 66% (64-68%), (2nd vs 3rd p=0.053), respectively (**Figure**). Corresponding retention rates for the individual registries ranged from 48-100% and 49-91%, respectively. If patients had stopped the 1st TNFi due to AE or LOE, 12-month retention rates for the 2nd TNFi treatment were 66% and 65%, respectively. In patients who stopped the 2nd TNFi due to AE or LOE, 12-month retention rates for the 3rd TNFi treatment were 65% and 63%, respectively.

For the 2nd and 3rd TNFi, 6 months LUNDEX adjusted DAS28 remission rates were 35% and 27% (p<0.001), respectively, and for DAPSA28 remission 14% and 10% (p=0.008) (**Table**).

Conclusion: The EuroSpA Collaboration demonstrated decreasing retention and remission rates with increasing number of previous TNFi, although with only minor difference between 2nd and 3rd. Patients who had withdrawn from the previous TNFi due to LOE had retention rates and remission rates similar to those who had withdrawn due to AE.

REFERENCES

[1] Brahe, et al. ACR 2018
[2] Arthritis Rheum, 2006, 54(2), p:600-6

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SAT0615 THE DIFFERENT EFFECTS OF CIGARETTE SMOKING ON ANTI-CITRULLINATED CYCLIC PROTEIN ANTIBODY AND RHEUMATOID FACTOR FORMATION IN RELATION TO SHARED EPITOPE ALLELES IN JAPANESE RA PATIENTS

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Background: In rheumatoid arthritis (RA), cigarette smoking affects both rheumatoid factor (RF) and anti-citrullinated cyclic peptide/protein antibody (ACPA) formation, but its association in relation to HLA-DRB1 alleles, especially shared epitope (SE) alleles, have been controversial among different races[1-5]. Furthermore, the impact of cigarette smoking and its cessation on levels of RF and ACPA have not been well documented.

Objectives: To investigate the impact of cigarette smoking and cessation on RF and ACPA levels in relation to HLA-DRB1 alleles in the largest RA cohorts in Asians.

Methods: A total of 6,239 subjects from two independent Japanese cohorts were enrolled. Their precise smoking histories both before and after the onset of RA were collected in questionnaires. The latest RF and ACPA levels were used (mean disease duration 15.6 years). We defined top quadrant of levels of RF or ACPA as high levels. Associations between smoking status and positivities or high levels of ACPA or RF as well as effects of HLA-DRB1 alleles on the associations were investigated by multiple logistic regression models.

Results: Smoking at onset was an independent risk of not only RF and ACPA positivities (RF, odds ratio (OR) 1.52, 95% confidence interval (CI) 1.26-1.85, $p=1.8x10^{-5}$; ACPA, OR 1.39, 95%CI 1.09-1.76, $p=6.8x10^{-3}$), but also high levels of these autoantibodies, especially RF (OR 2.06, 95% CI 1.70-2.48, $p=7.4x10^{-14}$; ACPA OR 1.29, 95%CI 1.06-1.57, $p=1.2x10^{-2}$). The larger ORs of RF than ACPA suggests that RF is more sensitive to cigarette smoking than ACPA. The effects of cigarette smoking were significantly larger in males than in females. The patients who quited smoking before onset had no longer significant risks of high autoantibody levels compared to subjects who had never smoked (RF, OR 1.33, p=0.099; ACPA, OR 1.19, p=0.093), and the risk was gradually attenuated depending on cessation years (RF, 0-10 years OR 1.34, 10-20 years OR 1.31, > 20 years OR 0.97; ACPA, 0-10 years OR 1.38, 10-20 years OR 1.01, > 20 years OR 1.12). The effect of smoking on ACPA positivity and its high level was apparent only in the presence of SE alleles, while the effect on RF positivity and its high level was apparent despite the presence of SE alleles (Table below).

Conclusion: Cigarette smoking especially at RA onset is a significant risk of future high levels of ACPA and RF preferentially in males, and RF is more sensitive to smoking status than ACPA. The effect on ACPA is apparent only in the presence of SE alleles, indicating that an interaction between cigarette smoking and SE alleles affects ACPA formation. On the other hand, the effect of cigarette smoking on RF formation may be independent of SE alleles. Our study imply a novel potential mechanism of RA pathogenesis.

ACPA positivity		smoking at onset	
		-	+
SE	-	1.000	1.081
	+	1.754***	2.665**

RF positivity		smoking at onset	
		-	+
SE	-	1.000	1.532
	+	1.131	1.599

ACPA High (≥ 236 (AU/mL))		smoking at onset	
		-	+
SE	-	1.000	0.434
	+	2.244****	3.051****

RF High (≥ 139 (IU/mL))		smoking at onset	
		-	+
SE	-	1.000	1.402
	+	0.906	1.539

** $p < 1.0X10^{-2}$, *** $p < 1.0X10^{-3}$, **** $p < 1.0X10^{-4}$

REFERENCES

[1] Klareskog L, Stolt P, Lundberg K, et al. Arthritis Rheum. 2006.
[2] Too CL, Yahya A, Murad S, et al. Arthritis Res Ther. 2012.
[3] Lee HS, Irigoyen P, Kern M, et al. Arthritis Rheum. 2007.
[4] Bang SY, Lee KH, Cho SK, Lee HS, Lee KW, Bae SC. Arthritis Rheum. 2010.
[5] Murphy D, Mattey D, Hutchinson D. PLoS One. 2017.

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SAT0616 DIETARY HABITS OF SIX AUTOIMMUNE DISEASES IN THE SPANISH POPULATION: A CROSS-SECTIONAL STUDY

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Background: In the last years multiple genetic variants have been associated with autoimmune disease (AD) risk. However, much less is known on the association with important environmental factors like diet.

Objectives: The objective of the present study is to characterize the dietary patterns of six prevalent ADs, including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE).

Methods: A cross-sectional cohort of 11,621 individuals from Spain encompassing 1,949 RA, 2,186 psoriasis (PS), 1,437 PsA, 699 SLE, 1,415 ulcerative colitis (UC), 1,952 Crohn's disease (CD) and 1,983 healthy controls, was recruited by the IMID-Consortium. The weekly consumption frequency of main food categories was recorded, together with drinking habits and smoking status. Multivariate linear models were used to test for association while adjusting for confounders.

Results: Patients with AD targeting the digestive system showed the largest differences in comparison to controls. In the rheumatic ADs several food categories were also found to be consumed differently compared to controls. SLE had a high consumption of sweets and pastries, and RA ate more fruit and bread/wholegrain foods and less meat and cold cuts compared to controls. In PsA the dietary pattern differences with controls

where milder, and non-overlapping with psoriasis. Disease activity was significantly associated with specific food categories in CD, UC and PS, mildly in RA and SLE, and PsA showed no association. High smoking cessation rates were observed in UC, CD and SLE, but not in Ps, RA and PsA. Tea/coffee and alcohol consumption was low in all ADs compared to controls.

Conclusion: Our results show previously unreported associations with dietary habits in rheumatic ADs.

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SAT0617 PRESENCE OF ANTI-BETA2-GLYCOPROTEIN-1 IGA ANTIBODIES MODERATES THE EFFECT OF INFLAMMATORY BURDEN ON CORONARY PLAQUE PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: Beta2-glycoprotein-1 (b2GPI), an apolipoprotein abundant in human plasma, is readily expressed in human atherosclerotic plaque. High frequencies of anti-b2GPI-IgA antibodies have been previously reported in both Rheumatoid arthritis (RA) patients and controls; their presence has been independently predictive of cardiovascular events in general patients.

Objectives: We explored the role of a-b2GPI-IgA presence and their interaction with inflammatory load on occult coronary plaque progression in patients with RA.

Methods: One hundred-one participants with a baseline plaque evaluation with coronary computed tomography angiography (CCTA) underwent follow-up assessment within 83±3.6 months. Coronary artery calcium (CAC) was quantified by the Agatston method. Subclasses (IgG, IgM, and IgA) of a-b2GPI Ab, anticardiolipin-Ab (ACL) and lupus anticoagulant (LA) were assessed on the day of baseline CCTA and reconfirmed 12 weeks later, if positive. Serum interleukin-6 (IL-6) was measured at baseline scan, while CRP was assessed on every clinic visit from baseline through follow-up scan. Multivariate linear regression models evaluated predictors of CAC progression; predictors entered as continuous variables included baseline CAC, age, waist-to-height ratio (obesity index), cumulative prednisone dose, years exposure to bDMARDs, statins and baseline IL-6 or time-averaged CRP. Gender, diabetes, hypertension, dyslipidemia, and a-b2GPI-IgA positivity were entered as dichotomous independent variables. Specific interactions between a-b2GPI-IgA presence (predictor) and time-averaged CRP or baseline IL-6 (moderator) where explored; the conditional effects of the predictor at values of the moderator and significance regions were defined with the Johnson-Neyman test.

Results: A-b2GPI-IgA antibodies were highly prevalent (34.7%) in contrast to other antiphospholipid-Ab subclasses (<4%). A-b2GPI-IgA presence predicted incident CAC [OR=3.69 (1.02-13.32), p=0.046] as well as greater CAC change from baseline, after adjustments for age, baseline CAC score and significant covariates [mean change (95%CI) = 93.2 (69.8-116.6) vs. 56.0 (39.0-73.0) units, p=0.012]. A significant interaction between a-b2GPI-IgA positivity and time-averaged CRP as well as baseline IL-6 on CAC progression was observed [beta=0.19, p=0.048 for time-averaged CRP and beta=0.26, p=0.029 for IL-6 respectively]; higher baseline IL-6 and time-averaged CRP associated with significant CAC progression exclusively in a-b2GPI-IgA positive patients but not in those without such Ab. Baseline IL-6> 4.66pg/ml and time-averaged CRP> 0.76mg/dl both associated with significantly higher CAC progression in a-b2GPI-IgA positive patients but not in negative ones (figure 1).

Conclusion: A-b2GPI-IgA antibodies independently contributed to occult coronary plaque progression in RA and specifically moderated the effect of inflammation on progression of atherosclerotic burden. Tight control of inflammation may be particularly important in Ab positive patients in order to prevent coronary plaque progression; additionally, a-b2GPI-IgA presence may serve as a predictive biomarker for atherosclerosis progression, especially in the context of higher inflammatory state.

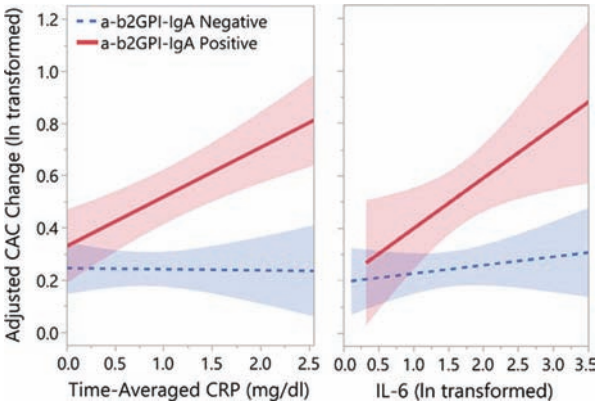


Figure 1. Interaction between b2GPI-IgA and time-averaged CRP and baseline IL-6 on CAC progression

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SAT0618 BASELINE CHARACTERISTICS AND TREATMENTS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: THE CREDIT STUDY IN CHINA, 2016-2018

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Background: Rheumatoid Arthritis (RA) has been a huge public health issue among the Chinese population, but little is known about the current treatments among RA patients, especially with different disease activity levels.

Objectives: To describe the baseline characteristics among all RA patients registered in the Chinese Registry of rhEumatoiD arthrITis (CREDIT) and the treatment patterns by patients' disease status.

Methods: A total of 25,191 RA patients registered in CREDIT from Nov, 2016 to Apr, 2018 were enrolled. Patients' baseline characteristics of demographics, disease characteristics, comorbidities, as well as treatment agents for RA were abstracted for analysis.

Results: The mean age of patients was 53.0 years and 79.9% of them were female. The median disease duration from diagnosis was 2.0 years. The proportions of moderate/high disease activity according to the Disease Activity Score-28 joint count using C-reactive protein (DAS28-CRP>3.2) and Clinical Disease Activity Index (CDAI>10) were 76.1% and 81.7%, respectively. Among those patients with treatment records, a similar conventional systematic disease-modifying antirheumatic drugs (cDMARDs) usage was observed in remission/low activity patients and

moderate/high activity patients categorized by DAS28-CRP. The results showed that 1639 (29.9%) remission/low activity patients and 4948 (28.3%) moderate/high activity patients received csDMARD monotherapy, while more combination therapies were prescribed in both groups (57.2% vs 55.1%, respectively). Furthermore, 337 (6.2%) patients received biologic disease-modifying antirheumatic drugs (bDMARDs) in remission/low activity group, while 1021 (5.9%) patients received bDMARDs in moderate/high activity group. In terms of tsDMARDs (only tofacitinib was approved in China), the proportions of usage were lower for remission/low activity patients (0.2%) than for the moderate/high activity patients (0.3%). On the other hand, the proportion of glucocorticoids usage in remission/low activity patients (15.5%) was lower than in moderate/ high activity patients (21.3%).

Conclusion: Over three-quarters of RA patients registered in CREDIT were in moderate/high disease activity. csDMARDs are the most frequently used medications for RA in China.

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SAT0619 ATTITUDES AND PERCEPTIONS OF PHYSICAL ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW

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Background: Patients with arthritis are less likely to adhere to physical activity recommendations than are individuals in the general population. In contrast to rheumatoid arthritis (RA), which affects predominantly peripheral joints, axial spondyloarthritis (axSpA) affects predominantly the axial skeleton and may result in restricted spinal mobility. Both RA and axSpA are associated with an increased risk of cardiovascular disease, the development of physical disability, and decreased levels of physical activity. However, the extent to which the distinct joint distributions in these forms of inflammatory arthritis might differentially affect physical activity behaviors is not known. Several studies have addressed the relationship between "physical activity behavior" and "disease-specific outcomes" among patients with RA, but information about this among patients with axSpA is more limited.

Objectives: To review systematically and synthesize qualitatively the literature about perceived facilitators and barriers to physical activity in patients with axSpA and identify the types of physical activity preferred by these patients.

Methods: PubMed and Scopus and reference lists were searched for quantitative and qualitative studies reporting on beliefs towards exercise in patients with axSpA. Searches were limited to studies published from 2000 through 2018. The PRISMA guidelines were followed. Systematic searches identified 125 publications which underwent a title, abstract, or full-text review. Studies were excluded if articles were not in English or did not include original data. We summarized the methodologic quality using modified criteria for quantitative and qualitative studies.

Results: Eight quantitative and three qualitative studies met eligibility criteria, with variable study quality. Based on self-reported data, 50% to 68% met established physical activity recommendations with walking, swimming/pool exercise, and cycling the most common forms reported. Intrinsic factors such as motivation and improvement in symptoms and health were commonly reported as facilitators associated with physical activity/exercise. Barriers included lack of time, fatigue, and symptoms such as pain.

Conclusion: Up to half of patients with axSpA do not meet established physical activity recommendations. Given the potential for regular physical activity to reduce symptom burden in this patient population and the recent 2018 EULAR recommendations for regular physical activity as part of the management of these patients, more rigorous studies of physical activity behaviors and attitudes will be useful to inform interventions and promote exercise among individuals with axSpA.

REFERENCES

[1] Ehrlich-Jones L, Lee J, Semanik P, Cox C, Dunlop D, Chang RW. Relationship between beliefs, motivation, and worries about physical activity and physical activity participation in persons with rheumatoid arthritis. Arthritis Care Res 2011;63:1700–1705.

[2] Iversen MD, Frits M, von Heideken J, Cui J, Weinblatt M, Shadick NA. Physical activity and correlates of physical activity participation over three years in adults with rheumatoid arthritis. Arthritis Care Res 2017;69:1535-1545.

[3]

[4] Rausch Osthoff A-K, Niedermann K, Braun J, Adams J, Brodin N, Dagfinrud H, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis 2018:annrheumdis-2018-213585. Available at: http://ard.bmj.com/lookup/doi/10.1136/annrheumdis-2018-213585.

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SAT0620 INCIDENCE AND TREND OF HIP FRACTURE IN SPAIN. FACTORS ASSOCIATED WITH THE VARIABILITY OBSERVED

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Background: It is known that in Spain there is a great variability between Autonomous Communities (CCAA) in the incidence and trend of hip fracture, with rates in certain regions that can double those of others. Although it is speculated with different hypotheses that explain it, there are no studies that demonstrate the reasons for this variability.

Objectives: 1.- To analyze the incidence and trend of hospital admissions for hip fracture, in Spain, during the period between 1999 and 2015.

2.- Analyze factors/risk markers (genetic, demographic, level and living conditions, health indicators, cohort effect centered on the period of the civil war, climatology and environment) that could explain the variability in incidence and trend between different CCAA.

Methods: Part 1: retrospective observational study, nationwide, based on the exploitation of an administrative database (MBDS) that collects hospital admissions from 1/1/1999 to 12/31/2015. Hip fractures were identified through the presence of ICD-9 820.0 to 820.9 as primary or secondary diagnosis. Only those that the patient was 50 or older were selected. The crude rates and adjusted for age of incidence of hip fracture were calculated, by sex, age groups and by CCAA. The population census issued by the National Institute of Statistics (INE) was used to calculate this rate. The trend over the 17 years covered in the study was analyzed using Poisson regression and negative binomial models.

Part 2: ecological study, based on the analysis of the results obtained in part 1, with different risk markers obtained from the INE (except the 4), by CCAA. The analyzed factors were: 1.- Genetic; 2.- Demographic; 3.- Level and conditions of life; 4.- Health; 5. Impact of the civil war. 6.- Environment; 7.- Climatological. This analysis was performed using bivariate correlations and univariate and multivariate linear regression.

Results: There were 744,848 patients diagnosed with hip fracture; 182,205 (24.4%) men and 562,643 (75.5%) women p <0.001. (Ratio M: V of 3.07). The mean age was 81.7 years (SD 8.9), 79.3 years (SD 10.3) in men and 82.5 years (SD 8.2) (p <0.001). In-hospital mortality was 5.7%, The average of the Charlson Index was 0.71 (SD1.14). The rate adjusted for the age of incidence of global hip fracture at the national level was 315.38/100,000 inhabitants * year (95% CI 312.36-317.45), 169.56 (95% CI 166.26-172.39).) in men and 434.89 (95% CI 430.66-438.17) in women. By CCAA the incidence of hip fx varied from 213,97 in the Canary Islands to 363,13 in Comunidad Valenciana and Cataluña).

The trend for both sexes was -0.67% (95% CI 0.9990-0.9957) (p <0.001); in men it was -0.06% (95% CI 0.9975-1.0013) (p = 0.537) and

in women -0.82% (95% CI 0.9992-0.9944) (p <0.001). The distribution by CCAA of the incidence and trend is represented in the following figure:



In the analysis of risk factors/markers that explain this distribution, we found significant correlations with genetic factors (H and J2 haplotypes), demographic (birth, fecundity, mean age and aging index), climatic factors (precipitation) and the time a region was on the Republican side. The linear regression model that includes the factors that show significant correlation justifies 96% of the variability observed.

Conclusion: In Spain, the rate adjusted for age of incidence of hip fracture is decreasing. There is a great variability in the incidence and tendency of hip fracture among the different CCAA. Genetic, demographic, climatological factors and due to the cohort effect of the civil war, explain 96% of this variability.

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SAT0621 IMPACT OF HINDFOOT CORONAL/SAGITTAL ALIGNMENT ON METATARSUS PRIMUS ELEVATUS IN RHEUMATOID FOOT DEFORMITIES

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Background: Typical foot deformity patterns of patients with rheumatoid arthritis (RA) include hallux valgus, claw toes, splay foot, flat foot, and hindfoot valgus deformities. However, some patients show deformities different from a typical pattern, including metatarsus primus elevatus, described as dorsal elevation of the first metatarsal in relation to the lesser metatarsals, as we reported previously. In the report, we speculated that metatarsus primus elevatus might be associated with calcaneal inclination and hindfoot varus alignment. However, there are no studies on the association of hindfoot alignment with metatarsus primus elevatus in patients with RA.

Objectives: To elucidate the impact of hindfoot coronal/sagittal alignment on metatarsus primus elevatus in patients with RA.

Methods: A retrospective study was performed of standing anteroposterior and lateral radiographs of 81 feet in 53 patients who underwent surgical treatment for metatarsalgia in our hospital. The distance between the dorsal cortical bones of the first and second metatarsals (MPE) was measured on the lateral radiograph for the degree of metatarsus primus elevatus. Using a two-dimensional coordinate system on the lateral radiographic image where lines along the calcaneus tuberosity were defined as X and Y axes, ten anatomic points of the foot were measured. Calcaneal pitch, talar declination angle, and naviculocuboid (N/C) overlap ratio were measured for assessment of hindfoot sagittal and coronal alignment, respectively. We assessed the hallux valgus angle (HVA), the inter metatarsal angle between first and 2nd metatarsals (M1M2A), and the intermetatarsal angle between first and 5th metatarsals (M1M5A) for axial foot alignment. The correlations of MPE with other radiographic angular and coordinate data were statistically assessed using Spearman rank correlation coefficient.

Results: Median MPE was 1.7 mm (interquartile range: 0–5.2 mm). The first metatarsal head, first metatarsal-cuneiform and posterior talocalcaneal joint were shifted dorsally (r=0.70, p<0.01; r=0.57, p<0.01; r=0.42, p<0.01, respectively). No correlation MPE with HVA and M1M5A were observed (r=-0.26, p=0.05; r=-0.25, p=0.07, respectively), however, M1M2A showed correlation with MPE (r=-0.52, P<0.01). On the other hand, MPE showed a high degree of correlation with talar declination angle, calcaneal pitch, and N/C overlap ratio (r=-0.45, p<0.01; r=0.35, p<0.01; r=-0.45, p<0.01, respectively).

Conclusion: In patients with RA, the hindfoot joints shifted dorsally in metatarsus primus elevatus. Moreover, hindfoot varus alignment and high-arched foot affect metatarsus primus elevatus. The results of the present study suggest the importance of evaluating hindfoot alignment when determining surgical treatment procedures for rheumatoid foot deformities.

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SAT0622 ROLE OF PREGNANCY IN FLARE AND PROGRESSION INTO DEFINED RHEUMATIC DISEASE IN WOMEN WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE: RESULTS FROM A MONOCENTRIC OBSERVATIONAL COHORT

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Background: Patients with Undifferentiated Connective Tissue Disease (UCTD) are at risk of disease worsening and progression into well-defined rheumatic disease over time[1]. Only a few studies[2-3] from small cohorts regarding the role of pregnancy in UCTD outcome are available, with no clear-cut factors associated with the evolution of the disease.

Objectives: To evaluate the impact of pregnancy on progression from UCTD into a well-defined rheumatic disease. To analyze the role of UCTD flares during pregnancy, as well as clinical and laboratory features in the evolution of the disease; to compare UCTD evolution in patients with or without pregnancy; to compare UCTD evolution in patients with or without UCTD diagnosis before pregnancy.

Methods: We collected clinical data from a rheumatologic outpatient clinic regarding women (aged 18-45) with UCTD, from diagnosis to last follow-up. Pregnant women with a previously undiagnosed UCTD were included using a validated two-steps screening method performed at the 1st trimester during the gynecological ultrasound evaluation, as previously reported[4]. We compared women with at least one pregnancy to non-pregnant women. Student's t test was applied for unpaired, continuous variables, while chi-square to compare percentages. The rate of progression was compared with Kaplan–Meier estimator and Log-rank test. A Cox regression model was fit to assess the association of flare during pregnancy and of clinical and laboratory features with the evolution of the disease.

Results: We retrieved data regarding 152 pregnant and 108 non-pregnant patients, mean age of 32 (±6.71) years. We recorded 201 pregnancies. The progression into well-defined disease was observed in 31 (20.4%) pregnant patients and in 5 (4.6%) non-pregnant patients (p<0.001) (fig.1). The most frequent evolution was into SLE (52%) in pregnant UCTD and into SSc (40%) in non pregnant patients.

We observed 32 flares during pregnancy, mostly with joints involvement (75% of the cases). Having at least one flare during pregnancy, a history of UCTD-related cytopenia and lower levels of C4 in the 6 months before conception were associated with disease evolution. No differences were found as for disease evolution in pregnant patients with or without a previous UCTD diagnosis.

Conclusion: The rate of progression from UCTD into a well-defined rheumatic disease is significantly higher in women who had a pregnancy. Having a history of UCTD-related cytopenia, or lower C4 levels before conception, or at least one flare of UCTD during pregnancy significantly increases the risk of progression. The timing of the diagnosis of UCTD, in respect with the pregnancy, does not change the risk of flare and progression.

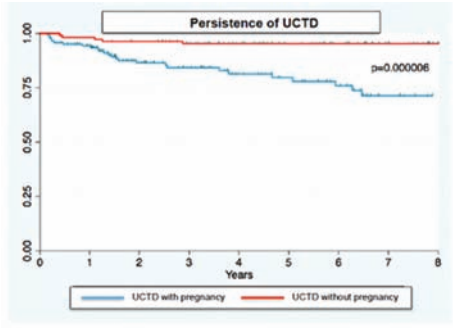


Figure 1. Persistence of UCTD in women with at least one pregnancy compared to non-pregnant women (Kaplan-Meier curve)

REFERENCES

[1] Mosca M, Tani C, Vagnani S, et al. The diagnosis and classification of undifferentiated connective tissue diseases. J Autoimmun. 2014

[2] Mosca M, Neri R, Strigini F, et al. Pregnancy outcome in patients with undifferentiated connective tissue disease: a preliminary study on 25 pregnancies. Lupus 2002

[3] Castellino G, Capucci R, Bernardi S, et al. Pregnancy in patients with undifferentiated connective tissue disease: a prospective case-control study. Lupus 2011
[4] Spinillo A, Beneventi F, Ramoni V, et al. Prevalence and significance of previously undiagnosed rheumatic diseases in pregnancy. Ann Rheum Dis. 2012

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SAT0622B SERUM URIC ACID LEVELS WERE INDEPENDENTLY ASSOCIATED WITH AORTIC ARCH CALCIFICATION IN MIDDLE-AGED AND ELDERLY CHINESE POPULATION

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Background: Aorta calcification are considered markers of subclinical atherosclerotic disease that are independent predictors of subsequent cardiovascular events. A growing number of studies have shown that serum uric acid is associated with the development of cardiovascular diseases.
Objectives: The main purpose of this study was to investigate the prevalence of aorta calcification and to determine the relationship between the levels of serum uric acid and aorta calcification in the middle-aged and elderly population.
Methods: From Jan 2018 to Dec 2018, totally 6152 consecutive participants aged >50 years old underwent annual health survey were included in this study. Detailed physical examination was performed as well as a thorough review from structured questionnaires, which in baseline demographics and medical history including alcohol consumption, smoking and physical activity status, BMI, blood pressure, blood glucose and serum lipid were all collected and recorded. Aortic calcification was analyzed by chest X-ray. All data were analyzed retrospectively.
Results: The prevalence of aortic arch calcification was 13.9% in these 6152 participants with age >50 years and was equally common in men and women. Aortic arch calcification prevalence was significantly increased in populations with hyperuricemia (defined as serum uric acid 420 umol/L), as compared with populations with normal serum uric acid levels (defined as serum uric acid ≤ 420 umol/L) (83.39% vs. 16.61%, $p < 0.001$). Participants were divided into three groups according to their uric acid levels.A more prevalent aortic arch calcification was identified in high uric acid level group than those in middle or low uric acid level group ($p < 0.05$). On logistic regression analysis, serum uric acid levels were found to be independently associated with aortic arch calcification (OR=1.469, 95%CI: 1.199~1.800, P<0.01) in these participants.
Conclusion: Serum uric acid levels were independently associated with aortic arch calcification in middle-aged and elderly Chinese population. These results may suggest the need for more aggressive actions for urate lowering therapy in middle-aged and elderly hyperuricemia patients, especially in patients coexist with other cardiovascular disease risks.

REFERENCES

[1] Gertler MM, Garn SM, Levine SA. Serum uric acid in relation to age and physique in health and in coronary heart disease. Ann Intern Med. 1951;34:1421–1431.
[2] Fang J, Alderman MH. Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971–1992. National health and nutrition examination survey. JAMA. 2000;283:2404– 2410.
[3] Wheeler JG, Juzwishin KD, Eiriksdottir G, et al. Serum uric acid and coronary heart disease in 9,458 incident cases and 155,084 controls: prospective study and meta-analysis. PLoS Med. 2005;2:e76.
[4] Culleton BF, Larson MG, Kannel WB, Levy D. Serum uric acid and risk for cardiovascular disease and death: the Framingham heart study. Ann Intern Med. 1999;131:7–13.
[5] 5.Moriarity JT, Folsom AR, Iribarren C, et al. Serum uric acid and risk of coronary heart disease: Atherosclerosis Risk in Communities (ARIC) study. Ann Epidemiol. 2000;10:136–143.

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SAT0623 CHARACTERIZING THE GUT AND PLASMA METABOLOMES IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: Although a link between gut microbiome and autoimmunity has been suggested, there is a gap in the understanding of the gut metabolome in ANCA-associated vasculitis (AAV).
Objectives: To explore the mechanisms by which an altered gut microbiota might predispose to ANCA-associated vasculitis (AAV), a comprehensive metabolic profiling of fecal and plasma bile acids, amino acids, and short chain fatty acids was performed in patients with AAV (granulomatosis with polyangiitis; microscopic polyangiitis; and eosinophilic granulomatosis with polyangiitis) and healthy controls.
Methods: Using cross-sectional and longitudinal designs, the fecal and plasma metabolomes of patients with newly diagnosed AAV (active and in remission) were compared to chronic AAV (active and in remission), and to healthy controls. All samples were analyzed by Liquid Chromatography/Mass Spectrometry for bile acids, aminoacids, and short chain fatty acids. Gut microbiome was analyzed on the same fecal samples by sequencing the bacterial 16S rRNA gene (V1-V2 region). Association between bacterial taxa and fecal metabolites was studied using logistic regression models, correcting for multiple comparisons.
Results: 78 fecal samples were studied: 37 active AAV (20 new diagnosis and 17 chronic), 25 remission, and 16 controls. 32 plasma samples were studied: 20 active AAV, 6 remission, and 6 controls.
Compared to remission states, the fecal amino acids phenylalanine and tyrosine were significantly diminished in active disease. Patients with chronic AAV in remission had higher levels of plasma phenylalanine and tyrosine compared to patients with a new diagnosis of AAV in remission (p=0.02 for both).
Patients with a chronic active AAV had higher levels of plasma taurolithocholic bile acid compared to patients with an active new diagnosis of AAV (**Figure 1A**). *Faecalibacterium* was associated with this plasma bile acid (p=0.02). Plasma glycholic and glycodeoxycholic acids were strongly associated with active disease (p<0.01 and p=0.01 for both).
Patients with chronic AAV in remission had higher levels of plasma taurochenodeoxycholic bile acid compared to patients with a new diagnosis of AAV in remission (**Figure 1B**). *Phascolarctobacterium, Sutterella, and Ruminococcus* were associated with this plasma bile acid (p<0.05).
Conclusion: Active AAV is associated with an altered fecal and plasma metabolome. Plasma taurochenodeoxycholic bile acid, and plasma and fecal amino acids are higher in chronic remission states compared to new diagnosis remission states, suggesting potential anti-inflammatory

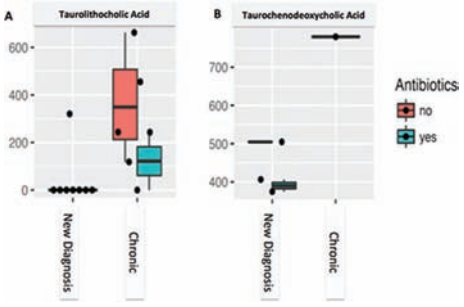


Figure 1. Differential Proportion of Plasma Bile Acids Between Various Subgroups of Patients with ANCA-Associated Vasculitis (AAV). (A) Compared to patients with a new diagnosis of active AAV, patients with chronic active AAV had a higher proportion of *taurolithocholic acid* (p=0.02). (B) Compared to patients with a new diagnosis of AAV in clinical remission, patients with a chronic AAV in remission had a higher proportion of *taurochenodeoxycholic acid* (p=0.04).

effects of these metabolites. Diminished metabolic diversity may be a feature of active AAV and potential biomarker to predict disease activity in AAV.

REFERENCES

[1] Scher J.U., et al., *Microbiome in Inflammatory arthritis and human rheumatic disease.* Arth Rheum, 2016. 68: p.35-45.

[2] Scher J.U. *Intestinal dysbiosis and potential consequences of microbiome-altering antibiotic use in the pathogenesis of human rheumatic disease.* J of Rheum, 2015. 42: p.355-357.

[3] Scher J.U., et al., *Decreased bacterial diversity characterizes an altered gut microbiota in psoriatic arthritis and resembles dysbiosis of inflammatory bowel disease.* Arth Rheum, 2015. 67(1): p.128-139

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SAT0624 VALIDATION PROCESS OF CASES OF RHEUMATOID ARTHRITIS IN A LARGE PROSPECTIVE COHORT OF FRENCH ADULT WOMEN: THE E3N COHORT

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Background: Rheumatoid arthritis (RA) is a complex multifactorial autoimmune disease in which genetic and environmental factors interact in the pathogenesis of the disease to trigger auto-immunity. Except for tobacco smoking, the role of environmental factors has been suggested yet poorly investigated, and results were rarely reproducible. More observational studies are requested to address the question. Cohort studies offer the advantage over case-control studies of having a prospective collection of environmental factors before disease onset, thus avoiding recall bias. However, collected information about disease phenotypes is usually limited, and a rigorous process of case validation is needed.

Objectives: To detect RA cases in a large prospective cohort of healthy French adult women and to assess the performance of the validation methods.

Methods: The French E3N cohort included 98,995 healthy women prospectively followed since 1990. Self-administered questionnaires were sent every 2–3 years to collect medical events, and general, lifestyle, and environmental characteristics. Potential cases of inflammatory rheumatic diseases (IRD), including RA cases, were identified through self-reports in three consecutive questionnaires. Self-reported RA cases were validated with two methods including sending of a specific validation questionnaire and the use of the reimbursement database. The sensitivities and specificities of each method were calculated using as a reference the analysis of available medical records reviewed by a panel of expert rheumatologists.

Results: Among the 3,192 identified potential IRD cases, 964 RA cases were validated, including 698 incident cases and 266 prevalent cases. Of them, 314 (32.6%) were seropositive, 23 (2.4%) seronegative and 627 (65.0%) had unknown antibody status. Mean age at diagnosis was 57.4 ± 13.9 years (40.9 ± 10.4 years for prevalent cases, and 63.8 ± 9.0 for incident cases). Sensitivities and specificities of the validation methods were 92.2 and 83.7% for the specific validation questionnaire and 69.8 and 97.0% for the reimbursement database.

Conclusion: This study enabled us to detect a large number of RA cases in a large general population prospective cohort of women with acceptable sensitivity and specificity. This will allow investigating a large number of potential endogenous and exogenous risk factors of RA in women.

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SAT0625 TREATMENT RESPONSE AND DRUG RETENTION RATES IN 23,956 BIOLOGIC-NAÏVE PATIENTS WITH AXIAL SPONDYLOARTHRITIS INITIATING TNFI TREATMENT – ROUTINE CARE DATA FROM 12 REGISTRIES IN THE EUROSPA COLLABORATION

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[1]EuroSpA Research Collaboration, On behalf of the DANBIO (Denmark), ARTIS (Sweden), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), biorx.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RRBR (Romania), ARC (Netherlands), BSRBR-AS (United Kingdom), GISEA (Italy), Denmark

Background: The efficacy of Tumour Necrosis Factor Inhibitor (TNFi) in patients with axial spondyloarthritis (axSpA) has been investigated in randomized controlled trials (RCTs) with strict inclusion and exclusion criteria. Patients treated in routine care are more heterogeneous and only ≈20-30% of patients receiving TNFi in routine care would have been eligible to be enrolled in the RCTs[1]. This emphasizes the need for real-world observational data as a valuable supplement to RCTs. Studying large patient groups from several European countries would increase the external validity of the results. Particularly, large data sets from patients with non-radiographic axSpA (nr-axSpA) are lacking.

Objectives: To investigate TNFi retention rates at 12 months (primary objective), 6 and 24 months, and response rates at the same time-points in biologic-naïve patients with axSpA from the EuroSpA Research Collaboration. Furthermore, to investigate if findings vary between patients with nr-axSpA and ankylosing spondylitis (AS).

Methods: Data from 12 European quality registries in rheumatology, prospectively collected in routine care, were anonymized and uploaded through the secure Virtual Private Network pipelines to the EuroSpA server. Baseline characteristics were investigated with non-parametric descriptive statistics. TNFi retention rates (Kaplan-Meier statistics), and Ankylosing Spondylitis Disease Activity Score (ASDAS) Inactive disease (<1.3) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≤4 were assessed, including LUNDEX adjustment[1]. For patients initiating 1st TNFi after January 1st 2009, the following sub-cohorts were also

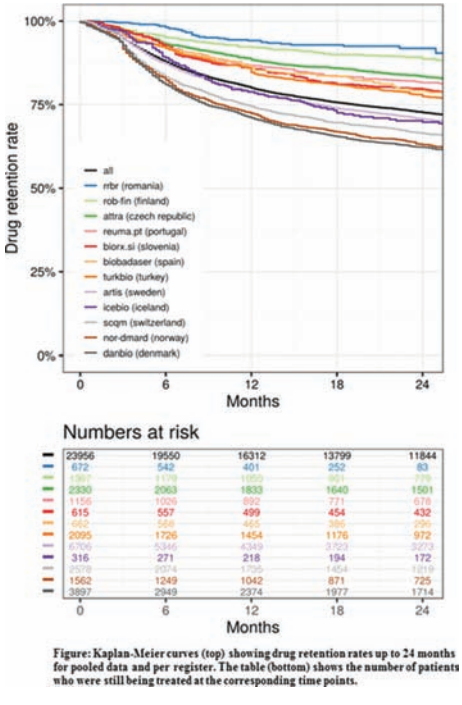


Figure: Kaplan-Meier curves (top) showing drug retention rates up to 24 months for pooled data and per register. The table (bottom) shows the number of patients who were still being treated at the corresponding time points.

studied: patients fulfilling the ASAS criteria for axSpA, the modified New York criteria for AS and ASAS criteria for nr-axSpA.

Results: First TNFi treatment was initiated in 23,956 axSpA patients. Baseline characteristics of the pooled population are shown in the **Table**. The 12-month retention rate (95%CI) was 80% (79-80%); 71-94% across registries (**Figure**). At 6 months, overall ASDAS Inactive disease/ BASDAI≤4 rates were: 33%/72% (LUNDEX adjusted: 27%/59%). Number of patients initiating 1st TNFi after 2009 and registered with fulfilment of axSpA (ASAS) was 6,097, Ankylosing Spondylitis (modified New York Criteria) was 2,935 and non-radiographic axSpA (nr-axSpA) was 1,178. We observed lower retention rate and marginally lower LUNDEX adjusted response rates in nr-axSpA patients (**Table**).

Table: Baseline characteristics, retention and response rates of all patients and the axSpA subgroups (ASAS criteria, modified New York criteria and nr-axSpA)

	All		ASAS criteria* (n=6,097)	Modified New York criteria** (n=2,935)	Nr-axSpA*** (n=1,178)
	Available data, n	Median(IQR) or %	Median(IQR) or %	Median(IQR) or %	Median(IQR) or %
Age, years	23,956	41 (33-50)	41 (33-50)	43 (34-52)	39 (31-48)
Male	23,956	61 %	63 %	67 %	52 %
HLA-B27-positive	12,388	68 %	76 %	69 %	68 %
csDMARD	23,745	31 %	29 %	26 %	25 %
Disease duration, years	18,939	2 (1-9)	2(1-8)	3 (1-10)	1 (0-3)
First TNFi drug					
Infliximab	6,874	29 %	19 %	20 %	16 %
Etanercept	6,034	25 %	19 %	22 %	20 %
Adalimumab	6,936	29 %	36 %	36 %	35 %
Certolizumab	868	4 %	4 %	3 %	5 %
Golimumab	3,244	14 %	23 %	20 %	24 %
CRP, mg/L	18,382	10 (4-23)	13 (5-26)	13 (5-27)	7 (2-19)
BASDAI, mm	14,351	60 (44-72)	64 (51-76)	66 (52-77)	65 (50-78)
BASFI, mm	4,551	24 (10-40)	20 (10-40)	30 (10-50)	20 (10-30)
BASMI	11,464	46 (26-66)	51 (33-69)	53 (34-70)	48 (29-68)
			Retention rates		
6 months (95% CI)	88% (87-88%)		89% (88-90%)	90% (89-91%)	84% (82-86%)
12 months (95% CI)	80% (79-80%)		81% (80-82%)	83% (82-85%)	73% (70-76%)
24 months (95% CI)	73% (72-73%)		74% (73-76%)	76% (74-78%)	64% (62-67%)
			Response rates		
	Crude****	LUNDEX adjusted*****	Crude****	LUNDEX adjusted** ***	Crude****	LUNDEX adjusted** ***	Crude****	LUNDEX adjusted*****
ASDAS inactive disease at 6 / 12 /24 months	33% / 35% / 38%	27% /24% / 19%	30% /33% / 38%	25% / 23% / 18%	25% / 29% / 32%	21% /21% / 16%	26% / 31% / 37%	20% / 19% / 15%
BASDAI ≤4 at 6 / 12 / 24 months	72% / 75% / 77%	59% / 51% / 38%	73% / 76% / 79%	60% / 52% / 37%	71% / 73% / 76%	60% / 52% / 37%	64% / 70% / 71%	50% / 43% / 29%

*Data are as observed, median (IQR) or percentage; csDMARD: conventional synthetic Disease Modifying Anti Rheumatic Drug; TNFi: tumor necrosis factor inhibitor; INF: infliximab; ETA: etanercept; ADA: adalimumab; CER: certolizumab pegol; GOL: golimumab; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BASFI: Bath Ankylosing Spondylitis Functional Index; VAS: visual analogue scale; *Patients registered as having axial SpA according to Axial Spondyloarthritis (ASAS) criteria, initiating treatment after 2009; **Patients registered as having Ankylosing Spondylitis (AS) according to New York Criteria, initiating treatment after 2009; ***Patients registered as having non-radiographic axSpA (nr-axSpA), initiating treatment after 2009; ****Crude value: The fraction responding of those still on drug at 6, 12 and 24 months, respectively; *****LUNDEX adjusted: crude value adjusted for drug retention*

Conclusion: In routine care ≈1/3 of patients with axSpA initiating 1st TNFi treatment were in ASDAS inactive disease after 6 months, while ¾ achieved BASDAI ≤4. Four out of five patients continued treatment after 1 year. Results were slightly inferior in nr-axSpA as compared to AS.

REFERENCES

[1] Clin Exp Rheumatol, 2018, 36(6):1068-1073
[2] Arthritis Rheum, 2006, 54(2): 600-6

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SAT0626

THE INFLUENCE OF MEDITERRANEAN DIET IN RHEUMATOID ARTHRITIS: A MONOCENTER CROSS-SECTIONAL STUDY

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Background: Mediterranean diet (MD) is considered a well-balance and potentially anti-inflammatory diet characterized by high consumption of olive oil, unrefined cereals, fresh or dried fruit and vegetables, fish, dairy, meat and with a moderate amount of red wine. Currently, there is conflicting data for the benefits of MD in RA, and no enough evidence to support a role of MD in the prevention and treatment of rheumatoid arthritis (RA) [1].

Objectives: The aim of our study was to evaluate the association between MD adherence and disease activity, general health (GH) and comorbidities in patients with RA.

Methods: Consecutive patients with RA (ACR/EULAR Criteria 2010) were enrolled in this cross-sectional study. For each patient, Disease Activity Score on 28 joints (DAS28), Simple Disease Activity Index (SDAI), patient GH and a self-reported questionnaire called MD score [2] were recorded. The association between MD score and the above mentioned variables was assessed through univariate regression models (MD score as response variable and the variables of interest as independent variables). Results from each model were reported in terms of: 1) test of association (Likelihood Ratio test, with a Chi-square distribution); 2) for categorical independent variables, estimated differences of mean MD score between groups, with respective 95% CI; 3) for numerical independent variables, estimate of correlation coefficient and regression slope coefficient, with respective 95% CI. All analyses were performed using the R software.

Results: 205 patients (197 Italian) were enrolled: median age at visit 53 (q1-q3: 44-59) years, age at onset 38 (q1-q3: 28-47), disease duration 12 (q1-q3: 7-19), female 80.49%, rheumatoid factor and/or anti–citrullinated protein antibody positivity 58.54%, radiographic damage 41.79%. Comorbidities were also assessed: gastrointestinal 19% (gastro-esophageal reflux disease; inflammatory bowel disease; gastritis; esophagitis), chronic renal failure 1%, arterial hypertension 21.95%, diabetes mellitus 3.9%, coronary artery disease 1.95%. A significant positive correlation was found between MD score and GH, as shown in the table below: this suggests a low/moderate tendency of having better GH with higher MD score. Although not statistically significant, a negative correlation was found with DAS28 and SDAI, suggesting an association between higher MD score with lower disease activity. Among comorbidities, a significant difference of mean MD score values between subjects with and without arterial hypertension was also found (mean difference -2.0 CI: -3.7, -0.2; p=0.029).

	Mediterranean diet score		
Numerical covariates	**Correlation coefficient (r): est (95% CI)**	**Regression coefficient (slope): est (95% CI)**	**LR test: p-value**
DAS28	-0,10 (-0.23, 0.04)	-0.45 (-1.05, 0.16)	0.149
SDAI	-0.12 (-0.25, 0.02)	-0,12 (-0.38, 0.15)	0.088
GH	0.19 (0.05, 0.31)	0.05 (0.01, 0.09)	**0.007***
Body mass index	-0.05 (-0.18, 0.09)	-0,06 (-0.22, 0.08)	0.483

Conclusion: In this Italian RA cohort, the adherence to MD was significantly associated with a better GH, but higher MD score was not significantly associated with lower disease activity. Arterial hypertension was the only comorbidity associated with lower MD score, probably due to the fact that the prevalence of the other comorbidities was low. Our study suggests an overall beneficial effect of MD in RA patients. Further studies are needed to better understand the impact of lifestyle modification (*e.g.* diet) in achieving RA disease control.

REFERENCES
[1] Forsyth C, et al. Rheum Intern 2018
[2] Demosthenes B, et al. Nutr metab cardiovasc dis 2006

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SAT0627

PSYCHOLOGICAL PROFILE IN PATIENTS WITH RHEUMATIC DISEASES IN CHINA: A STUDY OF HADS SELF-ASSESSMENT WITH SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: The patients with chronic diseases such as rheumatic diseases suffer from physical pain and/or disability. In addition, psychological morbidities have also been found in patients with rheumatic diseases. Hospital Anxiety and Depression Scale (HADS) is commonly applied to assess the mental health of patients with rheumatic disease.
Smart System of Disease Management (SSDM) is a mobile application which has two application systems for both patients and doctors for rheumatic diseases management. The patient application system provides functions including self-assessment, medication management, adverse events management and laboratory records. After input by patients, all the data will be synchronized to the mobile terminal of authorized rheumatologists. Based on these data, rheumatologists can evaluate and follow up with their patients and provide consultation service through SSDM in text or voice method. The rheumatologists can also adjust therapeutic regimens based on patients' profiles.
Objectives: The purpose of this study is to explore the profile of psychological morbidities in patients with rheumatic diseases.
Methods: The patients were educated and trained to perform HADS assessments using SSDM by the rheumatologists. The HADS self-assessments data could be extracted from the mobile terminal for further analysis. The HADS scale consists of two subscales for anxiety (HADS-A) and depression (HADS-D) which have 7 items, respectively. Both subscales range from 0 to 21, with higher scores indicating greater anxiety and depression. A score between 11 and 21 indicates a probable case of anxiety or depression.
Results: From June 2016 to January 2019, 13,830 adult patients (81% females; 19% males) with a mean age of 43.86 ± 17.29 years from 254 hospitals performed self-evaluation of HADS using SSDM. 34 rheumatic diseases were assessed, including RA (4,594; 33%), SLE (3054; 22%), SS (1,253, 9%), AS (975; 7%), gout (607; 4%), OA (590; 4%), MCTD (490; 4%), UCTD (443; 3%), PM/DM (405; 3%), etc.

Table 1 presents the number and percentage of patients with rheumatic diseases accompanied by anxiety or depression. The ratio of probable anxiety was 12% in RA, 14% in SLE, 15% in SS, 16% in AS, 10% in Gout, 11% in OA, 12% in MCTD, 14% in UCTD and 10% in PM/DM. The prevalence of probable depression was 19% in RA, 21% in SLE, 20% in SS, 21% in AS, 17% in Gout, 19% in OA, 21% in MCTD, 18% in UCTD and 16% in PM/DM.

Table 1. Prevalence of anxiety and depression in patients with rheumatic diseases

Disease	Frequency no. (%)	Age (years) Mean	Age (years) SD	Anxiety (%)	Depression (%)
RA	4,594 (33%)	51.17	18.72	12%	19%
SLE	3,054 (22%)	35.46	12.92	14%	21%
SS	1,253 (9%)	48.48	14.95	15%	20%
AS	975 (7%)	32.3	12.28	16%	21%
Gout	607 (4%)	44.57	16.35	10%	17%
OA	590 (4%)	50.25	15.22	11%	19%
MCTD	490 (4%)	43.28	14.92	12%	21%
UCTD	443 (3%)	38.02	12.68	14%	18%
PM/DM	405 (3%)	44.86	16.19	10%	16%
APS	200 (1%)	32.89	7.00	6%	9%
Scleroderma	201 (1%)	46.47	13.91	10%	20%
Vasculitis	163 (1%)	47.84	17.14	13%	17%
BD	134 (1%)	38.42	13.17	15%	16%
PsA	159 (1%)	40.34	12.7	10%	17%
Others	562 (4%)	42.18	15.35	11%	19%
Total	13,830 (100%)	43.86	17.29	12%	19%

Conclusion: SSDM can be used for HADS self-assessments by patients with rheumatic diseases. RA was recorded as the most prevalent condition, followed by SLE. 10% to 20% patients could be classified as probable case of anxiety or depression according to HADS scores. The prevalence of anxiety was usually lower than that of depression in patients with rheumatic diseases in this study.
Disclosure of Interests: None declared
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Validation of outcome measures and biomarkers

SAT0628

VALIDATION OF METHODS FOR PREDICTING LONG-TERM OUTCOME IN JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FOR CANADIAN AND NORDIC PREDICTION MODELS IN THE NORDIC COHORT

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Background: Models predicting outcome in juvenile idiopathic arthritis (JIA) have recently been proposed by Guzman *et al.*[1] and Rypdal *et al.*[2] Guzman *et al.* constructed a model for predicting severe disease course derived from the ReACCh-Out study, and Rypdal *et al.* constructed models for prediction of non-remission, functional disability and joint damage.
Objectives: To validate methods for prediction of long-term outcome in JIA by testing the ability of Guzman's model and Rypdal's model to predict severe disease course (the ReACCh-Out outcome) in the Nordic cohort.
Methods: The Nordic cohort is a prospective longitudinal multicenter cohort from defined geographical areas of 4 Nordic countries. Children with a baseline and an 8-year study visit were included. Missing data were imputed using low rank matrix factorization[3], and a K-medoids algorithm[4] was used to identify clusters corresponding to severe disease course in the ReACCh-Out study. With this outcome, the prediction model of Guzman *et al.* was tested with no re-estimation of parameters. A Receiver operating characteristic (ROC) curve and the corresponding area

under the curve (AUC) were computed. For the same outcome, prediction models were built using the method of Rypdal *et al.* on randomly sampled training sets, and tested on disjoint validation sets.
Results: In the Nordic cohort 98/440 (22%) patients were identified with a severe disease course. This ratio is similar to the 125/610 (20%) found in the ReACCh-Out study. Characteristics of groups of patients with severe and non-severe disease course are similar in the two cohorts. The model of Guzman *et al.* had an AUC of 0.85 for prediction of severe disease course and an AUC of 0.66 for predicting remission off medication. In repeated cross-validations, the model of Rypdal *et al.* had a median AUC of 0.90 (IQR 0.86-0.92) for prediction of severe disease course, and a median AUC of 0.78 (IQR 0.72–0.82) for remission off medication.
Conclusion: Tests in the Nordic cohort validate the ability of the model of Guzman *et al.* to predict severe disease course. Repeated cross-validations of the model of Rypdal *et al.* indicate that validation results are highly dependent of the chosen outcome, and that prediction of long-term remission status is more challenging than prediction of a severe disease course.

REFERENCES

[1] Guzman, J. et al., Predicting Which Children with Juvenile Idiopathic Arthritis Will Have a Severe Disease Course: Results from the ReACCh-Out Cohort, J Rheumatol, 44, 230-240, 2017.
[2] Rypdal, V. et al., Predicting unfavorable long-term outcome in juvenile idiopathic arthritis: results from the Nordic cohort study, Arthritis Res Ther, 20, 91, 2018.
[3] Liu, G. et al., Robust subspace segmentation by low-rank representation, Proceedings of the 27th International Conference on International Conference on Machine Learning, 663-670, 2010.
[4] Park, H.-S. et al., A simple and fast algorithm for K-medoids clustering, Expert Systems with Applications, 36, 3336-3341, 2009.

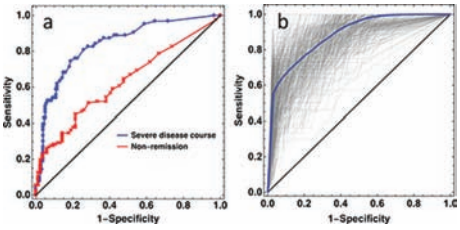


Figure. **a**, ROC-curves for Canadian model tested on Nordic JIA cohort. **b**, ROC-curves for the Nordic model tested on severe disease course.

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SAT0629

THERE ARE 4 MAIN QUESTIONNAIRES TO ASSESS ADHERENCE IN INFLAMMATORY ARTHRITIS BUT NONE OF THEM PERFORM WELL: A SYSTEMATIC LITERATURE REVIEW

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Background: Insufficient patient adherence to treatments in inflammatory arthritis (IA) including rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA), crystal-induced arthritis and connective tissue diseases (CTD) may lead to complications, unnecessary treatment switches, and increased costs. Patient adherence to treatment should be assessed, however how to evaluate it has not been determined.
Objectives: To assess the psychometric properties of questionnaires to measure adherence to treatment in IA.
Methods: We performed a systematic literature review (SLR) using three central databases (Pubmed, Cochrane, Embase) and several websites in January 2019. The scope was limited to IA (i.e., RA, SpA, PsA, CTD, crystal-induced arthritis, vasculitis, and auto-inflammatory diseases), and disease-modifying drugs (i.e., mainly conventional DMARDs, biologics and targeted synthetic DMARDs). All questionnaires used to assess adherence were collected, then a specific search using the questionnaire name was run to obtain data on their psychometric properties including overall validity (sensitivity (Se), specificity (Sp) and Cronbach coefficient (CC), reliability, and sensitivity of change, following the OMERACT filter. These properties were analyzed semi-quantitatively.
Results: After screening 1209 publications and 194 other documents, 242 relevant papers were analyzed for measuring adherence (63.6% in RA, 8.7% in SpA, 6.6% in PsA, 14.5% in CIA and 19.0% in CTD). The number of articles using adherence questionnaires by disease was: 69/154 in RA, 14/21 in SpA, 27/40 in systemic lupus erythematosus (SLE), 9/16 in PsA, 8/35 in crystal induced arthritis and 4/6 in other CTD. Four questionnaires were used to evaluate drug adherence (Table1). The most used questionnaire was the MMAS in all diseases except in RA where the CQR was more used. The CQR was validated in 85 patients with IA against as external standard, electronic medication monitoring (Se 62 to 98%, Sp 67 to 97% and CC of 0.71 to 0.85). The MASRI was validated in 55 patients with SLE against adherence based on pharmacy refill information (Se 87%, Sp 86% and CC of 0.70). The MMAS was validated in 91 patients with gout against medication possession ratio Se 81 to 93%, Sp 44 to 53% and CC of 0.54). The MARS was validated in 108 patients with RA (Se 13 to 53%, Sp 57 to 94% and CC 0.60 to 0.75). Reproducibility was correct but copyright posed isses (Table).

Table 1. Questionnaires performances to assess adherence in IA

	Compliance Questionnaire on Rheumatology: CQR-19/5 [1]	Medication Adherence Report Scale: MARS10/ 9RA/6/5/4 [2]	Medication Adherence Self-report Inventory: MASRI [3]	Morisky Medication Adherence Scale: MMAS-8/4 [4]
N studies on the questionnaire	48	13	7	62
Copyright	No	No	Yes	Yes
Reproductibility	++	++	+++	++
Validity assessed in rheumatology	Yes	No	Yes	+/-
Feasibility	+/+++	+++	+++	+++

The + represents a semi-quantitative summary of the available literature with more + meaning higher/better results (from - to +++)
Conclusion: Four questionnaires are being used to measure medication non-adherence in IA; the most used is the MMAS which is unfortunately copyrighted and not fully validated in rheumatology. The CQR and MASRI questionnaires were the most validated in rheumatology, but the CQR is long and the MASRI only used for SLE. Thus it appears that to date, a simple, reliable and valid questionnaire to assess drug adherence is lacking.

REFERENCES

[1] De Klerk E. et al., J. Rheumatol. 2003; Thompson K. et al., Schizophr Res 2000; Walsh JC. et al., AIDS. 2002; Morisky DE. et al., J Clin Hypertens (Greenwich) 2008

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SAT0630 DUTCH TRANSLATION AND PSYCHOMETRIC PROPERTIES OF A PATIENT REPORTED EXPERIENCE MEASURE (PREM) FOR PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS

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Background: Evaluating the quality of care provided as perceived by patients can be helpful in order to reveal areas for improvement, identify best practices and stimulate interventions to further improve these. This can be done with a patient reported experience measure (PREM). Such a PREM, containing 23 questions in 7 domains has been developed and validated specifically for patients with rheumatic conditions, including rheumatoid arthritis (RA) and spondyloarthritis (SpA) in the United Kingdom (box 1) (1). Until now, no translated and validated Dutch questionnaire is available for patients with SpA or RA in the Netherlands.
Objectives: To translate the PREM into Dutch and to study its psychometric properties in patients with SpA or RA.
Methods: The PREM was independently translated into Dutch by two researchers fluent in the English language (one rheumatologist and one healthcare scientist) and a consensus version was generated which was checked by two other researchers (one rheumatologist and one methodologist). The final version was piloted in two Dutch real-life quality registries for patients with SpA or RA; SpA-Net and DREAM-RA, respectively. Patients completed the PREM annually starting from December 2016. For the current cross-sectional analysis, the most recently completed PREM from each patient was included. Feasibility was assessed by the median and interquartile ranges (IQR) of completion times. Reliability was assessed by internal consistency (Cronbach's α) and homogeneity (corrected item-total correlations (r_p)) within each domain. Content validity was assessed by floor- and ceiling effects (>15%) for each question. Divergent validity was assessed by Spearman rank correlation coefficients (r_s) between the average score of each domain and outcome measures for disease activity (BASDAI, ASDAS or DAS28), daily functioning (BASFI, HAQ or HAQ-S), health status (ASAS-HI) and quality of life (SF-36).
Results: The PREM was completed by 282 patients with SpA and 378 patients with RA. The average age and the proportion of female patients with SpA was lower compared to patients with RA (54.2 (SD 12.2) versus 61.5 (SD 11.9) years and 47.9% versus 65.1% female patients, respectively). Average disease activity was high in patients with SpA but low in patients with RA (mean ASDAS 2.2 (SD 0.9), mean DAS28 2.3 (SD 1.2)). The median time to complete the PREM was 5.5 minutes (IQR 2.7) in SpA-Net and 5.4 minutes (IQR 2.3) in DREAM-RA. Internal consistency of all domains was considered good for patients with SpA or RA ($0.70 \geq \alpha \leq 0.95$), except for the domain *Daily living and physical comfort* in patients with RA (α=0.65). In both populations, thresholds for homogeneity were exceeded within three domains ($r_p > 0.7$) suggesting possible item redundancy. Ceiling effects were found in 75% (SpA) and 90% (RA) of the questions. As expected, correlation coefficients showed that nearly all domains of the Dutch PREM were independent of scores on outcomes measures in both patients with SpA and RA ($-0.3 \leq r_s \leq 0.3$).
Conclusion: The Dutch PREM has acceptable psychometric properties to assess perceived quality of care in patients with SpA or RA. The homogeneity within three domains could be improved. The results for perceived quality of care are not affected by scores on outcome measures for disease activity, physical functioning, health status and quality of life.

Box 1 Domains and number of questions in PREM

PREM domain	N questions
1. Needs and preferences	5
2. Coordination of care and communication	4
3. Information, education and self-care	4
4. Daily living and physical comfort	2
5. Emotional support	2
6. Family and friends	1
7. Access to care	1

REFERENCES

[1] Bosworth A, et al. Development and Validation of a Patient Reported Experience Measure (PREM) for Patients with Rheumatoid Arthritis (RA) and other Rheumatic Conditions. Curr Rheumatol Rev. 2015;11:1-7.

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SAT0631 CRITERION VALIDITY AND CUT-OFFS OF THE FLARE ASSESSMENT IN RHEUMATOID ARTHRITIS (FLARE-RA) QUESTIONNAIRE: INTERNATIONAL COLLABORATION

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Background: Flares are inherent to the rheumatoid arthritis (RA) disease course and associated with poor clinical outcomes. The self-administered Flare Assessment in Rheumatoid Arthritis (FLARE-RA) questionnaire was devised and validated for detection of current and recent flares in RA, taking into account both patient and provider perspectives [1, 2]. The FLARE-RA questionnaire includes arthritis-related subscale and general subscale. The overall score for the questionnaire is defined as the global scale, with scoring from 0 (no flare) to 10 (maximum flare).
Objectives: To define the cross-cultural criterion validity of the FLARE-RA questionnaire and cut-off(s) for definition and decision in four different countries, using different anchor items in patients with RA.
Methods: This cross-sectional study included adult patients with prevalent RA (per 2010 ACR/EULAR criteria) attending outpatient rheumatology clinics in France (n=138), Denmark (n=253), USA (n=75), and Argentina (n=105). Flare occurrence over the past 3 months was assessed using the FLARE-RA questionnaire. The cut-offs for the FLARE-RA score were defined using the following anchor items obtained at the same encounter: 1) Patient report of flare; 2) DAS28-CRP>3.2; 3) Change of anti-rheumatic treatment. Detection of the optimal cut-off for the FLARE-RA questionnaire was performed with distance (0,1) method, based on the area under the receiver operating characteristic curve (AUC).
Results: The study included 571 patients with RA (mean age 56.9 years, 75.3% female). The discrimination for the FLARE-RA was acceptable-to-excellent: AUC for the global FLARE-RA score ranged from 0.71 to 0.92. The summary of optimal cut-offs for the FLARE-RA questionnaire is presented in the Table. The cut-offs for the FLARE-RA score were overall lowest using "patient's report of flare" and highest using "change of anti-rheumatic treatment" as an anchor item: cut-offs for the global score for patients with RA duration 2-5 years: 1.82 and 4.55, respectively; for patients with RA duration >5 years – 2.18 and 3.18, respectively. The cut-offs corresponding to DAS28-CRP>3.2 were lower in patients with RA disease duration >5 years than in those with RA duration 2-5 years.

Table: Summary of FLARE-RA optimal cut-offs by RA disease duration using different anchor selection methods

	Disease duration 2-5 years			Disease duration > 5 years		
	Arthritis subscale	General subscale	Global scale	Arthritis subscale	General subscale	Global scale
Patient report of flare	2.80	1.00	1.82	2.20	1.40	2.18
DAS28 CRP >3.2	4.40	3.67	4.09	1.80	1.67	2.18
Change of anti-rheumatic treatment	4.00	4.50	4.55	4.80	2.33	3.18

Conclusion: The FLARE-RA questionnaire has acceptable-to-excellent discriminative capacity across the tested anchor items. Patient report of flare corresponds to a lower FLARE-RA cut-off score than DAS28-CRP and change of anti-rheumatic treatment, suggesting the hierarchy of flare recognition from flare self-perception to its detection by DAS28 to treatment change by the rheumatology provider. More studies are needed to ensure the early recognition of flares and the appropriate alignment between flare and the adjustment of anti-rheumatic and other medications.

REFERENCES

[1] Berthelot JM, et al. Ann Rheum Dis 2012, 71(7):1110-6.

[2] Fautrel B, et al. *Arthritis Rheumatol* 2017, 69(2):309-19.

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SAT0632 NEUTROPHIL ACTIVATION IDENTIFIES PATIENTS WITH ACTIVE POLYARTICULAR GOUT – A NOVEL BIOMARKER?

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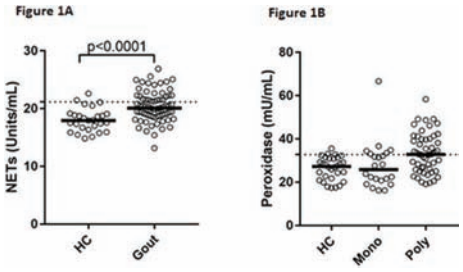
Background: Neutrophils are key immune cells participating in host defense through several mechanisms, including the formation of neutrophil extracellular traps (NETs). Although beneficial from a host-pathogen perspective, excessive neutrophil activation has been linked to inflammation and autoimmunity, including systemic lupus erythematosus (SLE) and gout.(1) In gout models, uric acid crystals induce NETosis. Though NETs are known to induce marked inflammation through TLR9- and cGAS-dependent pathways, as well as partake in induction of tissue damage and thrombotic events, the role of NETs in human gout has not been carefully investigated.

Objectives: Our objective is to investigate evidence of systemic neutrophil activation, and the clinical utility of neutrophil-derived biomarkers in gout. We hypothesize that uric acid crystals will activate neutrophils to undergo NET formation, with these processes contributing to immune cell activation, and local joint destruction.

Methods: Plasma samples from 75 gout patients participating in the 'Reade gout cohort Amsterdam' were compared with 30 healthy controls (HC). Levels of NETs, and NET-derived markers (cell-free DNA and peroxidase activity) were analyzed using a MPO-DNA ELISA, as well as fluorimetry.(2) Levels of calprotectin (S100A8/A9) were analyzed by ELISA. Mitochondrial (mt, COXII), as well as genomic (n, RPLP0) DNA levels were analyzed by qPCR. All of the analyzed markers were compared between gout patients and healthy individuals, and related to markers of inflammation and disease activity.

Results: Levels of NETs, as well as other neutrophil biomarkers, were significantly increased in gout patients as compared to healthy subjects ($p<0.01$, Figure 1A). In contrast to SLE, gout patients did not have elevated levels of circulating mtDNA ($p=0.96$), but only nDNA ($p=0.006$). No associations were found between markers of cell death (cfDNA and NETs) and disease activity. Peroxidase activity correlated with disease activity (RAPID score: $r=0.43$, $p=0.01$, RAPID function: $r=0.54$, $p=0.001$) and inflammation markers (CRP: $r=0.40$, $p<0.001$, and ESR: $r=0.43$, $p<0.001$). Involvement of ankle and wrist resulted in significant higher peroxidase levels compared to mono-articular disease ($p=0.01$, and $p=0.03$, respectively), suggesting peroxidase activity being a marker of polyarticular gout (Figure 1B). Calprotectin (S100A8/A9) correlated with the inflammation markers CRP and ESR ($r=0.30$, $p=0.01$, and $r=0.30$, $p=0.001$, respectively) and morning stiffness, especially in patients with chronic polyarticular gout ($r=0.61$, $p=0.001$).

Conclusion: To our knowledge, this is the first report demonstrating presence of NETs in the peripheral blood of gout patients. Although markedly elevated, levels of NETs did not associate with markers of disease activity or inflammation, possibly due to the lack of inflammatory mitochondrial DNA within the NETs. Even so, our data demonstrate an important role of neutrophils in gout pathogenesis, with neutrophil activation markers associating with characteristics of active, and more pronounced polyarticular disease.



REFERENCES

[1] Lee KH, Kronbichler A, Park DD, Park Y, Moon H, Kim H, et al. Neutrophil extracellular traps (NETs) in autoimmune diseases: A comprehensive review. Autoimmun Rev. 2017;16(11):1160-73.

[2] Lood C, Blanco LP, Purmalek MM, Carmona-Rivera C, De Ravin SS, Smith CK, et al. Neutrophil extracellular traps enriched in oxidized mitochondrial DNA are interferogenic and contribute to lupus-like disease. Nat Med. 2016;22(2):146-53.

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SAT0633 PREGNANCY SUCCESS RATE AND RESPONSE TO HEPARINS AND/OR ASPIRIN DIFFERS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS ACCORDING TO THE GAPSS SCORE

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Background: Current standard of care (SoC) in pregnancy for patients with Systemic lupus erythematosus (SLE) and/or aPL positivity includes treatment with low dose aspirin (75–100mg/day) and low molecular heparin or unfractionated heparin. However, up to 30% of women continue to have pregnancy complications despite SoC. Therefore, identifying patients that are at greater risk to develop pregnancy complications despite the SoC and might benefit from additional therapeutic approaches, is still an unmet clinical need.

Recently, our group conceived and validated the global antiphospholipid syndrome score (GAPSS) [1], as a risk score for predicting aPL-related clinical manifestations (thrombotic and/or pregnancy morbidity).

Objectives: We aimed to investigate response to SoC in women with SLE and/or aPL positivity when stratifying their risk according to GAPSS Score.

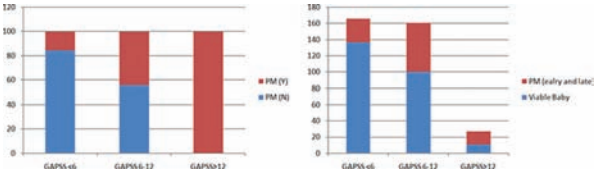
Methods: 143 women ever pregnant treated with SoC therapy with SLE and/or aPL positivity were included. Data on cardiovascular risk factors and aPL positivity were retrospectively collected. The individual GAPSS was calculated for each patient by calculating the sum of each risk factor score, as follows: 3 for hyperlipidaemia, 1 for arterial hypertension, 5 for anticardiolipin IgG/IgM, 4 for anti-β2glycoprotein I IgG/IgM, 3 for anti-phosphatidylserine/prothrombin antibodies IgG/IgM and 4 for lupus anticoagulant. The patients GAPSS was then grouped according to the patients' GAPSS into low risk (<6), medium risk (6-11) and high risk (≥12).

Results: The analysis included 143 patients (mean age 30.8 ±6.4) with SLE (122; 85.3%) and/or aPL positivity, for a total of 352 pregnancies.

	GAPSS <6 (n=72)	GAPSS 6-12 (n=66)	GAPSS ≥13 (n=5)
Demographics			
Age, mean (±S.D.)	30,7 (±5,9)	30,6 (±6,2)	34 (±11,1)
Diagnosis			

SLE, n (%)	55 (76%)	52 (79%)	4 (80%)
aPL positive, n (%)	17 (24%)	14 (21%)	1 (20%)
CardiovascularRiskFactors			
Hyperlipidemia, n (%)	14 (19%)	18 (27%)	2 (40%)
Arterial Hypertension, n (%)	13 (18%)	28 (42%)	1 (20%)
Smoking, n (%)	19 (26%)	15 (23%)	2 (40%)
Diabetes, n (%)	1 (1%)	1 (2%)	1 (40%)
aPLProfile			
LA, n (%)	0	32 (48%)	3 (60%)
aCL IgG/IgM, n (%)	10 (14%)	33 (50%)	5 (100%)
Anti-Beta2GPI IgG/IgM, n (%)	2 (3%)	10 (15%)	4 (80%)
Triple Postive, n (%)	0	0	2 (40%)
aPS/PT IgG/IgM, n (%)	7 (10%)	11 (17%)	1 (20%)

Overall, we observed a live birth rate of 70.5%, with a total of live birth of 248 out of the 352 pregnancies. Forty-five patients (31%) experienced at least one event of PM, defined as early or late. When considering patients who ever experienced PM while treated with SoC, all patients in the high risk group (GAPSS≥12) experienced PM, while patients in the medium group (GAPSS 6-11) had a significant higher rate of PM when compared to the low risk (GAPPS <6) group [29 (43.9%) patients V.s. 11 (15.3%), respectively; p<0.001]. When analysing the number of pregnancies in the three groups, patients in the high risk group had significantly lower live birth rates, when compared to the other groups [11 (40.7%) life births V.s. 100(62.1%) and 137(82.5%), respectively; p<0.05]. Furthermore, patients with medium risk group also had significantly lower live birth rates, when compared to the lower risk group (p<0.001).
Figure 1 resumes the results of PM and live births divided in the three groups.
Conclusion: GAPSS might be a valuable tool for identifying patients with a higher likelihood of response to SoC.



REFERENCES

[1] Sciascia S, Sanna G, Murru V, Roccatello D, Khamashta MA, Bertolaccini ML. GAPSS: the Global Anti-Phospholipid Syndrome Score. Rheumatology (Oxford). 2013 Aug [cited 2016 Sep 21];52(8):1397–403.

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SAT0634

CO-MORBIDITIES ASSOCIATED WITH DISCORDANCE BETWEEN STRUCTURAL SEVERITY AND PAIN IN OSTEOARTHRITIS: IMPLICATIONS FOR CLINICAL TRIAL DESIGN IN OA – A POST-HOC ANALYSIS OF DATA FROM TWO RANDOMIZED CONTROLLED TRIALS

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Background: Development of new disease-modifying drugs in OA (DMOADs) is complicated by heterogeneous study populations and insensitive endpoints of structural change and symptoms, and discordance between structural disease severity and reported symptoms. In such trials, counterintuitively, mild structural disease may be associated with severe symptoms and vice versa. Research to uncover factors distorting the perceived severity of symptoms is needed to better characterize the clinical relevance of structural improvement, if any, in DMOAD trials. Anxiety and depressive (AD) disorders are known to affect pain sensitivity and perception, and as common co-morbidities of OA, these conditions may partly explain the observed discordance between structure and symptoms. If established, exclusion of patients with AD in DMOAD trials could potentially improve the understanding of structural benefit in a clinical context.
Objectives: The main objective of this analysis was to investigate the impact of AD on the association between structural features of OA and patient-reported pain.

Methods: Baseline data from two phase 3 trials investigating oral salmon calcitonin in OA, NCT00486434 and NCT00704847 (total N=2206), was analyzed in a post-hoc cross-sectional analysis. Patients with self-reported current or previous depression, anxiety or post-traumatic stress syndrome (PTSD) were selected and compared to a control group, matched by sex, age, BMI and JSW. Spearman's correlation coefficient between JSW and WOMAC pain was calculated for both groups. Multiple regression analyses of both groups with WOMAC pain as the outcome variable, and age, sex, body mass index (BMI) and baseline JSW or KL-grade as explanatory variables were performed.
Results: In the AD group, 149 patients had AD in medical history of which 123 reported the condition as ongoing at baseline. The study groups of AD and matched controls (MC) were comparable in terms of age, sex, BMI, JSW, KL-grade and WOMAC pain. Associations between pain and JSW In the AD group, no significant correlation between JSW and WOMAC Pain score was found, while BMI was found to be weakly associated with WOMAC pain (R= 0.19, p=0.02) in the multiple regression analysis. In the MC group, a statistically significant (p=0.004), correlation (R= -0.24) was found between JSW and pain indicating that lower JSW was associated with higher pain, with JSW accounting for approximately 6% of the total natural variation behind reported pain. In addition, a positive significant association between male sex and WOMAC pain (R=0.18, p=0.04) was found. The univariate linear relationship between JSW and pain is illustrated in Figure 1, and multivariate analyses are shown in Table 1.

Table 1. Associations between WOMAC pain JSW (in red) and other baseline covariates

	Anx/Depr. group		Control group	
	$r_{partial}$	P-value	$r_{partial}$	P-value
Age	-0.04	0.60	-0.05	0.57
BMI	0.18	0.03	0.02	0.82
Male Sex	0.10	0.21	0.17	0.04
JSW	**0.03**	**0.75**	**-0.24**	**0.004**

Associations between pain and KL-Grade In the model evaluating associations between KL-grade and symptoms, there was no correlation between KL-grade and symptoms in the AD group. Similar to the findings relating to JSW, in the MC group, a weak (R=0.16), borderline

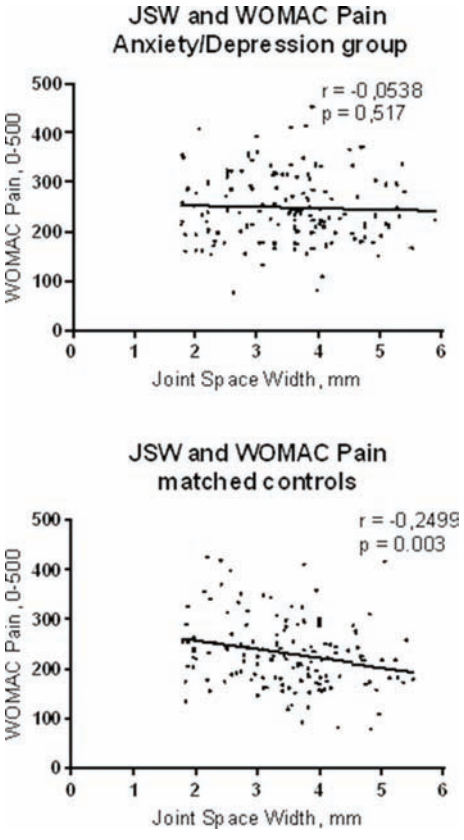


Figure. Linear correlations between WOMAC pain and JSW, with Spearman's R reported

statistically significant association (p=0.07) was found between KL-grade and WOMAC pain.

Conclusion: A marked structure-symptoms discordance was found in OA patients with AD, while a statistically significant correlation was seen in matched controls without AD. The results suggest that exclusion of trial patients with anxiety and depression in medical history may improve the accuracy of pain reporting in clinical OA trials.

Disclosure of Interests: Jonathan Jetsmark Bjerre-Bastos Employee of: Nordic Bioscience, Inger Byrjalsen Employee of: Nordic Bioscience, Morten Asser Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Jeppe Ragnar Andersen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Asger Bihlet Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience

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SAT0635 PATIENT-PERCEIVED RESIDUAL BURDEN OF PSORIATIC ARTHRITIS IN PATIENTS IN REMISSION/ LOW DISEASE: AN ANALYSIS OF 444 PATIENTS

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Background: The objective of treatment in psoriatic arthritis (PsA) is remission or low disease (ref1). However, there may remain residual patient burden in patients where inflammation is controlled.

Objectives: To explore patient-perceived burden of disease in PsA patients in remission or low disease, when using different definitions of remission.

Methods: ReFlap (NCT03119805, ref2) was an observational study in 14 countries of consecutive adult patients with definite PsA and >2 years of disease duration. Remission/low disease status was defined at the baseline visit using composite scores: Minimal Disease Activity (MDA), and Disease Activity in PSoriatic Arthritis (DAPSA)<=14 (both corresponding to a status of remission or low disease). Patient-perceived burden of disease was assessed through the PsA Impact of Disease (PsAID12) composite score and its individual components assessing physical and psychological impact (0-10 where 0 is the optimal status). Mean and median levels of patient-reported symptoms were assessed in remission/low disease status. P-values by Wilcoxon test were computed to compare patients in good status according to both MDA and DAPSA (n=161), versus in good status according to DAPSA only (n=90). There was no imputation of missing data.

Results: Of 466 patients, 444 had disease status and impact available: 220 (50.5%) were male, mean age was 52.2±12.6 years, mean disease duration was 10.1±8.1 years; 261 (62.9%) were taking a conventional DMARD and 255 (61.3%) a biologic. Disease activity was moderate: 154 (36.2%) had no current psoriasis skin lesions, mean tender joint count was 4.7±9.5, mean swollen joint count (SJC) was 2.2±7.0, and mean DAPSA was 16.6±17.2. Remission/low disease was more frequent when defined by DAPSA: 251 (56.5%) patients, than by MDA: 171 (38.5%) patients. As expected, objective measures of disease activity were minimal in the good status categories (e.g., SJC was 0.3±0.8 in MDA and 0.4±0.9 in DAPSA-remission/low disease). In remission/low disease, residual disease impact (assessed with PsAID12) was low: most median levels of symptoms were below 1 on a 0-10 scale; 5 aspects of impact had a median level >=1 (figure); only one had a median level of 2, and this was fatigue. Levels of impact were slightly though significantly higher in patients in DAPSA-defined good status than in patients in both MDA and DAPSA-remission/low disease (all p<0.001).

Conclusion: In this unselected population, residual symptoms were of low magnitude using both definitions of good status: DAPSA-based definitions (present in 56%) and MDA (38%), confirming the patient relevance of remission/low disease as a treatment objective. The predominant aspect of impact was fatigue, which is one of the most important domains of impact recognized by patients. Residual burden of disease was lower in the MDA group than in the DAPSA-remission/low disease group, which could indicate that MDA corresponds to a 'deeper' form of disease control, though the clinical relevance of the differences observed should be further explored. A holistic approach should be implemented when evaluating people with PsA including when disease control has been obtained.

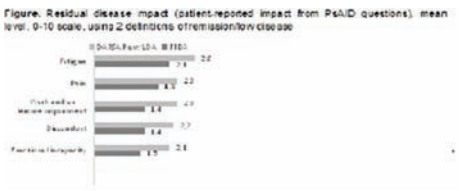


Figure. Residual disease impact (patient-reported impact from PsAID questions), mean level, 0-10 scale, using 2 definitions of remission/low disease

REFERENCES

[1] Gossec L, Smolen JS, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis. 2016;75(3):499-510.

[2] Gorlier C, et al. Comparing patient-perceived and physician-perceived remission and low disease activity in psoriatic arthritis: an analysis of 410 patients from 14 countries. Ann Rheum Dis. 2019;78(2):201-208.

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SAT0636 A DRUG INDUCED REMISSION SIGNATURE PROMISES PERSONALIZED THERAPY IN RA PATIENTS

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Background: Today the objective for efficient Rheumatoid Arthritis (RA) therapy is not restricted to reduced synovial inflammation but to induce immunological and clinicaly lasting remission. Despite improvement in therapy of RA, anti-TNF alpha or anti-IL-6 (Tocilizumab) biologicals provide less than 20% of clinical remission. Interestingly, the complete remission can last up to 12 months in about 40% of these patients despite discontinuation of the above biologicals. In order to set up optimized strategy to obtain persistent clinical remission, new predictive markers of complete remission are needed.

Objectives: By using Firalis' BIOPRED panel, an innovative targeted gene sequencing panel of 2155 mRNA targets associated with immune-inflammatory pathways, we identified candidate biomarkers that have the potential to stratify patients for personalized therapy.
Methods: Paxgene RNA samples obtained from 18 RA patients treated with Etanercept (n=11) and Tocilizumab (n=7) who had achieved remission (DAS28 < 2.6) were directly profiled without RNA extraction with BIOPRED panel, a targeted sequencing kit based on HTG EdgeSeq platform. Data were extracted using HTG Parser software and normalized using EdgeR method. Student T-test was applied to find out targets which are significantly regulated.
Results: In total, 37 mRNA targets are found to be significantly up- or down-regulated in Etanercept groups as compared to Tocilizumab group (p-value <0.05). 3 mRNA genes are found to be significantly upregulated with fold change of > 2 (p-value < 0.05) and 1 mRNA gene is found to be significantly downregulated with fold change of <0.5 (p-value < 0.05).
Conclusion: Our preliminary analysis shows that a panel of candidate predictive markers for biological specific (Etanercept) remission has the potential to stratify patients for personalized therapy in RA patients. Longitudinal studies are required with RA patients treated with all biologicals to validate this signature and explore further dimensions.
Disclosure of Interests: None declared
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SAT0637 THE DIAGNOSTIC VALUE OF SERUM IGG4 IN IGG4 RELATED DISEASES

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Background: IgG4–RD is a newly recognized autoinflammatory disease. Serum IgG4 is an important tool for the diagnosis of IgG4—RD. However, only a few articles have reported the value of serum IgG4 for the diagnosis ofIgG4–RD.
Objectives: To explore the diagnostic value of serum IgG4 in IgG4-related diseases,Whether 1350 mg/L as the cutoff concentration is suitable for Chinese people to identify IgG4-RD and other rheumatic immune diseases.
Methods: From October 2013 to December 2018,40 patients with IgG4-RD diagnosed in the rheumatic immunology department of people's hospital of Xinjiang Uygur Autonomous Region were collected.We also reviewed the of 90 other CTD patients and 40 healthy controls.The age, gender, diagnosis, serum IgG4 concentration and other data were collected. The cut off levels were determined by receiver operating characteristic (ROC) curve analysis
Results: The mean serum IgG4 concentration of 40 definite IgG4-RD was was significantly higher than that of other rheumatic immune diseases group and healthy control group. There was a significant serum IgG4 concentration difference between patients with IgG4-RD,Non-IgG4-RD and healthy control group(P<0.05 (Figure 1 . By the ROC curves of serum IgG4 levels in 170 patients. The optimal cutoff value of serum IgG4 for a diagnosis of IgG4-RD was 1440 mg/L, and the sensitivity and specificity were 90.0% and 80.8%, respectively. The area under the curve (AUC) was 0.926. When We using a ratio >0.07 as the cut-off for normal and the sensitivity and specificity were 90.0% and 77.7%, respectively. The area under the curve (AUC) was 0.925(Figure 2 .

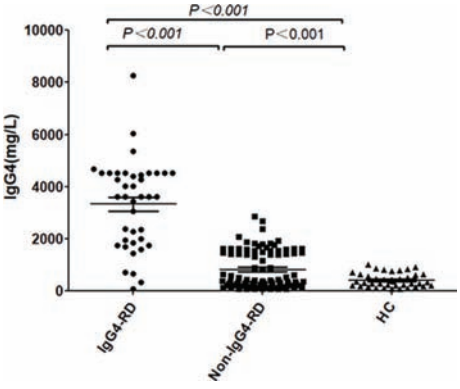


Figure 1. There were significant differences between IgG4-RD, Non-IgG4-RD and HC (P<0.05).

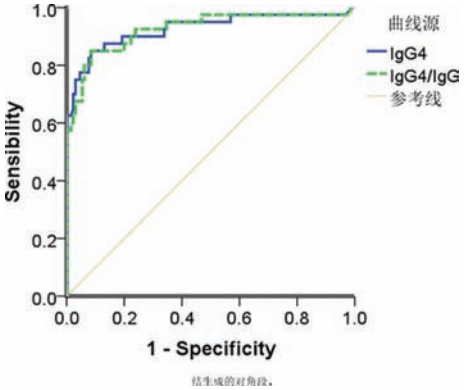


Figure 2. The ROC curve of IgG4 and IgG4/IgG ratio

Conclusion: The high levels of serum IgG4 are sometimes observed in not only IgG4-RD but also other rheumatic,malignancy diseases and common diseases. The cut of serum IgG4 is 1440mg/L,The usual cut-off value of 1350 mg/Lis useful for diagnosing whole IgG4-RD.

REFERENCES

[1] Kamisawa T, Funata N, Hayashi Y, et al. A new clinicopathological entity of IgG4-related autoimmune disease[J]. Journal of Gastroenterology, 2003, 38(10):982
[2] Takahashi H, Yamamoto M, Suzuki C, et al. The birthday of a new syndrome: IgG4-related diseases constitute a clinical entity.[J]. Autoimmunity Reviews, 2010, 9(9):591-594
SSadlerR,ChapmanRW,SimpsonD,etal.The diagnostic significance of serum IgG4 levels in patients with autoimmune pancreatitis: a UK study. Eur J Gastroenterol Hepatol. 2011;23:139–45.
Umehara H, Okazaki K, Masaki Y, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011[J]. Nihon Naika Gakkai Zasshi the Journal of the Japanese Society of Internal Medicine, 2012, 101 (3):795.
Stone JH, Zen Y, Deshpande V.IgG4-related disease J .N Engl J Med, 2012, 366(6 539-551.
Yamamoto M, Tabeya T, Naishiro Y, et al. Value of serum IgG4 in the diagnosis of IgG4-related disease and in differentiation from rheumatic diseases and other diseases[J]. Modern Rheumatology, 2012, 22(3):419-425.
Zen Y, Nakanuma Y. IgG4-RD: a cross-sectional study of 114 cases. Am J Surg Pathol 2010, 34:1812–19.
Carruthers M N, Khosroshahi A, Augustin T, et al. The diagnostic utility of serum IgG4 concentrations in IgG4-related disease.[J]. Annals of the Rheumatic Diseases, 2015, 74(1):14.
Masaki Y, Kurose N, Yamamoto M, et al. Cutoff values of serum IgG4 and histopathological IgG4+ plasma cells for diagnosis of patients with IgG4-related disease. Int J Rheumatol 2012;2012:580814.
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SAT0638 INCREASED LEVELS OF CIRCULATING EXTRA CELLULAR LONG NON-CODING RNAS MALAT1, MEG3 AND NEAT1 IN PATIENTS WITH RHEUMATOID ARTHRITIS AND THEIR IMPACT ON DISEASE ACTIVITY MEASURES

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Background: Deregulations of long non-coding RNAs (lncRNA) have been lately implicated in autoimmune diseases(1) including Rheumatoid arthritis (RA). However, their specific roles in disease pathogenesis, extra-cellular manifestations and clinical impact in RA remain largely unknown.
Objectives: To identify the intra- and extra-cellular expressions of lncRNAs, MEG3, MALAT1, NEAT1, in RA and their impact on disease activity.
Methods: Blood samples were collected from 82 active RA patients (DAS28-CRP: 4.7±0.2) and 15 age-sex matched healthy individuals. Knee synovial fluids (SF) were collected from 24 RA patients (among 82) and 10 osteoarthritis patients (as control). Sera were separated for cytokines

measurements. RNA, isolated from peripheral blood mono nuclear cells (PBMCs), plasma and synovial fluid were quantified by spectrophotometry. Levels of MALAT1, MEG3 and NEAT1 were determined using specific primers and real time PCR, 18S rRNA was the endogenous control. Fold changes were calculated using standard $2^{-\Delta\Delta Ct}$ method. Multivariate analysis was performed to analyze associations between the dependent variable (DAS28-CRP) and the predictor variables (CRP, MALAT1, MEG3 and NEAT1). Confidence interval of 95% ($p \leq 0.05$) was considered statistically significant for all analyses.

Results: All patients recruited were anti-CCP positive (122.5 ±28.3 IU/ml) and RF positive (166.5 ±37.3 IU/ml). Their systemic inflammation were high compared to controls ($p<0.05$) as reflected in serum CRP (47.4 ±26.2 mg/L), TNFα (140±29 pg/dl) and IL17 (270±33 pg/dl). Levels of MALAT1, MEG3 and NEAT1 were increased in the PBMCs ($p<0.05$) of RA patients compared to controls. Similar increases of these lncRNAs were seen in plasma and in SF. Spearman's correlation were performed with the fold changes of lncRNAs in PBMC, DAS28-CRP and its components. MEG3 significantly correlated with tender joint count (TJC) ($r=0.75$, $p=0.002$) whereas NEAT1 correlated with both TJC ($r=0.571$, $p=0.002$) and DAS28-CRP ($r=0.943$, $p=.001$). Multivariate analysis was performed with NEAT1 and MEG3 as the predictors and DAS28-CRP (model 2) as outcome and co-efficient of determinant (r^2) was compared to that of CRP as the predictor and DAS28-CRP as the outcome (model 1). Model 1 was made to set a cut-off mark for model 2. The r^2 for model 1 (0.862) was greater than that of model 2 (0.656) indicating the expressions of NEAT1 and MEG3 accounted more for variability in DAS28-CRP scores (86.2%) than CRP (65.6%). In model 2, β co-efficient of NEAT1 (β=0.868) was greater than that of MEG3 (β=0.397) suggesting a greater impact of NEAT1 on DAS28-CRP scores. The lncRNAs in plasma and in synovial fluids had shown similar trends.

Conclusion: Increased in lncRNAs in extra cellular fluid suggests their systemic regulation on RA pathogenesis. Increased predictability of DAS28-CRP by NEAT1 and MEG3 compared to CRP indicate their potentiality of being probable markers in monitoring disease activity. However, validation of this finding in larger cohort is necessary.

REFERENCES

[1] Wu GC, Pan HF, Leng RX, Wang DG, Li XP, Li XM, Ye DQ. Emerging role of long noncoding RNAs in autoimmune diseases. Autoimmun Rev. 2015 Sep;14(9):798-805.

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SAT0639 ACTIVE JAK/STAT SIGNALING IN CIRCULATING LEUCOCYTES DEFINES DISTINCT IMMUNOLOGIC ENDOTYPES OF RHEUMATOID ARTHRITIS

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Background: In rheumatoid arthritis (RA) stratification is considered an important step towards the development of patient-tailored therapeutic concepts. The fact that less than 50% of RA patients experience a substantial improvement in response to any single biologic therapy has brought up the idea that yet unidentified subtypes of RA (endotypes) might exist. This concept is in line with distinct microscopic patterns of synovitis found in biopsies of RA joints.[1] Furthermore, a subset of RA patients has leucocytes with interferon driven gene expression, whereas the majority of RA patients does not[2]. Interferons activate receptor associated Janus kinases leading to phosphorylation of STAT1 and STAT2. Other STAT family members are activated by cytokines such as IL-6 (STAT3) or IL-15 (STAT5). Therefore, the phosphorylation pattern of the different STAT molecules in circulating leucocytes might mirror the specific cytokine milieu of a given patient.

Objectives: To define endotypes of RA based on the phosphorylation patterns of the different STAT molecules in circulating leucocytes.

Methods: Cross-sectional study of 63 patients with established RA fulfilling the 2010 EULAR/ACR criteria (mean age: 64.5 ± 1.7 (SEM) years, female ratio: 0.79). Ten healthy subjects served as a control group. Flow cytometry was performed to detect the phosphorylated forms of STAT1-6 in Monocytes, Granulocytes, B cells, naïve-, effector-, and memory-T cells of the CD4+ and CD8+ lineage. All steps from blood draw to cell fixation were performed at 4°C to prevent auto-activation of leucocytes. The mean fluorescence intensity (MFI) of phosphorylated STATs in the different leucocyte populations was used for statistical analysis. MFIs were correlated with disease activity measured by the cDAI. MFIs of populations with elevated STAT phosphorylation not associated with disease activity were analyzed by unsupervised hierarchical clustering. The resulting groups were validated by principal component analysis. Finally, criteria for patient assignment to specific groups by MFI were generated by calculating ROC-curves.

Results: Pronounced *ex vivo* phosphorylation of STAT1-6 in any leucocyte population was detected in 20 of 63 (48%) RA patients but not in healthy subjects (n=10). Active STAT5 signaling in Monocytes, naïve CD4 + T cells and CD4+ effector T cells was significantly associated with disease activity. Unsupervised hierarchical cluster analysis of RA patients based on pSTAT MFIs not associated with disease activity resulted in 3 groups: 1) Patients with active STAT1 and STAT3 signal in Monocytes and Granulocytes (n=14/63, 22%), 2) Patients with active STAT5 signal in naïve CD8+ T cells, CD8+ effector T cells and CD4+ memory T cells (n=16/63, 25%) and 3) Patients without active STAT signal in any leucocyte population (n=33/63, 52%). cDAI, CRP, ESR, current treatment, RF and ACPA status did not differ significantly between the groups. To test if the assignment to a group changed over time, we performed a second analysis of STAT phosphorylation after 3-6 months. Eighty percent of the patients tested (12/15) were re-assignment to their initial group.

Conclusion: We identified three distinct RA endotypes based on active STAT signal. Whether patients within different endotypes respond differently to a given therapy will be subject to further research.

REFERENCES

[1] Orr C, Sousa E, Boyle DL, et al. Synovial tissue research: A state-of-the-art review. Nat Rev Rheumatol 2017;13:463–75. doi:10.1038/nrrheum.2017.115
[2] Wright HL, Thomas HB, Moots RJ, et al. Interferon gene expression signature in rheumatoid arthritis neutrophils correlates with a good response to TNFi therapy. *Rheumatol (United Kingdom)* 2014;54:188–93. doi:10.1093/rheumatology/keu299

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SAT0640 SHEAR-WAVE ELASTOGRAPHY OF SKIN STIFFNESS IN SYSTEMIC SCLEROSIS: A FIVE-YEAR FOLLOW-UP STUDY

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Background: Measurement of skin involvement is essential for diagnosis and assessment of prognosis in systemic sclerosis (SSc). The mRSS is the gold standard measure of skin thickness. The mRSS has been criticised for being associated with high inter-observer variability and being too insensitive to detect relevant changes in skin thickness over time. Previously, our group demonstrated that shear-wave elastography (SWE) offers a potential for objective and quantitative assessment of skin involvement in SSc patients.[1] However, no studies have evaluated its sensitivity to change over-time.

Objectives: To assess changes in skin stiffness in SSc patients using SWE over-time.

Methods: This study included 19 SSc patients [89.5% females; age 57.5 years (10.3), 53% with limited form; disease duration 11.4 years (8.5)] at baseline and, 13 healthy controls [69.2% females; age 53.4 years (11.5). Skin stiffness was measured by SWE, using virtual touch image quantification, at the 17 sites corresponding to the mRSS, in each participant, at baseline and follow-up [a mean of 4.9 ((4.6-4.9) years later]. mRSS was performed at both time points. Differences between groups were analysed using the related-samples Wilcoxon Signed Rank test. Results are presented as median (interquartile range (IQR)).

Results: In SSc patients, skin stiffness measured by SWE decreased in a strongly significantly way ($p \leq 0.001$), over time at all skin Rodnan sites, except the fingers (table 1). Interestingly, the same was observed in controls for all sites, except the leg. The effects of normal ageing correspond to 30 to 60% of the changes observed in SSc. Local Rodnan

scores only decreased significantly at the forearms and fingers of SSc patients. The reduction of mRSS at the fingers did not correspond to improvements in SWV. Shear wave velocity (SWV) measurements correlated with mRSS both at baseline (rs:0.56; p=0.0001) and at follow-up (rs:0.74; p=0.0001).

Conclusion: Although preliminary, this study provides the first evidence suggesting that 1. SWV of the skin is more sensitive to change over time than mRSS; 2. Skin stiffness reduces significantly over time in normal controls, and 3. Normal skin ageing may contribute to the overall decrease of SWV with time in SSc. Our results highlight the discriminant ability of SWV in detecting subtle skin changes not identified by mRSS. SWV may offer a significant improvement in the evaluation of skin stiffness and may provide relevant insights into the biology of healthy and scleroderma skin. Studies including a larger number of patients in different phases of skin involvement and data on normal reference values of these ultrasound measurements are needed to reach a definitive validation.

REFERENCES

[1] - Santiago T, et al; Clin Exp Rheumatol. 2016;100:137-141.

Table 1. - Comparison between skin stiffness – shear-wave velocity measurements – and mRSS at the site of analysis, at baseline and follow-up.

	SSc patients (SWV & mRSS)				Controls (SWV)			
	baseline median (IQR)	follow-up median (IQR)	change median	p	baseline median (IQR)	follow-up median (IQR)	Change median	p
SWV	2.9 (2.3-3.4)	1.5 (1.3-1.6)	-1.45	0.000	2.5 (2.2-2,8)	1.5 (1.3-1.7)	-0.92	0.002
mRSS	*0.42 (0-1)*	*0.32 (0-1)*		*0.48*				
SWV	2.4 (1.9-3.0)	1.4 (1.1-1.5)	-1.04	0.000	2.2 (1.8-2.6)	1.6 (1.5-1.8)	-0.53	0.003
mRSS	*0,16 (0-0)*	*0.11 (0-0)*		*0.564*				
SWV	2.9 (2.4-3.0)	1.3 (1.1-1.4)	-1.43	0.000	2.2 (1.7-2.4)	1.3 (1.1-1.4)	-0.87	0.002
mRSS	*0.42 (0-0)*	*0.21 (0-0)*		*0.317*				
SWV	3.1 (2.5-3.2)	1.75 (1.2-2.1)	-1.49	0.000	2.3 (2.1-2,4)	1.5 (1.4-1.7)	-0.70	0.001
mRSS	*1.42 (0-2)*	*0.63 (0-2)*		*0.041*				
SWV	3.6 (2.5-4.0)	2.32 (1.7-2.8)	-1.29	0.001	2.2 (2.2-2.5)	1.7 (1.4-1.9)	-0.62	0.003
mRSS	*2.21 (0-2)*	*1.37 (0-2)*		*0.084*				
SWV	3.78 (2.7-4.8)	4.11 (2.3-70)	0.79	0.748	2.1 (2-2.3)	1.8 (1.6-1.9)	-0.34	0.05
mRSS	*3,26 (2-4)*	*1,63 (1-2)*		*0.003*				
SWV	2.51 (2.3-2.8)	1.57 (1.4-1.8)	-0.87	0.000	2.0 (1.9-2.1)	1.5 (1.3-1.6)	-0.53	0.03
mRSS	*0.16 (0-0)*	*0.21 (0-0)*		*0.564*				
SWV	3.13 (2.3-3.8)	2.3 (1.8-2.5)	-0.83	0.001	2.5 (2.0-2.8)	2,2 (1.8-2.6)	-0.26	0.30
mRSS	*0.37 (0-1)*	*0.21 (0-0)*		*0.257*				
SWV	3.06 (2.4-3.8)	1.65 (1.5-1.9)	-1.40	0.000	2.1 (1.9-2.2)	1.6 (1.3-2.0)	-0.48	0.008
mRSS	*0.47 (0-1)*	*0.26 (0-1)*		*0.366*				

Disclosure of Interests: None declared

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SAT0641 RETINAL VASCULOMETRICS AS A POTENTIAL BIOMARKER FOR RISK OF POLYMYALGIA RHEUMATICA

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Background: Vascular risk factors are implicated in the aetiology of polymyalgia rheumatica (PMR) but lack sensitivity as a screening tool to assess risk of future disease or disease progression. Retinal vascular measures from digital images of the retinal fundus provide a direct objective measure of vascular health and have potential value in estimating future disease risk.

Objectives: The aim of this study was to determine if quantitative changes on retinal vasculometric imaging could be detected prior to the onset of PMR among a large prospective population-based cohort with a view to assessing their clinical utility as a biomarker of disease risk.

Methods: Known risk factors for vascular disease were obtained at enrolment to the EPIC-Norfolk cohort in 1993, with data available on BMI, blood pressure, smoking status and blood drawn for cholesterol and high-sensitivity C-reactive protein. Eye screening took place between 2004 to 2011. Cases of PMR were identified retrospectively among 8112 volunteers by: (i) free text questionnaire responses at baseline, 18 months, 3, 10 and 13 years; (ii) linkage to hospital electronic discharge summaries containing ICD codes (iii) linkage to key word searches (*polymyalgia or rheumatica)* of out-patient clinic letters. Case definition conformed to validated methods. Measures of retinal vessel width were generated by an automated software programme (QUARTZ), using Gaussian modelling to determine vessel widths and an ensemble classifier of bagged decision trees to classify vessels into either venules or arterioles with greater than 80% probability. Stepwise Cox modelling was used to investigate vascular risk factors, including vasculometric characteristics, and subsequent development of PMR, within a multivariate adjusted model.

Results: We identified 71 cases of PMR (median age at diagnosis: 70.5 years, minimum 50.5 years, maximum 87.0 years; mean ESR at diagnosis: 52 mm/hr; 67.6% female) amongst 5130 participants who attended ocular screening and had high quality retinal images acceptable for analysis. There were 50 incident diagnosis of PMR with vascular risk data recorded at enrolment into EPIC-Norfolk prior to their diagnosis of PMR. Results from the univariate Cox modelling revealed positive associations for age, female sex, low-density lipoprotein (LDL) and retinal venular width. There were no associations for arteriolar measures. After adjustment a positive association remained for age and venular dilatation: the hazard ratio for age was 1.14 (95% CI 1.09, 1.18) p<0.0001 and for venule width dichotomised at 90 microns was 2.88 (1.47, 5.66) p=0.002.

Conclusion: Retinal venular dilatation is a marker of vascular health and within this data an independent risk factor for subsequent development of PMR. Retinal fundus images are easily captured in the clinical setting. While validation of these findings in other datasets is warranted, they provide a potential biomarker for assessment of PMR risk.

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SAT0642 PROTEIN BIOMARKERS TO DIFFERENTIATE PSORIATIC ARTHRITIS FROM PSORIASIS

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Background: The BIOmarkers of COMorbidities (BIOCOM) in Psoriasis (Pso) study is a longitudinal study in which we aim to identify clinical, genetic and protein biomarker features associated with the development of co-morbidities, notably psoriatic arthritis (PsA), in patients with psoriasis (Pso). Pso usually precedes the development of PsA with an average interval of 10 years. Thus, patients with Pso are an ideal group in which to study the early events in the evolution to PsA.

Objectives: To use a targeted proteomics approach to identify a serum protein, or panel of proteins, which can predict the development of PsA in patients with Pso. As a first step, we initially sought to identify serum proteins capable of discriminating between patients with Pso only and patients with established PsA.

Methods: 30 patients with Pso and 30 patients with established PsA were selected from the BIOCOM-Pso database. Serum samples from these patients, taken at their initial assessment, were digested using an established in-house standard operating protocol (SOP). Once digested, a targeted proteomics approach using liquid chromatography – mass spectrometry (LC-MS) and a multiple reaction monitoring (MRM) assay called PAPRICA was used to measure candidate biomarker proteins. These 206 proteins (423 peptides) were previously identified as being potential biomarkers in a number of different inflammatory rheumatological conditions.

Results: The demographics of the 2 patient groups are shown in Table 1.

Table 1. Demographic & Clinical Characteristics of the Study Population

Patient Group	Pso	PsA
Age, mean +/- SD years	41.1 +/- 14.6	50.3 +/- 10.6
Male Sex, number (%)	20 (66.7)	21 (70)
Duration of Pso, mean +/- SD years	6.5 +/- 2.9	23.3 +/- 12.1
Duration of PsA, mean +/- SD years		14.8 +/- 10.1
PASI, mean +/- SD	8.1 +/- 3.7	2.8 +/- 2.7
CPDAI, mean		4.4

Targeted proteomics data from the PsA and Pso patients was subjected to univariate and multivariate analysis using a leave one out cross validation approach. The initial results revealed that the application of the PAPRICA method to the BIOCOM-Pso samples resulted in a dataset in which 88 of the 206 PAPRICA proteins could be reliably measured (CV Area < 20%; Signal to Noise ratio > 5; Library Dot Product > 0.8). This subset of the PAPRICA proteins was not able to discriminate between PsA and Pso and none of the associated peptides were significantly different between the two groups (p value < 0.05).

Conclusion: Analysis of a subset of 88 of the 206 biomarker proteins in the PAPRICA method, in patients with PsA and Pso, did not reveal peptides (proteins) that were statistically different between these two groups. Multivariate analysis generated a model that was unable to discriminate between patients with PsA and Pso. The possibility that the full PAPRICA assay may be able to discriminate between PsA and Pso will be explored, as will supplementing the PAPRICA method with additional biomarkers including proteins that may be identified in an unbiased proteome wide screen of PsA vs Pso serum samples.

Disclosure of Interests: None declared

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SAT0643 FACIT-FATIGUE TO PROMIS-FATIGUE CROSS-WALKED DATA FROM MONARCH, MOBILITY AND TARGET RANDOMIZED CLINICAL TRIALS OF SARILUMAB FOR THE TREATMENT OF MODERATELY-TO-SEVERELY ACTIVE RHEUMATOID ARTHRITIS (RA)

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Background: Fatigue is a common symptom in RA and increasingly recognized as an important therapeutic target in disease management. Phase 3 randomized clinical trials (RCTs) have shown significant improvements in fatigue for sarilumab, based on the 13-item Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue measure. In TARGET (n=546) and MOBILITY (n=1197), patients receiving sarilumab 150 or 200 mg subcutaneous (SC) every 2 weeks (Q2W) achieved clinically meaningful improvements in fatigue vs placebo. In MONARCH (n=369), there was a trend towards greater improvement in fatigue scores for sarilumab 200mg mg Q2W vs adalimumab 40 mg Q2W monotherapies. To facilitate comparability of fatigue outcomes across studies and measures, the National Institutes of Health (NIH)-funded Patient Reported Outcomes Measurement Information System® (PROMIS®) initiative developed a fatigue item bank of 95 items that includes the FACIT-Fatigue scale within it. This allows FACIT-F scores to be cross-walked to the PROMIS T-score metric, including the subset of 10 FACIT-F items deemed most relevant to RA patients.

Objectives: To describe patient-level, cross-walked PROMIS-fatigue and scoring service 13- and 10-item PROMIS-fatigue scores from TARGET, MOBILITY and MONARCH.

Methods: FACIT-Fatigue scores were cross-walked to PROMIS-Fatigue (using look up tables at the individual patient level), with PROMIS-Fatigue 10- and 13-item T-scores derived from individual patient level data via the publicly available scoring service (http://www.healthmeasures.net). Between-group comparisons of differences (Δ) on least-square mean (LSM) Week 24 change-from-baseline (CFB) scores were evaluated between sarilumab 150 or 200 mg SC Q2W vs placebo (+conventional disease modifying anti-rheumatic drugs in both arms) in TARGET and MOBILITY (including Week 52 CFB) and sarilumab 200 mg SC Q2W vs adalimumab 40mg Q2W monotherapies in MONARCH.

Results: In TARGET and MOBILITY, Week 24 LSM CFB for cross-walked PROMIS-Fatigue scores ranged from −6.10 to −7.22 for sarilumab 150mg and −6.76 to −7.05 for sarilumab 200mg (−6.72 and −6.94 Week 52 CFB in MOBILITY, respectively) and −4.08 to −4.90 for placebo (−4.34 Week 52 CFB). ΔLSM were significant ($p < 0.05$) for sarilumab vs placebo for both doses, in both RCTs. In MONARCH, Week 24 LSM was −5.80 for adalimumab and −7.24 for sarilumab, with non-significant ΔLSM. T-scores on 13- and 10-item PROMIS-fatigue obtained similar results across all studies (**Table**).

Conclusion: Consistent with trial results shown for FACIT-Fatigue, following cross-walk to PROMIS-Fatigue and on PROMIS-Fatigue 13 and 10 T-scores, patients treated with sarilumab demonstrated statistically greater and clinically meaningful improvement in fatigue vs placebo and a trend towards greater improvement vs adalimumab. Converting FACIT-fatigue data to PROMIS-fatigue using either the patient level cross-walk or via the patient level scoring service provides a common metric for comparisons of fatigue outcomes across treatments for RA and against US clinical population reference scores.

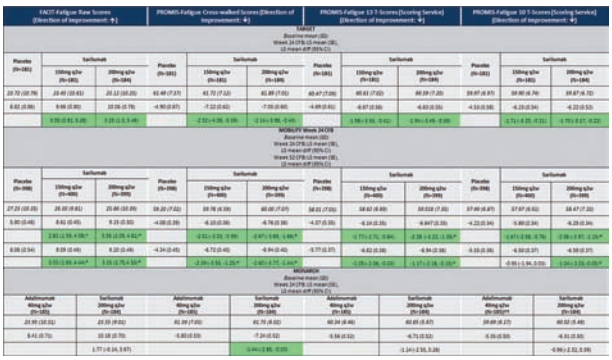
Green boxes $P < 0.05$; * $P < 0.001$

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Table. Week 24 least-square mean differences of change from baseline from TARGET, MOBILITY (and 52) and MONARCH from FACIT-Fatigue raw scores, cross-walked patient-level PROMIS-Fatigue scores and PROMIS-Fatigue 13 and 10 T-score scoring service



SAT0644 OUTCOME MEASURES IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Neuropsychiatric involvement in Systemic Lupus Erythematosus (NPSLE) is one of the most complex and severe expressions of the disease consisting of a variety of neurological and psychiatric syndromes. To date the NPSLE spectrum is lacking in validated disease activity instruments to support specific interventions. This absence of standardization for defining response to therapy is one of the most important barriers to test new therapeutic strategies or drugs in controlled clinical trials in NPSLE.

Objectives: To identify the instruments used to assess NPSLE in published studies according to the OMERACT (Outcome Measures in Rheumatology) Filter 2.0 [Ref].

Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for systematic reviews and Meta-analysis (PRISMA) statement. All articles available in English, published from June 1967 to March 1, 2018, in Pubmed, EMBASE, PsycINFO, Cochrane Library and EULAR Library for Outcome Measure were screened as well as extensive hand search. Study selection and data collection were performed by four independent reviewers. All data were extracted using a standardized template designed for this review. Each outcome was characterized according to the OMERACT Filter 2.0 considering core areas (pathophysiological manifestations, life impact, death, resource use) and domains [Ref].

Results: Results: Of 2,625 abstracts, we included in the review 62 studies of which 1 randomised clinical trial (1.6%, 32 patients), 4 systematic literature reviews (6.4%, 8,024 patients), 21 cohort studies (33.8%, 2,684 patients) and 36 observational studies (58.1%, 1,534 patients), with a total of 12,274 patients. Patients were predominantly female (89.6%) with a mean±SD age of 34.9±5.8 years. The mean disease duration was 5.1 ±2.2 years (range 1 - 9.6). The most frequent included events were seizures (34 studies, 54.8%), cerebrovascular disease (30 studies, 48.4%), psychosis and myelopathy (29 studies, 46.8%), mood disorders (28

Table 1. Health areas, domains and instruments pertinent to the core areas defined by OMERACT reported in the 62 selected articles.

Core Area	Domain	Instrument	No. of Studies Using the Instrument
Pathophysiological	Laboratory markers	• Complement level	3
		• Anti-dsDNA	2
		• Peripheral blood B cell subsets	2
		• Immunoglobulins (IgM, IgA, IgM) titer	1
		• Expression of functional molecules on CD4-positive cells (CD40L, ICOS; CD69, CD4)	1
		• PBMCs CD40-expressing and CD80-expressing CD19-positive cells, CD20-positive cells	1
		• CSF protein content, glucose, and differential cell count	1
		• CSF interleukin (IL)6 level	1
		• CSF GFAP level	1
		• CSF NFL	1
	Instrumental markers	• Fundoscopy	1
		• Electrophysiological studies	4
		• Brain computed tomography	1
		• Brain/spinal cord MRI	15
		• MTR-HPH	1
		• MTI	1
		• SPECT	5
		• 18FTG-PET	2
	Cognitive field	• ACR-SLE battery	1
		• MMSE	1
		• HDS-R	1
		• Cognitive Failures Questionnaire	1
		• Wechsler Adult Intelligence Scale	1
	Sensory-motor field	• ASIA Impairment Scale	1
	Depression/Anxiety field	• CES-D	2
		• HAM-D	1
		• HAM-A	1
		• HADS	1
	Psychiatric field	• BPRS	2
		• YMRS	1
	Pain	• The Short-Form McGill Pain Questionnaire	1
Life impact	Likert scale	• 7 or 5 -point scale	5
	Neuwelt's response criteria	• 20% disease change (composite measure after 4 months of treatment)	6
	GCS	• 3-15 points score	1
	PhGA	• Own definition	27
	PGA	• Patient's Assessment of Own Functioning Inventory	1
	Fatigue	• FSS	1
		• MAF	1
	Function	• EDMUS-GS	1
		• EDSS	3
		• modified Rankin Scale	1
		• Walking index for Spinal Cord Injury	1
	Quality of life	• SF-36	8
		• EuroQol-5D questionnaire	1
Death	Mortality	• Mortality rate	4
	Hospitalization	• Number	1
Composite measures	Disease activity	• SLEDAI-2K	8
		• SELENA-SLEDAI	2
		• ECLAM	2
		• BILAG	2
	Recurrence	• SFI	1
		• Own definition	4
	Damage	• SDI	2
Contextual factors	Side effects	• General	2
	Glucocorticoid therapy	• Minimal dose	2

List of abbreviation: CSF, cerebrospinal fluid analysis; GFAP, glial fibrillary acidic protein; neurofilament triplet protein, NFL; MRI, magnetic resonance imaging; MTR-HPH, magnetization transfer ratio histogram peak height; MTI, magnetization transfer imaging; SPECT, single photon emission computed tomography; PET, 18FTG-positron emission tomography; GCS, Glasgow coma scale; PhGA, physician global assessment; PGA, patient global assessment; MMSE, mini mental state examination; HDS-R, Hierarchic Dementia Scale-Revised; ASIA, American Spinal injury Association; CES-D, Center for Epidemiologic Studies Depression Scale; HAM-D, Hamilton Depression Rating Scale; HAM-A, Hamilton Rating Scale for Anxiety; HADS, Hospital Anxiety and Depression Scale questionnaire; BPRS, Brief Psychiatric Rating Scale; YMRS, Young Mania Rating Scale; Hierarchic Dementia Scale-Revised (HDS-R); Hamilton Depressive Score (HAM-D)FSS, The Fatigue Severity Scale; MAF, Modified Multidimensional Assessment of Fatigue Questionnaire; EDMUS-GS, European Database for Multiple Sclerosis grading scale; EDSS, Expanded Disability Status Scale, SLEDAI, Systemic Lupus Erythematosus Disease Activity Index 2000; SFI, SELENA-SLEDAI Flare Index; ECLAM, European Consensus Lupus Activity Measurement; BILAG, British Isles Lupus Assessment Group Index; SDI, The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index.

studies, 45.1%), headache (27 studies, 43.5%), cognitive dysfunction and cranial neuropathy (24 studies, 38.7%), polyneuropathy (22 studies, 35.5%). Four studies did not define the neuropsychiatric manifestation. Studies identified in this literature review include outcomes and instruments pertinent to all core areas defined by OMERACT, except resource use. The core areas most represented are pathophysiological manifestations and life impact which included a total of 8 domains for each [Table 1].

Conclusion: Our study revealed that a great heterogeneity exists in the assessment of NPSLE and this supports the development of a core outcome set in order to promote clinical research in this field and enhance comparability of studies.

REFERENCES

[1] Boers M, Kirwan JR, Wells G, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. J Clin Epidemiol 2014;67:745–53. doi:10.1016/j.jclinepi.2013.11.013

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SAT0645 ANTI-DFS70 AUTOANTIBODIES INDUCED BY ANTI-TNF THERAPY IN RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS PATIENTS

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Background: anti-DFS70 antibodies (anti-DFS70ab) were recently described as biomarkers clinically useful to discriminate Systemic Autoimmune Rheumatic Diseases (SARD) from non-SARD patients, especially if no concomitant SARD-specific autoantibodies were found. Several unanswered questions concerning the biological significance of this autoantibodies still remain. Objectives: to evaluate the prevalence of anti-DFS70ab in Rheumatoid Arthritis (RA) and Spondyloarthritis (SpA) patients and the influence of anti-TNF therapy on their development. Methods: sera from adult RA (n= 100) and SpA (n= 105) patients, included psoriatic arthritis, fulfilling ACR/EULAR 2010 and ASAS 2011 criteria, respectively, were studied for anti-DFS70ab as measured by IIF, then confirmed by immunoblotting. Medical history, demographic and clinical data were collected at enrolment.

Results: the prevalence of anti-DFS70ab was 4.00% (4/100) in the RA and 4.76% (5/105) in SpA cohort. All anti-DFS70ab in RA patients were monospecific, while only 1 sample in SpA showed concomitant anti-centromere positivity. The findings for the anti-DFS70ab positivity revealed no statistical differences between the groups (p>0.05). In RA cohort, there were no differences between anti-DFS70ab positive and negative patients regarding the F/M *ratio* (F/M, 3/1 *vs* 84/12, p>0.05), mean age (50.2 ±12.4 *vs* 55.6±11.7 yrs, p>0.05) and disease duration (18.2±15.2 *vs* 14.0 ±9.9 yrs, p>0.05). In SpA group, no significant differences were found between patients with and without anti-DFS70ab in F/M *ratio* (3/2 *vs* 43/57, p>0.05) and regarding disease duration (18.8±7.7 *vs* 19.0±20 yrs, p>0.05) while the mean age of anti-DFS70ab patients was significantly higher than the negatives (66.8±10.4 vs 53.5±15.0 yrs, p<0.05). Serological and clinical data of anti-DFS70ab positive patients were summarized in Table 1. In our cohort, all anti-DFS70ab were negative before initiating biologics.

Conclusion: based on our findings, detection of anti-DFS70ab reactivity cannot completely exclude the suspicion of SARD, especially for RA and SpA. In addition, the rate of anti-DFS70ab positivity resulted higher in RA and SpA patients than previously observed in a cohort of samples from outpatients clinics (2.1%) [1]. Immunogenicity of anti-TNF therapy has been also addressed in this study, showing that all detected anti-DFS70ab were induced by anti-TNF therapy. Further studies are needed to support these preliminary data.

REFERENCES

[1] Carbone T. et al. Prevalence and serological profile of anti-DFS70 positive subjects from a routine ANA cohort. *Scientific Report.* 2019, In press.

TABLE 1. Serological and clinical data of anti-DFS70ab positive patients.

Patient n°	*Diagnosis*	*ACPA*	*RF*	*ENA*	*Extra-articular manifestations*	*Comorbidity*
1	RA	-	-	-	None	AH
2	RA	+	+	-	None	EM
3	RA	+	+	-	Lung Fibrosis	OP, AH, HBV, DM, Dyslipidemia
4	RA	+	+	-	None	None
5	SpA	*na*	*na*	-	Erythema nodosum	Autoimmune thyroiditis
6	SpA	*na*	*na*	-	None	COPD, AH
7	SpA	*na*	*na*	-	Psoriasis	DM, AH, diverticulitis
8	SpA	*na*	*na*	-	Psoriasis	COPD, autoimmune thyroiditis, allergic asthma
9	SpA	*na*	*na*	+	Psoriasis	Autoimmune thyroiditis

RA, Rheumatoid Arthritis; SpA, *Spondyloarthritis; ACPA, anti-Cyclic Citrullinated Peptide Antibody; RF, Rheumatoid Factor; AH, Arterial Hypertension; EM, Endometriosis; OP, Osteoporosis; DM, Diabetes Mellitus; COPD, Chronic Obstructive Pulmonary Disease; na, not available; -, negative; +, positive.*

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THE EMERGING ROLE OF IGG ANTI-HIGH-DENSITY LIPOPROTEINS ANTIBODIES AS NOVEL BIOMARKER FOR THROMBOTIC ARTERIAL EVENTS IN ANTIPHOSPHOLIPID SYNDROME PATIENTS

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Background: The mechanisms underlying thrombosis and cardiovascular disease (CVD) in antiphospholipid syndrome (APS) are not completely understood, but recent evidences have brought to light the existence of a complex interplay between traditional CV risk factors and disease-specific features, such as the presence of autoantibodies [1]. Recent studies have discovered the existence of a heterogeneous group of autoantibodies specifically directed against lipoproteins and their components [anti-high density lipoproteins antibodies (anti-HDL)]. Anti-HDL showed promising results in predicting the development of CVD, lipoprotein dysfunction and clinical outcomes in autoimmune conditions. Nevertheless, the association between anti-HDL and clinical features of APS remains unclear.

Objectives: The aim the study was to evaluate the presence of IgG anti-HDL antibodies in a cohort of thrombotic APS patients and to investigate if these antibodies can discriminate between arterial and venous thrombosis.

Methods: This cross-sectional study included 60 patients with persistent antiphospholipid antibodies (aPL) positivity that fulfilled the Sydney criteria for thrombotic APS (venous and/or arterial) [2], and 20 age- and sex-matched healthy donors (HDs). Clinical data were retrospectively collected. Serum levels of total IgG, IgG anti-HDL antibodies and complete aPL profile were assessed, including lupus anticoagulant, anti-cardiolipin, anti-β 2glycoprotein I, and anti-phosphatidylserine/prothrombin both IgG and IgM antibodies.

Patients characteristics	APS patients (N=60)	HDs (N=20)
Female sex (n,%)	43 (71.6)	15 (70.0)
Age (mean, S.D.), years	50±10.8	45.1±11.6
Primary APS patients (n,%)	43 (71.6)	0 (0)
Concomitant diagnosis of SLE (n,%)	17 (28.3)	-
Disease duration since APS diagnosis (mean, S.D.), years	11.7±7.5	-
Thrombosis (n,%)	60 (100)	0 (0)
Venous thrombosis(n,%)	37 (61.6)*	-
Arterial thrombosis (n,%)	30 (50.0)	-
Pregnancy morbidity (n,%)	1 (1.6)	0 (0)
Arterial hypertension (n,%)	22 (36.6)	1 (5)
Hyperlipidemia (n,%)	19 (31.6)	0 (0)
Smoking (n,%)	5 (8.3)	2 (10.0)
LA (n,%)	49 (81.6)	0 (0)
aCL IgG/M (n,%)	38 (63.3)	0 (0)
Anti-β2GPI IgG/IgM (n,%)	29 (43)	0 (0)
aPS/PT IgG/IgM (n,%)	29 (48.3)	0 (0)
Triple aPL positivity (n,%)	20 (33.3)	-
Total cholesterol levels(mean, S.D.), mg/dl	187.4±51	145±32.2
HDL-cholesterol levels(mean, S.D.), mg/dl	64±9.1	72±15.3
Triglycerides levels(mean, S.D.), mg/dl	98.7±28.6	104±26.2
CRP levels(mean, S.D.), mg/dl	0.45±0.2	0.23±0.2
Statins (n,%)	20 (33.3)	0 (0)
Anti-hypertensive drugs (n,%)	19 (31.6)	1 (5.0)
HCQ (n,%)	15 (25.0)	0 (0)
Anticoagulant agents (n,%)	33 (55%)	0 (0)
Antiaggregant agents (n,%)	36 (60.0)	0 (0)

Table 1. Demographic, clinical and laboratory characteristics of the APS patients and HDs included in the study.

Results: 43 patients (72%) were primary APS and 17 patients (28%) had a concomitant diagnosis of systemic lupus erythematosus. Thirty APS patients (50%) presented previous arterial events and 37 (61%) venous events (7 patients experienced recurrent thrombotic events, both venous and arterial; the first event was taken as a reference for the analyses). The characteristics of the cohort are displayed in Table 1.

Higher levels of IgG anti-HDL were found in APS patients compared to HDs [mean 46 (±70) vs. 14 (±13) AU, respectively; p <0.001], even after correcting for total IgG levels [mean 13 (±16) vs. 4.6 (±5), respectively; p <0.001] (Figure 1.1). No association with traditional cardiovascular risk factors, except for smoking habit (p <0.0001) was found. No differences in anti-HDL levels were observed between patients with primary APS and those with a concomitant autoimmune disease (p >0.050). Patients who experienced at least one arterial event had significantly higher levels of anti-HDL antibodies when compared to patients with history of venous thrombosis [mean 53 (SD ±94) vs. mean 34 (SD ±29), respectively; p =0.046]. This difference became stronger when adjusting for total IgG levels [anti-HDL/IgG: mean 13.1 (SD ±16.7) vs. mean 9.5 (SD ±6.6); p =0.007] (Figure 1.2).

In addition, patients tested positive for aPS/PT (IgG/IgM) antibodies had significantly higher levels of anti-HDL antibodies [mean 53.1 (SD ±81.1) vs. mean 20.7 (SD ±17.6), p =0.045]. The levels of IgG anti-HDL antibodies were not influenced by pharmacological treatments (all p >0.050).

Conclusion: Our study demonstrates that thrombotic APS patients have higher levels of IgG anti-HDL antibodies, supporting the emerging role of these autoantibodies in APS setting. Moreover, our findings suggest that anti-HDL represent a promising tool for risk management and assessment and a potential biomarker for lipid dysfunction and arterial thrombotic events.

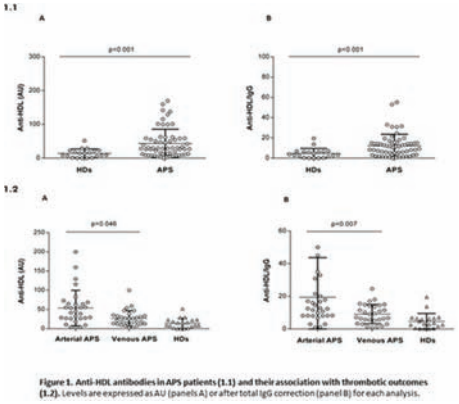


Figure 1. Anti-HDL antibodies in APS patients (1.1) and their association with thrombotic outcomes (1.2). Levels are expressed as AU (panels A) or after total IgG correction (panel B) for each analysis.

REFERENCES

[1] Meroni PL, et al. Pathogenesis of antiphospholipid syndrome: understanding the antibodies. Nat Rev Rheumatol 7:330–339 (2011).

[2] Miyakis S, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 4:295–306 (2006).

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SAT0647

MRI DATA FROM THE SPRIFERMIN PHASE II FORWARD STUDY: CONFIRMATION OF MANUAL CARTILAGE SEGMENTATION FINDINGS BY AUTOMATED SEGMENTATION

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Background: Sprifermin is under investigation as a potential disease-modifying osteoarthritis drug (DMOAD). 2-yr results from the FORWARD study showed significant dose-dependent modification of cartilage thickness in the total femorotibial joint (TFTJ), medial and lateral femorotibial joints

(MFTC, LFTC), and central medial and lateral TFTJ subregions, by quantitative (q)MRI.[1]

Objectives: To determine whether qMRI findings from FORWARD (manual segmentation) could be reproduced in the same cartilage regions using an independent method (automated segmentation), on the same dataset/ time period.

Methods: Pts were randomized 1:1:1:1:1 to: sprifermin 100 μg q6mo; 100 μg q12mo; 30 μg q6mo; 30 μg q12mo; and placebo (n=110/110/111/110/108).[1] Cartilage thickness was assessed at baseline and 6, 12, 18, and 24 months using 1.5- or 3-Tesla MRI images, analyzed manually.[1] The same images were analyzed by automated cartilage segmentation using active appearance models, a supervised machine learning method, to produce maps of cartilage thickness for weight-bearing femoral and tibial cartilage surfaces, subdivided into anatomical masks. Results were blinded for treatment and timepoint for both methods. No statistical comparisons between methods were conducted.

Endpoints were change from baseline in: 1) cartilage thickness in the TFTJ, MFTC and LFTC, using regions duplicated based on published data;[1] 2) cartilage thickness in the central subregion of the medial and lateral tibia and femur (cMT, cMF, cLT, cLF [conventions used by the automated analysis investigators]). As in previous analyses, treatment effect was assessed by observed changes and adjusted using repeated ANCOVA on change from baseline, including treatment group, timepoint, and country as fixed factors, baseline value as covariate and treatment by timepoint as interaction.

Results: Based on automated segmentation, statistically significant, dose-dependent structural modification of cartilage thickness was observed over 2 yrs with sprifermin vs placebo for the TFTJ (overall treatment effect and dose response across all doses, both P<0.001), MFTC (P=0.004 and P=0.044), and LFTC (both P<0.001). **Table 1** shows changes from baseline for sprifermin 100 μg q6mo and placebo. Statistically significant dose-dependent structural modification of cartilage over 2 yrs was observed for sprifermin vs placebo in the cMT (100 μg q6mo), cLT (100 μg q6mo, q12mo) and cLF (100 μg q6mo, q12mo). In the cMF, there was no treatment effect, but there was a linear trend for dose responsiveness. The results showed a consistent pattern to those obtained using manual segmentation.

Conclusion: Cartilage thickness assessed by automated segmentation provided a consistent pattern of structural modification in FORWARD compared with manual segmentation. This is the first time that two independent methods of image analysis have reached the same conclusions in an interventional DMOAD trial. The findings strengthen the conclusions that sprifermin modifies cartilage loss/structural progression in knee OA.

REFERENCES

[1] Hochberg, et al. ACR 2017

Table 1. Change in cartilage thickness with sprifermin 100 μg q6mo vs placebo using automated segmentation

	Mean (SD) change from baseline at Yr 2, mm		
Region	**Sprifermin 100 μg q6mo**	**Placebo**	**P value**
TFTJ	0.05 (0.11)	-0.04 (0.08)	P<0.001
MFTC	0.03 (0.15)	-0.04 (0.14)	P=0.011
LFTC	0.07 (0.12)	-0.04 (0.10)	P<0.001
cMT	0.02 (0.18)	-0.07 (0.17)	P=0.008
cLT	0.09 (0.20)	-0.05 (0.18)	P<0.001
cLF	0.09 (0.11)	0.00 (0.08)	P<0.001
cMF	0.02 (0.17)	-0.04 (0.16)	P=0.061

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SAT0648

RELIABILITY OF MAGNETIC RESONANCE IMAGING (MRI)-SCORING OF THE METATARSOPHALANGEAL-JOINTS ACCORDING TO THE RHEUMATOID ARTHRITIS-MRI SCORE (RAMRIS)

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Background: The Rheumatoid Arthritis Magnetic Resonance Imaging Score(RAMRIS) is validated for magnetic resonance imaging (MRI) of the hand. Its' reliability when applied to metatarsophalangeal(MTP-1-5)-joints is unknown.

Objectives: To assess the interreader- and intrareader-reliability of status scores and the interreader-reliability of change scores applied to the MTP-joints for the following MRI-outcomes: bone marrow edema, synovitis, tenosynovitis and erosions.

Methods: Patients underwent 1.5T MRI of MTP(1-5)-joints. Two readers scored bone marrow edema(BME), synovitis, tenosynovitis and erosions. Interreader reliability was assessed of 441 consecutive early arthritis patients at baseline, the first 215 by two readers, the remaining 226 by two different readers. Additionally, baseline MRIs of 82 consecutive patients with arthralgia were scored by two readers, a random set of 40 patients by seven additional readers (nine readers in total). Intrareader reliability was determined on a random set of 15 early arthritis patients, scored twice by two readers. For change-scores, 30 early arthritis patients with baseline and 1-year follow-up MRI were scored by two readers. Intraclass correlation coefficients(ICCs), Bland-Altman(BA)-plots and smallest detectable change(SDC) were determined.

Results: Interreader mean scores and ICCs in early arthritis are presented in Table 1; ICCs were good to excellent (0.85-0.92) In arthralgia-patients mean scores were lower, ICCs were comparable (Table 1). Intra-reader ICCs for MRI-features were good to excellent (0.84-0.98), but for erosions moderate for reader 1 (0.71 and excellent for reader 2 (0.92). Mean change scores and ICCs are presented in Table 2; ICCs were generally excellent (≥0.90), but moderate for erosions (0.77). SDCs were ≤1.0. BA-plots for status and change scores showed no systematic bias.

Conclusion: Status and change MRI-scores of BME, synovitis, tenosynovitis and erosions of MTP-joints can be assessed reliably by the RAMRIS. This is encouraging for the use of MRI of the MTP-joints in trials in early phases of RA.

Table 1. Interreader intraclass correlation coefficients and average status scores according to the RAMRIS in early arthritis patients (n=441 in total) and patients with arthralgia (n=82)

Patient population		Early arthritis n=215, k=2	Early arthritis n=226, k=2	Arthralgia n=82, k=2	Arthralgia n=40, k=9
MTP-joints					
BME	ICC (95%CI)	0.91 (0.90-0.93)	0.92 (0.90-0.94)	0.77 (0.64-0.85)	0.95 (0.93-0.97)
	Median (IQR, max)	0.5 (0.0-1.5; 20)	0.5 (0.0-1.5; 18)	0.0 (0-0.5; 6)	0.1 (0.0-0.4; 5.4)
	Mean (SD)	1.5 (2.6)	1.1 (2.0)	0.4 (0.9)	0.4 (0.9)
Synovitis	ICC (95%CI)	0.90 (0.84-0.94)	0.92 (0.88-0.94)	0.92 (0.87-0.95)	0.98 (0.97-0.99)
	Median (IQR, max)	1.0 (0.0-1.5; 8)	0.5 (0.0-1.5; 10)	0.0 (0-0.5; 6)	0.2 (0.0-0.8; 6.2)
	Mean (SD)	1.3 (1.7)	1.2 (1.7)	0.4 (0.9)	0.5 (1.0)
Tenosynovitis	ICC (95%CI)	0.85 (0.78-0.90)	0.80 (0.69-0.86)	0.96 (0.93-0.97)	0.99 (0.98-0.99)
	Median (IQR, max)	0.0 (0.0-1.5; 9)	0.0 (0.0-1.5; 12)	0.0 (0-0.0; 7.5)	0.0 (0.0-0.1; 6.8)
	Mean (SD)	1.1 (1.8)	1.1 (1.9)	0.2 (0.9)	0.3 (1.1)
Erosions	ICC (95%CI)	0.88 (0.84-0.91)	0.89 (0.86-0.92)	0.87 (0.81-0.92)	0.96 (0.93-0.97)
	Median (IQR, max)	0.5 (0.0-1.0; 9)	0.0 (0.0-1.0; 7)	0.0 (0-0.5; 2)	0.0 (0.0-0.7; 1.4)
	Mean (SD)	0.7 (1.0)	0.6 (0.9)	0.2 (0.5)	0.3 (0.5)

Results are based on a mean-rating, absolute agreement, two-way mixed effects model.
RAMRIS: Rheumatoid Arthritis Magnetic Resonance Imaging Score; MTP: metatarsophalangeal; MCP: metacarpophalangeal; BME: bone marrow edema; n: number of patients; k: number of readers; CI: confidence interval; IQR: interquartile range; SD: standard deviation; ICC: intraclass correlation coefficients.

Table 2. Change scores intraclass correlation coefficients and average status scores according to the RAMRIS in RA-patients (n=30) from baseline until 12 months of follow-up

	Median difference readers (IQR; max)	Mean difference readers (SD)	ICC change (95% CI)	SDC	Change, n (%)	Change >SDC, n (%)
MTP						
BME	0 (0-1; 3)	0.17 (0.99)	0.97 (0.94-0.99)	1.0	15 (50)	15 (50)
Synovitis	0 (0-0; 3)	0.20 (1.03)	0.90 (0.90-0.98)	1.0	12 (40)	12 (40)
Tenosynovitis	0 (-1-0; 2)	0.23 (0.73)	0.96 (0.91-0.98)	0.7	11 (37)	11 (37)
Erosions	0 (0-0; 1)	0.13 (0.57)	0.77 (0.52-0.89)	0.6	10 (33)	10 (33)

IQR: interquartile range; SD: standard deviation; CI: confidence interval; SDC: smallest detectable change; n: number; MTP: metatarsophalangeal; MCP: metacarpophalangeal; BME: bone marrow edema. 'Median and mean change' represents the average change over time of both readers, 'median and mean difference readers' represents the difference between the change scores of reader 10 substracted from reader 9. Change ICCs are based on a mean-rating, absolute agreement, two-way mixed effects model. 'Change, n' represents the number of patients with change before using any cut-off, 'Change >SDC, n' represents the number of patients with change after using the SDC as a cut-off.

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SAT0649 DEVELOPMENT AND VALIDATION OF A PATIENT-REPORTED OUTCOME ASSESSING ACTIVITY LIMITATION AND PARTICIPATION RESTRICTION OF PATIENTS WITH SYSTEMIC SCLEROSIS: THE COCHIN 17-ITEM SCLERODERMA FUNCTIONAL SCALE (CSF-17)

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Background: Few patient-reported outcomes measures (PROs) have been specifically designed to assess the functioning of patients with systemic sclerosis (SSc). In addition, the development of currently available instruments did not fully follow current guidelines (1)
Objectives: To develop and validate a PRO assessing activity limitation and participation restriction of patients with SSc.
Methods: A provisional International Classification of Functioning, Disability and Health (ICF)-based 65-item questionnaire previously developed from interviews of SSc patients was submitted online to French patients (n=184) of the Scleroderma Patient-centered Intervention Network e-cohort (2). Items were reduced according to their metric properties, dimensional structure of the questionnaire was assessed by principal component analysis, convergent and divergent validities using the Spearman correlation coefficient (ρ), internal consistency by the Cronbach α coefficient and reliability by a test-retest method using intraclass correlation coefficient (ICC) and Bland and Altman analysis.
Results: Overall, 113/184 (61.4%) patients completed the provisional questionnaire. The item-reduction process resulted in a 17-item questionnaire, the Cochin 17-item Scleroderma Functional scale (CSF-17). Principal component analysis extracted 2 dimensions: 10 items related to mobility (CSF-17 section A) and 7 items related to general tasks (CSF-17 section B). We observed convergent validity with global activity limitation, pain, depression and aesthetic burden and divergent validity with anxiety. The Cronbach α coefficient was 0.94 for section A and 0.95 for section B. ICC (n=25 patients) was 0.92 for CSF-17 total score. Bland and Altman analysis did not reveal a systematic trend for the test-retest.
Conclusion: The CSF-17 is a self-administered questionnaire assessing activity limitation and participation restriction of patients SSc with good content and construct validities

REFERENCES

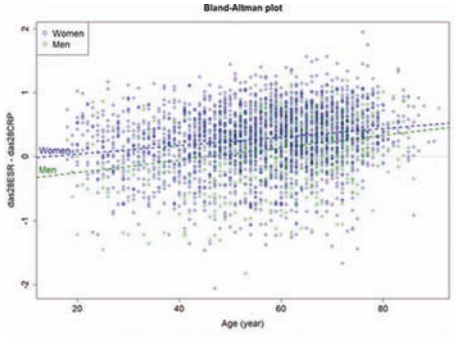
[1] Health USDo, Human Services FDA, Research, et al. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. Health Qual Life Outcomes. 2006;4:79.
[2] Kwakkenbos L, Jewett LR, Baron M, Bartlett SJ, Furst D, Gottesman K, et al. The Scleroderma Patient-centered Intervention Network (SPIN) Cohort: protocol for a cohort multiple randomised controlled trial (cmRCT) design to support trials of psychosocial and rehabilitation interventions in a rare disease context. BMJ Open. 2013;3(8).

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SAT0650 THE INFLUENCE OF PATIENT DEMOGRAPHICS ON DISEASE ACTIVITY MEASUREMENTS IN RHEUMATOID ARTHRITIS

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Background: Several indexes have been constructed for the measurement of disease activity in rheumatoid arthritis (RA) patients, including the Disease Activity Score 28-joint count, which either includes the Erythrocyte Sedimentation Rate (DAS28ESR) or the C-reactive protein concentration (DAS28CRP), and the Clinical Disease Activity Index (CDAI). The categorization of the results of these three indexes into levels of disease activity (Remission, Low, Moderate and High) is used to assess patient outcomes, and to guide medical decisions regarding treatment. However, the different indexes can lead to somewhat different classification, and hence influence treatment decisions.[1]
Objectives: To investigate how DAS28ESR, DAS28CRP and CDAI indexes are associated to age and sex in RA patients. To investigate the agreement between indexes and between categories of disease activity levels.
Methods: We identified a cohort of RA patients, registered in the Swedish Rheumatology Quality Register between January 1st2014 and December 31st2017. The indexes were obtained from the first visit at the time point of RA diagnosis, and at the visit registered at the start of a first ever biological treatment prescription. Linear models were used to investigate the correlation between the indexes, age and sex. The agreement between the indexes was explored with Bland-Altman plots. The agreement between disease activity levels was evaluated through kappa statistics.
Results: Data were analyzed for 3855 RA patients (2576 women, mean age ±SD=60±15) at their first diagnosis visit and for 3062 RA patients (2313 women, mean age ±SD=57±14) at the start of their first biologic. Similar results for all subsequently described analyses were obtained at both time points. The correlation coefficient and 95% confidence interval (95%CI) between the indexes and age were 0.093 (0.063-0.124) for DAS28ESR and 0.055 (0.025-0.085) for DAS28CRP at the first visit, while CDAI was not correlated to age. There was no difference between men and women for CDAI and DAS28CRP, while DAS28ESR presented a mean difference of 0.1 unit between men and women. The agreement between categories of disease activity was moderate: at the RA diagnosis visit, the kappa statistics and 95% CI were: 0.63 (0.61-0.65) between DAS28ESR and DAS28CRP, 0.59 (0.57-0.61) between DAS28ESR and CDAI, and 0.55 (0.53-0.57) between DAS28CRP and CDAI. About 25% of the patients were classified differently. The Bland-Altman plot revealed that the difference between DAS28ESR and DAS28CRP depended on sex and slightly increased with age.
Conclusion: Factors related to patient demographics might influence the results of disease activity indexes. This has a potential to affect clinical decisions, as the definition into disease activity categories can differ depending on the score used. This suggests the need to consider sex and age when defining such categories and interpreting results from these indexes.



The Bland-Altman plot show that the mean difference between DAS28ESR and DAS28CRP slightly increases with age, in both women and men (dotted lines). Both DAS28 were measured at start of biological treatment.

REFERENCES

[1] Shoels, et al. Arthritis Res. Ther. 2017,19:155

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SAT0651 GOOD DISCRIMINATIVE ABILITY OF THE SIMPLE EROSION NARROWING SCORE COMPARED TO THE SHARP/VAN DER HEIJDE SCORE

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Background: The Simple Erosion Narrowing Score (SENS), a simplification of the Sharp/van der Heijde score (SHS), has been recommended for use in clinical practice because it combines a simpler, less time-consuming scoring method with measurement properties comparable to the SHS [1]. The SENS assesses both joint space narrowing (JSN) and erosions in the same joints as the SHS, but the SENS sums the number of joints with erosions and the number of joints with JSN without grading per joint. However, some studies have suggested that the SENS is less sensitive to radiographic progression than the SHS. Further erosion of already eroded joints added to the discriminative ability of the SHS in the COBRA trial, suggesting some discrimination might be lost when using the SENS, especially in more advanced RA populations [2]. This is an important issue, as time savings using SENS are substantial (7 instead of 25 minutes [1,3]), but contrast between interventions is in general lower than in the early years of RA research as the standard of care improves and trials are more and more characterized by active controls and disease activity guided treatment strategies that tend to converge.

Objectives: To assess whether the SENS can discriminate between treatment groups when the treatment contrast is low, using data from the DRESS (Dose REduction Strategy of Subcutaneous TNF inhibitors) trial

Methods: The DRESS study (Dutch trial register, NTR 3216, CMO region Arnhem-Nijmegen, NL37704.091.11) is an open label non-inferiority randomised controlled trial in which RA patients with low disease activity on a stable adalimumab or etanercept dose were randomised 2:1 to disease activity guided tapering or usual care [4]. Radiographs of hand and feet at baseline and the end of follow up (18 months) were assessed independently in chronological order by 2 blinded trained readers using the SHS. The SENS was determined based on the individual joint scores of the SHS. For both scores, the mean of the two readers was used to minimise measurement error. In order to compare the discriminative ability of both scores, we repeated the analyses from the DRESS study using the SENS and compared the results. In addition, we performed bootstrapping (1000 replications) to investigate the consistency of the results.

Results: Table 1 shows baseline characteristics of the study population. A significant but clinically unimportant mean increase (95% CI) in radiographic progression of 0.60 (0.16-1.0) points SHS in the dose reduction group was found in the original study. Using the SENS score, this analysis shows a difference of 0.33 (0.11-0.54) points. In relation to the maximum score in each method (SHS: 448; SENS: 86), these changes are comparably low (SHS: 0.13% (0.04%-0.23%); SENS: 0.38% (0.13%-0.63%)). In bootstrapping replications of the DRESS study, using a T-test, the SHS detected a significant difference in progression in 86,0% of replications, the SENS did so in 91,3%.

Table 1. Baseline characteristics

	Dose reduction (n=116)	Usual care (n=59)
Age, mean (sd)	59 (10)	58 (9)
Female, n (%)	71 (61%)	41 (69%)
Disease duration, median (IQR)	10 (5-16)	10 (6-16)
Erosive disease, n (%)	65 (61%)	34 (62%)
Rheumatoid factor, n (%)	91 (78%)	49 (83%)
Anti-CCP, n (%)	82 (71%)	45 (76%)
Baseline SvdH, median (IQR)	23 (6-50)	18 (9-47)
Baseline SENS, median (IQR)	10 (4-22)	10 (5-20)

Conclusion: The SENS and SHS were equally able to detect a difference in radiographic progression, even with a very low treatment contrast between the two groups and in this relatively advanced RA population.

REFERENCES

[1] Van der Heijde, et al. Rheumatology (Oxford). 1999 Oct;38(10):941-7.
[2] Bruynesteyn, et al. Arthritis Rheum. 2002 Oct 15;47(5):532-6.
[3] Boini, et al. Ann Rheum Dis. 2001 Sep;60(9):817-27.
[4] Van Herwaarden, et al. BMJ. 2015 Apr 9;350:h1389.

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SAT0652 VALIDATION OF A RISK PERCEPTION QUESTIONNAIRE DEVELOPED FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Risk perception (RP) is a multidimensional phenomenon that describes the individual's judgment of the likelihood of experiencing something unpleasant. RP shapes health-related-behaviors and may be central for rheumatoid arthritis (RA) management, where treatment must be based on shared decisions between the patient and the rheumatologist. Rheumatologists can motivate successful self-care in RA patients with information that brings the physician vision closer to the patient's perceptions. Assessing patients-perceived risk may help explain how RA patients integrate their ideas concerning the disease and its treatments, and how this understanding drives their self-care management. There is no current validated instrument to assess RP in RA.

Objectives: Develop and validated a RP-Questionnaire (RPQ) for Spanish speaking RA patients.

Methods: Development and validation the RPQ was performed in 3 different steps, using 3 different convenience samples of RA outpatients attending a tertiary-care-level center. The construction process suggested by Streiner for health measurement scales when a current measure does not exist was followed[1]. Step 1 was the conceptual model construction and included: a literature review, semi-structured one-to-one interviews to 20 RA outpatients which were directed to answer open-ended questions about the likelihood of harms related to RA, and interviews to 6 rheumatologists and 5 RA-experienced physiotherapists who were directed to list and rate (according to severity and frequency) 15 RA-related components (symptoms, manifestations and/or complications). Step 2 consisted of item generation (theory, patients interviews and expert opinions were the sources considered), item reduction performed in 100 additional RA patients (from 108 to 27 items, that were ultimately distributed into 5 dimensions following conceptual construction), scaling responses, item scoring and feasibility. Step 3 consisted of RPQ psychometric validation performed in 270 additional RA outpatients, content and face validity (by experts agreement), construct validity (exploratory factor analysis) and consistency and stability (Cronbach's α and test-retest). Validation sample size was based on the methodological recommendations, which suggested a minimum of 50 patients for assessing construct validity, 100 patients for assessing internal consistency, and 5 to 10 patients for each item. IRB approved the study.

Results: The 390 patients included in the 3 samples were representative of typical RA outpatients from a tertiary care level center; they were primarily women, in their fifth decade of life, with basic formal education, medium low socioeconomic status and had long-standing disease; in addition, patients with a major comorbid condition and with surgical joint replacement were also represented.

RPQ included 27 items distributed in 5 factors (3 for likelihood, 1 for responsibility and prevention and 1 for disease control), which resulted in 68.8% of the variance explained. Cronbach's α for the total score was 0.90. Intraclass-correlation-coefficient in test-retest was 0.93 (95% CI=0.90-0.95). All items had $\geq$80% agreement from experts. Patients agreed about item´s semantic clarity (89%) and RPQ format adequacy (97%).

Conclusion: RPQ showed to be a valid and reliable instrument to evaluate RP in Spanish speaking RA patients. RPQ can be incorporated to clinical care and guide interventions to improve patient´s health behaviors.

REFERENCES

[1] Steiner D, Norman G. (Eds). Health Measurement Scales. A practical guide to their development and use. New York. Oxford University. Press 2003.

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SAT0653 PATIENT-ACCEPTABLE SYMPTOM STATUS IN RHEUMATOID ARTHRITIS: WEALTH AND AGE MATTER BEYOND DISEASE ACTIVITY AND IMPACT. AN ANALYSIS OF 548 PATIENTS

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Background: Patient Acceptable Symptom State (PASS) represents the maximum level of symptom intensity that patients consider acceptable[1]. Control of disease activity is associated to attainment of PASS[1]. Recognizing the factors associated with PASS status beyond disease activity, can be helpful in identifying the need for interventions beyond disease-modifying drugs, aimed at improving the satisfaction and well-being of patients with rheumatoid arthritis (RA).
Objectives: To explore the clinical and socio-demographic factors associated with PASS status in RA.
Methods: Data of patients with definite diagnosis of RA from 11 countries (*post-hoc* analyses of RAID Study[2], with additional data from Portugal) were used. PASS was assessed using the anchored method based on patients' perspective, through the question: "*Think about all the ways your RA has affected you during the last week. If you were to remain for the next few months as you were during the last week, would this be a) Acceptable b) Unacceptable*". Variables analysed for differences across PASS status were (a) disease activity based on DAS28-3values (joint counts and ESR) categories, (b) impact by the seven patient-reported domains included in the RA Impact of Disease (RAID) score, (c) demographics: age (above or below 50) and gender, and (d) Country gross domestic product (GDP) classified as High GDP (>35.000 USD per capita) and Low GDP. Differences between patients in PASS or not were assessed through t-test for independent samples or Chi-square test, as adequate. Variables with p<0.05, gender and GDP category were included in multivariate logistic regression (Forward Conditional) analysis. A subgroup analysis was performed for patients in DAS28-ESR remission.
Results: In all, 548 patients (80.5% female, mean (SD) age 55.8 (12.8) years, mean (SD) disease duration 13.6 (10.6) years, mean (SD) DAS28-3v 3.6 (1.5), 44.2% in LDA or remission) from 11 European countries (5 (n=230) with high GDP and 6 (n= 318) with low-GDP) were analysed. The majority of patients (65.7%) considered themselves to be in PASS; among them 40% were in remission and 16.7% in LDA. In multivariate analyses, factors associated to being in PASS were lower disease activity (OR 1.28; [1.08-1.52]), lower pain (OR 1.45; [1.27-1.64]) and better emotional well-being (OR 1.28; [1.13-1.45]), older age (OR 1.67; [1.04-2.67]), but not GDP country category. When analysing PASS for patients in DAS28 remission independent predictors were lower pain (OR 2.5; [1.79 -3.45]), older age (OR 3.30 [1.03-10.82]) and living in a low GDP category country (OR: 5.0; [1.35-20.0]).
Conclusion: PASS in RA is associated with lower inflammation, less symptoms and higher age, as expected. However, when analysing patients in DAS28 remission, thus taking out inflammation as a predictor, we found older age and living in a country with lower GDP were drivers of being in PASS. Thus, beyond disease activity and patient-reported impact, this observation underlines the potential effect of economical/cultural and personal aspects upon PASS, especially in the context of remission, suggesting the need for a holistic and personalized approach in the management of patients with RA.

REFERENCES

[1]) Heiberg T, et al. Ann Rheum Dis. 2008 Jul;67(7):967-71
[2]) Gossec L, et al. Ann Rheum Dis. 2011;70(6):935-42

Acknowledgement: Carmona L, Dijkmans BA, Englbrecht M, Gogus F, Heiberg T, Cerinic MM, Otsa K, Sokka T, Balanescu A
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SAT0654 SHOULD PATIENTS WITH RHEUMATOID ARTHRITIS (RA) ASK FOR A BETTER DEAL THAN MERELY AN ACCEPTABLE SYMPTOM STATE? AN ANALYSIS OF 1931 RA PATIENTS

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Background: Patients satisfaction with their symptoms state may be considered an acceptable outcome in RA. However, many patients who report being in an Acceptable Symptom State (PASS) have still moderate disease activity.[1]
Objectives: To explore whether it is possible to identify more stringent levels of symptom states in patients´ perspective.
Methods: A cross-sectional analysis of unselected adult patients with the diagnosis of RA from the RA Impact of Disease (RAID) validation study[2] (n=570, from 12 European countries), and from the Norwegian DMARD (NOR-DMARD)[3] registry (n=1372), was performed. Symptom state was calculated using the anchored method based on the patients' perspective, taking, as gold standard, the question: "*Think about all the ways your rheumatoid arthritis has affected you during the last week. If you were to remain for the next few months as you were during the last week, how would you consider this state*?", with five levels: Very bad/Bad/Acceptable/Good/Very good. Disease activity was assessed based on the DAS28-3v (joint counts and ESR). Impact was evaluated through the seven patient-reported domains included in the RAID score. The threshold levels of DAS28-3v, Individual RAID items and RAID score for Acceptable/Good/Very Good States were calculated using the receiver-operating characteristic (ROC) curve and the optimal cut-off was determined through Youden Index.
Results: Data from 1931 patients [74.5% female, mean (SD) age 54.4 (14.1) years, mean disease duration 13.8 (10.4) years, mean DAS 28-3v-ESR 3.0 (1.4)] were analysed. In all, 14.5% considered themselves as being in a "very good", 21% as "good" and 33.1% in a "acceptable" status. Disease activity, RAID global score and all individual seven domains of RAID were significantly different between patients across these 3 symptom states (p<0.001). Patients reporting a "Very Good" symptom status had disease activity in the range of remission (mean DAS28-3v-ESR: 1.99±0.91), while patients in "acceptable" status were in range of low disease activity (DAS28-3v-ESR:2.98±1.20) and in moderate disease activity in patients with "Bad" (DAS28-3v-ESR: 3.83±1.44) and "Very Bad status" (DAS28-3v-ESR: 4.10±1.59). Remission according the Boolean ACR/EULAR criteria was observed in 70.9% of patients in "Very Good" symptom status (versus 28% in "Good", 5% in "Acceptable" and inferior to 1% in "Bad" and "Very Bad" symptom status). The cut-off value for "Very Good" states was 0 for most individual RAID items, except for pain and fatigue ≤1 (Figure1).
Conclusion: Being in a "very good" symptom status showed a good correspondence to being in remission and having very low disease impact. This shows promising in identifying a status that patients would actually desire, more than accept for, while corresponding to a level of disease activity consistent with the long-term preservation of structure and function.

Figure 1: Thresholds for DAS28-3v-ESR, score of global RAID and each of its individual domains for Good and very good symptom sates.

	Cut-off	AUC	Sensitivity (%)	Specificity (%)
Cut-off for "Good"				
RAID Pain	≤2	0.78	64.7	80.8
RAID Function	≤2	0.78	71.8	73.4
RAID Fatigue	≤2	0.72	57.6	77.0
RAID Sleep	≤2	0.73	79.3	60.4
RAID Emotional Well-being	≤2	0.80	69.9	80.6
RAID Physical Well-being	≤2	0.73	73.8	62.7
RAID Coping	≤1	0.78	64.9	79.8
RAID Score	≤2.58	0.82	77.1	75.5
DAS 28-3v-ESR	≤2.61	0.65	65.5	57.9
Cut-off for "Very Good"				
RAID Pain	≤1	0.81	81.8	70.2
RAID Function	≤0	0.76	66.1	78.3
RAID Fatigue	≤1	0.76	76.7	64.0
RAID Sleep	≤0	0.38	73.6	61.0
RAID Emotional Well-being	≤0	0.81	57.2	91.6
RAID Physical Well-being	≤0	0.73	63.1	76.0
RAID Coping	≤0	0.75	74.7	71.6
RAID Score	≤1.02	0.84	80.0	77.1
DAS 28-3v-ESR	≤2.3	0.67	70.0	49.2

AUC: Area Under the Curve

REFERENCES

[1]) Heiberg T, et al. Ann Rheum Dis. 2008 Jul;67(7):967-71
[2] Gossec L, et al. Annals of the rheumatic diseases. 2011;70(6):935-42
[3] Kvien TK, et al. Clin Exp Rheumatol. 2005. 23: S188-94

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SAT0655 THE SPECTRUM OF MYOSITIS ANTIBODIES: CLINICAL CORRELATION AND PREVALENCE OF ANTI-DFS70

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Background: Myositis can be a clinical feature of several rheumatic diseases. In inflammatory idiopathic myopathies (IIM), such as Dermatomyositis (DM), Polymyositis (PM), Antisynthetase syndrome (ASS), muscular lesions are immune-mediated and may associate with skin, aesophagus, lung, heart and joint involvement. The role of myositis specific antibodies (MSA) and myositis associated antibodies (MAA) in determining the clinical phenotype is still unclear. Anti-dense fine speckled antibodies (anti-DFS70ab) show a low frequency in DM and are generally associated with DM-specific autoantibodies
Objectives: to characterize antibodies in IIM and myositis related to other rheumatic diseases and to correlate them to clinical features, cancer history and anti-DFS70ab presence.
Methods: 37 patients with myositis (including IIM, overlap syndrome and myositis related to other rheumatic diseases) were evaluated. Anti-DFS70ab pattern was determined by indirect immunofluorescence on HEp-2000 cells. Detection of anti-DFS70ab specificity (truncated sequence of the DFS70 antigen (residues 349-435)), of MSA (MDA-5, TIF 1-γ, SAE1, SAE2, NXP-2, Jo-1, PL-7, PL-12, EJ, OJ, KS, ZO, HA, SRP, Mi-2,), of MAA (U1-RNP, SSaRo52/60, PM-Scl100/75, Ku) and of other Scleroderma associated antibodies (Scl-70, CENP-A, CENP-B, RNA Polymerase III, Th/to, Fibrillarin) were performed using immunoblotting assay. Clinical, serological and instrumental data were recorded.
Results: 15 patients had a diagnosis of DM, 8 of PM, 3 of ASS, 5 of overlap syndrome (3 with Systemic Sclerosis (SSc), 1 with Sjogren Syndrome (SS), 1 with cryoglobulinemia), 6 of myositis related to other rheumatic disease (1 SSc, 1 Rheumatoid Arthritis, 2 Undifferentiated Connective Tissue Disease, 2 Systemic Lupus Erithematosus). In IIM, overall frequencies of MSA and MAA were 46.1% (12/26) and 38.4% (10/26), respectively, with concomitant expression in 5/26 cases. The 30.7% (8/26) of patients was negative for any type of antibodies. Mi-2 (4/15=26.6%), NXP-2 (3/15=20%) and SRP (2/15=15.3%) were detected in DM subset and were associated with typical skin lesions, muscle weakness, dysphagia and microvascular damage on capillaroscopy, while no interstitial lung disease, cardiac and articular involvement were recorded. Jo-1 was positive in 5/26 patients (2 PM, 2 ASS, 1 DM=19.2%) characterized by interstitial lung disease, arthritis, skin involvement and muscle weakness and by pulmonary hypertension when associated with TIF1- γ (1 DM=6.6%). Autoantibodies profile in overlap syndrome and myositis related to other rheumatic diseases was characterized by prevalence of MAA, more frequently PM-Scl100/75, RNP, Ku, SSaRo52/60. Only in 1 patient with an overlap syndrome SSc/PM HMGCR reactivity was detected. As far as cancer association, a positive history was found in 8.1% (3/37), related more frequently to Jo-1 and SSaRo52. Anti-DFS70ab were positive in 2/26 patients with IIM (7.6%; 1 DM and 1 PM) and in 1 with SSaRo60. No cases of anti-DFS70ab positivity was found in other subsets.
Conclusion: Prevalence of MSA and MAA and their clinical correlations in our population are comparable to data reported in literature. Mi-2, NXP-2 and SRP can be considered markers of DM, while Jo-1 a predictor of lung involvement. Jo1/SSaRo52 positivity is reported in association with lung cancer, but to our knowledge no data are present about melanoma. Our preliminary data confirm that, not only in DM but also in PM, anti-DFS70ab were observed with a low frequency; however more studies are needed to establish the pathogenetic role of these antibodies.
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SAT0656 DAPSA OR MDA/VLDA CRITERIA FOR DEFINING THE TREATMENT TARGET IN PSORIATIC ARTHRITIS? CROSS-SECTIONAL ANALYSIS FROM A MULTICENTER ITALIAN COHORT

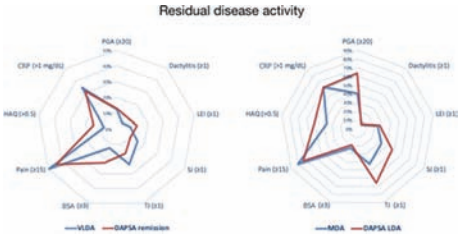
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Background: According to international recommendations, psoriatic arthritis (PsA) should be managed by a treat-to-target approach, but the identification of the best tool for defining the target of remission/low disease activity (LDA) is still controversial.
Objectives: To evaluate and compare the rates of remission/LDA by comparing Disease Activity in PSoriatic Arthritis (DAPSA) score with Very Low Disease Activity (VLDA)/Minimal Disease Activity (MDA) criteria in a real-life multicentre cohort of PsA patients.
Methods: We performed a cross-sectional analysis including the first consecutive 500 PsA patients evaluated in 8 Italian rheumatology centres since September 2017. The rates of patients achieving DAPSA remission/ LDA and VLDA/MDA were calculated and compared by a chi-square test. The agreement between the two criteria sets was established by Cohen's kappa. The proportion of patients with residual disease activity despite remission/LDA and VLDA/MDA was computed for: peripheral arthritis

(number of swollen [SJ] or tender joints [TJ] ≥1), Leeds Enthesitis Index (≥1), number of dactylitis (≥1), Body Surface Area (BSA, ≥3%), Patient Global Assessment (PGA, ≥20), Health Assessment Questionnaire (HAQ, ≥0.5), pain VAS (≥15), C-reactive protein (CRP, ≥1 mg/dL). Sub-analyses after stratification according to ongoing treatment (csDMARDs versus bDMARDs) were also performed.

Results: The study population (53.2% men; mean [± standard deviation, SD] age 52.9±12 years; mean [±SD] disease duration 8.6±7.7 years) included 200 patients treated with csDMARDs (71% methotrexate) and 300 with bDMARDs (73% anti-TNF agents). The rates of DAPSA remission and VLDA were similar in the overall population (25.8 vs 22.2%, respectively; p=0.18) and in bDMARD subgroup (27.3 vs 26.7%, respectively; p=0.85), but greater for DAPSA remission in csDMARD patients (23.5 vs 15.5%, respectively; p=0.04). DAPSA LDA was significantly more frequent than MDA (40.6 vs 26.4%, respectively; p<0.0001), with no significant difference in bDMARD vs csDMARD subgroups. The level of agreement was good between DAPSA remission and VLDA (kappa=0.72), but only fair between DAPSA LDA and MDA (kappa=0.30), with a higher agreement in bDMARD than csDMARD patients for both DAPSA remission/VLDA (kappa 0.74 vs 0.6, respectively) and DAPSA LDA/MDA (kappa 0.34 vs 0.23, respectively). Levels of residual disease activity (figure 1) were similar for DAPSA remission and VLDA, with the exception of skin domain (22.4 vs 12.6%, respectively; p=0.04). Compared with patients in MDA, those in DAPSA LDA showed more frequently residual joint involvement (SJ 47.3 vs 32.6%, respectively, p=0.007; TJ 66 vs 42.2%, respectively, p<0.0001), elevated PGA (63.5 vs 40.9%, respectively, p<0.0001), and elevated HAQ (50.7 vs 36.3%, respectively, p<0.009).

Conclusion: In our real-life cross-sectional analysis, the agreement between DAPSA and VLDA/MDA criteria was good only for the definition of remission, whereas DAPSA was significantly less stringent than MDA (especially in csDMARDs treated patients) in defining LDA, with a great proportion of patients showing residual arthritis and disability.



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SAT0657 MONOCYTE-LYMPHOCYTE RATIO AND PLATELET-LYMPHOCYTE RATIO: ROLE AS BIOMARKERS OF DISEASE ACTIVITY IN PSORIATIC ARTHRITIS PATIENTS

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Background: Monocyte-lymphocyte ratio (MLR), neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) had emerged as good indicators of systemic inflammation status in a variety of diseases like cancer, cardiovascular and autoimmune diseases. Furthermore, some recent data showed relevant association of this haematological parameters with others traditional inflammatory measures as serum c- reactive protein (CRP) levels in rheumatic patients, suggesting their use as a valuable indicator of disease activity.

Objectives: To assess the association between the NLR, MLR, eosinophil-lymphocyte ratio (ELR), basophils-lymphocyte ratio (BLR) and PLR with disease activity and functional parameters in psoriatic arthritis (PsA) patients.

Methods: An observational cross-sectional study was performed in patients with psoriatic arthritis before introduction of a bDMARD, followed at our Rheumatology department until December 2018. Demographic, clinic and laboratory information were collected from the national database (Reuma.pt). Available data of blood cell counts were consulted and NLR, MLR, ELR, BLR and PLR were calculated by dividing neutrophil, monocyte, eosinophil, basophils and platelet count by lymphocyte count, respectively. The following disease activity and functional scores were also registered: CRP and ESR levels, DAS28 4V and 3V (ESR and CRP), HAQ, BASDAI, ASDAS-CRP, BASFI, BASMI, swollen and tender joints counts (SJC and TJC), SPARCC index, patient global assessment (PtGA) and physician global assessment (PGA) rated on a visual analogue scale (VAS). Correlations between variables were evaluated with Spearman's test. The statistical analysis was performed using SPSS 21.0 software. Differences were considered statistically significant at p<0.05.

Results: A total of 83 patients were enrolled. Forty-three were females (51.8%) and forty were males (48.2%). The mean age was 47 years (±10.9) and the median disease duration at start of biological therapy was 6.9 years (min:1.4; max:32.4). In total, 67.5% of the patients had axial involvement (n=56), 91.6% articular involvement (n=76) and 43.4% enthesopathic involvement (n=36). Almost all patients fulfilled the CASPAR criteria for PsA (n=78; 94%). Thirty patients presented with dactylitis (36%). Most were non-smoking (n=48; 57.8%) and most didn't have history of alcohol consumption (n=55; 66.3%). According to ASDAS criteria, 25 patients (30.1%) had high disease activity and 45 patients (54.2%) very high disease activity. At time of evaluation, 71.1% were receiving csDMARDs. NSAIDs and corticosteroids were prescribed in 80.7% and 54.2% of the patients, respectively. We found statistically significant correlation between MLR values and CRP levels (r=0.276, p=0.014). MLR did not correlate with ESR levels, DAS28 4V and 3V (ESR and CRP), HAQ, BASDAI, ASDAS-CRP, BASFI, BASMI, SJC, TJC, SPARCC, PtGA and PGA. PLR values also had weak correlation with ESR (r=0.340, p=0.002), DAS 4V-ESR (r=0.260; p=0.027) and with DAS 3V-ESR (r=0.290, p=0.012). There was no statistically significant correlation between PLR values and others disease parameters. No significant correlation were found between NLR, ELR and BLR and the functional and disease activity scores evaluated.

Conclusion: Our study showed that MLR had a positive association with CRP and PLR with ESR, DAS 4V-ESR and DAS 3V-ESR. Evaluation of this novel inflammatory biomarkers may represent a simple, cost-effective and useful tool in monitoring disease activity in PsA patients.

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SAT0658 A LONGITUDINAL ANALYSIS OF ANTI-FHL1 ANTIBODIES IN A SWEDISH COHORT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Antibodies targeting a novel and muscle-specific autoantigen, the Four-and-a-half-LIM-domain 1 (anti-FHL1), have been identified in patients with idiopathic inflammatory myopathies (IIM).

Objectives: The aim of this project was to evaluate when anti-FHL1 autoantibodies are present in the course of the disease and if autoantibody titers vary over time.

Methods: The anti-FHL1 antibody status was obtained from a previous serological cross-sectional analysis from where we selected sera from IIM anti-FHL1$^+$ patients (n=25) and sex and age matched sera from IIM anti-FHL1$^-$patients (n=51), and healthy controls (HCs, n=50). Levels of anti-FHL1$^+$ autoantibodies were evaluated by ELISA. Patients included in the study had at least one sample available at time of diagnosis and one consecutive serum sample within an interval of 36 months. All patients were followed at the Division of Rheumatology, Karolinska University Hospital from January 1982 to December 2017. HCs sera collected at a single time point were tested.

Results: In the IIM group we included 76 patients with a total of 320 serum samples. Median follow-up time was 108 months, with median of 4 samples available per patient. In total, we identified the presence of anti-FHL1$^+$ antibodies in n=31 IIM patients, corresponding to the group of

anti-FHL1$^+$ (n=25) and in anti-FHL1$^-$ (n=6) from the cross-sectional analyses. One HC had positive anti-FHL1 titers. We subdivided the patients into 4 groups: anti-FHL1$^+$: "highly positive" (O.D.>1, n=11), "intermediate positive" (1>O.D.>0.75, n=6), "baseline negative" that seroconverted (O.D. >0.75, n= 14), and one anti-FHL1 "negative" group. All groups were compared by given OD medians at each of the point of observation. Highly positive patients had persisting high anti-FHL1 titers during the follow-up; on the contrary, both intermediate positive and baseline negative groups were fluctuating around the cut-off point. Eight of 14 (57%) patients from the group "baseline negative" seroconverted to anti-FHL1$^+$ within the first 36 months. The anti-FHL1 "negative" group presented constant low antibody titers during the longitudinal follow-up.

Conclusion: Anti-FHL1 antibody positivity was detected in patients with high titers of anti-FHL1$^+$ autoantibodies in the first available serum sample or developed within the first 36 months after diagnosis and persisted over many years. A group of patients with intermediate levels had fluctuating positivity over the years. It is still unknown if the anti-FHL1 antibody titer is a marker of prognosis and/or damage in IIM; thus, clinical data needs to be addressed, and *in-vitro* experiments and biochemical characterization of this autoantibody are still required.

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SAT0659 APPLYING THE OMERACT TRUTH FILTER TO A NEW ELECTRONIC SPINAL MOBILITY INDEX FOR AXIAL SPONDYLOARTHRITIS BASED ON INERTIAL MEASUREMENT UNIT (IMU) SENSORS

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Background: Loss of spinal mobility is one of the most characteristic problems for people with axial spondyloarthritis (axSpA) and is predictive of loss of function. Traditional measures such as the BASMI fail to capture many elements of spinal mobility and lack responsiveness to change. Inertial Motion Unit (IMU) sensors can be used to accurately measure spinal movement without requiring significant operator expertise.

Objectives: The primary objective of this study was to test the reliability of these new tools in patients with axSpA and to develop a new composite spinal mobility index. Our secondary objective was to apply the OMERACT 'Truth' filter to evaluate the new index for bias, for clinical relevance, and for convergent validity with existing measures[1].

Methods: Patients with axSpA fulfilling ASAS classification criteria were recruited. ViMove system was used to obtain ROM by attaching two IMU sensors at the cervical (Occiput-T3) and lumbar spine (L1-Sacrum). Intra-rater, inter-rater and test-retest reliability of IMU tests were assessed by intraclass correlation coefficients (ICC). The maximum range of movement for anterior flexion/extension (AFE), lateral flexion (Left+Right) and rotation (Left+Right) were obtained for the lumbar and cervical region. These six values were used in a composite score (IMU-ASMI) which referenced equivalent ROM values from normal subjects in an earlier criterion validity study. Pearson correlation coefficients with BASFI were calculated for each component as well as the overall score.

Results: The study included 40 patients (12 females, 28 males) with a mean age of 48 (27-41). Subjects had a wide range of severity of axSpA. The mean BASMI was 4.8 (range 0.7 to 8.2, SD 1.9). The mean IMU-ASMI was 4.0 (range 0.1-9.2, SD 2.1). The sensor based measurements had good to excellent reliability (Table 1) and correlated closely with BASMI (r=0.79). The mean BASFI was 4.6 and the IMU-ASMI correlated closely with BASFI (r=0.71).

Face Validity: Each IMU test presents spinal movement in angles and can also be represented as a normalized severity index analogous to BASMI. The mean cervical and lumbar IMU-ASMIs were 3.5 and 4.4 units, respectively.

Construct Validity: Do IMU movements correlate with their corresponding traditional measurements? As expected, the closest correlations were between IMU and goniometer cervical rotation (r=0.85) and between IMU and tape measure lumbar side flexion (r=0.84). Correlations between Schober's test and IMU lumbar AFE and between tragus to wall and IMU cervical FE were moderate (r=0.62, 0.65).

Do IMU movements correlate with BASFI? Correlation coefficients were as follows: lumbar AFE -0.57; rotation -0.59; side flexion -0.45; cervical F/E -0.55; rotation -0.61; side flexion -0.39. BASFI correlations with BASMI were comparable.

Content Validity/Comprehensiveness: No major ceiling or floor bias issues were found in the composite indices. Intermalleolar distance (BASMI) represents hip rather than spinal mobility, but it correlates with BASFI and is not in the IMU-ASMI. IMU-ASMI includes lumbar rotation which accounts for 27% (0-53%) of the lumbar mobility score.

	Cervical			Lumbar			
Movement	AFE	Lat	Rot	AFE	Lat	Rot	IMU-ASMI
Intra-rater	0.95	0.87	0.97	0.89	0.84	0.76	0.96
Inter-rater	0.96	0.96	0.98	0.94	0.94	0.77	0.98
Test-retest	0.88	0.96	0.85	0.91	0.94	0.81	0.97

Table 1. Results of ICC for different IMU spinal mobility tests

Conclusion: IMU sensors can be used by non-experts to accurately and reliably measure spinal mobility in patients with axSpA. Lumbar rotation is an important new outcome measure.

REFERENCES

[1] Tugwell P, et al. J Rheum 2014 41(5):1000-1004

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SAT0660 PROPOSAL OF CORE OUTCOME DOMAINS IN MIXED CRYOGLOBULINEMIC VASCULITIS

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Background: Cryoglobulinaemic vasculitis is immune complex mediated vasculitis of medium and small-size vessels. This vasculitis involves mainly kidneys, peripheral nervous system, skin and joints. Currently, no standardized outcome measures are available for the evaluation of treatments in patients with cryoglobulinemic vasculitis.

Objectives: To identify a core set of outcome measure (what to measure) for clinical studies for mixed cryoglobulinemic syndrome, following the OMERACT filter 2.0. [Ref]

Methods: A search was made in Medline (via PubMed) and Embase using a standardized search [filter https://omeracthandbook.org/]. This review considered studies that included patients with Mixed (type 2 and 3) cryoglobulinemic syndrome, any type of outcome measures, articles in

the English language and considered only SLR, RCT, cohort, case control and case series (>5 patients). Data were screened independently by three reviewers, recorded on a prespecified extraction form and summarized qualitatively. Considering core areas and core domain set was drafted. The results were presented and voted by a Consensus Committee including physicians with expertise in rheumatic, kidney and infectious diseases. Specific domains were separately voted and scored from 1 (strongly disagree) to 5 (strongly agree). Agreement was calculated as the percentage of agree/strongly agree. Consensus was reached in case of >70% of agreement.

Results: In the review were included 88 studies of which 4 randomised clinical trial (3%, 144 patients), 3 systematic literature reviews (9%, 401 patients), 25 cohort studies (27%, 1284 patients), and 56 other observational studies (61%, 2871 patients). The most frequent domains were : bio-humoral activity markers (e.g. cryocrit, rheumatoid factor, complementemia), viral infection and liver function, reversible and non reversible manifestation of skin, peripheral nerve, kidney, joint. Only a few studies included as life impact area, survival and safety. No studies analyzed included economical impact. Drafted core domains within core areas and percent agreement from the Delphi survey are reported in Table I. Additional core domains included adverse events and viral infection, considered as contextual factor.

Conclusion: This is the first study aimed at identifying the core outcome measures in cryoglobulinemic vasculitis. Further studies will be needed to evaluate appropriate instruments to measure these outcome domains to be applied in clinical trials and practice.

Table I – Outcome Domains in Mixed Cryoglobulinemic Vasculitis

Core Areas	Domains	Subdomains	Total studies (N-%)	RCT (N)	Delphi Overall (% agreement)
Pathophysiological	Laboratory markers	Bio-humoral activity	72 (81%)	4	90
	Clinical manifestation	Skin involvement	43 (48%)	3	100
		Peripheral nerve involvement	42 (47%)	4	100
		Articular involvement	27 (30%)	1	100
	Organ function	Renal function	46 (52%)	2	100
Life impact	Quality of life		1 (1%)	0	100
	Physical Functioning		1 (1%)	0	97
	Pain		1 (1%)	0	100
Death	Survival		10 (11%)	0	100
Economical impact			0 (0%)	0	97

REFERENCES

[1] Boers M, Kirwan JR, Wells G, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. J Clin Epidemiol 2014;67:745–53. doi:10.1016/j.jclinepi.2013.11.013

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SAT0661 MXA IS A CLINICALLY APPLICABLE BIOMARKER FOR TYPE I INTERFERON ACTIVATION IN SYSTEMIC LUPUS ERYTHEMATOSUS AND SYSTEMIC SCLEROSIS

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Background: Activation of the type I interferon (IFN) system has been found in large subsets of patients with systemic autoimmune diseases. This is usually assessed with a laborious quantification of IFN-stimulated genes. An easier and cheap biomarker would facilitate implementation of type I IFN measurements in diagnostic laboratories. Previously, we described Myxovirus resistance protein 1 enzyme immunoassay (MxA-EIA) for systemic evaluation of type I IFN activity in primary Sjögren's syndrome [1].

Objectives: To assess the applicability of the MxA-EIA to detect systemic type I IFN activation in patients with systemic lupus erythematosus (SLE) and systemic sclerosis (SSc).

Methods: Whole blood intracellular MxA protein levels were measured in SLE (discovery cohort: n=25; replication cohort retrieved from the CHILL-NL study [2]: n=102), SSc (n=28) and healthy controls (HC) using the MxA-EIA. IFN scores were determined from whole blood gene expression of interferon-stimulated genes IFI44, IFI44L, IFIT1, IFIT3, and MxA by RT-PCR.

Results: MxA levels were significantly elevated in patients with SLE and SSc compared to HC and highly correlated to IFN scores (r_s=0.735 to r_s=0.854, p≤0.003). MxA-EIA robustly discriminated (AUC=0.938 to AUC=0.991, p≤0.007) between low and high type I IFN activity in SLE and SSc patients with a specificity of 100% and a sensitivity of 87.5 to 94.7%. Patients with autoantibodies against SM, RNP, SSA/Ro, or SSB/La antigens showed higher MxA levels and IFN scores compared to patients without these antibodies.

Conclusion: Intracellular MxA is an easy applicable and clinically relevant biomarker for systemic type I IFN bioactivity in SLE and SSc. MxA-EIA could be used to identify patients eligible for IFN-targeting treatments and potentially to monitor treatment responses.

REFERENCES

[1] Maria NI, Brkic Z, Waris M, van Helden-Meeuwsen CG, Heezen K, van de Merwe JP, van Daele PL, Dalm VA, Drexhage HA, Versnel MA. MxA as a clinically applicable biomarker for identifying systemic interferon type I in primary Sjogren's syndrome. Ann Rheum Dis 2014;73:1052-9.

[2] Groot N, Shaikhani D, Teng YKO, de Leeuw K, Bijl M, Dolhain R, Zirkzee E, Fritsch-Stork R, Bultink IEM, Kamphuis S. Long-term clinical outcomes in a cohort of adults with childhood-onset Systemic Lupus Erythematosus. *Arthritis Rheumatol* 2018; doi: 10.1002/art.40697.

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SAT0662 SERUM INFLAMMATORY ANGIOGENIC AND TISSUE REMODELING BIOMARKERS IN PERIPHERAL SPONDYLOARTHRITIS BEFORE AND AFTER IL-17A BLOCKADE

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Background: Spondyloarthritis (SpA) is characterized by extensive angiogenesis, tissue remodeling and inflammation of both the enthesis and the synovial tissue. Several studies have shown a relation between angiogenic/tissue remodeling serum markers and disease progression. Secukinumab, an anti-IL-17A inhibitor, is an effective treatment in SpA, but it's effects on serum markers of angiogenesis, tissue remodeling and inflammation are largely unknown.

Objectives: The purpose of this study was to analyze several candidate biomarkers of these processes in patients with SpA treated with anti-IL-17A.

Methods: Serum samples from 20 active peripheral SpA patients that were included in a 12 week open-label trial with secukinumab were analyzed for several markers with luminex technology. Study design and primary results were previously published (1).

Results: Serum levels of IL-6, MMP-3, osteopontin (all P < 0.001), Vascular Endothelial Growth Factor A (VEGF-A), tumour necrosis factor (TNF)-alpha, IL-31, IL-33, S100A8, S100A9 (all P < 0.05) decreased

significantly upon treatment with anti-IL-17A. These serum level changes correspond with the clinical responses and the published effects on inflamed target tissues of this cohort. Meanwhile, serum levels of DKK-1, ROBO4, sclerostin and CD40L remained unchanged.
Conclusion: These results indicate that anti-IL-17A not only diminishes inflammation, but also impacts on other processes such as angiogenesis and tissue remodeling. Whether these observations are predictive of disease progression or outcome remains to be determined.

REFERENCES

[1] van Mens, L. J. J. et al. IL-17 blockade with secukinumab in peripheral spondyloarthritis impacts synovial immunopathology without compromising systemic immune responses. *Arthritis Rheumatol.* (2018). doi:10.1002/art.40581

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SAT0663 ABILITY OF THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE TO IDENTIFY RHEUMATOID ARTHRITIS PATIENTS IN REMISSION AT RISK OF RELAPSE AFTER TNF-BLOCKER TAPERING. AN ANCILLARY STUDY OF THE STRASS TRIAL

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Background: Rheumatoid arthritis (RA) patients in sustained remission are candidates for tapering of disease modifying anti-rheumatic drugs (DMARDs). However, no predictors of relapse have been clearly identified so far. The STRASS trial included 137 RA patients in sustained DAS28 remission with TNF blockers (TNFb) who were randomized to 2 strategy arms: maintenance of TNFb at full dose or progressive DAS28-driven spacing of TNFb injections [1]. RA relapses were significantly more common with TNFb spacing in STRASS but no baseline characteristics predicted the risk of relapse in either strategy arm. The multi-biomarker disease activity (MBDA) blood test measures 12 serum protein biomarkers and uses a validated algorithm to produce a score for RA disease activity on a scale of 1-100. In some studies, the MBDA score was a significant predictor of flare following DMARD tapering in well controlled RA patients.
Objectives: To test the ability of the MBDA score to identify rheumatoid arthritis patients who will relapse following continuation or tapering of TNF blocker (TNFb) treatment in the STRASS study
Methods: MBDA scores were determined in a central laboratory (Crescendo Biosciences, San Francisco, USA) for available archived serum samples that had been obtained at baseline from patients in STRASS (N=133). The ability of the MBDA score to predict relapse (defined as DAS28 >2.6 and increased >0.6 from previous study visit) in each arm of the 18-month STRASS trial was assessed by: 1) comparing MDBA scores in relapsing vs. non-relapsing patients by Wilcoxon rank sum or Fisher's test, and 2) determining the ability of the MBDA score to discriminate relapse, based on receiver operating characteristic (ROC) analysis summarized by C-statistic (i.e., area under the ROC curve [AUC]), and its 95% confidence interval (CI). Analyses were performed for intention-to-treat (ITT) and completer populations
Results: At 18 months, 48% and 77% of the patients relapsed in the full dose maintenance and the spacing arms, respectively. In each study arm, mean MBDA scores and the percentages of patients with low, moderate or high MBDA scores at baseline were not significantly different in relapsing vs. non-relapsing patients (Table 1). The ROC analyses displayed no statistically significant discriminating ability for the MBDA score in terms of relapse prediction over the 18-month period of the trial in either arm of the ITT population (Figure 1). However, a significant ROC result was obtained in the maintenance group in the completer analysis (AUC 0.638 [95% CI: 0.502, 0.774], p=0.01).

Table 1. MBDA scores at baseline in the STRASS trial

	Randomization arm			
	Maintenance		Spacing	
MBDA				
Mean MBDA score (SD) [Median]	29.7 (11.4) [30]		26.8 (10.3) [27]	
MBDA score < 30, N (%)	29 (43.28%)		35 (57.4%)	
30 ≤ MBDA score ≤ 44	33 (49.25%)		25 (41.0%)	
MBDA score > 44	5 (7.46%)		1 (1.64%)	
NA	2		3	
Outcome at Month 18	**No relapse**	**Relapse**	**No relapse**	**Relapse**
N (%)	36 (52.2%)	33 (47.8%)	15 (23.4%)	49 (76.6%)
MBDA scores				
Mean MBDA score (SD)	27.28 (11.4)	32.5 (11.1)	26.2 (12.5)	27.0 (9.7)
MBDA score < 30, N (%)	18 (50%)	12 (35.5%)	9 (60%)	26 (56.5%)
30 ≤ MBDA score ≤ 44	15 (41.7%)	18 (58.1%)	5 (33.3%)	20 (43.5%)
MBDA score > 44	3 (8.3%)	2 (6.4%)	1 (6.7%)	0 (0%)
NA	0	2	0	3

*Each comparison between No relapse vs. Relapse groups was not statistically significant (p >0.05).

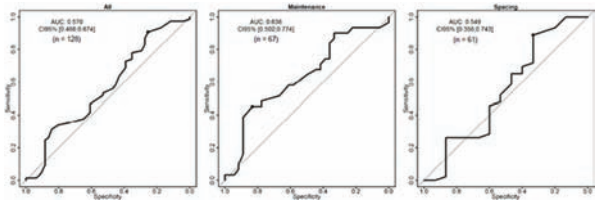


Figure 1. Discriminative ability of the MBDA test to identify RA patients at risk of relapse during the 18-month follow-up in the STRASS trial, based on ROC analyses of the ITT population.

Conclusion: The MBDA score did not display quantification of the risk of relapse in RA patients in remission, when assessed, in the context of the DAS28-driven TNFb tapering strategy in STRASS

REFERENCES

[1] Fautrel, et al. Ann Rheum Dis 2016;75(1):59-67

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SAT0664 RESPONSIVENESS OF PATIENT-REPORTED PHYSICAL FUNCTION OUTCOME MEASURES IN A REAL LIFE INTERNATIONAL COHORT OF 405 PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Physical function (PF) is a core domain to be measured in all trials for psoriatic arthritis (PsA); several instruments can be used but have not been compared.
Objectives: To evaluate the longitudinal construct validities of 3 physical function patient-reported outcome measures (PF-PROMs): HAQ-disability

index (HAQ-DI), physical functioning of SF12 (SF12-PF) and functional capacity of Psoriatic Arthritic Impact of Disease (PsAID-PF).

Methods: The Remission/Flare in PsA (ReFlap) study (NCT03119805), is a prospective longitudinal study in 14 countries of consecutive adults with definite PsA collecting validated PsA outcomes. We assessed longitudinal construct validity using correlation between change scores of PF-PROMs with other assessments, according to *a priori* hypotheses. Responsiveness was assessed using the change of PF-PROMs anchored with patient-defined improvement/worsening at follow-up. We calculated the relative effectiveness statistic (RE=Standardized response mean, SRM^2 ratios) for each PF-PROM comparing improved/worsened groups vs. no change at follow-up.

Results: Of 466 subjects recruited, 405 completed follow-up (50.8% male, mean(SD) age = 52.7 (12.6) years). After a mean (SD) follow-up of 4.3 (2.7) months, 27.6%, 55.0% and 17.4% reported improvement, no change and worsening. All change scores of the PF-PROMs met the *a priori* hypotheses (Table 1). PF-PROMs change scores were statistically different for improved and worse group from the no change group ($p<0.001$). All PF-PROMs were more sensitive to worsening than improvement (Table 2). PsAID-PF was more sensitive to change compared to the other two PF-PROMs.

Conclusion: Using data from this prospective longitudinal real-life study setting, HAQ-DI, SF12-PF and PsAID-PF fulfilled longitudinal construct validity for measurement of physical function in PsA. PsAID-PF had the highest responsiveness to change. These data will help to choose outcomes in PsA studies.

Abstract Table 1. Correlations of PF change with change in other outcomes, Spearman's rho correlation

	Δ HAQ-DI	Δ SF12-PF	Δ PsAID-PF
Δ HAQ-DI	-	-0.73 **	0.68 **
Δ SF12-PF	-0.73 **	-	-0.64 **
Δ PsAID-PF	0.68 **	-0.64 **	-
Δ Patient joint GA	0.56 **	-0.51 **	0.74 **
Δ Pain	0.56 **	-0.50 **	0.75 **
Δ Patient skin GA	0.28 **	-0.24 **	0.42 **
Δ Physician GA	0.44 **	-0.39 **	0.56 **
Δ Tender joint count	0.40 **	-0.37 **	0.47 **
Δ Swollen joint count	0.32 **	-0.26 **	0.33 **
Δ DAPSA	0.58 **	-0.49 **	0.69 **
Δ PsAID12 total	0.67 **	-0.64 **	0.90 **

**p<0.001; Δ: change scores; GA: global assessments

Abstract Table 2. Responsiveness of PF-PROMs in PsA

		Sample size	Change score (SD)	SRM (95% CI)	SRM^2 ratio¶
HAQ-DI (0-3)	Improved	111	-0.20 (0.85)	-0.23 (-0.43, 0.03)	3.56
	No change	221	-0.10 (0.79)	-0.12 (-0.25, 0.01)	-
	Worse	70	0.28 (0.79) **	0.36 (0.12, 0.62)	8.70
SF12-PF (0-100)	Improved	105	4.76 (45.61)	0.10 (-0.09, 0.31)	3.10
	No change	206	2.43 (40.95)	0.06 (-0.07, 0.20)	-
	Worse	68	-12.13 (42.65) **	-0.28 (-0.53, -0.03)	23.04
PsAID-PF (0-10)	Improved	111	-0.88 (4.12)	-0.21 (-0.40, -0.02)	6.39
	No change	220	-0.33 (3.91)	-0.08 (-0.23, 0.04)	-
	Worse	69	1.65 (3.94) **	0.42 (0.16, 0.69)	24.45

δ determined by the best cut-off point using ROC curve; ¶ comparing to the no change group; **p<0.001 by Kruskal-Wallis test; SD = standard deviation; SRM = standardized response means.

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SAT0665 PLASMA HSPRO-C2 LEVELS PREDICT RADIOGRAPHIC PROGRESSION IN SYMPTOMATIC KNEE OSTEOARTHRITIS PATIENTS

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Background: There is a lack of objective diagnostic modalities that identify patients at risk for severe osteoarthritis (OA), which complicates the development of disease-modifying OA drugs. The biochemical marker, high-sensitive PRO-C2 (hsPRO-C2)[1], is a measure of the propeptide of type IIB collagen and a blood measure of cartilage formation.

Objectives: The aim of this study was to determine whether hsPRO-C2 could predict radiographic progression in a knee OA population and stratify patients into high and low risk for joint destruction.

Methods: Subjects with varying degrees of symptomatic knee OA (n=106) were included from a New York University (NYU) progression cohort. Radiographic progression was assessed by medial joint space narrowing (JSN), based on the change in joint space width (JSW), of the signal knee at baseline and at 24months. Baseline plasma type II collagen formation biomarker (hsPRO-C2) levels were measured. Association between

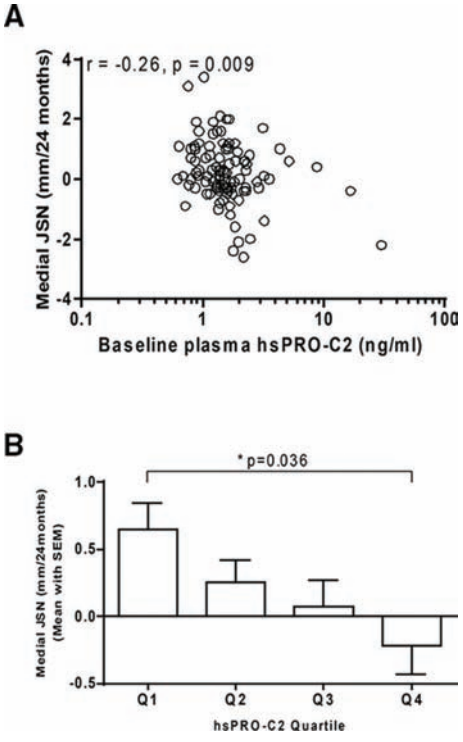


Figure 1. Association of baseline plasma propeptide of type IIB collagen (hsPRO-C2) levels with medial joint space narrowing (JSN) at 24 months from baseline shown as Pearson's correlation (A) and quartile groups (B). The values of quartiles were compared with one-way

baseline hsPRO-C2 and JSN was analyzed by Pearson's correlation, corrected for age, sex, BMI, race, baseline JSW, and non-steroids anti-inflammatory drugs (NSAID) use. Subjects were divided into quartiles of equal size depending on the hsPRO-C2 levels, and the difference in JSN was investigated. The median level of baseline hsPRO-C2 (1.48 ng/ml) was used as a cut-off for stratifying all the subjects. The difference in JSN over 24 months was investigated in patients dichotomized based on median level. The values were compared with two-way analysis of covariates (ANCOVA).

Results: Baseline plasma hsPRO-C2 levels were negatively correlated with the progression of radiographic joint space narrowing over 24 months ($r = -0.26$, $p = 0.009$) after adjustment for confounders (Figure 1A). Quartile analysis demonstrated a decreasing trend of hsPRO-C2 in the radiographic progression from quartile 1 to 4 (Figure 1B). One-way ANOVA revealed a significant difference in mean JSN between quartiles 1 and 4 (0.5073 mm versus -0.0691 mm, $p = 0.036$, Figure 1B). JSN was significantly larger in the low hsPRO-C2 patients (0.3710 mm) compared to the high hsPRO-C2 patients (0.0195 mm) (Figure 2).

Conclusion: These data suggest that symptomatic knee OA subjects with lower levels of hsPRO-C2 at baseline presented more radiographic medial JSN progression as compared to the subjects with higher levels of hsPRO-C2. The biomarker hsPRO-C2 may be useful for predicting OA progression.

REFERENCES

[1] Luo Y, He Y, Reker D, Gudmann NS, Henriksen K. A Novel High Sensitivity Type II Collagen Blood-Based Biomarker, PRO-C2, for Assessment of Cartilage Formation. Int J Mol Sci. 2018;19(11):3485. doi:10.3390/ijms19113485

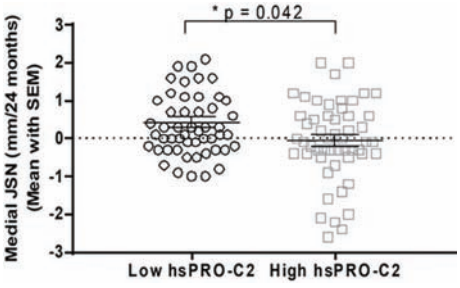


Figure 2. Medial joint space narrowing (JSN) on the signal knee over 24 months. The values were compared with two-way analysis of covariates (ANCOVA). Data were adjusted for BMI, sex, age, race, baseline medial JSW and NSAID user. Asterisks indicate the following: *$p < 0.05$. All values were presented as means and standard error of the mean (SEMs).

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SAT0666 ASSESSMENT OF INFLAMMATORY AND IMMUNE PATHWAYS IN RHEUMATOID ARTHRITIS PATIENTS USING BIOPRED KIT TO IDENTIFY CANDIDATE BIOMARKERS

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Background: Rheumatoid Arthritis **(**RA) is a chronic, progressive, inflammatory autoimmune disease associated with articular, extra-articular and systemic effects leading to joint destruction. T cells, B cells and the orchestrated interaction of pro-inflammatory cytokines play key roles in the pathophysiology of RA. Better comprehension of interaction between cytokines and their signaling pathways are key for the development of new strategies with small molecules or biologicals. Today, new technologies allow the specific investigation of inflammatory pathways at mRNA level without extraction step directly from the blood. The BIOPRED panel, Disease activity specific gene enrichment studies in RA & other autoimmune-inflammatory disorders would help pharmaceutical industry tailor target specific therapies and would help clinicians choose optimal & personalized therapy for their patients. Therefore, we have identified active biological pathways in RA patients associated with different disease activity status.

Objectives: By using Firalis' BIOPRED assay, a targeted gene sequencing panel including 2155 mRNAs from inflammatory and immune pathways, we aimed to identify active biological pathways in function to different disease activity status of RA and Healthy volunteer (HV) subjects.

Methods: Paxgene samples of active RA patients with DAS28>3.2 (n=178) and HV (n=25) are directly profiled without RNA extraction with BIOPRED assay and 2155 mRNA were quantified on HTG EdgeSeq platform, a combination of a nuclease protection assay & next generation sequencing (NGS). Subjects are categorized into three groups; High disease activity (HDA) group with DAS28 >5.1, Moderate disease activity (MDA) group with DAS28 between 3.2 and 5.1, and Healthy volunteer (HEV) group.

Results: After transformation and normalization of the gene expression data, 22 mRNA genes are found to be significantly upregulated in RA (p-value < 0.005, fold change > 2) as compared to HV group. After ANOVA analysis on three groups as stated above, 351 mRNA targets are significantly regulated (p-value <0.05). Pathway analysis based on protein-protein interaction from Biogrid, String and Intact database was used and score were generated based on fold change for 22 pathways to assess modification in HDA and MDA groups versus HV group. Various pathways including Jak/STAT pathway were shown to be significantly upregulated.

Conclusion: Our results identify a list of mRNAs relevant to RA pathology and pathways that have the potential to be candidate biomarkers for disease activity, disease severity or as therapeutic targets. Moreover, BIOPRED panel accurately measures 2155 mRNA (Coefficient of Variation is less than 20% for more than 1100 mRNAs) from inflammatory and immune pathways and can be further used to study pathway analysis in autoimmune-inflammatory disorders such as RA.

Disclosure of Interests: None declared

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SAT0667 TREATMENT RESPONSE CRITERIA FOR ANCA-ASSOCIATED VASCULITIS: RESULTS OF A SCOPING REVIEW

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Background: A comprehensive assessment of outcome measures to assess response to treatment in ANCA-associated vasculitis (AAV) is necessary to implement.

Objectives: To perform a review of outcome measures to assess response to treatment in AAV which will help advance methodology for clinical trials in this disease.
Methods: As part of an ongoing international project to develop response criteria, we performed a scoping review to assess the tools used as outcome measures in randomized clinical trials (RCTs) of AAV. Medline, Cochrane Central, and ClinicalTrials.gov were searched from inception until November 2018 to identify RCTs enrolling patients with granulomatosis with polyangiitis and/or microscopic polyangiitis.
Results: Among the 24 RCTs included in the review (Figure 1), various versions of the Birmingham Vasculitis Activity Score (BVAS) were the most widely used instruments for disease assessment. BVAS was almost always reduced to a dichotomous variable (0 or > 0) providing distinction between remission and active disease. Reduction in BVAS and/or achievement of BVAS=0 represented a main study outcome (primary or secondary endpoint) in 20/24 (83%) RCTs; 6 of these trials used the BVAS/WG. Damage, mainly assessed by the Vasculitis Damage Index (VDI), was an outcome for 14/24 (58%) RCTs. Physician global assessment and patient-reported outcomes (PROs) [measures of health-related quality of life (HRQoL) and/or patient global assessment] were assessed in 7 (29%) and 14 (58%) RCTs, respectively. Assessment of renal function or activity was a major outcome or specifically included in definitions of remission/relapse in 23/24 (96%) RCTs. Timing for outcome measure assessment differed substantially, with baseline, 6 months (15/20 RCTs), and 12 months (14/20) after enrollment being the most common time points for reporting BVAS and VDI. Assessment of disease state occurred as early as 1-4 weeks after enrollment.
Conclusion: Outcome measures used in RCTs of AAV include the repeated use of vasculitis specific tools to assess disease state, but with heterogeneity in the definitions for remission/relapse and timing of assessment. Intermediate states of disease activity are currently poorly defined or evaluated. Furthermore, other important outcomes in AAV, including PROs, damage measures, and global assessments are often not included as primary or confirmatory secondary outcomes in RCTs in AAV. This review highlights the need for more homogeneous outcome assessment in RCTs for AAV and the current lack of a composite measure that integrates various endpoints relevant to physicians and patients.

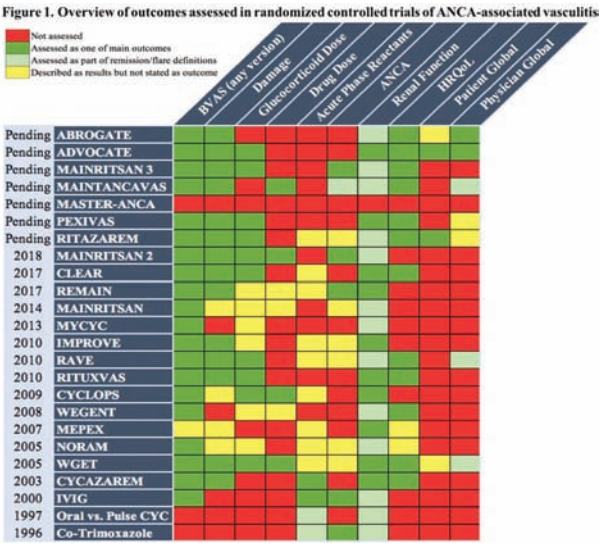


Figure 1. Overview of outcomes assessed in randomized controlled trials of ANCA-associated vasculitis

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SAT0668

"WHEN YOU READ THIS, YOU REALLY FEEL OLD!" PERSPECTIVES OF YOUNG PEOPLE WITH INFLAMMATORY ARTHRITIS ON PATIENT REPORTED OUTCOME MEASURES FROM A EUROPEAN QUALITATIVE STUDY

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Background: Although patient-reported outcome measures (PROMs) are extensively used in clinical practice and research, it is unclear whether the most commonly used instruments adequately cover the perspective of young people with chronic inflammatory arthritis.
Objectives: To investigate whether the aspects important to young people with inflammatory arthritis are sufficiently covered by the PROMs that are widely used in clinical practice and research.
Methods: A qualitative, multicentre focus group interview study was conducted in Austria, Croatia, Italy and the Netherlands in order to inform a EULAR-funded taskforce. Three groups of young people (aged 18-35 years) with either (1) rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA) and Still's disease, (2) psoriatic arthritis (PsA), or (3) axial spondyloarthritis (SpA) were interviewed at each centre. The interview guide was based on the WHO International Classification of Functioning, Disability and Health (ICF) to comprehensively cover all aspects of functioning in daily life. It also included questions on the perspectives and views of the participants on selected PROMs (Pain scales, Patient Global Assessment [PGA], FACIT Fatigue Scale, The Health Assessment Questionnaire [HAQ]/Bath Ankylosing Spondylitis Functional Index [BASFI], and The 36-Item Short Form Health Survey [SF-36]). All interviews were conducted by trained local investigators, audio-recorded, transcribed verbatim, and analysed using a modified form of 'meaning condensation'. During a face-to-face meeting of the task-force members, the concepts were reformulated and organized into a scheme of higher and lower-level concepts.
Results: Thematic saturation was reached after 12 focus groups with 53 participants (21 with RA/JIA/Still's, 15 with SpA, 17 with PsA; 72% female, mean age 28, SD±5), resulting in 18 hours and 22 minutes of recorded time and 269 pages of transcript. The analysis revealed aspects of functioning in daily life important to young people with inflammatory arthritis which were mentioned in all countries. Furthermore, 55 concepts emerged with regard to PROMs and were summarized into seven higher-level concepts. The table depicts these higher-level concepts including quotes from the interviews.
Conclusion: The evaluation of young patients' perspectives should probably reach beyond the topics/aspects covered in the most commonly used PROMs. Accordingly, tailoring the assessments to specific needs of young people should be considered.
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SAT0669

DISCRIMINANT ABILITY OF THE PARENT VERSION OF THE JUVENILE ARTHRITIS DISEASE ACTIVITY SCORE IN A LARGE MULTINATION COHORT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: The assessment of disease activity plays a pivotal role in the management of children with juvenile idiopathic arthritis (JIA). Most recent recommendations require that parents' and children's perception is incorporated in the evaluation of the disease course and of effectiveness of therapeutic interventions. A new disease activity tool, named parent Juvenile Arthritis Disease Activity Score (parJADAS) and based only on parent-centered outcome measures, is currently under development (1).

Objectives: To demonstrate, in a large multinational dataset of JIA patients, the discriminant ability of the parJADAS.

Methods: The parJADAS includes 4 measures: 1) parent assessment of disease activity; 2) assessment of pain intensity; 3) proxy assessment of joint disease; 4) assessment of morning stiffness (MS). Disease activity and pain are assessed on a 21-numbered circle VAS (0 = best and 10 = worst). The active joint count is based on the count of any swollen or painful joint, irrespective of its type, up to a maximum of 10 joints. MS duration is assessed on a Likert scale, ranging from no MS (0 points) to > 2 hours of MS (10 points). Validation was conducted on a dataset of 8,656 children with JIA from 49 countries, enrolled in the study of Epidemiology, treatment and Outcome of Childhood Arthritis (2), who had all the variables included in the parJADAS available. Discriminant ability was evaluated by comparing parJADAS levels (median, [IQR]) among patients with inactive disease (ID), low disease activity (LDA), moderate disease activity (MDA), and high disease activity (HDA) according to the cJADAS10; patients in remission, continued activity, or flare according to the attending physician; patients whose parents were satisfied or not with current disease state. To assess the possible influence of the articular and extra-articular damage on the parJADAS, the levels of the score in patients with or without damage (Juvenile Arthritis Damage Index > 0) were compared. For this analysis, only subjects in inactive disease and with at least 2 years of disease course were considered (n = 2,423).

Results: The levels of parJADAS in patients in ID, LDA, MDA, and HDA were 0.0 [0.0, 1.0], 3.0 [1.0, 6.0], 6.0 [2.0, 11.5], an 14.5 [8.5, 21.0], respectively (Kruskal-Wallis test, p < 0.001). The levels of par JADAS in patients in remission, continued activity, or flare according to the attending physician were 0.5 [0.0, 3.5], 9.0 [3.5, 17.0], 12.0 [5.5, 20.0], respectively (Kruskal-Wallis test, p < 0.001). Median parJADAS in patients whose parents were satisfied or not satisfied with disease course is 1.5 [0.0, 7.0] and 13.0 [6.6, 20.5], respectively (Mann-Whitney test p < 0.001). ParJADAS was not different in JIA patients in remission with or without damage measured with the JADI (Mann-Whitney test p = 0.08)

Conclusion: The parJADAS showed excellent discriminate ability in a large multinational cohort. The score did not show to be relevantly influenced by disease damage in JIA patients in remission.

Table. Overview of higher-level concepts and related quotes

Higher-level concepts	Quotes
Relevant issues for young people are not covered by widely used PROMs	*My appearance has never been brought up for discussion, but it impacts my teaching, my sex life, [...].* (male, 30, PsA)
Information, transparency and clarity regarding the purpose of PROMs are often missing	*Honestly, I have often thought that we should fill all those questionnaires to keep us quiet and to avoid that we will freak out!* (female, 27, PsA) *I do not understand the meaning. Why does the doctor care if I can wash my hair? Who will wash it instead? It is a stupid question!* (female, 27, PsA)
The individual life situation of a patient adds essential importance to the results of PROMs	*In my opinion it is problematic to estimate disease activity for today. With my medication, or without? At the moment, I am feeling fine, but it won't be like that without any medication, I guess. And that makes scoring a bit difficult.* (female, 27, PsA)
The scoring on a rating scale sometimes differs from the current health situation	*I am just putting my line anywhere and think – that's fine. (female, 27, PsA)* *I always score very low, like a 1, 2, or 3. which might look very harmless to the doctor. I often ask myself whether I should score worse, to get recognized.* (male, 30, PsA)
Certain PROMs were seen as outdated	*When you read this, you really feel old! (female, 21, RA)* *I think 'working on your computer' or 'typing' or something could be included. I mean how often do we still use a pen and pencil all day long? It should be a little more up to date.* (female, 25, PsA)
PROMs focusing on symptoms and physical function only, do not comprehensively cover patients' experiences	*I think it is also important what you [as an individual] need. Not only the physical part, but also the mental part, so how are you feeling. I think that is important too.* (male, 22, SpA)
The use of new technologies for data acquisition was suggested by some young patients	*Sometimes I do not want to answer with a whole story. [...] but I can also do that questionnaire [HAQ] digitally at my hospital. That is nice!* (female, 25, PsA)

REFERENCES

[1] Consolaro A, et al. "Development and Initial Validation of the Parent and Child Versions of the Juvenile Arthritis Disease Activity Score". Arthritis Rheumatol. 2016; 68 (suppl 10).

[2] Consolaro A, et al. "Phenotypic variability and disparities in treatment and outcomes of childhood arthritis throughout the world: results from an observational cohort study". The Lancet Child and Adolescent Health, In press.

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SAT0670

REDUCING THE IMPACT OF THE PATIENT GLOBAL ON BOOLEAN REMISSION CRITERIA FOR RHEUMATOID ARTHRITIS

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Background: The patient global assessment (PtGA) is a core set variable to assess disease activity in rheumatoid arthritis (RA). It is strongly linked to patient-reported pain and has shown to be a limiting factor for reaching remission in patients with remittent joint inflammation and normal acute phase response, particularly when the ACR/EULAR Boolean criteria are used. In these, the PtGA may not be greater than 10 on a 0-100 scale to reach remission.

Objectives: To analyse the impact of higher cut-offs for or removal of the PtGA applied in the ACR/EULAR Boolean remission on the consistency with the SDAI remission definition, and with respect to long-term structural and functional outcomes.

Methods: We retrieved data from six clinical trials testing the efficacy of tumor-necrosis factor inhibitors vs MTX or placebo/MTX. Three trials depicted early RA: ASPIRE (infliximab), Go Before (golimumab), PREMIER (adalimumab); and three late RA: ATTRACT (infliximab), DE019 (adalimumab) and Go Forward (golimumab). We increased the cut-off of the PtGA gradually by 5mm (mBoolean15-REM) up to 30mm, and also omitted the criterion completely (Boolean-NO REM, i.e. requiring only CRP, SJC, TJC≤1). We assessed frequencies of remission by these definitions at 6 and 12 months and evaluated agreement with the Index based (SDAI) definition of remission (which does not include an inherent cut-off for PtGA). Further the impact on functional and structural outcomes after 1 year were explored based on achievement of each of these remission definitions at 6 months.

Results: We included 3293 patients in our study, 2121 in early and 1172 in late RA (mean disease duration: 1.5±3.0 and 9.8±8.6 years, respectively). The rates of patients achieving Boolean remission increased with higher allowance for PtGA from 11.9% to 18.8% in early RA, and from 5.9% to 12.4% in late RA at 6 month, and from 19.7% to 29.9% and from 10.7% to 20.9%, respectively, at 1 year. Best agreement with SDAI occurred at a PtGA cut-off of 15mm and 20mm, while with higher allowances for PtGA the disconnect between Boolean and Index based remission increased again (**Figure**). Radiographic progression was very similar in the different Boolean groups (ranging from a mean of 0.27±4.7 to 0.41±5.1). As expected, removing the PtGA increased functional impairment in remission (% of patients scoring HAQ=0 in Boolean 10, 15, 20, 25, 30, and in the "no PtGA" definition were 68.2%, 63.7%, 60.4%, 56.0%, 54.6% and 47.9%, respectively. Functional scores in late RA were generally worse than in early RA. CRP levels across all definitions, including "no PtGA", were similar (data not shown).

Conclusion: Increasing the PtGA cut-off to 15mm would provide highest consistency between Boolean with the Index based remission, while the integer cut-off of 20mm (or 2/10) would also allow the use on numerical rating scales. This new cut-off would discount the overly stringency of the PtGA in the remission context, while keeping the patient perspective in the core of RA disease activity evaluation.

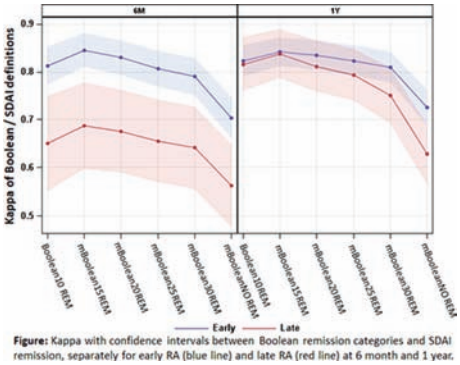


Figure: Kappa with confidence intervals between Boolean remission categories and SDAI remission, separately for early RA (blue line) and late RA (red line) at 6 month and 1 year.

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SAT0671

SEROCONVERSION OF AUTOANTIBODIES TO UH-RA.21 PEPTIDE IS ASSOCIATED WITH CDAI REMISSION IN RHEUMATOID ARTHRITIS PATIENTS OF THE CARERA COHORT

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Background: Autoantibodies are present in the majority of rheumatoid arthritis (RA) patients and are used clinically as diagnostic serum biomarkers. Insight in their role in prediction of therapy response and disease progression would provide a useful tool for patient stratification and personalized selection of a suitable treatment. In a previous pilot experiment, autoantibody levels to the University of Hasselt (UH) peptide UH-RA.21 have been correlated with response to DMARD treatment. In patients continuing the same DMARD during a 17 month follow-up period, which was taken as a proxy for treatment success, persistently positive anti-RA.21 antibody levels showed an overall decrease in titers (p=0.0334).

Objectives: Our aim is to determine the association between autoantibodies to the UH-RA.21 peptide and disease remission in early RA patients from the CareRA cohort.

Methods: In the CareRA trial, different COBRA treatment regimens consisting of synthetic DMARDs combined with a step-down glucocorticoid treatment, have been studied. Disease remission was defined as a DAS28CRP<2.6, CDAI<2.8 or SDAI<3.3. Custom peptide enzyme-linked immunosorbent assays were used to screen for the presence of antibodies to the UH-RA.21 peptide in serum samples of the CareRA cohort. Cut-off for seropositivity was defined by 2 x SD above the mean antibody level of the healthy control group. Antibody reactivity to UH-RA.21 was evaluated in baseline samples, collected before the start of treatment, of 223 early RA patients from the CareRA cohort. In patients that were positive for anti-UH-RA.21 antibodies at baseline, follow-up samples collected 16, 40, 52 and 104 weeks after the initiation of treatment were tested.

Results: Antibodies to UH-RA.21 were found in 21% (47/223) of the baseline samples from the CareRA cohort. Compared to baseline levels, combination therapy induced a 50% reduction of anti-UH-RA.21 antibody levels in 30% of patients after 16 weeks and in 47% of patients after 52 weeks. Seroconversion was observed in 16% (7/44) of patients after 16 weeks and 30% (10/34) after 52 weeks. Seroconversion was not correlated with remission according to the DAS28CRP or SDAI remission indices. However, of those patients which were UH-RA.21 positive at baseline, more seroconversion occurred in patients reaching remission (5/14, 36%) than in patients remaining in active disease (2/30, 7%), according to CDAI remission criteria (p=0.025).

Conclusion: A COBRA therapy induces a rapid decrease in anti-UH-RA.21 autoantibody levels in many patients. Moreover, early anti-UH-RA.21 seroconversion is associated with CDAI remission.

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SAT0672 THE DIAGNOSTIC VALUE OF SERUM KL-6 IN CONNECTIVE TISSUE DISEASE ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: The connective tissue diseases (CTDs) are a group of inflammatory, immune-mediated disorders. Involvement of the respiratory system, particularly interstitial lung disease (ILD), is common and is an important contributor to morbidity and mortality.Currently, high-resolution computed tomography (HRCT), bronchoscopic examination and surgical lung biopsy (SLB) are the basic methods for the diagnosis of ILD,But these tests require specific inspection machines,are less repeatable and cause considerable discomfort to the subject.

Objectives: To evaluate the diagnosis of the serum Krebs von den Lungen-6 (KL-6 for the interstitial lung disease(ILD) associated with connective tissue diseases(CTD).

Methods: Patients with CTDs who visited our Hospital between January, 2016 and December, 2017, and whose serum KL-6 level was measured were included. We analyzed 175 patients with CTDs,84 CTDs associated ILD,91 CTDs patients without ILD. Record age,gender,diagnosis,serum KL-6 levels,pulmonary function tests and performed in parallel were reviewed. Statistical analysis was performed using SPSS (version20.0) statistical package

Results: The significantly higher levels of KL-6 were determined in the CTD-ILD group than in the CTDs without pulmonary involvement group (P<0.05 (figure 1 .By the ROC curves of serum KL-6 levels in 175 patients. The optimal cutoff value of serum KL-6 for a diagnosis of CTD-ILD was 409U/ml, and the sensitivity and specificity were82.1% and 86.8%, respectively. The AUC was 0.905(figure 2).Serum KL-6 correlated negatively with vital capacity(VC) (%predicted),forced vital capacity(FVC%) (%predicted),forced expiratory volume in one second(FEV1%)(%predicted) and diffusing capacity of the lung for carbon monoxide (DLcoSB) (% predicted) (Table 1).

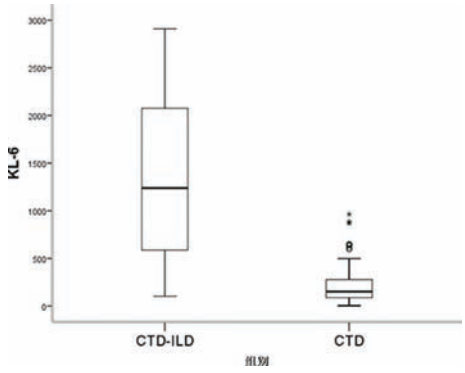


Fig1: Comparison of serum KL-6 concentrations in CTD-ILD group and CTD-ILD group.

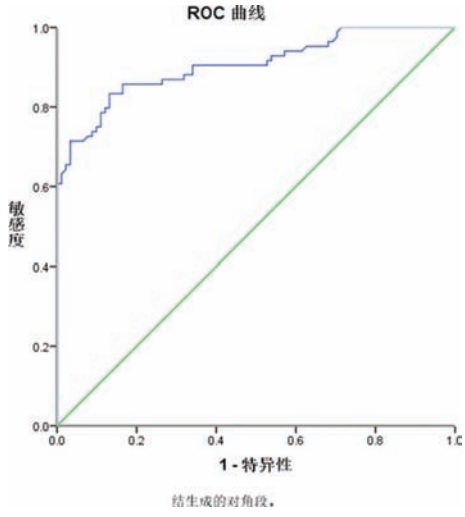


Fig.2 Receiver-operating characteristic curve(ROC) of KL-6 for the diagnosis of CTD-ILD

Table 1 Correlation. between KL-6 level and pulmonary function

	KL-6	
	r	*P*
VC%	-0.196	0.009
FVC%	-0.158	0.037
FEV1%	-0.173	0.022
FEF25%	-0.090	0.237
FEF50%	-0.058	0.447
FEF75%	-0.044	0.560
MMEF%	-0.075	0.323
DLcoSB %	-0.470	0.000

Conclusion: The serum KL-6 is a valuable biomarker for CTD-ILD diagnosis , and it is an important serum marker for detection of CTD-ILD activity.

REFERENCES

[1] Capobianco,J, et al. Thoracic manifestations of collagen vascular diseases. Radio -graphics 32.1(2012):33-50.
[2] Woodhead F, Wells A U, Desai S R. Pulmonary Complications of Connective Tissue Diseases[J]. Clinics in Chest Medicine, 2008, 29(29):149–164.
[3] Kohno N, Kyoizumi S, Awaya Y, et al. New serum indicator of interstitial pneum -onitis activity. Sialylated carbohydrate antigen KL-6. Chest 1989; 96:68–73.
[4] Ogz E O, Kucuksahin O, Turgay M, et al. Association of serum KL-6 levels with interstitial lung disease in patients with connective tissue disease: a cross-sectional study. Clinical Rheumatology, 2016, 35(3):663-666.

Disclosure of Interests: None declared

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SAT0673 ANTI-C1Q ANTIBODIES HAVE HIGHER CORRELATION WITH LUPUS NEPHRITIS DISEASE ACTIVITY

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Background: Systemic lupus erythematosus (SLE) is the prototype of autoimmune disease and is characterized by the production of a variety of autoantibodies. and lupus nephritis continues to be a principal cause of morbidity and mortality.The focus is to finding biomarkers that can monitor renal activity and predict prognosis for early diagnosis and treatment. Complement C1q is the starter molecule of the classical pathway

of complement activation and plays an important role in the clearance of immune complexes and apoptotic cell debris. Hereditary homozygous deficiency of C1q has been described to be the strongest risk factor for developing SLE.There are some cross-sectional studies on anti-C1q in which the antibody was found to have a significant association with renal involvement but the association of anti-C1q antibodies (antiC1q) with lupus nephritis (LN) still a matter of debate.

Objectives: We assessed the association between lupus nephritis disease activity and anti-C1q antibodies

Methods: We retrospectively analyzed the medical records of 88 patients with lupus nephritis, aged 35.7±10.8 years on the average, with SLE of average duration 12 (3, 57 years.In all examines the levels of anti-dsDNA and anti-C1q antibodies were measured using the ELISA, C3, C4, 24-hour urinary protein performed in parallel were reviewed. The Clinical manifestations of SLE was also collected.Lupus nephritis disease activity was measured by The SLICC Renal Activity Score of 2004,All biopsied tissues were scored based on the to ISN/RPS2003 lupus nephritis pathological typing standards,Acute Index,Chronic Index Score were used to evaluated the activities of lupus, All the analyses were performed by SPSS 20.0 software.

Results: Patients with active lupus nephritis had a higher levels of anti-C1q antibodies than inactive lupus nephritis (68.9(34.1, 140.1 vs. 11.6(5.5, 44.1 ; p<0.001)(Figure 1). Anti-C1q antibody levels were positively correlated with levels of 24-hour urinary protein(r=0.605; *P=0.000* ,AI score *(*r=0.337; *P=0.001),*and negatively correlated with serum C3(r=-0.573; *P=0.000* and C4 (r=-0.509; *P=0.000* .(Figure2).

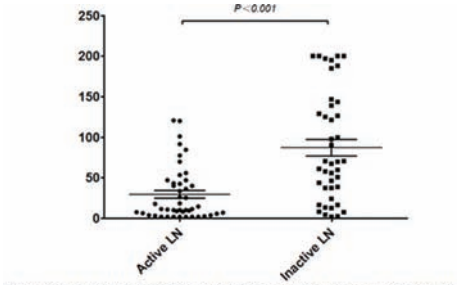


Figure 1:Comparison of serum Anti-C1q concentrations in activity LN group and Inactivity LN

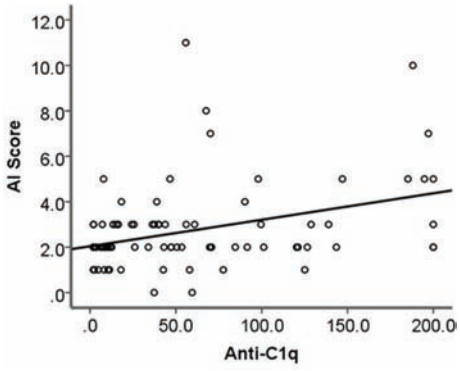


Figure 2 A: Anti-C1q antibody levels were positively correlated with AI score

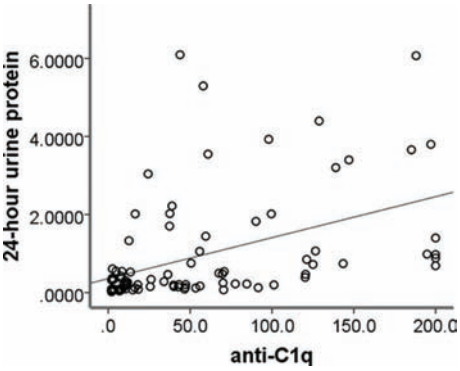


Figure 2 B: Anti-C1q antibody levels were positively correlated with levels of 24-hour urinary protein

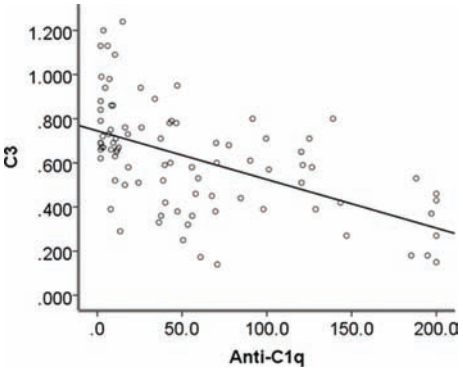


Figure2-C:Anti-C1q antibody levels were positively correlated with C3

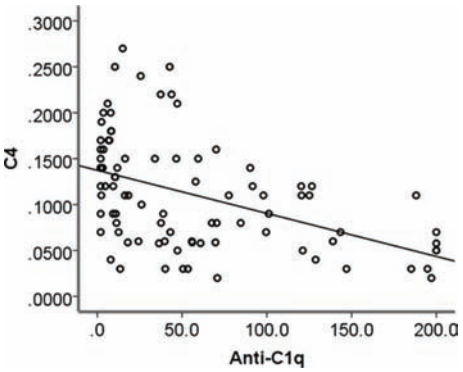


Figure2-D:Anti-C1q antibody levels were positively correlated with C4

Conclusion: Anti-C1q antibodies are more closely correlated with renal disease activity.

REFERENCES

[1] Clarke AE, Panopalis P, Petri M, Manzi S, Isenberg DA, Gordon C, et al. SLE patients with renal damage incur higher health care costs[J]. Rheumatology (Oxford, England). 2008;47(3):329-33.

[2] Walport MJ. Complement. First of two parts[J]. N Engl J Med. 2001;344 (14):1058.

[3] Walport MJ. Complement. Second of two parts[J]. N Engl J Med. 2001;344 (15):1140.

[4] Truedsson L, Bengtsson AA, Sturfelt G. Complement deficiencies and systemic lupus erythematosus[J]. Autoimmunity. 2007;40(8):560-6.

[5] Akhter E,., Burlingame RW, Seaman AL, Magder L,., Petri M,. Anti-C1q antibodies have higher correlation with flares of lupus nephritis than other serum markers[J]. Lupus. 2011;20(12):1267-74.

Disclosure of Interests: None declared

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SAT0674 **ADIPOKINES AND ENDOTHELIAL DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: Premature atherosclerosis is clearly described in systemic lupus erythematosus as a main cause of poor outcomes and mortality(1). Pleiotropic adipokines including adiponectin and visfatin are implicated in the inflammatory process of lupus disease that promote cytokines signaling leading accelerated endothelial disruption(2)

Objectives: To evaluate the endothelial dysfunction by measuring serum visfatin,adiponectin,leptin and HOMA-insulin Index as reliable biomarkers of atherosclerosis &estimating the FMD of brachial artery among lupus patients and correlating these parameters with clinical characteristics

Methods: A case-control study in which 150 systemic lupus patients who were fulfilling American College of Rheumatology revised classification were recruited consecutively from Internal Medicine department at Cairo University.They were compared to 90 age & sex matched healthy controls. Patients who were pregnant,smoker,diabetic,those with hepatic and

renal dysfunction, hypothyroidism,and familial dyslipidemia were excluded. Adiponectin,leptin,visfatin and HOMAIR were evaluated.Flow mediated dilatation of brachial artery was calculated as the maximum percent increase in artery diameter after cuff release compared to baseline

Results: Data revealed elevated levels of adiponectin,leptin,visfatin and HOMAIR in lupus cases compared to controls with reduced FMD percent. Clinical and laboratory background are summarized in table(1)

Table(1)

variables	Cases N=150	Controls N=90	p-value
Age(yr)	25.15±5.78	24.84 ±5.84	0.256
Female(N,%)	125	65(73%)	0.34
Male(N,%)	(84.66%) 25(16.44%)	25(27%)	
Disease duration in months	10±6		
BMI(Kg/m2)	25.56±3.66	22.74 ±2.13	<0.001
Clinical characteristic(N,%)	60(40%)		
- Mucocutaneous	123(82%)		
- Arthritis/arthralgia	100(75%)		
- Renal disease	12(8%)		
- Central nervous disease	68 (41.5%)		
- Cardiovascular disease	49(32.66%)		
- Vascular occlusion			
Lab characteristics	97±8	89±4	<0.001
Fasting glucose(mg/dl)	10.6±2.9	12.8±0.7	<0.001
Hemoglobin% (gm/dl)	126±59	94±18	<0.001
Triglycerides (mg/dl)	187±44	143±8	<0.001
Total Cholesterol(mg/dl)	118.2±33.7	64.6±7	<0.001
LDL(mg/dl)	48±14	49±3	0.138
HDL(mg/dl)	42±11	4±3	<0.001
ESR (mm/hr)			
HOMA IR	10.6±5.2	4.0±0.3	<0.001
Plasma Adiponectin (ng/ml)	16.5±3.2	12.2±0.3	<0.001
Serum Leptin(ng/ml)	25.4±10.7	7.8±0.5	<0.001
Serum Visfatin (ng/ml)	18.0±5.6	10±1.5	<0.001
FMD of brachial artery%	8.82±1.99	11.60±1.2	<0.001

None of adipokines is correlated to age,BMI,Disease duration or activity. An inverse correlation between FMD of the brachial artery and total cholesterol, visfatin, adiponectin, leptin and HOMAIR (r-value=-0.523,- 0.35,-0.27,-0.45,-0.56 respectively)with P<0.05.Adipokines and FMD did not differ regarding clinical presentations specially cardiovascular.Roc curve analyses studied the performance of adipokines.Adiponectin and visfatin are better to predict reduced FMD.Table(2)

Variable	AUC	Cut-off point	P value	Sensitivity	Specificity	Asymptotic 95% CI	
Homatest IR	0.466	12.15	0.718	50.7%	50.0%	0.268	0.663
Plasma Adiponectin	0.890	15.85	0.000	82.1%	80.0%	0.827	0.952
Serum Leptin	0.139	5.45	0.000	22.9%	20.0%	0.059	0.218
Serum Visfatin	0.890	17.50	0.000	82.1%	80.0%	0.828	0.952

Conclusion: Endothelial dysfunction is evident in SLE.Reduced FMD of brachial artery and increased adipokines &HOMAIR are noted.Adiponectin and visfatin could be predictors of atherosclerosis in lupus

REFERENCES

[1] Nassef S, Essam M, Abdelfattah D, et al. Evaluation of Impact of Interferon-Induced Helicase C Domain-Containing Protein 1 Gene in Egyptian Systemic Lupus Erythematosus Patients and its Relationship With Vascular Manifestations of the Disease. Arch Rheumatol 2018;33(2):181–9.

[2] Li H, Zhang T, Leng R, Li X. Emerging role of adipokines in systemic lupus erythematosus. Immunol Res. 2016;64(4):820–30.

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SAT0675

SERUM CALPROTECTIN IN EARLY RHEUMATOID ARTHRITIS: ASSOCIATION WITH DISEASE ACTIVITY AND CLINICAL REMISSION

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Background: Although remission is the goal of treatment in early rheumatoid arthritis (ERA), there is a lack of a sensitive biomarker for evaluating stringent clinical remission. Calprotectin is a potential biomarker for this purpose as it plays a critical role in synovial inflammation, cartilage destruction and bone resorption and its levels are reflective of local joint inflammation.[1,2]

Objectives: The study compares calprotectin with acute phase reactants such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in discriminating stringent clinical remission from low disease activity (LDA) to moderate disease activity (MDA) in patients with ERA.

Methods: A cross-sectional study was conducted on ERA patients from the Singapore Early Arthritis Cohort study. Serum calprotectin, ESR and CRP levels were measured. Receiver operating characteristics curves were used to compare the biomarkers in determining remission according to the Disease Activity Score in 28 Joints with ESR and CRP (DAS28ESR and DAS28CRP), Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI).

Results: Eighty ERA patients were included: 72.5% female, 61.3% Chinese, 66.3% seropositive, mean (S.D.) age 54.1 (12.2) and disease duration 2.3 (0.9) years. Calprotectin was significantly correlated with the DAS28ESR (r_s=0.509, *P*-value<0.001), DAS28CRP (r_s=0.486, *P*-value<0.001), CDAI (r_s=0.487, *P*-value=0.021) and SDAI (r_s=0.567, *P*-value=0.002). Calprotectin had the highest area under the curve (AUC) for discriminating remission based on the DAS28ESR (AUC=0.782, 95% CI 0.659 to 0.868), CDAI (AUC=0.753, 95% CI 0.627 to 0.855) and SDAI (AUC=0.829, 95% CI 0.693 to 0.937). A calprotectin cut-off of 98.9 ng/ml determined remission by the CDAI (sensitivity 0.82, specificity 0.53, 80.0% correctly classified) and a cut-off of 89.4 ng/ml determined remission by the SDAI (sensitivity 0.90, specificity 0.68, 87.5% correctly classified). 96.3% of patients were treated with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).

Conclusion: Calprotectin is a sensitive biomarker for evaluating stringent clinical remission and can potentially be integrated into treat-to-target algorithms to guide management in ERA patients with apparently quiescent disease activity.

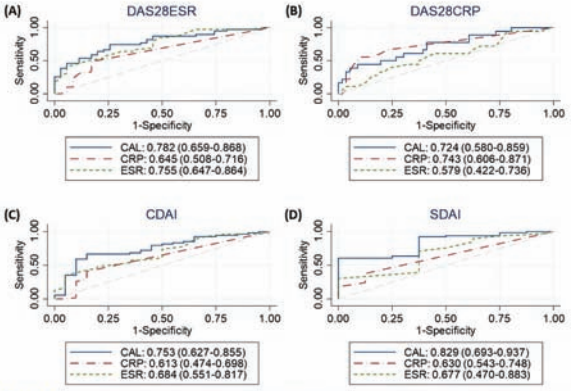


Figure 1 ROC curves comparing calprotectin, CRP and ESR in the evaluation of clinical remission based on **(A)** DAS28ESR **(B)** DAS28CRP **(C)** CDAI **(D)** SDAI. The AUCs and 95% CIs are indicated in the legends. CAL, Calprotectin; CRP, C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate.

REFERENCES

[1] Bae SC, Lee YH. Calprotectin levels in rheumatoid arthritis and their correlation with disease activity: a meta-analysis. Postgrad Med 2017;129 (5):531-7.

[2] Kopec-Medrek M, Widuchowska M, Kucharz EJ. Calprotectin in rheumatic diseases: a review. Reumatologia 2016;54(6):306-9.

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Disclosure of Interests: Yuhan Zou: None declared, Manjari Lahiri Grant/research support from: Grant support from Pfizer. I am the site PI for the Singapore National Biologics Register which is funded by multiple pharmaceutical companies; however I do not directly receive any funds for this., Consultant for: Advisory board for Elli Lilly, Lay Kheng Teoh: None declared, Bhushan Dharmadhikari: None declared, Nien Yee Kow: None declared, Anselm Mak: None declared, Peter Cheung: None declared

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SAT0675B ANTI-MODIFIED PROTEIN AUTOANTIBODIES IN RA DISPLAY IMPORTANT PEPTIDE CROSS-REACTIVITY BUT YET PROTEIN RECOGNITION SELECTIVITY

Peter Sahlström[1,2], Johanna Steen[1], Björn Forsström[3], Philip Titcombe[1,4], Ragnhild Stålesen[1], Ute Nonhoff[5], Zoltán Konthur[5], Luca Piccoli[6], Karin Lundberg[1], Holger Bang[7], Daniel Mueller[4], Anca Catrina[1], Lars Klareskog[1], Karl Skriner[2,8], Vivianne Malmström[1], Caroline Grönwall[1]. [1]*Karolinska Institute, Department of Medicine, Stockholm, Sweden*; [2]*Charité – Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany*; [3]*KTH Royal Institute of Technology, School of Biotechnology, Stockholm, Sweden*; [4]*University of Minnesota, The Center for Immunology, Minneapolis, United States of America*; [5]*Engine GmbH, Engine GmbH, Hennigsdorf, Germany*; [6]*Università della Svizzera italiana, Institute for Research in Biomedicine, Bellinzona, Switzerland*; [7]*Orgentec Diagnostika GmbH, Orgentec Diagnostika GmbH, Mainz, Germany*; [8]*Engine GmbH, Engine GmbH, Henningsdorf, Germany*

Background: The continuing increase of anti-citrullinated protein autoantibodies (ACPA) titers together with epitope spreading close to onset of disease, suggests that antibody responses to different citrullinated antigens may be critical in rheumatoid arthritis (RA) pathogenesis. Interestingly, monoclonal antibodies demonstrate reactivity to multiple cit-antigens that can even expand to other protein modifications. The width of this cross-reactivity is still not understood.

Objectives: To characterize the targets of monoclonal ACPA in relation to amino acid motif recognition, cross-reactivity with others post-translational modifications, and cellular localization.

Methods: A peptide array (NimbleGen, Roche) containing 16aa arginine- or lysine in pairs with citrulline- or homocitrulline peptides (53019 and 49211 cognate peptide pairs, respectively) derived from 1610 extracellular proteins and known RA cit-targets was used to screen 12 monoclonal ACPA with CCP2 reactivity. In addition, these ACPA were also screened for reactivity to acetylated-histone peptides and for reactivity to acetylated HeLa cell-extracts from cytosol, membrane, nuclear and cytoskeleton fractions. Three of the described mAbs together with polyclonal anti-CCP2 IgG were further evaluated on a macroarray platform (HEXselect, Engine) consisting of 20776 *E.coli* on-array expressed His-tagged protein fragments from 6909 genes originating from a human cDNA library. The array was enzymatically citrullinated with rabbit PAD and mAb-reactivity was scored from 0-3.

Results: On the peptide arrays, all 12 ACPA displayed low reactivity to unmodified peptides (<0.06%), while reacting to 1,000s of synthetically citrullinated peptides (>3,4% of the peptides). Based on the sequence from the positive peptides, consensus amino acids motifs were created, identifying aa-patterns with only a few critical citrulline-flanking residues (e.g. Cit-Gly; Gly-Cit; Arg-Cit-Asp). Intriguingly, five of the antibodies also reacted with the carbamylated peptides (>2.2%) and the recognition of certain homocitrulline-motifs also correlated with cross-reactivity to acetylated peptides. Interestingly, these AMPA reacted with acetylated-histones in NETs and apoptotic cells and in the nuclear fraction of *in vitro* acetylated cell-extracts. Three of the 12 ACPA were further screened on the macroarray and displayed multiple binding to citrullinated proteins and protein fragments identifying primarily previously unknown autoantibody targets (96, 210 or 917 positive hits for the mAbs, scoring 2-3), while limited binding was seen to native proteins.

Conclusion: ACPA display multi-reactivity to citrullinated peptides and proteins to a much greater extent than previously appreciated. Additionally, some ACPA, but not all, show distinct cross-reactivity to other post-translational modifications. Importantly, different autoreactive clones display modified protein recognition patterns dominated by proteins from different cellular structures. These reactivity profiles are likely to have impact on functionality and pathogenesis.

Disclosure of Interests: Peter Sahlström: None declared, Johanna Steen: None declared, Björn Forsström: None declared, Philip Titcombe: None declared, Ragnhild Stålesen: None declared, Ute Nonhoff: None declared, Zoltán Konthur Shareholder of: Engine GmbH, Luca Piccoli: None declared, Karin Lundberg: None declared, Holger Bang Shareholder of: Orgentec GmbH, Daniel Mueller: None declared, Anca Catrina Grant/research support from: Yes, but not for the presented study., Lars Klareskog Grant/research support from: Yes, but not for the presented study., Karl Skriner Shareholder of: Engine GmbH, Vivianne Malmström: None declared, Caroline Grönwall: None declared

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Education

SAT0676 SUPPORTING EARLY CAREER RESEARCHERS IN RHEUMATOLOGY AND MUSCULOSKELETAL MEDICINE: RESULTS FROM AN EMERGING EULAR NETWORK (EMEUNET) SURVEY

Meghna Jani[1], Alexandre Sepriano[2], Marloes van Onna[3], Katie Druce[1], Anne Troldborg[4], Aurelie Najm[5], Alessia Alunno[6], Elena Nikiphorou[7], EMEUNET Working Group 2018. [1]*The University of Manchester, Arthritis Research UK Centre for Epidemiology, Manchester, United Kingdom*; [2]*LUMC, Leiden, Netherlands*; [3]*Maastricht University Medical Center, Maastricht, Netherlands*; [4]*Aarhus University Hospital, Aarhus, Denmark*; [5]*Nantes University Hospital, Nantes, France*; [6]*University of Perugia, Perugia, Italy*; [7]*Kings College London, London, United Kingdom*

Background: Early career researchers (ECRs) across Europe face a number of challenges as highlighted by the European federation of education employers (EFEE) (1). Understanding the unmet needs of ECRs in rheumatology would allow development of targeted educational resources and support where required.

Objectives: To perform a Europe wide survey on the demographics of ECRs, current unmet needs and perceptions of possible solutions.

Methods: Clinical and non-clinical researchers who work in the field of rheumatology and under the age of 40, were invited to participate in an online-based survey. EMEUNET is a Europe-wide network of >2000 young researchers in rheumatology addressing educational needs and promoting research interests. Survey questions were devised and modified in collaboration with members of the EMEUNET education subgroup and steering committee. It was disseminated to EMEUNET members and national young rheumatology organisations. Participants were allowed to choose $\geq$1 answer options where applicable.

Results: 339 participants' anonymised responses were collected from 53 countries. The majority of participants were between 31-35 years (38.1%) and female (63.4%). Most were clinical researchers (including 33.3% rheumatology trainees) and 24.1% were non-clinical, including allied health professionals. The area of research of the participants was as follows: Epidemiology (40.0%), basic science/translational (39.6%), clinical trials (38.1%), imaging (17.7%), health services research (14.7%), other (7.5%). 48.6% did not feel they had adequate educational resources to develop their research skills locally. Obtaining grant funding as ECRs was deemed to be difficult (43.3%) or very difficult (31.4%) in their respective institutions/countries. Reasons listed are presented in figure 1. 98% were interested in developing new European collaborations in their research area either through: face to face interactions at conferences (82.1%), website forum (50.8%), email interactions (61.1%), teleconferences (43.5%). In addition, 93.7% felt they would apply for small European grants for ECRs, 81.6% would be interested in funding to spend short periods (4-8 weeks) at another European institute and 87.5% in focussed deep dive sessions on a topic of interest. The top 3 research skills that participants felt they would benefit from having more resources for as ECRs were: 1. Writing a study protocol (64.9%), 2. Writing a first grant application (64.0%), 3. Performing a systematic review (51.1%) (Figure 2).

Conclusion: A large proportion of ECRs in rheumatology felt they lack resources to develop their research skills locally. Small grant funding, research opportunities for pan-European collaborations, short periods of exchange to other institutes and targeted support to develop research skills can help address some of the current needs of ECRs.

Figure 1: Reasons for difficulties in obtaining grant funding amongst ECRs across Europe

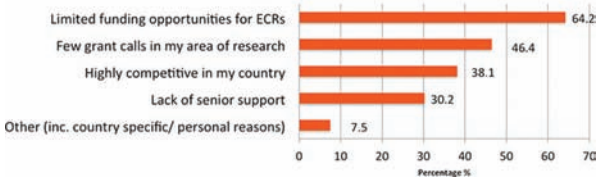
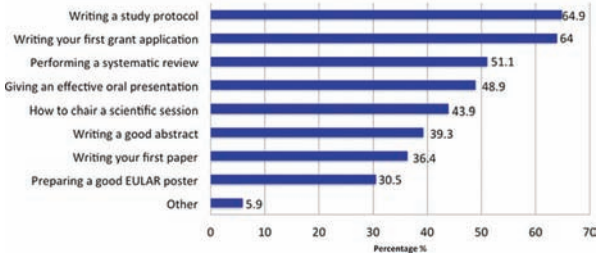


Figure 2: Research skills ECRs would prefer to have more resources for



REFERENCES

[1] Supporting Early Career Researchers in Higher Education: Summary report Feb 2015 https://www.ucea.ac.uk/en/empres/rs/ecr.cfm

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.2268

SAT0677

HETEROGENEITY OF STRATEGIES AND METHODS FOR ASSESSMENT OF COMPETENCES IN RHEUMATOLOGY TRAINING: RESULTS OF A SYSTEMATIC LITERATURE REVIEW TO INFORM EULAR POINTS TO CONSIDER

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Background: The structure and content of Rheumatology training programs vary widely among European countries. Harmonization of assessment methods of competences across EULAR countries could contribute to ensure a minimal standard of care.
Objectives: To identify and review the evidence on competence assessment methods and strategies in postgraduate medical training in rheumatology and other specialties.
Methods: As part of the EULAR project to develop points to consider on assessment of competences in rheumatology training, a systematic literature review (SLR) was performed. Two reviewers (AA and AN) independently identified eligible studies according to the PIM framework: P (population): trainees, fellows; I (instrument of interest): assessment strategies and methods; M (measurement of properties of interest): validity, discrimination, feasibility. Two searches were conducted: (i) for rheumatology, retrieving original studies; (ii) for related medical specialties, retrieving SLRs through which we identified original studies. Risk of bias was assessed using the medical education research study quality instrument (MERSQI) and the tool by Daly et al for qualitative studies. Studies were too heterogeneous to allow for any form of pooling, so descriptive results are presented.
Results: Of the 6276 articles from the rheumatology search, 4 met the inclusion criteria; of the 2,265 SLRs in other specialties, 36 were included, corresponding to a total of 133 original studies included. Studies on the assessment of competences in rheumatology were at variable risk of bias and explored only 2 methods: direct observation of practical skills (DOPS) and objective structured clinical examination (OSCE) (Table 1). Rheumatology OSCEs have been used to assess clinical and communication skills, professionalism and practical skills on musculoskeletal ultrasound, with conflicting evidence on internal consistency, reliability and inter-rater reliability. However, OSCEs including clinical, laboratory and imaging stations performed best, with a good to very good internal consistency (Cronbach's α = 0.83-0.92) and inter-rater reliability (r correlation coefficient= 0.80-0.95). A fair to moderate correlation (r= 0.44-0.52) between OSCEs and other assessment tools, including DOPS, has been found. The study on DOPS but not those on OSCE provided evidence for feasibility. Studies in other specialties were more heterogeneous for strategy/tools investigated, type and comprehensiveness of the analysis. The majority of studies on OSCEs to assess clinical skills showed a good to very good inter-rater reliability (r=0.60-0.95), while those on OSCEs to assess communication skills consistently demonstrated a good to very good internal consistency (Cronbach's α=0.7-0.98). Other tools such as multisource feedback (MSF) and mini-clinical evaluation exercise (mini-CEX) showed feasibility and a good to very good internal consistency, but results on validity and reliability were conflicting.
Conclusion: Although there is a consistent body of evidence about assessment of competence in postgraduate medical training in several specialities, data in rheumatology is scarce and this partial picture indicates some conflicting evidence. OSCEs represent an appropriate tool to assess clinical competences and correlate fairly well with other assessment strategies; DOPS, MSF and mini-CEX are other feasible alternatives. A mapping of European countries and a qualitative study will be additionally performed.

Figure 1: Studies addressing assessment of competences in rheumatology

Author, country, year	Humphrey-Murto S, Canada, 2009	Berman JR, USA, 2009	Kissin EY, USA, 2014	Pascual Ramos V, Mexico, 2015
Competence assessed	CanMEDS roles	Clinical skills, communication skills, professionalism	Practical skills (MSUS)	Clinical skills
Tool	DOPS	OSCE	OSCE	OSCE
Comparator tool	A national 10-station OSCE	Rating by program directors	A 76-question MCQ	Theory Test Board Exam (300 MCQ)
Sample size	73	70 (number of participants to year 4 NA)	35	68
Control population	none	none	3 faculty members	3 certified rheumatologists
MERSQI (0-18)	12.5	11	9.5	14.5
Revised tool by Daly et al (1-5)	5	2	5	1
Internal consistency (Cronbach alpha)	not performed	not performed	0.15-0.57	0.83-0.92
Inter-rater reliability	not performed	Correlation between faculty raters not significant	ICC 0.3 between live assessors and assessors on videotapes ICC 0.7 between assessors on videotapes	not performed
Test-retest reliability/intra-rater reliability	not performed	not performed	not performed	OSCE total and partial scores in Year 1 vs Year 2 r=0.80-0.95
Inter-method (or parallel forms) reliability /concurrent validity	DOPS vs OSCE r=0.48	OSCE vs rating by program directors r=0.48	OSCE vs MCQ r =0.52	OSCE total score vs MCQ Study year 1: r=0.203 Study year 2: r=0.436
Feasibility	14 forms per resident to achieve a g coefficient of 0.80	not performed	not performed	not performed
Construct validity	not performed	not performed	OSCE scores significantly discriminated fellows and fellows vs faculty	Significantly higher scores in higher levels of training

MSUS: musculoskeletal ultrasound; DOPS, direct observation of practical skills; OSCE, objective structured clinical examination; MCQ, multiple choice questionnaire; NA, not available; MERSQI, medical education research study quality instrument; ICC, intraclass correlation coefficient

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SAT0678

DEVELOPMENT AND VALIDATION OF A SELF-ADMINISTRATED QUESTIONNAIRE MEASURING ESSENTIAL KNOWLEDGE FOR PATIENTS WITH SPONDYLOARTHRITIS : THE SPONDYLOARTHRITIS ASSESSMENT KNOWLEDGE QUESTIONNAIRE(SPAKE):

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Background: Patient education is recommended for patients with inflammatory arthritis to enhance self-management. Only one Knowledge

Questionnaire (KQ) is available in spondyloarthritis (SpA) (ref 1) and needs to be updated according to the recent recommendations for SA and the patients' needs (ref 2).

Objectives: To develop and validate a new KQ in SpA

Methods: 4 steps. Step1. Selection of knowledge considered essential for patients with SpA through Delphi rounds by a working group of rheumatologists, health professionals (HPs) and patients, leading to a list of consensual items (ref2). Step2. Two rheumatologists and a rheumatology nurse constructed the first version of the KQ, each question of the KQ referring to a selected item on the list. The formulation was then amended by the working group. A new version was elaborated during a face-to-face meeting of 3 health professionals and one patient. Step3. The KQ was submitted to ten patients for cognitive debriefing, comments were analyzed and a final version was elaborated. Step 4. Multicentric validation in 13 rheumatology departments: acceptability was measured by the rates of missing data per item, reproducibility and sensitivity to change were assessed respectively by test/retest at a 2 weeks interval (Lin's concordance correlation coefficient) and by testing the KQ before and after patient education sessions.

Results: Step1 obtained 42 items, 32 considered essential and 10 considered useful, selected respectively by more than 2/3 or more than 50% of participants to the Delphi rounds, leading to the SPAKE: a 42-items questionnaire, with a 32-items short form. The SPAKE contains 6 knowledge domains: disease knowledge (12 items), pharmacological treatment (11), non -pharmacological treatment (8), comorbidities (1), self-care for pain and fatigue (4), adaptative skills to psychosocial, professional issues and health care system (6). The validation included 130 patients, 67 (51.5%) men, mean age 43.5±12.9 years, median disease duration 8 years [3;16]. There were no missing items in the KQ. The SPAKE's internal validity (Kuder-Richardson) was 0.85. Reproducibility (in 61 patients) was 0.81 [95% CI, 0.72; 0.89]. Sensitivity to change was measured in 55 patients. A statistically significant difference in total knowledge score was observed between the two assessment times: 29.1±6.4 vs. 34.7±5.9 ($p<0.001$), representing an effect size of 0.92 [0.52; 1.31]. The questionnaire's external validity was confirmed by a significant correlation with the patients' educational level ($p=0.02$).

Conclusion: This study enabled the development and the validation of the SPAKE, a knowledge questionnaire for patients with SpA, with a good acceptability, reproducibility and sensitivity to change. This KQ will be helpful to assess the process of knowledge acquisition in patient education approaches.

REFERENCES

[1] Lubrano E, et al. Br J Rheumatol. 1998;37:437-41.2 Beauvais C, et al. ARD 2015; 74, suppl 2

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SAT0679

EFFICACY OF A NURSE-LED PATIENT EDUCATIONINTERVENTION IN PROMOTING SAFETY KNOWLEDGE AND SKILLS OF PATIENTS WITH INFLAMMATORY ARTHRITIS (IA) TREATED WITH BIOLOGICS: A RANDOMIZED CONTROLLED TRIAL

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Background: Biologic disease modifying drugs (bDMARDs) are highly effective treatments of IA such as rheumatoid arthritis (RA) and axial or peripheral spondyloarthritis (SpA). However, they lead to risks of infections and other side effects. Some of these adverse events may be prevented by patient education (PE) aimed at promoting patients' safety skills.

Objectives: To investigate the effect of a nurse-led PE on safety skills of patients with IA at the introduction of a first subcutaneous bDMARD.

Methods: Multicentric randomized controlled trial comparing an intervention group (IG) to usual care (UC) at the time of the introduction of a first bDMARD. Inclusion criteria: patients with RA or SpA, biologic naïve, eligible for a subcutaneous bDMARD according to the rheumatologist's opinion. Intervention: a face-to-face nurse-led PE at baseline (BL) and 3 months later, ie, assessment by the nurse of the patients' health beliefs and educational needs, education focused on safety skills, self-injections and motivation. The primary outcome was the acquisition of safety skills at 6 months measured by the Biosecure Questionnaire (0-100 scale), a 55 item validated questionnaire assessing competences to deal with fever, infections, vaccination, and other daily life situations (ref). The secondary outcomes were quality of life, severe infections rate, coping, psychological well-being and disease activity. Data were anaysed as intent-to-treat using multiple imputations.

Results: 128 patients were included from 9 rheumatology departments between January 2017 and April 2018, 39 (30.7%) with RA, 72 (56.7%) with axial SpA, 16 (12.6%) with peripheral SpA; mean age 47.0 ±12.8 years, mean disease duration 6.1 ±7.5 years, 120 (94%) completed the study. BL mean self- reported information on RA treatments (0-10 numeric scale) was similar: 7.1±2.0 in IG; 6.8±2.1 in CG. The mean duration of the intervention was 65.5 ±17.9 minutes. The primary outcome was met: the Biosecure score at 6 months was 81.2 ±13.1 versus 75.6±13.0 in the IG and CG respectively ($p =0.016$), showing better skills in the IG. Secondary outcomes were also favorable.

Conclusion: Safety is an important issue in the management of IA treated with bDMARDs. In this trial, a nurse-led patient education was shown for the first time to be effective in teaching patients the essential safety skills.

REFERENCES

[1] Gossec, et al. Joint Bone Spine 2013;80:471-6.

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SAT0680 EDUCATIONAL NEEDS OF A LARGE COHORT OF PATIENTS WITH DIFFERENT RHEUMATIC AND MUSCULOSKELETAL DISEASES ATTENDING A HEALTH FACILITY IN AUSTRIA

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Background: Patient education is an important part of the management of rheumatic and other diseases. Since patients do not have the same needs, it is crucial to assess needs of a targeted group to be able to tailor educational interventions.

Objectives: To assess educational needs of a large cohort of patients with different rheumatic and musculoskeletal diseases attending a health facility in Austria.

Methods: We conducted an online survey with patients attending the Gastein Healing Galleries in Bad Gastein, Austria. Approximately 12,000 patients with a variety of diseases are treated in the centre every year. Of those, 6,465 patients were invited by email to fill out an anonymous online survey. Socio-demographics and health outcomes were collected from all respondents. In addition, the Educational Needs Assessment Tool (Austrian version - OENAT) was administered to a subset of respondents. The OENAT (39 items) assesses 7 domains of educational needs: Managing Pain, Movement, Managing Feelings, Arthritis/Disease process, Treatments, Self Help Measures, Support Systems.

Results: In total 2017 (31%) patients responded of which 516 had data on educational needs: AS (63%), RA (14%), and FM (24%). Their mean (SD) age was 56 (11), and 54% were male. Level of education was: Elementary School (32%), Junior High School (22%), High School (21%), College (12%), and University (14%). Table 1 presents differences in educational needs across disease groups. Across the groups, there were significant differences in following OENAT domains: Managing Pain, Feelings, Treatments, and Support Systems. There were no differences in the level of educational needs in Movements, Disease Process, and Self-Help Measures. Patients with FM had significantly lower needs for managing and higher needs for feeling education, compared to those with AS and RA (p<.05). The RA group had significantly higher needs than the AS (p<.05) and FM (p<.05) groups for treatments education - the AS group had significantly higher needs than the FM group (p<.05) in the same domain. AS patients had significantly higher needs for support system education than FM (p<.05) and RA patients (p<.05).

Table 1. Differences in educational needs across disease groups

	Managing Pain	Movements	Managing Feelings	Disease Process	Treatments	Self-Help	Support Systems
AS: Mean (SD)	14.54 (5.41)	10.20 (4.86)	8.33 (4.39)	16.74 (6.29)	13.98 (7.26)	15.07 (5.45)	7.85 (4.18)
FM: Mean (SD)	9.98 (6.49)	9.53 (5.13)	9.39 (4.53)	16.87 (6.37)	11.91 (7.57)	14.09 (6.36)	6.80 (4.54)
RA: Mean (SD)	15.30 (5.07)	10.07 (4.64)	7.94 (4.41)	18.15 (6.71)	16.85 (6.76)	15.82 (5.31)	6.41 (4.04)
F-Statistic	33.22***	.84	3.27*	1.43	10.34***	2.31	4.91**

*p < .05, **p < .01, ***p < .001

Conclusion: Educational needs vary by disease groups and depend on the domain under consideration.

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SAT0681 DEVELOPMENT, ACCEPTABILITY AND USABILITY OF HIBOOT : A SMARTPHONE APP TO IMPROVE MEDICATION ADHERENCE, SAFETY AND SELF-ASSESSMENT IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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Background: There is an increasing interest for mobile health applications (Apps) to enhance patients self-management in rheumatology. However few have been developed involving patients and health professionals.

Objectives: 1.To develop an App to improve medication adherence, safety and self-assessment in patients with inflammatory arthritis (IA) treated by biologics and/or methotrexate (MTX). 2. To assess its acceptability and usability.

Methods: 4 steps. Step1. In 2016, a qualitative ethnographic study and a quantitative study including 21 and 344 patients respectively explored 1. the impact of IA in daily life, treatment practices, relationship between adherence and safety 2. the patients' use of health Apps in general, their needs in terms of content and potential use (refs). Step2. A multidisciplinary team including 7 rheumatologists, 3 patients association representatives and 4 members of a Digital company developed the first version of the App through face-to-face meetings and qualitative interviews of patients along the development process. The content was collectively reviewed to be understandable by the patients and general population. After the launching of the App (step3), the assessment (step4), consisted in a) a qualitative study including 7 patients with different profiles (current users or non-users, satisfied or not) and 3 rheumatologists, having or not counselled the App to their patients, and b) the number of loadings and current users.

Results: Preliminary studies indicated numerous safety issues and needs on adherence and daily life counselling, leading the 5 mains functionalities of the App: a) a treatment reminder, b) a global well-being self-assessment c) a safety checklist before administration, d) help in daily life situations related to self-management and safety e.g. symptoms requiring to stop their treatment (infections, surgery) etc…e) periodic counselling messages. The presentation was a friendly companion called HIBOOT (OWL in English) that interacts with the user. The content was based on the French recommendations of the Club Rhumatismes Inflammation (www.cri-net.com) for biologics and MTX management, the drug leaflets and the public national health websites. In May 2017 : launching on the stores (GooglePlay and iTunes, with free uploading); May 2017-January 2018 : communication toward patients, rheumatologists and health professionals (flyers, postal letters, Facebook, Tweeter). Assessment showed 2 types of usability: a regular use by the patients who have adopted the HIBOOT companion and are in demand of more functionalities; a more punctual use on specific questions with the need of quick answers. The reminder system was particularly appreciated and the messages considered understandable and reliable. Patients suggested ways of improvement on the App navigation system and the check list. Rheumatologists appreciated the independent scientific content although having a low knowledge of the App. To date, the mean loading is ~500/months with a regular use of ~1500-1800 patients monthly.

Conclusion: The free App HIBOOT for patients with IA was developed through a formal methodology using preliminary qualitative studies, inclusion of patients all along the process and has a scientific validated content. Its acceptability and usability is good and will be improved according to patient's advices. Communication is still necessary to enhance rheumatologist's adherence to promoting the App.

REFERENCE

[1] Montagu, et al. ARD, 2017; 76,suppl 2 (3) Beauvais, et al. ARD, 2017; 76, suppl 2

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SAT0682 PATIENT EDUCATION IN THE EUROPEAN REFERENCE NETWORK ON RARE AND COMPLEX CONNECTIVE TISSUE AND MUSCULOSKELETAL DISEASES (ERN RECONNET): UNMET NEEDS FROM THE HEALTH CAREPROVIDERS SIDE AND FROM THE PATIENTS' SIDE

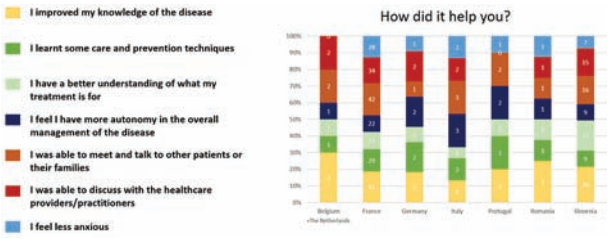
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Background: The ERN ReCONNET (European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases) is the ERN aimed at improving the management of Rare Connective Tissue and Musculoskeletal Diseases across the European Union (EU). The ERN ReCONNET involves 26 health care providers (HCPs), from eight different EU countries: Belgium, France, Germany, Italy, the Netherlands, Portugal, Romania, Slovenia and 7 european Patient Advocacy Group (ePAGs). An intense collaboration has been established between HCPs and ePAGs. Patient Education (PE) was defined in 1998 by the World Health Organization as a continuous process including organized awareness information, self-care learning and psychological support regarding the disease, treatment, care and health care setting. It is designed to help patients to maintain or improve their quality of life with specific PE programmes designed to help them acquiring new skills.

Objectives: To evaluate PE practice in the ERN ReCONNET based on a survey send to the HCPs members and to the patients of the corresponding countries.

Methods: A questionnaire designed on a google form was send to the HCPs members asking about their practices in PE in their department and an other one was send to ePAGs who translated the patients' survey in the different languages. Various versions of the same questionnaire was then send to patients' associations in the different countries.

Results: 33 HCPs members or representatives answered the survey. 52.9% (18) had no specific staff members dedicated to PE. In the department with staff trained in patient education, 33% (4) had no specific PE programmes. In the HCPs with dedicated staff for PE, 83.3% (10) estimated care providers are insufficient to meet the patients' needs. 1608 patients answered the patient survey (France, n=246; Germany, n=23; Italy, n=500; Portugal, n=339; Slovenia, n=240; Belgium, n=190; the Netherlands, n=42), mostly women (84,5%, n=1359), around 48,5 years old (SD=13,6). Patients suffered mostly from Connective Tissue Diseases and Ehler-Danlos disease. 68%% (1093) of the patients had never heard about PE and were for 74% (804) interested in taking part in a PE programme. In the remaining patients who had heard about PE, 66% (342) never took part in a programme. For patients who had already taken part in a PE programme, they expressed satisfaction in several domains listed in the following bar chart: For all respondents, patients expressed needs for a better knowledge in disease and symptoms, treatments, well-being, nutrition, exchanging experiences with other patients, and daily life with the disease.



Conclusion: Based on the EULAR recommendations for PE (Zangi HA et al.), PE should be apply in all EU countries. E-learning on PE for staff members and ePE for patients will be developed by the ERN ReCONNET.

REFERENCE

[1] Zangi HA, Ndosi M, Adams J, Andersen L, Bode C, Boström C, Van Eijk-Hustings Y, Gossec L, Korandová J, Mendes G, Niedermann K, Primdahl J, Stoffer M, Voshaar M, van Tubergen A; European League Against Rheumatism (EULAR). EULAR recommendations for patient education for people with inflammatory arthritis. Ann Rheum Dis. 2015 Jun;74(6):954-62. doi: 10.1136

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SAT0683 NORMATIVE DATA FOR THE DISEASE AND TREATMENT ASSOCIATED KNOWLEDGE SCORE (DATAK-RA) IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Having adequate disease-related knowledge is essential for patients with RA, since it may influence treatment decisions, shared-decision making, and the ability to perform self-management behavior. Patient Knowledge Questionnaires can be used to measure disease-related knowledge. We recently developed and validated the item response theory (IRT) based Disease and Treatment associated Knowledge in Rheumatoid Arthritis (DataK-RA) item bank, containing 42 multiple-choice items. In the present study we establish normative data to facilitate the interpretability of DataK-RA scores.

Objectives: To produce normative data for DataK-RA (IRT)-scores, stratified by sex and educational level.

Methods: Consecutive patients recruited from three hospitals in the Netherlands were asked to complete a form containing either 27 or 26 DataK-RA items. Datak-RA IRT-scores and standard errors (SEs) were obtained using the weight maximum likelihood estimator. The Dutch Committee on Tests and Testing (COTAN) quality criteria for test norms were followed. DataK-RA IRT scores and the precision of the scores (SE) were summarized using the mean (SD) or median and 1st – 3th quartile in case of non-normal distribution. Scores were compared between male

and female patients and patients with low, middle and high educational attainment, according to the International Standard Classification of Education, using One-way ANOVA with a significance level of $\alpha = 0.05$.

Results: In total 631 patients participated, most of them were female (60.9%). Mean age (SD) was 64.0 (11.6) years. Mean (SD) DataK-RA score was 52.5 (14.1) (range 11.7 – 104.7). Female patients had significantly higher Datak-RA scores compared with men ($F = 25.23$, $p < 0.01$). Mean (SD) DataK-RA-score was 54.6 (15.1) for women, and 48.9 (11.5) for men. The median (1^{st} – 3^{th} quartile) SE of the IRT-scores was 4.7 (4.1 – 5.8). Regarding education, higher-educated patients had a significant higher IRT-score than middle- and lower-educated patients ($p < 0.01$), as well as middle-educated versus lower-educated patients ($p < 0.01$). Table 1 shows the percentiles DataK-RA-scores, and DataK-RA scores stratified by age educational level.

Conclusion: We present normative data for DataK-RA scores generated from a sample of consecutive patients participating in an ongoing longitudinal study. A unique feature of IRT based DataK-RA scores is that they are expressed in a metric in which the unit of measurement is independent of the administered items. Hence these norm scores pertain to all applications of the DataK-RA item bank (e.g. computer adaptive tests, tailored short forms). According to the COTAN quality criteria, sample sizes for the overall percentile scores were 'good' ($n \geq 400$) and 'adequate' ($300 \geq n < 400$) for all stratified percentiles, except patients with high educational level.

Table I. Percentiles DataK-RA scores and percentiles DataK-RA scores stratified by age and educational level

	DataK-RA scores	DataK-RA scores by sex		DataK-RA scores by educational level		
	N = 631	**n = 382**	**n = 245**	**n = 222**	**n = 259**	**n = 103**
Percentile	All patients	Female	Male	Low	Middle	High
10	37	37	37	33	43	46
20	42	43	40	37	47	49
30	46	47	44	40	49	51
40	48	50	46	43	51	53
50	50	53	47	45	54	56
60	53	55	49	47	56	62
70	56	59	52	49	60	67
80	62	65	55	52	64	71
90	68	71	62	58	69	91

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SAT0684 A UNIQUE FREE EDUCATIONAL RESOURCE FOR RHEUMATOLOGISTS: WWW.RHEUMATOLOGYMINDMAP.COM

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Background: One of the challenges for doctors in training is fast and easy access to reliable, relevant, and up-to-date clinical information. It can be very difficult to find what you require in the middle of a busy clinic or a ward round. All widely used educational approaches have significant limitations: textbooks are often inaccessible at work and information there can be outdated, internet search is time consuming and results are often irrelevant even if you use trusted sources, there is no single place where you can find all applicable guidelines and documents, learning from seniors is always limited in time and coverage. Trainees who do not yet have comprehensive knowledge of relevant topics can miss important details when they see a patient (e.g., bits of clinical assessment, differentials, certain relevant investigations) and this can adversely impact patient care.

Mind mapping approach is a very effective strategy that can be used to address these issues. A mind map is an expandable structure consisting of radial hierarchic nodes. It is one of the simplest ways to visually organize and access information. A mouse click or a tap opens the next level and any subtopic is easily available within a few clicks. Online mind maps are still highly underrated but they have many important advantages offering visual structured approach, intuitive and logical search, easy modification, ability to embed documents, link topics, and use external hyperlinks. Evidence shows that mind maps facilitate learning [1-4].

Objectives: To create a free educational resource in rheumatology using mind-mapping techniques.

Methods: We used Mindjet MindManager 2017 (mind mapping software allowing export into HTML5 files that can be published online) to create the Rheumatology Mind Map website (www.rheumatologymindmap.com). A wide range of information relevant to adult rheumatology practice in the United Kingdom has been retrieved from various sources and structured in accordance with common standards used in medical education. The mind map embeds infographics currently used in rheumatology (diagnostic and classification criteria, activity and damage indices, treatment decision aids, downloadable templates, etc). Appropriate permissions from right owners have been obtained.

Results: The current version of the website (1.7, January 2019) contains an expandable mind map with above 1900 subtopics covering all aspects of adult rheumatology. It works with all modern desktop and mobile browsers. Examples of structure of the mind map and some subtopics are shown in figures 1 and 2. The main advantages of the mind map are the presence of the most up-to-date information, detailed lists of investigations relevant for each of rheumatic conditions, thorough differential diagnosis, subtopics on pregnancy issues, extensive information about medications used in rheumatology practice and treatment options for each condition. Specific attention is paid at the clinical information relevant for trainees, e.g., what to ask when you suspect a certain rheumatic illness, what to look for at the examination, and which investigations to order. The mind map has direct online links to appropriate NHS, NICE, BSR, SIGN, EULAR, and ACR guidelines and policies, and various resources including online calculators, relevant databases, websites providing support for patients, etc.

Conclusion: The website www.rheumatologymindmap.com is an attempt to create a unique comprehensive educational resource in rheumatology. It allows free access and structured approach to clinical information required by a trainee or an established rheumatologist. It is an up-to-date source of a wide range of information and is linking hundreds of current online sources together in one place.

REFERENCES

[1] P Farrand, et al. Med Educ. 2002 36(5):426-31
[2] V Vilela, et al. J Contemp Med Edu. 2013 1(4):199-206
[3] M Kalyanasundaram, et al. Indian J Community Med. 2017 42(1):19-23
[4] G Abdel-Hamid. MOJ Anat & Physiol 2017 3(3):00090

Figure 1

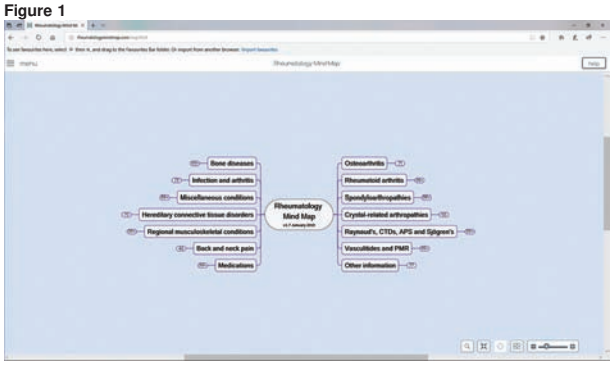
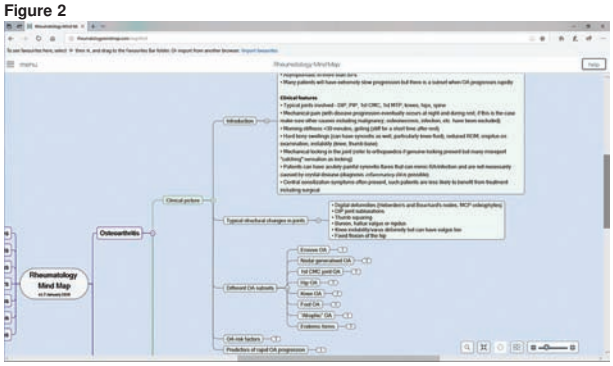


Figure 2



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SAT0685 USE AND IMPACT ON SOCIAL NETWORKS BY RHEUMATOLOGY JOURNALS

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Background: Traditional system for assessing the quality and impact of a scientific journal is based on the number of citations. One of the main forms of measurement is the impact factor, which measures the impact that a journal has on the scientific community. Despite its traditional use, this quality and impact assessment system has been criticized in recent years. The "Alternative Assessment Metrics" initiative (Altmetrics) seeks to define new measures of metrics for scientific publications[1]. Alternative metrics are based on the number of "mentions" of an article in various online sources, including blogs and social networking platforms[2]. The alternative metrics are more dynamic and accumulate quickly in real time. The social networks most frequently used by scientific journals are Facebook, YouTube and Twitter
Objectives: To evaluate presence, number of followers and activity of rheumatology journals in 3 social networks (Facebook, Twittter and Youtube).
Methods: Platform of scientific journals SCOPUS was consulted, selecting journals classified as rheumatology journals. Scimago Journal Rank (SRJ) of 2017 was taken to evaluate the quality of the journal. The social networks Facebook, Twitter and YouTube were consulted, searching for rheumatology journals of those found in SCOPUS with active accounts in these social networks. Date of consultation: 13-11-18
Results: 61 rheumatology journals in SCOPUS, of which only 8 (13.1%) had an active account in at least one of the social networks consulted. On Facebook the most active and most popular magazine was Nature Reviews, followed by the Journal of Rheumatology and Annals of the Rheumatic Diseases. It should be noted that Nature Reviews includes other journals in their social networks that cover other specialties of medicine such as cardiology, immunology, microbiology, oncology, among others. On Twitter, as on Facebook, magazine with largest number of followers was Nature Reviews, followed by Annals of the Rheumatic Diseases and Journal of Rheumatology. Activity on Twitter, measured as number of twits, had same behavior according to the number of followers. The only journal with channel on YouTube was Annals of the Rheumatic disease with 67 subscribers, 12 videos, of which the most watched has 315 reproductions. See table 1

Journal	SJR	Facebook	Twitter	Twits
Annals of the Rheumatic Diseases (Q1)	5.505	3.032	4.042	2.874
Nature Reviews (Rheumatology) (Q1)	2.951	426.513	7.146	3.976
Osteoarthritis and Cartilage (Q1)	2.290	NA	351	51
Arthritis Research and Therapy (Q1)	2.080	NA	2.756	718
Journal of Rheumatology (Q1)	1.687	4.012	3.341	843
Open Rheumatology Journal (Q2)	0.988	60	NA	NA
Journal of Clinical Rheumatology (Q2)	0.562	199	4	0
Acta Reumatologica Portuguesa (Q3)	0.266	456	NA	NA

Table 1. Characterization of scientific journals in social networks in rheumatology. SJR: Scimago Journal Rank. Facebook: Number of followers. Twitter: Number of followers. Twits: Number of twits reported on the platform

Conclusion: YT and FB are social networks with a high content of false information. The majority of available videos promise to cure different rheumatic diseases (even several simultaneously). This is the first work of a line of research that seeks to highlight the high degree of misinformation. We will continue to analyze other diseases and social networks, to make publications and communications in different media and to alert local regulatory entities.

REFERENCES

[1] Trueger NS, Thoma B, Hsu CH, et al. The Altmetric Score: a new measure for article-level dissemination and impact. Ann Emerg Med 2015; 66:549–53.
[2] Maggio LA, et al. Beyond Citation Rates: A Real-Time Impact Analysis of Health Professions Education Research Using Altmetrics. Acad Med 2017;92:1449-55

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SAT0686 ONLINE EDUCATION IMPROVES PHYSICIANS' KNOWLEDGE OF FAMILY PLANNING AND PREGNANCY MANAGEMENT IN WOMEN WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES

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Background: Chronic inflammatory rheumatic disease (CIRDs) often develop in women during their childbearing years. Preconception counselling and coordinated medical and obstetric care are essential to maintain control of the disease and maximize the chances of a successful pregnancy.
Objectives: This study assessed whether online CME can improve physicians' understanding of the risks of uncontrolled chronic rheumatic diseases in pregnancy and the benefits of proactive pregnancy planning, and enhance physician confidence in managing such patients.
Methods: Physicians participated in an online CME activity consisting of a 15-minute video discussion between 2 experts with accompanying slides. Educational effect was assessed using a 4-question repeated pairs, pre-/post-assessment. A Chi-square Test of Independence was used to determine if a statistically significant improvement (5% significance level, P <.05) existed in the number of correct responses between the pretest and posttest scores. Cramer's V was used to estimate the effect of the education. The CME accredited activity launched on August 2 2018, and data were collected through August 30 2018.
Results:

- Rheumatologists (n=47) had a high baseline knowledge of family planning and pregnancy management in women with CIRDs, but the activity had a signficiant impact (P =.0008) on rheumatologists' knowledge and the Cramer's V value of 0.199 indicates a considerable effect of the education
- The average percentage of correct responses for rheumatologists was 91% post–activity compared with 76% pre–activity
- 64% more rheumatologists answered all 3 questions correctly post–activity compared with pre–activity (74% vs. 45%)
- 26% of rheumatologists gained confidence in their ability to manage CIRDs in pregnant patients, with an average confidence shift of 9%
- Obstetricians/gynaecologists (n=40) also had a fairly high baseline knowledge of family planning and pregnancy management in women with CIRDs, but again, the activity had a significant impact (P =.0005) on their knowledge and the Cramer's V value of 0.226 indicates a considerable effect of the education
- The average percentage of correct responses for obstetricians/gynaecologists was 83% post–activity compared with 63% pre–activity
- 97% more obstetricians/gynaecologists answered all 3 questions correctly post–activity compared with pre–activity (65% vs. 33%)
- Almost half (45%) of obstetricians/gynaecologists gained substantial confidence in their ability to manage CIRDs in pregnant patients, with an average confidence shift of 22%

Conclusion: This online, 15-minute video discussion between 2 experts significantly improved rheumatologists' and obstetricians/gynaecologists' understanding of family planning and pregnancy management in women with CIRDs which may lead to improved outcomes for both women and babies. Both groups would benefit from further education to reinforce knowledge of disease activity on conception and pregnancy and to emphasize the need for collaborative proactive family planning in women with CIRDs.
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SAT0687

EVOLVING THE MANAGEMENT OF RHEUMATOID ARTHRITIS THROUGH DEVELOPMENT OF PRACTICAL AND EDUCATIONAL TOOLS

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Background: Despite advances in the treatment armamentarium for rheumatoid arthritis (RA) over the last decade, several unmet needs remain within RA management.
Objectives: To enhance scientific knowledge and improve patient care by providing practical tools and evidence-based awareness – in line with EULAR recommendations – on how to implement optimal RA management and address identified needs.
Methods: The eRA (evolving the management of RA) programme convened a Steering Committee (SC) of 17 European and International experts in RA, including representation from rheumatologists, nurses, health professionals and patients. Through literature search and assessment of expert opinion, 4 core areas of unmet need were identified: delays in referral and initiation of disease-modifying anti-rheumatic drugs, inconsistent application of treat-to-target strategy, sub-optimal identification and management of comorbidities, and a growing need to actively engage patients with their care. Several clinical and educational gaps associated with these unmet needs were also identified. To fill these gaps and support application of an optimal approach to RA management, practical and educational tools were developed. A cascade process engaging national leaders in rheumatology was then initiated to disseminate the tools to health professionals across Europe, with tools being updated in participating countries to ensure alignment with local practices and individual country needs. Broader programme dissemination is supported by congress activities and a digital communication plan. The eRA programme is funded by Sanofi Genzyme. Programme direction and content creation are driven by the SC.
Results: A suite of 12 educational tools was developed (Figure 1), including educational slides to raise awareness of unmet needs, self-reflection questionnaires to evaluate personal practice alongside EULAR recommendations, case scenarios outlining the optimal approach to management, and clinical checklists to support daily practice. The process to disseminate these tools commenced in November 2017 with a Multi-Country Workshop, which convened 43 national leaders in rheumatology from countries participating in the programme. Feedback on the eRA tools at this meeting was positive, and in 2018, additional countries were onboarded to the programme. Launch of a digital web-platform aims to further support dissemination of the eRA tools.
Conclusion: The content of the eRA programme has been well-received, largely due to the programme's flexible approach, which is sympathetic to individual country needs. As the cascade process continues, it is anticipated that many more health professionals and patients will benefit from the eRA tools. References: Disclosure of Interests: Gerd Rüdiger Burmester Consultant for: Roche, Sanofi-Genzyme, Speakers bureau: Roche, Sanofi-Genzyme, Mart van de Laar Grant/research support from: AbbVie, Eli Lilly, Janssen-Cilag, Merck Inc, Pfizer Inc, Sanofi Genzyme, Speakers bureau: Eli Lilly, Pfizer Inc, Jose-Maria Alvaro-Gracia Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer Inc, Roche, Sanofi, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer Inc, Roche, Sanofi, and UCB, Neil Betteridge Consultant for: Amgen, Eli Lilly, Grunenthal, GSK, Heart Valve Voice, Janssen, Roche, Sanofi Genzyme and Sanofi Regeneron, Speakers bureau: Amgen, Eli Lilly, Grunenthal, GSK, Heart Valve Voice, Janssen, Roche, Sanofi Genzyme and Sanofi Regeneron, Jaime Calvo Consultant for: Bristol-Myers Squibb, Janssen, Celgene, Sanofi Genzyme, Speakers bureau: Bristol-Myers Squibb, Bernard Combe Consultant for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB, Patrick Durez Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celltrion, Ricardo J.O Ferreira Consultant for: Sanofi Genzyme, Bruno Fautrel Grant/research support from: AbbVie, Lilly, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, Sanofi-Aventis, Sanofi Genzyme, SOBI, UCB, Cem Gabay Grant/research support from: Roche, Pfizer, AB2 Bio Ltd, Consultant for: Roche, Pfizer, Lilly, AbbVie, Sanofi, Regeneron, Bristol-Myers Squibb, Novartis, UCB, AB2 Bio Ltd, Debiopharm, Annamaria Iagnocco: None declared, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Mikkel stergaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Sofia Ramiro Grant/research support from: MSD, Consultant for: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Speakers bureau: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Andrea Rubbert-Roth Consultant for: Chugai, Eli Lilly, Roche, and Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Hexal/Novartis, Janssen, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, and Sanofi, Tanja Stamm Grant/research support from: TS has received grant support from AbbVie., Paid instructor for: TS has received speaker fees from AbbVie, Janssen, MSD, Novartis, and Roche., Zoltán Szekanecz Grant/research support from: Pfizer, UCB, Consultant for: Pfizer, Abbvie, Roche, Sanofi, Lilly, Novartis, Speakers bureau: Pfizer, Abbvie, Roche, Sanofi, Lilly, Novartis, Peter C. Taylor Grant/research support from: Celgene, Galapagos, Eli Lilly, UCB, Consultant for: AbbVie, Galapagos, Gilead, Eli Lilly, Pfizer Inc
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Figure 1. eRA toolkit

SAT0688

PATIENT STATE OF KNOWLEDGE ON BIOSIMILARS – DO PHYSICIANS NEED TO IMPROVE EDUCATION SKILLS?

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Background: Biosimilars are highly similar to original biological medicines[1].Worldwide prescription of biosimilars is still low because of the lack of understanding in manufacturing and approval process together with mistrust in the extrapolation of indication in clinical use[2].Lack of biosimilar awareness throughout rheumatic patients results in an unjustified underuse[2].
Objectives: To assess patients current knowledge and concerns on biosimilars and to investigate their expectations when receiving such a treatment following the principle of shared-decision making.
Methods: A national,cross-sectional survey was conducted in Romanian patients with rheumatoid arthritis(RA),spondyloarthritis(SpA),psoriatic arthritis (PsA)currently on a bio-originator or biosimilar.336 patients responded to

a survey distributed from August to December 2018,main topics being patient basic information on biosimilars,their efficacy,safety,price or differences to original drugs.

Results: Out of 336 patients,47.3% had RA,39.8% SpA,12.5% PsA with a mean age of 52.5.In the study cohort,13% received approved biosimilars while 87% bio-originators with different mechanisms of action.A *yes/no* type of question divided patients into those aware or not of biosimilars with further exclusion of those with lack of information.Half of the patients(48.8%) stated they never heard of biosimilars.Surprisingly, four of them were already on this type of treatment.Out of the 172 remaining patients,28.4% feared the risk of adverse events like infections or cancer while almost 20% expressed either insecurity on drug tolerability or the possibility that the biosimilar might be less efficient that the original drug. Another 19.7% certified they had no concerns related to these products and only 15.1% stated confusion regarding the potentially difference in the pharmacological structure of the drugs.Most patients(48.2%) are convinced that the price of a drug should not exceed its efficacy or safety. Half of the respondents say they could accept a switch from an original to a biosimilar if their rheumatologist advises them and 30% might agree but only after being informed.8.7% are interested in scientific proof of the drug and only 1% would consent to a change directly from the pharmacist.When handling prescription,37.7% of patients would want to know if it is an original drug or a biosimilar while 20% do not mind if they receive either.Another 30% trust their rheumatologist and 12.7% would feel more secure if receiving a patient card and written information.Most patients (73.2%)say that they feel completely confident in their rheumatologist if they would want to prescribe a biosimilar,18.6% will have doubts but they will accept the drug and 4% would ask for another medical opinion. After biosimilar initiation,45.9% would be cautious when administrating it,23.2% would stop the drug if an adverse event occured and 15% would have no fears.

Conclusion: Study results confirm there is still a significant information gap concerning biosimilars in patient population.Most concerns on biosimilars are related to adverse event occurrence.There is a need to improve patient education on biosimilars involving patients and health professionals.Shared-decision principle is more of a myth since most patients rely entirely on their physician for prescribing the most appropriate product.

REFERENCE

[1] Declerck P, et al. The Language of Biosimilars:Clarification,Definitions and Regulatory Aspects.Drugs 2017. 2.O'Callaghan J, et al. Regulatory Science Ireland:bridging the information gap on biosimilar medicines.*GaBI J* 2016.

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SAT0689 A NOVEL METHODOLOGY FOR TEACHING RHEUMATOLOGY TO NEW GENERATIONS

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Background: Teaching rheumatology to undergraduate students is every day more challenging. In order to motivate new generations and use time more efficiently, we explored new methods to incorporate active learning in our rheumatology course. Therefore, we developed a video library and turned the classical lectures into flipped classrooms.

Objectives: To evaluate the impact of this new teaching method of rheumatology in a cohort of medical students at Pontificia Universidad Catolica de Chile School of Medicine.

Methods: Fundamental lectures of rheumatology were recorded, edited and uploaded to YouTube, so the students were able to easily access the lessons from different electronic devices. A total of 10 videos were created, with an average duration of 6 minutes. A cohort of 120 fourth-year medical students took the rheumatology course between May 28th and June 11th of 2018. They were asked to watch the videos before the class, and during the classroom time the teacher could work on clinical classes, complement the information about the topic and answer questions. At the end of the course, the students evaluated this new methodology with a final online and anonymous survey. Performance analysis of each video was obtained from YouTube Analytics.

Results: Seventy-two students completed the survey at the end of the course (60%). One hundred percent thought that watching the videos before the class was useful for their learning. Moreover, 70 students (97%) would like to continue using flipped classrooms in the future, and 1/3 of them would even use them to replace traditional lectures. Overall, the rheumatology was evaluated with a 6.8 score in a 1 – 7 scale. A 100% of this cohort approved the course. Average view duration of all videos was 4:37 minutes.

Twenty-two students added positive comments about the use of flipped classroom in this course, and appreciated the videos were short enough to watch them before attending lectures.

Conclusion: Advances in technology have allowed developing innovating ways to teach. Flipped classroom encourages students to adopt a more active role in the learning process. This new methodology seems to be well accepted by students and shows a promising way to motivate new generations to learn rheumatology.

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SAT0690 HOW TO REDUCE THE NOCEBO EFFECT WHEN SWITCHING FROM ORIGINATOR INFLIXIMAB TO A BIOSIMILAR: POSITIVE RESULTS OF A MULTIDISCIPLINARY TEAM INTERVENTION

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Background: Nonspecific subjective adverse effects (NSAE), usually considered as related to a nocebo effect (NE), have been identified as a barrier to the acceptability of switches from biologic originators (BO) to biosimilars (BS).

Objectives: To assess the efficacy of a multidisciplinary team intervention to reduce the NE among inflammatory arthritis (IA) patients concerned by systematic switch from originator Infliximab (OI) to the biosimilar infliximab (BI) SB2.

Methods: The intervention was part of a multidisciplinary patient education (PE) program. It was developed in 4 steps. Step 1: we conducted first semi-directive qualitative interviews with 5 patients treated by other intravenous (IV) biologics. Interviews showed: fears about efficacy and tolerability of BSs, need for information (particularly on the difference between BSs and generics), importance of sharing their experience of adverse effects (AE) with health practitioners (HP), and having the opportunity to switch back. The wish to discuss the nurses' own experience of BSs was prominent. Step 2: a meeting with the multidisciplinary team (3 rheumatologists, 1 resident, 1 pharmacist, 3 nurses, 1 peer-patient from a patient's association) was set up for designing the intervention based on the interviews, on non-systematic literature review about switches and on patients' perspective regarding NE. Step 3: Consensual agreement on the intervention and the chosen pieces of language to be used by all HPs. The intervention included written and oral information by the nurses; nurse-led PE; if necessary, distribution of an informative leaflet made by the team. Step 4: Implementation of the intervention. The rheumatologist had the entire appreciation for discontinuing the BS or not.

Inclusion criteria were all IA patients treated with OI. The primary outcome was SB2 retention rate (RT) at 34 weeks, secondary outcomes were the number of NSAEs leading to SB2 discontinuation; the comparison of the RT and NSAE rate of the cohort with 1) RT and NSAEs rate of a systematic switch from another Infliximab BS (CT-P13) to SB2 made at the same period in the same rheumatology department 2) RT and NSAEs rate of switches in other published European cohorts (1,2,3).

Results: Fourty-five patients were included from March 12th, 2018 to May 25 th, 2018, median follow up was 34 weeks, 17 rheumatoid arthritis

(RA), 23 spondyloarthritis (SpA) and 5 psoriatic arthritis (PSA) patients were included. Mean OI duration before switch was 9.4 years. The switch RT from OI to SB was 41/45 (91,2%) and NSAE (1/45). RT was significantly higher than in other European cohorts ($p<0.05$) (table 1). Reasons for discontinuation were uveitis (1); demyelinating disorder (1) and peripheral synovitis (1) already present before the switch; 1 patient had NSAE (increased fatigue and pain). During the same period, 18 patients switched from CT-P13 to SB2 with a RT of 12/18 (66,7%) and 1 NSAE.

Conclusion: An intervention based on a multidisciplinary patient education team where nurses have a prominent role is effective in reducing the NE when switching from the originator infliximab to its biosimilar.

Table 1.

Study	Patients	Number of BS discontinuation	RT (%)	p value*
Tweehuysen L. et al. Arthritis Rheumatol. 2018, 70:60-68	192	47	24,5%	0.014
Scherlinger M. et al. Joint Bone Spine 2018, 5: 561-567.	89	25	28%	0.003
Avouac J et al. Semin Arthritis Rheum. 2018, 47; 741-748.	182	48	26,4%	0.006
Petit J et al.	45	4	8,9%	ref.

RT: Retention rate. BS: Biosimilar

Disclosure of Interests: None declared
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SAT0691 PHYSICIAN–PATIENT AGREEMENT IN A RHEUMATOLOGY CONSULTATION

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Background: Several aspects of the consultation have already been studied. These usually comprise the patient satisfaction, patient enablement, physician–patient interaction and physician–patient agreement.[1] After consultations, the physician's perceptions differed from the patient's in the illness level, cause and nature of the problem and the content of the consultation.[2] Greater physician–patient agreement on consultations was associated with higher patient global satisfaction.[3] Agreement on problems requiring follow-up was associated with a better outcome.[4]

Objectives: Assessment of physician–patient agreement in Rheumatology consultation.

Methods: A 10 item questionnaire - "Consultation Assessment Instrument" (CAI) - was constructed with the aim of assessing physician-patient agreement. It was anonymously applied, after the consultation, to the patient and physician. The higher the score obtained, the more positive the consultation experience. Patients above 18 years of age, with an established diagnosis of inflammatory joint disease under biological therapy were included. Items were evaluated and index of proportional agreement for the dichotomized answers - agree (P_{pos}) and disagree (P_{neg}) - was calculated.

Results: 102 observations were obtained, corresponding to 10 physicians and 102 patients. Most patients were female (53.9%) with a mean age of 51.5 ±12.7 years old. Rheumatoid Arthritis was the most prevalent diagnosis (40.2%) and more than half of patients were in disease remission [28-joint Disease Activity Score (DAS28) <2.6 or Ankylosing Spondylitis Disease Activity Score (ASDAS PCR) <2.1]. Higher CAI scores correlated with lower Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores ($r=-0.376$; $p<0.05$). Also, patients with mild disease (score <3.2) by DAS28 had higher CAI scores (low disease = 37±3.8; moderate disease = 35.8±4.3; high disease = 35±2.3; $p=0.039$). It was also found that the more satisfied the patient, the lower the Bath Ankylosing Spondylitis Functional Index (BASFI) ($r=-0.334$; $p<0.05$) and ASDAS PCR scores [low disease = 35.3±4.2; high disease = 30.5±7.8; $p=0.001$]. There was no statistically significant association between CAI total score and Health Assessment Questionnaire (HAQ) score, ASDAS PCR or BASFI. Patient's satisfaction did not show an association with DAS28, HAQ or BASDAI scores.Physician-patient agreement was high in 9 of the 10 items. Highest agreement was obtained for consultation satisfaction and the lowest for explanation of treatment importance in disease control. There was no statistically significant association between physician-patient agreement and disease activity, disability scores or patient satisfaction.

Conclusion: Both patient and physician tend to show a positive experience towards Rheumatology consultation. Patients with a more positive experience had lower disease activity scores. Physician–patient agreement was high in the majority of the consultation aspects. CAI could be useful as a mental checklist in daily practice or as an educational tool for training consultation skills.

REFERENCES

[1] GC Ahlén, et al. Physician–patient questionnaire to assess physician–patient agreement at the consultation, Family Practice. 2007:24(5):498–503.DOI.org/10.1093/fampra/cmm043
[2] Martin E, et al. Why patients consult and what happens when they do. BMJ. 1991;303(6797):289-92.
[3] Fagerberg C, et al. How well do patient and general practitioner agree about the content of consultations?, Scandinavian Journal of Primary Health Care. 1999:17(3):149-152.DOI: 10.1080/028134399750002557
[4] Starfield B, et al. The influence of patient-practitioner agreement on outcome of care. Am J Public Health. 1981;71(2):127-31.

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SAT0692 DEALING WITH COMORBIDITIES IN RHEUMATOID ARTHRITIS WITH MEDICAL ASSISTANTS. THE PATIENTS' OPINION ON ASSESSMENT AND EDUCATION BY MEDICAL ASSISTANTS DURING ROUTINE CLINICAL PRACTICE

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Background: In 2006 the curriculum for rheumatology health professionals of the Academy of the German Association of Rheumatologists (DGRh) was developed. [1]. Since then more than 1400 health professionals (medical assistants [medizinische Fachangestellte] and nurses) were trained and are currently playing an increasing role in rheumatology practices in Germany.

Objectives: To evaluate the patients' opinion on the assessment by medical assistants in general and regarding assessment and education on cardiovascular risk and vaccination.

Methods: Patients with rheumatoid arthritis were interviewed by a medical assistant in a rheumatology practice that is part of the public health care system with five rheumatologists in Erlangen, Germany A semi-standardized interview assessed disease activity, pain, medication, general health, and side effects of medication. A part of the patients was also assessed and educated regarding cardiovascular risk or vaccinations. Thereafter they were examined by the rheumatologist and finally asked to complete a questionnaire regarding their visit. The questions were numerical scales ranging from 0 [very good, very satisfied] to 10 [very poor/inadequate].

Results: 293 Patients (mean age 61.3 ± 13.5 years, mean DAS28 2.8 ± 0.9, mean FFbH 76,4 ± 20.8) were documented between August and December 2018. 212 completed the general questionnaire, 34 regarding a structured cardiovascular assessment and education, and 18 regarding a structured assessment of vaccinations.

Table 1 shows patients answers between 0 [very good, very satisfied] to 10 [very poor/inadequate]. Overall rating was excellent with a mean score of 1.0 (SD 1.5). The rating was only slightly different, if patients were assessed by medical assistants for the first time (n=111; mean score 1.2, SD 1.5), between the 2nd to 4th time (n=82; mean score 1.0, SD 1.3) or the 5th time or more (n=19; mean score 0.6, SD 0.6)

	Mean (0= very good/very satisfied; 10= very poor/ inadequate)	SD
General questions		
The prior consultation to a medical assistant is estimated as ? 0= good – 10 = bad	1.04	1.66
Regarding acquiring information and asking questions the form of consultation is ? 0 = better – 10 = worse	1.28	1.76
All of my questions were answered 0 = correct – 10 = incorrect.	0.89	1.55
The further consultation to the physician was ? 0 = adequate – 10 - inadequate	0.96	1.49
Cardiovascular assessment and education		
I was able to understand the information. 0 = correct – 10 = incorrect	0.50	0.96
I had the opportunity to ask questions. 0 = correct – 10 = incorrect	0.50	0.90
The information was helpful, I learned something new. 0 = correct – 10 = incorrect	1.32	1.93
I am planning to put the information into practice. 0 = correct – 10 = incorrect	0.74	0.86
Information on vaccination		
I was able to understand the information. 0 = correct – 10 = incorrect	0.17	0.38
I had the opportunity to ask questions. 0 = correct – 10 = incorrect	0.22	0.43
The information was helpful, I learned something new. 0 = correct – 10 = incorrect	1.06	1.35
I am planning to put the information into practice. 0 = correct – 10 = incorrect	0.44	0.78

Conclusion: The semi-standardized assessment of patients with rheumatoid arthritis by medical assistants, the cardiovascular risk assessment and education, and the assessment and information on vaccination was very well accepted and appreciated by patients. Currently, there is no reimbursement by the German health care system.

REFERENCE

[1] Schuch F, Kern P, Kreher G, Kruger K, Wendler J, Fiehn C. [Curriculum for "Rheumatology health professionals DGRh-BDRh" as a way of qualification for clinical nursing specialists : Concept and results of an evaluation]. Z Rheumatol. 2011 Oct; 70(8):670-677.

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SAT0693 ONLINE EDUCATION SIGNIFICANTLY IMPROVED RHEUMATOLOGISTS' UNDERSTANDING AND INTERPRETATION OF COMPARATIVE TREATMENT DATA FOR AS

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Background: With multiple therapeutic options now available for patients with ankylosing spondylitis (AS), clinicians and payers require evidence to guide their decision-making. Head-to-head randomized controlled trials (RCTs) are considered to provide the best evidence to inform treatment decisions, but in the absence of such trials, physicians often rely on their own experience and clinical trial data from single RCTs. In the absence of head-to-head RCTs, data from comparative studies such as network meta-analysis and matching adjusted indirect comparisons can be useful to help inform treatment choices.

Objectives: This study assessed whether the online CME accredited round-table-discussion with title "Comparing Treatment Alternatives in Ankylosing Spondylitis" improves physicians' understanding and interpretation of comparative effectiveness data for AS.

Methods: Rheumatologists participated in an online CME activity[1] consisting of a 30-minute video roundtable discussion between 3 experts with accompanying slides. Educational effect was assessed using a 4-question repeated pairs, pre-/post-assessment. A chi-square test was used to determine if a statistically significant improvement (P <.05 significance level) existed in the number of correct responses from the pretest and posttest scores. Cramer's V was used to estimate the level of impact of the education. The CME activity launched on December 20, 2017, and the data were collected through March 6, 2018.

Results: A total of 328 rheumatologists completed the pre- and post activity assessments. Overall the activity had a signficiant impact (P <.001) on rheumatologists' understanding of comparative effectiveness data in AS with a Cramer's V value of 0.189 indicating a considerable effect of the education. The average perecentage of correct responses rose from 22% pre-activity to 39% post-activity. A linked learning assessment (each individual tracked pre and posteducation) showed that 24% of learners improved their knowledge and 15% reinforced their knowledge. The change in percentage of correct responses from pre- to post-assessment achieved statistical significance (P <.05) for all 3 questions presented: (i) recommendations for biologic DMARD use in AS according to the ASAS-EULAR 2016 guidelines (34% at baseline rising to 67% post acivity; P <0.001), (ii) understanding the impact of treatment with biologic DMARDS on radiographic progression in AS (17% at baseline rising to 26% post acivity; P <.01), (iii) understanding comparative analysis of RCTs in AS (14% at baseline rising to 24% post acivity; P <.001) and (iv) a quarter of rheumatologists gained confidence in their ability to select a biologic DMARD based on comparative data and individual patient needs, with an average confidence shift of 14%.

Conclusion: This online CME activity significantly improved rheumatologists' understanding of how to compare treatments and interpret comparative effectiveness data in AS which may lead to improved treatment selection and better patient outcomes. However, there is clearly room for further improving physicians' knowledge of treatments & radiographic progression and comparative analysis of RCTs (since 75% of rheumatologists provided incorrect answers to questions 2 and 3 post-activity) which can be addressed in future education.

REFERENCE

[1] Comparing Treatment Alternatives in Ankylosing Spondylitis http://www.medscape.org/viewarticle/887334

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SAT0694 QUALITATIVE ANALYSIS OF MOBILE APPS DIRECTED FOR LUPUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is chronic disease that requires lifelong treatment with a multidisciplinary approach. Increasingly, patients use the internet and associated technology to access health-related information. Smartphone applications (apps) have become essential tools in this age and are widely-accessed by patients. These apps can be very helpful tools to inform patients about their illness, support them in their treatment plan, and help them connect with others. Unfortunately, healthcare apps remain largely unregulated.

Objectives: We aim to evaluate the overall quality of patient-directed lupus apps with a focus on the accuracy and appropriateness of the health information contained in these apps.

Methods: The 2 most commonly used app stores are Apple Store and Google Play. These stores were searched for the terms "lupus" and "SLE" during December 2018. The resulted apps (Patient oriented, English language, and free of charge) were analyzed and the following data was collected: app type (informational, tool, or both), features, and

content. Tool apps are those used by patients to track symptoms, contained lupus action plan, appointment and medication reminders, and/or quizzes/gamification. App features included connection to external sites (social media, professional societies, online patient communities, healthcare provider), and security features including login/password protection and privacy policy statement. Apps were then rated using (with permission from originator) a published reliable and multidimensional scale: Mobile App Rating Scale (MARS). The study authors were trained on MARS using the recommended slides and exercise. In addition, quality of health information contained in informational apps was rated using the published DISCERN instrument.

Results: The search terms SLE and Lupus retrieved a total of 471 apps on Google Play store and a total of 198 apps on Apple Store. On Google Play, 14/471 met our inclusion criteria compared to 11/198 on Apple Store. Majority of Google apps were in the tools category representing 44%, followed by apps that are both tools and informational (31%), whereas informational apps were 25%. On the other hand, majority of Apple Store apps were both tools and informational (64%), followed by tools only apps (27%), and finally informational only apps (9%). The most common apps features were email login (37%) and links to external sites including social media platforms (31%). Two apps were identified as a potential source for misleading information claiming that certain homemade herbs/food has anti-inflammatory properties to treat lupus. The average MARS score for Google apps was 2.7/5 indicating poor apps quality. The average MARS score for Apple apps was 3.7 indicating acceptable apps quality. Overall, the functionality score was the highest (3.9/5) while the engagement score was the lowest (2.7/5) for both app stores. For apps that contained information for patients, DISCERN score was 2.15/5 and 3.12/5 for Google and Apple apps respectively indicating potentially important shortcomings in the quality of health information provided in these apps.

Conclusion: Our study demonstrates that a larger need is emerging for designing high-quality apps for patients with lupus. Healthcare organizations, professional societies, rheumatologists, and allied health professionals are encouraged to participate in promoting and creating high-quality apps for lupus patients. These apps are likely to contribute to improving the quality of care provided to these patients and can potentially extend care in the looming global shortage of rheumatologists. This is also an acknowledgement of the need to adapt to advancing communications technology as it integrates into many patients' lives in this digital age.

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HPR Epidemiology and public health (including prevention)

SAT0695-HPR ASSOCIATION OF PHYSICAL FITNESS WITH HEALTH-RELATED QUALITY OF LIFE IN WOMEN WITH FIBROMYALGIA

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Background: Physical fitness (PF) represents a marker of health and is associated with health-related quality of life (HRQoL). Different components of PF have shown to be consistently associated with lower symptomatology in people with fibromyalgia[1,2]. Identifying which PF components are associated with HRQoL in people with fibromyalgia may contribute to the development of more specific therapeutic strategies.

Objectives: The aim was to examine the associations of different PF components with HRQoL in women with fibromyalgia.

Methods: This population-based cross-sectional study included 466 women with fibromyalgia. The Senior Fitness Tests battery plus handgrip test were used to assess PF and the 36-item Short-Form Health Survey (SF-36) was used to assess HRQoL. Tender points, cognitive impairment, anthropometric measurements and medication usage were also measured and used as confounders. Firstly, multivariate linear regression assessed the individual relationship of each PF test with the eight dimensions of the SF-36. Secondly, a standardized composite score was computed for each component of PF (aerobic fitness, muscular strength, flexibility and motor agility). Forward stepwise regression was performed to analyse which components of PF were independently associated with the SF-36 physical and mental component scales.

Results: Overall, higher performance on PF tests was associated with higher levels of HRQoL in all SF-36 dimensions and subscales (all $p<0.05$ or $p<0.001$) except for associations between handgrip with social functioning, emotional role, mental health and mental component scale, as well as the chair sit-and-reach test with the general health dimension. The muscular strength composite score was independently (from other fitness components and confounders) associated with the SF-36 physical component scale ($p<0.001$), while the flexibility composite score and cardiorespiratory fitness were independently (from other fitness components and confounders) associated with the SF-36 mental component scale (both $p<0.05$).

Conclusion: High PF is consistently associated with better HRQoL in women with fibromyalgia. Muscular strength, flexibility and cardiorespiratory fitness are independent indicators of HRQoL in this population. These results might have implications for future intervention studies because it could facilitate the selection of the most suitable exercise interventions according to the clinical profile of each patient.

REFERENCES

[1] Soriano-Maldonado A, Ruiz JR, Aparicio VA, Estévez-López F, Segura-Jiménez V, Álvarez-Gallardo IC, et al. Association of physical fitness with pain in women with fibromyalgia: The al-Ándalus project. Arthritis Care Res 2015;**67**.

[2] Estévez-López F, Gray CM, Segura-Jiménez V, Soriano-Maldonado A, Álvarez-Gallardo IC, Arrayás-Grajera MJ, et al. Independent and combined association of overall physical fitness and subjective well-being with fibromyalgia severity: the al-Ándalus project. Qual Life Res 2015;**24**.

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SAT0696-HPR THE PREVALENCE OF SEPTIC ARTHRITIS AT A LARGE UNIVERSITY TEACHING HOSPITAL

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Background: Septic arthritis (SA) is a rheumatological emergency requiring early treatment to prevent lasting joint damage. Treatment outcomes depend on prompt diagnosis, which currently rests on clinical suspicison, riased non-specifc inflammaotry markers and identification of a pathogen from synovial fluid.

Objectives: To establish the prevalence of SA in a large University teaching hospital. To review the microbiology results and identified pathogens in each positive case along with subsequent treatment regimes utilising outpatinet parenteral antimicrobial therapy (OPAT) with adherence to local guidelines.

Methods: Retrospective data collection of all samples identified as synovial fluid or joint aspiration sent to microbiology lab between 1st January 2016 and 31st December 2016. Electronic review of microbiology results to identify the causal pathogen and case notes to review treatment and outcomes.

Results: There were 364 samples identified as joint aspirate or synovial fluid, 54 of these grew a pathogen. Positive aspirates from native joints totaled 35 in 31 patients. Twenty-three of these patients accounting for 25 of the positive samples were treated clinically as SA. Sub analysis of this group revealed *Staph.aureus* was the most commonly identified pathogen in 14 cases (56%). There were however 8 other pathogens identified in the 25 positive samples. Fifteen patients (65%) underwent a joint washout in theatre, 7 of these patients had multiple washouts. Duration of antibiotic therapy was 5 weeks in 8 cases; 13 cases had therapy for >5 weeks and 2 cases with SA in the upper limb had treatment for < 5 weeks. There were 10 positive samples taken from 8 native joints that grew a pathogen and were not treated as SA. These were identified

on enrichment culture only n=3 or an alternative clinical diagnosis was clearly documented n=4. One case was incorrectly labeled as a joint aspirate. The remaining positive samples, 17 in 12 patients, came from prosthetic joint aspirates.

Conclusion: In line with known literature, *staph.aureus* was the most common pathogen[1], however there were a number of other bacteria identified which needs to be taken into account when formulating local antimicrobial guidelines. Current literature reports surgical treatment as not superior to medical[2], yet 65% of cases here under went joint lavage in theatre. This information will be used to inform local clinical practice, and, guide recruitment targets for a large multi-centre study collecting data and samples from patients presenting with a hot swollen joint, with the aim of identifying a specific biomarker for SA.

REFERENCES

[1] Rutherford A I, Kleymann A, Ibrahim F, Galloway J. The increasing incidence of septic arthritis in England between 1998 and 2013. Rheumatology April 2016 55(1):i51-i52

[2] Ravindran V, Logan I, Bourke B E. Medical vs Surgical treatment for the native joint in septic arthritis: A 6 year, single UK academic centre experience. Rheumatology Oct 2009 48(10):1320-1322

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SAT0697-HPR COMMON COMORBIDITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A UNICENTRIC BIG COHORT

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Background: Rheumatoid arthritis (RA) is a common systemic autoimmune disease characterized chronic joint inflammation. RA and ageing are associated with comorbidities such as cardiovascular disease, malignancies and osteoporosis, these conditions have an important effect on the management of RA. These comorbidities can be associated with higher mortality, poor life quality, and the increasing of costs for the health system.

Objectives: To describe the prevalence of comorbidities and characteristics of a Colombian unicentric big cohort that assist to a RA specialized center.

Methods: We performed a descriptive analysis; our main goal was to provide real-life data regarding characteristics of patients with RA. We collected sociodemographic information, DAS28, and prevalence of comorbidities regarding hypertension, cerebrovascular disease, diabetes mellitus, osteoporosis, renal chronic disease, or Sjogren's syndrome. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We estimated the prevalence of comorbidities and performed a bivariate analysis.

Results: We reviewed the medical charts of 6541 patients, 82% were female and 18% male; median age was 60 years RIQ (50-67), regarding disease activity, mean DAS28 was 3.34 ± 1.28. The prevalence of comorbidities was 36%, the most common disease was high blood pressure followed by osteoporosis, see table 1. When we compared DAS28 and comorbidities 11% of patients who were in moderate or severe disease activity had one or more comorbidities. The relationship between disease activity and comorbidities was not associated and it was not statistically significant (P>0.05)

Table 1. Comorbidities in patients with RA

Comorbidity	n	%
High Blood Pressure	1589	24
Osteoporosis	804	12
Diabetes Mellitus	319	5
Sjogren Syndrome	262	4
Chronic Renal Failure	54	0.83
Cerebrovascular Disease	30	0.46

Conclusion: As other studies have shown high blood pressure is the most common disease among patients with RA followed by osteoporosis (1, 3). s. According to these results it is important to consider the patient´s context, medical conditions, and the number of comorbidities in order to understand the complexity of the management of patient with RA. Additionally, it is important to explore barrier and health care services in order to plan a realistic plan where a patient is managed with all comorbidities.

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SAT0698-HPR SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS OF INFECTION TYPES AND THE EFFECT OF MEDICATIONS ON INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The infection incidence rates are high in systemic lupus erythematosus (SLE) patients[1] and the medical literature documents broad categories of specific bacterial infection risks for SLE patients.[2-4] However, there has not been a detailed incidence of infection types and infection predictors.

Objectives: In a systemic literature review (SLR) and meta-analysis, to describe the types and incidences of infections in SLE patients and to examine the effect of medications used to treat SLE.

Methods: An SLR of SLE and infection articles generated through a search of MeSH terms using PubMed and Medline generated 1,211 articles. Using predefined Incl/Exc criteria, data from 32 accepted articles were double-extracted and descriptive and multivariable analyses were conducted. Relative risks between drug classes were estimated using Arm-Based Network Meta-Analysis. Hypothesis tests were two-sided and a p-value <0.05 was statistically significant. Analysis was conducted in the R Statistical Computing Environment (R Core Team; Vienna, Austria).

Results: 4,130 patients were considered, 91% females, average age: 36.8 (10.9) years, mean disease duration: 6.9 (6.1) years, SLEDAI mean: 11.7 (4.6). In drug trials, 775 used conventional synthetic DMARDs (csDMARDs), 1,809 (43.8%) used biologic DMARDs (bDMARDs), 691 (16.7%) used placebo and the rest were in non-drug specific observational studies. 90.4% used background corticosteroid therapy.

Bacterial infections occurred most commonly, being 61% of the total of 315 non-serious infections, of which 28.4% were gram negative and 15.3% gram positive. 135 (42.9%) had viral infection – H zoster, HPV, and CMV were most common. 36 (11.4%) were opportunistic infections - 12 candida, 11 mycobacterial, 4 pneumocystis jiroveci pneumonia, and 9 unspecified infections.

There were 182 serious infections (SIE), of which 110 were bacterial (gram negative were the most common subtype (36.3%)). Serious opportunistic infections accounted for 31 (17%) of the SIEs, similar to serious viral infections 41 (22.5%).

Patients using csDMARDs had an absolute risk to develop H Zoster of 15.2% (95% CI: 7.7-28.2), while it was 8.2% (CI: 1.9-29.2%) when using bDMARDs. The next most likely infection for which these SLE patients were at risk was for gram negative infections, where csDMARDs demonstrated a 7% absolute risk (CI: 0.4-36%) of developing a gram negative

infection, compared to 5.6% (CI: 0.1-52.6%) for bDMARDs. The attributable risk for developing gram positive infections when using csDMARDs was 3.9% (CI: 0.2-25%) and 3.5% (CI: 0.1-41.6%) when using bDMARDs.
Conclusion: In this SLR and meta-analysis in SLE, the frequency of infections was bacterial>viral > opportunistic, in that order, although some details were unavailable. csDMARDs were associated with more infections than bDMARDs.

REFERENCES

[1] Ramos M, Cuadrado MJ, Abla P, et al. (2008) Acute viral infections in patients with SLE: description of 23 cases and review of the literature. Medicine (Baltimore) 87:311-318.
[2] Feldman, et al. (2015) Serious infections among adult Medicaid beneficiaries with SLE and lupus nephritis. Arthritis Rheumatol 67: 1577-1585.
[3] Dubula T, Mody GM (2015) Spectrum of infections and outcome among hospitalized South Africans with SLE. Clin Rheumatol 34: 479-488.
[4] Bouza E, Moya JG, Muñoz P (2001) Infections in SLE and RA. Infect Dis Clin North Am 15: 335-361.

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SAT0699-HPR ASSESSMENT OF HEALTH LITERACY IN A COHORT OF SYSTEMIC SCLEROSIS (SSC) PATIENTS

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Background: SSc is a chronic, complex and very debilitating disease, involving all the aspects of physical, mental and social life. Thus, the need of a first assessment of the degree of health literacy (HL) is required to develop useful tools for SSc patients to simplify their access to health care services. HL is defined as the ability to acquire, synthesize and understand health information and services required to make decisions regarding an individual or community's health.
Objectives: to assess the HL in SSc patients.
Methods: 25 SSc patients classified ACR/EULAR criteria (limited and diffuse subsets) were enrolled in September-October 2018 with the support of the local association of patients (ASSMAF). Patients have been evaluated for socio-demographic variables and the HLS-EU-Q16 questionnaire (Italian version).
Results: Questions 1 to 7 (on health information) are associated with age, educational qualifications and with the number of children; while 8 to 12 (on prevention) are associated with the number of children, but also with the type of employment and marital status; finally, questions 13-16 (on health promotion) are associated with age, educational qualifications and number of children. Moreover, our results show 20% of SSc patients with an inadequate level (0-8) of HL, compared to the 12% of the general population; 40% show a problematic level (9-12) of HL lower than that found in the general population (55%), while 40% of patients show an adequate level (13-16) of HL, higher than the 33% of the general population.
Conclusion: Health literacy level is an important parameter to consider and assess in SSc patients to facilitate their access to health care services and their understanding of the disease. Future researches with larger sample size are needed.
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SAT0700-HPR PHYSICAL AND PSYCHOLOGICAL DETERMINANTS OF FIBROMYALGIA SEVERITY: A STRUCTURAL EQUATION MODELLING FROM THE AL-ÁNDALUS CROSS-SECTIONAL STUDY

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Background: In fibromyalgia, the main aim of therapy is to reduce the severity or impact of the disease [1]. The effectiveness of the most commonly used therapies is modest in fibromyalgia. Therefore, identifying modifiable factors associated with lower fibromyalgia severity is a priority as these modifiable factors may be possible therapeutic targets [2-4].
Objectives: This study examined the determinants of fibromyalgia severity.
Methods: In this observational, population-based cross-sectional study, 569 people with fibromyalgia were assessed on resilience, catastrophizing, active lifestyle, declarative memory, subjective fitness, objective fitness, psychological distress, physical fatigue and disease severity. Structural equation modelling estimation was used to analyse the following hypotheses: (i) resilience, catastrophizing and active lifestyle through subjective fitness, objective fitness, psychological distress, and physical fatigue determine fibromyalgia severity; and (ii) these factors are distributed in two core pathways (one physical and one psychological) that interplay between each other.
Results: We confirmed the above-mentioned hypotheses. Our model explained 83% of fibromyalgia severity, which is a considerably large proportion.
Conclusion: Our findings not only corroborate the importance of the two core (i.e., physical and psychological) pathways but also their interaction in their association with fibromyalgia severity. The understanding of these interconnections between alleged predisposing and perpetuating factors may optimise current approaches for treating fibromyalgia. Although the present research is the most comprehensive model of fibromyalgia severity to date, its cross-sectional design impedes to determine causal relationships. Longitudinal research is warranted.

REFERENCES

[1] Macfarlane GJ, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis 2017;76:318–28. doi:10.1136/annrheumdis-2016-209724.
[2] Estévez-López F, et al. Adaptation profiles comprising objective and subjective measures in fibromyalgia: the al-Ándalus project. Rheumatology (Oxford) 2017;56:2015–24. doi:10.1093/rheumatology/kex302
[3] Estévez-López, F., Rodriguez-Ayllon, M., Soriano-Maldonado, A., Acosta-Manzano, P., Segura-Jiménez, V., Álvarez-Gallardo, IC., et al. Lower Fatigue in Fit and Positive Women with Fibromyalgia: The al-Andalus Project. Pain Med (In press). DOI: 10.1093/pm/pny304
[4] Estévez-López, F., et al. The discordance between subjectively and objectively measured physical function in women with fibromyalgia: association with catastrophizing and self-efficacy cognitions. The al-Ándalus project. Disabil Rehabil 2018;40: 329-337.

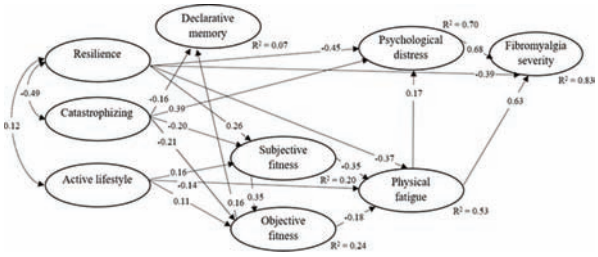


Figure 1. Estimated standardised regression and squared multiple regression (R^2) coefficients for the final model.

All the coefficients were significant.
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SAT0701-HPR SLE EXACERBATION PREDICTORS IN PATIENTS OF KYRGYZ NATIONALITY

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Background: Taken into account the wave-like multivariate flow of SLE, there are still difficulties in diagnosing conditions such as "remission" and "exacerbation". The questions of SLE "exacerbation" predictors and their influence on the further nature of the course and outcome of the disease remain little studied.
Objectives: Study of SLE exacerbations predictors in patients living in Kyrgyzstan.
Methods: The study included 150 (26.31%) Kyrgyz patients out of 570 with a reliable diagnosis of SLE, female (96%), young age (median - 34 [26; 44]), Kyrgyz nationality (89.33%), high - 61 (40.66%) and very high activity - 40 (26.67%), with the duration of SLE at 1 observation point from 7 months to 10 years, with dynamic observation from 1 year to 3 years.
To determine the gradation of the degree of reduction in glomerular filtration rate (GFR) and the severity of proteinuria in patients with lupus nephritis, used the classification of chronic kidney disease (CKD) according to KDIGO (2013).
The characteristic and frequency of SLE exacerbations were assessed by the SFI - R index: mild, moderate or severe.
Results: The results of the study showed that 84 (56%) Kyrgyz patients out of 150 had 192 SLE exacerbations by using the SFI index during 3 years of follow-up, with a frequency of 1 to 4 cases (2.82 ± 2.21) per patient. A mild exacerbation was observed predominantly in 103 patients (53.65%), manifested by skin - mucous syndrome - in 81 (78.64%) and febrile fever - in 22 (21.36%). A moderate exacerbation was noted in 48 (25%) patients in the form of polyserositis - in 18 (37.5%), articulations - in 16 (33.33%) and nephritis with minimal urinary syndrome - in 14 (29.17%) of them. Severe exacerbation was recorded in 41 (21.35%) patients, manifested mainly by kidney damage - in 28 (68.29%), lungs - in 4 (9.76%), central nervous system - in 4 (9.76%) and hematological disorders - in 5 (12.19%).
Severe exacerbations of the kidneys were characterized by nephritis with CKD C1 A1 in 6, CKD C1 A3 in 6, with CKD C2 A3 in 6, severe nephritis with CKD C3a A3 in 3, CKD C3b A3 in 2 and nephritis with nephrotic syndrome - in 5 patients.
SLE exacerbations in most cases resulted from self-withdrawal of glucocorticoid and cytostatic therapy in 44 (52.38%) and activation of the pathological process in 35 (41.67%) patients and in 5 (5.95%) of them were unknown.
Conclusion: On the background of careful dynamic monitoring of patients, predominantly mild SLE exacerbation was observed (53.65%), due to self-withdrawal of glucocorticoid and cytostatic therapy (52.38%).
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SAT0702-HPR FREQUENCY OF INFECTION AND PREDICTIVE FACTORS IN PATIENTS WITH BIOLOGICAL THERAPY

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Background: Infections represent an important cause of morbidity and mortality for patients with autoimmune inflammatory rheumatic diseases. CsDMARDs have a low risk of infection; however, exposure to glucocorticoids seems to be an important predictor of infection. Therapy with bDMARDS is associated with a higher rate of severe infections compared to csDMARD.
Objectives: To determine the prevalence and identify the predictive factors of infection in patients with autoimmune inflammatory rheumatic diseases with the use of biological therapy.
Methods: cross-sectional study, files of patients with autoimmune inflammatory rheumatic diseases were analyzed. Descriptive statistics were performed with mean, standard deviation and binary logistic regression to determine predictive factors of infection. We used SPSS software v. 21 (IL).
Results: 54 patients were included, 37% diagnosed with RA, followed by SLE 15%, psoriasis arthritis 9%, ankylosing spondylitis in 7%, Sjögren's syndrome 5.6%. Fifty nine percent used glucocorticoids. Of the bDMARD the most used was Rituximab 65%, abatacept 25%, tocilizumab 5%, adalimumab 4%, etanercept 2% and infliximab 2%. The mean time of use was 28.8 ± 21.1 months. 54% had infection, mainly genitourinary 30%, pneumonia 15%, others as skin or gastrointestinal were presented with lower frequency, out of all infections only 12% required hospitalization (serious adverse events).
No positive predictive factors for infection were found with the use of bDMARD, but adding this variable increased the risk of infection by 5%, however the use of concomitant therapy with mycophenolic acid was the most predictive risk for the presence of infection with an OR = 9,143 (95% CI 1.055 - 79.26) p = 0.045.
Conclusion: The patients on bDMARD presented a significant percentage of infections, in this study it was not shown that the use of biological therapy was a predictive factor for the risk of infections, but with the concomitant use of mycophenolic acid appears to increase the risk.

REFERENCES

[1] Cipriani P, Berardicurti O, Masedu F, D'Onofrio F, Navarini L, Ruscitti P, et al. Biologic therapies and infections in the daily practice of three Italian rheumatologic units: a prospective, observational study. Clin Rheumatol. febrero de 2017;36(2):251-60.
[2] atoid arthritis. Arthritis Care Res. julio de 2014;66(7):990-7.Curtis JR, Yang S, Patkar NM, Chen L, Singh JA, Cannon GW, et al. Risk of hospitalized bacterial infections associated with biologic treatment among US veterans with rheum
[3] Yun H, Xie F, Delzell E, Levitan EB, Chen L, Lewis JD, et al. Comparative Risk of Hospitalized Infection Associated With Biologic Agents in Rheumatoid Arthritis Patients Enrolled in Medicare. Arthritis Rheumatol Hoboken NJ. enero de 2016;68(1):56-66.

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SAT0703-HPR THE HEALTH INEQUALITIES ASSOCIATED WITH SEVERE MENTAL ILLNESS IN PEOPLE WITH RHEUMATOID ARTHRITIS

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Background: People with conditions such as schizophrenia, schizoaffective disorder, bipolar disorder, personality disorder and depression with psychosis are vulnerable and face a number of health inequalities,[1,2] including poorer healthcare. This may explain why those with a severe mental illness (SMI) die younger.[3] In arthritis, people with psychotic disorders who are over 65 are less likely to receive nonsteroidal anti-inflammatory drugs (NSAIDS) and disease-modifying anti-rheumatic drugs (DMARDS), than those without a psychotic disorder.[4] However, little is known about the prevalence of these conditions or whether disease outcomes differ to those in the broader rheumatoid arthirtis (RA) population.
Objectives: To establish the proportion of people with RA who are living with a SMI and whether fatigue, pain, function and disease activity differs to that of the general RA population.
Methods: The 2018 National Rheumatoid Arthirtis Society (NRAS) 'Emotional Health and Well-being Matters' survey was designed by people with RA and researchers. This included a questionnaire designed to capture self-reported co-morbidities and measures of fatigue and pain using a 100-point visual analogue scale, quality of life (using the shortened Arthritis Impact Measurement Scale[5]), functional disability (using the Health Assessment Questionnaire[6]) and patient-based disease activity.[7] Participants were recruited by NRAS via their social media platforms, membership and non-membership lists and in newsletters and the NRAS HealthUnlocked forum. The survey was open from May-July 2018. Recruitment was focused on those diagnosed with RA aged 18 years and over and living in the UK.
Results: A total of 1565 people with RA completed the survey, 2% (n=29) of whom reported having a diagnosis of SMI, the most common being bipolar disorder (n=12). After adjusting for age and gender, those

with RA and a SMI experienced significantly greater levels of pain (p=0.04), functional disability (p=0.01), along with poorer disease activity (p=0.03) and poorer quality of life (p<0.03) than those with RA, but without SMI. There was however, no significant difference in the receipt of DMARDS or NSAIDS between the two groups (p>0.12).

Conclusion: Prevalence rates of SMI are no greater in RA than the general population. Those with RA and a SMI do however experience significantly poorer clinical outcomes than people with RA but without SMI despite being in receipt of similar medications. Further research is needed to explore why these health inequalities exist and how best to ensure more positive outcomes for this vulnerable population.

REFERENCES

[1] Thornicroft G. Physical health disparities and mental illness: the scandal of premature mortality. Br J Psychiatry 2011; 199(6):441-442.
[2] Shiers D, Bradshaw T, Campion J. Health inequalities and psychosis: time for action. Br J Psychiatry 2015; 207(6):471-473.
[3] De Hert M, Correll CU, Bobes J, Cetkovich-Bakmas MARC, Cohen DAN, Asai I, et al. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. World Psychiatry 2011; 10(1):52-77.
[4] Redelmeier DA, Tan SH, Booth GL. The treatment of unrelated disorders in patients with chronic medical diseases. N Engl J Med 1998; 338 (21):1516-1520.
[5] Guillemin F, Coste J, Pouchot J, Ghézail M, Bregeon C, Sany J. The AIMS2−SF. A short form of the arthritis impact measurement scales 2. Arthritis Rheum 1997; 40(7):1267-1274.
[6] Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum 1980; 23(2):137-145.
[7] Choy EH, Khoshaba B, Cooper D, MacGregor A, Scott DL. Development and validation of a patient−based disease activity score in rheumatoid arthritis that can be used in clinical trials and routine practice. Arthritis Care Res (Hoboken) 2008; 59(2):192-199.

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SAT0704-HPR **PREVALENCE OF RHEUMATIC PATHOLOGY IN CHILDREN IN THE CENTRAL FEDERAL DISTRICT OF THE RUSSIAN FEDERATION, STRUCTURE OF MORBIDITY AND THERAPY**

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Background: Analysis of the incidence of rheumatic diseases in children can help to evaluate the real needs in treatment provision and improve medical service.
Objectives: To analyse the prevalence, structure of morbidity, and therapy of rheumatic pathology in children in the Central Federal District of the Russian Federation.
Methods: Statistical, sociological methods and content analysis were used. The study included generalised information on 3940 patients aged 1-17 years with various rheumatic diseases living in the 13 regions of the Central Federal District of the Russian Federation. The data is provided by the main paediatric rheumatologists of the regions.
Results: 5,999,124 children aged 0 to 17 years live on the territory of 13 regions of central Russia. In these regions, 3,940 patients with rheumatic diseases are observed. Our data allowed us to calculate the prevalence of rheumatic diseases per 100,000 children from 0 to 17 years. The prevalence of juvenile idiopathic arthritis (JIA) is 62.2, systemic lupus erythematosus - 0.7, juvenile dermatomyositis - 0.7, systemic scleroderma - 0.6. The overall incidence of the rheumatic disease is 65.7 per 100,000 children from 0 to 17 years. In the structure of rheumatic pathology, 94.7% are accounted for JIA, 1.1% for systemic lupus erythematosus, 1.0% for juvenile dermatomyositis, 0.9% for systemic scleroderma, 2.2% for other rheumatic diseases. 67.3% of patients receive disease-modifying anti-rheumatic drugs (DMARDs) (n = 2650), of which 80.1% receive methotrexate (n = 2122), 13.5% - sulfasalazine, 0.3% - leflunomide, 0.7% - cyclosporine A, 3.8% - corticosteroids, 0.7% - mycophenolate mofetil, 0.5% - hydroxychloroquine.
Biological therapy is received by 27.5% of patients suffering from JIA (n = 1026). The data differs depending on the region. In the Bryansk region, the proportion of patients receive biological therapy is 45.8%, in the Yaroslavl region - 41.2%, in Moscow - 40.7%. More rarely, the biological therapy is initiated in Kostroma - 11.9% and Oryol - 15.3% areas. The structure of biological therapy is dominated by TNF-alpha inhibitors - 71.3%. 41.6% of all children undergoing biologic therapy were prescribed etanercept, 27.2% - adalimumab. 18.1% of patients receive tocilizumab, 7.2% - abatacept, 1% - infliximab, 2.5% - canakinumab, 1.5% of patients receive golimumab.
Conclusion:
1. The overall incidence rate of rheumatic diseases in central Russian regions is 65.7 per 100,000 children from 0 to 17 years.
2. The prevalence of juvenile idiopathic arthritis is 62.2 per 100,000 children from 0 to 17 years old.
3. 67.3% of patients receive DMARDs. In 80.1% of cases, the drug of choice is methotrexate.
4. 27.5% of patients suffering from JIA receive biological therapy; data vary by region (45.8% –11.9%). The structure of biological therapy is dominated by TNF–alpha inhibitors – 71.3%.
5. At the level of various regions, countries, it is necessary to conduct research aimed at studying the causes influencing the overall incidence, the detectability of rheumatic diseases, and the structure of therapy.

REFERENCES

[1] Beukelman, T. The new Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry: design, rationale, and characteristics of patients enrolled in the first 12 months [Electronic resource]/T. Beukelman//Pediatric Rheumatology. – 2017. – Enable URL:

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HPR Measuring health (development and measurement properties of PROs, tests, devices)

SAT0705-HPR **PATIENTS' EXPERIENCES OF REASONS TO BEING PHYSICALLY ACTIVE IN EARLY RHEUMATOID ARTHRITIS – A MIXED METHODS STUDY**

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Background: The importance of physical activity in rheumatoid arthritis (RA) is well known and patients are informed about the importance of being physically active. Despite this knowledge there is a lack of compliance to this advice. Studies comparing physical activity in different groups of patients with RA and reasons influencing physical activity are needed.
Objectives: The objectives were to compare physical activity (PA) in workers, retired and patients with sick-leave with early RA and further to explore reasons to being physically active in these patients.
Methods: A total of 66 patients with early RA were included in the study. A sequential explanatory mixed methods design was used. The groups were compared with clinical data as: disease activity (DAS28); pain (VAS 0-100, best to worst); health-related quality of life (EQ5D, -0.594-1 worse to best) and a physical function (HAQ, 0-3 best to worst). ESR and CRP. Patients were dichotomized as being active on recommended levels of PA (MVPArec; physically active on a moderate level $\geq$150min/week (MPA) or on an intense level $\geq$75min/week (VPA)) or not (sedentary). The patients were grouped on self-reported working ability; workers, patients with sick-leave and retired patients.
Qualitative data was collected by a questionnaire with open-ended questions about reasons influencing PA. The qualitative data was analysed with a manifest qualitative content analysis to gain a greater understanding of patients' experiences of PA in early RA.
Results: There were no significant differences between the groups in disease activity, physical function, swollen joints, health-related quality of life

or inflammatory parameters (ESR, CRP). Patients on sick-leave had more tender joints median (min-max) 9 (2-18) vs. 4 (0-20) and 3 (0-10), p=0.013. Workers reported higher intensity of pain, though not significant. Retired patients fulfilled MVPA criteria to a higher rate (86%) than workers (42%) or patients with sick-leave (40%), p=0.010.
The qualitative content analysis resulted in three categories. Reasons to being physically active in patients with early RA were; limitations (pain, physical function, stiffness, limited strength and fatigue), awareness as motivation (fear of movement and health benefits) and external environment (weather, transports to activity, economy and time, especially for workers).
Conclusion: Knowledge of reasons to being physically active in patients with RA is important to facilitate and support the patients. Joint pain seems to be an issue for patients with sick-leave. This could be associated to fear of movement and in this aspect these patients need to be supported. Time could be a limiting issue for working patients, which need to be highlighted and solved for these patients.
Disclosure of Interests: None declared
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SAT0706-HPR THE RELATIONSHIP BETWEEN SUBJECTIVE AND OBJECTIVE METHODS FOR MEASURING PHYSICAL ACTIVITY STATUS OF AXIAL SPONDYLOARTHRITIS PATIENTS: QUESTIONNAIRE VERSUS ACCELEROMETER

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Background: Physical activity is getting more attention for the appropriate management of both disease itself and co-morbid conditions in patients with axial spondyloarthritis (axSpA). Many different tools are available for determining physical activity status. Although subjective tools such as questionnaires are quick and easy for gathering data, objective tools such as accelerometers might provide more accurate information.
Objectives: To investigate the relationship between a subjective physical activity questionnaire (International Physical Activity Questionnaire Short Form: IPAQ) and an accelerometer (Actigraph wGT3X-BT) for measuring physical activity status of axSpA patients.
Methods: Thirty-nine patients with axSpA (age 37.9±11.3 years, body mass index 26.9±5.3 kg/m^2, disease activity: 3.3±2.3 according to Bath Ankylosing Spondylitis Disease Activity Index, functional status: 2.9±2.8 according to Bath Ankylosing Spondylitis Functional Activity Index, 24 male) according to ASAS criteria were included to assess the subjective and objective physical activity status by using the Turkish version of IPAQ and an accelerometer (Actigraph wGT3X-BT), respectively. The accelerometer was worn by the patients on their waists at their first visit and it provides information about the light, moderate, vigorous physical activity times in minutes. On the seventh day when the accelerometer was removed, patients were asked to complete the IPAQ. The IPAQ inquires the physical activity performed previous week in minutes and categorizes into three sections as vigorous, moderate activity, and walking. The walking section in IPAQ was accepted as equal to light physical activity in Actigraph. The relationship between measurements was determined by using Spearman's Rank Correlation Coefficient.
Results: No significant correlations were determined between subjective and objective methods (p>0.05), except the time spent during moderate physical activity (rho: 0.457, p<0.05). It was also observed that IPAQ were underestimating the physical activity times for all types of physical activity (Table 1).

Abstract Table 1. The correlations between objective and subjective physical activity measurements

	Objective Measurement*	Subjective Measurement**	Spearman's Correlation	p
Light Physical Activity (min)	2270.26±1016.70	331.03±552.75	-0.037	0.825
Moderate Physical Activity (min)	243.97±167.9	90.26±241.39	**0.457**	**0.003**
Vigorous Physical Activity (min)	7.23±18.61	248.72±848.93	0.184	0.914
Total Physical Activity (min)	2521.46±1094.40	670.00±1183.30	0.271	0.095

*: Actigraph wGT3X-BT, **: IPAQ: International Physical Activity Questionnaire Short Form, p<0.05.

Conclusion: According to our results, IPAQ short version may not be an appropriate tool for determining physical activity status in axSpA patients. It seems that we need disease specific tools in axSpA.

REFERENCES

[1] Saglam M, Arikan H, Savci S, Inal-Ince D, Bosnak-Guclu M, Karabulut E, Tokgozoglu L. International physical activity questionnaire: reliability and validity of the Turkish version. Percept Mot Skills. 2010;111:278-84.

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SAT0707-HPR PATIENT AND CLINICIAN PERSPECTIVES USED FOR SURVEY DEVELOPMENT TO INVESTIGATE THE NATURE, EXTENT AND IMPACT OF FOOT PROBLEMS IN PEOPLE WITH PSORIATIC ARTHRITIS

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Background: Despite recognition that hallmark features of psoriatic arthritis (PsA), such as enthesitis, are predominant and persistent in the foot and ankle [1], limited research has focused on the foot. Few published studies have used RA-specific outcome measures unlikely to capture the dermatological impact in PsA and there has been little incorporation of the patient perspective [1]. The importance of patient and clinician involvement as a central component of research design has been identified in PsA [2, 3], and provides a basis for defining what should be measured to represent comprehensively the experience of people with PsA-related foot problems and important domains of impact.
Objectives: To develop a survey based on the views of people with PsA and clinicians on foot problems, their impact and the foot care needs.
Methods: Interviews of people with PsA-related foot problems and focus groups with clinicians on their understanding of the patient experience were undertaken in Sydney, Australia and Auckland, New Zealand. A representative sample from public and private sector, from lower and higher socioeconomic geographical areas, as well as clinicians with different professional backgrounds was sought. Based on the themes from the qualitative interviews, previous research [1, 3] and clinical experience, survey items were generated by the research team using a consensus based approach. The survey was pre-tested using a 4-stage method that comprised; cognitive de-briefing of people with PsA, expert review panels of subject and survey design experts, cultural sensitivity assessment and pilot testing. All focus groups and interviews were audio-record, transcribed verbatim and survey items were revised based on comments made.
Results: The final 60-item self-administered survey was developed based on feedback from each of the 4-stages, which related to wording, comprehension, timescales, content, repetition, number of survey items and overall survey design. Key survey domains included demographic (10%) and socioeconomic data (10%), global disease information (18%), foot and ankle characteristics (18%), and the impact of foot problems on daily

life including daily routine, footwear choice, family life, work and accessing health care (44%). Percentage coverage of items directly reflects the dominant concerns of people with PsA-related foot problems and clinicians. Whilst priorities for clinicians included the diverse expression of disease and determining the nature of foot symptoms as mechanical or inflammatory, a key theme from patients was the psychological impact of foot involvement on daily life coupled with self-management strategies (coping skills, self-care activities and availability of social support), which was poorly recognised by clinicians. Consequently, nearly a quarter of survey content was dedicated to these areas of impact highlight by patients (23%). Engaging patients and clinicians in the survey development methods ensured that face and content validity were confirmed and cognitive and usability standards were achieved.

Conclusion: By incorporating the views of those with the disease and of clinicians into the survey development process, good conceptual coverage of items important to both patients and clinicians was achieved whilst minimising responder burden. This is the first study to develop a survey on foot involvement in PsA based on best practice methods in qualitative survey design, which may have utility in the future development of assessment or screening tools.

REFERENCES

[1] Hyslop E, et al. Ann Rheum Dis. 2010;69:928.
[2] Carter K, et al. Clin Rheumatol. 2019;8:1-9.
[3] Orbai AM, et al. Ann Rheum Dis. 2016;76:673-680.

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SAT0708-HPR DEVELOPING AN ALLIED HEALTH CORE OUTCOME SET FOR PAEDIATRIC RHEUMATOLOGY MUSCULOSKELETAL CONDITIONS

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Background: Musculoskeletal (MSK) conditions are prevalent within the general population, including children and young people (CYP) with MSK pain. There is evidence that MSK pain in CYP is an antecedent of adult MSK pain. Paediatric Rheumatology Allied Health Professionals (PRAHPs) are well placed to manage these CYP, but there is no current standardisation in treatment, services or outcomes.

Objectives: To develop a core outcome measure set for clinical use by PRAHPs to facilitate national collaboration and standardisation of care.

Methods: A modified Nominal Group technique study was undertaken by an expert* panel of PRAHP's working in 8 Tertiary Paediatric and Adolescent UK centres. Literature search and presentation of findings informed expert panel discussion with particular reference to the following criteria: paediatric population specific, ease of clinical use, cost, general availability to clinicians, reliability, validity, length to administer/perform and previous research use. Expert panel discussion and ranking identified eight domains. A survey was sent to the 12 members of the expert panel asking participants to choose two measures or none, based on criteria above. Consensus was pre-determined as agreement between experts of 60% or more.

Results: Survey response rate was 83% with consensus achieved for 6 outcome measures- see table. Consensus could not be reached for hand function, sleep and goal-setting in part due to the large number of measures and variation in use, lack of paediatric specific measures, length of time taken to administer or costs involved. Psychological measures were not included within the scope of this work, but would be a valuable future addition.

Conclusion: This study informs a pilot outcome measure set for PRAHPs in clinical settings when time, space, money and ease of use are paramount.

Outcome domain selected by expert panel	Measure with consensus
Fatigue	Fatigue VAS
	PedsQL pain and fatigue scale
School attendance	% attendance rate
QoL	Peds QL
	MSK HQ
Muscle strength	Kendall scale
	MRC Oxford scale
Balance	Standardised single leg stand
Stamina	2 minute walk test
	Timed step test (1 minute)
Hand function	No consensus
Sleep	No consensus
Goal setting	No consensus

*Definition: Senior Level Tertiary PRAHP's

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SAT0709-HPR SPINAL MOBILITY IN SPONDYLOARTHRITIS PATIENTS: DO THE BASMI-MEASUREMENTS CORRELATE WITH THE DAVID BACK DEVICES-MEASUREMENTS?

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Background: The BASMI is a common used and well established index to measure spinal mobility in spondyloartritis(SpA)-patients, both in the clinic as well as for research. The David Back Devices (DBD) on the other hand, are used to measure and exercise lumbar and cervical mobility and strength in spine patients. The DBD might have the potential advance of not being operator dependent in contrast to the BASMI-measurements.

Hence, the question rose if the BASMI measurements that correspond with cervical rotation and lumbar lateral flexion movements on the DBD are correlated with one another.

Objectives: The aim of this study was to measure the spinal mobility in SpA-patients both by using BASMI measurements and by using the DBD and determine their relationship.

Methods: SpA-patients of the outpatient rheumatology department of the Ghent University Hospital (included in the Be-Giant cohort) were consecutively asked to participate in the study. After informed consent, BASDAI, BASFI and BASMI were evaluated. To measure mobility on the DBD both trunk and cervical range of motion for flexion, extension, lateral flexion and rotation were assessed. Spearman correlation coefficients were calculated for cervical rotation and lumbar lateral flexion.

Results: Thirty-one SpA-patients participated of which 18 were male (58%). Twenty-four (77%) were classified as axial SpA and 7 (23%) as peripheral SpA. Median time since diagnosis was 5 years. Mean age of the patients was 41 years (range: 21 – 58 years) and their BMI was on average 24 (range: 17-33). Averages for BASDAI, BASFI and BASMI were 2.6, 1.7 and 0.9 respectively.

There was a significant positive correlation between the cervical rotation measurement obtained by BASMI and DBD (ρ=0.84 for right and ρ=0.80 for left) as well as between the lateral flexion measurement obtained by BASMI and DBD (ρ=0.72 for right and ρ=0.65 for left). Due to the sitting position during testing the lumbar flexion by DBD, the range of motion was limited when the chest touched the thighs. Therefore, correlation could not accurately be determined between the modified Schöberindex and DBD lumbar flexion.

Conclusion: This study demonstrated that in SpA-patients, the BASMI measurements for cervical rotation and lumbar lateral flexion show high correlations when compared with the similar measurements on the DBD. The correlations for cervical rotation were better than those for lumbar lateral flexion.

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SAT0710-HPR RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY OSTEOPOROSIS DIAGNOSIS ON FEMORAL NECK: A SPANISH CLINICAL EXPERIENCE

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Background: Radiofrequency Echographic Multi Spectrometry (REMS) is an innovative echographic technology able to provide the most important densitometric parameters by a fully automatic approach. Its high accuracy with respect to the conventional Dual X-ray absorptiometry (DXA) has been shown in a very recently published multicenter clinical trial [1].
Objectives: To evaluate the performance of the REMS technology in osteoporosis diagnosis, with respect to DXA(Clinical Gold Standard), when applied on femoral neck.
Methods: DXA and REMS acquisitions were performed on the femoral neck in 324 female patients, aged between 51 and 70 year, recruited at the Department of Internal Medicine of the Hospital del Mar (Barcelona, Spain). REMS technology is based on a automatic integrated processing of the native unfiltered "raw" (RF) signals, which can be employed to assess the bone health status through comparisons with reference spectral models previously derived from osteoporotic and healthy patients. The data shown have been obtained in the strictest adherence to manufacturer's procedures and indications. REMS accuracy was assessed by investigating its discriminating ability between osteoporotic and non-osteoporotic patients and by evaluating the correlation between REMS and DXA measurements.
Results: The REMS approach is effectively able to discriminate between osteoporotic and non-osteoporotic patients with a sensitivity equal to 93% and a specificity equal to 95%. These data are further emphasized by the obtained Pearson Correlation value (r = 0.90; p<0.001). REMS accuracy was confirmed also by Cohen's kappa coefficient (k) equal to 0.76. Finally, a very low average difference (expressed as bias ± 2 SD) between REMS and DXA measured BMD (-0.006 ± 0.078 g/cm^2) was shown.
Conclusion: In conclusion, REMS technology has proven to be an accurate non-ionizing approach to detect osteoporosis disease at the femoral neck. The performance of this radiation-free technique opens new perspectives for early diagnosis and screening of osteoporosis in clinical and epidemiological studies.

REFERENCE

[1] Di Paola et al, Osteop. Int., 2018

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SAT0711-HPR ADDING INFORMATION ON WIDESPREAD PAIN TO THE START BACK SCREENING TOOL WHEN IDENTIFYING LOW BACK PAIN PATIENTSAT INCREASED RISK FOR POOR PROGNOSIS

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Background: Early identification of those with the highest risk of developing chronic low back pain (CLBP) is important but difficult. STarT Back Screening Tool (SBST) is reported to capture patients at high risk of developing CLBP, but does not include concurrent pain from other locations, which is a known risk factor for worse outcome.
Objectives: To study differences in self-reported health between patients with low, medium and high risk of developing CLBP identified by the combination of SBST and information on widespread pain.
Methods: Adults aged 18-67 seeking primary care for LBP in the southwest of Sweden were included. The STSB was used to differentiate between three risk levels; low, medium and high risk. When patients were classified as medium risk, information from a pain mannequin on widespread pain and multisite pain were added to further distinguish between high and medium risk. If widespread pain and pain from more than seven locations (multisite pain) were reported, patient was transformed from the medium risk to the high risk group. Differences between the three risk groups with regard to physical function (Roland Morrison Disability Questionnaire (RMDQ), 0-24 best-worst), mental health (Hospital Anxiety and Depression scale (HADa and HADd) 0-21 no distress-maximum distress), health related quality of life (EuroQol-5D (EQ5D), 0-1 worst-best), fear avoidance for physical activity (PA) and work (Fear-Avoidance Beliefs Questionnaire (FABQ) PA, 0-24, and work, 0-42 best-worst) were analyzed in an ANOVA.
Results: Ninety-five patients (61% women), mean (SD) age 42 years (14) seeking health-care for their LBP were included in the study. Of those scoring low risk on SBST (n=19), 3 also reported multisite CWP. Of those who scored medium risk on SBST (n=48), 8 reported multisite CWP and were moved to the high risk group. Of 17 scoring high risk on SBST, 4 simultaneously reported multisite CWP. After constructing three risk groups combining SBST and multisite CWP, there were 19 in the low risk group, 40 in the medium risk group, and 25 in the high-risk group. The low, medium, high risk groups identified by the combined method, differed statistically significant in reported RMDQ (low, medium, high mean respectively 7.0, 12.2, 13.4, p<0.001), HADa (3.7, 6.4, 10.1, p<0.001), HADd (2.9, 4.0, 8.4, p<0.001), FABQ PA (9.1, 12.7, 14.4, p=0.005), FABQ work (9.9, 16.7, 23.1 p=0.001), EQ5D (0.72, 0.53, 0.38, p=0.001).
Conclusion: Adding information on multisite widespread pain to the SBST resulted in classifying more patients in the high risk group as compared to using only SBST. The three groups identified by combing the screening tools differed significantly on all investigated health variables, indicating the combination may be capturing more patients at risk for CLBP.
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SAT0712-HPR VALIDATION OF THE TEST FOR SUBSTITUTION PATTERNS – IN INDIVIDUALS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS

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Background: Few tools evaluates quality of movements in individuals with knee osteoarthritis (OA). The Test for Substitution Patterns (TSP) is developed to measure the ability to perform five functional movements regarding postural control and altered movement patterns (1). TSP is validated and reliable in individuals with anterior cruciate ligament injury, but has not yet been evaluated in individuals with knee OA.
Objectives: To study the relationships between the OA modified TSP (OA-TSP) and self-reported knee function as measured with the Knee Injury and osteoarthritis Outcome Score (KOOS) and the 30-s chair stand test (30-s CST) in individuals with symptomatic knee OA. A second aim was to study the discriminative ability of the OA-TSP for unilateral knee pain.
Methods: Sixty-two individuals with symptomatic knee osteoarthritis were included using consecutive sampling. Health status was assessed with the EuroQol five dimension scale (EQ5D, 0-1 worst-best), and knee function in five subscales for KOOS (pain, symptoms, ADL, quality of life and sport/recreation, 0-100 worst-best). The 30-s CST-test measured the number of rises in 30 seconds. In the OA-TSP, substitution patterns are observed and scored from 0-3 (no substitution pattern-poorly performed) during five standardized functional movements. The maximum score is 54 points/side with score of 108 points. Median and min-max were used for all descriptive data. Spearman´s correlation and Wilcoxon signed rank test were used for analyzes. A correlation coefficient $r_s \geq \pm 0.50$ is considered large, ±0.30 to < 0.50 moderate and ±0.10 < 0.30 small.
Results: The median age was 54 years (30-61), 76% were women. The median Body Mass Index was 25 (18-48) and EQ5D 0.8 (0.29-1.00). There were no significant differences between the gender regarding BMI and EQ5D. Median OA-TSP total score was 29 (10-70). Median KOOS pain was 75 (36-100), symptoms 71 (21-96), ADL 87 (30-100), and sport/rec 50 (0-100). In the 30-s CST the median was 16 raises (5-32). Moderate, significant correlations were observed between TSP total score and KOOS pain and KOOS ADL (r_s=-0.30; p=0.03, r_s=-0.35; p=0.01

respectively) and small correlations between TSP and KOOS sport/recreation and KOOS symptoms (r_s=-0.13; p=0.36, r_s=-0.22; p=0.11 respectively). There was a moderate, significant correlation between TSP total score and 30-s CST (r_s=-0.34; p<0.01). Discriminative ability for the TSP for unilateral knee pain was found to be significant worse in the painful side, with median 18 (2-36) vs. 14 (7-37) in the not painful side, p=0.001.

Conclusion: The OA-TSP could be used as a functional test to detect altered knee alignment interpreted as an early sign of knee OA and assist the physiotherapist in functional testing during the rehabilitation of individuals with symptomatic knee OA.

REFERENCES

[1] Trulsson A, et al. Relationships between postural orientation and self reported function, hop performance and muscle power in subjects with anterior cruciate ligament injury. BMC Musculoskelet Disord. 2010;11:143.

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SAT0713-HPR DYNAMIC JOINT STABILITY MEASURED AS GAIT SYMMETRY IN PEOPLE WITH SYMPTOMATIC KNEE OSTEOARTHRITIS

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Background: Modern strategies for knee osteoarthritis (OA) treatment and prevention includes early detection and analyses about pain, gait and lower extremity muscle function including both strength and stability. The very first sign of knee OA is pain or perceived knee instability, often experienced during weight bearing activities e.g. walking. Increased muscle strength will provide dynamic joint stability, reduce pain, and disability. Specific measures of gait symmetry (GS) can be assessed objectively by using accelerometers, which potentially is a feasible method when evaluating early symptoms of symptomatic knee OA.

Objectives: The aim was to study if symptoms of early knee pain affected gait symmetry, and the association between lower extremity muscles function and gait symmetry in patients with symptomatic knee OA.

Methods: Thirty-five participants (mean age 52 SD 9 years, 66% women) with uni- or bilateral symptomatic knee OA, and without signs of an inflammatory rheumatic disease or knee trauma were included. Pain was assessed by a numeric rating scale (NRS, range 0-10 best to worse), tests of lower extremity muscle function with the maximum number of one leg rises. Dynamic stability was measured as GS by using wearable inertial sensors (PXNordic senseneering platform), during the 6 min walking test to obtain spatio-temporal gait parameters. GS was computed based on stride time (temporal symmetry, TS) and stride length (spatial symmetry, SS). Stride length was normalized by height. Kruskal-Wallis and Spearman's correlation coefficient were used for analyses.

Results: Reports of knee pain did not differ between gender (women 4.7, SD 2.4 vs. men 3.9, SD 2.4, p= 0.362), neither did one leg rises or gait symmetry. Participants who reported unilateral knee pain (left/right side n=9/13), had a shorter stride length on the painful side. The mean difference in stride length was 0.7% of the subject's height (SD 1.3). Participants with unilateral pain also presented less SS gait than those who reported bilateral pain (p=0.005). The higher number of one-leg rises performed, the better TS was observed. We found a significant relationship between TS and one-leg rise for the right r_s=-0.39, p=0.006, and left r_s=-0.40, p=0.004 left side). No significant relationship was observed between SS and one-leg rises.

Conclusion: Our results is in line with earlier findings stating that knee pain affects GS negatively and that lower extremity muscle function is an important feature for symmetry and dynamic joint stability in patients with symptomatic knee OA. We also found that pain in one leg was related to impaired GS. Bilateral knee pain was however more symmetrical and will need healthy controls for comparison to better understand the negative impact of symptomatic knee OA.

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SAT0714-HPR THE EFFECTS OF EXERCISE ON PAIN AND DEPRESSION IN MOTHERS OF DISABLED CHILDREN WHO SUFFER FROM BACK PAIN

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Background: The rate of back pain prevalence and its subsequent negative psychological effects is quite high in mothers of disabled children. Family caregivers of children with a disability demonstrate higher degrees of chronic conditions and are more likely to engage in health risk behaviors (1, 2).

Objectives: The purpose of this study was to investigate the effects of home exercise programs on mothers' back pain, relevant functional influence and the depression level (3).

Methods: Forty-two mothers aged 35,71±6,53 were included in this study whom children were diagnoses with cerebral palsy. Back pain level of the mothers was measured with Visual Analogue Scale (VAS), relevant functional disability was measured with Oswestry Disability index and depression level was measured with Beck Depression Scale. Disability level of their children was measured with Gross Motor Function Classification System (GMFCS). Following the assessments, a home exercise program consisting of Dynamic Lumbar Stabilization Exercises was given to mothers. They were asked to perform the exercises for three months and exercises were checked once in a month.

Results: GMFCS average of the children was 3,35±1,57. There was a significant difference in the pain level (VAS) changed from 4,90±2,67 to 3,21±2,50 after the exercise (p=0,000). The difference between the Oswestry Disability Index score before (13,92±8,32) and after the exercise (10,76±8.54) was statistically significant (p=0,001). Also there was a significant difference in the Beck Depression Scale score decreased from 25,16±9,46 to 12,76±7,50 (p=0,009).

Conclusion: Mothers with disabled children complain about back pain during activities such as caregiving their children (4). This study reveals that back pain, relevant functional influence and depression could be reduced in mothers by perform recommended exercises regularly.

REFERENCES

[1] Lee, M. H., Park, C., Matthews, A. K., & Hsieh, K. (2017). Differences in physical health, and health behaviors between family caregivers of children with and without disabilities. Disability and health journal, 10(4), 565-570.
[2] TeRzi, R., & Tan, G. (2016). Musculoskeletal system pain and related factors in mothers of children with cerebral palsy. Agri J. Turk. Soc. Algol, 28, 18-24.
[3] Murphy, K. M., Rasmussen, L., Hervey-Jumper, S. L., Justice, D., Nelson, V. S., & Yang, L. J. S. (2012). An assessment of the compliance and utility of a home exercise DVD for caregivers of children and adolescents with brachial plexus palsy: a pilot study. Pm&r, 4(3), 190-197.
[4] Glinac, A., Matović, L., Delalić, A., & Mešalić, L. (2017). Quality of Life in Mothers of Children with Cerebral Palsy. Acta clinica Croatica, 56(2.), 299-307.

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SAT0715-HPR BREAKING BAD: REPORTING OF VERTEBRAL FRAGILITY FRACTURES AND THE IMPACT TO MANAGEMENT OF BONE HEALTH

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Background: Vertebral fragility fracture (VFF) is the most common osteoporotic fracture and a strong predictor for future vertebral fracture(s) and/or hip fracture. A clear reporting of VFF by radiologists offers ample opportunity for early diagnosis and appropriate management of osteoporosis among treating physicians.

Objectives: The objectives of this study were two-fold; to evaluate 1) the reporting of VFF by radiologists at one of the largest acute hospitals in southern Ireland 2) the management of osteoporosis (adherence to

screening for secondary causes and commencement/switching of anti-resorptive therapy accordingly) for patients with VFF.
Methods: We conducted a retrospective cross sectional study involving all patients (n=199) who attended our specialist rheumatology outpatient clinics at University Hospital Kerry during the month of November 2018. Patients who previously had undergone plain radiography of the spine (PRS) in the previous 5 years were identified and reassessed for evidence of VFFs. Basic demographic, drug history, clarification of fragility fracture and previous related trauma, investigations for secondary causes of osteoporosis, and treatment received for osteoporosis were documented.
Results: 73 of the 199 patients had undergone previous PRS, 9 of which had evidence for VFFs. Only two patients (22.2%) were reported as having vertebral "fractures", while 7 others had different terms used to describe the fracture(s)-2 patients with "wedging", 1 with "compression", 2 with "loss of height" and 2 with "collapse". All (2 patients; 100%) with VFF reported as "fracture" had complete clarification of VFF, secondary osteoporotic work-up and treated with anti-resorptive therapy accordingly. Among the other 7 patients with VFFs but not reported as having "fracture", 1 patient had concomitant report of "osteoporotic" bones and had complete management for osteoporosis. 4 patients had concomitant report of "osteopenia", 3 (75%) of which received complete management for osteoporosis; while only 50% (1 patient) of the 2 remaining patients without further description of bone density received appropriate management. Further 6 patients with non-VFF were reported to have reduced bone density (1 reported as "osteoporotic" bones; 5 as "osteopenic" bones). Only one of them (16.7%) had further work-up, evaluation and management for osteoporosis.
Conclusion: Clear radiological report of PRS with VFFs using the word "fracture" is a strong predictor for appropriate management of bone health. It is essential that other terms used to describe VFFs such as "wedging", "compression", "loss of height" and "collapse" not to be used alone without the concomitant use of the word "fracture".
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SAT0716-HPR SYSTEMATIC REVIEW OF THE PSYCHOMETRIC PROPERTIES OF PATIENT-REPORTED OUTCOME MEASURES FOR FOOT AND ANKLE IN RHEUMATOID ARTHRITIS

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Background: Foot problems and pain are common in patients with rheumatoid arthritis. Patient-reported outcome measures provide a standardized method of capturing patients' perspectives of their functional status and wellbeing. There are many instruments specific to people with feet affected by rheumatoid arthritis but knowledge of their psychometric validation or methodological quality is lacking
Objectives: To identify patient-reported outcome measures specific to the foot and ankle and rheumatoid arthritis and investigate their methodological quality and psychometric properties
Methods:
Design: Systematic review. ***Data source***: A search was conducted for psychometric or validation studies on patient-reported outcomes in Rheumatoid Arthritis published in different languages, by examining the Pubmed; Scopus, CINAHL; PEDro and Google Scholar databases. ***Review methods***. The systematic review performed was based on the following inclusion criteria: psychometric or clinimetric validation studies on patient-reported outcomes specific to the foot and ankle that included patients with Rheumatoid arthritis. Two authors independently assessed the quality of the studies and extracted datas
Results: Of the initial 431 studies, fourteen instruments met the inclusion criteria. Significant methodological flaws were detected in most with only SEFAS met the COSMIN quality criteria.
Conclusion: SEFAS had the best quality and was ranked most appropriate for use with patients living with Rheumatoid Arthritis

REFERENCES

[1] Terwee CB, Jansma EP, Riphagen II, De Vet HCW. Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. Qual Life Res. 2009;18(8):1115–23.
[2] Prinsen CAC, Mokkink LB, Bouter LM, Alonso J, Patrick DL, de Vet HCW, et al. COSMIN guideline for systematic reviews of patient-reported outcome measures. Qual Life Res [Internet]. 2018;27(5):1147–57. Available from: http://dx.doi.org/10.1007/s11136-018-1798-3
[3] Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: An international Delphi study. Qual Life Res. 2010;19(4):539–49.
[4] Terwee CB, Lidwine @bullet, Mokkink B, Knol DL, Ostelo RWJG, Bouter LM, et al. Rating the methodological quality in systematic reviews of studies on measurement properties: a scoring system for the COSMIN checklist. Qual Life Res [Internet]. 2012 [cited 2018 Apr 4];21:651–7. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3323819/pdf/11136_2011_Article_9960.pdf
[5] Cöster MC, Bremander A, Rosengren BE, Magnusson H, Carlsson Å, Karlsson MK. Validity, reliability, and responsiveness of the Self-reported Foot and Ankle Score (SEFAS) in forefoot, hindfoot, and ankle disorders. Acta Orthop [Internet]. 2014 Apr 25 [cited 2018 Apr 24];85(2):187–94. Available from: http://www.tandfonline.com/doi/full/10.3109/17453674.2014.889979

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Table 1. Detailed COSMIN ratings

	Structural Validity	Internal Consistency	Reliability	Measurement Error	Hypotheses testing for construct validity	Cross Cultural Validity/ Measurement Invariance	Criterion Validity	Responsiveness
FFI	+	+	-	?	?	?	?	?
AOS	-	?	+	?	?	?	-	?
FHSQ	-	?	+	?	-	-	?	-
MFPDI	-	?	-	?	?	-	?	?
ROFPAQ	-	?	+	?	?	?	-	?
PHQ	-	?	?	?	?	?	-	?
RAOS	-	?	+	?	?	?	-	?
FAM	-	?	-	?	?	?	-	?
AAOS								
FAAM	-	?	+	+	-	?	-	+
BFS	+	+	-	?	?	?	?	?
LFIS	-	?	+	?	?	-	?	?
SAFE	-	?	+	?	-	?	+	-
SEFAS	-	?	+	?	+	?	-	+
FAOS	-	?	-	?	?	-	?	?

Rating: "+": Positive rating; "?": Indeterminate rating; "-": Negative rating

SAT0717-HPR CONSTRUCT VALIDITY AND RELIABILITY OF A PORTUGUESE VERSION OF THE ANIMATED ACTIVITY QUESTIONNAIRE (AAQ)

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Background: The AAQ assesses activity limitations in individuals with hip/knee osteoarthritis (HKOA), and consists video animations of 17 basic daily activities performed with different levels of difficulty (www.myaaq.com). The individuals choose the animation that best matches their own performance. The AAQ was developed in the Netherlands, and showed a good overall cross-cultural validity in 6 other languages.
Objectives: The aims of this study were to assess the construct validity and reliability of the Portuguese version of the AAQ.
Methods: In Diamantina, Brazil, men and women ($\geq$ 45 years) with clinical HKOA were included in the study. The exclusion criteria were: cognitive impairment, visual/auditory deficit, or any medical condition other than HKOA that could hamper activity. This study was approved by the UFVJM Ethics Committee. All participants completed the Portuguese version of the AAQ. Illiterate or functional illiterate participants were assisted by the researchers. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), to assesses pain, stiffness and function was administered to the participants. Performance-based tests were applied to a subgroup of 71 participants: Timed Up and Go (TUG) and Short Physical Performance Battery (SPPB). The first 53 participants completed the AAQ twice. To validate the AAQ, Spearman's rho coefficients were calculated between the AAQ score, each score of the WOMAC, the SPPB score, and TUG score. To evaluate the influence of education in completing the AAQ, the participants were divided in two groups, 0-3 years of education and $\geq$4 years of education. To evaluate internal consistency and test–retest reliability of the AAQ, we calculated the Cronbach's alpha coefficient and the intraclass correlation coefficient (ICC), respectively.
Results: 200 individuals, 85% female, mean age of 64.4 (SD 11.2) years, and a mean of 5.8 (SD 4.4) years of education, participated in the study. 72% of the participants had knee OA, 9% had hip OA, and 19% had both joints affected. The mean values on the different measures were as follow: AAQ = 72.7 (SD 16.1), WOMAC pain = 36.5 (SD 19.3), WOMAC stiffness = 37.1 (SD 26.2), WOMAC function = 39.1 (SD 19.6), SPPB = 8.0 (SD 2.1), and TUG = 16.2 (SD 12.7) seconds. The AAQ showed high internal consistency (Cronbach's alpha = 0.94) and good test-retest reliability was (ICC = 0.98). The AAQ showed a moderate correlation with WOMAC pain (r_s = -0.51, 95%CI = -0.61 to -0.39), and WOMAC stiffness (r_s = -0.46, 95%CI = -0.56 to -0.33), and a high correlation with WOMAC function (r_s = -0.77, 95%CI = -0.82 to -0.71), SPPB (r_s = 0.65, 95%CI = 0.48 to 0.77), and TUG (r_s = -0.71, 95%CI = -0.81 to -0.56). Regarding the level of education, the correlations between the AAQ score and the three domains of the WOMAC were similar when the participants with 0-3 years of education (n = 62) were compared to the participants with $\geq$4 years of education (n=138) (pain: r_s = - 0.51, 95%CI = -0.68 to -0.29 vs -0,52, 95%CI = -0.64 to -0.39; stiffness: r_s = - 0.54, 95%CI = -0.70 to -0.32 vs -0,41, 95%CI = -0.54 to -0.25; function: r_s = - 0.80, 95%CI = -0.88 to -0.68 vs -0,75, 95%CI = -0.82 to -0.66).
Conclusion: The Portuguese version of the AAQ showed good construct validity and reliability, and also seems to be applicable for patients with low literacy.

REFERENCE

[1] Peter WF, et al. Cross-cultural and construct validity of the Animated Activity Questionnaire. Arthritis Care Res. 2016.

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SAT0718-HPR VALIDATION OF THE DANISH VERSION OF THE BRISTOL RHEUMATOID ARTHRITIS FATIGUE QUESTIONNAIRES

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Background: The revised Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ) and the revised BRAF numerical rating scales (BRAF-NRSv2) are available in 33 languages and are validated in six countries (1), but not yet in Danish.
Objectives: To validate the Danish version of the BRAFs.
Methods: We surveyed patients with Rheumatoid Arthritis (RA) visiting one of three Danish outpatient clinics. The four-factor structure and internal consistency were explored by factor analysis and Chronbach's α. The fatigue construct validity was tested by Spearman correlations with the SF-36 vitality subscale and the VAS-fatigue. Wider construct validity was tested by correlations with VAS-pain, VAS-fatigue, VAS-global, Hospital Anxiety and Depression Subscales (HADS) and the Health Assessment Questionnaire (HAQ). We asked 120 of the patients to complete the BRAFs before and after their visit in order to be able to explore reliability.
Results: A total of 225 patients participated, 69.9% were female, mean (SD) age 59.3(0.87), disease duration 11.11(0.63) years, HAQ 0.71(0.05) and DAS28-CRP 2.55(0.08). The four-factor structure of the BRAF-MDQ and the uni-dimensionality of each of the four subscales were confirmed. Internal consistency for the BRAF-MDQ total was a Cronbach's α of 0.94 and 0.79-0.92 for the four subscales. The correlation coefficients between the BRAF-MDQ and the SF-36 vitality subscale were r=0.75, r=0.65 and r=0.74 for the anxiety and depression subscales of the HADS, respectively and r=0.62, r=0.73 and r=0.62 to VAS-pain, VAS-global and HAQ, respectively. Intra Class Coefficient for agreement was 0.995. The Bland-Altman plot showed a mean difference of 1.9 and a variance of 9.8 (-6.8 to 3.0) for BRAF-MDQ with 95% confidence interval. The correlation coefficients for the BRAF-NRS subscales and the subscales of the BRAF-MDQ, the SF-36 vitality subscale and the VAS-fatigue ranged between 0.57-0.93, 0.54-0.68 and 0.66-0.82, respectively.
Conclusion: The Danish version of the BRAF-MDQ identifies the same four aspects of fatigue as the original version, showed good internal consistency, moderate-good construct validity reflected by similar correlations to the SF-36 vitality subscale, HADS, HAQ and VAS for pain, fatigue and global health as the original UK-version and good reliability. The BRAF-NRS had moderate construct validity. The Danish BRAFs are considered valid and reliable for identifying aspects of fatigue among Danish patients with RA.

REFERENCES

[1] Hewlett, S; Kirwan J, Bode C, et al. (2018): The revised Bristol Rheumatoid Arthritis Fatigue measures and the Rheumatoid Arthritis Impact of Disease scale: validation in six countries. Rheumatology 57:300-308.

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SAT0719-HPR FOOT PRESSURE DISTRIBUTION AND FUNCTIONAL LEVELS: ANKYLOSING SPONDYLITIS VS CONTROLS

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Background: Ankylosing spondylitis (AS) is a chronic rheumatic disease characterized by the inflammation of the pelvis and spine with a tendency to bony ankylosis. The most common AS-related alterations in posture are, the limitation of spinal mobility, head protraction, loss of lumbar lordosis, increased dorsal kyphosis, flexion contracture of the hip and consequent flexion of the knee.

Objectives: The purpose of this study was to investigate the foot pressure distribution and functional levels differences in ankylosing spondylitis and also compare with healthy individuals.

Methods: Eighteen patients with ankylosing spondylitis (median age= 42.2 ±2.4 years, median BMI=25.27±1.27 kg/m^2) and 17 controls (median age= 43.1±2.4 years, median BMI=26.78±0.65 kg/m^2) were included in the study. Plantar pressure distribution was recorded by Digital Biometry Scanning System and Milletrix software (DIASU, Italy). The static test was used to determine the maximum foot pressure (N/cm^2) of the foot, forefoot weight ratio, rarefoot weight ratio, total load and foot angle axis (FAA). When evaluating spinal mobility; lumbar flexion, lateral flexion and tragus to wall distance were used in Bath Ankylosing Spondylitis Mobility Index (BASMI) sub-parameters. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to determine the disease activity; The Bath Ankylosing Spondylitis Functional Index (BASFI) was used to measure functional impairment; The Ankylosing Spondylitis Quality of Life (ASQoL) Questionnaire was filled out by the patients in an attempt to understand the impact of the disease on the quality of life. Mann-Whitney U test was used to compare AS groups with the control group. Spearman test was used for correlation analysis.

Results: No difference between age (p=0.031) and BMI (p=0.012) in both groups. There were no differences modified Schober (p=0.184), lumbar flexion (p=0.160) and tragus to wall distance (p=0.434). But lower right lateral flexion (p=0.003) and left lateral flexion (p=0.001) in ankylosing spondylitis group when compared to healthy individuals. Rearfoot load higher than forefoot load in ankylosing spondylitis group (p=0.001). There were no differences static and dynamic analysis parameters ankylosing spondylitis group and healthy group. In addition to right lateral flexion (r=0.645 p=0.005) and left lateral flexion (r=0.641 p=0.04) correlated foot angle axis; tragus to wall distance correlated maximum foot pressure (r=0.578 p=0.015) and average foot pressure (r=0.542 p=0.025).

Conclusion: Lumbar spine flexibility was lower and associated with foot pressure distribution in AS patients. In addition, the load distribution between the rare and fore foot was different in these patients. Therefore, the foot pressure distribution as well as the spine flexibility should be monitored closely, when implementing and designing the exercise programs in patients with AS.

REFERENCES

[1] Carroll, et al. Gait characteristics associated with the foot and ankle in inflammatory arthritis: a systematic review and meta-analysis. BMC Musculoskeletal Disorders (2015) 16:134

[2] Haddas, et al. Clinical Gait Analysis on a Patient Undergoing Surgical Correction of Kyphosis from Severe Ankylosing Spondylitis. Int J Spine Surg. 2017 Jun 21;11:18

[3] Zhang, et al. The gait deviations of ankylosing spondylitis with hip involvement Clin Rheumatol. 2019 Jan 4. doi: 10.1007/s10067-018-4401

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SAT0720-HPR PULMONARY FUNCTIONS AND RESPIRATORY MUSCLE PERFORMANCE CORRELATE WITH NIGHT PAIN IN PATIENTS WITH ANKYLOSING SPONDYLITIS COMPARED TO CONTROLS

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Background: In ankylosing spondylitis (AS), chronic systemic inflammation mainly affects the axial skeleton and involvement the costovertebral and costotransvers joints results in limitation of thoracic and spinal mobility (1,2). There is no study published to evaluate the endurance and strength of respiratory muscle and to investigate the relationship with pain.

Objectives: The aim of the study was to investigate the functional status, quality of life, pain, pulmonary function, respiratory muscle strength and endurance patients with AS and compare to healthy controls.

Methods: Standard pulmonary function tests, maximum inspiratory pressure (PImax), and maximum expiratory pressure (PEmax) for pulmonary volumes and respiratory muscle strength were applied. Respiratory muscle endurance was recorded using sustained threshold loading of 40% maximal inspiratory pressure. AS group were evaluated by using the functional status and quality of life, the Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL). The severity of night pain, morning pain and morning stiffness were evaluated by Visual Analog Scale (VAS) in patients with AS. Mann Whitney-U test and Student-t Test were used to compare to groups variables. To evaluate the correlation in AS group Spearman's Test was used.

Results: A total eleven patients (6 female, 5 male; mean age: 41±9.4yrs, body mass index (BMI): 26.1±6.3kg/m^2 and duration of disease 22 ±24.9months) and eleven controls (6 female, 5 male; mean age: 42.9 ±12.7yrs and BMI: 25±3.6kg/m^2) were included in this study. There were no differences in age (p=0.554) and BMI (p=0.922) between the groups. No difference between FEV1% (p=0.069), FEV1/FVC% (p=0.243), PEF% (p=0.490), FEF25-75% (p=0.297), MVV% (p=0.450), PImax (p=0.694), PEmax (p=0.358) and respiratory muscle endurance (p=0.341) in both groups. But FVC% (p=0.041) significantly lower in AS group compare to controls. In addition to PImax (r= -0.800, p=0.003), PEmax (r=-0.683, p=0.021) and respiratory muscle endurance (r=-0.683, p=0.021) were correlated the night pain level in AS group. The respiratory muscle endurance (r=-0.675, p=0.023) was correlated the duration of disease. No correlations to the functional status, quality of life indexes and pulmonary functions in AS group.

Conclusion: This study shows that patients with AS have clearly reduced maximal PImax and PEmax, indicating decreased respiratory muscle strength and endurance as night pain levels increased. If indeed the respiratory strength were to be unchanged or even increased the decreased respiratory muscle strength should be due to reduced strength or atrophy of intercostal or accessory muscles, or both. Although the present data do not provide the direct evidence of intercostal muscle atrophy, it is tempting to speculate that immobilization of these muscles due to thoracic rigidity and decreased inspiratory intercostal and accessory activation leading to disuse may be an important factor contributing to it.

REFERENCES

[1] Sahin G, Guler H, Calikoglu M, et al. A comparison of respiratory muscle strength, pulmonary function tests and endurance in patients with early and late stage ankylosing spondylitis. Z Rheumatol 2006; 65: 535–538.

[2] Basakci Calik B, Gur Kabul E, Taskin H, et al. The efficiency of inspiratory muscle training in patients with ankylosing spondylitis. Rheumatol Int 2018;38:1713–1720.

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SAT0721-HPR INVESTIGATION OF FUNCTIONAL OUTCOMES AND QUALITY OF LIFE IN YOUNG ADULTS WITH INTERNAL FIXATION SURGERY OF FEMORAL SHAFT FRACTURE

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Background: Femoral Shaft Fracture (FSF) is a severe injury with incidance 10-21 per 100,000 persons/year[1]. The union rate is reported between 95–99 %[2]. Unfortunately, even after union a number of patients still report impairments and limitations in functional outcomes and quality of life (QoL)[3]. The literature lacks studies evaluating long-term functional outcome and performance and QoL.

Objectives: The aim of this study was to compare the functional outcomes and quality of life of the young adults who underwent internal fixation (IF) surgery of femoral shaft fracture (FSF) to the healthy individuals.

Methods: Twenty patients who underwent IF surgery of FSF by the same surgeon and 20 healthy individuals were included in this retrospective study. Individuals with secondary osteoporosis risk were not included. Function of both two groups was assessed using Harris Hip Score. To evaluate performance Stair Climb Test (SCT) is applied. Quality of life was assessed by the EQ-5D-3L HrQoL. The Mann Whitney U-Test was used to compare the results of the function, performance and quality of life of the two independent groups. Statistically, $p<0.05$ was accepted as a significant difference.

Results: The mean time after surgery was 2.2±0.8 years. Comparing to the healthy group, the EQ-5D-3L VAS and TTO scores of the patient group were significantly lower ($p<0.001$). When the function results were compared between the groups, the mean total HHS of the patient group were found significantly lower ($p<0.001$). The results of mean stair climbing time in healthy group were significantly lower ($p<0.001$). Descriptive outcomes and results' details is shown in Table 1.

Abstract SAT0721HPR Table 1. Patient characterictics, functional outcomes and QoL scores

Patient Group	Healthy Group		
	M±SD	M±SD	p-Value
Age (year)	39,55 ± 11,92	42,75 ± 8,83	0,43
Height (cm)	170,70 ± 8,51	170,15 ±8,86	0,86
Body Weight (kg)	75,45 ± 12,68	74,01 ± 15,03	0,79
Body Mass Index (kg/m^2)	25,85 ± 3,76	25,40 ± 3,86	0,82
HHS Overall (point)	71,65 ± 15,42	94,99 ± 5,74	< 0,001**
SCT Overall (sec)	11,58 ± 6,55	5,53 ± 0,89	< 0,001**
EQ-5D-3L VAS	0,527 ± 0,182	0,849 ± 0,147	< 0,001**
EQ-5D-3L TTO	0,513 ± 0,266	0,874 ± 0,131	< 0,001**

Mann-Whitney U Test**, M±SD:** Mean score and Standart Deviation

Conclusion: The results of the study showed that there were deficiencies in long-term function, performance and quality of life in young adults after IF surgery compared to healthy individuals. Therefore, we suggest that the assessment of the in long-term functional outcomes and quality of life of the patients with FSF after IF surgery is necessary to plan appropriate rehabilitation programs by determining the patient's needs.

REFERENCES

[1] Enninghorst N, McDougall D, Evans JA. Population-based epidemiology of femur shaft fractures. J Trauma Acute Care Surg. 2013;74:1516–20.

[2] Deepak MK, Jain K, Rajamanya KA, et al. Functional outcome of diaphyseal fractures of femur managed by closed intramedul- lary interlocking nailing in adults. Ann Afr Med. 2012;11:52–7.

[3] El Moumni M, Voogd EH, ten Duis HJ, Wendt KW. Long-term functional outcome following intramedullary nailing of femoral shaft fractures. Injury. 2012;43:1154–8.

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SAT0722-HPR WHAT IS THE MOST AFFECTED BIOPSYCHOSOCIAL ASPECT IN RHEUMATIC DISEASES?

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Background: Rheumatic diseases are chronic illnesses that vary in the extent to different manifestations in musculoskeletal and internal organ systems. In addition to organ involvements, patients with these conditions suffer from biopsychosocial problems such as pain, stiffness, loss of functionality, social isolation, anxiety and depression, fatigue, sleep, and sexuality problems due to the chronic nature of these diseases (1). BETY-BQ is a newly developed biopsychosocial questionnaire that can be used in rheumatic diseases and assesses patients in regards to biopsychosocial status.

Objectives: The aim of this study was to investigate the most affected biopsychosocial aspect that rheumatic diseases cause to.

Methods: 343 patients with rheumatic diseases (283 females and 60 males, mean age: 45.95±10.6) who referred to Hacettepe University, Department of Internal Medicine-Rheumatology were included in this study. Biopsychosocial aspects were assessed by using Bilişsel Egzersiz Terapi Yaklaşimi-Biopsychosocial Questionnaire (BETY-BQ)(2). Rasch analysis was used to determine the different biopsychosocial aspects and the most affected one.

Results: It was found that BETY-BQ has 6 categories assessing pain, functionality & fatigue, emotional status, social participation, sexuality, sleep. When the residual correlation matrix was evaluated, substantial local dependency was observed among the items. Consequently, the sets of items within each of the six subscales were treated as one summary item (testlet) and the data fitted to the Rasch model. Following this, all items were found to fit the model (given a Bonferroni adjustment fit level of 0.0083) (Table 1). Overall, the resulting 6-item item bank was well targeted. The most affected biopsychosocial aspect was found to be 'social participation' and the less affected was 'sleep problems'.

Abstract SAT0722HPR Table 1. Fit of BETY-BQ to Rasch model

Items	Location	Standard Error	Individual Item Fit Residual	Chi-Square Test Statistics	p
Subtest of "pain" items	-0.101	0.017	1.026	4.350	0.500
Subtest of "functionality" and "fatigue" items	-0.080	0.011	1.190	5.440	0.365
Subtest of "emotional status" items	0.092	0.011	-1.730	4.445	0.487
Subtest of "social participation" items	0.156	0.021	-1.149	11.025	0.051
Subtest of "sexuality" items	0.140	0.023	2.201	6.831	0.234
Subtest of "sleep problems" items	-0.207	0.039	0.719	8.824	0.116

Conclusion: According to our results, social functioning is the most affected aspect of patients with rheumatic diseases. Following social functioning, sexuality, and emotional status were further affected. This results should be taken into consideration in the multidimensional rehabilitation programs.

REFERENCES

[1] Van Middendorp H, Evers AW, The role of psychological factors in inflammatory rheumatic diseases: From burden to tailored treatment. Best Pract Res Clin Rheumatol 2016;30(5):932-945.

[2] Unal E, Arin G, Karaca NB, et al. Romatizmali hastalar için bir yaşam kalitesi ölçeğinin geliştirilmesi: madde havuzunun oluşturulmasi. *J Exerc Rehabil* 2017;4(2):67-75.

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SAT0723-HPR **INVESTIGATION OF FUNCTIONAL CAPACITY AND AFFECTING FACTORS IN SYSTEMIC SCLEROSIS PATIENTS**

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Background: Systemic Sclerosis (SSc) is a rare, systemic connective tissue disease characterized by widespread microvascular damage and by increased production and deposition of extracellular matrix components both in the skin and internal organs (1).
Objectives: The aim of this study was to investigate the functional capacity and affecting factors in SSc patients.
Methods: Twenty-two SSc patients were included in the study. Functional capacities of patients were measured by 6 Minute Walking Test (6MWT). Lung volumes (FVC, FEV1, FEV1/FVC, PEF, VC) were performed with Pulmonary function tests-PFT. Respiratory muscle strength was evaluated with a muscle inspiratory pressure(MIP)-muscle expiratory pressure(MEP) modulated spirometer known as respiratory muscle strength meter. Peripheral muscle strengths (deltoid, biceps, quadriceps and iliopsoas muscles) were also evaluated with manual muscle strength meter.
Results: The mean age of the patients was 52.00±11.23 years and duration of diagnosis was 7.63±4.86 years. The patients' mean 6DWT distance was 430.40±50.25 meters, FEV1% were 78.52±22. 23 L, FVC% were 80.95±23.02 L, FEV1/FVC% were 102.56±9.58 L, VC% values were 72.95±22.75 L, MIP% were 54.27±34.85 L, and MEP% values were 56.59±3.56. The mean deltoid muscle strength of the patients was 5.88 ±1.26 kg, biceps were 6.48±1.68 kg, quadriceps were 6.06±1.55 kg, iliopsoas were 5.93±1.74 kg. It was found that there was a significant correlation between 6MWT distance and VC (p =0.009, r = 0.529), FEV1 (p =0.001, r = 0.659), FVC (p =0.005, r = 0.568), MIP (p =0.014, r = 0.506) and MEP (p =0.036, r = 0.449). There was significant correlation between the 6MWT distance and Deltoideus (p =0.024, r = 0.470), Biceps (p =0.001, r = 0.646), Quadriceps (p<0.001, r = 0.679) and İliopsoas (p=0.004, r = 0.576) muscles strengths.
Conclusion: The decrease in the functional capacity of the patients is accompanied by a decrease in pulmonary function, loss of respiratory and peripheral muscle strength in parallel. 6-min walk test showed negative effects in the pulmonary and musculoskeletal system or in the patients' clinic on SSc patients. To evaluate and improve functional capacity while performing medical and rehabilitation follow-up, respiratory functions, respiratory and peripheral muscle strengths should be evaluated and improved.

REFERENCE

[1] Hinchcliff, M., & Varga, J. (2008). Systemic sclerosis/scleroderma: A treatable multisystem disease. American Family Physician, 78(8), 961–968.

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HPR Service developments, innovation and economics in healthcare

SAT0724-HPR **PROMISING OUTCOMES IN PATIENTS WITH RA UNDER A T2T PROGRAM AND A MULTIDISCIPLINARY DISEASE MANAGEMENT MODEL – 5 YEARS RESULTS FROM A RETROSPECTIVE COHORT**

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Background: Rheumatoid arthritis (RA) is a common chronic inflammatory disease. It is characterized by progressive, irreversible joint damage, impaired joint function and pain, the disease causes disability and reduced quality of life. Treat-to-target (T2T) is a management strategy for RA. It proposes that the therapeutic goal in RA should be a state of remission, or an alternative goal could be a low disease activity, additionally it looks to achieve long-term health quality of life for the patients. Additionally, multiapproach programs for RA aim to take into account all components that interfere with the course of RA.
Objectives: To describe the effectiveness of a T2T strategy associated to a disease management model with a multidisciplinary approach of patients with RA, according to disease activity measured with Activity Score 28 (DAS28) in a 5-year period in patients who receive conventional or biological DMARDs in a Colombian specialized in RA center.
Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed during 2015-2017; those patients were followed-up under T2T standards and a multidisciplinary approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3-5 weeks (DAS28 > 5.1), every 7-9 weeks (DAS28 $\geq$ 3.1 and $\leq$ 5.1), and every 11-13 weeks (DAS28 < 3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 > 3.2 unless patient´s conditions don't permit it; we considered this follow-up type as implementation of a T2T strategy in patients with RA. Patients entered into a multidisciplinary program of care with periodic consultations not only to rheumatology but with a physiatrist, psychologist, physiotherapist, occupational therapy nutrition, and, a patient focused program. With a multidisciplinary model of care the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA. We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We compared disease activity at base line and at the end of follow-up.
Results: We included 4000 patients, 83% were female and 17% male; median age was 60 years RIQ (50-67). Regarding pharmacological therapy 77% were receiving conventional DMARDs while 37% were receiving biological DMARDs. At beginning 55% were in MDA, 26% in LDA and 19% and during 5 years 82% of our patients achieved remission. See table 1. We performed a Wilcoxon test in order to compare the mean DAS28 at baseline and at the end showing statistical significance (P<0.05)

ACTIVITY LEVEL	BASELINE		5 YEARS FOLLOW-UP	
	n	%	n	%
REM			3297	82.40
LDA	1049	26.23	322	8.05
MDA	2201	55.02	333	8.32
SDA	750	18.75	48	1.22

Conclusion: A T2T strategy associated with a multiapproach disease management model improves considerably disease activity in patients with RA. This evidence from a real-life setting that shows the advantages of treating RA patients with a multidisciplinary team under a T2T model with a low-cost treatment. It is important to explore other predictors that can improve disease activity.

REFERENCES

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SAT0725-HPR **A DISEASE MANAGEMENT MODEL TYPE CENTER OF ESCELLENCE IN SPONDYLOARTHRITIS – FIRST PILOT ANALYSIS RESULTS**

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Background: Ankylosing spondylitis (AS) mainly affects the spine and the sacroiliac joints, it is a chronic inflammatory disease that might be associated with a variety of extra spinal lesions involving the eyes, bowel,

and skin. In Colombia little is known in regards of this condition. Spondyloarthritis (SpA) is one the most prevalent musculoskeletal disease in the Americas, with an estimated prevalence of 0.5%. This group of patients present a number of unmet needs for accessibility to the consultation, diagnosis and adequate treatments. That for this reason it is necessary to develop a program of Centers of Excellence (CoE) in this pathology, which allows answer to these needs and at the same time to add values for our health systems.

Objectives: To describe the characteristics of patients with AS who attend to a specialized in SpA disease management model center.

Methods: We implemented a pilot SpA program under the scheme of CoE, as they are already delineated in projects like REAL-PANLAR for rheumatoid arthritis. We performed a cross sectional study and reviewed the medical charts of patients with AS. All patients had a confirmed diagnosis of AS. We collected demographic data (age, sex, smoking, alcohol consumption); BASDAI, BASFI, DAS, disease specific data treatment with csDMARDs or bDMARDs and comorbidities, evaluation period covered January to December 2018.

Results: During 2018 257 patients with AS entered to our program. 64% were men and 36% were female; mean age was 48 years ±14. 28% of our patients with SA had comorbidities the most common was high blood pressure 19% followed by diabetes mellitus 4%. Regarding behavioral habits 23% were current smokers and 11% reported to consume alcohol. When we evaluated clinical outcomes BASDAI mean score was 2.95 ± 2.06, BASFI mean score was 3.49 ± 2.36 and, ASDAS mean score was 1.70 ± 1.01. 60% of patients received biological DMARDs and 25% received conventional DMARDs. The remaining 15% received corticoids or pain medications.

Conclusion: Due to the need to develop CESPAs, in order to define treatment targets type T2T-SpA, we implemented an innovative program in a low-income country with the aim to improve clinical outcomes and avoid so much disability and health economic costs. This descriptive data is the starting point to collect evidence and demonstrate the impact of the program

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SAT0726-HPR EHEALTH CONSULTATIONS IN RHEUMATOLOGY MANAGED BY NURSING. SPANISH NATIONAL DESCRIPTIVE STUDY

Silvia Garcia Diaz, All the members from the Nursing Working Group from the Rheumatology Spanish Society (GTE-SER). *Hospital Sant Joan Despí Moisès Broggi-Hospital General de Hospitalet, Consorci Sanitari Integral (CSI), Rheumatology, Barcelona, Spain* Background

The increase in social media applications and electronic technology has made it possible to carry out consultations with patients using an electronic interface. These tools are used in the healthcare environment for the purpose of prevention, diagnosis, treatment, monitoring, and in health management, to save costs to the health system by improving its effectiveness [1-4].

For patients with rheumatic diseases these non-face-to-face eHealth consultations, carried out by specialized nurses have been shown to resolve a large part of the problems that these patients may present with [5-8]. However we do not know how many of these types of consultations are taking place in Spain.

Objectives: The aim of this study was to describe the content of these types of consultations, mostly managed by nursing, in the Spanish national territory.

Methods: A descriptive study of a group of nurses working actively in rheumatology was carried out in November 2018. The data collection was done using a Google-form questionnaire developed for that purpose by the members of the Nursing Working Group from the Rheumatology Spanish Society (GTE-SER). The main variables studied were the sociodemographic details of the group and the content of the activity carried out mainly by them in the eHealth consultations. This instrument had 31 questions, with wide variability of response. Statistical analysis: descriptive statistics was used.

Results: A total of 47 (out of 50) completed surveys were analysed. 94% of the nurses were women, from 15 Spanish Autonomous Communities, with an average age between 51-60yo; 52% had education at postgraduate level (17%) or master's degree (35%). 47% of professionals had been working in rheumatology for more than 10 years and 77% had received specific training in rheumatology. 37% reported having between 1-5 years experience of using e-Health consultation in rheumatology. The average of monthly consultations was between 50-100 sessions. Further details of the eHealth consultations in Rheumatology: see Table 1.

Table 1:

VARIABLES	Nursing professionals%
eHealth consultations ARE managed by nursing professionals	89%
The type of eHealth consultation is both scheduled and on demand	68%
The type of access to the consultation is telephone	72%
The management of the answer to the consultation is IMMEDIATE	68%
The space where the consultation is handled is in a quiet office	41%
eHealth consultations ARE always registered	76%
eHealth consultations ARE registered in the patient's clinical history	91%
eHealth consultations are computed as a clinical activity in the nursing agenda	79%
There are NO standards or protocols on the use of eHealth consultations in rheumatology in your centre	81%
There has not been any audit on the use of eHealth consultations in rheumatology in your centre	98%

Conclusion: EHealth consultations are already established in many Rheumatology services in Europe. However, this has not been described in Spain. The survey showed that there is a great variability in the way nurses carry out this type of consultations, including the number and type of consultation (on demand and/or scheduled), registration and analysis of the data of this consultation as well as its quality standards.

This study demonstrates a lack of regulated training and standardized protocols in managing this type of consultation at the national level. Therefore standards and protocols should be developed in the near future, so that patients receive a more consistent service from this type of consultation.

REFERENCE

[1] Chiranjeev Sanyal, et al. 2018; [2] Hughes RA, et al. (2002); [3] Royal College of Nursing (2006); [4] Ferreira R, et al. (2014); [5] GESVR 2013; [6] C. Nájera Herranz, et al. (2013); [7] C. Thwaites, et al. (2008); [8] Garcia-Diaz S, et al. (2015)

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SAT0727-HPR CHANGES IN ACHILLES TENDON STIFFNESS IN GOUT MEASURED BY ELASTOGRAPHY – A PRELIMINARY STUDY

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Background: In addition to acute attacks of severe joint pain and swelling, chronic gout has been associated with weaker foot/leg muscles, altered gait patterns and on-going foot pain. Inflammation associated with gout may change tissue elasticity and ultrasound imaging (US) utilising elastography is a non-invasive method of quantifying these changes in tendon stiffness and elastography findings have not previously been reported in individuals with gout.

Objectives: To determine differences in Achilles tendon stiffness in people with chronic gout compared to controls (non gout)

Methods: A cross sectional study comparing people with gout according to 2015 ACR/EULAR criteria and age/sex matched controls. Clinical and demographic data were collated and US imaging used to determine tendon thickness, presence of gouty tophi and/or aggregates and levels of angiogenesis. Previously validated protocols for conventional US imaging [1] and shear wave elastography [2] were used. Prior to data collection, intra-observer error was good (ICC (2) 0.69 (95%CI 0.62-0.89)). Ten elastography measures were taken along a longitudinal section of the midpoint of the Achilles tendon bilaterally. Data were summarised using descriptive statistics and a repeated measures ANCOVA was used to compare elastography outcomes between the two groups for the left and right foot separately after accounting for Body Mass Index (BMI).

Results: A total of 14 people with gout and 13 age/sex matched control subjects participated. Table 1 displays clinical and demographic data. A

small proportion of those with gout presented with intra-tendon aggregates and/or intra-tendon tophi in one or both tendons n=7 (27%) for both). There was no significant difference in tendon thickness between groups, neo-vascularity was present in n=3 (21%) gout participants. Elastography findings (table 2) demonstrated significantly reduced tendon stiffness in those with gout compared to controls.

Abstract SAT0727HPR Table 1. Clinical & demographic characteristics

	Gout	Non gout
Male:Female	11:3	11:2
Mean age (SD)	71.9 (10.54)	71 (10.8)
Mean BMI (SD)	30.8 (5)	27.8 (4.54)
Mean duration gout years (SD)	12.7 (9.88)	-
Comorbidities (%)	50	62
Diabetes	85	70
Hypertension	64	70
Dyslipiaemia	57	23
Cardiac disease	36	8
Chronic Kidney disease		
Gout management n (%)	3 (9)	
None	2 (7)	
NSAID (prn)	6 (21)	
Allopurinol	1 (3)	
Cholchine	2 (7)	
Prednisolone		

Abstract SAT0727HPR Table 2. Elastography findings (using marginal mean results and adjusted for BMI)

	Gout	Control	Difference (95% CI)	P value
Elastography Right Achilles m/s Mean (±SD)	8.38 (1.94)	9.70 (0.27)	1.625 (0.55-2.699)	0.005
Elastography Left Achilles m/s Mean (±SD)	8.73 (1.67)	9.63 (0.66)	1.214 (0.23-2.198)	0.018

Conclusion: Subjects with chronic gout show reduced Achilles tendon stiffness compared to controls. From a clinical standpoint, our findings were similar to elastography measurements in otherwise healthy subjects with Achilles tendinopathy and who did not have gout [3].

REFERENCES

[1] Carroll M, Dalbeth N, Allen B, et al. Ultrasound Characteristics of the Achilles Tendon in Tophaceous Gout: A Comparison with Age- and Sex-matched Controls. J Rheumatol. 2017 44(10):1487-1492.
[2] Payne C, Watt P, Cercignani M, Webborn N. Reproducibility of shear wave elastography measures of the Achilles tendon. Skeletal Radiol. 2017 17 2846-8.
[3] Payne C 2018 Clinical Applications of shear wave elastography to Achilles tendon imaging and monitoring of a rehabilitation protocol for Achilles tendonopathy PhD Thesis, University of Brighton

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SAT0728-HPR REVISION OF THE DUTCH GUIDELINE FOR PHYSIOTHERAPY IN PATIENTS WITH HIP AND KNEE OSTEOARTHRITIS: RECOMMENDATIONS FOR DAILY PRACTICE

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Background: Until 2018, the most recent update of the Dutch physiotherapy guideline for Hip and Knee Osteoarthritis (HKOA) was conducted in 2010. Since then, scientific developments changed the view on osteoarthritis and could have significant impact on daily practice. An update of the guideline was necessary with more applicable recommendations about the content of exercise therapy.
Objectives: To revise the Dutch guideline for physiotherapists in patients with HKOA
Methods: To develop more practical and widely supported guidelines, a guideline methodology was developed by the Royal Dutch Society for Physical Therapy (KNGF) in 2016. This methodology was based on GRADE, the most accepted approach in guideline development worldwide. According to the KNGF methodology, a guideline panel was formed out of 22 stakeholders, e.g. physiotherapists, general practitioners, orthopedic surgeons, patient representatives and healthcare insurers. Based on the scientific evidence and other considerations, the guideline panel formulated the recommendations in this guideline.
Results: Recommendations about diagnostics and therapeutic interventions formed the base of the new Dutch physiotherapy guideline for HKOA. Three indications were formulated, based on patient preferences, severity of the functional condition and existence of comorbidity. A fourth indication concerned pre- and postoperative physical therapy before or after a total joint replacement. It was recommended to restrict physical therapy in patients with minor functional limitations by informing and advising about osteoarthritis and how to deal with the disease. In contrast, extensive supervised exercise therapy was recommended in patients with severe functional restrictions and/or comorbidity. Besides informing and advising, supervised exercise therapy is stated as the intervention with the strongest recommendation. Frequency, Intensity, Type and Time (FITT factors) of exercise therapy are described extensively, based on evidence and strongly linked to (inter)national recommendation for physical activity. Besides informing and advising, other non-exercise therapeutic interventions were not recommended.
Conclusion: The new physiotherapy guideline for HKOA provides practical information and guidance to physiotherapists on diagnostics and therapeutic interventions. Extensive implementation is necessary to enhance conservative treatment of osteoarthritis and achieve uniform health care.

REFERENCE

[1] Rausch, et al. EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis. 2018 Sep;77 (9):1251-1260.

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SAT0729-HPR REVISION OF THE DUTCH GUIDELINE FOR PHYSIOTHERAPY IN PATIENTS WITH RHEUMATOID ARTRITIS: RECOMMENDATIONS FOR DAILY PRACTICE

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Background: The importance of exercise therapy in patients with rheumatoid arthritis (RA) is recognized in scientific evidence and clinical practice. The recommendations for physiotherapists concerning the diagnostics, treatment and evaluation of patients with RA are described in the Dutch guideline for physiotherapy (PT) in patients with RA from 2008. Since new scientific evidence was published and an up to date guideline is indispensable for the applicability in daily clinical PT practice, a revision is made.
Objectives: To revise the Dutch guideline for physiotherapy in patients with RA
Methods: A guideline panel with representatives of relevant stakeholders (such as PTs, general practitioners, rheumatologists, specialized nurses, a podiatrist and patients) was composed. Conform the Dutch Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach, research questions for systematic or narrative reviews were formulated after focus groups with patients and PTs, and consultation of experts. Evidence was synthesized by providing the estimates of the effect for each outcome and the quality of the evidence. A strong or conditional recommendation for or against an intervention was formulated by the panel, based on evidence together with additional considerations, as described in the GRADE evidence to decision framework.

Results: Three indications for PT are distinguished, based on the patients' health status and abilities of self-management: 1) patient education combined with instructions for mainly unsupervised exercise therapy, 2) patient education combined with exercise therapy with short-term supervision and 3) patient education combined with exercise therapy with intensified supervision. Exercise therapy is recommended for indication 2, and conditionally recommended for indication 1 and 3. Patient education consist of information and advice on RA and promotion of self-management. Specific recommendations concerning the frequency, intensity, type and time (FITT) of the exercise therapy are provided, based on studies performed in patients with RA, recommendations from The Dutch Health Council (2017), EULAR recommendation on Physical Activity (2018), and The American College of Sports Medicine guidelines for exercise testing and prescription (2018). Behavioral interventions to promote physical activity in patients with RA are also recommended. The guideline obtains practical advices for applying tailored behavioral interventions.
Conclusion: The indication for PT is divided in: instructions for mainly unsupervised exercise therapy, exercise therapy with short-term supervision and exercise therapy with intensified supervision. Based on scientific evidence and expert consensus on additional considerations among relevant stakeholders, exercise therapy with supervision of a PT is recommended in patients with RA, together with information and advice and promotion of self-management. Specific recommendations on dosage of exercise therapy (FITT) are provided. Behavioral interventions to promote physical activity are also recommended.

REFERENCES

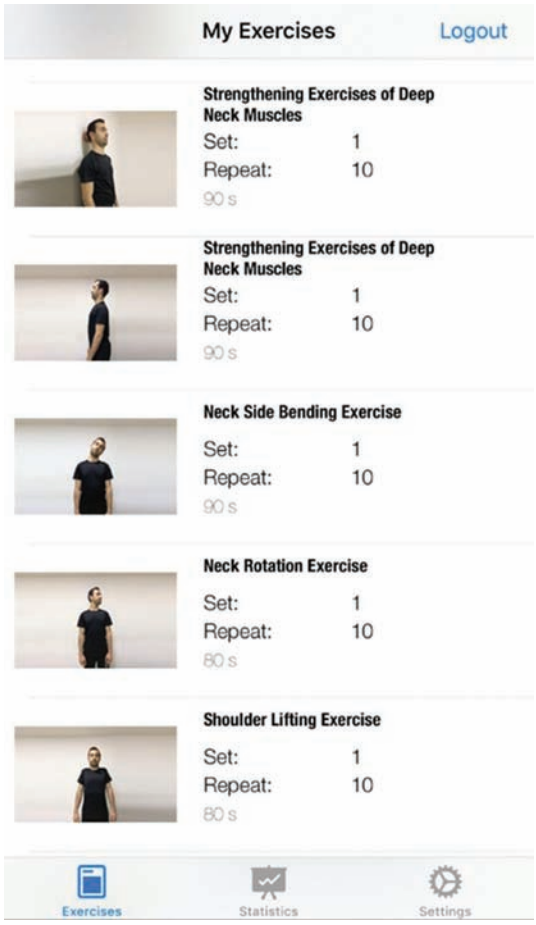
[1] Rausch, et al. EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis. 2018 Sep;77 (9):1251-1260.

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SAT0730-HPR DEVELOPMENT AND DESIGN OF SMARTPHONE APPLICATION FOR POSTURAL ALIGNMENT OF CERVICAL AND THORACIC SPINE FOR YOUNG ADULTS

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Background: Mobile health (mHealth) technologies offer personal, intelligent, cost-effective, access to health care services. Numerous smartphone applications exist to assist the users for management or prevention of the musculoskeletal disorder. But most of the apps were not designed with both users and experts focus. As our knowledge, there is no health exercise app for neck and upper back musculoskeletal prevention designed by experts with the user-centered method.
Objectives: The aim of our study is to develop a smartphone exercise application (app) for cervical-thoracic postural alignment for young adults.
Methods: We used a combination method of focus groups interviews and user-centered design approach. The mobile application was designed in three phases: (1) we conducted multidisciplinary focus group meetings to compromise the content, feature and design of app in the first phase (prototype smartphone app\MarNeckEx). Focus group consisted of software developers, 3 experienced physiotherapists on musculoskeletal ergonomics, 3 young smartphone users who have neck and upper back problems associated with an excess smartphone using. The focus group members discussed the variety of topics in subgroups (login parameters, self-monitoring, exercises content, video or animation types, exercise diary, reminders, encouragement method etc). We conducted 4 focus group meeting for phase 1. (2) After developing the prototype version of app 30 young adult downloaded the prototype app and used the app for one week, after one week we asked the satisfaction levels, barriers and facilitators of the app design and advice for usability. We conducted 2 focus group meetings for development of the revised application by modifying the errors taking into account feedbacks (revised MarNeckEx).
Results: Major themes identified for development app phase 1 were (a) self-assessment of musculoskeletal problems (b) Choosing the spinal stabilization and postural alignment exercises with well design videos (c) encouraging and notifications for exercise adherence. A second phase themes, (d) education for using the digital app for exercise, (e) positive or negative feedback notifications for improving adherence were added.



Conclusion: We conducted the smartphone-based cervico-thoracic postural alignment exercise app with multidisciplinary and user focus method. Usability of the application should be done before marketing the new mHealth app for exercise.

REFERENCES

[1] Dicianno, et al. (2015)."Perspectives on the evolution of mobile (mHealth) technologies and application to rehabilitation." Phys Ther 95(3): 397-405.
[2] Berolo, S., R. Wells, et al. (2011). Musculoskeletal symptoms among mobile hand-held device users and their relationship to device use: A preliminary study in a Canadian university population. Appl Ergon. 2011 Jan;42(2):371-8
[3] Gustovo C et. Al. (2016) Smartphone apps for the self-management of low back pain: A systematic review. Best Practice and Research in Clinical Rheumatology 30;1098-1109.

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SAT0731-HPR TRIAGE AD HOC REFERRAL BY RHEUMATOLOGY NURSE – AN ALTERNATIVE PATH TO CLINIC VISIT

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Background: Rheumatic diseases are chronic conditions characterized by disease flares and remissions. Patients are often referred back from other healthcare providers in between follow-up visits when they seek attention for disease flares or adverse effects from treatment. While prompt attention and assessment is important, the busy rheumatology clinic may not have the coping capacity for these ad hoc needs. Rheumatology nurse (RhN) can play a pivotal role in triaging these referrals.

Objectives: The study aims to evaluate the safety of referral triage by rheumatology nurse and the effectiveness in alleviating workload of the rheumatology clinic.

Methods: This was a retrospective study. Data were retrieved from November 2016 till December 2018. Ad hoc referrals to the rheumatology out-patient clinic were screened by rheumatologists and suitable cases were directed to RhN for further handling. The triage process included phone triage or attendance of RhN clinic for assessment and subsequent phone follow-up. Investigations including laboratory and radiography were arranged as indicated. Frequency of phone follow-up after the first contact depended on patients' needs. Patients would be referred to rheumatologist for further management if the condition worsened at or before the first phone follow-up.

Results: Totally 110 referrals were triaged by rheumatology nurse with 54 arthritis, 28 systemic lupus erythematosus, 10 vasculitis, 8 undifferentiated connective tissue disease and 5 others. Age ranged from 22 to 84 years and 82.7% were female. Sources of referral included general out-patient department (38.2%), emergency department (22.7%), other specialists (33.6%) and general practitioners (5.5%). Reasons for referral included disease flare-up (47.3%), drug-related problems (20.9%), abnormal investigation results (12.7%) and alarming clinical presentation (19.1%). Mean time interval from referral to first phone contact was 3.8 days. Of the 110 cases, 20 patients had follow up advanced; 1 patient was admitted before phone triage and 86 patients could follow original appointments. Two of the 110 patients' symptoms subsided spontaneously and no intervention was required; 1 patient was arranged admission after discussion with rheumatologist. No record of emergency attendance or admission for the 86 patients who kept the scheduled appointment. Nursing interventions included drug education and advice (64 episodes), disease education (20 episodes), investigation arrangement (50 episodes), counselling and emotional support (12 episodes). Three patients attended RhN clinic for assessment and education. The other 83 patients were managed through phone communication and majority (81.4%) had phone follow up once.

Conclusion: The result of the study showed that referral triage by rheumatology nurse is safe and effective in handling the majority of ad hoc referral requests. The service can promptly address patient needs and reduce clinic visit burden of the rheumatology clinic.

Disclosure of Interests: None declared

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Genomics, genetic basis of disease and antigen presentation

AB0001 ASSOCIATION OF MDR1 GENE G2677T POLYMORPHISM WITH METHOTREXATE RESISTANCE IN PATIENTS WITH UZBEK RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is the most widely prescribed disease-modifying antirheumatic drug (DMARD) for treatment of rheumatoid arthritis (RA)[1]. According to different authors, in 25–40% [3] of cases "complete clinical remission" or "low disease activity" is not achieved, by reason of refractoriness to methotrexate and this may be related to the activity of the MDR1 (ABCB1) gene which is involved in its metabolism. According to many studies on the C3435T isoform MDR1 polymorphism CC genotype is associated with methotrexate refractoriness [2]. But a certain interest is also influenced by the other isoform of the MDR1 gene (G2677T) for the presence of resistance to methotrexate.
Objectives: The aim of this research was to study the effect of MDR1 gene polymorphisms G2677T (rs2032582) on resistance to treatment with methotrexate in Uzbek patients with RA.
Methods: The study involved 76 patients with RA of uzbek nationality and 24 healthy people. The average age of patients was 48,9 ± 15,9 years. RA was diagnosed according to the criteria of the American College of Rheumatology (ACR). 75.6% of patients had high and 24.4% moderate RA activity (DAS 28). All patients took methotrexate in monoterapy, at a dose of 7.5-15 mg for 3-6 months. All patients were genotyped by the MDR1 gene G2677T polymorphisms by using the polymerase chain reaction (PSR-Real time).
Results: Genotyping of the G2677T isoform of MDR1 gene revealed the following results: in patients with CC genotype was found in 22 patients (28.9%), GT genotype was found in 31 patients (40.7%) and TT genotype was found in 23 patients (30.2%). In patients treated with methotrexate, the following disease activity was observed: in patients with CC genotype, the disease activity was Das28 <2.6, with CT genotype Das28 3.2–4.5. Patients with the TT genotype had an activity of Das28> 5.1. Despite the increase in the dose of methotrexate, the remission was not achieved.
Conclusion: TT genotype G2677T isoform of MDR1 gene is associated with resistance to methotrexate. Patients with TT genotype are recommended to replace methotrexate with other DMARD preparations. Patients are recommended to conduct genotyping to the MDR1 gene for personal selection of drugs.

REFERENCES

[1] Grabar P.B., Logar D. et al. (2008). Genetics determinants of methotrexate toxicity in rheumatoid artritis patients: a study of polymorphisms affecting methotrexate transport and folate metabolism. Eur J Clin Pharmacol. 64:1057-1068.
[2] Pawlik A., Wrzesniewska J., Fiedorowicz-Fabrycy I. et al. **The MDR1 3435 polymorphism in patients with rheumatoid arthritis**. Int J Clin Pharmacol Ther. 2004 Sep; 42 (9): 496-503.
[3] Samara S.A., **Irshaid** Y.M. wt al. **Association of MDR1 C3435T and RFC1 G80A polymorphisms with methotrexate toxicity and response in Jordanian rheumatoid arthritis patients.** International Journal of Clinical Pharmacology and Therapeutics, Vol. 52 - No. 9/2014 (746-755)

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AB0002 INCREASED SENSITIVITY TO DNA DAMAGING AGENTS IN HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder with not fully elucidate pathogenesis. Rheumatoid arthritis patients have increased risk of developing lymphomas. One of the possible mechanisms of this predisposition is increased genomic instability and impaired DNA repair. It is unclear how this genomic instability contributes to diseases pathogenesis.
Objectives: The aim of this study was to analyze the sensitivity and repair efficiency of mononuclear cells isolated from RA patients to DNA damaging agents.
Methods: The study group consisted of 22 patients with RA (age years - 60,77±13,00 women-17, men - 5) hospitalized in the Department of Rheumatology between 2017 and 2018 and 10 healthy controls without autoimmune and oncological diseases in clinical history (age 44,09±16,56; women-5, men-6). The peripheral blood mononuclear cells (PBMC) from all subjects were isolated. Using comet assay the degree of intracellular DNA damage as a result of exposure to standard damage factors: tert-butyl hydroperoxide (TBH), bleomycin, methyl methanesulfonate (MMS) and UV radiation was assessed.
Results: RA patients show a statistically significant higher level of endogenous damage in PBMC DNA than controls (mean RA- 8,64% vs 4,68% in control; p<0,001). The extent of the DNA damage induced by TBH, MMS as well as UV was significantly higher in PBMC derived from RA patients than in healthy counterparts (p<0,001). The DNA of RA patients treated with TBH was repaired less effectively than in control (p<0,0001). Significantly higher percentage of DNA damage in RA DNA (p<0,0001) under the influence of bleomycin and clearly marked repair processes were observed. Among the healthy controls lower percentage of DNA was damaged, and although the repair process was slower but the final percent of DNA damage was lower than in RA cases (p<0,0001).
Conclusion: DNA of people with rheumatoid arthritis is significantly more susceptible to damage in baseline and induced. The kinetics of DNA repair from RA patients after the introduction (TBH and bleomycin) was statistically less effective as compared to healthy control. Understanding the ethology of this phenomenon in RA may provide insight into disease pathogenesis and explain the increased susceptibility of patients to malignancies.
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AB0003 GENETICS OF PAIN IN WOMEN WITH FIBROMYALGIA: THE PROMISING ROLE OF REDUCING SEDENTARY BEHAVIOUR

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Background: Fibromyalgia is characterised by chronic pain and a heterogeneous presentation of other symptoms (e.g., fatigue and depression) [1]. It is widely accepted that pain is promoted by both genetic susceptibility and environmental factors such as people's behaviours [2]. In addition to genotype individual associations and gene-gene interactions, when considering complex phenotypes such as pain, gene-environmental interactions are likely present and can help to better understand the disease (i.e. by unravelling underlying mechanisms [3]).
Objectives: To test the individual association of 64 polymorphisms (34 candidate-genes) and the gene-gene, gene-physical activity, and gene-sedentary behaviour interactions with pain and pain-related cognitions in fibromyalgia.
Methods: In 274 women with fibromyalgia, saliva samples were collected for extracting DNA. We measured physical activity and sedentary behaviour by accelerometers for a week, pain with algometry and questionnaires, and pain cognitions with questionnaires. Age, body fat, and analgesics and antidepressants consumption were included as covariates. Significance was set at P-values lower than the Bonferroni's correction or P- and false discovery rate values lower than 0.05.
Results: The rs6311 and rs6313 polymorphisms were individually related to algometer scores. The interaction of rs4818 and rs1799971 polymorphisms was related to pain catastrophizing. Five gene-behaviour interactions were significant: the interactions of sedentary behaviour with rs1383914, rs6860, rs4680, rs165599, and rs12994338 polymorphisms were associated with the bodily pain subscale of the SF-36.
Conclusion: The HTR2A gene (individually), COMT and OPRM1 gene-gene interaction, and the interactions of sedentary behaviour with ADRA1A, CHMP1A, COMT, and SCN9A genes were associated with pain-related outcomes in fibromyalgia females. Besides indicating the relevance of genetic background for pain and pain-catastrophizing, the observed genotype-behaviour interactions suggest that the effects of sedentary behaviour on pain may depend on the genotype of women with fibromyalgia. Future clinical experimental research should examine whether reducing sedentary behaviour is particularly beneficial for reducing pain in women with specific genotypes.

REFERENCES
[1] Estévez-López F, et al. Rheumatology (Oxford). 2017 Nov;56(11):2015-2024
[2] Nielsen CS, et al. Pain. 2008 May;136(1-2):21-9
[3] Hunter DJ. Nat Rev Genet. 2005 Apr;6(4):287-98

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AB0004 DETECTION OF THE SNP-SNP INTERACTIONS IN THE JUVENILE ARTHRITIS SUSCEPTIBILITY USING MDR ANALYSIS

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic arthropathy of childhood which is considered to be a complex disease. The genes encoding HLA complex account for only 14% of the JIA risk. Hence, it is suggested that substantial role in genetic predisposition to JIA belongs to the non-HLA gene variations.
Objectives: The aim of the study was to estimate interactions between SNPs of the genes implicated in immune and inflammatory responses: *STAT4* (rs7574865), *CTLA4* (rs5742909), *MIF* (rs755622), *TRAF1/C5* (rs3761847), *RUNX3* (rs11249215) and their effect on the JIA susceptibility.
Methods: 119 patients diagnosed with JIA (mean age 8.48 ± 5.06), and 197 hospital controls with no signs of autoimmune or inflammatory diseases (mean age 14.19 ± 2.56) were included into the study. DNA extraction from peripheral blood samples was performed with phenol-chloroform method. SNPs were genotyped using the PCR-RFLP assay. Multifactor dimensionality reduction (MDR) analysis was performed using MDR 3.0.2 software package with the following configuration: attribute count range – from 1 to 5; cross-validation count – 10; track top models – 1000; search method configuration – exhaustive; ambiguous cell analysis – Fisher's exact test; ambiguous cell assignment – unclassified. The best model was selected on the basis of maximum crossvalidation consistency and testing balance accuracy values.
Results: Model-free nonparametric statistical approach of MDR analysis revealed the best model for JIA susceptibility prediction with cross-validation consistency of 9/10 and testing balanced accuracy of 0.5768. The model includes SNPs of *STAT4*, *TRAF1/C5* and *RUNX3* genes and is characterized by 0.6727 sensitivity; 0.7083 specificity, OR = 4.9921; 95%CI [2.4–10.20], $p < 0.0001$. Gene-gene interaction analysis discovered three genotype combinations for higher JIA risk. The most statistically significant was: GA (*RUNX3* rs11249215), GT (*STAT4* rs7574865) and GG (*TRAF1/C5* rs3761847), OR = 2.92, combined entropy – 4.83%. Separate data analysis for males and females didn't show any statistically significant model of SNP interactions associated with JIA. However, *MIF* rs755622 with entropy of 2.92% was more informative in females, while *STAT4* rs7574865 with entropy value of 1.12% – in males.
Conclusion: MDR analysis of the JIA case-control data set identified a statistically significant high-order interaction of three polymorphisms: *STAT4* (rs7574865), *TRAF1/C5* (rs3761847), *RUNX3* (rs11249215). This combination may contribute to JIA genetic susceptibility in the Belarusian population.
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AB0005 FAVORABLE RESPONSE TO RITUXIMAB IN A PATIENT WITH HYPOCOMPLEMENTEMIC URTICARIAL VASCULITIS ASSOCIATED WITH A HOMOZYGOUS FRAMESHIFT AGBL3 VARIANT

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Background: Last year we described a homozygous AGBL3 variant in a patient with autoinflammatory features and hypocomplementemic urticarial vasculitis. Whole exome sequencing revealed a deleterious homozygous c.769C>T mutation in AGBL3 (ATP/GTP binding protein-like 3) gene, which results in early termination of the protein (p.Gln257Ter) and deletion of the functional carboxypeptidase domain. This protein belongs to metallocarboxypeptidases that mediate both deglutamylation and deaspartylation of target proteins, and AGBL3 is suggested to catalyze the deglutamylation of polyglutamate side chains, especially in proteins such as tubulins. This variant was not found before in all reported databases including 1000 Genomes Project data.
Objectives: To define the clinical phenotype and treatment responses of a patient with newly defined monogenic hypocomplementemic urticarial vasculitis associated with a homozygous AGBL3 variant.
Methods: We collected all clinical, serologic, and pathological data regarding the clinical findings of the index case as well as recorded all treatment responses throughout the follow-up period during the last 8 years.
Results: The index case was 23-year-old male patient of Assyrian origin, who had consanguineous parents. He was evaluated in our clinic because of recurrent attacks of fever, urticarial rash on the extremities and trunk, conjunctival injections and arthralgia, without a trigger or more frequently following an infection. His 2 to 3 days lasting attacks started when he was 13 and recurred more frequently during warm weather conditions or following hot baths. He had highly elevated CRP and ESR during attacks, but his acute phase response did not return to normal values in between the flares. Low C3 and C4 values were also observed during asymptomatic periods. His ANA test became positive during the course of his disease with an increase in titers during the last years. The biopsy of skin lesions revealed findings compatible with urticarial vasculitis. He responded only partially to corticosteroids, canakinumab and anakinra treatments. His treatment was switched to rituximab last year, and a favorable response was observed following the first two infusions. He developed less frequent and milder attacks only after infections, and acute phase response was reduced to near normal values in between attacks.
Conclusion: The AGBL3 metallocarboxypeptidase gene was recently idenfied as a novel autoinflammatory gene associated with hypocomplementemic urticarial vasculitis phenotype, and it was different from the previously defined variants including DNASE1L3 mutations. The clinical features of the index case included both autoinflammatory and autoimmune findings including autoantibodies; and his inflammatory attacks did respond to rituximab treatment but not IL-1 blockade. Long term follow-up and search for other patients associated with AGBL3 variants among idiopathic hypocomplementemic urticarial vasculitis are required for better clarification of the AGBL3-associated clinical phenotype.
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AB0006 ASSOCIATION OF HLA-DPB1*16:01 ALLELE WITH PR3-ANCA POSITIVE GRANULOMATOSIS WITH POLYANGIITIS IN TURKISH PATIENTS

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Background: ANCA associated vasculitides (AAV) comprise an important subset of small vessel vasculitides with a multifactorial pathogenesis, which is considered to be associated with the interaction of genetic and environmental factors. Certain HLA Class 2 alleles have been reported among the genetic risk factors for AAV from different geographic regions such as Europe and Asia (1,2).
Objectives: In this study, we aimed to analyse the distribution of HLA Class 2 genotypes among a series of Turkish AAV patients in comparison with the healthy Turkish subjects and the previously reported data of AAV cohorts from other countries.
Methods: Ninety-eight patients (aged between 18–75 years) diagnosed with AAV according to 2012 Chapel Hill Consensus Criteria were enrolled into the study. Records of age-and birthplace-matched 196 healthy kidney donors were used as the control group. Patients were classified according to the clinical subgroups (GPA, e-GPA, MPA) and ANCA serotypes (MPO-AAV, PR3-AAV). HLA Class II genotyping were carried out by using NGS-Omixon Holotype HLA Kit at the EFI accredited HLA Typing Lab of Department of Medical Biology. Allele distributions were compared by Chi-square test, and P value lower than 0.05 was accepted as significant.
Results: AAV patients were classified as PR3-AAV (54%) and MPO-AAV (31.6%) according to autoantibodies and GPA (71.4%), MPA(20.4%), e-GPA (8.2%) according to clinical subgroups. HLA-DPB1*04:01 (8.5% vs. 35.9% $p<0.01$, OR= 0.16 %95 CI 0.08–0.34) and HLA-DPB1*02:01 (%7.5 vs. %22.4 $p<0.05$, OR=0.28 %95 CI 0.13–0.6) alleles were significantly lower in the PR3-AAV group. HLA-DPB1*16:01 allele was significantly higher in the PR3-AAV group (%8.5 vs. %0.26 $p<0.01$, OR=36.2 %95 CI 4.5–289.7). In clinical subgroups, HLA-DPB1*04:01 (%7.9 vs. %35.9 $p<0.01$, OR=0.15 %95 CI 0.08–0.29) and HLA-DPB1*02:01 (%7.9 vs. %22.4 $p<0.01$ OR= 0.29 %95 CI 0.15–0.57) alleles were significantly lower in the GPA-AAV group. HLA-DPB1*16:01 allele

was significantly higher in the GPA-AAV group (%7.14 vs. %0.26 p<0.01, OR=30, %95 CI: 3.8–237). No significant difference was detected between the MPO-AAV and control groups.
Conclusion: HLA analysis of this small series of Turkish AAV patients revealed a negative correlation between PR3-ANCA positivity and HLA-DPB1*04:01 and HLA-DPB1*02:01 alleles in opposition to the results reported from different European AAV cohorts (1,3). On the other hand, a significant increase in both GPA and PR3-AAV subgroups for a previously unpublished HLA-DPB1*16:01 allele may suggest that HLA association may show ethnic or regional differences, and further analyses in larger series of AAV patients may reveal the molecular basis of this observation.

REFERENCES

[1] Lyons PA, Rayner TF, Trivedi S, et al. Genetically distinct subsets within ANCA-associated vasculitis. N Engl J Med 2012; 367:214-223.
[2] Tsuchiya N. Genetics of ANCA-associated vasculitis in Japan: a role for HLA-DRB1*09:01 haplotype. Clin Exp Nephrol 2013; 17:628–630.
[3] Xie G, Roshandel D, Sherva R, et al. Association of granulomatosis with polyangiitis (Wegener's) with HLA-DPB1*04 and SEMA6A gene variants: evidence from genome-wide analysis. Arthritis Rheum. 2013;65(9):2457-68.

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AB0007 IL12B POLYMORPHISMS ARE ASSOCIATED WITH ELEVATED SERUM LEVELS OF IL-12P40, IL-23 AND GENETIC PREDISPOSITION TO RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is the most common type of autoimmune arthritis in which genetic predisposition in close interaction with environmental triggers seems to be the major factor in the disease pathogenesis. Genetic analyses suggest a polygenic inheritance, as the largest genetic contribution to RA susceptibility remains the HLA–DRB1 gene, residing within the HLA gene complex. Since immune dysregulation plays a key role in immune-mediated inflammatory disorders, genetic variations within cytokine loci may contribute to variability in the immune response determining susceptibility or resistance to a certain autoimmune disease.
Objectives: We aimed to investigate whether IL12B polymorphisms are involved in causation of RA and in variations of circulating IL-23 and IL-12p40 levels in our Bulgarian population.
Methods: A total of 125 RA patients aged from 18 to 79 years in comparison to 239 age- and sex-matched healthy controls (HC) were genotyped for rs17860508 and rs3212227. Both *IL12B* polymorphisms were investigated by polymerase chain reaction (PCR) - based methods. Serum IL-12p40 and IL-23 concentrations measurement was done using ELISA test in 67 RA patients and 55 age-matched HC.
Results: An association between the rs17860508 polymorphism and RA development was established under the allelic model (allele 2 vs allele 1; OR = 1.68, 95%CI = 1.17–2.42, p = 0.0044), the co-dominant model (2.2 vs 1.1, OR = 2.83, 95%CI = 1.37–5.86; 1.2 vs 1.1 OR = 1.76, 95%CI = 0.91–3.41; p = 0.017), the dominant model (1.2 + 2.2 vs 1.1; OR = 2.12, 95%CI = 1.15–3.90, p = 0.014), and the recessive model (2.2 vs 1.1 +1.2; OR = 2.00, 95%CI = 1.10–3.62, p = 0.022). These results suppose that the homozygous 2.2 genotype could be predisposing, while 1.1genotype might be protective factor to RA susceptibility. No association between the rs3212227 and RA risk was revealed under the same genetic models. Also, a combined two loci model was designed with a referent group - the individuals with the *IL12Bpro* 1.1 + *IL12B* 3' UTR AA genotype. We found that the combination of *IL12Bpro* 1.1 with *IL12B* 3' UTR AA genotype is protective factor for RA susceptibility, whereas the carriage of *IL12Bpro* allele 2 despite hetero- or homozygosity simultaneous with *IL12B* 3' UTR AC/CC genotypes increase the RA risk more than 3-fold. The highest risk for RA susceptibility was established in the carriers of *IL12B* 3′ UTR allele C in combination with *IL12Bpro* 2.2 genotype, which was estimated to be 12.6 (95%CI = 2.478–71.412; p < 0.001). Circulating IL-12p40 and IL-23 levels were increased in the RA patients as a difference was observed depending on genotypes of rs17860508 and rs3212227. We found a functional effect of the rs3212227; the AA genotype was associated with a higher production of both IL-12p40 and IL-23 in RA cases, whereas the lowest serum levels were seen in CC genotype carriers. Also, the rs17860508 2.2 genotype, identified as a risk for RA, was associated with a higher serum levels of IL-23 in all patients. Notably, the highest circulating IL-23 levels were observed in carriers of the rs3212227 AA genotype and rs17860508 2.2 genotype compared to the remaining genotypes.
Conclusion: *IL12Bpro* (rs17860508) and 3' UTR (rs17860508) polymorphisms does confer susceptibility to RA either as an individual or combinatorial effect and might influence the RA occurrence through regulating the expression of IL-12/IL-23 p40 and production of IL-23.
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AB0008 CLINICAL AND GENETIC FEATURES OF NON-BACTERIAL OSTEOMYELITIS IN RUSSIAN FEDERATION

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Background: Chronic non-bacterial osteomyelitis (CNO) is Data about incidence, prevalence and clinical and genetic features of chronic non-bacterial osteomyelitis (CNO) in Russia is scarce.
Objectives: The aim of our study was to evaluate clinical and genetic peculiarities of CNO in Russia.
Methods: The diagnosis of CNO was made with criteria, proposed by Jansson [1, 2], after the exclusion of other causes of bone disease. Our cohort consists of three main subtypes: i) early-onset (<5 years) CNO (n=22); ii) CNO, associated (n=20) and iii) not associated (n=59) with rheumatic diseases (RD). Targeted next generation sequencing (NGS) analysis of 302 genes related to primary immune defficiency syndromes and autoinflammatory syndromes was performed.
Results: We selected a subgroup of the CNO patients having the following features: 1) early disease onset (<5 years); 2) all children were initially diagnosed as having tuberculosis (TB) due to bone morphology findings (granulomatosus, e.g. tuberculosis-like inflammation), but had negative TB culture test; 3) initial treatment with combination of 3-4 anti-MBT drugs during 1-2 years was ineffective, and the patient continued to develop new inflammatory bone foci; 4) patients had very severe clinical (fever and symptomatic arthritis) and radiological signs of disease; 5) all patients were from areas with traditionally high prevalence of consanguinity (table).

Parameter	EO-CNO (n=22)	"CNO w/o RD" (n=59)	CNO with RD (n=20)	p
Onset age, years	3.0 (2.1-4.8)	7.3 (2.8-11.7)	10.3 (8.2-12.2)	0.0009
Fever at onset, n (%)	14/22 (64)	23 (39)	5 (25)	0.03
Foci number	5.0 (1.5-6.0)	3.0 (1.0-4.0)	2.0 (1.0-6.0)	0.048
Symptomatic arthritis, n (%)	20/22 (91)	33 (56)	17 (85)	0.003
North Caucasus origin, n (%)	22 (100)	0 (0)	0 (0)	<0.00001
Granulematosus inflammation (tuberculosis-like), n (%)	22 (100)	0 (0)	0 (0)	<0.00001
Prevalence of CNO	1: 42,000	1:450,000	1:1,375,000	<0.00001

In the subgroup patients with early onset we performed genetic tests. Rare variants of PID genes were detected in 7/22 (32%) patients. Mutations affecting the genes previously associated with CNO were found only in two patients: one of them carried heterozygous variant IL1RN c.170G>T (p.C57F) and another had IL1RN c.512T>C (p.V171A). No mutation of LPIN2 was revealed. Other detected variants included one pathogenic MEFV p.M694V mutation in heterozygous state and a number of VUS in CD40LG, NLRP12, CR2, NLRP3, IL12B, PLCG2, SH3BP2, CARD14, IRF8, CASP10 and NFKB1A genes.

Conclusion: We have found the unique regional subtype of CNO with early-onset in North Caucasus region with at least 10 times higher prevalence. We have not yet seen similar patients in other nationalities of Russia. Mutations in known genes were detected only in a minor fraction of CNO patients from Dagestan and Chechnya.

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REFERENCES

[1] Jansson AF, Müller TH, Gliera L, Ankerst DP, Wintergerst U, Belohradsky BH, Jansson V. Clinical score for nonbacterial osteitis in children and adults. Arthritis Rheum. 2009;60(4):1152-9.
[2] Jansson AF, Grote V; ESPED Study Group. Nonbacterial osteitis in children: data of a German Incidence Surveillance Study. Acta Paediatr. 2011;100(8):1150-7.

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AB0009 IDENTIFICATION OF A NOVEL POLYMORPHISM OF ERAP1 IN A GROUP OF ITALIAN PATIENTS WITH BEHÇET SYNDROME

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Background: The endoplasmic reticulum aminopeptidase protein 1 gene (*ERAP1*) was associated to several human diseases, including Behçet syndrome (BS), a multisystemic disorder with unknown etiology. ERAP1 protein is involved in immune response and its role can be influenced by gene single nucleotide variations (SNVs) with an unclear mechanism [1-5].
Objectives: We aim to genotype *ERAP1* whole structure searching for SNVs, in 50 consecutive BS patients and 50 sex and ethnically-matched healthy controls (HC) unrelated to each others and/or to BS patients.
Methods: We used both bioinformatics and molecular methodologies. Specific primers for the coverage of all *ERAP1* regions were designed using the NCBI Primer-Blast tool. Genomic DNA was extracted from whole blood and amplified using *in vitro* PCR. Good-quality PCR amplicons were directly sequenced using the GATC Biotech Sanger sequencing service and bioinformatically analysed using Mutation Surveyor software and NCBI-Blast Nucleotide on line similarity search tool. SNV functional impact was predicted using on line PolyPhen-2 [6], while the 3D protein prediction was obtained using 3D Protean server [7].
Results: Our study was performed recruiting an explorative cohort of BS patients from Southern Italy, a population characterized by low disease prevalence. We identified a novel heterozygous SNV at 18169 nucleotide position (NG_027839.1: g.18169A>T; HGVS nomenclature) within *ERAP1* exon 3 (Fig. 1a). It was found in 7/50 (14% of cases) of BS patients and in none of HC. The novel polymorphism was submitted and released in GenBank Database (MK252970 accession number). The SNV was a missense variation responsible for the substitution glutamate (hydrophilic amino acid) to valine (hydrophobic amino acid) at 183 position (NP_057526.3:p.Glu183Val; HGVS nomenclature) (Fig. 1b). This is a conserved site involved in the substrate binding, due to its significant role in the anchorage of the N-terminal amine group of the peptides. Because of the different amino acid chemical features, the computational assessment of the protein structure was performed (Fig. 1c) recognizing a change in the protein energy and stability: the SNV was associated to a more stable protein chain (ΔE: -2.022), probably affecting the enzyme conformational state change and activity, as well as the substrate binding process. The amino acid change was predicted to be damaging with maximum score when PolyPhen-2 prediction software was queried (score: 1.00) (Fig. 1d).
Conclusion: We found a SNV not previously reported in literature in a relatively small group of Italian BS patients. Our data need to be tested in a larger case-control study. In particular, the link between our SNV and the protein stability is to be validated in future functional studies.

REFERENCES

[1] A.L. Hanson, et al. Arthritis Rheumatol 2018.70:255.
[2] E. Reeveset al. J. Immunol 2013.191:35.
[3] G. Kochan, et al. Proc. Natl. Acad. Sci. USA 2011.108:7745.
[4] M. Takeuchi, et al. Ann. Rheum. Dis 2016.75:2208.
[5] M.J. Ombrello, et al. Curr. Opin. Rheumatol 2015.27:349.
[6] I.A. Adzhubei, et al. Nat. Methods 2010.7:248.
[7] T.N. Plasterer. PROTEAN. Protein sequence analysis and prediction. Mol Biotechnol 2000.16:117.

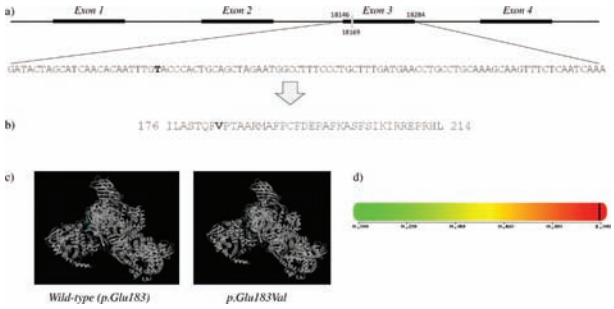


Figure 1. a) Localization of our *de novo* SNV and nucleotide sequence (polymorphic site in bold font). b) amino acid sequence (the polymorphic sites in bold font. c) 3D Protean software of wild-type and p.Glu183Val polymorphic sequences. d) PolyPhen-2 output showing the SNV maximum score of pathogenicity.

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AB0010 THE ASSOCIATION OF THE LTA AND PTPN22 GENES POLYMORPHIC VARIANTS WITH THE REDUCED IMMUNOGLOBULIN A LEVEL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Data from a number of studies indicate the presence of a genetic predisposition to the level of immunoglobulins [1]. The aberration in the distribution of serum immunoglobulin A (IgA) concentrations was previously shown in patients with juvenile idiopathic arthritis (JIA) [2].
Objectives: The goal of the study was to determine whether the *LTA* rs909253 and *PTPN22* rs2476601 polymorphic loci variants are associated with the reduced IgA level in JIA patients.
Methods: The study included 234 JIA patients (154 girls and 80 boys) from the Republic of Bashkortostan, Russia. IgA levels were measured in serum by the radial immunodiffusion method and considered reduced when they were less than the lower limit of established age-dependent reference intervals. Genotyping was performed by the real-time PCR method, and statistical processing of the results – using the two-tailed Fisher exact test (p) and the odds ratio (OR) with a 95% confidence interval (CI).
Results: Reduced IgA levels were detected in 10.68% of patients with JIA (n=25), and the majority of them were girls (n=21). There were only four boys with the reduced IgA level, and therefore the isolated analysis was not carried out for them.
The analysis of the *LTA* rs909253 polymorphic locus in the general JIA group, as well as in girls with JIA, showed that, in the presence of the reduced IgA level, the heterozygous genotype *LTA* rs909253*AG was significantly less common than in the absence of this IgA level abnormality (the general JIA group: 20.00% vs. 48.33%, p=0.010, OR=0.267, 95% CI 0.107-0.712; girls with JIA: 19.05% vs. 45.11%, p=0.031, OR=0.286, 95% CI 0.101-0.843, respectively).
When studying the *PTPN22* rs2476601 polymorphic locus in the general JIA group, the risk markers for the formation of the reduced IgA level were not established (p>0.1). At the same time, it turned out that in girls with JIA with the reduced IgA level, the genotype *PTPN22* rs2476601*GG was significantly more common, and the allele *PTPN22* rs2476601*A was significantly less common than in girls with JIA with normal or elevated IgA levels (*GG: 95.24% vs. 73.68%, p=0.028, OR=7.143, 95% CI 1.162-76.405; *A: 2.38% vs. 14.66%, p=0.025, OR=0.142, 95% CI 0.014–0.865, respectively).
Conclusion: As a result of the study, the association of the *LTA* rs909253 and *PTPN22* rs2476601 polymorphic loci variants with the reduced IgA level in girls with JIA was established.

REFERENCES

[1] Jonsson S, Sveinbjornsson G, de Lapuente Portilla AL, et al. Identification of sequence variants influencing immunoglobulin levels. Nat Genet. 2017 Aug;49(8):1182-1191.

[2] Cassidy JT, Petty RE, Sullivan DB. Abnormalities in the distribution of serum immunoglobulin concentrations in juvenile rheumatoid arthritis. J Clin Invest. 1973 Aug;52(8):1931-1936.

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AB0011 CLINICAL CHARACTERISTICS AND GENETIC EXPRESSION IN A COHORT OF PATIENTS WITH FAMILY MEDITERRANEAN FEVER

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Background: Familial Mediterranean fever (FMF) is the most frequent monogenic periodic fever syndrome and is characterized by recurrent episodes of fever, serositis, arthritis, dermal manifestations and long-term renal complications (amyloidosis is the most important complication). The genetic mutation of the disease is found in the MEFV gene located on the short arm of chromosome 16 and is inherited in an autosomal recessive manner. It affects the populations of the Mediterranean basin and is diagnosed according to the clinical evaluation.
Objectives: To describe the clinical characteristics of a cohort of patients with FMF and to study the different genetic mutations located in the MEFV gene.
Methods: Retrospective descriptive study of patients treated in our Hospital (2008-2018), with FMF diagnosis and MEFV gene mutation. The data was obtained through the review of medical records.
Results: We included 52 patients (29 men), mean age 41 years. The following mutations have been identified in alleles of the MEFV gene: Non-pathogenic in 34 patients (65%) (p 202Q 73%, p148Q 17%, p. 319K 6% and p339F 3%). Pathogenic in 18 patients (34%) (pr 202Q 22%, eg 148Q 27%, pr 653H 5%, pm 694V 16%, pi 159T 5%).
In 17% of the patients family history was documented. Elevation of acute phase reactants in 41 patients (79%) (C Reactive Protein 75%, Globular sedimentation rate 65%). Echocardiography was performed in 14 patients, with diagnosis of pericardial effusion in 6 of them. Two patients develop renal amyloidosis, one of them (homozygous for the mutation 148Q) died due to this complication.
54% of patients use colchicine as initial treatment, achieving 50% good response with control of symptoms. 19% undergo treatment with glucocorticoids (0.5-1 mg/kg/day), needing to add methotrexate in 1 patient and hydroxychloroquine in another. Four also use biological therapy (1 tocilizumab, 2 anakinra, 1 canakinumab) and 2 thalidomide to control skin manifestations.
Conclusion: The genetic study confirms the diagnosis of FMF, allowing it to be differentiated from other SAIs. It also has prognostic value, depending on the mutation detected and if it affects one or both alleles. In our series, the most prevalent symptoms in patients with pathogenic mutations were fever, abdominal pain and arthromyalgia.
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AB0012 GENETIC EXPRESSION AND CLINICAL MANIFESTATIONS IN A COHORT OF PATIENTS WITH AUTOINFLAMMATORY SYNDROME

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Background: The autoinflammatory syndromes (SAI) encompass a set of diseases in which there is an alteration of the innate immune response, contrary to what occurs in autoimmune diseases, in which the origin is due to pathological changes in the adaptive immune response. These diseases have common symptoms such as fever, skin, joint and lung involvement, among others, so they can be difficult to diagnose and classify.
Objectives: -Describe the clinical and genetic characteristics of a cohort of patients with autoinflammatory syndromes (SAI).
-To study the clinical manifestations of patients with SAI depending on the genetic alteration
Methods: Retrospective descriptive study of patients seen in our Hospital (2008-2018), with a diagnosis of SAI. The data was obtained through the review of medical records.
We have included data from patients who present a positive genetic study, both for described and pathogenic mutations, as well as nonpathogenic mutations, but which present a clinical picture according to this pathology.
Results: We included 80 patients (52 men), mean age 41 ± 13 years. Fourteen patients (17.5%) presented family history. Summary of diagnoses (TABLE 1) and associated mutations by order of frequency (TABLE 2).

DIAGNOSIS	FMF	52	65,0%
	TRAPS	13	16,3%
	SCHNITZEL SINDR	1	1,3%
	GEN NOD	0	0,0%
	GEN NLRP12	3	3,8%
	CRIOPIR	4	5,0%
	MUCKLE-WELLS	1	1,3%
	PFAPA	0	0,0%
	DITRA	1	1,3%
	DADA 2	1	1,3%
	PAPA	2	2,5%
	FCAS	1	1,3%
	CINCA	1	1,3%

GEN/ALTERED PROTEIN	MEFV(P.R202Q)	29	37,7%
	MEVF(p.E148Q)	12	15,6%
	MEFV(p.E319K)	2	2,6%
	MEFV(p.S339F)	1	1,3%
	TNFRSF1A(p.R92Q)	11	14,3%
	TNFRSF1A(p.P46L)	1	1,3%
	NLPR3(P.v198M)	3	3,9%
	NLRP12(F402L)	3	3,9%
	MEFVp.R653H	1	1,3%
	MEFV(p.M694V)	4	5,2%
	MEFV(pI159T)	1	1,3%

The most frequent clinical manifestations: Arthralgias 77.5%, followed by high fever (> 39) 73.8%, myalgias 72.5%, abdominal pain 56.3%, exanthema 47.5%, arthritis 35%, pericarditis 28.8%, headache 21.3%, pharyngitis 21.3% and canker sores 20%. The onset of the picture was a fever in 59 patients (73.8%) accompanied by cutaneous manifestations in 51.2% of the cases, with the rest of the symptoms being variable depending on the mutation studied.
The most affected joints were: Metacarpophalangeal in 18 patients (22.8%), ankles in 15 patients (18.8%), proximal interphalangeal in 8patients (10%), hips in 2 patients (2.5%) and knees in 2 patients (2.5%).
Elevated acute phase reactants were found in 53 patients (66.8%), with high sedimentation velocity in 56.3% and C reactive protein in 63.3%.
The initial treatment was based on colchicine in 45% of the cases, needing to add corticosteroids in 25% of the patients. 10.1% required drugs modifying the disease, being the most frequent methotrexate (74.25%).
Sixteen patients (20%) required biological therapy, being the most used anakinra (12.5%), followed by etanercept (2.5%) and canakinumab (2.5%).
In the period of time analyzed, 3 patients died due to causes unrelated to the SIA.
Conclusion: -The results obtained are consistent with what exists in the medical literature.The most frequent SAI in our center is the family Mediterranean fever, followed by the TRAPS.The most frequent mutation was the MEFV (P.R202Q), followed by the MEVF (p.E148Q).

- With our study we want to reflect the variety of symptoms presented by patients with SAI diagnosed in adulthood. Despite the great variability, the most frequent symptoms are arthralgia, fever greater than 39 °C and myalgias.
- The most used treatment in this type of patients is colchicine and respond to this positively in most cases.

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AB0013 GENOMIC PROFILING OF INFLAMMATION-RELATED GENES IN NEURO-BEHÇET SYNDROME: A PRELIMINARY ITALIAN STUDY

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Background: Behçet Syndrome (BS) is a chronic vasculitis characterized by a wide spectrum of clinical manifestations, including the rare nervous system

involvement, known as "Neuro-BS" (NBS) [1-3]. BS inflammatory features were studied in several genetics studies with focus on single nucleotide polymorphisms (SNPs) of genes involved in inflammation and immune response [4,5]. A very few papers assessed the mutational state of NBS patients and this characterization was limited to a small number of SNPs [3].

Objectives: The aim of this study was to analyse the genetic background of a homogenous group of Italian NBS (parenchymal form) to genotype some SNPs of inflammation-related genes.

Methods: NBS patients were extracted from our database and retrospectively studied. Molecular characterization was performed for a subset of 20 NBS patients and 42 sex-matched healthy controls (HC) via: a) bioinformatics consultation for SNPs selection and primer design; b) SNPs genotyping: DNA extraction, PCR amplification, direct sequencing; c) DNA variant analysis using similarity search tool and specific software. In a second phase of analysis, a group of 30 BS patients without neurological involvement (no-NBS) was also genotyped. The odds ratio (OR) was calculated to assess the strength of BS association for each genotype.

Results: NBS patients subset was formed by 14 males and 6 females with mean age equal to 44.20 (±10.73) years. Six SNPs were considered eligible for molecular analysis and genotyped. Our results underlined the major role of *ERAP1* rs17482078 (Table 1a). rs17482078 GG genotype frequency was higher in controls (p-value<0.01), while GA genotype frequency was lower in the same group (p-value<0.05). rs17482078 AA genotype was absent in control group, while its frequency was equal to 10% for the patients (p-value<0.05). rs17482078 GA frequency was higher in NBS patients compared with no-NBS patients (p-value<0.01) (Table 1b). No statistically significant differences were found for other SNPs of *ERAP1* neither for *IL-10* and *STAT4* polymorphisms when NBS patients and controls were compared.

Gene	SNP ID	Genotype	NBS patients (n=20) n (%)	Controls (n=42) n (%)	p-value	OR (95% CI)
ERAP1	rs30187	AA	4 (20.00)	11 (26.19)	0.5947	0.70 (0.19-2.57)
		AG	7 (35.00)	19 (45.24)	0.4451	0.65 (0.22-1.96)
		GG	9 (45.00)	12 (28.57)	0.2014	2.05 (0.68-6.18)
	rs17482078	GG	7 (35.00)	30 (71.43)	0.0063**	0.22 (0.07-0.67)
		GA	11 (55.00)	12 (28.57)	0.0440*	3.06 (1.01-9.24)
		AA	2 (10.00)	0 (0.00)	0.0467*	46.67 (0.08-∞)
	rs27044	CC	5 (25.00)	14 (33.33)	0.5058	0.67 (0.20-2.21)
		CG	5 (25.00)	16 (38.10)	0.3085	0.54 (0.17-1.78)
		GG	10 (50.00)	12 (28.57)	0.0993	2.50 (0.83-7.53)
IL-10	rs1800872	AA	2 (10.00)	4 (9.52)	0.9527	1.06 (0.18-6.31)
		AC	4 (20.00)	17 (40.48)	0.1113	0.37 (0.10-1.29)
		CC	14 (70.00)	21 (50.00)	0.2979	1.75 (0.61-5.04)
	rs1518111	AA	7 (35.00)	19 (45.24)	0.4451	0.65 (0.22-1.96)
		AG	4 (20.00)	13 (30.95)	0.3662	0.56 (0.16-2.00)
		GG	9 (45.00)	10 (23.81)	0.0907	2.62 (0.84-8.12)
STAT4	rs7572482	TT	6 (30.00)	8 (19.05)	0.3350	1.82 (0.52-6.22)
		TC	8 (40.00)	20 (47.62)	0.5731	0.73 (0.25-2.16)
		CC	6 (30.00)	14 (33.33)	0.7930	0.86 (0.27-2.17)

Table 1a. Genotype frequencies of *ERAP1*, *IL-10* and *STAT4* SNPs in NBS patients and controls

Gene	SNP ID	Genotype	NBS patients (n=20) n (%)	No-NBS patients (n=30) n (%)	p-value	OR (95% CI)
ERAP1	rs17482078	GG	7 (35.00)	18 (60.00)	0.0830	0.36 (0.11-1.16)
		GA	11 (55.00)	5 (16.67)	0.0044**	6.11 (1.66-22.49)
		AA	2 (10.00)	7 (23.33)	0.2293	0.37 (0.07-1.97)

Table 1b. Genotype frequencies of *ERAP1* rs17482078 in NBS and no-NBS patients

Conclusion: Our results reported for the first time the genotype distribution of several susceptibility loci in a group of Italian NBS patients. The data suggest a possible association between *ERAP1* rs17482078 and NBS. Larger analyses were required to verify our preliminary findings.

REFERENCES

[1] Saip S, et al. 2014. Handb Clin Neurol;121:1703-23;
[2] Noel N, et al. 2014. Rev Med Interne;35(2):112-20.
[3] Gheita TA, et al. 2015. Joint Bone Spine;82(3):213-5.
[4] Gul A. 2015. Current Opinion in Rheumatology;26:56-63.
[5] Takeuchi, et al. 2015. J Autoimmun. 2015;64:137-148.

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AB0014

A MIR146A POLYMORPHISM IS ASSOCIATED WITH ANTI-CARP ANTIBODIES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: (SLE) is a chronic autoimmune disease with a complex pathogenesis in which genes and environmental factors interact leading to a protean clinical picture. Joint involvement is one of the most common manifestations in SLE patients, with a prevalence ranging from 69 to 95%. This feature significantly influences the patients' quality of life, possibly leading to disability and impaired functional performance in daily activities. Identification of prognostic biomarkers, able to identify patients at risk to develop this more aggressive phenotype, is mandatory. Autoantibodies associated with inflammatory arthritis, such as Rheumatoid Arthritis (RA), have been shown to play a role also in SLE arthritis. For instance, ACPA can be found in approximately 16% of SLE patients and, recently, it was demonstrated that anti-carbamylated proteins antibodies (anti-CarP) can be identified in up to 28.3% of SLE patients (1).

Objectives: Thus, our aim was to analyze previously identified loci associated with SLE in a cohort of SLE patients to evaluate their influence on autoantibody production.

Methods: We recruited 52 Italian SLE patients. A panel of 34 SNPs in 19 genes involved in immune response, autophagy and inflammation, was selected. SNPs genotyping was performed by allelic discrimination assay by TaqMan assays (Applied Biosystems, Foster City, CA, USA) and ABI PRISM 7000. The main clinical/laboratory features (including injury index and disease activity) were collected on an electronic platform. The presence of Rheumatoid Factor (RF), ACPA, and anti-CarP antibodies was investigated. All autoantibody assays were carried out in duplicate, commercial enzyme-linked immunosorbent assay (ELISA) kits were used and the results were evaluated according to the manufacturers' instructions. Detailed methods are described in (1). A genotype/phenotype correlation analysis was performed.

Results: Clinical and demographic data of patients are described in table 1. The variant allele of rs2910164 (MIR146a) (P=0.03) was significantly associated with presence of anti-CarP antibodies in SLE. Specifically, patients carrying the C allele of MIR146a were more likely to have anti-CarP antibodies (P=0.01, OR 5.018, 95% CI 1.414-17.811). Among the clinical and laboratory features, the same polymorphism was associated with presence of arthritis in clinical history (P=0.02), and with anti-dsDNA positivity (P=0.025). In a multinomial logistic regression analysis, MIR146A was independently associated with anti-CarP (P=0.017, Exp(B)=5.433, 95%CI 1.345-21.944).

Conclusion: Carbamylation is a non-enzymatic process consisting in the addition of a cyanate group on self-proteins determining a modification in the tertiary structure. This change causes the generation of new epitopes and the consequent production of autoantibodies. This is the first report suggesting that anti-CarP production is genetically driven. Indeed, Mir146a expression is altered in SLE and has been linked with autoantibody production in lupus-prone mice models. Probably, the higher IFNa levels observed in patients carrying the C allele can be responsible for such higher autoantibody production.

Clinical/Laboratory features		
Age (mean ± SD)	47.51±9.080	
Sex (F:M, n/%)	49:3	94.23:5.77
Disease Duration (months, mean ± SD)	171.3±115.9	
Anti-CarP (n, %)	17	32.69
ACPA (n, %)	11	21.15
RF (n, %)	11	21.15
Articular Involvement		
Arthritis	52	100.00
Jaccoud's arthritis	9	17.31
SLEDAI (mean ± SD)	3.04±2.93	
SDI (mean ± SD)	1.8±2.05	
DAS28 (mean ± SD)	3.5±1.05	
CDAI (mean ± SD)	11.15±8.5	
SDAI (mean ± SD)	11.7±9.31	
STR (mean ± SD)	0.38±0.55	
Erosions	20	38.46
Cutaneous involvement (n, %)	32	61.54
Serositis (n, %)	10	19.23
Hematological involvement (n, %)	28	53.85
Renal involvement (n, %)	15	28.85
Neurological (n, %)	7	13.46
ANA	45	86.54
Anti-dsDNA	35	67.31
Anti-Sm	9	17.31
Anti-RNP	10	19.23
Anti-SSA	16	30.77
Anti-SSB	7	13.46
Anti-cardiolipin	12	23.08
Anti-beta2glycoprotein I	9	17.31
LA	9	17.31
Low complement (C3/C4)	21	40.38
Glucocorticoids	42	80.77
HCQ	41	78.85
CyA	9	17.31
MTX	23	44.23
CY	4	7.69
MMF	19	36.54
RTX	2	3.85
AZA	8	15.38
ASA	15	28.85
TAO	5	9.62
BLM	6	11.54

REFERENCE

[1] Massaro L, et al. Anti-carbamylated protein antibodies in systemic lupus erythematosus patients with articular involvement. Lupus. 2018;27:105-111.

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AB0015 MICRORNA-155 EXPRESSION IN BEHÇET'S DISEASE

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Background: Mature microRNAs (miRNAs) are a class of naturally occurring, small non-coding RNA molecules. MicroRNAs are partially complementary to one or more messenger RNA (mRNA) molecules, and their main function is to downregulate gene expression in a variety of manners, including translational repression, mRNA cleavage, and deadenylation.

Recent miRNA deletion studies have revealed a central role in the regulation of the immune response. The deletion of miRNA-155 impairs T and B cell differentiation in germinal centers, and greatly affects antibodies and cytokines production. Furthermore, aberrant expression of miR-155 has been reported in human autoimmune disorders such as rheumatoid arthritis and systemic lupus erythematosus.[1] Whether miR-155 plays a role in the pathogenesis of Behçet's Disease is not yet known and is therefore the subject of this study.

Objectives: The aim of this work is to study the expression of microRNA-155 as a molecular biomarker in Behcet's disease.

Methods: Thirty patients with Behçet's disease and 15 healthy matched controls were included. Patients fulfilled the International Study Group (ISG) diagnostic Criteria of Behçet's Disease. Exclusion Criteria included other types of primary or secondary vasculitis; reactive arthritis; inflammatory bowel disease; current or past history of cancer, chemotherapy or radiotherapy; current infection; long standing diabetes mellitus; and hypertension.

Total RNA, including miRNAs isolation, from peripheral blood mononuclear cells (PBMCs) was extracted by using miRNeasy Mini Kit (QIAGEN, cat. no. 217004). This was followed by reverse transcription into complementery DNA (cDNA). Expression of microRNA-155 was carried out using quantitative real time polymerase chain reaction (RQ_PCR). Relative expression of microRNA155 was calculated using $2 - \Delta\Delta^{ct}$ formula. Where ct = (ct miRNA – ct miRNA control) and Ct is the fractional cycle number at which the fluorescence passes the fixed threshold.

Results: Our results showed a significantly decreased expression of miR-155 in peripheral blood mononuclear cells (PBMCs) of Behçet's disease patients with active disease compared to that in patients with inactive disease as well as healthy control (p=0.026).

The level of miR-155 showed a significant positive correlation with patients' age (p=0.042), and significant negative correlation with BDCAF activity score of the disease (p=0.034), and platelets count (p=0.011) (Table1).

N=30	microRNA155	
	r_s	P
Age	0.374*	0.042*
BDCAF Activity Score	-0.389*	0.034*
Duration of the disease	0.143	0.450
ESR	0.159	0.402
CRP	0.038	0.841
Hemoglobin	0.065	0.735
Platelets	-0.458*	0.011*
White blood cells	0.166	0.381
Serum Urea	0.191	0.313
Serum Creatinine	-0.135	0.477

Table 1. Correlation between microRNA155 with different parameters in cases group

Conclusion: Downregulation of miR-155 expression in active BD patients may be used as a molecular biomarker for increasing activity and severity of Behcet's disease. This pathway could be a potential target for a new therapeutic strategy.

REFERENCES

[1] Kurowska-Stolarska M, Alivernini S, Ballantine LE, et al. MicroRNA-155 as a proinflammatory regulator in clinical and experimental arthritis. Proc Natl Acad Sci 2011;108: 11193–8.

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AB0016 COMBINED GENOME-WIDE ASSOCIATION AND GENE-EXPRESSION META-ANALYSIS IDENTIFIES NOVEL PSORIASIS GENES

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Background: Psoriasis (Ps) is a common, inflammatory disorder affecting skin, joints and associated connective tissue, with significant genetic underpinnings. Multiple genome-wide association studies (GWAS) have been conducted with identification of several Ps loci. However, these only explain about a third of Ps genetic risk indicating that additional loci of modest effect remain to be discovered (1).

Objectives: Identify novel psoriasis genes that have functional consequences for psoriasis by altered gene-expression

Methods: Association clustering methods such as gene- and locus-based tests are more powerful than single variant analysis for identifying modest genetic effects (2, 3). Here, a dbGAP GWAS dataset (4) for Ps (pha002855: 1348 Ps cases and 1368 controls, genotyped for 448K SNPs) was analyzed using the locus-based algorithm, OASIS (3), to identify 13 highly significant loci other than the *HLA-C* locus. In these loci 50 genes were identified using SNIPPER, which were then subjected to gene expression analysis in three Ps GEO datasets.

Results: This genetic and functional analysis identified a total of 18 genes that were significantly associated and had altered expression in psoriasis skin. The most significant of these were two genes that were two-fold upregulated in Ps, *IL12B* (P=9x10^{-11}) and *TTC39B* (P=3x10^{-12}) and two genes that were repressed

<50%, *MAML2* (P=8x10^{-19}) and *EBF1* (P=1x10^{-12}). Interestingly, the expression of *IL23R* remained unaltered. Other genes that were significantly upregulated (1.5 – 2.0 fold) were *IL12RB2*, *TTC1* and *PSMD6*. Genes that were also significantly repressed (0.5 - 0.8 fold) were *SERBP1*, *ATXN7*, *PSIP1*, *ZNF385D*, *SIPA1L1*.
Conclusion: This combined genetic and functional meta-analysis elucidated novel genes, functional networks and pathways for psoriasis. These results will lead to important insights into the immunopathogenesis and treatment of psoriasis.

REFERENCES

[1] Tsoi LC, Stuart PE, Tian C, et al. Large scale meta-analysis characterizes genetic architecture for common psoriasis associated variants. Nat Commun. 2017 May 24;8:15382. PMID: 28537254.
[2] Luo L, Peng G, Zhu Y, et al. Genome-wide gene and pathway analysis. Eur J Hum Genet. 2010 Sep;18(9):1045-53. PMID: 20442747.
[3] Saeed M. Novel linkage disequilibrium clustering algorithm identifies new lupus genes on meta-analysis of GWAS datasets. Immunogenetics. 2017 May;69(5):295-302. PMID: 28246883.
[4] Nair RP, Duffin KC, Helms C, et al. Genome-wide scan reveals association of psoriasis with IL-23 and NF-kappaB pathways. Nat Genet. 2009 Feb;41 (2):199-204. PMID: 19169254.

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AB0017 COMPARISON BETWEEN THE ALTERED PERIPHERAL BLOOD MIRNA EXPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTEMATOSUS

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Background: MicroRNAs (miRNAs) are a class of small, non-coding RNAs that negatively regulate gene expression at posttranscriptional level. Altered miRNA expression in the circulation has been described in inflammatory joint diseases such as rheumatoid arthritis (RA) as well as in systemic rheumatic diseases, such as systemic lupus erythematosus (SLE). miR-146a and miR-155 have been found to regulate key signaling pathways involved in the pathogenesis of RA and SLE [1-2].
Objectives: To compare the expression levels of miR-146a and miR-155 in peripheral blood (PB) from RA and SLE patients in regard to their use as disease biomarkers.
Methods: 63 RA patients and 40 SLE were included in the study. The expression levels of miR-146a and miR-155 in whole PB were determined by qPCR (Sybr-Green technology) and compared to healthy controls (HCs). Relative changes of gene expression levels of the studied miRNAs were calculated by $2^{-\Delta\Delta Ct}$ method. SPSS was used for statistical analysis.
Results: 29 (46.03%) of the RA patients showed overexpression of miR-146a in the PB when compared to HCs, but the levels were not statistically significant to differentiate patients from HCs (p=0.365). 34 (53.97%) of the RA patients didn't show a statistically significant expression of miR-155 in the PB when compared to HCs and PB expression of miR-155 couldn't be used for differentiating RA from HCs (p=0.074). In the group of SLE patients the PB levels of miR-146a were over-expressed in 25 (62.5%) and levels of miR-155 were increased in 20 (50.0%) of the patients (p<0.05).
Conclusion: Although miR-146a and miR-155 are involved in key signaling pathways in the pathogenesis of RA their whole PB expression could not fully reflect the local pathological process and thus to differentiate patients from HCs. The expression of both miRNAs in whole PB of SLE samples showed a possibility for discriminating patients from HCs. Further analysis with larger sets is needed to confirm if altered systemic miRNA expression levels could be used in the clinical practice as disease biomarkers.

REFERENCES

[1] Honarpisheh M, Köhler P, von Rauchhaupt E, Lech M. The Involvement of MicroRNAs in Modulation of Innate and Adaptive Immunity in Systemic Lupus Erythematosus and Lupus Nephritis. J Immunol Res. 2018; 2018:4126106.
[2] Zhou Q, Haupt S, Kreuzer JT, et al. Decreased expression of miR-146a and miR-155 contributes to an abnormal Treg phenotype in patients with rheumatoid arthritis. Anna Rheum Dis. 2015; 74:1265-1274.

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AB0018 TRANSCRIPTOMIC CHARACTERIZATION OF SINGLE PATHOGENIC MEMORY B CELLS IN RHEUMATOID ARTHRITIS

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Background: Autoantigen-specific B lymphocytes are crucial players in the development of rheumatoid arthritis (RA). Despite the fact that ACPA+ autoreactive memory B cells have been observed in the majority of RA patients for a long time, their properties still remain enigmatic.
Objectives: In this study, we aimed to reveal transcriptomic nature of single pathogenic memory B cells from RA patients.
Methods: Single-cell full-length RNAseq data was generated from ACPA+ and control memory B cells from 7 human donors with established rheumatoid arthritis and subjected to transcriptome analyses as well as B cell receptor (BCR) assembly.
Results: Both transcriptome and BCR data was successfully generated from the majority of the sequenced cells. The success rate depended on chosen sequencing parameters as well as on a BCR assembling algorithm that was used. We observed expression of genes defining memory B cell population in our data as well as pathways crucial for their function.
Conclusion: Taken together, gene expression and BCR sequence data obtained from the same single cell can give novel insights into the biology and role of B cells in the development of the disease.
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AB0019 REPLICATIVE STUDY OF GWAS-ASSOCIATED CANDIDATE GENE LOCI IN PATIENTS WITH OSTEOARTHRITIS FROM THE BASHKORTOSTAN REPUBLIC

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Background: Osteoarthritis (OA) is one of the most common joint diseases and a global socially significant problem. Currently, new methods of early diagnosis of the disease are being developed, before the development of destructive processes in various tissues of the joint. The leading role in determining the pathophysiology of OA is given to the identification of genetic and epigenetic mechanisms.
Objectives: The main goal of the study was replicative analysis of the associations of loci associated with OA according to the data of genome-wide analysis of associations (GWAS) located near the DOT1L, ALDH1A, GNL3, GLT8D1, ASTN2, FILIP1, SENP6, NCOA3, DVWA, CHA11 genes with various localization OA.
Methods: DNA samples from 410 women were used (mean age 45.45 ± 2.35). Patients with OA was carried out in accordance with the criteria of the American Association of Rheumatology (1995), the debut of the disease before the age of 55 years and radiographic confirmation. For genotyping, PCR-RFLP analysis using KASP$^{@}$ technology was used. As a calculation tool, MS Office Excel 2007 (Microsoft), Statistica v.6.2 (StatSoft), SPSS v.13 (SPSS Inc) software packages are used.
Results: We conducted replicative analysis of the 12 loci that were the most significantly associated with OA in the results of GWAS study, among which rs12982744 and rs2302061 (DOT1L), rs4836732 (ASTN2), rs9350591 (FILIP1 &

SENP6), rs6976 (GLT8D1), rs6094710 (NCOA3), rs11177 (GNL3), rs7639618 (DVWA/COL6A4P1), rs3204689 (ALDH1A2), rs11842874 (MCF2L), s6539153 and rs835487 (CHST11).
The rs4836732 locus of the ASTN2 gene showed an association of the *C*C genotype with OA in general ($\chi2 = 5.064$, p = 0.024, OR = 2.78; 95% CI (1.11-6.97), with early manifestation of OA (up to 50 years) ($\chi2 = 5.357$, p = 0.004, OR = 5.35; 95% CI 1.53-18.68) and with generalized osteoarthritis ($\chi2 = 8.071$, p = 0.004, OR = 5; 95% CI 1.52-16.35), which is consistent with the results of GWAS.
The *T allele of the rs7639618 locus of DVWA gene showed an association with late onset OA ($\chi2 = 5.21$, p = 0.022, OR = 1.88; 95% CI 1.09-3.24).
The *T*T genotype (0.676) of the rs835487 locus (CHST11) was associated with OA of the hip ($\chi2 = 6.284$, p = 0.012, OR = 2.57; 95% CI 1.21-5.48), which contradicts the results GWAS, where the allele *G was significantly associated with OA of the hip in European populations.
An association of the allele *C ($\chi2 = 4.558$, p = 0.032, OR = 2.04; 95% CI 1.05-3.95) and its homozygous genotype *C*C (0.115) ($\chi2 = 6.398$, p = 0.01, OR = 22.3; 95% CI 1.22-408.21) in rs2302061 locus of the DOT1L gene with knee OA was find.
The *T*T genotype of the rs6976 (GLT8D1) was associated with early manifestation of OA ($\chi2 = 5.213$, p = 0.022, OR = 2.58; 95% CI 1.14-4.26).
The study of the rs3204689 locus (ALDH1A) revealed an association of the genotype *C*G with the generalized osteoarthritis ($\chi2 = 6.071$, p = 0.013, OR = 2.52; 95% CI 1.19-5.33) and the genotype *C*C turned out to be protective ($\chi2 = 5.226$, p = 0.022, OR = 0.39; 95% CI 0.17-0.89).
Conclusion: Thus, the replication of GWAS results does not always confirm the associations identified earlier, which may be due to a number of reasons.
Disclosure of Interests: None declared
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Adaptive immunity (T cells and B cells) in rheumatic diseases

AB0020 INTERACTION MTHFR 677C/T AND PON1 -108C/T POLYMORPHISMS IS ASSOCIATED TO ATHEROGENIC RISK IN RHEUMATOID ARTHRITIS PATIENTS FROM SOUTHERN MEXICO

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Background: The risk of cardiovascular disease in rheumatoid arthritis (RA) patients is 1.5 times higher compared to the general population. Some factors relationships to cardiovascular disease in RA are high clinic activity of the disease, the autoantibodies-positive, the disease duration and pharmacological treatment[1], as well as single nucleotide polymorphisms. Methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism and is considered a drug-metabolizing enzyme; MTHFR 677C/T polymorphism was described leading to reduced enzyme activity, increasing serum concentration of homocysteine, an intermediate product of methotrexate metabolism. Paraoxonase 1 (PON1) is a multifunctional enzyme that can detoxify through its homocysteine thiolactonase activity, the polymorphism identified in the position PON1 -108C/T exerts effects on serum activity and expression levels.
Objectives: We evaluate the association between the interaction MTHFR 677C/T and PON1 -108C/T polymorphisms and cardiovascular risk (CVR) in RA patients.
Methods: A cross-sectional study was performed including 250 RA patients diagnosed according to ACR/EULAR 2010 criteria, attended in a public hospital from southern Mexico. MTHFR 677C/T and PON1 -108C/T genotypes were determined by PCR-RFLP method. The clinic and metabolic parameters were evaluated. CVR was defined using different diagnostic tools. Logistic regression models were used to evaluate the association between interaction polymorphisms and CVR.
Results: We show high CVR in a variable prevalence according to diagnostics tools: TGs/HDL-c (64.8%), Castelli (50%) and Kannel (43%). Alleles frequency of 667C/T were 33% for C and 67% for T allele; PON1-108C/T 52% for C and 43% for T allele. In a multiple regression model adjusting by duration of disease, pharmacological therapy and DAS28-hsCRP score, carriers of the 667TT and -108CC genotypes had higher CVR according to TGs/HDL-c (>3%) (OR=4.68, p=0.019), Castelli (>3%) (OR=2.99, p=0.03) and Kannel index (>4.5% in woman and >5% in men) (OR=2.03, p=0.13).
Conclusion: Our results demonstrate an interaction between MTHFR 677C/T and PON1 -108C/T polymorphisms on the CVR, associated to atherogenic indexes in RA patients from southern Mexico.

REFERENCES

[1] Mackey RH, Kuller LH, Moreland LW. Cardiovascular disease risk in patients with rheumatic diseases. Clin Geriatr Med. 2017;33(1):105-117. doi: 10.1016/j.cger.2016.08.008.

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AB0020B QUANTIFYING DIFFERENCES IN HERITABILITY AMONG PSORIATIC ARTHRITIS (PSA), CUTANEOUS PSORIASIS (PSC) AND PSORIASIS VULGARIS (PSV)

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Background: Epidemiological studies have established a large recurrence risk ratio among siblings suggesting a strong genetic component for psoriasis and psoriatic arthritis (1). Better understanding of the heritability of PsC, PsV and PsA will lead to more efficient genetic profiling for psoriatic disease.
Objectives: We set out to assess the heritability of cutaneous psoriasis without known arthritis (PsC); psoriasis vulgaris (psoriasis irrespective of arthritis, PsV) and psoriatic arthritis (PsA) by interrogating SNPs from a large scale genotyping array.
Methods: The heritability of PsC, PsV and PsA were estimated by interrogating 715 PsA, 1155 PsC, 2938 PsV patients and 3117 unaffected controls of European ancestry. The samples were genotyped on a custom Axiom Biobank plus genotyping array and core GWAS chip with 461,092 autosomal SNPs. Further imputation led to 1.3M well-imputed SNPs based on the autosomal reference panel of the HapMap Phase 3 (HM3) CEU cohort. After strict filtering, 230k autosomal SNPs without imputation and 401k autosomal SNPs after imputation were retained for heritability estimation.
The following two methods were used to determine the heritability of PsC, PsV and PsA from SNP based data: Linkage Disequilibrium Adjusted Kinships (LDAK) and GCTA which relies on the restricted maximum likelihood algorithm (ReML). Sex and the top 5 principal components were used as covariates to control for gender effect and population stratification in each analysis. Parallel analyses were performed after removing SNPs from the MHC region. The prevalence also was used to adjust the heritability estimation.
Results: The heritability assessment for psoriatic disease for each method is presented in the table with and without imputation. Although the heritability estimates vary depending on the method, the heritability of PsC appears to be greater than PsA, for analysis that was done with and without imputation. Similar trends are noted when non-MHC SNPs were assessed.

Table 1. Heritability estimation before and after imputation, including and excluding MHC SNPs

Test	PsA		PsC		PsV	
	h2 (sd)	Imp'ed h2 (sd)	h2 (sd)	Imp'ed h2 (sd)	h2 (sd)	Imp'ed h2 (sd)
LDAK (all SNPs)	0.45 (0.10)	0.48 (0.08)	0.81 (0.09)	0.72 (0.07)	0.68 (0.06)	0.60 (0.05)
LDAK (non MHC SNPS)	0.28 (0.10)	0.32 (0.09)	0.48 (0.09)	0.41 (0.08)	0.40 (0.07)	0.35 (0.05)
GTCA (all SNPs)	0.39 (0.09)	0.27 (0.07)	0.42 (0.06)	0.34 (0.05)	0.26 (0.03)	0.20 (0.03)
GTCA (non MHC SNPs)	0.32 (0.09)	0.20 (0.07)	0.34 (0.06)	0.27 (0.05)	0.22 (0.03)	0.16 (0.03)

Conclusion: SNP based heritability estimates suggest greater heritability for PsC as compared to PsA. Common environmental factors may need to be considered to account the strong recurrence rate of PsA over psoriasis among first degree relatives reported in previous epidemiological studies, as this finding is not noted from large SNP based association studies.

REFERENCES

[1] Chandran V, Schentag CT, Brockbank JE, Pellett FJ, Shaumugrajah S, Toloza SM, Rahman P, Gladman DD. Familial aggregation of psoriatic arthritis. Ann Rheum Dis. 2009; 68(5):664-7.

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Adaptive immunity (T cells and B cells) in rheumatic diseases

AB0021 IMMUNOGENICITY OF TNF ALPHA ANTAGONISTS IN RHEUMATIC INFLAMMATORY DISEASES : IMPACT ON CLINICAL RESPONSE

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Background: One of the mechanisms implicated in the loss of response to TNF alpha antagonists in rheumatic inflammatory diseases is the formation of antibodies against these drugs (anti-drug antibodies: ADAb).
Objectives: The objective of our study was to determine the incidence of ADAb anti Infliximab (IFX) and anti Adalimumab (ADA) and to evaluate the therapeutic impact of the presence of ADAb, the rate of ADAb and trough serum concentration of the drug at the time of sampling and six months later.
Methods: A longitudinal, prospective and multicenter study was conducted including patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA) treated with IFX or ADA as a first biotherapy for at least six months. ADAb and trough levels were measured. The evaluation of the therapeutic response was made at the time of sampling and six months later.
Results: Fifty patients were included (17 RA and 33 SpA). ADAb were positive in 39% of SpA and 35% of RA. They were positive in 40% of cases for IFX and 25% for ADA. The presence of ADAb was negatively related to the trough levels of IFX and ADA during RA ($p=0.01$ and $p<0.0001$) and SpA ($p<0.01$ and $p<0.0001$). For the two pathologies, no impact of the presence of ADAb, the rate of ADAb or the trough levels was noted on the therapeutic response at the time of sampling. However, the presence of ADAb was related to a higher activity of SpA six months after the sampling ($p=0.05$). Factors that were related to ADAb formation were a high BMI in RA ($p=0.05$) and a longer duration of evolution of RA ($p=0.03$).
Conclusion: The presence of ADAb and low trough levels seem to not affect the therapeutic response in patients on TNF alpha antagonists. Other tracks than immunogenicity should be investigated to explain the loss of response to these biotherapies.
Disclosure of Interests: None declared
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AB0022 STUDY OF FUNCTIONAL ORIENTATION OF B CELLS IN PHYSIOLOGY AND SJÖGREN'S SYNDROME

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Background: Sjögren's syndrome (SS) is a chronic systemic autoimmune disease, characterized by mouth and eye dryness, due to irreversible destruction of glandular tissue by infiltrated lymphocytes. It is now well established that B cells play a key role in the physiopathology of SS. Indeed, B cells exhibit various signs of hyperactivity and produce excessive amounts of pro-inflammatory cytokines and immunoglobulins (Ig), especially IgG type-antibodies (Abs) (Kroese et al.,2014). Currently, it is suggested that the interleukin (IL)-21 (Wang et al., 2018) and IFNα (Yao et al., 2013), promote the generation of autoreactive IgG-producing plasma cells (PC). On the other side, some studies highlight the protective role of IgM producing cells in autoimmunity through enhanced efferocytosis and immune-regulatory properties (Ehrenstein and Notley, 2010).
Objectives: This study aims to understand the influence of IL21 and IFNα on the B cell differentiation and the subsequent functional responses of the cells according to their maturation stage. Moreover, this will also enable a further understand of the contribution of these cytokines to the pathogenesis of SS.
Methods: We established *in vitro* models to study the differentiation of different B cell subsets in a T-independent (TI) and T-dependent (TD) manner, under different cytokine stimulations. Naïve, switched memory, unswitched memory and CD27-negative memory B cells were isolated from peripheral blood of healthy controls (HC) and SS patients and thereby cultured in those different conditions. After three days of culture, the expression of surface markers and transcription factors was analysed by flow cytometry and molecular identity was further determined by transcriptional analysis. Additional functional assay was also performed to measure Abs and cytokine secretion.
Results: First results on HC suggest that switched memory B cells differentiate into IgG and IgA-secreting plasmablasts (PB), when stimulated in a TI manner. This process is highly increased in presence of IFNα. Unswitched memory B cells mostly become PB able to secrete IgM and IL10.
IL21 and IFNα oppose distinct effector functions. IL21 promote activation of B cells with an upregulation of the surface marker CD11c and T-bet transcription factor.
Transcriptomic studies are still in progress to further define the molecular profile of those distinct effector B cells.
Preliminary results on SS patients suggest that B cell differentiation is altered with a biased ratio between activated cells and PB.
Conclusion: This work will allow us a better understanding of the heterogeneity of the distinct effector B cells and their involvement in SS pathogenesis.

REFERENCES

[1] Ehrenstein, M. R. & Notley, C. A. The importance of natural IgM: scavenger, protector and regulator. Nature Reviews Immunology 10, 778–786 (2010).
[2] Kroese, F. G. M. et al. B-cell hyperactivity in primary Sjögren's syndrome. Expert Rev Clin Immunol 10, 483–499 (2014).
[3] Wang, S. et al. IL-21 drives expansion and plasma cell differentiation of autoreactive CD11chiT-bet+ B cells in SLE. Nat Commun 9, 1758 (2018).
[4] Yao, Y., Liu, Z., Jallal, B., Shen, N. & Rönnblom, L. Type I interferons in Sjögren's syndrome. Autoimmun Rev 12, 558–566 (2013).

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AB0023 IMPACT OF METABOLIC CHANGES DURING AGING ON HUMAN EX VIVO NAÏVE AND MEMORY CD4+ T CELL FUNCTION

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Background: Age-related dysfunction in immune cells (immunosenescence), such as T cell dysfunction, may contribute to the development of rheumatoid arthritis (RA). In aged people, senescent T cells tend to produce low amounts of pro-inflammatory cytokines leading to low-grade inflammation. However, cellular metabolism modulates effector functions such as cytokine production and proliferation in T cells by providing energy and building blocks. Metabolically, naïve and memory CD4+ T cells are relatively quiescent immune cells. Currently, the metabolic phenotype of naïve and memory CD4+ T cells and how metabolism affects functions of naïve and memory CD4+ T cells in aged people are not well understood.
Objectives: Therefore, we analysed the differences in the metabolic phenotype of peripheral naïve and memory CD4+ T cells in young and aged healthy donors to explore fundamental processes of immune-aging in the pathogenesis of RA.
Methods: Naïve and memory CD4+ T cells were isolated from PBMCs of young donors (18-35 years) and old donors (>50 years) by using MACS™ technology. Purity of isolated cell fractions was assessed by flow cytometry. *Ex vivo* naïve and memory CD4+ T cells were analysed by Seahorse™ Technology to determine proton efflux rate (PER) as a measure of glycolysis (glycPER) and oxygen consumption rate (OCR) as a measure of mitochondrial respiration (mitoOCR). Cytokine expression and secretion was measured by flow cytometry and multiplex assay. Finally, TCR-stimulated memory CD4+ T cell proliferation was determined using CSFE and Ki-67 after 3 days and 4 days by flow cytometry.
Results: We included 9 young (20-32 years, 25.0±3.4 years) and 9 aged gender-matched donors (52-67 years, 57.8±5.7 years) for PER and OCR measurement. Memory CD4+ T cells demonstrated higher basal glycolysis, compensatory glycolysis as well as basal OCR and spare respiratory capacity than naïve CD4+ T cells. Memory CD4+ T cells from young donors had higher basal glycolysis, and compensatory glycolysis than aged donors, but lower ratio of basal mitoOCR/glycPER. Although we did not observe differences in intercellular cytokine expression measured by flow cytometry after 5h stimulation of memory CD4+ T cells, we determined a significant higher amount of secreted IL-6, IL-9, IP-10, monocyte chemotactic and activating factor in the supernatant of memory CD4+ T cells from aged donors as compared to those from young donors. Cell division index, proliferation index, percentage of divided cell, and Ki-67 expression after 3 and 4 days of stimulation showed no statistical differences between both groups.
Conclusion: Here, we demonstrate a higher basal glycolysis, basal OCR, mitochondrial and glycolytic capacity of human *ex vivo* memory CD4+ T cells as compared to naïve T cells. A decrease of basal glycolysis, compensatory glycolysis in memory CD4+ T cells of aged people which results in an enhanced cytokine expression can be assumed to culminate in T cell dysfunction leading to the development of RA during aging.
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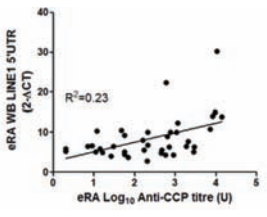
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AB0024 WHOLE BLOOD ENDOGENOUS RETROELEMENT ACTIVITY ASSOCIATES WITH ANTI-CCP TITRES IN EARLY DRUG NAÏVE RA AND IS PREFERENTIALLY INCREASED IN CD5+ AND NAÏVE B CELLS

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Background: Endogenous retroelements of which LINE1, Alu and LTR are the main subsets, constitute approximately 50% of the human genome. They are mobile genetic elements derived from the historical genomic integration of retroviruses. Whilst most are inactive, some expression of viral mRNA and subsequent protein is retained. This theoretically could promote immune activation, for example by triggering type 1 interferon (IFN-I) production and notably Alu has been identified as a target for Ro60 autoantibody. Retroelements may therefore provide a mechanism whereby tolerance is breached in autoimmunity.
Objectives: To examine the potential clinical impact of retroelement activity in early drug naïve rheumatoid arthritis (eRA). This stage of disease was chosen to minimise therapeutic confounding.
Methods: Drug-naïve eRA and healthy controls (HC) were recruited and clinical characteristics including disease activity, immunoglobulins (IgA, IgG, IgM), ESR, CRP, rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) autoantibody titres documented. Serum cytokines (IFN-γ, IL-6, IL-12 p70, TNF-α, IL-1β, IL-2, IL-13, IL-4, IL-10) were also measured. Whole blood (WB) RNA was extracted and expression of an IFN-I gene signature (IGS: *MxA, IFI6, OAS1, ISG15, IFI44L*) and LINE1 5'UTR activity quantified using RT-PCR. In addition anti-CCP and RF positive (double seropositive) eRA peripheral blood plasmacytoid dendritic cells (pDCs), myeloid DCs, $CD19^+$ B cells, monocytes, $CD4^+$ and $CD8^+$ T cells were flow cytometrically sorted. $CD19^+$ B cell subsets were further sorted from double seropositive eRA and disease controls (early, drug naïve, psoriatic arthritis, PsA) into $CD5^+$ B cells, age associated B cells ($CD19^{hi}CD11c^+CD21^-$), naïve (IgD^+CD27^-) and memory (IgD^-CD27^+) B cells. Cell specific expression of LINE1, Alu and LTR was quantified by NanoString nCounter and analysed using R Core Team (2013). WB RNA analysis for continuous and categorical variables included linear regression and Mann-Whitney U tests respectively (GraphPad Prism, significance $p<0.05$).
Results: WB LINE1 expression for 56 eRA patients (median age 58 [range 30-87], male:female 3:4, 77% seropositive for either RF or anti-CCP) and 23 HC (median age 39 [range 23-62], male:female 1:1) was obtained. WB LINE1 activity was not associated with age or gender and was comparable between cohorts. However in eRA a unique, robust positive association between WB LINE1 and anti-CCP titres was identified (see table and figure). Additionally, when comparing eRA circulating cell subsets, B cells had the highest expression of Alu, LINE1 and LTR (n=8, median age 56 [range 49-64], male:female 1:1). Furthermore, there was significantly increased expression of all retroelement classes in eRA CD5+ and naïve B cells compared with PsA (n=4, male:female 1:1 and median age 62 for both with age range [63-78] and [60-80] respectively).

Associations with eRA whole blood LINE1	
Variable	**Linear regression**
anti-CCP titres (U)	p<0.0001
RF titres (IU/ml)	p=0.490
CRP	p=0.123
ESR	p=0.106
DAS-28	p=0.335
IgM, IgG, IgA	All >0.4
Serum Cytokines	All >0.4
Interferon gene signature (IGS)	p=0.100



Conclusion: This is the first time peripheral blood retroelement activity has been examined in both HC and RA. It highlights intriguing, IFN-I independent, associations between anti-CCP titres, autoantibody producing B cells (CD5+) and retroelements. We suggest retroelements may play a more extensive role in autoantibody generation and may ultimately provide a novel target in the treatment or prevention of RA.

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AB0025 ATYPICAL, ACTIVATED MEMORY B CELLS ARE EXPANDED IN THE SYNOVIAL FLUID OF PATIENTS WITH OLIGOARTHRITIS COMPARED TO PERIPHERAL B CELLS

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Background: Juvenile idiopathic arthritis (JIA) is an umbrella term used to describe a group of chronic arthritides of unknown cause in children and adolescents. It is the most common rheumatic disease in children and young people under the age of 16, and if left untreated can cause significant morbidity. Oligoarthritis is the most common of the seven different JIA subtypes and is characterized by autoantibody production and the differentiation of autoreactive T cells. B lymphocytes are known to contribute to the pathophysiology of oligoarthritis by producing autoantibodies, but recent developments suggest that they may further contribute to disease by presenting auto-antigens to (autoreactive) T cells, or secreting by cytokines that influence the function of other inflammatory cell types.
Objectives: To carry out in-depth immunophenotyping of B cells in the peripheral blood (PB) and synovial fluid (SF) of patients with oligoarthritis. Greater understanding into the phenotype and function of B lymphocytes in oligoarthritis may help clinicians identify novel treatment targets for patients that fail first-line methotrexate therapy.
Methods: Patients with oligoarthritis (n=28, age 0-15), adult healthy controls (n=4, age>21) and child healthy controls (n=3, age 7-15) were included in this study. All patients and controls were recruited in the United Kingdom with fully informed and age-appropriate consent as approved by the London-Bloomsbury Research Ethics Committee (ref: 95RU04) in accordance with the Declaration of Helsinki. PB and SF mononuclear cells were prepared by density centrifugation and immunophenotyped by flow cytometry.
Results: CD19+CD24loCD38lo (atypical) and CD19+CD2hiCD38lo (memory) B cells were enriched in synovial fluid compared to peripheral blood, whereas CD19 +CD24hiCD38hi (immature) and CD19+CD24intCD38int (mature) B cells were depleted. The B cell activation markers CD27 and CD86 were also found to be upregulated on SF B cells compared to PB B cells. Further analysis using extracellular markers identified by single cell sequencing analysis revealed that SF B cells also express higher levels of complement receptor 4 (CD11c/CD18) and the oxysterol receptor GPR183 than PB B cells.
Conclusion: Flow cytometry analysis demonstrated that B cells in the synovial fluid have a distinct phenotype compared to B cells in the peripheral blood. Future work will investigate the functional implications of these results.
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AB0026 **LARGE JOINT ARTHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS IS CHARACTERISED BY T CELL RATHER THAN B CELL ACCUMULATION**

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Background: Musculoskeletal involvement is a common clinical feature of systemic lupus erythematosus (SLE), that can be present either at the onset or in later disease course. SLE related arthritis is usually non-erosive and non-deforming as opposed to rheumatoid arthritis (RA). While RA synovial pathology has been extensively studied, little is known about the pathophysiology of arthritis in SLE.
Objectives: to explore the cellular compartments in synovial fluid of SLE patients with arthritic manifestations.
Methods: paired synovial fluid (SF) samples from large joint aspiration and peripheral blood samples (PBMC) obtained at the same time point from five SLE patients were analyzed by multicolor flow cytometry. The patients fulfilled the ACR 1982 classification criteria for SLE [1]. Clinical records were reviewed in order to exclude the presence of comorbidities such osteoarthritis or overlap with RA. Three different lineage-specific panels for B cells, T cells (cytotoxic and helper) were developed.
Results: The overall frequency of CD4+ and CD8+ T cells was similar across the SF and PBMC samples. Among the CD4+ T cells, those co-expressing CCR4, showed a much higher frequency in the SF compared to the peripheral blood in 4 out of 5 patients (mean percentage 8.9±7.0% vs 2.1±1.6%, p=ns). In addition, in 4 out of 5 patients we could identify an increased frequency of CD4+ expressing CCR6+, a marker for Th17 cells in SF as compared to PBMC (mean percentage 35±16.6% vs 12.7±8.9%, respectively, p=ns). In all patients, a higher frequency of EOMES+ Granzyme A + CD4+ T cells was observed in SF when compared to PBMC (9.2±2.5% vs 4.5±2.5%, p=0.03). Moreover, in all patients, we could observe a higher proportion of regulatory T cells (FOXP3+/CD25+) in the SF (21.5 ±15.4% vs 8.4±7.8%, p=ns). No relevant differences were observed in the Th1 compartment (CXCR3+). CD19+ cells (B-lymphocytes) were scarcely present in the SF of SLE patients as opposed to the peripheral blood.
Conclusion: Although SLE is usually considered to be a B cell driven disease, its common clinical features like arthritis could be driven in situ by T cells, namely subtypes of CD4+ (helper) cells such as TH17 cells and CD4+ T cells with cytotoxic profile. Further confirmation of the present findings is needed.

REFERENCE

[1] Tan, E.M., et al., *The 1982 revised criteria for the classification of systemic lupus erythematosus*. Arthritis Rheum, 1982. 25(11

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AB0027 **ARE RHEUMATOID FACTORS AND ANTINUCLEAR ANTIBODIES ASSOCIATED WITH FRAILTY IN ELDERLY TUNISIAN POPULATION?**

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Background: An emerging concept is the 'frailty syndrome', which may explain diversity in clinical outcomes in the elderly population.
Objectives: The aim of the study was to investigate the possible association between antinuclear autoantibodies, different isotypes of Rheumatoid Factor and frailty in aged individuals.
Methods: Using a validated set of frailty criteria (the SEGA tool), we conducted a cross sectional observational study to evaluate the prevalence of antinuclear antibodies (ANA) (assessed by IFI) and different isotypes of Rheumatoid Factor (RF) (determined by ELISA) in 89 Tunisian individuals aged at least 65 years living in the community. The study population were categorized into three groups: severely frail (n=29), frail (n=31), and non frail (n=29) according to the validated and widely utilized frailty criteria (SEGA tool).
Results: ANA were detected in 36 of the participants. No Significant difference was observed between the three groups. Immunofluorescence patterns observed were speckled in 34%, homogenous in 3.3%, and nucleolar in 3.3% of individuals. Nineteen of the severely frail patients had positive IgA RF compared to 11 from the Frail group and 6 only from the non-frail group ($p<0.02$). RF isotypes showed low correlations with other features. Indeed, the IgA RF was correlated with the age ($r= -0.22$, $p<0.03$), the C-Reactive Protein level ($r= -0.45$, $p<0.01$), and the nutritional state of the patients assessed by the MNA score ($r=0.27$, $p<0.009$). The IgG RF was correlated with hemoglobin ($r= 0.22$, $p<0.03$) and creatinin ($r= -0.36$, $p<0.01$) levels.
Conclusion: Our study showed no significant difference in the frequency of ANA amongst nonfrail, prefrail, and frail aged individuals, whereas RF isotypes were found to be slightly correlated with several biological parameters and other features.

REFERENCES

[1] Renato Nisihara, et al.Antinuclear Antibodies and Rheumatoid Factor Positivity in Healthy Elderly Adults: A Cross-Sectional Study in 336 Individuals. J American Geriatric Society2013; 61, P : 2044-46

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AB0028 **SELECTIVE DEPLETION OF PLASMA CELLS IN VIVOBASED ON SPECIFICITY OF SECRETED ANTIBODIES**

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Background: Antibody-mediated diseases like allergies and chronic-inflammatory autoimmune diseases affect more than 10% of the human population, and for most, no cure is available. This is particularly true when pathogenic antibodies are secreted by long-lived plasma cells generated early in pathogenesis, which are refractory to conventional therapies. Therapeutic concepts for the generic ablation of plasma cells are currently being tested in clinical trials. These concepts target both plasma cells secreting pathogenic antibodies and those providing protective antibodies, i.e., humoral immunity. Efficient ablation of pathogenic plasma cells is inevitably accompanied by immunodeficiency and increased susceptibility to infection.
Objectives: We studied the use of an antigen-antibody conjugate to label plasma cell in vivo with the antigen and selectively ablate those that secrete antibodies specific for the antigen.
Methods: Balb/c mice were immunized with ovalbumin (OVA) and chicken gamma globulin (CGG), which resulted in the generation of OVA and CGG-specific long-lived plasma cells in the bone marrow. These mice were treated by a single intraperitoneal injection of a conjugate consisting of OVA and a monoclonal anti-CD138 antibody. The effect of this treatment on the long-lived plasma cells and antibody levels was analyzed by flow cytometry and ELISA, respectively.
Results: The single injection of an OVA-anti-CD138 conjugate resulted in a significant depletion of OVA-specific plasma cells while CGG-specific plasma cells were not affected. The selective depletion of OVA-specific plasma cells also led to stable reduction of serum anti-OVA antibody levels; circulating anti-CGG antibody levels remained unchanged.
Conclusion: The cellular antigen-affinity matrix strategy described here for the ablation of plasma cells *in vivo* according to the specificity of their antibodies enables a unique causative therapeutic approach in established antibody-mediated diseases without impairment of humoral immunity.

REFERENCES

[1] Taddeo, A. et al. Eur J Immunol 45, 317-319 (2015)

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AB0029 CITRULLINE REACTIVE B CELLS ARE PRESENT IN THE LUNGS OF EARLY UNTREATED RA

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Background: We have previously shown that structural changes, increased tissue citrullination, signs of local inflammation and ACPA are present in the pulmonary compartment of early seropositive RA. These findings suggest a potential role for the lungs in generation of RA-associated autoimmunity.
Objectives: To identify citrulline reactive B cells in the lung compartment of early untreated RA patients and to generate and characterize the corresponding monoclonal antibodies.
Methods: Bronchoalveolar lavage (BAL) fluid cells (13 and 22.5 million respectively) were obtained from two early untreated non-smoking ACPA positive RA patients and single CD19+ B cells were sorted by flow cytometry. Immunoglobulin variable region genes were sequenced and expressed to generate recombinant monoclonal antibodies (mAbs). The citrulline reactivity was determined by in-house ELISA against different citrullinated peptides and controls.
Results: Single sorted CD19+ B cells (n=768) from each patient (RA.1 and RA.2) were processed and the variable region amplification and sequencing yielded 192 (RA.1) and 213 (RA.2) paired heavy and light chain sequences. Based on previously published data showing SHM-introduced N-linked glycosylation in the Fab regions of ACPA [1], 22 sequences from each patient were pre-selected with such features, and monoclonal antibodies were expressed. Two antibodies from each patient were ACPAs as determined by their reactivity against CCP2. The 4 ACPAs have varying ACPA fine specificity against citrullinated enolase, filaggrin, vimentin and fibrinogen peptides (figure 1). Sequence analysis of the heavy chain variable region revealed unique V gene usage of the ACPAs arising from different patients, V4-39 for the 2 mAbs from RA.1 and V3-49 for RA.2.

Protein	Peptide	RA.1_10	RA.1_15	RA.2_23	RA.2_37
	CCP2	+	+	+++	++
α-Enolase	CEP-1	-	+	+++	+
Filaggrin	Fil 307-324	-	++	+++	+
Vimentin	Vim 2-15				
	Vim 60-75	-	+	+++	-
	Vim 435-455				
Fibrinogen α	Fib 36-52	-	+++	+++	++
	Fib 573	-	+	+++	+
	Fib 591	-	-	+++	-

Figure 1. ACPA fine specificities of the mAbs by ELISA against different citrullinated peptides. The green cells (+) represent reactivity against citrullinated peptides and the orange cells (-) represents non-reactivity.

Conclusion: We demonstrate for the first time that citrulline-reactive B cells are present in the lung compartment of early untreated RA. Further analysis and functional characterization are needed and ongoing to understand their role in RA.

REFERENCE

[1] Lloyd, K.A., et al., Variable domain N-linked glycosylation and negative surface charge are key features of monoclonal ACPA: Implications for B-cell selection. Eur J Immunol, 2018. 48(6): p. 1030-1045.

Disclosure of Interests: Vijay Joshua: None declared, Malena Loberg-Haarhaus: None declared, Heidi Wähämaa: None declared, Aase Hensvold: None declared, Magnus Sköld: None declared, Johan Grunewald: None declared, Lars Klareskog Grant/research support from: Yes, but not for the presented study., Vivianne Malmström: None declared, Anca Catrina Grant/research support from: Yes, but not for the presented study.
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AB0030 QUANTIFICATION OF CD27+ MEMORY B-CELLS IN RHEUMATOID ARTHRITISPATIENTS TREATED WITH RITUXIMAB

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Background: Rituximab (RTX) is being increasingly used in treatment of several autoimmune diseases, including Rheumatoid Arthritis (RA).RTX induces a deep depletion of all peripheral B-Cell subsets (memory and naïve B-cells). During the B-Cell repopulation phase, occurring approximately after 3 months of RTX administration, B-precursors and naïve cells reappear.Several studies have shown that relapsing RA patients are characterized by a relative expansion of memory B cells during the B-Cell repopulation phase
Objectives: The aim of this study was to quantify the memory B-Cell compartment in RA patients with different disease activity scores, evaluated by DAS28, during RTX treatment
Methods: 26 RA patients under RTX treatment were studied. At the end of th treatment 8/26 showed high-to-moderate activity risk (median DAS28=4.8) and 18 low activity risk or remission (median DAS28=2.69). After a median of 3 months from last RTX infusion, B-Cell subsets (precursors, naïve, memory B cells and plasma cells) were quantified in peripheral blood by flow cytometry, using a panel of 8 markers (CD3, CD4, CD8, CD19, CD20, CD27, CD38 and CD45). B naïve cells were identified as CD19+ CD20+ CD27-, B memory cells were identified as CD19+ CD20+ CD27+, plasma cells as CD19+ CD38++ CD27++ CD20- and B precursors as CD19+ CD38++ CD20- CD27-, respectively. Percent and absolute values were calculated for each subset. In adition 10 healthy subjects were included as negative control group (NC).
Results: The median percent and absolute values of B naïve cells, B memory cells and plasma cells identified in NC, non-responder RA patients with high/moderate disease activity and responder RA patients with low disease activity or in remission are reported in Table 1.

Median Values	Normal controls	Non Responder	Responder
CD19+CD20+%	15.5	0.5	0.75
Absolute B cells/μL	279	9	13
*Memory B cells %	28.8	36.5	7.75
Absolute memory B cells/μL	69.7	1.75	6.6
*B cell Naive %	71.2	63.5	92
Absolute naïve B cells/μL	198.6	5.7	72
*Plasmacells%	0.04	0.001	0.01
*As percentage of B cells			

The virtual absence of peripheral B-Cell was defined as <0.1 B-Cell/μL. In the responder group, 5/18 cases showed absolute B-Cell levels <0.1 cell/μL, while only in 1/8 of the non responder group a similar B-Cell depletion was found. The memory B-Cell% was significantly higher in non responder than in responders ($p<0.05$); the memory B-Cell level in non responders was similar to that of the NC group.
Conclusion: We used a sensitive and easily applicable flow cytometric multicolor panel that allowed the accurate and standardized identification and enumeration of peripheral blood B-Cell subsets. As reported by other studies, higher levels of memory B-Cells were found in non responder RA patients treated by RTX, approaching those of healthy individuals.

REFERENCES

[1] Lòpez J. Clin Exp Rheumatol 2018; Dec 19. Sellam J. Arthritis Rheum 2011; 63: 3692-3701.Dass S. Arthritis Rheum 2008; 58: 2993-2999

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7914

AB0031 IL-2 THERAPY AFFECT PERIPHERAL BLOOD LYMPHOCYTE LEVEL IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: PrimarySjogren'sSyndrome (PSS)is a chronic inflammatory autoimmune disease that mainly involves exocrine glands. Changes in the number of lymphocytes in PSS due to broken immune balance.
Objectives: Toexplorethe quantitative changes of peripheral Th17 cells and regulatory T cells (Tregs) in primarySjogren'ssyndrome before and after short-term low doseIL-2 treatment, and to explore the correlation between the level of peripheral blood lymphocytes and clinical indexes in patients with primary Sjogren syndrome.
Methods: Total172PSSpatients were enrolled,and 196 healthy adults were used as normal controls.Of them,53 cases were treated with low dose IL-2($5.0*10^5$ international units (IU) for 5 days).The median four quantile method was used for statistical description. Multiple samples were compared with Kruskal-Wallis H test, and the correlation between variables was Spearman rank correlation analysis.
Results: (1)The number ofT,Th1 cells were decreased as compared with that in the control group($p<0.05$).The number of total T,$CD8^+$ T,Th1,Th17,Treg and the ratio of Th17/Treg were significantly increased after IL-2 treated($p<0.05$).The ratio of Th17/Treg in the patients was not significantly different from that in the control group ($P>0.05$). (2) The Th17 cell levels, the ratio of Th17/Treg and $CD4^+$ T/$CD8^+$ T were negatively correlated with ESR ($p<0.05$). Th1,Th2,Th17 cell levels and the ratio of Th17/Treg were negatively correlated with CRP($p<0.05$).
Conclusion: The level of $CD4^+$T cells in peripheral blood of patients with PSS such as T,Th1,Th17,Treg cells were significantly decreased, Th17,Th17/Tregwere correlated with ESR,CRP.however, Th17,Treg cell levelswere increased after treatment with short term low dose IL-2,especially Treg cells .Itindicated that IL-2 promoted the differentiation of Treg cells, maintained the function of Treg cells.

REFERENCES

[1] Furuzawa-Carballeda J, Hernández-Molina G, Lima G, et al. Peripheral regulatory cells immunophenotyping in PSS: a cross-sectional study. Arthritis Res Ther 2013;15:R68

Table 1. Comparison oflymphocytes level sandratios between the two groups M(p25, p75)

Groups	T (ng/ml)	$CD4^+$ T (ng/ml)	$CD8^+$ T (ng/ml)	$CD4^+$ T/ $CD8^+$ T
Case group	1197.73 (783.00,1432.75)ab	650.08 (362.50,867.75)b	477.01 (275.00,551.00)b	1.64 (0.99,2.18)
Il-2 treatment group	1430.77 (927.00,1805.15)	383.78 (135.50,367.50)a	148.54 (2.21,162.60)a	1.83 (1.16,2.36)
Healthy control group	1335.11 (1072.00,1569.74)	693.47 (550.25,825.12)	510.45 (366.00,617.25)	1.56 (1.05,1.90)
*H*value	18.16	55.10	80.06	3.59
*P*value				0.166

Groups	Th1(ng/ml)	Th2	Th17(ng/ml)	Treg(ng/ml)	Th17/Treg
Case group	86.72 (25.61,135.24) ab	13.81 (6.02,16.15) a	6.99 (2.89,9.73)b	35.40 (17.07,44.42) b	0.30 (0.09,0.35) b
Il-2 treatment group	123.29 (34.80,182.25)	12.88 (5.14,17.19) a	11.42 (4.91,13.80) a	76.17 (39.80,96.97) a	0.54 (0.09,0.23) a
Healthy control group	107.05 (44.31,160.47)	8.85 (4.67,11.38)	7.17 (3.96,9.91)	31.21 (21.80,41.40)	0.26 (0.14,0.34)
*H*value	10.95	15.58	12.34	41.88	10.13
*P*value	0.004		0.002		0.006

Notes: [a]Comparison with healthy control group $P<0.05$; [b]Comparison with IL-2 treatment group $P<0.05$.

Disclosure of Interests: None declared
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AB0032 CASE REPORT: ADVANCED MELANOMA PATIENT WITH FAVORABLE RESPONSE TO IMMUNE CHECKPOINT INHIBITOR TREATMENT SHOWS SEVERE ERYTHEMA CIRCINATUM WITH ANTI-SS-A ANTIBODIES

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Background: Immune checkpoint inhibitors (ICI) targeting cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and programmed cell death protein 1 (PD-1) have been efficacious treatments in oncology. However, the use of ICI induces a large spectrum of immune side effects. The prevalence of autoimmune connective tissue diseases and the autoantibody profiles induced by ICI are largely unknown. The Ro52/TRIM21 antigen is known as a cytosolic Fc receptor that is found in almost all tissues. Its expression is regulated by interferons, and overexpression or hypoexpression has been observed in several cancers.
Objectives: In this study, we investigated autoantibodies produced after ICI treatments and analyzed the clinical characteristics of the patients.
Methods: Sera were collected from patients with unresectable metastatic or recurrent melanoma before and after treatment with ICIs such as ipilimumab, nivolumab or pembrolizumab. Autoantibodies were screened by Western blotting (WB) using A375 and HaCaT cell extracts. Antigenic proteins, which showed differences in reactivities in WB before versus after treatment, were purified by immunoprecipitation and analyzed by time-of-flight mass spectrometry. The identified proteins were tested for serum reactivities with ELISA.
Results: Of the 19 melanoma patients, 1 patient showed high titers of anti-SS-A/Ro52 and anti-SS-A/Ro60 antibodies after treatment. The other 18 melanoma patients were negative for both anti-SS-A/Ro52 and anti-SS-A/Ro60.
Case presentation: An 81-year-old Japanese male patient with multiple metastatic melanomas on the face (Figure 1A) was judged as unresectable, and treatment with pembrolizumab was started. After the fifth pembrolizumab administration, a grade 2 skin rash appeared (Figure 1B). The multiple metastatic lesions and the primary melanoma showed significant reductions, without new cancer lesions (Figure 1C). Pembrolizumab was ceased after the ninth administration with grade 3 skin erythema, and systemic prednisolone (PSL) at 1mg/kg/day was started. No other subjective symptoms, such as sicca, fever or fatigue, were observed. A biopsy specimen of erythema circinatum on the back showed strong liquefaction degeneration, individual cell keratinization and exocytosis. The reactive 52kDa and 60kDa polypeptides in WB (Figure 1D) were presumed to be SS-A/Ro52 and SS-A/Ro60, respectively, and the serum was confirmed to be reactive with these antigens by ELISA. The skin symptoms and anti-SS-A/Ro52 and anti-SS-A/Ro60 antibodies remained after the PSL treatment. Some of the erythema left incomplete depigmentation of the skin (Figure 1E, F). Anti-SS-A/Ro52 and anti-SS-A/Ro60 antibody titers increased along with the skin symptom in this melanoma patient who was being treated with an ICI (Table 1).
Conclusion: Anti-SS-A/Ro52 and/or anti-SS-A/Ro60 may have some association with cancer immunity.

REFERENCES

[1] Rhodes DA, Isenberg DA. TRIM21 and the Function of Antibodies inside Cells. Trends Immunol. 2017;38:916-926.
[2] Nguyen JQ, Irby RB. TRIM21 is a novel regulator of Par-4 in colon and pancreatic cancer cells. Cancer Biol Ther. 2017;18:16-25.

Table 1 Changes in anti-Ro52 and anti-Ro60 antibody titers

	Before PD-1 treatment	After PD-1 treatment	After PSL treatment
Anti-Ro52 titer (positive range: 50< unit)	44.48	240<	240<
Anti-Ro60 titer (positive range: 30< unit)	31.3	88.9	72.7

Table 2. Correlation of lymphocytes with inflammatory indexs in patients with lymphocyteslevels.

Indexs	T		$CD4^+$ T		$CD8^+$ T		$CD4^+$ T/$CD8^+$ T	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
ESR	-0.046	0.547	-0.098	0.202	-0.041	0.596	-0.156	0.041*;
CRP	-0.082	0.284	-0.121	0.114	-0.022	0.774	-0.071	0.354

Indexs	Th1		Th2		Th17		Treg		Th17/Treg	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
ESR	-0.100	0.191	-0.110	0.151	-0.249	0.001*;	0.016	0.837	0.211	0.005*;
CRP	-0.177	0.020*;	-0.217	0.004*;	-0.220	0.004*;	0.028	0.716	0.207	0.006*;

Notes: ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; *$P<0.05$.

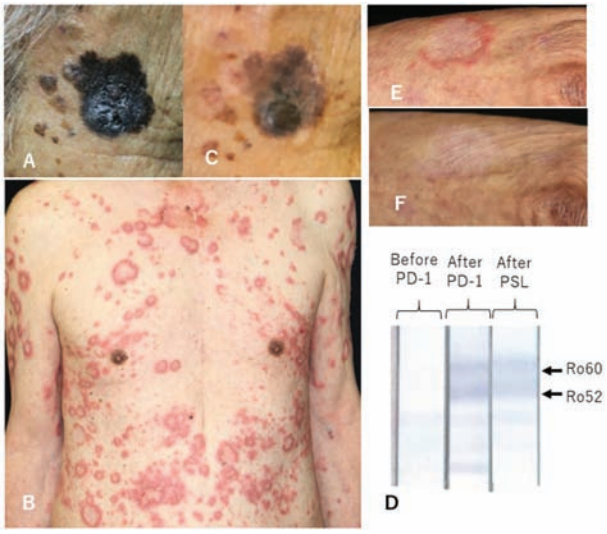


Figure 1

A. Primary melanoma lesion on the face. B. Systemic erythema circinatum. C. Primary melanoma lesion after the ninth pembrolizumab administration. D. Western blotting using A375 extract. E. Erythema circinatum. F. Remaining incomplete depigmentation.

Disclosure of Interests: None declared
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AB0033 AGE AND GENDER EFFECTS ON PROGRAMMED CELL DEATH-1 EXPRESSION IN HEALTHY DONORS

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Background: Giant cell arteritis (GCA) is the most frequent form of vasculitis affecting the large sized vessels. GCA occurs more frequently in females and exclusively in individuals > 50 years of age but it is unclear how gender and age relate to GCA pathogenesis.
In balancing the immune response and preventing immune dysfunction, immune checkpoints are crucial. Recently, the co-inhibitory checkpoint molecule programmed cell death-1 (PD-1) and its ligand PD-L1 were found to be aberrantly expressed in GCA (1). However, data on age and gender related effects on immune checkpoint expression is limited.
Objectives: To further investigate the contribution of immune checkpoints in GCA pathogenesis and how this relates to ageing and gender differences, we first studied PD-1 expression as a function of age and gender in healthy males and females.
Methods: Whole blood cells of 13 young healthy donors (mean age 25.5 years, female/male ratio 7:6) and 20 elderly healthy donors (mean age 72.7 years, female/male ratio 11:9) were stained for CD3, CD4, CD45RA, CD25 and PD-1 with monoclonal antibodies and expression was measured with flow cytometry.
Results: Percentages of PD-1+ cells within CD4+ T cells, memory CD4+ T cells and the subset of non-suppressive regulatory T cells (Tregs, defined as CD4 +CD45RA-CD25int) were decreased in elderly post-menopausal females compared to elderly males (Figure 1A-C; $p<0.05$). Furthermore, the frequency of PD-1 + cells within non-suppressive Tregs was also decreased in post-menopausal females compared to young females (Figure 1C; $p<0.05$).
Conclusion: PD-1 expression is decreased in (subsets of) CD4+ T cells of post-menopausal females when compared to younger females and elderly males. These findings suggest that post-menopausal status in females can influence PD-1 expression. Further studies on the relation between hormonal changes and immune checkpoint expression may contribute to understanding why elderly females are predisposed to develop GCA.

REFERENCE

[1] Zhang H, Watanabe R, Berry GJ, Vaglio A, Liao YJ, Warrington KJ, et al. Immunoinhibitory checkpoint deficiency in medium and large vessel vasculitis. Proc Natl Acad Sci. 2017 Feb 7;114(6):E970–9.

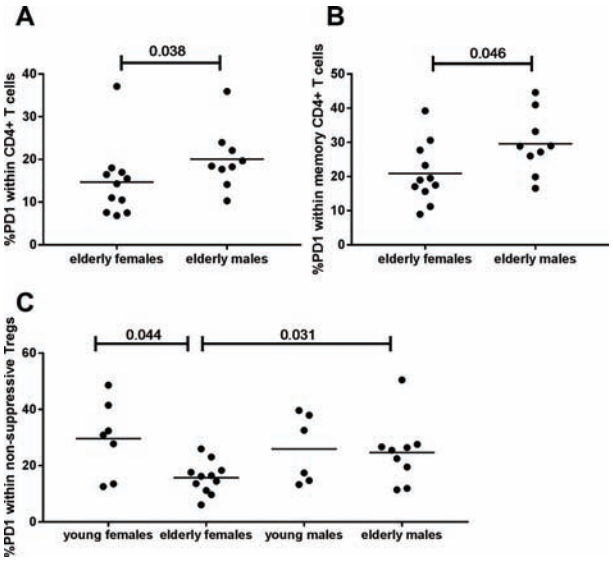


Figure 1. Expression of PD1 on (subsets of) CD4+ *T* cells. Graphs represent percentages of PD-1-expressing total CD4+ T cells (A) and memory CD4+ *T cells* (B) in elderly post-menopausal females and elderly males, and the percentages of PD-1-expressing non-suppressive Tregs (C) in young females, elderly females, young males and elderly males. Horizontal bars reflect median percentages. Statistical analyses of differences between young and elderly females and elderly females and elderly males were performed using Mann-Whitney U tests. P values are indicated in the graphs.

Disclosure of Interests: Rosanne Reitsema: None declared, Rebeca Hid Cadena: None declared, Sander Nijhof: None declared, Wayel Abdulahad: None declared, Minke G. Huitema: None declared, Annemieke Boots Grant/research support from: grant from MSD in 2010-2015, Consultant for: I was a consultant for Grunenthal Germany 2016-2017, Employee of: I was an employee of Organon, Shering-Plough and MSD from 1991-2011, Elisabeth Brouwer Speakers bureau: Dr. Brouwer as an employee of the UMCG received speaker fees and consulting fees from Roche which were paid to the UMCG, Peter Heeringa: None declared
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AB0034 INCREASED PRODUCTION OF HYDROGEN AND METHANE SUGGESTED BACTERIAL OVERGROWTH IN THE SMALL INTESTINE IN PATIENTS WITH AUTOIMMUNE DISEASE DETECTED BY LACTULOSE BREATH TESTS

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Background: Researchers have linked a species of intestinal bacteria to the onset of rheumatoid arthritis. The lactulose breath test detects small intestinal bacterial overgrowth (SIBO) can measure hydrogen and methane produced by intestinal bacteria.
Objectives: To investigate the intestinal flora of patients with autoimmune diseases through a lactulose breath test.
Methods: The study was conducted on 720 cases of autoimmune disease. The hydrogen value was increased by ≥20p.p.m and the methane value increased by ≥10p.p.m in 90 minutes was defined as positive for SIBO. Spearman's rank correlation analysis was used to determine the association between age and hydrogen values or methane values.
Results: A total of 75% of patients had a positive breath test. Among them, the positive rate of rheumatoid arthritis (RA) patients was 69.4%, systemic lupus erythematosus (SLE) 69%, Sjogren's syndrome (SS) 79.22%, ankylosing spondylitis (AS) 89.29%, and juvenile arthritis (JIA) 73.33%. In addition, patients with AS had significantly higher hydrogen value than that with RA, SLE, and SS ($p<0.05$) (Fig. 1). Sex was no statistically significant difference between lactulose breath test results. In female patients, age was positively correlated with hydrogen values ($r = 0.151$; $p = 0.049$) and methane values ($r = 0.248$; $p = 0.001$); in male patients, age was negatively correlated with hydrogen values ($r = -0.367$); $p=0.006$) (Fig. 2).
Conclusion: Patients with autoimmune disease have positive bacterial growth in the small intestine, and hydrogen production is significantly increased in patients

with AS, suggesting that hydrogen production in the small intestine may be related to inflammation. In addition, with increasing age of the female, hydrogen and methane produced in the small intestine may increase, with increasing age of the male, small intestine may reduce the production of hydrogen, suggesting a reason why there are more female patients than male in some autoimmune disease.

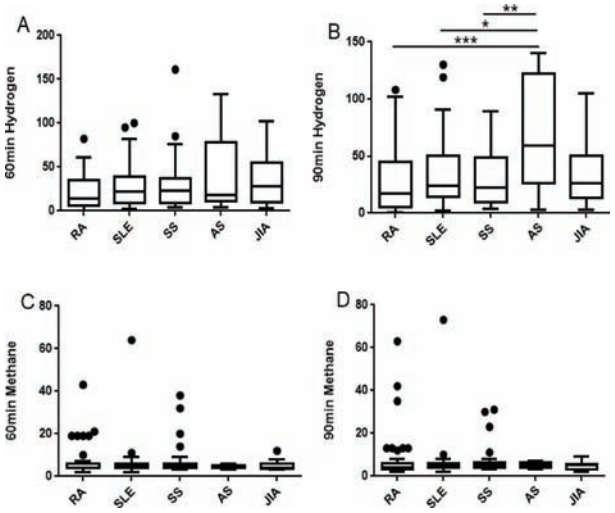


Figure 1. Differences in hydrogen and methane levels in different autoimmune diseases in the lactose breath test: (A and B) The production of hydrogen in the small intestine of patients with ankylosing spondylitis is significantly higher than that of other autoimmune patients. (C and D) Methane production in the small intestine showed no significant difference between the groups. *P < 0.05; **P < 0.01; ***P < 0.001. RA: rheumatoid arthritis, SLE: systemic lupus erythematosus, SS: Sjogren's syndrome, AS: ankylosing spondylitis, JIA: juvenile arthritis.

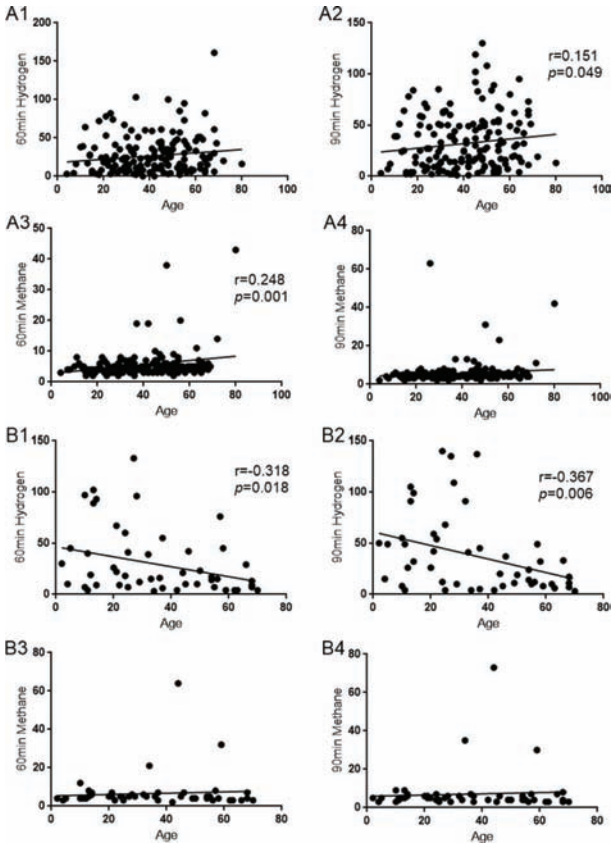


Figure 2. Correlation between the age of autoimmune patients and the hydrogen and methane values in the lactose breath test: (A1-A4) The age of female patients is positively correlated with the production of hydrogen and methane in the small intestine. (B1-B4) The age of male patients is negative related to the production of hydrogen in the small intestine.

REFERENCES

[1] Gislane Lelis Vilela de Oliveira, Aline Zazeri Leite, Bruna Stevanato Higuchi, Marina Ignácio Gonzaga, Vânia Sammartino Mariano.Intestinal dysbiosis and probiotic applications in autoimmune diseases. Immunology. 2017 Sep; 152(1): 1–12.doi: 10.1111/imm.12765

[2] Maria C. Opazo, Elizabeth M. Ortega-Rocha, Irenice Coronado-Arrázola, Laura C. Bonifaz, Helene Boudin, Michel Neunlist, Susan M. Bueno, Alexis M. Kalergis, Claudia A. Riedel. Intestinal Microbiota Influences Non-intestinal Related Autoimmune Diseases. Front Microbiol. 2018;9:432.doi: 10.3389/fmicb.2018.00432

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AB0035

THE CHARACTERISTICS OF CIRCULATING FOLLICULAR T LYMPHOCYTE SUBSETS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND THE EFFECT OF TFR/TFH BALANCE ON DISEASE ACTIVITY

Yan Yan Wang, Rui Su, Xiang-Cong Zhao, Jing Luo, LI Bao Chen, Qiao Ling Guo, LI Xiaofeng, Caihong Wang. *The second hospital of Shanxi Medical University, Department of Rheumatic Immunology, taiyuan city, China*

Background: Rheumatoid arthritis (RA) is a highly disabling autoimmune disease. T lymphocyte subsets imbalance causeing immune dysfunction is essential stages in the occurrence and development of RA diseases. Recent studies show that the interaction of both follicular helper T (Tfh) cells and follicular regulatory T (Tfr) cells are important frontier scientific direction to maintain autoimmune tolerance, and Tfr/Tfh balance may play a pivotal role in the formation of lymphoid germinal center and the production of autoantibodies[1-2].

Objectives: The aim of this study was to explore the clinical characteristic of peripheral follicular T cell subsets in patients with RA and healthy individuals,and the effects of Tfr/Tfh balance on autoantibody formation and disease activity. Searching for new immunomodulatory targets from it.

Methods: The study included 26 patients with a diagnosis of RA according to the 1987 revised criteria of the American College of Rheumatology and 17 healthy individuals as control group. All follicular T cell subsets from them were assessed by flow cytometry(Figure1). Using isotypic controls to distinguish follicular T cell subsets that were not clearly clustered. In addition, we measured all peripheral lymphocyte subsets in RA patients by Flow Cytometry. IgG, IgA, IgM,RF were measured using Turbidimetric inhibition immuno assay. Anti-CCP was measured using ELISA. We also collected relevant clinical information and made DAS28 score.

Results: (1)Compared with healthy controls, the proportions of $CD4^+CXCR5^+PD\text{-}1^{high}$Tfh cells were higher in RA patients (P=0.029), In contrast, patients with RA had much lower level of $CD25^+CXCR5^+FoxP3^+$Tfr cells (P=0.010). And there were significant differences of Tfr/Tfh between these two groups (P=0.000). (2)Among 26 RA patients, there was obvious correlation between Tfr/Tfh and the DAS28 value(r=0.422, P=0.032). But there was no correlation between Tfr/Tfh and ESR(P>0.05). Correlation between $CD4^+CD25^+FoxP3^+$Treg cells and Tfr cells was also analyzed(r=0.722, P=0.000)(Figure2). (3) We have not found correlation between Tfr/Tfh and autoantibodies maybe for the small sample content.

Conclusion: Treg cells have a negative immunomodulatory effect on inflammatory response, the high correlation between Tfr cells and Treg cells indicates that Tfr cells may come from directional transformation of Treg. There is a Tfr/Tfh imbalance in RA patients, which suggests a potential mechanism of RA disease severity. However, more samples are needed to confirm whether it is related to the production of autoantibodies to affect disease activity.

REFERENCES

[1] Wing J B, Tekgüc Murat, Shimon S. Control of germinal center responses by T-follicular regulatory cells[J]. Frontiers in Immunology, 2018, 9:1910-1922.

[2] Moschovakis G L, Bubke A, Friedrichsen M, et al. T cell specific CXCR5 deficiency prevents rheumatoid arthritis[J]. Scientific Reports, 2017, 7 (1):8933-8946.

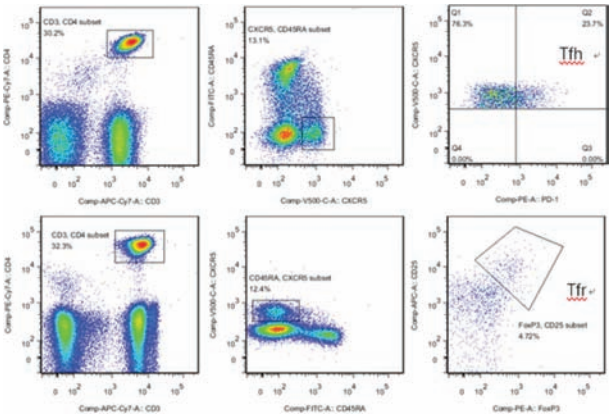


Figure 1. Follicular T lymphocytes from RA patients and healthy controls were analyzed through staining for CD3, CD4, CXCR5, CD45RA and PD-1 as Tfh cells, andCD3, CD4, CD25, CXCR5,CD45RAandFoxP3 as Tfr cells. Using isotypic control IgG1 to distinguish follicular T cell subsets that were not clearly clustered. Numbers indicate the percentage of cells of last gate.

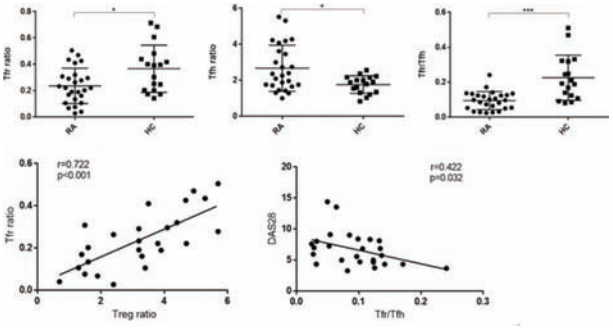


Figure 2. The percentage of circulating follicular T lymphocyte subsets in patients with RA and healthy controls (*p<0.05, ***p<0.001). Correlation between Treg cells and Tfr cells, and correlation between Tfr/Tfh and the DAS28.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3302

AB0036 THE IMPACT OF ANTI-TNF THERAPY ON CD4+T CELL SUBSETS IN DIFFERENT DIFFERENTIATION STAGES AND TREG CELLS IN ACTIVE ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondyloarthritis (AS) is a progressive, chronic, inflammatory skeletal disorder affecting the spine and sacroiliac joints. To date, the disease etiology remains unclear. Some studies have shown that T lymphocytes play important roles in the inflammatory process of AS, but imbalances in the numbers and functions of CD4+T cells and regulatory cells (Treg) in different differentiation stages are rarely mentioned. Tumornecmsis factor (TNF)-α blocker has been very effective in the treatment of ankylosing spondylitis, but its specific mechanism in the immune function of ankylosing spondylitis in active stage has not been fully revealed.
Objectives: To investigate the role of Treg and CD4+T cells of different differentiation stages on the pathogenesis of active AS, and to study the machanism of TNF-α blocker on the treatment of active AS by detecting the number of Treg cells and CD4+T cells before and after the treatment.
Methods: Ankylosing Spondylitis Disease Activity Score (ASDAS) was used to assess disease activity. AS patients who fulfilled the Assessment in Ankylosing Spondylitis Criteria in 1984 and ASDAS≥1.3 were enrolled in this study. The patients received subcutaneous injection of recombinant human tumor necrosis factor receptor-Fc fusion protein (rh TNFR-Fc) 50 mg weekly for 12 weeks. Healthy age and gender-matched subjects were also enrolled as control group. Flow cytometry analyses were carried out to detect the levels of a series of lymphocytes including different stages of differentiation CD4+T cells and Treg cells. C-reactive protein(CRP) levels in serum were determined by immunoturbidimetry.
Results: A total of 23 active AS patients(Age: 31.74±10.20 yrs, M/F:19/4) and 50 healthy subjects (Age: 34.66±9.72 yrs, M/F: 45/15) were included in the study. The percentage of initialization CD4+T cells(CD3+CD4+CD45RA+CCR7+) and central memory CD4+T cells (CD3+CD4+CD45RA-CCR7+) were found to be significantly higher in the AS groups compared with the healthy individuals (P < 0.05). However, the percentage of and Treg cells (CD3+CD4+CD25+CD127-) were significantly lower in the AS groups (P < 0.05). After 12 weeks rh TNFR-Fc treatment, the percentage of initialization CD4+T cells and central memory CD4 +T cells are significantly reduced. In contrast, the proportion of Treg cells increased significantly.
Conclusion: Initialization CD4+T cells (CD3+CD4+CD45RA+CCR7+), central memory CD4+T cells (CD3+CD4+CD45RA-CCR7+) and Treg cells (CD3+CD4 +CD25+CD127-) may play a role in the pathogenesis of AS. The down regulation of initialization CD4+T cells and central memory, and the up regulation of Treg cells in active AS patients are significant for the evaluation of the curative effect of rhTNFR-Fc.

REFERENCES

[1] Croft M: The TNF family in T cell differentiation and function-unanswered questions and future directions. Semin Immunol 2014; 26: 183-190.
[2] Dulic S: The Impact of Anti-TNF Therapy on CD4+ and CD8+ Cell Subsets in Ankylosing Spondylitis. Pathobiology 2018;85:201–210.
[3] Zhongliang Duan: The immune dysfunction in ankylosing spondylitis patients. BioScience Trends. 2017; 11(1):69-76.

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AB0036B LYMPHOCYTE SUBSET IMBALANCES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondyloarthritis (AS) is a progressive, chronic, inflammatory skeletal disorder affecting the spine and sacroiliac joints. To date, the disease etiology remains unclear. Some studies have shown that lymphocytes play important roles in the inflammatory process of AS. However, the role of comprehensive subtype lymphocyte subset imbalance in AS was rarely mentioned.
Objectives: In the present study, the correlation of lymphocyte subset changes with the progression of AS was investigated.
Methods: Flow cytometry analyses were carried out to detect the levels of a series of lymphocytes including different stages of differentiation CD4+T cells, CD8 +T cells, helper T cells (Th), cytotoxic T cells(Tc), regulatory cells (Treg), B lymphocytes and so on. Evaluation of hip joint disease were by using Bath Ankylosing Spondylitis hip X-ray index. Ankylosing Spondylitis Disease Activity Score (ASDAS) was used to assess disease activity and AS patients were divided into inactive disease group (ASDAS<1.3) and active disease group (ASDAS≥1.3). Bath Ankylosing Spondylitis Disease Activity Index(BASDAI) were also recorded.
Results: A total of 67 AS patients and 50 healthy subjects were included in the study. The percentage of Th2 cells, Th17 cells, Tfh2 cells, inactive phase-specific CD8+ T cells and B cells were found to be significantly higher in the AS groups compared with the healthy individuals (P < 0.05). However, the percentage of Th1 cells, Tc1 cells, Tfh1 cells, continuous expression of virus-specific terminally differentiated CD8+ T cellsplasma cells, memory B cells and convertible B cells were significantly lower in the AS groups (P < 0.05). As a result, the percentage of Th1/Th2 and (Th1+Th17)/Th2 ratios were significantly lower in AS patients (P < 0.05). In addition to the above differences, the percentage of Treg cells were higher but inactive phase-specific CD8+ T cells and continuous expression of virus-specific CD8+ T cells were lower in patients with hip joint involvement compared with the healthy individuals (P < 0.05). But there was no significantly differences between hip joint involvement AS group (58.7%) and no involvement AS group (41.3%). In patients who had a history of peripheral arthritis (excluding hip involvement), the proportion of plasma cells was significantly higher than in patients without a history of peripheral arthritis.The percentage of Th1 cells, Th2 cells, effector memory CD4+ T cells were higher but naive B cells were lower in patients have uveitis/iritis history compared with no uveitis/iritis history AS group (P < 0.05). AS patients with family history have significantly higher percentage of Treg cells and terminally differentiated CD8+ T cells but lower initialize CD8+ T cells and central memory CD8+ T cells compared with no family history group (P < 0.05). The percentage of depleted CD4+ T cells, terminally differentiated CD8+ T cells, Th17 cells and Tfh 17 cells were significantly higher but functional CD4+ T cells, central memory CD4+ T cells were significantly lower in active disease group compared with inactive disease group. Central memory CD4+ T cells and central memory CD8+ T cells were negatively correlated with ASDAS (P < 0.05). Depleted CD4+ T cells were positively correlated with BASDAI (P < 0.05) but functional CD4+ T cells were negatively correlated with BASDAI (P < 0.05).

Conclusion: Imbalances in the numbers and functions of specific lymphocyte cell subsets are key pathogenic derangements in AS, and these insights are leading to changes in clinical practice. The present study provided further evidence on the function and underlying mechanism of lymphocyte subsets, which may be useful in the diagnosis and treatment of ankylosing spondylitis.

REFERENCES

[1] Zhongliang Duan: The immune dysfunction in ankylosing spondylitis patients. BioScience Trends. 2017; 11(1):69-76.

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AB0036C IMMUNOPHENOTYPIC CHARACTERIZATION OF T-CELL IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH GOLIMUMAB

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Background: Golimumab is a human anti-TNF monoclonal antibody that has shown efficacy in RA. In the RA pathophysiology, the elevation of TNF modulates the cellular immune response, which leads to a sustained activation of T-cell response; however, it is unknown whether anti-TNF interferes with the immunophenotype of T-cell.
Objectives: To evaluate activation (CD25, CD69) and exhausted (PD-1, TIM-3, LAG-3, CTLA-4) markers of T-cells in RA patients treated with Golimumab.
Methods: We included 14 patients with RA diagnosis (Criteria ACR/EULAR 2010), with moderate to severe activity; 11 non-responders to synthetic DMARDs (NR-DMARDs) and 3 responders to synthetic DMARDs with pharmacological toxicity (R-DMARDs). All patients were treated with Golimumab during 24 weeks. The questionnaire SF-36, DAS28-CRP, power Doppler signal and expression of CD25, CD69, PD-1, TIM-3, LAG-3 and CTLA-4, in T-cell were evaluated at 0 and 24 weeks.

Table 1. Clinical variables evaluated in patients with Rheumatoid Arthritis

Clinical variables	Cases n=14
Gender	
Female	13 (92.8%)
Male	1 (7.14%)
Age (years)	52.4 ±8.91
Time of evolution (years)	10.5 ±5.91
Extra-articular activity	4 (28.57%)
Rheumatoid factor (UI/ml)	330.7 ±170.03
Anti-CCP (UI/mL)	351.0 ±106.69
DAS28-CRP	
Week 0	6.0 ±0.98
Week 24	2.8 ±1.24
Power Doppler signal (score)	
Week 0	2.4 ±2.71
Week 24	2 ±1.41

Table 2. Results of the SF 36 Questionnaire in patients with Rheumatoid Arthritis.

	Week 0 $\bar{x}$ ±SD	Week 24 $\bar{x}$ ±SD
Physical function	25.8 ±17.37	49.6 ±24.31
Physical role	39.3 ±41.14	54.1 ±38.20
Body ache	54.3 ±13.11	26.9 ±19.28
General health	28.7 ±3.85	34.2 ±11.72
Vitality	50.2 ±6.55	46.4 ±9.28
Emotional	53.3 ±38.01	48.6 ±38.45
Social function	63.6 ±10.51	30.0 ±9.53
Mental health	63.2 ±9.12	46.4 ±17.13

Results: Clinical variables evaluated in patients with Rheumatoid Arthritis are shown in tables 1 and 2.

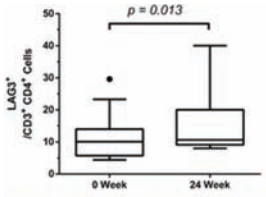


Figure 1. Expression of LAG3 on CD4+ T-cells in peripheral blood of RA patients treated with Golimumab. Mean fluorescence intensity (MFI).

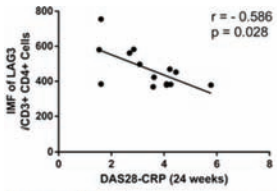


Figure 2. Correlation of LAG3+ on CD4+ T-cells in peripheral blood and the activity of the disease determined by DAS28-CRP after 24 weeks of treatment with Golimumab in patients with RA. MFI: the mean fluorescence intensity.

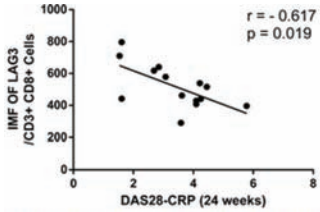


Figure 3. Correlation of LAG3+ on CD8+ T-cells in peripheral blood and the activity of the disease determined by DAS28-CRP after 24 weeks of treatment with Golimumab in patients with RA. MFI: the mean fluorescence intensity.

The frequency of LAG-3+ on CD4+ T-cells increased after 24 weeks of treatment with Golimumab (p = 0.013) (figure 1). The expression of LAG-3 in CD4+ T-cells (r = -0.586, p = 0.028) (Figure 2) and CD8+ T-cells (r = -0.617, p = 0.019) (Figure 3) inversely correlated with DAS28-CRP after treatment. At the beginning of treatment NR-DMARDs patients showed higher expression of CD25 in CD8+ T-cells and lower expression of TIM-3 in CD4+ and CD8+ T-cells with respect to R-DMARDs. After 24 weeks of treatment, a lower frequency of CD69+ and LAG-3+ T-cells was found and increased of CD25+ T-cells compared to R-DMARDs.
Conclusion: Golimumab treatment increased the expression of LAG-3 in T-cells, suggesting a negative regulator of antigen presentation of T-cells.

REFERENCES

[1] Tahir Z, Kavanaugh A. The role of golimumab in inflammatory arthritis. A review of the evidence. Ther Adv Musculoskel Dis 2018;9:181–194.
[2] Cuda C, Pope R, Perlman H. The inflammatory role of phagocyte apoptotic pathways in rheumatic diseases. Nat rev Rheumatol 2016;12: 543-555.
[3] Wherry E, Kurachi M. Molecular and celular insights into T cell exhaustion. Nat rev Inmunol 2015;15: 486-496.
[4] Burmester G, Feist E, Dörner T. Emerging cell and cytokine targets in rheumatoid arthritis. Nat rev Inmunol 2013;15:1-10.
[5] McKinney E, Lee J, Jayne D, Lyons P. T-cell exhaustion, co-stimulation and clinical outcome in autoimmunity and infection. Nat rev Inmunol 2015;523: 612-616.

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Innate immunity in rheumatic diseases

AB0037 NEUTROPHIL GRANULOCYTES ARE PRIMED IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: The adaptive as well as innate immunity is involved in JIA pathology. Neutrophils are key mediators of the innate immune response and is the most abundant cell type found in JIA synovial fluid. Studies of neutrophils in JIA have shown transcriptional abnormalities and neutrophil-derived S100A proteins have shown a potential role as biomarkers. Still, studies of neutrophils in JIA are scarce.

Human neutrophil lipocalin (HNL), also known as neutrophil gelatinase-associated lipocalin (NGAL), is a protein found in the secondary granules of neutrophil granulocytes. HNL can be found in epithelial cells as well, but only in its monomeric form. The dimeric form is only produced by neutrophil granulocytes. HNL resides in the secondary granules and is released upon stimulation, making HNL a unique marker of primed and activated neutrophil granulocytes, compared to myeloperoxidase (MPO) that resides in the primary granules and is released when neutrophils are activated, but also found in monocytes.

Objectives: To examine levels of the dimeric form of human neutrophil lipocalin (dHNL), to reveal if neutrophil granulocytes are primed in JIA, also analysis of myeloperoxidase MPO to reveal neutrophil activation. We aimed to compare the analyses to healthy controls and correlate the results to established measures of disease activity.

Methods: Blood samples from 75 patients with JIA (68% females) and 16 healthy controls were analyzed regarding HNL, using a dimer ELISA assay (Diagnostics Development, Uppsala, Sweden) specifically detecting the dimeric form of HNL (dHNL). We also analysed MPO (Diagnostics Development, Uppsala, Sweden), white blood cell count, neutrophil granulocyte cell count, ESR and CRP. All categories of JIA except the systemic category were included. Patient/parent and the physician filled out a global health assessment on a VA-scale (0-10). The number of active joints at sampling was collected and patients were classified according to the ILAR criteria. The participants with JIA had a median age of 12.1 (IQR: 7.7-15.3) years, the control group 5.3 (IQR: 2.0-9.5) years.

Results: The serum levels of dHNL and MPO were significantly elevated compared to healthy controls, ($p < 0.001$; $p = 0.002$), and correlated significantly with each other ($r_s = 0.68$, $p < 0.001$).

The levels of dHNL correlated best to the count of neutrophil granulocytes ($r_s = 0.54$, $p < 0.001$), total leukocyte count ($r_s = 0.43$, $p < 0.001$) and less well to CRP ($r_s = 0.42$, $p < 0.001$) and ESR ($r_s = 0.35$, $p = 0.002$) and not at all to the scoring system for disease activity, JADAS27 ($r_s = 0.06$, $p = 0.65$).

Conclusion: The increased levels of the dimeric HNL in serum confirmed the involvement of neutrophil granulocytes in JIA although dHNL did not correlate with disease activity. The mechanisms by which neutrophils are primed and activated in JIA, however, still remain an enigma.

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AB0038 S100A8/9 ASSOCIATES WITH PAIN PERCEPTION IN OA PATIENTS AND INDUCES NOCICEPTIVE PAIN BUT NOT ALLODYNIA IN EXPERIMENTAL SYNOVITIS

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Background: Inflammatory mediators released during synovitis, including S100A8 and -9, have been implicated in the regulation of pain. S100A8 and -9 may regulate pain either via direct stimulation of TLR4 on the nerve endings in the synovium or via stimulation at the site of the dorsal root ganglia (DRG), thereby inducing local inflammation which may cause sensitization.

Objectives: We aimed to elucidate the role of S100A9 in the pain response after induction of an acute synovitis using streptococcal cell walls (SCW) as a trigger, comparing $S100A9^{-/-}$ mice and their WT controls.

Methods: Synovial biopsies of 25 patients with early symptomatic OA were studied by micro-array analysis and subsequent functional annotation clustering (FAC). Patients with pain at t=5 years after biopsy isolation were compared to those without pain. Acute synovitis was induced by a single i.a. injection of SCW in the knee joint of C57Bl6 (WT) mice and $S100A9^{-/-}$ mice, control mice received an i.a. saline injection. Serum S100A8/A9 levels were investigated by ELISA and expression of S100A8 and S100A9 in synovium and DRG by immunohistochemistry (IHC). Joint swelling and cell influx was assessed by ^{99m}Tc accumulation and histology, respectively. Pain response were investigated Incapacitance Tester (weight bearing), Catwalk (gait analysis) and von Frey's filaments (mechanical allodynia). Gene expression of inflammatory mediators and neuron activation markers in DRG were determined by q-PCR. Monocyte influx and protein expression of NAV1.7 and GAP43 was monitored by IHC.

Results: In synovial biopsies of early symptomatic OA patients, approximately 750 genes were upregulated in patients that had pain 5 years after inclusion compared to patients without pain. FAC showed that inflammatory genes were highly significantly enriched ($p=6{,}4*10^{-12}$). Among the upregulated genes were the alarmins S100A8 and S100A9. In mice, a single i.a. injection of SCW resulted in increased synovial expression of S100A8 and S100A9 and subsequent increased serum S100A8/A9 levels (2.6-fold, $P < 0.001$) 1 day p.i., which returned to basal levels at 7 days p.i. The increased expression of S100A9 did not contribute to the development of inflammation since joint swelling and cell influx were similar in WT and $S100A9^{-/-}$ mice 1 day p.i.. WT mice showed a marked and significant decrease in percentage of weight bearing on the SCW injected hindpaw (28%) compared to saline injection (47%, $P < 0.001$) 1 day p.i., whereas $S100A9^{-/-}$ mice did not. Gait analysis confirmed that right paws were unloaded in WT mice, not in $S100A9^{-/-}$ mice. No difference in mechanical allodynia was observed, both mouse strains showed a similar reduction of paw withdrawal threshold (4.2 and 4.5 fold decrease respectively). Analysis of DRG showed no increased phagocyte infiltration after SCW injection as determined by S100A8 and S100A9 IHC and no change in inflammatory gene expression was measured. In addition, no change in F4/80 staining was seen in both WT and $S100A9^{-/-}$ mice. However, expression of neuron activation markers NAV1.7, ATF3 and GAP43 was significantly increased at 1 day after SCW injection in WT and not in $S100A9^{-/-}$ mice as compared to saline injected mice ($P = 0.022$, 0.004 and 0.030, resp.), which is in line in with the reduced pain response observed earlier in $S100A9^{-/-}$ mice. IHC confirmed the difference in NAV1.7 expression in the DRG at protein level.

Conclusion: These findings show that S100A9, which is released from the synovium upon inflammation, is an important mediator of inflammatory nociceptive pain response in the knee, rather than by being involved in peripheral sensitization. In acute inflammation S100A8/A9 is likely regulated via direct activation of TLR4 on nerve endings in the synovium.

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AB0040 JAK INHIBITORS – BARICITINIB AND TOFACITINIB – MODULATE THE IN VITRO INFLAMMATORY AND ALTERNATIVE POLARIZATIONS OF MACROPHAGES

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Background: Macrophages are major effector cells in inflammatory rheumatisms such as Rheumatoid arthritis (RA) and Psoriatic arthritis (PsA). Depending on their microenvironment, especially cytokines content, they can display various phenotypes or "polarizations" described as inflammatory (in the presence of IFNγ or GM-CSF) or as alternative (in the presence of IL-4 or IL-10). These cytokines involve JAK/STAT signaling pathway, and their action is expected to be inhibited by JAK inhibitors (JAKi) developed in RA and PsA. How JAKi modulate polarization of macrophage, and whether this phenomenon explains the clinical benefit in RA and PsA is not fully understood.

Objectives: To evaluate whether JAKi modulate *in vitro* polarization of monocytes derived macrophages.

Methods: ***[Cell culture]*** $CD14^+$ monocytes were isolated from healthy donors and differentiated as macrophages in the presence of M-CSF. Macrophages were then polarized as inflammatory macrophages (by LPS + IFNγ, or GM-CSF), or as alternative macrophages (by IL-4, or IL-10), in the presence or not of JAKi (500 nM): Baricitinib (JAK1/JAK2 specific), Tofacitinib (JAK1/JAK2/JAK3/Tyk2 specific).

[Membrane markers] Surface polarization markers were evaluated by flow cytometry.

[Functional assays] Cytokines production in supernatants of macrophages were quantitated by bead-based immunoassay and by ELISA. Reactive oxygen species (ROS) production triggered by LPS and/or IFNγ was assessed by flow cytometry. Phagocytosis of *E.coli* bioparticles was assessed by flow cytometry.

Results: We analyzed 12 donors. ***Membrane polarization markers*** were: CD40/CD80/CD206 for inflammatory macrophages, CD163/CD16/CD206/CD200R for alternative macrophages. Both JAKi modulated these markers. Regarding the inflammatory polarizations, Baricitinib and Tofacitinib respectively reduced CD40 and CD206 expression. Regarding the alternative polarizations, both drugs inhibited the expression of CD163, CD206 and CD200R.

At the ***cytokines*** level, both drugs did not significantly modulate the pro-inflammatory/anti-inflammatory balance in supernatants. We observed a slight increase in TNF and IL-6 resulting from LPS/NFkB pathway [1]. However, Baricitinib decreased the inflammatory IP-10, and increased IL-10 production. Both JAKi did not affect ***ROS production*** in the presence of LPS. Consistently with the absence of modulation of CD16 surface expression, Baricitinib and Tofacitinib did not affect CD16-dependent ***phagocytosis***.

Conclusion: Our study shows that despite distinct JAK specificity, Tofacitinib and Baricitinib maintained surface phenotypes close to those of non-activated macrophages This finding was observed whatever was the polarizing condition, thus supporting the potential benefit of JAK inhibitors in different immune diseases.

REFERENCES

[1] Pattison MJ, J Immunol, September 15, 2012, 189 (6) 2784-2792

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AB0041 DO FUNCTIONAL INTERACTIONS BETWEEN MACROPHAGES AND SYNOVIAL FIBROBLASTS DRIVE SYNOVIAL PATHOLOGY OR RESOLUTION OF INFLAMMATION?

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Background: We recently uncovered heterogeneity in human synovial tissue macrophages during inflammation and resolution of inflammation (remission) in rheumatoid arthritis (RA). The transcriptomic profiles of distinct macrophage subpopulations suggest distinct functions, ranging from inflammatory to regulatory. Prior studies propose reciprocal interactions between macrophages and synovial fibroblasts (FLS) exist in the joint; however, the exact contribution of these interactions to synovial pathology or resolution of inflammation remains unknown.
Objectives: The aim of this study was to examine the functional interactions between different macrophage phenotypes and synovial fibroblasts.
Methods: To model different macrophage phenotypes, monocyte-derived macrophages (MODM) were pre-stimulated (16h) with LPS (100ng/ml) to model inflammatory macrophages or with dexamethasone (Dex, 1µM) to model regulatory macrophages. After extensive washing, MODM were co-cultured with RA FLS for different periods of time. Prior to co-culture, FLS and MODM were labelled with CellTraceTM-Violet and CellTraceTM-Red, respectively. After 24 & 48 hours of co-culture, FLS and MODM were sorted based on positivity for CellTraceTM Violet (FLS) or Far Red (MODM) using FACS ARIA III, and expression of IL-6 and MMP1 in FLS analysed by ultrasensitive qPCR. In addition, the levels of IL-6 and MMP3 proteins were evaluated in co-culture supernatants by ELISA. To investigate the nature of the contact (40min meandering velocity) of individual MODMs on FLS monolayers was evaluated using Delta Vision fluorescence microscopy.
Results: FLS co-cultured with MODM showed an increased mRNA expression of IL-6 at both 24 and 48h, and MMP1 at 48h, compared to FLS cultured alone. This expression pattern was decreased when MODM were pre-treated with Dex and significantly up regulated when MODM were pre-treated with LPS. Consistently with mRNA expression, IL-6 protein was significantly increased when FLS were co-cultured with MODM (1192±137pg/ml) as compared to FLS cultured alone (445±78pg/ml). This production was significantly augmented when MODM were pre-treated with LPS (1985±25 pg/ml) and decreased when MODM were pre-treated with Dex (729±62pg/ml). Similarly, MMP3 protein level was increased when FLS were co-cultured with MODM (256±10pg/ml) as compared to FLS cultured alone (123±1 pg/ml). This production was significantly augmented when MODM were pre-treated with LPS (1960±34pg/ml) and decreased when MODM pre-treated with Dex (164±2pg/ml). These distinct effects of MODM phenotypes on FLS function were associated with different dynamics of their interactions. Our preliminary data reveal that MODM are quiescent on FLS monolayers unless MODM are pre-treated with Dex, which induced a patrolling behaviour.
Conclusion: Macrophages can actively increase or limit activation of FLS, depending on their inflammatory or regulatory phenotypes, respectively. These observations indicate the potential for different subsets of synovial tissue macrophages to drive or resolve synovial inflammation by influencing the stromal compartment.

REFERENCES

[1] Elmesmari A, Alivernini S, et al., Synovial tissue of RA patients in remission contains a unique population of regulatory macrophages. Annals of the Rheumatic Diseases, 2017;76 (Suppl2) 138-139.

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AB0042 PRECLINICAL EVALUATION OF JAK1 SELECTIVE INHIBITORS INCB039110 AND INCB054707 AS TARGETED THERAPY OF CUTANEOUS LUPUS ERYTHEMATOSUS

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Background: Cutaneous lupus erythematosus (CLE) is an autoimmune disease with heterogenous subtypes presenting with inflammatory skin lesions, a histological pattern called “Interface-dermatitis” and enhanced type-1-interferon (IFN)-regulated JAK/STAT (Janus kinase/signal transducers and activators of transcription) pathway signaling. Despite deeper understanding of the pathogenesis still no specifically approved drugs for CLE exist.
Objectives: The aim of our study was to investigate the effect of JAK1 selective inhibition as potential therapeutic approach for CLE in established preclinical models of cutaneous autoimmunity.
Methods: The expression of IFN-regulated proteins and genes after JAK1 inhibitor treatment was analysed in cultured, stimulated immortalized and primary human epidermal keratinocytes. In addition the impact of JAK1 inhibition on CLE-like skin lesions in lupus prone MRL/lpr- and TREX1-knockout-mice was determined.
Results: In vitro investigation revealed a significantly decreased gene- and protein expression of proinflammatory cytokines, in particular CXCL10 as key driver chemokine of lesional inflammation, and other pathophysiologic important IFN-regulated mediators in inflamed keratinocytes after treatment with JAK1 inhibitors. Moreover JAK1 inhibition generated an amelioration of skin lesions in lupus prone mice.
Conclusion: Our findings indicate that inhibition of JAK1 results in a decreased chemokine expression, subsequent less cytotoxic T cell induced keratinocytic cell death leading to an improvement of lesional skin. By breaking the vicious inflammatory cycle JAK1 inhibitors appear to be promising agents as targeted therapy of CLE. Further investigation has to be performed in clinical trials.

REFERENCES

[1] Wenzel, J.; Tüting, T. (2008): An IFN-associated cytotoxic cellular immune response against viral, self-, or tumor antigens is a common pathogenetic feature in “interface dermatitis”. In: The Journal of investigative dermatology 128 (10), S. 2392–2402.
[2] Kuhn, A.; Landmann, A.; Wenzel, J. (2016): Advances in the treatment of cutaneous lupus erythematosus. In: Lupus 25 (8), S. 830–837.
[3] Hornung, T.; Janzen, V.; Heidgen, F.-J.; Wolf, D.; Bieber, T.; Wenzel, J. (2014): Remission of recalcitrant dermatomyositis treated with ruxolitinib. In: The New England journal of medicine 371 (26), S. 2537–2538.
[4] Klaeschen, AS.; Wolf, D.; Brossart, Peter; Bieber, T.; Wenzel, J. (2017): JAK inhibitor ruxolitinib inhibits the expression of cytokines characteristic of cutaneous lupus erythematosus. In: Experimental dermatology 26 (8), S. 728–730.

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AB0043 EFFECT OF IN VIVO HYDROXYCHLOROQUINE AND EX VIVO ANTI-BDCA2 TREATMENT ON PDC IFNA PRODUCTION FROM PATIENTS AFFECTED WITH CUTANEOUS LUPUS ERYTHEMATOSUS

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Background: BIIB059 (aka 24F4A) is a monoclonal antibody that targets BDCA2, an inhibitory receptor expressed on pDCs. Plasmacytoid dendritic cells (pDCs) are a major source of Type-I Interferon (IFN-I), which is considered to be a key pathogenic driver in Cutaneous Lupus Erythematosus (CLE). Recent results from a Phase I clinical trial suggest that BIIB059 may ameliorate skin lesions in CLE patients. BIIB059 is currently evaluated in Phase II clinical trial for CLE with or without SLE.
Objectives: Given that Hydroxychloroquine (HCQ), a widely-used CLE therapy, and BIIB059 are both able to inhibit pDC-derived IFN-I production; this study aimed to determine whether BIIB059 would show an additional inhibitory effect on pDC response after *ex-vivo* or *in-vivo* treatment with HCQ.
Methods: The effect of BIIB059 on pDC-derived IFNα was measured from peripheral blood mononuclear cells (PBMC) either from healthy donors in presence or absence of HCQ or from CLE patients clinically exposed to various levels of HCQ. TLR7, TLR7/8, and TLR9 agonists (ssRNA, R848, and,CpG-A) were used for pDC stimulation.
Results: PDCs were the only producers of IFNα in response to CpG-A, R848, and ssRNA stimulation in PBMC cultures. CLE patients with high blood HCQ levels showed lower *ex-vivo* pDC responses to CpG-A, but not R848 or ssRNA. In contrast, BIIB059 reduced the amount of IFNα produced by pDCs from CLE patients in response to all TLR agonists, irrespective of the blood HCQ level. This effect was observed in patients with low or high blood IFN signature and in patients with or without concomitant SLE diagnosis.
Conclusion: Clinically-relevant HCQ concentrations partially inhibit the pDC response to TLR9 and weakly affect the response to TLR7/8 stimulation. BIIB059 robustly inhibits pDC responses even in the presence of HCQ, highlighting its unique potential to disrupt pDC disease relevant biology, which could provide additional therapeutic benefit for CLE patients.
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AB0044 PHARMACOLOGICAL MANIPULATION OF SIRTUIN 1 ACTIVITY IN EXPERIMENTALLY INDUCED ARTHRITIS

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Background: Sirtuin 1 (Sirt1) is a member of the sirtuin family of NAD+ dependent protein deacylases. This nuclear enzyme with deacetylase activity serves as a metabolic sensor and transcriptional regulator, and exerts its beneficial effects by promotion of cell viability, tissue regeneration, and inhibition of inflammation.
Objectives: 1) To investigate the effect of pharmacological modulation of Sirt1 enzymatic activity on disease outcomes of experimental rheumatoid arthritis in mice; and 2) To characterize surface marker and pro-inflammatory cytokine expression in neutrophils following Sirt1 activation or inhibition.
Methods: Arthritis was induced by intra-peritoneal administration of a cocktail of monoclonal antibodies against collagen type II in Balb/c mice (CAIA). We utilized synthetic compounds which specifically activate or inhibit Sirt1 activity - SRT2183 and EX527, respectively. We investigated the effect of Sirt1 activity modulation on clinical scores of arthritic mice after subcutaneous seven-day treatment initiated at Day 7 of CAIA. We used flow-cytometry for phenotyping and functional analysis of blood, and bone marrow (BM) derived neutrophils stimulated *in vivo*, and *in vitro*. The effects of the two compounds on Sirt1 activity and on cell viability were assessed using ELISA-based colorimetric assays.
Results: Activation and inhibition of Sirt1 activity led to CD11b down-regulation and CXCR2 up-regulation on healthy blood and BM neutrophils, suggestive of neutrophil mobilization from the BM to the periphery following treatment *in vivo*. Both SRT2183 and EX527 had a positive effect on clinical scores in CAIA mice. However, in EX527-treated mice the re-emergence of signs of joint inflammation was observed 14 days after cessation of treatment. Administration of SRT2183 was able to up-regulate IL-1beta in healthy and CAIA mice, which we also observed in un-stimulated neutrophils *in vitro*. Iso-nicotinamide, a compound which activates sirtuins via an alternative mechanism, had a similar effect on IL-1beta expression *in vitro*. Finally, Parp1 cleavage, a marker for cell death, was reduced in purified BM neutrophils following Sirt1 activation.
Conclusion: Sirt1 activity modulation, whether activation or inhibition, improved clinical scores in arthritis. This corresponds to the mobilization of neutrophils from the BM to the periphery. The selective increase of IL-1beta following Sirt1 activation indicates that while activation or inhibition achieves a similar outcome, this is done through different molecular pathways. Our results underscore that systemic pharmacological modulation of Sirt1 activity for a complex disease, such as rheumatoid arthritis, is complicated and attention should be paid to the schedule and duration of treatment, as well as to the progressive involvement of various cell types, in order to maximize the beneficial effects.
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AB0045 MESENCHYMAL STEM CELLS INHIBIT THE ACTIVATED COMPLEMENT C5 BY CLUSTERIN IN LUPUS NEPHRITIS

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Background: Dysregulation of clusterin (CLU) and over-activated complement C5 were involved in the development and progression of lupus nephritis (LN). Allogeneic mesenchymal stem cells (MSCs) transplantation has achieved good clinical efficacy for refractory LN, however, the exact mechanisms remain to be elucidated.
Objectives: To investigate the clinical effect of MSCs on SLE model mice (B6.lpr), and explore the mechanisms of MSCs inhibiting the activated complement C5 *in vivo* and *in vitro*.
Methods: 26-week-old female B6.lpr mice were randomly allocated in three groups, which were given the following treatments, CTX (200mg/kg), MSCs (1 x 10^6), and an equal volume of PBS. 24 hours urine and peripheral blood were collected periodically. All mice were sacrificed at 40 weeks of age. Urine protein to creatinine ratio and plasma creatinine were quantified to evaluate renal disease. Levels of C3, soluble C5b-9 (SC5b-9), CLU, and anti-dsDNA antibody were determined in the plasma by ELISA. Histopathological evaluation of renal lesions was undertaken by HE, PAS, PASM and Masson staining under light microscopy. Podocyte foot processes were assayed by the transmission electron microscopy. Accumulation of immunocomplexes (IC), C3, C5b-9, and CLU were detected in renal specimens by immunofluorescence or immunohistochemistry. Expressions of CLU in MSCs were detected by real-time PCR and ELISA. MSCs-derived CLU was purified and functional analysis was performed accordingly.
Results: Compared to the control mice, both proteinuria and plasma creatinine were significantly improved in each treatment group. Plasma C3 was significantly elevated in mice of MSCs and CTX groups. There were decline trends in plasma levels of anti-dsDNA and SC5b-9 in treated mice when compared to the control mice. Notably, plasma CLU was only significantly elevated in MSCs treated mice. Pathological analysis showed that the proliferation of glomerular cells and foot process fusion were significantly alleviated in MSCs treated mice. Immunofluorescence and immunohistochemistry showed that depositions of IC, C1q, C3 and C5b-9 were significantly decreased in the MSCs group, although the expression of CLU was obviously increased in these mice. Mechanistically, interferon-α promoted the secretion of functional CLU by MSCs *in vitro*.
Conclusion: Allogeneic MSCs transplantation can effectively improve the clinical outcome of lupus mice. Possible mechanisms of MSCs might be related to inhibit the activated C5 via clusterin, which would be a potential treatment target in the future.

REFERENCE

[1] Harris CL, et al. Mol Immunol. 2018

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AB0046 **COMPARATIVE ANALYSIS OF TLRS AND INFLAMMASOMES GENES EXPRESSION IN DIFFERENT ETHIOLOGY ARTHRITIS AFTER STIMULATION WITH INFLAMMATORY STIMULI AND VITAMIN D**

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Background: It has been shown that a variety of environmental and genetic factors, as well as deficiency of vitamin D plays a key role in outcomes of arthritis. Many studies have shown that the central feature of synovitis in rheumatoid arthritis (RA) is activated synovium fibroblasts (SF) that play a key role in expression and secretion of distinct patterns of inflammatory factors. Recent studies demonstrated that nucleotide-binding oligomerisation domain-like receptor (NLR) containing a PYRIN domain 1 (NLRP1) and NLRP3 inflammasomes as well as Toll-like receptors (TLR), may be important in pathogenesis of chronic autoimmune joint diseases such as RA and potentially in development of osteoarthritis (OA). Therefore, better understanding of the role of SF, TLRs and inflammasomes inflammatory pathways in different ethiology joint damage could make a significant contribution to the early disease prognosis, monitoring, and therapy.
Objectives: A pilot study, to evaluate the effects of tumour necrosis factor α (TNFα), lipoteichoic acid (LTA), lipopolysaccharide (LPS), vitD on expression levels of TLR, inflammasomes, and vitD receptor (VDR) in human SF different ethiology knee damage: OA, RA, early arthritis (EA) (duration <12 months), healthy controls (HC) (after meniscus tear due to trauma).
Methods: Synovial tissue and blood samples for vitD analysis were collected from patients undergoing joint replacement/artroscopic synovectomy surgery, following informed consent according to the permission Lithuanian Ethics Committee. The isolated cells were expanded in a monolayer and used between passages 2 and 4. The expression of *VDR, TLR1, TLR2, TLR4, NLRP1*, *NLRP3* inflammasomes genes was analysed by qRT-PCR after 24h of stimulation with LTA, LPS, TNFα, vitD.
Results: Analysis of gene expression results revealed that TNFα, LPS or LTA have no effect on *TLR4* and *TLR1* genes expression levels in SF. Downregulation of *NLPR1* expression and upregulation of *NLRP3* accompanied by enhanced expression of *TLR2* was determined after stimulation with all factors, particularly TNFα. Highest upregulation of *TLR2* was observed in RA and early arthritis patients, levels of other genes showed high variation between all patients, disrespectfully to diagnosis. Stimulation with TNFα resulted in 8-fold downregulation of *VDR* gene expression only in RA group, but not in OA, EA or HC. Stimulation with vitD had no effect on expression levels of studied genes in SFs *in vitro*, while the blood levels of vitD were neither associated with the ethiology of arthritis nor with VDR responses to stimulation with TNFα, LPS, LTA.
Conclusion: We demonstrated downregulated expression of NLPR1, associated with increased levels of NLRP3 and TLR2 upon inflammatory stimuli in human articular SF from patients with arthritis of different ethiology. These data further support active involvement of those cells in inflammatory responses. Downregulated expression of VDR by TNFα in SF of RA patients implies altered signalling of vitD in the disease.

REFERENCES

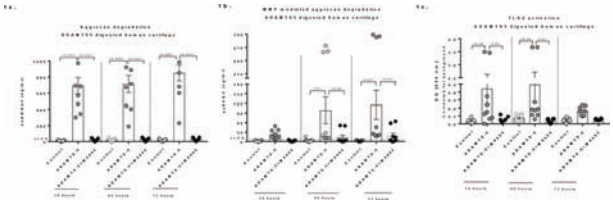
[1] Zao LR, et al. Mol Med Rep. 2018 Apr 17(4):5463-5469
[2] Guo C, et al. Clin Exp Immunol. 2018 Nov;194(2):231-243

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AB0047 **ACTIVATION OF TLR2 BY ADAMTS-5-MEDIATED DEGRADATION FRAGMENTS OF CARTILAGE EXPLANTS IS INHIBITED BY THE ANTI-ADAMTS-5 NANOBODY®, M6495**

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Background: Patients with joint diseases such as osteoarthritis (OA) are believed to have an abundance of endogenous Toll like receptor (TLR) ligands in their joints, which might be responsible for activating TLRs that may ultimately initiate a self-perpetuating inflammatory loop in the disease. TLR ligands may be generated from the breakdown of articular cartilage, which in turn arises from the activity of two key enzymes: A disintegrin and metalloproteinase with thrombospondin motifs 5 (ADAMTS-5) and Matrix metalloproteinases (MMPs).
Objectives: In this study, we investigate the effect of M6495, a novel anti ADAMTS-5 inhibiting nanobody® on TLR2 activation by ADAMTS-5 derived cartilage cleaved fragments
Methods: Human cartilage biopsies were retrieved from OA patients undergoing total knee replacement. The tissue cartilage was snap frozen in liquid nitrogen to eliminate underlying metabolic activity and then digested with recombinant human ADAMTS-5 (4 µg/ml) for 24, 48 and 72 hours respectively at 37 °C. The undigested remaining cartilage was discarded after each timeframe and the digested cartilage solution (DS) was used for further testing. Tissue cleavage was assessed by measuring the release of aggrecan degradation biomarkers: Aggrecanase mediated aggrecan degradation (AGNx1) and MMP mediated aggrecan degradation (FFGV). DS was tested for TLR activation in a secreted embryonic alkaline phosphatase (SEAP) reporter gene based HEK hTLR2 (human Toll like receptors) cell line. Cartilage tissue in buffer alone was used as control at each time point.
Results: Aggrecan degradation in cartilage was confirmed by increased release of AGNx1 ($p<0.0001$) (Fig. 1a) and FFGV ($p<0.01$ at 48 hours and $p<0.001$ at 72 hours) (Fig. 1b) in the DS compared to control. M6495 inhibited release of ADAMTS-5-mediated AGNx1 ($p<0.0001$, Fig. 1a) and FFGV ($p<0.05$ at 48 hours and $p<0.05$ at 72 hours, Fig. 1b). ADAMTS-5mediated DS showed TLR2 activation in the SEAP based reporter system when compared to control ($p<0.05$) (Fig. 1c). Adding M6495 blocked the ADAMTS-5-mediated DS TLR2 activation ($p<0.01$) (Fig. 1c).
Conclusion: ADAMTS-5-mediated cartilage degradation leads to release of aggrecan fragments, which activate the TLR2 receptor *in vitro* in a specialised reporter system. Anti-ADAMTS-5 inhibiting nanobody®, M6495, showed a suppression in release of degradation biomarkers leading to limited activation of TLR2. The data suggest a potential chondro-protective effect by M6495.



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AB0048 CHARACTERIZING THE ROLE OF NET-DERIVED IL-33 IN SLE PATHOGENESIS

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Background: Interleukin (IL)-33 is a cell necrosis-derived alarmin with immunostimulatory properties which depend on the context of immune cells and the inflammatory milieu (1). In Systemic Lupus Erythematosus (SLE), extracellular DNA (as in extracellular chromatin traps [NETs] or immune complexes [ICs]) combined with alarmins stimulate innate immunity receptors (such as Toll-like receptors [TLRs]) and the production of IFNa by plasmatocytoid dendritic cells (pDCs) (2, 3, 4).

Objectives: We propose that IL-33 is a potential NET-decorating protein and we want to investigate its pro-inflammatory properties. Additionally, NETs could also act as a platform mediating IL33's bioactivity taking into consideration the excessive accumulation of proteases on extracellular traps. We hypothesize that NET-derived IL-33 might enhance the interferogenic capacity of pDCs.

Methods: Peripheral blood polymorphonuclear cells (PMNs) were isolated from healthy and SLE individuals and their ability to form IL33-decorated NETs was assessed by confocal microscopy. Renal sections from active lupus nephritis patients were immunostained to observe any IL-33 decorated NETs. NET-supernatants from untreated and IC-treated SLE PMNs were administrated to healthy pDCs and type I IFN production was monitored by qPCR and ELISA. The contribution of IL-33 to the interferogenic capacity of NETs was assessed by pre-treating pDCs with a specific mAb against IL33-receptor (anti-ST2L). The effect of proteases on the IL33-mediated interferogenic potential of NETs was investigated by pharmaceutical inhibition of elastase and Cathepsin G.

Results: Spontaneous-released NETs from peripheral blood PMNs of active SLE patients were decorated with IL-33 to larger extent as compared to healthy PMN NETs. IL-33 decorated NETs were observed in renal sections from active lupus nephritis patients exhibiting mainly tubulointerstitial localization. Treatment of SLE PMNs with ICs led to the release of NETs with extended IL-33 decoration and enhanced interferogenic capacity. IL33 receptor blockade significantly decreased the type I IFN response of NET-treated control pDCs. Elastase and Cathepsin G inhibition on NETs decreased the interferogenic capacity of IC-SLE NETs in an IL-33-dependent manner.

Conclusion: NET-derived IL-33 is a novel mediator of the nucleic acid-driven aberrant type I IFN response which exacerbates SLE disease. NET structure may be crucial in regulating the bioactivity of IL-33.

REFERENCES

[1] Duan, et al. "**The Role of IL-33 in Rheumatic Diseases.**" Clinical and Developmental Immunology (2013): 1-5

[2] Garcia-Romo, et al. "**Netting Neutrophils Are Major Inducers of Type I IFN Production in Pediatric Systemic Lupus Erythematosus**." Science Translational Medicine 3.73 (2011)

[3] Lande R, et al. ''**Plasmacytoid dendritic cells sense self-DNA coupled with antimicrobial peptide.**'' Nature (2007), Vol 449

[4] Tian, et al. "**Toll-like Receptor 9–dependent Activation by DNA-containing Immune Complexes Is Mediated by HMGB1 and RAGE**." Nature Immunology 8.5 (2007): 487-96

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AB0049 REDUCED FCΓR IIB AND ENHANCED FCΓR III EXPRESSION ON MONOCYTES IN PATIENTS WITH BEHÇET DISEASE

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Background: Behcet's disease (BD) is a systemic inflammatory disease without clear pathogenesis. Previous studies have shown the association between FcγR gene polymorphisms and BD[1-2]. FcγRs, the receptor of IgG, has both activatory and inhibitory subtypes, and the imbalance of them on immunocytes has been illustrated to have significant pathogenetic roles in many autoimmune diseases[3-6].

Objectives: This study was aimed to investigate the potential abnormal expression of FcγRs in BD patients

Methods: We recruited 27 newly-onset treatment-naive BD patients (according to 2014 International Criteria for BD) and 23 gender-and age-matched healthy controls (HC). Flow cytometry was used for detecting the expression of the inhibiting receptor (FcγRIIB) and activating receptors (FcγRI and FcγRIII) on the neutrophils, monocytes, B cells, natural killer cells, dendritic cells, and T cell from the whole blood of BD and HC. The correlation between the expression of FcγR and disease activity index of BD was evaluated.

Results: BD patients had increased numbers of monocytes (60.14±3.387% vs 47.56±4.923%, p=0.0365) compared with HC. FcγRIIB expression on monocytes, rather than other immunocytes (p>0.05), was significantly lower in BD patients (4.87±0.61% vs 7.67±1.10%, p=0.0199). FcγRIIB expression on monocytes was negatively correlated to ESR (r=-0.576, p=0.031) and CRP (r=-0.539, p=0.047), positively correlated to serum IgA (r=0.785, p=0.001) and uncorrelated to serum IgG, IgM and PLT (p>0.05). FcγRIII expression on monocytes was higher in BD patients (19.61±3.046% vs 9.349±1.107%, p=0.0091). FcγRIII expression on monocytes was positively correlated to ESR (r=0.2551, p=0.0274) and CRP (r=0.2354, p=0.0352), and uncorrelated to serum IgG, IgM, IgA and PLT (p>0.05). Furthermore, FcγRIIB expressions of monocyte were comparable between BD patients in active disease or remission, while FcγRIII expression was significantly decreased (p=0.0158) after 3-month of treatment.

Conclusion: Our research demonstrated, for the first time, that the decreased expression of inhibitory receptor FcγRIIB and increased expression of activatory receptor FcγRIII on monocytes in BD. Furthermore, the abnormal expression was correlated with disease activity. These findings suggested that FcγRs *ratio imbalance might* play a *role* in the pathogenetic role of BD.

REFERENCES

[1] Aksu, K. et al. FcgammaRIIa, IIIa and IIIb gene polymorphisms in Behçet's disease: do they have any clinical implications? Clin Exp Rheumatol. 2008;26(4 Suppl 50):S77-83.

[2] Zhang, D. et al. Analysis of the association between Fc receptor family gene polymorphisms and ocular Behçet's disease in Han Chinese. Sci Rep 2018; 19;8(1):4850.

[3] Smith, KG. et al. FcgammaRIIB in autoimmunity and infection: evolutionary and therapeutic implications. Nat Rev Immunol 2010; 10(5): 328-43.

[4] Su, K. et al. Expression Profile of FcγRIIb on Leukocytes and Its Dysregulation in Systemic Lupus Erythematosus. J Immunol. 2007;178(5):3272-80.

[5] Li, Y. et al. Increased expression of FcgammaRI/CD64 on circulating monocytes parallels ongoing inflammation and nephritis in lupus. Arthritis Res Ther. 2009; 11(1):R6

[6] Catalán, D. et al. B cells from rheumatoid arthritis patients show important alterations in the expression of CD86 and FcgammaRIIb, which are modulated by anti-tumor necrosis factor therapy. Arthritis Res Ther. 2010;12(2): R68.

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AB0049B CHANGES OF INNATE LYMPHOID CELLS IN PERIPHERAL BLOOD OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME AND ITS CORRELATIONS WITH CLINICAL MARKERS

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Background: Innate Lymphoid Cells (ILCs) are a novel group of innate immune cells, according to the cytokine profile, they were divided into three major subsets:

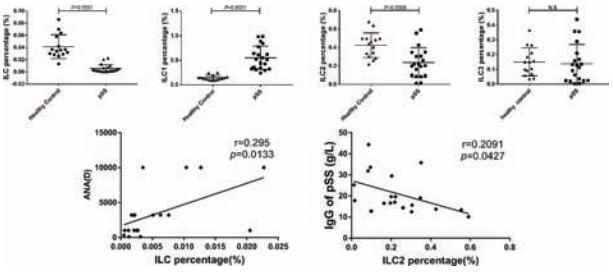
ILC1(Lin–IL7R+NKp46+ILCs), ILC2(Lin–IL7R+CRTH2+ILCs) and ILC3(Lin–IL7R+CRTH2–CD117+ILCs)[1]. Little research on ILC in the pathogenesis of Primary Sjögren's Syndrome(primary SS)

Objectives: Our purpose is to explore the function and role of ILC in the pathogenesis of Primary Sjögren's Syndrome and its correlations with clinical markers.

Methods: 20 patients with pSS and 15 age-matched healthy non-immune-related diseases controls were enrolled. The frequency of ILCs, B cells, CD4+T and CD8+T cells from PBMCs was detected by flow cytometry. Analysis the subsets of ILCs in each group which compared with B cells and T cell subsets respectively and correlation with clinical serologic markers. Analyze the levels of IL-4, IL-9, IL-33, IL-22 and IFN-γ in each group by ELISA.

Results: Compared with the control group, the percentage of ILC was decreased significantly in primary SS(P<0.0001); Meanwhile ILC1 was significantly increased in primary SS(P<0.0001), ILC2 was decreased significantly in primary SS(P=0.0009) and ILC3 has no significant difference in the primary SS (P>0.05). The frequency of ILCs in all patients positively correlated with antinuclear antibody titer (ANA(D)) (r=0.295, P=0.0133), moreover, the frequency of ILC2 in primary SS was positively correlated with B cells(r=0.3896;p<0.05), and the serum IgG was negatively correlated with ILC2 of all patients (r=0.2091,P=0.0427). Compared with Healthy control group, the level of IL-22 was significant higher in primary SS(P=0.0003), however, the levels of IL-4, IL-9, IL-33 and IFN-γ were not significant different with healthy control group(P>0.05).

Conclusion: The frequency of ILCs is related to ANA(D) of primary SS patients and ILCs play a critical role in the pathogenesis of primary SS. Its function and mechanism are worth further exploration.



REFERENCE

[1] Spits H., Artis D., Colonna M., et al. Innate lymphoid cells-a proposal for uniform nomenclature[J]. Nat Rev Immunol, 2013, 13(2): 145-149. doi: 10.1038/nri3365

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AB0049C INFLAMMASOME DRIVES RELEASE OF MITOCHONDRIAL DNA ENCLOSED IN EXTRACELLULAR MEMBRANE VESICLES AND PROPAGATION OF INFLAMMATION IN BEHÇET'S DISEASE

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Background: It has been reported that mitochondrial DNA (mtDNA) is released into the cytosol by mitochondrial stress and induces pro-inflammatory cytokine production via inflammasome and intracellular DNA sensors. Also, mtDNA in the extracellular space is known to result in sterile inflammation. However, the molecular mechanism of mtDNA release and its pathological significance in autoimmune diseases (ADs) has not been elucidated.

Objectives: To clarify the molecular mechanism of mtDNA release and its pathological significance in ADs.

Methods: We collected the serum from various AD patients and analyzed the levels of mtDNA in serum. We digested mtDNA in serum by DNase treatment. We purified the extracellular membrane vesicles (EMVs) and evaluated their inflammation-inducing potential. Also, we investigated the molecular mechanism behind mtDNA-induced inflammation by using inflammasome gene Knock out cell lines

Results: We first measured the levels of mtDNA in serum of the various ADs by quantitative PCR and found that serum mtDNA levels were significantly high in BD. Interestingly, mtDNA in BD serum could not be digested by DNase treatment and was detected in the extracellular membrane vesicles (EMVs) purified by ultracentrifugation. Since EMVs are known to deliver various molecules from one cell to another, we stimulated monocytic cells with BD-derived EMVs and found that these EMVs could induce IL-1β production in an NLRP3 inflammasome-dependent manner. We then studied the mechanism of secretion of mtDNA in EMVs and found that both human primary monocyte and monocyte-like cell line released mtDNA-containing EMVs after stimulation with ATP or LPS. Further, BD-derived monocytes secreted more abundant mtDNA in EMVs than monocytes derived from healthy donors. Additionally, the inhibition of caspase-1 activity reduced the secretion of mtDNA in EMVs

Conclusion: We revealed a novel mechanism of inflammation propagation involving inflammasome and mtDNA; activated inflammasome releases mtDNA-containing EMVs and subsequently leads to mtDNA-induced inflammation via NLRP3 inflammasome. Such inflammatory mechanism may contribute to the exacerbation of inflammation in BD.

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Cytokines and inflammatory mediators

AB0050 DETECTION OF SERUM AND SYNOVIAL FLUID LEVELS OF VISFATIN DURING FLARE-UPS AND REMISSION OF PRIMARY OSTEOARTHRITIS OF THE KNEES

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Background: OA is the most common form of joint disease and a major contributor of disability in older people. OA is a chronic joint disease characterized by cartilage breakdown, bone remodeling, osteophyte development and synovial inflammation [1]. Adipose tissue expresses and secretes a large number of proteins that often share functional and structural properties of cytokines and are there classified as adipokines [2]. These include leptin, adiponectin, resistin, visfatin, and others. These factors are associated with inflammation and immune response. Visfatin is an adipokines identified in 2004 and was identified first as Pre B cell Colony Enhancing Factor [3]. Visfatin is a potent inducer of PGE2 release in both human and immature mouse articular chondrocytes, as a result of increased messenger prostaglandin E synthase and decreased 15 15prostaglandine dehydrogenase syntheses [4].

Objectives: The aim of the study was to measure the level of visfatin in serum and synovial fluid from patients with knee osteoarthritis in flare-up and after they enter in remission.

Methods: to achieve the target of our study 20 patients with OA of the knee in flare-up were selected from out-patients clinic. The patients were followed up every two weeks after the first setting until they entered into remission. Twenty normal controls age, sex and body mass index (BMI) matched were recruited. In the first setting all patients had their sera, and synovial fluid measured for Visfatin, in the second setting sera and synovial fluid (if any) was drawn for visfatin measurement. Measurement of Visfatin by (ELISA) for quantitative determination of human visfatin in biological fluids.

Results:

1: serum visfatin of patients and control groups:

P value	t	Control ng./ml	Patients ng./ml	
0.0001	42.09	216.6000±30.25	847.90±59.86	Flare up
0.001	23.6	216.60±30.25	542.45±59.60	Remission

Patients recorded higher VIS-S readings than the controls with high significant difference in both situations.

2: serum and SF visfatin of patients during flare up and remission:

	Flare up ng./ml	Remission ng./ml	T	P value
Serum visfatin	847.90±59.86	542.45±59.60	19.65	0.0001
SF visfatin	694.60±77.35	384.00±30.61	7.85	0.001

There was a significant increase in Visfatin in serum and synovial fluid during flare-ups.

Conclusion: Visfatin was elevated both systemically and locally in the patients with knee OA, was elevated during flare-ups and decrease during remission, was higher in serum than in synovial fluid of patients and There was no difference in the level of visfatin in relation to aging or gender difference.

REFERENCES

[1] Lorenz H, Richter W (2006) Osteoarthritis: cellular and molecular changes in degenerating cartilage. Prog Histochem Cytochem 40(3):135–163.
[2] Kershaw EE, Flier JS (2004) Adipose tissue as an endocrine organ. J Clin Endocrinol Metab 89(6):2548–2556.
[3] O. Gualillo, J. R. Gonźalez-Juanatey, and F. Lago,(2007) "The emerging role of adipokines as mediators of cardiovascular function: physiologic and

clinical perspectives," Trends in Cardiovascular Medicine, vol. 17, no. 8, pp. 275–283, 2007.
[4] Duan Y, Hao D, Li M, et al. (2012) Increased synovial fluid visfatin is positively linked to cartilage degradation biomarkers in osteoarthritis. Rheumatol Int 2012; 32:985–90.

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AB0051 SEMAPHORIN 3A: A POSSIBLE MARKER FOR DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Sema 3A is concerned in the pathogenesis of many autoimmune diseases because it is involved in regulation of immune responses and maintenance of self-tolerance. Regulatory T cells play an important role in maintaining immunological self-tolerance by suppressing autoreactive T cells. Sema3A promotes regulatory T cells by enhancing IL-10 production
Objectives: The current study aimed at testing the possible role of Semaphorin 3A (Sema 3A) in activity and in remission in rheumatoid arthritis patients and to assess whether this level correlates with interleukin 10 (IL-10) level.
Methods: Sixty Egyptian patients with rheumatoid arthritis (RA) were divided into three groups according to modified Disease Activity Score (DAS28), RA in high activity (group II, n=20), RA in moderate activity (group III, n=20) and RA in remission (group IV, n=20) and compared with 20 normal individuals (group I). Serum levels of Sema 3A and IL-10 were measured and correlated with ESR, CRP, Rheumatoid factor, DAS28 and Health Assessment Questionnaire (HAQ).
Results: Serum Sema 3A levels were significantly lower in high activity (55.7 ± 15.5 pg/ml) than in moderate activity groups (72.9 ± 14.6 pg/ml, p = 0.002) and both levels are lower than those in remission group (77.2 ± 13.1pg/ml, p < 0.001 compared to high activity one) and the control groups (76.5 ± 23.6pg/ml, p < 0.001 compared to high activity one also), A significant negative correlation was detected between Sema 3A and each of ESR, CRP, DAS28 and HAQ. Serum IL-10 was higher in patient groups, with highest mean among group IV.
Conclusion: reduced serum level of Sema 3A was found to be correlated with disease activity and indicating its usefulness marker for RA disease activity.
Disclosure of Interests: None declared
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AB0052 GENE POLYMORPHISM TNFAIP3 RS6920220 IS ASSOCIATED WITH A SPECIFIC CYTOKINE PATTERN IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Genetic factors are known to substantially influence the production of cytokines.
Objectives: This prospective study was aimed to explore whether the polymorphisms of immune response genes were associated with cytokines/chemokine production in patients with early rheumatoid arthritis (eRA) and whether a biological therapy affected this association.
Methods: 44 eRA patients (36 females; median age 55.0 [46; 60,0]; median disease duration 7,0 [4,0; 11,0] months; DAS28 5.9 [4,8; 6,4]) were included. 89% were positive for IgM rheumatoid, 92% - anti-CCP positive. "Gene candidate" approach was used to search for the following gene polymorphisms (SNPs): P*TPN22* (+1858 C/T, rs2476601), *CTLA4* (+49A/G, rs231775), *TNFAIP3* (rs675520, rs6920220, rs10499194), *IL6* (-174G/C, rs1800795), *IL6R* (+358A/C, rs8192284), *TNFA* (-308A/G, rs1800629), *MCP1/CCL2* (+2581A/G, rs1024611), *IL10* (-592A/C, rs1800872, -1082 A/G, rs1800896). Serum levels of 27 cytokine/chemokines were measured using the xMAP multiplexing technology at baseline, at 12 and 24 weeks after initiation of therapy. All patients were treated with methotrexate and/or biological therapy in accordance with the treat-to-target strategy (REMARCA study).
Results: Among all studied SNPs only polymorphism rs6920220 of gene *TNFAIP3* was associated with a certain cytokine/chemokine production across all time-points: baseline, 12 and 24 weeks. At baseline, the carriers of GG genotype (27 pts) showed significantly higher serum levels of the following mediators, compared to the patients with GA/AA genotypes (17 pts): **IL8** (42.8± 23.0 pg/ml vs 25.5±8.4 pg/ml, p<0.0001), **IL-17** (20.4±15.8 pg/ml vs 11.5±12.1 pg/ml, p=0.017), **MIP-1a** (19.1±40.5 pg/ml vs 9.8±2.7 pg/ml, p=0.036), **MIP-1b (**155.4±45.0 pg/ml vs 117.6±47.2 pg/ml, p=0.013), **PDGF-BB (**6967.5±3275.7 pg/ml vs 4600.6 ±1826.0 pg/ml, p=0.018). At week 12th, **IL-8** serum levels were the only ones to remain associated with polymorphism rs6920220 (p=0.015). At week 24th, the carriers of GG genotype had higher serum levels of several cytokines/chemokines, compared to the patients with GA/AA genotypes**: IL-8** (47.9±26.2 pg/ml vs 33.7±19.3 pg/ml, p=0.05), **IP-10 (**2451.7±1825.2 pg/ml vs 1404.9±941.1 pg/ml, p=0,037), **MIP-1b** (150.7±68.2 pg/ml vs 89.7±33.8 pg/ml, p=0.004), **PDGF-BB** (6150.9±2667.6 pg/ml vs 3915.4±1343.5 pg/ml, p=0.046). There was no statistically significant difference in production of IL-8, IP-10, MIP-1b, and PDGF-BB prior to and after 24 weeks of therapy.
Conclusion: The results suggest that polymorphism rs6920220 of gene *TNFAIP3* is linked to a particular cytokine/chemokine pattern. Biological therapy used according to the treat-to-target strategy for 24 weeks does not lead to the reduced production of IL-8, IP-10, MIP-1b, and PDGF-BB in the carriers of GG genotype.
Disclosure of Interests: None declared
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AB0053 ACTIVIN A AND FOLLISTATIN AFFECT THE INTERACTION OF ENDOTHELIAL CELLS AND RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: Activin A and its antagonist follistatin are part of an autoregulatory cycle, which is well known in the hypothalamic-pituitary-gonadal axis. Activins also have an important function in autoimmune diseases, such as rheumatoid arthritis (RA). Due to inflammation, activin A is released systemically, causing an induction of its antagonist follistatin. The negative feedback mechanism is well described for hepatocytes, but seems to be inactive in synovial fibroblasts from patients with rheumatoid arthritis (RASF). Neoangiogenesis, which is mediated partially by local fibroblasts, is increased due to inflammation and tissue hyperplasia in RA synovium. Despite the fact that RASF contribute to cartilage destruction in RA and RASF are able to interact with endothelial cells, less is known about the effect of activin and follistatin in this context.
Objectives: The aim of this study was to examine the effect of activin A and follistatin on the interaction of RASF and endothelial cells.
Methods: Endothelial cells (HUVEC) were commercially obtained and RASF were isolated from synovial tissue of patients with RA undergoing joint replacement surgery, RASF and HUVEC were stimulated in mono-, or coculture with activin A (15ng/ml), follistatin (500ng/ml) and/or IL-1β (1ng/ml). The concentrations of activin A, follistatin, VEGF and IL-6 were measured by ELISA.
Results: IL-1β induced the release of activin A 8-fold in RASF alone ($p < 0.01$, n=5) as well as in direct coculture with HUVECs 4-fold ($p < 0.05$, n=5). The stimulation with follistatin together with IL-1β reduced the activin A concentration produced by HUVECs 9-fold ($p < 0.01$, n=5) as well as in cocultures (10- fold, $p<0.01$) in comparison to stimulation with IL-1β alone. This reduction could not be observed in RASF monoculture.
In HUVECs, the IL-6 release was reduced by 37.6% after stimulation with activin A and IL-1β (n=5,$p<0.05$) in comparison to the stimulation with IL-1β alone. In RASF monoculture the release of IL-6 was induced by 61.0% after stimulating with activin A combined with IL-1β in comparison to the stimulation with IL-1β alone. In direct coculture neither the induction, nor the reduction of the IL-6 concentration could be detected when stimulated with activin A and IL-1β.
The release of VEGF was induced in RASF with IL-1β (89%), activin A (55%), activin A combined with IL-1β (148%), follistatin and IL-1β (84%) compared to unstimulated control. In coculture with HUVECs, the induction was less distinct than in monoculture (IL-1β: 75%, activin A: 22%, activin A and IL-1β: 101%, follistatin and IL-1β: 67%, n=4).
Conclusion: The autoregulatory cycle of activin A and follistatin is active in endothelial cells and inactive in RASF. Due to the interaction of endothelial cells and RASF, the proinflammatory response of the RASF is weakened. This was shown in direct coculture with no induction in coculture compared to stimulation with activin A and IL-1β in RASF monoculture. Interestingly, in direct coculture, the effects of HUVECs appear to dominate resulting in a significant reduction of the activin A concentration in the presence of follistatin and IL-1β in comparison to RASF monoculture.

REFERENCES

[1] de Jong FH, Grootenhuis AJ, Klaij IA, Van Beurden WM: Inhibin and related proteins: localization, regulation, and effects. Adv Exp Med Biol 1990;274:271-293.

[2] de Kretser DM, O'Hehir RE, Hardy CL, Hedger MP: The roles of activin A and its binding protein, follistatin, in inflammation and tissue repair. Mol Cell Endocrinol 2012;359:101-106

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AB0054 SEQUENTIAL INTRA-ARTICULAR INJECTIONS OF LINEAR AND CROSS-LINKED HYALURONIC ACIDS IN THE TREATMENT OF GONARTHROSIS

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Background: Sequential intra-articular injections of linear and cross-linked hyaluronic acids in the treatment of gonarthrosis
Objectives: This study evaluates clinical and biochemical effects of sequential intra-articular (IA) injections of two different formulations of hyaluronic acid (HA) in gonarthrosic (GA) patients. The first formulation consists in linear HA (LHA, MW 800-1200kDa; Regenflex Starter, Regenyal Labs, Italy) and the second in an intercalated mixture of cross-linked and linear HAs (CL-LHA, MW 1-2 MDa the crosslinked form and 500kDa the linear, intercalated one; Regenflex BioPlus).
Methods: 39 knee GA patients, 19 adults (50–65 years) and 20 elderly (>65 years), underwent two IA injections, i.e. LHA only at baseline and CL-LHA after 1 week. The same injections were repeated after 6 months. Clinical assessment - visual analogic scale (VAS) for pain, range of motion (ROM) and WOMAC index for knee functional limitation - was performed at baseline and after 3, 6, 9, 12 months. Blood, collected at baseline, after 1 week and 3 months, was analysed for relevant cytokines and collagen telopeptide II (CTX-II). Synovial fluid (SF) from patients with recurrent knee effusion (GA worse group) was biochemically analysed at baseline and 1 week. SF proteomic analysis was also carried out at specific time points.
Results: This HA-regimen improved joint pain and function independently from the age; plasma and synovial biochemical analyses indicate the attenuation of inflammatory cytokines (IL-1β, IL-9 and IL-17) and the stabilization of CTX-II; ultrasonograph data show an improvement of cartilage conditions and thickness at 12 months.
Conclusion: Sequential IA injections of LHA and CL-LHA represent a highly effective treatment especially in low degree GA patients and produce a significant and perduring improvement also in the GA worse group. The efficacy is likely dependent on the sequential administration of LHA and CL-LHA: the pharmacokinetic rationale of this combination will be discussed.
References: E. Barbieri[1,2*], P. Sestili[1], F. Mannello[1], G. Annibalini[1], S. Contarelli[1], L. Vallorani[1], A. M. Gioacchini[1], D. Ligi[1], L. Croce[1], Tung Tran Dang Xuan[3], C. Bartolucci[1] V. Stocchi[1] and I. Capparucci[1]
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Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7357

AB0055 INFECTIONS WITH ANTI TNF ALPHA: PROSPECTIVE STUDY OVER 12 YEARS

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Background: Anti Tumor Necrosis Factor alpha (TNFα) has significantly improved the prognosis of some chronic inflammatory diseases (CID). Nevertheless, they carry with them a significant risk of opportunistic infections, imposing a rigorous surveillance and an adequate education of the patients. In a context of endemic tuberculosis, it is imperative to take the appropriate precautions to detect this kind of infection in rheumatisers under anti TNFα.
Objectives: The aim of our work was to study the profile of infectious incidents in patients treated with anti TNFα.
Methods: This is a prospective and descriptive study in patients treated with anti-TNFα over a 12-year period (2006- 2018). We examined all infectious complications for each patient who received an anti-TNFα for with CID while assessing the level of severity, the type of infection and the risk factors that may be related to this type of incident.
Results: During the study period, 134 patients were identified, these patients were followed for ankylosing spondylitis (AS) for 58 cases, 36 for enteric rheumatism, 23 for psoriatic arthritis and 17 for rheumatoid arthritis. The mean age was 46.3 years (19-64 years), the mean age of the disease was 44.2 months (8-140).
The molecules used were: infliximab, etanercept, adalimumab with a respective number n (%) = 29 (21), 44 (33), 61 (46). Of the 134 patients evaluated, 71 were diagnosed and treated by a physician (in 47 patients), only 5 were serious: 2 cases of tuberculosis were reported (intestinal and ganglionic tuberculosis), 1 case of chickenpox of the adult, 1 case with perianal abscess, 1 case of erysipelas of the lower limb. The infection was bacterial, viral or mycotic [n (%) = 38 (53), 61 (86), 7 (8)]. A large proportion of the patients were on conventional immunosuppressive therapy. The factors related to the occurrence of infectious incidents were: use of corticosteroids p <0.0001,habitat in rural areas p= 0,042.
Conclusion: More than a third of patients have infectious complications after TNFα treatment in our study sometimes with serious issue. Thus, with the emergence of these accidents, the physician has to be very vigilant when instituting this biotherapy, and secondly, a rigorous and prolonged monitoring of the patients.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3835

AB0056 CUTANEOUS ADVERSE EFFECTS WITH BIOLOGIC AGENTS

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Background: Biologic agents (BA) are designed to treat chronic inflammatory diseases (CID), however, the adverse effects inherent with these drugs are more and more encountered. Among them are dermatological manifestations : infections, allergic reactions or even skin cancers, which sometimes require stopping treatment temporarily or permanently.
Objectives: The goal of this work consists to identify the cutaneous manifestations (CA) that have been reported to the most commonly used biologics in CID.
Methods: It's a prospective study in patients received in day hospital and treated with BA for CID during a period of 9 months (October 2017 - June 2018), we recorded all the data on CA after a complete dermatological examination, nor forgetting that we appreciated the phototype of the patients, the level of exposure to the sun and means of photoprotection.
Results: We collected the data of 68 patients under BA for the study (Adalimumab = 21, Etanercept= 17, Tocilizumab = 12, Infliximab = 7, Rituximab = 11) with a clear female predominance 59.4%, the mean age was 39 years. 37 (54%) had cutaneous manifestations, the main CA occurred with TNFα inhibitors 21/68 (30%), with more often skin infections. The other CA encountered were cutaneous rashes and allergic reactions, appearance of psoriasis or eczema and injection site reactions, we didnt cross any skin cancer.
Conclusion: Cutaneous manifestations remain frequent and relatively benign with BA. This work confirms the importance of education and dermatological monitoring of patients treated with biologic drugs in the CID. This prospective study needs to be completed over a longer period especially to screen any skin cancer.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3830

AB0057 ASSESSMENT OF MATRIX METALLOPEPTIDASE 3 (MMP3) AS A POTENTIAL BIOMARKER FOR RHEUMATOID ARTHRITIS IN ALGERIAN PATIENTS

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Background: Matrix metallopeptidase 3 (MMP3) is a protease induced by rheumatoid pannus pro-inflammatory cytokines during rheumatoid arthritis (RA) and degrades many cartilage and bone components. Its serum level is a useful marker for predicting joint destruction and evaluating disease activity.
Objectives: First, compare MMP3 production in RA patients to controls, then try to place this marker in the evaluation of disease activity.
Methods: We subdivided the studied population into three groups:

- RA: n = 134; sex ratio: 1: 5; age: 50 ± 14 years; disease duration: 7 ± 9 years,
- Healthy controls: n = 67; sex ratio: 1: 7; age: 38 ± 11 years,
- Population control: Patients with:
  - Inflammatory rheumatism: n = 80,
  - Chronic inflammatory diseases (CID): 18 Connective tissue disease (CTD), 14 chronic hepatitis C and 2 Crohn disease (CD).

The serum MMP3 measurement was performed by ELISA assay.
Results: Serum MMP3 was significantly higher in RA patients vs. healthy controls ($p < 0.0001$), Inflammatory rheumatism ($p < 0.0001$) and CID ($p < 0.05$) and is particularly high in women with high Disease Activity Score 28 joints (DAS28) vs. Moderate DAS28 ($p < 0.05$). In addition, it is higher if patients have: positive CRP: $p < 0.05$; positive RF: $p < 0.05$; positive ACPA: $p < 0.05$ and Bone erosion: $p < 0.01$ compared to other patients. Finally, there is a positive correlation between MMP3 production and RF ($p < 0.0001$, Spearman $r = 0.35$) and ACPA ($p < 0.01$, Spearman $r = 0.26$) but not with DAS28 joining the results published by Mahmood *et al* (2013) and Fadda *et al* (2016). Furthermore, in RA patients, there is no significant difference in MMP3 levels according to whether the erythrocyte sedimentation rate (ESR) is accelerated or not, unlike CRP which represents the best marker of inflammation in this disease, according to the literature. Finally, the production of MMP3 is greater in case of erosion and is associated to bone and joint destruction.
Conclusion: MMP3 serum measurement is a particularly useful marker of inflammatory activity in RA and may have potential predictive value in the development of bone and joint destruction.

REFERENCES

[1] Mahmood M. T. M. Ally, Bridget Hodkinson, Pieter W. A. Meyer, Eustasius Musenge, Mohammed Tikly, and Ronald Anderson. Hindawi Publishing Corporation. Mediators of Inflammation. Volume 2013, Article ID 183653, 6 pages
[2] Fadda S, Abolkheir E, Afifi R, Gamal M. The Egyptian Rheumatologist. 2016;38(3):153-159.

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AB0058 SERUM OXYTOCIN LEVELS IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND NONRADIOGRAPHIC AXIAL SPONDYLARTHRITIS

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Background: Spondyloarthritis refers to a group of chronic inflammatory diseases with unknown etiologies that involve particularly sacroiliac joints and spine but may also affect the remaining joints and entheses and exhibit extra-articular involvement in some patients. Oxytocin is a peptide hormone released from hypothalamus and stored in pituitary gland. It has been known for a while that oxytocin has anti-inflammatory effects and can cause a reduction in TNF-alpha levels.
Objectives: The aim of this study was to investigate the serum levels of oxytocin and its potential association with disease activity, spinal mobility and some other laboratory parameters such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in patients with ankylosing spondylitis (AS) and non-radiographic axial spondylitis (nrAxSpA).
Methods: Seventy-one patients with nrAxSpA and 38 patients with AS who presented to the Outpatient Clinic of Physical Medicine and Rehabilitation of Dicle University Hospital between March 2017- October 2017 and 67 healthy control subjects were included in this study. All the subjects underwent a thorough physical examination. Disease activity was assessed by Bath Ankylosing Spondylitis Disease Activity Index, and spinal mobility by Bath Ankylosing Spondylitis Metrologic Index. Laboratory examinations included complete blood count, ESR, CRP, and oxytocin tests.
Results: There was no significant difference in serum levels of oxytocin among the three groups ($p= 0.973$). However, serum levels of oxytocin correlated negatively with both ESR ($r= -0.359$, $p=0.027$) and BASDAI scores ($r= -0,448$, $p=0.005$) in patients with AS. On the other hand, serum levels of oxytocin had a negative correlation only with ESR in the patients with nrAxSpA ($r= -0.321$ $p= 0.009$).
Conclusion: ESR is one of the parameters associated with disease activity in patients with inflammatory rheumatoid diseases. Serum levels of oxytocin correlating negatively with both ESR and BASDAI scores in patients with AS and only with ESR in patients with nrAxSpA suggests that low levels of oxytocin may be associated with increased disease activity. This study lays the foundation for further studies that may aim to investigate how addition of oxytocin to the treatment regimen impact on the disease activity in patients with AS who exhibit particularly low levels of oxytocin during active disease period.

REFERENCES

[1] Clodi M, Vila G, Geyeregger R, Riedl M, Stulnig TM, Struck J, et al. Oxytocin alleviates the neuroendocrine and cytokine response to bacterial endotoxin in healthy men. Am J Physiol Endocrinol Metab. 2008; 295(3): E686-91
[2] Garrido-Urbani S, Deblon N, Poher AL, Caillon A, Ropraz P, Rohner-Jeanrenaud F, Altirriba J. Inhibitory role of oxytocin on TNFα expression assessed in vitro and in vivo. Diabetes Metab. 2018 Jun;44(3):292-295.
[3] Tong Li, Ping Wang, Stephani C. Wang, and Yu-Feng Wang. Approaches Mediating Oxytocin Regulation of the Immune System. Front Immunol. 2016; 7: 693.

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AB0059 通过**MAPK**和**NF-KB**信号通路自动修饰药物抑制白细胞介素-**37**表达

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Background: Autophagy has been shown as an intrinsic cellular defense mechanism in innate and adaptive immune responses and is reported to regulate inflammation during infection [1], Accumulating evidence indicates that autophagy suppresses inflammasome activation [2-5]. IL-37 has been identified as an anti-inflammatory factor that translocates into the nucleus and downregulates other pro-inflammatory cytokines [6]. Nevertheless, whether autophagy regulates the expression of IL-37 has not been elucidated.
Objectives: The purpose of this study was to investigate the role of autophagy in regulating IL-37, an anti-inflammatory cytokine highly expressed in tissues of patients with inflammatory and autoimmune diseases.
Methods: PMA-transformed and LPS-stimulated U937 macrophages were treated with three autophagy-modifying reagents—3MA, chloroquine, and rapamycin. The expression of three IL-1 family cytokines (IL-37, IL-18, and IL-1β) and two receptors (IL-1R8 and IL-18RA) was determined by quantitative PCR. Intracellular IL-37 expression was detected by flow-cytometry. Western blot analysis and immunofluorescence assay were used to determine the levels of P62/SQSTM1 and LC3, and autophagic U937 cells were isolated by sorting for quantifying IL-37 expression. We also used agonists and antagonists of the MAPK and NF-κB pathways to investigate the possible pathway involved. Peripheral blood mononuclear cells from one healthy donor were also used for autophagy modification and intracellular IL-37 quantitation.
Results: IL-37 was upregulated by rapamycin and chloroquine in U937 cells stimulated by LPS. IL-37 was preferentially expressed in autophagic cells accompanied with LC3 conversion. Higher IL-37 expression was found in "Cyto-ID" positive cells than in negative cells. Inductive IL-37 expression, but not constitutive IL-37 expression, could be abolished by inhibitors of the MAPK and NF-κB pathways, whereas it was augmented by MAPK agonists.
Conclusion: IL-37 levels were enhanced by rapamycin and chloroquine dependent on MAPK and NF-κB pathway activation, probably through LC3 accumulation. This study suggests a possible novel mechanism of chloroquine and rapamycin action in autoimmune inflammatory diseases.

REFERENCES

[1] B. Levine, N. Mizushima, H.W. Virgin, Autophagy in immunity and inflammation, Nature 469(7330) (2011) 323-35.
[2] C. Lupfer, P.G. Thomas, P.K. Anand, P. Vogel, S. Milasta, J. Martinez, G. Huang, M. Green, M. Kundu, H. Chi, R.J. Xavier, D.R. Green, M. Lamkanfi, C.A. Dinarello, P.C. Doherty, T.D. Kanneganti, Receptor interacting protein kinase 2-mediated mitophagy regulates inflammasome activation during virus infection, Nature immunology 14(5) (2013) 480-8.
[3] C.S. Shi, K. Shenderov, N.N. Huang, J. Kabat, M. Abu-Asab, K.A. Fitzgerald, A. Sher, J.H. Kehrl, Activation of autophagy by inflammatory signals limits IL-1beta production by targeting ubiquitinated inflammasomes for destruction, Nature immunology 13(3) (2012) 255-63.
[4] Q. Liu, D. Zhang, D. Hu, X. Zhou, Y. Zhou, The role of mitochondria in NLRP3 inflammasome activation, Molecular immunology 103 (2018) 115-124.
[5] R. Zhou, A.S. Yazdi, P. Menu, J. Tschopp, A role for mitochondria in NLRP3 inflammasome activation, Nature 469(7329) (2011) 221-5.
[6] S. Sharma, N. Kulk, M.F. Nold, R. Graf, S.H. Kim, D. Reinhardt, C.A. Dinarello, P. Bufler, The IL-1 family member 7b translocates to the nucleus and down-regulates proinflammatory cytokines, J Immunol 180(8) (2008) 5477-82.

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AB0060 METHOTREXATE DOWNREGULATES P-GLYCOPROTEIN EXPRESSION AND INHIBITS THE ACTIVATION OF JAK2/STAT3 PATHWAY IN RHEUMATOID ARTHRITIS PERIPHERAL BLOOD MONONUCLEAR CELLS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by abnormal synovial hyperplasia, inflammatory cell infiltration, and destruction of cartilage or bone. Early use of disease-modifying anti-rheumatic drugs (DMARDs) can significantly improve the patient's condition. However, many patients had no response after treatment or gradually decreased after treatment for some time. DMARDs Multidrug resistance(MDR) is an important cause of the above phenomenon[1]. How to reverse MDR in RA patients, and then control the disease is a major problem in RA treatment. The mechanism of MDR is complex. ATP binding cassette transporter super family consists of 48 transporters, ABCB1/P-glycoprotein (P-gp) is one of the major proteins associated with MDR[2]. The expression of P-gp is induced not only by genotoxic mechanisms, but also by inflammatory cytokines such as IL-2, IL-4, IL-6, and TNF-α in some inflammatory diseases[3,4].

Objectives: The multiple drug resistance(MDR) to disease modifying anti-rheumatic drugs(DMARDs) is the key factor in Rheumatoid arthritis(RA) treatment field. P-glycoprotein (P-gp) encoded by multidrug resistance gene 1 (MDR1) is involved in the excretion of numerous DMARDs. We investigated the effects of methotrexate(MTX) alone and combined with interleukin 6 (IL-6) on P-gp expression and examined the signaling pathway involved in Peripheral blood mononuclear cells of RA patients.

Methods: The Peripheral blood mononuclear cells were extracted from Fifteen RA patients who were without any DMARDs and biological agents treatment. These cells were treated with IL-6, IL-6+MTX(0.01ug/m), IL-6+MTX (0.1ug/m), IL-6+MTX (1ug/m) for 72h. P-gp expression was measured by flow cytometry and real-time polymerase chain reaction (RT-PCR); JAK2 and STAT3 were measured by RT-PCR.

Results: Methotrexate produce a dose-responsive reduction of both P-gp, JAK2 and STAT3 expression induced by IL-6.

Conclusion: Methotrexate downregulates p-glycoprotein expression and inhibits the activation of JAK2/STAT3 pathway in rheumatoid arthritis peripheral blood mononuclear cells.

REFERENCES

[1] van der Heijden JW, Dijkmans BA, Scheper RJ, Jansen G. Drug Insight: resistance to methotrexate and other disease-modifying antirheumatic drugs-from bench to bedside. Nat Clin Pract Rheumatol. 2007 2007-01-01;3(1):26-34.

[2] Dean M, Rzhetsky A, Allikmets R. The human ATP-binding cassette (ABC) transporter superfamily. Genome Res, 2001,11:1156-1166.

[3] Tsujimura S, Saito K, Nakayamada S, Nakano K, Tanaka Y. Clinical relevance of the expression of P-glycoprotein on peripheral blood lymphocytes to steroid resistance in patients with systemic lupus erythematosus. Arthritis Rheum. 2005 2005-06-01;52(6):1676-1683.

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AB0061 INVESTIGATING THE ROLE OF TGF-B AND FATIGUE IN CHRONIC FATIGUE SYNDROME

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Background: Chronic fatigue syndrome (CFS) is estimated to affect up to 5% of people in Europe and is more common in women than men. It is characterised by unexplained fatigue, post-exertional malaise and a range of other symptoms. Recent studies indicate potential immune dysfunction in CFS, specifically regarding cytokines and the adaptive behavioural response.

Objectives: This study aims to investigate serum transforming growth factor-beta (TGF-β) and the expression of the TGF-β Receptor 1 (TGFBR1) and TGF-β Receptor 2 (TGFBR2) genes, in relation to the fatigue associated with CFS.

Methods: Serum active and total TGF-β concentrations were measured in 117 CFS patients and 40 HCs using a TGF-β responsive luciferase bioassay. Expression levels of TGFBR1 and TGFBR2 were analysed using quantitative PCR. Fatigue was measured using the fatigue impact scale (FIS)[1]. FIS was categorised into three groups; 'mild' (0-80), 'moderate' (81-120) and 'severe' (121-160). Linear and ordinal regressions were performed on the continuous FIS and FIS categories respectively.

Results: Serum TGF-β concentrations in the CFS group did not differ significantly compared with the HC group (p=0.58). TGF-β concentrations showed no correlation with disease duration but there was a trend towards decreased TGF-β with increasing symptom duration. There were no significant differences between the levels of TGFBR1 and TGFBR2 in any of the fatigue groups, or between HCs. Active TGF-β concentrations were significantly elevated in the 'severe' FIS group compared to the 'mild' FIS group (p=0.04). Active/total TGF-β levels were significantly higher in the 'severe' FIS group than the 'mild' and 'moderate' FIS groups (p=0.02, p=0.03 respectively).

Conclusion: These data suggest no differences in serum concentrations of TGF-β or expression of TGFBR1 and TGFBR2, between the HC and CFS groups. It also suggests no differences in expression levels of TGFBR1/2 between any of the CFS fatigue groups. However, active/total TGF-β levels were increased in more severely fatigued patients based on FIS. This finding could be due to higher levels of circulating TGF-β, or increased amounts of TGF-β activation. Further work is necessary to confirm this finding in a larger cohort of CFS patients, and to explore how this increase in TGF-β relates to fatigue.

REFERENCES

[1] Fisk JD, Ritvo PG, Ross L, Haase DA, Marrie TJ, Schlech WF. Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 1994;18 Suppl 1:S79-83.

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AB0062 P75NTR IN THE MODULATION OF INFLAMMATORY RESPONSE MEDIATED BY SYNOVIAL FIBROBLASTS

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Background: Our previous studies[1] showed high expression levels of p75NTR, the nerve growth factor (NGF) receptor, in mononuclear cells (MNCs) obtained from blood and synovial fluids of patients with juvenile idiopathic arthritis (JIA) and rheumatoid arthritis (RA). p75NTR binds with high affinity proNGF, the immature form of NGF whose concentration, as we recently demonstrated[2], is extremely high in the synovial fluids of arthritis patients. In ex vivo experiments we demonstrated that recombinant proNGF increases inflammatory cytokine production in patient MNCs, an effect that was abolished using p75NTR inhibitors[2].

We also found that synovial fibroblasts (SFs) represent the main source of proNGF in the inflamed synoviae.

At present it is not known whether proNGF can influence the activity of SFs that are key effector cells in synovia inflammation producing inflammatory mediators that regulate chondrocytes and osteoblasts activation.

Objectives: To investigate the mechanisms regulating p75NTR expression in synovial fibroblasts of arthritis patients and to evaluate the effects of its inhibition on the inflammatory response.

Methods: SFs from arthritis patients were used to study the activity of proNGF/p75NTR axis. SFs from osteoarthritis patiens (OA) and skin fibroblasts from healthy donors (HD) were used as controls. p75NTR, NGF, and cytokine transcripts were evaluated by quantitative PCR (qPCR). Protein expression of p75NTR, NGF, and proNGF were analyzed by Western Blot. ELISAs were used to evaluate NGF, proNGF and cytokine concentration in supernatants and synovial fluids. p75NTR was inhibited using LM11A-31, a synthetic inhibitor that blocks the binding between p75NTR and its specific ligand proNGF.

Results: mRNA and protein expression of p75NTR were up-regulated in arthritis SFs compared to OA SFs and skin fibroblasts. *In vitro* stimulation with recombinant cytokines (IL-1β, TNF, IL-6), TLR-ligands (such as LPS), and JIA synovial fluids, containing a mixture of inflammatory mediators, strongly increased p75NTR mRNA expression in arthritis SFs. Interestingly, after stimulation we observed that also OA SFs and HD fibroblasts up-regulated p75NTR transcript, suggesting that p75NTR levels are modulated by the inflammatory mediators.

SFs of arthritis patients spontaneously produced proNGF and its release was further enhanced by all the above-mentioned inflammatory stimuli, albeit with different ability. Thus patient SFs can both produce proNGF and bind it through p75NTR. The inhibition of proNGF binding to p75NTR using LM11A-31 in arthritis SFs, activated with inflammatory cytokines or with synovial fluids, significantly reduced the expression and release of pro-inflammatory cytokine.

Conclusion: In addition to inducing p75NTR up-regulation, inflammatory stimuli increase the release of proNGF in arthritis SFs. Autocrine proNGF binds to p75NTR and further enhances pro-inflammatory cytokine production, creating a vicious circle that amplifies the inflammatory response. Blocking the binding of endogenous proNGF to its receptor p75NTR strongly reduces the production of inflammatory mediators and prospects the use of p75NTR inhibitors as a new therapeutic approach to chronic arthritis.

REFERENCES

[1] Prencipe, et al., Nerve Growth Factor Down regulates Inflammatory Response in Human Monocytes through TrkA, J Immunol. 2014
[2] Minnone, et al., ProNGF-p75NTR axis plays a proinflammatory role in inflamed joints: a novel pathogenic mechanism in chronic arthritis, RMD Open. 2017

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AB0063 A SYSTEMS APPROACH TO INVESTIGATE INFLAMMATION RESOLUTION BY MULTICOMPONENT MEDICINAL PRODUCT TR14

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Background: Acute inflammation is a nonlinear, spatio-temporal process for the removal of invading pathogens and the repair of damaged tissues to re-establish homeostasis. If not resolved, it leads to chronic inflammatory clinical phenotypes. The current medical paradigm is based on using single-molecule inhibitors aiming to block certain molecular pathways involved in inflammation. Complex diseases, where large numbers of feedback mechanisms play a central role, require multi-target interventions [1]. Dynamics of feedback mechanisms associated with multiple therapeutic checkpoints require systems biology approaches.
Objectives: The objective of our study was to construct a comprehensive molecular interaction map (MIM) of acute inflammation and its resolution. We further aimed to understand the effect of Traumeel (Tr14), a multicomponent drug, on inflammation resolution, by mapping previously published Tr14 transcriptomics data [2] from a wound healing murine model onto the MIM.
Methods: We constructed a comprehensive MIM using damage-, and pathogen-associated molecular patterns (DAMPs and PAMPs) and established disease genes from selected acute inflammatory clinical phenotypes as seed molecules. From the MIM, we identified feedback loops (FBLs) with the NetDS Cytoscape plugin using our previously published methodology [1]. All FBLs were merged to create a core regulatory network responsible for the overall dynamics of acute inflammation initiation, transition and resolution.
Using Tr14 transcriptomics data to identify acute inflammatory processes enriched at various time points, we combined RPKM values of each individual splice variant into the parent gene using the RSEM method [3]. The expression profile of whole genes was favored due to the lack of splice variant-specific ontology data. Further, the fold change expression profile for each gene was calculated by comparing Tr14-treated vs untreated mice. These data were mapped to the core regulatory network, and time point-specific sub-networks were identified by keeping nodes with absolute fold change expression of ≥ 1.5 and a p-value ≤ 0.05. Furthermore, we identified enriched immune-related processes regulated by Tr14 at each time point using the Cytoscape ClueGo app.
Results: The MIM has, as of January 2019, 3300 interactions, which are divided into 24 functional modules based on acute inflammation-related gene ontology terms. From the MIM, we identified 435 FBLs which were merged to extract a core regulatory network. After mapping of Tr14 gene expression fold change data at time points 12h, 24h, 36h, 72h, 96h, 120h and 192h, we identified that large numbers of FBLs were differentially regulated at early time points. This number decreased substantially at later time points. At time point 192h, we could identify only 6 differentially regulated nodes with no specific role in immune regulation, indicating that the inflammation was resolved mostly before 192h after injury. Combined expression profile of all the genes associated with the "increase acute inflammation" ontology showed an approximately 24hrs shift towards faster resolution in Tr14-treated mice.
Conclusion: Molecular interaction maps facilitate gene expression data analysis to identify enriched molecular processes and cell/tissue specific-phenotypes. Tr14-induced gene expression changes can be linked to inflammation-related biological functions as defined by enriched GO terms. Our analyses suggest that Tr14 modulates multiple network components at early time points, which can be linked to inflammation resolution.

REFERENCES

[1] Khan FM, et al. Nat Commun. 2017;8(1):198.
[2] St Laurent G 3rd, et al. Front Mol Biosci. 2017;4:57.
[3] Zhao S, et al. Plos One. 2015;10(11):e0141910.

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AB0064 SERUM TENASCIN-C LEVELS ARE ELEVATED IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Tenascin-C (TNC) is a pro-inflammatory extracellular matrix glycoprotein that is synthesized in various pathological conditions. TNC induces inflammatory activity and promotes damage of joints. Its expression in adults is restricted to sites of tissue injury, particularly during phases of inflammation and active tissue remodelling. Only a few studies have described elevated serum TNC levels in ankylosing spondylitis (AS) compared to healthy controls (HC).
Objectives: The aim of this study was to examine the levels of serum TNC among different axial spondyloarthritis (axSpA) subsets and whether TNC levels are related to disease activity measures or other clinical features.
Methods: Sixty-one patients who fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA and twenty age and sex-matched HC were included in this study. Based on imaging, patients were further classified as AS (n = 45) and as nr-axSpA (n = 16). Patients with AS were further divided into two subsets based on the absence (n=22) or presence of syndesmophytes (n=23).
TNC serum levels were determined using ELISA. The following data were collected: clinical and laboratory disease activity measures; demographic status; disease-related factors such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and CRP levels. Statistical analyses were performed with GraphPad Prism 5.1. The data are presented as the median and interquartile range.
Results: TNC serum levels were elevated in axSpA patients (535.3 (457.7-677.2) ng/mL) compared to HC (432.1 (329.1-565.9) ng/mL, p= 0.007). Dividing axSpA into nr-axSpA and AS subsets the difference was observed only between AS patients and HC (535.3 (434.5-677.2) vs. 432.1 (329.1-565.9) ng/mL, p=0.022). TNC serum levels did not correlate with disease activity biomarkers (serum CRP or BASDAI) in patients with axSpA. Although we have not observed correlation between TNC and mSASSS radiographic score, weak correlation with disease subsets was found (r=0.25, p=0.025).
Conclusion: We demonstrated here elevated serum TNC levels in patients with axSpA, particularly in those with syndesmophytes, which may suggest its role in bone formation during radiographic stage of the disease.
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AB0065 THE ROLE OF "NEW" CYTOKINES IN THE PATHOGENESIS RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune rheumatic disease. Activated B- and T-lymphocytes, mast cells, macrophages, tissue fibroblasts play a leading role in its pathogenesis. The development of autoimmune inflammation is impossible without the influence of a large number of pro-inflammatory cytokines such as IL 1α and β, TNF α, IL 6, IL 17, IL 22. Currently, other classes of biologically active molecules, such as adiponectin, visfatin, nesfatin, fetuin A, are being actively studied in RA [1,2,3,4].
Pre-B-cell colony enhancing factor 1 (PBEF1) stimulates synthesis of matrix metalloproteinases and chemokines, supporting synovial inflammation caused by leukocyte infiltration. A positive correlation between visfatin and C-reactive protein confirms its role as a mediator of inflammation. It is believed that increased concentrations of PBEF1 can stimulate systemic inflammation.
Objectives: The study the relationship between serum PBEF1 level and disease activity in RA patients.
Methods: We observed 140 patients with a reliable diagnosis of RA, of whom 96 were women and 44 were men. The control group consisted of 20 women and 10 men aged from 22 to 55 years without complaints of pain in the joints during life.
PBEF1 concentration in blood serum were determined by indirect enzyme-linked immunosorbent assay using commercial test systems (RaiBiotech, catNº EIA-VIS-1) according to the manufacturer's instructions.
Results: The level of normal values of PBEF1 in healthy individuals with a BMI of 18.5 to 24.9 kg/m2 was 0.14–3.9 ng/ml, with a BMI of 25 to 29.9 kg/m^2–0 - 5.9 ng/ml. Elevated serum PBEF1 level was detected in 84.29% of RA patients. The ones with elevated PBEF1 levels of significantly more likely to have a higher degree of activity index DAS28 (χ^2=48,293; p<0,001,), high level of anti-cyclic citrullinated peptide (anti-CCP) (χ^2=5,386; p=0,0203), higher levels of C-reactive protein (χ^2=8,159; p=0,0043), erythrocyte sedimentation rate (p<0,001), extra-articular manifestations of the disease (χ^2=7,354; p=0,0067).
Conclusion: PBEF1 can be regarded as an important link in the pathogenesis of rheumatoid arthritis and for the potential molecule for biological therapeutic agents.

REFERENCES

[1] Adiponectin determination in Rheumatoid Arthritis patients complicated by osteoporosis. L.Seewordova, J.Polyakova, B.Zavodovsky [et al]. Annals of the Rheumatic Diseases; 2016;Vol. 75, Suppl 2, p. 970. DOI: 10.1136/annrheumdis-2016-eular.1076
[2] Laboratory markers of inflammation and serum Nicotinamide phosphoribosyltransferase level in Rheumatoid Arthritis patients. Y.Akhverdyan, B. Zavodovsky, J.Polyakova [et al]. Annals of the Rheumatic Diseases, 2017; Vol. 76, Suppl 2, P.1149. DOI: 10.1136/annrheumdis-2017-eular.1958.
[3] Elevated Nesfatin-1 levels in patients with Rheumatoid arthritis/T.Kvlividze, B.Zavodovsky, Y.Akhverdyan [et al]//Annals of the Rheumatic Diseases 2018, Vol.77, P.A1762. DOI: 10.1136/annrheumdis-2018-eular.4459.
[4] Fetuin-a: clinical and laboratory associations in women with Rheumatoid Arthritis. Papichev E., Sivordova L., Polyakova J [et al.] Annals of the Rheumatic Diseases 2018; Vol.77; P.1228. DOI: 10.1136/annrheumdis-2018-eular.2111.

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AB0066 THE JAK INHIBITOR (BARICITINIB) INHIBITS IFNΓ-INDUCED GLIOSTATIN EXPRESSION IN HUMAN FIBROBLAST-LIKE SYNOVIOCYTES

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Background: The JAK/STAT signaling pathways mediate the production of many cytokines and growth factors related rheumatoid arthritis (RA) [1]. Baricitinib is a novel oral JAK inhibitor and it has demonstrated high efficacy in RA [2]. Gliostatin (GLS) is known to have angiogenic and arthritogenic activities. GLS was expressed in inflamed synovial tissues of patients with RA. In cultured fibroblast-like synoviocytes (FLSs), GLS expression was found to be up-regulated by inflammatory cytokines, such as IL-1β, TNFα [3]. GLS acted as a cytokine in FLSs, augmenting its own synthesis, and also induced the extracellular secretion of matrix metalloproteinase (MMP)-1, -3, -9, and -13 [4]. Therefore the suppression of GLS production might be an effective therapy in RA. The mechanism of the action of baricitinib had not been determined in fibroblast-like synoviocytes (FLSs).
Objectives: The purpose of this study was to investigate the GLS production effect of interferon (IFN) γ and the inhibitory action of baricitinib in FLSs derived from patients with RA (RA-FLSs).
Methods: RA-FLSs were cultured from synovial specimens of patients with RA and stimulated by IFNγ with or without treatment of baricitinib. The expression levels of GLS were determined using reverse transcription-polymerase chain reaction (RT-PCR), enzyme immunoassay and immunocytochemistry.
Results: In cultured RA-FLSs, GLS mRNA and protein were significantly induced by stimulation with IFNγ and these GLS inductions were significantly suppressed by treatment of baricitinib in dose-dependent manners.
Conclusion: Our data demonstrated that JAK/STAT activation play a pivotal role in IFNγ mediated GLS up-regulation in RA-FLSs. Suppression of GLS production in inflamed synovia has been suggested as one of the anti-inflammatory effects of baricitinib.

REFERENCES

[1] Kawaguchi Y, et al. The Janus kinase inhibitor tofacitinib inhibits TNF-α-induced gliostatin expression in rheumatoid fibroblast-like synoviocytes. Clin Exp Rheumatol. 2018;36:559-567.
[2] Vollenhoven R, et al. Safety and Efficacy of Baricitinib in Patients Receiving Conventional Synthetic Disease-Modifying Antirheumatic Drugs or Corticosteroids. Rheumatol Ther 2018; 5:525–536.
[3] Ikuta K, et al. The Sp1 transcription factor is essential for the expression of gliostatin/thymidine phosphorylase in rheumatoid fibroblast-like synoviocytes. Arthritis Research & Therapy 2012; 14:R87.
[4] Tatematsu N, et al. Mithramycin has inhibitory effects on gliostatin and matrix metalloproteinase expression induced by gliostatin in rheumatoid fibroblast-like synoviocytes. Mod Rheumatol. 2018;28:495-505.

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AB0067 ASSOCIATION BETWEEN INTERLEUKIN-6–174 G/C POLYMORPHISMS AND VASCULITIS: A META-ANALYSIS

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Background: Interleukin (IL)-6 is associated with the development and progression of vasculitis, and inhibitors of this cytokine are used to treat this disease. Polymorphisms of the promoter region of IL-6 are associated with the production and expression of IL-6.
Objectives: The aim of this study was to perform a meta-analysis of eligible studies to derive a precise estimate of the association between IL-6 polymorphisms and susceptibility to vasculitis.
Methods: A meta-analysis was conducted on the associations between IL-6-174 G/C and vasculitis. The literature was searched using the PubMed and Embase databases to identify available articles in which IL-6 polymorphisms were analyzed in vasculitis patients. The associations between the -174 G/C alleles and vasculitis were estimated by evaluating odds ratio (OR) and 95% confidence interval (CI). We performed meta-analyses using the 1) allelic contrast (C vs. G), 2) recessive (CC vs. GC+GG), and 3) dominant (CC+GC vs. GG) models, and 4) heterozygote vs. dominant homozygote (GC vs. GG), 5) heterozygote vs. recessive homozygote (GC vs. CC), and 6) homozygote comparison (CC vs. GG).
Results: A total of 13 studies involving 1,294 vasculitis patients and 1,594 controls were considered in the meta-analysis. There were significant associations between IL-6-174 G/C polymorphisms and vasculitis in allele contrast, dominant genetic model, and heterozygote vs. dominant homozygote comparison (OR 0.80, 95% CI 0.67–0.94, *P* =0.009 and OR 0.76, 95% CI 0.63–0.92, *P* =0.005, respectively). In subgroup analysis based on subtype, there were significant associations between IL-6 polymorphisms and susceptibility in large and medium vessel vasculitis, but not in small and variable vessel vasculitis.

Conclusion: The GC genotype of IL-6-174 G/C was suggested by the analyses to be related to low prevalence of vasculitis, especially for large and medium vessels.

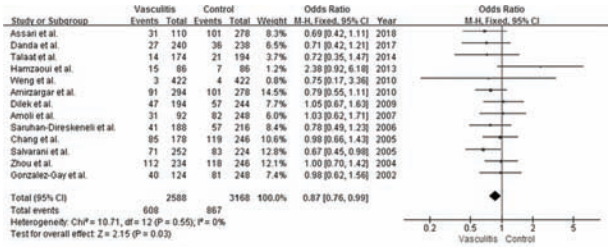


Figure 1. OR and 95% CI of individual studies and pooled data for the association between C allele of IL-6-174 and vasculitis in all study subjects.

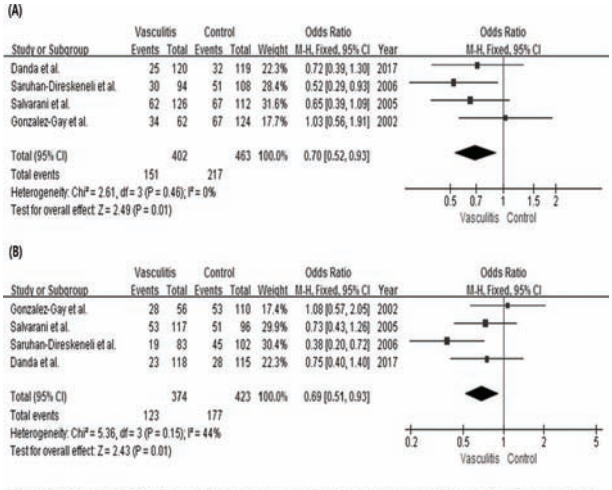


Figure 2. OR and 95% CI of individual studies and pooled data for the association between IL-6-174 G/C polymorphisms and large vessel vasculitis. **(A)** dominant model and **(B)** heterozygote vs. dominant homozygote comparison.

REFERENCES

[1] Assari R, Aghighi Y, Ziaee V, Sadr M, Rahmani F, Rezaei A, Sadr Z, Moradinejad MH, Raeeskarami SR, Rezaei N. (2018) Pro-inflammatory cytokine single nucleotide polymorphisms in Kawasaki disease. Int J Rheum Dis 21:1120-6.

[2] Berti A, Cavalli G, Campochiaro C, Guglielmi B, Baldissera E, Cappio S, Sabbadini MG, Doglioni C, Dagna L. (2015) Interleukin-6 in ANCA-associated vasculitis: Rationale for successful treatment with tocilizumab. Semin Arthritis Rheum 45:48-54.

[3] Salvarani C, Casali B, Farnetti E, Pipitone N, Nicoli D, Macchioni P, Cimino L, Bajocchi G, Catanoso MG, Boiardi L. (2005) Interleukin-6 promoter polymorphism at position -174 in giant cell arteritis. J Rheumatol 32:2173-7.

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AB0068 NOVEL ANTI-ANGIOGENIC EFFECTS OF TOFACITINIB IN FIBROBLAST-LIKE SYNOVIOCYTES DERIVED FROM PATIENTS WITH RA

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Background: Angiogenesis, which is the growth of new capillaries from pre-existing blood vessels, is an essential pathological feature of rheumatoid arthritis (RA). Gliostatin (GLS) is known to have angiogenic activity and thymidine phosphorylase activity. We have previously demonstrated that the production of GLS was enhanced by TNF-α and GLS induced vascular endothelial growth factor (VEGF) expression in fibroblast-like synoviocytes derived from patients with RA (RA-FLSs) [1]. The JAK/STAT signaling pathways mediate the effects of many cytokines and growth factors related RA. Tofacitinib is a novel oral JAK inhibitor and it has demonstrated high efficacy in RA, even in non-responder to anti-TNF treatment [2]. However it have been reported that RA-FLSs with the treatment of tofacitinib suppress the production of chemokines, IL-6 and granulocyte colony-stimulating factor [3, 4], the anti-angiogenic effects of tofacitinib remain to been elucidated.
Objectives: The purpose of this study was to investigate the suppression of angiogenic factors such as VEGF, tenascin-C (TNC) and GLS in RA-FLSs treated with tofacitinib.
Methods: RA-FLSs were stimulated by TNF-α with or without pre-treatment of tofacitinib. The expression levels of VEGF, TNC and GLS were determined using reverse transcription-polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay (ELISA).
Results: In cultured RA-FLSs, VEGF, TNC and GLS were significantly induced by stimulation with TNF-α alone and these inductions were significantly suppressed by treatment of tofacitinib in a dose-dependent manner.
Conclusion: These findings indicate tofacitinib inhibits the VEGF, TNC and GLS production through blockade of a JAK/STAT pathway. Tofacitinib may extinguish inflammatory synovitis through preventing excessive angiogenic factors in RA-FLSs.

REFERENCES

[1] Tanikawa T, et al. Gliostatin/thymidine phosphorylase-regulated vascular endothelial growth-factor production in human fibroblast-like synoviocytes. Rheumatol Int 2007; 27:553-559.

[2] Kawaguchi Y, et al. The Janus kinase inhibitor tofacitinib inhibits TNF-α-induced gliostatin expression in rheumatoid fibroblast-like synoviocytes. Clin Exp Rheumatol 2018;36:559-567.

[3] Migita K, et al. CP690,550 inhibits oncostatin M-induced JAK/STAT signaling pathway in rheumatoid synoviocytes. Arthritis Res Ther 2011;13:R72.

[4] Rosengren S, et al. The JAK inhibitor CP-690,550 (tofacitinib) inhibits TNF-induced chemokine expression in fibroblast-like synoviocytes: autocrine role of type I interferon. Ann Rheum Dis 2012;71:440-447.

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AB0069 THE DOWNSTREAM EFFECT OF ADALIMUMAB INVOLVES INHIBITION OF SYNOVIAL CXCL SUBFAMILY CHEMOKINE EXPRESSION

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Background: The many different disease modifying anti-rheumatic drugs used for the treatment of immune mediated inflammatory arthritis have very distinctive modes of action. However, the downstream effects of the different drugs are not completely understood. As more treatment options become available detailed knowledge about the different drugs will be important in the future when planning treatment strategies. Adalimumab is a fully humanized monoclonal antibody against tumor necrosis factor-alpha (TNFα). Earlier studies have found that TNFα inhibitors can decrease the production of interleukin 1 (IL-1), IL-6, IL-8 (aka CXC motif chemokine 8 (CXCL8)), monocyte chemotactic protein 1 (MCP-1) and granulocyte-macrophage colony-stimulating factor (GM-CSF).[1] However, these studies have been limited to the measurement of a subset of predefined downstream signaling molecules.
Objectives: The aim of this study was to make an unbiased investigation of downstream effects of adalimumab on production of a wide range of cytokines, chemokines and growth factors by synovial fluid mononuclear cells (SFMCs).
Methods: SFMCs were obtained from a study population consisting of patients with active RA or peripheral SpA with at least one swollen joint (for obtaining synovial fluid) (n=14). SFMCs were cultured for 48 hours with and without addition of adalimumab 5 µg/ml measuring the secretion of 96 cytokines, chemokines and growth factors by an Olink proseek multiplex panel.
Results: In SFMCs cultured for 48 hours, adalimumab decreased the production of IL-8 (CXCL8) (P=0.0001), CXC motif chemokine 5 (CXCL5) (P=0.0003), CXCL9 (P=0.03) and CXCL10 (P=0.03), and monocyte chemotactic protein 2 (MCP-2) (P=0.04) and increased the production of hepatocyte growth factor (HGF) (P=0.008) and tumor necrosis factor-like weak inducer of apoptosis (TWEAK) (P=0.03) after Bonferroni correction (all corrected P values). In this unbiased analysis, adalimumab did not change the production of several other

cytokines and chemokines including IL-12B (P=0.07), IL-6 (P=0.07), IL-10 (P=0.12), IL-18 (P=0.19), and IL-4 (P=0.63).
Conclusion: This study illuminates the downstream effects of neutralizing TNFα not previously investigated. Adalimumab had a pronounced effect on downregulation of the inflammatory CXCL subfamily chemokines IL-8, CXCL5, CXCL9, and CXCL10. This helps explain findings of diminished inflammatory cell migration into joints seen in the first trials with TNFα inhibitors and could be an important mechanism of action of TNFα inhibitors.[2] Further characterization of downstream effects of the multiple DMARDs used for the treatment of immune mediated inflammatory arthritis will help guide treatment strategies for these patients.

REFERENCES

[1] Brennan FM, Chantry D, Jackson A, Maini R, Feldmann M. Inhibitory effect of TNF alpha antibodies on synovial cell interleukin-1 production in rheumatoid arthritis. Lancet 1989;2:244–7.
[2] Taylor PC, Peters AM, Paleolog E, Chapman PT, Elliott MJ, McCloskey R, et al. Reduction of chemokine levels and leukocyte traffic to joints by tumor necrosis factor alpha blockade in patients with rheumatoid arthritis. Arthritis Rheum. 2000;43:38–47.

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AB0070 THE RELATIONSHIP BETWEEN THE LEVEL OF NESFATIN-1 AND THE CLINICAL MANIFESTATIONS OF RHEUMATOID ARTHRITIS

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Background: Nesfatin-1 is actively studied in the pathogenesis of metabolic disorders. An excess of this factor in the brain leads to loss of appetite, a feeling of fullness, as well as a decrease in body weight. Similarly, elevated levels of nesfatin are associated with depressive disorders [1]. We studied the level of nesfatin in the serum of patients with rheumatoid arthritis (RA) and found a relationship with systemic inflammation and functional impairment [2].
Objectives: To study the relationship of serum nesfatin-1 levels with the clinical manifestations of RA.
Methods: To identify the relationship between serum nesfatin-1 and the clinical manifestations of rheumatoid arthritis, all patients were divided into 2 groups. The first group - 1 (66 patients) with elevated serum nesfatin (> 37.95 ng/ml). The second group - 2 (44 patients) - with normal values (<37.95ng/ml). In both groups, we studied the clinical manifestations of RA.
Results: A high level of nesfatin in RA patients was typical for patients with a higher degree of activity in DAS28 ($\chi 2 = 8.37$; $p = 0.04$), seropositivity for the rheumatoid factor (RF) - ($\chi 2 = 5.53$; $p = 0, 02$), the duration of the disease is more than 10 years ($\chi 2 = 9.53$; $p = 0.01$). At the same time, there was no significant correlation between the level of nesfatin and the extra-articular manifestations of RA ($\chi 2 = 2.09$; $p = 0.14$) and the degree of radiological damage to the joints ($\chi 2 = 4.45$; $p = 0.21$).
Conclusion: This study shows that serum Nesfatin-1 levels are significantly higher in patients with more unfavorable RA, than in RA with minimal clinical manifestations. These data confirm the pathogenetic role of Nesfatin-1 in the development of clinical manifestations associated primarily with RA activity, but to a lesser extent with organ lesions in RA. The relationship of the level of nesfatin with the duration of the disease is of particular interest, since there is no correlation with the degree of X-ray damage to the joints and organ damage. There are literary data on the relationship of depression and late stage of RA [3].

REFERENCES

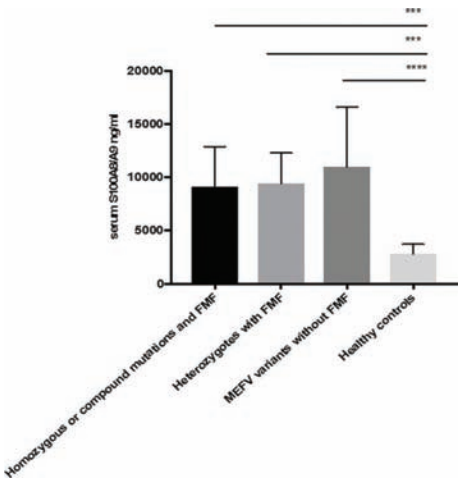
[1] Role of nesfatin-1 in anxiety, depression and the response to stress/Weibert E, Hofmann T, Stengel A//Psychoneuroendocrinology. 2018; 29;100:58-66. doi: 10.1016/j.psyneuen.2018.09.037.
[2] Elevated Nesfatin-1 levels in patients with Rheumatoid Arthritis/T.Z. Kvlividze, B.V. Zavodovsky, Y.R. Akhverdyan, L.E. Sivordova, Y.V. Polyakova, D.P. Lavrova, A.T. Yakovlev//Ann Rheum Dis, V.77, Suppl, 2018, P. A1762
[3] Waheed A., Hameed K., Khan A.M. et al. The burden of anxiety and depression among patients with chronic rheumatologic disorders at a tertiary care hospital clinic in Karachi, Pakistan//J Pak Med Assoc 2006; 56: 243–7.

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AB0071 SERUM S100A8/A9 (CALPROTECTIN) IN FAMILIAL MEDITERRANEAN FEVER DOES NOT CORRELATE WITH DISEASE ACTIVITY

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Background: Familial Mediterranean Fever (FMF) is caused by mutations in MEFV. The protein product pyrin is expressed in monocytes, neutrophils and eosinophils. Acute inflammatory attacks are accompanied by a dramatic hepatic acute phase response. S100A8/A9 is damage associated molecular pattern and a TLR4 ligand expressed in neutrophils, monocytes and early infiltrating macrophages. We aimed to investigate S100A8/A9 in 39 patients with FMF, 45 healthy carriers and wild type controls.
Objectives: To measure S100A8/9 in patients with FMF, carriers and healthy controls.
Methods: All patients were genotyped. Patients and healthy controls (HC) serum S100A8/A9 levels, cell surface expression on monocytes and neutrophils as well as intracellular peripheral blood mononuclear cells (PBMC) expression were measured by flow cytometry (FACS). CD14 cells were isolated and following overnight incubation with or without LPS, S100A8/A9 was measured in the supernatants by ELISA. Patient and HC monocyte apoptosis was compared.
Results: Serum levels were measures in 84 samples from 31 patients with homozygous or compound mutations (median 9061ng/ml [range 500-38470], 79 samples from 39 symptomatic patients who were MEFV heterozygotes (median 9394ng/ml [range 1744-38119], 80 samples from 45 individuals with MEFV variants but without clinical features of FMF (median 10939ng/ml [range 2447->40000]. There was no difference in calprotectin concentrations between the different mutations. All the groups described had significantly higher levels than healthy controls (n=16 median 2836ng/ml [range 1058-6175])($p<0.001$).Minimal monocyte and neutrophil cell surface expression was detectable. Following LPS stimulation there was significantly more S100A8/A9 detected in the supernatants in patients than healthy control CD14. There was also a trend to an increased intracellular monocyte S100A8/A9 expression.



Conclusion: Patients with pyrin mutations both with and without clinical disease have greatly elevated serum S100A8/A9 levels without detectable cell surface expression in well-controlled disease with a trend to an increased monocyte intracellular expression. Upon monocyte stimulation with LPS, increased S100A8/A9 is secreted. The exact mechanism by which these patients, especially those with mutations but no clinical disease, demonstrate sustained elevated serum S100A8/A9 remains to be elucidated but does not appear to result in a significant clinical sequelae.
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AB0072 BIOMARKER CHANGES FOR PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOFACITINIB WITH METHOTREXATE OR GLUCOCORTICOIDS VS TOFACITINIB MONOTHERAPY

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Herpes zoster is more common in patients (pts) with RA vs the general population.[1] This risk increases with tofacitinib use[2] and appears to be further increased with concomitant use of csDMARDs such as methotrexate (MTX), or glucocorticoids (GC).[3] The mechanism for these increases in risk may be linked to treatment-induced interferon (IFN) suppression,[3] given that replication of the varicella zoster virus appears to be limited by IFN activity.[4]
Objectives: To evaluate whether treatment of RA with tofacitinib + MTX or GC suppresses IFN pathway proteins to a greater extent than treatment with tofacitinib monotherapy.
Methods: This was a post hoc analysis of pooled data from 1 Phase (P)2 (Japan study [NCT00687193]) and 2 P3 (ORAL Scan [NCT00847613]; ORAL Start [NCT01039688]) tofacitinib studies. Serum samples were collected at baseline (BL), Week (W)12 and/or W24 from pts with RA treated with tofacitinib 5 or 10 mg BID, given as monotherapy (Japan study; ORAL Start) or with stable doses of MTX (15–25 mg weekly for ≥6 weeks; ORAL Scan) and/or GC (≤10 mg/day prednisone or equivalent; all studies). A total of 376 proteins associated with cellular and inflammatory processes, including 6 IFN pathway proteins (CXCL10, CXCL9, CXCL11, IL-12, IFNγ and IL-20), were measured using a homogeneous solution-based assay (Olink Proseek® Multiplex Assay, Uppsala, Sweden). Changes in protein levels from BL to W12 (Japan study, ORAL Scan) and/or W24 (ORAL Scan, ORAL Start) were compared for tofacitinib monotherapy vs tofacitinib + MTX or GC using linear regression models. The dependent variable was change from BL in protein levels at W12 or W24. The independent variable was MTX or GC status. Age, gender, GC status (in MTX model) and BL protein levels and tofacitinib dose were covariates. Regressions were performed separately for each study; results for GC were combined via meta-analysis using fixed and random effect models. Significance was considered at $p<0.1$ after controlling for false discovery rate (FDR). Data quality control included accounting for plate/batch defects and limits of detection, and removal of sample/analytes with excessive missing data.
Results: In total, 659 serum samples were collected from 321 pts. Of the 6 IFN pathway proteins, 2 (IFNγ and IL-20) were below the limit of detection. There was no strong evidence suggesting statistical differences between tofacitinib monotherapy and tofacitinib + MTX or GC in changes in levels of the 4 detectable IFN pathway proteins (CXCL10, CXCL9, CXCL11 and IL-12) from BL to W12 and/or W24. Significant differences were observed for 2 of the 370 other proteins: MMP-1 (FDR adjusted p=0.08) and IL1Ra (FDR adjusted p=0.09), where levels decreased from BL to W12 for tofacitinib + MTX to a greater extent than for tofacitinib monotherapy.
Conclusion: The results of this post hoc analysis suggest that tofacitinib + MTX or GC may not suppress circulating serum levels of IFN pathway proteins to a greater extent than tofacitinib monotherapy. Although there were differences at W12 for tofacitinib + MTX vs tofacitinib monotherapy in MMP-1 and IL1Ra, it is not yet clear whether these observations may be attributable to differences in the ethnicities of the study populations receiving these two treatment regimens (global vs Japan). Further analyses of biomarker changes with tofacitinib are ongoing.

REFERENCES

[1] McDonald JR, et al. Clin Infect Dis 2009; 48: 1364-71.
[2] Winthrop KL, et al. Arthritis Rheumatol 2014; 66: 2675-84.
[3] Winthrop KL, et al. Arthritis Rheumatol 2017; 69: 1960-8.
[4] Ku CC, et al. Cell Biosc 2016; 6: 21.

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AB0073 RELATIONSHIPS BETWEEN CYTOKINE PROFILES AND TH17/TREG BALANCE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune inflammatory disease. Cytokines serve as the mediators of cellular differentiation, inflammation, immune pathology, and regulation of immune response in this disease. [1] A previous study demonstrated that the imbalance between Th17 and Treg cells is an important mechanism which may lead to RA. [2] However, the effect of cytokines on the balance of Th17/Treg cells in patients with RA remains unknown.
Objectives: To investigate the relationships between various cytokine levels and Th17/Treg balance in patients with RA.
Methods: The study include75 RA patients, meeting the diagnostic classification criteria for RA revised by ACR in 1987 and with DAS28 scores were greater than 2.6, and 75 health controls. The absolute numbers of lymphocyte cell subsets and T subsets in peripheral blood were measured by Flow Cytometer (FCM). Serum levels of the following 6 cytokines were determined in the same samples using a cytometric beads array: Interleukin-2(IL-2), Interleukin-4(IL-4), Interleukin-6(IL-6), Interleukin-10(IL-10), Interferon-γ(INF-γ) and Tumor necrosis factor-α(TNF-α) for all RA patients.
Results: (1) Compared with healthy controls, the absolute counts of B cells (P=0.042), the absolute counts of Th1 cells (P=0.031) and the ratio of Th1/Th2 (P=0.000) are significantly increased in RA patients. In contrast, the absolute counts of NK cells (P=0.032) and the absolute count of Th2 cells (P=0.000) were significantly decreased in the RA patient. (Figure1) (2) There was no significant difference in the absolute number of Th17 cells between the two groups, but absolute counts of Treg cells are significantly decreased in RA patients, the ratio of Th17/Treg also have obvious difference, which was higher in RA patients. (Figure1) (3) Among 75 RA patients, two cytokines were significantly associated with the ratio of Th17/Treg, IL-4 (r=0.264, P=0.023) and TNF-α (r=0.270, P=0.020), while other cytokines have no correlation. (Figure2)
Conclusion: Rheumatoid arthritis (RA) is a chronic disease involving various immune cells, our research show that decreased NK cells, Th2 cells and Treg cells; increased B cells, Th1 cells and the ratio of Th17/Treg may be key pathophysiological features in patients with RA. Meanwhile, the level of serum IL-4 and TNF-α may influence the ratio of Th17/Treg, that means we can maintain the patient's Th17/Treg immune balance by regulating the levels of such cytokines. Further researches are needed to elucidate the possible mechanisms with this phenomenon.

REFERENCES

[1] Astry, B.; Harberts, E.; Moudgil, K.D. A cytokine-centric view of the pathogenesis and treatment of autoimmune arthritis. J. Interferon Cytokine Res. 2011, 31, 927–940.
[2] Liu J, Hong X, Lin D, et al. Artesunate influences Th17/Treg lymphocyte balance by modulating Treg apoptosis and Th17 proliferation in a murine model of rheumatoid arthritis[J]. Experimental and Therapeutic Medicine, 2017.13(5):2267-2273.

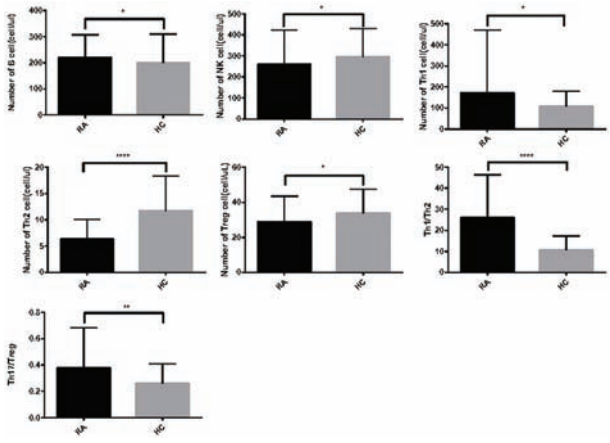


Figure 1. The absolute number of B cell, NK cell, Th1 cell, Th2 cell, Treg cell in RA patients and health controls, Data are expressed as means ±SD.

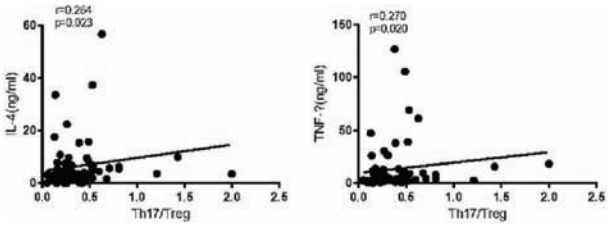


Figure 2. Correlation of the serum levels of IL-4 and TNF- α with the ratio of Th17/Treg.

Disclosure of Interests: None declared
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AB0074 INTERRELATIONSHIP BETWEEN NICOTINIC ACETYLCHOLINE RECEPTOR AND CYTOKINE PRODUCTION NOTED FOLLOWING T-CELL ANTIGEN RECOGNITION AND ACTIVATION

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Background: T cells express muscarinic and nicotinic acetylcholine receptors (mAChRs, nAChRs) that increase intracellular Ca^{2+} [1] on stimulation. The expression of these receptors on macrophages and their activation by vagal stimulation has recently been the focus for novel arthritis treatment [2].
Objectives: Our aim in the present study was to assess the effect of various peptides, on cytokine production and nAChRs inhibition.
Methods: nAChR heterologous subunits were expressed in *Xenopus* oocytes and the inhibitory activity of various peptides at ACh-evoked currents were assessed. The effect of these peptides on T-cell antigen recognition and subsequent cytokine production was assessed using an antigen presentation assay (APA). Briefly, the 2B4.11 murine T cell hybridoma recognizing cytochrome c as the antigen was co-cultured with the antigen presenting B cell hybridoma line LK35.2 (I-Ek bearing) and pigeon cytochrome c in the absence or presence of peptide or several nAChRs antagonists, including mecamylamine (broad nAChR antagonist), waglerin-1 (α1β1εδ), α-bungarotoxin (α7), RgIA (α9α10), Vc1.1 (α9α10) and dihydro-β-erythroidine hydrobromide (α4β4 and α4β2). ELISA and real-time PCR were performed to measure cytokine protein levels and nAChRs T-cells mRNA express levels separately.
Results: At 10μM, peptide W32052 had modest 50-55 % inhibition of human (h) α3β2 and hα4β2 nAChR subtypes, and 35% inhibition at hα9α10. W32052 greatly inhibited chimeric rat α1β1δ-mouse ε (85%) at 10μM. W32052 also inhibited IL-2, IL-6, TNF-α and GM-CSF production at 50μM in the APA. nAChRs antagonists, mecamylamine (100μM), RgIA (10nM), Vc1.1 (17.5μM) and dihydro-β-erythroidine hydrobromide (10μM) could decrease IL-2 production. However, waglerin-1 and α-bungarotoxin did not affect IL-2 production in the APA.
Conclusion: W32052, an antagonist of nAChR, inhibits cytokine production following antigen recognition suggesting that there is a close link between T-cell antigen activation, ion channel regulation mediated by AChR and cytokine production. Further experiments are in progress.

REFERENCES

[1] Masato M, Yukari I, Takeshi FJ, et al. Acetylcholine released from T cells regulates intracellular Ca2+, IL-2 secretion and T cell proliferation through nicotinic acetylcholine receptor, Life Science, 2017, 172: 13-18.
[2] Koopman FA, Chavan SS, Tak PP, et al. Vagus nerve stimulation inhibits cytokine production and attenuates disease severity in rheumatoid arthritis, PNAS, 2016, 113(29):8248-9.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3856

AB0075 EFFECT OF SIDAGURI EXTRACT (SIDA RHOMBIFOLIA L) ON URINARY CARBOXY-TERMINAL TELEPEPTIDES OF TYPE II COLLAGEN IN OSTEOARTHRITIC PATIENTS

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Background: Osteoarthritis is one of the most common joint diseases in Indonesia and elsewhere. Assessment of the effectiveness of osteoarthritis therapy with biomarkers should be developed. One of the biomarker that can be used to assess the activity of osteoarthritis is *Urinary Carboxy-Terminal Telepeptides of Type II Collagen*. Indonesia is the center of world biodiversity, and Sidaguri is one of the traditional plants that is believed to have many benefits including its anti-inflammatory effect and the ability to decrease level of uric acid. The β-sitosterol is an active component in Sidaguri that has anti-inflammatory activity in osteoarthritis.
Objectives: To compare the effect of sidaguri and meloxicam therapy with meloxicam alone in decreasing the levels of urinary Carboxy-Terminal Telepeptides Of Type II Collagen in osteoarthritis patients.
Methods: This study was conducted on 24 patients with osteoarthritis at H. Adam Malik General Hospital Medan from April to June 2018. Subjects were divided into 2 groups, namely placebo and Sidaguri group. Levels of uCTX II were assessed before and after intervention. T- test was used to analyze the data using SPSS version 22.
Results: 83.3% of osteoarthritis patients in H. Adam Malik hospital who participated in this study were women with mean age 60.58 ± 9.74 years in the placebo group and 63.08 ± 6.14 years in the sidaguri group. The results showed that subjects receiving Sidaguri showed significant decrease in uCTX II before and after intervention (521.42 ± 369.99 vs 330.75 ± 163.49 ng/mmol, p = 0.033). Meanwhile, in the placebo group also found decreased levels of uCTX II but it was not statistically significant (286.17 ± 163.82 vs. 218.25 ± 75.05 ng/mmol, p = 0.238). In addition, there was a significant difference between the mean of the two groups after the intervention (p = 0.046).
Conclusion: There was a significant decrease in uCTX II levels in osteoarthritis patients who received Sidaguri extract for 30 days compared to the placebo group.

REFERENCES

[1] Aigner, T, et al. 2015. Pathogenesis and Pathology of Osteoarthritis. In : Hochberg. M, Silman. A, Smolen. J, Weinblat. M, Weisman. M, editors. Rheumatology. 6th ed. Philadelphia : Elsevier; p. 1462-1476.
[2] Alpiansyah, A. 2015. Antihyperuricemia Potential of *Sida rhombifolia* L. as a Treatment for Gout. Journal Majority. Vol. 4 (3):9-13.
[3] Davies NM., Skjodt NM,. 1999. Clinical Pharmakinetics of Meloxicam. Clin Pharmacokinet Feb;36(2):115-126.
[4] Gupta MB, et al. 1980. Anti-inflammatory and antipyretic activities of beta-sitosterol. Planta Med. 1980 Jun;39(2):157-63
[5] Marpaung, B. 2010. Penggunaan Petanda Biokimia Asam Hialuronat Serum Dan CTX-II Urin Terhadap Penilaian Hasil Pengobatan Osteoartritis Lutut. Medan : University of Sumatera Utara Institutional Repository

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3977

AB0076 CAN DIFFERENT INTERLEUKIN LEVELS PREDICT RESPONSE TO BIOLOGICAL TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS?

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Background: The cytokine family interleukin IL-17 has an important pro-inflammatory role; stimulating tumour necrosis factor (TNF), interleukin IL-1 and IL-6 production. It is subclassified into IL-17A, IL-17F and IL-17AF[1]. The interleukin IL-10 acts by blocking the secretion of pro-inflammatory cytokines[2]. We hypothesised that patients whose disease activity is not adequately controlled by TNF therapies in Rheumatoid Arthritis (RA) may have IL-17 driven disease and that lower IL-10 levels may play a permissive role.
Objectives: To determine if pre-treatment or 3 month IL-17/IL-10 concentrations correlate with treatment response to anti-TNF drugs by 6 months of treatment.
Methods: Data was collected from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS). Patients were followed up at pre-treatment (baseline), 3 months, 6 months and 12 months with bloods, questionnaires and clinical data obtained. Patients were eligible for inclusion if commencing on adalimumab or etanercept and were designated good or poor EULAR responder status at 6-months. Wilcoxon rank sum compared interleukin levels at pre-treatment and 3 months- according to EULAR classification by 6 months. Logistic regression was carried out adjusting for gender, baseline DMARD use and disease activity scores (DAS-28).

Results: 152 patients were included, (80 adalimumab-treated and 72 etanercept-treated). No statistically significant difference between mean IL-17A, IL-17AF, IL-17F and IL-10 levels at baseline and 3 month follow-up were observed(figure 1). For IL-17A, those patients classified as good responders demonstrated an increase in mean serum levels of IL-17A from 1.06 pg/ml at baseline to 1.23pg/ml at 3 months. This came close to significance (p=0.07). Further analysis was carried out by drug group and also a subgroup analysis by drug group linked to responder status. No statistically significant results were obtained. Adjusting for gender, baseline DMARD use and DAS-28 scores did not alter findings.

Interleukin levels (pg/ml)	All Patients (n=152)	P-values	Good Responders (n =86)	P-values	Poor Responders (n= 66)	P=-values
Baseline IL-17A	1.16	-	1.06	-	1.29	-
3 month IL-17A	1.21	*(p = 0.76)*	1.23	*(p= 0.07)*	1.19	*(p = 0.49)*
Baseline IL-17AF	21.51	-	16.40	-	28.32	-
3 month IL-17AF	30.98	*(p = 0.57)*	21.89	*(p = 0.58)*	42.43	*(p =0.81)*
Baseline IL-17F	1.97	-	2.50	-	1.28	-
3 month IL-17F	1.59	*(p = 0.66)*	1.41	*(p = 0.89)*	1.81	*(p=0.42)*
Baseline IL-10	9.26	-	8.41	-	10.38	-
3 month IL10	10.52	*(p = 0.93)*	11.49	*(p = 0.59)*	9.33	*(p 0.42)*

Figure 1. Mean interleukin levels at pre-treatment and 3 months

Conclusion: There was a lack of statistically significant data to suggestion a correlation between pre-treatment and 3 month IL-17F, IL-17AF and IL-10 concentrations. However, an increase in IL17-A serum levels between baseline and 3 months may be associated with a good EULAR response status by 6 months. Larger sample sizes are required to confirm this.

REFERENCES

[1] Gaffen SL. Curr Rheumatol Rep 2009; 11(5): 365-370.
[2] Alanara T. Scand J of Rheumatol 2010; 39: 118-126

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AB0077 SERUM IL17 CORRELATED WITH INFLAMMATORY CHANGES BUT NOT WITH BONY CHANGES IN BOTH HAND OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

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Background: previous studies showed that serum IL17 is correlated with disease activity in both osteoarthritis and rheumatoid arthritis which may have therapeutic reflections (1,2). Taking in consideration that OA has different pathogenesis and presentations in comparison with RA; it is not known what the source of high serum level of IL17 in both diseases is?
Objectives: To evaluate the association of IL17 serum level with musculoskeletal ultrasound (MSK US) findings and clinical disease activity in Rheumatoid Arthritis (RA) and hand Osteoarthritis (OA) patients.
Methods: It is a randomized controlled clinical trial, which was done in the period between June 2017 and June 2018. The total number of the included subjects was 120 in 3 equal groups (RA, OA and control). All subject was subjected to serum IL17 level measurement. MSK US (of both wrists, MCPs, PIPs and DIPs) was done to all patients in RA and OA groups to. Disease activity was measured by disease activity score (DAS28) for RA patients. Visual analogue scale for pain (VAS) was obtained from patients in RA and OA groups. Functional assessment was done using health assessment questionnaire (HAQ) for RA patients and the Australian/Canadian (AUSCAN) Osteoarthritis Hand Index for OA patients
Results: Serum levels of IL17 were significantly higher (p<0.0001) in both RA group and OA (141.37±51.09 and 151.69±23.13) group in comparison to control group (32.46±20.71).
The serum level of IL17 was correlated with disease activity parameters (DAS28 & VAS for RA and VAS for OA) both RA and OA groups. As regards ultrasonographic findings, serum IL17 levels were correlated with the presence of synovitis in both RA and OA groups. Ultrasonographic detected bony changes (erosions and osteophytes) were not correlated with serum level of IL17 in neither RA nor OA group. As regards functional assessment, serum level of IL17 was correlated with HAQ in RA group but not correlated with AUSCAN in OA group.
Conclusion: Serum level of IL17 was correlated with inflammatory changes detected by US and not correlated with bonny changes (erosions and osteophytes). According to the results of this study, the inflammatory process is the source of increased level of IL17in OA and RA.

REFERENCES

[1] PLoS One. 2017; 12(6): e0178879.
[2] Ther Adv Musculoskelet Dis. 2013 Apr; 5(2): 77–94.

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DOI: 10.1136/annrheumdis-2019-eular.2253

AB0078 THE THERAPEUTIC EFFECT OF GPNMB IN A TRAUMATICALLY-INDUCED OSTEOARTHRITIC MODEL

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Background: Osteoarthritis is a severe joint disease that affects millions of people. At this time, the current treatment for osteoarthritis is total joint reconstruction surgery. GPNMB plays a key role in bone remodeling and bone growth. Data from our lab suggested that GPNMB is positive regulator of osteoblastogenesis and a negative regulator of osteoclastogenesis.
Objectives: The role of GPNMB in cartilage has not been investigated before. In this study we examined the therepaeutic effects of GPNMB on damaged cartilage using post-traumatic osteoarthritic mouse model.
Methods: The destabilization of the medial meniscus (DMM) surgery in mice has been found to be an excellent model for studying post-traumatic osteoarthritis. We performed the DMM surgery on 21 C57/BL6 mice. These mice were divided into three intra-articular injection treatment groups consisting of a control, low dose GPNMB, and high dose GPNMB. These mice were divided into three intra-articular injection treatment groups consisting of a control, low dose GPNMB, and high dose GPNMB. Moderate to severe osteoarthritis develops around six to eight weeks with this model.
Results: Here we present that damaged human cartilage has significantly higher levels of GPNMB compared to undamaged cartilage. In addition, human osteoarthritic chondrocytes treated with GPNMB showed a protective response to inflammation induced by IL1-beta. In this study, we examined whether recombinant GPNMB has an anti-inflammatory effect in a model of post-traumatic osteoarthritis. Based on studies performed in our lab, we expected cartilage degeneration to be dramatically decreased in response to the therapeutic effects of GPNMB. A protective factor against osteoarthritis progression, GPNMB-injected mice had significantly reduced cartilage damage and OARSI scores in comparison to the control group, proving GPNMB a promising therapy in lieu of total joint reconstruction. GPNMB-injected mice also had reduced expression of IL-6 and MMP13 but significantly increased expression of aggrecan in comparison to control mice.
Conclusion: Our data clearly showed that GPNMB has therapeutics anti-inflammatory effects on protecting cartilage damaged. Hence, future studies will be directed towards examining the therapeutic effects of GPNMB on larger animal models for osteoarthritis. Given the remarkable ability of GPNMB to reduce expression of key inflammatory markers, we conducted this study to reveal GPNMB therapeutic effects in traumatically-induced osteoarthritis.

REFERENCES

[1] The surgical destabilization of the medial meniscus (DMM) model of osteoarthritis in the 129/SvEv mouse. Methods in Molecular Biology: Osteoporosis and Osteoarthritis. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: A disease of the joint as an organ. Arthritis and Rheumatism. 2012. pp. 1697–1707.
[2] Zhou, L., Zhuo, H., Ouyang, H., Liu, Y., Yuan, F., Sun, L.,. .. & Liu, H. (2017). Glycoprotein non-metastatic melanoma protein b (Gpnmb) is highly expressed in macrophages of acute injured kidney and promotes M2 macrophages polarization. Cellular immunology, 316, 53-60.
[3] Ripoll, V.M., et al., Gpnmb is induced in macrophages by IFN-gamma and lipopolysaccharide and acts as a feedback regulator of proinflammatory responses. J Immunol, 2007. 178(10): p. 655766.
[4] Karlsson C, Dehne T, Lindahl A, Brittberg M, Pruss A, Sittinger M, Ringe J. Genome-wide expression profiling reveals new candidate genes associated with osteoarthritis. Osteoarthritis and Cartilage. 2010 Apr 1;18(4):581-92.

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AB0079 **EFFECT OF HYALURONIC ACIDLOCAL INJECTIONS ON ACHILLES TENDINOPATHIES: AN OBSERVATIONAL STUDY ON TENDON VISCOELASTIC PROPERTIES AND THEIR RELATIONSHIPS WITH CLINICAL OUTCOMES**

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Background: Effect of hyaluronic acid local injections on Achilles tendinopathies: an observational study on tendon viscoelastic properties and their relationships with clinical outcomes.
Objectives: Achilles tendinopathy (AT) affects athletes, recreational exercisers and also inactive people, where it is sometimes associated with arthritic phenotypes. The aim of this study was to evaluate the efficacy of a three-local injections regimen of hyaluronic acid (HA) in middle aged patients with a diagnosis of AT; the relationships of the functional, biochemical and clinical outcomes with the viscoelastic properties of the tendon were also studied
Methods: 8 patients previously diagnosed for monolateral AT were enrolled. AT was confirmed before the first local HA injection (T0) by clinical examination, MRI and thermography. At T0 patients were assessed for maximal voluntary isometric contraction (MVI) involving Achilles tendon (both injured and healthy), and pain level with a Likert scale; Achilles tendon viscoelastic state, i.e. tone and stiffness, were then measured at relaxed state and at 10% of MVI with MyotonPro (Myoton Ltd, UK). Finally patients received the first HA injection (RegenFlex T&M, a blend of 2 to 1000 KDa HA, Regenyal, IT). All the measurements were repeated at T1 (15 days after the first injections and immediately prior the second), at T2 (15 days after the second injection and prior the third) and at T3 (15 days after the third injection), i.e. over a total of 45 days in which clinical visits were also performed. Furthermore, before each injection, injured tendon exudates were collected by needle aspiration and the levels of IL-1β and matrix metalloprotease 3 (MMP-3) were determined with an ELISA test.
Results: At T0, pain score and MVI were significantly higher and lower in injured tendons, respectively. Accordingly, tone and stiffness values were significantly different between injured and contralateral tendons, especially when measured at the relaxed state. Interestingly, the above differences gradually disappeared at T1, 2 and 3. In keeping with these results, tendon exudates volumes also decreased over time, as well as the levels of IL-1β and MMP-3.
Conclusion: RegenFlex T&M promoted a progressive healing of AT, with recovery of clinical, functional and tendon's viscoelastic state.

REFERENCES

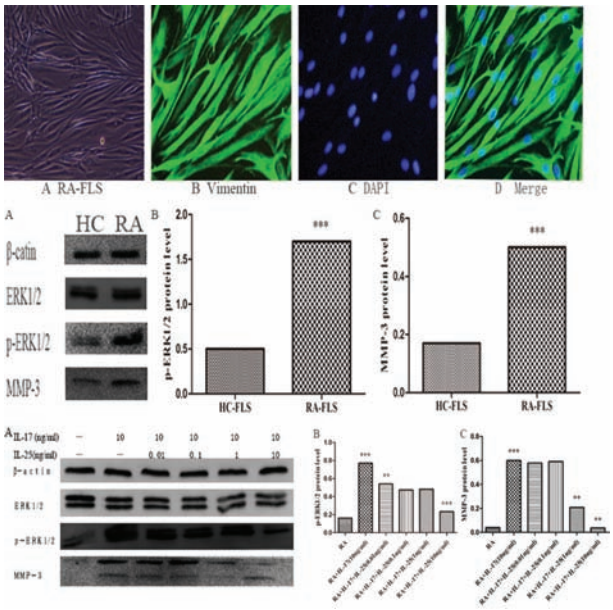
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AB0080 **THE INHIBITION OF IL-25 TO THE EFFECT OF IL-17 TO ERK1/2 AND MMP–3 IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIALCYTES**

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Background: Rheumatoid arthritis (RA) is a common chronic systemic autoimmune diseases characterized by the inflammation in joint and synovium. Synovitis leads to the destruction of cartilage and bone in joint subsequently joint dysfunction and even disability eventually.Recently, IL-25 has been found to play a role in regulating inflammation through Th1 and Th17 responses in inflammatory diseases[3], However, the function to fibroblast-like synoviocytes and its signaling pathway are not clear. This study aims to probe the effects of IL-25 on the expression of ERK1/2 and MMP-3 in RA fibroblast-like synoviocytes.
Objectives: To study the function of IL - 25 for rheumatoid arthritis (RA) fibroblast - like synoviocytes(FLS) differentiation as well as to the effects on the expression of extracellular regulating protein kinase (ERK) and matrix metalloproteinases-3 (MMP-3).
Methods: The differences on ERK1/2 and MMP-3 protein levels were tested in RA-FLS and healthy controls, then IL-17A (10ng/ml), different concentrations of IL-25 (0.01, 0.1, 1 and 10ng/ml) and IL-17A(10ng/ml) to co-stimulate the RA-FLS for 24 hours respectively.The expression of ERK1/2 and MMP-3 protein were detected by the Wesern blot. The results were expressed by ±*s*, *t* test was used for the comparison between different groups.
Results: The expression of ERK1/2 (1.71±0.17) and MMP-3 (0.50±0.13) proteins in RA-FLS was higher than the healthy controls (0.50±0.15, 0.17±0.05)(t=-9.13,P<0.001and t=-4.10,P<0.05), because of the stimulation of IL-17A, the expression of ERK1/2 (0.77±0.22) and MMP-3 (0.59±0.13) proteins in RA-FLS were increased compared with untreated groups (0.18±0.35, 0.04±0.03)(t=-4.69,P<0.01 and t=-7.47,P<0.01).with the increasion of the concentration on IL-25, the level of ERK1/2 (0.54±0.26, 0.48±0.18, 0.48±0.23, 0.23±0.06)and MMP-3 (0.58±0.09, 0.59±0.14, 0.21±0.04, 0.04±0.02)in RA-FLS which stimulated by IL-17A was decreased slowly (t=4.22,P<0.05 and t=4.95,P<0.01 and t=7.47, P<0.01).
Conclusion: IL-25 can inhibit the stimulation of IL-17A on ERK1/2 and MMP-3 fractionally,which imply that it may take part in the development of RA through this pathway and may play as a target for the RA treatment on IL-17A.



Disclosure of Interests: None declared
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AB0081 **NOVEL COOPERATION BETWEEN CCL26 AND CX3CL1 VIA CX3CR1 IN THE INJURY OF SMALL BILE DUCT IN PRIMARY BILIARY CIRRHOSIS**

Yihan Cao, SUN XIAOCHUAN, Zhilei Chen, Shuo Zhang, Hua Chen, Fengchun Zhang, LI Wang. *Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China*

Background: CX3CL1-CX3CR1 pathway has been found to be critically involved in the pathogenesis of primary biliary cholangitis (PBC)[1]. As a novel ligand to CX3CR1, CCL26 can promote chemotaxis of CX3CR1+ immune cells but its role in PBC remains elusive[2].
Objectives: This study aimed to explore the role of CCL26, together with CX3CL1-CX3CR1 pathway, in the pathogenesis of PBC.
Methods: We recruited 40 patients diagnosed with PBC in the Peking Union Medical College Hospital from Jan 2018 to May 2018 and 18 age and sex-matched healthy controls (HCs). Peripheral blood and liver tissue samples were collected. The plasma level of CX3CL1 and CCL26 were determined by ELISA. Flow cytometry was used to measure the percentage of CX3CR1+ cells in various subsets of PBMCs. The expression of CX3CL1 and CCL26 in liver tissues was revealed by immunohistochemical staining. Using ELISA and flow cytometry, the change of CX3CL1/CCL26-CX3CR1 pathway expression in human intrahepatic biliary epithelial cells (HIBECs) upon stimulation of various cytokines was studied.
Results: The plasma level of CX3CL1 and CCL26 was higher in patients with PBC than HCs with a P value of 0.044 and 0.104 respectively. The increased level of CCL26 was positively correlated with peripheral eosinophils, basophils and CRP level. In comparison with HCs, the expression of CX3CR1 was significantly higher in NKT-like and CD4+ T cells in PBC patients. In liver samples from PBC patients, CX3CL1 and CCL26 were significantly over-expressed in intrahepatic bile ducts and CCL26 also tended to be abundant in hepatocytes near portal areas and gradually weakened in distant regions. This distribution pattern was not observed in HCs. Upon stimulation of IFN-γ, the expression of CX3CR1 on HIBEC surface and CX3CL1 in culture supernatant was significantly up-regulated, while the expression of CCL26 was increased upon IL-4 and IL-13 stimulation.
Conclusion: CCL26 may cooperate with CX3CL1 to mediate the immune injury of intrahepatic bile ducts via CX3CR1 in PBC.

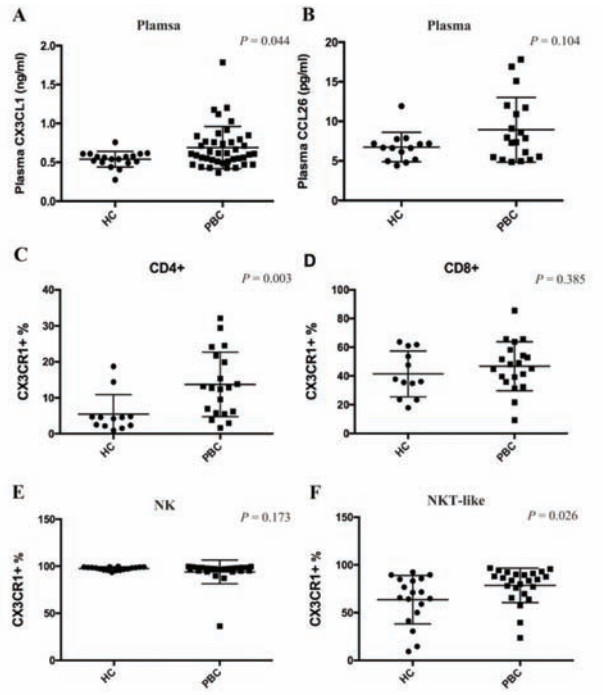


Figure 1: Plasma level of CX3CL1 and CCL26 and expression of CX3CR1 in various subsets of PBMCs. In comparison with HCs, patients with PBC present with following features. (A) A significantly higher plasma level of CX3CL1. (B) An increased tendency of CCL26 level in plasma. (C) A significantly larger percentage of $CX3CR1^+$ cells in $CD4^+$ T cells. (D) A comparable expression of CX3CR1 in $CD8^+$ T cells. (E) A comparable expression of CX3CR1 in NK cells. (F) A significantly larger percentage of $CX3CR1^+$ cells in NKT-like cells.

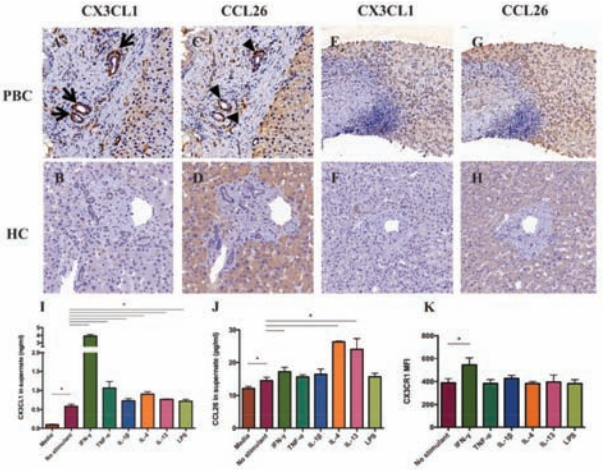


Figure 2: Expression of CX3CL1 and CCL26 in liver tissues and the change of CX3CL1/CCL26-CX3CR1 pathway expression in HIBECs upon stimulation of various cytokines. (A-D) In intrahepatic bile ducts, high expression of CX3CL1 and CCL26, which was indicated by arrows and triangles respectively, was observed in PBC patients. However, only weak expression of CX3CL1 and no expression of CCL26 were found in HCs. (E-F) Weak and no expression of CX3CL1 was revealed in hepatocytes in PBC patients and HCs respectively. (G-H) CCL26 was widely expressed in both PBC patients and HCs. However, in PBC patients, hepatocytes expressed with CCL26 tended to be abundant near portal areas and became scarce in distant regions. This distribution pattern was not observed in HCs. (I) IFN-γ up-regulated the expression of CX3CL1 in HIBEC culture supernatant. (J) IL-4 and IL-13 stimulated the expression of CCL26 in HIBEC culture supernatant. (K) IFN-γ stimulated the expression of CX3CR1 on HIBEC surface.

REFERENCES

[1] Isse K, Harada K, Zen Y, et al. Fractalkine and CX3CR1 are involved in the recruitment of intraepithelial lymphocytes of intrahepatic bile ducts. Hepatology. 2005;41(3):506-16.

[2] Nakayama T, Watanabe Y, Oiso N, et al. Eotaxin-3/CC chemokine ligand 26 is a functional ligand for CX3CR1. J Immunol. 2010;185(11):6472-9.

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AB0082

REDUCED STEROIDOGENIC ACTIVITY OF REPOSITORY CORTICOTROPIN INJECTION (RCI) INDUCES A DISTINCT CYTOKINE RESPONSE FOLLOWING T CELL ACTIVATION IN VIVO

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Background: Melanocortin receptor agonists, such as αMSH have been shown to reduce inflammation in preclinical models, suppressing the production of proinflammatory cytokines. Natural and synthetic ACTH analogues remain linked to the induction of corticosteroids as their primary mechanism of action, leading to the anti-inflammatory and immunosuppressive responses. Repository Corticotropin Injection (RCI) is a complex mixture containing purified porcine pituitary ACTH-analogue, and is an FDA-approved treatment for several inflammatory diseases. RCI has been shown to be effective in steroid-refractory autoimmune disease.
Objectives: We hypothesize that Acthar has an immune regulatory response distinct from synthetic ACTH and steroids. These studies sought to explore the differences between RCI and synthetic ACTH on corticosterone levels in rats and cytokine production in a murine T cell activation model.
Methods: RCI (10, 40, or 400 IU/kg) or ACTH (0.6, 1.2, or 2.4 mg/kg) was administered to Sprague Dawely rats, plasma samples collected and analyzed for corticosterone. To determine the effect on T cell cytokine production, Balb/C mice were treated with RCI (10, 40, and 400 U/kg), ACTH (0.6, 1.2, or 2.4 mg/kg) or prednisolone 1 hour prior to the administration of an anti-CD3. Two hours after antibody administration, plasma cytokines were measured using Meso Scale multiplex ELISA.
Results: RCI and ACTH peak corticosterone and area under the curve (AUC) were evaluated. RCI-induced corticosterone rapidly peaked between 2 -8 hrs. and was dependent on the dose. ACTH displays a delay in the peak time (8-24 hours) and was not dose dependent. When compared to the high dose ACTH, RCI reduced the AUC by 50.0 ± 2.6%, 45.5 ± 5.6% and 27.3 ± 12.5% respectively for 10, 40, and 400 IU/kg. However, there was no significant reduction between any of the ACTH doses tested.
To further explore functional differences between RCI and ACTH, we examined the effects on T cell activation. In vivo T cell activation with the anti-CD3 antibody (clone, 145-2C11) increased several cytokines, including IL-2, IL-6, IL-10, and IFNγ. Treatment with RCI, ACTH, or prednisolone significantly reduced the production of IL-2, IL-4, IFNγ, and TNFα. Interestingly, RCI showed an inverse dose-response on the production of IL-6 and IL-10. RCI inhibited the production of IL-6 at 74.7 ± 4.4% and 67.9 ± 8.5% and IL-10 at 39.1 ± 7.1% and 26.7 ± 9.3% for 10 and 40 IU/kg, respectively, whereas 400 IU/kg had no effect. ACTH inhibited the production of IL-6 at a similar level for all doses tested and had no effect on IL-10 production, whereas treatment with prednisolone inhibited all cytokines.
Conclusion: These data show that RCI has a reduced steroidal response compare to synthetic ACTH. RCI has a direct and distinct immunomodulatory response on T cells unique from both synthetic ACTH and steroids. These characteristic effects suggest a mechanism of action for RCI that is steroid-independent and may help explain its benefit in steroid refractory syndromes.
Disclosure of Interests: Dale Wright Shareholder of: Mallinckrodt Pharmaceuticals, Employee of: Mallinckrodt Pharmaceuticals, Ben Zweifel Shareholder of: Mallinckrodt Pharmaceuticals, Employee of: Mallinckrodt Pharmaceuticals, Prabha Sharma Shareholder of: Mallinckrodt Pharmaceuticals, Employee of: Mallinckrodt Pharmaceuticals, Karen Galen Shareholder of: Mallinckrodt Pharmaceuticals, Employee of: Mallinckrodt Pharmaceuticals, Rick Fitch Shareholder of: Mallinckrodt Pharmaceuticals, Employee of: Mallinckrodt Pharmaceuticals
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AB0083

ADIPONECTIN STIMULATES PRO-INFLAMMATORY CYTOKINE PRODUCTION BY PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH EARLY UNTREATED RHEUMATOID ARTHRITIS

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Background: The pathogenesis of rheumatoid arthritis (RA) involves the action of immune cells and fibroblast-like synoviocytes (FLS). Adiponectin, an adipokine produced mainly by adipocytes, is elevated in serum of RA patients compared to healthy controls; moreover, synovial fluid from RA subjects has higher levels of adiponectin compared to controls with osteoarthritis[1,2]. Adiponectin induces the production of pro-inflammatory cytokines, such as interleukin 6 (IL-6) and IL-8, by

FLS from RA patients [3,4]. However, it remains unclear whether the response to adiponectin in terms of cytokine production is different in immune blood cells from healthy donors compared to RA patients; moreover, it is not known if FLS from healthy subjects can also produce pro-inflammatory cytokines upon adiponectin stimulation.
Objectives: The study aims to analyse if adiponectin induces pro-inflammatory cytokine production by peripheral blood mononuclear cells (PBMCs) from both early RA patients and healthy controls. We also aim to study whether adiponectin induces pro-inflammatory cytokine production by FLS from healthy subjects.
Methods: PBMCs were isolated from whole blood obtained from 5 healthy donors and 3 early untreated newly diagnosed RA patients using Ficoll-Paque PLUS. FLS were isolated from synovial tissue obtained from 3 healthy donors after knee surgery due to injury. Healthy FLS were cultured in Dulbecco's Modified Eagle Medium (DMEM GlutaMAX) supplemented with 10% FBS, 1% Penicillin-streptomycin and 0.5% Gentamycin. Harvested PBMCs and FLS were resuspended in X-VIVO 15 serum-free hematopoietic cell medium and stimulated with different doses of human recombinant adiponectin (1, 5 and 10 μg/ml), and the culture media were collected at different time points. Concentrations of IL-6, IL-8 and TNF-α were measured with ELISA.
Results: Unstimulated PBMCs from early RA patients produced higher levels of IL-6 compared to healthy subjects ($P<0.001$). In healthy controls, both the production of IL-6 and TNF-α was higher in PBMCs stimulated with adiponectin compared to unstimulated PBMCs (n=5, $P<0.01$ for IL-6 and $P<0.01$ for TNF-α). Likewise, the production of both IL-6 and TNF-α was higher in PBMCs from early-RA patients after stimulation with adiponectin compared with unstimulated PBMCs (n=3, $P<0.01$ for IL-6 and $P=0.03$ for TNF-α) in a dose- and time-dependent manner. After stimulation with adiponectin, levels of IL-6, but not TNF-α, were higher in PMBCs from subjects with early RA compared to healthy controls ($P<0.01$). Adiponectin stimulation did not induce IL-8 production from PBMCs from either healthy donors or RA patients.
Adiponectin was able to induce the production of IL-6 and IL-8 by FLS isolated from heathy donors (n=3, $P=0.03$ for IL-6 and $P=0.02$ for IL-8), but not TNF-α.
Conclusion: Our results show that adiponectin induces the production of IL-6 and TNF-α from PBMCs from both healthy subjects and patients with RA and that adiponectin is able to stimulate the production of IL-6 and IL-8 by FLS isolated from healthy subjects. Those results suggest that adiponectin may play a role in the pathogenesis of RA.

REFERENCES

[1] Laurberg TB, et al. Plasma adiponectin in patients with active, early, and chronic rheumatoid arthritis who are steroid- and disease-modifying anti-rheumatic drug-naive compared with patients with osteoarthritis and controls. J Rheumatol 2009
[2] Tan W, et al. High adiponectin and adiponectin receptor 1 expression in synovial fluids and synovial tissues of patients with rheumatoid arthritis. Semin Arthritis Rheum 2009
[3] Tang CH, et al. Adiponectin enhances IL-6 production in human synovial fibroblast via an AdipoR1 receptor, AMPK, p38, and NF-kappa B pathway. J Immunol 2007
[4] Kitahara K, et al. Adiponectin stimulates IL-8 production by rheumatoid synovial fibroblasts. Biochem Biophys Res Commun 2009

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Cartilage, synovium and bone

AB0084 ASSOCIATION OF SYNOVITIS VERSUS CARTILAGE LOSS WITH PAIN SEVERITY AND FUNCTIONAL LIMITATION IN PRIMARY KNEE OSTEOARTHRITIS: CLINICAL, ULTRASONOGRAPHY AND MAGNETIC RESONANCE IMAGING

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Background: Osteoarthritis (OA) is a common and debilitating condition associated with pain and the loss of mobility that undermines quality-of-life. Magnetic resonance imaging (MRI) has become the most important modality for assessment of pathologic changes in knee cartilage, in both clinical and research environment, also Musculoskeletal Ultrasound (MSU) is a valuable tool for imaging musculoskeletal changes in osteoarthritis. It shows early and late changes.
Objectives: The aim of the study was to detect the association of MRI and musculoskeletal ultrasound detected synovitis versus cartilage defect with knee pain severity and functional limitation in patient with primary knee osteoarthritis
Methods: This study was carried out on fifty patients of primary osteoarthritis diagnosed as primary osteoarthritis of knee joints according to American College of Rheumatology Radiologic and Clinical Criteria for Knee osteoarthritis all patients were assed clinically and knee examined for any swelling tenderness, warmth, limitation of range of motion. Pain severity and functional limitation assessed by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Musculoskeletal ultrasound and M.R.I of osteoarthritic knee joints were done.
Results: MSUS synovitis of examined joinits was (0.93 ± 0.94) and cartilage thickness(3.95 ± 1.4). MRI synovitis of examined joinits was (0.89 ± 0.93) and cartilage thickness (39.9 ± 13.26), There was Correlation between WOMAC pain score and MSU synovitis and cartilage thickness with Significant difference ($p<0.01$), also there was Correlation between WOMAC pain score and MRI synovitis and cartilage thickness with Significant difference ($p<0.01$). a positive Correlation between MSU Synovitis and MSU cartilage thickness was detected Significant difference ($p<0.01$) r(0.38). Also a Correlation between MRI Synovitis and MRI cartilage thickness show Significant difference ($p<0.01$) r (0.39).



Sagittal an proton density–weighted magnetic resonance imaging shows focal cartilage loss in the lateral tibiofemoral joint
Conclusion: The severity of cartilage loss and severity of the synovitis/effusion are the most significant determinants of pain and functional disability. Synovitis has role on increasing cartilage los MRI and MSU are a non-invasive method which allows comprehensive assessment and detection of early structural changes in osteoarthritic joints



Longitudinal scan show first grade of synovitis of right knee

REFERENCES

[1] Gold GE, Chen CA, Koo S, et al. (2009): Recent advances in MRI of articular cartilage. AJR Am J Roentgenol 2009; 193(3):628–638.
[2] Iagnocco A (2010): Imaging the joint in osteoarthritis: a place for ultrasound? Best Practice & Research Clinical Rheumatology 2010, 24:27-38.
[3] Procházková M, Zanvit P, Dolezal T, et al. (2009): Increased gene expression and production of spinal cyclooxygenase 1 and 2 during experimental osteoarthritis pain. Physiol Res 2009;58:419Y25

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AB0085 ULTRASONOGRAPHIC EVALUATION OF THE METACARPAL CARTILAGE THICKNESS IN WEIGHTLIFTERS AND VOLLEYBALL PLAYERS

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Background: Articular cartilage is inevitably exposed to impact and loading in different sports play. Despite the fact that it is quite prone to different forms of overloading, the metacarpal cartilage has not been looked into in the pertinent literature. Accordingly, in this comparative study, we have assessed the metacarpal cartilage in volleyball players and weightlifters whereby different forms of stress is naturally prevalent in the athletes' hands.

Objectives: To evaluate the possible effects of impact and loading on the metacarpal cartilage and hand functions in young athletes.
Methods: A total of 42 male athletes (19 weight-lifters and 23 volleyball players) and 46 healthy control subjects were enrolled. Demographic and clinical characteristics (age, height, weight, smoking habit, duration/type of sport, dominant hand) were recorded. The 2nd to 5th finger metacarpal head cartilage thicknesses were measured bilaterally using ultrasonography. Handgrip strength was measured with Jamar dynamometer; pinch strengths (lateral, tip to tip and three jaw chuck pinch) were measured using a pinchmeter. Michigan Hand Outcomes Questionnaire was also completed for each and every participant.
Results: Metacarpal cartilage thicknesses of the athletes (more predominant in weightlifters) were found to be thicker than those of the healthy controls (all $p<0.001$). There were no differences between the dominant and non-dominant hands (all $p>0.05$). Athletes' handgrip and pinch strengths were higher than those of the controls. In the weightlifting group, Michigan Hand Outcome Questionnaire work performance and pain scores were worse than the other groups.
Conclusion: The presence of increased cartilage thickness measurements in the athletes suggests that sports activities might affect the metacarpal articular cartilage. Highest pain scores and lowest work performance scores in the weightlifters with highest metacarpal cartilage thickness might suggest that impact and loading during their sports play could lead to cartilage edema.

REFERENCES

[1] Gratzke C, Glaser C, Englmeier KH, et al. Comparison of cartilage morphology in professional weight lifters and sprinters with normal volunteers suggests that human articular cartilage cannot adapt to functional stimulation. Osteoarthritis Cartilage 2002;10: S11.
[2] Onat ŞŞ, Ata AM, Serrano S, et al. Ultrasonographic measurements of the metacarpophalangeal and talar cartilage thicknesses: A reliability study in healthy subjects. J Back Musculoskelet Rehabil. 2018; 31:253-7.
[3] Sun HB. Mechanical loading, cartilage degradation, and arthritis. Ann N Y Acad Sci 2010; 1211:37-50.
[4] Sadeghi H, Shepherd DET, Espino DM. Effect of the variation of loading frequency on surface failure of bovine articular cartilage. Osteoarthritis Cartilage. 2015;23(12):2252-2258.
[5] Eckstein F, Hudelmaier M, Putz R. The effects of exercise on human articular cartilage. J Anat 2006; 208:491-512.
[6] Yıldızgören MT, Ekiz T, Nizamoğulları S. et al. Effects of habitual knuckle cracking on metacarpal cartilage thickness and grip strength. Hand Surg Rehabil 2017; 36:41-3.

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AB0086 BCP AND CPPD CRYSTALS INFLUENCE THE CHONDROCYTE PHENOTYPE IN DIFFERENT WAYS

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Background: Calcification of cartilage with BCP crystals is a common finding during osteoarthritis (OA) and is directly linked to the severity of the disease and hypertrophic differentiation of chondrocytes. In some OA cartilage samples calcium pyrophosphate dihydrate (CPPD) crystals can be found. The mechanism underlying the formation of the CPPD crystals and their effects on the chondrocytes are not completely understood.
Objectives: The aim of this study was to evaluate the effect of CPPD compared to BCP crystals on the chondrocyte phenotype in OA cartilage.
Methods: Cartilage samples of patients with chondrocalcinosis were used and compared with samples of severe OA patients without chondrocalcinosis and healthy cartilage samples served as control. Radiological presence of chondrocalcinosis was evaluated using standard X-ray pictures, as well as macroscopically inspection. The cartilage samples were stained using von Kossa/Safranin-orange staining. These stainings were used for OA severity scoring using the Chambers-Score. Chondrocyte differentiation markers were evaluated using Collagen 2 and X, as well as Sox9 and aggrecan as markers for chondrocyte hypertrophic differentiation in immunohistochemistry and qRT-PCR. TUNEL staining was performed to investigate cell death. In vivo results were validated using qRT-PCR for the expression of the respective genes after stimulation of C28 chondrocytes with CPPD and BCP crystals.
Results: Radiologically detectable cartilage calcifications were evident in chondrocalcinosis patients, but absent in OA patients without chondrocalcinosis. Chondrocalcinosis cartilage exhibited an increased collagen 10 expression compared to healthy cartilage, as well as to severe OA cartilage containing BCP calcification. Interestingly, aggrecan and collagen 2 were not reduced in chondrocalcinosis cartilage, but markedly reduced in OA cartilage. TUNEL positive cells were significantly increased in CPPD cartilage compared to OA cartilage, although the histological OA severity was lower. qRT-PCR indicated no relevant influence of CPPD crystals on hypertrophic marker genes, whereas BCP crystals significantly induced hypertrophic differentiation.
Conclusion: BCP and CPPD crystals seem to trigger differential effects on the chondrocyte phenotype. BCP crystals induce hypertrophic differentiation, which is not induced by CPPD crystals.
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AB0087 DLX5 AND DLX6 PROMOTES THE COMMITMENT OF MSC TO OSTEOBLASTIC LINEAGE AND CORTICAL BONE FORMATION

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Background: Osteoporosis which affects 200 million women worldwide is the consequence of an imbalance of low anabolism to high catabolism, causing a risk of fracture. Impaired anabolism involved reduced osteoblast differentiation. The osteoblast differentiation is mediated by transcription factors, including Dlx5 and Dlx6. Dlx5 is known to have a role in osteoblast/osteoclast couple and as a promotor of osteoblast lineage commitment [1, 2]. Thus, Dlx5 is a transcriptional actor of Runx2 [3], a key element of osteoblastic differentiation.
Objectives: The goal of this project is to expand our knowledge about bone formation and cellular precursors of osteoblasts, focusing on Dlx5 and Dlx6.
Methods: We analyze the kinetic expression of Dlx5, Dlx6 and osteoblastic markers during the osteoblastic differentiation from murine osteoblastic progenitor derived from calvaria and bone marrow. Same analysis was carried out in osteoblastic precursors from control cells, Dlx5/Dlx6 cells with *ex vivo* recombination or from KO mice in parallel to human bone marrow cells. We analyzed the bone phenotype of mutated mice in the absence of expression of Dlx5 and Dlx6 under Osx promoter.
Results: Dlx5 and Dlx6 increases at D7 during osteoblastic differentiation in the murine bone marrow and then was stable to D21. The absence of Dlx5/6 in cells derived from calvaria and bone marrow resulted in decreased levels of osteocalcin and alkaline phosphatase. *Dlx5/6 $^{fl/fl}$ Osx-Cre* mice were lethal. Dlx5/6 $^{fl/+}$ Osx Cre mice does not affect cortical and trabecular parameters at 6 weeks but had a significant lower cortical thickness and also lower Tb. BV/TV and Tb. Th along with a lower BMD at 3 months in both sexes. Moreover, periosteal volume was also lower in mutated mice. The skulls revealed a lack of sutures closures and dental abnormalities at 6 weeks and 3 months in both sexes.
Conclusion: The deletion of these transcription factors under the action of the Osterix promoter generates lethality, in favor of an essential role in bone development. Heterozygous mutation show impaired bone acquisition during growth. To obtain a total deletion of Dlx5 and Dlx6 in osteoblastic precursor cells, a new murine model of conditional induced deletion is generated. Dlx5 and Dlx6 promote osteoblastic differentiation with an effect on late bone markers, in favor of a role in terminal differentiation. Analysis *in vitro* of Dlx5 and Dlx6 will be confirmed by ongoing *in vivo* experimentation.

REFERENCES

[1] - Samee N, Geoffroy V, Marty C, Schiltz C, Vieux-Rochas M, Levi G, et al. Dlx5, a positive regulator of osteoblastogenesis, is essential for osteoblast-osteoclast coupling. Am J Pathol 2008;173(3):773-80.
[2] - Samee N, Geoffroy V, Marty C, Schiltz C, Vieux-Rochas M, ClementLacroix P, et al. Increased bone resorption and osteopenia in Dlx5 heterozygous mice. J Cell Biochem 2009;107(5):865-72.
[3] - Hassan MQ, Tare RS, Lee SH, Mandeville M, Morasso MI, Javed A, et al. BMP2 commitment to the osteogenic lineage involves activation of Runx2 by DLX3 and a homeodomain transcriptional network. J Biol Chem 2006;281(52):40515-26.

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AB0088 **MECHANICAL STIMULUS INDUCED BY CHIROPRACTIC MANIPULATION REDUCES CARTILAGE, SUBCHONDRAL BONE DAMAGE AND SYNOVIAL INFLAMMATION IN AN EXPERIMENTAL MODEL OF OSTEOARTHRITIS**

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Background: Osteoarthritis (OA) is a degenerative joint disease characterized by cartilage degradation, although both subchondral bone deterioration and synovial inflammation are also hallmarks of the disease. Chiropractic manipulation (CM) is a therapeutic approach focused on the diagnosis, treatment and prevention of musculoskeletal disorders. It is essentially manual, allowing the chiropractor to restore the normal range of motion and function of the joints, muscles, and ligaments. Clinical evidences suggest that CM might exert positive effects in OA patients.
Objectives: The aim of this study was to evaluate the effects of CM on cartilage, subchondral bone and synovitis state in an OA rabbit model.
Methods: Ten (4 months old) male New Zealand rabbits underwent knee surgery to induce OA by transection of anterior cruciate ligament. One week after the surgery, CM was performed using the chiropractic adjusting instrument ActivatorV as follows: Force 2 setting was applied onto the tibial tubercle of the right hind limb (true manipulation, TM-OA group), at an angle of approximately 90°, from medial to lateral, whereas the corresponding left hind limb received a false manipulation (FM-OA group) consisting of ActivatorV firing in the air and slightly touching the tibial tubercle. These procedures were repeated 3 times a week for 8 weeks. Three healthy animals were used as control. Following sacrifice, µCT and histological damage evaluation (Mankin score) were done in femur and tibiae. RANKL/OPG protein expressions were studied by immunohistochemistry in tibia samples. Sinovitis was assessed by Krenn score and immunohistochemistry for macrophages (RAM11) and angiogenesis (CD31) were done. Protein expression of VEGF, COX2, TNFa, IL-1b and MMP3 were determinated by Western Blot.
Results: In the OA rabbits, subchondral BMD decreased in relation to control, been partially reversed in the tibiae of TM-OA group. When subchondral trabecular bone structural parameters were analyzed by microCT, a significant decrease of bone volume/trabecular volume (BV/TV), trabecular number (Tb.N) and trabecular thickness (Tb.Th) was observed in the OA rabbits, while trabecular separation (Tb.S) increased compared to control animals. TM-OA group showed a significant improvement of these parameters compare to FM-OA group. FM-OA joints had higher Mankin score (cartilage damage) than control joints, and TM decreased Mankin score compare to FM-OA ($p<0.05$). The study of RANKL and OPG in cartilage and subchondral bone showed that the significant increase in the RANKL/OPG ratio observed in both tissues respect to controls, was partially reversed in TM-OA group. OA synovial membranes presented a total Krenn synovitis score higher than healthy animals; however, TM-OA rabbits exhibited scores lower than FM-OA ($p<0.05$). RAM11 immunostaining revealed lower expression in TM-OA synovial membranes compared to FM-OA ($p<0.05$). Finally, the significant increase in proinflammatory cytokines (COX2, TNFa and IL-1b) and MMP3 were observed in the synovial membranes of OA rabbits respect to controls, being partially reversed in TM-OA group. Likewise, VEGF and CD31 expression was higher in FM-OA synovium compared to TM-OA.
Conclusion: These results suggest that mechanical stimulus induced by CM may retard the pathologic progression of OA. The beneficial effects of CM might be associated with an improvement in bone and cartilage damage and also inflammatory state.
Disclosure of Interests: None declared
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AB0089 **IN VITRO EFFECT OF FASCIOLA HEPATICA EXTRACT ON SYNOVIAL FIBROBLAST OF RHEUMATOID ARTHRITIS PATIENTS**

Suelen Dalmolin[1,2], Renata Ternus Pedo[1,2], Mirian Farinon[1,2], Jordana Miranda de Souza Silva[1,2], Vanessa Hax[3], Martin Cancela[4], Henrique Bunselmeyer Ferreira[4], Rafaela Cavalheiro Do Espírito Santo[1,2], Fabiany Gonçalves[5], Ricardo Xavier[2,3]on behalf of Laboratório de Doenças Autoimunes. [1]*Laboratório de Doenças Autoimunes, Porto Alegre, Brazil*; [2]*Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil*; [3]*Hospital de Clínicas de Porto Alegre, Serviço de Reumatologia, Porto Alegre, Brazil*; [4]*Universidade Federal do Rio Grande do Sul, Departamento de Biologia Molecular e Biotecnologia, Porto Alegre, Brazil*; [5]*Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands*

Background: Synovial fibroblasts (FLS) have an aggressive and invasive profile and play a major role in RA[1]. Available therapeutic options are effective for induction and maintenance of disease remission[2], but not all patients respond to treatment and there is no cure. So new therapeutic options need to be explored. Studies have shown that products secreted by helminths contain components with anti-inflammatory properties[3 4], capable of suppressing Th1 immune response[5] and the production of inflammatory cytokines[6]. One example is the immunomodulating properties[7] of the extract of *Fasciola hepatica*.
Objectives: To evaluate the effects of *F. hepatica* extract in FLS from RA patients.
Methods: Firstly, the cultures of FLS collected from the synovial fluid of RA patients were exposed at different concentration of *F. hepatica* extract (60µg/mL, 80µg/mL and 100µg/mL) and analyzed after 24h, 48h and 72h by MTT cell proliferation assay. FLS controls were exposed to standard culture medium. The effect of extract was also evaluated through adhesion and wound healing assay, and TNF-α production after IFN*g* stimulation. Statistical analysis was performed with ANOVA or T Test and the $p<0.05$ were considered statistically significant.
Results: *F. hepatica* extract decreased the cell proliferation of FLS at concentration of 100µg/ml after 48h (83.8% ± 5.0 extract *vs* 100.0% ± 0.0 control; $p<0.05$), and at concentrations of 80 µg/ml (88.4% ± 3.0 extract *vs* 100.0% ± 0.0 control; $p<0.05$) and 100 µg/ml (89.8% extract ± 3.8 extract *vs* 100.0% ± 0.0 control; $p<0.05$) after 72h, when compared with control group. Based on these results, the concentration of 100µg/ml and the time of 48h were chosen for the following tests. The treatment with extract showed a decreased of FLS adhesion (92.0 cells ± 5.8 extract *vs* 116.3 cells ± 7.9 control; $p<0.05$) and migratory potential (40.2 inch/h ± 13.9 extract *vs* 58.7 inch/h ± 6.5 control). Moreover, after treatment there was a trend of decreased TNF levels (7.0 pg/mL ± 0.5 extract *vs* 8.1 pg/mL ± 0.7 control).
Conclusion: Taken together, our results suggest that extract of *F. hepatica* is able to reduce the aggressive and invasive profile of FLS. However, further analyses are needed for a better understanding the mechanisms of the effect of *F. hepatica* extract on FLS and its different components, such as cystatin.

REFERENCES

[1] Bottini N, et al. Nat Rev Rheumatol. 2013;9(1):24–33.
[2] Tanaka Y. Korean J Intern Med. 2016;31(2): 210–218.
[3] Hamilton C, et al. Infect. Immun. 2009;(77):2488–98.
[4] Wang S, et al. Parasites & Vetors. 2016;(9):6.
[5] Donnelly S. Infection and immunity. 2005;(73):166–73.
[6] Ravidà A, et al. Molecular & cellular proteomics: MCP. 2016;15(3139–3153).
[7] Cancela M, et al. Parasitology. 2017;144(13):1695–707.

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AB0090 **INHERITED DEFICIT OF PROTEOGLYCAN MIMICKING SEPTIC ARTHRITIS**

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Background: Aggrecanopathies (AP) are a heterogeneous group of skeletal disorders caused by *ACAN* gene mutations leading to dysfunction of a proteoglycan called aggrecan that plays a pivotal role in the organization of the extracellular matrix of the growth-plate cartilage. Clinically, patients with AP display bone dysplasias ranging from severe spondyloepimetaphyseal dysplasia to familial cases of osteochondritis dissecans (OCD) associated with short stature and typical facial dysmorphisms[1].
Objectives: Herein we report a patient with AP referred to our Institute for an inflammatory articular involvement mimicking a septic arthritis.
Methods: Molecular analysis of the *ACAN* gene was performed using Sanger sequencing method.
Results: A 14-year-old boy displayed pain and swelling at the right elbow. Echoscan revealed an effusion in both coronoid and olecranon recess. Acute phase reactants were negative. A month later, since non-steroidal anti-inflammatory drugs were administered without benefit, the patient was admitted in our Institute.
On physical examination, acute arthritis at the right elbow was noted: it appeared painful, warm, and not erythematous. Laboratory test showed slight elevation of acute phase reactant (C reactive protein 1.7 mg/dl, normal value <0.5).

Arthrocentesis was performed and sterile synovial fluid was found. Magnetic resonance images displayed a bone fragment detachment from the humeral condyle of the right elbow with synovium thickening and persistent effusion: the diagnosis of OCD was pointed out.
The patient showed minor dysmorphisms (i.e. dolicocephaly, hypotelorism, arched palate and brachydactyly of the IV finger of both hands) and parents reported a previous episode of OCD when he was 12: at that time, symptoms resolved with non-weightbearing and non-steroidal anti-inflammatory therapy after few days. Furthermore, the patient went under regular endocrinologist follow-up for short stature since he was 8. At the age of 10, his height was 123 cm, SDS 2.4, and growth hormone (GH) stimulation tests showed partial response to insulin tolerance test (GH peak 6.27 ng/mL). Bone age at the X-Ray of right hand and wrist was delayed of 12 months. Human recombinant GH replacement therapy was administered without significant growth-velocity improvement. Although the patient came to observation because of suspected elbow septic arthritis, we re-considered the diagnosis: namely, i. recurrent episodes of OCD; ii. short stature that was poorly responsive to the human recombinant GH treatment, iii. mild skeletal and facial dysmorphisms, led us to hypothesize a form of aggrecanopathy. Molecular analysis of the *ACAN* gene revealed the novel missense variant c.6970T>C, p.Trp2324Arg in the G3 domain of the protein. Notably, another mutation of the G3 domain (c.7249G>A) has been previously related to aggrecanopathy2. Intra-familial molecular analysis allowed us to detect the same gene variant in other three subjects (the mother and 2 siblings) affected only by brachydactily and short stature.
Conclusion: A patient carrying a novel mutation of the ACAN gene presented an atypical form of aggrecanopathy mimicking inflammatory and/or septic arthritis associated with slight short stature and bone dysmorphisms. Further studies are needed to investigate a possible role of this novel ACAN gene variant in the inflammatory articular involvement.

REFERENCES

[1] [Gibson BG, Briggs MD.The aggrecanopathies; an evolving phenotypic spectrum of human genetic skeletal diseases Orphanet J Rare Dis. 2016; 11: 86.]
[2] [E.L. Stattin, F. Wiklund, K. Lindblom, et al.A missense mutation in the aggrecan C-type lectin domain disrupts extracellular matrix interactions and causes dominant familial osteochondritis dissecans. Am. J. Hum. Genet., 86 (2010), pp. 126-137]

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AB0091 SYNDECAN-4 IS INCREASED IN OSTEOARTHRITIC KNEE, BUT NOT HIP OR SHOULDER, ARTICULAR HYPERTROPHIC CHONDROCYTES

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Background: Syndecan-4 plays a critical role in cartilage degradation during osteoarthritis (OA).
Objectives: To investigate the expression and localization of syndecan-4 in different OA joint tissues.
Methods: Syndecan-4 mRNA levels were quantified by RT-PCR in human OA primary cells to compare non-hypertrophic vs hypertrophic articular chondrocytes, non-sclerotic vs sclerotic subchondral osteoblasts and normal/reactive vs inflamed fibroblasts-like synoviocytes. Syndecan-4 was localized by immunohistochemistry in knee, hip or shoulder OA bone/cartilage biopsies. Syndecan-4 was quantified by immmunoassay in chondrocytes culture supernatant and cell fraction.
Results: By immunohistochemistry, syndecan-4 was observed in chondrocytes clusters in the superficial zone of OA knee, but not in OA hip or shoulder cartilage. No staining was observed in the deep zone of cartilage and in subchondral bone. No difference between syndecan-4 expression level in sclerotic and non-sclerotic osteoblasts was observed. Syndecan-4 tended to be increased in inflamed synoviocytes compared to normal/reactive ones but difference was not significant. Differentiated hypertrophic chondrocytes from knee, but not from hip cartilage, expressed more syndecan-4 than non-hypertrophic cells. Using an immunoassay for the extracellular domain of syndecan-4, we found 68% of the syndecan-4 in the culture supernatant of OA chondrocytes culture, suggesting that a large majority of the syndecan-4 is shed and released in the extracellular medium. The shedding rate was not affected by hypertrophic differentiation state of the chondrocytes or their joint origin.
Conclusion: Syndecan-4 could be related to the hypertrophic differentiation of the OA chondrocytes, but the pathway seems to be knee specific. Even if chondrocytes clusters are seen in OA knee, hip and shoulder cartilage and hypertrophic differentiation appears in knee and hip OA articular chondrocytes, syndecan-4 synthesis only increased in knee. These findings suggests the presence of biochemical difference between articular cartilage according to their location and that syndecan-4 could be a biochemical marker specific for knee OA.
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AB0092 SERUM LEVELS OF COLL2–1, A SPECIFIC BIOMARKER OF CARTILAGE DEGRADATION, ARE NOT AFFECTED BY SAMPLING CONDITIONS, CIRCADIAN RHYTHM, SEASONABILITY AND PHYSICAL ACTIVITY

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Background: Coll2-1 is a nine amino acid sequence (HRGYPGLDG) specific of type II collagen which is released during cartilage degradation. This peptide is located in the triple helicoidal part of type II collagen molecule(1,2,3).
Objectives: This study aims to assess intra-individual biological variability of serum cartilage specific biomarker Coll2-1 and define the best standardized conditions for blood sampling in clinical trials.
Methods: Blood samples were taken from 122 subjects with diagnosed knee osteoarthritis (KOA) at a single timepoint as well as from 15 healthy subjects under various conditions, including fasting condition (before or after breakfast and lunch), sampling time (at 8am, 9am, 12pm, 2pm and 5pm), sampling season (at baseline and after 2, 16, 52 and 68 weeks), physical activity (after a resting weekend versus working day), blood treatment (blood clotting from 1h to 24h at room temperature or 4°C; centrifugation at room temperature or 4°C) and type of blood collection tube (dry tube versus dry tube with gel separator). Type II collagen-specific biomarker Coll2-1 was measured using ELISA (Artialis Groups SA, Liège, Belgium) on all collected samples.
Results: There was no significant difference on Coll2-1 values between samples collected at any of the five sampling times (p=0.85) or at any of the sampling days measured (p=0.58). None of the sampling parameters tested had a significant impact on Coll2-1 value (clotting time, clotting temperature and temperature of blood centrifugation (p=0.93), type of tube: p=0.38) when all data from healthy subjects were pooled (n=631 samples). On the contrary,subjects with knee OA had a significantly higher Coll2-1 concentration then healthy subjects (OA: 481+/-144nM vs Healthy 192+/-32nM, p<0,001).
Conclusion: Coll2-1 assay is sufficiently robust for use during OA clinical trials. Coll2-1 measurement is not affected by subject specific conditions such as fasting, resting state, circadian rhythm, seasonality, nor by sampling process factors such as type of dry tube, clotting patterns and centrifugation temperature.

REFERENCES

[1] Henrotin Y, Addison S, Kraus V, Deberg M: Type II collagen markers in osteoarthritis: what do they indicate? Curr Opin Rheumatol 2007, 19:444–450.
[2] Henrotin Y, Deberg M, Dubuc JE, Quettier E, Christgau S, Reginster JY: Type II collagen peptides for measuring cartilage degradation. Biorheology 2004, 41:543–547.
[3] Henrotin Y, Sanchez C, Cornet A, Van de Put J, Douette P, Gharbi M : Soluble biomarkers development in osteoarthritis: from discovery to personalized medicine. Biomarkers 2016, 20:8, 540-546.

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AB0093 EFFECTIVENESS AND SAFETY OF PRILOCAINE IN COMBINATION WITH HYALURONIC ACID IN KNEE OSTEOARTHRITIS: AN OPEN-LABEL STUDY

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Background: Knee osteoarthritis (OA) is a degenerative progressive, debilitating and painful joint disease. Apart from surgery, treatment of OA includes pharmacotherapy and non-medical treatment such as physical therapy, exercise and local applications. Local hyaluronic acid, steroids and local anesthetics provide symptomatic relief and delay surgery.
Objectives: The present study aimed to assess the effectiveness and safety local prilocaine + hyaluronic acid combination in patients with painful knee osteoarthritis radiologically classified as having grade 2 and 3 OA.
Methods: A total of 64 patients with knee OA diagnosed as per the American College of Rheumatology (ACR) criteria were enrolled in the study. Of these patients, 42 had grade 2 and others had grade 3 disease. A single injection of the combination product was administered to all patients. The combination product contained 1 mg hyaluronic acid, 14 mg cross-linked hyaluronic acid, 6.9 mg sodium chloride and 3 mg prilocaine hydrochloride in a 2 ml solution. The combination was injected into a single joint in the painful knee through the anteromedial aspect of the joint. Assessments were performed before the treatment and at 4 and 12 weeks post-treatment by the same physician. The study was designed as an open-label, observational study. The patients were assessed using the Lysholm Knee Scoring Scale. Patient scores were categorized as poor (0-64), fair (65-83), good (84-90) or excellent (91-100). Pain and functional measures were evaluated by this scale.
Results: There was a female (n=58) predominance in the study sample. The mean age of the patients was 56.4 ± 15.3 years. As rated by the Lysholm Knee Scoring Scale, the number of patients with poor scores was 50 before treatment which decreased to 40 at 4 weeks and 30 at 12 weeks post-treatment. There were 4 patients which scored good before treatment and the number of patients with good scores rose to 6 at 4 weeks and 16 at 12 weeks. These findings were statistically significant ($p<0.05$). None of the patients received any additional medication and all continued their daily activities. A home exercise program was followed by the patients throughout the study. Global evaluation of the study physician rated 40 patients in good or excellent condition, whereas 34 patients self-rated themselves in good or excellent condition. Six patients had local symptoms including swelling, pain and redness which were of mild-to-moderate intensity. These symptoms resolved in 1-3 days with simple interventions.
Conclusion: Local hyaluronic acid injections may represent an alternative to systemic medications in the treatment of knee osteoarthritis and they can provide long-term relief with minimal adverse effects when combined with local anesthetics without the need for additional drugs or treatments.
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AB0094 DIFFERENTIATION OF ADIPOSE DERIVED MESENCHYMAL STEM CELLS OBTAINED FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ANKYLOSING SPONDYLITIS AND SYSTEMIC SCLEROSIS

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Background: Cartilage and bone destruction occurs in many rheumatic diseases. While the use of biologic drugs may delay the destruction but still it cannot be averted. Adipose tissue is an easy accessible and rich source of MSCs. Application of mesenchymal stem/stromal cells (MSCs) may be promising option for successful tissue regeneration in therapy of ankylosing spondylitis (AS) systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) patients.
Objectives: The aim of this study was to compare differentiation potential of ASCs obtained from AS, SLE, SSc patients and ASCs line originating from healthy volunteers (hASCs).The phenotype of these cells has been also analysed.
Methods: ASCs obtained from AS (n=9), SLE (n=10), SSc (n=10) patients and 5 commercially available hASC lines were used in study. Cells in passage 4 were used in each experiment. Phenotype of ASCs was evaluated by flow cytometry. Differentiation was made by using osteogenic, chondrogenic or adipogenic media. At the end of differentiation process cells were harvested and total RNA was isolated. Relative quantification (RQ) of gene expression level were calculated by the $2-\Delta\Delta ct$ method.
After 4 weeks of chondrogenic differentiation, mRNA level of *SOX9* and aggrecan (*ACAN*) mRNA has been evaluated by RT-PCR. Additionally glycosaminoglycan (GAG) deposition was analysed by alcian blue staining. After 2 weeks of osteogenic differentiation, expression of *RUNX-2*, collagen 1a1 (*COL1a1*) and osteopontin (*OPN*) mRNA has been determined. Calcium deposition has been determined by alizarin red staining. After 3 weeks of adipogenic differentiation expression of CCAAT/enhancer-binding protein (*C/EBP*), peroxisome proliferator activated receptor-γ (*PPAR-γ*) and fatty acid binding protein 4 (*FABP4*) was determined.
Results: All ASCs cultured in osteogenic medium showed calcium deposition. The expression of *RUNX-2* and *OPN* mRNA was significantly higher in AS-ASCs. Cells obtained from SLE and SSc revealed significantly lower expression of *COL1a1* than hASCs lines.
The results of alcian blue staining showed chondrogenesis of cells obtained from all patients types. No statistically significant differences between AS, SLE, SSc and hASCa lines were observed in *SOX9* mRNA expression. However, all patients derived cells expressed a lower of *ACAN* mRNA level.
Deposition of oil droplets in cytoplama was observed in all cells cultured in adipogenic medium. There were no differences in expression of *C/EBP* and *FAB4*. Cell derived from SLE and AS expressed significantly higher level of *PPARγ*.
Conclusion: AS, SLE and SSc ASCs have phenotype comparable with hASCs lines. The patients derived ASCs are mighty to differentiate into any of the 3 cell types, although the process is altered.
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AB0095 A REGULATORY ROLE OF ANTXR1 IN RANKL-INDUCED OSTEOCLAST DIFFERENTIATION AND FUNCTION

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Background: Anthrax toxin receptor 1 (ANTXR1) has been known to have relationship with extracellular transmembrane protein deeply associated with the process of bone formation and exert important role in angiogenesis. However, there have been no reports to prove the effects of ANTXR1 on bone metabolism mediated by two types of bone cells, osteoclasts and osteoblasts. The aim of this study is to reveal the role of ANTXR1 in the differentiation and function of osteoclasts and osteoblasts.
Objectives: The aim of this study is to reveal the role of ANTXR1 in the differentiation and function of osteoclasts and osteoblasts.
Methods: To determine the effect of ANTXR1 on osteoclastogenesis or osteoblast differentiation, we examined TRAP staining, F-actin staining and Pit assay, or ALP and Alizarin Red-mineralization staining, respectively. The mechanism of ANTXR1 by transfection of retrovirus or siRNA analyzed using real-time PCR and western blot analysis. Also, the effect of ANTXR1 on osteoclast-mediated angiogenesis of endothelial cells assessed by in vitro vascular tubule formation assay of human umbilical vein endothelial cells (HUVECs).
Results: Through performing gain- and loss-of-function studies, we found that ANTXR1 positively regulated receptor activator of nuclear factor kappa B ligand (RANKL)-induced osteoclast differentiation and bone resorption with no effects on osteoblast differentiation. During ANTXR1-mediated regulation of osteoclastogenesis, phosphorylation of early signal transducers, c-jun N-terminal kinase (JNK), Akt, and inhibitor of kappa B (IκB) was affected, which in turn alteration of mRNA and protein levels of c-Fos and nuclear factor of activated T cells cytoplasmic 1 (NFATc1). In addition, genetic manipulation of ANTXR1 in bone marrow macrophages (BMMs) modulated the capillary-like tube formation by HUVECs via two kinds of angiogenic factors, matrix metalloproteinase-9 (MMP-9) and vascular endothelial growth factor-A (VEGF-A). These results explained the important role of ANTXR1 in osteoclast differentiation and functional activity, as well as, osteoclast-mediated angiogenesis of endothelial cells.
Conclusion: Taken together, it was proposed that ANTXR1 might be a promising candidate for gene therapy related with bone metabolic diseases and further, have potential to be served as an important biomarker in the research fields of bone metastasis associated with vascularization.
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AB0096 ANALYSIS OF THE GENE EXPRESSION OF URAT-1, ABCG2, GLUT-9, OCT3, IL1B, TLR4 AND ALPK1 IN MONONUCLEAR CELLS OF PATIENTS WITH INTER-CRITICAL GOUT

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Background: Gout is a common type of arthritis that has incresed in the world due to environmental and genetic factors that associate it with an altered metabolic state. In Mexico, overweight, obesisty, diabetes and metabolic syndrome have incresed in children and adult population, These alterations are associated with the development of gout in adults.

The gout is characterized by an inflammatory chronic process caused by the deposition of monosodium urate crystals (CUMs) in the joints. The recognition of these crystals by macrophages and neutrophils in the joint activates innate immunity. However, high levels of uric acid (UA) in intercritical phase could activate the expression of urate transporters and inflammation genes in other cell types such as monocytes and peripheral blood lymphocytes.

Objectives: The aim of this project was to analyze the changes in gene expression of SLC22A12, SLC2A9, SLC22A3, ABCG2, ALPK1, IL1β, TLR4 in peripheral blood mononuclear cells (PBMC) of mexican patients with inter-critical gouty arthritis and controls without hyperuricemia (HU) comparing it with their metabolic profile.

Methods: The determination of the biochemical parameters was performed by a serum - blood chemical test for uric acid, glucose, triglycerides, cholesterol, HDL, LDL and creatinine. through the use of **U**niCel DxC 600, Synchron Clinical System.

The total RNA of the PBMC cells was amplified by qRT-PCR using the GoTaq® 1-Step RT-qPCR System real kit (Promega) and the Qiagen Rotor Gene Q kit, using specific primers. The gene expression analysis were performed by the ΔCT and ΔΔCT method and using GAPDH as a reference gene to compare the expression of urate transporter genes and inflammatory genes in the study groups.

The expression results were associated to clinical and biochemical parameters such as levels of uric acid, triglycerides, and weight. All statistical analyzes were performed with the SPSS program (IBM 22 version for Windows, SPSS, Inc., Chicago, IL, EU), using student's t-test or U Mann-Whitney test, for the normal and non-normal data, when $p^* < 0.05$ or $p <^* 0.01$.

Results: In this study we compared 24 patients with inter-critical gout and 26 controls without HU. It was found that the expression of ABCG2 was higher in the patients and that the expression of OCT3 was higher in overweight people, regardless of whether they had gout or not compared with normal weigh people. The expression of ALPK1 was higher among patients and controls while the expression of TLR4 and IL1β was not different. The patients had a higher mean in the levels of UA, triglycerides, weight, age and hypertension, but lower HDL than the controls.

Conclusion: Patients with inter-critical gout maintain metabolic alterations associated with the metabolic syndrome although some of them are under treatment. They are also characterized by having overexpression of ABCG2 and ALPK1. These conditions could favor a new attack of gout.

REFERENCES

[1] Dalbeth, N.; Merriman, T. R.; Stamp, L. K., Gout. Lancet 2016, 388 (10055), 2039-2052.

[2] Merriman, T. R., An update on the genetic architecture of hyperuricemia and gout. Arthritis research & therapy 2015, 17, 98

[3] Ko, A. M.; Tu, H. P.; Liu, T. T.; Chang, J. G.; Yuo, C. Y.; Chiang, S. L.; Chang, S. J.; Liu, Y. F.; Ko, A. M.; Lee, C. H.; Lee, C. P.; Chang, C. M.; Tsai, S. F.; Ko, Y. C., ALPK1 genetic regulation and risk in relation to gout. International journal of epidemiology 2013, 42 (2), 466-74.

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AB0097 NOVEL EX VIVOMODEL OF SEPTIC ARTHRITIS DEVELOPED TO IDENTIFY BIOMARKERS RELEASED UPON ARTICULAR INFECTION

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Background: Septic arthritis (SA) is most commonly caused by infectious agents such as *Staphylococcus aureus*. Due to the morbidity and mortality associated with the disease, joint infections are treated as a medical emergency and therefore early diagnosis is essential. Unfortunately, no reliable biomarkers are available to assist diagnosis, beyond serum CRP and synovial fluid culture.

Objectives: To generate a novel *ex vivo* model of septic arthritis comprised of cartilage matrix, neutrophils and SA-associated *Staph. aureus*, to identify biomarkers released upon an inflammatory host response to infection.

Methods: Cartilage explants biopsied from human femoral heads were compared to chondrocyte disks differentiated from mesenchymal stem cells (MSC). MSC differentiation into chondrocytes under defined media and growth factor conditions was confirmed by IHC staining for collagen II on the disks. Explants and disks were infected for 48h with 10^6 cfu *Staph. aureus* (SA patient derived). Structural damage was measured by glycosaminoglycan (GAG) release. Neutrophils were purified from health donor blood samples using the StemCell whole blood isolation kit, and 10^6 cell were added in the final 4h of bacterial infection. Disks were stained with eosin to visualise microscopic damage, CMFDA for viability and PI to identify cell death.

Results: Co-culture of MSC-derived chondrocyte disks with neutrophils or *Staph. aureus* alone resulted in microscopically identifiable structural damage to the disk matrix. The addition of neutrophils in the final 4h of the *Staph. aureus* co-cultures resulted in enhanced structural damage. Assessment of cellular viability revealed that both neutrophils and *Staph. aureus* alone induced cell death throughout the disk whilst the combination of both resulted in total abrogation of viable chondrocytes. Subsequent evaluation of GAG release, however, showed no clear differentiation between the conditions and as such this model was judged not to be sufficient for biomarker development. In comparison, femoral head cartilage explants studies demonstrated that *Staph. aureus* infection in this explant model resulted in significant GAG release after 24h and 48h, which was consistent between donors.

Conclusion: Cartilage explants provide a superior and more physiologically relevant cartilage matrix model for the *ex vivo* analysis of septic arthritis. *Staph. aureus* infection resulted in reproducible damage to cartilage matrices that was not emulated in an MSC-derived chondrocyte disk system. These finding suggest that the femoral head cartilage explants are the optimal matrix model to identify biomarkers for joint infections.

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AB0098 GENE EXPRESSION AND FUNCTIONAL COMPARISON BETWEEN MESENCHYMAL STEM CELLS FROM LATERAL AND MEDIAL CONDYLES OF KNEE OSTEOARTHRITIS PATIENTS

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Background: Osteoarthritis (OA) is the most common degenerative joint disorder, mainly afflicting the weight–bearing joints, and is the leading cause of physical disability worldwide. Despite the identified risk factors, the exact pathogenesis of osteoarthritis remains unclear (1). Formation of mesenchymal stem cells' (MSC) clusters and their aberrant osteogenic differentiation in OA subchondral bone (SB) has been proposed as a key contributor to progression of OA in animal models (2) and in human hip OA (3). MSCs have a crucial role in joint repair but it remains unknown how OA severity affects MSC numbers or characteristics. Knee OA provides a good model to determine this as in knee OA, distribution of damage is usually asymmetrical and tends to be more severe in the medial (Med) compared to the lateral (Lat) compartment (4).

Objectives: The aim of this study was to determine whether there were differences in MSC numbers, topography and gene expression (GE) between Med and Lat femoral condyles of patients with knee OA.

Methods: Condyles were obtained from OA patients that underwent total knee replacement (n=16; UK Ethics Committee approval, 14/YH/0087). Decalcified samples were histologically evaluated for cartilage damage, bone sclerosis and CD271+ MSC distribution (2). MSCs were extracted from SB and sorted using the CD271+CD45- phenotype for GE analysis. Colony forming unit (CFU-F) (3), trilineage differentiation (5) and population doubling (PD) assays were performed. MSC numbers, topography and GE were compared between condyles.

Results: Med condyles presented significantly higher ($p<0.05$) degree of cartilage damage (median OARSI score 20, range 15-20) compared to Lat condyles

(score 3, range 1.5-15), and sclerotic SB area was higher in the Med condyles (64.3±7.0 vs 27.6±7.4%, p<0.05). CD271+ MSCs were found in bone-lining and perivascular locations, and accumulated in the areas of vascular invasion into the articular cartilage in both, Med and Lat condyles. No differences in the MSC numbers were found using CFU-F assay (1.4±0.7 and 1.6±0.8% of total cells in Lat and Med condyles, respectively), or by flow cytometry (4.4±3.9 and 5.9±6.8%, respectively). MSCs had similar PD and trilineage capacities *in vitro*. Out of 95 gene tested, 3 genes were significantly upregulated in Med condyle CD271+ MSCs: GREM1 (lateral MSCs below detection), PTHLH (2.4-fold, p=0.02) and STMN2 (10.5-fold, p=0.02), all implicated in osteogenic differentiation and mineralisation (6, 7, 8).

Conclusion: Upregulation of ossification-related genes in Med condyle MSCs suggest their potential contribution to sclerotic plate formation and OA severity. Further work is needed to establish if biomechanical or biological stimulation of these MSCs can result in GE modulation in preference of cartilage tissue formation and subchondral bone restoration.

REFERENCES

[1] Conaghan. Nat Rev Rheumatol (2013).
[2] Zhen. Nat Med (2013);
[3] Campbell. Arthritis Rheumatol (2016);
[4] Bae. Cartilage (2010).
[5] Altaie. Cytotherapy (2018);
[6] Hu. Mol Med Rep (2017);
[7] García-Martín. Mol Endocrinol (2014);
[8] Chiellini. Biochem Biophys Res Commun (2008)

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AB0099

COCULTURE OF SYNOVIAL MEMBRANE AND CARTILAGE: A POTENTIAL HUMAN EX VIVO CARTILAGE DEGRADATION MODEL

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Background: Cartilage degradation is a hallmark in both osteoarthritis (OA) and rheumatoid arthritis (RA). Ex vivo cartilage models offer the potential to study disease processes but are surprisingly rarely used.

Objectives: Here we investigate the effect of synovial tissue and stimulation with TNF-α on cartilage degradation in a physiologically relevant coculture-model of synovial membrane and cartilage.

Methods: Cartilage and synovial membrane were collected from patients with RA and OA who underwent joint replacement. Cartilage was cultivated either alone or with synovial membrane in medium with or without TNFα as a stimulant for up to 28 days. The explants were harvested at different time points and Safranin-O-staining was performed to visualize proteoglycan (PG) content. A scoring system from 0 (no PG content) to 3 (high PG content) was applied as a semi-quantitative measure for evaluation. Linear mixed modeling adjusted for gender and age was performed to identify factors influencing PG content.

Results: Samples of 18 patients (9 OA, 9 RA) were collected. Factors associated with proteoglycan loss in cartilage were the time in culture (p=0.02), stimulation with TNF-α (p=0.0007) and coculture with synovial membrane (p=0.00002) in univariate analysis with TNF-α (p=0.0009) and coculture (p=0.001) maintaining the level of significance in multivariate analysis. (Figure 1)

Conclusion: Exposure to synovial tissue and TNF stimulation drive cartilage proteoglycan loss in an ex vivo cartilage degradation model. This model may prospectively serve to investigate pathophysiologic pathways of cartilage degradation in both OA and RA.

REFERENCES

None

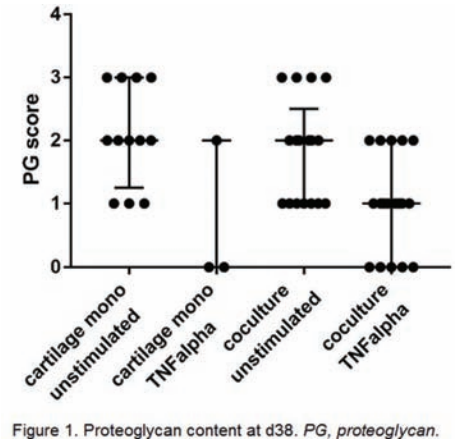


Figure 1. Proteoglycan content at d38. *PG, proteoglycan.*

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AB0100

COMPARATIVE ANALYSIS OF THE EFFECTIVENESS AND TOLERANCE OF INTRA-ARTICULAR INJECTION OF PLATELET RICH PLASMA VS HYALURONIC ACID AND NON-ARTHROSCOPIC JOINT LAVAGE IN PATIENTSWITH KNEE OSTEOARTHRITIS

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Background: Knee Osteoarthritis (KOA) is a common condition associated with pain and morbidity. The impact of this pathology makes it necessary to develop new procedures for joint regeneration. Regenerative treatments such as platelet-rich plasma (PRP) are being proposed as a safe alternative, capable of regenerating damaged tissues and improving the quality of life, reducing the need to surgical procedures (1-4).

Objectives: To compare the effectiveness of PRP treatment vs Hialuronic Acid (HA) and Non-Arthroscopic Joint Lavage (NAJL) in patients with KOA.

Methods: It was performed a prospective, 3-months observational study of 51 patients with KOA, from the OA clinic of the Reina Sofía Hospital of Córdoba. Patients were treated according to clinical practice in 1 of the 3 treatment arms (PRP, HA, NAJL). Pain and disability were evaluated using Visual Analogue Scale (VAS) of joint pain, WOMAC and OARSI. We compared the baseline data using simple ANOVA and chi-squared tests and the intra- and inter-group differences before and after treatment (0, 1 and 3 months) using the mixed ANOVA test. All comparisons were bilateral considering p≤0.05 as a significant result.

Results: 51 patients were enrolled, of which 52.9% were female. The average age (±SD) was 58.47 ± 7.48 years. The average Body Mass Index (BMI) was 30.64 ± 4.25 Kg/m^2. Characteristics at baseline were comparable among the 3 treatment groups (Table 1). An overall improvement was observed during the follow-up in the PRP group in terms of pain and disability with respect to the baseline, with a VAS MD of -3.00 [95% CI, -4.79 to -1.21] in the first month and -3.08 [CI 95%, -4.79 to -1.38] at 3 months (p <0.001), a MD WOMAC of -18.83 [95% CI, -30.62 to -7.05] (p = 0.001) in the first month, and a MD of OARSI of -19.32 [95% CI, -34.26 to -4.37], (p = 0.008) in the first month and -18.94 [95% CI, -36.81 to -1.07] at 3 months (p = 0.035). In addition, the PRP group was superior to the HA group, showing a significant improvement in the VAS at 1 and 3 months (p <0.005) and compared to the NAJL group, PRP showed better results in the WOMAC throughout the follow-up (p <0.01) and in the OARSI at 3 months (p = 0.013).

Conclusion: Based on our results, the intra-articular infiltration with PRP could therefore constitute a safe and effective treatment option in KOA patients, with short-medium term results superior in terms of pain and disability to conventional treatment with HA and NALJ.

Table 1. Baseline characteristics of patients:

Variable	PRP group (n=16)	HA group (n=22)	NALJ group (n=13)	P
Age (years) (x±SD)	59.56±8,70	63.32±5,49	62.23±7.73	NS*
BMI (kg/m^2) (x±SD)	30.31±3.75	30.3±3.36	31.99±5.94	NS*
Female (n,%)	8(50)	12(54.5)	7(53.8)	NS**
KOA stage (n,%)				NS**
II	5(33.3)	11(50)	6(46.2)	
III	10(66.7)	11(50)	7(53.8)	
Knee treated (n,%)				NS**
Left	4(25)	12(54.5)	7(58.3)	
Right	12(75)	10(45.5)	5(41.7)	
VAS pain (x±SD)	6.81±2.14	6.73±1.55	6.54±2.07	NS*
WOMAC (x±SD)	48.56 ±13.31	48.68 ±16.09	57.69±18.98	NS*
OARSI (x±SD)	63.92 ±17.48	57.03 ±18.78	70.80±13.51	NS*

NS: not significant. statistical significance based on: *the simple ANOVA test and ** on the Xi-square test.

REFERENCE

[1] Huang Y, et al. Orthopade. 2019 Jan 8. 2)Burke, et al. Clin trans Med (2016) 5-27. 3)Wroblewski AP, et al. Oper Tech Orthop 2010; 20: 98-105. 4) De La Mata J, et al. Reumatol Clínica. 2013; 9(3):166-71.

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AB0101 SECRETOME ANALYSIS OF CHONDROCYTES AND SYNOVIAL FIBROBLASTS IN OSTEOARTHRITIS: MODULATION BY VIP

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Background: Osteoarhthritis (OA) is a chronic, degenerative and multifactorial disease, and the main cause of pain and dysfunction among elder people. It is characterized by a progressive loss of function of synovial joints (1). The role of chondrocytes in this pathology has been widely studied (2), but other joint cells are also involved, including the synovial fibroblast (SF) (3-5). During joint destruction, inflammatory and degradative mediators are released by joint cells and from the extracellular matrix (ECM), including fibronectin degradation fragments (Fn-fs) (3, 4, 6). On the other hand, vasoactive intestinal peptide (VIP) exerts anti-inflammatory and immunomodulatory actions in several autoimmune and inflammatory disorders, including OA (3, 5). The study of the mediators released by joint cells and their modulation by pro- and anti-inflammatory mediators would be useful for the design of novel therapies for OA treatment.
Objectives: To analyse the mediators released from co-cultures of OA chondrocytes and SF, and to elucidate the effect of Fn-fs and VIP on these cells.
Methods: Human articular chondrocytes (HAC) and SF from 4 OA patients were provided by the Rheumatology Service at Complejo Hospitalario Universitario A Coruña. Isolated cells were recovered and plated in SILAC DMEM-Flex lacking Arginine and Lysine. In the case of medium and heavy media, isotope-labeled L-lysine and L-arginine were used. When 100% of labeling was reached, cells were put in co-culture and incubated in serum-free medium with or without Fn-fs (10^{-8}M) or Fn-fs + VIP (10^{-8}M) for 48h. Cell secretomes were separated on a 10% SDS PAGE gel. Gels were stained with Coomassie blue and the resulting lanes were cut into slices and subjected to in-gel digestion. Extracted peptide mixtures were desalted and concentrated via NuTip, subjected to liquid chromatography, using a Tempo nano LC equipped with a Sun Collect MALDI Spotter, and analyzed by MALDI-TOF/TOF. Identification of peptides and proteins and relative quantification were performed using Protein Pilot software (Sciex).
Results: Cell secretomes were analysed in 4 OA patients in duplicate. Database search (UniprotKB/Swissprot) and Venn's diagrams drawing tool (Venny 2.1.0) allowed us to identify 79 common proteins in the HACs-SF co-cultures. Among them, VIP was able to modulate 33 different proteins, significantly reducing 9 of them: CH3L1, PTX3, PGS2, MMP2, Complement C1R, Complement C3, TBA1, QSOX1, and CATB. These proteins include inflammatory and ECM proteins, proteases and complement system proteins among others, which play a main role in the OA pathogenesis.
Conclusion: VIP decreases inflammatory and degradative mediators in HAC-SF co-cultures, potentially slowing the progression of the disease and supporting its therapeutic role in osteoarthritis.

REFERENCES

[1] Loeser RF, et al. Arthritis Rheum. 2012;64(6):1697-707.
[2] Calamia V, et al. J Proteome Res. 2011;10(8):3701-11.
[3] Pérez-García S, et al. Journal of molecular neuroscience : MN. 2014;52 (1):18-27.
[4] Pérez-García S, et al. Am J Pathol. 2016;186(9):2449-61.
[5] Pérez-García S, et al. J Cell Mol Med. 2016;20(4):678-87.
[6] Zack MD, et al. Arthritis Rheum. 2006;54(9):2912-22.

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AB0102 GENERATION OF OSTEOARTHRITIC MESENCHYMAL STROMAL CELL LINES

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Background: Bone-marrow mesenchymal stromal cells (MSCs) are multipotent self-renewal adult cells with high potential to regenerate the damaged tissues in degenerative diseases such as osteoarthritis (OA). Nevertheless, their usefulness for osteochondral Regenerative Medicine research is hampered by their proneness to senescence when in vitro cultured. Currently, MSC lines available are scarce and present limitations regarding their differentiation capacities. In addition, there is none OA MSC line available for research on this disease.
Objectives: The aim of this study was to generate and characterize immortalized human OA and non-OA MSC lines for their use in osteochondral Regenerative Medicine research.
Methods: For the generation of the immortalized MSC lines, SV40 large T antigen (SV40LT) and GFP-fused human telomerase reverse transcriptase (hTERT) were used. Primary MSCs derived from two hip OA patients and one hip fracture patient without OA were transduced by spinoculation at 800 xg for 45 minutes. Transgene expression was induced by valproic acid. Nuclear expression of SV40LT and GFP was tested by immunofluorescence. Proliferation and senescence were investigated through calculation of population doublings (PDs) at each passage after immortalization and β-galactosidase staining after 100 PDs for each MSC line. Maintenance of MSC characteristics in immortalized MSCs was tested by analysis of CD29, CD44, CD73, CD90, CD105, CD34 and CD45 expression by flow cytometry and cell differentiation experiments. Multi-lineage differentiation potential was analysed histochemical, immunohistochemical and molecularly.
Results: Three MSC lines have been generated: two OA and one non-OA. As shown by immunofluorescence, SV40LT is expressed in the nucleoplasm of these cells, while GFP-fused hTERT is expressed in the nucleoli. A constant proliferation rate thoroughout subculturing in addition to β-galactosidase negative staining confirms that immortalized MSC lines do not senesce, unlike primary MSCs. Expression of CD29, CD44, CD73 and CD90 and lack of CD34 and CD45 was conserved in immortalized MSC lines, while CD105 expression was altered for transduction status and passage. Both OA and non-OA immortalized MSC lines maintain their multipotency (namely, osteogenic, chondrogenic and adipogenic differentiation capacity).
Conclusion: Both OA and non-OA MSCs are susceptible to immortalization by SV40LT and hTERT. For they increased lifespan combined with keeping of most

of primary MSC characteristics, these MSC lines are expected to be valuable tools for the research on Regenerative Medicine for OA as part of Tissue Engineering in vitro models.

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AB0103 A NOVEL PROTECTIVE ROLE OF GPNMB/ OSTEOACTIVIN IN POST-TRAUMATIC OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a chronic joint disease causes irreversible damage to the articular cartilage resulting in loss of joint function and subchondral bone remodeling. There is no cure for OA and currently the available treatment like pain management, and joint replacement surgery is used to treat this disease. GPNMB/Osteoactivin is a type-I transmembrane protein plays a vital role in osteogenesis and bone remodeling,

Objectives: Howver, the function of GPNMB/Osteoactivin in chondrogenesis and cartilage repair is unknown. Hence, in this study, we examined the role of GPNMB/Osteoactivin using post-traumatic osteoarthritis model and ex vivo chondrocytes cell culture and assessing the effects of GPNMB/Osteoactivin as anti-inflammatory factor in chondrocytes.

Methods: We first examined the expression GPNMB/Osteoactivin in noramal cartilage. Next, we assessed the effects of recombinant GPNMB/Osteoactivin on mouse primary chondrocytes profeliation/viabiltiy and extracellular matrix marekrs.

Results: We founad that GPNMB/Osteoactivin treatment did not have any effect on cell prolfieration/viability, howwever, there was an increased in Colllagen Type II and aggrecan expression in a dose- and time-dependent manner. These data sugges that GPNMB/Osteoactivin palys a role in cartilage maintainance. Next we determined whether GPNMB/Osteoactivin contributes to the OA disease progression. Human osteoarthritic damaged and undamaged cartilage harvested following knee replacement were used to examine GPNMB/Osteoactivin exmression and founad that GPNMB/Osteoactivin mRNA was 6-7-fold increased in damaged compared to undamaged cartilage. Similar results were obtained from mouse primary chondrocytes treated with IL1-b and showed a significant increase (4-fold) in GPNMB/Osteoactivin mRNA compared to untreated control. Next, we evalauted the effects of GPNMB/Osteoactivin deficiency on the OA progression usign the DMM model. GPNMB/Osteoactivin muntat (DBA/2J) mice showed significant increased in OARSI scores compared to WT mice.

Conclusion: Taken together, these data are the first to report a role for GPNMB/Osteoactivin in cartilage maintanance and protection again the prgoression of OA.

REFERENCES

[1] The surgical destabilization of the medial meniscus (DMM) model of osteoarthritis in the 129/SvEv mouse. Methods in Molecular Biology: Osteoporosis and Osteoarthritis. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: A disease of the joint as an organ. Arthritis and Rheumatism. 2012. pp. 1697–1707.

[2] Zhou, L., Zhuo, H., Ouyang, H., Liu, Y., Yuan, F., Sun, L.,. .. & Liu, H. (2017). Glycoprotein non-metastatic melanoma protein b (Gpnmb) is highly expressed in macrophages of acute injured kidney and promotes M2 macrophages polarization. Cellular immunology, 316, 53-60.

[3] Ripoll, V.M., et al., Gpnmb is induced in macrophages by IFN-gamma and lipopolysaccharide and acts as a feedback regulator of proinflammatory responses. J Immunol, 2007. 178(10): p. 655766.

[4] Karlsson C, Dehne T, Lindahl A, Brittberg M, Pruss A, Sittinger M, Ringe J. Genome-wide expression profiling reveals new candidate genes associated with osteoarthritis. Osteoarthritis and Cartilage. 2010 Apr 1;18(4):581-92.

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AB0104 ARE POLLUTANTS A NEW RISK FACTOR FOR OSTEOARTHRITIS? RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

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Background: Prevalence of knee osteoarthritis (OA) has doubled since the mid-20th century. Interestingly, this increase cannot be explained solely by longer life expectancy and the obesity epidemics (1). Therefore, other environmental factors known to have increased in the recent years could be part of the explanation.

Objectives: We performed a systematic literature review (SLR) to summarize the existing knowledge about associations between OA and pollutants.

Methods: Pubmed database was used to identify studies reporting data on OA and pollutants in humans (examples of MeSH terms: "Polychlorinated Biphenyls (PCB)" or "Lead"). Abstracts from international congresses were reviewed for the past 2 years, combined with manual curation. Studies were classified in epidemiological *clinical* studies, pollutants assessments in *ex vivo* OA joint tissues, and *in vitro* effect on human chondrocyte.

Results: As of January 15, 2019, 193 potentially relevant articles were screened. Among them, 14 were selected. After manual curation, a total of 21 full text articles were analyzed. Ten articles reported epidemiological clinical studies. Four articles underlined the link between PCB and OA: in the 3 articles reporting association with past exposure to PCB, the most robust one showed that risk of OA was significantly increased, at least in men (OR 4.1 [95%CI: 1.8-11.2] for men and 1.3 [95% CI: 0.8-2.3] for women). In the 4th study, the highest serum concentration of PCB was associated with a higher risk of arthritis: maximal adjusted OR (aOR) was 3.2 [95%CI: 1.6-6.7], p<0.01. However, sensitivity analysis of OA patients did not find any significant association in this study. Two articles focused on serum levels of perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS): aOR to have OA in the PFOA highest serum level quartile was 1.42 [95%CI: 1.26-1.59], p=0.00001 and 1.55 [95%CI: 0.99-2.43]. Data were conflicting for PFOS: aOR to have OA in the PFOS highest serum level quartile was 1.77 [95%CI: 1.05-2.96], p<0.05 and 0.76 [95%CI: 0.68-0.85], p=0.00001. Two articles showed an association between serum lead levels and knee OA in the general population. In Korea, the risk of radiographic OA was increased in the highest quartile of lead serum level compared to the lowest one (aOR 1.90 [95%CI: 1.09-3.32] for men and 1.81 [95%CI: 1.17-2.77] for women). In the United States, risk knee radiographic OA correlates with increased lead serum levels. In the last study, household air pollution induced by the cooking heat source was examined: compared to electricity, the risk of OA was increased with the use of liquids (kerosene/paraffin: aOR 1.73 [95%CI 1.33-2.25]) or solid (coal, wood: aOR 1.73 [1.32-2.27]), (agriculture/crop: aOR 2.0 [1.47-2.72]). Lead and zinc accumulation was reported in 7 articles: 4 of them analyzed the concentration in OA joint obtained during arthroplasty and showed highest concentration in cartilage versus bone. In another, lead serum levels were associated with biomarkers of joint tissue metabolism. Two studies with X-ray fluorescence on cadavers found a high accumulation of lead and zinc in the articular cartilage tidemark. Four studies assessed the in vitro effect of pollutants on human chondrocytes: the viability of chondrocytes was reduced in presence of PCB, gold, silver, fluvic acid and bisphenol A.

Conclusion: This SLR suggests a possible link between OA and pollutants but the designs of the studies, the populations investigated and the type of pollutants were still too heterogeneous and limited to conclude definitively that pollutants represent a new environmental risk factor for OA. However, this SLR highlights a critical need for novel epidemiological, clinical and basic research studies in order to identify other potential environmental factors in OA.

REFERENCES

[1] Wallace, PNAS 114(35), 2017

Disclosure of Interests: None declared

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AB0105 THE EFFECT OF TROMBOSIT RICH PLASMA APPLICATION ON DEGENERATED CARTILAGE: IN VITRO EXPERIMENTAL STUDY

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Background: Osteoarthritis is the most common problem among musculoskeletal system disorders. Platelet-rich plasma (PRP) has been suggested to be

beneficial in the treatment of degenerative musculoskeletal problems. The purpose of this study is to evaluate PRP treatment efficacy on degenerated cartilage.
Objectives: In this study, we aimed to determine the efficacy of platelet-rich plasma (PRP) on mechanically damaged chondrocyte cells by using different dose, different duration of exposure and different methods of activation of platelet.
Methods: Human source chondrocytes (CHON-001 ATTC CRL-2846) were used in thestudy. Chondrocyte cells were produced in appropriate medium and an experimental cartilage model was created. Theplatelet-rich plasma was produced from platelets obtained by apheresis in the laboratory, from blood of volunteer. Theplatelet-rich plasma was adjusted at five different doses as $4{,}8x10^6$, $2{,}4x10^6$, $1.2x10^6$, $6x10^5$, $3x10^5$. The first group of platelet rich plasma was left intact, the second group was detonated within seven minutes by applying ultrasound waves in water, the third group was activated with calcium chloride and thefourth group was determined as control group. Using a ten microliter pipette tip, a linear damage to theopposite side was created at the widest part of the well. Cell migration was monitored at 0-4-8-24 and 48 hours at x10 magnification by in vitro microscopy and wound healing was evaluated by photographing. Migration intervals were determined quantitatively using the program named Image J.
Results: When the rates of recovery were compared to the groups, no significant improvement was observed in the intact and detonated platelet groups at 4-8 and 24 hours compared to the control group. In the third group which was activated with calcium, no significant improvement was observed in all doses at 4 and 8 hours compared to the control group. However, at the 48th hours there was a significant improvement in the doses of $1.2x10^6$, $2.4x10^6$and $4.8x10^6$compared to the control group ($p < 0.0001$).
There were significant differences in intact and detonated platelets at $3x10^5$and $6x10^5$doses at 48th hours compared to controlgroup ($p < 0.0001$). Significant improvement was observed in all groups at levels of $1.2x10^6$and a bove ($p < 0.0001$).
When evaluated in terms of activation, there was a significant improvement in the exploded and intact groups at the 48th hour, compared to the calcium-activated group at doses of $3x10^5$ and $6x10^5$ ($p < 0.01$).
Conclusion: Cartilage damage is the main pathology in the pathogenesis of osteoarthritis. All doses of PRP used in the study contributed to improvement. Meanwhile, the most critical parameter for platelet migration was timing and significant improvement was started after 48 hours.

REFERENCES

[1] Nguyen RT, Borg-Stein J, McInnis K. Applications of platelet-rich plasma in musculoskeletal and sports medicine: an evidence-based approach. PM R 2011;3(3):226-50.
[2] Filardo G, Kon E, DiMatteo B, Merli ML, Cenacchi A, Fornasari PM, et al. Platelet-rich plasma vs hyaluronicacid to treat knee degenerative pathology: study designand preliminary results of a randomizedcontrolledtrial. BMC MusculoskeletDisord2012;13:229.
[3] Spaková T, Rosocha J, Lacko M, Harvanova D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. Am J Phys Med Rehabil 2012;91(5):411–7.
[4] Virchenko O, Aspenberg P. How can one platelet injection after tendon injury lead to a stronger tendon after 4 weeks? Interplay between early regeneration and mechanical stimulation. Acta Orthop 2006;77(5):806-12.

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AB0106 CHANGES IN THE MIRNA PROFILE AND HYPOXIC BEHAVIOUR OF HUMAN CHONDROCYTES BY THERAPEUTIC NUCLEAR MAGNETIC RESONANCE THERAPY (NMRT)

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Background: Therapeutically applied nuclear magnetic resonance (NMRT) is discussed to participate in repair processes regarding cartilage and influences pain signaling. Studies concerning NMR therapy implemented within the treatment of patients with degenerative rheumatic diseases outlined pain reduction as the main clinical outcome (1). NMRT is also known to lead to improvements in pain from patients with knee OA due to a chondroprotective effect on the articular cartilage. In spite of this significant reduction in pain, the mechanism of action of NMRT at the cellular level remains to be elucidated.
Objectives: To substantiate the application of NMRT the aim of this work targets the underlying mechanisms at the cellular level. We investigated NMRT induced changes of the miRNA profile of human healthy and OA chondrocytes and studied the respective miRNA targets. Based on the fact that articular cartilage functions as an avascular and hypoxic connective tissue we were further able to demonstrate that NMRT modulation seems to be more pronounced under hypoxic conditions.
Methods: Human primary chondrocytes and the chondrocyte cell line Tc28/2a were used for the experiments.
RNA was extracted using RNEasy Mini Kit and was used as input for the Thermo Fisher Ion Total RNA-Seq Kit v2. Sequencing was performed on Ion Proton sequencer using the Ion PI Hi-Q™ Sequencing 200 system. Signal processing and base calling was performed using Torrent Suite version 5.6. Hypoxic conditions were established and enabled cell growth in presence of 1-5% O2. Expression of miRNAs and target proteins was studied by a standard PCR procedure as well as protein detection by western blot. HDAC activity was measured by HDAC-Glo I/II assay.
Results: Characterization of the miRNA profile showed a slight up regulation of miR-24-1-5p and miR-502-5p while miR-25-5p and miR-365a-5p was down regulated. For miR-365a-5p known to directly targeting HDAC and NFkB a decrease of HDAC activity by NMRT was detected. The miR-25-5p target COX2 was changed in expression by NMRT whereas no influence on CDK4 knowing to be controlled by miR-24-1-5p was detected. NMRT treatment of chondrocytes under hypoxic conditions (0-5 % O_2) changed the expression profile with respect to NOS, IGF2, PDGF and IGFBP and a change in the expression of Hif1/2 under the influence of IL1b was observed. The hypoxic conditions changed apoptotic behavior of the cells, NMRT showed no influence.
Conclusion: A closer look into the mechanism of the NMRT at the cellular level revealed a modulatory effect on miRNA, their regulatory units and chondrocytes under hypoxic conditions. The results underline our former results indicating that NMRT counteracts IL-1b induced changes which mean that pain reduction by NMRT might be due to NMRT holding against inflammatory mechanisms under OA.

REFERENCES

[1] Kullich W, Overbeck J, Spiegel HU; Journal of Back and Musculoskeletal Rehabilitation 2013, 26:93-104.
[2] Steinecker-Frohnwieser B, Kullich W, Mann A, Kress H, Weigl L; Exp. Clin. Rheum. 2018, 36, 2:0294-0301.

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AB0107 S-ALLYL-L-CYSTEINE ATTENUATES INFLAMMATION RELATED OXIDATIVE STRESS PARAMETERS AND INCREASES ADHESION CAPACITY OF PRIMARY HUMAN OSTEOARTHRITIC ARTICULAR CHONDROCYTES

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Background: Osteoarthritis (OA) is characterized by progressive destruction of the articular cartilage, and chondrocytes, the only cells in articular cartilage, are in charge of maintaining the homeostasis of articular cartilage via modulating extracellular matrix anabolism and catabolism [1]. Due to the association of the degree of oxidative degeneration of chondrocytes and OA, preventing impaired redox signalling and oxidative death of chondrocyte are suggested as potential targets to relieve OA[2]. In this respect, some photochemicals have been shown to be potential agents for preventing or treating OA due to their antioxidant and anti-inflammatory properties [3].
Objectives: We studied the effects of an antioxidant S-allyl-cysteine (SAC), a major sulphur-containing amino acid compound of garlic[4], on the redox system, and its associations with the proliferation rate and index of human OA chondrocytes(OACs).
Methods: Chondrocytes were isolated from the joint cartilages of OA patients (grade 4, meanage= 66 years, BMI= 29.7 ± 4.4 kg/m^2).The alterations in cell proliferation (MTT), adhesion profile (RTCA-iCELLigence System), reactive oxygen species generation (ROS), lipid hydroperoxide levels (LPO), HNE-protein adduct levels (HNE), AGE-protein adduct levels(AGE), 3-nitrotyrosine levels (3-NT),

glutathione peroxidase activity (GPx), and inflammatory progenitors ICE/caspase-1 (ELISA) were determined.
Results: SAC increased OAC's proliferation rate and adhesion profile at relatively low concentrations (1, 10 and 100 nM),but inhibited at higher concentrations (1-100 μM). SAC (1 nM-10 μM) inhibited ROS, LPO and 3-NT, but not HNE- and AGE-modified proteins levels. SAC increased GPx but drastically down regulated ICE/caspase-1, indicating a potential redox regulating and anti-inflammatory effect.
Conclusion: Results suggest that SAC has favourable effects on OA chondrocytes through protecting proliferation capacity and ameliorating redox-mediated inflammatory pathways. Further studies are needed to investigate its therapeutic potential in patients with OA.

REFERENCES

[1] Lepetsos P, Papavassiliou AG. ROS/oxidative stress signalling in osteoarthritis. Biochim Biophys Acta. 2016 Apr;1862(4):576-591.
[2] Drevet S, et al. Reactive oxygen species and NADPH oxidase 4 involvement in osteoarthritis. Exp Gerontol. 2018 Oct 1;111:107-117.
[3] Goker B, et al. Luteolin Modulates Glyco-Lipo-Oxidative Protein Modifications and Inhibits Inflammatory Cytokine Release in Human Osteoarthritic Articular Chondrocytes: Comparison with Colchicine. 2018 ACR/ARHP Annual Meeting. Abstract Number: 1990.
[4] QianYQ, et al. Down regulating PI3K/Akt/NF-κB signalling with allicin for ameliorating the progression of osteoarthritis: in vitro and vivo studies. Food Funct. 2018 Sep 19;9(9):4865-4875.

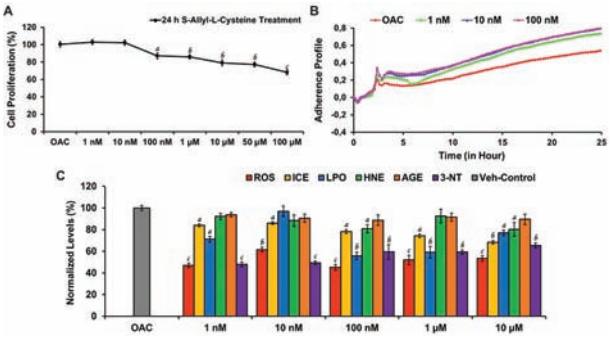


Figure.. Cell proliferation of human primary chondrocytes (A) and dynamic monitoring of adhesion profile of human primary chondrocytes during SAC (B) treated with SAC (24 h). ICE/caspase-1, ROS, LPO, HNE, AGE, 3-NT levels after SAC (24 h) treatment (C). [a]p<0.05, [b]p<0.01, [c]p<0.001 vs OAC. (Bland-Altman Statistics)

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Disclosure of Interests: None declared
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AB0108 **THE ROLE OF CD70 IN THE PATHOGENESIS OF RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is characterized by inflammation and cellular proliferation in the synovium. Activated lymphocytes and proinflammatory molecules are important in the pathogenesis of RA.
CD70 belongs to the tumor necrosis factor (TNF) ligand superfamily and is typically present on activated B and T lymphocytes, natural killer cells and mature dendritic cells.
CD70 expressing $CD4^+$ T cells are enriched in the peripheral blood and synovial fluid of patients with RA and promote autoimmunity via co-stimulatory CD70-CD27 interaction.
CD70 expression is associated with aggressive phenotype of cancer cells and it is mediated by hypoxia inducible factor 2α (HIF-2α).
Objectives: In this study, we examined the presence of CD70 on the surface of fibroblast-like synoviocyte (FLS) of patients with RA (RA-FLS) and investigate the role of CD70 in the pathogenesis of RA associated with HIF-2α.
Methods: RA FLS were obtained from 7 patients with RA who were undergone operation like total knee replacement or synovectomy. All patients were fulfilled the 2010 ACR-EULAR classification criteria for RA.
CD70 and HIF-2α messenger ribonucleic acid (mRNA) were analyzed in RA-FLS by *quantitative polymerase chain reaction* (*qPCR*).
CD70 and CD27 on the surface of RA-FLS were stained by PE-Anti CD70 antibody and PerCP-Cy5.5-CD27 antibody respectively and evaluated by flow cytometry.
Same experiments were performed after treatment with interleukin (IL)-17, TNF-α and HIF-2α blocking antibody (Anti HIF-2α antibody).
Results: CD70 and HIF-2α mRNA in the RA-FLS were elevated after treatment with IL-17 and TNF-α (Figure 1, 2).
The level of CD70 expression on the surface of RA-FLS was elevated after stimulation with IL-17 and TNF-α (Figure 3). And it was lowered after treatment with HIF-2α blocking antibody as dose dependent pattern (Figure 3).
CD27 wasn't present on the surface of RA-FLS (Figure 4).
Conclusion: We identified the expression of CD70 on the surface of RA-FLS.
And in inflammatory conditions like stimuation with IL-17 and TNF-α, both CD70 and HIF-2α mRNA were increased. The level of CD70 on the surface of RA-FLS also elevated by treatment with IL-17 and TNF-α.
The result of decreased level of CD70 after treatment with anti HIF-2α antibody suggest that CD70 expression on the surface of RA-FLS is associated with HIF-2α.
From these results, we expect that CD70-targeted therapy associated with HIF-2α may be effective for treatment with RA.

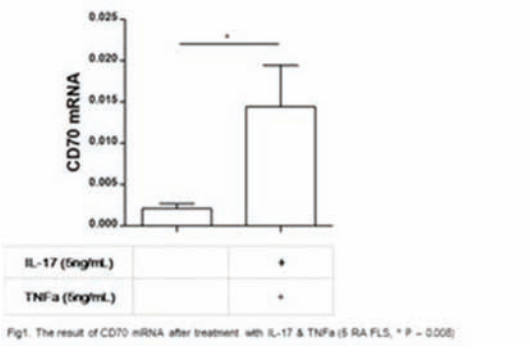


Fig1. The result of CD70 mRNA after treatment with IL-17 & TNFa (5 RA FLS, * P = 0.008)

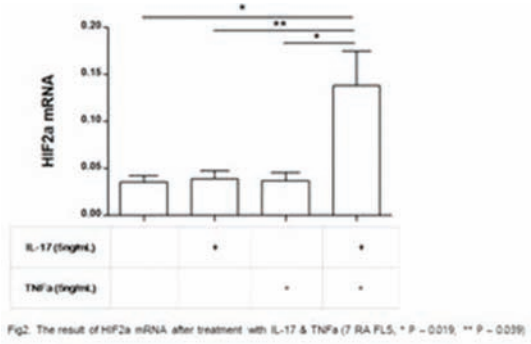


Fig2. The result of HIF2a mRNA after treatment with IL-17 & TNFa (7 RA FLS, * P = 0.019, ** P = 0.039)

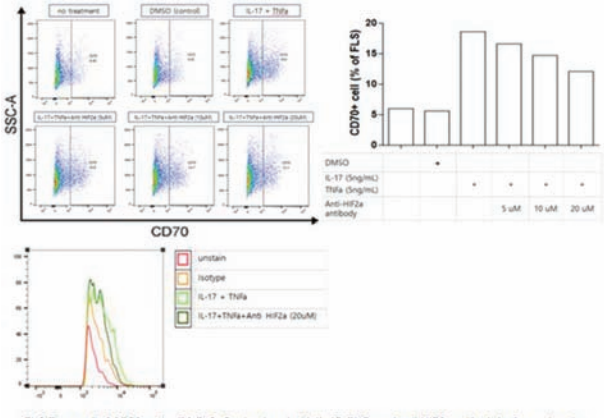


Fig3.The result of CD70 on the RA FLS after treatment with IL-17, TNFa and anti-HIF2a antibody by flow-cytometry

REFERENCES

[1] Han, B. K., Olsen, N. J., & Bottaro, A. (2016). The CD27-CD70 pathway and pathogenesis of autoimmune disease. Semin Arthritis Rheum, 45(4), 496-501.

[2] Kitajima, S., Lee, K. L., Fujioka, M., Sun, W., You, J., Chia, G. S. Poellinger, L.(2018). Hypoxia-inducible factor-2 alpha up-regulates CD70 under hypoxia and enhances anchorage-independent growth and aggressiveness in cancer cells. *Oncotarget, 9* (27), 19123-19135.
[3] Lee, W. W., Yang, Z. Z., Li, G., Weyand, C. M., & Goronzy, J. J. (2007). Unchecked CD70 expression on T cells lowers threshold for T cell activation in rheumatoid arthritis. *J Immunol, 179*(4), 2609-2615.
[4] Oflazoglu, E., Boursalian, T. E., Zeng, W., Edwards, A. C., Duniho, S., McEarchern, J. A. Grewal, I. S. (2009). Blocking of CD27-CD70 pathway by anti-CD70 antibody ameliorates joint disease in murine collagen-induced arthritis. *J Immunol, 183*(6), 3770-3777.
[5] Park, J. K., Han, B. K., Park, J. A., Woo, Y. J., Kim, S. Y., Lee, E. Y., Song, Y. W. (2014). CD70-expressing CD4 T cells produce IFN-gamma and IL-17 in rheumatoid arthritis. *Rheumatology (Oxford), 53*(10), 1896-1900.
[6] Ruf, M., Moch, H., & Schraml, P. (2015). Interaction of tumor cells with infiltrating lymphocytes via CD70 and CD27 in clear cell renal cell carcinoma. *OncoImmunology, 4*(12), e1049805.

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AB0108B PREVALENCE AND RISK FACTORS INFLUENCING THE DEVELOPMENT OF ARTERIAL HYPERTENSION IN PATIENTS WITH A GOUT

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Background: Cardiovascular diseases (CVD) is the leading cause of death for gout. Arterial hypertension (AH) is a proven CVD risk factor (CVD-RF).
Objectives: To assess the factors influencing on development of an AH in patients with a gout.
Methods: 286 male patients fulfilling Wallace proposed criteria for gout were included in the study: age 51.2 [42.8;59.4] years (ys), disease duration – 6.2 [3.8;12.1] ys, number of joints involved during disease course – 7[4;12], subcutaneous tophi – in 35% pts, intraosseous tophi – in 44% pts, nephrolithiasis – in 69% pts, abdominal obesity – in 71%. All pts underwent standard clinical examination, C-reactive protein (CRP), total cholesterol (TC), triglycerides (TG), low and high density lipoproteins (LDL/HDL), serum uric acid, serum creatinine, smoking, family history of AH, body mass index (BMI), diabetes mellitus was performed by standard procedure. We estimated the adjusted odds ratio (OR) and 95% confidence interval (95% CI).
Results: There were two groups of patients with AH diagnosed on clinical data: group 1 (with AH) - 244 (85%) pts, group 2 (without AH) - 42 (15%) pts. The 1st group pts were older (52.3[44.5; 61.1] vs 41.9[38.3; 50.1] ys), had longer duration of gout (6.7[3.9; 13.7] vs 4.5[3; 7.9]), a higher number of joints involved during disease course (8[4; 12] vs 5[3; 9]). The frequency of family history of AH (68.3% vs 48.8%), abdominal obesity (55.3% vs 33.3%), nephrolithiasis (71% vs 54.7%), intraosseous tophi (48% vs 21%) was higher in group 1 as compared with group 2, p<0,05. BMI and CRP level was higher in group 1 compared with group 2: 30.2[27.4; 33.1] vs 27.9[26.3; 30.5] kg/m2, and 12.7[5.84; 19.2] vs 7.8[3.7;16.4]mg/l, accordingly, p<0.05. We didn't find differences of lipid profile, serum uric acid, and serum creatinine level in 1 and 2 group. We also didn't find differences the frequency of smoking, diabetes mellitus, subcutaneous tophi in both groups (table 1).

Table 1

Parameters	Group 1	Group 2
Uric acid, mmol/l	494[420; 575.8]	466[397.3; 547]
Creatinine, mmol/l	94[84.7; 108]	93[83.8; 102]
TC, mg/dl	225[190; 266.8]	225[190; 251]
HDL, mg/dl	35.2[28; 44]	38[27.5; 46.8]
LDL, mg/dl	152.8[113.5; 182.4]	132.2[103;175.2]
TG, mg/dl	172.5[120; 262.3]	147[94;240]
Subcutaneous tophi,%	36.5	26
Smoking,%	29.9	28.6
Diabetes mellitus,%	17.6	11.9

Data are present in median values and interquartile range, *p<0,05 (nonparametric paired Mann-Whitney U-test).
Abdominal obesity (OR, 1.247; 95% CI, 1.063-1.462), family history of AH (OR, 2.8; 95% CI, 1.5-5.4), disease duration more 10 ys (OR, 4.5; 95% CI, 1.1-19.4), intraosseous tophi (OR, 3.0; 95% CI, 1.4-6.4), increased the risk for AH in patients with a gout.

Conclusion: Majority (85%) of patients with gout had AH. Abdominal obesity, family history of AH, disease duration more 10 ys, intraosseous tophi were associated with an increased risk of AH in pts with a gout.
Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3530

Rheumatoid arthritis - etiology, pathogenesis and animal models

AB0109 SYSTEMIC OVEREXPRESSION OF INTERLEUKIN-22 INDUCES EXPRESSION OF THE NEGATIVE IMMUNE-REGULATOR SOCS3 AND POTENTLY REDUCES COLLAGEN-INDUCED ARTHRITIS IN MICE

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Background: High interleukin-22 (IL-22) levels are detected in serum and synovial fluid of rheumatoid arthritis (RA) patients. The increased IL-22 serum levels in RA patients correlated positively with multiple clinical disease parameters like disease activity score (DAS)28 and serum levels of rheumatoid factor. The role of IL-22 in autoimmunity and inflammation appears to be greatly contradictory, being both pro- and anti-inflammatory. Especially the anti-inflammatory properties of IL-22 are not well understood.
Objectives: We aimed to investigate the anti-inflammatory and immune-suppressive effect of IL-22 during experimental arthritis.
Methods: Collagen-induced arthritis was induced in DBA1 mice by immunization and booster with bovine collagen type II (CII). After booster, but before arthritis onset, IL-22 was overexpressed either locally or systemically using an adenoviral construct (AdIL-22) or Luciferase as control (AdLuc). $1x10^7$ plaque-forming units (PFU) of the adenoviruses were injected intra-articularly for local overexpression, or $3x10^8$ PFU was injected intravenously for systemic overexpression in immunized mice, and mice were sacrificed 10 days later. Macroscopic scoring and histological analysis was performed, and mRNA expression and protein production of various pro- and anti-inflammatory mediators was determined in synovial tissue, spleen, and serum.
Results: Local overexpression of IL-22 by injection of AdIL-22 in the knee joint of CII-immunized mice resulted in an unaltered arthritis incidence and severity as compared to the control virus AdLuc. Accordingly, no changes in mRNA expression or protein production were observed in CIA mice locally overexpressing IL-22. In contrast, systemic overexpression of IL-22 potently reduced disease incidence and severity, which was also confirmed by histological analysis. Systemic levels of IL-1β, IL-17, GM-CSF and MCP1 were unaltered in mice overexpressing IL-22 systemically. However, these mice showed significantly lower serum levels of IFNγ, TNFα, MIP1α, and IL-10. Interestingly, the significantly enhanced splenic SOCS3 expression was found to negatively correlate to serum TNFα and MIP1α levels, which is in line with our hypothesis that that the observed reduction in the cytokine levels is mediated in a SOCS3-dependent manner.
Conclusion: With this study, we revealed clear anti-inflammatory effects of IL-22 overexpression during collagen-induced arthritis, which are completely dependent on the systemic route of administration. Additionally, we were the first to show that this protective effect of IL-22 during experimental arthritis is likely orchestrated via up-regulation of the negative regulator SOCS3.
Disclosure of Interests: None declared
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AB0110 RITUXIMAB INDUCED GRANULOMATOUS HEPATITIS WITH A SARCOIDOSIS LIKE REACTION: A BLINDED TRIAL IN MICE

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Background: Rituximab is useful in patients with rheumatoid arthritis (RA) with persistently active disease despite adequate trials with other disease-modifying antirheumatic drugs (DMARDs).
Objectives: To determine whether the inhibition of the B cell CD20 receptor by rituximab results in acute hepatitis in BALB/c mice.
Methods: Twenty BALB/c mice were studied. Ten mice received subcutaneous (SC) injection of rituximab (0.31mg per 25g body weight per 0.03 ml normal saline) at 0, 1, 2 and 4 weeks. For the control group, 10 mice received a SC injection of normal saline (NS) (0.03 ml). At the 10th week post injection, the mice were sacrificed, and histopathological studies were conducted
Results: Of the rituximab-treated group, 1/10 mice died. Liver histology for the rituximab -treated group showed that 7/9 displayed histopathological changes in the lobular cellular infiltrates of eosinophils, lymphocytes and histocytes, in addition to granuloma formation. In contrast, only minimal inflammation was observed in 3/10 mice in the control group (p=0.051).

Conclusion: To our knowledge this is the first experimental controlled study demonstrating rituximab may play a role in inducing granulomatous hepatitis with a sarcoidosis-like reaction.

REFERENCES

[1] Soliman MM, Hyrich KL, Lunt M, Watson KD, Symmons DP, Ashcroft DM. Rituximab or a second anti-tumor necrosis factor therapy for rheumatoid arthritis patients who have failed their first anti-tumor necrosis factor therapy? Comparative analysis from the British Society for Rheumatology Biologics Register. Arthritis Care Res (Hoboken) 2012;64:1108-15.
[2] Reuben A. Hepatotoxicity of immunosuppressive drugs. In: Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier;2011:569-91.
[3] Nard FD, Todoerti M, Grosso V, Monti S, Breda S, Rossi S, et al. Risk of hepatitis B virus reactivation in rheumatoid arthritis patients undergoing biologic treatment: Extending perspective from old to newer drugs. World J Hepatol 2015;7:344-361.
[4] Greenwald M, Tesser J, Sewell KL. Biosimilars Have Arrived: Rituximab. Arthritis 2018;2018.

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AB0111 THE ROLE OF KLOTHO IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic systemic and disabling disease affecting 0.5–1% of the general population. It is characterized by the presence of autoantibodies including rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA). Klotho is a membrane-bound protein predominantly expressed in the kidney, parathyroid gland and choroid plexus that displays enzymatic and co-receptor functions, being involved in the prevention of aging, in the calcium-phosphate balance and in the reparative and fibrotic processes. klotho seems to play an essential role in the maintenance of vessel tone control, in tissue regeneration and reparation and in the electrolytic balance.
Objectives: *We aimed to compare serum Klotho levels between RA patients and healthy controls and the p*ossible association between soluble Klotho with different characteristic of the disease.
Methods: This cross-sectional study was performed in Vega-Baja Hospital, Orihuela (Spain) from November 2016 to May 2018. We prospectively enrolled 63 consecutive women patients affected by RA and followed at the Vega-Baja Hospital (Orihuela, Spain) and 65 matched healthy women controls. All patients included in this study had normal serum creatinine (Cr) levels and met the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA. ACPAs were detected using a second-generation ELISA (ACPAs) kit (ORGENTEC Diagnostika GmbH. Mainz, Germany) while IgM RF was determined as part of routine analysis by turbidimetric assay (Siemmens Healthcare Diagnostic Inc. NY, USA) according to the manufacturers' instructions. Serum Klotho was analyzed using ELISA.
Results: The mean serum total ACPAs and RF were 571.22±1040.89 U/ml and 173.73±751.8 U/ml, respectively. Serum Klotho concentrations were significantly higher in the RA patients than those in the control group: [4.68 (1.4-7.8) vs. 3.5 (0.6-6.1), ng/mL; $P<0.0001$]. They were positively associated with the presence of ACPA and RF ($p<0.05$). Klotho serum levels were higher in RA patients treated with biologic agents than in those undergoing conventional therapy ($p=0.008$).
Conclusion: The increased serum klotho levels in RA patients, especially in those undergoing biologic therapy, may indicate a potential implication in the pathogenesis of the disease.

REFERENCES

[1] Kozera L, Andrews J, Morgan AW. Cardiovascular risk and rheumatoid arthritis—the next step: differentiating true soluble biomarkers of cardiovascular risk from surrogate measures of inflammation. Rheumatology. 2011; 50: 1944-1954.
[2] Hu MC, Shi M, Cho HJ, Adams-Huet B, Paek J, Hill K, et al. Klotho and phosphate are modulators of pathologic uremic cardiac remodeling. J Am Soc Nephrol. 2015; 26(6):1290–1302.
[3] Mazzotta C, Manetti M, Rosa I, et al. Proangiogenic effects of soluble -klotho on systemic sclerosis dermal microvascular endothelial cells. Arthritis Research & Therapy. 2017; 19(1): 27.

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AB0112 EVALUATION OF A NEW MULTIPLEX TECHNOLOGY ASSAY FOR ANTI-CITRULLINATED PEPTIDE ANTIBODIES DETERMINATION

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Background: Anti-citrullinated peptides antibodies (ACPA) are highly specific RA markers. In 2010, experts included them in the ACR/EULAR criteria for disease diagnosis, usually, measured by ELISA. However, a new assay has been developed, recently: Multiplex technology, which allows searching IgG ACPA directed against four citrullinated peptides: Human (HCP1 and 2) and Viral (VCP1 and 2).
Objectives: First, assess ACPA diagnostic performances using Multiplex technology and then compare them to those obtained with the reference technique (ELISA).
Methods: We studied sera of 273 RA patients versus 165 controls (64 healthy controls and 101 patients with other pathologies). We realized ACPA dosage by Multiplex technology and compared them with ELISA assay results. In the end, we looked for a correlation between ACPA production and shared epitope expression in RA patients.
Results: The overall agreement calculated between the two methods was about 91.3%. As to the comparison of diagnostic values of Multiplex technology vs. ELISA, it revealed a sensitivity of 80.2% vs. 82.4% and a specificity of 95.8% vs. 95.5%. Then, for a better evaluation, we plotted ROC curves for ACPA detected by Multiplex technology and ELISA ones. Therefore, we obtained the following areas under the curve (AUC) (p value <0.0001): Anti-: HCP1 (0.775), HCP2 (0.798), VCP1 (0.715) and VCP2 (0.837) and ACPA ELISA (0.867). Finally, our results reveal higher serum levels of ACPA detected by Multiplex technology, in case of SE expression [SE (+) vs. SE (-)] (p value <0.0001).
Conclusion: Diagnostic performance of ACPA detection methods is comparable with relatively good agreement. Our study demonstrated an association between elevated serum levels of anti-HCP and anti-VCP and SE expression, in RA patients.

REFERENCES

[1] Toussirot E, Roudier J. Joint Bone Spine. 2007 Oct;74(5):418-26.
[2] Pratesi F, Dioni I, Tommasi C, Alcaro MC, Paolini I, Barbetti F, Boscaro F, Panza F, Puxeddu I, Rovero P, Migliorini P. Ann Rheum Dis. 2014 Jul;73 (7):1414-22.
[3] Johansson L, Pratesi F, Brink M, Ärlestig L, D'Amato C, Bartaloni D, Migliorini P and Rantapää-Dahlqvist S. Arthritis Res Ther. 2016 Jun 3;18 (1):127.

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AB0113 ARTHRITIS IS ASSOCIATED WITH CEREBROVASCULAR ENDOTHELIAL DYSFUNCTION: MECHANISTIC INSIGHTS IN THE RAT ADJUVANT-INDUCED ARTHRITIS MODEL

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Background: Stroke is the second cause of premature mortality and sudden death in rheumatoid arthritis (RA) after myocardial infarction[1]. The mechanisms involved in the high risk of stroke are currently unknown, but data from the general population argue for a contribution of cerebrovascular dysfunction.

Objectives: The aim of our study was to investigate cerebrovascular function in the rat adjuvant-induced arthritis (AIA) model and to unravel the mechanisms involved, with special emphasis on the pathways regulating nitric oxide (NO) vascular availability.
Methods: Arthritis was induced in 6 weeks-old male Lewis rats by a single injection at the base of the tail of a suspension of *Mycobacterium butyricum* in Freund's incomplete adjuvant. A control group received saline. Thirty-three days after induction, middle cerebral artery (MCA) were dissected and mounted on two glass micropipettes in a small vessel arteriograph before being pressurized at 80 mmHg. Endothelial function was evaluated in vessels pre-contracted with serotonin (10^{-6} M) by measuring the relaxant effect of bradykinin (BK, 10^{-6} M), adenosine diphosphate (ADP, 10^{-6} M) and cumulative concentrations of acetylcholine (Ach, 10^{-12} to 10^{-4} M) in the presence or not of a Nitric Oxide Synthase (NOS) inhibitor (L-NAME, 10^{-4} M), an arginase inhibitor (nor-NOHA, 10^{-4} M), a NOS co-factor (BH_4, 10^{-7} M), an analog of superoxide dismutase (Tempol, 10^{-4} M). The relaxant response of vascular smooth muscle cells to a NO-donor (SNP, 10^{-12} to 10^{-4} M) was also evaluated.
Results: Vasodilation induced by BK, ADP and Ach were significantly reduced in AIA compared to controls rats ($p<0.0001$). L-NAME decreased Ach-induced relaxation in controls but not in AIA rats. By contrast, nor-NOHA ($p<0.0001$), Tempol ($p<0.0001$) and BH_4 ($p<0.02$) significantly improved Ach-induced relaxation in AIA but not in controls. The response to SNP was not different between the 2 groups.
Conclusion: Arthritis is associated with endothelial dysfunction in MCA. These results indicate that this model is relevant for mimicking the cerebrovascular impairments recently observed in RA patients[2]. Cerebrovascular endothelial dysfunction relies on a low NOS activity, a high arginase activity and excessive superoxide anions production. Overall data suggest that therapies able to reverse the imbalance in NOS/arginase pathways would be efficient for reducing the incidence of cerebrovascular events in RA.

REFERENCES

[1] Avina-Zubieta, J. A., Thomas, J., Sadatsafavi, M., Lehman, A. J. & Lacaille, D. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann. Rheum. Dis. 71, 1524–1529 (2012).
[2] Oláh C, Kardos Z, Sepsi M, Sas A, Kostyál L, Bhattoa HP, Hodosi K, Kerekes G, Tamási L, Valikovics A, Bereczki D, Szekanecz Z. Assessment of intracranial vessels in association with carotid atherosclerosis and brain vascular lesions in rheumatoid arthritis. Arthritis Res Ther. 19(1):213 (2017).

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AB0114 POTENTIAL THERAPEUTIC EFFECTS OF CENTAUREA CYANUS L. ON RHEUMATOID ARTHRITIS THROUGH CD38+ NK CELLS

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Background: CD38 catalyzes nicotinamide adenine dinucleotide (Coenzyme I, NAD+) to cyclic ADP ribose (cADPR). We previously reported that CD38 was specifically overexpressed in synovial membrane during rheumatoid arthritis (RA), and CD38+ natural killer (NK) cells are not only highly proportionate in the peripheral blood of RA patients but are also closely related to the disease severity. Cyanidin-3-O-glucoside (C3G) is an inhibitor of CD38 that has anti-inflammatory effects.
Objectives: This study aimed to determine the roles and mechanisms of CD38 and its inhibitor C3G on RA and provides a basis for C3G to become a potential therapeutic agent for RA.
Methods: This study employed bovine type II collagen-induced arthritis (CIA) rats, in vitro cultured RA synovial fibroblasts (RASFs) and mononuclear cells (MNCs) as models to explore the potential therapeutic effects and mechanisms of C3G on RA.
Results: Rats following C3G injections showed significantly alleviated CIA, while the concentrations of inflammatory interleukin (IL)-6 and interferon (IFN)-γ and the proportion of CD38+ NK cells decreased, the levels of anti-inflammatory IL-10 and the proportion of regulatory T (Treg) cells increased, in the peripheral blood and synovial fluids (Figure 1). After C3G treatment, the RASF proliferation and the level of IL-6 in the culture medium decreased, apoptosis increased. C3G also increased IL-2 and IL-10 secretion, and decreased IL-6 and IFN-γ level and the proportion of CD38+ NK in MNCs. The coculture of CD38+NK cells with MNCs depleted of CD38+ NK cells decreased the proportion of Treg cells and the IL-10 levels, meanwhile the coculture in the presence of C3G showed increased the proportion of Treg cells and the IL-10 levels and decreased IL-6 and IFN-γ level. However, C3G did not directly affect the Treg cell proliferation and their cytokine production. C3G treatment also increased sirtuin (Sirt)6 expression, while decreasing the expression of the NK activation receptor natural killer group 2D (NKG2D) in CD38+ NK cells. The expression level of NKG2D in CD38+ NK cells transfected with Sirt6 siRNA was not significantly changed in the presence of C3G. After CIA rats were injected with both C3G and OSS_128167, a Sirt6 inhibitor, the rats remained joint inflammation and the low proportion of Treg cells, although the proportions of CD38+ NK cells decreased in these CIA rats. After C3G treatment, the concentration of tumor necrosis factor (TNF)-α in the CD38+ NK culture medium increased and the concentration of IFN-γ decreased. When cocultured MNC and CD38+NK cells were treated with C3G and TNF-α or C3G and anti-IFN-γ antibody, the proportion of IL-10+ Treg cells increased significantly, while the proportion decreased when cocultured MNC and CD38+ NK cells were treated with C3G and IFN-γ or C3G and anti-TNF-α antibody. The secretion level of TNF-α decreased sharply, and the concentration of IFN-γ increased significantly in the CD38+NK cell culture treated with both Sirt6 siRNA and C3G.
Conclusion: C3G has therapeutic effects for CIA and RA. C3G decreases the proportion of CD38+ NK cells, and increases the expression of Sirt6 in CD38+ NK cells, which increases TNF-α secretion and decreases IFN-γ secretion and sequentially stimulates MNC differentiation into IL-10+ Treg cells and the secretion of IL-10. This study also suggests that the inhibition of MNC differentiation into Treg cells by CD38+ NK cells is an important cause of immune imbalance in RA and CIA (Figure 2).

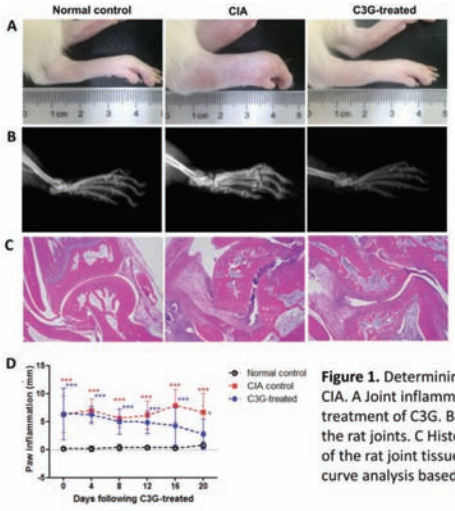


Figure 1. Determining effect of C3G on rat CIA. A Joint inflammation of CIA rats with treatment of C3G. B X-ray observation of the rat joints. C Histochemical observation of the rat joint tissues. D Inflammation curve analysis based on paw swelling.

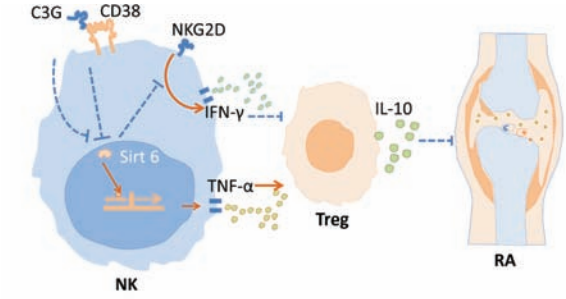


Figure 2. Pattern diagram explaining therapy mechanism of C3G to RA. C3G decreases CD38+ NK cells proportion and increases Sirt6 expression in CD38+ NK cells, which inhibits the NKG2D expression and results in increased TNF-α and decreased IFN-γ secretion. As a result, the proportion of IL-10+ Treg cells and IL-10 secretion elevates to exert therapy to RA

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AB0115 SEMAPHORIN 4A PERPETUATE SYNOVIAL FIBROBLAST INTERACTIONS WITH CD4+ T CELLS AND OSTEOCLAST DIFFERENTIATION: IMPLICATION IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis synovial fibroblast (RASF) and T cells are important contributors in the pathogenesis of RA. Semaphorin 4A has been reported to be elevated in RA patients and play crucial role in promoting inflammation of RA. However, whether semaphorin 4A could facilitate RASF interactions with $CD4^+$ T cells and osteoclastogenesis is less known.
Objectives: The present study aims to investigate the role of semaphorin 4A-Plexin B1 axis in RASF interactions with $CD4^+$ T cells and osteoclastogenesis in vitro.
Methods: Mouse synovial fibroblasts (SF) were isolated from collagen-induced arthritic mice and cultured in vitro with TNF-α and IL-β for 24h. Small interfering RNA (siRNA) against Semaphorin 4A and Plexin B1 were constructed and transfected into SF via adenovirus. Splenic $CD4^+$ T cells isolated from arthritic mice were cocultured with SF under anti-CD3 and anti-CD28. The proportion of $CD4^+IL\text{-}17^+$ Th17 cells was determined at day 5. PBMC isolated from blood of healthy donors were incubated with 1μg/ml Plexin D1 neutralizing antibody overnight. Cells were washed for monocyte enrichment and cultivated for 14 days in α-MEM supplemented with MCSF and RANKL. Osteoclast differentiation was evaluated by TRAP staining. Total RNA was extracted and expression of osteoclast markers were examined by quantitative real-time PCR.
Results: Adenovirus-Mediated siRNA efficiently inhibited expression of Semaphorin 4A and Plexin B1 in SF. The proportion of Th17 cells was significantly decreased in both Semaphorin 4A and Plexin B1 transfected SF cocultures. The number of Trap positive osteoclasts were significantly decreased in cultures that pretreated with Plexin D1. Consistently, blocking of Plexin D1 signaling dramatically downregulated mRNA expression level of Trap, Cathepsin K and NFATc1.
Conclusion: Semaphorin 4A perpetuate synovial fibroblasts interactions with $CD4^+$ T cells by promoting Th17 differentiation. Moreover, Semaphorin 4A-Plexin D1 axis promote osteoclastogenesis and therefore might serve as a potential therapeutic target in the treatment of RA.

REFERENCES

[1] Iyer AS, et al. Neuroimmune Semaphorin 4A in Cancer Angiogenesis and Inflammation: A Promoter or a Suppressor? Int J Mol Sci. 2018 Dec 30;20 (1).
[2] Chapoval SP, et al. Semaphorins 4A and 4D in chronic inflammatory diseases. Inflamm Res. 2017 Feb;66(2):111-117
[3] Wang L, et al. Expression of Semaphorin 4A and its potential role in rheumatoid arthritis. Arthritis Research & Therapy (2015) 17:227.

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AB0117 HOMOCYSTEINYLATED ALPHA 1 ANTI-TRYPSIN AS A POTENTIAL ANTIGENIC TARGET IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic, inflammatory, autoimmune disorder that primarily affects joints. Beside the well-known rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) have been reported to be a very useful diagnostic and prognostic marker of RA, recently antibodies against carbamylated proteins (anti-CarP) have been described also in ACPA negative RA patients. However, more than 20% of RA cases are still defined as seronegative forms. Therefore, the individuation of new antibody specificities in RA could be helpful for diagnostic and prognostic purposes.
Objectives: The goals of this study were the identification and the immunologic characterization of post-translational modified synovial fluid (SF) autoantigens, specifically targeted by autoantibodies from sera of seronegative RA patients.
Methods: SFs from 5 seronegative RA patients were collected, pooled and treated with hyaluronidase. After removal of both albumin and IgG, the sample was washed and cleansed, concentrated, separated by 2-dimensional electrophoresis (2-DE) and then transferred by Western blotting to nitrocellulose membrane, for autoantigen detection by immunoassay, using a pool of sera from 5 seronegative RA patients. The antigenic protein spots were identified by peptide mass fingerprint, using a Matrix-Assisted Laser Desorption/Ionization-Time Of Flight (MALDI-TOF) mass spectrometer.
This approach revealed Alpha 1 Anti-Trypsin (A1AT) as a target of RA patients autoantibodies.
Pooled SFs were also analyzed by reverse-phase nanoliquid chromatography and tandem mass spectrometry, to confirm the presence of A1AT and for the identification of A1AT post-translational modifications.
Homocysteinylated A1AT was immunoprecipitated from pooled SFs of RA seronegative patients and, after a diafiltration and concentration process, was used as an antigen to detect anti-homocysteinylated A1AT antibodies by Enzyme-Linked ImmunoSorbent Assay (ELISA). In order to this, consecutive patients with RA, osteoarthritis (OA), psoriatic arthritis (PsA), and healthy donors were enrolled and sera were collected.
Results: Homocysteinylated A1AT was identified as a potential antigenic target not only in ACPA and RF positive RA patients but, more importantly, also in RA seronegative patients.
Antibodies anti-homocysteinylated A1AT were found in 66.7% (44/66) RA patients seronegative for ACPA and RF, 88.6% (39/44) RA patients, 15% (3/20) OA patients, 26.3% (5/19) PsA patients and in none (0/41) of healthy donors.
Conclusion: Homocysteinylated A1AT was identified as a new possible antigenic target of autoantibodies in sera from RA patients, including RA seronegative patients. This tool may be useful in diagnosis and monitoring of the disease and may contribute to understand the immunopathogenic mechanisms of RA in future studies.
Disclosure of Interests: Tania Colasanti: None declared, Danilo Sabatinelli: None declared, Carmine Mancone: None declared, Arbi Pecani: None declared, Mariangela Speziali: None declared, Marta Vomero: None declared, cristiana barbati: None declared, Alessandra Ida Celia: None declared, Annacarla Finucci: None declared, Carlo Perricone Speakers bureau: BMS; Lilly, Celgene, Sanofi, Fulvia Ceccarelli: None declared, francesca spinelli: None declared, Vincenzo Barnaba: None declared, fabrizio conti: None declared, Guido Valesini: None declared, cristiano alessandri: None declared
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AB0119 MECHANISM OF NEUTROPHIL EXTRACELLULAR TRAP IN PROMOTING SYNOVIAL HYPERPLASIA IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis(RA)is an autoimmune disease characterized by chronic inflammation of the synovial membrane and pannus formation.With the discovery of Neutrophil extracellular traps (NETs) in 2004, its role in autoimmune diseases has received much attention [1].At present,studies on the pathogenesis of NETs in RA have focused on NETs as a source of citrullinated antigens [2], producing autoantibodies to citrullinated protein antigens (ACPAs) [3]. In addition, NETs can activate rheumatoid arthritis fibroblast-like synoviocytes (RA-FLSs) to produce inflammatory cytokines [2].Studies have reported that connective tissue growth factor (CTGF) is overexpressed in RA serum [4], and CTGF plays a key role in the proliferation of RA-FLSs, furthermore leads to joint destruction in RA patients [5]. Therefore, our study stimulated RA-FLSs with NETs to detect cell proliferation and CTGF mRNA, aiming to explore the pathogenesis of NETs involved in RA.
Objectives: To Explore the potential effects of Neutrophil extracellular traps (NETs) on rheumatoid arthritis synovial fibroblasts (RA-FLSs).
Methods: The synovial tissues of RA patients were isolated and cultured in vitro; peripheral blood neutrophils were extracted from healthy volunteers and stimulated to formation NETs, NETs were extracted as a stimulating agent; MTS proliferation assay was used to evaluate the effect of NETs on the proliferation of RA-FLSs; qRT-PCR was used to determine the expression of connective tissue growth factor (CTGF) mRNA in cells treated with NETs-stimulated RA-FLSs for 60h.
Results: The isolated and purified neutrophils could form NETs by stimulated in vitro. The concentration of extracted NETs -DNA was 58.5ng/ul (1×10^6 cells). Compared with the control group, NETs could promote the proliferation of RA-FLSs. With the increase of NETs concentration, the proliferation of RA-FLSs was also enhanced($F=99.519, P<0.05$);NETs stimulated the up-regulation of CTGF mRNA expression in RA-FLSs(30.696 ± 0.468 vs. 1, $p<0.01$)
Conclusion: NETs can promote the proliferation of RA-FLSs and stimulate the up-regulation of CTGF mRNA in RA-FLSs in vitro.

REFERENCES

[1] April Barnado, Leslie J. Crofford, Jim C. Oates. At the Bedside: Neutrophil extracellular traps(NETs) as targets for biomarkers and therapies in autoimmune diseases. Journal of Leukocyte Biology Vol.99, No.2, pp:265-278, July, 2017.

[2] Khandpur R, Carmona-Rivera C, Vivekanandan-Giri A, et al. NETs are a source of citrullinated autoantigens and stimulate inflammatory responses in rheumatoid arthritis. Sci Transl Med (2013) 5(178):178ra40.

[3] Corsiero E, Bombardieri M, Carlotti E,Pitzalis C, et al. Single cell cloning and recombinant monoclonal antibodies generation from RA synovial B cells reveal frequent targeting of citrullinated histones of NETs.Ann Rheum Dis 2016;75:1866–1875.

[4] Nozawa K, Fujishiro M, Kawasaki M, et al. Connective tissue growth factor promotes articular damage by increased osteoclastogenesis in patients with rheumatoid arthritis. Arthritis Res Ther. 2009;11(6):R174.

[5] S Ding, H Duan, F Fang, et al.CTGF promotes articular damage by increased proliferation of fibroblast-like synoviocytes in rheumatoid arthritis. Scand J Rheumatol 2016;45:4,282–287.

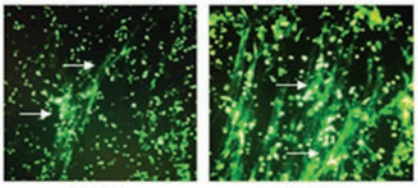


Fig.1.Identification of NETs by fluorescent staining

PicoGreen fluorescent staining showed extracellular fibrous network structure

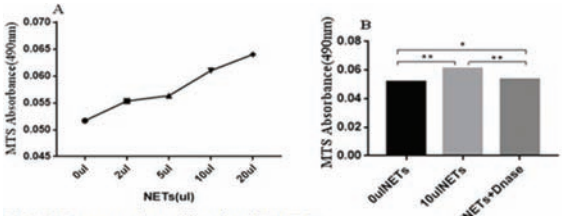


Fig.2.NETs promote the proliferation of RA-FLSs

(A)Different doses of NETs stimulated RA-FLSs, and the OD value at 490nm was detected after 60h culture.(B)The OD values of NETs group (10ul NETs) and DNaseI pretreated NETs group (DNaseI+10ul NETs) were higher than the control group (0ul NETs) . (*P<0.05, **P<0.01)

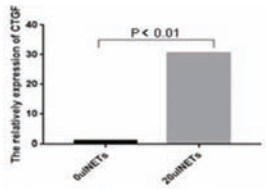


Fig.3.CTGF mRNA levels in RA-FLSs

The relative expression of CTGF mRNA in RA-FLSs between experimental group (20ul NETs) and control group (0ul NETs).

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AB0120 THE MECHANISM OF TRADITIONAL CHINESE MEDICINE PRESCRIPTION ER-MIAO-SAN IN THE TREATMENT OF RHEUMATOID ARTHRITIS BASED ON CHOLINERGIC ANTI-INFLAMMATORY PATHWAY

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Background: Rheumatoid arthritis (RA) is a chronic progressive autoimmune disease. The traditional Chinese herbal formula Er-miao-san (EMS) has been used to treat RA demonstrating significant clinical efficacy; however, the mechanism of action remains unclear. In view of the important role of α7 nicotinic acetylcholine receptor (α7nAChR) in the cholinergic anti-inflammatory pathway (CAP)for the regulation of inflammation and cytokines. Indeed, we previously found a correlation between *CHRNA7* (encoding α7nAChR) expression and EMS, we hypothesized that it may play a role in the anti-inflammatory effects of EMS.

Objectives: The mechanism of EMS in the treatment of RA based on *CHRNA7* involved in the regulation of CAP.

Methods: We established a CIA model with female Wistar, and the effects of intragastric administration of EMS on the expression of *CHRNA7*, arthritis score, inflammatory, and articular cartilage changes, was examined in the joints. The serum levels of TNF-α, IL-6, and IL-1β were determined using commercial ELISA kit.

Results: The CIA model was successfully established. Macroscopic changes of arthritis, such as redness and swelling, were clearly observed in the CIA rats, but were attenuated by the treatment of EMS. The mean arthritis score was markedly lower in the EMS-treated group (EG, $P < 0.05$). The serum level of TNF-α was significantly lower in EG compared with CIA group ($P < 0.05$). The same results were found in the serum levels of IL-6 and IL-1β. Synovial edema and extensive infiltration of inflammatory cells occurred in the CIA rats, but were repaired by the treatment of EMS. Cartilage tissue was thinning, dissolution and disappearance, as well as extensive inflammatory cell infiltration with plasma cells and lymphocytes, was observed in the articular cartilage of the ankles in CIA group. In contrast, EMS treatment prevented cartilage degeneration and markedly reduced inflammation. Immunohistochemistry (IHC) analysis showed positive signals of CHRNA7 was expressed on fibroblast-like synoviocytes, macrophages, and endothelial cells in the joints. Effect of EMS on the expression of CHRNA7 protein in the joint by Western blot (WB) analysis. IHC and WB relative optical density values of CHRNA7 was significantly higher in EG compared with CIA group ($P < 0.05$).

Conclusion: EMS can significantly alleviate the symptoms of arthritis in CIA rats by regulating the expression of CHRNA7 in CAP. It provides a scientific research foundation for the further development of EMS and explores more ways to treat RA.

REFERENCES

[1] Lam F. F., Ko I. W., Ng E. S., et al. (2008). Analgesic and anti-arthritic effects of Lingzhi and San Miao San supplementation in a rat model of arthritis induced by Freund's complete adjuvant. J Ethnopharmacol, 120 (1), 44-50.

[2] Chen G., Li K. K., Fung C. H., et al. (2014). Er-Miao-San, a traditional herbal formula containing RhizomaAtractylodis and Cortex Phellodendri inhibits inflammatory mediators in LPS-stimulated RAW264. 7 macrophages through inhibition of NF-κB pathway and MAPKs activation. J Ethnopharmacol, 154(3), 711-718.

[3] Wang H., Yu M., Ochani M., et al. (2003). Nicotinic acetylcholine receptor alpha7 subunit is an essential regulator of inflammation. Nature, 421, N, 6921, 384-388.

[4] Kanashiro A., Talbot J., Peres R. S., et al. (2016). Neutrophil Recruitment and Articular Hyperalgesia in Antigen-Induced Arthritis are Modulated by the Cholinergic Anti-Inflammatory Pathway. Basic & clinical pharmacology & toxicology, 119(5), 453-457.

[5] Li S., Zhou B., Liu B., et al. (2016). Activation of the cholinergic anti-inflammatory system by nicotine attenuates arthritis via suppression of macrophage migration. Molecular medicine reports, 14(6), 5057-5064.

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AB0121 EXPRESSION OF CHEMOKINES AND CHEMOKINE RECEPTORS IN DIFFERENT TISSUES AND THEIR LOCALIZATION IN THE JOINTS OF RATS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a complex, chronic, multisystem autoimmune disease characterized by a sustained immune response that leads to inflammation in the body and destruction of joints. While not completely understood, immune cells, as well as soluble factors such as cytokines and chemokines, are believed to be involved in the pathogenesis of RA. chemokines play an important role in the development of inflammation and the regulation of cytokines. However, studies of chemokines have focused mainly on their role in cancer, and

there is a lack of relevant reports on their function in chronic, multisystem autoimmune diseases.
Objectives: Here, using molecular biology techniques were performed to evaluate the expression of 7 chemokines/chemokine receptors in different tissues and their localization in the joints.
Methods: We established a collagen-induced arthritis (CIA) model in female Wistar rats and evaluated the expression patterns of 7 chemokines/chemokine receptors (CCR3, CCR5, CCR7, CCL5, CXCR3, CXCR4, and CXCL10) in different tissues using qRT-PCR and western blotting and their localization in the joints using immunohistochemistry.
Results: The mRNA expression of *CCR*3, *CCR*7, *CXCR*4, and *CXCL*10 was significantly higher in the spleen and joints, while that of *CCR*5 and *CCL*5 was significantly higher in the liver and that of *CXCR*3 was significantly higher in the lung, spleen, and joints (Fig. 1). Protein expression patterns largely corresponded to mRNA expression patterns. In the joints, CCR3, CCR5, and CCR7 were expressed in fibroblast-like synoviocytes (FLS), macrophages, stromal cells, and endothelial cells. CCL5, CXCR3, and CXCR4 were expressed in FLS, endothelial cells, and stromal cells. CXCL10 was expressed throughout the synovium, stromal cells, and endothelial cells (Fig. 2).

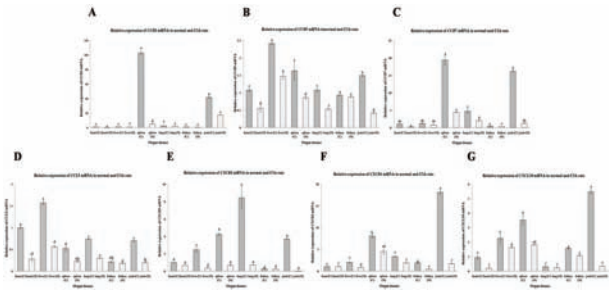


Figure 1. Relative expression levels of seven chemokine/chemokine receptor genes in different tissues of CIA rats

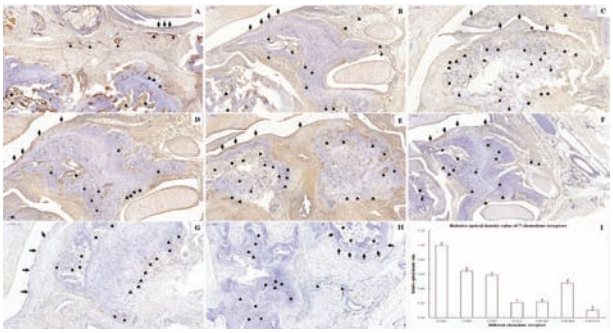


Figure 2. Representative images of immunostaining of chemokines and their receptors in CIA rat joints. Arrow, FLS; triangle, endothelial cell; pentagon, stromal cell; chevron, macrophage. A–G. Positive immunohistochemistry results for CCR3, CCR5, CCR7, CCL5, CXCR3, CXCR4, and CXCL10, respectively; H. Negative control. Scale bar, 200 μm.

Conclusion: Seven chemokines/chemokine receptors are widely expressed in different tissues in the CIA rat model, and all are involved in the inflammatory response. Our results provide a basis for investigations into the mechanism of action of RA and suggest that chemokines may become novel targets for RA treatment.

REFERENCES

[1] Li Z. C., Xiao J., Peng J. L., et al. (2014). Functional annotation of rheumatoid arthritis and osteoarthritis associated genes by integrative genome-wide gene expression profiling analysis. PloS one, 9(2), e85784.
[2] Pandya J. M., Lundell A. C., Andersson K., et al. (2017). Blood chemokine profile in untreated early rheumatoid arthritis: CXCL10 as a disease activity marker. Arthritis. Res. Ther., 19(1), 20.
[3] Rump L., Mattey D. L., Kehoe O., Middleton J. (2017). An initial investigation into endothelial CC chemokine expression in the human rheumatoid synovium. Cytokine, 97, 133-140.

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AB0122

TNF INHIBITION IN RHEUMATOID ARTHRITIS RESPONDERS TO CERTOLIZUMAB-PEGOL REDUCES LYMPHOCYTE RECRUITMENT FROM BLOOD WHILE MONOCYTE TURNOVER REMAINS INCREASED

Biljana Smiljanovic[1], Till Sörensen[2], Marc Bonin[2], Pascal Schendel[2], Sascha Johannes[2], Karl Skriner[2], Marina Backhaus[3], Silvia Pade[2], Gabriela Schmittat[2], Sandra Hermann[2], Sarah Ohrndorf[2], Bruno Stuhlmüller[2], Andreas Grützkau[4], Gerd Rüdiger Burmester[2], Thomas Häupl[2]. *[1]Charité – Universitätsmedizin Berlin, Rheumatology, Berlin, Germany*; *[1]Charité – Universitätsmedizin Berlin, Rheumatology, Berlin, Germany*; *[3]Park-Klinik Weißensee, Berlin, Germany*; *[4]Deutsches Rheuma-Forschungszentrum (DRFZ), Berlin, Germany*

Background: Increased turnover of monocytes is a hallmark of active RA [1]. Targeting the mediators of monocyte activation like TNF or IL6 is a successful strategy in reducing inflammation in RA.
Objectives: To investigate differential effects of anti-TNF treatment in responders and non-responder on turnover of peripheral leukocytes in patients with rheumatoid arthritis.
Methods: Immune cell profiling in a subgroup of 36 patients of the BIORAC open-label 52-weeks treatment study with certolizumab-pegol (CZP) by multicolor flow cytometry at baseline, week 12 and 52. Cell populations were analyzed with *immuno*Clust [2]
Results: Of the 36 RA patients with initial DAS28 of 4.75, response to CZP occurred in 18 patients after 12 weeks and 15 patients after 52 weeks (both Δ-DAS28 -1.4). When comparing populations during the course of treatment, there was no relevant change in the number of monocytes or granulocytes. However, as previously reported [1], the most characteristic observation was the reduced absolute number of non-classical $CD16^{+}CD14^{low}$ monocytes at baseline when compared to healthy controls. This corresponds to increased monocyte turnover and recruitment to inflamed tissue. In both, responders and non-responders this monocyte population did not increase or change over time despite reduction of DAS28 disease activity in responders. In responders to CZP, the absolute number of T-cells, B-cells and NK-cells as well as their subsets including naïve-, central- and effector-memory T-cells and naïve-, unswitched- and switched memory B-cells and plasmablasts increased compared to baseline. In non-responders to CZP, the absolute number of T-cells, B-cells and NK-cell remained unchanged. In CZP responders, the cell frequencies in T-cell subsets shifted from a naïve towards a central and effector phenotype, while in non-responder no changes were identified.
Conclusion: In responders, successful reduction of subsequent events of immune activation by anti-TNF drugs will decrease inflammation and thus decrease recruitment of lymphocytes to tissue. Initial triggering seems to involve especially monocytes, which are typical producers of TNF and which are still recruited to tissue much more than in healthy controls as indicated by persisting reduction of non-classical monocytes even in responders. Thus, increase of lymphocytes in the blood upon response seems to reflect ongoing mobilization from bone marrow and lymphatic organs into the blood but reduced recruitment to tissues when local inflammation is successfully suppressed. Altogether, these changes indicate that triggers for monocyte recruitment exist and persist despite immunosuppression with anti-TNF whereas lymphocyte recruitment is successfully suppressed in responders to anti-TNF.

REFERENCES

[1] Smiljanovic B, et al. Monocyte alterations in rheumatoid arthritis are dominated by preterm release from bone marrow and prominent triggering in the joint. Ann Rheum Dis. 2018;77(2):300-308.
[2] Sörensen T, et al. immunoClust-An automated analysis pipeline for the identification of immunophenotypic signatures in high-dimensional cytometric datasets. Cytometry A. 2015;87(7):603-615.

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DOI: 10.1136/annrheumdis-2019-eular.7612

AB0123 CCL17 IN SYNOVIAL FLUID AND PLASMA OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

Cecil Hor[1,2,3], Adrian Achuthan[2,3], [1,2]Keith Lim[3], John Hamilton[2,3]. *[1]Western Health, Rheumatology, Melbourne, Australia*; *[2]Australian Institute of Musculoskeletal Science (AIMSS), Melbourne, Australia*; *[3]University of Melbourne, Melbourne, Australia*

Background: Despite the advancements in management of rheumatoid arthritis (RA) in the last two decades, there are still a significant number of patients who cannot achieve low disease states or remission with the current available therapy. Granulocyte macrophage-colony stimulating factor (GM-CSF) is a key mediator in inflammation and autoimmunity, and has emerged as a novel therapeutic target in RA. However, potential adverse side effects warrant further investigation of a more specific target.
Objectives: Chemokine (C-C motif) ligand 17 (CCL17) is a downstream mediator of GM-CSF and has recently been shown to be regulated by GM-CSF in human monocytes. Significantly, CCL17 has a non-redundant role in inflammatory arthritis and pain. We investigated the expression levels of CCL17 in synovial fluid and plasma from RA patients.
Methods: We recruited RA patients with symptomatic swollen joints, who require joint aspiration for diagnostic and/or therapeutic purposes. Synovial fluid and plasma were collected and CCL17 protein levels were determined by ELISA.
Results: CCL17 protein was measured in synovial fluid and plasma samples from our cohort of RA patients. Levels of secreted CCL17 were higher in plasma [median 240 (40-580) pg/ml] compared to synovial fluid [median 100 (30-300) pg/ml] $p<0.05$.
Conclusion: Significant levels of CCL17 were detected in RA synovial fluid and plasma. This is a novel study which demonstrates and compares the presence of CCL17 in synovial fluid and plasma from matching RA patients. The expression of CCL17 in plasma can make it a useful potential biomarker for RA, while its expression in synovial fluid suggests that CCL17 may be a therapeutic target for treating RA.

REFERENCES

[1] Gibofsky, A., *Epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis: A Synopsis*. Am J Manag Care, 2014. 20(7 Suppl): p. S128-35.
[2] Hamilton, J.A., *GM-CSF as a target in inflammatory/autoimmune disease: current evidence and future therapeutic potential*. Expert Rev Clin Immunol, 2015. **11**(4): p. 457-65.
[3] Achuthan, A., et al., *Granulocyte macrophage colony-stimulating factor induces CCL17 production via IRF4 to mediate inflammation*. J Clin Invest, 2016. **126**(9): p. 3453-66.

Disclosure of Interests: Cecil Hor Speakers bureau: Mundipharma, Pfizer, Adrian Achuthan: None declared, Keith Lim Consultant for: Advisor for role of hepatitis and TB in Cimzia, UCB, Speakers bureau: Role of biological in pregnancy UCB, John Hamilton Grant/research support from: GSK
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AB0124 IMPACT OF INFLAMMATORY CYTOKINE IL-1B ON THE EXPRESSION OF MULTIPLE DRUG RESISTANCE PROTEIN BCRP/ABCG2 IN SYNOVIOCYTES OF PATIENTS WITH RHEUMATOID ARTHRITIS

Fang Yuan Hu[1], Ning Yan[1], Jie Liang[1], Xiang-Cong Zhao[1], LI Zhao-Hua[1], Chong Gao[2], LI Xiao-Feng[1], Caihong Wang[1]. *[1]The Second Hospital of Shanxi Medical Univerity, Taiyuan, China*; *[2]Department of Pathology, Brigham and Women's Hospital,Harvard Medical School, MA, United States of America*

Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by synovitis and vasospasm[1]. So far, The biggest challenge in the current field of RA treatment is the production of DMARDs multidrug resistance (MDR) and the most critical mechanism for the production of MDR is the ABC transporter family-mediated increase in target cell drug excretion, while inflammatory cytokines play an important role in its expression regulation. Our previous research have confirmed that IL-1β, IL-6 and IL-17 are involved in the regulation of P-glycoprotein (P-gp) expression in lymphocytes of RA patients. The breast cancer resistance protein (BCRP/ABCG2) is also a highly efficient efflux pump, which absorbs, distributes, and excretes drugs or exogenous substances in the body[2]. IL-1βis a cytokine involved in the whole process of RA, which can aggravate the inflammatory response. However, there is no research on the effect of IL-1β on the expression of BCRP in RA Fibroblast-like synoviocytes (FLS).
Objectives: To explore the effects of different concentrations of IL-1β on the expression of drug resistance proteins in FLS of RA patients at different time points.
Methods: Synovial tissues of untreated RA patients (n=3) were extracted by Joint surgery, FLS culture system in vitro was established and passaged to the fifth generation or so to do the experiments. FLS cells were divided into A, B, C, D four groups randomly with different treatments: Group A was the cell control group. Group B, C, D were respectively co-cultured with low (20ng/ml), middle (50ng/ml), high (100ng/ml) concentrations of IL-1β. They were cultured respectively for 24 hours, 48 hours, and 72 hours. The effect of IL-1β on the expression level of BCRP mRNA was observed at different concentrations and at different time points.
Results:

1. With the prolongation of IL-1βculture, the expression of BCRP mRNA increased. Under the same concentration of IL-1β(20ng/ml or 50ng/ml), the expression of BCRP mRNA in the 72h group was higher than that in the 24h group or 48h group ($P<0.05$). At the concentration of IL-1βof 20 ng/ml, the 48h group showed higher levels of BCRP mRNA expression than the 24h group ($P<0.05$).
2. The expression of BCRP mRNA increased with the increase of IL-1βconcentration. After 48h of IL-1βculture, the 100 ng/ml group showed high levels of BCRP mRNA expression compared with the 0 ng/ml group ($P<0.05$). After 72h of IL-1βculture, compared with the 0 ng/ml group, the expression of BCRP mRNA was significantly increased in the 20 ng/ml or 50 ng/ml or 100 ng/ml group ($P<0.01$); and the 100 ng/ml group showed high levels of BCRP mRNA expression compared with the 20 ng/ml group ($P < 0.05$).

Conclusion: The expression of BCRP mRNA in FLS of RA patients has a certain concentration and time dependence of IL-1β, suggesting that IL-1β is involved in BCRP-mediated multidrug resistance, which lays a foundation for exploring its specific mechanism.

REFERENCES

[1] Takase-Minegishi K, Horita N, Kobayashi K, et al. Diagnostic test accuracy of ultrasound for synovitis in rheumatoid arthritis: systematic review and meta-analysis[J]. Rheumatology, 2017.
[2] Chen Z, Shi T, Zhang L, et al. Mammalian drug efflux transporters of the ATP binding cassette (ABC) family in multidrug resistance: A review of the past decade[J]. Cancer Letters, 2016, 370(1): 153-164.

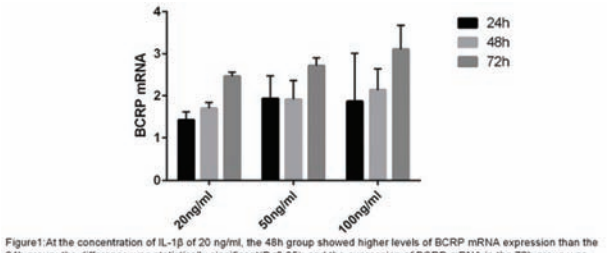


Figure1:At the concentration of IL-1β of 20 ng/ml, the 48h group showed higher levels of BCRP mRNA expression than the 24h group; the difference was statistically significant($P<0.05$); and the expression of BCRP mRNA in the 72h group was significantly higher than that in the 24h group or the 48h group; the differences were statistically significant ($P<0.01$). At the concentration of IL-1β of 50 ng/ml, the expression of BCRP mRNA in the 72h group was higher than that in the 24h group or 48h group; the difference was statistically significant($P<0.05$).

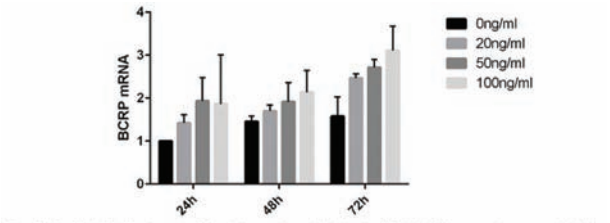


Figure2:After 48h of IL-1β culture, the 100 ng/ml group showed high levels of BCRP mRNA expression compared with the 0 ng/ml group; the difference was statistically significant ($P<0.05$). After 72h of IL-1β culture, compared with the 0 ng/ml group, the expression of BCRP mRNA was significantly increased in the 20 ng/ml or 50 ng/ml or 100 ng/ml group; the differences were statistically significant ($P<0.01$); and the 100ng/ml group showed high levels of BCRP mRNA expression compared with the 20 ng/ml group; the difference was statistically significant ($P < 0.05$).

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Disclosure of Interests: None declared
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AB0125 **CXCL17 IN RHEUMATOID ARTHRITIS: INTERFERONE-GAMMA INDUCIBLE EXPRESSION AND INHIBITION OF ANGIOGENESIS**

Anna Kernder[1], Johanna Mucke[1], Long Tang-Chieu[1], Torsten Lowin[1], Tim Claßen[2], Oliver Sander[1], Ellen Bleck[1], Claudia Heier[1], Georg Pongratz[1], Matthias Schneider[1], Stefan Vordenbäumen[1]. *[1]Heinrich-Heine-University Düsseldorf, Policlinic of Rheumatology and Hiller Research Unit, Düsseldorf, Germany*; *[2]St. Elisabeth Hospital, River Rhein Center for Rheumatology, Department of Orthopaedics, Meerbusch, Germany*

Background: CXCL17 is the latest chemokine discovered and was reported to influence angiogenesis and monocyte trafficking[1-2]. Its role in rheumatoid arthritis (RA) has not been assessed so far.
Objectives: To assess the role of CXCL17 and its putative receptor G-protein-coupled receptor 35 (GPR35) in RA.
Methods: Synovial tissue from joint replacements of RA and osteoarthritis (OA) patients was used for CXCL17 and GPR35 immunohistochemistry and in-situ-hybridization/immunofluorescence double-stainings. CXCL17 concentration in the synovial fluid of RA and CXCL17 production by synovial fibroblasts and smooth muscle cells after stimulation with TNF-α, INF-γ and IL-1β was quantified by qPCR and ELISA. Angiogenesis was assessed by a human umbilical vein endothelial cell culture assay.
Results: CXCL17 and GPR35 are widely expressed in the synovial membrane of RA compared to OA (p=0.006). Within the synovial membrane CXCL17-mRNA could be located to vascular smooth muscle cells. INF-γ significantly induced CXCL17-mRNA and protein production in RA synovial fibroblasts (1.88-fold, p=0.019 and 2-fold, p=0.0002 respectively) and rat smooth muscle cells (67-fold, p=0.02 and 3.7-fold, p<0.001). CXCL17 was detected in the synovial fluid of RA (mean 310 pg/ml). In vitro angiogenesis was inhibited by CXCL17. This effect was reversed by specific GPR35 antagonists.
Conclusion: CXCL17 is abundant in RA synovial tissue, localizes to vascular smooth muscle cells and fibroblasts, and is inducible by INF-γ. Antiangiogenic properties are mediated by GPR35. CXCL17 and GPR35 may constitute a hitherto unrecognized regulatory protein in RA pathogenesis and therefore be interesting drug targets.

REFERENCES

[1] Pisabarro MT, Leung B, Kwong M, Corpuz R, Frantz GD, Chiang N, et al. Cutting edge: novel human dendritic cell- and monocyte-attracting chemokine-like protein identified by fold recognition methods. J Immunol Baltim Md 1950. 2006;176(4):2069–73
[2] Lee W-Y, Wang C-J, Lin T-Y, Hsiao C-L, Luo C-W. CXCL17, an orphan chemokine, acts as a novel angiogenic and anti-inflammatory factor. Am J Physiol Endocrinol Metab. 2013;304(1):E32-40.

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AB0126 **ANTI-INFLAMMATORY EFFECTS OF SPLEEN TYROSINE KINASE (SYK) INHIBITOR, PICEATANNOL, ON FIBROBLAST-LIKE SYNOVIOCYTE IN RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation with subsequent cartilage and bone erosion leading to joint destruction. The fibroblast-like synoviocytes (FLS) have a central role in disease pathogenesis and in vitro FLS invasiveness correlates with articular damage in RA patients. Spleen tyrosine kinase (Syk) is an intracellular protein tyrosine kinase in the cells of joint tissues such as bone, cartilage, and synovium, where it is involved in tumor necrosis factor α (TNF-α) receptor signaling. Piceatannol, a naturally occurring hydroxylated analog of resveratrol, was reported to inhibit Syk.
Objectives: The aim of this study is to evaluate the effects of piceatannol on inflammation and the downstream signaling pathway of Syk in RA FLS.
Methods: FLS isolated from synovium of rheumatoid arthritis (RA) patients were cultured with DMEM supplemented with 10% FBS and 1% penicillin/streptomycin. FLS were stimulated with lipopolysaccharide (LPS) for 24 hr after 1 hr treatment of piceatannol. The cytokines were screened using human inflammatory and matrix metalloproteinase (MMP) antibody array kit (Abcam) in the culture supernatant. Also, IL-6, IL-8 and CXCL10 levels were measured by ELISA and the expression levels of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthases (iNOS) were determined by western blotting.
Results: Protein expression level of Syk was suppressed by piceatannol (50 μM treatment). Piceatannol inhibited the production of cytokines/chemokines such as IL-6, CCL-5, CCL-8 and MMP-1 in RA FLS stimulated with LPS. The levels of IL-6, IL-8 and CXCL10 in RA FLS were dose-dependently decreased. The viability and proliferation of the cells were not affected. Piceatannol significantly suppressed COX-2 and iNOS protein expressions.
Conclusion: Piceatannol had suppressive effects on pro-inflammatory cytokines/chemokines production and had anti-inflammatory effects in RA FLS.

REFERENCES

[1] Kjelgaard-Petersen CF, et al. Arthritis Rheumatol. 2018 Sep;70(9):1419-1428
[2] Mullard A. et al. Nature Reviews Drug Discovery 2018, 17:385

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AB0127 **VERY STRONGLY POSITIVE RHEUMATOID FACTOR LEVELS (10-FOLD HIGHER THAN THE UPPER NORMAL RANGE) RATHER THAN "RHEUMATOID FACTOR POSITIVITY" PER SEARE ASSOCIATED WITH SMOKING IN FEMALE RA PATIENTS WITHOUT A HISTORY OF OCCUPATIONAL DUST AND FUME EXPOSURE**

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Background: Rheumatoid factor (RF) forms part of the 2010 EULAR/ACR classification criteria[1].
A weakly positive RF is defined as up to 3-fold higher and a strongly positive RF >3-fold higher than the upper normal range.
However, a longitudinal study of individuals with RF levels at least 4-fold higher than the upper range of normal had an adjusted hazard ratio for RA development of 26 (95% CI 15 to 46) compared to only 6.0 (3.4 to 10) for individuals with levels 2 to 4-fold above the upper normal range[2].
We have recently reported median RFs of greater than 10-fold higher than the upper normal range in nodular RA which is far more prevalent in smokers than non-nodular RA[3]. We have arbitrarily defined this level of RF as very strongly positive as it defines a disease subtype.
Additionally, RF levels are strongly associated with additive exposures to both smoking and industrial vapours, gases, dust and fumes (VGDF) in male RA, with only 8% having been exposed to neither VGDF nor cigarette smoke[4].
Objectives: Accordingly, we have studied female RA in whom VGDF exposures are less common to compare RF levels in an appreciable number of smokers and non-smokers without the significant confounding effect of VGDF exposures to determine if smoking is specifically associated with a very strongly positive RF.
Methods: Medical record analysis yielded 241 female RA patients seen in clinic between January and June 2018 without exposures to industrial VGDF. These patients were stratified for a history of smoking. RF was measured with Tina-quant Rheumatoid Factors II Test System, by Roche Diagnostics Corporation at the time of RA diagnosis. A value of < 14 IU/ml was considered as negative as per manufacturer guidelines, a RF weakly positive (14-42 IU/ml), RF strongly positive (42.1-140 IU/ml) and RF very strongly positive (>140 IU/ml).
Results: There were 109 never smokers and 132 smokers with a median RF of 21 IU/ml and 53 IU/ml respectively, p<0.05. In never-smokers significantly more were seronegative 46/109 (42%) vs. 32/132 smokers (24%),odds ratio (OR)=2.22 (95% confidence interval (CI)1.28-3.83, P=0.004). Of never smokers 22/109 (20%) were weakly RF positive and very similar to smokers 28/132 (21%).29/109 (27%) of never smokers were strongly RF positive and a similar proportion of smokers 37/132 (28%) were strongly RF positive. Finally in never smokers, only 12/109 (11%) very strongly RF positive compared to 35/132 (27%) of smokers, OR=2.89 (95% CI 1.41-5.89, p=0.004).
Conclusion: Considering female RA smokers and non-smokers, the difference in RF positivity was exclusively accounted for by an increased prevalence of a very strongly positive RF in female smokers. This suggests that smoking has an impact on very strongly positive RF levels rather than RF positivity per se without the important confounding factor of VGDF exposure.

REFERENCES

[1] Aletaha D, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis & Rheumatism. 2010;62(9):2569-81.

[2] Nielsen SF, et al. Elevated rheumatoid factor and long term risk of rheumatoid arthritis: a prospective cohort study. BMJ. 2012;345:e5244.

[3] Murphy D, et al. Nodular rheumatoid arthritis (RA): A distinct disease subtype, initiated by cadmium inhalation inducing pulmonary nodule formation and subsequent RA–associated autoantibody generation. Medical hypotheses. 2019;122:48-55.

[4] Murphy D, et al. Vapour, gas, dust and fume occupational exposures in male patients with rheumatoid arthritis resident in Cornwall (UK) and their association with rheumatoid factor and anti-cyclic protein antibodies: a retrospective clinical study. BMJ open. 2018;8(5):e021754.

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AB0128 ANTIOXIDATIVE PROTECTION AND MONOXIGENASE SYSTEM ACTIVITY OF CYTOCHROME P450 (MOG) OF NEUTROPHYLIC LEUKOCYTES (NL) FROM SYNOVIAL FLUID (SF) IN RHEUMATOID ARTHRITIS (RA)

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Background: MOG system is present not only in the liver but also in far less quantities in other organs and tissues, including SF.
Objectives: SF in RA patient contains up to 95% of NL that determines the inflammation also by inhibiting MOG.
Methods: SF of knee joints of 8 patients with RA with active synovitis and 4 donors (D) were examined. NL have been isolated by standard methods. After the application of Triton-X-100 0,1% solution, NL has been centrifuged at 25000 g for 30 minutes. The supernatant has been used in the experiment. The activity of MOG has been estimated according to the level of cytochromes P450. P420 and b5 have been estimated by applying the method of differential spectrophotometry. Active forms of oxygen have been registered by applying electron paramagnetic resonance (EPR). The activity of the antioxidant enzymes - Cu-Zn superoxiddismutase (Cu-Zn SOD), Se-glutathione peroxidase (Se-GPO) and catalase (CAT) was estimated by employing classical enzymology methods.
Results: It has been found out that in RA, the level of active oxygen forms increases by 68%. Meanwhile, the enzymes level of antioxidant defense is insufficient. In RA the activity of SOD, GPO and CAT enzymes is inhibited at 52, 66 and 39% respectively. In RA the activity of MOG (P450 and b5) in NL is 4 times lower than normal. The concentration of the inactive form of cytochrome P420, however, doubles. Nevertheless, their ratio P450/P420 (when normal = 5) in case of RA = 5,6 hardly ever changes.

Cytochrome concentration P450, P420 and b5 (nmol/g of protein), level of active oxygen forms (Units/mg of protein) and antioxidant system activity (SOD, GPO - Units/mg of protein; CAT- μmol/min·mg of protein) in NL in RA

NL	P-450	P-420	b5	Level of active forms	Cu-Zn SOD	Se-GPO	CAT
D	1,25 ± 0,4	0,025 - 0,029 (0,027)	0,43 ±0,07	15,7 ± 4,1	19,7 - 34,4 (27,1)	1,8 - 2,3 (2,1)	10,8 - 15,3 (13,1)
PA	0,3 ± 0,1	0,054 - 0,063 (0,058)	0,11 ±0,03	49,4 ± 8,6	10,7 - 15,3 (13.1)	0,6 - 0,8 (0,7)	0,76 - 0,84 (0,8)

Conclusion: A fall in the level of free radical oxidation and antioxidant defense and faster generation of active oxygen forms in RA leads to NL being destroyed and creates favorable conditions for the development of autophagy and apoptosis. The oxidative stress during RA is accompanied by a fall in the activity of MOG and activation of lipid peroxidation and cytokine production in NL as shown earlier. A general fall in the activity of MOG (P-450 and b5) in NL in RA occurs against the background of enhanced conversion of P-450 into the inactive cytochrome P-420. This fact proves that the expression of isoenzymes P450s (CYPs) is reprogrammed whilst the autoimmune pathology is being developed and there is an unbalance of the immune oxygenase homeostasis in RA.

REFERENCE

[1] Shishkin V. I. et al. Ann Rheum. Dis. 2016;75: sup.2 - 5832.

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AB0129 ULTRA-MICROSCOPIC ANALYSIS OF NURSING PHENOMENON IN SYNOVIAL TISSUE OF RHEUMATOID ARTHRITIS

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Background: Applying recent advances in electron microscope technology, cells and cell-cell interactions are observable using virtual slides, three-dimensional (3D) imaging, and serial sections of ultrathin thickness. Inflammation in rheumatoid arthritis (RA) is caused by multiple cell types, including infiltrating inflammatory cells, such as lymphocytes, neutrophils, macrophages, and spindle-shaped fibroblasts. Especially, we are focusing on fibroblast-like synoviocytes (FLSs). These cells have been reported to be positive for multiple markers including CD14, CD68, HLA-DR and vimentin, and we have shown that these cells are dendritic cells in our previous study using electron microscopy. Therefore, FLSs are presumed to function as dendritic cells. and these cells involved in the nursing phenomenon.
Objectives: The objective of this study is to investigate the chronicity mechanism of immunological inflammation in RA by using electron microscopy.
Methods: Synovial tissues collected from RA patients undergoing elbow or knee joint surgery were prepared for this study. Using wide field of view images of the synovial tissue, areas containing the nursing phenomenon were selected by using multiscale electron microscopy. 3D structures of the features were constructed from series of micrographs obtained by using focused ion beam-scanning electron microscopy and those by using transmission electron microscopy with double-axis electron tomography (DA-ET).
Results: From multiscale electron microscopy, many synovial dendritic cells and plasma cells were present in various areas of the lymphnodular infiltration. Serial cross-sectional observation with an FIB-SEM and 3D images revealed that synovial dendritic cells patronized the plasma cells, wrapping around the plasma cells, by the long slender axes. A tomogram of an ultra-thin sliced section created by using DA-ET revealed that synovial dendritic cells formed a membranous fusion with the plasma cells.
Conclusion: The nursing phenomenon involves characteristic histopathological features, which may be a factor in the chronicity of the inflammation mechanism in RA synovial tissue.

REFERENCES

[1] Ochi T, Yoshikawa H, Toyosaki-Maeda T, Lipsky PE. Mesenchymal stromal cells. Nurse-like cells reside in thesynovial tissue and bone marrow in rheumatoid arthritis. Arthritis Research&Therapy 2007; 9(1): 201.

[2] Ochi T, Sawai T, Murakami K, Kamataki A, Uzuki M, Tomita T, et al. Nurse-like cells in rheumatoid arthritis: Formation of survival niches cooperating between the cell types. Mod Rheum 2018; 29: 1-5.

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AB0130 THE EFFECTS OF METHOTREXATE ON THE VASCULAR ENDOTHELIUM

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Background: Anti-inflammatory therapy has been recently validated as a treatment option for patients with cardiovascular disease (CVD) [1]. The anti-inflammatory drug methotrexate (MTX) reduces cardiovascular risk in patients with systemic inflammatory rheumatic diseases [2]; possibly by improving endothelial function [3]. However, the molecular basis of the drug's anti-inflammatory and potential anti-atherogenic effects on the vasculature is not well described.
Objectives: Our goal was to characterize the actions of MTX on vascular endothelial cells (EC).
Methods: MTX-treated human umbilical vein (HUVEC) or aortic endothelial cells (HAEC) were analyzed by quantitative real-time PCR (qRT-PCR), immunoblotting and phospho-kinase activity arrays. EC were treated with tumor necrosis factor (TNF)-α to induce pro-inflammatory activation. EC viability and cell cycle were evaluated by flow cytometry using Annexin V and/or propidium iodide staining. For selected experiments, EC were exposed to laminar (LSS; 20dyn/cm^2) or oscillatory shear stress (OSS; 0±5dyn/cm^2, 2Hz) using a parallel plate model.
Results: Under static conditions, MTX independently increased the activity of multiple kinases in quiescent and TNFα-activated EC. MTX-activated kinases

included the mitogen-activated protein kinase (MAPK) p38 and Akt. MTX did not inhibit TNFα-induced nuclear factor kappa B (NFκB) transcriptional activation, signaling or target gene expression. However, MTX induced pro-inflammatory markers such as vascular cell adhesion molecule (VCAM)-1 in an additive manner with TNFα. Functionally, MTX did not induce apoptosis but caused S-phase cell cycle arrest, which, along with p38 and Akt activation, could be abrogated by supplementation with folinic acid.

Findings to date in EC subjected to shear stress are somewhat different. MTX had no or a mild inhibitory effect on kinase signaling in EC under LSS and OSS respectively. MTX did not affect cell proliferation nor baseline or OSS-induced VCAM-1 expression in EC under shear stress.

Conclusion: In static EC, low-dose MTX caused cell cycle arrest through folate depletion, which is a known mechanism of action in other cell types. Of note, this response was not seen in EC pre-conditioned by shear stress and emphasizes the impact of biomechanical forces on endothelial phenotype and response to exogenous stimulation. This is the first report to study the effects of MTX on EC under shear stress, which will be crucial in understanding its molecular actions on the vasculature.

REFERENCES

[1] Ridker, P.M., et al., *Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease*. N Engl J Med, 2017. 377(12): p. 1119-1131.

[2] Micha, R., et al., *Systematic review and meta-analysis of methotrexate use and risk of cardiovascular disease*. Am J Cardiol, 2011. 108(9): p. 1362-70.

[3] Guin, A., et al., *Effects of disease modifying anti-rheumatic drugs on subclinical atherosclerosis and endothelial dysfunction which has been detected in early rheumatoid arthritis: 1-year follow-up study*. Semin Arthritis Rheum, 2013. 43(1): p. 48-54.

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AB0131 THE CORRELATION OF EXPRESSION OF DIFFERENTIAL DRUG-RESISTANT PROTEINS AND INFLAMMATORY CYTOKINES IN COLLAGEN INDUCED ARTHRITIS MODEL

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease. The most characteristic patho-logical changes are chronic synovitis. At present, the combination of traditional disease-difying anti-rheumatic drugs (DMARDs) and biological agents DMARDs has improved the therapeutic effect of RA, but some RA patients still have poor response due to Multidrug resistance (MDR) phenomenon. The main mechanism of MDR is related to the ATP-binding cassette (ABC) transporter superfamily members, which increases drug efflux and reduces intracellular drug concentration. We will study how cytokines regulate the expression of ABC transporters.

Objectives: By comparing the differential expression of ABC transporter family resistance-related proteins P-gp, BCRP, MRP1 and inflammatory cytokines IL-1β, IL-2, IL-6, IL-10, TNF-α and IL-17 in CIA model mice, to investigate the correlation between Inflammatory cytokines and drug-resistant proteins.

Methods: Fourteen DBA1 mice were successfully induced by collagen and Freund's Adjuvant. According to the scores of synovial pathology, the CIA group was divided into mild, moderate-to-severe groups, another four mice were selected as control. The mRNA expressions of P-gp, BCRP, MRP1 in splenic lymphocyte cells were measured by RT-PCR. The concentrations of IL-1β, IL-2, IL-6, IL-10, TNF-α, IL-17 in serum were detected by Cytometric Bead Array(CBA). Further analyze the correlation between different inflammatory cytokines and these proteins, then study one of the proteins which is most related with cytokines by immunohistochemical (IHC) in synovium. Two independent samples were analyzed by the Mann-Whitney U test. Non-parametric Kruskal- Wallis H test was performed on multiple independent samples. The correlation between variables was used by Spearman correlation analysis.

Results:

1. Compared with the normal controls, The level of IL-6 and TNF-α in the serum of mild CIA group, moderate-severe CIA group were significantly increased (Z_1=14.383, P_1<0.05, Z_2=8.375, P_2<0.05). Compared with the mild CIA group, the level of IL-6 in serum were significantly increased in the moderate-to-severe CIA group (P<0.05),but there was no distinct difference in the TNF-α level(P>0.05).
2. In the spleen lymphocytes, there was no significant difference in the the mRNA expression level of P-gp and BCRP among the groups, but the mRNA expression level of MRP1 were significantly increased (P<0.05). Compared with the mild CIA group, the MRP1 mRNA in the moderate-to-severe CIA group was higher, there was significant difference(Z=12.634, P<0.05). There was a correlation between mRNA expression of MRP1 and P-gp(r=0.635, P=0.015).
3. The mRNA expression of MRP1 was positively correlated with IL-6 level (*r*=0.711, P=0.004).
4. The expression of MRP1 in normal group, low-level IL-6 group and high-level IL-6 group were respectively as follows::1.08(0.65,1.30), 1.40 (1.13,2.07), 1.90(1.68,2.17).
5. Compared with the controls, the cytoplasm/membrane of the knee and ankle joint synovial tissue in the CIA group was yellowish-brown, which proved that MRP1 expression was positive.

Conclusion: In the CIA arthritis model, synovial tissue lesion is not only related to inflammatory cytokines, but also related to MRP1 expression in the ABC transport resistance protein family, and it is proved that IL-6 is highly correlated to MRP1.

REFERENCE

[1] Chen Z, Shi T, Zhang L, et al. Mammalian drug efflux transporters of the ATP binding cassette (ABC) family in multidrug resistance: A review of the past decade[J].Cancer Letters, 2016, 370(1):153-164. DOI: 10.1016/j.canlet.2015.10.

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AB0132 A NOVEL TARGET FOR TREATMENT OF INFLAMMATORY JOINT DISEASES

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Background: The bile salt-stimulated lipase (BSSL) is a hitherto unrecognized player in inflammation. Animals devoid of BSSL (knockout mice) are protected from developing collagen induced arthritis (CIA) and collagen antibody induced arthritis (CAIA), and antibodies directed towards BSSL has been proven to prevent or mitigate arthritis in mouse and rat arthritis models[1]. In humans, BSSL is present in blood[2] and accumulate at sites of inflammation. Patients with acute pancreatitis have significantly increased plasma BSSL levels compared to healthy controls. Whether BSSL in blood originates from pancreas, inflammatory cells, or both remains to be elucidated.

Objectives: To determine BSSL concentration in blood samples from patients with inflammatory joint disorders and to evaluate possible relationships between circulating BSSL levels and disease-activity variables.

Methods: BSSL concentrations in plasma or serum were determined in patients with rheumatoid arthritis (RA), psoriasis arthritis (PsA), and juvenile idiopathic arthritis (JIA) by a sandwich enzyme-linked immunosorbent assay (ELISA). Correlations between BSSL concentrations and disease activity score, erythrocyte sedimentation rate (ESR), blood levels of C-reactive protein (CRP), S100A8/9, leukocyte- and neutrophil counts, proinflammatory cytokines and chemokines were analyzed using Spearman rank-order correlation.

Results: Significant correlations between BSSL concentration in plasma and disease activity score (DAS28, r_S=0.31, p=0.007), ESR (r_S=0.58, p<0.000), CRP (r_S=0.42, p=0.012), leukocytes (r_S=0.66, p<0.000), and neutrophils (r_S=0.71, p<0.000) were found in RA. The BSSL plasma concentration decreased with duration of treatment with the TNFα inhibitor infliximab, in parallel with decreasing DAS28 score.

BSSL concentration was significantly higher in sera from PsA patients with both oligo- and polyarthritis compared with healthy controls. Moreover, BSSL concentration in serum correlated significantly with S100A8/A9 and CRP concentrations (r_S=0.54, p<0.001 and r_S=0.49, p<0.001, respectively). No correlation between levels of BSSL and cytokines or chemokines were found in RA or PsA plasma or serum, respectively.

In JIA, levels of BSSL in serum correlated significantly with JIA disease activity score (JADAS27) (r_S=0.26, p=0.007), ESR (r_S=0.47, p<0.000), and leukocytes (r_S=0.32, p<0.000).

Conclusion: BSSL concentration in serum and plasma correlated with disease activity in patients with inflammatory joint disorders, i.e. RA, PsA and JIA. These data in humans support the relevance of our previous studies in rodents and

therefore also our hypothesis [1] that BSSL is a novel target for treatment of inflammatory diseases.

REFERENCES

[1] Lindquist S, Andersson EL, Lundberg L, Hernell O. Bile salt-stimulated lipase plays an unexpected role in arthritis development in rodents. PLoS One. 2012;7(10):e47006.

[2] Blind PJ, Blackberg L, Hernell O, Ljungberg B. Carboxylic ester hydrolase: a serum marker of acute pancreatitis. Pancreas. 1987;2(5):597-603.

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AB0133 HUMAN UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS AMELIORATE COLLAGEN-INDUCED ARTHRITIS VIA IMMUNOMODULATORY EFFECT ON T LYMPHOCYTES

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Background: Rheumatoid arthritis (RA) is an autoimmune disease that results in cartilage and bone destruction. Overactivation of T lymphocytes and imbalance of T lymphocyte subsets are closely related to the occurrence and development of RA. These have become important mechanisms of inflammation, immune activation, and bone destruction. RA treatment ideally involves regulation of immune abnormalities and maintenance of immune homeostasis. Mesenchymal stem cells (MSCs) are multipotent adult stem cells with high proliferation, multi-differentiation, and immune regulation. They exert immunoregulatory effects on T lymphocytes to improve RA symptoms, inhibit synovial hyperplasia, and reduce cartilage and bone erosion. However, the specific molecular mechanisms have not been fully elucidated.

Objectives: This study investigated the effect of human umbilical cord mesenchymal stem cells (hUCMSCs) on collagen-induced arthritis (CIA) in rats in comparison with that of methotrexate (MTX), a classical drug for RA. It evaluated T lymphocyte proliferation, apoptosis, differentiation, and associated inflammatory factors, futher explored the regulatory mechanism of T lymphocyte differentiation at the gene transcription level. This study elucidated that hUCMSCs play an immunoregulatory role in T lymphocytes of CIA rats through multiple pathways and explored the possible mechanism of hUCMSCs in RA treatment via the immunomodulated T lymphocyte pathway.

Methods: The effects of hUCMSCs on arthritis, radiological and synovial pathological changes in CIA rats were assessed. Flow cytometry was conducted to detect T lymphocyte proliferation, apoptosis, the ratio of Th17 and Treg cells in the spleen, and IL-17 and TGF-β levels in the sera from CIA rats. Further, Foxp3 and ROR-γT expression in the spleen were assessed by immunohistochemistry, Foxp3mRNA and ROR-γTmRNA expression were assessed by reverse transcription-polymerase chain reaction (RT-PCR).

Results: hUCMSCs inhibited proliferation and promoted apoptosis of T lymphocytes, up-regulated Foxp3 mRNA and protein expression, increased the proportion of Treg cells, down-regulated ROR-γT mRNA and protein expression, and decreased the proportion of Th17 cells in the spleens of CIA rats. Correction of the Foxp3/ROR-γT imbalance to regulate the Treg/Th17 ratio, promoted anti-inflammatory factor TGF-β expression and inhibited pro-inflammatory factor IL-17 expression, thereby improving arthritis in CIA rats, delaying radiological progression, and inhibiting synovial hyperplasia. This effect was similar to that of MTX.

Conclusion: hUCMSCs exert immunoregulatory effects on T lymphocytes in CIA rats through many pathways and are expected to become a new immunoregulatory therapy for RA.

REFERENCES

[1] KONDO Y, YOKOSAWA M, KANEKO S, et al.: Review: Transcriptional Regulation of CD4+ T Cell Differentiation in Experimentally Induced Arthritis and Rheumatoid Arthritis. Arthritis Rheumatol 2018; 70: 653-61.

[2] ANSBORO S, ROELOFS AJ, DE BARI C: Mesenchymal stem cells for the management of rheumatoid arthritis: immune modulation, repair or both?. Current Opinion in Rheumatology 2017; 29: 201-7.

[3] SUN Y KW, HUANG S, SHI B, et al.: Comparable therapeutic potential of umbilical cord mesenchymal stem cells in collagen-induced arthritis to TNF inhibitor or anti-CD20 treatment. Clin Exp Rheumatol 2017; 35: 288-95.

[4] PARK KH, MUN CH, KANG MI, LEE SW, LEE SK, PARK YB: Treatment of Collagen-Induced Arthritis Using Immune Modulatory Properties of Human Mesenchymal Stem Cells. Cell Transplant 2016; 25: 1057-72.

[5] YANG Y, HU X, CHENG L, et al.: Periplocoside A ameliorated type II collagen-induced arthritis in mice via regulation of the balance of Th17/Treg cells. Int Immunopharmacol 2017; 44: 43-52.

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AB0134 ANALYSIS OF INTESTINAL MICROBIOME PROFILE OF PATIENTSWITH ESTABLISHED RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS

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Objectives: Describe the intestinal microbiome profile in RA patients and analyze the mechanisms through which intervenes in the pathogenesis RA.

Methods: Design: Controlled, observational, cross-sectional study of established RA cohort. Patients: Forty consecutive RA patients (ACR/EULAR 2010 criteria) >16 years, selected from a prospective inception cohort (2007-2011) and 40 sex-age matched healthy controls. Protocol: Cases and controls were evaluated by a rheumatologist. Clinical data of disease activity were collected during the follow-up and analytical values were determined. Fecal samples were frozen within 24 hours of collection. Main outcome: Fecal samples exam. Microbial DNA was extracted from fecal samples using QIAamp DNA stool Mini kit. The concentration and quality of DNA was determined by Nanodrop. Secondary Other variables: Demographic, clinical-analytical and therapies (DMARDs). Statistical analysis: Analysis of microbiota prole: UniFracPCoA (Principal Coordinate Analysis) was performed with the abundance data of operational taxonomic units (OTU) by means of the variancecovariance matrix implemented in Quantitative Insights Into Microbial Ecology(QIIME). The relative abundance of each OTU (taxa) was compared using a Wilcoxon test. The variations of abundance and diversity were compared by ANOSIM pathway. The calculation of α and β-diversity was carried out using QIIME.

Results: Most of subjects were women (75%) (table). In RA patients, the average DAS28 was 3.6. β-diversity data showed that patients tend to dier from healthy subjects according to their microbiota (p = 0.07). Patients with RA exhibited decreased gut microbiome diversity compared with controls, although was not statistically signicant. Regarding in species richness, the analysis suggested an increase of the Collinsella aerofaciens species and enterococcus genera in patients compared with controls. Likewise, an increase of arginine deaminase activity was observed, which belonged, in approximately 90%, to the RA genes of the genus Collinsela.The multivariate analysis identified ACPA positive (ß [95% CI], 0.33 [27.4-390]), smoking (0.3 [8.8-256.4]) and age (-0.3 [27.4-390.0]) as factors associated with Collinsela.Also, we observed a decrease in other bacterial lineages. On the other hand, RA patients showed an altered metabolic capacity for the transport of zinc and copper.

Conclusion: These observations suggest a dysbiosis in RA patients, resulting from the abundance of certain bacterial (i.e Collinsela) and decrease of other bacterial lineages. These alterations could inuence in a signicant way in the perpetuation of the autoimmunity of the disease.

VARIABLE	RA n=40	Control n=40	P - VALUE
Age (years), mean (SD)	58,5 (9,4)	58,5 (9,4)	0,998
Sex (female), n (%)	30 (75,0)	30 (75,0)	1,000
Rheumatoid factor, n (%)	32 (80,0)	2 (5,0)	<0,001
Anti–cyclic citrullinated peptide, n (%)	28 (70,0)	0 (0,0)	<0,001
DAS28 average value, mean (SD)	3,6 (0,5)		-
Metotrexato (%)	72,5	-	
biologic disease-modifying antirheumatic drugs (%)	37,5	-	

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AB0135 LEVELS OF MYOKINES AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Myokines, such as irisin and myostatin, are cytokines and growth factors mainly expressed in skeletal muscle, which is also their primary target tissue. They are released into circulation and exert a variety of systemic effects promoting crosstalk among different tissues [1]. Irisin is known to retrieve disuse-induced bone loss by stimulating the osteoblast pathways, while myostatin was demonstrated to be highly expressed in the synovial tissues of rheumatoid arthritis (RA) subjects, with direct role in osteoclastogenesis [2, 3].
Objectives: To investigate whether myokines serum levels can predict one-year radiographic progression in patients with RA.
Methods: Forty female patients with RA, according to ACR/EULAR 2010 classification criteria, were included in the study. Blood samples were collected, and ELISA was used to measure serum levels of irisin and myostatin. Radiographs of hands and feet, taken within three months of the blood collection and a year later, were evaluated using the Sharp-van der Heijde (SvH) score to verify the one-year radiographic progression. The RA activity was assessed by disease activity score based on evaluation of 28 joints (DAS28-ESR). Statistical analysis included Mann-Whitney U test and Spearman correlation. A value of $p<0.05$ was considered significant.
Results: The mean age of RA patients was 53 years old, mean DAS28-ESR was 4.09, mean disease duration was 11.2 years and mean BMI was 27.33 kg/m^2. The mean serum levels of irisin and myostatin were respectively 25.61 ± 8.25 ng/ml and 3011.28 ± 1271.11 pg/ml. Considering radiographic progression, the mean values of SvH score were 28.3 and 31.3 in the baseline and after one year, respectively, resulting in a mean ΔSvH of 3. Over one year, 89.2% of the patients presented radiographic progression (ΔSvH score >0), and 10.8% presented rapid progression (ΔSvH score >5).

SvH score	Irisin (ng/ml)	Myostatin (pg/ml)
ΔSvH = 0	31.66 ± 10.66	2943.94 ± 719.96
ΔSvH > 0	26.67 ± 7.28	2996.90 ± 1356.66
ΔSvH > 5	31.61 ± 8.31	3255.81 ± 975.68

Conclusion: The serum levels of irisin and myostatin were not correlated with one-year radiographic progression. There was a tendency of increased myostatin levels in patients with rapid progression compared to patients with no progression. More studies are needed to investigate whether the myokine levels in the joint environment differ from the circulating concentration.

REFERENCES

[1] Giudice J, et al. Muscle as a paracrine and endocrine organ. Curr Opin Pharmacol. 2017 Jun;34:49-55.
[2] Colaianni G, et al. The myokine Irisin increases cortical bone mass. Proc Natl Acad Sci U S A. 2015 Sep 29;112(39):12157-62.
[3] Dankbar B, et al. Myostatin is a direct regulator of osteoclast differentiation and its inhibition reduces inflammatory joint destruction in mice. Nat Med. 2015 Sep;21(9):1085-90.

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AB0136 EVALUATION OF ANALGESIC ACTIVITY OF ALLOPURINOL AND FEBUXOSTAT IN EXPERIMENTAL ANALGESIC MODELS IN MICE

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Background: Allopurinol and febuxostat are xanthine oxidase inhibitor which are used in the treatment of hyperuricemia and gout. Pain is one of the important symptoms in gout patients.
Objectives: The present study is to evaluate the analgesic activity of allopurinol and febuxostat in two analgesic models in mice.
Methods: The analgesic activity of allopurinol (39 mg/kg) and febuxostat (15.6 mg/kg) was evaluated by using central analgesic model of Eddy's hot plate and peripheral analgesic model of acetic acid induced writhing. Both drugs were compared with the positive control, pentazocin for hot plate method & aspirin for the Writhing method. Also both allopurinol and febuxostat were compared with each other.
Results: Both allopurinol and febuxostat showed significant increase in reaction time at various time periods in hot plate method & also showed significant delay in onset of writhing as well as decrease in number of writhes in writhing method. As compared to positive control result allopurinol and febuxostat result were lower. Febuxostat shows better analgesic activity as compared to that of allopurinol.
Conclusion: Allopurinol and febuxostat exhibited analgesic activity in both central and peripheral models of pain.
Disclosure of Interests: None declared
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AB0137 ROLE OF VIMENTIN AS A TARGET OF ANTIBODIES AGAINST CARBAMYLATED PROTEINS IN RHEUMATOID ARTHRITISPATIENTS

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Background: Patients with Rheumatoid Arthritis (RA) have an increased risk of cardiovascular diseases (CVD). Inflammation and autoantibodies indipendently promote endothelial dysfunction, which is the earliest, reversible stage of atherosclerosis. *In vitro* studies have demonstrated that antibodies against carbamylated proteins (anti-CarP), recently described in RA patients, can induce the production of proatherosclerotic molecules like *Vascular Cell Adhesion Molecule* (VCAM-1) and activate *Interleukin-1 Receptor-Associated Kinase* (IRAK-1), *Nuclear Factor kB* (NF-kB), *inducible Nitric Oxide Synthase* (iNOS) in endothelial cells (1,2). Moreover, anti-CarP are associated to endothelial dysfunction and subclinical atherosclerosis in RA patients (3).
Objectives: Aims of the present study were: 1) to analyze the role of vimentin as a target of autoantibody response in the serum of patients with RA and 2) investigate the expression of vimentin and carbamylated proteins in endothelial cells.
Methods: Consecutive RA patients were enrolled in this study. Vimentin was carbamylated and used as an antigen for the detection of anti-Vimentin Carbamylated antibodies (CarVim), through immunoenzymathic methods. Cells were incubated with anti-vimentin and carbamylated antibodies. The presence of vimentin and carbamylated proteins was investigated by immunofluorescence on the immortalized endothelial cell line EA.hy 926.
Results: Eighty-eight (88) RA patients were enrolled in this study (F:M = 79:9, mean age = 56 ± 13 years). Anti-CarVim antibodies were present in 9% of the patients with a mean titre of di 442 aU/ML (IQR 303 aU/ml). Vimentin and carbamylated proteins were detected in the endothelial cells by immunofluorescence (Figure 1).

Conclusion: The results of this study confirm that Vimentin is one of the antigenic targets of anti-CarP antibodies present in the serum of RA patients. The presence of carbamylated proteins and vimentin in endothelial cells suggests that anti-CarVim could bind the modified protein and determine endothelial activation and subsequent endothelial dysfunction.

REFERENCE

[1] Pecani A & Alessandri C et al, Arthr Res Ther 2016
[2] Pecani A et al, Reumatismo 2017
[3] Spinelli FR & Pecani A et al, BMC Musculoskelet Disord 2017.

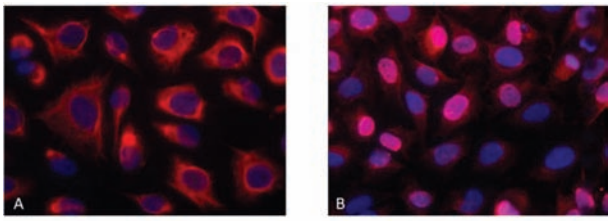


Figure 1. Immunofluorescence on endothelial cell line EA.hy 926 demonstrating the presence of Vimentin (A) and Carbamylated (B) proteins.

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AB0138 INDIVIDUALS WITH ACPA POSITIVE RA PRESENTING INITIALLY WITH PALINDROMIC SYMPTOMS ARE SIGNIFICANTLY LESS LIKELY TO BE RHEUMATOID FACTOR POSITIVE THAN CLASSICAL ACPA POSITIVE RA; COULD THE AETIOPATHOGENESIS DIFFER BETWEEN THESE TWO DISTINCT TYPES OF ACPA POSITIVE RA?

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Background: It remains unclear whether ACPA positive RA presenting initially with palindromic symptoms (PRA) has the same underlying pathophysiology as ACPA positive RA presenting without palindromic symptoms (classical ACPA positive RA). The lung is an initiating site in RA development and rheumatoid factor (RF) is generated within bronchial associated lung tissue (1). RF in combination with ACPA immune complexes can induce TNF∝ from joint macrophages and potentially induce synovitis (2). Unsurprisingly a positive RF is a risk factor for RA development. Alternatively, palindromic rheumatism in the absence of RA occurs commonly in RF negative individuals (58%) (3). Therefore this form of explosive synovitis often occurs independently of RF, but is commonly associated with ACPA positivity (56%) (3).
Objectives: To identify whether classical ACPA positive RA differs in terms of RF positivity compared to ACPA positive PRA.
Methods: A retrospective case note observational study was undertaken to identify ACPA positive RA patients with or without a palindromic onset. All patients fulfilled the RA 2010 EULAR/ACR classification criteria (4). Patients were stratified for a history of smoking. RF was measured with Tina-quant Rheumatoid Factors II Test System, by Roche Diagnostics Corporation at the time of diagnosis. A value of < 14 IU/ml was considered as negative, weakly positive (14-42 IU/ml) and strongly positive (>42.1 IU/ml) as per EULAR/ACR guidelines (4).
Results: 99 classical ACPA positive RA and 35 ACPA positive PRA were identified. The median RF for PRA was significantly lower than the non-PR onset RA group (25 vs 86 IU/mL, p = 0.001).Comparing classical ACPA positive RA with ACPA positive PRA revealed 8/99 (8%) vs. 8/35 (23%) to be RF negative, 23/99 (23%) vs. 11/35 (31%) to be RF weakly positive and 68/99 (69%) vs. 16/35 (46%) to be strongly RF positive. Classical RA patients were significantly less likely to be RF negative, odds ratio 0.25 (95%CI 0.09-0.73), P=0.01. RA patients were significantly more likely to be strongly RF positive OR 4.32 (1.88-9.89), P=0.0005.
Classical ACPA RA patients were more likely to be smokers than ACPA PRA patients 60/99 (61%) vs. 18/35 (51%), however this was not significant 0R 1.48 (95 CI 0.68-3.2), p=0.99. Classical ACPA RA patients accumulated a greater number of pack years, median of 17 vs 5, however, the difference was not significant p=0.12.
Conclusion: The majority of ACPA RA patients presenting with palindromic symptoms have either a negative or weakly positive RF (54%). This contrasts with classical ACPA RA (31%) and suggests that a strongly positive RF is more important in the pathogenesis of classical ACPA RA than ACPA PRA. We suggest that a strongly positive RF and palindromic rheumatism are likely to be independent risk factors for ACPA positive RA.

REFERENCES

[1] Rangel-Moreno J, et al. Inducible bronchus-associated lymphoid tissue (iBALT) in patients with pulmonary complications of rheumatoid arthritis. The Journal of clinical investigation. 2006 116(12):3183-94.
[2] Sokolove J, et al. Rheumatoid factor as a potentiator of anti–citrullinated protein antibody–mediated inflammation in rheumatoid arthritis. Arthritis & rheumatology. 2014; 66(4):813-21.
[3] Salvador G, et al. Prevalence and clinical significance of anti-cyclic citrullinated peptide and antikeratin antibodies in palindromic rheumatism. An abortive form of rheumatoid arthritis? Rheumatology. 2003; 42(8):972-5.
[4] Aletaha D, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis & Rheumatism. 2010; 62(9):2569-81.

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AB0140 EFFECT OF THE CO-TREATMENT WITH BACTERICIDAL/PERMEABILITY-INCREASING PROTEIN AND HYALURONIC ACID IN AN IN VIVO MODEL OF ARTHRITIS

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Background: Bactericidal/permeability-increasing protein (BPI) is an antibacterial, anti-inflammatory and antiangiogenic glycoprotein which has been detected in synovial fluid of patients with different arthritis [1].
Objectives: To investigate the effect of BPI alone or in combination with hyaluronic acid (HA) in a mouse model of collagen-induced arthritis (CIA).
Methods: CIA was induced in C57Bl/6 mice (n=12 per condition) by immunization with type II collagen/complete Freund's adjuvant emulsion at days 0 and 21 [2]. Development and severity of arthritis were monitored by measuring paw swelling with a caliper and scored (0-5) every 2 days. Arthritic mice (paw score=2) were intraperitoneally injected with 200 µl of BPI (50 µg/ml) in PBS in the presence or absence of HA (0.02%). Treatment and arthritis evaluation were carried out twice a week for 2 months. Untreated mice or animals that received HA alone (0.02%) were used as controls. At the experiment endpoints, mice were sacrificed to collect paw and blood samples. Hind paws were processed for histological analysis to assess inflammation, pannus formation, cartilage damage and bone resorption in ankle joints (score 0-5). CXCL1, TNF, IL-6, IL-1β and VEGF serum levels were determined by ELISA.
Results: All mice reached an arthritis score of 2 after 28-33 days and showed a progressive worsening of clinical signs that picked at day 49-56, and continued during the entire follow-up period only in control groups. At the end of the experiment, hind paw swelling and scores were lower in BPI-mice (paw thickness=4.76 ±0.33 mm; score=4.5±0.5) than in untreated mice (paw thickness=6.39±0.95 mm; score=5). Histological analysis revealed leukocyte infiltration (score 3.00±1.73), synovial proliferation (score 3.50±0.71), cartilage damage (score 2.50±0.71) and mild bone resorption (score 1.50±1.71) in ankle joints of untreated controls. All of these histological changes were decreased (50–80%) in the group that received BPI. CIA induction led to high levels of CXCL1 (834.08±68.8 pg/ml), TNF (277.72 ±15.24 pg/ml), IL-6 (376.04±46.33 pg/ml), IL-1β (656.80±45.6 pg/ml), and VEGF (347.48±75.58 pg/ml) which were reduced with BPI treatment by 1.9, 14.6, 1.8, 2.9 and 2.7 fold, respectively. Animals injected with HA alone displayed slight improvement of all parameters evaluated but the differences were not significant. The combined use of BPI and HA showed paw swelling (3.65±0.37 mm), arthritic score (0.67±0.75) and histological scores for pannus formation (0.4±0.55), inflammation (0.20±0.45), cartilage damage (0.0±0.0) and bone resorption (0.0±0.0) more remarkably reduced than their separate use. In addition, the lowest levels of CXCL1 (11.44±1.31 pg/ml), TNF (4.46±2.23 pg/ml), IL-6 (129.30±14.25 pg/ml), IL-1β (81.58±7.64 pg/ml), and VEGF (107.80±32.64 pg/ml) were observed in serum of mice co-injected with BPI and HA.
Conclusion: This study shows that BPI attenuates progression of CIA in mice, and this effect is greatly enhanced by co-administration of HA. The combined use of BPI and HA represents an interesting perspective for a new potential intervention in the treatment of arthritis.

REFERENCES

[1] Punzi L, et al. Clin Exp Rheumatol 2000;18:613-5
[2] Bevaart L, et al. Methods Mol Biol 2010;602:181-92

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AB0141 THE ROLE OF AIR POLLUTION ON EXTRACELLULAR VESICLES AS A POTENTIAL PRO-INFLAMMATORY STIMULUS IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an heterogeneous chronic autoimmune disorder potentially leading to a progressive joint damage with great impact on quality of life. RA pathogenesis is complex and involves environmental factors that trigger disease in genetically susceptible individuals. Extracellular vesicles (EVs) have been described to play an important role in RA pathogenesis and to modulate autoimmune response following environmental exposures, such as air pollution.

Objectives: Our aim was to evaluate the effects of particulate matter (PM) with aerodynamic diameter ≤ 10 μm (PM_{10}) and ≤ 2.5 μm ($PM_{2.5}$) on EVs in RA and osteoarthritis (OA) as control.

Methods: Plasma EVs were analyzed by Nanosight and flow cytometry: CD14 (monocyte/macrophage), CD61 (platelet), CD25 (T-reg), human endogenous retrovirus w (HERV-w), human leukocyte antigen G (HLA-G). Demographic and clinical data were collected for each patient. Plasma EV concentrations were measured in RA and OA patients and were analyzed by generalized linear regression models. Daily PM concentrations, estimated by Regional Environmental Protection Agency at municipality resolution, were used to assign short-term exposure (mean of the 7 days preceding the evaluation) to each patient.

Results: 12 consecutive patients with RA (median age 68.1, median disease duration 9.3, 12 female, median DAS28 2.25, 5 positive for rheumatoid factors, 6 positive for anti-citrullinated peptide antibodies) and 12 patients with OA (median age 67.1, median disease duration 9.3, 8 female) were enrolled. Analysis of EVs concentration, according to their dimensions, showed a negative association of exosomes (63-92nm) in RA compared to OA ($p<0.05$). The increase of $PM_{2.5}$ led to a decrease of CD14+ microvesicles (MV) (β=-0.13; $p<0.01$) and CD61+ (β=-0.08; $p=0.05$) in RA, and of HERV-w in OA (β=-0.09; $p=0.01$). Similar results were observed analyzing PM10 exposure. PM exposure was not observed to modify CD25+ and HLA-G+ MV release both in RA and OA patients (table below). Moreover, we compared plasmatic EVs mean concentration among patients with RA and OA, and we found a significant difference in the two groups in the HERV-w subpopulations (β_{AR} vs β_{OA} = 0.044 vs -0.091; p = 0.011). In RA patients we also observed a significant association between EVs (CD14+ and HLA-G+ MV) and DAS28 (β_{CD14+} = 0.03; p = 0.01 and β_{HLA-G+} = 0.04; p = 0.02). Finally, we observed a negative association between exosomes and C-reactive protein (CRP) (β=-1.99; p=0.03), and a positive association between HERV-w and Erythrocyte Sedimentation Rate (ESR) (β=0.53; p=0.06), and HLA-G+ and ESR (β=0.29; p=0.01).

EV	RA			OA		
	β	SE	P-value	β	SE	P-value
$PM_{2.5}$ exposure						
EV count						
Total EV	-0.04	0.02	0.08	0.02	0.03	0.49
Exosomes	-0.01	0.02	0.60	0.01	0.03	0.66
MV	-0.02	0.02	0.36	0.01	0.03	0.66
MV subtypes						
CD14+	-0.13	0.03	**<0.01**	-0.04	0.04	0.25
CD61+	-0.08	0.04	**0.05**	0.00	0.05	0.99
CD25+	-0.02	0.02	0.48	-0.02	0.03	0.48
HERV-w+	0.04	0.03	0.08	-0.09	0.04	**0.01**
HLA-G+	-0.03	0.02	0.18	-0.01	0.03	0.67
PM_{10} exposure						
EV count						
Total EV	-0.01	0.01	0.52	0.02	0.02	0.43
Exosomes	-0.02	0.02	0.26	0.04	0.03	0.14
MV	-0.01	0.01	0.63	0.02	0.03	0.52
MV subtypes						
CD14+	-0.09	0.02	**<0.01**	-0.01	0.04	0.72
CD61+	-0.06	0.03	**0.02**	-0.02	0.05	0.76
CD25+	-0.01	0.01	0.53	-0.02	0.03	0.50
HERV-w+	0.03	0.02	0.07	-0.07	0.04	**0.05**
HLA-G+	-0.01	0.02	0.46	0.00	0.03	0.97

Conclusion: The results of this pilot study show that PM exposure modulates the release of EVs carrying HLA-G and/or HERV-w in RA patients. This might be interpreted as an attempt of immune system to counteract the perturbation provoked by a pro-inflammatory environmental stimulus. More research is still needed to tie the genetic, epigenetic and environmental factors together and to determine their roles in RA pathogenesis.

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AB0142 IMMUNOREGULATORY ROLES OF B^2 INTEGRINS IN RHEUMATOID ARTHRITIS

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Background: Evidence is mounting that β^2 integrins, adhesion receptors that exist in a continuum between 'inactive' and 'active', facilitate not only inflammation but are also important in immune regulation. Elucidating their role on dendritic cells (DCs) is hereby of special interest due to the pivotal role DCs play in immune activation and tolerance. Previous research suggests that β^2 integrin-mediated immunoregulation is prominent in murine DCs[1], but a similar role in human cells has yet to be characterised.

Objectives: We hypothesised that altered β^2 integrin expression, activation or function in DCs may contribute to the immune dysregulation prevalent in autoimmune disorders such as Rheumatoid Arthritis (RA). To this end, we aimed to characterise β^2 integrin expression and activation in antigen-presenting cell (APC) populations from people with RA compared to healthy controls.

Methods: Using flow cytometry, we can detect both total and activated β^2 integrin subunits (CD11a, CD11b, CD18) on different APC populations present in human blood and synovial fluid.

Results: Based on our results so far, we found CD11b expression to be equivalent in APC populations between patients with RA and healthy controls. However, expression of both the total and active forms of CD11a was reduced across several APC populations in RA patients compared to healthy controls, with cDC2s (CD1c+) showing the most striking reduction. Interestingly, we found that cDC2s from matched RA synovial fluid samples express even lower levels of CD11a than blood cDC2s. Previous studies show that cDC2s are the DC population predominant in the RA joint, characterised by an increased capacity to attract T cells to the site of inflammation and activate self-reactive T cells[2]. As CD11a is described to have largely pro-inflammatory effects by contributing to immune cell contacts and recruitment to inflammatory sites, this could suggest that contrary to our initial hypothesis, cells downregulate CD11a as a means of limiting the aberrant inflammation present in the disease.

Furthermore, cDC2s from RA patients in remission express lower levels of active CD11a compared to those from patients with high disease activity. Upon stimulation of cDC2s with PMA, cells from patients with active disease decrease their activation of CD11a, while neither healthy controls nor patients in remission show any change in CD11a activation. This might suggest that CD11a activation is differentially regulated in patients with active disease, while remission signifies a return to a state of normal CD11a regulation on cDC2s. In additional work on exploring monocyte-derived DCs (MO-DCs) as a potential therapeutic for RA, we did not detect a reduction in CD11a expression in activated MO-DCs, suggesting that the effect may be specific to settings of chronic inflammation that cannot be easily modelled in vitro.

Conclusion: Further interrogation of our integrin expression data, including disease stratification, together with functional studies on RA patient cDC2s compared to MO-DCs, is currently under way to fully investigate the role of this immunoregulatory pathway in autoimmune disorders. In doing so, we will explore β^2 integrin subunits and signalling pathways as potential therapeutic targets in RA.

REFERENCES

[1] Morrison, Vicky Louise, et al. "Loss of beta2-integrin-mediated cytoskeletal linkage reprogrammes dendritic cells to a mature migratory phenotype." Nature communications 5 (2014): 5359.

[2] Moret, Frederique M., et al. "Intra-articular CD1c-expressing myeloid dendritic cells from rheumatoid arthritis patients express a unique set of T cell-attracting chemokines and spontaneously induce Th1, Th17 and Th2 cell activity." Arthritis research & therapy 15.5 (2013): R155.

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AB0143 PERIODONTITIS AND SALIVA ANTIBODIES TO CITRULLINATED PEPTIDES IN RHEUMATOID ARTHRITIS

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Background: Mucosal immunity, involving antibodies against citrullinated peptides (ACPA), is a prevailing hypothesis concerning the pathogenesis of rheumatoid arthritis (RA). The oral mucosa is a possible site that is involved. Several epidemiological studies have found an association between RA and periodontitis, and periodontal inflammation has been suggested as a possible pathogenic factor.

In established RA, periodontitis has been associated with ACPA positivity (1) although a recent large study (2) did not find any association between periodontitis and IgG ACPA. Previous studies only evaluate ACPA in serum, and as local mucosal immune responses are likely involved in periodontitis, saliva antibodies are of interest to investigate. Saliva IgA ACPA has in a pilot study of RA patients been associated with lower disease activity and less erosions(3), but has not previously been evaluated in relation to periodontitis.

Objectives: To evaluate if saliva or serum ACPA is associated to periodontitis, in patients with RA.

Methods: In this population-based cohort of patients with RA (n=132), we included all patients with RA older than 61 years, living in Karlskrona in southern Sweden, between October 21, 2013 and January 7, 2015.

The patients underwent a clinical examination by a rheumatologist, a dental clinical examination by a dental nurse and a panorama radiograph of the jaws and teeth. Periodontitis was defined as a distance from the cement-enamel junction (CEJ) to the bone level ≥ 5 mm, as defined by the radiographic assessment, at ≥ 30% of interproximal sites.

We analysed antibodies against second generation cyclic citrullinated peptides (anti-CCP) in enzyme immunoassays in serum and saliva. Saliva samples were analysed in parallel for anti-CCP and anti-CAP, the arginine containing control peptide. Serum ACPA positivity was defined as the 99th percentile of healthy controls. In saliva, a positive test was defined as a difference in optical density (OD) for IgA anti-CCP and IgA anti-CAP (delta OD)> 0.

Results: Saliva IgA ACPA was found in 11% of RA patients with periodontitis and in 24% of RA patients with no periodontitis (p=0.052). There was no difference between the groups concerning IgG or IgA ACPA in serum.

Table 1. Demographic and laboratory characteristics of the study participants

	Patients with RA and periodontitis N=80	Patients with RA no periodontitis N=52	P value*
	Mean or percent	Mean or percent	
Age at inclusion, years	71.4	69.0	0.034
Females%	71%	69%	0.847
Disease duration, years	12.1	12.3	0.930
DAS28 ESR	3.01	2.84	0.403
DAS28 CRP	2.81	2.80	0.936
Erosions in hands or feet %	59%	53%	0.584
Biologics currently%	21%	23%	0.806
Biologics ever%	36%	44%	0.577
Smoker (ever vs never)%	64%	60%	0.714
Serum IgG ACPA positive,%	66%	69%	0.849
Serum IgA ACPA positive,%	35%	43%	0.461
Saliva IgA ACPA positive,%	24%	11%	0.052

*Student's T-test was used for continuous variables and Fischer's exact test for categorical variables.

A logistic regression analysis adjusting for gender, age and smoking showed an Odds Ratio of 0.299 (95% CI=0.096-0.929, p=0.037) for RA patients with periodontitis to be positive for saliva IgA ACPA, compared to RA patients with no periodontitis.

Conclusion: A weak, negative, correlation was observed between periodontitis and saliva IgA ACPA, when adjusting for age, sex and smoking. No correlation was observed between periodontitis and IgA or IgG ACPA in serum. In this cohort of patients with established RA, our findings do not support the hypothesis that periodontitis leads to increased formation of IgA ACPA in saliva or serum.

REFERENCES

[1],Dissick
A, et al. J Periodontol. 2010;81(2):223-30.
[2] Eriksson K, et al. PloS one. 2016;11(5):e0155956.
[3] Svärd A, et al. Immunobiology. 2013;218(2):232-7.

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AB0144 EFFECTS OF AB501 (CERTOLIZUMAB MICE EQUIVALENT) IN ARTHRITIS INDUCED BONE LOSS

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Background: Rheumatoid arthritis (RA) is a chronic immune-mediated inflammatory disease, which causes local and systemic bone damage.

Objectives: The main goal of this work was to analyze, how treatment intervention with Ab501 (certolizumab mice equivalent) prevents the disturbances on bone structure and mechanics induced by arthritis.

Methods: Thirty one DBA/1 collagen-induced arthritis (CIA) mice were randomly housed in experimental groups, as follows: arthritic untreated (N=10), preventive intervention with ab501 2 days before arthritis induction (N=10) and treatment intervention upon arthritis onset with ab501 (N=11). A non-induced group (N=5) was used as a control. Mice were monitored during 70 days after disease induction for the inflammatory score, ankle perimeter and body weight. Non-induced mice were used as controls. After 70 days of disease progression mice were sacrificed and bone samples were collected for histology, micro-computed tomography (μCT) and 3-point bending analysis. In addition, blood samples were also collected for bone turnover markers quantification. Statistical differences were determined with Mann–Whitney tests using GraphPad Prism (GraphPad, California, USA). Data were expressed as median with interquartile range. Differences were considered statistically significant for p<0.05.

Results: Results showed that Ab501 administration was able to control and abrogate disease development both in preventive and early therapeutic intervention. μCT results revealed that ab501 was able to preserve bone structure when delivered before arthritis induction.

Conclusion: Ab501 preventive administration was able to control inflammation and prevent the degradative effects of arthritis on trabecular bone structure.

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AB0145 THE INHIBITION OF JAK PATHWAY WAS ASSOCIATED WITH REDUCTION OF AUTOPHAGY IN SYNOVIOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS

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Background: The pathway of Janus tyrosine kinases (JAKs) has a central role in the pathogenesis of rheumatoid arthritis (RA) by regulating multiple immune functions and cytokine production. The orally available JAK inhibitor CP-690,550, named tofacitinib, is able to inhibit Jak1, Jak2 and Jak3 and it showed a great clinical efficacy in RA patients not responding to methotrexate or TNF-inhibitors (1). Autophagy, a highly conserved mechanism involved in the degradation of intracellular components, was found to be dysregulated in several autoimmune diseases including RA (2). In fact, fibroblasts like synoviocytes (FLS) from RA patients showed a resistance to apoptosis associated with the induction of autophagy (3). Maeshima and colleagues recently demonstrated that tofacitinib suppressed proliferation, but not apoptosis, of CD4+ T cells derived from the synovium (4), but to date there are no data on the effect of inhibition of JAK pathway on autophagy.

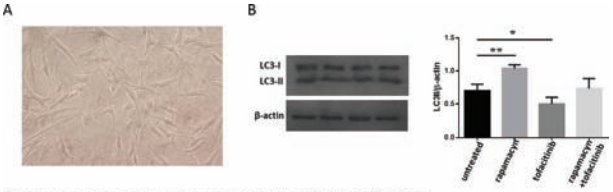
Objectives: Since hyperactive autophagy has been associated with impaired apoptosis of RA FLS, the aim of the study was to investigate the role of tofacitinib in modulating autophagy and apoptosis in FLS from RA patients.

Methods: Primary RA FLS isolated from RA biopsies (Figure 1A) were cultured in presence of autophagy inducer rapamycin (as control condition) and tofacitinib (1μM). After 24h of culture, autophagy was evaluated both by flow cytometry and

western blot analysis. Apoptosis was analyzing by annexin V (AV) and propidium iodide (PI) apoptosis detection kit by flow cytometry.
Results: As expected tofacitinib inhibited the expression of the phosphorylated form of STAT3 ($p<0.01$). Rapamycin caused an increase in autophagy, while the levels of autophagy marker LC3-II were reduced after treatment with tofacitinib in vitro ($p<0.001$ and $p=0.02$, respectively, Figure 1B). In addition, the analysis of autophagic vacuoles by specific fluorescence dye confirmed the reduction of autophagy in RA-FLS treated with tofacitinib. The percentage of annexin V-positive apoptotic cells was not influenced by the treatment with tofacitinib.
Conclusion: The results of this study elucidated a new mechanism of action of tofacitinib related to autophagy modulation and led to a better understanding of the role of autophagy in RA. This study was supported by an unconditioned Research grant from Pfizer Inc.

REFERENCES

[1] Burmester GR, Blanco R, Charles-Schoeman C, et al. Tofacitinib (CP-690,550) in combination with methotrexate in patients with active rheumatoid arthritis with an inadequate response to tumour necrosis factor inhibitors: a randomised phase 3 trial. Lancet 2013; 381: 451-60.
[2] Vomero M, Barbati C, Colasanti T, et al. Autophagy and Rheumatoid Arthritis: Current Knowledges and Future Perspectives. Front Immunol. 2018;9:1577.
[3] Shin YJ, Han SH, Kim DS, et al. Autophagy induction and CHOP underexpression promotes survival of fibroblasts from rheumatoid arthritis patients under endoplasmic reticulum stress. Arthritis Res Ther. 2010; 12: R19.
[4] Maeshima K, Yamaoka K, Kubo S, et al. The JAK inhibitor tofacitinib regulates synovitis through inhibition of interferon-γ and interleukin-17 production by human CD4+ T cells. Arthritis Rheum. 2012;64:1790-8.



A. Image of fibroblast-like synoviocytes obtained from synovial tissue of RA patients during total knee replacement and used for in vitro experiments. **B.** Western blot analysis of autophagy marker LC3-II after in vitro treatment with tofacitinib.

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AB0146 IDENTIFICATION A MARKED INFLAMMATION MEDIATED CARDIAC DYSFUNCTION DURING THE DEVELOPMENT OF ARTHRITIS IN COLLAGEN INDUCED ARTHRITIS MICE

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Background: Systemic inflammation is strong linked to the increased risk of cardiovascular diseases (CVD) in rheumatoid arthritis (RA)[1]. Increased cardiovascular risk in RA patients can not be fully explained by the traditional risk factors, such as hypertension, obesity, diabetes, age and smoking[2,3]. Much more work is needed to elucidate the mechanism of chronic inflammation bridging RA and cardiovascular disease.
Objectives: To investigate the cardiac changes during the development of arthritis in collagen induced arthritis (CIA) mice and to explore the potential role of inflammation on cardiac dysfunction in RA.
Methods: Arthritis severity was evaluated using clinical indices, micro-computed tomography and histopathology. Cardiac function was determined by transthoracic echocardiography at week 5, 7, 9 and 11 after immunization in mice. At week 7 (day 50), mice joints and hearts were removed for pathological study, and cardiomyocytes and cardiac fibroblasts were isolated using Langendorff perfusion method *Ex vivo* to measure expression of inflammatory and cardiac-related genes by real time PCR. The expression of key molecule in cardiac dysfunction (β-MHC) was also tested in H9c2 cardiomyocytetreated with sera derived from CIA mice or RA patients.
Results: At day 50 after immunization, cardiac function in CIA mice was prominently reduced as evidenced by decreased ejection fraction (EF) and fractional shortening (FS), increased left ventricular end-systolic volume (LVESV) and internal systolic diameter (LVIDs). Accordingly, enhanced inflammatory cells infiltration and fibrosis were identified in ventricular tissues pathologically, and increased inflammatory genes expression including TNF-α, IL-6, IL-17 and MMP3 detected in isolated ventricular cardiomyocytes and cardiac fibroblasts from CIA mice. Furthermore, H9c2 cells treated with sera from CIA mice or RA patients exhibited high levels of β-MHC.
Conclusion: Joint inflammation is associated with an obvious cardiac dysfunction and enhanced inflammation infiltration and inflammatory cytokines production in cardiomyocytes and cardiac fibroblasts during CIA development. Our data provide the direct evidence that inflammation contributes to development of cardiac diseases in RA patients.

REFERENCES

[1] SOLOMON DH, GOODSON NJ, KATZ JN, *et al.*: Patterns of cardiovascular risk in rheumatoid arthritis. Ann Rheum Dis. 2006;65:1608-12.
[2] JAFRI K, BARTELS CM, SHIN D, GELFAND JM, OGDIE A: Incidence and management of cardiovascular risk factors in psoriatic arthritis and rheumatoid arthritis: A population-based study. Arthritis Care Res (Hoboken). 2017;69:51-7.
[3] AN J, ALEMAO E, REYNOLDS K, et al.: Cardiovascular outcomes associated with lowering low-density lipoprotein cholesterol in rheumatoid arthritis and matched nonrheumatoid arthritis. J Rheumatol. 2016;43:1989-96.

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AB0147 RESEARCH PROGRESS OF MESENCHYMAL STEM CELL-DERIVEDMICROVESICLES BY DELIVERING MICRORNA IN RHEUMATIC DISEASES

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Background: Recently, studies have shown that Mesenchymal Stem Cell-derived Microvesicles(MSC-MVs) can play a role in immune regulation and tissue repair by transporting miRNAs, and their effects are not weaker than that of their mother stem cells. Rheumatoid arthritis is an autoimmune disease characterized by chronic synovitis and progressive cartilage and bone destruction. Current treatments include non-steroidal anti-inflammatory drugs, glucocorticoids, DMARDs, and biological agents, but 30% of patients with rheumatism are ineffective, so there is an urgent need to find a new treatment.
Objectives: To review the research progress of MSC-MVs by delivering microRNA(miRNA) in rheumatic diseases.
Methods: Literatures were searched by using MSC-MVs, autoimmune diseases and miRNA as keywords.
Results: In the field of rheumatology, Chen C showed that after MSCT transplantation, mir-151-5p was transferred through exosomes to damaged bone marrow MSC of systemic sclerosis(SSc) mice, and the activation of IL4R/mTOR pathway was down-regulated to improve the osteoporosis of SSc mice [1].Exosomes of human synovial mesenchymal stem cells overexpressing miR-140-5p promoted cartilage regeneration and prevented OA in rat models [2].In the field of autoimmune deseases, Chen L et al. demonstrated that BMSC-derived exosomes containing miR-223 play a important role in liver protection by down-regulating NLRP3 (nod-like receptor family protein) and caspase-1 (caspase-1) in the experimental model of autoimmune hepatitis[3].Human BMSC-derived exosomes transfected with siFas and anti-mir-375 plasmids down-regulated Fas and miR-375 in human NOD scid gamma (NSG) mice, thereby protecting islet function and inhibiting immune rejection in islet transplantation [4].
Conclusion: MiRNA targeting therapy with MSC-MVs as vector or the construction of MSC-MVs with overexpression of protective miRNA will provide new, accurate and promising treatment strategies for multiple rheumatic diseases.

REFERENCES

[1] Chen, C., et al.Mesenchymal stem cell transplantation in tight-skin mice identifies miR-151-5p as a therapeutic target for systemic sclerosis. Cell Res, 2017. 27(4): p. 559-577. DOI:10.1038/cr.2017.11.

[2] Tao S, C, Yuan T, Zhang Y. L,et al.Exosomes derived from miR-140-5p-overexpressing human synovial mesenchymal stem cells enhance cartilage tissue regeneration and prevent osteoarthritis of the knee in a rat model. Theranostics, 2017. 7(1): p. 180-195.
[3] Chen L, et al. BMSCs-derived miR-223-containing exosomes contribute to liver protection in experimental autoimmune hepatitis. Mol Immunol, 2018. 93: p. 38-46. DOI:10.1016/j.molimm.2017.11.008.
[4] Wen D, Peng Y, Liu D, et al.Mesenchymal stem cell and derived exosome as small RNA carrier and Immunomodulator to improve islet transplantation. J Control Release, 2016. 238: p. 166-175.DOI:10.1016/j.jconrel.2016.07.044

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AB0148 OSTEOBLASTS SECRETE A HIGH LEVEL OF OSTEOPROTEGERINE AND SUPPRESS OSTEOCLASTOGENESIS BY INHIBITING SOLUBLE RANKL – IMPLICATIONS FOR THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

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Background: Osteoclasts (OCs) are multinucleated cells of monocyte/macrophage lineage and are the only cells known to resorb bone matrix. Osteoblasts (OBs) have the ability to differentiate bone marrow cells (BMCs) into osteoclasts when co-cultured with BMCs in the presence of Vitamin D_3 ($1,25(OH)_2D_3$) and prostaglandinE_2(PGE_2). OBs produce both M-CSF, a survival factor for OC precursor cells, and RANKL, a differentiation factor. In rheumatoid arthritis (RA), synoviocytes may fulfill the functional role of OBs, since OBs are not observed in the synovium of the joints. Although human BMCs are difficult to obtain, mouse BMCs are known to respond to human M-CSF and RANKL, and differentiate into OCs in the presence of both cytokines.
Objectives: Our aim was to examine whether a co-culture system of human synoviocytes and mouse BMCs might be developed. Through this analysis, we attempted to clarify the characteristics of synoviocytes in the pathogenesis of bone destruction observed in RA
Methods: Human synoviocytes were prepared from synovium obtained in the course of joint replacement surgical operations performed at Saitama Medical University Hospital. Written informed consent, approved by the ethics committee of the hospital, was obtained from each patient prior to the experiment. Mouse OBs were obtained from the calvaria of newborn C57BL/6 mice. Mouse BMCs were co-cultured with either synoviocytes or OBs. OCs were detected by tartrate-resistant acid phosphatase (TRAP) staining. The concentrations of M-CSF, RANKL and the decoy receptor for RANKL, OPG, were quantified by ELISA in the culture supernatant of synoviocytes or OBs.
Results: When synoviocytes and BMCs were cultured with $1,25(OH)_2D_3$ and PGE_2, OCs were not induced. OC precursor cells did not seem to even survive. Next, we added human M-CSF to the system. This time, OC precursor cells remained, but TRAP-positive multinuclear cells were not observed. It was only in the presence of exogenous M-CSF and RANKL that BMCs transformed into OCs. RANKL was not detected in the culture supernatant of synoviocyte culture, but OPG and M-CSF were detectable at a level comparable to mouse OBs. Finally, we cultured mouse OBs and BMCs that were separated by a polycarbonate membrane in the presence of $1,25(OH)_2D_3$ and PGE_2. In this case, too, BMCs did not survive unless exogenous M-CSF was added, and they did not differentiate into OCs unless both M-CSF and RANKL were added to the system.
Conclusion: These results indicate that the M-CSF derived from OBs or synoviocytes is not sufficient to support the survival of OC precursors. Likewise, the soluble RANKL derived from OBs is by itself insufficient for the differentiation of OCs, confirming the importance of a cell-cell interaction between OBs and OC precursors. Thus, membrane-bound RANKL seems to play a role more important than soluble RANKL in the co-culture system of OCs *in vitro*. Soluble RANKL may be neutralized by the OPG that is produced at a fairly high level from both OBs and synoviocytes. We propose that this is the system by which ectopic differentiation of OCs is prevented.
Disclosure of Interests: None declared
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AB0149 ARSENIC TRIOXIDE IMPROVES TREG AND TH17 BALANCE VIA MODULATING STAT3 IN TREATMENT-NAÏVE RA PATIENTS

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Background: We have a long-term interest in novel arsenic trioxide As_2O_3 (ATO) medical application since some acute promyelocytic leukemia (APL) patients have been cured by first using ATO and survived for more than 45 years successfully treated by Prof. Zhang Tingtong in our institute. Moreover, our previous studies have shown that ATO significantly suppress angiogenesis and induced fibroblast like synoviocytes (FLS) apoptosis in collagen induced arthritis (CIA) model[1, 2]. However, the extract mechanism by which ATO anti-rheumatic and whether this occurs via modulation of immune system are still unclear.
Objectives: To investigated the immunologic mechanism by which ATO may inhibit T helper 17 cells (Th17) differentiation while promote regulatory T cells (Treg) generation via modulating signal transducer and activator transcription 3 (STAT3) in treatment-naïve RA patients.
Methods: Naïve $CD4^+$T cells sorted by fluorescence-activated cell sorting (FACS) from treatment-naïve RA patients and healthy controls were used to investigated the effect of ATO on its polarization process and related cytokines. Knockown or enforced expression of STAT3 transfection experiments were conducted by small interfering RNA (siRNA) and lentivirus STAT3 to verify the mechanism of ATO on Th17/Treg balance in vitro. Collagen-induced arthritis (CIA) model was constructed to detect the clinical score, histopathological change, bone destruction, Th17/Treg proportion and joint tissues immunohistochemistry. Single cell sequencing and other methods have been appplied too.
Results: We found that ATO prevented activated naïve $CD4^+$T-cell differentiate into Th17 cell and reduced cytokine production by activated Th17 cells by downregulating their signature transcription factors, STAT3 and orphan nuclear receptor (RORγt). Notably, ATO reduced Th17 cells frequency while increased Treg cells frequency under specific polarizing conditions from treatment-naïve RA patients by transfecting siRNA STAT3 and lentivirus STAT3. Furthermore, we have noticed that intervention of ATO in CIA model attenuated joint inflammatory infiltration and bone destruction, significantly improved the imbalanced Treg/Th17 ratio. In-detail single cell sequeining analysis is ongoing.
Conclusion: ATO may be a immune modulator candidate for treatment-naïve RA patients via balancing well Treg/Th17 cell ratio through STAT3 regulation.

REFERENCES

[1] Zhang, J., et al., *Inhibition of angiogenesis by arsenic trioxide via TSP-1-TGF-beta1-CTGF-VEGF functional module in rheumatoid arthritis.* Oncotarget, 2017. 8(43): p. 73529-73546.
[2] Mei, Y., et al., *Arsenic trioxide induces apoptosis of fibroblast-like synoviocytes and represents antiarthritis effect in experimental model of rheumatoid arthritis.* J Rheumatol, 2011. 38(1): p. 36-43.
[3] Vasheghani, F., et al., *PPARgamma deficiency results in severe, accelerated osteoarthritis associated with aberrant mTOR signalling in the articular cartilage.* Ann Rheum Dis, 2015. **74**(3): p. 569-78.

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AB0116 BROMODOMAIN INHIBITOR, I-BET762 INHIBITS PRODUCTION OF PRO-INFLAMMATORY MEDIATORS BY DOWN-REGULATING BROMODOMAIN AS AN EPIGENETIC READER IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder, characterized by joint inflammation and bone destruction. The fibroblast-like synoviocyte contributes to the pathogenesis of RA through proliferation and production of cytokines. Recently, blockade of the bromodomain and extra-terminal domain

(BET) family protein was reported to be a potential therapeutic target by inhibiting epigenetics interaction between bromodomains and acetylated histones.
Objectives: We aimed to investigate the effects of bromodomain-containing protein 4 (BRD4) inhibition on tumor necrosis factor (TNF)-α-stimulated rheumatoid arthritis fibroblast-like synoviocyte (RA-FLS) using BRD4 inhibitor, I-BET762.
Methods: We examined the effects of BET protein inhibitor on cytokine production and cellular proliferation in RA-FLS. RA-FLSs were treated with TNF-α (10 ng/ml) in the presence of I-BET762 for 48 h. The cell viability and proliferation were measured after 24, 48, and 72 h in I-BET762-treated RA-FLS using CCK-8 colorimetric assay. We then screened pro-inflammatory mediators by using the human inflammation antibody array (Abcam). The levels of interleukin (IL)-6 and IL-8 in culture supernatants of TNF-α-stimulated RA-FLS were measured by enzyme-linked immunosorbent assays (ELISA).
Results: I-BET762 had no significant effect on cytotoxicity and proliferation of RA-FLS. I-BET762 reduced the secretion of CXCL-10 and regulated upon activation, normal T cell expressed, and secreted (RANTES) from RA-FLS while increased the secretion of tissue inhibitor of metalloproteinase 2 (TIMP-2) in the antibody array. In addition, ELISA showed significantly decreased level of IL-6 and IL-8 in culture supernatant after treatment with I-BET762.
Conclusion: Inhibition of BRD4 by I-BET762 leads to down-regulation of pro-inflammatory cytokines and chemokines in RA-FLS. I-BET762 may have anti-inflammatory properties and provide a therapeutic target molecule in RA.

REFERENCES

[1] Sahai V, et al. Oncotarget 2016;6;7(33):53997-54009.
[2] Klein K, et al. Ann Rheum Dis 2016;75: 422–429.

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AB0139 ASSOCIATION OF RS17004921 ADORA2A GENE POLYMORPHISM WITH EFFICACY OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Adenosine A2A receptors (ADORA2A) are part of the adenosine-mediated antiinflammatory pathway. These receptors are over-expressed in peripheral blood leukocytes of patients with rheumatoid artritis (RA). Methotrexate (MTX), the gold standard for therapy, exerts its antiinflamatory effects via increased release of adenosine into the extracellular space. Adenosine binds to ADOR A2A and A3 and initiates an antiinflammatory response. Therefore, ADOR gene polymorphisms could have an impact on MTX therapy outcome.
Objectives: To examine the role of adenosine receptor 2A gene (*ADORA2A, rs 17004921*) polymorhism on outcome of MTX treatment in RA.
Methods: A total of 123 patients with RA (mean age 56.5±10.73, 91 (74% female), treated with MTX for 6 months (mean dose 12.22±3.20/weekly) were enrolled in a prospective study. Genotypisation within *ADORA2A* gene was performed using the KASP genotyping assays. MTX efficacy assessment was based on the changes in the Disease activity score (DAS28) after 6 months of treatment according to the EULAR response criteria. Patients with good and moderate response were classified as „responders“, whereas patients with poor response were considered „nonresponders“. Data of adverse effects were collected during this period. MTX efficacy and toxicity were compared among patients with different genotypes. All statiscal analyses were performed by SPSS version 16.0.
Results: Median DAS 28 at the beginning of MTX treatment was 7.43±0.89. According to EULAR response criteria, 111 (90.2%) patients with RA were classified as responders. Among all RA patients, 97 (78.9%) had CC, 20 (16.3%) CT and 6 (4.9%) TT genotype. The distribution of *ADORA2* genotypes in responders (CC 77.5%, CT 17% and TT 5.4%) was not significantly different from nonresponders (CC 91.7%, CT 8.3%), p>0.05. After 6 months, 26 carriers of T allele (CT +TT) had higher reduction DAS 28 (7.16 vs. 3.88) in comparison to other 97 patients (7.50 vs.4.64, p=0.013). Adverse effects were reported in 24 (19.5%) patients. Most of patients had hepatotoxicity and nausea, 14 (58%) and 9 (37%) respectively. No statistically significant association between *ADORA2*A genotype and side events has been observed (p>0.05).
Conclusion: According to our results, T allele of *ADORA2A rs17004921* polymorphism may have favourable influence on efficacy in RA patients treated with methotexatate.

REFERENCES

[1] Cronstein B, Sitkovsky M. Adenosine and adenosine receptors in the pathogenesis and treatment of rheumatic diseasess. www.nature.com/nrrheum
[2] Hider SL, Thomson W, Mack LF, et al. Polymorhisms within the adenosine receptor 2a gene are associated with adverse events in RA patients treated with MTX. Rheumatology 2008;47:1156-1159.

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Spondyloarthritis - etiology, pathogenesis and animal models

AB0150 IMMATURE GRANULOCYTES LEVEL IS A POTENTIAL BIOMARKER IN PERIPHERAL ENTHESITIS

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Background: Immature granulocytes (IG) level in peripheral blood is used as early sign of infection. On the other hand, IG could be elevated in other conditions like inflammatory or cancerous diseases and in pregnancy. Similar to CRP, we have observed a series of cases of peripheral enthesitis associated increased level of IG and correlated with CRP elevation and clinical activity.
Objectives: To test the concept of IG as a biomarker in peripheral enthesitis, This observation might be a reflection to the innate immunity role in pathogenesis of enthesitis.
Methods: We have identified 13 cases over the last 12 months at the Rheumatology clinic in our centre who have shared two features (clinical enthesitis and elevated IG) those 13 cases are mainly presented with recurrent foot and ankle pain and swelling of enthesitis nature.
Results: The cohort is of equal gender distribution 46/54% respectively and age range 31-53 years (mean age 38.5), only 3 patients are known to have Psoriatic arthritis whilst the rest either undiagnosed or diagnosed Rheumatoid arthritis or gout prior to clinic visit. The rheumatologist clinical diagnoses are of enthesitis of foot, ankle, knee and hip area as shown on the table [1] apart from one patient who has spinal symptoms mainly. 4/13 patients have the history of psoriasis and after their visits we find them fit in the CASPAR criteria for psoriatic arthritis. All these cases are associated with increased absolute number of IG as well as differential (IG) number compare to 10/13 of these cases are having high CRP. The 3 cases with normal CRP do have relatively slight increase in (IG) number. The main correlation is of response to therapy and was seen in 7 cases who have followed up at the time of submission and it shows a 100% correlation between CRP, absolute (IG) and differential (IG) values. There are 3 patients who have elevated (IG) but normal CRP and it would possible indicate (IG) test has a better yield than CRP in peripheral enthesitis.
Conclusion: Immature granulocytes can be elevated in inflammatory disease and more notably in peripheral enthesitis of the lower limbs of inflammatory rather than mechanical nature and do correlate with CRP elevation as well as response to therapy. Larger studies are needed to assess the usefulness and validity of (IG) level in clinical practice.

REFERENCES

[1] Rudwaleit M et al, The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in genera, Ann Rheum Dis. 2011;70(1):25
[2] Moots R et al, Low-density granulocytes: functionally distinct, immature neutrophils in rheumatoid arthritis with altered properties and defective TNF signaling, Translational & Clinical Immunology 2016 https://doi.org/10.1189/jlb.5A0116-022R
[3] Salvarani c et al, Isolated peripheral enthesitis and/or dactylitis: a subset of psoriatic arthritis. J Rheumatol. 1997 Jun;24(6):1106-10

Table 1: The table shows the CRP and immature granulocytes

F/M	Age	Diagnosis before referral	Diagnosis at rheumatology clinic	CRP (mg/L)	IG (%) 48.5%	IG (absolute) x10.3	Treatment	CRP after	IG%	IG (absolute)
M	40	Gout	Peroneal tenosynovitis	2	0.05%	0.04	Steroids	2	1.6*	0.9
M	50	Inflammatory arthritis	peroneal and Tibialis posterior tendonitis	19	0.90%	0.09	Steroids and MTX	10	0.50%	0.03
M	44	Undiagnosed	Peripheral enthesitis and spondyloarthritis	20	0.70%	0.07	Methotrexate	awaited	awaited	awaited
F	51	Seronegative arthritis	Seronegative arthritis on Sulphasalazine	24	0.83%	0.04	Increased dose	17	0.2	0.01
F	41	Rheumatoid Arthritis/Plaquenil	Enthesitis, Ant.Tibial, Achilles, planters	17	1.50%	0.06	steroids add MTX / remicade	awaited	awaited	awaited
F	67	Rheumatoid Arthritis/Enbrel	plantar fasciitis bilateral / Ischial pain	15	0.70%	0.07		12	0.50%	0.03
M	33	Planter fasciitis 13 years	Plantar fasciitis, thigh, seronegative arthritis	10	1.00%	0.1	Adalimumab	1	0.70%	0.03
M	42	Planter fasciitis	Planter fasciitis / at rest	4	0.90%	0.05	Etanizumb	awaited	awaited	awaited
F	31	Undiagnosed	Ankylosing Spondylitis/SI, Knees, plaure	30	0.50%	0.05	Secukinumab	awaited	awaited	awaited
M	32	Psoriatic TPSA	Psoriatic Arthritis / DIP	4	1.00%	0.07	Arcoxia	awaited	awaited	awaited
M	53	PSO, PSA, Spinal disease	PSO, PSA, Spinal disease/Enbrel	13	0.60%	0.06	Ixekizumab	7	0.30%	0.03
F	42	PSO	PsA, Achilles and Planters	21	1.00%	0.11	Golimumab	9	0.40%	0.04
F	35	PSO on Secukinumab /failing	PsA, Knees tendonopathy	9	0.70%	0.07	to switch	awaited	awaited	awaited

* Transient elevation due to steroid use

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AB0151 EXPRESSION OF ANXIETY AND DEPRESSION IN PATIENTS WITH ANKYLOSING SPONDILITE DEPENDING ON THE STATE OF THE AUTONOMIC NERVOUS SYSTEM AND INTENSITY OF THE PAIN SYNDROME

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Background: Chronic pain syndrome, immanent in the majority of immune-inflammatory processes, is one of the pathophysiological mechanisms of the development of emotional and affective disorders. It has been proven that high levels of "pro-inflammatory" mediators are predictors of depression, and increased anxiety leads to an imbalance in the autonomic nervous system (ANS). It is also known that the pain syndrome worsens the autonomic supply of the organism. However, this problem remains insufficiently studied today.
Objectives: To assess the severity of anxiety and depression in patients with ankylosing spondilite, depending on the state of the ANS and pain syndrome.
Methods: The study included 75 patients with ankylosing spondylitis (AS), who studied the frequency of anxiety-depressive disorders and their severity on the Spielberger anxiety and Hamilton depression scales. The autonomic status was investigated according to the methods "Wayne-patient" - WP, filled by the patient (more than 15 points - possible autonomic dysfunction (AD)) and "Wayne-doctor" - WD, filled by a doctor (more than 25 points - confirms the presence of signs of AD); we evaluated the indicators of heart rate variability (HRV) - mode (Mo), mode amplitude (AMo), autonomic equilibrium index (AEI), regulatory systems tension index (TI), the standard deviation of the normal RR intervals (SDNN), the square root of the mean squares of the difference between successive RR intervals (RMSSD) and the balance ratio of the activity of the sympathetic and parasympathetic divisions of the ANS (LF/HF). Pain syndrome and the patient's own health index (POH) were assessed by a visual analogue scale (VAS) by patients, and by a physician - by counting the number of painful joints (NPJ), index BASDAI and ASDAS indices.
Results: In 25.3% of patients with AS, a high situational anxiety was observed and in 36% of patients high personal anxiety (PA) was observed. Depressive disorders were found in 57 patients with AS (76%). The severity of pain in the joints and the spine influenced the increase in PA ($F = 2.75$, $p = 0.047$; $F = 3.54$, $p = 0.037$, respectively) and the level of depressive disorders ($F = 3.28$, $p = 0.03$; $F = 3.44$, $p = 0.047$, respectively), and the level of depression is also POH ($F = 3.49$, $p = 0.048$). 68% patients had an AD (according to WP and WD methods). They constituted the 1st group of observation, and the remaining 24 patients were included in the 2nd group. In group 1, signs of anxiety disorders were identified in 84.3% of cases, and in patients without AD in 45.8% of cases. Depressive disorders were observed in 94% patients with autonomic disorders (11 cases of psychotic, 37 - non-psychotic depression) and in 37.5% in patients without signs of AD - signs of non-psychotic depression.
In both groups, there was a decrease in SDNN and RMSSD in comparison with normative ones, which indicates an increase in sympathetic regulation. In the 1 st group, there was a more significant increase in LF/HF (4.15 ± 0.64) and a decrease in SDNN (22.4 ± 5.6 ms) than in the 2nd (3.0 ± 0.86; 29.1 ± 8.4 ms), which indicates the connection between the strengthening of the sympathetic regulation link and the presence of signs of psycho-emotional disorders. The growth of AMo in the 1st group (47.9 ± 8.4%) reflects the degree of mobilizing influence of the sympathetic division and indicates an increase in the activation of the central contour and the growth of sympathetic regulation in patients with AS with AD.
Conclusion: Patients with AS have a high incidence of clinically significant anxiety and depression, which were affected by the intensity of the pain syndrome. The presence of autonomic imbalance and dysregulation of the sympathetic link of the ANS also contribute to the strengthening of psycho-emotional disorders in this category of patients.
Disclosure of Interests: None declared
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AB0152 IL-23 INDUCES OSTEOCLASTS TO EXPRESS PRO-OSTEOGENIC FACTORS RATHER THAN ANTI-OSTEOGENIC FACTORS

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Background: The formation of new bone or syndesmophytes is the dominant factor of the damage caused by AS, but the mechanisms responsible for syndesmophyte formation in AS have not been elucidated.
Objectives: To explore whether IL-23 indirectly facilitates new bone formation through osteoclasts in ankylosing spondylitis, here we analyzed whether IL-23 enhances the expression levels of osteogenic factors by osteoclasts.
Methods: Mouse bone marrow mononuclear cells were cultured in the presence of M-CSF (50ng/ml) and receptor activator of NF-λB ligand (RANKL, 30ng/ml) to induce osteoclast formation *in vitro*. The mRNA and protein expression levels of the osteogenesis-modulating factors, such as ephrin B2, sphingosine kinase 1 (SPHKl), bone morphogenetic protein 2 (BMP2), BMP6, Wnt10b, semaphorin 4D and HtrA1, were analyzed by quantitative real-time RT-PCR and Western blotting.
Results: Mature osteoclasts were successfully induced from primary bone marrow mononuclear cells in the presence of both M-CSF and RANKL. Mature osteoclasts were identified by elevated expression levels of tartrate-resistant acid phosphatase (TRAP) and NFATc1, as well as positive TRAP staining with more than 3 nuclei. IL-23 increased the mRNA expression levels of pro-osteogenic ephrin B2, SPHKl and BMP2 in osteoclasts to 2.1, 2.46 and 1.46 folds, respectively. The elevated protein levels of ephrin B2 and SPHK1 in IL-23-stimulated osteoclasts were also confirmed by Western blotting. IL-23 failed to enhance the expression levels of pro-osteogenic BMP6 and Wnt10b and showed no effects on the expression levels of anti-osteogenic semaphorin 4D and HtrA1 in osteoclasts.
Conclusion: IL-23 induces osteoclasts to express pro-osteogenic factors rather than anti-osteogenic factors, suggesting IL-23 may indirectly promote the differentiation of osteoblasts through osteoclasts in ankylosing spondylitis.
Disclosure of Interests: None declared
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AB0153 CLINICAL SIGNIFICANCE OF MONOCYTE TO HEMOGLOBIN RATIO AND PLATELET TO ALBUMIN RATIO IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) is a progressive, chronic, inflammatory skeletal disorder. Platelet to hemoglobin ratio (PHR) and platelet to albumin ratio (PAR) have been recommended as prognostic factor of cancer. However, none of study has focused on the clinical significance of PHR, PAR, neutrophil to hemoglobin ratio (NHR), neutrophil to albumin ratio (NAR), monocyte to hemoglobin ratio(MHR), monocyte to albumin ratio(MAR) for axSpA.
Objectives: The study aims to determine the clinical significance of NHR, NAR, MHR, MAR, PHR, PAR for axSpA.
Methods: A total of 198 axSpA patients and 48 healthy subjects were enrolled in the study retrospectively. Neutrophil, monocyte, platelet, hemoglobin, albumin, NHR, NAR, MHR, MAR, PHR, PAR, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) were collected. AxSpA patients were divided into remission group (BASDAI<4) and active group(BASDAI≥4). Relationships between the parameters and BASDAI were assessed by the Sperman' s correlations analysis. Receiver operation characteristic (ROC) curves were used to discriminate axSpA patients from healthy subjects and active group from remission group.
Results: Neutrophil, monocyte, platelet, NHR, NAR, MHR, MAR, PHR, PAR, CRP, ESR in axSpA group were higher than those of control group, while albumin and hemoglobin were lower ($P<0.05$). ROC curve results showed that the AUC value of MHR for axSpA were 0.808 (CI95%: 0.738-0.878), yielding a highest AUC value than other parameters. The optimal cutoff value of MHR for axSpA was 0.002447, with the Youden index of 0.498, sensitivity of 87.4% and specificity of 62.5%. The closely positive correlations were found between PAR and BASDAI ($r=0.379$, $P<0.001$). Besides, platelet, NAR, MAR, PHR, PAR, CRP, ESR in active group were higher than those of remission group, while albumin were lower ($P<0.05$). ROC curve results showed that the AUC value of PAR for active group were 0.693 (CI95%: 0.610-0.775), yielding a highest AUC value than other parameters. The optimal cutoff value of PAR for active group was 5.967, with the Youden index of 0.354, sensitivity of 83.3% and specificity of 52.1%.

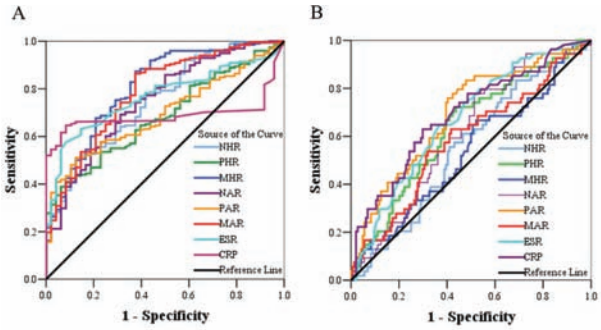


Figure.1 ROC curves were used to discriminate axSpA patients from healthy subjects**(A)** and active group from remission group**(B)**.

Conclusion: MHR was elevated in axSpA patients with a highest diagnostic value. PAR was elevated in active axSpA patients, showing a significant correlation to the disease activity.

REFERENCES

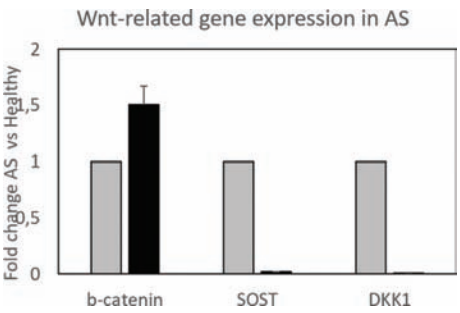
[1] Li Xing, Lin Zhi-Huan, Hong Ying-fen, et al. Platelet-to-hemoglobin ratio as a prognostic factor for hepatocellular carcinoma patients receiving transcatheter arterial chemoembolization.JOURNAL OF CLINICAL ONCOLOGY, 2016, 34(15): suppl. e15591

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AB0154 WNT-BETA CATENIN PATHWAY MAY BE UPREGULATED IN ANKYLOSING SPONDYLITIS

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Background: The Wnt–β-catenin pathway may play a critical role in new bone formation in ankylosing spondylitis. Wnt–β-catenin signaling depends primarily on the activity of glycogen synthase kinase-3β (GSK3β) that plays a key role in controlling β-catenin stability/degradation. It has been clearly established that phosphorylation of serine 9 in GSK3b correlates with the inhibition of its kinase activity and stabilization of β -catenin. Dickkopf-1 (DKK1) and sclerostin (SOST) are both upstream inhibitors of the Wnt/β-catenin pathway. Given that AS is associated with new bone formation we are interested in the molecular pathways that lead to this clinical phenotype
Objectives: The objective of our studies was to test the hypothesis that "alterations in the Wnt–β-catenin activity may be a contributing factor in the pathogenesis of AS"
Methods: 5 healthy donors and 12 patients (mean age 48 y.o., HLA-B27+ 70%) with AS based on New York classification criteria were enrolled. RNA was extracted from whole blood collected in PAX tubes following PreAnalytix kit protocol.Total mRNA was reverse transcribed using the high capacity cDNA Reverse Transcription Kit (Thermo Scientific) according to the manufacturer's instructions. TaqMan® Gene Expression Assays (IDT) were used to quantify mRNA levels of DKK1, SOST, and β-catenin. LightCycler480, and $\Delta\Delta C_T$ method were used to quantify the data (normalized to RPLP0(60S acidic ribosomal protein P0)). Protein lysates were prepared using NucleoSpin RNA/Protein kit (Takara) from PBMCs isolated from blood collected from the same 12 patients. Equal amounts of protein were loaded on 4–12% SDS gels and transferred to PVDF membranes. Membranes were blocked with 5% milk in TBST and probed at 4°C overnight with primary antibodies [rabbit anti-phosphoGSK3β (Ser9) (1:500; Cell Signaling, #9336), rabbit anti-GSK3β (1:1000; Cell Signaling, #9315), and mouse anti-β-actin (1:1000; Santa Cruz Biotechnologies, sc-47778)]. Appropriate HRP-conjugated secondary antibody was applied at room temperature for 1 hour. Immunoreactive protein bands were visualized using ECL (Pierce) and imaged with VisionWorks Image Acquisition and Analysis Software (Analytik Jena US, Upland, CA). β-actin was used as a loading control.
Results: Compared to healthy controls the mRNA levels of DKK-1 and SOST were significantly lower in AS patients ($p < 0.001$), while the mRNA level of β-catenin was significantly higher in AS patients than in healthy controls ($p < 0.05$) (Fig 1).



Compared to healthy controls, there was a several fold increase in the phosphorylation of GSK3b (Ser9) protein in the AS patient's sample.

Conclusion: These data indicate that altered Wnt- β -Catenin activity may be contributing to the new bone formation in AS patients and thereby contributing to the disease pathogenesis and can be targeted for therpaeutic development.
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AB0155 INTESTINAL MICROBIAL SIGNATURE IN ANKYLOSING SPONDYLITIS

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Background: Intestinal microbiota analysis is a current subject because of its important role in the pathogenesis of various autoimmune diseases such as intestinal inflammatory diseases or spondyloarthritis.
Objectives: The objective of this paper was to perform a quantitative determination of the intestinal microbiota in patients with ankylosing spondylitis (AS) and to highlight the main characteristics of intestinal dysbiosis in these cases.
Methods: We conducted a case-control prospective study that included 28 patients with AS and 32 control cases (healthy individuals). Intestinal microbiota analysis was performed by real-time PCR (polymerase chain reaction) in faeces. Intestinal microbiota analysis focused on the following bacterial species: *Bacteroides, Bifidobacterium, Clostridium coccoides* (XIVa) (*C. Coccoides*), *Clostridium leptum (IV) (C. Leptum), Faecalibacterium prausnitzii (F. Prausnitzii), Lactobacillus, Escherichia coli (E. coli).*
Results: Intestinal disbiosis in AS patients was characterized by a significant bacterial decrease compared to the control arm. Some bacterial species showed a numerical growth: *Bacteroides, C. coccoides* and *C. leptum, F. prausnitzii*. In other bacterial groups there was a significant decrease: *Bifidobacterium, Lactobacillus* and *E. coli*. Statistically significant correlations were observed only for *Bifidobacterium*, significantly increased in the axial form of AS compared to the peripheral form ($p = 0.035$). Other bacterial groups were numerically elevated in the axial form of AS (except *Bacteroides*), without statistically significant differences. In all AS cases, a moderate disease activity was evidenced (mean BASDAI = 4.83, mean BASFI = 9.11). BASDAI score inversely correlated with the total bacteria group ($p = 0.010$, $r = -0.606$) - intestinal dysbiosis worsens as disease activity increases. Also, direct proportional correlations were highlighted between BASDAI and *F. prausnitzii* ($p = 0.000$, $r = 0.764$), respectively *Lactobacillus* ($p = 0.047$, $r = 0.488$). An increase in AS activity is associated with an increase in proinflammatory bacteria. BASFI score statistically correlated with the total bacterial count ($p = 0.000$, $r = -0.764$), *F. prausnitzii* ($p = 0.010$, $r = 0.606$), *Bifidobacterium* ($p = 0.016$, $r = 0.843$) and *E. coli* ($p = 0.016$, $r = 0.575$). An important decrease in the functionality of these patients correlates with a decrease in total bacterial diversity. Improvement of intestinal dysbiosis has been observed in patients on synthetic and biological immunosuppressive therapy compared to the control arm.
Conclusion: The study highlightes the characteristics of intestinal dysbiosis in AS patients. There is a direct relationship between the composition of intestinal microbiota and the AS activity scores. Specific treatment for AS leads to a decrease in proinflammatory bacteria, improving gut dysbiosis.

REFERENCES

[1] Mancabelli L, Milani C, Lugli GA, et al. Identification of universal gut microbial biomarkers of common human intestinal diseases by meta-analysis. *FEMS Microbiol Ecol*. 2017 Dec 1;93(12).
[2] Breban M, Tap J, Leboime A, et al. Faecal microbiota study reveals specific dysbiosis in spondyloarthritis. Ann Rheum Dis. 2017 Sep;76(9):1614-1622.
[3] Breban M. Gut microbiota and inflammatory joint diseases. Joint Bone Spine. 2016 Dec;83(6):645-649.
[4] Gill T, Asquith M, Rosenbaum JT, Colbert RA. The intestinal microbiome in spondyloarthritis. Curr Opin Rheumatol. 2015 Jul;27(4):319-325.
[5] Stebbings SM, Taylor C, Tannock GW, et al. The immune response to autologous bacteroides in ankylosing spondylitis is characterized by reduced interleukin 10 production. J Rheumatol. 2009; 36:797–800.
[6] Stoll ML, Kumar R, Morrow CD, et al. Altered microbiota associated with abnormal humoral immune responses to commensal organisms in enthesitis-related arthritis. Arthritis Res Ther. 2014;16(6):486.

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AB0156 A NOVEL ASSOCIATION OF TLR-2 (23 BPINS/DEL: RS111200466) POLYMORPHISM WITH ANKYLOSING SPONDYLITIS – A POSSIBLE ROLE IN DISEASE SUSCEPTIBILITY: A HOSPITAL BASED CASE-CONTROL STUDY

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Background: Role of innate immunity in pathogenesis of ankylosing spondylitis (AS) has been well documented[1]. Higher expression of TLR2 has been reported in AS patients and associated with clinical severity[2]. Recently, a functional 23bp ins/del polymorphism at 5'UTR of TLR2 gene has been reported and association of variant with elevated TLR2 surface expression and proinflammatory molecules has been elegantly demonstrated[3]. This is associated with high TNF-alpha levels, one of the key molecules in the pathogenesis of AS [4]. In this preliminary study, we investigated the possible role of TLR2 (23bp ins/del) polymorphism with AS in a cohort from Odisha, India.
Objectives: To investigate the role of TLR-2 (23 bp ins/del: rs111200466) Polymorphism in Ankylosing Spondylitis
Methods: AS patients (n = 101), who fulfilled the ASAS classification criteria for axial spondyloarthritis or ASAS classification criteria for peripheral spondyloarthritis were enrolled along with 100 healthy age matched controls from similar geographical areas. Patients were examined in detail and BASDAI/BASFI recorded. TLR2 (23 bp ins/del) polymorphism was genotyped by polymerase chain reaction. Genotype and allele distribution among patients and controls were compared by Fisher's exact test.
Results: All patients enrolled in the present study were males. The mean age of AS patients and healthy controls was 31.21±11.43 and 28.28±9.62 years, respectively. At the time of enrolment, mean disease duration of patients was 2.07±1.13 years. BASDAI and BASFI scores were above 5. Distribution of TLR2 (23 bp ins/del) polymorphism was in accordance with Hardy-Weinberg Equilibrium. Prevalence of del/del genotype was significantly higher in AS patients compared to healthy controls (P=0.01, OR=5.65), indicating a possible contributory role of TLR2 on predisposition to AS. Distribution of heterozygous genotype (ins/del) and minor allele (del) were comparable among different clinical categories. Furthermore, no significant association of TLR-2 polymorphism was observed with disease severity.
Conclusion: TLR2 5'UTR homozygous mutants (23 bp deletion) were significantly associated with patients of AS in but not with disease severity. Larger sample size and levels of TNF alpha and IL17 in the mutants will further improve the understanding of its role in AS.

REFERENCES

[1] Vanaki N, Aslani S, Jamshidi A, Mahmoudi M. Role of innate immune system in the pathogenesis of ankylosing spondylitis. Biomedicine & Pharmacotherapy. 2018 Sep 30;105:130-43.
[2] McCormack WJ, Parker AE, O'Neill LA. Toll-like receptors and NOD-like receptors in rheumatic diseases. Arthritis research & therapy. 2009 Oct;11 (5):243.
[3] Das B, Tripathy R, Pattanaik S, Panda A. 270 Association of tlr2 (23bp ins/del) polymorphism with systemic lupus erythematosus (sle) and p. falciparum malaria: a study in malaria endemic area of odisha, india.
[4] Blandizzi C, Gionchetti P, Armuzzi AL, Caporali R, Chimenti S, Cimaz R, Cimino L, Lapadula G, Lionetti P, Marchesoni A, Marcellusi A. The role of tumour necrosis factor in the pathogenesis of immune-mediated diseases. International journal of immunopathology and pharmacology. 2014 Jan;27 (1_suppl):1-0.

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AB0157 SYNOVIAL FLUID PROTEOMICS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS), affecting 0.5% of the population, is a chronic inflammatory rheumatic disease affecting the axial skeleton and peripheral joints. When peripheral arthritis in ankylosing spondylitis (AS) develops early in the disease course it is a predictor of more aggressive disease. SF is in contact with the primary tissues affected by arthritic diseases and has been implicated in disease pathophysiology. Therefore it is an excellent source for discovery of biomarkers.
Objectives: We used proteomic analysis using SFs from AS patients and other arthritis patients in order to discover novel diagnostic markers for AS. Our aim was to identify differentially expressed protein mediators in synovial fluid of ankylosing spondylitis.
Methods: A Total of 40 SF samples from 10 AS and each 10 controls [Osteoarthritis (OA), Rheumatoid Arthritis (RA), gouty arthritis (Gout)] were collected. Liquid chromatography and tandem mass spectrometry (LC-MS/MS), to identify differentially expressed proteins based on the ratios of the extracted ion current of each protein between the four groups. Among the 9 proteins showing 1.5 fold change, 8 were verified with the exception of the abundant protein Haptoglobin (HP). Matrix metalloproteinase-1(MMP1) and Matrix metalloproteinase-3(MMP3) were used as a positive control, and the remaining 6 proteins were subjected to western blot analysis.
Results: We identified 9 proteins that were found to be more than 1.5-fold differentially expressed in SF of AS patients compared to control groups. Proteins such as HP, MMP1, MMP3, Serum amyloid P-component(APCS), Complement factor H-related protein 5(CFHR5), Fumarylacetoacetase(FAH), Mannose-binding lectin2(MBL2), Complement component C9(C9) and Complement C4-A(C4A) were found to be upregulated in the SF of AS patients. CFHR5 and C9 were reported in previous studies with AS serum. APCS was reported in SF as well as serum. However, FAH, C4A and MBL2 were newly discovered through this analysis. We were able to verify the unique expression level of C9 and CFHR5 in AS sample using western blot analysis compared to the other three diseases.
Conclusion: We performed quantitatively proteomic profiling of the respective SF sample from 4 diseases, i.e., AS, OA, RA, and GOUT, by LC-MS/MS. The systematic comparative proteomic analysis of the four groups together was carried out for the first time, leading to several differentially expressed proteins in AS. Among them, we expect C9 and CFHR5, which expression levels were confirmed by western blot analysis, can be a potential biomarker for AS.

REFERENCES

[1] Fischer R, et al. Mol Cell Proteomics 2012;11:M111.013904.
[2] Bhattacharjee M, et al. Clinical Proteomics 2013;10:11

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AB0157B FREQUENCY AND SPECTRUM OF ANEMIC SYNDROME IN PATIENTS WITH ANKYLOSING SPONDYLITIS, PECULIARITIES OF CYTOMETRIC CHARACTERISTICS AND HEMOPOIESIS

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Background: Anemia is one of the most common extraarticular manifestations in patients with ankylosing spondylitis (AS). According to various sources, from 18.5 to 45.8% of patients with AS have anemia. In the pathogenesis of anemic syndrome in the AS, a leading role is given to proinflammatory cytokines (IL-1, IL-6, and TNF-alpha), which is associated with the development of anemia of chronic disease (ACD) in this category of patients. Another type of anemia in patients with AS is iron deficiency anemia (IDA), and the relationship between the latter and the ACD varies significantly according to various literature data. As for other types of anemia in the AS, they are represented by anemia caused by drugs.
Objectives: The purpose of the work was to investigate the prevalence of anemia in the Ukrainian population of patients with AS and evaluate the hematopoiesis in patients with the main types of it.
Methods: The group with anemia included patients whose haemoglobin levels were below 120 g/l. The diagnosis of AS was determined according to the modified New York criteria (1984). Laboratory methods of research (general analysis of blood, erythrocytes, haemoglobin, color index, serum iron, total iron binding capacity (TIBC) included in the list of standard examinations of patients were performed according to standard methods. To verify the diagnosis of ACD, ferritin (FN) and levels of soluble transferrin receptor (sTfR) were determined.
Results: 118 patients with AS were included into the study, 11 (32.3%) females and 23 (67.7%) males. It was found that 34 patients (28.8%) had anemia. Anemia of mild degree was manifested in 27 (79.4%) patients and with moderate severity - 7 (20.6%) patients. Among 34 patients with anemia, patients with ACD - 15 (44.1%) predominated. In the second place, 10 (29.4%) showed a combination of ACD with functional deficiency of iron, and 8 (23.5%) patients had signs of IDA. Only one of the subjects had signs of scarce anemia. Consequently, anemic

syndrome in patients with AS is represented by ACD, ACD with iron deficiency and the actual IDA.
The analysis did not reveal significant differences in hemoglobin levels in the groups of patients with different types of anemia, depending on gender, age and duration of the disease.
The patients with different types of anemic syndrome did not have significant differences in haemoglobin content, the number of red blood cells and the magnitude of the MCH, but significantly differed in magnitude MCV. The lowest values of MCV (73.5 ± 3.14 ft) were in patients with IDA, intermediate (86.22 ± 2.6 ft) in the group of patients with ACD with functional deficiency of iron and the highest (94.2 ± 1.68 flask) among people with ACD ($p < 0.05$). According to cytometric distribution, ACD was mostly (80%) normocytic, 13.3% macrocytic and only 6.65% microcytic. ACD with functional deficiency of iron was normocytic in 70% of cases, in 20% and 10% of cases, microcytic and macrocytic, respectively. Microcytic changes of erythrocytes most often in 75% were registered in the group of patients with IDA.
The course of the AS was accompanied by significant violations of iron exchange. In particular, with anemia of the first degree, iron levels were 10.25 ± 0.26 mmol/l, and with anemia of the second degree 9.30 ± 0.63 mmol/l ($p < 0.05$). With regard to the types of anemic syndrome, in patients with IDA, serum iron levels were 8.30 ± 0.21 mmol/l, or it was probably (38%) lower than in patients with "pure" ACD. It was at the IDA that the total iron binding capacity (TIBC) was the highest. Patients with a combination of ACD with functional deficiency of iron with this indicator occupied an intermediate position between patients with IDA and ACD.
Conclusion: Thus, the most widespread variants of anemia in patients with AS are ACD, IDA and ACD with iron deficiency. ACD is in most cases a normocytic anemia, IDA - microcytic anemia, and ACD with iron deficiency mostly normocytic as well.
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AB0157C **OCULAR CAUSES OF THE INITIATION OF SYSTEMIC THERAPYIN PATIENTS WITH SPONDYLOARTHRITIS (SPA) AND UVEITIS**

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Background: Uveitis is the most frequent extra-axial manifestation in Spondyloarthritis (SpA). Even though, the criteria for the initiation of systemic therapy in patients with SpA are well defined, they are not when dealing with eye involvement.
Objectives: The main objective of this study is to determine which patients require treatment with systemic therapy (ST), understood as such the disease-modifying drugs (sulfasalazine and methotrexate) and the biological drugs (anti-TNF-α), due to ocular involvement.
Methods: This is an observational retrospective study carried out in the University Health Care Complex of León with patients diagnosed with SpA who have some episode of uveitis throughout the course of their disease and who are being treated with ST.
Results: We studied 28 patients, 67.9% men and 32.1% women, with a mean age at diagnosis of 34.48 ± 12.69 years. All patients had axial involvement and 64.3% had peripheral involvement. The initial ST was sulfasalazine (SSZ) in 50% of the patients, methotrexate (MTX) in 21.4% and anti-TNFα in 28.6%. Within those treated with antiTNFα, 50% was treated with adalimumab and the other 50% with golimumab (25%) and infliximab (25%). A 78.57% of the patients required a second systemic therapy to control the disease; a 50% required a third treatment and only 3 patients needed a fourth systemic drug that, in all cases, was adalimumab. The patients who started the ST were exclusively due to uveitis in 32.1% and both due to uveitis and SpA in 35.7%. When they need a second systemic treatment, it is still owing to an ophthalmological cause in 28.6% of the patients, and both due to ocular activity and SpA, in 33.4%. Nevertheless, when these patients require a third anti-TNFα, it is usually due to SpA (57.1%). A 10.7% of patients requiring a fourth ST was because of uveitis. 66.7% of the patients who started the ST due to uveitis were treated that way because of the uveitis severity. 60.7% of the patients with uveitis presented complications in the form of vitritis (70.6%), panuveitis (11.8%), hypopyon (5.9%), keratic precipitates (35.3%), fibrin (41.2%), synechiae (5.9%), pupillary membrane (23.5%), IOP increase (41.2%) and cataract (17.6%). The macular involvement was observed in 17.9% of the cases in the form of macular oedema (40%), papillary oedema (40%), epiretinal atrophy (20%), neurosensory detachment (20%) and epiretinal membrane (40%). In 61.9% of the patients, the ST started due to refractoriness, with the average number of uveitis after the initiation of systemic therapy of 4.32 ± 2.25 uveitis. When exclusive eye involvement is present, the treatment with SSZ is usually initiated (6 patients), although 2 patients required from the start the anti-TNFα and 1 MTX. The average number of uveitis in patients with BASDAI <4 is 5.27 CI 95% (3.90-6.63) versus 3.23 CI 95% (2.41-4.05) of patients with BASDAI> 4 ($p < 0.05$); while in patients without peripheral involvement is of 5.60 CI 90% (3.75-6.85) compared to 3.78 of the patients with peripheral involvement CI 90% (2.71-4.85) ($p < 0.05$).
Conclusion: The treatment of uveitis with ST in a patient with SpA is determined by the presence of complications and/or by the refractoriness of these, being the SSZ the most used drug at the beginning. It seems that the activity of the SpA is independent of uveitis and that patients with purely axial forms have more uveitis than those with peripheral involvement.
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SLE, Sjögren's and APS - etiology, pathogenesis and animal models

AB0158 **DECREASED AUTOPHAGY IN SALIVARY GLANDS OF PRIMARY SJÖGREN'S SYNDROME PATIENTS COULD BE ASSOCIATED WITH AN INCREASED EXPRESSION OF INFLAMMATORY MARKERS**

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Background: Salivary glands (SG) of primary Sjögren's syndrome (pSS) patients show high levels of IL-6 and endoplasmic reticulum (ER) stress[1]. In response to ER stress salivary epithelial cells trigger the unfolded protein response, seeking alleviate ER stress through several mechanisms, such as autophagy. The autophagy does not only eliminate misfolded protein aggregates, but also decreases the inflammation selectively removing proteins related to TLRs and inflammasomes. Interestingly, the activation of IL-6/JAK/STAT3 signaling pathway inhibits the autophagy through an increase in MCL-1 expression[2]. Given the role of the autophagy as anti-inflammatory mechanism, it is interesting to evaluate if SG from pSS patients show a decrease in autophagy and if this correlates with the increased expression of inflammatory markers.
Objectives: To evaluate the expression of autophagy markers in labial SG (LSG) from pSS patients and 3D-acini deficient in autophagy. In addition, the expression of inflammatory marker IL-6, as well as, autophagy inhibitor MCL-1 was determined in 3D-acini control or deficient in autophagy, evaluating the possible participation of IL-6/JAK/STAT3 signaling pathway.
Methods: In LSG of 11 anti-Ro/La seropositive pSS patients and 10 control subjects, mRNA levels of ATG5, mTOR and Beclin-1 were measured by qPCR. ATG5, p62 and LC3B protein levels were measured by Western blot in LSG or 3D-acini deficient in autophagy by knocking down ATG5. HSG cells were transduced with lentiviral vectors expressing shRNAs against ATG5 mRNA or a control vector. Later 3D-acini were generated from shATG5 and control cells. Acini were incubated with 10 ng/mL recombinant IL-6 in the presence or absence of 1.5 μM of JAK inhibitor tofacitinib for 24 h. The mRNA levels of IL-6 and MCL-1 were measured by qPCR.
Results: A significant decrease in mRNA levels of ATG5, mTOR and Beclin-1 was observed in LSG of SS-patients. In addition, a significant decrease of ATG5 protein levels together with an increase in p62 receptor protein levels was determined in LSG from SS patients. In shATG5 3D-acini an increase in p62 protein levels was observed similar to LSG from SS patients. Also, an increase in mRNA levels of MCL-1 was determined in 3D-acini stimulated with IL-6 and reverted with tofacitinib. Moreover, an increase in mRNA levels of IL-6 was measured in shATG5 3D-acini compared to 3D-acini control.
Conclusion: Our results suggest an attenuation of autophagy in salivary epithelial cells from anti-Ro/La seropositive pSS patients, which could be associated with an increased expression of inflammatory markers. We postulate that a plausible via involved in the autophagy attenuation in LSG from pSS patients could be the IL-6/JAK/STAT3 pathway, which induces MCL-1 expression. Further experiments are needed to elucidate this proposal.

REFERENCES

[1] Barrera, MJ., et al. Autoimmun Rev, 2018. 17(8):p.796-808.
[2] Qin, B., et al. Sci Rep, 2015. 5: p. 15701.

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AB0159 SILENT CEREBRAL MRI FINDINGS IN LUPUS NEPHRITIS AND NON NEPHRITIS PATIENTS

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Background: Lupus nephritis carries high morbidity and mortality and whenever added to neuropsychiatric manifestations lead to more unfavorable prognosis. The current work focused on LN patients comparing them to those without kidney affection, studying their cerebral MRI and its correlation with the histopathological classes of LN and disease activity.
Objectives: To study the effect of renal affection on the brain in SLE and their clinical significance with early detection and management of such lethal comorbidity
Methods: Cerebral MRI and MRA were studied in 40 SLE patients without neuropsychiatric manifestation; 20 LN patients with different histopathological classes and 20 patients without kidney affection. Disease activity was assessed for all patients using SLE disease activity index
Results: Abnormal MRI brain findings were more common in LN patients "though non significant" (P=0.9). The most common lesions were white matter hyperintense lesions. Number and size of such lesions were significantly higher in LN patients (1.8 fold that of non nephritis, P=0.003 and 0.03, respectively) and positively correlated with urea, creatinine, urinary albumin/creatinine ratio, SLEDAI, ESR, CRP, and grades of renal biopsy and negatively correlated with c3 and c4. cortical atrophy and prepontine space dilatation were also significantly higher in LN patients (P=0.01).
Conclusion: Asymptomatic MRI brain lesions in LN patients, they are usually clinically significant and correlate to laboratory parameters of LN, grades of renal biopsy, and disease activity independent to age, sex and hypertension.

REFERENCES

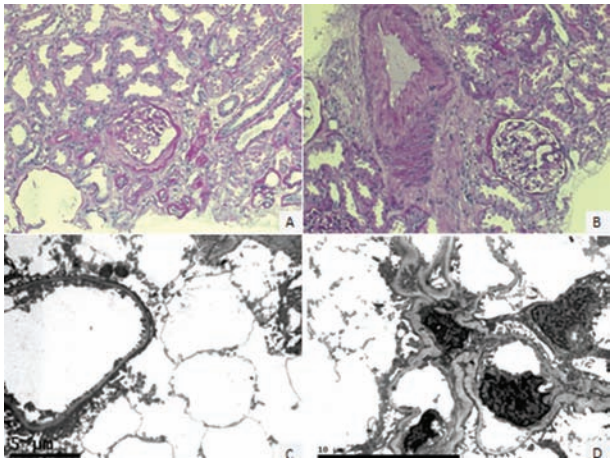
[1] Pons_Estel GJ, Alarcon GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematous. Semin Arthritis Rheum 2010;39:257-68.

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AB0160 LUPUS PODOCYTOPATHY-CASE REPORT

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Background: Lupus podocytopathy is a recently recognized new entity of lupus nephritis characterized by diffuse foot process effacement with or without mesangial expansion. Capillary wall immune deposits and glomerular proliferation are lacking in the histopathological analysis. (1) Clinically, it is manifesting as nephrotic proteinuria in the majority of reported cases.(1) Nevertheless, there is insufficient knowledge about the epidemiology, precipitant etiology and choices of management. Here, we describe a case presented with significant proteinuria secondary to foot process effacement with the absence of immunocomplement deposition or glomerular inflammation.
Objectives: To describe unusual presentation of proteinuria in lupus patient secondary to podocyte effacement which is unusual underlying pathology.
Methods: 45 years old female diagnosed to have SLE 14 years back in the setting of malar rash, alopecia, arthritis and positive serology (ANA, Ds DNA). She was doing fine on HCQ till a years ago when she presented to the clinic with gradual onset lower limbs swelling.
Laboratory results showed a significant proteinuria 2781 mg/dl/day, urine analysis showed RBC 1-2 cells/microliter, WBC 2-3 cells/microliter, normal renal profile and normal C3-C4 counts. Kidney
Kidney biopsy was taken and described a picture of minimal change glomerulonephritis with mild mesangial expansion. In addition, the study was negative for the presence of Immunocomplement deposition with the absence of capillary basement membrane and tubulointerstitial inflammation. Patient was treated with Mycophenolate Mofetil 2 grams twice per day and 1mg/kg/day oral steroid.
3 months later, protein was noticeably reduced in urine to 731 mg/dl/day but the patients had a side effect of MFM inform of significant weight loss, gastritis, and diarrhea. Azathioprine had been instituted alternatively with low dose prednisolone 10 mg. Proteinuria level had peaked again after 4 months of starting azathioprine to reach 5660 mg/dl. Kidney biopsy performed again which showed minimal light microscopic changes, the ultrastructural study showed extensive podocyte injury and foot process effacement up to 70% by the electron microscope. Mild mesangial proliferation and focal tubulointerstitial chronic changes. There was no evidence of endocapillary proliferation, subendothelial deposits or glomerular scarring. Immunoflourecance was negative for immunocompetent deposition. Mycophenolate Mofetil has been instituted again but unfortunately, proteinuria inadequately responded and remained between 3-4 grams. Lateraly, Cyclosporin 1.25 mg/kg/day has been commence few days ago. All laboratory results like renal profile and complements are with in normal values.
Results: Proteinuria was found to be attributed to diseased podocyte namely lupus podocytopathy. Unfortunately, she has inadequate response to azathioprine and mycophenolate mofetil.



Conclusion: Lupus podocytopathy is a recently recognized new entity of lupus nephritis characterized by diffuse foot process effacement without capillary wall immune deposits and glomerular proliferation. This case presentation illustrate an attention toward this new lupus entity. However, the lack of efficient knowledge about the frequency, clinical features and treatment necessitate further investigation. (2)

REFERENCES

[1] Weixin H, Yinghua C, Shaofan W, Hao C, Zhengzhao L, Caihong Z, Haitao Z, Zhihong L, Clinical–Morphological Features and Outcomes of Lupus Podocytopathy. CJASN.2016;11(4):585-592
[2] Suzuki K, Kaneko Y, Anan R, et al. FRI0370 Clinical features and outcomes of lupus nephritis with podocyte injury in patients with systemic lupus erythematosus. BMJ. 2018;77:720.

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AB0161 CLINICAL ASSOCIATIONS AND DIAGNOSTIC POTENTIAL OF REGULATORY-LIKE B-CELLS IN SJOGREN'S SYNDROME

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Background: Some B-cell subsets contribute to the regulation of immune responses, mainly through the secretion of interleukin-10, which suppresses T-helper 1 (T_h1) and T_h17 cells and induces regulatory T-cells (Tregs). The role of Bregs and Tregs in Sjögren's syndrome (pSS) pathogenesis is an active field of research.
Objectives: To evaluate the distribution of regulatory and effector T and B-lymphocytes, in patients with pSS and healthy controls (HC), and the relation between regulatory-like B-cell subsets and the pSS phenotype.
Methods: Fifty-seven pSS patients (2002 AECG criteria) and 24 HC were included. Circulating T and B-lymphocytes were characterized by flow cytometry and groups were compared. Significance was considered for $p<0.05$.
Results: Compared to HC, pSS patients had lower percentages (16.9 vs 32.0%, $p<0.001$) and absolute numbers (28 vs 81 cells/μL, $p<0.001$) of Breg-enriched $CD24^{hi}CD27^{+}$ B-cells, and a decrease in $CD24^{hi}CD38^{hi}$ B-cells percentages (6.2 vs 7.7%, p=0.09).
Lower frequencies of $CD24^{hi}CD27^{+}$ B-cells were found in anti-SSA-positive (n=38) compared to anti-SSA-negative (n=19) patients (15.0 vs 19.6%, p=0.170), as well as lower absolute counts (26 vs 31 cells/μL; p=0.173). Anti-SSA-positive patients presented higher $CD24^{hi}CD38^{hi}$ B-cells percentages (6.2 vs 4.2%;

p=0.260) and absolute counts (10 vs 5 cells/μL; p=0.343) compared to anti-SSA-negative patients.
Although $CD24^{hi}CD27^{+}$ B-cells frequencies and absolute counts did not differ between patients with active (n=27) or inactive disease (n=30), (16.9% vs 17.0%, p=0.946; 25 vs 31 cells/μl, p=0.179), patients with higher disease activity (ESSDAI≥5) (n=9) presented lower absolute counts of $CD24^{hi}CD27^{+}$ B-cells (18 vs 31 cells/μL, p=0.096) and lower $CD24^{hi}CD38^{hi}$ B-cells (4 vs 10 cells/μL, p=0.075), and higher Th1/Breg $CD24^{hi}CD27^{+}$ ratios, (16.2 vs 9.2, p=0.064).
Considering all patients, a negative correlation was found between the ESSDAI score and the absolute numbers of either $CD24^{hi}CD27^{+}$ B-cells (r= -0.277; p=0.037) and Tregs (r= -0.311; p=0.019).
Correlations with ESSDAI was stronger when looking at patients with ESSDAI≥5: for the percentages of $CD24^{hi}CD27^{+}$ B-cells, r=-0.705, p=0.023; for $CD24^{hi}CD27^{+}$ B-cells absolute counts, r= -0.644; p=0.045; and for the absolute counts of Tregs, r= -0.862; p=0.001.
Using ROC curves to discriminate pSS from HC, better AUCs were obtained for $CD24^{hi}CD27^{+}$Breg cells (cut-off 34 cells/μL, AUC=0.81), Tregs/$CD24^{hi}CD27^{+-}$ Breg ratio (cut-off 1.98, AUC=0.74) and $T_h1/CD24^{hi}CD27^{+}$Breg ratio (cut-off 12.23, AUC=0.70), corresponding to a specificity for pSS of 0.83, 0.75 and 0.70, respectively, and sensitivity of 0.75, 0.72 and 0.67, respectively.
In pSS, lower $CD24^{hi}CD27^{+}$ B-cell counts, as well as higher Tregs/$CD24^{hi}CD27^{+-}$ Breg and $T_h1/CD24^{hi}CD27^{+}$Breg ratios, were associated to a higher frequency of autoantibodies and higher gammaglobulin.
Conclusion: Our findings demonstrated a significant decrease in the Breg-enriched $CD24^{hi}CD27^{+}$ B-cell subset in pSS, which presented a negative correlation with the disease activity. We have demonstrated significant differences in the $CD24^{hi}CD27^{+}$ B-cell subset and respective ratios, presenting a good discriminatory capacity compared to HC. Therefore, this subset may have diagnostic utility in pSS, as it may support the presence of immune dysregulation in suspected cases that don't fulfil the pSS classification criteria. Further studies with increased number of samples and a prospective design are needed to explore this hypothesis.
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AB0162 IMPLEMENTATION OF HYDROXYCHLOROQUINE AT THE PRE-CONCEPTIONAL STAGE IN THE TREATMENT OF ANTIPHOSPOLIPID SYNDROME ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The problem of correcting the antiphospholipid syndrome (APS) at the planning stage of pregnancy of patients with systemic lupus erythematosus (SLE) is an important task of rheumatology.
Objectives: To study the effect of hydroxychloroquine (HC) on the level of antiphospholipid antibodies titer in women with SLE of low degree of activity at the planning stage of pregnancy.
Methods: The study included 7 women aged from 18 to 44 years with a definite diagnosis of low-level SLE (1–5 points according to the SLEDAI2K scale) and confirmed APS. All patients were characterized by a history of three or more reproductive losses in the gestational age of 10 weeks or more. According to standard laboratory tests, the level of antibodies to cardiolipin (*IgM/IgG*) and/or to β2-glycoprotein I (*IgM/IgG*) (β2GPI) in a titer above 99 percentile was determined twice in a 12-week interval. Before inclusion in the study, patients received methylprednisolone and acetylsalicylic acid in the recommended dosages. Other drugs potentially affecting the activity of SLE or hemostasis indicators of the patient during the observation period were not administered. At the time of inclusion, patients were prescribed with hydroxychloroquine (HC) in a dose of 400 mg per day orally, in addition to the therapy received earlier. The titer of antibodies to cardiolipin (*IgM/IgG*) and antibodies to β2GPI (*IgM/IgG*) was determined three times: initially, after 3 and 6 months from the start of therapy. Statistical data processing was performed using the MS Excel 2010 statistical software package and MedCalc Version 17.9.7. Data of laboratory parameters are presented in the form of median (Me) and 95% confidence interval (95% CI). Comparison of dependent samples was performed using non-parametric methods (Wilcoxon Signed Ranks Test). The statistical significance of the hypotheses was accepted at a level of $p < 0.05$.
Results: The initial SLEDAI2K index constituted 4.0±1.0 points. The median of the level of antibodies to cardiolipin is defined as 69.2 [95% CI 57.4 - 80.0] U/ml., antibodies to β2GPI - 69.24 [95% CI 49.7 - 87.5] U/ml. After 3 and 6 months from the start of HC administration, the SLEDAI2K index did not statistically significantly change (p=0.09). 3 months later, a statistically significant decrease in the level of antibodies to cardiolipin (*IgM/IgG*) by 30.4% was determined relative to the initial one [Me 21.43 (95% CI 20.2-46.1), p = 0.001]. By the 6th month of therapy, a reduced level of antibodies to cardiolipin remained unchanged; there was no statistically significant difference between the rates after 3 and 6 months of HC therapy. The level of antibodies to β2GPI (*IgM/IgG*) after three months from the start of therapy remained at the level of the indicator before inclusion in the study. A statistically significant decrease in the level of antibodies to β2GPI by 28.5% compared to the initial one was determined 6 months after the start of HC administration [Me 19.17 (95% CI 10.8-27.4), p = 0.003].
Conclusion: The study showed that, against the background of additional administration of hydroxychloroquine in patients with APS with low-level SLE, a decrease in the level of antibodies to cardiolipin (*IgM/IgG*) by 30.4% (p = 0.001) was observed after 3 months of therapy, to β2-glycoprotein I (*IgM/IgG*) - by 28.5% (p = 0.003) after 6 months of therapy.
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AB0163 THE ROLE OF IMMUNOREGULATORY MOLECULES ON FATIGUE IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a chronic autoimmune rheumatic disease characterized by exocrine gland dysfunction. The clinical presentation of pSS can vary considerably from predominantly 'sicca' symptoms such as dry eyes and dry mouth to systemic manifestations such as arthralgia, vasculitis and fatigue[1,2]. Previous work from our laboratory has suggested that immunoregulatory pathways might play a role in fatigue development in patients with pSS[3].
Objectives: The first aim was to measure the serum levels of three candidate immunoregulatory molecules (melatonin, TGF-β and IL-10) and determine any relationship with fatigue severity. The second aim was to compare molecular profiles of the immunoregulatory mediators between pSS patients and healthy controls. The third aim was to identify key predictors of fatigue in pSS.
Methods: Serum levels of the three molecules were measured in 124 patients with pSS and 28 healthy non-fatigued controls selected from the United Kingdom Primary Sjögren's Syndrome Registry using various assays. IL-10 concentrations were measured using a cytometric bead array-based immunoassay, melatonin levels were determined using ELISA and TGF-β concentrations were quantified using a bioassay in which HKC-8 cells were stably transfected with a TGF-β inducible CAGA-luciferase reporter construct. Patient fatigue levels were evaluated with a validated self-complete questionnaire and the scores were compared with the immunoregulatory molecular levels using analysis of variance. Significance in immunoregulatory mediators between the patients and controls was determined using the Wilcoxon test. Ordinal logistic regression analysis was performed in a smaller subset of patients (N = 75) to identify the key predictors of fatigue in pSS.
Results: IL-10 was significantly higher in the sera of patients with pSS compared to the healthy controls ($p<0.0001$). Melatonin showed a positive correlation with fatigue levels within the patient cohort ($\rho=0.1664$) whereas IL-10 and TGF-β were inversely related to fatigue severity ($\rho=0.1265$ and $\rho=0.0643$ respectively). The regression model used the three investigated immunoregulatory molecules, disease specific, haematological and clinical parameters as well as patient reported depression, anxiety and pain as predictors. The model was able to predict fatigue levels to a 67% accuracy.
Conclusion: The study suggests that melatonin may play a role in regulating the immune response in pSS and may affect fatigue levels in patients. Dryness, anxiety, pain and melatonin appear to be the most powerful predictors of fatigue in pSS. Further research into the effects of these immunoregulatory molecules is necessary to gain a better understanding of the pathophysiology of fatigue in pSS.

REFERENCES

[1] Shahane A, Patel R. The epidemiology of Sjogren's syndrome. Clinical Epidemiology. 2014;6:247-255.
[2] Ng W, Bowman S. Primary Sjogren's syndrome: too dry and too tired. Rheumatology. 2010;49(5):844-853.
[3] Howard Tripp N, Tarn J, Natasari A, et al. Fatigue in primary Sjögren's syndrome is associated with lower levels of proinflammatory cytokines. RMD Open. 2016;2(2):e000282.

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AB0164 **THE EXPRESSION AND CLINICAL SIGNIFICANCE OF DIFFERENT FORMS OF LILRA3 IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: LILRA3 is a member of the LILR family produced as a soluble molecule by monocytes and macrophages. A 6.7-kb deletion in the gene of LILRA3 results in a null allele and an absence of function. The frequencies of the 6.7-kb deletion vary greatly in different populations, considerably higher in Northeastern Asians (0.56–0.84) compared with Africans (0.10) or Europeans (0.17). The homozygous LILRA3 deletion (nonfunctional *LILRA3*) has been demonstrated to be associated with Sjogren's syndrome (SS) and multiple sclerosis (MS) in Caucasians. However, in our previous studies, we found that in Chinese Han population, the LILRA3 non-deletion (namely functional *LILRA3*) contributes to susceptibility and subphenotypes of SLE and SS. With respect to the significant role of LILRA3 in immune-modulatory functions, we studied the role of LILRA3 in SLE.

Objectives: Our previous study has shown that functional *LILRA3* contributes to susceptibility and subphenotypes of systemic lupus erythematosus (SLE). However, the mechanism remains unclear. We aimed to evaluate the role of LILRA3 in SLE.

Methods: 126 SLE patients and 48 healthy controls were recruited in this study. Functional studies were performed using intracellular flow cytometry and ELISA.

Results: Both LILRA3 levels in serum and $CD14^+$ monocytes were significantly elevated in SLE patients compared with healthy controls. Elevated LILRA3 level was found positively correlated with SLEDAI. Furthermore, more elevated LILRA3 levels were found in patients with higher SLEDAI, presence of lupus nephritis and thrombocytopenia.

Conclusion: Both LILRA3 levels in serum and $CD14^+$ monocytes significantly increased in SLE and positively correlated with disease activity and severity. The up-regulation of LILRA3 expression may serve as a biomarker of disease activity and severity of SLE.

Table 1. Correlations of LILRA3 levels with the studied parameters in SLE patients

Clinical manifestations	LILRA3 in monocytes (MFI)		LILRA3 in serum (pg/mL)	
	Spearman's *r*	*P* value	Spearman's *r*	*P* value
SLEDAI	**0.398**	**0.0018****	**0.257**	**0.0036****
24h proteinuria excretion	**0.328**	**0.024***	0.159	0.09
Leucocytes	-0.033	0.680	**-0.253**	**0.0037****
Thrombocytes	-0.176	0.213	-0.144	0.11
Anti-dsDNA Ab	0.066	0.627	-0.061	0.498
C3	-0.138	0.290	-0.076	0.392
C4	-0.140	0.282	-0.025	0.777
IgA	0.068	0.604	0.017	0.852
IgM	0.107	0.417	0.053	0.557
IgG	0.143	0.218	0.228	0.01*
CRP	-0.164	0.237	0.088	0.339

SLE: systemic lupus erythematosus; SLEDAI: systemic lupus erythematosus disease activity index; LILRA3: Leukocyte immunoglobulin-like receptor A3; ANA: antinuclear antibody; Anti-dsDNA Ab: anti-double strand DNA Antibody; ACL: anticardiolipin antibody; AnuA: antinucleosome antibody; Sm: anti-Smith antibody; SS: anti-SSA antibody; C3 Complement component 3; C4: Complement component 4. CRP: C-reactive protein. * $P < 0.05$, ** $P < 0.01$. Spearman's correlation coefficient (*r*) was applied to detect correlation between two types of numerical data.

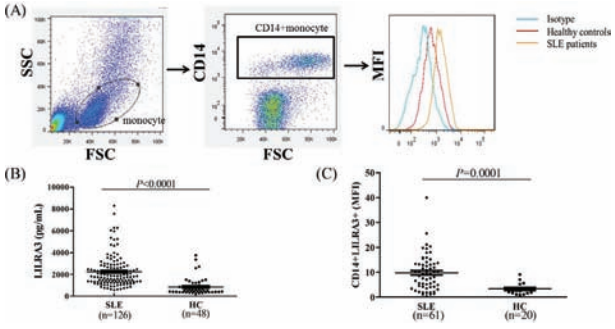


Figure 1

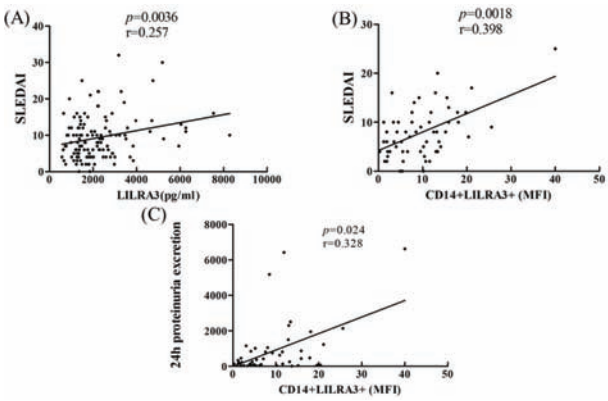


Figure 2

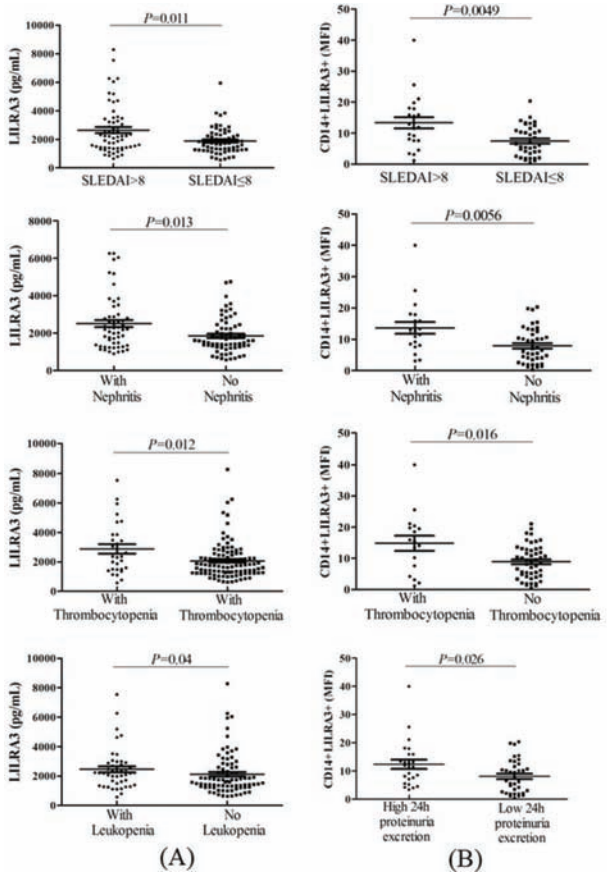


Figure 3

REFERENCES

[1] Du, Y., Y. Su, J. He, Y. Yang, Y. Shi, Y. Cui, C. Luo, X. Wu, X. Liu, F. Hu, X. Ma, L. Zheng, J. Zhang, X. Zuo, Y. Sheng, L. Wu, X. Zhang, J. Guo, and Z. Li, *Impact of the leucocyte immunoglobulin-like receptor A3 (LILRA3) on susceptibility and subphenotypes of systemic lupus erythematosus and Sjogren's syndrome*. Ann Rheum Dis, 2015. 74(11): p. 2070-5.

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AB0165 THE EUROPEAN REGISTRY ON OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (EUROAPS): A SURVEY OF 1100 CONSECUTIVE CASES

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Background: The obstetric antiphospholipid syndrome (OAPS) is an autoimmune disease defined by the presence of obstetric complications related to antiphospholipid antibodies. EUROAPS project is the biggest published European registry on obstetric antiphospholipid syndrome and it is ongoing.
Objectives: To analyse the clinical features, laboratory data and foetal-maternal outcomes, and follow them up on a cohort of 1100 women with obstetric antiphospholipid syndrome (OAPS).
Methods: Thirty hospitals throughout Europe have collaborated to carry out this registry. Cases with obstetric complaints related to antiphospholipid antibodies (aPL) who tested positive for aPL at least twice were included prospectively and retrospectively. The eight-year survey results are reported.
Results: 1100 women with 3653 episodes were included of which 2553 were historical and 1100 were latest episodes. All cases fulfilled the Sydney classification criteria. According to the laboratory categories: 29.2% were in category I,35.7% in IIa,22.4% in IIb and 12.7%) in IIc. Miscarriages appeared in 38.6% cases. Early preeclampsia and early foetal growth restriction appeared in 18.1% and 16.1%, respectively. Patients with recommended treatment had a good live-birth rate (85%), while patients with no treatment showed a poor birth rate (49.6%).
Conclusion: In this series, recurrent miscarriage is the most frequent poor outcome. To avoid false-negative diagnoses, all laboratory category subsets were needed. OAPS cases have very good foetal-maternal outcomes when treated. Results suggest that we were able to improve our clinical practice to offer better treatment and outcomes to OAPS patients.

REFERENCES

[1] Cervera R, Piette JC, Font J, Khamashta MA, Shoenfeld Y, Camps MT, et al. Antiphospholipid syndrome: clinical and immunologic manifestations and patterns of disease expression in a cohort of 1,000 patients. Arthritis Rheumatol 2002;46:1019–1027.
[2] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295–306.
[3] Esteve-Valverde E, Ferrer-Oliveras R, Alijotas-Reig J. Obstetric antiphospholipid syndrome. Rev Clin Esp 2016;216:135–45.

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Disclosure of Interests: Enrique Esteve-Valverde: None declared, Jaume Alijotas-Reig: None declared, Raquel Ferrer-Oliveras: None declared, Luis Sáez-Comet: None declared, Cristina Belizna: None declared, Amelia Ruffatti: None declared, Angela Tincani Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, AlphaSigma, Lillly, Jannsen, Cellgene, Novartis, Sara DeCarolis: None declared, Omar Latino: None declared, Ricard Cervera: None declared
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AB0166 ENHANCING THE QUALITY OF CLINICAL DATA THROUGH DATA CURATION IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's Syndrome (pSS) is a chronic systemic autoimmune disease that is affecting primarily women near the menopausal age, causing exocrine gland dysfunction, with clinical manifestations varying from dry eye and mouth to multi-systemic disorders [1]. The lack of automated means for data quality improvement in pSS cohorts and the huge time effort needed for manual curation, yield data that are irrelevant and incomplete, introducing undesirable implications in their analysis.
Objectives: To enhance the quality of the clinical data in pSS using automated data curation.
Methods: Anonymized clinical data were recruited from 380 patients with pSS from the University of Athens (UoA) cohort (300 patients, mean age 68.7914.84) and the Harokopio University of Athens (HUA) cohort (80 patients, mean age 59.2913.92). The features consist of SS-related measures (see [2] for details). The curation tool produces 3 files: (i) a quality report, including the metadata, the presence of outliers (using the z-score [3]), unknown data types, and missing values, on a feature-basis (data imputation [4] is used to fix features with < 50% missing values), (ii) the curated dataset, where the inconsistencies are marked using color notations, and (iii) a standardization report, where the features that share common terminology with those from a reference model [5] (i.e., a set of parameters that describe the pSS minimal requirements) are identified using lexical matching [6].
Results: For the UoA cohort, out of 167 features, 80 were classified as "bad", 30 with unknown data type, and 12 were marked for outliers (Fig. 1). An example of an outlier was found for the IgM (1370 mg/dL). For the HUA cohort, out of 204 features, 69 were classified as "bad", 5 with unknown data type, and 13 were marked for outliers. The standardization process succesfully matched 82 out of 88 (93.18%) pSS-related terms for the UoA cohort and 61 out of 69 (88.4%) terms for the HUA cohort.
Conclusion: Our strategy enhances the quality of the pSS clinical data through data curation and reduces the time effort needed for manual curation by the clinicians. The tool produces re-usable reports that can be used to fix inconsistencies, outliers, missing values, and harmonize pSS clinical data [6].

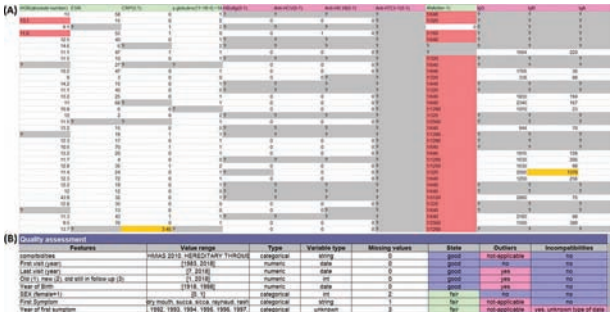


Figure 1. An instance of (A) the curated dataset, and (B) the quality assessment report, for the UoA cohort.

REFERENCES

[1] C. P. Mavragani, and H. M. Moutsopoulos, "Sjögren syndrome," Can. Med. Assoc. J., 2014;186(15):E579-86.
[2] S. Fragkioudaki, et al., "Predicting the risk for lymphoma development in Sjogren syndrome: an easy tool for clinical use," Medicine, 2016;95(25).
[3] P. J. Rousseeuw, and M. Hubert, "Robust statistics for outlier detection," Wiley Interdiscip. Rev. Data Min. Knowl. Disc., 2011;1(1):73-9.
[4] S. Van Buuren, "Flexible imputation of missing data," Chapman and Hall/CRC, USA, 2018.

[5] V. C. Pezoulas, et al., "Towards the establishment of a biomedical ontology for the primary Sjögren's Syndrome," in IEEE Eng. Med. Biol. Soc., 2018;4089-92.
[6] K. Kourou, et al., "Cohort Harmonization and Integrative Analysis from a Biomedical Engineering Perspective," IEEE Rev. Biomed. Eng., 2018.

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AB0167 SINGLE CELL RNA EXPRESSION IN LUPUS NEPHRITIS COMPARING AFRICAN-AMERICAN AND CAUCASIAN PATIENTS IDENTIFIES DIFFERENTIAL EXPRESSION OF TYPE I INTERFERON PATHWAY

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Background: African-American ethnicity is associated with a 3-fold higher risk of developing systemic lupus erythematosus (SLE). In addition, there is an increased risk of lupus nephritis (2-fold), high-risk histological features, and resistance to treatment. This may account for the increased mortality rate compared to Caucasian patients, especially in women.
Objectives: In Phase One of the Accelerating Medicines Partnership (AMP) study, we used single-cell RNA sequencing on kidney biopsies from patients with active lupus nephritis to identify pathways that were differentially expressed in African-American patients.
Methods: Single cell RNA sequencing was performed on renal biopsies obtained for clinical purpose for active nephritis using CEL-Seq2. Cell clusters with similar expression profile were identified using t-distributed stochastic neighbor embedding (t-SNE). First, the relative abundance of a cluster in AAs compared to Caucasian was determined using a logistic mixed model. Second, the differential expression profile was determined for each cell cluster and we applied Ingenuity Pathway Analysis (IPA) (QIAGEN Bioinformatics) to identify pathways of interest.
Results: Samples from 13 AA and 7 Caucasian patients were obtained. Of the 3097 sequenced cell libraries, we used 2354 which passed our quality filter for a total of 30155 unique molecular identifiers. We identified 16 cell clusters including CD4, CD8, B and plasma cells, NK, myeloid cells, and tubular cells. We identified 2 cell clusters unique to African-American patients, a T and a B cell population with high expression of interferon inducible genes. We also identified that same cell populations may have differential gene expression profiles across ethnicity. For example, CD4 T cells in African-Americans have a higher expression of type 1 and type 2 interferon pathways. In contrast, myeloid cells have several upregulated pathways in Caucasians, including ERK/MAPK signaling.
Conclusion: African-American lupus nephritis patients may have a stronger interferon pathway activation in infiltrating immune cells. Several other pathways, including ERK/MAPK, are differentially expressed in infiltrating cells based on ethnicity. These results suggest that ethnicity might predict a response to both current and upcoming treatments, paving the way for a more personalized approach to treatment in lupus nephritis. Further work in Phase 2 of AMP will confirm and extend these findings.
Disclosure of Interests: Andrea Fava: None declared, Yuji Zhang: None declared, Nir Hacohen: None declared, Arnon Arazi: None declared, Celine Berthier: None declared, Deepak Rao: None declared, Michael Brenner Grant/research support from: Roche: sponsored research agreement on stromal cells (but has nothing to do with checkpoint related disease), Consultant for: GSK: consultant. (I am part of their immunology network, a group of about 8 immunologists who advise them regularly and broadly in the areas of inflammation and infection)., David Wofsy Consultant for: GlaxoSmithKline – Member, data safety monitoring board
Novartis – Member, data safety monitoring board
Celgene – member, scientific advisory board, Anne Davidson: None declared, Matthias Kretzler: None declared, David Hildeman: None declared, E. Steve Woodle: None declared, Betty Diamond: None declared, Michelle A Petri Shareholder of: Pfizer, Merck, Grant/research support from: AstraZeneca, Exagen, Consultant for: Eli Lilly, GSK, Merck EMD Serono, Janssen, Amgen, Novartis, Quintiles, Exagen, Inova Diagnostics, AstraZeneca, Blackrock, Glenmark, UCB, and the Annenberg Center for Health Sciences
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AB0168 1,25 DIHYDROXYVITAMIN D IMPROVEMENTS ARTHRITIS BUT DOES NOT ALLEVIATE RENAL DAMAGE IN PRISTANE-INDUCED LUPUS MODEL

Eduarda Freitas[1,2], Thaís Karnopp[1,2], Jordana Miranda de Souza Silva[1,2], Rafaela Cavalheiro Do Espírito Santo[1,2], Thales Hein Da Rosa[1,2], Mayara Souza de Oliveira[1], Fabiany Gonçalves[2], Francine Hehn de Oliveira[3], Pedro Guilherme Schaefer[3], Odirlei Monticielo[1,2]. *[1]Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil*; *[2]Laboratório de Doenças Autoimunes, Porto Alegre, Brazil*; *[3]Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil*

Background: SLE is an autoimmune disease, characterized by the production of autoantibodies and tissue damage. The role of vitamin D (VD) in SLE has been increasingly explored. VD is a steroid hormone notably involved in the regulation of calcium and bone homeostasis, and its deficiency has been implicated in the development of SLE and other connective tissue diseases (2,3). The study of different murine models has provided a better understanding of these autoimmune phenomena. Pristane-induced lupus (PIL) represents a suitable model to study factors that could influence the induction and/or progression of SLE, including genetic factors.
Objectives: To evaluate the development and evolution of SLE after 1,25(OH)2D supplementation in the PIL model.
Methods: Female BALB/c mice divided into 3 groups: CO, PIL and PIL+VD. Lupus was induced in PIL and VD groups using pristane. VD group received a subcutaneous injection of calcitriol [2ug/kg] in PBS-Tween 20 buffer every second day during 180 days. Body weight, arthritis clinical score, edema and articular nociception was measured. On day 150 after pristane induction, the animals were placed in individual metabolic cages for urine collection for a period of 12h. Protein levels on urine were analyzed using urine test strips. At the end of the experimental period, serum, tibiotarsal joint and kidneys was collected. Hind paws were collected to confirm the development of arthritis by histological analysis with HE staining. The glomerular cellularity was quantified by counting the total cell nuclei per glomerulus on HE slides. Immune complex deposition (IgG and IgM) in kidney was examined by direct immunofluorescence. IL-2, IL-4, IL-6, IFN-γ and TNF-α were measured by Luminex technology in serum. Data was analyzed with ANOVA Two-Way followed by Bonferroni and independent sample t-test. $p<0.05$ was considered significant. All data are represented as mean±SD.
Results: PIL group showed arthritis and kidney injury, characterized by increased proteinuria, glomerular mesangial expansion and inflammation. Moreover, PIL model showed increased levels of IL-6, TNF-α and IFN-γ in serum. VD treatment reduced arthritis incidence compared PIL (42vs85%;$p<0.01$) at the end of the experimental period. The arthritis clinical score (1.00±1.15vs2.85±1.34;$p<0.001$) and the hind paws edema (0.20±0.03vs0.24±0.05 mL;$p<0.05$) in the VD group were also attenuated in relation to the PIL at day 180 after induction. VD was able to reduce synovial hyperplasia (0(0,1)vs2(2,3);$p<0.05$), erosion in bone (0(0,1) vs2(2,2);$p<0.05$) and cartilage (1(0,2)vs3(2,3);$p<0.05$) when compared to the PIL group. Treatment with VD was not able to reduce proteinuria levels (44.28vs47.14 mg/dL), decrease mesangial hypercellularity (31.48±2.6vs33.12±3.4nucleo/glomeruli) or IgG (17.88±6.0vs24.04±6.2) and IgM (12.62±6.9vs15.57±3.7) deposition in the kidney. VD supplementation did not alter IL-6, TNF-α, IL-2 and IL-4 cytokine levels, but reduce IFN-γ levels ($p<0.01$).
Conclusion: VD improves arthritis but does not influence renal injury despite reducing IFN-γ levels. These results support that the role of VD may be different depending on acting site, what could explain different responses according clinical phenotype. Therefore, further investigations of VD are needed to explore the supplement dosage, timing, and the molecular basis in SLE.

REFERENCES

[1] Pons-Estel GJ, et al. Seminars in Arthritis and Rheumatism. 2010. 2 Kamen DL, et al. Autoimmun Rev 2006; 5: 114–117. 3 Orbach H, et al. Ann N Y Acad Sci 2007; 1109: 385–400.

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Disclosure of Interests: None declared
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AB0169 **SNP (1513A>C AND 489C>T) OF P2X7 RECEPTOR IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH SEROSITIS**

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Background: our preliminary data demonstrated that expression and activity of P2X7R was impaired in Systemic Lupus Erythematosus (SLE) and associated with a reduced production of IL-1β[1]. Serositis is a typical manifestation of SLE characterized by a marked inflammation, which has been suggested to be an "inflammasome driven" manifestation.
Objectives: to investigate the role of 1513A>C (rs3751143) and 489C>T (rs208294) Single Nucleotide Polymorphisms (SNPs) which are differently associated with loss or gain of function, respectively, of P2X7R, a potent activator of the NLRP3 inflammasome and IL-1β release, in patients with SLE and with a history of serositis (SLE-S).
Methods: DNA was extracted from whole blood and used for evaluation of 2 P2X7R SNPs (1513A>C and 489C>T). Considering the combined action of these two SNPs, the overall activity of P2X7R was divided, into three groups: GOF (gain of function), normal function (NF), and LOF (loss of function). In addition, peripheral blood mononuclear cells (PBMCs) were isolated from venous blood and employed to evaluate P2X7R and NLRP3 expression by RT-PCR, assess P2X7R activity as Benzoyl ATP (BzATP)-induced intracellular Calcium ([Ca2+]i) increments and evaluate in vitro IL-1β following stimulation with lipopolysaccharide (LPS) and BzATP, either separately or in combination.
Results: 33 SLE patients (pts), 11 with (SLE-S) and 22 without serositis (SLE-NS) were enrolled. Mean age was 40.9±10.9 years and disease duration was 135.3± 108.6 months. No significant difference in disease activity and clinical characteristic was found between the two groups (table 1). Evaluating 1513A>C SNP, 20 pts were positive for A/A and 13 for A/C phenotype respectively, while in case of 489C>T SNP, 7 pts presented C/C, 12 C/T and 14 T/T phenotype with a comparable distribution between SLE-NS and SLE-S (table 1). After combination of different phenotypes, 9 pts presented normal function (NF), 22 gain of function (GOF) and 2 loss of function (LOF) with no significant difference between SLE-S and SLE-NS (table 1). P2X7R activity, (evaluated as IL-1 β production and [Ca2+] i increments,) and expression (evaluated with RT-PCR) were comparable between SLE-S and SLE-NS. No significant difference was found between expression and activity of P2X7R and NLRP3 and the two SNPs evaluated (table 2).

Table 1 Comparison between patients with a positive history of serositis (SLE-S) vs patients without history of s (SLE-NS)

	SLE-NS 22 (66.7%)	SLE-S 11 (33.3 %)	P (SLE-NS vs SLE-S)
Demografic parameters No. female/male	21/1	9/2	ns
Age. mean ± SE years	40.8± 8.4	44.2± 13.1	0.36
Disease duration (months)	134.7 ± 98.3	122.5± 96.2	0.28
Ongoing treatment Hydroxychloroquine (200 mg/day)	18 (81.8%)	8 (72.7%)	0.36
Corticosteroids (2.5 up to 12.5 mg/day)	18 (81.2%)	9 (81.2%)	1
Mayor immunosoppressive treatment (Mycophenolate mofetil, Cyclosporine A, Azathioprine, MTX, PEX, RTX)	10 (45.5%)	4 (36.6%)	0.25
Ongoing dosage of steroids mg mean ± SE	3.7 ± 0.59	5.1 ± 1.6	0.34
Cumulative dosage of steroids gr mean ± SE	19.8± 3.6	19.5 ±6.7	0.95
Current clinimetric parameters SLEDAI-2K. mean ± SE	3.3 ±0.7	3.9±0.8	0.61
SLICC. mean ± SE	0.33 ± 0.7	0.45 ±0.2	0.55
SNP 1513A>C= A/C	9 (40.9%)	4(36.4%)	0.55
SNP 1513A>C =AA	13 (59.9%)	7 (63.6%)	0.54
SNP 489C>T = CC	5 (22.7%)	2 (18.2%)	0.57
SNP 489C>T = CT	7 (31.8%)	5 (45.5%)	0.35
SNP 489C>T = TT	10 (45.5%)	4 (36.4%)	0.45
LOF	7 (31.8%)	4 (36.4%)	0.54
GOF	15 (68.2%)	7(63.4%)	0.55

Conclusion: our data indicate that the 1513A>C and 489C>T SNPs do not seem linked with reduced activity and expression of P2X7R that we previously observed in our cohort of lupus patients. Furthermore, no significant association was found between expression of these SNPs and development of serositis.

REFERENCES

[1] *P2X7 receptor in systemic lupus erythematosus (SLE). Exploring a novel pathogenetic pathway in lupus related serositis. F. Furini.* Ann Rheum Dis, *volume 77, supplement Suppl, year 2018, page A871*

Table 2: Activity and expression of P2X7R-NLRP3 inflammasome axis: influence of combinated effect of two SNP

	GOF	LOF	p (GOF vs LOF)
ΔCa^{2+} (Fura2) nM±SE	54.8± 40.0	74.2±14.5	0.42
IL-1β levels in monocytes supernatants pg/ml; mean ±SE			
RPMI	81.3± 29.9	48.2 ± 22.0	0.49
LPS	130.7± 26.9	231.1 ± 70.1	0.71
LPS+BZATP	2159.1± 203.2	2392.7 ± 166.9	0.46
BZATP	110.0 ± 31.6	153.9 ± 55.1	0.46
RT-PCR P2X7R mean (±SE)	1.1± 0.13	0.97±0.1	0.63
RT-PCR NLRP3 mean (±SE)	4.7±0.3	3.7±0.7	0.47

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AB0170 **TUBERCULOSIS IN PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES : THE TUNISIAN EXPERIENCE**

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Background: The incidence of tuberculosis among patients with systemic rheumatic **diseases is much higher than in the general population.** The clinical manifestations of both systemic rheumatic disease activity and tuberculosis, (i.e. fever, weight loss, asthenia) may overlap or lead to confusion. The immunosuppression of systemic diseases makes the management of patients with tuberculosis more complicated.
Objectives: The purpose of our study was to describe the clinical characteristics of patients with systemic rheumatic diseases and tuberculosis.
Methods: A retrospective study, from 1998 to 2018, in the internal medicine service in Fattouma Bourguiba hospital, Tunisia, of 59 patients suffering from connective tissues disease, treated by corticosteroids linked in one or several treatments to immunosuppressants, who subsequently developed tuberculosis.
Results: Fifty nine patients were included (46 women and 13 man) with a mean age of 47years (range from 18-83 years). Systemic illnesses were: systemic lupus erythematous (13.6%, n = 8), Gougerot-Sjögren syndrome (secondary or primary) (18.6%, n = 11), systemic scleroderma (5.1%, n = 3), rheumatoid arthritis (n = 1), Takayasu arteritis (n=1), Horton disease (n=2), periarteritis nodosa (n=1), Wegener's granulomatosis (n= 2) and Behçet's disease (n=1). 45 patients (76.6%) were treated with corticosteroids and/or immunosuppressants in 3 cases (methotrexate in one case, cyclophosphamide in one case and azathioprine in one case) before the tuberculosis was diagnosed. The clinical manifestations most commonly observed were : weight loss in 55.9%, fatigue in 50.8% and fever in 24.7%. The tuberculin skin tets was positive in 45.8%. Quantiferon-TB-Gold was positive in eleven cases. Twelve patients had an abnormal chest X-ray. The location of the tuberculosis was pulmonary (32.3%, n = 19), ganglionic (33.9%, n = 16), urogenital (20.3%, n = 12), lymphatic (n = 5), abdominal (n=4), cerebral (n=2), ocular (n=2), osteoarticular (n= 2) and more than one location in 23.7% of the cases. The diagnosis of tuberculosis was confirmed by bacteriology in 13,6% (n = 8) and in thirteen cases, histologically (22.03%).The systemic rheumatic disease was clinically active at the time of the diagnosis of tuberculosis in 8 patients.The diagnosis of **systemic** rheumatic **diseases** was made before that of tuberculosis in 13 patients and concomitantly in 5. Under tuberculosis treatment by four drugs then by two drugs, the evolution of tuberculosis was favourable in most of our patients. Three of the patients developed an allergy in isoniazid. Nine patients have developped hepatotoxicity with pyrazinamide. Retrobulbar neuritis was observed in 3 cases treated with ethambutol.
Conclusion: This study confirms the often extra-pulmonary character of tuberculosis in patients with systemic disease as well as the difficulty of diagnosis and problems multiplied by this association. The screening strategies for tuberculosis should probably be extended in all patients with systemic rheumatic diseases receiving glucocorticoids and/or immunosuppressive therapy.

REFERENCES

[1] SEGAL B, SNELLER M: Infectious complications of immunosuppressive therapy in patients with rheumatic diseases. Rheum Dis Clin North Am 1997; 23: 219-37.

[2] Hernández-Cruz B1 et al, Mycobacterium tuberculosis infection in patients with systemic rheumatic diseases. A case-series.Clin Exp Rheumatol. 1999 May-Jun;17(3):289-96.

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AB0171 THE REGULATION AND PHARMACOLOGICAL MODULATION OF IMMUNE COMPLEX INDUCED PRODUCTION OF TYPE III IFN BY PLASMACYTOID DENDRITIC CELLS

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Background: The type I Interferons (IFNs) are the most important drivers of the IFN gene signature in Systemic Lupus Erythematosus (SLE). However, both type II and type III IFNs (IFN-λ1-3) can be measured in a proportion of patients with SLE and contribute to the IFN signature. The exact role of type III IFNs in SLE is not completely clear, but serum levels of type III IFN correlate with disease activity and specific organ manifestations, such as arthritis, nephritis and anti-dsDNA antibodies. Type III IFN can be induced in pDCs by TLR9 agonist Oligodinucleotide (ODN) 2216 and many viruses. Whether type III IFN can also be induced in pDCs by nucleic acid containing immune complexes (IC), has, to our knowledge, not been investigated before.

Objectives: We asked if RNA containing immune complexes (RNA-IC), which trigger the synthesis of large amounts of IFN-α by plasmacytoid dendritic cells (pDCs), can act as stimuli for type III IFN production, and how this production is regulated by Natural Killer (NK) cells and different cytokines. We also investigated if the type III IFN production could be blocked by hydroxychloroquine (HCQ) and an interleukin receptor 1 associated kinase 4 inhibitor (IRAK4i).

Methods: Peripheral blood mononuclear cells (PBMCs) from SLE patients or healthy individuals were used to isolate PDCs and natural killer (NK) cells, or were depleted of monocytes. Cells were stimulated with RNA-IC, and cytokines were measured by immunoassays. mRNA expression in RNA-IC stimulated pDCs and NK cells cells was analyzed with a microarray. The effect of HCQ and IRAK4i on the IFN-λ1/3 production was investigated in pDCs and NK cells from healthy individuals.

Results: Type III IFN mRNA expression was strongly upregulated in co-cultures of pDC-NK cells stimulated with RNA-IC. High levels of IFN-λ1/3 and IFN-λ2 (medians 2000 pg/ml and 100 pg/ml) were detected in supernatants from RNA-IC stimulated pDC-NK cell co-cultures. IFN-λ2 enhanced IFN-λ1/3 and IFN-α production by purified pDCs. Interleukin (IL) -3, IL-6, and GM-CSF significantly enhanced IFN-λ1/3 production (4-5 fold) by RNA-IC stimulated pDCs. Monocyte depleted PBMCs and pDC-NK cell co-cultures from 15% and 9% of SLE patients produced IFN-λ1/3 in response to RNA-IC stimulation. Exogenous IFN-α2b and GM-CSF in pDC-NK cell co-cultures increased the proportion of patients responding to RNA-IC stimulation from 9 to 36%. IFN-λ1/3 production by RNA-IC-stimulated pDCs and pDC-NK cells was significantly inhibited by HCQ (by 99% and 93% respectively) and an IRAK4i (by 98% and 96% respectively).

Conclusion: pDCs produce both type I and type III IFN in response to RNA containing immune complexes. This is promoted by activated NK cells as well as a number of pro-inflammatory cytokines, including IFN type I and type III, considered important in SLE. Consequently, in order to achieve a proper control the IFN driven autoimmune process in SLE, both type I and type III IFN need to be targeted. In this system of stimulated, co-cultivated pDCs and NK cells, HCQ and an IRAK4 inhibitor blocked the type III IFN production.

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AB0172 EXPRESSION OF SLAMF6 AND ITS FUNCTIONAL SIGNIFICANCE IN PODOCYTES OF LUPUS NEPHRITIS

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Background: Systemic lupus erythematosus (SLE) is multisystem disorder that is caused by tissue damage resulting from antibody and complement-fixing immune complex deposition. Lupus nephritis (LN) is frequent complication and one of the most serious manifestations of SLE. The expression of nephrin, as podocyte marker, is reduced in various renal diseases that develop into nephrotic syndrome[1)]. The alteration of the structural protein in podocytes is known as a mechanism of proteinuria in LN.

Objectives: The signaling lymphocyte activation molecule family (the SLAM family) of type I transmembrane receptors consists of nine related members of the immunoglobulin superfamily and has been reported to mediate important regulatory signals between immune cells through their homophilic and heterophilic interactions[2)].The 1q23 region (*Sle1b* region in mouse) on human chromosome 1 including the SLAMF cluster of genes, containing SLAMF6 has been identified as a lupus susceptibility locus[3)].It has been shown that the expression of signaling lymphocyte activation molecule family 6 (SLAMF6) is enhanced in CD4+T cells of SLE patients and is involved in IL-17 production[4)]. We sought to examine the functional role of SLAMF6 in lupus podocytes.

Methods: We evaluated the co-expression of nephrin, a podocyte marker and SLAMF6 in kidney of normal controls and LN patients, also in B6 and MRL/*lpr* mice at the age of 8wk and 16wk by immunofluorescence analysis. We also examined nephrin positive SLAMF6 expression in isolated podocytes from B6 and MRL/*lpr* kidneys. Then, we analyzed the expression of SLAMF6 in CD4+T cells of isolated kidney and spleen in B6 and MRL/*lpr* mice. We treated human podocytes with IgG from healthy individuals and LN patients for 24 h and 48h and analyzed the expression of SLAMF6 by real-time PCR.

Results: In the histopathology, the expression of SLAMF6 was increased in nephrin positive area in LN patients and MRL/*lpr* mice compared to each control groups. Although the expression of nephrin in MRL/*lpr* mice kidney at 16 wk old decreased compared to B6 mice at same age, the expression of SLAMF6 in podocytes increased in diseased MRL/*lpr* mice compared to B6 mice. Similarly, the expression of SLAMF6 in CD4+ T cells increased in diseased MRL/*lpr* mice kidney and spleen compared to B6 mice. The level of SLAMF6 mRNA elevated in human podocytes exposed to LN-derived IgG compared to healthy individuals-derived IgG.

Conclusion: The expression of SLAMF6 is enhanced in LN podocytes, suggesting that the possibility of cooperating with CD4+T cells contributing to its dysfunction. Further examination is needed to investigate in detail how SLAMF6 is involved in the development of LN in the future.

REFERENCES

[1] J Am Soc Nephrol. 2003 Aug;14(8):2063-71.,

[2] Nat Rev Immunol. 2003 Oct;3(10):813-21.,

[3] Nat Rev Rheumatol. 2010 Jun;6(6):348-57.,

[4] J Immunol 2012; 188:1206-1212.

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AB0173 **LONG NON-CODING RNA, LINC00487 EXPRESSION IS UPREGULATED IN B CELLS AND CORRELATES TO DISEASE ACTIVITY IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME**

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by interferon signature [1] and exocrine gland dysfunction which leads to dryness of the eyes and mouth [2]. B cells are considered to play an important role in the pathogenesis of pSS. Dysregulation of B cells can lead to production of anti-Sjögren's syndrome-related antigen A (anti-SSA) autoantibodies.
Objectives: We investigated the differential gene expression of peripheral B cell subsets to reveal the precise role of B cells in the pathogenesis of pSS.
Methods: We enrolled pSS patients (n=6) and healthy controls (HC) (n=6), with matching for age and sex. Peripheral B cells acquired from the participants were separated by cell sorting into 4 subsets: $CD38^-IgD^+$, $CD38^+IgD^+$, $CD38^{high}IgD^+$ and $CD38^{\pm}IgD^-$. Total RNA was extracted and gene expression was measured using the Human Genome U133 Plus 2.0 Array (Affymetrix). The data were bioinformatically analyzed with reference to the corresponding clinical information.
Results: Using principal component and clustering analyses, we found that transcript expression patterns depended on cell type rather than clinical condition (pSS or HC). Interferon signaling was the most upregulated pathway in many of B cell subsets of pSS patients. As well as HLA and interferon signature genes, LINC00487 was upregulated significantly in all B cell subsets. Its fold changes in $CD38^-IgD^+$, $CD38^+IgD^+$, $CD38^{high}IgD^+$ and $CD38^{\pm}IgD^-$ were 8.4 (p=0.038), 11.3 (p=0.014), 8.5 (p=0.089) and 6.37 (p=0.078), respectively. In addition, the normalized intensity value of LINC00487 was significantly correlated with disease activity score in all pSS B cell subsets, namely $CD38^-IgD^+$(Figure A, r=0.96, p=0.002), $CD38^+IgD^+$(Figure B, r=0.90, p=0.015), $CD38^{high}IgD^+$ (Figure C, r=0.81, p=0.049) and $CD38^{\pm}IgD^-$ (Figure D, r=0.96, p=0.003). The expression of LINC00487 in B cell lines was regulated by IFNα.
Conclusion: Compared to HC, patients with pSS showed upregulation of the interferon signaling pathway and LINC00487 gene in all B cell subsets. This upregulation correlated with disease activity and regulated by IFNα in B cell lines. These results may suggest that long non-coding RNA contributes to B cell dysregulation in patients with pSS and the precise role of LINC00487 in B cell and pathogenesis of pSS requires further study.

REFERENCES

[1] Muskardin TLW, et al. Nat Rev Rheumatol 2018;14:214-228.
[2] Qin, B. et al. Ann Rheum Dis. 2015;74:1983-1989.

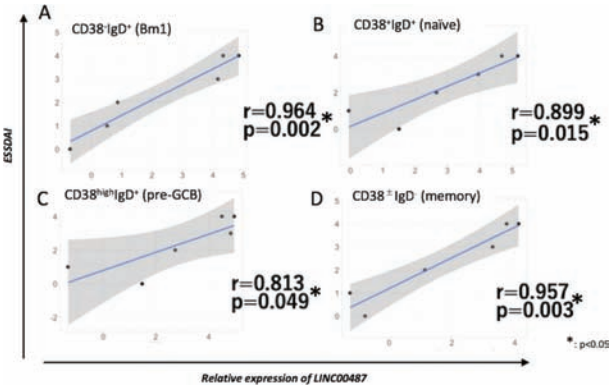


Figure. Correlation between the expression of LINC00487 and disease activity score in each B cell subset.

ESSDAI; EULAR Sjögren's Syndrome Disease Activity Index

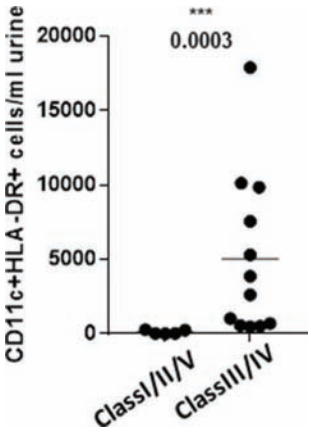
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AB0174 **CLINICAL SIGNIFICANCE OF THE URINARY CD11C+ MYELOID CELLS IN THE PATIENTS WITH LUPUS NEPHRITIS**

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Background: It is known that various immune cell populations play important pathogenic roles in lupus nephritis (LN). Kidney-infiltrating myeloid cells are responsible for the pathology in murine model for LN. However, the characteristics of myeloid cells in patients with LN have not previously been investigated because of difficulties of access to affected tissue. Recent studies have reported that the urine has become an alternative substitute for kidney tissue to study renal pathology.
Objectives: Therefore, we investigated the characteristics and functions of urinary myeloid cells in patients with LN.



Methods: Within viable CD45+ cells, the frequency and absolute numbers of myeloid cells in the urine were examined after exclusion of lymphoid cells by expression of CD3, CD19 and CD56. Expression of phenotypic markers and

production of pro-inflammatory cytokines were analyzed in urinary myeloid cells of patients with LN.
Results: Myeloid cells were identified by the expression of CD45+ and CD11c+ in the urine of patients with LN. The frequency and absolute numbers of myeloid cells were markedly increased in the urine of patients with proliferative LN than non-proliferative LN. In addition, titers of anti-dsDNA antibodies were correlated with the frequency or numbers of urinary CD11c+ myeloid cells. These urinary CD11c+ myeloid cells showed the phenotypes of infiltrated monocyte-derived cells rather than tissue-resident macrophage. In addition, CD11c+ myeloid cells were localized in tubulointerstitium and had capacity to produce pro-inflammatory cytokines including IL-6. Further, we found that there was a significant population of tubule cells in the urine, which is correlated with the frequency of CD11c+ myeloid cells.
Conclusion: Our results indicate that CD11c+ myeloid cells are present in the urine and contribute to tubulointerstitial inflammation in proliferative LN.
Disclosure of Interests: None declared
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AB0175 ABSOLUTE REDUCTION OF PERIPHERAL CD4+CD25+FOXP3+T REGULATORY CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: T lymphocytes are important contributors to systematic lupus erythematosus (SLE). Regulatory T (Treg) cells, with the capacity to suppress immune responses, effector T cells (Teff), which promote inflammation, have been intensively studied in recent years. However, previous reports describing the respective changes of Treg and Teff, especially T helper cells (Th17) in SLE patients were controversial. Here, we investigated both absolute number and percentage of CD4+CD25+Foxp3+Treg (CD4Treg) cells and effector cells on a large scale and the role of low-dose interleukin-2 (IL-2) in SLE.
Objectives: To investigate both absolute number and percentage of CD4+CD25+Foxp3+Treg (CD4Treg) cells and effector cells on a large scale and the role of low-dose interleukin-2 (IL-2) in SLE.
Methods: Two hundred and thirty-five SLE patients (219 women and 16 men), with mean age of 37.80 ± 14.00 years, were enrolled. The absolute count and percentage of subpopulation of peripheral blood (PB) lymphocyte in these patients were measured by flow cytometry combined with internal microsphere standard. And low-dose IL-2 was used among 127 patients at a dosage of fifty WIU every day for five days. Immunological and clinical assessments were performed again at the end of IL-2 treatment. Ninety healthy volunteers, matched for patients' age and gender, were also included for the estimation of lymphocyte subsets.
Results: As compared to healthy controls (median of Treg cells: 33.09 cells/ul), the absolute number of circulating CD4Treg cells were significantly decreased in SLE patients (median: 15.49 cells/ul, P<0.001). The median ratios of Th17/Treg cells in patients were greatly higher than those of healthy volunteers [0.42 (0.19, 0.88) vs. 0.21 (0.15, 0.34), P<0.001], while there was not significantly different in peripheral Th17 cell between two groups. Besides, Th1, Th2, CD8+T, B cells and their respective ratios to Treg cells were like that of Th17 cells as well. Moreover, CD4Treg cells were negatively correlated with ESR and SLEDAI score (r=-0.198, P=0.01; r=-0.25, P=0.002). While no obvious correlation was seen between Th17 cells and SLEDAI score. After IL-2 therapy in SLE, there was a four-fold increase in circulating CD4Treg cells [43.73 (24.08, 74.22) vs. 11.95 (7.51, 20.34), P<0.001], whereas Th17 cells were increased slightly. The ratio of Th17/Tregs was decreased significantly in patients with IL-2 treatment [0.19 (0.09, 0.41) vs. 0.52 (0.23, 0.95), P<0.001], tended to balance and had no difference with healthy individual (P=0.275). Similarly, there were same trends in Th1, Th2, CD8+T, B and NK cells.
Conclusion: The reduction of CD4Tregs but not the elevation of effector cells may be the major reason for imbalance of Teff/Treg, indicating that SLE is an autoimmune disease triggered by the defect of immunotolerance. More importantly, low-dose IL-2 might promote the proliferation of various lymphocyte subpopulation, and mainly modulated the abundance and immunosuppression activity of Tregs, which effectively induced autoimmune tolerance and further improved clinical symptoms.

REFERENCES

[1] Bonelli M, Goschl L, Bluml S, et al. (2014) CD4+CD25-Foxp3+T cells: a marker for lupus nephritis? Arthritis Research & Therapy. 16: R104.
[2] M Miyara, G Gorochov, M Ehrenstein, et al. (2011) Human FoxP3+ regulatory T cells in systemic autoimmune diseases. Autoimmunity Reviews. 10 (12): 744-55.
[3] Żabińska M, Krajewska M, Kościelska-Kasprzak K, et al. (2016) CD4(+) CD25(+) CD127(-) and CD4(+)CD25(+)Foxp3(+) Regulatory T Cell Subsets in Mediating Autoimmune Reactivity in Systemic Lupus Erythematosus Patients. Arch Immunol Ther Exp (Warsz). 64(5): 399-407.

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AB0176 MITOGEN- AND STRESS-ACTIVATED PROTEIN KINASE-1 (MSK1) AS THE LINK BETWEEN MIR-130A-DYSREGULATION AND CDC2-ACTIVATION IN SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands and dryness of mouth and eyes. T and B lymphocytes that infiltrate the salivary glands play a central role in local production of autoantibodies and cytokines, associated with dryness and tissue-damage. Type-2 conventional dendritic cells (cDC2) are very potent antigen-presenting cells and have the ability to produce a variety of cytokines involved in T and B cell activation, germinal centres formation and autoantibody production.
Objectives: Considering the critical role of microRNAs (miRNAs) in regulation of cell activation, we investigated their potential dysregulation in circulating cDC2s of patients with pSS compared to healthy controls (HC).
Methods: CD1c-expressing cDC2s were isolated from peripheral blood of pSS patients and controls from two independent cohorts. In the donors from the discovery cohort (15 pSS, 6 HC) the expression of 758 miRNAs was screened; the replication cohort (14 pSS, 11 HC) was used to confirm consistent differential expression of 18 identified miRNAs. A quantitative mass spectrometry-based technique (pSILAC) in HEK-293T cells was used to identify novel targets of the replicated miRNAs. Target-miRNA interaction was replicated in primary cDC2s. Differences in cytokine production between pSS and HC cDC2s were evaluated by FACS. cDC2s were cultured in the presence of different MSK1-inhibitors to examine their effect on cytokine production.
Results: The expression of miR-130a and miR-708 was consistently decreased in cDC2s from pSS patients compared to HC in both cohorts, and both miRNAs were downregulated upon stimulation via TLR3 and TLR7/8. MSK1 was identified as a novel target of miR-130a and overexpression of miR-130a reduced MSK1 protein expression in both HEK-293T cells and primary cDC2s. In-line with the regulation of MSK1 by miR-130a, MSK1 expression was higher in cDC2s of pSS patients as compared to controls. An increased frequency of cDC2s producing-IL-12 and TNF-α was observed in pSS patients compared to HC, consistent with the central role of MSK1 in regulation of cytokine production. Exposure to either of two different MSK1 inhibitors in vitro reduced cDC2 activation and the production of IL-12, TNF-α and IL-6.
Conclusion: We here provide the first evidence of molecular dysregulation of cDC2s in pSS, including decreased expression of miR-708 and miR-130a, which can result from TLR activation, and enhanced production of pro-inflammatory cytokines. In view of its central role in NF-κB signalling, inhibition of MSK1 to decrease cell activation and inhibit pro-inflammatory cytokine production represents a novel therapeutic avenue for treatment of Sjögren's Syndrome.
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AB0177 ARE THERE ANY CLINICAL AND SEROLOGICAL DIFFERENCES BETWEEN PATIENTS WITH PRIMARY AND SECONDARY (SLE) ANTIPHOSPHOLIPID SYNDROME?

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Background: Antiphospholipid syndrome (APS) could be diagnosed as primary (PAPS) or secondary (SAPS - accompanying other diseases, mainly found in patients with systemic lupus erythematosus -SLE)
Objectives: The aim of our study was to determine if pts with PAPS and SAPS had different clinical and serological status.

Methods: The study involved 80 (59-f and 21-m) APS patients (pts) 24 pts had PAPS and 56 pts had APS following SLE. In the whole study group the mean age was: 39.3± 12.7 years (range 18-71), the duration of the disease was 8.8 ± 8.3 years (range 0-37).

The presence of aPL was detected in patients' serum using the commercially available tests: aPL-immunodot assay Anti-Phospholipid 10 Dot, for the qualitative detection of IgG or IgM antibodies. The statistical data analysis was performed using Statistica v13.0

Results: In the study group of 80 patients we have detected the presence of the following aPLs: a- cardiolipin IgM -37%, IgG -50.6%; a-phosphatidic acid IgM -19.7%, IgG -13.3%; a-phosphatidylcholine IgM and IgG -1.2; a-phosphatidylethanolamine IgM -1.2% and IgG -0; a-phosphatidylglycerol IgM – 5.0%, IgG -12.5%; a-phosphatidylinositol IgM-10.0%, IgG-12.5%; a-phosphatidylserine IgM-31.0%, IgG-50.6%; a-annexin V IgM -20%, IgG -10%; a-β2-GP I IgM-44.5%, IgG-35.0%; a-prothrombin IgM -44.5%, IgG-30%.

Table 1

	PAPS n=24	SAPS n=56	P<0.05
aCL IgM aCL IgG	10 (41.6%)	20 (35.7%)	NS
	10 (41.6%)	31 (55.3%)	NS
a-phosphatidic acid IgM a-phosphatidic acid IgG	8(33.3%)	8(14.3%)	**P=0.0515**
	3 (12.5%)	8 (14.3%)	NS
a-phosphatidylcholine IgM a-phosphatidylcholine IgG	0(0%)	1(1.8%)	NS
	0(0%)	1(1.8%)	NS
a-phosphatidylethanolamine IgM a-phosphatidylethanolamine IgG	0(2.2%) 0(%)	0(%) 0(%)	NS NS
a-phosphatidylglycerol IgM a-phosphatidylglycerol IgG	2 (8.3%)	2 (3.6%)	NS
	3 (12.5%)	7 (12.5%)	NS
a-phosphatidylinositol IgM a-phosphatidylinositol IgG	5 (20.8%)	3 (5.4%)	**P=0.0345**
	3 (12.5%))	7 (12.5%)	NS
a-phosphatidylserine IgM a-phosphatidylserine IgG	11 (45.8%)	14 (25.0%)	0,0655
	12 (50.0%)	29 (51.8%)	NS
a-B2GPI IgM a-B2GPI IgG	17 (70.8%)	12 (28.6%)	P=0,0004
	7(29.2%)	21 (37.5%)	NS
a-annexin V IgM a-annexin V IgG	6 (25.0%)	10 (17.9%)	NS
	2 (8.3%)	6(10.7%)	NS
a-prothrombin IgM a-prothrombin IgG	16 (66.7%)	20 (35.7%)	**P=0.0108**
	8 (33.3%)	16 (28.6%)	NS

Table 2

Clinical symptoms	PAPS n=24	SAPS n=56
stroke	3 (12.5%) NS	5 (9.0%)
pulmonary embolism	6 (25.0%)	7 (12.5%)
thrombosis	14 (58.3%) NS	19 (34.0%)
obstetric complications	3/ (18.9%) NS	12/ (28.0%)
valve defects	4 (16.7%) NS	8 (14.3%)
livedo reticularis	2 (8.3%) NS	7 (12.5%)
nephropathy	5(20.8%) NS	19 (34.0%)
deep vein thrombosis	14 (58.3%) **P=0,0422**	19 (34.0%)
hypertension	12 (50.0%) NS	23 (41.0%)
convulsions/chorea	0(0%) NS	5 (8.9%)
migrene	1(0%) NS	4 (8.9%)
depression	1(4.2%)	2 (3.6%)

The following clinical symptoms of APS were also present: stroke -10%, arterial/venous thrombosis -34%, pulmonary embolism-16.3%, obstetric complications-25.4%, nephropathy – 30.0%, hypertension-43.8%, valve defects 15.0%, livedo reticularis 11.2%, convulsions/chorea-6.2%, thrombocytopenia- 23.7% of the study group.

During the study we detected statistically significant differences in the frequency of occurrence of **aPLs between groups with PAPS and SAPS:** a-phosphatidylinositol p=0,0345; a-β2-GP I IgM p=0.004; a-prothrombin IgM p=0.0108 a-phosphatidic acid IgM p=0.045 (table 1)

There are no differences in the assessed clinical symptoms between pts with PAPS and SAPS, apart from significantly higher frequency of the deep vein thrombosis in pts with PAPS (p- 0.04).

Conclusion: The clinical pictures of PAPS and SAPS are similar. Only deep vein thrombosis occurs more frequently in pts with PAPS.

Some classic and novel aPLs occur more frequently in pts with PAPS than in SAPS, and maybe could become a biomarker of PAPS

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AB0178

TRANSCRIPTION PROFILING OF PERIPHERAL B CELLS IN ANTIBODY-POSITIVE PRIMARY SJOGREN'S SYNDROME REVEALS INTERFERON SIGNATURE AND UPREGULATED EXPRESSION OF GENES WHICH MAY BE PREDICTIVE OF TRANSFORMATION TO LYMPHOMA AND CORRELATED TO CHRONIC PULMONARY NON-TUBERCULOUS MYCOBACTERIAL (NTM) INFECTION

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Background: Primary Sjögren's syndrome (pSS) is the second most common systemic autoimmune disease (after RA), with a prevalence of about 0.5% in the general population and it occurs primarily in women at a ratio of women to men of 9:1. Key features of the disease include infiltration of salivary and lacrimal glands by lymphocytes, production of inflammatory cytokines, and the production of autoantibodies. Nevertheless, systemic manifestations can arise in a proportion of pSS with pulmonary manifestation and higher incidence of NTM infection. Also, B-cell non-Hodgkin lymphoma (NHL) development represents a severe complication, afflicting approximately 5% of patients. The risk of NHL occurrence in the setting of pSS, has been previously estimated to be 7-19 fold higher than the general population. B activation is one of the proposed hypotheses, that accord with the known biological findings, including hypergammagolubinemia, presence of autoantibodies including SSA/Ro60/TROVE2, SSA/Ro52/TRIM21 and SSB/La48.

Objectives: B cells play a key role in the pathogenesis of pSS. The aim of this study was to analyze the transcriptome of B cells from patients with pSS and healthy controls to decipher the B cell-specific contribution to pSS.

Methods: RNA of negatively selected B cells from 5 ANA, SSA (both Ro60 and Ro 52), SSB and rheumatoid factor positive untreated female patients with pSS and 5 healthy controls was subjected to whole transcriptome sequencing. A false discovery rate corrected significance threshold of a < 0.1 was applied to define differential gene expression.

Results: RNA-sequencing identified 56 and 23 up and down differentially expressed genes, respectively, and hierarchal clustering showed a clear separation between the two groups. Ingenuity Pathway Analysis revealed that these genes may play a role in interferon signaling (IFIT3, IFIT1, OAS1, MX1, STAT2, IFI35, IFITM1, ISG15, IFI27, IFI44L, IFI44, and PARP9), chronic mycobacterial infection (IFI35,IFI44,IFI44L,IFIT1,IFIT3,IFITM1,MX1,OAS1,OAS2,OAS3, STAT2) and transformation to myeloproliferative disorders, especially B cell lymphomas (CD160, CD38, ENAM, FUT4, GADD45B, IFI35, IFI44, IFI44L, IFIT3, IFITM1, ISG15, JCHAIN, MX1, OAS1, OAS2, OASL, RGS16, RNF213, RSAD2, SARS2, SATB1, SMAD7, and STAT2).

Conclusion: Upregulated expression of type I and type II interferon (IFN)-induced genes was observed, establishing an IFN signature in pSS B cells. There are also genes that may play a role in other concomitant conditions like mycobacterial/NTM infection and higher risk for developing myeloproliferative conditions. This adds insight into the autoimmune process and suggests potential targets for future functional and prognostic studies.

REFERENCES

[1] Gottenberg, J.-E. Et al. Serum levels of β2-microglobulin and free light chains of immunoglobulins are associated with systemic disease activity in primary Sjögren's syndrome. PLoS ONE 2013

[2] Schulte-Pelkum J., Fritzler M., and Mahler M.: Latest update on the Ro/SS-A autoantibody system. Autoimmun Rev 2009

[3] Song J.S., Do J.H., and Lee S.W.: The prevalence and the clinical relevance of anti-Ro52 in Korean patients with primary Sjogren's syndrome. Rheumatol Int 2011
[4] Salomonsson S, Jonsson MV, Skarstein K, et al. Cellular basis of ectopic germinal center formation and autoantibody production in the target organ of patients with Sjogren's syndrome. Arthritis Rheum. 2003
[5] Imgenberg-Kreuz J, AC, Nordmark G, et al. Transcription profiling of peripheral B cells in antibody-positive primary Sjögren's syndrome reveals upregulated expression of CX3CR1 and a type I and type II interferon signature. Scand J Immunol. 2018

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AB0179 THE TRANSCRIPTION FACTORS IKZF1 AND IKZF3 CONTROL B CELL ACTIVATION AND DIFFERENTIATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The transcription factors *IKZF1* (Ikaros) and *IKZF3* (Aiolos), essential for the maturation, differentiation and survival of B cells, have been linked to Systemic Lupus Erythematosus (SLE). The cereblon modulator Iberdomide, which induces degradation of *IKZF1* and *IKZF3*, is undergoing clinical trials in SLE. However, the role of *IKZF1* and *IKZF3* in aberrant plasmablast development and pathogenesis of SLE has not been fully elucidated.
Objectives: To assess the mechanism of *IKZF1* and *IKZF3* control of gene expression underlying activation and differentiation of B cells in SLE patients.
Methods: $CD19^+$ B cells were isolated from the peripheral blood of patients with SLE recruited at Barts Health NHS Trust (n=25). B cells were cultured for 5 days and stimulated with IL-2, IL-10, IL-15, CD40L and TLR-7 ligand Resiquimod to induce plasmablast differentiation together with iberdomide (10 nM) or control at either day 0 or 18h prior to harvest at day 4. At day 5, cells were harvested for fluorescence-activated cell sorting (FACS) and measurement of IgG and IgM in supernatants by ELISA. RNA extraction and RNA-sequencing were performed on FACS-sorted $CD27^-IgD^+$ naïve B cells and $CD20^{low}CD27^+CD38^+$ plasmablasts and matched baseline B cells.
Results: Iberdomide from day 0 (n=9) significantly reduced the number of $CD20^{low}CD27^+CD38^+$ plasmablasts (number of sorted $CD20^{low}CD27^+CD38^+$ plasmablasts mean±SD 48727±86122 in untreated, 3248±8335 in iberdomide, p=0.03). Accordingly, iberdomide significantly inhibited the production of IgM and IgG from SLE B cells (p=0.017 and 0.050, respectively). Iberdomide given at day 4 did not affect the numbers of plasmablasts or the production of IgM and IgG (n=16). However, iberdomide induced a significant modulation of several genes both in naïve B cells and plasmablasts, as assessed by RNA-seq on sorted cells (400 and 461 differentially modulated genes in naïve B cells and plasmablasts, p adjusted <0.05). Pathway analysis showed that iberdomide treatment resulted in downregulation of JAK-STAT signalling downstream of IL12 (FDR=7.92E-04), IL12 signalling (FDR0.0014), and p53 signalling regulation of cell death (FDR=0.0043) and showed a trend to upregulation of RUNX1 signalling and Rho GTPase cycle.
Conclusion: Our work confirms the importance of *IKZF1* and *IKZF3* in modulating gene expression required for B cell differentiation in SLE, as shown by the ability of iberdomide to inhibit the differentiation of SLE B cells into plasmablasts. Inhibition of *IKZF1* and *IKZF3* modulated the expression of several transcriptional programmes in naïve B cells and plasmablasts. While larger scale analysis will be needed to confirm the functional consequences of *IKZF1* and *IKZF3* modulation in naïve B cells and plasmablasts, our results confirm their relevance in SLE as important regulators of B cell activation and differentiation.
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AB0180 VALIDATION OF COMPLEX IMMUNOPHENOTYPING STRATIFICATION OF PATIENTSWITH LUPUS AND SJÖGREN'S SYNDROME WITH THERAPEUTIC POTENTIAL

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Background: There is a current paucity in effective treatments for patients with primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE). Their overlapping symptoms mean that they are often treated with similar biologic therapeutics, despite being distinct diagnoses. Our pilot research sought to stratify patients by novel, complex immune signatures, to potentially facilitate a more personalised approach to prescribing medication, irrespective of clinical diagnosis. From a cohort of 40 patient patients with SLE, pSS or combined SS/SLE, and 33 healthy controls; five distinct clusters were originally identified.
Objectives: Here we aimed to validate the original patient endotypes from our pilot data with a new patient cohort, and refine the identified clusters to be of more realistic clinical benefit.
Methods: A new cohort of patients with SLE (n=32), pSS (n=31) and SS/SLE (n=15) donated peripheral blood samples while attending appointments at UCLH clinics. None had received B-cell depletion therapy in the preceding 48 months. Complex phenotyping of peripheral T and B-cell subsets was performed by flow cytometry. Unsupervised clustering, statistical comparison to healthies and Receiver Operator Characteristic (ROC) analysis, as per our previous work, were used to stratify patients using immune signatures into distinct endotypes considering only those markers where sensitivity and specificity were above 80% (AUC> 0.80). Characteristics of new clusters were compared with previous findings to refine the number of markers and unique groups.
Results: Five distinct endotypes across the three disease groups were identified after unsupervised clustering of CD19+ B-cell, CD4+ and CD8+ T-cell subsets. Two of these clusters serve to validate groupings from our original data- one with a distinct B cell fingerprint (Bm1, lBm5 and Total CD19+) with AUC=0.87, AUC=0.81 and AUC=0.83 respectively, and another with a T cell fingerprint (Total CD4+, Total CD8+, CD8+ naïve, CD8+ effector memory T cell subsets) with AUC>0.80 for all of them. Clinical diagnoses and symptoms treatment did not differ significantly between clusters.
Conclusion: Our results demonstrate a novel method to re-classify patients using clustered immune phenotype abnormalities. Two distinct groups demonstrated either B or T-cell immunophenotypes, likely reflective of their underlying immunopathogenesis. Stratification by patient endotype has the potential to facilitate a better-informed selection of biologic therapeutics for individual patients; and highlights pathways for further mechanistic research.
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AB0181 ASSOCIATION BETWEEN SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) OF THE BAFF GENE AND FATIGUE IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's Syndrome (SS) is characterized by B lymphocyte hyperactivity with B cell activating factor (BAFF) acting as an important regulator. Single Nucleotide Polymorphisms (SNPs) of the *BAFF* gene have been implicated in the pathogenesis of several autoimmune diseases including lupus and SS both of which are characterized by heightened fatigue levels, often compromising quality of life.
Objectives: To explore potential associations between several *BAFF* gene SNPs and fatigue status experienced by primary SS patients.
Methods: Fatigue status was assessed by Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) scale in 178 primary SS patients. Five SNPs (rs9514827, rs1041569, rs9514828, rs1224141, rs12583006) of the *BAFF* gene were tested in DNA extracted from peripheral blood of all patients enrolled in the study using the RFLP-PCR method. A cut-off value of <30 was used, which indicates severe fatigue. Analysis of BAFF SNPs in association with fatigue levels was performed by the online platform SNPStats.
Results: The frequency of T/T genotype of both rs9514828 and rs1224141 was reduced in primary SS patients with severe fatigue compared to those without

(17.9% vs 36.7%, p=0.0094 and 51.8 vs 69.2%, p=0.027, respectively. The corresponding ORs [95%CI] in the dominant model were 0.38 [0.17-0.82] and 0.48 [0.25-0.92], respectively. No statistically significant associations between fatigue status and other SNPs tested were detected.
Conclusion: We report novel associations between genetic makeup and primary SS-associated fatigue with the rs9514828 and rs1224141 *BAFF* T/T genotypes decreasing the likelihood of fatigue development among these patients. These findings need to be validated in multi-center studies.

REFERENCES

[1] Mavragani, C.P. and H.M. Moutsopoulos, *Sjogren's syndrome*. Annu Rev Pathol, 2014. 9: p. 273-85.
[2] Koçer, B., Tezcan, M. E., Batur, H. Z., Haznedaroğlu, Ş., Göker, B., İrkeç, C. and Çetinkaya, R., *Cognition, depression, fatigue, and quality of life in primary Sjögren's syndrome: correlations*. Brain and Behavior,2016. 6: p. 1–11.
[3] Karageorgas, T., et al., *Fatigue in Primary Sjogren's Syndrome: Clinical*, Laboratory, *Psychometric, and Biologic Associations*. Arthritis Care Res (Hoboken), 2016. 68(1): p. 123-31.
[4] Norheim, K.B., et al., *A possible genetic association with chronic fatigue in primary Sjogren's syndrome: a candidate gene study*. Rheumatol Int, 2014. 34(2): p. 191-7.

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AB0182 RECEPTOR ACTIVATOR OF NUCLEAR FACTOR-KAPPA B LIGAND (RANKL)/RANK AND OSTEOPROTEGERIN (OPG) PATHWAY ACTIVATION IN SJOGREN'S SYNDROME

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Background: Primary Sjogren's syndrome (SS) is an autoimmune exocrinopathy characterized by chronic salivary and lacrimal glands dysfunction. Recent studies suggest that activation of the receptor activator of nuclear factor-kappa B ligand (RANKL)/RANK and osteoprotegerin (OPG) pathway is implicated in the development of autoimmunity.
Objectives: The aim of this study is to investigate the contribution of RANK/RANKL/OPG pathway in primary SS pathogenesis.
Methods: Sixty-six primary SS patients fulfilling the American/European criteria and 13 subjects with oral and/or ocular dryness without satisfying the aforementioned criteria (sicca controls, SC) and 11 healthy controls (HC) have been enrolled. RANKL and OPG serum levels were determined by ELISA in 29 SS patients and 11 HC. Total RNA was extracted from minor salivary glands biopsies (MSG) from 43 SS patients and 13 SC and RANKL mRNA expression was assessed by qRT-PCR. Protein expression of RANKL was determined by Western Blot and immunohistochemistry (IHC) in total protein extract and paraffin embedded tissue respectively, derived from MSG biopsies of 6 primary SS patients and 5 SC. Statistical analysis was performed with SPSS 24.0 package.
Results: Increased serum levels (pg/ml) of RANKL (mean±SD=4.197±897.6vs mean±SD=144.8±290.2, p=0.013) and OPG (mean±SD=173.4±57.52, mean ±SD=48.42±21.89, p=0.015) were detected in SS patients compared to HC. Higher RANKL at both mRNA and protein level by IHC were detected, in MSG derived from primary SS patients compared to SC. RANKL protein expression was significantly increased in MSG biopsies from primary SS patients compared to SC by Western Blot (mean±SD=2.468±1.896 vs mean±SD=0.5138±0.823, p=0.0335).
Conclusion: Increased serum levels, mRNA and protein expression of RANKL in association with increased OPG titers in SS patients compared to controls, suggests that the activation of RANK/RANKL/OPG pathway contributes to SS pathogenesis.

REFERENCES

[1] Skopouli, F. N. & Moutsopoulos, H. M. Autoimmune epitheliitis: Sjögren's syndrome. Clin. Exp. Rheumatol. 12 Suppl 11, S9-11 (1994).
[2] Assmann, G. et al. Genetic variations in genes encoding RANK, RANKL, and OPG in rheumatoid arthritis: a case-control study. J. Rheumatol. 37, 900–904 (2010).

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AB0183 THE ROLE OF THE PHOSPHOLIPASE LP-PLA2 ACTIVITY IN SJOGREN'S SYNDROME RELATED LYMPHOMAGENESIS: A NEW SERUM BIOMARKER?

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Background: One of the major complications of primary Sjogren's syndrome (SS) is the development of B-cell non-Hodgkin's lymphoma (B-NHL). The contribution of tissue macrophages in the pathogenesis of B-NHL, based on previous histopathological studies, appears to be significant. Extracellular lipoprotein-associated phospholipase A2 (Lp-PLA2) is a product of tissue macrophages which is found in the circulation associated with lipoproteins and has been involved in both cardiovascular and malignant diseases, including B-NHL lymphoma.
Objectives: The purpose of the current study was to investigate the role of serum Lp-PLA2 activity as a potential biomarker for the development of B-NHL in the setting of primary SS.
Methods: Extracellular Lp-PLA2 activity was determined by measuring [^{3}H]PAF degradation products in liquid scintillation counter in serum samples obtained from 48 primary SS patients, 9 primary SS patients complicated by lymphoma (SS-lymphoma) and 40 healthy controls. Similar results were obtained in an independent cohort of 25 primary SS patients, 17 primary SS-lymphoma and 10 healthy controls, when a commercially available ELISA kit was implemented. Statistical analysis was performed with the Graph Pad software.
Results: The activity of Lp-PLA2 was statistically significant increased in patients with primary SS-lymphoma compared to primary SS patients without lymphoma [mean±SD (nmol/min/ml): 62.0±13.4 vs 47.7±14.7, p=0.003 and 19.7±4.7 vs 15.2 ±3.2, p=0.005, respectively], as well as healthy controls [mean±SD (nmol/min/ml): 62.0±13.4 vs 52.0±16.3, p=0.03 and 19.7±4.7 vs 15.7±3.1, p=0.06, respectively]. No statistical significant differences in Lp-PLA2 activity were detected between primary SS patients without lymphoma development and healthy controls.
Conclusion: Evaluation of extracellular Lp-PLA2 activity in primary SS patients could be a useful serological biomarker for B-NHL development in the context of primary SS.

REFERENCES

[1] Fragkioudaki S, Mavragani CP, Moutsopoulos HM. Predicting the risk for lymphoma development in Sjogren syndrome: An easy tool for clinical use. Medicine (Baltimore). 2016 Jun;95(25):e3766.
[2] Li D, Wei W, Ran X, Yu J, Li H, Zhao L, Zeng H, Cao Y, Zeng Z, Wan Z. Lipoprotein-associated phospholipase A2 and risks of coronary heart disease and ischemic stroke in the general population: A systematic review and meta-analysis. Clin Chim Acta. 2017 Aug;471:38-45.
[3] Markakis KP, Koropouli MK, Grammenou-Savvoglou S, van Winden EC, Dimitriou AA, Demopoulos CA, Tselepis AD, Kotsifaki EE. Implication of lipoprotein associated phospholipase A2 activity in oxLDL uptake by macrophages. J Lipid Res. 2010 Aug;51(8):2191-201.
[4] Lecointe N, Meerabux J, Ebihara M, Hill A, Young BD. Molecular analysis of an unstable genomic region at chromosome band 11q23 reveals a disruption of the gene encoding the alpha2 subunit of platelet-activating factor acetylhydrolase(Pafah1a2) in human lymphoma. Oncogene. 1999 May 6;18(18):2852-9.

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AB0184 FLOW CYTOMETRIC IMMUNOPHENOTYPING OF SALIVARY GLANDS IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's Syndrome (PSS) is a common autoimmune disease of unknown aetiology. It is characterised by inflammatory infiltration of exocrine glands, development of a sicca syndrome and a 20-fold increase in the risk of developing lymphoma. Standard pathological evaluation is based on a lymphocyte 'focus score' but little is known about the composition of the lymphoid infiltrate or its relationship to disease markers such as autoantibodies and the risk of lymphoma.
Objectives: The aim of the study was to use flow cytometry to characterise the lymphoid infiltrate in more detail.
Methods: Salivary glands were collected from 103 subjects attended the Newcastle Sjogren's clinic who had undergone minor salivary gland biopsy as part of the diagnostic investigations which also include testing for anti-SSA/SSB antibodies, Schirmer's tests and unstimulated oral salivary flow. 70 with confirmed PSS, 15 with potential or early-stage PSS and 18 with non-SS. Salivary glands were digested in collagenase for 3 hours and sort-analysed using a BD Biosciences FACSFusion flow cytometer. Sorted cells from 6 patients were Giemsa stained to observe cell morphology. All subjects have given their written informed consent according to the principles of Helsinki and the project has received local REC approval.
Results: Salivary glands contain multiple lymphoid populations including CD19+ B cells, CD19+CD38+ plasmablasts, CD19-CD38+ plasma cells, and predominantly central memory CD4+ and CD8+ T cells. The focus score is associated with an increase in the total number of lymphocytes of up to 10-fold. In particular there is a striking increase CD19-CD38+ cells with restricted kappa light chain expression associated with the most advanced cases. By morphology these cells have the appearance of plasma cells with frequent Russell bodies and occasional binucleated forms.
Conclusion: Flow cytometry of dispersed salivary gland demonstrates and association between lymphoid cells and the focus score in PSS patients. The dominant B cell population in PSS salivary gland is a CD19-negative tissue plasma cell with evidence of kappa light chain restriction in advanced disease.
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AB0185 INTERFERON-Γ AMPLIFIES IMMUNE RESPONSE MEDIATED BY TYPE I INTERFERONS IN PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS AND CORRELATES WITH DISEASE ACTIVITY

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Background: Paediatric systemic lupus erythematosus (pSLE) is an autoimmune disorder of childhood characterized by the production of autoantibodies against nuclear antigens. In the last decade, several studies showed an up-regulation of genes induced by type I interferons (IFNα) in peripheral blood and tissues of pSLE patients[2]. It has been reported that the expression of this group of genes, known as the type I IFN signature, correlates with disease activity[2]. More recently, also the type II interferon (IFNγ) has been implicated in pSLE; however, its precise role has not been clarified yet[3].
Objectives: To investigate the role of IFNγ in the pathogenesis of pSLE evaluating: 1) the expression levels of IFNγ-related genes in the peripheral blood of pSLE patients; 2) the possible cross-talk between IFNγ and type I IFNs.
Methods: Expression levels of IFNα-induced genes (IFI27, IFI44L, IFIT1, RSAD2, ISG15, SIGLEC1), IFNγ-induced genes (CXCL9, IDO1) and IFNγ itself were analysed by quantitative PCR (qPCR) in whole blood of pSLE patients and healthy donors (HDs). We developed a type II IFN score similarly to the type I IFN score described by Crow[4]. Peripheral blood mononuclear cells (PBMCs) from 6 HDs were stimulated *in vitro* with recombinant human IFNγ and IFNα2b; gene expression was evaluated by qPCR. CXCL9 and CXCL10 in sera and supernatants from stimulated cells were measured by ELISA. Whole blood of pSLE patients and HD was incubated with an anti-IFNγ neutralizing antibody and isotype control, and later type I and type II signatures were assessed. For each patient, SLEDAI was calculated.
Results: Expression levels of both IFNα-induced genes, IFNγ-induced genes and IFNγ were upregulated in pSLE patients with active disease (n = 21) compared to HDs and pSLE patients with inactive disease (n = 17). The type II IFN score correlated with the SLEDAI ($r = 0.64$, $P < 0.01$). As previously reported, also the type I IFN score correlated with SLEDAI ($r = 0.67$, $P < 0.01$). We also found increased serum levels of CXCL9 and CXCL10 in pSLE patients compared to HDs ($P < 0.05$).
In order to study a possible crass-talk between type I and type II IFNs, we stimulated *in vitro* HD PBMCs with recombinant IFNα2b and IFNγ for 6 hours: we analysed the expression levels of type I and type II IFN signatures and assessed the production of CXCL9 and CXCL10 in the supernatants. IFNα2b strongly up-regulated the expression of IFNγ, CXCL9 and IDO1. On the other hand, IFNγ induced the expression of the 6 IFNα-related genes. IFNγ, but not IFNα2b, induced the release of CXCL9 in supernatants. Both IFNγ and IFNα2b induced the production of CXCL10. IFNγ also up-regulated the expression levels of both TLR7 and TLR9, two potent inducer of IFNα. Finally, whole blood of pSLE was incubated with an anti-IFNγ neutralizing antibody for 24 hours: the type II signature was significantly downregulated ($P < 0.05$), whereas the type I signature was reduced without reaching statistical significance.
Conclusion: Our data suggest a potential role of IFNγ in the pathogenesis of pSLE. IFNγ-induced genes in whole blood and CXCL9 in serum are increased in pSLE patients. Type I and type II signatures are not strictly interferon-specific as IFNγ can induce the expression of type I genes. Moreover, blocking of IFNγ in the blood of pSLE patients reduces the type II signature confirming the presence of IFNγ in the blood of pSLE patients. IFNγ also induces the expression of TLR7 and TLR9, and IFNα induces the expression of IFNγ, thus establishing a positive crosstalk between IFNα and IFNγ that potentiate their reciprocal biological activity in pSLE.

REFERENCES

[1] Petri M, et al. Lupus. 2009 Oct;18:980-9.
[2] Munroe M, et al. Ann Rheum Dis 2016;75:2014-2021.
[3] Rice GI, et al. Lancet Neurol 2013;12:1159-69.

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AB0186 CORRELATIONS BETWEEN RENAL TRANSCRIPTOMIC PROFILES AND OUTOCOMES IN A MOUSE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Factors contributing to poor renal outcomes in lupus nephritis (LN) are poorly understood. In our previous research, we found an association between the presence of activated immune effectors in the lupus kidney and disease severity. Here we investigated correlations between patterns of renal genes expression and biological parameters of renal disease activity in a mouse model of systemic lupus erythematosus (SLE).
Methods: We collected blood, urine, kidneys and spleens from 33 B6/Sle1.Sle2.Sle3 congenic mice, before disease onset at 3 months (n=8), and at different stages of disease progression, at 6 (n=7), 9-10 (n=12) and 17-18 (n=5) months. RNA was extracted from kidneys, and hybridized on Mouse Gene 2.0 ST exon arrays. Unsupervized hierarchical clustering studies and pathways analyses were performed on Genespring and DAVID softwares. Spleen and kidney CD8 T cell activation and differentiation markers were evaluated by flow cytometry (CD8, CD69, CD62L, CD44, CD122, CD25, CD44, CCR7, CD279, CD152, CD11a, CD103). Plasma urea and albuminuria were measured by immunoassay.

Results: 712 (out of 33,793) transcripts were overexpressed in kidneys from diseased mice (age > 6 months). These transcripts were significantly enriched in the following pathways: response to type I interferons, antigen processing and presentation, activation and regulation of B cells, complement activation, and regulation of cytotoxicity mediated by T cells.
Proportions of renal CD8 T cells with an effector phenotype were significantly increased in the kidneys from 6 months and older compared to younger mice, and compared to paired spleens. Proportions of renal effector CD8 T cells correlated significantly with transcripts involved in interferon signature, adaptive immune responses, cytotoxic T cells, chemotaxis, and correlated negatively with pathways associated with renal tubular cell functions.
Finally, we found a correlation between biological parameters of kidney function (plasma urea, albuminuria) and transcripts involved in pro-fibrotic pathways, chemokines and adaptive immune responses.
Conclusion: Our results confirm the link between the presence of activated immune effectors in the kidney and renal outcomes in a mouse model of SLE, similar to our previous observations in human LN, and warrant further functional studies on the role of kidney-infiltrating T and B cells in this model.
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AB0187 CAN ARTIFICIAL INTELLIGENCE REPLACE MANUAL SEARCH FOR SYSTEMATIC LITERATURE REVIEW ON CUTANEOUS MANIFESTATIONS IN PRIMARY SJÖGREN'S SYNDROME?

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Background: Manual systematic literature reviews are becoming increasingly challenging due to the sharp rise in publications. The task is particularly daunting when the study topic is complex.
Objectives: The primary objective of this literature review was to compare manual and in-house computer software retrieval of publications on the cutaneous manifestations of primary Sjogren's Syndrome (pSS). The secondary objective was to evaluate the prevalence of cutaneous manifestations in pSS.
Methods: We compared manual searching and searching with the in-house computer software BIBOT (1) designed for article retrieval and analysis. Both methods were used for a systematic literature review on a complex topic i.e., the cutaneous manifestations of pSS. Articles published in French or English between 1 January 1990 and 30 May 2018 were sought.
Results: The manual search retrieved 855 articles and BIBOT 1042 articles. In all, 202 articles were then selecting by applying exclusion criteria. Among them, 155 were retrieved by both methods, 33 by manual search only, and 14 by BIBOT only. Further selection was performed by reading the 202 articles, of which 54 were deemed relevant, including 23 providing data on the prevalence of one or more cutaneous signs in a cohort of patients with pSS. Cohort sizes and the nature and prevalence of cutaneous manifestations varied across publications. In all, 52 cutaneous manifestations were reported, of which the most common were cutaneous vasculitis (561 patients), xerosis (651 patients), and annular erythema (215 patients).
Conclusion: Agreement was good between the two methods. BIBOT was faster and automatically classified the articles in a chart. Combining the two methods retrieved the largest number of publications. The prevalence of cutaneous manifestations in patients with pSS varied considerably across studies. The advanced machine learning techniques used in artificial intelligence hold promise for literature reviews.

REFERENCES

[1] Foulquier N, Redou P, Le Gal C, Rouvière B, Pers J-O, Saraux A. Pathogenesis-based treatments in primary Sjogren's syndrome using artificial intelligence and advanced machine learning techniques: a systematic literature review. Hum Vaccin Immunother 2018;14:2553-2558.

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AB0188 MOLECULAR NETWORKS IN MONOCYTES FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS RELATED TO THEIR PHYSIOPATHOLOGY. MODULATORY EFFECTS OF ANTI-DSDNA ANTIBODIES AND MOLECULAR MECHANISMS UNDERLYING IN VIVOSTATIN TREATMENT

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Objectives: 1. To characterize the mRNAs and microRNAs transcriptomes of monocytes from systemic lupus erythematosus (SLE) patients and their association with the pathophysiology of the disease. 2. To evaluate the role of anti-dsDNA antibodies in the regulation of these processes. 3. To investigate the molecular mechanisms involved in the efficacy of Fluvastatin in preventing the atherothrombotic risk.
Methods: Monocytes from peripheral blood of 81 SLE patients and 40 healthy donors (HD) were purified by negative immunomagnetic selection. Then, gene expression microarray (Agilent G4112F platform) and nCounter microRNA expression arrays (Nanostring) were performed. Functional categorization of altered genes and miRNAs was made using IPA software, and interaction networks were identified. Genes and miRNAs integrating the networks were validated in the whole cohorts by RT-PCR. Predicted miRNA-mRNA interactions were tested by microRNA over-expression or inhibition experiments. Serum and cellular inflammatory and oxidative profiles were evaluated by multiplex assay, PCR and specific commercial kits, respectively; phosphorylation status of intracellular proteins was analyzed by PathScan array. To evaluate the clinical significance of the parameters analyzed, correlation and association studies were performed. Mechanistic studies were developed to typify the specific effects of the anti-dsDNA antibodies on monocytes. Besides, the beneficial effects of ex vivo Fluvastatin treatment on the monocyte molecular profiles were assessed.
Results: Microarray identified 553 altered genes in SLE monocytes. Relevant biofunctions and disorders on which these genes were involved included inflammatory, immunological, cardiovascular, neurological, renal and reproductive disease. Analysis of miRNA profiles showed altered expression of 35 miRNAs in SLE monocytes. Sixty-one genes were inversely correlated and predicted as CVD-related target genes of 26 differentially expressed miRNAs. Transfection studies confirmed the relationship between specific miRNAs and their identified target genes.
Association of these genes and miRNAs with the anti-dsDNA positivity, early atherosclerosis and nephropathy, along with correlations with disease activity (SLEDAI), activation of some intracellular signaling proteins, and levels of serum inflammatory and oxidative markers were demonstrated. *In vitro* studies demonstrated the specific modulation of several genes/miRNAs by anti-dsDNA, along with the increase of prothrombotic and proinflammatory mediators, the induction of apoptosis and the phosphorylation of intracellular proteins participating in renal and CVD-related signaling pathways. Besides, treatment of HD-monocytes with SLE patients' serum after Fluvastatin supplementation prevented the proinflammatory altered gene/miRNA profiles induced by serum from those patients before treatment.
Conclusion: 1. Gene and microRNA expression profiles allowed the identification of relevant genes and pathways altered in monocytes of SLE patients, associated with the pathogenesis of the disease, and modulated by anti-dsDNA. 2. Specific microRNA-miRNA regulatory networks control the biological processes and factors related to the CV pathology in SLE, which are prevented by Fluvastatin treatment.
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AB0189 DECREASED URINE SEMAPHORIN 3A SECRETION PREDICTS THE EXTENT OF RENAL DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Semaphorins are a family of proteins, involved in axon-guidance, malignancy spread and angiogenesis. Semaphorin 3A (sema3A) is recognized also as "immune semaphorin", it is expressed on regulatory T cells and has been

shown to enhance their inhibitory effect of CD4+ T cell pro-inflammatory function and replication. We have reported a decreased serum levels of sema3A in systemic lupus erythematosus (SLE) compared to healthy controls and in correlation with SLE disease activity [1]. Sema3A was found to be over expressed in podocytes and epithelial cells in in animal models with diabetic nephropathy. Increased urinary sema3A was also detected in diabetic patients with proteinuria and in contrast-induced acute renal injury [2-3].

Objectives: To assess urine sema3A secretion in SLE patients with and without renal involvement compared to rheumatoid arthritis patients as disease control and healthy controls.

Methods: 50 ml of fresh urine samples were collected, centrifuged and the supernatant was then concentrated up to 50 times the initial concentration and subjected to specific human Sema3A ELISA kit (MBS732622, San Diego, CA, USA).

Results: Thirty-eight lupus patients fulfilling the 2012 SLICC criteria were recruited, 33 (87%) of whom were women, at a mean age of 35±12 years. Eight patients had active nephritis (21%) and additional 5 had a history of nephritis but were in remission. APLA was diagnosed in 13 (34%) of patients. Disease activity was evaluated by the Systemic lupus erythematosus disease activity index 2000 (SLEDAI 2K) and was 8.2±7.7.

Sema3A was lower in lupus patients compared to rheumatoid arthritis and healthy controls, 4.9±3.9 ng/mL, 8.5±2.7ng/mL, 9.855±1.7ng/mL, p=0.0006. Lupus nephritis patients demonstrated lower urine sema3A concentration compared to lupus patients without renal involvement 4±3.4 ng/ml, 6.5±3.8 ng/ml, p=0.03. Sema 3A reversely correlated with proteinuria r=-0.43 p=0.006 and SLEDIA2K -0.3, p=0.04, but not with creatinine concentration, disease duration and complement concentration. There was no difference in urinary sema3A between SLE patients with or without APLA syndrome.

Conclusion: Urinary excretion of Sema 3A was found to be decreased in the SLE patients with renal disease, reversely correlating with disease activity and proteinuria. These findings are in line with previous reports of decreased serum level of Sema3A in SLE, that may result in reduced efficacy of regulatory T cells, driving autoimmunity and kidney damage. The discrepancy between low sema3A urinary excretion in SLE nephropathy and increased urinary secretion in other "non- auto immune" conditions with renal damage, suggests that sema3A in the kidneys is protective in autoimmune diseases and detrimental in "non-auto immune" conditions. This differential effect of sema3A may has to do with different populations of effector cells and different expression of sema3A receptors (nuropilin1). Further studies should evaluate semphorin 3A role in lupus nephritis and its potential as a treatment option.

REFERENCES

[1] Vadasz Z, Haj T, Halasz K, Rosner I, et al. Semaphorin 3A is a marker for disease activity and a potential immunoregulator in systemic lupus erythematosus. Arthritis Res Ther;14(3):R146.

[2] Mohamed R, Ranganathan P, Jayakumar C, et al. Urinary semaphorin 3A correlates with diabetic proteinuria and mediates diabetic nephropathy and associated inflammation in mice. J Mol Med (Berl) 2014;92:1245-1256.

[3] Ning L, Li Z, Wei D, et al. Urinary semaphorin 3A as an early biomarker to predict contrast-induced acute kidney injury in patients undergoing percutaneous coronary intervention. Braz J Med Biol Res. 2018;51(4)

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AB0190 CROSSTALK BETWEEN SALIVARY GLAND EPITHELIAL CELLS AND B LYMPHOCYTES IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is an auto-immune disorder characterized by lymphocytic infiltrates and destruction of the salivary glands. Mechanisms leading to B lymphocytes chronic activation remain partially understood and we assumed that salivary gland epithelial cells (SGECs) might play a key role in B lymphocytes activation and differentiation.

Objectives: We aimed to study the interactions between SGECs from pSS patients or controls and B lymphocytes.

Methods: Patients with pSS according to 2016 EULAR/ACR criteria and controls with sicca symptoms were studied. RNASeq analysis was performed on SGECs and B lymphocytes sorted from salivary gland and blood using a FACS ARIA. Enrichment analysis was performed using Ingenuity Pathway Analysis software. Validation of the results was performed by qPCR (Biomark technology). Primary cultured SGECs from pSS patients (n=6) and controls (n=6) were co-cultured with B lymphocytes sorted from healthy donors blood and stimulated with or without PolyIC, INFα or IFNγ for 5 days. Transwell assays were performed. Survival, activation (CD38 positivity) and differentiation of B lymphocytes were assessed at day 5 by flow cytometry.

Results: The RNASeq analysis of B lymphocytes sorted from salivary gland showed an up-regulation of CD40 and CD48 which are involved in their activation. The analysis of sorted SGECs highlighted IL-7, interferon (IFN) signaling pathways and genes potentially involved in immune responses, including HLA-DRA, BST2 (bone marrow stromal cell antigen 2) and BAFF-R.

Co-culture experiments showed an increase of B lymphocytes viability when co-cultured with SGECs compared to B lymphocytes cultured alone ($p<0.05$). Co-culture with SGECs from pSS compared to controls lead to an increased survival of B lymphocytes (calculated as the percentage of alive co-cultured B lymphocytes – percentage of alive cultured alone B lymphocytes) without stimulation or stimulated with Poly(I:C) ($p<0.01$) (**Figure 1A**). Similarly, SGECs from pSS were more likely to induce higher activation of B lymphocytes compared to SGECs from controls, assessed by the percentage of CD38+ B lymphocytes (significant after stimulation with Poly(I:C)) (**Figure 1B**). To determine whether the activation of B lymphocytes and SGECs required a direct cell contact, we used transwell experiments. Preliminary results suggested that the increase of B lymphocytes viability could depend mostly on soluble factors that are currently being identified and will be communicated at the congress.

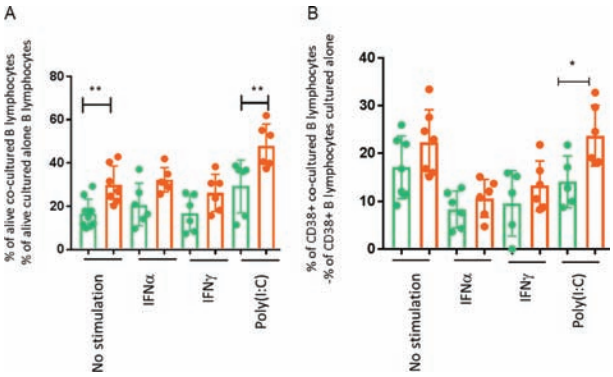


Figure 1. A: Difference between the percentage of alive B lymphocytes co-cultured with SGECs and the percentage of alive B lymphocytes cultured alone at day 5. **B**: Difference between the percentage of CD38+ B lymphocytes co-cultured with SGECs and the percentage of CD38+ B lymphocytes cultured alone at day 5. In green for SGECs from controls, in orange for SGECs from pSS patients. One asterisk indicates p-value <0.05, two asterisks indicate p value < 0.01.

Conclusion: Epithelial cells from patients with pSS have better ability than controls to stimulate survival and activation of B cells. According to preliminary results, this effect could be mediated at least partially by soluble factors. The pathways responsible for this stimulation are being determined by RNASeq analysis of purified epithelial cells and B lymphocytes and inhibitory experiments that can represent new therapeutic perspectives are ongoing.

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AB0191 ENDOTHELIN-1 LEVEL IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME, ITS ASSOCIATION WITH ENDOTHELIAL DYSFUNCTION AND ATHEROSCLEROSIS

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Background: It is known that endothelin-1 is one of the leading factors in the development of coronary artery disease, acute myocardial infarction, atherosclerosis of cerebral and peripheral vessels, pulmonary hypertension, ischemic lesion

of the brain vessels etc. Patients with rheumatic diseases also have an elevetaion of endothelin-1 in serum. But it remains unclear whether the endothelin-1 level may reflect endothelium dysfunction in patients with antiphospholipid syndrome (APS) and serve as an early marker of atherosclerosis.
Objectives: The aim of the study was to evaluate the endothelin-1 concentration, its association with antiphospholipid antibodies and atherosclerotic vascular lesions in patients with APS.
Methods: According to our observation, there were 82 patients, among which 34 (41.6%) with primary antiphospholipid syndrome (PAPS) and 48 (58.4%) with secondary antiphospholipid syndrome (SAPS). The control group consisted of 37 practically healthy persons. The groups of patients were comparable by age, sex, and duration of the disease. The APS diagnosis was established according to the international classification criteria (2006). The content of the anticardiolipin antibodies IgG, *anti-beta2-glycoprotein*-1 *antibodies* IgG, IgA, IgM and endothelin-1 were determined by the immune enzyme method using commercial sets of Trinity Biotech Captia USA - Ireland, ORGenTec GmbH Germany and «Endothelin-1» (Cormay, England). All patients were assessed for the level of endothelium-dependent vasodilation (EDVD), the thickness of the intima-media complex of the common carotid artery (IMT), the presence of atherosclerotic plaque (AP) and clinical manifestations of vascular involvement.
Results: The analysis of endothelin-1 levels has showed that its content was in 2.3 times higher in patients with APS than in the control group. The proportion of people with optimal endothelin-1 content was twice lower, and the proportion of people with extremely high and high rates was 1.6 and 5.3 times higher, respectively, among patients with APS, than in the control group. Also differences in the endothelin-1 level have been established depending on the type of APS. The content of endothelin-1 was significantly higher (1.3 times) in patients with SAPS, than in PAPS. Among the patients with SAPS, the proportion of patients with an optimal level of endothelin-1 was 1.7 times lower, and the proportion of patients with high levels was 1.6 times higher than in patients with PAPS. The significantly lower endothelin-1 level was recorded in patients with highly positive antibodies to cardiolipin and beta-2 glycoprotein-1. Correlation analysis has showen direct correlation between anticardiolipin antibodies of the IgG class and *anti-beta2-glycoprotein*-1 *antibodies* and endothelin-1 concentration (r=0.35 and 0.34). High endothelin-1 level was an adverse factor of structural and functional atherosclerotic changes of the heart and blood vessels in patients with APS. IMT increasing and EDVD decreasing were from 1.7 to 6.6 times more frequent among patients with high endothelin-1 level (>10 pg/ml), than patients with optimal endothelin-1 level (≤ 5.0 pg/ml).
Conclusion: Thus, the obtained data has showed that the excess concentration of endothelin-1 is a circulating marker of early atherosclerosis, since it is closely associated with subclinical manifestations of atherosclerotic vascular damage
Disclosure of Interests: None declared
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AB0192 ASYMPTOMATIC VERTEBRAL FRACTURES WORSEN ORGAN DAMAGE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background:
Objectives: To investigate the influence of asymptomatic vertebral fractures on organ damage and to identify risk factors associated with critical organ damage in women with systemic lupus erythematosus (SLE).
Methods: 207 women with SLE were included in this study. Bone mineral density (BMD) measurements of the hip and spine were performed using the dual energy X-ray absorptiometry (DXA). Vertebral fracture assessment (VFA) was done for detection vertebral fractures using a method described by Genant. Accumulated damage was scored using the SLICC/ACR damage index (SDI). Critical organ damage was defined as SDI>3.
Results: Vertebral fractures were developed in 55 (26.5%) women with SLE. Half of all women with SLE (n=31, 15.0%) had asymptomatic vertebral fractures which were diagnosed for the first time in this study. 131 (63.3%) women with SLE had critical organ damage (SDI>3). Average SDI before and after morphometry was 4,5±2,1 and 5,4±2,5 respectively. Multivariate analysis showed age (p=0,01) and cumulative dose of glucocorticoids (p=0,00005) were significantly associated with critical damage in women with SLE.
Conclusion: Detection of vertebral fractures helps in counting accumulated organ damage correctly. VFA in the combination with DXA in women with SLE is an effective method for diagnostic asymptomatic vertebral fractures.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3058

AB0193 THE EFFECTS OF NON-INVASIVE VAGUS NERVE STIMULATIONON FATIGUE AND NEUROCOGNITION IN PARTICIPANTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) sufferers have rated physical and mental fatigue ('brain fog') as the most important symptoms needing improvement. Previous data from our group suggest that stimulation of the vagus nerve can invoke immunological responses and concurrently an improvement of patient reported symptoms of fatigue[1].
Objectives: This follow up study uses the gammaCore device (electroCore) and a sham device to assess the effects of non-invasive vagus nerve stimulation (nVNS) on patient reported symptoms of fatigue in pSS. In addition, neurocognitive tests were used to assess the effect of nVNS on short term memory, executive function and attention.

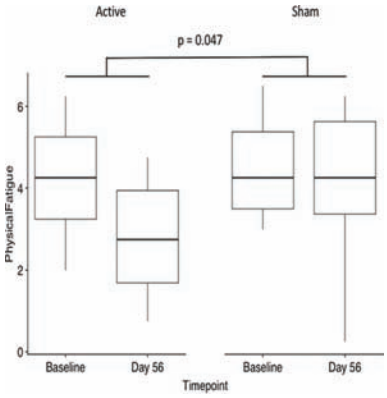


Figure 1

Methods: 40 pSS participants were assigned to use active (n = 20) or sham (n = 20) nVNS devices. Participants and research staff were blinded to the active/sham device assignment. The participants were instructed to use the device twice daily for a study period of 56 days. The following patient reported measures of fatigue and neuropsychological tests were collected at baseline and day 56; Profile of Fatigue (PRO-F, Physical and Mental), visual analogue scale (VAS) of abnormal fatigue, trail making, Digit Symbol Substitution Test (DSST), Stroop test and digit span. 7 subjects were excluded from the analysis due to withdrawal from the study. Changes in fatigue and test scores from baseline to day 56 were compared between devices using t-tests.
Results: Physical fatigue was significantly reduced between baseline and day 56 in the active group but not the placebo group (p = 0.047) The mean reduction in physical fatigue was 30% and 6% for the active and sham arms respectively (Figure 1). In both the active and sham subject groups there were no significant changes in the patient reported mental fatigue or neuropsychological test scores.
Conclusion: This sham controlled scientific study of vagus nerve stimulation in pSS suggests nVNS may improve patient reported symptoms of physical fatigue, which is consistent with our published data. There were no improvements in the neurosychological test scores which is consistent with no improvements in patient reported mental fatigue. nVNS has been shown to activate the anti-inflammatory reflex, therefore assessment of peripheral inflammatory markers may help our understanding of nVNS, inflammation and fatigue.

REFERENCE

[1] Tarn, J., Legg, S., Mitchell, S., Simon, B. & Ng, W.-F. The Effects of Noninvasive Vagus Nerve Stimulation on Fatigue and Immune Responses in Patients With Primary Sjögren's Syndrome. Neuromodulation 49, 844 (2018).

Disclosure of Interests: Jessica Tarn: None declared, Victoria Macrae: None declared, Sheryl Mitchell: None declared, Bruce Simon Shareholder of: Bruce Simon is an employee and shareholder of electroCore., Peter Gallagher: None declared, John-Paul Taylor: None declared, Stuart Watson: None declared, Mark Baker: None declared, Stephen Rushton: None declared, Andrew Blamire: None declared, Julia Newton: None declared, Wan Fai Ng: None declared
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AB0194 BTLA EXPRESSION IS REDUCED ON SLE B CELL SUBSETS

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Background: B- and T-lymphocyte attenuator (BTLA/CD272) is a co-receptor constitutively expressed on B cells [1, 2]. Upon B cell activation via the B cell receptor (BCR), BTLA co-localizes with Src homology region 2 domain-containing phosphatase-1 (SHP-1) and thus negatively regulates BCR signaling [2]. A recent study found that CD4+ T cells from SLE patients fail to upregulate BTLA upon activation [3], however, data on BTLA expression and function for B cells in autoimmunity is missing.

Objectives: To assess BTLA expression on conventional naïve ($CD20^+CD27^-$), conventional memory ($CD20^+CD27^+$) B cells and on $CD27^{++}CD38^{++}$ expressing plasma cells (PC) in peripheral blood mononuclear cells (PBMCs) of patients with systemic lupus erythematosus (SLE) and healthy donors (HD).

Methods: PBMCs were isolated from EDTA blood taken from 7 female SLE patients (age 38, mean disease activity 5 (SLEDAI)) and 6 female HD (mean age 28) by Ficoll density gradient centrifugation according to the manufacturer's protocol. Cells have been stained and expression of BTLA was assessed by flow cytometry.

Results: Analysis of BTLA surface expression on B cell subsets in SLE patients and HD revealed decreased expression of BTLA on naïve SLE B cells (*p=0.0173, Mann-Whitney U Test (MWU), BTLA median fluorescence intensity (MFI) 9006±1450) compared to naïve HD B cells (11957 ±941). A similar tendency was found for memory SLE B cells (p=0.0823 MWU) compared to HD memory but not SLE PC and HD PC. Remarkably, an inverse correlation was found for BTLA expression on naïve SLE B cells and SLE PC with Siglec-1 expression on monocytes (*p=0.0333 Spearman's rank correlation (SRC) naïve B cells, *p=0.0167 PC), a marker for interferon signature, and the same trend was seen for SLE memory B cells (p=0.0583 SRC). Inverse correlation of BTLA expression was also found with disease activity (SLEDAI) with these B cell populations but did not reach significance (p=0.0583 naïve B cells, p=0.1361 memory B cells, p=0.0833 PC).

Conclusion: Herein, we document that B cell subsets of SLE patients express lower levels of the negative regulator BTLA than HD. Additionally, an inverse correlation between BTLA expression on B cell subsets and Siglec-1 on monocytes were found suggesting its involvement in disease and consideration BTLA as therapeutic target in SLE. We hypothesize that reduced BTLA expression is a feature of post-activated B cells. Further studies need to delineate functional properties of BTLA expression and activation in autoimmune B cells.

REFERENCES:

[1] Watanabe N, Gavrieli M, Sedy JR, Yang J, Fallarino F, Loftin SK, Hurchla MA, Zimmerman N, Sim J, Zang X, et al: **BTLA is a lymphocyte inhibitory receptor with similarities to CTLA-4 and PD-1**. Nat Immunol 2003, **4**(7):670-679.

[2] Vendel AC, Calemine-Fenaux J, Izrael-Tomasevic A, Chauhan V, Arnott D, Eaton DL: **B and T lymphocyte attenuator regulates B cell receptor signaling by targeting Syk and BLNK**. J Immunol 2009, 182(3):1509-1517.

[3] Sawaf M, Fauny JD, Felten R, Sagez F, Gottenberg JE, Dumortier H, Monneaux F: **Defective BTLA functionality is rescued by restoring lipid metabolism in lupus CD4+ T cells**. *JCI Insight* 2018, **3**(13).

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AB0195 THE IMPACT OF KETOGENIC DIET AND HIGH-FAT-HIGH-GLUCOSE DIET IN PRISTANE INDUCED LUPUS-LIKE NEPHRITIS MURINE MODEL

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Background: Systemic lupus erythematous is a chronic systemic inflammatory disease which commonly involes kidneys[1]. Aside from the use of conventional immunosuppressants, dietary components and metabolites may likely affect our immune system.

Objectives: An interest in the anti-inflammatory property of ketogenic diet (KD) has recently come to attention.

It not only alters the balance between Th17 and Treg cells[2], its metabolite, beta-hydroxybutyrate was known to block NLRP3 inflammasome-mediated inflammation[3-6]. High-fat-high-glucose diet (HFGD), on the other hand, was known for a proinflammatory property. Aim to understand the immune modulatory effect of KD and HFGD in cases with systemic lupus erythematous, a chronic systemic inflammatory disease with glomerulonephritis, pristane induce lupus like nephritis murine model was used.

Methods: Pristane induced lupus nephritis mice were divided in to groups fed with regular chow (CD), KD and HFGD along with healthy controls. The diets were kept for 6 months with regular body weight and urine protein monitoring. Serum samples were collected for metabolic evaluation and immune survey bimonthly. The mice were sacrificed 6 months after diet change. Kidneys, lymph nodes, spleen, blood and guts were collected for evaluation.

Results: KD and HFGD were both well tolerated by experimental mice. Two months after diet change, higher level of beta-hydroxybutyrate and triglyceride but lower sugar level was noted in mice fed on KD when compared to those fed on CD and HFGD (all $p<0.05$). Mice fed on KD and HFGD have a much lower RBC and platelet count than those fed on CD in the experimental mice group (both $p<0.05$). Although global lymphocyte counts were much lower in those pristine treated mice, Th17 lymphocytes were significantly higher in the blood as well as kidneys among those fed on HFGD (all $p<0.05$). This is compatible with their high serum concentration of anti-dsDNA, anti-nRNP and anti-Sm and the rapid progressing proteinuria. Renal, hepatic and intestinal histopathology was still under analysis at present.

Conclusion: In conclusion, food plays a critical role in immune modification. Despite the reported anti-inflammatory effect of KD, it does not mitigate lupus nephritis progression. HFGD formula, however, accelerated the autoimmune phenotype for cases with lupus like glomerulonephritis.

REFERENCES:

[1] Borchers AT, Leibushor N, Naguwa SM, Cheema GS, Shoenfeld Y, Gershwin ME (2012) Lupus nephritis: a critical review. Autoimmun Rev 12:174-194.

[2] Ni FF, Li CR, Liao JX, Wang GB, Lin SF, Xia Y, Wen JL (2016) The effects of ketogenic diet on the Th17/Treg cells imbalance in patients with intractable childhood epilepsy. Seizure 38:17-22.

[3] Goldberg EL, Asher JL, Molony RD, Shaw AC, Zeiss CJ, Wang C, Morozova-Roche LA, Herzog RI, Iwasaki A, Dixit VD (2017) beta-Hydroxybutyrate Deactivates Neutrophil NLRP3 Inflammasome to Relieve Gout Flares. Cell Rep 18:2077-2087.

[4] Choi IY, Piccio L, Childress P, Bollman B, Ghosh A, Brandhorst S, Suarez J, Michalsen A, Cross AH, Morgan TE, Wei M, Paul F, Bock M, Longo VD (2016) A Diet Mimicking Fasting Promotes Regeneration and Reduces Autoimmunity and Multiple Sclerosis Symptoms. Cell Rep 15:2136-2146.

[5] Storoni M, Plant GT (2015) The Therapeutic Potential of the Ketogenic Diet in Treating Progressive Multiple Sclerosis. Mult Scler Int 2015:681289.

[6] Choi IY, Lee C, Longo VD (2017) Nutrition and fasting mimicking diets in the prevention and treatment of autoimmune diseases and immunosenescence. Mol Cell Endocrinol 455:4-12.

Disclosure of Interests: None declared

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AB0196 **MESENCHYMAL STEM CELLS TUNE THE DIFFERENTIATION OF MYELOID-DERIVED SUPPRESSOR CELLS IN SJÖGREN'S SYNDROME THROUGH INHIBITING IL-12**

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Background: The preliminary animal and human studies, including ours, showed that mesenchymal stem cell (MSC) transplantation could reestablish salivary function and reduce lymphocytic infiltration in salivary glands in Sjögren's syndrome (SS). However, the mechanisms of the encouraging results of MSCs on the SS remain to be elucidated. Myeloid-derived suppressor cells (MDSCs) represent an important class of immunoregulatory cells. MDSCs have multiple phenotypes which inhibit T cell responses by multiple mechanisms, and the environment dictates the development of suppressive properties and activation. Previous studies have demonstrated that MDSCs played important roles in systemic lupus erythematosus and rheumatic arthritis. However, the involvement of MDSCs in the immunopathology of SS is largely unknown.
Objectives: This study aims to investigate effects of MDSCs in SS progression and the potential association of MDSCs with the therapeutic effects of MSCs in the patients with SS and mice with SS-like symptoms.
Methods: The frequencies of MDSCs in the blood and bone marrow were detected by flow cytometry analysis in SS mice (NOD mice) and patients with SS. The NOD mice were adoptively transferred with MDSCs or treated with anti-Gr1 antibody to eliminate MDSCs. The salivary flow rate was measured and inflammatory infiltration in salivary glands was assessed. MSCs were infused into NOD mice to investigate the effects of MSCs on SS-like syndrome and changes of MDSCs. The percentages of MDSCs in SS patients before and after MSC transplantation were determined.
Results: The percentage of MDSCs increased significantly with the development of SS-like syndrome in NOD mice. The SS-like syndrome exacerbated after transfer of MDSCs, whereas deletion of MDSCs alleviated SS-like syndrome in NOD mice. MSC transplantation enhanced salivary flow rates and decreased lymphocyte infiltration in salivary glands in NOD mice. The percentages of MDSCs were down-regulated after MSC transplantation. MSC reduced IL-12 production in dendritic cells in vitro and in vivo. The IL-12 promoted generation of MDSCs in vitro. The numbers of MDSCs were positively correlated with disease activities of SS patients. The percentages of MDSCs were reduced after MSC transplantation in patients with SS.
Conclusion: 1. MDSC expansion positively correlated with inflammation during the progression of SS. 2. MSC transplantation had beneficial effects in SS mice. 3. IL-12 production by dendritic cells was reduced by MSCs. 4. The MDSCs expansion was induced by inflammatory IL-12 and reversed by MSC transplantation in SS. Thus, we have revealed a previously unrecognized function of MSC-mediated reduction of MDSCs in suppressing SS-like syndrome through inhibition of IL-12 production by DCs, which provided novel therapeutic strategies to treat patients with SS.
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Disclosure of Interests: None declared
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AB0197 **VITAMIN D PROTECTS PODOCYTES FROM AUTOANTIBODIES INDUCED INJURY IN LUPUS NEPHRITIS BY REDUCING ABERRANT AUTOPHAGY**

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Background: Recent data suggest that vitamin D insufficiency may play a role in the progression of SLE and the nephropathy such as chronic kidney disease[1]. We previously show that severe vitamin D deficiency increases the risk for moderate to severe disease activity[2]. Moreover, vitamin D has been demonstrated a protective effect on podocyte injury via diverse mechanisms in proteinuric glomerular disease[3-7]. However, there is a paucity of data to demonstrated the mechanisms through which the autophagy functions on the protective role vitamin D plays on podocyte in the pathogenesis of lupus nephritis
Objectives: The aim of this study was to investigate whether vitamin D play a protective role in podocyte injury induced by autoantibodies purified from lupus nephritis (LN) patients serum via autophagic way.
Methods: Autophagic activities of LN patients renal tissues were evaluated under transmission electronic microscope. IgG from patients with LN were purified to induce human podocyte injury and the role of vitamin D in injury was observed. Podocytes were observed under TEM and autophagic activity was evaluated by western blot analysis and qRT-PCR, mRFP-GFP-LC3B adenovirus were infected into HPC in vitro.
Results: Significantly higher autophagic levels were observed in LN patients($p<0.05$) and apparently greater autophagic levels in podocytes were shown ($p<0.05$). Among different classifications of LN, Class V(n=5), III+V(n=5) and IV+V (n=5) gained higher autophagic levels than Class III (n=5) and IV(n=5). Induced autophagy, which was evident by increased LC3B-II and Beclin 1 level, caused consumption of p62, more autophagosomes observed under TEM, and more LC3B dots observed under confocal microscope in IgG group, along with decreased Nephrin expression, which suggests podocyte injury. Reduction of autophagy as well as alleviated podocyte injury was observed in the IgG+ VD group.

CONCLUSION:
This study demonstrates that vitamin D plays a protective role in podocytes injury induced by autoantibodies from LN patients and that appears to be a novel therapy target in LN.

REFERENCES:
[1] Mok CC, Bro ET, Ho LY, Singh RJ, Jannetto PJ: **Serum 25-hydroxyvitamin D3 levels and flares of systemic lupus erythematosus: a longitudinal cohort analysis**. Clinical rheumatology 2018.
[2] Gao CC, Liu SY, Wu ZZ, Li TF, Gao GM, Liu ZS, Zheng ZH: **Severe vitamin D deficiency increases the risk for moderate to severe disease activity in Chinese patients with SLE**. *Lupus* 2016, **25**(11):1224-1229.
[3] **Vitamin D down-regulates TRPC6 expression in podocyte injury and proteinuric glomerular disease**. *The American journal of pathology* 2013, **182**(4):1196-1204.
[4] Zhang XL, Guo YF, Song ZX, Zhou M: **Vitamin D prevents podocyte injury via regulation of macrophage M1/M2 phenotype in diabetic nephropathy rats**. *Endocrinology* 2014, **155**(12):4939-4950.
[5] Guo J, Lu C, Zhang F, Yu H, Zhou M, He M, Wang C, Zhao Z, Liu Z: **VDR Activation Reduces Proteinuria and High-Glucose-Induced Injury of Kidneys and Podocytes by Regulating Wnt Signaling Pathway**. *Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology* 2017, **43**(1):39-51.
[6] Chandel N, Ayasolla K, Wen H, Lan X, Haque S, Saleem MA, Malhotra A, Singhal PC: **Vitamin D receptor deficit induces activation of renin angiotensin system via SIRT1 modulation in podocytes**. *Experimental and molecular pathology* 2017, **102**(1):97-105.
[7] Garsen M, Sonneveld R, Rops AL, Huntink S, van Kuppevelt TH, Rabelink TJ, Hoenderop JG, Berden JH, Nijenhuis T, van der Vlag J: **Vitamin D attenuates proteinuria by inhibition of heparanase expression in the podocyte**. *The Journal of pathology* 2015, **237**(4):472-481.

Disclosure of Interests: None declared
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AB0198 **THE ROLE OF LOW EXPRESSION OF MIR-127–3P IN THE PATHOGENESIS OF LUPUS NEPHRITIS**

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Background: Lupus nephritis (LN) is one of the most severe organ lesions in systemic lupus erythematosus (SLE). Overactivation of the type I interferon (IFN-I) signaling pathway is associated with the pathogenesis of LN. Overexpression of the IFN stimulated genes (ISGs) was found in the kidneys of LN patients, and the absence of the IFN receptor reduced nephritis in lupus prone mice. Abnormal expression of microRNA in renal tissue is involved in the pathogenesis of LN.
Objectives: We aimed to investigate the role of renal microRNA related to LN in the over-activation of the IFN signaling pathway of LN kidney.
Methods: The expression of microRNA was determined by Taqman method. Interferon stimulation response element (ISRE) -luciferase reporter gene assay and western blot assay were used to study the function of candidate microRNA in IFN signal transduction pathway. mRNA expression was measured by SYBR green method. Gene expression profile was detected by gene expression microarray. Antagomir and Agomir (chemically modified microRNA mimics and antagomir inhibitors) of candidate microRNAs were used for functional gain and functional loss experiments.

Results: Among differentially expressed renal microRNAs in LN, miR-127-3p was reduced in renal tissues of patients with LN. The miR-127-3p suppressed the fluorescase gene expression of ISRE induced by ISRE, and the phosphorylation of STAT1 and STAT2. By microarray analysis, we found that most ISG was inhibited by miR127-3p in IFN-stimulated Hela cells. The functional deletion of miR-127-3p enhanced the IFN response in human primary mesangial cells, which was manifested by enhanced ISRE mediated reporter gene expression, enhanced STAT2 phosphorylation and increased ISG expression. In addition, we found that JAK1, the upstream tyrosine kinase of STAT1 and STAT2, was a new target molecule for miR-127-3p.
Conclusion: Our study shows that miR-127-3p can inhibit IFN signal transduction by targeting JAK1. The decreased expression of miR-127-3p in the kidney is associated with an overactive IFN response in the renal tissue of patients with LN. Subsequent mouse model studies indicate the therapeutic potential of miR-127-3p in treating lupus associated organ damage.

REFERENCES:

[1] Han X, Wang Y, Zhang X, et al. MicroRNA-130b Ameliorates Murine Lupus Nephritis Through Targeting the Type I InterferonPathway on Renal Mesangial Cells. Arthritis Rheumatol. 2016 Sep;68(9):2232-43.
[2] Wu L, Qin Y, Xia S, et al. Identification of Cyclin-Dependent Kinase 1 as a Novel Regulator of Type I Interferon Signaling in Systemic Lupus Erythematosus. Arthritis Rheumatol. 2016 May;68(5):1222-32.

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AB0198B BENEFIT OF CRITHIDIA TESTS IN DIAGNOSING CONNECTIVE TISSUE DISEASES

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Background: The diagnosis of systemic lupus erythematosis(SLE) relies on autoantibody testing, including double stranded DNA (dsDNA), the testing of which has evolved over time from the FARR assay through to ELISA/ELiA. dsDNA assays can pick up non-specific single stranded DNA as false positives and can give occasional false negative results. To evaluate the implications of this we analysed our hospital's use of crithidia testing as a confirmatory assay of dsDNA results.
Objectives: Investigate the relation between dsDNA Abs measured by Crithidia test and ELiA. Define the clinical role for Crithidia testing.
Methods: All crithidia tests for an 8 months from January 2017 to August 2017 were reviewed and results of ANA, ENA, dsDNA and complement collected. Data were collected regarding referral to rheumatology and where possible rheumatology clinic letters were reviewed regarding final diagnosis.
Results: One hundred and fourcrithidia tests were undertaken of which 91 were negative and 13 positive.Sixteen of the 104 patients were ANA negative, 18 ANA 1:100, 70 ANA >/=1:400, and 14 patients had a positive ENA. Positive crithidias had a dsDNA range from 2 to 333 and negative crithidia from <1 to 131 however positive crithidias were more likely to have higher dsDNA and ANA titres. Of the 65 patients seen by rheumatology 4 did not have available notes for analysis. Ten of the 13 crithidia positive patients were seen by rheumatology, 6 diagnosed as SLE, 1 as TNF induced lupus, 1 MCTD, 1 RA and 1 had no clinical evidence of autoimmune disease. 88 patients were dsDNA positive (cut off of >/=9) of whom 11 were also crithidia positive. Of the 13 positive crithidia results, 2 had a negative dsDNA level, one of whom was ANA 1;400 Ro positive and diagnosed with RA, the other was diagnosed as TNF induced lupus. Of the crithidia negative patients the median dsDNA level was 20, a range of diagnoses were made including 5 patients with SLE who had a positive Ro or La, 3 patients with SLE who were ENA negative, 4 UCTD, 2 MCTD, 2 with GCA/PMR, 3 with RA and 5 with inflammatory arthropathy. Twenty patients were documented as having no evidence of connective tissue disorders (CTDs),others remain under assessment.
Conclusion: We have shown a significant number of patients using our ELiA assay are dsDNA positive and crithidia negative. In patients with crithidia positivity autoimmune disease is more likely to be diagnosed. Crithidia testing appears to influence whether or not a patient will be referred to rheumatology, with negative crithidias less likely to be referred. This highlights some of the limitations of dsDNA ELISA testing however there is a clear role for this assay as depicted above in preventing over diagnosis of CTDs and unnecessary commitment to immunosuppression.
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Systemic sclerosis, myositis and related syndromes – etiology, pathogenesis and animal models

AB0199 ASSESSING DISABILITY AND QUALITY OF LIFE IN ALGERIAN SYSTEMIC SCLEROSIS PATIENTS: CONSTRUCT VALIDITIES OF THE ARAB HAND FUNCTION INDEX AND HEALTH ASSESSMENT QUESTIONNAIRE (HAQ)

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Objectives: To assess the construct validity of the Arab Hand Function Index (AHFI), an Arabic and adapted version of the Cochin hand Functional scale (CHFS) and an Arabic version of the Health Assessment Questionnaire (HAQ) in SSc.
Methods: We evaluated 100 patients with SSc followed between 2015 and 2017. All patients were white and fulfilled the American College of Rheumatology/European League Against Rheumatism criteria and/or the Leroy and Medsger (2) criteria for SSc. Mean±SD age at the time of evaluation was 47.66±12.28 years. The mean±SD disease duration was 6.54±6.23 years. Forty-one (41%) patients had diffuse cutaneous SSc and 59 (59%) had limited cutaneous SSc. Global hand and wrist mobility were evaluated using the hand functional index (HFI) and Kapandji index. Global disability and hand disability were assessed by an Arabic and adapted version of the HAQ and by the Arab hand functional index, an Arabic and adapted version of the CHFS, respectively. Anxiety and depression significant symptoms were assessed with the Arabic version of Hospital Anxiety and Depression Scale (HADS) anxiety and HADS depression. Construct validity was assessed by convergent and divergent validity (Spearman's rank correlation coefficient) and factor analysis.
Results: The AHFI had correct convergent validity with global disability assessed by the HAQ (0.61) and the HFI (0.55), moderate correlation with the Kapandji Index (-0.48: inverse correlation), depression (HADd) (0.45) and anxiety (HADa) (0.42) and no correlation with the disease duration (0.29) and the age (0.19) (Table 1). Factor analysis (Table 2) extracted 2 factors that accounted for 64.45% of the total variance. The HAQ has a good correlation with hand disability (AHF: 0.61), anxiety (0.57) and the HFI (0.51), a moderate correlation with depression (0.47) and Kapandji index (-0.46) and a little correlation with the age (0.28) and the disease duration (0.10) (Table 1).The factor analysis of the HAQ, extracted 1 factor that accounted for 50.64% of the total variance (Table 2).
Conclusion: In patients with SSc, the AHFI and the Arabic HAQ have good construct validity. The total score of the AHFI explained 61% of the variance of the HAQ.
Acknowledgement: All the patients who participated in this study
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Table 1. Convergent and divergent validities of the AHFI and the HAQ for patients with SSc (correlation with other variables)*

Scales	Spearman's correlation Coefficient	P Value
AHFI		
Convergent validity		
HAQ	0.61	<0.001
HFI	0.55	<0.001
Kapandji	- 0.48	<0.001
Divergent validity		
Depression (HADd)	0.45	<0.001
Anxiety (HADa)	0.42	<0.001
Disease duration	0.29	0.003
Age	0.19	0.058

HAQ		
Convergent validity		
AHFI	0.61	<0.001
HFI	0.51	<0.001
Kapandji	- 0.46	<0.001
Divergent validity		
Anxiety (HADa)	0.57	<0.001
Depression (HADd)	0.47	<0.001
Disease duration	0.10	0.320
Age	0.28	0.005

Health Assessment Questionnaire; SSc : systemic sclerosis; AHFI: Arab hand functional index; HFI: Hand Functional Index.

Table 2. Factor analysis of the AHFI and HAQ

	Eigenvalue	Variance. %	Cumulative %
AHFI			
Factor 1	5.411	54.114	54.114
Factor 2	1.034	10.338	64.453
HAQ			
Factor 1	4.051	50.638	50.638

AHFI: Arab hand functional index; HAQ: Health Assessment Questionnaire.

AB0200 INHIBITION OF DOT1L ACTIVITY IN HUMAN SKIN FIBROBLASTS: A TRANSCRIPTOME ANALYSIS

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Background: The pathophysiology of fibrosis, a hallmark of diseases like Systemic Sclerosis, is still not well understood. The role of epigenetic factors is increasingly explored. DOT1L, the unique H3K79-methyltransferase, methylates histone 3 at the Lysine residue at position 79, thereby regulating gene expression programs. Inhibition of DOT1L in cartilage and bone has cell-type specific effects on Wnt signaling, a pathway suggested to play an important role in fibrotic disease.
Objectives: To study the changes in the transcriptome of dermal fibroblasts after DOT1L inhibition.
Methods: Primary human dermal fibroblasts isolated from abdominal skin were treated with DOT1L-inhibitor EPZ-5676 or vehicle and stimulated or not with TGF-β or CHIR99021 (activating Wnt signaling). RNAseq was performed using the NextSeq500 as a platform and TruSeq as library prep kit. The preprocessed reads were aligned to the reference genome of Homo-sapiens (Ensembl.GRCh38.88(GRCh38)). Statistical comparative analysis for differential expressed genes (DEG) was done using the edge package in R version 3.20.9. The resulting p-values were corrected for multiple testing with Benjamini-Hochberg to control for false discovery rate (FDR). DEG were selected based on FDR-value less than 0.05 and a fold change of an absolute $\log_2$-ratio larger than 1. Pathway analysis was done using PANTHER14.0. Western Blot for di-methylated H3K79 was performed to confirm successful DOT1L inhibition.
Results: The DOT1L-inhibitor EPZ-5676 effectively reduced H3K79 dimethylation in the treated samples. RNAseq analysis revealed 663 differentially expressed genes in dermal fibroblasts exposed to the DOT1L inhibitor, based on group analysis: 77 genes were downregulated and 556 upregulated. There was no significant interaction between inhibition of DOT1L and stimulation of the cells with TGF-β or CHIR99021. Pathway analysis showed involvement of primarily the integrin signaling, the cadherin pathway and Wnt signaling.
Conclusion: More than 600 differentially expressed genes were discovered by RNA sequencing in human dermal fibroblasts exposed to DOT1L inhibition (independent of TGF-β or CHIR 99021 stimulation). These gene lists and their networks indicate that DOT1L activity affects integrin signaling, the cadherin and Wnt pathway, suggesting a potential impact on the fibrotic process that is leading to pathology in SSc.
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AB0201 THE PATHOGENIC EFFECTS OF IMMUNE COMPLEXES CONTAINING SCLERODERMA-SPECIFIC AUTOANTIBODIES IN ENDOTHELIAL CELLS

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Background: In systemic sclerosis (SSc), autoantibodies provide the most reliable tool to predict disease subset and the pattern of organ involvement.
Objectives: Consistently with the diagnostic and prognostic role of these autoantibodies, our group has previously demonstrated that immune complexes (ICs) containing scleroderma specific autoantibodies elicit a pro-inflammatory and pro-fibrotic signalling cascade in healthy skin fibroblasts, thus contributing to SSc aetiopathogenesis. In addition, we showed that SSc-ICs upregulate Toll-like Receptors (TLRs) and that pre-treatment with DNase and RNase prevent SSc-IC-mediated effects in fibroblasts, thus suggesting that SSc-ICs might engage TLRs via their nucleic acid components. The objective of the present study is to investigate the pathogenicity of SSc-ICs in endothelial cells (ECs).
Methods: Human umbilical vein ECs (HUVECs) have been isolated from umbilical vein and cultured in adequate conditions. ICs have been purified from sera of SSc patients bearing different autoantibody specificities (antibodies against centromeric proteins, DNA topoisomerase I, RNA polymerase and Th/To), patients with systemic lupus erythematosus (SLE), primary anti-phospholipid syndrome (PAPS) or healthy controls using polyethylen glycol precipitation. Cell cultures have been incubated with pathologic and control ICs and TLR3 [Poly(I:C)] and TLR4 (LPS) agonists. Several parameters have been assessed: mRNA levels of endothelin-1 (ET-1) and type I interferons (IFN-α and IFN-β) have been investigated by real-Time PCR; ICAM-1 expression has been evaluated by cell-ELISA and the secretion of IL-6, IL-8, tumour growth factor (TGF)-β1 and Pro-Collagen Iα1 in culture supernatants has been measured by commercial ELISA kits. The involvement of intracellular signalling pathways culminating with the activation of p38MAPK has been assessed. Furthermore, skin fibroblasts from healthy controls were stimulated with supernatants from HUVEC incubated with scleroderma and control ICs. The mRNA levels of collagen (col)Iα1 and matrix metalloproteinases (MMP)-1 and the secretion of TGF-β1 were evaluated in fibroblasts. Statistical analysis was performed comparing ICs from SSc and disease controls to NHS-ICs.
Results: Stimulation of HUVEC with scleroderma and control ICs resulted in the modulation of study mediators, as detailed in Table 1. When skin fibroblasts from healthy controls were stimulated with supernatants from HUVEC incubated with scleroderma and control ICs, we observed a significant modulation of mediators (Table 2).
Conclusion: These data provide the first demonstration of the pathogenicity of ICs isolated from scleroderma patients with different autoantibody specificities in ECs. According to our preliminary data, the activation of ECs induced by SSc-ICs might ultimately lead to a pro-fibrotic phenotype in healthy skin fibroblasts. SSc-ICs might thus be at the crossroad of scleroderma pathogenesis, contributing to the recruitment of the many cells involved in disease onset.

Table 1. Modulation of study mediators in HUVEC.

	ICAM-1	IL-6	IL-8	TGF-β1	ColIIIα1	ET-1	IFN-α	IFN-β	P38MAPK
Poly(I:C)	***	***	***	NA		NA			***
LPS	***	***	***	NA		NA			***
ATA-IC		*	***	*		**			***
ACA-IC	**	*	***	*					***
ARA-IC		**	***	*					***
anti-Th/T0-IC	***	**		*		**			
PAPS-IC	**			NA		***			
SLE-IC			**	NA					**
NHS-IC									

*= p<0.05; **= p<0.001, ***=p<0.0001

Table 2. Modulation of study mediators in fibroblasts.

	TGF-β1	ColIIIα1	MMP-1
TGF-β	NA	***	
ATA-IC	*	**	
ACA-IC	***	**	*
ARA-IC			*
anti-Th/T0-IC	***	***	*
NHS-IC			

*= p<0.05; **= p<0.001; ***=p<0.0001

REFERENCE:
[1] Raschi E, Chighizola CB, Cesana L, et al. Arthritis Res Ther 2018;20:187

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AB0202 DYSPHAGIA: POOR PROGNOSIS IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Dysphagia has been reported to occur in 10% to 73% of these patients and can be present at any time during the disease process (1).
Objectives: The primary objective of the study was to evaluate the prevalence of dysphagia in a cohort of patients with idiopathic inflammatory myopathy (MII) and to evaluate factors associated with the presence of dysphagia. The secondary objective was to evaluate the factors associated with severe dysphagia.
Methods: Retrospective, observational study, which included patients with a diagnosis of MII according to modified classification criteria of Bohan and Peter (1992-2018). Demographic data, clinical characteristics, laboratory data, autoantibodies, imaging studies, videodeglution, muscle biopsy and EMG were recorded.
Severe dysphagia was considered: one in which oral feeding was contraindicated and/or which required nasogastric tube feeding (SNG) either by clinical evaluation or by videodeglution study. The rest of the patients with dysphagia who did not present a contraindication to oral intake during the course of the disease were considered mild/moderate dysphagia.
Results: 94/110 patients were included, 76% female, mean age at diagnosis: 48 years (SD ± 14). Idiopathic dermatomyositis was the most frequent subtype of myopathy (64%). Dysphagia occurred in 53/94 patients (56.4%) and it was presented at the beginning of the disease in 31/94 (32%). Severe dysphagia was found in (22/94) 23%.
When analyzing the clinical features of patients with myopathy and dysphagia, it was found that Idiopathic dermatomyositis was the most frequent MII in these patients (71%). Patients with dysphagia presented: proximal muscle weakness 90%, neck muscles weakness 47%, and respiratory muscle weakness 27%.
Treatment received: 90/94 (97%) oral glucocorticoids, mean dose 48 mg of prednisone (Range 4 -100 mg.), pulses of Intravenous methylprednisolone was indicated in 25 patients (27.5%).The main steroid sparing agents used were: 72% methotrexate, followed by 33% azathioprine.
Significant association was found between dysphagia and weakness of neck muscles, respiratory muscles, of glucocorticoid pulses, gamma globulin and mortality (data not shown). In the Logistic Regression analysis, no variable was independently associated with the presence of dysphagia.
When analyzing the relationship of severe dysphagia and factors associated, a significant association was found with the requirement of mechanical ventilation, hospitalization in an intensive care unit, serious infections, neoplasia and mortality (Table 1). In the multivariate analysis: no associated factors were found independently.

Table 1.

Variable	**severe dysphagia (present)** n=22 (%)	**severe dysphagia (absent)** n=72 (%)	*p*	OR	IC
Weak neck muscles	**15 (68%)**	**18 (25%)**	**<0.001**	**8.86**	**2.75-8.86**
Weakness of respiratory muscles	**10 (45%)**	**6 (8%)**	**<0.001**	**9.5**	**2.8-32**
pulses of corticosteroids	**17 (77%)**	**8 (11%)**	**<0.001**	**25**	**7.5-89.5**
intravenous gammaglobulin	**10 (45%)**	**7 (9%)**	**<0.001**	**7.73**	**2.46-24**
intensive care unit	**8 (36%)**	**8 (11%)**	**<0.001**	**4.57**	**1.46-14.26**
mechanical ventilation	**6 (27%)**	**5 (7%)**	**<0.001**	**5.02**	**1.36-18.55**
death	**16 (72%)**	**10 (14%)**	**<0.001**	**16.53**	**5.89-90**
neoplasms	**6 (27%)**	**9 (12%)**	**<0.001**	**2.62**	**0.65-9.2**
serious infections	**11 (50%)**	**10 (14%)**	**<0,002**	**4.95**	**1,71-14**

Conclusion: in patients with MII 56% course with dysphagia at some point in the evolution. Of which 23% of cases were characterized as severe dysphagia. Both dysphagia in general and severe dysphagia were associated with parameters of severity, high cost and poor prognosis. However, in the analysis of multiple variables, this relationship could not be demonstrated.

REFERENCE:
[1] Mayo Clin Proc. • April 2007;82(4):441-447

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AB0203 INTRAPLATELET ANGIOGENIC AND GROWTH FACTORS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SE) is a serious disease of the connective tissue characterized by dysfunction of the microcirculation. Angiogenesis is a complex process regulated by both angiogenic and angiostatic factors. Normally the functions of these factors are under an adequate balance, however, under certain conditions these factors can be induced initiating disorganized angiogenic phenomena.
Objectives: For the first time, the levels of intraplatelet growth and angiogenic factors (normalized by platelet number and volumen) are described in patients with systemic sclerosis.
Methods: We included 23 patients with systemic sclerosis (ACR/EULAR) and 16 controls. Patients underwent a platelet-apheresis to obtain platelet-rich plasma (PRP) and platelet-poor plasma (PPP). The samples were subjected to a freeze-thaw process to break the cell membranes and release the platelet content. Subsequently the various factors were measured (VEGF-α, PDGF $\beta\beta$, HGF, FGF2, G-CSF, MCP-1, IL-1α, IL-1β, IL-8, IL-6, IL-13). Finally, the results were normalized according to the value of the plaquetocrit (number and volumen of platelets). We compared the levels in platelet-rich plasma and in platelet-poor plasma. A cut-off value $p < 0.05$.
Results: The mean age of the patients was 52 years ± 9.71, with a duration of the disease of 8 years, 74% were patients with limited SE, 70% of the patients had pulmonary involvement. Both patientes and controls, the TFG-β was 12 times more concentrated in PRP than in PPP ($p < 0.0001$), IL-1b 13 times more ($p < 0.0001$), IL-6 10 times more ($p < 0.0001$), G-CSF 11 times more ($p < 0.0001$), VEGF- α more concentrated (11.6 times) $p < 0.005$. When the PRP of the patients with scleroderma was compared with the PRP of the controls, only differences were found in the VEGF concentrations, being decreased in the patients with scleroderma respect to controls ($p < 0.0001$). Table 1 and 2.
Conclusion: The levels of VEGF-α (intraplatelet) are lower in patients with SE vrs controls ($p < 0.0001$). The intraplatelet values of the growth and angiogenic factors are higher than the plasma (patients and controls), finally, the plasma levels of these factors are similar in patients compare with controls. In almost all studies until today the measured levels have been carried out in serum, which are not precise since, in serum, several cells and lysate residues can alter the values, therefore, quantification in plasma is important. The present work is the result of the doctoral thesis of the main author.

Table 1. Growth factors values (23 patients with SE and 16 controls)

Factor	*PPP (pg/mL)*	*PRP (pg/mL)*	*p*
TFG-β1	21149,7	237185,2	<0.0001
IL-1β	7,7	117	<0.0001

IL-6	8,1	39,7	<0.0001
IL-8	2,4	3,4	0.169
IL-13	5,4	7,82	0.005
G-CSF	20,9	278	<0.0001
HGF	73,0	109,7	<0.001
MCP-1	53,6	64,8	0.01
IL-1α	1,2	9,1	<0.001
FGF-2	2.9	25,5	<0.001
VEGF	32,3	406,6	<0.001
PDGF-β	8,2	329,7	<0.001

Table 2. Values of growth factors in platelet rich plasma (PRP), *n* patients= 23, controls= 16

Factor		***Mean (pg/mL)****	***p***
TFG-β1	Patients	220271,8	0,327
Controls	261498,1		
IL-1β	Patients	111,3	0,492
	Controls	125,3	
IL-6	Patients	41,4	0,575
	Controls	37,2	
IL-8	Patients	2,4	0,159
	Controls	2,4	
IL-13	Patients	8,1	0,574
	Controls	7,4	
G-CSF	Patients	282,0	0,820
	Controls	272,2	
HGF	Patients	105,5	0,598
	Controls	115,9	
MCP-1	Patients	66,9	0,841
	Controls	61,8	
IL-1α	Patients	8,4	0,517
	Controls	10,1	
FGF-2	Patients	29,4	0,257
	Controls	19,9	
VEGF	Patients	248,9	<0.0001***
	Controls	633,3	
PDGF-β	Patients	270,6	0,12
	Controls	414,7	

REFERENCE:

[1] Choi JJ, et al. Elevated vascular endothelial growth factor in systemic sclerosis. J Rheumatol2003; 30: 1529-33.

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AB0204 THE CLINICAL FEATURES OF ANTI-TIF1GAMMA ANTIBODY POSITIVE DERMATOMYOSITIS

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Background: Anti-TIF1gamma antibody positive dermatomyositis(TIF1γ-DM) has greater risk of complication with cancer.
Objectives: We aimed to analyze the clinical features of TIF1γ-DM and find the difference between cancer-associated TIF1γ-DM (CA-TIF1γ-DM) and non-cancer-associated TIF1γ-DM (nCA-TIF1γ-DM).
Methods: We investigated the clinical data of idiopathic inflammatory myositis (IIM) patients received remission induction therapy in out hospital between January 2006 and December 2018.
Results: We treated 148 patients with IIM in this period, 9 cases of them were TIF1γ-DM. Patients with CA-TIF1γ-DM and nCA-TIF1γ-DM were 4 and 5 cases, respectively. Average age at onset of 9 patients with TIF1γ-DM was 63 years old. CA-TIF1γ-DM was significantly older than nCA-TIF1γ-DM (average:78.0 vs 57.4). All of 9 TIF1γ-DM had distinctive skin rash and muscle weakness. Seven cases of them suffered from dysphagia. Interstitial lung disease was not seen in all patients with TIF1γ-DM. Serum creatine kinase (CK) levels of CA-TIF1γ-DM was significantly higher than those of nCA-TIF1γ-DM (average: 3405.5IU/L vs 719.8IU/L) (Fig 1.). Among the TIF1γ-DM patients, we administered glucocorticoid (GCs) for 8 cases, immunosuppresants for 4 cases, and intravenous immunoglobulins (IVIG) for 7 cases. All 4 cases of CA-TIF1γ-DM were treated with GC and IVIG. All TIF1γ-DM patients, especially 4 CA-TIF1γ-DM patients, seemed to have good response to treatment in serum CK levels. Although serum CK levels of these 4 cases were normalized within a month (Fig1.), their muscle weakness, skin rash and dysphagia which was associated with quality of life and the prognosis were poorly improved.

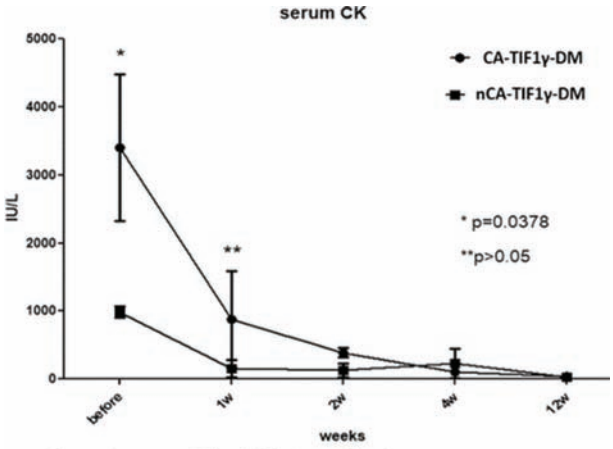


Figure 1: serum CK levels for 3months after treatment; Compared with cancer-associated TIF1γ-DM (CA-TIF1γ-DM) and non-cancer-associated TIF1γ-DM (nCA-TIF1γ-DM)

Figure 1

Conclusion: In our investigation, the age of onset and serum CK levels were significantly different between CA-TIF1γ-DM and nCA-TIF1γ-DM. We report our investigation of the phenotype and treatment of anti TIF1-gamma antibody positive dermatomyositis. TIF1γ-DM with high serum CK levels, we should perform appropriate tests to check for cancer throughout our treatment, and the improvement of serum CK levels is not equal to the success of our treatment.

Disclosure of Interests: None declared

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AB0205 TREATMENT OF INFLAMMATORY MYOSITIS IN CLINICAL PRACTICE: ANALYSIS OF THE REGISTRY OF INFLAMMATORY MYOSITIS FROM THE MADRID COMMUNITY (REMICAM)

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Background: Although glucocorticoids (GC) remain the cornerstone in the treatment of inflammatory myositis (IM), the management of these processes is not yet standardized. Experts recommend early use of immunosuppressants (IS), in order to prevent GC side effects. It is not known what is the actual management in clinical practice.
Objectives: To describe the management of IM in REMICAM registry, and to identify differences according to disease subtype (polymyositis (PM), or dermatomyositis (DM)), and to the year of diagnosis (before or after 2000).
Methods: All patients from REMICAM were included (1). A descriptive analysis of the different therapies (GC, IS, biologics, IV immunoglobulins

(IVIG), and hydroxychloroquine HCL) was performed, attending to possible differences between IM subtype and the year of diagnosis. T student and Chi square tests were used for quantitative and qualitative variables, respectively.

Results: From 479 patients (74% females, 52% PM, 44±22 y at diagnosis, 10±8 y follow up), 473 (99%) received oral GC, 50/344 (15%) pulses GC, 78 (16%) HCL, 355 (74%) IS (methotrexate MTX 228, leflunomide 10, azathioprine AZA190, cyclophosphamide 44, mycophenolate MP 38, cyclosporine 32), 55 (12%) biologics (rituximab 45, abatacept 2, aTNF 16) and 79 (17%) IVIG. Differences according to IM subtype (1), and to the year of diagnosis (2), are shown in Tables.

Table 1

	PM (n=251; 52%)	**DM** (n=228; 48%)	**p**
mean ± SD			
Time (T) initial symptoms- diagnosis (dx) (m)	19±43	11±28	**0.04**
T initial - any treatment (tt) (m)	15±42	7±15	**0.009**
T initial - GC (m)	16±42	8±18	**0,01**
n;%			
MTX	104/251 (41%)	124/228 (54%)	**0.006**
AZA	114/251 (45%)	76/227 (33%)	**0.009**
Mycophenolate	30/244 (12%)	8/224 (4%)	**0.001**
HCL	27/251 (11%)	51/228 (22%)	**0.001**
GC withdrawal due to improvement	52/245 (21%)	100/212 (47%)	**<0.0001**
Severe infections	75/241 (31%)	38/217 (17%)	**0.001**

Table 2

	Diagnosis <2000 (n=208, 43%)	**Diagnosis >2000** (n=271, 57%)	**p**
mean± SD			
T initial - dx (m)	22±48	11±26	**0.006**
T initial - any tt (m)	16±42	8±22	**0.02**
T initial - GC (m)	17±43	9±24	**0.02**
T initial - IS (m)	53±82	14±28	**<0.0001**
T dx – IS (m)	39±75	4±19	**<0.0001**
N° tt	2.3±1.6	2.8±1.3	**<0.0001**
N° IS	0.9±1	1.3±0.8	**<0.0001**
n;%			
Any IS	121/208 (42%)	234/271 (86%)	**<0.0001**
MTX	69/208 (33%)	159/271 (59%)	**<0.0001**
MP	9/205 (4%)	29/263 (11%)	**0.01**
Any biologic	12/208 (6%)	43/271 (16%)	**<0.0001**
RTX	8/208 (4%)	37/271 (14%)	**<0.0001**
IVIG	21/204 (10%)	58/271 (21%)	**0.001**
GC withdrawal due to improvement	75/189 (40%)	77/191 (29%)	**0.02**
All cause mortality	69/162 (43%)	45/247 (18%)	**<0.0001**
Severe infections	61/192 (32%)	52/266 (19%)	**0.003**

Conclusion: The therapeutic management of IM has changed over the last few years, with a clear increase and earlier use of IS in patients diagnosed after 2000. In spite of a more aggressive approach in recent years, severe infections are less frequent, perhaps as a consequence of lower GC doses. The management of PM and DM is similar.

REFERENCE:

[1] Nuño L, Rheumatol Clin 2017; 13:331-337

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AB0206

IS DISEASE SEVERITY A RISK FACTOR FOR CARDIOVASCULAR MORTALITY IN INFLAMMATORY MYOSITIS? ANALYSIS OF THE REGISTRY OF INFLAMMATORY MYOSITIS FROM THE MADRID COMMUNITY (REMICAM)

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Background: Inflammatory myositis (IM) are heterogeneous autoimmune diseases, characterized by muscular inflammation, which can associate systemic manifestations. In other inflammatory diseases, as rheumatoid arthritis, inflammation is a cardiovascular risk factor (CVRF), with clear influence on cardiovascular events and mortality (CVE, CVM).

Objectives: To analyze the influence of IM severity in the development of CVE and CVM in the REMICAM registry.

Methods: All patients from REMICAM were included(1). REMICAM is a retrospective multicentric registry of IM patients (n=479), performed in Madrid between 2012 and 2014, containing demographic, clinical and outcome data (1). The presence of extra muscular features (cardiac, pulmonary, cutaneous and systemic involvement), number of therapies, immunosuppressants (IS) need, and glucocorticoids (GC) withdrawal due to IM remission defined IM severity. Bi and multivariate logistic regression analysis were used to determine the association between these factors and CVE. Survival analysis and regression proportional hazard bi and multivariate Cox models were used to determine the effect of these factors on CVM. All factors with p< 0,2 in bivariate analysis were included in multivariate models. The effect was controlled for age, sex and CVRF.

Results: From 479 patients (74% females, 52% polymyositis, 44±22 years at diagnosis, 10±8 years follow up), 104/467 (22%) presented CVE and 24/409 (6%) died due to CVE. CVE were associated to age, male sex, CVRF number, diagnosis before year 2000, presence of arrhythmia or Raynaud (Table 1). Arrhythmia was the only independent risk factor for CVM. GC withdrawal due to IM remission, and a smaller number of therapies, were protective factors for CVM (Table 2).

Conclusion: In the REMICAM registry, extra muscular manifestations such as arrhythmia, were associated to CVE and CVM, as independent risk factors. A smaller number of treatment or GC withdrawal due to remission were protective factors for CVM. Our results support the hypothesis that more severe IM, with extra muscular involvement and persistent inflammation, could favor atherosclerosis and CVE development.

Table 1. Characteristics associated with cardiovascular event (ECV) development

	Bivariate		**Multivariate**	
	OR (IC 95%)	**P**	**OR IC 95%)**	**p**
Sex	1.7 (0.9-2.9)	0.06	**3.2 (1.4-7.4)**	**0.007**
Age at diagnosis	**1.04 (1.03-1-05)**	**<0.0001**	**1.04 (1.02-1.06)**	**<0.0001**
CVRF number	**2.2 (1.7-2.7)**	**<0.0001**	**1.9 (1.4-2.5)**	**<0.0001**
Raynaud	**2.01 (1.3-3.2)**	**0.003**	**2.3 (1.2-4.6)**	**0.015**
Arrhythmia	**9.7 (5.2-18.1)**	**<0.0001**	**5.7 (2.4-13.4)**	**<0.0001**
Pericarditis	**3.9 (1.8-8.3)**	**<0.0001**		0.06
Diagnosis after year 2000	0.7 (0.5-1.08)	0.1	**0.4 (0.2-0.7)**	**0.004**

REFERENCE:

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Table 2. Risk factors for cardiovascular mortality (MCV)

	Bivariate		Multivariate	
	HR (IC 95%)	p	HR (IC 95%	p
Sex		0.2		0.1
Arrhythmia	**3.8 (1.6-9.2)**	**0.003**	**3.4 (1.4-8.4)**	**0.007**
Number of therapies	**0.6 (0.4-0.9)**	**0.03**	**0.5 (0.3-0.9)**	**0.01**
GC withdrawal due to IM remission		0.2	**0.4 (0.1-1.005)**	**0.05**

AB0207

RECEPTOR EXPRESSION OF ANGIOTENSIN TYPE-1 AND 2 ARE DECREASED IN PATIENTS WITH SYSTEMIC SCLEROSIS AND PULMONARY ARTERIAL HYPERTENSION(PAH) AND CORRELATED WITH SEROLOGICAL LEVELS OF NT-PROBNP

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Background: Previous studies identified functional autoantibodies against the angiotensin receptor type-1 (AT1R) and the endothelin receptor type A (ETAR) in about 85% of the patients with systemic sclerosis (SSc, 1). The antibodies are cross-reactive, agonistic and functionally active by increasing the effects of the natural ligands as well as by specific activation of the receptors (2, 3). The levels of the antibodies are associated with clinical findings such as pulmonary arterial hypertension (PAH). Patients with highest antibody levels show worst prognosis and do not respond well to receptor blocker therapy (2-4). Several in vitro effects of the antibodies depend on the antibody levels and on the cell type bearing the receptors. Receptor expression of ETAR and AT1R was highest in early disease (3).
Objectives: To determine predictors of PAH, DU and clinical complications by measuring the antibody levels and the receptor expression on peripheral mononuclear cells in patients with systemic sclerosis.
Methods: The current study analyzed the serological levels of anti-AT1R and anti-ETAR antibodies and the extracellular and intracellular expression of AT1R, AT2R, ETAR and ETBR on circulating CD4pos T cells, CD8pos T cells, CD14pos Macrophages, CD15pos Granulocytes and CD19pos B cells in SSc (n=41) using sandwich ELISA and flow cytometry. Clinical data (PAH, history of digital ulcers, digital-ulcers score, mRSS, pulmonary fibrosis, therapy) and serological markers (ESR, CRP, NT-proBNP) were gathering at the time of serum sampling and every three-month up to 27month after baseline.
Results: Patients with PAH demonstrated a lower AT1R MFI and AT1R/AT2R MFI ratio on all PBMC. Levels of NT-proBNP correlated negatively with the AT1R MFI and AT1R/AT2R MFI ratio on all PBMC. The levels of anti-AT1R ab correlated with the NT-proBNP in SSc patients with levels of NT-proBNP <300pg/ml. AT1R MFI on T cells, Granulocytes and Macrophages distinguished between pathological and physiological levels of NT-proBNP. Using Log-rank test and Mantel-Cox proportional hazards model, decreased expression of AT1R MFI on T cells, Granulocytes and Macrophages identified trends of deterioration of NT-proBNP over 50%.
Conclusion: Expression of AT1R and AT2R on PBMC could be of diagnostic value identifying clinical progress and/or subgroups in SSc. Their role in the pathophysiology, e.g. their impact of endothelial damage, has to be further investigated in SSc.

REFERENCES:

[1] Riemekasten G. et al., Involvement of functional autoantibodies against vascular receptors in systemic sclerosis. Ann Rheum Dis. 2011 Mar;70 (3):530-6.
[2] Kill A. et al., Autoantibodies to angiotensin and endothelin receptors in systemic sclerosis induce cellular and systemic events associated with disease pathogenesis. Arthritis Res Ther. 2014 Jan 28;16(1):R29.
[3] Becker MO. Et al., Vascular receptor autoantibodies in pulmonary arterial hypertension associated with systemic sclerosis. Am J Respir Crit Care Med. 2014 Oct 1;190(7):808-17.
[4] Günther J. et al., Angiotensin receptor type 1 and endothelin receptor type A on immune cells mediate migration and the expression of IL-8 and CCL18 when stimulated by autoantibodies from systemic sclerosis patients. Arthritis Res Ther. 2014 Mar 11;16(2):R65.

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AB0208

UP-REGULATION OF TMEM176A AND TMEM176B IN PERIPHERAL BLOOD CELLS, A POSSIBLE BIOMARKER FOR THE DEVELOPMENT OF EARLY PULMONARY VASCULAR DISEASE IN SYSTEMIC SCLEROSIS

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Background: Pulmonary arterial hypertension (PAH) is prominent as a vascular involvement of systemic sclerosis (SSc), which remains a leading cause of death in spite of current best treatments. As the pulmonary vascular disease (PVD) can be well compensated for, more than 2/3 of the pulmonary circulation is impaired by the time of diagnosis. However, there were few studies focusing on the molecular mechanisms of PVD at the subclinical stage of PAH in SSc patients.
Objectives: To detect candidate genes involved in the development of PVD before diagnosis of PAH in SSc patients.
Methods: Total of 88 patients who had not met PAH criteria with Raynaud phenomenon (n=75), skin sclerosis (n=58) or SSc-related autoantibody (n=59) was enrolled. To detect the early PVD, exercise Doppler echocardiography (exDE) was carried out. The exercise induced pulmonary arterial hypertension (exPAH) group was segregated from normal response group (exN) with using the reported definition[1)]. The exDE was followed every 6 or 12 months for up to 3 years. For gene expression analysis, total RNAs from whole peripheral blood cells were extracted by PAXgene system and multiplex sequencing was done. To identify candidate genes involved in the pathogenesis of the early PVD, the differentially expressed genes (DEGs) between exPAH and exN group were visualized by volcano plots, a scatter plots calculated to show fold-changes and p-values of DEGs. After identifying the candidate genes, weighted gene co-expression network analysis (WGCNA) was performed to find the co-expressed gene cluster. And then, enrichment analysis using gene ontology (GO) terms were performed to investigate roles of the gene cluster in pathogenesis of PVD.
Results: Patients were fall into exPAH group (n=14) and exN group (n=74) at the baseline. After gene expression analysis, 1204 DEGs between exPAH and exN group were identified. Volcano plots indicated that expressions of TMEM176A and TMEM176B were prominent ($\log_2$ fold-change >1.25 and $-\log_{10}$p-value >3.5) in exPAH patients. We also found that the expressions of these genes were highly correlated with each other (R^2=0.9724, p<0.01). 11 out of 74 patients (14.9%) in exN group progressed to exPAH group during follow-up period (24.8±11.3 months). The expressions of TMEM176A/B at the baseline were significantly up-regulated in the group of clinical progression as compare with others ($\log_2$ fold-change from the average: TMEM176A: 0.78±1.31 vs. -0.35±1.65; p=0.022, TMEM176B: 0.71±1.38 vs. -0.38±1.78; p=0.034). By WGCNA and GO enrichment analysis, the terms, such as related to "apoptosis", "Toll-like receptor signaling" and "dendritic cell differentiation" were found in the co-expressed gene cluster of TMEM176A/B.
Conclusion: Although elucidating the mechanisms for progression of early PVD in SSc remains a major challenge, (1) we found up-regulation of TMEM176A/B was prominent in exPAH group; (2) TMEM176A/B was significantly up-regulated at the baseline in the patients progressed from exN to exPAH group during the follow-up period; (3) the co-expressed gene cluster of TMEM176A/B includes genes related to "apoptosis", "Toll-like receptor signaling" and "dendritic cell differentiation". TMEM176A/B was found initially to be a regulator for DC maturation in mice[2)] but functions of human ortholog of these genes remain still unclear. However, our findings suggest that the up-regulation of TMEM176A/B in peripheral blood cells is possible to be a biomarker for the development of early PVD in SSc.

REFERENCE:

[1] R. Naeije, et al., *Am J resp and critical care med* **187**, 576-583 (2013). 2) Condamine, T.et al., *J of leuko biol* 88, 507-515 (2010).

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AB0209 A STUDY OF CORRELATION BETWEEN PLATELETS AND LYMPHOCYTE SUBSETS IN SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, autoimmunity and widespread dermal and visceral fibrosis. There are existing evidence to support excessive platelet activation and their contribution to vascular function and fibrosis. Now we will focus on the immune role of PLT in SSC.
Objectives: By analyzing the correlation between platelet and lymphocyte subsets, CD4 + T cell subsets and disease activity in patients with diffuse SSc (dcSSc)/limitedSSc (lcSSc), and to explore the immune role of PLT in SSC.
Methods: The peripheral blood of 21 stable disease patients, 31 active disease patients and 20 healthy controls (HC) were collected. The clinical data and laboratory indicators of them were enrolled. The T, B, NK lymphocyte subsets and CD4 + T cell subsets were detected by flow cytometry (FCM). The CD4 + T cell subsets contains Th1, Th2, TH17, Treg, Th1/Th2 and Th17/Treg. Non-parametric Kruskal-Wallis H test was performed on multiple independent samples. The correlation between variables was used by Spearman correlation analysis.
Results: The PLT,PCT,MPV,PDW in peripheral blood of the stable group and active group were significantly higher than the HC group($P<0.05$). The amount of T cells in peripheral blood of active group were [1127.80 (796.66,1363.79)], which was lower than the percentage of HC group [1246.44(984.81,1497.84)] and stable group [1428.59(1179.09,2022.88)], there was significant difference between active group and stable group ($Z=6.525$,$P=0.038$). The amount of NK cells of the stable group [198.48 (140.22, 302.97)]and active group [143.76(89.00, 230.00)]were significantly lower than the HC group [224.81(155.04,350.51)]($Z=8.694$, $P<0.05$). The amount of Th cells of the stable group[888.11(679.55, 1430.70)] and active group[684.20(385,878)] were higher than the HC group[574.84 (493.22,728.00)], the former was significant, there was significant difference between active group and stable group($Z=8.694$, $P<0.05$). The Th17/Treg ratio of the stable group [0.18 (0.10, 0.34)] and active group [0.21(0.13, 028] were lower than the HC group [0.25 (0.12,0.31)], there was significant difference between active group and HC group($Z=0.508$, $P<0.05$). The ESR and CRP were positively correlated with PLT, PCT; The amount of Th cells and Th17 cells were positively correlated with PLT,PCT; The amount of Th2 cells and the ratio of CD4+T/CD8+ T were positively correlated with PCT; There was a negative correlation between the ratio of Th1/Th2 and PCT; The amount of Th2 cells was positively correlated with MVP, and the ratio of Th1/Th2 was negatively correlated with MPV.Among these immune cells, NK cells was negatively correlated with ESR and DSS(disease severity scale).
Conclusion: In scleroderma, NK cells are associated with the severity of the disease, and PLT affects the number of Th1/Th2, Th17, and disease activity.

REFERENCES:

[1] Ntelis K, Solomou E E, Sakkas L, et al. The role of platelets in autoimmunity, vasculopathy and fibrosis. Implications for systemic sclerosis[J]. Seminars in Arthritis and Rheumatism, 2017:S0049017217301105.
[2] Pauling J D, O'Donnell, V. B, Mchugh N J. The contribution of platelets to the pathogenesis of Raynaud\"s phenomenon and systemic sclerosis[J]. Platelets, 2013, 24(7):503-515.

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AB0210 THE GLOBAL EXPRESSION OF MIRNAS AND LNCRNAS IN THE EXOSOMES OF SYSTEMIC SCLEROSIS PLASMA AND NEUTROPHIL AND RELATED FUNCTIONS

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease with unknown pathogenesis. Exosomes (EXOs) are cell-derived vesicles 30-150 nm in size that contain various mRNAs, microRNAs (miRNAs), long non-coding RNAs (lncRNAs) and proteins. Plasma EXOs play wide roles in various diseased, however, little is known in SSc.
Objectives: Investigate the global expression of miRNAs and lncRNAs in the EXOs of SSc plasma and neutrophil. Explore the potential function of EXOs in the pathogenesis of SSc.
Methods: EXOs were respectively isolated from plasma, cultured neutrophil supernatants, and were identified by transmission electron microscopy. Global expression of miRNAs and lncRNAs form 5 SSc and 5 normal controls was analysis by IlluminaHiSeq 3000 platform. Differentiated expressed and bioinformatics analysis was performed by edgeR, limma package, GO, KEGG, and cytoscape. Furthermore, we used the EXOs stimulated human dermal microvascular endothelial cells (HDMECs) and human primary skin fibroblasts, and explore the potential functions of EXOs.
Results: 1. In plasma EXOs, we identified a total of 37 miRNAs and 479 lncRNAs that showed significant differences between the two groups. Among them, 26 of upregulated miRNAs were involved in the ErbB signalling pathway; 11 of downregulated miRNAs were involved in the MAPK signalling pathway, TGF-β signalling pathway, AMPK signalling pathway;299 of upregulated lncRNAs were involved in the PI3K-Akt signalling pathway, p53 signalling pathway;180 of downregulated lncRNAs were involved in lysosome.
2. In neutrophil EXOs, we identified a total of 22 miRNAs and 281 lncRNAs that showed significant differences between the two groups. Among them, 12 of upregulated miRNAs were involved in the Wnt signalling pathway; 10 of downregulated miRNAs were involved in the MAPK signalling pathway, AMPK signalling pathway; 119 of upregulated lncRNAs were involved in interleukin-23 signalling pathway;162 of downregulated lncRNAs were involved in the signalling by GPCR, signalling by NOTCH and TRAIL.
3. After stimulated with SSc plasma EXOs, the expression levels of has-miR-324-5p and SP1/SMAD2, has-miR-624-5p and PIK3RCB, has-miR-483-5p and MAPK1 were negatively correlated, the expression levels of ENST00000562409.1 and OSMR, ENST00000601511.1 and HMGB1/NRAS were positively correlated, variably in HDMECs and human primary skin fibroblasts.
4. After stimulated with SSc neutrophil EXOs, the expression levels of has-miR-1268a and PRKCA, has-miR-299-3p and IGF1R were negatively correlated, the expression levels of ENST00000520562.1 and IL23R, ENST00000596567.1 and TFDP2, ENST00000608572.1 and HDAC2 were positively correlated, variably in neutrophil, HDMECs and human primary skin fibroblasts.
5. These miRNAs and lncRNAs with consistent expression might be involved in the pathogenesis of SSc EXOs.
Conclusion: Our study identified and confirmed differentially miRNAs and lncRNAs in the neutrophil EXOs and plasma EXOs. Those genes may be involved in the pathological mechanism of SSc, such as has-miR-324-5p and SP1/SMAD2, has-miR-624-5p and PIK3RCB, has-miR-483-5p and MAPK1, ENST00000520562.1 and IL23R, ENST00000596567.1 and TFDP2, ENST00000608572.1 and HDAC2.
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AB0211 NEUTROPHIL-DERIVED EXOSOME S100A8/A9 INHIBITS ANGIOGENESIS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, inflammation, and extensive fibrosis of the skin and organs. Exosomes (EXOs) are cell-derived vesicles 30-150 nm in size that contain various mRNAs, microRNAs and proteins.
Objectives: Here, we aimed to investigate the roles of EXOs in SSc pathogenesis, especially in angiogenesis.
Methods: EXOs were respectively isolated from plasma, cultured peripheral blood mononuclear cells (PBMCs) and neutrophil supernatants, and were identified by transmission electron microscopy. The expression of S100A8/A9 was measured by real-time PCR and ELISA. Proliferation, migration and scratch assays in human dermal microvascular endothelial cells (HDMECs) were used to study the influence of neutrophil EXOs and neutrophil EXOs S100A8/A9. We also performed a genome-wide transcriptome analysis on PBMCs from 19 SSc patients and 18 matched normal controls (NC) using Illumina BeadChip arrays. The ingenuity pathway analysis (IPA) tool and Database for Annotation, Visualization and Integrated Discovery (DAVID) were used for bioinformatics analysis.
Results: Plasma EXOs and neutrophil EXOs from SSc patients suppressed the proliferation and migration of HDMECs. Using a microarray analysis we found 28% genes upregulated in PBMCs could exist in EXOs, especially the S100 protein family, including S100A8/A9. High levels of S100A8/A9 were consistently verified in SSc plasma, PBMCs, plasma EXOs, PBMC EXOs and neutrophil EXOs. Particularly, S100A8/A9 expression in neutrophil EXOs was distinctly higher than that in PBMC EXOs in SSc patients. Furthermore, we found that neutrophil EXOs S100A8/A9 inhibit the proliferation and migration of HDMECs, and that might through Toll-like receptor 4 (TLR4) pathway.
Conclusion: S100A8/A9 is one of components of neutrophil EXOs that regulates vascular endothelial cell angiogenesis in SSc patients, most likely by activating the TLR4 signalling pathway.
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AB0212 LONG-TERM TREATMENT WITH RITUXIMAB IN SYSTEMIC SCLEROSISMANAGEMENT: AN OVERVIEW OF THE CLINICAL EXPERIENCE FROM A REAL-LIFE SETTING

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Background: The treatment of systemic sclerosis (SSc) is a clinical challenge because of its complex pathogenesis. The rationale for the use of rituximab (RTX), able to downregulate the B-cell over expression, is demonstrated in different autoimmune diseases, some reports have suggested its key role in regulating both vascular, fibrotic, and immune T- and B-lymphocyte-mediated alterations that characterize several SSc manifestations. According to our previous experience with RTX [1], we suggested a possible therapeutical role of RTX in SSc, along with its good safety profile.
Objectives: To investigate the role and efficacy of RTX in our SSc patients' series.
Methods: A series of 24 SSc patients (M/F 7/17, mean age 55.2 ±14.7SD years, mean disease duration 11.7± 7.3SD years, L/D cutaneous subsets 11/13) were treated with one or more cycles of RTX (4 weekly infusions of 375 mg/m^2) and evaluated during a mean follow-up period of 12.3 ± 6.6SD years, range 2-26 years. The indications to RTX were interstitial lung disease, cutaneous, articular manifestations, evaluating its effects after 6 months of the first cycle and at the end of follow-up.
Results: After the first 6 months the extent of skin sclerosis measured with modified Rodnan skin score (mRSS) significantly improved (from 16.3±9.8 to 12.3±7.1; p<0.0001), and remained stable at the end of the follow-up (11.0±6.9; p=0.105). The effect on skin sclerosis was more evident in patients with diffuse cutaneous SSc (n=13) showing a significant decrease of mRSS after the first 6 months (from 24.3± 5.4 to 17.9±4.3; p=0.006) and at the end of the follow-up period (17.8±5.7; p=0.005). Similarly, a valuable improvement of other skin manifestations, namely hypermelanosis (17/20 pts), pruritus (18/21 pts), digital ulcers (8/18 pts) and calcinosis (6/3 pts), was observed. Moreover, arthritis revealed a good response to RTX treatment leading to a clear-cut reduction of swollen (from 2.0±2.8 to 0.3±1.3; p<0.0001) and tender joints (from 5.2±4.0 to 0.9±2.5; p<0.0001) in 20/24 patients. Finally, lung fibrosis detected in 19/24 on chest-CT remained stable during the entire follow-up, as well as pulmonary function tests (PFTs). These positive clinical changes were mirrored by the subjective improvement of patients' well being in all subjects (HAQ from 1.04±0.55 to 0.85±0.38; VAS from 71.0±15.2 to 28.0 ±10.3, p<0.0001). No significant side effects were observed during the entire follow-up. Only in one patient a severe urinary tract infection leading to the discontinuation of the treatment was detected.
Conclusion: The present study reinforces the previous trials and our preliminary researches on this topic, showing the efficacy of RTX in the management of SSc with good safety profile. The specific therapeutical role of RTX on B-cell-driven autoimmunity, might explain its beneficial effects on some SSc clinical alterations. The improvement of skin sclerosis, articular symptoms and the stabilization of lung involvement were identified as the main results. Further exploration of the potential clinical efficacy of RTX in SSc with multicentre, double blind, controlled study is needed.

REFERENCE:

[1] Giuggioli D, et al. Rituximab in the treatment of patients with systemic sclerosis. Our experience and review of the literature. Autoimmun Rev. 2015;14(11):1072-8

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AB0213 RELATED FACTORS TO RENAL INVOLVEMENT IN SYSTEMIC SCLEROSIS PERUVIAN PATIENTS

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Background: Systemic sclerosis (SSc) can affect multiple organ systems including the kidney. Renal disease, especially chronic kidney disease (CKD), remains an important cause of morbidity and mortality in SSc. The spectrum of renal complications in SSc include scleroderma renal crisis (SRC), normotensive renal crisis, antineutrophil cytoplasmic antibody associated glomerulonephritis, penicillamine-associated renal disease, and reduced renal functional reserves. Furthermore, subclinical renal impairment affects approximately 10-55% of SSc patients and might be associated with other vascular manifestations. However, the available evidence on CKD in patients with SSc residing in low-middle income countries (LMIC) is scarce. Because the health system of LMIC, and especially Peru, could have great differences in access to diagnosis and management of SSc, it is important to identify which clinical factors would be associated with CKD in patients with this autoimmune disease.
Objectives: To identify the associated factors to renal involvement in Peruvian patients with SSc.
Methods: We analyzed the associated factors to renal involvement in SSc patients at Hospital Nacional Edgardo Rebagliati Martins Lima-Peru, a national reference hospital in Peru. Between June 2001 and December 2018, we included ambulatory patients, older than 18-year-old with SSc that met the ACR-EULAR classification criteria. In patients who accepted to get informed consent, a complete clinical assessment and a sociodemographic survey were done. Additional clinical data were collected from their clinical records. Multiple Poisson regression with robust standard errors was used to identify significant and independently associated factor. Two models were estimated: one based on theoretically selected variables and another parsimonious model based on variables that was selected using a manual backward selection procedure with a predetermined alpha of 0.2. Adjusted prevalence ratio (aPR), 95% confidence interval and p-values were reported.
Results: One hundred and five patients with SSc were included in this study, 15.1% had chronic kidney disease. The average age was 57.8

years; 92% were women, and the average time of illness was 8.2 years. The model based on theory showed that age (aPR = 1.03, 95% CI = 0.99-1.07, p = 0.143) and exposure to Penicillamine (aPR = 0.51, CI 95% = 0.19-1.33, p = 0.170) were marginally associated (p <0.2) with CKD, while pulmonary hypertension (aPR = 2.76, 95% CI = 1.29-5.89, p = 0.009) and arterial hypertension (aPR = 3.51, 95% CI = 1.06-11.6, p = 0.04) were significantly associated (<0.05) with CKD. The parsimonious model retained pulmonary hypertension (aPR = 3.74, 95% CI = 1.67-8.36, p = 0.001) and arterial hypertension (aPR = 7.45, 95% CI = 3.31-16.7, p <0.001) as significantly associated factors to CKD.

Conclusion: Hypertension, a classic cardiovascular risk factor, and pulmonary hypertension were important factors associated with CKD. The appropriate management of these factors must be taken into account to prevent CKD. Prospective cohort studies should evaluate the influence of these factors in reducing the incidence of CKD.

REFERENCES:

[1] S.I. Nihtyanova VHOCPD. Current management strategies for systemic sclerosis. Clin Exp Rheumatol. 2014; 32(81: 156-154).

[2] Rosato E, Gigante A, Barbano B, Gasperini ML, Cianci R, Muscaritoli MPrognostic Factors of Renal Involvement in Systemic Sclerosis. Kidney Blood Press Res. 2018;43(3):682-689

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AB0214 MUSCLE INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: The prevalence of myopathy in systemic sclerosis (SSc) or scleroderma patients varies from 5% to 81% depending on the diagnostic criteria used to define the muscle involvement. The histopathological characteristics found in these patients and their correlation with the clinical features and autoantibody profile has not been fully characterized.

Objectives: To characterize the muscle involvement and histopathology findings in patients with SSc.

Methods: This retrospective cross-sectional study included all patients from Scleroderma Cohort of Vall d'Hebron General and Hospital Clínic de Barcelona with muscle biopsies available for review performed at the Muscle Research Unit of Hospital Clínic de Barcelona from May 2004 to November 2018. Muscle biopsies were performed, for weakness or raised CK and/or aldolase. Histological sections were independently evaluated by two myopathology experts looking for inflammation in the endomisium, perimisium and perivascular areas. The presence of necrosis, regeneration, fibrosis, neurogenic atrophy, and fiber type grouping as well as perifascicular atrophy were also recorded. Based on the autoantibody profiles patients were classified into five groups, "Scl70", "PM/Scl", "centromere", "U1-RNP", and "nucleolar and centromer IFI ANA pattern without specificity for anti-Scl70 or anticentromer". Demographic and clinical data were obtained by chart review.

Results: 42 subjects were included, 33 (78,6%) of them were women. Considering the immunological profile 12 had Scl70, 12 PM/Scl, 5 anticentromere, 2 U1RNP, and 11 had ANA pattern without specificity for anti-Scl70 or anticentromer. Most of patients (90.5%) were Caucasians, 2 (4.8%) were Hispanic, and 2 of other ethnic background. The mean age at the onset of SSc was 42.1 (SD 2.5) years and at the muscular symptoms 50.7 (SD 2.1) years, respectively. Twenty-two (52.4%) patients presented with high CK level (mean level of 1316 ± 353.8 U/L; normal value ≥200 U/L) whereas 38 (90.5%) exhibited high aldolase level (mean 19 ± 2.53 U/L, normal value < 6 U/L). Of note, 17 (40.5%) presented with high aldolase level and normal CK. Regarding the clinical manifestations of muscle involvement, 34 (80%) patients developed symmetrical distribution. Twenty-six (61,9%) had interstitial lung disease and 5 (11.9%) patients developed cancer.

Among the pathological features, 28 (66.7%) biopsies had fibrosis. Neurogenic atrophy was detected in 4 (9.5%) and fiber type grouping was present in 9 (21.4%) muscle biopsies. In near half of the muscle biopsies (45.2%) inflammatory infiltrate was present. Compared to other patients, those positive for PM/Scl had more perivascular (75%), endomysial (50%) and perimisial inflammation (75%) and perifascicular atrophy (42%) (all *p<0.05*), while a reduced prevalence of inflammatory infiltrates was noted in the Scl70 group (17%) (*p<0.05*).

Conclusion: In our cohort of SSc patients with muscle involvement, two main histopathological patterns were found, fibrosis and inflammation. Almost half patients presented with elevated aldolase with normal CK levels. The muscle disease heterogeneity suggests that a variety of pathologic mechanisms play a role in the scleroderma associated myopathy but those patients with histopathological inflammatory features deserve to be treated with immunosuppressive therapy.

REFERENCES:

[1] Arthritis Care Res (Hoboken). 2015; 67: 1416-25

[2] Ther Adv Musculoskelet Dis. 2017; 9: 3–10.

[3] Arthritis Res Ther. 2014; 16: R111.

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AB0215 A LATE ONSET OF SYSTEMIC SCLEROSIS IS ASSOCIATED WITH A MORE RAPIDLY PROGRESSING CLINICAL PHENOTYPE IN LCSSC PATIENTS

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Background: SSc is a heterogeneous multisystem connective tissue disease. The majority of patients (pts) develop initial clinical symptoms between the ages of 30-50 years (yrs).

It is not yet known whether the age of onset has an influence on the development of a distinct clinical phenotype.

Objectives: Investigating the relationship between age at disease onset and the development of clinical characteristics using data of the German Network for Systemic Scleroderma.

Methods: We evaluated 2928 patient data, subdivided them into 3 age groups at disease onset (<40 years, 40-60 years, and >60 years) and correlated the age at disease onset with specific clinical characteristics.

Results: Overall, 24% of pts developed first non-RP symptoms at the age of <40yrs, 53% between the age of 40-60yrs, and 23% were older than 60yrs. In particular, SSc pts with disease onset >60yrs developed significantly (p<0.001) more often the lcSSc subtype (64%) as well as ACA antibodies (42%) with a significantly lower mRSS. They, however, also suffered more often from pulmonary hypertension (PH) and developed less often digital ulcers. Especially lcSSc pts were associated with a more rapidly progressing clinical phenotype, i.e., 25% of the elderly lcSSc pts developed PH after five years. In contrast, less than 5% diagnosed with lcSSc at the age of <40yrs suffered from PH after five yrs (p<0.001).

Conclusion: In this registry, approximately one quarter of pts developed SSc at an age above 60yrs, predominantly having a lcSSc subtype. Although these pts have been diagnosed with the mild form of SSc, pts with a lcSSc subtype at a higher age (>60yrs) had more frequent a PH and showed a more rapid disease progression than the youngest pts. These findings may have an important influence on recommendations on

diagnosis, frequency of follow-ups and therapy of SSc in different age groups.

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AB0216 THE IMBALANCE OF ACTIVITIES OF PURINE AND PYRIMIDINE METABOLISM ENZYMES IN RED BLOOD CELLS OF SYSTEMIC SCLERODERMA PATIENTS

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Background: The systemic scleroderma (SSc) is connective tissue disease of unknown cause. The key points in development of SSc are the increased number of high collagen-producing fibroblasts in the skin, endothelial dysfunction and immune activation. Recent studies report various metabolic disturbances in SSc patients. Purine and pyrimidine metabolic pathways are underlies the central processes of cellular life. The changes in activity of purine and pyrimidine metabolism enzymes in blood plasma and lysed lymphocytes depending on the SSc activity were described by us earlier [1]. At the same time, there are publications that confirm the relationship between changes in ADA activity in red blood cells and pronounced immune disorders [2].

Objectives: to characterize enzymatic patterns of the major purine and pyrimidine metabolic pathways enzymes in lysed red blood cells depending on the SSc activity.

Methods: 51 SSc patients and 30 healthy controls were enrolled in the study. The diagnosis was verified in accordance with the international standards (ACR/EULAR 2013). Disease activity was assessed in accordance with the national classification [3]. Adenosine deaminase (ADA; EC 3.5.4.4); adenosine kinase (AK; EC 2.7.1.20); guanylate kinase (GK; EC 2.7.4.8), dihydroorotate dehydrogenase (DODH; DC 1.3.1.14); IMP dehydrogenase (IMPDH; EC 1.1.1.205); purine nucleoside phosphorylase (PNP; EC 2.4.2.1); thymidine kinase (TK; EC 2.7.1.21); thymidine phosphorylase (TP; EC 2.4.2.4); uracil/thymidine dehydrogenase (UDH; EC 1.17.99.4); cytidine deaminase (CDA; EC 3.5.4.5) activities were measured in lysed red blood cells.

Results: Mean age of patients (Mean± SD) was 42.8±1.3years, mean SSc duration was 7.9±0.7 years. We revealed substantial changes in enzymatic activities related to both purine and pyrimidine metabolism in lysed red blood cells of SSc patients. The increased ADA ($p<0,001$), AK ($p<0,001$), IMPDH ($p<0,001$), TK ($p<0,001$), UDH ($p<0,001$) activities and the decreased DODH ($p<0,001$), PNP ($p<0,001$) activities in lysed red blood cells were observed of SSc patients in comparison with healthy controls. AK, IMPDH, TK, UDH activities positively correlated with SSc activity. Negative correlations with SSc activity were revealed for ADA, CDA, DODG, GK, PNP, TP activities.

Conclusion: The progression of SSc goes with the imbalance of the purine and pyrimidine enzymes in a regular manner. Activity of the autoimmune inflammation is the factor that underlies the enzymatic pattern of purine and pyrimidine metabolism.

REFERENCES:

[1] Mozgovaya E., Bedina S., Trofimenko A., Zborovskaya I. The association between activity of purine and pyrimidine metabolism enzymes and disease activity in systemic scleroderma patients. Annals of the Rheumatic Diseases 2018;77(2):1280.

[2] Cowan M.J., Brady R.O., Widder K.J. Elevated erythrocyte adenosine deaminase activity in patients with acquired immunodeficiency syndrome. Proc Natl Acad Sci U S A. 1986 Feb;83(4):108.

[3] Guseva N.G. Systemic scleroderma. M.: Medicine,1993.268 p.

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AB0217 ASSOCIATION OF EUROPEAN SCLERODERMA STUDY GROUP ACTIVITY INDEX (ESCSG-AI) WITH PROGRESSION PULMONARY ALTERATIONS BY HRCT IN PATIENTSWITH SYSTEMIC SCLEROSIS OVER A FIVE YEAR PERIOD

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Background: Systemic sclerosis (SSc) is a rare connective tissue disease with a heterogeneous clinical course. Interstitial lung disease (ILD) is a common manifestation of SSc and a leading cause of death. Patients with early active SSc are at great risk for progressive ILD.

Objectives: To assess the EScSG-AI in patients with systemic sclerosis (SSc) and interstitial lung disease over a five year period.

Methods: It was a longitudinal study involving 77 pts with SSc-ILD (mean age was 46,2±13,4; 69% have limited subset of the disease; 93% were female). The mean duration of follow up was 58,9±11,4 months. Pts. were investigated with HRCT twice (at first visit and at the end of the study) and according the CT-changes were divided into 3 groups: the 1st group (16 pts) with improvement; 2nd group (39 pts) without any changes and 3rd group (22 pts) with worsening of fibrosis. Disease activity was assessed by the 2001 European Scleroderma Study Group Activity Index (EScSG- AI).

Results: There were no significant differences between groups related to sex, frequency of diffuse form and duration disease. Mean dates of EScSG-AI score of all pts and in the each groups in first visit and the end of follow up are present in table 1.

Table 1

Groups	First visit	At the end of the study	p
Group 1 (n=16)	1.9 ± 1.8	1.7 ± 0.9	P > 0.05
Group 2 (n=39)	2.0 ± 1.5	2.1 ± 1.3	P > 0.05
Group 3 (n=22)	2.4 ± 1.5	3.25 ± 2.0	P < 0.05
All pts (n= 77)	2.2 ± 1.6	1.9 ± 1.8	P > 0.05

After 5 years of follow up mean values of EScSG-AI score increased significantly in group 3 and was more than 3, this actually means the activity of the disease. The mean values of EScSG-AI score in group 3

was significantly higher than in groups 1,2 ($p < 0,01$ and $p < 0,04$ accordingly) at the end of the study.

Conclusion: Mean values of EScSG-AI score associated with and were accompanied by progression pulmonary alterations in pts SSc so EScSG-AI score can be used as valuable tool for long-term follow-up studies.

Disclosure of Interests: None declared

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AB0218 CORRELATION BETWEEN IMMUNOLOGICAL PARAMETERS AND PULMONARY FUNCTION PARAMETERS IN THE PATIENTS WITH SSC AND ILD OVER 5 YEARFOLLOW UP STUDY

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Background: Interstitial lung disease (ILD) is related to specific radiographic features in lung imaging and/or the presence of restrictive disorders in pulmonary function tests (PFTs). ILD is one of the leading causes of death in systemic sclerosis patients. Major risk factors of ILD associated with SSc (SSc-ILD) include male sex, diffuse type of cutaneous SSc and presence of anti-Scl-70 antibodies.

Objectives: Taking into account that anti-Scl-70 antibody is an unfavorable predictor of ILD, we have assessed the time course of FVC and DLco in anti-Scl-70-positive and anti-Scl-70-negative patients.

Methods: It was a longitudinal study involving 77 pts with SSc-ILD (mean age was 46,2±13,4; 69% have limited subset of the disease; 93% were female). The mean duration of follow up was 58,9±11,4 months. Pts. were investigated with HRCT twice (at first visit and at the end of the study) and according the CT-changes were divided into 3 groups: the 1st group (16 pts) with improvement; 2nd group (39 pts) without any changes and 3rd group (22 pts) with worsening of fibrosis. We evaluated the forced vital capacity (FVC), diffusing capacity of carbon monoxide (DLCO) in one year and in 5 years and anti-Scl-70 antibodies at the end of the study.

Results: In anti-Scl-70-negative patients the average FVC remained unchanged within a year (91.4 ± 17.4% и 91.6 ± 17%, respectively), however, within 5 years FVC significantly increased to 99.1 ± 20% ($p < 0.001$), while in anti-Scl-70-positive patients the average FVC was lower at the baseline and remained virtually unchanged both 1 year and 5 years later (85.4 ± 17.3%. 85.5 ± 17 и 86 ± 21%, respectively), as a result in 5 years' time the average FVC in anti-Scl-70-negative patients was significantly higher than in anti-Scl-70-positive patients ($p = 0.009$).

At the baseline average DLco were below normal and were similar in anti-Scl-70-positive and anti-Scl-70-negative patients: 60 ± 19% и 61.2 ± 14.3% respectively (p 0,05). Within 1 year DLco significantly decreased in all patients, however anti-Scl-70-positive patients demonstrated more pronounced DLco decrease to 53.4 ± 17.2% (p 0.0001), while in anti-Scl-70-negative patients it was less pronounced to 57.2 ± 12.8% ($p<0.05$), respectively. Within 5 years significant DLco decrease was found only in anti-Scl-70-positive patients: 53.9 ± 16.4% ($p<0.001$).

The time courses of DLco in anti-Scl-70-positive and anti-Scl-70-negative patients by group are shown in Table 1.

Significant DLco decrease over the 5-year period was observed in Group 2 and Group 3, and the lowest DLco (<50%) were observed in Group 3.

Table 1: The. time course of DLco in anti-Scl-70-positive and anti-Scl-70-negative patients by group over the 5 year observation period

Observation period	Group 1		Group 2		Group 3	
	With anti-Scl-70 (n = 4)	Without anti-Scl-70 (n = 11)	With anti-Scl-70 (n = 19)	Without anti-Scl-70 (n = 17)	With anti-Scl-70 (n = 17)	Without anti-Scl-70 (n = 3)
In 1 year (M ± δ)	78.5 ± 18	61.5 ± 18	62 ± 19	64.1 ± 11	52 ± 17	64 ± 1.8
In 5 years (M ± δ)	70 ± 12.5	57 ± 14	56 ± 14	61.5 ± 9	45 ± 16	52 ± 7
P	> 0.05	> 0.05	< 0.05	> 0.05	< 0.05	> 0.05

Conclusion: Therefore, the presence of anti-Scl-70 antibodies was associated with significantly lower pulmonary function parameters specifically in pts with progressive ILD.

Disclosure of Interests: None declared

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AB0219 BIOMARKER EXPRESSION IN MONOCYTE SUBPOPULATIONS IN SSC PATIENTS

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by vasculopathy and fibrosis, which can be classified into diffuse cutaneous (dSSc) and limited cutaneous (lSSc) subtypes. Monocytes are key agents in the pathophysiology of systemic autoimmune diseases, including systemic sclerosis (SSc). M1 cells (CD14++CD16-) represent a predominantly pro-inflammatory phenotype and M2 cells (CD14-/+CD16+/++) are more associated to an regulatory/pro-fibrotic phenotype.

Objectives: Our aim was to evaluate circulating blood monocyte subpopulations [classical (M1), intermediate and non-classical (M2)] and analyze the expression of CD163, CD169, CD206 and HLA-DR (function and activation monocytes receptors).

Methods: Fifty consecutive patients fulfilling the 2013 ACR/EULAR classification criteria for SSc were included in a cross-sectional study. Monocyte subpopulations were identified and characterized according to the expression of CD64, CD16, CD14, CD163, CD169, CD206 and HLA-DR. Thirty-eight age- and sex-matched healthy individuals were recruited as a control group.

Results: SSc patients mean age was 57.2 ± 12.8 years (HC 55.2 ± 11.4) and 94% were female. Limited form of disease was present in 72% of SSc patients and. SSc patients had an increased number of circulating peripheral blood monocytes compared to healthy subjects (table 1). Absolute counts of CD16+ (intermediary and non-classical) monocyte subpopulations were higher in SSc patients compared to HC [79.9 (53.4-103.5)/mm³ vs. 55.9 (26.8-85.8)/mm³, p=0.003]. HLA-DR intensity of expression was higher in all monocyte subsets from lSSc and dSSc patients when compared to control. There was a higher percentage of classical [1.56 (0.84-2.98) vs. 0.68 (0.37-1.88); p=0.003]and intermediate monocytes [15.9 (9.5-29.9) vs. 6.1 (3.7-11.5); p<0.001] with CD206 expression in SSc patients compared to HC, and a higher percentage of CD169 expression in dSSc patients compared to control and lSSc groups ($p<0.01$).

Table 1. Absolute value (/mm³) about monocytes subpopulations in all systemic sclerosis (SSc) patients compared to healthy controls (HC) and in limited (lSSc) and diffuse (dSSc) systemic sclerosis subtypes.

Monocytes subpopulations	SSc patients (n=50)	HC (n=38)	p *	lSSc (n=36)	dSSc (n=14)	p * (lSSc x dSSc)	p * (lSSc x HC)	p * (dSSc x HC)
Classical monocytes	346.2 (260.9-450.8)	209.8 (146.1-287.1)	<0.001	363.2 (262.9-451.8)	326.5 (231.2-461.9)	0.779	<0.001	0.003
Intermediate monocytes	38.2 (24.6-47.1)	25.4 (12.6-41.2)	0.005	38.5 (24.7-47.5)	37.1 (22.1-49.1)	0.795	0.009	0.069
Non-classical monocytes	41.2 (20.8-58.3)	28.3 (11.5-46.1)	0.006	42.5 (20.8-69.0)	37.1 (20.8-47.3)	0.310	0.005	0.201

Data are shown as median (interquartile range- IQR). * Mann-Whitney U test

Conclusion: In our study, SSc patients show greater monocytes counts than HC with a predominantly regulatory/pro-fibrotic phenotype (M2). dSSc seems to be more associated to CD169 than lSSc.

REFERENCES:

[1] Trombetta AC, Soldano S, Contini P, Tomatis V, Ruaro B, Paolino S, et al. A circulating cell population showing both M1 and M2 monocyte/macrophage surface markers characterizes systemic sclerosis patients with lung involvement. Respir Res. 2018.

[2] Lescoat A, Lecureur V, Roussel M, Sunnaram BL, Ballerie A, Coiffier G, et al. CD16-positive circulating monocytes and fibrotic manifestations of systemic sclerosis. Clin Rheumatol. 2017.

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AB0220 **ALPHA- SMOOTH MUSCLE ACTIN EXPRESSION ON ENDOTHELIAL PROGENITORS CELLS OF SYSTEMIC SCLEROSIS PATIENTS: POSSIBLE ROLE IN THE ENDOTHELIAL-TO-MESENCHIMAL TRANSITION PROCESS**

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Background: Endothelial-to-mesenchymal transition (EndoMT), a newly recognized type of cellular transdifferentiation, seems to be involved in Systemic Sclerosis (SSc) pathogenesis. In this process endothelial cells lose their specific markers, and acquire a mesenchymal phenotype, thus expressing cell products such as alpha smooth muscle actin (α-SMA) (1,2). Circulating endothelial progenitors cells (EPCs) derive from bone marrow stem cells and contribute to *de novo* vessels formation. Several studies, although with conflicting results, have shown that EPCs in the peripheral blood of patients with SSc are impaired in their number and function (3).
Objectives: to assess the expression of α-SMA, possibly associated with a pro-mesenchymal switch (EndoMT) of the circulating Early (CD34+KDR +CD 133+) and Late (CD34+KDR+) EPCs in the peripheral blood of SSc patients and of patients with Very Early Diagnosis of SSc (VEDOSS) compared with healthy controls (HC) using flow cytometry.
Methods: we enrolled 11 patients (7 SSc and 4 VEDOSS), classified according to the classification criteria for SSc (4) and for VEDOSS not fulfilling SSc criteria (5), and 10 HC. Phenotypic characterization was performed as previously described by Vasa et al. using a FACS Calibur (BD Immunocytometry Systems). EPCs number was expressed as a percentage of cells within the lymphocyte gate.
Results: we found a significantly higher percentage of α-SMA positive Early EPCs (CD34+KDR+CD 133+αSMA+) in all patients respect to HC (0,06% ±0,03 vs 0,03% ± 0,01; p=0,0149) particularly in VEDOSS patients (0,07%±0,01 vs 0,03±0,01 p=0,008). Moreover, in VEDOSS patients, also the percentage of Early EPCs (CD34+KDR+CD 133+), Late EPCs (CD34+KDR+)and α-SMA positive Late EPCs (CD34+KDR+αSMA+) were significantly higher than in HC (0,05%±0,01 vs 0,03%±0,01 p=0,05; 0,07%±0,01 vs 0,04%±002 p=0,04; 0,06%±0,01 vs 0,04%±0,02 p=0,05). Besides Early EPCs and α-SMA positive Early EPCs percentages seem to be significantly reduced in patients taking iloprost (p=0,05 and p=0,01 respectively), calcium channel blockers (CCB) (p=0,05 and p=0,03) and DMARDs (p=0,017 and p=0,013).
Conclusion: EndoMT seems to be involved in the pathogenesis of SSc and circulating EPCs seem to be impaired in number and function in SSc patients. In our study we found higher levels of EPCs, in particular α-SMA positive Early EPCs in both groups of patients (SSc and VEDOSS) respect to HC. Thus we can hypothesize a predominant pro-mesenchymal phenotype of this kind of EPCs. This could be considered the expression of the involvement of EPCs in EndoMT process and could better explain the controversial role of EPCs in SSc pathogenesis. Very interesting is the finding of a lower percentage of Early EPCs, and in particular of α-SMA positive Early EPCs, in those patients taking iloprost, CCB and DMARDs, suggesting a potential effect of these drugs on this subgroup of EPCs.

REFERENCES:

[1] Corallo C, et al. Arthritis Res Ther 2016;
[2] Manetti M, et al. Ann Rheum Dis 2017;
[3] Del Papa N, et al. Front. Immunol 2018;
[4] Van den Hoogen F, et al. Ann Rheum Dis 2013;
[5] Avouac J, et al. Ann Rheum Dis 2011.

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AB0221 **SEQUENCE OF CLINICAL SYMPTOMS ONSET AND ITS CORRELATION TO THE AUTOANTIBODIES PRESENCE IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES**

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Background: Idiopathic inflammatory myopathies (IIM) is a heterogeneous group of autoimmune diseases with a broad spectrum of clinical presentations including musculoskeletal, respiratory, neurological, dermatological, gastrointestinal and cardiovascular symptoms. It is known that presence of autoantibodies is a predictor of disease course. However, there is very limited data summarizing long-term observations assessing, when the particular symptoms are expected to occur.
Objectives: To assess the development of the symptoms in IIM patients during the disease course with respect to their serology patterns.
Methods: Medical history of IIM patients treated in our clinic between 2008 and 2019 were reviewed. We excluded patients with: insufficient data for the first period of disease course, history of IIM <6 months, IIM patients who do not fulfill Peter & Bohan 1975 diagnostic criteria (less than 4 points). Finally 103 IIM patients medical history were included for this analysis. EUROLINE test containing 16 myositis specific or associated antibodies (MSAs, MAAs) was used to determine serology for all of those patients. Onsets of symptoms were noted only in case when symptoms were confirmed objectively. Mean time since onset (MTSO) in months was counted for each symptom.
Results: Numbers below are presenting MTSO in months for each symptom.
Anti-Jo1 antibodies positive patients (n:30) have presented: rash (0), mechanic hands (1.2), myocarditis (5), muscle weakness (10.3), Raynaud's phenomenon (RP) (10.4), arthritis (20.7), interstitial lung disease (ILD) (23.5), fever (29.1), Gottron's sign (31.3), muscle pain (46.2), dysphagia (53.4).
Anti-Mi-2 antibodies positive patients (n:12) have presented: RP (0), mechanic hands (0), rash (0.2), Gottron's sign (0.3), fever (2.5), muscle weakness (4.5), dysphagia (4.5), muscle pain (9), ILD (15.5).
Anti-PM-Scl antibodies positive patients (n:7) have presented: rash (1), fever (1), Gottron's sign (1.25), mechanic hands (4), ILD (4), RP (5), arthritis (10.2), muscle weakness (46.3), muscle pain (108.5).
Anti-SRP antibodies positive patients (n:5) have presented: muscle weakness, fever, arthritis and ILD symptoms simultaneously (0), then dysphagia (4) and muscle pain (10).
Anti-NXP2 antibodies positive patients (n:4) have presented: muscle weakness and pain simultaneously with dysphagia (0), ILD developed 4 months later.
Anti-MDA5 antibodies positive patients (n:2) have presented: arthritis (0), fever (0.5), muscle pain (2), rash (3).
Anti-Ro52 antibodies positive patients (n:12) have presented: RP (3), Gottron's sign (3.3), rash (3.5), arthritis (5), muscle weakness (6.2), muscle pain (11), myocarditis (11), ILD (12), mechanic hands (13), dysphagia (18.3).
MSAs and MAAs negative patients (n:21) have presented: fever (0), RP (0), dysphagia (0,3), muscle pain (0,4), muscle weakness (1.9), rash (20), arthritis (66).
Conclusion: Our study shows differences in disease course in IIM patients with each serology pattern adding new data on chronology of appearances of each symptom, which is important in predicting the future course of the disease and planning long-term management.

REFERENCES:

[1] The Clinical Features of Myositis-Associated Autoantibodies: a Review. Gunawardena H, et al. Clin Rev Allergy Immunol. (2017)
[2] Specific autoantibodies in dermatomyositis: a helpful tool to classify different clinical subsets. Merlo, G., Clapasson, A., Cozzani, E. et al. Arch Dermatol Res (2017) 309: 87.

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AB0222

ASSOCIATION BETWEEN CENTROMERE AND TOPOISOMERASE SPECIFIC IMMUNE RESPONSES AND THE DEGREE OF MICROANGIOPATHY IN SYSTEMIC SCLEROSIS

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Background: In systemic sclerosis (SSc) more severe microangiopathy has been associated with worse disease outcome. In addition, auto-antibodies are important tools for disease prognostication. To what extent these two biomarkers reflect the same pathophysiological background is not clear. A better understanding of the interaction between the specific auto-immune response and the degree of microangiopathy could not only improve our insight in disease pathophysiology but could also contribute to more reliable disease prognostication. We hypothesized that an ongoing activated immune response, as reflected by higher anticentromere antibody (ACA) or anti-topoisomerase (ATA) specific IgG levels and higher number of ACA or ATA specific isotypes, associates with more severe microvascular damage and with more severe SSc.
Objectives: 1. To evaluate whether ACA and ATA isotype expression associates with the degree of microangiopathy in SSc.
2. To determine the additive value of more activated immune response for prediction of organ involvement.
Methods: ACA and ATA IgG, IgA and IgM levels were measured in serum samples of 129 ACA IgG+ or 102 ATA IgG+ SSc patients, respectively. The degree of microangiopathy was determined based on nailfold videocapillaroscopy (NVC) images, with SSc late pattern reflecting more severe microangiopathy. Associations between ATA and ACA isotype expression and NVC patterns were evaluated. Logistic regression analyses, with NVC pattern, autoantibodies, isotype expression and IgG levels as independent and disease characteristics as dependent variables were performed, adjusted for age, sex and disease duration.
Results: NVC images were available for 164 patients (n=100 ACA, n=64 ATA). Prevalence of SSc early, active and late pattern did not differ between ACA/ATA IgM+ and IgM – patients, nor between ACA/ATA IgA+ and IgA – patients. No associations between isotype expression (Figure 1) or IgG levels and NVC patterns were found. Logistic regression confirmed the association of ATA with pulmonary involvement (multivariable Odds Ratio [OR] 9.0 range 2.3-34.5) and of late SSc pattern with digital ulcers (multivariable OR 12.0 range 3.0-48.0) and pulmonary involvement (multivariable OR 5.0 range 1.5-16.1). Of note, higher topoisomerase and centromere specific IgG levels were independently associated with presence of digital ulcers (OR 3.5 range 1.1-11.0).
Conclusion: We did not observe an association between the quality of the anti-centromere specific or the anti-topoisomerase specific immune response and degree of microangiopathy in SSc patients. This might indicate that specific autoantibodies and stage of microangiopathy reflect different processes in the disease. The association between higher ATA or ACA specific IgG levels with digital ulcers, independent of specific autoantibody and NVC patterns suggests that an ongoing, active immune response is associated with more severe organ involvement.

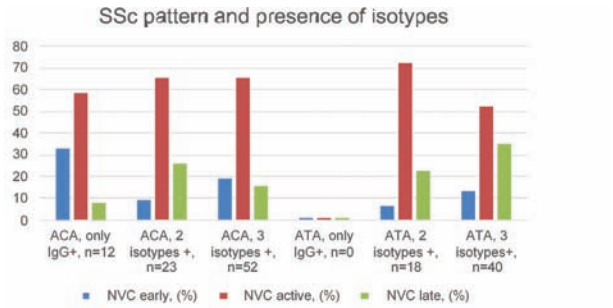


Figure 1. SSc patterns on nailfoldvideocapillaroscopy (NVC) stratified for number of isotypes expressed.

Figure 1

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AB0223

ASSESSMENT OF DISEASE ACTIVITY IN SYSTEMIC SCLEROSIS: THE COMPARISON BETWEEN REVISED EUSTAR AND ESCSG ACTIVITY INDEXES

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Background: Assessment of disease activity in systemic sclerosis (SSc) is challenging and usually hard to distinguish from damage or chronicity.
Objectives: We aimed to evaluate disease activity by different indexes and compare them in a SSc cohort.
Methods: Disease activity was evaluated by revised EUSTAR (European Scleroderma Trials and Research group) and EScSG (European Scleroderma Study Group) activity indexes in 131 SSc patients fullfiling ACR/EULAR classification criteria (2013). The patients with the scores of EUSTAR activity index $\geq$2.5 or EScSG activity index $\geq$3 were accepted as having active disease.

Table 1

	ATA Late NVC n=18	ATA Other NVC n=46	ACA Late NVC n=15	ACA Other NVC n=85
Female, n(%)	13 (72)	34 (74)	14 (93)	75 (88)
Age, mean (SD)	60 (14)	50 (15)	64 (11)	57 (13)
Since non RP, median(IQR)	6 (0-12)	2 (1-4)	15 (8-26)	4 (1-10)
DcSSc, n(%)	6 (33)	14 (30)	0 (0)	0 (0)
Digital Ulcers, n(%)	4 (22)	6 (13)	10 (67)	16 (19)
Pulmonary involvement, n(%)	5 (28)	3 (7)	2 (13)	5 (6)
Cardiac involvement, n(%)	4 (22)	7 (15)	4 (27)	8 (9)
PAH, n(%)	5 (28)	3 (7)	2 (13)	5 (6)
IgA positivity, n(%)	18 (100)	46 (100)	10 (67)	61 (72)
IgA level [aU/mL], median (IQR)	1810 (890-6868)	2782 (1148-9399)	102 (23-178)	67 (34-141)
IgM positivity, n(%)	14 (78)	30 (65)	12 (80)	65 (77)
IgM level [aU/mL], median (IQR)	1514 (492-7719)	693 (325-1818)	50 (23-1210)	110 (14-571)
IgG level [aU/mL], median (IQR)	394 (164-641)	498 (167-869)	630 (181-1094)	375 (169-1027)

Results: Demographics, disease characteristics and nailfold video-capillaroscopic (NVC) pattern details were summarised in table-1. The scores of EUSTAR and EScSG activity indexes were correlated well (r=0.576, p=0.000) and the agreement between two scores for activity was moderate (cohen kappa:0.407). The percentages of SSc patients described as having active disease or not according to two activity indexes were summarised in table-2. Of the patients, 9.9% had active and 70.9% had inactive disease according to both indexes in this SSc cohort. Twenty - one (for EUSTAR) and 4 patients (for EScSG) were described as active according to one index and not to the other. Revised EUSTAR activity index was found to have 76.5% sensitivity and 81.6% specificity when the activity was defined by EScSG activity index.

Table 1.

Table-1: Demographics, Characteristics and NVC pattern in SSc patients

		All SSc pts n=131
Age (years) ±SD		50,3±12,4
Gender F/M		122/10
Duration of Raynaud's (years) ±SD		9,6±8,9
Duration of non-Raynaud's (years) ±SD		6,2±6,5
Cutaneous involvement	diffuse	33 (24.4%)
	limited	93 (71%)
	sclerodermic	6 (4.6%)
ANA		120 (91.6%)
	anti-Scl70	38 (29%)
	anti-centromer	33(25.2%)
Clinical findings	Digital ulcer	60 (45%)
	Flex contr	18 (13.7%)
	Low DLCO	59 (45%)
	Lung disease	51 (38.9%)
	pulmHT	19 (14.5%)
NVC	Normal	7 (5.3%)
	Early	29 (22.1%)
	Active	23 (17.6%)
	Late	69 (52.7%)
	Cap number/mm	5,9±2,1
Mod Rodnan Skin Score		7,3±6,5
Disease Severity Score (Medsger)		5,3±3,6
ESR (mm/h)		30,2±18,3
CRP (mg/dl)		6,2±10,5
Treatment	Immunosuppressivas	68 (51.9%)
	Anti-vasculopathic	34 (26%)

Table 2.

Table-2: The percentage of the patients as having active or inactive disease according to indexes

		EUSTAR activity index	
		active	inactive
EScSG activity index	active	13(9.9%)	4(3%)
	inactive	21(16%)	93(70.9%)

Conclusion: This SSc cohort predominantly had limited cutanous disease, digital vasculopathy and late scleroderma pattern. Defining active disease was differed in 19% of the patients according to EUSTAR and EScSG activity indexes, former described higher frequency for activity. This difference might be related to validation procedures of these indexes in patients with different predominant stages of SSc disease, content of the index and the features of the cohort.

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AB0224 SYSTEMIC SCLEROSIS SINE SCLERODERMA: CHALLENGES WITH VERIFICATION IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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Background: Recognizing systemic sclerosis (SSc) in patients without cutaneous involvement is a real challenge due to inapparent clinical picture. 1980 ACR classification criteria for SSc fail to verify the diagnosis in the majority of cases. Therefore, the diagnosis is usually established years and decades after SSc onset at the stage of full-blown visceral disease. Introduction of 2013 ACR/EULAR classification criteria into clinical practice allow early diagnosis of SSc even in cases without skin involvement thanks to the fact, that list of considered criteria includes telangiectasia, pulmonary arterial hypertension (PAH), abnormal nailfold capillaries and SSc-related autoantibodies.

Objectives: To identify specific features in the clinical course of SSc sine scleroderma (ssSSc) in patients with PAH.

Methods: 11 patients with verified SSc diagnosis according to 2013 criteria were included; participants did not have any SSc-specific signs of skin involvement, such as puffy fingers, fingers' skin thickening/induration or skin atrophy. PAH was diagnosed in 11 patients during of right heart catheterization.

Results: Isolated Raynaud's phenomenon (RP) was along-standing diagnosis (more than 5 years) in all patients, except for one whoman, in whom the disease manifested with signs of Sjogren's syndrome (SjS) (parotitis). Benign, chronic, and gradually progressing during a long time disease was documented in all patients. In 7 patients out of 11 SSc diagnosis was initially suspected by cardiologists, and later confirmed by detection of antinuclear autoantibodies. The following signs were documented in SSc patients as initial manifesting non-Raynaud symptoms: esophageal dysmotility – in 3 patients, digital ulcers – in 2, telangiectasia – in 2 patients, and dyspnea (PAH symptom) – in 1 patient. None of the patients ever experienced skin thickening typical for SSc. RP was present in all 100%, but digital ischemic alterations – digital tip ulcers, pitting scars were found only in 3 patients. SSc diagnosis was verified based on abnormal nailfold capillaries (in 100% cases), and based on identification of SSc-specific antibodies (anticentromere antibodies – ACA) – in 7 patients. Anti-Ro-antibodies were found in 4 patients, anti-RNP-70 – in 3. SjS was established in 3 out of 4 anti-Ro-antibodies – positive patients and ruled out in one. Myositis was documented in past-medical history in one patient with anti-RNP-70-antibodies positivity. It should be noted, that 3 ACA-negative patients had, nevertheless, a "threshold" score value (9 scores) for SSc diagnosis, exhibiting many clinical features in favor of SSc diagnosis beyond any doubt. Esophageal dysmotility and associated symptoms were found in 10 out of 11 SSc patients. One patient had an SSc–rheumatoid arthritis overlap syndrome (erosive arthritis, joint deformities, positive ACA, rheumatoid factor, anti-CCP).

Conclusion: Introduction of 2013 ACR-EULAR classification criteria for SSc into clinical practice was highly relevant for identification of SSc cases without cutaneous involvement, providing therefore a timely diagnosis in this group of patients, and allowing to prognosticate the clinical course of PAH. 2013 ACR-EULAR classification criteria for SSc is an algorithm for SSc verification in patents with PAH, especially in the absence of typical for SSc cutaneous disease. The earlier PAH-SSc is diagnosed and PAH-specific therapy is initiated, the longer will be patient' lifespan.

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AB0225 CLINICALSUBTYPE OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS

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Background: Despite the similar pathogenesis and clinical picture, pulmonary arterial hypertension in systemic sclerosis (PAH-SSc) in comparison with idiopathic pulmonary arterial hypertension (IPAH) is characterized by a more severe course, an unsatisfactory response to PAH-specific therapy, a poor survival and a

disappointing prognosis. In this connection, before doctors of different specialties, first of all before rheumatologists, cardiologists and pulmonologists, there is a need to highlight the characteristics of the flow of PAH depending on the presence of SSc.

Objectives: To describe specific symptoms of PAH associated with SSc.

Methods: The study included 51 patients with PAH-SSc and 50 patients with IPAH formed the control group. To verify the diagnosis of PAH all patients underwent studies according to the program corresponding to the russian recommendations for the diagnosis and treatment of pulmonary hypertension with mandatory right heart catheterization. The diagnosis of SSc was established in accordance with the classification criteria ACR-EULAR 2013. Univariate logistic regression was used to calculate a probability (odds ratio (OR)) of SSc-associated symptoms.

Results: We identified 29 symptoms that were associated with PAH-SSc. The most significant of them, increasing the risk of detection of SSc in patients with PAH, were age over 45 years (OR 9.7, 95% CI 3.9-24.3, p <0.00001), serum uric acid level> 387 μmol/L (OR 3.8, 95% CI 1.5-9.6, p = 0.003), diffusion lung capacity (DLCO) <60% (OR 13.8, 95% CI 4.3-44.7, p <0.00001), ratio of forced vital capacity to DLCO <1.7 (OR 13.0, 95% CI 3.9-42.9, p <0.00001), level of C-reactive protein >2 mg/l (OR 12.9, 95% CI 3.96-41.8, p <0.00001), the presence of pericardial effusion (OR 2.3, 95% CI 1.0-5.1, p = 0.04), mean right ventricular pressure > 15.5 mm Hg. (OR 8.9, 95% CI 3.4-23.1, p <0.00001), diastolic right ventricular pressure > 4.5 mm Hg. (OR 4.6, 95% CI 1.9-11.2, p = 0.0003). Symptoms that reduce the risk of detecting SSc in patients with PAH include mean pulmonary artery pressure >55 mmHg. (OR 0.4, 95% CI 0.2-0.9, p = 0.03), pulmonary vascular resistance >12 units Wood (OR 0.4, 95% CI 0.2-0.9, p = 0.02), hemoglobin level >146 g/l (OR 0.3, 95% CI 0.2-0.8, p = 0.007), presense of syncope (OR 0.3, 95% CI 0.1-0.9, p = 0.02).

Conclusion: The selection of features of the course of PAH that increase the likelihood of detection of SSc will contribute to the timely diagnosis of SSc, will allow to predict the course of PAH, to approach more carefully the selection and monitoring of the effectiveness of PAH-specific therapy. That will contribute to improving the survival and functional status of patients with PAH-SSc.

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AB0226 NEUTROPHIL EXTRACELLULAR TRAPS ACTIVATE LUNG FIBROBLAST TO INDUCE MYOSITIS-RELATED INTERSTITIAL LUNG DISEASES IN MICE

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Background: Excessive neutrophil extracellular traps (NETs) formation may contribute to myositis-associated interstitial lung diseases (ILD), but the underlying mechanism is not fully revealed.

Objectives: This research aimed to elucidate the mechanism by which NETs contribute to myositis-associated ILD.

Methods: Myositis mice model was established by injected with the rat skeletal muscle homogenate and pertussis toxin. Expressions of ACTA2, CCN2, ADAM12, miR-7 and Smad2 were detected by quantitative real-time polymerase chain reaction (qRT-PCR). Smad2, α-SMA, CCN2 and TLR9 signaling-related proteins were measured by western blot. Soluble collagen I-IV were detected by Sircol collagen assay kit. The proliferation and apoptosis of lung fibroblasts (LFs) were detected by MTT assay or flow cytometry analysis. The interaction between miR-7 and the Smad2 was confirmed by dual-luciferase reporter gene assay.

Results: NET accelerated the progression of ILD and promoted pulmonary fibrosis *in vivo*. miR-7 expression was downregulated in lung tissue of myositis group than control group, and NETs further decreased miR-7 expression. TLR9 and Smad2 were upregulated in lung tissue of myositis group than control group, and NETs further increased TLR9 and Smad2 expressions. *In vitro* experiments showed that PMA-treated NETs accelerated the proliferation of LF and their differentiation into myofibroblast (MF), whereas DNAse I decreased the promotion effect of NETs. NETs components myeloperoxidase (MPO) and histone 3 also promoted the proliferation and differentiation of LF. In addition, we demonstrated that TLR9 involved in the regulation of NETs on LF proliferation and differentiation, and confirmed the interaction between miR-7 and Smad2 in LF. Finally, miR-7-Smad2 pathway was confirmed to be involved in the regulation of TLR9 on LF proliferation and differentiation.

Conclusion: NETs promote myositis-related ILD, and TLR9-miR-7-Smad2 signaling pathway is involved in the proliferation of LFs and their differentiation into MFs.

REFERENCES:

[1] A. Chrysanthopoulou, I. Mitroulis, E. Apostolidou, S. Arelaki, D. Mikroulis, T. Konstantinidis, E. Sivridis, M. Koffa, A. Giatromanolaki, D. Boumpas, K. Ritis, K. Kambas, Neutrophil extracellular traps promote differentiation and function of fibroblasts, J. Pathol. 233 (2014) 294-307.

[2] D. Storisteanu, J. Pocock, A. Cowburn, J. Juss, A. Nadesalingam, V. Nizet, E. Chilvers, Evasion of Neutrophil Extracellular Traps by Respiratory Pathogens, Am. J. Respir. Cell Mol. Biol. 56 (2017) 423-431.

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Basic science in paediatric rheumatology

AB0227 EXTENSIVE IMMUNOPHENOTYPIC ANALYSIS OF CO-INHIBITORY AND CO-STIMULATORY MOLECULES IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) PERIPHERAL LYMPHOCYTES

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Background: In a previous in-depth phenotypic analysis of PBLs in JIA, we detected differences in cell subpopulations dependent on the age and also some cellular changes that could be often associated with an exhausted phenotype.

Objectives: To analyze the expression of co-inhibitory and co-stimulatory molecules in different cellular subpopulations in Oligoarticular JIA patients stratified by age and treatment.

Methods: Exploratory cross-sectional study. 53 patients fulfilling Oligoarticular JIA (ILAR) criteria and 22 controls were included. All of them were children or young adults (2 to 35 years of age). JIA patients were either not treated (n=14) or treated with MTX (n=14), anti-TNF (n=8), or a combination of both (n=16). JIA disease activity was clinically and biologically assessed. Four flow cytometry panels were designed for the analysis of co-stimulatory/co-inhibitory markers, some typical of "exhausted" cells (PD1, TIM 3, TIGIT, CD226, CD137, HVEM, LIGHT, BTLA), assessed in memory, effector and naïve CD4+ and CD8+ T lymphocytes, and also in B lymphocytes and NK cells. Statistical analysis was performed, and FDR correction was applied for p values.

Results: No correlation was found among the different exhaustion/activation markers and age neither in JIA nor in controls. Interestingly, age-related differential trends were observed in the CD8+ compartment in controls, while in JIA patients were detected in the B cell compartment. We didn't observe, after correcting for treatment, any significant difference in lymphocyte subpopulations defined by the above co-inhibitory and co-stimulatory markers in JIA patients in relation to indexes of disease activity. However, there was a tendency towards a higher expression of CD137 in several CD8+ subpopulations of active patients as compared to inactive.

Conclusion: No clear differences were found in PBL subpopulations of oligoarticular-JIA patients regarding co-stimulatory/co-inhibitory molecules. This finding could be explained, at least in part, by the good therapeutic control achieved in this patient population, or by the particular characteristics of this group of patients, in which prevails a more localized expression of the disease. It could be of interest to carry out complementary analysis to further define the differential tendencies observed.

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AB0228

CHILDREN WITH EXTENDED OLIGOARTICULAR AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS HAVE A CYTOKINE PATTERN FAVOURING B CELL ACTIVATION IN CIRCULATION SIMILARLY TO EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS PATIENTS

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Background: The majority of polyarticular JIA (pJIA) and a large fraction of extended oligoarticular JIA (oJIA) patients fulfil classification criteria for rheumatoid arthritis (RA) in adulthood. B cells play several important roles in RA pathogenesis, but it is still unclear if the pattern of B cell involvement in pJIA and extended oJIA follows what has been described for adults with RA.
Objectives: The main goal of this study was to determine the concentration of cytokines potentially relevant for B cell activation in serum from children with pJIA and extended oJIA when compared to children with persistent oJIA, adult JIA, early and established RA patients.
Methods: Serum samples were collected from children with extended oJIA (n=8), persistent oJIA (n=6), pJIA (n=6), adult JIA (n=8), untreated early RA (< 1 year of disease duration, n=12), established RA patients treated with synthetic DMARDs (n=10) and two corresponding groups of age- and sex-matched healthy donors (children, n=6 and adults, n=10). A proliferation-inducing ligand (APRIL), B-cell activating factor (BAFF), interleukin (IL)-6 and IL-21 serum levels were measured by ELISA.
Results: Children with extended oJIA, early and established RA patients had significantly higher BAFF serum levels when compared to controls, but no significant differences were observed in children with persistent oJIA, pJIA and adult JIA when compared to all groups included. APRIL serum levels were significantly increased in all patient groups when compared to controls, except in adult JIA, who had similar APRIL concentrations in comparison to controls. In addition, children with extended oJIA and pJIA had significantly higher APRIL serum levels when compared to adult JIA. IL-6 serum levels were significantly increased in children with extended oJIA, pJIA, early and established RA when compared to controls, but no significant differences were found in children with persistent oJIA and adult JIA patients. IL-21 serum levels were significantly increased in early RA when compared to controls, but no significant differences were observed between any of the other groups included.
Conclusion: The similarity in B cell cytokine pattern found between extended oJIA, pJIA, early and established RA patients, contrarily to what was observed in persistent oJIA, suggests an early B cell involvement in the pathogenesis of extended oJIA and pJIA as described for RA.
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AB0229

RELATIVE MONOCYTE SUBSET DIFFERENCES BETWEEN JUVENILE- AND ADULT-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: 15-20% of patients with Systemic Lupus Erythematosus (SLE) develop the disease in childhood or adolescence (Juvenile-onset SLE, JSLE)[1]. Whilst it is recognised that JSLE is often more severe than adult-onset SLE[2], there is a lack of knowledge related to differences in the disease pathogenesis. Peripheral blood $CD14^+$ monocytes are thought to play a role in lupus development. $CD16^+$ Non-classical and Intermediate monocyte subsets, producing inflammatory cytokines and contributing to T-cell activation and B-cell proliferation, are enriched in adults with SLE[3]. Furthermore, $CD16^-$ Classical monocytes are important for phagocytosis of apoptotic cells - a process known to be aberrant in lupus- contributing to the generation of autoantibodies. Thus we hypothesised that monocyte subsets could be differentially dysregulated in SLE and JSLE and relate to the disparities seen in pathogenesis and clinical presentation.
Objectives: To compare relative percentages of classical, intermediate and non-classical monocyte subsets in patients with SLE and JSLE.
Methods: Peripheral blood from female patients with SLE (n=17) and JSLE (n=23) was collected at the UCLH rheumatology clinics after obtaining informed consent. In depth phenotyping of peripheral blood mononuclear cells was performed using multiparameter flow cytometry. GraphPad Prism was used for Mann-Whitney U-tests and Spearman's Correlations, and 'R' for logistic regressions.
Results: Non-Classical $CD14_{dim}CD16^{++}$ (p=0.007) and Intermediate $CD14_{high}CD16^+$ (p=0.039) monocytes had significantly increased frequencies in SLE patients compared to those with JSLE while no significant differences were seen in Classical $CD14_{high}CD16^-$ monocyte percentages between groups. Interestingly, non-classical monocytes correlated *positively* with age (p=0.006, rho=0.431), while classical monocytes negatively correlated with age (p=0.042, rho= -0.323), suggesting a relationship between age and increasing proinflammatory monocyte phenotype. No relationship was observed between dsDNA titre or C3 levels and monocyte subset frequencies in SLE or JSLE patients. Classical monocyte frequencies negatively correlated with ESR (p=0.027, rho= -0.323) in JSLE patients, but this correlation was lost when JSLE and SLE were grouped together, or when SLE was examined in isolation. Increased percentages of non-classical monocytes were associated with a higher odds of adult onset SLE relative to JSLE, after adjusting for the effects of disease activity (SLEDAI) (OR= 1.137, 95% CI= 1.021- 1.266, p= 0.018).
Conclusion: Pro-inflammatory $CD16^+$ subset percentages were higher in adults and increased with age. Studies have shown a similar correlation in healthy adults[4], suggesting that age-related differences in baseline immune cells may underpin differing mechanisms of monocyte involvement in lupus pathogenesis.

REFERENCES:

[1] Jimenez S. et al. (2003) The epidemiology of systemic lupus erythematosus. Clin Rev Allergy Immunology; 25: 3–12.
[2] Watson L. et al(2012) Juvenile-onset SLE; disease activity, severity and damage – the UK JSLE Cohort Study. Arthritis Rheum; 64: 2356–2365
[3] Zhu, H. et al(2016). CD16+ Monocyte subset was enriched and functionally exacerbated in driving T-cell activation and B-cell response in systemic lupus erythematosus. Frontiers in immunology; 7, 512.
[4] Seidler, S. et al(2010). Age-dependent alterations of monocyte subsets and monocyte-related chemokine pathways in healthy adults. BMC immunology; 11(1), 30.

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AB0230

CYTOKINE SIGNATURE DOES NOT CORRELATE WITH PAIN OR DISEASE ACTIVITY IN WELL CONTROLLED ERA

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Background: Inflammation is a mediator and primary driver of joint damage in juvenile idiopathic arthritis (JIA). Musculoskeletal pain can be experienced in the presence or absence of inflammation. Enthesitis related arthritis (ERA) is a subtype of JIA characterised by inflammation of the spine, enthesis, and peripheral joints. Cytokines and numerous other regulatory molecules are implicated in pain and inflammation, yet, to date, no reliable biomarkers have been identified.
Objectives: To assess if cytokine profiles correlate with pain or disease activity in patients with ERA.
Methods: 42 patients, with either a prior diagnosis of JIA or back pain, agreed to have a standard clinical MRI scan of lumbar spine, sacroiliac joints, and pelvis and to donate serum. Serum was also collected from 12 volunteer age matched healthy controls. Serum was analysed using a bead-based multiplex assay (Luminex) for the concentrations of the

following analytes: IL-6, IL-12, IL-17, IL-23, IL-27, TNFα, IFNγ, MIF, OPG, SOST, GM-CSF, VEGF, DKK-1, S100A8, MMP-3 and CRP. To assess pain levels, patients indicated on a scale of 0-10 the amount of back pain experienced at night and separately the amount of back pain experienced at any time during the last week. They also completed a Bath Ankylosing Spondylitis Disease activity Index (BASDAI) questionnaire to assess disease activity. Cytokine concentrations in patients with ERA were compared with those of controls. The levels were also correlated with the two measures of back pain as well as individual questions from the BASDAI questionnaire.

Results: Of all 54 samples tested, 11 patients and 5 controls cross-reacted with the negative control for the assay and thus were excluded from analysis. Based on MRI scan results, 14 patients had ERA, 8 had biomechanical pain, 7 had other subtypes of JIA, and 2 had non-specific features of spinal inflammation. The median overall back pain and the total BASDAI scores for the ERA group were 2.4 (IQR=1.45-5.55) and 2.5 (IQR= 0.75-6.25) respectively, suggesting well controlled disease on treatment and minimal residual symptoms. There was no statistical difference between cytokine levels in the ERA group compared to controls when corrected for multiple testing, with the exception of IL-12 which was significantly higher in controls (p=0.003). No correlation was found between cytokines and pain scores (at night or overall during the last week) or with the overall BASDAI score or any of the sub-component questions of the BASDAI questionnaire.

Conclusion: Well-controlled ERA patients on treatment have similar cytokine profiles as healthy controls and they do not correlate with clinical pain scores or disease activity.

Disclosure of Interests: None declared

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AB0230B STUDY OF CELIAC DISEASE ANTIBODIES IN PATIENTS WITH JUVENILE ONSET RHEUMATOLOGICAL DISORDERS

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Background: Preclinical autoimmunity can be detected in the form of circulating autoantibodies in the peripheral blood many years preceding the onset of the clinical disease. Celiac disease (CD) is an immunological response to gluten in genetically susceptible people. The clinical presentation of CD includes abdominal pain, diarrhea and nutritional deficiencies. However; clinical symptoms could be misleading in most of the patients presenting subclinical forms with only minor gastroenterological symptoms. Celiac disease will present in older children by atypical presentation. Most celiac disease patients show atypical symptoms and may remain undiagnosed; which makes screening is mandatory in high-risk patients with autoimmune diseases. This collectively highlights the need to check for clinical evidence of celiac disease among patients diagnosed as juvenile onset rheumatic diseases

Objectives: The aim of the work is to screen for celiac disease antibodies (anti-tissue transglutaminase IgA and IgG auto-antibodies) in the serum of juvenile onset rheumatic diseases patients in comparison with normal subjects

Methods: Serum tTG (both IgA and IgG) level was detected in 60 juvenile onset rheumatic patients and 20 age and sex matched healthy controls. We also assessed different clinical and laboratory markers of disease parameters; 31 juvenile onset systemic lupus erythematosus (SLE), 21 juvenile onset idiopathic arthritis (JIA), 4 juvenile onset systemic sclerosis and 2 juvenile onset behcet's disease and each disease activity score. We also correlated serum transglutaminase auto-antibodies with each disease activity. Endoscopic examination and histopathologic examination, for the patients with a least one positive anti-tTG Ab was done

Results: Serum anti-tTG Abs was no statistical significant differences in the patients group than in the control group, and there was no correlation between anti-tTG Abs with positive disease activity score

Conclusion: The presence of concomitant CD and another rheumatic disorder in the same patient is unlikely

REFERENCES:

[1] Roth B. Transglutaminase and peptidylarginine deiminase in the pathogenesis of autoimmune diseases. Doctorial Dissertation series. Sweden, Lund: Media-Tryck 2008.

[2] Vojdani A. Antibodies as predictors of complex autoimmune diseases and cancer. International Journal of Immunopathology and Pharmacology. 2008; 21(3):553–566.

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Rheumatoid arthritis – prognosis, predictors and outcome

AB0231 PAIN THRESHOLD IN RHEUMATOID ARTHRITIS AND ITS RELATED FACTOR

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Background: Pain remains the most important challenge for rheumatoid arthritis (RA) patients. In order to cope with pain in RA, clinicians firstly need to understand the degree of patients'pain. When self reported measures such as visual analog scale were used, inconsistency between clinicians' and patients' ratings of pain was demonstrated (1). As a result, inability to fully assess the pain will cause the inability to fully assess the impact of pain on disease severity. Measuring pressure pain threshold with pressure algometry may provide additional advantages for the evaluation of pain and disease severity when compared with self-reported measures.

Objectives: The aim of this study was to evaluate the pain threshold and to determine the variables associated with pain threshold in the patients with RA.

Methods: The current study included 100 RA patients and 80 age-sex matched controls with non-inflammatory chronic low back pain. Clinical parameters, functional status, disease activity, pain, fatigue, depression, anxiety, pain catastrophizing and laboratory activity of RA patients were recorded. The pressure pain thresholds on the dominant thumb nail bed, trapezius and wrist of the two groups were measured by the algometer. The pain thresholds of the paients with RA and controls were compared. Moreover, the relation between pain threholds and all evaluated parameters in RA patients was analysed.

Results: The mean age of RA patients was 55.93 ± 10.81; the mean age of the controls was
54,50 ± 9,47. The pain thresholds of RA patients and controls were statistically similar in all areas. When the parameters found to be significantly correlated with pain threshold in RA patients were analyzed by regression analysis, depression was the only factor associated with low pain threshold in all areas (Table 1).

Conclusion: We found that depression was the only factor associated with low pain threshold in the patients with RA. The use of pressure algometry in the evaluation of chronic pain could offer an additional method to detect pain/depression overlap.

Table 1. The correlation between pain threshold values and demographic, clinical and laboratory parameters of RA patients

	Nail PT		Wrist PT		Trapezius PT	
	p	r	p	r	p	r
Age	0,551	0,060	0,705	0,038	0,806	0,025
BMI (kg/m^2)	0,174	-0,137	0,066	-0,185	0,046*	-0,200
Duration of disease (year)	0,247	-0,117	0,144	-0,147	0,364	0,092
Morning stiffness (minute)	0,415	-0,082	0,592	-0,054	0,542	-0,062
Tender joint counts	0,046*	-0,200	0,099	-0,166	0,361	-0,092
Swollen joint counts	0,109	-0,161	0,227	-0,122	0,522	-0,065
CRP	0,681	-0,042	0,144	0,147	0,076	0,178
ESR	0,952	-0,006	0,330	0,098	0,453	0,076
VAS	0,056	-0,192	0,069	-0,182	0,086	-0,173
PCS	0,013*	-0,248	0,013*	-0,249	0,034*	-0,212
Fatigue Intensity Scale	0,107	-0,162	0,145	-0,147	0,422	-0,081
HADS-Anxiety	0,157	-0,143	0,118	-0,157	0,285	-0,108
HADS-Depression	0,010*	-0,256	0,005*	-0,282	0,003*	-0,293
HADS-Total	0,026*	-0,223	0,014*	-0,245	0,024*	-0,225
HAQ	<0,001*	-0,264	0,000*	-0,287	<0,001*	-0,315
DAS28-ESR	0,013*	-0,248	0,091	-0,170	0,211	-0,126
DAS28-CRP	0,009*	-0,261	0,066	-0,185	0,220	-0,124

PT: pain threshold, BMI: Body mass index, PCS: Pain Catastrophizing Scale, *VAS:* Visual Analog Scale, HAQ: The health assessment questionnaire

*p < 0.05

REFERENCE:
[1] Bagnato G, De Andres I, Sorbara S, Verduci E, Corallo G, Ferrera A, et al. Pain threshold and intensity in rheumatic patients: correlations with the Hamilton Depression Rating scale. Clinical rheumatology. 2015;34(3):555-61.

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AB0232 TIGHT CONTROL MANAGEMENT OF EARLY RA ACHIEVES MORE PATIENTS IN REMISSION AT 6 MONTHS AND IMPROVES PAIN, FUNCTION AND FATIGUE AT 24 MONTHS COMPARED TO A CONTROL GROUP

Maria Aronsson[1,2], Annika Teleman[1], Stefan Bergman[2,3], Kristina Forslind[4], Maria Andersson[2,5]. **Background:** Even with modern antirheumatic treatment, many patients experience chronic pain and loss of function despite less disease activity. The understanding of how this chronic pain development can be prevented is sparse. There is furthermore little knowledge if a tight control management without specific treatment schemes and instructions for the physicians to follow could increase the remission frequency.
Objectives: To determine whether solely a tight control management of patients, without further intervention in the physician's work, can increase the remission frequency and improve patient reported outcome in early RA.
Methods: In all, 96 patients with early RA were consecutively included in a tight control study group (TCS). Inclusion criteria were early RA patients (<13 month duration) with no previous history of rheumatic disease. **A control group, with so far 27 patients receiving standard care, has been analyzed.** The tight control management included monthly visits to the physician the first 6 months, followed by visits at 9, 12 and 24 months. If not in remission at 6 months the patients' monthly visits could continue to 12 months. The study did not include any treatment guidelines for the physicians. Pain, Fatigue and the Patient's Global Assessment of the General Health (**PtGA)** were reported on a Visual Analogue Scale (VAS). The 28 tender and swollen joint score, DAS28, C-Reactive protein, Erythrocyte sedimentation rate and Health Assessment Questionnaire (HAQ) were assessed.
Results: There was no significant difference between the groups at baseline in gender, age, smoking, disease duration, disease activity, pain, HAQ, fatigue, RF and ACPA. There was a significant difference between groups in outcome, with 70% of TCS and 37% of control patients in remission (DAS28 <2.6), p=0.010, at 6 months, figure 1A. At 12 and 24 months there was no significant difference in the remission frequency, figure 1A. The TCS group improved more than the control group in Pain, Fatigue and HAQ during follow up, figure 1B-D. The median VAS pain at 24 months was 11 (IQR 2-22) in the TCS group and 22 (IQR 6-42) in the control group, p=0.036. The median VAS fatigue was 13 (IQR 2-38) in the TCS group and 33 (IQR 8-70) in the control group p=0.028 at 24 months. The difference in HAQ reached significant numbers solely at 6 months where the median was 0.13 (IQR 0-0.50) in the TCS group and 0.57 in the control group (IQR 0.16-0.94).

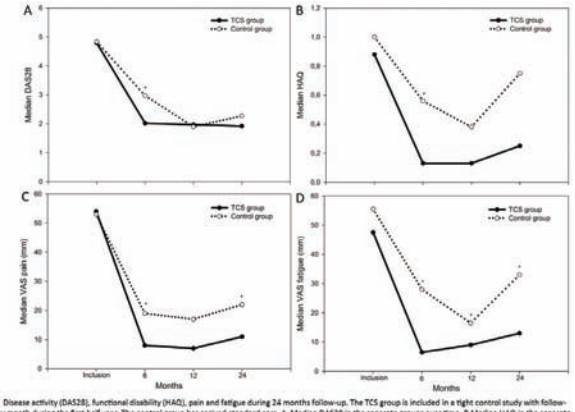


Figure 1. Disease activity (DAS28), functional disability (HAQ), pain and fatigue during 24 months follow-up. The TCS group is included in a tight control study with follow-ups every month during the first half year. The control group has recived standard care. A. Median DAS28 in the separate groups over time. B Median HAQ in the separate groups over time. C. Median VAS pain in the separate groups over time. D. Median VAS fatigue in the separate groups over time.
* significant difference p≤0.05

Figure 1

Conclusion: Patients in tight control reached remission faster than patients receiving standard care. They also reported less pain and fatigue, despite the fact that there was no difference in remission frequency at 24 months. The results indicate that a tight control scheme could influence pain development in patients with early RA, but further studies are required.
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AB0233 ASSESSMENT OF THE RESPONSE TO THERAPY WITH CSDMARDS AND BDMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The significant economic burden of rheumatoid arthritis (RA) and new treatment options, consuming much of the healthcare resources, pay attention on appropriate management strategies. These strategies are due to the need for an adequate assessment of the response to treatment and changes if it is necessary. Currently used American College of Rheumatology (ACR) response criteria and disease activity score (DAS28-CRP) allows on time evaluation of the results and facilitate decision process when is the right time to switch patient's therapy.
Objectives: The aim of the study is to evaluate the effectiveness and response to the treatment with csDMARDS and/or corticosteroid and bDMARDS in patients with RA after one year follow up period using ACR 20/50/70/90 response criteria and DAS28-CRP.
Methods: A total of 220 patients with a mean age 55.05±10.63SD meeting the 1987 ACR classification criteria for RA were included in the study. The mean disease duration was 9.97±5.78SD. Patients were stratified according to treatment regimens into age-matched treatment groups: 96 on csDMARDs and/or corticosteroid (Sulfasalazine ? 15, Methylprednisolone ? 15, Chloroquine – 16, Methotrexate – 20, Methotrexate and Methylprednisolone –30) and 124 on bDMARD (Tocilizumab ? 30, Certolizumab pegol ? 16, Golimumab – 22, Etanercept – 20, Adalimumab – 20, Rituximab – 16). All participants were evaluated for ACR 20/50/70/90 response to therapy on 6-th and 12th month of the follow up period, DAS28-CRP was calculated via licensed calculator. Comparison was performed by analysis variance ANOVA
Results: The majority of patients (71%) on bDMARDS achieved ACR 50 response criteria and 16% achieved ACR 70, indicating a significantly better therapeutic effect compared to the group on csDMARDS (ACR 50 - 11% ACR 70-1%) at 6th month follow up (p <0.001, p = 0.002). Only 3% of bDMARDS patients achieved ACR 90 response on the 6th month. Most of the patients on csDMARDs (64%) reach ACR 20 response criteria after the same period of therapy. At 6th month of follow-up, best response was achieved by the patients on combined MTX and corticosteroid (CS) therapy (50%) achieved ACR 20, 27% - ACR 50 and 3% - ACR 70. At the 12th month, a significant proportion of patients on bDMARDS reached the ACR 50 (36%) and ACR 70 (52%) response criteria compared to the csDMARDS group(ACR 50 – 20%, ACR 70 – 10%) (p = 0.0102; p <0.001). We evaluated the response to therapy according to the DAS28-CRP categories. On baseline patients on bDMARDS had higher disease activity in comparison to patients on csDMARDS (p=0.0004). In the follow-up to the 6th month, we observed a significant reduction in the proportion of patients (on bDMARDS) with severe disease activity - 2.4%, compared to csDMARDS group - 13.5% (p = 0.0019). In 26.6% of patients on bDMARDS, we found minimal disease activity, which was significantly more than 13.5% for the csDMARDS group (p = 0.0186). A remission was found in 5.6% of patients on bDMARDS which is significantly less than 14.6% for the group on csDMARDS. In contrast to the results obtained at the 6th month of follow-up, at 12th month we observed significantly higher percentage of patients on bDMARDS who had reached the remission category - 29.8%, in comparison with csDMARDS group - 12.5%, (p = 0.0025).
Conclusion: Patient treated with bDMARDs showed better response to treatment and lower disease activity than those on therapy with csDMARDs within a period of 12 months of treatment. Current management strategies should focus on switching on another medication earlier in the treatment plan when patients inadequately respond to therapy after 6 months of follow up.
Disclosure of Interests: None declared

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AB0234 AN INTEGRATED PROTEOMICS AND ANTIBODY ANALYSIS OF THE U-ACT-EARLY TRIAL TO IDENTIFY MARKERS OF TREATMENT RESPONSE AND DISEASE PROGRESSION IN EARLY RHEUMATOID ARTHRITIS

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Background: Predictive markers of treatment response in rheumatoid arthritis (RA) are necessary to stratify patients to devise personalised treatment strategies. The U-Act-Early trial [1], in which disease-modifying antirheumatic drugs (DMARD) naïve early RA patients initiated either methotrexate (MTX) or tocilizumab (TCZ) in monotherapy or in combination, offers a unique opportunity to assess the capacity of many baseline –omics markers (i.e. genomics, transcriptomics, proteomics, metabolomics, auto-antibodies) to predict clinical outcomes.
Objectives: To identify predictive markers of treatment response by developing a statistical machine learning methodology for correlating baseline clinical and –omics variables with clinical response data over time.
Methods: We developed a multi-omics approach that combines longitudinal statistical modelling of clinical data with Bayesian machine learning variable selection to identify the most predictive markers of treatment response. The time course of clinical outcomes was fit using a non-linear mixed longitudinal model, that characterise each patient of the U-Act-Early trial (n=317) by three parameters: a baseline value, an asymptotic value and a velocity (describing the speed at which the asymptote is reached). Supervised machine learning methods (such as Bayesian sparse regression as well as tree-based algorithms) were subsequently employed to find predictive markers for each of the longitudinal model parameters. We specifically focused on 85 auto-inflammatory proteins and 450 auto-antibodies markers, including 41 citrullinated-peptides antigens. The analysis was repeated for the three treatment-arms since DAS28-subscores response markers may vary across treatment strategies and clinical outcomes. We finally investigated whether predictions are enhanced by incorporating known networks of protein-protein interactions, rather than considering the predictive power of each protein independently.
Results: Preliminary results are that some proteins (e.g. sCD14, VEGF) were moderately predictive of the disease status at baseline. Specifically, the available inflammatory proteins predicted baseline DAS28, swollen and tender joints and ESR with R^2 values of 0.25, 0.32, 0.16 and 0 respectively. Surprisingly, these proteins did not improve the prediction of treatment-response (i.e. the velocity and asymptotic parameters) after controlling for the baseline disease status. Protein networks marginally improved prediction when compared to prediction of individual proteins. Citrullinated peptide antigens did not appear predictive of the baseline disease status nor the treatment response.
Conclusion: In our initial investigation inflammatory proteins, especially when considered as part of interaction networks, appear to be predictive of the baseline status of the disease but not of treatment-response. The most predictive marker of treatment response appears to be disease activity at baseline.

REFERENCES:

[1] Bijlsma JWJ, et al. Lancet. 2016;388:343-55.

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AB0235 THE LIFETIME RISK OF KNEE AND HIP REPLACEMENT FOLLOWING A DIAGNOSIS OF RHEUMATOID ARTHRITIS: FINDINGS FROM ROUTINELY COLLECTED DATA FROM ENGLAND

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Background: Understanding the lifetime risk of knee and hip replacement following a diagnosis of rheumatoid arthritis (RA) would help provide patients and clinicians with an indication of long-term prognosis and future health care utilisation.
Objectives: To estimate the lifetime risk of knee and hip replacement following a diagnosis of RA.
Methods: Routinely collected data from the English NHS was used to inform the analysis. Diagnosis of RA was identified using primary care records, with knee and hip replacement observed in linked hospital records. Parametric survival models were fitted for up to 15 years of follow up, with age, sex, Charlson comorbidity score, socioeconomic status, BMI, and smoking status included as explanatory variables. A decision model was used to combine and extrapolate survival models to estimate lifetime risk. Lifetime risk was estimated for individuals with average characteristics (median for continuous variables and mode for categorical ones). The partial effect of explanatory factors on lifetime risk was assessed by re-running models with participant profiles varying in the explanatory factor of interest, while holding other characteristics constant at their average.
Results: 13,961 study participants with a diagnosis of RA were included. Lifetime risk of knee replacement and hip replacement was estimated to be 22% (95%CI 16% to 29%) and 17% (11% to 26%) following a diagnosis of RA for the average patient profile (non-smoking women aged 64 with no other comorbidities, BMI of 27 and in the top socioeconomic quintile). Risks were higher for younger patients, but broadly similar for men and women. Comorbidities, socioeconomic status, BMI, and smoking status had relatively little impact on lifetime risk.
Conclusion: This study has estimated lifetime risk of knee and hip replacement following a diagnosis of RA, allowing for a better understanding of long-term prognosis and healthcare resource use. These risks are more than double those of the general UK population.
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AB0236

WHAT FACTORS ARE ASSOCIATED WITH THE EVOLUTION TOWARDS RHEUMATOID ARTHRITIS, USE OF BIOLOGICAL THERAPY AND DEVELOPMENT OF CARDIOVASCULAR EVENTS IN A COHORT OF PATIENTS WITH UNDIFFERENTIATED ARTHRITIS?

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Objectives: To describe the clinical-demographic characteristics and behaviour over time (12, 24 and 60 months) of a cohort of Undifferentiated Arthritis (UA), as well as to analyze which factors are associated with the evolution towards Rheumatoid Arthritis (RA), use of Biological Therapy (BT) and the development of Cardiovascular Disease (CVD).
Methods: Ambispective cohort study of patients with UA evaluated longitudinally from January 2009 to 2019. We analyzed baseline clinical and laboratory variables and a Multivariate Logistic Regression was performed to determine the factors associated with RA development after 5 years of follow-up. To analyze what factors were associated with the use of BT and the presence of CVD chi-square or Fisher's test were used for binary variables, and U-Mann Whitney for continuous variables.
Results: 180 patients were included, 55% were women, with an average age of 49.3 (SD 16.1) years. The average duration of symptoms before the first visit was 6.9 (SD 9.9) months. 47.2% were FR+, 41% ACPA+, 20.6% HLA-DRB1 shared epitope.
At the end of follow-up: 33.3% evolved to RA, 17.2% remained as palindromic rheumatism, 25% were diagnosed other chronic rheumatic diseases, 21.1% remitted spontaneously and 3.3% remained as UA. Of the 60 AR, 37 were diagnosed in the first year, 13 at second and 10 at 5 years of follow-up. During follow-up, 13 patients with RA started BT, and 12 patients presented CVD (7 of them died).

Table 1:. Factors associated with RA after 5 years of follow-up.

Baseline data	Total patients N=180	RA N = 60	No RA N =120	OR (95%IC)	p-value
Sex (women)	99 (45.7%)	34 (56.7%)	65 (54.2%)	1.11 (0.69-2.07)	0.751
Duration of symptoms (months)	7.7 (8.8)	7.5 (6.5)	7.8 (9.8)	0.99 (0.96-1.03)	0.864
Age at diagnosis	49.3 (16.1)	49.4 (14.5)	49.3 (16.9)	1.00 (0.98-1.02)	0.961
-Oligoarthritis	84 (46.7%)	20 (33.3%)	64 (53.3%)	2.34 (0.49-11.14)	0.284
-Polyarthritis	79 (43.9%)	38 (63.3%)	41 (34.2%)	**6.95 (1.49-32.42)**	**0.014**
Morning stiffness>1h	43 (23.9%)	22 (36.7%)	21 (17.5%)	**2.73 (1.35-5.52)**	**0.005**
RF+	85 (47.2%)	47 (78.3%)	38 (31.7%)	**7.8 (3.78-16.1)**	**<0.001**
ACPA+	73 (41.0%)	50 (83.3%)	23 (19.5%)	**20.6 (9.1-46.7)**	**<0.001**
High ESR	104 (57.8%)	40 (66.7%)	64 (53.3%)	1.75 (0.92-3.34)	0.089
Hight CRP	100 (55.6%)	40 (66.7%)	60 (50%)	**2.0 (1.05-3.81)**	**0.035**
HLADRB1 Shared epitope	37 (20.6%)	32 (53.3%)	5 (4.2%)	**26.3 (9.39-73.55)**	**<0.001**
Smoker	72 (40%)	25 (41.7%)	47 (39.2%)	1.11 (0.59-2.08)	0.747
Family history RA	39 (21.7%)	17 (28.3%)	22 (18.3%)	1.76 (0.85-3.64)	0.127
Tto glucocort (5mg/d)	88 (48.9%)	40 (66.7%)	48 (40%)	**3.0 (1.57-5.74)**	**0.001**
Tto dolquine (200mg/d)	50 (27.8%)	25 (41.7%)	25 (20.8%)	**2.71 (1.38-5.34)**	**0.004**
Tto mtx (15mg/w)	16 (8.9%)	14 (23.3%)	2 (1.7%)	**17.9 (3.93-82.12)**	**<0.001**

Table 1 identifies the factors associated with the development of RA. The MLR identified **ACPA +, OR (95% CI) = 10.69 (4.43 - 25.78), and the HLA-DRB1 shared epitope OR (95% CI) = 9.18 (2.96 - 28.48) p <0.001** as factors associated to the development of AR. We failed to identify factors associated with the use of BT, possibly due to the sample size. The factors associated with the development of CVD, where only the use of glucocorticoids as a factor associated with the presence of CVD shows statistical significance.

Conclusion: 1) Useful clinical and laboratory characteristics have been identified to predict which patients are at risk of developing persistent arthritis. 2) HLADRB1 shared Epitope and ACPA are predictive factors of evolution to RA. 3) Possibly the continued use of glucocorticoids, even at low doses, may be related to the development of long-term CVD
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AB0237

WHAT DO SPANISH RHEUMATOLOGISTS THINK ABOUT THE EFFICACY OF THE DRUGS USED IN THE MANAGEMENT OF PATIENT WITH RHEUMATOID ARTHRITIS AND POOR PROGNOSIS FACTORS? PROGRESAR-2 PROJECT

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Background: Currently, patients with rheumatoid arthritis (RA) have a wide range of treatments available to achieve a good control of the disease and avoid progression. However, some patients, especially those with poor prognostic factors, need to switch drugs to achieve remission or low disease activity. If we can predict the response to a drug, given specific prognostic profiles, we may be able to choose the best drug for individual patients.
Objectives: To assess the degree of confidence of rheumatologists regarding the efficacy of biologic therapies and specific targeted synthetic molecules in patients with RA harbouring poor prognostic factors.
Methods: A Delphi survey was sent to a group of rheumatologists with the aim to capture the perceived efficacy of a group of drugs (antiTNF, T-cell co-stimulants, B-cells depletors, anti IL6, and JAK inhibitors) given different poor prognostic factors are present at the onset of the disease. These factors were: interstitial lung disease, elevated HAQ, positive rheumatoid factor (RF), presence of anti-citrullinated protein antibody (ACPA), elevated acute phase reactants (APR), and bone erosions observed by simple x-ray/ultrasound. The survey was circulated in two rounds, with feed-back from the first round. The degree of confidence in the efficacy of the therapies for each specific prognostic profile was collected on a Likert scale from 1 to 9. The mean (m) and standard deviation (SD) were calculated; agreement was considered if SD ≤1 and 80% of the scores were in one of the three levels (correspondingly it would be agreement on "ineffectiveness", ldquo;neutrality" and "effectiveness").

Table 1:.

	Agreement on the efficacy of therapy m (SD)				
Prognostic factor	AntiTNF	T-cell co-stimulants	Depletion of B cells	Anti IL-6	Jak inhibitors
Interstitial Lung Disease	2.5 (1.5)	**8.6 (0.7)**	7.0 (1.4)	6.2 (1.4)	5.1 (1.6)
High HAQ	**8.1 (0.7)**	**7.4 (1.0)**	7.0 (1.0)	**8.1 (0.7)**	**7.9 (0.9)**
RF positive	**7.7 (0.8)**	**8.1 (0.6)**	**8.3 (0.5)**	**7.8 (0.8)**	**7.6 (0.8)**
ACPA positive	**7.8 (0.8)**	**8.6 (0.5)**	**8.2 (0.7)**	**7.5 (0.8)**	**7.4 (0.7)**
Elevated APR	**7.9 (0.7)**	**7.2 (0.7)**	7.0 (0.9)	**8.7 (0.5)**	**7.9 (0.9)**
Bone erosions by Rx	**8.1 (0.8)**	**7.9 (0.6)**	**7.3 (0.8)**	**8.2 (0.5)**	**7.8 (0.8)**
Bone erosions by US	**8.2 (0.9)**	**7.9 (0.7)**	**7.3 (1.0)**	**7.9 (0.8)**	**7.8 (0.8)**

Conclusion: There is agreement among rheumatologists regarding the behaviour of particular drugs on particular prognostic profiles, except in the case of interstitial pulmonary involvement, HAQ, ACPA+ and acute

phase reactants, where there may be differences in the perception of efficacy. This perception of efficacy should be contrasted with scientific evidence

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AB0238 14–3–3H AND CALPROTECTIN PROTEINS IN PLASMA AS NEW BIOMARKERS IN EVALUATION OF THE ACTIVITY IN PATIENT WITH RHEUMATOID ARTHRITIS

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Background: The determination of rheumatoid arthritis (RA) activity remains an important clinical task nowadays and it is a long and difficult process. There is no single approach to assess the activity of RA. The gold standard for evaluating RA activity is composite indexes, for example, DAS28. However, composite indices are not reliable in evaluation of the disease activity in patients with RA, as having a subjectity assessment. New biomarkers that reflect the immune inflammatory process in joints in RA is of great scientific importance. 14-3-3η and calprotectin markers in plasma are considered as promissing.

Objectives: To assess the value of 14-3-3η and calprotectin in plasma as additional markers in RA activity determination.

Methods: 48 patients were examined with reliable diagnosis of RA, according to the ACR 2010 criteria. The mean age was 59 years, mean duration of the disease was 12.8 years. 4 patients in the group were in remission, 2 had low degree of RA activity, 20 - moderate, 22 – high. RA activity was determined according to the DAS28 ESR index. The concentrations of 14-3-3η and calprotectin in the blood plasma were determined by ELISA (LLC «SPF «Abris+»). The obtained results were compared with laboratory (ESR, CRP) and clinical (tender joint count (TJC), swollen joint count (SJC), VAS, DAS28) parameters of RA activity.

Results: 14-3-3η and calprotectin proteins in plasma and ESR highly correlated with DAS28 ($r = 0.84$; $r = 0.65$; $r = 0.53$), while CRP had moderate correlation with RA activity ($r = 0.34$). 14-3-3η and calprotectin proteins had high correlation with TJC ($r = 0.68$; $r = 0.61$) and moderate correlation with SJC ($r = 0.56$; $r = 0.41$); ESR and CRP had weaker correlation ($r = 0.15$; $r = 0.13$; $r = 0.02$; $r = 0.08$) respectively.

The ROC analysis showed that sensitivity, specificity, and diagnostic accuracy of high RA activity determination are significantly higher for 14-3-3η (AUC = 0.98, $p < 0.001$) and calprotectin (AUC = 0.89, $p < 0.001$) than for ESR (AUC = 0.81, $p < 0.001$) and CRP (AUC = 0.72, $p < 0.001$). The proteins 14-3-3η and calprotectin reflect the relationship with the SJC (AUC = 0.89, $p < 0.0001$; AUC = 0.79, $p = 0.002$) with higher diagnostic accuracy, sensitivity and specificity, comparing with ESR (AUC = 0.63, $p = 0.19$) and CRP (AUC = 0.51, $p = 0.88$).

It was also found, that calprotectin (AUC = 0.8, $p < 0.001$) and 14-3-3η (AUC = 0.79, $p < 0.001$) had greater sensitivity and specificity, as well as diagnostic accuracy, in TJC determination, compared with ESR (AUC = 0.57, $p = 0.4$) and CRP (AUC = 0.52, $p = 0.8$). Determining the relationship between biomarkers and the patient's subjective assessment of RA activity (VAS), significant difference between 14-3-3η (AUC = 0.68, $p = 0.06$), calprotectin (AUC = 0.63, $p = 0$, 16), ESR (AUC = 0.64, $p = 0.14$) and CRP (AUC = 056, $p = 0.57$) was not detected.

Conclusion: 14-3-3η and calprotectin proteins in plasma are new promising biomarkers of immunoinflammatory process in joints in RA assessment, because they are more sensitive and specific markers of the disease activity, than conventional acute-phase proteins ESR and CRP.

Disclosure of Interests: None declared

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AB0239 EFFECT OF SMOKING ON THE EFFICACY OF TNF INHIBITORS IN THE TREATMENT OF CHRONIC INFLAMMATORY IMMUNE-MEDIATED DISEASES: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Chronic inflammatory immune-mediated diseases, as rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis (Ps), ankylosing spondylitis (AS), ulcerative colitis (UC) and Crohn's disease (CD), have higher risks of morbidity and mortality and a great impact on quality of life of patients[1]. Drug inhibitors of tumor necrosis factor (TNF inhibitors) have demonstrated an adequate efficacy and security profile in these patients when classical treatments (as disease-modifying antirheumatic drugs) have been failed or patients were intolerant. TNF inhibitors are used to control inflammatory response and to improve quality of life, pain, functional capacity and progression of the disease[2]. Studies in RA show that smoking habit is related to more articular and extra-articular damage, worse prognosis, higher basal activity and higher risk of seropositive RA. It has been related also to greater number of different treatments and higher doses needed for patients by pharmacokinetic and pharmacodynamic processes. Data published until now suggest that smoking habit decreases efficacy of TNF inhibitors[3].

Objectives: To analyze the smoking habit influence on the efficacy of TNF inhibitors in patients diagnosed of chronic inflammatory immune-mediated diseases (RA, PsA, Ps, AS, UC, CD).

Methods: It was made a systematic literature search using Cochrane Library, Medline, the Web of Science and Embase databases. Meta-analyses were performed using a random-effects model.

Results: 37 of 3677 identified articles met the inclusion criteria. No documents with GOL were found. The analysis of all the diseases together gives a significant decrease on the response to TNF inhibitors in smoking patients [OR 0.812 (0.662-0.996), p=0.046]. This response also has a significant decrease in IBD maintained response in smoking patients [OR 0.467 (0.257-0.848), p=0.012]. A non-significant decrease in the treatment response of smoking patients with IBD clinical remission was found, in smoking patients versus ex-smoking and never smoking patients with IBD response, in ex-smoking patients versus never smoking patients with IBD partial response, in current and ex-smoking patients versus never smoking patients with IBD partial response, in current smoking patients versus ex-smoking patients with IBD partial response, in current smoking patients versus never and ex-smoking patients with IBD partial response, in current smoking patients versus never smoking patients with IBD partial response, in patients with AR EULAR and in patients with AR EULAR moderate response.

Conclusion: Smoking habit is a poor prognosis factor in RA, AS, Ps, PsA, UC and CD. Its leaving will decrease cardiovascular risk, joint and bowel damage, will increase the efficacy of TNF inhibitors and will benefit the health of patients, not only in their particular disease, and it can be the first step on their treatment.

REFERENCES:

[1] Gabriel SE. Cardiovascular morbidity and mortality in rheumatoid arthritis. Am J Med 2008;121(10):9-14.

[2] Seymour HE. Anti-TNF agents for rheumatoid arthritis. Br J Clin Pharmacol 2001;51(3):201-8.

[3] Arnson Y. Effects of tobacco smoke on immunity, inflammation and autoimmunity. J Autoimmun 2010;34(3):258-65.

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AB0240 ALCOHOL CONSUMPTION AND DEVELOPMENT OF ARTHRITIS AMONG PATIENTS WITH ANTI-CITRULLINATED PEPTIDE ANTIBODIES AND MUSCULOSKELETAL PAIN

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Background: Individuals with anti-citrullinated peptide antibodies (ACPA) and arthralgia are at increased risk of developing rheumatoid arthritis (RA). Predictors of disease development are important within this category of patients in order to improve treatment and follow-up decisions. Although excessive use of alcohol is well-known to cause harmful medical and social consequences, an inverse association between alcohol consumption and RA development has been proposed. Phosphatidylethanol (PEth) has shown to be a reliable biomarker to measure recent (up to four weeks) alcohol consumption with high specificity.
Objectives: The aim of this study was to, in relation to other possible clinical and laboratory predictors, pinpoint the association between biochemically determined alcohol consumption and development of arthritis in ACPA-positive individuals with musculoskeletal pain.
Methods: The study was performed as part of an observational prospective cohort (TIRx), including 104 ACPA-positive individuals with musculoskeletal pain and maximally one arthritis upon clinical examination. Exclusion criteria were >1 clinical arthritis, previous inflammatory rheumatic disease, and oral or intraarticular corticosteroid treatment within 6 weeks prior to screening. Participants were enrolled between 2010 and 2013 and were carefully followed during 72 months in median (range 23-91). The primary outcome measure was development of arthritis upon clinical examination. In baseline samples, we assessed ACPA levels in serum (2^{nd} generation cyclic citrullinated peptides (CCP) as antigen), rheumatoid factor (RF), and the presence of shared epitope. PEth 16:0/18:1 was measured by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) in whole blood from baseline, and the results were categorized into three groups: no/low, moderate, or high consumption. Cox regression analyses were performed adjusting for smoking, symptom duration, age, sex, shared epitope, RF, and treatment with disease modifying antirheumatic drugs (DMARDs) and oral glucocorticoids.
Results: In TIRx, 82 patients had no swollen joints at inclusion, of whom 39 (48%) developed arthritis during follow-up after median 6 months (range 1-71). Of those, 48 (59%) patients were classified according to PEth values with no/low alcohol consumption, 28 (34%) with moderate consumption and 5 (6%) patients with high alcohol consumption. There was no significant difference in PEth values between patients with one baseline arthritis compared to those without (p=0.09). Neither were there any significant differences in arthritis-free survival across PEth categories versus arthritis development (p=0.64). Unadjusted hazard ratios (HRs) were numerically, but not significantly, increased among moderate (HR 1.22 95% CI 0.63-2.37, p=0.56) and high consumers (HR 1.69 95%CI 0.50-5.68, p=0.40) as compared to those classified as no/low consumers. There was an increased risk of arthritis development regarding RF positivity (adjusted HR 3.13, 95% CI 1.36-7.19, p=0.007) and higher ACPA levels (adjusted HR 1,001 95% CI 1.000-1.001, p<0.001), respectively.
Conclusion: This study does not show a significant association between biochemically assessed recent alcohol consumption and arthritis development in ACPA-positive individuals with musculoskeletal pain. Thus, PEth does not appear to be a clinically useful biomarker to predict disease development in ACPA-positive at-risk populations. Whether it may predict arthritis in a seronegative population remains to be determined. We confirm that RF positivity and ACPA levels associate with arthritis development in an ACPA-positive population.
Disclosure of Interests: Emma Eloff: None declared, Michael Ziegelasch Consultant for: AbbVie, MSD, Pfizer, and BK-Medical, Klara Martinsson: None declared, Jan Cedergren: None declared, Åsa Reckner: None declared, Thomas Skogh: None declared, Louise Karlsson: None declared, Andreas Ärlemalm: None declared, Alf Kastbom Consultant for: Roche and Pfizer, Employee of: Sanofi, Speakers bureau: UCB and BMS
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AB0241 DISEASE COURSE AND COSTS OF A COHORT OF RHEUMATOID ARTHRITIS PATIENTS OVER A PERIOD OF 6 YEARS

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Background: A previous multicenter, cross-sectional study showed a substantial economic burden of rheumatoid arthritis (RA) in Turkey with significant positive correlation between disease severity and total costs (1).
Objectives: To calculate the annual costs and to assess disease activity and functional outcome of RA patients from a single center over a period of 6 years.
Methods: The previous study on healthcare costs in RA was performed in the outpatient clinics of 10 university hospitals between May 2011 and August 2012 (1). A total of 689 RA patients (all fulfilling ACR 1987 criteria) were studied of whom 75 (11%) being from our center. In March 2018, we called back our patients to the clinic for re-evaluation by using the questionnaire of the previous study containing questions on demographics, medication use and RA-related direct and indirect costs. We assessed disease activity with the Routine assessment of Patient Index Data 3 (RAPID3), functional status with HAQ-DI and Steinbrocker functional index and quality of life (QoL) with EuroQol Quality of Life Scale (EQ-5D).
Results: We could interview 62 patients (83%) in the clinic. Of the remaining 13 patients, 7(9%) had died, 3 were receiving palliative care following cardio-vascular events, 2 went to other centers and 1 declined to participate. The mean age and mean disease duration of the 62 re-evaluated patients (52 women, 10 men) were 56.8±13.3 SD years and 225±120 SD months, respectively. Forty-nine (79%) had used at least 1 biologic agent during follow-up and 34 (55%) were still on biologics at the time of re-evaluation. Disease activity was lower but was not significantly different from that of the previous study. However, functional status and QoL had improved significantly over time (Table 1). The majority of the patients (89%) were in Steinbrocker Class 1 or 2 with only 7 (11%) being in Steinbrocker Class 3. Of the 7 deceased patients (4 women 3 men; mean age: 68.2±8.12 SD years; mean disease duration: 127.6±73.8 SD months) 3 were on Rituximab, 2 were on synthetic DMARD's (one being biologic naïve) and 2 were free of RA medications (one was biologic naïve) at the time of death. Serious infections were the cause of death in 4 patients followed by hepatic failure due to hepatitis B, abdominal bleeding under anticoagulation and multi organ failure in 3 patients, respectively. Direct costs were higher than indirect costs and made up two thirds of RA related total costs (Table 1).
Conclusion: Disease activity remained stable and functional status and QoL improved among our patients over 6 years. Biologic usage was increased. Cardiovascular events and serious infections were major determinants of morbidity and mortality. Direct costs were the main determinants of RA related cost.

Table 1:. RAPID 3, HAQ-DI, EQD5 Scores and annual cost

	Previous study (n=62)	Current study (n=62)	*P*
Mean (SD) RAPID3 Score	4.85±1.64	4.36±1.54	0.06
Mean (SD) HAQ-DI Score	1.86±0.59	0.69±0.57	0.001
Mean (SD) EQ-5D Score	0.57±0.21	0.68±0.21	0.003
Annual mean (SD) direct costs (€)	NA*	2262±2227	
Annual mean (SD) indirect costs (€)	NA*	1220±2449	

Results: The survey was replied by 41 rheumatologists, representing all regions in the country. Table 1 shows a summary of the results of the second round in terms of m and SD. To summarize, there was an agreement regarding the drugs that might be more adequate for patients with particular prognostic factors, except in the case of pulmonary involvement, in which agreement was only met for T-cell co-stimulation, and for elevated HAQ and acute phase reactants, where the use of B-cell depressant treatments did not reach an 80% of agreement.
NA*= not available

REFERENCE:

[1] Hamuryudan V, et al. Clin Exp Rheumatol 2016; 34: 1033

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AB0242 RADIOLOGICAL EVALUATION OF FOREFOOT INVOLVEMENT IN RHEUMATOID ARTHRITIS

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Background: Severe and often debilitating involvement of the forefoot is seen frequently in patients with rheumatoid arthritis (RA)

Objectives: We aim to determine the prevalence and the characteristics of radiological forefoot involvement

Methods: Monocentric retrospective study of 52 consecutive patients with RA, hospitalized in the Rheumatology Department between 2012 and 2018. Radiological measurements included the modified Sharp/van der Heijde method (SHS) for the feet and forefoot angles: The angle between the longitudinal bisection of the first metatarsal and the first phalanx of the first finger (Hallux valgus: H1M1$\geq$20°), the intermetatarsal angle between the 1st and 2nd metatarsals (Metatarsus primus varus: M1M2$\geq$ 10°) and the intermetatarsal angle between the 1st and 5th metatarsals (splaying foot: M1M5$\geq$ 35°) measured on antéroposterior radiographs.

Results: The average age was 53 ± 15 years and the sex-ratio was 0.21. The average disease duration was 8 ± 10 years and the average disease activity index DAS28 was 5.65±1.12. The prevalence of forefoot erosion and joint space narrowing were 35% and 58%, respectively. In 85% of patients, both $\geq$1 forefoot erosion score and $\geq$1 forefoot joint space narrowing score were present. Erosions were the most frequent in the 5th metatarsophalangeal joints (MTP) and 1st interphalangeal joint (50% and 47% of eroded joints, respectively) and the least frequent in 4thMTP (27%). The forefoot erosion score was significantly correlated with age, disease duration and hand erosion score and weakly but statistically significantly with titer of ACPA ($p \leq 0.05$). Obesity was an independent protective factor (OR = 0.25; $p < 0.05$) of forefoot erosions. Foot deformities were observed in 71% of the patients; Metatarsus primus varus(MV) (56%), hallux valgus(HV) (38.5%) and splaying foot(SF) (13.5%). The HV was significantly correlated with forefoot damage (erosion score r=0.67, joint space narrowing r=0.7; $p<0.01$), extra-articular manifestations of RA, disease duration and rheumatoid factor titer. Multivariate analysis showed that the extra-articular manifestations was an independent risk factor for HV (OR = 9.39, $p < 0.05$). There was significant correlation between the MV and forefoot damage (erosion score: r=0.4, joint space narrowing: r=0.5, $p<0.05$). There was no correlation between the splaying foot and the forefoot damage. The splaying foot was associated with the hallux valgus (OR = 5.7, p = 0.05).

Conclusion: In our study, forefoot involvement is common in patients with RA and it isn't associated with disease severity. Deformities (HV, MV) are associated with forefoot joint damage and splaying foot is associated with hallux valgus.

REFERENCES:

[1] Baan H, & Drossaers-Bakker w, et al. We should not forget the foot: relations between signs and symptoms, damage, and function in rheumatoid arthritis. Clin Rheumatol (2011) 30:1475–1479

[2] Matsumoto, et al. Radiologic Patterning of Joint Damage to the Foot in Rheumatoid Arthritis. Arthritis Care & Research.2014;66 (4):499–507.

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AB0243 CYSTEINE RICH 61 (CYR61): A POTENTIAL BIOMARKER ASSOCIATED WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Numerous preclinical studies have revealed a critical role of Cysteine rich 61 (Cyr61) in the pathogenesis of rheumatoid arthritis (RA). However, little is known about the potential value of circulation Cyr61 in clinical RA patients.

Objectives: To compare serum Cyr61 level in patients with RA and healthy controls, and to characterize the potential association between Cyr61 and RA disease activity.

Methods: In training cohort, serum samples were obtained from 177 patients with definite RA and 50 age- and gender- matched healthy controls. Medical records were collected and serum Cyr61 concentration was detected by enzyme-linked immunosorbent assay. Correlations between Cyr61 levels with clinical disease activity were analyzed. Furthermore, a validation cohort consisting of 77 active RA patients who received uniform biologic therapy for 12 weeks was set up (ClinicalTrials.gov identifier: NCT02320630). Paired serum samples were collected at baseline and after 12-week treatment for each individual and prepared for detection of Cyr61. Comparisons between groups were made using Mann-Whitney U test or Wilcoxon matched-pairs signed rank test, as appropriate.

Results: Significant elevation of serum Cyr61 concentration was found in RA patients, demonstrating excellent diagnostic ability to discriminate RA with healthy controls (area under the curve (AUC) = 0.98, $P < 0.001$). In training cohort, Cyr61 level in active RA patients was significantly lower than that in inactive RA, and it was inversely with measures of clinical disease activity in statistic. Findings were further confirmed in our validation cohort. Active RA patients who had a reduction in disease activity showed a significantly increase of Cyr61 level after effective treatment (in terms of achieving ACR20/50/70 improvement criteria). RA patients who did not achieve ACR response showed no significant difference of Cyr61 level before and after treatment. Multivariate logistic regression analysis revealed that increase of Cyr61 level as well as younger age were independent indicators for achieving ACR20 response.

Conclusion: Serum Cyr61 levels were remarkably increased in RA patients compared with healthy control. More intriguingly, the level of Cyr61 was inversely associated with RA disease activity and increased after effective treatment.

REFERENCES:

[1] Zhang Q, Wu J, Cao Q, Xiao L, Wang L, He D, et al. A critical role of Cyr61 in interleukin-17-dependent proliferation of fibroblast-like synoviocytes in rheumatoid arthritis. Arthritis & Rheumatism. 2009;60(12):3602-12.

[2] Chen CY, Su CM, Hsu CJ, Huang CC, Wang SW, Liu SC, et al. CCN1 Promotes VEGF Production in Osteoblasts and Induces Endothelial Progenitor Cell Angiogenesis by Inhibiting miR-126 Expression in Rheumatoid Arthritis. J BONE MINER RES. 2017 2017-01-01;32(1):34-45.

[3] Barranco C. CCN1, a novel RA target? NAT REV RHEUMATOL. 2016 2016-08-19;12(10):561.

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Disclosure of Interests: None declared

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AB0244 THE IMPORTANCE OF TREATMENT STRATEGY FOR THE OUTCOME OF EARLY RHEUMATOID ARTHRITIS PATIENTS NOT RESPONDERS TO THE FIRST LINE THERAPY WITH METHOTREXATE

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Background: According to EULAR recommendations for the management of Rheumatoid Arthritis (RA), if the treatment target is not reached with the first conventional synthetic (cs)-disease modifying antirheumatic drugs (DMARDs), addition of another csDMARD or of a biological (b)-DMARD should be considered [1].

Objectives: To evaluate the clinical and radiological outcome under combination therapy of either cs-DMARDs or b-DMARDs in our cohort of early rheumatoid arthritis (ERA) patients treated according to the treat-to-target (T2T) strategy.

Methods: A total of 384 ERA patients with less than 12 months of disease duration (mean age 54.6±14.6 years, 75% female, 73.3% seropositive) were enrolled in the study. ERA patients fulfilled the 2010 ACR criteria for RA and were followed according to the T2T strategy. At baseline, and every three months, the ACR/EULAR core data set variables were recorded. At baseline and every year, hand and foot radiographs were examined according to modified Total Sharp score (mTSS). At each visit, clinical improvement and remission were evaluated according to EULAR criteria. The achievement of Comprehensive Disease Control (CDC) (28-joint Disease Activity Score using C reactive protein <2.6, Health Assessment Questionnaire <0.5 and change from baseline in mTSS ≤0.5) was assessed every year of follow-up (FU). The mean FU duration was 45.5±40.6 months. In patients not reaching the target with methotrexate (MTX) after the 3rd-6th month of FU, the addition of another csDMARD (chloroquine, leflunomide or sulfasalazine) or a bDMARD was considered in order to attain at least a good EULAR response.
Results: At the twelfth month of FU, out of the 174 ERA patients (45.3%) not reaching the target with MTX, 97 (25.3%) were in combination therapy with csDMARDs and 77 (20.1%) were treated with csDMARDs in association with bDMARDs.
Similar percentages of good EULAR response, DAS remission and CDC were registered in the two groups of patients, both at 12th month of FU and at the last FU.
Although not statistically significant, fewer bDMARD treated patients showed 5-year radiographic progression (RP) (21.7%) compared to subjects in csDMARD combination (36.8%, p=0.13).
A higher BMI was observed in ERA patients who started bDMARDs (26.0±4.1) compared to subjects in combination therapy with csDMARDs (24.8±4.2, *p=0.02*).
No differences were founded regarding age and disease duration. Autoantibody positivity was comparable between the two groups.
Conclusion: Our results support data suggesting that the treatment strategy is more important than the therapy used to achieve remission.
In fact, when a strict protocol of tight control is applied, similar clinical and radiological outcome is achieved both in patients treated with csDMARD combination, and in subjects in bDMARD association, regardless of RA prognostic factors.
A higher BMI is associated with a major frequency of bDMARD therapy, underlying a possible more csDMARD refractory disease.

REFERENCES:

[1] Smolen JS et al, Ann Rheum Dis 2017; 76:960-977

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AB0245 PREDICTORS OF BIOLOGIC THERAPY DISCONTINUATION IN RHEUMATOID ARTHRITIS PATIENTS AFTER REMISSION ACHIEVEMENT: A MONOCENTRIC OBSERVATIONAL STUDY FROM BIOLOGIC APULIAN REGISTRY (BIOPURE)

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Background: Thanks to biologic therapies, disease remission in Rheumatoid Arthritis (RA) patients is not a wishful thinking but an achievable goal. Nevertheless, some patients experienced treatment discontinuation after obtaining disease remission. EULAR recommendations suggest to suspend steroids as soon as possible[1], but in real life-setting this point is not always hold in esteem.
Objectives: The objective of our study was to assess the impact of steroids on the long-term drug survival and the possible predictors of drug discontinuation in RA patients who achieved Simplified Disease Activity Index (SDAI) remission at 1-year upon treatment with a first biologic disease modified anti-rheumatic drug (bDMARD).
Methods: Data of RA patients naïve to bDMARDs, registered in Biologic Apulian Registry (BIOPURE) between 1st January 2008 to 31st December 2017, were retrospectively analysed. Demographic and clinical data of all RA patients were acquired at the initiation of first bDMARDs ("screening-time") and after 1-year follow-up ("baseline-time"). The inclusion criterion in this study was the achievement of SDAI remission (SDAI ≤ 3.3) at 1 year of treatment with a first bDMARD. At "baseline-time", RA patients on SDAI remission were divided, according to steroid administration, into concomitant "steroid-no" and "steroid-yes" groups. Drug retention rate and mean survival time (MST) were estimated using Kaplan-Meier (K-M) life-table method. Estimated hazard ratios (HRs) of discontinuing bDMARD were assessed by performing a multivariate Cox-regression analysis with stepwise backward methods.
Results: 216 RA patients started their first bDMARDs between 1st January 2008 to 31st December 2017. Among these, 86 (39.8%) patients achieved SDAI remission at 1-year of whom 54 (62.8%) were steroid free while 32 (37.2%) were still intaking low-dose steroids (mean 3.8 mg/die; SD ±1.4). Considering patients who achieved SDAI remission at "baseline-time", global drug retention was 81.4% [MST=88.5 (95% CI: 80-97) months], higher for "steroid-no" patients [90.7%, MST=98.2 (95% CI: 89-107) months] than "steroid-yes" ones [68.8%, MST=68.9 (95% CI: 57-81) months] (long rank 7.086, p=0.008) (Figure 1). This difference was also seen when drug discontinuation by ineffectiveness was calculated [96.1%, MST=103 (95%CI: 96-110) months vs 72.4%, MST= 70.6 (95%CI 57-84) months, long rank 10.101, p=0.001], but not by adverse events. Moreover, no steroid administration (HR = 0.31, 95% CI:0.10-0.93) and concomitant Methotrexate therapy (HR = 0.34, 95% CI:0.12-0.98) were independently associated with low risk of bDMARDs interruption after the achievement of SDAI remission.
Conclusion: This study provided evidence that, among RA patients who achieved SDAI remission, those who stopped steroids and continued combination therapy with MTX had a very long drug survival with just the first bDMARD in a real-life setting. These results can help rheumatologists to precociously select RA patients who might start a tapering or spacing strategy of biologic drug.

REFERENCE:

[1] Smolen JS, Landewé R, Bijlsma J, Burmester G. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun;76(6):960-977.

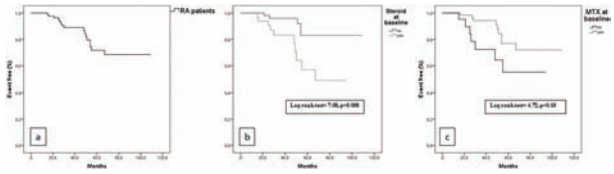


Figure 1. Retention rate on first bDMARD of Rheumatoid Arthritis (RA) patients in remission assessed by Simplified disease activity index (SDAI) after 1 year of follow-up: global population (a), concomitant steroid (b) and concomitant MTX (c).

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AB0246 PREDICTORS OF FATIGUE IN RHEUMATOID ARTHRITIS PATIENTSWHO RECEIVE BIOLOGICAL AND TARGETED SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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Background: Fatigue is one of the most frequent symptoms in patients with rheumatoid arthritis (RA), affecting more than 80% of them. Despite

being a very disabling symptom, the variables that predict it are still unknown.

Objectives: To identify potential factors associated with fatigue.

Methods: Cross-sectional study. 60 patients were included, patients were being followed up in the rheumatology outpatient clinic of Hospital Clínico San Carlos, Madrid, Spain. Data were collected between July 2018 and January 2019. All patients met the ACR/EULAR 2010 criteria and they were in treatment with Biological agents or Targeted Synthetic DMARDs. **Main variable:** Fatigue was assessed by the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ) and the Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS). **Covariables:** Sociodemographic, clinical, Disease-related variables and treatment. **Statistical analysis.** A descriptive analysis was carried out for the different variables. To identify factors independently associated to BRAF-MDQ a multivariable linear regression was applied. Results were expressed as β with their corresponding 95% CI. A value of $p < 0.05$ was accepted as statistically significant.

Results: A total of 60 patients, comprising of 53 females (88%) and 7 males (12%) with a mean age of 56.45±11.89 years and mean disease duration of 14.11±7.79 years were evaluated. RF was positive in 60% of patients. 65% of the patients were in active on work and 23% were retired. Regarding comorbidities, 43% had dyslipidemia, 42% hypertension, 17% hypothyroidism and 15% depression. The DAS28-ESR and SDAI scores of the patients were 2.68 ± 0.86, 8.56 ± 5.96 respectively. The rest of the clinical, treatment characteristics, and the scores of the fatigue instruments used in the study are shown in **Table 1**. Physical dimension was the most affected according to patients, who perceive an average severity and affectation, and insufficient coping. The factors affecting the total BRAF-MDQ was evaluated in multivariate analyze **Table 2.** We found that patients with Disability ($p < 0.0001$) and those in treatment with Non anti-TNF (p 0.048), experienced more fatigue while a positive RF (p 0.022) decreases overall fatigue.

Conclusion: Fatigue is a substantial symptom in RA patients and should be evaluated on the daily clinical practice. The results of our study indicated that disability and type of treatment were the dominant factors in the experience and degree of fatigue. Disease activity (DAS28 and SDAI) was not associated to fatigue. The evaluation and management of fatigue should be one of the objectives in the treatment of patients with RA

Table 1. Characteristics of the sample

Variable	Descriptive statistics
Glucocorticoids mg/day, mean ± SD	4.86 ± 1.65
Treatment, n (%)	47 (78.33)
Conventional DMARDs	40 (66.67)
Anti TNF	16 (26.67)
Non-Anti TNF	4 (6.67)
Synthetic target DMARD (Jakinibs).	
HAQ (0-3) mean ± SD	0,86 ± 7,7
VAS pain mean ± SD	39.3 ± 24.27
Sleep quality self-report, n (%)	23 (39.66)
Good	35 (60.34)
Poor	
BRAF-MDQ (0-70), **mean ± SD**	21.95 ± 15.01
Physical (0-22)	10.6 ± 5.49
Living (0-21)	5.08 ± 5.04
Cognitive (0-15)	3.3 ± 3.38
Emotional (0-12)	2.96 ± 2.75
BRAF-NRS, mean ± SD	
Fatigue severity (0-10)	4.75 ± 2.33
Effect of fatigue (0-10)	4.8 ± 2.43
Coping with fatigue (0-10)	3.73 ± 2.29

Table 2. Multivariate analyses of Total-BRAF-MDQ

Total BRAF	Coef.	Std. Err.	t	p	IC 95%
Age	-0.041	0.141	-0.29	0.769	-0.325 0.242
Sex	-6.933	4.985	-1.39	0.170	-16.938 3.071
FR positive	-9.589	3.467	-2.77	0.008	-16.546 - 2.631
Non Anti-TNF	7.348	3.621	2.03	0.048	0.082 14.614
HAQ >1.1	15.863	3.290	4.82	0.000	9.259 22.467

Disclosure of Interests: None declared

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AB0247

INSIGHTS INTO ADHERENCE AND PATIENT-INITIATED MONOTHERAPY FOR RHEUMATOID ARTHRITIS VIA A GLOBAL SURVEY OF PATIENTS, CAREGIVERS AND PHYSICIANS

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Background: Treatment satisfaction and adherence remain issues affecting outcomes for patients (pts) with rheumatoid arthritis (RA). A better understanding of the reasons for non-adherence, and differences between pt, caregiver and healthcare professional (HCP) views on adherence, may improve decision-making and outcomes.

Objectives: To survey pts, caregivers and HCPs, in order to investigate pt behaviours and attitudes, and communications between pts, caregivers and HCPs regarding adherence to RA therapy.

Methods: Surveys were conducted online by Harris Poll between Oct and Nov 2018, among pts/caregivers and HCPs from Australia, Brazil, Canada, Germany, Japan, Spain, Taiwan, UK and US. The pt survey included pts aged ≥18 years with a diagnosis of RA who had taken conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) with biological (b)DMARDs in the past 3 years. The caregiver survey included adults aged ≥18 years who lived with/provided care to a spouse/family member with RA and were involved in ≥2 care activities for a pt with RA who had taken csDMARDs with bDMARDs in the past 3 years. The HCP survey included responses from licensed rheumatologists (orthopaedists in Japan) who saw ≥10 pts with moderate/severe RA per month, ≥10% of whom had been prescribed a bDMARD. A post-weight was applied to raw data to adjust for the relative adult population size of each country vs the total for all 9 countries surveyed.

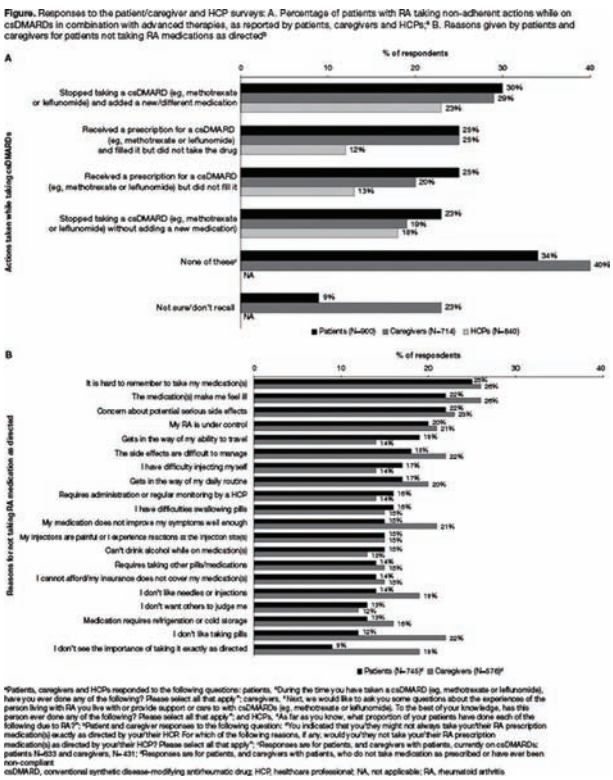


Figure 1

Results: In total, 900 pts, 714 caregivers and 840 HCPs responded to the surveys. Overall, 50% of both pts and caregivers reported that pts always took their current RA prescription medications exactly as directed. However, 67% of pts reported that they had not always adhered to dosing regimens (most common deviations: skipping doses [45%]; extending time between doses [44%]; taking other medications without HCP direction [38%]; taking less than the prescribed dose [34%]; dose splitting [31%]; and stopping medications altogether [28%]). Among HCP

respondents, 98% reported asking pts about adherence to RA medication, even though 61% felt there was no way of knowing if pts were taking medications as prescribed and, overall, HCPs responded that 64% of pts did not always take RA medication as prescribed. While 87% of HCPs agreed that bDMARDs were most effective when taken in combination with csDMARDs and 92% reiterated this to pts, 62% were concerned that pts take bDMARDs without csDMARDs. Pts and caregivers reported that pts often stopped taking csDMARDs; however, HCPs underestimated the number of non-adherent pts (Figure A). The most common reason given by pts and caregivers for non–adherence to RA medication was difficulty in remembering to take medication; however, concerns about feeling ill and potential side effects were also common (Figure B). Despite this, 47% of pts and 51% of caregivers responded that pts often don't share all side effects caused by their RA medication with HCPs, while 38% of HCPs believed that pts did not inform them of all side effects.

Conclusion: This study from a large, multinational cohort of pts with RA, caregivers and HCPs describes medication adherence patterns. Pts on bDMARDs often did not take their background csDMARDs; however, the extent of pt non-adherence was underestimated by HCPs. These results highlight gaps in communication and understanding of non-adherence between pts, caregivers and HCPs.

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AB0248 DISEASE ACTIVITY IS ASSOCIATED WITH FATIGUE IN THE FOLLOW-UP OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Chronic fatigue negatively impacts on quality of life in Rheumatoid Arthritis (RA) patients (1,2), does not allow optimal clinical results, being an negative predictor for clinical remission (3,4).

Objectives: The objective was to determine whether disease activity correlates with increased fatigue in the follow-up of a RA patients.

Methods: Prospective study of the RA-Almenara cohort (criteria ACR87/ ACR-EULAR2010). Patients were included with at least two evaluations (half-yearly). Patients with fibromyalgia, major depression and/or anxious depressive disorder, chronic neuropathic pain or active systemic manifestations (including interstitial lung disease) were excluded. Disease activity was evaluated with SDAI (Simple Disease Activity Index) and fatigue with FACIT questionnaire (Functional Assessment of Chronic Illness Therapy-fatigue). A generalized estimation equation model was used to determine the association between SDAI and FACIT, at each visit according with two models of analyses. Model 1 considered SDAI value as a linear variable; Model 2 considered each category of SDAI (high, moderate and low) activity, using remission as reference. Multivariable analyses were adjusted by possible confounders: gender, age at diagnosis, instruction, socio-economic level (Graffar), disease duration, tobacco, ACPA level, disability (MDHAQ), use of conventional (c) and biologic(b) DMARDs and corticosteroids (current use, past or non-use).

Results: Four hundred and twenty patients were included, 372 (88.6%) women, age at diagnosis was 44.1 (13.2) years, disease duration 17.7 (11.6) years. At the baseline 4.2% 13.6%, 41.0% and 41.2% were in remission, low, moderate and high activity respectively; 40% were using corticosteroids, 256 (61%) cDMARDs and 25 (6%) bDMARDs. Basal SDAI was 23.7 (20.4) and FACIT 17.2 (8.8). We analyzed 1233 follow up visits [2.2 (1.2) visits per patient]. Multivariablee analysis: In model 1 were associated with FACIT: SDAI [B: -0.03 (IC95%: - 0.06- -0.01;p=0.013] and MHAQ [B: -9.55 (IC95%: - 10.55- -0.54), p = <0.001]. In model 2, were associated with FACIT: the categories high [B: -4.92 (IC95%: -6.87 – -2.7); p <0.001], moderate [B: -3.75 (IC95% : -5.70- -1.89), p <0.001] and low [B: -2.22 (95% CI: - 4.05- -0.39); p = 0.018] disease activity by SDAI, in addition with MHAQ [B: -9.11 (IC95%: - 10.11- -8.11), p <0.001] and tobacco use [B: -3.37 (95% CI: - 6.56- -0.18, p = 0.039)]

Conclusions: Higher disease activity correlates with worse fatigue scores, at each follow-up visits of patients with RA

REFERENCE:

[1] Balsamo. Isr. Med. Assoc. J. 2014, 16, 57–60. 2. Alomari. Sci. World J. 2012:580863. doi: 10.1100/2012/580863. 3. Roodenrijs. Ann Rheum Dis. 2018 Sep 7. pii: annrheumdis-2018-213687. 4 Uhlig. J Rheumatol. 2016;43(4):716–23

Disclosure of Interests: None declared

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AB0249 EFFECT OF RF AND ACPA NEGATIVATION IN CLINICAL RESPONSE IN RA PATIENTS UNDER BIOLOGIC THERAPY

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Background: Both rheumatoid factor (RF) and antibodies against cyclic citrullinated peptide (ACPA) are regarded as serological markers of Rheumatoid Arthritis (RA), being well recognized as diagnostic and prognostic tools. However, their potential role in the disease's monitoring and clinical response is still under debate.

Objectives: To assess the effect of RF and ACPA negativation in clinical response to biologic therapy in RA patients.

Methods: Longitudinal retrospective study of RA patients treated with biologic therapy as first line option. Demographic and clinical data were collected at baseline and at 24 months follow-up, including: RF and ACPA status (negative or positive), ESR, CRP, DAS28 4v ESR, CDAI, SDAI, HAQ, EULAR and ACR response. RF was considered positive if $\geq$ 30 U/ml and ACPA if $\geq$ 7 U/ml. SPSS statistics 22.0 was used for statistical analysis.

Results: 169 patients were included with mean (±SD) age of 50.7 ± 10.6 years and median disease duration (min-max) of 10.2 (0.69-39.4) years. The majority were female (84%). At baseline 160 (94.7%) were positive for RF and 166 (98.2%) were positive for ACPA. 77 (45.6%) turned negative for RF and/or ACPA at a median time of 20.3 months after biologic therapy begining. 63 out of 169 patients become negative for RF (37.3%) and 17 patients for ACPA (10.1%). 52 (30.6%) patients were treated with etanercept, 39 (22.9%) adalimumab, 27 (15.9%) rituximab, 19 (11.2%) tocilizumab; 16 infliximab (9.4%); 14 (8.2%) golimumab; 1 (0.6%) certolizumab and 1 (0.6%) anakinra. The mechanism of action of the drug didn't differ between patients who became seronegative for RF and/or ACPA and those who remained seropositive (70.2% under anti-TNFα agents vs 73.9% for the other biologics). Most of the patients in the first group began adalimumab (32.5%) and most of the patients in the latter began etanercept (34.8%). Demographic characteristics like age, sex, disease duration, and extraarticular manifestations were comparable in both groups. They weren't comparable in terms of smoking habits (p=0.014): just 3 (3.9%) current smokers in those who became negative for RF and/or ACPA vs 17 (18.5%) among those who remained seropositive. Nevertheless, there weren't statistically significant differences in ΔDAS28 4v ESR, ΔERS, ΔCRP, ΔCDAI, ΔSDAI, ΔHAQ, EULAR or ACR response at 24-months between patients with negativation of at least one antibody and those who remained seropositive.

Conclusion: In our sample, change of antibody status wasn't predictor of better response to biologic therapy. Therefore the results did not support the association between the persistence of RF or ACPA and the lack of effectiveness of biologic therapy at 2 years of treatment, but further studies are needed.

REFERENCE:

[1] Alexandra B. et al. Prospective cohort study of effects of infliximab on rheumatoid factor, anti-cyclic citrullinated peptide antibodies and antinuclear antibodies in patients with long-standing rheumatoid arthritis; Joint Bone Spine 76 (2009) 248e253.

Disclosure of Interests: None declared

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AB0250

REAL-WORLD OUTCOMES IN STABLE ORIGINATOR BIOLOGIC-TREATED ADULT PATIENTS WHO STAYED ON THE THERAPY VERSUS THOSE WHO SWITCHED TO BIOSIMILAR: A RETROSPECTIVE CHART REVIEW STUDY IN EUROPE

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Background: Biologic therapies have considerably improved clinical management of autoimmune diseases. Over the past few years, several biosimilars have been introduced in Europe for these conditions. Limited information is available evaluating the impact of switching stable patients from originators to their respective biosimilars in clinical practice for non-medical reasons.

Objectives: This real-world study reported and compared patient characteristics, clinical outcomes, and healthcare resource utilization (HRU) associated with stable patients who switched from the originator biologic etanercept to its biosimilar (switchers) vs. those who stayed on the originator (non-switchers) in adults with a rheumatic condition such as ankylosing spondylitis (AS), psoriatic arthritis (PsA), or rheumatoid arthritis (RA).

Methods: Medical record data were retrospectively collected anonymously from rheumatologists in the UK and Germany. Adult patients who were diagnosed with RA, AS, or PsA, treated with originator etanercept for at least 6 months with a stable dosing schedule, and had no emergency department visit or hospitalization for the disease of interest over the 6-month period were eligible for the study. The index date for a non-switcher was the prescription date closest to one year after the initiation of originator etanercept and with a stable dosing for at least 6 months. The index date for a switcher was the biosimilar initiation date. Chart data available for at least 12 months prior to and post the index date were required. Patient characteristics, disease severity, symptoms and signs, and HRU were extracted anonymously. Unadjusted and adjusted comparisons of the outcomes between non-switchers and switchers were conducted among all patients and for each individual disease.

Results: Data were extracted from 242 patient records (non-switchers = 123, 50.8%; switchers = 119, 49.2%; AS=26.4%; PsA=26.0%; RA=47.5%) from 162 rheumatologists. At baseline, non-switchers were significantly younger than switchers (44.5 vs. 48.4 years, p<0.05), had a significantly shorter time on the originator etanercept (11.7 vs. 23.8 months), and more patients had been treated with NSAIDS (55.3% vs. 37.8%). Significantly more non-switchers had moderate, or severe disease (27.6% vs 16.0%, p<0.05; 26.8% vs 5.9%, p<0.01) and non-switchers on average had worse joint or spine pain (4.4 vs 2.4, p <0.01) than switchers. During the follow-up period, significantly more non-switchers' disease status improved (58.5% vs. 25.2%. p<0.01), resulting comparable disease severity (moderate: 10.6% vs 10.9%; severe: 0% vs 0%) and joint or spine pain scale (2.0 vs 1.0) between the two cohorts. After adjusting for potential confounding factors, compared to switchers, more AS and PsA non-switchers improved in disease severity (AS: p<0.05; PsA: p<0.01), and RA non-switchers had a fewer number of swollen joints (0.5 vs 1.5, p<0.01). Non-switchers generally had numerically lower HRU than switchers during the one-year follow-up period (patients with outpatient visits: 76.4% vs 89.1%; average number of outpatient visits: 1.8 vs 2.0).

Conclusion: When compared with stable patients who underwent non-medical switching, stable patients who continued therapy with the originator biologic demonstrated significantly more improvement in disease severity. Other outcomes such as HRU appeared more similar between patients who underwent non-medical switching and patients who continued therapy with the originator biologic. The value of biosimilar non-medical switching requires continued evaluation in real-world clinical practice.

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AB0251

ASSESSMENT OF CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS AND ITS RELATION WITH LEPTIN AND INTERLEUKIN-6

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Background: In rheumatoid arthritis patients the risk of cardiovascular affection is 2–3 times higher than the general population (Hollan, Meroni et al. 2013), with increased morbidity and mortality(Perles, Sánchez et al. 2013). This is due to increase in the traditional and nontraditional risk factor(Skeoch and Bruce 2015).

Objectives: The aim of this study is to determine the cardiovascular risk in patients with RA using four established CV risk algorithms Framingham Risk Score (FRS), Systematic Coronary Risk Evaluation Score (SCORE], Reynolds Risk Score (RRS), Q II Risk Score and there relation with serum levels of leptin and interleukin-6 (IL-6).

Methods: Sixty seven RA patients were enrolled in this study. The 10-year CVR for RA patients were calculated using FRS, SCORE, RRS and Q II Risk Score. Serum leptin and IL-6 were estimated.

Results: The results showed a significant difference between higher leptin values and disease activity, obesity, positive RF and longer disease duration, On the other hand, we found a significant difference between higher IL-6 values and disease activity, and hypertriglyceridemia.

As regarding correlations of IL-6 and Leptin with different cardiovascular scores, there were no significant correlations with exception of moderate significant correlation between IL-6 and RRS (r= 0.42, *P*< 0.001).

Conclusion: New models of CVD risk prediction incorporating RA specific variables or imaging techniques are needed.

Table 1. Relationship between serum leptin levels and cardiovascular risk factors

Variables	Serum concentrations of leptin (ng/ml)		*P*
	Yes	No	
Age > 40 years	25.25 (2.50- 160)	9.8 (2.7- 116)	0.05
Body mass index> 30 kg/m^2	39.1 (2.50- 160)	18.15 (3- 116)	**0.02**
Diabetes mellitus	28.40 (10.60- 120)	20.30 (2.50- 160)	0.29
Hypertension	28.40 (4- 120)	19.3 (2.50- 160)	0.26
Cholesterol ≥ 200 mg/dl	31.75 (8.60- 98.50)	18.10 (2.50- 160)	0.05
LDL ≥ 130 mg/dl	28.75 (2.70- 98.50)	18.8 (2.50- 160)	0.34
HDL*	28.40 (28.40- 160)	20.30 (2.50- 160)	0.83
Triglyceride≥ 150 mg/dl	30.1 (6.60- 120)	18.8 (2.50- 160)	0.06
DAS-28 ESR > 2.3	31.20 (2.70- 160)	18.8 (2.50- 130)	**0.04**
Duration of illness > 10 year	31.50 (2.70- 130)	17 (2.50- 160)	**0.04**
Positive RF	25.70 (2.70- 160)	18.95 (2.50- 120)	**0.03**

Table 2. Relationship between IL- 6 levels and cardiovascular risk factors

Variables	Serum concentrations of IL- 6		*P*
	> 5 pg/ml (n= 37)	< 5 pg/ml (n= 30)	
Age > 40 years	31 (83.8%)	19 (63.3%)	0.05
Body mass index> 30 kg/m^2	24 (64.9%)	22 (73.3%)	0.31
Diabetes mellitus	4 (10.8%)	3 (10%)	0.61
Hypertension	9 (24.3%)	8 (26.7%)	0.52
Cholesterol ≥ 200 mg/dl	12 (32.4%)	4 (13.3%)	0.06
LDL ≥ 130 mg/dl	9 (24.3%)	5 (16.7%)	0.32
HDL*	12 (32.4%)	13 (43.3%)	0.83
Triglyceride≥ 150 mg/dl	12 (32.4%)	2 (6.7%)	**0.02**
DAS-28 ESR> 2.3	28 (75.7%)	13 (43.3%)	**<0.001**
Duration of illness > 10 year	14 (37.8%)	16 (53.3%)	0.15
Positive RF	18 (48.6%)	18 (60)	0.25

REFERENCES:

[1] Hollan, I., P. L. Meroni, J. M. Ahearn, J. C. Tervaert, S. Curran, C. S. Goodyear, K. A. Hestad, B. Kahaleh, M. Riggio and K. Shields (2013). "Cardiovascular disease in autoimmune rheumatic diseases." Autoimmunity reviews 12(10): 1004-1015.

[2] Perles, C. M., J. A. Sánchez, B. García-Magallón and C. S. Gómez (2013). "Artritis reumatoide (II)." Medicine-Programa de Formación Médica Continuada Acreditado 11(30): 1850-1855.

[3] Skeoch, S. and I. N. Bruce (2015). "Atherosclerosis in rheumatoid arthritis: is it all about inflammation?" Nature Reviews Rheumatology 11(7): 390.

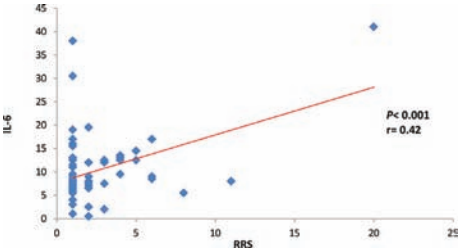


Figure 1. Correlation of RRS with IL-6

Disclosure of Interests: None declared
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AB0252 RACIAL DISPARITIES IN OUTCOMES FOR PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING TOTAL KNEE OR TOTAL HIP ARTHROPLASTY

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Background: Race is linked to delays in healthcare. Black and Hispanic patients with osteoarthritis have worse pain and function than Whites before arthroplasty. Whether Black and Hispanic patients with RA similarly delay care is unknown.
Objectives: To assess whether Black and/or Hispanic (minority) RA patients have worse pain, function and disease activity at the time of arthroplasty.
Methods: We used prospectively acquired data on RA patients between 10/2013 and 11/2018 prior to total knee arthroplasty (TKA) or total hip arthroplasty (THA). Pain, function, and disease activity were assessed using the visual analogue scale (VAS), the Multidimensional Health Assessment Questionnaire (MD HAQ), and the Disease Activity Score (DAS28). Race, ethnicity, education, income, insurance and medications were collected via self-report questionnaire. Multivariable linear and logistic models examined whether minority status predicted pain, function and disease activity.
Results: 37 (23%) of the 164 patients were minorities (Table 1). MD HAQ and DAS28 were worse in minorities, only VAS was significant (p-value= 0.029). There was no significant difference in education. Unadjusted comparisons indicated no difference in pain, function, disease activity or medication use between groups. Insurance varied significantly between groups (p= <0.0001). In the multivariable analyses (Table 2), minority status was not significantly associated with worse function (MD HAQ) [p=0.26], disease activity (DAS28-ESR) [p=0.658], or VAS pain [p=0.18]. Increased age was significantly associated with better function (p=0.004).
Conclusion: For Black and/or Hispanics with RA undergoing THA or TKA at a high-volume specialty hospital, minority status was not significantly associated with pain, disability or RA disease activity at the time of elective arthroplasty.
Disclosure of Interests: Julianna Hirsch: None declared, Bella Mehta: None declared, Jackie Finik: None declared, Serene Mirza: None declared, Mark Figgie: None declared, Collin Brantner: None declared, Iris Navarro-Millan: None declared, Susan Goodman Grant/research support from: Novartis: research support, Consultant for: Novartis, UCB, Pfizer: consulting
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Table 1. Cohort

	Overall (N=164)	Minority* (N=37)	Non-minority (N=127)	p-value
Age, years, median [IQR]	62.5 [54.7, 71.2]	56.8 [51.0, 68.8]	64.0 [55.1, 71.5]	0.063
VAS Pain Score, median [IQR]	**6.0 [4.0, 8.0]**	**7.5 [4.0, 8.0]**	**6.0 [4.0, 8.0]**	**0.029**
MD HAQ Score, mean ± SD	11.8 ± 5.3	12.3 ± 5.1	11.6 ± 5.3	0.528
DAS28, mean ± SD	3.8 ± 1.3	4.1 ± 1.3	3.8 ± 1.2	0.181
Sex				
Males	22 (13.41%)	3 (8.11%)	19 (15.08%)	0.412
Education				
Graduated HS	18 (11.76%)	4 (12.90%)	14 (11.48%)	0.762
Some college or above	135 (88.24%)	27 (87.10%)	108 (88.52%)	
Insurance				
Commercial	**54 (33.13%)**	**9 (29.03%)**	**45 (41.28%)**	**<0.001**
Medicare	77 (47.24%)	13 (41.94%)	64 (58.72%)	
Medicaid	9 (5.52%)	9 (29.03%)	0 (0.0%)	
N/A	23 (14.11%)	6 (16.22%)	17 (13.49%)	
Biologics				
Yes	90 (55.56%)	23 (62.16%)	67 (53.60%)	0.452

*Minority status: Black or African American, Hispanic or Mixed.
IQR: Interquartile Range
VAS: Visual Analogue Scale
MD HAQ: Multidimensional Health Assessment Questionnaire
DAS28: Disease Activity Score28
HS: High School

Table 2. Multivariable analysis to determine the risk of DAS28, VAS Pain Score, and MD HAQ Score (Generalized Logistic Model)

	DAS28-ESR Odds ratio (95% CI)	VAS Pain Score β ± SE	MD HAQ Score β ± SE
Minority (Yes)	1.29 (0.41, 4.05)	0.87 ± 0.66	1.44 ± 1.27
Education (Some college +)	**9.57 (2.17, 42.21)**	0.12 ± 0.77	-0.24 ± 1.49
Medicaid*	4.30 (0.28, 66.69)	-0.13 ± 1.37	-2.60 ± 2.66
Medicare*	1.48 (0.49, 4.45)	0.22 ± 0.67	2.31 ± 1.28
Age	0.97 (0.92, 1.02)	0.02 ± 0.03	**-0.17 ± 0.06**
Sex (Female)	2.35 (0.74, 7.49)	0.16 ± 0.70	0.26 ± 1.37
Biologics (Yes)	0.64 (0.27, 1.48)	0.81 ± 0.50	0.13 ± 0.97
MD HAQ Score	**1.09 (1.00, 1.17)**	**0.17 ± 0.05**	

*Ref: Commercial
Significant variables in bold

AB0253 BIOMARKERS OF CLINICAL RESPONSE TO IL6-R BLOCKADE IN DMARDS INCOMPLETE RESPONDERS (AR-BIOM TRIAL): IL23 AND BAFF AS BIOLOGICAL TARGETS, AND ALBUMIN AS BIOLOGICAL PREDICTOR

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Background: The therapeutic algorithm in persistently active Rheumatoid Arthritis, despite conventional synthetic DMARDs(csDMARDs), identifies TNFα blockers and other biologics as first line treatment, without clear indications of which biologic should be adopted first in persistently active patients.
Objectives: In the AR-BIOM trial we analyzed several biomarkers to define which one could help to identify the best responder to IL6-R blockade.
Methods: Sixty-nine RA persistently active despite csDMARDs treatment, were enrolled in this Interventional Phase IV, prospective, multicenter, non-randomized, no-profit study(Clinical Trial:n.2012-001760-30) and followed for 18 months after Tocilizumab(TCZ) treatment monotherapy or in combination with csDMARDs. The study was conducted in 10 outpatient clinics of "Gruppo Italiano di Studio sulle Early Arthritis" network(GISEA Study Group) in Italy. The primary end point was the clinical response to TCZ, as LDA(DAS<2.4) at 12 months follow-up(FU), correlated with Matrix 1 (pathway of Innate inflammation:IL-8,MCP1,Chemerin) vs Matrix 2(Pathway of IL1/IL6/TH17:IL1α,IL1β,IL17,IL23) along with the Pathway of regulatory T cells activity(IL-10,BAFF) and acute phase reactants (Albumin, Fibrinogen,CRP,ESR) as biomarkers of interest. DAS and SDAI remission were secondary end-points at 12 and 18 months FU. A ROC analysis of soluble biomarkers was performed to obtain thresholds allowing the prediction of DAS-remission or LDA at 12 months FU. A multivariate logistic analysis, in which "LDA or DAS/SDAI remission at 12 months FU" were the dependent variables, was performed.
Results: During the 18 months of the study, 9/69 patients(13.0%) discontinued the study because of treatment failure, 2(2.9%) for an AE, 2 for a SAE, and 5(7.2%) for other reasons. At 12 months FU, LDA was achieved in 75.0% and DAS-R and SDAI-R in 63.3% and 41.7%

respectively, of RA patients, without significant differences between mono and combination therapy. Considering baseline biomarkers predictive of LDA at 12 months FU, IL23 plasma levels ≥43.6pg/ml arose as potent predictor [OR(95%CIs):20.0(1.9-211.2)], whereas the best predictors of DAS-R were baseline BAFF plasma levels ≥563.3pg/ml [OR(95%CIs):3.9 (1.1-14.3)] and IL23 plasma levels ≥43.6pg/ml [OR(95%CIs):4.1(1.1-15.2)]. In addition, Albumin levels ≥4.25g/dl at 3 months FU, arose as a biochemical parameter predicting DAS-R [OR(95%CIs):26.0(3.9-173.1)] and SDAI-R [OR(95%CIs):5.3(1.2-22.9)] at 12 months FU.

Conclusion: IL23 and BAFF related inflammation are targets of IL6 blockade that significantly increases Albumin levels. High plasma levels of IL23 and BAFF at baseline represent biomarkers for LDA and DAS-R achievement in RA inflammation driven by IL6. Albumin after three months of therapy represents the strongest predictor of remission at 12 months.

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AB0254 NEUTROPHIL-LYMPHOCYTE RATIO AND PLATELET-LYMPHOCYTE RATIO IN PATIENTSRECEIVING ANTIRHEUMATIC THERAPY: RELATIONSHIP TO CLINICAL AND LABORATORY MARKERS OF DISEASE ACTIVITY

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Background: The use of antirheumatic drugs is key to limit or prevent inflammation and joint damage in rheumatoid arthritis (RA). Recently, neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) has been considered markers of clinical activity in RA[1], however its relationship with serological and clinical parameters in patients receiving disease modifying drugs (DMARDs) therapy has been poorly evaluated.

Objectives: To analyze the association of NLR and PLR with serological and clinical parameters related to the clinical prognosis in RA patients with antirheumatic treatment.

Methods: A cross-sectional study was carried out in 150 women with RA (mean age of 45.5 years, and mean duration of disease of 8 years) all diagnosed according to ACR/EULAR 2010 criteria and receiving DMARDs and corticosteroids (Cs) therapy. The clinical features and DAS-28 score were analyzed by a rheumatologist professional. The NLR and PLR, as well as the e*rythrocyte sedimentation rate* (ESR), high sensitivity C reactive protein (hsCRP) levels, rheumatoid factor (RF) and anti-cyclic citrullinated peptides (anti-CCPs) antibodies, were determined in the laboratory.

Results: The medical schemes prescribed commonly were: Methotrexate (MTX) monotherapy and MTX combination with chloroquine, sulfasalazine, leflunomide and Cs. The NLR was correlated with DAS28-ESR and DAS28-hsCRP scores. The values of NLR >2.2 (percent neutrophil/percent lymphocyte) were associated with hsCRP >12 mg/L (OR=2.45, p=0.036), DAS28-hsCRP >5.1 (OR=2.69, p=0.07) and with anti-CCPs-positive (>5 U/mL) (OR=1.57, p=0.41). While, PLR >10.4 (platelet count×10^3/mm^3/percent lymphocyte) was too associated (OR=3.72, p=0.004; OR=2.51, p=0.08; OR=2.96, p=0.07, respectively). Serological autoantibodies, when was considered in combination, the anti-CCPs/RF-positive patients showed a higher correlation between NLR and PLR with the parameters of clinical activity [tender joints count (r=0.19, p=0.036; r=0.16, p=0.07), swollen joints count (r=0.15, p=0.08; r=0.14, p=0.11) and DAS28-hsCRP score (r=0.16, p=0.06; r=0.17, p=0.05)], however this correlation was higher in anti-CCPs-positive but RF-negative patients. In addition, was observed that patients with DMARDs combination and a greater number of drugs had increased NLR and PLR.

Conclusion: NLR and PLR could be considered markers for the evaluation of the clinical course and response to therapy DMARDs in RA patients.

REFERENCE

[1] Sargin G, Senturk T, Yavasoglu I, et al. Relationship between neutrophil-lymphocyte, platelet-lymphocyte ratio and disease activity in rheumatoid arthritis treated with rituximab. Int J Rheum Dis. 2018. doi.org/10.1111/1756-185X.13400

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AB0255 CLINICO- BIOLOGICALPROFILE OF RHEUMATOID ARTHRITIS WITH PERIODONTITIS AND PORPHYROMONAS GINGIVALIS

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Background: The Periodontitis (PD) is currently recognized as a risk factor of occurrence of the rheumatoid arthritis(RA). The porphyromonas gingivalis (P.gingivalis) figure among the main germs incriminated in the occurrence of the PD. Previous studies have shown that antibodies to P. gingivalis are associated with anti-CCP antibody in patients with RA. However others studies have not demonstrated this association.

Objectives: The aim of this study was to seek for a possible association between clinico-biological parameters of the RA and the presence of the P.gingivalis.

Methods: We conducted a prospective study of 69 patients with early rheumatoid arthritis (≤2 years), naive of biotherapy. Smokers, diabetics, and subjects who received dental care and those who used antibiotics in the previous 6 months were not included. Periodontal status, demographic, clinical activity, and anticyclic citrullinated peptide antibodies (anti-CCP) parameters were determined. The P. gingivalis has been searched in patients with a PD. We sought to investigate an association between Rheumatoid disease activity (DAS28), anticyclic citrullinated peptide antibodies (anti-CCP) and P.gingivalis.

Results: The mean age of our patients was 40.75 ± 12.04, the mean duration of the illness was 14.30±6.76 months (extremes: 1-24 months). ACPA was detected in 88% of patients and the mean titre was 255.57±409.78.

43% of patients have presented a PD. The P.gingivalis has been detected in 59% of PD. The means DAS28 of patient with and without P.gingivalis is respectively 4.40±1.32 and 4.15±1.45, and there was no significant difference (p=0.65). There was also no association observed between anti CCP and the presence of P.gingivalis(the mean titre of anti CCP was 249.47±294.58 with P.gingivalis and 258.67 ±93.48 without P.gingivalis, p= 0.74).

Conclusion: This study showed that periodontitis is frequent in rheumatoid arthritis. More than half of our patients suffering of periodontitis were infected by porphyromonas gingivalis. Rheumatoid disease activity does not seem to be related to porphyromonas gingivalis. In addition therewas no association between anti-CCP antibody and the presence of porphyromonas gingivalis.

REFERENCES

[1] Johansson L, Sherina N, Kharlamova N, Potempa B, Larsson B, Israelsson L, Potempa J, Rantapää-Dahlqvist S, Lundberg K. Concentration of antibodies against *Porphyromonas gingivalis* is increased before the onset of symptoms of rheumatoid arthritis. Arthritis Research 18: 201.

[2] Bello-Gualtero JM, Lafaurie GI, Hoyos LX et al. Periodontal Disease in Individuals With a Genetic Risk of Developing Arthritis and EarlyRheumatoid Arthritis: A Cross-Sectional Study. J Periodontol. 2016;87(4):346-56.

[3] Fisher BA, Cartwright AJ, Quirke AM, de Pablo P, Romaguera D, Panico S et al. Smoking, *Porphyromonas gingivalis* and the immune response to citrullinated autoantigens before the clinical onset of rheumatoid arthritis in a Southern European nested case-control study. BMC Musculoskelet Disord. 2015;16:331.

[4] Cheng Z, Meade J, Mankia K, Emery P, Devine DA. Periodontal disease and periodontal bacteria as triggers for rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2017;31(1):19-30.

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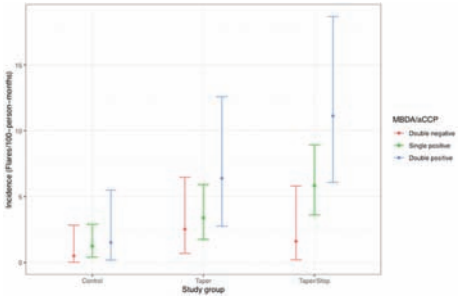
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AB0256

PREDICTION OF DISEASE RELAPSES BY MULTIBIOMARKER DISEASE ACTIVITY SCORE AND AUTOANTIBODY STATUS IN RA PATIENTS TAPERING DMARD TREATMENT – AN UPDATE OF THE RETRO STUDY

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Background: Achieving remission is the ultimate treatment goal in patients with rheumatoid arthritis (RA). With the development and wider use of highly effective disease modifying anti-rheumatic drugs (DMARD) about half of RA patients reach the disease remission state (1), raising the question about tapering or stopping anti-rheumatic treatment and appropriate predictors (2).
Objectives: The purpose was to analyze the effect of multi-biomarker disease activity (MBDA) score and anti-citrullinated protein (ACPA) on relapse rates in RA patients in sustained remission enrolled in the prospective randomized controlled RETRO study (3,4,5).
Methods: MBDA scores and ACPA status were determined in the baseline samples of patients in sustained DAS28-ESR remission fulfilling RETRO inclusion criteria. Patients were unblended and either continued DMARDs (Control), tapered dose by 50% (Taper) or stopped DMARDs after tapering (Taper/Stop) for one year according to the RETRO study protocol. MBDA and ACPA status were used as relapse predictors. Relapse was defined as the loss of a DAS28-ESR remission. We calculated incidence of flares and 95% Poisson confidence intervals by baseline ACPA and MBDA status in each study group (double negative, single positive, double positive). We compared the risk of flare in the treatment arms with a Cox regression model and calculated hazard ratios (HR) and 95% confidence interval (CI) for relapses.
Results: Serum samples and follow-up data of 203 patients included in the RETRO trial were analyzed. A flare was observed in 8/59 patients (13.6%) in the Control group, 24/60 (40.0%) patients in the Taper group and 37/68 (54.4%) patients in the Taper/Stop group among the 187 patients that completed their 1-year follow-up. HR (95%CI) for a relapse was 3.43 (1.54-7.66) in the taper group and 5.32 (2.47-11.46) for the control group. HR of flare of a positive MBDA and ACPA was 4.00 (1.72-9.31) compared to a negative MBDA and ACPA. Flare incidence did not differ with baseline MBDA/ACPA status in the control group, whereas in the taper/stop group, number of positive biomarkers could identify three distinct subgroups with a graded incidence of flare (Figure).



Conclusion: Tapering or stopping DMARDs after stable remission was associated with an increased risk of RA flares. Incidence of flares in ACPA/MBDA double-negative patients after tapering and stopping RA treatment was comparable to those that continued treatment within the precision limits of our subgroups. Lack of blinding is a shortcoming of our study.

REFERENCES

[1] Aga AB et al. Ann Rheum Dis. 2013;74:381-8.
[2] Schett G et al. Ann Rheum Dis. 2016 Aug;75(8):1428-373.
[3] Haschka J et al, Ann Rheum Dis. 2016;75:45-51.
[4] Rech J et al, Ann Rheum Dis. 2015; Oct 19.
[5] Hagen M et al, J Rheum. 2018

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AB0257

FATIGUE LEVELS PREDICT OTHER PATIENT REPORTED OUTCOMES AND DISEASE ACTIVITY SCORES: RESULTS FROM A LONGITUDINAL STUDY OF RA PATIENTS INITIATING BDMARD THERAPY

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Background: Fatigue is a sensation of weakness and lack of energy which is common in patients with rheumatoid arthritis (RA), contributing to reduced quality of life. However, there are few studies on the longitudinal influence of fatigue on patient reported outcome measures (PROMs).
Objectives: The present study explores the impact of fatigue on PROMs, clinical, laboratory and ultrasound (US) assessments.
Methods: A total of 208 patients with established RA (mean (SD) age 53 (13) years, disease duration 10 (9) years, 81% women, 79% anti-CCP positive) were examined when initiating bDMARDs and assessed at baseline and after 1, 2, 3, 6 and 12 months, including fatigue (0-10, as part of the RAID score), PROMs (joint pain VAS, patient's global disease activity VAS (PGA), MHAQ, pain catastrophizing (PC), SF-36 Mental Health scale score (SF36MH)), clinical examinations (performed by a study nurse including examiner's global disease activity VAS (EGA), 28 tender and swollen joint counts (TJC, SJC)) and laboratory variables (ESR and CRP). US examinations (semi-quantitative scoring (0-3)) of grey scale (GS) and power Doppler (PD) were performed of 36 joints and 4 tendons by one rheumatologist (HBH; Siemens Acuson Antares, excellence version, 5-13 MHz probe). The clinical disease activity scores (CDAS) DAS28, CDAI and SDAI were calculated for all visits. Correlations were assessed by Spearman's rho. The predictive value of baseline fatigue on several dependent variables (PROMs, CDAS, clinical assessments) at all visits after baseline was explored by use of multiple linear regression analysis with adjustment for demographic values (age, sex and disease duration) and baseline inflammatory activity (CRP and sum score GS).
Results: Fatigue levels diminished during follow-up (baseline median (IQR) 5 (3-7), 12 months 2 (1-5)). Table 1 shows the high cross-sectional correlations between fatigue and PROMs/CDAS scores, low correlations with EGA/SJC/CRP and lack of correlations with US assessments. Baseline fatigue predicted PROMs and CDAS scores at all examinations (table 2). No/low associations were found between baseline fatigue and SJC/EGA/sum score PD at follow-up.
Conclusion: Fatigue was highly correlated with PROMS and composite scores at all timepoints. The level of baseline fatigue predicted PROMs and composite scores at follow-up, but not objective inflammatory measures. Thus, the degree of fatigue should be taken into account when composite scores are used for evaluation of inflammatory activity in established RA patients.

Table 1.

Table 1.
Cross-sectional correlations between fatigue and several variables (Spearman's rho) at all visits *p<0.05, **p<0.001

	Baseline n=208	1 month n=208	2 months n=204	3 months n=197	6 months n=183	12 months n=152
Patient's global VAS	0.72**	0.73**	0.69**	0.70**	0.74**	0.67**
Joint pain VAS	0.64**	0.69**	0.63**	0.62**	0.67**	0.49**
MHAQ	0.63**	0.59**	0.53**	0.51**	0.57**	0.47**
SF36 Mental Health scale score	-0.57**	-0.66**	-0.54**	-0.56**	-0.55**	-0.52**
Pain catastrophizing	0.58**	0.61**	0.53**	0.49**	0.46**	0.45**
DAS28	0.60**	0.56**	0.44**	0.45**	0.51**	0.38**
CDAI	0.56**	0.52**	0.46**	0.47**	0.52**	0.41**
SDAI	0.56**	0.52**	0.45**	0.47**	0.51**	0.41**
28 tender joint count	0.47**	0.50**	0.40**	0.46**	0.47**	0.32**
Assessor's global VAS	0.31**	0.29**	0.26**	0.29**	0.32**	0.21*
28 swollen joint count	0.20*	0.12	0.12	0.05	0.11	0.01
CRP	0.14*	0.11	0.11	0.10	0.18*	0.08
Sum score GS	0.00	0.01	0.00	0.01	0.04	0.04
Sum score PD	0.02	0.02	0.01	0.01	0.04	0.04

Table 2.

Table 2.
The predictive value of baseline fatigue on PROMs, CDAS and clinical scores at follow-up, adjusted for age, sex, disease duration, baseline CRP and baseline sum score GS, and given as the standardized regression coefficient (β) and partial R square.

	1 month	2 months	3 months	6 months	12 months
Patient's global VAS	β=0.57, R=0.34**	β=0.53, R=0.29**	β=0.45, R=0.21**	β=0.50, R=0.26**	β=0.47, R=0.23**
Joint pain VAS	β=0.54, R=0.30**	β=0.46, R=0.22**	β=0.41, R=0.18**	β=0.47, R=0.22**	β=0.42, R=0.18**
MHAQ	β=0.50, R=0.27**	β=0.15, R=0.02*	β=0.34, R=0.16**	β=0.43, R=0.21**	β=0.46, R=0.23**
SF36 Mental Health scale score	β=-0.45, R=-0.30**	β=-0.45, R=-0.30**	β=-0.46, R=-0.21**	β =-0.52, R=-0.26**	β =-0.47, R=-0.22**
Pain catastrophizing	β=0.54, R=0.30**	β=0.52, R=0.26**	β=0.49, R=0.23**	β=0.40, R=0.15**	β=0.39, R=0.15**
DAS28	β=0.42, R=0.24**	β=0.36, R=0.16**	β =0.40, R=0.19**	β=0.38, R=0.18**	β=0.31, R=0.11**
CDAI	β=0.36, R=0.17**	β=0.32, R=0.12**	β=0.35, R=0.14**	β=0.33, R=0.13**	β=0.25, R=0.07**
SDAI	β=0.35, R=0.17**	β=0.30, R=0.12**	β=0.33, R=0.14**	β=0.33, R=0.13**	β=0.24, R=0.07*
28 tender joint count	β=0.41, R=0.18**	β=0.35, R=0.13**	β=0.39, R=0.15**	β=0.37, R=0.14**	β=0.27, R=0.07*
Assessor's global VAS	β=0.18, R=0.04*	NS	β=0.18, R=0.04*	β=0.20, R=0.06*	NS
28 swollen joint count	NS	NS	NS	NS	NS
Sum score PD	NS	NS	NS	NS	NS

NS=Not Significant, *p<0.05, **p<0.001

Disclosure of Interests: Hilde Berner Hammer Grant/research support from: AbbVie, Pfizer and Roche, Paid instructor for: AbbVie, Pfizer, UCB, Novartis, Roche, Speakers bureau: AbbVie, Pfizer, UCB, Novartis, Roche, Brigitte Michelsen Grant/research support from: Unrestricted grant: Novartis, Consultant for: Novartis, UCB, Sella Aarrestad Provan Consultant for: Novartis, Speakers bureau: Lilly, Till Uhlig Consultant for: Grünenthal, Novartis, Speakers bureau: Grünenthal, Novartis, Tore K. Kvien Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB., Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB
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AB0258 POTENTIAL ROLE OF MEAN PLATELET VOLUME AND RED BLOOD CELL DISTRIBUTION WIDTH AS A BIOMARKER FOR CLINICAL AND SONOGRAPHIC ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Red cell distribution width (RDW) reflects the variation in the circulating erythrocytes size (anisocytosis) that can increase in chronic inflammation due to ineffective erythropoiesis [1], while mean platelet volume (MPV) reveals the average size of platelets and may disclose its activation. Both are typically included in the complete blood count (CBC) and have been studied as a possible indicator of disease activity in many inflammatory conditions [2].
Objectives: This study aimed to assess the relationship between MPV and RDW levels and various rheumatoid arthritis (RA) clinical,laboratory and ultrasongraphic disease activity parameters in patients with recent onset RA before and after initiation of therapy.
Methods: We assessed MPV and RDW in blood samples obtained from 60 recent onset RA patients and 30 healthy controls at baseline and 4 months after initiation therapy with non-biological disease modifying anti-rheumatic drugs (DMARDS). Disease activity was calculated using the 28 joint counts (DAS28) and musculoskeletal ultrasound examination (MSUS) was performed at baseline and after 4 months using a 12-joint score (bilateral elbow, wrist, 2nd metacarpophalangeal (MCP), 3rd MCP, knee, ankle) [2]; Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, rheumatoid factor (RF) titre and anti-cyclic citrullinated peptide (anti-CCP) antibodies titre were measured and the health assessment questionnaire (HAQ) score was documented.
Results: Baseline RDW was significantly increased in RA (15.16 ± 3.63%) compared to its level in the healthy controls (12.16 ± 1.43%) (p<0.001). While, there was no significant difference in MPV between RA and control groups (10.92 ± 2.02 fl and 10.08 ± 0.88 fl respectively) (p=0.2). In RA patients, baseline RDW significantly correlated with CRP(r=0.39, p<0.05), DAS28 (r=0.47, p<0.05), grey scale (GS) (r=0.53, p<0.05) and power Doppler (PD) (r=0.56, p<0.001) synovitis scores. Also, RDW at 4 months follow up significantly correlated with the DAS28 (**r** =0.42, p<0.05), GS score (r=0.45, p<0.05). MPV showed no significant correlation with clinical, laboratory and ultrasonographic parameter of RA disease activity. Baseline RDW (p =0.02) was shown to be comparable to ESR (p =0.03) but less than CRP (p =0.001) at predicting PD synovitis score.
Conclusion: Rheumatoid arthritis patients have significantly increased RDW levels that remarkably correlated with clinical, laboratory and MSUS parameters of inflammations suggesting that it could be a useful marker to reflect RA disease activity. RDW could be a useful biomarker to predict treatment outcome in RA patient. In this regard, MPV had poor correlations.

REFERENCES

[1] Aksoy ŞN, Savaş E, Sucu M, Kisacik B, Kul S, Zengin O. Association between red cell distribution width and disease activity in patients with Behçet's disease. J Int Med Res. 2015 Dec;43(6):765-73.
[2] Tecer D, Sezgin M, Kanık A, İncel NA, Çimen ÖB, Biçer A, Şahin G. Can mean platelet volume and red blood cell distribution width show disease activity in rheumatoid arthritis?. Biomark Med. 2016 Sep; 10(9):967-74.
[3] Naredo E, Rodríguez M, Campos C, Rodríguez-Heredia JM, Medina JA, Giner E, et al. Validity, reproducibility, and responsiveness of a twelve-joint simplified power Doppler ultrasonographic assessment of joint inflammation in rheumatoid arthritis. Arthritis Rheum 2008;59(4):515–22.

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AB0259 FOUR COMORBIDITY INDEXES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Previous studies have reported an increased risk of multiple comorbidities in people with RA therefore it is necessary to systematically quantify the comorbidity burden of these patients.[1] The comorbidity index is a tool developed under this concept and has multiple clinical and research uses.
Objectives: We compared four comorbidity indexes and mortality rate in patients with rheumatoid arthritis in Taiwan (Charlson Comorbidity Index (CCI), Elixhauser Comorbidity Index (ECI), Mutimorbidity index (MMI), Rheumatic Disease Comorbidity Index (RDCI))
Methods: All patients with rheumatoid arthritis diagnosed during 1998-2008 in Taiwan were identified using the Taiwan National Health Insurance Database and followed up to 31 Dec 2013. One-year mortality rate and 5-year mortality rate were compared using CCI, ECI, MMI and RDCI. High risk group for each index was defined as around the top 20% patients. A discrimination analysis was performed to compare the predictive ability of the model against the base model using the change of Harrell's c-statistics and the Akaike information criterion (AIC).
Results: Among 24767 patients with rheumatoid arthritis, median age at diagnosis is 51 years old and female is 79.2%. The one-year and 5-year mortality rate (per 1000 people) is 41 vs. 177 in CCI, 43 vs. 135 in ECI, 43 vs. 169 in MMI, 43 vs. 159 in RDCI. (Low risk group vs. high risk group) The one-year and 5-year mortality rates all are higher in the high risk group compared with low risk group using four comorbidity indexes. The 5-year mortality rate rises up rapidly both in low risk group and high risk group using four comorbidity indexes. The discrimination analysis showed MMI predicted one-year and 5-year mortality best. (Harrell's c-statistics 0.796 in one-year mortality and 0.802 in 5-year mortality) ECI, MMI and RDCI are all good at predicting mortality as well.
Conclusion: Our study showed mortality rate increased in patients after rheumatoid arthritis was diagnosed. All four comorbidity index score during diagnostic period predicted one-year and 5-year mortality rate well both in high risk and low risk group. Clinicians should screen different comorbidities, determine primary prevention and control disease activity to improve the functional status, quality of life and mortality of rheumatoid arthritis, especially in the patients with initial high comorbidity index scores.

REFERENCE

[1] Baillet, A., et al., *Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative*. Ann Rheum Dis, 2016. 75(6): p. 965-73.

Table 1. 1-year and 5-year mortality analysis for four comorbidity indexes.

	Mortality rate (per 1000 people)	
Comorbidity indexes	**1-year**	**5-year**
CCI		
Low risk (0-1)	**3**	**41**
High Risk (>1)	**23**	**177**
ECI		
Low risk (0-3)	**4**	**43**
High Risk (>3)	**15**	**135**
MMI		
Low risk (0-1)	**4**	**43**
High Risk (>1)	**19**	**169**
RDCI		
Low risk (0-2)	**4**	**43**
High Risk (>2)	**18**	**159**

High risk group for each index was defined as around the top 20% patients.

Table 2. The four comorbidity indexes discrimination for 1- and 5-year survival in patients with RA.

Models	1-year mortality		5-year mortality	
	Harrell's c-statistics	AIC	Harrell's c-statistics	AIC
Base model	**0.744**	**1868**	**0.777**	**10281**
Base model+ CCI	**0.796**	**1783**	**0.802**	**9879**
Base model+ ECI	**0.772**	**1829**	**0.793**	**10024**
Base model+ MMI	**0.779**	**1821**	**0.792**	**10038**
Base model+ RDCI	**0.773**	**1817**	**0.791**	**10048**

Base model included age, gender, income quartiles, urbanization and occupation groups. The Harrell's c-statistic indicates model prediction as the followings: 0.5 (as well as chance), 0.7–0.8 (acceptable), 0.8–0.9 (excellent), and 0.9–1 (outstanding prediction). The AIC statistic was calculated, and a small AIC indicates better prediction of the model.

Disclosure of Interests: None declared

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AB0260 TREATMENT WITH BIOTECHNOLOGICAL DRUGS ACCORDING TO PRE-DEFINED SELECTION CRITERIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: PRELIMINARY RESULTS OF A SINGLE COHORT

IACONO DANIELA, Ilenia Pantano, Serena Fasano, Giuseppe Scalise, Francesco Ciccia. *University of Campania Luigi Vanvitelli, Rheumatology, Naples, Italy*

Background: Current recommendations on the treatment of Rheumatoid Arthritis (RA) are based on a treat to target approach, nevertheless which biologic drug should be used in an unresponsive patient is not clarified (1). Such a strategy is essentially justified by the fact that no biotechnological drug has proved to be superior to any other (2).

Recent studies have reported some disease or patient features that are associated with a greater or lesser likelihood of response (3). Nevertheless, an adapted therapy to the single patient and based on physiopathological mechanisms has not been acquired yet.

Objectives: Aim of this study was to evaluate if the choice of a tailored therapy, based on patient and disease features, would be an effective strategy.

Methods: From April 1st 2017, at our Department of Rheumatology of the University of Campania, each patient with RA has been characterized, at enrolment, for demographic and disease features, and started a biological Disease-modifying antirheumatic drug based on an established algorithm **(Figure 1)**. Attainment of the targeted end point i.e. remission (R) as assessed by Simplified Disease Activity Index (SDAI) <3.3 or at least low disease activity (LDA), SDAI<11, has been evaluated at 3, 6 and 12 months.

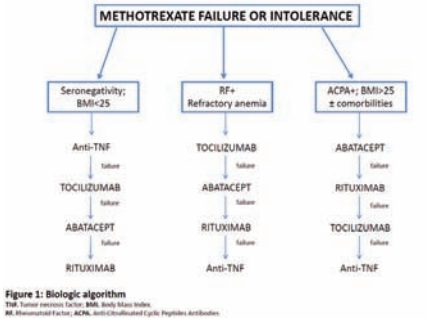


Figure 1: Biologic algorithm

Figure 1

Results: Forty-nine patients were admitted to our centre from April 1st2017 to December 31st2018. Out of them, 36 patients have been followed up at least for 3 months and were included in the study (algorithm+ patients). Out of them, 26 (72.2%) reached 6 months of treatment, while 16 (44.4%) 12 months of treatment. Among the 26 patients evaluated at 6 months, 23(88.5%) achieved the targeted end point. At 12 months, 16/16 patients (100%) preserved a status of remission or at least low disease activity. We compared our results to those registered, from January 2015 to September 2016, in a RA cohort of 79 patients (RA general cohort). We found a significant difference in regard to attainment of the target at 6 months (23/26 patients, 88.5% algorithm+ vs 45/67 patients, 67.2% RA general cohort; p=0.04) and at 12 months (16/16 patients, 100% algorithm+ vs 40/57 patients, 70.2% RA general cohort; p=0.01) **(Table 1)**. Notably, 32 out of the 79 patients had undergone a biological drug which didn't follow the predefined algorithm. These patients (algorithm- patients) presented a further lower incidence of response with regard to those enrolled according to the algorithm: 22/32 patients (68.7%) at 3 months; p=0.4; 17/29 (58.6%) at 6 months; p=0.001; 17/24 (70.8%) at 12 months; p=0.03).

Conclusion: The choice of a personalized approach toward treatment of RA might be an effective strategy to achieve the targeted end point of remission or at least low disease activity in every patient.

REFERENCES

[1] Smolen JS et al. Ann Rheum Dis 2017;76:960–77
[2] Pierreisnard A et al. Joint Bone Spine. 2013;80:386-92.
[3] Daïen CI et al. Mediators of Inflammation 2014;2014:386148

Table 1. Comparison of percentage of response between Algorithm + patients (n.36) and RA general cohort (n.79)

	Algorithm+ patients	RA general cohort	p
LDA/R 3 months	28/36 (77.7%)	51/76 (67.1%)	0.25
LDA/R 6 months	23/26 (88.5%)	45/67 (67.2%)	0.04
LDA/R 12 months	16/16 (100%)	40/57 (70.2%)	0.01

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AB0261 TARGET SETTING OF FUNCTIONAL REMISSION FOR HAND AND WRIST SURGERIES USING GRIP POWER AND PATIENT-REPORTED OUTCOME MEASURES IN PATIENTS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE COHORT STUDY

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Background: The treatment aim of rheumatoid arthritis (RA) is achieving and maintaining functional remission via tight medical control. However, if adequate medication is not administered in the very early stage of the disease, surgical reconstruction for the structurally damaged hand and wrist is sometimes required.

Objectives: To evaluate the effect of surgical treatment of the hand and wrist**(1)** and to set the target of functional remission using grip power and patient-reported outcome measures (PROs) at baseline.

Methods: A prospective observational cohort study was performed in RA patients who were scheduled to have primary hand and/or wrist surgeries. Assessments were performed at baseline and 12 months after surgery using grip power (GP), pain visual analogue scale (pain VAS), general health (GH), disease activity score 28- C-reactive protein(4) (DAS28-CRP (4)), disabilities of the arm, shoulder and hand (DASH), European quality of life scale with five dimensions (EQ-5D), Beck depression inventory -II (BDI-II) and health assessment questionnaire- disability index (HAQ-DI) for all registered patients. Baseline data for each item in the group with HAQ remission (HAQ-DI≤0.5) at 12 months (REM) were compared with those in the group without remission at 12 months (non-REM).

Results: There were 137 sites (63 hands, 74 wrists) in 119 patients whose average age was 62 (19-88) years and average disease duration was 14 (1-45) years. Overall, the physical function (GP, pain VAS, DASH, HAQ-DI), quality of life (HAQ-DI, GH, EQ-5D), depression (BDI-II) and disease activity (DAS28-CRP(4)) had significantly improved at 12 months (p<0.01) **(Table 1)**. In the REM group (n=47), the GP and EQ-5D were significantly higher (p<0.01) and the HAQ-DI, DASH and BDI-II significantly lower (p<0.01) than in the non-REM group **(Table 2)**. The cut-off value at baseline for achieving HAQ remission at 12 months after surgery was 119 mmHg (sensitivity: 0.70, specificity: 0.64) in GP, 0.81 (0.81, 0.77) in HAQ-DI, 36.9 (0.74, 0.73) in DASH, 0.69 (0.87, 0.74) in EQ-5D and 9.5 (0.72, 0.60) in BDI-II.

Abstract Table 1. Changes in the GP and each PRO (n=119)

item	Baseline	12 months after op.	P
GP (mmHg)	125.6	139.2	0.009
Pain VAS (mm)	32.3	20.1	1E-07
GH (mm)	35.2	24.1	4.6E-07
DAS28-CRP(4)	3.1	2.2	3.1E-15
DASH	42.1	35.1	6E-05
EQ-5D	0.72	0.76	0.0005
BDI-II	13.4	11.9	0.008
HAQ-DI	1.07	0.91	0.0021

Abstract Table 2. Baseline value in the REM group (n=47) and the non-REM group (n=72)

item	REM	Non-REM	P
GP (mmHg)	151	109	8.35E-05
DASH	26.1	52.2	1.54E-11
EQ-5D	0.80	0.66	3.51E-09
BDI-II	10.1	15.5	0.0011
HAQ-DI	0.5	1.4	7.19E-14

Conclusion: GP and other four PROs were validated as good objective tools for assessing the physical function after hand and wrist surgeries. It would be helpful for rheumatologists to consider the timing of surgery in RA patients based on the cut-offs determined in this study[(2)].

REFERENCES

[1] Ishikawa H. The latest treatment strategy for the rheumatoid hand deformity. J Orthop Sci. 2017; 22: 583-592.

[2] Kojima T, Ishikawa H, Tanaka S, et al. Target setting for lower limb joint surgery using the timed up and go test in patients with rheumatoid arthritis: A prospective cohort study. Int J Rheum Dis. 2018; 21: 1801-1808.

In the other items, there was not a significant difference between two groups

Disclosure of Interests: Hajime Ishikawa: None declared, Asami Abe: None declared, Toshihisa Kojima: None declared, Masayo Kojima: None declared, Yoichi Kurosawa: None declared, Eriko Hasegawa: None declared, Satoshi Ito Speakers bureau: Mitsubishi Tanabe Pharma Corporation., Naoki Ishiguro: None declared, Akira Murasawa: None declared

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AB0262

SERUM CALPROTECTIN AS A MARKER OF DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Calprotectin is a heterodimeric complex of S100A8 and S100A9 calcium-binding proteins. Stored in the cytosol of granulocytes, it is released under cell stress and acts as an endogenous damage-associated pattern molecule. In contrast to C-reactive protein (CRP), it is not an acute phase protein. Serum calprotectin levels correlate with disease activity of several inflammatory rheumatic diseases.

Objectives: To investigate association of serum calprotectin with clinical activity in rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA).

Methods: We performed retrospective analysis of patients with RA, axSpA and PsA from the Swiss Clinical Quality Management (SCQM) registry. Age- and sex-matched asymptomatic first-degree relatives of RA patient without sign of autoimmunity were used as healthy controls (HC, n=72). Serum calprotectin was measured by ELISA (Inova Diagnostics, research use only). Calprotectin levels were categorized into quartiles for each disease. Clinical outcomes included swollen joint count (SJC), CDAI, HAQ and ultrasound power Doppler (USPD) score for RA patients; BASDAI, BASFI and ASDAS for axSpA; SJC and DAPSA for PsA. Comparison of outcomes by calprotectin quartile levels was performed using Kruskal-Wallis tests for continuous outcomes or trend tests for categorical. We used multivariable regression models to compare association of CRP and calprotectin with USPD. Proportions of explained variances were estimated using R^2.

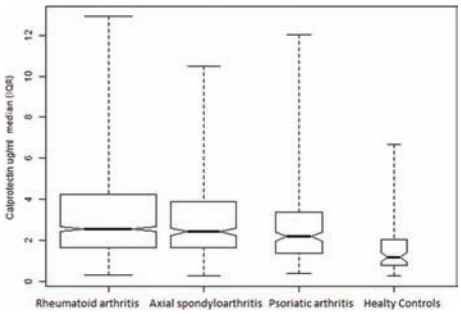


Figure: Serum calprotectin level by diagnosis

Results: 1729 subjects [RA=969, axSpA=451, PsA=237 and HC=72] were included. 209 RA patients had an ultrasound performed at time of blood collection. Median levels of serum calprotectin were higher in each disease compared to HC (p<0.01; Figure). In RA, all clinical scores were statistically different across quartiles indicating an association between calprotectin levels and higher disease activity (SJC, CDAI) and severity (HAQ) (Table). In univariable regression models, both CRP (R^2=0.02, p=0.04) and calprotectin (R^2=0.10, p<0.001) were associated with USPD scores. Multivariable model analysis revealed that calprotectin alone was as predictive of USPD scores as calprotectin and CRP together (likelihood ratio test between models p=0.14). In axSpA, an association between level of calprotectin and ASDAS score (p<0.01) was observed. For PsA, SJC, DAPSA and CRP did not differ across calprotectin quartiles.

Table: Clinical outcomes by calprotectin quartile levels. * Results are mean (SD) except for those with an asterisk which represent median (IQR):

Calprotectin quartiles [µg/ml]	**1**	**2**	**3**	**4**	**p**
RA quartiles (n)	**[0-1.7] (243)**	**[1.7-2.6] (242)**	**[2.6-4.3] (242)**	**[4.3-13] (242)**	
SJC	1.3 (2.5)	1.7 (2.8)	2.2 (3.3)	3.4 (4.5)	<0.001
HAQ	0.6 (0.6)	0.8 (0.7)	0.8 (0.7)	1.0 (0.7)	<0.001
CDAI	7.3 (7.9)	9.8 (9.9)	11.2 (11.7)	12.3 (13.4)	0.002
USPD	2.2 (5.9)	2.0 (4.0)	2.0 (3.0)	4.7 (6.1)	0.01
CRP mg/l*	2.0 [1.0,4.6]	2.0 [1.0,7.0]	2.2 [1.0,7.0]	4.2 [2.0,12.0]	<0.001
AxSpA quartiles (n)	**[0-1.6] (113)**	**[1.6-2.4] (113)**	**[2.4-3.9] (112)**	**[3.9-13] (113)**	
BASDAI	3.6 (2.3)	4.0 (2.4)	3.5 (2.4)	4.1 (2.3)	0.2
BASFI	2.1 (2.3)	2.7 (2.6)	2.3 (2.3)	2.8 (2.5)	0.2
ASDAS	2.1 (0.9)	2.4 (1.0)	2.2 (1.1)	2.7 (1.0)	0.01
CRP mg/l*	3.0 [1.0,8.0]	2.0 [1.0,8.0]	3.0 [1.0,8.0]	4.0 [2.0,13.0]	0.002
PsA quartiles (n)	**[0-1.4] (60)**	**[1.4-2.2] (59)**	**[2.2-3.4] (59)**	**[3.4-12] (59)**	
SJC	1.8 (4.5)	1.3 (2.5)	1.1 (2.5)	2.2 (4.4)	0.3
DAPSA	18.2 (23.5)	15.6 (17.5)	18.4 (16.8)	21.1 (24.2)	0.8
CRP mg/l *	2.2 [1.0,8.0]	2.0 [1.0,5.5]	4.0 [1.9,7.0]	3.9 [1.8,7.8]	0.2

Conclusion: This large study supports the association of serum calprotectin levels with disease activity and severity in RA and shows an association between serum calprotectin and ASDAS in axSpA.

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AB0263 **ASSOCIATED FACTORS OF RESIDUAL SYMPTOMS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN REMISSION OR LOW DISEASE ACTIVITY**

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Background: Treatment outcomes for rheumatoid arthritis (RA) have been improved by advances in drugs. In daily clinical practice, treatment outcomes are assessed with both inflammatory findings and based on swollen joints (SJ), tender joints (TJ), a patient's global assessment on visual analogue scale (GVAS) score, a physician's GVAS score, etc. Although composite measures indicate suppressed inflammatory or articular symptoms, many patients show no improvement in GVAS scores. The reported residual symptoms include morning stiffness (MS), pain (P), and dullness (D).
Objectives: We investigated the residual symptoms of patients achieving low disease activity (LDA) or complete remission (CR).
Methods: His study included 111 RA patients who received outpatient treatment at our department (31 men and 80 women). The mean age was 65.1 (range, 27–89) years. The disease stages were distributed as follows: 36 patients with Stage 1, 23 patients with Stage 2, 20 patients with Stage 3, and 32 patients with Stage 4. The severity of dysfunction was distributed as follows: Class 1 in 73 patients, Class 2 in 25 patients, Class 3 in 11 patients, and Class 4 in 2 patients (Steinbrocker classification). Based on the disease activity score in 28 joints using the erythrocyte sedimentation rate, disease activity was graded as CR in 54 patients, LDA in 19, moderate disease activity in 37, and high disease activity in 1. Questionnaire forms were used to assess the presence or absence and duration of MS and the presence or absence and severity of P (Pain VAS) and of D (Dullness VAS). These variables were assessed to determine how they were associated with clinical outcome measures, drugs, and surgery.
Results: The following residual symptoms were observed in 73 patients who achieved the treatment target of LDA or CR: MS in 34 patients (46.6%), P in 48 (65.6%), and D in 38 (52.8%). In the LDA+CR group, the Pain VAS ($P < 0.001$, $r = 0.612$) and Dullness VAS ($P = 0.0131$, $r = 0.193$) were significantly correlated with the GVAS. In patients with P in the LDA+CR group, the use rates for analgesics ($P = 0.0047$) and biological disease-modifying antirheumatic drugs (bDMARDs) ($P = 0.0295$) were significantly higher. In the LDA+CR group, Dullness VAS scores were significantly improved by the use of bDMARDs ($P = 0.0074$). No association was observed between surgical interventions (42 patients) and residual symptoms.
Conclusion: Residual symptoms were frequently observed even in patients achieving LDA or CR, which is regarded as the treatment target. Because P and D were significantly correlated with the GVAS, relief of these residual symptoms is expected to improve treatment effects. Although D was relieved by bDMARDs, further studies on the treatment of residual P in patients achieving LDA or CR are necessary.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.4049

AB0264 **THE EXTENT OF JOINT DESTRUCTION IN THE KNEE JOINT AT THE INITIATION OF BDMARDS TREATMENT IS A PREDICTIVE FACTOR OF SUBSEQUENT TOTAL KNEE ARTHROPLASTY AND PROGRESSION OF JOINT DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS DURING LONG-TERM BDMARDS TREATMENT**

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Background: The joint destruction inhibitory effect of biological disease-modifying anti-rheumatic drugs (bDMARDs) in patients with rheumatoid arthritis (RA) has been reported in a lot of studies. Most of them are evaluated in small joints such as hands and feet, there are few reports on the joint destruction inhibitory effect in large joints such as knees which are frequently affected in disease course of RA[1]. Although bDMARDs is very effective drugs, we experience RA patients in whom total knee arthroplasties (TKA) are performed after the initiation of bDMARDs treatment[2].
Objectives: To investigate the rate of TKA during bDMARDs treatment and to explore associated factors of subsequent TKA after the initiation of bDMARDs treatment in RA patients.
Methods: 356 knee joints of 184 RA patients who initiated bDMARDs treatment in our institute from March
2004 to November 2013 were included in this retrospective study. They were retrospectively studied over the course of a minimum of 5 years of follow up. Knees in which TKA were already performed before the initiation of bDMARDs treatment were excluded in this study. Patients' characteristics and rates of subsequent TKA over time were investigated. Next, factors associated with subsequent TKA were explored using univariate and multivariate analysis. The X-ray change (Larsen grade[3]), ARASHI score[4]) at the last observation after 5 years or more was also examined. ARASHI score was developed in Japan to assess destruction of large joints such as knees or hips.
Results: Baseline patients' characteristics were below. Mean age was 57.1 years old. 152 female and 32 male. MTX was concomitant in 85.7% of patients. Prednisolone was concomitant in 53.7% of patients, First bDMARDs were infliximab in 67 cases, etanercept in 67 cases, adalimumab in 35 cases, tocilizumab in 6 cases, abatacept in 9 cases, golimumab in 0 cases and certolizumab in 0 cases. Agents were changed according to clinical necessity. The median follow-up period was 7.8 years. TKA were performed in 20 knees (5.95%) in total. Baseline extent of joint destruction of knees which was evaluated using Larsen grade and ARASHI score, joint destruction, age, disease duration, steinbrocker class, concomitant corticosteroids, concomitant methotrexate, DAS28-CRP, SDAI, MMP-3, mHAQ, swelling of the knees,and tenderness of the knees were associated with subsequent TKA in univariates analysis. Multivariate analysis revealed that the extent of baseline joint Destruction and mHAQ were associated with subsequent TKA (Larsen grade: Odds ratio; 6.17, 95%, confidence interval; 2.93-12.98, ARASHI score: Odds ratio; 3.50, 95% confidence interval; 2.18-5.62, mHAQ : Odds ratio; 3.56, 95% confidence interval; 1.06-11.93). Cut-off value was calculated as 2 in Larsen grade, 3 in ARASHI score and 1.5 in mHAQ using receiver operating characteristic analysis. There were significant differences in the rates of subsequent TKA if knees were divided according to baseline Larsen grade, ARASHI score and mHAQ (Fig1). Baseline ARASHI status score in progressed knees which was worsened after over 5 years were increased compared with that in knees which was stable. There was no significant difference in baseline Larsen grade between progressed knees and non-progressed knees.
Conclusion: It was suggested that baseline joint destruction and mHAQ at the initiation of bDMARDs in RA patients was predictive factors of subsequent TKA and progression of joint destruction of knees during long-term bDMARDs treatment. Early intervention with effective bDMARDs is necessary to prevent destruction of knee joints and subsequent TKA in RA patients whose knee joints are affected.

REFERENCES

[1] Drossaers-Bakker, et al. Rheumatology. 2000
[2] Seki, et al. Clin Rheumatol. 2009
[3] Larsen, et al. Scand J Rheumatol. 1979
[4] Kaneko, et al. Mod Rheumatol. 2013

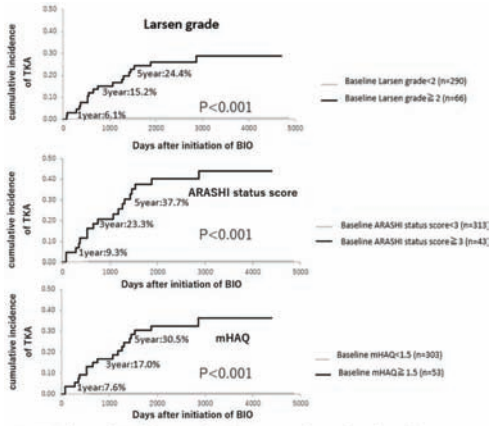


Fig.1 Incidence of total knee arthroplasties according to baseline values
Kaplan-Meier method and Log-rank test were used for statistical analysis.
TKA: total knee arthroplasty, BIO: biological agent,
ARASHI: Assesment of Rheumatoid Arthritis by Systemic Histological and radiological Imaging
mHAQ: modified health assessment questionnaire

Disclosure of Interests: None declared
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AB0265

ASSOCIATION OF CUMULATIVE ANTI-CYCLIC CITRULLINATED PROTEIN ANTIBODIES WITH RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Antibody against cyclic citrullinated proteins (ACPA) is counted as one of the most important biomarkers in diagnosis, classification, and prognosis of rheumatoid arthritis (RA). The clinical implications of change in ACPA level over time remain undetermined.
Objectives: We examined the evolution of ACPA during disease course and assess predictive value of time-weighted cumulative ACPA titer on radiographic progression in patients with RA.
Methods: A group of 734 patients with RA was followed longitudinally over 2 years, with annual measurements of IgM rheumatoid factor (RF) and ACPA. Radiographs of the hands were scored with the modified Sharp score (SHS). Cumulative ACPA antibody titers were calculated using the trapezoidal rule.
Results: The patients with radiographic progression had a higher SHS at baseline; and smoking status, diabetes, RF positivity, and use of biologic DMARDs were independently associated with radiographic progression (all $P<0.05$). As for ACPA, reversion happened more commonly in men and was associated with younger onset age and lower titer at baseline, but it had no direct relevance to radiographic outcome. In multivariable regression analysis, only high cumulative or baseline titer of ACPA had a predictive power for rapid radiographic progression (all $P<0.05$), and cumulative ACPA titer was superior in terms of statistical significance (Cohen's d, 0.637 versus 0.583).
Conclusion: High cumulative ACPA titer was an independent predictor for accelerated radiographic progression, especially with initiation of joint damage. Serial measurement of ACPA titer can provide information about its dynamics over the clinical course and can facilitate an additional assessment of radiographic progression.
Acknowledgement: Nothing specified.
Disclosure of Interests: None declared
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AB0266

THREE NOVEL BIOMARKERS PRDICTING THE SHORT-TERM RESPONSE TO IFX + MTX + LEFTRIPLE THERAPY IN RA

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Background: For rheumatoid arthritis (RA), nearly one-third of patients still have poor response to biological agents. In addition, infliximab, methotrexate and leflunomide are the most widely used three drugs in the clinic, but there remains no unified and precise indicators capable to predict the clinical response to their combination therapy.
Objectives: The purpose of this experiment is to identify a protein biomarker panel for predicting the outcome of RA patients who have received a triple therapy combining of infliximab, methotrexate and leflunomide (IFX+MTX+LEF).
Methods: All incorporated RA patients with DAS28-CRP>5.1 accepted IFX +MTX+LEF therapy. At 14th week, they were divided into good responder (GR), moderate responder (MR), and non-responder (NR) in accordance with the EULAR response criteria. After removal of the 14 high-abundance proteins, serum samples from patients (4 GR and 4 NR) at baseline and 14th week, and 4 healthy subjects (HS) were screened for candidate biomarkers via isobaric tags for relative and absolute quantification (iTRAQ). After an in-depth technical feasibility analysis, Parallel Reaction Monitoring (PRM) was performed in 20 RA patients and 20 HS for further validation
Results: A total of 590 proteins were identified by iTRAQ, and 51 proteins of which showed significant differences between NR and GR (Figure 1). PRM showed that levels of catalase, epididymal secretory protein Li 282, and hemoglobin subunit δ of the GR+MR group at baseline was higher than that of the NR group (Figure 1), and they were involved in the process of oxidative stress.
Conclusion: The RA patients with higher pre-treatment levels of the three proteins responded better to IFX+MTX+LEF triple therapy at 14th week; Inhibitor of oxidative stress might be a new therapeutic target of RA in the future.

REFERENCES

[1] Tracey D, Klareskog L, Sasso E H, Salfeld J G and Tak P P. Tumor necrosis factor antagonist mechanisms of action: a comprehensive review. Pharmacol Ther, 2008, 117(2):244-279.

[2] Isaacs J D, Ferraccioli G. The need for personalised medicine for rheumatoid arthritis. Ann Rheum Dis, 2011, 70(1):4-7.

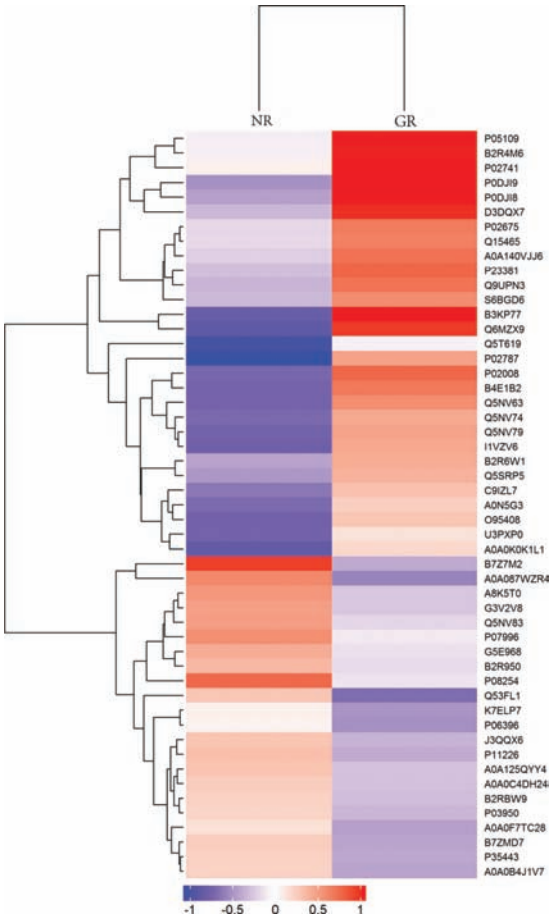


Figure 1. **Hierarchical cluster.** Hierarchical cluster of proteins differentially expressed between good responders and non-responders with an FDR < 1% identified by MaxQuant from iTRAQ. Red, high expression; green, low expression. Two main clusters of proteins can be observed, one up-regulated (left) and other down-regulated (right) in the serum of patients. Abbreviation: GR, good responder; NR, non-responder; Red, high expression; Blue, low expression.

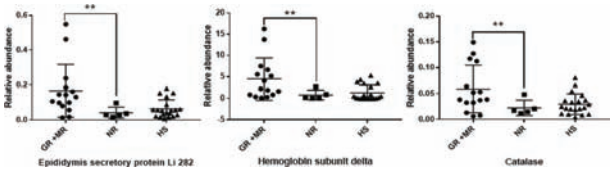


Figure 2. **Expression levers of the three protein.** Comparison of epididymis secretory protein Li 282, hemoglobin subunit delta and catalase at baseline from PRM among groups of GR+MR, NR and HS, $^{**}P<0.05$.

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AB0267

ROLE OF FCGAMMA RECEPTORS IIA, IIIA, AND IIIB POLYMORPHISMS IN RHEUMATOID ARTHRITIS SEVERITY

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Background: Fc gamma receptors (FcgR) type IIA IIIA and IIIB play an important role in the recognition of immune complexes (ICs) by

binding their Ig-Fc portion. However, it has been demonstrated that FcgR single nucleotide polymorphisms (SNP) leads to low binding affinity alleles (FcgRIIA-131R, IIIA-158V and IIIB NA2). Therefore, we can make an assumption that the presence of these risk alleles could influence the outcome of immune mediated disease such as rheumatoid arthritis (RA).

Objectives: The aim of this study was to assess the relationship between functional SNP of FcgR IIA H13R, IIIA V158F and IIIB NA1/NA2 and disease severity scores in RA.

Methods: We assessed disease severity in RA patients based on the Health Assessment Questionnaire (HAQ) and Sharp/van der Heijde (mSharp) method. To reduce selection biais, all recruited patients were treated with conventional DMARDs.We considered patients with HAQ score ranged from 2 to 3 as having severe disability. For radiographic evaluation, since there is not validated threshold for joint damage severity, we took mSharp score median value of our population as a reference. Patients underwent FcgRIIA, FcgRIIIA and FcgRIIIB SNP study using PCR-SSP and direct sequencing process. Then, biallelic polymorphisms were examined for association with HAQ and mSharp score.

Results: Fifty-eight RA patients were enrolled. The mean duration of the disease was 11.77 years [0.5-24]. Among these patients, 34 (58.62%) had severe disability according to HAQ score. The mSharp median value was 43,5 [0-232] and 28 (48.28%) patients had a score above this value.

Genotypic study showed that FcgR IIIB-NA2 was significantly associated with severe disability (p=0.021) (Table 1).

Table 1. Correlation between FcgR biallelic polymorphisms and disability level

Gene	Genotype	HAQ<2	HAQ>=2	OR (95% CI)	P-value
FcgR IIIB	NA1/NA1	10 (41.7%)	5 (14.7%)	1.00	**0.021**
	NA1/NA2 – NA2-NA2	**14 (58.3%)**	**29 (85.3%)**	4.14(1.19-14.44)	
FcgR IIIA	V/V	4 (16.7%)	7 (20.6%)	1.00	0.71
	F/F-F/V	**20 (83.3%)**	**27 (79.4%)**	1.30 (0.33-5.04)	
FcgR IIA	H/H	3 (12.5%)	5 (14.7%)	1.00	0.81
	H/R-R/R	**21 (87.5%)**	**29 (85.3%)**	0.83 (0.18-3.86	

Table 2. Correlation between FcgR biallelic polymorphisms and radiographic evaluation

Gene	Genotype	Sharp < 43.5	Sharp >=43.5	OR (95% CI)	P-value
FcgR IIIB	NA1/NA1	7 (23.3%)	8 (28.6%)	1.00	0.65
	NA1/NA2 – NA2-NA2	23 (76.7%)	20 (71.4%)	0.76 (0.23-2.47)	
FcgR IIIA	V/V	5 (16.7%)	6 (21.4%)	1.00	0.64
	F/F-F/V	25 (83.3%)	22 (78.6%)	1.36 (0.37-5.09)	
FcgR IIA	H/H	5 (16.7%)	3 (10.7%)	1.00	0.51
	H/R-R/R	25 (83.3%)	25 (89.3%)	1.67 (0.36-7.74)	

Furthermore, FcgRIIIA-158F and IIA-131R carriers were more frequent in patients with severe disability but the association was not statistically significant. Finally, no correlation was found between radiographic evaluation and FcgR SNP study (table 2).

Conclusion: FcgR low affinity alleles seem to confer susceptibility to severe functional impairment in RA but not to structural damage. However further studies on larger population must be done to corroborate these findings.

REFERENCES

[1] Brun JG, Madland TM, Vedeler CA. Immunoglobulin G Fc-receptor (FcgammaR) IIA, IIIA, and IIIB polymorphisms related to disease severity in rheumatoid arthritis. J Rheumatol. 2002;29:1135–40.

[2] Kastbom A, Ahmadi A, Soderkvist P, Skogh T. The 158V polymorphism of Fc gamma receptor type IIIA in early rheumatoid arthritis: increased susceptibility and severity in male patients (the Swedish TIRA project) Rheumatology (Oxford) 2005;44:1294–8.

[3] Lee YH, Bae SC, Song GG. FCGR2A, FCGR3A, FCGR3B polymorphisms and susceptibility to rheumatoid arthritis: a meta-analysis.Clin Exp Rheumatol. 2015 Sep-Oct; 33 (5):647-54.

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AB0268

MORTALITY RATE OF RHEUMATOID ARTHRITIS PATIENTS EVEN IN THE NEW ERA OF BIOLOGICS IS HIGHER THAN THE CONTROL GROUP: EIGHT YEARS OF THE TOMORROW STUDY

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Background: Patients with rheumatoid arthritis (RA) have a high mortality rate compared to the general population[1]. However, the mortality rate of patients with RA might be improved by advances in therapy[2].

Objectives: We investigated the risk factors for mortality in patients with RA from TOMORROW study.

Methods: This study included 413 participants, comprising 208 patients with RA and 205 age- and sex- matched healthy volunteers (Vo) from the prospective "TOMORROW" cohort study that has been ongoing since 2010 were included in this study (women, 84%; mean age, 58 years old). Median disease duration was 10.3 years.

Results: The rate of accomplishment for 8 years was 83.2% in the RA group and 92.7% in the Vo group. There were 14 deaths in the RA group (8.7/1000 person-years) and two in the Vo group (1.2/1000 person-years) (p=0.0025) for 8 years. Infection was the most common cause of death in the RA group (43%). Cox proportional hazard analysis showed that having RA was significant risk factor for death (hazard ratio [HR]: 6.9, 95%CI: 1.6 - 30.4, p=0.01) adjusting by age (Figure). In the RA group, glucocorticoid (GC) use (HR: 3.6, 95%CI: 1.1 -10.4, p=0.032) was significant risk factor for death. Disease activity, duration of disease, use of biological products, use of methotrexate, presence of cardiovascular disease, and smoking were not significant factor.

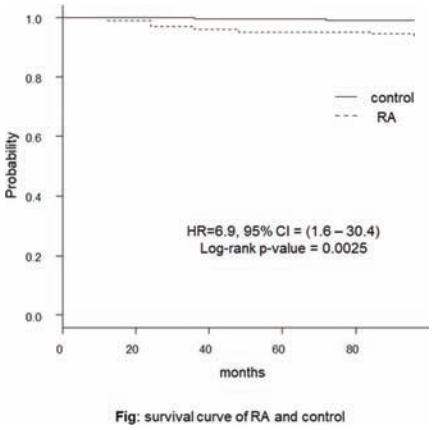


Fig: survival curve of RA and control

Figure 1

Conclusion: RA was still significant risk factor of death. GC use was independent factors of death in RA patients.

REFERENCES

[1] van den Hoek J, Boshuizen HC, Roorda LD, et al. Mortality in patients with rheumatoid arthritis: a 15–year prospective cohort study. Rheumatol Int (2017) 37:487–493

[2] Lacaille D, Avina-Zubieta JA, Sayre EC, et al. Improvement in five-year mortality in rheumatoid arthritis compared to the general population – closing the mortality gap. Ann Rheum Dis. 2017 June; 76(6): 1057–1063.

Disclosure of Interests: Koji Mandai: None declared, Tatsuya Koike Speakers bureau: AbbVie, Astellas Pharma Inc., Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB, Yuko Sugioka: None declared, Kentaro Inui Speakers bureau: Takeda Pharmaceutical, Pfizer Japan, Daiichi-Sankyo Co.Ltd., Abbvie, Mitsubishi Tanabe Pharma Corporation, Janssen Pharmaceutical, Chugai Pharmaceutical, Ono Pharmaceutical, Eisai Co. Ltd., Eli-Lilly, Nippon Kayaku Co.,Ltd., Maruho Co.,Ltd, Kaken

Pharmaceutical Co.,Ltd., Tadashi Okano Speakers bureau: AbbVie, Yutaro Yamada Speakers bureau: Abbvie, Chugai, Mitsubishi Tanabe, Masahiro Tada Speakers bureau: Abbvie, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Ono Pharmaceutical, Pfizer Japan, Takeda Pharmaceutical, Kenji Mamoto: None declared, Shohei Anno: None declared, Hiroaki Nakamura: None declared

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AB0269 COMPARISON BETWEEN DIFFERENT DISEASE ACTIVITY SCORES IN ELDERLY ONSET RHEUMATOID ARTHRITIS

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Background: Elderly onset rheumatoid arthritis (EORA) has several peculiarities. Which activity index should we use in this age group is still an unresolved issue. The use of ESR in DAS28 is widespread, but it is well known that ESR could increase with age, overestimating activity. DAS28-PCR or SDAI, which uses PCR, or CDAI that does not use analytical data, could be more suitable alternatives.
Objectives: To describe disease activity scores evolution in EORA and to analyse the correlation and concordance between them.
Methods: Longitudinal observational study in naïve treatment EORA patients (ACR/EULAR 2010 criteria). Study visits were carried out basally (pre-treatment) and at month 1, 3, 6 and 12. DAS28 VSG, DAS28 PCR, SDAI and CDAI were calculated at each visit, and ACR/EULAR remission index at 12 months. The same rheumatologist made all visits and explorations. Correlations were analysed using the Spearman or Pearson correlation index (p value ≤ 0.001). The concordance was evaluated with the kappa index. The statistical study was performed with Stata 15.1.
Results: 45 patients with EORA were enrolled. Table 1 and 2 summarize the clinical and analytical characteristics.
All the scores had a very good linear correlation both at baseline and at follow-up (correlation score: 0.83-0.98). A moderate concordance was observed from the baseline visit between DAS28-VSG and DAS28-PCR (k=0.43-0.52, p <0.001), which decrease to low at 12 months (k=0.32, p <0.001). A concordance of 100% was observed at baseline analysing DAS28-VSG and SDAI (k=1; p <0.001), but worsened during follow-up being moderate (k=0.40-056; p<0.001). A very good concordance was observed comparing DAS28-VSG to CDAI at the baseline visit (k=0.88, p<0.001), which decreased to good-moderate during follow-up (k=0.40-0.63, p<0.001). Between DAS28-PCR and SDAI a moderate concordance was observed up to 6 months (k=0.43-0.57, p <0.001), which worsened to low at 12 months (k=0.32, p<0.001). The concordance between DAS28-PCR and CDAI was low-moderate (k=0.26-0.48, p <0.001). On the other side, the agreement was very good between SDAI and CDAI throughout the follow-up (k=0.86-0.93, p <0.001). The ACR/EULAR index had a very low concordance with DAS28-PCR (k=0.17, p <0.001), moderate with DAS28-VSG (k=0.49, p<0.001) and the results are good with SDAI and CDAI (k=0.64, p<0.001).
Conclusion: The correlation between the different scores was good. However, the concordance between all the scores decreases as time passes, according to a higher percentage of patients in remission or low activity. This low-moderate concordance is demonstrated even between DAS28-PCR and DAS28-VSG, and when these are compared with CDAI and SDAI. CDAI and SDAI are the only ones that maintain a good concordance between them, even when the number of patients in remission or low activity increases. ACR/EULAR only maintains an acceptable concordance with the most restrictive scores, SDAI and CDAI. By contrast, agreement is very low with DAS28, especially by DAS-PCR.
Disclosure of Interests: None declared

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	N=45
Epidemiological data	
Women n (%)	21 (46.7)
Age (mean ± σ)	74.8 ± 7.5
Symptoms n (%)	
Shoulder girdle	34 (75.6)
Pelvic girdle	20 (44.4)
Peripheral joints	45 (100)
Oedema	21 (46.7)
Small joints of hands	42 (93.3)
Analytical and radiological data n (%)	
FR +	15 (33.3)
ACPA +	13 (28.9)
FR and ACPA +	10 (22.2)
Bone erosions	4 (8.8)
Treatments n (%)	
Glucocorticoids	43 (95.5)
DMARDs	40 (91.1)

	Baseline N = 45	Month 1 N=45	Month 3 N=44	Month 6 N=44	Month 12 N=44	% remission Month 12 N=44
DAS28-VSG (mean ±σ)	6.3 ± 1.0	2.9 ± 1.7	3.0 ± 1.4	2.8 ± 1.3	3.1 ± 1.3	40.9
DAS28-PCR (mean ±σ)	5.7 ± 1.0	2.5 ± 1.4	2.4 ± 1.3	2.2 ± 1.1	2.5 ± 1.0	70.4
SDAI (mean±σ)	41.0 ± 13.8	9.3 ± 11.1	7.9 ± 10.7	6.9 ± 8.7	7.5 ± 8.0	31.8
CDAI (mean±σ)	36.9 ± 11.6	8.7 ± 10.4	7.4 ± 10.5	6.4 ± 8.5	6.8 ± 7.9	31.8
ACR/EULAR remission						18.2

AB0270 POSITIVE ACPA WITHOUT EVIDENCE OF ARTHRITIS – A RARITY?

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Background: Rheumatoid Arthritis (RA) follows a variable disease course in regards to joint damage and functional outcome, therefore an early diagnosis is crucial for its management. However, occasionally, this diagnosis can be a challenge. Rheumatoid Factor (RF) and Anti-citrullinated peptide antibodies (ACPA) are the most useful biomarkers in the diagnosis of RA and, although individually they do not dictate the final diagnosis, they present high specificity and may be positive even before clinical manifestations of the disease occur.
ACPA is detected in approximately two thirds of the patients with RA and presents a superior diagnostic specificity when compared to RF. This specificity of 95-98% may present an increased value if it is three times superior to its value of reference.
Objectives: Share with the medical community and alerting them for the existence of patients with positive ACPA with no clinical evidence of RA.
Methods: By consulting the electronic clinical records of patients observed by a Rheumatologist, we identified and analyzed the patients that presented positive ACPA in their blood tests and no evidence of signs or symptoms of RA, during at least six years of follow-up. Patients with other rheumatic diseases, history of tuberculosis or chronic pulmonary diseases were excluded.
Results: We identified seven patients (average of 61 years old) with positive ACPA in at least two different blood tests, of which five presented a value three times superior to its normal value (<15UA/mL). It should be noted that, four patients presented both positive ACPA and RF. Clinically, all patients referred mechanical symptoms that varied between cervical, low back, shoulder and knee pain and did not present any record of swollen joints without trauma. Radiologically, in most cases we observed joint degenerative damage. Six years after the first positive ACPA, none of the patients developed any manifestation of inflammatory joint disease.
Conclusion: Studies reveal that positive ACPA in healthy patients may precede the clinical diagnosis of RA. The specificity of positive ACPA and RF one and a half years before the diagnosis of RA is approximately 99-100%. However, as we demonstrated, it is not uncommon to find during clinical practice individuals with positive ACPA without evidence of arthritis, which leads us to emphasize the importance of a detailed anamnesis with a meticulous physical examination before establishing a diagnosis based on the patient's blood tests.

REFERENCES

[1] Moeez S, et al. Anti-citrullinated protein antibodies: role in pathogenesis of RA and potential as a diagnostic tool. Rheumatol Int. 2013;33(7):1669–73
[2] Brito Rocha, et al. Clinical and pathophysiologic relevance of autoantibodies in rheumatoid arthritis. Advances in Rheumatology. 2019;59:2
[3] Nielsen SF, et al. Elevated rheumatoid factor and long term risk of rheumatoid arthritis: a prospective cohort study. BMJ. 2012;345:e5244
[4] Rantapää-Dahlqvist S. What happens before the onset of rheumatoid arthritis? Curr Opin Rheumatol. 2009;21:272
[5] Bugatti S, et al. The Clinical Value of Autoantibodies in Rheumatoid Arthritis. Front. Med. 2018;5:339

[6] Avouac J, et al. Diagnostic and predictive value of anti-cyclic citrullinated protein antibodies in rheumatoid arthritis: a systematic literature review. Ann Rheum Dis 2006; 65:845

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AB0271 FACTORS ASSOCIATED WITH HOSPITAL ADMISSIONS MORTALITY IN RHEUMATOID ARTHRITIS PATIENTS IN SPAIN. (TREND-AR STUDY)

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Background: There have been significant changes in the management of rheumatoid arthritis (RA) during the past 20 years. The potential impact of these changes on hospital admissions mortality is unknown.
Objectives: To analyse the factors associated with hospital admissions mortality in rheumatoid arthritis patients in Spain from 1999 to 2015.
Methods: This is a retrospective population study. We have analized a national administrative database that includes a Minimum Basic Data Set (MBDS) of hospital admissions of RA patients during the period 1999 to 2015. We studied all the cases of hospital admissions mortality. Patients were identified by concatenation of clinical record number and birth date. The analyzed factors were identified by the presence in primary and secondary diagnosis of the ICD9 codes, during the first hospital admission. Hazard Ratio (adjusted by sex and age) were calculated using Cox regression analyses.
Results: There were a total of 338.343 hospital admissions in RA patients during the study period, accounting for a total of 186.491 patients (127.203 women (68,21%) and 59.288 men (31,79%). The mean number of hospital admissions was 1,81(SD 1,7), with a minimum of 1 and a maximum of 43. The median time of follow-up was 11,85 months (DE 27,4). There were a total of 18.641 exitus (5,5%). The HR (adjusted by sex and age) of the factors associated with hospital admissions mortality are shown in the next table:

Risk factor	Adjusted by sex and age Cox reg analyses		
	HR	IC	p
Gender (Male/Female)	1,242	1,20-1,28	<0,001
Age	1,066	1,064-1,068	<0,001
Charlson Index	1,276	1,268-1,284	<0,001
Stay	1,004	1,003-1,005	<0,001
Cardiovascular disease	1,318	1,274-1,362	<0,001
Dementia	1,852	1,696-2,021	<0,001
Diabetes Mellitus	1,093	1,05-1,137	<0,001
Neoplasm	2,432	2,313-2,556	<0,001
Hepatopathy severe-moderate	3,189	2,752-3,695	<0,001
COPD	1,113	1,071-1,156	<0,001
Pressure ulcers	1,115	1,006-1,235	0,036
Renal Disease	1,758	1,683-1,837	<0,001
Infectious disease during stay	1,593	1,545-1,642	<0,001
S. Felty	1,531	1,18-1,985	<0,001
Amyloidosis	2,957	2,627-3,327	<0,001
Hip fracture	0,731	0,664-0,804	<0,001
Tuberculosis	1,066	1,064-1,068	<0,001

Conclusion: In Spain, during the period of 1999-2015, the factors associated with hospital admission mortality (first admission) are: age, male sex, higher Charlson Index and longer hospital stay. The associated clinical variables are chronic hepatopathy, amyloidosis and neoplasm.
Disclosure of Interests:
None declared

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AB0272 EVALUATION OF CXCL13, SICAM-1, MMP-3 AND S100A8/A9 AS SERUM BIOMARKERS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB

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Background: Serum levels of C-X-C motif chemokine ligand 13 (CXCL13) and soluble intercellular adhesion molecule-1 (sICAM-1) have been associated with response to tocilizumab (TCZ) in patients with rheumatoid arthritis (RA); levels of matrix metalloproteinase-3 (MMP-3) and S100A8/A9 have also been associated with RA disease activity and joint damage.
Objectives: To evaluate the association of CXCL13, sICAM-1, MMP-3 and s100A8/A9 levels with disease activity and response to TCZ in patients with RA who achieved low disease activity with 24 weeks of TCZ + methotrexate (MTX) treatment and were subsequently randomized to TCZ monotherapy (mono) or TCZ + MTX in the COMP-ACT trial (NCT01855789).
Methods: US patients with RA who had an inadequate response to MTX received initial combination therapy of MTX plus TCZ 162 mg subcutaneous for 24 weeks. Patients who achieved Disease Activity Score in 28 joints calculated with erythrocyte sedimentation rate (DAS28-ESR) ≤ 3.2 at Week 24 were randomized 1:1 (double-blind) to receive either TCZ mono or continue TCZ + MTX until Week 52. Randomized patients were included in the present study based on baseline, Week 24 and Week 40 sample availability; serum levels of CXCL13, sICAM-1, MMP-3 and S100A8/A9 were measured by immunoassay. Correlations between CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels and DAS28-ESR at baseline, Week 24 and Week 40 were determined according to Spearman correlation coefficient. Changes in CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels from baseline to Week 24 (open-label period) were determined using Wilcoxon test. Mean changes in CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels from Week 24 to Week 40 (randomized period) were compared between treatment arms using analysis of covariance.
Results: Of 296 randomized patients, 249 were included (TCZ mono, n = 126; TCZ + MTX, n = 123). Biomarker levels were well balanced across treatment arms at baseline and Week 24 (randomization). At baseline, there were weak to mild correlations between DAS28-ESR and biomarker levels (CXCL13 [r = 0.13, *P* = 0.0411], sICAM-1 [r = 0.20, *P* = 0.0015], MMP-3 [r = 0.19, *P* = 0.0021], S100A8/A9 [r = 0.25, *P* = 0.0001]). Significant reductions in mean biomarker levels were observed from baseline to Week 24 (open-label period) among the total randomized patients (*P* < 0.0001). CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels were relatively stable between Week 24 and Week 40 (randomized period), with no significant differences between TCZ mono and TCZ + MTX (**Table**).

Table 1. Adverse Events During the 12-Month Post-Index Period, Stratified by OGC Daily Dose

	Dose Q1 ≥ 1.00 to ≤ 13.75 mg N = 184	Dose Q2 > 13.75 to ≤ 25.00 mg N = 184	Dose Q3 > 25.00 to ≤ 40.00 mg N = 198	Dose Q4 > 40 mg N = 161
Patients without type 2 diabetes and without HbA1c ≥ 7.5 in the pre-index period, n	120	136	130	110
With type 2 diabetes diagnosis or HbA1c ≥ 7.5 in the post-index period, n (%)	9 (7.5)	16 (11.8)	16 (12.3)	27 (24.5)
Maximum HbA1c value across HbA1c lab results during post-index, mean (SD)	7.75 (2.46)	8.30 (2.86)	8.25 (2.42)	8.61 (3.09)
Patients with diabetes diagnosis in the pre-index period but without HbA1c ≥ 7.5 in the pre-index period, n	31	18	40	15
With worsening diabetes with HbA1c ≥ 7.5 in the post-index period, n (%)	10 (32.3)	6 (33.3)	20 (50.0)	4 (26.7)
Patients without blood glucose level ≥ 200mg/dL in the pre-index period, n	173	169	179	147
With blood glucose level ≥ 200mg/dL in the post-index period, n (%)	13 (7.5)	15 (8.9)	24 (13.4)	22 (15.0)
Adverse events in the post-index period, n (%)				
Serious infection requiring hospitalization for infection and/or IV antibiotics	31 (16.8)	39 (21.2)	44 (22.2)	40 (24.8)
Serious infection requiring IV antibiotics	29 (15.8)	33 (17.9)	42 (21.2)	35 (21.7)
Serious infection requiring hospitalization for infection	6 (3.3)	12 (6.5)	12 (6.1)	8 (5.0)
Cataracts	22 (12.0)	27 (14.7)	34 (17.2)	35 (21.7)
Gastrointestinal bleeding or ulcer	11 (6.0)	11 (6.0)	13 (6.6)	19 (11.8)
Patients with BMI in pre- and post-index, n	171	162	181	141
Increase in BMI by 5, n (%)	7 (4.1)	5 (3.1)	9 (5.0)	9 (6.4)

BMI, body mass index; HbA1c, hemoglobin A1c; IV, intravenous; Q, quartile.

Conclusion: In agreement with previous studies, the association between baseline disease activity and CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels was weak to mild; TCZ + MTX treatment from baseline to Week 24 (open-label period) resulted in significant reductions in all biomarkers. Changes in levels of CXCL13, sICAM-1, MMP-3 and S100A8/A9 from Week 24 to 40 (randomized period) were similar between treatment groups, consistent with the finding of non-inferiority of TCZ mono compared with TCZ + MTX in patients with RA who achieve low disease activity with TCZ + MTX.
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Sornasse Employee of: Genentech, Inc., Michael J. Townsend Shareholder of: Stockholder of Genentech/Roche, Employee of: Genentech/Roche, Jinglan Pei Employee of: Genentech, Margaret Michalska Employee of: Genentech, Inc.
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AB0273 THE ANALYSIS OF THE CLINICAL COURSES OF THE ACPA POSITIVE PATIENTS WITHOUT SYNOVITIS: WHETHER TO FOLLOW UP THEM

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Background: ACPA (anti-citrullinated peptide antibody) is a major risk factor for the onset of RA (rheumatoid arthritis)[1]. As ACPA becomes a common test in non-rheumatologists, ACPA positive patients not diagnosed with RA are increasing. However, it is unclear whether follow-up of ACPA-positive patients without synovitis leads to early treatment and consequently to the improvement of prognosis.
Objectives: To reveal whether to follow up the ACPA positive patients without synovitis.
Methods: In the four years from January 2015 to December 2018, we extracted the ACPA positive patients introduced from other hospitals, among which patients not diagnosed as RA at the first visit were selected. Then, their clinical courses and ACPA titers were retrospectively analyzed. The 2010 ACR-EULAR classification criteria was used for the diagnosis of RA[2]. For the significance test, a χ 2 test and a t test with α = 0.05 were used.
Results: Thirty six patients met the conditions, and then 10 patients, previously treated as RA, and 8 drop-out patients were excluded. In 18 patients remaining, 10 patients developed RA (follow-up days: avg. 404, max. 983) and the other 8 were non-RA, predisease patients (follow-up days: avg. 424, max. 926). All 10 RA patients initially started the treatment with MTX (methotrexate). Five of them reached remission with only MTX. Of the other five, three needed other csDMARDs because of an inadequate amount of MTX due to adverse events, and two had insufficient observation period. The ACPA titer was significantly higher in the RA patients than the predisease patients (468 versus 26.3 U/ml (P=0.0075)). Tenderness of DAS 28 subject joints at the first visit was a significant predictor of RA onset when trying to extract from clinical findings. (10 of 10 in RA patients vs. 2 of 8 in predisease patients (P=0.0044)).
Conclusion: In our research, the predictors of RA onset are not only high ACPA titer but also tenderness of DAS28 subject joints at the first visit. The early treatment with MTX could contribute to improved prognosis, so it would be useful to follow up the ACPA positive patients without synovitis. The frequency of hospital visits and the modality to detect synovitis are the subject of our analysis from now on.

REFERENCES

[1] Solbritt Rantapaa-Dahlqvist, et al.: Antibodies against cyclic citrullinated peptide and IgA rheumatoid factor predict the development of rheumatoid arthritis. Arthritis Rheum., 48 (10),2741-2749,2003.
[2] Aletaha,D.,Neogi,T.,Silman,A.,et al.: 2010 Rheumatoid arthritis classification criteria. Arthritis Rheum., 62,2569-2581,2010.

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AB0274 THE PREDICTIVE VALUE OF RHEUMATOID FACTOR, ANTI-CITRULLINATED PROTEIN ANTIBODIES, ANTI-CARBAMYLATED PROTEIN: ANTIBODIES AND ANTI-PEPTIDYL ARGININE DEIMINASE TYPE-3 ANTIBODIES, ALONE OR IN COMBINATION, ON RADIOGRAPHIC DAMAGE IN RHEUMATOID ARTHRITIS

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Background: Autoantibodies such as anti-citrullinated protein antibodies (ACPA), anti-carbamylated protein antibodies (CarP) and anti-peptidyl arginine deiminase 4 (PAD4) antibodies have been associated with disease severity and radiographic progression in rheumatoid arthritis (RA). However, very little is known about the anti-PAD 3 (PAD3) antibodies and of the added value of combining multiple autoantibodies to predict radiographic damage.
Objectives: To investigate the capability of rheumatoid factor (RF), ACPA, anti-CarP and anti-PAD3 antibodies to predict radiographic damage in RA, both individually and in combination.
Methods: We performed a nested cohort study within the « Swiss Clinical Quality Management » (SCQM) RA registry. Biobank samples were tested for RF [QUANTA Lite (QL), IgM and IgA], ACPA IgG [QL CCP3 and QUANTA Flash (QF) CCP3], anti-CarP IgG [using carbamylated fetal calf serum as antigen by prototype ELISA, research use only (RUO)] and anti-PAD3 IgG [QF PAD3, RUO] (all methods Inova Diagnostics). Outcome: radiographic damage assessed with a validated scoring method, the Ratingen (Rau) score. We examined the association of each autoantibody both separately and combined, with radiographic damage at baseline and over time with linear mixed-effects models. Multivariable analyses were corrected for age, sex, smoking status, disease duration, disease activity (DAS28), number of prior biologics and calendar year of biosampling.

Figure: Radiographic damage at baseline and progression over time based on a) the presence of anti-PAD3 antibodies and b) the number of autoantibodies present (RF IgM, QL CCP3 IgG, anti-CarP and anti-PAD3). Number of patients per biomarker subgroup – 0: 177, 1: 161, 2: 335 and 3-4: 178.

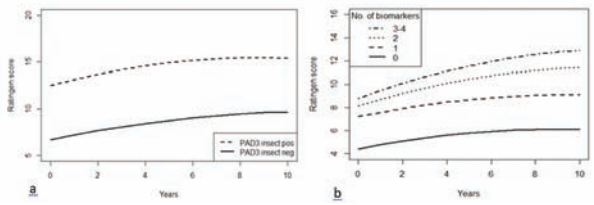


Figure 1

Results: A total of 851 RA patients were included with a median of 4 Ratingen scores per patient. Autoantibodies were positive in the following proportion of patients: RF IgM 66.3%, RF IgA 56.9%, QL CCP3 63.8%, QF CCP3 63.3%, anti-PAD3 10.7% and anti-CarP 22.4%. Significantly higher baseline Ratingen scores were associated with the presence of RF (IgM and IgA) and anti-CCP3 (QL and QF) and greater progression over time with RF IgM and QL CCP3 IgG (p=0.01 and p=0.04 respectively). Patients' positive for anti-PAD3 demonstrated higher mean baseline Ratingen scores compared with anti-PAD3 negative patients (14.9 vs. 8.8 respectively) which was significant in both univariable (Figure) and multivariable analyses (p=0.0002 and p=0.02 respectively). In the QL CCP3 negative subgroup (n= 308), baseline Ratingen scores were significantly higher in anti-PAD3 positive patients (p=0.01).There were no significant differences with regards to anti-CarP, either in the whole population or in the seronegative cohorts. The presence of multiple autoantibodies was associated with higher baseline Ratingen scores, particularly the combination of RF IgM, RF IgA, QL CCP3, and anti-PAD3, with a baseline Ratingen score of 16.1 (p<0.00001 compared to those with no autoantibodies). The presence of at least 3 of the following autoantibodies: RF IgM, QL CCP3, anti-CarP and anti-PAD3, was associated with significantly greater radiographic progression over 10 years (Figure) than if these autoantibodies were absent (p=0.03).
Conclusion: The presence of anti-PAD3 antibodies was associated with significantly higher scores of radiographic damage at baseline, in both the overall population and in the subgroup of ACPA-negative patients. Combinations of autoantibodies (including anti-CarP and anti-PAD3) predicted both higher baseline radiographic damage and greater radiographic progression over time.
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AB0275 RHEUMATOID ARTHRITIS IN HISPANIC PATIENTS: DEMOGRAPHIC AND BASELINE CLINICAL CHARACTERISTICS IN AN EARLY REFERRAL COHORT IN MEXICO VERSUS ROUTINE CARE IN THE UNITED STATES

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Background: Hispanics are the largest minority group in the United States (US) and his percentage is expected to increase (28.6% by 2060)[1], being Mexicans the largest group (67.9%). RA patients from Latin-America have distinctive features from White patients. The literature highlights a younger age at presentation and a different clinical expression compared with White[2] but few data for Hispanic patients in US are available.
Objectives: We compared baseline demographic, clinical features and disease management among Hispanic RA patients from two well characterized cohorts, in the USA and Mexico city.
Methods: An early arthritis clinic (EAC) was established at Site 1 (Mexico City); patients with recent-onset RA (<1 year of symptoms) had a standardized assessment and received "treat to target" treatment. At Site 2 (US), a "routine care" cohort was initiated in 2011, and all patients completed a multidimensional health assessment questionnaire (MDHAQ) as part of their routine care. Patients from both sites had baseline complete evaluation including sociodemographic data, patient-reported outcomes (PROs) (patient global assessment, pain-VAS, HAQ/MHAQ, RAPID3), laboratory data, and tender joint counts. Initial treatment was noted. Data from both sites were compared and appropriate statistics was used.
Results: 201 patients from site 1 and 179 from site 2 were included (table 1); among them, 105 (52%) and 37 (19%), respectively, were DMARDs-naïve at baseline. Patients from site 2 were older and had longer disease duration, however demographic characteristics did not differ. Naïve-DMARDs patients from site 2 scored significantly higher pain-VAS and tender joint counts, and had higher ESR values ($p \leq 0.05$, Mann Withney); a similar tendency was seen for other PROs. Time to DMARDs initiation was shorter in the EAC.

Table.. Demographic and clinical characteristics at first rheumatology visit for RA patients. All data as median (IQR) unless otherwise indicated. *$p \leq 0.003$. NA, not applicable

	Site 1: Mexico-Early Arthritis Clinic		Site 2: US-RA Routine Care	
	Patients on DMARD N=96	DMARD Naïve N=105	Patients on DMARD N=142	DMARD Naïve N=37
DEMOGRAPHICS				
Age, years, mean (SD)	38.6 (13)	38.8 (12.9)	55.7 (15.4)	45.5 (12.6)
Female,%	87.5%	93%	87%	83%
Yrs of formal education	12 (9,16)	12 (9, 14)	12 (9, 14)	12 (9.5, 14)
Symptom duration-first visit, mo	5.6 (3.9, 7.9)	4.7 (2.9, 6.5)	NA	22.7 (3.0, 47.9)
% treated as early RA (<6m)	59.4	70	NA	34
PROs				
Pain (0-10)	4.2 (2.4, 6)	6.2 (3.8, 7.8)	6 (2.7, 8)	8 (6, 8.5)
Patient global assessment (0-10)	4.4 (2.3, 6.8)	6.7 (3.9-8.2)	5.5 (2.5, 8)	7.5 (4, 8.5)
Tender Joint Counts (TJC28 or self-reported RADAI48)	11 (6, 18)	14 (9, 20)	12 (3, 24)	20 (7,32)
RAPID3 (0-30)	11.0 (6.8-16.3)	15.5 (10.3-19.1)	13.6 (6, 20)	15.3 (10, 21.5)
Physical Function-MHAQ (0-10)	2.2 (1-4)	3 (1.3-4.3)	3.0 (0.6, 4.2)	2.4 (1.2, 4.8)
SEROLOGIC DATA				
RF,%	82	82	75	72
ACPA,%	84	86	67	81
ESR, mm/hr	21.5 (11, 48)	23 (12.5, 38)	NA	35.5 (14, 55)
CRP, mg/dl	0.68 (0.22, 2.22)	0.67 (0.27, 2.48)	NA	0.69 (0.54, 1.23)
TREATMENT				
MTX,%	89	93	NA	63*
Other DMARDs,%	59	66	NA	44*
Prednisone,%	47	59	NA	80*
Mean dose (SD), mg	7.5 (2.3)	7.7 (3.5)		9.3 (3.4)
Time to initiate DMARD, mo	NA	0.2 (0-0.4)	NA	0.7 (0.4, 1.4)*

Conclusion: Hispanic patients with RA from different regions in America may differ in their initial presentation. Naïve DMARDs patients belonging to an early RA cohort had shorter presentation to rheumatology resulting in earlier treatment initiation, which has been associated to better outcomes. EACs facilitate the identification of patients with recent-onset disease and help provide early access to effective therapies.

REFERENCES

[1] Public Health Reviews 2016; 37:31.
[2] Best Pract Clin Rheumatol 2008; 22:621-41.

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AB0276 IS PREDICTION OF CLINICAL RESPONSE TO METHOTREXATE IN INDIVIDUAL RHEUMATOID ARTHRITIS PATIENTS POSSIBLE? RESULTS OF A SYSTEMATIC LITERATURE REVIEW

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Objectives: To identify, by a systematic literature review, predictors of clinical response to methotrexate (MTX) treatment in rheumatoid arthritis (RA) patients, which would facilitate personalised treatment.
Methods: PubMed and Embase databases were searched for original articles. Additionally, congress abstracts of European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) annual meetings of the past 2 years were screened. Articles describing baseline predictors of clinical response to MTX after 3 to 6 months were included, since this reflects the time span used to determine treatment effectiveness and decide on treatment changes in treat-to-target recommendations.
Results: 30 articles were included, containing 100 different predictors and 11 predictive models, but only 19 predictors and 2 predictive models were studied in multiple similar RA cohorts. Of these 19 predictors, 4 were described in multiple articles sharing details on statistical analyses and response outcomes, allowing pooling of the predictive values of these 4 factors (Figure 1). Conflicting non-statistically significant associations between age and response were found (Figure 1a).[1-4] Female gender was found to be a predictor of non-response in two studies (OR (odds ratio) 0.55 and 0.54), but these findings could not be replicated in two other studies (Figure 1b).[1-4] In two studies, smoking predicted non-response (adjusted OR 0.35 and 0.60), but this was inconsistent over all response criteria assessed (Figure 1c).[3,5] Higher disease activity score was a predictor of response in two studies (adjusted OR 1.12 and 2.7), conflicting and non-statistically significant predictive values were found in two other studies (Figure 1d).[2-4,6] Rheumatoid factor positivity predicted non-response in two studies (adjusted hazard ratio 0.61, adjusted OR 0.4), although this was not found in three other studies.[2-4,7,8] Heterogeneity between studies prohibited pooling of predictive values. Additionally, a validated epigenetic model was found: area under the receiver operating characteristic curve 0.90 in the development cohort and 0.91 in a validation cohort.[9]
Conclusion: No predictors were identified reliably predicting clinical response to MTX after 3 to 6 months in the individual patient: clinical predictors were weak. However, a promising epigenetic model was found that needs further validation. Future studies on prediction of response to MTX should focus on combining clinical characteristics with genetic and other laboratory biomarkers and on predicting outcome after 3 to 6 months of treatment, to get closer to personalised medicine.

REFERENCES

[1] Kavanaugh, et al. Ann Rheum Dis 2017;76:822-3.

[2] Ponchel, et al. Ann Rheum Dis 2014;73:2047-53.
[3] Saevarsdottir, et al. Ann Rheum Dis 2011;70:469-75.
[4] Wessels, et al. Arthritis Rheum 2006;54:2830-9.
[5] Saevarsdottir, et al. Arthritis Rheum 2011;63:26-36.
[6] Tan, et al. Int J Rheum Dis 2016;19:482-9.
[7] Bugatti, et al. Ann Rheum Dis 2017;76:790-1.
[8] Stühlmuller, et al. Clin Immunol 2016;171:50-61.
[9] Carini, et al. J Transl Med 2018;16:1-11.

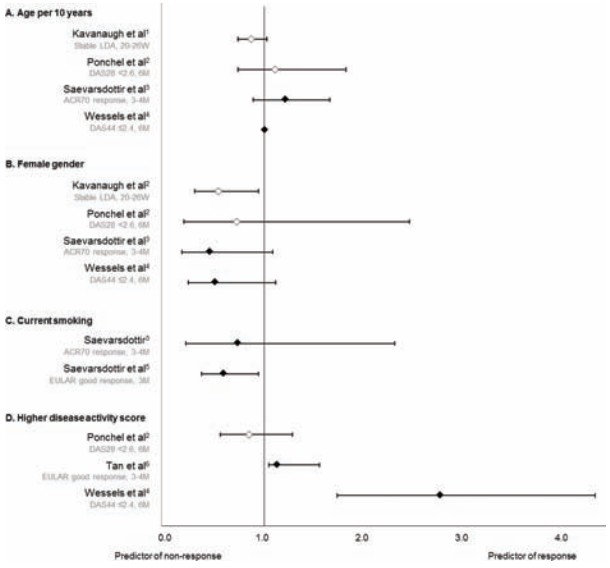


Figure 1. Associations between baseline predictors and response to MTX according to different outcome criteria and at different time points, in odds ratios with 95% confidence interval.
Odds ratios are shown as diamonds: White diamonds represent univariate analyses; black diamonds multivariate analyses; and whiskers 95% confidence intervals. Used response criteria and time points of clinical response are shown in grey type for each study.
DAS28: disease activity score assessing 28 joints; DAS44: disease activity score assessing 44 joints; LDA: low disease activity (definition not specified in article); M: months; W: weeks.

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University Medical Center Utrecht, Utrecht University, Consultant for: SUN Pharma, Speakers bureau: Lilly, Roche, Johannes W. G. Jacobs Grant/research support from: Roche, Consultant for: Roche
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AB0277 EFFECT OF DISEASE DURATION AND OTHER PATIENT BASELINE CHARACTERISTICS ON OUTCOMES IN TOCILIZUMAB-TREATED RHEUMATOID ARTHRITIS PATIENTS: A POOLED ANALYSIS

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Background: Tocilizumab (TCZ) efficacy and safety in rheumatoid arthritis (RA) have been well established by numerous phase 3 and 4 studies and observational studies.
Objectives: To explore the extent to which disease duration, inflammation, disease burden, and other baseline factors explain variations in outcomes in studies of RA patients treated with TCZ.
Methods: This was a pooled analysis of methotrexate-inadequate responding (IR)/conventional synthetic disease-modifying antirheumatic drug (csDMARD)-IR patients with RA allocated to TCZ (intravenous or subcutaneous, monotherapy + combination therapy) in phase 3 and 4 studies. End points were change from baseline to week 24 in Clinical Disease Activity Index (CDAI) and quality of life (Health Assessment Questionnaire–Disability Index [HAQ-DI]) and week 24 ACR50 and CDAI remission (≤2.8). Using a combination of clinically informed and mathematically driven variable selection techniques, models (with study included as a random effect to account for intracorrelation of observations within each study) were built to optimize fit and explain outcome variance. Analysis of covariance and logistic regression were used for CDAI/HAQ-DI change from baseline and for ACR50/CDAI remission, respectively.
Results: The analyses were performed on 5462 patients from 12 studies. Analysis of baseline characteristics (before TCZ administration) revealed that patients with longer disease duration had been exposed to more csDMARDS and had worse HAQ-DI than patients with shorter disease duration. Statistical modeling of clinical outcomes showed that disease duration accounted for <2% of the variation in HAQ-DI and CDAI change from baseline. Baseline CDAI explained 32% of the variation in CDAI change from baseline. Patients with higher baseline CDAI values tended to have greater improvements, likely due to having more "room" for improvement and to a higher risk for regression to the mean resulting from the fact that inclusion criteria for most trials required defined thresholds of disease activity, including joint counts. Baseline HAQ-DI, neither an inclusion criterion itself nor influenced by other inclusion criteria, explained 15% of the variation in HAQ-DI change from baseline. The odds of achieving ACR50 decreased by 9.2% if disease duration was doubled. The odds of achieving CDAI remission decreased by 15% per 5 additional years of disease duration and decreased by 22% per 10 additional score units of CDAI at baseline.
Conclusion: In this pooled analysis of TCZ-treated RA patients, disease duration explained statistically significant but practically small variations in clinical outcomes. These findings indicate that TCZ treatment outcomes are not heavily influenced by disease duration or other baseline characteristics.
Disclosure of Interests: Andrea Rubbert-Roth Consultant for: Chugai, Eli Lilly, Roche, and Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Hexal/Novartis, Janssen, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, and Sanofi, Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Jenny Devenport Employee of: F. Hoffmann-La Roche, Paris N. Sidiropoulos Shareholder of: Roche, Employee of: Genentech, Yves Luder Shareholder of: F. Hoffmann-La Roche, Employee of: F. Hoffmann-La Roche, Michael Edwardes Consultant for: Roche, Johannes W. G. Jacobs Grant/research support from: Roche, Consultant for: Roche
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AB0278 DISCRIMINANT VALIDITY OF THE HANDGRIP STRENGTH TEST IN PATIENTS WITH RHEUMATOID ARTHRITIS: A COHORT STUDY

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Background: Hand involvement is one of the major determinants of disease outcome affecting the ability to perform activities of daily living and other functional activities in rheumatoid arthritis (RA). Handgrip strength (HS) provides a clinically validated marker of functional disability.
Objectives: The aim of this study was to assess discriminant validity of HS and to compare it with the Quick Disabilities of Arm Shoulder and Hand (Quick-DASH) (1), Arthritis Impact Measurement Scales 2 (AIMS-2), Hand Health Assessment Questionnaire (Hand HAQ) and Recent-Onset Arthritis Disability **(**ROAD) upper extremity index (2).
Methods: In this transversal study, a total of 291 patients with RA responding to the ACR 2010 criteria were evaluated. HS was measured twice for both hands by the use of an electronic grip device. The instrument consists of a cylindrical-shape grip device made of 5 force sensors connected to a microcontroller. The correlations between indices were studied through the Pearson's correlation coefficient (r). The discriminatory ability of HS [cut-off values, male ≤ 27Kg, female ≤16Kg], QuickDASH [range 0-100], AIMS-2 hand/finger function [range 0-10], Hand HAQ [range 0-21], and ROAD upper extremity function [range 0-10] were assessed using receiver operating characteristic (ROC) curves analysis. The external anchor was the general question on Patient Acceptable Symptom State (PASS) (3).
Results: The 239 female and 52 male patients (sex ratio: 4.5F/1M) were of a mean age of 56.5 ±12.3 years (20–81) and a disease duration of

8.5±3.3 years (2 months–22 years). The HS mean (Kg) was 20.9±7.1 [95%CI 20.07-21.7]. The Quick-DASH mean was 28.08±11.90 [95%CI 26.7–29.45]. The AIMS-2 hand and finger mean score was 4.5±2.21 [95%CI 4.24–4.75]. The Hand HAQ mean score was 9.8±4.3 [95%CI 9.3-10.31] and the ROAD-upper extremity mean score was 4.75±2.11 [95%CI 4.5–5]. A positive statistically significant correlation was noted between the five indices (p<0.0001). The area under the ROC (AUC-ROC) were similar in all the measures although the HS showed the greatest discriminative ability (Table I and Figure 1).

Table 1. ROC curve analysis for the discriminatory power of functional disability, according to the different measures

Variable	AUC	SE [a]	95% CI [b]
AIMS-2 hand/finger function	0,839	0,0317	0,792 to 0,879
Hand HAQ	0,846	0,0306	0,799 to 0,885
QuickDASH	0,863	0,0239	0,818 to 0,900
ROAD upper extremity function	0,816	0,0279	0,766 to 0,858
Handgrip strength (Kg)	0,900	0,0206	0,860 to 0,932

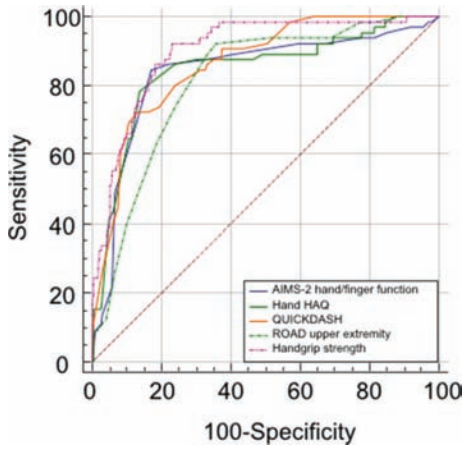


Figure 1. ROC of measures of upper extremity disease activity measures used in rheumatoid arthritis. ROC illustrating the relationship between sensitivity and complement of specificity (100-specificity) in RA for functional measures using PASS as an external indicator.

Conclusion: HS is a good alternative to the self-assessment functional indices for the evaluation of functional disability in RA. The use of an electronic grip device for HS measurement makes it easier to collect data and should be applied in both clinical trials and routine clinical care settings.

REFERENCES

[1] Salaffi F, Di Carlo M, Carotti M, Farah S. "**Validity and interpretability of the QuickDASH in the assessment of hand disability in rheumatoid arthritis**". Rheumatol Int. 2018 Dec 3.
[2] Salaffi F, Carotti M, Gutierrez M, Di Carlo M, De Angelis R. "**Patient Acceptable Symptom State in Self-Report Questionnaires and Composite Clinical Disease Index for Assessing Rheumatoid Arthritis Activity: Identification of Cut-Off Points for Routine Care**". *Biomed Res Int.* 2015
[3] Salaffi F, Stancati A, Neri R, Grassi W, Bombardieri S. "**Measuring functional disability in early rheumatoid arthritis: the validity, reliability and responsiveness of the Recent-Onset Arthritis Disability (ROAD) index**". *Clin Exp Rheumatol.* 2005 Sep-Oct;23(5 Suppl 39):S31-42.

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AB0279

RENAL INVOLVEMANT AND CAUSES OF DEATH IN RHEUMATOID ARTHRITIS PATIENTS ACCORDING TO THE AUTOPSY DATA

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Background: Renal involvement is a clinically significant manifestation in rheumatoid arthritis (RA) patients with potential influence on the treatment, prognosis and outcome of this disease while rare publications are available on kidney damage in RA [1,2].
Objectives: To estimate the frequency and characteristics of renal involvement and causes of death in RA patients on the basis of autopsy data reports and postmortem microscopic examinations.
Methods: We have analyzed 21 814 autopsy data reports performed during 10-year period (2001-2010) and 6720 cases of autopsy performed 5 years later (2016-2018) in the Minsk City Clinical Pathologoanatomic Bureau (The Republic of Belarus).
Results: For the period 2001-2010 autopsies were performed in 110 RA patients: 91 women and 19 men of 67.0 (13.1) years old, M (SD). Renal involvement was revealed in 75 patients (68.2%). The most common type of renal involvement was secondary AA amyloidosis - 44 patients (40%). Other types of revealed renal lesions (n=31, 28.2%) were mesangial proliferative glomerulonephritis (n=3; 2.7%), nephroangiosclerosis (n=14, 12.8%), tubulointerstitial nephritis (n=2, 1.8%), chronic pyelonephritis (n=10, 9.1%) and renal vessel vasculitis (n=2, 1.8%).
The main cause of death in RA patients with amyloidosis was end-stage renal disease (ESRD, 43.2%), whereas in other patients the common causes of death were cardiovascular events (43.2%) and secondary infections (33.3%). In case of secondary amyloidosis the deposits of amyloid were found in kidney of all RA patients (100%), in adrenal glands – in 36.4% and in spleen – in 34.1% of RA patients. Amyloid deposits in other internal organs were not nearly as common.
In 2016-2018 50 patients with RA have been autopsied with mean age of death 72.0 (15.2) years old. Renal involvement was revealed in 34 (68.0%) of autopsies: as secondary amyloidosis in 29 patients (58.0%) and as focal segmental glomerulosclerosis or mesangial proliferative glomerulonephritis in 5 patients (10.0%). The most common cause of death in this group of RA patients were cardiovascular events (58.0%), fatal infectious complications developed in 16.0% of patients, ESRD was revealed only in 4.0% of patients.
Conclusion: 1. We have revealed an increase in secondary amyloidosis frequency in RA patients over the studied period of time from 40% to 58% (p=0.041, Fisher's exact test) while ESRD as a cause of death in RA patients decreased from 17.3% to 4% (p=0.023, Fisher's exact test).
2. Secondary amyloidosis is the most common type of renal involvement in RA according to the autopsy data.

REFERENCES

[1] Makino H. et al. // Mod. Rheumatol. 2002;12(2):148-54.
[2] Icardi A. et al. // Reumatismo. 2003;55(2):76-85.

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AB0280

DIFFERENCE BETWEEN PATIENT'S GLOBAL HEALTH AND PATIENT'S GLOBAL ASSESSMENT OF DISEASE ACTIVITY, AND DIFFERENT FACTORS INFLUENCE ON THESE SCALES IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Evaluation of rheumatoid arthritis (RA) activity is crucial measurement in achieving remission or low disease activity. Visual analogue scale (VAS) by patient's evaluation has been used for the outcome measure for RA patients because of its feasibility, reliability, sensitivity to change, and it directly reflects the patient's overall perspective. Patient's evaluation is a component of multiple composite indices used in assessing RA activity and treatment response. There are two measurements that patient's evaluation. One is patient's global assessment of disease activity (PtGA), and the other is patient's assessment of global health (PtGH)[1)]. PtGA was originally developed as a component of American College of Rheumatology Core Set and used for Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI); while PtGH was originally developed as a component of 28-joint Disease Activity Score (DAS28). PtGA and PtGH have been considered equivalent in a

large scale of study[2]. In daily practice or observation, "patient's VAS" is usually used without specifying whether it refers to PtGA or PtGH. The factors which influence the change in PtGA or PtGH have not been demonstrated concomitantly in daily practice.

Objectives: We investigated the difference between PtGA and PtGH, especially each change obtained after intensification of treatment in 12 weeks and identified the factors that influence on each measurement in RA patients.

Methods: Consecutive patients were enrolled to this retrospective study at our hospital from October 2017 to September 2018. Demographic and clinical data at enrollment as well as treatment regimens were collected by review of medical charts. At first, we examined the baseline data and the changes in 12 weeks of PtGA and PtGH in their relations. The second, we divided those patients into two subsets according to medications intensified by methotrexate (MTX) subset and biological disease-modifying antirheumatic drugs (DMARDs) or janus kinase (JAK) inhibitor (B/J) subset. We compared the difference of the changes in PtGA from the baseline to 12 weeks (ΔPtGA) and those in PtGH (ΔPtGH) between MTX subset and B/J subset. Finally, the logistic regression analysis was performed to identify factors that differently influence for each scale in 12 weeks.

Results: Consecutive 38 RA patients were enrolled. Women were 76%. The median age [IQR] was 66.5 [55-75] years old. Disease duration was 2.5 [1-15] years. DAS28 was 2.61 [2.02-3.17]. SDAI was 16.8 [11.1-24.6] and CDAI was 15.3 [9.38-23.9]. MTX was initiated or increased in 24 patients (63%). The baseline median dose of MTX was 6 [3.5-8] mg/week. Biologics or JAK inhibitor were initiated in 8 patients (21%); tocilizumab (n=5), golimumab (n=1), abatacept (n=1) and tofacitinib (n=1). Other DMARDs were used in 6 patients (16%). ΔPtGH in 12 weeks was -1.68 ($p<0.01$), and ΔPtGA in 12 weeks was -2.22 ($p<0.01$). ΔPtGH and ΔPtGA correlated significantly ($r=0.785$, $p<0.01$). ΔPtGA in MTX subsets was not different from that in B/J subsets in ($p=0.50$) and ΔPtGH was not either ($p=0.57$). No significant improving factor in ΔPtGA was identified, whereas, woman ($p<0.05$) and usage of steroid ($p<0.01$) were improving factors in ΔPtGH.

Conclusion: Intensification of treatment significantly improved in both ΔPtGA and ΔPtGH but we need to pay attentions that there were different improving factors between these two patient's measuremet.

REFERENCES

[1] Koevoets R, et al. Simplified versions of the original disease activity score: validation in BeSt trial. Ann Rheum Dis 2011; 70: 1471.

[2] Khan NA, et al. Patient's global assessment of disease activity and patient's assessment of general health for rheumatoid arthritis activity assessment: are they equivalent? Ann Rheum Dis 2012; 71: 1942.

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AB0281 UTILIZATION OF SMART PHONE APPLICATION TO ASSESS THE DISEASE OUTCOMES IN RHEUMATOID ARTHRITIS: SMART- RA STUDY

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder which if not managed properly leads to joint destruction, disability, poor quality of life and premature mortality. Disease modifying antirheumatic drugs (DMARDs) have considerably improved disease outcome in RA. However, poor patient compliance significantly limits the benefits that could be accrued from DMARDs. In a technology driven era, with more people having access to smart phones, unique opportunities exist for use of phone-based technologies to improve patient care in chronic diseases. This study aims to investigate whether the use of HealthCius smart phone application for self management can influence quality of life for patients with RA and improve inflammatory disease activity.

Objectives: To investigate the impact of smart phone application (HealthCius) on inflammatory disease activity and quality of life in RA.

Methods: 38 RA patients fulfilling the 2010 Rheumatoid Arthritis Classification Criteria were recruited. Subjects were randomized into 2 groups. First, having access to a smart phone were assigned to the intervention group using the Healthcius application (n=23) and second, the control group not using the application (n=15). The patients in two groups received standard treatment of RA. The application was designed after obtaining feedback from health care providers, patient counselors and RA patients using a questionnaire. To the patients, the app was their individual treatment plan. It helped them comply with the plan by providing an easy to refer checklist, reminders, alerts and a visual dashboard of their progress through the day. The app served as the doctor's virtual assistant inside the patient's smart phone. For the doctor, it was a live dashboard of all patients and their real time compliance levels. The data reported by the patients was available to the doctor in the form of time sliced charts and trend lines. Therefore, this app is designed to leverage technology to shift the patients' focus every day on to their treatment plan thereby driving up compliance and better health outcomes.

Outcome measures included erythrocyte sedimentation rate (ESR), C-Reactive protein (CRP), disease activity score (DAS28) and health assessment questionnaire (HAQ-DI) at baseline and at 12 weeks.

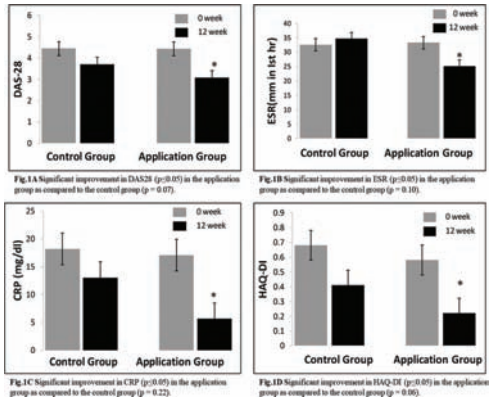


Figure 1

Results: Baseline characteristics were similar between groups with no significant difference. There was a significant difference between the control and intervention group for DAS28 ($p<0.05$), ESR ($p\leq0.05$), CRP ($p\leq0.05$) and HAQ-DI ($p\leq0.5$) after 12 weeks in favor of smart phone application. Analysis within the groups revealed significant improvement in DAS28 ($p<0.05$) (Fig.1A), ESR ($p=0.01$) (Fig.1B), CRP ($p=0.001$) (Fig.1C) and HAQ-DI ($p=0.01$) (Fig.1D) in the application group as compared to control group. Impact of DMARDs usage was also evaluated at the end of the study and it was found that the average drug usage of DMARDs was more in control group than the intervention group.

Conclusion: The study suggested that there was greater improvement in inflammatory disease activity and quality of life in smart phone application assisted RA patients suggesting that smart phone technology can be used to leverage health benefits in RA.

REFERENCE

[1] Azevedo R, Bernardes M, Fonseca J, Lima A. Smartphone application for rheumatoid arthritis self-management: cross-sectional study revealed the usefulness, willingness to use and patients' needs. Rheumatol Int. 2015 Oct; 35(10):1675-85. doi: 10.1007/s00296-015-3270-9. Epub 2015 Apr 24.

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AB0282 SYSTEMATIC REVIEW OF STUDIES REPORTING ON COGNITIVE FUNCTION IN RHEUMATOID ARTHRITISCOMPARED TO THE GENERAL POPULATION

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Background: Rheumatoid arthritis (RA) patients often complain of "brain fog" as a symptom when their disease activity is greater. The exact areas of cognition that this "brain fog" means are not yet understood. Previous studies have found that people with RA have lower cognitive function (CF) than healthy controls and age based population norms. A study by Shin et al which looked at prevalence of cognitive impairment

in persons with RA found that 31% of their 115 person sample was cognitively impaired and stated that further studies should be done to identify the specific domains of cognitive function that are most commonly affected (1). In this project, I will be looking at and summarizing all the data and findings that have been collected and reported on CF in the RA population and seeing which domains of cognition differ and which do not differ when compared to the general population and aged based population norms.

Objectives: To conduct a systematic review of studies reporting on cognitive function (CF) in rheumatoid arthritis (RA) patients compared to non-RA populations (based on comparison with a control group or age-based population norms).

Methods: We conducted a comprehensive literature search of MEDLINE, EMBASE, and PUBMED databases using the following search terms: rheumatoid arthritis or arthritis or inflammatory arthritis, and cognitive function or cognition. The search was conducted with no limit for years, and confined to only articles in English or French. After title and abstract screen, relevant articles were selected for review. Only full length articles were considered. Study selection criteria included: 1) must be presenting original data, 2) must contain RA group with confirmed diagnosis, 3) must be reporting on CF in RA, 4) must use a validated measure of CF (self-reported or from conducting CF tests), and 5) must contain a healthy control group or age-based populations norms. Selected articles were critically appraised using the SIGN Methodology Checklist and data extracted using a standardized form.

Results: Our initial literature search yielded 747 titles, and after screening for irrelevant titles and duplicates, 28 abstracts remained. Upon excluding non-full length articles and articles which did not report on CF, 13 abstracts remained. Of these 13 articles, 8 met our selection criteria. All studies were published after the year 2000, 3 were from the USA, 1 from Canada, 1 from the UK, 1 from Australia, 1 from Egypt, and 1 from Taiwan. Sample sizes for RA and control groups varied from 15 to 120. Of these 8 articles, 6 found a significant difference in cognitive function in the RA group compared to control group or age-based population norms in at least one domain of CF. All articles that found a significant difference in CF used standardized neuropsychological tests. Domains of CF that differed included fluency, attention, visual-spatial learning, memory, decision making time, and simple reaction time. Domains of CF that were not found to differ from general population across all studies included reasoning, comprehension, and intelligence (IQ).

Conclusion: Overall, 75% of the articles reviewed found a significant difference in at least one domain of CF in RA patients compared to healthy controls or age-based population norms. The domains of CF most commonly affected are those related to processing and speed rather than intellectual ability. Further studies are needed to explore these differences in greater depth and to understand the underlying reasons for these differences.

REFERENCE

[1] Shin, So Young, Patricia Katz, Margaret Wallhagen, and Laura Julian. 2012. “Cognitive Impairment in Persons with Rheumatoid Arthritis.” Arthritis Care & Research.

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AB0283 IDENTIFICATION OF NEW AUTOANTIBODIES FOR RHEUMATOID ARTHRITIS USING HUMAN PROTEOME MICROARRAYS

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Background: Rheumatoid arthritis is an autoimmune disease characterized by symmetrical small arthritis. Anti-cyclic citrullinated peptide antibodies and rheumatoid factor are commonly used to diagnose RA[1]. However, the early diagnosis of RA is sometimes difficult, due to the heterogeneity and negative anti-CCP antibody or RF in some patients. Therefore, it is urgent to find autoantibodies with high sensitivity and specificity as diagnostic markers for RA.

Objectives: To screen autoantibodies of RA with high sensitivity and specificity using human proteome microarrays[2].

Methods: Firstly, a case-control method was used to analyze the serum antibodies of RA patients using human proteome microarray which composed of 20,000 proteins, and identified RA-related antibodies. Then, expanded the sample size and analyzed the expression of these candidates between RA patients and healthy controls.

Results: The serum of five RA patients and five healthy controls were selected to detect the RA-related autoantibodies by microarray, and 25 candidates were screened. Then the IgG and IgM RA-focused microarrays composed of the 25 proteins were screened with additional cohorts of 72 RA patients and 106 healthy controls. The results of IgG protein microarray showed: (1) Expression of these 25 autoantibodies in RA patients was significantly higher than those in healthy controls (P<0.05). (2) There was nodifferentially expressed protein between anti-CCP antibody and RF-negative RA patients (n=18) and anti-CCP antibody and/or RF-positive RA patients (n=54) (P>0.05). (3) ROC analysis showed that the combination of anti-RBPJ, anti-SH3BGR and anti-PAFAH1B3 autoantibody can be highly RA-specific biomarkers, with 66.7% sensitivity and 74.2% specificity, and the area under the curve is 0.734; meanwhile the sensitivity and specificity of the anti-CCP antibody and RF-negative RA patients diagnosis were 77.8% and 65.6%, and the area under the curve was 0.720. The results of IgM protein microarray showed: (1) Only 10 out of the 25 candidates’ expression was significantly higher in RA patients than healthy controls (P<0.05). (2) Compared with anti-CCP antibody and/or RF-positive patients, the expression of anti-PAFAH1B3, anti-RBPJ, anti-SH3BGR, anti-UBA5, anti-ANP32A, anti-PAGE2, anti-SHFM1 and anti-PDE1B was found significantly higher in anti-CCP and RF-negative patients (P<0.05). (3) ROC analysis showed that anti-PAFAH1B3 antibody was identified to diagnose RA with 76.2% sensitivity and 72.9% specificity, and the area under the curve was 0.768; however, there were no significance for the diagnosis of anti-CCP antibody and RF-negative RA patients (P=0.160).

Conclusion: The combination of IgG-type antibodies anti-RBPJ, anti-SH3BGR and anti-PAFAH1B3, the IgM-type antibody anti-PAFAH1B3 as well, has high sensitivity and specificity for the diagnosis of RA; especially the IgG-type autoantibody combination has great value for the diagnosis of anti-CCP and RF-negative RA patients.

REFERENCES

[1] Silveira IG, et al. Anti-CCP antibodies have more diagnostic impact than rheumatoid factor (RF) in a population tested for RF. Clinical Rheumatology, 2007. 26(11): p. 1883-1889.
[2] Song Q, et al. Novel Autoimmune Hepatitis-Specific Autoantigens Identified Using Protein Microarray Technology. Journal of Proteome Research, 2010. 9(1): p. 30-39.

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AB0284 HEMATOLOGICAL MARKERS OF SYSTEMIC INFLAMMATION CORRELATE WITH CLINICAL, LABORATORY AND ULTRASOUND DISEASE ACTIVITY PARAMETERS IN RHEUMATOID ARTHRITISPATIENTS

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Background: An accurate measurement of disease activity and inflammation is essential for customizing the most appropriate management and treatment strategy in patient with rheumatoid arthritis (RA). Current data suggest that hematological markers of systemic inflammation [peripheral blood neutrophil-to-lymphocyte (NLR), platelet-to-lymphocyte (PLR) and monocyte-to-lymphocyte (MLR) ratios] could be used as novel, sensitive measures of inflammatory response, additionally to conventional laboratory and clinical markers [erythrocyte sedimentation rate (ESR), C-reative protein (CRP), Disease Activity Score of 28 joints (DAS28), tender joint count (TJC), swollen joint count (SJC)]. The ultrasonography US) of joints enables the disease activity assessment by quantifying thickening and vascularity of the synovium.

Objectives: The goal of the study was to assess the relationship of NLR, PLR, MLR with the conventional disease activity markers (ESR, CRP, DAS28, TJC, SJC) and results of joints US, in patients with RA.
Methods: The study was conducted in the consecutive 72 patients with RA (60 women, 12 men), with the mean (SD) age 53.4 (8.9) and disease duration 16.8 (10.3) years. The following procedures were assessed for all patients: joint counts,DAS28, complete blood cell counts, ESR, CRP, US of 24 small joints.
Results: The mean (SD) values of hematological markers were as follows: NLR 3.24 (2.7) (range 0.2-13.96); PLR 193.26 (88.3) (range 71.2-560.8); MLR 0.3 (0.16) (range 0.06-0.87). The mean values of NLR and PLR were significantly lower in patients with low (DAS28 ≤3.2) vs moderate/high (DAS28 >3.2) disease activity; respectively NLR 2.4 (1.7) vs 4.0 (3.2), p=0.004; PLR 168.7 (58.0) vs 215.8 (104.9), p=0.4. Hematological markers of systemic inflammation were significantly, positively correlated with clinical, laboratory and US markers of the disease activity. Significant correlations were found between: NLR and DAS28, TJC, SJC, ESR, CRP, vascularity of synovium in US; PLR and DAS28, TJC, SJC, ESR, CRP, vascularity and hypertrophy of synovium in US; MLR and DAS28, SJC, ESR, CRP, vascularity and hypertrophy of synovium in US. In multiple regression test significant correlations were confirmed for: NLR and SJC (p=0.008), ESR (p<0.001), CRP (p<00.1), vascularity of synovium in US (p=0.02); PLR and ESR (p=0.03), CRP (p=0.03); MLR and DAS28 (p=0.04), ESR (p<0.001), hypertrophy of synovium in US (p=0.02).
Conclusion: The results of the study suggest that hematological markers of systemic inflammation (NLR, PLR, MLR) may serve as reliable, inexpensive and effective measure of inflammation in RA. The strong association with US imaging is an attractive result because of its predictive value and usefulness in clinical practice
Disclosure of Interests: Bozena Targonska-Stepniak Speakers bureau: Sandoz, Berlin-Chemie, Robert Zwolak: None declared, Mariusz Piotrowski: None declared, Maria Majdan Speakers bureau: MSD, UCB, Abbvie, Roche
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AB0285 PREDICTORS OF UNACCEPTABLE PAIN, AND UNACCEPTABLE PAIN WITH LOW INFLAMMATION, IN EARLY RHEUMATOID ARTHRITIS

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Background: Pain is a major symptom in many patients with rheumatoid arthritis (RA). In early RA, pain is usually due to active synovitis, but over the disease course some patients experience pain without elevated laboratory markers of inflammation.
Objectives: To investigate predictors of unacceptable pain, and unacceptable pain with low inflammation, in patients with early RA.
Methods: Consecutive patients with early RA (symptom duration <12 months), recruited in 1995-2005 from a defined area, were followed through 5 years. Patients were managed according to usual care, with no pre-specified treatment protocol. Pain was assessed using a visual analogue scale (VAS; 0-100 mm). Unacceptable pain was defined as VAS pain>40 based on the patient acceptable symptom state (PASS) (1), and low inflammation as CRP<10 mg/l (2). Baseline predictors of unacceptable pain, and of unacceptable pain with low inflammation, were evaluated using logistic regression analysis.
Results: A total of 233 patients with early RA (73% female, 57% anti-CCP positive, mean age 60 years, median symptom duration 7 months) were included. Of these, 179 attended the 5-year follow-up. At 5 years, 34% had unacceptable pain, and 23% had unacceptable pain with low inflammation. High VAS scores for pain and patient's global assessment (PGA) at baseline were associated with unacceptable pain at 5 years (Table). There was a negative association between baseline swollen joint count (SJC28) and unacceptable pain at the 5 year follow-up. In multivariate logistic regression analysis including VAS PGA and SJC28, both had an impact on unacceptable pain after 5 years (adjusted odds ratios per standard deviation (SD), with 95% CI 1.78 (1.26-2.52) and 0.61 (0.42-0.89), respectively). Anti-CCP positive patients were significantly less likely to experience unacceptable pain with low inflammation at 5 years (Table).

Table 1.

Baseline predictors of unacceptable pain or unacceptable pain with low inflammation in the early RA cohort after 5 years, bivariate logistic regression

	Unacceptable pain		Unacceptable pain with low inflammation	
Variable	**Odds ratio**	**95 % CI**	**Odds ratio**	**95 % CI**
Female	1.24	0.62 – 2.47	1.87	0.80 – 4.40
RF positive	0.88	0.46 – 1.67	0.54	0.26 – 1.09
Anti-CCP positive	0.77	0.39 – 1.49	0.50	0.22 – 0.98
Erosion	0.62	0.26 – 1.49	0.62	0.22 – 1.72
Age	1.09	0.80 – 1.49	0.97	0.68 – 1.38
Symptom duration	1.28	0.93 – 1.76	1.19	0.83 – 1.71
VAS pain	1.40	1.02 – 1.91	1.34	0.94 – 1.92
DAS28	1.03	0.76 – 1.41	1.00	0.70 – 1.42
SJC28	0.71	0.51 – 0.99	0.70	0.47 – 1.03
TJC28	0.98	0.71 – 1.35	1.04	0.72 – 1.50
HAQ	1.01	0.74 – 1.37	1.01	0.72 – 1.43
CRP > 9 mg/l	0.64	0.29 – 1.41	0.62	0.23 – 1.72
ESR	0.79	0.57 – 1.09	0.74	0.50 – 1.11
VAS PGA	1.60	1.16 – 2.21	1.39	0.98 – 2.00

Odds ratios per SD for continuous variables

Conclusion: More than 1/3 of early RA patients experienced unacceptable pain after 5 years. Extensive synovitis in early RA was associated with a reduced risk of unacceptable pain at 5 years, likely due to positive effects of treatment on inflammation related pain. Non-inflammatory pain may be a greater long term problem in anti-CCP negative patients.

REFERENCES

[1] Tubach, et al. Arthritis Care Res 2012; 64: 1699-707
[2] Lourdudoss, et al. Arthritis Care Res 2018; 70: 205-12.

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AB0286 STATINS TO PREVENT RHEUMATOID ARTHRITIS (STAPRA TRIAL): CHALLENGES IN RECRUITMENT AND RETENTION

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Background: Primary prevention may be possible in subjects at high risk to develop rheumatoid arthritis (RA). We designed a placebo controlled randomized trial to investigate if atorvastatin can halt RA development in persons at risk for this disease (STAPRA, Netherlands Trial Register NTR5265). A statin was chosen because these drugs reduce disease activity in RA (1), hyperlipidemia patients on statins have a lower risk for developing RA (2) and dyslipidemia increased the risk for RA in a seropositive arthralgia cohort (3). We assumed that high risk-subjects would be attracted to this trial. However, we experienced severe difficulties with patient inclusion and treatment adherence.
Objectives: To explore difficulties with patient recruitment and retention.
Methods: The STAPRA study is a multicenter, 3-year, randomized, placebo controlled, double-blind clinical trial to assess the efficacy of atorvastatin 40 mg daily in delaying or preventing RA development in persons at high risk, defined by the presence of arthralgia and the presence of high titers of anti-citrullinated protein antibody (ACPA) or presence of both ACPA and rheumatoid factor (RF). Eligible participants were ≥18 years, did not use lipid lowering agents and had no synovitis. Five centers participated. Our goal was to recruit 220 study subjects based on an expected risk reduction of 21%. The unexpected low recruitment rate prompted us to evaluate the reasons to decline participation or to discontinue the study drug prematurely.
Results: Details were available from the initiating center (Reade) and 1 participating center (Sint Maartenskliniek (SMK)). During a period of 36 months, 164 eligible patients were asked to participate of whom 58 patients (35%) consented. Most common reasons to decline were: unwillingness to use study medication (49%) and the feeling that participation was too time-consuming (14%). Fifty-four patients were randomized since 4 failed screening due to hyperlipidemia or seronegativity on repeated testing. Currently, 11 participants (20%) have developed arthritis. Twelve

dropped out for various reasons, including adverse events (33%). Thirty-one persons are still being followed, but of these 10 stopped study medication after a median of 3 months. The main reason to discontinue therapy was side effects (80%), notwithstanding a standardized approach for dose reduction and temporary discontinuation as needed.

Conclusion: In this RCT in persons at risk for RA we identified a major obstacle to the successful conduction of such trials, namely the difficulty to enter and retain participants. The primary reported reason was unwillingness to use study medication. This is different from many successfully completed trials on optimal medical treatment in early RA patients, where large inclusion goals have been met within a relatively short timeframe and adherence overall was good. This issue is highly relevant to the current inclination to move the start of drug intervention in RA to ever earlier phases. Further research into patients' motivation and barriers for participation in intervention trials in the at risk phase of RA is necessary to enable intervention research in this phase of the disease.

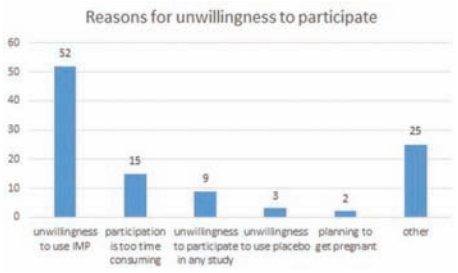


Figure 1

REFERENCES

[1] Xing B, et al. Medicine (Baltimore). 2015;94(8):e572.
[2] Chodick G, et al. PLoS Med. 2010;7(9):e1000336.
[3] van de Stadt LA, et al. Ann Rheum Dis. 2012;71(11):1915-6.

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AB0287

BENEFITS OF PAIN RELIEF ON FATIGUE, FUNCTION, AND QUALITY OF LIFE WHEN JOINT INFLAMMATION IS CONTROLLED IN PATIENTS WITH RA

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Background: The ultimate goals for rheumatoid arthritis (RA) treatment are to achieve disease activity control and the best potential health state throughout the course of disease.[1] In prior analyses of the Phase 3 trial, RA-BEAM (NCT01710358), baricitinib was associated with significant clinical improvements and patient-reported pain relief in RA patients (pts) who had had an inadequate response to methotrexate.[2,3] The additional benefits of pain relief when inflammation is controlled are not well characterized.

Objectives: To quantify the contribution of pain relief to other PROs, fatigue, physical function, and quality of life, in pts who achieved control of inflammation, defined as swollen joint count (SJC) ≤1 and C-reactive protein (CRP) ≤1 mg/dL, at Week (Wk) 24 in a post hoc, pooled analysis of RA-BEAM.

Methods: Among pts with inflammation control, PROs were compared between pts who also achieved thresholds of pain relief at Wk 24 vs those who did not. Pain was measured with a visual analogue scale (VAS, range: 0-100 mm) and divided into ≤20, >20, ≤40, >40 mm.[4,5] PROs included: the Health Assessment Questionnaire-Disability Index (HAQ-DI) normative value (<0.5), to compare with a general population, and minimum clinically important differences (MCID, ≥0.22), SF-36 physical and mental component scores (PCS and MCS) MCID (≥5), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F, range of 0–52, higher scores represent less fatigue) normative value (≥40.1) and MCID (≥3.56). Logistic regression models were adjusted for age, gender, BMI, geographic region, duration of disease, baseline SJC, baseline pain, and baseline value of PRO under evaluation. Missing data were imputed using modified last observation carried forward.

Table 1.

Percentage of patients achieving improvement in PROs by pain relief thresholds in patients who achieved control of inflammation at Week 24

	20 mm threshold			40 mm threshold		
	≤20 mm (N=212)	>20 mm (N=159)	p-values	≤40 mm (N=297)	>40 mm (N=74)	p-values
HAQ-DI <0.5	67	19	<0.0001	56	7	<0.0001
HAQ-DI MCID, 0.22	89	72	<0.0001	84	73	<0.0001
SF-36 PCS MCID, ≥5	81	57	<0.0001	74	58	<0.0001
SF-36 MCS MCID, ≥5	48	44	<0.05	47	44	<0.05
FACIT-F ≥40.1	80	41	<0.0001	71	32	<0.0001
FACIT-F MCID, ≥3.56	77	64	<0.0001	71	70	<0.01

FACIT-F: the Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI: Health Assessment Questionnaire-Disability Index; MCID: minimum clinically important difference; MCS: mental component score; SF-36: 36-item Short Form Health Survey, PCS: physical component score

Results: Of the total 1305 patients in RA-BEAM, 371 pts treated with adalimumab (121/330), baricitinib (187/487), or placebo (63/488) and background methotrexate achieved inflammation control at Wk 24. Among patients who achieved inflammation control, those who also achieved each pain relief threshold were statistically significantly more likely (p<0.05) to report benefit in physical function, general quality of life, and fatigue than patients who did not reach the pain relief thresholds. (Table)

Conclusion: When inflammation is controlled (SJC ≤1 and CRP ≤1 mg/dL), more pain relief is associated with better physical function, quality of life, and reduced fatigue. This may support consideration of pain relief as an additional goal of therapy, even when inflammation is controlled. Further investigation should evaluate this benefit with other patient populations and outcomes.

REFERENCE

[1] Smolen, et al. ARD 2017; 76: 960-77; 2. Taylor, et al. NEJM 2017; 376: 652-62; 3. Taylor, et al. Arthritis Rheumatol 2017; 69 (Suppl 10); 4. Wolfe & Michaud, J Rheumatol 2007; 34: 1674-83; 5. Tubach, et al. Arthritis Care Res 2012; 64:1699-707.

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AB0288 PERSISTENTLY ACTIVE DISEASE IN PATIENTS WITH NEW-ONSET RHEUMATOID ARTHRITIS DURING THE FIRST YEAR OF TIGHT CONTROL AND AGGRESSIVE THERAPY: PREVALENCE AND CLINICAL PREDICTORS IN DIFFERENT CRITERIA SETS

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Background: Early intervention and aggressive therapy of rheumatoid arthritis (RA) improves prognosis, however a substantial proportion of patients under guideline-based care remain persistently active disease (PAD) in the first year.
Objectives: To investigate the proportion of PAD (LDA/MDA/HDA) in real-life practice and identify its prognostic factors in early RA (≤2 years) patients receiving tight-controlled conventional synthetic disease-modifying antirheumatic drugs (csDMARD) treatment at 1 year of follow-up.
Methods: In our observational RA cohort, patients were usually three-monthly followup and step-up csDMARD escalation treatment at the discretion of physicians in the first year. Disease activity and remission were assessed by four commonly-used indices (DAS28-ESR, CDAI, SDAI, and Boolean criteria). Logistic regression was used to estimate odds ratios (ORs) and their 95% confidence intervals (CIs) for PAD by 12 months.
Results: The study included 303 DMARD-naïve early RA patients completing one year follow-up schedule, who were mostly female (72%) with a mean age of 55, and a median disease duration of 6 months. Most patients were in MDA or HDA at baseline and most of them (83.5%) received csDMARDS combination in the first year. 26.4-55.1% of participants did not reach remission by 12 months. Compared to patients experienced remission, patients in PAD were frequently in female, elder, shorter disease duration, and high baseline disease activity components, including SJC, TJC, PGA, EGA, ESR, CRP and glucocorticoids use. In multivariate logistic regression analyses, female (OR=1.34-1.58), increasing age (OR=1.03-1.10), longer disease duration (OR=1.45-1.78), higher baseline SJC (OR=1.11-1.25), EGA (OR=1.02-1.08) showed the independent association with the increased risk for PAD, across all criteria. Higher ESR (OR=1.05) was an independent risk factor for PAD, measured by DAS28-ESR.
Conclusion: Our results indicated around one-third of RA participants receiving guideline-based healthcare had PAD in the first year. Female, increasing age, long disease duration, higher SJC, EGA, and ESR at baseline independently increased the risk of PAD.
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AB0289 PREDICTION OF CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS PATIENTS USING PROTEIN BIOMARKERS AND CLINICAL FACTORS

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Background: The ACC/AHA recommends preventive strategies for patients with a high-predicted risk of atherosclerotic cardiovascular disease (CVD). RA patients are at higher risk for CVD events, yet the role of systemic inflammation and the influence of traditional CVD risk factors are unclear with respect to risk prediction in RA.
Objectives: A simple and accurate algorithm for predicting CVD event risk that considers systemic inflammation might help risk assessment for RA patients and optimize preventive care.
Methods: We derived a U.S. cohort of RA patients by linking multi-biomarker disease activity (MBDA) test data to Medicare claims data. Patients had to have ≥1 year Medicare coverage prior to the date of their first MBDA test, which was designated as baseline. Exclusions were past MI, stroke, or cancer. Follow-up ended at the earliest of: 1) CVD event; 2) death; 3) loss of coverage; or 4) 12/31/2016, the latest date for which the Medicare claims database was evaluated. CVD events were defined as incident MI, stroke or fatal CVD event, and were identified using validated algorithms (PPV >=80%). The leptin-adjusted MBDA score (Curtis et al., *Rheumatology* 2018) and its 12 individual protein biomarkers were evaluated as predictors of CVD events, as were other variables, including demographics, healthcare utilization, CVD-related comorbidities and medications, and RA-related features (e.g. DMARD/biologic use, glucocorticoid use). The cohort was randomly split 2:1 to use 2/3 of patients for training and 1/3 for validation. Cox proportional hazard regression with LASSO was used for variable selection based on minimization of 10-fold cross-validated error + 1 SE. Model calibration (observed vs. expected) and discrimination were assessed for predicted CVD events at 3 years. Analyses are ongoing; model performance results are reported for the cross-validated training data.
Results: A total of 26,261 eligible RA patients were analyzed; mean (SD) age 68.6 (10.2) years, 80.1% female, 72.6% white, 23% diabetes, 43% statin use, 56% methotrexate, 44% on biologics/tofacitinib, 55% steroids, and median (IQR) adjusted MBDA score 40 (32-49). A total of 477 CVD events occurred over mean (SD) follow-up time of 1.7 (1.2) years yielding a CVD incidence rate of 16.5 (95% CI 15.0-18.0)/1000py. The most important predictors in these LASSO-selected models were age, beta-blocker use, sex, diabetes, adjusted MBDA score and a subset of individual MBDA biomarkers. The best performing model had a cross-validated area under the receiver operator curve of 0.70 and good observed: expected prediction at 3 years (Figure).

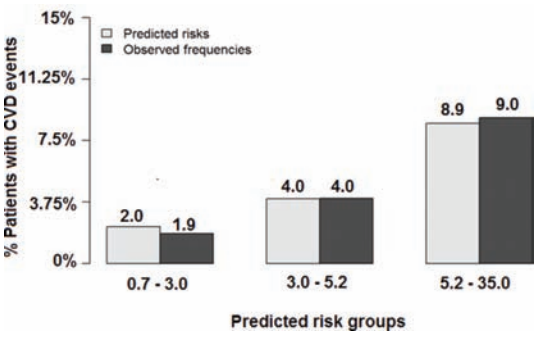


Figure 1

Conclusion: Preliminary results from this approach suggest that a simple algorithm consisting of a limited number of protein biomarkers and clinical measures can provide an accurate method to predict short-term CVD risk in RA.**Acknowledgement:** The work for this abstract was funded by an industry/academic collaboration between Myriad and University of Alabama at Birmingham.
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AB0290 TREAT-TO-TARGET (T2T) IS NOT ENOUGH: IDENTIFY FACTORS LEADING TO A MISMATCH BETWEEN T2T AND HAQ AMONG RA PATIENTS THROUGH DATA MINING FROM SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: T2T, achieving a DAS28 score lower than 2.6 (remission) or below 3.2 (low disease activity), is the main management strategy recommended by ACR and EULAR. HAQ is the most widely used in assessments of physical function in RA. However, the T2T may not always associate with good HAQ.
Objectives: To quantify phenomenon of mismatch between the T2T and the HAQ in RA patients and identify influential factors from real-world data mining in SSDM.

Methods: SSDM is a novel mobile tool of disease management. The patients were trained to master SSDM by health care professionals and conducted their DAS28 and HAQ self-assessments. The data were synchronized to the mobile of physicians and uploaded onto cloud for analysis.

Results: From Jun 2014 to Jan 2019, 44,698 RA patients from 587 hospitals in China used SSDM, of which 32,058 patients made 67,845 DAS28 and HAQ self-assessments. The T2T rates were 27% at baseline, and 60% after 6 months among 4,768 patients who have been followed up longer than 6 months.

In 25,820 assessments of patients who achieved T2T at baseline or repeat assessments, 76% (19,552) assessments had normal physical function (HAQ = 0), but 24% (6,268) were with HAQ score higher than 0, which mean score for 8 functional tests was 3.67, indicating physical dysfunction. The "Bend down to pick up clothing from the floor" was the one being affected most, with a mean score of 0.81, significantly higher than other functional test score, P<0.001. The mean numbers of tender and swollen joints among T2T patients were 1.53 and 1.32 respectively. The analysis of correlation between physical dysfunction and the affected joints showed the knees were the major contributor to the mismatch, following by wrist and shoulders. Table 1 showed the mean scores for each functioning category in HAQ and the top target joints.

In patients who did not achieve T2T, 32% had HAQ scores of 0, showing that these patients had normal physical function despite failure in achieving T2T. The mean number of tender and swollen joints in these patients was 4.31 and 2.85, respectively. The affected joints were mainly hand joints. According to the cluster weights for the impacts of affected joints on physical function, the weighted coefficient of affected joints impacting factors (IF) on physical function was obtained. The highest IF was for knee (4), followed by wrist (3.4), shoulder (2.3), middle finger (2.1), elbow (2), index finger (2), other fingers (1), respectively.

Conclusion: 1/4 RA patients suffer from physical dysfunctions even though T2T are achieved. Diseased knees, wrists and shoulders are the top three joints that lead to corresponding physical dysfunctions and contribute to a mismatch between T2T and HAQ. Conversely, diseased elbow and finger joints are less likely to cause physical dysfunction. Therefore, not all joints are equal. Joints of knees, wrists and middle fingers deserve higher IF (2.1-4) in evaluation of disease activity. T2T guided by current DAS28 lead to mismatch with HAQ and may be misleading. A modified DAS28 should be considered with IF and a special attention should be paid on these top three joints for rehabilitations.

Table

Table 1. The mean scores for each functioning category in HAQ and the top 3 target joints.

	Mean score	Knee	Wrist	shoulder	middle finger	elbow	Index finger	Other fingers
1 Dress yourself including shoelaces and buttons	0.43		0.43	0.34	0.22			0.12
2 Get in and out of bed	0.3	0.3	0.24	0.15				
3 Lift a full glass to your mouth	0.32		0.32	0.26	0.16			
4 Walk outdoors on flat ground	0.38	0.38	0.3	0.19				
5 Wash and dry your body	0.48		0.48	0.38		0.24		
6 Bend down to pick up clothing from the floor *	0.81*	0.81	0.65	0.42				
7 Turn faucets (or cocks) on and off	0.47		0.47		0.38		0.24	
8 Get in and out of a car	0.48	0.48	0.38	0.24				
Total scores	3.67	1.97	3.27	1.98	0.76	0.24	0.24	0.12
Mean score	0.46	0.49	0.41	0.28	0.25	0.24	0.24	0.12
impact factors		4	3.4	2.3	2.1	2	2	1

* p<0.001

Disclosure of Interests: None declared

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AB0291 SHORT TERM EFFECTIVENESS OF JANUS KINASE INHIBITORS AND BIOLOGIC DRUGS IN RHEUMATOID ARTHRITISPATIENTS FROM THE APULIAN REGISTRY BIUOPURE

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Background: Randomized clinical trials have provided evidence that janus kinase inhibitors (Jak-i) induce a quick response in patients affected with rheumatoid arthritis (RA), especially in terms of perception of pain. However, a few data are available on this issue in RA patients upon treatment with Jak-i in the settings of real life.

Objectives: We aimed at evaluating the early clinical response in RA patients treated with Jak-i or biologic disease modifying drugs (bDMARDs) from the Apulian registry BIOPURE.

Methods: We retrospectively evaluated patients with RA, according to 2010 ACR/EULAR Criteria, who begun Jak-i or biologic drugs from December 2017 (since baricitinib was available onto the market) through December 2018. We included 189 patients (female 146, 77.25%) with age (mean ±SD) of 57.8 ±12 years. Of them, 143 (75.6%) were treated with bDMARDs, whereas 46 (24.3%) were on JAK Inhibitors, namely baricitinib or tofacitinib (Table 1). Disease activity score on 28 joints (DAS28) and reported pain on a 0-100 visual analogue scale (VAS) were estimated at baseline, 3 and 6 months. Intra-group changes from baseline of DAS28 and VAS-pain was assessed by t-test. Mean difference changes in VAS-pain at 3 months between Jak-i and bDMARDs were compared by t-test. Possible predictors of the achievement of EULAR good-response at 3 months were estimated by binary logistic multiple regression analysis.

Table 1. Frequency of different Jak-I and bDMARDs

	n	%
Tofacitinib	4	2.12
Baricitinib	42	22.22
Abatacept	43	22.75
Adalimumab	13	6.88
Anakinra	1	0.53
Certolizumab	18	9.52
Etanercept	17	8.99
Golimumab	5	2.65
Infliximab	4	2.01
Rituximab	4	2.12
Tocilizumab	38	20.11
Total	189	100.00

Results: Considering the whole cohort, mean DAS28 at baseline was 3.70 (±1.4) and significantly decreased to 2.76 (±1.1) at 3-months (p<0.001) and to 2.99 (±1.4) at 6-months (p<0.001). Likewise, VAS-pain was significantly improved from baseline, either at 3 and 6 months (p<0.001). Also VAS-pain significantly decreased in patients on treatment with Jak-i (3 months p=0.0001, 6 months p=0.008) and bDMARDs (3 months p=0.0001, 6 months p=0.009). Of note, mean difference from baseline of VAS pain at 3 months was significantly higher in patients treated with JAK-i than in those on bDMARDs (p=0.0005) (Figure 1). An EULAR good response was reached by 37.5% at 3 months and by 56.4% of patients at 6 months. In particular, patients with JAK Inhibitors met this goal at 3 months significantly more frequently than others (p=0.003). EULAR good response at 3 months was strongly associated with Jak-i treatment (OR 3.1, 95%CI 1.4-6.6).

Conclusion: Despite the usual flaws of the analysis from registries, such as comorbidities, concomitant therapies, adherence, different disease activity or line of treatment, our study suggests that Jak-i allow to achieve an early clinical benefit in terms of patient reported pain at greater extent than classical bDMARDs in real-world.

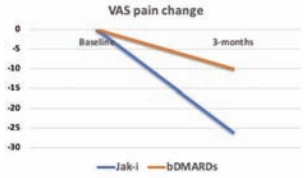


Figure 1. Comparison of mean difference at 3 months from baseline between Jak-i and bDMARDs.

Disclosure of Interests: Carmelo Zuccaro Consultant for: C Zuccaro has received consultancy fees and/or speaker honoraria from MSD, AbbVie, Novartis, Pfizer, Janssen outside this work, Speakers bureau: C Zuccaro has received consultancy fees and/or speaker honoraria from MSD, AbbVie, Novartis, Pfizer, Janssen outside this work, Leonardo Santo Consultant for: L Santo has received consultancy fees and/or speaker honoraria from AbbVie, MSD, Novartis UCB outside this work, Speakers bureau: L Santo has received consultancy fees and/or speaker honoraria from AbbVie, MSD, Novartis UCB outside this work, Laura Quarta: None declared, Nicola Maruotti Speakers bureau: N Maruotti has received speaker

honoraria from Pfizer outside this work, Giorgio Carlino Consultant for: G Carlino had has received consultancy fees from Pfizer, Janssen, AbbVie, MSD, BMS., Romano Bucci Consultant for: R Bucci has received consultancy fees and/or speaker honoraria from Pfizer, Sanofi, MSD, BMS, Speakers bureau: R Bucci has received consultancy fees and/or speaker honoraria from Pfizer, Sanofi, MSD, BMS, Angelo Semeraro Speakers bureau: A Semeraro has received speaker honoraria from Sanofi, Roche, AbbVie, BMS, MSD, Novartis, Antonio Marsico: None declared, Daniela Mazzotta: None declared, Paola Chiara Francesca Falappone Consultant for: PC Falappone had received consultancy fees and/or speaker honoraria from Amgen, Abbott, MSD, BMS, outside this work, Speakers bureau: PC Falappone had received consultancy fees and/or speaker honoraria from Amgen, Abbott, MSD, BMS, outside this work, Florenzo Iannone Consultant for: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work

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AB0291B A COMPARISON OF THE JOINTS ULTRASONOGRAPHY IN THE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED BY BIOLOGICAL AGENTS AND THE CORRESPONDING SYNOVIAL HISTOLOGICAL FINDINGS

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Background: In the treatment of Rheumatoid arthritis (RA), early diagnosis and early treatment with tight control have become increasingly important with the advent of biological therapy. Ultrasonography (US) of the various joints enables the real-time evaluation of synovial hypertrophy, effusion and bone erosion, Power Doppler (PD) ultrasound is able to identify both subclinical synovitis and early erosive disease.
Objectives: The objectives of this study were to investigate whether the image of US at the operated joint reflect synovium histological findings or clinical indicators, and to compare the results in the patient treated by non-biological agent (NonBio) and biological agent (Bio)
Methods: RA related orthopaedic surgery was performed at 1287 joints including 17 shoulders, 160 knees, 96 elbows, 378 wrists, 364 fingers, 38 ankles and 234 toes during the period between January 2011 and December 2018 at our rheumatic center. Preoperatively, ultrasound evaluations were performed and grade of PD signal was determined at the part with the highest signal. PD signal consists 4 grades from grade 0 to 3. The operations were performed within one week after the ultrasound evaluations. Rooney score of the synovium histology, DAS28-ESR (4), MMP-3, CRP were investigated. Rooney score represents the histologic features in the synovium of RA. It includes 6 features i.e. synoviocytes hyperplasia, fibrosis, proliferating blood vessels, perivascular infiltrates of lymphocytes, focal aggregates of lymphocytes, diffuse infiltrates of lymphocytes. They were scored separately on a scale of 1-10. The treatments that the patients received included: biological agents (Bio) (n=389 30%), etanercept (ETN) (n= 102), tocilizumab (TCZ) (n=105), infliximab (IFX) (n=29), adalimumab (ADA) (n=28), certlizumab pegol (CZP) (n=12), golimumab (GLM) (n=56), and abatacept (ABT) (n=55), tofacitinib (TOF) (n=2).
Results: PD signal (0.97±0.88), DAS28 (3.23±1.13), CRP(0.5±1.25 mg/dL), MMP-3 (119.0±119.0 ng/mL) and Rooney score (23.5±7.7) in the patients treated with Bio were significantly lower than those (1.39±0.95, 3.66±1.07, 0.78±1.37 mg/dL, 146.3±150.0ng/dL, 28.5±9.26) in the patients treated with NonBio. Rooney score fibrosis (9.57±1.44) in patients treated with Bio was significantly higher than those (8.64±2.48) in patients treated by NonBio. Rooney score, synoviocyte hyperplasia (1.16±1.26) and three items of lymphocyte (1.59±2.91, 1.68±2.54, 1.11±2.20) in patients treated with Bio were lower than those (1.72±1.30, 3.79±3.56, 3.73±3.53, 2.40 ±2.98) in patients treated with NonBio. TCZ, ADA, ABT and IFX had some significant differences for Rooney score and Rooney item score between the patients treated with NonBio.
Conclusion: The activity of RA synovitis at operated site was suppressed in patients treated with Bio. There were some differences in clinical data, histological score, PD signal and DAS28 among Bio.
Disclosure of Interests: None declared
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AB0291C REMISSION IN RHEUMATOID ARTHRITIS: CONSIDERING NEW CUT-POINTS OF COMPOSITE DISEASE ACTIVITY INDICES ACCORDING TO THE ABSENCE OF SYNOVITIS BY ULTRASONOGRAPHY

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Background: Achieving the state of remission in RA according to currently available criteria does not entirely prevent patient from radiological progression. On the contrary, the presence of subclinical synovitis by means of ultrasonography (US) correlates with radiological progression.
Objectives: To stablish cut-off values of composite disease activity indices (DAS28-CRP, DAS28-ESR, CDAI and SDAI) that adjust better to remission according to the absence of synovitis by US.
Methods: Observational, cross-sectional study that included 126 patients with diagnosis of RA who were in remission or low disease activity (DAS-ESR ≤3.2). For each patient we calculated the DAS28-ESR, DAS28-CRP, CDAI, SDAI. For US assessment we used the 12 joint simplified score. We considered the state of remission by US if synovial hypertrophy (SH) ≤1 and power Doppler (PD) signal= 0 in all joints. The cut-off values of the disease activity indices to define remission according the proposed US definition of remission were determined by ROC curves.
Results: Patients had a median (ICR) DAS28-ESR of 2.32 (0.60), DAS28-CRP= 1.89 (0.55), CDAI= 3.56 (3.0) and SDAI= 3.0 (4.7). The sensitivity, specificity, positive and negative predictive value of each of the selected cut-off points for the DAS28-CRP, DAS28-ESR, CDAI and SDAI for the definition of remission are shown in the Table.
Conclusion: In this study we describe new cut points of the different composite disease activity indices for the definition of remission. These cut points improve the accuracy of the definition of remission. However, they differ scarcely from the reference values making its impact uncertain in the long term management of patients with RA. Longitudinal studies are, therefore, warranted in order to elucidate the performance of these new cut points.

REFERENCE

[1] Aletaha D, Smolen JS. Clin Exp Rheumatol 2006; 24(6 Suppl 43): S-45-51.

Cut-off values	Sensitivity% (IC95%)	Specificity% (IC95%)	PPV% (IC95%)	NPV% (IC95%)
Taking as reference SH definition of remission.				
DAS28-ESR	81 (70-88)	50 (37-63)	68 (58-77)	66 (51-78)
≤2.6	65 (54-75)	63 (56-73)	70 (58-80)	58 (45-69)
≤2.5				
DAS28-CRP	86 (76-92)	26 (16-39)	61 (51-70)	58 (39-76)
≤2.6	57 (45-68)	55 (41-68)	63 (51-74)	48 (36-61)
≤2.0				
CDAI	61 (50-72)	74 (61-84)	76 (64-85)	59 (47-70)
≤2.8	60 (48-70)	74 (61-84)	75 (63-85)	58 (46-69)
≤2.1				
SDAI	52 (40-63)	72 (59-82)	71 (58-82)	53 (42-64)
≤3.3	52 (41-64)	80 (68-89)	78 (64-88)	55 (44-66)
≤3.0				
Taking as reference the PD definition of remission.				
DAS28-ESR	71 (61-80)	43 (28-59)	76 (66-84)	37 (25-52)
≤2.6	58 (48-68)	60 (44-74)	79 (68-87)	36 (25-48)
≤2.5				
DAS28-CRP	80 (71-87)	17 (8-33)	72 (62-79)	25 (18-45)
≤2.2	64 (53-73)	56 (40-71)	79 (68-87)	38 (26-52)
≤1.96				
CDAI	55 (44-64)	47 (58-86)	85 (73-92)	38 (28-50)
≤2.8	53 (43-63)	74 (58-86)	84 (73-92)	38 (27-50)
≤2.15				
SDAI	46 (36-56)	71 (55-84)	81 (68-89)	34 (24-489)
≤3.3	46 (36-57)	82 (67-92)	87 (74-94)	33 (28-49)
≤3.0				

Disclosure of Interests: None declared
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AB0291D

PREDICTORS OF NEW BONE EROSION IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING CSDMARDS: ANALYSIS OF DATA FROM THE DRIVE AND DESIRABLE STUDIES

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Background: Suppression of joint destruction is an important target for the treatment of rheumatoid arthritis (RA). Most previous studies have proposed prediction models for joint destruction to detect the risk of rapid radiographic progression (change in mTSS ≥5). As joint destruction progresses irreversibly, even slight progression of joint destruction might impact the prognosis. Therefore, our study focused on the onset of new bone erosion in RA patients.

Objectives: To clarify predictors for new bone erosion in RA patients treated with csDMARDs.

Methods: Predictive factors were analyzed using data from the placebo groups of the DRIVE [1] and DESIRABLE [2] studies, which were 12-month, randomized, double-blind, phase 2 and 3 trials for evaluating the efficacy of denosumab in RA patients. New bone erosion was defined as change from baseline in erosion score (ES) ≥1.0 at 12 months, which was assessed as "progressed" by two readers. In addition to newly emerging erosion, new bone erosion also included enlargement of erosion size which is the result of new erosion at a site adjacent to an existing bone erosion. To evaluate predictors for new bone erosion, a logistic regression model was applied. Significant predictors (p value of <0.1) were selected from the univariate analysis and one variable from each correlated pair that showed significance was removed. Multivariate analyses were performed using the selected predictors.

Results: In a total of 306 patients, baseline DAS28-CRP (mean±SD) was 3.58±1.03. New bone erosion was observed in 90 patients (29.4%).

In the univariate analysis, female sex, anti-CCP antibody positivity, rheumatoid factor (RF) positivity, tender joint count (TJC)≥6, CRP≥0.3 mg/dL, erythrocyte sedimentation rate (ESR) ≥28 mm/h, and baseline ES≥3 were identified as significant predictors for new bone erosion. RF and ESR were not included in the multivariate analysis because they were strongly correlated with anti-CCP antibody and CRP, respectively. In the multivariate analyses, female sex, anti-CCP antibody positivity, TJC≥6, CRP≥0.3 mg/dL, and baseline ES≥3 were identified as predictors for the development of new bone erosion.

Abstract AB0291D Table 1. Univariate and multivariate analyses for a change in ES ≥1.0

			Univariate		Multivariate	
Variables		Reference	Odds ratio	P value	Odds ratio	P value
Sex	Female	Male	1.78	0.089	1.85	0.097
Age	≥65 years	<65 years	0.79	0.423		
Duration of disease	≥3 years	<3 years	1.06	0.844		
Anti-CCP antibody	Positive	Negative	5.95	<0.001	4.01	<0.001
RF	Positive	Negative	2.67	<0.001		
Glucocorticoid use	Yes	No	0.99	0.963		
TJC	≥6	<6	1.66	0.047	1.70	0.060
Swollen joint count	≥10	<10	1.26	0.353		
CRP	≥0.3 mg/dL	<0.3 mg/dL	2.84	<0.001	2.02	0.013
ESR	≥28 mm/h	<28 mm/h	2.08	0.007		
Baseline ES	≥3	<3	3.32	<0.001	2.29	0.005
Study	DESIRABLE	DRIVE	1.16	0.602		

Conclusion: In RA patients whose disease activity was controlled on csDMARDs, positive anti-CCP antibody/RF status, elevated CRP/ESR levels, baseline ES≥3, TJC≥6 and female sex were identified as predictors for new bone erosion.

REFERENCES

[1] Takeuchi T, et al. Ann Rheum Dis 2016;75:983–90
[2] NCT01973569 (Takeuchi T, et al: in submission)

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AB0291E **THE EFFECT OF HUMAN UMBILICAL CORD MESENCHYMAL STEM CELLS-DERIVED EXOSOMES ON CHEMOKINES IN COLLAGEN-INDUCED ARTHRITIS RATS**

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Background: *Umbilical cord mesenchymal stem cells (UCMSC) derived exosomes could simulate the function of MSC and avoid the limitations of MSC, which is being hotspot in the research of rheumatoid arthritis (RA) treatment. Chemokines can recruit inflammatory cells and osteoclasts in inflammatory joints, and participate in the synovial inflammation and bone destruction of RA. The mechanisms of UCMSC- derived exosomes on chemokines have less understood in RA*

Objectives: The aim of this study was to investigate the effect of UCMSC and UCMSC-derived exosomes on the chemokines CCL2, CXCL10 and CXCL12 in CIA rats.
Methods: Human umbilical cord mesenchymal stem cells (UCMSCs) were cultured in vitro and separated using a differential centrifugation methods. The CIA rats model was set up by freund's complete adjuvant and type II collagen, then randomly divided into control, CIA, MTX, UCMSCs, UCMSCs exosomes low and high concentration groups. Rats in UCMSCs group were injected in double ankle joint with UCMSCs $2X10^6$/L weekly for 3 weeks. Rats in UCMSCs exosomes low and high group were injected in double ankle joint with UCMSCs exosomes 30μg and 90μg weekly for 3 weeks, respectively. Rats in MTX group were given intraperitoneal injection with MTX (0.9mg/kg) weekly for 3 weeks. Serum concentrations of CCL2 and CXCL10 were detected by flow cytometry. CXCL12 serum level was tested by enzyme-linked immunosorbent assay (ELISA). The protein expressions of CCL2, CXCL10 and CXCL12 in synovial tissue were detected by immunohistochemistry. CCL2, CXCL10 and CXCL12 mRNA levels in synovial joint and spleen were measured by reverse transcription-polymerase chain reaction (RT-PCR).
Results: Intra-articular injection of UCMSC exosomes decreased CCL2 and CXCL12 levels in serum and improved synovial hyperplasia and inflammatory cell infiltration in the CIA rats. UCMSC exosomes suppressed the protein expressions of CCL2, CXCL10, CXCL12 in synovial tissue. It also inhibited transcript levels of CCL2, CXCL10, CXCL12 in synovial tissue and spleen. UCMSC had similar effect on CCL2, CXCL10, CXCL12 in CIA. The high concentration group was more effective than the low concentration in preventing CCL2,CXCL10,CXCL12 protein expressions of synovial tissue and CCL2 transcript level of spleen.
Conclusion: UCMSC exosomes alleviates synovial inflammation in CIA rats through suppression of CCL2, CXCL10, CXCL12 release. The inhibitory effect of on chemokines simulate UCMSC, their cell of origin, the high concentration was better than low concentration.

REFERENCES

[1] F. Djouad, V. Fritz, F. Apparailly, P.Reversal of the immunosuppressive properties of mesenchymal stem cells by tumor necrosis factor α in collagen-induced arthritis[J]. Arthritis Rheum., 52 (5) (2005), pp. 1595-1603.
[2] A. Augello, R. Tasso, S.M. Negrini, R. Cell therapy using allogeneic bone marrow mesenchymal stem cells prevents tissue damage in collagen-induced arthritis[J]. Arthritis Rheum., 56 (4) (2007), pp. 1175-1186.
[3] Y. Liu, R. Mu, S. Wang, L. Long, Therapeutic potential of human umbilical cord mesenchymal stem cells in the treatment of rheumatoid arthritis[J]. Arthritis Res Ther., 12 (6) (2010), p. R210.
[4] Rani S,Ryan AE,Griffin MD, Ritter T.Mesenchymal stem cell-derived extracellular vesicles:toward cell-free therapeutic applications[J].Mol Ther,2015,23(5):8 12-823.
[5] Szekanecz Z, Kim J, Koch AE. Chemokines and chemokine receptors in rheumatoid arthritis. Semin Immunol. 2003 Feb;15(1):15-21.

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Rheumatoid arthritis - comorbidity and clinical aspects

AB0292 **EFFECTS OF ACETAMINOPHEN ON THE KIDNEY FUNCTIONS OF PAITIENTS WITH MUSCULOSKERLTAL DISEASE TREATED WITH LONG-TERM NONSTEROIDAL ANTI-INFRAMMATORY DRUG THERAPY**

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Background: While nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently used therapeutic agents, they are known to cause side effects, such as gastrointestinal disorders and kidney dysfunction. As the proportion of patients with chronic kidney disease (CKD) increases with age, dealing with NSAIDs requires particular care in areas with aging populations. However, in many cases, prescriptions are continued without any particular plan. Hence, the effects of acetaminophen (AAP), which does not cause kidney dysfunction, are being revisited. Opportunities are increasing for using formulations containing tramadol hydrochloride in patients with chronic pain or intravenous agents for perioperative pain management.
Objectives: In this study, we investigated the kidney functions of patients with musculoskeletal disease who had been using NSAIDs for a long time and examined the possibility of switching to AAP.
Methods: The subjects were 105 patients with musculoskeletal disease (42 men and 63 women) who were being treated as outpatients in the orthopedics department of our hospital and had been using NSAIDs for at least 3 months. They primarily had 5 musculoskeletal diseases, including degenerative osteoarthritis (OA), rheumatoid arthritis (RA), osteoporosis (OP), polymyalgia rheumatica (PMR), and gout (G). After checking their background characteristics, we measured their kidney functions and visual analogue scale (VAS) scores, and then switched them from NSAIDs to AAP. Kidney functions were evaluated by classifying CKD using glomerular filtration rate (eGFR) and urinary protein, and by using the Cockcroft-Gault equation to calculate creatinine clearance (Ccr). The patients were given the NSAIDs that they had been taking for single use. Six months after the switch, we remeasured their kidney functions and VAS scores, and investigated whether they could continue using AAP and whether they had used NSAIDs.
Results: The patients' mean age at the time of switching from NSAIDs to AAP was 76 years, and their mean duration of NSAID use was 43 months. For the diseases, 63 patients had OA, 20 had RA, 14 had OP, 6 had PMR, and 2 had G. Before the switch, the mean VAS score was 41.6 mm and mean eGFR was 67.0 mL/min/1.73 m^2. On the basis of the eGFR, the CKD classification was G3 or higher in 38.1% of patients. The CKD classifications with the amounts of urinary protein added to the eGFR were as follows: green, 44.7%; yellow, 33.0%; orange, 14.6%; and red, 7.8%, with 55.4% classified as having CKD. By age, the proportions of patients with CKD based on eGFR and CKD classification were as follows, respectively: 0.0% and 12.5% for those in their 50s, 16.7% and 25.0% for those in their 60s, 29.3% and 48.8% for those in their 70s, and 59.5% and 69.0% for those in their 80s and older. The mean AAP dose was 455 mg.
Six months after the switch, 69 patients had continuously used AAP without regular NSAID use. Of these patients, 13 had used NSAIDs for rescue purposes. Thirty-six patients had stopped using AAP, the most common reason being ineffectiveness (15 patients), although 9 patients did so because they no longer needed any analgesic. Three patients stopped using the drug owing to palpitations or other side effects, although none stopped because of liver dysfunction. Overall, the mean VAS score declined significantly as compared with before the switch, as did the mean eGFR. Of those who continued to use AAP, 56 patients who did not use any NSAIDs exhibited significantly lower mean VAS scores, but not a significant decline in mean eGFR.
Conclusion: The proportion of patients with CKD who were receiving long-term NSAID therapy was higher than that of the general population for all age groups. Halting NSAIDs and switching to AAP could help maintain kidney functions, which could continue to decline with NSAID use.

REFERENCES

[1] CKD guidebook;2012

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AB0293 ASSOCIATION OF HOMOCYSTEINE WITH BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease with unknown etiology that primarily affects the peripheral joints and, over time, leads to loss of mobility if untreated. RA is an important risk factor of osteoporosis and occurrence of fractures. Many authors describe a significantly higher frequency of osteoporosis and fractures in patients with RA in comparison to a control group. The aetiology of progressive bone mass loss in RA patients is multi-factorial and remains obscure. Factors related to the pathological process – activity of RA and applied therapy – seem to be significant. Homocysteine (Hcy) is a sulfhydryl containing amino acid produced by demethylation of an essential amino acid (methionine). A high serum level of Hcy has been recently recognized as a risk factor for osteoporosis and osteoporotic fractures in postmenopausal women.
Objectives: The purpose of this study was to evaluate serum Hcy levels in RA patients compared with healthy controls, examine possible associations between Hcy and bone mineral density.
Methods: This cross-sectional study was performed in Vega-Baja Hospital, Orihuela (Spain) from November 2016 to May 2018. We prospectively enrolled 63 consecutive women patients affected by RA and followed at the Vega-Baja Hospital (Orihuela, Spain) and 60 matched healthy women controls. All patients included in this study had normal serum creatinine (Cr) levels and met the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA. Serum Hcy was analyzed using immunonephelometric method. Bone mineral density (BMD) of femoral neck and lumbar spine was measured by dual-energy X-ray absorptiometry (DXA).
Results: A total of 63 female patients were included in our study, with a mean (SD) age of 53 ± 8 years. The majority were Caucasian (90.5%). Thirty-four patients were menopausal and twenty-nine non-menopausal patients. The mean duration of RA was 8.5 ± 5.8 years. The mean disease activity scores in 28 joints (DAS28) according to the erythrocyte sedimentation rate (ESR) indicated low disease activity 3.0 ± 1.3. The mean health assessment questionnaire (HAQ) was 0.75 ± 0.67. Twenty-eight patients were treated with methotrexate, with a median weekly dose of 11.5 ± 4.8 mg, all the patients received 10 mg folic acid supplementation per week. Serum Hcy concentrations were significantly higher in the RA patients than those in the control group: [9.93 (5.6-18.8) vs. 7.11 (4.9-11.1), pg/mL; P<0.001]. Serum levels of Hcy were inversely related to lumbar spine BMD and femur neck BMD (r -0.28; P < 0.05).
Conclusion: Patients with RA have high levels of Hcy that correlate, inversely, with bone mass suggesting that hyperhomocysteinemia is a risk factor for osteoporosis in patients with RA.

REFERENCES

[1] Kim SY, Schneeweiss S, Liu J, Daniel GW, Chang CL, Garneau K, Solomon DH. Risk of osteoporotic fracture in a large population-based cohort of patients with rheumatoid arthritis. Arthritis Res Ther. 2010; 12: 154–164.
[2] Macovei L, Ancuta C, Belibou C, Chirieac R. Bone mineral density in patients with rheumatoid arthritis. Rev Med Chir Soc Med Nat Iasi. 2011; 115 (3): 723–730.
[3] Gjesdal CG, Vollset SE, Ueland PM, Refsum H, Drevon CA, Gjessing HK, Tell GS. Plasma total homocysteine level and bone mineral density: the Hordaland Homocysteine Study. Arch Intern Med. 2006; 166:88-94.
[4] Bucciarelli P, Martini G, Martinelli I, et al. The relationship between plasma homocysteine levels and bone mineral density in post-menopausal women. Eur J Intern Med. 2010; 21:301-305.

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AB0294 THE EFFECT OF SMOKING ON ENDOTHELIN-1 IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is one of the chronic autoimmune diseases with an estimated prevalence of 1 to 2 percent of the total population in the world. RA patients have an increased risk of morbidity and mortality from cardiovascular (CV) events as a result of accelerated atherosclerosis. Endothelin-1 (ET-1) is a hormone with strong vasoconstrictor properties, secreted in excessive amounts by damaged endothelial cells. However, the effect of this hormone depends on the presence of specific ET-1 receptors as well as their density and location. ET-1 is a mediator-activating autocrine and paracrine, primarily in the circulatory system. It induces the production of proinflammatory cytokines, exacerbating the inflammatory process.
Objectives: The objectives of this study were: *to compare serum ET-1 levels between RA patients and healthy controls and* observe the relationship between tobacco smoking and serum levels of ET-1 in RA patients.
Methods: This cross-sectional study was performed in Vega-Baja Hospital, Orihuela (Spain) from November 2016 to May 2018. We prospectively enrolled 63 consecutive women patients affected by RA and followed at the Vega-Baja Hospital (Orihuela, Spain) and 65 matched healthy women controls. All patients included in this study had normal serum creatinine (Cr) levels and met the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA. Current smokers were defined as those who reported having smoked $\geq$1 cigarette per day regularly during the year preceding the examination. Serum ET-1 was analyzed using ELISA.
Results: A total of 63 female patients were included in our study, with a mean (SD) age of 53 ± 8 years. The majority were Caucasian (90.5%). The mean duration of RA was 8.5 ± 5.8 years. The mean disease activity scores in 28 joints (DAS28) according to the erythrocyte sedimentation rate (ESR) indicated low disease activity 3.0 ± 1.3. The mean health assessment questionnaire (HAQ) was 0.75 ± 0.67. Fourteen (22%) patients had a smoking history. Serum ET-1 concentrations were significantly higher in the RA patients than those in the control group: [30.6 (0-50) vs. 21.7 (0-50), pg/mL; P<0.001]. Higher plasma ET-1 concentrations were significantly associated with smoking (r 0.29; p<0.05).
Conclusion: Our data shows a significant difference in the concentration of serum ET-1 between RA patients and controls. We report significant positive association between serum levels of ET-1 and smoking status.

REFERENCES

[1] Gibofsky A. Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. Am J Manag Care. 2012; 18(13): S295-302.
[2] Castañeda S, Nurmohamed MT, González-Gay MA. Cardiovascular disease in inflammatory rheumatic diseases. Best Pract Res Clin Rheumatol. 2016; 30(5):851-869.
[3] Kowalczyk A, Kleniewska P, Kolodziejczyk M, Skibska B, Goraca A. The Role of Endothelin-1 and Endothelin Receptor Antagonists in Inflammatory Response and Sepsis. Arch. Immunol. Ther. Exp. 2015; 63:41–52.
[4] Mayes MD. Endothelin and endothelin receptor antagonists in systemic rheumatic disease. Arthritis Rheum. 2003; 48: 1190–1199.

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AB0295 CLINICAL CHARACTERISTICS OF 31 CASES OF MALIGNANT SOLID TUMORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: A recent meta-analysis shows patients with rheumatoid arthritis (RA) are at increased risk of lung and lymphoid malignancies compared with general populations[1)]. Rheumatologists perform cancer screening before treatment of biological disease-modifying anti-rheumatic drugs (DMARDs), and do routine blood, urine and imaging tests to find adverse effects of DMARDs. However, they can't always find malignant solid tumors (cancers) at the early stage in patients with RA.

Objectives: We examine characteristics of cancers in patients with RA and use the data to help diagnose the cancers in early stages during medical checkups.

Methods: In this retrospective study, we studied 397 patients with RA who visited our rheumatology clinic from April 2011 to December 2018. Thirty-one cancers in 29 patients with RA were reviewed. The onset of RA and cancer, the medication situation and prognosis were analyzed.

Results: Twenty-five were female, and 4 males. The mean age of diagnosis of RA and cancer were 55 years old (SD 15.0) and 66 (SD 11.4). The median duration of RA prior to cancer diagnosis was 8 years (IQR 4-18). The median follow-up was 4.3 years (range 0.2-7.8). One case of breast cancer was diagnosed with RA at the same time. Breast, Lung and Gastrointestinal cancers were the most common, followed by uterine cervix and skin. Two female patients had metachronous double cancers (uterine cervix and lung, skin and lung). Sex cancers; uterine cervix 3, breast 2, and anal melanoma 1, were found by cancer screening tests that the patients received voluntarily. Twelve cases were detected by blood tests or imaging tests performed in outpatient settings. Three lung cancers were found by the chest CT at the diagnosis of RA and before treatment of biological DMARDs, which were all at the early stage and cured by the resection. A gastric and a colon cancer, which were detected by worsening of microcytic anemia, were in advanced stage with hepatic metastases. Nineteen patients were treated with methotrexate (MTX) before detection of cancers. But only 4 patients continued MTX after detection of cancers. Six patients were treated with biological DMARDs (TNF inhibitor 3, tocilizumab 2, abatacept 1) before detection of cancers. Two patients were treated with TNF inhibitor until just before the admission for cancer treatment, because the rheumatologists did not notice their patients' cancers. After treatment of cancer, 3 patients were treated with tocilizumab and abatacept. The prognosis of 29 patients were as follows; death by cancers 4, death by pneumonia 2, undergoing chemotherapy 6, in remission 17.

Conclusion: The consultation rates for breast and cervix cancer screening are lower in Japan than in European nations. Rheumatologists should encourage their patients to have usual age and sex appropriate cancer screening. A large cohort study showed biological DMARDs did not increase risk of second malignant neoplasm among RA patients with a history of cancer[2)]. However, in this study, no patients were treated with TNF inhibitor after treatment of cancer.

REFERENCES

[1] Simon TA, et al. Incidence of malignancy in adult patients with rheumatoid arthritis: meta-analysis. Arthritis Research and Therapy 2015; 17:212

[2] Dreyer L, et al. Risk of second malignant neoplasm and mortality in patients with rheumatoid arthritis treated with biological DMARDs: a Danish population-based cohort study. Ann Rheum Dis 2017; 0:1-5

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AB0296 ARTERIAL STIFFNESS IN RHEUMATOID ARTHRITIS PATIENTS: DO DISEASE ACTIVITY AND DURATION OF ILLNESS MATTER?

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Background: Recent evidence has demonstrated that the increased risk of mortality in rheumatoid arthritis (RA) patients is largely related to cardiovascular disease (CVD). Overall, RA increases the risk of cardiovascular (CV) mortality by up to 50% for reasons which are insufficiently understood. Chronic inflammation may impair vascular function and lead to increase of arterial stiffness. Measurement of arterial stiffness provide an independent risk factor of CV mortality and morbidity. Brachial pulse-wave velocity (BPWV) is a reproducible method to estimate of arterial stiffness. Whether the disease activity or duration of illness has more contribution in arterial stiffness of RA patients is still controversial.

Objectives: To investigate the correlation of disease activity and duration of illness in RA patients with pulse-wave velocity as a measure of arterial stiffness, free of cardiovascular disease and risk factors.

Methods: RA patients aged 55 years-old or younger were screened for the absence of clinical cardiovascular disease or risk factors (diabetes mellitus, dyslipidemia, hypertension, chronic kidney disease, smoking, obesity, cancer, prolong infections, excessive steroid use, or other inflammatory diseases). Patients were subjected to full history taking, clinical examination, and laboratory investigations including serum lipid profile, CRP, and ESR. Then they were recorded for their brachial pulse-wave velocity using PWV Sphygmograph.

Results: There were 30 suitable patients (all were female, mean age was 44.17 ± 7.98 years-old, mean duration of illness was 1.88 ± 0.94 years). Average systolic blood pressure was 121.67 ± 7.46 mmHg, mean diastolic pressure was 74.00 ± 4.98 mmHg. Average body mass index was 22.43 ± 1.18. Mean DAS28-ESR was 3.29 ± 1.32, and mean DAS28-CRP was 3.30 ± 4.02. Average of BPWV was 14.44 ± 3.86 m/s. This study did not show any correlation between duration of illness and arterial stiffness ($p=0.832$). But it revealed moderate correlation between disease activity (either DAS28-ESR or DAS28-CRP) with arterial stiffness ($r=0.441$ with $p=0.015$ and $r=0.501$ with $p=0.005$).

Conclusion: This preliminary suggests that disease activity of RA is correlated with arterial stiifness free of cardiovascular disease or risk factors. But duration of illnes does not show any correlation with arterial stiffness as believed before, it may need more sample size to determine that. This findings support the importance of inflammation control in RA patients not just to improve quality of life but also to decrease cardiovascular mortality in RA.

REFERENCES

[1] Klocke R, Cockcroft JR, Taylor GJ, Hall IR, Blake DR. Arterial stiffness and central blood pressure, as determined by pulse wave analysis, in rheumatoid arthritis. Ann Rheum Dis 2003; 62:414-418.

[2] Provan SA, Angel K, Semb AG, Mowinckel P, Agewall S, Star D, Kvien TK. Early prediction of increased arterial stiffness in patients with chronic inflammation: A 15-year followup study of 108 patients with rheumatoid arthritis. *The J of Rheumatol* 2011; 38:606-612.

[3] Avina-Zubieta JA, Thomas J, Sadatsafavi M, Lehman AJ, Lacaille D. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis 2012; 71: 1524–1529.

[4] Youssef G, Allam NT, Gaber W, Afifi A, Hesham D. Increased arterial stiffness in rheumatoid arthritis and Its relation to disease activity: A cross sectional study. *The Egyptian Heart J* 2018; 70: 35-40.

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AB0297 **HOW OFTEN IS THE COMBINATION OF NSAID-INDUCED LESIONS OF THE UPPER AND LOWER GI TRACT?**

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) can damage all parts of the gastrointestinal tract (GIT). However, the frequency of the combination of lesions in different parts of the gastrointestinal tract has not been studied.
Objectives: To assess the frequency of the combination of NSAID-induced lesions of the upper GI tract, small and large intestine.
Methods: The study group consisted of 112 patients with rheumatic diseases (62.5% of women, 56.2 + 14.6 years), who regularly took NSAIDs. All patients underwent endoscopy of the upper GI tract and colon. Capsule endoscopy was performed in 35 patients with signs of NSAID-gastropathy.
Results: NSAID-gastropathy (erosions and/or gastric or duodenum ulcers) were detected in 43.8%, NSAID enteropathy (hemorrhages, erosions and ulcers of the small intestine) in 68.6%, NSAIDs-colopathy (hemorrhages, erosions and ulcers of the colon) - 14.3% patients. The combination of NSAID-gastro- and colonopathy was detected in 28.6% of patients (odds ratio 12.2, 95% CI 2.619-56.84), the combination of NSAID-gastro, entero- and colopathy - in 10 patients (20.4% of the number of patients with NSAID-gastropathy). There was a significant risk association for the development of NSAID-induced lesions in all parts of the GI tract with a diagnosis of spondyloarthritis, the presence of abdominal pain, small intestine bacterial overgrowth, as well as in the polymorphism of the CYP2C19 gene (CYP2C19 * 17 * 1/* 17 allele).
Conclusion: The combined NSAID-induced damage of various parts of the GI tract is a frequent and serious pathology requiring complex diagnostics and the combined use of prophylactic agents with a different mechanism of action.
Disclosure of Interests: None declared
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AB0298 **COMPLICATIONS OF RHEUMATOID ARTHRITIS AND ALLIED DISORDERS– A STATISTICAL COMORBIDITY STUDY OF 234 AUTOPSY PATIENTS**

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Background: Complications of rheumatoid arthritis (**RA**) may modify the clinical course and symptoms of allied disorders leading to missed diagnosis or late recognition of associated diseases.
Objectives: The **aim** of this study was to determine the possible role of classic **complications** of **RA**: systemic autoimmune vasculitis (**AV**), AA amyloidosis (**AAa**), lethal cardiac insufficiency (**CI**) caused by endo-, myo- or pancarditis, furthermore lethal septic infection (**SI**) on **prevalence** and **mortality** of coexistent **associated diseases**: atherosclerosis (**Ath**), hypertension (**HT**), type 2 diabetes mellitus (**DM**) and tuberculosis (**Tb**) with miliary dissemination (**mTb**).
Methods: 234 non- selected autopsy patients with **RA** were studied. **RA** was confirmed clinically according to the criteria of the **ARA**.
The presence of **AV**, **AAa**, **CI** and **SI** was determined at autopsy and confirmed by a detailed review of extensive histological material. The prevalence and mortality of associated diseases **Ath**, **HT**, **DM**, **Tb** or **mTb** were analyzed retrospectively, reviewing the clinical and pathological reports.
The link between **AV**, **AAa**, **CI** or **SI** and **Ath**, **HT**, **DM**, **Tb** or **mTb** was analyzed by (χ^2) test.
Results: RA was complicated by **AV** in **43** (**18.4**%), by **AAa** in **48** (**20.5**%), by **CI** with lethal outcome in **15** (**6.4**%), and by lethal **SI** in **33** (**14.1**%) of **234** patients.
RA associated with severe **Ath** in **106** (**45.3**%), with **HT** in **41** (**17.5**%), with **DM** in **41** (**17.5**%), and with **Tb** in **28** (**11.9**%), with active **mTb** in **9** (**3.8**%) of **234** patients.
As a basic disease **Ath** led to death in **61** (**26.1**% of 106), **HT** in **2** (**0.9**% of 41), **DM** in **none** (**0**% of 41), and **Tb** with **mTb** in **3** (**1.3**% of 28) of **234** patients. **Tb** without miliary dissemination was not lethal in our patient population.
The statistical links ("p" values of significance) between complications of **RA** and prevalence or mortality of allied disorders are summarized in Table.
(*asterisk indicates a negative value of associations' coefficient with inverse relationship).

Complications of RA	**AV n=43** of 234	**AAa n=48** of 234	**CI n=15** of 234	**SI n=33** of 234
Allied disorders in RA				
Ath n=106 of 234	**χ^2=6.43*, p<0.01**	**χ^2=10.04*, p<0.001**	χ^2=0.92*, p<0.33	**χ^2=5.03*, p<0.02**
Ath lethal n=61 of 106	**χ^2=15.92*, p<0.00**	**χ^2=11.04*, p<0.00**	**χ^2=4.29*, p<0.03**	**χ^2=12.01*, p<0.00**
HT 41 of 234	χ^2=3.30*, p<0.07	χ^2=0.03*, p<0.86	χ^2=0.00*, p<0.92	χ^2=1.27*, p<0.25
HT lethal n=2 of 41	χ^2=0.05*, p<0.80	χ^2=0.02, p<0.87	χ^2=1.16*, p<0.28	χ^2=0.19*, p<0.65
DM 41 of 234	χ^2=0.04, p<0.8	χ^2=0.84*, p<0.35	χ^2=0.92, p<0.33	χ^2=0.01, p<0.91
Tb 28 of 234	**χ^2=4.02, p<0.04**	χ^2=2.61*, p<0.10	χ^2=0.33, p<0.56	χ^2=0.37, p<0.54
Tb lethal n=3 of 28	χ^2=0.00*, p<0.93	χ^2=0.02*, p<0.86	χ^2=0.53*, p<0.46	χ^2=0.01*, p<0.89
mTb 9 of 28	**χ^2=4.24, p<0.03**	χ^2=0.08, p<0.77	χ^2=0.01, p<0.91	χ^2=0.05, p<0.82
mTb lethal n=3 of 9	χ^2=0.00*, p<0.93	χ^2=0.02*, p<0.86	χ^2=0.53*, p<0.46	χ^2=0.01*, p<0.89

Conclusion: The inverse correlations between **AV**, **AAa**, **CI**, **SI** and **Ath**, **HT**, **DM**, **Tb** or **mTb** indicate that the prevalence and mortality of allied disorders were not influenced basically by the complications of **RA**.
The consequently inverse and (in most cases) significant correlations between prevalence of **AV**, **AAa**, **CI**, **SI** and the prevalence and mortality of **Ath** show that these are are independent entities in **RA**. The **AV**, **AAa**, **CI** and **SI** are the most important complications of **RA**, and are characterize severe forms of disease, mostly involving younger patients, with an earlier onset (without pronounced Ath); while **Ath** is basically an age dependent phenomenon, characteristically present in **RA** patients with advanced age. **RA** patients with **Ath** may represent a special group of **RA**, characterized by lower incidence of **AV**, **AAa**, **CI** or **SI**, and a better prognosis.
The positive and significant relations **AV** to **Tb** or **mTb** suggest an increased risk of Tb, e.g. the presence of **AV** may promote **Tb** or endogenous exacerbation and miliary dissemination of **Tb**.
Disclosure of Interests: None declared
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AB0299 **COXITIS DURING CHRONIC INFLAMMATORY RHEUMATISM**

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Background: The occurrence of coxitis in chronic inflammatory rheumatism is a prognostic factor of great importance given the functional repercussions of the involvement of the coxofemoral joint.
Objectives: The aim of this work is to evaluate the prevalence of this lesion in chronic inflammatory rheumatism (PR/JIA/SpA) and to describe the evolution of this disorder according to the pathology.
Methods: Eighty-two patients with chronic inflammatory rheumatism were enrolled. These patients were followed by the rheumatology department rabta since 2004 until March 2018. The clinical demographics, activity scores, treatment background (all our patients in this series were under biotherapy) and the need PTH were identified.
Results: The eighty-two patients were distributed as follows: 36.58% (n = 30) patients with RA, 36.58% (n = 30) SpA and 26.83 (n = 22) JIA. The average age was 48.3 years, 47.6 years and 32.17 years. For the rheumatoid arthritis population 26.67% (n = 8) of the patients had a coxite of which 62.5% (n = 5) was bilateral and 37.5% (n = 3) unilateral. The mean time to discovery of coxite was 11.7 years and the evolution was in 50% (n = 4) to worsening requiring in 3 cases a bilateral PTH and a case of synoviorthesis.
In the SpA group, 23.33% (n = 7) of patients had coxitis, of which 57.14% (n = 4) were bilateral and 32.86% (n = 3) unilateral. The average time to discovery was 8.22 years. PTH was performed in 71.43% (n = 5) of patients.
For the JIA population, 45.45% (n = 10) of the patients had a coxite of which 80% (n = 8) was bilateral and 20% unilateral. The average time to discovery of this lesion was 14 years, with 60% of cases progressing to an aggravation requiring 40% of the cases for synoviorthesis and 60% for PTH.
Conclusion: SpA is the most common chronic inflammatory rheumatism with cxo-femoral involvement with the most pejorative evolution despite the biological treatment

REFERENCES
none
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AB0300 LIVER DISORDERS DURING RHEUMATOID ARTHRITIS

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Background: Hepatic disease in rheumatoid arthritis (RA) are rare, but can be impactful for patients. Though some hepatic manifestations are directly related to RA, whereas others may be sequelae of treatment or caused by concomitant autoimmune diseases.
Objectives: We have tried through this study to focus on the liver disorders during the monitoring of rheumatoid arthritis and to identify the different etiologies.
Methods: This is a retrospective descriptive study of patients with rheumatoid arthritis (ACR-EULAR 2010 criteria) followed a rheumatology department between 2012 and 2018 with liver function disorder. We have specified the epidemiological, clinical, biological and therapeutic characteristics and the different explorations carried out for these patients.
Results: We included 61 patients in our study (3 men and 58 women). Mean age was 52.13 years [26-82]. Average duration of RA was 9.2 years [0.5-30]. Mean DAS28 was 5.95 [3-8.33]. RA was immunopositive in 88,5% of the cases and erosive in 93,44% of the cases. Most of patients received symptomatic treatment (98% paracetamol, 87% non-steroidal anti-inflammatory drugs, 84% corticosteroids).As for conventional csDMARD, 72% of patients were treated with methotrexate, 8.2% with anti-malarial, 22.95% with salazopyrine and 11.47% with leflunomide. Three patients received biologic DMARDs (1 rituximab and 2 TNF-Blockers).
Hepatic disorders were:cholestasis (95%), cytolysis (33%) and concomitant cytolysis and cholestasis (28%). The etiological investigation undertaken linked these disorders of the liver function disorders to the RA treatment in 50% of the cases.Methotrexate was incriminated in the genesis of this liver enzyme abnormalities in 14 cases, the salazopyrine in 2 cases, the leflunomide in 1 case, paracetamol and nonsteroidal anti-inflammatory drugs in 11 cases and rituximab in 1 case. Hepatic immunological investigation was negative in all cases. We have not noted any hepatitis B seroconversion. Two patients had hepatitis C. One patient presented active hepatitis C serology with signs of fibrosis (A2F2) at the liver biopsy puncture. Abdominal ultrasound showed signs of non-alcoholic fatty liver disease in 34.42% of cases. The biopsy puncture of the liver was performed in 9 patients showing chronic hepatitis lesions (n=1), hepatic atrophy (n=1), steatosis with portal and peri-sinus fibrosis (n=1). The etiological investigation was negative in 10% of cases.
Conclusion: In our study, the liver function disorders during RA are in half of the cases of iatrogenic origin. This requires rigorous monitoring of patients followed for RA in order to improve their management.
Disclosure of Interests: None declared
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AB0301 ANTIMICROBIAL USE IS HIGH IN PATIENTS WITH INFLAMMATORY ARTHRITIDES, AND FURTHER INCREASES WITH FIRST-LINE TNFI THERAPY – NATIONWIDE RESULTS

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Background: Infections are well-known adverse effects of tumor necrosis factor inhibitors (TNFi) and increased hospitalization rates due to infections have also been reported. To our knowledge, this is the first study to report the effect of TNFi initiation on outpatient antimicrobial prescription patterns.
Objectives: To investigate the use of antimicrobial agents (antibacterials, antifungals and antivirals; excluding antimycobacerials) in patients with rheumatoid arthritis, psoriatic arthritis, and axial spondyloarthritis in relation to the initiation of the first TNFi in biologic-naïve patients.
Methods: All patients with inflammatory arthritides who are treated with biologic DMARDs in Iceland are registered in ICEBIO, a nationwide registry. On February 1st 2016, ICEBIO contained information on 1058 individuals. The Icelandic Directorate of Health operates the Icelandic Medicine Database (IMD), a registry that includes over 95% of all filled drug prescriptions in Iceland. From the IMD, filled antimicrobial prescriptions were extracted two years before and two years after the initiation of first-line TNFi therapy for all patients in ICEBIO with rheumatoid arthritis (RA; n=366), psoriatic arthritis (PsA; n=250) and axial spondyloarthritis (AS; n=218). As controls, five individuals, age and sex matched, for the same calendar time were randomly selected. Antimicrobial use was determined from defined daily dose per 1000 capita (DID).
Results: The use of antimicrobials prior to TNFi treatment was greater in the patient group when compared to controls (mean 43 DID vs 21 DID; p<0.01). The patient group received more DID of antimicrobials following the start of TNFi, with a statistically significant increase in PsA (33.9 to 45.2; p<0.01), AS (37.2 to 46.8; p<0.01) and nonsignificant in RA (46.8 to 49.7; p=0.066). Antibacterial use increased from 115 DID to 137 DID for the whole group, most prominently in the PsA and AS groups (Table I). Antifungal use increased in patients with RA and antiviral use in RA and PsA (Table I).
Table I: Antibacterial, antifungal and antiviral use in DID two years before and after TNFi therapy.

	RA *n = 366*	Control *n = 1830*	PsA *n = 250*	Control *n = 1250*	AS *n = 218*	Control *n = 1090*
Antibacterial	45.7	23.7	32.7±48.3	19.2	36.6±68.6	16.6
Before	±97.1	±47.8		±34.5		±37.2
After	47.5	23.8	43.3	21.2	45.6	17.5
	±80.4	±53.7	±70.2**	±41.0	±74.8*	±40.3
Antifungal	0.60±4	0.18±1.7	0.32±2.3	0.37±3.6	0.44±2.4	0.13±1.1
Before						
After	1.06	0.32	0.42±2	0.41±3.6	0.60±3.4	0.13±1.1
	±6.3*	±2.6*				
Antiviral	0.49±4.7	0.42±4.5	0.88±9.8	0.21±1.8	0.19±1.5	0.18±3.2
Before						
After	1.06	0.46±4.9	1.52±11*	0.36±3.5	0.63±3.6	0.29±4.3
	±5.5*					

*p<0.05; **p<0.01

Conclusion: Patients with active chronic arthritidies use statistically significantly more antimicrobials two years antedating TNFi treatment compared to controls. TNFi treatment further increases antimicrobial use in this patient population, especially in patients with PsA and AS. Meanwhile, antifungal use increased in RA and antiviral use increased in both RA and PsA. Further analysis needs to be done on the effect of co-medicines such as glucocorticoids, DMARDs and disease activity.
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AB0302 INTEREST OF THE SYSTEMATIC ELECTROCARDIOGRAM IN THE DETECTION OF CARDIAC INVOLVEMENT DURING SPONDYLOARTHROPATHIES AND RHEUMATOID ARTHRITIS

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Background: Cardiovascular risk is not uncommon in patients with chronic inflammatory rheumatism.
Objectives: The objective: To evaluate the interest of systematic electrocardiogram (ECG) as a tool for detecting cardiac abnormalities during spondyloarthropathies (SA) and rheumatoid arthritis (SA).
Methods: Consecutive patients suffering from SA, RA, hospitalized during the period from 2016 to 2017 and free from cardiovascular events were included. An ECG - 12-lead - was performed and interpreted by a cardiologist without the diagnosis.

Results: A total of 44 patients with SA were included (average duration 9 ± 8 years), 56 patients with RA (average duration 11 ± nine years). They were all asymptomatic on the cardiac level and without a cardiovascular history. The population was homogeneous, concerning the presence of the cardiovascular risk factors, except for the diabetes, more frequent in the RA groups. The proportions of extra systoles, atrioventricular blocks (2.2% in the SA group, 1.4% in the RA group), complete or incomplete left branch block (respectively: 0.7%, 0.6%), complete right limb block or left branch block (respectively: 0.8%, 2.7%) and abnormality suggestive of myocardial ischemia (5.2%, 10.8%)
Conclusion: In patients with no history of cardiovascular disease who are asymptomatic, performing a systematic ECG does not reveal the increased risk of specific cardiac complications related to these conditions in patients with SA and RA.

REFERENCES

[1] Danesh J, Whincup P, Walker M, et al. Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses. BMJ 2000;321:199–204.
[2] Bulkley BH, Roberts WC. Ankylosing spondylitis and aortic regurgitation. Circulation 1973;48:1014–27:
[3] Nitter Hauge S, Otterstad JE. Characteristics of atrioventricular conduction disturbances in ankylosing spondylitis. Acta Med Scand 1981;210:197–200.
[4] Brunner F, Kunz A, Weber U, et al. Ankylosing spondylitis and heart abnormalities. Clin Rheumatol 2006;25:24–9.
[5] Yildirir A, Aksoyek S, Calguneri M, et al. QT dispersion as a predictor ofarrhythmic events in patients with ankylosing spondylitis. Rheumatology 2000;39:875–9

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AB0303 METABOLIC SYNDROME IN TUNISIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The rheumatoid arthritis (RA) is responsible of a high cardiovascular morbi-mortality. This could be related to an increased prevalence of metabolic syndrome in patients with (RA)
Objectives: The aim of our study was to determine the prevalence of metabolic syndrome in RA, to identify factors associated with its presence and to evaluate the influence of antirheumatic drugs on its occurrence.
Methods: A cross-sectional study was conducted in the Internal Medicine department over a period from July 2016 to June 2017, including 50 RA patients classified according to the 1987 ACR and/or 2010 ACR/EULAR criteria. We used the National Cholesterol Education Program/Adult Panel Treatment III 2005 (NCEP/ATP III 2005) definition for the metabolic syndrome.
Results: There were 50 patients (sex-ratio = 0.28) with a mean age of 50.84 ± 12.52 years. The mean age at the onset of RA was 42.04 ± 12.76 years with duration of 17.52 months (0.8-120 months). The evaluation of the disease showed an average DAS28-VS score of 5.37 ± 1.24 and a significant functional impact (HAQ score $\geq$ 1) in 36% of patients. The prevalence of metabolic syndrome in RA was 40%. Its presence was associated with higher age (p = 0.003), greater disease activity (p=0.044), the presence of a biological inflammatory syndrome (p=0.032) and hyperuricemia (p=0.005). An association was also found with long-term corticosteroid use (p = 0.03).
Conclusion: Our results are consistent with most of the literature data. Throughout our study, we emphasize the importance of continuous monitoring of disease activity and the need for cortisone-sparing.

REFERENCES

[1] Da Cunha VR, Brenol CV, Brenol JCT, Fuchs SC, Arlindo EM, Melo IMF, et al. Metabolic syndrome prevalence is increased in rheumatoid arthritis patients and is associated with disease activity. Scand J Rheumatol. 2012; 41 (3): 186–91.
[2] Chung CP, Oeser A, Solus JF, Avalos I, Gebretsadik T, Shintani A, et al. Prevalence of the metabolic syndrome is increased in rheumatoid arthritis and is associated with coronary atherosclerosis. Atherosclerosis. 2008; 196 (2): 756–63.
[3] Dao H-H, Do Q-T, Sakamoto J. Increased frequency of metabolic syndrome among Vietnamese women with early rheumatoid arthritis: a cross-sectional study. Arthritis Res Ther. 2010; 12 (6): R218.

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AB0304 EXTRA-ARTICULAR MANIFESTATIONS IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING BIOLOGIC TREATMENT

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Background: Extra-articular manifestations (EAM) in rheumatoid arthritis (RA) are more prevalent in patients with seropositive, nodular and long term disease. Around 40% of patients with RA can develop EAM, although the incidence has decreased with the "treat to target" strategy.
Objectives: To describe EAM in a cohort of patients with rheumatoid arthritis.
Methods: Retrospective descriptive study of patients diagnosed with RA between 2000 and 2018 who are currently under active biological treatment. Cardiovascular risk factors, baseline characteristics of RA and EAM during their evolution are collected. Statistical analysis is performed with SPSS 24.
Results: We recruited 108 patients, 81.5% female, with mean age at onset of RA of 50 ±15 years (range 17-82). RF was positive in 84.3% and ACPA in 81.3%. Erosions were observed on hands or feet at diagnosis in 35.2%. Mean follow up period: 12±8 years. The most common initial treatment was methotrexate (82.4%) and 44.4% received other DMARDs: leflunomide (32.3%), hydroxychloroquine (16.2%) and others (9.1%).
DAS28VSG at diagnosis was 4.15±1.18 (1.89-6.02) and at the introduction of the first biological drug it was 5.02 ±1.16 (mean years since diagnosis 6±5).
The first biological drug was etarnecept (40.7%), followed by adalimumab (17.6%), abatacept (15.7%), rituximab (7.4%), tocilizumab (7.4%) and infliximab (4.6%). 57.4% discontinued the first biologic: secondary failure (58.1%) or adverse effects (20.6%).
65.7% (71 patients) developed some EAM during disease evolution and 14.8% appeared during the first year. During this first year, secondary Sjögren (37.5%) was the most frequent, followed by rheumatoid nodules (18.7%), EPID (18.7%) and osteoporosis (18.7%). Two or more EAMs were present in 33.3% of patients.
Fifty-four patients (56.3%) did not present any EAM at the beginning of the biological treatment and 29.6% (21 patients) developed EAM afterwards, with an average of 1±3 years. Pulmonary involvement was the first EAM to appear after the onset of biological treatment, followed by anemia (both in the first year).
Summarizing the data of all patients over time, the most frequent EAMs were: osteoporosis (28.7%, mean appearance: 5 years from diagnosis); secondary Sjögren syndrome (27.8%, mean 6 years); normochromic normochromic anemia (21.3%, mean 8 years) and pulmonary involvement (17.6%, mean 4 years), presented as EPID (63.3%), NINE (25%), NIU (8.3%) and pulmonary nodules (8.3%). Other EAM observed were: cutaneous involvement in the form of rheumatoid nodules (15.7%, mean 5 years); ophthalmological involvement (6.5%, mean 18 years) (PUK 2.8%, uveitis 1.9%, scleritis 0.9%, episcleritis 0.9%); amyloidosis (3.7%, mean 16 years) and vasculitis (2.4%, mean 14 years).
Conclusion: EAM have a high prevalence in RA patients receiving biologic treatment (76.6%). A third part of patients had 2 or more EAMs. 14.8% develop the first EAM during the first year of evolution of RA and 30% in the first 5 years. The most frequent are osteoporosis and Sjögren's syndrome, according to what is described in the literature. Pulmonary involvement is the most rapid during the evolution of RA with an average of 4 years.

REFERENCES

[1] Marcucci E, Bartoloni E, Alunno A, Leone MC, Cafaro G, Luccioli F, et al. Extra-articular rheumatoid arthritis. Reumatismo. 2018 Dec 20;70(4):212-224

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AB0305 **ALLERGIC SYMPHTOMS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: One of the hypothesis of RA pathogenesis is that autoimmune process in rheumatoid arthritis starts within the airways. The factors leading to increased antiCCP antibodies formation within the airways are not fully understood. People with allergies to inhaled allergens suffer from chronic inflammation within upper and lower airways.
Objectives: The aim of this study was study was to assess the prevalence of symptoms of upper and lower airways allergic diseases in patients with rheumatoid arthritis as compared to general population prevalence.
Methods: The study group consisted of 96 patients with RA (age years – 46,69±15,70 women-93%, men – 7%). Control group consist 1685 subjects from Lodz population (47,89±15,11 women-55%, men-45%). All responders completed a screening test for allergy symptoms, 60 of RA and all controls were asked to complete a detailed survey consisting of 30 questionnaires based on GA^{2}LEN Global Allergy and Asthma Network protocol include diagnoses and separate symptoms of allergic diseases.
Results: In screening questionnaire 16,84% of RA patients and 7,24% control declare that suffer from asthma (p<0,001). The incidence of wheezing in both groups was statistically insignificant (30,00% RA vs 20,65% control; p>0,05), however the coexistence of dyspnoea and wheezing was more frequent in the group of patients with RA (44,83% vs 14,01%; p<0,001) as well as wheezing without symptoms of infection (55,56% vs 15,37% p<0,001). The frequency of waking up at night due to dyspnea or coughing did not differ significantly between the study and control group (respectively 18,67% vs 12,82 and 33,33% vs 33,35%).
The symptoms of upper airway chronic inflammation were also more prevalent in patients with RA as compared to controls. Chronic sinusitis was declared by 26,67% of patients and 10,62% controls (p<0,001), as well as the symptom of post-nasal drip was significantly twice more frequent than in the study group (20,00% vs 9,08%; p<0,005). Symptoms of a nasal allergy are insignificantly more often in RA group (38,33 vs 33,06%).
Conclusion: Increased prevalence of symptoms of upper and lower allergic diseases in patients with RA requires further investigation as chronic inflammation within airways can lead to posttranslational modification of proteins and autoantigen formation.
Disclosure of Interests: None declared
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AB0306 **DISEASE ACTIVITY AND PREVALENCE OF CAROTID PLAQUE ARE INCREASED IN SEDENTARY RHEUMATOID ARTHRITISPATIENTS**

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Background: Multiple benefits from physical activity (PA) in rheumatoid arthritis (RA) patients have been described; exercise in RA is associated with a cardiovascular (CV) protective role, resulting in lower waist-hip ratio, vascular stiffness and hypertension (1). Other important advantage of PA in RA is the impact observed in disease activity; regular PA is associated with reduced DAS28 (2). There are no previous studies evaluating the effect of exercise on disease activity and carotid Ultrasound (US) findings in Mexican-mestizo RA patients.
Objectives: To compare clinical characteristics and carotid US findings of Mexican-mestizo RA patients who perform PA to sedentary RA patients.
Methods: Cross-sectional, observational, comparative study. We included RA patients aged 40 to 75 years that fulfilled the 2010 EULAR criteria. Patients with prior atherosclerotic CV diseases and overlap syndromes were excluded. Clinical history, blood samples, physical exam and carotid US were performed. Carotid plaque (CP) was defined as a focal narrowing $\geq$0.5 mm of the surrounding lumen or a carotid intima media thickness (cIMT) $\geq$1.2 mm, and increased cIMT was defined as $\geq$0.9 mm. Patients were classified in two groups: those who are sedentary and those who regularly perform PA (defined as $\geq$120 min/week). The Kolmogorov-Smirnov test was used to determine normal distribution. Categorical variables are expressed as total number (%), and numerical variables as median (q25-q75). Chi square and Mann-Whitney U-test were used to compare groups and considered significant if p<0.05.
Results: A total of 334 RA patients were included. Clinical characteristics are shown in table 1. Patients who exercised had lower disease activity and BMI. Carotid US was performed in 127 patients (Table 2). There was a higher prevalence of CP, bilateral CP and increased cIMT in sedentary patients. Sedentary RA patients had an increased risk of CP (OR 3.1 [IC95% 1.0-9.7, p=0.04]).

Table 1. Clinical characteristics

Variables	Physically active (n=80)	Sedentary (n=254)	p
Age (years), median (q25-q75)	55.3 (46-58.7)	55.7 (49-61.6)	*NS*
Women, n (%)	72 (90)	236 (92.9)	*NS*
Disease duration (years), median (q25-q75)	5 (2-11.3)	9 (3.7-15.5)	***0.002***
Past or current smoker, n (%)	16 (20)	63 (24.8)	*NS*
BMI (kg/m^2), median (q25-q75)	26.4 (24.7-29.1)	28 (25.2-31.8)	***0.004***
Diabetes Mellitus, n (%)	10 (12.5)	38 (15)	*NS*
Dyslipidemia, n (%)	27 (33.8)	67 (26.4)	*NS*
Hypertension, n (%)	16 (20)	77 (30.3)	*NS*
DAS28-CRP, median (q25-q75)	2.6 (1.8-3.8)	3.4 (2.3-4.4)	***0.001***
CDAI, median (q25-q75)	6 (2-16)	11 (3.7-20.2)	***0.005***
SDAI, median (q25-q75)	7 (2.5-17.3)	12.5 (4.5-22)	***0.004***

Table 2. Carotid US

Carotid US findings n (%)	Physically active (n=28)	Sedentary (n=99)	P
CP	4 (14.3)	34 (34.3)	***0.041***
Increased cIMT	9 (32.1)	55 (55.6)	***0.029***
Unilateral CP	3 (10.7)	15 (15.2)	*NS*
Bilateral CP	1 (3.6)	19 (19.2)	***0.045***

Conclusion: Patients who perform PA had significantly lower disease activity and BMI. A higher prevalence of CP, increased cIMT and bilateral CP was found in sedentary patients. Sedentary RA patients had an increased risk of CP. These results are similar to previously described in other populations and may be indicators of the protective effect of PA in RA patients. Rheumatologists should encourage their patients to exercise regularly.

REFERENCES

[1] Byram KW. et al. Exercise is associated with increased small HDL particle concentration and decreased vascular stiffness in RA. Journal of Clinical Rheumatology. 2018;00(00):1-5
[2] Sandberg ME. et al. Patients with regular physical activity before onset of RA present with milder disease. Ann Rheum Dis. 2014;73:1541-1544

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AB0307 **A.P.R.A.N. ASSESSMENTS OF TENDER AND SWOLLEN JOINTS COUNT SCORE PERFORMED BY A RHEUMATOLOGIST AND RHEUMATOLOGY NURSES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is a multisystem and debilitating disease. Fortunately, there is now a wide range of available treatments for these patients[2]. Also, guidelines recommend a « treat to target »[1] involving strict follow-up of the patients. The recommended target is remission. But, in Canada, especially in rural areas, there are few rheumatologists facing a growing number or RA patients. Innovative solutions are needed in order to face this challenge. One solution is to work with a nurse assistant performing the joint count evaluation between the rheumatologist's visits. The consistency of examinations and disease activity evaluation is therefore.
Objectives: The primary objective is to validate the accuracy of the assessment of RA and Psoriatic arthritis disease activity by a nurse in comparison to assessments conducted by rheumatologists for CDAI and

DAS-28. The secondary objective is to validate the accuracy of different parts of the CDAI and DAS-28. Comparison with the patient's joint count is done as well.
Methods: The trial was conducted in a private clinic. The patient was examined at first by the physician and afterward by the nurse. The 2 nurses participating to the trial were trained for joint count during a 14 hours course. Finally, a brief training was given to the patient who performed a self-evaluation. The study consisted of one visit where all the different information was collected. The different data collected concerned: the patient's medical history, medication, diagnostic, joint count by the nurse and the physician, VAS by nurse and physician. The patient's self-joint count was done for a subgroup of the patients. The Rho of Spearman was used for the correlation analysis.
Results: The overall correlation between the patient DAS-28 and physician DAS-28 was good (r=0,701) and it was very good between the nurse and the physician (r=0,846).The correlation between the nurse CDAI and the physician CDAI was also very good (r=0,765). The correlation between the different parts of the DAS-28 was less impressive. But in the same way, the correlation was better between the nurse (nr) and the physician, than between the patient (pt) and the physician (MD) and the least between the patient and the nurse. Respectively the correlation for TJC pt-nr is r=0,452, pt-MD is r=0,537, nr-MD is r=0,693, for the SJC the correlation is with pt-nr=0,390, pt-MD=0,414, nr-MD=0,699. The VAS-pt correlates poorly with both the nurse and the doctor VAS, respectively r=0,428 and r=0,392.No significant difference was found between the two nurses.
Conclusion: The primary end point is attained. There is a very good correlation between the nurse and the physician's evaluation. These results are congruent with those of previous studies[3]. So, this study is another argument to work with a nurse assistant and to use DAS-28 or CDAI in order to save time as we can be confident that the results of the nurse examination is accurate and valuable. This team work is a way to improve patient care following the guidelines. Treat to Target is possible even in remote areas lacking of resources.

REFERENCES

[1] Smolen JS, et al. Treating rheumatoid arthritis to target: recommendations of an international task force; Ann Rheum Dis 2010; 69: 631-6372- Anderson, et al., Rheumatoid Arthritis Disease Activity Measures: American College of Rheumatology Recommendations for Use in Clinical Practice; Arthritis Care & Research, Vol. 64, No 5, May 2012, pp 640-6473-Cheung PP, Gossec L, Mak A, March L. Reliability of joint count assessment in rheumatoid arthritis: A systematic literature review. Semin Arthritis Rheum. 2014 Jun;43(6):721-9.

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AB0308 THE ASSOCIATION OF PARKINSON DISEASE WITH RHEUMATOID ARTHRITIS

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Background: Parkinson disease (PD) is a progressive neurological disease, characterised with tremor, spasticity, arthrosis, dementia, loss of mobility and generalised pain. PD affects mainly elderly population. Activity of PD patients is restricted because of spasticity and severe arthrosis. Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease which can cause disability in elderly population. Patients with can admit to rheumatology clinics with generalised pain or restricted mobilisation. In contrast, in some PD patients with generalised pain on joints, RA may be overlooked
Objectives: We aimed in this study to evaluate the characteristics of patients with RA and Parkinson patients.
Methods: 842 RA patients screened retrospective for PD from the patient files.10 patients with both RA and Parkinson disease were included to study. 3 female and 7 male patients with **mean age 76,4 (with a standard deviation 5,4) were evaluated. The characteristics of patientsare evaluated from the patient files.**
Results: All patients were older than 75 years. Mean RA duration time was 14 months and PD duration time was 34 months. All patients admitted outpatient clinic with leg pain and inability to walk. 4 of 10 patients had mild dementia. Median ESR was 36 mm/h and median CRP value was 0,68 mg/dl. 6 of 10 patients had positive ANA result with 1/100 ratio, but rheumatoid factor and anti CCP were negative.
Conclusion: PD is one of the disorder that may cause severe disability in very old ages. RA may be an additional factor for pain and loss of function in PD patients. Patients with generalised pain and difficulties with walking should be evaluated for PD especially in old ages. PD patients with generalised pain on joints should be evaluated for inflammatioy arthritis.
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AB0309 THE FREQUENCY OF HEMATOLOGICAL MALIGNANCIES IN AUTOIMMUNE RHEUMATIC DISEASES

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Background: Autoimmune rheumatic diseases are associated with increased risk of hematological malignancies. The pathogenesis of autoimmunity can cause of malignancies or immunosuppressive agents may increase the risk of malignancies.
Objectives: We aimed in this study to determine the frequency, type and characteristic of hematological malignancies in rheumatology practice.
Methods: 1640 rheumatology outpatient patient with autoimmune rheumatic diseases (Rheumatoid arthritis (RA), SLE, Sjogren's syndrome (SjS), myositis, systemic Sclerosis, undifferentiated connective tissue diseases (UCTD)) are screened for hematological malignancies. 16 patients are found with hematological diseases. The characteristics of these patients are reported retrospective from their outpatient clinic case files.
Results: The frequency of hematological diseases was found%0.04 in study group. 4 patients had myeloproliferative diseases (1 polycythaemia vera (PV), 1 primary myelofibrosis (MyF), 2 patients with essential thrombocythemia (ET)). Patients with PV and MyF had severe rheumatoid arthritis and because of unresponsiveness of MTX, they used rituximab for severe disease activity. Patient with ET had only minimal arthralgia and are followed under HCQ therapy. As lymphoproliferative diseases 4 patients had chronic lymphoid leukemia (CLL). 3 of them had RA and 1 of them had (SjS). 2 patients had non-Hodgkin lymphoma and these patients are seen after autolog bone marrow transplantation because of arthralgia, bur not detected arthritis. 1 patient had Hodgkin disease in her history, and had both RA and SjS, and receiving MTX therapy. 2 patients had multiple myeloma (MM). One of them is new diagnosis arthritis plus elevated sedimentation rate. Second one was seen with arthralgia after MM treatment and autologous bone marrow transplantation. 3 patients had mycosis fungoides, 1 of them had UCTD and received hydroxychloroquine. The other patient had RA under MTX therapy and one patient received rituximab therapy for severe RA activity.
Conclusion: Hematological malignancies are rare diseases in rheumatology practice, although expected high rate because of using immunosuppressive treatment and autoimmunity. The increased frequency of lymphoproliferative disorders are expected and associated with autoimmunity, but we don't found a high rate for lymphoproliferative malignancies. Myeloproliferative malignancies possibly not associated with the pathogenesis of autoimmune rheumatic diseases.
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AB0310 THE INCIDENCE OF EXTRA-ARTICULAR MANIFESTATIONS IN SOUTHERN CHINESE PATIENTS WITH INFLAMMATORY JOINT DISEASES

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Background: Inflammatory joint diseases (IJDs) are chronic arthritis, but frequently present with co-morbidities of other organs and systems, which is known as extra-articular manifestations (EAMs) [1]. It is still unclear which clinical characteristics or bio-markers can predict the development of EAMs[2].

Objectives: The aim of this study was to estimate the proportion of EAMs in southern Chinese patients with IJDs and to explore the risk factors.
Methods: This was a retrospective cohort study of a total 1135 IJDs patients, including 788 rheumatoid arthritis (RA) patients, 307 ankylosing spondylitis (AS) patients and 40 psoriatic arthritis (PsA) patients. Demographic data, disease characteristics, laboratory blood tests, medical imaging, and the presence of EAMs were recorded.
Results: We found 459 (40.44%) of them presented with EAMs: 30.84% had cardiovascular; 7.67% had pulmonary, 5.29% had osteoporosis/low bone mineral density, 2.29% had ocular, 0.79% had gastrointestinal and 0.26% had renal involvements. Multivariate logistic regression showed older age (OR: 1.05, P<0.001) and higher anti-cyclic citrullinated peptide antibody (anti-CCP) levels (OR: 1.003, P=0.011) were independent risks of EAMs in RA patients. In AS group, older age (OR: 1.07, P<0.001) and higher disease activity (OR: 2.06, P<0.001), were independent risks of EAMs. As in PsA group, longer disease duration (OR: 1.01, P=0.046) and higher disease activity (OR: 1.15, P=0.011) were independent risks.
Conclusion: These results suggested the high prevalence of EAMs, and it is important to regularly screen on EAMs, as it influences treatment decision and impacts on patients' quality of life.

REFERENCES

[1] Agca R, Heslinga SC, van Halm VP, Nurmohamed MT. Atherosclerotic cardiovascular disease in patients with chronic inflammatory joint disorders. Heart 2016;102:790-5.
[2] Carmen Stolwijk AvT, José Dionisio Castillo-Ortiz AB. revalence of extra-articular manifestations in patients with ankylosing spondylitis: a systematic review and meta-analysis. Ann Rheum Dis 2015;74:65–73.

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AB0311 HEMOSTASIS IN AFRICAN BLACK COMPARED TO WHITE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Aberrant hemostasis is implicated in the increased CVD risk experienced by patients with rheumatoid arthritis (RA) (1). Large circulating concentrations of plasminogen activator inhibitor-1 (PAI-1) predict cardiovascular event rates (2). PAI-1 levels are markedly smaller in American and African black populations than in those of European descent (3,4). Whether this protection persists in black persons who have RA is unknown.
Objectives: This study compared hemostasis factors among African black and white RA patients
Methods: PAI-1, tissue factor pathway inhibitor (TFPI) and tissue plasminogen activator (t-PA) levels were measured by ELISA in 236 (114 black; 122 white) African RA patients. Data were analysed in mixed regression models.
Results: In age and sex adjusted analysis, PAI-1 concentrations were larger in black compared to white patients with RA (median (interquartile range (IQR))=12.4 (3.1-28.7) versus 5.4 (1.5-25.0) ng/ml, p=0.006). In all patients, body mass index (BMI) (β (SE)=0.022 (0.007), p=0003), waist circumference (β (SE)=0.007 (0.003), p=0.04) and tetracycline use (β (SE) =0.291 (0.133), p=0.03) were associated with logarithmically transformed PAI-1 levels. Population grouping did not influence these relationships (interaction p>/=0.8) but impacted rheumatoid factor (RF) positivity- and azathioprine use-PAI-1 level associations (interaction p=0.03 and 0.004, respectively). In stratified analysis, RF positivity was associated with PAI-1 levels in white (β (SE)=0.344 (0.139), p=0.01) but not black patients (β (SE)=-0.102 (0.143), p=0.5), and azathioprine use was associated with PAI-1 levels in black (β=0.400 (0.155), p=0.01) but not white patients (β (SE)=0.305 (0.184), p=0.1). In age, sex, BMI, RF positivity and azathioprine and tetracycline use adjusted analysis, black population origin remained associated with PAI-1 levels (β (SE)=0.175 (0.091), p=0.05). In age and sex adjusted analysis, TFPI and t-PA levels did not differ in black compared to white RA patients (median (IQR)=221.0 (149.8-410.5) versus 225.0 (130.4-357.2) pg/ml, p=0.6, and 6.7 (4.9-9.1) versus 7.4 (4.4-10.0) pg/ml, p=0.3).
Conclusion: PAI-1 concentrations are substantially larger in African black compared to white patients with RA.

REFERENCES

[1] Van den Hoever IAM, Sattar N, Nurmohamed MT. Thromboembolic and cardiovascular risk in rheumatoid arthritis: role of the haemostatic system. Ann Rheum Dis 2014;73:954-7.
[2] Jung RG, Motazedian P, Ramirez FD, et al. Association between plasminogen activator-1 and cardiovascular events: a systematic review and meta-analysis. Thrombosis J (2018) 16:12.
[3] Festa A, D'Agostino R, Rich SS, et al. Promoter (4G/5G) plasminogen activator inhibitor-1 genotype and plasminogen activator inhibitor-1 levels in blacks, Hispanics and non-Hispanic whites. The Insulin Resistance Atherosclerosis Study. Circulation 2003;107:2422-7.
[4] De Lange Z, Rijken DC, Hoekstra T, et al. In black South Africans from rural and urban communities, the 4G/5G PAI-1 polymorphism influences PAI-1 activity, but not plasma clot lysis time. PLoS One 2013;8 (12): e83151.

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AB0312 CARDIOVASCULAR RISK FACTOR´S BEHAVIOR AND CARDIOVASCULAR RISK IN HISPANIC EARLY RHEUMATOID ARTHRITIS PATIENTS: A COHORT STUDY

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Background: Rheumatoid arthritis (RA) patients present an increased risk of cardiovascular (CV) morbidity and mortality compared to the general population[1]. Patients from Latin-America exhibit younger age, female preponderance, less severe disease and dyslipidemia, which are relevant when assessing CV risk[2]. In order to impact CV morbidity/mortality, control of reversible CV-risk factors need to be achieved[3]. Cohorts allow prospective evaluation of long-term outcomes. In 2004 we initiated an early RA cohort. Up to June 2018, the cohort comprised 185 RA patients with prospective assessments of CV risk and at least one year of follow-up.
Objectives: To monitor CV risk-factor´s behavior during the first year of follow-up and to identify if traditional CV risk scores predict major CV events (MACE) in our population.
Methods: Once enrolled patients had complete rheumatic evaluations at regular intervals. Baseline CV-risk factor´s assessments included age, gender, ethnicity, physical activity and history of first-degree relatives with premature heart disease. CV-risk factors assessments at baseline and at least 6 months apart included blood pressure, serum total cholesterol (CHO) and HDL cholesterol (Castelli ratio CHO/HDL was derived), serum glucose (GLU, in mg/dL), body mass index (BMI), CRP (in mg/dL) and (at least) the following comorbidities: Hypertension (HT, and HT treatment), diabetes mellitus (DM), advanced chronic kidney failure (CKF) and atrial fibrillation (AF). Smoking status was assessed at baseline and last follow-up. Incident MACE were defined according to standard definitions[4]. Cox regression´s model identified predictors of incidental MACE. Patients gave written informed consent.
Results: At cohort entry, the 185 patients (all Hispanic) which data were analyzed were primarily middle-aged females (87.6%) and had 5.3 months (3.3-7.1) of disease duration. Most prevalent CV risk factors were CRP >1 mg/dL (90%), Castelli ratio > 3 (84%) and low HDL levels (74%).
During the first year of follow-up, smoking status, systolic blood pressure $\geq$ 140 mm Hg, diastolic blood pressure $\geq$ 90 mm Hg, low HDL, Castelli ratio > 3, high CRP and patients with active disease progressively decreased; meanwhile, the opposite figure was true for BMI $\geq$ 30 kg/m² and patients on corticosteroids. At 12 months of follow-up, number of patients with incident CV risk factor was higher for Castelli-ratio > 3 (23%), low HDL (16.3%), high CHO (10.6%), BMI $\geq$ 30kg/m² (10%), CRP >1 mg/dL (7.5%) and age $\geq$45 years old (3.3%).
During the first year of follow-up, 45.8% of the patients had age between 40-79 years old, required to apply American Heart Association (AHA) criteria; these identified 12 patients with high CV-risk.
Up to June 2018, the cohort had 1358 patient/years follow-up and 6 patients had incidental MACE after (median, IQR) 6.5 years of follow-up (3.3-9.5). High CV-risk score at baseline failed to predict incidental MACE. Meanwhile, BMI $\geq$30kg/m² was a predictor of incidental MACE in our population.

Conclusion: Hispanic RA patients from an early RA cohort present a distinctive pattern of CV risk factors. Due to younger age at RA presentation, a minority of the patients had CV risk scored. Obesity was a predictor of incidental MACE in our population.

REFERENCES
[1] Avina-Zubieta JA, et al. Arthritis Rheum 2008;59:1690-7.
[2] Parra-Salcedo F, et al. Arthritis Res Ther 2015;17:34.
[3] Primdahl J, et al. Ann Rheum Dis 2013;72:1771-6.
[4] Hicks K, et al. Draft Definitions for CDISC 2014;7:1-33.

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AB0313 THE PREDICTORS OF UNDIAGNOSED DYSGLYCAEMIA IN PATIENTSWITH ESTABLISHED RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease with an increased risk of diabetes and insulin resistance.[1, 2] The prevalence of type 2 diabetes mellitus (T2DM) were demonstrated to be 10.4% as compared to only 7.6% in 1:4 controls matched for age, sex and geographical region, with an odds ratio of 1.4.[3]
Objectives: To determine the prevalence of dysglycaemia (T2DM, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT)) and the factors associated with dysglycaemia in patients with established RA.
Methods: This is a cross-sectional study conducted in a rheumatology centre in Malaysia. Patients with established RA aged 30 years or more were included. Exclusion criteria were overlap syndrome, pre-existing diabetes or pre-diabetes, pregnant and within 6 weeks of post-partum period. An oral glucose tolerance test (OGTT) was performed for all patients. Comparison of various factors between dysglycaemia and normoglycaemia were analysed. Multivariate analysis was performed using logistic regression analysis to ascertain the true effects of significant factors found on univariate analysis.
Results: The mean age of patients was 57.2 ± 8.1 years and 87.7% were female. Of 155 patients included in this study, 55 (35.5%) were found to have dysglycaemia; 40 (72.7%) had IGT, 11 (20%) had T2DM, 3 had IFG and IGT (5.5%) and 1 had IFG (1.8%). Significant factors between dysglycaemia and normoglycaemia is tabulated in Table 1. The predictors of dysglycaemia were previous or current smoker (OR 4.28, 95% CI 1.02 – 17.90) and raised triglycerides (OR 3.29, 95% CI 1.29 – 8.37).
Conclusion: One third of 155 patients had dysglycaemia and majority had IGT. The predictors of dysglycaemia in patients with established RA aged 30 years and more, were previous or current smoker and raised triglycerides.

Table 1. Factors investigated for differences between dysglycaemia and normoglycaemia.

Risk factors	Dysglycaemia n=55	Normoglycaemia n=100	p-value
Previous or current smoker, n (%)	7 (13.0)	3 (3.0)	0.02
Waist circumference (cm), mean ± SD	89.0 ± 12.5	83.1± 9.6	<0.01
Weight (kg), mean ± SD	65.5 ± 12.3	60.7 ± 10.6	0.01
Systolic blood pressure (mmHg), mean ± SD	134.5 ± 17.5	128.2 ± 18.1	0.04
Diastolic blood pressure (mmHg), mean ± SD	79.7 ± 8.7	76.3 ± 10.5	0.04
High density lipoprotein (mmol/L), mean ± SD	1.4 ± 0.3	1.5 ± 0.4	0.02
Triglycerides (mmol/L), mean ± SD	1.3 ± 0.5	1.1 ± 0.5	<0.01

REFERENCES
[1] Su C-C, Chen I-C, Young F-N, Lian I-B. Risk of diabetes in patients with rheumatoid arthritis: a 12-year retrospective cohort study. The Journal of rheumatology. 2013;40(9):1513-8.
[2] Ursini F, Russo E, D'Angelo S, Arturi F, Hribal ML, D'Antona L, et al. Prevalence of undiagnosed diabetes in rheumatoid arthritis: an OGTT study. Medicine. 2016;95(7):e2552
[3] Han C, Robinson DW, Hackett MV, Paramore LC, Fraeman KH, Bala MV. Cardiovascular disease and risk factors in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. The Journal of rheumatology. 2006;33(11):2167-72.

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AB0314 QUALITY OF LIFE IN WOMEN WITH RHEUMATOID ARTHRITIS DEPENDING ON ANXIETY AND DEPRESSION

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes joint damage, deformity, and pain. This can lead to loss of functionality and mobility, which entails a decrease in the quality of life and the possible occurrence of anxiety and depressive disorders[1].
Objectives: Assess the quality of life in women with RA, depending on the severity of anxiety and depression.
Methods: The study included 104 women with reliable RA according to the ACR1987 and/or EULAR/ACR2010 criteria (mean age 53,7 ± 10,9 years, mean duration of RA – 10,1 [4;14] years, DAS28 – 4,96 [4,27;5,77]). An assessment of the severity of anxiety and depression was conducted using a questionnaire for the hospital scale of depression and anxiety (HADS). Evaluation of the quality of life of patients with rheumatoid arthritis was performed using the EQ-5D index. Depending on the degree of functional impairment, according to the HAQ questionnaire, were regarded as minimal (0,5-1 point), moderate (1-2) and pronounced (2-3 points), the population norm was 0-0,5 points. The severity of pain was determined by VAS: no pain (0–4 mm), mild pain (5–44 mm), moderate pain (45–74 mm), severe pain (75–100 mm). Statistical processing was performed using the program STATISTICA 10.0.
Results: The frequency of occurrence of anxiety-depressive disorders in patients with RA was determined: clinically significant anxiety was detected in 20 (19.2%) patients, depression - in 19 (17,3%); subclinical anxiety - in 26 (25%), depression - in 27 (25,9%) patients; the absence of reliably expressed symptoms of anxiety in 58 (55,8%) patients, depression - in 59 (56,8%) patients.
HAQ functional impairment was absent in 11 (10,6%) patients, minimal impairment was detected in 20 (19,2%), moderate - in 52 (50%), and pronounced in 21 (20,2%) patients.
Severe pain in the VAS was noted by 38 (36.6%) patients, moderate - 51 (49%), in 15 (14.4%) patients the pain syndrome was weakly expressed.
The HAQ and EQ-5D indices for women were 1,26 [0,88;1,75] and 0.41 [0,07;0,59], respectively. The relationships between the HAQ and EQ-5D indices (r = 0,67, p <0,05), the HAQ index and the age of the patients (r = 0,33, p <0,05), and the duration of the disease (r = 0,29, p <0,05), ESR indicator (r = 0,28, p <0,05), CRP (r = 0,37, p <0,05), the level of pain in VAS (r = 0,4, p <0,05), DAS28 index (r = 0,32, p <0,05), anxiety severity (r = 0,22, p <0,05), depression severity (r = 0,31, p < 0,05). The relationship between the EQ-5D index and the age of the patients (r = 0,29, p <0,05), with the duration of the disease (r = 0,22, p <0,05), CRP (r = 0,32, p <0,05), the level of pain in VAS (r = 0,45, p <0,05), the severity of anxiety (r = 0,28, p <0,05), the severity of depression (r = 0,35, p <0,05).
To clarify the relationship between the quality of life of patients and the level of depression and anxiety, two groups were identified: no anxiety-depressive disorders (N = 43) and the second group with their presence (N = 30). The EQ-5D index in the first group was 0,59 [0,52; 0,62] and in the group with anxiety and depressive disorders it was 0,27 [-0,02; 0,52] (p = 0,005). The HAQ index significantly differed in women without anxiety and depressive disorders 1,0 [0,625; 1,5] with the index in the other group 1,75 [1,0; 2,125] (p = 0,01).
Conclusion: Thus, every fifth patient with RA suffers from clinically significant anxiety and depression; subclinical anxiety and depression were found in 26% of patients with RA. Interrelations between the indicators of quality of life of patients with RA and the patient's age, duration, activity of RA, severity of anxiety and depressive disorders.

REFERENCES

[1] Lisitsyna TA, Veltishchev DYu. Mental disorders in patients with rheumatic diseases: Diagnosis and treatment. Nauchno-Prakticheskaya Revmatologiya = Rheumatology Science and Practice. 2015;53(5):512-21

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AB0315 EVALUATION OF SLEEP QUALITY, FATIGUE AND SEXUAL PROFILE IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: People over the age of 60 with rheumatoid arthritis (RA) often complain of fatigue, which is considered an extra-articular symptom. This problem has a multidimensional character and sounds on the quality of sleep and on the sexual profile.
Objectives: Our study consists in assessing the prevalence of fatigue and studying the quality of sleep and the sexual profile of patients over 60 years of age with RA compared to subjects suffering from the same illness of younger age.
Methods: This is a prospective study involving 100 patients at the Rheumatology department of Fattouma Bourguiba university hospital in Monastir over a period of 6 months: 40 patients more than 60 years of age with RA compared with 60 patients with RA of younger age.
Data collection was based on scales and specific questionnaires (Visual Analogue Fatigue Scale (VAS-F), Multidimensional Fatigue Inventory (MFI-20), Pittsburgh Sleep Quality Index (PSQI), Female sexual Function Index (FSFI), Sexual Health Inventory for Men (SHIM).
Results: The average age was 55.8 years [25-84]. The most represented age group was over 60 (40%). The sex ratio was 5.6.
73% of our patients were married and 81% had children with an average number of 3 children in charge and extremes between 1 and 9. Fatigue, sleep quality and sexual profile were analyzed comparatively and respectively between the 2 groups (1st group≥60 and second <60 years). The average of the VAS-F was 60.25 compared to 53.5. Fatigue (via MFI-20) was present in all its domains in our patients. General fatigue and physical fatigue were the highest, averaging 13.98 vs. 13.07 and 12.98 vs. 12.33 respectively. Sleeping insomnia (PSQI> 5) was found with the same proportion of 65% in both groups. Low sleep quality was found in 90% versus 93%. A sleep latency> 31 minutes was found in 37.5% against 30%. Sleep duration <6 hours per night was found in 52.5% versus 50%. Sleep efficiency <85% was found at an equal percentage of 75%. Sleep disorders> 10 times in the last 4 weeks were found at an equal percentage of 15%. Regular female sexual activity was found in 42.5% versus 71% and dysfunction (FSFI≤26.55) was noted in 35% against 63.3%. Regular male sexual activity was found in 54.5% against 75% and mild erectile dysfunction (SHIM≤21) was noted in 83.3% against 20%.
Conclusion: A multidimensional approach is needed to explore the different components of fatigue, sleep quality and sexual profile in patients with RA and its very diverse consequences. This should lead to an improvement in the quality of life in the current medical practice.
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AB0316 ESTABLISHED SERONEGATIVE RHEUMATOID ARTHRITIS IS CONSIDERED A MILD FORM OF THE DISEASE, ALSO WILL IT BE THE SAME REGARD FOR VERY EARLY SERONEGATIVE RHEUMATOID ARTHRITIS?

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Background: Established Seronegative Rheumatoid Arthritis (ESNRA) is considered a mild form of the disease with a good prognosis and response to therapy compared with seropositive (SP) form [1]. Lately evidence indicates that seronegative (SN) form of arthritis in early stage is serious and should not be underestimated in terms of disease activity, response to therapy and radiographic damage [2,3,4]. At present, the influence of SN status of clinical course and treatment choice in very early stages, in other words less than 3 months from time at onset of disease, is still controversial [5].
Objectives: To evaluate demographical, clinical and treatment differences between Very Early Seronegative Rheumatoid Arthritis (VESNRA) and Very Early Seropositive Rheumatoid Arthritis (VESPRA) in a Mexican cohort.
Methods: 64 patients with Very Early Rheumatoid Arthritis [(VERA), < 3 months from time at onset of clinical manifestations] that fulfilled ACR/EULAR 2010 criteria (≥18 years) from a Mexican cohort recruited from 2015 to 2018 were examined and followed to 3, 6 and 12 months. Patients without presence of rheumatoid factor (RF) and anticitrullinated protein antibodies (ACPA) were considered SN. Demographic factors, clinical features, disease activity measured using DAS28, functional status evaluated using HAQ, comorbidities and pharmacologic treatments were examined for patients with VESNRA and VESPRA. Charlson's clinical comorbidity index was used to analyze comorbidities. Chi-square and Student-t test was performed by univariate analysis and logistic regression was used by multivariate analysis, both were adjusted for age and gender. Statistical test were conducted at 5% level of significance.
Results: Of 64 patients with VERA 79% were women. The mean age [standard deviation (SD)] was 49.8 (13.5) years. The mean of time at onset of VERA (SD) was 77.8 (15.5) days. A total of 20 (31.2%) patients had VESNRA. In the univariable analyses VESNRA patients were more likely to have minor disease activity and better functional status during their follow-up to 3, 6 and 12 months [Table 1]. Moreover, VESNRA patients were more likely to present lesser work disability, lower comorbidities including fibromyalgia, to use fewer sulfasalazine, leflunomide, biologic agents and corticosteroids. As expected, the modified Charlson's comorbidity index score was lower in VESNRA patients through all their follow-up. In multivariable analyses less frequently use of corticosteroids (OR 0.68, 95% CI 0.42-0.88, p=<0.001) remained significant in VESNRA patients
Conclusion: This study suggests that in very early stage of disease, SN form presents minor disease activity, better functional status, lower comorbidities, also require less aggressive therapy using biologic agents and corticosteroids than SP form in the course of one year. By these clinical and therapeutic differences should be considered VESNRA a mild form of the disease like as ESNRA. These observations must be confirmed in larger studies with further follow-up.

REFERENCES

[1] Ann Rheum Dis 2018;77:A936; (2) J Rheumatol 2014;41;2361-2369; (3) Ann Rheum Dis 2012;71:245–248; (4) Arthritis Res Ther 2014;16: R13; (5) Ann Rheum Dis 2011;70:949-55

Table 1. Disease activity and functional status in VESNRA and VESPRA Patients

Feature	VERA		*p* value
	Seropositive (68.8)	***Seronegative*** n= 44 n= 20 (31.2)	
Disease activity (DAS28), mean score (SD)			
Baseline	5.99 (0.85)	5.09 (0.76)	NS
3 months	3.43 (1.09)	2.42 (0.85)	0.003
6 months	2.76 (0.97)	2.04 (0.72)	0.008
12 months	2.25 (0.57)	1.74 (0.22)	0.002
Functional status (HAQ), mean score (SD)			
Baseline	2.19 (0.30)	1.72 (0.28)	NS
3 months	1.86 (0.32)	1.29 (0.33)	0.007
6 months	1.49 (0.42)	0.87 (0.35)	0.019
12 months	0.99 (0.36)	0.56 (0.17)	0.025

VESNRA: Very Early Seronegative Rheumatoid Arthritis; VESPRA: Very Early Seropositive Rheumatoid Arthritis; **SD:** Standard deviation**; NS**: Not significant

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AB0317 THE EFFECT OF ANEMIA ON THE CARDIAC FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic disease that is characterized by defeat of the musculoskeletal system and is often accompanied by the anemia.

Objectives: The aim of our study was to determine the effect of anemia on the structural and functional state of the heart in patients with rheumatoid arthritis.
Methods: The 154 patients with rheumatoid arthritis were included in the study: 37 patients with anemia (1st group) and 117 – without systemic manifestations of rheumatoid arthritis (2nd group). RA activity was estimated by index DAS-28. All patients underwent echocardiography.
Results: Both groups were comparable in age, sex, ratio of seropositive and seronegative patients. A comparative analysis of both groups revealed that in 1st group DAS-28 was higher than in 2nd group ($p<0.05$). According to the results of echocardiography, the left ventricular myocardial mass index was higher in 1st group than in the 2nd group ($p<0.05$). The same applies to the end-diastolic size of the left ventricle: in patients with anemia, it was more than in patients without it ($p<0.05$). Our results suggest that patients with anemia often have a violation of diastolic myocardial function, which is accompanied by an increase in myocardial mass. The correlation analysis in both groups revealed a direct relationship between the age and the left ventricular mass index ($r=0.62$, $p<0.0005$), between the age and the mitral E/a ($r=-0.55$, $p<0.00001$). In addition, in 1st group we revealed the inverse relationship between the DAS-28 and the tricuspid E/a ($r=-0.43$, $p<0.05$).
Conclusion: Thus, regardless of the presence of anemia, the patients with rheumatoid arthritis observed dependence of structural and functional changes in the heart of age: a violation of diastolic function of the left ventricle, an increase of the left ventricular myocardial mass index,. However, in patients with anemia, an increase in the activity of the disease is accompanied by diastolic dysfunction of the right ventricle that requires correction in the tactics of patient management.

REFERENCES

[1] rheumatoid arthritis, anemia, echocardiography

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AB0318 BAROPODOMETRIC COMPARISON OF PLANTAR PRESSURE IN KNEE OSTEOARTHRITIS PATIENTS AND RHUMATOID ARTHRITIS PATIENTS

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Objectives: To compare the plantar pressure between patients with Knee Osteoarthritis and patients with rhumatoid arthritis
Methods: This is a cross-sectional study, included 41 patients with rheumatoid arthritis (87.8% female, mean age 49 ± 11.9 [27-83] years, median duration of evolution was 9 (4.20)) months, and 40 knee osteoarthrosis patients (100% female, mean age 57.6 ± 5.2 [50-67] years, median evolution time was 36 (24, 69) months).
The two groups were matched by BMI (27.5 vs. 29.6, p> 0.05).
In the rheumatoid arthritis group: The mean DAS28 was 3.9 ± 1.3 [2-6] and the knee joint was affected in 22% of cases.
In the knee osteoarthritis group: The knee osteoarthrosis was bilateral in 80% of the cases and the radiological severity (Stages 3 or 4 of Kellgren and Lawrence classification) was found in 27.5%.
The baropodometric study was performed using a PRESSCAM® platform (SIDAS®, 38,000 VOIRON, MEDICAPTEURS®). The static analysis was done in free position, for 30 seconds at 50 Hz with measure of plantar pressure parameters.
Results:

Baropodometric characteristics	Rheumatoid arthritis	Knee osteoarthritis	p
Surface of whole foot (cm2)	105.2	123.7	<0.001
Maximum pressure of whole foot(g/cm2)	667,8	655,8	0,72
Average pressure of whole foot (g/cm2)	307,3	307	0,98
Surface of foorefoot (cm2)	39.1	44.5	0.02
Surface of hindfoot (cm2)	64.1	60.7	0.2
Thrust of foorefoot(%)	15.5	23.4	<0.001
Thrust of hindfoot(%)	33.9	29.1	<0.001
Thrust of the whole foot (%)	50.1	52.5	0.06

P significatif si≤0,05; Test utilisé : t-student

Conclusion: This comparative static baropodometric study of patients with RA and patients with knee osteoarthritis shows significant differences in bearing surface, which appears to be lower in the RA group, especially in the forefoot. The thrust on the forefoot is also less important in the RA group.
these results could be explain by the rheumatoid forefoot, which decreased support and pressure on the forefoot.
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AB0319 ABATACEPT IN RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE. A MULTICENTRE STUDY OF 181 PATIENTS

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Background: Interstitial Lung Disease (ILD) is a severe extraarticular manifestation of rheumatoid arthritis (RA).
Objectives: Our aim was to assess the efficacy of abatacept (ABA) in RA patients with ILD.
Methods: Retrospective multicenter study of RA patients with ILD treated with ABA. ILD was diagnosed by HRCT. We have analyzed the following variables: **a)** 1-point change the Modified Medical Research Council (MMRC); **b)** FVC improvement $\geq$10%; and improvement $\geq$10% in DLCO; **c)** radiological improvement in HRCT scan, **d)** changes in DAS28 score. Values were compared with baseline **e)** prednisone doses
Results: We studied 181 patients (94women/87 men) with ILD associated to RA. The follow-up was 12.1[6.2-24.1] months. The mean age was 64.54 ± 9.7 years. The median to progression of ILD was 12 [3-43.75] months. 81 patients were treated in monotherapy, 100 patients in combination therapy. The most frequent pattern was UIP 45,3%.
The most of patients who did not have dyspnea remained asymptomatic. See results in Figure1. DAS28 also improved. We appreciate a decrease in the dose of prednisone compared to the initial dose.
Conclusion: ABA seems to be effective. However, should be verified in prospective and randomized studies.

Table 1.

	Evolution at last observation.
MMRC, available data, n - Stable - Improvement - worse	 (76,5%) (20,6%) (2.9%)
FVC, available data, n - Stable - Improvement - Worse	 (70,3%) (12,9%) (16,8%)
DLCO, available data, n - Stable - Improvement -worse	 (71,6%) (18,2%) (10,2%)
HRCT, available data, n - Stable - Improvement - worse	 (21%) (20%) (21%)

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AB0320

FATIGUE PATTERNS IN RHEUMATOID ARTHRITIS PATIENTSWHO RECEIVE BIOLOGICAL AND TARGETED SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

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Background: Fatigue is one of the most frequent symptoms in patients with rheumatoid arthritis (RA), affecting more than 80% of them. The experience of fatigue is multidimensional.
Objectives: To identify the factors associated with fatigue on its different subscales (Physical, Living, Cognitive and Emotional).
Methods: Cross-sectional study. 60 patients were included, they were being followed up in the rheumatology outpatient clinic of Hospital Clínico San Carlos, Madrid, Spain. Data were collected between July 2018 and January 2019. All patients met the ACR/EULAR 2010 criteria and they were in treatment with Biological or Targeted Synthetic DMARD. **Main variable:** Fatigue was assessed by the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ). **Covariables:** Demographic, clinical and treatment. **Statistical analysis.** A descriptive analysis was carried out for the different variables. To identify factors independently associated to BRAF-MDQ and its subscales, multivariable linear regression was applied. Results were expressed as coef with their corresponding 95% CI. A value of $p < 0.05$ was accepted as statistically significant.
Results: A total of 60 patients, comprising of 53 females (88%) and 7 males (12%) with a mean age of 56.4±11.8 years and mean disease duration of 14.1±7.7 years were evaluated. RF was positive in 60% of patients. 65% were in active on work and 23% retired. Regarding comorbidities, 43% had dyslipidemia, 42% hypertension, 17% hypothyroidism and 15% depression. The DAS28-ESR and SDAI scores of the patients were 2.6±0.8, 8.5±5.9 respectively. The HAQ was 0,86 ± 7.7. The rest of the clinical, treatment characteristics, and the scores of the fatigue instruments are shown in **Table 1.** The factors affecting the BRAF-MDQ and its subscales was evaluated in multivariate analyze **Table 2.** Our results shows a correlation between disability and the different dimensions ($p < 0.001$). Patients who reported good sleep quality had less physical fatigue, while those under Non Anti-TNF treatment perceived more physical and living fatigue. In addition, an association was observed between depression and cognitive fatigue, disease activity (DAS28-ESR) and living fatigue and between VAS-pain score and emotional fatigue. A positive RF was associated with less physical and living.
Conclusion: It is important to evaluate fatigue in a multidimensional perspective, each of the different subscales could be modulated by different factors. The results of our study indicated that disability predicts in all subscales of fatigue, however, other factors can configure different patterns of fatigue in RA patients, and identify them is key to the approach of this complex symptom.

Table 1. Characteristics of the sample

Glucocorticoids mg/day, mean ± SD	4.8 ± 1.6
Treatment, n (%)	47 (78.3)
Conventional DMARDs	40 (66.6)
Anti TNF	16 (26.6)
Non-Anti TNF	4 (6.6)
Synthetic target DMARDs	
VAS pain mean ± SD	39.3 ± 24.2
Sleep quality self-report, n (%)	23 (39.6)
Good	35 (60.3)
Poor	
BRAF-MDQ (0-70), **mean ± SD**	21.9 ± 15.0
Physical (0-22)	10.6 ± 5.4
Living (0-21)	5.08 ± 5.0
Cognitive (0-15)	3.3 ± 3.3
Emotional (0-12)	2.9 ± 2.7

Table 2. Multivariate analyses of BRAF-MDQ and its subscales. *p < 0.001, **p < 0.05. Cells represent beta coefficients with standard error

	Physical	Living	Cognitive	Emotional
Age	-0.10 (0.04)**	0.00 (0.04)	-0.00 (0.03)	0.04 (0.02)
Sex	-2.65 (1.70)	-0.74 (1.64)	-1.93 (1.26)	-1.21 (0.97)
RF positive	-3.80 (1.15)**	-2.85 (1.13)**		
HAQ≥1.1	4.76 (1.14)*	4.05 (1.13)*	1.83 (0.90)**	1.91 (0.70) **
Non Anti-TNF	3.33 (1.18)**	2.60 (1.23)**		
VAS Pain				0.02 (0.01)**
DAS28-ESR		1.75 (0.65)**		
Depression			3.10 (1.19)**	
Good Sleep quality	-2.75 (1.10)**			

Disclosure of Interests: None declared
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AB0321 MORTALITY AND COMPLICATION OF PATIENTS WITH RHEUMATOID ARTHRITIS ADMITTED TO INTENSIVE CARE UNIT IN KYUSHU UNIVERSITY HOSPITAL

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Background: The patients with rheumatoid arthritis (RA) are associated with high mortality caused by comorbidity and complication, and are often required the intensive treatment. Severe infections are among the most common causes of their mortality in intensive care unit (ICU)[1)2)].
Objectives: To determine prognostic factors and mortality in patients with RA, including juvenile idiopathic arthritis (JIA), admitted to the ICU in Kyushu University Hospital, we examined the treatments of RA and JIA, comorbidities, complications, the reasons admitted to the ICU, intensive treatments, mortalities within 30 days, 90 days, and a year.
Methods: Between January 2008 and March 2018, 70 patients (20 males, 50 females) with RA (68) or JIA (2) staying at the ICU of our institution for 48 hours and over were included in this study. The admission to the ICU were performed total 77 of times because 5 patients were readmitted. The average of age and RA duration at the admission was 65.8 ±17.7 years (5-96) and 13.5±14.8 years (0-61), respectively, and the average of follow-up duration was 879.9±992.0 days (3-3988).
Results: The mortality within 30 and 90 days were 21.4% (15/70) and 27.1% (19/70), respectively, and 24 of 65 patients (36.9%), excluded 5 patients due to the change of hospital, were dead within a year. The reasons for ICU admission included cardiovascular complications (22.9%), infection (30.0%), neurological complications (7.1%), respiratory problem (15.7%), gastrointestinal problems (4.3%), endocrinological cause (2.9%), liver problems (7.1%), kidney problems (4.3%), and others (5.7%). The average of ICU length of stay was 7.2±7.6 days (2-39). The group of 30 days mortality was significantly higher in the amount of prednisone (8.1 ±5.8 vs 4.5±4.9), Charlson Comorbidity Index3) (5.1±2.5 vs 2.7±1.4), and APACHEII4) (21.7±9.2 vs 14.5±5.5) scores. The fatal outcomes within 30 days was mainly caused by infection (46.7%). In blood data, the low levels of platelet number, total protein, and albumin, and the high levels of creatinine and prothrombin time international normalize ratio at the time of admission of ICU were significantly poorer prognoses.
Conclusion: Our study has shown the high mortality of RA patients admitted to the ICU, and some blood data could be predicted poor prognosis.

REFERENCES

[1] Moreels M, et al.: Intensive Care Med 2005
[2] Brunnler T, et al.: Intern Med 2015
[3] Quan H, et al.: Am J Epidemiol 2011
[4] Knaus WA, et al.: Crit Care Med 1985

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AB0322 BIOMASS SMOKE EXPOSURE LINKED TO HIGHER ACPA LEVELS IN MEXICAN-MESTIZO RA-PATIENTS

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Background: Rheumatoid arthritis (RA) is a chronic, inflammatory, autoimmune disease of the joints. Current classification criteria for RA diagnosis requires the presence of either rheumatoid factor (RF) or anti-citrullinated protein antibodies (ACPA). These have also been linked to chronic air pollutants exposure, such as tobacco smoke and biomass fuel smoke. Patients with COPD and biomass exposure have higher levels of ACPA (1). Nearly 50% of the world's population still rely on biomass fuels for cooking, heating and industry, especially in low-income countries (2).
Objectives: To investigate the prevalence of biomass exposure in a cohort of Mexican-mestizo RA-subjects, and the effect of it in their RF and ACPA levels.
Methods: A cross-sectional, observational trial with RA-subjects that fulfilled the 2010 ACR/EULAR classification criteria, recruited at a rheumatology clinic in northeastern Mexico. Patient evaluation included a complete clinical history, somatometry, and blood samples to measure hs-CRP, RF isotypes (IgA, IgG, IgM) and ACPA. Biomass exposure was documented using the biomass exposure index (BEI), defined as: average hours exposed per day multiplied by years of exposure. Descriptive analysis was done using frequencies (%) and median values (q25-q75). Subjects were divided into 3 groups according to their BEI: non-exposed, BEI <30 and BEI >30. Comparisons were done by Chi-square and Kruskal-Wallis test and correlation by Spearman's rho test.
Results: A total of 285 subjects were included, 154 (54%) of them had history of exposure. Comparisons are shown in Table 1. A significant difference in age was found (p=0.006), this being caused by a difference between the BEI=0 and BEI >30 groups (p<0.001). We also found a higher prevalence of dyslipidemia and hypertension in subjects with a BEI >30 (p<0.05). A significant correlation between a rising BEI and a higher value of ACPA (rho=0.14, p=0.016) was found; this correlation was not found with any subtype of RF (p>0.05).

Table 1. Demographic and clinical characteristics of RA according to BEI groups.

	BEI = 0	BEI < 30	BEI > 30	*p* value
Age, years, *median (q25-q75)*	54 (47.9-59.3)	55 (49.2-61.4)	58.2 (51.8-65.4)	NS
Women*, n (%)*	120 (92.3)	72 (91.1)	71 (94.7)	NS
BEI, hours/year *(median, q25-q75)*	0 (0-0)	15 (2-19)	72 (42-160)	**<0.001**
Dyslipidemia, *n (%)*	32 (24.8)	19 (24.4)	33 (44.0)	**0.011**
Type 2 diabetes, *n (%)*	18 (13.7)	9 (11.4)	15 (20.0)	NS
Hypertension, *n (%)*	32 (24.4)	21 (26.6)	33 (44.0)	**0.007**
Body mass index, kg/m²*, median (q25-q75)*	27.66 (25.07-31.6)	27.25 (24.32-31.6)	27.83 (25.52-31.2)	NS
Disease Duration, years*, median (q25-q75)*	9.03 (3.4-15.03)	9.5 (4.01-14)	9.04 (3.6-15.6)	NS
DAS 28-CRP, *median (q25-q75)*	3.17 (1.9-4.1)	3.38 (2.2-4.3)	3.39 (2.07-4.5)	NS
Negative ACPA*, n (%)*	46 (38.3)	20 (25.3)	20 (27.8)	NS
Group 1 ACPA, *n (%)*	26 (21.7)	19 (24.1)	14 (19.4)	NS
Group 2 ACPA, *n (%)*	31 (25.8)	21 (26.6)	18 (25.0)	NS
Group 3 ACPA, *n (%)*	17 (14.2)	19 (24.1)	20 (27.8)	**0.016**

Conclusion: In our cohort of Mexican-mestizo RA subjects, 54% had positive biomass exposure. Subjects with a BEI >30 were older and had a higher prevalence of dyslipidemia and hypertension. A significant correlation was found between higher BEI index and a higher value of ACPA antibodies.

REFERENCES

[1] Sigari N, et al. (2015). Anti-cyclic citrullinated peptide (CCP) antibody in patients with wood-smoke-induced chronic obstructive pulmonary disease (COPD) without rheumatoid arthritis. Rheumatology International.

[2] Yang, DH, et al. (2014). Circulating anti-cyclic citrullinated peptide antibody in patients with rheumatoid arthritis and chronic obstructive pulmonary disease. Rheumatology International.

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AB0323 CARDIOVASCULAR RISK ESTIMATION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS OR C-DMARDS

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Background: Patients with Rheumatoid Arthritis (RA) are at increased risk of developing atherosclerotic cardiovascular (CV) disease. The impact of treatment with conventional or biological disease modifying drugs (c- or b-DMARDs) on inflammation of systemic circulation is an important question.
Objectives: The aim of this study is to determine the influence of therapy (c-DMARDs or b-DMARDs) on 10 year CV risk in patients with RA, over a period of 18 months.
Methods: A single center, observational study of 229 consecutive RA patients, who were treated with c-DMARDs or b-DMARDs mono/combination therapy for at least 18 months. The 10 year CV risk was calculated with Framingham risk score (FRS).
Results: A total of 229 patients were included, 111 received b-DMARDs and 194 c-DMARDs. The mean age was comparable between 2 groups (62.45±12.74 vs 64.56±12.48years, p: 0.1596) and 148 (64.63%) were female. Patients receiving b-DMARDs had longer disease duration compared to c-DMARDs group (14.34±9.89 vs 9.99±9.3 years respectively, p: 0.001) and comparable baseline FRS 10-year percent CV risk (10.74 ±8.88 vs 11.68±8.78 respectively, p: 0.3710). Baseline patient distribution across intermediate (9.6% vs 16.6%) and high (10.91% vs 16.16%) FRS 10-year CV risk categories was comparable between treatment groups (b-DMARDs vs c-DMARDs, p: 0.208), except low FRS category (27.51% vs 51.53% respectively, p<0.001). At month 18, FRS 10-year CV risk category remained stable in b-DMARDs patients (low: 31.88%, intermediate: 10.92%, high: 5.24%, p: 0.47), whereas a significant shift in FRS 10-year CV risk category was observed in c-DMARDs patients (low: 58.1%, intermediate: 17.03%, high: 9.17%, p: 0.001). Within-group the mean (SD) change in FRS 10-year percent CV risk from baseline to month 18 was statistically significant for both b-DMARDs (Δ: 10.74-8.94= 1.8 (1.14), p<0.001) and c-DMARDs (Δ: 11.68-8.73= 2.95 (0.91), p<0.001).
Conclusion: Patients treated with b-DMARDs had lower baseline and month 18 10-year CV risk. However, both treatment arms induced significant improvement of 10-year CV risk at 18 months.

REFERENCES

[1] Ann M. Chodara, MD, Aimée Wattiaux, BS, and Christie M. Bartels, MD, MS. Managing cardiovascular disease risk in rheumatoid arthritis: clinical updates and three strategic approaches. Curr Rheumatol Rep. 2017 Apr; 19(4): 16.

[2] Meyer PW1, Anderson R2, Ker JA3, Ally MT4. Rheumatoid arthritis and risk of cardiovascular disease. Cardiovasc J Afr. 2018 Sep/Oct 23;29 (5):317-321.

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AB0324 PAIN IMPROVEMENT IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BARICITINIB: RESULTS OF A PROSPECTIVE STUDY

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Background: Assessment of pain improvement during treatment for Rheumatoid Arthritis (RA) may be useful to clinical decision between providers and their patients (pts).
Baricitinib (BARI) once daily, an oral, selective Janus Kinase (JAK)1/JAK2 inhibitor, reduced disease activity levels in Rheumatoid Arthritis (RA) patients (pts) with an inadequate response (IR) to methotrexate (MTX).
Objectives: To Evaluate the likelihood of achieving different levels of pain control with BARI 2 mg or 4 mg in patients with RA with inadequate response to traditional DMARDs or biological DMARDs.
Methods: Prospective observational registry of pts with RA who start treatment with BARI, in a third level Spanish Hospital (October 2017- June 2018). BARI 2 mg is started in patients with inadequate response to traditional DMARDs and BARI 4 mg in patients with inadequate response to biological DMARDs. The pts were assessment of pain was assessed with 0-100 mm visual analog scale (VAS) at each study visit. The likelihood of achieving >=25%, >=50% and >=70% pain VAS improvement through week 12 and analyze if there are significant differences between the group of patients with BARI 2 mg and BARI 4 mg (Mann-Whitney test). The statistical study was carried out with the SPSS15 computer package.
Results: We included 38 pts (28 women), mean age 52 ± 12 years. Pain VAS improvement for all patients, baseline pain and weeks 12. The frequency is the percentage of improvement with respect to the baseline. In BARI 2 mg group, 58% of pts (p75) have experienced a decrease greater than pain VAS improvement than baseline and in BARI 4 mg group, 55% of pts (p75) have experienced a decrease greater than pain VAS improvement than baseline.
No statistically significant differences were found in the two treatment groups (BARI 2 mg and BARI 4 mg) (p 0.847).
Conclusion: Our results, in general, agree with what is published in the literature (RA treated with BARI reported greater improvements in pain control when compared to adalimumab or placebo, a post-hoc analysis of the Phase 3 RA-BEAM study). BARI treated pts reported significantly greater and more rapid reductions in pain severity as measured by the pain VAS, improvements were sustained 12 weeks, without finding differences in pts receiving BARI 2 mg or BARI 4 mg.

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AB0325 PREVALENCE OF ANXIETY/DEPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS AT THE UNIVERSITY OF CHILE`S CLINICAL HOSPITAL AND THEIR ASSOCIATIONS WITH DISSEASE ACTIVITY INDEXES AND QUALITY OF LIFE

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Background: Rheumatoid Arthritis is a chronic inflammatory disease with great impact in quality of life. Anxiety and depression could be frequently present in RA patients and may impact the disease activity evaluation. However psicological evaluation or therapy are not part of the standard of care of RA patients.
Objectives: To evaluate the prevalence of anxiety/depression in rheumatoid arthritis patients in control at the University of Chile`s Clinical Hospital and to investigate the association of anxiety/depression with disease activity and quality of life.
Methods: The Hospital Anxiety Depression Scale (HADS) was applied to measure depression and anxiety in a cross-section patients with RA meeting the ACR/EULAR 2010 criteria in control at the University of Chile`s Clinical Hospital. All patients included gave their inform consent. Demografic characteristics, Disease variables and activity, measure as DAS28-VHS, DAS-28 CRP, CDAI and SDAI and HAQ were evaluated at the same time. Spearmen correlation, Fisher exact test, Chi-Square and Kruskal-Wallis test were used according to variables at evaluation. Statistical analysis was perform by Stata v12.1 sfotware. The study was approved by the Hospital Ethic Review board.
Results: 122 patients were enrolled in the study between december 2017 and December 2018. 103 (84.45%) were female. 56 (46%) had depression and/or anxiety according to HADS. 24% of the patients (n=24) had only depression. The severity of the depression symptoms was mild in 71%, moderate in 21% and severe in 8% of the patients. 42%, 40% and 18%of the patients with anxiety (n=55) had mild, moderate and severe anxiety symptoms respectively. The disease activity was significantly higher in patients with as compared to those without anxiety/depression, measure with all of the following indexes: DAS28-VHS (4.33 vs 2.75, p<0.001, DAS-28 CRP (4.13 vs 2.75, p<0.001), CDAI (15 vs 7 p<0.001)and SDAI (17 vs 7.5, p<0.001). The HAQ was also significantly higher in patients with anxiety/depression (1.18 vs 0.29, p<0.01

Conclusion: Depression/anxiety symptoms was very frequent in our cohort of RA patients. The disease activity measure with different indexes and the HAQ was significantly higher in the patients with depression/anxiety. It is possible that psychological factors influence the RA treatment outcomes. Therefore screening and therapy of anxiety and depression should be consider in the regular management of RA patients.

REFERENCES

[1] Michelsen B, Kristianslund EK, Sexton J, Hammer HB, Fagerli KM, Lie E, Wierød A, Kalstad S, Rødevand E, Krøll F, Haugeberg G, Kvien TK. Do depression and anxiety reduce the likelihood of remission in rheumatoid arthritis and psoriatic arthritis? Data from the prospective multicentre NOR-DMARD study. Ann Rheum Dis. 2017 Nov;76(11):1906-1910.

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AB0326 RECOGNITION AND IMPLEMENTATION OF EULAR RECOMMENDATIONS FOR RHEUMATOID ARTHRITISCARDIOVASCULAR RISK MANAGEMENT AMONG INTERNAL MEDICINE AND RHEUMATOLOGY FELLOWS: DATA FROM AN ACADEMIC TERTIARY CARE LEVEL CENTER

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Background: Rheumatoid arthritis (RA) patients present an increased risk of cardiovascular (CV) morbidity and mortality compared to the general population. Patients from Latin-America present distinctive features and some of them are relevant when assessing CV risk. EULAR recommendations include CV risk assessment for all the patients at least once every 5 years and its reconsideration following major changes in anti-rheumatic therapy. Importantly, failure to identify and manage CV comorbidity in RA patients has been recognized by rheumatologists, although there is no information in Latin-America.
Objectives: To investigate knowledge about EULAR recommendations for RA-CV risk assessment/management (K-EULAR-R) among internal medicine and rheumatology fellows from an academic and tertiary care level center, to identify physician´s perception about responsible(s) for CV risk assessments and about major barriers to perform the assessments and to investigate the appropriated identification of major CV risk factors. Potential differences among both group of trainees were additionally investigated.
Methods: Internal medicine fellows (N=105, 1st to 4th grade participants were represented) and rheumatology fellows (N=10, 4 from first grade and 6 from second grade) were invited to anonymously answer a questionnaire designed by 2 investigators to investigate K-EULAR-R and integrated by 11 items classified in 3 categories: "general knowledge about CV risk in RA patients" (4 items), "timing of CV risk assessment" (4 items) and "appropriated statin use" (3 items). In addition, fellows were directed to select and rate main responsible for CV risk assessment (5 options), major barriers to apply EULAR recommendations (6 options), and to correctly identify CV risk factors (20 options). After questionnaire completion, an overall-CV-knowledge-Likert scale (superior, borderline or inferior) was assigned to each participant by an independent observer. The study received IRB approval. Descriptive statistic was used and questionnaire was scored to a decimal scale.
Results: Ninety-three (85%) internal medicine fellows and 10 (100%) rheumatology fellows participated. Rheumatology fellows scored higher in the K-EULAR-R questionnaire when compared to internal medicine fellows (6.9±1.4 vs. 5.5±1.4, p=0.004) and the higher score was replicated in the category of "general knowledge about CV risk" (8.3±2.0 vs 5.3±2.5, p=0.001), meanwhile no differences were detected in the scoring of the categories "timing of CV risk assessment" and "appropriated statin use". No differences among grades within each group were identified.
The majority of the rheumatology fellows rated themselves as the specialist responsible for CV risk assessment (80%); meanwhile this percentage decreased to 45.7% among the internal medicine fellows (p=0.084); fellows from both groups identified lack of time during rheumatic evaluations as the main barrier to perform CV risk assessment (60% and 57%, respectively).
Adequate CV risk factor identification varied from 30% (for contraceptive use) to 100% (for smoking habit), and these% were similar among both groups. Up to 82.5% of the fellows identified incorrectly $\geq$ 1 CV risk factor and high serum triglyceride levels was the highest (49%).
Conclusion: Knowledge about CV risk management in RA patients was suboptimal among trainees in internal medicine and rheumatology from an academic and tertiary care level center in México City; trainees in rheumatology performed better. There is a need to reinforce the topic during fellow´s residency.
Disclosure of Interests: None declared
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AB0327 RHEUMATOID ARTHRITIS PATIENTS HAVE VITAMIN-D DEFICIENCY COMPARED TO AGE SEX MATCHED CONTROL. WHAT CONTRIBUTE TO THIS DEFICIENCY?

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Background: Vitamin-D (vit-D) is believed to have an immunomodulatory and anti-inflammatory action. As a result, low vit-D has been proved to increase susceptibility to the development and to increase the inflammatory activities of rheumatoid arthritis (RA). This study looked at 25-vit-D level in RA patients and in their matched age and sex controls, and investigated what contribute to the risk of low 25-vit-D in RA.
Objectives: The study looked at RA diseases activities, renal function, demographic features and blood biochemistry relation to 25-vit-D level.
Methods: 62 RA patients and 82 control were recruited for the study. 25-vit-D level, RA diseases activity parameters and blood biochemistry (full blood count, liver function test, and renal profile) were obtained on the same day. Estimated glomerular filtration rate (eGFR) calculated with Modification of Diet in Renal Disease (MDRD) formula. Body mass index (BMI) calculated as mass (kg)/Height $(m)^2$. Univariate regression analysis was carried out to determine the relationship between 25-vit-D level and all the parameters of interest (as above).
Results: 65 RA, and 82 controls matching for age (48±13 years for RA, and 47±14 years for the controls, p=0.58) and sex (57 F (88%), M=8 (12%) RA, 67 F (82%), 5 M (18%) controls, p=0.23) were included for the study. The mean 25-vit-D level was 41±31 nmol/l for the RA patients (normal range: 50-80), and 52±33 nmol/l for the controls (p=0.03).
Univariate linear regression among RA patients revealed a positive linear relationship between 25-vit-D level and age of the patients (p=0.02, CI: 0.08, 1.24), creatinine level (p=0.01, CI: 0.13, 0.96), body surface area (p=0.02, CI: 9.47, 111), body mass index (BMI) (p=0.03, CI: 0.17, 3.18), and calcium level (p=0.04, CI: 1.38, 69.6). 25-vit-D level was negatively associated with eGFR (p=0.04, CI: -0.20, -0.01), microalbuminuria level (p=0.03, CI: -0.26, -0.00), and CRP level (P=0.03, CI: -0.47, -
Conclusion: Vit-D receptors are present in most cells in the body and in the T and B lymphocytes. The active form of vit-D (1, 25 vit-D) is one of the most potent modulators of the immune system. Hence, the negative relationship between 25-vit-D and CRP support 25-vit-D deficiency role in the exacerbation of the inflammatory status, and possibly in the subclinical renal impairment; as shown by the negative association between eGFR and the 25-vit-D. The relation between the subclinical renal impairment and the vit- D deficiency is further supported by e the negative linear relationship between 25-vit-D and the urine microalbumin level and the positive linear relationship association between 25-vit-D and the serum creatinine level. The positive association between 25-vit-D and the age of the participants might reflect the awareness of the older population about the importance of sun exposure for health. Screening for vit-D deficiency might be an important step to detect subclinical renal insufficiency in RA. Vit-D supplement might help in ameliorating the inflammation of RA and the subclinical renal impairment especially its well known that our general population is already Vit-D deficient and this worsen by the inflammatory conditions that they develop.

REFERENCES

[1] Kostoglou-Athanassiou I, Athanassiou P, Lyraki A, Raftakis I, Antoniadis C. (2012) Vitamin D and rheumatoid arthritis. Ther Adv Endocrinol Metab 3 (6): 181–187.

[2] Adorini L. (2005) Intervention in autoimmunity: the potential of vitamin D receptor agonists. Cell Immunol 233: 115–124
[3] Hewison M. (2012) Vitamin D and immune function: autocrine, paracrine or endocrine? Scand J Clin Lab Invest Suppl 243: 92–102

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AB0328 SECONDARY SARCOPENIA IN RHEUMATOID ARTHRITIS PATIENTS TREATED BY BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

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Background: Sarcopenia is characterized by a loss of muscle mass and strength, which leads to a reduced physical ability, poor quality of life (QoL), frailty and mortality. Rheumatoid arthritis (RA) is considered a cause of secondary sarcopenia.
Objectives: To clarify the effectiveness of biologic disease-modifying anti-rheumatic drugs (bDMARDs) on sarcopenia, including the physical ability, body composition and nutritional status.
Methods: This was a prospective cohort study including consecutive 41 patients (11 men, 30 women, 63.6±16.1 years old) with RA who started bDMARDs for the first time at Niigata Rheumatic Center. The diagnosis of secondary sarcopenia was made according to the diagnostic algorithm of the Asian Working Group for Sarcopenia (AWGS), excluding the criteria about older age. We observed the disease activity of RA, physical ability, body composition, nutritional status and QoL at baseline and 6 months. The disease activity was assessed by the disease activity score-28 joint count erythrocyte sedimentation rate (DAS28-ESR) and clinical disease activity index (CDAI). The physical activity was determined using the health assessment questionnaire (HAQ), 10-m walking test (10MWT) and timed up and go test (TUG). The nutritional status was determined based on the controlling nutrition status (CONUT) score and prognostic nutritional index (PNI). The overall QoL was measured by European quality of life scale- 5 dimensions (EQ-5D).
Results: Among 41 patients who started bDMARDs, 19 were classified as having sarcopenia, and 7 were classified as having pre-sarcopenia. The bDMARD was certolizumab pegol in 10 patients, adalimumab in 7, abatacept in 7, golimumab in 6, tocilizumab in 5, infliximab in 3 and etanercept in 3. The DAS28-ESR (4.7±1.3 vs. 2.6±1.3, p<0.001) and CDAI (18.6±9.4 vs. 7.2±7.3, p<0.001) decreased significantly after 6 months of bDMARDs therapy. The physical activity was significantly improved after 6 months of bDMARDs: HAQ (1.1±0.9 vs. 0.7±0.9, p<0.001), 10MWT (1.5±0.7 vs. 1.6±0.6 m/s, p=0.046) and TUG (10.0±5.0 vs. 9.5±6.2 s, p=0.024). Regarding the nutritional status, the CONUT score (3.8±0.5 vs. 1.1±1.2, p<0.001) and PNI (44.9±6.4 vs. 49.7±4.1, p<0.001) were significantly improved after 6 months of bDMARDs. The EQ5D was also improved after 6 months of bDMARDs (0.64±0.15 vs. 0.71±0.20, p=0.010). The body composition analysis showed a significant increase in the body weight (54.3±13.2 vs. 55.4±14.4 kg, p=0.006) and fat mass (16.3±7.3 vs. 17.4±7.8 kg, p<0.001) after 6 months of bDMARDs but no significant increase in the appendicular skeletal muscle mass (14.7±4.3 vs. 14.8±4.5, p=0.111). The proportion of patients classified as having sarcopenia showed a decreasing trend after 6 months of bDMARDs therapy (46.3% vs. 24.4%, p=0.0637).
Conclusion: After 6 months of bDMARDs therapy, the physical ability, nutritional status and QoL were significantly ameliorated. While the muscle mass was not markedly increased, the proportion of patients with sarcopenia showed a decreasing trend. The administration of bDMARDs might be useful for preventing secondary sarcopenia in RA patients.
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AB0329 CERVICAL SPINE INVOLVEMENT IN RHEUMATOID ARTHRITIS

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Background: After the small peripheral joints, the cervical spine is the second most involved region in rheumatoid arthritis (RA). The most frequent radiological features are the atlantoaxial subluxation (AAS) which can be anterior, posterior or vertical. During the course of the disease, the affection of the cervical spine has no symptoms for a long time due to the adaptability of neurological structures. The onset of myelopathy can occur at any time. MRI assessment compared to functional cervical spine X-ray is more sensitive method to provide not only AAS but also soft tissue involvement such as periodontal synovitis or fibrous pannus and even more odontoid erosion. New data show that there is a decreasing prevalence of cervical involvement because of the biologics.
Objectives: We assessed RA patients in permanent remission with MR imaging. RA patients have no cervical pain or any neurological symptoms. We wished to explore the cervical spine involvement: AAS, odontoid erosion or periodontal soft tissue thickening. We also wished to determine the affectation of cervical spine in RA patients receiving different treatment strategies.
Methods: Altogether 49 RA female patients were included. Among them, 15 were MTX-treated, biologic-free, 34 patients received biologics (17 infliximab [IFX] and 17 tocilizumab [TCZ]) as first-line biologic treatment, in combination with MTX. There was no significant difference between the main characteristics of these subgroups. ESR, CRP and DAS28 were determined in all RA patients in every 3 months. We calculated sumESR, sumCRP and sumDAS28 indices from the past 3 years.
Results: We detected anterior AAS in one-quarter of RA patients (13 affected patients from the total 49) (26,5%). There was no significant difference between the therapeutic subgroups. No posterior or vertical AAS occurred. Compared with patients without cervical involvement, the patients with AAS showed higher sumCRP and sumESR levels, higher sumDAS28 scores and more frequent seropositivity, but these differences were not significant. Soft tissue involvement of the cervical spine was detected in 33,3% of MTX-treated, in 35,3% of IFX-treated and in 5,9% of TCZ-treated RA patients. Eight RA patients had odontoid erosion (16,3%), 3 from the MTX, 2 from the IFX and 3 from the TCZ-treated subgroups. In relation to soft tissue involvement and odontoid erosion we did not find any correlation with age, disease duration, seropositivity, sumESR, sumCRP or sumDAS28 indices.
Conclusion: These findings suggest that the presence of cervical involvement in RA patients is an important and frequent phenomenon even in asymptomatic patients. Higher ACPA titer, high disease activity and erosive disease at baseline are predictors of atlantoaxial involvement. With the appropriate disease control with conventional or biologic treatment, progression of cervical spine involvement can also be prevented.

REFERENCES

[1] The Craniovertebral Junction in Rheumatoid Arthritis: State of the Art. Ferrante A, Ciccia F, Giammalva GR, Iacopino DG, Visocchi M, Macaluso F, Maugeri R. Acta Neurochir Suppl. 2019;125:79-86.
[2] Magnetic resonance imaging of the craniovertebral junction in early rheumatoid arthritis. Carotti M, Salaffi F, Di Carlo M, Sessa F, Giovagnoni A. Skeletal Radiol. 2018 Sep 11.

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AB0330

RELATIONSHIP BETWEEN FOREFOOT SYNOVITIS IN RHEUMATOID ARTHRITIS AND WORSENING FOREFOOT DEFORMITY

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Background: While the number of rheumatoid arthritis (RA) surgeries has been declining due to advances in pharmacotherapies for RA, forefoot surgeries are on the rise. In recent years, the common use of joint ultrasonography in RA consultations has led to the early detection of synovitis. However, little is known about how much forefoot deformities such as hallux valgus and metatarsophalangeal (MTP) joint dislocation are affected by synovitis in the forefoot of RA patients.
Objectives: The present study examined factors involved in forefoot deformity among patients with foot synovitis identified on joint ultrasound.
Methods: Subjects (71 patients, 91 feet) were RA patients who had undergone foot joint ultrasonography more than 2 years earlier and underwent standing X-rays of the feet before and after ultrasonography. Surgery cases were excluded. Mean age was 64.9 years (range, 15-90 years). Disease stage was Stage 1 in 14 patients, Stage 2 in 14 patients, Stage 3 in 16 patients, and Stage 4 in 27 patients. According to the Steinbrocker functional classification, RA was Class 1 in 45 patients, Class 2 in 19 patients, Class 3 in 6 patients and Class 4 in 1 patient. Twenty-five patients had been administered biological drugs. At the time of joint ultrasonography, patients were questioned regarding whether they had any complaints involving the forefoot, midfoot or hindfoot (noted separately). The following scans were performed: forefoot (MTP joints 1-5); midfoot (calcaneocuboid, calcaneocuboid and cuneonavicular joints) and hindfoot (peroneal muscle tendon, talocrural joint, talocalcaneal joint and posterior tibial muscle tendon). Foot deformity score (FDS) (hallux valgus angle + first-second intermetatarsal angle [M_1M_2 angle] + first-fifth intermetatarsal angle [M_1M_5 angle]) was used as the benchmark for forefoot deformity, and an increase >5° was considered to indicate worsening deformity.
Results: Forefoot deformity had progressed in 25 patients. Mid- and hindfoot synovitis and the presence of complaints were not associated with deformity. However, significant worsening of FDS was observed in patients with forefoot synovitis or forefoot complaints. While no difference in age, disease activity, biologic disease-modifying antirheumatic drug usage or health assessment questionnaire results were seen in the advanced deformity group, duration of disease was significantly shorter in this group.
Conclusion: Mid- and hindfoot synovitis was unrelated to forefoot deformity. MTP joint synovitis in the forefoot was related to forefoot deformity. Continuous synovitis in the forefoot must damage the articular capsule and ligament structure, leading to progression of deformity. As shown by the short duration of the disease in the advanced deformity group, deformity may progress in the early stages among patients with forefoot deformity.
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AB0331

DEPRESSION AND ANXIETY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory joint disease leading to substantial morbidity and mortality and had a major economic and psychological impact on individuals with RA and their families. The prevalence of depressive disorder in RA was 17% and associated with poorer outcomes
Objectives: To evaluate prevalence of depression and anxiety and their related factors in patients with RA.
Methods: In this cross-sectional study, 464 patients with RA from two RA registries, the Siriraj Rheumatoid Arthritis (SiRA) registry and the Thai Army Rheumatoid Arthritis Cohort (TARAC) were enrolled. Demographic data and clinical variables, including disease activity, functional status, health-related quality of life, and cognitive function, were collected. Depression and anxiety were assessed using the Thai version of the Hospital Anxiety and Depression Scale (Thai HADS).
Results: Based on the Thai HADS cutoff value of more than 8 out of 21, 12.5% and 14.5% had some degrees of depression and anxiety, respectively. The proportion of depression and anxiety elevated with increasing disease activity or worsening functional status. However, in multivariate analyses, only global health [RR (95%CI) 0.98 (0.96 - 0.99), p 0.001] was negatively associated with depression, after adjusted for covariate. For anxiety, functional disability [RR (95%CI) 2.46 (1.33 - 4.54), p 0.004] and marital status [married: RR (95%CI) 2.43 (1.25 - 4.73), p 0.009] significantly increased the risk, while disease duration 10 years or more [RR (95%CI) 0.45 (0.25 - 0.80), p 0.007] and global health [RR (95%CI) 0.97 (0.95 - 0.98), p < 0.001] decreased this risk.
Conclusion: Depression and anxiety are common in patients with RA. Patients' perception of their current health is significantly related to mood disorders. Therefore, mental health status, especially mood disturbances, should be addressed in routine practice to improve quality of life in RA.

Table 1 Multivariate analyses for depression and anxiety

Factors	Depression		Anxiety	
	RR (95% CI)	P value	RR (95% CI)	P value
DAS28 > 2.6	1.66 (0.49 – 5.70)	0.418		
HAQ > 0.5	1.38 (0.75 – 2.54)	0.303	2.46 (1.33 – 4.54)	0.004
Comorbidity	1.04 (0.58 – 1.89)	0.890	1.05 (0.59 – 1.86)	0.875
Global health	0.98 (0.96 – 0.99)	0.001	0.97 (0.95 – 0.98)	< 0.001
Cognitive impairment	1.12 (0.59 – 2.15)	0.727	1.66 (0.84 – 3.30)	0.144
Pain score	1.07 (0.95 – 1.20)	0.275	1.01 (0.90 – 1.14)	0.819
Disease duration ≥ 10 years			0.45 (0.25 – 0.80)	0.007
Marital status (married)			2.43 (1.25 – 4.73)	0.009

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AB0332

CLINICAL FEATURES AND RISK FACTORS OF CHRONIC HEART FAILURE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS PRIOR TO THERAPY WITH BASIC ANTI-INFLAMMATORY DRUGS

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Background: Heart failure (HF) is a major cause of premature mortality, there is little information regarding its prevalence and associated risk factors in patients (pts) with early rheumatoid arthritis (RA).
Objectives: to study the frequency, clinical manifestations and risk factors associated with the development of HF in pts with early RA prior to therapy with basic anti-inflammatory drugs.
Methods: A total of 74 pts with early RA (ACR/EULAR criteria, 2010) were included in the study: 78% of women, median (Me) age - 56 years [47; 61], Me of disease duration - 7 [4;8] months; Me DAS28 5.3 [5.0;6.2], IgM RF seropositive (87%) and/or ACCP (100%), without any experience of administration of disease-modifying antirheumatic drugs and glucocorticoides. All pts underwent blood pressure monitoring, echocardiography, tissue Doppler imaging, NT-proBNP. The normal range for NT-proBNP was less than 125 pg/ml. HF was diagnosed according to the recommendations of the European Society of Cardiology (2012).
Results: HF was diagnosed in 24 (33%) pts: in 23 pts - HF with preserved ejection function (EF), in 1 pts - HF with reduced EF. Dyspnea was detected in 21 (87%) RA pts with HF (positive predictive value (PPV)-33%), in 6 (25%) - ankle edema (PPV-35%), in 24 (100%) - fatigue (PPV-38%). In 5 (21%) pts dyspnea NYHA=1 was observed, 15 (63%) - NYHA=2, in 1 (4%) - NYHA=3. Diastolic dysfunction of the left ventricle was detected in all pts with HF (PPV-69%). Elevated NT-proBNP level wasn't highly indicative for HF in early RA (PPV=41%).
All pts with early RA were divided into 2 groups: 1- with HF, 2-without HF. Pts with RA and HF were older (61 [58;65] vs 51 [36;56] years), had higher BMI (28 [25;32] vs 24 [22;29] kg/m^2, p<0,05), NT-proBNP level (192.0 [154.9;255.7] vs 77.0 [41.1;191.2] pg/ml, p<0.05), more likely to have arterial hypertension (AH) (83% vs 51%, p<0.05), carotid atherosclerosis (91% vs 48%, p<0.05), coronary artery disease (CAD) (40% vs

7%, p<0.05) then RA pts without HF. DAS28, CRP and ESR did not differ in two groups.

In order to identify factors associated with the risk of development of HF, a step-by-step linear regression analysis was performed. The multiple coefficient of determination is R^2 = 57.1 (R-0.76, p<0.001) (Tabl.1).

Table 1. Risk factors of HF in patients with early rheumatoid arthritis

Model	Non-standard coefficient β	p	95% CI	
Abdominal obesity, yes/no	0,249	0,025	0,032	0,466
CRP, mg/l	0,004	0,003	0,001	0,006
Dyslipidemia, yes/no	0,255	0,024	0,034	0,476
AH, yes/no	0,004	0,144	0,001	0,010
TIM carotid arteries, mm	0,758	0,026	0,091	1,423
CAD, yes/no	0,226	0,073	0,021	0,474

According to ROC analysis, the diagnostic significance of studied factors was high with 88% sensitivity and 88% specificity.

Conclusion: HF mainly with preserved EF was found in 1/3 of pts with early RA with high and moderate activity. Clinical manifestations of HF had low diagnostic value. The risk factors of HF in pts with RA were the level of CRP and traditional risk factors (abdominal obesity, AH, dyslipidemia), the value of TIM of carotid arteries and the presence of CAD.

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AB0333 EFFECT OF OBESITY ON THE COURSE OF RHEUMATOID ARTHRITIS AND CARDIOVASCULAR RISK

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Background: The literature shows that the level of pro-inflammatory cytokines increases in obesity. High body mass index (BMI) is increasingly common in rheumatoid arthritis (RA), which can aggravate cardiovascular risks.

Objectives: The aim is to study the effect of obesity on the course of RA and cardiovascular risk.

Methods: 100 patients (male-7%, female-93%) aged from 21 to 81 years (average age 55 ± 12.4) with reliable RA were examined. High activity in DAS28 scale was observed in 68%, moderate - in 30%, low - in 2%, rheumatoid factor (RF) positivity - in 88%, ACCP - 81%. DMARDs received 78%, glucocorticosteroids 60% of patients. Arterial hypertension (AH) was present in 45% of patients. BMI ranged from 15 to 46.5 kg/m^2 (average 26.8±5.7). The patients were divided into three groups: the 1st (n=38) with a normal BMI up to 25 kg/m^2, the 2nd (n=24) - with heightened BMI 25-29.9 kg/m^2, the 3rd group (n=28) - more than 30 kg/m^2. Patients were examined in standard laboratory tests, all of them had echocardiogram.

Results: Patients in the groups with normal and heightened BMI had no statistical differences in manifestations of articular syndrome. In the 3rd group with obesity reliably higher (pThe level of systolic blood pressure (BP) correlated with BMI, although even in the group with obesity it was 136.4±21.9 (pThe increase in LVMI correlated (p**Conclusion:** RA in patients with obesity is characterized by a higher activity first of all because of pain syndrome. Increased BMI leads to bad prognostic myocardial changes in patients with RA, while cholesterol and blood pressure may stay within the normal range. This causes the need of using the echocardiography for this group of patients.

REFERENCES

[1] rheumatoid arthritis, body mass index

Disclosure of Interests: None declared

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AB0334 THE OVARIAN RESERVE MEASURING THE ANTI-MÜLLERIAN HORMONE IS NOT DIMINISHED IN PATIENTS WITH RHEUMATOID ARTHRITISCOMPARED TO THE HEALTHY POPULATION

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Background: Rheumatoid Arthritis (RA) is the most prevalent chronic inflammatory arthritis, affecting 0.5-1% worldwide population and predominates in females. Altered fertility has been reported due to a decrease in ovarian reserve secondary to sustained inflammation. The anti-Müllerian Hormone (AMH) is currently the most reliable biomarker of ovarian reserve. However, few and contradictory studies have been reported to analyze the relationship between fertility in RA women patients and AMH.

Objectives: The aim of present study is to determine the AMH serum concentrations in a long-standing RA patients and control group. We also sought to determine the correlation between AMH serum levels and disease activity measured by different parameters and the effect of biological DMARDs.

Methods: Serum AMH levels were measured in 60 women with long-standing RA aged 20-50 y.o. and compared to 59 healthy women. AMH was assessed by ELISA (*Gen II Beckman Coulter Inc.*) and a large data set of clinical and molecular data was annotated. Demographic parameters, RA disease activity measured by DAS28 score and inflammatory biomarkers such as ESR, CRP, lymphocyte CD4+, CD8+, NK cells, IL-10 and IL-6 were determined. A comprehensive gynecological self-administered questionnaire was given. Serum AMH levels were age-correlated. Differences between groups were calculated using Student's t-test or Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables. Multivariate analysis was conducted by the partial correlation coefficient. Linear regression analysis was performed to study the effect of different variables on proportional AMH change. *P* value <0.005 were considered significant.

Results: The median age was similar in AR and control groups (37.4 ±6.23 *vs* 37.3±6.27 *P*=0.937). Mean disease duration was 8.37±5.36 years. The number of previous treatments was <3 in 71.7% of patients and ≥3 in 28.3%. Disease activity measured by DAS28 was 2.89± 1.54. The age-adjusted mean serum concentration of HAM was 1.27 ng/ml [IQR 0.42; 2.24] in RA patients and 1.31 ng/ml [IQR 0.46; 3.09] in controls (*P*=0.608). Neither disease activity (*P*=0.862), nor current or previous bDMARDs treatments (*P*=0.871) were associated with HAM levels. However, a negative linear correlation was observed between HAM and IL-10 levels (*P*= 0.033).

Conclusion: Our study shows that ovarian reserve determined by HAM serum levels is not reduced in rheumatoid arthritis patients compared with healthy controls. In our series, HAM levels were not affected by disease activity however a significant correlation was observed between HAM and IL-10 levels. These results support the role of cytokines profile in the female reproductive system and will focus further investigations in this critical area, mainly once biological DMARDs have be recommended in RA pregnant patients.

REFERENCES

[1] Brouwer J, Fleurbaaij R, Hazes JM, Dolhain RJ, Laven JS. Subfertility in rheumatoid arthritis is often unexplained or caused by anovulation. Arthritis Care Res (Hoboken). 2016.

[2] Brouwer J, Hazes JM, Laven JS, Dolhain RJ. Fertility in women with rheumatoid arthritis: influence of disease activity and medication. Ann Rheum Dis. 2015;74(10):1836-1841.

[3] Brouwer J, Laven JS, Hazes JM, Schipper I, Dolhain RJ. Levels of serum anti-Mullerian hormone, a marker for ovarian reserve, in women with rheumatoid arthritis. Arthritis Care Res (Hoboken). 2013;65(9):1534-1538.

[4] Del Junco DJ, Annegers JF, Coulam CB, Luthra HS. The relationship between rheumatoid arthritis and reproductive function. Br J Rheumatol. 1989;28 Suppl 1:33; discussion 42-35.

[5] Dewailly D, Andersen CY, Balen A, et al. The physiology and clinical utility of anti-Mullerian hormone in women. Hum Reprod Update. 2014;20 (3):370-385.

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AB0335

THE CORRELATION OF CORRELATION OF TH17 AND TREG CELL LEVELS OF IN CORONARY HEART DISEASE PATIENTS WITH RHEUMATOID ARTHRITIS

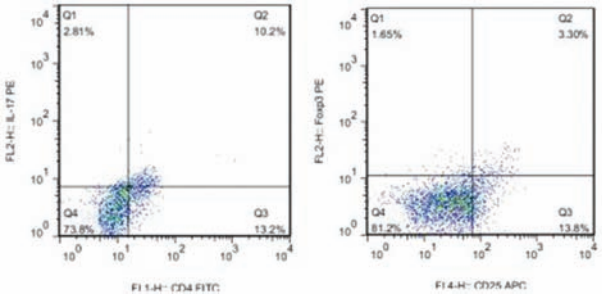
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Background: Rheumatoid arthritis (RA) is a prevalent chronic autoimmune inflammatory disease. Also acute coronary syndrome (ACS) is a prevalent chronic inflammatory disease. Now more and more studies have also shown that coronary heart disease is also associated with immune inflammationWe will discuss Th17 and Treg cell levels in patients with rheumatoid arthritis combined with coronary heart disease and simple rheumatoid joints as well as normal people. Its pathogenesis is closely associated with a failure of endogenous immune tolerance that caused by the imbalance of CD4/CD8.New T subgroup Th17 Treg,T lymphocytes play an important role in the occurrence and development of RA and ACS,Moreover, T lymphocytes are one of the first cells to be recruited into atherosclerotic plaques[1], and most adhesion molecules and chemokines that promote the migration of monocytes to the intima are also related to T cell recruitment.T lymphocytes mainly divided into two major subsets of CD4/CD8, including CD4 $^{+}$T helper cells, which are classified into Th1Th2 and newly discovered Th17 cells and regulatory T cells subgroup, have the effect of the immune response to promote the immune, and CD8 $^{+}$play the role of killer cells and suppress the immune response,Similar to CD8, (Treg) lymphocytes can reduce the body's antitumor ability by inhibiting cell contact and the production of inhibitory factors and effector T cells

Objectives: Through clinical studies, we want to explore whether the proportion of Th17/Treg in peripheral blood of RAwithACSpatients is reduced to indicate whether the immune balance is broken, thus providing further data for clinical studies

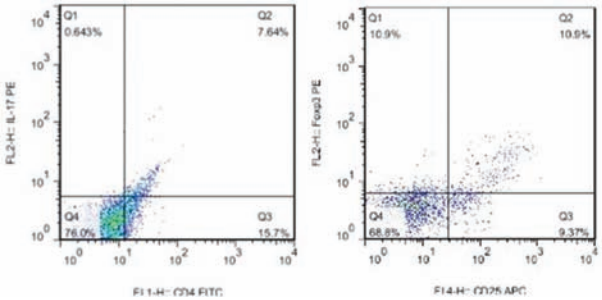
Methods: In April 2017 to September 2018 in our hospital Patients with RAand ACS diagnosed by Coronary angiography in our hospital of 20 cases male:9 female:12 into the research object, the diagnosis of ACS combined with clinical data of 20 patients as Observation group, These patients have been diagnosed with rheumatoid arthritis. Another 20 rheumatoid arthritis patientsmale: 11 female:9were collected from the rheumatology department of our hospital, and 20 normal healthy peoplemale:10female:10 were collected from the physical examination center of our hospital,as control group

Chart-1

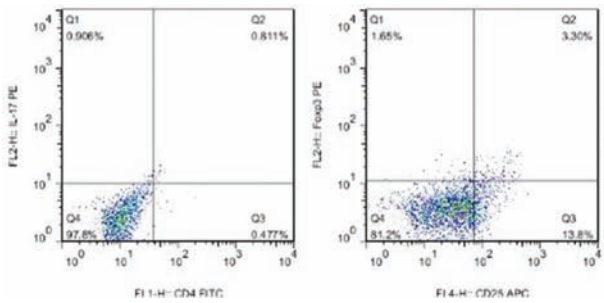


RA with ACS group

Chart-2



RA group



Control group

Results: Compared with the control group, the proportion of Th17 cells and Treg cells in peripheral blood of RA with ACS and RA groups increased and decreased respectively ($P < 0.05$).Compared with the RA group, the proportion of Th17 cells in the peripheral blood of RA with ACS group increased, while the proportion of Treg cells decreased ($P < 0.05$).The proportion of Th17 cells in RA with ACS group was higher than that in RA group and control group ($P < 0.05$).Th17/Treg ratio in control group, RA group, ACS and RA groups were respectively Compared with the control group, Th17/Treg increased in the RA with ACS and RA groups, and the RA with ACS group was higher than the RA group, with statistically significant differences ($P < 0.05$),but the ratio between the RA group and the control group was not significant

Conclusion: Through this rare clinical study, it was found that the levels of Treg cells and Th17 cells in patients with rheumatoid arthritis combined with coronary heart disease were to some extent higher than those in patients with rheumatoid arthritis alone and normal healthy people.We can speculate whether it is possible to find a target for Treg cell Th17 cell levels in patients with RA with ACS expanding the sample study again, so as to intervene as early as possible and regulate the immune balance to avoid the progression of coronary heart disease and adverse cardiovascular events

REFERENCES

[1] Libby, P.; Ridker, P. M.; Hansson, G. K.; Leducq Transatlantic Network on, A., Inflammation in atherosclerosis: from pathophysiology to practice. J Am Coll Cardiol 2009, 54 (23), 2129-38.

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AB0336

COMPARATIVE ANALYSIS OF ESTIMATED BONE MASS AND BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM THE CHIKARA STUDY

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Background: Patients with rheumatoid arthritis (RA) have lower muscle mass and a higher rate of sarcopenia than healthy individuals. The relationship between rheumatoid arthritis and bone loss is well known. Dual energy X-ray absorptiometry (DEXA) and bioelectrical impedance analysis (BIA) are used to diagnose sarcopenia, but the correlation between bone mineral density and estimated bone mass is unknown.

Objectives: To investigate the correlation between bone mineral density and bone mass in RA patients.

Methods: Data from a prospective observational study (CHIKARA study) were analyzed. Bone mineral density (BMD) was measured by DEXA, and bone mass was measured by BIA on the same day, and the correlations between BMD at each measurement site and bone mass were evaluated.

Results: A total of 90 RA patients (women, 83%; mean age, 67.2±12.1 years) were included. The median disease duration was 8.5 (interquartile range (IQR): 4.9, 17) years, the mean DAS28-ESR was 2.92±1.2, and the median MTX dose was 10 (IQR: 8, 12) mg/week. Nineteen patients (21%) used a biologic agent. There was a significant correlation between total hip BMD and bone mass (r=0.64, p<0.001). The details are shown in Figure 1. Bone mass was significantly correlated with femoral neck BMD (r=0.62, p<0.001), whole body BMD (r=0.60, p<0.001), and lumbar BMD (r=0.49, p<0.001). Bone mass was significantly lower by DEXA (1.9 ±0.5 kg) than by BIA (2.0±0.4 kg) (P<0.001).

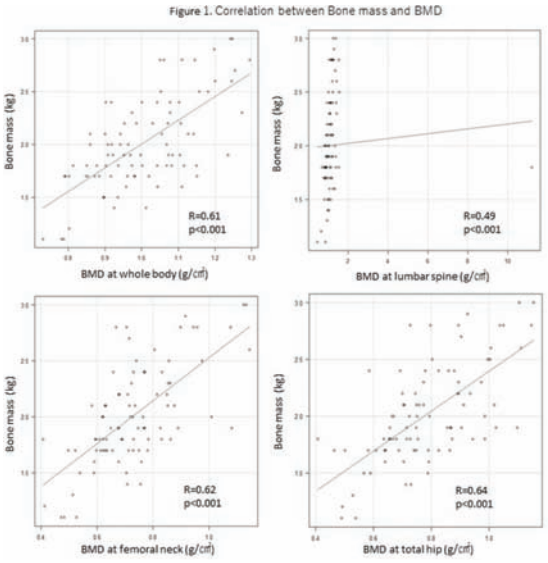


Figure 1

Conclusion: There was a significant correlation between bone mass by BIA and BMD by DEXA. Bone mass by BIA and total hip BMD had the strongest correlation. Bone mass is likely to be overestimated by BIA. Thus, we need to evaluate it with appropriate caution.

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AB0337 IS THE RADIAL DEVIATION ASSOCIATED WITH MEDIAN NERVE SWELLING IN PATIENTS WITH RHEUMATOID ARTHRITIS?

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Background: Rheumatoid arthritis (RA) and carpal tunnel syndrome (CTS) are known to be associated and also RA may lead to swelling of the median nerve without the presence of CTS.

Objectives: This study was conducted to test the hypothesis that one of the causes of this median nerve swelling may be radial deviation developing after wrist involvement of RA.

Methods: Of a total of 138 cases, 51 that met the inclusion criteria were included in the study. Electroneuromyography (ENMG) was performed on each patient and those with a CTS diagnosis were excluded from the study. Duruöz hand index, visual analog scale and painDETECT questionnaire was performed in clinical assesment. Radiographic measurements including radial inclination angle were performed with radiography. Using ultrasonography, the median nerve cross-sectional areas (CSAs) of the patients were measured from the four levels of the distal 1/3 of the forearm, radioulnar joint, pisiform bone and hook of hamate, and the ulnar nerve CSAs were measured from the pisiform bone.

Results: The study completed with 102 hands of 51 patients. 27% of these RA patients without clinical and electrophysiological findings were diagnosed as CTS by ultrasonography. A negative correlation was found between the radial inclination (RI) and the median CSAs measured from the radioulnar joint (R: - 0.49; p: 0.00), the pisiform bone (R: - 0.45; p: 0.00), and hook of hamate (R: - 0.60, p: 0.00). When the hands were divided into three groups according to the ranges of RI specified in the literature, the median nerve CSA was found to be significantly higher in the group with a low RI at these levels (p < 0.001).

Conclusion: The median nerve CSAs increased as the radial deviation increased in RA patients. The prevention of disease progression may prevent the increase in median nerve CSA by preventing deviations in patients with RA. And the development of CTS may also be prevented.

REFERENCES

[1] Yagci I, Akdeniz Leblecicier M, Mansiz Kaplan B, Ozturk Gokbakan D, Akyuz G. Sonographic measurements can be misleading for diagnosis carpal tunnel syndrome in patients with rheumatoid arthritis. Acta Reumol Port. 2016;41:40-4

[2] Joshua Broder. Diagnostic imaging for the emergency physician. Elsevier Healh Science. Philadelphia, 2011; page 783.

[3] Ito J, Koshino T, Okamoto R, Saito T. Radiologic Evaluation of the rheumatoid hand after synovectomy and extensor carpi radialis longus transfer to extensor carpi ulnaris. J Hand Surg Am. 2003;28(4):585-90.

[4] Hammer BH, Hovden IA, Haavardsholm EA, Kristian Kvien T. Ultrasonography shows increased cross-sectional area of the median nerve in patients with arthritis and carpal tunnel syndrome. Rheumatology (Oxford). 2006;45(5):584-588.

[5] Hammer BH, Haavardsholm EA, Kristian Kvien T. Ultrasonographic measurement of the median nerve in patients with rheumatoid arthritis without symptoms or signs of carpal tunnel syndrome. Ann Rheum Dis. 2007;66:825-7

[6] Sakthiswary R, Singh R. Has the median nerve involvement in rheumatoid arthritis been overemphasized? Rev Bras Reumol. 2017;57(2):122,128.

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AB0338 ELDERLY ONSET RHEUMATOID ARTHRITIS AND POLYMYALGIA RHEUMATICA: COMPARATIVE CLINICAL STUDY

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Background: Polyarthritis at the elderly people usually has a similar onset with an acute inflammatory character and scapular girdle involvement. Differentiating elderly onset rheumatoid arthritis (EORA) and polymyalgia rheumatica (PMR) can be a diagnostic challenge.

Objectives: To analyse the clinical and analytical differences between EORA and PMR.

Methods: Longitudinal observational study of patients older than 60 years newly diagnosed with EORA (ACR/EULAR 2010) and PMR (ACR/EULAR 2012). Inclusion: consecutive and voluntary. Follow-up time: 12 months. A single rheumatologist made all follow-up visits. The clinical-epidemiological and analytical characteristics were collected. The statistical study was performed with Stata 15.1.

Results: 45 EORA were recruited (53% women; mean age 74.8 ± 7.5) and 20 PRM (85% women; mean age 76.6±5.0).

75% of EORA had scapular girdle involvement, but only 44% of the pelvic girdle. All had peripheral arthritis, and the small joints of the hands were involved in 93.3%, with edema in 46.7%. Forty percent of EORA patients were seropositive (RF> 20 IU/mL and/or ACPA> 20 U/mL): 33% RF positive (132.8 ± 126 IU/mL), 28.9% for ACPA (2 cases [15.4%] from 100 to 250 U/mL and 11 cases [84.6%] above 250 U/mL) and in 10 patients [22.2%] double positive). All patients with PMR patients had shoulder girdle involvement and 90% of the pelvic girdle. None of them had peripheral arthritis. RF was positive in one patient (73 IU/mL) and ACPA in 2 patients (titers between 20-40 U/mL). No patient was double positive. Table 1 and 2.

	RA N = 45 n (%)	**PMR** N = 20 n (%)	**p value**
Fever	1 (2.2)	2 (10.0)	0.222
Weight loss	16 (35.6)	8 (40.0)	0.732
Asthenia	31 (68.9)	14 (70.0)	0.929
Anorexia	20 (44.4)	7 (35.0)	0.476
Morning stiffness	43 (95.6)	19 (95.0)	0.922
Oedema	21 (46.7)	0 (0)	**<0.001**
Shoulder girdle	34 (75.6)	20 (100)	**0.014**
Pelvic girdle	20 (44.4)	18 (90.0)	**<0.001**
Peripheral arthritis	45 (100)	0 (0)	**<0.001**
Small joint of the hands	42 (93.3)	0 (0)	**<0.001**
	RA N = 45 n [%]	**PMR N = 20 n [%]**	**p value**
RF positive	15 (33.3)	1 (5.0)	**0.014**
ACPA positive	13 (28.9)	2 (10.0)	0.095

After 12 months of follow-up, there was no difference between the dose of glucocorticoids received in patients with EORA and PMR (p = 0.684). There were also no differences in glucocorticoids adverse effects according to the diagnosis (p = 0.734).

Regarding the use of immunosuppressors, this was higher in patients with EORA (91% EORA and 20% PMR), according to the usual clinical practice guidelines.

The percentage of remission in PMR at 12 months was 95%. However, using DAS 28-VSG, only 40.9% of patients with EORA were in remission at 12 months (p=0.003).

Conclusion: The female predominance was higher in PMR than in EORA. The scapular girdle involvement, but especially the pelvic girdle, was more frequent in PMR. In contrast, involvement of peripheral joints and edema were more frequent in EORA. RF and ACPA were more frequent in EORA. There were no other analytical differences that would help their differential diagnosis. The mean and accumulated doses of glucocorticoids during the first 12 months were similar, as well as the percentage of side effects. Immunosuppressors are more frequently used in EORA than in PMR. Remission is achieved more commonly in PMR than in EORA.

REFERENCES

[1] Olivieri I, Pipitone N, D' Angelo S, Padula A, Salvarani C. Late-onset rheumatoid arthritis and late-onset spondyloarthritis. Clin Exp Rheumatol 2009;27(4 Suppl 55):S139-145.

[2] Pease CT, Haugeberg G, Montague B, Hensor EMA, Bhakta BB, Thomson W, et al. Polymyalgia rheumatica can be distinguished from late onset rheumatoid arthritis at baseline: results of a 5-yr prospective study. Rheumatology 2009;48(2):123-7.

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AB0339 HYPERURICEMIA AMONG A MOROCCAN POPULATION WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a known cause of cardiovascular disease (CVD). Several studies suggest that serum uric acid (SUA) is significantly associated with CVD in RA. However, the association between SUA and inflammation remains controversial.

Objectives: The aim of the present study is to determine the prevalence of hyperuricemia in RA patients, to assess its association with inflammation and to evaluate whether disease modifying anti rheumatic drugs (DMARDs) have a hypouricemiant effect.

Methods: We have conducted a cross-sectional study over four months in our department of rheumatology. A total of 204 RA patients receiving DMARDs in their treatment were enrolled. All patients fulfilled the RA ACR-EULAR criteria. SUA and inflammatory markers were studied. Hyperuricemia was defined as SUA>70mg/L for males and >60mg/L for females. Data analysis was carried out using the SPSS 20 Software. Univariate and multivariate regressions were performed to identify the impact of hyperuricemia in RA patients.

Results: The mean age was 51.76±12.84 and the mean age at RA diagnosis was 42.5 ± 15.23. Fourteen patients (6.9%) had hyperuricemia and the average rate of SUA was 41.99 ± 11.85 mg/L. All patients were taking Methotrexate, 34% received also Sulfasalazine, 6.4% Hydroxychloroquine and 77% steroids. Males and post-menopausal women had significantly higher SAU levels (p<0.001 and p<0.0001, respectively). Univariate analysis showed a positive relationship between SUA levels and age (p=0.004), gender (p=0.002), age at RA diagnosis (p=0.03), smoking (p=0.046), use of alcohol (p=0.025), high body mass index (BMI) (p=0.012), elevated blood pressure (p<0.0001), dyslipidaemia (p<0.001) and high doses of steroids (p=0.001). The association between RA and gout was noted in one case. We found no correlation between inflammation, DMARDs, CVD and SUA. In multivariate regression In multivariate analysis adjusted for age, gender, BMI and steroids maintained a significant correlation with SAU.

Conclusion: The prevalence of hyperuricemia is low in our RA patients and similarly gout remains infrequent. However, RA patients must be screened for hyperuricemia. There is growing evidence that higher doses of steroids can cause hyperuricemia. Practitioners should be aware that these patients are at risk of having high SUA levels as well as more traditional cardiovascular risk factors. Thus, appropriate preventive interventions in these patients should be introduced.

REFERENCES

[1] J.-Y. Choe, S.-K. Kim. Association between serum uric acid and inflammation in rheumatoid arthritis: Perspective on lowering serum uric acid of leflunomide. Clin Chim Acta. 2015 Jan 1;438:29-34.

[2] Kuo D, et al. Hyperuricemia and incident cardiovascular disease and noncardiac vascular events in patients with rheumatoid arthritis. International Journal of Rheumatology, 2014 Aug 17;523897-7.

[3] Zaragoza-García O, et al. Hypertriglyceridemic waist is associated with hyperuricemia and metabolic syndrome in rheumatoid arthritis patients. Diabetes Metab Syndr. 2019 Jan - Feb;13(1):722-729.

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AB0340 PATIENTS WITH RHEUMATOID ARTHRITIS COMPLICATED WITH DEPRESSION HAVE A HIGHER FREQUENCY OF EXPERIENCING PHYSICAL DEPRESSIVE SYMPTOMS

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Background: Approximately 15% of patients with rheumatoid arthritis (RA) experience depression with an odds ratio of 1.42 (95% CI 1.3–1.5) compared to healthy people. Depression is related to disease activity and activities of daily living (ADL) of patients with RA. Previous studies have reported depressed mood, sleep disorder, and other such symptom separately with no reports addressing the factors constituting depression together.

Objectives: To examine the factors constituting depression in RA patients.

Methods: The subjects were 124 registered RA patients. The following patient characteristics were investigated: age, gender, body mass index, smoking history, and presence or absence of hypertension and diabetes. Baseline steroid dosage, methotrexate dosage, and serum matrix metalloproteinase–3 levels and creatinine level were examined. For evaluation, we used the simplified disease activity index (SDAI) for RA disease activity, the health assessment questionnaire disability index (HAQ-DI) score for ADL, and the Hamilton depression rating scale (HAM-D) score for depression status. Different items on the HAM-D scale were analyzed, and the correlation between HAM-D and each item was examined.

Results: Although 42 patients (33.9%) answered that they experienced "depressed moods", more than 50% of the patients answered that they had "anxiety somatic (79 patients, 63.7%)" and "somatic symptoms general (69 patients, 55.6%)". Patients, who responded that they had "work and activities (57 patients, 46.0%)", "hypochondriasis (53 patients, 42.7%)," and "genital symptom (49 patients, 36.5%)," exceeded the number of patients claiming to experience depression. "Depressed mood" correlated with SDAI (r=0.31, p<0.01) and HAQ-DI (r=0.26, p<0.01). "Somatic Symptoms General" correlated with SDAI (r=0.30, p<0.01) and HAQ-DI (r=0.29, p<0.01) as well. "Anxiety somatic" correlated with age (r=0.24, p<0.01) only and no other factor.

Conclusion: Patients with rheumatoid arthritis patients experiencing a depressed state of mind have a high chance of exhibiting physical symptoms as compared to patients with "depressed mood" alone. These factors are not necessarily associated with RA disease activity or HAQ-DI.

Acknowledgement: Cooperation on data collection: All Showa University in Rheumatoid Arthritis (ASHURA) group
Disclosure of Interests: YUSUKE MIWA Grant/research support from: Mitsubishi Tanabe Pharma Corporation and AbbVie CK. Astellas Pharma Inc., Mitsubishi Tanabe Pharma Corporation, AbbVie CK, Pfizer Japan Inc., Chugai Pharmaceutical Co., Ltd., Eizai Co., Ltd, Asahi Kasei Pharm Co., Ltd, YL Biologics Ltd., Japan Blood Products Organization, Ono Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., and Teijin Pharma Ltd.
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AB0341 REASONS FOR DROP-OUT IN RHEUMATOLOGY SPECIALTY CARE OF ELDERLY RHEUMATOID ARTHRITIS PATIENTS

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Background: The difference between total and healthy life expectancies were 12.3 and 8.8 years for women and men respectively in 2016, in Japan. Rheumatoid arthritis (RA) not only reduces daily living activities due to joint symptoms but also deteriorates the life prognosis due to systemic inflammation. That is, patients with RA are short for both total and healthy life expectancy. In recent years, the need for rheumatologist to provide specialty medical care to elderly patients with RA has been expanding. However, some elderly patients drop out of specialty treatment and care. To date, there are little information concerning background of patients who drop out.
Objectives: To investigate reasons and characteristics of elderly RA patients who drop out from rheumatology specialty medical care.
Methods: Of RA patients who had been visited our rheumatology specialty facility in 2016, we defined as drop-out when the patients did not return to the hospital in 2017. We surveyed age, gender, disease activity, and reason for drop-out retrospectively from medical records and questionnaires.
Results: Of 2,092 patients with RA who visited to our department, 156 patients (7.5%, 95% confidential interval: 6.4 – 8.6%) dropped out. Among drop-out patients, 101 patients were older than 65. 37 patients (37%) dropped out due to comorbidities including death (group C), 32 (32%) patients were introduced certified rheumatologists near the patients' residences (group R). Twenty-two patients were due to unknown reasons, nine were due to remission, and one patient moved out to other area. Average age of both group C and R were eighty years old. Glucocorticoid user rate (C: 89%, R: 71%) and dose (C: 5.6 mg, R: 5.7 mg) were similar in the both two groups. Patients in group C showed less use of methotrexate (C: 19% vs R: 58%, P < 0.01) compared with group R patients. Simple disease activity index was similar, however, higher modified health assessment questionnaire was observed in group C patients (C: 1.13 vs R: 0.25, p=0.01).
Conclusion: Some elderly RA patients, especially may drop out from rheumatology specialty care due to comorbidities. Regional co-management should be constructed so that elderly patients could continue receiving RA specialized care.
Disclosure of Interests: None declared
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AB0342 DEPRESSION ON PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic representative inflammatory autoimmune disease. The association of disease activity and pro-inflammatory cytokines with depression has not been sufficiently investigated.
Objectives: The aim of this study is to analyze the association between disease activity and depression using Patient Help Questionnaire (PHQ-9) in patients with rheumatoid arthritis (RA). We also examined the outcome of intervention on depression score and determined the prevalence of depression and risk factors for depression and deterioration of depressive symptoms in RA patients.
Methods: 146 RA patients with a mean age of 51,3±11,2 years were included in the study. Demographic and laboratory data were examined. Disease activity score 28-joint count C-reactive protein (DAS 28-CRP) was performed to assess disease activity of RA. PHQ-9 scores were collected at each clinic visit. Physicians assessed corresponding disease activity using Clinical Disease Activity Index (CDAI). Patients with at least moderate depression (PHQ-9 _10) were offered depression intervention, counseling or medications. PHQ-9 was re-administered after intervention.
Results: 119 of RA patients were females, the average disease duration was 6,8 ± 5,9 years. Depression was diagnosed in 38 of RA patients: 18 - mild, 13 - moderate and 7 - moderately severe. Severity of depression positively correlated with disease activity in RA patients ($p < 0.05$). RA patients with moderate/high CDAI had significantly higher PHQ-9 than those with low CDAI ($p<0.001$). Of 7 patients who met criteria for depression intervention, 6 were treated and 1 - declined. With treatment 5 patients had improved PHQ-9 scores, 1 patient worsened, and 1 patient had no change in score. The risk of developing a depressive disorder is highest between 5 and 10 years of onset of the disease and depression is a better predictor of work disability than disease activity and response to treatment. Depression is associated with more pain, fatigue and impaired quality of life. Therefore, the risk to develop a depression is increased with impaired function as measured by the health assessment questionnaire (HAQ). Increased disease activity increases the risk for depression in RA. The severity of disease activity of RA, DAS 28-CRP [OR 1.75, 95% CI 1.08-2.64]) and severity of fatigue (OR 1.32 95% CI 1.12-1.27) were associated with depression and deterioration of depressive symptoms in the multivariate analysis. Among the components of DAS 28-CRP, patient assessment for global health and abilities for daily performance were more related to depression. Depression unfavorably influences the response to therapy, the rate of remission is lower and the mortality is increased in RA patients. Taken together, this indicates that it is necessary to detect a depression in patients with RA as early as possible in order to initiate appropriate treatment of depression in such cases.
Conclusion: Our study shows depression in 19,18% of patients. Correlation between disease activity and depression score is found in RA patients. Depression intervention resulted in PHQ-9 improvement in some patients, supporting the benefit of depression screening and treatment in rheumatology practice. Depression was related with the level of fatigue and high RA disease activity, which was associated with impaired ability to perform activities of daily life. Strict control of fatigue and disease activity to improve one's capacity to perform daily life activities would be important to regulate depression. Depression is common and associated with worse outcomes among patients with RA.
Disclosure of Interests: None declared
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AB0343 ANTIRHEUMATIC THERAPY IS NOT ASSOCIATED WITH CHANGES IN CIRCULATING N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE (NT-PROBNP) LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) are predisposed to impaired cardiac function and heart failure (HF). While the pathophysiology has not been fully elucidated yet, inflammation is suspected to play an important role. However, the impact of disease-modifying antirheumatic drugs on cardiac dysfunction in RA remains controversial. Although anti-inflammatory drugs might have protective effects, some of them, i.e. tumour necrosis factor inhibitors (anti-TNF), might also negatively influence cardiac function. Serum NT-proBNP (s-NT-proBNP) is used as a biomarker of cardiac function, and levels ≤125 ng/L with high probability exclude HF[1].
Objectives: To examine effects of methotrexate (MTX) and anti-TNF regimens on s-NT-proBNP in patients with active RA, and to assess associations between s-NT-proBNP and endothelial function (EndoF).

Methods: From the observational PSARA study, we examined 64 RA patients starting with MTX monotherapy (n=34) or anti-TNF with MTX comedication (n=30) due to active disease. All patients starting with anti-TNF regimens had been previously unsuccessfully treated with MTX. s-NT-proBNP (ELISA), EndoF (measured by finger plethysmography), and other laboratory and clinical parameters were evaluated at baseline and after 6 weeks and 6 months of treatment.
Results: Median age was 57 years (range 28-79), and 73% were women. 17 (27%) patients had CVD (history of angina, MI, heart surgery, PTA, cerebrovascular disease, thromboembolism, aortic aneurysm, peripheral artery disease). None of the patients had known/symptomatic HF. There were no statistically significant differences between s-NT-proBNP levels at baseline (median 2241 ng/L [IQR 9002]) and after 6 weeks (median 2300 ng/L, [IQR 8960]) and 6 months (median 2358 ng/L [IQR 7772]) of antirheumatic therapy (p=0.992 and p=0.528, respectively). There were no significant differences in the effects of MTX monotherapy and anti-TNF regimens on s-NT-proBNP levels ($p_{baseline\text{-}6weeks}$=0.779; $p_{baseline\text{-}6months}$=0.421).
At baseline, 57 (89%) patients had s-NT-proBNP>125 ng/L, and 44 (69%) had high s-NT-proBNP levels (s-NT-proBNP>450 ng/L in patients <50 years old and >900 ng/L in patients ≥50 years old), and these frequencies did not significantly change with antirheumatic treatment. s-NT-proBNP was not related to EndoF.
Conclusion: A large proportion of RA patients without known HF had elevated s-NT-proBNP levels, which might indicate subclinical impairment of cardiac function. s-NT-proBNP levels were not influenced by six-month MTX and/or anti-TNF treatment. Thus, in contrast to some previous studies, our data does not support the notion that anti-inflammatory treatment protects against HF, and that anti-TNF treatment has negative effect on cardiac function in RA. Nevertheless, definitive conclusions cannot be drawn by our study, e.g. due to limitations of s-NT-proBNP as surrogate marker of HF. Cardiac function in terms of s-NT-proBNP levels was not related to EndoF.

REFERENCES

[1] Ponikowski P, et al. European journal of heart failure. 2016;18:891-975.

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AB0344 COMPARATIVE ANALYSIS OF SIDE EFFECTS BETWEEN PATIENTS TREATED WITH AND WITHOUT CORTICOSTEROID AT DMARDS-STARTING POINT. SINGLE CENTER RETROSPECTIVE REAL WORLD DATA ANALYSIS

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Background: In the EULAR recommendation on rheumatoid arthritis (RA) treatment, short-term steroid combination should be considered at the start of DMARDs treatment. In this study, we analyzed the present condition of steroid combined use in Japan and the actual situation of side effects in recent years.
Objectives: RA patients who started treatment with DMARDs at our hospital during July 2008 to April 2018,
Methods: A new incidence of hypertension (HTN), diabetes (DIB), dyslipidemia (HLP), infection (INF) were compared between the two groups of steroid combined use group (D_PSL) and noncombined group (D_nonPSL) and analyzed by Cox regression analysis. The cases had there complications before the start of RA treatment were excluded from the analysis.
Results: The number of cases of analysis was 573 (D_PSL = 216, D_nonPSL = 357, average observation period: 5.22±2.70 year), and the new incidence of each complication was INF 50/561 (D_PSL 16.2%vs. D_nonPSL 4.56%[16/351], p=0.000094), HTN 48/527 cases (13.3%[25/188] vs.6.78%[23/339], P = 0.0148), DIB 24/558 (6.16%[13/211] vs. 3.17%[11/347], p = 0.136), HLP 72/542 (15.8%[32/202] vs. 11.8%[40/340], p = 0.198). The incidence of INF was high in D_PSL group in both groups over 65 and under 65 years old (p = 0.00658, p = 0.00267), HTN was high in D_PSL group only in group over 65 years old (*p=0.0276, p=0.0554*). Average starting amount of steroids was 6.07±10.2 mg, cases of non-withdrawal of steroid at 1, 2, 3 years later is 79.7%, 72.2% and 66.3% respectively.
Conclusion: Combined use of steroid at the start of DMARDs increased the rate of mortality of infection requiring hospitalization and hypertension. More than half of them were difficult cases of withdrawal of steroids. From the viewpoint of side effect, it is necessary to study the optimization of steroid therapy in the future.
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AB0345 A PILOT ATTEMPT TO USE THE CONSTANT GENETIC MARKERS IN CARDIOVASCULAR RISK STRATIFICATION IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is associated with early atherosclerosis and high mortality. Routine riskometers developed for a common population usually underestimate a true cardiovascular (CV) risk in RA-patients. For early prevention additional criteria is needed to evaluate CV risk in RA-patients. It's known, that early CV accidents in relatives relate to elevated risk. Nevertheless, specific constant genetic markers don't use in risk stratification. Single nucleotide polymorphisms in regulatory regions of genes, participating in immune interaction, can potentially play a role in progression atherosclerosis and used in CV-prevention algorithms.
Objectives: to develop the model for cardiovascular risk stratification in RA-patients including constant genetic markers.
Methods: Two hundred and twelve Caucasian patients with RA (age – 58.0 yrs [48.3; 65.0]; DAS28 4.96 [3.86; 5.85]) were included in our study. Patients had American College of Rheumatology (ACR)-defined RA (1987 classification criteria). All patients gave written informed consent before enrollment. Traditional and "non-traditional" (e.g. RA-associated factors) were analyzed [1]. Carotid atherosclerotic plaques had been found by ultrasonography. Single nucleotide polymorphisms were determined by restriction fragment length polymorphism (*TNFA G-308A* (rs1800629), *TNFA C-863A* (rs1800630), *TNFA G-238A* (rs361525), *IL6 G-174C* (rs1800795), *VEGFA C-2578A* (rs699947), *MMP3 5-1171 6A* (rs 3025058), *MMP9 -1562T* (rs3918242)) and polymerase chain reaction (*IL1B T-31C* (rs1143627), *IL4 C-590T* (rs2243250), IL10 C-592A (rs1800872), *IL10 A-1082G* (rs1800896), *VEGFA C+936T* (rs3025039), *MMP2 C-1306T* (rs2438650)). Descriptive statistics, Chi-squared test, logistic regression with Wald statistics were used for data analysis. Results are presented as median and 25th/75th percentiles (Me [25th percentile; 75th percentile]).
Results: Atherosclerotic plaques (APl) were found in 59 (27.8%) patients. API revealed were strongly associated with age (66.0 yrs [59.0; 73.0] with API vs 55.0 yrs [42.0; 61.0] without API, p<0.001) and sex (51.6% for man vs 23.8% for woman, p<0.001). Then, a logistic regression was performed to determine which variables analyzed are predictors of a carotid atherosclerotic lesion. Regression results had demonstrated that the model was statistically reliable in distinguishing between patients with API and without [-2 Log Likelihood = 146.53, p<001]. The model correctly classified 85.3% of cases. The Wald statistics showed that at least 6 parameters were principal – age (B=0.123, p<0.001), hypertension (B=3.114, p<0.001), smoke (B=2.167, p<0.001), positive rheumatoid factor (B=1.674, p=0.038), body mass index (B=-0.098, 0.019) and recessive allele in *TNFA C-863A* (B=1.338, p=0.005). Using parameters obtained the ROC-curve was constructed. Area under ROC curve were 0.900 (SE 0.022; 95%CI 0.857-0.942, P<0.001). Sensitivity and specificity calculated by Youden's Index were 79.7% and 87.5%, respectively.
Conclusion: Age, hypertension, smoke, positive rheumatoid factor, low body mass index and recessive allele in *TNFA C-863A* were associated with carotid atherosclerosis.

REFERENCES

[1] Amaya-Amaya J. et al. Novel risk factors for cardiovascular disease in rheumatoid arthritis//Immunol. Res. 2013. Vol. 56, No 2–3. P. 267–286

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AB0346 TREND OVER TIME OF AORTIC STIFFNESS IN RHEUMATOID ARTHRITISPATIENTS AND ITS RELATION WITH CARDIOVASCULAR EVENTS

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Background: Ascending aorta has an increased stiffness (AoSI) in rheumatoid arthritis (RA) patients due to their chronic inflammatory status. We assessed prevalence and modification of AoSI during a follow up period and its prognostic role on cardiovascular events (CVE) in a large cohort of RA patients

Objectives: Prognostic role of AoSI and its modification over time on CVE.

Methods: We prospectively followed 146 RA patients without overt cardiac disease with periodic echocardiographic examination. Abnormally high AoSI was diagnosed if AoSI > 6.07% (95th percentile of the AoSI detected in our reference healthy population). AoSI was assessed at the level of the aortic root by two-dimensional guided M-mode evaluation as part of a thorough echocardiography performed in all patients. CVE information were collected during follow up

Results: Of our 146 RA patients, 89 had a normal AoSI at baseline, in the remaining 57 it was abnormally high. After a mean follow up of 27 months: among patients with normal baseline AoSI it stayed normal in 64 (6 to 5,6%) and in 25 raised to an abnormal high AoSI (from 3,7 to 11,9%); of the 57 patients with high baseline AoSI, 33 went back to normal values (9,4 to 3,1%) and in 24 it remained high. Of these 4 groups divided by AoSI trend over time the group with de novo high AoSI showed the highest prevalence of new CVE (33%), together with the group with persistent high AoSI (16%). Much lower prevalence was observed in the other two groups (persistent normal 5%, normalized at follow up 6%).

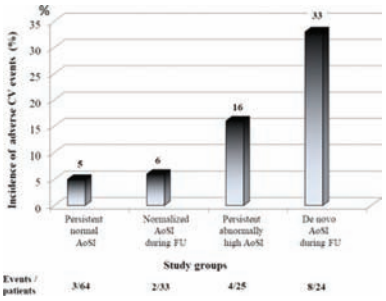


Figure 1

Conclusion: Abnormally high AoSI is common in RA patients, rapid increase through time or persistent high AoSI identify those patients that are more prone to develop CVE. On the contrary, patients that showed a normalization of AoSI demonstrated to have a similar low incidence of CVE as patients who ever had a normal AoSI.

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AB0347 CLINICAL RELEVANCE OF ANTI-CARBAMYLATED PROTEIN ANTIBODY: IS IT SAME AS CAUCASIANS IN ASIANS?

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Background: Recently, there was an interesting study demonstrating that anti-CarP was associated with more inflammation and higher baseline disease activity in French ESPOIR cohort [1]. However, all of the investigated patient cohorts have been Caucasian. However, considering the genes associated with RA are different in Caucasians and Asians, PTPN22 in Caucasians and PADI4 in Asians, and those genes contribute to the loss of tolerance and autoantibody production, clinical relevance of anti-CarP might be different in Asians.

Objectives: Therefore, we investigated the clinical significance of anti-CarP in Korean patients with early RA focused on initial presentations and treatment outcome.

Methods: The anti-CarP antibodies were analysed by commercial ELISA (Novateinbio, USA) in the Korean Intensive Management of Early Rheumatoid Arthritis cohort. All patients were DMARD-naïve RA patients with symptom duration less than 1 year. They were intensively treated by adjusting medications every 4 weeks, and treated to target as disease activity score (DAS)28 of < 2.6. Baseline clinical characteristics and disease outcomes were compared according to the presence of anti-CarP antibodies.

Results: A total of 128 patients were included, 67 patients (52.3%) were positive for anti-CarP antibody at presentation. After 2 years of treatment, proportion of anti-CarP positivity decreased to 38.1% (p=0.049), but titration did not change (6.87 to 4.45 ng/ml, p=0.074). Patients without anti-CarP antibody presented with more tender joint count (TJC) (7.3 vs. 5.2, p=0.055), swollen joint count (SJC) (4.1 vs. 2.6, p=0.019) and higher baseline physician global VAS (5.5 vs 4.7, p=0.005) than patients with anti-CarP antibody. Subgroup analysis with ACPA negative patients, patients without anti-CarP antibody showed more TJC (13.7 vs. 4.7, p=0.043), SJC (7.9 vs. 3.0, p=0.076), higher patient global VAS (5.9 vs. 3.7, p=0.044) and DAS28-ESR (6.1 vs. 4.7, p=0.051). After intensive treatment, there were no differences in remission rate and DAS28-ESR at 12, 24, and 36 months.

Conclusion: Interestingly, RA patients without anti-CarP antibody presented with more TJC/SJC than those with anti-CarP antibody in Korean patients. This finding is contrast to previous studies which were done with Caucasians. Further investigation is needed to conclude the clinical implications of anti-CarP.

REFERENCES

[1] Truchetet ME, Dublanc S, Barnetche T, Vittecoq O, Mariette X, Richez C, et al. Association of the Presence of Anti-Carbamylated Protein Antibodies in Early Arthritis With a Poorer Clinical and Radiologic Outcome: Data From the French ESPOIR Cohort. Arthritis Rheumatol 2017;69(12):2292-302.

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AB0348 PREVALENCE AND SAFETY OF BIOLOGIC THERAPY IN A CHILEAN COHORT OF RHEUMATOID ARTHRITIS PATIENT, A RETROSPECTIVE STUDY

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Background: Interstitial lung disease (ILD) is a common extra-articular condition in rheumatoid arthritis (RA). New-onset ILD or ILD worsening has also been reported as a possible consequence of biologic therapy. These associations are based on case reports. The present study evaluated ILD prevalence and exacerbation among users of abatacept (T-cell inhibitor), rituximab (B-cell inhibitor), and anti-TNFα agents in a cohort of adult RA patients.

Objectives: In the present study, we aimed to assess the safety of biologic therapy in patients with ILD associated to RA and patients without a history of ILD.

Methods: Data from RA patients beneficiaries of the Ley Ricarte Soto (LRS) program, at the Hospital Clínico de La Universidad de Chile, who received abatacept, rituximab, or anti-TNFα agents for at least a year, were reviewed.

Results: Seventy four patients were reviewed retrospectively between January 2016 and December 2018 (55 female; mean disease duration, 7 years; mean age, 55 years). Mean (SD) $DAS_{28\ ESR}$ was 6.9 (±0.1) previously to initiate therapy. RA was seropositive in 65 patients (87.8%). Eighteen patients (24.3%) had been previously diagnosed with ILD, with a median duration of 4 years. Most common patterns of RA-associated ILD were UIP (n=5 [46%]) and CPFE (n=3 [23.1%]). Patients with ILD at baseline as compared to patients without history of ILD were more frequently males (27.8% vs 7.5%, p < 0.05), had an older age (64±12 vs 52±13, p < 0.005), a higher positivity of anti-cyclic citrullinated protein antibodies (CCP) (87.5% vs 80%, p < 0.005) and a more frequent history of smoking (50% vs 28%, p < 0.005). The treatment received by patients with RA-associated ILD previously to start biologics under LRS program were: metotrexate [MTX] (n=5), leflunomide [LFN] (n=14),

sulfasalazine [SSZ] (n=8), etanercept [ETN] (n=1), adalimumab [ADA] (n=1), abatacept ABA (n=3) and rituximab [RTX] (n=1). When the patients were enrolled to LRS program 83.3% received abatacept, 11.1% anti-TNFα agents and 5.5% rituximab. All patients with RA-associated ILD remained stable at 1 year follow-up. RA patient without ILD who started biologic therapy did not had ILD at 1 year follow-up.

Conclusion: There were no significant differences in the risk of complications between patients with a baseline history of ILD receiving different biologic agents. The present study found that male sex, older age, seropositive RA and patients with a history of smoking, were at increased risk for developing ILD. These data are largely consistent with those of the existing literature. Patients without a history of ILD did not develop pulmonary complications, but these data may be affected by the short follow-up window. Further studies are needed to evaluate the risk of RA-associated ILD and its complications.

REFERENCES

[1] Curtis, J (2015). Incidence and complications of interstitial lung disease in users of tocilizumab, rituximab, abatacept and anti-tumor necrosis factor α agents, a retrospective cohort study. Arthritis Research & Therapy 17:319.
[2] Fernández-Díaz, C (2018). Abatacept in patients with rheumatoid arthritis and interstitial lung disease: A national multicenter study of 63 patients. Seminars in Arthritis and Rheumatism 48: 22–27.
[3] Shaw, Megan (2015). Rheumatoid arthritis-associated lung disease. European Respiratory Review 24: 1-16.

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AB0349 DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS AND RISK OF LUNG INVOLVEMENT

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Background: Rheumatoid arthritis (RA) is a common inflammatory disease developing within joints but extra-articular organs such as the lung could be involved.

Objectives: To determine the relationship between disease activity and lung involvement in rheumatoid arthritis (RA) Tunisian patients.

Methods: We performed a retrospective study of patients with RA diagnosed according to American College of Rheumatology-European League Against Rheumatism classification criteria for RA 2010 between 2014 and 2017 in a department of rheumatology in the north of Tunisia. The prevalence of pulmonary involvement was determined based on combined results from chest-X-ray, computed tomography of the chest and pulmonary functional tests. Disease activity was evaluated based on number of night waking, morning stiffness duration, painful joints number and swelling joints number, erythrocytes sedimentation rate (ESR) and C-reactive protein levels (CRP). Specific disease activity scores were also noted including the 28-joint Disease Activity Score Index (DAS28), Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI).

Results: Sixty five patients were collected. Mean age was 56 years ± 12.8 years and mean age of disease onset was 46.4 ± 13.8 years ranging from 17 to 75 years. Mean disease duration was 9.6 ±10.1 year ranging from 1 to 38 years. Number of painful joints was 13.71 at mean and swelling joints number was 5.98. Morning stiffness duration was 1.03 hour at mean and number of night waking was 2.31. Concerning laboratory investigations, mean ESR was 49.7 mm ant mean CRP level was 13.6 mg/l. The average of DAS28 was 5.8. The overall frequency of lung involvement based on different lung investigations was 27.6% (18 patients). Interstitial lung disease was found in 7 cases, bronchiectasis was found in 5 cases, rheumatoid nodule in 4 cases and pleural disease in 2 cases.
Patients with lung involvement had significantly higher painful joints number (p=0,034) and no difference was seen concerning swelling joints number. Number of night waking and morning stiffness duration had no impact in lung involvement (p=0,651, p=0,907 respectively). RA patients with lung involvement displayed higher ESR level (p=0,032) and no difference was seen concerning CRP level. No association was found between lung involvement and specific disease activity scores (DAS28, CDAI, SDAI).

Conclusion: Our study showed that only high level of ESR could be associated with lung involvement in RA Tunisian patients.

REFERENCES

[1] Pérez-Doramea R, Mejiaa M, Mateos-Toledoa H,Rojas-Serranob J.Rheumatoid arthritis-associated interstitial lung disease: Lung inflammation evaluated with high resolution computed tomography scan is correlated to rheumatoid arthritis disease activity. Clin Rheumatol. 2015;11(1):12-6.
[2] Jearn LH, Kim TY. Level of anticitrullinated peptide/protein antibody is not associated with lung diseases in rheumatoid arthritis. J Rheumatol 2012;39:1493-4.2] Jearn LH, Kim TY. Level of anticitrullinated peptide/protein antibody is not associated with lung diseases in rheumatoid arthritis. J Rheumatol 2012;39:1493-4.

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DOI: 10.1136/annrheumdis-2019-eular.8050

AB0350 RHEUMATOID ARTHRITIS MANAGEMENT IN SOUTHEAST TURKEY, EXPERIENCE FROM RURAL AREA

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Background: Rheumatoid arthritis is a chronic disease affecting more commonly women in all age groups. Access to healthcare, taking part in decision making and compliance with the treatment are very important in management. In Turkey, after completion of their fellowships, rheumatologist work for a limited time in state hospitals mandatorily (especially in under-developed cities of the country). Batman city lies in the southeast of Turkey with a population of 585.000 people; 7% of whom is illiterate. Due to ethnic and cultural reasons women suffer more commonly in obtaining and maintaining education and healthcare.

Objectives: To define the clinical characteristics, adherence to follow-up appointments and treatments ever received in patients with rheumatoid arthritis in Batman State Hospital.

Methods: Hospital records between July 15th 2017 and January 1st 2019 were viewed retrospectively. Only 1 rheumatologist works in the hospital. Appointments were scheduled between 1-3 months intervals, patients were defined as 'lost to follow-up' if there was no clinical appointment in last 3 months. Patients were categorized as recently or formerly diagnosed and according to receiving conventional synthetic disease modifying agents (DMARDs) (methotrexate, leflunomide, hydroxy-chloroquine, sulfasalazine) or biologic DMARDs (adalimumab, etanercept, infliximab, golimumab, certolizumab pegol, rituximab, tociluzimab, abatacept, tofacitinib). Most of the patients received low-dose steroids.

Results: Patient characteristics and treatments are displayed in the table. Follow-up duration for the patients who continued follow-ups was 8.9 months on average (max: 17 months). Average follow-up duration for patients who lost to follow-up was 2.8 months (min: 1 month, max:13 months). Seventy-one of 146 patients who lost to follow-up came to appointment only once. Route of administration was very important in biological treatment decisions, oral treatments and intravenous administration in hospital were favored over subcutaneous administration especially for elderly illiterate patients.

Table: Patient characteristics, treatments

Age	Mean 51 years (min:16 y, max:85 y)
Sex	Female:432, Male:86 (F/M=5)
RF or Anti-CCP positivity	Seropositive: 308 patients Seronegative: 210 patients
Lost to follow-up (total)	146 patients (28%)
Continuing follow-up (total)	372 patients (72%)
Recently diagnosed (135 patients) (26%)	Lost to follow-up: 37 (27%) Continuing follow-up: 98 (73%)
Formerly diagnosed (383 patients) (74%)	Lost to follow-up: 108 (28%) Continuing follow-up: 275 (72%)
Conventional Synthetic DMARDs (397 patients) (77%)	Lost to follow-up: 135 (34%) Continuing follow-up: 262 (66%)
Biologic DMARDs (121 patients) (23%)	Lost to follow-up: 11 (10%) Continuing follow-up: 110 (90%)
Biologic DMARDs (route of administration ever received, including switches)	Subcutaneous : 52 (35%) Intravenous: 67 (45%) Per oral: 28 (20%)

Conclusion: Even though management goal is directed at remission induction in the earliest stages of rheumatoid arthritis with molecular targeted therapies in most of the developed countries, in rural parts of the developing countries low rate of adherence to follow-up appointments and medications is still an important difficulty in management. Patients receiving biologic DMARDs have higher adherence to treatment. Awareness and education of patients in rheumatoid arthritis, as well as in all chronic diseases, is most important aspect of management.

Disclosure of Interests: None declared
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AB0351 ELDERLY-ONSET RHEUMATOID ARTHRITIS (EORA): DIFFERENCES ACCORDING TO CLINICAL DEBUT AND SEROLOGICAL POSITIVITY

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Background: In patients with Elderly-onset Rheumatoid Arthritis (EORA) has been described a clinical debut mimicking polymyalgia rheumatica with rhizomelic *pseudopolyarthritis,* in contrast with the classical profile of patients with Rheumatoid Arthritis similar to younger patients. We compare in our study these two profiles of the disease.
Objectives: To describe and compare the differences according to clinical debut, serological positivity and its implications in terms of treatment and prognostic factors in patients with Elderly-onset Rheumatoid Arthritis (EORA).
Methods: Patients with a diagnosis of RA over 65 years of age according to ACR/EULAR 2010 criteria were included. A database was created including the age of onset, the presence of polymyalgia-like symptoms (*rhizomelic pseudopolyarthritis*), the positivity of rheumatoid factor (RF) and anti-c*itrullinated* protein *antibodies* (ACPAs), elevation of acute phase reactants (APR), the presence of erosions and the treatment required. Finally, data was analyzed according to clinical debut, serological positivity and prognostic factors.
Results: 83 patients diagnosed of EORA were included, with an average age of 73.8 years. 71.25% had positive RF (58.75% high titers) and 62.5% had positive ACPA (52.3% high titers). 24/83 patients (29%) debuted with a polymyalgia-like symptoms. 47.5% had persistent APR elevation during follow-up. Regarding treatment, 15% were treated only with corticosteroids, 81.5% required treatment with DMARDs and 15% were receiving biological treatment. 42/83 patients (50%) had erosions on plain X-rays. Of those patients with a polymyalgia-like profile, 52.2% (43/83) had positive RF but most of them had low titers (61%). On the other hand, patients without polymyalgia-like symptoms had positive RF in 78% of the cases and most of them at high titers (66%, p = 0.01). In the first group there was less positivity for ACPAs (26%, p = 0.00004) and half of them had low titers. Erosions were observed in only 30% of the patients with polymyalgia-like symptoms, while those without this profile had more erosions (58%, p = 0.02) and higher APR (50%, p = 0.026). Regarding treatment, in the group with polymyalgia-like symptoms only 34% were treated with corticosteroids, 65% required DMARDs and no patients had received biological treatment, whereas in the non-polymyalgic group, 88% required DMARDs and 21% required biologics (p = 0.01 for both results). Analyzing patients with positive RF and ACPAs at high titers, 93% received treatment with DMARDs and 24% required biological treatment. 65% had persistent elevation of APR and 48% presented erosions on plain X- rays. Only 2 patients with positive RF and ACPAs at high titers debuted with a polymyalgia-like symptoms.
Conclusion: Patients with EORA with polymyalgia-like symptoms tend to have less erosions and a higher prevalence of negative RF and ACPA or at low titers. These patients usually require less DMARDs and biological treatments to control the disease unlike patients with non-polymyalgia symptoms. On the other hand, patients with high RF and ACPA titers have more erosions and elevated APR during follow-up but do not usually experience polymyalgia-like symptoms.

REFERENCE

[1] Tutuncu Z, Reed G, Kremer J, Kavanaugh A. Do patients with older-onset rheumatoid arthritis receive less aggressive treatment?. Ann Rheum Dis. 2006;65(9):1226-9.

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AB0352 HIGH PREVALENCE OF ANTICIPATORY AND ASSOCIATIVE SYMPTOMS OF METHOTREXATE INTOLERANCE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is the most widely used anti-rheumatic drug in the treatment of Rheumatoid Arthritis (RA) due to low costs, efficacy and an acceptable safety profile. However MTX has certain side effects. The most common side effects include the gastrointestinal tract not only after taking MTX, but also before MTX intake (anticipatory) and when thinking of MTX (associative).
Objectives: The aim of this study was to assess the prevalence of MTX intolerance and particularly the anticipatory and associative symptoms using the validated methotrexate intolerance Severity Score (MISS) (1).
Methods: We performed a cross-sectional descriptive study that involved patients with RA and treated by MTX for more than 3 months, compiled from Charles Nicolle hospital's rheumatologic department. The tolerance of MTX was assessed by the MISS questionnaire. The MISS Questionnaire includes five elements: abdominal pain, nausea, vomiting, fatigue, and behavioral symptoms of restlessness, crying, irritability and drug refusal. Each symptom is evaluated after intake of MTX, before taking MTX (anticipatory) and on thinking about MTX (associative). MTX intolerance was defined as $\geq$6 points on the MISS, with at least 1 point on anticipatory, associative or behavioral adverse effects.
Results: A total of 100 RA patients (87 women and 13 men) with a mean age of 53,5 years. The MTX was administrated by oral route in 91% of patients; the other 9% received it by intramuscular way. The average MTX weekly dose was 15,4mg. The average MTX duration was 76,7 months. All patients received folic acid with an average of 7,6 mg a week. MTX intolerance was found in 36% of patients. Abdominal pain was the most common symptom occurring in 55% of patients and up to 91.66% in MTX-intolerant patients, followed by nausea in 51% of patients and in 86.11% of MTX-intolerant patients and vomiting in 16% of patients and in 44.44% of MTX intolerant-patients. Anticipatory and associative abdominal pain affected 72,2% and 69,4 of intolerant-patients respectively. Anticipatory and associative nausea were found in 58,3% and 59% of intolerant-patients respectively. Anticipatory vomiting occurred in 16.6% of intolerant-patients. Overall, behavioral symptoms occurred in 75% of intolerant-patients, of whom 19.4% refused MTX. Older age was significantly correlated with better tolerance to MTX (p=0,02). There was no correlation between the dose of MTX, the duration of MTX intake and the route of MTX and the MISS score (respectively p=0,7, p=0,07and p=0,2). Also, the use of other disease modifying drugs didn't worsen the tolerance of MTX.
Conclusion: To conclude intolerance to MTX is frequently seen in RA. In addition to gastrointestinal symptoms after taking MTX, RA patients can suffer from anticipatory and associative gastrointestinal symptoms. We should screen these symptoms earlier using MISS questionnaire in order to improve MTX compliance.

REFERENCE

[1] Bulatovic M, Heijstek MW, Verkaaik M, van Dijkhuizen EH, Armbrust W, Hoppenreijs EP, et al. High prevalence of methotrexate intolerance in juvenile idiopathic arthritis: development and validation of a methotrexate intolerance severity score. Arthritis and rheumatism. 2011;63(7):2007-13.

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AB0353 WORSE OFFICE AND 24-HOUR BRACHIAL AND CENTRAL AORTIC BLOOD PRESSURE MONITORING PROFILE IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARED TO CONTROLS

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Background: Hypertension (HTN) contributes to increased cardio-vascular (CV) morbidity and mortality in RA. Recent European guidelines on the management of HTN encourage wider use of ambulatory blood pressure

(BP) monitoring (ABPM) that provides more accurate information about BP control compared to conventional BP measurement. Central blood pressure (CBP) may be a better predictor of CV risk compared to brachial BP

Objectives: To evaluate office and ambulatory brachial and central BP levels in patients with RA compared to the controls.

Methods: Study group included 85 patients with RA (77.6% females,age 59.7±14.3 years, HTN 65%, median HTN duration 6.6 years, RA duration - 7 years, seropositive RA 65%, DAS-28(CRP) 3.7±1.1, median hsCRP 10 mg/dl, RF 51.3 IU/ml, all received DMARDs) and control group (40 patients matched by gender, age and risk factors). All hypertensives received antihypertensive therapy. Office CBP was measured with applanation tonometry. CBP elevation was assessed according to individual reference values by gender and age. 24-hour ABPM of peripheral and central BP was performed with BPLab Vasotens. $p<0.05$ was considered significant.

Results: In patients without HTN mean office brachial and central BP levels were similar in RA and control groups. In patients with HTN corresponding BP levels were: 138±17/82±10 vs 130±16/74±11 mmHg ($p=0.04$ for SBP;$p<0.001$ for DBP) and 132±20/82±10 vs 120±17/74±12mmHg ($p=0.01$ for SBP;$p=0.001$ for DBP). Rate of BP control was 58% in RA and 67% in the controls ($p=0.48$). CBP elevation was observed in 42.4% of RA patients and 17.5% controls ($\chi^2=14.9$,$p=0.0001$):16.7% vs 0% in the normotensive group ($\chi^2=6.0$,$p=0.01$) and 56.4% vs 29.2% in HTN group ($\chi^2=9.9$,$p=0.002$), respectively. In the normotensives mean daytime, nighttime and 24-h BP levels were similar in RA and control groups. In HTN 24-h brachial SBP levels for RA and control group were 134±17 vs 125±9mmHg for daytime ($p=0.02$); 128±17 vs 113±10 mmHg for nighttime ($p=0.01$) and 131±16 vs 123±9 mmHg for 24-h BP ($p=0.02$), respectively. The 24-h central BP levels were 124±14 vs 115±14 mmHg for daytime ($p=0.02$), 121±16 vs 111±10 mmHg for the nighttime ($p=0.02$) and 123 ±15 vs 115±8 mmHg for 24-h BP ($p=0.02$), respectively. Group with RA had higher incidence of masked and isolated nocturnal HTN compared to controls (35.3 vs 17.5% ($\chi^2=3.7$,$p=0.05$) and 29.4 vs 12.5% ($\chi^2=4.3$, $p=0.04$). In normotensives corresponding frequencies of masked and isolated nocturnal HTN were 33.3 vs 12.5% ($p>0.05$) and 26.7 vs 6.3% ($\chi^2=3.3$,$p=0.04$), respectively. In HTN group rate of masked uncontrolled HTN was 36.3 vs 2.5%, respectively, rate of uncontrolled night HTN-30.9 vs 20.8% ($p>0.05$).

Conclusion: Despite similar BP control rate, patients with RA were characterized by significantly higher levels of office brachial and central BP, worse control of CBP and higher frequency of masked and isolated nocturnal HTN compared to controls. Hypertensive RA patients had higher 24-h brachial and central SBP. This indicates the importance of 24-h ABPM in RA.

REFERENCES

[1] Panoulas VF, et al. Prevalence and associations of hypertension and its control in patients with rheumatoid arthritis. Rheumatology 2007; 46:1477-82.

[2] Herbert A. et al. Establishing reference values for central blood pressure and its amplification in a general healthy population and according to cardiovascular risk factors. Eur Heart J. 2014;35(44):3122-33

[3] Williams B, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. J Hypertens 2018;36(10):1953-2041

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AB0354 CAN CANCER TRIGGER AUTOIMMUNITY DISEASE? FEATURES OF AUTOIMMUNE DISORDER OF CANCER PATIENTS

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Background: Association between cancer and autoimmune diseases are reconsidered by frequent use of immune checkpoint inhibitor and its adverse effects. In addition, the childhood cancer patients have the higher possibility of developing autoimmune disease than general population in previous research, though this may be related to cancer therapy. Furthermore the development of scleraderma in cancer patients harboring the rPOLAR3A cancer mutation suggests that cancer may directly induce autoimmune disease.

Objectives: We examine the features of autoimmune diseases in the patient with pre-exisiting cancer.

Methods: Date on clinical characteristics, laboratory features, and treatment response from patients with autoimmune disease in our hospital were analyzed retrospectively. We excluded patients who had diagnosed cancer more than 5 years ago, who use immune check point inhibitor, whose symptom became clear by the drug toxicities and endocrine disease, and who had no symptoms but only test abnormalities.

Results: 149 patients consulted our department and 111 patients were included; their medina duration of follow-up was 39 months. The median period of diagnosing cancer from autoimmune disease was 17 months, and median age of the patients with autoimmune diseases at diagnosis was 68 years. Baseline manifestations included rheumatoid arthritis (RA) 42%, polymyalgia rheumatica (PMR) 20%, systemic scleroderma (SSc) 10%, Sjoegren syndrome (SjS) 7.3%, IgG4-related disease 6.3%, vasculitis 5.5%, polymyositis and dermatomyositis 5.5%, interstitial pneumonia 2.7%.

In patients with RA, 53% were positive for both rheumatoid factor (RF) and anti-CCP antibody (median RF 155IU/mL, anti-CCP antibody 380U/mL). The median age of diagnosis was 68 years, and 52% were female. The average serum C-reactive protein (CRP) was 1.7mg/dL. Patients who experienced only operation for previous cancer therapy was 44%. 39% patients developed RA symptoms with in half year. As a treatment, MTX were used in 44%, SASP in 26%, PSL alone in 11%. The response to therapy was 70% overall. One patient who used MTX developed MTX-LPD (DLBCL) after 10 months.

In PMR, all cases were seronegative. The median age of diagnosis was 71 years, and 63% were female. The average CRP was 5.4mg/dL. 41% of patients had operation for previous cancer therapy and 32% had operation and chemotherapy. All cases started using PSL (15-40mg) and responded to treatment. They all tapered PSL.

In SSc, all cases were female and mean age was 63 year old. 33% of them had breast cancer. 82% had centromere antibody and the median titer of the antibody were 1280. Interestingly, even in SjS patients, the same antibody was positive in 38%.

In myositis, 4 out of 6 patients had ARS antibodies and their main symptom was interstitial pneumonia. No patients were positive for TIF-1γ.

Seeing from cancer side, 18% had colorectal cancer, 17% had breast cancer, 11% had lung cancer, 9% had gastric and uterine cancer.

Conclusion: Patients with cancer developed autoimmune diseases, and had different characteristics from primary autoimmune disease. This suggest that cancer itself and it's therapy somehow influence to our immune systems.

Disclosure of Interests: None declared

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AB0355 CAROTID ULTRASOUND IS MORE EFFECTIVE THAN CORONARY CALCIFICATION ASSESSMENT FOR DETECTING INDICATIONS TO STATIN THERAPY IN RHEUMATOID ARTHRITIS PATIENTS

Helen Udachkina, Diana Novikova, Tatiana Popkova, Irina Kirillova, Eugenia Markelova, Helen Gerasimova. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation* **Objectives:** To compare the significance of the carotid ultrasound and the MDCT assessment of coronary calcification in the stratification of cardiovascular risk and the detection of indications for lipid-lowering therapy in patients with RA.

Methods: Ninety two patients with RA are included (ACR/EULAR, 2010), 74% are women, the median of age is 54 [41.5; 60] years, median of disease duration - 6 [5; 21] months, median of DAS28 (ESR) – 5.2 [5.0; 6.0], without cardiovascular diseases and diabetes mellitus, severe chronic renal failure (GFR <60 ml/min x 1.73m^2). Arterial hypertension was detected in 57% of patients, dyslipidemia – in 50%, 63% of women were in postmenopause. Initially, the cardiovascular risk was assessed using the mSCORE scale, and then again, taking into account the results of carotid ultrasound and MDCT assessment of coronary calcification.

Results: After assessing the cardiovascular risk on the mSCORE scale 41.3% of patients with RA were classified as low risk (n = 38), medium risk – 38% (n = 35), high risk – 15.2% (n = 14), very high risk– 5.5%

(n = 5). Non-target lipid levels were detected in 44.7% of low-risk patients, in 83% of medium risk patients, in 78.6% of high risk patients, in 100% of very high risk patient. Absolute indications for statin therapy were detected in 17.4%.

Hemodynamically insignificant carotid plaques (stenosis <50%) was detected in 56.5% of patients with RA: in 23.7% of low risk category, in 74.3% of medium risk patients, in 85.7% of high risk patients, in 100% of very high risk patients. A sever calcification of the coronary arteries was detected in 25% (the coronary index is more than 300 U or > 75 percentile of the age- and sex-related reference values, in according to MESA): in 5.3% of low risk patients, in 37% of medium risk patients, in 28.6% of high risk patients, in 80% of very high risk.

After carotid ultrasound 38% (34/92) of RA patients were reclassified from the category of low and medium cardiovascular risk on the mSCORE scale to the high risk category. The proportion of patients with high cardiovascular risk increased in 3.5 times (53.2%, p <0.001). There were 42 patients with non-target lipid levels in the high risk category. The proportion of patients with absolute indications for statins increased in 2.9 times compared with the results of the mSCORE evaluation (n = 47/92; 51%; p <0.001).

After MDCT assessment of coronary calcification 16.3% (15/92) of RA patients were reclassified from the category of low and medium cardiovascular risk on the mSCORE scale to the high risk category. The proportion of patients with high cardiovascular risk increased in 2.1 times (31.5%, p <0.001). There were 24 patients with non-target lipid levels in the high risk category. The proportion of patients with indications for statins increased in 1.8 times compared with the results of the mSCORE evaluation (n = 29/92; 31.5%; p <0.001). Carotid ultrasound more often reveals indications for statin therapy, p <0.001.

Conclusion: The use of the mSCORE scale is not sensitive enough for stratification of cardiovascular risk in RA patients due to the high incidence of subclinical atherosclerosis in this population. The use of carotid ultrasound and the MDCT assessment of coronary calcification significantly improve the stratification of cardiovascular risk in patients with RA, which helps to identify patients requiring intensive prevention of cardiovascular complications. The frequency of identifying patients with absolute indications for statin therapy when performing carotid ultrasound is significantly higher than MDCT assessment of coronary calcification.

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AB0356 COMPARISION FOREARM BONE MINERAL DENSITY BETWEEN LUMBAR SPINE AND HIP: A USEFUL TOOL TO SCREEN OSTEOPOROSIS IN FEMALE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: DXA is widely used in clinical practise in BMD measurement of osteoporosis. Forearm and axial BMD is the most common site to define in clinical practise. However, the relationship between forearm and axial BMD is not confirmed in RA patients.

Objectives: To compare the forearm (bone mineral density) BMD between lumbar spine and left hip BMD by dual-energy X-ray abosorptionmetry (DXA), and explore the diagnostic value of the forearm BMD in rheumatoid arthritis (RA) patients.

Methods: In the study, 200 female patients with established RA underwent DXA of the lumber, left hip and non-superiority forearm DXA at the same time. We compared BMD at different sites, and the diagnostic cut-off value of abnormal axial BMD by forearm BMD was explored. Data analysis was performed by independent-sample *t* test and Pearson's correlation test. The area under the receiver operating characteristic curve (AUC) and calibration of predictions were assessed. Sensitivity and specificity were calculated to determine the correlation between cases of osteoporosis detected by the axial DXA scan and forearm.

Results: (1) The mean age of the 200 female patients was (55.9±13.8) years. Twenty (10.0%) patients had the fragility fracture history. Based on their axial DXA data and fracture history, 30 (15.0%) patients had normal BMD (T score≥-1.0), 170 (85.0%) patients had abnormal BMD. The mean forearm BMD was (0.35±0.13) g/cm2, and T score was -2.3±1.9. (2) Compared with abnormal axial BMD group, forearm BMD in normal axial group was significantly decreased [(0.33±0.13) g/cm2 vs (0.44±0.06) g/cm2, t=4.29, P<0.01], forearm T score was also significantly decreased [(-2.6±1.9) vs (-0.71±0.9), t=4.35, P<0.01]. T score of the forearm BMD was positively correlated with axial BMD T score, both at lumber and left hip respectively (r=0.488, 0.543, P<0.01). After correction by age, T score of the forearm remained positively correlated with axial T score by partial correlation analysis (Pearson partial vertebral r=0.46, P<0.001; left hip r=0.502, P<0.001). (3) The area under the ROC curve for diagnosis of lumber and hip osteoporosis were 0.757 (95%CI: 0.638, 0.876) and 0.615 (95%CI: 0.481,0.749) separately. (4) The sensitivity and specificity for identifying osteoporosis in lumber were 86.5% and 50.1% respectively when the T-score threshold of forearm was defined as -3.52; however, the sensitivity and the specificity for identifying osteoporosis at left hip were 66.2% and 76.2% when T score threshold of forearm was defined as -2.5.

Conclusion: Our study has confirmed that DXA measurement performed of forearm analysis is capable of screening osteoporosis defined by axial BMD in female RA patients.

REFERENCES

[1] Siris ES, Adler R, Bilezikian J, et al. The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group[J]. Osteoporos Int,2014,25(5):1439-1443. DOI: 10.1007/s00198-014-2655-z.

[2] Hangartner TN, Warner S, Braillon P, Jankowski L, Shepherd J. The Official Positions of the International Society for Clinical Densitometry: acquisition of dual-energy X-ray absorptiometry body composition and considerations regarding analysis and repeatability of measures[J]. J Clin Densitom. 2013. 16(4): 520-536. DOI: 10.1016/j.jocd.2013.08.007

[3] Kilic G, Ozgocmen S. Hand bone mass in rheumatoid arthritis: A review of the literature[J]. World J Orthop. 2015. 6(1): 106-116.DOI: 10.5312/wjo.v6.i1.106

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AB0357 CORRELATION BETWEEN DISEASE ACTIVITY AND MENTAL HEALTH OF RA PATIENTS- ASSESSMENT WITH SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOLS

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Background: WHO survey showed that the prevalence of anxiety and depression in Chinese population and Chinese patients with chronic diseases were between 3.1% - 4.2% and 3.1% - 7.3%, respectively. DAS28, HAQ, Hospital Anxiety and Depression Scale (HADS) are commonly used to evaluate RA patients' disease activity, physical function and mental health. All of those evaluations were mainly conducted by health professionals with paper questionnaire previously. SSDM is a novel smart disease management tool that allows patients to do self-evaluation on DAS28, HAQ and HADS by mobile terminal.

Objectives: To estimate the prevalence of anxiety and depression in Chinese patients with RA and to analyze the potential association between disease activity and mental health.

Methods: Under the guidance and training by health professionals, RA patients downloaded SSDM and performed self-evaluation bundle of DAS28, HAQ and HADS with SSDM. DAS28<=3.2 and HAQ=0 are criteria for Treat-to-Target (T2T) and normal physical function, HADS score >=8 can be diagnosed with anxiety or depression.

Results: From June 2016 to Jan 2019, 2,635 RA patients (461 male, 2,174 female) with a mean age of 49.94 ± 14.23 (11-88) years and the median disease duration of 25.37 months from 175 hospitals performed bundle self-evaluation for 7,455 times in total. According to the HADS and DAS28 assessment results, the prevalence of anxiety and depression in all patients was 33.30% and 39.04% respectively, which was significantly higher than that in the WHO survey in Chinese population and chronic disease patients. The proportion of patients achieved and failed on T2T was 29% and 71%, respectively. The prevalence of anxiety and

depression was 20% and 25% among T2T achievers; and 31% and 38% among T2T failures, respectively (P_A<0.05, P_D<0.05).
According to DAS28, the prevalence of anxiety was 19%, 20%, 27% and 41% in Remission (Rem), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) subgroups respectively, the prevalence of depression was 24%, 26%, 33% and 49% respectively. The correlation coefficients of anxiety (A) and depression (D) with DAS28 were r_A=0.9318 and r_D=0.9334, respectively. It suggested that with the increase of disease activity, the proportion of RA patients with anxiety and depression increased significantly.
Combined with physical function evaluation results, the overall prevalence of anxiety (23.65%) and depression (33.20%) in the normal HAQ group was significantly lower than that in the abnormal HAQ group (A: 36.37%, D: 43.19%, x_A^2 = 4.52, x_D^2 = 6.21, p_A<0.05, p_D<0.05). 30.50% of the patients with HAQ=0 and DAS28<=2.6 were still depressed. The analysis showed that these subgroup patients comorbid with other rheumatic diseases (SS 37%, SLE 15%) or suffer adverse events (abnormal WBC count: 19%, abnormal liver function: 15%) during treatment.
Conclusion: Higher prevalence of anxiety and depression were associated with higher levels of disease activity and worse physical function. Rheumatic comorbidity and adverse events (ADEs) were potentially associated with depression in the Rem subgroup patients with normal physical function. SSDM is an effective mobile interface to monitor and study entanglement of disease activity, physical function and mental health in RA patients, which build a foundation for proactive interventions in future.
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AB0358 WRIST BONE MINERAL DENSITY AND WRIST SYNOVITIS IN RHEUMATOID ARTHRITIS

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Background: Bone involvement in rheumatoid arthritis is characterized by focal articular bone loss around inflamed small joints of the hands.[1] Therefore, precise quantification of hand bone loss may predict the severity and the progression of the disease.
Objectives: The aim of this study is to find a correlation between wrist bone mineral density (BMD) and sonographic wrist synovitis in patients with rheumatoid arthritis (RA).
Methods: RA patients were examined by bone mineral density (BMD) measurement of the wrist using dual-energy X-ray absorptiometry (DXA) according to standard protocols for positionning and analysis (area measured at a level of 33%). Patients were diagnosed as having osteoporosis when the minimum T-score measured was less than -2.5 SD, osteopenia if T-score between -2,5 and –1 SD [2]. Ultrasound of the wrist was done by an operator with experience in musculoskeletal ultrasound with an esaote My lab60 machine. The wrist joint (inferior radio-ulnar joint, mediocarpal joint and ulnar recessus) was assessed on dorsal side in Gray and Power Doppler (PDUS) scales. Semi-quantitative score was used to sum the synovitis score.[3]
Statistical analysis comparing synovitis and BMD was performed using Kruskal Wallis Test, a non-parametric test (Mann–Whitney U-test) and chi-square, as appropriate.
Results: The study included 24 RA patients with female predominance (sex ratio=0,3). The mean age was 59.3 [47-71] years-old. The duration of the disease was 10.2 years [0,83 -23] and the body mass index was 27.3 (18.97-36.98) kg/m2. RA was erosive in 75% of cases. Sixty-seven percent of patients received calcium supplementation. All women experienced already menopause. Most of them (75%) were on corticosteroids at the average dose of 5 mg [5-15], two of whom were not supplemented. Only one quarter of patients had physical activity. BMD showed that 45% of patients suffered from osteoporosis and 25% are osteopenic with a mean T-score of -1.92 [-4.3; 1.4] and mean bone mass of 0.475 g/cm²[0.239,0.712]. Forty-eight wrists were assessed by ultrasound. Mediocarpal joint was the most affected in Gray scale and Doppler. Fifty-eight percent of patients had moderate to severe synovitis when combined scoring was used. Twenty nine percent of patients (29,1%) had grade 3 at Gray Scale and 25% had Doppler scale grade 3.The wrist BMD (T-score) in RA with high disease activity was lower than those with moderate or low disease activity (-2.21 vs -2.05 and -2,21 vs 0.6 respectively; p=0,431). There was no correlation between BMD of the wrist and the disease duration as well as the activity of the disease DAS28 VS (respectively p = 0.4, p = 0.58).The percentages of wrist synovitis in osteoporosis group were significantly higher than in osteopenia group (81.8% vs. 66%, p=0,03).Moroever, Gray scale grade 3 synovitis in osteoportic patients was higher than osteopenic patients (62,5% vs 25% respectively,p=0,041). Results also showed a correlation between BMD and doppler mode grade 3 (83%vs 16,7 respectively,p=0,014).
Conclusion: This study shows a highly significant correlation between the BMD of the wrist and synovitis. Local inflammation of the wrist is an important factor of local bone loss that should be acted upon in order to avoid fractures, especially Colles' fracture.

REFERENCES

[1] Hansen M,et al. Bone loss in rheumatoid arthritis.. Scand J Rheumatol. 1996;25:367–376
[2] World Health Organization (2004) WHO scientific group on the assessment of osteoporosis at primary health care level.p. 5–7.
[3] D'Agostino M L, et al.Scoring ultrasound synovitis in rheumatoid arthritis : a EULAR-OMERACT ultrasound taskforce—Part 1: definition and development of a standardised, consensus-based scoring system.RMD Open; 2017;000428.

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AB0359 TREATING STRATEGY FOR ELDERLY RHEUMATOID ARTHRITIS PATIENT, ESPECIALLY WHOSE AGE IS MORE THAN 75

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Background: A population of elderly rheumatoid arthritis (ERA) is increasing, probably due to treatment developed and simply elderly population increase. In aging, functional activity in daily life, immunity, especially T-cell function, and neural response decline and deteriorations become manifested. Treatment must not be same as that of young patient.
Objectives: To evaluate our treatment method and strategy for ERA.
Methods: From August 2010 to July 2015, 576 patient who have been treated in the institute continuously for more than 3 years were referred. In these, patients were classified in according with age at baseline (BL); younger than 65 (G-Y), from 65 to 74 (G-O), and no less than 75 (G-OO). Mean 28-joints disease activity score (DAS28), Health Assessment Questionnaire Disability Index (HAQ), Pain Score with visual analog scale (PS-VAS), drug administration history and dosage, were recorded.
For ERA, we have adopted a treating strategy called "Touch Down Strategy", what configures three tactics; 1) From BL, methotrexate (MTX) 6mg/week or tacrolimus (TAC) 1.5mg/day administer. 2) Increase or maintain drug dosage until clinical remission is attained or start bDMARDs when remission is not attained in 3 months, and in case, glucocorticoid (GCS) administered with every other month interval. 3)When clinical remission is attained, GCS tapering started immediately and csDMARDs tapering considered. Tapering of bDMARDs is the last order.
ERA patients were treated under these tactics. Monitored DAS28, HAQ score and PS-VAS were calculated for each group and compared with ANOVA with Bonferroni correction.
Results: HAQ at baseline demonstrated significantly higher in G-OO than the other groups. Prevalence of DAS28 remission were 76.4%, 89.6%, and 87.2%, while mean length from BL to DAS28 remission was 2.9, 2.5 and 4.0 months for G-Y, G-O, and G-OO, respectively. bDMARDs administration ratio was 19.8%, 20.6%, and 18.0%, while mean MTX dosage was 8.6mg, 8.6mg, and 7.4mg/week, for G-Y, G-O, and G-OO respectively. GCS administration ratio and mean dosage until DAS28 remission were 24.2% and 2.96mg, 38.0% and 2.41mg, and 42.6% and 2.71mg/day, while after remission 19.3% and 5.68mg, 21.1% and 4.58mg, and 26.4% and 2.14mg/day, for G-Y, G-O, and G-OO, respectively (Table).
Conclusion: Our Touch Down Strategy can work effective for ERA, especially for elderly ERA whose age is over 75 years old. Just by doing take care for risk of comorbidities, ERA can be well controlled their disease activity.

Table: Characteristics of G-Y, G-O, and G-OO

	G-Y	G-YO	G-OO	S.S.
Cases	207	142	227	n.s.
female (%)	154 (74.4)	103 (72.5)	167 (73.6)	n.s.
age at onset	48.1	61.8	71.4	p<0.01
age at baseline	50.8	65.1	78.1	p<0.01
ACPA	123.7	156.8	229.3	n.s.
DAS28 at baseline	2.7	3.2	3.1	n.s.
Sharp/van de Heijde score at baseline	30	46.6	65.6	n.s.
HAQ at baseline	0.292	0.478	0.84	p<0.01
PS-VAS at baselline	37.3	41.5	43.4	n.s.
DAS28<2.3 prevalence (%)	76.4	89.6	87.2	n.s.
length untilDAS28<2.3 from baseline	2.9	2.5	4	n.s.
mean DAS28 at follor up	1.6	1.4	1.5	n.s.
mean DAS28 after DAS28 remission	2.0	1.8	2.0	n.s.
b-/ts-DMARD administration case and ratio (%)	41 (19.8)	29 (20.6)	41 (18.0)	n.s.
mean MTX dosage	8.6	8.6	7.4	n.s.
GCS administration dosage and ratio (until DAS28 remission)	2.96, 24.2%	2.41, 38.0%	2.71, 42.6%	n.s.
GCS administration dosage and ratio (after DAS28 remission)	5.68, 19.3%	4.58, 21.1%	2.14, 26.4%	n.s.

Disclosure of Interests: None declared
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AB0360 EVALUATION OF HEALTHCARE RESOURCE UTILISATION AND COSTS OF SJÖGREN'S SYNDROME: PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ABATACEPT OR ANTI-TNF DMARDS

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Background: Sjögren's syndrome (SS) is considered an extra-articular manifestation of RA and is an autoantibody-mediated condition similar to RA. In an open-label, prospective, observational multicentre study, abatacept (ABA) was found to be effective for both RA and SS-related manifestations.[1] However, there are limited data on the healthcare resource utilisation (HCRU) and cost in patients (pts) with RA with SS managed with ABA compared with those managed with anti-TNFs.
Objectives: To evaluate the HCRU and cost for pts with SS associated with RA treated with ABA or anti-TNF DMARDs.
Methods: Pts (≥18 years) from the Truven MarketScan™ administrative claims database with incident RA (≥2 claims for RA using International Classification of Diseases [ICD]-9 or ICD-10 codes and ≥1 claim for a conventional DMARD), incident SS (≥1 claim for SS using ICD-9 or ICD-10 codes) and with a prescription for ABA or an anti-TNF on or after the first diagnosis of SS from Jan 2011 to Sep 2017 were included. Pts were divided into two mutually exclusive cohorts. Pts with prescriptions for both ABA and an anti-TNF were excluded. The index date was the date of ABA or anti-TNF prescription. All-cause HCRU (healthcare visits) and costs were captured during the 2-year enrolled period prior to the index date (baseline) and in the 2-year enrolled follow-up period or until the pt was taken off the index drug, whichever occurred earlier. The baseline and follow-up periods were divided into intervals of 6 months each. Total healthcare visits (inpatient, outpatient, emergency care, urgent care and pharmacy) and total healthcare costs associated with these visits were calculated for each interval. A fixed-effects model was used to compare the HCRU and costs for pts taking ABA vs anti-TNFs after controlling for baseline Charlson Comorbidity Index and other comorbidities of interest.

Table 1.

Table 1. Baseline characteristics for pts in the ABA and anti-TNF cohorts

	ABA pts (n=148)	Anti-TNF pts (n=1219)
Age, years	56.0 (11.0)	53.0 (11.0)*
Female, n (%)	136 (91.9)	1065 (87.4)
Disease duration, days	336.0 (427.5)	285.0 (375.2)
CCI score	2.3 (1.6)	1.8 (1.2)*

Mean (SD) reported, unless stated otherwise
*p<0.05 vs ABA pts
ABA=abatacept; CCI=Charlson Comorbidity Index; pt=patient

Results: Overall, 1367 pts met inclusion criteria, of which 148 (10.8%) and 1219 (89.2%) were treated with ABA and anti-TNFs, respectively. ABA (vs anti-TNF) pts were older and had a higher comorbidity index (Table 1). Overall HCRU decreased in both the ABA and anti-TNF groups (relative to pts not being treated with biologic DMARDs). The HCRU was lower in ABA pts vs anti-TNF pts (average visits 20.0 vs 20.8, Figure 1) in the adjusted analysis. The average adjusted total healthcare cost for ABA (vs anti-TNF) pts was lower in the four 6-month cycles evaluated (average cost $17,050 vs $27,469; Figure 1). The overall healthcare costs were primarily driven by all-cause pharmacy cost (data not shown).
Conclusion: Pts with RA with SS managed with abatacept had lower HCRU and costs relative to pts managed with anti-TNFs. Further analysis is warranted to understand the drivers of the differential economic burden among pts with RA with SS.

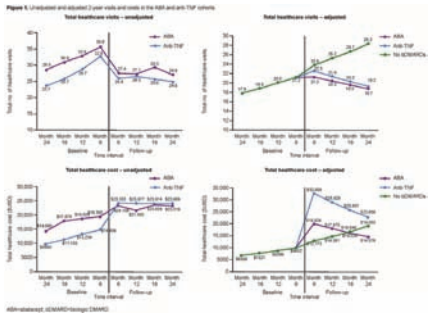


Figure 1

REFERENCES:
[1] Tsuboi H, et al. Mod Rheumatol 2016;26:891–9.

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AB0360B ANALYSIS OF SEQUENTIAL DEVELOPMENT OF PULMONARY LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Pulmonary involvement is critical for the management of RA. Pulmonary involvement shows various features in pathology and imaging such as interstitial pneumonia (ILD) and airway diseases (ADs). Importantly, pulmonary abnormalities coexist with other ones. We have previously reported that there were coexpstence patterns and ADs were shared abnormalities of patients with pulmonary lesions. However, it remains unknown through what pathways various pulmonary lesions develop.
Objectives: The purpose of this study was to determine the sequential development of pulmonary abnormalities in RA.
Methods: A retrospective cohort study. Subjects were consecutive 208 RA patients who were treated with bDMARDs as the first one from Feb.2004 to Sep. 2015 in our department and received HRCT scan before and during the therapy. Based on HR-CT imaging, pulmonary abnormalities were classified into 4 categories (ILD, nodular lesions, airway disease (AD) and others) and 20 lesions such as ground-glass opacity (GGO), reticular pattern, bronchiolitis and bronchiectasis. We recorded their existence and distribution and examined their changes. Cluster analysis was conducted according to new lesions at the second CT scans during the biological DMARDs, by Ward method. A checkerboard analysis with Chi-square test followed by residual analysis was conducted to examine the relation between pre-existing and newly emerging lesions. We compared the frequencies and pattern of newly emerging lesions in patients with or without pre-existing lesions.
Results: Subjects were 208 RA patients; M/F; 64/144, mean age; 59.2 years old, disease duration; 7.9 years, positive for RF in 84.1%. bDMARDs used for the longest period were TNF inhibitors in 79.8% of the subjects, abatacept in 15.4% and tocilizmab in 4.8%. Pulmonary

abnormalities were found in 146 (70.2%) of patients at the entry (ILD 81, (38.9%); nodular lesions 45, (21.6%); and AD 115, (55.3%)). During the observation period (3.26±2.61 years), newly emerging pulmonary lesions were found in 31.3% of patients and the incidence of which was 11.1/100 person-year. Cluster analysis of newly emerging lesions showed 7 clusters (Fig.1); Cluster 1; no new lesions, Cluster 2; nodular lesions, Cluster3; curved linear opacities, Cluster 4; bronchioectasis, Cluster 5; consolidations, Cluster 6; new bronchiolitis, and Cluster 7; GGO.

Newly emerging lesions frequently occurred in patients with pre-existing pulmonary lesions. Notably, curved linear opacities and bronchiolitis were developed in patients without pre-existing lesions with high frequencies compared to those with pre-existing ones (Fig.1). In patients with pre-existing lesions, various lesions were developed, particiraly GGO and consolidation.

The checkerboard analysis of pre-existing and newly emerging lesions revealed relation between 1) pre-existing honeycomb, small nodular lesions, bronchiolitis or bronchioectasia and newly emerging GGO and 2) pre-existing nodules and new bronchial wall thickening. In addition, bronchoectasia has the tendency to develop in patients with bronchitis, and conversely bronchiolitis occurred in patients with bronchioectasia. The relation between pre-existing small nodules or bronchiolitis and GGO was shown by analysis of pre-existing lesions and clusters of newly emerging ones.

Conclusion: Pulmonary lesions were developed in several patterns, not at random. Pre-existing pulmonary abnormalities induced new pulmonary lesions. Airway diseases, particularly bronchiolitis, might be important initial lesions that induce new pulmonary lesions, especially GGO.

Disclosure of Interests: None declared

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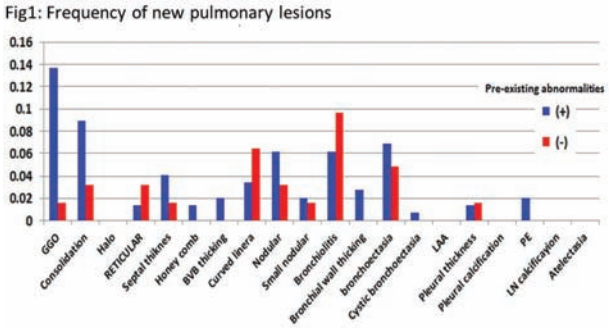


Figure 1

AB0360C **AN OBSERVATIONAL STUDY INTO THE RELATIONSHIP OF ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY AND RHEUMATOID FACTOR WITH LUNG DISEASE**

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Background: Extra-articular disease in rheumatoid arthritis (RA) occurs in nearly 50% of patients, the lung being a common site of complication. (1) Raised RF and anti-CCP titers have been associated with the development of pulmonary disease. Smoking in genetically susceptible individuals can result in protein citrullination and enhancement of autoimmune reactivity (2).

Objectives: Our aim was to explore the relationship between the presences of RhF and anti-CCP antibody with pulmonary manifestations in the following groups: RF positive only (group 1), Anti-CCP factors positive only (group 2) RF and anti-CCP positive in combination (group 3) we also explored the relationship between smoking, seropositivity and lung disease.

Methods: In this retrospective cross-sectional observational study of 2088 patients who had a RF and anti-CCP antibodies tested during Nov-2015 and Oct-2016 at Royal Wolverhampton Trust. Out of 2088, 1662 patients tested negative for both anti-CCP and RF and were excluded from analysis. 426 out of 2088 tested positive, of which 89 patients were anti-CCP only positive, 100 patients were RF only positive and 237 patients were positive for both antibodies. Data was collected on 89 patients from each group. Data collection included patient age, gender, smoking status, pulmonary manifestations, RF and anti-CCP titer, background of RA and current medications including DMARDS and biologics.

Results: In group 1 (30) 33.7% of RF positive patients suffered from RA, with (63) 70.7% in group 2 and (82) 92.1% in group 3(P=0.00001). In group 1 17% were current or ex-smokers, 29% in group 2 and 52.7% in group 3(P=0.02). Lung disease was present in 13.4% from group 1, 7.8% from group 2 and 12.3% from group 3 with no significant statically difference between the three groups (p=0.376). In group 2 and 3 all patients with lung disease had RA. From group 1, 50% of those with lung disease had a diagnosis of COPD, followed by 20% with bronchiectasis and 10% with ILD. Of note patients with a diagnosis of COPD had a higher titer of RF. In group 2 a third of patients with lung disease had a diagnosis of COPD and ILD respectively, and again these patients had higher titers of anti-CCP. In group 3 13.4% suffered from lung manifestations and 37.5% had a diagnosis of pulmonary fibrosis, 12.5% diagnosed with ILD and the remaining 50% had COPD and pleural disease.

Conclusion: Antibody positivity was associated with higher prevalence of RA. Our data provide evidence for the association between smoking and raised antibody titers, especially with anti-CCP antibodies. Lung disease was more strongly associated with RF than anti CCP even though the proportion of smokers was higher in patients with positive anti CCP compared than RF. However lung pathology varied with airway obstruction being more prevalent in RF positive patients compared with fibrosis in patients who were RF and CCP positive. Furthermore, our findings suggest that RF is more strongly associated with lung disease than anti CCP though citrullination is thought to start in the lungs. Our findings demonstrate that lung disease is prevalent in patients with RA and should be anticipated and treated accordingly in order to reduce mortality. Seropositivity of both RF and anti-CCP can be linked with a higher prevalence and greater severity of pulmonary disease activity however this requires replication in a larger cohort.

REFERENCES

[1] Turesson C, O'Fallon WM, Crowson CS, et al. Occurrence of extraarticular disease manifestations is associated with excess mortality in a community based cohort of patients with rheumatoid arthritis. J Rheumatol. 2002;29 (1):62–7.

[2] Mikuls TR, Payne JB, Deane KD, Thiele GM. Autoimmunity of the lung and oral mucosa in a multisystem inflammatory disease: The spark that lights the fire in rheumatoid arthritis? J Allergy Clin Immunol 2016; 137:28

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AB0360D **ADHERENCE TO THERAPY IN RHEUMATIC PATIENTS TREATED WITH SUBCUTANEOUS BIOLOGICS**

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Background: Patients' adherence to treatments is undoubtedly a fundamental part of a successful therapeutic strategy, even for rheumatic patients. In fact, the lack of adherence to treatment should be considered in all cases of "supposed" inefficacy of therapy prescribed.

Objectives: We aimed to evaluate the adherence to treatment in a series of rheumatic patients from a single Centre (Catania, Sicily, Italy).

Methods: We recruited 85 consecutive patients (M/F: 25/60; mean age 52.713.5 years) affected by chronic inflammatory arthropathies treated with subcutaneous biologics. All patients completed the 5-item version of Compliance Questionnaire for Rheumatology (CQR 5)[1] and the Morisky Medication Adherence Scales (MMAS-8)[2], in order to estimate their adherence to therapy. Moreover, all patients completed the Patient Global Assessment (PGA), the Visual Analogue Scale (VAS) for articular pain, and the Health Assessment Questionnaire (HAQ), in order to estimate their personal judgments on the effectiveness of therapies. Finally, the eventual presence of adverse events were reported.

Results: Considering MMAS-8, 7/85 (8.2%) patients were low adherent to treatment (score <6), and 27/85 (31.8%) presented medium-grade adherence (score 6-7). Interestingly, the CQR 5 failed to precisely identify these patients. Adherence to therapy was not related to age, gender, education level, articular disease, adverse events, association with DMARDs. Notably, the use of etanercept (originator or biosimilar) was significant more frequent in low-adherent patients (5/7 vs. 19/78; p=0.017). Finally, a trend to higher mean levels of PGA (57.1 vs. 37.6; p=0.06), VAS (68.6 vs. 42.6; p=0.06), and HAQ (1.3 vs. 0.7; p=0.052) was reported in low-adherent patients.

Conclusion: Our preliminary study confirmed that the low adherence to therapy (better identified with MMAS-8) is a relevant issue in the management of rheumatic patients treated with biologics. Moreover, low-

adherent patients tend to perceive a worse disease condition. Further studies can clarify if low adherence is causally associated with less efficacy of therapy.

REFERENCES

[1] Hughes, et al. BMC Musculoskeletal Disorders 2013; 14:286. 2. Morisky DE, et al. J Clin Hypertens 2008; 10:348–354.

Disclosure of Interests: None declared
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AB0360E SLEEP DISORDER OR DEPRESSION IN KOREAN RHEUMATOID ARTHRITIS, AND ITS ASSOCIATION WITH DISEASE ACTIVITY

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Background: Rheumatoid arthritis is a chronic autoimmune disease. Psychological stress and mood disorders such as sleep disorder or depression are more frequent in patient with RA.
Objectives: The aim of this study was to evaluate the relationship between disease activities and sleep disorder or depression in Korean patients with RA.
Methods: The study enrolled 334 patients with RA who visited Hallym University Sacred Heart Hospital (South Korea). The diagnosis of insomnia and depression is based in patient questionnaire such as Pittsburg sleep quality index (PSQI) and Beck depression inventory (BDI). Insomnia was defined as PSQI>5 and depression was defined as BDI $\geq$13. Patients were divided into two groups (insomnia vs no-insomnia, depression vs no-depression) and the clinical aspects were compared by Mann-Whitney U-test. Age, gender, erythrocyte sedimentation rate (ESR), 28 joint disease activity score (DAS28), DAS28-P score (the subjective components of the DAS28 relative to the total components), tender joint count (TJC) and swollen joint count (SJC), quality of life measured with health assessment questionnaire (HAQ) were analyzed.
Results: The median (inter-quartile range) disease duration was 6 (4–9) years and the mean DAS28 score was 3.6±1.1. Seventy percent of the patient had insomnia and 8% had depression. Compared with patients without insomnia, insomnia patients had a higher DAS28 (3.7±1.16 *vs.* 3.21±1.0, *P*<0.001), higher pain DAS28-P (0.37±0.17 *vs.* 0.32±0.16, *P*=0.004), higher TJC (4.63±5.68 *vs.* 2.38±3.45, *P*<0.001) and higher HAQ score (0.49±0.53 vs 0.18±0.36, *P*<0.001). Compared with no depression patients, depression patients had a higher DAS28 (4.07±1.37 *vs.* 3.51±1.11, *P*<0.001), higher pain DAS28-P (0.44±0.17 *vs.* 0.35±0.44, *P*=0.015), higher TJC (6.59±6.57 *vs.* 3.71±5.02, *P*=0.006), higher SJC (1.81±5.2 *vs.* 0.67±1.28, *P*=0.003), and higher HAQ score(0.63±0.51 vs 0.38±0.5, *P*=0.021).
On univariable logistic regression analysis, insomnia was positively associated with age, DAS28, DAS28-P and BDI score. After adjustment, insomnia was positively associated with sex (female), age, BDI and DAS28 score. On univariable logistic regression analysis, depression was positively associated with PSQI, DAS28 and DAS28-P score. After adjustment, depression was positively associated with PSQI and DAS28-P score.
Conclusion: Rheumatoid arthritis patient with the sleep disorder or depression had worse clinical symptoms than those without. Rheumatologist should take sleep disorder or depression into consideration on evaluation of disease severity in RA patients.
Disclosure of Interests: None declared
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AB0360F GENDER DIFFERENCES IN CLINICAL CHARACTERISTICS AND COMORBIDITIES AND THEIR IMPACT ON CLINICAL OUTCOME IN KOREAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic auto-immune disease that is more common to female than male. Gender-based differences in clinical features, comorbidities, and disease outcomes have been fragmentarily described. However, systematic analysis focusing on gender differences in a large RA population is scarce.
Objectives: We aimed to elucidate gender differences in clinical characteristics and comorbidities and their potential impact on clinical outcome in a large Korean cohort of patients with RA.
Methods: A total of 5,376 RA patients were included from the KORean Observational study Network for Arthritis (KORONA) database. Each patient was examined at baseline and three consecutive years. RA disease activity, functional disability, and quality of life were assessed by disease activity score 28 (DAS28), health assessment questionnaire (HAQ) and EuroQoL-5D (EQ-5D), respectively. The subjective health-related outcomes including visual analog scale (VAS) scores for patient's and physician's global health, patient's pain, fatigue, and sleep disturbance were collected. Clinical characteristics and comorbidities at baseline were compared according to gender. Gender impacts on clinical outcome during the four years were analyzed using generalized estimating equations (GEE) models for repeated measures. In addition, the gender effect on achieving clinical remission was analyzed using Cox-proportional hazards regression.
Results: At baseline, females (n=4,574) were younger, more erosive, and had longer disease duration than male (n=802). Females showed significantly higher scores in DAS28, HAQ, EQ-5D, and VAS for all patients' health-related outcomes. In terms of comorbidities, the prevalence of male RA was significantly higher than that of female RA in most illnesses including interstitial lung disease, cardiovascular disease, diabetes and other pulmonary disease except for depression. In the GEE model, gender was found to significantly influence the rate of change of DAS28 (p=0.041), and also independently associated with this outcome (p<0.001) after adjusting for age, disease duration, and baseline DAS28. Females were associated with a reduced rate of achieving DAS28 remission (HR 0.41, 95% CI 0.28-0.58) compared to male.
Conclusion: In Korean patients with RA, most comorbidities were more prevalent in male than in female. But for RA-related health outcomes, the longitudinal change in disease activity and the rate of achieving clinical remission over time were found to be worse in female RA.

REFERENCES

[1] Jawaheer D, Maranian P, Park G, Lahiff M, Amjadi SS, Paulus HE. Disease progression and treatment responses in a prospective DMARD-naive seropositive early rheumatoid arthritis cohort: does gender matter? J Rheumatol 2010;37:2475-85

[2] Aurrecoechea E, Llorca Díaz J, Diez Lizuain ML, McGwin G Jr, Calvo-Alen J. Gender-associated comorbidities in rheumatoid arthritis and their impact on outcome: data from GENIRA. Rheumatol Int 2017;37:479-85.

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AB0360G DETECTABLE HBV DNA AT TREATMENT BASELINE PREDICTED HEPATITIS B VIRUS REACTIVATION IN INFLAMMATORY ARTHRITIS PATIENTS WITH NEGATIVE HEPATITIS B SURFCE ANTIGEN BUT POSITIVE ANTI-HEPATITIS B CORE ANTIGEN

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Background: Hepatitis B virus (HBV) reactivation in inflammatory arthritis IA (rheumatoid arthritis, psoriatic arthritis, and peripheral spondyloarthritis) patients with positive hepatitis B surface antigen (HBsAg+) is one of the treatment-related complications. The risk of reactivation in patients with negative hepatitis B surface antigen but positive anti-hepatitis B core antibody (HBsAg+/anti-HBc-) is less well defined.
Objectives: This retrospective, single centre study aimed to study the prevalence of HBV reactivation (defined as HBV DNA becoming detectable during treatment if it was untectable at baseline, or an increase in HBV DNA titre if detectable at baseline) among IA patients with HBsAg+/anti-HBc+ status, and to investigate any factors predicting reactivation.
Methods: IA patients attending the rheumatology specialist clinic in a local tertiary hospital between 1stJanuary 2011 and 31st December 2016 were included if they had HBsAg-/anti-HBc+ status. Demographic data, clinical parameters including treatments for IA and any use of antiviral prophylaxis, and laboratory results including anti-hepatitis B surface antibody (anti-HBs) and serial HBV DNA levels were obtained. Logistic regression was used to identify factors predicting HBV reactivation.

Results: Around 1/3 (68%) of the 206 included patients included were female and the mean age was 61.7-year-old. 75% had rheumatoid arthritis and the remaining had psoriatic arthritis or peripheral spondyloarthritis. Most patients (94%, n=194) were on conventional synthetic DMARD csDMARD (25 on monotherapy and 169 on combination therapy). 35% patients (n=72) were on biologic DMARD (with or without csDMARD). As antiviral prophylaxis was not mandatory in HBsAg-/anti-HBc+ patients according to local protocol, only 17 patients (8.3%) were on preemptive antiviral against HBV.

Thirteen patients (6.3%) experienced HBV reactivation during their disease course and four of them were on antiviral prophylaxis. All of these reactivations were only transient low-grade viraemia with HBV DNA level ≤ 20IU/ml. Spontaneous resolution of viraemia were observed in all these patients. None of the reactivation resulted in acute hepatitis, hepatic failure or mortality.

Presence of detectable HBV DNA at baseline predicted HBV reactivation (OR 21.0, p<0.005). Other parameters including age, the lack of antiviral prophylaxis, negative anti-HBs status and anti-HBs titre were not significant predictors of HBV reactivation. None of the synthetic and biologic DMARDs were associated with HBV reactivation.

Conclusion: HBV reactivation was infrequent among IA patients with HBsAg-/anti-HBc+ status and was unlikely to be associated with adverse clinical outcome. It could occur in patients with positive anti-HBs or on antiviral prophylaxis. Detectable HBV DNA at baseline was a predictor of HBV reactivation.

REFERENCES

[1] Mod Rheumatol. 2018 Jan 22:1-6
[2] Clin Exp Rheumatol. 2017 Sep-Oct;35(5):831-836

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Rheumatoid arthritis – biological DMARDs

AB0361 ASCORE, A 2-YEAR, OBSERVATIONAL, PROSPECTIVE MULTICENTRE STUDY OF SUBCUTANEOUS ABATACEPT FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN ROUTINE CLINICAL PRACTICE: 1-YEAR INTERIM ANALYSIS

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Background: ASCORE (Abatacept [ABA] SubCutaneOus in Routine clinical practicE; ClinicalTrials.gov: NCT02090556) is an ongoing, 2-year, observational, prospective, multicentre study of patients (pts) with RA initiating SC ABA in routine clinical practice.

Objectives: To present for the first time 1-year interim retention rates and clinical outcomes by previous biologic (b)DMARD exposure.

Methods: Pts (≥18 years) with moderate-to-severe RA, who initiated SC ABA 125 mg weekly, were enrolled (Mar 2013–Jan 2017) across 10 countries in two cohorts: biologic-naïve pts and those who had failed ≥1 prior bDMARD. Pt and disease characteristics were recorded. ABA retention rates (95% CI) were estimated at 1 year by Kaplan–Meier analysis. Good/moderate EULAR response rates based on DAS28 (ESR, otherwise CRP), LDA or remission according to DAS28 (ESR; ≤3.2), SDAI (≤11), CDAI (≤10) and Boolean criteria were assessed at 1 year.

Results: A total of 2843/2949 enrolled pts were evaluable: 1162 (40.9%) were biologic naïve; 740 (26.0%) had failed 1 and 941 (33.1%) had failed ≥2 prior biologics. At baseline, pts with a higher vs lower number of prior bDMARDs had longer disease duration and greater presence of erosive disease vs pts who were biologic-naïve; CRP was higher in biologic-naïve vs -failure pts; disease activity was similar across treatment exposures. Overall SC ABA retention (95% CI) at 1 year was 65.3% (63.4, 67.0); retention was higher in pts receiving ABA as a first vs later bDMARD (71.1% [68.3, 73.7] in biologic-naïve pts vs 61.9% [58.2, 65.4] and 60.7% [57.4, 63.8] in those with 1 and ≥2 prior biologic failures, respectively; Figure). At 1 year, 943 pts had discontinued ABA: 465/936 [49.7%] due to inefficacy and 218/936 [23.3%] due to safety (data unavailable, n=9/943). Among pts continuing ABA at 1 year, good/moderate EULAR response rates for pts who were biologic-naïve and those with 1 and ≥2 prior biologic failures were 81.0%, 70.0% and 66.4%, respectively. Corresponding rates for LDA outcomes were also higher with ABA as an earlier vs later bDMARD. The safety profile was similar across patient cohorts and consistent with real-world IV ABA studies.[1,2]

Conclusion: In routine clinical practice, overall retention of SC abatacept at 1 year was around 65% and comparable with that of IV abatacept.[2] Among pts continuing abatacept at 1 year, good/moderate EULAR response rates were consistently >65% irrespective of prior bDMARD exposure. Better retention and clinical response rates were achieved with abatacept earlier in bDMARD treatment history.

REFERENCES

[1] Nüßlein HG, et al. Clin Exp Rheumatol 2016;34:489–99.
[2] Alten R, et al. *RMD Open* 2017;3:e000538.

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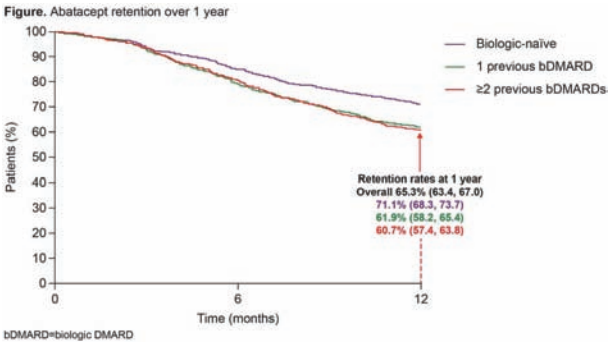


Figure 1

Disclosure of Interests: Rieke Alten Grant/research support from: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, Xavier Mariette Consultant for: Honorarium from Bristol-Myers Squibb, GlaxoSmithKline, Gilead, Janssen, Pfizer, UCB, Maya Buch Grant/research support from: Pfizer LTD, UCB, Consultant for: AbbVie, Eli Lilly, EMD Serono, Pfizer Ltd., Sanofi, Roberto Caporali Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Roche, Genzyme, Lilly, MSD, Pfizer, UCB, Rene-Marc Flipo Consultant for: Advisory board: Bristol-Myers Squibb, Adrian Forster Consultant for: Consultant for Pfizer, MSD, Grünenthal, Novartis and Roche, Michael Nurmohamed Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Yusuf Patel: None declared, Peter Peichl Speakers bureau: Speaker: Eli Lilly, Pfizer, Bristol-Myers Squibb, Raimon Sanmarti Grant/research support from: Research support: Bristol-Myers Squibb, Speakers bureau: Speakers bureau: Bristol-Myers Squibb, Melanie Chartier Employee of: Bristol-Myers Squibb, Julia Heitzmann Employee of: Employee of Excelya which received funding from Bristol-Myers Squibb as contract research organization for this study., Christiane Rauch Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Sean Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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AB0362 HIGH UNMET NEED AMONG RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO BIOLOGIC DMARD: REAL-WORLD ANALYSIS OF 2012–2016 US MEDICARE DATA

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Background: Within treat-to-target approach, ACR recommends biologic DMARD (bDMARD), with or without methotrexate, in rheumatoid arthritis (RA) patients whose disease is active despite methotrexate treatment[1]. ACR further defines bDMARD failure as the lack of efficacy (desired response) or side effects. Understanding the real-world characteristics and treatment patterns of the patients who become bDMARD inadequate responders (IR) may help clinicians tailor the next treatment to patient needs and health status.

Objectives: This study described treatment patterns, treatment duration, and characteristics of RA patients who became IR to their first bDMARD.

Methods: The study population included adult patients with Medicare medical and pharmacy insurance coverage (20% sample) who became bDMARD IR: ≥2 RA claims, newly initiated bDMARD (initial therapy) and then switched (index date) to another bDMARD or JAKi (index therapy). Patients with cancer, non-RA autoimmune disease, or pregnancy were excluded. At least 1 year pre- (baseline) and 1-year post-index enrollment was required. Patient characteristics and treatment allocation and duration were assessed.

Results: A total of 528 bDMARD IR patients met the study selection criteria. At baseline, these patients used monotherapy (n=165, 31.2%) or bDMARD+csDMARD combination (n=363, 68.8%).

Patient baseline demographics were comparable between monotherapy and combination therapy groups: mean (SD) age 65.6 (11.0) years, 82.0% female, 81.6% white. The mean (SD) Charleson Comorbidity Index was 1.8 (1.1) for monotherapy and 1.6 (1.0) for combination therapy (P=0.084). On average, patients used 14.8 (7.1) concomitant medications (comparable between groups).

The original bDMARD treatment lasted for median 211 days, including 211 days for monotherapy and 212 days for combination therapy.

As bDMARD IR patients switched treatment regimen, they started using either monotherapy (n=187, 35.4%) or combination therapy (n=341, 64.6%). The median duration of subsequent therapies was 287 days overall, including 224 days for monotherapy and 319 days for combination therapy (P=0.0063).

Conclusion: Among Medicare bDMARD IR patients, the median duration of the initial bDMARD therapy lasted for 212 days or less and the subsequent treatments lasted for 319 days or less. This analysis suggests that bDMARD IR patients require alternative efficacious and well-tolerated treatments.

Table 1. Frequencies of monotherapy and combination therapy for initial and post-switch treatments.

Initial (first bDMARD) therapy	Total		Post-switch (index) therapy			
			Monotherapy		Combination therapy	
	N	%	N	%	N	%
Monotherapy	165	31.2	133	80.6	32	19.4
bDMARD + csDMARD combination	363	68.8	54	14.9	309	85.1
Total	528	100	187	35.4	341	64.6

REFERENCES

[1] 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care & Research DOI 10.1002/acr.22783 V C 2015, American College of Rheumatology

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AB0363 TREATMENT PATTERNS IN RHEUMATOID ARTHRITIS PATIENTS INITIATING DMARDS: ANALYSIS OF US HEALTH PLAN CLAIMS

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Background: The ACR treat-to-target approach for rheumatoid arthritis (RA) recommends regular assessments of disease activity and adjustment of medication regimen until efficacy goals are met.[1] Given recent advances in pharmacologic therapy, this study assessed recent treatment patterns in RA patients with a newly-initiated DMARD.

Objectives: To describe current treatment patterns among RA patients initiating their first DMARD treatment.

Methods: Adults with ≥2 RA claims, initiating the first DMARD between 1/2012–9/2016 (index date; ID) were identified in fully-adjudicated commercial medical and pharmacy health insurance claims (includes self-insured, full-risk, and Medicare policies for approximately 40 million lives annually). Those with 12-months continuous enrollment pre- and post-ID and without DMARD claims 12 months pre-ID were selected. Initiation of conventional synthetic DMARDs (csDMARDs), tumor necrosis factor inhibitors (TNFi), anti-interleukin-6 pathway antibodies (anti-IL6), other biologic DMARDs (bDMARDs), and janus kinase inhibitor (JAKi), as monotherapy or in combination with csDMARDs was summarized with descriptive statistics. Median therapy duration was assessed with the Kaplan-Meier method. End of treatment was defined as drug discontinuation, switch to a new therapy, or addition of another DMARD.

Results: Among 26,808 identified patients (74.2% female; mean age 51.9 ±11.0 years), 97.7% initiated monotherapy and 2.3% started combination therapy. The most commonly-prescribed monotherapies were csDMARD (91.3%) and TNFi (6.6%). The most commonly-prescribed combination therapies included TNFi+ csDMARDs (88.0%) and other bDMARDs+ csDMARDs (7.3%). The median duration of csDMARD monotherapy was 230 days. The median treatment duration (combination vs monotherapy) was: 225 vs. 206 days (TNFi), 227 vs. 203 days (anti-IL6), 198 vs. 182 days (other bDMARDs), and 347 vs. 301 days (JAKi) (Table). JAKi treatment had the longest therapy duration when combined with csDMARDs (347 days), and other therapies lasted for median 198-230 days. As monotherapy, JAKi duration lasted for median 301 days, and other monotherapies lasted for median 182-227 days.

Table. Median treatment duration in adult rheumatoid arthritis patients initiating a first DMARD

	Median Treatment Duration, days	
	Monotherapy	Combination Therapy
TNFi	206	225
anti-IL6	203	227
other bDMARD	182	198
JAKi	301	347

Conclusion: Real-world data from US longitudinal healthcare claims showed that in RA patients newly initiating DMARDs, the median duration of therapy was less than a year, suggesting a need for treatment with improved response durability. Duration of JAKi therapy was longer than the median duration of other therapies. Further research is needed to determine the reasons for the longer persistence of JAKi therapy and why persistence is low with RA therapies overall.

REFERENCES

[1] Singh JA, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2016 Jan;68(1):1-26.

Disclosure of Interests: Robin K Dore Grant/research support from: Gilead Sciences, AbbVie, Amgen, Lilly, Pfizer, Regeneron, Sanofi, Consultant for: AbbVie, Amgen, Lilly, Speakers bureau: AbbVie, Amgen, Lilly, Sanofi, Regeneron, Pfizer, UCB, Jenya Antonova Shareholder of: Gilead Sciences, Employee of: Eli Lilly and Company, Medimmune, Genentech, Gilead Sciences, Jerrold Hill Grant/research support from: Gilead Sciences

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AB0364

DISCONTINUATION OF CONCOMITANT METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB: AN INTERVENTIONAL STUDY

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Background: Methotrexate (MTX) is an important anchor drug for rheumatoid arthritis (RA) patients and is used alone or in combination with biologics. However, some patients discontinue MTX due to toxicity including gastrointestinal (GI) disorders [1]. Thus, de-escalation of MTX while maintaining a favourable disease activity state—a challenge in RA clinical research—may be beneficial from the perspective of reducing adverse events. The efficacy of tocilizumab (TCZ) has been demonstrated in monotherapy as well as with concomitant MTX [2], opening up the possibility of MTX discontinuation in these patients if disease control can be maintained.

Objectives: This study aimed to evaluate the efficacy and safety of MTX discontinuation in RA patients with sustained low disease activity undergoing combination therapy with TCZ plus MTX.

Methods: This multicentre, open-label, uncontrolled, prospective 64-week study included RA patients maintaining low disease activity (Clinical Disease Activity Index [CDAI] ≤10) for ≥12 weeks with TCZ plus MTX. MTX was discontinued following 12 weeks of biweekly administration while continuing TCZ therapy. The rescue treatments were performed if the CDAI score was >10 and at the discretion of the investigator and/or upon patient request. The primary endpoint was the proportion of patients maintaining low disease activity with no flare at week 36 (24 weeks after MTX discontinuation). Disease flare was defined as a CDAI score >10 or intervention with the rescue treatments for any reasons. Assuming that 80% of patients would maintain low disease activity at week 36, 43 patients were calculated as necessary to prove the clinical feasibility of discontinuing MTX at a power of ≥80% with a threshold response rate of 60%. Secondary endpoints were GI symptoms, physical function, and quality of life.

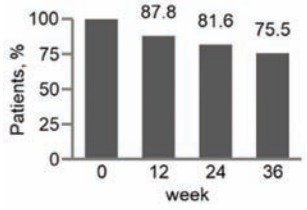


Figure 1. Proportion of patients maintaining low disease activity without a flare.

Figure 1

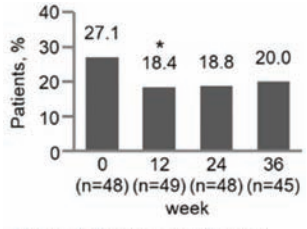


Figure 2. Prevalence of gastro-oesophageal reflux disease defined as a FSSG score ≥8. *P < 0.05 vs. week 0 by McNemar's test.

Figure 2

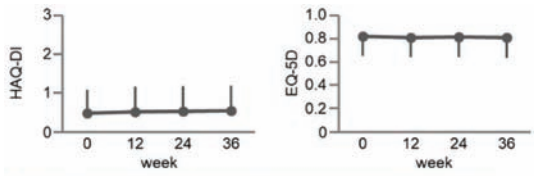


Figure 3. Changes in Health Assessment Questionnaire Disability Index (HAQ-DI) and EuroQol-5 dimension (EQ-5D) from week 0 to 36. Values represent mean (standard deviation).

Figure 3

Results: A total of 49 patients completed 36 weeks of therapy. Table 1 shows the baseline (week 0) characteristics of patients included in the efficacy analyses. The proportions (95% CI) of patients who maintained low disease activity without a flare at weeks 12, 24, and 36 were 87.8% (75.2 – 95.4%), 81.6% (68.0 – 91.2%), and 75.5% (61.1 – 86.7%), respectively (Fig. 1). The lower limit of the 95% CI at week 36 exceeded the assumed threshold response rate of 60%, demonstrating the clinical feasibility of MTX discontinuation. The prevalence of gastro-oesophageal reflux disease, defined as a Frequency Scale for Symptoms of Gastro-oesophageal reflux disease score ≥8, significantly decreased from week 0 to 12 (27.1% to 18.4%; P = 0.025) (Fig. 2). No significant changes were observed in the HAQ-DI and EQ-5D from week 0 to 36 (Fig. 3).

Table 1. Patient characteristics at baseline (week 0)

	Total, n = 49		
Age, years	62	±	10
Female,%	84		
Weight, kg	55	±	11
Disease duration, years	11	±	8
Route of TCZ, intravenous/ subcutaneous,%	65/35		
Rheumatoid factor positive,%	79		
Anticyclic citrullinated peptide positive,%	90		
MTX dose, mg/week	8.2	±	2.3
Use of glucocorticoids,%	29		
CDAI	2.7	±	2.5
CDAI ≤2.8,%	67		
CRP, mg/dl	0.04	±	0.06
HAQ-DI	0.472	±	0.613
EQ-5D	0.822	±	0.170

Data are shown as mean ± SD or percentage.

Conclusion: Discontinuation of concomitant MTX is clinically feasible for maintaining low disease activity, and may be beneficial from the perspective of reducing GI symptoms in RA patients treated with TCZ.

REFERENCES

[1] Bologna C, et al. Br J Rheumatol 1997;36:535-40.
[2] Dougados M, et al. Ann Rheum Dis 2013;72:43-50.

Disclosure of Interests: Shuji Asai Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Janssen, Takeda, and UCB Japan, Toshihisa Kojima Grant/research support from: Chugai Pharmaceutical (Investigator Initiated Study), Novartis, Nippon Kayaku, Eli Lilly, Eisai, Speakers bureau: Chugai Pharmaceutical, Takeda Pharmaceutical, Pfizer, Eli Lilly Japan, Bristol Myers Squibb, Ono Pharmaceutical, Daiichi Sankyo, Astelas, UCB, Janssen Pharmaceutical, Tanabe Mitsubishi, Nobunori Takahashi Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Eisai, Mitsubishi Tanabe, and Pfizer. YS has received speakers' fees from Astellas, Bristol-Myers Squibb, and Ono, Yachiyo Kuwatsuka: None declared, Masahiko Ando: None declared, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant for: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama
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AB0365 EFFICACY OF TOCILIZUMAB FOR CORTICOSTEROID AND METHOTREXATE SPARING IN RHEUMATOID ARTHRITIS

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Background: Successful management of rheumatoid arthritis (RA) depends on the early administration of DMARDs and biologic DMARDs. The biologic agent tocilizumab, an interleukin-6 receptor inhibitor, has been used for the management of RA.
Objectives: The aim was to describe a cohort of RA patients treated with tocilizumab and the effect of this treatment on the other DMARDs used, namely methotrexate and corticosteroids.
Methods: In a cohort of 80 patients with rheumatoid arthritis the biologic agent tocilizumab was administered in combination with methotrexate administered sc and 10 mg prednisolone. Within this cohort, 26 patients were on tocilizumab administered iv 8 mg/kg/4wks (maximum dose 800 mg) and 54 were on tocilizumab administered sc 162mg/wk. As corticosteroid administration is characterized by adverse effects, such as osteoporosis and diabetes mellitus, in the course of the disease, in all patients an effort was made to reduce and, if possible, withdraw corticosteroids. An effort was also made to reduce methotrexate dosage. After a year, prednisolone was either significantly reduced or withdrawn. The final dosage of prednisolone was either 2.5-5 mg or complete withdrawal. The successful reduction of methotrexate dosing schedule was also achieved. The final methotrexate dose was either 12.5 mg sc or complete withdrawal. After a period of 52 weeks in this cohort 42 of 80 patients (52.5%) were on monotherapy with tocilizumab.
Results: In a cohort of 80 patients with RA the administrations of tocilizumab, either iv or sc, proved safe and effective. Remission or low disease activity of RA was achieved. Corticosteroid dosage was reduced. Methotrexate dosage was also reduced. After 52 weeks within the group of RA patients on treatment with tocilizumab, in 42 complete withdrawal of corticosteroids and methotrexate proved feasible. Patients on tocilizumab monotherapy remained in remission.
Conclusion: It appears that tocilizumab is safe and effective for the treatment of RA. Tocilizumab treatment may permit withdrawal of both corticosteroids and methotrexate in patients with RA. The management of active RA initially with low dose corticosteroids in combination with methotrexate sc and, in the case of failure to achieve remission, with the addition of the biologic agent tocilizumab had as a result either significant corticosteroid reduction or complete withdrawal and reduction of methotrexate dosage, the disease remaining in remission.
Disclosure of Interests: None declared
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AB0366 COMPARISON OF THE EFFECT OF RITUXIMAB (ROCHE) AND RITUXIMAB BIOSIMILAR – BCD-020 (BIOCAD) ON INFLAMMATORY AND IMMUNOLOGICAL BIOMARKERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: BCD-020 (BIOCAD) is the first Russian rituximab (RTX) biosimilar which was approved for medical use in rheumatoid arthritis (RA) patients in Russia and some CIS countries
Objectives: To evaluate the changes in acute phase reactants, autoantibodies, immunoglobulins, cytokine profile and CD19+B lymphocytes in patients (pts) with RA during RTX and RTX biosimilar therapy
Methods: The study included 54 RA patients (pts), divided into two groups. The first group included 34 pts with RA (31 women, mean age 49(42-64), mean disease duration 66(36-132) months, mean DAS 28 6.2 (5.5-6.8)) who received two infusions of RTX - 35% at a dose of 500 mg, 65% of the dose of 1000 mg every two weeks in combination with DMARDs and glucocorticoids; 33 pts achieved a good/moderate EULAR response at week 24. The second group - 20 pts with RA (18 woman, mean age 61.5(54-66.5) years, mean disease duration 39.5(20-84) months, mean DAS 28 5.6(4.9-6.8)) who received two intravenous BCD-020 infusions (600mg No 2) in combination with DMARDs and glucocorticoids; 17 pts achieved a good/moderate EULAR response at week 24. Laboratory biomarkers were assessed at baseline and weeks 12 and 24 after the first infusion of RTX. ESR (mm/hr) (Westergren method); serum concentrations of CRP (mg/L), IgM RF (IU/ml) (laser nephelometry); anti-CCP2 (U/ml), IgA RF (U/ml), anti-MCV (U/ml) (ELISA kits); cytokine profile (xMAP technology) were assessed
Results: RTX and BCD-020 induced decreases in ESR, levels of CRP, IgMRF, IgARF, anti-MCV at week 12 and 24, $p<0.05$ (tabl.1). At week 24 – 20% of IgMRF positive pts at baseline (in the first group) and 10% of IgMRF positive pts (in the second group) turned negative. Levels of anti-CCP2 did not reduced. At week 24 – 7% of anti-CCP2 positive pts at baseline (in the first group) and 15% of anti-CCP2 positive pts (in the second group) turned negative. Depletion of CD19+B-cells was achieved at week 12 in all patients (absolute number 0), with an increase in the level of B cells at week 24, tabl.1. The immunoglobulin level decreased at week 24, but remained normal. In the first group RTX induced reduction in proinflammatory (IL-1b, IL-2, IL-6, IL-12, IL-15, IFN-γ, TNF-α), anti-inflammatory cytokines (IL-1Ra, IL-5, IL-9, IL-10, IL-13), growth factors (IL-7, GM-CSF, FGF-basic) and chemokines (MC-1) at week 24 (fig.1). In the second group BCD-020 induced reduction in IL-1b, IL-1Ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-17, Eotaxin, G-CSF, IFN-γ, IP-10, MC-1, MIP-1β, TNF-α, VEGF at week 24 $p<0.05$, fig.1.

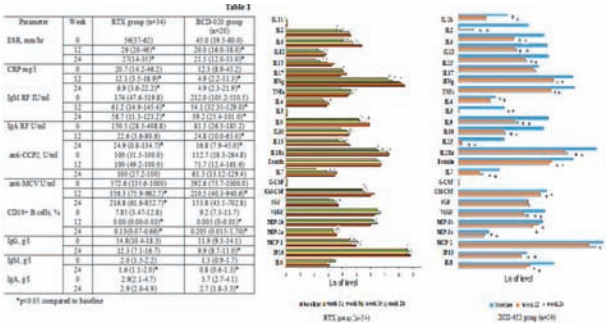


Figure 1

Conclusion: RTM biosimilar (BCD-020) has a similar effect on inflammatory and immunological biomarkers to the original RTM. BCD-020 therapy induced a rapid and significant improvement in ESR, levels of CRP, IgM/IgARF, anti-MCV, proinflammatory, anti-inflammatory cytokines, growth factors, chemokines levels and CD19+B cells depletion in RA pts
Disclosure of Interests: Anastasia Avdeeva: None declared, Maria Cherkasova: None declared, Alexander Artyuhov: None declared, Eh. Dashinimaev: None declared, D. Kusevich: None declared, Alexander Lila Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc., Evgeny Nasonov: None declared
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AB0367 REASONS FOR DISCONTINUATION OF BIOLOGICAL DRUG AND TARGETED SYNTHETIC DRUGS AMONG PATIENTS WITH INFLAMMATORY ARTHRITIS IN THE UNITED ARAB EMIRATES (UAE)

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Background: In routine clinical care of Rheumatoid arthritis (RA) Spondyloarthritis(SPA) and Psoriatic arthritis (PSA) there is a high rate of discontinuation of biologic disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs) due to loss of efficacy, side effects or lack of adherence. This can impact on the ability to achieve low disease activity.
Objectives: To evaluate the use of bDMARDs and tsDMARds and analyze the reasons for discontinuation of these drugs and to compare them to our standard DMARD Methotrexate.
Methods: In this retrospective cohort analysis we included consecutive patients aged $\geq$ 18 years with RA/SPA/PSA attending 2 Rheumatology clinics in the UAE from August- December 2019. Statistical analysis was performed using STATA version 13 and R-studio. Continuous data were

summaries as mean and SD. Dichotomous data were presented as percentage. Chi square test, Proportion test and T-test were applied based on the data type and its distribution to calculated P-value at a 5% level of significance

Results: Of 745 patients who were included, 453 (60.8%) had RA,165 (22.5%) SPA, and 127 (16.7%) PSA. Of these a total of 353(47.3%) received 565 treatment courses with bDMARDs and 106patients had (14.2%) had110 treatment courses with tsDMARD, and 480(64.4%) Methotrexate(MTX)

100/353(28.3%) of patients discontinued bDMARds; 35/106(33.0%) of patients discontinued tsDMARds; and 254/480(52.9%) MTX. 52% of treatment courses of bDMARD andd 36% courses of tsDMARD were discontinued. Reasons for discontinuation are in table 1.

Factors such as age, gender,ethinicity were not significantly associated with the rate of discontinuation of medications (Chi-square test). 647/745 (86.6%) of patients had medical insurance, however lack of insurance did not lead to discontinuation of bDMARDs (OR=0.54 95% CI (0.22 to 1.32)) and tsDMARDs (OR= 1.59 95% CI:(0.3 – 8.3)). A significant proportion of patients (15% -18%) in all the three groups have stopped the drugs of their own choice. We did not observe any statistical significant difference between the active and discontinued categories with respect to disease activity scores das 28 for RA; BASDAI for SPA and HAQ score for PSA.

Table 1. Distribution of different medications

Number of patients	bDMARDS (n=353)		tsDMARDS (n=106)		Methotrexate (n=480)		P value
Actively on Rx	253	72%	71	67%	226	47%	<0.001*
Discontinuation	100	28%	35	33%	254	53%	
Total	353	100%	106	100%	480	100%	
Reasons for Discontinuation							
Unknown reason	8	8%	4	11%	18	7%	0.66
Side effect	8	8%	4	11%	92	36%	<0.001*
Primary loss of efficacy	10	10%	9	26%	18	7%	0.001*
Secondary loss of efficacy	27	27%	10	29%	46	18%	0.101
Doctors choice	7	7%	1	3%	11	4%	0.486
Patient choice	17	17%	1	3%	37	15%	0.118
Pregnancy	5	5%	0	0%	24	9%	0.075
Remission	10	10%	3	9%	8	3%	0.025*
Financial	6	6%	3	9%	0	0%	<0.001*
Infection	2	2%	0	0%	0	0%	0.001*
Total	100	100%	35	100%	254	100%	

P value is computed using proportion test

* statistical significance difference at 5%

Conclusion: A significantly higher proportion of patients discontinued MTX as compared to bDMARDs and tsDMARDs. Major reason for stopping MTX was side effects while bDMARDs and TsDMARDS were mainly stopped due to loss of efficacy or financial reasons. Safety and tolerability of bDMARDs and tsDMARDs was good in our cohort of patients.

REFERENCES

[1] Ebina K,et al. Drug retention and discontinuation reasons between seven biologics in patients with rheumatoid arthritis -The ANSWER cohort study. PLoS One. 2018 Mar 15;13(3)

[2] Favalli EG, et al. Real-life 10-year retention rate of first-line anti-TNF drugs for inflammatory arthritides in adult- andjuvenile-onset populations: similarities and differences. ClinRheumatol. 2017Aug;36(8):1747-1755.

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AB0368 SAFETY OF COMBINATION THERAPY WITH TWO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: About 20% to 40% of patients with rheumatoid arthritis (RA) treated with biologic therapies fail to achieve remission consequently requiring additional treatment (1-4). Combining different biologic agents could be a promising therapeutic strategy. However, the safety and tolerability of combining different biologic agents is one of the major concerns of this treatment approach.

Objectives: We performed a systematic review and meta-analysis of the current literature to assess the safety of combining two bDMARDs (biologic disease-modifying anti-rheumatic drugs) in the treatment of patients with RA.

Methods: We searched PubMed, the Cochrane Library, Scopus, ClinicalTrials.gov, and the WHO International Clinical Trials Registry platform through 12/18/17. Our eligibility criteria included human RCTs or observational or non-randomized comparative studies in adults ($\geq$ 18 years of age) that recorded safety of combination therapy with two bDMARDs in RA patients. We used R version 3.1.2 to perform meta-analysis between groups on combination therapy and placebo/single therapy alone using random effect model calculating odds ratio (OR) as well as 95% confidence interval (CI). Cochran Q statistic and I^2 statistic was used to identify heterogeneity between studies. The primary outcome was the rate of major serious events. Additional outcomes were the rate of total adverse events, total infectious events and major infectious events.

Results: Six studies with a total of 623 patients (410 on combination therapy and 213 on single therapy) were included for meta-analysis. Median follow-up was 9.5 months (range 6-12 months). There was a significant increase in SAEs in the combination group (14.9 vs 6.0%, OR 2.51, 95% CI 1.29-4.89, $I^2$0%) as well as in total adverse events (94.6 vs 89.1%, OR 2.07, 95% CI 1.11-3.86, $I^2$0%). When performing subgroup analysis in patients receiving only full-dose of both bDMARDs there was a significant increase in serious infections (6.7 vs 0.6%, OR 5.58, 95% CI 1.25-24.90, $I^2$0%) and the risk of SAEs remained significantly higher (17.1 vs 6.2%, OR 2.72, 95% CI 1.30-5.69, $I^2$0%).

Conclusion: Our findings suggest that combination therapy with two bDMARDs in RA patients appears to increase the risk of SAEs during the first twelve months of treatment.

REFERENCES

[1] -Lipsky PE, et al. Infliximab and methotrexate in the treatment of rheumatoid arthritis. Anti-Tumor Necrosis Factor Trial in Rheumatoid Arthritis with Concomitant Therapy Study Group. N Engl J Med. 2000 Nov 30;343 (22):1594–602.

[2] Weinblatt ME, et al. Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate: the ARMADA trial. Arthritis Rheum. 2003 Jan;48(1):35–45.

[3] Keystone ECet al. Once-weekly administration of 50 mg etanercept in patients with active rheumatoid arthritis: results of a multicenter, randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2004 Feb;50 (2):353–63.

[4] Weinblatt ME, et al. A trial of etanercept, a recombinant tumor necrosis factor receptor:Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate. N Engl J Med. 1999 Jan 28;340(4):253–9.

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AB0369 SAFETY, EFFICACY AND RETENTION RATE OF BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (BDMARDS) IN ASSOCIATION WITH DENOSUMAB: COMPARISON OF COMBINATION AND MONO-THERAPY REGIMENS

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Background: Osteoporosis is a frequent complication of rheumatic muscle-skeletal diseases (RMD), with high impact from steroid treatment. It is known that bDMARD impact positively on patients' prognosis and this is also known for Denosumab, a monoclonal antibody for osteoporosis. The combination treatment with two monoclonal antibodies, bDMARD & denosumab, has addressed the problem of safety and efficacy, with incomplete answers from the available literature.

Objectives: to evaluate the impact of the combination treatment bDMARD +Denosumab (COMBO group), compared to mono-therapy with bDMARD (MONO group), on clinical efficacy, safety and treatment retention of bDMARD in patients with RMD.

Methods: RMD patients treated with COMBO therapy where enrolled from a single centre rheumatology unit; for each case, at least one MONO therapy control (matched per age±5 years, sex, bDMARD, RMD, without osteoporosis) was enrolled. Data on clinical efficacy (3-points Likert scale for physician and patient – improved/stable/worse), safety (locl reaction, serious and non-serious adverse events) and bDMARD treatment retention at 12, 18 and 24 months.
Results: Out of 129 eligible patients, 77 were enrolled in the protocol: 49 in the MONO and 28 in the COMBO group. The two groups were different of age (slightly higher in the COMBO group), for tender joint count, erythrocyte sedimentation rate and c-reactive protein (higher in the MONO group). Efficacy analysis showed higher percentage of clinical improvement at 12 months in the MONO group at 12 months, being not significant at 18 and 24 months (possibly explained by a different disease activity at baseline visit, corresponding to the overlap of denosumab on top of bDMARD in the COMBO and to the initiation of bDMARD in the MONO group). Between the 2 groups, no difference about safety and retention rate was found.
Conclusion: the efficacy of COMBO treatment is similar to MONO therapy. Moreover, the data show that also safety and retention rate are similar. Therefore, the COMBO treatment with 2 different monoclonals can be safely employed in the treatment of RMDs and osteoporosis.
Disclosure of Interests: Cosimo Bruni: None declared, Cosimo Cigolini: None declared, Giulia Tesei: None declared, Francesca Bartoli: None declared, Ginevra Fiori: None declared, Maria Letizia Conforti: None declared, Silvia Bellando Randone: None declared, Serena Guiducci: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS; MSD, Janssen
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AB0370 EFFICACY AND SAFETY OF BIOLOGIC TREATMENT IN ELDERLY RHEUMATOID ARTHRITISPATIENTS: A WIDE COHORT STUDY

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Background: Given the data on efficacy and safety of biologic treatment in rheumatoid arthritis (RA), more and more patients older than 65 years are starting these drugs.
Objectives: This study aims to evaluate safety and efficacy of biologics in elderly patients.
Methods: four-hundred and thirteen patients with RA were enrolled and divided in two group, i.e. older or younger than 65 years old. Data on disease characteristics, treatment and adverse reactions were collected. In addition, comorbidities were evaluated by the Rheumatic Disease Comorbidity index (RDCI).
Results: Seventy-seven patients were male and 87 were older than 65 years. The elderly patients had a higher RDCI as compared to those younger than 65 years (1.0 ± 3.0 vs. 0.0 ± 10 respectively, p<0.001). Mean DAS28 at the beginning of biologic treatment was 4.46 ± 1.16. Most of patients started etanercept (41.4%) or adalimumab (26.9%) and 37.1% were on monotherapy. None of these variables were statistically different between age groups. The figure shows the differences in retention rate of first biologic at 60 months in the two groups that was found to be significantly higher in older than younger patients (43.3 vs. 48.5, p=0.023). This result was confirmed also after correcting for comorbidities as defined by RDCI (p=0.014). On the contrary, no differences were found in retention rate on any biologic (i.e. not only first line) between age groups (p=0.509). The main reason for biologic treatment discontinuation was inefficacy in both groups (74.7% in <65 years old and 58.6% in ≥65years old, p=0.161). The most common side effects in elderly patients were hematological complications (30.4%) while in younger patients muco-cutaneous (32.4%) adverse reactions. Infections were a reason for discontinuation in 17.4% in old patients and 20.6% in younger ones (p=1.000).
Conclusion: RA patients aged over 65 years have been found to have even a better retention rate at first biologic than youngers one, probably because of less strict targets in disease control and a more frequent follow up. In addition, safety has been found to be as good as in younger patients. Comorbidities do not seem to affect retention rate.

Figure. Retention rate in patients <65 years old (blue line) vs patients ≥65years old (green line) (p=0.023).

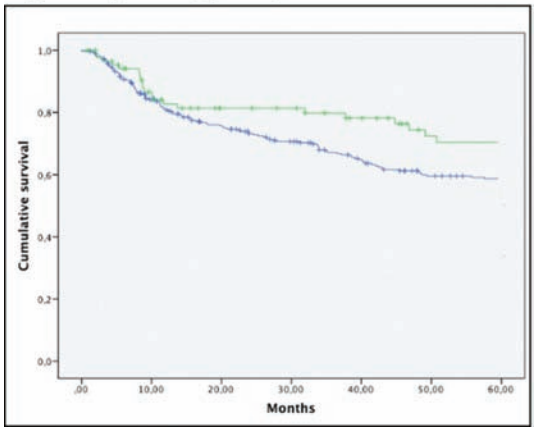


Figure 1

Disclosure of Interests: Cristian Caimmi: None declared, Federica Martinis: None declared, Ilaria Montanari: None declared, Alice Dellaidotti: None declared, Elena Fracassi Speakers bureau: Novartis, Ombretta Viapiana Speakers bureau: Novartis, Abbvie, Eli-Lilly, Sanofi Genzyme, Domenico Biasi: None declared, Maurizio Rossini: None declared, Antonio Carletto Speakers bureau: Roche, Novartis, MSD, Abbvie, Bristol, Jannsen, Celgene, Pfizer
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AB0371 LONG TERM RITUXIMAB PERSISTENCE FOR RHEUMATOID ARTHRITIS IN THE REAL WORLD: THE RITAR STUDY

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Background: Rituximab (RTX) is a B-lymphocyte depleting monoclonal antibody that was approved for rheumatoid arthritis (RA) treatment in Europe in 2006.
Objectives: To analyse factors affecting long term persistence of RTX for the treatment of RA patients in daily clinical practice.
Methods: RITAR (RITuximab en Artritis Reumatoide) is a retrospective, open-label, observational study that describes the patterns of use and long term persistence of RTX in a tertiary university hospital from 2003 to 2015. We collected demographic, clinical and therapeutic variables. Patients who discontinued RTX were considered events whereas patients lost for follow-up and non-RTX-related deaths were censored. Statistical analysis was performed with STATA 12. Kaplan-Meier survival analysis, Log-rank test and Cox Regression were used. A multivariable Cox-proportional hazards model was fitted to determine which variables were most likely related to RTX persistence.
Results: 114 patients were included: 80.7% women, median age 60 years (IQR 51-69) and median RA duration 11 years (IQR 6-16). Most patients were FR/ACPA positive (93.0%). Retreatment schedule was 94.6% on demand and 5.4% fixed-retreatment every 6 months. In the 1st cycle RTX monotherapy used in 12.2% and gradually increased over time. The mean RTX dose by cycle was 1,733 mg (DE: 294): 324 x 2000 mg and 130 x 1000 mg. RTX was used as 1st biologic in 19.3%. Median response duration was 10 months (IQR 7-13).
We observed 38 events, 22 patients were censored and 54 remained on RTX treatment at the end of the study. Follow-up time in analysis was 484.84 years. Median survival was 9.98 years, withdrawal rate was 7.67/100 patients-year. Reasons for discontinuation were 21.0% ineffectiveness, 8.7% adverse events and 3.5% deaths probably related with RTX.

Table 1. Univariate Cox regression analysis

Variable	N (%)	HR	IC 95%	P>[z]
Sex, ref. men	22 (19%)	1.06	0.47-	0.883
- Women	92 (81%)		2.42	
Age at RTX start, ref. <45 years	14 (12%)	0.58	0.24-	0.221
- 45-65 years	61 (54%)	0.53	1.38	0.193
- > 65 years	39 (34%)		0.21-	
			1.38	
RF/ACPA, ref. negative	8 (7%)	**0.32**	0.12-	**0.018**
- positive	106		0.82	
	(93%)			
DAS28, ref. baseline < 5,1	35 (39%)	0.86	0.43-	0.659
- baseline ≥5,1	55 (61%)		1.71	
RTX 1st cycle, ref. csDMARD	95 (83%)	**2.42**	1.16-	**0.017**
- monotherapy	19 (17%)		5.02	
RTX monotherapy%, ref. ≤50%	95 (83%)	2.00	0.94-	0.071
- >50% monotherapy	19 (17%)		4.27	
RTX biologic line, ref. 1st line	22 (19%)	1.80	0.70-	0.220
- ≥2nd line	92 (81%)		4.62	
RTX dose, ref. ≤ 1,500 mg/cycle	31 (27%)	1.26	0.58-	0.556
- ≥1,500 mg/cycle	83 (73%)		2.77	
Retreatment schedule, ref. on	99 (87%)	1.28	0.58-	0.531
demand	15 (13%)		2.81	
- fixed-retreatment/6 months				

Table 2. Multivariate Cox-Regression analysis

Variable	HR	IC 95%	P>[z]
RF/ACPA, ref. negative	0.25	0.09-	**0.005**
		0.66	
RTX monotherapy%, ref.	3.10	1.37-	**0.007**
≤50%		7.02	

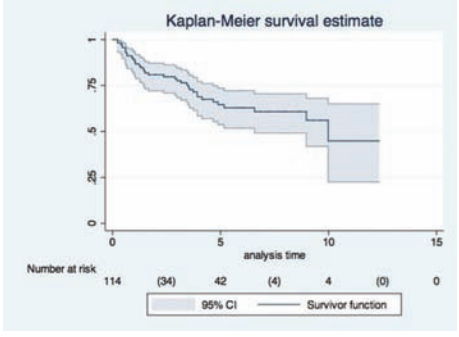


Figure 1. Persistence of RTX in daily clinical practice

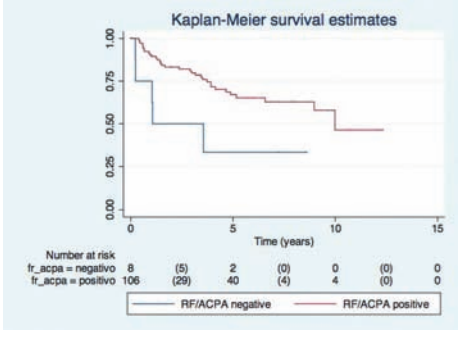


Figure 2. Persistence by RF or ACPA status

Log-Rank test: p=0.013

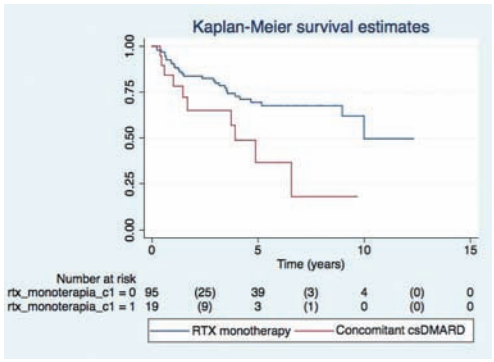


Figure 3. Persistence by monotherapy status in 1st cycle.

Log-Rank test: p=0.014
Log-Rank test: p=0,066

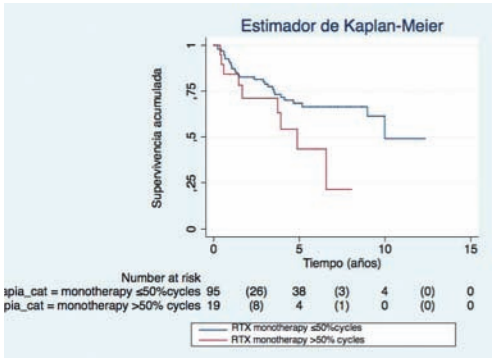


Figure 4

Conclusion: In our hospital RTX treatment has a long median survival that is significantly higher in seropositive patients and in those treated in combination with csDMARDS. The RTX dose by cycle did not affect the persistence.

REFERENCE

[1] Cañamares-Orbis I, Merino L, Lopez J, Llorente I, Garcia-Vadillo A, Ramirez E, et al. Experience With the Use of Rituximab for the Treatment of Rheumatoid Arthritis in a Tertiary Hospital in Spain: RITAR Study. J Clin Rheumatol. 2018.

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AB0372 EXPLORING REFRACTORY DISEASE & PERSISTENT SYMPTOMS IN RA/POLYJIA DESPITE BDMARDS: PATIENT & PROFESSIONAL EXPERIENCES

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Background: Refractory disease is defined as not achieving a low disease activity target despite DMARDs. This definition does not account for patients with well controlled inflammation who experience persistent symptoms, or who have a high perceived disease impact. Furthermore, variations in professionals understanding of refractory disease and related concepts exists, with potential discordance when compared to patients understanding.

Objectives: To qualitatively explore patients and professionals understanding and experiences of refractory disease and persistent symptoms.

Methods: Semi-structured interviews were conducted with 13 RA and 3 Polyarticular JIA patients (on bDMARD not responding with DAS28>3.2) attending four UK Rheumatology clinics. Thirty-two healthcare professionals (working in Rheumatology >1year) were interviewed across 11 UK hospitals. Inductive thematic analysis was conducted, with descriptive statistics reported for quantitative data.

Results: Patients had not responded to on average 3 csDMARDs and 3.5 bDMARDs, with mean MSK-HQ=24.6, mean DAS28=4.60, and mean Patient Global=55.4. Healthcare professionals interviewed were predominantly adult trained (25/32), with mean 11.7 years' experience, comprising rheumatologists, nurses, physiotherapists, occupational therapists, psychologists, pharmacist, podiatrist, and social worker.

Key themes for both patients and professionals' experiences of refractory disease and persistent symptoms explored were: 1) Frustrations with the disease, non-response to medication and side effects, 2) Importance of areas not captured by the DAS28, 3) Patient-centred targets/care, 4) Role of other specialties, 5) Role of comorbidities, infections and/or joint damage, and 6) Patient acceptance, adjustment and resilience. Although patients expressed hopeful expectations despite poor experiences, this was in discordance to professionals' accounts of loss of trust/hope, disengagement and limited treatment options, with hope mainly for stratified medicines.

Patient specific emergent themes identified: 1) Disease not controlled fully but manageable, 2) Drugs do not work: at all versus over time, 3) Persistent pain, fatigue and restricted mobility are most problematic symptoms, 4) Life-limiting impact: practically, psychologically/emotionally and socially, and 5) Good support from rheumatology team but holistic approach needed.

Professionals grouped refractory disease into four key areas: 1) Refractory Inflammation vs Refractory Symptomology, 2) Biological processes, 3) Drug inefficacy/tolerability, and 4) Patient health beliefs/behaviours.

Those with JIA had a greater variety in their experiences compared to those with RA. In addition to above themes they all highlighted the challenges of having a long-term illness so young, e.g. not knowing a life without pain or disease and lack of understanding in both themselves and others. Paediatric/Adolescent professionals noted differences in treating JIA compared to RA, e.g. joints affected and treatment guidelines/availability not based on DAS equivalent scores.

Conclusion: These results highlight the potential need for a broader definition for refractory disease, and the need for holistic approaches to treatment that better support both patients, and professionals, in managing their condition.

Disclosure of Interests: Hema Chaplin: None declared, Ibone Verhey: None declared, Nora Ng: None declared, James Galloway Consultant for: Pfizer Inc, Ian Scott: None declared, Debajit Sen: None declared, Rachel Tattersall: None declared, Heidi Lempp: None declared, Sam Norton: None declared

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AB0373 A COMPARATIVE EFFECTIVENESS STUDY OF ABATACEPT AND TNFI AGENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS USING REAL-WORLD DATA

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Background: Introduction of multiple biologic DMARDs, targeted synthetic DMARDs and biosimilars has led to a paradigm shift in the management of patients (pts) with RA. There are, however, limited head-to-head studies comparing these agents to guide evidence-based treatment decisions. Abatacept versus adaliMumab comParison in bioLogic-naivE RA subjects with background MTX (AMPLE) was the first head-to-head randomised controlled trial to evaluate the efficacy of abatacept (ABA) and adalimumab. However, there are limited data replicating AMPLE findings in real-world settings.

Objectives: To compare effectiveness of ABA versus TNF inhibitors (TNFis) in pts with RA by line of therapy (LOT) and by LOT stratified by anti-citrullinated protein antibody (ACPA) status using data from real-world clinical practice.

Methods: Data from two independent RA registries comprising pts treated by physicians in routine care were used for the analysis. An RA disease-specific registry provided data on pts treated with TNFis; the other was a product-specific RA registry and provided data on pts treated with ABA.[1,2] The disease-specific registry was a US-based single-centre registry; the product-specific registry was a multi-centre, 12-country registry excluding the US. Frequency matching on age (in years [yrs]; ±4 yrs' window), RA disease duration (in yrs; ±4 yrs) and baseline CDAI category (remission [≤2.8], low activity [≤10], medium activity [≤22], high activity [>22]) between TNFi and ABA pts was done for biologic-naïve and -experienced pts. Descriptive statistics were used to summarise baseline demographics, disease activity measures and serostatus for both treatment groups by LOT. Disease activity in the follow-up period was measured at the 12-month mark (±6 months). Change in disease activity after 12 months was evaluated for TNFi and ABA pts by LOT, and statistical comparison using Kruskal–Wallis test was performed. The analysis was repeated for pts stratified by ACPA status.

Table 1.

Table 1. Baseline characteristics by LOT and ACPA status

	ACPA+				ACPA–			
	First-line		Subsequent-line		First-line		Subsequent-line	
	ABA (n=68)	TNFis (n=68)	ABA (n=60)	TNFis (n=60)	ABA (n=31)	TNFis (n=31)	ABA (n=21)	TNFis (n=21)
Age, years	54.9 (12.9)	57.0 (13.3)	55.7 (10.3)	58.2 (10.4)	54.3 (8.5)	56.4 (9.5)	52.0 (12.4)	54.8 (12.3)
RA duration, years	9.9 (9.3)	11.0 (9.4)	17.0 (10.7)	17.9 (10.1)	4.1 (4.6)	4.4 (4.2)	9.2 (9.6)	10.3 (8.9)
Female, n (%)	52 (76.5)	55 (80.9)	45 (75.0)	54 (90.0)*	21 (67.7)	26 (83.9)	18 (85.7)	19 (90.5)
CDAI score	24.6 (10.9)	26.9 (14.8)	25.9 (14.9)	25.7 (15.3)	25.6 (10.6)	30.6 (15.8)	28.5 (17.1)	26.8 (15.7)

Mean (SD) reported, unless otherwise stated
*p<0.05 for ABA vs TNFi
ABA=abatacept; ACPA=anti-citrullinated protein antibody; LOT=line of therapy; TNFi=TNF inhibitor

Table 2.

Table 2. Change in disease activity (CDAI) by LOT and by LOT and ACPA status

		Baseline CDAI score	Follow-up CDAI score	CDAI reduction from baseline, %	Absolute CDAI reduction from baseline
Biologic naïve	TNFis (n=105)	28.4 (16.1)	13.3 (13.8)	53.3	15.1 (15.7)
	ABA (n=105)	24.2 (10.1)	9.5 (6.6)	61.0	14.8 (10.8)
Biologic experienced	TNFis (n=91)	24.6 (15.9)	19.4 (16.9)	21.2	5.2 (15.5)
	ABA (n=91)	23.8 (14.5)	13.6 (10.1)*	43.0	10.2 (13.4)*
ACPA+ biologic naïve	TNFis (n=68)	26.9 (14.8)	12.6 (11.8)	53.2	14.3 (15.7)
	ABA (n=68)	24.6 (10.9)	8.2 (6.0)	66.6	16.4 (10.8)
ACPA+ biologic experienced	TNFis (n=60)	25.7 (15.3)	19.6 (16.6)	24.0	6.2 (13.7)
	ABA (n=60)	25.9 (14.9)	12.6 (8.5)*	51.2	13.3 (14.3)*

Mean (SD) reported, unless otherwise specified
*p<0.05 for ABA vs TNFi
ACPA=anti-citrullinated protein antibody; LOT=line of therapy; TNFi=TNF inhibitor

Results: Data for 105 first-line and 91 second- or further-line (subsequent-line) matched pairs of TNFi and ABA pts were included in the analysis (68 first-line and 60 subsequent-line matched pairs of TNFi and ABA pts, respectively, in ACPA+ cohort; 31 first-line and 21 subsequent-

line matched pairs of TNFi and ABA pts, respectively, in ACPA– cohort; Table 1). In the biologic-experienced pts, ABA (vs TNFi) had a higher reduction in CDAI score (10.2 vs 5.2, p=0.035; Table 2). In the biologic-experienced ACPA+ pts, ABA (vs TNFi) had higher reduction in disease activity (CDAI: 13.3 vs 6.2, p=0.023; Table 2; SDAI: 13.9 vs 7.0, p=0.046). No difference in disease activity was observed between the two groups among the ACPA– pts.

Conclusion: Real-world RA registry data further confirm findings from the AMPLE study that the overall efficacy of ABA is similar to TNFi agents in biologic-naïve pts with RA. Efficacy of ABA (vs TNFis) in biologic-experienced pts is greater, and greater reductions in joint disease activity in ACPA+ ABA (vs TNFis) pts were observed.

REFERENCES

[1] Brigham and Women's Hospital. BRASS. https://www.brassstudy.org/. Accessed September 12, 2018.
[2] Alten R, et al. *RMD Open* 2017;3:e000538.

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AB0374 ADALIMUMAB DISCONTINUATION IN PATIENTSWITH RHEUMATOID ARTHRITIS AFTER ACHIEVING SUSTAINED REMISSION

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Background: the most important factor in the progress of pharmacotherapy of RA was the widespread implementation of therapy with biological disease-modifying antirheumatic drugs (bDMARD). Recently, the issues of optimizing the management of patients have attracted more and more attention. First of all, we are talking about the possibility of reducing the dose and the abolition of bDMARD with the maintenance of remission ("biological-free remission").

Objectives: to assess whether adalimumab (AD) can be gradually discontinued during continuous methotrexate (MTX) use in patients with early rheumatoid arthritis (ERA).

Methods: Within the REMARCA (the Russian study of methotrexate and biological agents in early active arthritis) study, the investigators examined 20 patients (17 women and 3 men; median age, 51 [41.5; 56] years) with ERA (disease duration, 10 [5.5; 20] months; DAS28, 5.17 [4.37; 6.51]; 85% of the patients were seropositive for rheumatoid factor and 85% for anti-cyclic citrullinated peptide antibodies.

All the patients received subcutaneous MTX 25 mg/week. Twelve weeks after beginning therapy with MTX, due to its inefficiency, ADA was added according to the standard scheme. Clinical and laboratory data was analyzed just before the therapy (point-3 months), then at the term of 6 (n=20), 12 (n=17), 24(n=17) and 36 (n=17) months. To assess the effectiveness of therapy, indices of activity DAS28, CDAI and SDAI were used. The everyday life functioning of the patient was assessed quantitatively using the Russian version of the HAQ questionnaire.

Results: At week 24, with the combined therapy of methotrexate and adalimumab, about 75% of patients have reached remission/low disease activity: the median DAS28 was 3.0 [1.65; 3.73]; 85% of the patients achieved remission or low disease activity. After 3 months of ADA therapy, high or moderate disease activity remained in 3 (15%) patients; median DAS28 was 4.4 [4.3; 6.1]; the drug was discontinued in them due to ineffective therapy. After 12-month follow-up, low DAS28 scores were observed in 5 (29.4%), DAS28 remission was in 12 (70.6%) of the 17 patients who continued ADA treatment; after 24 months, all the 17 patients were noted to have remission. After achieving sustained remission (≥ 6-month duration during ADA therapy), there was a carefully controlled reduction (titration) in the dose of ADA with its complete discontinuation, by maintaining remission at 36-month follow-up; the median DAS28 was 1.6 [1.4; 2.2].

The disease duration up to 1 year and functional class reduction to I in the first year of observation (or=46,2; 95% CI 1,870-1141,178; P=0.019 and or=44,2; 95% CI 1,795-1088,143; P=0.02) were identified as predictors of maintaining long-term remission after the discontinuation of ADA. RF positivity and the presence of erosion initially determined the impossibility of ADA withdrawal. (fig.1)

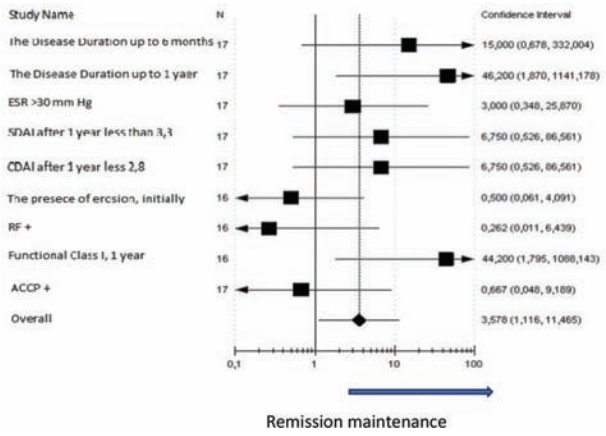


Figure 1. Influence of different factors on the possibility of withdrawal of ADA in patients with RA in remission.

Remission maintenance

Conclusion: In most patients with early rheumatoid arthritis, early induction of remission can be maintained after stopping the biologic therapy, under condition that the therapy was carried out by a combination of bDMARD and methotrexate. The maintenance of remission after discontinuation of ADA therapy was influenced by the duration of the disease and the depth of remission.

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AB0375 HYPOGAMMAGLOBULINEMIA AFTER RITUXIMAB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS IS NOT RARE AND IS ASSOCIATED WITH BETTER RESPONSE

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Background: Rituximab (RTX) is used as a second line treatment in rheumatoid arthritis (RA), with well-established efficacy. One of the most common adverse events of RTX use is hypogammaglobulinemia (HGG).

Objectives: To define, in RA patients treated with Rituximab, the frequency of HGG (IgG<700mg/dL or IgM<40mg/dL or IgA<70mg/dL) and to identify associations between its occurrence and clinical, epidemiological and other disease related features at baseline, RA outcomes and adverse events.

Methods: The patients received RTX for RA in two rheumatology centers from 1/2007 to 12/2018 were included. Demographical, clinical and laboratory parameters were recorded at baseline and at the last visit of the follow-up. Time of follow-up was defined as the time interval between the first RTX infusion and the last visit. Patients with monoclonal gammopathy and patients that received only one cycle of treatment were excluded. Severe infections were recorded defined as those which required hospitalization or antibiotics intravenously. Binomial regression analysis using stepwise backwards model having as dependent variables the "low IgG" or "low IgM" and independent variables: gender, age,

follow-up duration, RF levels, number of cycles received, DAS28(CRP) at baseline and IgG or IgM levels at baseline. SPSS software 21.0 and GraphPad Prism 5.00 were used for statistical analyses.

Results: 76 patients were included followed up for a median (range) of 48 (6-135) months. 65 were female (84.4%) with a mean±SD age of 63.5±11.8 and baseline DAS28(CRP) of 5.98±1.25. 67.8% and 65.2% of patients were RF positive, respectively (Table). At baseline, none of them had low IgG or IgA levels while 4 patients had IgM levels below 40mg/ml. The patients received median (range) 8 (2-20) cycles of RTX. In total, 43.4%, 25%, 28.9% and 5.3% developed HGG, low IgG, IgM and IgA, respectively. In 15.8% of the patients, at least 2 immunoglobulins subclasses were low. Levels of IgG and IgM, at the last visit, were negatively correlated with the number of RTX cycles received (IgG: p=0.02, r=-0.27; IgM: p=0.03, r=-0.25). At baseline, no differences were recorded between patients that developed HGG and those who did not (Table). Patients who developed low IgG or IgM had lower baseline levels of IgG or IgM levels, respectively (Table). Multivariable analyses revealed number of cycles received (p=0.03) and baseline IgM levels (p=0.03) as predictors of "low IgM" occurrence, while no variable was identified for "low IgG". At the end of follow up, the patients who developed HGG or low IgM compared to those who did not, exhibited lower DAS28 (Table). Concurrent treatment, during follow up or at the time of the last visit did not differ between the various groups, except from co-administration of methotrexate, which was more frequent at the time of last visit in patients who did not develop HGG (43.5% Vs 30.3%, p=0.04). No difference was observed in infections rate, among all analyses performed.

Table 1.

Characteristic	Not developed Hypogammaglobulinemia	Developed Hypogammaglobulinemia	p-value
Baseline characteristics			
Disease duration (months), mean ± SD	44.6 ± 25.1	55.9 ± 30.7	0.125
Number of cycles, median (range)	8 (2-20)	8 (2-13)	0.157
Age (years), mean±SD	61.5 ± 12.2	66.2 ± 11.0	0.085
Female gender, n (%)	37/43 (86.1)	28/33 (84.9)	1.000
Smoking, n (%)	7/13 (53.8)	3/10 (30.0)	0.402
RF positive, n (%)	20/31 (65.5)	18/24 (75.0)	0.558
DAS28 (baseline), mean±SD	5.46 ± 1.07	4.99 ± 0.91	0.092
Outcomes			
DAS28 (end of follow-up), mean±SD	4.16 ± 1.36	3.12 ± 1.32	0.003
Infections rate (95% CI)	4.81 (2.19 – 9.13)	1.62 (0.33 – 4.75)	0.09
	Normal IgG	**Low IgG**	
Baseline characteristics			
Disease duration (months), mean ± SD	46.0 ± 25.1	60.2 ± 35.4	0.232
Number of cycles, median (range)	8 (2-13)	9 (2-20)	0.157
Age (years), mean±SD	62.2 ± 12.4	67.7 ± 9.0	0.169
Female gender, n (%)	47/57 (82.5)	18/19 (94.7)	0.273
Smoking, n (%)	9/17 (52.9)	1/6 (16.7)	0.179
RF positive, n (%)	28/41 (68.5)	10/14 (71.4)	1.000
IgG levels (mg/dl) (baseline), mean±SD	1098 ± 291.0	1213 ± 280.0	0.09
DAS28 (baseline), mean±SD	5.32 ± 1.07	5.12 ± 0.88	0.654
Outcomes			
DAS28 (end of follow-up), mean±SD	3.87 ± 1.42	3.27 ± 1.39	0.146
Infections rate (95% CI)	3.88 (1.86 – 7.14)	1.75 (0.20 – 6.31)	0.312
	Normal IgM	**Low IgM**	
Baseline characteristics			
Disease duration (months), mean ± SD	48.1 ± 28.2	53.1 ± 24.6	0.314
Number of cycles, median (range)	8 (2-20)	8.5 (2-17)	0.303
Age (years), mean±SD	61.8 ± 12.1	67.8 ± 10.1	0.06
Female gender, n (%)	47/53 (88.7)	18/23 (78.3)	0.291
Smoking, n (%)	7/17 (41.2)	3/6 (50.0)	1.000
RF positive, n (%)	26/39 (66.7)	12/16 (75.0)	0750
IgM levels (mg/dl) (baseline), mean±SD	76.7 ± 31.0	143.1 ± 79.0	0.001
DAS28 (baseline), mean±SD	5.41 ± 1.01	4.86 ± 1.01	0.094
Outcomes			
DAS28 (end of follow-up), mean±SD	4.03 ± 1.38	2.92 ± 1.26	0.003
Infections rate (95% CI)	3.53 (1.61 – 6.70)	2.57 (0.52 - 7.51)	0.671

Table: comparison of patients who developed hypogammaglobulinemia with those who did not. Further analysis was performed stratifying patients according to the immunoglobulin subclass. SD: standard deviation, n: number, RF: rheumatoid factor, DAS: disease activity score, RTX: rituximab, CI: confidence interval.

Conclusion: HGG following RTX can be developed in about 40% of RA patients even after several treatment cycles. It is related to baseline immunoglobulin levels and possibly combined with better disease outcomes. The latter is observed primarily with IgM. No increased risk of major infections was identified.

Disclosure of Interests: None declared

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AB0376 RESULTS OF A MANDATORY SWITCHING FROM ORIGINATOR TO BIOSIMILAR ETANERCEPT IN 117 PATIENTS WITH INFLAMMATORY ARTHRITIS FROM A SINGLE CENTER

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Background: Currently available evidence indicates that a single switch from a bio-originator to one of its biosimilars is safe and effective and has cost benefits to the National Health Systems. However, there is some reluctance to switch patients due to lack of real-world data and differences between patients treated in the setting of real clinical practice and those of clinical trials

Objectives: We aimed to investigate the efficacy and safety of Etanercept-biosimilar (SB4), in a non-medical switch in patients with inflammatory arthritis (IA)

Methods: At Cabueñes Hospital a non-medical switch from Etanercept (ETN) to SB4 was carried out in March 2018. Inflammatory arthritis patients (rheumatoid arthritis (AR), psoriatic arthritis (APS), axial spondyloarthritis (AS), juvenile idiopathic arthritis (JIA)) were included in this single-center retrospective observational study from March 2018 to December 2018. Reasons for SB4 withdrawal were categorized as lack of effect (LOE), adverse events (AE) or others.

Results: A total of 117 patients were identified, 100% were switched to SB4 maintaining the same dose. Disease duration was 5 (2–8,5) years. 49 patients (41%) had basal optimized dose of ETN (dose down-titration or dose interval expansion). In most patients ETN was the first biologic.

31 patients (26%) stopped SB4 treatment during follow-up, mainly due to LOE (67%) or AE (25%), with median duration of SB4 3,5 months (1,9-5,9). Most AE that led to withdrawal were dermatological (injection-site reactions, skin rash). 11 patients switched back to ETN, 15 to others. Two patients died, both were APS (one sudden death and one aneurysmal subarachnoid hemorrhage). After switching to SB4, one stable patient with AS had recurrent acute anterior uveitis, and psoriasis worsening were noted in 2 patients with APS. 2 patients needed reinstatement of the full dose of biologic because of LOE. The clinical situation on ETN was stable in 23 of the 31 (74%) patients who stopped SB4 (no flares or changes in treatment in the last 6 months before switch).

Table 1 summarizes baseline characteristics and treatment outcomes.

Conclusion: Biosimilar switch of SB4 was successful in over 74% of cases and was well tolerated.

Most patients who stopped SB4 due to LOE had a clinical stable situation in this observational study. Some concerns regarding the safety profile and interchangeability have raised and further evidence on the efficacy of transitioning from reference ETN is needed.

REFERENCES

[1] Kay J, Schoels MM, Dörner T, et al. Ann Rheum Dis 2018;77:165-174
[2] Emery P, Vencovsky J, Sylwestrzak A, et al. Ann Rheum Dis 2017;76:51–57
[3] Glintborg B, et al. Ann Rheum Dis 2019 Feb;78(2):192-200

Table 1:

	RA (n=47)	APS (n=29)	AS (n=30)	JIA (n=8)
Age (years)	62 (53-71)	51 (46-60)	49 (42-60)	42 (30-51)
Female, n (%)	33 (70,2%)	11 (37,9%)	4 (13,3%)	2 (25%)
Monotherapy, n (%)	17 (36%)	16 (55%)	30 (100%)	6 (75%)
Dose optimization, n (%)	18 (38,6%)	13 (44,8%)	12 (40%)	5 (62,5%)
Duration of ETN (years, median IQR)	4 (1,8-6)	4,2 (2-6)	5,9 (2-10,6)	6 (4,1-8,2)
Other biologic drug prior to ETN, n (%)	6 (12,7%)	7 (24,1%)	6 (20%)	1 (12,5%)
9-month treatment outcomes				
Withdrawal during follow-up, n (%)	15 (31,9%)	8 (27.5%)	6 (20%)	1 (12,5%)
Duration of SB4 (months, median IQR)	3,8 (1,9-5,1)	4,3 (2-6,1)	2,3 (1,4-5,6)	5,9

Disclosure of Interests: None declared

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AB0377 CLINICAL SIMILARITY OF ABP 710 WITH INFLIXIMAB (REFERENCE PRODUCT) IN SUBJECTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

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Background: ABP 710 is being developed as a biosimilar to infliximab. Both ABP 710 and infliximab reference product (RP) inhibit tumor necrosis factor-alpha and have been shown to be structurally and functionally similar in analytical assessments. In a phase 1 clinical pharmacokinetic (PK) study both were shown to be bioequivalent for PK

parameters. The final step in the demonstration of biosimilarity is a comparative phase 3 clinical trial in a representative indication

Objectives: The objective of this study was to evaluate the similarity of ABP 710 compared to RP with respect to efficacy and safety.

Methods: In this multicenter, randomized, double-blind study, the efficacy and safety of ABP 710 was compared with the RP in subjects with moderate to severe rheumatoid arthritis. Subjects were maintained on a stable 7.5 to 25 mg/week dose of methotrexate and received 3 mg/kg infusions of the investigational products (IPs) at predetermined intervals. The primary endpoint of the study was risk difference (RD) of ACR20 at week 22; secondary endpoints included DAS28-CRP and safety at week 22. The confidence intervals (CI) for RD of ACR20 were estimated using the intention-to-treat analysis set with non-responder imputation based on the subject's randomized treatment. Clinical equivalence was evaluated by comparing the 2-sided 90% CI with the equivalence margin of (-15%, 15%) of the RD of ACR20. For change of DAS28-CRP at week 22 from baseline, the CI of the mean difference was estimated using an analysis of covariance model with relevant baseline values and stratification factors as covariates.

Results: Of the 558 randomized subjects, 556 were treated (ABP 710 n=278; RP n=278). For ACR20, the RD was 9.3% and the lower bound of the 90% CI (2.67%, 15.96%) was within the pre-specified criteria, thus confirming non-inferiority; the upper bound slightly exceeded the pre-specified criteria such that superiority cannot be ruled out statistically. In post-hoc analysis when the impact of random imbalance in baseline demographic and disease characteristic between the 2 treatment arms was adjusted, the RD was reduced to 7.18% and the 90% CI was narrowed to (0.75%, 13.62%). Results of change of DAS28-CRP at week 22 showed a difference in mean change from baseline of -0.01 with 90% CI of (-0.20, 0.17). Since this difference is less than the suggested EULAR threshold of 0.6 for clinically meaningful difference, the result supports both non-inferiority and non-superiority. Through week 22, percentage of subjects reporting any serious adverse events was 4.1 (ABP 710=3.2; RP=5.0) and the binding/neutralizing antibody positive post-baseline in subjects were 58.9/19.4 (ABP 710=57.1/18.0; RP=60.6/20.8).

Conclusion: The results of this study indicate that ABP 710 is similar to the RP. Although we were unable to statistically confirm non-superiority, post-hoc analysis is supportive of non-superiority. The DAS28-CRP difference of less than 0.6 is believed to not be clinically meaningful. These efficacy and safety results support similarity between ABP 710 and infliximab RP.

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AB0378 AN UPDATE AND SYSTEMATIC REVIEW ON USING BIOLOGICALS DURING PREGNANCY IN INFLAMMATORY AUTOIMMUNE DISEASES

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Background: The effects of biologicals on reproduction are unknown. Therefore pregnancy during biologicals use is discouraged. However biologicals are frequently prescribed in patients of childbearing potential and many patients become pregnant while using these drugs.

Objectives: In 2015 EULAR published a broad review article on this matter. Our aim was to update the data based on newly published articles.

Methods: A search was conducted at 18/10/2017 and then 21/11/2018 in Embase, Medline Ovid, Web Of Science, Cochrane CENTRAL and Google Scholar with specific search terms for each database. Articles were excluded based on title/abstract (double blind, two researchers, NG and HJMJC) and then full text (one researcher, NG). A chart was made based on outcomes of interest(see Table1). The references of included articles were reviewed to include and minimize the missing articles.

Results: Totally 137 articles were included (79 articles at first round, 51 articles at second round and 7 found after screening the references of the included articles). A descriptive analysis was performed to sum up the data on each separate biological and all the biologicals together. The results are shown in Table1. It should be notified that due to heterogeneity of the data the calculated percentages are up to individual interpretations and cannot be compared to each other.

Conclusion: From 2015 onwards, there have been many articles published regarding use of biologicals during pregnancy. Despite limitations of our study, such as heterogeneity in being prospective or retrospective and quality of the included articles, no alarm is raised concerning safety issues.

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Table 1. Results of the final chart. The denominator is the sum up of total cases recruited from the articles, for each outcome the denominator is defined as the population for which the specific outcome was reported. The other cases, which haven't mentioned the outcome in their results, were excluded from the denominator for that specific outcome. Both spontaneous and elective abortion cases are excluded from the denominator of preterm birth and major congenital malformations.

Drug	Maternal exposed pregnancies	Abortion		Live birth	Preterm birth	Major congenital malformations	Serious infections in children	ADRs to vaccine
		Elective	Spontaneous					
Abatacept	153	13.1% (20/153)	26.1% (40/153)	60.8% (93/153)	-	6.8% (6/88)	-	0.0% (0/93)
Adalimumab	2518	0.1% (3/339)	0.4% (16/432)	95.5% (424/444)	3.2% (7/213)	3.7% (23/608)	7.9% (4/501)	0.5% (1/205*)
Anakinra	34	2.9% (1/34)	2.9% (1/34)	94.2% (32/34)	20.0% (2/10)	3.4% (1/29†)	0.0% (0/30)	-
Certolizumab pegol	767	4.7% (27/574)	8.2% (47/574)	86.9% (527/606)	10.7% (41/380)	1.9% (10/510)	4.0% (2/50)	0.0% (0/26)
Etanercept	801	7.6% (30/393)	17.4% (69/397)	87.4% (702/803)	11.5% (40/347)	6.2% (37/597)	0.0% (0/140)	0.4% (1/269)
Infliximab	2174	5.1% (90/1759)	9.6% (169/1759)	79.3% (1483/1869)	5.9% (111/1892)	10.9% (22/2014)	13.7% (21/153)	18.2% (6/33)
Rituximab	27	0.0% (0/11)	12.5% (2/16)	87.5% (14/16)	18.2% (2/11)	0.0% (0/8)	0.0% (0/18)	-
Tocilizumab	368	14.6% (37/254)	20.9% (53/254)	64.2% (163/254)	18.1% (32/177)	4.9% (8/164)	0.0% (0/3)	-
Tofacitinib£	47	19.5% (8/41)	17.1% (7/41)	63.4% (26/41)	7.7% (2/26)	3.8% (1/26)	0.0% (0/26)	-
Ustekinumab	46	0.0% (0/28)	7.1% (2/28)	92.6% (25/27)	3.8% (1/26)	0.0% (0/21)	0.0% (0/10)	0.0% (0/3)
Vedolizumab	59	11.1% (6/54)	18.5% (10/54)	70.4% (38/54)	2.9% (1/34)	10.0% (2/20)	0.0% (0/28)	-

ADR= Adverse Drug Reaction * mild fever after rotavirus vaccination. † unilateral agenesis and ectopic neurohypophysis. £ Just one article had information in this regard.

AB0379 GENDER DIFFERENCES IN RHEUMATOID ARTHRITIS: EFFECT OF ANTI-TUMOR NECROSIS FACTOR THERAPY

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Background: Rheumatoid arthritis (RA) is more prevalent in women than men (F:M=4:1), due to hormonal, genetic and environment factors. Women present higher disease activity markers as Disease Activity Score-28 (DAS28) and Health Assessment Questionnaire (HAQ), at the onset and after c-DMARDs therapy, without correlation with radiographic damage.
Objectives: The purpose of this study was to assess gender differences in RA patients after anti- tumor necrosis factor (TNF) α treatment.
Methods: Ninety-six patients were enrolled at the beginning of anti-TNF α therapy (etanercept and adalimumab). All patients satisfied 1987 and 2010 ACR criteria for RA. They underwent to clinical and clinimetric evaluation at baseline (T0) and after three (T3) and six (T6) months of therapy with: tender and swollen joints, Visual Analogic Scale (VAS) pain, VAS patient and physician, DAS28, Clinical/Simplified clinical disease activity index (CDAI/SDAI) and HAQ. The evaluation of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Rheumatoid Factor (RF) and anti-citrullinated protein antibody (ACPA) was performed in all patients.
Results: Among these patients, 70 were women and 26 men; 81 patients (58 female, 23 male) started etanercept and 15 adalimumab (12 female, 3 male). They presented a mean age of 56.4 ± 14.5 years (women 55.2 ± 15.4, men 60 ± 11.2) and mean disease duration of 11 ± 6.8 years (woman 11.51 ± 6.3, men 9.6 ± 8.1). Both women and men had a DAS28 reduction after 3 and 6 months therapy ($p<0.05$) but DAS28 in women was higher than men at T0, T3 and T6 ($p<0.05$). Women presented higher number of tender joints in all evaluations, and more swollen joints than men at T0 and T6 ($p<0.05$). Women felt more active disease at T6 (VAS patient) ($p<0.05$). CDAI was higher in woman after 3 and 6 months ($p<0.05$). There were no differences about physician evaluation, inflammation markers, RF and ACPA titles.
Conclusion: In this study, both women and men had a good response to anti-TNF treatment but women presented worse clinical response. Female gender resulted the only variable associated with DAS28 reduction differences. We could hypothesize that beyond to biological factors, also social contest, daily life and work activity could explain a worse impact of disease on women.

Table 1.

Patients clinical characteristics (n=96)									
	T0			T3			T6		
	F (n=70)	M (n=26)	p	F (n=70)	M (n=26)	p	F (n=70)	M (n=26)	p
TJ (mean; CI)	12.16 (10.2-14.2)	8.44 (5.08-11.8)	0.0025	4.86 (3.65-6.06)	2.64 (0.68-4.6)	0.0046	4.75 (3.49-6.02)	2.16 (0.98-3.34)	0.0106
SJ (mean; CI)	5.32 (4.22-6.42)	3.56 (1.8-5.32)	0.0046	2.29 (1.59-2.82)	1.36 (0.45-2.27)	ns	2.12 (1.40-2.83)	0.6 (0.22-0.98)	0.032
CDAI (mean; CI)	27.73 (24.57-30.89)	23.63 (16.32-30.95)	ns	14.28 (12.02-16.54)	10.99 (5.11-16.87)	0.0098	12.95 (10.46-15.45)	6.78 (4.21-9.36)	0.0037
DAS28 (mean; CI)	5.25 (4.99-5.51)	4.38 (3.76-5.01)	0.0162	3.89 (3.62-4.16)	3.19 (2.6-3.77)	0.0176	3.74 (3.45-4.03)	3.00 (2.47-3.52)	0.0156
VAS pain (mean; CI)	5.55 (5.01-6.09)	5.23 (4.13-6.33)	ns	3.56 (2.85-4.28)	2.37 (1.60-3.13)	ns	3.47 (2.85-4.09)	2.84 (1.21-4.47)	ns
VAS patient (mean; CI)	5.61 (5.16-6.07)	5.22 (4.19-6.25)	ns	3.50 (2.98-4.02)	2.79 (1.74-3.84)	ns	3.32 (2.76-3.89)	1.98 (1.21-2.74)	0.017
VAS physician (mean; CI)	4.49 (3.96-5.02)	4.27 (3.29-5.26)	ns	2.78 (2.38-3.19)	2.1 (1.27-2.94)	ns	2.52 (2.05-2.99)	1.67 (1.01-2.32)	ns
ESR (mean; CI)	25,84 (21,51-30,17)	24,64 (17,41-31,87)	ns	15,99 (13,05-18,92)	16,48 (8,54-24,42)	ns	16,36 (13,25-19,48)	15,12 (8,98-21,26)	ns
CRP (mean; CI)	12,26 (7,45-17,07)	11,86 (5,55-18,16)	ns	6,36 (2,19-10,53)	9,75 (2,82-16,68)	ns	3,7074 (1,9065-5,5083)	6,1912 (2,3178-10,0646)	ns

CI (confidence interval); TJ (tender joints); SJ (swollen joints); CDAI (Clinical Disease Activity Index); DAS28 (Disease Activity Score 28); VAS (Visual Analogue Scale); ESR (erythrocyte sedimentation rate); CRP (C-reactive protein)

REFERENCES

[1] Neovius M, Ann Rheum Dis 2011;
[2] O.L. Quintero, et al., Journal of Autoimmunity 2012.
[3] M Ahlm en, Ann Rheum Dis 2010.
[4] Jawaheer, et al, The Journal of Rheumatology 2010.
[5] Jawaheer, et al, The Journal of Rheumatology 2012.
[6] Arnett FC, Arthritis Rheum 1988.
[7] Aletaha D, Arthritis Rheum 2010.

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AB0380 ISTHERE AN EFFECT OF TOCILIZUMAB IN SERUM AUTOANTIBODIES LEVELS IN RHEUMATOID ARTHRITIS?

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Background: Interleukin 6 (IL-6) plays a role on B cell differentiation and antibody production. However, few information is available considering the effect of tocilizumab (TCZ) on rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs) levels in Rheumatoid Arthritis.
Objectives: To compare serum levels of RF and ACPAs on RA patients at the beginning of therapy with TCZ and at 6 and 12 months under TCZ, assessing if its variations correlate with the several disease activity scores.
Methods: Longitudinal retrospective study of RA patients ever treated with TCZ at a Rheumatology Department. Serum levels of RF and ACPAs at 0, 6 and 12 months after starting anti-IL6 treatment were collected, as well as DAS28, DAS28 CRP, CDAI, SDAI, HAQ, ESR, CRP, patient's global assessment (PGA), physician's global assessment (PhGA), swollen joint count (SJC) and tender joint count (TJC). Demographic and clinical data were collected. SPSS statistics 22.0 was used for statistical analysis; p values under 0.05 were considered significant.
Results: 75 patients were included, 93.3% female (N=70), with a median (min-max) age of 58 (33-80) years and median disease duration at TCZ initiation of 10.7 years (1.0-43.3); 33.3% were on TCZ monotherapy (N=25). At baseline, forty-two (56.0%) were RF positive (>=30UI/ml) and 47 (62.7%) were ACPAs positive (>=10UI/ml). Median serum RF levels were 255.0 UI/mL (37.20-5560.00), 193.5 UI/mL (9.80-5270.00) and 131.0 UI/mL (9.40-6260.00) at 0, 6 and 12 months respectively; serum RF levels were only statistically different (p=0,006) between 0 and 6 months. Median serum ACPAs levels were 278.5 UI/mL (17.00-9300.00), 348.0 UI/mL (19.00-4720.00) and 277.0 UI/mL (16.00-4400.00) at 0, 6 and 12 months respectively, without any statistically significant differences. Considering the autoantibodies levels variation, ΔRF at 6 months correlated positively with ΔHAQ (r=0.482; p=0.009) and ΔCPR (r=0.413; p=0.026). After one year, ΔRF correlated positively with ESR (r=0.426; p=0.019) and DAS28 (r=0.428; p=0.018). As for ΔACPAs at 6 months, it correlated positively with PhGA (r=0.461; p=0.035). At 12 months, there was a positive correlation between ΔACPAs and ΔCDAI (r=0.385;p=0.036) and between ΔACPAs and ΔSJC (r=0.469;p=0.002).
Conclusion: In our RA sample, serum RF levels showed a significant titre difference past 6 months of treatment with TCZ. Moreover, a moderately strong correlation was found between ΔACPAs/ΔRF at 12 months months and the variations in several disease activity scores. Thus, this study reinforces the evidence of an impact of IL-6 inhibition on autoantibodies production in RA patients, as well as a relation between autoantibodies titre variation and clinical response. These findings need to be assessed in larger, prospective studies.

REFERENCES

[1] Modi S, Soejima M, and Levesque MC. The effect of targeted rheumatoid arthritis therapies on anti-citrullinated protein autoantibody levels and B cell responses. Clin Exp Immunol. 2013 Jul; 173(1): 8–17.
[2] Maneiro RJ, Salgado E, Carmona L, Gomez-Reino JJ. Rheumatoid factor as predictor of response to abatacept, rituximab and tocilizumab in rheumatoid arthritis: Systematic review and meta-analysis. Semin Arthritis Rheum. 2013 Aug;43(1):9-17.

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AB0381 CERTOLIZUMAB PEGOL IN AUTOIMMUNE DISEASES. REAL LIFE EXPERIENCE IN PREGNANCY

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Background: Certolizumab pegol (CZP) is a Pegylated, Fc free monoclonal antibody that is useful in different autoimmune conditions. It does not bind FcRn and is not expected to undergo transfer across the placenta and probably there is a minimal placenta transfer of CZP in humans. On the other hand, most chronic inflammatory diseases are prevalent in women and 50% of these diseases need active treatment. We describe our experience for more than 7 years in patients with inflammatory arthritis and pregnancy that received CZP.
Objectives: We describe our experience in patients with inflammatory artropathy that received CZP during their pregnancy.
Methods: We review our cohort of patients with Rheumatoid Arthritis, Spondyloarthritis and psoriatic arthritis from 2011 to 2017 that received CZP and analyzed those cases of pregnancy and described the clinical characteristic, the medication concomitant and the course of the pregnancy.
Results: We review more than 750 patients with inflammatory arthritis that received CZP and found 15 cases that was in pregnancy. See table 1.

Table 1. The use of CZP was effective, good tolerated and the profile of safety for the mother and the product was acceptable.

Age (years)	Disease	Drug exposure (months)	Clinical course	Breastfeeding. Comments
28	RA. (Rheumatoid Arthritis).	5	Normal.	+
30	RA	7.5	Pretèrm. 34 weeks.- 1500 grams	+ 3 month
38	RA	2	Miscarriage. 8 weeks.	Methotrexate Use. NA.
48	RA	5	Miscarriage. 5 weeks. uterine curettage. previous tubal ligation.	Methotrexate use. NA
32	Seronegative Spondyloarthritis.	4	Normal.	-
36	RA	8	Caesarean section. 1400 grams. Gestational age 31weeks. Preterm.	+
24	Seronegative Spondyloarthritis	9	Normal	+
29	RA	9	Normal.	+
31	RA	4	Normal.	+
33	Seronegative Spondyloarthritis	9	Normal. Caesarean section. (C-section).	+
37	RA	8	Preterm. 33 weeks. Arterial Hypertension, Gestational Diabetes.	Baby Kangaroo. 1640 grams.
32	RA	9	Normal. Caesaran section. (C-section).	+
31	Psoriatic Arthritis	6.5	Normal	NA
20	RA	10	Normal	+
21	Psoriatic Arthritis	9	Normal.	+

Conclusion: CZP is a useful alternative of treatment for pregnant patients and with inflammatory arthropaties that required therapeutic agent. This topic has been recently review and show that this agent is safe for pregnant women and for those breastfeeding and support continuation of CZP during pregnancy, when considered necessary.
There has been clear evidence during the last few years that this is the treatment of choice for women in fertile age with autoimmune diseases which requires immunomodulation.

REFERENCES

[1] Mariette X., et al. Ann Rheum Dis 2017.doi.10.1136/2017-212196.
[2] Clowse MEB., et al. Arthritis Rheumatol 2017.69.suppl 100. Abstract 1309.

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AB0382 TROUGH VERSUS NON-TROUGH ADALIMUMAB DRUG LEVEL MEASUREMENTS

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Background: Over the last years there has been an increasing interest for measuring drug levels to guide decision-making. Serum samples used for these measurements are often obtained prior to the next injection, at trough level. However, Jani et al. (2015) analyzed drug levels of randomly acquired serum samples from patients with rheumatoid arthritis (RA) treated with either etanercept or adalimumab and found a significant relationship with clinical disease activity. This indicates that random drug level measurements might also be useful (1). However, more aspects should be considered before deciding to use non-trough measurements.
Objectives: To assess the effect of non-trough measurements, compared to trough measurements, on serum drug level.
Methods: Patients with RA starting adalimumab treatment were included in this prospective observational cohort study, named the Reade Rheumatology Registry. Serum samples were obtained during every visit and these were analyzed for drug levels using a regular enzyme-linked immunosorbent assay (Sanquin, Amsterdam). The date of a patients' last injection with adalimumab was documented. Samples were included in the analyses if the interval between the last injection and serum sampling did not exceed 28 days, as in general patients do not have such long dosing-intervals. The analysis was performed using Spearman correlation.
Results: In total, 121 RA patients were included in this study. The median follow-up period of these patients was 156 (interquartile range (IQR) 78-247) weeks. Drug level measurements were performed in all serum samples that were obtained. In total, 310 measurements were included in the analyses, as from this subset the date of the previous injection with adalimumab was documented. The median drug level during adalimumab treatment was 6.6 (IQR 4.2-9.8) µg/ml, and the median number of days between the previous injection of adalimumab and serum sampling was 8 (5-13). The latter was divided into quartiles and plotted against drug level (Figure 1). The first quartile (median 2 (IQR 1-3) days) had a median drug level of 8.0 (4.7-11.0) µg/ml, the second quartile (7 (6-8) days) of 6.9 (5.4-10.0) µg/ml, the third quartile (11 (10-12) days) of 6.1 (3.4-9.5) µg/ml, and the fourth quartile (14 (13-14) days) of 5.7 (3.1-8.5) µg/ml. A weak association was found between the number of days between the previous injection of adalimumab and serum sampling and adalimumab drug level (Spearman's ρ: -0.182, p=0.001).

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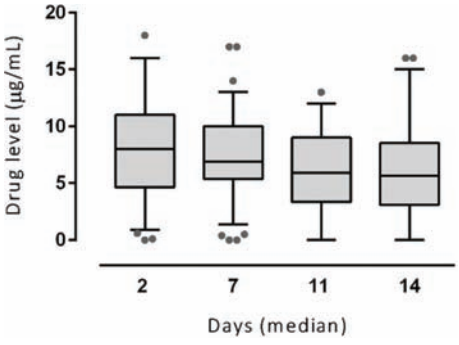


Figure 1

Conclusion: The growing interest to apply therapeutic drug monitoring (TDM) within the field of rheumatology forces us to discuss which measurements, trough or non-trough, are most informative. We found a correlation between the number of days between the previous injection of adalimumab and serum sampling, and adalimumab drug level. This might suggest that the timing of serum sampling affects the measured drug level, which could have consequences for treatment decisions based on these drug levels.

REFERENCES

[1] Jani M, Chinoy H, Warren RB, Griffiths CEM, Plant D, Fu B, et al. Clinical Utility of Random Anti-Tumor Necrosis Factor Drug-Level Testing and Measurement of Antidrug Antibodies on the Long-Term Treatment Response in Rheumatoid Arthritis. Arthritis & Rheumatology. 2015;67 (8):2011-9.

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AB0383 LATENT TUBERCULOSIS INFECTION SHOULD BE MONITORED IN BOTH TUMOR NECROSIS FACTOR INHIBITORS AND NON-TUMOR NECROSIS FACTOR INHIBITORS IN BIOLOGICAL-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The risk of latent tuberculosis infection (LTBI) increased during the treatment of biologic agents for patients with rheumatoid arthritis. Taiwan rheumatology association recommend performing at least annual interferon-gamma release assays (IGARs) testing during biologic treatment course because of the moderate prevalence of tuberculosis in Taiwan.[1] Although increased tuberculosis reactivation rate in patients with TNF inhibitor is reported, the risk of LTBI in patients with RA treated by non-TNF inhibitors is limited.
Objectives: The aim is to use serial interferon-gamma release assays (IGRAs) as a diagnostic tool for LTBI in biologic-naïve patients with rheumatoid arthritis treated with TNF and non-TNF inhibitors in Taiwan.
Methods: We retrospectively collected 313 biologic-naïve patients with rheumatoid arthritis receiving biologic agents between 2013 to 2017 in Chang Gung Memorial hospital in Taiwan. All RA patients underwent semi-annual IGRA test during biologic agent treatment. Cox proportional hazard model was used for analysis to compared RA patients with TNF and non-TNF inhibitors.

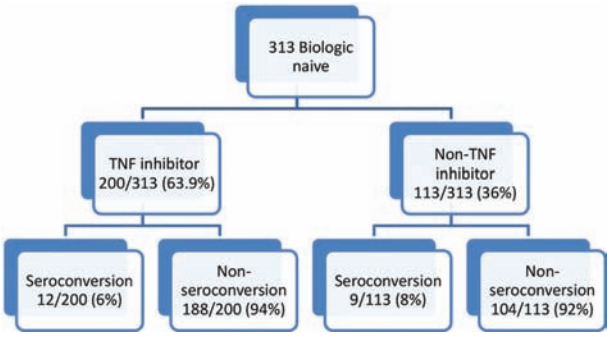


Figure 1

Results: The age of patients and disease duration are 55.9 13.1 year-old and 5.2 2.0 years(Table 1). The LTBI rate in patients with rheumatoid arthritis after biologic treatment is 6.7%. Out of the 21 patients with LTBI, 12(6%) patients were treated with TNF inhibitors, 9(8%) patients were treated with non-TNF inhibitors (Figure 1). 42.9%(9/21) received chemoprophylactic therapy by isoniazid but no patient suffered from active TB till the end of study period. Patients with TNF inhibitors was associated with a hazard ratio (HR) of 4.43 (95% CI, 0.80-24.39) after adjusted age, sex, diabetes history, prednisolone use and disease duration. This Cox regression analysis of RA patients found that the risk of LTBI was not different in TNF or non-TNF inhibitors.
Conclusion: Our study revealed biologic-naïve patients with rheumatoid arthritis have the same risk of LTBI. All RA patients who need either TNF or non-TNF inhibitors should be monitored LTBI in moderate prevalence TB area.

REFERENCES

[1] Chen, Y.-H., 2015 *TRA revised recommendations for screening and management of tuberculosis infection in patients before and after anti-tumor necrosis factor-alpha biological treatment*. Vol. 29. 2015. 1-8.

Table 1. Baseline characteristics in patients with RA treated with TNF or non-TNF inhibitors

	Total (n=313)	TNF inhibitors (n=200)	Non-TNF inhibitors (n=113)	p-value
Gender, female	259 (82.7%)	169(84.5%)	90(79.6%)	0.109
Age (Mean± standard deviation)	55.9	55.0	57.6	0.102
	13.1	12.3	14.4	
Disease duration (Mean± standard deviation)	5.2	5.5	4.7	**0.001***
	2	1.8	2.2	
Diabetes mellitus	28(8.9%)	12(6.0%)	16 (5.1%)	**0.019***
Liver cirrhosis	2(0.6%)	2(1.0%)	0(0.0%)	0.280
Prednisolone mean dose (mg/day)	223 (71.2%)	145(72.5%)	78 (69.0%)	0.479
	8.0	8.2	7.6	0.623
	7.7	9.1	3.8	

Disclosure of Interests: None declared
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AB0384 PROMISPAIN INTERFERENCE 6B AND FATIGUE 7A SHORT FORMS AND PROFILE-29 IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TNF INHIBITORS

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Background: PROMIS (Patient Reported Outcomes Measurement Information System) has been used in rheumatoid arthritis (RA) patients (Pts) to assess disease activity across multiple domains (i.e. physical function, fatigue, pain interference). AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis) is an ongoing Phase 4 study designed to provide a real-world assessment of intravenous Tumor Necrosis Factor inhibitor (TNFi) medications in RA pts. The study utilizes PROMIS and Clinical Disease Activity Index (CDAI) to assess effectiveness.
Objectives: This analysis examined select PROMIS measures to assess (1) relationship between baseline (BL) CDAI and PROMIS-scores, (2) responsiveness of PROMIS after initiation of TNFi and (3) relationship between PROMIS T-scores of the 4 item Profile29v2 Fatigue and Pain Interference domains and respective PROMIS Short Forms (SF).
Methods: AWARE is a prospective, noninterventional, 3-year study at 100 US sites. RA pts were enrolled when initiating TNFi treatment. Treatment decisions are at the discretion of the treating rheumatologist. We report on data from Pts' BL PROMIS Pain Interference 6b (PI), Fatigue7a (F), Profile29v2 and CDAI. PROMIS T-scores were compared across CDAI disease category (high, moderate etc) using ANOVA. We dichotomized pts based on whether their BL T-score was within 0.5SD of the population mean (i.e. 'normal') or not to evaluate for effect modification in the subsequent change in PROMIS T-scores. Data shown are mean ± std dev.
Results: Pts (N=1220) were 59.5± 13.2 yrs, disease duration 8.2 ± 9.9 yrs, 83.4% female, body weight 85.1± 24.2 kg, BMI 31.4 ± 8.51, BL CDAI 32.4 ± 15.6. A significant relationship between PROMIS T-scores (PI, F) and BL CDAI disease activity category was confirmed. There was minimal change in T-score of pts with BL PI and F T-scores </=55 and PF>/=45 over 5 infusions (approx. 5-7 months). Depending on domain,

14.7-27.3% of pts had initial PROMIS T-scores within 0.5SD of normal. There was a significant (p<0.0001) relationship between PI and F T-scores and the respective 4 questions on the P29v2.

Conclusion: Avoiding floor effects in pts who initiated TNFi therapy with near-normal PROMIS scores, PROMIS instruments demonstrated a robust T-score change in response to initiation of TNFi therapy.

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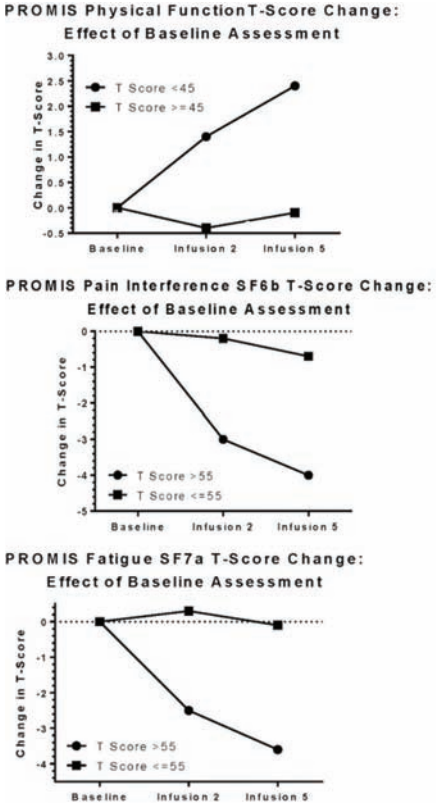


Figure 1

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AB0385

INTEGRATED SAFETY ANALYSIS ACROSS PHASE 3 CLINICAL STUDIES INCLUDING THE CONTROLLED AND UNCONTROLLED PERIODS FOR INTRAVENOUS GOLIMUMAB IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND ANKYLOSING SPONDYLITIS

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Background: The GO-FURTHER, GO-VIBRANT, and GO-ALIVE randomized controlled trials evaluated the efficacy and safety of intravenous (IV) golimumab (GLM) in patients (pts) with active rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS), respectively.

Objectives: This integrated analysis assessed safety events across indications in pts who received IV GLM.

Methods: Integrated safety data from 3 Phase 3, double-blind, placebo (PBO)-controlled trials were analyzed up to week (WK) 112 in RA pts and up to WK 60 in PsA and AS pts. Pts received either IV PBO or IV GLM (2 mg/kg) at 0, 4, 12, and 20 WKS. PBO pts crossed over to IV GLM at WK 24, except RA pts randomized to PBO who met early escape criteria crossed over at WK 16 and AS pts randomized to PBO who crossed over at WK 16. Cumulative adverse events (AEs) were reported by indication and pooled by treatment. Anti-drug antibodies (ADAs) were evaluated.

Table 1.

Table 1. Summary of Adverse Events During the Placebo-controlled and Uncontrolled Study Periods

Variables	RA[a] IV GLM	PsA[b] IV GLM	AS[b] IV GLM	All IV GLM
Treated patients, n	584	460	204	1248
Average duration of follow up, wks	95.9	47.2	51.8	70.7
Patients who discontinued due to an AE	41 (7.0)	17 (3.7)	4 (2.0)	62 (5.0)
Patients with ≥1 AE	462 (79.1)	234 (50.9)	113 (55.4)	809 (64.8)
Patients with ≥1 SAE	106 (18.2)	24 (5.2)	7 (3.4)	137 (11.0)
Patients with ≥1 infection	287 (49.1)	105 (22.8)	67 (32.8)	459 (36.8)
Patients with ≥1 serious infection	36 (6.2)	10 (2.2)	3 (1.5)	49 (3.9)
Patients with ≥1 infusion reaction	27 (4.6)	4 (0.9)	3 (1.5)	34 (2.7)
ADA-positive patients[c], %	23.4	22.0	20.2	22.3

Patients n (%) reporting safety events during the placebo-controlled and uncontrolled study periods are reported, unless otherwise specified.
[a]Based on safety events that occurred up to week 112; [b]Based on safety events that occurred up to week 60
[c]Assessed using a drug-tolerant enzyme immunoassay based on IV GLM patients with appropriate samples through week 52 (RA, n=552; PsA, n=450; AS, n=203; and All, n=1205)
ADA, anti-drug antibody; AE, adverse event; AS, ankylosing spondylitis; IV GLM, intravenous golimumab; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SAE, serious adverse event

Table 2.

Table 2. Incidence of Safety Events Per 100 Patient-Years

Variables	RA[a]		PsA[b]		AS[b]		All	
	IV GLM	Placebo	IV GLM	Placebo	IV GLM	Placebo	IV GLM	Placebo
Treated patients, n	584	197	460	239	204	103	1248	539
Average duration of follow up, wks	95.9	21.0	47.2	23.2	51.8	16.1	70.7	21.0
Opportunistic infections	0.4	0	0	0	0	0	0.2	0
(95% confidence interval)	(0.1, 1.0)	(0, 3.8)	(0, 0.7)	(0, 2.8)	(0, 1.5)	(0, 9.4)	(0.1, 0.6)	(0, 1.4)
All malignancies	0.5	0	0.5	1.9	0	0	0.4	0.9
(95% confidence interval)	(0.2, 1.1)	(0, 3.8)	(0.1, 1.7)	(0.2, 6.8)	(0, 1.5)	(0, 9.4)	(0.2, 0.9)	(0.1, 3.3)
Active TB	0.2	0	0.5	0	0.5	0	0.3	0
(95% confidence interval)	(0, 0.7)	(0, 3.8)	(0.1, 1.7)	(0, 2.8)	(0, 2.7)	(0, 9.4)	(0.1, 0.7)	(0, 1.4)
Death	0.5	1.3	0.2	1.9	0	0	0.4	1.4
(95% confidence interval)	(0.2, 1.1)	(0, 7.0)	(0, 1.3)	(0.2, 6.8)	(0, 1.5)	(0, 9.4)	(0.1, 0.8)	(0.3, 4.0)

Incidence per 100 patient-years are reported, unless otherwise specified.
[a]Based on safety events that occurred up to week 112
[b]Based on safety events that occurred up to week 60
AS, ankylosing spondylitis; IV GLM, intravenous golimumab; PsA, psoriatic arthritis, RA, rheumatoid arthritis; TB, tuberculosis

Results: Overall, 1248 pts were treated with IV GLM across indications. A numerically greater proportion (%) of IV GLM pts with RA reported safety events than pts with PsA or AS (Table 1): SAEs (18.2 vs 5.2 vs 3.4), infections (49.1 vs 22.8 vs 32.8), serious infections (6.2 vs 2.2 vs 1.5), and infusion reactions (4.6 vs 0.9 vs 1.5). Incidence (per 100 pt-years) of opportunistic infections, malignancy, active tuberculosis, and death with IV GLM was low (≤0.5) across indications (Table 2). Infections were the most commonly reported type of SAE among pooled IV GLM pts; the most frequent was pneumonia (10 [0.8%]). Incidence (per 100 pt-years) of serious infections was similar among IV GLM pts with and without corticosteroid use (3.35 vs 3.37, respectively). Overall, 1 IV GLM pt (PsA) experienced a demyelination event. A numerically greater proportion of IV GLM pts discontinued due to an AE than PBO pts (5.0% vs 0.9%, respectively). In IV GLM pts with baseline alanine aminotransferase (ALT) ≤ upper limit of normal (ULN), 1.2% had post-baseline ALT elevations ≥5X ULN. The proportion of IV GLM and PBO pts with post-baseline ALT elevations ≥5X ULN was 2.1% vs 0% with methotrexate and 0.7% vs 1.4% without methotrexate use at baseline, respectively. Using a drug-tolerant enzyme immunoassay, the incidence of ADAs was 22% through WK 52 across indications, which primarily consisted of low titer ADAs.

Conclusion: IV GLM demonstrated a consistent safety profile across indications in the PBO-controlled (up to WK 24) and uncontrolled study periods. Similar to WK 24 (1), more safety events occurred in RA pts, who represented the largest study population with older pts, longer disease duration, and more concomitant medication use.

REFERENCES

[1] Husni ME, et al. Presented at EULAR 2018, Amsterdam, the Netherlands.

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AB0386 RESPONSE TO BIOLOGIC THERAPY IS INFLUENCED BY THE BODY MASS INDEX IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Biologic therapies have been bringing huge advantage in the treatment of rheumatoid arthritis, but response to the therapy is heterogeneous. The influence of the body mass index to the treatment is still controversial.
Objectives: To identify the factors influencing in the response to biologic therapy (bio naïve).
Methods: The analysis of the patients with rheumatoid arthritis who were initiated biologics therapy (bio naïve) between January 2011 to December 2016 in the rheumatology department of a hospital in Japan, was conducted. The effects were evaluated by EULAR response criteria after 6 months of biologic therapy, and factors influencing the response were analyzed in terms of the baseline characteristics (sex, age, disease duration, body mass index, tender joint count, swollen joint count, Patient's visual analog scale, Doctor's visual analog scale, erythrocyte sedimentation rate, C-reactive protein, Disease Activity Score in 28 joints, Modified Health Assessment Questionnaire, Methotrexate use, Prednisolone use).

Table 1.

Table 1. Difference of the baseline characteristics of RA patients between "Good or Moderate response" and "No response" of EULAR response criteria after 6 months of biologic therapy.

	Good or Moderate response (n=82)	No response (n=63)	p-value
Female sex, no. (%)	69 (84.1%)	53 (84.1%)	0.9975
Age, years	55.4 ± 15.6	59.2 ± 12.9	0.1115
Disease duration, years	6.6 ± 3.6	7.8 ± 3.9	0.0477
BMI, kg/m^2	22.0 ± 3.4	24.4 ± 5.2	0.0008
≧ 25, no. (%)	12 (14.6%)	22 (35%)	0.0043
TJC	5.6 ± 6.1	4.0 ± 5.4	0.0972
SJC	3.4 ± 4.8	1.5 ± 2.4	0.0018
Patient's VAS (range 0-100)	46.6 ± 24.6	34.4 ± 27.4	0.0052
Doctor's VAS (range 0-100)	44.6 ± 25.8	34.3 ± 28.0	0.0223
ESR mm/hour	62.8 ± 34.2	59.0 ± 31.8	0.5702
CRP mg/dL	1.7 ± 2.1	0.9 ± 1.7	0.0094
DAS28-ESR	4.9 ± 1.2	4.2 ± 1.3	0.0015
DAS28-CRP	3.9 ± 1.2	3.1 ± 1.3	<0.001
mHAQ	0.5 ± 0.5	0.5 ± 0.6	0.3829
Concomitant therapy			
MTX, no. (%)	62 (75.6%)	47 (74.6%)	0.8894
MTX dose, mg/week	7.4 ± 4.6	7.8 ± 5.0	0.7134
Steroid, no. (%)	46 (56.1%)	48 (76.2%)	0.0120
Prednisolone dose, mg/day	1.6 ± 2.3	3.9 ± 8.8	0.5156

* Values are the mean ± SD unless otherwise indicated. RA = rheumatoid arthritis; BMI = body mass index; TJC = tender joint count; SJC = swollen joint count; VAS = visual analog scale; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; DAS28 = Disease Activity Score in 28 joints; mHAQ = Modified Health Assessment Questionnaire; MTX = Methotrexate; PSL = Prednisolone.

Table 2.

Table 2. Logistic regression analysis of "Good or Moderate response" of EULAR response criteria after 6 months of biologic therapy by baseline body mass index among Tumor Necrosis Factor users, IL-6 receptor inhibitor users and CTLA4-Ig users.

Biologics	Odds Ratio	95% confidence interval	p-value
TNF inhibitor	0.88	0.78-0.99	0.0428
IL-6 receptor inhibitor	0.75	0.61-0.93	0.0093
CTLA4-Ig	0.95	0.79-1.13	0.5757

Results: There were differences of baseline characteristics in disease duration and body mass index between the patients who achieved "Good or Moderate response" and "No response" of EULAR response criteria after 6 months of biologic therapy (table 1). The latter was more significant, and the difference was found among biologics (table 2).
Conclusion: Body mass index influence in the response to first biologic therapy in patients with rheumatoid arthritis.
Disclosure of Interests: None declared
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AB0387 SATISFACTION OF PATIENTS AND PHYSICIANS WITH TREATMENTS FOR RHEUMATOID ARTHRITIS: A NATIONWIDE SURVEY IN CHINA

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Background: Treatment satisfaction is important for adherence to therapy both for patients and physicians. There is no full understanding of the treatment satisfaction for rheumatoid arthritis (RA) in China.
Objectives: The aim is to explore the treatment satisfaction between rheumatologists and RA patients across China and the factors associated with patients' satisfaction.

Table 1.

Table 1. TSQM-II summary scores of patients' and physicians' satisfaction.

Treatment		Patients	Physicians	*P*
All medications for patients/ csDMARDs for physicians	*N*	1237	146	
Effectiveness	Median (range)	83.3 (0–100)	66.7 (33.3–100)	
Side effects	Median (range)	100 (16.7–100)	75 (16.7–100)	
Convenience	Median (range)	81.3 (18.6–100)	68.8 (31.3–100)	
Global satisfaction	Median (range)	83.3 (8.3–100)	66.7 (16.7–100)	
bDMARDs	*N*	335	146	
Effectiveness	Median (range)	83.3 (0–100)	75 (33.3–100)*	0.302
Side effects	Median (range)	100 (8.3–100)	87.5 (16.7–100)*	<0.001
Convenience	Median (range)	75 (0–100)	68.8 (12.5–100)	0.001
Global satisfaction	Median (range)	75 (0–100)	75 (16.7–100)*	0.889

*p <0.05, bDMARDs vs.csDMARDs in physicians.

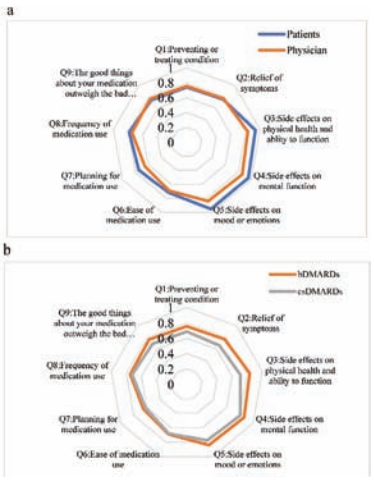


Figure 1 Radar charts with each item for the satisfaction between patients and physicians.

Methods: We conducted a prospective, multicenter, observational study of physicians and patients in 12 centers from 11 provinces across China between March and April 2018 (NCT03483597). The Treatment Satisfaction Questionnaire for Medication version II (TSQM-II) was used to assess the treatment satisfaction of patients and physicians regarding to csDMARDs and bDMARDs therapy. Multiple linear regression analysis was used to determine the factors independently associated with patients' satisfaction.
Results: 1237 patients (82.5% female) with a mean age (SD) of 48.9 (13.4) years and 146 rheumatologists (72.6% working>5 years) were included in this survey. The patients' satisfaction (n=335) with bDMARDs was higher than physicians' satisfaction (n=146) regarding the side effects (95.0±14.3 vs. 84.6±15.7, p<0.001) and convenience (74.6±21.2 vs. 69.1 ±16.5, p=0.002) (Table1). Among physicians, global satisfaction with bDMARDs was higher than that with csDMARDs (75.0 vs. 66.7, p<0.05) (Table1). Satisfaction of each questionnaire item toward therapy in patients and rheumatologists were also shown in radar charts (Figure 1). The multivariable regression analysis showed that age and quality of communication with physician was positively associated with patients' satisfaction, while level of education (bachelor or above), self-assessment of disease severity and treatment costs were inversely associated with satisfaction.
Conclusion: For bDMARDs, the treatment satisfaction of patients with RA is generally better than that of physicians. Physicians' satisfaction with bDMARDs is higher than that with csDMARDs. The independently factors associated with the treatment satisfaction of patients with RA are age, education, disease severity, the patient-physician communication, and treatment costs, which could be targeted in routine clinical care.

REFERENCES

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AB0388 COMPARATIVE EFFECTIVENESS OF RITUXIMAB, TOCILIZUMAB AND TNFI BIOLOGICS IN RHEUMATOID ARTHRITIS PATIENTS. INFLUENCE OF CLINICAL AND INFLAMMATORY PROFILES

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Objectives: 1) To compare the real-world effectiveness among RA patients starting 3 biologic DMARDs (bDMARDs). 2) To evaluate whether patients' clinical characteristics influence the response to specific bDMARDs. 3) To analyze the impact of bDMARDs on inflammatory profiles.
Methods: Eighty RA patients initiating TNFi, 22 patients treated with TCZ and 28 treated with RTX, the last ones after switching from TNFi and given as second bDMARDs, were included in the study. Effectiveness was assessed before and after 3 and 6 months of treatment by the European League Against Rheumatism (EULAR) criteria. Adjusted differences were estimated with multivariable linear regression. Differences in treatment outcomes were calculated as a function of patients' characteristics, through regression modelling. Extensive analysis of the inflammatory profile using a multiplex were also performed.
Results: A high proportion of patients starting TNFi showed early EULAR Good Response (65,8% responders at 3 months). After 6 months of therapy this percentage even increased (70,6%), so that tender joints' counts, swollen joints count, SDAI and HAQ improved significantly.
After switching from a first TNFi, RTX treatment promoted better early response (81,8% responders after 3 months) than TCZ (67% responders). Differences remained significant after adjusting for potential confounders. Yet, after 6 months, efficacy was similar among both non-TNFi DMARDs, even improving the effectiveness in TCZ-treated RA patients based on EULAR response rate (DAS28 change: 5.09±1.4 to 2.7±1,17) vs RTX-treated patients (DAS28 change: 4.8±1.3 to 3-1±1.3).
Patients older, and those suffering arterial hypertension (AH) or hyperlipidemia showed less effectiveness for both, TNFi and non-TNFi DMARDs, most remarkable for RTX and after 6 months of treatment.
Analysis of the inflammatory profile, by evaluating 27 key biomarkers of inflammation, showed, in patients' responders to therapy, specific profiles depending on the biologic DMARD administered. Thus, after 6 months of RTX, a generalized reduction in the expression levels of 22/27 proteins evaluated was observed, while TCZ mainly inhibited proteins involved in cell maturation, proliferation and leukocytes recruitment (IL6, GCSF, IP-10, IFNγ, RANTES). On the other hand, TNFi mainly reduced molecules related to leukocytes' recruitment (IL-2, IL-8, MIP1β, RANTES).
Conclusion: 1) Treatment outcomes among RA patients treated with non-TNFi bDMARDs in standard clinical practice, are in line with a superior early effectiveness of RTX compared with TCZ. However, effectiveness in TCZ-treated RA patients increases after 6 months of treatment vs RTX. 2) Patients characteristics influence the response to bDMARDs, suggesting the need of evaluating the benefit risk/ratio based on a personalized clinical evaluation. 3) Anti-inflammatory benefits associated with bDMARDs treatments can differ despite similar drug efficacy against RA, indicating that drug-specific mechanisms are involved in regulating these processes.
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AB0389 BIOSIMILAR ETANERCEPT VERSUS ORIGINATOR: RESULTS FROM A LONGITUDINAL PROSPECTIVE MONOCENTRIC STUDY

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Background: The introduction of TNF inhibitors have revolutionized the outcome of patients affected by Rheumatoid Arthritis (RA). In the last years, pharmaco-economic implications determined the introduction of biosimilar as alternative to originator biological drugs. Phase I and head-to-head phase III clinical studies demonstrated pharmacokinetic equivalence and comparability in terms of efficacy, safety, immunogenicity and tolerability. However, biosimilar drugs demonstrated some differences related to charge and glycosylation, not influencing the function and the ability to

bind the soluble TNF. To date, very few data are available concerning the use of biosimilar drugs in a real-life setting. Results from DANBIO registry suggested a lower retention rate in RA patients switchers from Etanercept originator (ETA) to biosimilar (SB4) versus the historic ETA cohort and higher in comparison with historic SB4 patients (1).

Objectives: To compare the efficacy of ETA versus SB4 in a cohort of RA patients in a real life setting.

Methods: In this monocentric case-control prospective study, we consecutively enrolled RA patients starting ETA or SB4 treatment from 2015. RA diagnosis was made according with ACR/EULAR 2010 criteria (2). Data were collected and entered into a standardized, computerized, electronically filled-in form. We included patient demographics, date of diagnosis, comorbidities and previous and concomitant medications. The clinical evaluation included the count of swollen and tender joints and the patient's and physician's global disease assessment based on a visual analogue scale (VAS; range, 0 to 100 mm). Disease activity was measured according to the disease activity score in 28 joints (DAS28ESR) (3). The patients were asked to fill in the Health Assessment Questionnaire (HAQ). All the patients were evaluated at the beginning of treatment (T0) and after 4 (T1) and 12 months (T2). Clinical response to treatment was evaluated by using EULAR criteria (4).

Results: We evaluated 35 RA patients treated with SB4 (M/F 2/33; median age 63 years, IQR 21; median disease duration 108 months, IQR 138) and 40 with ETA (M/F 5/35; median age 60.5 years, IQR 20; median disease duration 102 months, IQR 141). Biologic drug was prescribed as first-line biological treatment in 71.4% of SB4 cohort and in 80.0% of ETA. At T0 no significant differences were observed among the two groups in terms of DAS28ESR [SB4 median 4.6 (IQR 1.8), ETA 4.3 (IQR 1.9), p=ns] and HAQ [SB4: median 1 (IQR 1.05), ETA median 1 (IQR 0.85), p=ns]. In both groups we observed a significant reduction of DAS28 values at T1 (BS4 p=0.01; ETA p<0.0001) and T2 (SB4 p=0.0007; ETA p= 0.0002; Figure 1A). When evaluating the remission rate (DAS28ESR<2.6) at T1, we observed a significant higher rate in ETA (53.8%) versus SB4 (26.7%; p= 0.0002; Figure1B). No differences were found after 12 months of treatment.

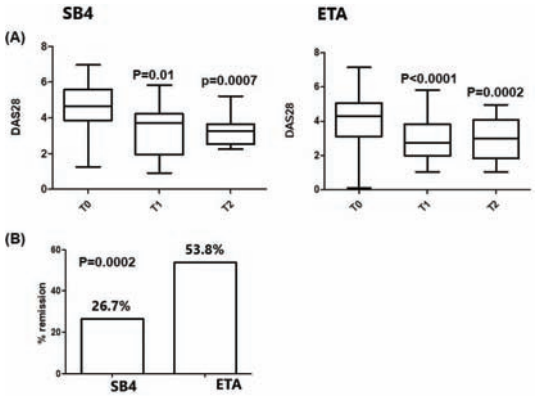


Figure 1

Conclusion: The results of our study confirmed in a real-life setting the efficacy of SB4 in RA patients, as demonstrated by the significant reduction of DAS28ESR values after 4 and 12 months of treatment, similarly to ETA. Nonetheless, ETA seems to be able to induce a remission status earlier than SB4.

REFERENCES

[1] Glintborg B, et al. Ann Rheum Dis. 2018
[2] Aletaha D, et al. Arthritis Rheum. 2010
[3] Anderson JK, et al. Arthritis Care Res. 2011
[4] van Gestel AM, et al. Arthritis Rheum. 1996

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AB0390

CORRELATION BETWEEN TNF-BLOCKERS BIOAVAILABILITY AND FCGRIIA H131R POLYMORPHISM IN TUNISIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA)'s prognosis drastically improved with the introduction of TNF-blockers. However, reasons behind therapeutic failure in some patients remain unclear. Several factors might influence pharmacokinetics of these drugs by reducing their half-life and, consequently, their effectiveness. Considering Fc-containing biologics like infliximab (IFX) and adalimumab (ADL), Fc gamma receptors (FcgRs) polymorphism would be an interesting genetic candidate to focus on.

Objectives: The aim of our study was to determine the influence of low affinity allele FcgRIIA-131R on ADL and IFX bioavailability.

Methods: We enrolled RA patients treated with IFX and ADL for over six months. Blood samples were collected for each patient immediately prior to drug administration. Quantitative measurements of the residual drug concentration (DC) was carried out by a commercial enzyme-linked immunosorbent assay (ELISA) kit (Promonitor®). Then, we identified patients with DC above therapeutic cut-off (DC+) for each biologic. EULAR criteria were considered to determine treatment outcome. FcgRIIA H131R polymorphism was genotyped using PCR-SSP.

Results: Twenty-nine patients were included (13 treated with ADL and 16 with IFX). We identified 31.3% and 23.1% non-responders among patients treated with IFX and ADL respectively. Patients with DC+ were more frequent in ADL group (76.9%) than IFX group (43.75%).

For IFX, DC+ was significantly correlated with the presence of FcgRIIA 131-R (p=0.033). In fact, none of the HH-genotyped patients had DC+. Furthermore, an association between FcgRIIA 131-R allele and poor response to IFX was noted (p=0.059) while all HH-genotyped patients responded to IFX. For ADL, no correlation was found with both of residual DC and response to treatment.

Conclusion: The presence of FcgIIA-131 R allele might be a predictive factor of non-responsiveness to TNF-blockers. It also appears to be associated to a higher residual DC. That might be explained by a reduced biologic clearance due to a lower binding affinity to Fc portion compared to wild allele FcgRIIA-131H. Therefore, FcgR polymorphism assessment in RA patients would be a decision-making parameter to consider, as part of the personalized medicine approach.

REFERENCES

[1] Montes A, Perez-Pampin E, Narváez J, et al. Association of FCGR2A with the response to infliximab treatment of patients with rheumatoid arthritis. Pharmacogenet Genomics. 2014;24(5):238-245
[2] DávilaáFajardo CL, van der Straaten T, Baak-Pablo R, et al. FcGR genetic polymorphisms and the response to adalimumab in patients with rheumatoid arthritis. Pharmacogenomics. 2015;16(4):373-381
[3] Cañete JD, Suárez B, Hernández MV, et al. Influence of variants of Fc gamma receptors IIA and IIIA on the American College of Rheumatology and European League Against Rheumatism responses to anti-tumour necrosis factor alpha therapy in rheumatoid arthritis. Ann Rheum Dis. 2009;68(10):1547-1552.

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AB0392

ASSOCIATION BETWEEN FCGRIIA R131H, FCGRIIIA NA1/NA2 AND FCGRIIIB V158F POLYMORPHISM AND RESPONSIVENESS TO BIOLOGICS IN RHEUMATOID ARTHRITIS TUNISIAN PATIENTS

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Background: Even though biologics have been used for several years in treatment of rheumatoid arthritis (RA), little is known about factors that modify their pharmacokinetics and therefore their efficacy. Polymorphisms (SNPs) in receptors for constant region Fc of IgG (FcgR) might influence the therapeutic outcome of molecules that incorporate an Fc fragment in

their structure such as etanercept (ETA), adalimumab (ADL) infliximab (IFX) and rituximab (RTX).
Objectives: The aim of our study was to determine whether the presence of low affinity allele of FcgR (FcgRIIA-131R, FcgRIIIA-158F and FcgRIIIB-NA2) influences efficiency and immunogenicity of ETA, ADL, IFX and RTX in RA Tunisian patients.
Methods: We included RA patients treated with biologics for at least six months. Response to treatment was assessed according to EULAR criteria. Quantitative measurement of antidrug antibodies (ADAb) for each biologic agent was carried out by a commercial enzyme-linked immunosorbent assay (ELISA) kit (Promonitor®). To do so, blood samples were collected for each patient right before drug administration. FcgRIIA, FcgRIIIA and FcgRIIIB SNPs was genotyped for all patients using PCR-SSP and direct sequencing process.
Results: Seventy-nine RA patients treated with biologics were enrolled (18 with ETA,13 with ADL,16 with IFX and 32 with RTX). Regardless of biologic type, 61 patients (77.2%) responded to treatment and 14 patients (17.7%) developed ADAb. Genotypic study revealed a correlation between poor response to treatment and the presence of at least one FcgRIIA 131-R allele (94.7% for RH/RR genotypes versus 5.3% for H/H genotype). But, the difference was not statistically significant (p=0.25). Besides, this mutant allele was significantly associated to the presence of ADAb (71.4% of ADAb positivity for RH/RR genotypes versus 28.6% for H/H genotype: p=0.041). The haplotypic study shows that the risk allele combination of FcgR IIA-131R/IIIA-158F/IIIB-NA2 was more frequent in ADAb+ (27%) compared to ADAb- subjects (23%) and in non-responders (27%) versus good responders (23%). But, neither of these associations was statically significant.
Conclusion: Our study suggests that RA patients FcgRIIA-131R allele carriers are more susceptible to develop ADAb than those with HH wild genotype. That could be explained by a higher biologic clearance in H-carrier patients, resulting in a decreased half-life and ultimately a lower risk of ADAb formation. Thus, FcgR polymorphism genotyping may be a useful marker for predicting response to Fc-containing biologics in Tunisian RA patients. Further studies need to be done on larger population.

REFERENCES

[1] Romero-Cara P, Torres-Moreno D, Pedregosa J, Vílchez JA, García-Simón MS, Ruiz-Merino G, Morán-Sanchez S, Conesa-Zamora P. A FCGR3A Polymorphism Predicts Anti-drug Antibodies in Chronic Inflammatory Bowel Disease Patients Treated With Anti-TNF. Int J Med Sci 2018; 15(1):10-15
[2] Lee YH, Bae SC. Associations between PTPRC rs10919563 A/G and FCGR2A R131H polymorphisms and responsiveness to TNF blockers in rheumatoid arthritis: a meta-analysis. Rheumatol Int. 2016 Jun;36(6):837-44.
[3] Lee YH, Bae SC, Song GG,Functional FCGR3A 158 V/F and IL-6 -174 C/G polymorphisms predict response to biologic therapy in patients with rheumatoid arthritis: a meta-analysis. Rheumatol Int. 2014 Oct;34 (10):1409-15.

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AB0393 IMPROVING DRUG SOLUBILITY FOR INFLAMMATORY ARTHRITIS TREATMENT: SULFASALAZINE NIOSOME

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Background: Newly, many studies have been assumed upon vesicular drug delivery systems like niosomes to make an effective formulation of drugs in soluble state that can lead to enhance bioavailability as well as to provide controlled drug release [1]. Niosomes due to their capability and efficient mechanism have been proposed to explain the ability of those as potential nanocarriers for poorly soluble drugs [2].
Objectives: In this study, niosomes have emerged as a drug delivery system to load sulfasalazine (SSZ) that is used to treat rheumatoid arthritis.
Methods: Niosomes were prepared by amphiphilic self-assembly of tween 80 and squalene through thin film hydration method. The optimal hydration condition that maximizes noisome yield was hydration duration of 24 hours at 30-35 •C. The encapsulation of sulfasalazine drug into niosome was characterized by Fourier transform infrared spectroscopy (FT-IR), UV-visible, Zeta potential, particle size, field emission scanning electron microscopy (FE-SEM), and transmission electron microscopy (TEM) to evaluate size, charge, morphology and functional properties.
Results: By using this method, the percentage of loaded drug, resulted by the encapsulation of micellar/niosomes was found to be 99 ± 0.2% for 5% of SSZ weight in total ingredients weight of micellar/niosomal vesicles (w/w). The drug-entrapped sulfasalazine niosomes (SSZN) nanoformulations indicated controlled release of drugs in phosphate buffer saline (PBS) at pH 7.2 making these nanoformulations ideal for colon-targeted drug delivery. It was also seen that a slower rate of the SSZ releasing of the drug encapsulated noisome was, in the range of 2-24 hours at PH 4.5-7.2. TEM examinations also confirmed the formation of 15-25 nm thick walls for the prepared SSZN particles. MTT assay revealed that the blank noisomes exhibited excellent biocompatibility. The in vitro drug loading and release behavior studier indicated the as prepared nano-noisome presented ultrahigh performance as drug carrier. Cell toxicity assay was carried out by HeLa cell line and A549 cell line demonstrated the half maximal inhibitory concentration (IC_{50}) of SSZ to 162 μM and 173 μM, respectively.
Conclusion: Niosomal formulation are introduced as a novel nano drug carriers to design effective drug delivery systems. They offer a great opportunity for loading hydrophilic, lipophilic drugs, or both drugs together. Niosomal formulation has been evaluated as a safe drug delivery system. In this study, we showed that SSZN has more stability and more efficiently affect the cancer cells. It seems that SSZN is a great candidate for future in vitro and in vivo researches for evaluating potential clinical applications.

REFERENCES

[1] P. Mokhtary, B. Javan, M. Sharbatkhari, A. Soltani, V. Erfani-Moghadam, Cationic vesicles for efficient shRNA transfection in the MCF-7 breast cancer cell line, International Journal of Nanomedicine 2018:13 7107–7121
[2] R. RAJERA, K. NAGPAL, S. Kumar SINGH, D. Nath MISHRA, Niosomes: A Controlled and Novel Drug Delivery System, Biol. Pharm. Bull. 34(7) (2011) 945-953.

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AB0394 SERUM CALPROTECTIN AS A PREDICTIVE MARKER OF THERAPEUTIC RESPONSE TO ADALIMUMAB IN RHEUMATOID ARTHRITIS

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Background: Adalimumab significantly reduces the activity of rheumatoid arthritis (RA), but reliable biomarkers of inflammation are still lacking to predict and evaluate the therapeutic response. Serum calprotectin is a mainstay of endogenous activation of the inflammatory response that can be useful as a marker of response to treatment in RA.
Objectives: To compare the evolution over time of serum calprotectin and C-Reactive Protein (CRP) after initiation of adalimumab.
Methods: Serum levels of calprotectin, CRP and adalimumab concentration were measured at visits V1 (week 0), V2 (week 4), V3 (week 8), V4 (week 12) and V5 (week 26). Changes in each variable were analyzed at each visit and each variable was compared to each other using a correlation test. Receiving operating characteristic curves were used to estimate the predictive value of response at V5 for calprotectin and CRP at each visit.
Results: Data from 66 patients were analyzed. Serum calprotectin level decreased from V1 to V5 (3.76 μg/mL [0 – 17.47] to 2.74 μg/mL [0 – 18.83]; $p < 0.05$). A positive correlation was observed between serum calprotectin and $DAS28_{ESR}$ (Spearman 0.244; $p < 0.01$), and between CRP and $DAS28_{ESR}$ (Spearman 0.512; $p < 0.01$) for all visits combined. In contrast to CRP, serum calprotectin and serum calprotectin variation from V1 at each visit, were not predictive of $DAS28_{ESR}$ at V5.
Conclusion: Serum calprotectin decreases after initiation of adalimumab in RA but was weakly correlated with disease activity at week 26. Serum calprotectin cannot be considered as superior to CRP as predictive marker of therapeutic response in RA after initiation of adalimumab.

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AB0395 NO CLINICAL RELEVANT CHANGES IN EFFICACY, QUALITY OF LIFE AND TOLERABILITY FOR RA PATIENTS IN CLINICAL REMISSION 16 WEEKS AFTER SWITCHING TO THE BIOSIMILAR IFX CT-P13 COMPARED TO THE ORIGINATOR; A DESCRIPTIVE REPORT

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Background: Switching patients from originator infliximab (IFX) to biosimilar IFX can reduce healthcare costs. Several studies have shown that switching does not affect the efficacy for rheumatoid arthritis (RA) patients(1,2), however prospectively collected data on pharmacokinetics, immunogenicity and quality of life (QoL) is scarce.
Objectives: We report data collected from RA patients in clinical remission enrolled in the SECURE study (IFX4501; registered at www.clinicaltrialsregister.eu 2014-004904-31). In SECURE we collected IFX serum concentrations, efficacy, quality of life (QoL) and safety data of patients switched from originator IFX to biosimilar IFX CT-P13 for up to 16 weeks. The IBD cohort of this study has been published elsewhere (3).
Methods: In this prospective, open-label, interventional, non-inferiority, multicenter, phase IV trial, adult RA patients in clinical remission >30 weeks (DAS<3.2) at stable IFX dose were switched from originator IFX to CT-P13. Patients were followed for 16 weeks (2 infusions) after switching. Primary endpoint was the IFX serum concentration at through measured with a bridging enzyme-linked immunosorbent assay (ELISA) 16 weeks after switch. Secondary endpoints included antidrug antibodies (ADA), clinical disease activity measured with the DAS score, CRP and quality of life measured with the EQ5D, 8 and/or 16 weeks after switching.
Results: Between July 2015 and December 2016, 34 RA patients were recruited. Two patients were excluded from the safety population (1 no IMP exposure; 1 no efficacy assessment) and two patients discontinued before week 16 (1 AE: renal colic; 1 personal reasons), leaving 30 patients in the intent to treat population.
For 11 patients, blood samples were obtained at baseline and week 16. The IFX ratio at week 16 (biosimilar) compared to baseline (originator) was 107.40 (90% CI 90.35;127.66), indicating non inferiority. The number of included patients was too low for firm conclusions.
The mean difference (95% CI) at week 16 compared to baseline was for the CRP -0.22 (-1.80,1.37); for DAS 0.12 (-0.06,0.30), for EQ5D thermometer -3.19 (-9.78,3.41) and EQ5D Health status -0.05 (-0.08,-0.01). These changes were not clinical relevant.
In total 76 AEs were reported by 29 (90.6%) patients; 27 of these AEs were related to the study treatment. The most frequently reported AEs (≥5% subjects) were fatigue (9.4%), headache (6.3%), arthralgia (15.6%), back pain (9.4%), cough (6.3%), viral upper respiratory tract infection (15.6%) bursitis (6.3%) and pain in extremity (6.3%). Two non-related serious AEs were reported (ovarian cyst and benign parathyroid tumour). No ADA's were detected by inclusion or during the follow-up period.
Conclusion: In this prospective, interventional study in RA patients in clinical remission there were no clinically relevant changes in clinical and biochemical efficacy, quality of life and tolerability 16 weeks after switching to the biosimilar IFX CT-P13 compared to the originator.
This study is sponsored by Mundipharma Pharmaceuticals BV.

REFERENCES

[1] Park, W. et al. Ann Rheum Dis 76,346-354 (2017)
[2] Jorgensen, K.K. et al. Lancet 389, 2304-2316 (2017)
[3] Strik, A.S. et al. Lancet Gastroenterol & Hepatol 6(3),404-412 (2018)

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AB0396 MONITORING OF PATIENTS WITH RHEUMATOID ARTHRITIS BY INDOCYANINE GREEN (ICG) ENHANCED FLUORESCENCE OPTICAL IMAGING TREATED WITH ANTI-TNFI THERAPY

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Background: Indocyanine (ICG)-enhanced fluorescence optical imaging (FOI) by the Xiralite® system enables visualization of inflammation in the hands in rheumatic joint diseases.
Objectives: To investigate the ability of monitoring treatment response under Certolizumab pegol (CZP) in patients with rheumatoid arthritis (RA) by the ICG-enhanced FOI method Xiralite® as compared to clinical disease activity, laboratory parameters, and musculoskeletal ultrasound (US).
Methods: CZP-naive patients with RA were eligible for this study, which consisted of an open-label 52-weeks treatment period with CZP. Disease activity was monitored by the clinical score DAS28, laboratory parameters for systemic inflammation (CRP and ESR), ultrasonography (US7 score [1]) and by FOI at baseline (before CZP) and after 6, 12, 24, and 52 weeks under CZP therapy.
Results: In this study, 28 patients (female 92.9%, mean age 49.4±13.3) with RA were included and treated with CZP over a period of 52 weeks. All patients received CZP for at least 12 weeks (w), n=27 until w24, and n=18 received CZP throughout the entire 52 weeks. DAS28 decreased from moderate disease activity (median 4.6) at baseline to low disease activity (median 2.7) at w52 (p <0.001). CRP/ESR values also reduced from baseline to w52 (n.s.). FOI in phase 1 showed a continuous decrease of enhancement during the course of the treatment period: from baseline (median 1.5, IQR 0-9.5) to w6 (median 1.0, IQR 0-3), to w12 (median 0.5, IQR 0-3), to w24 (median 0.0, IQR 0-3) and visit w52 (median 0.0, IQR 0-2). An image example is given by the **Figure** for baseline and w52. The results for other FOI phases 2, 3 and PVM did not show a decrease over the treatment period. US-detected synovitis and tenosynovitis by the US7 score also presented to be responsive under therapy. Especially US7-synovitis in Power Doppler (PD) was reduced from baseline (median 2.0, IQR 1-4) to w52 (median 0.5, IQR 0-2).
Conclusion: FOI in phase 1 appears to be a valuable tool for fast and easy monitoring of treatment response to CZP in a clinical setting. FOI may provide an additional method to evaluate inflammation of wrist and finger joints of RA patients in follow-up studies.

REFERENCES

[1] Backhaus M, Ohrndorf S, Kellner H, et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. Arthritis Rheum. 2009;61(9):1194-201

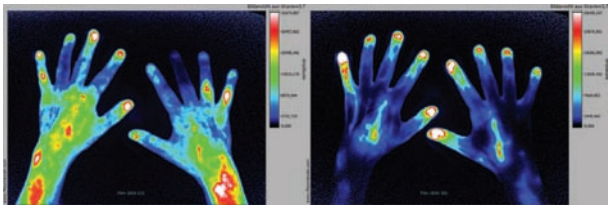


Figure 1. Decrease of ICG-enhancement in FOI, phase 1 (P1). Left image shows P1 of both hands at baseline (before CZP). Right image shows FOI in P1 of the same patient at w52 under CZP.

Legend: ICG: indocyanine green; FOI: fluorescence optical imaging; CZP: Certolizumab pegol; w52: week 52

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AB0397 PREDICTION OF RECURRENCE AFTER DISCONTINUATION OF ADALIMUMAB BY USING ULTRASOUND ASSESSMENT -THE PROUD STUDY-

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Background: Tapering of biological disease-modifying anti-rheumatic drugs (DMARDs) is recommended by European League Against Rheumatism (EULAR) in patients with stable rheumatoid arthritis (RA) disease activity. Discontinuation of biological DMARDs can be successful in some patients. However, the predictive factors enabling established patients with RA to remain free of biological DMARDs is unclear. Recently, ultrasonography (US) has become an important imaging tool to identify subclinical synovitis, even in patients with remission. There have been few reports on whether residual synovitis as shown by US can predict relapse of disease activity after discontinuation of biological DMARDs.

Objectives: We aimed to investigate the usefulness of US for predicting relapse in patients in remission for RA after discontinuation of adalimumab (ADA).

Methods: Patients who were using ADA and in remission (Disease Activity Score 28-joint count C reactive protein (DAS28-CRP) <2.6) for longer than 24 weeks were included in this multicenter prospective study. ADA was stopped and patients were followed up until week 52. Predictive factors for relapse at 24 and 52 weeks were analyzed from baseline clinical data, including a US examination. ADA was restarted at the time of relapse (DAS28-CRP $\geq$3.2). US assessment was performed at 0, 12, 24, 36, and 52 weeks and at the time of relapse. A US examination was performed at the bilateral first to fifth metacarpophalangeal joints, first interphalangeal and second to fifth proximal interphalangeal joints, and first to fifth metatarsophalangeal joints, by using a high-frequency linear transducer. The gray scale (GS) and power Doppler (PD) signals were scored in each synovial site using a semi-quantitative scale from 0 to 3. Moreover, the modified Total Sharp Score (mTSS) was evaluated at 0, 24, and 52 weeks by conventional radiography. The patients who relapsed were administrated ADA again.

Results: Fifty-three patients were included. Ten (18.9%) patients relapsed up to week 24 and 20 (37.7%) patients relapsed up to 52 weeks. The relapsed patients tended to have a long disease duration, but baseline US findings could not predict relapse. Increases in the PD score were observed during follow-up in some relapsed patients. Disease activity control was good after ADA was restarted in the relapsed group, and there was no difference in progression of the mTSS in the relapsed and non-relapsed groups.

Conclusion: Predicting relapse by baseline US findings after discontinuation of ADA in remission is difficult. However, an increased PD score in a following US examination might be useful for early detection of relapse. Radiographic progression is not significantly different in patients with relapse and those without relapse.

REFERENCES

[1] Iwamoto T, Ikeda K, Hosokawa J, et al. Prediction of relapse after discontinuation of biologic agents by ultrasonographic assessment in patients with rheumatoid arthritis in clinical remission: high predictive values of total gray-scale and power Doppler scores that represent residual synovial inflammation before discontinuation. Arthritis Care Res (Hoboken). 2014;66:1576-81.

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, Takanori Fujimura: None declared, Sho Sendo: None declared, Takaichi Okano: None declared, Yoshihide Ichise: None declared, Ikuko Naka: None declared, Heiseki Yu: None declared, Akihiko Nakabayashi: None declared, Yoshinobu Matsuura: None declared, Takahiro Yoshikawa: None declared, Masao Tamura: None declared, Masayasu Kitano: None declared, Yasuhide Kanayama: None declared

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AB0398 COMPARATIVE SAFETY OF ABATACEPT AND OTHER NON-TUMOR NECROSIS FACTOR INHIBITORS IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS

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Background: Abatacept has shown equivalent efficacy with other targeted therapies in rheumatoid arthritis (RA) patients[1], and equivalent or, in some cases, superior safety compared with tumor necrosis factor inhibitors (TNFi)[2,3]. However, there is limited evidence of its safety profile relative to other non-TNFi.

Objectives: To evaluate the class-level safety profile of abatacept compared with other non-TNFi in adults with moderate-to-severe RA in phase 3 and 4 clinical trials.

Methods: A systematic literature review (SLR) of phase 3 and 4 randomized controlled trials (RCTs) of adults with RA was conducted. The non-TNFi included were abatacept, tocilizumab, sarilumab, tofacitinib, baricitinib and rituximab. A search from database inception until Febuary 2018 was performed on MEDLINE®, Embase, CENTRAL, and the US and EU clinical trials registries. Conference proceedings from ACR and EULAR from 2015 to end of 2017 were also reviewed. Patients who were cDMARD-naive or not receiving concommitant cDMARD treatment were excluded from the main analysis. In Bayesian network meta-analysis (NMA) random effects model, drug class-level comparisons were made with respect to the risk of total aggregated adverse events (AEs), serious AEs (SAEs), treatment-related AEs, infection, serious infection, and cancer.

Results: We identified 39 RCTs that met the eligibility criteria for this SLR. The risk of bias was found to be low as assessed by the Cochrane Collaboration's tool for assessing risk of bias in randomized trials. Eight studies investigated abatacept (T-cell inhibitor), with no head-to-head comparison to other non-TNFi. Other interventions evaluated were

IL-6 inhibitors (tocilizumab, n=13; sarilumab, n=3), JAK inhibitors (tofacitinib, n=7; baricitinib, n=4), and B-cell depleting agent (rituximab, n=4).
The pooled study population of 27,215 moderate-to-severe RA patients primarily consisted of middle-aged Caucasian females (mean age: 47-55 yrs;% Caucasian: 44% - 97%;% female: 69% - 88%). Thirty three trials were on patients previously treated with cDMARD or TNFi, while 6 trials were on cDMARD-naive patients. Total aggregated AEs (total AEs, n=37; SAEs, n = 37; treatment-related AEs, n = 14) and infection (serious infection, n = 35; total infection, n = 26) were the most frequently reported safety outcomes.
The NMA was performed on 23 trials. Indirect comparisons were made between IL-6 inhibitors, JAK inhibitors, B cell depleting agent and abatacept, with TNFi or cDMARD as direct comparators. The risk of total AEs was significantly higher for IL-6 inhibitors compared with abatacept (RR = 1.13, 95% CrI = 1.05 – 1.22). For SAEs and other analyzed safety outcomes, no significant difference was observed between abatacept and other non-TNFi drug classes. Similar results were observed in sensitivity analyses for all patients on concomitant cDMARD, including those who were treatment-naive before the study (n=26 trials).
Conclusion: When comparing aggregated safety outcomes, abatacept shared a similar safety profile with most non-TNFi RA treatments. However, patients on abatacept had a statistically significantly lower risk of total AEs compared to US recommended doses of IL-6 inhibitors. More studies with head-to-head comparison in clinical trials and real-world setting are required to provide further understanding of the safety profile and risk of specific adverse events for non-TNFi in order to optimize treatments for moderate-to-severe RA patients.

REFERENCES

[1] Schoels M, et al. Ann Rheum Dis 2012;71(8):1303-1308
[2] Christensen R, et al. *Int J Clin Rheumatol* 2013; 8(6):647-655
[3] Jin Y, et al. J Rheumatol 2018; 45(9): 1240-1248

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AB0399 EVOLUTION OF BIOLOGIC/SMALL MOLECULE SWITCHING PATTERNS IN RA BETWEEN 2016 AND 2018

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Background: TNF therapy has been the standard of care for adult patients diagnosed with autoimmune conditions and are typically used as a first-line biologic/small molecule in the treatment of rheumatoid arthritis (RA). However, the adoption of systemic agents with alternate mechanisms of action (AMOA) such as JAK and interleukin inhibitors have increased in recent years across many indications. As such, the practice of sequential TNF prescribing following an initial TNF discontinuation is becoming less common, with switches to AMOAs, such as JAK and IL-6 inhibitors, becoming more popular.
Objectives: This research sought to track the evolution of biologic/small molecule switch patterns among US RA patients between 2016 and 2018 and to identify differentiating patient characteristics between the switch patterns.
Methods: An independent market analytics firm collaborated with US rheumatologists to conduct a retrospective chart review of RA patients who switched biologic/small molecule treatment 12 weeks prior to being surveyed. Physicians were able to submit up to 7 patient charts. Data were collected via a HIPAA-compliant online audit in January 2016 (n=198 rheumatologists/980 patient charts), in September 2017 (n=176 rheumatologists/1,002 patient charts), and September 2018 (211 rheumatologists/1,074 patient charts). Results were analyzed in SPSS.
Results: Analysis of patients recently switched from one biologic/small molecule to another revealed the decreasing popularity of cycling to another TNF after initial TNF discontinuation. TNF cycling accounted for 46% of all switches in 2016, 41% in 2017, and 40% in 2018. Conversely, switches from TNFs to JAK inhibitors accounted for 13% in 2016, 12% in 2017, and 15% in 2018. Switches to IL-6 inhibitors increased from 8% of all switches in 2016, to 9% in 2017, and 11% in 2018. The number of patients switched from a TNF to abatacept or rituximab remained stable over the study periods.
Patients who were cycled to another TNF were diagnosed with RA for a shorter amount of time, had been on a biologic for less time, had a lower swollen joint count and CRP level, were more likely to be males, were least likely to require a prior-authorization for treatment, and more likely to have been switched due to tolerability issues.
Consistent in all three years of data, patients switched to JAK inhibitors played a larger role in the switching decision, had a higher physician global assessment rating of global health, had a lower cardiovascular risk profile, were less likely to be prescribed concomitant methotrexate, and were more likely to participate in a manufacturer-sponsored co-pay assistance program.
Patients switched to an IL-6 inhibitor were largely indistinguishable from those undergoing other types of switches; however, they were slightly more likely to have more severe RA, have a slightly lower average physician global health assessment rating, were more likely to be obese, and have an elevated cardiovascular risk.
Conclusion: While the practice of TNF cycling is still the most predominant switch pattern among RA patients migrating from a first-to-second line biologic/small molecule therapy, the practice has been declining over the last three years. Over time, rheumatologists are increasingly likely to introduce a JAK or IL-6 inhibitor in the second-line setting following discontinuation of a first-line TNF.
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AB0400 FREQUENCY OF BIOLOGIC/SMALL MOLECULE MONOTHERAPY FOR RHEUMATOID ARTHRITIS IN THE EU: REAL-WORLD EVIDENCE FROM A PATIENT AUDIT STUDY

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Background: Biologic/small molecule therapy has been the standard of care for adult patients diagnosed with rheumatoid arthritis (RA) who have failed conventional DMARD therapy, resulting in familiarity, comfort, and satisfaction among physicians. Prior recommendations of combining biologics/small molecules with a DMARD like methotrexate (MTX) have recently been challenged by clinical data demonstrating the effectiveness of IL-6 and JAK inhibitors as monotherapy.
Objectives: This research sought to evaluate the frequency of biologic/small molecule monotherapy regimens among European RA patients who were recently switched from one biologic/small molecule to another.
Methods: An independent market analytics firm collaborated with rheumatologists in France (n=62), Germany (n=66), Italy (n=61), Spain (n=68) and the UK (63) to conduct an online retrospective chart review of RA patients who had switched treatment from one biologic/small molecule to another in the prior twelve weeks. Rheumatologists were able to submit up to seven RA patient charts. A total of 1,312 patient charts were collected via a market-specific compliant audit form in September 2018 and included patient and physician demographics, patient treatment history, and clinical/non-clinical patient parameters.
Results: Overall, the analysis of patient chart audits revealed that 22% of all recently switched patients were switched to a biologic/small molecule monotherapy regimen. The frequency of monotherapy was highest in Germany (32%) and lowest in the UK (13%). Monotherapy was more frequent for patients switched to infliximab (39%) and tofacitinib (39%) and lowest for those switched to tocilizumab IV (12%) and rituximab (11%). When combined into classes of agents, frequency of monotherapy among recently switched patients was 25% for TNFs, 24% for JAK inhibitors, 23% for IL-6 inhibitors, and 16% for non-JAK/IL-6 AMOAs (abatacept or rituximab).
On a country-specific level, rates of TNF monotherapy were highest in Germany (38%) and lowest in the UK (16%). IL-6 monotherapy was also more common in Germany (27%) but least common in France (17%). JAK monotherapy was highest in France (34%) and lowest in the UK (7%), while monotherapy for abatacept/rituximab was highest in Germany (32%) and again lowest in the UK (13%).
Conclusion: The popularity of biologic/small molecule monotherapy varies by EU5 country and while rates are highest for TNF inhibitors, use of biologic/small molecule monotherapy for patients recently switched to a JAK or IL-6 inhibitor are comparable.
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AB0401 SWITCH FROM ETANERCEPT ORIGINATOR TO ETANERCEPT BIOSIMILAR: DATA FROM REAL LIFE

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Background: Biosimilars of antiTNF-α are now available for the treatment of arthritis. There are a lot of data about maintenance of clinical efficacy after switching from originator to biosimilar but also reports about flares and adverse events (AE). Controversies still exist due to ethical and economic reasons. We describe the disease activity trend after switching from etanercept originator (oETA) to its biosimilar (bETA) in a population of Turin, Piedmont, Italy. In this region switch to biosimilar is mandatory by law except in case of patients with history of allergy, off-label, psycological reasons, active disease that required different treatment.
Objectives: To evaluate the disease activity trend before and after switch from oETA to bETA.
Methods: We switched 82 patients (M/F 33/49, mean age 59.65±11.5, duration of disease 17.56±10.3 years) in stable state of disease from oETA to bETA; 49 patients affected by RA, 24 by PsA, 10 by AS. The mean of duration of oETA and bETA treatment was respectively 129.2 and 6.2 months. We evaluated VAS-pain, Global-Health, CRP, number of swollen and tender joints, DAS28 for RA, DAPSA for PsA, HAQ and HAQ-S, BASDAI for AS patients.
Results: Differences of variables between oETA and bETA are summarized in table1.
We didn't find any significant difference between oETA and bETA in order to efficacy. However 8 patients, 5 RA and 4 PsA(9.75%) discontinued bETA because arthritis flare(7) or AE(1).
Conclusion: Data about maintenance of efficacy and percentage of discontinuation were similar to the literature. We didn't find significant differences on efficacy after switching from originator to biosimilar.
However, considering the rate of flares and AE, further strong studies are required.

Treatment	DAS28 RA	HAQ RA	DAPSA PsA	HAQ PsA	BASDAI SA	HAQ-S SA
oETA	2,61 (±0.92)	0.85 (±0.52)	8.15 (± 5.6)	0.88 (0.6)	2.88 (±2.6)	0.85 (±0.42)
bETA	2.68 (±1.21)	0.92 (±0.7)	11,66 (±9.63)	0.9 (±0.69)	2.7 (±2.16)	0.58 (±0.26)

Tab. 1 The analysis of variables between Etanercept originator (oETA) and Etanercept biosimilar (bETA)

REFERENCES

[1] Jørgensen, K. K. et al. Lancet 2017 Jun 10;389(10086):2304-2316.
[2] Kay J and KL Winthrop Nat Rev Rheumatol 2017 Jul;13(7):391-392.
[3] Toussirot E, Marotte H. RMD Open 2017;3:e000492.

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AB0402 MEASURING PATIENT EXPERIENCE OF SWITCHING BIOLOGIC TREATMENT – A SYSTEMATIC LITERATURE REVIEW

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Background: Biologics have transformed the treatment of inflammatory arthritis (IA).However, the complexity of disease management has increased with the introduction of biosimilars and novel treatments. Hence, patient experience and satisfaction has become increasingly important in treatment individualization.
Objectives: Firstly, to assess to what extent IA patient experience of switching biologics is measured in the literature; secondly, to summarize patient-reported outcomes (PROs) as well as medical/non-medical reasons associated with switching.
Methods: A systematic literature review (SLR) was performed in accordance with PRISMA guidelines. EMBASE and MEDLINE were searched for relevant publications from 2013 to present day, together with relevant conference abstracts from 2018 (ACR-ARHP, EULAR, and ISPOR). Studies published in English including either a) patient-reported outcomes (PROs) associated with switching biologics, or b) reasons for switching and/or discontinuing biologics treatment as noted by health care professionals and/or patients were included. The scope was limited to European and North American populations. While the initial search included patient populations with ulcerative colitis in addition to IA patients, results presented within this abstract focus on IA populations only.
Results: After initial screening of 1781 abstracts, sixty-eight studies including IA patients were identified for inclusion in the analysis. Of the remaining studies, 39/68 (57%) included ≥1 treatment switch. The majority of studies were conducted in Europe (36/39; 92%), with the proportion of female patients ranging between 12-90%. Thirteen studies (18%) included at least one PRO, 4 of which only recorded PROs prior to switch (6%). The most commonly reported PRO was PGA/VAS, followed by HAQ and questions asking patients to rank their switching experience using various pre-defined categories (Figure 1). While the most common reasons for discontinuing treatment, which may or may not include switching, was provided in 33 studies (loss of efficacy and safety), reasons strictly for switching are infrequently reported.
Conclusion: Patient satisfaction is important, as it has been linked to clinical safety, treatment effectiveness, and adherence (Doyle et al., 2013). However, this SLR highlights a notable lack of information regarding patient-reported experience of switching biologic treatment. The PROs reported in a minority of studies encompass several regions related to patient well-being – such as pain, fatigue, etc. – but provides very limited information on the experience of switching. Hence, to improve disease management and treatment individualization, further research is required.

REFERENCE

[1] Doyle, et al. A systematic review of evidence on the links between patient experience and clinical safety and effectiveness. BMJ Open, 2013.

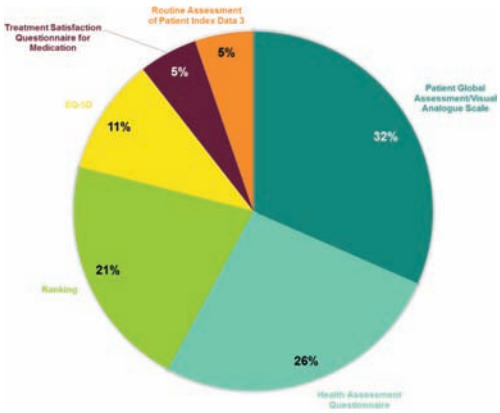


Figure 1

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AB0403 PREDICTORS OF PERSISTENCE OF BIOLOGIC DRUG STEP-DOWN STRATEGIES IN INFLAMMATORY ARTHRITIS: A LONGITUDINAL STUDY IN CLINICAL PRACTICE WITH A LONG FOLLOW-UP

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Background: Recommendations for the management of Rheumatoid Arthritis (RA) and spondyloarthritis (SpA) with bDMARD include dose-tapering

as an adequate option for patients on persistent remission. Although data regarding these strategies has increased in recent years, there is scarce evidence about their long-term effect.

Objectives: Our aim was to analyze the persistence of bDMARD dose-reduction in clinical practice and evaluate its predictors in patients with RA and SpA

Methods: Retrospective longitudinal study from 2006 to 2018. From a cohort of 153 patients with chronic inflammatory arthritis treated with bDMARD (TNF inhibitors, rituximab, tocilizumab, and abatacept) we recruited those with RA and SpA receiving reduced-dose regimens.[1]

Variables analyzed were: persistence of bDMARD dose-reduction, predictors of this persistence reported in the literature such as treatment with glucocorticoids (GC) or conventional synthetic DMARD (csDMARD), disease activity and duration of disease at dose-reduction as well as demographic and other clinical features.

A Cox proportional hazards model was used to identify factors associated with persistence on reduced-doses during the study period.

Results: 56 patients (RA:33; SpA:23) on tapered bDMARD (etanercept 51.8%, adalimumab 32.1%, Infliximab 3.6% and tocilizumab 12.5%) at study entry were included. Their clinical and laboratory features are shown in table 1.

After a mean follow-up on tapered-dose of 4.4 years (range 0.35-8.72), 42.9% of subjects overall remained on reduced doses (RA: 36.4%; SpA: 52.2%). (*Fig.1*)

From those who required discontinuation of the step-down regimen, 16 (48.4%) achieved the therapeutic objective and 7 (22.6%) failed after returning to standard dose respectively.

bDMARD were discontinued in 4 (12.9%) patients due to sustained disease remission (RA=3; SpA=1), 3 (9.7%) due to adverse events and 2 (6.4%) due to other reasons. No significant differences in the variables analyzed were found between patients continuing vs discontinuing reduced-dose regimens.

After adjusting for age, sex, diagnosis and disease duration, the concurrent use of GC at the time of dose-reduction was an independent predictor of discontinuation of the step-down regimen [aHR 3.6 (1.4 – 9.3)]

Conclusion: A significant proportion of patients with RA and SpA (36.4% and 52.2% respectively) can be maintained with reduced doses of bDMARD after a long-term follow-up.

Concurrent use of GC at the time of dose-reduction was found an independent predictor of discontinuation of the step-down regimen.

REFERENCES

[1] Inciarte-Mundo J, et al. Reumatol Clin. 2014;10(1):10–16

Table 1. Demographic and clinical features at bDMARD dose-reduction.

	Total n: 56	Continue tapered bDMARD n: 24	Withdrawn tapered bDMARD n:32
Age	52.3 ± 14.3	54 ±13.9	51.1 ± 14.7
Female	32 (57.1%)	10 (41.7%)	22 (68.8%)
Ever-smokers	25%	23.8%	26.1%
Diagnostics	33	12 (36.4%)	21 (63.6%)
RA	23	12 (52.2%)	11 (47.8%)
SpA			
Mean disease	14.4 ±	18.5±7.9	12.1 ± 4.9
duration	6.8	13.9 ± 7.53	14 ± 5
RA	13.9 ±		
SpA	6.3		
Disease activity	2.3 ± 0.5	2.3 ± 0.3	2.3 ± 0.6
RA (DAS28)	1.6 ± 1.7	1.7 ± 1.8	1.5 ± 1.7
AS (BASDAI)			
Antibody Status	28 (85%)	9 (75%)	19 (90.5%)
(RA)	29 (88%)	9 (75%)	20 (95.2%)
RF			
ACPA			
Erosive disease	24/33	9/12	15/21
(RA)			
bDMARD Naive	28 (85%)	11(91.7%)	17(81%)
RA	17	9 (75%)	8 (72.7%)
SpA	(73.9%)		
Concomitant	19	7(58.3%)	12(55%)
csDMARD	(57.6%)	1(8.3%)	4(36.3%)
RA	5(21.7%)		
SpA			
Concomitant GC	8(24.2%)	2(16.7%)	6(28.6%)
RA	2(9%)	0	2(18.2%)
SpA			

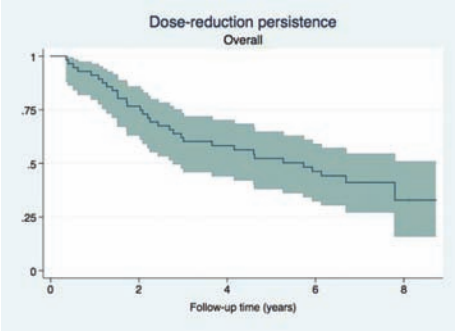


Figure 1. Survival curve for persistence on tapered-dose strategy. Data are proportion (solid line) and 95 CI (coloured area)

Disclosure of Interests: Sebastian C Rodriguez-García: None declared, Raul Castellanos-Moreira Speakers bureau: MSD, Lilly, Victoria Hernandez: None declared, Jose Inciarte Employee of: Lilly, Virginia Ruiz-Esquide Speakers bureau: Sanofi, Lilly, MSD, Jose A. Gómez-Puerta Consultant for: Pfizer, Roche, Speakers bureau: Abbvie, BMS, Janssen, MSD, Pfizer, Roche, Raimón Sanmartí Speakers bureau: PFIZER, SANOFI, LILLY, MSD, UCB, NOVARTIS, JANSSEN

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AB0404 VALIDATION OF A THERAPEUTIC DRUG MONITORING TEST TO MEASURE THE ADALIMUMAB BIOSIMILAR SB5 IN COMPARISON WITH THE REFERENCE ADALIMUMAB

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Background: Validation of therapeutic drug monitoring (TDM) tests is an essential requirement for using these tools to help assess reasons for non-response. The arrival of biosimilars has prompted a need to validate that existing TDM tests are suitable to determine drug levels for all versions of a given molecule. The adalimumab (ADL) biosimilar SB5 (Biogen) was authorised by the European Commission in August 2017, and has recently become available for prescription in several European countries. Promonitor®-ADL test is routinely used to monitor IBD patients treated with ADL.

Objectives: In this study we validated the suitability and performance of Promonitor-ADL CE-marked TDM test for quantifying SB5 serum concentrations in comparison to reference adalimumab (Abbvie).

Methods: The study evaluated imprecision and bias applied to the reference ADL and SB5 biosimilar. The validation study was in line with the design requirements established in the Clinical & Laboratory Standards Institute (CLSI) guideline EP10-A3 for the determination of imprecision and bias. Imprecision was evaluated using three replicates of five human serum sample matrices representative of clinically relevant ADL concentrations and spanning the measurement range of Promonitor-ADL.[1] Validations were ran on one instrument with one kit lot by one operator over six non-consecutive operating days and one run per testing day, with an acceptance criterium of CV%≤20%. The Lower Limit of Quantification (LLOQ) of Promonitor-ADL was determined according to CLSI guideline EP17-A2.

Results: The imprecision of Promonitor-ADL was calculated by estimating the components of variance due to within-run and between-day factors meet the accuracy goals proposed at all concentration levels of SB5 vs the reference adalimumab (CV% between 5% and 12%). The assessment of accuracy showed that Promonitor-ADL equally measures the active moiety of the reference adalimumab or the adalimumab biosimilar SB5. The test is able to quantify SB5 in the measurement range of 0.9 to 10.9 mg/mL with a bias estimate of -0.124 (1%) to 0.897 (10%) mg/mL and an overall imprecision of 5% to 11%. The measurement range includes the recommended clinical decision points. LLOQ of the test to determine ADL was determined to be 0.36 mg/mL.

Conclusion: This study demonstrates that Promonitor-ADL test can measure either the reference ADL drug or the adalimumab biosimilar SB5 with equivalent sensitivity, precision and accuracy.

REFERENCES

[1] Feuerstein, et al 2017. Gastroenterology 153: 827–834 AGA Institute Guideline on Therapeutic Drug Monitoring in IBD.

Disclosure of Interests: M. Begoña Ruiz-Argüello Employee of: Progenika Biopharma - Grifols employee, Ainara Maguregui Employee of: Progenika Biopharma - Grifols employee, Antonio Martínez Employee of: Progenika Biopharma - Grifols employee, Daniel Nagore Employee of: Progenika Biopharma - Grifols employee
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AB0405 ADALIMUMAB THERAPEUTIC DRUG MONITORING TEST VALIDATED FOR MEASURING ABP 501 BIOSIMILAR

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Background: Promonitor®-ADL test is routinely used to monitor IBD patients treated with adalimumab (ADL). ABP 501 (adalimumab biosimilar; Amgen) was authorised throughout the European Union in March 2017 and has been recently launched in several countries. Therapeutic drug monitoring (TDM) is broadly used as an aid for patient management. However, all TDM tests available should be properly validated against each new approved biosimilar in order to ensure safe application for patient monitoring as these may guide dose adjustments.
Objectives: Here we validate the suitability and performance of Promonitor-ADL CE-marked test for quantification of the adalimumab biosimilar ABP 501 in comparison to the reference adalimumab drug (Abbvie).
Methods: The validation study was in accordance with the design requirements established in the Clinical & Laboratory Standards Institute (CLSI) guideline EP17-A2 (Lower Limit of Quantification, LLOQ) and EP10-A3 (imprecision and bias). CLSI guidelines set a standard for the diagnostic industry accepted by all regulatory agencies. LLOQ was determined with four independent human serum sample matrices per each of three low level ADL concentrations, replicated three times per two lots of Promonitor-ADL (Progenika, Spain) kits for each drug, the reference drug and the adalimumab biosimilar ABP 501, over three days by one operator. Imprecision was evaluated using three replicates of five human serum sample matrices representative of clinically relevant ADL concentrations and spanning the measurement range of Promonitor-ADL, run on one instrument with one kit lot by one operator over six non-consecutive operating days and one run per testing day, with an acceptance criteria of CV%≤20%.
Results: The LLOQ of Promonitor-ADL for the adalimumab biosimilar ABP 501 and reference adalimumab were 0.34 mg/mL and 0.36 mg/mL, respectively. LLOQ values met accuracy goal proposed based on total error ≤25% and precision. The imprecision of Promonitor-ADL calculated by estimating the components of variance due to within-run and between-day factors meet the accuracy goals proposed at all concentration levels of ABP 501 vs the reference adalimumab (CV% between 5% and 10%). The bias study showed that Promonitor-ADL can equally measure the active moiety ADL either in the reference biologic ADL or in the biosimilar ABP 501. The test is able to quantify the adalimumab biosimilar ABP 501 in the measurement range of 0.9 to 10.9 mg/mL with a bias estimate of -0.089 to 0.306 mg/mL and an overall imprecision of 6% to 9%. The measurement range includes the recommended clinical decision points.
Conclusion: Promonitor-ADL test can equivalently measure either the reference ADL or the approved adalimumab biosimilar ABP 501 with the same sensitivity, precision and accuracy.
Disclosure of Interests: M. Begoña Ruiz-Argüello Employee of: Progenika Biopharma - Grifols employee, Ainara Maguregui Employee of: Progenika Biopharma - Grifols employee, Antonio Martínez Employee of: Progenika Biopharma - Grifols employee, Daniel Nagore Employee of: Progenika Biopharma - Grifols employee
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AB0406 THE POTENT WEAPON FOR RHEUMATOID ARTHRITIS-INTERSTITIAL LUNG DISEASE : RITUXIMAB EXPERIENCES

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Background: Rheumatoid arthritis (RA) is a common inflammatory disease with unknown etiology and systemic involvement (1). About 40% of RA patients have extraarticular involvement. Lung involvement is the most common extraarticular finding. The use of rituximab (RTX) in the treatment of rheumatoid arthritis- interstitial lung disease (RA-ILD) has been increasing in recent years (2).
Objectives: To present our rituximab experience in patients with RA-ILD.
Methods: Between April 2015 and April 2018, sixteen patients with RA-ILD who were followed up with RTX treatment in our university internal medicine-rheumatology department were included in this study. High resolution computed tomography (HRCT), carbon monoxide diffusion measurement (DLCO), pulmonary function test (PFT) and routine laboratory tests were examined.
Results: The median age of the patients was 68 years (min: 52-max: 77). 4 patients (25%) were male and 12 (75%) patients were female. Four of our patients (25%) were active smokers. Non-specific interstitial pneumonia (NSIP) was seen in 10 (62.5%) patients and usual interstitial pneumonia (UIP) was seen in 6 (37.5%) patients. Before RTX, 8 patients were receiving methotrexate and 8 patients were using leflunomide. Four patients had anti-TNF (tumor necrosis factor) treatment. Median during treatment time was 6 months. Other features of the patients are summarized in Table 1. All patients had dyspnea with exertion before treatment. The Forced Vital Capacity (FVC) median was% 70 and DLCO was% 66. Although 2/16 patients received cyclophosphamide treatment, there was no clinical response and then RTX treatment was started. Protocol of treatment was every 6 months (days 0 and 15 days 1 g). After 6 months, FVC values improved with NSIP pattern (p= 0.04). There was no improvement in the UIP pattern but remained stable (Table 2). Clinically, patients' exertional dyspnea improved. There were no serious side effects in the follow-up of the patients.
Conclusion: There is no valid guideline for RA-ILD treatment. Patient-based decision-making is important in the treatment of these patients. In recent years, RTX seems to be quite effective in RA-ILD. However, long-term and extensive studies are needed in terms of maintenance treatment and possible side effects.

REFERENCES

[1] McInnes IB, G. Schett, The pathogenesis of rheumatoid arthritis. N Engl J Med 2011; 365: 2205-19.
[2] Deborah Assayag, Joyce S. Lee, Talmadge E. Kıng, Jr., Rheumatoid Arthritis Associated Interstitial Lung Disease: A Review, MEDICINA (Buenos Aires) 2014; 72: 158-165

Table 1. Clinical and epidemiological Features of the RA patients

Age	68 (min:52-max:77)
Gender: Male	4 (25%)
Female	12 (75%)
Serology: Positive	14 (87.5%)
Negative	2 (12.5%)
Smoking history	4 (25%)
Medication: Methotrexate	8 (40%) patients
Leflunomide	8 (40%)
Anti-TNF	4 (20%)
Duration of disease	10 years
Duration of treatment	6 months
İAH pattern: NSIP	10 (62.5%)
UIP	6 (37.5%)

Table 2. The FVC and DLCO values of pre- and post- treatment

	UIP	NSIP	
Pre FVC	70	76	
Post FVC	70	80	p=0.04
	p>0.05		
Pre DLCO	65	70	
Post	66	71	p>0.05
DLCO	p>0.05		

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7559

AB0407 HIGH REMISSION RATES IN PATIENTS WITH RHEUMATOID ARTHRITIS USING BIOLOGICS UNDER A TREAT TO TARGET STRATEGY AND A COMPREHENSIVE DISEASE-MANAGEMENT MODEL. FIVE YEAR FOLLOW-UP RESULTS FROM A REAL-LIFE SETTING

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Background: Treat to target (T2T) strategy for rheumatoid arthritis (RA) aims to achieve remission or low disease activity. On the other hand, biological disease-modifying antirheumatic drugs (bDMARDs) have shown to be effective to achieve clinical remission or, at least, low disease activity in patients with RA. On the other hand, comprehensive healthcare programs have demonstrated good clinical outcomes in patients with chronic conditions.

Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) in patients receiving biological therapy during 5 years, and who were subjected to a multidisciplinary care program.

Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed during 2015-2017; those patients were followed-up under T2T standards and a multidisciplinary approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3-5 weeks (DAS28 > 5.1), every 7-9 weeks (DAS28 $\geq$ 3.1 and $\leq$ 5.1), and every 11-13 weeks (DAS28 < 3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 > 3.2 unless patient´s conditions don't permit it; we considered this follow-up type as implementation of a T2T strategy in patients with RA. Patients entered into a multidisciplinary program of care with periodic consultations not only to rheumatology but with a physiatrist, psychologist, physiotherapist, occupational therapy nutrition, and, a patient focused program. With a multidisciplinary model of care the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA. We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We compared disease activity at base line and at the end of follow-up.

Results: 747 patients meet our inclusion criteria, 85% of our patients were women, median age was 57 years RIQ (50-64); The most prescribed bDMARD was certolizumab 25% followed by etanercept 14%, tocilizumab 12%, abatacept 12%, golimumab 10% rituximab 8%, adalimumab 7%, infliximab 6% and Tofacitinib 6%. At beginning 53% of patients were in moderate disease activity and, 25% in high disease activity while at the end of follow up 89% of patients had achieved remission. See Table 1. It was stablished statistical significance between changes in median DAS28 at beginning and, at the end of follow-up (P<0.05).

Table 1. Comparison of DAS28

ACTIVITY LEVEL	BASELINE		5 YEAR FOLLOW-UP	
	n	%	n	%
REM			653	88.60
LDA	177	23	37	5.02
MDA	388	53	47	5.97
HDA	182	24	3	0.41

Conclusion: Biological therapy is effective for treating patients with RA, there was an evident global improvement of DAS28 in a cohort of RA patients. Also, our findings agree with other studies where T2T programs have shown improvements in disease activity in patients with RA. Thus, multidisciplinary T2T comprehensive healthcare programs should be widely implemented in patients with RA.

Disclosure of Interests: Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Michael Cabrera: None declared, Diana Buitrago-Garcia: None declared, Eva Cardozo: None declared, Ivania Ramirez: None declared, Danny Gomez: None declared, Edwin Castillo: None declared, Sandra Farietta: None declared

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AB0408 FIXED-INTERVAL VERSUS ON-DEMAND RETREATMENT STRATEGY WITH RITUXIMAB IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY

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Background: Rituximab (RTX), a monoclonal anti CD20 B-cell antibody is safe and effective in the treatment of Rheumatoid Arthritis (RA). The most optimal retreatment strategy in responding patients is still unclear.

A recent study by Chatzidionysiou et al suggests that RTX retreatment with Fixed-Interval (FI) strategy is better than retreatment with an On-Demand (OD) strategy. [1] However, whether FI treatment strategy is also superior in a treat to target setting is not known.

At our centre (Sint Maartenskliniek, the Netherlands), patients were retreated with RTX using the FI strategy and the OD strategy, by discretion of the rheumatologist, and using treat to target of DAS28CRP <2.9 in all patients.

In the FI strategy, patients receive retreatment after a predefined fixed period, mostly every 6 months. In the OD strategy, patients receive retreatment in case they experience increase in disease activity. In our hospital, most of the OD strategy patients were switched to the FI strategy in 2014 based on best evidence at that time, enabling us to retrospectively compare effectivity of these strategies.

Objectives: To compare the effectivity of retreatment of RA patients with RTX following the FI or OD retreatment strategy.

Methods: Adult ($\geq$18) RA patients (clinical diagnosis) who started RTX treatment (1 or 2 x 1000mg or 2 x 500mg intravenous) between 1-1-2008 and 1-6-2016 and received at least 3 infusion cycles were included. Patients were treated with either FI or OD strategy, or crossed over from OD to FI. For on demand treatment, RTX retreatment could be planned at the daycare within 2-4 weeks.

Primary outcome was DAS28-CRP, secondary outcome was mean yearly dose of RTX. Baseline characteristics and follow up data (DAS28-CRP scores, information on RTX infusions, and steroid injections) were retrospectively extracted from patients' health records.

A linear mixed model was used to analyse the influence of the strategies on DAS28-CRP score. Time since start of RTX, calendar year, RTX dose, intra-articular (IA) or intramuscular (IM) steroid injection <6 weeks ago, concomitant csDMARD use at start of treatment and RF status were added to the model as fixed effects. Data was analysed using Stata 13.1.

Table 1. Baseline patient characteristics

Age, mean (sd)	59.6 (12.4)
Disease duration at RTX start, median (IQR)	11 (5-17)
csDMARD use at RTX start, n (%)	124 (58%)
Rheumatoid factor positivity, n (%)	166 (78%)
Anti-CCP positivity, n (%)	152 (72%)
Baseline DAS28CRP, mean (sd)	4.0 (1.2)
Strategy, n (%)	154 (72%)
Fixed interval	25 (12%)
On demand	34 (16%)
Both strategies	

Results: 213 patients were included. 154 following FI strategy, 25 following the OD strategy and 34 switching from OD to FI. Median duration of follow up was 38 months (IQR: 23-64), with a median number of 8 (IQR 5-12) DAS28-CRP measurements per patient. Patient characteristics are shown in Table 1. The OD strategy was not associated with higher DAS28-CRP score compared to FI strategy: adjusted difference was 0.09 DAS28-CRP point (95% CI: -0.08 to 0.26). Regardless of used strategy, DAS28-CRP improved significantly both over year of treatment, and by time from the start of RTX treatment. Furthermore was rheumatoid factor positivity associated with an lower DAS28-CRP in all patients, with adjusted difference of - 0.37 (95%CI: - 0.60 to - 0.14). Average yearly RTX dose was 1899mg/yr (SD: 604) under the FI strategy and 1740mg/yr (SD: 732) under the OD strategy (95% CI difference: -336 to 34mg/yr).

Conclusion: Retreatment of RA patients with a fixed interval strategy does not seem to lead to better disease control or more drug use compared to an on demand strategy. A possible explanation might be the use of treat to target in our centre. Our study suggests that either strategy might be chosen in shared decision making and following treat to target.

REFERENCES
[1] Chatzidionysiou, et al. J Rheumatol. 2017 Feb;44(2):162-169.

Disclosure of Interests: None declared
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AB0409 B CELLS PROFILE AS A BIOMARKER FOR EARLY IDENTIFICATION OF OPTIMAL RESPONDERS TO TNF INHIBITORS IN RHEUMATOID ARTHRITIS

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Background: The most common biological agents used as disease-modifying treatment in rheumatoid arthritis (RA) are TNF inhibitors (TNFi). Although these new strategies to treat RA have improved the course of the disease, approximately 30-50% of patients do not respond to this therapy. Early identification of optimal responders is crucial in the clinical setting.
Objectives: The aim of this study was to investigate if baseline percentages of different leukocyte subsets in peripheral blood (PBMCs) can contribute to identify RA patients who will respond to TNFi.
Methods: This was a prospective bi-center pilot study including 100 RA patients under TNFi therapy. Clinical activity was assessed at baseline and 6 months of treatment by disease activity score 28 (DAS28), considering optimal responders if they reached remission at 6 months (DAS28≤2.6). PBMCs were obtained before treatment and different leukocyte subsets were evaluated by flow cytometry (FACSCantoII instrument). The association between the percentage of PBMCs at baseline and clinical response at 6 months was evaluated through logistic regression models (odds ratio; 95% CI). All the analyses were adjusted by sex, age, disease duration, concomitant methotrexate, baseline DAS28 and seropositivity (ACPA and/or RF).
Results: Demographic characteristics are shown in Table 1. After 6m of TNFi treatment, 40% of the patients achieved clinical remission. A significant association between higher percentage of total B cells (OR=1.19; 95%; CI:1.05-1.35; p=0.007) and naive B cells (Bn; OR=1,32; 95%; IC:1.08-1.61; p=0.007) at baseline and clinical response was found. The other PBMC subsets (monocytes, NK cells, CD4+ and CD8+ T cells subtypes) did not show statistical differences (Figure 1).
Conclusion: Our results suggest that basal B cells profile may contribute to identify optimal responders to TNFi in RA. (Funding: ISCIII (PI16/01092, PI16/00474).

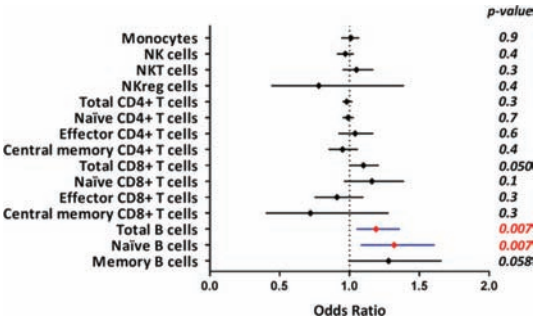


Figure 1. legend: Association between the percentage of PBMC subset before TNFi and the clinical remission. Multivariate logistic regression analysis was performed for each PBMC subset. The percentage of total B cells and in naïve B cells were independently associated with the clinical response. No association was found in other PBMC subsets. The analyses were adjusted by sex, age, disease duration, concomitant-methotrexate, seropositivity and baseline-DAS28.

Baseline patients' characteristics	Total patients (n=100)
Age (years); *mean±SD*	*53±13*
Female; n (%)	*84 (84)*
Disease duration (years); *median (IQR)*	*8 (4-12)*
Rheumatoid factor positive; n (%)	*77 (77)*
ACPA positive; n (%)	*83 (83)*
Smoking habit; n (%)	
no	*46 (46)*
smoker	*20 (20)*
ex-smoker	*34 (34)*
Body mass index (kg/m^2); *median (IQR)*	*24.8 (22.9-29.6)*
DAS28; *mean±SD*	*4.8±1.2*
CRP (mg/L); *median (IQR)*	*5.7 (2.2-12.4)*
Previous TNFi treatment; n (%)	*13 (13)*
TNFi type; n (%)	
Monoclonal antibodies	*55 (55)*
Etanercept	*45 (45)*
TNFi monotherapy	*4 (4)*
Concomitant csDMARD; n (%)	*96 (96)*
OnlyMethotrexate (MTX)	*51 (51)*
*OnlyothercsDMARDs (OD)**	*18 (18)*
MTX + OD	*27 (27)*
Prednisone; n (%)	*57 (57)*

Table1

Disclosure of Interests: Cristina Sobrino: None declared, Borja Hernández-Breijo: None declared, Carlota García-Hoz: None declared, Israel Nieto-Gañán: None declared, Victoria Navarro-Compán: None declared, ANA MARTÍNEZ-FEITO: None declared, Javier Bachiller-Corral: None declared, Gemma Bonilla: None declared, Paloma Lapuente-Suanzes: None declared, Cristina Pijoan Moratalla: None declared, DORA PASCUAL-SALCEDO Grant/research support from: Pfizer, Speakers bureau: Pfizer, Abbvie, Takeda, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Garbiñe Roy: None declared, Mónica Vázquez: None declared, Luisa María Villar: None declared, Chamaida Plasencia Speakers bureau: Pfizer, MSD, Eulalia Rodríguez-Martín: None declared
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AB0410 DISCONTINUATION OF ORAL GLUCOCORTICOID AFTER INITIATION OF BIOLOGICAL DMARD DUE TO A HIGHER DOSE OF METHOTREXATE; A RETROSPECTIVE OBSERVATIONAL STUDY BASED ON DATA FROM A JAPANESE MULTICENTER REGISTRY STUDY

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Background: In the treatment of rheumatoid arthritis, glucocorticoid that provide anti-inflammatory effects in the early stage of treatment is an important drug. We recommend discontinuing of glucocorticoid as much

as possible within 6 months[1], but many patients have taken oral glucocorticoid for the long term in daily clinical practice. The frequency of use of glucocorticoid has gradually declined, and there are several reports on discontinuation of glucocorticoid due to the initiation of bDMARD[2, 3]. However, there is no report showing the relation between discontinuation of glucocorticoid and MTX dose.

Objectives: The aim of this study is to examine association of methotrexate (MTX) dose with discontinuation of glucocorticoid after one year since initiation of biological DMARD (bDMARD) as 1st bDMARD.

Methods: We established the large observational cohort, the Nagoya University orthopedic facility multicenter study (TBCR), and a total of 3119 patients used biological DMARD. 564 patients who used glucocorticoid and MTX when bDMARD was initiated as 1st bDMARD were enrolled. In the first study, we examined predictive factors of discontinuation of glucocorticoid after one year since initiation of bDMARD by using multivariate analysis in the two groups, which patients continued to use glucocorticoid and discontinued to use glucocorticoid. In the second study, we adjusted the background at the time of initiation of bDMARD by using propensity score matching (PS) in the two groups, MTX≤8mg (L group) and MTX>8mg (H group).

Results: 400 patients continued to use glucocorticoid and 164 patients discontinued to use glucocorticoid. In the multivariate analysis, age (Odds ratio (OR)0.98), MTX dose (OR1.09) and glucocorticoid dose (OR0.88) were independently predictive factors of discontinuation of glucocorticoid. When we adjusted age, disease duration, sex, disease activity, RF/ACPA, glucocorticoid dose by using PS matching, 105 pairs were extracted. There were obvious significant differences between 24 patients (22.9%) in the L group and 43 cases (41.0%) in the H group (P = 0.007), where glucocorticoid was discontinued at one year after the initiation of bDMARD.

Conclusion: This cohort study investigated the association with discontinuation of oral glucocorticoid and MTX dose in the patients treated with bDMARD. TBCR revealed that, in the clinical practice, glucocorticoid use was decreasing in the patients treated with bDMARD. MTX dose at the time of initiation of bDMARD was predictive factor of discontinuation of glucocorticoid. A higher dose of MTX associated with discontinuation of glucocorticoid in the patients treated with bDMARD.

REFERENCES

[1] Smolen JS, Landewe R, Bijlsma J, Burmester G, Chatzidionysiou K, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun; 76(6):960-977.

[2] Shimizu Y, Tanaka E, Inoue E, Shidara K, Sugimoto N, Seto Y, et al. Reduction of methotrexate and glucocorticoids use after the introduction of biological disease-modifying anti-rheumatic drugs in patients with rheumatoid arthritis in daily practice based on the IORRA cohort. Mod Rheumatol. 2018 May; 28(3):461-467.

[3] Seror R, Dougados M, Gossec L. Glucocorticoid sparing effect of tumour necrosis factor alpha inhibitors in rheumatoid arthritis in real life practice. Clin Exp Rheumatol. 2009 Sep-Oct; 27(5):807-813.

Disclosure of Interests: Mochihito Suzuki Speakers bureau: Bristol-Myers Squibb, Toshihisa Kojima Grant/research support from: Chugai Pharmaceutical (Investigator Initiated Study), Novartis, Nippon Kayaku, Eli Lilly, Eisai, Speakers bureau: Chugai Pharmaceutical, Takeda Pharmaceutical, Pfizer, Eli Lilly Japan, Bristol Myers Squibb, Ono Pharmaceutical, Daiichi Sankyo, Astelas, UCB, Janssen Pharmaceutical, Tanabe Mitsubishi, Nobunori Takahashi Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Eisai, Mitsubishi Tanabe, and Pfizer. YS has received speakers' fees from Astellas, Bristol-Myers Squibb, and Ono, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant for: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama

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AB0411

TNF ALPHA INHIBITORS INFLUENCE THE CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) patients die because of cardiovascular diseases more often than the general population. Nowadays RA is considered as an independent risk factor for cardiovascular disease (CVD). A long-lasting inflammatory process, immunological dysregulation and endothelial dysfunction play an important role in the pathogenesis of progressive atherosclerosis in RA [1,2].

Objectives: The aim of the study was to assess the influence of biological treatment on cardiovascular risk factors in RA population

Methods: 38 RA patients with active disease (DAS28>5.1) and 22 age and sex matched healthy controls were enrolled in the study. All the patients were treated with TNF alpha inhibitors (n=20 etanercept, n=18 adalimumab), with the background methotrexate (10-25mg weekly). The clinical state was assessed at the beginning of the study and 6, 12 and 18 months after. All the patients underwent the following tests: DAS 28 assessment, basic laboratory measurements (including homocysteine levels, fibrinogen, lipid profile), electrocardiogram (ECG), flow-mediated dilation (FMD) and cartoid intima-media thickness (cIMT) assessment and echocardiography. The local bioethics committee approved the study (KB-753).

Results: 27 woman and 11 man (71% and 29% respectively) with high disease activity despite long-term treatment with synthetic disease modifying antirheumatic drugs were enrolled in the study. Mean age was 52 years (SD ± 9,6), 95% of the patients were RF-positive, 63% anti-CCP-positive. Of them 24% were current smokers, 58% had arterial hypertension and 66% had concomitant hypercholestrolaemia. In comparison to the control group, there were statistically significantly higher values of cIMT in RA patients. Moreover there was a positive correlation between cIMT thicknes and duration of RA. A reduction of cIMT (mainly during first 12 months) and an increase in FMD values were observed in the course of the treatment ($p<0.05$). The increase in FMD value (0.03 vs 0.37) correlated with decrease of the inflammatory markers, which may be a result of an improvement in endothelial dysfunction due to anti-TNF-alpha treatment. The decrease in total cholesterol ($p<0.05$), LDL cholesterol ($p=0.03$) and Castelli risk index ($p<0.05$) were also noted, no changes of the doses of cholesterol-lowering theraphy were done during the follow up. There was a positive correlation between homocysteine and uric acid levels and there was a statistically significant decrease in both parameters in the course of the treatment (11.31 vs 8.91 [mol/l] and 5.92 vs 4.77 [mg/dl], respectively). Normal left ventricular geometry was observed after 12 months of biological therapy in patients with concentric remodeling of the left ventricle. Furthermore echocardiography revealed a significant decrease in LVEDD, IVSD, LA, FS, RVEDD after 18 months of the biologic treatment.

Conclusion: Our results confirm earlier data that TNF alpha inhibitors may favorably influence on endothelial dysfunction. Besides TNF inhibitors can protect against increase in relative wall thickness of left ventricle. The anti-TNF alpha therapy not only reduces the activity of the disease in affected joints but also has a positive impact on selected cardiovascular risk factors in RA population.

REFERENCES

[1] Solomon DH., Goodson NJ., Katz JN., i wsp. Patterns of cardiovasular risk in rheumatoid arthritis. Ann Rheum Dis. 2006; 65: 1608-1612

[2] Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD. Metabolic syndrome in rheumatoid arthritis. Maedica (Buchar). 2012 Jun;7(2):148-52.

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AB0412 **FACTORS THAT AFFECT THE RESPONSE TO TOCILIZUMAB WITH REGARD TO WORK PRODUCTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A 2-YEAR FOLLOW-UP OF THE FIRST ACT-SC STUDY**

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Background: Rheumatoid arthritis (RA) is a major cause of work disability, sickness-related absence from work, presenteeism, and loss of productivity. The decrease in work productivity that results from persistent pain, impaired mobility and function, and reduced quality of life (QOL) has important personal, societal, and economic consequences[1]. The efficacy of tocilizumab (TCZ) as monotherapy and in combination with methotrexate for RA is well known. Thus, in this study, we expected TCZ treatment to improve work productivity on the basis of interim results of up to 52 weeks[2].

Objectives: We aimed to evaluate the long-term (104 weeks) control of RA in Japanese paid workers and house workers treated with TCZ and identify factors affecting the response (responder/non-responder) to TCZ in terms of work productivity.

Methods: The FIRST ACT-SC Study (UMIN-CTR: UMIN000012306) was a cohort study that assessed the 2-year treatment outcome of TCZ-SC (administered alone or with disease modifying anti rheumatic drugs) in biologics-naive Japanese patients with RA. Logistic regression analysis was performed to determine the factors contributing to treatment response in terms of activity impairment (AI) in the WPAI questionnaire, which is an index for the evaluation of overall daily life performance. In addition, the associations of these responses to treatment withdrawal rate and QOL were also evaluated.

Results: Of the 377 enrolled participants, 357 who were treated with TCZ-SC were included in the analysis. AI was improved from 56.2% at baseline to 22.9% at 104 weeks in the patients who received TCZ. In the single regression analysis, the factors that were statistically significant in the logistic regression analysis were job type (p=0.045), K6 as a measure of psychological distress (p=0.030), Health Assessment Questionnaire-Disability Index (HAQ-DI; p=0.023), and EuroQol five-dimensional descriptive system (EQ-5D) score (p=0.006). In the multiple logistic regression analysis, disease duration, academic background, AI, EQ-5D score, ESR, and CRP level were identified as factors that affected response. The results showed a strong association between the results of the subjective assessments such as the utility value of EQ-5D. At 104 weeks, the mean difference in AI between the EQ-5D scores of <0.6 at baseline and ≥0.6 was significant (−22.94% vs −30.50%; p=0.029). Moreover, the mean difference between the HAQ-DI of <1.5 at baseline and ≥1.5 was significant (−20.46% vs −29.08%; p=0.013). A disease duration of <1 year was also associated with being an AI responder. A significant difference in withdrawal rate was found between the responders and non-responders (27.0% vs. 46.9%; p<0.001), and the 2-year quality-adjusted life-year was also significantly higher in the AI responders.

Conclusion: Starting TCZ-SC treatment at an early stage while taking into consideration the subjective self-assessments of the patients may contribute to improvements in labour productivity and QOL, and long-term treatment continuation.

REFERENCES

[1] Best Pract Res Clin Rheumatol. 2015;29(3):495-511.
[2] Arthritis Res Ther 2018;20:151.

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AB0413 **THE PROSPECTIVE ASSESSMENT OF RITUXIMAB AND TOCILIZUMAB TREATMENT EFFECT ON RF-IGM AND ACPA TITRES IN RHEUMATOID ARTHRITIS PATIENTS**

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Background: Rheumatoid arthritis (RA) is associated with several specific autoantibodies, which can be used as diagnostic and prognostic markers. These include rheumatoid factor IgM (RF-IgM) and anti-citrullinated protein autoantibodies (ACPA). The data reporting an impact of biological disease modifying anti-rheumatic drugs (bDMARDs) on RA serological markers are divergent, probably depending on the type of treatment.

Objectives: The goal of this study was to prospectively evaluate the impact of bDMARDs [rituximab (RTX) and tocilizumab (TCZ)] on titers of RA serological markers (RF IgM, ACPA), in correlation with the disease activity assessment.

Methods: The study was conducted in the consecutive 42 patients with RA (36 women, 6 men), with the mean (SD) age 48.9 (13.8) and disease duration 9.2 (3.8) years. The treatment with RTX was administered to 30 patients and with TCZ to 12 patients. The following parameters were assessed for all patients: joint counts, disease activity index of 28 joints (DAS28), complete blood cell counts, erythrocyte sedimentation rate (ESR), serum concentration of serum amyloid A (SAA), RF-IgM, ACPA. Blood samples were taken before the drug administration (baseline) and in consecutive months (3, 6 and 9 months).

Results: Parameters of the disease activity decreased significantly in consecutive months, in comparison with the baseline assessment, in both treatment groups. The mean (SD) DAS28 decreased significantly in both groups (RTX and TCZ): respectively at baseline: 5.75 (0.69) and 5.47 (0.51); month 3: 3.92 (1.13) and 2.84 (0.76); month 6: 3.23 (1.09) and 2.3 (0.94); month 9: 3.67 (1.19) and 2.12 (0.81). The mean (SD) SAA concentration was significantly lower in consecutive months, in both groups (RTX and TCZ): respectively at baseline: 408.5 (268.2) and 402.0 (291.0) ug/ml; month 3: 214.2 (255.3) and 83.6 (157.8) ug/ml; month 6: 100.2 (154.9) and 31.5 (46.3) ug/ml; month 9: 108.5 (128.8) and 26.7 (32.4) ug/ml. The significant reduction of RA specific autoantibodies (RF-IgM and ACPA) was noted in the group of patients treated with RTX (Figure 1, Figure 2). Treatment with TCZ did not affect significantly RA specific autoantibodies up to 6 months of therapy; the significant decrease of ACPA concentration was noted only between baseline and

month 9 (Figure 3); no significant change of RF-IgM was observed (Figure 4).

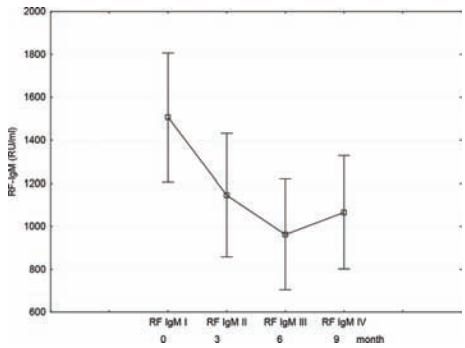


Figure 1. RF-IgM concentrations during RTX treatment.

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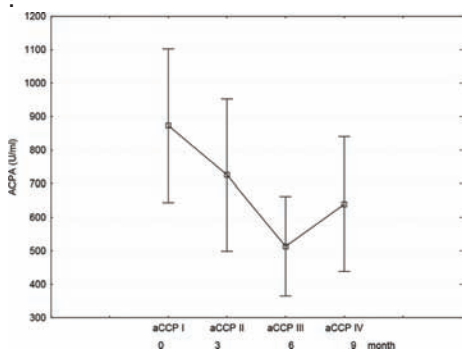


Figure 2. ACPA concentrations during RTX treatment.

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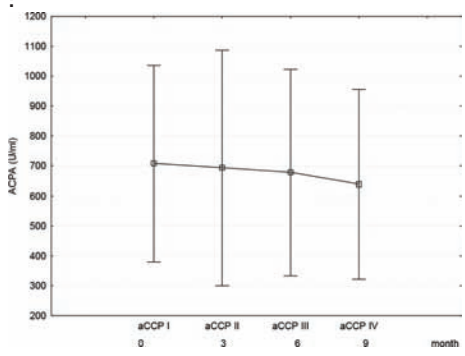


Figure 3. ACPA concentrations during TCZ treatment.

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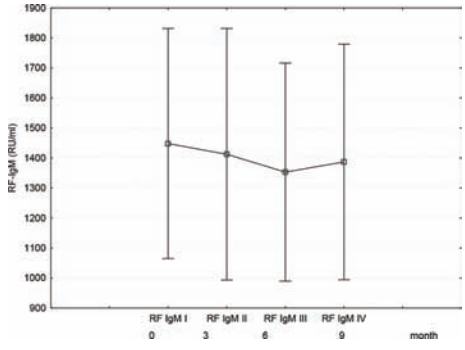


Figure 4. RF-IgM concentrations during TCZ treatment.

Conclusion: The results of the study suggest that both bDMARDs reduced significantly the disease activity in RA patients. The treatment with both drugs was associated with a significant reduction of SAA. However only RTX treatment affected significantly the production of disease specific autoantibodies. Long-term observation is necessary to assess a reliable effect of bDMARDs on the production of marker autoantibodies in association with the disease activity. **Disclosure of Interests:** Olga Borys: None declared, Bozena Targonska-Stepniak Speakers bureau: Sandoz, Berlin-Chemie, Magdalena Dryglewska: None declared, Maria Majdan Speakers bureau: MSD, UCB, Abbvie, Roche DOI: 10.1136/annrheumdis-2019-eular.3476

AB0414

THE IN VITRO EFFECT OF BIOLOGICAL AND CONVENTIONAL DISEASE MODIFYING ANTI RHEUMATIC DRUGS (DMARDS) ON FIBROCYTE DIFFERENTIATION IN RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY CONTROLS

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Background: Fibrocytes are circulating cells with both myeloid and haemopoietic properties. They home in tissues with active inflammation, where they differentiate into mature fibrocytes that are involved in several inflammatory pathways. One complication of Rheumatoid Arthritis (RA) is Interstitial Lung Disease (ILD) resulting in high mortality and with limited treatment options. Fibrocyte levels are elevated in RA patients compared with healthy individuals and further increased in RA patients with signs of ILD (reduced diffusion capacity) and in patients with idiopathic lung fibrosis (IPF) or scleroderma. Thus, fibrocytes have been proposed as a future treatment target.

Objectives: We investigate the effect of corticosteroids, conventional Disease Modifying Anti Rheumatic Drugs (cDMARDs) and biological DMARDs (bDMARDs) on the *in vitro* differentiation of isolated peripheral blood mononuclear cells (PBMCs) into mature fibrocytes.

Methods: 10 participants were included (five patients with RA and five healthy controls). Information on current medication, sex, age, serology and disease activity were collected. PBMCS were isolated and cultured for 5 days in four wells per drug. Drugs included prednisolone, cDMARD (Methotrexate, Sulfasalasine, Hydroxycloroquine) and bDMARD (Inflectra, Etanecept, Tocilizumab, Adalimumab, Abatacept, Rituximab), and control wells with no drugs.

Results: Overall, abatacept and prednisolone significantly suppressed differentiation of PBMC into fibrocytes compared to control wells, see Figure 1 ($p=0.02$ and $p<0.01$, respectively) (n=10). The reductive effect of Abatacept was significant among RA patients ($p=0.009$ and) but not among healthy subjects. In overall analysis (n=10), Abatacept reduced fibrocyte levels with an average of 44% overall and in the RA group 71% compared to control wells. Tocilizumab reduced the fibrocyte count with 63% overall and 45% in the RA group, although not significant ($p=0.07$ and $p=0.06$ respectively).

Conclusion: Abatacept and prednisolon suppress the differentiation of mononuclear cells to mature fibrocytes *in vitro* in RA patients and data indicating a similar effect of Tocilizumab. Prednisolone are used in the treatment of RA-ILD but has a marked toxicity, so new treatment modalities are desirable. Our findings are in line with the fact that fibrocytes have the receptors targeted by abatacept, furthermore recent scleroderma research has shown Abatacept to reduce fibrocyte levels *in vitro* and Tocilizumab to potentially reduce lung and skin affection(1, 2) Further research using abatacept and tocilizumab to target fibrocytes are needed in order investigate the treatment potential of these drugs in RA-ILD.

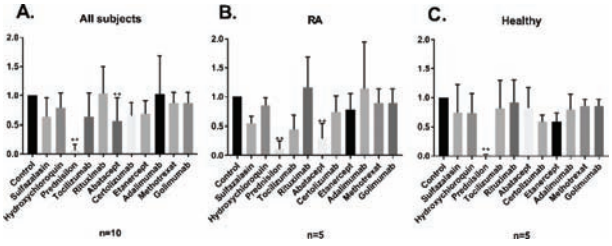


Figure 1. Effect of csDMARD, bDMARD and prednisolon on fibrocyte differentiation.

Ledgend: Demonstrates the different medical agents used and the number of cultured fibrocytes counted after 5 days of incubation. Values are mean +/- SEM. ** indicates statistical significance compared with the control well by ANOVA compared to the control ($p<0.05$)

REFERENCES

[1] Cutolo M, et al. Effects of CTLA4-Ig treatment on circulating fibrocytes and skin fibroblasts from the same systemic sclerosis patients: an in vitro assay. Arthritis Research & Therapy. 2018;20.

[2] Khanna D, et al. Safety and efficacy of subcutaneous tocilizumab in systemic sclerosis: results from the open-label period of a phase II randomised controlled trial (faSScinate). Ann Rheum Dis. 2018;77(2):212-20.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.1915

AB0415 **SURVIVAL OF BIOLOGIC AGENTS WITHIN A COHORT OF GREEK PATIENTS WITH RHEUMATOID ARTHRITIS. REAL WORLD DATA.**

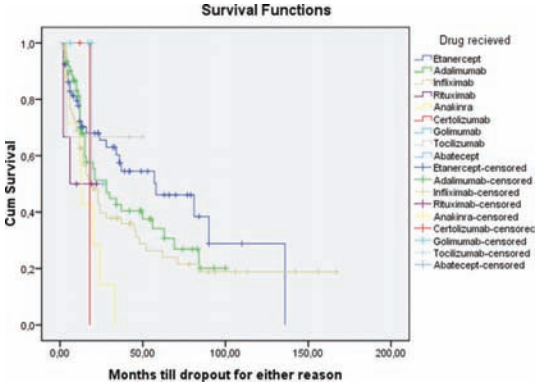
Olga Katsouli[1], Georgia Liantinioti[1], Panagiota Katsouli[1], Mary Pappa[1], Markos Patsouras[1], Theodoros Angelopoulos[2], Sotiris Roussos[3], VLACHOYIANNOPOULOS PANAYIOTIS[1]. *[1]Medical School National and Kapodistrian University of Athens, Department of Pathophysiology, Athens, Greece*; *[2]Medical School National and Kapodistrian University of Athens, Athens, Greece*; *[3]Medical School National and Kapodistrian University of Athens, Hygiene, Epidemiology and Medical Statistics, Athens, Greece*

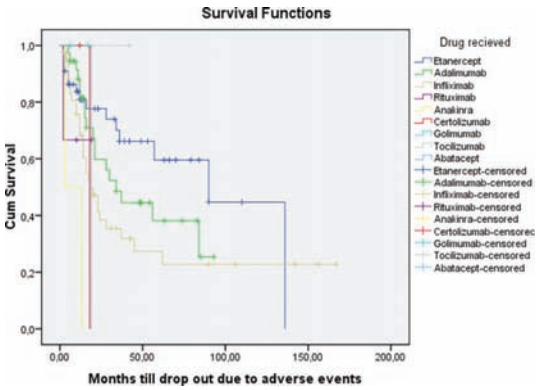
Background: Rheumatoid arthritis (RA) is treated successfully with biologic disease-modifying anti-rheumatic drugs (bDMARDs). However, a significant withdrawal rate, due to non-responsiveness or toxicity, remains a major barrier for their long-term use.
Objectives: To determine the withdrawal rate of the first bDMARD in a large cohort of RA patients due either, to non-responsiveness or toxicity.
Methods: In this study, were included retrospectively 220 patients from our outpatient clinic. The following bDMARDs were evaluated: Etanercept (n=66 patients), Adalimumab (n=61 patients), Infliximab (n=70 patients), Rituximab (n=6 patients) and others, such as Certolizumab pegol, Golimumab, Tocilizumab, Anakinra and Abatacept (n=17 patients). Disease activity was regularly measured by DAS-28 until the end of follow up. Kaplan-Meier plots were performed to examine the withdrawal rate of each biologic agent. Severity of AEs was classified according to the Common Terminology Criteria for Adverse Events (CTCAE, version 4.03).
Results: A total of 220 patients (49 men, 171 women) were included in the analysis. The most frequently used first-line bDMARDs were Infliximab (31.8%), Etanercept (30%) and Adalimumab (27.7%). The median of treatment duration with the first bDMARD was 15 months (Q1:8, Q3:40.5). Taking all bDMARDs as a whole, 126 patients (57,27%) discontinued the first bDMARD, either due to AEs(n=66, 52.38%), or loss of efficacy (n=60,47.62%) after a follow-up of 167 months. However the most withdrawals (53.18%) occurred within the first 60 months of follow-up. Mean initial and final DAS-28 were: for those who discontinued treatment due to AEs 4.96±1.33(95%CI 4.64-5.28) and 3.43±1.47(95%CI, 3.08-3.79), respectively, for those who discontinued due to failure of therapy: 5.04 ±1.37(95%CI, 4.70-5.39) and 4.91±1.27(95%CI, 4.59-5.23) respectively and for those who continue 4.79±1.55(95%CI, 4.47-5.10) and 2.63±1.06(95% CI, 2.41-2.84), respectively.
Differences in survival among bDMARDs are attributed to their AEs and not to their efficacy. As far as the AEs are concerned, infections constituted the majority of cases (n=23, 34.8%), from which 34.8% needed hospitalization (CTCAE 3-4). The percentage of 12,1% of AEs is attributed to cancer cases, while allergic reactions counted for 31,8% of them. Survival of Etanercept within our cohort was significantly longer than those of other bDMARDs.
Conclusion: Biologic agents are important drugs in our armamentarium to combat RA. However nearly 50% of patients discontinue these agents after 60 months of treatment due either to AEs or inefficacy. Differences in survival of bDMARDs were associated not to their inefficacy, but to their AEs. Choosing the right drug for the right patient is a matter of advanced research involving a better understanding of the plasticity of the pathways of inflammation and specific biomarker selection.

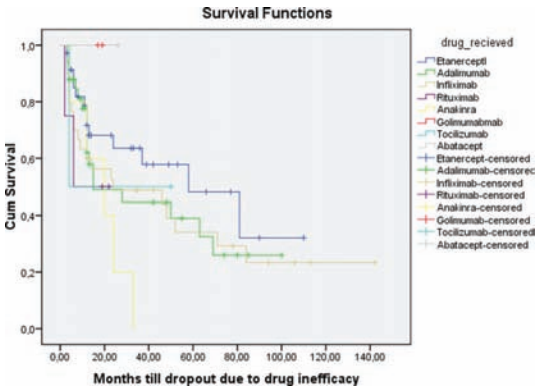
REFERENCES

[1] C. Lampropoulos, P. Orfanos, M. Manoussakis, A. Tzioufas, H. Moutsopoulos, P. Vlachoyiannopoulos. Treat-to-target biologic therapy in patients with rheumatoid arthritis is more efficacious and safe compared to delayed initiation of biologics:A real-world study.ClinExpRheumatology.2017;35:192-200.

[2] C. Lampropoulos, P. Orfanos, V. Bournia, T. Karatsourakis, C. Mavragani, D. Pikazis, M. Manoussakis, A. Tzioufas, H. Moutsopoulos, P. Vlachoyiannopoulos.Adverse events and infections in patients with rheumatoid arthritis treated with conventional drugs or biologic agents: a real world study. ClinExpRheumatology.2015;33:216-224.







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AB0416 A COMPARATIVE STUDY TO ASSESS THE EFFICACY, SAFETY, AND IMMUNOGENICITY OF YLB113 AND ETANERCEPT REFERENCE PRODUCT FOR THE TREATMENT OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: YLB113 is an investigational biosimilar of the reference product etanercept (ETN), being developed for the treatment of patients with moderate-to-severe rheumatoid arthritis (RA) and other approved indications of the reference product ETN.
Objectives: The phase 3 study of YLB113 was conducted in Europe, Japan, and India across more than 100 rheumatology clinics to compare efficacy, safety, and immunogenicity of YLB113 with ETN in patients with RA.
Methods: A total of 528 patients with moderate-to-severe RA receiving concomitant treatment with methotrexate were randomized to receive a once-weekly dose of 50 mg of subcutaneously administered YLB113 or ETN. The primary end point was the ACR20 response rate at Week 24, with equivalence confirmed if the 95% confidence interval (CI) was within the range of –15% to 15%. Other efficacy end points, such as DAS28 with safety and immunogenicity end points, were assessed periodically up to Week 52.
Results: The ACR20 response rate at Week 24 was 81.2% for YLB113 and 86.8% for ETN in the full analysis set, with a treatment difference of –5.6% (95% CI: –11.6, 0.5), which was completely within the predefined equivalence margin of −15% to 15%. The result for sensitivity analysis using the per protocol set population revealed that the proportion of subjects who showed ACR20 response at Week 24 was similar between both treatment groups, at –4.6% (95% CI: –10.1, 0.8). The incidence of treatment-emergent adverse events was comparable between YLB113 and ETN (55.5% vs 65.7%), and the incidence of antidrug antibody development up to Week 24 was in favor of YLB113 (0.8% vs 8.3%).
Conclusion: The present comparative study demonstrated the biosimilarity of YLB113 to ETN on the triad of efficacy, safety, and immunogenicity in patients with moderate-to-severe RA, and thus can be extrapolated to other therapeutic indications approved for ETN. The therapeutic equivalence of YLB113 and ETN in terms of the primary efficacy end point at Week 24 and long-term safety comparability until Week 52 was established with lower immunogenicity.
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AB0416B EFFICACY OF INFLIXIMAB IN RA PATIENTS BASED ON TOTAL COUNT OF INFUSIONS

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Objectives: To analyze the correlation between cumulative dose of infused infliximab and its' therapeutic and antidestructive effect in patients with rheumatoid arthritis (RA).
Methods: 135 patients with confirmed RA were included into a 1-year study. All patients were assigned to a recommended dosing regimen of 3 mg/kg infliximab as an intravenous induction at 0, 2 and 6 weeks followed by a maintenance 3 mg/kg dose every 8 weeks thereafter. Clinical (TJC and SJC), laboratory (CRP and ESR) parameters and quality of life assessments (HAQ) were performed during each visit.
The score trends of DAS28 disease activity scale were used as the primary criterion for evaluation of infliximab therapeutic effect. Sharp Vander Heijde (SvH) modification scoring method was used for dynamic assessment of erosion and for joint space narrowing. All patients were assessed and examined according to the Protocol before each infusion of infliximab. Therapeutic results were evaluated in all ITT population at Week 54 from the initiation of treatment (including those who did not complete the envisaged course of infliximab).
The patients were divided into three groups:

1. those who received ≤ 4 infusions of infliximab (N=63);
2. those who received 5–7 infusions of infliximab (N=31);
3. those who received ≥ 8 infusions of infliximab (N=41).

Patients from Group 1 received at average 2.5 infusion of infliximab, from Group 2 - 5.8 infusion, and from Group 3 – 8,8 infusion.
Results: High disease activity based on DAS 28 (>5,1) score was documented in the majority of participants at baseline: in 69% - in Group 1, in 86,6% - in Group 2, and in 62.1% - in Group 3. Moderate RA activity (3.2 < DAS 28 ≤ 5,1) was found in 31% in Group 1, in 13.4% - in Group 2, and in 37.9% - in Group 3.
All patients demonstrated rapid (already by Week 14 on-treatment) and significant ($p<0.05$) decrease of RA activity. This reduction remained significant by the end of the study at Week 54 as compared to baseline scores. Meanwhile, by the end of the study the mean DAS 28 score in Group 1 was significantly higher compared to Groups 2 and 3. No significant differences were found between Groups 2 and 3 during the FUP.
Similar patterns in RA activity differentiation were identified within individual groups: the highest proportion of pts with high laboratory activity at Week 54 was found in Group 1, receiving ≤ 4 infliximab infusions. The Group 3 showed the highest proportion of patients with low laboratory RA activity at Week 54 (including patients in remission according to DAS 28 criteria) (53.9% compared to 27.3% and 50% in Groups 1 and 2, respectively). Percentages of remissions in Groups 3 and 2 were comparable (28.6% and 23.1%, respectively), while in Group 1 the remission rates were lower (18.2%).
We analyzed the dynamics of total Sharpe score during 54 weeks FUP in all three groups, and found that patients receiving ≤ 4 infliximab infusions demonstrated more significant radiological progression as compared to patients from two other groups.
Conclusion: Low cumulative dose of infliximab can induce a long-lasting clinical effect, but does not significantly inhibit further destruction of joints. There were no significant differences between Groups 2 and 3 in the degree of radiological progression.
Disclosure of Interests: None declared
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AB0416C THE RESULTS OF THE USE OF TOFACITINIB (TOFA) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) IN MOSCOW. ANALYSIS DATA FROM MOSCOW UNIFIED ARTHRITIS REGISTRY(MUAR)

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Background: Moscow Unified Arthritis Registry (MUAR) started at 01 DEC 2012. By 01 DEC 2017, 829 RA patients were included in the register.
Objectives: The aim of the study was to evaluate the effectiveness and treatment survival of TOFA and identify predictors of the effectiveness of TOFA.

Methods: The inclusion criteria were diagnosis of RA, established at any time according to ACR (1987) or ACR/EULAR (2010) criteria; persons receiving or planning to receive targeted therapy for RA; signed informed consent to participate in the study. All episodes of treatment with TOFA in which there was at least 1 visit not earlier than 6 months since the start of the drug were included for efficacy analysis.

Results: Data of 48 patients treated with TOFA were extracted from the registry. Women were 41 (85,4%), mean age was 55,1 ± 12,4 years; age at the disease beginning was 44,3 ± 14,0; 6 (12,5%) of patients were smokers; mean time on TOFA was 552 ± 259 days. One of the independent predictors of achieved DAS28 was sex - 0.49 lower in men (p<0.001). There was no correlation of achieved disease activity with number of previous failures with biologics. Patients seropositive for rheumatoid factor achieved significantly lower activity (p =0,015). There was also a trend towards lower achieved activity in patients with rheumatoid nodules (p = 0,059).

On the first line of targeted treatment, survival of TOFA was significantly better than Infliximab, Adalimumab and Certolizumab pegol. On the second line – better than Infliximab. On the following lines TOFA was better than Adalimumab, but worse than Etanercept. Due to the fact that most of treatment episodes with TOFA are not completed, the average duration of treatment may be underestimated. There was no significant decrement of retention on therapy after multiple treatment failures (tab.).

Conclusion: The effectiveness and treatment survival of TOFA does not depend on the number of previous failures with biologics; the best results of TOFA can be expected in men and seropositive patients; the presence of rheumatoid nodules can be considered as a special indication for TOFA.

Table. Retention of targeted therapies in patients with rheumatoid arthritis

Drug	The 1-st line of therapy		The 2-nd line of therapy		The 3-d and subsequent lines of therapy	
	Number of cases / completed	Average duration estimate (95% confidence interval)	Number of cases / completed	Average duration estimate (95% confidence interval)	Number of cases / completed	Average duration estimate (95% confidence interval)
Tofacitinib	27/3	64,7 (55.8; 73.5)	27/7	28.5 (22.9; 34.2)	25/4	28.0 (23.5; 32.4)
Abatacept	81/24	109,1 (87.9; 130.3)	73/34	63,4 (43.7; 83.1)	36/18	73,7 (43.5; 103.8)
Adalimumab	166/82	**57,1 (47.3; 66.9)***	36/23	44,6 (28.6; 60.6)	16/11	**23,6 (12.1; 35.0)***
Certolizumab pegol	39/27	**49,8 (31.7; 68.0)***	13/8	22,7 (10.5; 34.9)	5/3	25,8 (5.77; 45.9)
Etanercept	117/43	99,2 (77.5)	53/19	98,8 (73.2; 124.4)	24/13	**43,7 (27.1; 60.2)***
Infliximab	129/115	**28,1 (22.6; 33.5)***	14/12	**11,3 (6.26; 16.2)***	3/2	14,8 (4.25; 25.4)
Rituximab	74/26	78,4 (64.2; 92.7)	41/18	66,1 (46.4; 85.7)	31/11	54,2 (37.8; 70.5)
Tocilizumab	74/27	101,3 (77.6; 125.0)	24/9	59,4 (43.3; 75.5)	20/6	41,2 (31.5; 50.9)
All	707/347	74,7 (66.5; 82.9)	281/130	67,2 (54.3; 81.1)	160/68	69,8 (46.5; 93.2)

* - statistically significant difference with Tofacitinib (log-rank test)

Figure 1

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Rheumatoid arthritis – non biologic treatment

AB0417

EFFICACY AND SAFETY OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS ACCORDING TO DURATION OF PRIOR CSDMARD TREATMENT AND NUMBER OF PRIOR CSDMARDS: A POST HOC ANALYSIS OF PHASE 3 AND PHASE 3B/4 TRIALS

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Previous analyses have reported greater improvements in efficacy outcomes with tofacitinib 5 mg twice daily (BID) ± conventional synthetic DMARDs (csDMARDs) in patients (pts) with early vs established RA.[1,2]

Objectives: To evaluate the efficacy and safety of tofacitinib in pts with RA, stratified by prior csDMARD treatment duration and number of prior csDMARDs.

Methods: This was a post hoc analysis of pooled data from 4 Phase (P) 3 trials (ORAL Scan [NCT00847613]; ORAL Solo [NCT00814307]; ORAL Sync [NCT00856544]; ORAL Standard [NCT00853385]) and 1 P3b/4 trial (ORAL Strategy [NCT02187055]) of tofacitinib in pts with RA and an inadequate response to ≥1 DMARD. Pts treated with tofacitinib 5 mg BID as monotherapy or with csDMARDs were included. Outcomes were evaluated according to csDMARD treatment duration (≤1, 1–2, >2 years *y+) and number of csDMARDs (1, 2, 3, ≥4) prior to baseline (BL). Efficacy outcomes assessed at Months (M)3, 6 and 12 were: change from BL (Δ) in CDAI and HAQ-DI, and rates of CDAI-defined low disease activity (LDA; ≤10) and remission (≤2.8). Safety outcomes, including treatment-emergent adverse events (AEs), serious AEs (SAEs) and AEs of special interest, were evaluated throughout the studies.

Results: In total, 1584 pts were included in the analysis; of these, 27.2% (n=431) had received csDMARDs for ≤1 y, 20.5% (n=325) for 1–2 y, and 52.1% (n=825) for >2 y prior to BL (duration unknown for 3 pts). Roughly half (53.2%, n=842) had received 1 prior csDMARD; 26.4% (n=418), 13.8% (n=219) and 6.6% (n=105) had received 2, 3 and ≥4 prior csDMARDs, respectively. Most pts had previously received MTX (50.8%, n=805) or MTX + other csDMARDs (46.3%, n=733); 2.9% (n=46) received other csDMARDs only. Mean BL CDAI and HAQ-DI scores were similar, irrespective of prior csDMARD treatment duration or number of prior csDMARDs (Table). Generally, up to M12, no trends were observed for ΔCDAI, ΔHAQ-DI or CDAI LDA rates regardless of prior csDMARD treatment duration or number of prior csDMARDs (Table). When CDAI remission rates data were stratified by csDMARD treatment duration, no differences between pt groups were observed at M3 and M6; however, a numerically higher proportion of pts with prior csDMARD treatment duration ≤1 y achieved remission at M12 vs 1–2 y and >2 y pts. Use of fewer prior csDMARDs appeared to be associated with higher remission rates up to M12. Although safety outcomes were similar when data were stratified by prior csDMARD treatment duration, there was generally a trend for increased rates of AEs, SAEs and AEs of special interest (serious infections, herpes zoster and opportunistic infections [excluding TB]) with increasing number of prior csDMARDs (Table).

Conclusion: In this post hoc analysis of pooled data from P3 and P3b/4 trials, no differences in the efficacy or safety of tofacitinib 5 mg BID were observed when pts were stratified by prior csDMARD treatment duration. Although pt numbers were small, use of fewer prior csDMARDs may be associated with improved remission rates and safety outcomes for pts treated with tofacitinib.

REFERENCES

[1] Hall S et al. Arthritis Rheum 2016; 68 (S10): 1999-2001.
[2] Fleischmann RM et al. RMD Open 2016; 2: e000262.

Table: Baseline demographics and disease characteristics, and efficacy and safety outcomes for patients treated with tofacitinib 5 mg BID + background csDMARDs, by prior csDMARD treatment duration and number of prior csDMARDs

	Prior csDMARD treatment duration			Number of prior csDMARDs			
	≤1 year (N=431)	1–2 years (N=325)	>2 years (N=825)	1 (N=842)	2 (N=418)	3 (N=219)	≥4 (N=105)
Baseline demographics and disease characteristics							
CDAI score, mean (SD)	38.8 (12.8)	37.8 (12.3)	37.7 (12.3)	38.6 (12.4)	37.3 (12.5)	38.0 (12.4)	36.9 (12.7)
HAQ-DI score, mean (SD)	1.5 (0.7)	1.4 (0.6)	1.5 (0.6)	1.5 (0.6)	1.5 (0.7)	1.5 (0.6)	1.5 (0.7)
Efficacy							
ΔCDAI, mean (SD)							
Month 3	-21.4 (13.7)	-21.0 (14.2)	-20.7 (13.2)	-22.3 (13.8)	-19.5 (13.4)	-20.1 (12.6)	-16.9 (12.7)
Month 6	-24.3 (14.1)	-23.7 (14.5)	-23.7 (13.6)	-25.1 (14.2)	-22.4 (13.7)	-23.4 (13.5)	-20.2 (14.3)
Month 12	-27.1 (13.1)	-24.9 (14.6)	-26.3 (13.3)	-27.3 (13.9)	-24.6 (13.2)	-25.9 (12.5)	-23.1 (12.9)
ΔHAQ-DI, mean (SD)							
Month 3	-0.6 (0.7)	-0.5 (0.6)	-0.5 (0.6)	-0.5 (0.6)	-0.5 (0.6)	-0.5 (0.6)	-0.5 (0.5)
Month 6	-0.6 (0.7)	-0.6 (0.6)	-0.5 (0.6)	-0.6 (0.6)	-0.6 (0.6)	-0.6 (0.6)	-0.5 (0.6)
Month 12	-0.7 (0.7)	-0.6 (0.7)	-0.6 (0.6)	-0.7 (0.6)	-0.6 (0.6)	-0.6 (0.6)	-0.6 (0.6)
CDAI-defined LDA (≤10), n (%)							
Month 3	138 (34.0)	95 (31.4)	265 (33.7)	279 (34.8)	129 (33.0)	67 (32.4)	24 (24.5)
Month 6	178 (45.6)	121 (41.4)	346 (45.7)	369 (47.7)	157 (42.0)	81 (40.3)	40 (43.5)
Month 12	168 (58.7)	129 (52.7)	330 (55.8)	352 (56.8)	151 (54.3)	86 (57.0)	38 (52.1)
CDAI-defined remission (≤2.8), n (%)							
Month 3	24 (5.9)	20 (6.6)	45 (5.7)	54 (6.7)	24 (6.1)	10 (4.8)	2 (2.0)
Month 6	46 (11.8)	32 (11.0)	79 (10.4)	92 (11.9)	42 (11.2)	18 (9.0)	6 (6.5)
Month 12	58 (20.3)	37 (15.1)	102 (17.3)	112 (18.1)	51 (18.4)	25 (16.6)	9 (12.3)
Safety							
AEs, n (%)	300 (69.6)	219 (67.4)	582 (64.5)	582 (69.2)	280 (67.0)	163 (74.4)	79 (75.2)
SAEs, n (%)	45 (10.4)	33 (10.2)	85 (10.3)	76 (9.0)	42 (10.0)	27 (12.3)	18 (17.1)
AEs of special interest, IR* (95% CI)							
Serious infections	1.14 (0.59, 1.99) [n=12]	1.14 (0.55, 2.10) [n=10]	1.15 (0.73, 1.70) [n=24]	1.04 (0.62, 1.62) [n=19]	1.17 (0.64, 1.96) [n=14]	0.77 (0.23, 1.80) [n=5]	2.26 (0.97, 4.45) [n=8]
Herpes zoster	0.77 (0.33, 1.52) [n=8]	1.17 (0.56, 2.16) [n=10]	1.17 (0.75, 1.74) [n=24]	0.94 (0.55, 1.50) [n=17]	1.02 (0.53, 1.78) [n=12]	0.63 (0.17, 1.60) [n=5]	3.83 (1.29, 8.93) [n=6]
Opportunistic infections (excluding TB)*	0.19 (0.02, 0.68) [n=2]	0.34 (0.07, 0.99) [n=3]	0.05 (0.00, 0.26) [n=1]	0.11 (0.01, 0.39) [n=2]	0.08 (0.00, 0.46) [n=1]	0.31 (0.04, 1.11) [n=2]	0.28 (0.01, 1.57) [n=1]

*IR in patients with events per 100 patient-years
†Opportunistic infections recorded included the following adjudicated events: herpes zoster (n=2), herpes zoster disseminated (n=1), cytomegalovirus chorioretinitis (n=1), esophageal candidiasis (n=1), and pneumocystis jiroveci pneumonia (n=1)
Δ, change from baseline; AE, adverse event; CDAI, Clinical Disease Activity Index; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, incidence rate; LDA, low disease activity; SAE, serious adverse event; SD, standard deviation; TB, tuberculosis

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AB0418 INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB

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Background: The presence of interstitial lung disease (ILD) is a common extra-articular manifestation in patients diagnosed with Rheumatoid Arthritis (RA), dyspnea being its cardinal symptom. Several of the drugs commonly used to treat this condition, such as TNF inhibitors (anti-TNF) and Disease Modifying Antirheumatic Drugs (DMARDs), have been implicated in the development or exacerbation of ILD. In regard to Tofacitinib, results of post hoc analysis of its pivotal and extension studies report a numerically lower ILD incidence rate in the group that received this drug compared with placebo.
Objectives: To describe the evolution of dyspnea, spirometric parameters, DLCO and high resolution computed tomography (HRCT) findings in patients with RA diagnosis with associated PID who received Tofacitinib for a period of 12 months.
Methods: Patients with a diagnosis of RA who fulfilled criteria ACR 1987/ ACR-EULAR 2010, with interstitial lung disease previously diagnosed from clinical findings, spirometry and/or HRCT were included. Tofacitinib was used in dose of 10 mg/day orally. Design: Descriptive, retrospective, multicentric study. The following variables were analyzed: change at 12 months from baseline in the degree of dyspnea (according to the modified scale of dyspnea MMRC), forced vital capacity (FVC), DLCO and findings in HRCT. Continuous variables were reported as mean and standard deviation or median and interquartile range as appropriate. The categorical variables were reported as percentages.
Results: Fifteen patients were included. 60% (n: 9) were women. The mean age was 64.4 years (± 10.92). The median time of evolution of RA was 9 years (IQR: 4-40). The median time of evolution of interstitial lung disease was 4 years (IQR: 1-24).13% (n: 2) of the patients were receiving methotrexate (MTX) at the time of evaluation, 60% (n: 9) of the patients had previously received it. 80% (n: 12) had previously received DMARD different from MTX. 33% of the patients (n: 5) had received previous biological treatment. All patients received tofacitinib at a dose of 10mg/day. 47% of patients (n = 7) received tofacitinib monotherapy and 53% (n = 8) received it combined with DMARDsc. 27% (n: 4) of the patients had grade 3-4 dyspnea at baseline.Improvement in the dyspnea scale was observed in 8 patients, while in the rest, it remained stable. The forced vital capacity (FVC) at baseline was <80% in 5 patients and> 80% in 2 patients. At 12 months, 4 patients achieved a FVC> 80%.The average of DLCO at baseline was 45.6 (± 18.84), with an improvement of 30% at 12 months in 4 patients. No progression of the disease was observed in the HRCT at 12 months in any of the patients evaluated.
Conclusion: The present preliminary study was performed with patients of daily practice, not being available in all cases, the corresponding respiratory functional examinations. However, despite these limitations, none of the patients showed worsening of dyspnea, with improvement in some patients. Regarding respiratory functional examinations and DLCO, not only they remained stable after treatment in the majority of patients evaluated, but 4 patients presented improvement with respect to baseline parameters. It is necessary to perform more studies, with systematized controls of the pulmonary function and images, to corroborate this hypothesis.
Disclosure of Interests: Marisel Bejarano: None declared, Maria Natalia Tamborenea: None declared, Mario Alberto Goñi: None declared, Lina Saldarriaga: None declared, Cecilia Pisoni: None declared, Rodrigo Garcia Salinas: None declared, Mariana Salcedo: None declared, Claudia Helling Employee of: I am an employee of Pfizer, Adrian Salas Consultant for: Pfizer, Employee of: I am an employee of Pfizer

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AB0419 FRACTURE RISK IN PATIENTS ON LONG TERM GLUCOCORTICOIDS WITH INFLAMMATORY ARTHRITIS

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Background: A main stay treatment of inflammatory arthritis is glucocorticoids (GCs)[1]. However, long term use of GCs has been associated with an increased risk of fracture, with studies estimating up to 12% of patients having sustained a fracture whilst on GC treatment[1][2].
Objectives: The aim of this study was to determine the prevalence of fractures in a cohort of patients on long term GCs with a diagnosis of inflammatory arthritis.
Methods: A database of patients with inflammatory arthritis attending the rheumatology department at the Midlands Regional Hospital Tullamore, since 2009, was reviewed. Patients on long term GCs were identified and outpatient summaries were analysed. Data collection included age, sex, diagnosis, vertebral fracture, other fracture sites and osteoporosis treatment.
Results: As of September 2018, out of the 2118 patients with a diagnosis of inflammatory arthritis 364 were on long term GCs. 10% of patients had reported vertebral fractures on imaging. 36.4% of patients had other types of fractures reported on imaging; 20%, and the most common site of fracture, were wrist fractures. 83.7% of those who suffered from a vertebral fracture were female. 18.2% of those who sustained fractures were not on any osteoporosis treatment.
Conclusion: The incidence of fracture in our cohort of patients was higher than suggested in previous studies. Furthermore, it highlights the need for patients on long term GCs to be given osteoporosis prevention therapy.

REFERENCES

[1] Buckley L, Guyatt G, Fink HA, Cannon M, Grossman J, Hansen KE, et al. 2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. Arthritis Rheumatol. 2017;69:1521–37
[2] Dam Kim, Soo-Kyung Cho, Byeongju Park, Eun Jin Jang, Sang-Cheol Bae and Yoon-Kyoung Sung. The Journal of Rheumatology March 2018, jrheum.170054

Disclosure of Interests: None declared

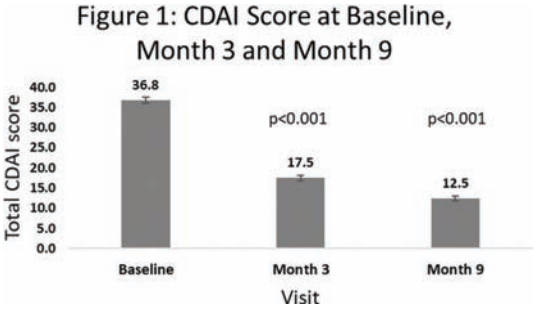
DOI: 10.1136/annrheumdis-2019-eular.8014

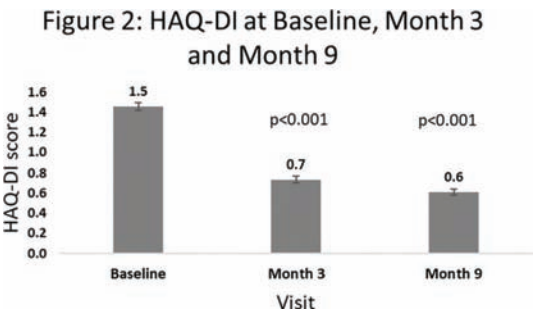
AB0420 A PROSPECTIVE, OBSERVATIONAL STUDY ON THE CLINICAL EFFICACY AND SAFETY OF LEFLUNOMIDE IN EGYPTIAN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: CLEAR STUDY

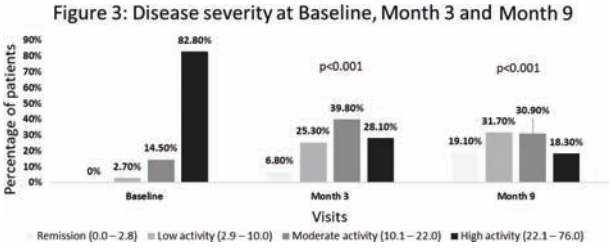
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Background: Due to its anti-inflammatory and immunomodulatory properties, leflunomide can be used as a monotherapy or in combination with other conventional synthetic DMARDs (csDMARDs) in treating active RA.[1]
Objectives: The aim of this observational study was to assess efficacy and safety of leflunomide in Egyptian patients with active RA, whether used as first-line and/or add-on therapy to other csDMARDs, with or without steroids.
Methods: Adult Egyptian patients with active RA, fulfilling the ACR/EULAR 2010 classification criteria, for whom leflunomide was prescribed, were included and followed up for 9 months. Leflunomide was prescribed at the physicians' sole discretion for patients who have previously experienced resistance, inadequate response or intolerance to other csDMARDs. Data about CDAI score and HAQ-DI score were acquired from patients who fulfilled the eligibility criteria, along with patients' demographics, medical history, physical examination, concomitant medications, and RA history including disease duration, previous RA medications and treatment response. This study was registered on clinicaltrials.gov (NCT03599986) and the preliminary results were previously published in 2018.[2]
Results: A total of 398 patients were enrolled in this study. Three hundred sixty-six patients with a mean age of 43.7 (SD 10.2) years and median disease duration of 2 (IQR 5.5) years were eligible for efficacy evaluation; 309 (84.4%) were female. We found that 86.1% of patients were leflunomide naïve. Patients who previously received leflunomide (13.9%) had a wash out period of at least 6 months prior to study enrolment. Patients were either prescribed leflunomide 20 mg/day (37.7%) or were prescribed a loading dose of 100 mg/day for the first 3 days of treatment then maintained with 20 mg/day (62.3%). Leflunomide was prescribed as first-line therapy in 21.1% of patients, as add-on therapy to other csDMARDs without steroids in 34%, and as add-on therapy to other csDMARDs with steroids in 44.9%. The mean total CDAI score

was significantly decreased (p<0.001) from 36.8 (14.9) at baseline, to reach 12.5 (10.3) after 9 months of treatment, with a reduction of 64%. In a similar pattern, the mean HAQ-DI score was significantly decreased (p<0.001) from 1.5 (0.7) at baseline to reach 0.6 (0.6) after 9 months of treatment, with a reduction of 57%. Figures 1 and 2 show changes in both CDAI and HAQ-DI scores throughout the study.







Abstract Figure 3. shows that disease severity was significantly improved (p<0.001) throughout the study, and 19.1% of patients were at remission after 9 months of treatment.

Twenty-three adverse events (AEs) were reported in 20 patients (5%) throughout the study period; most frequently, increased hepatic enzymes (6 cases, 1.5%), increased swollen/tender joint count (2 cases, 0.5%), decreased white blood cell count (2 cases, 0.5%), and abdominal discomfort (2 cases, 0.5%). None of the reported AEs were related to treatment with leflunomide.

Conclusion: Results from this study demonstrate that leflunomide may offer an effective, tolerable and safe treatment –whether used as a monotherapy or in combination with other csDMARDs- in Egyptian patients with active RA.

REFERENCES

[1] Alldred A, Emery P. Leflunomide: a novel DMARD for the treatment of rheumatoid arthritis. Expert opinion on pharmacotherapy. 2001;2(1):125-137.

[2] El Sayed A, Clinical efficacy and safety of leflunomide in Egyptian patients with active rheumatoid arthritis: CLEAR interim results. The open rheumatology journal. 2018;12(1):323-331.

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AB0421 METHOTREXATE COMPLIANCE AMONG PATIENTS WITH CHRONIC INFLAMMATORY DISEASE OR CONNECTIVE TISSUE DISEASE

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Background: Methotrexate (MTX) is widely used in rheumatology. About 30% of patients receiving MTX do not respond. One of the explanations could be poor adherence.

Objectives: The purpose of this study was to assess adherence and to identify predictive factors influencing it.

Methods: 188 patients with MTX for at least 3 months (rheumatoid arthritis (RA), peripheral spondyloarthritis (PS), psoriatic arthritis (PA), lupus, Sjögren's Syndrome (SS)) were enrolled between May 2017 and May 2018. Each patient completed a questionnaire including socio-demographic data, disease and MTX characteristics, 4-question Morisky, rheumatism activity scores including DAS 28, quality of life (EQ-5D), fibromyalgia (FiRST), anxiety and depression (HADS), catastrophism (PCS-CF), coping (WCC-R) and whether or not to participate in a therapeutic education program.

Results: 188 were recruited, of which 75% were women, with a mean age of 61.4 +/- 13.24 years: RA (77.12%), PS (7.98%), PA (10.11%), lupus (2.66%) and SS (2.13%). 68.6% were observant, versus 31.4% unobservant minor (28.2%) or major (3.2%) patients. In multivariate analysis, two models were performed and found a poor adherence in case of depression OR: 3.120 [1.051; 9.354], catastrophism OR: 3.974 [1.119; 14.108], anti-CCP antibodies OR: 4.019 [1.277; 12.653] in RA patients and depression OR: 2.715 [1.237; 5.963], absence of comorbidities OR: 2.309 [1.085; 4.915] with all rheumatism.

Conclusion: Some modifiable factors such as depression and catastrophism were associated with the risk of non-adherence with MTX. It is important to consider depression and catastrophism when taking care of our patients to improve adherence and avoid therapeutic escalations.

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AB0422 ACHIEVEMENT OF PATIENT ACCEPTABLE SYMPTOM STATE (PASS) IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BARICITINIB

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Background: Baricitinib, a newly approved drug for the treatment of patients with moderate to severe rheumatoid arthritis (RA), is a selective inhibitor of Janus kinase 1 and 2. In a patient-centered care, patient-reported outcomes (PROs) are really helpful to better evaluate the disease activity and the response to therapy. Between them, Patient Acceptable Symptom State (PASS) is defined as the highest level of symptoms beyond which patients consider themselves well [1], and consists of a single question with dichotomized answer (yes or no): "Considering all the different ways your disease is affecting you, if you would stay in this state for the next months, do you consider that your current state is satisfactory?". In randomized controlled trials baricitinib showed significant improvement of pain, fatigue, tiredness and assessment of disease [2].

Objectives: The aim of the present study was to investigate the effect of baricitinib on PASS one month from the beginning of therapy. Further aim was to quantify the time patients needed to reach an acceptable state of health and determine the clinical variables associated with PASS.

Methods: Patients affected by RA according to 2010 ACR criteria, starting treatment with baricitinib as clinically indicated, were consecutively enrolled; PASS was determined after 1 month of treatment (T1); days to

achieve PASS were estimated at T1; activity indices were calculated after 1 month of therapy and correlated with PASS.
Results: Thirty-four RA patients were enrolled (age median-IQR 58-16 years; disease duration median-IQR 144-138 months; DAS-28 median-IQR 5.09-1.92). After 1 month of therapy, 30 of 34 patients achieved PASS, of which 73% in the first 2 weeks of treatment (days to achieve PASS median-IQR 12-22) (figure). At T1, patients achieving PASS, compared to those who did not, reported less pain (median VAS 30/100 *vs* 72/100, p= 0.025), a better global assessment of disease (median 40/100 *vs* 72/100, p=0.023), lower CDAI (median 12 *vs* 31, p= 0.048), SDAI (median 12.8 vs 33.95, p=0.011) and DAS-28 (median 3.67 *vs* 5.54, p= 0.082). 10 out of 30 PASS positive patients (33%) achieved a DAS-28 low-disease activity or remission at T1 *vs* 0% of the PASS negative cohort (p= 0.169). Age, disease duration and number of previous bDMARDs did not significantly differ between the two subgroups.
Conclusion: Baricitinib was able to induce an acceptable state of health in about 90% of patients after the first month of therapy. The prompt effect of baricitinib on pain and fatigue could partially explain the rapid achievement of PASS, as shown by the decrease of VAS and improvement of the global assessment of disease.



REFERENCES

[1] Maksymowych WP, et al. Evaluation and validation of the patient acceptable symptom state (PASS) in patients with ankylosing spondylitis. Arthritis Rheum 2007
[2] Schiff, et al. Patient-reported outcomes of baricitinib in patients with rheumatoid arthritis and no or limited prior disease-modifying antirheumatic drug treatment. Arthritis Res Ther. 2017

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AB0423 CHANGES IN DISEASE ACTIVITY, PAIN, GLOBAL HEALTH AND PHYSICAL FUNCTION AFTER SWITCHING FROM ORAL TO SUBCUTANEOUS METHOTREXATE: RESULTS OF THE SIX-MONTH OBSERVATIONAL PROSPECTIVE STUDY IN CROATIA

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Background: In rheumatoid arthritis (RA) and psoriatic arthritis (PsA) methotrexate (MTX) is usually the first choice in the treatment strategy. Bioavailability of oral MTX reaches plateau in doses ≥15 mg weekly, and this is the reason of its lower clinical efficacy.
Objectives: The objective of this observational longitudinal study was to evaluate the changes in disease activity, intensity of pain, global health, and physical function when switching from oral (P.O.) to subcutaneous (S.C.) MTX in patients with RA and peripheral form of PsA.
Methods: Forty-eight consecutive patients (79.2% women) with established diagnosis of RA (77.1%) and peripheral PsA were enrolled from the outpatient clinics in six centres in Croatia. Median age was 61 (39-79) years, and the median of disease duration was 120 (3-528) months. Data were collected at baseline (T0) including retrospective data collection from the previous 3 months (on P.O. MTX), at day 90 (±10 days) (T1) and at day 180 (±10 days) (T2) for the previous periods, both of them during S.C. MTX treatment. Dose of MTX remained stable during the study. Domains of interest were Disease Activity Score on 28 joints measured using ESR (DAS28-ESR), level of pain, Patent's Global Health Assessment (PtGHA) and Physician's Global Health Assessment (PhGHA) were measured on horizontal 100 mm VAS, while physical function was measured by Health Assessment Questionnaire – Disability Index (HAQ-DI).
Results: Out of 48 patients 41 patients were switched to S.C. MTX monotherapy and 7 to S.C. MTX in combination with another csDMARD. At T1 40 patients were on S.C. MTX monotherapy and 8 on S.C. MTX in combination with another DMARD, and at T2 39 patients were on S. C. MTX monotherapy, 4 on S.C. MTX in combination with another DMARD, 1 on another DMARD and 4 were lost to follow-up. DAS28 showed trend of decrease from 4.9 at baseline to 4.6 at T1 and 4.2 at T2. Analysis of transition of patients according to DAS28 EULAR criteria has shown that percentage of patients with low disease activity has raised from 4.3% at T0, to 21.7% at T1, and 24.3% at T2, while percentage of patients with high disease activity has declined from 38.3% at T0 to 21.7% at T1 and 13.5% at T2. Recommendation for prednisone therapy > 7.5 mg/QD had 12.5% patients at T0 and T1, and only 6.8% patients at T2. There was a significant decrease in adjusted mean values for level of pain (-1.46; 95%CI -1.55, -0.35), PtGHA (-1.12; 95%CI -1.50, -0.73) and PhGHA (-1.15; 95%CI -1.50, -0.80). HAQ-DI showed significant improvement during the 6-month follow-up (-0.25; 95%CI -0.32, -0.17).
Conclusion: Patients who switched from P.O. to S.C. MTX showed improvement in all observed parameters: decrease of disease activity, reduction of pain, better global health, and physical function. Results of our study are in line with previously published literature data.
Disclosure of Interests: None declared
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AB0424 A RETROSPECTIVE STUDY OF ARTHROSCOPIC SYNOVECTOMY FOR REFRACTORY KNEE ARTHRITIS COMPLICATED WITH POPLITEAL CYST

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Background: Baker's cyst or popliteal cyst is the most common mass surrounding the knee joint that results from inflammatory knee arthritis. With increasing number of arthroscopic synovectomy performed for refractory knee arthritis annually, we aim to explore its value in baker's cyst treatment.[1]
Objectives: To investigate the efficacy of arthroscopic synovectomy on refractory knee arthritis complicated with popliteal cyst.
Methods: A retrospective analysis of 153 patients (RA= 95, SpA= 58) with refractory knee arthritis, underwent knee arthroscopic synovectomy in our hospital from 2010 to 2017, was performed. Among them, 20 patients (RA= 16, SpA= 4) complicated with popliteal cyst. We compared the changes in inflammation makers, disease activity score, imaging manifestations, symptoms, the rate and the grading of popliteal cyst[2] before and after the operation to evaluate the efficacy of knee arthroscopic synovectomy.[3]
Results: inflammation markers[ESR(49.42±32.54 *vs* 24.46±24.17, *P*<0.001), CRP(8.55±16.43 *vs* 5.60±22.45, *P*<0.001)], Rheumatoid Factor(191.29 ±373.72 *vs* 74.90±158.31, *P*<0.001), DAS28 score(4.67±1.25 *vs* 2.81 ±1.23, *P*<0.001), knee joint discomfort score(5.2±1.7 *vs* 1.9±1.5, *P*<0.001) and the amount of knee joint effusion by ultrasound scanning (*P*<0.05) in 95 RA patients were significantly decreased compared to those before the operation; Inflammation markers[ESR(36.76±28.71 *vs* 21.19±9.79, *P*<0.001), CRP(21.19±9.79 *vs* 3.36±6.44, *P*<0.001)], knee discomfort score (4.48±1.06 *vs* 2.51±1.54, *P*<0.05), back pain VAS score(2.74±2.88 *vs* 1.56±1.70, *P*<0.001), and the amount of knee joint effusion by ultrasound

scanning (*P*<0.001) in 58 SpA patients were significantly lower than those before the operation; the rate(16.84% vs 6.32%, *P*=0.023) and grading (*P*=0.007) of popliteal cyst in RA were decreased after the operation; No statistically difference was observed in the rate(6.90% *vs* 5.17%, *P*=0.697) of popliteal cyst in SpA, but the grading were all decreased in 4 patients.

Tab.2 Comparison of pre- and postoperative data in RA patients

	Pre	Post	*P*
ESR($\bar{x} \pm s$)	49.42±32.54	24.46±24.17	<0.001
CRP($\bar{x} \pm s$)	8.55±16.43	5.60±22.45	<0.001
RF($\bar{x} \pm s$)	191.29±373.72	74.90±158.31	<0.001
DAS28($\bar{x} \pm s$)	4.67±1.25	2.81±1.23	<0.001
Knee discomfort score ($\bar{x} \pm s$)	5.2±1.7	1.9±1.5	<0.001
Popliteal cyst(n,%)	16（16.84）	6（6.32）	0.023

Tab.4Comparison of pre- and postoperative data in SpA patients

	Pre	Post	*P*
ESR($\bar{x} \pm s$)	36.76±28.71	21.19±9.79	<0.001
CRP($\bar{x} \pm s$)	9.16±21.46	3.36±6.44	<0.001
Knee discomfort ($\bar{x} \pm s$)	4.48±1.06	2.51±1.54	<0.05
Back pain ($\bar{x} \pm s$)	2.74±2.88	1.56±1.70	<0.001
Popliteal cyst(n,%)	4（6.90）	3（5.17）	0.697

Conclusion: This study provide evidence that knee arthroscopic synovectomy has a good effect for refractory knee arthritis, which can reduce disease activity, improve joint symptoms and decrease the grading of popliteal cyst.

REFERENCES

[1] Zhou X N, Li B, Wang J S, et al. Surgical treatment of popliteal cyst: a systematic review and meta-analysis[J]. Journal of Orthopaedic Surgery & Research, 2016, 11(1):22.
[2] Rauschning W, Lindgren P G. Popliteal cysts (Baker's cysts) in adults. I. Clinical and roentgenological results of operative excision.[J]. Acta Orthop Scand, 1979, 50(5):583-91.
[3] [3]Rupp S, Seil R, Jochum P, et al. Popliteal cysts in adults. Prevalence, associated intraarticular lesions, and results after arthroscopic treatment[J]. Am J Sports Med, 2002, 30(30):112-115.

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AB0425 CONVERSE RELATIONSHIP OF URIC ACID AND VITAMIN D3 IN ADULT BAHRAINI PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The relationship between serum levels of uric acid (UA) and serum vitamin D3 (25(OH)D) in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) has been revealed separately. However, a possible link between these two factors in RA in comparison to SLE has not been clarified yet. This is the first study investigating the joint association between 25(OH)D and UA in two related rheumatic diseases in Bahrain.
Objectives: We aimed to evaluate the possible correlation between serum UA and serum 25(OH)D in adult Bahraini patients with RA and SLE and to examine if there are any differences or similarities between these two patient's groups.
Methods: Eighty adult Bahraini patients (RA=30 and SLE=50) were included in this longitudinal study (two-time points). The mean age of the patients was 45.21 years (range 16–77 years, SD=14.82). Females were 70 (87.5%). Only data for serum UA taken at the same time with vitamin D3 before and after vitamin D3 therapy were collected retrospectively from the patients' records at Salmanyia Medical Complex, Bahrain. The patients received oral vitamin D therapy at a dose of 50.000 IU weekly for 3 months.
Results: Our results showed that in our studied group the mean serum level of 25(OH)D was significantly increased from 48.17 at baseline to 78.87nmol/l after therapy with an increment of 30.71 (P<0.0001). Conversely, the mean serum level of UA in our cohort was significantly decreased from 333.26 at baseline to 304.67μmol/l after therapy (P<0.001). When segregated the group by disease: The mean serum level of 25(OH)D was significantly increased in SLE from 38.39 at baseline to 72.41 nmol/l after therapy (P=0.000), similarly in RA patients 25 (OH)D was significantly increased from 61.67 at baseline to 87.03nmol/l after therapy (P=0.002). In SLE serum UA decreased after vitamin D3 therapy, but the difference was not significant, while in RA the mean serum UA was significantly decreased from 309.83 to 262.03 after therapy (P=0.001). The SLE patients had statistically significant lower serum levels of 25(OH)D at baseline compared to RA (p=0.000). Conversely, RA patients had statistically significant lower serum levels of UA after vitamin D3 therapy compared to SLE (p=0.016). Age group >40 years had significant lower serum UA than those <40 before (p=0.015) and after therapy (p=0.037)
Conclusion: Our study showed that vitamin D3 therapy brought about 1.5 and 2.0 folds increment in its mean serum level in RA and SLE patients, respectively. RA patients showed more reduction in serum uric acid after vitamin D3 therapy compared to SLE, however, similar results manifested by age group>40 years compared to age group <40 yrs. The current study established that serum 25(OH)D levels were inversely correlated with serum uric acid levels in adult Bahraini patients with RA and SLE, thus, the correction of hypovitaminosis resulted in reduction of serum UA.

REFERENCES

[1] Costenbader, K.H., et al., Vitamin D intake and risks of systemic lupus erythematosus and rheumatoid arthritis in women. Ann Rheum Dis, 2008. 67(4): p. 530-5
[2] Jebakumar, A.J., et al., Occurrence of gout in rheumatoid arthritis: it does happen! A population-based study. Int J Clin Rheumtol. 8(4): p. 433-437

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AB0426 COMPARISON OF INFLUENCES OF DIFFERENT CONCOMITANT DRUGS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH IGURATIMOD, A CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUG DEVELOPED IN JAPAN, IN REAL-WORLD CLINICAL SETTING

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Background: Iguratimod (IGU) is csDMARDs developed in Japan and used in Japanese daily practice since 2012. Although IGU was developed as an anti-inflammatory drug at first, anti-rheumatic effect was found in experiments using type II collagen-induced arthritis model mice [1)]. Main mode of action of IGU was thought to be inhibition of NF-kB resulted in decreased production of IL-6, IL-8 and TNF-alpha [2)]. Clinical trials performed in Japan showed that efficacy of IGU was equal to sulfasalazine when used as monotherapy in patients with RA [3)]. Additive efficacy to MTX was also shown in double-blind randomised trial in RA patients [4)]. We reported efficacy of IGU in daily clinical practice in EULAR2017 [5)]. IGU is prescribed as monotherapy or concomitantly with other DMARDs such as MTX, csDMARDs other than MTX or biological DMARDs.
Objectives: Influences of different concomitant drugs were compared in RA patients treated with IGU in this retrospective study.
Methods: 178 RA patients treated with IGU in our institute from April 2013 to June 2017 were included. Patients were divided into four groups. (1) Group in which IGU was started as monotherapy (MONO-G: n=59). (2) Group in which IGU was added on to MTX treatment without bDMARDs (MTX-G: n=81). (3) Group in which IGU was added on to csDMARDs treatment other than MTX (sulfasalazine, tacrolimus, bucillamin) (CSD-G: n=26). (4) Group in which IGU was added onto bDMARDs treatment. (BIO-G: n=12). Patients' characteristics, time course of disease activity (LOCF analysis), continuation rates of IGU (Kaplan-Meier) and reasons of stopping IGU were investigated and compared between groups.

Results: Baseline characteristics was as below. Mean age was 71.4 years old (yo) in MONO-G, 58.3 yo in MTX-G, 70.1 yo in CSD-G, and 58.7 yo in BIO-G. RA duration was 10.2 years in MONO-G, 8.9 years in MTX-G, 11.2 years in CSD-G, and 15.1 years in BIO-G. SDAI at initiation of IGU was 14.2 in MONO-G, 12.8 in MTX-G, 21.3 in CSD-G, and 18.4 in BIO-G. SDAI was significantly improved over time in all four groups (Fig. 1). There were no significant differences in ΔSDAI from baseline to 1 year between groups by one-way ANOVA (Bonferroni). Continuation rates of IGU at one year and three years were 66.6% and 21.2% in MONO-G, 77.8% and 57.1% in MTX-G, 69.2% and 39.7% in CSD-G and 75.0% and 75.0% in BIO-G. Continuation rate in MTX-G was significantly favorable compared with that in MONO-G and CSD-G by Log-rank test (Fig. 2). Most frequent reason for stopping IGU was liver damage (10 cases). Second frequent reason was intermittent pneumonia in 4 cases and infectious pneumonia in 4 cases.

Conclusion: IGU seemed to be the most tolerant in MTX-G and the second most tolerant in BIO-G. Although higher aged population who might have several comorbidities was included in MONO-G and CSD-G, moderate efficacy of IGU was seen in those groups. Although biological DMARDs is effective in RA patients, the cost is very expensive. IGU is comparative cheap (¥9,200/month) and suitable for RA patients with economic difficulties. As IGU decreased TNF-alpha production via inhibition of NF-kB, MTX+IGU may have similar mode of action with MTX+TNF inhibitor. Although small cases were included in BIO-G, Continuation rate of IGU in BIO-G was good.

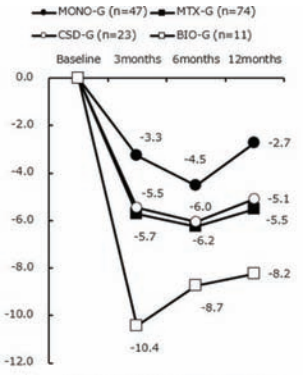


Fig 1. ΔSDAI from baseline
Only patients in whom iguratimod was continued over 3 months were included. Last observation carried forward.

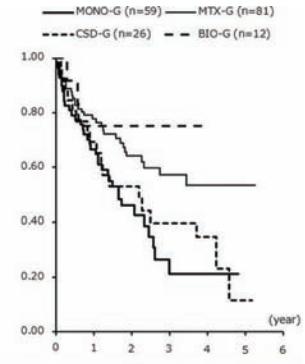


Fig 2. Continuation rates of iguratimod
All patients in whom iguratimod was prescribed were included. Kaplan-Meier.

REFERENCES

[1] Aikawa, et al. Inflamm res. 51; 188-194 2002.
[2] Kohno, et al. J Rheumatol. 28; 2591-2596 2001.
[3] Hara, et al. Mod Rheumatol. 17; 1-9 2007.
[4] Ishiguro, et al. Mod Rheumatol. 23; 430-439 2013.
[5] Hirano, et al. Ann Rheum Dis. suppl2; 285 2017.

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AB0427 **DIFFERENCES IN DRUG USAGE BETWEEN EORA AND YORA PATIENTS WITH TARGET OF LOW DISEASE ACTIVITY**

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Background: Along with the present aging population, development of new therapies such as biological disease-modifying anti-rheumatic drugs for rheumatoid arthritis (RA) has resulted in an increasing number of elderly patients with RA seeking treatment. Furthermore, the onset age of RA has been reported to be trending higher. Elderly onset RA (EORA) is defined as that which develops after 60 years of age, and shown to differ from young onset rheumatoid arthritis (YORA) in regard to background and drug treatment.[1] Although many EORA cases have acute onset, cases with polymyalgia rheumatica (PMR)-like symptoms and negative for rheumatoid factor (RF) have recently been observed at a relatively high rate.[2] In fact, we have found it occasionally difficult to distinguish between EORA and PMR in clinical settings. For both EORA and YORA patients, treat-to-target (T2T) is necessary, though it is considered that EORA should be treated with the goal of acquiring low disease activity (LDA) from the viewpoint of side-effects of administered therapeutic drugs.

Objectives: In this study, we examined the number of drugs given to EORA and YORA patients treated for RA at our hospital who achieved LDA.

Methods: We enrolled 260 patients into the EORA (n=70) and YORA (n=190) groups, and investigated background and treatment protocols.

Results: As for background, there was a significant difference between the EORA and YORA groups for mean age, mean disease duration, and female ratio, whereas the difference was not significant in regard to antibody positive rate, SDAI, or DAS28-CRP. In those groups, average age was 73.8 and 57.8 years, disease duration was 6.66 and 14.7 years, and female ratio was 62.9% and 83.7%, respectively. Furthermore, RF positivity was 85.3% and 80.7%, and ACPA positivity was 86.5% and 87.7%, respectively, while SDAI was 4.28 and 4.59, and DAS28-CRP was 1.99 and 2.04, respectively (Table 1). As for treatments given to the patients, the rates of prednisolone (PSL) use (37.1% vs. 36.3%), and dosage of methotrexate (MTX) (1.45 vs. 1.41 mg) and its usage rate (55.7% vs. 65.3%) were not significantly different between the groups. On the other hand, MTX weekly administration (2.89 vs. 4.09 mg, p=0.009) and biologics usage rate (32.9% vs. 56.3%, p=0.0012) were significantly lower in the EORA group (Table 2).

Table 1

	EORA	YORA
Average age (yrs)	73.8±0.75	57.8±0.91
Average Disease Duration (yrs)	6.7±0.57	14.7±0.81
Female rate (%)	62.9	83.7
RF positive rate (%)	85.3	80.7
ACPA positive rate (%)	86.5	87.7
SDAI	4.28±0.38	4.59±0.22
DAS28CRP	1.99±0.08	2.04±0.05

Table 2

	EORA	YORA
Rate of PSL use (%)	37.1	36.3
PSL amount (mg)	1.45±0.29	14.1±0.21
Rate of MTX use (%)	55.7	65.3
MTX amount (mg/W)	2.89±0.36**	4.09±0.25
Rate of bio use (%)	32.9**	56.3

** $P < 0.01$

Conclusion: Age of onset of RA has been increasing with the aging of society. Therefore, it is important to consider the features of EORA and YORA when considering therapy. For the present investigation, we considered the goal of treatment to be acquisition of LDA rather than

remission, and our findings indicate that EORA patients may be better able to achieve that goal with lower MTX dosage and biological product usage as compared to YORA patients. In addition, EORA patients might achieve LDA with a lower amount of drugs.

REFERENCES

[1] El-Labban AS, et al. Arthritis Musculoskelt Disord. 2010.
[2] Bajocchi G, et al. Clin Exp Rheumatol. 2000.

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AB0428 PATIENT-PHYSICIAN INTERACTION AS A PREDICTOR OF METHOTREXATE ADHERENCE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Recent years have seen numerous encouraging developments in the treatment of patients with rheumatoid arthritis (RA) with significant improvement in disease control. However, methotrexate (MTX) remains a cornerstone therapy and first-line drug for majority of patients with RA, commonly associated with prolonged or even lifelong treatment, which takes the risk for decreasing medication adherence over time Therefore, prompt recognition of predictive factors for MTX non-adherence is one of the most important challenges related to treatment of patients with RA.
Objectives: The aims of this study were to assess patients' self-reported adherence to MTX, as well as to investigate predictive role of physician-patient interaction satisfaction for MTX adherence. Namely, it could be hypothesized that patients' perceptions of multiple specific components of relationship with their physician are associated with patient trust in their physician, which is strongly related to treatment adherence.
Methods: In the period between May 1 and September 15, 2018, 98 consecutive RA patients who were treated in Clinical center of Montenegro and private clinic "Merkur Nera" were enrolled in this multi-centric cross-sectional study. Non-adherence to MTX was defined as $\geq$1 dose missed against medical advice. Patients field in the questionnaire consisted of MTX-specific queries, including the questions related to therapy-related communication with their physician. Possible interaction of the investigated confounders and their joint effect on the MTX adherence were analyzed using ordered logistic regression analysis. A multivariate logistic regression analysis was performed including all covariates that appeared to be associated with the endpoint in the univariate models ($p<0.1$). Odds ratio was used to express the strength of the association between independent predictors and MTX non-adherence as a dependent variable.
Results: Study population was predominantly female (87.8%), and the average age was 56.4±12.1 years. The median duration of RA was 8 years (range 0-34 years), while the median duration of MTX treatment was 6 years (range 0-26 years). The median current dose of MTX which responders received was 15 mg per week. The overall prevalence of non-adherence to MTX was 32.7%. According to the results of univariate regression analysis the following factors are significantly associated with adherence to MTX: younger age (OR=0.942; p=0.065), employment (OR=0.956; p=0.095), working capacity (OR=0,342; p=0.057), marital status (OR=0.342; p=0.001) and expressed need for more communication with the doctor regarding RA treatment (OR=1.410; p=0.021). Finally, in the multivariate regression model the following variables remained statistically significant: marital status (OR=0.406; p=0.007) and expressed need for more communication with the doctor related to RA treatment (OR=1.303 p=0.044). Namely, married RA patients were 2.46 times less likely to MTX non-adherence compared to others, while the patients who stated the need for more communication with the doctor regarding RA treatment has 1,30 times greater chances to MTX non-adherence.
Conclusion: The results of our study have shown that about one third of RA patients met the criteria for non-adherence to MTX. Identification of the patient's need for more communication related to RA therapy as independent predictor for MTX non-adherence suggests that physician-patient relationship quality is an important point of intervention for efforts to improve patients' medication adherence.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7828

AB0429 THE EFFICACY OF TOFACITINIB TREATMENT IN RHEUMATOID ARTHRITIS PATIENTSWITH HIGH DISEASE ACTIVITY IN REAL-WORLD PRACTICE

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Background: JAK-kinase inhibitors are the promising option for patients with severe rheumatoid arthritis (RA). Evaluation of the effectiveness and results of long-term use of tofacitinib (TOFA) seems relevant for clinical practice.
Objectives: To evaluate the efficacy of TOFA in achievement of remission or low disease activity (LDA) in RA patients after 12 months of treatment and follow-up in real-world practice.
Methods: In this open study 30 patients (22 women and 8 men) with severe RA (average DAS28>5,8) with inadequate response to methotrexate in effective dose were enrolled and started TOFA 5 mg BID. Average age was 57 (29-71), average disease history – 6,2 (1,5-12,5) years. Patients evaluated at baseline, after3, 6 and 12 months of treatment: number of painful and swollen joints, ESR, CRP, RF, anti-MCV, DAS28, SDAI. The joints ultrasound (US) with Power Doppler (PD) (German US7 score) helped to estimate synovial inflammation. After 12 months of treatment the patients were under follow-up in real-world practice.
Results: By 3rd month of treatment the average mean of ESR and CRP returned to normal range, the number of painful and swollen joints decreased to 2 times, DAS28 - from 5,8 to 3,8, SDAI – from 41,0 to 18,0. 6 patients achieved remission, 3 – LDA, 2 had high activity (DAS28>5,1) and the rest – moderate activity. We achieve the aim of T2T strategy by 12th month: average ESR and CRP normalized, DAS28 – 2,92 (1,39; 6,21) and SDAI – 7,0 (1,57; 36,4). 33% of patients achieved remission according to DAS28 and SDAI. RF decreased by 37%, anti-MCV stayed high during the year. There was temporary increase of AST, ALT in 4 patients (13,3%), but did not require TOFA discontinuation. By 12 thmonth of treatment in PDUS mode number of joints with hypervascularized synovium decreased from 3 (2; 7) to 0 (0; 1), number of bone erosions has not changed. 1 patient (3,3%) had severe herpes zoster infection, no other infections occurred. In 1 patient (3,3%) TOFA showed no efficacy (DAS28>6,21).
22 patients have finished 12-months course of TOFA at the moment and moved to follow-up period. 13 of them (59%) continue the same dose of TOFA: 8 have remission and 5 – LDA, 2 patients continued TOFA 5 mg/day for 1 year, then stopped and are in remission for 8 months. 1 patient had temporary withdrawal of treatment due to surgery without exacerbation of RA. 4 patients have stopped TOFA for non-medical reasons: 1 is still in remission and 1 – LDA for 12 months, 2 had worsening of RA and treated by low doses of glucocorticoids. At the moment 3 patients (13,6%) have long-term remission for 18 months after the end of TOFA treatment.
Conclusion: TOFA is effective and safe treatment option for severe RA in real-world practice. The effect develops by 3 months and continues to grow to 12 months. When remission is achieved, we recommend a reduced dose before withdrawal. Exacerbation of RA is effective solved by retreatment with TOFA.
Disclosure of Interests: None declared
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AB0430 DEVELOP A REPLICABLE MODEL FOR RATIONAL SELECTION OF STRATEGIES IN TREAT-TO-TARGET AND MAINTAIN-BEING-TARGET: REAL WORLD DATA MINING VIA SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: Daily health care in the real world is different from a clinical trial setting, which deals with a wide spectrum of RA patients from statuses of remission to disease activities at mild, moderate and severe based on DAS28. Due to lack of information and knowledge about optimal regiments for both treat-to-target (T2T) and maintain-being-target (MbT), physicians make choices on treatment strategies based on their own experience or intuition.

Objectives: To develop a replicable model for rationalizing the strategies for T2T and MbT using data mining via smart system of disease management (SSDM)

Methods: SSDM is an interactive mobile disease management tool, including two application systems (APPs) for both the doctors and the patients. The patients can input medical records (including medication and laboratory test results) and perform self-evaluation (DAS28, HAQ) via App. The data synchronizes to mobiles of authorized rheumatologists through cloud and advices could be delivered. In previous studies, we demonstrated that patients could master SSDM after training.

Up to January of 2019, totally 106,647 patients with rheumatic diseases using SSDM, among them, 38% are RA patients who receive more than 1,400 different regiments of treatments. Here we select MTX, Hydroxychloroquine (HCQ) and prednisone (GS) based therapies for model development.

Results: Totally1571 patients were treated with MTX (640), HCQ (397), GS (131), MTX+HCQ (253), MTX+GS (47), HCQ+GS (61), MTX+HCQ +GS (42), respectively. Among the patients whose DAS28<3.2 at baseline, 72% with MTX, 75% with HCQ, 78% with MTX+HCQ and 73% with MTX+HCQ+GS are MbT (DAS28<3.2) after 6 months, which are significantly different comparing with those 52% with GS, 57% with MTX+GS and 57% with HCQ+GS ($p<0.01$). Among the patients whose DAS28>5.1 at baseline, 81% with GS, 72% with MTX+GS and 100% with HCQ+GS achieved T2T (DAS28<3.2) after 6 months, which is significantly different compared to 25% with MTX, 24% with HCQ, 45% with MTX+HCQ and 37% with MTX+HCQ+GS ($p<0.01$). Among the patients whose 3.2<DAS28<5.1 at baseline, there is no statistic significant differences for the rates of achieving T2T, which rates ranging from 39% to 50% across all the 7 regiments.

Conclusion: With MTX, HCQ and GS based regiments in RA, the rational selections of strategies for MbT are mono therapy with MTX, HAQ, or MTX+HCQ, strategies for T2T on high disease activity group are GS, GS +MTX or GS+HCQ. In view of 1400 regiments with clinical outcomes being available in SSDM, the model developments can be replicated in rationalizing strategies through data mining.

Disclosure of Interests: None declared

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AB0431 EFFECTS OF LOW-LOAD RESISTANCE EXERCISE OF LOW EXTREMITY IN WOMEN WITH RHEUMATOID ARTHRITIS

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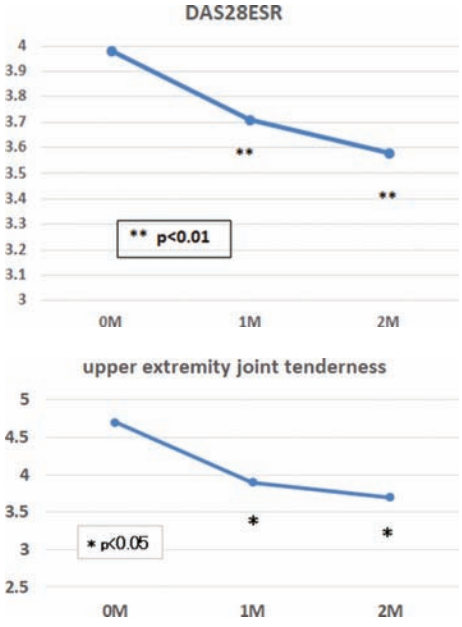
Background: Some skeletal muscles communicate with other organ by secreting proteins and peptides called myokine. Some myokines have anti-inflammatory effect[1]. As regards rheumatoid arthritis (RA), many studies have shown that aerobic and resistance exercise programs do not change the number of inflammatory joints and RA disease activity, whereas other studies showed improved the marker. And almost studies were performed by high-load resistance training protocols. Meanwhile lately Schoenfeild showed that muscle hypertrophy can be equally achieved across a spectrum of load ranges with meta-analysis[2].

Objectives: To investigate the efficacy of low-load resistance exercise of low extremity protocol on RA.

Methods: Twenty-four patients with RA were enrolled. Inclusion criteria were receipt of a stable dose of biologics, JAK inhibitory, and conventional DMARDs more than 3months prior to the first exercise, and corticosteroid and NSAIDs more than one month prior to the first exercise. The exercise circuits consisted of 6 different low extremity exercises intended to improve arthritis. Within the exercise circuits, each exercise was repeated 8-12 times and less than 50% of the 1-repitition maximum. The exercise circuits were performed 3 times a week. Disease activity parameters and inflamed joint of upper extremity and lower extremity were collected at base line and 2 months after exercise started. The Wilcoxon signed-rank test was used to examine the difference between the parameter of the base line and the 2 months.

Results: All patients were female. Mean age was 68.7 years., and mean disease duration 15.3 years. Seven patients (29%) used methotrexate, 5 patients (21%) used prednisolone and 13 patients (54%) used biologics. Mean DAS28(ESR) was 3.98 at base line and 3.58 at 2 months, mean DAS28(CRP) 3.46 and 3.06, mean SDAI 15.4 and 12.5, and mean CDAI 14.5 and 11.5, and mean upper extremity joint tenderness 4.7 and 3.7, mean upper extremity joint swelling 1.6 and 1.8, mean lower extremity joint tenderness 5.8 and 2.2, mean lower extremity joint swelling 4.0 and 2.0 respectively. Every index except upper extremity joint swelling improved significantly ($p<0.05$) at 2 months than baseline.

Conclusion: Low intensity exercise of low extremity was efficacious against not only lower extremity arthritis but also upper extremity joint arthritis in patients with rheumatoid arthritis



REFERENCES

[1] Fabiana B Benatti, Bente K Pedersen: Exercise as an anti-inflammatory therapy for rheumatic diseases-myokine regulation. Nat Rev Rheumatol 11: 86-97, 2015.

[2] Brad J Schoenfeld, et al.: Strength and hypertrophy adaptations low- vs. high-load resistance training a systemic review and meta-analysis. Strength Cond Res 31(12): 3508-3523, 2017

Disclosure of Interests: None declared
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AB0432 BURDEN OF ILLNESS AND CURRENT UNMET NEEDS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH CONVENTIONAL AND ADVANCED DISEASE-MODIFYING THERAPIES: A TARGETED LITERATURE REVIEW

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Background: The development of advanced therapies for the treatment of moderate to severe rheumatoid arthritis (RA) has changed the paradigm of management goals for the condition. However, even with currently available therapies, many patients fail to achieve adequate improvement or disease remission, and thus residual unmet needs exist.
Objectives: To examine the burden of RA with respect to the clinical, humanistic, and economic outcomes among RA patients treated with conventional and advanced disease-modifying therapies.
Methods: A targeted review of the literature published between January 2013 and September 2018 was conducted. EMBASE and MEDLINE databases were searched using terms related to the clinical, humanistic, and economic outcomes associated with conventional and advanced disease-modifying therapies currently available for moderate to severe RA. The search was limited to English-language articles, which reported data from France, Germany, Italy, Spain, United Kingdom, Sweden, Israel, Canada, Brazil, Japan, and Australia. This returned 1,833 records which were assessed for relevance in terms of study methodology, patient population, and outcomes.
Results: A total of 48 articles were included in the qualitative synthesis. Across these studies, disease activity score (DAS) remission rates (DAS28 ≤2.6) ranged from 14.7% to 26.4% over 6–12 months and 10.2% to 53.4% over 3–20 months for patients treated with conventional synthetic disease-modifying antirheumatic drug (csDMARD) monotherapies and biologic monotherapies, respectively. Figure 1 presents country-specific DAS28 remission rates for some of the included regions. Clinical disease activity index (CDAI) remission rates (CDAI ≤2.8) were reported to be <50% among patients who received biologics for a period of up to 12 months. The unemployment rate due to RA was as high as 58.3%, and employed patients lost 1.7 to 16.0 workdays per month at baseline. Following treatment with biologic therapy (over 24–104 weeks), employed patients lost 0.5 to 8.0 working days per month. Costs of treatment with advanced therapies were routinely investigated, but limited data were available regarding the economic burden associated with outcomes such as disability, depression, lack of sleep, and anxiety among RA patients treated with advanced therapies.
Conclusion: Despite advanced treatments, a significant proportion of the RA patient population do not achieve disease remission, and face the substantial burden of reduced productivity and lost work days.
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Figure 1: Country specific disease activity score (DAS 28) remission rates

Country	Treatment	DAS28 remission rate (% of patients)	# of studies
France	TCZ (mono/combination therapy)	29% at 4 months	1
Germany	ETN monotherapy	26.6–32.5% at 26-52 weeks	1
	ETN +MTX	31.2–38.8% at 52 weeks	
Italy	ADA/CTZ/ETN/GOL/IFX (mono or combination therapy)	18%. 19% and 21% at 3, 6, 12 months, respectively	1
	TCZ	52-58% at 6 months	
	ABA	33-35% at 6 months	
	anti-TNF	32-34% at 6 months	
United Kingdom	anit-TNF (ADA/ETN/IFX)	24–43.6% at 6-12 months	2
	csDMARDs	13.8–34.6% at 6-12 months	
Canada	CTZ	29.5% at 6 months; 20.0 % at 24 months	2
Japan	Biologics monotherapy (ADA/ABA/ETN/GOL/IFX/TCZ+MTX) or csDMARDs monotherapy	10–83% at 24-52 weeks	3
	Biologics + csDMARD combination therapy	32.9-83% (time period not reported)	
Australia	csDMARDs/biologics and/or MTX	41.6% at 12 months	1

DAS: Disease activity score; DAS28 remission defined as DAS28<2.6
Note: The presented data do not include all the studies from the review.

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AB0433 TREATMENT PATTERNS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS WHO RECEIVE METHOTREXATE: TARGETED LITERATURE REVIEW

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Background: Methotrexate (MTX) monotherapy or in combination with other disease modifying agents is a common first-line treatment option for patients with rheumatoid arthritis (RA). However, treatment patterns and associated patients' perceptions and preferences of MTX therapy may not be fully understood.
Objectives: To assess treatment patterns of MTX therapy in RA by evaluating real-world adherence and persistence, patients' preferences and reasons for discontinuation, as well as the economic burden of therapy.
Methods: A targeted review of the literature published between January 2010 and March 2018 was conducted by searching the MEDLINE and EMBASE databases. Searches were limited to English-language articles and included original research and reviews. All articles were assessed for relevance, in terms of study methodology, patient population and outcomes by a single reviewer.
Results: The search resulted in 444 hits of which 29 articles were included in the qualitative synthesis. Data pertaining to adherence and patient-reported reasons for non-adherence were extracted from 11 publications. MTX therapy non-adherence was high, with up to 42% of patients reporting not taking MTX as prescribed. Among these patients, many reported taking smaller doses than prescribed (53%) or intentionally skipping doses (52%). Common patient-reported reasons for non-adherence included upcoming surgery, and experience of, or concerns regarding, adverse events (AEs). Data pertaining to therapy discontinuation were extracted from 21 publications. Across the studies sampled, rates of discontinuation at one year were 24–50%. MTX toxicity was responsible for 5–34% of all discontinuations. Among patients who switched from orally to parenterally administered MTX, 29% discontinued due to gastrointestinal AEs within one year. Patient-reported reasons for therapy discontinuation, other than experiencing AEs, included concerns regarding MTX AEs, drug price and lack of perceived need. No studies examining the costs associated with MTX monotherapy monitoring and AE management were identified in the search.
Conclusion: Findings from the review indicated that MTX therapy is associated with substantial non-adherence and discontinuation, thus adding to patient burden. Patient-reported reasons for non-adherence/poor treatment persistence were varied but most commonly included experience of, or concerns regarding AEs.
Acknowledgement: The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of this publication.
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AB0434

EARLY EXPERIENCE WITH JAK INHIBITOR PRESCRIBING IN THE UK: RESULTS FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER FOR RHEUMATOID ARTHRITIS (BSRBR-RA)

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Background: In 2017 a new class of oral disease modifying anti-rheumatic drugs (DMARDs), janus kinase inhibitors (JAKi), were licensed for rheumatoid arthritis (RA): baricitinib and tofacitinib. In the UK, they are approved for use in patients with high disease activity with or without methotrexate, following failure of conventional synthetic (cs) DMARDs or biologic DMARDs, the latter when rituximab is contraindicated. As a new therapy option, it is currently unclear how and when these drugs are being prescribed in patients with RA.
Objectives: This analysis aims to describe the characteristics of patients starting JAKi and registered with the BSRBR-RA.
Methods: The BSRBR-RA aims to capture exposure and outcome data in patients with RA receiving biologics, biosimilars and targeted synthetic DMARDs. At the start of therapy, demographic and clinical data, including past treatment data, are collected. Characteristics of all patients receiving a JAKi for the first time with data recorded in the BSRBR-RA up to 30/11/2018 are described.
Results: To 30/11/2018, 443 patients in the BSRBR-RA have been treated with a JAKi; 374 patients baricitinib and 69 tofacitinib (Table). Twenty-eight percent of baricitinib and 13% of tofacitinib patients received a JAKi following csDMARDs, with no prior biologic exposure. Of these, 15% had a prior malignancy history. Of those with prior exposure, the median number of previous biologics was 3 (IQR 2-4) and 52% had received rituximab. Forty-three percent were receiving concurrent methotrexate.
Conclusion: To date, more patients have been recruited starting baricitinib than tofacitinib, likely owing to the later licensing of tofacitinib. Two groups are emerging with a quarter of patients receiving JAKi immediately after csDMARDs and a majority as a later stage alternative following multiple biologics. Further recruitment and follow-up patients will allow for analysis of real-world safety and effectiveness, but differences in patient characteristics will need to be considered in any comparative effectiveness analyses.

Characteristics of the first 443 patients in the BSRBR-RA treated with JAKi

	Ever exposed [N = 443]	**No biologic exposure [N = 112]**	**Previous biologic exposure [N = 331]**
Baricitinib	374 (84%)	103 (28%)	271 (72%)
Tofacitinib	69 (16%)	9 (13%)	60 (87%)
Age (years)	61 (53 to 69)	62 (51 to 71)	61 (53 to 69)
Female	335 (76%)	81 (72%)	254 (77%)
Disease duration (years)	12 (6 to 21)	6 (3 to 15)	14 (8 to 22)
Number of previous biologics	-	-	3 (2 to 4)
No prior biologics	112 (25%)	112 (100%)	0 (0%)
1 prior biologic	63 (14%)	-	63 (19%)
≥2 prior biologics	211 (48%)	-	211 (64%)
Unknown	57 (13%)	-	57 (17%)
Type of previous biologic exposure	-	-	-
TNF inhibitor	-	-	248 (91%)
Rituximab	-	-	143 (52%)
Abatacept	-	-	95 (35%)
Tocilizumab	-	-	139 (51%)
Concurrent Methotrexate	185 (43%)	51 (48%)	134 (42%)
Concurrent oral steroids	133 (31%)	22 (21%)	111 (34%)
Comorbidities#	-	-	-
None	170 (38%)	58 (52%)	112 (34%)
1 comorbidity	125 (28%)	25 (22%)	100 (30%)
2+ comorbidities	148 (34%)	29 (26%)	119 (36%)
Prior Cancer	38 (9%)	15 (15%)	23 (7%)
Pulmonary Fibrosis	11 (4%)	3 (3%)	8 (4%)
DAS28	5.7 (5.1 to 6.4)	5.6 (5.2 to 6.2)	5.8 (5.0 to 6.6)
HAQ	2 (1.4 to 2.5)	1.9 (0.9 to 2.4)	2.1 (1.5 to 2.6)

Results presented as N (%) or median (IQR).#Comorbidities - hypertension, ischaemic heart disease, stroke, lung disease (asthma and COPD), renal disease, diabetes, depression, liver disease.

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AB0435

REAL WORLD DATA OF A PATIENT COHORT WITH RHEUMATOID ARTRITIS TREATED WITH JAK/STAT INHIBITORS

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Background: We present the real World data of a patient cohort with rheumatoid arthritis (RA) that received one of the two JAK/STAT inhibitors approved by the EMA for this indication.
Objectives: To describe the Real World Data of a patient cohort attending Rheumatology consult of a reference hospital in Valencia with RA diagnosis and that were treated with JAK/STAT inhibitors.
Methods: A descriptive retrospective study was carried out. There were revised medical histories of 28 patients with a RA diagnosis that attended our consults between 2017 and 2018. All 28 patients were JAK/STAT treatment receivers of one of the two JAK/STAT inhibitors approved: Tofacitinib 10 mg oral QD or Baricitinib 4 mg oral QD. There were collected patient baseline demographic data: sex, age, BMI, activity disease score measured by DAS28-CRP and visual pain analogue scale for patient's assessment (VAS). In addition, there were collected the previous synthetic(s) and biological (s) DMARD treatments, as well as the associated treatments. Efficacy and security were also analysed. There were assessed serum biochemical variables, among them acute phase reactants such as CRP and and ESR
Results:

The study population consisted in 28 patients with the following distribution:

M/F	Mean age (years)	BMI (kg/m2)	Baricitinib	Tofacitinib	DAS28/CRP (at de begining)	Mean treatment time (days)
12 (42%)/ 16 (58%)	58.39	30.12	9 (32.14%)	19 (67.85%)	4.81	230.11

With regards to the previous treatments received, we obtained the following results:

Previous DMARDb				Previous DMARDc			
3TB	2TB	1TB	Naïve	3	2	1	Naïve
5	3	10	10	2	9	15	2

DMARDb: Number of previous biological treatment
DMARDc: Number of synthetic previous treatments
With regards to efficacy, there were collected 6 treatment withdrawals: 1 primary treatment failure (in Tofacitinib Group) and 5 secondary treatment failures (1 in Baricitiib Group and 4 in Tofacitinib Group) and the mean treatment duration was 152 days.
Conclusion: Despite the study population was small and the follow-up time was short, we highlight in our patients that both JAK inhibitor alternatives have shown a security and efficacy profile similar to the results shown in pivotal clinical trials. Despite the previous biological treatment failure and obesity are considered as predictors of bad response to treatment, in our cohort did not represent a high risk to treatment failure, it can be an alternative in the same scenary.

Disclosure of Interests: Isabel de la Morena Speakers bureau: Abbvie, Celgene, Pfzier, UCB, Ghebro, Roche, Sanofi, Janssen., Juan Alberto Paz Solarte Employee of: He is working at UCB since December 2018, when the patient recruitment ended., Speakers bureau: Abbvie, Roche, Pfzier, Novartis, Celgene, Amgen, MSD, Janssen, Diego Bedoya: None declared, Pilar Trenor Larraz: None declared
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AB0436 ADHERENCE TO DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN RHEUMATIC DISEASES

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Background: There has been seen a low adherence to treatment in patients with rheumatic diseases, which can have important consequences in disease prognosis. Although literature in Latin-American population is scarce, a previous study evaluating medication adherence in this population reported a 16.4% prevalence of adherence in Rheumatoid Arthritis (RA) and 45.9% in Systemic Lupus Erythematosus (SLE) patients (1). It has been demonstrated better outcomes in patients with rheumatic conditions who have good adherence to treatment therapies (2).
Objectives: To describe the adherence to synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) in patients with rheumatic diseases from a Mexican outpatient rheumatology clinic.
Methods: This study was conducted in the outpatient rheumatology clinic of University Hospital in Monterrey, México, cross-sectional, descriptive, self-report adherence study. Consecutive patients with RA, SLE, Inflammatory Myopathies, Psoriatic arthritis (PsA), Systemic Sclerosis (SSc) were approached during their normal routine rheumatology appointments, in the March 2018 to December 2018 period. They were asked how many days of the last month they forgot or took their DMARDs. We classified the adherence rate in 4 categories based on the days of the last month it took the indicated medication; good: 75%-100% (> 21 days), regular 50-74% (21-15 days), bad 25-49% (14-8 days) and null: <25% (< 7 days). When adherence was not good we interrogated about the cause. Data was obtained from REPAIR ® (internal electronic patient record) and analyzed with the statistical package SPSS version 24.

Table 1. Adherence for Rheumatic Disease Group

	n (DMARDs)	Good n (%)	Regular n (%)	Bad n (%)	Null n (%)
Rheumatoid Arthritis	1,686	1442 (85.5)	105 (6.2)	47 (2.8)	92 (5.5)
Systemic Lupus Erythematosus	440	393 (89.3)	16 (3.6)	12 (2.7)	19 (4.3)
Inflammatory Myopathies	91	83 (92.1)	2 (2.2)	0 (0)	6 (6.6)
Psoriatic arthritis	84	76 (90.5)	1 (1.2)	3 (3.6)	4 (4.8)
Systemic Sclerosis	91	80 (87.9)	6 (6.6)	1 (1.1)	4 (4.4)
N	2,392				

Table 2. Reasons for Bad or Null adherence

	Rheumatoid Arthritis %	Systemic Lupus Erythematosus %	Inflammatory Myopathies %	Psoriatic arthritis %	Systemic Sclerosis %
Economic	30.1	33.3	37.5	37	20
Own decision	27.9	33.3	12.5	25	40
Side effects	11.5	11.1	12.5	12.5	0
Lack of availability	15	13.3	12.5	12.5	40
forgetfulness of dose	11.9	4.4	25	12.5	0
Other	3.5	4.4	0	0	0

Conclusion: Adherence in this group of patients was good, for the definition used in our study.
The method used (self-report) is very sensitive to detect non-adherence, but it overestimate good adherence, therefore the potential bias of results must be considered and confirmed whit objective measurement.
The main reason for poor or no adherence was the economic, with the exception of the Ssc group it was their own decision and the patients with SLE that had the same percentage for economic and self-decision.

REFERENCES

[1] - Resende Prudente L, Souza Diniz J, Matteucci Ferreira TXA, Marçal Lima D, Antônio Silva N, Saraiva G, et al. Medication adherence in patients in treatment for rheumatoid arthritis and systemic lupus erythematosus in a university hospital in Brazil. Patient Preference and Adherence. 2016:10 863–870

[2] - Waimann ChA, Marengo MF, de Achaval S, Cox VL, Garcia-Gonzalez A, Reveille JD. Electronic Monitoring of Oral Therapies in Ethnically Diverse and Economically Disadvantaged Patients With Rheumatoid Arthritis. Arthritis & Rheumatism. 2013:6 1421-1429.

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AB0437 SAFETY OF JAK INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CONDITIONS OF DAILY CLINICAL PRACTICE

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Background: Efficacy and safety of the new JAK inhibitors is supported by phase I, II and III studies with a large number of patients included in the follow-up, although it is of vital importance behavior of new molecules in routine clinical practice, and until now we still have few clinical data.
Objectives: To describe the adverse effects observed, as well as the income Hospitals and description of them during treatment with JAK inhibitors in a series of patients with RA.
Methods: This is a retrospective descriptive study in patients with RA treated with JAK inhibitors in follow-up by the Rheumatology Unit of Virgen de Valme Hospital. We included demographic, related to the disease and treatment and security variables.
Results: We included 31 patients with rheumatoid arthritis with a mean age of 57.58 ± 11.31 years and mean time of evolution of the disease of 9.42 ± 6.62 years, 61.3% positive FR and 61.3% ACPA positive. The female sex represents 74.2% of the sample. The mean of the baseline DAS28 was 4.90 ± 0.95.
Regarding the treatment analysis initiated 12 patients (38.7%) receive baricitinib and 19 (61.3%) tofacitinib. 93.5% were in treatment with steroids at low doses and 80.64% in treatment combined with at least 1 associated DMARD (75% baricitinib group, 84.2% tofacitib group). The subanalysis of concomitant treatment reveals that up to 31.5% of patients undergoing treatment with tofacitinib initiated treatment with $\geq$2 FAMEs. 61.3% of patients had previously received at least one biological drug, among which the antiTNFs stand out for their frequency; 31.5% with one biological, 9.7% with 2 previous biologicals and 16.5% had used three. A total of 14 adverse effects were recorded in 10 of the 31 patients which are described below: baricitinib group a total of 6 events (50%); 1 toxic hepatitis, 1 respiratory infection, 2 cases of urinary tract infection, 1 case of canker sores, and 1 cold sore. Tofacitinib group a total of 8 events (42.1%): 2 cases of Herpes zoster, 1 case of headache and dizziness, 2 perianal abscesses and 1 abscess submandibular There were 3 hospital admissions with independence of its relationship with the treatment analyzed; barcitinib group: 1 patient with upper respiratory tract infection and decompensated heart failure, 1 patient with toxic hepatitis. Tofacitinib group: 1 patient with post-traumatic humerus fracture.
Conclusion: The main side effect observed was infection, in general mild-moderate that only motivated hospital admission in a patient in treatment with barcitinib due to decompensation of its pathology base. Stresses the development of uncomplicated perianal abscess in 2 patients on treatment with tofacitinib, one of them with perianal fistula known, and a recurrence of submental abscess in a patient with antecedent of repetition abscesses in said location. I only know observed elevated transaminases in a patient undergoing treatment with baricitinib showing in general an optimal hepatic safety profile. No primary cardiovascular events of interest have been recorded, neoplasms or other gastrointestinal events. Everything described, considering the high rate of concomitant treatment with steroids at low doses (93.5%) and up to 80.64% of patients in treatment with at least 1 concomitant DMARD.

REFERENCES

[1] Caporali R, Zavaglia D : Real-world experience with tofacitinib for treatment of rheumatoid arthritis. Clin Exp Rheumatol. 2018 Aug 29.

[2] Fleischmann R, Mysler E, Hall S Et Al.: Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy): a phase 3b/4, double-blind, head-to-head, randomised controlled trial. Lancet 2017; 390: 457-68.

[3] Smolen JS, Genovese MC, Takeuchi T, et al. Safety profile of baricitinib in patients with active rheumatoid arthritis with over 2 years median time in treatment [published online September 15, 2018]. J Rheumatol.

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AB0438 **A STUDY COMPARING EFFICACY OF INTRA-ARTICULAR STEROID (IAS) VS INTRAARTICULAR SCLEROSANT IN PATIENTS WITH PERSISTENT SYNOVITIS OF KNEE IN RHEUMATOID ARTHRITIS**

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Background: Chronic persistent synovitis is commonly seen in inflammatory arthritis like RA where despite adequate DMARD therapy, few joints are chronically inflamed. They are the reason for increasing morbidity and poor functional status in these patients. Some patients show persistent synovitis despite intra-articular steroids and hence they is need to identify other drugs like sclerosant which can be of use in improving pain and functional status.
Objectives: To compare the efficacy of Intra-articular steroid versus sclerosant in rheumatoid arthritis (RA) with persistent synovitis despite optimum dose of csDMARDS and to determine, if sclerosant is superior/non-inferior to steroids.
Methods: This is a single blinded-observational pilot study, conducted in Institute of Rheumatology, Madras Medical College for a period of 1 year. 20 patients with persistent synovitis (knees) despite optimum DMARD therapy are recruited as per inclusion and exclusion criteria. Disease and joint related activity and functional status are documented. Ethical committee approved the study. After getting written informed consent patients were randomized into two groups (A and B). Group A received IAS (Triamcinolone Acetonide) and group B received sclerosant (1% Polidocanol). They are assessed at 1, 4, 12 and 24 week and various parameters documented. The results are analysed with SPSS v22 software.**Inclusion Criteria:** 1. RA diagnosis according to ACR/EULAR2010 criteria in the age between 20 and 70years with persistent synovitis of knee. 2.Patients not willing for biological therapy. **Exclusion Criteria:** 1. Age <20->70yrs. 2. Pregnant & Lactating women. 3. Severe co-morbidities, clotting disorders and local infections. 4. Contraindications for intra-articular procedure. 5. Osteoarthritis and other arthritis and CTD. 6 Recent intra-articular injection within 3months.
Results: 40 patients were recruited for the study, with 20 in each group. 45% patients in group A and 65% patients in group B, showed significant improvement in DAS28, CRP, VAS pain and function. VAS scores improved within 1 week and no adverse effects were noted. Both the interventions found to be effective in reducing the pre operative VAS pain and function scores. However, Mean VAS Scores after 1 week of sclerosant injection found to be lesser than that of steroid group and the difference was statistically significant ($p<0.05$).
Conclusion: Intra-articular sclerosant (1%Polidocanol) is non-inferior to steroids in patients with persistent knee synovitis. It could be used as an effective alternative to steroids considering their side effect profile.

REFERENCES

[1] Use of objective measure of articular stiffness to record changes in finger joints after intra-articular injection of corticosteroid, annals of rheumatic diseases, 1997: 56:71-73
[2] Intra-articular injection with triamcilone hexacetonide in patients with rheumatoid arthritis: prospective assessment of goniometry and joint inflammation parameters. Rita Nely Vilar Furtado et al, Revista Brasileira de Reumatologia 2017:57(2):115-121
[3] Zulian F, Martini G, Gobber D, Agosto C, Gigante C, ZacchelloF. Comparison of intra-articular triamcinolone hexacetonide and triamcinolone acetonide in oligoarticular juvenile idiopathic arthritis. Rheumatology (Oxford). 2003; 42:1254–9.7.
[4] Hochberg MC, Chang RW, Dwosh I, Lindsey S, Pincus T, WolfeF. The American College of Rheumatology 1991 revised criteria for the classification of global functional status in rheumatoid arthritis. Arthritis Rheum. 1992; 35:498–502.9.

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AB0439 **YTTRIUM-90 SYNOVIORTHESIS. OUR EXPERIENCE FOR 25 YEARS**

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Background: Radioactive synoviorthesis (RS) is the intra-articular injection of a colloidal suspension of particles marked with a radioisotope that selectively irradiates the synovial membrane, respecting bone and cartilage. The radiocolloid is phagocytosed by type 2 synoviocytes of the synovial membrane, causing fibrosis and decreased production of synovial fluid. Intra-articular puncture is ensured by obtaining synovial fluid and then the radiopharmaceutical is instilled followed by 1ml of triamcinolone acetoide (40mg). After the procedure a graphic gamma image is made to assess the adequate distribution of the radionuclide in the joint cavity. With a half-life of 2.5 days, the drug will continue to emit radiation for weeks, with symptomatic improvement which is observed from the second week. The main indication of this technique is refractory chronic synovitis to local and/or systemic treatment.
Objectives: To describe the clinical-demographic characteristics of patients treated with SR in our hospital, and to asses the efficacy and safety of this technique.
Methods: Retrospective observational study that analyze the radiosynoviorthesis practiced in the Nuclear Medicine service of the Doce de Octubre Hospital between January 1994 and December 2018 is analyzed. A total of 113 techniques were analyzed in 89 patients from our center and other hospitals without Nuclear Medicine service, and data of 72 patients could be obtained from their clinical history. The efficacy of the technique was defined as total or partial, considering objective data (swelling and joint function) and subjective data (patient evaluation).
Results: 95 articular instillations were included in 72 patients, 46% women and 54% men; with an average age of 51.4 ± 15 |21-82| years, the knee articulations were injected with Yttrium-90 (5 millicuries). The patients had knee effusions lasting for an average of 18 months (IR 10-60). The temporal distribution was very heterogeneous, decreasing over the years (1994-1998: 23%, 1999-2003: 32%, 2004-2008: 20%, 2009-2013: 16%, 2014-2018: 9%). 93% of RS were indicated by the rheumatology service and 7% by traumatology. In the classification by pathologies, 72.2% had systemic rheumatological disease. The most frequent causes of indication were rheumatoid arthritis (25%), psoriatic arthropathy (24%), spondyloarthropathy (17%) and pigmented villonodular synovitis (11%). Less frequent were juvenile idiopathic arthritis (5%), arthrosis (4%), microcrystalline arthritis (5%) and non-specific chronic synovitis (9%). 79% had been previously infiltrated with steroid, with an average of 2.8 ± 1.8 |1-10| injections/knee. The 79% had maintained treatment with NSAID, the 42% with systemic steroid, the 55% with DMARDs and the 14% with biological therapy; appearing the therapeutic effect in the first 8 weeks in the 80% of the patients. 13 patients needed a reinstill with an average between radiosynoviorthesis of 25 ± 21 |6-80| months. Side effects were scarce (2.8%) and local in nature; 8.3% required a knee prosthesis.
Conclusion: RS has demonstrated acceptable efficacy and safety in cases of refractory synovitis of both mechanical and inflammatory etiology. Despite this, it is a procedure little used nowadays.
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AB0440 **CHANGES IN KEY LABORATORY VALUES WITH TOFACITINIB 5 MG BID TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS AND RHEUMATOID ARTHRITIS**

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of psoriatic arthritis (PsA) and rheumatoid arthritis (RA). In most countries where tofacitinib is approved, 5 mg twice daily (BID) is the recommended dose for PsA and RA. An important component of any product labelling is information on the need for laboratory monitoring.

Objectives: This post hoc analysis aimed to provide information on the effect of tofacitinib 5 mg BID on laboratory values in PsA and RA patients (pts).

Methods: For analysis of pts with active PsA treated with tofacitinib 5 mg BID, data were pooled from 2 Phase 3 studies and an ongoing long-term extension (LTE) study (data cut-off, 25 January 2017; database not locked; data may change). For analysis of pts with moderate or severe RA treated with tofacitinib 5 mg BID, data were pooled from 8 Phase 2, 7 Phase 3, and 1 LTE studies (data cut-off, 2 March 2017; for LTE, database not locked; data may change). All PsA and most RA pts received a background conventional synthetic disease-modifying antirheumatic drug. Data (to Month 12) for pts receiving constant tofacitinib 5 mg BID were evaluated, comprising pts who received tofacitinib 5 mg BID across studies, either at randomisation or following switch from placebo. Pts in the placebo groups who switched to tofacitinib 5 mg BID at Month 3 were included from the time they first received tofacitinib. Pts who switched tofacitinib dose were excluded. Change from baseline in haematologic (haemoglobin, neutrophils, lymphocytes) and lipid (low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, total cholesterol, triglyceride) levels and key liver tests (bilirubin, alanine aminotransferase, aspartate aminotransferase) were analysed. Although not addressed in the product labelling, creatine kinase, creatinine and C-reactive protein levels were also assessed. Pts meeting protocol-defined discontinuation criteria for laboratory values were evaluated.

Results: The constant tofacitinib 5 mg BID group comprised 348 PsA pts and 3040 RA pts. Mean (standard error) changes/percentage changes from baseline for laboratory values are presented in the table. Laboratory values generally stabilised after 1 to 3 months, and lymphocyte levels stabilised by 24 months (data not shown). In both PsA and RA, ≤3.0% of patients met discontinuation criteria for any laboratory values.

Conclusion: In this post hoc analysis of laboratory data with tofacitinib 5 mg BID, changes in key laboratory values were similar for PsA and RA, and discontinuations due to protocol criteria being met for laboratory values were infrequent. These results provide further information on the effect of tofacitinib on laboratory values in PsA and RA.

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Table. Changes in selected haematologic and lipid levels, key liver tests and C-reactive protein, creatine kinase and serum creatinine levels to Month 12 in the constant tofacitinib 5 mg BID group (safety analysis set)

	PsA[a] (data cut-off, 25 January 2017) N=348						RA[b] (data cut-off, 2 March 2017) N=3040					
	Mean (SE)	Mean (SE) change from baseline					Mean (SE)	Mean (SE) change from baseline				
	BL	M1	M3	M6	M9	M12	BL	M1	M3	M6	M9	M12
Haemoglobin, g/dL	13.88 (0.07)	-0.01 (0.04)	0.00 (0.05)	-0.04 (0.05)	0.05 (0.07)	0.10 (0.06)	12.73 (0.03)	0.10 (0.01)	0.18 (0.02)	0.21 (0.02)	0.17 (0.02)	0.23 (0.02)
Neutrophils, $10^3/mm^3$	4.85 (0.08)	-0.39 (0.08)	-0.31 (0.10)	-0.24 (0.12)	-0.32 (0.11)	-0.33 (0.12)	5.54 (0.04)	-0.75 (0.04)	-0.83 (0.04)	-0.80 (0.04)	-0.85 (0.04)	-0.88 (0.04)
Lymphocytes, $10^3/mm^3$	1.84 (0.04)	0.06 (0.03)	-0.03 (0.03)	-0.05 (0.03)	-0.05 (0.04)	-0.11 (0.04)	1.83 (0.01)	0.17 (0.01)	0.06 (0.01)	0.01 (0.01)	-0.04 (0.01)	-0.13 (0.01)
Bilirubin, mg/dL	0.46 (0.01)	0.03 (0.01)	0.05 (0.01)	0.04 (0.01)	0.05 (0.01)	0.05 (0.01)	0.41 (<0.01)	0.02 (<0.01)	0.04 (<0.01)	0.05 (<0.01)	0.05 (<0.01)	0.05 (<0.01)
ALT, IU/L	25.36 (0.91)	1.19 (0.81)	2.95 (0.87)	3.79 (1.00)	4.13 (1.11)	3.39 (1.08)	20.90 (0.26)	2.30 (0.52)	3.14 (0.35)	3.93 (0.34)	4.27 (0.42)	4.81 (0.61)
AST, IU/L	21.92 (0.57)	1.67 (0.48)	2.72 (0.55)	2.81 (0.63)	2.65 (0.74)	2.92 (0.75)	20.60 (0.18)	2.64 (0.26)	3.64 (0.24)	4.43 (0.26)	4.80 (0.29)	5.34 (0.38)
CRP, mg/L	12.08 (1.05)	-7.20 (0.89)	-6.16 (1.06)	-7.25 (1.20)	-7.56 (1.30)	-8.18 (1.41)	18.46 (0.43)	+1.70 (0.42)	+11.57 (0.45)	+12.12 (0.47)	+12.31 (0.47)	+12.11 (0.49)
Creatine kinase, U/L	99.87 (3.64)	36.37 (3.90)	50.57 (7.47)	51.69 (6.17)	54.13 (5.84)	64.45 (6.28)	70.14 (1.28)	31.76 (1.63)	46.96 (4.78)	50.50 (2.51)	66.42 (10.11)	61.47 (2.32)
Serum creatinine, mg/dL	0.81 (0.01)	0.02 (<0.01)	0.02 (0.01)	0.03 (0.01)	0.03 (0.01)	0.04 (0.01)	0.73 (<0.01)	0.04 (<0.01)	0.04 (<0.01)	0.06 (<0.01)	0.06 (<0.01)	0.07 (<0.01)
	Mean (SE)	Mean (SE) % change from baseline					Mean (SE)	Mean (SE) % change from baseline				
	BL	M1	M3	M6	M9	M12	BL	M1	M3	M6	M9	M12
LDL-c, mg/dL	117.32 (1.76)	7.39 (1.00)	8.43 (1.13)	9.91 (1.32)	10.35 (1.55)	10.99 (1.89)	113.70 (0.62)	10.96 (0.51)	13.85 (0.58)	14.08 (0.56)	13.93 (0.78)	15.02 (0.62)
HDL-c, mg/dL	55.59 (0.92)	9.55 (0.99)	10.34 (1.13)	9.94 (1.22)	9.67 (1.39)	10.13 (1.46)	58.92 (0.31)	13.00 (0.41)	13.97 (0.50)	13.21 (0.44)	13.87 (0.63)	13.98 (0.52)
Total cholesterol, mg/dL	201.39 (2.18)	7.08 (0.68)	7.92 (0.80)	8.72 (0.87)	8.98 (1.01)	9.33 (1.22)	197.51 (0.76)	9.90 (0.32)	12.10 (0.37)	12.18 (0.34)	13.20 (0.45)	13.33 (0.39)
TG, mg/dL	145.82 (5.55)	8.59 (2.32)	8.71 (2.24)	10.21 (2.56)	14.22 (2.93)	16.67 (3.44)	125.44 (1.24)	8.25 (0.87)	12.90 (0.95)	14.21 (0.90)	18.26 (1.43)	16.38 (1.07)

[a]Includes OPAL Broaden (NCT01877668; 12-month study), OPAL Beyond (NCT01882439; 6-month study) and OPAL Balance (NCT01976364; LTE study; data cut-off, 25 January 2017) studies. All studies were complete except for the LTE study; [b]Includes studies A3921019 (NCT00147498), A3921024 (NCT00413699; LTE study; data cut-off, March 2, 2017), A3921025 (NCT00413660), A3921032 (NCT00960480), A3921035 (NCT00550446), A3921044 (NCT00661661), A3921045 (NCT00814307), A3921046 (NCT00856544), A3921064 (NCT00853385), A3921068 (NCT01164579), A3921069 (NCT01039688), A3921073 (NCT00976599), A3921109 (NCT01059864), A3921129 (NCT01359150), A3921187 (NCT02187055) and A3921237 (NCT02147587). All studies were complete except for the LTE study

Safety analysis set: patients who received ≥1 dose of tofacitinib

Baseline is the latest pre-tofacitinib dose measurement, and includes patients with a baseline and ≥1 post-baseline measurement

Constant tofacitinib 5 mg BID: patients assigned to tofacitinib 5 mg BID, or advanced from placebo to tofacitinib 5 mg BID in the index studies, where Day 1 is the first dose of tofacitinib 5 mg BID, and includes data from LTE studies when exposure in index studies is <12 months

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; BL, baseline; CRP, C-reactive protein; HDL-c, high-density lipoprotein-cholesterol; LDL-c, low-density lipoprotein-cholesterol; LTE, long-term extension; M, month; N, number of patients included in the analyses. Number of patients for each laboratory parameter at each visit may be fewer than N due to missing values; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SE, standard error; TG, triglyceride

Figure 1

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AB0441 THERAPY WITH TOFACITINIB IN A COLOMBIAN POPULATION WITH RHEUMATOID ARTHRITIS: RESULTS OF THE DAILY CLINICAL PRACTICE

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects the quality of life and reduces life expectancy. It is characterized by the presence of autoantibodies and erosive synovitis that mainly involves small joints (1). Tofacitinib is the first oral Janus Kinase (JAK) inhibitor approved in 2012 for the treatment of patients with active, moderate to severe RA that does not respond to other therapies (2).

Objectives: The objective was to describe demographic and clinical results of a cohort of Colombian patients with RA treated with tofacitinib.

Methods: Descriptive observational study of a historical cohort of RA patients in a specialized center for the management of inflammatory arthropathies, from April 2014 to February 2018. The following variables are described: age, sex, time evolution of the disease, type of AR, comorbidities, disease activity (DAS-28), schedule and treatment time. For the descriptive analysis, categorical variables are presented as absolute and relative frequencies; while continuous variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR) according to distribution. The outcome of DAS 28 ≤ 3.2 was estimated by incidence rate, defined as the number of patients who presented the outcome divided by the summation of total exposure time of the patients.

Results: Of 59 patients included, 88.1% (52) were women, with a median age of 58.8 years (IQR 49-68 years), 74.6% were seropositive, the median time from diagnosis was 18.2 years (IQR 12- 28.3 years). High blood pressure was the most common comorbidity (40.7%) and 7% had tuberculosis history. The median number of bDMARD prior to tofacitinib was 2 (IQR 1-3). Sixty six percent patients (39) were on monotherapy while 34% (20) were on combination with leflunomide (19) and methotrexate (1). The median time of treatment was 1.2 years (IQR 0.6-2 years). At the beginning, 84.7% patients (50) were in moderate or high disease activity and 15,3% (9) in remission or low activity; at the end of follow-up, 47.5% (28) were in remission or low activity and 52.5% (31) in moderate or high activity (p = 0.000). The mean DAS28 at the beginning of tofacitinib was 4.6 ± 1.55 and at the end of the follow-up was 3.5 ± 1.49, with a difference of means of 1.10 (IC95% 0.62-1.57), (p 0.00). During the follow-up period, the rate of development of remission or low activity was 11.92 (95% CI 8.35-16.51) cases per 100 people-month observed (p 0.00). Only 2 patients developed therapeutic failure.

Conclusion: Tofacitinib shows a good profile of effectivity in patients with failure to prior bDMARD. Almost 50% patient reaches low disease activity or remission during follow up and low number of therapeutic failure was found.

REFERENCES

[1] Picchianti-Diamanti A, et al. Front Microbiol. 2018;8(2696):1-9
[2] Cohen S, et al. Rheumatol Ther. 2018;5(1):283-291

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AB0442 RESPONSE TO BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITISWITH FAILURE TO CONVENTIONAL SYNTHETIC DMARD AND/OR BIOLOGICAL DMARD: DATA FROM A LOCAL REGISTRY

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Objectives: To know the characteristics of patients with rheumatoid arthritis (RA), in treatment with baricitinib (BARI), who have failed to conventional synthetic DMARD (DMARDcs) and/or biological DMARDs (DMARD).
Methods: Prospective observational study, in real life, of patients with RA, under treatment with BARI. General data of the patients, (age, gender, comorbidity), RA and treatment were collected (time of evolution, presence of RF and ACPA, efficacy indexes at the beginning of BARI and the last visit: DAS28-VSG and CDAI, previous or concomitant treatment with DMARDcs and/or DMARDb, end of treatment and cause, time in BARI, serious adverse effects during treatment with BARI.
Results: Of 529 patients in follow-up, who have received at least one dose of DMARDb, 224 (42%) are diagnosed with RA, and 58 (26%) of them receive some drug inhibitor of the JAK pathway; 40/224 (18%) of them BARI.
The patients treated with BARI, 77% were women, mean age of 58.95 ± 10.8 years and mean evolution of RA of 9.6 ± 8.8 years. The mean BMI is 28.8 ± 1.8. The FR and ACPA are positive at 86% and 89%, respectively. 94% of patients continued concomitant treatment with some DMARDcs.
BARI is the first drug after failure of DMARDcs (F1) in 24/40 (60%) patients, and in 16/40 (40%), after failure to some DMARDb: second drug after failure to DMARDb (F2) in 2 (6%), third (F3) in 5 (13%) patients, fourth (F4) in 6 patients (17%) and fifth (F5) in 3 (9%) patients. The mean global time in BARI is 9.6 ± 3.2 months, being for F1, F2, F3, F4, F5, of 7, 5.2, 7.7, 6.9 and 11.1 months, respectively. BARI patients, such as F1 versus F2-F5, presented significantly higher BMI (30.83 ± 2.6 vs. 26.95 ± 4.4, p <001), higher percentage of ACPA (100% vs. 74%, P = 0.026), and lower mean time of evolution of RA (5.3 years, range: 0.7-25 vs 14.75 years, range: 2-36 years, p <0.001). In patients F2-F5, patients had failed to some DMARDb before initiating BARI, in F2 to 1 therapeutic target, in F3 to 2 targets and in F4 and F5 to 2 or 3 targets.
Regarding safety, 1 patient presented herpes zoster. The results of clinical efficacy with DAS28-VSG and baseline CDAI and in the last evaluation are shown in the table.
Conclusion: • 1. Baricitinib is effective and safe in real clinical practice.

- 2. It is competent of achieving clinical remission or low activity, in a high percentage of patients, even in those who have failed several biological drugs or several therapeutic targets previously.

	DAS28-ESR		p	CDAI		P
	Baseline	Last visit		Baseline	Last visit	
BARI F1	5.4	2.5	**0.0001**	26.0	5.0	**0.001**
BARI F2-F5	5.6	2.6	**0.0001**	27.8	5.8	**0.001**

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AB0443 GAYET WERNICKE'S ENCEPHALOPATHY SECONDARY TO METHOTREXATE INTOLERANCE: A SERIOUS COMPLICATION OF CHRONIC VOMITING

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Background: Gayet-Wernicke's encephalopathy is a serious complication of thiamine deficiency. Chronic alcoholism is recognized as the most commun cause of Gayet-Wernicke's encephalopathy, but other causes including malnutrition, chronic vomiting, prolonged fasting, and exclusive artificial feeding have been documented.
Objectives: We report a case of Gayet-Wernicke's encephalopathy complicating uncontrollable vomiting secondary to severe Methotrexate intolerance.
Methods: Case report
Results: A 47-year-old women with rheumatoid arthritis. She was put under methotrexate at the dose of 15 mg/week, 1 month prior to admission into our department for the management of an acute febrile polyarthritis associated to severe and uncontrollable gastrointestinal intolerance to Methotrexate. There was no abdominal pain or transit problem. One month later, she experienced temporo-spatial disorientation, somnolence, horizontal nystagmus, and vertigo attacks with visual hallucinations and memory problems. The muscular forces at the four limbs were decreased to 3/5 with abolished osteotendinous reflexes at the two lower limbs. MRI showed hyperintense signals on T2 and FLAIR image in thalamus, periaqueducal area and mamillary bodies. Electroneuromyography (ENMG) showed axonal motor neuropathy in all 4 limbs. The hemogram showed normochromic normocytic anemia. Laboratory testing for Vitamin B12, vitamin D, folate and minerals showed multiple deficiencies. A multivitamin supplementation was introduced with good evolution.
Conclusion: This is the first case of severe digestive intolerance to methotrexate leading to a serious neurological complication. Although digestive intolerance to methotrexate is considered benign, it can be daunting. Thorough knowledge of complications and close monitoring of patients must be imperative. Gayet Wernicke encephalopathy is a rare and serious pathology. We should keep it in mind and prevent it in risky situations.

REFERENCES

[1] Seci G, Sera A. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol. 2007;6 (5):442-55.
[2] osiezagha K, ali s, freeman c, et al. thiamine deficiency and delirium. Innov clin neurosci 2013;10:26-32.
[3] manzo g, de gennaro a, cozzolino a, et al. mr imaging findings in alcoholic and nonalcoholic acute wernicke's encphalopathy : a review. Biomed res Intern 2014; 2014:503596.

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AB0444 RISK FACTORS OF JOINT SURGERY IN RHEUMATOID ARTHRITIS TUNISIAN PATIENTS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by polyarticular synovial inflammation and progressive joint destruction. Orthopedic surgery is an integral part of the treatment of RA and it is mainly reserved for severe and advanced forms where there is a failure of medical treatment.
Objectives: To assess the rate of joint surgery in rheumatoid arthritis (RA) Tunisian patients and to determine the risk factors of surgical treatment
Methods: A retrospective cross sectional study over a period of 15 years including 500 Tunisian patients with RA was conducted. The prevalence of joint surgery indication has been evaluated. Clinical, paraclinical and therapeutic characteristics of RA were compared according to the need of surgical treatment
Results: Mean age was 53.4 years. Female to male ratio was 5. The indication of joint surgery was noted in 59 patients (12%). Factors associated with joint surgery were delayed diagnosis (p = 0.037), long RA duration (p = 0.017), young onset of RA (p <0.001), presence of joint deformities (p = 0.034), presence of osteoporosis (p = 0.029), presence

of antinuclear antibodies<0.001), combination therapy of methotrexate with other conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) (p = 0.001), a short period of first medical treatment (p = 0.012) and high erythrocyte sedimentation rate (ESR) (p = 0.027). In multivariate analysis, three factors were independently related to the need of joint surgery: age at disease onset (OR 2.799 95%CI: 1.49-5.22 p=0.01), high ESR level (OR 2.807 95%CI: 1.5-5.24 p=0.01), and association of Methotrexate with other csDMARDs (OR 3.500 95%CI: 1.61-7.56 p=0.01)

Conclusion: Twelve percent of RA patients needed joint surgery treatment. Predictive factors of surgical treatment were young age at disease onset, high ESR level and association of methotreaxte with other csDMARDs

REFERENCES

[1] Waljee J, Zhong L, Baser O, Yuce H, Fox DA, Chung KC. The incidence of upper and lower extremity surgery for rheumatoid arthritis among medicare beneficiaries. J Bone Joint Surg Am. 2015;97(5):403-10.

[2] Kapetanovic MC, Lindqvist E, Saxne T, Eberhardt K. Orthopaedic surgery in patients with rheumatoid arthritis over 20 years: prevalence and predictive factors of large joint replacement. Ann Rheum Dis. 2008;67(10):1412-6.

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AB0445 REMARKABLE OUTCOMES IN PATIENTS WITH RA USING CONVENTIONAL DMARDS UNDER A T2T STRATEGY AND A DISEASE MANAGEMENT MODEL – RESULTS FROM A FIVE YEAR REAL-WORLD REGISTRY

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Background: Rheumatoid arthritis (RA) is a common chronic inflammatory disease. Treat-to-target (T2T) is a management strategy for R that proposes as the therapeutic target a state of remission or low disease activity, additionally a multidisciplinary management of patients with RA has demonstrate to be an additional aid to achieve remission or low disease activity. Real-world evidence (RWE) refers to information coming from electronic health records, billing data, registries among others. RWE shows results that are difficult for clinical trials to demonstrate due to ideal conditions(1, 2).

Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy during 5 years in a cohort of patients receiving conventional DMARDs that attend to a specialized RA center.

Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed during 2015-2017; those patients were followed-up under T2T standards and a multidisciplinary approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3-5 weeks (DAS28 > 5.1), every 7-9 weeks (DAS28 $\geq$ 3.1 and $\leq$ 5.1), and every 11-13 weeks (DAS28 < 3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 > 3.2 unless patient´s conditions don't permit it; we considered this follow-up type as implementation of a T2T strategy in patients with RA. Patients entered into a multidisciplinary program of care with periodic consultations not only to rheumatology but with a physiatrist, psychologist, physiotherapist, occupational therapy nutrition, and, a patient focused program. With a multidisciplinary model of care the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA. We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We compared disease activity at base line and at the end of follow-up.

Results: During 5 years we included 2.128 patients. 83% were female and 17% were male, mean age was 57 years ±14. At baseline median DAS28 4.34 RIQ (3.76-5.06) and at 5 years 2.02 RIQ (1.46-2.38). At the end of our follow-up 81% were remission and 7% in LDA. See table 1. I our study DAS28 was not normally distributed, thus we performed a Wilcoxon test in order to compare the mean DAS28 at baseline/5-year showing statistical significance (P<0.05).

ACTIVITY LEVEL	BASELINE		3 YEARS FOLLOW-UP	
	n	%	n	%
REM			1726	81
LDA	5	0.24	147	6
MDA	1628	76.37	230	11
SDA	495	23.39	25	2

Conclusion: In our patients T2T improves associated with a disease management model improves disease activity in patients with RA. This evidence from a real-life setting that shows the advantages of treating RA patients with a multidisciplinary team under a T2T model with a low-cost treatment. It is important to explore other predictors that can improve disease activity.

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AB0446 REAL-LIFE USE OF BARICITINIB IN RHEUMATOID ARTHRITIS: A MULTICENTER OBSERVATIONAL STUDY OF 150 PATIENTS

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Background: Baricitinib is an oral selective JAK1/2 inhibitor recently approved in the EU for the treatment of rheumatoid arthritis (RA). No real-life data are available about its efficacy and safety.

Objectives: To investigate the efficacy and safety profiles of baricitinib in a real-life setting.

Methods: We performed a multicenter prospective observational study on adult RA patients starting JAK inhibitors between 12/2017 and 12/2018. Demographic and clinical data as well as laboratory values and adverse events were collected at baseline and after 12 and 24 weeks. Disease activity was measured by DAS28-CRP at baseline, after 12 and 24 weeks.

Results: We obtained data from 150 patients with RA (women 116 – 77.3%; median age 60 years, inter-quartile range IQR 54-68; median disease duration 10 years, IQR 4-18) treated with baricitinib 2 or 4 mg QD, however only 2/150 (1.3%) at the reduced dosage. At the time of database lock 95/150 (63%) patients have completed the 12 weeks follow-up, 38/150 (25%) patients have completed the 24 weeks follow-up. Baricitinib was started after at least one conventional synthetic DMARD in all 148/150 cases (99%), being in all of cases methotrexate, while was started prior to a biologic DMARD in 57 (38%) patients. It was prescribed as a second line in 17/93 (18%) patients, third in 27 (29%), fourth or higher in 49 (53%). Baricitinib was prescribed as monotherapy in 57/150 (38%) patients, while combined with methotrexate in 65/150 (43%), at a median dosage of 15 mg/week. Oral corticosteroids were used by 105/150 (70%) patients, at a median dosage of 5 mg/day. Mean DAS28-CRP at baseline was 4.92 (standard deviation 1.22), with 65 (43.3%) patients having a DAS28-CRP>5.1. At both 12 and 24 weeks, a significant reduction of disease activity scores was observed (DAS28-CRP mean 3.07, SD 1.36, and 2.85, SD 1.35, respectively; *p* values<0.001). Sixteen (11%) patients discontinued the treatment, with 8 (50%) due to primary inefficacy, mainly in the first 3 months of therapy (5/8– 63%). Adverse events were observed in 19/150 (13%) patients, 7 being non-serious infections (4

upper respiratory tract infections, 2 urinary tract infection, 1 *Herpes labialis*), while 3 patients manifested Herpes Zoster reactivation, 2 deep vein thrombosis (one with pulmonary embolism), 2 discontinued due to severe anemia and pancytopenia, and 2 developed self-limiting liver enzymes elevation.

Conclusion: In our real-world dataset, baricitinib is effective in reducing RA disease activity, after 12 weeks, being generally well-tolerated with few severe adverse events.

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AB0447 BIOLOGICAL THERAPY AND RADIOSYNOVIORTHESIS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: The treatment of patients with rheumatoid arthritis (RA) has been spectaculary changed since the 1950's. Introduction of the steroid compounds and their local application, the chemical and radionuclide synovectomy, surgical synovectomy, use of non steroid drugs, the basic treatment and the spread of biological therapy are the most important steps. Introduction of the biological therapy has changed the quality of life for these patients.

Objectives: During biological therapy sometimes 1 or 2 joints could be affected by inflammation. In this cases always the question is how to solve the problem. Change of the biological or basic therapy, use surgical synovectomy or radiosynovectomy (RSO)?

Methods: In our rheumatological department 2100 patients with RA and PA were treated with biological therapy between 2002 and 2015. In 100 patients we applied RSO because of the inflammation of the knee joint during biological therapy. We made a long term follow-up in 72 patients. All participants provided written informed consent.

62 participants inflammatory knee joint disease was diagnosed on the basis of the American College of Rheumatology. 55 of 62 patients with rheumatoid arthritis were seropositive, 7 seronegative. Steinbrocker functional stadium II was observed in 52, stadium III in 10. 10 patients were psoriatic arthritis. Mean age of 13 male and 61 female patients was 51.4 years (range 24-79) years. In 38 patients the right knee, in 34 the left knee was treated by radiosynovectomy. Mean duration of disease was 7.3 years (range 0.5-25), of synovitis (6.3month (range 3-8) Mean number of punctions of the treated joint prior to radiosynovectomy was 4,2 per patient and of steroid administrations prior to radiosynovectomy 3,0. In 12 patients a systemic steroid therapy has been performed.

Results: During the study period, inflammation decreased. In the first two years excellent and good results were recorded in 82,2%. Two years after radiosynoviorthesis 83.3% of patients did not need another punction. Before the knee inflammation patients were in complete remission which status has been achieved after RSO as well. DAS: 2,4+-0,4.

Conclusion:

1. RSO is an effective method to treat the inflammation of the knees.
2. The RSO performed during biological tehrapy is as effective as in the case of patients without biological therapy.
3. In case of a succesful RSO there is no need for biological or basic therapy neither for surgical synovectomy.
4. However an intraarticular injection has a low risk for infection it is recommended to avoid the biological therapy during the RSO.

REFERENCES

[1] Szekanecz Z.: Célzott terápia a reumatológiában. Klinikum és Tudomány, MOTESZ Magazin; 2010;XVIII(2):31–44.
[2] McInnes IB, Schett G. Cytokines in the pathogenesis of rheumatoid arthritis. Nat Rev Immunol. 2007 Jun;7(6):429-42
[3] Klippel JH. Primer on the Rheumatic Disease. 12th ed. 2001.
[4] Lipsky PE. Harrison's Principles of Internal Medicine. 16th ed. 2005
[5] EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update
[6] Fellinger K. and Schmid J.: Die lokale Behandlung der rheumatischen Erkrankungen. Z. Inn. Med. 33. 351. 1952.
[7] Stucki G., Bozzone P., Treuer E., Wassmer P. and Felder M.: Efficacy and safety of radiation synovectomy with Yttrium-90: A retrospective long term analysis of 164 applications in 82 patients. British J. of Rheumatology 32. 5. 383-386. 1993.
[8] Combe B., Krause E. and Sany J.: Treatment of chronic knee synovitis with arthroscopic synovectomy after failure of intra-articular injection of radionuclide. Arthritis Rheum. 32. 1. 10-14. 1989.
[9] Feldmann M, Maini RN.:Lasker Clinical Medical Research Award. TNF defined as a therapeutic target for rheumatoid arthritis and other autoimmune diseases. Nat Med. 2003 Oct;9(10):1245-50.

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AB0448 SAFETY AND EFFICACY OF FILGOTINIB IN JAPANESE PATIENTS ENROLLED IN A GLOBAL PHASE 3 TRIAL OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGIC DMARDS

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Background: Filgotinib (FIL), an oral, selective inhibitor of Janus kinase 1 (JAK1), has demonstrated efficacy in a phase 3 study in bDMARD-IR patients with active rheumatoid arthritis (RA).

Objectives: We report results of Japanese patients enrolled in the FINCH2 study (ClinicalTrials.gov Identifier: NCT02873936) of FIL in patients with RA and an inadequate response or intolerance to $\geq$1 bDMARDs.

Methods: FINCH2 (ClinicalTrials.gov: NCT02873936) was a 24-week, randomized, placebo-controlled, phase 3 trial conducted globally at 114 sites, including at sites in Japan, from July 2016–June 2018. Male and female adults with moderately-to-severely active RA and inadequate response/intolerance to $\geq$1 prior bDMARDs were randomized 1:1:1 to oral doses of FIL 200 mg, FIL 100 mg, or placebo (PBO) once daily (QD) for 24 weeks; patients continued background therapy with conventional synthetic DMARDs.

Results: Primary and all key secondary endpoints were met for both global (N=448, Genovese, 2018) and Japanese patient populations (n=40; FIL 200 mg, n=12; FIL 100 mg, n=15; and PBO, n=13). ACR20 response rates, HAQ-DI LS mean changes from baseline, and the percentage of Japanese patients with DAS28(CRP) $\leq$3.2 at week 12 are shown in Table 1. In Japanese patients, treatment-emergent adverse event (AE) rates were similar for FIL 200 mg, FIL 100 mg, and PBO (75%, 60%, and 77%, respectively) and there were no serious AEs; there was 1 case of uncomplicated herpes zoster (FIL 200 mg); and no

venous thrombotic events, opportunistic infection/active TB, malignancy, GI perforation, or death.

Table 1. Efficacy measures in the Japanese subgroup at weeks 12 and 24.

	FIL 200 mg QD (n=12)	FIL 100 mg QD (n=15)	PBO QD (n=13)
ACR20 (%) Week 12	83% (p=0.015)	53% (p=0.28)	31%
ACR20 (%) Week 24	92% (p<0.001)	60% (p=0.024)	15%
HAQ-DI (LSM CFB) Week 12	–0.55 (95% CI: -0.81, –0.29)	–0.30 (CI: -0.53, -0.07)	0.09 (CI: -0.16, 0.35)
DAS28(CRP) ≤3.2 (%) Week 12	67% (p<0.001)	47% (p=0.007)	0%

LSM CFB, least square mean change from baseline. P-values are vs PBO.

Conclusion: In this phase 3 study in bDMARD-IR patients with active RA, treatment with FIL over a 24-week period was associated with significant improvements in signs and symptoms of RA, with a safety and efficacy profile in Japanese patients consistent with that in the global population. Thus, FIL may provide a novel treatment option for patients who continue to have active RA despite prior biologic therapy.

REFERENCES

[1] Genovese MC, et al. ACR 2018. Abstract L06.

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Ltd., and UCB Japan, Speakers bureau: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Speakers bureau: AbbVie GK., Bristol–Myers K.K., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Astellas Pharma Inc, Diaichi Sankyo Co. Ltd., Eisai Co. Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co. Ltd., Novartis Pharma K.K., Tsukasa Matsubara Consultant for: Nichi-Iko Pharmaceutical Co., Ltd, Pfizer Japan Inc., Speakers bureau: Astellas Pharma Inc, SEKISUI MEDICAL CO., LTD., UCB Japan Co. 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AB0449

PAIN REDUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOFACITINIB MONOTHERAPY WITH OR WITHOUT PAIN MEDICATION: A POST HOC ANALYSIS OF POOLED DATA FROM PHASE 2, PHASE 3 AND PHASE 3B/4 STUDIES

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. Pain is the most common symptom reported by patients (pts) with RA,[1,2] thus reduction of pain is an important treatment goal.
Objectives: To evaluate the effect of tofacitinib monotherapy ± pain medication on pain in pts with RA.
Methods: This pooled post hoc analysis included pts who received tofacitinib 5 mg BID monotherapy (ie without csDMARDs) in Phase (P)2 (NCT00550446), P3 (ORAL Solo; NCT00814307) and P3b/4 (ORAL

Strategy; NCT02187055) studies. Pts were stratified by concomitant use of 'any pain therapy' (opioids, plain analgesics [eg acetaminophen], NSAIDs or glucocorticoids [GC; ≤10 mg of prednisone or equivalent per day]), 'pure analgesics' (opioids or plain analgesics) and 'adjuvant analgesics' (NSAIDs or GC). Pts receiving pain medication at baseline (BL) maintained a stable dose during the studies; opioid and/or acetaminophen dose could be increased as rescue therapy. Efficacy outcomes were assessed at Month (M)3 and M6: change from BL (Δ) in Pt Assessment of Pain (Pain; visual analogue scale [VAS]) and ΔPain stratified by DAS28-4(ESR)-defined low disease activity (LDA; ≤3.2) status at M3 and M6.

Results: Of 676 pts who received tofacitinib 5 mg BID monotherapy, 604 (89%) received 'any pain therapy', 141 (21%) received 'pure analgesics' and 589 (87%) received 'adjuvant analgesics'. Demographics and BL disease characteristics, including disease activity and Pain VAS, were generally similar when stratified by use/type of pain medication. Reductions in pain (ΔPain VAS) at M3 and M6 were generally similar for pts who received tofacitinib with 'any pain therapy' vs those who did not receive 'any pain therapy' (Figure 1a). There was a trend for a numerically greater reduction in pain at M3 and M6 in pts who received tofacitinib with 'any pain therapy' and who achieved LDA at M3 and M6 vs those who received tofacitinib with 'any pain therapy' and did not achieve LDA (95% CI overlapped; Figure 1b). By contrast, pain reductions were similar for pts who received tofacitinib without 'any pain therapy', irrespective of LDA status. Similar trends were seen when pts were stratified by use of 'pure analgesics' and 'adjuvant analgesics' (data not shown).

Conclusion: In this pooled post hoc analysis, pain reduction was similar in pts with RA receiving tofacitinib, regardless of pain medication use. Pain reduction was similar in pts receiving tofacitinib without 'any pain therapy', irrespective of LDA status. These results should be interpreted with caution, as pain medication could be used as rescue therapy, few pts received tofacitinib without 'any pain therapy', and confounding by indication cannot be excluded. Further analyses are required to explore the impact of tofacitinib on the relationship between reductions in pain and disease activity.

REFERENCES

[1] Walsh DA, McWilliams DF. Curr Pain Headache Rep 2012; 16: 509-17.
[2] American College of Rheumatology Pain Management Task Force. Arthritis Care Res (Hoboken) 2010; 62: 590-9.

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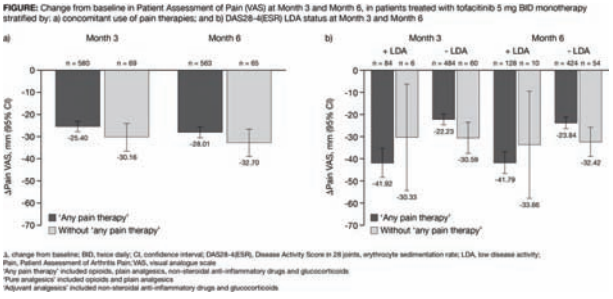


Figure 1

Disclosure of Interests: Peter C. Taylor Grant/research support from: Celgene, Galapagos, Eli Lilly, UCB, Consultant for: AbbVie, Galapagos, Gilead, Eli Lilly, Pfizer Inc, Mart van de Laar Grant/research support from: AbbVie, Eli Lilly, Janssen-Cilag, Merck Inc, Pfizer Inc, Sanofi Genzyme, Speakers bureau: Eli Lilly, Pfizer Inc, Jeffrey R. Curtis Grant/research support from: Abbvie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB, Crescendo Bioscience Inc., Consultant for: Abbvie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB, Crescendo Bioscience Inc., Valderilio F Azevedo Grant/research support from: AbbVie, GSK, Janssen, Merck Serono, Novartis, Pfizer Inc, UCB, Consultant for: AbbVie, GSK, Janssen, Merck Serono, Novartis, Pfizer Inc, UCB, Jose Luis Rivas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Palle Dahl Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lisy Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Noriko Iikuni Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Harry Shi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, John Woolcott Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Salim Benkhalifa Shareholder of: Pfizer SAS, Employee of: Pfizer SAS, Juan Jose Gomez-Reino Grant/research support from: Biogen, Gilead, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, Consultant for: Biogen, Gilead, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma
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AB0450 METHOTREXATE ADHERENCE IN MOROCCAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Adherence to conventional DMARDs (disease-modifying antirheumatic drugs) is highly variable in rheumatoid arthritis (RA), ranging from 22 to 107%. Many studies have evaluated these drugs adherence, but only one single systematic review evaluated specifically methotrexate adhesion in patients with RA.

Objectives: The aim of this study is to evaluate the adherence to methotrexate (MTX) in Moroccan patients with rheumatoid arthritis (RA) and to investigate factors that may influence it.

Methods: A cross-sectional study enrolled subjects suffering from rheumatoid arthritis according to ACR/EULAR 2010 criteria, with a history of methotrexate treatment for more than 6 months, either as monotherapy or in combination with other conventional or biological DMARDs.

The evaluation of therapeutic compliance with methotrexate was realized using two validated self-questionnaires; the Morisky-Green (MG) questionnaire consisting of 6 questions, and the CQR (Compliance Questionnaire on Rheumatology) consisting of 19 questions.

Adherence levels were defined according to the validated thresholds of the questionnaires.

The factors likely to influence the adhesion were researched by a standardized questionnaire.

Results: A total of 61 subjects were studied. The mean age was 53.4 ±12.5 years, with a weekly methotrexate average dose of 18.2 ± 4.5 mg. In combination methotrexate 77% of patients were receiving corticosteroids, 21% biological DMARDs, 19.7% other conventional DMARDs, and 42% folic acid.

The methotrexate adherence levels are presented in figure 1.

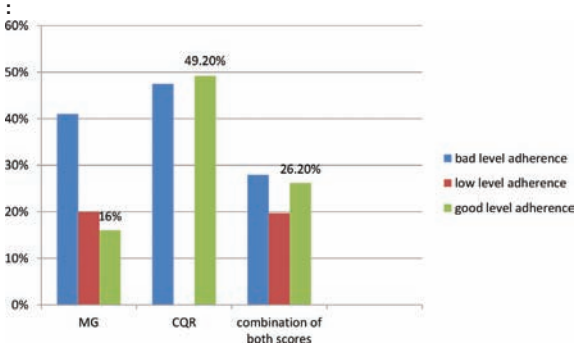


Figure 1. methotrexate adherence levels

Lack of resources and adverse effects were the main factors behind methotexate's low level adherence. The patients with these levels had a longer duration of disease progression and higher parameters of disease activity.

Conclusion: This study shows that the methotrexate adherence level in Moroccan patients with RA is low. The patient's education should be improved in the Moroccan population for a better control of the disease.

Disclosure of Interests: None declared
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AB0451

PROSPECTIVE STUDY OF REASONS FOR DISCONTINUATION OF TOFACITINIB IN SELF-FUNDED PATIENTS WITH RHEUMATOID ARTHRITIS FROM A SINGLE CENTRE

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of Rheumatoid Arthritis (RA). There can be potential differences in the adherence and compliance to therapies in real world compared to clinical trials especially in a non-reimbursable setup. Hence, it is very important to see the patient persistence to Tofacitinib therapy in a real world practice.
Objectives: To evaluate the reasons for discontinuation of Tofacitinib in RA patients in real world set-up.
Methods: Data of RA patients treated with Tofacitinib 5mg BID from a rheumatology center in South India was collected from September 2016 to January 2019 using standardized formats at baseline, 1, 3, 6 and 12 months. Efficacy was evaluated by DAS28-ESR and safety by listing of Adverse Events (AE). Reasons for discontinuation were objectively recorded. Concomitant RA treatment type/dose adjustments were as per the clinician's discretion. Analysis was based on observed values without imputation for missing data. For calculating persistence at a time point, the patients still taking the drug with treatment duration lower than that particular time point were excluded from the calculation.
Results: Fifty seven RA patients were treated with Tofacitinib. Average age and disease duration were 50 (20-77) years, 9 (1-22) years respectively. Most patients were females (88%); seropositive (89%) and all had erosive disease. Tofacitinib was used as a second line drug after inadequate response with conventional Disease Modifying Anti Rheumatic Drugs. Average Tofacitinib follow up was 6 (1-16) months. Thirty nine patients who discontinued Tofacitinib were analyzed. Eighteen patients were at various stages of therapy including 8 patients completing 12 months. Persistence with Tofacitinib at 3, 6 and 12 months was 85, 50 and 17 percent respectively. Details of the reasons for discontinuation are given in Table and Figure.
Conclusion: Tofacitinib was effective and well tolerated in Indian patients. However, majority of patients (80%) discontinued at various time points after feeling better. Only 13% discontinued due to AEs and 7% due to inadequate response. This data brings into light the difficulties faced by health providers for implementing 'treat to target' approach in real world practice.

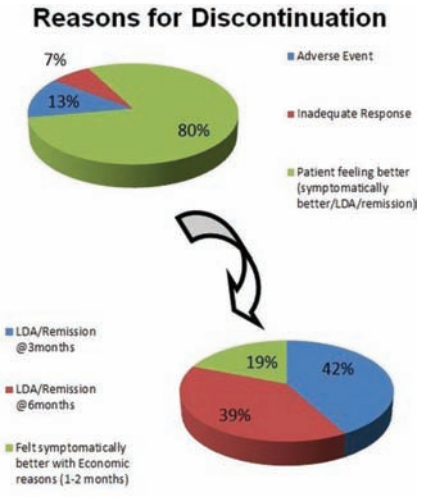


Figure 1

REFERENCES

[1] Marchesoni et al, Ann NY Acad Sci 2009, 1173: 837–846

Table

Reasons for Discontinuation	Duration of treatment (Months)			Number of patients
	1-3 months	3-6 months	6-12 months	
Adverse events (AE)	**1**	**4**		**5 (13%)**
Inadequate response (IR)	**1**	**1**	**1**	**3 (7%)**
Symptomatically better/LDA/ Remission				
• Patients' perception as 3 month course only		**13 (42%)**		**31 (80%)**
• Patients' perception as 6 month course only			**12 (39%)**	
• Economic reasons	**6 (19%)**			
Number of patients	**8**	**18**	**13**	**39**

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AB0452

SYSTEMATIC REVIEW OF GUIDELINES ON THE USE OF METHOTREXATE IN RHEUMATOID ARTHRITIS

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Background: Most guidelines on the use of methotrexate (MTX) in rheumatoid arthritis (RA) are issued by developed countries. MTX use in African 'least developed countries' (LDCs) requires considering costs of medical care, limited manpower and patients' beliefs. It is unknown whether current available MTX guidelines are relevant to LDCs.
Objectives: To review existing guidelines/recommendations on the use of MTX for the treatment of RA prior to developing recommendations for LDCs.
Methods: Electronic databases and guideline registries were searched for guidelines on MTX use in RA. Reviewers eliminated duplicates and selected the most updated guidelines. Similarities and discrepancies among recommendations are reported.
Results: From 2111 citations, 23 full texts were screened and 13 included in the qualitative synthesis. Guidelines targeted rheumatologists (3/13) and other physicians involved in RA care (7/13). Half (6/13) of the guidelines comment on patient education. MTX is suggested as the first DMARD choice by 5/13 guidelines. Screening for risk factors associated with a higher risk of MTX toxicity (e.g. alcohol) is suggested in 4/13 guidelines. Eight guidelines discuss pre-MTX tests: all recommend baseline CBC, liver (mainly albumin and liver function tests), renal function tests (mainly serum creatinine) and HBV/HCV serologies. Seven recommend a baseline chest X-ray. Only 4/8 and 2/8 guidelines recommend HIV and TB screening respectively. Pneumococcus and influenza immunization are suggested by 3/13 guidelines that comment on vaccines, whereas HBV and HZV vaccines by 2/13. Pregnancy and lactation are stated as MTX contraindications by 5/13 guidelines; four recommend MTX discontinuation 3 months prior to conception in females. Only 2/13 guidelines comment on the need of contraception in patients of reproductive age on MTX. MTX starting dose is discussed by 7/13 guidelines: $\geq$10mg/wk (5/7); 12.5 -15 mg/week (1/7); and 6-8mg/week (1/7, guideline from Japan). The maximal dose of MTX recommended by 8/9 guidelines is 20-30mg/week. Dose escalation (2-5 mg) every 2-6 weeks is discussed by 4/9 guidelines. There is no uniformity on the initial administration route of MTX (3/6 oral, 3/6 either oral or parenteral). The use of higher MTX doses, increasing adherence, and inadequate clinical responses or intolerance are suggested indications for switching from oral to parenteral route (8/13). Folic acid supplementation is recommended by 8/13 guidelines; however specific dose and time intervals are not defined. CBC, liver and kidney monitoring are recommended for MTX treated patients by 8/13 guidelines. Specific laboratory investigations and monitoring intervals vary between guidelines. Eight guidelines agree that MTX could be continued throughout the perioperative period of elective orthopedic surgery. Three guidelines recommend MTX discontinuation in case of severe infection. MTX dose reduction is discussed by 3/13 guidelines, which recommend considering reduction with sustained remission ($\geq$ 6 months).
Conclusion: Existing guidelines do not uniformly address all aspects related to the MTX use in RA, and do not include a cost-effectiveness analysis. Adaptation of these guidelines for their implementation in LDCs is needed.

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AB0453 RED RICE YEAST. AN ALTERNATIVE IN RHEUMATOID ARTHRITIS AND HYPERLIPIDEMIA

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Background: Lipid profile control is essential in patients diagnosed with inflammatory disease such as rheumatoid arthritis (RA), since cardiovascular events (CV) are still the first cause of mortality. According to the EULAR recommendations on CV risk, in those patients with a low or moderate CV risk index, for whom diet and exercise have not been effective to diminish low density lipoprotein (LDL) cholesterol below 190 and 100 respectively, we must prescribe a statin. These are the most commonly used drugs with undoubted benefits shown in medical literature. However, often-polymedicated patients may present intolerances or adverse side effects that limit their use. Red rice yeast, whose main active ingredient is monacolin K, has been used in traditional Chinese medicine since 800 AD as a remedy to reduce the total cholesterol level (TC) in blood, LDL and triglycerides (TG). In addition, some studies underline its anti-inflammatory effect and its benefit in patients with inflammatory pathology. In recent years, its use has spread throughout the western world.

Objectives: To evaluate the efficacy of red rice yeast in patients with elevated levels of TC and LDL in rheumatology clinic.

Methods: Prospective study that includes two cohorts of 30 patients with similar demographic characteristics. One cohort with RA patients and the other one without inflammatory disease. Both groups present high levels of TC and LDL. We study the demographic, clinical and lipid levels. A standard dose of red rice yeast is administered to every patient and we evaluate the analytical response after 3 and 6 months of treatment. For the statistical analysis, we used the SPSS program 22.0 version. Quantitative variables are presented as means ± standard deviation and qualitative variables as percentages. The comparisons between the quantitative variables are made with the Student´s T-test. We compared the mean values for each visit with the Anova test. A p <0.05 is considered significant.

Results: In the group of patients without inflammatory pathology (n = 30), 73% are women with an average age of 63.9 ± 7 years. The mean of baseline TC is 265.2 mg/dL ± 13.7 and LDL 176.4 ± 16. After 3 and 6 months of treatment, a significant decrease in both values was obtained (TC 231 ± 19 and 209.8 ± 19 F: 26.71 p 0.000 and LDL 143.9 ± 20 and 123.6 ± 19 F 22.51 p 0.000)

In the cohort of patients with RA (n = 30), 66% were women with an average age of 62.1 ± 10. The mean baseline TC is 258.2 ± 14 and LDL is 176.7 ± 10. After 3 and 6 months of treatment a significant decrease of both values was obtained (TC 224 ± 24 and 196.1 ± 28 F: 21.55 p 0.000 LDL 149.5 ± 12 and 122.4 ± 25 F: 28.28 p 0.000)

There were no significant changes in HDL or TG levels. Neither adverse effects were detected nor treatment was abandoned.

Conclusion: The red rice yeast significantly decreases the levels of TC and LDL in the two cohorts. In patients with RA and mild or moderate CV risk, where a close control is necessary, the use of red rice yeast could be an effective therapeutic alternative free of adverse side effects. More studies are needed with a greater number of patients to corroborate these data

REFERENCES

[1] Agca R, Heslinga SC, Rollefstad S, et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update *Annals of the Rheumatic Diseases* 2017;76:17-28.

Disclosure of Interests: None declared

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AB0454 FREQUENCY AND DURATION OF EARLY NON-SERIOUS ADVERSE EVENTS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB 5 MG TWICE DAILY AS MONOTHERAPY AND COMBINATION THERAPY

Ara Dikranian[1], Jürgen Wollenhaupt[2], Valderilio F. Azevedo[3], Louis Bessette[4], David Gold[5], Jose Luis Rivas[6], Harry Shi[7], Lisy Wang[8], John Woolcott[7], Andrea Shapiro[9], Peter Nash[10]. [1]*Cabrillo Center for Rheumatic Disease, San Diego, CA, United States of America*; [2]*Schön-Klinik Hamburg-Eilbek Teaching Hospital of the University of Hamburg, Hamburg, Germany*; [3]*Universidade Federal do Paraná, Curitiba, Brazil*; [4]*Laval University, Kirkland, QC, Canada*; [5]*Pfizer Canada, Montreal, QC, Canada*; [6]*Pfizer SLU, Madrid, Spain*; [7]*Pfizer Inc, Collegeville, PA, United States of America*; [8]*Pfizer Inc, Groton, CT, United States of America*; [9]*Pfizer Inc, Peapack, NJ, United States of America*; [10]*University of Queensland, Brisbane, Australia*

Background: Tolerability remains ill-defined in clinical trials and commonly refers to non-serious adverse events (AEs) impacting patient (pt) satisfaction and treatment adherence. Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: This update to a previously published post hoc analysis[1] describes the frequency and duration of the most common tolerability-related non-serious AEs in pts with RA receiving tofacitinib 5 mg BID as monotherapy or with conventional synthetic (cs)DMARDs in Phase (P)3 and P3b/4 studies.

Methods: Data were pooled from: ORAL Step (NCT00960440); ORAL Solo (NCT00814307); ORAL Scan (NCT00847613); ORAL Sync (NCT00856544); ORAL Standard (NCT00853385); and ORAL Strategy (NCT02187055). This post hoc analysis included data from pts receiving tofacitinib 5 mg BID monotherapy (ORAL Solo, ORAL Strategy), placebo (PBO; ORAL Solo), or tofacitinib 5 mg BID or PBO with csDMARDs (all studies except ORAL Solo). Non-serious AEs (affecting pts' day-to-day experience and ability to tolerate therapy) with incidence rates (IRs, pts with events/100 pt-years) ≥5 were evaluated up to Month (M)3. Infections, laboratory test abnormalities, general disorders or events not directly reported by pts, and musculoskeletal disorders likely due to underlying RA, were excluded.

Results: Of the 2657 pts included in the analysis, 1976 received tofacitinib 5 mg BID (monotherapy: N=627; combination: N=1349) and 681 received PBO (monotherapy: N=122; combination: N=559). The most frequent non-serious AEs up to M3 are shown in the Table. IRs ≥10 were seen for headache and diarrhoea (tofacitinib 5 mg BID monotherapy, combination therapy and PBO monotherapy), and nausea (PBO monotherapy and PBO combination therapy). Non-serious AE duration was ≤4 weeks for most pts with headaches, diarrhoea or gastric discomfort (any gastrointestinal pain, dyspepsia, epigastric discomfort or abdominal discomfort/pain). With tofacitinib 5 mg BID and PBO, respectively, duration of AEs was ≤2 weeks for 43.2% and 64.7% of pts with headaches; 66.1% and 81.3% with diarrhoea; and 36.2% and 58.6% with gastric discomfort. Most non-serious AEs were mild/moderate.

Table. Non-infectious, treatment-emergent non-serious adverse events[a] in Phase 3 and Phase 3b/4 studies up to Month 3

Non-serious AE, n (%), *IR [95% CI]*	Monotherapy		Combination therapy		Overall	
	Tofacitinib 5 mg BID (N=627)	PBO[b] (N=122)	Tofacitinib 5 mg BID (N=1349)	PBO[c] (N=559)	Tofacitinib 5 mg BID (N=1976)	PBO[b,c] (N=681)
Headache	21 (3.3) *13.7 [8.5, 21.0]*	3 (2.5) *10.1 [2.1, 29.4]*	50 (3.7) *15.3 [11.3, 20.1]*	13 (2.3) *9.5 [5.1, 16.3]*	71 (3.6) *14.8 [11.5, 18.6]*	16 (2.3) *9.6 [5.5, 15.6]*
Diarrhoea	18 (2.9) *11.7 [7.0, 18.5]*	3 (2.5) *10.0 [2.1, 29.2]*	41 (3.0) *12.5 [8.9, 16.9]*	13 (2.3) *9.5 [5.1, 16.3]*	59 (3.0) *12.2 [9.3, 15.8]*	16 (2.3) *9.6 [5.5, 15.6]*
Nausea	15 (2.4) *9.8 [5.5, 16.1]*	3 (2.5) *10.0 [2.1, 29.2]*	29 (2.1) *8.8 [5.9, 12.6]*	15 (2.7) *11.0 [6.2, 18.2]*	44 (2.2) *9.1 [6.6, 12.2]*	18 (2.6) *10.8 [6.4, 17.1]*
Vomiting	7 (1.1)	2 (1.6)	18 (1.3) *5.4 [3.2, 8.6]*	8 (1.4) *5.8 [2.5, 11.4]*	25 (1.3) *5.1 [3.3, 7.6]*	10 (1.5) *6.0 [2.9, 11.0]*
Dyspepsia	4 (0.6)	4 (3.3)	20 (1.5) *6.0 [3.7, 9.3]*	7 (1.3) *5.1 [2.1, 10.5]*	24 (1.2)	11 (1.6)
Abdominal pain upper	7 (1.1)	0 (0.0)	17 (1.3) *5.1 [3.0, 8.2]*	6 (1.1) *4.4 [1.6, 9.5]*	24 (1.2)	6 (0.9)

[a]Defined as AEs with an IR (pts with events per 100 pt-years) ≥5 in at least one treatment group under monotherapy, combination therapy or overall therapy. IRs (and 95% CI) that did not meet this criterion (ie, IR <5) are not shown; [b]Pts receiving PBO without background csDMARDs in ORAL Solo (only concomitant antimalarial medications were allowed); [c]Includes pts receiving PBO with background csDMARDs in Phase 3 and Phase 3b/4 studies

AE, adverse event; BID, twice daily; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IR, incidence rate; PBO, placebo; pt, patient

Figure 1

Conclusion: Overall, non-infectious non-serious AEs were mild/moderate and the majority were self-limiting. Non-serious AE frequency was similar for tofacitinib monotherapy and combination therapy, and for tofacitinib and PBO.

REFERENCES

[1] Dikranian A, et al. Arthritis Rheumatol 2013; 65: S192.

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AB0455 FACTORS ASSOCIATED WITH DAS28 RESPONSE IN BIOLOGIC-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: 10 YEAR FOLLOW-UP

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Background: Access to adequate care is limited in Mexico as biologics or targeted therapies are unavailable for a proportion of patients with rheumatoid arthritis (RA) and only methotrexate and other conventional (c) DMARDs are employed as therapeutic options in many cases.
Objectives: To determine the factors associated to DAS28 response in patients with rheumatoid arthritis followed up to 10 years and who never received biologic or targeted therapy, being treated only with cDMARDs.
Methods: We analyzed a prospective cohort of 543 patients with RA followed for 10 years (March 2006 to February 2016) at the Hospital General de Cuernavaca, in central México. Demographic data, shared epitope (SE; HLA-DR*0101, *0102, *0401, *0404, *0405, *0408, *0410, *1001, *1402) status, date since onset of disease and treatment, clinical and disease activity characteristics as well as treatment data was obtained and followed through time. Patients were seen by a rheumatologist every three months and blood samples obtained on each visit. The DAS28 score was determined on each visit and treatment adjusted accordingly. They were treated with prednisone (PDN; ≤10 mg/day), Methotrexate (MTX; 7.5-25 mg/week), Cloroquine (CLQ; 150-300 mg/day), Sulphasalazine (SSZ; 1-3 gr/day) or a combination of these. Descriptive statistics were used for the analysis of demographic data and parametric correlation tests (Spearman) were employed in the analysis.
Results: Of the 543, 94.3% of patients were women; mean age at baseline was 54.1 years (23-89; SD 12.4), mean time since onset of disease was 6.6 years (0-49; SD 7.9) and mean time since onset of treatment was 3 years (1-9; SD 2.12). HLA was determined in 57 patients and 36.8% of these patients were SE positive (one or two alleles). Most patients received treatment on the baseline visit based mainly on MTX (72.7%) combined with CLQ (63%) and low-dose PDN (76.4%). Less than 5% was under treatment with a non-MTX cDMARD. Baseline mean DAS28 was 4.9 (0.9-8.3; SD 1.41). At 6 months since DMARD-onset mean DAS28 was 3.8 (0.42-8.0; SD 1.46), at 12 months mean DAS28 was 3.6 (0.14-7.6; SD 1.34). At 2 years of follow-up, mean DAS28 remained at 3.6 (1.27-7.43; SD 1.35). Over the course of the next 8 years patients maintained a mean DAS28 between 3.5-3.6, with no significant changes in spite of continuing cDMARD treatment. Apart from being under treatment, which correlated with a better DAS28 score, being female correlated with a poorer DAS28 response ($p<0.05$). The other baseline factor significantly associated to an improved long-term outcome regarding disease activity was time since onset of disease, which correlated with a higher DAS28 score during the first two years of follow up but tapered after two years of follow-up ($p<0.001$). One of the limitations of the study was the significant drop-out rate (>20%) seen during follow up.
Conclusion: DAS28 response occurs mainly in the first 2 years of treatment. After that, cDMARD treatment is associated to a stationary effect over DAS28 in patients with no access to biologics or targeted therapies. This is an important factor to consider when establishing long-term therapeutic strategy from a cost-effective point of view.

REFERENCES

[1] Hazlewood, G. S. et al. Methotrexate monotherapy and methotrexate combination therapy with traditional and biologic disease modifying antirheumatic drugs for rheumatoid arthritis: abridged Cochrane systematic review and network meta- analysis. BMJ 353, i1777(2016).
[2] Salliot, C. & van der Heijde, D. Long-term safety of methotrexate monotherapy in patients with rheumatoid arthritis: a systematic literature research. Ann. Rheum. Dis. 68, 1100–1104 (2009).

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AB0456 PERCEPTIONS OF GLUCOSTEROID SIDE EFFECTS IN RHEUMATOID ARTHRITISPATIENTS

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Background: Most of the new recommendations proposed for the management of Rheumatoid arthritis (RA) emphasize the involvement of patients in therapeutic decision-making. This should encourage us to evaluate their level of information, fears and beliefs about the different treatments especially corticosteroids.
Objectives: The aim of this study was to evaluate the fears and beliefs of Tunisian patients with RA regarding corticosteroids.
Methods: A prospective study including 35 RA patients according to the ACR/EULAR 2010 criteria was performed. All of them were treated with corticosteroid therapy in addition to DMARDs and their usual long-term treatment. Every patient included in the study completed a questionnaire, containing sociodemographic component and evaluating corticosteroid modality use as well as side effects[1].
Results: The study included 35 patients with female predominance (74, 3%).The mean age was 57 years (29-72). The mean duration of the disease was 8 years (2-13 years). All RA patients were immunopositive for rheumatoid factor and/or for Anti-cyclic citrullinated peptide antibody (anti-CCP). Twenty-six patients were on Methotrexate, 6 on Infliximab, and 3 on Rituximab. Corticosteroid therapy was prescribed at a mean dose of 7.5 mg prednisone (5 to 10 mg).The level of education of our patients was generally low: 17 were illiterate, 10 had received a primary or secondary education, only 8 attended college. None of them was part of a medical or paramedical profession. Twenty patients, of whom eight diabetic, had an idea about the potentially harmful effect of corticosteroids on glycemic equilibrium (14 patients reported hyperglycemia and six patients mentioned hypoglycemia). Forty percent were aware of obesity as an effect correlated with corticotherapy. Moreover, 34.3% of patients talked about the hypertensive peak as a serious complication. Osteoporosis was mentioned in 17.1% of cases. About 10 patients had no idea about the adverse effects of steroids. When asking them about their source of information: they mentioned respectively television and radio programs with medical informative content, environment and medical or paramedical medical staff.
Conclusion: This study highlights the insufficiency of the level of information provided for RA patients regarding corticosteroids side effects. New awareness-raising materials should be reinforced and adapted to make full use of their potential with less likelihood of adverse effects.

REFERENCES

[1] Oray M, Abu Samra K, Ebrahimiadib N, Meese H, Foster CS. Long-term side effects of glucocorticoids. Expert Opin Drug Saf. 2016;15:457-65

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SLE, Sjögren's and APS – treatment

AB0457 AUDIT ON HYDROXYCHLOROQUINE RELATED RETINOPATHY SCREENING IN RHEUMATOLOGY PATIENTS IN SVUH

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Background: Hydroxychloroquine (HCQ) is a medication commonly used to treat rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and other rheumatological conditions. A known adverse effect associated with long-term use of these medications is vision loss resulting from irreversible retinal toxic effects. Recent guidelines emphasized on routine ophthalmological examination and to adhere on real weight-based dosages.

Objectives: This audit conducted to evaluate adherence rate on standard recommendation on HCQ related retinopathy screening in rheumatology patients in St Vincent's University Hospital (SVUH).

Methods: Patient were on HCQ and attended rheumatology clinics at SVUH with rheumatic diseases selected randomly from on 01/08/2017 and end on 01/04/2018. A total sample size of 56 patients received a questionnaire that included information on HCQ dose, duration and actual body weight. Other information included precipitant factors and ophthalmology examination reports were retrieved retrospectively form patient's chart. Standards were measured against recommendations on screening for HCQ retinopathy published by American Academy of Ophthalmology, 2016 Revision.

Results: Total 56 patients on HCQ with different rheumatic disease studied. Out of 56 patients studied, 6/56 (10.7%) were <25 years (young), 45/56 (80.4%) were 25-65 years (middle age), and 5/56 (8.9%) were >65 years (elderly). Sex distribution showed that 7/56 (12.5%) were males and 49/56 (87.5%) were females. Around 35.7% (20/56) were in HCQ dose >5mg/kg, and 64.3% (36/56) were on standard HCQ dose (<=5mg/kg of real body weight. The were 44.6% (25/54) patients on HCQ for a period <5 years, the rest, 55.4% (32/56) were on HCQ for a period of 5-20years, and none of these patients were on it for >20 years duration. There were only 1/56 (1.8%) patient with history of HCQ toxicity, 98.2% (55/56) showed no history of HCQ related toxicity. None of the 56 patients had any of the following influencing factors: renal impairment, Tamoxifen usage, coagulopathies, hepatic impairment, or pre-existing retinal/macular disease. However, there were 8.9% (5/56) of this group their age was > 65years (verses 51/56 91.1% were <65years age. Only 69.6% (39/56) of these patients underwent retinal baseline screening, were 17/56 (30.4%) did not receive any baseline screening after commencing HCQ therapy. Frequency of follow up retinal screening were done annually in 19/56 (33.9%), 5 yearly in 6/56 (10.7%). However, it was not done in 21/56 (37%) and it was not due in 9/56 (16.1%). Out of those who underwent the screening at any time, 32/56 (57.1%) showed normal examination results, only 1/56 patient (1.8%) showed abnormal results. Rest of the patient data either were not available, or examination were not done.

Conclusion: Above data emphases the need to adhere on standards HCQ retinal screening as baseline and follow up. Furthermore, adherence on real weight calculated dose rather than estimated/average body weight.

REFERENCES

[1] -Michael F. Marmor, Ulrich Kellner, Timothy Y.Y. Lai, et al. Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision). Ophthalmology. 2017 Mar;124(3):e28-e29.

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AB0458 A PHASE II RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PROOF OF CONCEPT STUDY OF ORAL SELETALISIB IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME (PSS)

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Background: Seletalisib is a potent, selective oral inhibitor of phosphoinositide-3 kinase delta (PI3Kδ). Preclinical data have shown that the PI3Kδ pathway is upregulated within salivary glands of patients with PSS and contributes to disease pathogenesis.[1]

Objectives: To assess the efficacy and safety of seletalisib in patients with PSS.

Methods: In this Phase II, double-blind, proof of concept study (NCT02610543), patients with PSS having an EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score ≥5 were randomised 1:1 to seletalisib once daily or placebo (PBO) in addition to current PSS therapy for 12 weeks. The primary endpoint was change from baseline in ESSDAI at Week 12. The study was designed to have 80% power to detect a difference of 3.8 points in change from baseline in ESSDAI between seletalisib and PBO at Week 12 and required 58 patients to complete treatment. Other endpoints included EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), salivary gland biopsy changes, Schirmer's I test, immunoglobulin concentrations and incidence of treatment-emergent adverse events (TEAEs).

Table 1. Change from baseline to Week 12 for secondary and exploratory endpoints (full analysis set)

	Seletalisib n=13, LS mean (SE)	PBO n=14, LS mean (SE)	Difference (95% CI)
ESSPRI score[a]	–2.13 (0.68)	–0.57 (0.56)	–1.55 (–3.39, 0.28)
Stimulated salivary flow rate, mL/min[a]	–0.08 (0.11)	–0.11 (0.08)	0.02 (–0.27, 0.31)
Schirmer's I test score[b]	–0.9 (3.3)	0.5 (2.6)	–1.41 (–10.35, 7.52)
Immunoglobulin G, g/L[a]	–2.36 (0.71)	1.17 (0.64)	–3.53 (–5.55, –1.51)
Immunoglobulin M, g/L[a]	–0.33 (0.10)	0.07 (0.09)	–0.40 (–0.68, –0.12)
Immunoglobulin A, g/L[a]	0.03 (0.13)	0.06 (0.12)	–0.03 (–0.40, 0.34)

LS, least squares; SE, standard error

[a] Mixed model for repeated measures analysis

[b] Analysis of covariance

Results: The study was terminated early due to slow recruitment, which led to study power decreasing to 36%. Twenty of 27 patients randomised (seletalisib n=13, PBO n=14) completed treatment. Demographic characteristics were generally similar between groups. Mean (SE) change from baseline in ESSDAI at Week 12 was seletalisib –5.4 (1.7) vs PBO –2.8 (1.5); treatment difference vs PBO (95% CI) was –2.59 (–7.30, 2.11; p=0.266). The percentages of patients achieving a ≥3 point reduction in ESSDAI were seletalisib 66.7% vs PBO 54.5%. Post-hoc Bayesian analyses of treatment difference showed an 86.5% probability of being superior to PBO and a 48.8% probability of a >3 point difference from PBO. Clinically notable improvements in some secondary endpoints were also observed in the seletalisib group (Table 1). Minor salivary gland biopsies had broadly similar histological features across groups at baseline. At

Week 12, seletalisib treatment led to a reduction in the size and cellular organisation of mononuclear inflammatory cell foci vs PBO (Table 2). TEAEs were reported by 13/13 (100.0%) seletalisib and 13/14 (92.9%) PBO patients; most frequently reported: diarrhoea (5/13 [38.5%] vs 0/14 [0%]) and headache (3/13 [23.1%] vs 2/14 [14.3%]). Serious TEAEs were reported by 3/13 (23.1%) vs 1/14 (7.1%), and discontinuations due to TEAEs by 5/13 (38.5%) vs 1/14 (7.1%) seletalisib and PBO patients, respectively.

Table 2. Change from baseline at Week 12 in characteristics of mononuclear inflammatory cell foci from paired minor salivary gland biopsies

	Seletalisib n=7 Mean (SD)	PBO n=11 Mean (SD)
Average focus area, mm^2	−0.02 (0.02)	0.01 (0.06)
Focus score, number foci present/4 mm^2 biopsy tissue	−0.43 (0.99)	0.20 (2.73)
Percentage infiltration	−1.3 (1.4)	2.5 (8.0)
Percentage of germinal centres	−13.5 (14.3)[a]	−0.9 (15.8)[b]
Percentage of T/B cell segregation	−17.6 (8.6)[c]	−12.7 (32.3)[d]
Percentage of foci with follicular dendritic cells	−23.2 (17.1)[e]	15.1 (40.7)

SD, standard deviation

[a] n=3; [b] n=7; [c] n=4; [d] n=9; [e] n=6

Conclusion: Although this Phase II PSS study was terminated early due to slow recruitment, seletalisib demonstrated a trend to clinical improvement in patients with PSS and acceptable safety and tolerability. Histological analyses demonstrated encouraging effects of seletalisib on the organisation and extent of salivary gland lymphocytic infiltration in patients with PSS.

REFERENCES

[1] Nayar S, et al. Ann Rheum Dis. 2019;78:249–260

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AB0459 IMMUNOGLOBULINS COMBINED WITH STANDARD THERAPIES FOR THE PREVENTION OF RELAPSES IN REFRACTORY OBSTETRICAL ANTIPHOSPHOLIPID SYNDROME: A SERIES OF 103 CASES

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Background: Optimal standard therapy in obstetrical antiphospholipid syndrome (APS) (aspirin and LMWH) is effective in 72- 80% of pregnancies (1). Intravenous immunoglobulins (IVIG) are not more efficient than standard therapy (2, 3) and seems to be reserved to high risk pregnant APS patients (4) and/or refractory cases (5).
Objectives: The main aim of this study was to analyse the outcome of pregnancies in APS patients with recurrent obstetrical event despite conventional treatment, who received IVIG.
Methods: We have performed a retrospective multicentre open-labelled study (2010-2018).
Results: 103 patients (107 pregnancies) with obstetrical APS from 8 international centres were included. In all cases, the previous standard treatment was inefficient. Obstetrical APS was present in 73%, while 27% had obstetrical and thrombotic APS. Median age was 28 years. Triple antiphospholipid antibody (tAPL) positivity was found in 51% of patients and lupus anticoagulant (LA) in 60%. IV IG use was associated with favourable outcome in 101/107 pregnancies (94%). In multivariate analysis, previous history of prematurity and Ig use were associated with live-birth pregnancy (odds-ratio 0.12 95%CI 0.03-0.37, p 0.005). The dosages of IV IG were variable: 0.4g/kilo day-2g/kilo day but without differences on outcomes between patients (p 0.8). There were no differences in outcomes of pregnancies between patients with tAPLand/or LA positivity and patients with other antibodies profiles (p 0.8).
Conclusion: IVIG could be effective in cases of refractory obstetrical APS but prospective studies are necessary.

REFERENCES

[1] Cervera R, Serrano R, Pons-Estel GJ, Ceberio-Hualde L, Shoenfeld Y, de Ramón E, Buonaiuto V, Jacobsen S, Zeher MM, Tarr T, Tincani A, Taglietti M, Theodossiades G, Nomikou E, Galeazzi M, Bellisai F, Meroni PL, Derksen RH, de Groot PG, Baleva M, Mosca M, Bombardieri S, Houssiau F, Gris JC, Quéré I, Hachulla E, Vasconcelos C, Fernández-Nebro A, Haro M, Amoura Z, Miyara M, Tektonidou M, Espinosa G, Bertolaccini ML, Khamashta MA. Morbidity and mortality in the antiphospholipid syndrome during a 10-year period: a multicentre prospective study of 1000 patients. Ann Rheum Dis. 2015;74:1011-8.
[2] Branch DW, Porter TF, Paidas MJ, Belfort MA, Gonik B. Obstetric uses of intravenous immunoglobulin: successes, failures, and promises. J Allergy Clin Immunol. 2001;108:S133-8.
[3] Dendrinos S, Sakkas E, Makrakis E. Low-molecular-weight heparin versus intravenous immunoglobulin for recurrent abortion associated with antiphospholipid antibody syndrome. Int J Gynaecol Obstet. 2009;104:223-5.
[4] Ruffatti A, Favaro M, Hoxha A, Zambon A, Marson P, Del Ross T, Calligaro A, Tonello M, Nardelli GB. Apheresis and intravenous immunoglobulins used in addition to conventional therapy to treat high-risk pregnant antiphospholipid antibody syndrome patients. A prospective study. J Reprod Immunol. 2016;115:14-9.
[5] Prete M, Urso L, Fatone MC, Pinto V, Perosa F. Antiphospholipids Syndrome Complicated by a Systemic Capillary Leak-Like Syndrome Treated With Steroids and Intravenous Immunoglobulins: A Case Report. Medicine. 2016;95:e2648.

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AB0460 USE OF PLATELET RICH PLASMA (PRP) IN TREATMENT OF DRY EYE SYNDROME IN THE PATIENTS WITH SJÖGREN SYNDROME: PRELIMINARY RESULTS

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Background: Xeroftalmia and xerostomia are the hinge symptoms of Sjögren Syndrome and often they negatively influence patients' quality of life. The eyewashes use based on Platelet Rich Plasma (PRP) has been applicate in the treatment of the xeroftalmia, both primitive and secondary.
Objectives: To evaluate the effect of subconjunctival injections and PRP based eyewashes on the ocular dryness (subjective and objective) in patients suffering of primary Sjögren syndrome (pSS).
Methods: Six pSS patients (6 females, age at the beginning 48.2±9.7 years) have been recruited in the study. All patients were reaching the criteria for pSS diagnosis; for each patient clinical and immunological data have been recorded. Patients with Schirmer Test value, in at least an eye, inferior to 10 mm after 5 minutes, and suffering from severe dryness calculated by OSDI score (between 33 and 100, severe condition of dry eye) in spite of therapies with tear substitutes were selected. The OSDI (Ocular Surface Index) is a questionnaire for the evaluation of the subjective ocular dryness. Selected patients have been addressed to treatment with PRP. The PRP is constituted by human plasma enriched with plaques by means of the utilisation of a special kit, therefore each patient has been subjected to a blood drawing, from which PRP has been extracted. Of this, a part has been injected in subconjunctival seat; from remained one, an eyewash has been extracted that the patients have assumed 6 times in the day up to exhaustion (about 5 days) during which another topic therapy was not used. The patients have been valued to the basal time and after ten days of the procedure; besides follow-up visits each three months are scheduled. To each evaluation Schirmer Test data and OSDI have been checked.
Results: Each patient had severe xeroftalmy, evaluated by Schirmer Test (right Eye: 3.33±2.66; left eye: 6.83±6.5) and index OSDI (59.71±20.72). All the patients had Schirmer Test values, in at least an eye, lesser than 10 mm after 5 minutes. The analized cohort had homogeneous clinical characteristics (presence of xerostomy and absence of inflammatory indexes, hypergammaglobulinemia, arthritis and linfoadenomegaly). After one week (T1), OSDI values were significantly more reduced compared to the basal time (38.89±15.12; p=0.028). The Schirmer Test values were not significative different to the follow-up visit compared to the basal one. No patients presented pre- and post-procedural complications, neither related infectious events. At 3 months follow up after first treatment (T2) no statistically significant difference in OD/OS Schirmer test values and OSDI score compared to the basal time were observed.
Conclusion: The use of PRP in dry eye syndrome in patients with Sjögren syndrome seems to be effective in alleviating symptoms and improving patients' life quality. Is need further follow-up to confirm data, to value effect also on the objective tests and to evaluate necessity of repeating treatment.

REFERENCES

[1] ShiboskiSC;Arthritis Care Res, 2012; 64(4): 475–487
[2] AlioJ; OphtalmicResearch, 2017; 39: 124–129
[3] AlioJ; CurrPharm Biotech, 2012; 13: 1257-1265

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AB0461 BELATACEPT IN SLE KIDNEY TRANSPLANT PATIENTS

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Background: Lupus nephritis (LN) results in the need for renal replacement therapy (RRT) in 10-30% of LN pts; of these 30% receive a kidney transplant (KT). Belatacept (bela) is a second-generation selective T-cell co-stimulator blocker (inhibits CTLA-4) used as an alternative to calcineurin inhibitors (CNI) for maintenance regimens after KT. The pathogenic relevance of CTLA-4 inhibition and the favorable cardiovascular profile of bela make it an attractive therapeutic option in SLE. Additionally, bela IV ensures therapeutic adherence.
Objectives: The current study was initiated to evaluate the effect of bela on graft function and extrarenal SLE.
Methods: This retrospective single-center study evaluates the outcomes of LN KT recipients treated with bela from 2006–2018 at the Columbia University Lupus and Renal Transplant Cohorts. The bela regimen was 5mg/kg every 2 weeks x 5 doses, then monthly. CNI weaning among the bela group was not standardized. Immunosuppressive regimen, kidney allograft function, and SLE activity were examined.

Figure 1: Creatinine trend before and after bela

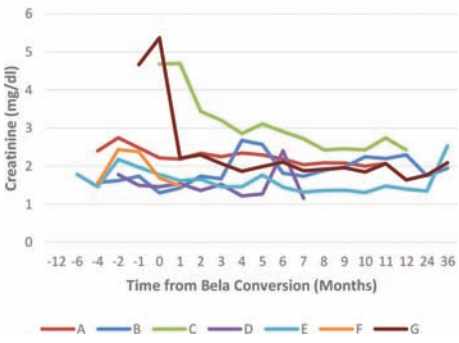


Figure 2: SLEDAI-2KG before and after bela

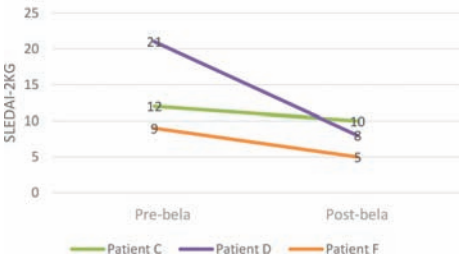


Table 1: Characteristics of patients on bela.

ID	Age at SLE dx	Race	LN class	Time to KT (yrs)	Type KT	Induction	Reason for conversion	Immunosuppressive regimen before conversion
A	16	Black	IV, VI	13	DDKT	ATG	Non-adherence	TAC, MMF
B	30	Asian		2	LRKT	ATG	Mod IFTA & Arteriosclerosis	TAC, MPA, PRED
C	18	White	IV, V	23	DDKT	ATG	Cortical necrosis	CYC, MMF, PRED
D	19	Black	V	9	LUKT	ATG	CNI side effects	TAC, MPA, PRED
E	22	Asian		5	LRKT	ATG	CNI side effects	TAC, MMF, PRED
F	18	Black	V	17	DDKT	Alemtuzumab	CNI side effects	TAC, MMF, PRED
G	25	White (Hispanic)	III, IV	23	DDKT	Basiliximab	TMA (biopsy)	TAC, MPA, PRED

Results: 48 pts with LN had undergone KT between 2006–2018 with follow-up time of 72.2 ± 74.6 months. Bela was started in 7 pts on CNI regimens (TAC N=6, cyclosporine N=1) at 15.5 ± 17.1 months after KT. All pts were female, age at SLE diagnosis 21.1 ± 4.9 yrs; 5 had undergone RRT prior to KT (4 hemodialysis, 1 peritoneal dialysis) for 38.7 ± 37.8 months. The interval between SLE diagnosis and KT was 13.1 ± 8.3 yrs. At the time of bela initiation, all pts were also treated with prednisone (7.1 ± 2.7 mg/day), 6 with mycophenolate (1123 ± 625 mg/day), and 1 azathioprine (25mg/day). CNIs were continued in 5/7 patients at 6 months after bela. 2 pts were on hydroxychloroquine, 2 took it only prior to KT. In 5 patients, creatinine stabilized 6 months after bela, 1 returned to HD due to CNI-toxicity and pyelonephritis and 1 is relisted for KT due to ACR and cortical necrosis (Fig. 1). No allograft failure due to recurrent

LN was noted in any of the 7 pts. 5 pts are followed by Rheumatology for extrarenal SLE; no extrarenal manifestations are documented in the other 2. Data on SLE Disease Activity pre and post bela were available and scored in 3/5 pts using the SLEDAI-2KG which accounts for clinical and laboratory manifestations, as well as steroid use (Fig. 2). Mean ds-DNA pre and post bela was 133 ± 178 UI/mL and 58 ± 72 UI/mL; C3 89 ± 31mg/dL pre and 91 ± 21 mg/dL post; C4 35 ± 15 mg/dL pre and 38 ± 7 mg/dL post.

Conclusion: Bela in LN KT recipients may decrease extrarenal manifestations, attenuate CNI toxicity and stabilize allograft function, providing a better alternative to CNI regimens. Furthermore, these data suggest that bela may be a therapeutic option in SLE.

REFERENCES

[1] Almaani, Salem, Alexa Meara, and Brad H. Rovin. Update on lupus nephritis. Clinical Journal of the American Society of Nephrology 12.5 (2017):825–835.

[2] Ortega, L. M., et al. Lupus nephritis: pathologic features, epidemiology and a guide to therapeutic decisions. Lupus 19.5 (2010):557-574.

[3] Sexton, Donal J., et al. ESRD from lupus nephritis in the United States, 1995–2010. Clinical Journal of the American Society of Nephrology 10.2 (2015):251-259.

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Disclosure of Interests: None declared

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AB0462 IMMUNIZATIONTO RITUXIMAB IS MORE FREQUENT IN AUTOIMMUNE SYSTEMIC AUTOIMMUNE DISEASES THAN IN RHEUMATOID ARTHRITIS AND MAY BE MANAGED BY SWITCHING FROM RITUXIMAB TO OFATUMUMAB

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Background: The most widely used B cell targeted therapies in autoimmune diseases (AID) is Rituximab (RTX), a murine chimeric monoclonal antibody. Among RTX's side effects, immunization and anti-drug antibodies to RTX (RTX-ADA) production have been reported but their consequences are poorly described. The immunization rate against RTX in rheumatoid arthritis (RA) is 2,7-9,2% and it seems to be higher in other sAID although data is lacking.

Objectives: We aimed to evaluate the frequency, consequences and predictive factors of RTX-ADA in RA and sAID, as well as the use of an alternative B-cell targeted therapy, ofatumumab (OFA) in case of RTX-ADA.

Methods: All patients with RA or sAID treated with RTX from 2012 to 2017 in our tertiary reference centre for sAID were retrospectively studied. Patients who were tested for RTX-ADA were identified. Clinical and biological characteristics of RTX immunized patients were compared to those of non-immunized patients. For patients treated with OFA, clinical and biological efficacy was obtained before and after treatment.

Results: 199 patients were treated with RTX (RA: 124, sAID: 75 including 38 primary Sjögren's Syndrome (pSS), 15 systemic lupus erythematous, 7 myositis, 6 overlap syndrome, 5 ANCA-associated vasculitides and 4 other sAID). Among the 62/199 (31.1%) tested for RTX-ADA, 14 were positive: 3/35 RA (8,6%) and 11/27 (40,7%) other sAID, (p=0.005). Among the whole RTX-treated patients, the frequency of RTX-ADA was 2,4% and 14,7% (p=0.003) in RA and in other sAID, respectively. Most of the immunized patients experienced delayed infusion reactions (11/14 [78,5%]). Delayed reactions were observed within the first 15 days after the infusion, and after a median 2 cycles [range; 1-2]. They were mainly rash (72,7%), fever (54.5) and/or abdominal pain (36,3%). Predictive factors of immunization were a sAID compared to RA (40,7% vs 8,6%, p=0.005), and young age (50.5 vs 61.5 years, p=0.003). Neither hypergammaglobulinemia, rheumatoid factor, disease activity, nor associated immunosuppressive therapy were associated with RTX-ADA. Among 23 tested patients with SLE or pSS, anti-SSA antibodies tended to be more frequent in immunized patients than non immunized (9/10 (90.0%) vs. 8/13 (61.5%), p=0.18). Three pSS patients immunized against RTX were treated with OFA because of associated cryoglobulinemic vasculitis or MALT lymphoma. All 3 experienced complete remission of their disease. Relapse occurred in 2 patients, one with MALT lymphoma after 14 months, one with cryoglobulinemic vasculitis after 10 months and were retreated successfully with OFA. No adverse events were reported.

Conclusion: Our results show that immunization against RTX is more frequent in other sAID than in RA. Testing for ADA must be performed in patients with infusion reactions. Patients immunized to RTX might be treated efficiently with OFA, which should be further evaluated in sAID.

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AB0463 BELIMUMAB IV EFFECT IN GLUCOCORTICOID TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune chronic disease produced by aberrant immunological response that consequently, causes a widespread organic damage. Treatment leads to regulating this disrupted immunological response. As a result, in 2011 Belimumab was approved for adults patients diagnosed with SLE, what is a monoclonal human antibody whose target is a B-lymphocyte stimulator (BLyS), a protein involved in the disease pathogeny.

Objectives: To evaluate the glucocorticoesteroid dose variation in adult patients with systemic lupus erythematosus during Belimumab IV treatment.

Methods: Retrospective, observational study that includes patients diagnosed with SLE according to SLICC 2012 criteria, who are treated with Belimumab IV. Treatment has been administrated as an initial dose: 10 mg/kg every 14 days and then, a maintenance dose: 10 mg/kg every 28 days. Data form serological profile, clinical manifestations at diagnoses and at the onset of treatment, existence of comorbidities or other diseases, concomitant therapy directed to the main disease or to the complications that came from the disease, non administration causes and definitive treatment discontinuation were collected from July 2012 until December 2018.

Results: A total of 19 patients (94.74% women) with 28 years old (Q1 14, Q3 31.82) as a median age at diagnosis and 11 (Q1 6.5, Q3 20) years since disease diagnosis were included. Follow up mean was 29 (Q1 7.5, Q3 37) months.

Regards to concomitant therapies, 5 patients (26.31%) were treated with Azatioprine and 3 patients with Methotrexate (15.79%). At the onset of biological therapy, 17 patients were treated with glucocorticoids, at a dose of 10 mg (Q1 9.38, Q3 10.63). At the end of follow up, 18 patients (94.73%) were treated with corticoid and the mean dose was 8.75 mg (Q1 8.75, Q3 8.75).

Table 1. Characteristics of patients on bela.

ID	Age at SLE dx	Race	LN class	Time to KT (yrs)	Type KT	Induction	Reason for conversion	Immunosuppressive regimen before conversion
A	16	Black	IV, VI	13	DDKT	ATG	Non-adherence	TAC, MMF
B	30	Asian		2	LRKT	ATG	Mod IFTA & Arteriosclerosis	TAC, MPA, PRED
C	18	White	IV, V	23	DDKT	ATG	Cortical necrosis	CYC, MMF, PRED
D	19	Black	V	9	LUKT	ATG	CNI side effects	TAC, MPA, PRED
E	22	Asian		5	LRKT	ATG	CNI side effects	TAC, MMF, PRED
F	18	Black	V	17	DDKT	Alemtuzumab	CNI side effects	TAC, MMF, PRED
G	25	White (Hispanic)	III, IV	23	DDKT	Basiliximab	TMA (biopsy)	TAC, MPA, PRED

We observed a mean corticoid dose reduction of 4.02 mg (Q1 2.5, Q3 5). Dose was not modified in 4 patients after the beginning of Belimumab IV. As exceptions, in 1 patient we added corticoids to treatment (dose of 5 mg/day) and in another one we doubled corticoid dose, until a maximum dose of 20 mg/day.
Belimumab treatment was definitive discontinued in 5 patients because of peripheral venous insufficiency, pregnancy, itchy skin lesions, uncertain drug allergy and primary pulmonary hypertension.
Conclusion: As we observed, an important percentage of patients (in our sample close to 90%) take usually corticoids, with the clinical consequences and development of comorbidities in a long time and adverse events related to this therapy. Diary dose is reduced in 57.9% of our patients, even in those patients who have discontinued Belimumab treatment, in which we observed a dose reduction too.
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AB0464 EFFECTIVENESS AND SAFETY OF ABATACEPT FOR 24 MONTHS FOR TREATING PATIENTS WITH PRIMARY SJOGREN'S SYNDROME (PSS)

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Introduction: Primary Sjögren's syndrome (SSp) is a systemic autoimmune disease concerning the exocrine glands and internal organs. Therapeutic options mainly include symptomatic and supportive measures, whereas traditional immunosuppressive drugs have not presented efficacy in randomized trials. Abatacept is a T-cell co-stimulation modulator and there are evidences that this drug may be effective for treating Pss.
Objectives: The objective of this trial was to evaluate effectiveness and safety of abatacept for 24 months in the treatment of pSS.
Methods: Observational prospective study for 24 months. It was included 11 patients that filled the American-European Consensus criteria (2002). Patients received abatacept according the weight < than 60 kilos (500mg), 60 kilos to 100 kilos (750 mg) per month for 24 months. It was evaluated Sjögren's syndrome disease activity index (ESSDAI), salivary flow with no stimulation for 15 minutes, Schimer's ophthalmologic evaluation tests, Ocular Staining Score (OSS) e Break up time, quality of life by Medical Outcome Survey Short Form 36 (SF-36) and fatigue by FACIT Fatigue - The Functional Assessment of Chronic Illness Therapy. For statistical analysis was used the Wilcoxon's test for related samples and test T of Student to paired samples. The significance level of 5% was adopted and analyzes were accomplished in the R program (version 3.5.1).
Results: This study was constituted from 11 women between the ages 25 to 81 years (average: 53.73 ± 15.07 years), being the majority afro-descendant women (54.5%). Of this total, 90.9% presented positive anti-nuclear antibody (ANA), 81.8% positive anti/SSA, and 90.9% positive rheumatoid factor. In relation to ESSDAI, 81.8% of the participants presented scores greater than 5. There was a statistically significant reduction in the ESSDAI IC 2.99 [-0.49; 7.99] (p = 0.013). Between the sub items of the ESSDAI, the ones that demonstrated the greatest modifications were articular and glandular. There was a significant increase in the salivary flow of the participants (dif = -0.90; IC-95%: -1.50; -0.50] after 24 months of treatment. There was no statistical difference between the beginning and after 24 months of treatment in the different evaluations, Schimer's ophthalmologic right eye IC 2.26 [-3.50; 12.5] p=0.423, Break up time OD 0.50 [-1.00; 2.49] p=0.307, OSS right eye IC: 0.50 [-2.50; 5.50] p=0.721. In the SF36 only in the Limitation for Emotional Aspects sub scale reported significant improvement (dif = 36.4; IC95%: -67.1; -5.57; p = 0.025), and FACIT presented no evidences of significant changes between pre and post treatment p = 0.356.
Conclusion: The study demonstrates limitations due to the few number of patients included and for being an open study not controlled, but we observed a statistically significant reduction in the ESSDAI, increase in the salivary flow and in the sub scale Limitation for Emotional Aspects of the SF36, indicating a positive effect in the disease.

REFERENCES

[1] Clair E.W. ST. Sjögren's syndrome in: Gary S. Firestein MD, Ralph C. Budd MD, Sherine E. Gabriel MD MSc, et al.Kelley & Firestein's Textbook of Rheumatology, Tenth Edition. Elsevier 2017 73:1221-44.
[2] Tsuboi H, Matsumoto I, Hagiwara S, et al. Effectiveness of abatacept for patients with Sjögren's syndrome associated with rheumatoid arthritis. An open label, multicenter, one-year, prospective study: ROSE (Rheumatoid Arthritis with Orencia Trial toward Sjögren's syndrome Endocrinopathy) trial. Mod Rheumatol 2016; 26(6):891-899

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AB0465 EFFICACY AND SAFETY OF IGURATIMOD IN PATIENTS WITH PRIMARY SJOGREN SYNDROME: A FOLLOW-UP STUDY

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Background: Primary Sjogren syndrome (pSS) is a chronic autoimmune disorder affecting 0.2–3% of the population. However, there are currently no effective systemic therapies. Anti-Ro, anti-La and rheumatoid factor(RF) as well as hyper γ-globulinaemia indicate a degree of B cell hyperactivity. In the recent ten years, iguratimod (T-614) has been used to treat RA as a novel immunomodulatory, which functions by suppressing the production of some inflammatory cytokines, as well as reducing immunoglobulin production by acting directly on human B lymphocytes without affecting B lymphocyte proliferation.
Objectives: We evaluated the effectiveness and safety of iguratimod on pSS patients in this follow up study.
Methods: A total of 21 pSS patients without severe systemic damage needing corticosteroid were recruited to receive iguratimod 25mg Bid for 12 weeks.
Results: Among them, 1 patient and 2 patients withdrew because of kidney dysfunction and ineffectiveness. For those 18 patients who finished the follow up, 94.4% were females and average age were 46.5±13.8 year-old with median disease duration of 22.0 (9.8, 58.5) months. Compared with baseline, ESSDAI score, hyperglobulinaemia and ESR was significant decreased after iguratimod treatment (Table). Two of the 18 patients presented with decreased white blood cell count. This side effect ameliorated in one patient after tapering the dose to 25mg Qd and in another patient after 2 weeks without any intervention.

Table. Effectiveness of iguratimod in pSS

	Baseline (B)	12w	P value (vs. B)	24w	P value (vs.12W)	P value (vs. B)
IgG	23.19±5.50	20.19±5.21	**0.009**	18.52±4.64	0.064	**0.001**
IgM	1.27±0.39	0.98±0.42	**0.000**	0.97±0.39	0.908	**0.001**
IgA	4.16±1.30	3.51±1.41	**0.000**	3.29±1.07	**0.045**	**0.000**
ESR	26.69 ±17.68	19.62 ±10.89	**0.015**	15.57 ±11.28	0.929	**0.043**
ESSDAI	4.5±2.5	3.0±2.4	**0.001**	2.08±1.44	0.237	**0.004**

Conclusion: This is the first follow study of iguratimod in pSS to show benefit with good tolerance.

REFERENCES

[1] Saraux, A., et al. (2016). "Treatment of primary Sjogren syndrome." Nat Rev Rheumatol 12(8): 456-471.
[2] Li, J., et al. (2013). "Efficacy and safety of iguratimod for the treatment of rheumatoid arthritis." Clin Dev Immunol 2013: 310628.
[3] Ramos-Casals, M., et al. (2010). "Treatment of primary Sjogren syndrome: a systematic review." JAMA 304(4): 452-460.

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AB0466 ADVERSE EVENTS AND THE RELAPSE RISK OF SYSTEMIC LUPUS ERYTHEMATOSUS DURING HYDROXYCHLOROQUINE TREATMENT

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Background: The antimalarial drug hydroxychloroquine (HCQ) is used worldwide to control the disease activity of systemic lupus erythematosus (SLE). In Japan, HCQ was not approved until September 2015 due to the problem of retinopathy induced by chloroquine. There is insufficient evidence of the effects of HCQ or adverse events linked to HCQ treatment.
Objectives: Here, we evaluated adverse events and the relapse risk of SLE during HCQ treatment.
Methods: We retrospectively analyzed the data of 109 patients diagnosed with SLE and treated with HCQ for ≥12 months at Nagasaki University Hospital and community hospitals. The demographic data included the patient's age at the onset of SLE, gender, the disease duration of SLE (the time from the diagnosis of SLE until the renal biopsy), comorbidities of Sjögren syndrome (SS)/anti-phospholipid syndrome (APS), and the treatment for induction. We identified the risk of adverse events and relapse at 12 months after the introduction of HCQ. Decision tree models predicting relapse were built with the Classification and Regression Trees (CART) algorithm. The data of the length of time between a patient's HCQ induction to the first observation of relapse was analyzed by the Kaplan-Meier method with a log-rank test.
Results: Most of the patients were female (88.1%). The median age at the introduction of HCQ was 40.0 years (interquartile range [IQR] 30.5–50.0 years), and the SLE disease duration was 95 months (IQR 38.0–184.5 months). The mean observation period after HCQ introduction was 12 months. The comorbidity rates of SS and APS were 25.7% and 20.2%, respectively. The SELENA-SLEDAI scores were significantly decreased at 3 months post-HCQ introduction. The dose of oral prednisolone was significantly decreased at 6 months post-HCQ introduction. Eighty-six patients (78.9%) were continuing HCQ at 12 months post-introduction. Adverse events occurred in 27 patients (24.8%), including skin rashes (n=11, 10.1%) and gastrointestinal symptoms (n=6, 5.5%). The sole predictive factor for adverse events was the white blood cell (WBC) count at baseline (odds ratio: 0.9997, 95%CI: 0.9994–0.9999, p=0.0285). Twelve of 86 patients (14.0%) experienced relapse that required the start of prednisolone or an immunosuppressant or an increased prednisolone dose. The multivariate analysis revealed that the C4 value at baseline was a predictive factor of relapse (odds ratio: 0.841, 95%CI: 0.718–0.984, p=0.0097). The cut-off point determined by the CART algorithm showed that C4 ≥9.3 mg/dl at baseline provides the best performance for predicting relapse. The Kaplan-Meier analysis showed that compared to C4<9.3 mg/dl at baseline, C4 ≥9.3 mg/dl at baseline was correlated with being free from relapse (p=0.0032).
Conclusion: A lower C4 value at HCQ introduction was a predictive factor for the relapse of SLE, and a lower WBC count was a predictive factor for adverse events.

REFERENCES

[1] Ponticelli C, Moroni G. Hydroxychloroquine in systemic lupus erythematosus (SLE). Expert Opin Drug Saf. 2017 Mar;16(3):411-419. doi: 10.1080/14740338.2017.1269168.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.1171

AB0467 IMPROVED DISEASE CONTROL OF SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS POSSIBLE ASSOCIATION WITH AGGRESSIVE USE OF IMMUNOSUPPRESSANTS

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Background: The outcome of patients with systemic lupus erythematosus (SLE) has considerably improved in recent decades.
Objectives: The aim of this retrospective study was to examine whether the disease control has been actually improved and its possible association with the altered balance between the use of immunosuppressants and glucocorticoids.
Methods: We enrolled SLE patients who visited Toho University Ohashi Medical Center during 2012-2017 (Group A, 79 patients), and compared them with patients during 1999-2003 (Group B, 68 patients; not overlapping with Group A). All the patients met the American College of Rheumatology 1997 revised criteria for SLE classification. Patient backgrounds, the dose of glucocorticoids and the use of immunosuppressants at the times of SLE onset and disease flare were reviewed from the medical records. The disease flare was defined as a new BILAG 2004 A or B score in at least one system.
Results: The age at disease onset and sex, as well as the presence of lupus nephritis and serositis were comparable between 2 groups, although central nervous system manifestations were less frequent in Group A (7% versus 19% in Group B, p=0.04). The average number of flare per person-year was significantly reduced in Group A than Group B (0.26 versus 0.4, respectively, p<0.01). In the initial treatment, the median dosage of oral prednisolone was equivalent in both groups (30 mg day, p=0.64), while the total glucocorticoid dosage in the initial 16 weeks was significantly reduced in Group A (1,960 mg prednisolone equivalent versus 2,913 mg in Group B, p=0.01). And the inclusion rate of immunosuppressants in the initial SLE treatment was significantly higher in Group A (43% versus 6% in Group B, p<0.01). Further, upon disease flare, the dose of prednisolone for it was significantly lower in Group A (6.5 mg/day versus 14 mg/day in Group B, p<0.01) and the rate of introduction or alteration of immunosuppressants were significantly higher in Group A (81% versus 24% in Group B, p<0.01). Infection rates were similar between the groups (p=0.44).
Conclusion: Aggressive use of immunosuppressants in recent years resulted in the reduction of the rate of SLE flare as well as that of cumulative glucocorticoid dosage.

REFERENCES

[1] Bernatsky S, et al. Arthritis Rheum 2006; 54: 2550-7
[2] Lee Y, et al. Lupus 2016; 25: 727-34.
[3] Guillermo R.I. Rheumatology 2012; 51: 1145-53
[4] Ugarte A, et al. Lupus 2011; 4: 423
[5] Pepper R, et al. Nephrol Dial Transplant 2009; 24: 3717-23.
[6] Saag KG, et al. Am J Med 1994;96: 115-23
[7] Ruiz-Irastorza G, et al. Arthritis Res Ther 2009;11:R109.

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AB0468 QUALITY OF LIFE IN SYSTEMIC LUPUS WOMEN WITH CUTANEOUS DAMAGE ON THE FACE: COSMETIC CAMOUFLAGE IMPACT

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Background: Health-related quality of life (HRQoL) can be negatively impacted by visible skin lesions.[1]
Objectives: To investigate the effect of cosmetic *camouflage* on health-related quality of life of systemic lupus erythematosus (SLE) women presenting sequelae of cutaneous manifestations on the face.
Methods: This is a randomized controlled clinical trial (Universal Trial Number: U1111-1210-2554e) with outpatients SLE women according to ACR/1997 and/or SLICC/2012 criteria, aged over 18 years old with sequelae of cutaneous lupus manifestations on the face, recruited in two tertiary centers. Exclusion criteria were: moderate to severe systemic lupus activity (SLEDAI 2k-modified>4), no understanding of the questionnaires or psychological and/or psychiatric treatment initiation or modification during the study. A final sample of 43 patients was divided into group I (cosmetic *camouflage* n=28) and group II (control n=15). Patients in group I were instructed to use cosmetic *camouflage* daily; Group II patients did not use any *camouflage*. SLE Quality of Life (SLEQoL) and Dermatology Quality of Life Index (DLQI) questionnaires were used to evaluate HRQoL, higher scores meaning worse HRQoL. All patients answered the questionnaires at baseline (T0) and after 12 (±2) weeks (T1). The primary end point was a change on HRQoL after *camouflage* cosmetic use. Continuous variables were described as median (interquartile range). The Wilcoxon signed rank test and the Mann-Whitney U test were used for the analysis as indicated. End points were investigated per-protocol analysis, and a 2-sided p value <0.05 was considered to be significant.
Results: Both groups were similar at baseline regarding age [group I:45.0 (37.3-55.7) years old *versus* group II: 50.0(43.0-55.0) years old, p=0.575], disease duration [group I: 17.5 (7.3-26.5) years *versus* group II: 15.0 (9.0-17.0) years, p=0.452] and modified SLEDAI-2k [group I: 0 (0-2) *versus* group II: 2 (0-2), p=0.301]. Also, they were similar considering the sociodemographic, clinical and treatment characteristics of the disease. The DLQI and SLEQoL scores decreased in the cosmetic *camouflage* group from baseline: DLQI [T0: 8.5 (4.0-16.0) *versus* T1: 3.0 (1.0-7.5), p=0.008]; SLEQOL [T0: 118.0 (91.0-154.3) *versus* T1: 95.5 (76.0-135.0), p=0.003]; while there was no variation in the control group: DLQI [T0: 8.0 (3.0-12.0) *versus* T1: 7.0 (4.0-12.0), p=0.196]; SLEQOL [T0: 89.0 (65.0-127.0) *versus* T1: 95.5 (65.0-164.0), p=0.532]. The difference on the variations of HRQoL scores between groups I and II was statistically significant: ΔDLQI [group I: -3.0 (-10.8-0.0) *versus* group II: 1.0 (-1.0-6.0), p=0.003] and ΔSLEQoL [group I:-14.5 (-33.0-0.0) *versus* group II:3.0 (-8.0-10.0), p=0.009]. The SLEQoL score variations were on physical function (p=0.033), humor (p = 0.033) and self-image (p=0.031) domains.
Conclusion: In this group of SLE women with low systemic disease activity and sequelae of cutaneous manifestations on the face, we observed an improvement of HRQoL after daily use of cosmetic *camouflage*. It is an effective intervention that should be recommended by the rheumatologists.

REFERENCES

[1] - Klein R, et al. Quality of life in cutaneous lupus erythematosus. J Am Acad Dermatol. 2011; 64 (5): 849-58.

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AB0469 THE EFFECTS OF ACUPUNCTURE ON XEROSTOMIA, XEROPHTHALMIA AND ANTIBODY MODIFICATION IN PATIENTS WITH SJŐGREN SYNDROME: A META-ANALYSIS

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Background: Xerostomia and xerophthalmia are common chief complaints among patients with Sjőgren syndrome (SS) but there has been no satisfying pharmacy to relieve the associated symptoms; hence the effectiveness of other non-pharmacological interventions such as acupuncture should be accessed.
Objectives: To access the therapeutic effects of acupuncture on xerostomia and xerophthalmia in patient with SS.
Methods: We conducted a meta-analysis of randomized clinical trials (RCTs) which evaluated the effectiveness of xerostomia and xerophthalmia in SS. PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Chongqing Weipu Database (CQVIP), China Academic Journals Full-text Database, AirititLibrary, Chinese Electronic Periodicals Service (CEPS), China National Knowledge Infrastructure (CNKI) Database were searches through Oct, 2018 to select studies. Data for evaluation of subjective and objective xerostomia was extracted and was assessed with random-effects meta-analysis.
Results: After searching, a total of 680 references were yielded and five RCTs were included, covering 460 patients dry mouth resulted from SS, among whom 229 patients received acupuncture and 231 patients were control group. Acupuncture group was associated with higher subjective response rate (odds ratio 3.036, 95% confidence interval [CI] 1.828 – 5.042, P < 0.001, Fig. 1) and increased salivary flow rate (weighted mean difference [WMD] 3.066, 95% CI 2.969 – 3.164, P < 0.001, Fig. 2), as an objective marker. Regarding xerophthalmia, acupuncture group revealed less dry eye visual analog scale (VAS, WMD -1.035, 95% CI -1.457 - -1.673, P < 0.001, Fig. 3), better Schirmer test (WMD 2.357, 95% CI 1.021 – 3.692, P = 0.001, Fig. 4) and trend of longer break-up time (WMD 4.927, 95% CI -0.055 – 9.908, P = 0.053, Fig. 5). In addition, two studies examined IgG levels, which were lower in the acupuncture group (WMD -166.857, 95% CI -233.138 - -100.576, P < 0.001, Fig. 6).
Conclusion: In the present meta-analysis, acupuncture improves both subjective and objective markers of xerostomia and xerophthalmia in patients with SS and is considered as an option of non-pharmacological treatment.

REFERENCES

[1] Vivino FB. Sjogren's syndrome: Clinical aspects. Clin Immunol. 2017;182:48-54.
[2] Kuklinski E, Asbell PA. Sjogren's syndrome from the perspective of ophthalmology. Clin Immunol. 2017;182:55-61.

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AB0470 IMMUNOREGULATORY THERAPY EFFECTIVELY PROMOTES THE BALANCE BETWEEN TREG CELLS AND PRO-INFLAMMATORY LYMPHOCYTES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Recent studies have reported that some drugs such as low-dose interleukin-2, rapamycin, metformin, retinoic acid and coenzyme Q10 could promote the proliferation and functional recovery of regulatory T cells (Treg) in patients with autoimmune diseases. However, the effects on the balance of Treg cells and pro-inflammatory lymphocytes and long-term efficacy have rarely been reported.

Objectives: To evaluate the changes of peripheral lymphocyte subsets, conventional drugs and remission rate in patients with systemic lupus erythematosus (SLE) after immunomodulatory therapy.
Methods: A total of 89 patients with SLE from the Second Affiliated Hospital of Shanxi Medical University from January 2016 to April 2018 were enrolled, who were divided into well-controlled group and untargeted control group taking a full consideration of the patient's symptoms, signs and related laboratory findings. We measured the absolute counts of B, NK, CD8+T and helper T 1 (Th1), helper T 2 (Th2), helper T 17 (Th17) and Treg cells in peripheral blood of patients before immunomodulatory therapy and during the 3 months and 6 months of follow-up and 93 sex- and age- matched control individuals using flow cytometry. Moreover, the ratios of various cells to Treg cells were calculated.
Results: Compared with healthy controls, Treg cells in SLE patients were significantly lower before the treatment with immunomodulator, while the ratios of various pro-inflammatory lymphocytes to Treg cells (such as Th2/Treg, Th17/Treg, CD8+T/Treg, etc.) were higher. After 3 months and 6 months with immunomodulatory therapy, the absolute number of Treg cells in peripheral blood of SLE patients increased obviously reaching to normal level. Accordingly, the ratios of various pro-inflammatory lymphocytes to Treg cells recovered. At the same time, the dose of glucocorticoid and disease-modifying antirheumatic drugs (DMARDs) decreased distinctly. Additionally, the well-controlled group was able to maintain a high remission rate, and the untargeted control group could achieve a higher response rate after immunomodulatory treatment.
Conclusion: The imbalance between pro-inflammatory lymphocytes and Treg cells caused by the significant decrease of Treg cells may be the main cause of SLE. And immunomodulatory therapy we came up with may reverse the imbalance of proinflammatory lymphocytes and Treg cells, which is an potential and effective treatment for SLE.

REFERENCES

[1] Chen YJ, Chang YT, Wang CB, et al. Malignancy in systemic lupus erythematosus: a nationwide cohort study in Taiwan[J]. Am J Med, 2010 Dec;123(12):1150.
[2] Noack M, Miossec P. Th17 and regulatory T cell balance in autoimmune and inflammatory disease[J]. Autoimmun Rev, 2014, 13(6): 668-677.
[3] Yu A, Snowhite I, Vendrame F, et al. Selective IL-2 responsiveness of regulatory T cells through multiple intrinsic mechanisms supports the use of low-dose IL-2 therapy in type 1 diabetes. Diabetes. 2015;64: 2172–2183.
[4] Zeiser R, Leveson-Gower DB, Zambricki EA, et al. Differential impact of mammalian target of rapamycin inhibition on CD4 + CD25 + Foxp3+ regulatory T cells compared with conventional CD4+ T cells. Blood. 2008; 111:453–462.
[5] Schuiveling M, Vazirpanah N, Radstake TRDJ, Zimmermann M, Broen JCA. Metformin, A New Era for an Old Drug in the Treatment of Immune Mediated Disease?[J]. Curr Drug Targets, 2017;18:1-15.

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AB0471 **VITAMIN D SUPPLEMENTATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH VITAMIN D DEFICIENCY AND INSUFFICIENCY: THE EFFECT ON DISEASE ACTIVITY, FATIGUE AND INTERFERON SIGNATURE GENE EXPRESSION**

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Background: Vitamin D deficiency is highly prevalent among patients with systemic lupus erythematosus (SLE) [1]. Evidence from multiple studies has shown that vitamin D deficiency in SLE is associated with a higher disease activity [2]. There is conflicting evidence with regards to the relationship between fatigue and vitamin D level [3,4].
Objectives: The principal aim of this study was to establish any potential effect on the level of fatigue, disease activity (measured by SLE disease activity index-2K (SLEDAI-2K)) and interferon signature gene expression, from vitamin D supplementation to SLE patients with vitamin D deficiency or insufficiency.
Methods: 33 SLE patients, 13 with vitamin D deficiency and 20 with vitamin D insufficiency, gave informed consent to participate in this 12 month prospective study. Their participation consisted of an interview, filling of the Fatigue Severity Scale (FSS), and blood tests. The patients were advised to take vitamin D3 8000IU daily for 8 weeks if they were vitamin D deficient, or 8000IU daily for 4 weeks if they were insufficient. This was followed by 2000IU daily maintenance. The patients were re-assessed after 6 and 12 months of vitamin D supplementation. RNA was extracted from whole blood taken from the patients at baseline and after 6 months of vitamin D supplementation. The expression of 12 interferon signature genes was measured in the extracted RNA by using QuantiGene Plex technology. Approval to carry out this study was obtained from the University Research Ethics Committee.
Results: 87.9% of SLE patients studied were female. The mean age was 47.6 years and the mean duration of SLE was 13.8 years. Table 1 shows the results obtained for several variables at baseline, after 6 months and after 12 months. The expression of all 12 interferon signature genes measured, was noted to decrease following 6 months of vitamin D supplementation. This reached statistical significance for two of the genes measured (OAS1, p=0.014; SOCS1, p=0.003).

Variable	Time	Mean	Standard Deviation	p-value
SLEDAI-2K	Baseline	3.97	3.359	0.210
	6 months	3.36	2.924	0.009
	12 months	2.61	2.193	
Anti-dsDNA level (IU/mL)	Baseline	210.31	234.416	0.032
	6 months	194.08	214.129	0.030
	12 months	190.50	208.131	
Prednisolone daily dose (mg)	Baseline	1.93	3.458	0.043
	6 months	2.30	4.089	0.042
	12 months	1.33	2.931	
FSS	Baseline	4.21	1.536	0.206
	6 months	3.93	1.577	0.053
	12 months	3.81	1.859	
25-hydroxyvitamin D (ng/mL)	Baseline	21.91	6.336	<0.001
	6 months	32.88	6.594	0.001
	12 months	28.48	9.291	

Abstract AB0471 Table 1. Table showing results at baseline, after 6 months and after 12 months of vitamin D3 supplementation.

Conclusion: The results indicate that vitamin D supplementation in SLE patients who are deficient or insufficient, results in an improvement in disease activity, and possibly also in the level of fatigue. This could be explained by the decrease in the expression of interferon signature genes.

REFERENCES

[1] Kamen DL, Aranow C. The link between vitamin D deficiency and systemic lupus erythematosus. Curr Rheumatol Rep 2008; 10: 273–280.
[2] Sahebari M, Nabavi N, Salehi M. Correlation between serum 25(OH)D values and lupus disease activity: an original article and a systematic review with meta-analysis focusing on serum VitD confounders. Lupus 2014; 23:1164-77.
[3] Ruiz-Irastorza G, Egurbide MV, Olivares N, Martinez-Berriotxoa A, Aguirre C. Vitamin D deficiency in systemic lupus erythematosus: prevalence, predictors and clinical consequences. Rheumatology 2008; 47:920–923.
[4] Ruiz-Irastorza G, Gordo S, Olivares N, Egurbide MV, Aguirre C. Changes in vitamin D levels in patients with systemic lupus erythematosus: Effects on fatigue, disease activity, and damage. Arthritis Care Res 2010; 62:1160–1165.

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AB0472 PRIMARY SJOGREN SYNDROME ASSOCIATED INTERSTITIAL LUNG DISEASE: FEATURES, TREATMENT AND OUTCOME OF A MONOCENTRIC COHORT

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Background: Primary Sjögren's syndrome (pSS) is an autoimmune systemic disease characterized by lymphocytic infiltration of exocrine glands, mainly resulting in dysfunction of salivary and lachrymal glands and symptomatic xerostomia and xerophthalmia. About one third of patients also present extra-glandular manifestations and,among them, interstitial lung disease (ILD) is one the most frequent, occurring in about 10– 20% of patients. ILD is associated with an impaired quality of life and physical capacity and to a reduced 10-year survival. Despite it seems to bemore frequently detected in late stages of thedisease, some authors suggest that ILD can be diagnosed before pSS in 20% of cases. Main predictive factors of progression of pSS-ILD have not been clearly investigated in previous studies and no evidence-based treatment is defined for these patients.

Objectives: To describe the clinical and serologic features and the outcome of a monocentric cohort of pSS-ILD and the possible differences between patients treated or not with immunosuppressive treatment

Methods: We retrospectively evaluated the 37 pSS-ILD patients followed at our Rheumatology Unit (male/female ratio 1/6.4, mean age 69.6±11.3 years, mean disease duration of pSS 5±5.2 years).

Among them, 18 patients (48.6%; group 1) underwent immunosuppressive treatment because of lung disease, namely mycophenolate mofetil (9 patients, 50%), cyclophosphamide (3, 16.7%), azathioprine (5, 27.8%), high dose steroids (1, 5.6%), while 19 patients were not treated (group 2).

Results: No significant differences were observed in regard of age, male/female ratio, and disease duration of ILD and pSS, while a significant difference was observed regarding the lung function of the 2 groups; the forced vital capacity (FVC) and the diffusion lung capacity of CO (DLCO) at baseline were significantly lower in the group 1 (FVC 78.6% vs 99.4% p=0.008; DLCO 45.7% vs 56.9%, p=0.025; in group 1 and group 2, respectively). No significant difference was observed between baseline and follow-up for FVC and DLCO in both groups, regardless the immunosuppressive drug (fig. 1). At the end of follow-up FVC increased, decreased and remained stable in 5.3/10.5/84.2% and 16.7/27.8/55.6%, in group 1 and group 2, respectively; DLCO increased, decreased and remained stable in 10.5/21.1/68.4% of group 1, while remained stable or decreased in 61.1 and 38.9 of treated patients, respectively (figure 1).

Figure 1. Evolution of lung function pSS patients treated (group 1) or not (group 2) with immunosoppressive drugs

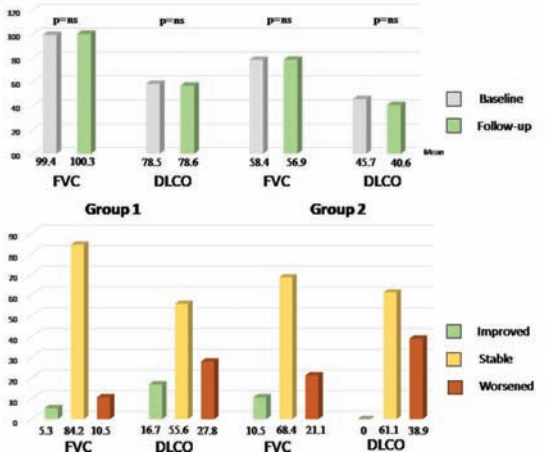


Figure 1

Conclusion: At our knowledge, few studies have investigated the features of pSS-ILD and the role of immunosuppressive drugs in these patients. Our data suggest that the decline of lung function is one of the most significant parameters to guide the prescription of immunosuppressive drugs, but no differences can be observed according to the treatment in term of effectiveness. However, no studies have investigated the correctness of this approach or the efficacy of the MMF or CFX in pSS-ILD. Our study is strongly limited by the retrospective design and the low number of patients evaluated, but these data set attention on this unmet need. Further prospective studies are mandatory to clarify the impact of ILD in pSS patients and the correct therapeutic approach.

REFERENCES

[1] Baldini C, Pepe P, Quartuccio L, et al. Primary Sjogren's syndrome as a multi-organ disease: impact of the serological profile on the clinical presentation of the disease in a large cohort of Italian patients. Rheumatology. 2014; 53: 839-844

[2] Manfredi A, Sebastiani M, Cerri S, et al.Prevalence and characterization of non-sicca onset primary Sjögrensyndrome with interstitial lung involvement. Clin Rheumatol. 2017;36:1261-1268.

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AB0473 HYPOGAMMAGLOBULINEMIA AND INFECTIONS IN RHEUMATOLOGIC PATIENTS TREATED WITH RITUXIMAB

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Background: Treatment with rituximab (RTX) for rheumatologic diseases may produce hypogammaglobulinemia (hypoglb) (1,2), and that way increase the risk to acquire certain infections (3,4). There are no stablished guides to evaluate and treat hypoglb in these patients. In our hospital, the percentage of patients who develop hypoglb and severe infections is unknown.

Objectives: To analyse the effect of RTX on immunoglobulin (Ig) levels and to evaluate the severe infections and hepatitis B reactivations that could be related to this treatment.

Methods: This is a descriptive, retrospective study of patients followed up in the Rheumatology Unit of the Alicante General University Hospital (HGUA) who had received at least one course of RTX. Clinical characteristics and laboratory parameters were obtained from the electronic charts: type of disease, posology and total amount of RTX, Ig levels before and after treatment with RTX, the concomitant treatment with disease-modifying drugs (DMDs), hepatitis B virus's (HBV) reactivations and infections that required hospitalization. Hypoglb was assessed when IgG< 750 mg/dL, and severe hypoglb if IgG <450 mg/dl. The association of hypoglb with disease and treatment´s aspects was studied by t-Student, U-Mann-Whitney and Chi-2. Multiple logistic regression was conducted to study the independent risk factors associated with hypoglb. The study was approved by the Hospital Ethics Committee.

Results: Finally 106 patients were included, 85 women (80.2%) and 21 men (19.8%). The more frequent conditions were rheumatoid arthritis (47.2%), Sjögren syndrome (16%), Systemic Lupus Eritematosus (13.2%), vasculitis (6.6%) and other connective tissue diseases (10.4%). Characteristics of the sample are shown in table 1. A correct follow up of the Ig levels during the treatment was shown to be undergone in 87.7% of the cases. It was found that 35.8% of the patients presented hypoglb and 13,2% presented severe infections after receiving RTX. No HBV reactivations were found. Among the patients with hypoglb, 78.9% received concomitant treatment with other immunosuppressants (methotrexate 23.6%, leflunomide 23.6%). Hypoglb was more frequent in rheumatoid arthritis (44%), lupus (42.8%) and vasculitis (28.6%). Through simple logistic regression hypoglb during treatment was associated with the presence of previous hypoglb (p=0.025), higher doses received (p=0.01) and longer treatment (p=0.003). In the multiple logistic regression, only low levels of Ig before treatment turned out to be an independent risk factor for hypoglb during treatment (OR 6.86; IC 1.25-37.57). The IgM and IgA levels, but no the IgG levels were significantly lower in patients who has severe infections.

Duration of treatment with RTX (months)	34.7 ± 30
Total dosage (grames)	12.7 ± 9,6
RTX posology	79 (74.5%)
Standard	10 (9.4%)
Single iv dose every 6 months	11 (10.4%)
On demand	
Ig levels followed up during treatment	YES: 93 (87.7%)
	NO: 13 (12.3%)

Patients with hypoglb during RTX	38 (35.8%)
Severe hypoglb	4 (3.8%)
Patients with severe infections which required hospitalization	14 (13.2%)
With hypoglb	7 (6.6%)
Without hypoglb	7 (6.6%)
Severe infections which required RTX discontinuation	2 (1,9%)
Respiratory	0
HBV reactivation	2 (1,9%)
Skin (Erisipela and celulitis)	
Exitus	0 (0%)

Conclusion: Hypogammaglobulinemia happens in a third of the patients who receive RTX, especially in those who have low previous IgG levels; therefore a follow up during the treatment should be encouraged. Low IgM and IgA levels during the treatment could also be associated with severe infections.

REFERENCES

[1] Christou EAA. Int Rev Immunol. 2017;3:352.
[2] Roberts DM. Journal of Autoimmunity 2015;57:60
[3] Gea-Banacloche, JC; Seminars in Hematology 2010;47:187.
[4] Salliot C.Ann Rheum Dis 2009;68:25

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AB0474 MORTALITY ACROSS RITUXIMAB-TREATED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE BRITISH ISLES LUPUS ASSESSMENT GROUP (BILAG) REGISTRY

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Background: Mortality in Systemic Lupus Erythematosus (SLE) is elevated in comparison to the general population. Previously we have demonstrated improved disease control in response to Rituximab (RTX) therapy in a cohort of refractory SLE patients.
Objectives: To investigate mortality in refractory SLE patients treated with RTX and identify risk factors that may be associated with death.
Methods: All patients recruited to the BILAG-BR (both RTX treated and standard of care-SOC) were included from initial study visit to death or 3 years post last treatment change. Demographics, concurrent medication use, disease activity (BILAG/SLEDAI) and damage scores (SLICC-DI) were recorded. Information regarding mortality was collected from study centres and NHS digital national death registry. Baseline demographic data are presented using descriptive statistics performed using Stata (version 14).
Results: 830 patients were included (715 RTX-treated, 115 standard therapy). RTX-treated patients tended to have longer disease duration (10 vs 6.5 years respectively) and were more likely to have active musculoskeletal disease (% BILAG A or B: 39% vs 23%). Rates of renal (11% vs 16%) and neurological disease (12% vs 9%) were comparable between groups as were baseline SLICC-DI and SLEDAI scores.
33 deaths were reported. 28 (3.9%) RTX-treated patients (1.2 deaths/100 pt yrs follow up) and 5 (4.3%) non-RTX patients (1.5 deaths/100 pt yrs follow up).
Cause of death was identifiable in 20 RTX treated patients. Infection was the commonest cause of death (10/20, 50%) followed by ischaemic heart disease (5/20, 25%) and malignancy (3/20, 15%). Median time to death for RTX-treated was 481 days.
Risk factors associated with mortality within the RTX group included male gender, older age at diagnosis, renal disease, hypogammaglobulinaemia, high SLICC-DI and higher steroid use at last review (Table 1). Median cumulative RTX dosing was 2g for deceased and alive.
Deceased RTX patients had a greater total number of co-morbidities at baseline (2.5 vs 0, $p < 0.01$) driven predominantly by the presence of hypertension (11/28, 39% vs 159/687, 25%, $p = 0.05$), ischaemic heart disease (4/28, 14% vs 11/687, 2%, p= 0.00) and diabetes (7/28, 25% vs 15/687, 2%, p = 0.00).
Conclusion: RTX treated patients do not appear to have higher mortality rates compared to patients starting SOC treatment. Mortality is associated with cardiovascular risk factors, higher steroid doses, hypogammaglobulinaemia and renal disease. Active management of these risk factors may lead to improved mortality outcomes.

Table 1. Deceased and alive RTX treated patients

	Deceased (n=28)	Alive (n=687)
Gender (M: F%) (n= 708)	7:21 (25% M, 75% F)	63:617 (9.26% M, 90.74% F)
Median Age at Diagnosis in years (IQR) (n = 713)	51.5(42.5-66.5)	39(30-49)
Median Disease duration in years (IQR) (n=647)	13(11-19)	12.27(6-16)
Median Cumulative Rituximab dose in mg (IQR) (n=567)	2000 (2000-4000)	2000 (2000-4000)
Ethnicity (Caucasian: Non-Caucasian) (n =491)	17:5 (77.27% Caucasian, 24% Non-Caucasian)	291:178 (62.05% Caucasian, 37.95% Caucasian)

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AB0475 BELIMUMAB: EXPERIENCE IN CLINICAL PRACTICE SETTINGS AT A RHEUMATOLOGY DEPARTMENT IN A TERTIARY HOSPITAL

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Background: Belimumab is a human IgG1l monoclonal antibody directed against BAFF, a B lymphocyte survival factor. It is indicated as adjuvant treatment in adult patients with active systemic lupus erythematosus (SLE), with positive autoantibodies and with a high degree of activity of the disease despite standard treatment.

Case	Gender	Age	Indication	Start date	Withdrawal	Reason for withdrawal	Initial and final daily prednisone dose	Time in treatment
1	♀	56	thrombocytopenia	26/01/2012	Yes	Inefficiency	0 → 0	8 months
2	♀	33	arthritis	17/03/2012	No		10 → 5	6 years and 6 months
3	♀	48	arthritis	22/03/2012	Yes	Neutropenia	7.5 → 2.5	8 months
4	♀	64	thrombocytopenia	03/04/2012	Yes	Urothelial carcinoma	15 → 2.5	5 years
5	♀	45	cutaneous	07/05/2012	Yes	Inefficiency	30 → 30	4 months
6	♀	70	cutaneous thrombocytopenia	09/12/2013	No		15 → 2.5	4 years and 9 months
7	♀	54	arthritis	18/12/2014	No		15 → 2.5	3 years and 9 months
8	♀	46	arthritis	30/11/2015	No		0 → 0	2 years and 10 months
9	♀	58	arthritis	30/05/2017	No		7.5 → 5	1 year and 4 months
10	♀	31	arthritis	17/01/2018	No		10 → 5	8 months
11	♀	46	arthritis	15/02/2018	No		5 → 2.5	7 months
12	♀	49	serositis	11/04/2018	No		5 → 5	5 months

Objectives: This study aims to describe a sample of patients diagnosed with SLE who received treatment with belimumab in a tertiary hospital.

Methods: Retrospective longitudinal unicentric observational study. Clinical records of all patients diagnosed with SLE who had received treatment with belimumab were reviewed. Demographic characteristics, clinical manifestations and reason for belimumab indicaton were collected.
Results: The twelve patients included in the sample were women. Median age was 48.5 years (31-70). The most frequent reason for indication of belimumab was uncontrolled arthritis. The average time of treatment with belimumab in the total sample was 27.5 (+/- 26.24) months, with a median of 12 months (4-78). Mean treatment time (cases in which belimumab was discontinued excluded) was 31.25 (+/- 26.98) months with a median of 25 (5-78). The average dose reduction of prednisone after initiation of treatment with belimumab (in patients in which it was considered effective) was 5 mg per day (+/- 5). It should be noted that of the 14 cases, treatment was only discontinued in 4 patients, 2 of which were withdrawn due to ineffectiveness. There were 2 adverse events that required drug withdrawal: neutropenia and urothelial carcinoma. (Table).
Conclusion: BLM is a well tolerated drug and effective in clinical practice. Adverse effects leading to drug withdrawal are infrequent.
Disclosure of Interests: Carolina Merino Argumánez: None declared, Olga Rusinovich: None declared, Consuelo Ramos Giráldez Speakers bureau: Sanofi, María Espinosa: None declared, Hilda Godoy: None declared, Carmen Barbadillo Mateos: None declared, Jose Campos Esteban: None declared, Mercedes Jiménez Palop: None declared, Jesus Sanz: None declared, Luis Fernando Villa Alcázar: None declared, Carlos Isasi Zaragoza : None declared, Monica Fernandez Castro: None declared, José Luis Andréu Sánchez: None declared
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AB0476 SPECIAL ASPECTS OF GLUCOCORTICOID THERAPY IN PATIENTSWHO TREATED WITH ANTI-B-CELL AND ANTI-BLYS THERAPY

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Background: The basis of treatment of SLE are glucocorticoids (GCs), which since their introduction into clinical practice, have led to increased survival and reduced early mortality of SLE patients. However, the need to use high doses of GCs, as well as long-term use of medium doses to maintain disease remission, leads to the development of serious adverse reactions. This leads to an increase in the risk of irreversible organ damage. In this regard, it is important to search for ways to prevent the use of high doses of GCs, minimizing the dose of GCs.
Objectives: To assess special aspects and dynamics of oral glucocorticoid (GC) therapy in SLE patients treated with anti-B-cell and anti-BlyS therapy.
Methods: The study included 64 SLE pts (5M/58F), divided into 3 groups: Group I - 47 patients (SLEDAI2K 16[11;20] scores), receiving rituximab (RTX) i/v infusions by drop at 500 - 2000 mg dose-range. Group II included 10 patients (SLEDAI2K 10[8;11] scores) treated with Belimumab (BLM) at 10 mg/kg once a month. The remaining 7 patients from Group III (SLEDAI2K 10[9;16] scores) were administered a combination of RTX and BLM. They started treatment with RTX 500 (2 patients) or 1000 mg (5 patients) infusions, and 3 months later BLM at standard scheme of 10 mg/kg once a month was initiated for 8 months. SLICC damage index (DI) was documented at baseline - before initiation of RTX and BLM - in 26 out of 64 patients (40%) with SLICC DI score > 1 (1 - 5 scores); 20 patients out of them were administered RTX.
Results: 47 patients on RTX therapy received different oral GCs doses: high GCs doses (Me 40[30;50]mg/day) were documented in 11 (24%) patients, moderate doses (Me 13[10;20]mg/day) – in 29 (61%) patients, and low doses (Me 5[5;7,5]mg/day) - in 7 (15%) patients. Patients on BLM and combination therapy were administered GCs at doses ≤ 20 mg (Me 15[5;20]mg/day and Me 8,75[5;15] mg/day, respectively)
During first 3 month of treatment GCs doses in all 3 Groups remained unmodified. By Mo 6 25% reduction in oral GCs doses was documented in: patients on RTX - 20[15;20]mg/day, 10[8,75;10]mg/day, 5[5;5] mg/day (respectively, in the groups with initially high, moderate and low GCs doses); BLM 10[7,5;10] mg/day, combination therapy 8,75[5;15] mg/day. By Mo 12 Me GCs dose in all 3 Groups did not exceed 10 mg/day. In view of SLE exacerbations in patients from Group I (RTX) additional RTX infusions at Mo 6, 9 and 12 were administered in 8 (20%) patients. Figure 1 presents the dynamics of oral GCs doses in patients from Group I (RTX), who were divided in 3 subgroups based on baseline (high, moderate or low) GCs dose, and also dynamics of GCs dose in patients from Groups II (BLM) and III (RTX+BLM).
Increase in SLICC score by Mo 12 of follow up was documented in patients on RTX therapy with baseline pre-existing organ damage (5 patients). There was no increase in SLICC scores in BLM and RTX +BLM treatment groups.
Conclusion: Combination therapy results in achieving rapid control of SLE activity thanks to RTX effects, and the combination with BLM allows significantly prolongs this result, minimizing the risk of exacerbation. And a very specific gain from combination RTX+BLM therapy is a chance to manage patients on moderate-to-low oral GCs doses, therefore, reducing the risk of irreversible organ damage. Increasing organ damage score in RTX Group is most likely associated with intake of higher GCs doses.

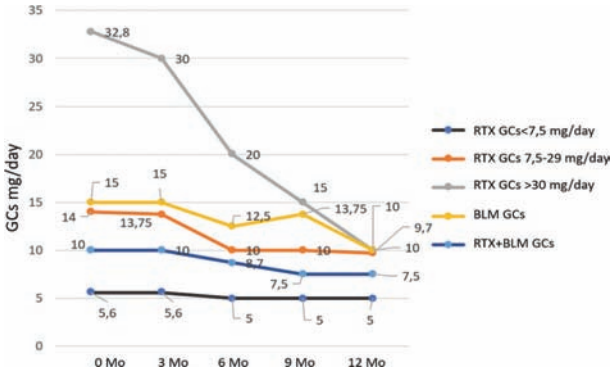


Figure 1. The dose of oral GCs in patients treated with RTX, BLM and combined treatment, Me

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AB0477 THE EFFECT OF CLOSTRIDIUM BUTYRICUM ON INTESTINAL FLORA OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ZHANG MINGXING*[1], XU-FANG YIN[1], XIAO-FENG LI[2]

zhang mingxing[1], Xu-Fang Yin[1], LI Xiao-Feng[2]. *[1]2The Second Hospital of Shanxi Medical University, Tai Yuan, China*; *[2]The Second Hospital of Shanxi Medical University, Taiyuan, China* **Objectives:** To investigate the effect of Clostridium butyricum on intestinal flora in patients with systemic lupus erythematosus.
Methods: Forty-four patients with systemic lupus erythematosus who were randomly selected from our hospital were given the oral administration of Clostridium butyricum live capsule 840mg twice a day. The concentration of methane and hydrogen at each time point before and after treatment for 44 patients was detected and compared by hydrogen and methane in lactulose breath test (LBT).
Results: After 28 days of treatment with Clostridium butyricum capsules, there was no significantly statistical difference in exhaled hydrogen concentration or methane concentration between 0 min, 30 min, 60 min and 90 min before and after treatment. See Table 1.
Conclusion: Numerous studies have shown that taking probiotics can promote the growth of normal flora and reduce the reproduction of other abnormal flora, which has a certain impact on the structure and quantity of There was no significantly statistical difference in exhaled hydrogen concentration or methane concentration at various points in time between the 44 patients before and after treatment, suggesting that there was no significant change in the structure and quantity of intestinal flora.
intestinal flora, which may be resulted from our low dose Clostridium butyricum live capsules or short treatment time, or need to be combined with other probiotics. These hypothesis above need us to further explore, in general, using microbes as a therapeutic target spot to regulate the illness of SLE by interfering with intestinal flora through diet, probiotics or fecal transplantation provides a promising prospect for clinical treatment of SLE.

Table 1. Methane and hydrogen concentrations before and after intervention by the experimenter[*PPM,Md(P25,P75)]*

	before intervention	after intervention	p
H2(0min)	16(8.5,30)	21(5.5,35)	0.697
H2(30min)	27(13,45)	27(6,61)	0.872
H2(60min)	27(11,49.5)	21(5.5,58.5)	0.977

H2(90min)	27(14,59)	27(11.5,55)	0.600
CH4(0min)	4(3,5)	4(3,5.5)	0.699
CH4(30min)	5(4,6)	5(3.5,7)	0.776
CH4(60min)	5(4,5)	5(3.3,6)	0.057
CH4(90min)	5(4,5)	5(4,6.5)	0.142
H2+CH4(0min)	20(12.5,35.5)	26(9,39)	0.747
H2+CH4 (30min)	32(19,50)	32(12,67)	0.872
H2+CH4 (60min)	31(17,54)	30(13.5,64.5)	0.909
H2+CH4 (90min)	31(20,63.5)	31(19,60)	0.000

Using Wilcoxon test, P<0.05.
Disclosure of Interests: None declared
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AB0478 PREGNANCY OUTCOME IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH HYDROXYCHLOROQUINE: 10 YEARS EXPERIENCE

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Background: Pregnancy in SLE patients is closely associated with the usage of hydroxychloroquine [1].
Objectives: To determine pregnancy outcomes in women with Systemic Lupus Erythematosus who were treated with hydroxychloroquine in Universiti Kebangsaan Malaysia Medical Centre.
Methods: Pregnant women with Systemic Lupus Erythematosus who had antenatal follow up and delivery in Universiti Kebangsaan Malaysia Medical Centre between 1st January 2007 and 1st January 2017 were retrospectively analyzed. Data collection was done via medical case notes and laboratory investigations. Study population was categorised into two groups based on hydroxychloroquine treatment during pregnancy. Incomplete pregnancy records were excluded.
Results: There were 82 completed pregnancies included with 47 (57.3%) in HCQ group and 35 (42.7%) in non HCQ group. Amongst HCQ users, there were significantly more pregnancies with musculoskeletal involvement (p=0.03), heavier mean neonatal birth weight (p=0.02) and prolonged duration of pregnancy (p=0.001). In non-HCQ users, the rate of recurrent miscarriages (p=0.003), incidence of hypertension (p=0.01) and gestational diabetes mellitus (p=0.01) and concurrent medical illness (p=0.005) were significantly more. Hydroxychloroquine use during pregnancy was protective against hypertension (p=0.001) and the gestational age at delivery had significant effect on the neonatal birth weight (p=0.001). However, duration of the disease had significant negative effect on the neonatal birth weight (p=0.016).
Conclusion: HCQ enhance better neonatal outcomes and reduce adverse pregnancy outcome and antenatal complications such as hypertension and diabetes.

REFERENCES

[1] M Leroux, C Desveaux, M Parcevaux. Impact of hydroxychloroquine on preterm delivery and intrauterine growth restriction in pregnant women with systemic lupus erythematosus: a descriptive cohort study. Lupus 2015. https://doi.org/10.1177/0961203315591027

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AB0479 RITUXIMAB MAY BE BENEFICIAL IN THE TREATMENT OF SEVERE FORMS OF SYSTEMIC AUTOIMMUNE DISEASES REFRACTORY TO STANDARD IMMUNOSUPPRESSIVE THERAPY. NINE-YEARS EXPERIENCE FROM SINGLE CLINICAL CENTRE

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Background: Rituximab (RTX) is anti-CD20 monoclonal antibody, registered for the treatment of rheumatoid arthritis (RA). It has been used in clinical practice "of label" in various other conditions including systemic autoimmune diseases – systemic lupus erythematosus (SLE), systemic scleroderma (SScl), Sjögren´s syndrome (SjS), polymyositis (PM) and dermatomyositis (DM) and ANCA associated vasculitides, but the results of clinical studies are inconherent. Nevertheless, RTX is frequently used in patients with severe forms of systemic autoimmune diseases with organ involvement after failure of conventional immunosupressive treatment. In Czech Republic, RTX may be used "of label" upon a special request in these special cases.
Objectives: To evaluate indications, clinical characteristics, general efficacy, safety and the impact of RTX therapy in patients with systemic autoimmune diseases treated in the Institute of Rheumatology, Prague since 2009 (a retrospective study).
Methods: The medical reports of all patients treated with RTX for other diagnosis than RA were analyzed and the clinical data (diagnosis, previous treatment with glucocorticosteroids and immunosuppressive drugs, number of RTX infusion, side effects and global evaluation of the efficacy by physician) were collected and analyzed.
Results: In the years 2009 – 2018, 50 patients with various systemic autoimmune diseases were treated with RTX in our clinic (SLE: n=8, SjS: n=2, SScl: n=16, PM: n=6, DM: n=3, MCTD: = 1, ANCA associated vasculitides: n=11, overlap syndromes: n=3). Mean age of the group was 48,12 ±12,9 years at the first RTX treatment and all of the patients experienced previous failure of treatment with 1-6 immunosuppressants. The total number of RTX infusions was 208 with mean 5,32 applications per patient. We have followed the patients for 37,1 months (mean), ranging from 2-114 months. During the follow-up two patients died due to complications of the disease, two patients were lost from the follow-up. The treatment was effective in majority of patients (n=27) and global efficacy was evaluated as "excellent" in 2, "very good" in 10 and "good" in 15 patients. In seven patients the treatment had no effect and in 4 patients the effect could not be evaluated due to short time follow-up. The treatment was well tolerated by patients and we have experienced 39 moderate or severe infections (requiring antibiotics or hospitalization) mostly in patients with ANCA associated vasculitides. In several patients, mild decrease of IgG levels following the RTX treatment was observed but only in one patient required a subsequent substitution with immunoglobulines. We have not observed any malignancy in the group. The detailed characteristics and results of the patients by diagnosis are provided.
Conclusion: Rixuximab may be beneficial in some patients with severe forms of systemic autoimmune diseases refractory to the standard immunosuppressive therapy. The treatment is generally well tolerated and the infections are the most common side effect.
Acknowledgement: This study was supported by the Research Project No. 0002372801 of the Czech Ministry of Health.
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AB0480 PROLONGED CLINICAL REMISSION AND LOW DISEASE ACTIVITY STATUSES ARE ASSOCIATED WITH BETTER QUALITY OF LIFE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background:
Treat to target (T2T) strategies in systemic lupus erythematosus (SLE) have been developed in order to control disease activity, improve health-related quality of life (HRQoL), reduce organ damage and decrease mortality. Previous studies revealed that both remission and low disease activity (LDA) had comparable damage accrual as well as mortality. However, studies of HRQoL in these two targets are few and there has been no comparative study between them:
Objectives: To determine the association between disease activity status (DAS) and HRQoL in SLE patients.
Methods: SLE patients in out-patient clinic during the previous 12 months were included in the study. Systemic Lupus Erythematosus-specific Quality-of-Life questionnaire (SLEQoL) was measured at the last visit. DAS was determined retrospectively during the previous year. Three categories of DAS were defined: clinical remission (CR): clinical quiescent disease according to Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), prednisolone < 5 mg/day; low disease activity (LDA): SLEDAI-2K (without serological domain) ≤ 2, prednisolone < 7.5 mg/day; and non-optimally controlled status: those who were not in CR/LDA. Immunosuppressive drugs (maintenance dose) and antimalarials were allowed. Both CR and LDA have been maintained for at least 1 year. The

association between DAS and HRQoL was assessed by using multiple linear regression analysis adjusting for other covariates.
Results: Of 237 SLE patients (pts), 100 pts (42.2%) achieved prolonged CR, 46 pts (19.4%) achieved prolonged LDA, and 91 pts (38.4%) were not in CR/LDA. Non-CR/LDA pts had significantly higher total SLEQoL score and in all domains compared with CR/LDA pts. No significant difference in SLEQoL domain scores was found between CR and LDA groups. Multivariable analysis revealed that non-CR/LDA was positively associated with SLEQoL score compared with CR/LDA (β 20.02, 95% confidence interval (CI) 6.81-33.23, p < 0.003). Moreover, non-CR/LDA was at a higher risk of impaired QoL (SLEQoL score > 80) compared with CR (hazard ratio (HR) 3.8; 95% CI 1.82-7.95; p < 0.001). However, there was no significant difference between CR and LDA in term of SLEQoL score or impaired QoL. Other factors associated with higher SLEQoL score were damage index (β 10.55, 95% CI 4.63-16.48, p = 0.001) and anemia (β 27.84, 95% CI 8.48-47.19, p = 0.001).
Conclusion: Prolonged CR and LDA are associated with better HRQoL in SLE patients and have a comparable effect. Prolonged CR or optional LDA may be used as the treatment goal of T2T approach in SLE.

REFERENCES

[1] Tselios K, et al. Clinical remission and low disease activity have comparable outcomes over 10 years in systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2018 Jul 28.
[2] Golder V, et al. Association of the lupus low disease activity state (LLDAS) with health-related quality of life in a multinational prospective study. Arthritis Res Ther. 2017 Mar 20;19(1):62.
[3] Mok CC, et al. Prevalence of remission and its effect on damage and quality of life in Chinese patients with systemic lupus erythematosus. Ann Rheum Dis. 2017 Aug;76(8):1420-1425.
[4] Tsang-A-Sjoe MWP, et al. The relationship between remission and health-related quality of life in a cohort of SLE patients. Rheumatology (Oxford). 2018 Dec 4.

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AB0481 AUTOANTIBODIES' TITRE MODULATION BY ANTI-BLYS TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Belimumab is a human monoclonal antibody that inhibits soluble B lymphocytes stimulator (BlyS) and represents the only biological drug approved for Systemic Lupus Erythematosus (SLE) (1). Belimumab is effective in reducing disease activity, number of flares and blocking damage progression (2,3). Pooled data derived from clinical trials reported a reduction of anti-dsDNA,analysed by ELISA, anti-cardiolipin (aCL) and anti-Sm and anti-ribosomal protein antibodies (2,4). No data were published on anti-beta2glycoprotein I (GPI) antibodies and other antiENA specificities.
Objectives: Our aim was to analyse the effect of Belimumab therapy on high avidity anti-dsDNA, aCL, anti-beta2GPI, and other relevant anti-ENA specificities.
Methods: 50 patients with active SLE (mean SLEDAI-2K score: 7,18; SD:3), with a mean age of 39 years (SD:11) and mean follow-up of 13 years (SD: 7,8) were enrolled. Sera were collected at Belimumab starting (T0) and every 6 months until 24th month. Disease activity index (SLEDAI-2K) was collected at every timepoints. High avidity anti-dsDNA were detected by radioimmunological method, anti-ENA, anti-cardiolipin (aCL), anti-β2 glycoprotein I (anti-β2GPI) were analysed by ELISA.
Results: At baseline 86% of sera were positive for anti-dsDNA, 50% for anti-ENA, 20% for aCL and 28% for anti-beta2GPI. Anti-dsDNA became negative in 21%, anti-beta2GPI IgG in 33% and aCL IgG in 30% of sera, mostly at T6. Among anti-ENA, 6/10 (60%) anti-ribosomal and 3/17 (17.6%) anti-Sm positive sera became negative. A significant decrease of anti-dsDNA and anti-beta2GPI IgM titers were observed at all timepoints. IgG aCL titre showed significant decrease only at T18. Anti-ribosomal showed a significant titre decrease at T6 and T12, with seroconversion to negative at T18. Anti-Sm titre significantly dropped down at T6, then remained stable during time. A significant correlation between anti-dsDNA and anti-ribosomal titre, and between SLEDAI ratio (SLEDAI value/SLEDAI T0) and anti-ribosomal titer ratio (value/value T0) were found.
Conclusion: Belimumab treatment induced a significant reduction of SLE-specific autoantibodies titre and IgM anti-beta2GPI. Anti-ribosomal titre decrease correlates with anti-dsDNA titre and improvement of disease activity.

REFERENCES

[1] Stohl W, et al. Nat. Biotechnol. 2012; 30: 69-77.
[2] Ginzler EM, Wallace et al. J Rheumatol 2014; 41:300-9.
[3] Iaccarino et al. Arthritis care Res 2017; 69: 115-123.
[4] Stohl W, et al. Arthritis Rheum 2012; 7: 2328-37.

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AB0482 MORE THAN ONE POSITIVITY FOR ANTIPHOSPHOLIPID SYNDROME DETERMINES LONG TERM ANTIBODY PERSISTENCE

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Background: It is generally assumed that once Antiphospholipid syndrome (APS) is diagnosed, patients should be treated with anticoagulation (ACO), possibly for a lifetime[1].
Objectives: Our main objective was the characterization of a group of patients with primary APS, evaluation of clinical profile, presence of APS antibodies (Ab) over time, recurrent thrombotic events and treatment.
Methods: Demographic and clinical features of patients with APS were identified through the Unit´s database. APL significant titers were retrospectively collected, 3, 6 and 9 months, every 6 months until year 6, every year until the last follow-up. LAC and aPL Ab (anticardiolipin IgG and Beta-2 Glycoprotein 1 IgG) were considered positive or negative by DRVVT/ELISA. Comparisons were made using the Wilcoxon Rank Sum and Chi square tests, p values < 0.05 were considered statistically significant (SPSS 22).
Results: 67 patients were analysed; the majority were female (n=49); mean average age of APS diagnosis was at 40[±13] y-old. Evaluation period: 2 - 20 years. 52 patients had at least one thrombotic event: 7 arterial thrombosis, 30 venous thrombosis and 8 both arterial and venous thrombotic events; 7 patients had obstetrical APS and one of these had both thrombotic and obstetrical APS; 9 had severe non-thrombotic APS manifestations. Fifty-four patients are currently under warfarin, 8 of which had a thrombotic event despite ACO. Patients could be grouped into two distinct patterns: those that became persistently antibody negative (aPL-; n=19) and those in whom the antibodies remained positive, persistently or intermittently (aPL+; n=48). The major difference between groups was the occurrence of cumulative double or triple positivity in 69% of aPL+ versus 37% in aPL- (p=0.026). There were no significant differences in age, age at diagnosis, duration of the disease and frequency/type of thrombosis, between each group (Table I). From the group that became persistently aPL-, 3 patients suspended ACO, without any event after 2 years of follow-Up.
Conclusion: Our study suggests that more than one aPL/LAC positivity is associated with antibody persistence over time. In our small series, as previously reported, ACO was safely discontinued in selected patients that become aPL-, in the absence of other risk factors for thrombotic events[2]. Regular antibodies measurements may help identify a subset of patients in whom ACO may be safely discontinued under careful observation.

Table I. Demographic, clinical, laboratory and therapeutic characteristics of patients according to presence of aPL/LAC persistence

Characteristics	aPL/LAC neg (n=19)	aPL/LAC pos (n=48)	Statistic test	p
Current Age (median ± IQR range, y)	52 (±16)	53	Wilcoxon rank sum (WRS)	0,6

Age at diagnosis (median ± IQR, y)	40 (±15)	41	WRS	0,54
Disease duration (median ± IQR, y)	11 (±12)	9	WRS	0,2
Number of events (median ± IQR, n)	1 (±1)	1	WRS	0,59
Arterial thrombosis, n (%)	6 (32)	22 (46)	Chi^2	0,4
Venous thrombosis, n (%)	12 (63)	27 (56)	Chi^2	0,7
Hydroxychloroquine therapy (n,%)	2 (10)	11 (23)	Chi^2	0,3
> 1 positivity (n,%)	7 (37)	33 (69)	Chi^2	0,026

References:
[1] J Thromb Haemost 2006;4(2):295-306; 2. Immunol Res 2013;56(2-3):358-61.

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AB0483 A SYSTEMATIC LITERATURE REVIEW ON THE USE OF BIOLOGICS IN SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a systemic chronic autoimmune disease characterized by dryness of the eyes and mouth. Current treatments provide modest benefit, leaving patients with limited therapeutic options. The pathophysiology of pSS involves hyperactivity of autoreactive lymphocytes. Biologic medications target mediators of the immune response. Modulation of autoimmunity in pSS with biologics has gained interest with open-label studies showing promising results.
Objectives: This review aims to conduct a systematic literature review of interventional studies investigating the efficacy of biologics in the treatment of pSS.
Methods: Literature was searched using the MEDLINE, EMBASE and PubMed databases as well as abstracts in EULAR, ACR and BSR.
Results: A total of twelve studies met the inclusion criteria. Infliximab and etanercept showed no significant improvements in fatigue and dryness in pSS compared to placebo. Anakinra showed improvement in fatigue after *post-hoc* analysis. Small trials in rituximab showed significant improvements in oral and ocular dryness but failed to replicate this in two larger randomised control trials. Belimumab significantly reduced overall disease activity which was driven by improvements in dryness and parotid gland swelling. Open-label studies in epratuzumab and abatacept showed significant reductions in fatigue with abatacept also improving salivary flow and pain in pSS.
Conclusion: Intervention with biologics in pSS has shown efficacy in alleviating pSS-associated fatigue and dryness in small RTCs and open-label trials. Larger randomised placebo-controlled trials have been inconsistent in replicating these results. This may be overcome by subgroup analysis, uptake of validated disease activity measuring tools, well-defined selection criteria to increase sample size and further understanding of pathophysiology in pSS. The small number of trials to date means the evidence base for biologics in pSS remains inconclusive.

REFERENCES

[1] Mariette X, Ravaud P, Steinfeld S, Baron G, Goetz J, Hachulla E, et al. Inefficacy of infliximab in primary Sjögren's syndrome: Results of the randomized, controlled trial of remicade in primary Sjögren's syndrome (TRIPSS). Arthritis Rheum. 2004 Apr;50(4):1270–6.
[2] Devauchelle-Pensec V, Mariette X, Jousse-Joulin S, Berthelot J-M, Perdriger A, Puéchal X, et al. Treatment of Primary Sjögren Syndrome With Rituximab. Ann Intern Med. 2014 Feb 18;160(4):233–42.
[3] Bowman SJ, Everett CC, O'Dwyer JL, Emery P, Pitzalis C, Ng W-F, et al. Randomized Controlled Trial of Rituximab and Cost-Effectiveness Analysis in Treating Fatigue and Oral Dryness in Primary Sjögren's Syndrome. Arthritis Rheumatol. 2017 Jul;69(7):1440–50.
[4] Mariette X, Seror R, Quartuccio L, Baron G, Salvin S, Fabris M, et al. Efficacy and safety of belimumab in primary Sjögren's syndrome: results of the BELISS open-label phase II study. Ann Rheum Dis. 2015 Mar;74 (3):526–31.

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Disclosure of Interests: Asaad Qadri: None declared, Syed Mujtaba Bilgrami: None declared, Marwan Bukhari Speakers bureau: Bristol-Myers Squib, UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Mennarini, Sanofi-aventis, Eli-Lilly, Janssen and Novartis.
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AB0484 EXPERIENCE WITH THE USE OF RITUXIMAB FOR THE TREATMENT OF SYSTEMIC AUTOIMMUNE DISEASES (SAD) IN A TERTIARY HOSPITAL

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Background: Rituximab is a chimeric anti-CD20 monoclonal antibody used in various clinical scenarios for the treatment of SAD, especially when immunocomplexes and/or limphocyte B proliferation plays a central role.
Objectives: The objective of this study was to retrospectively assess the efficacy and safety of use of rituximab in a cohort of patients with SAD in a tertiary hospital within the last 12 years.
Methods: We carry out a retrospective study of 48 patients with a diagnosis of SAD in our Autoimmune and Minority Diseases Department using Google Sheets.
Results: Our cohort is mostly female (48 women and 8 men). The mean age is 40.9 ±13.1 years (median 38 years). It is composed of different SAD: erythematous systemic lupus (22), granulomatosis with polyangiitis (6), dermatomyositis (6), eosinophilic granulomatosis with polyangiitis (3), rheumatoid arthritis (2), Takayasu's arteritis (1), Kikuchi-Fujimoto disease (1), mixed connective tissue disease (i), dermatomyositis with scleroderma overlap (1), systemic sclerosis (1) foliaceus pemphigus (1), gangrenosum pyoderma, (1) polimyositis (1) and orbital pseudotumor (1). The mean time from diagnosis to rituximab was 7.7±7.1years. the efficacy of RTX in reducing **disease activity** after 6 month was 64.6% patients -according to the disease recommended scales-. Nevertheless, 39% maintained 1 year remission.
The indications for rituximab were: persistant activity despite improvement of clasical immunosuppressive strategies (36), corticodependency (4), new relapses (3), corticoresistance (3) and toxicity (others immunosuppressant) (2). The drugs used when rituximab was used: cyclophosphamide (24), hydroxychloroquine (21), mycophenolate mofetil or mycophenolic acid (20); cyclosporine (7), immunoglobulines (7), leflunomide (4), and methotrexate (6). 5 patients did not receive any immunosuppressant. 61.3% were taking at least 2 drugs. All of them were taking glucocorticoids.
In terms of security and side effects, we observed 11 (22.9%) adverse reactions related to the administration. We detect 3 infusion reactions (mild severity), 1 severe mucocutaneous reaction, 1 moderate herpes zoster, 1 fungic invasive infection and 5 severe bacterial infections (1 of them lead to rituximab suspension). We did not detect any hepatitis B virus reactivation, multifocal progressive leukoencephalopathy, cytomegalovirus infections nor herpes simplex infections.
We observed 65 different haematologic adverse events: lymphopenia (34), anemia (15), neutropenia (12) and hrombocytopenia (4). No one needed specific treatment.
Conclusion: Rituximab is a second line therapeutic alternative in patients with SAD in whom other treatments have failed. It is a effective drug that rescues a 65% of patients in whom other treatments have failed. Furthermore, rituximab is a safe immunosuppressant.

REFERENCES

[1] Oon S, Huq M, Godfrey T, Nikpour M. Systematic review, and meta-analysis of steroid-sparing effect, of biologic agents in randomized, placebo-controlled phase 3 trials for systemic lupus erythematosus. Semin Arthritis Rheum. 2018 Jan 6. pii: 0049-0172(17)30579-6
[2] Tesfa D, Ajeganova S, Hägglund H, Sander B, Fadeel B, Hafström I, Palmblad J. Late-onset neutropenia following rituximab therapy in rheumatic diseases: association with B lymphocyte depletion and infections. Arthritis Rheum. 2011;63(8):2209

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AB0485

INTRAVENOUS HIGH DOSE GLUCOCORTICOIDS CAUSE PROLONGATION OF QT INTERVAL IN CONNECTIVE TISSUE DISEASE PATIENTS EXCEPT ANTI-RO POSITIVE SUBGROUP

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Background: Recent literature indicates that anti-Ro antibodies may be associated with prolongation of corrected QT (QTc) interval in the adult patients with connective tissue diseases. Moreover, glucocorticoids (frequently used in the therapy) are known to probably induce electrocardiographic changes including prolongation of QT interval. Prolongation of QTc interval is a risk factor for malignant ventricular arrhythmias. We hypothetised that patients with anti-Ro positivity have a higher risk of QT prolongation especially in the case of high dose intravenous glucocorticoids (IVGC) treatment.
Objectives: The aim of the study was to analyse risk of QTc interval prolongation in anti-Ro and anti-La positive patients before and after high dose IVGC treatment in patients with connective tissue diseases.
Methods: We performed a retrospective study of 115 patients (21 males), mean age of 48±14.7 years, range 19-78 years with connective tissue disease. Anti-Ro antibodies were examined in all patients before IVGC treatment. The patients were given 5x1000 mg methyprednisolon i.v. during five consecutive days. ECG recording was performed at baseline and after IVGC. The QT intervals were measured in each of 12-lead standard ECGs from two consecutive cycles. The QT intervals were measured from the onset of QRS complex to the end of the T wave by the means of a tangential method. Fridericia formula was used to obtain heart rate-corrected values for QT intervals.
Results: Comparing patients with anti-Ro positivity (n=39; 33.9%) and anti Ro-negativity (n=76, 66.1%), we found insignificant difference in QTc interval; QTcRo+ =417.2±28.4ms and QTcRo- =420,8±26.4ms (P=0.51), respectively. Admission of IVGC showed significant prolongation of QTc in all patients, mean QTc1 before treatment was 399.4±26.2ms, and QTc2 after therapy 412.7±27.2ms, P=0.00021. On the other hand, anti-Ro and anti-La positivity showed shorter QTc interval 391±18.7ms, to compare patients without these antibodies QTc=414.8±25.7ms, P=0.019 after treatment.
Conclusion: IVGC treatment significantly prolongs QT interval. Prolongation of QT over 445 ms was found in nine patients, but ventricular arrythmias were not observed. The presence of anti-Ro and anti-La antibodies did not show QT prolongation. Therefore, shortening of QT/QTc iterval needs further confirmation. Motivated by this experience, we consider ECG monitoring and careful observation of patients during IVGC treatment.
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AB0486

LACK OF CONSISTENT STANDARD OF CARE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN REAL WORLD

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Background: Current guidelines do not necessarily reflect current standard of care (SOC) or treatment patterns in SLE in real world.
Objectives: To describe SLE SOC in the EU5 and US and assess need for a more efficient and defined treatment pathway.
Methods: A cross-sectional study of 263 rheumatologists in the US and EU5. Data were collected from the Adelphi Real World 2015 Lupus Disease Specific Programme (DSP). Physicians were asked to complete patient record forms (PRFs) for the next 5 patients consulting with SLE; the same patients were asked to complete patient self-completion (PSC) forms describing how SLE affected them. PRFs collected data pertaining to the patient's diagnosis, disease history, current clinical outcomes, treatment and management history. PSCs focused on similar data collection and included patient reported outcome measures (PROs) to assess the humanistic burden. Chi-squared tests were conducted to ascertain significance.
Results: Data was extracted from 1376 PRFs, and 591 PSCs. 35.6% of patients were currently on their first line of therapy, 40.0% second line, and third line or more 24.4%. Significant differences were observed between US and EU5 in current treatment classes for first line ($p<0.0001$) and second line ($p=0.0007$). Descriptive differences were observed in the third line.
In the US monotherapy is used more often first line with antimalarial (AM) (monotherapy EU5 12.5% vs. US 19.3%) and immunosuppressant (IM) (monotherapy EU5 4.6% vs. US 11.1%). Glucocorticoids (GCS) use is higher in the EU5 at 1st line; both monotherapy (EU5 13.7% vs. US 11.8%) and combination (GCS+AM EU5 28.3% vs. US 16.7%). At second line, IM use (no bio) is higher in EU5 (EU5 64.9% vs. US 56.7%) and biologic use is higher in the US (EU5 5.0% vs. US 8.3%); GCS use is similar (EU5 19.2% vs. US 19.0%).
Globally, 84.4% of patients receiving GCS received it continuously with no significant differences observed between markets, EU5 85.5% vs. US 81.9%. A higher proportion of patients in the EU5 have been on GCS for 6 months or longer when compared to the US; EU5 79.9% vs. US 72.5%. Statistically significant differences were seen in the perception of GCS importance between markets (p=0.0004) and concerns with taking GCS (p=0.0140). A higher proportion of patients in the US regarded the use of GCS to at least be very important (very important/essential EU5 65% vs. US 80.6%). A higher proportion of patients in the US were concerned with the use of GCS (somewhat concerned/very concerned EU5 56% vs. US 61.2%).
Conclusion: Significant differences in treatment approach between regions highlights the need for a better understanding of this disparity and a united approach to SLE treatment. Despite the high profile of risk factors linked to GCS use in SLE, it continues to be a continuously utilized by a large proportion of SLE patients and there is poor use of flare preventing agents such as antimalarials. Patients and physicians recognize the role of GCS in the management of SLE but also express concerns. Impact of an update to the SLE guidelines and their dissemination with better understanding of risk benefits of GCS vs. immunosuppressive and biologic therapy is warranted.
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AB0487

HCQ COULD ACT ON SLE PATIENTS THROUGH THE MODULATING EXPRESSION OF IL-8 ALONG WITH S100 PROTEINS

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Background: Some reports revealed that S100A8 and S100A9 proteins were associated with disease activity of lupus nephritis(LN) [1]. However, there have been no reports about the mechanism of additional hydroxychloroquine (HCQ) treatment for systemic lupus erythematosus (SLE) patient with low disease activity.
Objectives: To clarify the mechanism of additional HCQ treatment for Japanese SLE patients with low disease activity.
Methods: All the 44 patients were enrolled in this study. These patients had been receiving additional oral HCQ sulfate continuously for at least 3 months. These patients had no need for additional immunosuppressants including glucocorticoids, during this study because of their sustained low disease activity for 3 months prior to starting HCQ. Low disease activity was defined as SELENA-SLEDAI score of 8 or less with no activity in major organ systems. As conventional immunological and clinical assessment for SLE disease activity were determined to examine the levels of complement (C3, C4, CH50), anti-dsDNA antibody, blood cell count, SELENA-SLEDAI and CLASI score. Serum levels of S100A8 and S100A9 reported as novel markers for SLE disease activity[1] were measured using ELISA (CircuLex ELISA Kit, MBL) at the time of HCQ administration as well as 3 months later. In addition, several expressions of cytokines (IFN-α, IFN-γ, TNF-α, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-17, IL-1α, IL-1β, IL-1ra, VEGF, GM-CSF, G-CSF, CCL2, CCL3, CCL4, CXCL) were measured by multiplex assay (Human Luminex assay, R&D systems).

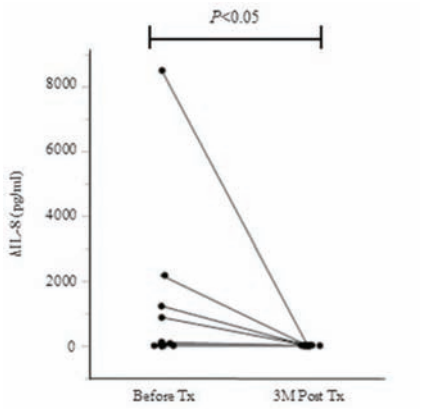


Figure 1. Serum level of IL-8 decreased significantly 3 months after additional HCQ treatment.

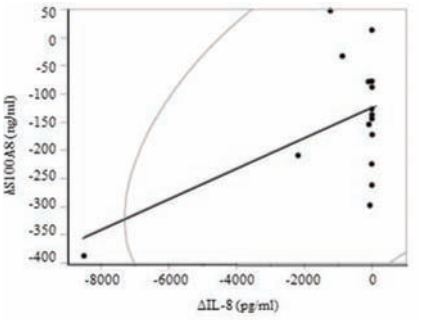


Figure 2. Correlation between the change of IL-8 and that of S100A8 protein (r=0.51, p=0.044).

Results: We enrolled 44 patients. Prednisolone dose during this study was fixed at the mean of 5.0±2.9 mg per day. SELENA-SLEDAI scores, CLASI scores, anti-dsDNA antibody and serum levels of C3 improved significantly, and serum levels of S100A8 and S100A9 proteins decreased significantly 3 months after additional HCQ treatment. The changes in serum S100A8 and S100A9 levels in SLE patients with LN were more significantly higher than in those without LN.

Among these patients, the changes of serum cytokine expressions were measured in 18 patients. The expressions of IFNs were not detected in almost of all patients. Serum levels of TNF-α, IL-6, IL-8, IL-1β, IL-1ra, VEGF, CCL3 and CCL4 decreased significantly 3 months after additional HCQ treatment (Figure1).

Seven of 18 SLE patients had a history of LN. These patients have been in sustained complete remission(CR) of LN for over one year(mean duration of CR was 5.0 ± 3.5 years).

The reductive effect of additional HCQ treatment on serum S100A9, TNF-α, IL-6 and IL-8 levels was much more apparent in those with history of LN (LN: S100A9, p=0.016, TNF-α, p=0.016, IL-6 p=0.031, IL-8, p=0.031; no LN: S100A9, p=0.065, TNF-α, p=0.083, IL-6 p=0.090, IL-8, p=0.557). The changes of serum S100A8 and S100A9 levels were correlated with those of serum IL-8 and IL-1ra (Figure2).

Conclusion: HCQ could reduce the serum levels of S100 protein and several cytokines in SLE Japanese patients with low disease activity. Recently, some reports showed that novel biomarker including IL-8 or S100 proteins was correlated with severity of LN [1, 2]. Our findings suggest that HCQ treatment without any additional immunosuppressant could reduce the expression of serum S100 proteins, IL-8 and IL-1ra, which were considered to be associated with the improvement of renal and life prognosis. Our data also indicated that S100 protein is closely related to IL-8 or IL-1ra expression in SLE pathogenesis, especially in LN. Farther investigations are needed to more clarify the significance of HCQ treatment in SLE.

REFERENCES

[1] P Tantivitayakul, et al. Lupus. 2016(25):38-45.
[2] A El-shehaby, et al. J Clin Immunol. 2011(5):848-56.

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AB0488 **RITUXIMAB THERAPY IN LUPUS NEPHRITIS RESISTANT TO CONVENTIONAL THERAPY – A SINGLE CENTER EXPERIENCE (CASE SERIES)**

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Background: Lupus nephritis(LN) can be a cause of morbidity and mortality in a significant portion of patients. The treatment of lupus nephritis can be challenging in some patients who are resistant to conventional immunosuppressive treatment.

Objectives: Rituximab is a promising agent for treating resistant patients. We evaluated the response of lupus nephritis patients who were treated with rituximab treatment in our clinic retrospectively.

Methods: We evaluated LN patients who were followed and treated with at least one course of rituximab in our clinic between 2013-2018. Remission was defined as proteinuria below 500 mg/day. Also, we evaluated the reason behind the cessation of rituximab during the follow-up whether it is a side effect or lack of efficacy. A final 24-hour proteinuria level was also analyzed at the end of the follow-up.

Results: 33 patients (20 F, 13 M) were treated with rituximab. All patients had active lupus nephritis at initiation. Mean of disease duration was 6.7 years. Diagnosis was proven by renal biopsy, except two (Table). Patients received an average of 4.2 courses. All patients were treated with high dose steroids. The other medications, the patients were previously treated with, were Cyclophosphamide (n=26), Azathioprine (n=7), Mycophenolate mofetil (n=17). Also one patient was treated with plasmapheresis due to thrombotic thrombocytopenic purpura. 2 patients were lost in follow-up. 13 patients (39%) are still on rituximab. Six of them (46%) still have active LN. Among 18 patients in whom rituximab therapy was terminated, 3 had inadequate response, 2 had severe infection (cellulitis, pneumonia), 1 had Rituximab-induced serum sickness, 1 had will of pregnancy. Treatment of 11 patients was terminated owing to remission of disease. All of the patients whom rituximab was terminated in disease remission did not flare, except one. The mean level of pretreatment proteinuria was 3356 ± 2478 mg/day. The mean level of proteinuria after the final course was 1025 ± 982 mg/day (p<0,0001). Mean erythrocyte sedimentation rate (ESR) was reduced from 28,62 ± 22,95 mm/h to 14,97 ± 12,32 mm/h (p<0,005). While initial steroid dose was 24 ± 19,3 mg/day, steroid dose at last rituximab course was 7,84 ± 6,13 mg/day (p<0,0001). None of the patients had a new organ involvement during therapy. End stage renal disease was developed in 3 patients. During the treatment 7 patients had infections, 2 had herpes zoster, 1 had cellulitis, 3 had pneumoniae and 1 had frequent upper respiratory infections.

Table. Histological characteristics of patients

RPS/ISN Classification	Number of patients
Class II	1
Class III	4
Class IV	11
Class V	7
Class III+IV	6
Class IV+V	2

Conclusion: In lupus nephritis patients resistant to conventional therapy, rituximab can be tried as an alternative treatment choice. In our single center, most of the patients were class IV nephritis whom we observed the efficacy of rituximab. Generally, the side effects were acceptable. Rituximab can be a steroid sparing agent in these patients.

REFERENCES

[1] Iaccarino L, Bartoloni E, Carli L, Ceccarelli F, Conti F, De Vita S, Ferraccioli G, Galeazzi M, Gatto M, Gerli R, Govoni M, Gremese E, Iuliano A, Mansutti E, Moroni G, Mosca M, Nalli C, Naretto C, Padovan M, Palma L, Raffiotta F, Roccatello D, Tincani A, Valesini G, Zen M, Doria A. Efficacy and safety of off-label use of rituximab in refractory lupus: data from the Italian MulticentreRegistry. Clin Exp Rheumatol. 2015 Jul-Aug;33(4):449-56.

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SLE, Sjögren's and APS – clinical aspects (other than treatment)

AB0490 **FIBROBLAST GROWTH FACTOR-23 IN SYSTEMIC LUPUS ERYTHEMATOSUSPATIENTS**

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that affects multiple organs including the kidneys and the heart. Chronic kidney disease (CKD) is common among SLE patients. SLE is also associated with increased left ventricular (LV) mass. LV hypertrophy (LVH) may have an additional role in the increased morbidity and mortality among in SLE patients. Fibroblast growth factor 23 (FGF23) is a phosphatonin that steadily increases in serum of CKD patients. High FGF23 is associated with inflammation, CKD progression, and LVH.

Objectives: The aim of this study is to determine the serum level of FGF23 in SLE patients with and without lupus nephritis looking for its possible association with the inflammatory and cardiovascular manifestations encountered in this disease.

Methods: Sixty SLE patient were recruited and appointed into 2 groups based on renal function; group I composed of thirty patients that had normal kidney functions or stage 1 CKD (eGFR>90 ml/min/1.73m^2) and group II of thirty cases with significant renal involvement defined as stage 2 to 4 CKD (eGFR <90 - >15 ml/min/1.73m^2). After history taking and complete clinical examination of every patient, we measured body weight, height, Systemic lupus erythematosus disease activity index (SLEDAI), Systemic lupus erythematosus International Collaborating Clinics (SLICC), serum level of creatinine, calcium, phosphorus, albumin, complement 3 (C3), complement 4 (C4), interleukin 6 (IL6), fibroblast growth factor 23 (FGF23), estimated glomerular filtration rate (eGFR), 24 hour urine protein, complete blood count, erythrocyte sedimentation rate (ESR), antinuclear antibody (ANA), and left ventricular mass index (LVMI). Sixty normal healthy adults were included as control group. They were tested for serum FGF23 level.

Results: Serum level of FGF23 in SLE patients was comparable to normal control subjects (99.6±79.86 vs. 139±12.3 pg/mL,P>0.05). In addition, there was no significant difference in FGF23 between the two studied groups (106.49± 88.2 vs. 93.84± 74.67 pg/mL,P>0.05). In addition, there was no significant difference in serum IL6 between the two groups (58.6 ± 63.69 vs 55.9 ± 47.97 ng/L, P=085). On the other hand, LVMI was significantly higher in Group II(138.6 ± 36.59 vs. 187.6 ± 81.7 gm/m^2 in group I vs. group II respectively, P=0.0045). FGF23 showed significant positive correlation with IL6 (r= 0.776, P<0.001) and failed to show significant correlation with LVMI, serum creatinine, eGFR or serum phosphorus.

Conclusion: FGF23 behaves differently in SLE patients; in spite of significant increase in inflammation and the frequent renal involvement, FGF23 level remains normal in SLE patients. There is a possible existence of an inhibitor to FGF23 production in SLE. This possibility should trigger further studies.

REFERENCES

[1] Podolska MJ, et al., Inflammatory etiopathogenesis of systemic lupus erythematosus: an update. J Inflamm Res. 2015 Aug 20;8:161-71

[2] Pieretti J1, et al., Systemic lupus erythematosus predicts increased left ventricular mass. Circulation. 2007 Jul 24;116(4):419-26.

[3] Liu S, et al., How Fibroblast Growth Factor 23 Works. J Am Soc Nephrol. 2007 Jun;18(6):1637-47.

[4] Lai CC, et al., Increased serum fibroblast growth factor-23 and decreased bone turnover in patients with systemic lupus erythematosus under treatment with cyclosporine and steroid but not steroid only. Osteoporos Int. 2015 Feb; 26(2):601-10.
[5] Durlacher-Betzer K, et al., Interleukin-6 contributes to the increase in fibroblast growth factor 23 expression in acute and chronic kidney disease. Kidney Int., 2018 Aug; 94(2):315-325.
[6] Faul C, et al. FGF23 induces left ventricular hypertrophy. J Clin Invest., 2011 121:4393–4408.

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AB0491 THE PERFORMANCE OF A RENAL ACTIVITY INDEX IN LUPUS NEPHRITIS IN INDUCTION THERAPY

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Background: Renal involvement in systemic lupus erythematosus (SLE) is associated with high morbidity and mortality[1]. Current standard tools to monitor lupus nephritis (LN) are suboptimal compared to the invasive renal biopsy[2]. The renal activity index in lupus (RAIL) was developed using 6 urinary biomarkers to reflect disease activity. In children this tool was 92% accurate in identifying active LN[3].
Objectives: We aim to study the changes in this score in relation to induction treatment in LN.
Methods: Urine samples were collected from active LN patients prior to induction treatment for LN and serially afterwards, coinciding with clinical visits. Luminex Bead Multiplex Assay was used for the analyses of urine biomarkers included in the RAIL score (neutrophil gelatinase-associated lipocalin, ceruloplasmin, monocyte chemoattractant protein-1, adiponectin, hemopexin, kidney injury molecule-1). RAIL scores were calculated per the defined algorithm for each urine sample. Data collected include LN histologic classification (International Society of Nephrology (ISN)/Renal Pathology Society (RPS) classification system), renal SLE disease activity index (rSLEDAI) score and type of therapy.
Results: At the time of the analysis, data from 6 active LN patients were collected longitudinally. Patients were all females and all had class IV LN per the ISN/RPS. Renal SLEDAI scores were on the higher end (*M*=11.3, SD=3.9). All patients were started on intravenous (IV) methylprednisolone and cyclophosphamide (CYC) therapy. All but one patient completed 6 doses of monthly CYC before switching to oral mycophenolate mofetil therapy. The RAIL scores for the 6 patients ranged between -1.8 and 3.29. All patients had reductions in their RAIL score at 2-3 months period at an average of 322% decline from baseline (Figure 1). At the end of induction treatment or at the 5-6 months interval, 5/6 samples were available for analysis and showed that 4/5 patients maintained a decline of RAIL scores below the baseline. Of note the patient with higher RAIL score at the end of treatment had only 3 monthly doses of CYC. All rSLEDAI scores decreased between baseline and the 6 months interval. However, one patient with known medication non-adherence had a flare of LN at the 6 months point leading to increased rSLEDAI.
Conclusion: RAIL scores show overall improvement from baseline with LN induction therapy. Lack of improvement was associated with flare of disease. Additional data points and a larger study sample are required to study the ability of the RAIL score to reflect clinical improvement of LN.

REFERENCES

[1] Almaani S, Meara A, Rovin BH. Update on Lupus Nephritis. Clinical Journal of
[2] the American Society of Nephrology : CJASN 2017: 12(5), 825-835.
[3] Sule SD, Moodalbail DG, Burnham J, Fivush B, Furth SL. Predictors of kidney disease in a cohort of pediatric patients with lupus. Lupus 2015; 24: 862–68.
[4] Brunner HI, Bennett MR, Abulaban K, et al. Development of a novel renal activity index of lupus nephritis in children and young adults. Arthritis Care Res (Hoboken) 2016; 68(7): 1003-11.

Disclosure of Interests: NAJLA ALJABERI: None declared, Theresa Hennard: None declared, Arjun Mathur: None declared, Hermine Brunner Grant/research support from: Bristol-Myers Squibb, Pfizer, Consultant for: Pfizer, Bristol-Myers Squibb, Janssen, Novartis, Lilly, Roche, GlaxoSmithKline, Sanofi, Speakers bureau: Novartis, Roche

Appendix:

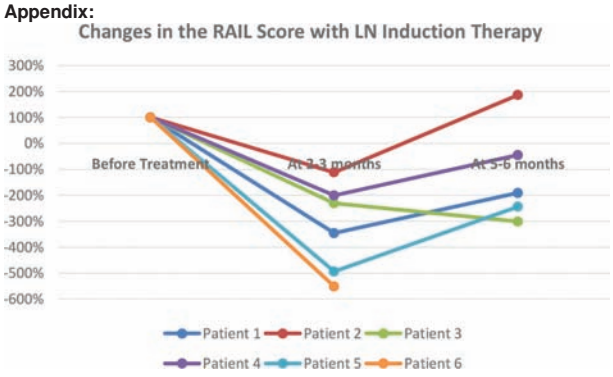


Figure 1. Changes in the RAIL score from baseline, at 2-3 months and at 5-6 months in 6 patients with LN. Baseline value is assigned 100%.

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AB0492 PREVALENCE OF IGA ANTICARDIOLIPIN ANTIBODY AND ITS ASSOCIATION WITH PREGNANCY MORBIDITY IN ASIAN INDIAN PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID ANTIBODY SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS – A CROSS SECTIONAL STUDY

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Background: There are many clinical and laboratory parameters which have been proven to be associated with increased risk of pregnancy morbidity in patients with SLE and APS. This study was undertaken as there is a lacuna in explaining all the pregnancy related morbidity in this group
Objectives: Primary: Correlation of IgA anticardiolipin antibody with the risk for pregnancy morbidity in patients with APS/SLE
Secondary: Association of IgA Anticardiolipin antibody with the risk of thromboembolic events
Methods: Patients diagnosed as SLE and/or Primary APS who are married and conceived atleast once were recruited and 3ml blood sample was obtained from them. Patients with history of recurrent infections, which could suggest probable IgA deficiency, were excluded. Demographic data including duration of illness, number of pregnancies, thromboembolic events, disease activity were noted. They were categorized into two different groups depending on whether they had a pregnancy morbidity or not. The blood samples were subjected to IgA Anticardiolipin assay by ELISA.
Results: A total number of 186 patients were recruited with mean age 34.54(+/-7.32)years, mean duration of illness of 5.52(+/-4.31)yrs with a diagnosis of 76.88% SLE, 7.53% primary APS and 15.59% SLE with secondary APS. On assessment of disease activity, mean SLEDAI score was found to be 4.46+/-6.32. Out of the total, 14.71% patients had conceived once, 14.56% twice, 16.72% patients thrice and 18.41% had conceived more than three times. 36.56% patients had pregnancy morbidity (majority being pregnancy induced hypertension 14.52%, prematurity 11.29%, IUGR 10.22%, pre-ecclampsia in 3.76%, eclampsia 1.08%,), 19.35% patients had history of thromboembolic events (6.45% pulmonary embolism, 5.38% deep vein thrombosis, 3.76% visceral vessel thrombosis, 0.54% cortical vein thrombosis, 6.99% other vessel thrombosis). 33.87% patients had positivity for antiphospholipid antibodies with 27.82% lupus anticoagulant positive, 20.97% IgG Anticardiolipin positive and 17.35% anti-beta2 glycoprotein positive. IgA Anticardiolipin was found to be positive in 4.84%(n=9) out of which, 10.29% were in the group with pregnancy morbidity as against 1.69% without pregnancy morbidity. Out of the total positives titre in 37.5% were indeterminate, 25% low positive and 37.5% high positive. All patients who had high titre positivity had pregnancy morbidity. The positivity of IgA anticardiolipin in the patient group with thromboembolic events was 5.56%.

IgA Anticardiolipin	Pregnancy morbidity	No pregnancy morbidity
Positive	7(10.29%)	2(1.69%)
Negative	69(89.71%)	116(98.31%)

Conclusion: Among patients with SLE, APS or SLE and APS, the overall prevalence of IgA anticardiolipin antibody was found to be about 4.84%, which is much less as compared to the percentages reported by other groups[1] IgA Anticardiolipin antibody positivity was more in patients with pregnancy morbidity compared to patients without a pregnancy morbidity. In this study however, statistical significance was not reached. Similar studies with larger number of patients are required. We also need to prospectively follow up such patients with IgA ACLA and evaluate for morbidity during pregnancy

REFERENCES

[1] Clinical significance of IgA anticardiolipin and anti-beta2-GP1 antibodies in patients with systemic lupus erythematosus and primary antiphospholipid syndrome, Clin Rheumatol. 2006 Mar;25(2):199-204

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DOI: 10.1136/annrheumdis-2019-eular.7181

AB0493 IMMUNOGLOBULINS AFTER ACUTE PHYSICAL EXERCISE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Moderate exercise improves the functions of the immune system. The results of serum immunoglobulins in response to acute physical exercise are conflicting, but in general, there is an increase in serum immunoglobulins in athletes and non-athletes after maximal and submaximal exercise. The effects of acute physical exercise on serum immunoglobulin in patients with systemic lupus erythematosus are unknown.
Objectives: To determine the serum levels of IgG, IgM and IgA immunoglobulins in patients with systemic lupus erythematosus after a single session of acute aerobic exercise.
Methods: Thirty-one women with SLE (ACR1997 and/or SLICC 2012 criteria),11 with active lupus and 20 with inactive lupus, and 24 healthy women, who were matched by gender, age, and body mass index, participated in this study. All subjects underwent a maximal exercise test on motorized treadmill, with increases in velocity every minute until exhaustion, to evaluate the speed (km/h), heart rate, Borg scale (6-20), and the reason for stopping the test (fatigue and/or dyspnea). Samples of blood were collected in the morning, after an 8-hour fast and immediately after acute physical activity, and stored in a freezer at -80°C until the tests were performed. Immunoglobulin IgG, IgM and IgA assay was performed by turbitometry according to the manufacturer (Turbiquest, Labtest Diagnostic S.A).
Results: There was an increase in both IgG and IgA serum levels after physical activity in SLE patients ($p = 0.004$ for IgG and $p = 0.002$ for IgA) and healthy controls ($p < 0.001$ for IgG and $p < 0.001$ for IgA) (Figure1). Inactive SLE patients showed higher levels of IgG and IgA after exercise ($p = 0.006$ and $p = 0.010$, respectively) (Figure 2), in comparison with the active SLE patients. There was no difference in IgM serum levels before and after the exercise test in both groups.

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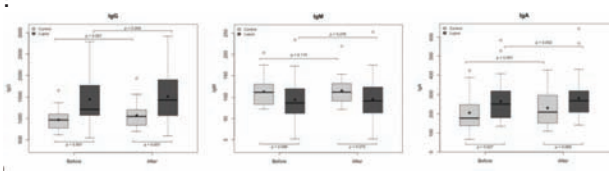


Figure 1. Comparison of IgG, IgM and IgA immunoglobulins intra and inter-group lupus and control ▲ = Average

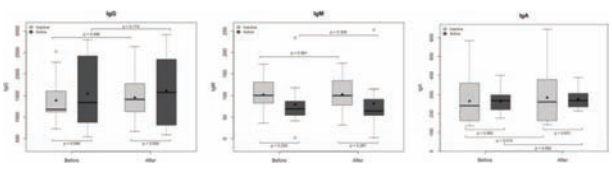


Figure 2. Comparison of IgG, IgM and IgA immunoglobulins intra- and inter-group of active and inactive lupus. ▲ = Average

Conclusion: Patients with SLE, mainly with inactive disease, responded to acute physical exercise with increased IgG and IgA serum levels, similarly to healthy controls.

REFERENCES

[1] Nehlsen-Cannarella SL, et al. The effects of acute moderate exercise on lymphocyte function and serum immunoglobulin levels. Int J Sports Med. 1991; 12(4): 391-398..
[2] Nieman DC and Nehlsen-Cannarella SL.The effects of acute and chronic exercise of immunoglobulins. Sports Med. 1991; 11(3): 183-201.
[3] Ochoa-Martínez PY, et al. Cinética de la inmunoglobulina-A salival (IgAs) en adultos jóvenes con capacidad aeróbica promedio o excelente antes y después de una prueba de esfuerzo máximo. Revista Chilena de Infectología, 2017; 34: 27-32.

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AB0494 ACTIVITY OF PURINE AND PYRIMIDINE METABOLISM ENZYMES IN SYSTEMIC LUPUS ERYTHEMATOSUS: ENZYMATIC PATTERNS OF BLOOD PLASMA AND LYSED LYMPHOCYTES

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Background: Cytotoxic immunosuppressants are widely used nowadays for outcome improvement and better quality of life in severe systemic lupus erythematosus (SLE). As purine and pyrimidine metabolism suggest to be the major targets of most cytotoxic immunosuppressants, enzyme profiling of these metabolic pathways is recognized as an important step for a better balance between efficiency and safety in clinical practice.
Objectives: To characterize enzymatic patterns of the major enzymes of purine and pyrimidine metabolic pathways in systemic lupus erythematosus.
Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles. 50 adult SLE patients from the rheumatology unit of Volgograd Clinical Emergency Hospital #25 and 30 healthy controls were included in the study. Diagnosis of SLE had been established using ACR criteria (1997), and activity was assessed by means of ECLAM scale. Activities of 10 major enzymes involved in purine and pyrimidine metabolic pathways: adenosine deaminase (ADA; E.C. 3.5.4.4), adenosine kinase (AK; E.C. 2.7.1.20), guanylate kinase (GK; E.C. 2.7.4.8), dihydroorotate dehydrogenase (DODG; E.C. 1.3.5.2), IMP dehydrogenase (IMPDG; E.C. 1.1.1.205), purine nucleoside phosphorylase (PNP; E.C. 2.4.2.1), thymidine kinase (TK; E.C. 2.7.1.21), thymidine phosphorylase (TP; E.C. 2.4.2.4), uracil/thymidine dehydrogenase (UDG; E.C. 1.17.99.4), cytidine deaminase (CDA; E.C. 3.5.4.5) were measured in blood plasma and lysed lymphocytes. Results are expressed as mean ±standard error. Statistical comparison tests are selected in line with common guidelines, differences were considered significant when $p<0.05$.
Results: Enzymatic profiles in plasma of SLE patients are characterized by increased PNP, AK, UDG, IMPDG, CDA, TK, and DODG activities; ADA and GK were found to decrease. Lyzed lymphocytes are revealed however to increased AK, IMPDG, TK, as well as decreased PNP, ADA, GK, CDA, and TP activities. We have also found that most enzyme activities significantly correlate with ECLAM score in accordance with our previous results [1]. Plasma PNP, AK, UDG, IMPDG, CD, TK and DODG activities positively correlated with ECLAM score, as well as lymphocyte AK, IMPDG, and TK activities did. Negative correlations with ECLAM score were revealed for plasma ADA and TP, and also for lymphocyte PNP, ADA, GK, UDG, CD, TP, and DODG. Plasma PNP, AK, IMPDG, and lymphocyte PNP, ADA, AK activities had the closest relations with minimal SLE activity, being a candidate markers of it.
Conclusion: The enzymatic patterns studied can be used as auxiliary markers of SLE activity, with special emphasis on minimal disease activity.

REFERENCES

[1] Zborovskaya IA, Martemyanov VF, Zborovsky AB, et al. Purine nucleoside phosphorylase activity in rheumatic diseases. Ann Rheum Dis. 2009;68 (Suppl3):764.

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AB0495 **INCREASED WORK LOSS DURING PREGNANCY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS COMPARED TO MATCHED HEALTHY CONTROLS**

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Background: Women with systemic lupus erythematosus (SLE) might be more vulnerable to reduce or stop working during pregnancy because of the increased risk of pregnancy complications compared to the general population. However, no data on work loss during pregnancy and return to work after maternity leave in patients with SLE are available.
Objectives: We aimed to investigate several work outcomes during and after pregnancy in women with SLE compared to matched pregnant controls.
Methods: A case-control study on employment was performed in pregnant women with SLE and matched controls. Matching criteria were age, year of delivery, and number of living infants. Employment was defined as having ≥8 hours/week of paid work before conception. Four work outcomes were investigated: interruption of work for >1 week during pregnancy, complete cessation of work for >1 week until delivery, reduction in working hours during pregnancy, and the time in weeks to return to work after maternity leave.
Results: A total of 42 women were included (21 SLE patients, 21 controls). Mean SELENA-SLEDAI before pregnancy in SLE patients was 2.6 (SD 2.3). Interruption of work for >1 week or completely stop working during pregnancy occurred in 10 SLE women, compared to 2 controls (OR=8.6, 95% CI [1.6-46.8], p=0.012). From the women who completely stopped working until delivery (n=8), 7 women had SLE (OR=1.4, 95% CI [0.07-28.1], p=0.826). In addition, in women continuing work, reduction of working hours occurred in 5 women with SLE versus 3 controls (OR=1.9, 95% CI [0.4-9.1], p=0.436).
After delivery, the median (IQR) duration of return to work after maternity leave was 4 weeks after maternity leave (0 - 6.8) for women with SLE and 2 weeks later (0 - 4) for controls (Mann-Whitney U test; p=0.977). No difference in number of women with delay of return to work after maternity leave (yes/no) was found between women with SLE and controls (n=9 versus n=11, respectively; OR=1.0, 95% CI [0.3-3.7], p=0.973).
Conclusion: Pregnant women with SLE more frequently completely stop working or reduce working hours compared to matched healthy controls. These findings warrant improved counseling of these women and attention of health care providers, including company doctors.
Disclosure of Interests: Birgit Blomjous Speakers bureau: UCB Pharma BV, Marieke ter Wee Grant/research support from: Nonrestricted grant from Lilly Netherlands BV, Speakers bureau: ARC Preceptorship program, Alexandre Voskuyl: None declared, Hanneke de Vries Grant/research support from: Pfizer, Speakers bureau: UCB Pharma BV, Irene E.M. Bultink Consultant for: Consultant fee from Sanofi Genzyme, Speakers bureau: Speaker fees from Lilly Netherlands BV, MSD Corp, Amgen BV, UCB Pharma BV, Roche Netherlands BV and Sanofi Genzyme
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AB0496 **18F-FDG-PET/CT, 11C-METHIONINE-PET/CT AND MULTI-PARAMETRIC MRI IN THE EVALUATION OF DISEASE ACTIVITY AND GLAND FUNCTION IN PRIMARY SJÖGREN'S SYNDROME**

Michele Bombardieri[1], Coziana Ciurtin[2], Michalis Kostapanos[3,4], Elisa Astorri[1], Anwar Tappuni[1], Natasha Jordan[3], Saleem Azeem[5], Teresa Fuller[6], Kathleen Port[6], Nirav Ratia[6], Andre van Maurik[6], Calum Gray[7], Lucy Kershaw[7], Rob Janiczek[6], Graham Searle[5], Paul Galette[6], Marius de Groot[6], Neel Patel[6], Nicolas Wisniacki[6], Mats Bergstrom[6], Pilar Jimenez-Royo[6], Ruth Tarzi[6]. [1]*Queen Mary University of London, London, United Kingdom*; [2]*University College London, London, United Kingdom*; [3]*Addenbrooke's Hospital, Cambridge, United Kingdom*; [4]*GSK, Cambridge, United Kingdom*; [5]*Invicro, London, United Kingdom*; [6]*GSK, Stevenage, United Kingdom*; [7]*University of Edinburgh, Edinburgh, United Kingdom*

Background: Saliva and tear flow rates and minor salivary gland biopsy are typically used to assess gland function and disease activity in primary Sjögren's syndrome (pSS); however, these have limitations. Imaging methods can directly visualize and generate quantitative values in individual glands. ^{18}F-FDG-PET/CT (^{18}F-FDG) measures glucose metabolism, a potential surrogate for inflammation; ^{11}C-methionine-PET/CT (^{11}C-met) is an amino acid PET tracer that assesses protein synthesis, a potential surrogate for gland synthetic function.
Objectives: Explore the potential of molecular imaging and multi-parametric MRI to characterize and quantify pSS disease manifestations.
Methods: In this pilot imaging study (203818), patients with pSS diagnosed per AECG criteria, with a EULAR Sjögren's syndrome disease activity index score ≥5, and basal salivary flow >0.0 mL/min or stimulated salivary flow rate ≥0.05 mL/min, underwent ^{18}F-FDG and ^{11}C–met and dynamic contrast-enhanced and diffusion-weighted MRI, followed by minor salivary gland biopsy for histological analysis. Age- and sex-matched healthy volunteers (HV) underwent MRI and ^{11}C-met. HV-pSS mean differences (m-diff; 95% confidence intervals [CI]) were calculated and Pearson's correlation coefficients (r) estimated. Peak PET standard uptake values (SUVpeak) were used in the correlations and SUVmax values were recorded. All methods were compared with routine clinical and laboratory tests.
Results: 12 patients had MRI, ^{18}F-FDG and ^{11}C–met; while HV (n=12) had MRI (n=12) and ^{11}C–met (n=8). A lower ^{11}C-met SUVpeak was seen in the parotid (m-diff: 1.4 g/mL [0.4, 2.3]) and submandibular (m-diff: 2.0 g/mL [0.9, 3.2]) glands in pSS versus HV, as was a trend for lower lacrimal gland uptake (m-diff: 0.5 g/mL [-0.2, 1.3]) in patients with pSS. On structural MRI, the fat fraction (mean%) was higher in pSS vs HV in the submandibular glands (m-diff: -14.8 [CI: -29.3, -0.4]), with similar trends observed in the parotid glands (-11.2 [-24.3, 1.9]). There was a negative correlation between ^{11}C-met uptake and fat fraction (r: -0.7 [-0.9, -0.4]) in the combined parotid glands. There was positive correlation between ^{11}C-met uptake and stimulated salivary flow (r: 0.5 [0.03, 0.8]) and negative correlation for stimulated salivary flow and fat fraction (r: -0.5 (-0.8, -0.1)] in the parotid glands; similar correlations were also seen in the submandibular glands. There was negative correlation between the global lymphoid aggregation score on minor salivary gland biopsy and the combined salivary gland fat fraction (r: -0.7 [-0.9, -0.2]). Parotid gland SUVmax ^{18}F-FDG uptake was higher than historical control values (mean: 1.9 g/ml, [SD: 0.5][1]) in some patients (pSS mean SUVmax: 2.8 g/mL [SD: 0.8, range 1.7–4.6]), with positive correlation between ^{18}F–FDG and ^{11}C-met uptake (r: 0.7 [0.2, 0.9]) in the combined salivary glands.
Conclusion: Imaging showed clear differences between pSS and HV and correlated with clinical endpoints. Low ^{11}C-met uptake and high fat fraction on MRI may indicate poor residual gland function, while high ^{18}F-FDG and stable ^{11}C-met uptake may define a subpopulation that responds well to anti-inflammatory therapies.

REFERENCES

[1] Basu S, et al. Nucl Med Commun 2008; 29:367–73.

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AB0497 **SERUM CALPROTECTIN IN SYSTEMIC LUPUS ERYTHEMATOSUS: IS IT A GOOD ACTIVITY BIOMARKER?**

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Background: Clinical manifestations of systemic lupus erythematosus (SLE) and infections sometimes are difficult to distinguish. In clinical practice low complement and anti(ds)DNA levels are used to assess lupus activity but

its determination usually requires some days. Leukocyte count, CRP and ESR cannot discriminate SLE from infectious processes. Calprotectin could be a good biomarker to assess lupus activity since it is more specific than CRP and ESR and faster to analyse than anti(ds)DNA.

Objectives: Our aim is to determine serum calprotectin levels in patients with SLE, and its correlation with analytical and clinical manifestations, especially with disease activity.

Methods: A total of 148 patients were included. All patients included fulfilled the SLE criteria (SLICC 2012). A quantitative ELISA analysis was performed to assess levels of serum calprotectin (CALPRO AS, Norway). Other biomarkers of lupus disease activity were also assessed (levels of anti(ds)DNA, hypocomplementemia, ESR and CRP). Clinical variables and activity/damage index (SLEDAI/SLICC) were also evaluated. The study was approved by the Clinical Research Ethics Committee of the hospital and all patients signed an informed consent. The results were compared with a healthy control group of similar age and sex (n=20).

Results: 134 patients (92%) were women with a mean age of 46±12 years and an average SLE evolution of 12±7 years. Mean SLEDAI was 2±2 (105 inactive [<3], 43 mild [4-12], 0 severe [>13]). Mean SLICC was 0.31±0.70. No significant differences were observed in serum calprotectin levels between patients with SLE and healthy controls (2.93±2.35 vs 2.17 ±1.49 µg/mL, p=0.160). Calprotectin was positively correlated with CRP (r=0.447, p=<0.001) and leukocyte count (r=0.462, p=<0.001). Additionally, patients with higher anti(ds)DNA levels (>100UI/mL) had higher calprotectin compared to patients with lower anti(ds)DNA (3.20±2.63 vs 2.42±1.57 µg/mL; p=0.027), however this pattern was not observed with hypocomplementemia. Contrary to what we expected, we did not observe significant differences on calprotectin levels depending on SLEDAI index classification (cutoff at 4 and 12). Moreover, no differences were observed on calprotectin levels between those patients with/without clinical manifestations such as serositis, arthritis or glomerulonephritis. Patients with antiphospholipid antibodies had higher calprotectin levels (3.75±2.04 vs 2.77±2.38 µg/mL;p=0.045).

Conclusion: Serum calprotectin levels were positively correlated with CRP levels and leukocyte count. Patients with higher anti(ds)DNA levels had higher calprotectin levels, however we did not observe significant differences depending on SLEDAI index or the presence of arthritis, serositis neither glomerulonephritis. Even that calprotectin determination is faster than anti(ds)DNA levels and could be helpful in assessing inflammatory activity. There is an interesting relation between antiphospholipid antibodies and calprotectin. This study should be continued in a larger sample of active SLE patients to assess its utility in clinical practice as a discriminating biomarker for flares and even infection

Disclosure of Interests: None declared

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AB0498 GYNECOLOGICAL SYMPTOMS AND SEXUALITY IN SJOGREN'S SYNDROME

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Background: Patients with Sjogren's syndrome (SS) have symptoms such as vaginal dryness and dyspareunia.

Objectives: In this study we aimed to present of primary SS (pSS) and secondary SS (sSS) patient's gynecological symptoms and effects of the disease on sexuality.

Methods: 60 pSS, 42 sSS, 52 healthy controls (HC) were interviewed. It was asked questions about sexuality, SF-36, HAD scale, pSS and sSS patients were also administered HAQ and Modified Hiil questionnaire[1].

Results: The mean age of the patients was 52 ± 11 years in the pSS, 54 ± 11years in the sSS and 46 ± 9 years in the HC. Although there was no significant difference in term of age in pSS and sSS groups, mean age was lower in HC group. There were no significant differences in SF-36 mental index score, SF-36 physical index score, HAD-Anxiety score and HAD-Depression score among 3 groups. 62% of patients in the pSS, 79% in the sSS and 33% in HC were in menopause. Vaginal and vulvar dryness were significantly higher in SS, especially in the pSS than HC. The proportion of sexually active women was lower in sSS group. Spontaneous genital pain and dyspareunia were found to be high in pSS and it was statistically significant. Decreased sexual desire was significantly higher in SS groups (Table1).

HAQ score was significantly lower in pSS group than sSS group. Dyspareunia, dysuria, vaginal dryness and fatigue were significantly higher in pSS (Table2). There was no significant difference between two groups in terms of the effect of vulvar, vaginal dryness, dyspareunia, decreased sexual desire, myalgia, arthralgia and fatigue on sexuality

In the pSS group, it was seen that disease had a negative effect on sexuality. There were no significant differences between the two groups when asked whether they enjoyed sexuality and the sexual problems create problems between their partners. In both groups, 97% of patients stated that they had not been questioned about their sexuality before. 80% of pSS patients and 88% of sSS patients stated that they did not talk about sexuality problems.

Conclusion: Gynecological and sexual problems are seen in SS patients. Menopause also contributes to this situation. Patients should be informed about these problems and directed to gynecologists when necessary, and enough time should be reserved as we do.

Table 1. Groups Data

N(%)	Primary SS (60)	Secondary SS (42)	Healthy Control (52)	p
Age	52±11	54±11	46±9	*0.001*
Menopausal state	37(62)	33(79)	17(32)	*0.000*
Menopause Age	47±5	48±4	45±4	0.722
Hormone replacement therapy	8(13)	3(7)	3(6)	0.334
Sexual activity	46(77)	25(60)	43(83)	*0.033*
Vaginal dryness	38(63)	18(43)	11(21)	*0.000*
Vulvar dryness	26(43)	17(41)	8(15)	*0.004*
Dyspareunia	34(57)	14(33)	16(31)	*0.010*
Spontaneous genital pain	17(28)	5(12)	5(10)	*0.019*
Reduced sexual desire	44(73)	34(81)	26(50)	*0.003*
SF-36 mental index	43.5±10	45±12	47±9	0.237
SF-36 physical index	43±11	43±10	45±9	0.537
HAD- Anxiety	7±4	7±5	7±4	0.879
HAD- Depression	5±4	5±5	5±4	0.824

Table 2. Brief Survey Results of Primary and Secondary Sjögren Patients

N(%)	Primary SS	Secondary SS	p
Vaginal dryness	38(63)	18(43)	*0.041*
Vulvar dryness	26(43)	17(41)	0.774
Dyspareunia	34(57)	14(33)	*0.020*
Spontaneous genital pain	17(28)	5(12)	*0.047*
Dysuria	13(22)	2(4.8)	*0.018*
Dysuria	44(73)	34(81)	0.372
At least one gynecological symptom	49(82)	34(81)	0.927
Arthralgia	33(55)	23(55)	0.981
Myalgia	38(63)	23(55)	0.385
Fatigue	48(80)	26(62)	*0.044*
At least 1 muscle-skeletal symptom	47(78)	27(64)	0.118
HAQ	0.19±0.33	0.45±0.82	*0.013*

REFERENCES

[1] S. Maddali Bongi at all.Gynaecological Symptoms and Sexual Disability in Women with Primary Sjögren's Syndrome and Sicca Syndrome.Clinical and Experimental Rheumatology 2013; 31: 683-690

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AB0499 FINGERSTICK BLOOD TRANSCRIPTOMICS: A PATIENT-CENTRIC APPROACH TO ENABLE PRECISION MEDICINE?

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Background: Venous blood collection using PAXgene RNA blood stabilization (PAX) is a routine method to obtain blood for gene expression (GE) analysis requiring phlebotomy and cold chain transport. DxCollect® is a fingerstick blood micro collection device (MCD) that circumvents phlebotomy and is reported to stabilize blood RNA for up to 14 days at ambient temperature potentially enabling collected blood to be shipped by mail.

Objectives: We evaluated DxCollect® as an alternative to the conventional method to potentially improve convenience and cost effectiveness of blood transcriptomic analysis and allow high frequency transcriptomic assessment.

Methods: Heparinized blood samples were treated with interferon-α for 3h *in vitro* and transferred to 3 PAX and 3 MCD tubes. One PAX and

MCD for each treatment was stored at ambient temperature for 7 and 14 days or frozen. RNA from PAX tubes and MCD was extracted and GE performed by qPCR and DxDirect® platform respectively. Interferon-inducible gene signature was compared between the two platforms. In addition, RNASeq was performed on immediately frozen PAX and MCD to examine suitability for broad transcriptomics.

Results: IFN-GE was comparable between PAX and MCD samples when frozen directly after collection. Stability of MCD IFN-GE was largely unchanged at 7 and 14 days of ambient storage while PAX IFN-GE decreased over storage period. Comprehensive QC of RNA-Seq showed no significant differences in the two platforms in terms of RNA quality and integrity. Transcriptional diversity and levels were comparable with an overall correlation between PAX and MCD > 95%.

Conclusion: MCD showed greater stability at ambient temperature and required minimal blood collection volumes. Downstream GE data from MCD finger stick blood collected was comparable to current PAX method. MCD in clinical trials may enable better resolution of temporal transcriptional changes and the ability to capture unpredictable events such as disease flare through ad hoc home collections allowing high frequency transcriptomic assessment. MCD coupled with a gene expression platform could become an opportunity for diagnostic development in the growing field of precision medicine.

REFERENCES

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AB0500 FLARES AND DISEASE-RELATED DAMAGE IN LATE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Late-onset systemic lupus erythematosus (SLE) and its disease-related outcomes have not been previously examined in a multi-ethnic Southeast Asian cohort.

Objectives: To compare the following outcomes between patients with adult-onset versus late-onset SLE a) Disease manifestations at baseline b) Frequency of flares, defined by the SELENA Flare Index (SFI) c) Baseline damage and damage accrual, defined by the SLICC/ACR Damage Index (SDI)

Methods: We prospectively enrolled patients ≥ 21 years old with SLE who fulfilled either the 1997 ACR Criteria or the 2012 SLICC Classification Criteria and followed each patient at three-monthly intervals for up to 5 years. Baseline demographics, disease manifestations, antibody profile were captured. At each visit, disease activity was measured using SLEDAI-2k. SDI was measured annually. We defined late-onset SLE as onset of symptoms at ≥50 years of age and adult-onset SLE as onset of symptoms at ≥18 but <50 years of age. We excluded patients with symptom onset before 18 years of age.

We compared the baseline demographic, disease manifestations and antibody profile between the adult-onset and late-onset patients. We analysed continuous variables using the Mann-Whitney U test and categorical variables using the Chi-square test. Bonferroni correction for multiple comparisons was done. We then compared the time to first flare between the two groups using the logrank test. Baseline SDI scores and the proportion of patients who have increased SDI ≥1 over follow-up were compared using Chi-square tests.

Results: Of the 214 patients recruited, 154 (72.0%) were Chinese and 197 (92.1%) were females. One-hundred and ninety-three (90.2%) were on anti-malarial therapy and 141 (66.2%) were on immunosuppressive agents other than corticosteroids. The median (SD) age of recruitment of the 184 adult-onset SLE patients was 30.0 (22.5-37.5) years while the median (SD) age of recruitment of the 30 late-onset SLE patients was 53.0 (50.0-56.5) years. The median (IQR) disease duration was 8.12 (2.75-13.5) years among the adult-onset patients and 5.73 (1.52-9.95) years among the late-onset patients. Arthritis was the only disease manifestation that was different between the two groups (66.8% in the adult-onset group versus 36.7% in the late-onset group, p=0.002). There were no significant differences in the demographics and antibody profile between the two groups.

The median (IQR) baseline Systemic Lupus Erythematosus Disease Activity Index-2k (SLEDAI-2k) was 3 (1-5) and 2 (0-4) in the adult-onset and late-onset patients respectively (p=0.086). The median (IQR) number of all flares per year was 0.41 (0-0.91) among adult-onset patients and 0.25 (0-0.55) among late-onset patients (p=0.206). There was no significant difference in the time to first flare or time to first severe flare between the two groups [mean (SD) time to any flare 2.51 (0.15) years in the adult-onset group versus 2.77 (0.34) years in the late-onset group, p=0.521; mean (SD) time to severe flare 3.90 (0.14) years among adult-onset patients versus 4.27 (0.28) years among late-onset patients, p=0.336].

The median (IQR) SDI at baseline was 0 (0-1) in adult-onset patients and 1 (1-2) in late-onset patients (p=0.049). There was no significant difference in the proportion of patients who accrued further damage during follow-up (7.9% of adult-onset patients versus 14.3% of late-onset patients, p=0.268).

Conclusion: Although Southeast Asian patients with late-onset SLE have higher disease-related damage at recruitment, baseline disease activity and frequency of flares were similar to patients with SLE of adult-onset.

REFERENCES

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AB0501 CLINICAL ANALYSIS OF BONE MINERAL DENSITY IN PATIENTS WITH NEW-ONSET SYSTEMIC LUPUS ERYTHEMATOUS

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Background: Osteoporosis in patients with systemic lupus erythematosus (SLE) is always thought to be GIOP (induced by glucocorticoid). Yet in our practice, there were some patients who developed osteoporosis at the onset of SLE, before the use of glucocorticoid and immunosuppressants. The clinical feature of these patients were not known by us clearly.

Objectives: This study aimed to investigate the BMD (bone marrow density) status and clinical characteristics of treatment-naive patients with newly diagnosed SLE.

Methods: Patients admitted to Peking University Third Hospital from 2009-2016, who were newly diagnosed as SLE and had no previous medical history that would had affected their BMD, were enrolled in this study. Demographic and clinical data were recorded. BMD of the lumbar vertebrae and femoral necks were measured with dual-energy X-ray absorptiometry, and patients were stratified as normal and abnormal BMD groups (including ostepenia and osteoporosis).

Results: Eighty-nine SLE patients with a mean age of 28.7 ± 8.9 years were included in the study (Table1).

Abstract AB0501 Table 1. Demographics of newly diagnosed SLE patients

Variables	SLE patients (n=89)
Age (year)	28.7±8.9
Menarche age (year)	13.1±1.3
BMI (Kg/m^2)	21.7±3.8
Male	7%
Smoking history	3%
Fracture history	0%
SLEDAI	10.0±5.0

Approximately 36% of these patients had normal BMD, 49% had osteopenia, and 15% had osteoporosis. The SLE Disease Activity Index (SLEDAI) in the abnormal BMD group was lower than that in the normal BMD group (9.4 ± 4.5 vs 12.1 ± 5.8, P= 0.028). The body mass index (BMI) was significantly lower in the abnormal than normal BMD group (20.5±3.5 kg/m^2 vs 24.2±3.2 kg/m^2, P = 0.00). The total cholestenone (TC) and low density lipoprotein (LDL) were lower in the abnormal than normal BMD group (4.3±1.7 mmol/L vs 2.4±1.2 mmol/L, P =0.04; 4.9±1.3 mmol/L vs 2.9±0.9 mmol/L, P = 0.033). The multisystem damage and

nervous system involvement were less in the abnormal than normal BMD group (χ^2 = 5.996, P = 0.014 and χ^2= 8.169, P = 0.004). Multivariate analysis showed that BMI (correlation coefficient = 0.484, P < 0.001) and multisystem damage (correlation coefficient = 0.258, P = 0.003) were positively correlated with BMD.

Conclusion: Low BMI, SLEDAI and less multisystem damage may be risk factors of BMD abnormalities in newly diagnosed SLE patients.

REFERENCES

[1] Rivas-Larrauri, F. and M.A. Yamazaki-Nakashimada, Systemic Lupus Erythematosus: Is It One Disease? Reumatología Clínica (English Edition), 2016. 12(5): p. 274-281.

[2] Bultink, I.E. and W.F. Lems, Systemic lupus erythematosus and fractures. RMD Open, 2015. 1(Suppl 1): p. e000069.

[3] ROSALIND RAMSEY-GOLDMAN, J.E.D., CHENG-FANG HUANG,et al, FREQUENCY OF FRACTURES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS Comparison with United States Population Data. ARTHRITIS & RHEUMATISM, 1999. **42**.

[4] Carli, L., et al., Risk factors for osteoporosis and fragility fractures in patients with systemic lupus erythematosus. Lupus Sci Med, 2016. 3(1): p. e000098.

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AB0502 IMPROVING RATES OF CERVICAL CANCER SCREENING AND PREVENTION IN PATIENTS WITH LUPUS

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Background: Recent studies suggest that patients with lupus have higher rates of cervical dysplasia and pre-malignant lesions. We have a large population of lupus patients at our institution that may be at increased risk of dysplastic lesions due to suboptimal rates of HPV vaccination and cervical cancer screening. The aim of this study was to determine the rate of HPV vaccination completion and cervical cancer screening compliance among the lupus patients seen in our institution. In addition, we developed a process to increase patient education and improve both HPV and cervical cancer screening rates at the level of the outpatient renal, dermatology and rheumatology clinics.

Objectives: To improve rates of cervical cancer screening and HPV vaccination among patients with Lupus

Methods: A comprehensive list was compiled of all patients with a diagnosis of lupus seen in the clinics over a 3 year period. A chart review of 332 patients was subsequently performed to determine the rate of HPV vaccination completion and the rate of compliance with cervical cancer screening. Methods were developed to improve these rates by streamlining access to HPV vaccination sites or facilitating referral for screening exams. Patients were also provided education through brochures about their increased risk.

Results: Our results revealed that rates of HPV vaccination among lupus patients at our institution were lower than national averages by 11%. Rates of cervical cancer screening were also 21% lower compared to national average for this group of patients. In creating a system to flag providers and increase patient education, we were able to improve these rates. In the first two months, 73.7% of all patients seen in the clinics were provided education and 61.5% of eligible patients that were seen in clinic were appropriately referred to either their PCP or to gynecology to complete cervical cancer screening and prevention.

Conclusion: Initial review of the lupus population at our institution highlighted a strong need to develop an intervention to improve vaccination and screening compliance in this population. By raising awareness amongst providers, we were able to significantly increase the number of at risk patients referred for cervical cancer screening and prevention. Given that the United States Food and Drug Administration has recently approved to expand the use of the HPV vaccine to women and men up to age 45, future efforts will be made to expand our eligble population to reflect these recommendations.

REFERENCES

[1] "FDA Approves Expanded Use of Gardasil 9 to Include Individuals 27 through 45 Years Old." *FDA News Release*, 5 Oct. 2018, www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm622715.htm.

[2] "Gynecologic Cancers." Centers for Disease Control and Prevention, 27 June 2018, www.cdc.gov/cancer/cervical/basic_info/test-results.htm.

[3] "Practice Bulletin No. 140." *Obstetrics & Gynecology*, vol. 122, no. 6, 2013, pp. 1338–1366., doi:10.1097/01.aog.0000438960.31355.9e.

[4] "Vaccines & Immunizations." Centers for Disease Control and Prevention, 4 Sept. 2018, www.cdc.gov/vaccines/index.html.

[5] Feldman, C H, et al. "Risk of High-Grade Cervical Dysplasia and Cervical Cancer in Women with Systemic Lupus Erythematosus Receiving Immunosuppressive Drugs." Lupus, vol. 26, no. 7, 2016, pp. 682–689., doi:10.1177/0961203316672928.

[6] Grein, Ingrid Herta Rotstein, et al. "HPV Infection and Vaccination in Systemic Lupus Erythematosus Patients: What We Really Should Know." *Pediatric Rheumatology*, vol. 14, no. 1, 2016, doi:10.1186/s12969-016-0072-x.

[7] Santana, I U, et al. "Systemic Lupus Erythematosus, Human Papillomavirus Infection, Cervical Pre-Malignant and Malignant Lesions: a Systematic Review." Clinical Rheumatology., May 2011

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AB0503 THE LUNG IN SJÖGREN'S SYNDROME PATIENTS – AN OVERVIEW OF CLINICAL CHARACTERISTICS AND DISEASE OUTCOME

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Background: Lung involvement has been reported in 10-20% of patients (pts) with primary Sjögren's syndrome (pSS) and mostly affecting parenchyma and airways. Its occurrence significantly impacts both quality of life and mortality in pSS pts.

Objectives: To characterize lung involvement in a cohort of pSS pts and present our experience with immunosuppressive drug treatment for pSS-interstitial lung disease (ILD).

Methods: Retrospective analysis of pSS pts followed in our Rheumatology department until December 2018. Lung involvement was based on imaging and/or histopathological alterations described in the spectrum of pSS-associated lung disease. Patients with and without lung disease were compared using parametric and non-parametric tests.

Results: In total, 137 pSS pts who fulfilled the European-American consensus criteria 2002 were identified, 130 (94.9%) females, with mean age at pSS diagnosis of 56.1 (±12.2) years; median disease duration 6 [IQR 3-10] years and median follow-up 6 [IQR 3-10.25] years. Antinuclear antibodies were positive in 113 (82.5%) pts, with 95/134 (70.9%) pts presenting positive anti-SSA and 60/128 (46.9%) anti-SSB. Specific immunoassays performed in 82 pts allowed identification of anti-Ro52 antibody in 48 (58.5%) of them. Rheumatoid factor was positive in 48/91 (52.7%).

During follow-up 3 pts died, 1 due to ILD progression and 2 due to sepsis (respiratory and abdominal), both under immunosuppression.

Lung involvement occurred in 17 (12.4%) pts; median time to lung disease was 2 years [IQR 0-8] after pSS diagnosis.

Mean EULAR SS disease activity index (ESSDAI) at the time of lung involvement diagnosis was 13.1 (±5).

Differences between pts with and without lung involvement are shown in table 1.

Table 1. – Comparison between pts with and without lung involvement

	Lung involvement (n=17)	No-lung involvement (n=120)	p-value
Female	17 (100%)	113 (94.2%)	0.31
Age at pSS diagnosis (mean±SD)	60.9±8.6	55.4±12.4	**0.04**
Disease duration (median IQR)	8 [2.5-12]	5 [3.9.75]	0.24
ANA	15 (88.2%)	99 (82.5%)	0.56
Anti-Ro52	7 (63.6%)	41 (57.7%)	0.72
Hypergammaglobulinemia during follow-up	10 (58.8%)	48 (40%)	0.14
Constitutional involvement during follow-up	6 (35.3%)	5 (4.2%)	**<0.001**

Legend: pSS - primary Sjögren's syndrome; ANA- antinuclear antibodies

Regarding pattern of lung involvement, 9 (52.9%) pts had ILD, 6 (35.3%) isolated bronchiectasis and 2 (11.8%) follicular bronchiolitis.
In ILD pts, non-specific interstitial pneumonia (NSIP) was documented in 6 pts, lymphocytic interstitial pneumonia in 2 and 1 pt had unclassifiable ILD pattern with lymphocytic alveolitis in bronchoalveolar lavage. One of the pts with NSIP later developed radiographic characteristics suggestive of usual interstitial pneumonia (UIP).
Six ILD pts were treated with immunosuppressive drugs. One received cyclophosphamide (CYC), 2 azathioprine (AZA) and 4 mycophenolate mofetil (MMF). From pts receiving MMF, 1 was previously treated with CYC as induction treatment and the other with AZA, but with inefficacy.
Rituximab (RTX) was given to 1 pt with refractory arthritis and new ILD onset. After 11 years on RTX (total 10 cycles) the pt complained of persistent dyspnoea and fatigue on minor exertion (cardiac causes excluded), with onset of subtle honeycombing in high resolution computed tomography. At this point pirfenidone was added to RTX, with clinical improvement. Detailed lung function and imaging evolution of pSS-ILD pts is shown in table 2.

Table 2 – Evolution of patients with interstitial lung disease treated with immunosuppressive drugs

Patient	Current immunosuppression	Baseline		6-12 months		≥ 24 months		Lung CT 6-12 months	Lung CT ≥ 24 months
		FVC (%)	DLCO (%)	FVC (%)	DLCO (%)	FVC (%)	DLCO (%)		
1†	AZA	52.8	27.7	42.1	7.4	35.2	Unable to perform	Progression, assuming UIP pattern	Stable
2	MMF	87.6	69.3	95	72.7	-	-	-	-
3	MMF	37.1	Unable to perform	45	Unable to perform	-	-	Progression	-
4	MMF	98.6	84.7	112.2	90	-	-	Improvement	-
5	MMF	76,7	39,6	*	*	*	*	*	*
6	RTX	45.8	40.9	-	-	46.5	36.7	Stable	Progression

† Patient 1 died due to lung disease progression, after 3 years on AZA and before there was experience with anti-fibrotic drugs
*This patient is under treatment for less than 6 months and has no follow-up assessment yet
Legend: AZA – azathioprine; MMF – mycophenolate mofetil; RTX – rituximab; FVC – forced vital capacity; DLCO- gas transfer; CT – computed tomography; UIP – usual interstitial pneumonia

Conclusion: Lung involvement occurred in 12.4% of our cohort and was associated with older disease at pSS diagnosis and presence of constitutional involvement.
Small airways disease and ILD had nearly the same prevalence and in the ILD sub-group, NSIP was the commonest pattern.
Despite the small number of ILD pts receiving immunosuppression, these drugs seemed to be associated with disease stabilization in most of them. Only 1 pt with UIP pattern had disease progression and eventually died.
Disclosure of Interests: None declared
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AB0504 CLINICOPATHOLOGICAL CHARACTERISTICS AS POSSIBLE PREDICTOR OF RENAL OUTCOME IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS FOLLOWING THE INDUCTION OF REMISSION PHASE

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Background: Systemic lupus erythematosus is polygenic autoimmune rheumatic disease with heterogeneous manifestations. Lupus patients with nephritis signal represents management challenge. With current induction and maintenance therapy the risk of developing lupus nephritis related ESRD at five, ten and fifteen years remains 11,17 and 22% for the last decade
Objectives: To study clinicopathological characteristics of lupus nephritis patients as well as short term renal outcome following induction of remission attempts.
Methods: Retrospective, prospective observational study. We enrolled all patients with suspected active Lupus nephritis attending Dubai Hospital Rheumatology services. Data collected during outpatient, inpatient consultation using medical electronic system for all patients newly diagnosed to have lupus with renal involvement or patients who had nephritic or nephrotic flare from June 2016 till December 2018
Results: Of 71 patients included during the study period, mean age was 36.4 years, 93% were female while 7% were males.56 Out of 71 were Arab (78%) while the rest 15 out of 71 (22%) from non-Arab ethnicity. 84% (60/71) patients suspected to have active lupus nephritis underwent ultrasound guided kidney biopsy unless contra-indicated or the patient refused to sign the consent for the procedure. The commonest histopathological class according ISN/RPS 2003 Classification was class III. Induction of remission attempted with Mycophenolate Mofetil in 29% of patients (21/71). Around (8/71) received Rituximab regimen while more than 50% of the patients (39/71) received Cyclophosphamide Euro lupus protocol. At 6 months assessment following induction of remission 40/71 showed complete response and 26/71 responded partially, 5/71 required dialysis 2 of them required short term dialysis. On the other hand 3/71 (4%) progressed to end stage renal disease. Among patients who developed end stage renal disease there was signal of less favorable prognostic indicators such comorbid condition with possible glomerulopathy complications such as diabetes mellitus and hypertension. Moreover 2 of the 3 patients end with long term dialysis observed to have positive Antiphospholipid antibody status which may reflect co-existing thrombotic angiopathy. Among biopsy criteria predicting worse outcome was the presence of Cellular crescents on background of Class III or IV lupus nephritis.
Conclusion: Our study is unique in the region, characterizing high risk group of SLE patients. The signal of co morbid conditions such as hypertension, diabetes mellitus and antiphospholipid antibody positivity as well as class III/IV Lupus nephritis with cellular crescents as predictor of worse renal outcome raise the unmet need for further study with large sample involving more than single center to determine clinical, serological and histopathological predictors of renal outcome in short term as well as long term with the available immune suppressive regimens.

REFERENCES

[1] G K Bertsias, Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis, Ann Rheum Dis. 2012; 71(11): 1771–1782.
[2] JAN J. WEENING, The Classification of Glomerulonephritis in Systemic Lupus Erythematosus Revisited, J Am Soc Nephrol 2004, 15: 241–250

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AB0505 AGE AT DIAGNOSIS AND HEALTH-RELATED QUALITY OF LIFE ARE ASSOCIATED WITH FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Fatigue can be defined as feeling tired and exhausted and lacking energy (1). It is associated with a poor quality of life; 53 to 80% of SLE patients identify fatigue as their main symptom (2)
Objectives: To define factors associated with fatigue in Mestizo patients with Systemic Lupus Erythematosus (SLE).
Methods: This is a cross-sectional study of SLE patients from a single center cohort. Visits were performed every six months. For these analyses, the first visit between October 2017 and December 2018 was included. Demographic and clinical characteristics as well as treatment were recorded at every visit. Socioeconomic status (SES) was defined using the Graffar's method (ref). Fatigue was ascertained with the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-FT), Health-Related Quality of Life (HRQoL) with the LupusQoL, disease activity with the Systemic Lupus Erythematosus Disease Activity Index –2K (SLEDAI-2K), and damage with the Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) damage index (SDI). Prednisone use was recorded as current daily dose. Immunosuppressive drugs and antimalarial use was recorded as current, past or never. Univariable and multivariable analyses were performed using linear regression models. For the multivariable analyses, model selection was based on backward elimination.
Results: Two hundred and twenty-six patients were evaluated. The mean (SD) age at diagnosis was 35.6 (13.1) years, 211 (93.4%) were female; and disease duration was 11.0 (7.3) years. The mean SLEDAI and SDI were 2.4 (3.5) and 1.3 (1.5), respectively. The mean FACIT-Fatigue was 33.1 (10.8). In the univariable analyses, FACIT-Fatigue correlated with age at diagnosis, SES, disease duration and all the HRQoL domains like physical health, pain, planning, intimate relationships, burden to others, emotional health, body image and fatigue. On the multivariable analysis, however, only age at diagnosis; and some domains of HRQoL (physical

health, emotional health and fatigue) remained associated. Theses analyses are depicted in table 1.
Conclusion: Age at diagnosis is negatively associated with fatigue; HRQoL domains like physical health, emotional health and fatigue are positively associated with fatigue.

Table 1: Factors associated with fatigue in systemic lupus erythematosus patients. Univariable and multivariable analyses.

	Univariable analysis		Multivariable analysis	
	B (SE)	p value	B (SE)	p value
Age at diagnosis, years	-0.30 (0.06)	<0.001	-0.08 (0.04)	0.034
Gender, female	-4.99 (3.05)	0.102		
Socioeconomic status				
Low/medium low	-6.88 (2.60)	0.008		
Medium	-2.81 (1.76)	0.110		
High/medium high	Ref.			
Disease duration, years	0.23 (0.10)	0.025		
SLEDAI	0.04 (0.23)	0.850		
SDI	-0.80 (0.56)	0.150		
Fibromialgia	-4.51 (3.17)	0.155		
Physical health	0.33 (0.02)	<0.001	0.14 (0.04)	<0.001
Pain	0.27 (0.02)	<0.001		
Planning	0.26 (0.02)	<0.001		
Intimate relationship	0.14 (0.02)	<0.001		
Burden to others	0.19 (0.02)	<0.001		
Emotional health	0.27 (0.02)	<0.001	0.08 (0.02)	0.001
Body image	0.15 (0.02)	<0.001		
Fatigue	0.30 (0.02)	<0.001	0.13 (0.03)	<0.001
Prednisone daily dose, mg/d	-0.15 (0.21)	0.490		
Antimalarial use				
Present	1.85 (4.11)	0.653		
Past	-0.36 (4.93)	0.942		
Never	Ref.			
Immunosuppressive drugs use				
Present	1.01 (2.04)	0.622		
Past	1.35 (2.51)	0.592		
Never	Ref.			

SE: Standard error.

REFERENCES

[1] Omdal R, et al. Fatigue in patients with systemic lupus erythematosus: lack of associations to serum cytokines, antiphospholipid antibodies, or other disease characteristics. J Rheumatol. 2002;29(3):482-6.
[2] Ahn GE, Ramsey-Goldman R. Fatigue in systemic lupus erythematosus. Int J Clin Rheumatol. 2012;7(2):217-27.

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AB0506 MICRORNA A POTENTIAL MARKER OF LUPUS ACTIVITY IN AN EGYPTIAN LUPUS COHORT

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Background: MicroRNAs play central roles in different stages of cellular activity, as well as contribute extensively to multifaceted aspects of systemic lupus erythematosus (SLE) pathogenesis. Screening from approximately a thousand human miRNAs, studies have concluded that their dysfunction has been related to the development and activity of diseases.(1) In addition, The expression levels of miRNAs in serum are stable, reproducible, and consistent. Thus, testing serum microRNA sequence provide novel biomarkers and potential therapeutic strategies in SLE patients.(2)
Objectives: To study the role of micro-RNA-142-3p expression in SLE in an Egyptian cohort and its role as a potential biomarker of lupus activity.
Methods: Expression of microRNA- 142-3p extracted from peripheral blood mono-nuclear cells determined using quantitative reverse transcription–polymerase chain reaction assay. A total of 60 plasma samples were obtained from 30 SLE patients without clinical and laboratory evidence of lupus nephritis (group A) and 30 SLE patients with clinical and laboratory evidence of lupus nephritis confirmed by renal biopsy (group B).
Results: We found a significant correlation between micro-RNA-142-3p expression levels and serum level of anti ds-DNA in both group A (p=0.007) and group B (p=019). We also found no significant correlation between micro-RNA-142-3p expression levels and C3 (p=0.399) & C4 (p=0.375) in group A, while there was a significant correlation in group B with both C3 (P=0.005) and C4 (P=0.002).In addition to, We demonstrated a significant correlation between micro-RNA-142-3p expression levels and SLEDAI score in both group A (P=0.001) and group B (P=0.007).
Conclusion: The expression level of micro-RNA-142-3p could be considered a potential activity marker in SLE patients with and without lupus nephritis.

REFERENCES

[1] Amarilyo G, La Cava A. miRNA in systemic lupus erythematosus. Clin Immunol 2012; 144:26–31.
[2] Wang Z, Chang C, Peng M, Lu Q. Translating epigenetics into clinic: focus on lupus. Clin Epigenetics 2017; 9:78.

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AB0507 HEARING LOSS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus(SLE) is a systemic disease that may affect the inner ear.
Objectives: To study hearing function in SLE and its possible association with clinical and serological profile as well as with antimalarial use.
Methods: Cross sectional study of 84 individuals(43 SLE patients and 41 controls) with audiometry and impedanciometry tests. Epidemiological, clinical, serological and treatment profile of SLE patients were extracted from the charts.
Results: SLE patients had more sensorineural hearing loss than controls (23.2% vs 0; p=0.001). The hearing loss was seen at 250 Hz, 500 Hz, 1000 Hz and 4000 Hz. No bone conduction impairment was observed. Serological and clinical profile in patients with and without hearing loss was the same (all p=ns). Patients on antimalarial had the same prevalence of hearing loss than those not using it but at 8.000 Hz, antimalarial non-users performed worse than users(p=0.03).
Conclusion: There is a high prevalence of hearing loss in SLE that is not affected by disease characteristics neither by antimalarial use.

REFERENCES

[1] - Di Stadio A, Ralli M. Systemic Lupus Erythematosus and hearing disorders: Literature review and meta-analysis of clinical and temporal bone findings. J Int Med Res. 2017; 45:1470-80.
[2] - Ralli M, D'Aguanno V, Di Stadio A, De Virgilio A, Croce A, Longo L, et al. Audiovestibular symptoms in systemic autoimmune diseases. J Immunol Res. 2018; 2018: 5798103. eCollection 2018.
[3] - Jourde-Chiche N, Mancini J, Dagher N, Taugourdeau S, Thomas G, Brunet C, et al. Antimalarial ototoxicity: an underdiagnosed complication? A study of spontaneous reports to the French Pharmacovigilance Network. Ann Rheum Dis. 2012; 71: 1586.

TABLE 1. Comparison of median auditory perception(in decibels) according to the studied frequency of the sound, speech recognition threshold and tympanometry between SLE patients and controls

	SLE patients (86 ears)	Controls (82 ears)	p
MAC	8.75 (5.00-13.75)	10.00 (5.93-12.50)	0.54
AC 250 Hz	10.00 (5.00-15.00)	15.00 (10.00-20.00)	< 0.0001
AC 500 Hz	10.00 (5.00-10.00)	12.50 (5.00-20.00)	< 0.0001
AC 1.000 Hz	5.00 (0-10.00)	5.00 (5.00-15.00)	0.03
AC 2.000 Hz	5.00 (0-15.00)	10.00 (5.00-15.00)	0.65
AC 3.000 Hz	10.00 (5.00-15.00)	10.00 (5.00-15.00)	0.40
AC 4.000 Hz	15.00 (5.00-20.00)	10.00 (5.00-15.00)	0.002
AC 6.000 Hz	15.00 (8.75-25.00)	15.00 (10.00-25.00)	0.37
AC 8.000 Hz	15.00 (10.00-30.00)	10.00 (8.75-15.00)	0.09
SRT (%)	96.0 (96.0-100.0)	100.0 (100.0-100.0)	< 0.0001
TIMP	0 (0-0)	0 (0-0)	0.99

MAC= mean air conduction; Hz=Hertz, SRT= speech recognition threshold; TIMP= tympanometry.

TABLE 2. Comparison of clinical data, auditory perception (in decibels) according to the studied frequency of the sound, speech recognition threshold and tympanometry in SLE patients using and not using antimalarials

	With antimalarials N= 74 ears	Without antimalarials N=12 ears	P
Mean Age (years) (SD)	46.4±12.7	40.9±13.9	0.22
Median Disease duration (years)	8.50 (5.00-14.25)	12.00 (8.25-21.25)	0.19
MAC	8.75 (5.00-13.75)	8.75 (5.31-13.44)	0.63
AC 250 Hz	10.00 (5.00-18.75)	10.00 (5.00-15.00)	0.81
AC 500 Hz	10.00 (5.00-10.00)	7.50 (5.00-15.00)	0.63
AC 1.000 Hz	5.00 (0-10.00)	2.50 (0-10.00)	0.47
AC 2.000 Hz	5.00 (3.75-15.00)	10.00 (0-15,0)	0.64
AC 3.000 Hz	10.00 (5.00-15.00)	12.50 (5.00-18.75)	0.43
AC 4.000 Hz	10.00 (5.00-20.00)	15.00 (7.50-20.00)	0.39
AC 6.000 Hz	12.50 (5.00-21.25)	20.00 (15.00-25.00)	0.07
AC 8.000 Hz	10.00 (8.75-25.00)	22.50 (16.25-33.75)	0.03
SRT (%)	96.00 (96.00-100.00)	96.00 (96.00-100.00)	0.50
TIMP	0 (0-0)	0 (0-0)	0.99
Tinnitus	15/37 (40.5%)	4/6 (66.6%)	0.38
Subjective hearing loss	10/37 (27.0%)	1/6 (16.6%)	1.00
Vertigo	4/37 (10.8%)	2/6 (33.3%)	0.18

Between parenthesis - interquartile rate; n= number; AC= airway conduction; MAC= mean airway conduction; SRT= speech recognition threshold; TIMP= tympanometry.

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AB0508 SCHIRMER TEST, VAN BIJSTERVELD, OSS, AND BREAK-UP TIME TEST IN PRIMARY SJOGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is an autoimmune disease characterized by lymphocytic infiltration of exocrine glands and other organs, resulting in dry eye, dry mouth, and systemic findings. [1]
Objectives: The American College of Rheumatology/AECG group diagnostic criteria for pSS have included three items related to ocular involvement: The Schirmer test type 1, van Bijsterveld score, and Ocular Staining Score (OSS). They are time-consuming and employ costly dyes and instruments. In this context, we analyzed 66 patients with pSS to ascertain correlation between these tests and assess the possibility of streamlining ophthalmologic examination.
Methods: Sixty-six patients (180 eyes) from the Federal University of Sao Paulo outpatient cornea clinic were analyzed prospectively from 2017 to 2018. Those with suspicion of pSS were tested according to the 2016 ACR-EULAR diagnostic criteria. A protocol consisting of the Schirmer, tear-film break-up time (TBUT), van Bijsterveld, and OSS tests was applied to all patients by a cornea specialist. Results were analyzed for correlation and interrater reliability using the kappa coefficient.
Results: Of the 66 patients, 64 were female; 36 were white; median age was 53.3 (11,3) years. The Schirmer I test was done in 177 eyes, it was positive in 57.6%. TBUT was tested in 175 eyes and was positive in 96%. The van Bijsterveld score was done in 128 eyes and was positive in 61.7%. The OSS was done in 177 eyes and was positive in 68.9%. All four tests could be performed in 128 eyes. The results were confirmed at the same proportions. Correlation between tests was then calculated through the kappa coefficient (Table 1).
Overall agreement was weak (κ = 0.340, p<0.001). Agreement between TBUT and other tests was particularly poor (κ = 0.112–0.144). On the other hand, good agreement was observed between the van Bijsterveld score and OSS (κ = 0.781, p<0.001). Overall and pairwise kappa coefficients are illustrated in Figure 1.
Conclusion: Schirmer's test without anesthesia has been part of the AECG diagnostic criteria for pSS since 1989. [2].
Our study demonstrates the low sensitivity of the Schirmer I test and the possibility of removing it from the diagnostic criteria. Limitations include our small sample size and lack of comparison group. We hope that, in future, use of objective tests for pSS will become routine ophthalmology practice, reducing costs and facilitating diagnosis.

REFERENCES

[1] Shiboski CH, Shiboski SC, Raphaèle S, et al. 2016 American College of Rheumatology/European League Against Rheumatism classification criteria for primary Sjögren's syndrome. Ann Rheum Dis 2016;0:1–8.
[2] Workshop on Diagnostic Criteria for Sjögren's syndrome. I. Questionnaires for dry eye and dry mouth. II. Manual of methods and procedures. Clin Exp Rheumatol 1989;7:212–19.

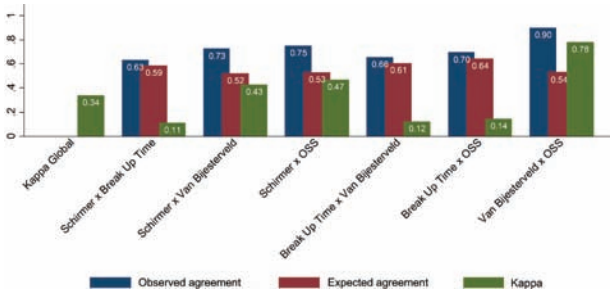


Figure 1. – Overall and pairwise kappa coefficients

Table 1. – Kappa coefficients for classification of primary Sjogren's syndrome

	Kappa	Standard Error	z	p	Observed agreement	Expected agreement
Pairwise comparison	**0.340**	**0.036**	**9.42**	**<0.001**	-	-
Schirmer I x Break-Up Time	0.112	0.041	2.76	0.003	63.28%	58.64%
Schirmer I x Van Bijsterveld	0.428	0.088	4.85	<0.001	72.66%	52.20%
Schirmer I x OSS	0.469	0.088	5.35	<0.001	75.00%	52.93%
Break-Up Time x Van Bijsterveld	0.123	0.043	2.90	0.002	65.63%	60.80%
Break-Up Time x OSS	0.144	0.046	3.15	0.001	69.53%	64.40%
Van Bijsterveld x OSS	0.781	0.088	8.87	<0.001	89.84%	53.66%

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AB0509 PREVALENCE AND INCIDENCE OF SJÖGREN'S SYNDROME AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-WORLD COMMUNITY PRACTICE SETTINGS

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Background: Sjögren's syndrome (SS) is a rheumatic disease that may coexist with RA, and is often considered a common extra-articular manifestation of RA. However, few studies have examined the prevalence and incidence of SS in patients with RA in real-world community practice settings.
Objectives: To estimate the prevalence and incidence of SS in patients with RA, and to summarise the characteristics of patients with SS associated with RA compared with those of patients with RA alone.
Methods: We analysed data from 1 Jan 2014 to 30 Jun 2018 in a large rheumatology database in the USA, which provides electronic medical record data from 120 community-based rheumatology providers. Adult patients with ≥2 RA diagnoses were identified from 1 Jan 2015 to 30 Jun 2018 (index period). The baseline period was from 1 Jan 2014 to 31 Dec 2014. Among patients with RA, we identified patients with ≥2 SS diagnoses in the index period (prevalent SS patients and patients with ≥2 SS diagnoses in the index period who had not been diagnosed with SS in the baseline period [incident SS patients]). Crude and age- and sex-standardised prevalence and incidence of SS were calculated among patients with RA. Characteristics of prevalent SS patients and patients with RA alone (as a control group) were summarised.
Results: A total of 53,156 patients with RA were identified. Among them, we identified 2451 prevalent SS patients and 1450 incident SS patients. The age- and sex-standardised prevalence of SS in patients with RA was 3.48%, and the age- and sex-standardised incidence rate was 0.66 per 100 patient-years. Female patients had a higher prevalence (5.23%

vs 1.68%) and incidence (0.96 vs 0.36 per 100 patient-years) of SS than male patients. Compared with other age groups, patients with RA aged 30–49 years had the highest prevalence (3.80%) and incidence (0.77 per 100 patient-years) of SS (Table 1). Compared with patients with RA only, those with both SS and RA were more likely to be female (92% vs 76%), had higher Charlson Comorbidity Index and lower CDAI scores, and were more likely to have prior use of biologic/targeted synthetic DMARDs (30% vs 10%) and conventional DMARDs (48% vs 18%) (Table 2).

Conclusion: This study estimated the prevalence and incidence of SS among patients with RA in real-world community practice settings, and provided insights on clinical characteristics of these patients. Patients with both SS and RA have less joint disease activity and greater DMARD exposure than those with RA only. The findings underscore the complexity of SS secondary to RA and highlight the important role of epidemiological research in understanding this condition.

*b/tsDMARDs: abatacept, infliximab, etanercept, adalimumab, certolizumab pegol, golimumab, tocilizumab, rituximab and tofacitinib; cDMARD: MTX, sulfasalazine, azathioprine, tacrolimus, gold thiomalate, leflunomide, aurothioglucose, auranofin, cyclosporine, penicillamine, cyclophosphamide and hydroxychloroquine b=biologic; c=conventional; IQR=interquartile range; RAPID3=Routine Assessment of Patient Index Data 3; SS=Sjögren's syndrome; ts=targeted synthetic

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Table 1. Prevalence and incidence of SS in patients with RA

	Patients with RA, n	Prevalent SS patients, n	Prevalence, %, crude (standardised*)	Incident SS patients, n	IR per 100 PY, crude (standardised*)
Total	53,156	2451	4.61 (3.48)	1450	0.81 (0.66)
Sex					
Female	40,843	2263	5.54 (5.23)	1331	0.98 (0.96)
Male	12,312	188	1.53 (1.68)	119	0.28 (0.36)
Age, years					
18–29	1427	51	3.57 (2.70)	36	0.74 (0.57)
30–49	9951	512	5.15 (3.80)	333	1.00 (0.77)
50–69	27,053	1327	4.91 (3.76)	805	0.89 (0.70)
≥70	14,725	561	3.81 (3.22)	276	0.56 (0.46)

*Age and sex-standardised to the 2017 USA population; one patient was excluded from the calculation due to lack of information on sex

IR=incidence rate; PY=patient-years; SS=Sjögren's syndrome

Table 2. Characteristics of patients with RA and SS vs RA only

Characteristic	RA and SS	RA only
n	2451	50,705
Age, years		
n	2451	50,705
Median (IQR)	63.00 (15.00)	62.00 (20.00)
Female, n (%)	2263 (92.33)	38,580 (76.09)
Charlson Comorbidity Index score		
n	2451	50,705
Median (IQR)	1.00 (1.00)	0.00 (0.00)
BMI, kg/m²		
n	1571	10,850
Median (IQR)	28.13 (8.43)	29.09 (8.76)
CDAI score		
n	284	1262
Median (IQR)	11.75 (16.50)	16.00 (17.00)
RAPID3 score		
n	127	875
Median (IQR)	9.20 (12.60)	12.30 (11.20)
Comorbidities, n (%)		
Vasculitis	16 (0.65)	34 (0.07)
Lymphoma	5 (0.20)	11 (0.02)
Neuropathy	65 (2.65)	197 (0.39)
Pulmonary fibrosis	16 (0.65)	26 (0.05)
Pulmonary nodules	9 (0.37)	28 (0.06)
Prior RA treatment, n (%)*		
0	997 (40.68)	38,317 (75.57)
1	753 (30.72)	9037 (17.82)
≥2	701 (28.60)	3351 (6.61)
Prior cDMARD, n (%)*	1173 (47.86)	9160 (18.07)
Prior b/tsDMARD, n (%)*	731 (29.82)	5067 (9.99)

Disclosure of Interests: Leticia Ferri Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Ying Bao Employee of: Bristol-Myers Squibb, Sonie Lama Employee of: Bristol-Myers Squibb, Varshini Rajagopalan Consultant for: Bristol-Myers Squibb, Evo Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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AB0510 LUNG ULTRASOUND OF PLEURAL IRREGULARITIES IN SUB-CLINICAL PRIMARY SJÖGREN'S SYNDROME-LUNG INVOLVEMENT: A SINGLE CENTRE EXPERIENCE

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Background: Ultrasound of Pleural Irregularities (PI-US) has recently been suggested as a useful tool for the diagnosis and quantification of severity in connective tissue diseases (CTD)-related lung involvement. However, no data are available regarding its role in the sub-clinical phase of primary Sjögren's syndrome (pSS)-related lung involvement.

Objectives: Aim of this study was to describe the role of lung ultrasound analyzing pleural irregularities in asymptomatic pSS-patients in order to early detect lung abnormalities/alterations.

Methods: pSS patients regularly followed-up at our Sjögren's Clinic and asymptomatic for dyspnea and cough, undergoing to CT or HRCT exam for lymphoproliferative and/or neoplastic screening, were included in the study. Demographic, clinical, biological and serological data were collected. PI-US was performed by a single operator using a MyLab ClassC (Esaote), 13-18 MHz, 5 cm linear probe. PI was defined as the loss of normal hyperechoic linear pleural contour (score 0-2: normal, minimal and major changes at each intercostal space). PI-US total score represented the sum of partial scores assigned to 6 lung fields (2 for the anterior, 2 for postero-superior and 2 for postero-inferior chest surface). CT-abnormal findings, distinguishing typical (interstitial pattern) from atypical lung alterations (non specific findings), were analyzed by an expert radiologist.

Results: 24 pSS patients (AECG criteria), 20 F:4 M, mean age =58 ±12.2 yrs, mean follow-up duration 8.6±12.2 yrs, were included in the study. All patients were positive for ANA, 21/24 for anti-Ro/SSA, 15/24 for Rheumatoid Factor (RF) and 6 of them for cryoglobulins.

Four patients (16.67%) had a previous history of pSS-related lymphoproliferative disorder.

None of the included patients reported cough or dyspnoea and the thoracic examination did not arise any abnormalities suggestive for lung disases.

The mean PI-US total and postero-inferior partial score resulted 22.75 ±19.72 and 8.29±8.60 respectively. CT/HRCT resulted normal in 9/24 patients (37.5%) and showed abnormal findings in 15/24 (62.5%). The latter consisted of non- Interstitial Lung Disease (ILD) alterations in 13/15 cases (i.e 13/13 fibrotic striae and/or micro/macronodularities, 5/13 disventilatory striae and/or medium lobe syndrome, 3/13 bronchiectasias and/or bronchioloectasias and 3/13 thin-walled cysts/atypical emphysema). In 2/15 patients a new diagnosis of Interstitial Lung Disease (ILD) was made with patients presenting a typical NSIP-pattern. Both the mean PI-US total score and the postero-inferior partial score resulted significantly higher in patients with abnormal CT/HRCT compared to those with normal CT findings (p =0.003 and p= 0.001 respectively). On the contrary, PI-US total and partial scores were not significantly different between ILD and non-ILD pSS patients (p= 0.103).

Conclusion: this study highlights the potential usefulness of PI-US as a sensitive, non invasive tool for the diagnosis of sub-clinical early lung alterations in pSS.

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AB0511

A COMPARATIVE STUDY ON CLINICAL AND SEROLOGICAL CHARACTERISTICS BETWEEN PATIENTS WITH RHUPUS AND PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Concomitant presence of two autoimmune diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) is known as "Rhupus". Although poliautoimmunity is not uncommon phenomenon, only a small series of patients have been described so far with Rhupus.

Objectives: Our purpose was to analyze the clinical and serological characteristics of patients with Rhupus and compare them with a cohort of patients with SLE.

Methods: In this cross-sectional study, we included cases of Rhupus (ACR/EULAR 2010 plus ACR 1987 criteria) from 11 different Rheumatology Departments at Catalonia, Spain. We included patients with a diagnosis of SLE in a 2:1 ratio matched by sex, race and disease duration. To avoid misclassification, those patients with Rhupus but who had Jaccoud's arthropathy or with overlap syndromes were excluded.

Results: A total of 120 patients were included, 40 cases with Rhupus and 80 cases with SLE. Most of patients were female (95%) and Caucasian (75%). Mean age was 51.0 ± 14.7 years with a mean disease duration of 12.9 ± 9.2 years. Main clinical characteristics were articular involvement (93.3%), cutaneous involvement (77.5%), haematological (72.5%), secondary Sjögren syndrome (38.7%) among others. Clinical and serological characteristics according different groups are shown in Table.

	Total N=120	Rhupus n =40	SLE n = 80
Gender (Female),%	114 (95%)	38 (95%)	76 (95%) 1
Mean age, years ± SD	51,0 ± 14,7	57,10 ± 14,1[§]	47,9 ± 14,2
Disease duration, years ± SD	12,9 ± 9,2	13,6 ± 7,9	12,6 ± 9,8
Race (Caucasian),%	84 (75%)	25 (78,1%)	59 (73,8%)
Clinical characteristics			
Cutaneous involvement,%	93 (77,5%)	31 (77,5%)	62 (77,5%)
Articular involvement,%	112 (93,3%)	40 (100%) [§]	72 (90,0%)
• Arthritis,%	96 (80,0%)	40 (100%) [§§]	56 (70,0%)
• Erosive disease,%	25 (20,8%)	24 (60,0%) [§§]	1 (1,3%)
• Tenosynovitis,%	37 (30,8%)	22 (55,0%) [§§]	15 (18,8%)
Renal involvement,%	24 (10%)	4 (10,0%) [§]	20 (25,0%)
Mean SLEDAI *	2,9 ± 2,8	2,6 ±2,5	3,0 ± 3,0
Immunological features			
Positive RF,%	37 (32,7%)	32 (80%) [§§]	6 (6,8%)
Positive anti-CCP,%	33 (30,6%)	31(81,6%) [§§]	2 (2,9%)
Comorbidity [¥]	44 (36,7%)	20 (50,0%) [§]	24 (30,0%)
SLICC *	0,8 ± 1,36	1,3 ± 1,55 [§§]	0,6 ±1,2
Treatment (ever)			
Prednisolone,%	100 (84,7%)	39 (97,5%) [§§]	61 (78,2%)
Antimalarial	109 (91,6%)	35 (89,7%)	74 (92,5%)
MTX%	58 (48,7%)	33 (82,5%)[§§]	25 (31,6%)
Rituximab,%	24 (20,2%)	13 (33,3%)[§]	11 (13,8%)

* Last visit, [¥] Comorbidities included: Hypertension, DM, dyslipemia, osteoporosis or Cushing.

Conclusion: We found some clinical and serological differences among patients with Rhupus vs SLE alone. As expected, articular domains and positive RF and ACPAs were higher in Rhupus. By other hand, renal involvement was more common among "pure" SLE patients. Rhupus patients were more commonly treated with prednisolone, MTX and rituximab, and had more comorbidities and organ damage. If Rhupus represent a different condition, requires further analysis in bigger cohorts.

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AB0512

ANTI-CARBAMYLATED PROTEIN ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS: ARE THEY USEFUL?

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Background: Anti-carbamylated protein antibodies (anti-CarP) have been described not only in Rheumatoid arthritis but in other systemic autoimmune diseases. Recently, they have been reported in different cohorts of Systemic Lupus Erythematosus (SLE) with a prevalence of 9-28% (1-4). Anti-CarP have been proposed as a marker of erosive arthitis in SLE(4).

Objectives: The aim of this work was to assess the prevalence of anti-CarP in SLE patients from a single center cohort and their association to clinical and laboratory data.

Methods: Anti-CarP were evaluated using a home-made ELISA (5), with some modifications: all the incubations has been reduced to 1.5 hrs at room temperature and the reaction was developed with diethanolamine and read at 405nm.The cut-off value of 0.350 optical density (OD) was set up, testing 230 healthy controls sera, calculating the average plus 3 times standard deviation. The ROC curve analysis demonstrated a specificity and sensitivity of 0,98 and 0,32, respectively. The OD was converted to arbitrary units (AU) with 20 AU as cut-off value. Clinical data were obtained from clinical charts.

Results: Anti-CarP antibodies were found in 80/282 (28,3%) SLE patients. Complete clinical and serological data were available for 217 patients (76,9%): 71 positive and 146 negative. No clinical associations were found with anti-CarP antibodies. However, cytopenia and renal involvement were more frequently assessed in patients without anti-CarP antibodies (p: 0,019; OR 0,49; 95%CI 0,26-0,91 and p: 0,07, respectively). Among the patients evaluated, 56 were treated with anti-Blys therapy (belimumab). In this subgroup, sera collected at the first administration (T0), after 6 months (T6) and after 12 months (T12) were tested. At baseline anti-CarP were positive in 10 (17,8%) with a mean titre of 37 AU (SD: 17,9). AntiCarp titre significantly decreased at T6 (p: 0.006) and T12 (p. 0.01). Negative seroconversion was observed in 7/10 sera.

Conclusion: the prevalence of anti-CarP antibodies found in our cohort is in line with to what previously reported. In our hands, anti-CarP antibodies are not associated to any clinical SLE features.

REFERENCES

[1] Ziegelasch M, et al. Arthritis Res and Ther 2016; 18: 289.
[2] Nakabo S, et al. J Rheumatol 2017 Sep;44(9):1384-1388.
[3] Pecani A, et al. Arthritis Res Ther 2016 Nov 25;18(1):276.
[4] Ceccarelli F, et al. Arthritis Res Ther 2018 Jun 14;20(1):126.
[5] Shi J, et al. Proceedings of the National Academy of Sciences of the United States of America. 2011;108(42):17372-7.

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AB0513 UTILITY OF RENAL REBIOPSY IN PATIENTS WITH LUPUS NEPHRITIS

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Background: The pathological class of lupus nephritis (LN) may change to a different class during the course of the disease. Renal biopsy is repeated is repeated in many patients during a flare but there is there is no agreement about systematically recommending them because proliferative lesions on their original biopsy rarely switch to a pure nonproliferative nephritis during a flare. However, renal rebiopsy may be useful in some cases to make appropriate adjustments or changes of treatment.
Objectives: To analyze the impact of renal rebiopsy on the therapeutic approach in patients with previous histological diagnosis of LN who experience a worsening in the clinical parameters of renal involvement.
Methods: Retrospective study of patients with histological diagnosis of NL subjected to at least one renal biopsy. We studied the demographic, clinical, histopathological variables of the first and subsequent renal biopsies, received treatment and the therapeutic modifications in relation to the result of the rebiopsies.
Results: We analyzed 35 patients diagnosed with LN between 1978 and 2017. 9 of them had been rebiopsied at least on one occasion and made a total of 11 rebiopsies (7 patients with a rebiopsy and 2 patients with 2 rebiopsies). All patients were female and Caucasian, except for a Hispanic woman, with a mean age at the time of the rebiopsy of 31 ± 12 years (14-55). The mean serum creatinine at the time of the first rebiopsy was 0.8 ± 0.17 mg/dl (0.5-1.06) and in the second, 1.18 ± 0.05 mg/dl (1.15-1.23). The fundamental indication for the rebiopsy was the increase in proteinuria, up to non-nephrotic range in 64% of the patients and within the nephrotic range in 36%. In comparison with the previous biopsy, 3 of the rebiopsies (27%) showed evolution from a non-proliferative to a proliferative form (from II to III, from II to IV and from V to V + IV). 4 of the rebiopsies (36%) started from a proliferative class and changed class but within these forms (3 from IV to III and and 1 from III to IV). The remaining 4 rebiopsies (27%) showed no change in the histological type. Regarding the baseline biopsy, we observed a decrease in the index of activity of the rebiopsies (5.4 ± 2.2 vs 3.4 ± 2.5, p = 0.017) and an increase in the chronicity index (0.8 ± 0.7 vs 2.9 ± 3.2, p = 0.027). In all cases, therapeutic modifications were carried out. In 9 cases (82%) the immunosuppression was increased and in two of them (18%) it was decreased.
Conclusion: The repetition of renal biopsy in cases of LN with clinical data of renal deterioration is relevant. The change of histological class and the evolution of activity and chronicity indexes support the decision to increase immunosuppression and are fundamental to diminish it.

REFERENCES

[1] Narváez J, et al. The value of repeat biopsy in lupus nephritis flares. Medicine (Baltimore). 2017;96:e7099.

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AB0514 PARATHORMONE BUT NOT VITAMIN D SERUM LEVELS ARE ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Growing evidence supports a link between alterations in bone metabolism and cardiovascular (CV) disease in both general and autoimmune populations.
Objectives: In the current study we aimed to explore whether vitamin D deficiency and/or increased parathormone (PTH) levels, as well as impairment of bone mass density, influence CV risk in patients with systemic lupus erythematosus (SLE).
Methods: 138 consecutive SLE patients were enrolled in the study. Clinical features, hematological, serological and immunological profile, as well as therapeutic regimens was recorded in all patients. Classical CV and osteoporosis risk factors were assessed in all participants. Intima-medial thickness scores (IMT) and carotid and/or femoral (C/F) plaque formation were evaluated by ultrasound. Assessment of bone mineral density (BMD) and asymptomatic osteoporotic fractures was also performed by dual X-ray absorptiometry and lateral thoracic and/or lumbar spine X-rays, respectively. Univariate and multivariate models were implemented for statistical analysis.
Results: PTH -but not 25(OH)vitamin D3- serum levels were found to be increased in lupus patients with subclinical atherosclerosis (plaque formation and/or arterial wall thickening) compared to those without (51.1±27.7 vs 37.4±18.4 pg/ml, p= 0.003 and 54±32.7 vs 40±18.3 pg/ml, p= 0.02, respectively). Abnormal PTH serum concentrations (>65 pg/ml) in SLE patients was identified as a risk factor for both plaque formation and high IMT scores (>0.9mm) [OR 95% (CI): 8.2 (1.8-37.4) and OR 95% (CI): 3.9 (1.3-11.8), respectively]. High PTH levels were found to be associated with low 25(OH)vitaminD3 levels, advanced age and increased triglycerides in the lupus cohort. Moreover, SLE patients with plaque formation exhibited increased rates of osteoporosis (based on WHO classification) compared to those without [19.5% vs 5.3%, p= 0.017, OR 95% (CI): 4.4 (1.2-15.9)]. Finally, an inverse correlation between femoral neck BMD values and total IMT scores was observed (r:-0.42, p=0.008).
Conclusion: Subclinical atherosclerosis in patients with lupus is associated with increased serum PTH levels and reduced bone mass density. These findings further support the presence of shared etiopathogenetic mechanisms between atherogenesis and altered bone metabolism.
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AB0515 OBESITY AND WEIGHT LOSS IMPACT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Obesity is considered a chronic low-grade inflammatory status due to the release of bioactive substances, as pro-inflammatory cytokines, by the adipose tissue, and it is known negatively affecting some autoimmune inflammatory diseases, like Rheumatoid Arthritis. Few data are available on the role of obesity in Systemic Lupus Erythematosus (SLE) disease.
Objectives: To evaluate the distribution of Body Mass Index (BMI) categories in SLE patients and the association between SLE disease activity and BMI groups. Furthermore, to dissect the impact of weight loss in a cohort of overweight/obese SLE patients, evaluated with a multidisciplinary approach.
Methods: Consecutive SLE patients, diagnosed according to the 2012 SLICC criteria, were enrolled. Clinical and demographic characteristics, disease duration, BMI category, laboratory indices and current therapies were collected at baseline and at follow-up visits. A subgroup of SLE patients with BMI$\geq$25 Kg/m^2 underwent a scheduled diet under a Nutritionist guide (1200 calories/daily) and Psycologist support when necessary, maintaining the SLE therapy unchanged and were evaluated by a rheumatologist and a nutritionist every 3 months and clinical and laboratory data and the ACR/EULAR core data set were registered at each follow-up(FU) visit.
Results: Of the 277 patients (age 42.2±14.4 years, disease duration 8.4 ±8.0 years, SLEDAI-2K 6.6±7.6, SLICC 1.9±1.5), 47.6% had articular, 32.3% renal, 23.6% neurological and 21.9% had serositic involvement, respectively. Considering the whole cohort, 66 (23.9%) patients had BMI between 25 and 30 Kg/m^2 and 34 (12.3%) a BMI$\geq$30 Kg/m^2 [of which 15 (5.4%) with BMI $\geq$35 Kg/m^2]. Overweight/obese SLE patients were predominantly male (20.0%) with respect to patients with BMI<25 Kg/m^2 (4.5%, p<0.001). Considering the therapeutic regimens, antimalarials treatment was ongoing in 39.4% of overweight SLE patients and in 61.8% of obese SLE patients compared to 28.7% in normal weight SLE patients (p< 0.001 for overweight and p<0.001 for obese patients), without any significant correlation between BMI and cumulative steroid dose during

the follow-up. Considering the whole SLE cohort, cardiovascular events were more frequent in obese patients (14.7%) than in overweight (7.6%) and normal weight (2.9%) SLE patients (ANOVA test: p=0.01). Twenty-nine SLE patients with BMI≥25 Kg/m^2 (BMI: 33.5 ± 5.1 Kg/m^2, age: 47.7 ± 12.3 years, disease duration: 11.9 ± 9.0 years; SLEDAI: 10.5 ± 5.7, SLICC: 1.3 ± 1.1) underwent a scheduled low calories diet. A significant reduction in BMI was observed at 6 and 12 month follow-up [6.6 ± 5.7% at 6 months FU (p = 0.001) and 7.0 ± 7.2% at 12 months FU (p=0.002), respectively] as well as a reduction in disease activity [SLEDAI at 6 months FU: 4.5 ± 4.0 (p=0.001) and at 12 months FU (0.7 ± 0.9 (p <0.001)]. Finally, a significant decrease of systemic inflammatory markers as C-Reactive Protein (p<0.05) was observed in SLE patients who achieved >5% weight loss compared to SLE patients who did not.

Conclusion: Obesity represents a modifiable factor for improving outcomes among obese SLE. A weight loss obtained with a controlled diet may reduce cardiovascular events and reduce the state of chronic inflammation subtended by the activity of adipose tissue.

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AB0516 AUTOANTIBODY PROFILE ANALYSIS AND ITS ASSOCIATION WITH CLINICAL MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune systemic disease characterized by autoantibody production. The presence of some of them is related to specific clinical manifestations. Previous studies have classified SLE patients according to an autoantibody profile, associating them to specific clinical groups.

Objectives: To define SLE patient groups according to an autoantibody profile and to analyze the correlation of these profiles to clinical manifestations, clinical activity and accumulated damage.

Methods: A cross-sectional observational study of SLE patients diagnosed according to SLICC 2012 criteria was conducted. A clinical and analytical evaluation was performed in all cases. Clinical manifestations were described according to RELESSER study. We selected 8 autoantibodies to classify SLE patients in different subgroups according to autoimmune similar profiles: anti-dsDNA, anti-Sm, anti-RNP, anticardiolipin IgG o IgM (aCL IgG/M), anti-B2microglobulin IgG o IgM (aB2M IgG/M), lupus anticoagulant (LA), anti-Ro and anti-La. Biostatistical analysis was performed using software R and immunological profiles were created according to previous study of Artim-Esen B et al. 2014.

Results: 142 SLE patients were evaluated (94.4% female) with a mean age at diagnosis of 33.29 (13.53) and a mean time of disease evolution of 15.82 (10.56) years. Mean SLEDAI score was 5.91 (5.6) and mean SLICC value 1.1 (1.46). Frequency of the selected autoantibodies was: ANAs 87.3% (n=124), anti-dsDNA 36.62% (n=52), anti-Sm 9.2% (n=13), anti-RNP 3.5% (n=5), aCL IgG/M 20.15% (n=27), aB2M IgG/M 21.88% (n=28), LA ANTI–LA? 26.27% (n=31), anti-Ro 45.07% (n=64) and anti-La 16.2% (n=23).

Profile n°2 included SLE patients with anti-Sm/RNP positivity. Profile n°3 included patients with anti-Ro/La positivity and not included in profile n°2. Profile n°4 included patients with aCL IgG/M or aB2M IgG/M or LA positivity and not included in previous profiles. Profile n°5 included patients who exclusively showed anti-DNA positivity. Profile n°1 included all patients excluded from the other profiles.

Depending on the results obtained, we analyzed autoantibody levels in order to assess its association with the presence of the described clinical affections. A significant association among hematological affection and high levels of anti-Ro (P<0.0001), anti-La (P=0.022) and anti-Sm (P=0.018) was observed. We also observed a tendency of presenting a higher rate of mucocutaneous affection, musculoskeletal and renal affection and Sjögren syndrome in patients classified in Profile 3.

Conclusion: Profile n°1 patients (absence of autoantibodies) were diagnosed earlier and had a longer disease evolution, whereas Profile n°5 patients (only anti-DNA positivity) were diagnosed at a mean age of 36 years and had a shorter disease evolution. We observed an association between the presence of anti-Ro/La and hematological affection, as well as high incidence of Sjögren syndrome in these subgroup of patients.

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AB0517 CORRELATION BETWEEN PATIENT-REPORTED OUTCOMES OF HEALTH-RELATED QUALITY OF LIFE AND CLINICAL ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Patient-Reported Outcomes (PROs) allow us to know the way the disease could affect patients, and maybe could not be detected in clinical measures. Among these, PROs of health-related quality of life (PRO-QL) represents patient evaluation of its health status and treatment, which affects the functional, psychological, social and emotional capabilities. In fact, patients with the same health status could show different PROs-QL. In the case of systemic lupus erythematoSus (SLE), patients experience many inflammatory symptoms and all of them can affect the health-related quality of life in different ways.

Objectives: We aimed to measure the PRO-QL in SLE patients and correlate them with the clinical activity of the disease.

Methods: A cross-sectional observational study with SLE patients diagnosed according to SLICC 2012 criteria was performed. In all cases SLEDAI score was carried out, and patients full-filled questionnaires of fatigue (FACIT-FATIGUE), quality of life (EQ-5D-5L), disability (HAQ) and a Global Health Status Scale (GHS) (0-100). Biostatistical analysis with software R was performed, using the multivariate analysis of variance by Pillai test.

Results: 54 SLE patients (91.84% female) participated in the study, with a mean age at diagnosis of 27.55±13.21 years *and a mean time of disease evolution* of 20.45±9.7 years. Mean SLEDAI score was 6.63±6.89, with a 37.04% of patients with SLEDAI>6. The 64.66% of patients were under glucocorticoid treatment, 38.77% under immunosupressants (methotrexate, azatioprine o mycophenolate) and 51.02% under antimalarials.

Patients showed a mean score of 34.02±12.38 in FACIT-FATIGUE, 0.72 ±0.26 in EQ-5D-5L, 0.62±0.71 in HAQ and 64.02±25.93 in GHS.

Statistical analysis showed correlation between SLEDAI score and the four questionnaires of PROs-QL (P<0.001). Particularly in those cases with high clinical activity we observed low scores of EQ-5D-5L, FACIT-FATIGUE and GHS, and an increment in HAQ. We performed the previous analysis considering as correcting factors the age, years of disease evolution, glucocorticoid treatment, antimalarials and inmunosupressants. We also obtained a correlation between clinical activity and PROs-QL (P=0.0107).

Conclusion: We observed a correlation between PROs-QL full-filled by SLE patients with the clinical activity of the disease, independently of glucocorticoid treatment, antimalarials and inmunosupressants, the age and the disease evolution.

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AB0518 - JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS RELATED PANCREATITIS: AN UNCOMMON MANIFESTATION OF A COMMON DISEASE

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Background: Pancreatitis is a rare but potentially life-threatening complication of juvenile systemic lupus erythematosus (jSLE).
Objectives: We report 3 children with SLE who presented with acute pancreatitis.
Methods: We have reviewed the clinical records of 140 children with SLE between period of 1993-2018. Three of them present with acute pancreatitis.
Results: Case 1-12-year-girl presented with fever of 1 month and alopecia. Examination revealed pedal oedema, periorbital puffiness, generalised lymphadenopathy, large joint arthritis and mild hepatomegaly.Investigations were consistent with lupus.Renal biopsy revealed Class 3 lupus nephritis and initiated on intravenous methylprednisolone.Two days after beginning her medication,she developed severe epigastric pain and vomiting which did not respond to antacids and analgesic.Serum amylase and lipase were elevated.Clinical possibilities included steroid induced pancreatitis and lupus pancreatitis.Intravenous methylprednisolone was continued following which she showed a dramatic improvement.**Case 2-**A-6-year-old presented with pain abdomen and vomiting. Physical examination showed epigastric tenderness.Investigations showed elevated amylase levels.Computerised tomography(CT) abdomen revealed acute necrotising pancreatitis. A ultrasound abdomen revealed a pancreatic pseudocyst.He had a second episode of acute pancreatitis along with anasarca after 3 months.In follow-up,he presented with anasarca. Investigation were consistent with lupus.Following the initiation of steroids,he improved and there has been no recurrence of pancreatitis over the next 4 years.**Case 3-** 9-year-girl presented with generalised rash and alopecia for 5 months.She also had pain abdomen for last 2 months.Investigations showed elevated amylase and ultrasound abdomen revealed acute pancreatitis. She had undergone a laparotomy elsewhere.Examination showed generalised pigmented rash, periorbital edema, alopecia, periorbital puffiness, hard palate ulcer and surgical scar on the abdomen.Urinalysis showed nephrotic range proteinuria.Serum amylase levels were elevated. Ultrasound abdomen revealed a pancreatic pseudocyst.Further investigations were suggestive of lupus. Workup for APLA revealed positive lupus anticoagulant. She was initiated on oral prednisolone and was given pulses of intravenous cyclophosphamide.There has been no recurrence of pancreatitis over 12-years follow-up.

Investigation	Case 1	Case 2	Case 3
Haemoglobin (g/L)	92g/L	96 g/L	80 g/L
White cell counts	7.7 X 10^6/L	7.8 X 10^6/L	7.5 X 10^6/L
Lymphocyte count	2.15x 10^6/L	1.9 X 10^6/L	1.95X10^6/L
Platelets	130×10^9/L	150 ×10^9/L	420 x 10^9/L
Urine routine	10-12 RBC, 3 + albumin -	Few RBC, 3 + albumin 82 mg/m^2/hr	No RBC, 3+ albumin 40 mg/m^2/hr
Urine protein (mg/m^2/hour)			
C3 (Normal 50-150 mg/dL)	23.4mg/dl	129 mg/dL	34 mg/dl
C4 (Normal 20-50 mg/dL)	2.98mg/dl	37mg/dL	10 mg/dl
ANA	4+ diffuse	3 +	3+ diffuse
Anti dsDNA (N: <60 IU/mL)	890	<60	123
Antiphospholipid antibodies: a) Lupus anticoagulant b) Anticardiolipin antibody (IgG and IgM) c) Anti ß2 Glycoprotein -1 antibody (IgG & IgM)	Negative Negative Negative	Negative Negative Negative	Positive Negative negative
Skin biopsy	Not done	Positivity of lupus band test with high positive IgG, IgA, IgM and C3 in dermal vessels	Lupus band test -positive
Renal biopsy	Class 3 lupus nephritis	IgG, Ig A, Ig M positivity in the mesangium as well as capillary loops and C3 in small sized blood vessels	Class 4 lupus nephritis
Serum amylase (< 100 U/L)	238 U/L	400 U/L	290 U/L
Serum lipase (< 60 U/L)	231U/L	Not done	Not done

Conclusion: Pancreatitis can at times, be the presentation of childhood lupus and requires prompt and aggressive management.
Disclosure of Interests: None declared
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AB0519 VITAMIN D CUT-OFF POINTS RELATED WITH CLINICAL FEATURES IN PATIENTSWITH ACTIVE LUPUS OR LUPUS NEPHRITIS

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Background: Vitamin D (25OHD) has immunomodulatory properties that can play a major role in patients with active lupus or lupus nephritis. His immunomodulatory function could be influenced by demographic factors, comorbidities (Charlson score), bone supplements, and other features.
Objectives: We explored the association between the best 25OHD cut-off points and specific clinical features that were present in patients with active lupus or lupus nephritis.
Methods: A retrospective descriptive research using clinical registers of patients diagnosed with systemic erythematosus lupus, attended in two rheumatology clinics was performed. A decisions tree model was used to identify the best cut-off points of 25OHD [ng/mL] and clinical features associated with active lupus (SLEDAI-2k >6) or lupus nephritis.
Results: We identified 81 patients, median age 41 years, women 91.3%. Active lupus and lupus nephritis were present in 69.1% and 29.6%, respectively. Median 25OHD was 26.49, without a difference at comparing with active lupus patients 24.85, but lower in lupus nephritis patients 21.50 (p: 0.015). Lupus nephritis was absent in patients with 25OHD cut-off points >38.8 (alone) or ≤38.8 if they were older than >57 years. Active lupus was always present in patients ≤44 years with **1.** High comorbidity or **2.** Low comorbidity plus cut-off point 25OHD >35; in >44 years, both a euthyroid state and the absence of bone supplements were present in patients with active lupus.
Conclusion: Exist a strong relationship between vitamin D levels and LES activity.

REFERENCES

[1] American College of Rheumatology. Guidelines for referral and management of systemic lupus erythematosus in adults. Arthritis Rheum. 1999 Sep;42(9):1785-96
[2] Simioni J, Heimovski F, Skare T. On lupus, vitamin D and leukopenia. 2016;56(3):206-211.
[3] Guzman R.A, Piñeros L.G, Theran A, Flechas J, Mejía M. AB0795 Hypovitaminosis D and Calcium Intake of Adult Population in Bogota (DICAVITD). Ann Rheum Dis 2016;75:1175-. 1176.

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AB0520 A COMPARISON OF SHEAR WAVE ELASTOGRAPHIC FINDING OF SUBMANDIBULAR GLANDS IN PATIENTS WITH EARLY-STAGE AND NON-SJÖGREN'S SYNDROME

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Background: Salivary gland (SG) ultrasonography proved valuable for assessing SG involvement in Sjögren's syndrome (SS) and seemed to exhibit good diagnostic properties. We have reported that the submandibular gland ultrasonography (SGUS) is a useful noninvasive and inexpensive procedure for the evaluation of the structural changes of SG in SS (ISSS 2002, EULAR 2009, EULAR 2012, EULAR 2015). However, our previously study demonstrated that although SGUS findings were useful for the diagnosis of SS with low salivary flow they were not for early stage SS with normal salivary flow (EULAR 2016). Recently, we reported that the tissue elasticity was decreased due to structural changes in the SG at the advanced stage of the disease and that the shear wave

elastography (SWE) is useful to distinguish pathological changes of the SG between early stage with normal salivary flow and advanced stage (EULAR2018). The present study we demonstrated that the tissue elasticity was increased due to inflammation and high viscosity in the SG at the early stage of SS with normal salivary flow comparing that in non-SS patients, but was decreased due to structural changes in the SG at the advanced stage of the disease. The SWE may be a useful tool for elucidation of early stage pathological changes of the SG when salivary gland functions are not impaired in SS.

Objectives: The aim of this study was to elucidate the usefulness of SWE in early-stage SS patients.

Methods: Seventeen non-SS patients and eighty patients who fulfilled the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for SS were studied. SS patients were divided into three groups according to salivary flow using gum test (VL/SS: <5mL/10min. (n=33), L/SS: 5-10mL/10min. (n=32) and N/SS: ≧10mL/10min. (n=15)). All patients were examined SGUS by a single investigator who was blinded to device (TUS-A300; Canon Medical Systems, Tokyo, Japan) with a linear transducer (7.5-10MHz). The examination consisted of conventional B-mode US (US staging score), pulsed wave Doppler US (PD grading score) and SWE with quantitative assessment. US staging scores were assessed by glandular size, inhomogeneity and contrast of diagastric muscle (stage 0 to 3). PD grading scores were graded by pulsed wave pattern in pulsed wave Doppler US at the internal SG facial arteries (grade 0 to 2). With the region-of-interest (ROI) placed over the stiffest areas of the lesion on SWE, the quantitative mean of the elasticity values were measured by shear wave velocity (Vs: m/s) and elasticity (E: kPa) for each lesion.

Results: The Vs and E values were correlated with US staging score ($r=-0.56$, $p<0.001$, $r=-0.58$, $p<0.001$) and PD grading score ($r=-0.51$, $p<0.001$, $r=-0.52$, $p<0.001$) in all patients. There was no significant difference between non-SS and N/SS in early-stage SS by US staging score (0.77±0.90 vs 1.20±0.86) and PD grading score (0.18±.053 vs 0.53±0.19). However, the values of Vs and E were highest in N/SS as compared with all groups, and significantly higher in N/SS than in non-SS (Vs: 1.73 ±0.18 vs 2.03±0.28m/s, $p<0.01$, E: 9.38±1.17 vs 12.73±3.63kPa, $p<0.01$).

Conclusion: The present study we demonstrated that the tissue elasticity was increased due to inflammation and high viscosity in the SG at the early stage of SS with normal salivary flow comparing that in non-SS patients. The SWE may be a useful tool for the differential diagnosis between patients with non-SS and early-stage SS with normal salivary flow in contrast to conventional SGUS.

Disclosure of Interests: None declared

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AB0521 EVALUATION OF LARYNGEAL IMPAIRMENT IN PATIENTS WITH SJÖGREN´S SYNDROME

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Background: Hyposalivation in patients with Sjögren´s Syndrome is causative for oral dryness, one of the main symptoms of this disease. So far only little attention has been paid to a possible impairment of laryngeal functions due to the hyposalivation, even though, especially in younger and working patients, signs of laryngeal involvement often have an impact on the patient´s quality of life.

Objectives: The objective of this study is to evaluate the laryngeal impairment in patients with Sjögren`s Syndrome.

Methods: Patients with Sjögren´s Syndrome diagnosed according to the AECG classification criteria were included in this study. Salivary function was evaluated by the measurement of the unstimulated salivary flow (USF). The laryngeal function was evaluated according to the European Laryngological Society protocol[1], which includes five different items: perception (roughness, breathiness, hoarseness), videostroboscopy, acoustics (jitter, dysphonia severity index, DSI), aerodynamics and subjective rating by the patient (voice handicap index, VHI).

Results: Eighteen patients (15 female, mean age 63 years) were included in the examination. Mean USF was 0.6 ml/5 min (±0.5). The auditory-perceptual assessment resulted in slight and moderate deviance in 14 and 2 patients for roughness of the voice, in slight and moderate deviance in 12 and 3 patients for breathiness and in slight, moderate and severe deviance in 14, 3 and 1 patient for hoarseness. Evaluation of acoustics resulted in abnormal values in 12 patients (67%). DSI revealed mild dysphonia in 7, moderate dysphonia in 6 and severe dysphonia in 1 patient. Evaluation of aerodynamics was abnormal in 12 (maximum phonation time) and 11 (phonation quotient) patients. Analysis of the VHI resulted in grade 0 in 5 patients (almost certainly not noticeable suffering), grade 1 in 8 patients (more likely unnoticeable than conspicuous suffering), grade 2 in 3 patients (more probably noticeable than not) and grad 3 in 2 patients (certainly noticeable suffering).

Conclusion: The evaluation of various laryngeal functions in patients with Sjögren´s Syndrome unfolded an impairment of different aspects. Questions on laryngeal involvement should be implemented in the anamnesis of these patients and the application of screening methods should be further investigated.

REFERENCES

[1] Dejonckers PH, et al. A basic protocol for functional assessment of voice pathology, especially for investigating the efficacy of (phonosurgical) treatment and evaluating new assessment techniques. Guideline elaborated by the Committee on Phoniatrics of the European Laryngological Society (ELS). Eur Arch Otorhinolaryngol 2001.

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AB0522 SEASONAL DIFFERENCE IN CEREBRAL STROKE FREQUENCY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The incidence of stroke is well-known as increased in winter season in general population, but seasonal difference in the systemic lupus erythematosus remain unclearified.

Objectives: The aim of study was to assess seasonal difference in cerebral stroke among patients with systemic lupus erythematosus.

Methods: We conducted a retrospective case-control study analyzing hospital database of a tertiary referral center in Taiwan. From January, 2002 to December 2017, subjects with systemic lupus erythematosus and cerebral stroke were enrolled. To examine the seasonal incidence of cerebral stroke, we analyzed data from the date of CT scan/MRI/MRA. The onset time was divided into four seasons (according Local season classification): spring (March, April, May), summer (June, July, August), autumn (September, October, November), and winter (December, January, February).

Results: In total, 4313 systemic lupus erythematosus patients were identified, 261 patients with cerebral stroke. Age of patients with cerebral stroke ranged 27 between 77 years, a mean age was 55-62 years. Female was predominant. Disease duration was longer in ischemia stroke group (4.8 years). According CT or MRI results, divided 4 types (Ischemia stroke (IS), ICH, SAH, SDH), 83% (150/180) cerebral stroke was ischemia stroke. 8.3% ICH, 5.5% SAH, 2.8% SDH found respectively. We noted a higher incidence of SLE with ischemia stoke in summer season (38.7%), the lowest incidence of ischemia stroke in winter season (18.7%). Patient with ICH has similar trend. But not found in SAH and SDH.

Conclusion: Incidence of systemic lupus erythematous with cerebral stroke varied in different pattern. The present findings suggested an increase in the incidence of Ischemia stroke and ICH in summer season. Awareness of risk factors (esp. antiphsopholipid antibodies) was essential to prevent cerebral stroke in SLE.

Table Seasonal difference in different types of cerebral stroke

	IS (n=150)	ICH (n=15)	SAH (n=10)	SHA (n=5)
Age	60 (46.8-75.0)	59.0 (35.0-68.0)	60.5 (43.3-77.3)	55.0 (27.0-71.0)
Gender% (F/M)	73.3/26.7	66.7/33.3	90.0/10.0	60.0/40.0
Disease duration	4.8(0.3-8.7)	2.5 (0.0-5.5)	3.9 (0.0-11.6)	0.0 (0.0-11.5)
Season				
Spring (3-5)	21.3%	26.7%	20.0%	60.0%
Summer (6-8)	38.7%	53.3%	20.0%	20%
Autumn (9-11)	21.3%	6.7%	30.0%	20%
Winter (12-2)	18.7%	13.3%	30.0%	0%

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AB0523 MENOPAUSE IN AN EGYPTIAN COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: EFFECT OF THE DISEASE

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Background: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease that mainly affects females in the reproductive age[1]. Although SLE generally emerges during reproductive ages, it was found that lupus patients experience menopause at younger age than the general population; however, whether the occurrence of menopause at a younger age in lupus patients results from the gonadotoxic effects of Cyclophosphamide treatment or from an autoimmune-mediated ovarian injury is debated[2].
Objectives: To identify menopause characteristics in an Egyptian cohort of women with SLE with effect of the disease on menopausal symptoms and the characteristics of disease activity and disease damage in peri-menopausal and post-menopausal patients.
Methods: In this cross-sectional observational study, data of 120 consecutive SLE female patients who fulfilled the 2012 ACR/SLICC criteria[3], above the age of 35. Disease activity was assessed by using the SLE disease activity index (SLEDAI)[4], and accumulated damage was assessed by Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI)[5]. Laboratory assessment was done to all patients including follicle stimulating hormone (FSH) and *luteinizing hormone* (LH) blood levels.
Results: The mean age of the patients was 45.067 ± 8.211 years and median disease duration was 5.074 ± 5.567 years (min 0.08 – max 21 years). It was found that the mean of total SLEDAI score was 4.667 ± 3.537 and mean of total SLICC/ACR damage index was 0.633 ± 0.819. Of 120 patients 20% had premature menopause, 29.17% had natural menopause and 50.83% were still menstruating (table 1). It was found that the age at menopause (either natural or premature menopause) ranged from 26 to 54 years with the mean 45.170 ± 7.278 years. There was a statistically significant negative correlation between LH and total SLEDAI (r = - 0.178, P = 0.052). It was also found a statistically significant positive correlation between FSH and cumulative Cyclophosphamide dose (r = 0.440, P < 0.001) and between LH and cumulative Cyclophosphamide dose (r = 0.214, P = 0.046) (table 2).

Table 1. Menstrual status:

	Positive	
	N	%
Premature menopause	24	20.00
Natural menopause	35	29.17
Menstruating	61	50.83

Conclusion: SLE has a reproductive and hormonal impact on female patients, either because of disease activity or due to pharmacological adverse effects. The mean age at menopause (either natural or premature menopause) is 45 years. High LH is associated with lower disease activity. High cumulative Cyclophosphamide dose is associated with high FSH and LH.

REFERENCES

[1] Mills JA. Systemic lupus erythematosus. New Engl J Med 1994; 330: 1871–1879.
[2] Sammaritano LR. Menopause in patients with autoimmune diseases. Autoimmun Rev. 2012; 11(6-7).
[3] Petri M., Orbai AM., Alarcón GS, et al. Derivation and Validation of the Systemic Lupus International Collaborating Clinics Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheum. 2012; 64: 2677-86.
[4] Bombardier C, Gladman D, Urowitz M, et al. Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. Arthritis Rheum 1992, 35, 630–640.
[5] Gladman D, Ginzler E, GoldsmithC, et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum. 1996; 39: 363-369.

Table 2. Correlation study between FSH & LH and Cyclophosphamide:

Correlations				
	FSH (mIU/ml)		LH (mIU/ml)	
R	P-value	R	P-value	
Cumulative Cyclophosphamide (mg)	0.440	< 0.001*	0.214	0.046*

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AB0524 SERUM BAFF AND APRIL AS CANDIDATE BIOMARKERS IN SYSTEMİC LUPUS ERYTHEMATOSUS (SLE): A PROSPECTIVE FOLLOW-UP STUDY

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Background: BAFF and APRIL are cytokines involved in B cell development and they take place in the pathogenesis of SLE.
Objectives: The aim of this study was to investigate the relationship between serum BAFF/APRIL levels with clinical features and disease activity in SLE patients.
Methods: We included 79 patients with SLE (ACR criteria) and 27 healthy controls into the study. Serum BAFF and APRIL levels were assessed by ELISA. In 19 patients with active disease at the time of the assessment BAFF/APRIL levels were reassessed at least 6 months later (mean 7.8 months) and disease activity was evaluated by SLEDAI. New renal involvement was observed in 16 patients during the study and renal involvement was previously detected in 12 patients.
Results: Although both BAFF (median 0.7 vs 0.41 ng/ml) and APRIL (median 2.3 vs 1.05 ng/ml)levels were higher in patients with SLE compared to the control group (p <0.001), no correlation was found between BAFF/APRIL levels and SLEDAI scores. Only 9 patients (11.4%) had both BAFF and APRIL in normal range (95% confidence interval). When patients were grouped according to disease activity as no activity (SLEDAI = 0), low disease activity and active disease, there was no difference in BAFF/APRIL levels between groups. Serum BAFF levels were higher in patients with renal disease activity (median 0.94 ng/ml vs 0.61 ng/ml, p=0,01), and there was a positive correlation between APRIL levels and proteinuria (r=0.42, p=0,02). There was no association between BAFF/APRIL levels and anti-dsDNA positivity but a weak inverse correlation was observed between BAFF and C3 levels (r=0.25, P=0.02). No correlation was found between BAFF/APRIL levels and renal SLEDAI score, renal histopathology activity and chronicity index scores. In the active disease group after follow-up, there was no significant change in BAFF (from 1,63 ng/ml to 1,2 ng/ml) and APRIL levels (from 2,11 ng/ml to 2,31 ng/ml).
Conclusion: BAFF/APRIL levels were found to be significantly higher in patients with SLE compared to controls, but no association with disease activity was found. BAFF levels are correlated with decreased C3 levels. These results suggest that both cytokines are involved in the pathogenesis of SLE, and that serum BAFF and APRIL levels can be valuable as a biomarker in SLE especially in patients with renal activity. Long-term studies on the effect of treatment are needed.
Disclosure of Interests: None declared
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AB0525 ANTI-SMITH ANTIBODY IS ASSOCIATED WITH DISEASE ACTIVITY IN PATIENTS WITH NEW-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Anti-Smith (Sm) antibody is a highly specific antibody for systemic lupus erythematosus (SLE). Despite the remarkable specificity of anti-Sm antibodies for SLE, the association between anti-Sm antibody level and the clinical manifestation of SLE is still unclear.
Objectives: We aimed to evaluate the association between anti-Sm antibodies and disease activity in patients with new-onset SLE.

Methods: We included patients who were repeatedly tested for anti-Sm antibodies at SLE diagnosis and within 12 months after SLE diagnosis. The clinical and laboratory profiles, and SLE disease activity index (SLEDAI) were collected at the time of the anti-Sm antibody test. SLEDAI and laboratory variables associated with disease activity were compared at baseline between patients with and without anti-Sm antibodies. The longitudinal association between disease activity and anti-Sm antibodies was also evaluated in total patients and in those with anti-Sm antibodies.
Results: Of 92 patients who were tested for anti-Sm antibodies at the time of SLE diagnosis, 67 and another 67 patients were followed up for the presence of anti-Sm antibodies at 6 and 12 months, respectively. Although the baseline SLEDAI was comparable in SLE patients with and without anti-Sm antibodies, the serum anti-Sm antibody level at diagnosis was significantly correlated with SLEDAI (P = 0.003). Patients with anti-Sm antibodies at 12 months had higher SLEDAI and anti-dsDNA levels than those without anti-Sm antibodies (P = 0.002, respectively). The changes in anti-Sm antibody levels over 12 months were also correlated with the alterations in SLEDAI (P = 0.029).
Conclusion: This study suggests that anti-Sm antibody level is associated with disease activity in patients with new-onset SLE, and that monitoring of anti-Sm antibody levels could help assess the disease activity.

REFERENCES

[1] Migliorini, P., et al., *Anti-Sm and anti-RNP antibodies.* Autoimmunity, 2005. 38(1): p. 47-54.
[2] *Clinical associations of anti-Smith antibodies in PROFILE: a multi-ethnic lupus cohort.* Clin Rheumatol, 2015. 34(7): p. 1217-23.
[3] *What is the clinical significance of anti-Sm antibodies in systemic lupus erythematosus? A comparison with anti-dsDNA antibodies and C3.* Clin Exp Rheumatol, 2017. 35(4): p. 598-606.

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AB0526

PRIMARY SJOGREN'S SYNDROME AND ORGAN SYSTEM INVOLVEMENT: A RETROSPECTIVE STUDY OF 153 PATIENTS FROM WESTERN INDIA

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Background: Primary Sjogren's syndrome (pSS) is under diagnosed and improperly treated disease because of its variable modes of presentation. Limited data is available on pSS from India.
Objectives: To describe organ system involvement in patients with pSS and compare to other studies.
Methods: Retrospective proforma based analysis of patients with pSS (AECG 2002 criteria) from 2002-2012 at a tertiary rheumatology centre was done. Demographic data and systemic organ involvement of patients was noted.
Results: We had 153 consecutive patients of pSS (135 females, 18 males) in the 10 years which were included. Mean age at diagnosis was 47±11.62 years. Mean duration of sicca symptoms was 32 (±31) months prior to presentation. Organ system involvement was seen in 93 (60.7%) patients as follows:- Musculoskeletal involvement in 90 (58.8%) patients, Skin involvement in 48 (31%) patients, Lung involvement in 27 (17.6%) patients, Renal involvement in 22 (14.3%) patients, Neurological involvement in 21 (13.7%) patients, GI involvement in 6 (3.9%) patients and Lymphoma in 2 (1.3%) patients. Comparison of organ system involvement with other major studies of pSS is shown in table 1.

Table 1. Comparison with major studies of pSS from different populations:

Parameter	Spanish[1] (1994-2007)	Italian[2]	Chinese[2] (1985-2006)	Vellore[2] (2004-2011)	Our study (2002-2012)
Criteria used	European community	European community	AECG	AECG ACR	AECG
No. of patients	1010	1115	573	332	153
Females (%)	937 (93%)	1067 (95.7)	524 (91.5)	315 (94.9)	135 (88.2)
Mean age (yrs)	53.8±0.5	57.5±13.7	39	44.5±10.6	47±11.6
Disease duration (months)	74.9±4	72	-	62.6 ±65.67	35±41
Xerostomia (%)	975 (96)	1033 (92.6)	484 (84.5)	313 (94.3)	146 (95.4)
Xerophthalmia (%)	968 (96)	1054 (94.5)	401 (70)	295 (88.9)	148 (96.7)
Ocular test positive (%)	898 (94)	982 (88.1)	-	-	149 (97.4)
Sialadenitis (%)	269 (27)	346 (31)	-	28 (8.4)	42 (27.5)
Arthralgia/arthritis (%)	640 (63)	806 (72.3)	274 (47.8)	275 (82.8)	90 (58.8)
Skin involvement (%)	91 (9)	106 (9.5)	-	35 (10.5)	48 (31)
Raynaud's phen (%)	187 (18)	239 (21.4)	101 (17.6)	1 (0.3)	2 (1.3)
Lung involvement (%)	112 (11)	60 (5.4)	221/522 (42.3)	40 (12.1)	27 (17.6)
Renal involvement (%)	48 (5)	-	192 (33.5)	49 (14.8)	22 (14.4)
Neurological inv (%)	131 (13)	59 (5.3)	68 (11.9)	32 (9.6)	21 (13.7)
GI involvement (%)	5 (0.5)	-	188 (32.8)	29 (8.7)	6 (3.9)
Lymphoma (%)	-	50 (4.5)	-	-	2 (1.3)
ANA (%)	859 (85)	941 (84.4)	474/565 (83.9)	206/312 (66)	151/151 (100)
Anti-Ro (SS-A) (%)	518 (52)	762 (68.3)	474/568 (83.5)	148/232 (63.8)	137/141 (97.2)
Anti-La (SS-B) (%)	343 (34)	410 (36.8)	231/568 (40.7)	88/231 (38.1)	108/119 (90.8)
RF (%)	467 (48)	582 (52.2)	292/476 (61.3)	180/301 (59.8)	95/106 (89.6)
Hyperglobulinemia (%)	-	530 (47.5)	-	50/261 (15.4)	56/135 (41.5)

Conclusion: Indian pSS patients are younger than their European counterparts. Majority of these patients show organ system involvement. Raynaud's phenomenon is rare in Indian patients. Lung, renal and gastrointestinal involvement in Indian patients is more prevalent than in European patients, but less prevalent than in Chinese patients. Musculoskeletal and neurological involvement is similar across different populations.

REFERENCES

[1] Ramos-Casals M, Solans R, Rosas J, et al. GEMESS Study Group. Primary Sjögren syndrome in Spain: clinical and immunologic expression in 1010 patients. Medicine (Baltimore) 2008; 87: 210-9.
[2] Sandhya P, Jeyaseelan L, Scofield RH, Danda D. Clinical Characteristics and Outcome of Primary Sjogren's Syndrome: A Large Asian Indian Cohort. The Open Rheumatology Journal. 2015;9:36-45.

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AB0527

PREDICTIVE VALUE OF MIR200B-5P IN THE LYMPHOMAGENESIS IN SJÖGREN'S SYNDROME (SS): COMPARISON WITH THE PUBLISHED PREDICTION MODELS. PRELIMINARY RESULTS

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Background: miR200b-5p expression levels are decreased in the minor salivary glands of SS patients who have or will develop non-Hodgkin's lymphoma (NHL), discriminate them from those who will not (p<0.0001) and independently predicted NHL development (p<0.0001)[1].
Objectives: To compare the predictive performance of low miR200b-5p levels with the previously published multifactorial predictive models.
Methods: 27 SS patients who didn't develop NHL during follow up (median follow up time upon biopsy performance, range: 8.9yrs, 1.33-14yrs) and 17 diagnosed with NHL during follow up (pre-lymphoma, median follow-up till lymphoma diagnosis, range: 3.67yrs, 0.42-8.5yrs) were studied. The multifactorial predictive models examined were: 1. Ioannidis et al[2] who defined patients expressing at least one of low C4 levels, salivary gland enlargement (SGE) and purpura as high-risk, 2. Baimpa et al[3] who designed 3 models (1, 2 and 3) based on the expression of at least 1, 2 or ≥3, respectively, of neutropenia, cryoglobulinemia, splenomegaly, lymphadenopathy and low C4 levels, 3. Quartuccio et al[4] who identified as high risk patients those having SGE and at least two of the following: low C4 levels, cryoglobulinemia, anti-La antibodies and leukopenia, and 4. Fragkioudaki et al[5] that defined as high-risk group those carrying ≥3 of the independent risk factors including SGE, lymphadenopathy, Raynaud phenomenon, anti-Ro/SSA and/or anti-La/SSB antibodies, rheumatoid factor positivity, monoclonal gammopathy and low C4 levels. Analyses were performed by estimating the area under the ROC curve (AUC), Kaplan-Meier (KM) lymphoma-free survival curves

compared by the log-rank test, the positive and negative predictive values, sencitivity (Se) and specificity (Sp), as well as the PSEP index of the model intrinsic prognostic value[6].

Results: ROC analysis identified low miR200b-5p levels as the better prognostic tool from the other multifactorial models. Its predictive value was further supported by the other analyses (including PSEP index), where it ranked among the two best models, whereas it had the better combination of sensitivity and specificity (Table).

Table. Comparison of models predicting NHL development in SS

	ROC		KM							
	AUC	**p value**	**p value**	**p value**	**PPV**	**NPV**	**PSEP**	**Se**	**Sp**	**Se +Sp**
Ioannidis et al	0.748	0. 006	0.006	0.006	0.57	0.94	0.51	0.94	0.56	1.50
Baimpa et al, model 1	0.775	0.002	0.002	0.003	0.63	0.90	0.53	0.88	0.67	1.55
Baimpa et al, model 2	0.687	0.038	0.038	0.006	0.88	0.72	0.60	0.41	0.96	1.37
Baimpa et al, model 3	0.647	0.104	0.104	0.008	1.00	0.69	0.69	0.29	1.00	1.29
Quartuccio et al	0.794	0.001	0.001	≤0.0001	1.00	0.79	0.79	0.59	1.00	1.59
Fragkioudaki et al	0.830	≤0.0001	≤0.0001	≤0.0001	0.71	0.91	0.63	0.88	0.78	1.66
Low miR200b-5p levels	0.863	≤0.0001	≤0.0001	≤0.0001	0.87	0.86	0.73	0.76	0.93	1.69

Conclusion: Low miR200b-5p levels associated with the incidence of NHL in SS, exhibiting consistently higher values than the other multifactorial models; however, larger cohorts are required to verify its statistical and clinical significance.

REFERENCES

[1] Kapsogeorgou et al, Ann Rheum Dis 2018
[2] Ioannidis et al, Arthr Rheum 2002
[3] Baimpa, et al. Medicine 2009
[4] Quartuccio et al, J Autoim 2014
[5] Fragkioudaki et al, Medicine 2016
[6] Altman and Royston, Stat Med 2000

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AB0528 ANALYSIS OF THE CASES OF 33 SLE PATIENTS THAT NECESSITATED CARDIOVASCULAR SURGERY

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Background: In SLE, immune complexes are overproduced and deposited in tissues where they ultimately cause damage. The immunocomplexes, which are deposited in the myocardium, blood vessels and atrioventricular valves, have been suggested to cause damage to the relevant tissues, but it remains unclear in which cases tissue damage progresses to a point that surgical treatment is required.

Objectives: The purpose of our study was to classify heart diseases into valvular heart diseases (V), ischemic heart diseases (I) and aortic aneurysms (A), to compare each class in terms of the correlation between the activity of SLE and the progression and exacerbation of heart disease, and in the future, to use the features of the correlations to carry out the prevention and treatment of heart diseases complicating SLE.

Methods: Between the years 2012 and 2018, a total of 2852 patients diagnosed with SLE were admitted to our hospital, and 33 had heart surgery; however, 2 patients with infective endocarditis and one patient, who had not been diagnosed with SLE before surgery, were excluded from the study, therefore 30 cases were examined. Comparative studies were also carried out to examine the association between the levels of various autoantibodies and IgG and the onset of heart disease, the association between the total administered doses of steroids, the concomitant use of immunosuppressants as well as the association between DNA antibodies and complement.

Results: At the time of the surgical treatment of the heart diseases, the mean duration of illness was 25.4 years, and the age was V vs. I vs. A=56.7 (44-79, median value: 56.2) vs. 55.1 (34-72, median value: 57.0) vs. 63.2 (41-78, median value: 65.5), showing that the age tended to be higher in the A group. The integrated value of the duration of illness and the level of anti-DNA antibodies, which served an index of activity, was calculated, and the findings revealed that V vs. I vs. A was (14020 vs. 32966 vs. 29444), showing that the values tended to be slightly lower in valvular heart diseases. As for antiphospholipid antibodies, the rate of positivity of either CLβ2GPI or anti-CL antibodies or LA was as follows: V vs. I vs. A (58% vs. 28% vs. 33%), showing that the rate tended to be higher in valvular heart diseases and that anti-CL antibody-positive patients were particularly higher in number among those with valvular heart diseases (V). The maximum preoperative levels of IgG were as follows: V vs. I vs. A (2803 vs. 1889 vs. 1708), which showed that the levels were higher with valvular heart diseases (V); those of SS-A antibodies were as follows: (36% vs. 43% vs. 42%), which showed high positive rates in all cases; and RNP antibody-positivity rates were as follows: (9% vs. 29% vs. 25%), and were relatively lower in valvular heart diseases (V). Regarding the medical treatment, the total administered doses of steroids were (25g vs. 39g vs. 63g) and tended to be lower in valvular heart diseases (V); use of immunosuppressants was found in 5 of 30 patients (16%); and concomitant use of both was particularly low in valvular heart diseases (V) as it accounted for only one case.

Conclusion: Our study findings suggested that in SLE patients, prolonged duration of illness, positivity of SS-A antibodies and the absence of intake of immunosuppressants were highly likely to lead to cardiovascular diseases that need surgical treatment. Low integrated DNA antibody levels and the absence of concomitant use of immunosuppresants, despite high levels of IgG and the positivity of SS-A antibodies and anti-CL antibodies, might be risk factors for valvular heart diseases necessitating surgical treatment.

REFERENCES

[1] Yasuhiro Sakaguti, et al. Journal of Cardiology. 1995;25:181-188
[2] Stephane Zuily, et al. Curr Rheumatol Rep (2013) 15:320
[3] Zawadowski GM, et al. Lupus. 2012;21(13):1378-84

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AB0529 SICCA SYNDROME DURING CHRONIC HEPATITIS C: PREVALENCE AND CHARACTERISTICS

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Background: The prevalence of Sicca Syndrome (SS) in patients with Chronic Hepatitis C (CHC) ranges from 5% to 33%. A link between hepatitis C virus (HCV) and SS was evoked given the strong association of these two pathologies with mixed cryoglobulinemia (MC) on one hand and with the salivary tropism of HCV on the other hand.

Objectives: To study the prevalence and the characteristics of Sicca Syndrome during CHC.

Methods: All patients suffering from CHC followed over a period of 11 years (2002 – 2012) were retrospectively included. Only patients having clinical SS (xerostomia and/or xerophthalmia) were selected. We have analyzed all data concerning the patient, the hepatitis and the SS.

Results: Two hundred and four patients affected by CHC were included. A clinical SS was found in 17 patients (8.39%). There were 15 women and 2 men with an average age of 45.6 years. A High viral load and an advanced hepatic fibrosis were respectively found in 94 and 88% of cases. Cryoglobulinemia and antinuclear antibodies were found in 37.5% and 53% of patients, respectively. Four patients (3 women and 1 man) had also presented the criteria of Sjogren Syndrome. Their average age was 47 years. MC was positive in all 4 patients whereas anti-SSA and

anti-SSB were absent in the 4 patients. Biopsy of accessory salivary glands revealed the presence of a grade 4 lymphocytic sialadenitis according to the Chisholm and Masson classification in 3 patients, while the remaining case had a lymphocyte grade 2 sialadenitis. The evaluation of hepatic fibrosis did not reveal cirrhosis in the 4 cases.
Conclusion: The prevalence of Sicca syndrome during hepatitis C is estimated at 8% in our study. It was mainly reported in women with perimenopausal age and seems to be associated with cryoglobulinemia, a high viral load and and an advanced fibrosis.
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AB0530 THE EFFECT OF MYCOPHENOLATE MOFETIL ON NON-RENAL MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS FROM 2014 TO 2018: OBSERVATION STUDY FROM KOREAN LUPUS NETWORK (KORNET) REGISTRY

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Background: Mycophenolate mofetil (MMF) has been established to a potent therapeutic drug for regulate renal involvement in systemic lupus erythematosus (SLE).
Objectives: The object of this study is to identify the effect of MMF on non-renal manifestations in SLE.
Methods: The study population was total 439 SLE patients enrolled from Korean Lupus Network (KORNET) registry. The KORNET registry was followed up annually and completed from baseline survey to the 2nd visits from 2014 to 2018. In the subgroup analysis, the effect of MMF on clinical features was also evaluated in 110 patients with histologically confirmed lupus nephritis (LN). The changes of clinical features including mucocutaneous lesions, arthritis, serositis, neurologic disorder, and hematologic abnormalities were assessed between MMF and non-MMF groups during follow-up period. Statistical analysis was used by multiple comparison analysis, considering time, group, and interaction of follow-up time and treatment group.
Results: There was significant difference of malar rash and renal disorder between MMF and non-MMF groups considering time and group in total SLE patients ($p = 0.025$ and $p < 0.001$, respectively). In hematologic abnormalities, proportion of leukopenia was significantly different between two groups during follow-up periods ($p_{time} < 0.001$, $p_{group} < 0.001$, and $p_{time\ \&\ group} = 0.004$). In 110 LN patients, there was not difference of non-renal clinical features between them. In contrast, proportion of leukopenia in patients with LN was significantly different between two groups during follow-up periods ($p_{time} < 0.001$, $p_{group} = 0.003$, and $p_{time\ \&\ group} = 0.004$).
Conclusion: This study showed that MMF might be beneficial to treatment for hematologic abnormalities in SLE.

REFERENCES

[1] Yahya F, Jasmin R, Ng CT, Cheah TE, Sockalingam S. Open label randomized controlled trial assessing the efficacy of mycophenolate sodium against other conventional immunosuppressive agents in active systemic lupus erythematosus patients without renal involvement. Int J Rheum Dis. 2013 Dec;16(6):724-30.
[2] Ginzler EM, Wofsy D, Isenberg D, Gordon C, Lisk L, Dooley MA; ALMS Group. Nonrenal disease activity following mycophenolate mofetil or intravenous cyclophosphamide as induction treatment for lupus nephritis: findings in a multicenter, prospective, randomized, open-label, parallel-group clinical trial. Arthritis Rheum. 2010 Jan;62(1):211-21.
[3] Pisoni CN, Sanchez FJ, Karim Y, Cuadrado MJ, D'Cruz DP, Abbs IC, Khamasta MA, Hughes GR. Mycophenolate mofetil in systemic lupus erythematosus: efficacy and tolerability in 86 patients. J Rheumatol. 2005 Jun;32 (6):1047-52.
[4] Moder KG, Amin S, Mazlumzadeh M, Crowson C, Ytterberg S. The effect of mycophenolate mofetil on patients with active non-renal SLE. Clin Exp Rheumatol. 2007 Nov-Dec;25(6):932.

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AB0531 OBESITY INCREASES THE INCIDENCE OF NEW-ONSET LUPUS NEPHRITIS AND ORGAN DAMAGE DURING FOLLOW-UP IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background:
Objectives: This study investigated the detrimental effects of obesity on clinical manifestations, disease activity, and organ damage in Korean patients with systemic lupus erythematosus (SLE).
Methods: We obtained data on 393 SLE patients from the Korean Lupus Network registry. Demographic variables, clinical manifestations, laboratory findings, Physician Global Assessment (PGA), Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)-2000 and Systemic Lupus International Collaborating Clinics Group (SLICC) damage index scores were recorded at the time of enrollment. The tests were repeated annually for 3 consecutive years. We divided the patients into groups according to their body mass index (BMI) using the Asia-Pacific classification (normal, BMI < 23; overweight, 23 ≤ BMI <25; obese, BMI ≥ 25). Univariate and multivariate analyses were performed to assess the impact of obesity on clinical outcomes.
Results: Of the 393 patients, 59 (15.0%) were obese at the time of enrollment. Obese patients had more comorbidities, such as diabetes (P=0.002), hypertension (P=0.005), hyperlipidemia (P=0.005), and pulmonary hypertension (P=0.036) than non-obese patients. Nephritis at enrollment and newly developed nephritis during follow-up were more common in obese patients than in non-obese patients (P=0.002 and P=0.002, respectively). In addition, obese patients had higher daily and cumulative prednisolone doses (P=0.010 and P=0.010, respectively) and higher rates of intravenous cyclophosphamide (P=0.008), mycophenolate (P=0.030), tacrolimus (P=0.007), and cyclosporine (P=0.019) use than non-obese patients. Furthermore, the PGA and SLICC damage index scores were higher in obese patients than in non-obese patients (P=0.017 and P=0.039, respectively) for all 3 consecutive years. In the multivariate analysis, obesity was significantly associated with male gender (OR = 0.141, 95% CI: 0.047–0.419, P<0.001), newly developed nephritis (OR = 2.741, 95% CI: 1.080–6.957, P=0.034), and annual increase in SDI (OR = 2.185, 95% CI: 1.229–3.885, P=0.008).
Conclusion: Obese SLE patients had a higher incidence of newly developed nephritis and cumulative organ damage than non-obese patients. Therefore, lifestyle modifications, including those aimed at weight loss, should be recommended for these patients to improve their clinical outcomes.
Disclosure of Interests: None declared
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AB0532 SOLUBLE SIGLEC-5 IS A NOVEL SALIVARY BIOMARKER FOR PRIMARY SJOGREN'S SYNDROME

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Background: Despite advances in the understanding of the pathogenesis, disease-specific biomarkers have not been included in the classification criteria for Primary Sjogren's syndrome (pSS).
Objectives: Based on the microarray of peripheral blood mononuclear cell (PBMC) of pSS patients, we aimed to investigate whether sialic acid-binding immunoglobulin-like lectin (siglec)-5 might serve as a biomarker for pSS.
Methods: Microarray of PBMCs obtained from 26 pSS patients and 10 healthy control (HC)s was performed to screen potential biomarkers for pSS. The concentration of siglec-5 in saliva and sera was determined by ELISA. Clinical parameters related with pSS were obtained from pSS registry and correlation with salivary siglec-5 level was evaluated. Receiver operating curve (ROC) analysis was performed to determine cut off value. A separate validation cohort consisted of subjects with suspicious pSS was evaluated to determine the performance.
Results: The level of salivary siglec-5/14 was significantly higher in pSS patients (n=170) compared with HCs (n=25) or non SS sicca patients (n=78) (1346.8 [202.8-4280.0] pg/mL, 6.08 [0-134.0] pg/mL, and 195 [0-947.5] pg/mL, median [interquartile range], P<0.001), meanwhile the serum level was not different between the groups. Clinical parameters were available in 170 patients in pSS registry. Salivary siglec-5 level negatively correlated with salivary flow rate (spearman's rho: -0.420, P<0.001), and positively correlated with ocular surface score (rho: 0.331, P<0.001) and serum immunoglobulin G level (rho = 0.202, P=0.008). However, the level

of salivary siglec-5 was not correlated with ESSDAI or focus score. On ROC analysis, area under the curve was 0.774(0.724-0.826). With cut off value 400pg/mL, sensitivity and specificity was 0.69 and 0.70 respectively. In validation cohort (45 pSS patients and 45 non SS sicca patients) where patients without sicca symptom but have 1 or more positive items in ESSDAI were included, sensitivity and specificity of siglec-5 was 64.4% and 77.8%, respectively.

Conclusion: The level of soluble siglec-5 is significantly increased in the saliva of pSS patients and reflects the severity of hyposalivation and ocular surface damage. Although the mechanism of the contribution to gland dysfunction is unclear yet, this easily obtainable salivary biomarker may add benefits on the diagnosis of pSS.

REFERENCES

[1] Shiboski CH, Shiboski SC, Seror R, et al. 2016 American College of Rheumatology/European League Against Rheumatism classification criteria for primary Sjogren's syndrome: A consensus and data-driven methodology involving three international patient cohorts. Ann Rheum Dis 2017;76:9-16.

[2] Katsiougiannis S, Wong DT. The Proteomics of Saliva in Sjogren's Syndrome. Rheum Dis Clin North Am 2016;42:449-56.

[3] Lee J, Lee J, Kwok SK, et al. Janus kinase 1 inhibition suppresses interferon-induced B cell activating factor production in human salivary gland: potential therapeutic strategy for primary Sjogren's syndrome. Arthritis Rheumatol 2018.

[4] Macauley MS, Crocker PR, Paulson JC. Siglec-mediated regulation of immune cell function in disease. Nat Rev Immunol 2014;14:653-66.

[5] Ali SR, Fong JJ, Carlin AF, et al. Siglec-5 and Siglec-14 are polymorphic paired receptors that modulate neutrophil and amnion signaling responses to group B Streptococcus. J Exp Med 2014;211:1231-42.

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AB0533 POSITIVE RATE OF SMALL INTESTINAL BACTERIAL OVERGROWTH TEST (SIBO) WAS SIGNIFICANT CORRELATIONS TO DISEASE ACTIVITY OF PRIMARY SJOGREN'S SYNDROME (PSS)

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Background: Primary Sjogren's syndrome (pSS) is a chronic inflammatory autoimmune disease that primarily affects the exocrine glands, which is involved in gastrointestinal unavoidably. Once intestinal flora imbalance, it will have a major impact on health. The Small intestinal bacterial overgrowth test (SIBO) is an important method for detecting bacterial growth in the small intestine.

Objectives: To investigate the difference in the positive rate of SIBO between disease active and stable patients with pSS, and to retrospectively analyze the correlation between disease activity and SIBO.

Methods: Total 51 patients with pSS diagnosed and treated in our hospital were selected as subjects of this study from October 2018 to December 2018, according to the PSS Disease Activity Rating System (SSDAI) scores. They were divided into Group A: active period (point≥5 points), 25 cases and group B: stable period (point<5 points), 26 cases. Two sets of clinical data were collected, including SSDAI scores and SIBO. The difference between the percentage of active and stable SIBO positive patients was compared. The maximum sum of hydrogen and methane in the two groups was tested by rank sum test, and the correlation between pSS disease activity and SIBO positive rate was analyzed.

Results: The positive rate of SIBO in patients with active pSS was significantly higher than that in stable phase, and the difference was statistically significant (P=0.026), as shown in Table 1. The two groups were compared with H2MaX or CH4MaX, and the Mann-Whitney U test results were statistically significant (P=0.001, P=0.006), as shown in Table 2.

Conclusion: SIBO positive rate was significant correlations to pSS disease activity. So, correcting intestinal flora imbalance combined with conventional treatment may bring greater benefits to patients with Sjogren's syndrome.

REFERENCES

[1] Lazarosl,Sakkas,Theodora,Simopoulou,Dimitrios,Daoussis,Stamatis-Nick, Liossis, Spyros, Potamianos.Intestinal Involvement in Systemic Sclerosis: A Clinical Review. [J]. Digestive diseases and sciences,2018,63(4):834-844.

[2] Hongjun, Zhao,Lijuan, Zhao,Wei, Shi,Hui, Luo,Liping, Duan,Yunhui, You, Yisha, Li,Xiaoxia, Zuo.Is it bowel-associated dermatosis-arthritis syndrome induced by small intestinal bacteria overgrowth?[J].SpringerPlus,2016,5 (1):1551.

[3] Coyte KZ, Schluter J, Foster KR. The ecology of the microbiome:Networks, competition, and stability [J]. Science, 2015, 350(6261): 663-666.

[4] Schirmer M, Smeekens SP, Vlamakis H, et al. Anticancer Immunotherapy by CTLA-4 blockade relies on the gut microbiota Commensal Bifidobacterium promotes antitumor immunity and Convenience anti-PD-L1 efficacy [J]. Cell, 2016, 167 (4):1125-1136.

[5] Neuman H, Koren O. The gut microbiota: a possible factor Influencing systemic lupus erythematosus [J]. Curr Opin Rheumatol, 2017, 29 (4) : 374-377.

Table 1. Comparison of SIBO positive rate between active period and stable period [n (%)]

SIBO positive	SIBO negative	total
active period 23(92.00%)	2 (8.00%)	25(100%)
stable period 16(61.50%)	10 (38.50%)	26(100%)
Total 39 (76.50%)	12 (23.50%)	51(100%)

Table 2. Mann-Whitney U test of two sets of H2MaX or CH4MaX independent samples

Disease active(25 cases)	Disease stable(26 cases)	difference
H2MAX 51.00(50.50)	17.50(22.50)	P=0.001
CH4MaX 6.00(2.00)	5.00(2.00)	P=0.006

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AB0534 DEVELOPMENT OF A MULTI-MODALITY IMAGING APPROACH TO EVALUATE LUPUS NEPHRITIS AND INITIAL RESULTS

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Background: Lupus nephritis (LN) remains a significant cause of morbidity and mortality in subjects with Systemic Lupus Erythematosus (SLE). The gold standard for evaluation of LN remains the kidney biopsy, whereas renal function is usually evaluated by eGFR and urinary protein: creatinine ratio. More effective and sensitive methodology is needed to assess LN and also the response to treatment. Functional imaging of the kidney using quantitative techniques has great potential, as it can assess kidney function and pathologic changes non-invasively by evaluating perfusion, oxygenation, cellular density and fibrosis.

Objectives: To develop a multi-modality imaging approach for the evaluation of the spectrum of pathologic changes in LN.

Methods: In this multi-center study, subjects who were having a standard of care renal biopsy for LN were asked to participate in the imaging evaluation. Local Institutional Review Board approval was obtained, and subjects signed an Informed Consent Form. Dynamic contrast enhanced MRI (DCE-MRI) was employed to detect changes in vascularization and perfusion[1], Diffusion Weighted Imaging (DWI) to assess interstitial diffusion, T2*Map/BOLD - the tissue oxygenation and T1rho to evaluate fibrosis[2]. The imaging scores will be compared to renal biopsy, including ISN/RPS classification of LN, activity index and chronicity index.

Results: Five patients have been evaluated to date and their imaging data assessed for quality. The initial results have demonstrated the feasibility of acquiring multi-modality imaging data, including dynamic imaging sequences, in the multi-center trial setting. Figure 1 illustrates scans from a representative patient. This study will determine whether multi-modality imaging could become an effective, non-invasive tool to assess renal function and pathology in LN.

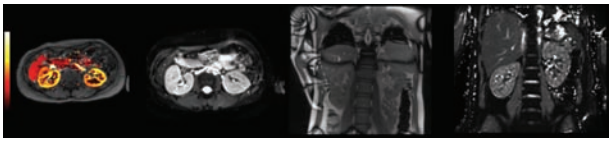


Figure 1. Multi-modality imaging from a representative LN patient. Left: Map of the initial rate of enhancement (DYNAMIKA™) from DCE-MRI showing the degree of perfusion (the white-yellow colors correspond to increased and the redder colors decreased perfusion) in which decreased perfusion can be seen in the anterior pole of the right kidney (arrow); Left center: DWI sequence that shows diffusion; Right center: T1rho illustrating fibrosis; and Right:T2*Map/BOLD to investigate tissue oxygenation within the renal medullary tissue.

Conclusion: The initial assessment of 5 LN subjects has established the feasibility of multi-modality imaging as a tool to evaluate LN in a multi-center study. By assessing functional and structural MRI outcomes and correlating them to clinical data, this study will provide essential preliminary evidence on the value of multi-modality imaging in diagnosis and evaluating the response to treatment of LN patients.

REFERENCES

[1] Rappachi S, et al. Magnetic Resonance Imaging, 2015 Nov;33(9):1066-1074.
[2] Boesen M, et al. PET Clin. 2018 Oct;13(4):523-550.

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AB0535 FACTORS RELATED TO FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS: A COHORT CROSS-SECTIONAL STUDY

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Background: Fatigue is the most prevalent symptom in Systemic Lupus Erythematosus (SLE) as it is present in up to 90% of patients; it is considered to be the most disabling symptom in around half of the patients [1,2]. Its aetiology is multi-factorial and there is conflicting evidence on the relationship between fatigue and SLE disease activity, and between fatigue and vitamin D deficiency. The Ad Hoc Committee on Systemic Lupus Erythematosus Response Criteria for Fatigue recommended the Fatigue Severity Scale (FSS) for the measurement of fatigue in SLE [2,3].
Objectives: The aim of the study was to characterise the relationship between fatigue and other factors, including disease activity, vitamin D level, pain, depression, anxiety, sleep quality and exercise in SLE. Moreover the prevalence of fatigue in the Maltese population of SLE patients was established.
Methods: 92 SLE patients, who fulfilled the SLICC classification criteria for SLE, gave informed consent to participate in the study. This consisted of an interview, blood and urine tests, and filling the questionnaires: Fatigue Severity Scale (FSS), visual analogue scale (VAS) for fatigue, Hospital Anxiety and Depression Scale (HADS), VAS for pain, Pittsburgh Sleep Quality Index (PSQI) and modified Health Assessment Questionnaire (mHAQ). SLE disease activity was measured by SLE disease activity index-2K (SLEDAI-2K). Approval to carry out this study was obtained from the University Research Ethics Committee.
Results: The mean age of the cohort studied was 46.9 years. 92.4% were females and the median disease duration was 13 years. 56.5% had an abnormal level of fatigue (FSS >3.7) and the median FSS was 4.17. Fatigue measured by FSS, had a significant correlation with VAS Pain ($R=0.536$, $p<0.001$), HADS-D ($R=0.535$, $p<0.001$), HADS-A ($R=0.395$, $p<0.001$), PSQI ($R=0.551$, $p<0.001$) and mHAQ ($R=0.435$, $p<0.001$). VAS fatigue had a significant correlation with SLEDAI-2K ($R=0.247$, $p=0.018$). There was no significant relationship between fatigue and vitamin D level or regular exercise. ANCOVA analysis showed that fatigue measured by FSS and VAS fatigue was significantly dependant on depression measured by HADS-D ($p<0.001$) and VAS pain ($p<0.001$).
Conclusion: Fatigue is highly prevalent in SLE patients. This study identified a number of factors that are significantly related to fatigue; of these it is most strongly dependent on depression and pain. This suggests that the aetiology of fatigue in SLE is multi-factorial and that in SLE patients reporting fatigue, the underlying cause needs to be identified and treated.

REFERENCES

[1] Zonana-Nacach A, Roseman JM, McGwin G, Friedman AW, Baethge BA, Reveille JD, et al, and the LUMINA Study Group. Systemic lupus erythematosus in three ethnic groups. VI.Factors associated with fatigue within 5 years of criteria diagnosis. Lupus 2000;9:101–9.
[2] Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46:1121–3.
[3] Ad Hoc Committee on Systemic Lupus Erythematosus Response Criteria for Fatigue. Measurement of fatigue in systemic lupus erythematosus: a systematic review. Arthritis Rheum 2007;57:1348–57.

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AB0536 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND LYMPHOMA AT A TERTIARY HOSPITAL: DESCRIPTIVE ANALYSIS OF NINE PATIENTS

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Background: Evidence of an increased risk to develop haematological malignancy, and especially non-Hodgkin's lymphoma (NHL) in autoimmune diseases, has been gathered since the 1970s. In the last decade studies from SLE cohorts have consistently shown a markedly increased risk of NHL.
Objectives: To analyze clinical and disease characteristics in SLE patients who developed a lymphoma during follow-up, as well as to define characteristics of the lymphoma and its evolution.
Methods: Retrospective observational, longitudinal study conducted in a tertiary hospital. Medical records of 362 patients with $\geq$4 SLICC classification criteria of SLE were reviewed, including those with lymphoma diagnosis. Demographic and clinical data, comorbidities, SLE manifestations and therapy, data related to lymphoma and outcome were collected. Descriptive statistic analysis with measures of central tendency and measures of variability was performed.
Results: Of the 362 SLE patients, 9 (2.5%) were diagnosed of lymphoma, of which 100% female. Mean age at SLE diagnosis was 34 y.o (SD 11) and average duration from SLE diagnosis to lymphoma was 17 years (SD 14). 7 patients were caucasian and 2 hispanic. Observed comorbidities were hypertension (6 pt, 67%), diabetes (2 pt, 22%), dyslipidemia (3 pt, 33%), HBV infection (1 pt, 11%) and active smoking (6 pt). No malignancy history was detected. Most frequent SLE features were haematological (9 pt, 100%), joint (5 pt, 56%) and skin (5 pt) involvement. The serious ones were: 3 patients with haemolytic anaemia (1 of them, platelets <20000), 2 epilepsia (1 of them with CNS vasculitis), 1 glomerulonephritis, 1 pulmonary hypertension and 1 hemophagocytic syndrome. Only 1 patient had overlap with Sjögren's syndrome. At the time of lymphoma diagnosis, 7 patients were on steroids, 4 on immunosuppressants (2 mycophenolate, 1 azathioprine and 1 rituximab) and 3 on antimalarials (Table 1). Mean age at lymphoma diagnosis was 51 y.o (SD 10). 5 patients (56%) had diffuse large B-cell lymphoma (DLBCL), 1 had NHL, 1 had Hodgkin's lymphoma, 1 had mantle B-cell lymphoma and 1 had MALT lymphoma. Only 1 patient, of 4 with available data, had EBV positive in the tissue. 7 patients (78%) received chemotherapy and 2 patients completed treatment with autologous peripheral stem-cell transplantation. Three patients died, 2 due to lymphoma and one due to other causes (severe flaccid paralysis, Miller Fisher syndrome). Overall survival after lymphoma diagnosis was 8 years (SD 6).
Conclusion: In our patients, unlike that reported in the literature, lymphoma diagnosis was in SLE with longer duration of the disease, and all cases were female. Most frequent subtype was NHL, and all patients had previous haematological manifestations. Regarding previous SLE treatments, 5 patients had been exposed to immunosuppressants.

n	Manifestations	Haematological	Immunological	Steroid at lymphoma diagnosis[a]	Immunosuppressant at lymphoma diagnosis[a]
1	Rash, photosensitivity, arthritis, pleuritis, pericarditis	Leucopenia	ANA, DNA, SS-A, low C	**Yes**	**Azathioprine (AZA)**
2	Arthritis	Haemolytic anaemia	ANA, Sm, SS-A	No	No
3	Rash, photosensitivity, discoid, oral ulcers, pericarditis	Lymphopenia	ANA, RNP	**Yes**	No
4	Rash, arthritis, epilepsia, fever, adenopathies	Leucolymphopenia	ANA, DNA, Sm, low C	**Yes**	**Mycophenolate** (previous AZA)
5	Discoid, photosensitivity, fever, hemophagocytic syndrome	Leucolymphopenia thrombocytopenia		**Yes**	Previous cyclophosphamide
6	Oral ulcers	Platelets <20000, haemolytic anaemia	ANA, SS-A, low C	**Yes**	**Rituximab**
7	Rash, photosensitivity	Leucolymphopenia	ANA, SS-A, SS-B, low C	Previous	No
8	Arthritis, epilepsia, CNS vasculitis, stroke, pleuritis, pericarditis	Thrombocytopenia	ANA	**Yes**	No
9	Arthritis, stroke, glomerulonephritis	Haemolytic anaemia, thrombocytopenia	ANA, DNA, RNP, SS-A, low C	**Yes**	**Mycophenolate**

[a]Mean time with immunosuppressant previous to lymphoma was 2 years and with steroid 12 years

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AB0537 CHRONIC DAMAGE CONTRIBUTION TO COGNITIVE IMPAIRMENT IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Background: There is a gamut of affections at neurological level in patients with primary APS (PAPS) including cognitive impairment (CI). It presents in middle age population carrying a high risk of dementia.
Objectives: To analyze the impact of chronic damage in CI and its associated factors in patients with PAPS.
Methods: Cross-sectional study in patients with PAPS (Sidney criteria). Demographic, clinical data, comorbidities and treatment were investigated. For the diagnosis of CI, MoCA version 8.1 questionnaire was employed and HAD questionnaire for depression screening. Patients were divided into 2 groups: with and without CI. Chronic damage was measured with DIAPS, considering chronic damage as the damage established for over 6 months and with a score $\geq$1. Descriptive statistics, and chi square test were used.
Results: Sixty PAPS patients were included, 76.7% were females. Clinical characteristics, associated risk factors and cognitive assessment by domain in both groups are shown in table 1.Only 1 patient presented depression and 3 had anxiety/depression by HAD test. Mild CI was present in 61.7%, moderate CI in 6.7% and no CI in 31.7%. Median DIAPS score was 3,Interquartile Range 2-5.75.Thirty patients with CI had a DIAPS score $\geq$3 (p=007). Persistence of positivity for aCL was associated to CI (p=0.004)
Conclusion: The high score of DIAPS and persistence of aCL were associated with CI in PAPS. Chronic stress generated by accumulated chronic damage coupled with APS vasculopathy may contribute to cognitive deterioration. Prevention of chronic damage as well as a cognitive intervention are necessary in order to decrease CI.

REFERENCES

[1] Tektonidou MG, Varsou N, Kotoulas G, et al. Cognitive deficits in patients with antiphospholipid syndrome. Association with clinical, laboratory, and brain magnetic resonance imaging findings. Arch Intern Med 2006; 166: 2278 – 84.
[2] Kozora E, Erkan D, Zhang L, et al. Cognitive dysfunction in antiphospholipid antibody (aPL)-negative systemic lupus erythematosus (SLE) versus aPL-positive non-SLE patients. Clin Exp Rheumatol 2014; 32: 34 – 40.

Table 1.Demographic characteristics, risk factors and cognitive evaluation in PAPS patients.

	Without CI (n=19)	With CI (n=41)
Demographic factors		
Age (years)	48.1 ± 14.7	49.0 ± 12.8
Education (years)	13.8 ± 3.5	12.0 ± 4.3
Disease characteristics		
Age at diagnosis (years)	36.0 ± 12.5	35.7 ± 10.9
Course (months)	229.9 ± 182.6	222.8 ± 144.8
Stroke history (%)	15.8	41.0
+aCL (%)*	73.7	92.0
B2GPI-1 (%)	52.6	35.9
Triple aPL (%)	23.1	42.1
Use of drugs associated to cognitive impairment		
Benzodiazepines (%)	10.5	20.5
Cognitive impairment by domain		
Cognitive alteration (%)	63.2	76.9
MoCA test score	26.8 ± 1.2	22.1 ± 2.8
Executive-Visuospatial (Mdn, range)	5, 3 – 5	4, 2 - 5
Identification (Mdn, range)	3, 3 - 3	3, 1 – 3
Attention (Mdn, range)	6, 4 – 6	5, 1 –6
Language (Mdn, range)	2, 1 - 3	2, 0 – 3
Abstraction (Mdn, range)	2, 1 - 2	2, 0 – 2
Deferred memory (Mdn, range)	3, 0 - 5	1, 0 – 5
Orientation (Mdn, range)	6, 5 - 6	6, 5 - 6
Dementia risk (%)	5.3	46.2

*p <0.05

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AB0538 INFLUENCE OF IMMUNOLOGICAL FEATURES, DISEASE ACTIVITY AND FATIGUE ON THE HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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Background: Studies show that the health-related quality of life (HRQoL) is significantly reduced in patients with primary Sjogren's syndrome (pSS). However, potential predictors of HRQoL in these patients are not well known.
Objectives: To investigate potential influence of main immunological features, fatigue and disease activity on the HRQoL in patients with pSS.
Methods: We studied 41 consecutive in- and outpatients with pSS diagnosed according to the AECG criteria in the Clinic of Allergy and Immunology. The SF-36 questionnaire has been used to assess HRQoL. The SF-36 values have been compared with the population based reference values. Fatigue was assessed using Fatigue Severity Scale (FSS). ESSDAI was used for the evaluation of systemic involvement and disease activity and ESSPRI for the evaluation of the patient-reported outcomes.
Results: There were 38/41 female patients. The mean age was 56.2 ±13.5 years and the mean disease duration was 3.9 ±5.8 years. HRQoL was reduced in almost all SF-36 domains in the comparison to healthy population: physical functioning (PF) (p=0.0161); role physical (RP) (p=0.0005); social functioning (SF) (p=0.0234); role emotional (RE) (p=0.0421). The mean value of FSS score was 4.6±2.2, with 53.6% of patients having FSS score more than 4.8 (which is considered to be pathological). There were no significant differences in HRQoL depending on the presence of ANA (p=0.44), anti-SSA Abs (p=0.0756), anti-SSB Abs (p=0.218), cryoglobulins (p=0.8), complement consumption (p=0.122). Patients with elevated values of RF had significantly higher HRQoL (p=0.00453). Serum IgG concentrations positively correlated with HRQoL (rho=0.488, p=0.00139), and especially with the domains of SF (rho=0.502, p=0.0005) and PF (rho=0.491, p=0.00129). We found a significant negative correlation between HRQoL and FSS score (rho=-0.794, p<0.001). The mean ESSDAI score was 3.8 (0-23), and 75.6% of patients had some level of disease activity according to ESSDAI. Patients with low disease activity had higher HRQoL compared to those with moderate disease activity in following SF-36 domains: physical composite score (PCS) (p=0.0148), PF (p=0.0328), RP (p=0.00697) and vitality (VT) (p=0.05). The mean ESSPRI score value was 5.1±2.7 (dryness scale – 6.1, fatigue scale - 5.4, limb pain scale – 3.8). ESSPRI score negatively correlated with HRQoL (rho=-0.763, p<0.001) in all SF-36 domains.
Conclusion: Our study identified ESSDAI, ESSPRI and FFS scores, serum RF and IgG concentrations as potential predictors of HRQoL in patients with pSS.

REFERENCES

[1] Ibn Yacoub Y, Rostom S, Laatris A, Hajjaj-Hassouni N (2012) Primary Sjogren's syndrome in Marroccan patients: characteristics, fatigue and quality of life. Rheumatol Int 32:2637-43.

[2] Chou A, Gonzales JA, Daniels TE, et al. (2017) Health-related quality of life and depression among participants in the Sjogren's International Collaborative Clinical Alliance registry. RMD Open 3:e000495.

[3] Seror R, Bootsma H, Saraux A, et al. (2016) Defining disease activity states and clinically meaningful improvement in primary Sjogren's syndrome with EULAR primary Sjogren's syndrome disease activity (ESSDAI) and patient-reported indexes (ESSPRI). Ann Rheum Dis 75:382-389.

[4] Cho HJ, Yoo JJ, Yun CY, et al. (2013) The EULAR Sjogren's syndrome patient reported index as an independent determinant of health-related quality of life in primary Sjogren's syndrome patients: in comparison with non-Sjogren's sicca patients. Rheumatology 52:2208-2217.

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AB0539 TEN YEARS OF THE MONASH LUPUS CLINIC: INSIGHT INTO THE CHARACTERISTICS AND OUTCOMES OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN AUSTRALIA

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Background: The Monash Lupus Clinic, based at Monash Health in Melbourne, is Australia's first multi-disciplinary specialist lupus clinic that services a broad community and acts as a research hub, particularly as the foundation site and headquarters of the Australian Lupus Registry and Biobank (ALRB). Since its inception in 2007, the clinic has been co-run by rheumatologists and nephrologists. A carefully curated clinical dataset has been collected since clinic inception.
Objectives: We provide an overview of the characteristics and longitudinal outcomes of adult lupus patients treated at the Monash Lupus Clinic over the last ten years.
Methods: A ten-year-long dataset from the original Monash Lupus Clinic cohort, of patients subsequently enrolled in the Australian Lupus Registry and Biobank, was used for the analysis. The dataset included information on patient demographics, lupus diagnosis, serological profile, treatments, disease activity, damage accrual and other medical outcomes such as renal failure, adverse pregnancy outcomes and hospitalisations. Descriptive statistics were used to summarise the characteristics of the study population. Bivariate tests and regression analyses were used for comparisons between inception cohort patients, enrolled in the registry within 15 months of their Systemic Lupus Erythematosus (SLE) diagnosis, and existing SLE patients enrolled later in their disease course.
Results: Of the 329 enrolled patients, the median age at enrolment was 38.0 years and 87.8% of were female. Most patients were either of Caucasian (48.6%) or Asian (36.5%) ethnicity. Patients were enrolled a median of 4.0 years after their SLE diagnosis; 31.0% of patients were inception cohort patients. Most patients (95.4%) had an abnormal titre of anti-nuclear antibodies; 65.0% of the cohort were positive for anti-dsDNA autoantibodies. Included patients were observed for a median observation period of 3.9 years. The median adjusted mean SLEDAI score over the observation period was 4.0; 49.1% of the cohort spent $\geq$50% of the observation period in the Lupus Low Disease Activity State and 43.5% had ever had a SLEDAI score $\geq$10. Just over half (57.4%) had accrued damage at the end of the observation period; however, pleasingly only a very small minority had an adverse pregnancy outcome (2.7%), developed renal failure (2.4%) or died (2.4%) during the observation period. Inception cohort patients did not appear to be different to existing SLE patients except for being a population of patients earlier in their disease course.
Conclusion: Running a multi-disciplinary clinic alongside research activity is both feasible and worthwhile. Systematic collection of longitudinal data on SLE patients has shown that adverse outcomes such as end-stage renal disease and death are rare; however, with more than half of the cohort having damage present at the end of the observation period, there is still work to be done to improve outcomes for SLE patients in Australia. Expansion of the Australian Lupus Registry and Biobank beyond the Monash Lupus Clinic will provide further insight into the characteristics and outcomes of SLE patients in Australia and provide a beneficial framework for future studies.
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AB0540 CAN LOW SERUM VITAMIN D LEVELS AFFECT THE COGNITIVE FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS?

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease involving various organs and systems including the nervous system. Neuropsychiatric SLE (NPSLE) occurs in 30 - 40% of SLE patients. One of the most common manifestations of NPSLE is cognitive dysfunction (CD) which is found in 20 - 80% of SLE patients. Epidemiological studies have reported vitamin D to be a potentional risk factor of cognitive impairment within the general population. There have also been found associations between vitamin D levels and CD in multiple disease states, such as Alzheimers´s disease, multiple sclerosis and SLE. It is hypothesized that vitamin D contributes to neuroprotection by modulating the production of proinflammatory cytokines. Vitamin D deficiency is highly prevalent in SLE patients due to photoprotection, renal insufficiency and use of different medication.
Objectives: To establish a possible association between serum vitamin D levels and cognitive function in SLE patients. To determine the presence of certain auto-antibodies (anti-dsDNA, antinucleosomal, anti-P protein, and antiphospholipid) in the serum, and the disease activity.
Methods: We included a total number of 70 patients diagnosed with SLE according to the American College of Rheumatology (ACR) classification criteria. We assessed disease activity according to SLE Disease Activity Index (SLEDAI). CD was evaluated on the basis of psychological analysis of cognitive functions with testing of attention, memory, psychomotor speed, visual spatial skills and speed of cognitive information processing. Serum vitamin D levels were measured by standardized immunochemical assay from blood samples.
Results: We analyzed 70 patients, 64 (91.4%) women and 6 (8.6%) men. The cognitive dysfunction with moderate to severe disability was found in 43 (61.4%) patients. There was found the statistically significant difference between two groups (with and without CD) in serum levels of vitamin D, 54.01 nmol/l (±22.6) and 68.48 nmol/l (±27.1), resp. ($p<0.01$). The average value of the activity index (SLEDAI) in group with CD was 8.49 (±8.4), vs 5.07 (±4.9) in group without CD ($p<0.01$). Antiphospholipid antibodies were positive in 17 (39.5%) patients with CD and in 6 (22.2%) patients without CD ($p<0.05$). The other antibodies were positive in almost 50% (anti-dsDNA, antinucleosomal), P protein only in 8.8% in group of patients with CD.
Conclusion: On the basis of obtained results it can be stated that cognitive dysfunction was present in a high number of SLE patients. We demonstrated a high frequency of vitamin D deficiency among SLE patients with CD and statistically significant lower levels of vitamin D than in patients without CD. These results suggest that low vitamin D level could be associated with impaired cognitive function.

REFERENCES

[1] Hussein HA Daker LI, Fouad NA, et al. Does Vitamin D Deficiency Contribute to Cognitive Dysfunction in Patients with Systemic Lupus Erythematosus? Innov Clin Neurosci. 2018;15(9-10):25-29.

[2] Balion C, Griffith LE, Strifler L, et al. Vitamin D, cognition, and dementia: a systematic review and meta-analysis. Neurology. 2012;79(13):1397-405.

[3] Tay SH, Ho CS, Ho RC, et al. 25-Hydroxyvitamin D3 Deficiency Independently Predicts Cognitive Impairment in Patients with Systemic Lupus Erythematosus. PLoS One. 2015;10(12)

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AB0541 LUPUS MANIFESTATIONS IN A PATIENT WITH SPONDYLOARTHRITIS TREATED WITH TUMOUR NECROSIS FACTOR-ALPHA ANTAGONIST: SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) OR DRUG-INDUCED LUPUS ERYTHEMATOSUS (DILE)?

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune inflammatory disease. Drug-induced lupus erythematosus (DILE) is defined as the development of lupus-like symptoms that is temporarily related to continuous drug exposure which resolves with cessation of the offending drug. It is usually accompanied by serologic findings of a positive antinuclear antibody (ANA) and anti-histone antibodies. Tumour necrosis factor-α (TNFα) antagonist-induced lupus-like syndrome (TAILS) is a well-known side effect of this class of substances. A retrospective study reported twenty two cases whose lupus manifestations abated within a few weeks (median eight weeks) in all patients except one with longer-lasting evolution of six months.
Objectives: We reported a case which posed a diagnostic challenge to us, a patient with spondyloarthritis (SpA) who presented with lupus-like features during treatment with Golimumab.
Methods: Case report
Results: A 36-year-old lady was diagnosed as spondyloarthritis when she presented with peripheral arthritis, plantar fasciitis, right eye anterior uveitis and bilateral chronic sacroiliitis confirmed via sacroiliac magnetic resonance imaging. Investigations revealed raised erythrocyte sedimentation rate (ESR) and negative HLA-B27. She developed allergic reaction to sulfasalazine and non-steroidal anti-inflammatory drugs (NSAIDS), thus intravenous Golimumab was initiated. Although she responded to this therapy and ESR had reduced during assessment at 24 weeks, Golimumab was stopped due to funding issue. It was restarted after six months but had to be discontinued again after four months because she developed recurrent fever and malar rash. During this presentation, investigations revealed leukopenia of 2.46 $x10^9$, ESR of 93 mm/hr, low complements and positive direct coombs' test. ANA, anti-double stranded DNA, anti-histone antibody and anti-smith antibody were all negative. Infective screening was negative. TAILS secondary to Golimumab was diagnosed. Apart from discontinuation of Golimumab, 0.5mg/kg/day of prednisolone was started which resulted in improvement of the malar rash and leukopenia. However, four months after the last dose of Golimumab, recurrent fever and leukopenia recurred when the prednisolone dose was reduced to 5mg on alternate-days. At this time, we considered diagnosis of SLE rather than TAILS because of persistent SLE manifestation despite cessation of Golimumab and improvement with oral corticosteroid. Furthermore, although not pathognomonic, the anti-histone antibody was negative.
Conclusion: This case posed a diagnostic challenge as both SLE and DILE can present similarly. The approach to managing this patient with coexisting SpA and SLE is also a challenge since there is a dilemma as to what can be offered after failure of NSAIDs and conventional disease-modifying antirheumatic drugs since anti-TNFα is contraindicated in SLE.

REFERENCES

[1] Vasoo S. Drug-induced lupus. Lupus, 2006; 15: 757–761
[2] Brussano AM, Aberer W, Massone C. Subacute lupus erythematosus during treatment with golimumab for seronegative rheumatoid arthritis. Lupus, 2014; 23: 201-3.
[3] De Bandt M, Sibilia J, Le Loet X, et al. Systemic lupus erythematosus induced by anti-tumour necrosis factor alpha therapy: A French National survey. Arthritis Res Ther, 2005; 7: R545-51
[4] Oscar M. Pérez-Fernández, et al. Spondyloarthropathies in Autoimmune Diseases and Vice Versa. Autoimmune Diseases, 2011: 2012

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AB0542 PREGNANCY OUTCOMES IN ANTIPHOSPHOLIPID SYNDROME: 8 YEAR-EXPERIENCE FROM A MULTIDISCIPLINARY UNIT

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Background: Women with antiphospholipid syndrome (APS) are at increased risk of recurrent miscarriage, fetal death, placental insufficiency, preeclampsia and fetal growth restriction. Although treatment improves fetal-maternal outcomes, there are still some unsuccessful pregnancies. A multidisciplinary approach with strict monitoring is essential in order to attain obstetrical success.
Objectives: To assess pregnancy outcomes in portuguese women with APS who were surveilled at a multidisciplinary unit.
Methods: Pregnant women fulfilling the Sydney classification criteria for definite APS, who attended our specialized Rheumatology and Obstetrics outpatient clinic between 2010 and 2018, were included in this retrospective observational study. Cases of suspected APS not meeting the classification criteria were excluded. All pregnancies were followed by a multidisciplinary team (rheumatologists, obstetricians and nurses). Data was collected from medical records. Adverse Pregnancy Outcomes (APO) were defined as: spontaneous abortion (<10w), fetal death (≥10w), neonatal death, fetal growth restriction (FGR) and delivery prior to 36 weeks of gestation with or without preeclampsia (PE).
Results: A total of 35 pregnancies were identified in 25 women with APS. Twelve (48%) patients had thrombotic APS, 9 (36%) had obstetric APS and 4 (16%) had mixed APS. Primary APS was seen in 56% of patients, while systemic lupus erythematosus was found in 44%.
The average maternal age at conception was 32.8 ± 5.2 years. Mean duration of disease prior to pregnancy was 6.4 ± 5.5 years. In regard to antiphospholipid antibody (APL) profile, 28.6%, 25.7% and 28.6% of patients were triple, double and single positive, respectively. Although they had fulfilled laboratorial criteria in the past, 17% of patients were negative for all APL. All patients were instructed to receive prophylactic or therapeutic low-molecular-weight heparin combined with low dose aspirin for the duration of pregnancy.
Regarding fetal outcomes, there were 2 (5.7%) cases of first-trimester miscarriage, 1 (2.9%) medical abortion due to exposure to teratogenic drugs at the time of conception and 4 (11.4%) fetal deaths. Among the cases of fetal death, one concerned a patient who suspended heparin on her own initiative and another one who became pregnant under warfarin and whose fetus had trisomy 18. The other cases occurred at 11 and 18 weeks of gestation, under regular therapy. There were no cases of neonatal death or other fetal malformations. The rate of live births was 80%, with a mean gestational age of 37.3 ± 1.5 weeks and mean birth weight of 2796.4 ± 462 g. Most women delivered by cesarean section (54.3% of cases). There were 6 (17.1%) cases of preterm birth, three (8.6%) corresponding to fetus with FGR. Concerning maternal outcomes, there was one single case (2.9%) of PE. There were no cases of eclampsia or HELLP syndrome.

Table 1. Clinical and serological features of adverse pregnancy outcomes and successful pregnancies.

	APO, n=11 (32.4%)	Successful pregnancies n= 23 (67.6%)	*p*-value†	OR (CI 95%)
Maternal age, mean	32.3 ± 5.8	33.2 ± 4.2	0.244 ‡	-
Disease duration, mean	7.7 ± 6.6	5.8 ± 5.0	0.358 ‡	-
History of thrombosis	9 (81.8%)	14 (60.9%)	0.271	-
History of previous APOs	7 (63.6%)	12 (52.2%)	0.715	-
Concomitant SLE	8 (72.7%)	11 (47.8%)	0.270	-
Lupus anticoagulant	11 (100%)	11 (47.8%)	**0.003**	25 (1.32 – 474.08)
IgG aCL	6 (54.5%)	8 (34.8%)	0.458	-
IgM aCL	0 (0%)	5 (21.7%)	0.150	-
IgG anti-B2GPI	7 (63.6%)	8 (34.8%)	0.151	-
IgM anti-β2GPI	2 (18.2%)	4 (17.4%)	0.999	-
Single Positivity	2 (18.2%)	7 (30.4%)	0.682	-
Double Positivity	3 (27.3%)	6 (26.1%)	0.999	-
Triple Positivity	6 (54.5%)	4 (17.4%)	**0.045**	5.7 (1.15 – 28.33)
Negative APL	0 (0%)	6 (26.1%)	0.145	-
Low complement levels *	4 (50%)	5 (23.8%)	0.209	-
Anti-dsDNA ♦	3 (37.5%)	2 (18.2%)	0.603	

The only patient who had a medical abortion was excluded from this analysis.
† Fisher's exact test, except otherwise indicated.
‡ Independent t-test.
*Data available for 29 pregnancies.
♦ Applied only to patients with SLE (n=19).

Lupus anticoagulant (*p*= 0.003, OR 25, CI 95% 1.32 – 474.0) and triple APL (*p*= 0.045, OR 5.7, CI 95% 1.15 – 28.33) positivity were associated with adverse pregnancy outcomes. In this cohort, no association was

found between poor obstetric outcomes and history of thrombosis, presence of SLE or low complement levels (table 1).
Conclusion: In our study, most pregnancies were uneventful. Despite the small sample size, we reinforce the importance of a multidisciplinary evaluation and surveillance before, during and after pregnancy in women with APS in order to implement early treatment and to optimize fetal-maternal outcomes.
Disclosure of Interests: None declared
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AB0543 FEATURES ASSOCIATED WITH RENAL DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DECEASED OVER A 10-YEAR PERIOD

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Background: Renal damage (RD) is one of the most important contributors to morbidity and mortality in patients with systemic lupus erythematosus (SLE).
Objectives: We aimed to assess features associated with RD in a group of 90 deceased SLE patients routinely followed-up at our institution, which serves as a national referral center for SLE.
Methods: We retrospectively analyzed 90 SLE patients (68 females) deceased from 2002 to 2011. All patients were ≥18 years of age at death, fulfilling ≥4/11 classification criteria of the American College of Rheumatology (ACR). We identified patients with RD, as defined by the Systemic Lupus International Collaborating Clinics (SLICC)/ACR index. An extensive set of variables was compared between patients with and without RD (RD and RD-N, respectively): demographics, ACR criteria at diagnosis and cumulatively at death, total damage and its components one year following diagnosis and non-renal damage and its components cumulatively at death, as well as components of the metabolic syndrome, smoking, sicca and Hughes syndrome. Frequencies were compared using the chi-square and Fisher´s exact test, and continuous variables using the t-test and Mann-Whitney U test. Variables associated with RD were analyzed using multivariate logistic regression.
Results: We identified 25/90 patients who accrued RD over the course of their disease. In the univariate analysis, we found no difference between RD and RD-N patients in any of the following parameters: demographics, total count of ACR criteria at diagnosis and death, as well as damage at one year after diagnosis and cumulative non-renal damage at death. Compared to RD-N patients, RD patients had a higher proportion of malar rash at diagnosis (11/25 vs. 13/65, p=0.021) and a higher cumulative proportion of renal disorder (19/25 vs. 30/65, p=0.011), including proteinuria and urinary casts (17/25 vs. 23/65, p=0.005, for both). RD patients also had a higher proportion of myocardial infarction as an item of cumulative damage (7/25 vs. 6/65, p=0.023) and were more frequently obese (11/25 vs. 15/65, p=0.049). Conversely, hematological disorder and leukopenia at diagnosis were less frequent in RD compared to RD-N patients (4/25 vs. 30/65, p=0.008 and 1/25 vs. 21/65, respectively). In the final multivariate model (adjusted for gender, age at diagnosis and disease duration), malar rash at diagnosis and the cumulative presence of renal disorder (classification criteria of the ACR) were positively associated with RD. Conversely, leukopenia at diagnosis was inversely associated with RD (Figure 1).

Variable	OR	95% CI	p
Malar rash (dg)(yes/no)	**27.416**	**3.586-209.620**	**0.001**
Leukopenia (dg)(yes/no)	**0.016**	**0.001-0.273**	**0.004**
Renal disorder (cum)(yes/no)	**7.141**	**1.091-46.760**	**0.040**
Myocardial infarction (cum)(yes/no)	6.117	0.319-117.197	0.229
Obesity (cum)(yes/no)	1.917	0.425-8.638	0.397
Male gender (yes/no)	1.913	0.335-10.916	0.465
Age (dg)(years, cont)	1.018	0.969-1.070	0.481
Disease duration (cum)(years, cont)	0.940	0.826-1.070	0.352

dg - at diagnosis, cum - cumulatively, yes/no - binary variable, cont - continuous variable

Figure 1. Features associated with renal damage (multivariate logistic regression model)

Conclusion: More than a quarter of deceased patients accrued RD. While malar rash at diagnosis may be associated with a higher likelihood of developing RD, early leukopenia may be associated with its lower likelihood in deceased patients.

REFERENCES
[1] Davidson A. Nat Rev Rheumatol. 2016;12:143-53.

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AB0544 ECHOCARDIOGRAPHIC CHANGES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS BEFORE TO INITIATION OF IMMUNOSUPPRESSIVE THERAPY

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Background: Cardiovascular diseases are becoming the leading cause of death among SLE patients due to increasing life-spans. Transthoracic echocardiography (TTE) is a routine and widely available modality in everyday clinical practice useful to identify specific pathological cardiac changes and predictors of heart failure (HF).
Objectives: Obtaining of specific TTE findings in SLE patients prior to initiation of pathogenic immunosuppressive therapy was the objective in this study.
Methods: Thirty four pts (91% females, aged 30[26-34]years (median [interquartile range 25%-75%]) with "non-treated" SLE (ACR 1997 and SLICC 2012 criteria) were included. None of pts was treated either with prednisone or cytotoxic drugs at the moment of inclusion.
Results: Median SLE duration was 18[6-60]months, SLEDAI-2K - 13[8-19], SLICC/DI - 0[0-0]scores. Leading SLE clinical manifestations included: hematological changes (74%), kidney involvement (59%), joints (50%) and skin involvement (50%). Immunological abnormalities were detected in all patients and were as follows: ANA positivity – in 100%, anti-dsDNA antibodies – in 76% of SLE patients. Concurrent antiphospholipid syndrome was found in 2(6%) patients. Valve insufficiency with varying degree of regurgitation was the commonest pathology found in "non-treated" SLE patients based on TTE data: mitral valve insufficiency – in 31(91%), tricuspid valve – in 31(91%), pulmonary valve insufficiency – in 21(62%), aortic valve insufficiency – in 4(12%) patients. Endocarditis was a rare pathology found in 5(15%) patients, while mitral and tricuspid valves prolapse was seen more often – in 16(47%), while not a single case of valve stenosis was found. Pericardial pathology was detected in 16(47%) patients: exudative – in 9(26%), and adhesive (thickening, hardening and separation of leaflets) – in 7(21%).
There were no cases of CAD or MI, although there were 2(6%) documented cases of cerebral stroke in past history, and 1(3%) case of confirmed CHF. Most common TRF were dyslipidemia and hypertension - in 15(44%) and 11(32%) SLE patients respectively.
Median LVEF was 64[59-67]%, LV end-systolic dimension– 30[27-32]mm, LV end-diastolic dimension – 48[45-51]mm, pulmonary artery systolic pressure – 24[22-32]mm Hg. LV diastolic disfunction (LVDD) was found in 10 (29%), systolic dysfunction (LVSD) – in 4(12%), LV myocardial hypertrophy (LVH) – in 5(15%); left atrium dilatation (LAD) was found in 4(12%), and increased dimensions of right atrium was detected in 3(9%) SLE patients.
Conclusion: Most common cardiac abnormalities in "non-treated" SLE patients with high activity (SLEDAI-2K 13 scores) were valve dysfunction (insufficiency with regurgitation), mitral and tricuspid valve prolapse and pericarditis. Of importance is the presence of early subclinical features of HF almost in 1/3 of naïve to treatment SLE patients: LVDD (29%), LVH (15%), and LAD (12%). SLE patients should be thoroughly monitored both for adequate control of SLE activity, and cardiac pathology with correction of TRF, regular assessments by a cardiologist, TTE, and early administration of cardio-protection therapy in view of increased HF risk in SLE patients, predetermining unfavorable prognosis.
Disclosure of Interests: None declared
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AB0545

DYNAMICS OF N-TERMINAL FRAGMENT OF BRAIN NATRIURETIC PEPTIDE PROGENITOR LEVEL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, WITHOUT HEART FAILURE SIGNS BEFORE AND AFTER IMMUNOSUPPRESSIVE THERAPY

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Background: Cardiovascular mortality is increased in systemic lupus erythematosus (SLE). Elevated plasma concentration of N-terminal fragment of brain natriuretic peptide progenitor (NT-proBNP) is a laboratory marker of heart failure (HF), associated with cardiovascular morbidity and mortality in the general population.
Objectives: To measure NT-proBNP serum levels in SLE patients without HF signs before initiation of the therapy. To monitor NT-proBNP levels during therapy up to achieving SLE remission.
Methods: The study included 15 patients (87% females, aged 31[29-33] years (median [interquartile range 25-75%]) with untreated SLE (ACR 1997 and SLICC 2012 criteria) without HF. These were patients with a new-onset and long-standing disease, who discontinued administered therapy. The control included 39 healthy donors (27[24-44]years, 87% females). A comprehensive SLE patients' evaluation was made twice: at baseline and at the end of follow up (FUP), median FUP was 7[2-7] years. Serum levels of NT-proBNP (pg/ml) were measured using electrochemiluminescence method Elecsys proBNP II (Roche Diagnostics, Switzerland). Normal NT-proBNP levels should vary within ≤125pg/ml.
Results: At enrollment medial SLE duration was 1[1-7]years, SLEDAI-2K - 10[8-20], SLICC/DI - 0[0-1]scores, SLE patients had elevated (vs controls) values of NT-proBNP: 150,7[77,6-550,2] vs 44,6[29,7-66,91]pg/ml, *p<0,001,* NT-proBNP concentrations >125pg/ml were found in 8(53%) SLE patients without HF. Glucocorticoids and hydroxychloroquine were initiated in all patients, and additionally cyclophosphamide was administered in 7(47%) patients, mycophenolate mofetil – in 10(67%), azathioprine – in 5(33%), rituximab – in 3(20%). By the end of FUP patients' median age was 36 [34-39]years *p<0,001*, SLE duration - 8[7,5-11]years, stable remission was achieved in 14(93%) patients, a relapse of exacerbation was documented in 1(7%) patient, SLEDAI-2K - 2[0-4] *p<0,01*, SLICC/DI - 1[0-2]scores *p<0,05*, NT-proBNP levels were comparable to values in the control group: 26,6[19,3-64,9] vs 44,6[29,7-66,91]pg/ml, *p>0,05*, with only one case (7%) with NT-proBNP level >125pg/ml.
Median NT-proBNP concentration dropped from 150,7[77,6-550,2] to 26,6 [19,3-64,9]pg/ml, *p<0,001* when remission was achieved, therefore baseline rate of 53% of participants with elevated NT-proBNP concentration decreased to 7%, *p<0,01*. Patients achieving SLE remission on treatment also succeeded to normalize their NT-proBNP levels, and didn't show any signs of cardiovascular (CV) pathology or HF.
In "naïve" to treatment SLE patients NT-proBNP levels showed positive correlation with concentrations of creatinine (r=0,614, p<0,05), urea (r=0,614, p<0,05), and also with interventricular septum myocardial thickness (r=0,557, p<0,05), and showed negative correlation with glomerular filtration rate (GFR) (r=-0,579, p<0,05). There was no association between NT-proBNP levels and clinical & immunological SLE features, as well as markers of inflammation (CRP, IL-6, TNF-α), and TRF.
Conclusion: NT-proBNP concentrations in "untreated" SLE patients with high disease activity and without CV pathology and HF were significantly higher than in the control group *(p<0,001),* and more than 50% of these patients had elevated NT-proBNP (>125pg/ml) baseline concentration. Elevated NT-proBNP concentrations were associated with markers renal function (creatinine, urea, GFR). Adequate immunosuppressive therapy resulted in achievement of SLE remission and normalization of NT-proBNP concentrations.
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AB0546

IS IMMUNOLOGICAL PROFILE THE PRIMARY DRIVING FORCE BEHIND CLINICAL PICTURE OF SJÖGREN SYNDROME?

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Background: Primary SS (pSS) is a unique autoimmune disorder with a diverse spectrum of clinical and serological manifestations. Multiple clinical and laboratory determinants have been suggested to affect disease progression. Among these, early-onset (up to 35 years) has been proposed to indicate more severe disease[1].
Objectives: To determine possible clinical and laboratory differences between pSS patients diagnosed at 35 years or younger and those diagnosed after the age of 35.
Methods: We analyzed a single-centre cohort of 228 adult patients with pSS. For 189 consecutive patients diagnosed between the years 2002 and 2008, the data were collected retrospectively from medical charts, while 39 consecutive patients diagnosed from 2016 to 2018 were followed prospectively. Clinical and laboratory data at diagnosis were collected as defined by ESSDAI. The patients were monitored for new organ involvement during the follow-up period. Categorical variables were compared between those diagnosed ≤ 35 years and after 35 years using the χ^2-test or Fisher's exact test. Continuous variables were compared using the Mann-Whitney U test. A multivariate logistic regression model was used to test the association between early- and over 35 years-onset pSS, anti-SSA positivity, baseline ESSDAI, the duration of follow-up period and the progression of pSS defined as new organ involvement during the follow-up period.
Results: All patients in our cohort fulfilled the 2002 classification criteria [2]. There were 24 (87.5% female, median age 32.5 (IQR 29-34)) early-onset patients and 204 (92.9% female, median age 59 (IQR 51-67)) patients diagnosed after the age of 35. The patients were monitored for new organ involvement during the follow-up period ((6.5 (IQR 3-13) years in the early-onset group and 5 (IQR 2-10) years in the > 35 years group). The early-onset group presented with a significantly higher frequency of salivary gland enlargement (25.0% vs 7.8%, p = 0.017), cutaneous involvement (25.0% vs 5.9%, p = 0.006) cryoglobulinaemia (37.5% vs 12.3%, p<0.004), RF positivity (50% vs 25.5%, p <0.028), anti-SSA positivity (87.5% vs 51.5% (p<0.001) and anti-SSb positivity (50% vs 22.8% (p<0.004). The presence of anti-SSA (odds ratio (OR) 3.93, 95% CI 1.69–9.12, p=0.001), and longer period of follow-up (OR 1.16, 95% CI 1.09–1.25, p<0.001), but not early onset of pSS (OR 0.68, 95% CI

Case	Age (years)	SLE evolution time	SLEDAI	Diarrhea	Abdominal pain	Vomit	Sickness	Fever
1	29	12 years	29	0	1	1	1	0
2	24	2 years	24	1	1	1	0	1
3	25	4 years	25	1	1	0	0	0
4	23	1 years	23	1	1	0	0	0
5	16	6 months	16	1	1	1	1	0
6	22	8 months	23	1	1	0	1	0

ANA	AntiDNAds	C3	C4	CRP mg/dl	Leukocytes	Hemoglobin (g/dl)	Creatinine (mg/dl)	Proteinuria	Kidney Biopsy	CT Findings	Treatment	Intestinal Biopsy
Homogeneous 1: 1280	NA	60	12	12.3	8.5	8.3	1.45	0.3 gr/lt	NA	Target Shooting	mPDN + CYC	NA
Homogeneous 1: 1280	NA	27	7.6	5.9	15.6	12	1.06	0.22 gr/lt	NA	Target Shooting	mPDN + CYC	NA
Fine speckled 1:320	NA	34.5	10	1.6	7.38	16	0.82	1 gr/lt	NA	Target Shooting	mPDN + MMF	NA
Homogeneous 1: 1280	NA	102.2	22	0.3	8.1	12.2	0.9	> 3gr/lt	NA	Target Shooting	mPDN + CYC	Rectal ampulla biopsy: Chronic non-specific mild colitis
Homogeneous 1: 1280	140 UI	29	8	0	2.6	11	0.55	3 gr/lt	III	Target Shooting	mPDN + CYC + RTX	NA
Homogeneous 1: 1280	NA	34	7	0.5	8.4	10.6	1.74	> 3gr/lt	III	Target Shooting	mPDN + CYC	NA

0.24–1.88, p=0.452), were independently associated with new organ involvement during the follow-up. There was a tendency for an association of higher ESSDAI at baseline with adverse outcome (OR 1.06, 95% CI 0.99–1.12, p=0.075).
Conclusion: Data from our cohort suggest that more aggressive disease course was associated with the presence of anti-SAA regardless of the age of pSS onset.

REFERENCES
[1] Anquentil C, et al. Rheumatology (Oxford). 2018 doi:10.1093/rheumatology/key392.
[2] Vitali C, et al. Ann Rheum Dis 2002;61:554–8.

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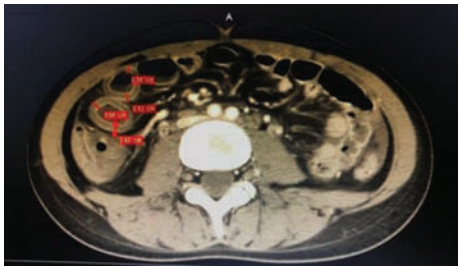
AB0547 LUPUS ENTERITIS SERIES OF CASES IN DEVELOPING COUNTRY: FROM CLINICAL FINDINGS TO THERAPEUTIC MANAGEMENT

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Background: The prevalence of lupus enteritis (LE) is 2% one of gastrointestinal manifestation of the involvement of the LES. The rapid onset of these symptoms requires determining the life-threatening conditions, but their detection becomes a challenge. We present a series of 6 cases of LE, the most clinical findings and limitations in our environment.
Objectives: Our objective was to describe six cases of lupus enteritis, its diagnostic challenge in our country with limited resources, frequent clinical presentations and its management.
Methods: We retrospectively reviewed the medical records of 6 patients in our hospital with a diagnosis of SLE according to SLICC ACR 2010 criteria between 2017-2018 for suspicion of lupus enteritis. we discard infectious etiology.

Case	Age (years)	SLE evolution time	SLEDAI	Diarrhea	Abdominal pain	Vomit	Sickness	Fever
1	29	12 years	29	0	1	1	1	0
2	24	2 years	24	1	1	1	0	1
3	25	4 years	25	1	1	0	0	0
4	23	1 years	23	1	1	0	0	0
5	16	6 months	16	1	1	1	1	0
6	22	8 months	23	1	1	0	1	0

ANA	AntiDNAds	C3	C4	CRP mg/dl	Leukocyt es	Hemoglobin (g/dl)	Creatinine (mg/dl)	Proteinuria	Kidney Biopsy	CT Findings	Treatment	Intestinal Biopsy
Homogeneous 1: 1280	NA	60	12	12.3	6.5	8.3	1.45	0.3 gr/h	NA	Target Shooting	mPDN + CYC	NA
Homogeneous 1: 1280	NA	27	7.5	5.9	15.6	12	1.06	0.22 gr/h	NA	Target Shooting	mPDN + CYC	NA
Fine speckled 1:320	NA	34.5	10	1.6	7.38	10	0.82	1 gr/h	NA	Target Shooting	mPDN + MMF	NA
Homogeneous 1: 1280	NA	102. 2	22	0.3	9.1	12.2	0.9	> 3gr/h	NA	Target Shooting	mPDN + CYC	Rectal ampulla biopsy: Chronic non-specific mild colitis
Homogeneous 1: 1280	140 UI	29	9	0	2.6	11	0.55	3 gr/h	H	Target Shooting	mPDN + CYC + RTX	NA
Homogeneous 1: 1280	NA	34	7	0.5	8.4	10.6	1.74	> 3gr/h	H	Target Shooting	mPDN + CYC	NA



Results: We describe 6 cases, all the patients were woman with a mean age of 23.1 years and an average of 3.6 years until the presentation of enteritis. The clinical symptoms included mainly abdominal pain (100%), vomiting (50%), diarrhea (83%), nausea (50%) and fever (16%). The laboratory characteristics mainly reflect the high lupus activity: SLEDAI 23 pts. Low levels of complement (83%), anemia (50%). The homogeneous pattern predominated in 83%, antiDNA was quantified only in one patient due to a lack of resources, with high titers. The median level of CRP was 3.3 mg/dL. Only two patients (33%) presented class III lupus nephritis by biopsy. In CT, the sign of target shot was present in all cases. Only 1 patient could be biopsied with non-specific chronic colitis. All patients received corticosteroids as first-line treatment, with additional immunosuppressants with significant improvement. One patient died due to pulmonary complications.
Conclusion: We should consider lupus enteritis as a possible initial digestive manifestation in patients with SLE. Its diagnosis requires a high index of suspicion, being the CT one of the fundamental pillars for the diagnosis. There is no consensus in the management, however, it was initiated with pulses of methylprednisolone, with limitations to request immunological studies and biological therapy due to economic implications.Finally, we emphasize the need for a prospective evaluation of this rare disease by encouraging the establishment of an international registry.

REFERENCES
[1] Li Z, Xu D, Wang Z, et al. Gastrointestinal system involvement in systemic lupus erythematosus. Lupus 2017; 26: 1127–1138.
[2] Yang C, Chen S, Gaut JP, Dehner LP. Smooth-muscle myopathy in systemic lupus erythematosus presenting with intestinal pseudo- obstruction. Am J Gastroenterol 2016; 111: 1501–1502

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AB0548 SELF-REPORTED NEUROPATHIC PAIN IN A COHORT OF PRIMARY SJOGREN'S SYNDROME

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Background: Although pain has been generally accepted being a cardinal symptoms of primary Sjogren's Syndrome (pSS), its cause remains unclear. It can be articular, muscular, neuropathic or related to fibromylagia. Neuropathic pain in pSS has often been associated with peripheral neuropathy, either small-fibre neuropathy or sensory neuropathies, one of the most common neurological complications of pSS.
Objectives: The aim of this work is to assess the prevalence and associated factors of self-reported neuropathic pain in a cohort of pSS.
Methods: Questionnaires for screening for neuropathic pain was giving out during routine clinic appointment. The first part of the questionnaire was adapted from the Neuropathic Pain Questionnaire – Short Form(1). The second part was adapted from the Neuropathic Pain Diagnostic Questionnaire (DN4)(2), but only including the self-reported items (7 items related to symptoms), which is scored with a cut-off value of $\geq$3/7.
Results: Data from 44 patients attending the Sjogren's clinic were analysed, yielding a female preponderance (86%), with a mean age of 59,6 years old. pSS disease duration on average 9,7 years, antibody positivity of 43% and 34% for anti-Ro and anti-La, respectively. 35 had salivary gland biopsy for diagnosis, the majority (48,6%) having a Focus Score (FS) of 1; 28,6% and 17,1% with FS of 2 and 3, respectively. Also worth mentioning 2 patients had lymphoma in the salivary gland biopsy (DLBC and MALT lymphoma). As for disease scores, ESSDAI mean was

2,5±4,1 and ESSPRI 5,8±2,5. A total of 10 patients (23%) had peripheral neuropathy.
For part I: 19 patients (43%) may have neuropathic pain. Overall, patients with neuropathic pain were similar to those without, even considering previous diagnosis of peripheral neuropathy. The exception was the ESSPRI score, in which patients with neuropathic pain had a higher score (6,9±2,4 vs 4,9±2,9, p-value 0.02). As for the individual components of the questionnaire: numbness mean was 37,2, tingling means was 33,7 and increased pain due to touch mean was the lowest with 25,5. None of them was significantly associated with ESSPRI.
For part II: 59% of patients may have neuropathic pain. Anti-Ro positivity was lower among patients with neuropathic pain (42% vs 58%, p-value 0.04), biopsy score distribution was different with a predominance of FS 1 in the group with neuropathic pain (88% vs 12%, p-value=0.03) and ESSPRI was again higher in patients with neuropathic pain (6,9±1,4 vs 4,5±2,9; p-value=0.008). Of the individual items: tingling and numbness, pins/needles and itching, burning, painful cold and electric shocks were reported in 57%, 48%, 45%, 34% and 27% respectively.
Finally, 36% (16) of the total of patients were positive for neuropathic pain for both parts of the questionnaire.
Conclusion: The prevalence of neuropathic pain appears to be common among pSS patients, in particular in seronegative patients and associated with lower focus score on salivary gland biopsy.
Interestingly, there was no association between neuropathic pain and the previous diagnosis of peripheral neuropathy. This may result of peripheral neuropathy no longer active, and therefore asymptomatic, but may also account for undiagnosed peripheral neuropathy in the group of neuropathic pain or other more general causes of neuropathic pain.

REFERENCES

[1] Backonja M-M, Krause SJ. Neuropathic Pain Questionnaire—Short Form. Clin J Pain. 2003;19:315–6.
[2] Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain. 2005;114(1–2):29–36.

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AB0549 NEUROPSYCHIATRIC DISEASE IN SYSTEMIC LUPUS ERYTHEMATOUS AND PRIMARY SJÖGREN'S SYNDROME: THE ADAPTATION OF A QUESTIONNAIRE

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Background: Systemic Lupus Erythematous (SLE) and Primary Sjögren Syndrome (pSS) are systemic autoimmune diseases, both associated with neurological and psychiatric manifestations. In SLE there are several questionnaires used for neuropsychiatric screening and evaluation, however for pSS there are no specific tools available. Their development is required in order to standardize symptom assessment and allow for accurate disease prevalence estimation.
Objectives: The main objective of this project is to assess the prevalence of neurological and psychiatric manifestations in our cohort of SLE and pSS patients through the adaptation to Portuguese of a screening questionnaire developed by Mosca et al 2010(1) and its relationship to quality of life.
Methods: A cross sectional study was performed by applying a screening questionnaire, adapted from Mosca et al (1), to patients with SLE and pSS. The outcomes were evaluated both as binary (neurologic (ND$\geq$9 pts) and psychiatric (PD$\geq$10 pts) disease versus no disease) and continuous variables (score average) and in relationship to demographic data, disease scores (SLEDAI and SLICC, and ESSDAI and ESSPRI) and a quality of life instrument (VAS score).
Results: A total of 70 participants (16 pSS and 54 SLE patients) participated in the study. Neurological disease was present in 63% and 48% and psychiatric disease in 25% and 15% of pSS and SLE patients, respectively. There was a statistically significant association between the presence of neurological and psychiatric disease and quality of life (pSS PD 20 vs 75, p-value 0.004; SLE ND 60 vs 80, p-value 0.001 and PD 50 vs 76.5, p-value 0.008). There was a trend for higher ESSPRI scores, with higher psychiatric scores (0.54 Spearman correlation coefficient; p-value=0.03). SLE higher neurological scores correlated with older age (0.34 Spearman correlation coefficient, p-value=0.01).
Conclusion: The questionnaire yielded a frequency of neurological and psychiatric disease similar to literature, as well as correlation to quality of life. This study represents the first step in the validation process for the Portuguese language but results should be regarded with caution considering this questionnaire was designed for screening and not for diagnosis.

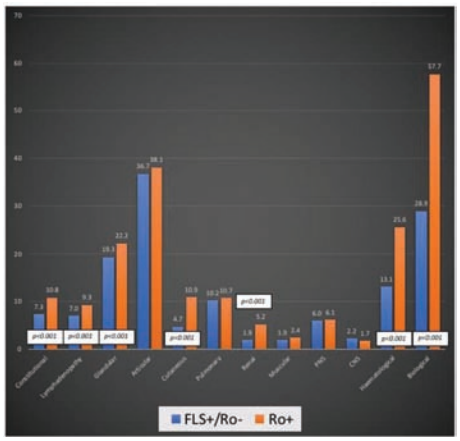
REFERENCES

[1] - Mosca M, Govoni M, Tomietto P, Aringer M, Boumpas D, Cervera R, et al. The development of a simple questionnaire to screen patients with SLE for the presence of neuropsychiatric symptoms in routine clinical practice. Lupus. 2011

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Disclosure of Interests: None declared
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AB0550 PHENOTYPE OF BIOPSY-PROVEN PATIENTS WITH PRIMARY SJÖGREN SYNDROME LACKING RO AUTOANTIBODIES: HIGH FREQUENCY OF DRYNESS SYMPTOMS WITH LOW SYSTEMIC ACTIVITY (BIG DATA SJÖGREN PROJECT)

Soledad Retamozo[1], Nihan Acar-Denizli[2], Wan Fai Ng[3], Ildiko Fanny Horváth[4], Astrid Rasmussen[5], Raphaèle Seror[6], LI Xiaomei[7], Chiara Baldini[8], Jacques-Eric Gottenberg[9], Pulukool Sandhya[10], Luca Quartuccio[11], Roberta Priori[12], Gabriela Hernandez-Molina[13], Berkan Armagan[14], Aike A. Kruize[15], Seung-Ki Kwok[16], Marika Kvarnstrom[17], Sonja Praprotnik[18], Damien Sene[19], Roberto Gerli[20], Roser Solans-Laqué[21], Maureen Rischmueller[22], Thomas Mandl[23], Yasunori Suzuki[24], David Isenberg[25], Valeria Valim[26], Agata Sebastian[27], Gunnel Nordmark[28], Hendrika Bootsma[29], Hideki Nakamura[30], Roberto Giacomelli[31], Valerie Devauchelle-Pensec[32], Benedikt Hofauer[33], Michele Bombardieri[34], Virginia Fernandes Moça Trevisani[35], Daniel Hammenfors[36], Sandra Pasoto[37], Tamer A. Gheita[38], Fabiola Atzeni[39], Jacques Morel[40], Cristina Vollenveider[41], Sandra Consani-Fernández[42], Xavier Mariette[6],Manuel Ramos-Casals[43,44]. *[1]IUCBC, INICSA-UNC-CONICET, Córdoba, Argentina*; *[2]Mimar Sinan Univ, Istanbul, Turkey*; *[3]Newcastle Univ, Newcastle, United Kingdom*; *[4]Debrecen Univ, Debrecen, Hungary*; *[5]OMRF, Oklahoma City, United States of America*; *[6]Université Paris Sud, INSERM, Paris, France*; *[7]Anhui Provincial Hosp, Hefei, China*; *[8]Pisa Univ, Pisa, Italy*; *[9]Strasbourg Univ, CNRS, Strasbourg, France*; *[10]Christian Med College and Hosp, Vellore, India*; *[11]Hosp "Santa Maria della Misericordia", Udine, Italy*; *[12]Sapienza Univ, Rome, Italy*; *[13]INCMNSZ, Mexico, Mexico*; *[14]Hacettepe Univ, Ankara, Turkey*; *[15]Univ Medical Center, Utrecht, Netherlands*; *[16]Catholic Univ of Korea, Seoul, Korea, Rep. of (South Korea)*; *[17]Karolinska Institute, Stockholm, Sweden*; *[18]Univ Medical Centre, Ljubljana, Slovenia*; *[19]Univ Paris VII Publique, Paris, France*; *[20]Perugia Univ, Perugia, Italy*; *[21]Vall Hebron, Barcelona, Spain*; *[22]Western Australia Univ, Crawley, Australia*; *[23]Malmö Hosp, Lund Univ, Lund, Sweden*; *[24]Kanazawa Univ Hosp, Ishikawa, Japan*; *[25]University College, London, United Kingdom*; *[26]Federal Univ Espírito Santo, Vitória, Brazil*; *[27]Wroclaw Medical Hosp, Wroclaw, Poland*; *[28]Uppsala Univ, Uppsala, Sweden*; *[29]Univ Medical Center, Groningen, Netherlands*; *[30]Nagasaki Univ, Nagasaki, Japan*; *[31]L'Aquila Univ, L'Aquila, Italy*; *[32]Brest Univ Hosp, CERAINO, Brest, France*; *[33]Technische Univ, München, Germany*; *[34]Queen Mary Univ, London, United Kingdom*; *[35]Federal Univ Sao Paulo, Sao Paulo, Brazil*; *[36]Haukeland Univ Hosp, Bergen, Norway*; *[37]Hospital das Clínicas, USP, São Paulo, Brazil*; *[38]Cairo University, Cairo, Egypt*; *[39]Messina and Milan Univ, Milan, Italy*; *[40]Montpellier Univ Hosp, Montpellier, France*; *[41]German Hosp, Buenos Aires, Argentina*; *[42]Hospital Maciel, UdelaR, Montevideo, Uruguay*; *[43]H. Clinic, IDIBAPS, Barcelona, Spain*; *[44]H. CIMA- Sanitas, Barcelona, Spain* **Objectives:** To analyze the clinical phenotype of primary Sjögren syndrome (SjS) with focal lymphocytic sialadenitis (FLS) without Ro autoantibodies (FLS+/Ro-).
Methods: The International Big Data Sjögren Project was designed in 2014 to take a "high-definition" picture of the primary SjS at diagnosis (2002 criteria) by merging international databases. 2716 FLS+/Ro- patients were compared with 8315 Ro+ patients



Results: FLS+/Ro- patients were predominantly White (82% vs 77%), had a higher frequency of oral (97% vs 92%) and ocular (95% vs 91%) dryness, a lower frequency of ANA (60% vs 87%), hypocomplementemia (13% vs 23%), rheumatoid factor (26% vs 56%), cryoglobulins (5% vs 9%), a lower mean ESSDAI score (4.6 vs 6.6), and a lower systemic activity in the constitutional, lymphadenopatic, glandular, cutaneous, renal, hematological and biological domains (p<0.001 for all comparisons). Abnormal salivary flows and ANA remained significant independent variables after adjustment by age and gender.

Conclusion: Biopsy-proven primary SjS with negative anti-Ro antibodies is characterized by high frequency of sicca symptoms, mild immunological profile and low systemic activity.

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AB0551 **SEXUALITY ASSESSMENT IN LATIN AMERICAN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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Background: The influence of systemic lupus erythematosus (SLE) in sexual behavior has been one of the less studied areas, being a forgotten part of quality of life, and not routinely evaluated by a rheumatologist. The seeming lack of interest in sexual problems is explained by the underlying difficulty to talk about this topic, the uncertainty of the role and capability of the rheumatologist to treat any difficulties in this area.

Objectives: Determine the prevalence of sexual assessment in women with SLE by their rheumatologist in the daily practice, as well as their characteristics and the possible difficulties that doctors deal with during this process.

Methods: A cross-sectional study, where women between 18 and 60 years with SLE diagnosis (according to SLICC 2012 criteria) were evaluated consecutively at the rheumatology clinic at Hospital Universitario "Dr. José Eleuterio González". 102 women with SLE were asked two questions: "Question 1. In the last year, has your rheumatologist asked about your sexual life?", and "Question 2. In case of having a trouble or disorder in your sexual life, would you ask your rheumatologist about it? (if not, why?)". Demographic and disease associated variables were analyzed with Chi-square test and Mann-Whitney U test.

Results: Baseline characteristics according to answers to each question are shown in Table 1. Most of the patients (62.74%, n=64) denied being asked about their sexual life in the last year; in this group, the prevalence of menopause was significantly higher than in the group that had been asked about this (30% vs 11%, p=0.025). Whilst, 82% (n=89) of patients said they were willing to talk about this topic with their doctor. The patients that answered "no" to the second question had the following characteristics: older age (45.5±10.5 vs 35.0±11.2 years; p=0.002), were in their menopause (46% vs 19%; p=0.042), had fibromyalgia (39% vs 10%, p=0.015), and had children (92% vs 64%, p=0.024). When asking the reason why they wouldn't ask, 70% (n=9) said they were ashamed to, 23% (n=3) ignored if this belonged to the rheumatologist and 7% (n=1) because of lack of time at consultation.

Table 1. Demographic characteristics.

	Question 1.			Question 2.		
	Yes (n=38)	No (n=64)	*p**	Yes (n=89)	No (n=13)	*p**
Age (years), mean ± SD	33.7 ± 9.0	37.9 ± 12.8	0.133	35.0 ± 11.2	45.5 ± 10.5	***0.002***
Menopause, n (%)	4 (10.5)	19 (29.7)	***0.025***	17 (19.1)	6 (46.2)	***0.042***
Has children, n (%)	25 (65.8)	44 (68.8)	0.757	57 (64.0)	12 (92.3)	***0.024***
Education (less tan 10 years), n (%)	19 (50)	39 (60.9)	0.281	48 (53.9)	10 (76.9)	0.118
Fibromyalgia, n (%)	5 (13.2)	9 (14.1)	0.898	9 (10.1)	5 (38.5)	***0.015***
Depression, n (%)	5 (13.2)	4 (6.3)	0.243	7 (7.9)	2 (15.4)	0.408

*- *p* value was obtained by Chi-square test. SD – Standard deviation.

Conclusion: Rheumatologists rarely approach or evaluate the sexuality topic with their patients. However, in our population, patients are willing to talk about this with their doctor. Sexuality must be assessed in all patients; but special attention must be paid to women with SLE and menopause, children, fibromyalgia and/or age over 35, because they're prone to not discuss this topic with their doctor.

REFERENCES

[1] Perdriger A, Solano C, Gossec L. Why should rheumatologists evaluate the impact of rheumatoid arthritis on sexuality? Jt Bone Spine. 2010;77:493-495. doi:10.1016/j.jbspin.2010.07.005

[2] Tseng J-C, Lu L-Y, Hu J-C, et al. The Impact of Systemic Lupus Erythematosus on Women's Sexual Functioning. J Sex Med. 2011. doi:10.1111/j.1743-6109.2011.02464.x

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AB0552 **25 HYDROXY-VITAMIN D LEVEL IN SYSTEMIC LUPUS ERYTHEMATOSUS: IS IT RELATED TO DISEASE ACTIVITY AND LUPUS NEPHRITIS?**

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. SLE is attributed to different autoimmune mechanisms leading to the production of several autoantibodies and formation of immune complexes with subsequent organ damage. 25 hydroxy-vitamin D3 (25(OH)D3) plays a significant role in immune system regulation and is an important immunomodulatory hormone involved in various biochemical reactions.
Objectives: Are to assess the levels of 25(OH)D3 in patients with SLE and to investigate the relationship between 25(OH)D3 levels and disease activity in patients with and without lupus nephritis.
Methods: 300 subjects were included in the study and were divided into 3 groups: group 1 consisted of 100 patients with SLE and lupus nephritis (LN), group 2 consisted of 100 patients free from LN and group 3 consisted of 100 healthy volunteers as a control group. All patients fullfilled the American College of Rheumatology criteria for diagnosis of SLE and were recruited from Internal Medicine department and out-patient clinics, Cairo University Hospital. Exclusion criteria included diseases and drugs which affect the endothelial function such as: smoking, diabetes mellitus, essential hypertension, and coronary artery disease and drugs such as nitrates, hypolipidaemic drugs and aspirin. Disease activity was evaluated by systemic lupus erythematosus disease activity index (SLEDAI). 25(OH)D3 was measured using ELISA. 25(OH)D3 level ≥30 ng/ml was considered as recommended, <30 ng/ml was considered as vitamin D insufficiency and <25 ng/ml was considered vitamin D deficiency.
Results: The mean value of 25(OH)D3 was significantly lower in patients with lupus nephritis (17.1±5.5 ng/ml) and those without lupus nephritis (16.6±5.9 ng/ml) than in controls (36.7±3.3 ng/ml) (p-value 0.001). Serum 25(OH)D3 level was inversely correlated with the duration of SLE disease (r -0.676, p-value <0.001) and with the duration of lupus nephritis (r -0.363, p-value<0.001). There was strong negative correlation between 25 (OH)D3 levels and serum urea, creatinine, ANA titre, anti-dsDNA titre, C3 and C4. 25(OH)D3 level was negatively correlated with, ESR, CRP and SLEDAI score (r=-0.811, p-value=0.001). There was also highly significant negative correlation between 25(OH)D3 level and prednisolone dose, hydroxychloroquine, cyclophosphamide and mycophenolate mofetil but not with NSAIDs.
Conclusion: 25(OH)D3 levels are markedly lower in patients with SLE. Low 25(OH)D3 levels are significantly correlated with disease activity parameters, disease duration and disease treatment.

REFERENCES

[1] Mok CC. Emerging biological therapies for systemic lupus erythematosus. Expert Opin Emerg Drugs. 2014;19(2):303–22.
[2] Yeap SS, Othman AZ, Zain AA, Chan SP. Vitamin D levels: its relationship to bone mineral density response and disease activity in premenopausal Malaysian systemic lupus erythematosus patients on corticosteroids. Int J Rheum Dis. 2012;15(1):17–24.
[3] Borges MC, Martini LA, Rogero MM. Current perspectives on vitamin D, immune system, and chronic diseases. Nutrition. 2011;27(4):399–404.

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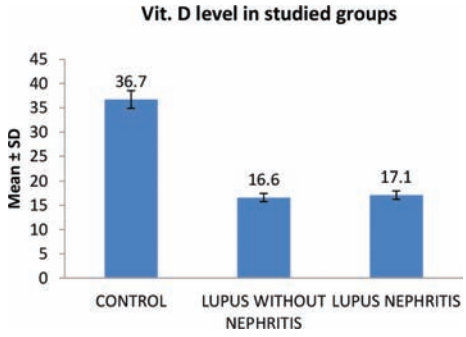


Figure 1. Level of serum 25(OH)D3 in patients with SLE and controls:

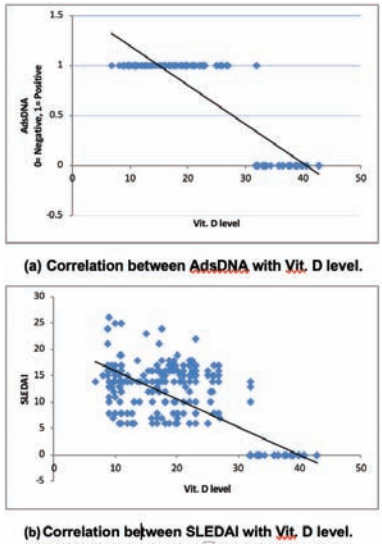


Figure 2. Correlation between 25(OH)D3 levels and SLEDAI and anti-ds DNA

Table 1. 25(OH)D3 levels and SLEDIA in patients with and without lupus nephritis

SLEDAI grade	25(OH)D3 level				
	WITHOUT LUPUS NEPHRITIS		LUPUS NEPHRITIS		P- value
	<30	≥30	<30	≥30	
Mild (1-5)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0.001**
Moderate (6-12)	4(100.0%)	0(0.0%)	69(98.6%)	1(1.4%)	
Severe (13-20)	94(97.9%)	2(2.1%)	30(100.0%)	0(0.0%)	

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AB0553 **STUDY OF ANXIETY AND DEPRESSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)**

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Methods: Cross-sectional study of a cohort of patients with SLE.All patients with SLE who had been included in the IMPARTs project(Integrating Mental and Physical healthcare:Research,Training and Services) were recruited between 2012-2016.All patients filled out the following questionnaires on a tablet device:PHQ9(Patient Health Questionnaire) (Scores of 10 or more have an sensitivity and specifity close to 90% for major depression) and GAD-7(7-item Generalized Anxiety Disorder)(Scores of 10 or more have an sensitivity and specifity close to 89% and 82% for GAD).Variables:demographic, duration of the disease(months)and the profile of autoantibodies.Previous history of depression or anxiety. SLEDAI,treatments,ESR, CPR,C3 and C4.Statistical analysis:descriptive, bivariate using T-Student and $\chi 2$.

Table 1

Variables	
Sex (female),*n (%)*	76 (91.6)
Age (years),median(IQR)	41 (18)
Race,n(%)	
White	12 (14.5)
Black	55 (66.3)
Asiatic	6 (7.2)
Other	10 (12)
Smoker,*n(%)*	13 (15.6)
Duration of the disease (months),median(IQR)	116 (112)
SLEDAI,median(IQR)	2 (4)
ESR,median(IQR)	25 (42.5)
CRP,median(IQR)	2 (7.32)
ANA,*n(%)*	82 (98.8)
dsDNA,n*(%)*	36 (46.8)
Anti-SM,*n(%)*	37 (44.6)
AntiRNP,*n(%)*	41 (49.4)
Anti-SSA 52 kD,*n(%)*	18 (26.9)
Anti-SSA 60 kD,n*(%)*	29 (43.3)
Anti-SSB,*n(%)*	14 (16.9)
Anti cardiolipin,*n(%)*	17 (20.5)
Anticoagulante lúpico,*n(%)*	7 (8.4)
Anti Beta-2-gicoproteina,*n(%)*	1 (1.2)
Treatments	**n (%)**
HCQ	83 (64.3)
MTX	9 (10.8)
AZA	11 (13.3)
CF	1 (1.2)
Micofenolic acid	25 (30.1)
Steroids	41 (49.4)
Rituximab	3 (3.6)
Mepacrine	3 (3.6)

Results: A total of 129 patients with SLE were included.Clinical characteristics in Table 1.38 patients (29.5%)had some degree of major depression and 27(20.9%)generalized anxiety disorder(Table 2).The prevalence of major depression was higher in patients with anti RO52(42.3%vs23.8%, p=0.06),with generalized anxiety (81.5%vs 15.7%,p<0.001)and in patients with black(35.2%vs 17.1%,p=0.03).The prevalence of generalized anxiety was higher in smokers(35%vs18.3%,p=0.09),patients receiving antidepressant treatment(57.1%vs13.9%, p<0.001)and patients taking azathioprine (36.8%vs18.2%,p=0.06).The prevalence of both major was higher in those who had higher fatigue and VAS higher(mean67.1s44.8 and 60.8vs32.3 in major depression, respectively; p<0.001) (65.3 vs 48.1 and 60.74 vs 35.4 in generalized anxiety respectively, p<0.001).The SLEDAI,ESR, duration of the disease and age were associated with generalized anxiety in a non-significant way.CRP,ESR and the duration of the disease were higher in patients with major depression

Table 2

Variables	n (%)
Previous depression	23 (17.8)
Antidepressants	17 (13.2)
GAD 7 total	
>15:Severe Anxiety Disorder	20 (15.5)
>10:Moderate Anxiety Disorder	7 (5.4)
>5:Mild anxiety disorder	12 (9.3)
PHQ 9 total	
>20:Severe major depression	11 (8.5)
>15:Moderately Severe Depression	20 (15.5)
>10:Moderate major depression	7 (5.4)
>5:Mild depression	7 (5.4)

Conclusion: The prevalence of anxiety and depression in our group of patients was high,both related, as well as with the perception of pain and fatigue.A correct assessment of these manifestations and early treatment could help improve the quality of life of patients

Disclosure of Interests: None declared
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AB0554 RISK OF CORONARY ARTERY DISEASE AND STROKE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS USING JAPANESE HEALTH INSURANCE DATABASE

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Background: Patients with systemic lupus erythematosus (SLE) have higher risk of coronary artery disease (CAD) and stroke than the general population [1-2]. Because these comorbidities influence on patients' vital prognosis and quality of life, it is essential for rheumatologists to manage them appropriately. Considering differences in life style and ethnicity, it is of great interest and needed to investigate risk of these comorbidities in Asia. However, to date, such evidence is scarce.
Objectives: To estimate incidence rate (IR) and identify risk factors of CAD and stroke in patients with SLE using a Japanese health insurance database.
Methods: This retrospective longitudinal population-based study was conducted using claims data provided by Medical Data Vision Co., Ltd (Tokyo, Japan). We defined individuals as SLE cases if they met all of the following: 1) had at least one ICD10 code (M321 or M329); 2) had at least one prescription of oral corticosteroids (CS), methylprednisolone (mPSL) pulse therapy, immunosuppressive drugs (IS) (azathioprine, mizoribine, tacrolimus, mycophenolate mofetil, cyclophosphamide, methotrexate), biologics (belimumab, rituximab) or hydroxychloroquine between April 2008 and July 2017; 3) were 16 years old or over. The start of observation was defined by the first month in which cases met all of the above criteria. Patients were followed until the earliest of date of first CAD event or stroke, date of loss of follow-up, or the end of follow-up (June 2018). CAD and stroke were defined as follows: for CAD, at least one ICD10 code (I20.x or I21.x or I23-24.x) and either percutaneous coronary intervention, coronary artery bypass procedure, or thrombolytic agents during hospitalization: for stroke, at least one ICD10 code (I60-62.x or I63-64.x) and either cerebrovascular procedures, thrombolytic agents, or antiplatelet drugs during hospitalization. Patients were excluded if they had a previous diagnosis of CAD or stroke and were prescribed antiplatelet drugs or anticoagulants during the first 3 months. We defined baseline characteristics using the data from the first 3 months, and calculated IR and adjusted hazard ratio (HR) of risk factors for CAD or stroke after adjusting for baseline characteristics using a Cox proportional hazard model.
Results: In this study, 19,138 cases were included. The median age was 53 years and 81.3% were female. Median observation period was 3.1 years. IR [95% CI]/1,000 patient-years (PY) of CAD or stroke was 1.41 [1.11-1.77] and 4.10 [3.56-4.70], respectively. IR of any CAD or stroke was increased age-dependently (2.06 [1.47-2.80] for 16-39 years-old, 5.07 [4.36-5.86] for 40-69, 13.0 [10.9-15.5] for 70-). Adjusted HR [95% CI] was 1.37 [95% CI, 1.27-1.47] for age by decade, 3.34 [1.78-6.28] for CS use, 1.46 [1.16-1.84] for presence of hypertension (HT), 1.38 [1.04-1.85] for diabetes mellitus (DM), 1.73 [1.25-2.38] for chronic kidney disease (CKD), and 1.95 [1.15-3.32] for atrial fibrillation (AF).
Conclusion: This is the first study investigating the risk of CAD or stroke in Japanese patients with SLE using a large health insurance database. Older age, use of CS, and presence of HT, DM, CKD, and AF were identified as significant risk factors of these comorbidities.

REFERENCES

[1] Am J Cardiol. 2004:198-200
[2] Arthritis Rheum 2009:1396-1402

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AB0555 POTENTIAL ROLE OF PAROTID ELASTOGRAPHY IN DIAGNOSIS AND CLASSIFICATION OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Despite the improvements in classifying patients with primary Sjögren's syndrome with usage of the new 2016 ACR/EULAR classification criteria, there remains to be a need for improvement and investigating the value of new modalities in diagnosing as well as classifiying these patients.

Objectives: to investigate potential role of parotid elastography in diagnosis and classification of patients with primary Sjögren's syndrome (pSs)

Methods: This is a cross sectional analysis of patients with primary Sjögren's syndrome followed up in our out-patient Rheumatology clinic. We performed chart reviews and retrospectively investigated the available data on files to search whether or not our clinically diagnosed patients satisfied the 2002 AEG and/or 2016 ACR/EULAR criteria sets. Ultrasonographic and elastographic evaluation of parotid and submandibular glands bilaterally were performed on consecutive patients with clinical diagnosis of pSs and contributions of these findings to classification criteria sets were interpereted

Results: There were 95 pSs patients and 30 healthy gender and age matched controls. Strain ratio, shearwave velocity and Pascal values of the glands were examined. Parotid strain ratio, submandibular velocity and submandibular pascal values were statistically significantly different compared to healthy controls (Table).%86 of patients considered clinically as Sjögren syndrome satisfied 2016 ACR/EULAR (criteria patients) and% 84 satisfied 2002 AER classification criteria. We grouped patients with respect to parotid strain ratio taking 1.0875 as the cut-off value. Those patients who did not satisfy 2016 ACR/EULAR criteria, but clinically diagnosed as pSs (non criteria pSs patients), also had significantly higher parotid strain ratio and submandibular velocity compared to healthy controls (p:0,016 and p<0,001 respectively). Interestingly, both criteria and non-criteria pSs patients had similar parotid strain ratio and submandibular velocity value (p:0,892 and p:0,260, respecitively)

Conclusion: Parotid shear elastography is an easy and nonivasive method and can be a useful tool for the diagnosis and classification of patients with pSs (1).

REFERENCES

[1] Mossel E, Delli K, van Nimwegen JF, Stel AJ, Kroese FGM, Spijkervet FKL, Vissink A, Arends S, Bootsma H; EULAR US-pSS Study Group. Ultrasonography of major salivary glands compared with parotid and labial gland biopsy and classification criteria in patients with clinically suspected primary Sjögren's syndrome Ann Rheum Dis. 2017 Nov;76(11):1883-1889. doi: 10.1136/annrheumdis-2017-211250

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AB0556 PARTICULARITIES OF PULMONARY HYPERTENSION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that primarily affects young women. It is characterized by the production of autoantibodies and immune complexes. Vascular pulmonary involvement has long been considered rare, a consequence of thromboembolic events. It is in fact a proper entity, often of multifactorial mechanism, with spontaneous evolution to pulmonary arterial hypertension (PAH), which makes its gravity

Objectives: The objective of our study is to determine the particuliarities of PAH during SLE.

Methods: We conducted a mono-centric, retrospective and descriptive study of the follow up of patients in the internal medicine department of the Military Hospital of Tunis for LES (diagnosis according to the ARA criteria) between January 2010 and December 2015.

All patients underwent external echocardiography or during their stay in the department

Results: We collected 87 patients diagnosed with SLE. PAH was recorded in 16 patients (38%) including 6 men and 10 women with a F/M sex ratio of 1.66. The average age was 37.23 years with extremes ranging from 16 to 70 years old. Clinically, we observed dyspnea in 10 patients (62%), chest pain in 7 cases (43%), dry cough in 2 cases (12%), palpitations in 1 case (6%),%) and right heart failure in 1 case (6%). At cardiac auscultation, 5 patients were tachycardic (31%), 5 had a tricuspid systolic murmur and 1 had an irregular rhythm. A burst of B2 in the pulmonary focus was noted in 3 patients (18%). Nine of the 16 patients with PAH had electrical signs: five had sinus tachycardia (31%), two had signs of right ventricular hypertrophy. A complete arrhythmia with atrial fibrillation was noted in one patient. The chest X-ray showed cardiomegaly in 6 patients (37%). Among the 16 patients, there was a tricuspid valve insufficiency associated with PAH in 7 patients (43%), 2 had mitral valve insufficiency (12%), 6 patients had pericarditis, one patient had endocarditis (6%) and myocarditis was found in another one (6%). PAH was isolated in 12% of cases. In Immunological tests, NAAs were positive in all patients. Three quarters of the patients (12) had native anti-DNA positive (75%) and ¼ of the patients (4) had anti-Sm positive and anti-RNP positive antibodies (25%). The complement was consumed in 5 cases (31.2%). Anti-phospholipid antibodies were noted in 4 cases (25%). Added to non-specific measures (smoking cessation, elimination of intense physical effort ...) adopted for all patients, oxygen therapy was indicated in four patients. Diltiazem 180 mg/day vasodilator therapy was prescribed in 3 patients. Effective anti-vitamin K anticoagulation was prescribed in a patient with severe PAH at 80 mmHg.

Conclusion: Pulmonary arterial hypertension (PAH) is a rare complication of systemic lupus erythematosus, its prevalence varies from 0.5 to 17.5% depending on the series. SLE is the second leading cause of PAH in connective tissue disease after systemic sclerosis. This vascular involvement is essential for the prognosis and is an important evolutionary step in the management.

Disclosure of Interests: None declared

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AB0557 NON-CORONARY CARDIAC MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN ADULTS

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Background: Systemic lupus erythematosus (SLE) is a common chronic multi-system autoimmune disorder of unknown etiology causing injury to many organ Systems. It predominantly affects young women. Cardiac manifestations develop in the majority of patients with SLE at some time during the course of their disease.

Objectives: The aim of our study is to assess cardiac abnormalities in patients with systemic lupus erythematosus (SLE) by echocardiography and to compare the 2 groups of patients with and without cardiac manifestations.

Methods: We have performed a transversal, descriptive study of SLE patients hospitalized in the Internal Medicine department at the Military Hospital of Tunis between January 2016 and June 2018. Diagnosis of SLE was made according to the criteria of ACR. All patients underwent a cardiac ultrasound externally or during their stay in our department.

Results: The patients were 61 females and 19 males (sex-ratio=3) with a mean age of 38 years.
Fourty two patients had cardiac involvement. They were 33 female and 9 male with a mean age of the disease of 31,8 years (16-80 years) at the beginning of the disease and 41 years at the time of the study.
83% of patients were symptomatic. The symptoms were dominated by objectified chest pain (43%). In Doppler echocardiography, pericarditis was found in 23 patients (55%) with a single case of cardiac tamponade. Libman Saks endocarditis and lupus myocarditis were found in one case each. Pulmonory hypertension (HTP) was observed in 16 patients (38%) and valvular disease in 22 patients (52%). Cardiomegaly was observed in 9 patients (21%). Electrical abnormalities were dominated by microvoltage found in 8 patients. The general symptoms (83%), skin lesions (76%) and musculoskeletal involvement (64%) were the most frequent events associated with the cardiac manifestations in group 1. ANA were positive in 97% of cases and antiphospholipid antibodies in 24%. Prednisone: 1mg/kg/day and immunosuppressive therapy were indicated respectively in 71% and 38% of patients.
Conclusion: Cardiac abnormalities are very common in lupus patients even when clinically asymptomatic. SLE is among systemic diseases most providers of heart disease. Echocardiography is an excellent non-invasive tool for cardiac evaluation. Their research must be systematic with echocardiography in order to reduce subsequent cardiac morbidity and mortality among the lupus patients.
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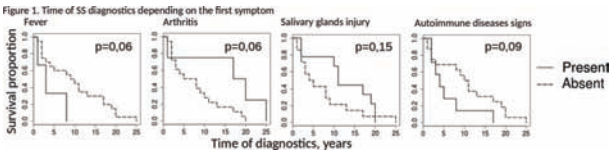
AB0558 TIME OF DIAGNOSTICS OF SJOGREN'S SYNDROME DEPENDING ON ITS FIRST MANIFESTATION

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Background: Sjogren's syndrome (SS) is a rare autoimmune disease with multisystem manifestations. Diagnostics of SS is intricate due to its low prevalence and deed of invasive tests for diagnosis confirmation.
Objectives: To investigate influence of the first symptom of SS on the time of diagnosis establishment.
Methods: The study was conducted at Dnipropetrovsk Mechnikov Regional Hospital, Dnipro, Ukraine. 23 patients (1 male and 22 females, mean age 54 [47;61] years) with SS that received medical care at Rheumatology Department from 2007th to 2017th were enrolled to the study. Diagnosis of SS was provided according to American-European Consensus Group criteria (2002). We analyzed time from the first symptom appearance to diagnosis of SS establishment. Symptoms of the disease onset were classified into 4 groups: fever (body temperature>37 C), arthritis (swelling and/or tenderness of $\geq$1 joints), signs of salivary glands injury (swelling of salivary glands, dry mouth syndrome) and other signs of autoimmune diseases (Rhaynaud's phenomenon, rash, myalgia).
Results: Median time between the first symptoms and SS diagnostics was 8 [2;17] years. Time to SS diagnostics depending on the first manifestation is in the table below.

Table 1. Time of SS diagnostics depending on the first symptom.

Symptom	Present	Absent	Log-rank test (p)
Fever	3 [1;8]	9,5 [2,2;17]	0,06
Arthritis	17 [6;22,5]	6,5 [2;11,5]	0,06
Salivary glands injury	11 [6;19,5]	4,5 [2;10]	0,15
Symptoms of autoimmune diseases	4 [2;8]	10,5 [2;18]	0,09



Presence of fever or symptoms of autoimmune diseases led to faster diagnostics of SS. Presence of salivary glands injury didn't influence time of SS diagnostics, while arthritis enlarged it (Figure 1).

Conclusion: Fever and signs of autoimmune diseases may be useful in diagnostics of SS. Greater alertness of symptoms of salivary glands injury is needed.

REFERENCES

[1] Vitali C, Bombardieri S, Jonsson R, et al. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis. 2002;61 (6):554-8.

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AB0559 ASSOCIATED FACTORS AND PREVALENCE OF OSTEONECROSIS IN A COHORT STUDY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) FROM HOSPITAL DEL MAR/PARC DE SALUT MAR.

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Background: Although the pathophysiology of osteonecrosis (ON) is not completely well-understood, it is likely the result of multiple combined effects such as environment, metabolic or genetic factors.
Clinical presentation of ON may be silent or may appear in a variable range of gradual-onset pain. The prevalence of ON in patients with SLE varies according to whether the lesions are symptomatic or asymptomatic.
Corticosteroid therapy (CT) has been recognized as a main risk factor to develop ON. Nevertheless, it looks like ON is more frequent in patients with SLE than in any other disease requiring systemic CT, which suggests that the use of corticosteroids may not be the only risk factor in those patients.
Objectives: To evaluate the prevalence of ON and to determine the association between ON and other variables such as sociodemographic factors, cardiovascular risk factors, SLE symptoms, autoimmunity, treatment received and disease activity in patients with SLE from Hospital del Mar.
Methods: 177 medical records were reviewed. Inclusion criteria included patients with SLE that met at least 4 of 11 ACR-LUPUS criteria revised in 1982 and updated in 1997. We identified six ON cases. The ON variable was evaluated by nuclear magnetic resonance in symptomatic patients. Afterwards, we matched ON patients with controls according to age and gender in a 1:2 proportion.
A bivariate descriptive analysis between cases and controls was made including demographic and clinical variables, cardiovascular risk factors and treatment received. The association between ON and the previously mentioned variables was evaluated by Fisher's Exact test and Chi-square test.
Results: The prevalence of ON was 3.4% (CI 95%: 0.01% - 0.07%), lower than that described in other series. We found statistical significance association between ON and arterial hypertension (patients with ON and hypertension: 62.5% vs patients with ON without hypertension: 10%; p-value 0.043), as well as between ON and CT evaluated by its presence in the last hospital follow-up (patients with ON under CT: 100% vs patients with ON without CT: 20%; p-value 0.025). The association between ON and the use of corticosteroid pulse therapy (CPT) was also statistical significance (patients with ON who received CPT: 80% vs patients with ON who did not receive CPT: 15.3%; p-value 0.022). Finally, we found a marginal association, although relevant, between ON and the SLICC damage index (p-value 0.057) (Table/Fig-1).
Conclusion: We found a statistical significance association between ON and hypertension (classical known cardiovascular risk factor) as well as between ON and CT (in the last visit) and the use of CPT (risk factor known as an etiological agent in ON). We did not find a statistical significance association between ON and lupus disease activity (SLEDAI), but a trend to statistical significance was noticeable with respect to the accumulated irreversible damage on lupus disease (SLICC). In order to confirm the results obtained, it is necessary to carry out other studies, with a larger sample and a longer follow-up period.
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TABLE/FIG-1. Demographic and clinical variables of our cohort and their association with ON.

Variables	CASES (6)	CONTROLS (12)	p-value
Gender:			
Female	5 (33.3%)	10 (66.6%)	1.00
Male	1 (33.3%)	2 (66.6%)	
Age*	32.50 ± 18.38	33.33 ± 11.83	0.511
Ethnic group:			
Caucasian	5 (35.7%)	9 (64.2%)	
Hispanic American	1 (33.3%)	2 (66.6%)	1.000
Afro-American	0 (0%)	0 (0%)	
Asian	0 (0%)	1 (100%)	
Body Mass Index (BMI) *	25.72 ± 2.38	22.89 ± 3.79	0.134
Smoking:			
Yes	0 (0%)	3 (100%)	0.312
Former smoker	2 (66.6%)	1 (33.3%)	
Dyslipidemia	2 (40%)	3 (60%)	1.000
Hypertension	5 (62.5%)	3 (37.5%)	**0.043**
Diabetes Mellitus	2 (100%)	0 (0%)	0.098
Photosensitivity	4 (33.3%)	8 (66.6%)	1.000
Oral ulcers	3 (60%)	2 (40%)	0.268
Arthritis	6 (37.5%)	10 (62.5%)	0.529
Pleuritis	0 (0%)	1 (100%)	1.000
Pericarditis	0 (0%)	2 (100%)	0.529
Leukopenia	3 (30%)	7 (70%)	1.000
Nephritis	2 (40%)	3 (60%)	1.000
Antinuclear antibody	5 (29.41%)	12 (70.59%)	0.333
Anti-dsDNA	3 (25%)	9 (75%)	0.344
Anti-Sm	0 (100%)	4 (100%)	0.245
Anti-SSA (Ro)	2 (28.57%)	5 (71.43%)	1.000
Anti-RNP	0 (0%)	4 (100%)	0.245
Hypocomplementemia	3 (25%)	9 (75%)	0.344
SLICC:			
0	2 (16.67%)	10 (83.3%)	
1	3 (60%)	2 (40%)	*0.057*
2	0 (0%)	0 (0%)	
3	1 (100%)	0(0%)	
SLEDAI *	2.33 ± 2.34	2.50 ± 2.28	0.883
APS associated	1 (50%)	1 (50%)	1.000
Corticosteroids (past YES/NO)	6 (35.2%)	11 (64.7%)	1.000
Corticosteroids (last visit YES/NO)	3 (100%)	0 (0%)	**0.025**
Corticosteroids pulses (YES/NO)	4 (80%)	1 (20%)	**0.022**

*: mean ± standard deviation.

AB0560

A 10-YEAR REVIEW OF DAMAGE ACCRUAL AND PROGRESSION IN A MULTI-ETHNIC COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN MALAYSIA

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Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with an unpredictable course of disease. The severity and outcomes of SLE vary across different ethnicities.
Objectives: This study is aimed to determine the pattern of development and progression of organ damage in a cohort of multi-ethnic SLE patients followed for at least 10 years, and to identify the factors associated with the damage accrual.
Methods: We reviewed the medical records of an inception cohort of patients who attended regular monitoring since 2007 at the Rheumatology and Nephrology/SLE Clinic, National University of Malaysia Medical Centre (UKMMC). Their medical records were retrospectively reviewed to obtain information on SLE disease characteristics, frequency of disease flares, cumulative corticosteroid dose and the use of other immunosuppressive treatment from 2007 until their last visit in 2017. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index (SDI) was used to determine the organ damage at baseline and after 10 years of being followed up. For patients who have succumbed or lost to follow up during the 10-year observation period, the SDI scores just before death or time of follow up loss were recorded.
Results: A total of 258 patients were included with majority of them were Malays (n=145, 56.2%), followed by Chinese (n=100, 38.8%) and Indians (n=13, 5.0%). The mean SDI score increased from 0.39±0.79 at baseline to 1.13±1.47 after 10 years, p<0.001. At 10 years, Indian patients were found to have a significant increase in their SDI scores from baseline compared to Malay and Chinese (p<0.05). New damage accrual was recorded in 38.8% patients with the most common new organ damage significantly occurred in renal (p<0.001), ocular (p=0.05) and cardiovascular (p=0.07). Higher age at baseline, higher ACR criteria at diagnosis, persistent active disease $\geq$ 6 months, and prednisolone use of $\geq$ 1mg/kg were independently associated with higher risk of damage accrual. In contrast, hydroxychloroquine treatment was associated with lower risk of damage accrual.
Conclusion: The SDI scores of our SLE cohort increased significantly over 10 years which predominantly affecting the renal. Indian patients accumulated higher SDI scores while persistent active disease, higher ACR criteria at diagnosis, and the use of high dose steroid were associated with new organ damage.

REFERENCES

[1] Bruce IN, O'Keeffe AG, Farewell V, et al. (2015) Factors associated with damage accrual in patients with systemic lupus erythematosus: results from the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort. Ann Rheum Dis 74(9):1706-13.
[2] Yee CS, Su L, Toescu V, et al. (2015) Birmingham SLE cohort: outcomes of a large inception cohort followed for up to 21 years. Rheumatology (Oxford) 54(5):836-43.

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AB0561

RISK FACTORS FOR ADVERSE PREGNANCY OUTCOMES AND LOW RISK FACTORS FOR ADVERSE PREGNANCY OUTCOMES AND LOW APGAR SCORES OF NEWBORNS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that occurs in women of childbearing age, and has high risk for adverse pregnancy outcomes (APOs) (1,2). Moreover, it is unclear whether maternal SLE influences the growth and development of children born from SLE mothers. Apgar scores at five minutes is a predictive factor of neurological development of newborns. However, there is no report about the association between maternal SLE and Apgar score of newborns.
Objectives: The aim of this study was to identify risk factors for APOs and for low Apgar scores of newborns from SLE mothers.
Methods: We investigated 50 SLE patients who were delivered from May 2006 to December 2018 in our institution. We examined retrospectively regarding APOs including spontaneous abortions, preterm births, premature rupture of membranes (PROM), light-for-date (LFD) newborns, and low Apgar scores of newborns. We analyzed the association between disease activity, laboratory findings, treatment agents, and APOs or Apgar scores.
Results: As for APOs of SLE mothers, cases with preterm births showed higher SLE disease activity index (SLEDAI) during the first trimester (P = 0.01) and higher titers of anti-double-stranded DNA (anti-dsDNA) antibodies at the time of conception (P < 0.01) compared to full-term births. In these cases, mean glucocortitcoid doses during pregnancy (P = 0.02) and the rate of treatment intensification (P < 0.01) was higher than full-term birth. In the mothers who delivered LFD newborns, serum complement levels at conception were lower than in those with non-LFD newborns (C3: P = 0.02; CH50: P = 0.05). Cases with spontaneous abortions and PROMs did not differ significantly from the cases without spontaneous abortions and PROMs. Apgar scores at one minute were correlated with SLEDAI during the third trimester (P < 0.01) and with the titer of anti-dsDNA antibodies at conception (P < 0.01). Additionally, Apgar scores at five minutes were correlated with the titer of anti-dsDNA

antibodies (P < 0.01). In multivariate analysis, there were significant association between Apgar scores at five minutes and the titer of anti-dsDNA antibodies (P < 0.01, Table 1).

Abstract AB0561 Table 1. Multivariate analysis of risk factor for Apgar score at 5 minutes

Variable	Standard β	P-value
SLEDAI at third trimester	0.361	0.05
C3 at conception	0.068	0.62
Anti-dsDNA antibody at conception	-0.964	< 0.01*
		(R^2=0.589, P<0.001)
Variable	**Standard β**	**P-value**
SLEDAI at third trimester	0.367	0.06
C4 at conception	0.047	0.74
Anti-dsDNA antibody at conception	-0.973	< 0.01*
		(R^2=0.589, P<0.001)
Variable	**Standard β**	**P-value**
SLEDAI at third trimester	0.400	0.03*
CH50 at conception	0.162	0.22
Anti-dsDNA antibody at conception	-0.969	< 0.01*
		(R^2=0.610, P<0.001)

Conclusion: In SLE, immunological abnormalities at conception, high SLEDAI and glucocorticoid doses were risk factors for preterm birth and having a LFD newborn. Apgar scores at five minutes were significantly associated with the titer of anti-dsDNA antibodies. Minimizing disease activity before pregnancy may decrease risks for mothers and their newborns. In preconception counseling, it is important for rheumatologists to explain these risk factors to patients with SLE who hope to conceive. There is a need for long-term follow-up studies focusing on the neurological development of children born from SLE mothers.

REFERENCES

[1] Clowse ME, Jamison M, Myers E, James AH. A national study of the complications of lupus in pregnancy. Am J Obstet Gynecol 2008;199:127.e1-6.
[2] Bundhun PK, Soogund MZ, Huang F. Impact of systemic lupus erythematosus on maternal and fetal outcomes following pregnancy: a meta-analysis of studies published between years 2001–2016. J Autoimmun 2017;79:17-27.

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AB0562 CARDIOVASCULAR RISK FACTORS AND FRAMINGHAM RISK SCORE IN PRIMARY SJÖGREN SYNDROME PATIENTS: A COMPARATIVE STUDY WITH MATCHED CONTROLS

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Background: The association between cardiovascular (CV) risk and chronic systemic inflammatory diseases has been an issue of debate. There is compelling evidence of increased CV morbidity in conditions such rheumatoid arthritis (RA) and systemic lupus erythematous (SLE) (1). Primary Sjögren's syndrome (pSS) is a chronic immune-mediated disease characterized by glandular and systemic manifestations, sharing clinical and immunological similarities with RA and SLE. However, in pSS patients the weight of cardiovascular disease attributed to traditional CV risk factors remains unclear.
Objectives: To determine the prevalence of traditional CV risk factors and long-term CV events based on the risk prediction tool of the Framingham risk score (FRS) in pSS patients.
Methods: The study included patients diagnosed with pSS, fulfilling both the 2016 ACR/EULAR and 2002 AECG criteria for the disease, followed-up at our Rheumatology department and 49 age and sex-matched controls. Inclusion criteria were age 30 to 74 and no history of CV events in order to calculate the FRS. In total, 46 out of 54 patients were eligible for the study. Data on the prevalence of traditional CV risk factors (diabetes, arterial hypertension and smoking), systolic blood pressure (SBP) values, total and high-density lipoprotein (HDL) cholesterol levels were collected and compared between groups. The 10-year risk for CV events according to FRS was calculated and means of patients and controls were compared. Parametric and nonparametric tests were used and the level of significance was defined as p<0.05.
Results: The mean age of pSS patients and healthy individuals was 58.0 ±11.6 and 54.1±13.6 years, respectively. The prevalence of arterial hypertension was higher in pSS patients than controls (52.2% versus 24.5%, p=0.005). The prevalence of diabetes and smoking did not differ significantly between the two groups (p=0.674 and p=0.949, respectively). The SBP values, total and HDL cholesterol levels were also similar between pSS patients and healthy subjects (p=0.063, p=0.413 and p=0.217, respectively).
Mean 10-years risk for CV events assessed by FRS was 11.8±8.3 for pSS patients and 7.8±8.4 for matched controls, with statistically significant difference (p=0.013).
Conclusion: In our study, pSS patients had a higher prevalence of arterial hypertension, which is in agreement with the M. Juarez *et al* (1) study. Although there were no significant differences in the other traditional CV risk factors, the results showed an increased 10-year risk for major CV events based on FRS assessment in pSS patients in comparison to age and sex-matched controls.

REFERENCES

[1] M. Juarez, et al. Cardiovascular Risk Factors in Women With Primary Sjogren's Syndrome: United Kingdom Primary Sjogren's Syndrome Registry Results. Arthritis Care & Research. Vol. 66, No. 5, May 2014, pp 757-764.

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AB0563 TRAUMA AND SLE-CONSIDERATIONS REGARDING A GROUP OF PATIENTS FROM ROMANIA

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Background: Systemic lupus erythematosus (SLE) represents a complex disease, which hasn't got a clear etiology established yet. Many genetic-susceptibility factors, environmental triggers, antigen-antibody (Ab) responses, B-cell and T-cell interactions, and immune clearance processes interact to generate and perpetuate autoimmunity. One of the triggers could be trauma-surgeries, serious infections or accidents.
Objectives: To assess the presence of history of trauma in patients diagnosed with SLE admitted in our Department, as well as the association with different co-morbidities.
Methods: We included 62 patients, admitted in the Rheumatology Department of the Tirgu-Mures Emergency Clinical County Hospital between 01.01.2018-29.01.2019, previously diagnosed with SLE. We performed a retrospective analysis of their medical documents, looking for evidence of traumatic risk factors.
Results: The majority of the patients were female (17=88.70%) and had some kind of trauma before being diagnosed with SLE (17=27.41%). Among the operations the most frequent were hysterectomy with bilateral oophorectomy and classical appendectomy, respectively (6=9.67% each), followed by cholecystectomy and tonsillectomy (2=3.22%). There were also one case of cerebral injury following a car accident and a complicated peritonitis-related to IUD extraction. The majority of co-morbidities was represented by neurologic involvement (16=25.80%), followed by thyroid (13=20.96%) and renal involvement (12=19.35%).
Conclusion: Patients with SLE from our department have a significant history of traumatic triggers, mainly open surgeries, which might explain the development of autoimmunity. They also have various organ involvement that sometimes warrants aggressive measures. Further studies have to be conducted in order to better examine the possible link between traumatic events and development of this multifaceted disease.

REFERENCES

[1] Christie M Bartels- Systemic lupus erythematosus (SLE) on Medscape Drugs & Diseases

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AB0564 THE CONTROVERSIAL ROWELL SYNDROME: TO BE OR NOT TO BE?

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Background: Rowell syndrome is a rather rare and highly debated entity, initially defined by Rowell et all as discoid lupus associated with

erythema multiforme-like (EM) lesions, positive speckled ANA, RF and Anti-SJT antibody, later known as anti Ro/La antibodies. In 2000, Zeitouni et al extended the definition by including all types of systemic lupus erythematosus (SLE) and proposed major and minor criteria, while in 2012 Torchia et al proposed another set of criteria defining Rowell syndrome as a distinct subtype of chronic cutaneous lupus. To date, Rowell syndrome as a distinct entity remains in question.

Objectives: To establish whether patients with clinically suggestive Rowell syndrome, meet the proposed criteria and form a distinct SLE subgroup.

Methods: A retrospective study which included SLE patients who associated EM-like lesions was carried out in the Rheumatology Department Cluj-Napoca, between 2008 and 2019. Clinical, immunological and histopathological parameters were recorded.

Results: Among 200 patients who fulfilled the 2012 SLICC criteria, 12 patients with target lesions, resembling EM, were identified. Four patients were excluded: 3 were not fully investigated and 1 was *My. pneumoniae* positive, thus 8 patients were studied. The majority of patients (87.5%) developed the cutaneous lesions after diagnosis. In all cases, the erythematous maculopapular rash with targetoid aspect was present, with poorly defined borders and a dusky center and a diameter between 2 to 6 cm. The lesions extended to the trunk and limbs, sparring the acral and mucosal areas. Five patients associated pruritus. The lesions could not be linked to any viral or bacterial infection in any of the cases. With regard to drug allergies, a link with AZA and HCQ was suspected in three patients – which was infirmed.

The majority of patients (87.5%) had negative anti-ds DNA, 87.5% presented speckled pattern ANA, one patient exhibited ANA rods and rings pattern, with a negative serology for B and C hepatitis and no antiviral therapy. Of note, 25% had positive rheumatoid factor, 87.5% had positive anti-Ro antibody and 37.5% of patients exhibited chilblains.

The first three classifications were tested on all patients: 25% met Rowell's criteria, 12.5% met Lee's criteria and 87.5% met Zeitouni's criteria, with only 1 patient meeting all 3, and 1 patient meeting none of them.

In the cases in which the SLE etiology of the lesion was in question from a clinical point of view, a biopsy was performed. In one case the histopathological examination described lymphocytic infiltrates and few eosinophils in the dermis, suggestive of drug allergy. Interestingly, this patient met all 3 classification criteria. Another report described thin epidermis, parakeratosis, dyskeratosis and spongiosis with dermis and perivascular lymphocytic infiltrate- findings highly suggestive for EM; this report belonged to the patient who met neither of the 3 classifications, but who associated a rods and rings ANA pattern. The third histopathological report was inconclusive.

Conclusion: Our study shows that patients with suspected clinical, immunological or histological Rowell syndrome do not meet all studied classifications criteria. Furthermore, studied classifications are incongruent. Should Rowell syndrome be a distinct entity it would most certainly be a very rare one. Further study is needed to better frame LES and EM.

REFERENCES

[1] ROWELL, N. R. (1963). *Lupus Erythematosus and Erythema Multiforme-like Lesions.* Archives of Dermatology, 88(2), 176.

[2] Torchia, D., Romanelli, P., & Kerdel, F. A. (2012). *Erythema multiforme and Stevens-Johnson syndrome/toxic epidermal necrolysis associated with lupus erythematosus*. Journal of the American Academy of Dermatology, 67(3), 417–421.

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AB0565 EXPERIENCE IN THE USUAL PRACTICE OF PATIENTS WITH INFLAMMATORY MYOPATHIES AT THE DONOSTIA UNIVERSITY HOSPITAL

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Background: Inflammatory myopathies (IM) are a heterogeneous group of acquired diseases, characterized by the presence of muscle weakness and inflammation. This group includes idiopathic polymyositis (PM), idiopathic dermatomyositis (DM), PM/DM associated with neoplasia, associated with rheumatic autoimmune diseases, juvenile PM/DM, inclusion body myositis (MCI) and immunomediated necrotizing myopathies (IMNM).

Objectives: Inflammatory myopathies (IM) are a heterogeneous group of acquired diseases, characterized by the presence of muscle weakness and inflammation. This group includes idiopathic polymyositis (PM), idiopathic dermatomyositis (DM), PM/DM associated with neoplasia, associated with rheumatic autoimmune diseases, juvenile PM/DM, inclusion body myositis (MCI) and immunomediated necrotizing myopathies (IMNM).

Methods: A retrospective search of all patients assessed in the service diagnosed with IM was performed. The computerized medical records were reviewed. The variables collected were: sex, age, underlying disease and immunosuppressive and biological treatments used, antibodies, and complementary tests. The immunosuppressant sought were methotrexate (MTX), azathioprine (AZA), hydroxychloroquine (HCQ), tacrolimus, mycophenolate (MMF), cyclophosphamide (CFM), cyclosporine (CsA), chloroquine; intravenous immunoglobulins (IVIG), rituximab (RTX). The quantitative variables are shown with the median and interquartile range; the qualitative ones are shown with the absolute value and its percentage

Results: 42 patients were found diagnosed with IM; the average age of diagnosis was 54 years, with a predominance of women with 71.4%. Table 1 shows the clinical characteristics, complementary tests and treatments used in these patients. The registered deaths were 8 (19%); of which 6 (75%) were related to their cancer, one patient with IM with pulmonary involvement died in the context of a respiratory infection at 91 years of age, and the other patient in the context of a bowel obstruction with 87 years of age. Two (4.7%) patients presented an overlap syndrome, one with scleroderma and the other with systemic lupus erythematosus. The median CPK was higher at the time of diagnosis in patients in the IM group with pulmonary involvement. We also observed a greater involvement of the swallowing muscles, 7 (16%) in patients with IM associated with malignancy, and those who were more associated in the initial IVIG treatment, 9 (21%). The mean follow-up time of these patients is 94 months. The most widely used immunosuppressant drug was MTX 76%; followed by 50% IVIG and 38% AZA; among those who maintain current treatment the most used is MTX 28% second of RTX 17%.

Conclusion: Despite the fact that IM are a serious disease, more than 80% of patients continue to follow up, IM presented more aggressively in IM patients associated with malignancy, and presented less aggressively in patients diagnosed at the juvenile age. In 40% of the patients, no specific antibody was found; possibly due to the fact that most of these patients were diagnosed more than 7 years ago, where the antibody pool was much more restricted than today's

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AB0566 POLYAUTOIMMUNITY AND MAJOR ORGAN INVOLVEMENT PREVALENCE IN SJÖGREN´S SYNDROME: THYROID, LIVER, LUNG AND KIDNEY AS TARGETS. A SINGLE CENTER CROSS SECTIONAL STUDY

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Background: Polyautoimmunity has been described to be associated with primary Sjögren´s syndrome (SjS) and the most frequent observed associated autoimmune diseases (AID) are autoimmune thyroid disease, autoimmune hepatitis and primary biliary cirrhosis, which are common organ-specific AID. In the same track, renal and lung involvement has increasingly been documented in SjS further highlighting its systemic nature.

Objectives: To describe and classify prevalence of polyautoimmunity and major organ involvement in a primary SjS-cohort.

Methods: This cross-sectional study included 179 patients [160 (89%) females and 19 (11%) males] diagnosed with primary SjS and fulfilling the ACR classification criteria (1) that had been admitted to our outpatient clinic between December 2008 and December 2018. Demographic and disease-specific characteristics were recorded in all patients.

Results: In our cohort the median age at diagnosis was 57 years (range: 20-85). Thyroid AID was found in 55/179 (30%) patients, with the following distribution: Hashimoto thyroiditis without (n=21) and with hypothyroidism (n=22), Graves's disease without (n=4) and with thyroidectomy (n=8). Liver AID was detected in 8/179 patients (4%), 3 patients with autoimmune hepatitis and 5 patients with primary biliary cirrhosis. Regarding major organ involvement, 20/179 (11%) patients had renal manifestations: renal insufficiency (n=12), glomerulonephritis (n= 3), interstitial nephritis (n=2) and IgA nephritis (n=3). Eight/179 (4%) patients had lung manifestations: interstitial fibrosis (n=6), emphysema (n=1) and chronic obstructive pulmonary disease (n=1).

Conclusion: Our results add evidence for the presence of polyautoimmunity and major organ involvement in SjS. We found a slightly lower prevalence of polyautoimmunity and major organ involvement compared to recently reported data (2). Nonetheless, extra-glandular organ involvement should be assessed in order to elucidate cumulative damage and how it might impact outcome, prognosis and therapeutic approaches in SjS.

REFERENCES

[1] Shiboski SC, et al. American College of Rheumatology classification criteria for Sjögren's syndrome: a data-driven, expert consensus approach in the Sjögren's International Collaborative Clinical Alliance cohort. Arthritis Care Res (Hoboken) 2012;64(4):475-87.
[2] Both T, et al. Reviewing primary Sjögren's syndrome: beyond the dryness - From pathophysiology to diagnosis and treatment. Int J Med Sci. (2017) 23;14(3):191-200.

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AB0567 DISEASE PATTERN IN EARLY AND NON-EARLY SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with a high degree of variability at onset, creating challenges in the accurate estimation of it's pattern in early stages[1].
Objectives: To evaluate the pattern of the disease in patients with early and non-early systemic lupus erythematosus from physician's perspective.
Methods: Performed case-control study included SLE patients that fulfilled SLICC classification criteria, 2012. The research included two groups: patients with early SLE – 1st group (disease duration ≤24 months) and non-early SLE – 2nd group (disease duration 24 months). The pattern of the disease activity was assessed by SLEDAI-2K, SLAM, PGA and PhGA for SLE activity, SLICC/ACR DI for disease irreversible changes and SF-8 for the quality of life (QoL). We correlated disease activity scores within groups and activity indices with the QoL using intra- and inter-class correlation coefficients
Results: A total of 101 SLE patients was analyzed. First group (early SLE) included 34 patients while the second group (non-early SLE) included 67 patients. The disease duration ± SD (range) was 12,42±8,70 (0.1-24) and 146,41±81,64 (31-432) months, respectively. The disease activity was high in both groups. The QoL was appreciated as low, compared to general population, by both components, in 2 groups. The damage index was higher in the 2nd group, which can be explained by longer disease duration and development of irreversible changes during the course of lupus.
The PhGA showed stronger and higher correlation with disease activity and QoL in patients with longer disease duration. These can be explained by the more accurate assessment of patients that have longer disease duration, while the unpredictable evolution and the assessment of early SLE is being challenging for the physician. Also, physician's judgment was influenced by the presence of irreversible organ damage in patient with longer disease, while in early disease course they where concerned mostly about disease activity.
Conclusion: The clinical picture of SLE was characterized by high disease activity and low QoL in both, early and non-early lupus, while occurrence of irreversible organ changes was more characteristic for the longer disease. The disease parameters (activity, damage and QoL) correlated with PhGA mostly in patients with non-early SLE, the appreciation of the disease pattern being challenging in the early disease course.

REFERENCES

[1] Cervera R. et al. Lessons from the "Euro-Lupus Cohort". Ann Med Interne, 2012 Dec;153(8):530-6

Table 1. General characteristic of the study group

Parameters of the disease	Gr I, Nr 34	Gr II, Nr 67	p
SLAM ± SD (range), points	7,47±4,40 (0-24)	7,31±4,10 (1-19)	>0,05
SLEDAI ± SD (range), points	7,02±4,16 (0-17)	6,26±4,43 (0-18)	>0,05
PhGA ± SD (range), points	45,61±19,45 (10-82)	48,35±19,50 (5-82)	>0,05
PGA± SD (range), points	46,97±19,39 (10-93)	47,98±22,41 (5-90)	>0,05
SLICC/ACR DI	0,23±0,43 (0-1)	1,07±1,29 (0-5)	<0,001
SF-8 ± SD, points	38,79±10,60 41,80	36,76±10,33	>0,05
PCS (physical component status)	±10,83	41,97±10,47	>0,05
MCS (mental component status)			

Table 2. Correlation of PhGA with other SLE parameters

	Early SLE group PhGA (correlation coefficient r)	Non-early SLE group PhGA (correlation coefficient r)
PGA	0,86*	0,81*
SLAM	0,48***	0,60*
SLEDAI	0,20	0,50*
SF-8 PCS	0,56*	0,54*
SF-8 MCS	0,41**	0,50*
SLICC/ACR DI	0,12	0,37**

*<0,001 **<0,01 ***<0,05

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AB0568 THE EFFECT OF DEPRESSIVE AND ANXIETY ON QUALITY OF LIFE IN PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUSIN RENAISSANCE COHORT

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Background: Systemic lupus erythematosus (SLE) patients are at high risk of depression and anxiety. These two states cause severe loss of health related quality of life (HRQoL) for patient with SLE.
Objectives: The aim of the current study was to assess the effect of depressive and anxiety on HRQoL in a cohort of patients with systemic lupus erythematosus in Russian Federation (RENAISSANCE).
Methods: Consecutive patients who fulfilled SLICC 2012 criteria for SLE were recruited. Depressive and anxiety symptoms were assessed by the Hospital Anxiety and Depression (HAD) scale (0-21 points). Health-related quality of life (HRQoL) was assessed by the validated specific questionnaires LupusQoL-Russian. Disease activity was evaluated by the SLEDAI-2K, and chronic damage by the Systemic Lupus International Collaborating Clinics Damage Index score (SDI).
Results: 328 Russian SLE patients were enrolled in the study (M/F 30/298, mean age 34.4±11.5 years, mean disease duration 106.3±97.9 months; mean SLEDAI 2K 9.6±8.0; mean SDI 0.2±0.6. 34 (10,3%) patients had HADS-depression score of ≥10 and 76 (23,1%) of patients had HADS-anxiety score of ≥10. Patients with depressive score of ≥10 had significantly lower the scales "Planning", "Emotion health" and "Fatigue" (p<0,0001) of the LupusQoL than those with score <10. Similarly, significant lower "Emotion health" and "Fatigue" (p<0,0001) were noted in those patients with HAD-anxiety score ≥10 compared to those <10 and they also had low score of "Burden to others" unlike those who are not anxiety. (Table 1).
Conclusion: Depressive and anxiety symptoms in SLE patients and were associated with significantly poorer HRQoL.

Table 1. Effect of anxiety and depressive on HRQoL in SLE patient

LupusQol domains	HADS-anxiety<10	HADS-anxiety ≥10	p	HADS – depressive<10	HADS-depressive ≥10	p
Physical health	70,3±22,2	50,2 ±21,2	<0,0001	67,9±23,1	48,2±18,7	<0,0001
Pain	73,8±23,3	52±22,3	<0,0001	71,2±23,8	50,7±26,9	<0,0001
Planning	68,4±26,8	42,8 ±26,3	<0,0001	65,8±21,2	35,3±21,2	<0,0001
Intimate relationship	75,9±30,6	56,7 ±29,8	<0,0001	73,2±31,1	58,3±33,6	0,05

Burden to others	60,4±27,2	39,5 ±23,1	<0,0001	57,7±27,3	42±29,9	0,001
Emotion health	70,8±21,2	37,9±22	<0,0001	66,6±24,2	40,1±20,3	<0,0001
Body image	69,8±25,7	48±27,6	<0,0001	67±26,8	45,7±28,6	0,001
Fatigue	67,9±22,4	40±22,4	<0,0001	64,4±24,3	41±21,7	<0,0001

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AB0569 THE EFFECT OF CUTANEOUS AND MUSCULOSKELETAL SYMPTOMS ON QUALITY OF LIFE IN PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN RENAISSANCE COHORT

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Background: Cutaneous and musculoskeletal symptoms is one of the most frequent clinical complaints of patients with systemic lupus erythematosus(SLE) and has been found to occur in up to 70%-95% of patients during the course of the disease. For these reasons, SLE can affect different aspects of the patient's life, leading to an impairment of HRQOL.
Objectives: The aim of the current study was to assess the effect of cutaneous and musculoskeletal symptoms on HRQoL in a cohort of patients with systemic lupus erythematosus in Russian Federation (RENAISSANCE).
Methods: Consecutive patients who fulfilled SLICC 2012 criteria for SLE were recruited. Health-related quality of life (HRQoL) was assessed by the validated specific questionnaires LupusQoL-Russian. Disease activity was evaluated by the SLEDAI-2K, and chronic damage by the Systemic Lupus International Collaborating Clinics Damage Index score (SDI).
Results: 328 Russian SLE patients were enrolled in the study (M/F 30/298, mean age 34.4±11.5 years, mean disease duration 106.3±97.9 months; mean SLEDAI 2K 9.6±8.0; mean SDI 0.2±0.6. Musculoskeletal symptoms were observed in 142 patients, cutaneous and mucosal lesion symptoms -147 patients, respectively. When comparing HRQOL in patients with lesions skin and mucousal revealed (Table 1) significant decline HRQoL on the scales "Planning" (58.5 ± 28.9), "Intimate Relationships" (65.9 ± 32.1), "Burden to other" (52.9 ± 26) and "Body Image" (57.4 ± 29.1) of the LupusQol questionnaire compared with the patients without skin and mucosal lesions (p≤0.002; p≤0.001; p≤0.03; p≤0,0001 respectively). When evaluating HRQoL in patients with SLE and musculoskeletal symptoms (Table 2) reduction of almost all scales LupusQoL.
Conclusion: Cutaneous and musculoskeletal symptoms in SLE patients were associated with significantly poorer HRQoL.

Table 1. Dependence of indicators of the scales of the LupusQol on the presence of the skin and mucosal lesions (p <0.05).

LupusQoL	No involved skin and mucosal lesions (N=181)	Involved skin and mucosals lesions (N=147)	P
Physical health	68,03±23	65,03±23,5	0,2
Pain	66,2±26,7	62,6±21,8	0,2
Planning	72,19±25	67,2±24	0,07
Intimate relationship	64±24,6	61±24,8	0,3
Burden to others	68,1±27,4	58,5±28,9	0,002
Emotion health	78,4±29	65,9±32	0,001
Body image	59,5±29	52,9±26	0,03
Fatigue	71,7±24	57,4±29	<0,0001

Table 2. The dependence of the indicators of the questionnaire scales LupusQoL from musculoskeletal symptoms (p <0.05).

LupusQoL	No musculoskeletal symptoms (N=186)	musculoskeletal symptoms (N=142)	p
Physical health	69,6±23	62,8±22,6	0,008
Pain	67,2±28	62,8±22,6	0,1
Planning	74,5±24	64±23,7	0,001
Intimate relationship	45,9±7,6	44±7,5	0,04
Burden to others	68±28,4	58,3±27	0,02
Emotion health	77±29,9	67,2±31	0,01
Body image	58,6±27	54±28,6	0,02
Fatigue	65,2±25	59,3±23	0,03

Disclosure of Interests: None declared
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AB0570 CLINICAL STUDY OF THE DISEASE ACTIVITY AND IMMUNE SCREENING OF PRIMARY SJOGREN'S SYNDROME

Yin Xufang, Zhang Mingxing, Ming Yan, LI Xiao-Feng. *The Second Hospital of Shanxi Medical University, Taiyuan, China* **Objectives:** To evaluate the change features of peripheral blood lymphocyte subsets and disease activity in patients with primary Sjogren's syndrome before and after treatment.
Methods: A total of 30 patients with primary Sjogren's syndrome in the Department of Rheumatology from the Second Hospital of Shanxi Medical University from January 2016 to December 2018 were enrolled. According to the treatment time of patients, they were divided into baseline group, 0-3 months group, 3-6 months group, 6-12 months group, and the absolute counts of T, B, NK, Th1, Th2, Th17 and regulatory T cells(Tregs) in peripheral blood of patients before and during the treatment were measured by flow cytometry. The ratio of various cells to Tregs was calculated as well.The primary Sjogren's syndrome disease activity was assessed according to the Sjögren's syndrome disease activity index (ESSDAI) score and compared with 30 healthy people.
Results: The Tregs counts in the disease group were significantly lower than those in the healthy control group (p<0.05), and the ratio of proinflammatory lymphocytes to Tregs (Th17/Treg) was higher(p<0.05).Tregs counts in peripheral blood of patients with primary Sjogren's syndrome has increased significantly after 3-month treatment,at the same time, the inflammatory index ESR was significantly lower (p<0.05), the ESSDAI score was significantly lower (p<0.05), and the high remission rate was maintained. However there was no statistically significant increase in Treg cell growth before treatment at 3-6 months and 6-12 months, (p>0.05).

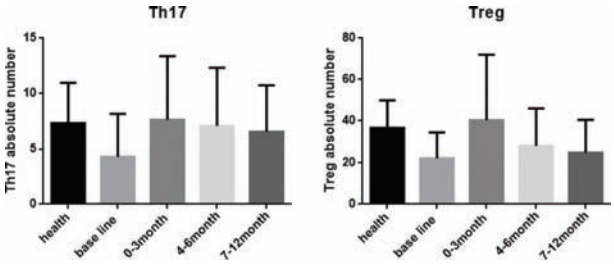


Figure 1 The. Tregs counts in the disease group were significantly lower than those in the healthy control group (p<0.05), and the ratio of proinflammatory lymphocytes to Tregs (Th17/Treg) was higher(p<0.05).Tregs counts in peripheral blood of patients with primary Sjogren's syndrome has increased significantly after 3-month treatment.

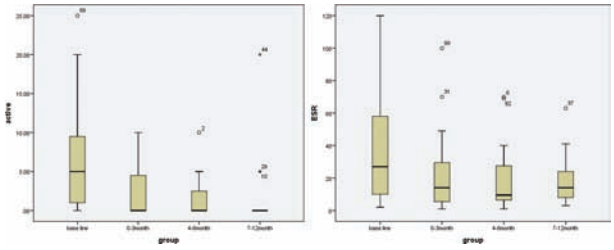


Figure 2the. inflammatory index ESR was significantly lower (p<0.05), the ESSDAI score was significantly lower (p<0.05), and the high remission rate was maintained.

Conclusion: The imbalance between pro-inflammatory lymphocytes and Tregs caused by the significant decrease of Tregs may be the cause of primary Sjogren's disease activity. We propose to promote the growth of Tregs and maintain the balance between pro-inflammatory lymphocytes and Tregs,which provides a new idea for disease relief of primary Sjogren's syndrome.

Disclosure of Interests: None declared
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AB0571 BENEFICIAL EFFECTS OF VACCINATION ON REDUCING RISKS OF INFLUENZA INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: In patients with systemic lupus erythematosus (SLE), infection is a major cause of morbidity and mortality. Influenza is one of the most common infectious diseases which can be prevented in a certain degree by vaccination, while in fact, influenza vaccination rates of SLE are really low in China.
Objectives: To investigate the influenza vaccination rate of SLE patients and the reasons for nonadherence to vaccination. To evaluate beneficial effects and safety of influenza vaccination.
Methods: A cross section study was performed among patients with SLE regular follow-up in Distinct HealthCare between June 1 and November 31. Vaccination status and influenza infection condition were surveyed. Demographic information, clinical features and laboratory characters were collected and systemic lupus erythematosus disease activity index (SLEDAI) was documented.
Results: 109 SLE patients were recruited, including 42 immunized with trivalent or quadrivalent split virion influenza vaccine and 67 non-vaccinated. There were no significant differences in demographic and clinical characteristics (p>0.05). The influenza vaccination rate was 38.5%. Influenza infection rates in the vaccinated and non-vaccinated were 7.1% (3/42) and 23.9% (16/67), respectively, with statistic difference (p<0.05). Reasons that non-vaccinated patients reported for nonadherence included refused by the community health workers due to basic disease of SLE (32.3%), vaccine shortages (27.7%), concerns for potential side effects (23.1%) and insufficient patient education (16.9%). No systemic adverse reactions were observed and no significant increase of disease activity was found in vaccinated patients.
Conclusion:
- 1. Split virion influenza vaccine is effective in reducing risks of influenza infection in patients with SLE, and also safe.
- 2. Influenza vaccination is insufficient in SLE patients.
- 3. Education of the community health workers and patients is important to increase influenza vaccination rate.

REFERENCES

[1] Belongia EA, Skowronski DM, McLean HQ, et al. Repeated annual influenza vaccination and vaccine effectiveness: review of evidence. Expert Rev Vaccines. 2017 Jul;16(7):1-14.
[2] Baillet A, Gossec L, Carmona L, et al. Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. Ann Rheum Dis. 2016 Jun;75(6):965-73.
[3] Chang CC, Chang YS, Chen WS, et al. Effects of annual influenza vaccination on morbidity and mortality in patients with Systemic Lupus Erythematosus: A Nationwide Cohort Study. Sci Rep. 2016 Dec 2;6:37817.
[4] Lawson EF, Trupin L, Yelin EH, et al. Reasons for failure to receive pneumococcal and influenza vaccinations among immunosuppressed patients with systemic lupus erythematosus. Semin Arthritis Rheum. 2015 Jun;44(6):666-71.
[5] Murdaca G, Orsi A, Spanò F, et al. Influenza and pneumococcal vaccinations of patients with systemic lupus erythematosus: current views upon safety and immunogenicity. Autoimmun Rev. 2014 Feb;13(2):75-84.

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AB0572 INVASIVE MYCOSES IN PATIENTS WITH CONNECTIVE TISSUE DISEASE FROM SOUTHERN CHINA: CLINICAL FEATURES AND ASSOCIATED FACTORS

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Background: Invasive fungal disease (IFD) was well studied in patients with AIDS and organ transplant recipients. A few researches illustrated that patients with connective tissue disease (CTD) were also predisposed to IFD. However, few researches were designed to focus on invasive mycosis (IM) in patients with CTD.
Objectives: To investigate the clinical features and associated factors of IM in patients with CTD from Southern China.
Methods: A retrospective study CTD was performed. Demographic and clinical data were recorded. Associated factors were analyzed by logistic regression analysis.
Results: A total of 32 patients with CTD were included. The incidence of IM was 0.5% in patients with CTD (32/6911) and the highest in patients with ANCA-associated vasculitis (AAV) (7/480, 1.5%). Molds were isolated in 20 sputum specimens (20/29, 69.0%). *Aspergillus* spp. (81.3%) were the leading strain. Positivity of serum G-test and GM-test was 47.8% (11/23) and 34.6% (9/26), respectively. GM-test was positive in BALF from seven patients. Lung was commonly involved (30/32, 93.8%). Pulmonary nodules (46.7%) and cavitary lesions (36.7%) were common. Ten patients died (31.3%), including three with AAV (42.9%) and seven with SLE (36.8%). Multivariate logistic regression analysis showed that lymphopenia [odds ratio (OR) =3.28, 95% confidential interval (CI) 1.29-8.38, *P*=0.01] and median-to-high dose of glucocorticoid (GC) [OR=3.40, 95% CI 1.04-11.13, *P*=0.04] was associated with IM in patients with CTD. Patients with lymphopenia experienced higher risk of co-infection (50.0% *vs* 0%, *P*=0.01) and mortality (45.5% *vs* 0%, *P*=0.01) compared with patients with normal lymphocyte count.
Conclusion: IM tended to develop in patients with AAV, resulting in high mortality. Sputum culture could be an effective and non-invasive method to diagnose IM. Lymphopenia, and median-to-high dose of GC are associated with IM in patients with CTD.
Acknowledgement: no
Disclosure of Interests: None declared
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Vasculitis

AB0573 ASSESSMENT OF PRESENCE, SEVERITY AND RISK FACTORS OF POST- THROMBOTIC SYNDROME IN VASCULAR BEHÇET DISEASE: MUTICENTERED RETROSPECTIVE STUDY

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Background: DVT(deep venous thrombosis) is the most common form of vascular Behçet Disease(VBD).Post-trombotic syndrome(PTS) developing after a thrombotic event in lower extremity is the most important complication of DVT and affects negatively patients' quality of life.
Objectives: We aimed to assess presence,severity and risk factors of PtS and venous disease spesific quality of life in VBD

		Post-thrombotic Syndrome		P Value
		No	Yes	
BSAS score (n:93)		10 (0-47)	20 (1-69)	.002
Standing time (hours)		8.09±3.9	8.24±3.97	.856
VCSS score (n:85)		2.27±1.64	6.54±4.09	.000
VDS	0	18 (50%)	11(19.3%)	.003
	1	15(41.7%)	34(59.6%)	
	2	3 (8.3%)	12(21.1%)	
Veines QoL total score (n:93)		97.19±17.8	77.75±17.3	.000
Veines symptom score		44.3±9.9	35.2±9.1	.000
CEAP		1.53±1.34	2.94±1.83	.000
DVT	1	24(40%)	36(60%)	.888
	2 and over	12 (36.7%)	21 (63.3%)	
Treatment	IS	13 (39.4%)	20 (60.6%)	.817
	IS+AC	17 (36.2%)	30 (63.8%)	
Treatment duration (months)	IS	39(1-200)	36 (3-256)	.600
	AK	12(1-60)	12 (1-156)	.772
Duration of trombosis (years)	<5	15 (40.5%)	22 (59.5%)	.872
	>5	20 (36.4%)	35 (63.6%)	
Compression stocking treatment	No	18 (42.5%)	24 (57.5)	.357
	Yes	12 (24.5%)	27(75.5)	

Methods: This study included 96 BD patients (Female/Male:18/78,mean age: 38.8±8.74)with DVT from 3 tertiary Rheumatology centers in Turkey. When vascular involvement developed, mean age was 32.7±8.65(female: 35.4±10.7; male: 32.09±8; p>.005) Villalta scale is used to assess PTS and according to scale; PTS is present if score >4 and degree of PTS mild, moderate and severe if score 5-9,10-14,>14 respectively. The Venous Disability Score(VDS) and the Venous Clinical Severity Score

(VCSS) were used for the assessment of venous disease. Venous disease-specific QoL was measured through Venous Insufficiency Epidemiological and Economic Study Quality of Life/Symptom (VEINES-QoL/Sym) questionnaire.All patients were reanalyzed using color Doppler USG in the Radiology Department,by a radiologist.In each patient, a total of 16 superficial and deep veins in both legs were assessed for the presence or absence of obstruction, recanalization,reflux, and collaterals within 1 weeks following the clinical examination.

Results: During venous assessment,median disease duration was 9(0-34) years. Eighty(84.2%) patients were under ımmunsupressive(IS) treatment and 13 of these patients were under anticoagulation treatment in addition to ISs. Duration between first vascular event and venous assessment was 6(1-26) years. PTS was present in 57(61.3%) out of 93 patients and severe PTS was present in 19(19.8%)patients.There was no association between the presence of PTS and sex,disease diagnosis age,age during DVT,presence of relaps. There was no difference between patients with or without PTS according to the anticoagulant usage (p=0.817).Doppler ultrasound examination showed bilateral at 31(31.4%) patients and both upper and lower involvment at 40(47.6%) patients.But there is no statically significant relationship between presence of PTS and Doppler findings. In addition to these, there is no statically significant association between PTS and presence of refluxtrombosis at any vessel in the affected leg, but there is a correlation between severe PTS and reflux(r=0.224, p:0.096).VCSS have positive correlation with the presence of reflux(p:0.041, r:0.224). VEINES-QoL/Sym,VCSS and BSAS were significantly worse in patients with PTS.(Table1)

Conclusion: In this study, we found that PTS in lower extremity develops in more than half of the patients with VBD during follow-up, and didn't found any predictor factor for develeopment of PTS. About one third of patient with PTS had severe PTS. PTS is an important clinical problem for physicians treating VBD in daily practice.It should be taken into account as much as preventing vascular relapses during follow-up of patients with VBD.

Table 1. Clinical and characteristic features of PTS

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AB0574

A MONOGENIC DISEASE WITH WIDE RANGE OF SYMPTOMS: DEFICIENCY OF ADENOSINE DEAMINASE 2

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Background: Deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessive autoinflammatory disorder caused by *ADA2* mutations.

Objectives: We aimed to investigate the characteristics of DADA2 patients along with the ADA2 enzyme levels.

Methods: 24 DADA2 patients who admitted to the Adult and Pediatric Rheumatology, Pediatric Haematology, and Pediatric Immunology Departments were included. All exons of the *ADA2* gene were screened by Sanger sequencing in all DADA2 patients. Serum ADA2 enzyme activity was measured by modified spectrophotometric method.

Results: 24 DADA2 patients were included; Group 1, 14 DADA2 patients with polyarteritis nodosa (PAN)-like phenotype; Group 2, 9 patients with Diamond-Blackfan anemia (DBA)-like features and one with immune deficiency. 14 PAN-like DADA2 patients did not have the typical thrombocytosis seen in classical PAN. Inflammatory attacks were evident in only Group 1 patients. Serum ADA2 was low in all DADA2 patients except one who was tested after hematopoietic stem cell transplantation. There was no significant difference in ADA2 levels between PAN-like and DBA-like DADA2 patients (Figure 1). ADA2 activities of heterozygote family members were about half the level of the control subjects. However, in heterozygote DADA2 patients, serum ADA2 levels were as low as the ones of homozygote DADA2 patients. *ADA2* mutations were affecting the dimerization domain in Group 1 patients and in the catalytic domain in Group 2 patients (Table 1).

Table 1. Molecular results of *ADA2* gene analyses in DADA2 patients (D, dimerization; C, catalytic)

Group number	Patient numbers	Mutation position	Mutation type	The affected domain of ADA2 protein
1	11	Exon 2: c.139G>A	Homozygous missense	D
1	1	Exon 2: c.139G>A/ Exon 2: c.140G>T	Compound heterozygous missense	D
1	2	Exon 2 c.139G>A	Heterozygous missense	D
2	1	Exon 4: c.620T>C/ Exon 9: c.1360G>C	Compound heterozygous missense	C
2	2	Exon 7: c.1072G>A	Homozygous missense	C
2	1	Exon 4: c.629delT/ Exon 2: c.144_145ins	Compound heterozygous Del/ins_frameshift and non-sense	C
2	1	Exon 10: c.1445A>G	Homozygous missense	C
2	1	Exon 4: c.680-681delAT	Homozygous deletion-Frameshift non-sense	C
2	1	Exon 9: c.1367A>G	Homozygous missense	C
2	2	Exon 6: c.916C>T	Homozygous non-sense	C
2	1	Exon 9: c.1392_1393insG	Homozygous missense	C

Conclusion: We suggest that enzyme activity of ADA2 should be assessed along with genetic analysis since there are heterozygote patients with absent enzyme activity. Our data confirms a possible genotype phenotype correlation where dimerization domain mutations are associated with a PAN-like phenotype whereas catalytic domain mutations are associated with hematological manifestations.

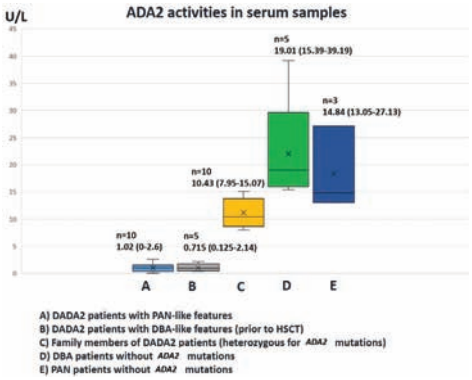


Figure 1

REFERENCES

[1] Navon Elkan P, et al. Mutant ADA2 in a PAN vasculopathy. N Engl J Med 2014;370(10):921-931
[2] Zhou Q, et al. Early-onset stroke and vasculopathy associated with mutations in ADA2. N Engl J Med 2014;370(10):911-920

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AB0575 THE EFFECT OF METABOLIC SYNDROME ON CARDIOVASCULAR DISEASE AND CUMULATIVE ORGAN DAMAGE IN TAKAYASU'S ARTERITIS

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Background: As a result of arterial ischemia, the frequencies of hypertension (HT), ischemic heart disease, congestive heart failure and atherosclerosis have been shown to increase and contribute to mortality in patients with Takayasu's arteritis (TAK). Determining cardiovascular disease (CVD) and associated risk factors in TAK is important for a comprehensive treatment approach and better disease prognosis. Data about the effect of metabolic syndrome (MetS) which is known as a risk factor for CVD on TAK are limited.
Objectives: The aim of this study was to determine the prevalence of MetS in patients with TAK and its effect on CVD and cumulative organ damage.
Methods: A total of 122 TAK patients, followed by Turkish Takayasu Study Group in 7 tertiary Centers and diagnosed according to the 1990 ACR criteria were consecutively assessed for cumulative organ damage (VDI score), history of CVD and MetS as defined by the National Cholesterol Educational Program Adult Treatment Panel III (NCEP ATP III). CVD was defined as coronary artery disease or cerebrovascular event (myocardial infarction or stroke).
Results: Eighty-seven percent of patients were female and the median age was 39 (17-65) years. The frequency of MetS was 14.7% and CVD was 13.1%. The median age, disease duration, smoking prevalence and CVD were found slightly higher in MetS group, without reaching statistical significance. There were no differences in VDI score between the groups (Table 1).

Table 1. Cardiovascular disease (CVD) and cumulative organ damage distributions according to the presence of MetS in patients with Takayasu's arteritis

	MetS+TAK n: 18	MetS-TAK n: 104	p values
Age (median, min-max)	44 (27-63)	37 (18-65)	0.056
Disease duration (year, mean±SD)	11.7±9.2	10.0±9.3	0.535
Female n (%)	17 (94)	89 (86)	0.273
Smoker n (%)	3 (17)	10 (10)	0.583
CVD n (%)	4 (22)	12 (16)	0.202
Cumulative GC(g, mean±SD)	9.8±6.1	10.1±9.1	0.872
NIH-Aktive n (%)	3 (17)	13 (13)	0.462
VDI (mean±SD)	4.1±2.6	4.2±2.6	0.941

(TAK: Takayasu's arteritis, MetS: Metabolik sendrom, SD: Standart deviation, GC: Glucocorticoids, NIH: "National Institutes of Health", VDI: "Vasculitis damage index")

Conclusion: MetS frequency in our TAK patients was observed to be less than the normal population data obtained from METSAR (Turkish MetS study in normal population) in Turkey (female: 39.6%, male: 28%). The discrepancy with SLE, which is another inflammatory autoimmune disease having a higher frequency of MetS related with organ damage, may be explained with the potentially more severe disease course in SLE patients requiring higher cumulative doses of glucocorticoids (1).

REFERENCE

[1] Demir S, Artim-Esen B, Şahinkaya Y, Pehlivan Ö, Alpay-Kanıtez N, Omma A, et al. Metabolic syndrome is not only a risk factor for cardiovascular diseases in systemic lupus erythematosus but is also associated with cumulative organ damage: a cross-sectional analysis of 311 patients. Lupus. 2016;25:177-84.

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AB0576 SERUM CATHELICIDIN (LL 37) LEVELS IN PATIENTS WITH BEHCET'S DISEASE AND ITS ASSOCIATION WITH DISEASE ACTIVITY

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Background: Behcet's disease (BD) is a recurrent multisystem inflammatory disease which is characterized by recurrent episodes of oral aphthous and genital ulcers, ocular inflammation and skin lesions. Antimicrobial peptides (AMPs) such as the cathelicidin (LL-37) and defensins have recently been implicated in the pathogenesis of autoimmune and autoinflammatory diseases.
Objectives: The aim of this study was to investigate the serum levels of cathelicidin and its potential association with disease activity, and some other laboratory parameters such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), white blood cell count (WBC) in patients with BD.
Methods: A total of 45 patients who presented to Dicle University Rheumatology clinics between September 2018 and December 2018 and met the International Study Group Classification Criteria for BD and 37 healthy control subjects who presented to Dicle University Physical Medicine and Rehabilitation clinics for various reasons other than rheumatoid complaints between the same dates were included in this study. Patients' demographic features, including age and sex, were noted. Duration of disease was also noted, and the disease activity was assessed by means of BD Current Activity Form (BDCAF). Laboratory investigations included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), complete blood count and routine biochemical analyses. Serum levels of cathelicidin (LL 37) were determined by means of human cathelicidin antimicrobial peptide ELISA Kit according to the manufacturer's protocol.
Results: Serum mean level of cathelicidin (LL 37) in patients with BD was lower than healthy controls but this result was not statistically significant. Cathelicidin levels were not correlated with ESR, CRP, BDCAF and WBC ($p>0.05$).
Conclusion: However serum mean levels of cathelicidin (LL 37) were lower in patients with BD compared to healthy controls, this result was not statistically significant. It may may be sourced from our relatively small sample size. To validate cathelicidin (LL 37) value as a prognostic or pathophysiologic biomarker, future studies should investigate the levels of cathelicidin LL37 in patients with BD in large cohorts of patients with different levels of disease activity, remission, and relapse.

REFERENCE

[1] Hoffmann MH, Bruns H, Backdahl L, et al. The cathelicidins LL-37 and rCRAMP are associated with pathogenic events of arthritis in humans and rats. Ann Rheum Dis. 2013;72(7):1239-48
[2] Gasim A. Cathelicidin antimicrobial peptide as a serologic marker and potential pathogenic factor in antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Res Ther. 2014: 28;16(1):105

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AB0577

TOCILIZUMAB IN GIANT CELL ARTERITIS. ROUTE OF ADMINISTRACION: INTRAVENOUS OR SUBCUTANEOUS

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Background: Recently, based on the GiACTA trial results, weekly subcutaneous Tocilizumab (TCZ) has been approved for the treatment of Giant Cell Arteritis (GCA). It has showed to be effective and safety.
Objectives: Our aim was to compare the efficacy of TCZ according the route of administration.
Methods: Multicenter study of 134 GCA patients in treatment with TCZ. It was performed a comparative study between 2 groups according the route of administration of TCZ, intravenous (IV) or subcutaneous (SC).
Results: We study 134 patients divided in 2 groups: a) IV TCZ, 104 cases and, b) SC TCZ, 30 cases, with a mean age 73.4±8.2 years vs 71.9±10.6 years, respectively (p=0.501). Disease duration, clinical manifestations and acute phase reactants at TCZ onset were similar in both groups with non-statistical difference. 91.7% patients who received SC TCZ achieved prolonged remission after 12 months of treatment (p=0.043). And the glucocorticoid sparing effect of TCZ was greater in the same group, reaching a statistical difference at 3 and 24 months (p=0.017 and p=0.021). Patients under IV TCZ treatment suffered more adverse event during follow up (p=0.043). **TABLE 1** and **2** summarizes the comparative study.
Conclusion: Patients in treatment with SC TCZ, reached prolonged remission after 12 months of treatment and were able to discontinue prednisone dose after 24 months of follow up. The incidence of adverse events was more frequent in the IV TCZ group, without difference in relation to infections.

REFERENCES

[1] Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, et al. Trial of Tocilizumab in Giant-Cell Arteritis. N Engl J Med. 2017; 377:317-28.

[2] Calderón-Goercke M. Tocilizumab in giant cell arteritis. Observational, open-label multicenter study of 134 patients in clinical practice. Semin Arthritis Rheum. 2019 Jan 5. pii: S0049-0172(18)30571-7. doi: 10.1016/j.semarthrit.2019.01.003. [Epub ahead of print]

TABLE 1

	TCZ IV (n=104)	TCZ SC (n=30)	p
BASAL FEATURES AT TCZ ONSET			
GENERAL FEATURES			
Age, years, mean± SD	73.4 ± 8.2	71.9 ± 10.6	0.501
Sex, female/male n (%)	77/27	24/6	0.504
Time from GCA diagnosis to TCZ onset (months), median [IQR]	14.5 [5-35]	11.5 [5-25.5]	0.447
AORTITIS AND ANOTHER LVV involvement, n (%)	49 (47.1)	9 (30)	0.096
ACUTE PHASE REACTANTS			
ESR, mm/1st hour, mean (SD)	41.8 ± 31.2	35.9 ± 31.7	0.301
CRP, mg/dL mean (SD)	3.3 ± 5.8	2.1 ± 3.1	0.191
Hemoglobin, g/dL, mean (SD)	12.1 ± 1.4	12.7 ± 1.6	0.145
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	16.9 ± 13.2	13.6 ± 11.2	0.457

TABLE 2

	TCZ IV (n=104)	TCZ SC (n=30)	p
EFFICACY AND SAFETY AFTER TCZ			
Prolonged remission n (%)			
Month 6	45 (56.3)	13 (65)	0.712
Month 12	35 (61.4)	11 (91.7)	**0.043**
Month 24	21 (63.6)	6 (85.7)	0.257
Relapses n (%)			
Month 1	2 (2.0)	2 (6.9)	0.184
Month 3	3 (3.1)	4 (15.4)	**0.017**
Month 6	5 (6.3)	0	0.251
Month 12	9 (15.8)	0	0.140
Month 24	7 (21.2)	0	0.180
Corticosteroids sparing effects, median [IQR]			
Month 1	16.9 [7.5-23.8]	13.6 [7.5-15]	0.257
Month 3	10.6 [5-12.5]	9.2 [5-10.6]	0.359
Month 6	6.9 [2.5-7.6]	3.8 [1-5]	**0.032**
Month 12	3.7 [0-5]	1.7 [0-4.4]	0.085
Month 24	2.4 [0-5]	0 [0-0]	**0.021**
Side effects, n (%)			
Relevant adverse events	29 (27.9)	3 (10)	**0.043**
Serious infections	14 (13.5)	2 (6.6)	0.544

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AB0578

DIFFERENCES AND CHARACTERISTICS OF PRIMARY LARGE VESSEL VASCULTIS AND LARGE VESSEL VASCULITIS ASSOCIATED WITH GIANT CELL ARTERITIS. STUDY OF 28 CASES FROM THE SAME CENTER

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Background: Large vessel vasculitis (LVV) is a severe entity with non-specific clinical symptoms, which contributes to a delay in diagnosis and sometimes to serious complications. LVV can be primary or secondary, with giant cell arteritis (GCA) being the most common association.

Objectives: To describe the characteristics and differences between patients with primary LVV and LVV associated with GCA in a single center.

Methods: Retrospective study of patients with LVV in a University Hospital (January 2013-December 2018). Patients diagnosed with aortitis using an imaging test (PET-CT/angioCT/CT/MRI) were included. GCA was diagnosed by biopsy and/or ultrasound of the temporal artery. The primary LVV was considered by exclusion of inflammatory or infectious causes. Epidemiological, clinical and analytical variables, affected vascular territories and the treatment received in both groups were reviewed.

Frequencies and percentages were used in qualitative variables, mean ±SD in quantitative and for the comparison between groups Chi2 test or Fisher test was used in categorical variables and Student T test or U of Mann-Whitney in quantitative. The statistical analysis was performed with IBM SPSS v.23.

TABLE 1. CHARACTERISTICS OF PRIMARY LVV AND LVV ASSOCIATED WITH GCA.

	Primary LVV, n=15	LVV associated with GCA, n=13	P
Age, mean±SD	66.33±10.16	76.77±8.9	**0.004***
Age ≥ 70 years, n (%)	8 (53.3%)	10 (76.9%)	0.254
Sex (M/F)	4/11	3/10	1
VASCULAR RISK FACTORS			
High blood pressure, n (%)	3 (20%)	7 (53.8%)	0.114
Diabetes, n (%)	2 (13.3%)	0 (0%)	0.484
Dyslipidemia, n (%)	4 (26.7%)	5 (38.5%)	0.689
Tobacco, (%)	2 (13.3%)	3 (23.1%)	0.598
CLINICAL FEATURES AT AORTITIS DX			
Constitutional syndrome, n (%)	10 (66.7%)	9 (69.2%)	1
Fever, n (%)	6 (40%)	2 (15.4%)	0.221
Atypical PmR, n (%)	10 (66.7%)	6 (46.2%)	0.274
Inflammatory low back pain, n (%)	7 (46.7%)	1 (7.7%)	**0.038***
Irradiated lower limb pain, n (%)	2 (13.3%)	2 (15.4%)	1
LABORATORY TEST AT AORTITIS DX			
Hemoglobin, mean±SD	12.07±1.85	11.1±1.13	0.108
Platelets, mean±SD	310013±112683	308538±80075	0.751
CRP, mean±SD	2.94±1.94	5.52±5.7	0.118
ESR, mean±SD	70.2±31.02	65.31±23.79	0.683
AFFECTED TERRITORIES			
Superior limbs, n (%)	1 (6.7%)	1 (7.7%)	1
Supra-aortic trunks, n (%)	10 (66.7%)	10 (76.9%)	0.686
Aortic arch, n (%)	11 (73.3%)	7 (53.8%)	0.433
Thoracic aorta, n (%)	11 (73.3%)	12 (92.3%)	0.333
Abdominal aorta, n (%)	10 (66.7%)	6 (46.2%)	0.445
Iliac arteries, n (%)	1 (6.7%)	4 (30.8%)	0.153
Femoropoplíteal arteries, n (%)	1 (6.7%)	2 (15.4%)	0.583
TREATMENT OF AORTITIS AT DX			
Prednisone dose (mg/day), mean±SD	44.33±17.2	38.46±17.8	0.387
Patients receiving CS pulses, n (%)	4 (26.7%)	3 (23%)	0.827
Patients receiving MTX, n (%)	8 (53.3%)	10 (76.9%)	0.184
MTX dose (mg/week), mean±SD	12.81±4.1	11.25±3.58	0.460
Patients receiving biololgical therapy, n (%)	0 (0%)	2 (15.4%)	0.206
EVOLUTION AT 4 MONTHS			
Asymptomatic/partial improvement/no change, n	8/6/1	7/5/1	0.993
Prednisone dose (mg/day), mean±SD	16.5±8.1	20.2±8.06	0.254
Patients receiving MTX, n (%)	12 (80%)	11 (84.6%)	1
MTX dose (mg/week), mean±SD	15.83±5.6	12.05±4.3	0.091
Patients receiving biololgical therapy, n (%)	1 (6.7%)	2 (15.4%)	0.583
CRP, mean±SD	0.84±2.12	0.59±0.82	0.698
ESR, mean±SD	23.4±27	18.7±19.1	0.609
Hemoglobin, mean±SD	13.45±1.53	12.75±1.43	0.230

LVV: large vessel vasculitis, GCA: giant cell arteritis, DX: diagnosis, PmR: polymyalgia rheumatic, CPR: C-reactive protein, ESR: erythrocyte sedimentation rate, CS: glucocorticoids, MTX: methotrexate

Results: We included 28 patients diagnosed with LVV (9 between 2013-2015 and 19 between 2016-2018). 75% were female with an average age±SD of 71.18±10.8 years. They were divided into two groups: primary LVV (n=15) and LVV associated with GCA (n=13). The diagnosis of GCA was made by ultrasound (n=6), biopsy (n=5) and both tests (n=2). In 7 patients (54%) aortitis and GCA diagnosis was simultaneous. In LVV with GCA, headache was observed in 84.6% of patients and constitutional syndrome in 53.8%.

Primary LVV was characterized by lower age at onset, inflammatory low back pain, fever, atypical polymyalgia rheumatica and lower CRP levels; only the first two variables reached statistical significance, probably due to sample size. TABLE 1

The mean number of affected vascular territories was 3 and thoracic aorta was the most affected territory in both groups.

The steroid treatment was similar in both groups, whereas methotrexate (MTX) was used more frequently in the LVV associated with GCA. In the first 4 months, 1 patient with primary LVV required Tocilizumab (TCZ).

The final clinical evolution was similar and favorable in both groups. At the last visit, after a mean follow-up of 11.94±8.5 months in the primary LVV and 29.63±14.8 months in the LVV secondary to GCA, 93% of patients were asymptomatic with a mean ESR of 24,07±20 and CRP 0.56±0.91. Treatment used in primary LVV were: glucocorticoids (CS) (n=4), mean dose 8.75±7.4mg; MTX (n=11), mean dose 18.18±5.6mg/week and TCZ (n=2). In LVV associated with GCA, 2 patients were without treatment; CS (n=9), mean dose 4.75±4mg; MTX (n=8), mean dose 13.44±6mg/week and TCZ (n = 2).

15 imaging tests were performed 6-10 months after diagnosis. Later, after an average time of 28.77±10.7 months 9 more control PET-CT were requested. TABLE 2.

TABLE 2. EVOLUTION OF IMAGE TESTS PERFORMED.

	Primary LVV, n=15	LVV associated with GCA, n=13	TOTAL=28
AT 6-10 MONTHS, (total of tests performed, n)	**6**	**9**	**15**
Full resolution, n (%)	0 (0%)	2 (22.2%)	2 (13.3%)
Partial improvement, n (%)	5 (83.3%)	4 (44.4%)	9 (60%)
Without changes, n (%)	1 (16.7%)	2 (22.2%)	3 (20%)
Worsening, n (%)	0 (0%)	1 (11.1%)	1 (6.7%)
LAST PET-CT, (n)	**3**	**6**	**9**
Time of evolution (months, mean±SD)	22.67±7.51	31.83±11.29	28.77±10.7
Full resolution, n (%)	1 (33.3%)	0 (0%)	1 (11.1%)
Partial improvement, n (%)	0 (0%)	2 (33.3%)	2 (22.2%)
Without changes, n (%)	1 (33.3%)	3 (50%)	4 (44%)
Worsening, n (%)	1 (33.3%)	1 (16.7%)	2 (22.2%)

Conclusion: In this study, younger age at onset and inflammatory low back pain were more frequent in primary LVV with statistical significance. The most affected vascular territory was the thoracic aorta in both groups.

The clinical and analytical evolution was similar in both populations. In the treatment, the only notable thing was the increased use of MTX in the LVV associated with GCA.

68% of the aortitis were diagnosed in the last 3 years due to greater clinical suspicion. PET-CT is a useful tool in the diagnosis of this pathology.

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AB0579

COMPARISON OF CLINICAL CHARACTERISTICS OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS BETWEEN RHEUMATOLOGY AND RESPIRATORY MEDICINE: A SINGLE CENTER, RETROSPECTIVE STUDY

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare but potentially life-threatening systemic necrotizing vasculitis. Multiple organs may be involved and patients initial consulting different departments may have different clinical manifestations.

Objectives: To explore the clinical characteristic of EGPA diagnosed in different departments in our hospital.

Methods: A retrospective study of EGPA patients in Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China. All patients fulfill the ACR 1990 classification criteria or the EULAR/ACR 2017 draft classification criteria. Demographic and clinical data of EGPA patients were collected and compared between different departments.

Results: 1) There were 45 EGPA patients diagnosed between December 2003 and January 2019. There were 29(64.4%) male, with median onset age 46(36~56) years, median time required for diagnosis 24(3~96) months. There were 8(17.8%) patients had history of drug allergy. There were 31(68.9%) patients fulfill the ACR 1990 classification criteria and 40 (88.9%) fulfill the EULAR/ACR 2017 draft classification criteria.

2) The main clinical manifestations included asthma-like symptoms (82.2%), limb numbness (37.8%), rash (22.2%), fever (20.0%), gastrointestinal symptom (11.1%) and arthralgias (8.9%). There were 91.1% (41/45) patients had serum eosinophil >10%, 77.8% (35/45) serum eosinophil $>1.0\times10^9$/L, 77.5% (31/40) elevated serum IgE, 7.8% (3/44) positive MPO-ANCA or p-ANCA and 18.4% (7/38) positive ANA.

3) There were 21(46.7%) patients diagnosed at rheumatology, 22(48.9%) at respiratory medicine, 1(2.2%) at dermatology and 1(2.2%) at pediatrics.

Compared with patients diagnosed at respiratory medicine, patients diagnosed at rheumatology had a higher frequency of fever (33.3% vs. 0), rash (33.3% vs. 4.5%), arthralgias (19.0% vs. 0) and limb numbness (57.1% vs. 22.7%), but lower frequency of asthma-like symptoms (66.7% vs. 100%; all $P<0.05$). There were more patients diagnosed at rheumatology received treatment of glucocorticoid (100% vs. 72.7%), immunosuppressive agents (85.7% vs. 4.5%) and intravenous immunoglobin (28.6% vs. 0) than those diagnosed at respiratory medicine (all $P<0.01$). Patients diagnosed at rheumatology also received higher initial dose of glucocorticoid than those diagnosed at respiratory medicine [50(50~100) mg/d vs. 28(10~40) mg/d of prednisone dosage, $P<0.001$].

4) Among the 21 patients diagnosed at rheumatology, 14(66.7%) had asthma-like symptoms, who showed significant longer time required for diagnosis than those without asthma-like symptoms [36(24~120) months vs. 2(2~13) months, $P=0.020$], but showed no significant difference of onset age between these two groups ($P>0.05$).

5) The median revisited Five-Factor Score (FFS) was 0(0~1). There were 17(37.8%) patients had FFS$\geq$1, who had older diagnostic age than those with FFS=0 [65(46~68) years vs. 48(42~53) years, $P<0.05$], but with no significant difference of onset age or time required for diagnosis. Patients with FFS$\geq$1 had higher level of serum IgE [1280(515~4895) IU/mL vs. 243(72~587) IU/mL] than those with FFS=0 ($P<0.05$).

Conclusion: Clinical manifestations of EGPA were different between rheumatology and respiratory medicine. Rheumatologist may be more aggressive treating EGPA patients with glucocorticoid and immunosuppressive agents than respiratory physician. Multidisciplinary team is needed for the diagnosis and management of EGPA.

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AB0580 A VISION OF THE CHARACTERISTICS AND COMORBIDITIES OF GIANT CELL ARTERITIS FROM THE HOSPITAL RECORDS OF THE NATIONAL HEALTH SYSTEM

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Background: Gigant cell arteritis (GCA) is the most frequent systemic vasculitis in older than 50 years old, with serious repercussions on the quality of life and survival of patients. The low prevalence and heterogeneous presentation make progress in the diagnostic and the knowledge of the disease difficult.

Objectives: The objective of this study has been to gather a large database to analyze the epidemiological characteristics, the comorbidities and the causes of mortality associated with the hospitalizations by ACG in our country.

Methods: Retrospective observational study based on data from the Database of Hospital from the Spanish National Health Service with primary or secondary diagnostic of GCA between January 1st, 2005 and December 31th, 2015. The included variables were sex, age, main reason for admission, secondaries diagnostics, time of stay, costs, comorbidities, temporal artery biopsy and mortality.

Results: The study cohort included 29.576 patients with GCA, 18.568 (62,8%) women, and the mean age was 80 ± 8 years. The number of hospital admissions with this diagnostic has increased between 2008 and 2013 with an annual cumulative increase rate of 3%, passing from 2.487 to 2.997 patients/year. We have found a different disease affectation pattern in men and women in terms of distribution by age group and the comorbidities associated. We have found that the mortality risk increases with the age and with the presence of cardiovascular disease OR 1,816 (1,484-2,221), ischemic heart disease OR 1,590 (1,302-1,941), renal disease OR 1,386 (1,225-1,569) and cancer OR 2,428 (2,039-2,891). While, a decrease in the risk of death was observed in patients who associated polymyalgia rheumatica OR 0.682 (0, 5810,801).

Table 1. Comorbidities and mortality in hospitalized with ACG

		Men		Woman		Both sexes	
		N	%	N	%	N	%
DM2 *		2948	26,8%	4669	25,1%	7617	25,8%
PMR *		1474	13,4%	2715	14,6%	4189	14,2%
ICC*		1298	11,8%	2854	15,4%	4152	14%
ENF.		1556	14,1%	2413	13,0%	3969	13,4%
RENAL *							
Cancer		809	7,3%	499	2,7%	1308	4,4%
IHD *		626	5,7%	565	3,0%	1191	4%
ECV *		502	4,6%	651	3,5%	1153	3,9%
EPOC		289	2,6%	559	3,0%	848	2,9%
CCI*	No comorbidities	4833	43,9%	9174	49,4%	14008	47,4%
	≤ 2 Comorbidities	5635	51,2%	8697	46,8%	14332	48,5%
	> 2 Comorbidities	539	4,9%	697	3,8%	1236	4,2%
Mortality		712	6,5%	1083	5,8%	1795	6,1%

*Statistically significant differences ($P < 0.05$) **DM2:** Diabetes mellitus Type 2 **PMR**: Polymyalgia rheumatica **ICC:** Congestive heart failure **IHC:** ischemic heart disease **ECV:** Cerebrovascular disease **CCI:** Charlson Index of Comorbidities

Conclusion: In recent years the number of GCA hospital admissions has increased. The presence of comorbidities is high and greater in men. An increase in deaths for ischemic cause and a reduction of mortality in patients with PMR associated is observed.

Disclosure of Interests: None declared

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AB0581 AN ATYPICAL PRESENTATION OF GIANT CELL ARTERITIS WITH SCALP LUMPS: A CASE REPORT

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Background: Giant cell arteritis (GCA) also referred as temporal arteritis is a systemic inflammatory vasculitis of unknown etiology which can result in wide range of systemic, neurologic and ophthalmic complications. It predominantly occurs in older people and may be associated with Polymyalgia Rheumatica. It must be treated urgently as it is associated with significant risk of permanent visual loss, stroke, aneurysm and possible death. Diagnosis of GCA can be based on clinical findings such as headache, scalp tenderness, jaw claudication and temporal artery problems, an elevated ESR and biopsy temporal artery showing typical histopathological findings. Diagnosis of GCA may be delayed when presentation is atypical.

Objectives: We report a case of an elderly lady presenting with scalp lump as an unusual presentation of GCA.

Methods: 70 years old lady presented with multiple painful scalp lumps to the surgeon was referred to the Rheumatologist when the excision biopsy of the lump diagnosed the GCA. (Sub cutis medium sized artery with severe arteritis composed with lymphocytes, neutrophils and occasional Eosinophills). On enquiry she revealed a history of generalized malaise and lethargy at the outset of the illness preceded by jaw pain

She had been initially referred to the dental surgeon which resulted in multiple carious tooth extractions without a relief. She didn't have any eye symptoms or headache at the outset. She lately developed headache and pain on touching the lumps.

On examination she had bilateral hardened thickened palpable non pulsatile temporal arteries. Her scalp was tender with multiple small cystic lumps. Her ESR was highly elevated 141mm/hr. WBC 9.7, Hb 9.5 and PLT 283. Her ANA, liver and renal profiles were normal. Her BL Doppler USS was consistent with BL temporal arteritis.

Results: She was soon started on high dose prednisolone with low dose aspirin which improved her systemic symptoms along with inflammatory markers significantly over a few days. She was referred for eye assessment and the involvement of other systemic larger arteries was ruled out.

Conclusion: Most of the cases the diagnosis of GCA is obvious but in patients with uncommon clinical presentation the diagnosis may be difficult.GCA is classified as disease of large vessel vasculitis but typically also involves medium and small arteries.The granulomatous inflammation in the vessel wall leads to obstruction of the lumen and ischemia in the territory distal to it. GCA involves almost all speciality and it is associated with increased mobility and mortality if not diagnosed and treated early. Awareness of rare presentation of GCA avoids unnecessary investigation and delaying the treatment.If there is no rapid improvement of symptoms within few weeks of starting treatment other diagnosis should be considered.

REFERENCES

[1] Gunawardena H, Kyle M.V, Atypical presentation s of Giant cell arteritis-A District General Hospital perspective, Rheumatology, volume 44, Issue suppl_3, 1 July 2005, pages iii17-iii18

[2] Weyand CM,Goronzy JJ. Giant cell arteritis and Polymalgia rheumatica. *N Engl J Med* 2014;371:50-7

[3] Shambu.S, Suarez. L, Giant cell arteritis: An atypical presentation diagnosed with the use of MRI imaging, *Case Reports in Rheumatology*, volume 2016, article ID8239549

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AB0582 NEUROLOGIC INVOLVEMENT IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS –EXPERIENCE FROM A PORTUGUESE CENTER

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Background: Involvement of peripheral (PNS) and central nervous system (CNS) in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis has been reported in 15-60% and 5-15% of patients (pts), respectively. PNS involvement occurs mainly in eosinophilic granulomatosis with polyangiitis (EGPA) and CNS involvement has been almost exclusively described in granulomatosis with polyangiitis (GPA). Neurologic involvement is associated with a higher morbidity and implies more immunosuppressive treatment in most pts.
Objectives: Evaluate prevalence and clinical features of PNS/CNS involvement in pts with ANCA-vasculitis in a Portuguese center.
Methods: Retrospective analysis of ANCA-vasculitis pts with neurologic involvement followed in our department from January 2016 to December 2018.
Data was collected from the Portuguese database REUMA.PT and included demographic data, vasculitis subtype, date of diagnosis, neurologic manifestations and treatment approach.
Results: In total, 11 pts were identified, mostly female (7/11) with mean age of 61±13.3 years (yrs). Five pts had EGPA, 5 GPA and 1 microscopic polyangiitis (MPA). Neurologic involvement was part of disease presentation in 8 pts (5 EGPA, 3 GPA). The other 3 pts had neurologic involvement 7±2.2 yrs after vasculitis diagnosis. At the time of neurologic involvement diagnosis, Birmingham Vasculitis Activity Score was 8.8±4.3.
PNS involvement occurred in 9 pts, all presenting mononeuritis multiplex (MM). From these, 5 had EGPA, 3 GPA and 1 MPA.
CNS involvement was reported in 3 pts, 2 with GPA and 1 with EGPA. Pachymeningitis was diagnosed in 1 GPA pt with persistent headache, refractory to analgesics, and thickening and enhancement of the dura mater on postcontrast magnetic resonance imaging. Two pts had cranial mononeuropathy, 1 with EGPA and MM who developed VI palsy 2 yrs after vasculitis diagnosis and 1 pt with GPA and VII palsy at disease presentation who developed XII palsy 8 yrs later.
All pts were treated with prednisolone (1mg/kg/day), mostly in combination with other immunosuppressive drugs. The choice of the treatment was based on the age of the pt and other comorbidities.
Detailed treatment of these pts and subsequent responses are shown in table 1.

Table 1 – Detailed data on patients with neurologic involvement in relation to ANCA-vasculitis

Patient	Gender/Age	ANCA-vasculitis	Interval from vasculitis onset to neurologic manifestations (years)	Type of neurologic involvement	Evolution
1	Male / 54	GPA	0	Mononeuritis multiplex	Improvement with CYC; disease progression after RTX + MMF (IVIg as bridging therapy until RTX retreatment)
2	Female / 69	GPA	0	Mononeuritis multiplex	Improvement with RTX + IVIg
3	Male / 43	GPA	10	Mononeuritis multiplex	Less than 6 months of treatment
4	Male / 78	GPA	6	Pachymeningitis	Improvement with RTX
5	Female / 36	GPA	0	VII palsy	Resolution with CYC
			8	XII palsy	Resolution with RTX
6	Female / 73	MPA	5	Mononeuritis multiplex	No response to RTX; improvement after 3 months on CYC
7	Female / 71	EGPA	0	Mononeuritis multiplex	Resolution with PDN
8	Male / 47	EGPA	0	Mononeuritis multiplex	Less than 6 months of treatment
9	Female / 61	EGPA	0	Mononeuritis multiplex	Improvement with CYC, followed by maintenance with AZA
10	Female / 69	EGPA	0	Mononeuritis multiplex	Improvement with IVIg followed by AZA
11	Female / 70	EGPA	0	Mononeuritis multiplex	Improvement with IVIg
			2	VI palsy	Resolution with RTX

Legend – GPA - granulomatosis with polyangiitis; MPA - microscopic polyangiitis; EGPA - eosinophilic granulomatosis with polyangiitis; CYC - cyclophosphamide; RTX – rituximab; MMF – mycophenolate mofetil; IVIg – intravenous human immunoglobulin; PDN – prednisolone; AZA – azathioprine

Figure 1

In our cohort there were 2 pts with serious infections: 1 with oropharyngeal and esophageal candidiasis and another with bacteraemia to *Pseudomonas aeruginosa*. Both pts were under immunosuppressive agents including corticosteroids and rituximab or cyclophosphamide.
Conclusion: Neurologic involvement was part of disease presentation in most pts and the commonest manifestation was mononeuritis multiplex.
PDN was prescribed to all pts, in most cases in association with other immunosuppressive drugs. Cyclophosphamide and rituximab (RTX) were used as induction treatment, and mycophenolate mofetil, azathioprine and RTX as maintenance. Intravenous human immunoglobulin was used in pts colonized by multiresistant microorganisms/severe infection with immunosuppression and as a bridging therapy to further immunosuppression. Most pts achieved clinical improvement, documented in electromyography.

REFERENCES

[1] Graf J. Central Nervous System Disease in Antineutrophil Cytoplasmic Antibodies–Associated Vasculitis. Rheum Dis Clin N Am. 2017 Nov;43 (4):573–8.

[2] Wolf J, Schmitt V, Palm F, Grau AJ, Bergner R. Peripheral neuropathy as initial manifestation of primary systemic vasculitides. J Neurol. 2013 Apr;260(4):1061–70.

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AB0583 100 GCA REFERRALS TO A TERTIARY CARE CENTRE: INFLAMMATION, HEADACHES AND CPAP MASKS

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Background: Giant cell arteritis (GCA) is a large vessel vasculitis typically affecting patients above the age of 50 years. It is the most common cause of vasculitis affecting adults with a UK prevalence of approximately 0.25% of the population above the age of 55 years [1]. Whilst its clinical presentation can often be non-specific, if left undiagnosed it can lead to devastating visual impairment. However, this has to be balanced with the potential for corticosteroid related adverse effects. The threshold for suspected diagnosis and referral to rheumatology centres from the community and acute medical services is therefore low, leading to a relatively high number of referrals with a wide range of clinical features and potential differential diagnoses.
Objectives: To assess the referral characteristics, demographics, management, corticosteroid adverse effects and differential diagnosis of 100 consecutive patients referred with suspected GCA to a tertiary rheumatology centre.
Methods: The notes of 100 consecutive patients referred to the rheumatology department at Addenbrookes hospital between August 2016 and January 2018 with suspected GCA were reviewed. Information on patient demographics, comorbidities, presenting symptoms, availability of up to date inflammatory markers, dates of treatment and clinic review, temporal artery biopsy (TAB) date and result, diagnosis and corticosteroid adverse effects were retrieved.
Results: Seventy three female and twenty seven male patients (average age 72.3 years) were referred within the time period. General practice referred 69% of the cases and common comorbidities included hypertension and type II diabetes. The most common symptoms were headache (97%), scalp tenderness (79%), jaw claudication (35%) and polymyalgia symptoms (34%). Up to date inflammatory markers were available for 91% of referrals and 92% were commenced on corticosteroids before or at the time of referral with an average starting dose of 43.9mg oral prednisolone. A TAB was performed on 85% of patients, with an average time of 9 days between referral and TAB and 40 days between referral and clinic appointment. TAB was positive for GCA in 13/85 patients. Temporal artery ultrasound (TAU) was not available at our centre. The American College of Rheumatology (ACR) classification criteria for GCA were met by 85% of the patients, but only 69% were given a diagnosis of GCA. Other diagnoses included trigeminal neuralgia, temporo-mandibular dysfunction, toothache and a poorly fitted CPAP mask. Corticosteroid adverse effects were experienced by 45% of patients including weight gain, poorly controlled diabetes, mood and sleep disturbance, and 4% suffered severe complications requiring hospital admission (pneumonia, disseminated nocardia infection and two episodes of upper gastrointestinal bleed).
Conclusion: Suspected GCA is a common referral to rheumatology but the non-specific symptoms, quality of referral and potential for visual loss can lead to over-diagnosis. We have found the majority of our referrals to have been appropriate and complete with 85% meeting ACR criteria for GCA and 92% having up to date inflammatory markers. Despite this, 31% of patients received an alternative diagnosis. Increasing the availability of

TAU may improve the time to diagnosis and therefore potentially reduce unnecessary exposure to corticosteroids. Our experience highlights the fact that despite a good standard of referral, GCA remains a difficult condition to diagnose and poses an on-going challenge to the rheumatologist.

REFERENCES

[1] Yates, M., et al., *The prevalence of giant cell arteritis and polymyalgia rheumatica in a UK primary care population*. BMC Musculoskelet Disord, 2016. 17: p. 285.

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AB0584 JOINT PROFILE OF BEHÇET'S DISEASE

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Background: Joint manifestations during Behçet's disease (BD) are frequent and polymorphic.
Objectives: To analyze these manifestations through 41 cases.
Methods: A retrospective study of 41 patients, collected at the rheumatology department of Farhat Hached University Hospital over a period of 19 years, meeting the criteria of the international study group on BD.
Results: 41 patients with a mean age of 40.21 years [16-66] were collected. The sex ratio=2.41. The articular and mucocutaneous involvement were constant. Also were found ocular manifestations (5cas), neurological (1cas), cardiac (1cas), gastro-intestinal (1cas), venous thrombosis (5 cases), arterial thrombosis (1 case) and an aneurysm (2 cases). Joint involvement was revealing in 21 cases (51.2%) occurring during evolution in 20 cases with an average delay of 102 months [6-360]. The most frequent manifestations were arthralgia in 24 cases (58.5%) and arthritis in 17 cases. It was predominantly asymmetric (21 cases), mono articular (13 cases), oligoarticular (16 cases) and polyarticular (12 cases). The knees and ankles were the most affected joints in 32 cases and 25 cases respectively, followed by wrist involvement (12 cases), MCP (5 cases) and elbows and shoulders in 4 cases each. A knee flessum was found in 2 cases. X-rays were mostly normal (35 cases). They showed erosive involvement (1case), joint narrowing (1case), osteonecrosis (2cases) and sacroiliitis (2cases). The presence of a popliteal cyst was noted in 2 cases.
Conclusion: Joint manifestations during the BD can be inaugural and take on several clinical aspects. They usually heal without sequelae and do not engage functional prognosis with the exception of rare cases of destructive arthritis.
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AB0585 REJA-VASCA: JAVERIAN REGISTRY OF PATIENTS WITH POSITIVE ANCA VASCULITIS AT THE UNIVERSITY HOSPITAL SAN IGNACIO 2005–2017

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Background: Vasculitis associated with cytoplasmic antibodies (VAAC) are heterogeneous entities with low prevalence and high morbidity and mortality. These include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (PAM), and eosinophilic granulomatosis with polyangiitis (GEPA). European retrospective records report an annual incidence of 10-20 cases per million, with peak presentation between 65-74 years, predominantly in males. It has diverse clinical manifestations in multiple systems. In Colombia, there are few clinical records that describe the clinical characteristics of these patients.
Objectives: To describe the clinical characteristics of patients with VAAC in the University Hospital San Ignacio between 2005-2017
Methods: Descriptive cross-sectional study. Patient records were reviewed between January 2005 and December 2017. The records were obtained using search systems in patients who were requested Antineutrophil cytoplasmic antibodies - ANCAS (Searching softeare: DISEARCH, LABCORE), obtaining 2072 results. 106 patients met the criteria for classification of the American College of Rheumatology for VAAC.
Results: 106 patients diagnosed with ANCA positive vasculitis. Average age 55 years (± 14.7). 48.4% were women. In-hospital debut in 68.8%. The average number of days of stay was 16.6 days (± 12.22), 56 patients (52.8%) had granulomatosis with polyangiitis GPA, 45 patients (42.4%) with microscopic polyangiitis (MAP) and 5 patients with eosinophilic granulomatosis with polyangiitis EGP (4.8%). 37 patients (35%) presented with alveolar hemorrhage, 22 patients (20.7%) presented renal compromise with rapidly progressive glomerulonephritis. Central nervous system compromise was documented in 25 patients (24%). Regarding treatment, 97 patients (91.5%) received treatment with intravenous or oral corticosteroid, 66 patients (62.2%) received treatment with cyclophosphamide. Plasma exchange therapy was performed in 15 patients (14.1%). 44 patients (41.5%) required renal replacement therapy. The in-hospital mortality of this group of patients was 20.4%, with sepsis being the most frequent cause of death (55%).
Conclusion: In this study, the most frequent positive ANCA vasculitis was granulomatosis with polyangiitis. Multisystemic compromise was present in all groups of patients, the most common being pulmonary and renal, mainly in patients with microscopic polyangiitis, similar to that reported by Solans-Laqué et al in Spain. Within the demographic characteristics, the average age at the time of diagnosis is around 50 years, predominantly in women related to the Mexican study by Hinojosa-Azaola et al. The most frequent cause of in-hospital mortality was sepsis. Clinical information of patients with VAAC is presented in a reference hospital in Colombia. Data are concordant with literature.
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AB0586 TAKAYASU ARTERITIS: REVIEW OF DIAGNOSTIC AND CLASSIFICATION CRITERIA IN A 9 CASE SERIES

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Background: Takayasu arteritis (TA) is a rare large vessel vasculitis that affects the aorta (Ao) and its main branches. Early diagnosis and the rapid establishment of treatment are key points in the prognosis of the disease. Despite the existence of different classification and diagnostic criteria, early diagnosis of TA continues to be a challenge.
Objectives: 1) To analyze the concordance between the different classification and diagnostic criteria in patients with TA, 2) To describe the demographic, clinical and analytical characteristics of TA.

Methods: Retrospective observational study that included all patients diagnosed with TA according to medical criteria between 1981 and 2018, visited in a Rheumatology unit. Demographic, clinical, analytical and image data were collected. It is assumed that the vascular territories affected and the type of vascular involvement can be evaluated by angio-CT, angio-MRI and PET-CT with contrast iv. in case angiography is not performed. Ishikawa diagnostic criteria, 1990 ACR classification criteria and Ishikawa's diagnostic criteria modified by Sharma were evaluated.
Results: We included 9 patients (77.8% women) diagnosed with TA. The age at diagnosis was 33.3 ±16.3 years with a time of evolution of 5.1 ±9.4 years. The other variables are shown in Table 1.

Variables	
CRP, mg/L, mean (SD)	42,8 (65,37)
ESR, mm/h, mean (SD)	33,3 (35,3)
HTA, n (%)	4 (44,4)
Limb claudication, n (%)	4 (44,4)
BP difference >10 mmHg, n (%)	5 (55,6)
Vascular pain, n (%)	4 (44,4)
Constitutional clinic, n (%)	3 (33,3)
Arthromyalgia, n (%)	1 (11,1)
Cefalea, n (%)	2 (22,2)
Syncope, n (%)	1 (11,1)
Decreased artery pulse, n (%)	5 (55,6)
Paresthesia, n (%)	2 (22,2)
Bruit, n (%)	4 (44,2)

The most frequent vascular territories afected were abdominal Ao (7), descending thoracic Ao (5) and iliac arteries (5). The most common type of arterial lesion was stenosis (8) followed by dilation and aneurysm. 6 patients were treated with corticotherapy as an induction treatment, 5 required chronic immunosuppression and 6 patients required surgery.
When reviewing the criteria we observed that all patients met the ACR criteria and 7 patients met the modified criteria by Sharma. However, the agreement with Ishikawa's diagnostic criteria was poor since 7 patients did not meet them. The different criteria are shown in Table 2.

Ishikawa, n (%)		**1990 ACR,** n (%)		**Modified Ishikawa,** n (%)	
Age ≤40 yrs	7 (77,8)	Age <40 yrs	7 (77,8)	Left subclavian lesion	4 (44,4)
Left subclavian lesion	4 (44,4)	Claudication of extremities	5 (55,6)	Right subclavian lesión	3 (33,3)
Right subclavian lesion	3 (33,3)	Decreased brachial artery pulse	4 (44,4)	Clinic at least 1 month duration,	9 (100)
VSG ≥20 mm/h	4 (66,6)	BP difference >10 mmHg	5 (55,6)	VSG >20 mm/h	4 (66,6)
Carotid artery tenderness	0	Bruit over subclavian arteries or Ao	4 (44,4)	Carotid artery tenderness	0
HTA	4 (44,4)	Arteriogram abnormality	9 (100)	HTA	4 (44,4)
Aortic regurgitation	3 (37,5)			Aortic regurgitation	3 (37,5)
Pulmonary artery lesion	0			Pulmonary artery lesion	0
Common carotid lesion	2 (22,2)			Common carotid lesion	2 (22,2)
Distal brachiocephalic trunk lesion	2 (22,2)			Distal brachiocephalic trunk lesion	2 (22,2)
Descending thoracic Ao lesion	5 (55,6)			Descending thoracic Ao lesion	5 (55,6)
Abdominal Ao lesion	7 (77,8)			Abdominal aorta lesion	7 (77,8)
				Coronary artery lesion	2 (33,3)

Conclusion:
- The most frequently affected vascular territory was the abdominal Ao, and the most common type of injury was stenosis.
- The most common clinical presentation was asymmetry of blood pressure between extremities and peripheral pulses, HTA and limb claudication.
- All patients met the ACR 1990 classification criteria and the great majority met the criteria modified by Sharma. The concordance with Ishikawa's criteria was poor so they should be used cautiously.

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AB0587 CLINICAL MANIFESTATIONS OF BEHCET'S DISEASE DEPENDING ON GENDER: A REVIEW OF 425 CASES IN RUSSIA

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Background: The gender-related differences in clinical course of Behcet's disease (BD) are well-established, and more severe course is usually observed among young males.
Objectives: To analyze the effect of gender on the severity and clinical features of BD.
Methods: The study included 425 patients (male – 285, female – 140) with BD (according to ISGBD 1990 and ICBD criteria 2014) [1, 2]. The male-to-female ratio was 2:1, the mean age was 33,2±10,2 yrs, the median of disease duration - 134,3 [60,0; 192,0] months.
Results:

General characteristics of BD-patients depending on gender

General characteristics	Male, n=285	Female, n=140	p
Age of pts, yrs (M±SD)	32,5±9,72	34,9±10,8	ns
Disease duration (Me [25%; 75%])	96,0 [60,0; 192,0]	108,0 [60,0; 216,0]	ns
Age of disease onset, yrs (M±SD)	21,2±9,71	22,8±11,5	ns
Activity (BDCAF), (M±SD)	3,71±2,02	2,64±1,45	0,0002
HLA-B5(51) +, n (%)	129 from 193 (67)	52 from 101 (51,5)	0.007

BD severity depending on gender

BD severity, n (%)	Male, n=285	Female, n=140	p
Mild	48 (17)	57 (41)	<0,001
Moderate	29 (10)	14 (10)	ns
Severe	208 (73)	69 (49)	<0,001

We observed the following gender-related differences in clinical manifestations of BD: males significantly more often had uveitis (74% vs 57%, p=0,0003), optic neuritis (11% vs 0%, p=0,0004), blindness (9% vs 2,5%, p=0,04); cutaneous lesions (89% vs 71%, p<0,001), such as pseudo-folliculitis (53% vs 21%, p=0,001), positive pathergy test (39,6% vs of 24,3%, p=0,001); severe vascular involvement (vena cava and iliac vein thrombosis, deep vein thrombosis, arterial thrombosis and arterial aneurism) (27% vs 11%, p=0,001), cerebral sinus thrombosis (9% vs 3%, p=0,015) and genital ulcers (77,9% vs 67,1%, p=0,012) compared with females. Male BD-pts more often had HLA-B5(51)-positivity (67% vs 51,5%, p=0,007), higher BD activity (BDCAF - 3,71±2,02 vs 2,64±1,45, p<0,001) and BD-severity (severe BD-course – 73% vs 39%, p<0,001). Mortality rate in this BD cohort was 1,2%, and all 5 cases were young males aged under 30 years.
Conclusion: An association of severe clinical manifestations (ophthalmological and vascular, such as large vessels and cerebral sinus thromboses), higher disease activity & severity, as well
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AB0588 GASTROINTESTINAL INVOLVEMENT OF BEHCET'S DISEASE IN RUSSIA

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Background: Behcet's disease (BD) is a multisystem vasculitis with unknown etiology and a unique geographical distribution. Intestinal manifestations of BD (IBD) are of particular importance as they are associated with significant morbidity and mortality. Although ileocecal involvement is most commonly described, BD may involve any segment of the intestinal tract as well as the various organs within the gastrointestinal system.
Objectives: To analyze the severity and clinical features IBD in Russia
Methods: The study included 250 patients (male – 177, female – 73) with BD (according to ISGBD 1990 and ICBD criteria 2014). The male-to-female ratio was 2,4:1, the mean age was 31,5±9,3 yrs, the age of disease onset - 21.8±9.62 yrs, the median of disease duration - 10.25 ±8.32 yrs. All those with gastrointestinal symptoms were subject to a gastroscopy and/or colonoscopy through which Crohn's disease and ulcerative colitis were excluded by the proctologists.
Results: Patients with gastrointestinal symptoms were 63 of 250 - 25.2% pts, (male – 40, female – 23). Symptoms of IBD include the abdominal pain in 62% pts, distension –55%, diarrhea – 14%, nausea – 13%, blood in the bowel movement – 4,7%. The examination revealed: esophageal ulcers (1.6%, four cases), gastric ulcers (3.2%, eight cases), and duodenal ulcers (1.2%, three cases) were found using endoscopy. Also, 6.8% (17 patients) had gastro duodenal ulcers and 14.3% (nine patients) combined gastrointestinal involvement including esophageal and had gastro duodenal ulcers. Colonic ulcers were detected in 9.2% (23 cases) by colonoscopy, two patients had multisegmental diffuse ulceration, three patients had in the sigmoid colon and of everyone else in the ileum. Ccolitis without ulcers found in 5,6% (14 cases). Two patients had a clinic of appendicitis, the operation found that the appendix is not inflamed. Two patients were 0.8% (were on treatment) urgently operated due to perforation of ulcers of the ileum, the woman held suturing of perforated ulcer, and a man - hemicolectomy. The last patient has a relaparotomy after 1 month and removal of the entire colon.
Conclusion: The IBD in Russia is affected in 1/4 of patients, but heavy refractory forms not often.

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AB0589 ANCA ASSOCIATED VASCULITIS: OUR EXPERIENCE FROM A TERITIARY CARE CENTER OVER 10 YEARS

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Background: The anti-neutrophil cytoplasmic antibody (ANCA)- associated vasculitides (AAV) are a group of disorders characterized by necrotizing inflammation of the small to medium vessels in association with autoantibodies. Childhood ANCA vasculitides are rare but can cause organ or even life-threatening systemic vasculitis. Children most frequently present with rapidly evolving, severe disease.
Objectives: To describe the clinical spectrum of ANCA associated vasculitis, the treatment given and follow up
Methods: A single-centre retrospective analysis of ANCA associated vasculitis over a period of 10 years from 2008 to 2018
Results: Six children (2 boys; 4 girls) were diagnosed to have AAV during this period. Median age at diagnosis was 11.25 years (range 8-18 years). Median delay in diagnosis was 1.5 months (range 1-8 months). Presenting clinical features included lung disease- 4 children; arthritis- 3 (knee, right ankle-left 3rd MCP, left elbow-knee) hemoptysis- 2 children; ear discharge- 1; redness of eye-1; oliguria, gross hematuria-2; anasarca-2; 2 children had concomitant neurological symptoms (left foot drop, quadriparesis with seizures). All children had fever at presentation. Laboratory investigations showed elevated erthrocyte sedimentation rate(ESR) and C-reactive protein(CRP). ANCA testing was positive in 6 children (3 c-ANCA, +PR3, 3 p-ANCA, +MPO). Deranged renal function tests, proteinuria, microscopic hematuria) were seen in 4 out of 6 children. Renal biopsy showed pauci immune glomerulonephritis in 4 cases who presented with nephritis. All patients were treated with 5 pulses of intravenous methylprednisolone(30 mg/kg/day) with tapering doses of oral steroids. Intravenous cyclophosphamide pulses was given in 5 children while 1 received additional plasmapheresis (PLEX)- 8 cycles. Mintainence therapy included azathioprine(given in 5 children), low-dose prednisolone. Thrombocytopenia was noted in 1 child while on azathioprine; this was subsequently substituted with mycophenolate mofetil. Two children have been lost to follow-up. Median duration of follow-up is 35.5 months (range 8-124 months). All 4 children have attained remission with good compliance and there are no relapses.
Conclusion: While an evidence base treatment of AAV in children is limited, our data suggests that prolonged remission can be achieved with aggressive immnosupressive therapy, however prognosis of childhood AAV remains guarded.

Table: Characteristics of children enrolled in study

Patients/ features	Age of diagnosis(years)/ year of diagnosis	Lower airway (Lung)	Upper airway	Renal	CNS	Arthritis	ANCA	Therapy	Follow up (months)	Mortality
Patient 1	8/M (2007)	+ Hemoptysis	-	++	-	-	P ANCA	Steroids	Lost to follow-up	-
Patient 2	11.5/M (2008)	+	+	+	+	+	C ANCA	Steroids, cyclophosphamide, azathioprine, MMF	124	+
Patient 3	9/F (2013)	+	+	++	Seizures + quadriparesis	+	P ANCA	Steroids, cyclophosphamide, PLEX	Lost to follow-up	+
Patient 4	11/F (2015)	+	+	++	+	+	C ANCA	Steroids, cyclophosphamide, azathioprine	46	+
Patient 5	12/F (2016)	+ Hemoptysis	-	+	Left foot drop	+	P ANCA	Steroids, cyclophosphamide, azathioprine	25	+
Patient 6	18/F (2018)	+	-	++	-	+	C ANCA	Steroids, cyclophosphamide, azathioprine	8	+

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8244

AB0590 A SINGLE CENTER RETROSPECTIVE ANALYSIS OF EFFICACY AND SAFETY BETWEEN LOW-DOSE VERSUS HIGH-DOSE RITUXIMAB AS REMISSION INDUCTION THERAPY IN JAPANESE PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: Administration of four once-weekly doses of 375 mg/m^2 rituximab (RTX) has been indicated for ANCA-associated vasculitis (AAV) as remission induction therapy. However, randomized controlled trial for Japanese AAV patients have never been conducted, although Japanese AAV patients are characterized by the predominance of elderly patients with microscopic polyangiitis (MPA).
Objectives: To compare the efficacy and safety between low-dose versus high-dose RTX therapy as remission induction therapy in Japanese patients with AAV.
Methods: A single center retrospective analysis of 27 consecutive AAV patients with RTX therapy was performed. Clinical and laboratory variables at diagnosis, rates of complete remission (CR), defined as Birmingham Vasculitis Activity Score (BVAS)=0 and prednisone <7.5 mg/day, adverse effects, and vasculitis relapses following RTX use.
Results: Twenty-five MPA patients and 2 GPA patients (14 males and 13 females) were included in the present study. Twenty-six patients were positive for MPO-ANCA. Their median age was 77 years (range: 40-85 years). Treatments were determined according to the discretion of the attending physician. As remission induction therapy, 18 patients were treated with once or twice (1/2) RTX infusions (375 mg/m^2), while 9 patients with 3 or 4 times (3/4) RTX infusions. At 6 months, 55.6% of the 1/2 infusion group (10/18) and 44.4% of the 3/4 infusion group (4/9) reached CR. At 6 months, mean PSL levels were 7.8 mg/day in the 1/2 infusion group and 6.6 mg/day in the 3/4 infusion group. At 18 months, 88.9% of the 1/2 infusion group (16/18) and 77.8% of the 3/4 infusion group (7/9) were survived. 0% of the 1/2 infusion group (0/18) and 33.3% of the 3/4 infusion group (3/9) were relapsed. Severe adverse effects occurred in 38.9% of the 1/2 infusion group (7/18) and in 22.2% of the 3/4 infusion group (2/9).
Conclusion: Our retrospective analysis indicated that cumulative CR rates and PSL tapering did not significantly differ between low-dose versus high-dose RTX as remission induction therapy in Japanese AAV patients, mostly elderly MPA patients, although there was no significant difference in severe adverse effects such as opportunistic infections between them.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.4450

AB0591 POSITIVE PREDICTIVE VALUE OF THE GIANT CELL ARTERITIS DIAGNOSIS IN THE DANISH NATIONAL PATIENT REGISTRY: A VALIDATION STUDY

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Background: Giant cell arteritis (GCA) is the most frequent systemic vasculitis[1]. The diagnosis is clinical and based on symptoms, histopathology, biochemistry and imaging. In Denmark, diagnostic codes for all in- and out-patient hospital diagnoses are registered in the Danish National Patient Registry (DNPR) [2]. Since GCA can be difficult to diagnose and treatment is initiated on suspicion, we hypothesized that the overall positive predictive value (PPV) of the GCA diagnosis code in the DNPR is low. High data quality is important for future epidemiological research in GCA.
Objectives: To establish PPV of the diagnostic code of GCA in the DNPR. Furthermore, to identify characteristics associated with a high PPV of the diagnostic code.
Methods: 293 patients aged ≥50 years with a first-time register-based GCA diagnosis were included from the DNPR in the period January 2012-January 2018. Patients were sampled based on the ICD-10 codes (M31.5 and M31.6) from two regional hospitals and one university hospital in the Central Region of Denmark. As gold standard we used the medical records (including biochemistry, histopathology and imaging results) and categorized each patient as true GCA or non-GCA. Based on the data from the prescription database, patients were divided into four categories depending on the number of prednisolone prescriptions they received. Two independent investigators (PH and PT) reviewed the medical records. In case of disagreement the final diagnosis was reached by consensus or by expert opinion (ITH). To test how the PPV varied,

sub-analyses were performed for number of prescriptions, specific symptoms, temporal artery biopsies (TAB), number of visits and number of prescriptions..

Results: We confirmed 183 of 293 diagnoses resulting in a PPV of 62.8% (95% CI: 57.1-68.2). In patients having at least three admissions, 95 of 110 diagnoses were confirmed (PPV: 86.4%; 95% CI: 78.5-91.7). We confirmed 82 of 95 patients with at least three visits and a TAB. This resulted in a PPV of 86.3% (95% CI: 77.7-91.9). The highest PPV was observed in patients with at least 3 visits and $\geq$3 prescriptions of prednisolone. In this sub-analysis we confirmed 88 of 95 diagnoses resulting in a PPV of 92.6% (95% CI: 85.2-96.5).

Conclusion: This is the first study to validate the diagnostic code of GCA in the DNPR. The overall PPV of a first-time diagnosis of GCA in the DNPR is low. The probability of identifying true cases of GCA increases substantially when diagnostic codes are combined with 3 visits and $\geq$3 prescriptions of prednisolone.

REFERENCES

[1] Gonzalez-Gay, M.A., et al., *Epidemiology of giant cell arteritis and polymyalgia rheumatica*. Arthritis Rheum, 2009. 61(10): p. 1454-61.

[2] Schmidt, M., et al., *The Danish National Patient Registry: a review of content, data quality, and research potential*. Clin Epidemiol, 2015. 7: p. 449-90.

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Disclosure of Interests: None declared
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AB0592 SYSTEMIC

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Background: Systemic vasculitis involving the breast is a rare clinical condition and may mimic breast cancer or mastitis clinically or radiographically.

Objectives: In this article, we reported a case of polyarteritis nodosa (PAN) with breast involvement and made a summary on the published cases of systemic vasculitis affecting breasts in order to better understand this disorder.

Methods: We reported a case of PAN affecting breast and conducted a retrospective review of literatures reporting patients with the diagnosis of systemic vasculitis involving breasts by using MEDLINE, EMBASE, Web of Science, the Cochrane Library, and Scopus database in any language up to June 1st, 2018.

Results: A case of a 27-year-old female patient presented with a painful mass of the right breast was diagnosed as PAN by the biopsy. After six months of treatment of full dose prednisone and methotrexate, her condition kept stable and inflammatory markers remained normal. A total of 67 cases were included, with granulomatosis with polyangiitis (GPA), giant cell arteritis (GCA) and PAN as the main types. The typical manifestation was mass (79.2%, 53/67) in the breast. All the diagnoses were made according to the pathology of the breast biopsy. Glucocorticoid and immunosuppressant were the main therapies. 74.6% (50/67) patients achieved remission during follow-up.

Conclusion: In total, we reviewed the clinical features and outcome of 67 cases of the systemic vasculitis involving the breast including the case we reported. Definite diagnosis depends on tissue biopsy, which is important, as the prognosis of diseases is upon to the types of vasculitis.

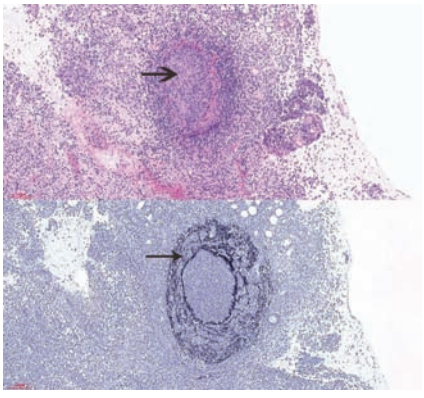


Figure 1

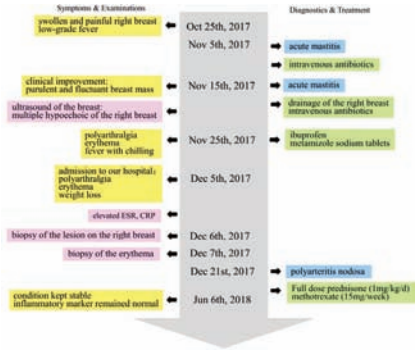


Figure 2

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3591

AB0593 INTERSTITIAL LUNG DISEASE ASSOCIATED WITH ANCA POSITIVITY: A RETROSPECTIVE ANALYSIS

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Background: The association between interstitial lung disease (ILD), antineutrophil cytoplasmic autoantibodies (ANCA) and vasculitis has been described in case reports and small series. Treatment approaches have been diverse and include the use of various immunosuppressive agents. To date, little is known about the clinical phenotype and outcomes of ANCA associated ILD.

Objectives: The objectives of this study were to ascertain the prevalence of ANCA in ILD patients at a tertiary respiratory centre; describe the clinical phenotype; describe lung function outcome and examine the progression of computed tomography (CT) patterns in patients with ANCA-associated ILD.

Methods: This retrospective observational study was conducted at a tertiary ILD centre. Patients with ILD and coexistent ANCA were identified from review of a clinical database. All patients had a multidisciplinary team diagnosis of ILD confirmed on CT scan and had no other underlying cause of ILD identified. Data regarding clinical characteristics, CT scan pattern of ILD, pulmonary function tests (PFTs) and treatment were collected retrospectively.

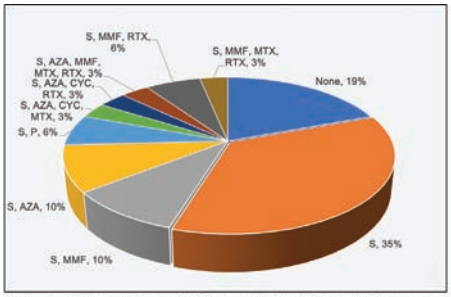
Results: Sixty-nine patients that fulfilled the criteria of coexistent ILD and ANCA were identified. Thirty-one patients were cANCA positive and 38 patients pANCA positive with a median age of 67 years (interquartile range 15 years). Sixteen patients were positive for MPO–ANCA and eight for PR3-ANCA. Only 26% of the cANCA and 24% of the pANCA population had coexistent ANCA-associated vasculitis diagnosed by a MDT clinic comprising of rheumatology, respiratory and renal physicians.

Figures 1 and 2 show the treatment distribution in c and pANCA populations respectively. Approximately 23% of the entire study population did not require treatment. Of the patients that required treatment, steroids were used in 81% of cANCA and 61% of pANCA patients. The most commonly used disease modifying anti-rheumatic drug was mycophenolate mofetil followed by azathioprine and/or methotrexate. Only a small proportion of patients required cyclophosphamide or rituximab.

At 24-months follow-up, 68% were alive, 22% deceased and data unavailable for 10% of the cANCA group compared to 61% alive, 2% end-of-life, 16% deceased and 21% unavailable data in the pANCA group. Diffusing capacity of the lungs for carbon monoxide (DLCO) declined in both p and cANCA groups over the first 12 months before improving. This improvement in PFTs is likely due to treatment escalation over time. Overall the pANCA group showed a mixture of progressive fibrotic and inflammatory CT features while the cANCA and MPO-ANCA groups showed predominantly progressive fibrotic CT findings.

Kruskal-Wallis test was used to determine whether there was an association between the PFTs of the p and cANCA population at three to six months, 12 months and 24 months. This test was then repeated for comparison of the MPO-ANCA and PR3-ANCA study population. There was no significant difference in lung function over time between the pANCA and cANCA group or MPO-ANCA and PR3-ANCA group.

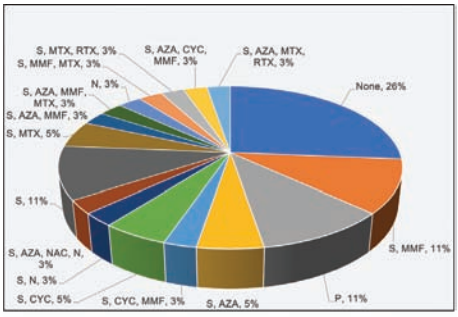
Conclusion: Although pANCA is thought to be associated with ILD or pulmonary fibrosis, we detected equal numbers of c and pANCA in a well characterised population of ILD patients. Approximately one quarter of patients with p or cANCA had an MDT diagnosis of ANCA-associated vasculitis. The clinical and CT characteristics did not differ between c and pANCA ILD patients. The two-year mortality of patients with ANCA and ILD was significant (22% in cANCA-ILD and 16% in pANCA). In surviving patients, the FVC and DLCO improved over a 24-month period.



S:Corticosteroids; MTX: Methothrexate; AZA: Azathioprine; NAC: N-acetylcysteine; CYC: Cyclophosphamide, RTX: Rituximab; P: Pirfenidone; MMF: Mycofenolate mofetil

Figure 1 Distribution of treatments used for cANCA patients over study period

Figure 1



S: Corticosteroids; MTX: Methothrexate; AZA: Azathioprine; NAC: N-acetylcysteine; CYC: Cyclophosphamide, RTX: Rituximab; P: Pirfenidone; N: Nintedanib; MMF: Mycofenolate mofetil

Figure 2 Distribution of treatment used in pANCA patients over study period

Figure 1

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.6254

AB0594 THE CLINICAL SPECTRUM OF HENOCH-SCHÖNLEIN PURPURA IN CHILDREN: A PROSPECTIVE SINGLE-CENTER STUDY

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Background: Henoch–Schönlein purpura (HSP) is the most common vasculitis of children. Predicting the risk factors at the time of diagnosis for systemic involvement may facilitate the management of the disease.
Objectives: The aim of this study is to evaluate the demographic and clinic findings of patients with HSP and also to determine predictive factors for assessing the development of gastrointestinal system (GIS) and renal involvement.
Methods: This study was performed prospectively among children with HSP who are under 18 years of age and being followed-up in the Pediatric Rheumatology Unit of Health Sciences University Kanuni Sultan Süleyman Training and Research Hospital between January 2016 and January 2018.
Results: A total of 265 patients, 137 boys (51.7%) and 128 girls (48.3%) were involved to the study. The mean ± standard deviation of age at the diagnosis was 7.5±3.2. The most common disease onset season was spring (31.7%). The rate of arthritis, GIS involvement and renal involvement was 54%, 51.3% and 29.1% respectively. GIS bleeding was more frequent in males than females (p=0.007). Boys over 7 years of age had significantly more common GIS bleeding (p=0.04). Intussusception, relapse and serious GIS involvement requiring hospitalization and steroid treatment were highly associated with severe renal involvement.
Conclusion: Intussusception, relapse and serious GIS involvement requiring hospitalization and steroid treatment were highly associated with severe renal involvement. We recommend at least 2 years follow-up for not overlooking renal involvement of HSP

REFERENCES

[1] Yang YH, Hung CF, Hsu CR, Wang LC, Chuang YH, Lin YT, Chiang BL (2005) A nationwide survey on epidemiological characteristics of childhood Henoch-Schonlein purpura in Taiwan. Rheumatology (Oxford) 44 (5):618-622. doi:10.1093/rheumatology/keh544
[2] Wang K, Sun X, Cao Y, Dai L, Sun F, Yu P, Dong L (2018) Risk factors for renal involvement and severe kidney disease in 2731 Chinese children with Henoch-Schonlein purpura: A retrospective study. Medicine (Baltimore) 97 (38):e12520. doi:10.1097/MD.0000000000012520

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AB0595 THE USEFULNESS OF 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY CT (18F-FDG PET/CT) AS AN IMAGING BIOMARKER IN TAKAYASU ARTERITIS TREATED WITH TOCILIZUMAB

Mikiya Kato[1,1], Hanae Okuda[2], Tomohiro Kameda[1], Taichi Miyagi[1], Risa Wakiya[1], Shusaku Nakashima[1], Hiromi Shimada[1], Mai Mahmoud Fahmy Mansour[1], Yuka Yamamoto[2], Hiroaki Dobashi[1]. *[1]Kagawa university, Division of Hematology, Rheumatology and Respiratory Medicine, Kagawa, Japan*; *[2]Kagawa university, Department of Radiology, Kagawa, Japan*

Background: Disease activity in large vessel vasculitis (LVV) including TAK is traditionally assessed by clinical and serological (ESR, CRP) parameters. Imaging assessment, including FDG-PET, may also be useful to monitor LVV. On the other hand, Tocilizumab (TCZ) treatment showed a favorable trend toward refractory Takayasu arteritis (TAK) (1). Because the TCZ could suppress the CRP or ESR elevation strongly despite the exist of TAK disease activity, clinical and serological (ESR, CRP) parameters could not reflect the disease activity of TAK appropriately.
Objectives: This study objective was to determine the efficacy of 18F-FDG PET/CT on the evaluating the disease activity of TAK treated TCZ compared with clinical and serological parameters.
Methods: Five Patients with TAK were recruited into a prospective, observational cohort. All patients in this study underwent FDG-PET/CT scans at 6 - 12 month intervals before and after TCZ treatment. Serological (ESR, CRP) and clinical assessment were determined at each visit. Disease activity was determined whether scans were active or inactive based on visual inspection of arterial 18F-FDG uptake. To determine the score of arterial FDG uptake assessed qualitatively relative to liver activity in 10 vascular beds with higher scores indicating more vascular inflammation. Additionally, scoring of FDG uptake was conducted to caluculate as divided into 4 grade compared with liver activity: 0, no uptake present; I, low-grade uptake (uptake present but lower than liver uptake); II, intermediate-grade uptake (similar to liver uptake); III, high-grade uptake (higher than liver uptake) (2). Clinical and imaging assessments were performed blinded to each other.
Results: All 5 cases (one male and 4 female) were initiated by TCZ treatment. The average age was 42.2±11.6 years old. The disease duration at the administration of TCZ was 176±136 months. The mean dosage of PSL was 6.40±3.72 mg/day. After initiating TCZ treatment, mean CRP values decreased from 1.44±1.80 to 0.032±0.034, and the PSL dose was reduced to 4.00±2.61 mg/day. No serious adverse events were observed. Though serum level of inflammatory biomarker such as CRP or ESR had become into normal range in all patients, arterial 18F-FDG uptake also remained in all patients after TCZ treatement. Additionally, clinical manifestations were correlate with site numbers and score of FDG uptake. The change of FDG score could reflect the improvement of clinical manifestation compared than serological biomarkers.
Conclusion: Serological biomarker such as CRP or ESR could not reflect disease activity appropriately in TAK patients treated with TCZ. 18F-FDG PET/CT was more useful for evaluating disease activities in Takayasu arteritis treated with TCZ. Further study might be needed to determine the definition of complete remission in TAK patients treated with TCZ.

REFERENCES

[1] Nakaoka Y, Isobe M, Takei S, et al. Ann Rheum Dis 2018;77:348–354

[2] Ingo Einspieler, et al. Eur J Nucl Med Mol Imaging 2015 42:1012–1024
[3] Quinn KA, et al. Ann Rheum Dis 2018;77:1166–1172.

Disclosure of Interests: None declared
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AB0596 ASSESMENT OF DAMAGE IN TAKAYASU ARTERITIS PATIENTS WITH VASCULITIS DAMAGE INDEX (VDI) AND TAKAYASU ARTERITIS DAMAGE SCORE (TADS)

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Background: Evaluation of damage in patients with takayasu arteritis is important because of the mortality and morbidity burden caused by the disease. Damage can be associated with treatment or with the disease itself (1).
Objectives: In this study we aimed to evaluate the damage in our Takayasu arteritis patients by using VDI and TADS scores.
Methods: Takayasu arteritis patients fullfilling the ACR 1990 criteria and had >3 months follow-up were enrolled in this study. TADS and VDI scores calculated at the end of the follow-up evaluated and compared.
Results: 114 patients (F/M: 101/13) were included in the study. The mean age at diagnosis, median symptom duration at baseline visit and mean follow-up duration were 35.3±13.3 years, 12 (0-360) months and 76.9 ± 51.4 months respectively. Mean VDI score was 5.1±2.5 and mean TADS score was 7.9±3.5. At least one disease-related damage item was present in all of the patients for both VDI and TADS meanwhile ≥1 treatment-related damage item was established in 69 (66.1%) patients with VDI and 46(40.7%) patients with TADS scoring system. Median treatment related-item number was 1 (0-6) in VDI and 0(0-3) in TADS. This difference may be due to the lack of disease-related parameters such as diabetes, cataract, osteoporosis, avascular necrosis in TADS. The median number of disease-related items was higher in TADS scoring (4 items vs 8 items). TADS scores include more detailed and higher number of items under vascular intervention and pulse loss categories. Also bruit and systolic hypertension data is only available in TADS(Table1).
There was no significant difference between patients with relapsing disease and patients with no relapses for both TADS and VDI scores. There was a weak corelation between VDI and cumulative steroid dose (p=0.002, r=0.32), and VDI-disease duration (p=0.001, r=0.29). A weak corelation between TADS and disease duration was established(p=0.04 r=0.19). No corelation was detected for TADS and cumulative steroid dose.
Conclusion: In Takayasu arteritis, detecting the disease-related and treatment-related part of damage must be considered while monitoring the disease. VDI seems to be predominant evaluating the treatment-related damage. TADS provides more detailed information on disease-related damage.

REFERENCES

[1] Omma A., Erer B., Karadag O.et al. (2017). Remarkable damage along with poor quality of life in Takayasu arteritis: cross-sectional results of a long-term followed-up multicentre cohort. Clin Exp Rheumatol., 35, 77-82.

Table 1. Comparison of VDI and TADS scores in our Takayasu patients

Categories	VDI n (%)	TADS n (%)
Musculoskeletal	23 (20)	-
Osteoporosis	15 (13.6)	
Avascular necrosis	6 (5.4)	
Skin	14 (12.6)	-
Ocular	37 (33.3)	8 (7.1)
Cataract	11 (9.9)	-
Retinal change	19 (17.1)	-
Visual impairment/diplopia	14 (12.6)	8 (7.1)
ENT	1 (0.8)	-
Pulmonary	20 (18)	16 (14.2)
Cardiovascular	79 (71.2)	114 (100)
Bruit	-	92 (81.4)
Pulse loss	—	79 (69.9)
Valvular diasease	44 (39.6)	-
Ischemic cardiac pain	-	18 (15.9)
Myocardial infarction	8 (7.2)	-
Aortic Incompetence	—	27 (23.9)
Diastolic BP > 95	46 (40.7)	—
Peripheral vascular disease	110 (99.1)	—
Absent pulses in one limb	78 (70.3)	—
Claudication > 3 months	89 (80.2)	-
Major/minör tissue loss	1 (0.9)	-
Venous thrombosis	1 (0.9)	
Gastrointestinal	3 (2.7)	-
Renal	4 (3.6)	47 (41.6)
Diastolic BP > 95	–	46 (40.7)
Neuropsychiatric	18 (16.2)	14 (12.4)
Vascular Intervention	—	45 (39.6)
Other	13 (11.7)	14 (12.4)
Malignancy	2 (1.8)	2 (1.8)
Infertility	1 (0.9)	1 (0.9)
Diabetes	8 (8.1)	-

VDI: Vasculitis Damage Index
TADS: Takayasu Arteritis Damage Score
ENT: Eye-Nose-Throat
'-' this item is not included in this scoring system
'—' this item is categorized in another category in the scoring system mentioned

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.6025

AB0597 CAN A ONE-HOUR QUANTITATIVE ASSESSMENT OF FDG-PET-CT (MODIFIED-PETVAS) BE USEFUL IN TAKAYASU'S ARTERITIS?

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Background: FDG-PET-CT is suggested as an imaging method for the assessment of disease activity in Takayasu's arteritis (TAK). Recently PETVAS, a quantitative score assessed at 2-hours is suggested as an imaging tool for TAK (1). However, most studies with FDG-PET-CT in the literature is performed at one-hour, similar to suggested as the minumum time in recent EULAR recommendations for the use of imaging in large-vessel vasculitis (2).
Objectives: In this study, we aimed to evaluate the value of a modified *PET Vascular Activity Score (PETVAS)* (performed at one-hour) during the initial diagnosis and follow-up of TAK patients.
Methods: Patients who are diagnosed with Takayasu's arteritis and underwent FDG-PET-CT imaging during their follow-up were evaluated in this study retrospectively. FDG-PET-CT imaging was performed at the first hour of FDG uptake. Demographic and clinical characteristics of the patients were recorded from patients' charts. Physician's Global Assessment (PGA) was used to determine clinical activity. In the modified PET-VAS scoring system, 9 arterial areas (Ascending Aorta, Aortic Arch, Descending Thoracic Aorta, Abdominal Aorta, Right Carotid Artery, Left Carotid Artery, Innominate Artery, Right Subclavian Artery, Left Subclavian Artery) were scored between 0 and 3 according to the FDG uptake, as originally suggested. The degree of arterial involvement was scored as 0= no uptake, 1=less than liver involvement, 2=equal involvement to liver, 3=greater than liver involvement (maximum score = 27). The visual analysis using the liver FDG uptake as the reference was also assessed and compared with m-PETVAS score.
Results: Thirty-eight imagings of 28 patients (F/M=22/6, mean age=39,7 ± 14,8 years) were evaluated. Median CRP level was 16,7 (2-126) mg/L. Median m-PETVAS score was 5 (0-27) and m-PETVAS was significantly higher in patients who were accepted as active according to PGA (median PETVAS score 6,0 vs 1,5, p=0.03). Similarly, patients who have an active PET assessed with only visual analysis (VA) have higher m-PETVAS scores than patients who were VA inactive (median score 9,0 vs 2,5, p= 0.000). A positive correlation was observed between the CRP levels before imaging and total m-PETVAS scores (p=0.01, rho=0.52). In 35/38 imaging assessments the score was >0 and the immunosuppressive agent was changed in 24 (63%) of these patients. Twenty-seven patients received corticosteroids before imaging. No difference in PETVAS scores were present between patients who were taking steroids vs non-steroid use. In 11 patients (29%), PET involvement other than the 9 arterial areas used for assessing the score, were observed. The mean age of this group was higher than the rest of the group (47,2±14,7 vs 35,7 ±11,2 years).
Conclusion: FDG-PET-CT assessment with a modified PETVAS (assessed at one hour) demonstrated higher scores in patients with Takayasu's

arteritis who were considered clinically active or had increased CRP. However, the scores were lower compared to the original scoring performed at two hours. Therefore, whether one hour investigations have sufficient discriminatory value requires further studies.

REFERENCES

[1] - Grayson PC, Alehashemi S, Bagheri AA, et al. 18 F-Fluorodeoxyglucose-Positron Emission Tomography As an Imaging Biomarker in a Prospective, Longitudinal Cohort of Patients With Large Vessel Vasculitis. Arthritis Rheumatol. 2018;70:439-449.

[2] - Dejaco C, Ramiro S, Duftner C, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheum Dis. 2018;77:636-643.

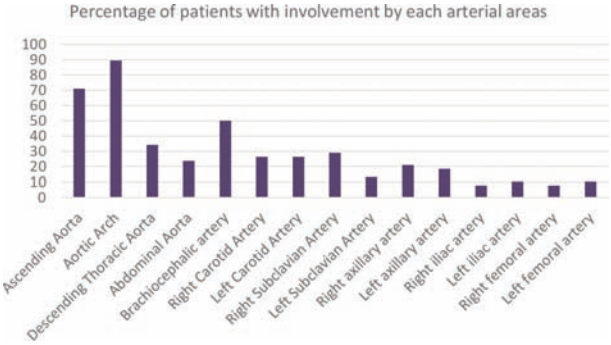


Figure 1

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AB0598 OSTEOPOROSIS AND RISK OF GIANT CELL ARTERITIS: A COMPARATIVE STUDY

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Background: Giant cell arteritis (GCA) and osteoporosis (OP) share many epidemiological features, such as occurrence in people >50 years old and increased incidence in women and northern Europe. Some known risk factors of OP, such as early menopause, nulliparity, low body mass index (BMI) and smoking, have also been linked to increased risk of GCA.
Objectives: We performed this study to investigate a potential link between OP and GCA onset by screening for OP by computed tomography (CT).
Methods: We retrospectively analyzed consecutive patients who underwent temporal artery biopsy (TAB) for suspected GCA in 4 hospitals. Cases and controls were defined by TAB-proven GCA and non-GCA diagnosis, respectively. Selection criteria additionally included 18F-FDG PET/CT at ±30 days (GCA cases) or ±90 days from the date of TAB (non-GCA controls). A radiologist blinded to patients' case or control status used CT images to measure the mineral density of trabecular bone in the first lumbar vertebra of all patients. OP was defined by previously identified thresholds of ≤110 Hounsfield units (HU) or ≤135 HU (1). We compared cases and controls for proportion of OP for the entire population and by sex. Statistical analyses involved chi-square and Student t tests for categorical and continuous variables, respectively.
Results: We included 50 cases and 59 controls. The most common diagnoses for controls were neurological disorders (n=21), autoimmune diseases (n=8), infections (n=10) and lack of an identifiable acute disease (n=9). Main demographic characteristics, prior cardiovascular and OP risk factors, and laboratory results are in the Table. Cases and controls did not differ in proportion with OP in the overall population (46% vs 49% [≤110 HU] and 60% vs 69% [≤135 HU]) or by sex (Table).
Conclusion: This study confirms that OP risk factors, that is, low BMI and nulliparity, are overrepresented in GCA, but our data do not suggest higher OP frequency in patients with new-onset GCA than controls. The high absolute proportion of OP in patients with new-onset GCA deserves further investigation because it may have practical implications in these patients at risk of glucocorticoid-induced bone loss.

	GCA cases n=50	Controls n=59	*P*
Age at TAB, mean (SD)	72.6 (8.3)	70.4 (10.6)	0.227
Women, n (%)	30 (60)	35 (59)	1
Ever smoking, n (%)	22/47 (47)	20/50 (40)	0.499
Nulliparous women, n (%)	10/27 (37)	3/30 (10)	0.015
Body mass index, mean (SD)	24.0 (3.5) [47]*	25.9 (4.9) [51]*	0.030
History, n (%)			
Diabetes	6 (12)	18/58 (31)	0.020
Hypertension	31 (62)	44/58 (76)	0.119
OP fractures or OP treatment	3/42 (7)	7/59 (12)	0.516
Hypercholesterolemia	9/49 (18)	21/58 (36)	0.041
CRP (mg/l) at TAB, mean (SD)	96.9 (58.3) [47]*	45.9 (68.2) [59]*	<0.0001
Hb level (g/dl) at TAB, mean (SD)	11.5 (1.7) [44]*	12.2 (2.1) [59]*	0.048
OP (≤110 HU) at TAB, n (%)			
All	23 (46)	29 (49)	0.743
Women	17/30 (57)	20/35 (57)	0.970
Men	6/20 (30)	9/24 (38)	0.601
OP (≤135 HU) at TAB, n (%)			
All	30 (60)	41 (69)	0.300
Women	21/30 (70)	27/35 (77)	0.514
Men	9/20 (45)	14/24 (58)	0.378

*No. of patients with available data.
GCA: giant cell arteritis; TAB: temporal artery biopsy; OP: osteoporosis; CRP: C-reactive protein level; Hb: hemoglobin level

REFERENCE

[1] Pickhardt PJ et coll. Opportunistic screening for osteoporosis using abdominal computed tomography scans obtained for other indications. Ann Intern Med. 2013 16;158:588-95.

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AB0599 CLINICAL MANIFESTATIONS OF BEHÇET'S SYNDROME IN A LARGE COHORT OF ITALIAN PATIENTS: FOCUS ON GENDER DIFFERENCES

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Background: Behçet's syndrome (BS) is a chronic multisystemic inflammatory disorder classified among primary vasculitis. BS clinical hallmarks are mucocutaneous manifestations which include oral aphtosis (OA), genital ulcers (GU) and a wide spectrum of skin lesions. Other BS features include ocular inflammation, articular, gastrointestinal, vascular and neurological involvement. Some evidences suggest that in non endemic regions the disease tend to be less severe and women seem to be more commonly affected [1-3].
Objectives: The aim of this study was to investigate the clinical phenotypes of Italian BS patients with respect to gender and HLA-B51 status.
Methods: We retrospectively evaluated 324 Italian patients (185 males and 139 females), seen consecutively at Rheumatology Institute of Lucania (IReL) from 1st January 2000 to 31th December 2017. Demographics, clinical features during follow-up and HLA status were obtained from a review of medical records. The analysis was limited to patients fulfilling the ISG criteria.
Results: 324 BS patients were identified in our database. 39 (17 males and 22 females) were excluded because did not satisfied ISG criteria and 285 (168 males and 117 females) resulted eligible for the present study. Results are summarized in table 1. We found statistically significant differences in papulopustolar lesions, posterior uveitis and deep venous thrombosis (DVT), which occur more frequently in males compared with females (83.3% versus 46.2%, 37% versus 18.8% and 8.3% versus 0.9% respectively; p<0.01). Erythema nodosum (EN) (59% versus 41,1%, p<0,01), arthralgia (52.1% versus 31.5%, p<0.01) and intestinal involvement (11.3% vs 21.4% p<0.05) resulted more frequent in females compared with males. No differences were found in HLA status (M 67.9% vs F 61.5%).

Conclusion: In our cohort of Italian BS patients the disease results slightly more prevalent in males. Gender-related differences were observed for posterior uveitis, DVP and papulopustolar lesions which are more frequent in males, whereas EN-like lesions, arthralgia and intestinal involvement are more frequently observed in females. These data confirm that BS tend to be less aggressive in Italian female patients. No sex-differences were observed in HLA-B51 status.

Table 1. Clinical manifestations of male and female BS patients

Clinical Manifestations	Overall (285) n(%)	Male (168) n(%)	Female (117) n(%)	OR (95%CI)	p-value
OA	285 (100.0)	168 (100.0)	117 (100.0)	1.44 (0.00-9231)	NS
GU	171 (60.0)	95 (56.5)	76 (65.0)	0.70 (0.43-1.14)	NS
EN	138 (48.4)	69 (41.1)	69 (59.0)	0.48 (0.30-0.78)	0.0029**
Follicolitits	50 (17.5)	32 (19.0)	18 (15.3)	1.29 (0.69-2.44)	NS
Papulopustolar lesions	194 (68.1)	140 (83.3)	54 (46.2)	5.83 (3.38-10.06)	0.0000**
Pathergy test	20 (45.5)	12 (7.1)	8 (6.8)	1.05 (0.41-2.65)	NS
Posterior uveitis	84 (29.5)	62 (37.0)	22 (18.8)	2.53 (1.44-4.42)	0.0010**
Anterior uveitis	51 (17.9)	29 (17.3)	22 (18.8)	0.90 (0.49-1.66)	NS
Panuveitis	24 (8.4)	17 (10.1)	7 (6.0)	1.77 (0.71-4.41)	NS
Episcleritis	4 (1.4)	2 (1.2)	2 (1.7)	0.69 (0.10-4.49)	NS
Arthralgia	114 (40.0)	53 (31.5)	61 (52.1)	0.42 (0.26-0.69)	0.0005**
Arthritis	74 (26.0)	44 (26.2)	30 (25.6)	1.03 (0.60-1.76)	NS
Deep venous thrombosis (DVT)	15 (5.3)	14 (8.3)	1 (0.9)	10.55 (1.37-81.35)	0.0054**
Superficial venous thrombosis (SVT)	33 (11.6)	18 (10.7)	15 (12.8)	0.82 (0.39-1.69)	NS
Neurological involvement	70 (24.6)	36 (21.4)	34 (29.1)	0.67 (0.39-1.15)	NS
Fatigue	72 (25.3)	37 (22.0)	35 (29.9)	0.66 (0.39-1.13)	NS
Fever	119 (41.8)	76 (45.2)	43 (36.8)	1.42 (0.88-2.31)	NS
Intestinal involvement	44 (15.4)	19 (11.3)	25 (21.4)	0.47 (0.24-0.90)	0.0208*
HLA-B51 positivity	186 (65.3)	114 (67.9)	72 (61.5)	1.32 (0.81-2.16)	NS

Abbreviations: n, number of subjects; OR, odds ratio; CI, confidence interval
statistically significant: *p<0.05; **p<0.01

Figure 1

REFERENCE

[1] Leccese P, et al. Curr Opin Rheumatol.2017;29(1):12-16. [2] Hatemi G, et al. Clin Exp Rheumaology.2016;34 Suppl 102:10-22. [3] Pipitone N, et al. Clin Exp Rheumatol.2004;22(6 Suppl 36):S46-51.

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AB0600

APREMILAST EFFECTIVENESS IN REFRACTORY ORAL AND GENITAL ULCERS OF BEHÇET'S DISEASE: DATA FROM REAL LIFE SETTINGS

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Background: Mucocutaneous lesions represent the earliest and the most frequent manifestations of Behçet's disease (BD), and may become disabling leading to substantial effect on quality of life. Recently the efficacy of the small molecule inhibitor of phosphodiesterase 4 apremilast in treating oral and genital ulcers has been shown in a phase 2 trial (1), whereas to date no results from real world data are available.

Objectives: The purpose of the present study was to describe our experience with apremilast in treating BD patients with oral and genital ulcers refractory to traditional therapies and previous biologic agents in real life settings

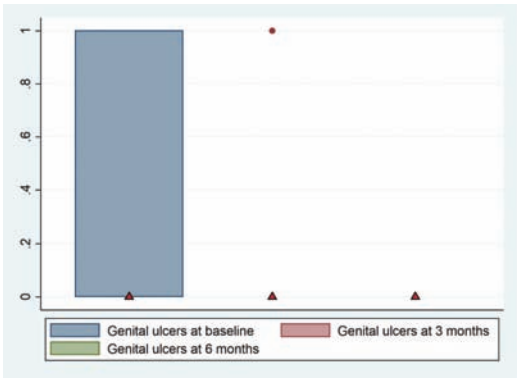


Figure 1

Methods: We retrospectively evaluated BD patients according to ICBD (2) and/or ISG (3) criteria who had undergone apremilast therapy (30 mg twice daily) for oral and/or genital ulcers from November 2017 to January 2018 in four different specialized referral Units in Italy (Bari, Firenze, Potenza, Siena). Retrieved data including previous treatments were also collected. Our endpoint was to assess the number of oral and genital ulcers under apremilast treatment. Moreover pain due to ulcers was evaluated with a 100-mm visual-analogue scale (VAS), whereas disease activity was assessed by means of BDCAF score. Paired t-test or Wilcoxon matched-pair signed rank test, if applicable, were used for statistical analysis.

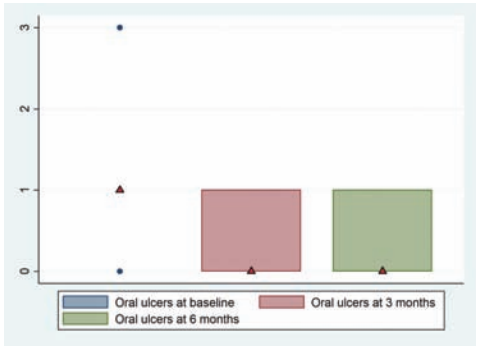


Figure 2

Results: Thirteen patients (9 females, 69.2%) with disease duration (mean ±SD) of 154.2 ± 167.7 months underwent apremilast treatment because of oral and genital ulcers inadequately responsive to previous immunosuppressant and/or biologic agents. At baseline, patients complained of 1 (1-1) (median (IQR)) oral and 0 (0-1) genital ulcers. At 3-month follow-up (data collected for 12/13 patients) the median number was 0 (0-1) for oral ulcers, and 0 (0-0) for genital ones, showing a significant improvement (p=0.02 for both). However, after 3 months, 3/12 patients (25%) stopped the treatment due to diarrhoea. Thereafter, at 6-month follow-up, a significant improvement of oral ulcers was observed (data collected for 8/13 patients, p=0.03), whereas a statistical significance for genital ulcers was not reached, even in the presence of a positive trend (p=0.07). A notable reduction in VAS and BDCAF scores was observed either after 3 months (p=0.004 and p=0.02, respectively) and 6 months (p=0.01 and p=0.02, respectively). The mean number of relapsing oral and genital ulcers during the first 3 months of therapy was significantly lower than that observed in the four weeks prior to apremilast (p=0.01 for both). Similarly, the average number of the sole oral ulcers appreciably decreased in the first 6 months of therapy (p=0.03). Notably no infections were reported during the whole observation period.

Conclusion: Our results, despite the small sample size, corroborate apremilast employment in real-life settings as viable treatment option in BD patients with mucosal involvement multi-refractory to standard treatments.

REFERENCES

[1] Hatemi G, Melikoglu M, Tunc R, Korkmaz C, Turgut Ozturk B, Mat C, et al. Apremilast for behcet's syndrome-a phase 2, placebo-controlled study. N Engl J Med 2015;372:1510-8.

[2] International Team for the Revision of the International Criteria for Behcet's D. The international criteria for behcet's disease (icbd): A collaborative study of 27 countries on the sensitivity and specificity of the new criteria. J Eur Acad Dermatol Venereol 2014;28:338-47.

[3] O'Neill TW, Rigby AS, Silman AJ, Barnes C. Validation of the international study group criteria for behcet's disease. Br J Rheumatol 1994;33:115-7.

Disclosure of Interests: Giuseppe Lopalco Speakers bureau: SOBI, BMS, vincenzo venerito: None declared, Pietro Leccese: None declared, Giacomo Emmi: None declared, Luca Cantarini: None declared, Nancy Lascaro: None declared, Gerardo Di Scala: None declared, Stefano Gentileschi: None declared, Anna Abbruzzese: None declared, Marco Fornaro: None declared, Fabio Cacciapaglia: None declared, Giovanni Lapadula: None declared, Florenzo Iannone Consultant for: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work

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AB0601 UTILIZATION OF A MULTISPECIALTY TEAM FOR THE DIAGNOSIS OF GIANT CELL ARTERITIS REDUCES PATIENT MORBIDITY

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Background: Giant Cell Arteritis (GCA) is an autoimmune vasculitis, most commonly seen in older adults with a peak incidence in the seventh decade of life. A diagnosis of GCA is often considered in any patient over the age of 50 years who complains of or is found to have new onset headache, acute visual disturbances, jaw claudication, unexplained fever, or elevated inflammatory markers. Because the manifestations of GCA can vary considerably from patient to patient, often with transient and fluctuating symptoms, an accurate diagnosis can be challenging. Even in the setting of a negative temporal artery biopsy, many patients are treated empirically based on the perceived probability of disease. This approach can lead to significant morbidity from prolonged medication exposure and unnecessary procedures.
Objectives: The aim for this project was to look at the impact of a collaborative effort amongst three specialties, rheumatology neurology and ophthalmology, which composed a consultation based "GCA team", the goal of which was to improve how GCA is diagnosed and subsequently managed.
Methods: We conducted a retrospective study of all patients suspected to have GCA at our institution over the last 2.5 years that had either been seen by the GCA team or not. The GCA team met either in person or had a conference call to discuss each case and make a joint decision regarding the diagnosis and treatment. Data extracted included patient demographics, symptoms on presentation, labs, biopsy results and accumulative prednisone dose.
Results: A total of 30 patients (19 female, 11 male) were evaluated; 19 were seen by the GCA team and 11 were not. The mean ages of the patients in each group were the similar (GCA Team 70.6 (SD 12.5) vs no GCA Team 70.3 (SD 12.3)). The mean ESR between the two groups was also similar (GCA Team 53.3 (SD 30.2) vs no GCA Team 53.8 (SD 27.2)). The presenting clinical symptoms between the two groups were also comparable: visual complaints (63% vs 73%), headache/jaw claudication/temporal artery tenderness (42% vs 45%), and cranial neuropathy (11% vs 9%).
All of the patients not seen by the GCA team underwent bilateral temporal artery biopsy; however none were positive on histology. Regardless, all were continued on high dose prednisone with a 6 month cumulative mean dose of 5,350mg.
Of the 19 patients seen by the GCA team, 8 were determined to be low probability for GCA and thus were spared temporal artery biopsy. Furthermore, all of the patients were recommended a rapid steroid taper and the cumulative mean dose of prednisone was only 490mg. Over 6 months of follow-up, none of the 8 patients deemed low probability had a subsequent diagnosis of GCA given.
Compared to patients deemed high probability by the GCA team, low probability patients were younger (68.6 vs 71.2), more often female (75% vs 45%), had lower ESR (40.5 mm/hr vs 66.1 mm/hr), and presented with more visual complaints (86% vs 46%).
In the 11 high probability GCA patients, 10 underwent temporal artery biopsy (one refused) with 4 biopsies read as positive for GCA. Over 6 months of follow up, none of these patients had flares after they were started on treatment.
Conclusion: While the accuracy of a GCA diagnosis cannot be determined in our cohort of patients not seen by the GCA team, it is likely that evaluation by a multispecialty team would have found several to be low probability for GCA, especially as none of the patients had a positive temporal artery biopsy. We have demonstrated that by adopting a collaborative approach to diagnosing GCA, unnecessary biopsies can be avoided as well as limiting unnecessary prednisone exposure. More prospective data is needed to provide an accurate assessment of this team approach for GCA which can serve as a model for other healthcare facilities.
Disclosure of Interests: Arash Hassantoufighi: None declared, Rachel Lu-Do: None declared, Joshpaul Dhillon: None declared, Christopher Collins Grant/research support from: Exagen, Consultant for: Exagen, AbbVie, Speakers bureau: Exagen, AbbVie, Novartis, Florina Constantinescu: None declared
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AB0602 CLINICAL USEFULNESS OF LUNG ULTRASOUND IN ACTIVE GRANULOMATOSIS WITH POLYANGIITIS WITH LUNG INVOLVEMENT – PRELIMINARY DATA

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Background: Lung involvement is observed in 43% to 94% of patients with granulomatosis with polyangiitis (GPA) (1). In about 10% of cases, the lung is the only organ affected and in as many as 30% of patients without clinical symptoms of lower respiratory tract involvement, abnormalities in chest imaging examinations can be found (2). The efficacy of lung ultrasound (LUS) is very well documented in many pulmonary diseases (3,4). Single publications indicate its applicability also in diagnostics of complications secondary to systemic connective tissue disease, e.g., lung fibrosis or diffuse alveolar hemorrhage (5,6). The necessity of repeating chest imaging examinations increases the patient's exposure to ionizing radiation. Thus, the possibility of limiting such exposure through the application of LUS as the diagnostic modality appears extremely inviting.
Objectives: The aim of this study was to assess lesions detected by ultrasound in patients with active granulomatosis with polyangiitis (GPA) in comparison to abnormalities found by computed tomography (CT).
Methods: We analyzed the clinical and radiological data of 12 patients (5 women/7 men, mean age 47.9 years/range 18-80) with active PR3-ANCA-associated vasculitis with lung involvement (Birmingham Vasculitis Activity Score, BVASv3 mean 5.7/range 1-12). LUS was performed in the sitting and lying positions, using the convex (2-6 MHz) and linear (4-12 MHz) transducers placed to each intercostal space over the chest wall (anterior, lateral and inferior). Chest CT was performed according to a standard protocol with the use of a 64-slice CT scanner made by GE. The images obtained in LUS were compared to changes detected in CT scans. The study protocol was approved by an independent local Bioethics Committee (NKBBN/474/2018).
Results: In all patients with lungs infiltrations, changes were visible in the LUS, but the visualized infiltrates and caves include only these lesions that were adjacent to the line of pleura. LUS revealed infiltrates as well as infiltrates with features of disintegration and cavities. Subpleural infiltrates in ultrasound were visualized as hypoechoic round or oval consolidations, without central flow visible in color Doppler (CD) and power Doppler (PD) modes. Caves visualized in LUS were round and anechoic; flow in CD and PD modalities was also absent. In some cases, we observed hypoechoic round or oval infiltrates with features of disintegration, partly filled in with fluid content (anechoic).
Conclusion: Due to the harmlessness of ultrasonography, LUS can be repeatedly performed. In addition, ultrasound examination can be performed during hospitalization at the patient's bedside as well as during a visit to the rheumatologist's office.

REFERENCES

[1] Anderson, et al. Wegener's granuloma. A series of 265 British cases seen between 1975 and 1985. A report by a sub-committee of the British Thoracic Society Research Committee. Q J Med. 1992; 83:427-438.
[2] Brown. Pulmonary vasculitis. Proc Am Thorac Soc. 2006; 3:48-57.
[3] Volpicelli, et al. International evidence-based recommendations for point-of-care lung ultrasound. Intensive Care Med. 2012; 38:577-591.
[4] Buda, et al. Polish recommendations for lung ultrasound in internal medicine (POLLUS-IM). J Ultrason. 2018; 18:198-206.
[5] Masiak, et al. Diffuse alveolar hemorrhage as an initial presentation of ANCA–associated vasculitis in an 80–year–old man. Pol Arch Intern Med. 2017; 127:365-367.
[6] Buda, et al. Serial Lung Ultrasonography to Monitor Patient With Diffuse Alveolar Hemorrhage. Ultrasound Q. 2017; 33:86-89

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AB0603 SCOTLAND'S FIRST FAST TRACK TEMPORAL ARTERY ULTRASOUND REFERRAL PATHWAY FOR SUSPECTED GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is associated with loss of vision (LOV). Rapid referral for specialist assessment including temporal artery ultrasound (TAU) reduces the risk of LOV and the need for temporal artery biopsy (TAB). Two

Consultant Rheumatologists (JSM & JHG), formally trained in TAU, established Scotland's First Fast Track Referral Pathway for Suspected GCA using TAU on 21.03.17. A third Consultant (SJH), whose formal Vascular ultrasound training occurred later, joined the Service on 10.04.18. We present here our Outcome data and also our experience of this new Service for NHS Fife, the first of it's kind in Scotland.

Methods: We prospectively recorded data on all referrals to our Fast Track Service for patients with suspected GCA from 21.03.17 onwards. NHS Fife covers a population of 370,000 and constitutes 6.8% of the Scottish Population (5,425,000).

Results: Up until 20.11.17 (20 months) we received a total of 142 referrals, representing an average of 7 per month, or around 2 per week. 54 (38%) were deemed to have a very low probability of GCA based on their age, history & CRP and were not seen or scanned. 88 (62%) of referrals underwent Fast Track assessment including TAU (62 F; 26 M); Mean age 71 (range 52-88). Time from referral to assessment was as follows : (25) 28% were seen on the same day; (60) 68% were seen by the next day; (69) 78% were seen within 2 days of referral; (84) 95% were seen within 3 days of referral. 25/88 (28%) patients were diagnosed with GCA. Of these, 14 patients had a positive TAU and did not require TAB. 9 patients had an equivocal or negative TAU and were diagnosed on TAB. Only 1/25 GCA patients experienced LOV (4%). The patient was an 82 year old male diabetic who presented to Ophthalmology with unilateral LOV but no symptoms of GCA and also with a normal CRP (4.1mg/L). However, he had stopped 1mg of prednisolone for PMR 2 weeks prior to developing LOV. TAU was positive, but in view of the atypical nature of his symptoms ("silent GCA") & normal CRP, he also underwent TAB, which was positive confirming the diagnosis of GCA. I patient had a negative TAU and TAB, but was subsequently diagnosed with LVV on Axillary artery US.

Conclusion: A previous survey of 20 GCA patients diagnosed in Fife over a 2 year period (Jan 2007 - Jan 2009) recorded a 50% rate of LOV. This was largely attributed to delayed referral. We have now successfully introduced Scotland's First Fast Track Referral Pathway for Suspected GCA using TAU. This has led to a dramatic reduction in Morbidity in terms of LOV (< 5%).

Disclosure of Interests: None declared

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AB0604 CLINICAL FEATURES AND TREATMENT IN A COHORT OF PATIENTS WITH BEHÇET DISEASE IN A TERTIARY HOPITAL OF BARCELONA

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Background: Behçet disease (BD) is considered a systemic vasculitis according to the Chapel-Hill classification, which occurs most frequently between latitudes 30 and 45° north and in the area of the Old Silk Route. Turkey has the highest prevalence, followed by Japan. In Spain, a prevalence of 7.5 cases per 100000 persons has been estimated. The epidemiological and clinical characteristics of European patients with BD vary with respect to those of the Turkish and Japanese cohorts.

Objectives: Description of clinical features and treatment received in a cohort of patients diagnosed with BD in an Internal Medicine Unit of a tertiary centre from Barcelona.

Methods: Retrospective, observational study. Epidemiological, clinical and laboratory data were obtained from clinical charts. SSPS package was used to perform statistical analysis.

Results: 132 patients (56.6% men) diagnosed over the last 30 years and followed-up until the censoring data were included. 112 (84.8%) were Caucasians, 15 (11.4%) from North Africa, 4 (3%) Asiatic and 1 (0.8%) from South America. 2 (1.5%) patients had a family history of BD and 9 patients (6.8%) a family history of other rheumatic diseases. 43.9% (58 patients) were HLA-B51. Oral or genital ulcers were present in 131 (99.2%) patients and skin involvement in 106 (80%) cases, 44.6% had erythema nodosum, 59% had acne-like lesions and 9% had cutaneous vasculitis. Ocular involvement was observed in 69 cases (52.3%): 27 patients unilateral and 8 bilateral anterior uveitis; 14 unilateral and 3 bilateral posterior uveitis; 10 patients unilateral and 14 bilateral panuveitis; 19 unilateral retinal vasculitis and 12 bilateral. Neurological involvement was present in 37 (28%) patients: 10 parenchimal disease and 17 cases non-parenchymal disease (aseptic meningitis or vasculitis); 8 patients benign intracranial hypertension, and 3 had dural sinus thrombosis. Articular involvement was recorded in 79 (59.8%) patients (it was observed 25 monoarthritis, 24 oligoarthritis, 6 poliarthritis and 58 patients had arthralgia). Vascular involvement was present in 43 (32.6%) cases: deep venous thrombosis in 38 patients (11 cases in locations other than the extremities); pulmonary embolism in 7; 21 thrombophlebitis; and 6 patients aneurysms (only 2 pulmonary arterial aneurysms). Digestive involvement was present in 12 (9,1%) patients, with predominant colon involvement (8 cases).

The most prescribed drugs were corticosteroids (85.6%) and colchicine (77.3%), followed by azathioprine (36.4%) and cyclosporine A (33.3%). Other prescribed drugs were thalidomide (6.1%), chlorambucil (6.9%), methotrexate (4.5%), anti-TNF-alpha therapies (infliximab 6.8% and adalimumab 2.3%), cyclophosphamide (3%), mycophenolate (3.8%), leflunomide (1.5%) and 22% received anticoagulation.

Conclusion: Clinical features of our patients are similar to those of other European cohorts, although a high prevalence of organic involvement (ocular, neurological, vascular and joint) should be highlighted.

REFERENCES

[1] Saadoun D, Wechsler B. Behçet's disease. Orphanet J Rare Dis. 2012 Apr 12;7;20. doi: 10.1186/1750-1172-7-20.

[2] Mendes D, et al. Behçet's disease – a contemporary rewiew. J Autoimmun. 2009 May-Jun; 32 (3-4): 178-88. doi: 10.1016/j.jaut.2009.02.011.

[3] Leccese P, et al. Behçet's síndrome in nonendemic regions. Curr Opin Rheumatol. 2017. doi: 10.1097/BOR.0000000000000349

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AB0605 SERUM NEOPTERIN AND ISCHEMIA MODIFIED ALBUMIN LEVELS ARE ASSOCIATED WITH THE DISEASE ACTIVITY OF ADULT IMMUNOGLOBULIN A VASCULITIS (HENOCH-SCHONLEIN PURPURA)

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Background: Immunoglobulin A vasculitis (IgAV) [formerly called Henoch–Schönlein purpura (HSP)] is an IgA mediated systemic vasculitis which primarily affects skin, gastrointestinal system and small vessels of kidneys. Exact pathogenesis of IgAV remains unknown. A fewclinicalstudiesevaluatedthe role of oxidativeinjury in thepathogenesis of vasculitis. Ischemia modified albumine (IMA) and Neopterin increased status of oxidative stress.

Objectives: The aims of the study are to investigate serum neopterin and IMA levels in patients with IgAV and evaluate the association of these markers with disease activity and relapse.

Methods: Thirty-four consecutive adult patients (24 males and 10 females) admitted to the rheumatology clinic of Ankara Numune Training and Research Hospital meeting the IgAVAmerican College of Rheumatology (ACR) criteria were enrolled in this cross-sectional study. Demographic and clinical features of IgAV and control group were recorded into a predefined protocol. Disease activity was categorized as "remission" or "active" according to BVAS. BVAS $\geq$1 was accepted "active".Serum neopterin levels, hsCRP and IMA were evaluated according to BVAS and compared to healthy control group.

Results: Serum median (IQR) neopterin, IMA levelsandhsCRPwerehigher in thestudygroupthan in controlgroup [2.01 (12.5) ng/mL vs. 1.77 (1.37) ng/mL, 0.67 (0.2) ng/mL vs. 0.43 (0.17) ng/mL, 5.6 (17.1) mg/L vs. 1.55 (1.6) mg/L, p=0.095, p<0.001and p=0.002,respectively). When evaluated according to BVAS, IMA and hsCRP levels were significantly higher in the group with active disease [0.77 (0.12) vs. 0.61 (0.13) and 14.85 (4.6), p=0.009 and p=0.03, respectively]. Serum neopterin levels were significantly higher in the active group compared to BVAS [18.95 (32.36) vs. 1.63 (1.48), p<0.001].

Conclusion: Oxidative stress is important in HSP pathogenesis. Roles of hsCRP,Neopterin and IMA as potential markers of diagnosis and disease activity seem to be worth studying in the future studies with larger study groups.

Disclosure of Interests: None declared

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AB0606

LONG-TERM BIOLOGICAL TREATMENT IN LARGE VESSELS VASCULITIS: A RETROSPECTIVE SINGLE-CENTER STUDY ON 30 PATIENTS FROM 2011 TO 2018

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Background: Glucocorticoids (GC) are the mainstay in the treatment of large vessels vasculitis (LVV), while conventional immunosuppressants have modest GC-sparing effect. Recent studies show that biological drugs could represent a valid therapeutic option, especially in patients with severe and/or relapsing LVV. Their role in the treatment of LVV is expanding, but only few data are available on their long-term efficacy and safety [1,2].
Objectives: Our aim is to describe the 8 years' experience of a single Italian center in biological treatment of patients with large vessels vasculitis (LVV).
Methods: We collected retrospectively clinical data from 30 patients affected by LVV and treated with biological drugs. Data from 18F-FDG PET and CT or MRI associated with improvement of clinical and inflammatory index (ESR and CRP) were used as criteria of response to treatment.
Results: Between 2011 and 2018 we treated 30 LVV patients (22 women and 8 men) with biological drugs: 10 patients with Takayasu arteritis (TAK), 17 patients with large-vessel giant cell arteritis (LV-GCA) and 3 patients with aortitis. The median age (10^{th}–90^{th} percentile) at the diagnosis was 63 (21-79) years. Biological treatment was started right after the diagnosis in 15 patients, while 15 patients had a long-standing relapsed disease (time between diagnosis and biological therapy 6 (1-43) months). The mean follow-up time of patients was 26 (4-72) months.
Anti-TNF-α drugs (infliximab, adalimumab, golimumab) were used in 9 patients; while anti-IL6r (tocilizumab) was used in 30 patients. During the follow up, 9 patients (23%) switched to another biologic for relapse of the disease or for infusive adverse reactions; in 3 cases multiple switches were made.
Infliximab (IFX) was used in 7 patients for a median period of 12 (3-33) months: 3 patients archived stable remission, 3 had an infusive adverse reaction, 1 had a relapse of the disease after 60 months of therapy. Adalimumab (ADA) was used in 3 patients and then suspended in all of them for relapse of the disease after 3, 12 and 93 months of therapy, respectively. Golimumab was used in 2 patients: one suspended therapy for developing follicular thyroid cancer, one switched to another biologic for persistent active disease.
Tocilizumab (TCZ) was used in all 30 patients for a median period of 20 (4-54) months: in 25 cases it was the first line therapy, in the other 5 cases it was used after an anti-TNF-α drug. 25 patients out of 30 (84%) archived stable remission and in 6 of them a dose tapering was possible, with no sign of relapse.
Three patients in TCZ had an adverse reaction; one developed a uveitis and one had a relapse of TAK.
In our last examination 29 out of 30 patients in biological therapy demonstrated a good control of the disease with clinical improvement, also confirmed by PET, TC and/or MRI, and reduction of inflammatory index (ESR and CRP), compared to before starting treatment. Biologics also demonstrated an important steroid sparing effect: mean prednisone dose at the beginning of treatment was 25 mg/day (12-50), while at the last follow-up was 6 mg/day (1-15) ($p<0.0001$; Wilcoxon test)
Conclusion: In our cohort of 30 patients biological treatments demonstrated long-term efficacy and acceptable safety profile and important steroid sparing effect.

REFERENCES

[1] Pazzola G, et al. Rev Med Interne, 2016
[2] Samson M, et al. Eur J Intern Med, 2018

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AB0607

SELF-MANAGEMENT BEHAVIOURS IN ANCA-ASSOCIATED VASCULITIS: SECONDARY ANALYSIS OF INTERVIEW DATA

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Background: ANCA-associated vasculitis (AAV) is a significant cause of morbidity and mortality. Meeting the challenges of AAV effectively requires patients to engage in self-management, including medical management, role management, and emotional management.[1] Self-management is recognised as a key aspect of chronic disease management and forms an important part of the National Health Service 5-year forward plan and the UK strategy for rare diseases.[2,3] Nonetheless, there has been limited specific research into the role of self-management in the AAV literature.
Objectives: To explore experiences and views of self-management amongst AAV patients.
Methods: A secondary analysis of all interview transcripts from a previous project exploring health-related quality of life in relation to AAV was performed.[4] Deductive analysis was used to map appropriate areas discussed by patients to the self-management framework proposed by Lorig and Holman.[1] Inductive analysis was used to identify emergent themes that did not fit into this framework.
Results: Interview data were collected from 50 patients with AAV (25 men), from the UK (n=18), USA (n=17) and Canada (n=15). Diagnoses included GPA (n=26), EGPA (n=17) and MPA (n=7). Thirty-four patients were diagnosed within the last 2 years and 16 were diagnosed more than 2 years ago.[4]
From the core tasks proposed in Lorig and Holman's framework, patients with AAV appear to attribute particular importance to maintaining life roles and to a lesser extent medication management and dealing with the emotions of chronic disease. Core skills necessary to self-manage in AAV include learning to take action as part of self-efficacy, forming productive health-care partnerships, learning about decision making (requiring disease and self-awareness), utilising resources effectively, and problem-solving.
Three themes emerged that were not included in Lorig and Holman's framework that respondents related to self-management abilities including: 1) support received from family, support groups, and religion; 2) the influence of pre-morbid personality factors; 3) the role patients attributed to developing a foundation of specific AAV knowledge in their subsequent ability to self-manage.
Conclusion: Patients with AAV self-manage in a variety of ways and their needs may change over time. Patients may benefit from support to help manage changing life roles and to deal with the challenges of having a chronic disease. Over time, support may need to shift focus onto core skills including recognising when to take action; forming effective partnerships with healthcare providers, family, and friends; adaptations to day-to-day changes in their condition; utilising resources appropriately; and strategies for problem-solving.

REFERENCES

[1] Lorig, K.R. and Holman, H.R., 2003. Self-management education: history, definition, outcomes, and mechanisms. Annals of behavioral medicine, 26 (1), pp.1-7.
[2] NHS England. Five year forward view. Oct 2014. Available from:https://www.england.nhs.uk/ourwork/futurenhs/
[3] UK Strategy for Rare Diseases. Department of Health, 2013.
[4] Robson, J.C., Dawson, J., Cronholm, P.F., Milman, N., Kellom, K.S., Ashdown, S., Easley, E., Farrar, J.T., Gebhart, D., Lanier, G. and McAlear, C. A., 2018. Health-related quality of life in ANCA-associated vasculitis and item generation for a disease-specific patient-reported outcome measure. Patient related outcome measures, 9, p.17.

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AB0608 TOCILIZUMAB TREATMENT FOR LARGE VESSELS VASCULITIS: REAL LIFE PRELIMINARY EXPERIENCES

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Background: IL-6r targeting therapy has been proven to be effective and safe in Giant Cell Arteritis (GCA) as well in Takayasu Arteritis (TA) in RCTs, probably because of the similar pathologic findings and vessel size (Large Vessel Vasculitis, LVV). However, real world data are scarce.
Objectives: The aim of the study was to evaluate the effectiveness of Tocilizumab for LVV in real life settings.
Methods: We retrospectively evaluated, from 2011 to 2017, the outcomes (including glucocorticoid dosage) in patients affected by LVV (according to 1990 ACR classification criteria) who received 8 mg/kg iv Tocilizumab (TCZ) monthly, due to the inadequate response to immunosuppressant. Demographic and clinical characteristics and laboratory findings were collected at baseline and consecutive follow up visits, over 52 weeks. Statistical analysis was performed using the GraphPad Software ver. 6.0 (San Diego CA USA) using appropriate tests.
Results: We analyzed n.10 patients (6/10 GCA, 4/10 TA) with mean age (± SD) 56 ± 21 years and mean disease duration 41±38 months. Eight out of 10 patients were female. Over the entire observation period, 7/10 also received concomitant methotrexate (mean dose 12.8 ± 2.7 mg/week) while 2/10 received azathioprine (100 mg/day). Median (IQR) prednisone equivalent dose at baseline was 22.5 (10-25) mg/day. At baseline, median ESR was 49 (31-58) mm/h and median CRP level was 15.4 (1.95-28.53) mg/l. Upon TCZ treatment we observed a good disease control in absence of headache, fever and other LVV clinical signs through 52-week follow up. At 52 weeks, we observed a significant reduction of ESR down to 6.5 (2.75-12.25) mm/h as well as of CRP level, down to 1.5 (0.67-3.47) mg/l ($p<0.001$). A meaningful steroid sparing effect was also achieved as a significant reduction in prednisone dose down to 5 (1.87-6.25) mg/day ($p<0.001$). During the 52-week follow up period, 3 patients discontinued TCZ treatment for side effects: 1 for severe neutropenia (at 12 weeks), 1 for hemorrhagic pancreatitis (after 24 weeks), and 1 for diverticulitis (after 52 weeks).
Conclusion: In our real life experience iv TCZ was effective and safe in LVV treatment, with a good disease control and a significant steroid-sparing effect. Our preliminary findings need to be confirmed in larger cohorts and prolonged follow-up.

REFERENCES

[1] Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, Brouwer E, Cid MC, Dasgupta B, Rech J, Salvarani C, Schett G, Schulze-Koops H, Spiera R, Unizony SH, Collinson N. Trial of Tocilizumab in Giant-Cell Arteritis. N Engl J Med. 2017 Jul 27;377(4):317-328. doi: 10.1056/NEJMoa1613849. PubMed PMID: 28745999.

Disclosure of Interests: giulia righetti: None declared, vincenzo venerito: None declared, maria giannotta: None declared, Giuseppe Lopalco Speakers bureau: SOBI, BMS, margherita giannini: None declared, Fabio Cacciapaglia: None declared, Laura Coladonato: None declared, Florenzo Iannone Consultant for: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work

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AB0609 NAILFOLD VIDEO CAPILLAROSCOPY AS A POTENTIAL DIAGNOSTIC TOOL IN SYSTEMIC VASCULITIS

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Background: Vasculitides are formally classified by artery size: large, medium or small, yet some overlap is evident as in Takayasu, a large vessel vasculitis manifesting also in retinal arterioles. Nailfold videocapillaroscopy (NVC) enables us to inspect changes in microvasculature. Only several small uncontrolled case series of light capillary microscopy in adult patients with vasculitis were reported in the literature, describing avascular areas and microhemorrhages in granulomatosis with polyangiitis (GPA) patients [1-2] and in [4] Behcet disease, and thin and tortuous capillaries in Takayasu arteritis [5].
Objectives: To characterize nailfold capillary changes by NVC in patients with autoimmune vasculitis compared to healthy controls.
Methods: Consecutive autoimmune vasculitis patients fulfilling the ACR criteria and age and gender matched healthy controls were evaluated by NVC using Optilia Mediscope with a magnification of X200. Patients with peripheral artery disease and ischemic heart disease were excluded. Capillaroscopy images were centrally analyzed. NVC was analyzed, noting: architecture, number of capillaries per field, capillary width, capillary morphology, microhemorrhages, peri-capillary stippling (PCS)- hemosiderin deposits probably representing former capillary leak, slow capillary flow ("rolling" or sludging of red blood cells) and avascularity. Continuous data are presented as the mean ± SD. Categorical variables are presented as frequencies and percentages. Comparisons of continues variables were made using 2-tailed t-tests and differences between groups by a 1-Way ANOVA.
Results: Seventeen patients with active vasculitis, 8 patients with vasculitis in remission (11 polyarteritis nodosum, 2 GPA, 3 eosinophilic granulomatosis with polyangiitis, 2 microscopic polyangiitis, 2 Takayasu, 3 Sjogren vasculitis (one with cryoglobulinemia), 1 primary central nervous system vasculitis and 1 lupus vasculitis) were compared to 25 age and sex matched healthy controls. The mean age (59 ±18 vs. 51±19 vs. 52 ±15), and the percent of females (53%, 50%, 60%), were similar between the groups.
Patients with active vasculitis demonstrated higher rate of "rolling", 74.1% ±27 vs. 12.5%±22 vs. 6.5%±12.7, $p<0.001$; microhemorrhages or PCS 30.1%±26.4 vs. 1.5%±4.5 vs. 1.9%±1, $p<0.05$, which reversely correlated with disease duration r=-0.4, P=0.05;avascular areas 76%±19.5 vs. 23.4% ±28 vs. 26%±18.5, $p<0.01$ and neoangiogenesis 57%±23% vs 26.5% ±22.5 vs. 6% ±10.5, $p<0.01$. PCS was observed exclusively in 5 of 17 patients with active vasculitis.
Conclusion: Patients with active vasculitis demonstrate capillary abnormalities, namely: "rolling", microhemorrhages, avascular areas and neoangiogenesis. PCS may be a specific sign of active vasculitis. NVC is an easy, readily available additive tool in the management of vasculitis. Further studies are needed to ascertain the role of NVC in vasculitis.

REFERENCES

[1] Sendino Revuelta A, Barbado Hernández FJ, Torrijos Eslava A, González Anglada I, Peña Sánchez de Rivera JM, Vázquez Rodríguez JJ. Capillaroscopy in vasculitis.An Med Interna. 1991;8(5):217-20. Spanish.
[2] HJ Anders, C Headecke, T Sigl, K Kruger. Avascular areas on nailfold capillary microscopy of patients with Wegener's granulomatosis. Clin Rheumatol. 19:86-8, 2000
[3] Aytekin S, Yuksel EP, Aydin F, Senturk N, Ozden MG, Canturk T, Turanli AY. Nailfold capillaroscopy in Behçet disease, performed using videodermoscopy. Clin Exp Dermatol. 2014;39(4):443-7.
[4] Javinani A, Pournazari M, Jamshidi AR, Kavosi H. Nailfold videocapillaroscopy changes in Takayasu arteritis and their association with disease activity and subclavian artery involvement. Microvasc Res. 2019;122:1-5

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AB0610 PERSISTENT INFLAMMATION DESPITE TOCILIZUMAB TREATMENT IN 2 PATIENTS WITH LARGE VESSEL VASCULITIS AND AORTIC INVOLVEMENT REQUIRING AORTIC VALVE REPLACEMENT

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Background: Tocilizumab (TCZ) has recently been approved for treatment of giant cell arteritis (GCA). Despite clinical, radiologic and serologic improvement in the majority of patients, it remains unclear whether inflammation of the vascular wall in patients with large vessel vasculitis may persist.
Objectives: To report 2 patients who were treated with TCZ for large vessel vasculitis involving the ascending aorta. The patients underwent aortic valve replacement in both cases and partial replacement of the ascending aortic arch in one case.
Methods: Following therapy with glucocorticosteroids (GC) and TCZ, replacement of the aortic valve and of the partial ascending aorta were performed, followed by a histopathologic examination of the surgical specimen.
Results: We report two female patients, aged 40 and 67 years, both diagnosed with large vessel vasculitis involving the aortic arch. Aortitis of the ascending aorta and significant aortic insufficiency were demonstrated in both patients by PET-CT, MR angiography and transesophageal cardiac ultrasound.
In Pat 1, PET CT and MR angiography revealed vascular inflammation. Intravenous pulse GC was initiated, followed by oral prednisone with stepwise tapering and TCZ iv 8mg/kg/month. Two weeks after the 2nd infusion of TCZ, MR angiography showed significant reduction of gadolinium enhancement in the wall of the ascending aorta and the patient subsequently underwent valve replacement.
Pat 2 was diagnosed with vasculitis of the aortic arch by MR angiography. Therapy with oral GC (1mg prednisone/kg) and methotrexate was initiated. After 12 months, the treatment was switched to TCZ 162mg sc once weekly because of inadequate control of disease. The patient was monitored clinically and by PET CT and GCA was considered well controlled over 4 years. Due to continuous enlargement of the ascending aorta resulting in significant aortic insufficiency, the patient underwent replacement of the aortic valve and the ascending aorta.
Both patients showed normalization of CRP and ESR during TCZ treatment.
In summary, despite PET-CT and MR angiography showing reduction in vascular wall inflammation before surgery and CRP and ESR normalized, both patients showed histologically persistent lymphoplasmacellular infiltrates (predominantly CD3+CD4+ T cells in patient 1) and, in addition, giant cells in pat 2.
Conclusion: Despite adequate control of large vessel vasculitis involving the ascending aorta clinically as well as by imaging, the 2 patients reported here had to undergo valve replacement which showed persistent inflammation of the aortic wall despite treatment with TCZ.
Disclosure of Interests: Andrea Rubbert-Roth Consultant for: Chugai, Eli Lilly, Roche, and Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Hexal/Novartis, Janssen, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, and Sanofi, Thomas Langenegger: None declared, Peter Karl Bode: None declared, Claudia Pfofe: None declared, Olaf Chan-Hi Kim: None declared, Johannes von Kempis: None declared
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AB0611 A NEW SHAPE OF THE TREATMENT OF VASCULITIDES: SINGLE CENTER BIOLOGICAL AGENTS EXPERIENCE

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Background: Vasculitides are a group of inflammatory diseases with different clinical and pathological features of vital importance in various sized and types which may lead to organ failure and inflammation of the vascular wall. The framework for the treatment of vasculitis is similar to that used for many other systemic autoimmune rheumatic disorders, while the specific therapeutic regimen depends upon the nature and severity of the particular disorder (1,2).
Objectives: The aim of this study is to evaluate the efficacy of biological agents in 56 vasculitides patients with resistant/intolareted to cDMARDs.
Methods: Between January 2015 and December 2018, fifty six patients who were diagnosed as vasculitis (Takayasu arteritis-TA, Granulomatosis with polyangiitis(GPA), Giant cell arteritis (GCA) and Behçet Syndrome (BS) at Sivas Cumhuriyet University Medical Faculty Rheumatology-Internal Medicine Department were included in to the study.
Results: 24 (43%) male and 32 (57%) female were included in the study. The median age of the patients was 56 years (min:19-max: 77) and the median age at diagnosis was 39 years (min 17-max 73). 14 (25%) patients with TA, 22 (39%) patients with GPA, 3 (5%) patients with GCA and 17 (31%) patients with BS included in this study.Tocilizumab treatment was used 6 of 8 patients who were resistant to anti-TNF. In 22 GPA patients with pulmonary and kidney involvement, Rituximab (RTX) treatment was started in 18 patients who were unresponsive to cDMARD and cyclophosphamide therapy. Plasmaexchange were used in 4 (18%) patients with alveolar hemorrhage. Indication of anti- TNF agents in behçet's syndrome were as follows panuveitis 70%, neuro-behcet 17.5% and vessel involvement 12.5% (Table 1). 1 GPA patient was died and other GPA, TA and BS patients have clinically response. Biological treatment is continued as maintenance therapy.
Conclusion: Biological treatments were used safely and effectively in vasculitis. In particular, RTX treatment is recommended for both induction and maintenance of GPA. Tosilizumab treatment is very effective in TA and GCA. However, large and long-term studies are needed in terms of long-term effects.

REFERENCES

[1] Specks U, Merkel PA, Seo P, et al. Efficacy of remission-induction regimens for ANCA-associated vasculitis. N Engl J Med 2013; 369:417.
[2] Mukhtyar C, Guillevin L, Cid MC, et al. EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis 2009; 68:318.

Abstract AB0611 Table 1:. Clinical Features Of Patients And Treatment Modalities

	n	Clinical features	cDMARDs	Anti-TNF	RTX
Takayasu	14 (25%)		6 (43%)	2 (14%)	6 (43%)
GPA	22 (39%)	Renal+pulmoner 18 (82%) Limited 4 (18%)	4 (18%)		18 (% 82)
Behçet	17 (31%)	Uveitis 12 (70%) Neuro-behçet 3 (17.5) Vessel inv. 2 (12.5%)		17 (31%)	
GCA	3 (5%)		2 (66%)	1 (33%)	

Disclosure of Interests: None declared
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AB0612 TEMPORAL ARTERY BIOPSYIN GIANT CELL ARTERITIS. INTERRELATION OF INFLAMMATORY PATTERNS WITH ANALYTICAL DATA AND CLINICAL MANIFESTATIONS

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Background: Giant cell arteritis (GCA) is a systemic vasculitis that affecting large and medium vessels, mainly the temporal artery and other arteries of extracranial localization **(1).**
Objectives: A series of 24 patients with clinical suspicion of GCA proved by a positive temporal artery biopsy (TAB) has been reviewed. Our aim was to asses a) histologic inflammatory patterns in the TAB and b) their possible correlation with analytical and clinical data.
Methods: Prospective study of 24 patients with positive TAB between January of 2016 until January of 2018. Clinical data, included: age, sex, symtomatology (craneal, visual or systemic manifestations) and physical examination of the temporal artery.
The analytical data registered were: ESR, CRP and haemoglobin. Furthermore, it has been considered if patients were receiving treatment with corticosteroids at the time of the biopsy.
Positive biopsies were classified into four categories: a) inflammation limited exclusively to the small vessels of the adventitia (SVV); b) vasa

vasorum vasculitis (VVV); c) inflammation limited to the adventitia (ILA); and d) transmural inflammation (TMI). The presence of giant cells, thrombosis and distrophic calcification was also noted.

Results: We included a total of 24 patients with positive TAB: a) 19 patients (79.16%) presented TMI and b) 5 patients (20.84%) presented ILA. There were no cases with SVV or VVV.

No significant differences at baseline were observed between the 2 groups regarding sex and age, with a mean of 79.6 ± 7.2 years in TMI group and 78.8 ± 7.3 years in ILA group (p = 0.83).

There were no significant differences between the correlation of the clinical and analytical data and the 2 patterns of inflammation observed in the biopsy **(TABLE-1).**

Regarding the treatment at the time of performing the BAT, 16 (of 19) patients in the group with TMI (84.2%) and 4 (of 5) patients in the group with ILA (80%) were receiving treatment with oral glucocorticoid (Prednisone). No significant differences between the two groups were found in terms of treatment duration prior to BAT and nor in the dose recived **(TABLE-2).**

Conclusion: In our sample, we didn't observe differences between the patterns of inflammation and the analytical and clinical data. It is important to recognise these patterns of inflammation in the TAB to avoid false negatives.

REFERENCES

1- MA González-Gay, T Pina, D Prieto-Peña, M Calderon-Goercke, R Blanco, S Castañeda (2018) Current and emerging diagnosis tools and therapeutics for giant cell arteritis,Expert Review of Clinical Immunology, 14:7, 593-605, DOI: 10.1080/1744666X.2018.1485491.

TABLE-1. CLINICAL AND ANALYTICAL DATA.

Variables	TMI (n=19)	ILA (n=5)	P
Sex (women), n (%)	10 (52.6)	5 (100.0)	0.12
Age at disease onset , (mean ± SD)	79.6 ± 7.2	78.8 ± 7.3	0.83
CLINICAL DATA			
Any cranial symptoms	17 (89.5)	3 (60.0)	0.18
Headache	15 (78.9)	3 (60.0)	0.57
Scalp Tenderness	6 (31.6)	2 (40.0)	0.99
Abnormalities of temporal arteries	9 (47.4)	1 (20.0)	0.36
Jaw claudication	9 (47.4)	2 (40.0)	0.99
Visual loss	5 (23.8)	1 (20.0)	0.99
Any visual symptoms	15 (78.9)	3 (60.0)	0.62
Systemic signs/symptoms	11 (57.9)	4 (80.0)	0.51
PMR	5 (26.3)	3 (60.0)	0.29
Peripheral synovitis	0 (0.0)	0 (0.0)	0.99
ANALYTICAL DATA			
ESR (mean ± SD) (mm/H)	64.2 ± 36.7	74.0 ± 32.2	0.57
CRP (mean ± SD) (mg/dL)	10.2 ± 9.0	9.5 ± 8.8	0.75
Hemoglobin (mean ± SD) (g/dL)	11.6 ± 1.5	11.1 ± 2.4	0.43

TABLE-2. TREATMENT.

Variables	TMI (n=19)	ILA (n=5)	P
TREATMENT			
Patients taking Prednisone at the time of TAB	16 (84.2)	4 (80.0)	0.99
Prednisone dose at the time of TAB (median [IQR]) (mg/d)	40.0 [30.0-60.0]	270.0 [23.0-875.0]	0.44
Duration of Prednisone treatment before TAB (median [IQR]), days	5.0 [1.0-8.0]	3.0 [1.0-30.0]	0.90

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AB0613

PRESENTATION OF TAKAYASU ARTERITIS ACCORDING TO THE AGE OF ONSET IN A MONOCENTRIC ITALIAN COHORT

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Background: Takayasu arteritis (TA) is a large-vessel vasculitis usually affecting young women. The age of onset is though variable. Controversial data are reported about differences in disease features according to the age of onset.

Objectives: To compare clinical and vascular TA features according to TA age of onset.

Methods: We retrospectively evaluated onset demographic and disease features in TA patients followed-up at our Hospital between January 2000 and August 2018. We divided our cohort into 3 groups according to the age of onset: ≤20 (Group 1), 21-40 (Group 2), >40 (Group 3) years. Diagnostic delay (DD) was defined as the time interval between the first TA symptom and TA diagnosis. Non parametric statistic tests were used.

Results: 126 patients (12 male, 114 female) were analyzed. Mean age at onset was 31.46±13.38 years. Group 1 and 3 included 30 (23.81%) patients each, Group 2 66 (52.38%). Mean age at onset was 16.23±3.20 years in Group 1, 29.59±5.80 in Group 2 and 50.8±7.16 in Group 3. Mean DD was different between the 3 groups: 117.63±129.79 months in Group 1, 56.47±76.98 in Group 2 and 30.80±40.53 in Group 3 (Group 1 vs 2, p=0.021; Group 1 vs 3, p<0.001; Group 2 vs 3, p=0.089). Clinical and laboratory features at TA onset are summarized in Table 1. Among all disease features only arterial hypertension was statistically more prevalent in Group 3 vs Group 1 and 2 (56.67% vs 36.67% and 30.30% respectively, p=0.048). When evaluating vascular involvement, abdominal aorta was more frequently affected in Group 1 (63.33% vs 34.85% and 56.67%, p=0.018) while right iliac and left iliac arteries in Group 3 (40% vs 23.33% and 10.61%, p=0.004; 36.67% vs 23.33% and 12.12%, p=0.024 respectively).

Abstract AB0613 Table 1

Clinical and laboratory features	Group 1 n 30 (%)	Group 2 n 66 (%)	Group 3 n 30 (%)	p-value
Systemic symptoms	21 (70)	37 (56.06)	15 (50)	0.254
Carotidynia	11 (36.67)	12 (18.18)	5 (16.67)	0.116
Lower extremities claudication	7 (23.33)	18 (27.27)	4 (13.33)	0.363
Upper extremities claudication	10 (33.33)	31 (46.97)	7 (23.33)	0.083
Δ blood pressure	10 (33.33)	16 (24.24)	6 (20)	0.526
Reduced/absent pulse	18 (60)	29 (43.94)	11 (36.67)	0.178
Bruits	15 (50)	20 (30.30)	8 (26.67)	0.114
Angina abdominis	6 (20)	6 (9.09)	3 (10)	0.376
Myocardial infarction	0	5 (7.58)	4 (13.33)	0.154
Heart failure	0	6 (9.09)	0	0.078
Arterial hypertension	11 (36.67)	20 (30.30)	17 (56.67)	**0.048***
Headache	10 (33.33)	9 (13.64)	8 (26.67)	0.067
Syncope	9 (30)	9 (13.64)	6 (20)	0.180
Stroke	2 (6.67)	6 (9.09)	2 (6.67)	1
Amaurosis	4 (13.33)	4 (6.06)	3 (10)	0.499
↑ inflammatory markers	25 (83.33)	52 (78.79)	25 (83.33)	0.869
Vascular surgery	8 (26.67)	13 (19.70)	11 (36.67)	0.202

Abstract AB0613 Table 2

Artery	Group 1 n 30 (%)	Group 2 n 66 (%)	Group 3 n 30 (%)	p-value
Coronary	2 (6.67)	7 (10.61)	4 (13.33)	0.274
Pulmonary	5 (16.67)	12 (18.18)	1 (3.33)	0.146
R subclavian	14 (46.67)	32 (48.48)	17 (56.67)	0.771
L subclavian	18 (60)	43 (65.15)	22 (73.33)	0.554
R CC	19 (63.33)	36 (54.55)	18 (60)	0.701
L CC	21 (70)	38 (57.58)	19 (63.33)	0.497
R vertebral	3 (10)	11 (16.67)	3 (10)	0.648
L vertebral	4 (13.33)	12 (18.18)	6 (20)	0.863
Brachiocephalic	10 (33.33)	22 (33.33)	6 (20)	0.425
Ascending ao	11 (36.67)	19 (28.79)	6 (20)	0.369
Arch	9 (30)	20 (30.30)	11 (36.67)	0.821
Descending ao	10 (33.33)	17 (25.76)	9 (30)	0.756
Abdominal ao	19 (63.33)	23 (34.85)	17 (56.67)	**0.018***
Celiac	7 (23.33)	23 (34.85)	12 (40)	0.344
Superior mesenteric	8 (26.67)	22 (33.33)	6 (20)	0.398
R renal	9 (30)	16 (24.24)	4 (13.33)	0.297
L renal	7 (23.33)	15 (22.73)	5 (16.67)	0.843
R iliac	7 (23.33)	7 (10.61)	12 (40)	**0.004***
L iliac	7 (23.33)	8 (12.12)	11 (36.67)	**0.024***

Abbreviations: right (R), left (L), common carotid (CC), aorta (ao)

Conclusion: TA patients <20 years might experience a longer DD. Arterial hypertension seems to be a prevalent feature in TA patients >40 years. Vascular involvement seems also be influenced by the age of onset with the abdominal aorta being more frequently affected in younger patients and iliac arteries in older patients.**Disclosure of Interests:** Silvia Sartorelli: None declared, Corrado Campochiaro Consultant for: Dr Corrado Campochiaro received consultation honoraria from Pfizer., Alessandro Tomelleri: None declared, Elena Baldissera Consultant for: Consultation honoraria from Novartis and Rottapharm, Speakers bureau: Pfeizer, Sobi, Novartis, Lorenzo Dagna Consultant for: Prof Lorenzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI.
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AB0614 A SINGLE, SUCCESSFUL INFLIXIMAB INFUSION FOR BEHCET'S DISEASE ASSOCIATED SIGHT-THREATENING UVEITIS ATTACK, FOLLOWED BY 2 ADDITIONAL INFUSIONS, PRODUCE LONG TERM OCULAR REMISSION

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Background: Recommendations on the use of anti-TNF agents in **Behcet's disease** BD include the administration of a single infusion of infliximab, 5 mg/kg for bilateral posterior eye segment inflammation as a first-line agent to achieve a fast-onset response (Sfikakis PP et al, Rheumatology 2007). On the other hand, long-term remission is feasible after discontinuation of successful anti-TNF treatment given for severe BD, including posterior ocular inflammation (Sfikakis PP et al. Arthritis Rheumatol 2017).
Objectives: To report the long-term outcome of successful short-term Infliximab treatment for sight-threatening uveitis in Behcet's disease.
Methods: In this retrospective single-center analysis, we identified all patients with BD followed up in our center at least once yearly since 2001, who received one successful IV infusion of Infliximab (5mg/kg) for bilateral sight threatening posterior uveitis attack, followed by 2 additional infusions 2 months apart. Other severe BD manifestations at the time of attack included severe mucocutaneous disease (n=3), arthritis (n=2), vascular (n=1), and gastrointestinal involvement (n=1).The first Infliximab infusion was considered successful if complete suppression of acute ocular inflammation was achieved. Study's endpoint was the proportion of patients remaining in complete ocular remission for at least 5 years after cessation of Infliximab.
Results: We identified 10 patients (aged 52±14.3 years, 60% men, disease duration 12±5.2 years) who received 3 IV Infliximab infusions (5 mg/kg each) for sight-threatening posterior ocular inflammation (20 eyes), either at the first attack (n=5) or for relapsing attacks (n=5). Infliximab was given as add-on to azathioprine (n=7) or to azathioprine in combination with cyclosporine (n=2). Nine of ten patients (90%) achieved the study's endpoint, i.e. after cessation of short-term Infliximab treatment remain in complete ocular remission for a mean of 9.5±4.2 years (range 5-15.3 years). The last patient relapsed 6 months after Infliximab discontinuation, but subsequently responded to antiTNF re-treatment, which is continued to date. Notably, four of the nine patients who achieved the study's endpoint were also able to discontinue azathioprine and are currently any drug free.
Conclusion: The majority of patients with sight-threatening uveitis who responded completely to a first Infliximab infusion and received 2 additional infusions, remain in remission for many years thereafter. Additional studies to confirm that short term infliximab treatment with observation for objective improvement should be promptly administered in every BD patient with sight-threatening uveitis attack are warranted.

REFERENCES

[1] Sfikakis PP, Markomichelakis N, Alpsoy E, Assaad-Khalil S, Bodaghi B, Gul A, Ohno S, Pipitone N, Schirmer M, Stanford M, Wechsler B, Zouboulis C, Kaklamanis P, Yazici H. Anti-TNF therapy in the management of Behcet's disease-review and basis for recommendations. Rheumatology (Oxford). 2007 May;46(5):736-41.
[2] Sfikakis PP, Arida A, Panopoulos S, Fragiadaki K, Pentazos G, Laskari K, Tektonidou M, Markomichelakis N. Brief Report: Drug-Free Long-Term Remission in Severe Behçet's Disease Following Withdrawal of Successful Anti-Tumor Necrosis Factor Treatment. Arthritis Rheumatol. 2017 Dec;69 (12):2380-2385.

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AB0615 PREVALENCE OF DEPRESSION, ANXIETY, FATIGUE AND SLEEP DISTURBANCES IN PATIENTS OF RA, SLE AND GPA

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Background: The relative frequencies of co-morbidities like depression, anxiety, fatigue and sleep disturbance in RA, SLE and GPA are not fully elucidated.
Objectives: To estimate and correlate the prevalence of depression, anxiety, fatigue and sleep disturbances in patients with RA, SLE and GPA by using time honored scales and PROMIS-HAQ[1].
Methods: This was a cross sectional study of 183 patients (RA – 57, SLE – 64, GPA – 62). Diagnosis and assessment of depression, insomnia, anxiety and fatigue was established by patient health questionnaire 9 (PHQ 9), Epworth sleepiness scale (ESS), generalized anxiety disorder assessment scale 7 (GAD 7) and fatigue severity scale (FSS) respectively. PROMIS-HAQ short form 8a was also used to diagnose depression, insomnia, anxiety and fatigue and its correlation with the above time honored scales was studied.
Results: Mean age of RA, SLE and GPA patients was 45.5 ± 12, 31 ± 9.5 and 42.7 ± 13.5 years respectively. Mean disease duration was 5.7 ± 5.1, 3.3 ± 2.4 and 4.6 ± 4 years in RA, SLE and GPA respectively. Prevalence of depression, anxiety, fatigue, insomnia in RA, SLE and GPA as per standard scales and PROMIS HAQ is depicted in table 1. The corelation between the standard scales and PROMIS HAQ for depression [RA (r- .816, p< .001), SLE (r- 0.625, p< 0.001), GPA (r-0.772, p <0.001)], anxiety [RA (r- .804, P< .001), SLE (r- 0.709, p<0.001), GPA (0.888, p<0.001)], sleep disturbance [RA (r- .872, p<0.001), SLE (r- 0.784, p< 0.001), GPA (r-0.917, p <0.001)] and fatigue [RA (r- .815, p< .001), SLE (r- 0.798, p< 0.001), GPA (r-0.805, p <0.001)] was significant.

Table 1. Prevalence of depression, anxiety, fatigue and insomnia by various scales

	Depression		Anxiety		Fatigue		Sleep/Insomnia	
	PHQ9	PROMIS HAQ	GAD7	PROMIS HAQ	FSS	PROMIS HAQ	ESS	PROMIS HAQ
RA	49.2%	35.1%	45.6%	38.5%	40.4%	49.1%	19.3%	17.5%
SLE	60.9%	43.7%	51.6%	40.6%	51.6%	57.8%	15.6%	14.1%
GPA	46.8%	21%	29.0%	24.0%	38.7%	40.3%	16.1%	12.9%

Conclusion: Depression, anxiety, fatigue and sleep disturbance are common in RA, SLE and GPA. PROMIS HAQ has good correlation with time honoured scales for assesment of depression, anxiety, fatigue and sleep disturbance in these disorders.

REFERENCES

[1] Cella D, Riley W, Stone A, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. J Clin Epidemiol 2010;63:1179–94.

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AB0616 HISPANIC AMERICAN PATIENTS WITH ANCA ASSOCIATED VASCULITIS AND DIFFUSE ALVEOLAR HEMORRHAGE RESPOND COMPARABLY TO INDUCTION THERAPY

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Background: Hispanic American patients with ANCA-associated vasculitis (AAV) have been reported to have more severe disease and higher

damage indices at presentation. One rare but life-threatening complication of AAV is diffuse alveolar hemorrhage (DAH).
Objectives: To study the clinical features, course and response to therapy in Hispanic American patients with AAV and DAH seen at a large public teaching hospital that serves medically underserved and low income patients with chronic poor health maintenance.
Methods: Among 60 Hispanic American patients with AAV, we retrospectively studied 13 patients with DAH from 2003-2017. Clinical features, laboratory results, diagnostic modalities and treatments given were studied.
Results: A total of 13 patients were identified; 6 men and 7 women, mean age of 51± 11 years. Anti-PR3 was found in 5 patients, anti-MPO in 8. Nine patients were diagnosed with microscopic polyangiitis and 4 with granulomatous polyangiitis based on ACR criteria or Chapel Hill Consensus Conference definitions. DAH was a presenting manifestation in 12 patients. Gross hemoptysis with hypoxia, drop in hematocrit and chest X-ray infiltrates were seen in all patients diagnosed with DAH. Bronchoscopy with BAL washings confirming diagnosis was done in 10 patients.
All patients had multi-organ involvement including nephritis (n= 8), peripheral neuropathy (n= 1), palpable purpura (n=2), upper respiratory tract involvement (n= 4) and eye involvement (n=2). Serum C3 was normal in 12 patients. Renal biopsy in 9 patients showed pauci-immune crescentic glomerulonephritis. Mean BVAS at time of DAH was 21.2 ± 5.1.
All patients underwent induction-remission therapy with pulse methylprednisolone followed by tapering oral prednisone. Induction therapy included IV cyclophosphamide (n=6), rituximab (n=6) and IV cyclophosphamide/rituximab combination therapy (n=1). Nine patients underwent plasma exchange and 5 received IV gamma globulin. Eleven patients required mechanical ventilation; 6 patients needed hemodialysis, 2 temporarily.
All 13 patients responded to induction therapy; mean post-induction therapy BVAS was 9.3 ± 3.5. Pulmonary fibrosis after DAH was noted in 2 patients. No early deaths (<6 months) were observed, however 1 patient died within 3 years due to infection. Mean follow-up period was 69 ± 54 months. Maintenance therapy used included prednisone (n=13), mycophenolate mofetil (n= 2), azathioprine (n= 6) and IV rituximab (n= 8).
Five patients had clinical relapse, 3 with recurrent DAH. Two patients had minor relapse, defined by their treating physician as requiring increased prednisone dose or worsening proteinuria. Mean BVAS at relapse was 15.2 ± 5.5.
Conclusion: This first in-depth study of DAH in Hispanic American AAV patients shows that in this socioeconomically disadvantaged patient population, the response to induction therapy is not significantly different from other ethnic groups reported in the literature. DAH remains a severe clinical manifestation of AAV and should be recognized without delay. If treated promptly following EULAR/ERA-EDTA recommendations, good short term response is to be expected.

REFERENCES

[1] Yates M, Watts RA, Bajema IM, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Ann Rheum Dis 2016;75:1583-1594
[2] Jennette JC, Falk RJ, Bacon PA, et al. 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013;65:1-11

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AB0617 CUTANEOUS POLYARTERITIS NODOSA TREATMENT: A RETROSPECTIVE CASE SERIES

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Background: Cutaneous polyarteritis nodosa (CPAN) is a small-to-medium vessel vasculitis limited to the skin. As it is a rare condition, there is little data available to guide treatment. Previous articles have suggested that colchicine and dapsone be used in mild disease and glucocorticoids in acute flares, with DMARDs such as methotrexate or azathioprine being reserved for moderate to severe disease, or steroid-refractory disease.
Objectives: Our objective was to review therapeutic regimens used to treat CPAN and to evaluate patient response.
Methods: A retrospective chart review including records from January 2003 to June 2017 was performed to identify patients with both histologic and clinical features of CPAN. We extracted information regarding patient age, clinical presentation, biopsy results, and response to treatment.
Results: Thirteen patients were identified who had clinical features of CPAN that were supported by histologic findings on biopsy. The majority of patients were female (92.3%). The average age at diagnosis was 44.9 years and mean duration of follow up was 53 months. All patients had involvement of the lower limbs with the most common cutaneous manifestation being subcutaneous nodules (92.3%), followed by papules (46.2%) and livedo reticularis (30.8%). Eight out of thirteen patients (61.5%) received steroids and three did not experience clinical benefit. Another patient did not respond to prednisone and hydroxychloroquine, but had significant improvement of her symptoms on prednisone and methotrexate. Seven out of nine patients (77.8%) who were treated with methotrexate had a favourable response. Three of those patients responded to methotrexate after failing other therapies such as dapsone, azathioprine, and prednisone.
Conclusion: In this case series, we found that most patients had a favorable response to methotrexate and thus the role of methotrexate in treating CPAN merits further investigation. As CPAN often has a chronic relapsing and remitting course, initiating methotrexate at the same time as steroid therapy may lower overall lifetime exposure to steroids.

REFERENCES

[1] Daoud MS, Hutton KP, Gibson LE. Cutaneous periarteritis nodosa: a clinicopathological study of 79 cases. Br J Dermatol. 1997 May;136(5):706–13.
[2] Ross K, Contreras J, Aung-Din D, Lien M. Asymptomatic cutaneous polyarteritis nodosa: treatment options and therapeutic guidelines. Cutis. 2017 Aug;100(2):125–8.
[3] Maillard H, Szczesniak S, Martin L, Garot D, Machet MC, Machet L, et al. [Cutaneous periarteritis nodosa: diagnostic and therapeutic aspects of 9 cases]. Ann Dermatol Venereol. 1999 Feb;126(2):125–9.
[4] Khoo BP, Ng SK. Cutaneous polyarteritis nodosa: a case report and literature review. Ann Acad Med Singapore. 1998 Nov;27(6):868–72.
[5] Schartz NEC, Alaoui S, Vignon-Pennamen MD, Cordoliani F, Fermand JP, Morel P, et al. Successful treatment in two cases of steroid-dependent cutaneous polyarteritis nodosa with low-dose methotrexate. Dermatology. 2001;203(4):336–8.

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AB0618 A SNAPSHOT OF DISEASE ACTIVITY IN PATIENTS WITH BEHCET'S SYNDROME: PREDICTIVE FACTORS AND RELATIONSHIP WITH QUALITY OF LIFE

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Background: Behçet's Syndrome (BS) is globally characterized by a variable spectrum of disease profile: while prevalent muco-cutaneous lesions and arthritis represent the only clinical features in patients with a benign disease subset, there are other patients who develop potentially sight or life-threatening manifestations, due to ocular, neurological or major vascular involvement. Beside the organ involvement, demographic factors could considerably influence the long-term and short-term outcomes of BD
Objectives: The primary aim of the study was to evaluate disease activity in a cohort of BS patients consecutively followed in a BS clinic of a tertiary centre; the secondary aims were to identify potential predictive factors of disease activity and to compare disease activity with quality of life.
Methods: One-hundred and thirty patients (71 males and 59 females; mean age 42±8 years, mean disease duration 11±4) with a diagnosis of BS according to the ISG criteria were studied. Disease activity has been evaluated by BDCAF and quality of life by the Short Form (SF) 36. Patients were also categorized in major or minor involvement of BS according or not to the presence of ocular, neurological and vascular involvement in the course of disease Predictors of long-term outcome were identified by univariate analysis using the log-rank test and by multivariate analysis using Cox proportional hazards regression models.

Results: At time of the evaluation, 39% of BS patients presented an active disease. Thirty-six patients presented muco-cutaneous involvement, 21 ocular disease, 10 joint involvement, 6 neurological impairment and 4 gastro-enteric involvement. Sixty-two percent of patients presented in the course of the disease a severe BS involvement and, among these, the majority was represented by males HLAB51 positive patients. The major limitations of quality of life related to disease activity were represented by vitality, physical functioning, bodily pain, general health perception.
Conclusion: Younger men patients affected by BS are more suitable to have a more severe disease, due to an increased frequency both of morbidity and mortality, secondary to ocular, vascular and neurological involvement. The variable prognosis associated to different gender or age, may represent an essential and useful element to tailor the management not only to the type and severity of symptoms, but also to the epidemiological profile of BD patients.
Disclosure of Interests: Rosaria Talarico: None declared, Alice Parma: None declared, Eralda Zera: None declared, Emanuele Calabresi: None declared, Chiara Tani: None declared, Chiara Baldini: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB
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AB0619 FAMILY MEMBERS WITH BS MAY NOT CLUSTER IN SIMILAR CLINICAL CHARACTERISTICS

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Background: Both genetic and environmental factors may have roles in the pathogenesis of Behcet's Syndrome (BS). Likewise, occurrence of different clinical cluster of BS may be also influenced by the combination of these two factors. But we do not know the weight of the factors during the emergence of the disease and clinical clusters.
Objectives: We conducted a study for evaluating the frequency of family history for BS in different clinical BS clusters. Furthermore, we assessed the hypothesis that "BS patients in the same family generally accumulate in the similar clinical cluster."
Methods: Eighty-five patients and their relatives in our BS cohort were participated to the study. We used International Study Group Criteria for Behçet Disease (ISBD) criteria (1) for classifying our index patients and their first and second degree relatives as BS. We sub-classified BS patient to mucocutenous, vascular, acne-arthritis-enthesis, eye, neurologic, intestinal and undetermined clusters (2). Firstly, we re-evaluated the family history of our BS patients. Then, the relatives of the patients with already known BS or with having symptoms related with BS were interviewed with phone. All participants have been informed about the study and we have taken consent from them.
Results: Twenty-two (25.9%) of the patients had first or second degree relatives with BS. Furthermore, 27 (31.8%) of our patient were classified to mucocutenaous cluster. In our study, the BS patient with enthesis-arthritis-acne cluster had highest frequency (44.4%) of family history. However, there was no apparent accumulation of similar findings in index BS cases and their close relatives (Table).
Conclusion: According to result of these studies, there was no finding that supports the hypothesis"*BS patients in the same family generally accumulate in the similar clinical cluster".* Still genetic may have major role in the emerging of the BS, such as it is accepted as a member of a group of diseases called MHC-I –opathy (3). However, like most of the diseases, genetic background is not enough for the expression of full-blown disease. Briefly, even in the similar genetic background, multiple and separate hits of environmental or non-genetic factors may take role in the pathogenesis.

Table. Features of the clusters' family history

Mucocutenaous Cluster	**n=27**
*Family history for BS n(%)**	10/27(37.0)
Mucocutenaous	5(50.0)
Eye	3(20.0)
Vascular	2(20.0)
Eye Cluster	**n=18**
*Family history for BS n(%)**	1/18(5.6)
Undetermined	1(100.0)
Enthesis-arthritis-acne Cluster	**n=18**
*Family history for BS n(%)**	8/18(44.4)
Mucocutenaous	3(37.5)
Enthesis-arthritis-acne	3(37.5)
Neuro-Behçet	1(12.5)
Undetermined	1(12.5)
Vascular Cluster	**n=12**
*Family history for BS n(%)**	2/12(16.7)
Mucocutenaous	1(50.0)
Eye	1(50.0)
Neuro-Behçet Cluster	**n=3**
*Family history for BS n(%)**	0/3(0.0)
Intestinal Cluster	**n=1**
*Family history for BS n(%)**	0/1(0.0)
Undetermined Cluster	**n=6**
*Family history for BS n(%)**	1/6(16.7)
Eye	1(100)

BS: Behçet's syndrome
* First or second degree relatives

REFERENCES
[1] Criteria for diagnosis of Behcet's disease. International Study Group for Behcet's Disease. Lancet. 1990;335(8697):1078-80.
[2] Tunc R, Keyman E, Melikoglu M, Fresko I, Yazici H. Target organ associations in Turkish patients with Behcet's disease: a cross sectional study by exploratory factor analysis. J Rheumatol. 2002;29(11):2393-6.
[3] McGonagle D, Aydin SZ, Gul A, Mahr A, Direskeneli H. 'MHC-I-opathy'-unified concept for spondyloarthritis and Behcet disease. Nature reviews Rheumatology. 2015;11(12):731-40.

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AB0620 EFFICACY AND SAFETY OF TOCILIZUMAB IN GIANT CELL ARTERITIS: A MONOCENTRIC REAL-LIFE EXPERIENCE

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Background: Giant cell arteritis (GCA) is a large-vessel vasculitis that generally affects people older than 50 years[1]. Glucocorticoids are the mainstay treatment[2]. Tocilizumab (TCZ) has recently been shown in clinical trials to be effective and safe for the treatment of GCA[3].
Objectives: To describe our real-life experience with TCZ in a cohort of GCA patients from a single Italian Centre.
Methods: We included GCA patients diagnosed according to the 1990 ACR criteria, followed-up at our Large Vessel Vasculitis Clinic, and treated with TCZ. We retrospectively evaluated demographic features, disease characteristics, reasons for TCZ introduction and discontinuation, concomitant therapies and response to treatment. For each patient we evaluated potential eligibility for GiACTA trial. For statistical comparisons, we used non-parametric tests.
Results: 40 patients (32 women, mean age 71±10 years) were included. Table 1 summarizes clinical features, tools for GCA diagnosis (imaging and/or biopsy) and reasons for TCZ introduction. Mean disease duration before TCZ introduction was 21.5±29.1 months. Only 12 patients (30%) met both GiACTA inclusion and exclusion criteria at TCZ introduction. 31 patients were followed-up for 3 months, 23 for 6 months, 17 for 12 months. Mean prednisone (PDN) dose at TCZ introduction was 21.9±13.2 mg. Mean PDN dose was 8.4±6.5 mg ($p<0.001$) at month 3, 4.8±5.6 mg ($p=0.002$) at month 6 and 2.3±2.3 mg ($p=0.012$) at month 12. PDN was stopped in 9 patients (2 at month 3, 5 at month 6, 2 at month 12) due to optimal disease control with TCZ alone. At TCZ introduction, 7 patients were already on methotrexate (MTX). MTX was subsequently stopped in 2 patients (1 at month 3, 1 at month 6) due to disease control. TCZ was temporarily held-off in 2 patients due to zoster reactivation and in 2 patients due to mild infections. TCZ was definitively stopped after 2 months (when PDN dose was still high) in 2 patients due to severe infections and after 6 months in 1 patient due to diverticulitis. No patient experienced severe neutropenia or liver enzymes elevation. In no case, TCZ was judged inefficient.

Table 1. TAB, temporal artery biopsy; PMR, polymyalgia rheumatica; GC, glucocorticoids; PET, positron emission tomography; MRA, magnetic resonance angiography.

Patient	Age at TCZ introduction/ sex	TAB (performed/ diagnostic)	Imaging	PMR	Cranial	Extra-Cranial	GiACTA inclusion criteria	GiACTA exclusioncriteria	Disease length before TCZ (months)	GC side effects/ contra-indications	GC dependence
1	80/M	+/+	MRA	-	+	-	+	-	9	+	+
2	70/F	+/+	PET	+	+	+	-	-	5	-	+
3	70/M	-	-	-	+	-	+	-	23	-	+
4	81/F	+/+	PET, MRA	-	+	-	+	-	9	-	+
5	61/F	-	MRA	+	+	+	-	-	16	-	+
6	68/F	-	-	+	+	-	-	-	3	-	+
7	80/F	+/+	-	-	+	-	+	-	6	+	+
8	76/F	-	-	+	+	-	-	-	3	+	+
9	56/F	-	PET, MRA	+	-	+	+	-	3	-	+
10	74/F	-	-	-	+	-	-	+	84	-	+
11	88/F	-	-	-	+	-	-	-	5	-	+
12	77/M	-	-	-	+	+	+	-	2	-	+
13	78/F	-	PET	-	+	+	+	-	30	-	+
14	52/M	-	-	-	+	-	-	-	24	-	+
15	57/F	-	-	+	+	-	-	-	0	+	-
16	79/F	+/+	-	-	+	-	-	-	4	+	+
17	67/M	-	PET, MRA	+	+	-	-	+	21	-	+
18	86/F	+/+	-	+	+	-	-	+	56	-	+
19	73/F	-	-	-	+	-	-	+	15	+	+
20	82/F	+/+	-	+	+	-	+	-	14	-	+
21	58/F	-	PET	-	+	+	-	-	7	-	+
22	59/M	-	PET, MRA	-	-	+	-	-	12	-	+
23	77/F	+/+	PET	+	+	+	-	+	18	-	+
24	91/M	-	-	-	+	-	+	-	3	-	+
25	57/F	-	PET	-	+	+	-	+	28	+	+
26	85/F	+/+	-	+	+	-	+	-	71	+	+
27	71/F	-	PET	-	-	+	-	-	22	+	+
28	67/F	+/+	PET, MRA	+	-	+	-	+	6	+	+
29	66/F	-	-	+	+	-	-	+	9	-	+
30	62/F	-	PET	-	+	+	+	-	29	+	+
31	62/F	-	-	-	+	-	-	-	6	+	+
32	79/F	+/-	PET	-	+	+	+	-	12	-	+
33	70/F	-	PET	-	+	-	+	+	8	-	+
34	85/F	-	PET, MRA	+	+	-	-	-	8	-	+
35	58/M	-	MRA	+	+	+	-	+	108	-	+
36	63/F	+/-	PET, MRA	+	-	+	-	-	132	-	+
37	71/F	-	-	+	+	+	-	-	3	-	+
38	77/F	-	PET	+	+	+	+	+	21	-	+
39	63/F	+/-	-	+	+	+	-	+	12	-	+
40	65/F	-	PET, MRA	+	+	+	-	-	12	+	-
TOTAL		**13/10**	**21**	**20**	**34**	**20**	**14**	**28**		**13**	**39**

Conclusion: Our data confirm TCZ is highly effective in GCA treatment and has a significant steroid-sparing effect. In our real-life retrospective study, TCZ was also shown to be a safe option in patients with relapsing or refractory GCA.

REFERENCES

[1] Salvarani C., et al. Polymyalgia rheumatica and giant-cell arteritis. Lancet (2008)
[2] Proven A., et al. Glucocorticoid therapy in giant cell arteritis. Arthritis Rheum (2003)
[3] Stone JH, et al. Trial of Tocilizumab in Giant-Cell Arteritis. *N Engl J Med* (2017)

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AB0621

GENDER DIFFERENCES IN CLINICAL PRESENTATION AND VASCULAR PATTERN IN PATIENTS WITH TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) is a chronic large-vessel vasculitis that predominantly affects aorta and its major branches. Although it is more commonly observed in Asian population, it can occur worldwide. TAK affects more frequently women in their second and third decades of life, but occurrence in patients older than 40 years is not rare[1]. Female to male ratio is commonly reported as 9:1[2].
Objectives: To compare clinical characteristics and pattern of vascular involvement at disease onset according to gender specificity in patients affected by TAK.
Methods: Data from 117 TAK patients (11 male, 106 female) diagnosed according to the ACR criteria from our Centre were retrospectively collected. Differences between men and women with regard to demographic features, diagnostic delay, signs and symptoms attributed to TAK, and arteries involved at diagnosis were compared. Data from 3 published

articles describing sex differences in TAK patients were obtained[3,4,5]. A global analysis of these 3 cohorts plus ours (for a total of 578 patients, 108 men and 470 women) was performed.

Results: In our TAK cohort, age at disease onset and age at diagnosis were not significantly different between men and women. Diagnostic delay was slightly higher in men. Male patients showed higher involvement of iliac arteries (right, p=0.016; left, p=0.021); female patients suffered more frequently from upper limbs claudication (p=0.026). In the overall analysis, men had higher prevalence of arterial hypertension (p=0.007) and more frequent involvement of abdominal aorta (p=0.026), renal arteries (right, p<0.001; left, p<0.001) and iliac arteries (right, p=0.009; left, p=0.002). Women more frequently exhibited upper limb claudication (p=0.042) and involvement of left subclavian artery (p=0.005), carotid arteries (right, p<0.001; left, p<0.001) and supradiaphragmatic aorta (ascending, p=0.050; arch, p<0.001; descending, p=0.003). Inflammatory markers were more frequently raised in women (p=0.005).

Conclusion: In TAK patients, gender has a strong influence on pattern of vascular involvement and consequently on clinical presentation. Specifically, women have higher involvement of the supradiaphragmatic vessels, whereas in men the abdominal vessels are more frequently affected.

REFERENCES

[1] Numano, et al. Takayasu arteritis. Lancet (2000).
[2] Fatos, et al. Epidemiology of Takayasu arteritis. Presse Med (2017)
[3] Lim AY, et al. Gender differences in clinical and angiographic findings of patients with Takayasu arteritis. Clin Exp Rheumatol (2015)
[4] Sharma BK, et al. A possible role of sex in determining distribution of lesions in Takayasu Arteritis. Int J Cardiol (1998)
[5] Mont'Alverne AR de S, et al. Features of the onset of Takayasu's arteritis according to gender. Arq Bras Cardiol (2013)

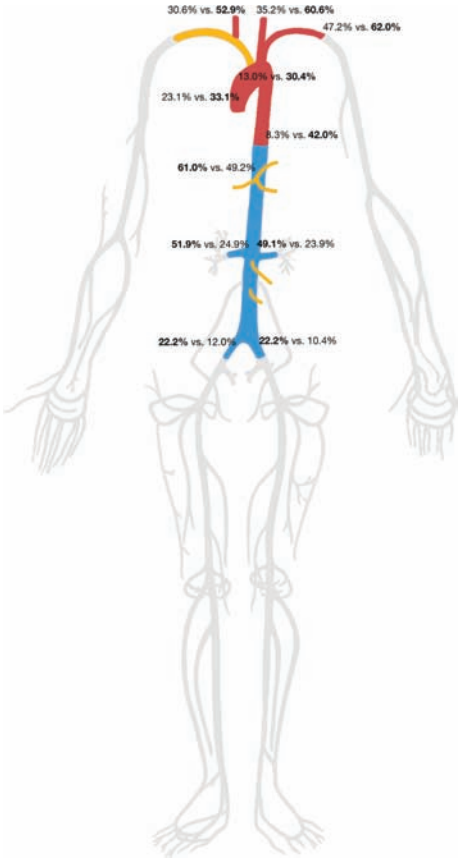


Figure 1. Vessels affected at disease onset in 578 patients with TAK (108 male, 470 female) from 4 different cohorts, according to gender. Red: higher involvement in women, with statistical significance. Blue: higher involvement in men, with statistical significance. Yellow: no statistically significant difference between women and men.

Disclosure of Interests: Alessandro Tomelleri: None declared, Corrado Campochiaro Consultant for: Dr Corrado Campochiaro received consultation honoraria from Pfizer., Silvia Sartorelli: None declared, Giulio Cavalli Consultant for: Dr Giulio Cavalli received consultation honoraria from Pfizer, Novartis and SOBI., Giacomo De Luca Speakers bureau: Pfeizer, Sobi, Elena Baldissera Consultant for: Consultation honoraria from Novartis and Rottapharm, Speakers bureau: Pfeizer, Sobi, Novartis, Lorenzo Dagna Consultant for: Prof Lorenzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI.
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AB0622 THE EFFICACY OF ADDITIONAL TOCILIZUMAB IN PATIENTS WITH SEVERE POLYMYALGIA RHEUMATICA WHO WERE RESISTANT TO OR INTOLERANT OF CONVENTIONAL THERAPY

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Background: Polymyalgia rheumatica (PMR) is the most common inflammatory disease in the elderly. The 2015 EULAR/ACR recommendations indicate that the management of PMR should be started with glucocorticoids (GCs) and if needed, followed by addition of methotrexate (MTX). The anti-interleukin-6 (IL-6) receptor antibody, tocilizumab (TCZ), has been shown to be effective for PMR.

Objectives: To determine the efficacy and safety of TCZ in patients with refractory PMR who were resistant to or intolerant of GCs plus MTX and characterize the clinical profile of patients who need TCZ.

Methods: Patients were diagnosed with PMR by the 2012 EULAR/ACR provisional classification criteria and treated according to the 2015 ACR/EULAR recommendations for the management of PMR. TCZ was further added to the patients who were GC plus MTX (GC/MTX)-resistant or -intolerant. The efficacy of treatment was determined by measuring the disease activity with PMR activity score (PMR-AS). We statistically analyzed the differences in clinical indicators between GC-responders, GC/MTX-responders, and GC/MTX-non-responders who need TCZ therapy.

Results: Ninety-three patients (53 females and 40 males) were the average of 72.1 ± 9.4 years old, serum CRP 63 ± 42 mg/L, ESR 84 ± 34 mm/hr and blood platelet counts 331 ± 86 $\times 10^3/\mu l$, at the first visit, and had been followed up for 25.4±19.6 months. All of them were treated first with prednisolone (PSL) (15.7± 4.3 mg/day). Relapses occurred in 43 patients (46.2%), at the PSL dose of 6.0 ± 5.6 mg/day, after 8.8 ± 6.7 month-GC treatment. GC was increased in 7 patients, and MTX (8.6 ± 2.9 mg/week) was added in 36 patients. Thirteen patients successfully discontinued GC, while 23 patients (24.7%) were resistant to or intolerant of GC/MTX. Ten of 23 patients agreed with TCZ therapy. Before TCZ addition, they were treated with PSL of 6.0 ± 2.2 mg/day plus MTX of 6.0 ± 3.8 mg/week, and serum CRP 9.7 ± 9 mg/L, blood platelet counts 271 ± 32 $\times 10^3/\mu l$ and PMR-AS 15.5 ±13.5. After 7.3 ± 4.2 month-TCZ treatment, PSL and MTX were reduced to 1.3 ± 1.6 mg/day and 2.2 ± 3.0 mg/week, and CRP, blood platelet counts and PMR-AS decreased to <0.2 mg/L, 191 ± 28 $\times 10^3/\mu l$ and 5.7 ± 8.3, respectively. GC could be withdrawn in 7 patients, and 4 patients reached drug-free remission. There were significant differences in blood platelet counts and the initial PSL amount between GC/MTX responders and GC/MTX-resistant patients (p<0.05; Mann-Whitney U test).

Conclusion: TCZ may provide a therapeutic option for patients with refractory PMR who were resistant to or intolerant of GC/MTX. Our retrospective results suggest that patients with severe PMR, who show thrombocytosis and need high dose GC for initial therapy, may be considered for early induction of TCZ.

Disclosure of Interests: None declared
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AB0623 ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS AND RISK OF CEREBROVASCULAR ACCIDENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: An increased risk of cardiovascular disease, including cerebrovascular accident (CVA), among patients with chronic inflammatory immune-mediated disorders is well-recognized, especially among patients with rheumatoid arthritis and systemic lupus erythematosus [1]. Patients with anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) may

be at an increased risk of CVA as well although the data are still inconclusive as most studies addressing this association were small in size.
Objectives: The current systematic review and meta-analysis was conducted with the aims to comprehensively identify all relevant studies and summarize their results together to better characterize the risk of CVA among patients with AAV.
Methods: Two investigators independently searched for published studies indexed in MEDLINE and EMBASE database from inception to October 2018 using the search strategy that included the terms for anti-neutrophil cytoplasmic antibody-associated vasculitis and cerebrovascular accident. Eligible studies must be cohort studies (either retrospective or prospective) that compared the risk of incident CVA between patients with AAV and individuals without AAV. They must also report the relative risk or hazard ratio with 95% confidence interval (CI) of this comparison. Point estimates and standard errors from each study were extracted and combined together using the random effect, generic inverse variance technique of DerSimonian and Laird.
Results: A total of 5 studies fulfilled the inclusion criteria and were included in this meta-analysis. The risk of incident CVA among patients with AAV was significantly higher than individuals without AAV with the pooled risk ratio of 1.49 (95% CI, 1.06–2.10). The statistical heterogeneity was insignificant with an I^2 of 11%. The forest plot of this meta-analysis is shown as figure 1. The funnel plot of this study was relatively symmetric and did not suggest the presence of publication bias.
Conclusion: A significantly increased risk of CVA among patients with AAV was demonstrated by this meta-analysis. Physicians who take care of patients with AAV should be aware of this risk and focus on interventions to modify other conventional risk factors for CVA may be warranted.

REFERENCES

[1] Hintenberger R, et al. Cardiovascular disease in patients with autoinflammatory syndromes. Rheumatol Int. 2018;38:37-50.

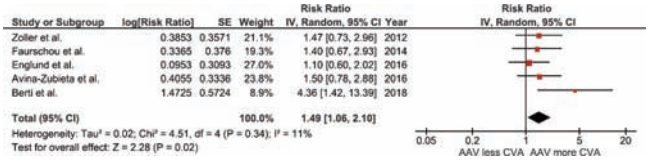


Figure 1. Forest plot of the studies on risk of incident CVA among patients with AAV

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AB0624 SAFETY OF RITUXIMAB BIOSIMILAR FOR THE TREATMENT OF CRYOGLOBULINEMIC VASCULITIS

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Background Rituximab (RTX) represents a milestone in the treatment of mixed cryoglobulinemic vasculitis (MCV). Despite usually well-tolerated, RTX may induce different types of adverse drug reactions, including exacerbation of vasculitis. RTX biosimilars have been recently approved in Europe in the treatment of rheumatoid arthritis, but no data are available about effectiveness and safety of RTX biosimilars in the treatment of MCV.
Objectives Aim of the study was to analyse the safety of RTX biosimilar in patients with MCV treated in first-line or after a shift by RTX originator.
Methods In a multicenter, prospective, open-label study, we enrolled all MCV patients treated with RTX biosimilar, both in first-line or after a shift by RTX originator. Nineteen consecutive MCV patients (F/M 13/6, mean age 68.3±11.5 months, mean disease duration 94±86 months, 10/19 HCV+ and 6/19 HBV+) were treated with RTX in a six-month period (July-December, 2018). Nine patients were treated with RTX for the first time, while the other 9 patients have been already treated with RTX originator and were switched to RTX biosimilar. Twelve patients received a dose of 250 mg/m^2 of RTX every other week, while 6 were treated with 1 gram of RTX every other week.
Results During a month-period after the last infusion, 5 adverse events (AE) were observed, namely 2 vasculitis flares, and 1 urticaria, atrial fibrillation occurred during infusion, and septicaemia, respectively.
Three of 5 AE were observed in patients treated with the higher dose of RTX (in particular both cases of vasculitis flare were recorded in patients treated with 1 gram of RTX), while no differences were observed according to the previous treatment with RTX originator (2/9 vs 3/9 AE in patients switch or naïve, respectively).
Conclusion Despite the low number of patients, the switch among RTX originator and biosimilar appear to be safe and the number of AE were in line with previous reports about RTX originator. The main limit of this study is the absence of a control group, that doesn't allow a direct comparison of the safety between RTX originator and biosimilar. Previous reports suggested that higher dosage of RTX are associated to a higher risk of side effects. Also, in our study the occurrence of AE, mainly vasculitis flare, seem to be associated to the dose of RTX, rather than to the switch to biosimilar

REFERENCES

[1] Ferri C, Cacoub P, Mazzaro C, Roccatello D, Scaini P, Sebastiani M, Tavoni A, Zignego AL, De Vita S. Treatment with rituximab in patients with mixed cryoglobulinemia syndrome: results of multicenter cohort study and review of the literature. Autoimmun Rev. 2011;11:48-55
[2] Sène D, Ghillani-Dalbin P, Amoura Z, Musset L, Cacoub P. Rituximab may form a complex with IgMkappa mixed cryoglobulin and induce severe systemic reactions in patients with hepatitis C virus-induced vasculitis. Arthritis Rheum. 2009;60:3848-55.

Disclosure of Interests None declared
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AB0625 EXPERIENCE IN THE USUAL PRACTICE OF PATIENTS WITH BEHÇET'S DISEASE WHO ARE IN FOLLOW-UP IN THE UVEITIS UNIT OF THE DONOSTIA UNIVERSITY HOSPITAL

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Background: Behçet's disease (BD) is an inflammatory, chronic, recurrent, multisystemic process of unknown origin, characterized by the simultaneous or sequential presence of oral aphthae, genital ulcers, uveitis, inflammatory skin lesions, arterial or venous thrombosis, arthritis, inflammatory bowel disease and involvement of the central nervous system (CNS). The highest incidence figures correspond to the countries of the Middle East and the Far East (prevalence's of 20-42/100,000), decreases in the Western Mediterranean (<10) and is much less frequent in the rest of the world (<2). The uveitis unit was created in our hospital in 2007, where a rheumatologist and an ophthalmologist jointly visit, so our aim is to report our experience for almost 12 years with this rare disease.
Objectives: To describe the demographic, clinical, and analytical characteristics, as well as immunosuppressive and biological treatments used, type of ocular and extra ocular involvement, presence of sequelae, and visual acuity (VA) affectation, of the patients that are in follow-up in the uveitis unit of the Donostia University Hospital (DUH).
Methods: A retrospective search of all patients with BD and ocular involvement evaluated the uveitis unit since 2007. The computerized medical records were reviewed. The variables collected were: sex, age, immunosuppressive and biological treatments used, and complementary tests. The immunosuppressant's sought were methotrexate (MTX), azathioprine (AZA), tacrolimus, sulfasalazine (SSZ), cyclosporine (CsA), leflunomide (LFN), cyclophosphamide (CFM); adalimumab (ADA); infliximab (IFX), golimumab (GLM), intravenous immunoglobulins (IVIG). The quantitative variables are shown with the median and interquartile range; the qualitative ones are shown with the absolute value and its percentage.
Results: We found 22 patients diagnosed with BD, the average age was 42 years, with a predominance of women (59%). Table 1 shows the clinical characteristics, complementary tests and treatments used in these

patients. The most frequent type of ophthalmological affectation was panuveitis with retinal vasculitis in 40%, followed by uveitis in 36%. The median VA at the first visit (RE 0.85 LE 0.85), and at the last follow-up visit (RE 1 LE 1), observing an improvement in VA after follow-up. The most common extra ocular involvement was the presence of oral aphthae in 90%, followed by erythema nodosum and arthritis in 45%. Positivity for HLA B51/B57 was observed in 81% of the patients. The most frequent immunosuppressant used was CsA 59%, followed by ADA 40%. Among the main aftermath, the presence of cataract was observed in 40% and synechia in 27%. The mean follow-up of these patients was 85 months.
Conclusion: We observed an improvement in VA during the follow-up of these patients compared to VA at the beginning; 70% of patients continued with immunosuppressive treatment with good control of the disease at more than 85 months of follow-up.
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AB0626 INCIDENCE OF SERIOUS INFECTIONS AND PATTERNS OF COTRIMOXAZOLE PROPHYLAXIS IN PATIENTSWITH ANCA-ASSOCIATED VASCULITIDES

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Background: Infections are among the most serious complications in patients with ANCA-associated vasculitides (AAV) and contribute significantly in overall mortality.
Objectives: To describe the incidence and risk factors for serious infections, as well as the patterns of cotrimoxazole prophylaxis in AAV patients (GPA and MPA).
Methods: Retrospective, descriptive study of AAV patients followed in a tertiary referral center (Clinical Immunology-Rheumatology Unit and Nephrology department). Patient and disease characteristics treatments and serious infections were recorded.
Results: 56 AAV patients were included (women: 50%, mean age at diagnosis: 59.8 years, mean disease duration: 5.1 years, GPA: 68%, generalized disease: 82%). Most frequent organ involvement was renal (71%), lung (68%), nervous (20%), skin (18%) and mucous membranes/eyes (14%). 21 serious infections were recorded in 16 patients (incidence: 7.2 per 100 patient-years), with respiratory tract infections (43%) and herpes zoster (19%) being the most frequent. Incidence was 6.2-times higher in patients with severe combined lung-kidney involvement compared to those without (20 vs 3.2 per 100 patient-years, p<0.001). Plasma exchange and/or hemodialysis (44% vs 12%, p=0.01), age >60 years (62% vs 35%) and treatment with cyclophosphamide (CYC)/rituximab (RTX) combination (38% vs 3%, p=0.001) were more common among those who developed a serious infection. Lung-kidney involvement and combined CYC/RTX treatment remained statistically significant in multivariate logistic regression analysis. Cotrimoxazole prophylaxis was given in 70% of patients treated with CYC and/or RTX (n=46). Patients with combined lung-kidney involvement were more likely to receive prophylaxis (82% vs 58%, p=0.08). No case of pneumocystis pneumonia was diagnosed during follow-up.
Conclusion: In this real-life cohort, more than one out of four AAV patients experienced a serious infection during follow-up, with pneumonia and herpes zoster being the most frequent. Patients with combined lung and kidney involvement had a ~6 times higher risk for developing a serious infections and were more likely to receive appropriate cotrimoxazole prophylaxis.
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AB0627 INTESTINAL BEHCET'S DISEASE: THE CLINICOPATHOLOGY ANALYSIS OF 38 CASES

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Background: Due to the rarity of GI involvement in BD, the diagnosis of intestinal BD relies on a combination of both vasculitis and IBD type characteristics. Histopathology play an important role in differentiation.
Objectives: To invastigate the clinic features, findings of endoscopy and histopathology of intestinal Behcet's disease.
Methods: The clinical features, findings of endoscopy and histolopathology of 38 intestinal Behcet's disease were analyzed retrospectively.
Results: The mean age of 38 cases were 44.1±15.6 years, the mean course were 64.8±90.4 months. Typical clinic manifestations and endoscopic finding existed in 24(63.2%) and 22(57.9%) patients with intestinal Behcet's disease respectively. The most common(33, 86.8%) symptoms were abdominal pain and diarrhea. The sites of intestinal ulcer were seen more often(22, 57.9%) at the ileum, ileocecal area, on the ileocecal valve. Most colonoscopic appearance of ulcers were usually well demarcated, oval or round (28, 73.6%). The suggestive histopathological changes were massive neutrophilic infiltration (20, 52.6%), inflammatory granuloma(14, 36.8%) and vasculitis(8, 21%) especially phlebitis.
Conclusion: The diagnosis of intestinal Behcet's disease depends on the combination of clinic features, endoscopic appearance and histopathological findings. massive neutrophilic infiltration, inflammatory granuloma and vasculitis point to the possibility of intestinal Behcet's disease.

REFERENCES

[1] Dong Y, Shi G. The synopsis of the 8th international meeting on BD [J]. Chin Med J, 1999, 38(2):135–136
[2] Davatchi F, Assaad Khalil S, Calamia KT, et al. The International Criteria for Behçet's Disease (ICBD) : a collaborative study of 27 countries on the sensitivity and specificity of the new criteria [J]. J Eur Acad Dermatol Venereol, 2014, 28 (3):338-347.
[3] Cheon JH, Kim ES, Shin SJ, et al. Development and validation of novel diagnostic criteria for intestinal Behçet's disease in Korean patients with ileocolonic ulcers [J]. Am J Gastroenterol, 2009, 104 (10):2492-2499.
[4] Valenti S, Gallizzi R, De Vivo D, et al. Intestinal Behçet and Crohn's disease: two sides of the same coin [J]. Pediatric Rheumatology, 2017, 15 (1):33-40.
[5] Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. N Engl J Med [J]. 1999, 341(17):1284–91.
[6] Zhuoli Zhang • Fang He • Yanjun Shi. Behcet's disease seen in China: analysis of 334 cases [J]. Rheumatol Int, 2013, 33 (3):645–648
[7] Park J, Cheon JH, Park YE, et al. Risk factors and outcomes of acute lower gastrointestinal bleeding in intestinal Behcet's disease [J]. Int J Colorectal Dis 2017, 32(5):745–51.
[8] Cheon JH, Kim WH. An update on the diagnosis, treatment, and prognosis of intestinal Behc¸ et's disease [J]. Curr Opin Rheumatol, 2015, 27(1):24–31.
[9] Lee SK, Kim BK, Kim TI, et al. Differential diagnosis of intestinal Behcet's disease and Crohn's disease by colonoscopic findings [J]. Endoscopy, 2009, 41(1):9–16.
[10] Hayasaki N, Ito M, Suzuki T, et al. Neutrophilic phlebitis is characteristic of intestinal Behcet's disease and simple ulcer syndrome [J]. Histopathology, 2004, 45(4): 377–83.
[11] Demirkesen C, Oz B, Go¨ksal S. Behcet's disease: pathology. In: Yazici Y, Yazici H, editors. Behcet's syndrome. New York: Springer; 2010. p. 215–43.

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AB0628 ANALYSIS OF CLINICAL FEATURES OF 15 CASES OF IGG4-RELATED DISEASES

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Background: IgG4-related disease is an autoimmune disease of unknown cause.

Objectives: Summarizing the clinical characteristics of IgG4-related diseases to improve the understanding of clinicians and achieve early diagnosis and reasonable treatment.
Methods: The clinical data of 15 patients with IgG4-related diseases diagnosed in our hospital from 2014 to 2018 were retrospectively analyzed.
Results: The ratio of male to female was 2:1 in 15 patients. The average age of onset was 56.8 years (34 to 84 years of age). From the first symptom to the diagnosis of 8 days to 4.75 years, the most common first symptom in 15 patients was Submandibular gland swelling, pain, anorexia, cough, the most common affected organs are the pancreas, lungs, submandibular glands. There were 11 cases of histopathological examination by surgery or needle biopsy. The histopathology showed interstitial fibrous tissue hyperplasia with more lymphocyte and plasma cell infiltration. Immunohistochemistry showed that the number of IgG4-positive cells was >50/HPF, and IgG4/IgG was >40%.Two of the 15 patients underwent surgical resection of the affected organ occupying lesions before definitive diagnosis. One patient was treated with mycophenolate mofetil and one patient was given a medium dose of hormone combined with tamoxifen. The remaining 13 patients were treated with simple hormones or combination immunosuppressive agents, including hydroxychloroquine, mycophenolate mofetil, azathioprine, and cyclophosphamide.
Conclusion: The organs involved in IgG4-related diseases are diverse, the clinical manifestations are not specific, and the hormone combined immunosuppressive therapy is effective.

REFERENCES

[1] Umehara H, Okazaki K, Masaki Y, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011[J]. Japanese Journal of Rheumatology, 2012, 22(1):21-30.
[2] Okazaki K, Kawa S, Kamisawa T, et al. Japanese clinical guidelines for autoimmune pancreatitis[J]. Pancreas, 2009, 38(8):849-866.

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AB0629 CIRCULATING ENDOTHELIAL CELLS MAY BE A MARKER FOR VASCULAR INVOLVEMENT IN BEHCET DISEASE

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Background: Circulating endothelial cells (CEC) are defined in conditions which vascular damage is seen in course of disease such as systemic vasculitis, coronary artery disease and chronic renal failure. CEC is thought to be an indicator of vascular damage (1).
Behcet disease (BD) is a systemic vasculitis mostly known with recurrent oral and genital ulceration, uveitis and mucocutaneus lesions. On the other hand vascular involvement such as deep venous thrombosis, cerebral sinus thrombosis and pulmonary artery aneurysm, is an important clinical finding of disease which may cause mortality (2).
Objectives: Our aim in this study was to analyse CEC levels in patients with Behcet disease, to compare them between patients with vascular (Group 1) and mucocutaneous (Group 2) involvement. Also we have compared the results of Behcet patients with patients with thrombosis due to other causes (Group 3) and healthy controls (Group 4). Each group involved 20 participant.
Methods: Blood samples of the patients and healthy controls are drawn into tubes containing etylene-diamine-tetra-acetic acid (EDTA). A panel of monoclonal antibodies, including anti-CD45 to exclude hematopoietic cells, anti-CD31, -CD34, -CD36, -CD105, -CD106, -CD133,and –CD 146 and appropriate analysis gates were used to enumerate resting and activated CECs and circulating and endothelial progenitor cells (CEP).
A hundred microlitre complete blood was added and incubated for 20 minutes at room temperature in the dark. After incubation for 10 minutes with erythrocyte lysing solution at room temperature, centrifugation at 1,800 rpm for 5 minutes was performed. Supernatant was removed and washed with phosphate buffer saline (PBS) for two times. Pellet was resuspended with PBS and 300.000–400.000 cells were counted with FACSCalibur flow cytometry device.
Results: Mean age, sex distribution and duration of disease were similar in all groups (Table 1).

Table 1. Demographic features of the study population

		Group				p
		Group 1	Group 2	Group 3	Group 4	
		mean ± standart deviation				
Age		43.55 ± 8.31	46.85 ± 9.43	42.50 ± 15.22	41.65 ± 6.54	0.323**
Duration of disease		14.90 ± 8.69	11.30 ± 8.80	-	-	0.109*
				n (%)		
Sex	**Female**	9 (% 45.0)	12 (% 60.0)	11 (% 55.0)	14 (% 70.0)	0.447***
	Male	11 (% 55.0)	8 (% 40.0)	9 (% 45.0)	6 (% 30.0)	

* Mann Whitney U Test
** Kruskal Wallis H Test
**** Pearson Chi Square Test

CEC levels did not show a statistically significant difference between all groups. CEPs, activated CECs (aCEC) and resting CECs (rCEC) were also compared between groups. CEPs were higher in Behcet patients with thrombosis similar to patients with thrombosis due to other causes (p:0.042). Activated CECs levels did not show a difference between groups (p>0.05).
Resting CECs are higher in Groups 1 and 3 than Groups 2 and 4. The detailed analysis of CEC, CEP, activated and resting CECs between groups is listed in Table 2.

Abstract AB0629 Table 2. Comparision of CEC, CEP, aCEC and rCECs between groups

	Group				p	Multi analysis
	Group 1	Group 2	Group 3	Group 4		
	mean ± standart deviation					
CEC	5.09 ± 4.7	2.52 ± 2.55	4.89 ± 3.83	4.09 ± 4.9	0.077**	-
CEP	13.49 ± 9.38	7.62 ± 4.02	15.6 ± 11.21	13.71 ± 10.1	0.042**	1-2: 0.015 2-3: 0.009
aCEC	4.39 ± 5.78	2.24 ± 2.14	8.17 ± 13.26	8.78 ± 13.21	0.054**	-
rCEC	6.44 ± 5.4	5.43 ± 3.49	9.03 ± 7.79	3.52 ± 2.34	0.007**	1-4: 0.034 3-4: <0.001

Conclusion: Increased levels of aCECs may be an indicator of active vascular involvement in BD. But in the current study aCEC levels did not show a difference between groups but none of the patients had active vascular involvement which may cause of this sameness. CEP and resting CEC levels were elevated in both groups of patients with thrombosis. So CEC may be a marker for vascular damage but it is not specific for BD.

REFERENCES

[1] Woywodt A Circulating endothelial cells in vasculitis and transplantation. Pathophysiol Haemost Thromb. 2003;33:500-2
[2] Kutlay S, Calayoglu R, Boyvat A, Turkcapar N, Sengul S, Keven K, Nergizoglu G. Circulating endothelial cells: a disease activity marker in Behçet's vasculitis. Rheumatol Int 2008;29:159-162

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AB0630 CLINICAL CHARACTERISTICS ANALYSIS AND LITERATURE REVIEW OF 55 CASES OF PANNICULITIS

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Background: Panniculitis is a heterogeneous inflammatory disease involving subcutaneous fat. It can be divided into different subtypes according to the clinical characteristics and pathological changes of the disease. Because the cause of panniculitis is unclear, clinical manifestations are diverse, lack of specificity, early diagnosis is difficult, and misdiagnosis and missed diagnosis are prone to occur.
Objectives: To improve the clinical understanding of the disease by retrospective analysis of 55 cases of patients with panniculitis.
Methods: The hospitalized patients with panniculitis were collected from December2011 to October 2018 in the Shanxi Dayi Hospital Affiliated to Shanxi Medical University. The demographics, clinical manifestations, auxiliary examinations and treatments were analyzed and summarized.
Results: The proportion of males and females in the 55 patients was 1:2.23, with an average of 53.3 years (18-82 years). A total of 52 cases

of nodular panniculitis (including 14 cases of mesenteric involvement) and 3 cases of special type of panniculitis were collected. Patients with nodular panniculitis often find subcutaneous nodules or masses. According to the affected parts, they are divided into skin type and system type. Among them, 10 cases are skin type and 42 cases are system type. The most common parts is mesenteric and kidney involvement. 9 of 55 patients was combined with tumor. Patients with mesenteric panniculitis mainly present abdominal pain and bloating, which are mainly diagnosed according to CT. Patients with systemic panniculitis can be significantly relieved after treatment with hormones and immunosuppressive agents.

Conclusion: Panniculitis is an inflammatory disease of unknown etiology. It is common in middle-aged and elderly people. It has various clinical manifestations and lacks specificity. The diagnosis is mainly based on pathological results. It is easy to be combined with tumors. When subcutaneous nodules are found, pathological examination should be improved in time in order to avoid misdiagnosis.

REFERENCES

[1] Daskalogiannaki M1, Voloudaki A, Prassopoulos P, et al.CT evaluation of mesenteric panniculitis: prevalence and associated diseases[J].AJR Am J Roentgenol. 2000 Feb;174(2):427-31.doi:10.2214/ajr.174.2.1740427.

[2] Chinese Medical Association Rheumatology Branch. Guidelines for the diagnosis and treatment of nodular panniculitis (draft). Chinese Journal of Rheumatology, 2004, 8 (4): 253-255. Doi:10.3760/j:issn:1007-7480.2004.04.017.

[3] Hongyan Liu, Juan Meng, Yuewu LIu, et al. Report of seven cases of lipitis in the pancreatitis and literature review [J]. Chinese Journal of Rheumatology, 2018, 22 (9): 627-630, after insertion 3.doi: 10.3760/cma. j.issn.1007-7480.2018.09.010.

[4] Litong Wang, Yujian Cai. Multi-slice spiral CT imaging features of mesenteric panniculitis[J].Chinese Journal of Digestive Surgery,2017,16(6):624-628.doi:10.3760/cma.j.issn.1673-9752.2017. 06.018.

[5] Gaobiao Zhou, ZhiyongYao, Bin Sun, et al.A case report of nodular panniculitis with lung and kidney damage as the first manifestation[J].Chinese Journal of Urology,2007,28(4):283.doi: 10.3760/j:issn:1000-6702.2007.04.028.

[6] Moraes AJ, Soares PM, Zapata AL, et al.Panniculitis in childhood and adolescence[J].Pediatr Int. 2006 Feb;48(1):48-53. doi:10.1111/j.1442-200X.2006.02169.x

[7] Jinfang Gao, Zhang Liyun Zhang, Xiaofeng Li, et al. Clinical characteristics and prognosis of 25 cases of nodular panniculitis[J].Chinese Remedies & Clinics, 2013,13(8):1093—1095. DOI: 10.11655/zgywylc2013.08.060.

[8] López-Lerma I, Peñate Y, Gallardo F, et al.Subcutaneous panniculitis-like T-cell lymphoma: Clinical features, therapeutic approach, and outcome in a case series of 16 patients[J].J Am Acad Dermatol. 2018 Nov;79(5):892-898. doi: 10.1016/j.jaad.2018.05.1243.

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AB0631 INTERSTITIAL LUNG DISEASE – A RARE MANIFESTATION OF MICROSCOPIC POLYANGIITIS

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Background: Interstitial lung diseases (ILD) are a group of diffuse inflammatory and/or fibrotic lung disorders with similar clinical, radiologic and histopathologic features. The coexistence of ILD and ANCA-associated vasculitis has been reported in case reports and small case series.

Objectives: The aim of this study was to assess the prevalence, clinical and radiological characteristics of ILD in MPA patients admitted to the Rheumatology Department of our hospital.

Methods: This retrospective single center cohort study included 102 patients diagnosed with MPA according to CHCC 2012 and EMA algorithm. We assessed Birmingham Vasculitis Activity Score (BVAS) at disease onset and VDI (Vasculitis Damage Index) at the end of the follow up in each patient. ANCA type and titer were assessed by enzyme-linked immunosorbent assay (ELISA). The results of repeated high resolution computed tomography (HRCT) of the chest were analyzed and interstitial changes (focal ground-glass opacity, reticular changes, honeycombing, traction bronchiectasis) were classified in four patterns: non-specific interstitial pneumonia (NSIP), typical interstitial pneumonia, possible interstitial pneumonia, and "inconsistent" usual interstitial pneumonia (UIP).

Results: ILD-features on HRCT was found in 11 (11.8%) of 102 patients with MPA. Their median age was 55 [53; 63] years. All of them were ANCA-positive (Table 1). In 5 cases interstitial pneumonia was the first and the sole manifestation that preceded for the occurrence of overt systemic vasculitis for a median of 3 years. The radiologic patterns included non-specific interstitial pneumonia in 5 cases, usual interstitial pneumonia in 3 cases and unclassifiable interstitial pneumonia in 3 cases. The most common clinical manifestations were non-productive cough (82%), progressive dyspnea (82%) and crepitation (27%). The most common extrathoracic manifestations of MPA in patients with ILD were glomerulonephritis with decreased renal function (91%), fever (100%) and arthritis (91%). All patients received induction therapy with glucocorticosteroids combined with cyclophosphamide, rituximab, azathioprine or methotrexate.

Abstract AB0631 Table 1.. Characteristics of patients with MPA and ILD

	n = 11
Male gender, n (%)	7 (64)
Age of the onset of ILD, Me, IQR, years	55 [53; 63]
Age of the onset of MPA, Me, IQR, years	59 [54; 65]
ILD onset	
Before systemic manifestations of MPA, n (%)	5 (45)
At MPA onset, n (%)	6 (55)
ANCA specificity	
MPO-ANCA, n (%)	6 (55)
PR3-ANCA, n (%)	2 (18)
unidentified ANCA, n (%)	3 (27)
Clinical symptoms	
Fatigue, n (%)	11 (100)
Fever, n (%)	11 (100)
Weight loss, n (%)	4 (36)
Arthralgia, n (%)	10 (91)
Skin vasculitis, n (%)	5 (45)
Renal manifestations, n (%)	10 (91)
Ear, nose and throat involvement, n (%)	4 (36)
Chronic cough, n (%)	9 (82)
Hemoptysis, n (%)	2 (18)
Dyspnea, n (%)	9 (82)
Crackles, n (%)	3 (27)
Laboratory and instrumental findings	
Increasing of ESR and/or CRP, n (%)	10 (91)
Anemia, n (%)	7 (64)
24-hours proteinuria, g/day	0.61 [0.25; 1.95]
Estimated GFR, ml/min/1.73 m^2	39 [19; 60]
Radiological patterns	
UIP, n (%)	3 (27)
NSIP, n (%)	5 (45)
Unclassified IP, n (%)	3 (27)
Mediastinal lymphadenopathy, n (%)	3 (27)
Emphysema, n (%)	2 (18)
Remission induction therapy	
Glucocorticosteroids, n (%)	11 (100)
Cyclophosphamide, n (%)	7 (64)
Rituximab, n (%)	1 (9)
Azathioprine, n (%)	1 (9)
Methotrexate, n (%)	1 (9)

Conclusion: ILD is a rare manifestation of MPA, which can precede systemic manifestations. ANCA-associated vasculitis should be included in the spectrum of differential diagnosis in patients with ILD.

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AB0632 MAINTENANCE RITUXIMAB IN ANCA ASSOCIATED VASCULITIS – OBSERVATIONAL DATA FROM UNIVERSITY HOSPITAL COVENTRY, UK

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Background: Rituximab is considered an effective[1] maintenance therapy in anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV), with reduced relapse rates post induction therapy and comparable adverse event profile to other agents such as Azathioprine[2].

Objectives: To describe the clinical outcomes of all patients receiving maintenance Rituximab for AAV in University Hospital Coventry in UK.

Methods: Records from the Renal and Rheumatology units were used to identify patients receiving maintenance Rituximab. Electronic patient records (EPR) were used to collate laboratory and clinical data.

Results: We identified 38 patients, with the diagnosis of AAV made 11 months to 19 years previously. 16 (42%) had been diagnosed within the last five years. Age range was 19-87 years old with roughly half (21; 54%) being male. Maintenance Rituximab was started between January 2010 and September 2018. Most patients received a fixed 6 monthly protocol. Seven patients (18%) died within the observation period. More details in table 1 below.

Table 1. Results

Total number (n) patients = 38	n (%)
Serology	32 (84.2%)
ANCA positive	21 (55.3%)
PR3 positive	9 (23.7%)
MPO positive	
Previous cyclophosphamide (2/38 unknown)	20/36 (55.6%)
Indication for starting Rituximab	9 (23.7%)
Failure of cyclophosphamide	20 (52.6%)
Flare/worsening disease despite disease-modifying therapy	3 (7.9%)
Intolerant of other disease-modifying therapies	3 (7.9%)
Young patient of child-bearing potential	2 (5.3%)
Patient preference	1 (2.6%)
Not documented	
Concurrent medication	12 (31.6%)
Azathioprine	11 (26.3%)
Mycophenolate mofetil	3 (7.9%)
Methotrexate	1 (2.6%)
Hydroxychloroquine	1 (2.6%)
Tacrolimus†	12 (31.6%)
Prednisolone monotherapy	1 (2.6%)
Nil	
Cotrimoxazole	20 (52.6%)
Prescribed	2/20 (10%)
Intolerant	
Infections	18 (47.4%)
Documented in clinic letters	13 (34.2%)
Any infection	10 (26.3%)
Respiratory tract infection	
Requiring admission	
Immunoglobulins post-Rituximab	4 (10.5%)
Hypogammaglobulinaemia	1/4 (25%)
Of which treated with IV immunoglobulins	3 (7.9%)
Low IgG and IgM	17 (44.7%)
Isolated low IgM	3 (7.9%)
Not tested	
Clinical response to Rituximab	31 (81.6%)
Full	2 (5.3%)
Partial; requiring addition of further disease-modifying therapy	2 (5.3%)
Mild disease progression	3 (7.9%)
Flare within first 2 years of treatment‡	
First 2 years of Rituximab treatment	11 (28.9%)
Ongoing	24 (63.2%)
Completed	3 (7.9%)
Not completed	1 (2.6%)
Discontinued due to infections	2 (5.3%)
Patient died	
Subsequent treatment^{Y} (n=24)	6/24 (25.0%)
Rituximab continued as primary therapy	6/24 (25.0%)
Regular Rituximab restarted following flare	1/24 (4.2%)
Mycophenolate mofetil	4/24 (16.7%)
Azathioprine	2/24 (8.3%) 5/38 (13.2%)
Prednisolone monotherapy Patient died	

† Renal transplant patient ‡ In 2/3 (67%) patients associated with poor compliance/missed doses

Y In patients who completed 2 years maintenance Rituximab

Conclusion: The effectiveness of Rituximab as a maintenance therapy in AAV is borne out by this real world data, with 31/38 patients demonstrating full clinical response. Longer term treatment and low grade disease continue to be issues as evidence for optimal management strategies is lacking. Infections, including severe infections necessitating admission, were common. PR3 positive patients are over-represented, in keeping with the known higher rate of relapse.

REFERENCES

[1] Smith, Rona M., et al. "Rituximab for remission maintenance in relapsing antineutrophil cytoplasmic antibody–associated vasculitis." Arthritis & Rheumatism 64.11 (2012): 3760-3769.

[2] Guillevin, Loïc, et al. "Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis." New England Journal of Medicine 371.19 (2014): 1771-1780.

I confirm that the abstract fulfils the requirements for a late breaking submission and that the research results were not available at the time of the original deadline (31 January 2019)

Yes

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AB0632B TB OR NOT TB, THAT IS THE VASCULITIC QUESTION

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Background: It is important to remember that there are many disorders that can mimic the clinical, radiographic and histological features of vasculitis. Tuberculosis (TB) is often referred to as the great imitator and therefore, needs to be considered early in the differential diagnosis of vasculitis.

Objectives: To emphasize the importance of being aware of noninflammatory mimics of vasculitis to be able to avoid unnecessary and potentially harmful immunosuppression.

Methods: We report a challenging case of a patient presenting with an inflammatory subglottic lesion.

Results: A 81-year-old lady initially presented to otorhinolaryngology (ENT) with hoarseness and and restriction of breathing. Nasendoscopy revealed a subglottic lesion with oedema and inflammation. Biopsy showed florid necrotising granulomatous inflammation. Upon questioning, patient revealed one year history of epistaxis and nasal crusting requiring regular nasal douching. She also reported lack of energy, loss of appetite, but denied any rash, weight loss or night sweats. She suffered with a severely dry mouth that was causing difficulty swallowing. She also complained of an occasional cough with small amount of phlegm which she attribute to the difficulty with swallowing. Rheumatology team felt that this could be a possible localised Granulomatosis with polyangiitis and requested ANCA and a vasculitis screen.

Interestingly, the patient's chest x-ray showed apical scarring, consistent with healed mycobacterial disease. A CT neck/thorax and abdomen was done which showed diffuse mucosal thickening of the subglottis and reticulonodular changes in the lungs. She was also noted to have deranged liver function test around this time. Gastroenterology advised that there was no clear cause for the transaminitis and an autoimmune screen was requested. Given the chest findings on CT, a sputum sample was sent for microscopy and culture. The patient had been started on dexamethasone on admission by ENT and reported substantial improvement in the hoarseness of voice and shortness of breath. ANCA then came back negative, as did the connective tissue screen. While the rheumatology team was considering how to further manage the possible vasculitis, the sputum smear came back positive for acid fast bacilli and the diagnosis was clinched: our patient was suffering with the extremely rare laryngeal tuberculosis, along with pulmonary TB. She was started on anti-tuberculous medication that have been introduced incrementally given the deranged liver function tests. The patient was doing well on her most recent follow up in the respiratory department.

Conclusion: Greater awareness of vasculitis mimics like TB and a high index of suspicion are needed when assessing a patient presenting with the protean manifestations of suspected vasculitis. It is therefore prudent to include TB in the differentials, whenever consider vasculitis.

REFERENCES

[1] Naeem Ullah Khan Seb Wallis and Naeem Siddiqui. Laryngeal tuberculosis: a diagnosis not to be missed BMJ Case Rep. 2009; 2009: bcr11.2008.1228.

[2] Jain A, Misra DP, Ramesh A, Basu D, Jain VK, Negi VS. Tuberculosis mimicking primary systemic vasculitis: not to be missed! Trop Doct. 2017 Apr;47(2):158-164.

[3] Suresh E. Diagnostic approach to patients with suspected vasculitis. Postgrad Med J. 2006 Aug; 82(970): 483–488.

[4] Khasnis A; Molloy E. Mimics of primary systemic vasculitides. International Journal of Clinical Rheumatology. 4(5):597–609, OCT 2009



Abstract AB0632B Figure 1:. View of the larynx on endoscopy showing the suspicious nodules of granulomatous inflammation

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Scleroderma, myositis and related syndromes

AB0633 FECAL CALPROTECTIN IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a connective tissue disease with heterogeneous symptoms and a non-predictable process. The most involved organ after the skin is the gastrointestinal tract (GI tract) and any part of it can be affected. The calprotectin level is increased in plasma, urine, sputum and feces when an inflammatory process is occurring with the presence of neutrophils which is measurable.
Objectives: So we decided to examine fecal calprotectin as a simple method to diagnose GI disorders and disease activity in SSc.
Methods: Totally 46 patients with SSc were invited by telephone, who have been referred to sayyad shirazi Hospital and the rheumatologists' offices in Gorgan and their information has been registered there. Seven patients did not enter our study because of having the items in exclusion criteria like Diabetes, a history of GI operation and having other connective tissue diseases at the same time.for the other 39 patients who was remained, a questionnaire about GI symptoms (UCLA SCTS 2.0) was filled in and then their skin was examined and the skin score was determined (the score more than 14 was considered as positive). Blood sample was taken from all patients to do tests as ESR,CRP, Magnesium, Albumin, Ferritin, Folic Acid, Vitamin B12 and Zinc and use them as a scale for malnutrition. Then the stool samples were collected to measure the calprotectin level. At last to determine GI disorders in a non-aggressive way, Barium Swallow (Esophagus malfunction) and CT Enterography (intestinal disorders) was done. The patients in our study according to the median of age which was 42, was divided in to two groups: young and middle aged. Due to the fact that FC level wasn't less than 50µgr/gr in any of our cases, the patients was divided in to two groups: the one with FC level less than 200 µgr/gr and the one with FC level as 200 µgr/gr or more than 200 µgr/gr and the latter was considered as positive.
Results: As we didn't have any male patients, the correlation between FC level and sex was not verifiable. Increased levels of FC didn't have any correlation with age (P Value=0.79), disease type (P Value=0.59), small intestine wall thickening (P Value=0.10), esophageal dilatation (P Value=0.18), skin score (P Value=0.25), final GI score (P Value=0.30) and none of serum tests. One of the most important reasons, was low sample size.In our study just 5 cases had evidence of wall thickening in CT Enterography and all that 5 cases had increased levels of calprotectin so we see that if we have a lrager sample size we may ensure the connection between these two variables. Also as most of our patients take vitamin and mineral supplements, we couldn't find any signs of micronutrient deficiencies and any correlation with FC level as well.
Conclusion: Although there was no statistical correlation between FC level and variables, the results are in favor of FC's specificity for assessing intestinal wall thickening.

REFERENCES

[1] -Marie I, Leroi AM, Menard JF, Levesque H, Quillard M, Ducrotte P. Fecal calprotectin in systemic sclerosis and review of the literature. Autoimmunity reviews. 2015;14(6):547-54.
[2] - Andreasson K, Scheja A, Saxne T, Ohlsson B, Hesselstrand R. Faecal calprotectin: a biomarker of gastrointestinal disease in systemic sclerosis. J Intern Med. 2011;270(1):50-7.
[3] - Affandi AJ, Radstake TR, Marut W. Update on biomarkers in systemic sclerosis: tools for diagnosis and treatment. Seminars in immunopathology. 2015;37(5):475-87.

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AB0634 FINDINGS OF EXERCISE ULTRASOUND CARDIOGRAPHY IN PRE-PAH PATIENTS WITH SYSTEMIC SCLEROSISARE CORRELATED WITH EXTENT OF CAPILLARY LOSS DETECTED BY NAILFOLD VIDEOCAPILLAROSCOPY

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Background: Systemic sclerosis (SSc) is characterized by excessive fibrosis, injuries in vasculature, and production of autoantibodies (1). Patients with SSc are complicated with various organ involvements, which can give a great impact on their prognosis (2). Of these, pulmonary arterial hypertension (PAH) is one of leading causes of death and the determinant of prognosis in SSc (3). And early diagnosis is an important key to improve their prognosis. The nailfold videocapillaroscopy (NVC) is a non-invasive modality which can evaluate the status of microvasculature of patients with SSc. However, the significance of NVC in patients with "pre-clinical" PAH was unclear.
Objectives: To examine the significance of detection of microvascular injury by NVC in patients with pre-clinical PAH patients with SSc.
Methods: Patients with SSc who newly visited the outpatient clinic at Fujita Health University Hospital between August 2015 to March 2016 were consecutively involved. All the patients fulfilled the 1980 preliminary classification criteria for SSc (4). The diagnosis of PAH was based on the definition in 2015 ESC/ERS guideline. The NVC (Medcap®3.0, DS MEDICA) was used to detect microvascular change and average capillary density and the number of capillaries/view were calculated. Also, existence of giant capillaries, hemorrhage and patterns of capillary changes were also documented. Transthoracic ultrasound cardiography (UCG) was performed using iE33 with 5MHz sector probe S5-1 (Philips). Exercise loading was done with an ergometer (Lode). Ejection fraction, E/e', velocity of tricuspid regurgitation jet (TR jet), tricuspid annular plane systolic excursion (TAPSE) were examined in a supine position. Tricuspid regurgitation pressure gradient (TRPG) was calculated using velocity of TR jet based on Bernoulli principle. Exercise loading was started at 25 Watt, and then increased 25 Watt every 3 minutes and TRPG at maximum exercise was also calculated. Parameters of NVC were compared with those of UCG. Patients with "pre-clinical" PAH were defined as patients 1) asymptomatic, 2) who did not meet the definition of PH by right heart catheterization (RHC), 3) whose probability of PH is lower than "intermediate" by UCG, 4) who did not see any UCG signs for PH based on the guideline and 5) who did not have severe interstitial lung disease, especially% FVC> 70% and/or area of ILD based on CT scan was <20% of the entire lung field.
Results: Nineteen patients with SSc were newly visited. Male to female ratio was 4:15, mean age 63 ± 13 years, and mean disease duration was 138 ± 109 months. Ratio of limited skin type was 79%. 37% were with ILD and 11% were with PAH confirmed by RHC. There is no correlation between TRPG at rest and the density of capillaries. However, there is a significant, negative correlation between TRPG at exercise and the capillary density ($r = 0.57$, $P < 0.02$). Furthermore, the same result was observed even with seventeen "pre-PAH" cases ($r = 0.67$, $P < 0.04$).

Conclusion: Our study suggests that the finding of NVC, especially the extent of capillary loss, is correlated with disease process of PAH, even subclinically, and may predict the progression to PAH in SSc. Since NVC is non-invasive, NVC can detect earlier PAH candidates and contribute to the improvement of prognosis.

REFERENCES

[1] Denton CP, et al. Trends Immunol 2005; 26: 596.
[2] Steen VD, et al. Ann Rheum Dis 2007; 66: 940.
[3] Avouac J, et al. J Rheumatol 2010; 37: 2290.
[4] The Subcommittee for Scleroderma Criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee. Arthritis Rheum 1980; 23: 581.

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AB0635 POTENTIAL BIOMARKERS OF SKIN CHANGES IN SYSTEMIC SCLEROSIS

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Background: Skin fibrosis is a hallmark of systemic sclerosis (SSc). There are no widely accepted biomarkers of skin involvement in this condition. Several serum or plasma markers have been studied in patients with SSc - monocyte chemoattractant protein-1 (MCP-1), chemokine (C-X-C motif) ligand 8 (CXCL8), interleukin-13 (IL-13), and some more recognized such as - platelet derived growth factor (PDGF), transforming growth factor-beta 1 (TGF-beta 1), epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF).
Objectives: The aim of this study was to assess several circulating biomarkers which may be relevant to the fibrosing process and further to correlate the obtained data with clinical indicators specific for SSc skin involvement.
Methods: 59 SSc patients (M/F 9/50; mean age 52.1 years, mean disease duration 6.7 years, 36 patients with limited cutaneous SSc and 23 with diffuse cutaneous SSc. As a control group 36 healthy individuals matched to sex and age were examined. Serum concentrations of bFGF, granulocyte-colony stimulating factor (G-CSF), granulocyte-macrophage-colony stimulating factor (GM-CSF), MCP-1, PDGF, IL-8 and 13 were analysed using commercial multiplex kit. The following clinical examinations were performed: modified Rodnan skin score (mRSS), Hand Mobility in Scleroderma Test (assessing hand function) (HAMIS), Cochin Hand Function Scale (hand function) (CHFS), Delta Finger-to-Palm Distance (extension-flexion) (dFTP), Inter-lip Distance (inter-lip), Inter-incisor Distance (inter-incisor), and Mouth Handicap in Systemic Sclerosis Scale (mouth opening) (MHISS). For statistical evaluation Spearman's correlation coefficient was used.
Results: When compared with healthy controls serum concentrations of bFGF ($p<0.001$), G-CSF ($p<0.0001$), GM-CSF ($p<0.0001$), MCP-1 ($p<0.0001$) IL-8 ($p<0.0001$), and IL-13 ($p<0.001$) were significantly elevated in SSc cohort. PDGF levels were increased in SSc patients with only a lower significance ($p<0.01$). bFGF, G-CSF, MCP-1 and IL-8 levels correlated significantly ($p<0.05$) with mRSS and HAMIS. GM-CSF levels correlated with mRSS and HAMIS and there was only a trend for negative correlation with inter-incisor. The was no correlation of IL-13 and PDGF levels with the evaluated clinical data.
Conclusion: Our results have shown that G-CSF, GM-CSF and IL-8 play a substantial role in SSc fibrosing process. Potential biomarkers as bFGF, G-CSF, MCP-1 and IL-8 correlated with a few clinical indices of SSc skin involvement.

REFERENCES

[1] Carulli MT, Handler C, Coghlan JG, Black CM, Denton CP. Can CCL2 serum levels be used in risk stratification or to monitor treatment response in systemic sclerosis? Ann Rheum Dis 2008;67:105-9.
[2] Chujo S, Shirasaki F, Kondo-Miyazaki M, Ikawa Y, Takehara K. Role of connective tissue growth factor and its interaction with basic fibroblast growth factor and macrophage chemoattractant protein-1 in skin fibrosis. J Cell Physiol 2009;220:189-95.
[3] Fuschiotti P, Larregina AT, Ho J, Feghali-Bostwick C, Medsger TA Jr. Interleukin-13-producing CD8+ T cells mediate dermal fibrosis in patients with systemic sclerosis. Arthritis Rheum 2013;65:236-46.
[4] Hasegawa M, Fujimoto M, Matsushita T, et al. Serum chemokine and cytokine levels as indicators of disease activity in patients with systemic sclerosis. Clin Rheumatol 2011;30:231-7.

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AB0636 INFLUENCE OF CARDIOVASCULAR RISK FACTORS ON NAILFOLD VIDEOCAPILLAROSCOPY IN THE STUDY OF CONNECTIVE TISSUE DISEASES

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Background: Nailfold videocapillaroscopy is a non-invasive technique used to assess Raynaud syndrome. It is mainly used for the early diagnosis of connective tissue disorders (CTD) such as systemic sclerosis. There is some evidence that capillaroscopy findings may be altered by microcirculation abnormalities in patients with cardiovascular risk factors (CVRF).
Objectives: to analyze the influence of cardiovascular risk factors on naildfold capillaroscopy in patients with Raynaud or suspect of CTD.
Methods: An observational and descriptive study of consecutive patients that underwent a videocapillaroscopy examination for the study of Raynaud syndrome was conducted. A "Capiscope" model videocapilaroscope from Optilia was used, with a fixed magnification of 200x. Examination was made on 8 hand fingers, with 2 images per finger. The patients had to be at least 30 minutes in a fixed warm temperature room and without smoking 1 hour before the performance of the test. The following capillaroscopic parameters were considered: nailfold morphology, capillary loop enlargements, megacapillaries, microhaemorrhages, avascular areas and signs of neoangiogenesis. Demographic information (including age, gender and previous diagnosis) and cardiovascular risk factors (including arterial hypertension (HT), diabetes mellitus (DM), dyslipidemia (DL) and smoking habit), were collected. The influence of cardiovascular risk factors on naildfold capillaroscopy was analyzed, using univariate and multivariate logistic regression models, adjusted for possible confounders.
Results: Out of the 136 included patients, 91% were women. Mean age was 54,6 ± 18,7 years. Raynaud syndrome was reported in 83% patients, with a mean duration of 6,1 ± 5,7 years and 12% of the patients had a previous diagnosis of CTD, including systemic lupus erythematosus (5%), systemic sclerosis (4%), undifferentiated connective tissue disorder (2%) and mixed connective tissue disease (1%). Regarding CVRF, HT was observed in 25%, DM in 7%, DL in 23% and past or current smoking habit in 32%. Capillaroscopic findings were: loop enlargements (81%), megacapillaries (30%), microhaemorrhages (46%), signs of neoangiogenesis (71%) and avascular areas (20%).
Regarding the capillaroscopic pattern, 46% presented a normal or non-specific pattern; 31% a microangiopathy pattern and 23% a scleroderma pattern (of which 58% had an early or active scleroderma pattern and 42% a late scleroderma pattern). A new diagnosis of CTD was made in 24 patients (18% of the cohort). In the group of patients without CTD, HT was associated with microhaemorrhages ($p = 0.02$) and avascular

areas (p = 0.007), and there was a tendency to association between smoking habit and megacapillaries (p = 0.08). After adjusting for confounding factors for this group, an association between CTD and microhaemorrhages (OR = 1.9; p = 0.01) and avascular areas (OR = 2.12; p = 0.007) was found. The multivariate study showed no relationship between CVRF and capillaroscopy patterns.

Conclusion: In our cohort we found an increased frequency of microhaemorrhages and avascular areas in the naildfold capillaroscopy in patients with arterial hypertension. The presence of cardiovascular risk factors could have an influence on the microvasculature and therefore on the findings of the capillaroscopy. More studies are required to better assess these findings.

REFERENCES

[1] Cutolo, et al., Best Pract Res Clin Rheumatol.2013;27:237-248.

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AB0637 IS VERY EARLY SYSTEMIC SCLEROSIS (SSC) A COMBINATION OF MILD AND EARLY DISEASE?

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Background: SSc has a high morbidity and mortality, therefore it is important to detect the disease at an early stage. Very early detection of SSc allows early management, which has been shown to profoundly impact on the disease course in different inflammatory rheumatic diseases. However, patients fulfilling criteria for the diagnosis of very early SSc could also be patients with a very mild, very slowly progressing, long-standing disease.

Objectives: To identify a subgroup of patients with long-standing, very mild SSc among the patients fulfilling the criteria for the very early diagnosis of SSc by analyzing clinical, epidemiological and immunological characteristics of the Zurich patient cohort.

Methods: Baseline data of the SSc patients from the University Hospital of Zurich cohort are analyzed in this study. Demographic and disease characteristics of the patients enrolled between January 2009 and June 2018 into the Very Early Diagnosis of Systemic Sclerosis (VEDOSS) cohort were analyzed. Patients fulfilling the ACR/EULAR2013 criteria and patients with primary Raynaud phenomenon were excluded. Disease duration was calculated as the difference between the baseline visit date and the date of the first Raynaud's phenomenon (RP) symptom reported by the patient. For further analysis, the cohort was divided into two subgroups using a cut off value of </≥5 years disease duration. Data were expressed as absolute and relative frequencies (n/total valid cases (%)) and percentages for categorical variables or as means ± SD and medians ± interquartile range for continuous variables.

Results: A total of 107 patients met the inclusion criteria. The patients' demographic and disease characteristics are shown in Table 1 and Table 2. The majority of patients had a short disease duration measured from first Raynaud attack of < 5 years. However, 43/107 patients (40.2%) had a long-standing disease with long-standing Raynaud`s (Figure 1). Further analysis of the clinical characteristics of early patients with </≥5years disease duration showed no significant differences in demographics and disease manifestations between the subgroups.

Abstract AB0637 Table 1. Description of the study cohorts at baseline (total N=107)

Age (years)	53 (43,64)	***Musculoskeletal***	
Female	96 (89.7)	Synovitis	13/103 (12.6)
Disease duration RP (years)*	4 (1, 10.25)	Tendon friction rubs	1/103 (0.9)
Disease duration NRP (years)*	4 (1.75, 7)	Muscle weakness	4/17 (23.5)
Raynaud's Phenomenon	100/107 (93.5)	***Cardiopulmonary***	
Puffy fingers (ever)	19/101 (18.8)	Dyspnea (NYHA) Stage I/II	88/88 (100)
Digital ulcers (ever)	2/80 (2.5)	Dyspnea (NYHA) Stage III/IV	0/88
Modified Rodnan skin score	0	Lung fibrosis on HRCT	4/80 (5.0)
Laboratory markers		Forced vital capacity<80%	8/97 (8.2)
ANA	99/103 (96.1)	Total lung capacity<80%	2/15 (13.3)
ACA	49/103 (47.6)	DLCO<70%	8/97 (8.2)
Anti-Scl70	1/103 (47.6)	PAH by right heart catheterization	0/0
Anti-U1RNP	3/92 (3.2)	***Gastrointestinal* symptoms**	36/103 (35.0)
Anti-RNA polymerase III	5/96 (5.2)	Immunosuppressive treatment	2/107 (1.9)
Creatine kinase elevation	12/103 (11.7)	Abnormal nailfold capillaroscopy	62/80 (77.5)
C reactive protein elevation	7/101 (6.9	Telangiectasia	14/86 (16.3)

ACA, ANA, Anti-Scl70, U1-RNP- anticentromere, antinuclear, anti-topoisomerase I, anti-U1 ribonucleoprotein antibodies, respectively. DLCO, diffusing capacity of the lung for carbon monoxide; PAH, pulmonary arterial hypertension.

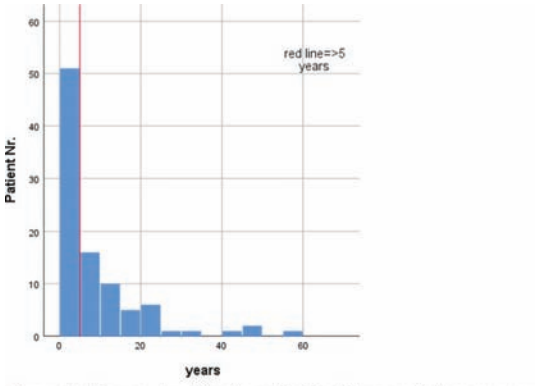


Figure 1. Disease duration from the first Raynaud phenomenon

Conclusion: This analysis is showing that patients fulfilling VEDOSS criteria include a subgroup of patients with very mild, long-standing disease. This observation has major impact on the management of VEDOSS patients, as this subgroup requires different follow up and treatment strategies compared to VEDOSS patients with early, progressive disease.

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AB0638 **ABSENCE OF LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS WITH SILICONE IMPLANTS**

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Background: Although many cases have been reported for the last 3 decades, the correlation between silicone breast implants (SBI) and systemic sclerosis (SSc) is yet unclear.
Objectives: To assess the prevalence of breast implants in a well characterized SSc cohort followed at a dedicated tertiary center and to define charcteristics that might differ between SSc patients with implants and those without.
Methods: A prospectively maintained database was interrogated regarding the prevalence of breast implants and the disease characteristics. Female patients aged 20 to 55y (215 patients) followed at our center between 2003-2018 were included. SBI cases were identified and their characteristics tabulated. Each SBI patient was matched with 2 controls matched for age, disease duration and type of disease. We used descriptive statistics, multivariate comparisons and multivariate analysis for correlations.
Results: 11 pts with SBI were found, 6 with diffuse (median age 37.5, range 32-55, median disease duration 3.5 y, range 1.5-8y, median mRSS 13.5, range 8-26) and 5 with limited SSC (median age 38,range 33-45, median disease duration 8y, range 3-22y, mRSS 2, range 2-5). The prevalence of SBI in the 20 to 55 y cohort is 5%, similar to the estimated prevalence in the general population. All had their implants instilled before the diagnosis of SSC (median 10y, range 4-13y). Four pts were first diagnosed with SSC within a year from diagnosis of silicon leakage. RNA polymerase 3 was positive in 3 patients, Scl70 in 3 others, anticentromere in 1 patient and 4 others were positive only for antinuclear antibody. There were no differences in the prevalence of digital ulcers, gastrointestinal involvement, skin score or the serologic profiles between the two groups. However, none of the SBI pts developed interstitial lung involvement, compared to 72% of the matched diffuse patients (p=0.001). There were neither renal crises in the SBI group (compared to 5 cases in the matched group) nor cardiac involvement.
Conclusion: The temporal relation and the different clinical features might generate a theory that silicone might induce a particular type of SSC, as the idea that silicone protects against lung involvement seems unreasonable. We plan a further prospective study.
Disclosure of Interests: None declared
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AB0639 **PREDICTION OF MAJOR VASCULAR COMPLICATIONSIN SYSTEMIC SCLEROSIS (SSC)**

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Background: in SSc, Digital ulcers (DU), scleroderma renal crisis (SRC) and pulmonary arterial hypertension (PAH) are major vascular complications (MVCs). Among the variables used to follow-up SSc patients, nailfold videocapillaroscopy pattern (NVCp), estimated pulmonary systolic arterial pressure (sPAP), diffusion capacity of carbon oxyde (DLco) and renal resistive index (RRI) on renal vascular Doppler ultrasound have previously shown to be predictive for MVCs development. Moreover, circulating endothelin-1 (ET1) levels have been associated with MVCs.
Objectives: to identify clinical, instrumental and laboratory predictors of MVCs development in SSc.
Methods: SSc patients fulfilling the 2013 ACR/EULAR criteria were enrolled from two SSc-care units. Data regarding clinical manifestations, instrumental and laboratory evaluation for renal, cardiac and cardiovascular involvement were collected. ET1 serum levels were measured with human ET-1 ELISA kit.
Results: 380 patients [aged 57 (46-68) years, 12% males] were enrolled in the study, with 42.4% prevalence of MVCs at baseline. Previously known associations were significantly confirmed between presence of MVCs and NVCp, sPSP, Dlco, RRI. The levels of ET1 were increased in the SSc MVCs without reaching a statistical significance.
In the whole population, modified Rodnan skin score (mRSS) [OR 1.081 (95% CI 1.032-1.132), p=0.001], presence of telangectasias [OR 2.246 (95% CI 1.201-4.201), p=0.11] and presence of dyspnoea [OR 2.100 (95%CI 1.029-4.286), p=0.041] were predictive for MVCs at baseline on multivariate regression analysis. During a 3-years follow-up, 21 patients developed a new MVCs and sPAP was the only independent predictor [HR 1.057 (1.016-1.100), p=0.006] at multivariate analysis. When evaluating only MVCs naive patients (n=179), 15 new MVCs developed during the follow-up and joint involvement was the only independent predictors [HR 8.355 (1.741-44.233), p=0.037].
Conclusion: The data show that the most stringent factors predicting MVCs are sPAP and joint involvement in MCVs complicated and naive patients, respectively. These 2 items, together with mRSS and teleangectasias, should always considered in SSc long-term follow up to shape up a tailored therapeutic approach.
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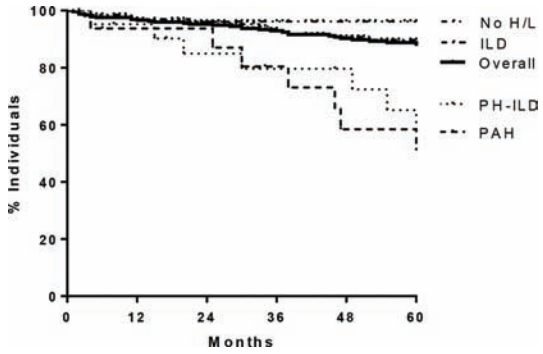
AB0640 **SURVIVAL AND MORTALITY PREDICTORS IN SYSTEMIC SCLEROSIS: RESULTS FROM A MONOCENTRIC ITALIAN COHORT**

Fabio Cacciapaglia, Marco Fornaro, Fabio Montini, Livio Urso, Sergio Colella, Laura Coladonato, Maria Grazia Anelli, Emanuela Praino, Giuseppe Lopalco, Florenzo Iannone. *Policlinico of Bari, Rheumatology Unit, Department of Emergency and Organ Transplantations, Bari, Italy*

Background: Systemic sclerosis (SSc) is a connective tissue disease with a poor prognosis and disease-related pulmonary fibrosis, pulmonary arterial hypertension (PAH) and cardiac involvement accounted for most deaths (1). However, a decrease in mortality is seen in the last decades thanks to the opportunity of new screening and therapeutic strategies (2).
Objectives: To estimate the global survival and any predictor of mortality in a monocentric cohort of SSc patients with a 10-years follow-up.
Methods: We performed a retrospective analysis examining the medical records of our longitudinal SSc cohort with a median (IQR) follow-up of 56 (25-82.5) months in our Scleroderma Unit since January 2009. All clinical, laboratory and instrumental findings have been recorded and analyzed using Chi-squared tests, Kaplan-Meier curves, log-rank tests, and Cox proportional hazards modeling.
Results: We collected data from 347 SSc patients (female n. 319 (91.9%); mean (SD) age at diagnosis 50.6 (15.9) years, median (IQR) disease duration 8.75 (4.1-14.9) years; diffuse cutaneous involvement (dsSSc) n.57 (16.4%) patients) fulfilling the 1980 ARA and/or 2013 ACR/EULAR classification criteria. All patients were positive for ANA, while anti-Topo-I were found in 145 (41.8%), CENP-B in 139 (40.1%) patients. Fifteen (4.3%) patients were positive to other autoantibodies (Anti-RNA polymerase III, anti-Pm/Scl) while anti-ENA were negative or unknown for 48 (13.8%) SSc patients. Interstitial lung disease (ILD) was present in 158 (45.5%), pulmonary arterial hypertension, diagnosed by right heart catheterism, (Group 1 PAH) was found in 17 (4.9%), and 22/347 (6.3%) patients presented pulmonary hypertension combined with ILD (Group 3 PH-ILD). The overall survival rates were 89.1% and 87.3% at 5 and 10 years, respectively. As reported in Figure 1, the 5-years global survival was significantly impaired by the presence of PAH or PH-ILD, while isolated ILD did not impact the survival. The univariate and multivariate analysis showed that dsSSc, higher age at diagnosis, delayed referral to our Scleroderma Unit, body mass index and absence of heart (H) or lung (L) involvement (No H/L) were independent predictors of 5-years mortality (Table I). While gender, disease duration, specific autoantibodies, basal Rodnan skin score, smoking, renal or gastrointestinal comorbidities, NYHA functional class, steroid or immune-suppressive treatments did not reach the statistically significance.
Conclusion: Our study demonstrated a global 10-years survival rate over 85%, and the presence of PH with or without ILD represents the main negative predictor. The rapid referral to a specialized centre for SSc and early treatment with effective agents for PH could further improve prognosis.

REFERENCES

[1] Tyndall AJ, et al. Ann Rheum Dis. 2010.
[2] Allanore Y, et al. Expert Opin Pharmacother. 2007.



Abstract AB0640 Figure 1.. Kaplan-Meier curves for 5-years survival in SSc patients (Log-rank 33.40, p<0.001).Abbreviations: No H/L: absence of heart or lung involvement; ILD: interstitial lung disease; PH-ILD: Pulmonary hypertension associated to ILD; PAH: pulmonary arterial hypertension.

Table I. Statistically significant prognostic factors for 5-years mortality at univariate and multivariate analysis (Cox proportional hazards modelling).

	UNIVARIATE ANALYSIS			MULTIVARIATE ANALYSIS		
	HR	**95%IC**	***P***	**HR**	**95%IC**	***P***
dcSSc	**3.45**	**1.33-8.95**	**0.01**	**4,02**	**1.86-8.71**	**0.0001**
Age at diagnosis	**2.63**	**1.01-6.75**	**0.04**	**2.71**	**1.12-6.61**	**0.03**
Delay in referral	**2.64**	**1.00-6.84**	**0.05**	**2.73**	**1.11-6.7**	**0.03**
BMI	**0.90**	**0.82-0.99**	**0.03**	**0.91**	**0.84-0.98**	**0.02**
No H/L Involvement	**0.45**	**0.21-0.97**	**0.04**	**0.17**	**0.06-0.5**	**0.001**

Abbreviations: dcSSc: diffuse cutaneous involvement; BMI: body mass index; H/L: heart or lung involvement; HR: hazard risk.

Disclosure of Interests: Fabio Cacciapaglia: None declared, Marco Fornaro: None declared, Fabio Montini: None declared, Livio Urso: None declared, Sergio Colella: None declared, Laura Coladonato: None declared, Maria Grazia Anelli: None declared, Emanuela Praino: None declared, Giuseppe Lopalco Speakers bureau: SOBI, BMS, Florenzo Iannone Consultant for: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work

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AB0641 VITAMIN D SERUM LEVELS AND THE RISK OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS: A LONGITUDINAL STUDY

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Background: Vitamin D is known to influence the immune system in many different diseases although longitudinal studies on systemic sclerosis (SSc) are still missing.
Objectives: this study wants to investigate if variations in vitamin D serum levels (25OHD) over time affect digital ulcers (DU) in SSc.
Methods: this is a retrospective study on 65 patients. Data on disease characteristics and 25OHD were collected in 2011 and 2016.
Results: The mean age of our cohort was 58 (12) years with a mean disease duration of 9.5 (5.3) years. Most of our patients had a limited subset (69.2%). At baseline 50.8% and 41.5% after 5 years had 25OHD <30 ng\mL. Supplemented patients (8750 IU\week) at baseline were 39 (60.0%) and 45 (69.2%) at the end of follow up. Nevertheless, 31 (47.7%) had a decrease of 25OHD in 5 years. In univariate analysis, patients with incident digital ulcers (DU) had a decrease in 25OHD as compared to patients with no incident DU (-17.4 (37.0) vs. 13.0 (89.5), p=0.018). No differences in 25OHD variations were found for other disease characteristics. In multivariate analysis correcting for previous DU and mRSS at baseline, patients with a decrease in 25OHD had an increased risk of developing DU (OR (IC95%): 16.6 (1.7 to 164.5), p=0.017).
Conclusion: In this study we have shown that a decrease in 25OHD increases the risk of developing DUs and that vitamin D supplementation with the doses currently recommended may be insufficient in SSc. Further studies in wider cohorts are needed to confirm these results and to evaluate the effectiveness of a more aggressive or different vitamin D supplementation.
Disclosure of Interests: Cristian Caimmi: None declared, Eugenia Bertoldo: None declared, Alice Pozza: None declared, Paola Caramaschi: None declared, Giovanni Orsolini Speakers bureau: Grunenthal, Davide Gatti Speakers bureau: Abiogen, Amgen, Janssen-Cilag, Mundipharma, Pfeizer, Maurizio Rossini: None declared, Ombretta Viapiana Speakers bureau: Novartis, Abbvie, Eli-Lilly, Sanofi Genzyme

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AB0642 DESCRIPTION OF SAE1/2 ANTIBODY IN A DERMATOMYOSITIS COHORT

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Background: Myositis specific antibodies have gained special importance in last years. Its knowledge has allowed stratifying patients in different clinical phenotypes, predicting with greater accuracy prognosis and establishing a clinical attitude to follow. SAE1/2 antibody (anti-small ubiquitin-like modifier activating enzyme) was first described in 2007 in patients with amyopathic dermatomyositis with cutaneous and digestive involvement. Its prevalence ranges from 8% in European cohorts to 3% in Asians.
Objectives: Describing myositis specific antibodies (MSA) in a cohort of inflammatory myopathies. To characterize the clinical phenotype of SAE1/2 antibody and to compare it with the rest of MSA.
Methods: Patients diagnosed of dermatomyositis in a tertiary hospital from 1978-2018, according to the criteria of Bohan and Peter (1975) and according to Dalakas classification criteria (2015). Clinical and analytical data, including the immunological profile were collected, as well as the treatments received and the evolution of the disease.
Results: Out of 46, 41 dermatomyositis had positive antinuclear antibodies (ANA). 55% percent had ANA titles≥640, being the fine speckled pattern the most frequent (43%) followed by coarse speckled and homogeneous (13.6% each).
72% had MSA, the most frequent being antiJo1 (27.3%) followed by MDA5 (18.2%) and SAE1/2 (15%). Up to 40% had two or more antibodies, being the association with antibodies Ro52 and Ro60, the most frequent.
5 patients presented positivity against SAE antibody. In comparison to the rest of MSA, 80% presented with cutaneous debut (p = 0.00), being the most frequent manifestations heliotrope erythema (p = 0.00), Gottron papules (p = 0.10) and skin rash (p = 0.00). 60% had pathological capillaroscopy compared to 15% (p = 0.00). Muscular balance was preserved in 60% of patients. Sixty percent had dysphagia vs 9% (p = 0.00). Two of them had lung involvement (alveolar hemorrhage and rapidly progressive pneumonitis). In comparison with SAE negative group, patients presented more pulmonary hypertension (44.5vs34 mmHg), without reaching significant differences. No significant differences were found between muscle enzyme levels' neither acute phase reactants.
As complications, one patient presented a myocarditis with quickly rapidly progressive pneumonitis that required high doses of corticotherapy and another one alveolar hemorrhage, which was treated the same way. All patients required corticotherapy at doses of mg/kg, requiring two of them to be treated with DMARDs (methotrexate and dolquine) and one of them with immunoglobulins due to cutaneous involvement.
Mortality rate was 40% due to rapidly progressive lung affectation and cardiorespiratory arrest.
Conclusion: Higher prevalence of SAE1/2 antibody in our cohort may be explained due to the use of amplified myositis antibodies kit that specifically includes this antibody. These patients typically present with cutaneous involvement and dysphagia but also lung affectation as a complication. Studies with larger samples should be performed in order to know the prognosis of this antibody specificity.
Disclosure of Interests: None declared

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AB0643 CLINICAL AND ANALYTICAL DESCRIPTION OF A DERMATOMYOSITIS SERIES OF PATIENTS

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Background: Dermatomyositis (DM) is an idiopathic inflammatory myopathy. The recent years has increased its knowledge thanks to best characterization of myositis-specific antibodies that correlate with different clinical phenotypes.with different clinical phenotypes.

Objectives: To describe the clinical and analytical features of a series of dermatomyositis: clinical debut, clinical manifestations as well as the treatments received and the evolution of the disease.

Methods: Patients diagnosed of dermatomyositis in a tertiary hospital between the years 1978-2018 according to the criteria of Bohan and Peter (1975) and according to Dalakas' classification criteria (2015). Clinical, analytical and immunological profile data were collected, as well as treatments received and the evolution of the disease.

Results: A total of 59 inflammatory myopathies diagnosed between the years 1985 and 2018 were included. 46 were dermatomyositis (78%), 9 polymyositis (15%) and 4 necrotizing myositis (7%). 69% were women and 22% were smokers. Clinic started at 54 ± 17 years. The initial manifestation was pulmonary in 26.7% followed by cutaneous manifestations (24.4%) and the muscular (22.2%), while a 17.8% started skin and muscular manifestations at the same time. 45.5% behaved like a myopathic DM while a 28% as amyopathic DM and antisynthetase syndrome respectively. 38% presented interstitial involvement being the most common non-specific interstitial pneumonitis (76%)followed by usual interstitial pneumonitis (17%). In these patients,

DLCO was decreased (mean of 58.9% and 13.2) as well as the FVC (average of 58%, 2.5L). 73.3% presented cutaneous involvement being the most common manifestations the Gottron papules (37.8%) and the heliotrope rash (35.6%), and up to 27% had cuticular affectacion. 64% had muscle involvement, afecting proximal and symmetrical. Neck flexors were affected in a 38% of patients while 20% had dysphagia.Only 3 patients presented dysphonia (7%) and 2 myocarditis

Analytical data

Muscular enzyimes	
CK	821 ± 1260U/mL
LDH	425 ± 300U/L
Aldolase	11.5 ± 11U/L
Acute phase reactants	
ESR	30 ± 23 mm
RCP	13 mg/L ± 25
Myositis specific antibodies	
AntiJo1	27%
MDA5	18%
SAE1/2	15%

Conclusion: 80% received corticotherapy at a dose of mg/kg/day and 20% required high doses of metilprednisolone due to muscular involvement or pulmonary. 18% immunoglobulins and 11% cyclophosphamide. As maintenance 80% received disease modifiying antirheumatic drug in addition to corticosteroid therapy in descending doses (azathioprine 22%, dolquine 15%, tacrolimus 13.3%, rituximab 11%) due to muscle (29.9%), cutaneous (24.4%) and pulmonary involvement (22.2%). As complications, 2 cases of the syndrome were registered hemophagocytic Virtually all patients they presented pulmonary hypertension (mean 34 ± 12 mmHg). 5 patients (11.1%) were diagnosed with neoplasia, two of them after the diagnosis of DM. The mortality was 24%. 3 patients died due to a rapidly progressive pneumonitis, another 2 due to alveolar hemorrhage and three of them due to complication of the neoplastic disease.

Dermatomyositis occurs in a variable way, with predominance of pulmonary, skin and muscle manifestations. They require corticotherapy and immunosuppressive treatment for maintenance, even so, mortality is high.

Disclosure of Interests: None declared

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AB0644 RESULTS OF A TRAINING COURSE FOR CALCULATION OF THE MODIFIED RODNAN SKIN SCORE IN SCLERODERMA

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Background: Scleroderma is a connective tissue disease that is characterized by fibrosis of the skin.The modified Rodnan Skin Score (mRSS) is a measure generally used to assess the skin thickness in patients with scleroderma.Data on the effectiveness of the mRSS training courses differ in the literature.

Objectives: The objective of our study was to evaluate the effectiveness of the mRSS training course in rheumatology fellows in the rheumatology departments.

Methods: The study included 6 fellows from the departments of rheumatology.Participants were given a 1-hour-long theoretical training, including dermal involvement, and mRSS assessment by 3 rheumatology experts experienced in scleroderma, which was followed by an applied training on 4 patients for one-hour.Participants scored two patients before and after training on a form, which included 17 domains with a total score-range between "0" and "51". Then using the SPSS15 software program, inter-rater reliability was assessed with intraclass correlation(**ICC**) analysis for both pre- and post-training mRSS.Fleiss' kappa was used to measure the degree of agreement according to 12 Rodnan score areas before and after the training.

Results: The ICC value for pre-training and post-training total Rodnan scores was 0.867 (95% CI-0.625-1.00, P=0.05), and 0.905(95% CI 0.045-1.00, P=0.02), respectively. Individual analysis of score areas showed that after the training there was an increase in degree of agreement in some of these areas, while there was no difference in one area, and it decreased in others (Table 1).

Table 1: The ICC value and percentage of agreement for pre-training and post-training total Rodnan scores

	Pre-training		Post-training	
Body area	Fleiss's Kappa (%95 CI)	Agreement, %	Fleiss's Kappa (%95 GA)	Agreement, %
Right fingers	0.38 (0.003, 0.73)	**53.3**	0.60 (-0.18, 1.00)	**70.0**
Left fingers	0.42 (0.16, 0.68)	56.6	0.29 (0.29, 0.29)	46.6
Right hand	0.02 (0.02, 0.02)	**26.6**	0.11 (-0.06, 0.29)	**33.3**
Left hand	0.16 (-0.11, 0.42)	**36.6**	0.16 (-0.11, 0.42)	**36.6**
Right forearm	0.29 (0.29, 0.29)	46.6	0.02 (0.02, 0.02)	26.6
Left forearm	0.29 (0.29, 0.29)	46.6	0.02 (0.02, 0.02)	26.6
Right upper arm	0.11 (-0.06, 0.29)	33.3	-0.22 (-0.11, 0.06)	23.3
Left upper arm	0.24 (0.16, 0.33)	43.3	0.02 (0.02, 0.02)	26.6
Face	0.24 (0.16, 0.33)	43.3	0.02 (0.02, 0.02)	26.6
Anterios chest	0.24 (0.16, 0.33)	43.3	0.16 (-0.11, 0.42)	36.6
Abdomen	0.16 (-0.11, 0.42)	36.6	0.11 (-0.06, 0.29)	33.3
Right thigh	0.02 (0.02, 0.02)	**26.6**	0.29 (0.29, 0.29)	**46.6**
Left thigh	0.02 (0.02, 0.02)	**26.6**	0.20 (-0.50, 0.90)	**40.0**
Right leg	0.38 (0.003, 0.73)	53.3	0.24 (0.16, 0.33)	43.3

Conclusion: Several studies have demonstrated the applicability, reliability, and validity of mRSS, a measure of dermal involvement, and that evaluation of the score requires experience, and an attentive learning process.In the literature, the inter-rater ICC values during previous training courses are reported to range between 0.378 and 0.92(1). These studies show differences in terms of the number and experience of participants,

number of patients, course-length, and repeated courses. Similar to the observation by Ionescu *et al*(2), the pre-training inter-observer ICC value was very high(0.867), and it increased to 0.905 after the training. Presence of an increase in some areas, and reduction in some others in individual analysis of areas after the training may suggests the need for repeated training. Our limitations were low number of participants and patients. We obtained very good inter-rater ICC values in the mRSS training course given to rheumatology fellows; however we may benefit from new studies for optimization of these conclusions by increasing the numbers of trainees, patients, and the lenght of courses.

REFERENCES

[1] Czirjak, L., et al., The EUSTAR model for teaching and implementing the modified Rodnan skin score in systemic sclerosis. Ann Rheum Dis, 2007.
[2] Ionescu, R., et al., Repeated teaching courses of the modified Rodnan skin score in systemic sclerosis. Clin Exp Rheumatol, 2010.

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AB0645 CANNABINOIDS IN THE TREATMENT OF PAIN RELATED TO SYSTEMIC SCLEROSIS SKIN ULCERS: OUR EXPERIENCE

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Background: Skin ulcers (SU) represent one of the most frequent complications of Systemic Sclerosis (SSc), characterized by severe chronic pain and frequent complications. Pain related to SSc SU(SSU) remains yet an area of significant unmet need. Moreover, pain control is fundamental for the wound care procedures in SSc patients (pt), increasing treatment adherence and compliance to skin ulcers dressing changes. The pain relief provided by standard therapy (i.e. NSAIDs, tramadol) is often inadequate or dose limited by side effects. Opioids currently are the mainstay of SSU pain treatment but burdened by side effect profile and/or ineffective. Thus, novel analgesic strategies need to be investigated. Cannabidiol (CBD), one of many constituents of the Cannabis sativa, has received renewed interest in the treatment of numerous pathological conditions.
Objectives: Evaluate our experience to define the efficacy of CBD preparation in patients with SSU.
Methods: 25 SSc pt (F/M 22/3, mean age 52.3 ± 12.9-SD-years), referred to our Scleroderma Unit during 2018, were consecutively included. In all pt the disease was complicated by long-standing, painful SU resistant to opioids. Pain was classified as severe, according to WHO guidelines in all subjects. 25/25 pt carried out systemic (calcium-channel blockers, prostanoids and/or anti-ET receptors) and local (debridement and dressing) therapies. The CBD (10% oral administration oil) was used daily for the treatment of SSU-related pain. We performed both an oral (five drops bid) as local treatment (two drops in the site of SSU) during surgical debridement of SSU for a period of 5.9 ± 3.2 SD months. Patients have been provided with a diary to record the following symptoms daily: self-evaluation of pain at the same time in the evening, using a visual analog scale (VAS), use of other analgesics, eventual side effects. Health Assessment Questionnaire-Disability Index (HAQ-DI) was administrated baseline and at the end of treatment. Safety of CBD was evaluated by patient's records of side effects, while vital signs and laboratory parameter variations were monitored at each weekly medication.
Results: The local treatment with CBD produced a significant reduction of SSU-related pain. After 1 month of therapy, pain VAS decreased from 94.8 ± 8.72 SD to 54.7 ± 9.4 SD (P<0.0001), total hours of sleep increased from 2.56 ±1.28 SD to 5.67 ± 0.85 SD (P <0.000). Additional analgesic therapy was necessary in 12/25 (48%). After 2 months, further clinical improvement was observed: the pain VAS reduced to 40.9 ± 12.9 SD, the mean total hours of sleep per night was 6.10 ± 0.85 SD and the HAQ-DI decreased from 1.1 ± 0.67 SD (baseline) to 0.46 ± 0.46 SD at the last patients' evaluation, when complete healing of SSU and pain relief were obtained and CBD was discontinued. 20/25 (80%) pt registered a better compliance to the local wound management.
No reported significant side effects with CBD oil.
Conclusion: Our study suggests that the use of CBD as a local therapy is effective and safe in maintaining analgesia in patients with SSU; not secondarily it could be essential for an adequate healing of a local wound with consequent improvement of SSc patients' quality of life and compliance on local SSU management. Further larger-scale studies will be needed to finally demonstrate CBD efficacy and to monitor long-term effects.
Disclosure of Interests: None declared
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AB0646 HEALTHCARE UTILIZATION AMONG INCIDENT CASES OF SYSTEMIC SCLEROSIS: RESULTS FROM A POPULATION-BASED COHORT (1988–2016)

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Background: Systemic sclerosis (SSc) is an autoimmune disorder associated with multi-organ dysfunction including but not limited to vascular, cardiac and pulmonary involvement. Few studies have estimated the healthcare resource usage of patients with SSc.
Objectives: To compare healthcare utilization among incident cases of SSc vs age- and sex-matched comparators.
Methods: This study utilized a retrospective, population-based cohort of physician-diagnosed patients with SSc in a geographically well-defined area from Jan 1, 1988 to Dec 31, 2016. A 2:1 cohort of age- and sex-matched non-SSc subjects from the same population base was randomly selected for comparison. Inpatient and outpatient utilization data were obtained from the Rochester Epidemiology Project beginning 12 months prior to the SSc incidence/index date. Patients were followed until death, migration from Olmsted County, or December 31, 2017. A maximum of 5 years following the incidence/index date was used for analysis and the follow-up of each matched triple was further truncated at the shortest length of follow-up for any member, to ensure similar periods of observation for SSc cases and non-SSc comparators. Services were summarized as visit-days (number of days at least one service in the category was billed) to avoid overestimation of services provided. Utilization was compared between SSc and non-SSc cohorts using negative binomial models.
Results: The cohort included 69 incident SSc cases and 138 non-SSc comparators (mean age of 57 ± 16 years at diagnosis/index, 90% female for both cohorts; 87% [SSc] and 95% [non-SSc] Caucasian). Patients with SSc had the highest utilization of outpatient physician, laboratory and combined radiology visit-days during the year of the SSc diagnosis compared with the year prior to diagnosis or years 1-4 after diagnosis of SSc (Table). Patients with SSc had higher utilization of outpatient physician, laboratory and combined radiology visit-days annually for the year prior to diagnosis of SSc and for each of the first 5 years after diagnosis of Ssc compared to patients without SSc. Rate ratios comparing utilization in patients with and without SSc ranged from 1.8 to 3.0 for all comparisons.
Conclusion: A higher utilization of outpatient physician, laboratory and radiology visits was observed among patients with SSc compared to non-SSc subjects throughout 5 years of disease duration, indicating high and continued care needs in this patient population.

Table. Comparison of outpatient visits, labs and imaging visit-days in patients with and without incident SSc

Services	Time Interval (years)	Number of patients, SSc/Non-SSc	SSc Median visit-days (IQR)	Non-SSc Median visit-days (IQR)	Rate Ratio (95% CI)
Outpatient visits	-1-0	69/138	4 (1–9)	2 (0–6)	1.8 (1.2–2.7)
	0-1	69/138	7 (4–12)	3 (0–5)	2.4 (1.7–3.3)
	1-2	66/132	4 (2–11)	2 (0–4)	2.0 (1.4–2.9)
	2-3	54/108	4 (2–10)	3 (0-5)	1.9 (1.4–2.7)
	3-4	48/96	4 (2–10)	3 (1–5)	1.9 (1.3–2.6)
	4-5	43/86	5 (2–12)	3 (0–6)	2.1 (1.4–3.0)
Labs	-1-0	69/138	3 (0-8)	1 (0-3)	2.1 (1.4–3.3)
	0-1	69/138	4 (2-10)	2 (0–3)	3.0 (2.0–4.6)
	1-2	66/132	5 (1-8)	1 (0–3)	2.0 (1.3–3.2)
	2-3	54/108	3 (1-9)	1 (0–4)	2.6 (1.7–4.3)
	3-4	48/96	3 (1-10)	1 (0–3)	2.7 (1.7–4.1)
	4-5	43/86	3 (1-12)	1 (0–3)	2.9 (1.7–4.7)
Radiology	-1-0	69/138	2 (0–5)	0 (0–2)	2.1 (1.6–4.2)
	0-1	69/138	3 (1–6)	1 (0–3)	2.6 (1.8–3.9)
	1-2	66/132	2 (1–6)	0 (0–2)	1.9 (1.8–3.1)
	2-3	54/108	2 (1–4)	1 (0–2)	2.1 (1.3–3.1)
	3-4	48/96	2 (1–4)	1 (0–2)	2.0 (1.3–3.1)
	4-5	43/86	2 (1–7)	1 (0–2)	2.6 (1.6–4.2)

IQR: interquartile range; CI: confidence interval

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AB0647 ASSOCIATION OF VASCULAR BIOMARKERS WITH SYSTEMIC SCLEROSIS CLINICAL FEATURES AND NAILFOLD VIDEOCAPILLAROSCOPY ALTERATIONS-CROSS SECTIONAL STUDY

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Background: The most reliable markers reflecting endothelial activation and injury in Systemic sclerosis (SSc), are intercellular adhesion molecule (ICAM1), vascular cell adhesion molecule (VCAM1), E selectin (Es) and P selectin (Ps) (1).
Objectives: To assess concentrations of these vascular biomarkers in SSc patients (pts) in comparison to healthy controls (HC) and in relation to disease manifestations.
Methods: Patients who fulfilled the 2013 ACR/EULAR SSc classification criteria and have never been treated with endothelin receptor antagonist, phosphodiesterase 5 inhibitors or prostanoids were eligibile. Exclusion criteria were overlap syndromes, other autoimmune and cardiovascular diseases, diabetes mellitus, thrombosis, pregnancy, active infection or neoplastic diseases. Our study included 53 SSc pts [34 limited (lcSSc) and 19 diffuse cutaneous SSc (dcSSc)] and 31 age- and sex matched HC. Serum concentration of ICAM1, VCAM1, Es and Ps were measured using a commercial ELISA kit (Quantikine; R&D Systems), expressed as ng/mL. Clinical evaluation of patients was obtained, including nailfold videocapillaroscopy (NVC). Disease activity was assessed by the revised EUSTAR activity index. Statistical analysis was done in R. Student's t-test or ANOVA, otherwise Mann-Whitney U or Kruskal-Wallis tests were used. Pearson's or Spearman's correlation were done depends on nature of data. ICAM1 cut off value were assessed with ROC analysis. Association were performed with univariate logistic regression for NVC alterations and multivariate for Anti-Topol/Scl70 antibodies (aTSa).
Results: Concentration of all markers were elevated in SSc pts compared to HC (ICAM1 $p<0.001$, VCAM1 $p<0.001$, Es $p<0.05$, Ps $p>0.05$). Different disease subsets exhibited higher values of ICAM1 and VCAM1 respect to HC (lSSc $p<0.05$, dSSc $p<0.001$). Concentration of ICAM1 was higher in dcSSc compared to lcSSc ($p<0.05$). ICAM1 level were independently associated with positive aTSa (OR 1.2, 95% CI 1.02–1.35, $p<0.001$), with distinguishing cut off value of 34.94 (Sn 0.90%, Sp 0.60%, AUC 0.85). ICAM 1 was positively correlated with the erythrocyte sedimentation rate (r 0.3, $p<0.05$) especially within disease duration > 3 years group (r 0.4, $p<0.05$). Higher levels of ICAM1 was found in diffusing capacity of the lungs for carbon monoxide<70% ($p<0.05$), modified Rodnan skin score >14 ($p<0.05$) and active disease ($p<0.05$) group. Calcinosis group had decreased level of Es ($p<0.05$) and increased Ps ($p<0.05$). Es was lower in group with acroosteolysis ($p<0.05$). Trends towards increasing markers concentration from early to late NVC pattern were observed for all biomarkers except Es which showed the highest concentration in active group, but without significant differences ($p>0.05$). Few megacapilaries were associated with ICAM1 (OR 1.2, 95% CI 1.06–1.34, $p<0.05$) and Ps (OR 1.2, 95% CI 1.08–1.39, $p<0.05$), while presence of bushy capillaries were associated with ICAM1 (OR 1.3, 95% CI 1.06–1.36, $p<0.05$) level.
Conclusion: Our results support the role of vascular biomarkers in SSc pathogenesis. Besides anti-Topol/Scl70 antibodies, ICAM-1 could be used as an additional marker of dSSc. Elevation of ICAM1 and Ps concentration might be associated with late NVC alterations.

REFERENCES

[1] Mostmans Y, Cutolo M, Giddelo C, et al. The role of endothelial cells in the vasculopathy of systemic sclerosis: A systematic review. Autoimmun Rev 2017;16:774–86. doi:10.1016/j.autrev.2017.05.024

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AB0648 CORRELATIONS BETWEEN NEUTROPHIL/LYMPHOCYTE RATIO AND CLINICAL CHARACTERISTICS OF PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: The ratio of neutrophils to lymphocytes (NRL) is considered a novel inflammatory marker. Recently studies are ongoing for objective and easy markers (1)
Objectives: In this study, we aimed to identify the possible relationship between NRL and clinical characteristics inn patients with systemic sclerosis (SSc)
Methods: Our study is based on a retrospective analysis. We collected in a data base clinic and epidemiological characteristic of SSc patients. Fifty-two patients (46 female; 10 subset diffuse) with SSc were enrolled consecutively for analyser the correlations. We considered the correlation with NRL and skin core, ulcers, pitting scars, gastro-intestinal events, fibrosis on HTCR, respiratory parameters (FVC, DLCO), PAPs, diastolic abnormalities, capillaroscopy alterations and activity index (2). Student's t-test was used for comparison averages, correlation among variables were assessed by Sperman's correlation testing.
Results: sociodemographic and clinical characteristic were reported in table 1. The correlation analysis statistically significant is summarized in table 2: NLR vs skin score, DLCO, PAPs, and activity index. The correlation analysis between NLR and presence of ulcers and pitting scars was considered not quite significant. There were no correlations between other parameters and NLR.
Conclusion: NLR values correlated negatively with DLCO value, and positively with PAP value, skin score and activity index NLR level may serve as inflammatory marker in patients with SSc.

REFERENCES

[1] Absenger G. et al. Br J Cancer 2013; 109:395
[2] Valentini G. et al. Ann Rheum Dids 2001; 60:592

Table 1. Sociodemographic and clinical characteristics

	Patients n=52
Age (years) mean ±sd	53.58±13.99
Sex (M/F)	6/46
Disease duration (years) mean ±sd	8.68±9.6
WBC count (K/μL) mean ± sd	6748±2302
NLR, mean ± sd	2398±1290
Skin score, mean ±sd	3.94±6.26
DLCO% of predict, mean ±sd	71.4±23.4
PAPs mmHg, mean ±sd	19.9±19.1
Ulcers (yes/no)	5/47
Pitting scars (yes/no)	18/34
Cpillaroscopy alterations, normal/early/active/late	6/17/17/12
Activity index, mean ±sd	1.86±1.48

Tabel 2. Correlation analysis between NLR and skin score, DLCO, PAPs, activity index

		Skin score	DLCO	PAPs	Activity index
NLR	r value	0.28	-0.30	0.29	0.28
	p value	0.045	0.035	0.033	0.042

Disclosure of Interests: None declared
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AB0649 **B CELL DEPLETION THERAPY IN VERY EARLY SYSTEMIC SCLEROSIS. A POTENTIAL WINDOW OF OPPORTUNITY?**

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Background: Our group, among others, has shown that B cell depletion therapy may improve skin thickening and interstitial lung disease (ILD) related to systemic sclerosis (SSc). All studies assessing the clinical efficacy of B cell depletion therapy in SSc have recruited patients with established disease fulfilling the old classification criteria. In our previous studies we have found that patients with shorter disease duration had a better clinical response to RTX.
Objectives: It is unknown whether treatment in very early SSc can affect long term outcomes. We aimed at assessing the effect of rituximab (RTX) in patients with very early SSc.
Methods: We report 2 cases where RTX was administered within 24 months from the appearance of Raynaud's.
Results: A 56 year-year-old female with an 18-month history of Raynaud's developed interstitial lung disease (ILD) with extensive ground glass lesions, a normal FVC (82%) but decreased DLco (44%). A diagnosis of SSc was made based on the presence of positive anti-centromere antibodies, puffy fingers, telangiectasias, positive capillaroscopy, ILD and Raynaud's. Six months following RTX treatment, her PFT's had increased (FVC 94% and DLco 55%) and chest HRCT showed an obvious improvement. One year later the patient no longer reported dyspnea. She remained on RTX for 5 years with no respiratory symptoms, stable PFTs and no evidence of disease progression. The second case is a 27-year old female with a 1-year history of Raynaud's, puffy fingers, positive anti-Scl70 and capillaroscopy. Within a few months her skin thickened rapidly reaching an MRSS of 12 and developed tendon friction rubs. Six months following RTX treatment skin thickening had almost resolved; she only had mild sclerodactyly. Tendon friction rubs disappeared. The patient received 8 consecutive RTX courses throughout a period of 4 years. During this period the patient remained in a steady clinical condition with no signs of disease progression.
Conclusion: It is generally accepted that autoimmunity/immune dysregulation and vasculopathy are the primary events in SSc that eventually trigger the fibrotic process. Based on this pathogenetic model, one can hypothesize that a therapeutic intervention very early in the disease course, prior to the appearance of fibrotic manifestations could potentially prevent permanent organ damage. Our data suggest that there may be a window of opportunity in SSc. This is why we propose that large scale, controlled studies assessing the efficacy of RTX (or other immune based therapies such as mycophenolate) in patients with very early disease are highly needed.
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AB0650 **PERSPECTIVES AND UNMET NEEDS OF PATIENTS WITH POOR PROGNOSIS SYSTEMIC SCLEROSIS ON AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION CARE: A QUALITATIVE STUDY**

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Background: Autologous hematopoietic stem cell transplantation (HSCT) can induce long-term remission in patients with diffuse cutaneous systemic sclerosis (dcSSc). Nevertheless, it is an intensive treatment with risk of treatment-related mortality and associated adverse events requiring long-term hospital admission. Little is known about the psychosocial impact of HSCT on patients with dcSSc. Additionally, post-discharge care is currently not standardized.
Objectives: To gain more insight in the experiences of patients during and after HSCT and to identify unmet needs in current care.
Methods: Semi-structured interviews were conducted with dcSSc patients that underwent HSCT in four academic hospitals in the Netherlands. Interviews were transcribed verbatim and analyzed with NVIVO12.
Results: Eight patients were interviewed (5 males and 3 females, mean age 48 years (SD 10), mean disease duration 4.6 years (SD 1.9), mean time since HSCT 3.2 years (SD 2.4). At inclusion mean SHAQ was 1.3 (SD 1.1) and mean EQ5D-5L 0.86 (SD 0.21). While patients were satisfied with the frequent, low-threshold contacts with physicians and nurses, the decision-making process followed by HSCT and recovery was mentally taxing. Although patient education was experienced as extensive pre-treatment, participants reported they only felt the real impact of it during therapy. Patients felt anxious throughout the hospital stay and they could not recall most events from that period. Feelings of losing control over health and over time were frequently described. Support of family and friends was important during treatment. Apart from the practical aid, they provided emotional support, helping to cope with emotions and to find purpose. Furthermore, a specialized nurse involved in psychosocial support and care management was highly valued. Still, participants felt lonely and misunderstood due to invisible disabilities, such as fatigue and pain. After HSCT, patients experienced more physical limitations than they expected, i.e. low energy levels and limited hand function. They worried about contracting infections and relapse risk. Professional rehabilitation was often hindered. There were unmet needs. Patients preferred to be better informed about what to expect after admission. Structured and written instructions should include themes such as self-management, practical tips and prognosis of recovery. Participants would advise peers to keep a diary and even take photos during HSCT and hospital stay, in order to help recollect and assimilate past events. Peer-support was recommended by most patients.
Conclusion: HSCT had a large impact, both physical and emotional. We identified unmet needs regarding patient education on rehabilitation and psychosocial support in the period following HSCT.
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AB0651 **THE INFLUENCE OF RITUXIMAB THERAPY ON THE DYNAMICS OF THE BASIC PARAMETERS AND ACTIVITY OF SYSTEMIC SCLEROSIS**

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by skin and multi- organ involvements induced by overproduction of autoantibodiies by B cells.
Objectives: To assess the influence of Rituximab (RTX) therapy on the dynamics of the basic parameters and activity of SSc during long-term follow-up.
Methods: There were 90 SSc patients (pts) in the prospective study. 75% were women. 57% pts had diffuse SSc. SSc was confirmed ACR/EULAR criteria. The average duration of the disease was 5,8 years and of the study was 27 months. For the purpose of the analysis, a group of pts was selected that had no less than two evaluation points from 12 to 42 months and having received 2,9±1.1 g RTX in average during such period. The examination included both routine clinical laboratory parameters and special research. We evaluated the modified Rodnan skin score (mRSS), forced vital capacity (FVC), diffusing capacity of carbon monoxide (DLCO), the Valentini Disease Activity index, estimated glomerular filtration rate (eGFR) before and after completed RTX. All pts included in the study received treatment with vascular, anti-inflammatory and/or immunosuppressive medicines. The average dose of prednisolone was 11,8±4,4 mg/day.
Results: In general, more than 90% pts demonstrated different kinds of improvements. A reliable improvement was documented based on a number of indicators, which reflect typical features of the disease. Thus, skin induration was reduced (skin score decreased), lung functional capacity

increased (increase of FVC of more than 5%). The skin score was reliably decreased from 11,2±9,3 to 6,2 ±4,9 (p<0.0001), FVC was increased from 76,9±19,9 to 84,7±20,9% (p<0.0001), also the increase of DLCO from 46,3±18,3 to 47,8±16,9% from the proper amount was detected. The Valentini Disease Activity index reliably reduced from 2,93±1,7 to 1,38±1,2 points (p<0,0001). Under the RTX therapy, the decrease of glucocorticoids dose was insignificant, but statistically reliable. Thus, prednisolone dose reduction from 11,8±4,4 to 9,22±3,2 mg/day was achieved. Clinically insignificant but reliable decline of eGFR from 100,2±23 to 94,6 ±22 ml/min/1,73m2 was detected.

Conclusion: Thus, RTX has a positive influence on the basic parameters of SSc, mainly on skin damage and lung functionality, reduces the general disease activity. The influence of the RTX on kidney function requires further long-term study.

Disclosure of Interests: None declared

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AB0652 QTC INTERVAL PROLONGATION IN A SCANDINAVIAN COHORT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES AND SYSTEMIC SCLEROSIS: CORRELATIONS WITH CLINICAL VARIABLES

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Background: Idiopathic inflammatory myopathies (IIM) are rare devastating diseases characterized by progressive muscle weakness and muscle fatigue. IIM frequently affects other organs pointing to IIM as a systemic inflammatory disease. Cardiac involvement is associated with poor prognosis. The symptoms are often subclinical and therefore overlooked. QTc prolongation has been detected in patients with systemic sclerosis (SSc). Autoantibodies are important diagnostic tools to confirm IIM and are present in approx. 60% of IIM patients. Autoantibodies are increasingly being recognized as markers for specific organ involvement. A biomarker for cardiac involvement has yet to be elucidated.

Objectives: The aim is to generate new knowledge about cardiac involvement in IIM detected by electrocardiography (ECG) and to evaluate possible associations between autoantibodies and cardiac involvement detected on ECG in a cohort of IIM patients compared with ECG changes in a cohort of SSc patients.

Methods: In a Scandinavian cohort, 263 IIM patients (130 polymyositis patients, 77 dermatomyositis patients, and 56 inclusion body myositis patients) and 102 SSc patients were investigated by ECG and basic cardiovascular and disease specific assessments according to international guidelines. IIM patients were tested for myositis specific autoantibodies (MSAs; anti-Jo-1, anti-PL-7, anti-PL-12, anti-OJ, anti-EJ, anti-SRP, anti-Mi-2, anti-MDA5, anti-TIF1 γ, anti-NPX2, anti-SAE1, anti-HMGCR) and myositis associated autoantibodies (MAAs; anti-PM/Scl75, anti-PM/Scl100, anti-Ro52, anti-Ku, anti-cN1A).

Results: Twenty two IIM patients (8.49%) had abnormal QRS duration versus one SSc patient (1.06%) (P = 0.012). SSc patients had significantly longer QTc duration than IIM patients (QTc = 432.7 ms ± 22.2 and 426.4 ms ± 23.6, respectively) (P = 0.03).

Multivariate regression analysis revealed that increased C-reactive protein (CRP) (P = 0.008), gender (P = 0.002), and hypertension (P = 0.007) were associated with QTc duration in IIM patients. Likewise, pulmonary arterial hypertension was associated with QTc duration (P < 0.001) in SSc patients.

In analysis of pooled data for IIM patients and SSc patients, factors associated with QTc duration were increased CRP (P = 0.005), gender (P = 0.001), and hypertension (P = 0.01).

Conclusion: Both IIM patients and SSc patients had ECG changes though no particular pattern was shown. The findings support our hypothesis on cardiac involvement in IIM patients. No significant association was found between presences of either myositis specific or myositis associated autoantibodies and ECG changes. This could be due to the relatively low number of each autoantibody. There is a need to conduct larger prospective studies to identify a possible autoantibody for cardiac involvement in IIM.

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AB0653 SERUM CARDIAC BIOMARKERS BUT NOT SUBCLINICAL CARDIOVASCULAR MAGNETIC RESONANCE ABNORMALITIES IN SYSTEMIC SCLEROSIS ASSOCIATE WITH THE DEVELOPMENT OF CARDIOVASCULAR EVENTS

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Background: Primary cardiac disease in systemic sclerosis (SSc-PCD) is associated with a poor prognosis when clinically evident. Subclinical SSc-PCD is described in up to 2/3 of SSc patients when sensitive methods are employed. The prognostic implication of these findings is not clear.

Objectives: To describe the prevalence of cardiovascular magnetic resonance (CMR) abnormalities, their association with clinical phenotype and cardiac biomarkers, and whether cardiac biomarkers and CMR predict the development of cardiovascular (CV) events.

Methods: Patients fulfilling the ACR/EULAR criteria for SSc, with no CV disease (CVD), diabetes and no more than 1 CV risk factor had 3Tesla CMR, including late gadolinium enhancement (LGE), myocardial perfusion, T1 mapping for T1 native and extracellular volume (ECV) quantification, and cardiac biomarkers measured. CV events were defined as episode of myocarditis, heart failure, rhythm disturbances and/or any echocardiographic abnormalities including systolic dysfunction, diastolic dysfunction > grade 1 or regional wall motion abnormalities. 47 healthy volunteers (HV) with comparable age and gender served as controls.

Results: 83 SSc patients were recruited, median (IQR) age of 54 (49, 54), 84% females and 33% dcSSc, 40% had ILD, 24% a history of digital ulceration (HxDU) and 29% were Scl70+.

CMR showed higher ECV% and T1 native, markers of diffuse fibrosis in SSc compared to HV [mean (SD) 30 (4) vs 25 (3), p= 0.000; 1241 (76) vs 1206 (55), p=0.003]. Lower myocardial perfusion reserve (MPR) was also noted in SSc patients [mean (SD) 2 (0.8) vs 3 (1), p=0.000]. None of the HV had LGE-fibrosis, whilst 16 (20%) of the patients had a non-ischemic LGE pattern. Left ventricular (LV) volume and function were similar between HV and SSc patients.

Presence of LGE associated with hsTnI and lower forced vital capacity (rho=0.283, p=0.032; rho=-0.217, p=0.5). Multivariate analysis revealed an association of T1 native with mRSS and CRP (B=0.5, p=0.02; B=0.218, p=0.049). ECV% associated with NTproBNP and HxDU (B=0.032, p=0.034; B=0.310, p=0.005). 73/83 had ≥1 year available clinical and echocardiography follow up data with a mean (SD) duration of 24(20) months. 12/73 had a CV event judged to be SSc-PCD. LV mass associated with CV events(p=0.043) (Table 1), whilst univariate regression analysis showed that both hsTnI (OR=1.014, p=0.014) and NTproBNP (OR=1.005, p=0.026) but none of the CMR variables associated with the development of CV events.

Conclusion: Asymptomatic SSc patients with no overt CVD demonstrate both focal and diffuse fibrosis, which are associated with cardiac biomarkers and markers of SSc disease activity. Whilst hsTnI and NTproBNP associated with the development of CV events, none of the measures of fibrosis did although a higher LV mass was noted in this

group. The prognostic implications of subclinical CMR findings remain unclear and would benefit from longer follow-up.

Abstract AB0653 Table 1. CMR measures in SSc patients with CV events versus SSc patients with no CV events

CMR variable	SSc patients with CV events n=12 Mean (SD)	SSc patients with no CV events, n=61 Mean (SD)	p value
LVEDV/BSA (ml/m^2)	83 (17)	76 (15)	0.158
LVESV/BSA (ml/m^2)	33(12)	30(9)	0.222
LVSV/BSA (ml/m^2)	50(7)	47(7)	0.259
LV mass/BSA (g/m^2)	49(10)	43(11)	0.043*
LVEF%	61(7)	62(5)	0.494
ECV%	31(2)	30 (4)	0.572
T1 native(ms)	1210 (78)	1238 (72)	0.262
LGE, n Scar mass	1 0.80 (1.68)	9 0.41(1.14)	0.678 (X^2 test) 0.359
MPR	1.8(0.5)	2.2(0.8)	0.375

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AB0654 NAILFOLD MICROVASCULAR CHANGES IN MIXED CONNECTIVE TISSUE DISEASE: DIFFERENCES WITH SYSTEMIC SCLEROSIS

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Background: Detailed nailfold capillary abnormalities have not been described in mixed connective tissue disease (MCTD) as well as their changes over time, unlike systemic sclerosis (SSc) which microvascular damage has been classified and validated by nailfold videocapillaroscopy (NVC) in specific and progressive scleroderma patterns ("Early", "Active", "Late") (1-5).
Objectives: Aim of this study was to retrospectively compare detailed MCTD nailfold capillary abnormalities with those of SSc patients at first visit, and to monitor MCTD capillary changes over time.
Methods: Ten patients (mean disease duration 6.4±4.2 years, mean age 50±19 years,) affected by MCTD (Kasukawa's criteria) were enrolled. Patients with either anti-extractable nuclear antigen positivity different from U1RNP or anti-dsDNA antibodies were excluded. Main capillary parameters (scores of enlarged capillaries, giant capillaries, microhemorrhages, capillary ramifications, as well as absolute number of normal and total capillaries per linear millimetre) were assessed in MCTD patients at their first NVC analysis (T0), and during a three year follow-up. Furthermore, NVC parameters were compared at T0 with 10 random SSc patients matched for disease duration (6.4±4.2 years) and age (51±17 years). Statistical analysis was performed by non parametric tests.
Results: The capillaroscopic scores of enlarged capillaries, giant capillaries and microhemorrhages were found significantly higher in SSc versus MCTD patients at T0 (2.50±0.5 vs 1.90±0.6 p=0.04, 1.63±0.7 vs 0.70±0.7 p<0.02, 1.25±0.7 vs 0.70±0.7 p=0.05, respectively). Moreover, the absolute number of both total capillaries and normal capillaries were found significantly lower in SSc versus MCTD patients (5.8±1.9 vs 7.6±1.6 p=0.04 and 0.45±1.0 vs 3.03±2.9 p= 0.009). On the contrary, no statistically significant difference was observed at T0 for the other capillary parameters (including capillary ramifications) between the two groups of patients. With the limit of a different pharmacological background among patients, no statistically significant variation of the scores, as well as of the absolute value of the above reported capillary parameters was observed during the 3 years of follow-up in MCTD patients. No statistically significant correlation was observed between capillary parameters and MCTD clinical aspects (Raynaud phenomenon, dysphagia, dyspnoea, sclerodactily, sicca syndrome, teleangectasias and artharlgia) at first visit and during follow-up.
Conclusion: In a limited cohort of MCTD patients with an average disease duration of 6.4 years and a follow-up of three years, the nailfold microvascular damage does not seem to be significantly progressive. Patients with MCTD seem to show less enlarged/giant capillaries, and larger absolute number of total and normal capillaries than SSc patients.

REFERENCES

[1] De Holanda Mafaldo DA, et al. Lupus. 2007; 16:254–8.
2.. Cappelli S, et al. Semin Arthritis Rheum. 2012; 41:589-98.
[3] .Cutolo M. et al. Best Pract Res Clin Rheumatol 2008; 22:1093-108.
[4] .Cutolo M. et al. J Rheumatol. 2000; 27:155-60.
[5] Sulli A, et al. Arthritis Rheum. 2012;64:821-5.

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AB0655 SCLERONET®: A PATIENT-CENTERED MULTIDISCIPLINARY APPROACH TO SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) is a rare connective tissue disease which may affect almost the whole body[1]. Because of its clinical complexity and heterogeneity, a multidisciplinary approach is helpful to patients.
Objectives: The project aims at providing evidence that a multidisciplinary approach allows to early detect and rightly treat diseases linked to SSc determining an improvement of the Quality of Life (QoL) for patients.
Methods: GILS, the Italian SSc Patient Organisation, selected 4 expert centers in Milan (where over one thousand patients are treated), among those able to diagnose and cure SSc in its different and difficult aspects. Inside these hospitals excellences have been identified: immuno-rheumatologists (overall management of SSc), cardiologists (cardio-pulmonary involvement and Pulmonary Arterial Hypertension - PAH), maxillofacial and plastic surgeons (lipofilling), odontologists (difficult dental cure due to microstomia), dermatologists (prevention of skin cancer), ophthalmologists (dryness of the eye), vasculars (digital ulcers - DUs), pneumologists (lung fibrosis), gynaecologists (dryness of the vagina) and nutritionists (malabsorption). Specialists can share, care and cure inside this net. A monthly meeting is held with patient representatives (PRs). No private data are disclosed. Hospitals General and Sanitary Managers must give a positive evaluation every year in order to continue ScleroNet® project.
Results: The monthly meeting allows to understand strength and threads and find the way to improve ScleroNet®. The PRs point out the unmet needs[2], to keep ScleroNet® patient-centered and to focus the attention on the QoL whose improvement has been described by patients but not yet supported for all interventions by questionnaires.
Common inclusion and exclusion criteria have been established.
Cardiologists performed 110 assessments through EKG, echocardiography and cardiopulmonary exercise testing. These tests gave the following diagnosis: 16 non-ischemic cardiomyopathy (after BNP and troponin dosage as well as cardiac MRI) got an immunosuppressive therapy; 22 PAHs; 34 diastolyc disfunctions; 23 respiratory disease. The rest did not receive a specific diagnosis but still in follow up.
70 perioral lipofillings have been carried out: body weight rose by 2 to 3 kg after 4 months in patients with low BMI thanks to a greater mouth opening. Moreover, a better elasticity of the perioral area led to better oral hygiene, speech and self-perception.
115 patients before Anti-TNF therapy have been screened to prevent non-melanoma skin cancer; 6 the diagnosis.
10 lipofillings for DUs nonresponsive to pharmacological therapy.
UCLA/MUST questionnaires were given to selected patients in order to evaluate the GI involvement and undergo a nutritionist evaluation.
A non-rheumatologist made his first SSc diagnosis due to the personal increased knowledge.
Conclusion: ScleroNet® provides a fruitful practical support to patients in order to receive the best care and cure inside the experts centers in a

delimited area, according to their specific problems. ScleroNet® seems to enable the experts to networking specifically on SSc, giving the opportunity of sharing their knowledge. Without ScleroNet® the timing of treatment and/or diagnosis would have been delayed. Nevertheless, due to the fact that it is a work-in-progress and some experts have been enrolled in a second stage, data are available only for some interventions. The use of validated questionnaires and indicators are necessary to measure and prove the value of ScleroNet®.

REFERENCES

[1] - Kowal-Bielecka O, Fransen J, Avouac J EUSTAR Coauthors, *et al* Update of EULAR recommendations for the treatment of systemic sclerosis *Annals of the Rheumatic Diseases* 2017;**76:**1327-1339.

2 . - Smith V, Scirè CA, Talarico R, *et al* Systemic sclerosis: state of the art on clinical practice guidelines *RMD Open* 2019;**4:**e000782. doi: 10.1136/rmdopen-2018-000782

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AB0656 ANTISYNTHETASE SYNDROME: CLINICAL VALUE OF SOLOMON´S AND CONNORS´ DIAGNOSIS CRITERIA

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Background: Two antisynthetase syndrome (ASSD) diagnosis criteria sets have been proposed; both consider mandatory the presence of anti-aminoacyl transfer RNA synthetase (ARS) autoantibodies. Solomon´s criteria consider major clinical criterions (interstitial lung disease (ILD) and fulfillment of Bohan and Peter criteria for DM/PM) and minor criterions (arthritis, Raynaud´s phenomenon (RP) and mechanic´s hands (MH)) (1). In contrast, Connors criteria evaluate the presence of at least one of the previously mentioned clinical features except myositis, and includes the presence of fever without other cause (2).
Objectives: 1) To evaluate the performance of Solomon´s and Connors´ criteria in patients with clinical suspicion of ASSD or myositis and positive ARS. 2) To describe their clinical characteristics.
Methods: We performed an observational retrospective study in two centers. All patients with clinical suspicion of ASSD or myositis, and positive ARS in the myositis immunoblot (Euroimmun assay) were included.
Results: We analyzed 37 patients; 70.3% woman, with a mean age at the moment of the ARS detection of 51.4 (SD±14.0) years, median time from the first symptom to the ARS detection of 4.0 (SD±5.8) years, and time of evolution of 7.69 (SD±6.51) years. The frequency of ARS was: anti-Jo1 (n=17), anti-PL-12 (n=8), anti-PL-7 (n=4), anti-EJ (n=4), and anti-OJ (n=4).
Diagnosis criteria fulfillment and clinical manifestations:
1) Patients that met Solomon and Connors´ criteria (n=17, 45.9%):
- At disease onset: ILD (n=6, 35.9%), muscle weakness (MW) (n=5, 29.4%), and arthritis (n=4, 23.5%).
- During disease development: ILD (n=14, 82.3%); arthritis (n=13, 76.5%); MW (n=10, 58.8%); mechanic hands (n=10, 58.8%); Raynaud phenomenon (n=8, 47.0%); and fever (n=3, 17.5%).
2) Patients that only met Connors´ criteria (n=17, 45.9%):
- At disease onset: ILD (n=5, 29.4%), MW (n=3, 17.6%), or arthritis (n=5, 29.4%).
- During disease development: Arthritis (n=8, 47.0%); ILD (n=6, 35.3%); MW (n=6, 35.3%); Raynaud phenomenon (n=6, 35.3%); fever (n=5, 29.4%); and mechanic hands (n=1, 5.9%).
Relative risk (RR) of the different clinical manifestation for Solomon´s criteria fulfillment:
- MH RR=2.98 (95%CI 1.5-5.6; P=0.002), ILD RR=3.2 (95%CI 1.1-9.2; P=0.013); other manifestations does not presented significant RR.
Conclusion: More than three quarter of all patients presented as first clinical manifestation one of those included in the ASSD classic triad (ILD, MW and arthritis). These manifestations showed increasing rates during the disease development, being more frequent in patients that met Solomon´s criteria than in those who only met Connor´s criteria; more than twice as high in for ILD, and almost twice for MW and arthritis. This suggests that patients who met Solomon´s criteria, at disease onset presented incomplete clinical forms, and their clinical progression favored the criteria fulfillment. On the other hand, we cannot predict if the patients that only met Connors´ criteria are going to fulfill Solomon´s criteria; nevertheless, our results suggests it.
To conclude, our results suggest that: 1) Connors criteria might be considered for screening of ASSD; 2) Solomon´s criteria can be considered at the moment the gold standard for the ASSD diagnosis; 3) the presence of mechanic hands or ILD indicates a high probability of Solomon´s criteria fulfillment in patients with positive ARS.

REFERENCES

[1] Solomon J, et al. Jornal brasileiro de pneumologia. 2011;37(1):100-9.
[2] Connors GR, et al. Chest. 2010;138(6):1464-74.

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AB0657 ANTISYNTHETASE SYNDROME: NON-ANTISYNTHETASE ANTIBODIES, CLINICAL MANIFESTATIONS AND OVERLAPS

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Background: The antisynthetase syndromes (ASSD) are characterized by the presence of anti-aminoacyl transfer RNA synthetase (ARS) autoantibodies and clinical features including myositis, arthritis, interstitial lung disease (ILD), Raynaud's phenomenon (RP), mechanic hands (MH), and fever. Two ASSD diagnosis criteria have been developed; those proposed by Connors, and the stricter criteria proposed by Solomon (1, 2). Additionally, other symptoms of connective tissue diseases (CTD) can be present.
Objectives: To describe a series of patients with positive ARS and analyze: 1) the associated non-ARS antibodies, 2) the clinical manifestations that are not included in the different ASSD diagnosis criteria; and 3) the initial diagnosis attributed by the Rheumatologist in the clinical records.
Methods: We performed an observational retrospective study in two hospitals. All patients with clinical suspicion of ASSD or myopathy and positive ARS in the myositis immunoblot (Euroimmun assay) were included.
Results: We analyzed 37 patients; 70.3% woman, with a mean age at the moment of the first symptom of 50.5 (SD±14.0) years, and 51.4 (SD ±14.0) years at the moment of the ARS detection. The frequency of ARS was: anti-Jo1 (n=17), anti-PL12 (n=8), anti-PL7 (n=4), anti-EJ (n=4), and anti-OJ (n=4). The rate of the ASSD clinical manifestations was: arthritis (56.7%), ILD (54.1%), muscle weakness (48.6%), RP (37.8%), MH (29.7%) and fever (21.6%). Thirty-four patients (91.9%) met Connors' criteria and 17 of them (45.9%) also met Solomon's criteria.
Non-antisynthetase characteristics:
- Associated non-ARS antibodies: anti-Ro52 (n=17, 46%); anti-PM/Scl75 (n=6, 16.2%); anti-PM/Scl100 (n=5, 13.5%); anticentromere (n=3, 8.1%); rheumatoid factor (n=2, 5.4%); anti-CCP (n=2, 5.4%); and anti-DNAds (n=2, 5.4%). Other antibodies detected only once: Anti-SRP, lupic-anticoagulant, anti-Ku, anti-Mi2, Anticardiolipin, Nor90, Th/To.
- Most frequent clinical manifestations not included in the ASSD diagnosis criteria: dysphagia (n=10, 27%); dermatomyositis rash (n=9, 24.3%); and SICCA sympthoms (n=7, 18.9%).
- First diagnosis attributed by the clinicians in the medical records: ASSD (n=19, 51.35%), dermatomyositis/polymyositis (DM/PM) (n= 3), overlap syndrome (n= 3), systemic lupus erythemoatous (SLE) (n= 3), primary Sjögren´s syndrome (SS) (n=2); rheumatoid arthritis (RA) (n=2); undifferenciated-CTD (UCTD) (n=2); and Systemic Sclerosis (SSc) (n=1; 2.7%). Overlaps included 2 DM/PM-SSc and 1 DM/PM-SS, and both UCTD was described with SSc pattern. Thus, of the 18 cases not diagnosed as ASSD, 6 (33.3%) presented DM/PM diagnosis pattern and 6 (33.3%) SSc pattern.

- Additionally, when we applied the ASSD diagnosis criteria, 7 of the 18 cases (38.8%) not diagnosed as ASSD by the Rheumatologist fulfilled Solomon´s criteria.

Conclusion: In our series, the most frequent non-ASSD profiles associated to ARS positivity was DM/PM, SSc and Sjögren´s syndrome. This, considering the most frequently associated non-ARS, the most frequent non-ASSD clinical manifestations and that the most frequent non-ASSD diagnosis diagnoses or profiles described by the Rheumatologist. Our results suggest that ARS can be present in patients with other CTD without presenting ASSD, and additionally that ASSD can be present in overlaps with other CTD.

REFERENCES

[1] Solomon J, et al. Jornal brasileiro de pneumologia. 2011;37(1):100-9.
[2] Connors GR, et al. Chest. 2010;138(6):1464-74.

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AB0658 ROLE OF NAILFOLD CAPILLAROSCOPY IN MONITORING LUNG INVOLVEMENT OF SYSTEMIC SCLEROSIS

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Background: The usefulness of capillaroscopy in the follow-up of scleroderma (SSc) patients and the possible prognostic role for the appearance of visceral involvement is suggested by many authors but still under debate.

Objectives: The aim of this study was to assess the role of monitoring capillaroscopic abnormalities (qualitative and semiquantitative) in relation with parameters of interstitial lung involvement and pulmonary arterial hypertension(PAH).

Methods: Longitudinal prospective study, 118 SSc patients, follow-up 2000-2017 based on MEDS evaluation sheets. Student t-test/Mann-Whitney test, chi-square test were used to evaluate differences across subgroups. Pearson's bivariate correlation/Spearman's rank correlation coefficient were used to evaluate the association between variables. Nailfold videocapillaroscopy (NVC) was performed by a trained physician: qualitative (scleroderma pattern) and semiquantitative scoring (microangiopathy evolution score-MES) were evaluated.

Results: 118 patients were included, 103 females (87,29%), 50,58(12,71) years old at diagnosis, 53.39% diffuse subset, mean disease duration 2,81(4.3) years, mean follow-up duration 4.42(3.16)years. At baseline 43.22% of the patients had lung fibrosis,18.64% had PAH, 9,32% had both. At first capillaroscopic evaluation: 12.7% had early, 46.61% active and 37.29% late pattern, medium MES was 4,76(1.43).

Baseline active and late capillaroscopic pattern were correlated with lung fibrosis ($\chi2$=9.62, p=0.047) and PAH ($\chi2$=15,36, p=0.004).

A strong correlation was identified between initial MES and FVC (r=-.47, p=0.002), FEV(r=-.45, p=0.003), DLCO (r=-.51, p< 0.001) and sPAP (r=0.34, p<0.001).

At the 2nd evaluation 5.93% of the patients had early, 0.85% active and 54,24% late scleroderma pattern, mean MES was 5.88(1.74). 19.49% had one step progression of capillaroscopic pattern, 1.69% had 2 steps progression. Lung involvement worsening was defined as decrease of FVC >15%, DLCO>10%, new diagnosis of alveolitis on high resolution computerized tomography or new diagnosis of PAH.

Active and late capillaroscopic pattern were correlated with diagnosis of lung fibrosis ($\chi2$=14, p=0.007) and pulmonary hypertension at follow-up examinations ($\chi2$=14,2, p=0.007). Progression of capillaroscopic pattern at follow-up evaluations was not correlated with significant worsening of lung volumes, DLCO, sPAP. Instead, progression of MES (>1) was associated with worsening of FVC (r=0.32,p<0.001), FEV(r=0.18,p=0.04), DLCO (r=0.21,p=0.02) and new diagnosis of lung fibrosis on HRCT (r=0,19, p=0.035).

Conclusion: Active and late capillaroscopic pattern are associated with increased frequency of interstitial lung disease and pulmonary hypertension in SSc patients. Semiquantitative scoring (microangiopathy evolution score), rather then qualitative capillaroscopic assessment can have a predictive role for new involvement or worsening of previous lung involvement (especially interstitial lung disease) in scleroderma patients, confirming the putative role of capillaroscopy as biomarker in SSc.

REFERENCES

[1] Sulli A How to Score the Qualitative Capillaroscopic Patterns in Systemic Sclerosis Annals of the Rheumatic Diseases 2013;72:A11

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AB0659 CARDIOPULMONARY EXERCISE TEST (CPET) IS A POTENTIAL NON-INVASIVE METHOD TO PREDICT DISEASE PROGRESSION IN SYSTEMIC SCLEROSIS

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Background: CPET is a widely used examination to predict the prognosis of chronic obstructive pulmonary disease or post-transplant lung function, and it has also been examined in the context of respiratory tract involvement and pulmonary hypertension in systemic slerosis (SSc).

Objectives: As CPET provides a general overview of the aerobic metabolism, influenced by pulmonary, cardiac and vascular function, the purpose of this investigation was to assess if development of poor overall disease outcome could be predicted by CPET.

Methods: Twenty-nine SSc patients (M/F=5/24 DcSSc/LcSSc=16/13) were investigated repeatedly with CPET and followed for a mean of 3.7 (range 1-7) years. The clinical features of the patients were the following: alveolitis (n=15), pulmonary fibrosis (n=16), digital ulcers (n=13), 5 of them required bosentan therapy, macroangiopathy (n=8), GERD (n=26), Barrett metaplasia (n=19), gastrintestinal angiopathy (n=5), motility disorder (n=10), pulmonary artery hypertension (pPulm >40 mmHg) (n=4). The average disease duration was 8.9 years. A composite end point was set up: death or digital ulceration necessitating bosentan therapy or pulmonary hypertension (Ppulm>40mmHg) or the decrease of carbon-monoxide diffusion capacity (δDLCO) > 2%/year, or increase in pulmonary artery pressure (δPpulm) >3mmHg/year). Paralell with the CPET, conventional disease activity check-ups have been performed too (echocardiography, chest CT, resting lung function tests, clinical examinations). The correlations between the CPET mesurements and conventional findings and the predictive value of CPET parameters at the first visit to the future development of the composite end-point have been examined.

Results: Various CPET results (anaerobic threshold (AT), work rate (WR), desaturation) have significantly correlated with worsening DLCO (p<0,05; Pearson's correlation). The change of AT per year (δAT/yr) and the degree of desaturation during exercise predicted the development of poor prognostic end-point (p<0.05 with logistic regression), and the detection of desaturation at the first CPET test was associated with a higher risk of poor prognosis (OR: 5,265 [95% CI 1,077-29,38] p=0.057). In contrast, none of the standard pulmonary or cardiac parameters have proved to be predictive to the end-point in this cohort.

Conclusion: CPET parameters correlate well with the standard assessment tools, indicating that this test is feasible in SSc patients too. The changes of AT during follow-up and desaturation are predictive to the appearence of the end point designed to comprise multiple features of the disease. This makes CPET a promising non-invasive examination method to estimate the progression of disease in patients suffering from systemic sclerosis.

Disclosure of Interests: None declared
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AB0660 SEXUAL HEALTH IMPAIRMENT IN WOMEN WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Idiopathic inflammatory myopathies (IIM) are a group of disorders characterized by skeletal muscle inflammation that can cause functional impairment including sexual dysfunction.
Objectives: To assess sexual function, pelvic floor function and sexual quality of life of women with IIM compared to age-/sex-matched healthy controls (HC). To subanalyze sexual function in sexually active individuals.
Methods: In total 27 women with IIM [mean age: 54.2, disease duration: 7.3 years, dermatomyositis (DM, 10)/polymyositis (PM, 13)/necrotizing myopathy (IMNM, 3)/inclusion body myositis (IBM, 1)], who fulfilled the Bohan/Peter 1975 criteria for DM/PM, and 27 healthy women (mean age: 54.2) filled in 11 well-established and validated questionnaires assessing sexual function, pelvic floor function, quality of life, fatigue, physical activity and depression. Data are presented as mean±SEM.
Results: Compared to HC, patients with IIM had significantly higher prevalence and greater severity of sexual impairment (FSFI, BISF-W), dysfunction of pelvic floor (PISQ-12), and worse sexual quality of life (SQoL-F) (table 1). There were no significant differences in sexual function between PM and DM. Even sexually active IIM patients reported significantly greater sexual health impairment compared to sexually active HC. Sexual health impairment in IIM was associated with laboratory markers of disease activity, health status, physical activity, fatigue and depression (table 2).

Table 1.

Questionnaire: score range	IIM (n=27)	HC (n=27)	p-value	IIM SA (n=16)	HC SA (n=16)	p-value
FSFI :2(worst)-36 (best)	15.7 ±2.5	23.0 ±2.2	p=0.0296	23.8±2.6	29.6±0.8	ns
BISF-W:-16(worst)-75(best)	15.9 ±3.5	27.4 ±3.5	p=0.0212	25.2±4.3	39.2±2.3	p=0.0151
SQoL-F: 0(worst)-100(best)	21.5 ±4.5	83.3 ±2.9	p<0.0001	31.9±6.4	85.7±3.0	p<0.0001
PISQ–12: 0(best)-48 (worst)	14.0 ±1.0	8.7±0.9	p=0.0007	11.4±1.1	9.2±1.0	ns
PFIQ7: 0(best)-300 (worst)	20.5 ±6.9	6.0±2.1	ns	17.6±10.8	10.4±4.2	ns

Abbreviations: FSFI: Female Sexual Function Index; BISF-W: Brief Index of Sexual Function for Women; SQoL-F: Sexual Quality of Life Questionnaire; PISQ–12: Pelvic Organ Prolapse/ Urinary Incontinence Sexual Questionnaire short form; PFIQ7: Pelvic Floor Distress Inventory Questionnaire, SA: sexually active; ns: not significant

Table 2.

Parameter: score range	Correlated parameters	r	p-value
FIS (fatigue): 0(best)-160(worst)	FSFI (sexual function)	-0.406	p=0.0353
	BISF-W (sexual function)	-0.424	p=0.0272
	SQol-F (sexual quality of life)	-0.562	p=0.0027
	PISQ-12 (pelvic floor function)	0.459	p=0.0157
HAP (physical activity): 0(worst)-94 (best)	FSFI (sexual function)	0.429	p=0.0252
LD	FSFI (sexual function)	-0.411	p=0.0327
	BISF-W (sexual function)	-0.466	p=0.0141
BDI II (depression): 0(best)-63(worst)	PISQ-12 (pelvic floor function)	0.322	p=0.0400
HAQ (health status): 0(best)-3(worst)	PISQ-12 (pelvic floor function)	0.477	p=0.0117
	BISF-W (sexual function)	-0.411	p=0.0329

Abbreviations: FIS: Fatigue Impact Scale; BDI-II: Beck's Depression Inventory II; HAP: Human Activity Profile; HAQ: Health Assessment Questionnaire; LD: lactate dehydrogenase
Conclusion: Women with IIM reported significantly impaired sexual function, sexual quality of life and pelvic floor function than age-matched HC. Worse scores in IIM were associated with disease activity/health status, physical activity, fatigue and depression.**Acknowledgement:** Supported by AZV-16-33574A, MHCR 023728.
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AB0661 ASSOCIATION OF ANTI-MDA-5 AUTOANTIBODY WITH AUTOIMMUNE ASSOCIATED HEMOPHAGOCYTIC SYNDROMEIN DERMATOMYOSITIS

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Background: Autoimmune associated hemophagocytic syndrome (AAHS) is a rare complication in dermatomyositis (DM). We previously demonstrated by multivariate analysis that one of factors associated with mortality in AAHS is DM (OR 5.57 [95% CI 1.08–28.65], P 0.05) among connective tissue diseases (1).
Objectives: To find out underlying immunological characteristics, we examined the DM patients with AAHS.
Methods: We examined 31 new onset patients with idiopathic inflammatory myopathies (IIM) including clinically amyopathic dermatomyositis (CADM) admitted to our hospital between January 2009 and December 2018. Three patients had been diagnosed as AAHS proven by bone marrow aspiration. We examined these patient clinical and laboratory characteristics.
Results: Two patients were diagnosed as DM and one was CADM. We found that these 3 patients were associated with interstitial pneumonia. Laboratory tests of all 3 patients showed hyperferritinemia and high titer of anti-MDA5 antibody. All patients were diagnosed as AAHS by bone marrow aspiration smears. Two of them died on the 12th and on the 75th hospital day, respectively, in spite of intensive therapies.

	age/ sex	diag.	CK (n)	ferritin (n)	antibodies			
					MDA5	Ro	PM-SCL100	others*
1	63/F	DM	8430 (36-216)	59,877 (5-120)	>150	+	-	-
2	50/M	CIDM	32 (59-248)	11,498(23-250)	>150	±	±	-
3	57/F	DM	277 (41-153)	4,876 (5-120)	>150	+	-	-

* examined antibodies against Jo1, SRP, Mi2, Ku, PL-7, OJ, EJ,Tif1-γ,

Conclusion: Anti-MDA5 may relate not only interstitial pneumonia but also AAHS.

REFERENCES

[1] 1. Kumakura S and Murakawa Y: Arthritis Rheum 2014;66:2297

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AB0662 UTILITY OF NAILFOLD CAPILLAROSCOPY FOR THE EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS SPECTRUM OF DISEASES IN ASIA

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Background: The utility of nailfold capillaroscopy (NFC) has largely been evaluated in patients with Raynaud's Phenomenon (RP). However, in equatorial countries, RP occurs in only 79% (1) and 84% (2) of patients in Singapore and Malaysia respectively. In the early stages of Systemic Sclerosis (SSc), patients may develop autoantibodies or puffy fingers before the onset of RP (3).
Objectives: There is no data on the utility of NFC in patients with non-RP features suggestive of the scleroderma-spectrum of diseases (SSc, mixed connective tissues disease, dermatomyositis). We aim to compare the utility of NFC for the early diagnosis of the SSc-spectrum of diseases in patients who present with and without RP.
Methods: Patients referred to our institution for NFC evaluation from March 2010 – March 2017 were recruited. Patients with confirmed diagnosis of a connective tissue disease were excluded. Eligible patients were divided into 4 groups: (I) RP with or without positive ANA; (II) Undifferentiated non-RP features to suggest SSc-spectrum diseases and negative ANA; (III) Undifferentiated non-RP features to suggest SSc-spectrum diseases and positive ANA $\geq$1/400 and (IV) Positive SSc-associated autoantibodies without features to suggest SSc-spectrum diseases. Images were analysed at 200x magnification using a software analysis program. Patients were noted to have normal, aspecific or SSc pattern on NFC, defined by the presence of $\geq$1 giant capillary, avascular areas or >2 dilated capillaries with areas of hemorrhage.
Results: 133 patients were recruited (mean age 55 years, 87% female; 76% Chinese, 7% Malay, 10% Indian, 7% other ethnicity). ANA was positive in 74 (82.2%) patients (n=25 anti-centromere, n=3 anti-Scl70). Taking into consideration NFC patterns, the clinical outcomes were normal in 32 patients (35.6%), connective tissue disease (CTD) suspected in 33 patients (36.7%), and definite CTD in 25 patients (27.8%). Diagnostic yield for SSc-spectrum of diseases was highest in Groups I and III (Table 1).

Abstract AB0662 Table 1.

	Definite SSc-spectrum diseases n (%)	Suspected CTD n (%)	No CTD n (%)
Group I	24 (47.1%)	16 (31.4%)	11 (21.6%)
Group II	5 (31.2%)	5 (31.2%)	6 (37.5%)
Group III	14 (35.9%)	17 (43.6%)	8 (20.5%)
Group IV	2 (12.5%)	9 (56.2%)	5 (31.2%)

Conclusion: In patients without RP, NFC was most useful to confirm a diagnosis in those with undifferentiated features to suggest SSc-spectrum of diseases and positive ANA.

REFERENCES

[1] Santosa A, Tan C, Teng G, et al. Lung and gastrointestinal complications are leading causes of death in SCORE, a multi-ethnic Singapore systemic sclerosis cohort. Scand J Rheumatol 2016 Nov;45(6):499-506.
[2] Pagalavan L, Ong S. Demography, clinical and laboratory features of systemic sclerosis in a Malaysian rheumatology centre. Med J Malaysia. 2007 Jun;62(2):117-21.
[3] Englert H, Champion D, Wu J, et al. Antitopoisomerase antibody positivity predates nailfold capillaroscopy abnormalities in scleroderma. Postulated classification of 'prescleroderma'. Intern Med J. 2011 Feb;41(2):197-9.

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AB0663 ASSESSMENT OF HEALTH RELATED QUALITY OF LIFE AND FUNCTIONAL DISABILITY AMONG SCLERODERMA PATIENTS IN BANGLADESH

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Background: Systemic sclerosis (SSc) is a complex autoimmune disorder that is characterized by overproduction and deposition of collagen in the skin and visceral organs, abnormalities of the microcirculation, and autoimmunity. SSc is responsible for skin, tendon, joint, and vessel damage, which leads to disability, handicap, and worsening of quality of life.
Objectives: The objective of the study was to assess the relationship between health-related quality of life (HRQoL) and functional disability among scleroderma (Systemic sclerosis, SSc) patients.
Methods: A cross-sectional study was conducted among 78 patients in Scleroderma clinic of *BSM Medical University (BSMMU).* Patients were selected according to American College of Rheumatology/European League Rheumatism (ACR/EULAR) classification criteria for SSc. The validated Bengali version of the Short Form 36 (SF-36) and Health Assessment Questionnaire (HAQ) were used to assess the HRQol and functional disability respectively.
Results: The mean age of the patients was 36.47

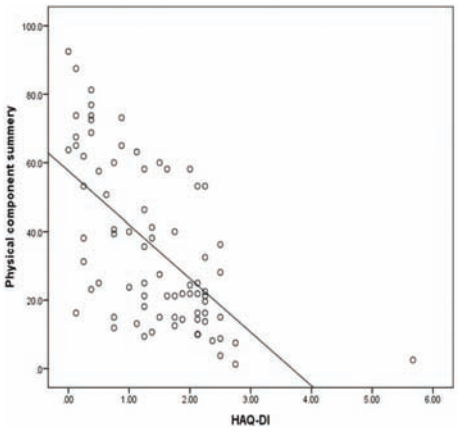
11.28 years and most of them were female (91.0%). Majority of the patients (76.9%) had diffuse whereas 23.1% patients had limited SSc. Out of 78 patients, antibody profiles were available for 63 patients. The frequency of Antinuclear, Anti-topoisomerase and Anticentromere antibody were 58.7%, 38.1%, 3.2% respectively. Sclerodactyly was present in 84.6% patients and 78.2% had pinch nose and 60.3% had calcinosis. Pitting scars of finger tips was present in 67.9% patients. Raynaud's Phenomenon was present in 89.7% patients and Musculoskeletal manifestations was present in 47.4% patients. Among the patients, 78.2% patients had microstomia and 60.3% had esophageal involvement. The mean MRSS was 21.39±13.02. SF-36 score showed that the mean Physical Component Summary (PCS) and Mental Component Summary (MCS) were 35.65 ± 23.65 and 41.36 ± 25.94 respectively. The mean HAQ-DI was found 1.40±0.95. The PCS of the SF-36 was moderately correlated with the HAQ-DI (r=-0.641, p=<0.001) and the MCS of the SF-36 was weakly correlated with the HAQ-DI (r=-0.360, p=<0.001) (Spearman's Correlation).
Conclusion: Functional disability significantly affects health related quality of life. Treatment strategies should include multi-disciplinary approach such as physiotherapy, psychotherapy, social support and occupational therapy to reduce the functional disability which will further enhance the HRQoL of SSc patients.

REFERENCES

[1] Medsger TA Jr (1997) Systemic sclerosis (scleroderma): clinical aspects. In: Koopman WJ (ed) Arthritis and allied conditions: a text-book of rheumatology, pp.1433–64. Williams & Wilkins, Baltimore.
[2] Poole JL, Steen VD (1991) The use of the Health Assessment Questionnaire (HAQ) to determine physical disability in systemic sclerosis. Arthritis Care Res 4,27–31.

Abstract AB0663 Table 1:. Outcome measure scores (SF-36 and HAQ-DI) of patients with SSc

SF-36 Scores Whole group (n=78)	DcSSc (n=60)	LcSSc (n=18)
PCS 35.65 ± 23.65	34.56 ± 22.90	39.31 ± 26.36
MCS 41.36 ± 25.94	39.82 ± 26.27	46.51 ± 24.84
HAQ DI scores		
HAQ-DI 1.40 ± 0.95	1.43 ± 0.99	1.31 ± 0.78



Abstract AB0663 Figure 1:. Correlation HAQ-DI with physical component summery (r=-0.641, p=<0.001)

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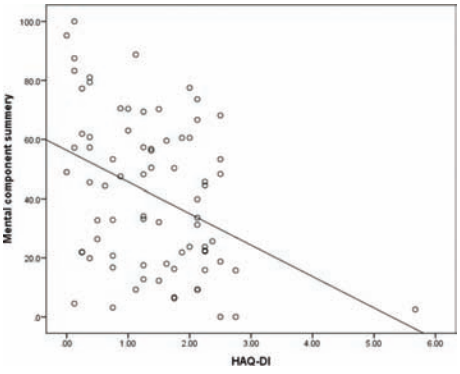
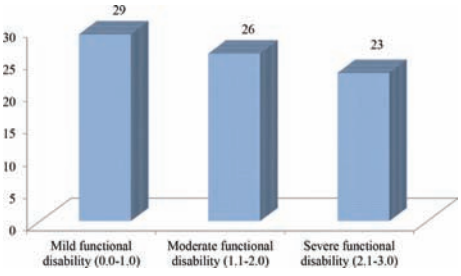


Figure 2. Correlation HAQ-DI with mental component summery (r=-0.360, p=0.001)

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Abstract AB0663 Figure 3. Distribution of SSc patients by functional disability (n=78)

Disclosure of Interests: None declared
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AB0664 REYNOLDS SYNDROME: ABOUT 7 CASES

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Background: Reynolds syndrome is a rare condition defined by the association of primary biliary cholangitis (PBC) with CREST syndrome. The frequency of scleroderma during PBC varies between 3 and 17%. The diagnosis is most often done during systematic search for autoimmune diseases associated with CBP.
Objectives: To determine the epidemiological, clinical, paraclinical and evolutionary features of Reynolds syndrome
Methods: We report 7 cases of Reynolds syndrome collected in the our department between 1996 and 2014
Results: There were 7 middle-aged women with an average age of 49.2 years (32-61 years old). The diagnosis of CREST syndrome with anti centromeric positive antibodies was retained in 6 cases. Extensive trunk sclerosis associated with diffuse sclerodacty and anti centromeric antibodies was noted in 1 case. An isolated acrosyndrome was noted in 1 case. The hepatic assessment found non icteric cholestasis in 6 patients. Anti-mitochondrial antibodies type M2 were positive in 6 cases. Liver biopsy showed histologic lesions consistent with primary biliary cholangitis PBC in 5 cases. Sjörgen's syndrome was confirmed histologically in 1 case. Autoimmune diseases (rheumatoid arthritis and lymphocytic thyroiditis) were associated with Reynolds Syndrome in 2 cases. The treatment consisted of ursodeoxycholic acid alone (N = 4), or combined with D-penicillamine (N = 1), azathioprine-associated prednisone (N = 1) or a calcium channel blocker alone (N = 1). The evolution was favorable in 2 cases. In the other 3 patients, worsening of cholestasis and complications such as oedemato-ascitic decompensation and gastrointestinal haemorrhage were noted during the course of the study. One patient died of cataclysmic gastrointestinal bleeding by rupture of oesophageal varices.
Conclusion: Reynolds syndrome is a rare entity that should be discussed in the presence of liver function disturbances in patients with CREST syndrome. Conversely, the CREST syndrome should be referred to and sought systematically in case of PBC.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8189

AB0665 OUTCOME OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SCLERODERMA, A 5 YEAR PROSPECTIVE COHORT STUDY

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Background: Systemic sclerosis (SSc) is a multi-system disorder characterized by a disturbance in fibroblast function, microvascular disease, and immune system activation, resulting in fibrosis of the skin and internal organs.
Objectives: To study changes in lung function in patients with scleroderma with ILD on treatment followed up prospectively over a period of 5 years
Methods: In this study, 73 patients with scleroderma with ILD were prospectively followed up from July 2013 to July 2018. Patients' clinical features, investigations, treatment and complications were recorded at regular interval
Results: Of 73 patients, 68 were females and 5 were males. 4 had only one visit and 11 had incomplete data. Baseline characteristics are shown in table 1. Mean PAH at baseline was 35.95±14.26 mmHg and at end of study was 39.44±14.44 mmHg. Immunosuppressant's used were MMF in 52, cyclophosphamide in 15, azathioprine in 13, and methotrexate in 17 patients. 61 patients received oral prednisolone with mean dose of 6.46±7.10 mg/day during maintenance and mean dose 15±8.95 mg/day during exacerbation of ILD. There was no statistically significant difference in mean FVC of 59 patients at baseline (59.76±16.91) and at end of the study (57.03±16.77) and in subgroup analysis of patients who received MMF ($p > 0.05$).Mean 6MWD at baseline was 370±58.83 meters and at end of study was 377±88.96 meters. Comorbidities seen were hypertension in 15, DM in 6, osteoporosis in 23 (of which one had vertebral fracture), AVN in 3 patients. 5 patients died because of ILD. 13 patients needed home O2.

Table: Mean age, duration of disease and age and follow up.

Parameter	Mean	SD
Mean age at enrollment (yrs)	43.24	11.70
Mean duration of disease (yrs)	10.02	6.86
Mean duration of ILD (yrs)	6.02	2.94
Mean duration of prospective follow up (yrs)	3.80	2.28

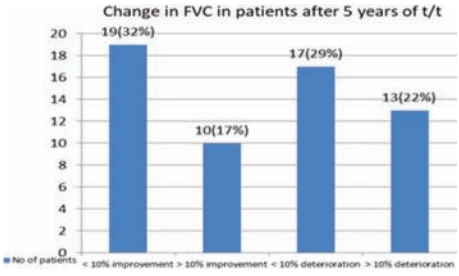


Figure 1. Change in FVC of 59 patients of SSc with ILD after 5 years of follow up

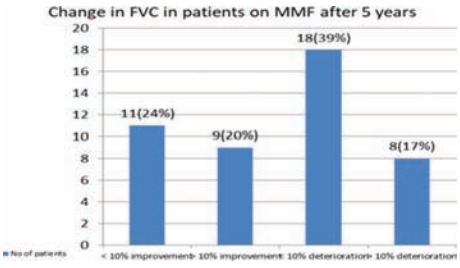


Figure 2. Change in FVC of 46 patients of SSc with ILD taking MMF after 5 years of follow up

Conclusion: This prospective study was carried out with aim to determine progression of ILD in patients with systemic sclerosis with ILD over period of 5 years.In our study, there was no statistically significant change of FVC over period of time. Worsening of lung function with deterioration in FVC >10% was seen in only 13 patients (22%) (P<0.01). Our findings are similar to study done by Le Gouellec etal in which 75 patients with scleroderma and ILD were followed over period of 72 months of which 26% patients showed significant worsening of FVC (≥ 10%)[1].In our study there statistically significant decline in DLCO and increase in PAH over period of 5 years(p>0.001). In study carried out by Le Goullec et at studying Scleroderma/ILD, there was significant decline in DLCO over period of 72 months of follow up[1]. In study done by Stephen C. Mathai et al, there was progressive increase in PAH when patients with scleroderma and ILD with PAH were followed up for period of 4 years[2]..

REFERENCES

[1] Le Gouellec N, Duhamel A, Perez T, et al. Predictors of lung function test severity and outcome in systemic sclerosis-associated interstitial lung disease. PLoS One. 2017;12(8):e0181692. Published 2017 Aug 1. doi:10.1371/journal.pone.0181692

[2] Stephan mathai etal,ARTHRITIS & RHEUMATISM,February 2009, pp 569–577 DOI 10.1002/art.24267 © 2009, American College of Rheumatology

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AB0666

ALL-CAUSE AND CAUSE-SPECIFIC MORTALITY TREND IN PATIENTS WITH SYSTEMIC SCLEROSIS: A POPULATION-BASED STUDY

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Background: Systemic sclerosis (SSc) is a disease with one of the highest mortality rates among connective tissue diseases with 5-year survival ranging from 68-88%[1]. Recent research has shown an improvement in survival for some rheumatic diseases at the population level [2, 3]. Contemporary data on mortality trends in SSc is scarse, especially at the general population level.
Objectives: 1) To investigate all-cause and cause-specific mortality in patients with newly diagnosed systemic sclerosis (SSc) compared to the general population.
2) To assess mortality trends between 2 calendar time periods, 1997–2004 and 2005–2012
Methods: Using an administrative health database, we compared all patients with new diagnosis of SSc with non-SSc individuals randomly selected from the general population matched for sex, age, and time of entry into the study. The study cohorts were divided into 2 groups based on the year of diagnosis ("early cohort [1997–2004] and "late cohort" [2005–2012]). The outcome was death (all-cause and cause specific including cancer, cardiovascular disease [CVD], infections, renal disease, pulmonary disease and other causes) during the follow-up period. Hazard ratios (HR) were estimated using Cox proportional hazards models, first adjusted for age, sex, and entry cohort time and then adjusted for selected baseline covariates (health care resource utilization, medications, pre-existing comorbidities, and socioeconomic status), based on a purposeful selection algorithm.
Results: We included 874 patients with SSc (83.6% female and mean age of 54.19 in the early cohort, and 81.7% female and mean age of 55.32 in the late cohort) and 8,740 non-SSc individuals in this study, contributing 4,083.8 and 47,515.8 person-years of follow-up, respectively. We observed 168 deaths in the SSc cohort, and 504 deaths occurred in the non-SSc cohort during the follow-up. Overall, the age-, sex-, and entry time–adjusted all-cause mortality HR in the SSc cohort was 4.47 (95% CI 3.72–5.37), and the fully adjusted remained significant [HR=2.87 (95% CI 2.35-3.50)]. Moreover, there was excess mortality due to CVD-related causes in the age-, sex-, and entry time–adjusted model (HR= 2.65 [95% CI 1.68 – 4.18]), but it did not persist in the fully adjusted model (HR= 1.52 [95% CI 0.93-2.48]). There was no significant difference in other cause-specific mortalities, including cancer mortality (HR=0.91 [95% CI 0.56-1.49]). As a consequence of the residual disclosure policy of Population Data BC to ensure patient confidentiality, we were not allowed to report on the deaths due to infection, renal or pulmonary disease, as <5 deaths were associated with each outcome. There was no improvement in all-cause mortality between the early and late cohort (fully adjusted HR= 3.73 and 95% CI 2.49-5.59; HR 2.51 and 95% CI 1.88-3.34, respectively).
Conclusion: This population-based study showed that people with SSc have a 3-fold increase risk of death when compared with the general population. The risk of death has not improved over time and this calls for further research to close this gap.

REFERENCES

[1] Nikpour M, Baron M. Mortality in systemic sclerosis: lessons learned from population-based and observational cohort studies. Curr Opin Rheumatol. 2014;26(2):131-137.

[2] Tan, J. A., Choi, H. K., Xie, H., Sayre, E. C., Esdaile, J. M. and Aviña Zubieta, J. A. All Cause and Cause Specific Mortality in Patients With Granulomatosis With Polyangiitis: A Population Based Study. Arthritis Care Res. 2019. 71: 155-163.

[3] Zhang Y, Lu N, Peloquin C, et al. Improved survival in rheumatoid arthritis: a general population-based cohort study *Annals of the Rheumatic Diseases* 2017;76:408-413.

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AB0667

SPECIFICITY OF ANTI-TRNA SYNTHETASE AUTOANTIBODIES CORRELATED WITH CLINICAL COURSE AND PROGNOSIS OF MYOSITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is associated with mortality among patients with idiopathic inflammatory myopathy (IIM). Anti-amino-acyl-tRNA synthetase (anti-ARS) autoantibodies have been identified highly specific for IIM and coincidence of ILD. It has been identified that non-Jo1 positive anti-ARS patients may have decreased survival rate. However, differences of characteristics and prognosis in myositis-associated ILD with an individual anti-ARS autoantibody have not been clarified.
Objectives: To compare the characteristics and cumulative survival of myositis-associated ILD with different positivity of anti-ARS antibodies.
Methods: We investigated retrospectively all consecutive patients with myositis -associated ILD evaluated from 1999-2017.All autoantibodies were screened by using RNA and protein immunoprecipitation assays. Demographic data, laboratory findings and chest computed tomography (CT) images were obtained.
Results: Among 105 patients with myositis-associated ILD, enrolled, 47 had anti-Jo1 antibody and 58 had non-Jo1 antibody: anti-EJ (n=20), anti-PL12 (n=12), ant-PL7 (n=11), anti-KS (n=8) and anti OJ (n=7). The diagnosis at first visit were polymyositis (PM; n=28), dermatomyositis (DM; n=42), clinically amyopathic dermatomyositis (CADM; n=3) and antisynthetase syndrome (ASS; n=31). Most common causes of death in this study were exacerbation of ILD (n=10, 71.4%). Anti-Jo-1 positive patients had better ILD prognosis than non-Jo1 patients (log rank test, p = 0.03). The prevalence of rapidly progressive ILD (RP-ILD) and upper lung field lesions in CT scans were significantly higher in anti-EJ positive patients (p=0.02 and p=0.05, respectively). Although the prognosis of ILD was not significantly different among 6 anti-ARS antibodies, anti-EJ positive patients had poor ILD prognosis than anti-Jo1 patients with the 5-year unadjusted cumulative survival was 73% and 95%, respectively.
Conclusion: Our data confirm that the characteristics and outcomes of myositis-associated ILD are distinct by anti-ARS antibodies and highlighted that anti-EJ antibody positivity associated with relatively poor prognosis and RP-ILD.

REFERENCES

[1] McHugh NJ, Tansley SL. Nat Rev Rheumatol. 2018; 20;14(5):290-302.
[2] Aggarwal, R. et al. Ann. Rheum. Dis. 2014; 73: 227–232
[3] Shi J. et al. J Rheumatol 2017; 44: 1051-1057
[4] Takanashi S, et al. Rheumatology (Oxford). 2019 Jan 8. doi: 10.1093/rheumatology/key420.

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AB0668

ASSOCIATION OF ANTI-RNA POLYMERASE III ANTIBODY AND BREAST IMPLANTS RUPTURE IN ITALIAN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Several epidemiological studies have investigated the link between silicone breast implants (SBI) and Systemic Sclerosis (SSc). Although discordant data were reported, a recent analysis of SBI followed by United States Food and Drug Administration post approval studies, including nearly 100,000 individuals, described an association of SBI with a higher rate of SSc (Standardized incidence ratio 7.00), compared with normative data[1]. The analysis of clinical associations in patients with SSc is complicated by the heterogeneity of the disease, both on immunological and clinical terms. Interestingly, a specific association of anti-RNA polymerase III antibody (anti-RNAP3) and SBI in Japanese patients with SSc was described in a single-center cohort[2]. Moreover, an association of anti-RNAP3 with breast cancer, particularly when synchronous with SSc onset, was also demonstrated[3,4].
Objectives: To evaluate the association of SBI with SSc in Italian patients classified according to their SSc-related autoantibodies.
Methods: 562 consecutive women with SSc, classified according the 2013 ACR/EULAR criteria, were evaluated for the presence of SSc-specific autoantibodies (anti-Topoisomerase-I (anti-Topo-I), anticentromere (ACA), and anti-RNAP3) in two Italian University centres. For each patient, history of breast cancer and SBI were recorded.
Results: Anti-RNAP3 antibodies were found in 4.6%, anti-Topo-I in 22.2% and ACA in 57.3% of total SSc women (Table 1). Comparing anti-RNAP3+ vs anti-RNAP3- patients, a significantly higher frequency of breast cancer (15.3% vs 4.1%; p=0.026), SBI (11.5% vs 1.1%; p=0.006) and SBI rupture (11.5% vs 0.2%; p=0.0003) was found. Notably a higher rate of SBI rupture without breast cancer in anti-RNAP3+ vs anti-RNAP3- was also noted (2/22 (9.1%) vs 0/514 (0%); p=0.0016).
Conclusion: In this large Italian cohort, a higher prevalence of SBI and SBI rupture in anti-RNAP3+ compared to anti-RNAP3- SSc patients was confirmed, regardless of the history of breast cancer. This preliminary observation should be confirmed in multicentre cohorts, particularly regarding the connection between SSc and SBI rupture.

REFERENCES

[1] Coroneos CJ, et al. Ann Surg 2019;269:30-6.
[2] Saigusa R, et al. J Dermatol 2016; 43:808-10.
[3] Moinzadeh P, et al. Arthritis Res Ther. 2014;16(1):R53.
[4] Lazzaroni MG, et al. J Rheumatol. 2017;44(5):639-47.

Table 1. *Frequency of SBI, SBI rupture and breast cancer in 562 SSc patients, divided according to the autoantibody status.*

	Patients	SBI	SBI rupture	Breast cancer
ACA	322	4	1	16
Anti-TopoI	125	0	0	2
Anti-RNAP3	26	3	3	4
Others	89	2	0	4
Total	**562**	**9**	**4**	**26**

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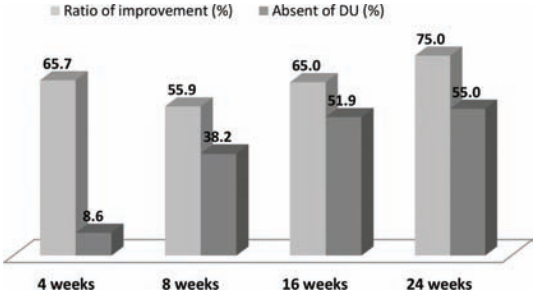
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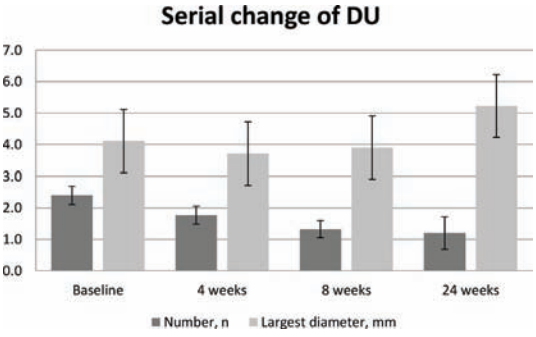
THE EFFECTS OF BOSENTAN FOR TREATMENT OF DIGITAL ULCER IN KOREAN PATIENTS WITH SYSTEMIC SCLEROSIS: PROSPECTIVE, MULTICENTER, OPEN-LABEL TRIAL

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Background: Bosentan is an orally administered dual endothelin-1 (ET-1) receptor antagonist approved in the EU for reducing the number of new digital ulcers in patients with systemic sclerosis (SSc) and ongoing digital ulcer (DU). Oral bosentan therapy was beneficial and generally well tolerated in patients with DU associated with SSc. A total of 3 RCTs were identified. The first two were high quality (RAPIDS-1 and RAPIDS-2) with 122 and 188 patients and treatment durations of 16 and 24 weeks, respectively. Both studies showed that, compared with placebo, bosentan significantly reduced the number of new ulcers; however, it did not have an effect on the healing of preexisting ulcers and pain.
Objectives: This study evaluated the efficacy and safety of bosentan in DU secondary to SSc in Korean patients.
Methods: From December 2013 to Decemver 2017, a prospective, multicenter, open-label trial was performed to investigate the complete healing of DU and tolerability of bosentan in Korean patients with SSc. The SSc

patients were included as having active DU or pulmonary arterial hypertension who had active DU in the last 3 months. A DU was defined as an area with visually discernable depth and a loss of continuity of epithelial coverage, which could be denuded or covered by a scab or necrotic tissue. If the area was denuded, the ulcer was designated active. If denudation could not be judged because of the presence of overlying scab or necrotic tissue, ulcers presenting with features, including underlying pain, based on investigator clinical judgment to be consistent with loss of epithelialization, epidermis, or dermis, and requiring treatment, were designated as active. The effectiveness and tolerability of bosentan was monitored within 24 weeks of study treatment, while healing of DU, largest diameter and the new incidence were also assessed up to week 24.





Results: The primary objective of this study was to assess the efficacy of bosentan in reducing DU including the complete healing rate. Secondary endpoints included development of new DU, assessment of discontinuation, measures of nailfold capillaroscopic (NFC) change. Thirty-five SSc patients were enrolled and seventeen patients were included in the NFC analysis. Mean age was 50.5 year-old, 85.7% was woman, 68.6% were diffuse type of SSc, mean mRSS was 15.4 and mean disease duration was 77.9 months. Among 35 patients, 20 patients was finished 24 weeks treatment duration. The main reason for discontinuation is when the patient wants to stop because of the full effect of the drug (n=12, 80%). The side effects of the drug occurred in 4 cases during the treatment period. The mean number of DUs before treatment was 2.4 and was statistically decreased to 1.2 (p=0.001). From the 4th week of bosentan treatment, improvement of DU number was observed in 65.7% and complete healing was observed in 55% at 24 weeks. However, the mean size of largest DU diameter, remained at the end of treatment, was slightly increased from 4.1 to 5.2 mm, with no statistical significance. There was no statistically significant difference in the semi-quantitative changes of NFC before and after bosentan treatment.
Conclusion: Administration of bosentan over 24 weeks was statistically associated with complete healing and significant reduction in net number of DU in Korean patients with SSc. However, the size of the remaining DU, that did not respond to bosentan, has rather increased.
Disclosure of Interests: None declared
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AB0670 INTESTINAL ANGIODISPLASIAS IN THE PATIENT WITH SYSTEMIC SCLEROSIS

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Background: Gastric angiodysplasia and the typical "watermelon stomach" aspect is one of the most characteristic vascular manifestations in systemic sclerosis (SS). These angiodysplasias can affect the intestine ocasionally as well as the stomach.
Objectives: Description of a series of 5 patients with systemic sclerosis and presence of intestinal angiodysplasia (IA).
Methods: Retrospective unicentric observational study in a tertiary hospital. Demographic data, comorbidities, manifestations of the disease, serological profile, concomitant treatments and bleeding manifestations, as well as endoscopic findings and received treatment were collected. Descriptive statistics was used to present the data.
Results: We reviewed the medical records of the 88 patients with a diagnosis of SS followed up in the Rheumatology Service. Five cases (5.6%) of IA were identified (4 women and one male), with a mean age of 73 years (SD 13.71). In one case, the diagnosis of SS and IA was simultaneous. In the remaining 4 cases, the mean time from the diagnosis of ES to the diagnosis of the IA was 7.75 years (SD 2.6). Regarding the clinical presentation, 4 of the cases presented as anemia with iron deficiency. In these cases IA were found in the endoscopic studies. In one case, IA were a finding in the context of the study of diarrhea. In 4 of the cases, the IA were in the small intestine, so the diagnosis was made using an endoscopic capsule. In one case they were found in the colon, so the diagnosis was by colonoscopy. Only one of the cases of angiodysplasias in the small intestine required specific treatment with argon laser by enteroscopy. One case required a transfusion of packed red blood cells. In the remaining cases, treatment with oral or intravenous iron therapy was enough. In all 5 cases, it was a limited form of the SS with the presence of anticentromere antibodies. All cases presented Raynaud's phenomenon, 3 of them with digital ulcers. Three of the cases associated primary biliary cholangitis, 3 cases pulmonary hypertension, 3 cases peristaltic involvement, 1 case interstitial lung disease and 1 case restrictive cardiomyopathy. As comorbidities, we identified 1 case of essential mixed cryoglobulinemia associated with hepatitis C virus, 2 cases of valvular heart disease, 2 cases of atrial fibrillation.
Conclusion: The extragastric localization of the angiodysplasias should be taken into account in the patient with SS and iron deficiency, especially in those with a limited form of the illness and positive anticentromere antibodies
Disclosure of Interests: Carolina Merino Argumánez: None declared, Olga Rusinovich: None declared, María Espinosa: None declared, Consuelo Ramos Giráldez Speakers bureau: Sanofi, Carmen Barbadillo Mateos: None declared, José Luis Andréu Sánchez: None declared, Hilda Godoy: None declared
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AB0671 DISCORDANCE IN ANTI-TIF-1γ ANTIBODIES DETECTION THROUGH COMMERCIAL KIT IN COMPARISON WITH HOMEMADE IMMUNOBLOT: CLINICAL EVALUATION

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Background: The antibody against the transcriptional intermediate factor 1γ (Anti-TIF1γ or Anti-p155), is considered specific for dermatomyositis (DM) and its a marker of cancer risk. Our center carries out the determination of Anti-TIF1γ by a homemade immunoblot (IB) technique with a 155 kDa TIF1γ human recombinant protein (OriGene). Currently there is

a commercial technique of IB to detect TIF1γ (Euroimmun), however, commercial kits sometimes elaborate antigens without using whole protein structure. To date, there are no studies that study the agreement between the commercial kit and homemades IB.
Objectives: 1-To compare the commercial IB results of Anti-TIF1γ with homemade IB.
2-To describe and compare the clinical characteristics of the patients analyzed by both techniques.
METHODS: Observational retrospective study that included adult patients with some determination of Anti-TIF1γ antibodies since 2014 in two tertiary-level university hospitals. We collected demographic and clinical data of all patients. Taking into account their diagnoses we grouped them into: Cancer Associated Myositis (CAM), DM without cancer, Systemic Autoimmune Diseases (SAD) non-DM and other diagnoses. Subsequently, the clinical agreement with the IB results of Anti-TIF1γ performed by commercial (cIB) and homemade (hIB) technique were analyzed. A p value < 0.05 was considered statistically significant.
RESULTS: 48 patients were recruited (77.1% women). 13 had diagnosis of CAM, 19 of DM without cancer, 7 of other non-DM EAS, and 9 had other diagnoses.
Of all DM (CAM and DM without cancer), 12 were positive for both techniques. 5 presented discordant results (4 hIB positive with negative cIB and 1 cIB positive with negative hIB). 15 DM were negative for the two techniques, of which 8/15 had other antibodies associated with Autoimmune Myopathy (3 NXP-2, 1 Mi2, 1 MDA5, 1 SAE, 1 Jo1 and 1 Ro52). When we analyzed patients with CAM with both techniques, 10/13 presented positive hIB vs 8/13 cIB positive. DM without cancer, 6/19 had positive hIB vs 5/19 cIB positive. The sensitivity and specificity of each test was evaluated in CAM and DM without cancer, being 61.5% and 73.7% respectively for cIB (p = 0.071), compared to 76.9% and 68.4% for hIB (p = 0.029).
In non-DM SAD group, 1 patient had positive determination for both techniques, 3 had positive cIB with negative hIB, and 3 cIB negative with positive hIB. We also found other antibodies in 6/7 patients with non-DM SAD. The 9 patients with other diagnoses were: 1 positive for both techniques and 8 positive for cIB and negative for hIB.
CONCLUSIONS: Homemade IB with 155 kDa recombinant protein was superior to cIB to detect TIFγ in our serie of patients with CAM. This could have clinical implications in screening and early detection of neoplasia that affect false negative by cIB.
A positive cIB in patients not suspected as a SAD were negative for hIB in the major part of cases.
It would be recommended to check the commercial IB using homemade IB, due to its known clinical-therapeutic implications.
Disclosure of Interests: Ana Milena Millán Arciniegas: None declared, M. ANGELES MARTINEZ: None declared, ANAIS MARISCAL: None declared, ANDRES BAUCELLS: None declared, Leticia Alserawan: None declared, Ernesto Trallero: None declared, Cesar Díaz-Torné: None declared, Ana Laiz Consultant for: Lilly, Novartis, AbbVvie, MSD, UCB and Janssen, Speakers bureau: Lilly, Novartis, Abvvie, MSD, UCB and Janssen, Berta Magallares: None declared, Patricia Moya: None declared, HyeSang Park: None declared, Andrea García-Guillén: None declared, Sycille Jeria: None declared, DAVID LOBO: None declared, Albert Gil: None declared, Coral Gozalvez: None declared, Susana P. Fernandez-Sanchez: None declared, Laura Martínez-Martínez: None declared, Esther Moga: None declared, Hector Corominas: None declared, Cándido Juarez: None declared, Ivan Castellví Consultant for: I received fees less than 5000USD as a consultant for Kern and Actelion, Paid instructor for: I received fees less than 2000USD as a instructor for Boehringer -Ingelheim, Novartis and Gebro, Speakers bureau: ND, Albert Selva-O'Callaghan: None declared
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AB0672 RENAL INVOLVEMENT IN PATIENTS WITH DERMATOMYOSITIS AND POLYMYOSITIS

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Background: Dermatomyositis (DM) and polymyositis (PM) are characterized by moderate to severe muscle weakness and inflammatory lesions in the muscle. They lead to frequent, and, in some cases, life-threatening extramuscular (lung, cardiac, neurologic, kidney) complications.
Objectives: The aim of this study was to determine the incidence, the severity, the course and outcome of renal diseases in patients with DM or PM.
Methods: We identified 84 patients (68 female, 16 male) with the diagnosis of DM and 23 (14 female, 9 male) with PM. Diagnosis of DM and PM was based on the ENMC classification. The mean follow-up was 5,6 ± 3,8 years. Evaluation of extramuscular involvement was mainly performed in the presence of suggestive clinical signs. Autoantibodies were detected by ELISA. Acute kidney injury (AKI) was defined as an acute doubling of serum creatinine level. Chronic kidney disease (CKD) was defined if an estimated glomerular filtration rate (eGFR) <60 mL/min on at least 2 measurements 3 months apart.
Results: Of the 107 patients, 26 were found to have suffered varying degree of renal involvement. All the 26 patients (22 patients with DM and 4 with PM) had varying degree of proteinuria and haematuria. Renal involvement consisted of AKI in 8 patients and CKD in 18 patients. Among patients with AKI, 6 (75%) progressed to CKD, including 2 patients who reached end-stage renal disease (ESRD). Acute tubular necrosis with renal failure developed in 3 patients with PM and in 4 patients with DM. In descriptive analysis, male sex, cardiovascular risk factors, the severity of muscle injury, heart involvement, and initial proteinuria (>0.3 g/d) were associated with AKI. In multivariate survival analysis, only age at disease onset, male sex, history of cardiovascular events, and a previous episode of AKI were identified as risks factors of CKD. Although the proteinuria and haematuria responded to therapy (except in 2 cases), the creatinine clearance remained decreased during the treatment. Kidney biopsy was performed in 16 patients and showed chronic tubulointerstitial nephritis (7 cases), minimal change disease (2 cases), focal segmental glomerulosclerosis lesions (3 cases), IgA nephropathy (2 cases), membranous nephropathy (1 case), and amyloid deposits (1 case).
Conclusion: Our data clearly indicate that DM and PM are associated with a wide range of renal disorders. Renal damage was noted in 24,3% of all included patients. AKI occurred in 7,48% of cases and CKD developed in 16,82% of the patients. AKI and CKD contribute to an increased morbidity in these patients. AKI and CKD are probably not a direct manifestation of PM or DM, but rather result from drug and myoglobin-induced renal damage. However, AKI and CKD contribute to increased morbidity in these patients
Disclosure of Interests: None declared
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AB0673 CHARACTERISTICS OF THE CAPILLAROSCOPY PATTERN IN SYSTEMIC AUTOIMMUNES DISEASES

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Background: Nailfold capillaroscopy (CP) is a simple, safe, low cost and non-invasive screenig test and together with the study of autoantibodies, is useful in the diagnosis of systemic sclerosis (SSc). It demonstrates certain specific patterns which are characterized by the presence of dilated capillaries, haemorrhages and avascular areas. Other systemic autoimmune diseases (SAD) do not have a specific pattern, but certain alterations in the morphology of the capillaries such as increased tortuosity have been described in SLE. In other diseases such as mixed connective tissue disease (MCTD), inflammatory myopathies and overlap syndromes, findings may be different to the pathological findings consistent with scleroderma pattern.
Objectives: Description of nailfold capillaroscopic findings in different SAD.
Methods: The study included 255 patients referred for CP that was performed in 8 fingers, and always by the same observer. The following findings were considered as "scleroderma pattern": Local or global capillary loss (> 20%), haemorrhages: two or more in at least two fingers and enlarged capillaries: two or more capillary with double caliber or more in at least two different fingers. Abundant evidence of tortuosity (> 20%) as ringlets tangles and no evidence of disorders described above, was considered nonspecific, tortuous pattern or suspects SAD. Statistical analysis was performed with SPSS 19.0 program.
Results: CP was performed in 255 patients, 31 males (12%) and 224 (88%) women. 23 patients (9%) had a diagnosis of SSc, 6 patients (2%) of SLE, other 6 (2%) of Sjögren's syndrome, 7 (3%) of MCTD, 4 (1.5%) of inflammatory myopathy and 2 (0.8%) of overlap syndrome. 18 patients (7%) had positive ANA and Raynaud without another data suggestive of SAD, 76 patinents with primary Raynaud (30%) and 66 patients (26%) with a miscellany of other diseases such as antiphospholipid syndrome, vasculitis, fibromyalgia and psoriatic arthritis. Also, 29 patients (12.4%) were sent for performing CP for suspected systemic sclerosis and 16

patients (6.3%) presented with only positive anti-centromere. CP was normal in 191 patients, while in 45 patients scleroderma pattern was observed and in 19 patients nonspecific pattern suggestive of SAD was seen. Capillaroscopic findings: in each of the 23 patients diagnosed with SSc, 21 patients had scleroderma pattern. Of the 6 patients with SLE, CP was normal in 4 patients, while one patient had abundant tortuosity. Likewise, the 6 patients with Sjögren's syndrome, only one patient had a nonspecific pattern suggestive of SAD. Of the 7 patients with MCTD, four had normal CP, two had a scleroderma pattern and one had tortuous pattern. The 2 patients with overlap (myopathy-scleroderma and Lupus-scleroderma) both had a pathological CP with scleroderma pattern.

Conclusion: Our study demonstrates that the evidence of scleroderma pattern is very specific of SSc. However, in certain diseases such as MCTD, overlap syndromes and inflammatory myopathies, we can also see this pattern. In other SAD, CP is usually normal or may show some nonspecific changes.

References: The contribution of capillaroscopy to the differential diagnosis of connective autoimmune diseases. Best Practice & Research Clinical Rheumatology Vol. 21, No. 6, pp. 1093–1108, 2007

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AB0674 RETROSPECTIVE STUDY OF A COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS IN A TERTIARY CARE HOSPITAL

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Background: Systemic sclerosis (SS) is an autoimmune disease of unknown etiology, characterized by the presence of fibrosis and vasculopathy in skin and multiple internal organs such as the lungs, the kidneys and the digestive tract. The course of the disease is unpredictable and could remain relatively stable or have a rapid evolution. Multiple studies have been carried out to determine the clinical characteristics and survival prognosis on SS patients.

Objectives: To analyze the demographic characteristics, clinical features, treatment and prognosis in a SS disease cohort.

Methods: We performed an observational and retrospective study of patients whit SS. The patients had been attended by the Rheumatology department of a tertiary care hospital. We collected demographic, clinical and analytical variables, as well as treatment and prognosis. We classified the disease employing the LeRoy and Medsger, VEDOSS criteria and 2013 ACR/EULAR criteria.

Results: Of our 43 patients, 36 (83.7%) were female and only 7 (16.3%) were male. The average age was 60.4 years (SD 15.6), the average age at diagnosis was 53.3 years (SD 17.6) and the mean time of evolution of the disease was 7.9 years (SD 6.3). Of all the patients, 3 patients (6.9%) died, the mean age at death being 53.6 years (SD 23.7) and the mean time from diagnosis to death of 19 years (SD 10.1). The most frequently ocurring presentation was limited SS (with 18 patients (41.9%), followed by preescleroderma with 14 patients (32.6%), diffuse SS with 6 patients (14%) and escleroderma sine escleroderma with 2 patients (4.7%). Three patients (7%) were labeled with MCTD. SS was associated with other autoimmune diseases in 20% of patients. Five (11.6%) patients developed neoplasms throughout the course of the study. The rest of the clinical characteristics are listed in Table 1 and 2, as well as the strength of association of these with the type of SS, calculated using chi square and Fischer test.

Conclusion: Worthy of noting in our cohort is the absence of scleroderma in more than 40% of our patients, probably because the new criteria have allowed us to diagnose the disease at an earlier stage and also due to the scarce frequency of puffy fingers with respect to other larger series. Digestive involvement was the most frequent visceral manifestation, followed by pulmonary manifestations, specifically interstitial lung disease (ILD). Despite the small sample size, lung disease was significantly associated with the two forms of systemic sclerosis, but not with the antibody pattern. Both the ILD and the pulmonary arterial hypertension (PAH) were more frequent in patients with SSd. Mortality in all cases was due to interstitial lung involvement. As is frequently described, SS is associated with other systemic autoimmune diseases, constituting an overlap syndrome.

REFERENCES

[1] Cañete Crespillo, J. (2008). *Manual SER de las enfermedades reumáticas*. Madrid: Editorial Médica Panamericana.

[2] Dougherty, D., Kwakkenbos, L., Carrier, M., Salazar, G., Assassi, S., Baron, M., Bartlett, S., Furst, D., Gottesman, K., van den Hoogen, F., Malcarne, V., Mouthon, L., Nielson, W., Poiraudeau, S., Sauvé, M., Boire, G., Bruns, A., Chung, L., Denton, C., Dunne, J., Fortin, P., Frech, T., Gill, A., Gordon, J., Herrick, A., Hinchcliff, M., Hudson, M., Johnson, S., Jones, N., Kafaja, S., Larché, M., Manning, J., Pope, J., Spiera, R., Steen, V., Sutton, E., Thorne, C., Wilcox, P., Thombs, B. and Mayes, M. (2018). The Scleroderma Patient-Centered Intervention Network Cohort: baseline clinical features and comparison with other large scleroderma cohorts. Rheumatology, 57(9), pp.1623-1631.

[3] CLINICAL FEATURES AND PROGNOSTIC FACTORS FOR SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE. (2018). Respirology, 23, pp.155-155.

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AB0675 DECREASED CAPILLARY DENSITY IS ASSOCIATED WITH DECREASED HAND MOBILITY IN SYSTEMIC SCLEROSIS

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Background: Nailfold videocapillaroscopy (NVC) is a simple method to evaluate capillary density and morphology. Systemic sclerosis (SSc) is characterized with decreased hand mobility and joint contractures evolving in hands in early disease stage. Movement ability (MA) of hands can be measured with different methods including Hand Mobility Index in Scleroderma (HAMIS), hand anatomic index (HAI), delta finger-to-palm index (ΔFTP), and number of joints with decreased range of motion (joint contractures-JC).

Objectives: To examine correlation between capillary density and MA of hands in patients with SSc.

Methods: 136 patients with SSc underwent detailed examination of MA and capillary density measured with videocapillaroscop. 70 patients had limited cutaneous SSc (lcSSc) and 66 had diffuse cutaneous SSc (dcSSc). 48 patients had ≤5 years of disease duration (early SSc) and 88 patients had disease duration>5 years (late SSc) calculated from the first non-Raynaud symptoms.

Results: DcSSc patients had significantly higher HAMIS score than lcSSc patients (4.5/1.5;6.5/ vs. 2/0.5;4.5/; p<0.01). HAMIS score showed negative correlation with capillary density in the entire cohort (rho: -0.269, p<0.01) and in dcSSc patients (rho:-0.487; p<0.0001), but not in lcSSc ones.

HAI showed a significantly higher value in lcSSc patients than in dcSSc patients (3.79/3.18;4.39/vs.3.19/2.64;3.76/, p<0.01). Significant positive correlation between HAI and capillary density was found in dcSSc patients (rho: 0.377, p<0.01).

DcSSc patients showed significantly lower ΔFTP value than lcSSc patients (73.88/65.63;87.00/ vs. 82.81/73.63;90.5/; p<0.05). Positive correlation was found between capillary density and ΔFTP in the entire cohort, in dcSSc patients even if dcSSc was examined separately as early dcSSc and late dcSSc. No significant correlation was found between capillary density and ΔFTP in lcSSc patients.

The number of JC was significantly higher in dcSSc patients than in lcSSc patients (16/0;28/ vs. 0/0;11/; p<0.01), and no statistically significant difference was found between early SSc patients and late SSc patients. Strong negative correlation was found between JC count and capillary density in the entire cohort (rho -0.376; p<0.0001), in dcSSc patients (rho -0.501; p<0.0001), in early SSc patients (rho-0.583; p<0.0001) and late SSc patients (rho -0,262 p<0.05), but not in lcSSc patients.

Conclusion: Decreased capillary density correlated with decreased hand mobility and higher number of JCs. Tissue ischemia may play role in the development of joint contractures and it might be a contributing factor to decreased hand mobility impairment in SSc.

REFERENCES

[1] Torok KS, Baker NA, Lucas M, et al. Reliability and validity of the delta finger-to-palm (FTP), a new measure of finger range of motion in systemic sclerosis. Clin Exp Rheumatol. 2010;28(2)(Suppl 58):S28-S36.

[2] Sandqvist G, Nilsson JA, Wuttge DM, Hesselstrand R. Development of a modified hand mobility in scleroderma (HAMIS) test and its potential as an

outcome measure in systemic sclerosis. J Rheumatol. 2014;41(11):2186-2192.
[3] Sebastiani M, Manfredi A, Colaci M,et al. Capillaroscopic skin ulcer risk index: a new prognostic tool for digital skin ulcer development in systemic sclerosis patients. Arthritis Rheum 2009; 61: 688-694
[4] Ruaro B, Sulli A, Smith V, et al. Advances in nailfold capillaroscopic analysis in systemic sclerosis. JSRD 2018; 3: 122 –131.

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AB0676 BODY COMPOSITION IN MYOSITIS PATIENTS AND THE ASSOCIATION WITH DISEASE SPECIFIC FEATURES, PHYSICAL ACTIVITY AND PLASMA LEVELS OF INFLAMMATORY CYTOKINES

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Background: Skeletal muscle, pulmonary, and articular involvement in idiopathic inflammatory myopathies (IIM) limit the mobility/self-sufficiency of patients, and can have a negative impact on body composition.
Objectives: To assess body composition and physical activity of IIM patients and healthy controls (HC) and the association with selected inflammatory cytokines in IIM.
Methods: 54 patients with IIM (45 females; mean age 57.7; disease duration 5.8 years; PM, (22)/DM, (25)/IMNM, (7)) and 54 age-/sex-matched HC (45 females, mean age 57.7) without rheumatic/tumor diseases were included. PM/DM patients fulfilled Bohan/Peter criteria for PM/DM. We assessed body composition (densitometry: iDXA Lunar, bioelectric impedance: BIA2000-M), physical activity (Human Activity Profile, HAP questionnaire), disease activity (MITAX and MYOACT activity score), muscle involvement (manual muscle test, MMT-8 and functional index, FI2) and plasma levels of 27 cytokines (commercial multiplex ELISA kit, Bio-Rad Laboratories). Data are presented as mean±SD.
Results: Compared to HC, patients with IIM had a trend towards significantly increased body fat% (BF%) as assessed by iDXA (39.9±7.1 vs. 42.4±7.1 %, p=0.077), but significantly decreased lean body mass (LBM) as assessed both by iDXA (45.6±8.1 vs. 40.6±7.2 kg, p=0.001) and BIA (52.6±8.8 vs. 48.7±9.0 kg, p=0.023), and increased extracellular mass/body cell mass (ECM/BCM) ratio (1.06±0.15 vs. 1.44±0.42, p<0.001), reflecting deteriorated nutritional status and worse muscle predispositions for physical activity. Compared to HC, IIM patients had significantly lower bone mineral density (BMD: 1.2±0.1 vs. 1.1±0.1 g/cm^2, p<0.001). Disease duration negatively correlated with BMD (r=-0.392, p=0.004) and LBM-BIA (r=-0.272, p=0.047). Disease activity assessed by both MITAX and MYOACT positively correlated with LBM-BIA (MITAX: r=0.294, p=0.031; MYOACT: r=0.335, p=0.013) and LBM-DXA (MITAX: r=0.341, p=0.012; MYOACT: r=0.368, p=0.007), similarly as with basal metabolic rate (BMR; MITAX: r=0.336, p=0.014; MYOACT: r=0.351, p=0.010), and fat free mass (FFM; MITAX: r=0.338, p=0.014; MYOACT: r=0.356, p=0.009). CRP was positively associated with BF% assessed both by DEXA (r=0.276, p=0.035) and BIA (r=0.306, p=0.025). Higher BF%-DEXA was associated with worse physical endurance (FI2: r=-0.311, p=0.026) and worse ability to perform physical activity (HAP: r=-0.292, p=0.032). MMT-8 score negatively correlated with ECM/BCM ratio (r=-0.385, p=0.006). Plasma levels of IL-1ra positively correlated with body mass index (BMI, r=0.359, p=0.009), BF% (r=0.363, p=0.009), and visceral fat (VF, r=0.409, p=0.003). Plasma levels of MCP-1 positively correlated with ECM/BCM ratio (r=0.387, p=0.005). Increased plasma levels of IL-10 were associated with decreased LBM (r=-0.473, p=0.014).
Conclusion: Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our IIM patients, which are associated with their disease activity and duration, inflammatory status, skeletal muscle involvement, and physical activity. Plasma levels of several inflammatory cytokines were associated with alterations of body composition in IIM patients and highlight the potential role of inflammatory status on impaired body composition during the course of IIM.
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AB0677 TREATMENT OF IDIOPATHIC INFLAMMATORY MYOPATHIES – A SINGLE CENTRE EXPERIENCE

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Background: There is no consensus or recommendations for the treatment of idiopathic inflammatory myopathies (IIM).
Objectives: We explored how we treated incipient IIM patients in our secondary/tertiary rheumatology centre.
Methods: We retrospectively included cases with IIM diagnosed between January 2010 and June 2018, who were followed at least 6 months. The remission inducing treatment and the treatment at the last follow-up were recorded.
Results: During the 102-month period we identified 102 IIM cases (71.6% female, median (IQR) age 62.7 (52.2–72.1) years): 27.5% dermatomyositis, 22.5% anti-synthetase syndrome, 14.7% myositis in an overlap syndrome, 13.7% immune mediated necrotizing myopathy, 11.5% polymyositis, 6.9% cancer associated myositis, 2.9% inclusion body myositis (IBM), 1% unspecified myositis. 94 (92.2%) patients received glucocorticoids (GC), 18/94 (17.6%) as monotherapy. The remaining 81 (79.4%) were treated with additional immunomodulatory agents (Table 1), most commonly methotrexate. In addition to therapy presented in Table 1, 13 (12.7%) also received human immunoglobulins (IVIG), one (1%) received plasma exchange therapy.
Of the 8 (7.8%) cases who were not treated with GC 3 received methotrexate, 1 rituximab, and 4 no additional treatment (1 paraneoplastic polymyositis received chemotherapy, 2 IBM, 1 mild polymyositis in elderly, multimorbid patient).
In the first 6 months following diagnosis, 11 patients died (3 due to infection, 2 as a consequence of IIM, 1 due to haemorrhagic shock, 5 of unknown causes), and 5 were lost to follow-up. The remaining 86 patients were followed for a median (IQR) 37.7 (20.2–62.6) months. At last follow-up 49 (57%) patients were still receiving GC, 8 (9.3%) in monotherapy. 9 (10.5%) cases were off GC and other maintenance treatment. Maintenance treatment at last follow-up is presented in Table 2. Treatment was changed in 13 (15.1%) patients (due to progression of pulmonary involvement in 3, active myositis in 4, pulmonary involvement progression and active myositis in 1 and due to intolerance to medication in 6 cases). In addition to therapy presented in Table 2, 2 (2.3%) patients received IVIG (1 concurrently with rituximab and mycophenolic acid due to recalcitrant anti-synthetase syndrome and 1 due to IBM complicated with dysphagia).

Table 1. Induction treatment of idiopathic inflammatory myopathy

Type of treatment	N (%)
Cyclophosphamide; median dose (range)	23 (22.5); 6 (2–12) g
Methotrexate	43 (42.2)
monotherapy	30 (69.8)
+ cyclosporine A	8 (18.6)
+ cyclosporine A and rituximab	4 (9.3)
+ chloroquine	1 (2.3)
Rituximab monotherapy	4 (3.9)
Azathioprine	3 (2.9)
Mycophenolic acid	3 (2.9)
Cyclosporine A monotherapy	1 (1.0)

Table 2. Maintenance treatment of idiopathic inflammatory myopathy

Type of treatment	N (%)
Methotrexate	35 (40.7)
monotherapy	20 (57.1)
+ cyclosporine A	11 (18.6)
+ rituximab	2 (5.7)
+ chloroquine	2 (5.7)
Azathioprine monotherapy	13 (15.1)
Rituximab monotherapy	3 (3.5)
Mycophenolic acid	15 (17.4)
monotherapy	13 (86.7)
+ tacrolimus	1 (6.7)
+ rituximab	1 (6.7)
Cyclosporine A	1 (1.2)
Tocilizumab*	1 (1.2)

* Anaphylactic reaction to rituximab, received tocilizumab due to pulmonary fibrosis progression as part of anti-synthetase syndrome

Conclusion: GC, methotrexate and cyclophosphamide (in case of pulmonary involvement) were the cornerstone treatment in our cohort.

REFERENCES

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AB0678 ANTIPROLIFERATIVE AND VASOACTIVE TREATMENT MODALITIES IN 457 CONSECUTIVE PATIENTS WITH SYSTEMIC SCLEROSIS FROM ACADEMIC CENTERS IN GREECE

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Background: The pathophysiology of Systemic Sclerosis (SSc) encompasses autoimmunity, microvascular damage and fibrosis of the skin and internal organs. Accordingly, the two mainstays of treatment comprise antiproliferative and vasoactive regimens. So far there are limited data regarding the actual use of these agents in daily clinical practice.
Objectives: To describe current treatment modalities based on standard practice decisions according to published recommendations and/or guidelines for SSc, as well as to determine to which extent different disease modifying agents, namely antiproliferative and vasoactive drugs, are administered to these patients.
Methods: Consecutive patients from 7 academic rheumatology departments across Greece who fulfilled the 1980 American College of Rheumatology criteria for classification of SSc and were examined between January 2016 and December 2018 at least once, were included in the study. Patients' medical records were analyzed and antiproliferative and vasoactive agents administered anytime during the disease course were recorded.
Results: A total of 457 patients (87% women, 51% diffuse SSc, 62% with pulmonary fibrosis, 55% with digital ulcers, mean±SD age at diagnosis 49.2±13.1 years, disease duration 10.4±8 years) were studied. Methotrexate was the most frequent antiproliferative agent ever administered (53% of patients, 55% of them with diffuse SSc) followed by cyclophosphamide (26%, 78% of them diffuse), mycophenolate (11%, 63% of them diffuse), azathioprine (10%, 64% of them diffuse), rituximab (9%, 84% of them diffuse) and tocilizumab (3%, 68% of them diffuse). Among vasoactive agents, endothelin receptor antagonists (ERA) were most frequently ever administered in 39% of patients (64% with diffuse SSc) followed by iloprost in 7% (55% diffuse) and 5 phosphodiesterase (5PDE) inhibitors in 5.5% of patients (62% diffuse). Among all antiproliferative/vasoactive agents used, the greatest retention rate at last follow-up visit since initiation had ERA (82%) and 5PDE inhibitors (86%). Of note, 20% of SSc patients (90% women, 70% limited SSc, age at diagnosis 50.4±13.2 years, disease duration 8.4±6.4 years) had never been treated with either antiproliferative or vasoactive agents, whereas 41% had ever received only antiproliferative and 8% only vasoactive therapy. Moreover, 1/5 of patients with pulmonary fibrosis had never received antiproliferative treatment, whereas 1/3 of patients with digital ulcers had never received vasoactive drugs (Table).
Conclusion: About 20% of contemporary SSc patients, including patients with pulmonary fibrosis and digital ulcers, have never received antiproliferative or vasoactive therapy, possibly reflecting the spectrum of benign disease and/or a subgroup of under-treated patients.

REFERENCES:

Table 1. Treatment modalities in consecutive SSc patients

	Combined antiproliferative and vasoactive agents	Only antiproliferative agents	Only vasoactive agents	Without antiproliferative and vasoactive agents
All patients n=457	31%	41%	8%	20%
Diffuse SSc n=233	43%	39%	7%	11%
Limited SSc n=224	17%	45%	11%	27%
Pts with Pulmonary fibrosis n=285	38%	40%	8%	14%
Pts with ulcers and/or pulmonary hypertension n=251	52%	23%	13%	12%

Disclosure of Interests: None declared
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AB0679 SKIN ULCERS IN SYSTEMIC SCLEROSIS: 10 YEARS' FOLLOW-UP OF 211 PATIENTS FROM A MONOCENTRIC COHORT IN THE NORTH EAST OF ITALY

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Background: Microvascular involvement plays a pivotal role in the pathogenesis of systemic sclerosis (SSc). Among vasculopathic manifestations, skin ulcers (SU) stand out for their high prevalence.
Objectives: The aim of this study was to evaluate the prevalence and the subtype of SU, the association with clinical phenotype and pharmacological approach in the cohort of scleroderma patients attending our tertiary referral Centre.
Methods: We retrospectively evaluated clinical records of patients affected with SSc according to ACR/EULAR 2013 criteria, attending the Rheumatology Unit of Padova University. Patients with SSc *sine scleroderma*, *overlap* syndrome and with a follow-up lower than 24 months were excluded. We evaluated the epidemiological and clinico-serological data, including autoantibody pattern, laboratory data (such as haemoglobin, ESR, CRP), organ involvement and pharmacological treatments. Prevalence of SU, type of occurrence (isolated, recurrent and persistent episodes) and site (digital and localized at the lower limbs, between knees and ankle-feet) were recorded. Statistical analysis was performed by SPSS v. 24.
Results: 211 patients were included in the study: 187 female and 24 male, aged 60.8 ±12.4 years, 147 (70%) with limited cutaneous and 64 (30%) with diffuse form. During the follow-up period of 120 months (50-216), 105 (50%) patients experienced at least one episode of SU: 74 experienced digital ulcers, 11 presented only SU at lower limbs and 20 both kinds of ulcers. Demographic, laboratoristic and clinical features of our cohort are shown in Table 1. At the multivariate analysis, diffuse cutaneous form, younger age at diagnosis, telangiectasias and joint involvement were independently associated to SU. Among 105 patients who experienced at least one episode of SU, 69 (66%) had recurrent/persistent ulcers. The latter group needed a combination of drugs, including: calcium-channel blockers (90%), low-dose aspirin (75%), prostanoids (85%) and/or endothelin receptor antagonists (58%); 27% requested opioids for analgesia. Concerning SU at lower limbs, 19/31 patients (61%) had macrovascular involvement and 14/31 (45%) persistent ulcers; 6/31 (19%) underwent autologous skin grafting.
Conclusion: In our cohort SU occur more frequently in SSc diffuse cutaneous form and are associated with visceral and articular involvement.

Digital ulcers tend to recur during the disease course requiring several drugs, while SU at lower limbs tend to be more persistent.

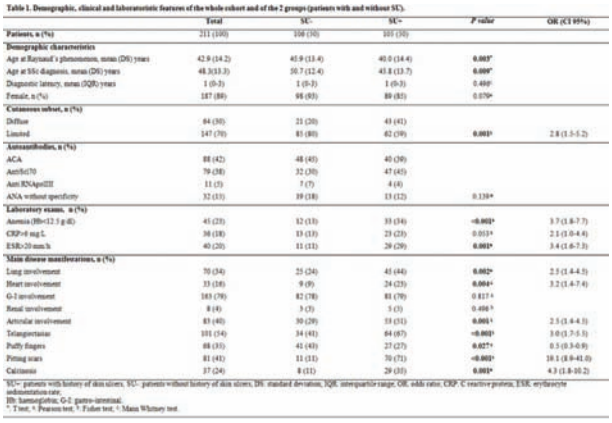


Table 1. Demographic, clinical and laboratoristic features of the whole cohort and of the 2 groups (patients with and without SU).

	Total	SU+	SU-	*P* value	OR (CI 95%)
Patients, n (%)	211 (100)	106 (50)	105 (50)		
Demographic characteristics					
Age at Raynaud's phenomenon, mean (DS) years	42.9 (14.2)	40.9 (13.4)	40.0 (14.4)	**0.003***	
Age at SSc diagnosis, mean (DS) years	48.3(13.3)	50.7 (12.4)	45.8 (13.7)	**0.000***	
Diagnostic latency, mean (IQR) years	1 (0-3)	1 (0-3)	1 (0-3)	0.460°	
Female, n (%)	187 (88)	98 (93)	89 (85)	0.070*	
Cutaneous subset, n (%)					
Diffuse	64 (30)	21 (20)	43 (41)		
Limited	147 (70)	85 (80)	62 (59)	**0.001***	2.8 (1.5-5.2)
Autoantibodies, n (%)					
ACA	88 (42)	48 (45)	40 (38)		
Anti-Scl70	79 (38)	32 (30)	47 (45)		
Anti-RNApolIII	11 (5)	7 (7)	4 (4)		
ANA without specificity	32 (15)	19 (18)	13 (12)	0.138*	
Laboratory exams, n (%)					
Anemia (Hb<12.1 g/dl)	45 (23)	32 (33)	33 (34)	**<0.001***	3.7 (1.8-7.7)
CRP>6 mg/L	36 (18)	13 (13)	23 (23)	0.053*	2.1 (1.0-4.4)
ESR>20 mm/h	40 (20)	11 (11)	29 (29)	**0.001***	3.4 (1.6-7.3)
Main disease manifestations, n (%)					
Lung involvement	70 (34)	25 (24)	45 (44)	**0.002***	2.5 (1.4-4.5)
Heart involvement	33 (16)	9 (9)	24 (23)	**0.004***	3.2 (1.4-7.4)
G-I involvement	163 (79)	82 (78)	81 (79)	0.817*	
Renal involvement	8 (4)	3 (3)	5 (5)	0.466°	
Articular involvement	83 (40)	30 (29)	53 (51)	**0.001***	2.5 (1.4-4.5)
Telangiectasias	101 (54)	34 (41)	64 (67)	**<0.001***	3.0 (1.7-5.3)
Puffy fingers	68 (33)	41 (40)	27 (27)	**0.027***	0.5 (0.3-0.9)
Pitting scars	81 (41)	11 (11)	70 (71)	**<0.001***	18.1 (8.9-41.0)
Calcinosis	37 (24)	8 (11)	29 (35)	**0.003***	4.3 (1.8-10.2)

SU+: patients with history of skin ulcers, SU-: patients without history of skin ulcers, DS: standard deviation, IQR: interquartile range, OR: odds ratio, CRP: C reactive protein, ESR: erythrocyte sedimentation rate.
Hb: haemoglobin, G-I: gastro-intestinal.
* T test, ° Pearson test, § Fisher test, ‡ Mann Whitney test.

REFERENCES

[1] Hughes M, Herrick AL. Digital ulcers in systemic sclerosis. Rheumatology (Oxford). 2017;56:14–25.

[2] Giuggioli D, Manfredi A, Lumetti F, Colaci M, Ferri C. Scleroderma skin ulcers definition, classification and treatment strategies our experience and review of the literature. Autoimmun Rev. 2018;17:155–64.

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AB0680 NAIFOLD VIDEOCAPILLAROSCOPY PATTERN CORRELATES WITH ORGAN INVOLVEMENT AND DISEASE OUTCOME IN SYSTEMIC SCLEROSIS: A SINGLE-CENTER OBSERVATIONAL STUDY

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Background: Systemic sclerosis (SSc) is characterized by systemic autoimmunity, vasculopathy and fibrosis. Nailfold Videocapillaroscopy (NVC) is a safe method to detect and to analyze morphological microvascular abnormalities in SSc patients. There is circumstantial evidence to suggest an association between NVC abnormalities and disease severity, particularly vascular manifestations.[1]
Objectives: To evaluate the association of NVC patterns with demographic, clinical, laboratory features and disease progression in the SSc cohort of University Hospital of Heraklion.
Methods: Retrospective study (2011-2018) of SSc patients who underwent NVC. NVC findings were classified into three distinct patterns namely early, active and late according to *Cutolo et al*[2]. NVC patterns were correlated with the clinical characteristics of the patients. We also correlated baseline NVC patterns with the progression of the disease at 3 years.
Results: 62 patients [(88.8% women, mean age of diagnosis 49.8 years, range 18-82)] were included. Compared to early/active pattern, patients with late pattern were more likely to have diffuse SSc (dSSc) (p=0.006), Interstitial Lung Disease (ILD) (80.0% vs 38.1% p=0.002) and esophageal involvement (80.0% vs 47.6% p=0.0034). There was a trend for increased frequency of Pulmonary Arterial Hypertension (PAH), digital ulcers (DU) and calcinosis in patients with late pattern (p=0.079, p=1.103 and p=0.079 respectively). Patients with active NVC pattern were more likely to have arthritis (early/active/late: 36.4%/75.9%/55.0%, p=0.054). A total 42 patients had NVC data at the time of SSc diagnosis. At 3 years there were no significant differences regarding disease progression, although patients with late NVC pattern had more hospitalizations due to infections (33.3% vs 9.1%, p=0.191), higher death rate (16.7% vs. 8.3%, p=0.543), need to use cyclophosphamide (33.3% vs 17.4%, p=0.391) and/or bosentan (40.0% vs 22.7%, p=0.426).
Conclusion: In this single-center SSc cohort, NVC pattern was found to correlate with organ involvement especially ILD, esophageal involvement and dSSc. Serious infections and treatment intensification were also more frequent among patients with late NVC pattern. NVC may be a useful prognostic marker for SSc patients.

REFERENCES

[1] Paxton D et al, Semin Arthritis Rheum. 2018 Dec;48(3):482-494

[2] Cutolo M, et al. Assessing microvascular changes in systemic sclerosis diagnosis and management, Nat Rev Rheumatol. 2010

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AB0681 SCLERODERMIC HAND: SUBCLINICAL JOINT INVOLVEMENT?

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Background: Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disorder of not fully understood aetiology characterized by vascular and fibrotic abnormalities in the skin and internal organs. Musculoskeletal involvement, mainly affecting hands and feet, is frequent in SSc and represents a major cause of disability. Ultrasonography is a non-invasive, cost-effective imaging modality which is able to detect the presence of joint involvement in SSc.
Methods: 61 consecutive patients (60 women) were enrolled. Each patient has completed a dichotomous survey to evaluate the presence of joint symptoms (presence of pain, swelling, morning stiffness in the last 3 months). Subsequently a rheumatologist - blinded to clinical data and survey results - performed the ultrasound examination of hands and wrists to evaluate the presence of effusion, synovial hypertrophy, power-Doppler signal, erosions and tenosynovitis defined according to the OMERACT definitions. The ultrasound examination was performed using the Esaote MyLab70 with a multifrequency linear probe (6-18 MHz).
Results: Of the 61 patients analyzed, 29 showned joint involvement on the ultrasound examination (47.54%), in particular, 37.93% had tendon involvement and 72.41% joint involvement (Table 1). 31 patients did not report joint symptoms (50.82%) but 13 (41.93%) still had ultrasound alterations (Table 2).

Table 1. Musculoskeletal involvement in SSc

	n. pazienti (%)
Joint effusion	14/29 (48.28%)
Synovial hypertrophy	18/29 (62.07%)
Erosions	2/29 (0.69%)
Tenosynovitis	11/29 (37.93%)
Power-Doppler signal	9/29 (31.03%)

Table 2. Musculoskeletal involvement in asymptomatic patients

	n. pazienti (%)
Joint effusion	3/13 (23.08%)
Synovial hypertrophy	8/13 (61.54%)
Erosions	0/13 (0%)
Tenosynovitis	5/13 (38.46%)
Power-Doppler signal	3/13 (23.08%)

Conclusion: Musculoskeletal involvement is frequent in SSc and can be asymptomatic in more than 20% of patients. The ultrasound examination can make it possible to detect articular and periarticular involvement at an early stage of the disease before the onset of disability.
Disclosure of Interests: Laura Belloli: None declared, Cinzia Casu: None declared, Mariaeva Romano Speakers bureau: janssen, Elisa Verduci: None declared, Maria Di Cicco: None declared, Emanuela Schito: None declared, Valeria Campanella: None declared, Michel Chevallard: None declared, Marina Muscarà: None declared, Davide Antonio Filippini: None declared, Oscar Massimiliano Epis Speakers bureau: BMS
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AB0682 CIRCULATING FIBROCYTES IN LIMITED CUTANEOUS SYSTEMIC SCLEROSIS PATIENTS: CORRELATION WITH DERMAL THICKNESS

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Background: Systemic sclerosis (SSc) is characterized by early skin impairment (1,2) and the modified Rodnan skin score (mRSS) is the validated method to assess the severity of this impairment. Whilst skin high frequency ultrasound (US) is a relatively new technique to measure dermal thickness (DT) (2-4).
Recent findings have reported the important contribution circulating fibrocytes make in the early stage of dermal repair and fibrosis. Indeed, as fibrocytes may be an important source of activated fibroblasts/myofibroblasts, it is reasonable to presume that they could be responsible for the increase in these cells observed in the tissue of SSc patients (5-7).
Objectives: The aim of this study was to identify any correlation between the modified Rodnan skin score (mRSS), dermal thickness (DT), measured by skin high frequency ultrasound (US) and the percentage of circulating fibrocytes in patients with limited cutaneous systemic sclerosis (lcSSc).
Methods: After obtaining approval and written informed consent and the Ethics Committee approval 8 lcSSc patients (7 females, 1 male) and 5 (4 females, 1 male) age-matched healthy volunteers (CNT) were enrolled. The lcSSc patients fulfilled the 2013 ACR/EULAR criteria for SSc (8). DT was evaluated by both mRSS and US (18 and 22 MHz probes), in all SSc patients and CNT, in the standard 17 skin areas evaluated by mRSS. The percentage of circulating fibrocytes was obtained by isolating them from the peripheral blood mononuclear cells (PBMCs) in all lcSSc patients and CNTs. Non-parametric tests were used for the statistical analysis.
Results: The percentage of circulating fibrocytes was positively correlated with DT-US, evaluated by the 22 MHz and the 18 MHz probes ($p=0.04$ and $p=0.03$, respectively) and mRSS ($p=0.04$) in lcSSc patients. Conversely, there was no correlation between these parameters in the CNT group ($p>0.05$).
Conclusion: The study demonstrates a significant relationship between DT, evaluated by both mRSS and US and the percentage of circulating fibrocytes in lcSSc patients. This observation may well support the hypothesis that circulating fibrocytes make a crucial contribution to skin fibrosis progression.

REFERENCES

[1] Cutolo M, et al. Best Pract Res Clin Rheumatol. 2016;30:670-87. 2. Krieg T, et al. Rheumatology 2009;48:iii14-8. 3. Clements PJ, et al. J Rheumatol 1995;22:1281-5. 4. Ruaro B, et al. Arthritis Rheumatol 2015; 67 (suppl 10). 5. Cutolo M, et al. Arthritis Res Ther. 2018;20:157. 6. Brunasso AM, et al. F1000Res. 2016 Apr 22;5. doi: 10.12688/f1000research.7986.1. 7. Reilkoff R, et al. Nat Rev Immunol. 2011;11:427-35. 8. van den Hoogen F, et al. Ann Rheum Dis. 2013;72:1745-55.

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AB0683 ROLE OF ELASTIN AND ELASTASE ANTIBODIES IN DEVELOPMENT OF PNEUMOSCLEROSIS IN PATIENTS WITH SYSTEMIC SCLERODERMA

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Background: Disturbed elastin metabolism, emerging pathological soluble isoforms followed by triggering of autoimmunity show that the biopolymer under study is associated with the pathogenesis of polyorganic lesions in systemic sclerosis. Elastin catabolism is promoted by elastase, an enzyme with a broad–range substrate specificity. It is the balance of a dynamic elastin–elastase system that determines physiological functioning of organs and tissues containing elastic fibres: the skin, ligaments, lungs, and vascular walls. Antibodies to elastin and elastase are unique predictors of development of pulmonary conditions in systemic scleroderma, which is now considered to be one of risk factors for pulmonary lesion.
Objectives: Developing highly sensitive markers of pulmonary remodeling at early stages of systemic scleroderma with participation of humoral immunity to the elastin–elastase system in the development of pulmonary lesion in systemic scleroderma requires further detailed study.
Methods: Patients for the study were selected from the department of rheumatology at the Emergency Care Municipal Hospital 25 in the city of Volgograd. The main group incorporated 42 persons with the diagnosis of systemic scleroderma verified by ACR/EULAR diagnostic criteria of 2013, without any exclusion criteria. There were 11 men and 31 women aged 22–72 among the systemic scleroderma patients. The mean age of patients was 44.1±15.4. The control group incorporated 30 healthy donors at the Volgograd Regional Blood Transfusion Station. Antibodies to elastin and elastase were determined in the blood serum by indirect enzyme immunoassay utilizing insoluble forms with enhanced antigen content according to the original technique by Gontar et al (1990).
Results: Compared with the control group, patients with systemic scleroderma showed a considerably higher rate of antibodies to elastase (52%) and elastin (38%). The upper normal level of antibodies to elastin was in the range of 0.131 absorbance units, of antibodies to elastase – 0.131 absorbance units. The mean value of elastin antibodies in the blood of systemic scleroderma patients was 0.125 ± 0.068 absorbance units. The value of elastase antibodies was 0.143 ± 0.071 absorbance units. The elevated level of elastin and elastase antibodies in the patients was associated with pulmonary lesion (basal pulmonary fibrosis – 20 (47.6%), pulmonary hypertension – 11 (26.2%), and adhesive pleurisy – 7 (16.7%)). In one half of cases the pulmonary lesion was asymptomatic, detected by accessory investigations like X-ray of chest organs, respiratory function study, EchoCG which were administered to assess the extent of abdominal organ inflammation and in differential diagnosis with cardiac insufficiency. The level of elastin antibodies in systemic scleroderma patients with pulmonary lesion was 0.149 ± 0.074 absorbance units, and of elastase antibodies – 0.146 ± 0.043 absorbance units, which was considerably higher than mean values in the control group.
Conclusion: By determining antibodies to elastin and elastase by the proposed technique of enzyme immunoassay at early stages of systemic scleroderma one can predict lesions of pulmonary parenchyma presenting with various clinical signs, and exacerbation of fibrosis processes.
Disclosure of Interests: None declared
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AB0684 DO WE DIAGNOSE ALL THE ANTISYNTHETASE SYNDROME?

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Background: Antisynthetase syndrome (AS) is an autoimmune disease characterized by the presence of antiaminoacyl tRNA-synthetase antibodies (anti-ARS) and clinical manifestations that may include interstitial lung disease (ILD), myositis, non erosive arthritis, Raynaud´s phenomenon (RP), fever and mechanic's hands. Until the Connors diagnostic criteria appeared in 2010, these patients with anti-ARS antibody were classified as an idiopathic inflammatory myopathy, or if they did not present myositis, they remained undiagnosed.
Objectives: To identify patients with anti-ARS antibodies from our hospital since June 2015, when the immunology laboratory was inaugurated, and to verify if they fulfilled the AS criteria.
Methods: Retrospective observational study carried out in a regional hospital in Barcelona with a reference population of 260,000 inhabitants. All patients with any anti-ARS antibody (Jo1, PL7, PL12, EJ) positive were selected, determined by the Dot Blot Polymyositis/Scleroderma IgD D-Teck. We applied Connors diagnostic criteria and collected demographic, clinical and instrumental data, and types of antibodies.
Results: We identified 18 patients with anti-ARS antibody, 9 anti-Jo1 (53%), 4 anti-PL7, 3 anti PL-12 and 1 anti-EJ. Of these, 13 had values of ANA > 1/80, 3 values of 1/80 and 1 negative. Other antibodies identified were anti-Ro52 in 4, anti-DNA in 4 and anti-Scl70 in 1. All pacients except one met AS criteria. None of anti-DNA positive subjects met criteria for erythematosus systemic lupus or systemic sclerosis. The majority

were women (88%) with a mean age at diagnosis of 62 years (27-83 years), 16 Caucasians and 1 Asian. The clinical manifestations reported were: 5 myositis (29%), 11 ILD (6 BOOP and 5 NSIP) (65%), 6 arthritis (2 polyarthritis, 2 oligoarthritis, 1 palindromic, 1 shoulder girdle syndrome) (35%), 3 Raynaud's phenomenon (17.5%), 2 mechanic´s hands (11%) and 6 fever (35%). Only one patient had the classic triad (myositis, arthritis, ILD, Jo1), 2 had myositis with ILD (Jo1), 1 myositis with arthritis (PL12), 1 ILD with arthritis (PL7), 7 ILD (Jo1, PL7, PL12), 3 arthritis (Jo1), 1 RP (Jo1) and 1 fever (EJ). Ten had a nailfold capillaroscopy performed, 7 of them had any alteration: 1 active systemic sclerosis pattern and 6 nonspecific (6 ramified capillaries and 3 microhemorrhages).

Conclusion: Our immunologically defined cohort has fewer clinical manifestations than described in clinically defined cohorts (AENAS group and EuroMyositis). Only 30% of patients had myositis and 70% had a single non-myositis clinical manifestation associated with anti-ARS antibody. Actually, it involved de-novo diagnosis of AS in half of them.

In patients with suspected AS with low or negative ANA, antibody blot determination is definitive.

Nailfold capillaroscopy in undefined cases is a fundamental tool for diagnosing AS.

Disclosure of Interests: None declared

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AB0685 ACROOSTEOLYSIS AND BONE METABOLISM PARAMETERS DISTINGUISH FEMALE PATIENTS WITH LIMITED SYSTEMIC SCLEROSISWITH AND WITHOUT CALCINOSIS: A CASE CONTROL STUDY

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Background: Calcinosis represents a late manifestation of limited systemic sclerosis (lSSc), inducing tissue damage and chronic calcifications. Bone metabolism studies in lSSc patients are rare in literature and there are few studies that analyzed clinical, laboratory and bone mineral density (BMD) parameters together.

Objectives: The aim of this study was to compare and analyze clinical aspects and laboratory parameters, including bone metabolism variables in female lSSc patients with and without calcinosis, paired by age, disease duration and body mass index (BMI).

Methods: Thirty-six female lSSc patients with calcinosis were compared to 36 female lSSc patients without calcinosis, matched by age, disease duration and BMI. Organ involvement, autoantibodies, BMD by DXA and laboratory parameters were analyzed. The past and current treatment modalities were also questioned. Statistical significance was considered if $p \leq 0.05$.

Results: Esophageal hypomotility, digital ulcers, and interstitial lung disease were the most frequent clinical manifestations of lSSc patients, present in similar frequency in both groups. Calcinosis was significantly associated with acroosteolysis (69% vs. 22%, p<0.001), higher modified Rodnan skin score (mRSS: 4.28±4.66 vs 1.17±2.50, p<0.001), higher 25OHD (24.46±8.15 vs. 20.80±6.60ng/ml, p=0.040) and phosphorus (3.81 ±0.41 vs. 3.43±0.45mg/dl; p<0.001) serum levels. 25OHD levels >30ng/ml were also significantly more frequent in patients with calcinosis (p=0.041). ANA was positive in 89% in both groups. Anticentromere antibody was frequent (44% and 31%), while positive anti-Scl70 was rare in both groups. Regarding treatment, current use of corticosteroids was lower in patients with calcinosis compared to patients without calcinosis (8% vs. 28%; p=0.032). Osteoporosis was more frequent in the group with calcinosis (31% vs.17%), although not statistically significant.

Conclusion: This study showed that lSSc patients with calcinosis can present a distinct clinic and biochemical profile when compared to a matched group without calcinosis. Presence of calcinosis in female patients with lSSc can be associated with acroosteolysis and higher serum levels of 25OHD and phosphorus when compared with patients without calcinosis paired by age, disease duration and BMI.

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AB0686 REDUCTION IN THE ABSOLUTE NUMBER OF PERIPHERAL REGULATORY T CELLS CORELATED TO CLINICAL FEATURES IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: The role of regulatory T cells (Tregs) in the development of SSc has started being studied during the last decade with new aspects being disclosed continuously. Although there is a general agreement in the medical literature regarding the decreased functional capacity of circulating Tregs in SSc, the alteration of absolute number of Treg and Th17 cells as well as their associations with clinical characteristics of SSc are still unclear.

Objectives: The present study was to investigate the relationship between multiple system impairments, disease activity and the absolute number of CD4+CD25+FOXP3+ regulatory T cells (Treg cells) and Interleukin 17 producing T help cells (Th17) in peripheral blood of patients with systemic sclerosis (SSc).

Methods: Clinical indicators were collected from total 54 patients with SSc[8 with localized SSc (lcSSc) and 46 with diffuse SSc (dcSSc)] who were divided into two groups, mainly with skin lesions (n=11) and with multiple system and organ besides skin lesions (n=43). Then According to the SSc EUSTAR index, we divided 54 SSc patients into the inactive (EUSTAR < 2.5 points, n = 22 cases) and the active group (EUSTAR score $\geq$ 2.5 points, n = 32 cases). The levels of peripheral T lymphocyte were detected with flow cytometry.

Results: We found that SSc, especially dcSSc patients, had significantly fewer peripheral CD4Treg cells (both absolute number and proportion, p<0.01) than healthy controls (Figure 1). In addition, the absolute number of peripheral Treg cells was significantly reduced in SSc patients with multiple system impairments (P<0.001), however, the number of Th17 cells were significantly increased in SSc patients with simple skin involvement (P = 0.002) (Figure 2). Also the absolute number of peripheral CD4Treg cells in active group with SSc decreased more significantly, thus causing an increase in the ratio of Th17 and Treg cells (Figure 2).

Conclusion: The reduced absolute number of peripheral Treg cells in SSc patients was contributed to the imbalance of Th17/Treg cells and involved in the pathogenesis of SSc, and may promote multiple system impairments and disease activity.

REFERENCES

[1] Liu M, Wu W, Sun X, et al. New insights into CD4(+) T cell abnormalities in systemic sclerosis. Cytokine Growth Factor Rev. 2016 Apr; 28:31-6. doi: 10.1016/j.cytogfr.2015.12.002.

[2] Lee GR. The Balance of Th17 versus Treg Cells in Autoimmunity. Int J Mol Sci. 2018 Mar 3;19(3). pii: E730. doi: 10.3390/ijms19030730.

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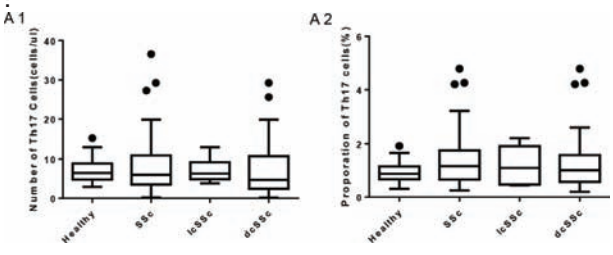


Figure 1. Absolute number of peripheral Th17 and Treg cells of patients with SSc. (A1 and A2) Neither absolute number nor proportion of Th17 cells was increased. *P<0.05; **P<0.01; ***P<0.001. lcSSc: localized sclerosis, dcSSc: diffuse sclerosis.

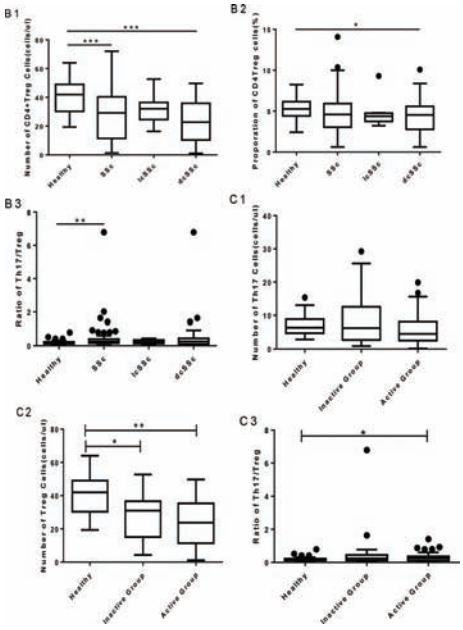


Figure 2. Absolute number of peripheral Th17 and Treg cells in SSc patients with different performance and disease activity. (B1 and B2) The absolute number of Treg cells was significantly reduced in patients with SSc, particularly more pronouncedly in patients with dcSSc. (B3) The ratio of Th17/Treg cell was increased in SSc patients. (C1) The absolute number of Th17 cells was not significantly changed but (C2 and C3) that of CD4Treg cells in active group with SSc decreased significantly, thus causing an increase in the ratio of Th17 and Treg cells. *P<0.05; **P<0.01; ***P<0.001. lcSSc: localized sclerosis, dcSSc: diffuse sclerosis.

Disclosure of Interests: None declared
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AB0687 **EFFECTIVENESS OF SPECIALIZED AND INTENSIVE ADL TRAINING IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES – PRELIMINARY RESULTS OF A ONE-YEAR CONTROLLED STUDY**

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Background: Idiopathic inflammatory myopathy are characterized by muscle weakness, caused by inflammation and immune changes in the affected muscles, which lead to a limitation in the execution of day-to-day activities (ADL). The aim of our study was to investigate the impact of specialized and intensive ADL training on muscle strength and endurance, depression and QoL of IIM patients.

Objectives: The study included a total of 50 IIM patients who fulfilled the Bohan and Peter 1975 criteria and had skeletal muscle involvement. 27 patients were recruited into the intervention group (IG) and 23 patients into the control group (CG). Both groups received an educational material for home exercise, but only the IG underwent a 6-month intensive training with a subsequent 6-month follow-up period.

Methods: Patients were assessed by a physician and a physiotherapist blinded to intervention at months 0, 3, 6, and 12. Patients also filled out patient reported outcomes questionnaires and provided blood for routine laboratory analysis and bio-banking. Data analysis was performed between groups and within the group.

Results: Compared to the observed statistically significant deterioration in the CG over the intervention period, we found a statistically significant improvement in the IG in objectively assessed strength and endurance of muscles as well as in subjectively assessed functional abilities and depression (Table). During the follow-up period, there was a significant deterioration or stagnation of the achieved positive results in the IG. Nevertheless, improved functional ability during the intervention period persisted in the IG in the follow-up period as well. Only numerical improvements in the IG during the intervention compared to the numerical deterioration in CG, that did not reach statistical significance, were observed in some subjectively assessed domains of QoL (SF-36) and fatigue (FIS – in physical dimension).

Parameter (unit)	Intervention group Mean ± SEM	Control group Mean ± SEM	Intra-group analysis (Friedman +Dunn)		Inter-group analysis (2WA)
			Interevention gr.	Control group	
MMT8	m0: 54.7 ± 2.6 m3: 60.7 ± 2.4 m6: 69.1 ± 1.9 m12: 64.0 ± 2.5	m0: 63.6 ± 2.0 m3: 57.9 ± 1.8 m6: 54.2 ± 1.9 m12: 56.5 ± 2.2	m0-3: p<0.01 m3-6: p<0.0001 m0-6: p<0.0001 m6-12: p<0.05	m0-3: p<0.05 m3-6: NS m0-6: p<0.0001 m6-12:NS	p<0.0001
FI-2 (%)	m0: 30.0 ± 4.4 m3: 46.9 ± 4.7 m6: 70.6 ± 4.9 m12: 58.4 ± 5.8	m0: 38.3 ± 5.3 m3: 29.6 ± 4.6 m6: 26.1 ± 4.1 m12: 25.7 ± 3.6	m0-3: p<0.01 m3-6: p<0.0001 m0-6: p<0.0001 m6-12: p<0.05	m0-3: NS m3-6: NS m0-6: p<0.01 m6-12: NS	p<0.0001
HAQ	m0: 0.9 ± 0.2 m3: 0.7 ± 0.1 m6: 0.6 ± 0.1 m12: 0.8 ± 0.2	m0: 1.3 ± 0.2 m3: 1.4 ± 0.2 m6: 1.4 ± 0.2 m12: 1.5 ± 0.2	m0-3: NS m3-6: NS m0-6: p<0.01 m6-12: p<0.05	m0-3: NS m3-6: NS m0-6: NS m6-12: NS	p=0.0002
BDI-II	m0: 11.9 ± 2.1 m3: 10.7 ± 1.7 m6: 8.9 ± 1.5 m12: 10.5 ± 2.0	m0: 13.0 ± 1.4 m3: 14.3 ± 1.7 m6: 15.7 ± 1. m12: 16.0 ± 2.0	m0-3: NS m3-6: NS m0-6: p<0.05 m6-12: NS	m0-3: NS m3-6: NS m0-6: NS m6-12: NS	p=0.0025

Conclusion: Our specialized and intensive ADL workout led to a significant improvement in the observed parameters that was clinically significant in a substantial proportion of patients, and prevention of the expected worsening of muscle weakness and QoL.

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AB0688 NEOPLASTIC RISK IN SYSTEMIC SCLEROSIS: A MONOCENTRIC STUDY

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Background: an increased risk of malignancies (1.5-5 times) was found in Systemic Sclerosis (SSc). Well recognized risk factors are the diffuse form, advanced age and (1), more recently, the positivity for anti-RNA Polimerase III antibodies (aRNAP3) has assumed considerable importance (2).
Objectives: the aim of this study was to evaluate the frequency of neoplasms and precancerous conditions, as well as the main risk factors, in our cohort of patients with SSc.
Methods: we enrolled 312 consecutive patients (288/92% females and 24/8% males, mean age 62.3 years, average disease duration 108 months) afferent at our department from 2000 to 2018, with a diagnosis of SSc confirmed according to the 2013 ACR/EULAR criteria (3). All patients underwent clinical, instrumental and laboratory evaluation. In 93 patients, negative for anti-topoisomerase I antibodies (aScl70) and anti-centromere antibodies (ACA), the presence of aRNAP3 antibodies was evaluated by an ELISA method (QUANTA LiteTM RNA Pol III).
Results: we found a limited form of disease in 229 patients (73.4%) and a diffuse form in 83 (26.6%). Eighty eight (28.2%) patients were positive for aScl70, 112 (35.9%) for ACA and 17 (5.4%) for aRNAP3. In the whole group, 44 (14%) patients had a positive familiar history for neoplasm while 105 (33.65%) had a history of neoplasms and/or precancerous conditions. Among these 105 cases, 44 (41.9%) were malignant, 50 (47.6%) benign and 11 (10.5%) had precancerous conditions. The most frequent neoplasms were breast carcinomas (14 cases/14.9%), thyroid (7 cases/7.4%), lung and kidney (3 cases/3.1%), melanomas (5 cases/5.3%). The most frequent precancerous condition was Barrett's esophagus (7 cases/63.3%). Regarding the antibody profile, 5 (4.8%) patients were positive for anti-RNAP3 and only 2 (1.9%) of these patients presented a malignant neoplasm, breast cancer in both cases. In 30 cases (28.6%) these neoplastic/precancerous conditions had arisen in the close period (± 36 months) at the SSc diagnosis and only 3 of them were anti-RNAP3 positive. Among the evaluated risk factors. Only familiarity was significantly associated with the development of neoplasia (p = 0.003), confirmed at the multivariate analysis (OR 2.9, IC95% [1,5-5,7]; p=0,002).
Conclusion: our study evaluated not only malignant neoplasms, but also benign neoplasms and precancerous conditions and identified familiarity as the only significant risk factor. In our cohort we did'nt find any relationship between the presence of anti-RNAP3 antibodies and the development of neoplasms, not even stratifying for the type of neoplasm. However, to better define our data, we should analyze anti-RNAP3 also in the double negative (antiScl70 and ACA) cases, in light of the recent evidence of double antibody positivity, as well as other newly investigated rare autoantibodies, associated with neoplasm in many connective tissue diseases, including SSc.

REFERENCES

[1] Szekanecz E, et al. (2012) Autoimmun Rev 11, 852;
[2] Shaha AA et al(2017) J Scleroderma Relat Disord. 2, 153;
[3] Van den Hoogen F, et al. (2013) Ann Rheum Dis 72, 1747–55.

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AB0689 EVALUATION OF CARDIOVASCULAR DETERMINANTS OF DISEASE OUTCOME IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by microvascular abnormalities. Cardiopulmonary and vascular manifestations in SSc are the most important survival factors in the disease.
Objectives: Correlations between different cardiovascular parameters (ejection fraction (EF), diastolic dysfunction, wall motion disturbance, estimated systolic pulmonary arterial pressure (sPAP), flow-mediated vasodilatation, arterial stiffness parameters (augmentation index - AIx, pulse wave velocity - PWV) and disease outcome and death were measured.
Methods: Thirty-six SSc patients were involved who underwent detailed arterial stiffness and vasodilatation examinations in 2007. In our work a 10-year period was analysed till 2017 following the progression of organ manifestations and survival.
Results: During the 10-year follow-up, 13 of the 36 patients died. The average survival time was 26.59 (22.36-37.64) years. Significant correlation was found between the initial AIx and PWV with cardiac wall motion disturbance (p = 0.018 and p = 0.016), AIx with restrictive ventilation dysfunction (p = 0.029) and PWV with obstructive ventilation dysfunction (p = 0.015). During the 10-year period, the occurrence of diastolic dysfunction was significantly increased (p = 0.0016), the incidence of arrhythmia did not change significantly. A significant risk factor for survival has been the decrease in EF (p = 0.011), where 1% reduction in EF was associated with 1.9% increase in mortality and 1 mmHg increase in sPAP involved 13% increase in mortality.
Conclusion: Based on our findings vascular stiffness parameters can be the predictors not only of the cardiovascular mortality but pulmonary manifestations with restrictive ventilation disturbances also in SSc.
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AB0690 USE OF MYCOPHENOLATE IN SYSTEMIC SCLEROSIS. CASE SERIES

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Background: At present, there are not specific targets to treat or prevent Systemic Sclerosis (SSc), but there are some to reduce the impact of its associated complications. Although mycophenolate (MP) is not recommended in latest EULAR SSc guidelines to treat cutaneous and pulmonary manifestations, its efficacy is known, based on observational studies and the Sclerodermalungstudy II.
Objectives: To describe our center's experience in treating SSc patients with MP.
Methods: Descriptive series of SSc patients treated with MP from November 2017 to December 2018. Demographic, clinical, analytical, spirometric, radiological (HR-CT) and modified Rodnan skin score (mRSS) data were collected.
Results: Case 1: woman diagnosed at 42 years old with diffuse SSc, having positive anti-toposiomerase-I antibody (ATA), telangiectasias, pitting scars, scleroderma and Non-specific Interstitial Pneumonia (NSIP) without significant alterations in spirometry. One year after diagnosis, as a result of skin worsening (mRSS 21), we started MP in association with prednisone (mean dose 5 mg. a day). After treatment for 14 months, she showed significant improvement (mRSS 9) without spirometric changes.
Case 2: woman diagnosed at 30 years old with diffuse SSc, having positive ATA, pitting scars, gastroesophageal reflux disease (GERD) and scleroderma. This same year, we started MP due to skin involvement (mRSS 14), improving significantly (mRSS 9) after 14 months of treatment.
Case 3: woman diagnosed at 35 years old with diffuse SSc, having positive anti-RNA polymerase-III (ARA), pitting scars, telangiectasias, calcinosis, myopathy and scleroderma. 40 months after diagnosis, MP and prednisone (mean dose 5mg. a day) were started to treat skin (mRSS 19) and muscle (confirmed by biopsy) involvement. Both showed significant improvement after 8 months of treatment, with mRSS 13, myopathy symptoms resolution and creatine kinase (CK) normalization.
Case 4: a woman diagnosed at 35 years of age with limited SSc, having positive anti-Ro52, telangiectasias, skin involvement (mRSS 14) and NSIP with non-assessable spirometry. Clinical respiratory improvement was shown after just 1 month of treatment, without mRSS changes.
Case 5: woman diagnosed at 54 years old with diffuse SSc, having positive ATA, hands edema, scleroderma (mRss 11), GERD and NSIP (FVC 56%, FEV1 64%, non-assessable DLCO). After 25 months of disease

progression and skin involvement, we started MP with prednisone (mean dose 8mg. a day), observing no significant changes after treating for 8 months on skin or lung disease, only improving the hands edema.
Case 6: woman diagnosed at 47 years old with diffuse SSc, having telangiectasias, scleroderma, positive ATA and NSIP. At 100 months from diagnosis, after 6 cyclophosphamide cycles followed by azathioprine (both ineffective) due to lung function (FVC 76%, FEV 83%, DLCO 26%) and skin (mRSS 30) worsening, MP and prednisone (mean dose 15mg. a day) were started. Currently, we are still waiting to assess clinical response.
Conclusion: Despite it is not included in EULAR current recommendations for SSc complications, our patients have remarkably improved with MP, especially skin involvement, with a good safety profile. These data reaffirm those obtained in previous studies and encourages us to continue considering its use.
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AB0691 INCREASED CARDIOVASCULAR RISK IN MIXED CONNECTIVE TISSUE DISEASE: EVALUATION OF MACROVASCULAR INVOLVEMENT AND ITS PREDICTORS BY AORTIC PULSE WAVE VELOCITY

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Background: Macrovascular involvement and cardiovascular (CV) risk have not been sufficiently studied in patients with mixed connective tissue disease (MCTD). In particular, the gold standard assessment method of aortic stiffness carotid-femoral pulse wave velocity (cfPWV) (1) has never been evaluated in patients with this disease.
Objectives: Aims of the present study were to examine cfPWV in MCTD and to evaluate its associations with MCTD associated parameters and traditional CV risk factors.
Methods: cfPWV measurements were performed in 43 MCTD patients and 107 healthy controls. The difference between cfPWV in the two groups was statistically examined and subsequently controlled for the effect of possible confounding factors. Association of cfPWV with MCTD associated organ involvement, routine laboratory parameters and immunoserological markers was also evaluated. Finally, relationship of cfPWV with medications and traditional CV risk factors was examined.
Results: Adjusted statistical analyses for confounding factors showed significantly higher cfPWV values in MCTD patients in comparison to controls (p_{adj}<0.001). cfPWV correlated in both the patients and the control group significantly with age (*rho*=0.69, *p*<0.001 and *rho*=0.67, *p*<0.001 respectively), diastolic arterial pressure (p_{adj}=0.024 and p_{adj}=0.032 respectively) and mean arterial pressure (*rho*=0.44, *p*=0.004 and *rho*=0.49, *p*<0.001 respectively). Moreover, cfPWV correlated in the control group with systolic arterial pressure (p_{adj}<0.001) (Fig. 1). Higher cfPWV values could be documented in the subset of MCTD patients without lung involvement (p=0.049).
Conclusion: To our knowledge, this is the first study to show that patients with MCTD have significantly higher aortic stiffness and thus CV risk in comparison to controls. Except the disease itself, age and blood pressure were the main predictors of cfPWV.

REFERENCES

[1] Bortel LM Van, Laurent S, Boutouyrie P, et al. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity.
[2] J Hypertens 2012; 30: 445–448.

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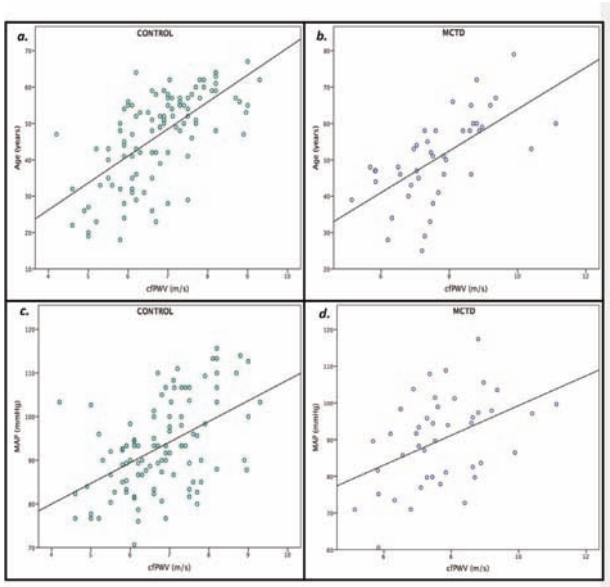


Figure 1 ***(a, b, c, d).*** Correlations of cfPWV (m/s) with age (years) and MAP (mm Hg) in the control and the MCTD group (all; $*p < 0.05$).

cfPWV carotid femoral pulse wave velocity, *MAP* mean arterial pressure, *MCTD* mixed connective tissue disease

AB0692 ASSESSING RECOVERY TIME AFTER COLD CHALLENGE AND THUMB INVOLVEMENT CAN HELP TO RULE OUT SYSTEMIC SCLEROSIS IN PATIENTS PRESENTING WITH RAYNAUD'S PHENOMENON

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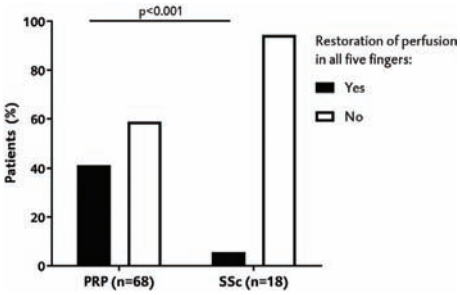
Background: Distinguishing primary Raynaud's phenomenon (PRP) from Raynaud's phenomenon secondary to systemic sclerosis (SSc) is crucial in the early detection of SSc. Recently we reported that patients with more severe vasculopathy suffer from a prolonged ischemia time during Raynaud's attack. [1] Additionally, it appears that the thumb is more frequently involved in SSc, where it seems to be spared in PRP. [2] These two characteristics are easily recognized by patients and physicians, and can help rising awareness for SSc.
Objectives: The aim was to study if the recovery of a Raynaud's attack and involvement of the thumb are differentiators for SSc in patients with Raynaud's phenomenon (RP).
Methods: A stepwise cooling and recovery procedure was performed, provoking an RP attack, in patients with PRP and SSc. One hand was submerged up till the radiocarpal joint in water. The water temperature was lowered in steps of 3 degrees Celsius every four minutes, from 33 until at least 9 degrees Celsius. Afterwards ten minutes of recovery in room air of 23 degrees Celsius was observed. During the procedure perfusion of the fingertips was assessed by photo-electric plethysmography.
Results: In total 18 patients with SSc and 68 patients with PRP underwent the procedure. Seventeen (94%) SSc patients had no restoration of perfusion after ten minutes in one or more fingers, compared to 28 (41%) PRP patients (figure 1), with a negative predictive value of 98%. During cooling, 17 (94%) SSc patients developed abnormal perfusion in the thumb compared to 48 (71%) PRP patients (p=0.036), with a negative predictive value of 95%. There was no difference in involvement of the other fingers during cooling (all p>0.05). Positive predictive values were low.
Conclusion: In patients with RP, when there is restoration of perfusion in all fingers after ten minutes or when the thumb is spared, the presence of an underlying SSc is very unlikely. Although this objective measurement needs to be verified with patient's reports, these results suggest that these simple signs can help physicians to assess if the patient needs to be referred for additional tests.

REFERENCES

[1] van Roon AM, Smit AJ, van Roon AM, Bootsma H, Mulder DJ. Digital ischaemia during cooling is independently related to nailfold capillaroscopic pattern in patients with Raynaud's phenomenon. Rheumatology (Oxford) 2016;55:1083-1090.

[2] Chikura B, Moore T, Manning J, Vail A, Herrick AL. Thumb involvement in Raynaud's phenomenon as an indicator of underlying connective tissue disease. J Rheumatol 2010;37:783-786.

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Abstract AB0692 Figure 1.. Percentage of patients with and without restoration of perfusion in all fingers during 10 minutes of recovery, measured in one hand by photoplethysmography.

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AB0693 DUROMETRY: HARD FACTS IN SYSTEMIC SCLEROSIS – A SYSTEMATIC LITERATURE REVIEW

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Background: Fibrosis represents one of the main characteristics of systemic sclerosis (SSc), with skin and internal organ involvement being its main clinical expressions. The modified Rodnan Skin Score (mRSS), using clinical palpation to estimate skin thickness, is considered the current "gold standard" to measure skin involvement in a semi-quantitative way. The mRSS has been judged as fully valid through the Outcome Measures in Rheumatology Clinical Trials (OMERACT) Filter, however a high risk of observer bias exists. Therefore, a new challenge for the SSc community is to define a reliable tool, able to more precisely investigate skin involvement in SSc patients, which would be of great value in clinical trials. Durometry, able to objectively investigate skin hardness, might address this need.
Objectives: To appreciate the validation status of durometry in SSc patients, guided by a systematic literature review.
Methods: Relevant full-text articles using durometry in SSc patients were identified through a systematic literature search in in PubMed, EMBASE and Web of Science, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Besides this systematic search, an additional hand search was performed through reference list screening. All retrieved records were screened by two raters based on title, abstract and full-text level to finally include manuscripts eligible for quality appraisal and data extraction. The finally included manuscripts were analysed according to the OMERACT Filter 2.0.
Results: The systematic search yielded 94 records, of which 50 were unique. Seven records were retained for full-text review and analysis, comprising one randomised clinical trial (RCT). The pillar feasibility was well documented in 3 studies [1-3]. Of note, the credibility (i.e. having face validity) of durometry was considered to be valid, as was stated by Kissin et al. [1]. Concerning the pillar truth: content validity was confirmed as durometry correlated well with histological findings (i.e. myofibroblast score and hyalinized collagen, r=0.69 and 0.78 respectively) [4], construct validity was confirmed as a moderate to high significant correlation with the total mRSS was documented in 5 studies (correlation coefficients ranging 0.59-0.81) [1, 3-6]. Concerning the pillar discrimination, the sensitivity to change in the context of one RCT was confirmed [3], inter-rater reliability was confirmed as intraclass correlation coefficients (ICC) ranged from 0.61-0.91 in 2 studies, of which one RCT [1, 3], intra-rater reliability has not been confirmed as this was domain was only investigated in a cohort 5 SSc patients (ICC 0.86-0.94) and thus solid evidence was lacking [1]. The sensitivity to change in situations of change (i.e. change over time, discrimination between SSc patients or between SSc patients and controls) was not confirmed, since solid evidence was lacking in literature.

Table 1: Validation of durometry according to the OMERACT Filter 2.0

Pillar	Subdomain		Reference
Truth	Face validity		[1]
	Content validity		[4]
	Construct validity		[1,3-6]
Discrimination	Sensitivity to change in the context of a RCT		[3]
	Detecting change in situations of change		
	- Sensitivity to change over time		[1]
	- Discrimination between disease subsets		[1,5]
	- Discrimination between SSc and HC		[1,2]
	Stability in situations of no change	Intra-rater reliability	[1]
		Inter-rater reliability	[1,3]
Feasibility			[1-3]

Green: a criterion was judged valid, if appropriate evidence from studies including SSc patients indicated that durometry met the requirements to be valid. Amber: a criterion was judged partially valid, if appropriate evidence from studies including SSc patients indicated that durometry only partially met the requirements to be valid. White: a criterion was judged with a white rating if appropriate evidence from studies including SSc patients was lacking. Exceptions are face validity and feasibility, in general evaluated by the judgement of experts as an appropriate measure rather than by specific studies.

Conclusion: Current systematically identified evidence suggests partial validation of durometry in SSc patients according to the OMERACT Filter 2.0. Further dedicated studies are needed to completely validate this tool in SSc, more specifically concerning the pillar 'discrimination'.

REFERENCES

[1] Kissin & Schiller. Arthritis Rheum 2006;55(4):603–9
[2] Falanga. J Am Acad Dermatol 1993;29(1):47–51
[3] Merkel. Arthritis Care Res 2008;59(5):699–705
[4] Kissin & Merkel. Arthritis Rheum 2006;54(11):3655–60
[5] Moon. Rheumatol Int 2012;32(8):2465–70
[6] Wiese. Arthritis Care Res 2014;66(11):1731–9

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AB0694 IS DUROMETRY A RELIABLE TOOL TO INVESTIGATE SKIN HARDNESS IN SYSTEMIC SCLEROSIS? A PILOT STUDY AND SYSTEMATIC LITERATURE REVIEW

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Background: Fibrosis of skin and internal organs is a hallmark feature of systemic sclerosis (SSc). The modified Rodnan Skin Score (mRSS) is routinely used to measure skin involvement, however this method has only an inter-rater reliability ranging from 0.38-0.92 and intra-rater reliability ranging from 0.74-0.76. Hence, finding a more reliable tool, capable of investigating skin involvement in SSc patients more reliably and precisely, would be of great significance. Durometry has been proposed as an objective technique to investigate skin hardness.
Objectives: To identify and critically appraise literature on the reliability of durometry in SSc patients by a systematic literature review and to perform a pilot study to investigate the intra-rater reliability of durometry in SSc patients.

Methods: Relevant full-text articles using durometry in SSc patients were identified through a systematic literature search in 3 electronic databases and a hand search of reference lists, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. All retrieved articles were screened on title, abstract and full-text level.
Additionally, a pilot study was conducted in a cohort of non-selected consecutive SSc patients to assess the intra-rater reliability of durometry, by having an anchor rater performing 3 cycles of durometry measurements at 17 skin sites approximating those of the mRSS. Reliability was described by calculating the intraclass correlation coefficient (ICC).
Results: A total of 94 records were identified through the systematic search of which a total of 40 unique titles were screened. After a thorough screening of all titles and abstracts,7 manuscripts were eligible for full-text review. Finally, of these, only 2 manuscripts fulfilled the predetermined inclusion criteria to be included, as they documented the reliability of durometry as an outcome. Hence, both manuscripts were included in the final analysis for quality appraisal and data extraction. Regarding intra-rater reliability, Kissin et al. reported ICC values ranging from 0.86-0.94 in a small cohort study including 5 diffuse SSc patients (DcSSc) [1]. Regarding inter-rater reliability, ICC values ranged from 0.82-0.96 according to a multicentre randomised clinical trial (n=43 DcSSc) by Merkel et al. and 0.61-0.85 according to Kissin et al. [1,2]. Finally, only 5 fulfilled the predetermined eligibility criteria to be included for quality appraisal and data extraction.
Subsequently to this systematic review, an additional pilot study investigating the intra-rater reliability was performed. Seventy-four SSc patients (61 women; 13 LSSc, 53 LcSSc and 8 DcSSc) underwent durometry assessment in this pilot study. The ICC values for intra-rater reliability ranged between 0.93-0.99.
Conclusion: The systematic literature review revealed that reliability, in particular intra-rater reliability, of durometry in SSc is nearly unexplored territory. The findings of our very pilot study, demonstrating as first an excellent intra-rater reliability of durometry measurements in a large unselected cohort of SSc patients, could confirm the explorative findings previously reported in a small cohort study. Hence, our results stepped forward to the need for intra-rater validation of durometry.

REFERENCES

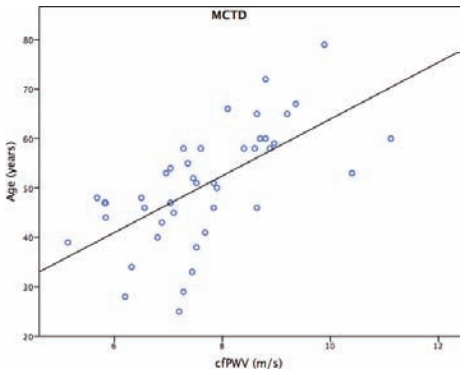
[1] Kissin. Arthritis Rheum 2006;55(4):603-9
[2] Merkel. Arthritis Care Res 2008;59(5):699-705

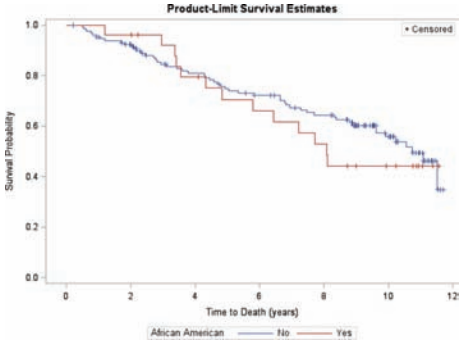
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AB0695 **LONG-TERM OUTCOMES OF AFRICAN AMERICAN PATIENTS WITH SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE**

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Background: Observational studies have demonstrated that African American patients with Systemic Sclerosis (SSc) have a more unfavorable prognosis compared with non-African Americans. However, no studies have evaluated racial disparities using data from a randomized controlled trial (RCT) where all patients have equal access to care and standard treatment and follow-up during the trial.
Objectives: To compare morbidity and mortality in African American and non-African American patients who participated in the Scleroderma Lung Study (SLS) I and II.[1,2]
Methods: SLS I randomized 158 SSc patients with interstitial lung disease (ILD) from 13 US SSc centers to 1 year of oral CYC (cyclophosphamide) versus placebo. SLS II randomized 142 SSc-ILD participants from 14 US SSc centers to 1 year of oral CYC, followed by 1 year of placebo, versus 2 years of mycophenolate (MMF). Up to 12 (SLS I) and 5 (SLS II) years after randomization, we contacted enrolled patients or designated surrogates to assess the following: mortality, cause of mortality, and development of organ failure. We used cox proportional hazard modeling to determine the variables associated with survival.
Results: Baseline characteristics of the SLS I and II cohorts were similar. In SLS I, African American participants (N=26) were younger than non-African American participants (N=132) (43.1 vs. 49.5 years, P=0.015). In SLS II, African American participants (N=33) had slightly increased baseline forced vital capacity (FVC) (69.2 vs 65.6, P=0.038), compared with non-American American participants (N=109). There were no significant baseline differences in the extent of cutaneous sclerosis (Modified Rodnan Skin Score [MRSS]), presence of diffuse cutaneous disease or serological profiles between racial groups. After adjusting for age, MRSS, FVC, there was no difference in long-term mortality outcomes (due to all causes or due to respiratory failure) in African American versus Non-African American SSc-ILD participants in SLS I or II (Figure 1). There was also no difference in time to the development of respiratory failure in African American versus Non-African American SSc-ILD participants in SLS I or II.





Conclusion: Data from two of the largest RCTs in SSc-ILD demonstrated that African American patients with SSc-ILD have similar morbidity and mortality outcomes compared with non-African American SSc-ILD patients, even after adjusting for age and baseline disease severity. These findings contrast with the racial disparities described in previous observational studies and warrant further investigation.

REFERENCES

[1] Tashkin, et al. *NEJM* 2006;354:2655.
[2] Tashkin, et al. *Lancet Resp Med* 2016;4:708.
Figure 1a. Time to death in African American participants of SLS I (red line) and non-African American participants of SLS I (blue line).
Figure 1b. Time to death in African American participants of SLS II (red line) and non-African American participants of SLS II (blue line).
Disclosure of Interests: Elizabeth Volkmann Shareholder of: Pfizer, Inc., Consultant for: Boehringer Ingelheim, Speakers bureau: Boehringer Ingelheim, Ning Li: None declared, Dinesh Khanna Shareholder of: Eicos Sciences, Inc, Grant/research support from: Bayer, BMS, Pfizer, Horizon, Consultant for: Actelion Acceleron, Arena, Bayer, BI, BMS, CSL Behring, Corbus, Cytori, GSK, Genentech/Roche, Galapagos, Employee of: Elcos Sciences, Inc, Philip Clements: None declared, Daniel Furst Grant/research support from: F. Hoffmann-La Roche, Genentech, Shervin Assassi: None declared, Michael Roth Grant/research support from: Genentech/Roche, Robert Elashoff: None declared, Donald Tashkin Consultant for: EMD Serono
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AB0696 **DETECTION OF COEXISTING MYOSITIS-SPECIFIC AUTOANTIBODIES WITH LINE AND DOT IMMUNOASSAYS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES**

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Background: Myositis-specific autoantibodies (MSAs) can be identified in up to 60% of patients with idiopathic inflammatory myopathies (IIM) (1). Based on previous immunoprecipitation studies, MSAs are considered to be mutually exclusive (1), but detection of coexisting MSAs with line or dot immunoassay (LIA/DIA) has been described (2-3).
Objectives: To determine the prevalence of detection of coexisting MSAs with different LIAs/DIAs in patients with IIM, assess the concordance between different assays and describe the clinical phenotype of patients with coexisting MSAs.
Methods: Cross-sectional assessment of prevalence of coexisting MSAs as detected by two LIAs (Euroline Autoimmune Inflammatory Myopathies, Euroimmun, Lübeck, Germany; and ImmcoStripe Myositis Advanced LIA, Trinity Biotech, Buffalo, USA) and 1 DIA (12 IgG Dot, Alphadia, Mons, Belgium), concordance between these assays and clinical phenotype of patients with coexisting MSAs in a single-center cohort of patients with a diagnosis of one of the subtypes of IIM as diagnosed by the treating physician.
Results: Nineteen of 145 patients (12%) had coexisting MSAs on at least one assay: 5 on the DIA (3,5%) and 5 (3,5%) and 11 (7,6%) on the LIA of Euroimmun and Trinity Biotech respectively. The results were concordant between 2 assays for more than one MSA in only 3 patients. The three combinations of these patients were anti-Jo-1 and anti-NXP-2, anti-Jo-1 and anti-TIF1-gamma, and anti-SAE and anti-NXP2 autoantibodies. The first two patients had an antisynthetase syndrome and the last patient an overlap myositis phenotype. All assays combined, anti-TIF1-gamma (9/19), anti-Jo-1 (7/19) and anti-NXP2 (6/19) autoantibodies were the most detected MSAs with concurrent detection of another MSA, though concordance between assays for these MSAs was low to moderate.
Conclusion: Detection of coexisting MSAs with LIA or DIA occurs in a minority of patients with IIM with varying prevalence between assays from different manufacturers. The combination of more than 1 MSA is not concordant between LIAs/DIAs in the vast majority of patients, suggesting that in most patients detection of coexisting MSAs with LIAs/DIAs reflects a problem of specificity of the assays for the involved autoantibodies.

REFERENCES

[1] McHugh NJ, Tansley SL. Autoantibodies in myositis. Nature Reviews Rheumatology. 2018.
[2] Brouwer R, Hengstman GJD, Egberts V, Ehrfeld H, Bozic B, Ghirardello A, et al. Autoantibody profiles in the sera of European patients with myositis. Ann Rheum Dis. 2001;60:116–23.
[3] Cavazzana I, Fredi M, Ceribelli A, Mordenti C, Ferrari F, Carabellese N, et al. Testing for myositis specific autoantibodies: Comparison between line blot and immunoprecipitation assays in 57 myositis sera. J Immunol Methods. 2016;

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AB0697 **LOW DOSE CYCLOPHOSPHAMIDE AND PIRFENIDONE MIGHT WORK IN SYNERGY TO RELIEVE INTERSTITIAL LUNG DISEASE WITH CONNECTIVE TISSUE DISEASE: A PRELIMINARY OBSERVATIONAL STUDY**

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Background: There are anti-inflammation and anti-fibrosis agents available for connective tissue disease associated interstitial lung disease (CTD-ILD). A clinical study has been initiated to assess the combination of the two (NCT03221257), but whether they can spare dose for each other is unknown.
Objectives: This preliminary study is aimed to observe outcomes of CTD-ILD patients receiving cyclophosphamide plus pirfenidone as a rescue therapy, with each agent at about one third of routine dosage.
Methods: We enrolled CTD-ILD patients who did not improve their symptoms (dyspnea or cough) after at least one-month steroids treatment (prednisone≥1mg/kg daily). Patients who had adjusted immunosuppressive agents other than steroids or had received anti-fibrotic medications within three months before enrollment were ruled out. We switched the treatment into pulse cyclophosphamide (0.4g/m2 monthly) combined with pirfenidone (300mg twice per day). Besides, we reduced the steroids to prednisone 0.5mg/kg daily and then tapered routinely. All the patients were followed up for 12 months.
Results: We enrolled seven patients, of whom two had anti-synthetase syndrome, two had Sjögren syndrome, two had scleroderma and one had mixed connective tissue disease. The media DLCO was 51% of prediction (range47.7% to 63%) and media FVC was 72.3% of prediction (range 39% to 81%). The media 6MWD was 275m (range202 to 324m). At the end of 12-month follow-up, all the patients regained functional independence with a media 52.7% increase of 6-minute walk distance (range34.4% - 86.3%). Pulmonary function tests showed improved forced vital capacity (median improvement 13.4%, range 0-35.9%) and DLCO (median improvement 6.3%, range 1.7%-16%). The HRCT score had a median decrease of 20.1% (range 11.7% to 29.6%). For quality of life assessment, the SGRQ total score had a median improvement of 53.3% (range 19.5% to 61.7%). Of note, no adverse events were observed during the 12-month follow-up.
Conclusion: Our Study provided preliminary but promising clinical evidence for a new strategy in treating CTD-ILD, that cyclophosphamide and pirfenidone might work in synergy and spare dose for each other. A well-designed controlled study is needed to further establish its safety and efficacy.

REFERENCES

None.
Disclosure of Interests None declared
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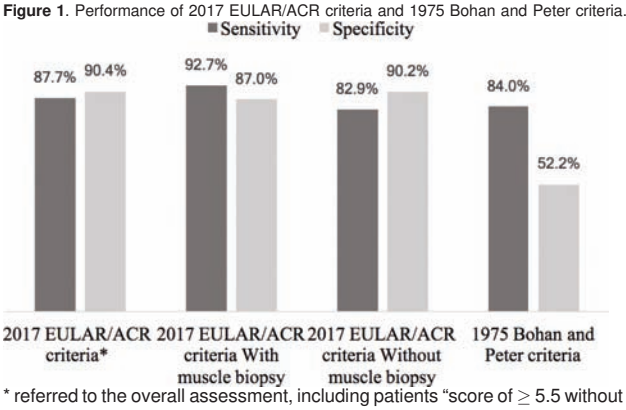
AB0697B **VALIDATION OF 2017 CLASSIFICATION CRITERIA FOR ADULT AND JUVENILE IDIOPATHIC INFLAMMATORY MYOPATHIES PROPOSED BY EULAR/ACR IN CHINESE PATIENTS**

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Background: Idiopathic inflammatory myopathies(IIMs) are heterogeneous disorers characterized by muscle weakness and muscle inflammation. Although the Bohan and Peter criteria proposed in 1975 are most widely used[1,2], there are some limitations. Firstly, they did not clearly specify how to exclude other forms of myopathy disease. Secondly, each criterion is not well defined either. EULAR and ACR jointly proposed the classification criteria for adult and juvenile IIMs and their major subgroups in 2017. The data-driven criteria exhibited high sensitivity and specificity. But most of the patients (62.6%) in the data were Caucasians, the performance of the criteria in Asian patients is unknown, which was one of the important limitations[6,7].
Objectives: To evaluate the ability of 2017 EULAR/ACR Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies (IIM) to

classify IIM in comparison with 1975 Bohan and Peter criteria in Chinese patients.
Methods: Two hundred and twenty-one in-patients with suspected IIM (including 40 children) were retrospectively included in this study. The performance of 2017 EULAR/ACR criteria was evaluated by sensitivity, specificity, positive predictive value, negative predictive value and classification rate, in comparison to the 1975 criteria, with clinical diagnosis as the gold standard.
Results: The sensitivity, specificity, positive predictive value, negative predictive value of the 2017 EULAR/ACR criteria in IIM classification were 92.7%, 87.0%, 90.1% and 90.4% respectively, in contrast to the 1975 Bohan and Peter criteria of 84.0%, 52.2%, 61.8%, and 77.9%(Fig 1). The classification rate of 2017 criteria was also much better than that of 1975 criteria (90.2% vs. 67.4%). The performance of the new criteria in general, as well as the new criteria with muscle biopsy was better. Most IIM patients were correctly further subclassified by the classification tree. The positive rate of myogenic lesion in electromyography (EMG), muscular inflammatory edema in magnetic resonance Imaging (MRI) and specific antibodies of myositis were significantly higher in IIM group than those in control group (p<0.001, all).
Conclusion: The 2017 EULAR/ACR criteria exhibited high sensitivity, specificity, classification rate in the Chinese IIM patients, which was superior to the 1975 criteria. The new criteria showed potentials as clinical classification criteria in the future.

Figure 1. Performance of 2017 EULAR/ACR criteria and 1975 Bohan and Peter criteria.



* referred to the overall assessment, including patients "score of $\geq$ 5.5 without biopsies and score of $\geq$ 6.7 with biopsies

REFERENCES

[1] Bohan A, Peter JB: Polymyositis and dermatomyositis (first of two parts). N Engl J Med 1975, 292:344-347.
[2] Bohan A, Peter JB: Polymyositis and dermatomyositis (second of two parts). N Engl J Med 1975, 292:403-407.
[3] Lundberg IE, Tjarnlund A, Bottai M, Werth VP, Pilkington C, de Visser M, Alfredsson L, Amato AA, Barohn RJ, Liang MH, et al: 2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups. Arthritis Rheumatol 2017, 69:2271-2282.
[4] Lundberg IE, Tjarnlund A, Bottai M, Werth VP, Pilkington C, Visser M, Alfredsson L, Amato AA, Barohn RJ, Liang MH, et al: 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. Ann Rheum Dis 2017, 76:1955-1964.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.2716

AB0697C

THE ASSOCIATION OF ANTI-MELANOMA DIFFERENTIATION-ASSOCIATED PROTEIN 5 AND SEASONAL PATTERNS IN ONSET OF IDIOPATHIC INFLAMMATORY MYOPATHIES IN KOREA

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Background: There was some reports of seasonal association with myopsitis onset. With the discovery of new myositis-specific autoantibodies (MSA), detailed grouping of idiopathic inflammatory myopathies was possible. Therefore, we evaluated the seasonal patterns in the onset of idiopathic inflammatory myositis (IIM) with MSA in Korea.
Objectives: To evaluate the correlation between MSA and seasonal patterns of IIM in Korea.
Methods: A total of 90 patients who met the criteria for probable or definite PM or DM and for whom data were collected from 7 referal centers in korea. 16 myositis-specific autoantibodies were detected by immunoblot with patient's serum. Statistical analyses were performed using a Poisson model that assessed associations of sex, MSA, and month of onset of symptoms or month of diagnosis.
Results: There were no significant seasonal patterns of disease onset in total IIM patients. Among MSAs, anti-synthetase (n=18), anti-transcriptional intermediary factor 1 γ (TIF1γ) (n=13), anti-melanoma differentiation-aasociated protein 5 (anti-MDA5) (n=12), and anti–signal recognition particle (SRP) (n=12) were analyzed. Among 55 patients with dermatomyositis, patients with anti-MDA5 showed a significant peak in winter (n=12, P=0.05). This seasonal association was significant in women (n =10; P=0.045). Patients with anti–synthetase, anti-TIF1 γ or anti-SRP antibodies did not have a significant seasonal onset patterns. There were no significant seasonal patterns in patients without myositis-specific autoantibodies.
Conclusion: Patients with anti-MDA5 showed a seasonality of myositis onset, in winter.
Disclosure of Interests: None declared
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AB0697D

CARDIOVASCULAR RISK FACTORS ARE HIGHER IN MALNOURISHED PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Cardiovascular disease (CVD) is a well known complication in rheumatoid arthritis and systemic lupus erythematosus. Atherosclerosis (ATS) and its impact on CVD in patients with systemic sclerosis (SSc) still remains unclear. Most of studies are suggesting higher frequency of CVD in SSc in comparison to healthy controls. CVD is a leading cause of death in most developed countries, whereas in SSc population it ranges from 20 to 30%. The etiology of ATS in SSc is unknown. Traditional risk factors, endothelial dysfunction and inflammation can contribute to ATS in SSc population. However, there is lack of data about the impact of the nutritional status on CVD factors in SSc patients.
Objectives: The aim of the study was to determine CVD factors among SSc patients depending on the nutritional status.
Methods: In 55 patients with SSc (72,7% well-nourished, 18,1% malnourished, 9,1% pre-cachexia) and 49 healthy controls we measured markers of endothelial dysfunction (asymmetric dimethylarginine - ADMA), inflammation (C-reactive protein - CRP, high sensitivity C-reactive protein - hsCRP, interleukin 6 - IL-6) and dyslipoproteinemia (oxidized low-density lipoprotein - ox-LDL, high-density lipoprotein- HDL, low-density lipoprotein – LDL and total cholesterol). Nutritional status was determined with subjective global assessment (SGA), body mass index (BMI), bioelectrical impedance analysis (BIA) and anthropometric measurements.
Results: Well-nourished SSc patients had significantly higher level of IL-6 (6,4±10,1 vs. 2,8±3,6 pg/ml; p=0,002) and lower HDL cholesterol (49,9 ±11,6 vs. 57±13,6 mg/dl; p=0,011) in comparison to healthy control. In malnourished SSc patients there was higher concentration of ADMA (1,68 ±0,53 vs. 1,24±0,34 μmol/l; p=0.003), CRP (18±28,8 vs. 2,4±2,5 mg/l; p=0.04), IL-6 (21,6±34,9 vs. 2,8±3,6 pg/ml; p=0.004) and lower HDL cholesterol (42,5±18,3 vs. 57±13,6 mg/dl; p=0.01) in comparison to healthy control. Pre-cachexia SSc group had significantly lower total cholesterol (166,8±28,5 vs. 219,3±40,9 mg/dl; p=0.008) and LDL cholesterol (96,8 ±21,6 vs. 139,6±36 mg/dl; p=0.007). There were no differences in concentration of oxLDL and hsCRP in those groups.
Conclusion: Nutritional status may play role in risk of CVD in SSc patients. Although its contribution to morbidity and mortality rates in CVD in SSc is yet to be established.
Disclosure of Interests: None declared
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Spondyloarthritis – treatment

AB0698 EFFECTIVENESS AND SAFETY OF CERTOLIZUMAB PEGOL FOR THE TREATMENT OF AXIAL SPONDYLOARTHRITIS IN REAL-WORLD CLINICAL PRACTICE IN EUROPE: RESULTS FROM A PROSPECTIVE NON-INTERVENTIONAL 12-MONTH COHORT STUDY

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Background: Certolizumab pegol (CZP) is an Fc-free, PEGylated anti-TNF with an established efficacy and safety profile in axial spondyloarthritis (axSpA) in clinical trial settings.[1]
Objectives: To report CZP effectiveness and safety in patients (pts) with axSpA, including ankylosing spondylitis (AS; radiographic axSpA) and non-radiographic (nr-) axSpA subpopulations, in routine clinical practice in Europe.
Methods: CIMAX (NCT02354105) was a non-interventional multicentre prospective cohort study observing CZP treatment response and safety over 12 months in a real-world clinical cohort of axSpA pts newly prescribed CZP. The primary outcome was change from baseline (CFB) in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) to Week (Wk) 52 in pts with available data, with additional outcomes pertaining to effectiveness and safety. Outcomes were evaluated for AS and nr-axSpA subpopulations (diagnosed according to local practice). Pts who received ≥1 dose CZP were followed up for adverse events (AEs) (Safety Set [SS]); those with baseline and ≥1 post-baseline BASDAI assessment were included in the effectiveness analyses (Full Analysis Set [FAS]). Outcomes are reported using observed case data with no imputation.
Results: 682 axSpA pts were enrolled from 101 European sites, of whom 490 (71.8%) completed the study. Of those enrolled, 672 formed the SS (AS: 469; nr-axSpA: 201) and 564 the FAS (AS: 384; nr-axSpA: 179); 2 (SS)/1(FAS) pts with unconfirmed AS/nr-axSpA were included in the overall axSpA population. 27.5% (185/672[SS]) axSpA pts had previous anti-TNF exposure (AS: 31.1% [146/469]; nr-axSpA: 18.4% [37/201]). BASDAI data were available for 77.8% (439/564) pts at Wk52. In pts with available data, all clinical outcomes were improved at Wk52 in both subpopulations (**Table**). At baseline, the mean BASDAI was 6.1. At Wk52, the mean BASDAI CFB in pts with available data (n=439) was −2.9 (AS: −2.9 [n=301]; nr-axSpA: −2.8 [n=137]). For pts with and without prior anti-TNF exposure, BASDAI at baseline was 6.1 in both groups (n=165 vs n=399, respectively), and at Wk52, the mean BASDAI CFB was −2.6 (n=127) vs −3.0 (n=312) (AS: −2.7 vs −3.0; nr-axSpA: −2.2 vs −3.0). In the SS, 37.9% (255/672) pts experienced AEs; 20.7% (139/672) experienced drug-related AEs and 6.3% (42/672) serious AEs (1.8% [12/672] reported serious infections); these data were comparable between AS and nr-axSpA (**Table**).
Conclusion: This is the first multicentre European study to evaluate CZP effectiveness and safety in both axSpA subpopulations in routine practice. Improvements were observed in all signs and symptoms in pts who remained on treatment to Wk52; >70% of those enrolled completed the study. No new safety signals were identified following application of CZP to real-world rheumatological practice.

Table: Clinical and safety outcomes at Week 52 for patients with axSpA in CIMAX

Clinical outcomes (FAS)	AS (N=384)		nr-axSpA (N=179)		Overall axSpA [a] (N=564)	
	BL	Wk52	BL	Wk52	BL	Wk52
BASDAI Mean (SD)	6.1 (1.8) n=384	3.2 (2.1) n=301	6.1 (1.7) n=179	3.2 (2.2) n=137	6.1 (1.8) n=564	3.2 (2.2) n=439
BASDAI CFB Mean (SD)	-	−2.9 (2.2) n=301	-	−2.8 (2.4) n=137	-	−2.9 (2.3) n=439
ASAS20 % (n/N) [95% CI]	-	72.3 (209/289) [67.2, 77.5]	-	64.3 (81/126) [55.9, 72.7]	-	69.7 (290/416) [65.3, 74.1]
ASAS40 % (n/N) [95% CI]	-	51.5 (150/291) [45.8, 57.3]	-	48.4 (62/128) [39.8, 57.1]	-	50.5 (212/420) [45.7, 55.3]
ASDAS (CRP) [b] Mean (SD)	3.7 (0.9) n=345	2.1 (1.0) n=267	3.5 (0.8) n=158	2.0 (1.0) n=115	3.6 (0.9) n=504	2.1 (1.0) n=383
ASDAS-ID [b] % (n/N)	0.9 (3/351)	24.1 (65/270)	0.6 (1/160)	25.6 (30/117)	0.8 (4/512)	24.5 (95/388)
BASFI Mean (SD)	5.4 (2.4) n=383	3.1 (2.4) n=301	5.1 (2.3) n=179	2.9 (2.5) n=137	5.3 (2.4) n=563	3.1 (2.4) n=439
Total back pain [c] Mean (SD)	6.8 (2.2) n=382	3.3 (2.3) n=297	6.8 (2.4) n=177	3.3 (2.6) n=137	6.7 (2.3) n=560	3.3 (2.4) n=435
PtGADA Mean (SD)	6.9 (2.2) n=384	3.2 (2.4) n=295	6.9 (1.9) n=177	3.3 (2.6) n=135	6.9 (2.1) n=562	3.2 (2.5) n=431
PhGADA Mean (SD)	6.5 (1.7) n=378	2.4 (1.9) n=295	6.2 (1.7) n=177	2.1 (1.9) n=137	6.4 (1.7) n=556	2.3 (1.9) n=433

Safety outcomes (SS), % (n)	AS (N=469)	nr-axSpA (N=201)	Overall axSpA [a] (N=672)
Any AE	36.9 (173)	39.8 (80)	37.9 (255)
Serious AEs	6.2 (29)	6.5 (13)	6.3 (42)
Serious infections	1.5 (7)	2.5 (5)	1.8 (12)
Drug-related AEs	18.6 (87)	24.9 (50)	20.7 (139)

(Observed data are presented. [a] Includes 1 patient with unconfirmed AS/nr-axSpA classification; [b] CRP values <2 were replaced with 2 to compute ASDAS; [c] Measured using a numeric rating scale where 0 is "no pain" and 10 is "worst possible pain". AE: adverse event; AS: ankylosing spondylitis; ASAS20/40: Assessment of Spondyloarthritis international Society 20%/40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-ID: ASDAS Inactive Disease; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BL: baseline; CFB: change from BL; CI: confidence interval; CRP: C-reactive protein; FAS: Full Analysis Set; nr-axSpA: non-radiographic axSpA; PhGPADA: Physician's/Patient's Global Assessment of Disease Activity; SD: standard deviation; SS: Safety Set; Wk: week.

REFERENCES
[1] van der Heijde D. Rheumatology (Oxford) 2017;56:1498–509.

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AB0699 EFFECT OF SWITCHING BETWEEN TUMOR NECROSIS FACTOR INHIBITOR IN SPONDYLOARTHRITIS

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Background: The introduction of new drugs, in particular tumour necrosis factor inhibitor (TNFi) has revolutionized the treatment of spondyloarthritis (SpA). Meanwhile, about 30% of patients do not react to first-line TNFi. To date,there is no recommendations available forthe treatment of SpA patients after first TNFi failure.
Objectives: In this study we assessed the effectiveness of a second and third biotherapy in patients with SpA with an inadequate response to previous TNFi and to analyze the survival of the second biotherapy
Methods: This study included patients with SpA who had had at least two biotherapies. Treatment response was noted at 3 months. At 6 months, we assessed the maintaining of effectiveness in Spa. We studied the elements of a good response to the second biotherapy.
Results: Our population of study included 30 SpA. During the second treatment, response rate was achieved by 80% after 3 months. No difference was noted between first and second TNFi among switchers. 86, 7%maintained response at twelve months. For axial forms, decrease in BASDAI was significant at 3 months. For peripheral forms, an improvement of the swollen and tender joint counts was observed and was significant at 3 months. Four patients have received a third TNFi. Response rate was achieved by all of them after 3 months. All of them maintained response at 6 months.The elements of a good response founded were;the early age of the SpA starting(<30y.o), the high value of initial CRP,the use of ESSG criteria,the SpA type,the extra articular signs, the first biotherapy and the reponse at 3 months to it, the drugs taken when second biotherapy were initiated a low initial EVA and BASFI.
Conclusion: These real-life data show that, after discontinuation of a first TNFi, switching to a second biotherapy in SpA is related to significantly improving of clinical effectiveness compared to a first TNFi.

REFERENCES
none

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AB0700

GOLIMUMAB PERSISTENCE IN BIOLOGIC NAÏVE AND NON-NAÏVE PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS OF THE GO-PRACTICE STUDY

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Background: Golimumab (**GLM**) was the latest anti-TNFα therapy to be indicated in the treatment of chronic inflammatory rheumatic diseases. The pivotal GO-AFTER study **[1]** and the ongoing observational GO-BEYOND study investigate GLM efficacy in rheumatoid arthritis (**RA**) patients who previously received biologics. However, clinical studies of GLM in axial spondyloarthritis (**AS**) are lacking. Using data from the GO-PRACTICE study, we examined GLM persistence in patients with AS.
Objectives: Primary objective was to estimate GLM persistence at 2 years from initial prescription, as a first line of treatment (in biologic naïve patients:**BN**) and as a second or further line of treatment (in biologic pre-treated patients:**BP**). Persistence was estimated with the Kaplan-Meier method. Secondary outcomes included assessing disease activity (**ASDAS**) evolution and patient-reported evaluations of disease activity (**BASDAI**), pain (**VAS**), functional ability (**HAQ**) and quality of life (**EQ-5D** and **SF-12**).
Methods: Observational, prospective, multicenter French study, that recruited adult patients with RA, psoriatic arthritis or AS, who were newly prescribed GLM. Patients were followed-up over 2 years; data were collected at baseline (**BL**), 1 year and 2 years. This abstract presents results from the AS cohort of GO-PRACTICE.
Results: 478 patients with AS (constituting 63% of the total cohort) from 134 sites were included from January 2015 to March 2016. Mean age was 43 years, 55% were female; 61% were BN (n=291) and 39% (n=187) were BP. Mean duration of AS was 5.5 and 10.7 years in BN and BP patients, respectively (*P*<.001). At BL most were prescribed 50 mg GLM monthly (97%). Co-treatments were disease-modifying anti-rheumatic drugs (34%), corticosteroids (17%) and NSAIDs/analgesics (90%). GLM persistence over 2 years was significantly higher in BN than BP patients (59.2% vs 45.1%, *p*<.01). For those still on GLM at 2 years, disease activity (Table1) and patient assessments showed significant improvements for both, BN and BP patients, with improvements being greater in BN patients. GLM was well tolerated in AS patients (n=478), with 46 (9.6%) discontinuing due to intolerance. Among BN patients, 18 (6.2%) discontinued GLM due to primary treatment failure, compared to 28 BP patients (15%). GLM was re-prescribed for 213 (88%) of the 241 patients persisting on GLM at 2-years. Post-hoc multivariate analysis showed that being female was a risk factor for GLM discontinuation in AS patients (HR1.9, IC95% 1.4-2.6).

Table 1. Disease activity at BL and 2 years for BN and BP patients with AS persisting on GLM

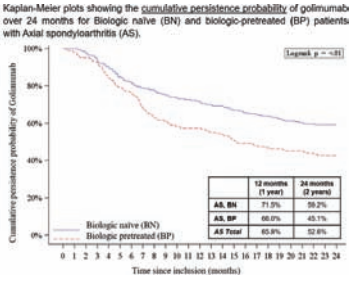
	BN patients		BP patients		
	BL	2 years	BL	2 years	*P**
ASDAS-CRP, Mean (SD)	3.2(0.8)	1.5(0.9)	3.1(0.8)	2.0(1.0)	*P*=.0051
BASDAI, Mean (SD)	5.3(1.7)	2.6(1.9)	5.7(1.6)	3.1(2.0)	*P* <.0001

**P* is from a 2-factor repeated-measures model testing the significance of the effect of prior biologic treatment on score evolution, adjusted to time

Conclusion: GLM is associated with clinical improvements and good persistence in AS patients, especially those who are biologic naïve.

REFERENCES

[1] Smolen JS, et al; Arthritis research & therapy 2015,17:14



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AB0701

REAL-WORLD EXPERIENCE OF SECUKINUMAB FOR AXIAL SPONDYLOARTHRITIS: SPECIFIC POPULATION CHARACTERISTICS

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Background: IL-17 inhibition has been proved effective in patients with ankylosing spondylitis (AS) in clinical trials and it has been added to the most recent national and international treatment guidelines. However, real-world data of its use is still scarce.
Objectives: This study aims to describe the axial spondyloartrhtitis (AxSpA) population receiving secukinumab therapy under non-experimental conditions.
Methods: Multicentric observational, retrospective, longitudinal study conducted in 4 tertiary hospitals of the Madrid region. Patients over 18 y.o. with clinical diagnosis of AxSpa and having received at least one dose of secukinumab were included. Medical records were reviewed to collect demographic and clinical data related to AxSpA, its features and treatment. Descriptive statstic analysis with measures of central tendency and measures of variability was performed.
Results: 143 patients, of which 68 women (47.6%) were included. Mean age was 50.6 y.o.(26-74) and average duration of the disease was 12.4 years (1-54). 105 AS patients (73.4%) and 38 non radiographic AxSpA patients (26.6%). 85 of them were HLAB27 positive (62%)
Observed comorbidities were hypertension (37pt, 25.8%), diabetes mellitus (12pt, 8.4%), dyslipidemia (43 pt,30.1%) and active smoking (41pt,28.7%) Average BMI was 27.1 (15.8-43.4), with an obesity rate of 27.6% (29pt). Other comorbidities highlighted were ischemic heart disease (10pt, 7%), HBV infection (10pt, 7.5%), malignancy (14pt, 9.8%) and renal transplantation (2 pt, 1.4%). No HVC nor HIV infections were detected.
In terms of axial disease, 97 (65.7%) patients showed grade 2 or higher sacroilitis. In sacroiliac joint MRI studies 35 patients (42.7%) had acute and chronic lesions, 13 (15.9%) had acute lesions, 17 (20.7%) had chronic lesions and 17 (20.7%) were normal. Syndesmophytes were present in 49 patients (34.5%) and hip arthropathy in 15 patients (11.4%).
In addition, peripheral disease was present: 77 patients (53.8%) had arthritis, 80 patients (55.9%) had enthesitis and 9 patients (6.3%) showed dactilitis. Joint erosions in hand and feet X-rays were reported in 6 patients (6.8%).
Extraarticular SpA features found were inflammatory bowel disease in 3 patients (2.1%), uveitis in 17 pts (11.9%) and psoriasis in12 pts (8.4%). 2 patients (1.4%) presented secondary amiloidosis.
Regarding previous treatments, 97.2% had used NSAIDs and 38.5% glucocorticoids. 100 patients (84.1%) had received DMARDs, particularly sulfasalazine (84 pts, 58.7%). 38 patients were naïve to biologic therapy (26.6%); 36 (34.3%) had been exposed to one bDMARD, 39 (37.1%) to two and 30 (28.6%) to three or more. Besides all TNF inhibitors, 13

treatments with abatacept, tocilizumab, rituximab or ustekinumab were recorded.
Average baseline BASDAI was 6.54 (0.4-12.8), and 5.01 (0-10) after 6 mo SCK therapy. Baseline BASFI was 5.8 (0.4-10) and 4.8 (0-9.6) at 6 months. Adverse events did not differ from those reported in clinical trials.
Conclusion: Population receiving SCK in real-world setting is different to clinical trials: more complex patientes, with higher disease activity, higher use of previous bDMARDs and higher comorbidity, particularly cardiovascular risk, infections or malignancy that could preclude the use of other biologic therapies. A relevant percentage of off-label prescription in nrAxSpA is reported. Further studys are needed to characterize this population and its clinical response and tolerability to SCK therapy.
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AB0702 TREATMENT EFFECT OF TUMOR NECROSIS FACTOR A INHIBITORS ON MAGNETIC RESONANCE IMAGING PROGRESSION IN PATIENTS WITH SPONDYLOARTHRITIS: A META-ANALYSIS

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Background: Treatment effect of tumor necrosis factor α inhibitors (TNFi) in patients with spondyloarthritis (SpA) had been proved by plenty of studies that could remarkably eliminate symptoms, signs, and laboratory inflammatory manifestations [1,2]. Simultaneously, the treatment effect of TNFi on delaying radiographic progression in SpA was often reported [3,4], including magnetic resonance imaging (MRI) which has a high sensitivity on detecting the earliest inflammation [5].
Objectives: A meta-analysis was performed to summarize the treatment effect of TNFi on MRI progression reflected by SPARCC score in SpA patients
Methods: Comprehensive search was conducted in the electronic databases of OVID Medline, OVID EMBASE and Cochrane library on Nov.27, 2018. All randomized controlled trials (RCTs) focused on MRI progression and disease activity in SpA patients treated with TNFi were included. Primary outcome was the Spondyloarthritis Research Consortium Canad (SPARCC) MRI scoring system, accompanied with or without other outcomes, including Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis disease activity index (BASDAI), Bath Ankylosing Spondylitis functional index (BASFI), C-reactive protein (CRP). Data were pooled by mean differences (MD) with 95% confidence intervals (CI) and publication bias was assessed by funnel plot. Sensitivity analysis was performed to test the result robustness. Jadad scale was applied to assess the methodology quality of included trials. Two reviewers independently selected studies, extracted data, and assessed study quality.
Results: Totally 10 RCTs enrolled 1006 patients with high methodology were included. Compared with control group, TNFi significantly improved SPARCC score at sacroiliac joint (SIJ) (MD=2.84, 95% CI 2.43-3.25), SPARCC score of spine (MD=1.87, 95% CI 1.27-2.46), ASDAS (MD=0.96, 95% CI 0.71-1.20), BASDAI (MD=1.15, 95% CI 0.51-1.78), BASFI (MD=0.95, 95% CI 0.51-1.40), and CRP (MD=4.64, 95% CI 1.06-8.23) in double-blind phase. Subgroup analyses by disease subgroup and individual TNFi showed treatment effect of TNFi on delaying MRI progression was not affected by disease subgroup and individual TNFi. Sensitivity analysis showed the treatment effects of TNFi versus placebo were consistent with TNFi versus controls, suggesting the results of the study were robust. The funnel plot of SPARCC score at SIJ based on TNFi versus control in double-blind phase was asymmetric, suggesting there might have potential publication bias.
Conclusion: TNFi are effective to treat SpA patients and delay MRI progression which are assessed by SPARCC score and treatment effect is consistent among disease subgroups and individual TNFi.

REFERENCES

[1] Baraliakos X, Listing J, Fritz C, et al. Persistent clinical efficacy and safety of infliximab in ankylosing spondylitis after 8 years–early clinical response predicts long-term outcome. Rheumatology (Oxford). 2011; 50(9):1690–9.
[2] Sfikakis PP. The first decade of biologic TNF antagonists in clinical practice: lessons learned, unresolved issues and future directions. Curr Dir Autoimmun. 2010;11:180–210.
[3] Wanders A, van der Heijde D, Landewe R, et al. Nonsteroidal antiinflammatory drugs reduce radiographic progression in patients with ankylosing spondylitis: a randomized clinical trial. Arthritis Rheum. 2005;52(6):1756-65.
[4] Poddubnyy D, Rudwaleit M, Haibel H, et al.Effect of nonsteroidal antiinflammatory drugs on radiographic spinal progression in patients with axial spondyloarthritis: results from the German Spondyloarthritis Inception Cohort. Ann Rheum Dis. 2012;71:1616-22.
[5] Puhakka KB, Jurik AG, Schiottz-Christensen B, et al. Magnetic resonance imaging of sacroiliitis in early seronegative spondylarthropathy. Abnormalities correlated to clinical and laboratory findings. Rheumatology (Oxford). 2004;43(2):234–7.

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AB0703 INFLAMMATORY BOWEL DISEASES AMONG SECUKINUMAB-TREATED PATIENTS: FIRST RESULTS OF THE MISSIL REGISTRY

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Background: Interleukin 17 (IL17) blockade is a therapeutic alternative for patients who are Tumor Necrosis Factor inhibitor-Inadequate Responders. However, in randomized controlled trials, cases of de novo inflammatory bowel diseases (IBD) have been reported in patients treated by IL17 inhibitors.
Objectives: To describe patients treated by IL 17 inhibitors developing new onset IBD (Crohn's disease and ulcerative colitis).
Methods: A French national registry called MISSIL was started in February 2018 to collect the cases of these patients. This registry is conducted by rheumatologist, dermatologist and gastroenterologist learned societies specialized on immune-mediated inflammatory diseases (IMID). In France, secukinumab has been granted market authorization in June 2016 and ixekizumab in April 2018.
Results: 12 cases were reported between February and December 2018 : 11 patients with new onset Crohn's disease and one with ulcerative colitis. Mean age was 51 ± 14.3 years old and 8/12 were female. 6 presented an axial spondyloarthritis, 3 a peripheral spondyloarthritis and 3 both. 9/10 were HLA-B27 positive. 4/10 have a radiographic sacroiliitis and 3/10 a MRI sacroiliitis. Only one was biological Disease-modifying antirheumatic drug (bDMARD)-naïve. Crohn's disease was mainly located at the ileum, colon and rectum. The mean time to onset of symptoms was 4.9 ± 5.6 months. The main symptoms were diarrhoea, nausea and vomiting and loss of weight. Median CRP at the onset of symptoms was 107 mg/L (66.5-200.7). 9 patients underwent biopsies. 5 were in favour of Crohn's disease. IL17 inhibitors were consistently stopped. Patients were treated by corticosteroids (9/12), mesalazine (3/12), methotrexate (2/12), thiopurines (1/12), infliximab (3/12), adalimumab (1/12), golimumab (1/12), ustekinumab (3/12). The evolution was favourable under treatment with healing (5/12), improvement (4/12) or stabilization (1/12). One patient worsened under treatment and one died (massive myocardial infarction).
Conclusion: IBD under IL 17 inhibitors are rare and lead to discuss the potential iatrogenic role of IL 17 inhibitor drugs. Further cases and case control studies are needed to better characterize this complication and identify patients at risk to develop IBD under IL 17 inhibitor.
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AB0704 EFFECTIVENESS AND SAFETY OF INFLIXIMAB AND GOLIMUMAB IN ANKYLOSING SPONDYLITIS PATIENTS FROM A PROSPECTIVE OBSERVATIONAL REGISTRY

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Background: Long-term registries are essential to evaluate new therapies in a patient population that differs from clinical trial and usually varies over time.
Objectives: To describe the profile of ankylosing spondylitis (AS) patients treated with infliximab (IFX) or golimumab (GLM) treatment in Canadian routine care along with its long-term effectiveness and safety.
Methods: 810 AS patients treated with IFX or GLM were enrolled into the Biologic Treatment Registry Across Canada (BioTRAC) registry between 2005-2015 and 2010-2017, respectively. Study visits occurred at baseline and every 6 months thereafter, as needed per routine care. Effectiveness was assessed with changes in ASDAS, BASDAI, BASFI, MDGA, HAQ-DI, PtGA, back pain and acute phase reactants. Safety was evaluated with the incidence of adverse events (AEs) and drug survival rates.
Results: Of the 389 IFX- and 421 GLM-treated patients, the proportion of males were 62.7% and 59.1%, the mean age were 45.6 and 45.7 years and the mean disease duration were 8.6 and 6.0 years, respectively. Most patients were bio-naive (>82.7%). Interestingly, we observed a significant decrease in disease duration in the IFX cohort from a median of 8.0 to 3.5 and 1.0 years in 2005-2008, 2009-2012 and 2013-2015, respectively ($p<0.001$). A reduction in baseline BASFI score (6.3 vs. 5.9 vs 5.1; P=0.011) and in the proportion of patient in ASDAS very high disease activity (48.4%, 43.8%, 30.3%; p=0.004) were also observed. As for the GLM cohort, most disease parameters including median disease duration (1.6 years), mean baseline BASFI (5.3) and the proportion of patients in ASDAS very high disease activity (48%) remained similar from 2010-2017.
Treatment with both IFX and GLM significantly improved all disease parameters over time ($P<0.001$) from baseline up to 120 and 84 months, respectively, with similar efficacy between agents.
AEs were reported for 67.9% and 70.5% (136 and 131 events/100 PYs) and SAEs for 15.4% and 8.1% (10.5 and 22.7 events/100 PYs) covering 1251.3 and 674.8 years of exposure for IFX- and GLM-treated patients, respectively. The most frequently occurring AEs (>7% of patient in either group) were upper respiratory tract infection, arthralgia and back pain. Two deaths occurred in IFX-treated patients (myocardial infarct, drowning) and two among GLM-treated patients (oropharyngeal cancer; neutropenia, staphylococcal/pseudomonas infections, septic shock).
The proportion of patients who discontinued treatment were 65.8% over a mean 3.2 years of exposure in the IFX cohort and 56.8% over 1.6 years in the GLM cohort.
Conclusion: Both IFX and GLM treatment significantly reduced disease activity and improved functionality in a similar fashion and were well tolerated in patients with AS. Differences in baseline characteristics over time demonstrate improvement in early diagnosis of AS and earlier access to biologic therapies.

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AB0705 AQUILA STUDY IN GERMANY – REAL WORLD ADHERENCE AND PERSISTENCE OF SECUKINUMAB TREATMENT IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS PATIENTS – AN INTERIM ANALYSIS

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Background: Secukinumab (SEC) has been shown to be an effective treatment for patients (pts) with ankylosing spondylitis (AS) and psoriatic arthritis (PsA) in several phase III studies[1,2]. Clinical studies reduce confounding factors, but do not guarantee the same results in real world where treating physicians deal with comorbidities, adherence and persistence challenges. Especially medication adherence has a direct impact on health outcomes. However, there is limited information on the adherence and persistence of SEC in routine care.
Objectives: The aim of this interim analysis is to report baseline (BL) characteristics and to assess adherence rate as well as treatment persistence of SEC in AS and PsA pts under real world conditions.
Methods: AQUILA is an ongoing, non-interventional study enrolling 2000 pts with active AS or PsA in Germany. Adherence was calculated as the proportion of the accumulated actual dose divided by the accumulated target dose (according to summary of product characteristics) during the maintenance phase (week 6 to 52). Adherence rate was calculated as the proportion of pts who achieved an adherence of >80% at wk 52. These calculations included pts who discontinued treatment with SEC; still ongoing pts were excluded from this interim analysis. Treatment persistence (time from study inclusion, i.e. date of informed consent, until treatment discontinuation) stratified by biologic/biosimilar (Bx) pretreatment was analyzed using Kaplan-Meier plots.
Results: This interim analysis describes 952 pts (AS n=311, PsA n=641) who were included at BL. In total, 51.4% (n=489) of the pts were female and 48.6% (n=463) male, mean age was 50.8 years, and 67.8% (n=645) were pretreated with Bx. At treatment start with SEC, pts presented with a number of extra-articular manifestations/comorbidities: plaque psoriasis 11.6% (n=36) in AS and 66.3% (n=425) in PsA, uveitis 6.4% (n=20) in AS and 1.7% (n=11) in PsA, depression 15.4% (n=48) in AS and 15.4% (n=99) in PsA, coronary heart disease 3.5% (n=11) in AS and 7.9% (n=51) in PsA, stroke 0.6% (n=2) in AS and 1.9% (n=12) in PsA, and heart insufficiency 1.6% (n=5) in AS and 3.0% (n=19) in PsA.
Adherence rates for SEC [95% CI] at week 52 were 64.5% [58.3,70.5] and 56.0% [51.5; 60.4] for AS and PsA, respectively.
In both AS and PsA, more Bx-pretreated pts discontinued treatment than Bx-naïve pts (AS: 38.0% versus 18.9%; PsA: 32.3% versus 20.7%). The most frequent reason for discontinuation was "adverse event/insufficient response/loss of efficacy" in both Bx-pretreated (n=73, 33.0%/n=111, 26.2%) as well as in Bx-naïve (n=10, 11.1%/n=34, 15.7%) AS/PsA pts. Moreover, Kaplan-Meier analysis showed that in both AS (Figure 1a) and PsA (Figure 1b) groups, Bx-naïve pts who received SEC as first line therapy had a higher persistence rate than those pretreated with Bx.

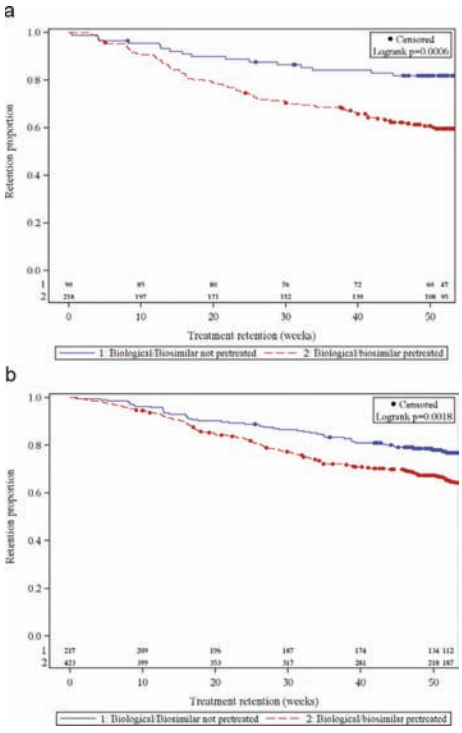


Figure 1.

Conclusion: AQUILA study revealed high disease burden at BL across AS and PsA pts characterized by the presence of extra-articular manifestations and cardiovascular diseases. Adherence rates under real-world conditions were consistent and comparable with published literature regarding immune-mediated inflammatory diseases[3]. SEC demonstrated a high drug persistence in real world in particular in Bx-naive pts. Overall, this interim analysis demonstrated that SEC is a reliable treatment in Bx-naïve as well as Bx-pretreated pts with AS or PsA in a daily routine setting.

REFERENCES

[1] Baeten D et al. *Lancet*. 2013;382(9906):1705-13;
[2] McInnes IB et al. *Lancet*. 2015;386(9999):1137-46;
[3] Vangeli E et al. *Adv Ther*. 2015;32:983-1028

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AB0706 DIFFERENCES IN RHEUMATOLOGISTS' TREATMENT PREFERENCES FOR ANKYLOSING SPONDYLITIS AND NON- RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Background: The lack of a formal indication for Non-Radiographic Axial Spondyloarthritis (nr-axSpA) has meant that many US rheumatologists fundamentally treat it as an early manifestation of Ankylosing Spondylitis (AS) and seldom differentiate their treatment approach when using biologics/small molecules.
Objectives: This study sought to gain a better understanding of the number of AS and nr-axSpA patients rheumatologists manage, recent changes made in treatment, and how AS and nr-axSpa patients are differentiated beyond radiographic evidence. The study also evaluated the differences in use of biologics/small molecules for the treatment of AS and nr-axSpA and rheumatologist projected changes in the management of these two conditions.
Methods: An independent market analytics firm administered a survey with US rheumatologists (n=104) on the treatment landscape for AS and nr-axSpA. To qualify, rheumatologists had to spend the majority of their professional time in clinical practice, manage a minimum of 50 AS or nr-axSpA patients, and have been in practice between 2 and 35 years. Respondents answered questions pertaining to their practice, the demographics of their AS/nr-axSpA patients, their treatment approaches for each type, as well as attitudinal statements. The survey was administered online in February 2018 and respondents were compensated for their participation. A similar study was also conducted in 2017 allowing for year over year comparison. The data were collected and analyzed in SPSS.
Results: Three-quarters of rheumatologists reported they treated their AS and nr-axSpA patients in a similar manner, though there was a higher use of NSAIDs and local steroids in non-radiographic disease, and more biologic/JAK use in AS. More established TNF inhibitors such as adalimumab, etanercept, and infliximab dominated biologics/small molecule preference, collectively accounting for approximately three-quarters of all biologic-treated AS and nr-axSpA patients. However, use of adalimumab, etanercept, and infliximab was expected to decline or stay flat in the next three months, while use of secukinumab, tofacitinib, golimumab IV, and both infliximab biosimilars, was anticipated to increase.
Although not indicated for either condition, 28% of respondents reported off-label use of tofacitinib for AS, and 25% for nr-axSpA, a significant increase from 2017. Projected off-label use of tofacitinib in the following three months is also expected to increase.
Conclusion: Rheumatologists are less likely to use biologics/small molecules for nr-axSpA, but when they do, use of brands is similar to those used in AS. While TNF inhibitors continue to account for the majority of biologic/small molecule prescriptions for these conditions, rheumatologists project increased use of agents with alternative mechanisms of action in the future.
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AB0707 LTBI SCREENING IN SPONDYLOARTHRITIS PATIENTSPRIOR TO ANTI-TNF TREATMENT AND FOLLOW-UP IN AN ENDEMIC AREA

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Background: Screening for latent tuberculosis infection (LTBI) remains a concern in endemic regions for anti-TNF eligible patients and recent researches have shown peculiarities between the inflammatory arthropathies such as different groups of spondyloarthritis (SpA).
Objectives: To evaluate the long-term efficacy of LTBI screening and treatment in patients with Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA) receiving TNF blockers in a single center.
Methods: A total of 218 SpA patients (135 AS and 83 APS) were screened for LTBI before receiving anti-TNF (infliximab, adalimumab, etanercept, certolizumab pegol and golimumab) treatment using the tuberculin skin test (TST), chest X-ray (CXR) and history of previous exposure to tuberculosis (TB). Patients were regularly followed every 2-3 months and asked about infectious symptoms or new exposure. TST was not repeated regularly. LTBI patients were treated with isoniazid (300 mg/day) for 6 months, according local guidelines.
Results: One hundred and eight patients (49.5%) were treated with a single anti-TNF agent and the total duration of biological treatment was approximately six years (5.9 ± 4.0). INF and ADA were most often used among the 422 treatment cycles analyzed, representing 45% and 30% respectively. LTBI screening was positive in 82 patients (38%): 69 (84%) were TST-positive, 23(28%) had a history of TB exposure and 5(6%) had an abnormal CXR. As isolated variables TST positivity and previous exposure accounted for 58(71%) and 11 (13%) LTBI diagnosis. There were some distinct patterns between APS and AS patients screening: despite APS patients had more cases of previous TB than AS patients (6% vs 0.7%, P= 0.03), they had a lower frequency of LTBI (30% vs 42%, P = 0.04). Among LTBI patients, TST positivity was lower in SpA than AS patients (64% vs 93%, P = 0.002), even with more previous exposure (52% vs 18%, P = 0.02) and in patients with peripheral arthritis (27% vs 42%, P = 0.03). During follow-up, 11 patients developed active TB: 5 under ADA, 5 under INF and 1 under ETA treatment. Five cases (45%) were extrapulmonary: 3 pleural, 1 peritoneal and 1 spondylodiscitis. Four (36%) cases occurred in patients with a positive LTBI screening and 7 in patients without LTBI. There was no difference in drug survival

according to type or class of anti-TNF, disease subgroups, duration or use of synthetic drugs and prednisone. Four (36.3%) cases occurred in the first year, median 5.3 (1.2-8.8) months after initiating anti-TNF exposure, 2 of them (50%) in patients with positive LTBI. Seven cases were probably due to re-exposure since occurred later, median 21.9 (14.2-42.8) months (5 in patients with negative LTBI screening). Six patients (54.5%) re-initiated treatment with ETA. Only the patient who developed pulmonary TB under ETA had a second TB infection after 18 months of therapy.

Conclusion: Despite the adequate screening and treatment of LTBI, according to local guidelines, TB still occurs in spondyloarthritis patients under anti-TNF therapy, even in the first year of treatment. These data point to LTBI screening/treatment failure, maybe to due to anergy, mainly in PsA patients, with peripheral disease, low adherence or re-exposition in an endemic environment. The high frequency of extrapulmonary disease is also a diagnostic challenge.

REFERENCES

[1] Cantini F, Nannini C, Niccoli L, et al; SAFEBIO (Italian multidisciplinary task force for screening of tuberculosis before and during biologic therapy). Guidance for the management of patients with latent tuberculosis infection requiring biologic therapy in rheumatology and dermatology clinical practice. Autoimmun Rev. 2015 Jun;14(6):503-9.

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AB0708 INFLUENCE OF IMMUNOGENICITY ON LONG-TERM MAINTENANCE OF ADALIMUMAB IN SPONDYLOARTHRITIS

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Background: Immunogenicity of anti TNF monoclonal antibodies leads to poor or secondary loss of response. Methotrexate reduces anti-drug antibodies (ADA) to adalimumab at week 26 in spondyloarthritis (SpA).[1]

Objectives: Herein we sought to examine adalimumab long term persistence in ADA positive versus ADA negative SpA patients.

Methods: The CoMARIS study (Combination of Methotrexate and Adalimumab to Reduce Immunization in patients with axial SpA) is a 26-week prospective, randomised, open-labelled, multicentre study in which patients received adalimumab 40 mg subcutaneously (s.c.) every other week either in combination with MTX 10 mg s.c. for 26 weeks or without MTX. In a post hoc analysis, we reviewed the charts of patients to assess adalimumab persistence. A Cox model analysis was performed to test the following covariates: MTX combination or not, sex, presence of ADA at week 26.

Results:

Data from 104 patients (54 without MTX and 50 with MTX) were reviewed, and time of adalimumab discontinuation was collected. The median time of follow-up was 210.57 weeks. ADA positivity at week 26 was the only covariate associated with adalimumab persistence. The median retention rate of adalimumab in ADA positive patients was 56.9 weeks, as compared with 98.6 weeks in those without ADA (log rank: p=0.015). In the Cox model analysis, the presence of ADA at week 26 increased the risk of adalimumab discontinuation by 1.78 [IC 95%=1.11-2.85], p=0.016.

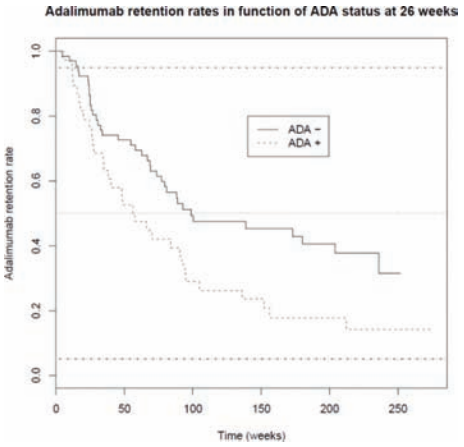


Figure. adalimumab retention rate in ADA positive patients (n=38) at week 26 versus ADA negative patients (n=66), log rank: p=0.015

Conclusion: Immunogenicity is a key factor that contributes to adalimumab discontinuation in SpA. MTX at initiation may therefore be considered in combination to adalimumab in SpA patients.

REFERENCES

[1] Ducourau E, et al. Methotrexate reduces adalimumab immunogenicity in patients with spondyloarthritis: a randomized clinical trial. EULAR17-1527.

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AB0709 **INFLUENCE OF DIETETARY INTAKES ON SPONDYLOARTHRITIS : AN OBSERVATIONAL PROSPECTIVE STUDY**

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Background: Dysbiosis can be found in inflammatory joint diseases and induces alterations of the protective function of the intestinal barrier (1). Yet intestinal inflammation exists in ankylosing spondylitis, which is as much severe as the disease is active (2). Benefits of diets and their influence on the microbiota diversity and inflammation deserve to be studied in spondyloarthritis.
Objectives: The aim of the study was to investigate the nutritional profil in active spondyloarthritis.
Methods: An observational prospective monocentric study based in a french rheumatology department based in Limoges was conducted between February and July 2018, demographic and disease data were collected, in addition to the treatments and the food frequency questionnaire. Voluntary patients over 18 years of age with spondyloarthritis defined by ASAS classification were included. Patients with a diagnosis of inflammatory bowel disease or a bariatric surgery history were excluded of the study. The primary outcome was the correlation between omega-3, vitamin C, refined sugars, fibers and ultra-processed food intakes and the disease activity assessed by ASDAS CRP and BASDAI scores.
Results: Among 140 patients included, there was no statistically significant difference in omega-3, vitamin C, refined sugars, fibers or ultra-processed food intakes between patients with active spondyloarthritis (BASDAI $\geq$ 4 or ASDAS CRP $\geq$ 1,3) and very active (ASDAS $\geq$ 2,1) and patients with unactive disease. The quality of life score and fatigue score were more important in the active and very active disease forms, likewise for the digestive symptoms but there was no link founded in the different nutrients intakes, neither with the associated treatment.
Conclusion: Althouth our study did not find any nutritional profil in active spondyloarthritis, there was an alteration of quality of life and more digestive symptoms in the active group. Future researches are however required to explore the impact of dietatary intakes on the disease activity of spondyloarthritis.

REFERENCES

[1] Costello M-E, Robinson PC, Benham H, Brown MA. The intestinal microbiome in human disease and how it relates to arthritis and spondyloarthritis. Best Pract Res Clin Rheumatol. Avr 2015;29(2):202-12
[2] Hascelik G, Oz B, Olmez N, Memis A, Yoruk G, Unsal B, et al. Association of macroscopic gut inflammation with disease activity, functional status and quality of life in ankylosing spondylitis. Rheumato Int. mai 2009;29 (7):755-81)

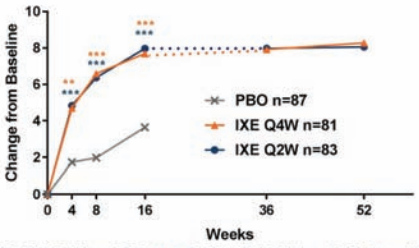
Disclosure of Interests: None declared
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AB0710 **IXEKIZUMAB SIGNIFICANTLY IMPROVES SELF-REPORTED OVERALL HEALTH AS MEASURED BY SF-36 IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS/RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS NAIVE TO BIOLOGICAL THERAPY: 52 WEEK RESULTS OF A PHASE 3 TRIAL**

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Background: Using the Short-Form-36 (SF-36) questionnaire, previous studies have determined that ankylosing spondylitis/radiographic axial spondyloarthritis (AS/r-axSpA) significantly impairs patients' health-related quality of life (HRQoL).[1] Ixekizumab (IXE), a humanized anti-interleukin-17A monoclonal antibody, improves disease signs and symptoms in patients with AS/r-axSpA.[2]
Objectives: To quantify the effect of 52 weeks of IXE treatment on self-reported HRQoL in patients with active AS/r-axSpA who are naïve to biologic therapy (NCT02696785).
Methods: COAST-V is a randomized, double-blind clinical trial that is active- and placebo-controlled in its first 16 weeks. Enrolled patients were adults with active AS/r-axSpA with ASAS criteria who fulfilled mNY of sacroiliitis (central reading), with a BASDAI and back pain $\geq$4, and with no prior treatment with biologic agents. Patients were initially randomized 1:1:1:1 to 80 mg IXE every 4 weeks (Q4W) or every 2 weeks (Q2W), adalimumab (ADA), or placebo (PBO) groups. Changes from baseline in SF-36 up to Week 16 were analyzed by mixed model for repeated measures. Changes from baseline in SF-36 for Weeks 36-52 had no model applied. Missing data were imputed by modified baseline observation carried forward (mBOCF).
Results: By Week 4, statistically significant differences in Physical Component Summary (PCS) were observed between PBO and both IXE Q4W and Q2W groups (Figure; p$\leq$0.002). Further differences in PCS between PBO and IXE groups were observed up to 16 weeks (p<0.001) and maintained through 52 weeks. The change in Mental Component Summary (MCS) was modest (Table). Improvements in all domains were reported at 52 weeks for both the Q4W and Q2W doses of IXE, with the largest improvements observed in the bodily pain domain (Table).
Conclusion: Improvement in self-reported HRQoL in patients with AS/r-axSpA as measured by SF-36 was observed as soon as Week 4 of IXE treatment and maintained for at least 52 weeks.

Figure. SF-36 Physical Component Summary Mean Change from Baseline.



**p=0.002 IXE Q4W vs. PBO; ***p<0.001 IXE Q4W vs. PBO, ***p<0.001 IXE Q2W vs. PBO.
Dotted lines indicate different analyses were performed at Weeks 4 -16 compared to Weeks 36-52. For Weeks 4-16, change from baseline was estimated by mixed model for repeated measures. For Weeks 36-52, observed change from baseline is presented with no model applied, and missing data was imputed by modified baseline observation carried forward.

REFERENCES

[1] Yang, et al. (2016). Qual Life Res. 25:2711-23.
[2] van der Heijde, et al. (2018). Lancet. 392(10163):2441-51.

Table: SF-36 Baseline Scores and Mean Change at Week 52

	IXE Q4W (n=81)		IXE Q2W (n=83)	
	Baseline	Mean Δ at Week 52	Baseline	Mean Δ at Week 52
Physical Component Summary	36.4	8.3	36.6	8.1
Mental Component Summary	50.7	2.2	46.9	4.5
Domains:				
Physical Function	39.2	7.0	38.1	8.0
Role-Physical	39.3	6.9	38.6	6.7
Bodily Pain	36.7	9.7	36.4	9.3
General Health	41.8	4.2	40.2	5.8
Vitality	45.9	6.1	44.9	6.9
Social Functioning	46.2	4.1	42.9	6.0
Role-Emotional	46.2	4.3	43.3	5.0
Mental Health	48.2	2.5	44.4	5.7

SF-36=Short-Form-36 Questionnaire; IXE Q2W=IXE dosed every 2 weeks; IXE Q4W=IXE dosed every 4 weeks; n=number of patients in analysis population; Mean Δ= mean change from baseline value with mBOCF.

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AB0711

IXEKIZUMAB IMPROVES SIGNS AND SYMPTOMS AND SPINAL INFLAMMATION OF ANKYLOSING SPONDYLITIS/RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS THROUGH ONE YEAR OF TREATMENT IN BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUG-NAÏVE PATIENTS

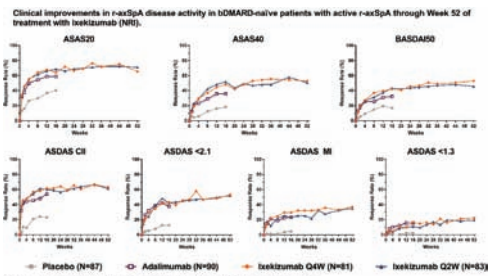
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Background: During 16 weeks (wks) of blinded treatment, ixekizumab (IXE) and an adalimumab (ADA) active reference arm were superior to placebo (PBO) in improving signs and symptoms of radiographic axial spondyloarthritis (r-axSpA).[1]

Objectives: To assess the safety and efficacy of continuous treatment with IXE through 52 wks in patients (pts) with r-axSpA and to describe clinical response at Wk 52 for pts who switched to IXE following 16 wks of treatment with either ADA or PBO.

Methods: Participants were biologic disease-modifying anti-rheumatic drug (bDMARD)-naïve adult pts with active r-axSpA per Assessment of Spondyloarthritis (SpA) international Society (ASAS) criteria (sacroilliitis centrally defined by modified New York criteria and ≥1 SpA feature) and inadequate response or intolerance to non-steroidal anti-inflammatory drugs. Pts were randomized 1:1:1:1 to receive 80 mg IXE every 2 (Q2W) or 4 wks (Q4W), 40 mg adalimumab (ADA) Q2W (active reference arm), or PBO. At Wk 16, pts assigned to IXE continued their assigned treatment and pts receiving PBO or ADA were re-randomized 1:1 to IXE Q2W or IXE Q4W through Wk 52.

Results: Of 164 pts initially randomized to IXE, 146 (89%) completed Wk 52. IXE Q4W and IXE Q2W led to persistent improvements in disease activity, function, objective inflammation (MRI and C-reactive protein), quality of life, health status, and overall functioning for up to 52 wks (Figure and Table). For pts initially assigned to PBO or ADA, ASAS40 response showed a numerical increase upon switching to IXE (Table). Frequencies of treatment-emergent adverse events (AEs) were similar between IXE dosing regimens. Among pts with ≥1 dose of IXE (N=336), serious AEs occurred in 20 (6%) pts. There were no deaths and 11 (3%) pts discontinued due to AEs.



Efficacy of IXE in bDMARD-naïve patients with active r-axSpA

Mean (± SD) change from baseline, Week 52 mBOCF (intent-to-treat)	IXE Q4W (N=81)	IXE Q2W (N=83)
ASDAS-CRP	-1.7 (1.2)	-1.6 (1.0)
BASDAI[a]	-3.3 (2.5)	-3.1 (2.3)
C-Reactive Protein (mg/L)	-9.2 (12.4)	-9.6 (14.5)
BASFI	-2.8 (2.5)	-2.8 (2.4)
SF-36 PCS[b]	8.3 (9.5)	8.1 (7.5)
ASAS Health Index	-2.7 (3.3)	-3.3 (3.6)
SPARCC Spine Score (observed)[c]	-8.8 (17.3)	-8.5 (15.9)
Response (%)	**PBO/All**	**ADA/All**	**All IXE/All**
NRI, extended treatment period population[d]	**IXE (N=86)**	**IXE (N=86)**	**IXE (N=164)**
ASAS40			
Week 16	18.6	36.0	50.0
Week 52	46.5	51.2	51.8

[a]BASDAI items were scored on a 0-10 numeric rating scale
[b]SF-36 analyses based on 2009 US norms
[c]SPARCC Spine: N=72 (IXE Q4W), N=68 (IXE Q2W)
[d]Patients who received ≥1 dose of IXE during Weeks 16-52
ADA=adalimumab; BASFI=Bath Ankylosing Spondylitis Functional Index; IXE=ixekizumab; mBOCF=modified Baseline Observation Carried Forward; NRI=nonresponder imputation; PBO=Placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SF-36 PCS=Medical Outcomes Study 36-Item Short-Form Health Survey Physical Component Summary; SPARCC=Spondyloarthritis Research Consortium of Canada

Conclusion: Persistent improvements in the signs and symptoms of r-axSpA were observed through Wk 52 in pts who received continuous treatment with IXE. ASAS40 response rates at Wk 52 were numerically similar between pts who received continuous treatment with IXE and pts who switched from ADA to IXE. No unexpected safety signals were observed through 52 wks of treatment.

REFERENCES

[1] van der Heijde, et al. Lancet, 2018

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Spondyloarthritis – clinical aspects (other than treatment)

AB0712

RETINAL AND CHOROIDAL VASCULAR STRUCTURES ARE AFFECTED IN AXIAL SPONDYLOARTHRITIS: AN OPTICAL COHERENCE TOMOGRAPHY STUDY

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that mainly affects axial skeleton. Ocular inflammation is one of the most common extra-articular manifestations of axSpA, mainly form of acute anterior uveitis (AAU). However posterior segment of the eye was rarely evaluated. The inaccessibility of posterior structures like choroid and retina to direct examination led clinicians to use non-invasive imaging technics. Optical coherence tomography (OCT) is an imaging technology

providing, high-resolution, and non-invasive cross-sectional view of microscopic, anterior and posterior ocular structures.
Objectives: To evaluate the retina and choroidal vascular structures in axSpA patients by using the advantage of OCT and to compare the changes (if any) with healthy control subjects.
Methods: In total 70 (66% male; mean age 39.7 ± 10.4 years) axSpA patients (50 radiographic- and 20 nr-axSpA) and 50 (mean age 41.2 ± 6.2 years) healthy control subjects were included in the analysis. All patients underwent a detailed ophtalmalogic examination by the same opthtalmologist. All individuals with significant refractive errors (>3 diopters of spherical equivalent refraction) and intraocular pressure ≥21 mmHg were excluded from the analysis. Choroidal thicknes (ChT), macula, and the ganglion cell complex (GCC) were measured by spectral domain optic coherence tomography (SD-OCT) by the same experienced operator.
Results: Mean (± SD) BASDAI score was 3.6 ± 2.5, BASFI score was 3.4 ± 2.9, ASDAS-CRP was 2.6 ± 1.3 in axSpA patients and 14% of them has a history of AAU and 61% ever treated with TNFi agents. There was no significant difference between groups regarding refractive error (*P*=0.640), intraocular pressure (*P*=0.815) and BMI (*P*=0.124) that could affect the OCT measurements. ChT (*P*<0.001) were increased and GCC thickness (*P*<0.001) were decreased in axSpA patients however both layer thicknesses were similar between r- and nr-axSpA patients (*P*=780 and *P*=0.677) (Table). History of uveitis was not associated with ChT and GCC. Although GCC was further decreased in TNFi treated patients (105.8 vs 113.3) this difference did not reach significance (*P*=0.058). Education level was associated both ChT and GCC measurement. GCC thickness was also releted with BMI and sex in univarite analysis. Other disease related characteristics including the ones related with disease activity were not related with posterior segment measurements.
Conclusion: Our results showed that beside anterior segment inflammation, posterior segment of the eye could be affected in both r- and nr-axSpA patients. Retina and choroidal vascular network forms the posterior segment of the eye. The thinning of GCC which form the inner neural layer of the retina is a good indicative of micro-neurotoxicity in axSpA. Elevation of the ChT may be an important indicator of inflammation.

Table. Demographic features and eye assessment results of study population

Variables	r-axSpA (n=50)	nr-axSpA (n=20)	AxSpA (n=70)	Control (n=50)	P*
Age, mean (SD)	41.3 (11.1)	35.8 (7.3)	39.7 (10.4)	41.2 (6.2)	>0.05
BMI, mean (SD)	25.1 (4.3)	26.3 (4.1)	25.5 (4.2)	25.9 (1.3)	>0.05
Education years, mean (SD)	9.1 (4.0)	10.6 (3.6)	9.5 (3.9)	N/A	-
History of AAU, n (%)	6/42 (14.3)	2/16 (12.5)	8/58 (13.7)	N/A	-
TNFi usage, n (%)	32 (64)	11 (55.0)	43 (61.4)	N/A	-
Intraocular pressure, mmHg, mean (SD)	15.0 (2.3)	14.6 (1.9)	14.8 (2.2)	14.8 (2.2)	>0.05
Choroid thickness μM, mean (SD)	333.3 (68.8)	329.8 (69.8)	332.3 (68.6)	263.3 (26.9)	**<0.001**
Macula thickness μM, mean (SD)	255.9 (32.3)	256.1 (16.8)	255.9 (28.6)	262.6 (20.8)	>0.05
GCIPL μM, mean (SD)	106.9 (8.7)	113.2 (27.2)	108.7 (16.3)	112.7 (7.3)	**<0.001**

* P between AxSpA and controls.

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AB0713 MAGNETIC: RESONANCE IMAGING AND ULTRASONOGRAPHIC MEASUREMENTS OF THE FEMORAL CARTILAGE THICKNESS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a progressive inflammatory disease involving cartilaginous structures in the spine and peripheral joints.
Objectives: To examine the role of musculoskeletal ultrasound (MSUS) and magnetic resonance imaging (MRI) in assessing femoral cartilage thicknesses in patients with AS and healthy controls, and to study the correlation between femoral cartilage thicknesses measurements and disease parameters
Methods: Twenty five patients with AS (17 males and 8 females), and twenty five age, sex and BMI matched healthy individuals were included. For all patients assessment of disease activity, spinal mobility, functional limitation and radiological changes were done. Thickness of the femoral articular cartilage was measured by MSUS using a 10-18 MHz linear probe, three mid-point measurements were taken from each knee at the lateral condyle, intercondylar area, and medial condyle. Thickness of the femorotibial articular cartilage was measured by MRI using 1.5 Tesla MR machine.
Results: AS patients had thinner femoral cartilage thickness than the healthy controls at all MSUS measurement sites, with statistically significant differences at medial femoral condyle and intercondylar area in both right and left knees (p<0.05). According to MRI examination, AS patients had statistically significant (p<0.05) thinner cartilage thickness at all subdivisions of femoral and tibial condyles than the healthy controls. Femoral cartilage thickness measurements either assessed by MSUS or MRI was negatively correlated with age, age at onset of the disease, and measures of disease activity and radiological changes. Positive correlation between ultrasonographic total femoral cartilage thickness and MRI total femoral cartilage thickness was found (r=0.49, p=0.02).
Conclusion: Patients with ankylosing spondylitis seem to have thinner femoral cartilage thickness than healthy controls. Correlations of knee cartilage thickness (assessed by MSUS and MRI) with demographic data and disease parameters reflect useful value of MSUS and MRI in determining early cartilage loss in AS patients.

REFERENCES

[1] **AlDhaheri F, Almteri T, Dwid N, Majdali A, Janoudi N and Almoallim H(2017).** Rituximab Can Induce Remission in a Patient with Ankylosing Spondylitis Who Failed Anti-TNF-α Agent. Am J Case Rep.; 18 :143-147.
[2] **Amin S, LaValley MP, Guermazi A, Grigoryan M, Hunter DJ, Clancy M, et al (2005).** The relationship between cartilage loss on magnetic resonance imaging and radiographic progression in men and women with knee osteoarthritis. Arthritis Rheum; 52: 3152-3159.
[3] **Andriacchi TP and Favre J (2014).** The nature of in vivo mechanical signals that influence cartilage health and progression to knee osteoarthritis. CurrRheumatol Rep.; 16(11) :463.
[4] **Anwar F, A-Khayer A, Joseph G, Fraser MH, Jigajinni MV and Allan DB (2011).** Delayed presentation and diagnosis of cervical spine injuries in long-standing ankylosing spondylitis.Eur Spine J.; 20(3) :403-7.

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AB0714 BALANCE AND FALLS IN AXIAL SPONDYLOARTHRITIS: A CROSS SECTIONAL STUDY

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Background: Spondyloarthritis (SpA) patients may suffer of balance loss predisposing them to falls.
Objectives: To study balance impairment and falls in SpA patients and its association with clinical and epidemiological variables, disease activity, functional and metrology indexes.
Methods: Cross sectional study of 55 SpA patients with axial disease. Clinical and epidemiological were collected from the charts. Balance was accessed by Berg Balance Scale(BBS). The following instruments were applied: ASDAS (Ankylosing Spondylitis Disease Activity Score)-ESR, ASDAS-CRP, BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), BASFI(Bath Ankylosing Spondylitis Functional Index), BASMI(Bath Ankylosing Spondylitis Metrology Index) and ASQoL (Ankylosing spondylitis quality of life questionnaire). The number of falls in the last year was collected.
Results: In this sample, 30.9% had high risk of falls by the BBS and 25.4% recalled having at least one fall in the last years. The BBS values were lower in those with white ethnic background(p=0.01); and smokers(p=0.03) and with HLA-B27(p=0.03) and correlated inversely with BASDAI(rho=-0.28), ASDAS-ESR(rho=-0.32) and ASDAS-CRP(rho=-0.33), BASFI(rho=-0.71,p<0.0001), BASMI(rho=-0.80; p<0.0001), ASQoL(rho=-0.57; p<0.001) and age(rho=-0.50;p<0.001). Multivariated analysis showed that BASFI and BASMI were independently associated with BBS(p=0.02 and

0.0001 respectively). Patients with falls had lower BBS (p=0.03) and loss of balance correlated with impairment of the quality of life(rho=-0.56; p<0.001).

Conclusion: Balance is impaired in 1/3 of SpA patients and the BBS is associated mainly with functional and metrology indexes, showing that patients with severe cumulative damage are more affected.

REFERENCES

[1] - Pompeu JE, Romano RS, Pompeu SM, Lima SM. Static and dynamic balance in subjects with ankylosing spondylitis: literature review. Rev Bras Reumatol. 2012; 52:409-16.

[2] - Sawacha Z, Carraro E, Del Din S, Guiotto A, Bonaldo L, Punzi L, et al. Biomechanical assessment of balance and posture in subjects with ankylosing spondylitis. J. Neuroeng Rehabil. 2012; 9:63.

TABLE 1. - STUDY OF BBS(BALANCE BERG SCALE) VALUES ACCORDING TO EPIDEMIOLOGICAL, CLINICAL AND TREATMENT VARIABLES

	Median BBS with the variable (IQR)	Median BBS without the variable (IQR)	p
Male gender	51(44.0-55.0)	51.0(44.2-53.7)	0.80
White ethnic background	49.0(42.5-53.0)	54.0(30.2-55.0)	0.01
Exposed to tobacco (ex and current)	46.0(41.5-54.0)	52.0(46.5-55.0)	0.03
Bilateral sacroiliitis	51.0(45.0-55.0)	53.5(46.2-55.0)	0.63
Enthesitis	50.0(38.5-55.2)	51.0(44.5-55.0)	0.45
Dactilitis	50.5(42.0-54.2)	51.0(44.0-55.0)	0.73
Uveitis	51.0(46.5-55.0)	50.5(41.7-55.0)	0.26
Peripheral arthritis	52.0(40.7-55.7)	51.0(33.0-54.0)	0.92
HLA B27 presence	52.0(44.5-55.0)	48.5(39.5-51.1)	0.03
Anti TNF-α users	50.5(45.0-54.7)	52.0(39.0-55.0)	0.67
History of falls in the last year	46.5(40.0-50.2)	52.0(44.5-55.0)	0.03

TABLE 2. - CORRELATION STUDIES OF BBS (BERG BALANCE SCALE) VALUES WITH AGE, DISEASE DURATION, DISEASE ACTIVITY INDEXES, FUNCTIONAL AND METROLOGY INDEXES AND QUALITY OF LIFE

	Rho	95% confidence interval	p
BASDAI	-0.28	-0,51 to -0,008	0.03
ASDAS VHS	-0.32	-0,54 to -0,05	0.01
ASDAS CRP	-0.33	-0.55 to -0.06	0.01
BASFI	-0.71	-0.82 to -0.55	<0.0001
BASMI	-0.80	-0.88 to -0.67	<0.0001
ASQoL	-0.56	-0.72 to -0.35	<0.0001
Age (years)	-0.50	-0.68 to -0.25	<0.0001
Disease duration (years)	-0.10	-0.36 to 0.17	0.44

BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; ASDAS=Ankylosing Spondylitis Disease Activity Score, ESR=erythrocyte sedimentation rate; CRP=C reactive protein; BASMI=Bath Ankylosing Spondylitis Metrology Index; BASFI=Bath Ankylosing Spondylitis Functional Index; ASQol-Ankylosing Spondylitis Quality of Life questionnaire.

Disclosure of Interests: None declared

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AB0715 ASSESSMENT OF BODY COMPOSITION IN LEAN MASS AND FAT MASS IN SPONDYLOARTHRITIS

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Background: Mohamed Montacer Kchir bsorptiometry Absorptiometer (DEXA) is the gold standard for the study of body composition. It allows to sepMohamed Montacer Kchirarate the 2 compartments lean mass (LM) and fat mass (FM), and to study their distribution at the android and gynoid level

Objectives:

- Evaluate the change in total body composition measured the DEXA in patients with spondyloarthritis (SpA) compared to a control group.
- Evaluate the distribution of LM/FM at the android and gynoid levels.
- Study the influence of disease activity and bone mass on body composition.

Methods: This was a case-control study involving 50 patients with SpA compared to 50 controls. Each control was comparable in age and sexe to the matched patient.

Results: The mean age was 36 years in the SpA group and 35,5 years in the control group. Eighty per cent of the patients with SpA were male. The mean BASDAI was 4,64 ± 2,5. The mean ESR rate was 32,37 ± 20,95, the mean CRP rate was 18,05 ± 27,22 [0-141]. The mean body mass index (BMI) was 25,4 Kg/m² (25,74 Kg/m² in the control group). The mean bone mineral density (BMD) at the lumbar spine was 1.033 g/cm² (with a mean T score of -1.5 DS and Z score -1.3 DS) while it was 0.956 g/cm² at upper end of the femur level (with a mean T score of -0.8 and a mean Z score of -1.2 DS). In controls, the mean BMD was 1.055 g/cm² and 1.013 g/cm² at the lumbar spine and upper end of the femur respectively (with a mean T score of -1.4 DS and -0.5 SD and a mean Z score of -1.4 and -0.3 respectively at the lumbar and superior femoral sites). In the SpA group, the mean value of whole body FM was 31.6%, whereas this average was around 36% in controls. FM was distributed as follows: 39.2% at the android level versus 37.7% at the gynoid level. For LM, the whole body average was 68.4%, while the average was 60.8% at the android level and 62.3% at the gynoid level. The 2 groups (patients and controls) were comparable in terms of BMD, T score and Z score measurements at different lumbar and superior femoral sites. The SpA group and their healthy controls were comparable in terms of FM and LM measurements and their distributions. We found a significant correlation between the rate of CRP and the measurements of FM at the android level (r = -0.358, p = 0.023) (and conversely the LM at the android level). However, we found no association between disease activity (BASDAI) and body composition.

Conclusion: Changes in body composition (MM/MG) related to chronic inflammatory status may occur during chronic inflammatory diseases. However, few studies in the world have focused on changes in the bodily compartments and their distribution in SpA.

Disclosure of Interests: None declared

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AB0716 ESTABLISHMENT OF BASDAI CUT-OFFS FOR THE DISEASE ACTIVITY STATES BASED ON ASDAS CUT-OFFS IN TAIWANESE ANKYLOSING SPONDYLITIS PATIENTS

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Background: The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) has been widely utilized to evaluate disease activity in patients with ankylosing spondylitis (AS). However, the cut-off of BASDAI used to indicate high disease activity (i.e., ≥4) was determined arbitrarily and was suggested as a criterion to initiate biological therapy for AS patients. The Ankylosing Spondylitis Disease Activity Score (ASDAS) has been developed as a new composite index to assess AS disease activity. The cut-off values for disease activity states has been defined and validated. ASDAS≥2.1 was selected as a criterion of starting biological therapy. However, the BASDAI cut-off values corresponding to the ASDAS cut-off values for disease activity states were unknown.

Objectives: The purpose of this study was to estimate the corresponding BASDAI and ASDAS cut-off in a Taiwanese AS cohort.

Methods: Since November 2016, we assessed the Ankylosing Spondylitis Disease Activity Score (ASDAS) and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) regularly and recorded demographic data, comorbidity, family history, medication use for AS patients in Taichung Veterans General hospital (TCVGH) using an electronic patient reported data system linked to an electronic medical record system. We identified 489 AS patients with complete baseline demographic and assessment data from the TCVGH electronic data system during 2016/11–2018/10. We used receiver operating characteristic (ROC) curves with Youden's J statistic to determine the cut-off values of BASDAI that correspond to ASDAS disease activity cut-offs (i.e., 1.3, 2.1 and 3.5).

Results: We included a total of 489 AS patients [114 (23.3%) females, mean age 44.1 years (S.D. 13.9), mean symptom duration 18.0 years (S.D. 11.9), 152 (31.1%) current biologic users]. Mean BASDAI, ASDAS-ESR and ASDAS-CRP scores were 2.1 (S.D. 1.5), 1.6 (S.D. 0.8) and 1.5 (S.D. 0.9) respectively. Mean levels of CRP and ESR were 0.6 (S.D. 1.5) mg/dl and 12.2 (S.D. 14.0) mm/hr respectively. Based on ASDAS-CRP, the numbers (%) of AS patients with inactive disease (<1.3), low disease activity (1.3-2.1), high disease activity (2.1-3.5) and very high disease activity (≥3.5) were 210 (42.9), 171 (35.0), 88 (18.0) and 20 (4.1) respectively. Based on ASDAS-ESR, the numbers (%) of AS patients with inactive disease, low disease activity, high disease activity and very high disease activity were 202 (41.3), 174 (35.6), 96 (19.6) and 17 (3.5)

respectively. The best trade-off BASDAI values corresponding to ASDAS -CRP 1.3, 2.1 and 3.5 were 2.1, 3.1 and 3.7 respectively. The optimal BASDAI values corresponding to ASDAS-ESR 1.3, 2.1 and 3.5 were 2.0, 2.6 and 4.8 respectively.

Conclusion: The estimated optimal BASDAI value that corresponds to the recommended ASDAS cut-off ≥2.1 for biologial therapy initiation was lower than the recommended BASDAI cut-off of ≥4 in this Taiwanese AS cohort.

Abstract AB0716 Table 1.. Optimal BASDAI cut-off values corresponding to ASDAS cut-offs using ROC curve with Youden's J statistic in AS patients.

	BASDAI cut-off	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
ASDAS-CRP 1.3	2.1	0.76 (0.72–0.80)	0.70 (0.65–0.75)	0.82 (0.75–0.88)
ASDAS-CRP 2.1	3.1	0.78 (0.74–0.82)	0.69 (0.62–0.76)	0.87 (0.83–0.91)
ASDAS-CRP 3.5	3.7	0.82 (0.75–0.89)	0.84 (0.66–0.95)	0.81 (0.77–0.84)
ASDAS-ESR 1.3	2.0	0.80 (0.77–0.84)	0.74 (0.69–0.78)	0.87 (0.80–0.92)
ASDAS-ESR 2.1	2.6	0.79 (0.76–0.83)	0.81 (0.74–0.86)	0.78 (0.73–0.82)
ASDAS-ESR 3.5	4.8	0.79 (0.70–0.89)	0.67 (0.46–0.83)	0.92 (0.89–0.94)

REFERENCES

[1] Machado P, et al. 2011. Ankylosing Spondylitis Disease Activity Score (ASDAS): defining cut-off values for disease activity states and improvement scores. Ann Rheum Dis 2011;70:47-53.

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AB0717 RELIABILITY OF SACROILIAC JOINT RADIOGRAPHS IN THE EARLY SPONDYLOARTHRITIS ESPERANZA COHORT

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Background: X-Ray sacroiliitis is the cornerstone in the diagnosis of the ankylosing spondylitis (AS). It is clear that the presence of sacroiliitis is a specific lesion in long standing AS, but little evidence exists on the reliability of this image technique in early axial spondyloarthritis (axSpA), which associates with reduced structural damage. This is relevant because some rheumatologists and pharmacological authorities feel more confident with the diagnosis of AS rather than with non radiographic axial spondyloarthritis (nr-axSpA) forms. On the other hand, according to various research studies, clinicians are subject to potential bias when interpreting radiographs, influenced by their pretest clinical judgment

Objectives: The main objective of this study is to determine the reliability of X-Ray sacroiliitis in the early diagnosis of axSpA.

Methods: This study included 290 radiographs of the SI joints from patients of the Esperanza early spondyloarthritis cohort. Nine readers, blinded for the diagnosis, participated in the reliability exercise, all of them experienced rheumatologists and members of the Spanish spondiloarthritis working group (GRESSER). Patients with axSpa were classified as having AS if the radiographic criteria of the modified NY criteria (presence of radiographic changes in the SIJ of at least grade II bilaterally or at least grade III unilaterally) were fulfilled. The gold standard was the categorical opinion of at least five of the expert readers. For the statistical analysis, the Chi-square and Kappa tests were performed.

Results: The table shows mean kappa values and the agreement reached by each reader. The mean kappa achieved was fair (0.375, range 0.146 - 0.652) and the mean agreement was 73.7% (range: 58.7% - 90%). When the categorical opinion of X-Ray sacroiliitis of at least 5 readers as gold standard was applied, 61 patients were classified as AS and 229, as nr-axSpa. Nevertheless, this scenario varied from 31 to 138 among the readers when the x-ray evaluation was performed by only one reader.

Conclusion: Reliability of X-Ray SIJ in an early SpA cohort was weak among nine experimented readers and the diagnosis of AS was subject to a high variability. At least in doubtful cases, a central evaluation performed by highly qualified readers is advisable.

	Gold standard	Reader 1	Reader 2	Reader 3	Reader 4	Reader 5	Reader 6	Reader 7	Reader 8	Reader 9
Kappa		.716	.345	.468	.606	.599	.459	.612	.513	.809
Agreement		90.97	68.06	85.52	84.48	85.12	73.79	87.59	78.47	94.14
SIJ mNY+	61	54	138	31	92	80	137	55	115	48
SIJ mNY TP	61	44	53	25	54	49	61	40	57	46
SIJ mNY FP	229	10	85	6	38	31	76	15	58	2
Sensitivity		73.33%	88.33	59.02	88.52	80.33	100	65.57	93.44	75.41
Specificity		95.61%	62.72	97.38	83.41	86.40	66.81	93.45	74.45	91.13
LR +		16.70	2.369	22.53	5.336	5.907	3.013	10.01	3.657	8.502

SIJ = (SI) joint; mNY+ = number of patients that meet diagnosis of ankilosing spondylitis; TP = true positives; FP = false positives; LR+ = Likelihood ratio +

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AB0718 IDENTIFYING AXIAL SPONDYLOARTHRITIS IN THE UNITED STATES: A POSSIBLE ROLE FOR CHIROPRACTORS

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Background: Approximately 19% of the general population in the United States has chronic back pain (CBP), with 5%-6% of these cases classified as inflammatory back pain (IBP).[1] According to the US National Health and Nutritional Examination Survey, ≈ 15% of patients with IBP have axial spondyloarthritis (axSpA),[1,2] which can cause irreversible structural damage in the spine, loss of function, and a decreased quality of life. The diagnosis of axSpA is commonly missed, as patients seek care for back pain (BP) from a variety of non-rheumatology providers, including chiropractors.[3] Overall, nearly 50% of patients seek chiropractic care for BP.[4] However, not much is known about the prevalence of different types of BP (acute, chronic, IBP, and BP due to axSpA) in patients seeking chiropractic care in the United States.

Objectives: To investigate the types of providers sought by patients with BP and the prevalence of acute BP, CBP, IBP, and axSpA in patients with BP seeking chiropractic care in the United States. A secondary objective was to investigate how frequently chiropractors refer patients with BP to a rheumatologist.

Methods: PubMed literature searches were performed for all English language articles published through December 2017 to determine which providers are sought by patients with BP as well as the percentage of patients with BP being referred to a rheumatologist following chiropractic consultation. Search terms included "chiropractic," "chiropractor," "axial spondyloarthritis," "ankylosing spondylitis," "inflammatory back pain," "chronic back pain," "acute back pain," "low back pain," "sacroiliac joint," "sacroiliac pain," "back pain epidemiology," "rheumatologist," and "rheumatology." The full text of relevant articles was evaluated for specific data and BP statistics in this care setting.

Results: Only 7 articles that described the types of providers sought by patients with BP were identified (Table 1). Among patients with BP, 7%-45% sought chiropractic care; 26%-70% sought care from general practitioners, and 3%-37% sought care from rheumatologists. Patients who sought chiropractic care were mainly white, female, aged < 65 years old, and of higher socioeconomic and education status. Patients with CBP seeking rheumatologic care had a mean duration of CBP of 14-28 years and were mostly women (56%; age range, 41-50 years)[5]; of these, 1% were referred to a rheumatologist by chiropractors for symptoms suggestive of SpA.[5] Data regarding the prevalence of different types of BP (eg, acute, CBP, IBP) in US chiropractic practices were not available. No articles describing axSpA in patients in chiropractic care were identified.

Table 1. Diagnosis and Management of Back Pain in the United States: Practitioner Specialties

Study Description	Practitioner Specialties, %							
	Chiropractor	General Practitioner	Orthopedist	Rheumatologist	Other Specialist	Physical/ Massage Therapist	AC/CAM	Other
Gallup-Palmer College of Chiropractic 2016 Annual Report - Survey of adult preferences (n = 7586) for back pain care if costs were equal Reference: http://www.palmer.edu/uploadedFiles/Pages/Alumni/gallup-report-palmer-college-2016.pdf	28	53[a]	NR	NR	NR	13	1	4
Ghildayal 2016 - Analysis of Alternative Health Supplement NHIS data for 9665 adults with LBP Reference: Ghildayal N, et al. *Glob Adv Health Med.* 2016;5:69-78.	15	NR	NR	NR	NR	12	41	NR
Wilson 2015 - Analysis of data from the 2002-2012 MEPS for patients with back/joint pain diagnosis (n = 16,762) Reference: Wilson FA, et al. *J Eval Clin Pract.* 2015;21:952-957.	24	43	13	3	11	5	1	NR
Deodhar 2016 - Analysis of US commercial claims database of AS in 3336 patients with back pain diagnosed by a non-rheumatologist Reference: Deodhar A, et al. *Clin Rheumatol.* 2016;35:1769-1776).[b]	7[c]	26	4	37	NR	NR	NR	26
Sherman 2004 - Survey of 249 adults with CBP about their interest in CAM Reference: Sherman KJ, et al. *BMC Complement Altern Med.* 2004;4:9.	45	NR	NR	NR	NR	24	11	7
Carey 2010 - Telephone survey of 3276 adults in North Carolina with chronic back or neck pain, stratified by race (range) Reference: Carey TS, et al. *J Pain.* 2010;11:343-350.	22-34	50-70	24-42[d]	NR	NR	10-31[e]	2-7[f]	NR
Carey 1995 - Telephone survey of 4437 adults in North Carolina; CBP prevalence and care-seeking Reference: Carey TS, et al. *Spine (Phila Pa 1976).* 1995;20:312-317.	25	64	55	NR	NR	29	NR	NR

AC, acupuncturist; AS, ankylosing spondylitis; CAM, complementary and alternative medicine; CBP, chronic back pain; LBP, low back pain; MEPS, Medical Expenditure Panel Survey; NHIS, National Health Interview Survey; NR, not reported.
[a]Reported as medical doctor or primary care doctor in original study; [b]Data reported in this article are for a diagnosis of AS made by a given specialty; [c]Includes physical therapist visits; [d]Includes neurosurgeon visits; [e]Physical therapist visits only; [f]Massage therapist and/or AC visits.

Conclusion: Chiropractors, as primary spine care providers in the United States, are playing an increasingly larger role in the diagnosis and treatment of BP, with 7%-45% of patients with BP seeking chiropractic care. However, there are conflicting data on the types of BP treated by chiropractors in the United States. Nonetheless, since approximately 15% of patients with IBP have axSpA,[1,2] it is very likely that many patients seeking care from chiropractors in the United States have undiagnosed axSpA. This reveals a need for a systematic investigation for the presence of axSpA among patients being treated by chiropractors. Specific educational strategies targeted to chiropractors should be applied to increase awareness of axSpA and achieve early referral to rheumatologists for these patients.

REFERENCES

[1] Weisman MH, et al. Ann Rheum Dis. 2013;72:369-373.
[2] Reveille JD, et al. *Arthritis Care Res (Hoboken).* 2012;64:905-910.
[3] Danve A, et al. Clin Rheumatol. 2018 Dec 26. [Epub ahead of print].
[4] Beliveau PJH, et al. Chiropr Man Therap. 2017;25:35.
[5] Deodhar A, et al. *Arthritis Rheumatol.* 2016;68:1669-1676.

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AB0719

PREVALENCE OF UNDIAGNOSED AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC LITERATURE REVIEWAND PRIMARY RESEARCH STUDY

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Background: Axial spondyloarthritis (axSpA) encompasses psoriatic arthritis with axial disease, ankylosing spondylitis and non-radiological axSpA. Patients with axSpA have a high burden of inflammatory bowel disease (IBD) but few studies have investigated the proportion of IBD cases that have undiagnosed axSpA. Untreated axSpA could have a significant impact on the general health and quality of life of patients; therefore early diagnosis and treatment is crucial[1].
Objectives: This systematic literature review (SLR) aimed to identify the prevalence of undiagnosed axSpA in IBD cases based on cross-sectional imaging (MRI and CT scans) of the axial skeleton from published data.
Methods: This SLR was performed in keeping with MOOSE guidelines for observational studies. Original articles in all languages from 1990-2018 were retrieved from PubMed, Embase and Cochrane databases. Article reference lists were checked for further literature. Rheumatology conference (ACR, EULAR, GRAPPA, BSR, Gent Spondyloarthritis) abstract lists from 2012-2018 were reviewed and authors contacted for any additional unpublished data. All abstracts were reviewed by two authors to determine eligibility for inclusion.
Results: Twenty observational studies were identified: twelve published papers and eight abstracts. Thirteen studies assessed the prevalence of CT-sacroiliitis in IBD cases, two used magnetic resonance enterography (MRE) imaging and five used MRI imaging. The studies included a variety of patient demographics and IBD types. Sample sizes ranged between 25-1247 patients. Eleven studies included 2 independent radiology readers. The presence of inflammatory back pain was assessed in 7/20 studies, 5/20 included a control group and only 3/20 included a clinical rheumatology assessment. Thirteen studies used IBD imaging to assess for sacroiliitis compared to seven using dedicated MRI or CT imaging of the sacroiliac joints. The prevalence of sacroiliitis ranged from 2.2% to 68%. Eleven studies included patients with Crohns disease (average sacroiliitis prevalence 18.6%) and Ulcerative colitis (average sacroiliitis prevalence 17.4%), with 7/11 studies stating no significant difference in the prevalence of sacroiliitis between the two groups. Four studies identified an association of sacroiliitis with increased disease duration, two with increasing age and only one with IBD location.
Conclusion: From these studies, it appears that axSpA may affect a substantial number of patients with IBD and is likely to be significantly underdiagnosed. Cross-sectional imaging intended for the assessment of IBD can be utilised to screen for the presence of axSpA, perhaps even before the onset of musculoskeletal symptoms. Such patients could then be triaged for detailed rheumatological assessment. This review highlights the sparsity of data on the prevalence of axSpA in IBD cases. Few studies have included a clinical rheumatological assessment and just over half assessed for any potential difference in the prevalence of sacroiliitis in the Crohn's disease (CD) and Ulcerative colitis groups. This review has informed our prospective cross-sectional single-centre observational study, due to start in February 2019. We will assess the sensitivity and specificity of MRE as a screening tool for axSpA in a cohort of 600 CD cases, using clinical assessment and a dedicated axial MRI scan as the gold standard.

REFERENCES

[1] Ozgul, A., et al., *Effect of ankylosing spondylitis on health-related quality of life and different aspects of social life in young patients.* Clin Rheumatol, 2006. 25(2): p. 168-74.

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AB0720 IMPACT OF SPONDYLOARTHRITIS ON THE MALE SEXUAL FUNCTION: LIMITING FACTORS

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Background: The impact of Spondyloarthritis (SpA) on patients' sexual life and erectile function has been gathering the attention of the scientific community over the last decade [1,2]. Several factors may condition sexual function for SpA patients: microangiopathy, pain, decreased range of motion, joint swelling and extraarticular features such as fatigue.
Objectives: To assess the erectile function and the sexual desire in a cohort of male patients with SpA and to identify the factors related to the disease limiting the sexual life.
Methods: This is a cross sectional study including sexually active male patients with SpA (ASAS criteria). A questionnaire was performed, consisting in two parts. One part filled by a rheumatologist with data of the disease (comorbidities, the presence of a coxitis, disease activity (BASDAI and ASDAS), function index (BASFI) and current treatment). The other part consisted in a questionnaire filled by an urologist, with data on pain during intercourse, the international index of erectile function (IEEF5), intensity and frequency of sexual desire and disease impact on private life. For statistical analysis, we used Khi^2-test for qualitative variables and Student-test for quantitative variables. A p value ≤0.05 was considered significant.
Results: We included 37 male patients with SpA, 18.9% had psoriatic arthritis, 51.4% had ankylosing spondylitis and 29.7% had inflammatory bowel disease spondyloarthritis. The mean age was 42.5 ± 1.8 years. Sixty two percent of patients were married. Mean disease duration was 11.4 ± 7.1 years. The mean disease activity and functional scores were as follow: BASDAI=2.57 ± 1.96, ASDAS CRP=2.36 ± 1.09, BASFI=2.59 ± 2.54). For the treatment side: 40.5% were on NSAIDs, 70.3% on csDMARDs and 56.8% of patients were on biotherapy (33.3% on Adalimumab, 52.4% on infliximab and 14.3% on Etanercept). The mean visual analog pain scale during intercourse was 2.97 ± 1.89 and the erectile function was deteriorated in 80.6% of patients.
Conclusion: Our results suggest the impact of SpA on patients' sexual function. Pain during intercourse and the limitation of the sexual desire were the most limiting factors of the sexual function.

REFERENCES

[1] Tristano AG. The impact of rheumatic diseases on sexual function. Rheumatol Int 2009;29:853–60.
[2] Bal S, et al. sexual functions in ankylosing spondylitis. Rheumatol Int 2011;31(7):889-94.

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AB0721 EPIDEMIOLOGICAL, CLINICAL AND PROGRESSION FACTORS OF SPONDYLOARTHRITIS IN A TERTIARY CARE HOSPITAL

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Background: Spondyloarthritis (SpA) is a heterogeneous group of diseases that predominantly affect the axial skeleton, with a debut generally before 45 years. Among the factors favoring radiological progression[1] are, among others, high levels of CRP, tobacco consumption and diagnostic delay.
Objectives: To describe clinical-epidemiological characteristics and analyze possible factors of radiological progression (based on the development of syndesmophytes) in patients with a diagnosis of SpA in our hospital.
Methods: Retrospective, descriptive observational study of patients diagnosed with SpA (New York, ASAS and AMOR criteria) in the University Health Care Complex of León for 45 years (1973-2018).
Results: A total of 218 patients were collected, 59.6% were men and 40.4% were women with an average age of onset of symptoms of 30.56 ± 12.06 years and a diagnosis of 35.59 ± 12.26 (diagnostic delay defined by a median of 2 years before the great dispersion of data). 81.2% have HLA-B27 positive. 64.2% come predominantly León capital, also highlighting other areas such as La Bañeza (9.6%) and Astorga (6.4%). 13.8% are ex-smokers, 18.8% are active smokers and 67.4% are non-smokers. 68.3% made their debut with inflammatory low back pain. 67% developed some anterior uveitis throughout its evolution. 72.9% have axial involvement and 27.1% joint axial and peripheral involvement. 89.9% met criteria New York (NY), 8.3% criteria ASAS and 1.8% criteria AMOR for the diagnosis of SpA. 17.4% developed syndesmophytes. The activity of the disease was assessed by BASDAI and PCR (taking the reference point of our laboratory, 5 mg/l as the cut-off point) at the time of diagnosis and in the last control performed, showing that 87.6% presented a BASDAI> 4 at the time of diagnosis while in the last revision 84.9% has BASDAI <4; the elevated levels of CRP appeared in 54.45%, normalizing in 73.9% in the last control. We observed that the age of diagnosis <45 years (p 0.000289) in our sample is related to less progression due to the probable early initiation of biological treatment (18.2% in <45 years, 11% in> 45 years); while both elevated CRP at diagnosis (p 0.003) and exposure to tobacco (p 0.036) present a higher rate of syndesmophytes due to a probable higher inflammatory activity. For other variables (Sex, HLA-B27, BASDAI, diagnostic delay, presence of uveitis and NSAIDs), we did not obtain a statistically significant relationship.
Conclusion: - Most part of patients with SpA are young men, with HLA-B27 positive and axial involvement with debut as inflammatory back pain that meet NY criteria.
- High levels of CRP at diagnosis (p 0.003) and tobacco consumption (p 0.036) have been associated, in our sample, with greater radiological progression while the age of diagnosis <45 years is related to lower progression (p 0, 000289) may be due to the early introduction of biological treatment (18.2% in <45 years, 11% in> 45 years).

REFERENCES

[1] Poddubny D, Haibel H, Listing J, Märker-Hermann E, Zeidler H, Braun J, et al. Baseline radiographic damage, elevated acute-phase reactant levels, and cigarette smoking status predict spinal radiographic progression.

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AB0722 DOES THE ULTRASOUND OF SACROILIAC JOINTS CONTRIBUTE TO THE DIAGNOSIS OF SPONDYLOARTHRITIS?

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Background: Although pelvic radiography is a robust imaging modality to detect sacroiliitis, radiographic changes require at least 5 years to develop after symptom onset, hence the increasing interest in new imaging tools in the field of spondyloarthritis (SpA). Whereas the diagnostic utility of magnetic resonance imaging (MRI) and computed tomography (CT) of sacroiliac joints (SIJ) has been extensively studied in many cohorts, the contribution of SIJ ultrasound (US) in the diagnostic of SpA has been little-studied.
Objectives: The objective of this study is to assess the performance of SIJ US for detecting sacroiliitis and to determine its sensitivity and specificity in patients with SpA.
Methods: Consecutive patients, aged 16 years and over, consulting for symptoms suggestive of SpA (inflammatory back pain, enthesitis or dactylitis…) from February 2014 to February 2017 were enrolled in this cohort. Eligible patients underwent physical examinations, laboratory tests, SIJ US, CT and/or MRIs, following a standardized protocol. Patients with a conventional radiography showing a confirmed sacroiliitis (grade 3 or 4) were not included. The US was considered positive when showing a unilateral or bilateral vascularization (Doppler signals). Then, resistive index (RI) was measured. After analyzing clinical and radiological data and HLA typing, two experienced rheumatologists, blinded to US results, proceeded to the classification of the patients into 2 groups: confirmed SpA or no SpA. Their final diagnosis was considered the gold standard in interpreting the results of US examination.
Results: Forty-five patients, 10 men and 35 women, with an average age of 39 years were included. The mean duration of symptoms was 75 months (6 years). A family history of SpA was noted in 2.22% of

patients. A personal history of Reiter's syndrome was noted in 2.22% of patients and of uveitis in 6.66%. Morning stiffness was noted in 60% (n=27) of patients. Good response to nonsteroidal anti-inflammatory drugs (NSAIDs) and to physical activity were respectively reported by 42.22% (n=19) and 57.8% (n=26) of patients. Twenty-seven per cent of the patients were HLA-B27+. Fifty-one per cent of the studied patients fulfilled the ASAS criteria for axial SpA and 46.7% fulfilled the Amor criteria. After a follow-up between 2 and 3 years, the diagnosis of SpA was confirmed by the referring rheumatologists in 31 (68.9%) patients and excluded in 14 (31.1%) patients. Among the 31 patients with confirmed SpA, 61.3% (n=19) had a positive US (with a mean RI estimated at 0.75) and 38.7% (n=12) had a normal US. Among the 14 patients in whom SpA was excluded, 50% (n=7) had a positive US (with a mean RI estimated at 0.7) and 50% had a normal US. Sensitivity and specificity of US examination were estimated at 61.3% and 50%. Positive and negative likelihood ratio were estimated at 73% and 36.8%. Association between US findings and rheumatologists' diagnosis of SpA was not statistically significant (p=0.47).

Conclusion: US contribution in the diagnostic of SpA has been little-studied. In our study, although US of SIJ lacked specificity, it has a satisfactory sensitivity and positive likehood ratio. In fact, this tool is more valuable by its positivity which indicates a high probability of sacroiliitis. However, further investigation is needed in order to assess its performance for ascertaining sacroiliitis.

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AB0723

SMOKING MAY BE RELATED TO SACROILIITIS IN ENTEROPATHIC ARTHRITIS PATIENTS: TREASURE REAL-LIFE PRELIMINARY DATA

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Background: Articular manifestations may differ in ulcerative colitis (UC) and Crohn's disease (CD). Genetic and non-genetic factors like sex, smoking, and presence of HLA-B27 were previously shown to modify the expression of articular and other extraintestinal manifestations of IBD.

Objectives: The aim of this study is to document disease features and factors affecting the expression of articular manifestations in Turkish patients with IBD-related (enteropathic) arthritis under treatment with disease modifying antirheumatic drugs (DMARDs).

Methods: Data regarding enteropathic arthritis (EA) were collected from the TReasure database, a nation-wide multicenter observational registry of inflammatory arthritis patients.

Table 1. Demographic and clinical features of enteropathic arthritis patients with respect to inflammatory bowel disease form

	N	Sacroiliitis (-) (n=18)	Sacroiliitis (+) (n=138)	p
Female, n (%)	156	11 (61.1)	55 (39.9)	0.086
Age, years (Q1-Q3)	156	44 (31-58)	46 (38-51)	0.754
EA duration, months (Q1-Q3)	156	61 (24-146)*	85 (36-146)*	0.385
Syndesmophytes, n (%)	115	0 (0)	28 (27.2)	**0.037**
Enthesitis, n (%)	110	6 (50)	31 (31.6)	0.214
Dactylitis, n (%)	128	0 (0)	3 (2.6)	Ns
Psoriasis, n (%)	153	1 (5.6)	5 (3.7)	Ns
Family history of SpA, n (%)	118	2 (22.2)	32 (29.4)	1
HLA-B27 positivity, n (%)	90	1 (7.1)	24 (31.6)	0.1
Smoking, n (%)	146	6 (35.3)	80 (62)	**0.035**
ESR, mm/h, (Q1-Q3)	106	46 (14-74)	37 (21-52)	0.442
CRP, mg/L, (Q1-Q3)	106	29 (11.8-55.3)	16.1 (8.12-38.1)	0.367
BASDAI, (Q1-Q3)*	100	5.8 (4.5-8)	5.6 (3.9-7)	0.597
BASFI, (Q1-Q3)*	87	3.4 (2-6.1)	3.2 (2-5)	0.886
ASDAS-ESR, (Q1-Q3)*	72	3.25 (2.46-4.12)	3.4 (2.59-3.91)	0.948
ASDAS-CRP, (Q1-Q3)*	73	3.85 (2.72-4.73)	3.53 (2.63-4.09)	0.446

Results: Among 4066 patients with seronegative spondyloarthropaties (SpA), 156 (3.8%) had EA, not reflecting a true prevalence due to selection bias. Demographic and clinical features according to IBD groups were summarized in Table 1. Rates of presence of sacroiliitis were similar between patients with UC and CD (39.9% and 60.1%, p=0.086 respectively). Rates of HLA-B27 positivity were 31.6% and 7.1% in patients with and without radiographic sacroiliitis, respectively (p=0.101). Enthesitis, dactylitis, psoriasis, family history forSpA, ESR, CRP, BASDAI and ASDAS levels had similar distributions in patients with and without radiographic sacroiliitis. Rates of "never-smoked" (26.5% vs 64.7%) and "current smoking" (32.4% vs 17.6%) significantly differed in patients with and without sacroiliitis (overall p=0.012)

Conclusion: Our data confirm an association between smoking status and disease manifestations, particularly radiographic sacroiliitis.

REFERENCES

[1] Fries W. Clinical features and epidemiology of spondyloarthritides associated with inflammatory bowel disease. World J Gastroenterol 2009; 15: 2449-2455.

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declared, Bahar Keleşoğlu: None declared, Sedat Yılmaz: None declared, Yavuz Pehlivan: None declared, Ender Terzioğlu: None declared, Levent Kılıç: None declared, Sukran Erten: None declared, Koray Taşçılar: None declared, Umut Kalyoncu Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim

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AB0724 DOSE PREGNANCY AND VAGINAL DELIVERY WORSEN ANKYLOSING SPONDYLITIS?

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Background Ankylosing spondylitis (AS) affects the sacroiliac joints and commonly occurs in those at the reproductive age. Women with AS have a higher rate of cesarean section (CS) compared with healthy controls.

Objectives This study determined the effect of pregnancy and delivery methods on AS worsening by analyzing prescription pattern.

Methods Based on the Korean Health Insurance Review and Assessment Service claims database, subjects comprised female patients aged 20–49 years with an AS. Alteration of prescriptions was defined by changing the at two time periods of 1–2 years pre-delivery and 1-year post-delivery. We compared alteration of prescriptions between AS patients with delivery and 1:1 matched AS patients without delivery. In addition, among AS patients with delivery, alteration of prescriptions according to delivery method was evaluated.

Results Among 6,821 female patients with AS, 996 patients in the delivery group were younger, had a higher proportion of non-drug use, and had lower rates of comorbidity than the no delivery group. The alteration of prescriptions did not differ between the AS with delivery and the AS without delivery groups (OR 0.76, 95% CI 0.56–1.05). Furthermore, the overall alteration of prescriptions did not differ significantly between vaginal delivery (VD) and CS (OR 0.72, 95% CI 0.45–1.14).

Conclusion The rate of alteration of prescriptions was comparable between the AS patients with and without delivery. There was no association between VD and alteration of prescriptions compared with CS. Taken together, pregnancy and VD may not be assumed to be factors of AS worsening.

Disclosure of Interests None declared

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AB0725 ASSOCIATION BETWEEN RADIOGRAPHIC PROGRESSION AND CARDIOVASCULAR RISK IN SPONDYLOARTHRITIS: DATA FROM COSPAR REGISTRY

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Background: Studies suggest that radiographic damage is associated with cardiovascular (CV) risk in axial spondyloarthritis (axSpA). However, the relationship among disease characteristics directly related to structural damage and CV risk has not yet been fully clarified.

Objectives: To analyze the association of structural damage with the presence of atherosclerotic plaques via carotid ultrasound (US) and the increased CV risk in a registry of patients with SpA.

Methods: Eighty-five patients with SpA (ASAS criteria) from the SpA registry from Cordoba (CoSpaR) were selected for a cross-sectional study and underwent a complete clinical history, physical examination and biochemical analysis. Variables about demographics, clinical parameters and CV risk factors were collected. CV risk was evaluated by estimating SCORE index and assessing presence of atherosclerotic plaques through carotid US performed by a qualified radiologist. Independent-samples t test was used to evaluate the association between radiological characteristics and presence of atherosclerosis. Multiple lineal regression (MLR) was performed to assess the variables potentially associated with increased SCORE. All comparisons were bilateral.

Results: Baseline characteristics are shown in the table. Values are mean±SD for quantitative and N (%) for qualitative variables. Regarding characteristics related with radiographic damage and CV risk, they exhibited a mSASSS of 14.84±18.4 (7.27±9.64 in cervical spine and 7.72 ±10.14 in lumbar spine). Average BMI 26.88±4.13, 33 (38.8%) were smokers, 16 (18.8%) had diagnosis of arterial hypertension, 1 (1.2%) of diabetes mellitus, 13 (15.3%) of hyperlipidemia, and 8 (9.4%) took lipid lowering drugs. Examination with carotid US found that 14 (16.5%) patients had previously unknown atherosclerotic plaques. After classification according to SCORE index, 60 (76.9%) had low CV risk, 10 (12.8%) moderate, and both high and very high CV risk categories had 4 (5.1%) patients each.

In patients with atherosclerotic plaques, age, disease duration and variables related to radiographic damage (mSASSS [total, cervical and lumbar], and bone bridges) were significantly higher ($p<0.05$). In addition, mSASSS in cervical spine ($p=0.063$) and age ($p<0.001$) were associated with the SCORE and were predictors of increased CV risk in MLR analysis.

Age (years) (N=85)	44.5±12.2
Sex (males) (N=85)	59 (69.4)
HLA B27 (N=83)	71 (83.5)
axSpA (N=85)	79 (92.9)
Radiographic axSpA (N=77)	63 (74.1)
BMI (kg/m^2) (N=80)	26,9±4.13
Disease duration (years) (N=82)	18.01±13.62
Smokers (N=84)	33 (38.8)
ASDAS-CRP	3.13±1.05
ASAS HI (N=82)	4.05±3.8

Conclusion: Presence of atherosclerosis is associated with age, disease duration and radiographic damage in SpA. Age and structural damage especially in the cervical spine predicted a greater CV risk. Thus, it is important to identify these patients in order to maintain tight control and avoid development of CV disease.

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AB0726 WHAT IS THE IMPACT OF MRI ON THE PERFORMANCE OF THE ASAS CLASSIFICATION CRITERIA IN PATIENTS PRESENTING WITH UNDIAGNOSED BACK PAIN?

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Background: Several cohorts have reported the performance of the ASAS classification criteria in settings where clinical, radiographic, and MRI features have been simultaneously incorporated into the diagnostic evaluation in arriving at a gold standard for the testing of the criteria. MRI improves diagnostic precision but access is limited and it is therefore still important to understand how the criteria perform in a setting where diagnostic evaluation can be conducted sequentially before and after MRI assessment. We hypothesized that the ASAS criteria would demonstrate enhanced specificity when MRI is available due to enhanced diagnostic precision.

Objectives: We aimed to test the impact of adding MRI to the diagnostic evaluation on the performance of the classification criteria in unselected patients referred with undiagnosed back pain who have presented with acute anterior uveitis (AAU), psoriasis, or colitis to their respective specialists.

Methods: Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation is ordered per rheumatologist decision. The rheumatologist determines the presence or absence of axial SpA and the degree of confidence in the diagnosis (-10 (definitely not SpA) to +10 (definite SpA)) at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. We calculated the sensitivity and specificity of the ASAS criteria and the component imaging and clinical arms using the stage 2 and 3 diagnostic assessments by the local rheumatologist as gold standard.

Results: A total of 246 patients were recruited, 47.6% being diagnosed with axSpA (61.5% male, age 33.7 years, symptom duration 7.6 years, B27 positive 52.1%), after final diagnostic evaluation. Sensitivity/specificity of the ASAS criteria, imaging arm, clinical arm after stage 2 diagnostic evaluation for the entire cohort were 67.4/85.7%, 39.7/95.2%, 48.9/87.6%, respectively (Table). For the subset of 146 patients who had MRI and had diagnostic evaluation at both stage 2 (pre-MRI) and stage 3 (post-MRI), sensitivity of the criteria was greater but specificity was lower when tested against the stage 3 diagnosis. This was particularly apparent in the clinical arm.

Tab

Patient Category	Stage of evaluation	Number	ASAS criteria		Imaging arm		Clinical arm	
			Sen	Spec	Sen	Spec	Sens	Spec
All patients	2	246	67.4	85.7	39.7	95.2	48.9	87.6
Patients diagnosed with confidence >7 for axSpA and <-4 for not axSpA (-10 to +10 scale)	2	144	86.4	85.9	65.2	96.2	56.1	87.2
Subset of patients with MRI	2	146	58.9	83.9	23.3	94.6	46.7	85.7
Subset of patients with MRI	3	146	67.2	74.7	44.8	92.4	47.8	77.2
Subset of patients with MRI and confidence rating of >7 for axSpA and <-4 axSpA for not axSpA (-10 to +10 scale)	2	111	74.1	82.1	44.4	92.3	51.9	84.6
Subset of patients with MRI and confidence rating of >7 for axSpA YES and <-4 for not axSpA (-10 to +10 scale)	3	111	80.5	78.6	58.5	91.4	53.7	81.4

Conclusion: The ASAS criteria were less specific when MRI assessment was added to the process of diagnostic evaluation, which could reflect rheumatologist over-interpretation of both clinical and radiographic findings in this population with higher pre-test probability of axSpA.

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AB0727

MAGNETIC RESONANCE IMAGING IN SYMPTOMATIC BACK PAIN IN INFLAMMATORY BOWEL DISEASE: STRUCTURAL LESIONS AND HLA-B27 IMPROVE THE DIAGNOSTIC ACCURACY IN AXIAL SPONDYLOARTHRITIS

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Background: Inflammatory bowel disease (IBD) related arthropathy may manifest as peripheral arthritis, dactylitis or enthesitis as well as inflammatory back pain (IBP) due to sacroiliac joint (SIJ) and/or spinal inflammation. HLA-B27 correlates with the presence of MRI determined SIJ bone marrow oedema (BMO) in axial spondyloarthritis (axSpA) and axial psoriatic arthritis (PsA) patients. The prevalence of HLA-B27 positivity is low in IBD and patients may already be on therapy that potentially modifies MRI spinal lesions at the time of imaging.

Objectives: To evaluate the utility of MRI to aid the diagnosis of axSpA in IBD patients with IBP and to explore the relationship of MRI abnormalities with HLA-B27 status.

Methods: Cross-sectional, retrospective audit of consecutive MRI scans of the SIJ and spine performed (2008-2018) in a large teaching hospital. All scans were requested in IBD patients presenting with IBP and clinical suspicion of axSpA. Demographic and clinical data were retrieved from the medical notes. Decision from the clinician whether the patient had axSpA related to the IBD was also recorded. MRI scans were scored by 2 readers using the semiquantitative Leeds Scoring System (BMO grade from 0 to 3)[1]. An overall score for inflammatory (sum of SIJ and Spine BMO scores) and structural lesions (sum of lesions per quadrant) was calculated.

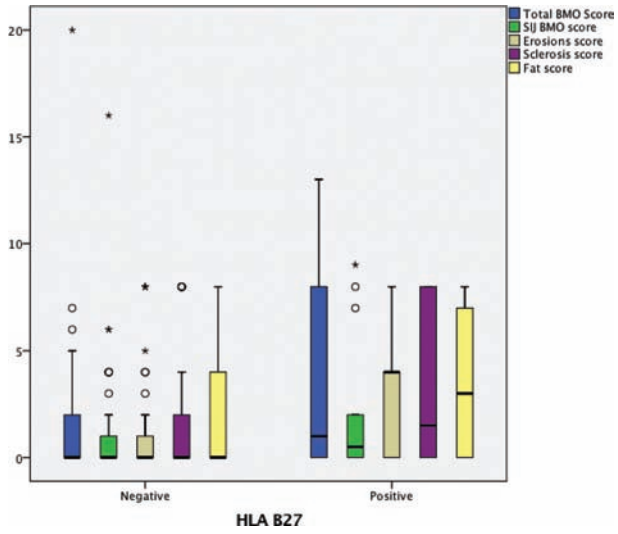
Results: MRI scans from 119 IBD (Crohn's n=82, ulcerative colitis n=31, and undifferentiated IBD n=6) patients were available for analysis. 63.9% were female, mean age 38.7 years at time of MRI with mean age of IBP onset 36.3 years. The majority (n=65/83, 78.3%) were HLA-B27 negative (missing data n=36). Thirty subjects were receiving biologic therapy for IBD. A summary of MRI findings (SIJ and spine) is shown on Table 1.

Abstract AB0727 Table 1

Abnormal SIJ MRI	BMO	Grade 1 N=20 (16.8%)
		Grade 2 N=24 (20.2%)
	Structural lesions	Fat deposition N=46 (38.7%)
		Sclerosis N=45 (37.8%)
		Erosions N=39 (32.8%)
		Ankylosis N=4 (3.4%)
Abnormal Spine MRI	BMO	<3 lesions N=17 (14.3%)
		3 lesions N =7 (5.9%) (ASAS criteria)
	Structural lesions	Posterior fusion N=1 (1%)
		Syndesmophytes N=1 (1%)

Degenerative disc disease was common in the cohort with 55/119 having at least one affected level. Other incidental findings included: hemangiomas (n=8), osteoporotic fractures (n=2) and myeloma (n=1). The total BMO MRI scores (Spine plus

SIJ), SIJ only BMO score, erosions, sclerosis and fat scores were higher in the HLA-B27 positive group as seen in Figure 1, with only differences in the erosion (P=0.002) and sclerosis score (P=0.038) being statistically significant.



Abstract AB0727 Figure 1

Less active (BMO) and structural lesions were seen in the biologic treated group, reaching statistical significance in total BMO (P=0.041), erosions (P=0.039), fat (P=0.003) and sclerosis (P=0.013) scores. A clinical diagnosis of axial SpA was made in 42/119 (35%) cases. Of these, n=25/42 had BMO (SIJ or spine) and structural lesions. Structural lesions alone were evident in 13/42 of these cases. BMO lesions alone with no structural changes was found in 2 cases (grade 1).

Conclusion: MRI findings of sacroiliitis and spinal involvement, defined as a combination of active and structural lesions, are common in IBD subjects with symptomatic back pain. The low prevalence of BMO seen in this cohort may represent partially treated disease. The addition of structural lesions to the current definitions of a positive MRI, may help with the diagnosis of axSpA. The presence of HLA-B27 positivity appears to define a more severe axial phenotype in IBD associated axSpA.

REFERENCES

[1] Marzo-Ortega H, et al. Ann Rheum Dis 2009; 68:1721–7.

Disclosure of Interests: Xabier Michelena-Vegas: None declared, Leticia Garcia-Montoya: None declared, Gabriele De Marco: None declared, Dennis McGonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB, John Hamlin: None declared, Christian Selinger: None declared, Helena Marzo-Ortega Grant/research support from: Janssen, Novartis and Pfizer, Consultant for: AbbVie, Celgene, Janssen, Eli-Lilly, Novartis and UCB, Speakers bureau: AbbVie, Celgene, Janssen, Eli-Lilly, Novartis and UCB
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AB0728 PREVALENCE AND SEVERITY OF CLINICAL AND IMAGING AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Some patients with inflammatory bowel disease (IBD), such as ulcerative colitis (UC) and Crohn's disease (CD), develop spondyloarthritis (SpA). Inflammatory back pain (IBP) is one of the most important signs of axial SpA. However, changes in conventional radiography take a long time to appear as typical changes, such as erosion, sclerosis, or ankylosis. Magnetic resonance imaging (MRI) is useful for assessing axial involvement. High-quality imaging modalities can detect the inflammatory condition in the joints and enthesis more sensitively than clinical assessment or conventional radiography.

Objectives: This study aimed to examine the clinical and imaging prevalence or severity of axial SpA in patients with IBD.

Methods: A total of 56 patients, including 39 with UC (19 males, 20 females) and 17 with CD (10 males, 7 females) were included. The Assessment of SpondyloArthritis international Society (ASAS) Expert Criteria were used to assess IBP. The criteria were fulfilled if at least four of five of the following questions were answered by "yes": (1) did your back pain start when you were aged 40 or younger?; (2) did your back pain develop gradually?; (3) does your back pain improve with exercise?; (4) do you find that there is no improvement in your back pain when you rest?; and (5) do you suffer from back pain at night, which improves upon getting up? Image evaluation was performed blindly by two readers. Conventional radiography was evaluated by the modified Stoke AS Spine Score (mSASSS) in the spine and the Grade of modified New York criteria (mNY) in the sacroiliac joints. In MRI, spinal and sacroiliac joints were evaluated by the Spondylo-arthritis Research Consortium of Canada (SPARCC) score.

Results: Among the 56 patients with IBD, 21 had IBP by clinical examination and 11 had pain in the sacroiliac joints. In conventional radiography, the average mSASSS score was 8.9 in patients with IBP and 6.5 in patients without IBP ($p = 0.257$). Eleven patients had bilateral Grade 2 or unilateral Grade 3 of the mNY, and three (27.3%) of these patients had sacroiliac pain and eight (17.8%) did not have sacroiliac pain ($p = 0.477$). In spine MRI, nine (42.9%) patients with IBP and nine (25.7%) patients without IBP had an SPARCC score of > 2 ($p = 0.184$). In sacroiliac MRI, one (9.1%) patient with sacroiliac pain and 12 (26.7%) patients without sacroiliac pain had an SPARCC score of > 2 ($p = 0.216$).

Conclusion: Even without clinical symptoms of SpA, significant inflammatory findings are detected by MRI. Imaging might be important, regardless of the presence or absence of clinical symptoms, in patients with IBD.

REFERENCES

[1] Eshed I, Hermann KG. Novel imaging modalities in spondyloarthritis. Curr Opin Rheumatol. 2015;27:333-42.

Disclosure of Interests: Tadashi Okano Speakers bureau: AbbVie, Kentaro Inui Speakers bureau: Takeda Pharmaceutical, Pfizer Japan, Daiichi-Sankyo Co.Ltd., Abbvie, Mitsubishi Tanabe Pharma Corporation, Janssen Pharmaceutical, Chugai Pharmaceutical, Ono Pharmaceutical, Eisai Co. Ltd., Eli-Lilly, Nippon Kayaku Co.,Ltd., Maruho Co.,Ltd, Kaken Pharmaceutical Co.,Ltd., Koji Mandai: None declared, Yutaro Yamada Speakers bureau: Abbvie, Chugai, Mitsubishi Tanabe, Yuko Sugioka: None declared, Tatsuya Koike Speakers bureau: AbbVie, Astellas Pharma Inc., Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB, Hiroaki Nakamura: None declared
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AB0729 ASSESSING THE DIFFERENCES IN TIMES TO GENERAL PRACTITIONERPRESENTATION AND DIAGNOSIS, AND OUTCOMES FOR AXIAL SPONDYLOARTHRITIS PATIENTS IN DIFFERENT ETHNIC GROUPS

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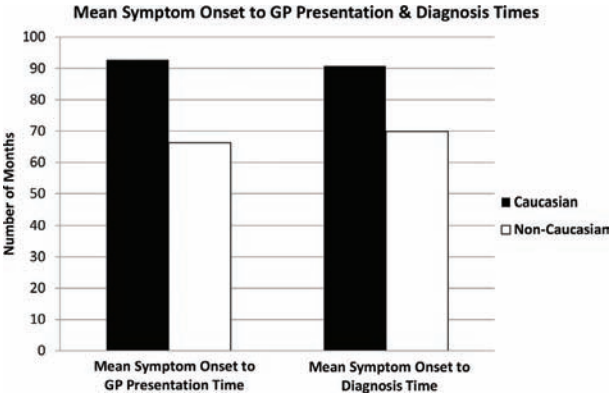
Background: Axial spondyloarthritis (axial SpA) is a condition characterised by inflammatory back pain +/- extra-articular manifestations. There is a known delay to diagnosis[1]. Management includes physiotherapy, non-steroidal anti-inflammatory drugs (NSAIDs) and biologic agents[2]. The Luton & Dunstable University Hospital, UK Rheumatology department looks after an ethnically diverse population of patients with the condition.

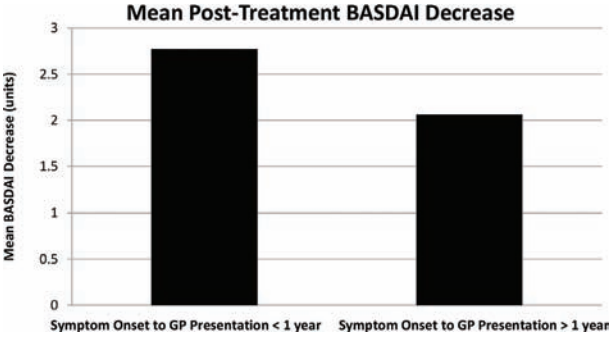
Objectives: The objectives of this study were to compare time from symptom onset to General Practitioner (GP) presentation, time from symptom onset to diagnosis, and response to treatment between different ethnic groups.

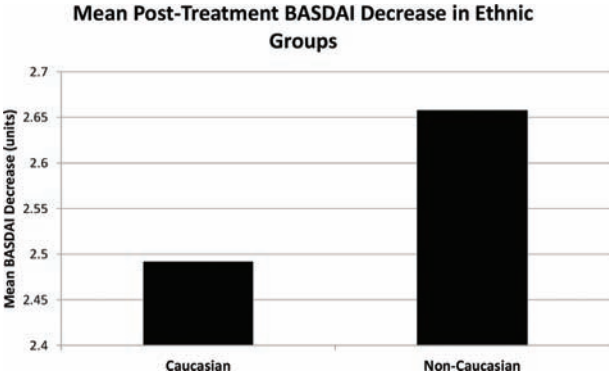
Methods: 124 patients with an axial SpA diagnosis, according to the Luton & Dunstable University Hospital Infoflex database, were identified. 24 patients were excluded due to a peripheral spondyloarthritis diagnosis. A retrospective case note review of 100 case records was undertaken. A Microsoft Excel spreadsheet was used to analyse data.

Results: The mean age was 44 years. 64 (64%) patients were male and 36 (36%) were female. 48 (48%) and 27 (27%) patients were HLA-B27 positive and negative respectively. HLA-B27 status was not available for 25 (25%) patients. Ethnicity breakdown showed 58 White British patients; 12 Pakistani; 7 White Other; 6 Bangladeshi; 5 White Irish; 5 Asian; 4 Indian and 3 Black Caribbean. There were 70 Caucasian (White British,

Irish or Other) and 30 non-Caucasian patients. 49 patients (36 Caucasian and 13 non-Caucasian) had confirmed radiographic axial SpA. 17 patients (10 Caucasian and 7 non-Caucasian) had confirmed non-radiographic axial SpA.







Based on available data for 57 patients, the median time of symptom onset to GP presentation was 48 months. Based on available data for 49 patients, the median time of symptom onset to diagnosis was 53 months. The mean time of symptom onset to GP presentation was 93 months in Caucasians compared to 66 months in non-Caucasians. The mean time of symptom onset to diagnosis was 91 months in Caucasians compared to 70 months in non-Caucasians. 12 patients presented within 1 year of symptom onset.

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) data were available for 7 out of 12 patients who presented within 1 year of symptom onset and 25 out of 45 patients who presented after 1 year. Following NSAIDs or biologics, there was a larger decrease in the first measured BASDAI for those who presented within 1 year of symptom onset (Mean BASDAI decrease: 2.77 compared to 2.06).

For those presenting within 1 year of symptom onset, BASDAI data were available for 5 out of 7 Caucasian and 2 out of 5 non-Caucasian patients. The mean BASDAI decrease was 5.65 in non-Caucasian patients compared to 1.62 in Caucasian patients.

For those presenting after 1 year of symptom onset, BASDAI data were available for 15 out of 26 Caucasian and 10 out of 19 non-Caucasian patients. Mean BASDAI decrease was 2.26 in non-Caucasian and 1.93 in Caucasian patients.

BASDAI data were available for 43 out of 70 Caucasian patients and 18 out of 30 non-Caucasian patients, regardless of time of presentation. The mean decrease in first measured BASDAI was smaller in Caucasian patients compared to non-Caucasian patients (Mean BASDAI decrease: 2.49 compared to 2.66).

Conclusion: There is a shorter mean time of symptom onset to GP presentation and diagnosis in non-Caucasian patients compared to Caucasians. There is a higher response to treatment in patients who present within one year of symptom onset. This may support the hypothesis that early diagnosis leads to better outcomes.

REFERENCES

[1] Hamilton L, Gaffney K, et al. Services for people with ankylosing spondylitis in the UK – a survey of rheumatologists and patients. Rheumatology (Oxford) 2011; 50:1991-1998.

[2] Van der Heijde D, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Annals of the Rheumatic Diseases. 2017; 76:978–991.

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AB0730

RECLASSIFICATION INTO VERY HIGH CARDIOVASCULAR RISK AFTER CAROTID ULTRASOUND IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (a-SpA) are associated with an increase in cardiovascular (CV) morbidity and mortality. Subclinical atherosclerosis, in the form of carotid plaques, is more frequent in this patients than in healthy controls. How the presence of carotid plaque affects the reclassification of CV risk in a-SpA has not been study before. Besides, it is not known if this reclassification can be explained by characteristics related to the disease.

Objectives: To analyze whether the reclassification of CV risk after performing carotid ultrasound is more frequent in this patients compared to controls and whether this reclassification can be explained by characteristics related to the disease such as activity, functional damage or metrology scores.

Methods: Study of 343 a-SpA patients according to ASAS criteria and 177 controls with no previous history of CV events, diabetes or chronic kidney disease. The clinical characteristics and risk profile were analyzed in patients and controls by SCORE. The presence of plaques and intima-media thickness (cIMT) was determined by carotid ultrasound. The differences in the presence of reclassification between patients and controls and the factors associated with this in patients with a-SpA, were analyzed by multivariated regression analysis.

Results: Patients with a-SpA compared to controls disclosed a higher presence of hypertension (p=0.000), dyslipidemia (p=0.000) and smoking (p=0.000). Consequently, patients also showed a significantly higher SCORE than controls (0.6 IQR [0.1-2.0] vs. 0.1 [0.0-0.4], p=0.000). The presence of carotid plaque (36% vs. 25%, p=0.010) and cIMT (0.641 ± 0.121 vs. 0.602 ± 0.115 mm, p=0.001) were higher in patients compared to controls. Moreover, the possibility of being reclassified into very high-risk category after ultrasound was superior in patients (34% vs 25%, p=0.037). The possibility of being reclassified was associated, both in patients and controls, with an older age, male sex, abdominal circumference, hypertension and dyslipidemia. Contrary, body mass index and

serum levels of cholesterol, LDL cholesterol and atherogenic index only showed association with reclassification in controls. The effect of each factor associated with reclassification in patients and controls was compared by the addition of interaction factors in the regression model. In this sense, age (beta coef 2.74 [IC95% 1.34-5.62] in controls vs. beta coef 0.63 (95% CI 0.40-0.99) in patients, interaction p=0.001) and serum LDL cholesterol levels (beta coef 1.03 [IC95% 1.02-1.04] vs. beta coef 1.00 [0.99-1.01], interaction p=0.002), cholesterol and atherogenic index, showed a greater effect in controls than in patients. The reclassification in patients with a-SpA was associated with a higher ASDAS-PCR (2.2 ± 1.0 VS. 2.5 ± 1.0, p=0.041), BASFI (3 [1-5] vs. 4 [2-7], p=0.000) and BASMI scores (2 [1-4] vs. 4 [2-5], p=0.000). However, these differences were lost when they were analyzed adjusting for CV risk factors.

Conclusion: Patients with a-SpA are more likely to be reclassified into very high-risk after carotid ultrasound compared to controls. Traditional CV risk factors have less effect on this reclassification in patients than in controls. The activity, functionality and metrology scores of the a-SpA have a univariate positive relationship with this reclassification.

Disclosure of Interests: Juan Carlos Quevedo-Abeledo: None declared, Javier Rueda-Gotor: None declared, Fernanda Genre: None declared, Alfonso Corrales: None declared, Vanessa Hernández-Hernández: None declared, Esmeralda Delgado-Frías: None declared, Sonia Peña Montelongo: None declared, Carlos Rodríguez-Lozano: None declared, Miguel A González-Gay Grant/research support from: Prof. MA Gonzalez-Gay received grants/research supports from Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker´s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Iván Ferraz-Amaro: None declared
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AB0731 RATE OF SACROILIITIS RADIOGRAPHIC PROGRESSION IN MALE AND FEMALE PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS

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Background: According recent studies radiographic progression (mSASSS) of male patients (pts) with ankylosing spondylitis (AS) higher than in female pts [1, 2].

Objectives: to compare radiographic progression of early axial spondyloarthritis (axSpA) in male and female pts over 2 years (y) of follow-up (FUP).

Methods: The research included 68 pts with early axSpA (ASAS criteria, 2009) from Moscow CORSAR cohort with disease duration <5 and age onset <45 years. The mSASSS index is not suitable for assessing radiographic progression at an early stage of axSpA, because at that stage of the disease, the cervical and lumbar spine have practically no damage. Sacroiliac joints (SIJ) radiographs and CRP performed at baseline and after 2 y FUP. Radiographic SIJ stages scored according to the modified New York criteria grading system. To assess the progression in SIJ, total stage of sacroiliitis (TSS) calculated, by determining sum score stages of sacroiliitis (SI) in the left and right SIJ (from 0 to 8 points). The following formula used to calculate the rate of SI radiographic progression:

$$\text{Rate of SI radiographic progression} = \frac{(\text{TSS}^2 - \text{TSS}^1)\text{x}12}{\text{FUP}}$$

*TSS¹ - initial total score stages of SI, TSS² - FUP total score stages of SI

Pts mean age was 28,5 (5,8) y, average disease duration - 24,1 (15,4) mo, 63 (92,6%) pts were HLA-B27 positive.

Results: Initially, among men there were more pts with AS than among women and they had a higher TSS and higher CRP level (table 1). Rate of SI radiographic progression in male and female pts with axSpA at baseline did not differ.

Abstract AB0731 Table 1.. Outcome parameters at baseline.

	Men (n=33)	Women (n=35)	p
Ankylosing spondylitis, n,%	25 (75,5%)	15 (42,8%)	**0,007**
Non-radiographic axSpA, n,%	8 (24,5%)	20 (57,2%)	**0,005**
Total stage of sacroiliitis, mediane [IQR]	4,0 [4,0; 5,0]	3,0 [2,0; 4,0]	**0,021**
Rate of SI radiographic progression, mediane [IQR]	2,3 [1,3; 4,0]	2,0 [1,0; 4,0]	0,364
CRP, mediane [IQR]	12,8 [1,7; 31,8]	4,3 [0,9; 9,8]	**0,041**

After 2 y FUP, pts with AS still prevailed among men (table 2). TSS increased in both groups: in female pts from 3[2,0; 4,0] to 4 [3,0; 4,0] (p<0,05), in male pts from 4,0 [4,0; 5,0] to 4 [4,0; 6,0] (p<0,05). But, however, in female pts TSS remained less than in male pts over 2 y FUP (table 2). CRP level still was higher in male pts (p <0,05). Progression from non-radiographic axSpA to AS between male and female pts didn't differ - 5 (15,5%) vs 6 (17,2%), p>0,05 respectively, after 2 y FUP. In both groups rate of SI radiographic progression after 2 y decreased (p<0,05) and did not differ between them.

Abstract AB0731 Table 2.. Outcome parameters after 2 y of FUP.

	Men (n=33)	Women (n=35)	p
Ankylosing spondylitis, n,%	30 (90,9%)	21 (60,0%)	**0,003**
Non-radiographic axSpA, n,%	3 (9,1%)	14 (40,0%)	**0,003**
Total stage of sacroiliitis, mediane [IQR]	4,0 [4,0; 6,0]	4,0 [3,0; 4,0]	**0,006**
Rate of SI radiographic progression, mediane [IQR]	0 [0; 1,0]	0 [0; 0,5]	0,98
CRP, Me, [25‰; 75‰]	5,0 [1,0; 12,7]	1,2 [0,6; 4,0]	**0,005**

Conclusion: 1. Rate of SI radiographic progression in male and female pts with axSpA in the first 2 y from the onset of disease is higher than in further. 2. Rate of SI radiographic progression between male and female pts with axSpA is not differ. 3. Male pts with AS more than female pts in CORSAR cohort. It can be explained that male pts had higher CRP level than female pts.

REFERENCES

[1] Baraliakos X, et al. The natural course of radiographic progression in ankylosing spondylitis: differences between genders and appearance of characteristic radiographic features. Current rheumatology reports 2011;13 (5):383.

[2] Rudwaleit, M. et al. The early disease stage in axial spondylarthritis: results from the German Spondyloarthritis Inception Cohort. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology 2009;60(3):717-727.

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AB0732 THE ASSOCIATION BETWEEN PERIODONTAL DISEASE AND RISK OF ANKYLOSING SPONDYLITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: The association between periodontal disease and rheumatoid arthritis is well-recognized [1]. *Porphyromonas gingivalis* is probably the link between the two conditions. On the other hand, the data on the

association between periodontal disease and ankylosing spondylitis are still relaitvely limited.

Objectives: The current systematic review and meta-analysis was conducted with the aims to identify all publsihed studies that investiagted the risk of ankylosing spondylitis among patients with periodontal disease versus individuals without periodontal disease and summarize their results together to better characterize this relationship.

Methods: Two investigators independently searched for published studies indexed in MEDLINE and EMBASE database from inception to October 2018 using the search strategy that included the terms for periodontal disease and ankylosing spondylitis. The inclusion criteria are as follows: (1) Case-control or cohort studies that compared the risk of ankylosing spondylitis between patients with periodontal disease versus individuals without periodontal disease (2) Individuals without periodontal disease were used as comparators in cohort studies while individuals without ankylosing spondylitis were used as controls in case-control studies and (3) Effect estimates and 95% confidence intervals (CI) of the association of interest were reported. Point estimates and standard errors from each study were extracted and combined together using the random effect, generic inverse variance technique of DerSimonian and Laird.

Results: Of 554 retrieved articles, a total of 7 case-control studies with 41,575 participants met the eligibility criteria and were included into the meta-analysis. The risk of ankylosing spondylitis among patients with periodontal disease was significantly higher than individuals without periodontal disease with the pooled odds ratio of 2.16 (95% CI, 1.48–3.16). The statistical heterogeneity was low with an I^2 of 45%. The forest plot of this meta-analysis is shown as **Abstract AB0732 figure 1**.. Funnel plot was created for evaluation of publication bias. The plot was relatively symmetric which did not suggest the presence of publication bias in favor of studies with positive results.

Conclusion: A significantly increased risk of ankylosing spondylitis among patients with periodontal disease was demonstrated in this study. This observation may provide more understanding of the pathogenesis of this chronic inflammatory arthritis.

REFERENCES

[1] Leech MT, Bartold PM. The association between rheumatoid arthritis and periodontitis. Best Pract Res Clin Rheumatol 2015;29:189-201.

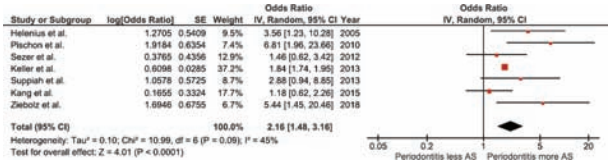


Figure 1. Forest plot of the meta-analysis on the association between periodontal disease and risk of ankylosing spondyltiis

Disclosure of Interests: None declared

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AB0733 AN EYE FOR THE HEART: ARE RETINAL VASCULAR PARAMETERS ASSOCIATED WITH CARDIOVASCULAR DISEASE IN ANKYLOSING SPONDYLITIS?

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Background: Chronic systemic inflammation in patients with ankylosing spondylitis (AS) contributes to the development of cardiovascular disease (CVD). Microvascular changes are thought to precede clinically overt CVD and its early recognition could improve timely treatment. The microvasculature of the retina and fingertips are easily accessible for non-invasive visualization. Furthermore, previous studies have shown an association between CVD and respectively retinal morphology and digital microvascular function (fingertips), in patients without rheumatic diseases. The retinal and digital vasculature could provide an unique opportunity to recognize early signs of CVD in AS patients.

Objectives: To investigate whether retinal vascular parameters and digital microvascular function in AS patients are associated with the 10 year CVD risk.

Methods: Cross-sectional study in AS patients (diagnosis according to modified New York criteria) between 50-75 years without a history of diabetes mellitus or cerebrovascular disease. Consecutive patients were recruited consecutively from the Rheumatology outpatient clinic of the Amsterdam UMC, location VUmc and Reade. Patient characteristics, CVD (risk factors), disease duration/activity (ASDAS), C-reactive protein and lipid profile were assessed. The digital microvascular function (the reactive hyperemia index, RHI) was tested through endo Peripheral Arterial Tone measurement at the finger tips (EndoPAT). Retinal vascular parameters were assessed through fundus photography, and identified with Singapore I Vessel Assessment (SIVA) software: central retinal artery and vein equivalent (CRAE, CRVE), arteriovenous ratio (AVR), curvature tortuosity arterioles and venules (cTORTa, cTORTv), fractal dimension of arteries and venules (FrDiA, FrDiV). SIVA parameters were reported as continuous values. The Framingham risk score (FRS) was calculated and classified based on the 10 years CVD risk (low risk <10%, intermediate risk 10-20%, high risk >20%). Linear regression analyses were used to determine the association between the FRS categories and retinal parameters or digital microvascular function (RHI), correcting for age and disease duration.

Results: Fifty-three AS patients were included (age 60±6 years, 55% female, 74% HLA-B27 positive, disease duration 35 years ±13, ASDAS 2.3±1.0). Fifty-five% was currently treated with NSAIDs and 47% with a TNF inhibitor. Based on the FRS, 36% had a high risk of CVD in the next 10 years, 42% an intermediate and 12% a low risk. In multivariable analyses, patients with an intermediate and high risk of CVD (FRS) had a significantly lower diameter of the central retinal artery (CRAE; $p<0.01$ for both risk groups) and arteriovenous ratio (AVR; only for high risk; $p=0.03$) as compared with patients with a low risk. There was no association between the RHI and the cardiovascular risk.

Conclusion: This study suggests an association between the 10 years CVD risk and the morphology of the retinal arterial vessels in older AS patients ($\geq$50 years). This is in accordance with some other studies reporting on atherosclerosis in the general population. No association was found between CVD risk and microvascular function in the fingertips. In conclusion, the measurement of retinal vascular parameters might be a new technique to detect early stages of atherosclerosis in AS.

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AB0734 CHANGES IN HEIGHT AND BODY MASS INDEX OVER TIME IN PATIENTS WITH AXIAL SPONDYLOARTHITIS, TREATED WITH TUMOR NECROSIS FACTOR-A INHIBITORS

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Background: Monitoring of height and body mass index (BMI) is an important for patients with axial spondyloarthritis (axSpA). Reduction of height not only reflects spine remodeling, but affects various indexes, such as BMI (fig.1). However, BMI calculations assume that the adult patient‘s height is a constant. Therefore these calculations may be inaccurate in patients whose height is susceptible to decrease.

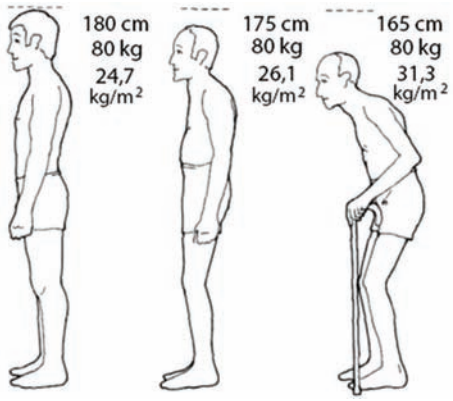


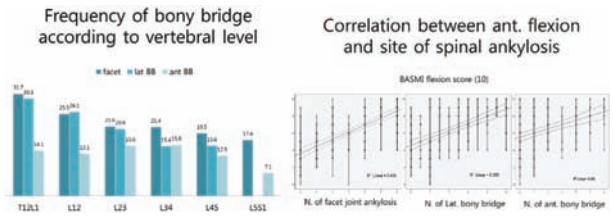
Figure 1. Difference in BMI in the person with unstable height and stable body mass.

Objectives: To evaluate changes in height and BMI over time in patients with axSpA, treated with tumor necrosis factor-α inhibitors (iTNF-α).
Methods: The study included 51 patients with axSpA (ASAS criteria 2009). All the patients were treated with iTNF-α for one and > years. The patient's height and weight measured before the beginning TNF-α inhibitors and during the treatment. Only patients with stable weight (variability ± 2.0 kg from baseline) were included in the study.
Results: Mean age of axSpA patients at baseline was 40.22±13.51, 38 (74.5%) were male, disease duration 12.77±6.82, duration of TNF-α inhibitors treatment 5.64±2.21 years, all the patients had inactive disease. In 19 patients with axSpA diagnostic delay was 8 years.
Patients' height varied between 1.55 – 1.92 m (average height 1.73±0.07 m). Male's mean height was 1.78±0.05 m, women's – 1.63±0.05 m. Height decrease over time in patients with AxSpa was 3.74±1.83 cm (from 1.0 to 15.0 cm). Maximal decrease in height was shown in patients with 10 years after the first symptoms emerged. Mean weight in patients who had height loss was 79.75±12.7 kg. Among patients who had decrease of height and stable body mass the difference between BMI at subsequent measurement and the time of treatment initiation (ΔBMI) was 1.15 kg/m^2: BMI at baseline = 26.25±3.34 kg/m^2, over time of observation BMI = 27.39±3.38 kg/m^2).
Conclusion: Height loss in axSpA is significant even in patients with inactive disease. Height loss affects BMI calculation that could lead to overestimation of cardiovascular risk, obesity and could change all of the BMI-dependent areas. Correction of BMI calculation for the patients with unstable height is needed.
Disclosure of Interests: Elizaveta Vasilenko: None declared, Olga Nikolaeva: None declared, Anna Dadalova: None declared, Ekaterina Gaydukova: None declared, V Mazurov Grant/research support from: JSC BIOCAD, Inna Gaydukova Grant/research support from: JSC BIOCAD, Speakers bureau: paiment from Pfizer, Novartis, Abbvie, Biocad, Selgene, MSD, Sanofy not exceed 10 000 euros
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AB0734B BONY BRIDGE ON FACET JOINT OR LATERAL SIDE OF LUMBAR VERTEBRA IS MORE FREQUENT AND CORRELATED WITH LUMBAR FLEXION FUNCTION THAN THAT ON ANTERIOR SIDE OF LUMBAR VERTEBRA IN ANKYLOSING SPONDYLITIS; ANALYSIS OF ANKYLOSIS REGISTRY OF AXIAL SPONDYLOARTHRITIS (ANKAS)

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Background: Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis characterized by sacroiliitis and a marked propensity for sacroiliac joint and spinal fusion. The modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) has been used when measuring radiographic progression in AS, which only measures bony changes of anterior side in vertebral body (AV). Variation of this score is too small to assess radiographic progression in AS. Some patients have syndesmophytes on lateral side in vertebral body (LV) or ankylosis in facet joints (FJ).
Objectives: We planned this study to know which side of lumbar vertebra ankylosis more frequently develops in and is more correlated with lumbar flexion function.
Methods: We analyzed ANKylosis registry of Axial Spondyloarthritis (ANKAS). In this cohort, the patients with AS are examined by antero-posterior and lateral view of X-ray every 2 years and low dose whole spine computed tomography (CT) every 5 years to determine radiographic progression. We analyzed the location of near total or total bone bridge at each level of lumbar spine by X-ray and CT in 518 patients with AS.
Results: Male was 78% and mean age was 38.8 ± 2.8. Ankylosis or bony bridge in sacroiliac joint (SIJ), FJ, LV and AV was respectively 55.2%, 22.8%, 21.6% and 13.1%. T12L1 was the most frequent level of ankylosis in FJ (31.7%) and LV (30.3%). For FJ and LV, there was a tendency that upper levels of spine have more ankylosis, but not in AV. The patients who didn't have SIJ ankylosis also have a tendency of not having any bony bridge in lumbar spine (negative predictive value: 92.24%, OR 28.1, 95% CI:16.3-48.4, p=0.000). We analyzed the correlation between the flexion score of Bath AS Metrology Index (BASMI) 10 and the site of ankylosis. FJ ankylosis showed the strongest correlation with lumbar flexion range (R^2=0.456, p=0.000), but bony bridge of LV and AV showed weak correlation with that (respectively, R^2=0.288, R^2=0.155, p=0.000). We analyzed the correlation between ankylosis of FJ and bony bridge of AV or LV respectively. Ankylosis of FJ and bony bridge of LV showed a stronger correlation (R^2=0.712, p=0.000) than that of AV (R^2=0.515, p=0.000)



Conclusion: Bony bridge in LV is not only more developed and correlated with ankylosis in FJ, but also more correlated with limitation of anterior lumbar flexion than that in AV. We suggest bony changes of LV should be also included in radiographic score system for more sensitive detection of radiographic progression in AS.
Disclosure of Interests: None declared
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AB0734C REMISSION IN AXIAL SPONDYLOARTHRITIS: A DELPHI-METHOD QUESTIONNAIRE AMONG EXPERTS TO EVALUATE THE AVAILABLE ASSESSMENT TOOLS TO MEASURE DISEASE ACTIVITY AND TO DEVELOP A CONSENSUS DEFINITION OF REMISSION

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Background: Several definitions of remission in axial spondyloarthritis (axSpA) have been proposed based on the available disease activity assessment tools, but to date we lack a universally accepted definition of remission for the development of clinical trials or routine clinical practice.
Objectives: To explore the degree of agreement that exists among the experts managing patients with axSpA regarding the assessment tools available to evaluate disease activity in these patients and to develop a consensus definition of clinical remission in axSpA.
Methods: As a consensus method, we followed the modified Delphi methodology. A scientific committee developed 80 statements that were submitted in 2 rounds (in September and October 2018, respectively) to a panel of 152 rheumatologists from GRESSER (GRupo de Estudio de ESpondiloartritis de la Sociedad Española de Reumatología), the Spanish working group with common interests in spondyloarthritis, addressing controversial issues regarding the current assessment of remission; clinical features, laboratory and imaging tests results, and if they should be included in the definition of remission; general recommendations for outpatient visits and the use of disease activity scores.

Results: Agreement was reached for 56 of the 80 proposed items (70%). The panelists concluded that although a definition of remission in axSpA is not currently available, there is consensus that it is possible to achieve remission in this disorder. There was agreement that the definition of remission in axSpA should include: pain, fatigue, functional impairment, mobility, extra-articular manifestations, peripheral involvement, joint inflammation, disease activity, laboratory tests, quality of life, need for treatment, progression of the disease, and both physician and patient global assessments. It is recommended to set a therapeutic goal when starting treatment in patients with axSpA, the ideal objective being remission, but low disease activity (LDA) may also be acceptable as an alternative objective, being ASDAS the preferred tool to assess disease activity with cut-off values of < 1.3 for remission and ≥ 1.3 to < 2.1 for LDA. A proposal for clinical remission in axSpA based on the ASDAS cut-off value associated to the absence of extra-articular (psoriasis, uveitis, inflammatory bowel disease) and peripheral (arthritis, enthesitis, dactylitis) activity, as well as the absence of inflammation assessed by the normalization of CRP levels and absence of radiographic progression.
Conclusion: This work offers consensus recommendations and a proposal of clinical remission that may be useful in the management of patients with axSpA.
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Psoriatic arthritis

AB0735 SAFETY AND EFFECTIVENESS OF USTEKINUMAB IN PSORIATIC ARTHRITIS. A MULTICENTRIC STUDY

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Background: Ustekinumab (UST) is an anti- interleukin (IL) 12/23 monoclonal antibody that has been shown to be effective and safe in psoriatic arthritis (PsA) in two phases III clinical trials. However, we have very few UST data in a real- life setting.
Objectives: To assess the effectiveness, safety and survival of UST among patients with PsA treated under routine clinical care.
Methods: Retrospective and multicentric study. Epidemiological and clinical data were collected through the electronic medical record of all patients with PsA who started UST due to rheumatological indication in 14 hospitals of Catalonia and the Balearic Islands (Spain).
Results: 152 patients were included, 116 (76.3%) with 45mg and 36 (23.8%) with 90mg. 55.9% were women, mean age 54.79 (12.5) years, and mean disease duration 209 months. 132 patients (87%) had oligo (30.3%) or polyarticular involvement (56.6%). 26.8% had enthesitis and 36.2% dactylitis. 48p(35.6%) had erosions. 94p (61.8%) had previously received another biological therapy, and 39 of them (38.8%) had received 2 or more. 54.6% of the patients were taking DMARDs and 39.5% glucocorticoids. The baseline DAS 28 was 3.97 (1.45), C reactive protein (CRP) was 2 mg/dl (2), SJC was 4.0 (5.4), and PASI was 6.5 (8.4). There were no significant differences in clinical and epidemiological data between patients at 45 or 90 mg except in obese patients (58.4% in 90mg vs 40% in 45mg, p = 0.038). Overall, there was a significant decrease in DAS28, SJC, TJC and PASI in the first month of treatment, with more pronounced improvement in skin (PASI and BSA) than in joints outcomes, where the curves reached a plateau at 6 months. There were no significant differences between joint and/or skin outcomes between 45 and 90 mg doses.
Patients naive to biological therapy had an earlier skin improvement than patients with previous biological failure. Likewise, the improvement in joint outcomes was also faster in naive vs biological experienced patients (DAS28 and SJC 4m, p = 0.01 and 0.01, respectively).
After an average of 19m of follow-up, 94 out of 152p (61.8%) continued with UST, 54.4% started at 45mg and 72.2% at 90mg (p = 0.04). 42p (28.2%) stopped UST due to joint inefficacy, 8p (5.4%) for skin inefficacy and 4 (2.7%) for adverse effect. Although survival was better in patients with fewer previous biological agents, no significant differences were achieved (p = 0.233 for naive and p = 0.072 for patients with 1 biological failure).
Conclusion: This analysis demonstrates that UST, administered to PsA patients in a routine clinical care setting, is safe and effective in improving skin and joint outcomes. 61.2% of the patients continued with the treatment after an average of 19m of follow-up. Joint and skin outcomes reached significant differences from the first month. The efficacy seems faster in those patients with fewer lines of previous biological therapies. One third of the patients interrupted the therapy due to joint inefficacy.
Acknowledgement: JANSSEN
[1] [1] **Disclosure of Interests:** Ana Belén Azuaga-Piñango: None declared, Beatriz Frade-Sosa: None declared, Ana Laiz Consultant for: Lilly, Novartis, AbbVvie, MSD, UCB and Janssen, Speakers bureau: Lilly, Novartis, Abvvie, MSD, UCB and Janssen, Paula Estrada: None declared, Luciano Polino: None declared, Emma Beltrán: None declared, Águeda Prior-Español: None declared, Lourdes Mateo Soria: None declared, Carme Moragues Pastor : None declared, Agusti Sellas-Fernández: None declared, ANA URRUTICOECHEA-ARANA: None declared, Mireia Moreno : None declared, Javier Garcia Miguel: None declared, José L Tandaipan: None declared, Manel Pujol: None declared, Vicenç Torrente Segarra : None declared, Inmaculada Ros Vilamajo : None declared, Sergi Ordoñez : None declared, Delia Reina-Sanz: None declared, Andrea Cuervo: None declared, Juan D. Cañete: None declared, Julio Ramirez: None declared
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AB0736 GENDER INFLUENCE ON TREATMENT EFFECTIVENESS IN PSORIATIC ARTHRITIS

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Background: Gender has been lately suggested as influential in the response to treatment with biological drugs in spondyloarthritis, such as psoriatic arthritis (PsA). However, data about the association between gender and treatment response in axial PsA (axPsA) or peripheral PsA (pPsA) are scarce.
Objectives: To analyze the association between gender and clinical response to biological therapy in patients with axPsA and pPsA.
Methods: An observational cohort study was conducted, prospectively collecting data from 108 patients treated with biological therapy (93% TNFi and 7% IL-17i) from 2002-2018. Patients were divided into two groups according to their clinical predominant manifestation: axPsA or pPsA. Disease activity indexes (ASDAS and BASDAI for axPsA and DAPSA and DAS28 for PsA) were collected before starting drug and 6 months later (baseline and 6m visit, respectively). Low disease activity (LDA) was defined as ASDAS <2.1 or BASDAI <4 (axPsA) and DAPSA ≤14 or DAS28 ≤ 3.2 (pPsA). Clinical improvement was defined as an improvement ≥ 1.1 points in ASDAS (dASDAS) or 50% in BASDAI (BASDAI50) for axPsA, and an improvement of 50% in DAPSA (DAPSA50) or dDAS28 ≥ 1.2. First, the frequency of male- and female-patients achieving LDA and clinical improvement at 6m were compared using Fisher test, separately for axPsA and pPsA. Second, the association between gender and each of the clinical outcomes was analyzed using logistic regression models adjusted for confounders (age, disease duration, previous biologics, smoking habit, body mass index (BMI), baseline DMARDs and baseline disease activity (ASDAS or BASDAI for axPsA and DAPSA or DAS28 for pPsA).
Results: Out of 108 included patients, 55 (51%) had predominant axPsA and 54 (49%) pPsA. In the group of axPsA, 35 (64%) were males, 33 (60%) were non-smokers, 33 (60%) had a BMI ≥25, with mean (SD) baseline disease activity of ASDAS: 3.3 (1.0) and BASDAI: 5.4 (2.0). The frequency of patients achieving clinical response was higher in males than females (LDA: 74% vs 37%; p=0.02, respectively) (Table 1). After adjusting for confounders, male gender was significantly associated with higher probability of achieving LDA (ASDAS OR=4.4; p=0.03 and BASDAI OR=6.0; p=0.01), and clinical improvement (dASDAS: OR=4.8; p=0.04 and BASDAI50: OR=5.19; p=0.03). In the group of pPsA, 20 (37%) were

males, 37 (68%) were non-smokers, 34 (63%) had a BMI ≥25, with mean (SD) baseline disease activity indexes of DAPSA: 26 (14.9) and DAS 28: 4.8 (1.2). The frequency of patients achieving LDA was higher in males than females (74% vs 39%; p=0.02, respectively). After adjusting for cofounders, male gender was independently associated with higher probability of achieving LDA by DAPSA (OR=4.0; p=0.03) and DAS28 (OR= 2.1; p=0.3). Finally, an association between male gender and clinical improvement was also observed but this was statistically significant only when using dDAS28 as the outcome: OR=2.9; p=0.1 for DAPSA50 and OR=5.8; p=0.02 dDAS28.

Conclusion: Male gender is associated with a higher rate of response to biological treatment (TNFi and IL-17i) in both predominant articular manifestations: axPsA and pPsA. This association is robust despite using the new recommended disease activity indices and cut-off points for clinical practice. Further investigations of these gender-related differences are important for a better management of PsA.

REFERENCES

Abstract AB0736 Table 1. Response rates after 6 months of biological therapy, stratified for PsA subtype and gender.

axPsA (n= 55)				pPsA (n= 54)			
	Males (n= 35)	Females (n= 20)	p-value		Males (n= 20)	Females (n=34)	p-value
LDA							
ASDAS <2.1	25 (74 %)	7 (37 %)	0.02	DAPSA ≤14	14 (74 %)	12 (39 %)	0.02
BASDAI < 4	24 (72 %)	5 (26 %)	0.02	DAS28 ≤ 3.2	13 (68 %)	6 (31%)	0.09
Clinical Improvement							
dASDAS ≥ 1.1	20 (59 %)	7 (37 %)	0.15	DAPSA50	10 (53 %)	11 (36 %)	0.25
BASDAI50	16 (48 %)	3 (16 %)	0.04	dDAS28 ≥ 1.2	11 (57 %)	8 (42 %)	0.15

axPsA (n= 55)				pPsA (n= 54)			
	Males (n= 35)	Females (n= 20)	p-value		Males (n= 20)	Females (n=34)	p-value
LDA							
ASDAS <2.1	25 (74 %)	7 (37 %)	0.02	DAPSA ≤14	14 (74 %)	12 (39 %)	0.02
BASDAI < 4	24 (72 %)	5 (26 %)	0.02	DAS28 ≤ 3.2	13 (68 %)	6 (31%)	0.09
Clinical Improvement							
dASDAS ≥ 1.1	20 (59 %)	7 (37 %)	0.15	DAPSA50	10 (53 %)	11 (36 %)	0.25
BASDAI50	16 (48 %)	3 (16 %)	0.04	dDAS28 ≥ 1.2	11 (57 %)	8 (42 %)	0.15

Disclosure of Interests: Diego Benavent: None declared, Chamaida Plasencia Speakers bureau: Pfizer, MSD, Victoria Navarro-Compán: None declared, Alejandro Villalva: None declared, Diana Peiteado: None declared, Gemma Bonilla: None declared, Elisa Fernández: None declared, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly

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AB0737

ACHIEVEMENT OF RAPID3 NEAR REMISSION OR LOW SEVERITY IS ASSOCIATED WITH RESIDUAL LEVELS OF ARTICULAR AND EXTRA-ARTICULAR MANIFESTATIONS OF ACTIVE PSORIATIC ARTHRITIS IN SUBJECTS TREATED WITH APREMILAST

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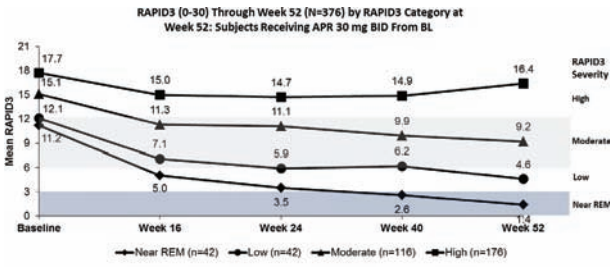
Background: The Routine Assessment of Patient Index Data 3 (RAPID3) is an outcome measure of disease activity widely used in the USA as part of routine care[1] and is entirely derived from patient self-reported measures (Health Assessment Questionnaire-Disability Index [HAQ-DI] or multidimensional HAQ [MDHAQ], Pain visual analog scale [VAS] and Patient's Assessment of Disease Activity [PtGA] VAS). However, the lack of more objective, traditional physician assessments, such as joint counts, may lead to residual active disease that will be missed.

Objectives: To examine trajectories for improvement in RAPID3 score over time and PsA manifestations not measured specifically by RAPID3 in subjects achieving RAPID3 near remission (REM) or low disease severity at Week 52.

Methods: Pooled analyses of the phase III PALACE 1, 2 and 3 studies were performed for subjects assigned to receive APR 30 mg twice daily (BID) at baseline (BL). Subjects with available scores on RAPID3 components (HAQ-DI, Pain VAS and PtGA VAS) at Week 52 were included and grouped according to RAPID3 categories at Week 52 (near REM: ≤3; low: >3 to ≤6; moderate: >6 to ≤12; and high: >12 to 30). Mean RAPID3 scores were assessed from BL through Week 52. Other measures of PsA disease activity were reported longitudinally by RAPID3 category at Week 52.

Results: The analysis included 376 APR subjects, with 42 with near REM and 42 with low severity at Week 52. Overall, mean RAPID3 trajectories improved overtime with greater mean improvements observed for those achieving RAPID3 near REM and low disease severity by Week 52. At a mean level, subjects in moderate RAPID3 at baseline were associated with achievement of RAPID3 near REM or low disease severity by Week 52 with APR (Figure). Many subjects who achieved RAPID3 near REM or low disease severity at Week 52 showed improvements in articular and extra-articular disease activity, although not all manifestations were controlled at Week 52 (Table); mean TJC was higher than expected in subjects achieving RAPID3 targets at Week 52 and there was no association between low mean RAPID3 and mean Psoriasis Area and Severity Index (PASI) scores.

Conclusion: At a mean level, subjects in moderate RAPID3 at baseline were associated with achievement of RAPID3 near REM or low disease severity targets with APR by Week 52. Achievement of RAPID3 targets was associated with improvement, but not necessarily control, of all articular and extra-articular manifestations. Complementing the RAPID3 measure with joint and skin assessments may help to evaluate achievement of treatment goals in clinical practice.



Includes subjects randomized at baseline who had RAPID3 components available at Week 52; data are as observed. RAPID3 Near remission: ≤3; low severity: >3 to ≤6; moderate severity: >6 to ≤12; and high severity: >12 to 30. REM=remission.

Articular and Extra-Articular Disease Activity in Subjects With Low Severity or Near Remission RAPID3 Scores at Week 52

	Near Remission at Week 52 n=42				Low Severity at Week 52 n=42			
Mean	BL	Week 16	Week 24	Week 52	BL	Week 16	Week 24	Week 52
SJC (0-66)	10.2	3.9	3.2	1.6	8.4	4.4	2.5	2.1
TJC (0-68)	14.6	4.7	4.3	2.5	14.8	7.6	5.9	6.3
Pain VAS (0-100 mm)	45.8	16.8	11.7	5.7	45.4	24.7	22.5	19.4
PtGA VAS (0-100 mm)	44.1	26.6	17.4	7.2	44.9	28.6	23.3	15.4
PhGA VAS (0-100 mm)	48.5	20.3	19.1	12.8	50.8	24.5	15.7	15.4
PASI* (0-72)	9.4	4.8	4.5	5.2	6.9	3.8	3.4	2.4
MASES§ (0-13)	2.7	1.1	0.7	0.9	3.6	2.2	2.2	2.0
Dactylitis count‡ (0-20)	3.1	1.0	0.8	0.6	2.6	1.5	0.9	0.6
HAQ-DI (0-3)	0.7	0.2	0.2	0.0	0.9	0.5	0.4	0.3

Data are as observed and n values vary by time point based on number of subjects with available data for a given time point. *Assessed in subjects with ≥3% psoriasis-involved body surface area at BL. §Assessed in subjects with enthesitis at BL. ‡Assessed in subjects with dactylitis at BL. MASES=Maastricht Ankylosing Spondylitis Enthesitis Score; PhGA=Physician Global Assessment of Disease Activity.

REFERENCES

[1] Coates LC, et al. Arthritis Care Res. 2018;70:1198-1205.

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AB0738 DUAL NEUTRALISATION OF INTERLEUKIN (IL)–17A AND IL–17F WITH BIMEKIZUMAB IN MODERATE-TO-SEVERE PLAQUE PSORIASIS: 60-WEEK RESULTS FROM A RANDOMISED, DOUBLE-BLINDED, PHASE 2B EXTENSION STUDY

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Background: Psoriasis is a chronic, systemic, immune-mediated inflammatory disease associated with prominent skin manifestations. One in four patients with psoriasis also has psoriatic arthritis,[1] with skin disease preceding joint manifestations in most patients.[2] Interleukin (IL)-17F shares structural homology and pro-inflammatory function with IL-17A. Preclinical and early clinical data support dual neutralisation of IL-17F, together with IL-17A, as a novel targeting approach for the treatment of immune-mediated inflammatory diseases. Bimekizumab, a monoclonal antibody that potently and selectively neutralises both IL-17A and IL-17F, is in development for the treatment of psoriasis, psoriatic arthritis and ankylosing spondylitis.[3–5] In the 12-week BE ABLE 1 study (NCT02905006), bimekizumab provided rapid and substantial clinical improvements in patients with moderate-to-severe plaque psoriasis, with a safety profile consistent with previous bimekizumab studies.[3]
Objectives: The objectives of this Phase 2b extension study (BE ABLE 2; NCT03010527) were to assess the long-term safety and efficacy of subcutaneous bimekizumab every four weeks for an additional 48 weeks (60 weeks' total exposure).
Methods: BE ABLE 1 responders (≥90% reduction in Psoriasis Area Severity Index [PASI90] at Week 12) receiving placebo or bimekizumab 64mg, 160mg, 160mg (320mg loading dose [LD]) remained on the same dose; non-responders (<PASI90 at Week 12) were re-assigned from placebo/bimekizumab 64mg to 160mg or from 160mg/160mg (LD) to 320mg. Patients previously receiving bimekizumab 320mg/480mg received 320mg. The primary variable was the exposure-adjusted incidence rate (EAIR) of treatment-emergent adverse events (TEAEs); efficacy assessments were secondary.
Results: 217 patients were enrolled. Across all doses, BE ABLE 1 responders generally maintained complete or almost complete skin clearance for up to an additional 48 weeks: PASI90: 80−100%, non–responder imputation (93−100%, observed); PASI100: 70−83% (80−96%); Investigator's Global Assessment: 78−100% (98−100%). PASI100 was achieved by 33−76% (40−82%) of non-responders (Week 48). EAIR of TEAEs was 206.1/100 patient-years (n=184/217 [85%]). EAIR of serious TEAEs was 6.2/100 patient-years (n=15/217 [7%]); no serious TEAE was reported by >1 patient. The most frequent TEAEs were oral candidiasis and nasopharyngitis. No cases of suicidal ideation/behaviour, major adverse cardiac events, or inflammatory bowel disease were reported. No new safety findings were observed.
Conclusion: Nearly all BE ABLE 1 responders completing 60 weeks of bimekizumab treatment maintained complete or almost complete skin clearance, with a safety profile consistent with previous studies.[3]

REFERENCES

1 . Alinaghi et al. *J Am Acad Dermatol* 2019;80:251-65;
2 . Gladmann et al. *Ann Rheum Dis* 2005;64:ii14–17;
3 . Papp et al. *J Am Acad Dermatol* 2018;79:279–286;
4 . Van der Heijde et al. *Ann Rheum Dis* 2018;77:A70;
5 . Ritchlin et al. *Arthritis Rheumatol* 2018;70(S10):L17

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AB0739 THE PREVALENCE OF PSYCHOLOGICAL DISORDERS IN PATIENTSWITH SEVERE PSORIASIS WITH/WITHOUT PSORIATIC ARTHRITIS IN CLINICAL PRACTICE: DATA FROM A SINGLE DERMATOLOGICAL SETTING

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Background: Psoriatic arthritis (PsA) and Psoriasis (PsO) are associated with different psychological disorders. Depression is a risk factor for development of PsA among PsO patients (pts). Diagnosis of PsA in dermatological practice is still problematic. The prevalence of psychological disorders in patients with severe PsO with/without PsA are limited in the Russian Federation.
Objectives: To study the prevalence of anxiety, depression and fatigue in pts with severe PsO with/without PsA in a single dermatological setting.
Methods: 99 unselected pts (male-23/female-76) with severe plaque PsO, mean age 45.82±14.04 years, BSA 56.35±9.11%, PASI 22.50 ± 5.13 were included. PsA was diagnosed by the CASPAR criteria. Anxiety, depression and fatigue were identified by the Hospital Anxiety Scale (HADS-A), HADS-Depression (HADS-D) and Functional Assessment of Chronic Illness Therapy (FACIT) (points) accordingly. The HADS-A/HADS-D was defined as normal - 0-7; presence of disorders - 8-10; psychiatric morbidity >11 points accordingly. FACIT 43.6±9.4 matched with healthy control. The lower the level of FACIT corresponded to higher fatigue. The number of pts with FACIT≤30 were calculated. All pts were treated with different synthetic DMARDs, mostly Methotrexate (subcutaneous 15-20 mg every week), biological DMARDs according local therapy according

to the national guidelines. M±m,%, chi², t-test were performed. All p<0.05 were considered to indicate statistical significance.
Results: 20 out of 99 pts (20.2%) had PsA. In all group mean HADS-D/HADS-A/FACIT were 2.59±3.88/4.61±6.54/41.47±6.41 accordingly. In PsO pts without PsA presence of disorders/psychiatric morbidity by HADS-A were seen in significantly more cases compare to PsO pts with PsA: totally in 30 out of 79 pts (38%)/in 2 out of 20 pts (10%) accordingly (chi^2, p=0.025). In PsO pts without/with PsA presence of disorders/psychiatric morbidity by HADS-D were seen totally in 20 out of 79 pts (25.3%)/in 2 out of 20 pts (10%) accordingly (chi^2, p=0.24). No significant difference were found between groups. In PsO pts without/with PsA FACIT≤30 were seen in 2 out of 79 pts (2.53%)/in 2 out of 20 pts (10%). No significant difference were found between groups (chi^2, p=0.17).
Conclusion: In our real dermatological clinical practice cohort of pts with severe PsO subclinical and clinical anxiety and depression were detected in about 30% of cases. This fact should be taken into account for the early detection of pts at risk for developing PsA.

REFERENCES

[1] Lewinson RT, Vallerand IA, Lowerison MW. Depression Is Associated with an Increased Risk of Psoriatic Arthritis among Patients with Psoriasis: A Population-Based Study. J Invest Dermatol. 2017;137(4):828-835. doi: 10.1016/j.jid.2016.11.032.

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AB0740 USE OF SECUKINUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS. IMPACTS OF COMBINATION WITH METHOTREXATE

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Background: Secukinumab (SECU) is a human IgG1κ monoclonal antibody that binds to the protein interleukin-17A approved for the treatment of psoriasis, ankylosing spondylitis, and psoriatic arthritis (PsA). Recently presented data suggest that combination with methotrexate (MTX) in patients with PsA may not be as necessary as in rheumatoid arthritis as it improves neither efficacity nor sustainability (1,2,3,4).
Objectives: This analysis describes the use of SECU with or without MTX.
Methods: The data of patients with psoriatic arthritis seen since January 1, 2015 (date at which SECU appeared in the Canadian market) at the *Institut de Recherche en Rhumatologie de Montréal* (IRRM) and the *Centre de l'Ostéoporose et de Rhumatologie de Québec* (CORQ) was extracted from the Rhumadata® clinical database and registry on January 7, 2019. Selected patients initiated SECU either without (MTX-) or with MTX (MTX+). The collected data include baseline characteristics (socio-demographic variables, concomitant and past medication, comorbidities and the Charlson comorbidity index (CCI)), variables measured over time (laboratory test results, patient and physician-reported outcomes, and disease activity measures such as minimal disease activity (MDA), CDAI and DAS28(4)-ESR) and persistence data (treatment duration, reason for cessation). The groups were compared to identify potential confounder, and persistence data were analyzed using Kaplan-Meier and proportional hazard methods.
Results: A total of 96 patients were prescribed SECU since January 1, 2015. Of those, 49% (n=47) treated with MTX. No significant differences in baseline (at treatment initiation) were observed between the MTX+ and MTX- groups. Average age at treatment initiation was 52.4 (standard deviation=11.3) and 53.7 (13.4) in the MTX+ and MTX- groups respectively. Women represent 45% and 55% of these groups, and the average body mass index was 29.9 (6.2) and 28.1 (6.0) kg/m2. Patient global, pain and fatigue assessments, made on a visual analogue scale ranging from 1 to 10, were 4.9 (2.6), 5.3 (2.9) and 4.3 (2.9) in the MTX+ group and 6.3 (2.2), 6.9 (2.1) and 6.5 (2.9) in the MTX- group. Among the 38 (40%) patients ceasing therapy, the principal reason for cessation was "inefficacy" (MTX+: 15/17 (88%) vs MTX-: 15/21 (71%)). Patients remaining on treatment at last follow-up had an average treatment duration of 1.7 (0.8) and 1.5 (0.7) years. The improvement in CDAI, HAQ and the percentage of patients reaching MDA are similar for both groups. No difference in retention was observed between the MTX+ and MTX- groups (log-rank p=0.4867). These results remain unchanged when we adjust for age at treatment initiation, gender, disease duration, and comorbidities (Charlson comorbidity index).
Conclusion: Combining MTX to SECU does not improve its sustainability over time. Efficacy was also the same for both cohorts.

REFERENCES

[1] Mease PJ, et al. *Arthritis Rheumatol.* 2018; 70 (suppl 10). Abstract L11
[2] Benryane O, et al. *Arthritis Rheumatol.* 2018; 70 (suppl 10). Abstracts 693 and 694
[3] Benryane O, et al. CRA-2019, Montréal, Canada.

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AB0741 ACHIEVEMENT OF CDAPSA LOW DISEASE ACTIVITY OR REMISSION IS ASSOCIATED WITH CONTROL OF ARTICULAR AND EXTRA-ARTICULAR MANIFESTATIONS OF ACTIVE PSORIATIC ARTHRITIS IN SUBJECTS TREATED WITH APREMILAST

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Background: Therapeutic targets for psoriatic arthritis (PsA) include the achievement of remission (REM) or low disease activity (LDA), measured by the Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA [0-154]), a composite of swollen and tender joints counts (SJC and TJC), Patient's Assessment of Pain (PAP) and Patient's Global Assessment of Disease Activity (PtGA).
Objectives: We examined the trajectories for improvement in cDAPSA, its core components and PsA manifestations not measured by cDAPSA among subjects achieving cDAPSA REM or LDA by Week 52.
Methods: Pooled analyses of the phase III PALACE 1, 2 and 3 studies were performed for subjects assigned to receive apremilast (APR) 30 mg twice daily at baseline (BL). Subjects with cDAPSA components available to calculate responses at Week 52 were included and grouped according to the cDAPSA categories reached at Week 52 (REM: ≤4; LDA: >4 to ≤13; moderate disease activity: >13 to ≤27; high disease activity: >27). We then traced their mean cDAPSA trajectory from BL to Week 52. Mean disease activity in core PsA domains were reported longitudinally by cDAPSA category reached at Week 52.

Results: A total of 375 APR subjects were included in the analyses. Achievement of REM or LDA by Week 52 was associated with lower mean cDAPSA at BL, and these subjects had continuous improvements in disease activity from BL to Week 52 (Figure). Among subjects who achieved REM or LDA by Week 52, most were classified as having LDA (mean cDAPSA: 8.5) or moderate disease activity (mean cDAPSA: 16.6), respectively, at Week 16. Furthermore, subjects who achieved REM or LDA by Week 52 showed early improvement, with no/mild articular and extra-articular disease activity by Week 52 with APR (Table).

Conclusion: In the subgroup of subjects who achieved cDAPSA REM or LDA, early improvement was seen in disease activity by Week 16 and sustained to Week 52 with continued treatment. Subjects achieving cDAPSA REM or LDA exhibited no or mild disease activity in enthesitis, dactylitis, function and skin psoriasis by Week 52.

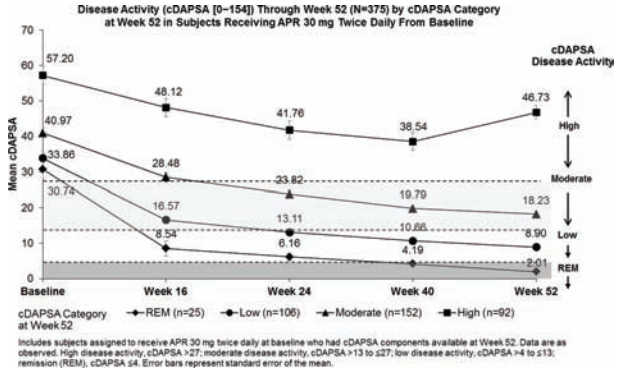


Figure 1

Articular and Extra-Articular Disease Activity in Subjects With REM or LDA at Week 52

	Subjects With REM at Week 52 n=25				Subjects With LDA at Week 52 n=106			
	Time Point				Time Point			
Mean	BL	Week 16	Week 24	Week 52	BL	Week 16	Week 24	Week 52
SJC (0-66)	9.1	2.2	1.2	0.1	8.8	3.5	2.0	1.1
TJC (0-68)	12.2	3.2	1.8	0.4	14.8	6.1	4.5	2.5
PAP (VAS 0-100 mm)	50.6	14.4	13.1	7.2	51.2	32.5	32.5	25.1
PtGA (VAS 0-100mm)	44.5	17.0	18.6	7.7	51.5	38.7	34.2	28.0
PhGA (VAS 0-100 mm)	48.8	16.0	12.4	8.4	50.7	24.0	18.9	13.7
PASI* (0-72)	9.5	4.2	3.5	2.7	8.2	3.7	3.4	4.0
MASES§ (0-13)	1.9	0.4	0.1	0.4	3.3	1.7	1.2	1.2
Dactylitis count‡	2.3	0.7	0.2	0.0	2.8	1.0	0.6	0.5
HAQ-DI (0-3)	0.9	0.3	0.2	0.1	1.0	0.7	0.7	0.6

Includes subjects assigned to receive APR 30 mg twice daily at BL who had cDAPSA (as calculated with SJC [0-66] and TJC [0-68]) components available at Week 52. Data are as observed and n values vary by time point based on number of subjects with available data for a given end point. *Assessed in subjects with ≥3% psoriasis-involved body surface area at BL. †Assessed in subjects with enthesitis at BL. ‡Assessed in subjects with dactylitis at BL. REM, cDAPSA ≤4; LDA, cDAPSA >4 to ≤13. VAS=visual analog scale; MASES=Maastricht Ankylosing Spondylitis Enthesitis Score.

Figure 1

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AB0742

ACHIEVEMENT OF PASDAS LOW DISEASE ACTIVITY AND VERY LOW DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH CERTOLIZUMAB PEGOL OVER 4 YEARS AND THE OVERLAP WITH DAPSA AND MDA DISEASE ACTIVITY TARGETS

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Background: Psoriatic Arthritis Disease Activity Score (PASDAS),[1]Disease Activity Index for Psoriatic Arthritis (DAPSA),[2] and the minimal disease activity (MDA) criteria[3] are instruments recommended for evaluating disease activity (DA) in psoriatic arthritis (PsA). RAPID-PsA demonstrated the sustained efficacy of certolizumab pegol (CZP) across the spectrum of PsA symptoms.[4] A substantial proportion of patients (pts) completing 4 years' treatment achieved DA targets; ~75% reached DAPSA low DA (LDA) or remission (REM), and almost 60% had MDA (≥5/7 MDA criteria), half of whom also achieved very low DA (VLDA) (7/7 MDA criteria).[5]

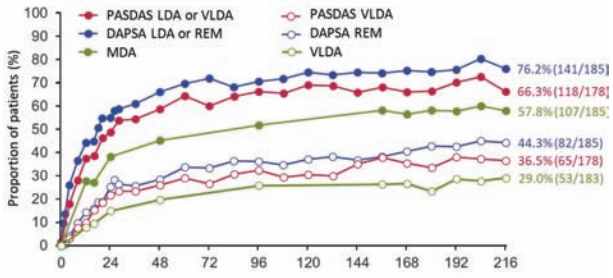
Objectives: To report the proportion of pts who achieved PASDAS VLDA and LDA over 216 weeks' (wks') CZP treatment, and the overlap in pts achieving PASDAS, DAPSA and MDA.

Methods: RAPID-PsA (NCT01087788) was double-blind and placebo-controlled to Wk24, dose-blind to Wk48, and open-label (OL) to Wk216.[5] Outcomes reported for pts randomised to CZP at Wk0 (200 mg every 2 wks or 400 mg every 4 wks, following a 400 mg loading dose at Wks0/2/4) are PASDAS change from baseline (CFB); pts achieving PASDAS LDA (>1.9−<3.2), PASDAS VLDA (≤1.9), DAPSA LDA (>4−≤14), DAPSA REM (≤4), MDA and VLDA to Wk216; and the overlap in pts achieving PASDAS VLDA, DAPSA REM, and VLDA, at Wk216. Data are summarized for observed cases per visit. Pts withdrawing between scheduled visits had their final assessment values assigned to the next scheduled visit timepoint.

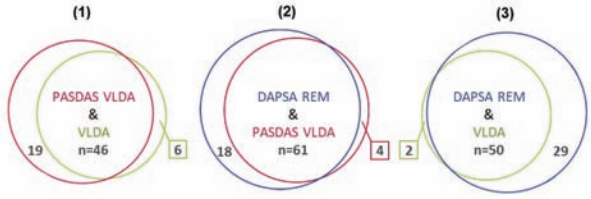
Results: Of 409 pts randomised, 273 received CZP from Wk0, of whom 248 (90.8%) completed Wk24 and 183 (67.0%) completed Wk216. The mean (SD) baseline PASDAS was 6.0 (1.0): in the high DA range, CFB at Wk216 was −3.4 (1.5). Of pts completing Wk216, 66.3% (118/178) were in PASDAS LDA or VLDA (PASDAS VLDA: 36.5% [n=65]): less than the proportion reaching DAPSA LDA or REM (76.2%), but more than those achieving MDA or VLDA (57.8%) (**Figure A**).

At Wk216, of pts achieving PASDAS VLDA, a large proportion (71% [46/65]) had VLDA based on MDA criteria (**Figure B1**) and most (94% [61/65]) achieved DAPSA REM (**Figure B2**). Almost all pts achieving VLDA (96.1% [50/52]) were also in DAPSA REM (**Figure B3**). After 4 years' CZP treatment, 25.8% (46/178) pts achieved the PASDAS VLDA, DAPSA REM and VLDA.

Figure: A) Patients with PsA achieving PASDAS, DAPSA and MDA disease activity targets over 4 years' CZP treatment (OC)



B) Overlap in patients with PsA achieving PASDAS VLDA, DAPSA REM and VLDA upon completing 216 weeks' CZP treatment (OC)



Data are for OC per visit. Patients withdrawing between scheduled visits had their final assessment values assigned to the next scheduled visit timepoint. CZP: certolizumab pegol; DAPSA: Disease Activity index for PSoriatic Arthritis; LDA: low disease activity; MDA: Minimal Disease Activity; OC: observed case; PASDAS: Psoriatic Arthritis Disease Activity Score; PsA: psoriatic arthritis; REM: remission; VLDA: very low disease activity.

Conclusion: A substantial proportion of pts completing 4 years' CZP treatment achieved PASDAS LDA or VLDA, and the vast majority who achieved PASDAS VLDA at Wk216 also reached DAPSA REM and/or VLDA. 1 in 4 pts achieved the most stringent DA target with all 3 instruments.

REFERENCES

[1] Helliwell P. Ann Rheum Dis 2013;72:986–91; 2. Schoels M. Ann Rheum Dis 2016;75:811–18; 3. Coates L. Ann Rheum Dis 2010;69:48–53; 4. van der Heijde D. RMD Open 2018;4:e000582.

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AB0743

REAL-WORLD EFFECTIVENESS AND SAFETY OF APREMILAST IN BELGIAN PATIENTS WITH PSORIATIC ARTHRITIS: ANALYSIS FROM THE MULTICENTRE, PROSPECTIVE, NON-INTERVENTIONAL APOLO STUDY

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Background: Real-world evidence on effectiveness and safety data for patients (pts) with psoriatic arthritis (PsA) in the Belgium clinical practice setting is lacking.

Objectives: To assess the effectiveness and safety of apremilast (APR) in pts with active PsA from routine clinical practice in Belgium.

Methods: In this multicentre, prospective, non-interventional study (APOLO), the PsA Response Criteria (PsARC) response 6 months after APR initiation was the primary endpoint. PsARC response was defined as improvement in ≥2 and no worsening of any of the following 4 measures: tender joint count (TJC; 0-68), swollen joint count (SJC; 0-66), Physician's Global Assessment of Disease Activity (PhGA) and Patient's Global Assessment of Disease Activity (PtGA). Other endpoints included PsAID12, HAQ-DI, Physician's and Patient's Numerical Rating Scale (NRS) assessing disease activity for the most affected joint, psoriasis-affected body surface area (BSA), enthesitis, dactylitis, pain and pruritus. The current analysis is based on observed data.

Results: The first 55 of a planned 150 Belgian pts receiving APR for up to 6 months were evaluated. Mean age was 52.5 yrs, mean BMI was 27.1 kg/m^2 and 47.3% were female. Mean durations of psoriasis and PsA were 15.8 yrs and 8.1 yrs, respectively; ≈80% of pts were biologic-naive. At baseline (BL), mean (SD) SJC was 8.0 (5.4), mean (SD) TJC was 12.7 (9.5) and mean (SD) body surface affected was 12.3% (20.8%); 31.0% of pts had dactylitis and 47.8% had enthesitis. In total, 35 pts (63.6%) continued APR treatment for 6 months; 20 (36.4%) had discontinued APR (insufficient effectiveness: 21.8%; adverse events: 10.9%, intolerance: 3.6%). After 6 months of APR initiation, 69.6% of pts had a PsARC response. Mean changes from BL in SJC were −4.4 (Month 3) and −5.7 (Month 6), with improvements in SJC (defined as ≥30% decrease per PsARC) observed in most pts (Month 3: 78.3%; Month 6: 83.3%). Comparable results were seen for TJC: Mean changes from BL were −7.2 (Month 3) and −6.7 (Month 6), with improvements observed in most pts (Month 3: 78.3%; Month 6: 80%). Decreases in PhGA score of ≥1 from BL were observed in most pts at Months 3 (73.7%) and 6 (66.7%). Mean (SD) Physician's NRS scores decreased from 5.6 (2.6) at BL to 2.5 (2.0) at Month 6. Among pts with enthesitis at BL who had data available at Month 6, 54.5% achieved a score of 0. Among pts with dactylitis at BL who had data available at Month 6, 44.4% achieved a score of 0. BL mean (SD) PsAID12 score of 5.9 (1.6) decreased to 3.7 (1.8) at Month 6. Mean (SD) BSA improved from 12.3% (20.8%) at BL to 7.5% (14.7%) at Month 6. An improvement of ≥20% in HAQ-DI at Month 6 was achieved by 73.1% of pts. Improvements were also seen in PtGA score, overall pain and pruritus. No new safety and tolerability concerns from known overall safety profile of APR.

Conclusion: Results from this real-world PsA study confirmed an improvement in disease activity with APR in both physician-assessed and pt-reported outcomes for most pts. Overall, improvements were observed after 3 months of APR treatment and were maintained up to the 6-month observation period. Safety and tolerability were similar to the known profile of APR.

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AB0744

EFFICACY OF IXEKIZUMAB IN ACTIVE PSORIATIC ARTHRITIS (PSA) PATIENTS WITH AXIAL PAIN STARTING BEFORE AGE 45: A SUBGROUP ANALYSIS OF SPIRIT-P1 AND SPIRIT-P2 PHASE 3 CLINICAL TRIALS

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Background: The efficacy and safety of ixekizumab (IXE), an IL-17A antagonist, was investigated in patients with active psoriatic arthritis (PsA) in the SPIRIT-P1 and SPIRIT-P2 clinical trials.

Objectives: To investigate the efficacy of ixekizumab on axial pain, fatigue, stiffness, and physical function in a subset of patients with PsA self-reporting axial pain starting before the age of 45 years at baseline.

Methods: Patients with PsA in the intent-to-treat populations of SPIRIT-P1 (Biologic-naïve; NCT01695239) and SPIRIT-P2 (Inadequate responders or intolerant to 1 or 2 TNF inhibitors; NCT02349295) with baseline patient-reported axial pain (≥4 Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] question 2), high-sensitivity C-reactive protein (hsCRP) >5mg/L, and <45 years old were included in this post-hoc integrated analysis. SPIRIT-P1/P2 did not include axial imaging. Patients were treated with placebo (PBO) or ixekizumab 80-mg every 2 weeks (IXEQ2W) or 4 weeks (IXEQ4W) after a 160-mg starting dose for 24 weeks. The efficacy of ixekizumab on axial pain (BASDAI question 2), fatigue (BASDAI question 1), stiffness (mean of BASDAI questions 5/6), total BASDAI, Health Assessment Questionnaire Disability Index (HAQ-DI), and 36-Item Short Form Health Survey Physical Component Summary (SF-36 PCS) was analyzed at Weeks 16 and 24 using mixed model for repeated measures with treatment, region, baseline conventional DMARD experience, visit, and treatment-by-visit interaction as fixed factors, and response value at baseline as a covariate.

Results: Axial pain and stiffness significantly improved at Weeks 16 and 24 in patients with PsA treated with IXEQ4W or IXEQ2W versus PBO (p<.05; Table 1). Fatigue significantly improved at Week 16 in patients treated with IXEQ4W or IXEQ2W versus PBO and at Week 24 with IXEQ2W versus PBO (p<.05). Total BASDAI scores significantly improved at Weeks 16 and 24 in patients treated with IXEQ4W or IXEQ2W versus PBO (p<.01). Physical function significantly improved at Weeks 16 and 24 in patients treated with IXEQ4W or IXEQ2W versus PBO when assessed by HAQ-DI or SF-36 PCS (p<.05).

	PBO N=32		IXEQ4W N=36		IXEQ2W N=37	
	Week 16 n=28	Week 24 n=13	Week 16 n=36	Week 24 n=29	Week 16 n=37	Week 24 n=33
BASDAI total	-0.78±0.51	-1.29±0.56	-2.80±0.45†	-3.28±0.45†	-3.32±0.47‡	-3.53±0.47‡
Question 1 (Fatigue)	-0.53±0.49	-1.07±0.56	-1.84±0.43*	-2.17±0.44	-2.52±0.46‡	-2.72±0.46†
Question 2 (Axial Pain)	-1.26±0.55	-1.85±0.61	-3.25±0.48†	-3.53±0.47*	-3.19±0.49†	-3.45±0.48*
Questions 5/6 (Stiffness)	-0.32±0.58	-0.86±0.65	-2.40±0.50†	-3.09±0.52†	-3.01±0.51‡	-3.16±0.52‡
HAQ-DI	-0.02±0.13	-0.15±0.13	-0.40±0.12†	-0.52±0.12*	-0.52±0.11‡	-0.51±0.11*
SF-36 PCS	1.53±5.15	3.64±5.44	15.56±4.73*	22.38±4.71†	18.33±4.77†	17.26±4.71*

*p<0.05, †p<0.01, ‡p<0.001, all vs. PBO.

Conclusion: Ixekizumab treatment yielded significantly higher improvements than placebo in axial pain, fatigue, stiffness, and physical function at Weeks 16 and 24 in the integrated PsA subpopulation self-reporting axial pain at baseline. These analyses were limited by a lack of baseline axial imaging.

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AB0745

ASSESSMENT OF DISEASE ACTIVITY USING RAPID3 AND EVALUATION OF TREATMENT EFFECT OF GUSELKUMAB IN PATIENTS WITH PSA: RESULTS FROM A RANDOMIZED PLACEBO-CONTROLLED PHASE 2 CLINICAL TRIAL

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Background:

Objectives: To evaluate the effect of guselkumab (GUS) on Routine Assessment of Patient Index Data 3 (RAPID3) in patients with psoriatic arthritis (PsA).

Methods: In a phase 2 trial, patients with active PsA and ≥3% body surface area of plaque psoriasis despite current or previous treatment with standard-of-care therapies, including anti-TNFα agents, were randomized 2:1 to receive GUS 100 mg (n=100) or placebo (PBO, n=49) subcutaneously at wks 0, 4, and every 8 wks (q8w) thereafter through wk44. At wk16, patients from either group with <5% improvement from baseline in both swollen and tender joint counts were eligible for early escape to open-label ustekinumab. At wk24, all remaining PBO patients crossed-over to receive GUS 100 mg, and then received GUS at wk28 and q8w thereafter through wk44. RAPID3 (0-30) is derived from the Multi-Dimensional Health Assessment Questionnaire (MDHAQ) and numerical rating scales (0-10) for pain and patient global assessment. A change of 5.1 in RAPID3 score was identified as the minimally important difference (MID) in PsA, and RAPID3 ≤3.0 was used to define PsA remission. Change in RAPID3 and proportion of patients achieving MID were compared between treatments. Correlations of RAPID3 scores with the PsA Disease Activity Score (PASDAS), GRACE index, Disease Activity in Psoriatic Arthritis (DAPSA), and Modified Composite Psoriatic Disease Activity Index (mCPDAI) were evaluated using Spearman correlation.

Results: The mean (SD) RAPID3 score at baseline was 16.9 (5.19). At wk24, patients in the GUS group (n=100) achieved statistically significantly greater decrease from baseline (improvement) in RAPID3 (-5.81 ± 6.0) than the PBO group (n=49) (-0.57 ± 5.1, p<0.001), and 50% of patients in the GUS group vs. 20.4% in the PBO group achieved an MID (p<0.001). Higher RAPID3 remission rate in the GUS than the PBO group (14.0% vs. 2.4%, p=0.022) was observed. The mean ±SD decrease from baseline in RAPID3 was -6.36 ±6.2 at wk24, and -7.48 ± 6.3 at wk44 in those who continued Guselkumab (N=86). Among patients who switched from PBO to GUS at wk24 (N=28), mean ± SD change from baseline (improvement) in RAPID3 was -2.28 ± 5.2 at wk24 while on placebo and -7.60 ± 6.6 at wk44 after switching to GUS. The RAPID3 score was highly correlated with PASDAS (r=0.84, p<0.001), GRACE index (r=0.89, p<0.001), DAPSA (r=0.77 p<0.001) and mCPDAI (r=0.65, p<0.001) at wk16.

Conclusion: GUS-treated PsA patients demonstrated significant improvement in RAPID3 compared to PBO. RAPID3 is simple and feasible to use in routine clinical care, and it correlates well with other comprehensive PsA-specific disease activity measures.

Disclosure of Interests: Atul Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, L Bruce Kirkham Grant/research support from: Investigator for Janssen Research & Development, LLC, Consultant for: Abbvie, Eli Lilly and Company, Janssen, Novartis, Proton Rahman: None declared, Philip Helliwell Grant/research support from: Paid to charity: from AbbVie, Janssen and Novartis, Consultant for: Paid to charity: from AbbVie, Amgen, Pfizer, and UCB and Celgene. Paid to self: from Celgene and Galapagos, Alice B Gottlieb Grant/research support from: PI: Incyte Corporation, Janssen-Ortho Inc., Lilly ICOS LLC, Novartis, UCB, XBiotech, Consultant for: AbbVie, Dermira, Incyte Corporation, Lilly ICOS LLC, Novartis, Sun Pharmaceutical Industries Ltd., Avotres (unpaid), XBiotech (unpaid), Speakers bureau: AbbVie, Eli Lilly and Company, Janssen Biotech; advisory board:

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AB0746 WORKING STATUS AND FACTORS ASSOCIATED WITH WORK PRODUCTIVITY AMONG PEOPLE WITH PSORIATIC ARTHRITIS

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Background: Work disability is an important functional outcome measure in psoriatic arthritis (PsA) and includes unemployment and loss of work productivity.
Objectives: The aim of this study is to investigate the working status and the factors associated with work productivity in patients with PsA.
Methods: Patients with PsA according to Classification Criteria for Psoriatic Arthritis (CASPAR) were included in the study consecutively, without sample selection. Data about age, sex, disease duration (month) were noted. Disease activity was assessed with DAPSA (Disease Activity in Psoriatic Arthritis) and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index). The Health Assessment Questionnaire (HAQ) was used to evaluate physical disability. The Psoriatic Arthritis Quality of Life (PsAQoL) scale was used to assess the quality of life. Fatigue and stiffness were assessed on the Visual Analogue Scale (VAS). Anxiety and depression were evaluated with HAD (Hospital Anxiety and Depression) scale.
Assessing work disability, we asked some questions to the patients including employment status, and early retirement, changing or reducing work due to PsA. We used WPAI: PsA (Work Productivity and Activity Impairment Questionnaire) to evaluate the impact of PsA on work productivity. WPAI: PSA consists of six questions and gives four scores: the percentage of absenteeism (work time missed due to PsA), the percentage of presenteeism (reduced productivity at work due to PsA), an overall work impairment (combines absenteeism and presenteeism) and percentage of impairment in daily activities.
The association between WPAI: PsA scores and HAQ, PsAQoL, HAD, fatigue and stiffness was determined by Spearman's correlation coefficient. The Mann Whitney-U test was used to compare the means of groups. The descriptive analysis was done for demographic data. $P<0.05$ accepted as significant. SPSS 20.0 (Statistical package for social sciences for Windows 20.0) program was used for the statistical analysis.
Results: The mean age of 60 patients (38 female, 22 male) with PsA was 48.13 (SD: 11.53) years. The median (min-max) duration of disease was 36 (3-384) months.
63.33% of the patients were not working and 57.89% of these patients were housewives, and 23.68% were retired. 11.66% of the patients with PsA were unemployed. There were no patients who were retired early due to the disease. Percentage of the stopping work, changing work or reducing working hours due to PsA was 3.3%, 6.7% and 10%, respectively.
There was no significant difference between the working and not-working groups of patients according to the disease duration, DAPSA, BASDAİ and HAQ scores ($p>0.05$). The mean age was higher in the non-working group ($p<0.005$).
There was no absenteeism in 63.3% of patients. The mean percentage of the presenteeism was 36 (SD: 30.79) and the mean percentage of the overall work impairment was 41 (SD: 34.06). There were no significant correlations between WPAİ: PsA scores and age, disease duration, DAPSA score ($p>0.05$). Presenteeism and overall work impairment had significant moderate correlations with fatigue (rho: 0.639, p: 0.001; rho: 0.607, p: 0.003), morning stiffness (rho: 0.424, p: 0.049; rho: 0.484, p: 0.023), HAQ (rho: 0.532, p: 0.011; rho: 0.551, p: 0.008), PsAQoL (rho: 0.481, p: 0.023; rho: 0.510, p: 0.015), HAD depression (rho: 0.650, p: 0.001; rho: 0.634, p: 0.002), and HAD anxiety scores (rho: 0.486, p: 0.022; rho: 0.527, p: 0.012), respectively.
Conclusion: Psoriatic arthritis can cause loss of work productivity. The severity of work impairment is associated with fatigue, stiffness, physical disability, depression, anxiety and health-related quality of life. In our study population, the percentage of housewives and retired was high and the rate of unemployment was 11.66%. This is a preliminary study and will continue in larger patient populations.
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AB0747 RESPONSE TO SECUKINUMAB AMONG NAIVE AND BIOLOGICALLY EXPERIENCED PATIENTSIN PSORIATIC ARTHRITIS

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Background: Secukinumab is a recombinant human monoclonal immunoglobulin IgG antibody that selectively targets IL-17A and blocks its interaction with the IL-17 receptor. Inhibition of the downstream effects of this proinflammatory cytokine thereby interferes with key psoriasis disease pathways while promoting normalization of immune function and skin histology.
Objectives: The aim of the study was two-fold; firstly, to compare the response to Secukinumab in psoriatic arthritis (PsA) patients who were biologically naive and experienced, and secondly to compare the response between smokers and non-smokers.
Methods: In collaboration with the National Psoriatic Arthritis Registry of Ireland, patients who were diagnosed and treated as PsA at University Hospital Kerry between March 2017 and October 2018 were included in this population-based cohort study.Patients demographic, clinical characteristics, treatment strategies (including response rates and adverse effects) were captured at baseline and at follow-up outpatient visits.
Results: A total of 96 patients were identified and included in the study (mean age of 56.6 years; male to female ratio of 1:1, 49 males, 47 females). Of these patients, 15 received Secukinumab (7 biologically-naive patients, 8 patients with previous treatment failure to anti-TNF agents (3 patients received one anti-TNF, 5 received two different anti-TNFs). In the biologically-naive group, 5 patients(71%) had completeresponse to Secukinumab, one patient (14.3%) had complete improvement of joint symptoms but remained fatigued (high BRAF score) while 1 patient (14.3%) had no improvement. All 7 of these patients were exposed to cigarette smoking (6 current smokers, one ex-smoker). In patients who previously failed anti-TNF, five(62.5%) remained symptomatic (tender & swollen joints, PROMs and BRAF score remained high) despite treatment with Secukinumab. Only three patients (37.5%) responded well to treatment. Two of the eight patients never smoked (both did not respond to Secukinumab) while the other 6 patients (3 responded, 3 had no response) were ex-smokers.
Conclusion: In our study, Secukinumab demonstrated better response to the biologically-naive PsA patients, while smoking did not increase the risk of disease activity among PsA patients receiving Secukinumab.
Disclosure of Interests: None declared
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AB0748 EVOLUTION ON HEALTH-RELATED QUALITY OF LIFE IN PSORIATIC ARTHRITIS PATIENTS

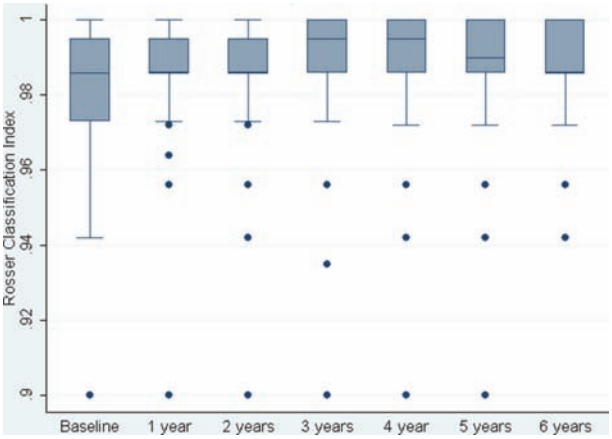
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Background: Psoriatic arthritis (PsA) is a chronic, progressive and inflammatory arthritis. It is consider a multifaceted disease, with a high impact on patient's psychological and physical well-being, with patients reporting lower health-related quality of life (HRQoL). Data of burden of disease is substantial and even though there are some studies that identify risk factors with longstanding PsA, there exists a need for properly designed studies to learn more about the evolution of HRQoL throughout the follow-up in this condition.
Objectives: To analyze the evolution on HRQoL in patients with PsA and to to evaluate factors that may influence this evolution.
Methods: Retrospective longitudinal observational study including incident patients diagnosed with PsA from 2007 to 2016, and followed-up until loss of follow-up or December 2017; with at least two registered visits; having received any ICD9/ICD10 diagnosis code of PsA; and with symptoms onset after 16 years of age. Patients were collected from the rheumatology outpatient clinic of a tertiary hospital (Hospital Clínico San Carlos, Madrid, Spain). Clinical information was collected from a departmental electronic health record, including demographic, clinical, comorbidities, treatment, and HRQoL related variables (measured with the Rosser

Classification Index). The influence of these variables in repeated measures of HRQoL was analysed using bivariate and multivariate generalized estimating equations (GEE) models nested by patient. Those variables with a p-value <0.20 (plus age, gender, follow-up time, and calendar year of diagnosis) were introduced in the multivariate analysis. Bonferroni p-value threshold adjustment was carried out.

Results: We included 187 patients, with a median follow-up of 3.6 years (interquarltile range: 0.8 to 6.3). 48% were women, with a median age at the onset of symptoms and diagnosis of 45 and 49 years, respectively. 86% of patients had a personal history of Psoriasis. Regarding clinical manifestations during the follow-up, 83%, 30%, 26%, and 22% of the patients presented with peripheral arthritis, inflammatory low back pain, enthesitis and dactylitis, respectively. In addition, they received treatment with nonsteroidal antiinflammatory medications (NSAIDs), oral glucocorticoids and disease-modifying antirheumatic drugs (DMARDs) 71%, 52% and 82%, respectively. 20% received biological agents. The Rosser median value at the first visit was 0.986, with an slight increase alter the first 2 years and a decline after 5 years of follow-up (Figure 1).

With respect to the variables independently associated with HRQoL during follow-up, the history of osteoporotic fractures (p = 8.1x10-18) and chronic obstructive pulmonary disease (p = 5.0x10-8) were associated with a poorer quality of life. Conversely, treatment with methotrexate (p=6.4x10-5), and the use of bone-forming agents (p = 7.8x10-4) were associated with better HRQoL. History of osteoporosis and use of biphosphonates and denosumab were also associated with HRQoL, although not significantly after p-value adjustment.



Conclusion: We have identified different factors associated with HRQoL during the evolution of patients with PsA. We observed that the presence of certain comorbidities were independently associated with a worse HRQoL. In addition, regarding different treatments, the use of methotrexate and bone-forming agents were independently associated with a better HRQoL.

Disclosure of Interests: None declared

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AB0749

ARE THERE ANY DIFFERENCES IN THE EFFECTIVITY AND SAFETY OF CERTOLIZUMAB PEGOL IN PATIENTS WITH PSORIATIC ARTHRITIS ACCORDING THEIR GENDER?

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Background: Gender-related biochemical, hormonal and psychological factors could play an important role in the response to TNF blocker therapy in psoriatic arthritis (PsA). Scarce data are available analyzing differences in effectiveness and safety of the antiTNFs, and none in particular with Certolizumab Pegol (CZP) according to the gender.

Objectives: To evaluate the influence of the gender in the effectiveness and safety of CZP in the routine clinical setting in PsA patients.

Methods: Observational, national and muticentric cohort (approved by local ethical committee), PsA patients treated with CZP according to routine clinical practice were studied for 12 months. Clinical and disease characteristics and disease activity between gender were compared. Safety analysis: adverse events and withdrawn.

Results: 347 PsA patients were analyzed. No statistical differences were found between women and men at baseline in demographics, clinical variables, except for previous biologic treatment and ESR (Table 1). In both genders, a statistical significant decreased was observed after 1 year of CZP treatment in the following variables: DAS28(CRP); SJC; TJC; PGA (patient global ssesment);% patients with enthesitis, dactilytis and nail disease; but with no differences between females and males. Variables that influence the response at 12 months are: disease duration, CRP and TJC at baseline. Drug survival of CZP was 80.1%, and no differences were observed in gender. Adverse events related to CZP were observed in 9.5% and 19.9% withdrawn treatment: 12.4% due to lack of effectiveness, 4.0% due to intolerance and 3.5% other reasons.

Conclusion: CZP has shown to be effective and safe in PsA patient after a year of treatment in clinical practice regardless patient's gender.

Abstract AB0749 Table 1. Baseline demographic, clinical and disease activity characteristics.

Demographic variables	Female	Male
Gender, n (%)	196 (56.5) N=347	151 (43.5) N=347
Age, median (min-max), years	48.5(22.3;81.1) N=188	50.5 (22.0;78.0) N=137
No smoking, n (%)	137 (79.2) N=173	79 (56.8) N=139
Disease characteristics		
Disease duration, mean (Q1-Q3)	6.5 (1.8-8.7) N=188	6.9 (1.2-10.0) N=137
Presence of HLAB27	28 (20.3) N=138	13 (13.0) N=100
Previous biologics	N=155	N=124
• 0	37 (23.9)	48 (38.7)
• 1	67 (43.2)	42 (33.9)
• ≥2	51 (32.9)	34 (27.4)
Disease activity		
TJC (28 joints), mean (Q1-Q3)	7.3 (4.0-10.0) N=167	6.5 (3.0- 8.0) N=125
SJC (28 joints), mean (Q1-Q3)	5.2 (2.0-8.0) N=156	4.8 (2.0-6.0) N=116
PtGA (VAS), mean (Q1-Q3)	7.0 (6.0-8.0) N=195	6.8 (6.0-8.0) N=150
PhGA (VAS), mean (Q1-Q3)	6.2 (5.0-8.0) N=193	6.1 (5.0-7.0) N=150
CRP (mg/L), mean (Q1-Q3)	10.1 (1.0-14.0) N=195	9.4 (0.9-11.4) N=151
ESR (mm/h), mean (Q1-Q3)	24.8 (8.8-37.3) N=90	16.6 (5.0-21.3) N=58

Abstract AB0749 Table 2.. CZP effectiveness at 1 year of treatment

	Basal		3 months		12 months	
	F	M	F	M	F	M
DAS28 (CRP); mean (SD)	4.7 (0.9)	4.5 (0.8)	3.9 (0.9)	3.9 (1.0)	3.7 (1.0)	3.4 (1.0)
TJC; mean (SD)	7.3 (5.1)	6.5 (4.4)	5.2 (4.3)	5.1 (4.3)	4.4 (4.3)	4.0 (4.3)
SJC; mean (SD)	5.2 (3.8)	4.8 (3.5)	3.8 (3.1)	3.9 (3.3)	3.6 (3.1)	3.7 (3.4)
Enthesitis, n (%)*	38 (21.3)	35 (25)	30 (16.9)	26 (18.6)	12 (9.8)	8 (9.8)
Dactlylitis, n (%)*	48 (26.4)	48 (34.8)	27 (14.8)	31 (22.5)	7 (5.6)	10 (12.5)
Presence of nail disease, n (%)*	21 (24.7)	28 (38.4)	17 (20.0)	25 (34.2)	5 (9.8)	10 (25.0)

Disclosure of Interests: Rosa García : None declared, Manuel Fernandez-Prada: None declared, Arantxa Conesa: None declared, Jose Campos Esteban: None declared, ANA URRUTICOECHEA-ARANA: None declared, Alejandro Olive: None declared, SILVIA PAREDES Speakers bureau: Bristol, Roche, Amgen, Pfiser, Abbvie, lilly, UCB, Delia Taverner Speakers bureau: amgen, pfiser, Bristol, Lilly, Roche, Carlos Gonzalez Consultant for: Celgene, Gilead, Janssen, Merk, Novartis, Pfizer, Speakers bureau: Celgene, Roche, UCB

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AB0750

INFLUENCE OF AXIAL INVOLVEMENT ON FREQUENCY OF ENTHESITIS AND DACTYLITIS, PATIENTS' REPORTED OUTCOMES AND THEIR FUNCTIONAL CAPACITY. DATA FROM THE RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PSART)

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Background: The latest data show that axial involvement in psoriatic arthritis (PsA) patients (pts) is associated with significantly worse disease status and widespread impairment of patient-reported outcomes (PRO's) (1).

Objectives: To analyze clinical characteristics and PRO's in PsA pts with and without radiographic sacroiliitis (rSI) in the Russian Psoriatic Arthritis Registry (RU-PsART).I

Methods: 385 pts (M/F–172/213) with PsA according to CASPAR criteria were included in the RU-PsART. Data was collected from 25 rheumatology clinics from various regions of the Russian Federation. Median age 45 (Min 20-Max 80) years (yrs), disease duration 3.4 yrs (4 months-32 yrs). Pts underwent standard clinical examination of PsA activity. All pts were studied for patient global disease activity (PGA) and patients' pain measured by Visual Analogue Scale (VAS), and Health Assessment Questionnaire (HAQ). Physician's global assessment of disease activity (PG) was measured by VAS. The examination included X-ray of sacroiliac joints (pelvic radiographs). rSI was defined as bilateral grade $\geq$2 or unilateral grade $\geq$3. Pts were split into two groups (gr.): those with rSI [rSI(+)] and those without rSI [rSI(-)]. Medians and quartiles [Me (Q25; Q75)], [Min; Max], U-test and ORs with 95% CI were performed. All CI >1, p <0.05 were considered to indicate statistical significance.

Results: gr. rSI(+) included 214 (55.6%) cases (M/F–106/108), gr. rSI(-) included 171 (44.4%) cases (M/F–66/105). Median age in gr. rSI(+) was 45 [Min 20-Max 80] yrs, in gr. rSI(-) it was 46 [Min 21- Max 82] yrs. Significant differences were revealed between gr. rSI(+) and gr. rSI(-). ***In Leeds Enthesitis Index (LEI)***: in gr. rSI(+) LEI was 0 [0-2], in gr. rSI(-) it was 0 [0-1] (p=0.02). ***In frequency of dactylitis***: in gr. rSI(+) 71 pts had dactylitis, 143 did not have; in gr. rSI(-) 32 pts had dactylitis, 139 did not have. OR 2.2 [1.3-3.5]. ***In PGA:*** in gr. rSI(+) it was 56.5 [42.3-70.0], in gr. rSI(-) it was 50.0 [30.0-60.0] (p= 0.00). ***In patients' pain:*** in gr. rSI(+) it was 50.0 [40.0-70.0], in gr. rSI(-) it was 50.0 [20.5-58.8] (p=0.00). ***In PG:*** in gr. rSI(+) it was 54.0 [40.0-69.5], in gr. rSI(-) it was 40.0 [25.5-50.0] (p=0.00). ***In HAQ scores***: in gr. rSI(+) it was 1.0 [0.6-1.5], in gr. rSI(-) it was 0 [0-2.2] (p=0.02).

Conclusion: Axial involvement is identified in more than half (55.6%) of the PsA pts. The presence of axial involvement in PsA pts is associated with significantly worse disease status as measured by frequency of enthesitis and dactylitis, worse PRO's and with the reduction of patient's functional capacity. Consequently, the diagnostics of axial involvement is critical in clinical practice.

REFERENCES

[1] P. J. Mease, et al. J Rheumatol 2018;45:1389-96

Disclosure of Interests: ELENA GUBAR: None declared, Elena Loginova Speakers bureau: Novartis, Celgene Corporation, Biocad, Janssen, AbbVie Inc, Anastasia Koltakova: None declared, Yulia Korsakova Speakers bureau: Celgene Corporation, Janssen, Tatiana Korotaeva Consultant for: Pfizer, MSD, Novartis, AbbVie, Celgene, Biocad, Janssen, UCB, Lilly and Novartis-Sandoz, Speakers bureau: Pfizer, MSD, Novartis, AbbVie, Celgene, Biocad, Janssen, UCB, Lilly and Novartis-Sandoz, Evgeny Nasonov Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc., Maria Sedunova: None declared, Igor Pristavsky: None declared, Irina Umnova: None declared, Irina Bondareva: None declared, Snezana Kudishina: None declared

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AB0751

ASSOCIATION OF AXIAL INVOLVEMENT WITH MORE SEVERE DISEASE: HIGH DISEASE ACTIVITY, SEVERE PERIPHERAL ARTHRITIS AND WORSE SKIN LESION. DATA FROM THE RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PSART)

[1]Gubar Elena*, Elena Loginova[1], Anastasia Koltakova[1], Yulia Korsakova[1], Tatiana Korotaeva[1], Evgeny Nasonov[1], Maria Sedunova[2], Igor Pristavsky[2], Irina Umnova[3], Irina Bondareva[4], Snezana Kudishina[5]. *[1]Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*; *[2]St. Petersburg Clinical Rheumatology Hospital No.25, Rheumatology, St. Petersburg, Russian Federation*; *[3]Omsk Regional Hospital, Rheumatology, Omsk, Russian Federation*; *[4]Kemerovo Regional Hospital, Rheumatology, Kemerovo, Russian Federation*; *[5]Vladivostok Clinical Hospital No.2, Rheumatology, Vladivostok, Russian Federation*

Background: The latest data show that axial involvement in psoriatic arthritis (PsA) patients (pts) is associated with significantly more severe disease status (1).

Objectives: To analyze, in clinical practice, disease activity and characteristics of PsA pts with and without radiographic sacroiliitis (rSI).

Methods: 385 pts (M/F–172/213) with PsA according to CASPAR criteria were included in the RU-PsART. Data was collected from 25 rheumatology clinics from various regions of the Russian Federation. Median age 45 (Min 20-Max 80) years (yrs), disease duration 3.4 yrs (4 months-32 yrs). Pts underwent standard clinical examination of PsA activity. Disease activity was measured by DAPSA, DAS28, BASDAI. The examination involved HLA B27 antigen status and X-ray of sacroiliac joints (pelvic radiographs). rSI was defined as bilateral grade $\geq$2 or unilateral grade $\geq$3. Skin lesion severity was evaluated in terms of body surface area (BSA) affected, and Psoriasis Area Severity Index (PASI). When BSA was $\geq$3%, PASI was calculated. Pts were split into two groups (gr.): those with rSI [rSI(+)] and those without rSI [rSI(-)]. Gr. rSI(+) included 214 (55.6%) cases (M/F–106/108), gr. rSI(-) 171 (44.4%) cases (M/F– 66/105). Median age in gr. rSI(+) was 45 [Min 20-Max 80] yrs, in gr. rSI(-) it was 46 [Min 20-Max 82] yrs. Medians and quartiles [Me (Q25; Q75)], [Min; Max], U-test and ORs with 95% CI were performed. All CI >1, p <0.05 were considered to indicate statistical significance.

Results: Significant differences were revealed between gr. rSI(+) and gr. rSI(-). ***In HLA-B27 antigen status:*** in gr. rSI(+) it was positive in 62 pts, negative in 64 pts, while in gr. rSI(-) it was positive in 26 pts, negative in 52 pts. OR 1.9 [1.1-3.5]. ***In tender joint count (TJC):*** in gr. rSI(+) TJC was 9 [14-18], in gr. rSI(-) it was 6 [3-12] (p=0.02). ***In disease activity measured by DAPSA:*** in gr. rSI(+) DAPSA was 28.40 [15.65-43.65], in gr. rSI(-) it was 20.0 [12.45-30.0] (p=0.00). ***In DAS28***: in gr. rSI(+) DAS28 was 4.3 [3.3-5.6], in gr. rSI(-) it was 4.1 [3.0-4.9] (p=0.02).]. ***In disease activity measured by BASDAI***: in gr. rSI(+) BASDAI was 1.6 [0-5.1], in gr. rSI(-) it was 0 [0-4.5] (p=0.00). ***In frequency of erosive radiographic arthritis of feet:*** in gr. rSI(+) 58 pts had erosive arthritis of feet, 156 did not have, while in gr. rSI(-) 29 pts had erosive arthritis of feet, and 142 did not have. OR 1.8 [1.1-3.0]. ***In more extensive skin lesion area:*** in gr. rSI(+) BSA <3% had 120 pts, BSA >3% had 94 pts; while in gr. rSI(-) BSA <3% had 141 pts, BSA >3% had 57 pts. OR 0.6 [0.4-0.97]. ***In CRP:*** in gr. rSI(+) CRP was 0.9 [0.4-2.2] mg/dl, in gr. rSI(-) it was 0.8 [0.3-1.3] mg/dl (p=0.03).

Conclusion: Axial involvement in PsA patients is associated with HLA-B27 positivity. Patients with axial involvement have significantly worse disease status as measured by disease activity and a higher CRP level; they are more likely to have more severe (erosive) peripheral arthritis and more extensive skin lesion area. Early detection of axial involvement is critical for choice of treatment approach and good prognosis.

REFERENCE

[1] P. J. Mease, et al. J Rheumatol 2018;45:1389-96

Disclosure of Interests: ELENA GUBAR: None declared, Elena Loginova Speakers bureau: Novartis, Celgene Corporation, Biocad, Janssen, AbbVie Inc, Anastasia Koltakova: None declared, Yulia Korsakova Speakers bureau: Celgene Corporation, Janssen, Tatiana Korotaeva Consultant for: Pfizer, MSD, Novartis, AbbVie, Celgene, Biocad, Janssen, UCB, Lilly and Novartis-Sandoz, Speakers bureau: Pfizer, MSD, Novartis, AbbVie, Celgene, Biocad, Janssen, UCB, Lilly and Novartis-Sandoz, Evgeny Nasonov Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc., Maria Sedunova: None declared, Igor Pristavsky: None declared, Irina Umnova: None declared, Irina Bondareva: None declared, Snezana Kudishina: None declared

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AB0752

DRUG RETENTION AND REMISSION RATES IN 14,261 BIOLOGIC-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS STARTING TNF INHIBITOR TREATMENT IN ROUTINE CARE – RESULTS FROM 12 REGISTRIES IN THE EUROSPA RESEARCH COLLABORATION

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[1]EuroSpA Research Collaboration, On behalf of the DANBIO (Denmark), ARTIS (Sweden), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), biorx.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RRBR (Romania), ARC (Netherlands), BSRBR-AS (United Kingdom), GISEA (Italy), Denmark

Background: The efficacy of Tumour Necrosis Factor Inhibitor (TNFi) in patients with psoriatic arthritis (PsA) has been investigated in randomized controlled trials (RCTs) with strict inclusion and exclusion criteria. Patients treated in routine care are more heterogeneous and only ≈20-30% of patients receiving TNFi in routine care would have been eligible to be enrolled in the RCTs[1]. This emphasizes the need for real-world observational data as a valuable supplement to RCTs. Studying large patient groups from several European countries would increase the external validity of the results.

Objectives: To investigate Tumour Necrosis Factor inhibitor (TNFi) retention rates at 12 months (primary objective), 6 and 24 months, and remission rates at the same time-points in biologic-naïve patients with PsA from the EuroSpA Collaboration.

Methods: Prospectively collected data on PsA patients from 12 European registries were uploaded through the secure Virtual Private Network pipelines to the EuroSpA server, and pooled. Baseline characteristics were investigated with non-parametric descriptive statistics. TNFi retention rates (Kaplan-Meier statistics), and 28-joint count Disease Activity Score (DAS28)<2.6 and 28 joint Disease Activity index for Psoriatic Arthritis (DAPSA28)≤4 were calculated, including LUNDEX adjustment[2]. For patients initiating 1st TNFi after January 1st 2009, the following subcohorts were also studied: patients known to be fulfilling ClASsification for Psoriatic ARthritis (CASPAR) criteria and patients with one or more swollen joints (swollen joint count (SJC)≥1) at baseline.

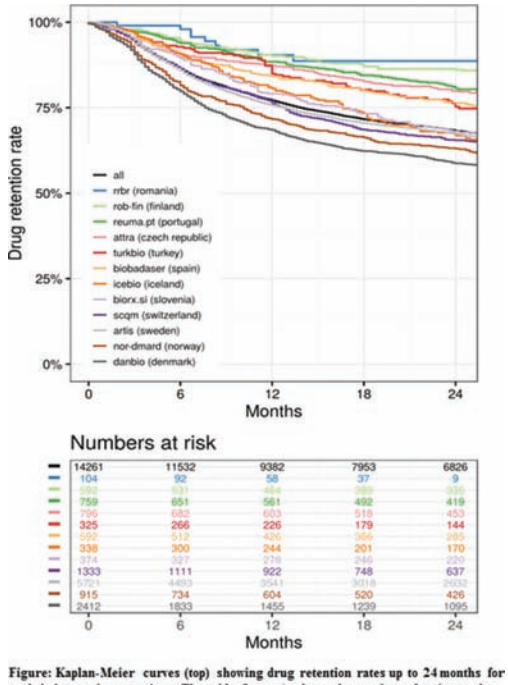


Figure: Kaplan-Meier curves (top) showing drug retention rates up to 24 months for pooled data and per register. The table (bottom) shows the number of patients who were still being treated at the corresponding time points.

First TNFi drug

Infliximab	3,089	22 %	12 %	18 %
Etanercept	4,788	34 %	25 %	31 %
Adalimumab	4,364	31 %	36 %	32 %
Certolizumab	524	4 %	5 %	5 %
Golimumab	1,516	11 %	22 %	15 %
DAS28	9,450	4.3 (3.4-5.1)	4.4 (3.5-5.3)	4.5 (3.8-5.2)
DAPSA28	8,717	26.7 (17.6-39.2)	28.4 (18.4-42.2)	29.9 (21.5-41.2)
CRP, mg/L	11,138	7 (3-17)	8 (3-17)	7(3-18)
SJC (0-28)	10,777	3 (1-6)	3 (1-7)	4 (2-7)
TJC (0-28)	10,764	5 (2-9)	5 (2-10)	6 (3-10)
SJC (0-66)	3,815	4 (1-7)	4 (2-8)	5 (3-8)
TJC (0-68)	4,655	8 (4-14)	7 (3-14)	9 (5-15)
	Retention rates			
6 months (95% CI)	86 % (86-87%)		88 % (87-90%)	85 % (84-86%)
12 months (95% CI)	77 % (76-78%)		78 % (77-80%)	76 % (74-77%)
24 months (95% CI)	68 % (67-69%)		69 % (67-71%)	67 % (65-68%)
	Remission rates			
	Crude**	LUNDEX adjusted ****	Crude**	LUNDEX adjusted ****	Crude**	LUNDEX adjusted ***
DAS28 remission at 6 months	56 %	45 %	59 %	49 %	55 %	43 %
DAS28 remission at 12 months	61 %	40 %	65 %	43 %	63 %	38 %
DAS28 remission at 24 months	65 %	31 %	68 %	32 %	69 %	29 %
DAPSA28 remission at 6 months	27 %	22 %	30 %	25 %	27 %	21 %
DAPSA28 remission at 12 months	30 %	20 %	33 %	22 %	32 %	20 %
DAPSA28 remission at 24 months	33 %	16 %	34 %	16 %	34 %	14 %

Data are as observed, median (IQR) or percentage; csDMARD: conventional synthetic Disease Modifying Anti Rheumatic Drug; TNFi: tumor necrosis factor inhibitor; SJC: swollen joint count; TJC: tender joint count; VAS: visual analogue scale; CRP: C-Reactive Protein; DAS28: Disease Activity Score 28 joint-count; DAPSA28: Disease Activity index for Psoriatic Arthritis 28 joint-count; *CASPAR criteria: CIASsification Criteria for Psoriatic Arthritis initiating treatment after

Results: Overall, 14,261 patients with PsA initiated a 1st TNFi. Baseline characteristics of the pooled population are shown in the **Table**.

The median 12-month retention rate (95%CI) was 77% (76-78%), ranging from 68-90% across registries (**Figure**). Overall, DAS28/DAPSA28 remission rates at 6 months were 56%/27% (LUNDEX-adjusted: 45%/22%). In patients initiating a 1stTNFi after 2009 with registered fulfillment of CASPAR criteria (n=1,980) or registered ≥1 swollen joint at baseline (n=5,803), the retention rates and remission rates were similar to those found overall (**Table**).

Conclusion: Approximately half of >14,000 patients with PsA who initiated 1st TNFi treatment in routine care were in DAS28-remission after 6 months, and three out of four were still on the drug after 1 year.

REFERENCES

[1] Clin Exp Rheumatol, 2018, 36(6):1068-1073

[2] Arthritis Rheum, 2006, 54(2): 600-6

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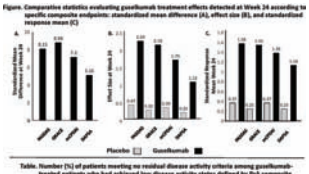
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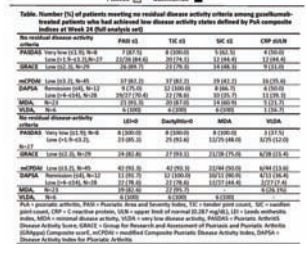
Have received research grants (not current) from the British Society for Rheumatology, who received the funds from Abbive, Pfizer and UCB.
Have received research grant (current) from the British Society for Rheumatology, who received the funds from Celgene., Florenzo Iannone Consultant for: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Lise Hyldstrup: None declared, Niels Steen Krogh: None declared, Mikkel Østergaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Merete L. Hetland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Bioepis
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AB0753 COMPARING COMPOSITE MEASURES OF DISEASE ACTIVITY IN PSORIATIC ARTHRITIS: RESULTS FROM A RANDOMIZED PHASE 2 TRIAL WITH GUSELKUMAB

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Background: Psoriatic ArthritiS Disease Activity Score (PASDAS), GRAppa Composite scorE (GRACE) Index, modified Composite Psoriatic Disease Activity Index (mCPDAI), and Disease Activity Index for PSoriatic Arthritis (DAPSA) are composite indices recently developed to assess disease activity in psoriatic arthritis (PsA).1,2 Guselkumab (GUS) is a monoclonal antibody targeting interleukin-23 that has demonstrated efficacy in a phase 2 PsA trial.3
Objectives: To compare the effect of GUS on disease activity in psoriatic arthritis (PsA) as measured by these composite indices.
Methods: In this Phase-2 trial, patients with active PsA (≥3 tender, ≥3 swollen joints, C-reactive protein ≥3 mg/L, ≥3% body surface area) were randomized 2:1 to subcutaneous GUS 100mg (n=100) or placebo (PBO, n=49) at Wk0, Wk4, and every 8 wks through Wk44. At Wk16, patients with <5% improvement in swollen plus tender joints could early-escape (EE) to open-label ustekinumab. Patients continuing PBO crossed-over to receive GUS 100mg at Wks 24/28/36/44 (PBO to GUS). PsA composite indices PASDAS, GRACE, mCPDAI, and DAPSA were analyzed using last-observation-carried-forward for missing/post-EE data through Week24. Instruments were validated using SF-36 physical component summary (PCS) score as an anchor. Sensitivity was assessed via standardized mean differences (SMDs), effect size (ES) and standardized response means (SRMs).





Results: Changes in SF-36 PCS score were consistent with disease activity states at Wk24 for each PsA composite index in guselkumab-treated patients. The SMD, ES and SRM indicated that guselkumab elicited a substantial effect in treating the diverse manifestations of PsA compared with placebo, regardless of composite index employed (Figure). PASDAS and GRACE indices appeared to be more sensitive than mCPDAI and DAPSA in detecting changes upon treatment and distinguishing guselkumab treatment effects relative to placebo. Residual disease activities among guselkumab-treated patients who achieved low disease activity at Week24 based on each PsA composite index are summarized in the Table.
Conclusion: Regardless of the PsA-specific composite index employed, GUS significantly improved disease activity and achieved clinically meaningful therapeutic targets such as low/minimal disease activity or remission. PASDAS and GRACE indices were more sensitive than mCPDAI and DAPSA in detecting changes in disease activity by guselkumab treatment.

REFERENCES

[1] Helliwell PS, et al. JRheumatol 2014;41:1212-1217.
[2] Scholes MM, et al. AnnRheumDis 2016;75:811-818.
[3] Deodhar A, et al. Lancet 2018;391: 2213–24.

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AB0754 CLINICALLY MEANINGFUL IMPROVEMENT IN SKIN AND NAIL PSORIASIS IN BIO-NAÏVE ACTIVE PSORIATIC ARTHRITIS PATIENTS TREATED WITH INTRAVENOUS GOLIMUMAB: RESULTS THROUGH WEEK 52 FROM A PHASE-3 STUDY

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Background: GO-VIBRANT is a Phase 3 trial of intravenous (IV) golimumab (GLM) in adult patients (pts) with active psoriatic arthritis (PsA). Clinically meaningful improvements in skin and nail psoriasis (PsO) and in Dermatology Life Quality Index (DLQI) that were significantly greater than placebo (PBO) at weeks (wks) 14 & 24 were previously reported.1
Objectives: To evaluate improvement in skin and nail PsO and DLQI with IV GLM through wk52.
Methods: Adult bio-naïve PsA pts with active disease(≥5 swollen & tender joints, CRP ≥0.6mg/dL, active plaque psoriasis or documented history), despite treatment w/csDMARDs &/or NSAIDs, were randomized to IV GLM 2mg/kg at wks 0/4 & every 8 wks thereafter or PBO at wks 0/4/12/20 with crossover to GLM at wk24. Pts with ≥3% body surface area (BSA) psoriasis at baseline (BL) were assessed using Psoriasis Area and Severity Index (PASI, 0-72) of 75/90/100% improvement scale,

modified Nail Psoriasis Severity Index (mNAPSI, 0-130) in pts with mNAPSI >0 at BL, and DLQI (0-30) scale.

Results: 394 pts (PBO:n=198; GLM:n=196) had ≥3% BSA psoriasis at BL; 76.5% had mNAPSI>0 at BL(mean 18.6). Pts on IV GLM achieved a greater PASI 75 response rate (RR) vs PBO at wk24 (64.8% vs 13.1%, p<0.001). At wk52, PASI 75 RR was maintained in pts who continued IV GLM treatment and increased numerically in those who crossed-over from PBO to IV GLM at wk24 (71.9% and 60.6%, respectively). At wk24, pts on IV GLM achieved significantly greater PASI 90/100 RR vs PBO. At wk52, PASI 90/100 RR was maintained among those continually on IV GLM and increased numerically in PBO to IV GLM pts(Table). At wk24, significantly greater proportions of pts on IV GLM ± BL methotrexate (MTX) achieved PASI 90/100 vs PBO. By wk52, both ± BL MTX, PASI 90/100 responses were maintained in those continually on IV GLM and increased numerically in PBO to IV GLM pts (Table). The mean decrease (improvement) from BL in the mNAPSI score was also greater with IV GLM vs PBO at wk24, overall and in groups ± BL MTX. At wk52, mNAPSI RR was maintained with continual IV GLM and increased numerically in PBO to IV GLM pts(Table). At wk24, the mean decrease (improvement) from BL in DLQI was greater with IV GLM vs PBO (−8.1 vs −1.9, p<0.001). At wk52, mean DLQI improvement was maintained in pts continually on IV GLM and increased numerically in PBO to IV GLM pts (-7.8 vs -5.8). Similar patterns were seen in subgroups ± BL MTX. In pts with DLQI improvement >1 at baseline, rate of simultaneous achievement of both PASI 50 response & improvement in DLQI ≥5 was greater at wk24 with IV GLM (59.2%) vs PBO (8.1%, p<0.001). At wk52, both were achieved by 56.6% continually on IV GLM vs 41.4% of PBO to IV GLM pts. Similar patterns were seen for simultaneous achievement of both improvement in DLQI ≥5 &PASI 75/90/100 at wks 24 and 52.

Table. Change from Baseline in PASI 90/100 and mNAPSI through Week 52

	Week 24		Week 52	
	PBO	IV-GLM 2 mg/kg	PBO→ IV-GLM 2 mg/kg at Wk 24	IV-GLM 2 mg/kg
Pts evaluable for improvement from BL in PASI, n	198	196	198	196
PASI 90 (%) % Diff (95% CI)	7.6	42.9 35.3 (27.4, 43.1)*	41.9	56.1
PASI 100 (%) % Diff (95% CI)	5.6	25.5 20.0 (13.2, 26.9)*	18.7	28.6
+ BL MTX, n	142	131	142	131
PASI 90 (%) % Diff (95% CI)	9.2	45.8 36.6 (26.9, 46.4)*	40.8	58.0
PASI 100 (%) % Diff (95% CI)	7.0	30.5 23.5 (14.6, 32.4)*	18.3	32.8
- BL MTX, n	56	65	56	65
PASI 90 (%) % Diff (95% CI)	3.6	36.9 33.4 (20.7, 46.1)*	44.6	52.3
PASI 100 (%) % Diff (95% CI)	1.8	15.4 13.6 (4.2, 23.0)**	19.6	20.0
Pts (mNAPSI >0) evaluable for change from BL in mNAPSI, n	170	197	170	197
Mean mNAPSI (SD) LS Mean diff (95% CI)	-3.7 (14.5)	-11.4 (16.4) -8.4 (-10.8, -6.0)*	-12.9 (16.2)	-12.1 (16.7)
+ BL MTX, n	121	129	121	129
Mean mNAPSI (SD) LS Mean diff (95% CI)	-5.8 (14.9)	-10.0 (15.6) -7.3 (-10.2, -4.4)*	-14.4 (16.1)	-10.1 (15.4)
- BL MTX, n	49	68	49	68
Mean mNAPSI (SD) LS Mean diff (95% CI)	1.7 (11.7)	-14.1 (17.6) -12.2 (-16.6, -7.8)*	-9.3 (16.0)	-15.8 (18.5)
	*p<0.001; **p=0.010 BL, baseline; CI, confidence interval; GLM, golimumab; MTX, methotrexate; PASI, Psoriasis Area and Severity Index; PBO, placebo; Pts, patients			

Conclusion: Clinically meaningful improvements in skin and nail psoriasis and psoriasis quality of life after IV GLM treatment of PsA pts were maintained from 24 to 52 weeks of treatment.

REFERENCES

[1] Mease P, et al. EULAR. June 2018, Amsterdam, NL.

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AB0755

REGIONAL AND TEMPORAL VARIATION IN THE BASELINE PROFILE OF PSORIATIC ARTHRITIS PATIENTS INITIATING ADALIMUMAB FOLLOWING FAILURE OF NON-BIOLOGIC TREATMENT IN CANADIAN ROUTINE CARE

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Background: Treatment selection in routine clinical care is driven by treatment guidelines, physician judgment, patient preferences, and regional reimbursement policies, which may vary over time and among geographic regions.

Objectives: The objective of this analysis is to investigate the regional and temporal variability of the profile of anti-TNF naïve psoriatic arthritis (PsA) patients at initiation of adalimumab (ADA) treatment following failure of initial non-biologic treatment.

Methods: COMPLETE-PsA is an ongoing Canadian observational study of anti-TNFα naïve adults with active PsA who require change in their current treatment as per the judgement of their treating physician. Patients are followed for up to 2 years. Regional variation was assessed for the following regions: British Columbia/Manitoba (BC/MB), Newfoundland/Nova Scotia (NL/NS), Ontario (ON), and Quebec (QC). Temporal variation was assessed for the following periods: 2012-2014 and 2015-2017. Multivariate linear regression was used to evaluate the independent impact of region and time period on disease activity (DAS28) and patient function (HAQ).

Results: A total of 278 patients were included**,** of whom 68 (24.5%) were from BC/MB, 25 (9%) from NL/NS, 104 (37.4%) from ON, and 81 (29.1%) from QC. One hundred fifty-three patients (55%) were enrolled in 2012-2014 and 125 (45%) in 2015-2017.

Using univariate analysis, significant regional variation at ADA initiation was observed for the following disease parameters: BSA<3% (from 42.3% in ON to 76% in NL/NS; *p*=0.003), morning stiffness (from 60.9 min in QC to 119.7 in BC/MB; *p*=0.049), WLQ productivity loss score (from 8.4% in BC/MB to 12.9% in NL/NS; *p*=0.028), and DLQI (from 3.5 in NL/NS to 7.9 in ON; *p*=0.007); and for the initiation of ADA monotherapy vs. ADA combination therapy (range from 9.9% in QC to 27.9% in ON; *p*=0.022). No differences were observed in demographics (other than race: Caucasian range from 85% to 100%; *p*=0.006), **or** other disease parameters (DAS28, HAQ, SJC, TJC, DAPSA, PtGA, BDI). A statistical trend towards lower DAS28 (2012-14 vs. 2015-17: 4.9 vs. 4.6; *p*=0.070), SJC (8.3 vs. 6.4; *p*=0.001), TJC (9.5 vs. 8.1; *p*=0.074), and DAPSA (30.8 vs. 27.8; *p*=0.083) at ADA initiation was observed for the more recent time period. Using multivariate analysis to adjust for age, gender, BSA levels, and corticosteroid use, there was no regional or temporal variation in DAS28 and HAQ.

Conclusion: The results of this analysis demonstrate that there is significant regional and temporal variation in the profile of PsA patients initiated on ADA treatment in Canadian routine care. The impact of this profile variation on treatment outcomes requires further investigation.

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AB0756

COMPARATIVE CHANGE IN QUALITY OF LIFE MEASURES IN PRECLINICAL AND ESTABLISHED PSORIATIC ARTHRITIS PATIENTSUNDER SECUKINUMAB TREATMENT. DATA DERIVED FROM THE PROSPECTIVE OPEN LABEL PSARTROS STUDY

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Background: Psoriasis (PsO) and psoriatic arthritis (PsA) differentially impact patients' quality of life (QoL) due to pain, mental changes in the context of chronic inflammation and impaired physical function. Effective anti-inflammatory therapy has shown to be effective to improve QoL in PsO and PsA patients. However, the impact of ant-inflammatory therapy on QoL may be different in the earliest stages of PsA as compared to established disease.

Objectives: To perform a detailed comparative investigation of the effect of interleukin (IL)-17 inhibition with 300 mg secukinumab (SEC) on QoL in patients with very early PsA/pre-PsA and established PsA.

Methods: Patients from the IVEPsA study (1) on very early PsA/pre-PsA (N=20) and the PSARTROS (2) study on established PsA (N=20) were longitudinally assessed for SF-36, DLQI, PsAID and HAQ-DI at baseline and after 4, 12 and 24 weeks. All patients received SEC treatment; 19/20 pre-PsA patients and 17/20 established PsA patients completed the study. Changes from baseline values were evaluated using linear mixed effects models adjusted for baseline values of each scale, gender, age and disease duration, and plotted as model coefficients and respective 95% confidence intervals that represent adjusted mean absolute improvement from baseline. Scale signs were inverted as necessary to ease interpretability. Further subgroup analysis was conducted using Mann-Whitney.

Results: Significant and rapid improvements were observed in both pre-PsA and established PsA treated with SEC with regard to pain (SF-36 bodily pain, BP), general health perception (GH), dermatology quality of life index (DLQI) and PsA impact of disease (PsAID), as well as in the SF-36 component scores (mental component score of SF-36, MCS and physical component score of SF-36, PCS). Physical function- oriented instruments like SF-36 physical functioning (PF), role limitation due to physical problem (RP) and HAQ-DI were preferentially affected in established PsA group due to the higher functional burden of disease (*Figure*). There were more differences with respect to the course of QoL improvements through week 12 and 24, as established PsA patients showed an incremental improvement in SF-36 BP, PF and GH from week 12 to 24 while most of the responses plateaued in the pre-PsA group. Furthermore, established PsA patients who achieved minimal disease activity showed a significantly higher improvement in PsAID, HAQ-DI, SF-36 PF, RP and BP (all $p < 0.05$).

Conclusion: Pain, mental health, general health perception and impact of disease rapidly improve in both very early PsA/pre-PsA and established PsA patients treated with SEC. These data support the concept that very early treatment of PsA leads to significant improvement in QoL with the additional benefit of prevention of bone damage as previously shown (1, 2).

REFERENCES

1. . OP0305 Disease interception in psoriasis patients with subclinical joint inflammation by interleukin 17 inhibition with secukinumab – data from a prospective open label study. Kampylafka et al, ARD June 2018, Volume 77, Suppl. 2

[2] Resolution of synovitis and arrest of catabolic and anabolic bone changes in patients with psoriatic arthritis by IL-17A blockade with secukinumab: results from the prospective PSARTROS study. Kampylafka et al, Arthritis Res Ther. 2018 Jul 27;20(1):153

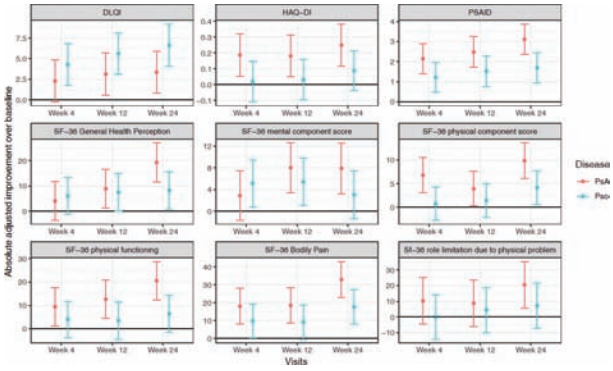


Figure:

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AB0757

ANALYSIS OF THE PROGNOSTIC VALUE OF THE 12-ITEM PSORIATIC ARTHRITIS IMPACT OF DISEASE (PSAID-12) QUESTIONNAIRE FOR EVALUATION OF PSORIATIC ARTHRITIS ACTIVITY(PSA) BY DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS (DAPSA) IN ROUTINE CARE: DATA OF THE RUSSIAN PSORIATIC ARTHRITIS REGISTRY(RU-PSART)

[1]Anastasia Koltakova*, Elena Loginova[1], Elena Gubar[1], Yulia Korsakova[1], Tatiana Korotaeva[1], Maria Sedunova[2], Igor Pristavsky[2], Irina Umnova[3], Irina Bondareva[4], Snezana Kudishina[5], Evgeny Nasonov[2]. [1]*Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*; [2]*St. Petersburg Clinical Rheumatology Hospital No.25, St. Petersburg, Russian Federation*; [3]*Omsk Regional Hospital, Omsk, Russian Federation*; [4]*Kemerovo Regional Hospital, Kemerovo, Russian Federation*; [5]*Vladivostok Clinical Hospital No.2, Vladivostok, Russian Federation*

Background: The PsAID-12 is an instrument for assessment the impact of PsA on patients` lives by examine both physical and psychological components of health. DAPSA is a valid and discriminative tool for evaluation of the PsA activity. There is limited data about the PsAID-12 correlations with PsA activity by DAPSA in clinical care [1].

The Russian Psoriatic Arthritis Registry (RU-PsART) collected data from 25 rheumatology clinics in the Russian Federation regions.

Objectives: to investigate the predictive value of the PsAID-12 for evaluate PsA activity by DAPSA in real-world settings.

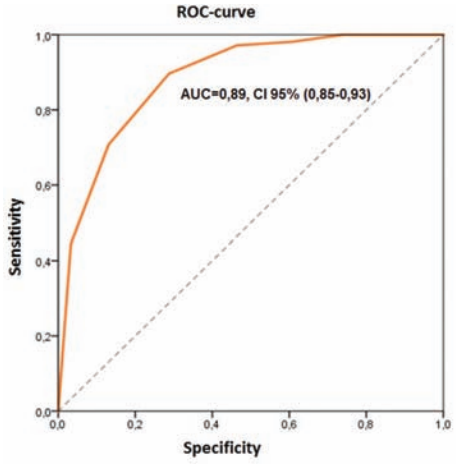
Methods: 138 (male/female–79/59) patients (pts), median age 40 (Min-Max/23-71), with PsA, according to CASPAR criteria, were included in

the RU-PsART after signing consent participation forms. Every 6 months (259 visits total) all pts underwent evaluation of PsA activity: The Tender Joint count (TJC68), Swollen Joint Count (SJC66), Leeds Enthesitis Index (LEI), physician´s global disease activity (PhGA) VAS, CRP (mg/l), ESR (mm/h), by PROs - patient pain global assessment VAS, Patient global disease activity (PGA) VAS and the PsAID-12. PsA activity was calculated by DAPSA. All pts were divided into 2 groups based on disease activity state by DAPSA: the first one with results ≤14 that interpreted as Remission and Low Disease Activity (REM and LDA) and second one with results >14 that interpreted as Moderate and High Disease Activity (MoDA and HDA). Pearson correlation coefficient and ROC-curve analysis were performed. All $p<0.05$ were considered to indicate statistical significance.

Results: The Significant positive correlations between the PsAID-12 and all parameters of PsA activity, PROs were found (table 1). The Significant positive correlations for DAPSA (r=0,71) were found. The high prognostic value of the PsAID-12 for PsA activity by DAPSA showed by ROC-curve analysis (AUC=0,89, CI 95% (0,85-0,93)). The threshold for MoDA and HDA (DAPSA >14) by PsAID was 1.

Parameters	r
Patient global disease activity VAS	0,81
patient pain global assessment VAS	0,78
PhGA	0,74
DAPSA	0,71
HAQ	0,70
DAS 28	0,67
SJC66	0,59
TJC78	0,57
LEI	0,41
CRP (mg/l)	0,39
ESR (mm/h)	0,31

Conclusion: The PsAID-12 has a significant prognostic value for PsA activity by DAPSA. The questionnaire doesn`t include any physician`s or laboratory`s data, so it could be useful as a simple instrument for pts` self-control and prognosis disease activity in daily clinical practice.



REFERENCES

[1] Di Carlo M, Becciolini A, Lato V. et al. The 12-item Psoriatic Arthritis Impact of Disease Questionnaire: Construct Validity, Reliability, and Interpretability in a Clinical Setting. J Rheumatol. 2017;44(3):279-285. doi: 10.3899/jrheum.160924

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AB0758

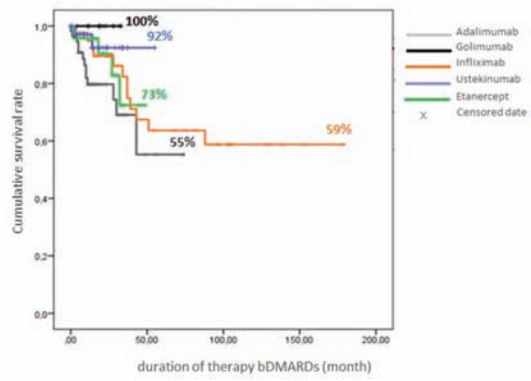
PERSISTENCE AND DRUG SURVIVAL RATES OF THE FIRST-LINE BIOLOGICAL (B) DMARDS IN PATIENTS (PTS) WITH PSORIATIC ARTHRITIS (PSA) FROM THE RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PSART)

[1]Tatiana Korotaeva*, Elena Loginova[1], Anastasia Koltakova[1], Elena Gubar[1], Yulia Korsakova[1], Maria Sedunova[2], Igor Pristavsky[2], Irina Umnova[3], Irina Bondareva[4], Snezana Kudishina[5], Evgeny Nasonov[1]. *[1]Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*; *[2]St. Petersburg Clinical Rheumatology Hospital No.25, St. Petersburg, Russian Federation*; *[3]Omsk Regional Hospital, Omsk, Russian Federation*; *[4]Kemerovo Regional Hospital, Kemerovo, Russian Federation*; *[5]Vladivostok Clinical Hospital No.2, Vladivostok, Russian Federation*

Background: Persistence with bDMARDs has only been studied recently in the last few years. But this information is very relevant for choice of bDMARDs treatment in real-life practice. RU-PsART collected data from 25 rheumatology clinics in the Russian Federation.

Objectives: to investigate drug survival and persistence rates, reasons for discontinuation of first-line bDMARDs in PsA pts in clinical practice.

Methods: 170 (M/F–87/83) PsA pts according to CASPAR criteria, median (Me) age 43 (Min 19 – Max 74) years (yrs.) who were treated with first-line bDMARDs were included in the present analysis. All information concerning the data for starting/withdrawing bDMARDs and reasons for discontinuation were taken at the time of being included to the RU-PsART registry. Pts took the following bDMARDs: Adalimumab (ADA) (57pts), Infliximab (INF) (40pts), Ustekinumab (UST) (36pts), Etanercept (ETN) (23pts), Golimumab (GOL) (14pts). Drug survival rate was evaluated with Kaplan-Meier cumulative analysis, Me [Min-Max],%, Breslow, Tarone-Ware, Log Rank tests were performed. All $p\leq0.05$, were considered to indicate statistical significance.



Results: 71 out of 170 pts (41.8%) were treated with mono-bDMARDs and 99 out of 170 pts (58.2%) were treated with a combination with different sDMARDs. Among them ADA/INF/UST/ETN/GOL were used in combination with MTX in 66.7%/72.5%/33.3%/65.2%/35.7% of pts accordingly Average (Me) duration of bDMARDs therapy was 13.5[0-74]/39[2-179]/15[0-55]/26[2-49]/19[4-33] months for ADA/INF/UST/ETN/GOL accordingly. 31 out of 170 pts (18.2%) stopped bDMARDs. INF/ADA/ETN/UST/GOL were stopped in 30%/22%/17%/5%/0% of cases accordingly. Among them 4 pts (2.35%) stopped due to inefficacy, 13 pts (7.6%) - due to loss of efficacy, 8 pts (4.7%) - due to adverse events, 6 pts (3.5%) - due to other reasons. No significant differences in drug survival rates were seen between all bDMARDs within two years of therapy. During long-term observations GOL had better persistence among iTNF agents. UST has shown significantly higher cumulative survival and persistence rates compared to ADA ($p<0.05$, Log Rank tests). No significant differences were found between UST and other iTNF biologics (Fig.1). **Fig.1.** Cumulative survival rates for all bDMARDs.

Conclusion: In our real practice PsA pts cohort bDMARDs with different mechanisms of action were well tolerated and effective. During long-term observational periods UST has shown better cumulative survival rates compared to ADA.

Disclosure of Interests: Tatiana Korotaeva Speakers bureau: Novartis, Celgene Corporation, AbbVie Inc, Biocad, Janssen, Pfizer, UCB, Lilly, Elena Loginova Speakers bureau: Novartis, Celgene Corporation, Biocad, Janssen, AbbVie Inc, Anastasia Koltakova: None declared, ELENA GUBAR: None declared, Yulia Korsakova Speakers bureau: Celgene Corporation, Janssen, Maria Sedunova: None declared, Igor Pristavsky: None declared, Irina Umnova: None declared, Irina Bondareva: None declared, Snezana Kudishina: None declared, Evgeny Nasonov Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc.
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AB0759 **BIOLOGICS IMPROVES ARTERIAL STIFFNESS WITH CS DMARDS-RESISTANT ACTIVE PSORIATIC ARTHRITIS. A COHORT STUDY**

Kensuke Kume[1,2], Kanzo Amano[3], Toshikatsu Kanazawa[3], Kazuhiko Hatta[3], Naohiko Matsumoto[2]. *[1]Hiroshima Clinic, rheumatology, Hiroshima, Japan; [2]Hiroshima Clinic, medical research, Hiroshima, Japan; [3]Hiroshima Clinic, rheumatology, Hiroshima, Japan*

Background: Patients with psoriatic arthritis (PsA) have an increased cardiovascular (CV) risk. We should have strategies for primary cardiovascular prevention in PSA[1)]. But there is no evidence of CV risk management and arterial stiffness about biologics in patients with PsA
Objectives: To examine the effect of biologics plus conventional synthetic (cs) DMARDs on arterial stiffness in cs DMARDs resistant PsA patients in a cohort study design.
Methods: 38 PSA and patients with moderate to severe active disease despite cs DMARDs treatment (disease activity score: DAPSA[2)] score>14) were received Biologics plus cs DMARDs. All patients have no previous history of CV. Arterial stiffness was assessed with cardio-ankle vascular index (CAVI, modified pulse wave velocity(PWV)) and augmentation index corrected for a heart rate of 75 beats per minute (AIx@75) at baseline and 24 weeks follow-up. Clinical data were collected at regular visits. CAVI is very similar to pulse wave velocity (PWV), and CAVI measures arterial wall stiffness independent of blood pressure and it is superior to brachial ankle PWV as an index of arterial stiffness[2].
Results: 35 PsA patients(18 patients adalimumab,13 patients infliximab, and 4 patients ustekinumab, respectively) completed this study, Treatment with biologics(10.88 ± 1.86 and 9.46± 1.14%; p = 0.006), attenuated the CAVI significantly from baseline to 24 weeks follow up. Treatment with biologics (36.4 ± 8.6, 32.1 ± 3.8%; p = 0.008) attenuated the Aix@75 significantly from baseline to 24 weeks follow up. DAPSA score improved significantly from baseline to 24 weeks(17.45±6.33, 5.44±3.43: p=0.01). There are no significant differences among biologics about CAVI and Aix@75. Surprisingly, improvement of CAVI and AIx@75 were not correlated disease activity at 24 weeks of biologics treatment (CAVI: p=0.91, AIx@75: p=0.88). Biologics improves arterial stiffness independently of its effects on disease activity, since even in high disease activity (4 cases; DAPSA score>28) is halted.
Conclusion: These findings suggest that combination therapy, biologics with cs DMARDs not only reduced PsA disease activity but also limited vascular damage in patients with cs DMARDS resistant active PsA

REFERENCES

[1] Søren Lund Kristensen, et al. Psoriasis, psoriatic arthritis and cardiovascular risk: are we closer to a clinical recommendation? Ann Rheum Dis. 2015; 74: 321-2.
[2] Schoels MM, et al. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. Ann Rheum Dis, 2016; 75: 811-8.

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Disclosure of Interests: None declared
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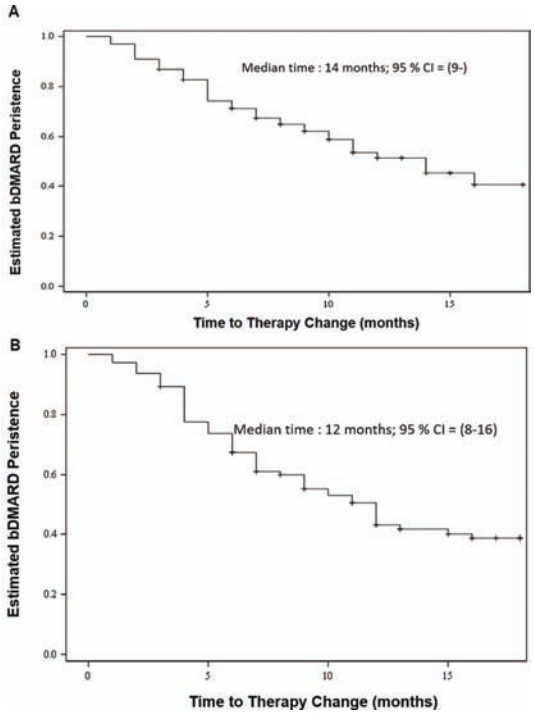
AB0760 **DRUG SURVIVAL AND EFFICACY OF USTEKINUMAB AND SECUKINUMAB IN PSORIATIC ARTHRITIS: A REAL-WORLD MULTICENTRIC COHORT OF 186 PATIENTS**

[1]Jean-Guillaume Letarouilly*, Jeremie Sellam[2], Pascal Richette[3], Philippe Dieudé[4], Pascal Claudepierre[5], Corinne Miceli Richard[6], Eric Houvenagel[7], Chi Duc Nguyen[8], Marie-Hélène Guyot[9], Nicolas Segaud[10], Laurent Marguerie[11], Xavier Deprez[12], Jean-Hugues Salmon[13], Guy Baudens[14], Maeva Kyheng[15], Julien Paccou[1], Elisabeth Gervais[16], René-Marc Flipo[1]. *[1]Lille University Hospital, Rheumatology, Lille, France; [2]Saint-Antoine University Hospital, Rheumatology, Paris, France; [3]Lariboisière University Hospital, Rheumatology, Paris, France; [4]Bichat University Hospital, Rheumatology, Paris, France; [5]Henri Mondor University Hospital, Rheumatology, Créteil, France; [6]Cochin University Hospital, Rheumatology, Paris, France; [7]Saint-Philibert Hospital, Rheumatology, Lomme, France; [8]Béthune Hospital, Rheumatology, Béthune, France; [9]Roubaix Hospital, Internal medicine, Roubaix, France; [10]Armentières Hospital, Internal Medicine, Armentières, France; [11]Calot Institute, Rheumatology, Berck-sur-mer, France; [12]Valenciennes Hospital, Rheumatology, Valenciennes, France; [13]Reims University Hospital, Rheumatology, Reims, France; [14]Rheumatology, Private Practice, Valenciennes, France; [15]Lille University Hospital, Methodology-Biostatistics and Date Managment Department, Lille, France; [16]Poitiers University Hospital, Rheumatology, Poitiers, France*

Background: Ustekinumab (UST) and secukinumab (SEK) are new Biologic Disease-modifying AntiRheumatic Drugs (bDMARDs) available in psoriatic arthritis (PsA), targeting respectively IL12-23 and IL 17. Real-world data are missing for these drugs, despite the wide use. There is only one previous published study including 160 patients (1) receiving UST, but not SEK.
Objectives: To evaluate the characteristics of the patients with PsA treated by UST or SEK and to assess real life drug survival and efficacy of UST and SEK in PsA.
Methods: This is a national, retrospective, multicentric study from patients suffering from PsA (CASPAR criteria) from July 2011 to April 2018. Drug survival was defined as the time from initiation to discontinuation (stop/switch) of bDMARDs. Kaplan-Meier survival curves and Cox-regression analyses [hazard ratios (HR) and 95% confidence intervals (CIs)] were used adjusting for patient demographics, disease characteristics, co-therapy with methotrexate, and line of treatment with ustekinumab. For peripheral involvement, treatment was considered to be effective for patients with a combined favorable expert opinion and/or > 30% clinical improvement of swollen and tender joint counts. For axial involvement, efficacy criteria were: improvement of BASDAI by at least 2 points on a scale from 0 to 10 or 50% improvement and/or expert opinion.
Results: 186 patients were included with a mean follow-up ≥ 6 months: 111 patients under UST and 75 under SEK. The mean age was 51.5 (12.9) years old, 55% of patients were women and the body mass index was 27.3 (5.8) kg/m². The disease duration was 10.8 (8.1) years. Patients were bDMARDs-naïve in 15%. The median drug survivals for UST and SEK were respectively 12 and 14 months (Fig1). A propensity score cannot be used to compare the two bDMARDs, since the number of patients was too small. Smoking was associated with an unfavourable drug survival for SEK (HR= 0.22, 95%CI 0.91), whereas CRP levels were associated with a favorable one for UST (HR=1.009, 95%CI 1.003–1.016). Nine patients under SEK and 2 under UST stopped their treatments due to side effects.
Conclusion: This is the first real-world study for drug survival on PsA for SEK and one with the largest number of patients for UST. Drug survival of UST and SEK seems similar to TNF inhibitors' (2).

REFERENCES

[1] Iannone F, et al. Drug survival and effectiveness of ustekinumab in patients with psoriatic arthritis. Real-life data from the biologic Apulian registry (BIOPURE). Clin Rheumatol. 2018;37:667–75.
[2] Walsh JA, et al. Care Spec Pharm. 2018;24:623-631



Abstract AB0760 Figure 1. Drug survival of secukinumab (A) and ustekinumab (B) in psoriatic arthritis

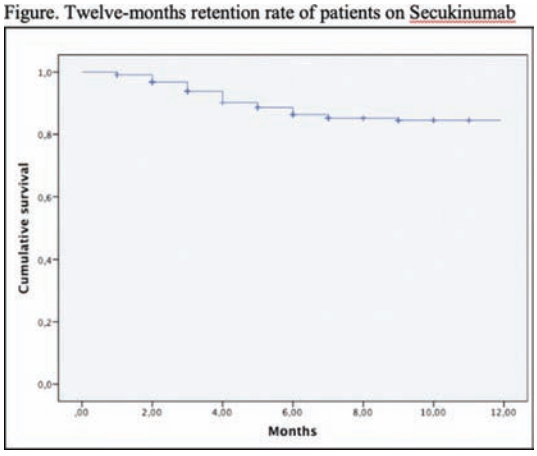
Disclosure of Interests: Jean-Guillaume Letarouilly: None declared, Jeremie Sellam: None declared, Pascal Richette Consultant for: Grunenthal, Horizon, Speakers bureau: AstraZeneca, Grunenthal, Philippe Dieudé: None declared, Pascal Claudepierre Consultant for: Honoraria from Novartis as steering committe of this survey, Corinne Miceli Richard Grant/ research support from: MSD, Pfizer, AbbVie, Biogen, UCB, Novartis, Consultant for: Abbvie, Novartis, BMS, Eric Houvenagel Speakers bureau: Lilly, Novartis, Janssen, Chi Duc Nguyen: None declared, Marie-Hélène Guyot: None declared, Nicolas Segaud: None declared, Laurent Marguerie: None declared, Xavier Deprez Speakers bureau: Novartis Janssen, Jean-Hugues Salmon Speakers bureau: Janssen Novartis, Guy Baudens Grant/research support from: Financial Grant from NordicPharma, Consultant for: Roche SAS, Maeva Kyheng: None declared, Julien Paccou Speakers bureau: Novartis Janssen, Elisabeth Gervais Grant/research support from: Roche, Pfizer, Consultant for: Bristol-Myers Squibb, UCB, René-Marc Flipo Consultant for: Honoraria from Novartis as steering committe of this survey
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AB0761 SECUKINUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS IN REAL LIFE: AN ITALIAN EXPERIENCE

[1]Federica Martinis*, Cristian Caimmi[1], Rosario Foti[2], Elisa Visalli[2], Giorgio Amato[2], Roberta Ramonda[3], Augusta Ortolan[3], Mariagrazia Lorenzin[3], Angelo Semeraro[4], Leonardo Santo[5], Emanuela Praino[5], Maria Sole Chimenti[6], Roberto Perricone[6], Favia Sunzini[6], Raffaele Scarpa[7], Francesco Caso[7], Luisa Costa[7], Elena Fracassi[1], Maurizio Rossini[1], Antonio Carletto[1]. *[1]Rheumatology Unit, University of Verona, Verona, Italy*; *[2]Rheumatology Unit, A.O.U. Policlinico Vittorio Emanuele, Catania, Italy*; *[3]Rheumatology Unit Department of Medicine, DIMED, University of Padova, Padova, Italy*; *[4]Rheumatology Unit, ASL Taranto, Taranto, Italy*; *[5]Rheumatology Unit, ASL BT Andria – DSS4 Barletta, Italy, Barletta-Andria-Trani, Italy*; *[6]Rheumatology, allergology and clinical immunology, University of Rome Tor Vergata, Roma, Italy*; *[7]Rheumatology Unit, Department of Clinical Medicine and Surgery, University Federico II, Napoli, Italy*

Background: Secukinumab is a novel treatment for psoriatic arthritis (PsA) but data from real life are still missing.
Objectives: The aim of this study is to evaluate a wide cohort of PsA patients on secukinumab followed in 7 Italian rheumatologic centers.
Methods: Two-hundred and seventy-nine patients affected by PsA and on secukinumab were enrolled. Data on disease characteristics, previous and ongoing treatments, comorbidities and duration of follow-up were collected. In particular DAPSA and ASDAS were used to assess articular and axial disease activity.
Results: Mean age of our cohort was 53±11 years and BMI 26.4±5.1 kg \m^2 with the majority of patients being female (63.8%). Mean disease duration was 9.7±7.5 years and mean follow-up was 10.9±6.8 years. For 100 patients (35.8%) secukinumab was their first line biologic treatment and 41 (50.5%) were in monotherapy. DAPSA was 25.9±10.5 at baseline, 15.9±9.7 at M3, 12.9±8.4 at M6, 9.8±7.1 at M12 with a significant downward decrease at every visit as compared to baseline (p<0.001 for each comparison to baseline). ASDAS at baseline was 3.27±1.15, 2.32±0.99 at M3, 2.04±1.12 at M6, 1.96±0.88 at M12 with a significant downward decrease at M3 and M6 (p<0.001) and a downward trend for M12 (p=0.064), probably because of the small number of patients with axial involvement at M12 (15). After 12 months of treatment 70.6% with axial involvement and 76.6% with articular manifestations had an inactive disease\low disease activity, accordingly to ASDAS and DAPSA respectively. Forty patients (14.3%) stopped the treatment during the follow up mainly because of primary or secondary loss of efficacy (18 and 10, respectively). Only 9 patients suspended the treatment because of adverse events, of which 5 because of reactions at site of injection.
The retention rate at 12 months was very good in the whole population (figure), and in particular in patients with entesitis at the baseline (10.5 vs, 11.2, p=0.038). No differences in survival were found when dividing patients accordingly to BMI, although overweight or obese patients showed a trend for a better retention rate (10.6 vs 10.9, p=0.089). Interestingly no differences were found between naïve and non-naïve patients (p=0.895) and between those in monotherapy or in combination therapy (p=0.925).
Conclusion: This is one of the first real life studies on secukinumab and shows a very good efficacy and safety of this treatment in PsA patients, also for the articular manifestations, as shown by a significant decrease of DAPSA over a 12-months follow up.

Figure. Twelve-months retention rate of patients on Secukinumab



Disclosure of Interests: Federica Martinis: None declared, Cristian Caimmi: None declared, Rosario Foti: None declared, Elisa Visalli: None declared, Giorgio Amato: None declared, Roberta Ramonda: None declared, Augusta Ortolan: None declared, Mariagrazia Lorenzin: None declared, Angelo Semeraro: None declared, Leonardo Santo: None declared, Emanuela Praino: None declared, Maria Sole Chimenti: None declared, Roberto Perricone: None declared, Favia Sunzini: None declared, Raffaele Scarpa: None declared, Francesco Caso: None declared, Luisa Costa: None declared, Elena Fracassi Speakers bureau: Novartis, Maurizio Rossini: None declared, Antonio Carletto Speakers bureau: Roche, Novartis, MSD, Abbvie, Bristol, Jannsen, Celgene, Pfizer
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AB0762 TREATMENT WITH TOFACITINIB IN REFRACTORY PSORIATIC ARTHRITIS. MULTICENTER STUDY OF CLINICAL PRACTICE

[1]José Luis Martín-Varillas*, Eva Galindez[2], Esteban Rubio Romero[3], Agusti Sellas-Fernández[4], Roberto Daniel Gonzalez Benitez[5],Beatriz Joven-Ibáñez[6], José Campos Esteban[7], Olga Rusinovich[7], Vanesa Calvo-Río[1], Francisco Ortiz-Sanjuán[8], Clara Ventín-Rodríguez[9], Luis Fernández-Dominguez[10],Antia Crespo Golmar[11], Ximena Elizabeth Larco Rojas[11],Manuel Moreno[12], Alejandro Escudero Contreras[13], Emma Beltrán[14], Rafael Melero[15], Maria Jose Moreno[16], Enrique Raya[17], Beatriz Arca[18], María-Luisa Peral[19], Olga Maiz[20], Raul Veroz Gonzalez[21], Alfonso Corrales[1], Natalia Palmou-Fontana[1], Belén Atienza-Mateo[1], J. Loricera[1], Miguel A. González-Gay[1], Ricardo Blanco[1]. *[1]H.U.M. Valdecilla, Santander, Spain*; *[2]H. Basurto, Bilbao, Spain*; *[3]H. Virgen del Rocío., Sevilla, Spain*; *[4]H. Vall d'Hebron, Barcelona, Spain*; *[5]H.G.U. Gregorio Marañón, Madrid, Spain*; *[6]H. 12 de Octubre, Madrid, Spain*; *[7]H. Puerta de Hierro, Madrid, Spain*; *[8]H. La Fe, Valencia, Spain*; *[9]H.U. A Coruña, A Coruña, Spain*; *[10]H. Ourense, Ourense, Spain*; *[11]H. León, León, Spain*; *[12]H. Virgen Arrixaca, Murcia, Spain*; *[13]H. Reina Sofia, Córdoba, Spain*; *[14]H. del Mar, Barcelona, Spain*; *[15]H. Vigo, Vigo, Spain*; *[16]H. Rafael Méndez, Lorca, Spain*; *[17]H. San Cecilio, Granada, Spain*; *[18]H. San Agustín, Avilés, Spain*; *[19]H.G.U. Alicante, Alicante, Spain*; *[20]H. Donosti, San Sebastián, Spain*; *[21]H. Mérida, Mérida, Spain*

Background: Tofacitinib (TOFA) is the first inhibitor of JAK kinases with approval for the treatment of psoriatic arthritis (PsA) in Europe (July 2018)[1]. TOFA has shown efficacy in refractory patients to anti-TNF[2].
Objectives: A) to assess efficacy and safety of TOFA in the first cases in Spain in clinical practice. **B)** to compare the profile of clinical practice patients with clinical trial.
Methods: Study of 41 patients of clinical practice with PsA treated with TOFA in Spain. The diagnosis of PsA was made using CASPAR criteria. Patients who received at least one dose of TOFA were included. Results are expressed as percentage, mean±SD or median [IRQ].
Results: 41 patients (23♀/18♂), mean age of 50.2±10.7 years (**table 1**). Pattern joint involvement was as follows: peripheral (n=25), axial (1) and mixed (15). During the PsA evolution, in addition to arthritis, patients also presented enthesitis (60.9%), nail involvement (39%) and dactylitis (31.7%).

Table 1.

	CLINICAL TRIAL *Gladman D, et al.* (N=131)	CLINICAL PRACTICE (N=41)
Baseline demographic parameters		
Age, years (mean±SD)	49.5±12.3	50.2±10.7
Sex, n (%)	67M/64F (51/49)	18M/23F (46.6/53.4)
Disease Characteristics		
Duration of psoriatic arthritis, year (mean±SD)	9.6±7.6	12.6±9.1
HAQ-DI	1.3±0.7	1.9±0.4 *(n=11)*
Swollen joint count, mean±SD	12.1±10.6	5.7±5.3
Painful joint count, mean±SD	20.5±13.0	8.7±6.1
Elevated CRP, n (%)	85 (65)	33 (80.5)
PASI score, median [IQR]	7.6 [0.6–32.2]	6 [0-15]
Day 1 oral glucocorticoid use, n (%)	37 (28)	25 (60.9)
Concomitant synthetic DMARD, n (%)		
- Methotrexate	98 (75)	25 (60.9)
- Leflunomide	12 (9)	8 (19.5)
- Sulfasalazine	21 (16)	0 (0)
- Others	2 (2)	0 (0)
N. of previous Anti-TNF inhibitors, mean±SD	1.7±1.0	2.5±1.4
N. of previous other biological no anti-TNF, n (%)	11 (8)	52 (126.8)
Adverse event, n (%)	72 (55)	10 (24.4)
Discontinuation due to adverse event, n (%)	2 (2)	1 (2.4)

Table 2.

	Baseline (N=41)	1st month (N=41)	6th month (N=13)
Prednisone, n (%)	25 (60.9%)	8 (43.9%)	6 (46%)
Dose (mean±SD)	9.4±6.1	7.6±4.7	5.6±2.9
Methotrexate, n (%)	9 (21.9%)	6 (14.6%)	3 (23%)
Dose (mean±SE)	18.8±5.8	19.5±3.3	21.6±2.8
N. Patients: Skin involvement, n (%)	22 (53.6%)	8 (19.5%)	2 (15.4%)
N. Patients: Nail involvement, n (%)	12 (29.2%)	7 (17.1%)	6 (46.2%)
N. Patients: arthritis, n (%)	38 (92.6%)	8 (19.5%)	2 (15.4%)
- Swollen joint count, median [IQR]	4 [2-7]	2 [1-4.3]	0 [0-1.5]
- Painful joint count, median [IQR]	7 [4.3-11.5]	2 [1-5]	1 [0-2]
N. Patients: enthesitis, n (%)	11 (26.8)	8 (19.5)	1 (7.7%)
N. Patients: dactylitis, n (%)	7 (17.1)	4 (9.7)	ND
CRP mg/dl, median [IQR]	2.36 [0.95-7.5]	1.7 [0.5-4.5]	0.98 [0.4-5]
DAS28, median [IQR]	5.1 [4.7-5.7]	3.8 [3.2-4.6]	2.9 [2.4-3.3]
DAPSA, median [IQR]	28.3 [23.2-32.3]	14 [7.2-31.1]	7.6 [4.8-13.2]
PASI, median [IQR]	6 [0-15]	5 [0.7-9.5]	2 [0-8]

Prior TOFA, most patients had received oral prednisone or equivalent (max. 17.9±13.6 mg/d), synthetic immunosuppressants (mean 1.9±0.7) and biological therapy (TB) (3.4±1.9). TB were as follows: etanercept (29), adalimumab (29), Infliximab (16), golimumab (13), certolizumab (14), secukinumab (30), ustekinumab (22). Apremilast was used in 10.

After a mean follow-up of 12.6±9.1 years after the PsA diagnosis, TOFA was started (5 mg/12 h). 60.9% associated prednisone (9.4±6.1 mg/d). In 17 (41.5%) TOFA was started in combined therapy: methotrexate (9) and leflunomide (8); in the remaining 24, monotherapy was prescribed. In addition to active arthritis patients presented skin involvement (53.6%), enthesitis (26.8%), nail involvement (29.2%) and dactylitis (17.1%).

Patients of clinical practice compared with clinical trial have a longer duration of PsA, functional disability (HAQ) and received a higher proportion of corticosteroids and TB (anti-TNF and non-anti-TNF) (**table 1**).

After a median follow-up of 4 [3-10.5] months, patients showed prompt improvement in the main variables, both in activity indexes (PASI, DAS28, DAPSA) and laboratory test (**table 2**). Minor side effects were reported in 10 patients (gastrointestinal symptoms), and TOFA was discontinued in 1 due to persistent symptoms.

Conclusion: In this preliminary study, first patients of clinical practice in Spain with TOFA in PsA had a longer evolution and received a greater number of TB than those of clinical trial. As in the TOFA clinical trial, it seems effective, rapid and relatively safe in daily clinical practice for refractory PsA.

REFERENCES

[1] https://www.ema.europa.eu/documents/overview/xeljanz-epar-medicine-overview_es.pdf

[2] Gladman D. N Engl J Med 2017; 377: 1525-36.

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AB0763

SAFETY OF ABATACEPT TREATMENT OVER 2 YEARS IN A PHASE III ACTIVE PSORIATIC ARTHRITIS RANDOMIZED TRIAL (ASTRAEA)

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Background: In the placebo (PBO)-controlled Phase III ASTRAEA study (ClinicalTrials.gov, NCT01860976) in psoriatic arthritis (PsA), abatacept (ABA) 125 mg SC weekly significantly increased the ACR20 response rate at Week 24 versus PBO (39.4% vs 22.3%, respectively; p<0.001; primary endpoint).[1] Numerical benefits in physical function, enthesitis and dactylitis and a modest impact on psoriasis lesions were also seen at Week 24. Efficacy was maintained or improved up to Week 52.[1]

Objectives: To assess ABA safety up to 2 years in patients (pts) enrolled in ASTRAEA.

Methods: Pts with active PsA were randomised 1:1 to ABA or PBO for 24 weeks followed by 28 weeks' open-label (OL) ABA (total time on study: 52 weeks); pts without ≥20% improvement in joint counts at Week 16 (early escape) were switched to OL ABA (total time on study: 44 weeks).[1] Pts could subsequently receive OL ABA in a 52-week long-term extension (LTE; Year 2) for the collection of safety data. The proportions of pts in the cumulative ABA population (all pts who received ≥1 dose of ABA at any time in the study) with AEs (all AEs, serious AEs [SAEs], deaths, AEs leading to discontinuation), laboratory marked abnormalities and anti-ABA antibodies over the cumulative ABA period (date of first treatment dose to end of LTE) were recorded in 1-year and 6-month intervals.

Table 1. Summary of safety up to Year 1 and Year 2 (cumulative ABA period; cumulative ABA population)

	From baseline up to Year 1 (N=398)		From baseline up to Year 2 (N=398)	
	n (%)	Incidence rate per 100 patient-years	n (%)	Incidence rate per 100 patient-years
Deaths	0	0	0	0
SAEs	34 (8.5)	12.1	50 (12.6)	8.9
Treatment-related* SAEs	5 (1.3)	NA	10 (2.5)	NA
Discontinued due to SAEs	8 (2.0)	NA	8 (2.0)	NA
AEs	273 (68.6)	184.9	322 (80.9)	151.2
Treatment-related AEs	81 (20.4)	NA	104 (26.1)	NA
Discontinued due to AEs	13 (3.3)	NA	18 (4.5)	NA
AEs reported in ≥5% of patients				
Nasopharyngitis	25 (6.3)	9.0	44 (11.1)	7.7
Upper respiratory tract infection	28 (7.0)	10.2	40 (10.1)	7.0
Bronchitis	26 (6.5)	9.4	38 (9.5)	6.6
Urinary tract infection	18 (4.5)	6.4	29 (7.3)	5.0
Influenza	–	–	29 (7.3)	4.9
Back pain	–	–	23 (5.8)	3.9
Diarrhoea	–	–	22 (5.5)	3.7
Sinusitis	–	–	21 (5.3)	3.5
AEs of special interest				
Infections†	162 (40.7)	75.9	226 (56.8)	62.7
Malignancies‡	4 (1.0)	1.4	4 (1.0)	0.7
Autoimmune events§	1 (0.3)	0.4	4 (1.0)	0.7
Local injection-site reactions¶	5 (1.3)	1.8	6 (1.5)	1.0
AEs within 24 hours¶	94 (23.6)	38.7	141 (35.4)	34.0

*Causal relationship between study drug and an AE was determined by an investigator physician

†SAEs of infection reported during the LTE included osteomyelitis, intervertebral discitis and cellulitis. Three pts discontinued during the LTE due to the following infections: hepatitis A, Epstein-Barr virus infection and intervertebral discitis

‡Bowen's disease, carcinoma in situ of skin, prostate cancer and transitional cell carcinoma. Only transitional cell carcinoma was treatment related. No malignancies were reported during the LTE

§Uveitis, hyperthyroidism, Sjogren's syndrome and celiac disease. No autoimmune events reported in the LTE were serious or led to discontinuation of ABA therapy

¶No local injection-site reactions led to treatment discontinuation

¶None were suggestive of systemic immune reactions

ABA=abatacept; LTE=long-term extension; NA=not available; pt=patient; SAE=serious AE

Results: Overall, 398 pts were included in the analysis of the cumulative ABA period (213 received ABA from study Day 1; 185 completed initial randomisation to PBO and received ABA thereafter). Of these, 322 pts entered the LTE (initial randomisation: ABA, n=162; PBO, n=160) and continued to receive OL ABA beyond the 28-week OL period. Of 162 and 160 pts initially randomised to ABA and PBO, respectively, 19 (11.7%) and 21 (13.1%) pts discontinued ABA in the LTE. Median (range) number of ABA injections in the cumulative ABA period to end of LTE was 80 (1–133). Safety during the cumulative ABA period over 2 years is shown (Table 1); 6-month interval safety data will be available at time of presentation. In the LTE, there were 3 SAEs of infection (osteomyelitis, intervertebral discitis and cellulitis) and 3 pts discontinued due to infection (hepatitis A, Epstein-Barr virus, intervertebral discitis). No malignancies or deaths were reported, and no autoimmune events were reported as serious or led to ABA discontinuation during the LTE. AEs, SAEs and AEs of special interest occurred with a similar frequency regardless of concomitant MTX or prior TNF inhibitor (TNFi) use. The proportion of pts with anti-ABA antibodies during the cumulative ABA period was higher during the post-treatment period (≥22 days after last dose; 37.1% [91/245]) than in the on-treatment period (first treatment dose date to ≤21 days after last dose; 7.1% [28/392]). No apparent relationship between anti-ABA antibodies and efficacy in the on-treatment period or AEs suggestive of systemic immune reactions was seen.
Conclusion: Abatacept was well tolerated up to 2 years with no new safety signals during the LTE in this Phase III study in PsA. There was no impact of concomitant MTX use or prior TNFi exposure on the safety profile of abatacept. The occurrence of anti-abatacept antibodies had no impact on abatacept efficacy or safety.

REFERENCES

[1] Mease PJ, et al. Ann Rheum Dis 2017;76:1550–8.

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AB0764 USE OF IXEKIZUMAB IN A THIRD LEVEL HOSPITAL

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease mediated by the immune system, which affects the musculoskeletal system and the skin. It is a disease with increased expression of TNF-alpha and IL23/IL17 cytokines, which are therapeutic targets whose neutralization has a great impact on the control of the disease.
Ixekizumab is a monoclonal antibody inhibitor of IL-17 indicated for the treatment of moderate-severe psoriasis and PsA. Ixekizumab is administered subcutaneously every 4 weeks, and according to the latest studies, it is a well-tolerated drug and an effective treatment option with significant improvement in the quality of life of patients with cutaneous psoriasis and PsA.
Objectives: -Describe the clinical characteristics, tolerance, safety and survival of a cohort of patients diagnosed with psoriasis or PsA, who have started treatment with Ixekizumab.
-Correlate skin involvement and joint with the quality of life of the patient through the life questionnaire (DLQI) in patients treated with Ixekizumab.
Methods: An observational, cross-sectional and retrospective study was conducted on a cohort of 29 patients who started treatment with Ixekizumab in our hospital in the last year (2018). The data were obtained through the review of patients' medical records and through telephone contact to carry out quality of life questionnaires (DLQI).
Results: Twenty-nine patients were included, of which 22 were males (79.5%). The mean age of the patients was 47 years. Of the cases included, 22 of the patients presented cutaneous Psoriasis (75.8%), 6 of the patients with PsA (20.7%) and 1 patient presented with Dermatomyositis antiMDA 5 (3.5%). Of the 29 patients included, 24 (82.2%) did not present adverse effects. Of the 5 patients who presented adverse effects, in 100% of the cases they were mild. All patients had received prior therapy with disease modifying drugs (DMARDs), and 31% were naive to biological therapy. A total of 4 patients required concomitant therapy with corticosteroid treatment, 3 of them with PAs and 1 with dermatomyositis anti MDA 5. The average of the DLQI of the patients analyzed was 4 and an average PASI of 1 after the start of the treatment, obtaining an Overall improvement of the skin.
A statistically significant Pearson correlation of 0.895 was found between DLQI and PASI (dependent variable), with a strong degree of association. In which patients with a lower score in the DLQI had a lower PASI.
Regarding the pain produced by the autoinjector, measured according to the EVA scale, it was 2 (mild pain), and none would abandon the treatment for this reason. Of all the patients, 9.1% abandoned the treatment due to inefficiency.
Conclusion: The treatment with Ixekizumab presents some promising results in the treatment of cutaneous psoriasis and PsA.
Treatment with Ixekizumab presents a significant improvement in the quality of life of patients.
Ixekizumab is a well-tolerated drug with good efficacy in the short-medium term. It has also been shown to be a safe drug among the patients included in the study.
However, long-term studies with a larger number of patients are required to evaluate the efficacy and safety of Ixekizumab.
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AB0765 THE IMPACT OF PSORIASIS SEVERITY ON OUTCOMES AMONG PSORIATIC ARTHRITIS PATIENTS RECEIVING ADALIMUMAB

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Background: Psoriatic arthritis (PsA) is a heterogeneous, chronic, immune mediated disease associated with psoriasis (PsO). The American College of Rheumatology (ACR) and National Psoriasis Foundation (NPF) recently released a guideline for treatment of PsA, in which TNF inhibitors are recommended over IL-17 or IL-12/23 inhibitors in pts with active PsA.[1] The ACR/NPF conditionally recommend that IL-17 or IL-12/23 inhibitors may be used instead of TNF inhibitors in pts with severe PsO (defined as a psoriasis activity and severity index [PASI] ≥12 or a body surface area [BSA] of ≥10%).
Objectives: Evaluate the impact of PsO severity on clinical, functional, and structural outcomes among PsA pts treated with adalimumab (ADA) or placebo (PBO).

Table. Clinical, Functional, and Structural Outcomes Through 24 Weeks Among Adalimumab- and Placebo-treated Patients Having Severe[a] or Mild-to-Moderate[b] Psoriasis at Baseline Relative to the Overall Study Population.

	ADA 40 mg eow				PBO eow			
n (%)	Severe Ps (N=17)	Mild-to-Moderate Ps (N=66)	Mild-to-Severe Ps (N=83)	Total study populatio n (N=151)	Severe Ps (N=20)	Mild-to-Moderate Ps (N=60)	Mild-to-Severe Ps (N=80)	Total study populatio n (N=162)
MDA	5 (29)	29 (44)	34 (41)	53 (35)	3 (15)	6 (10)	9 (11)	11 (7)
DAPSA ≤4	4 (24)	19 (29)	23 (28)	33 (22)	1 (5)	1 (2)	2 (3)	4 (2)
DAPSA >4, ≤14	4 (24)	10 (15)	14 (17)	33 (22)	3 (15)	5 (8)	8 (10)	14 (9)
HAQ-DI ≤0.25	6 (35)	29 (44)	35 (42)	70 (46)	4 (20)	12 (20)	16 (20)	33 (20)
ΔHAQ-DI ≥0.22	12 (75)	43 (80)	55 (79)	99 (79)	5 (31)	16 (38)	21 (36)	52 (42)
ΔmTSS ≤0[c]	14 (82)	46 (70)	60 (72)	120 (79)	11 (55)	33 (55)	44 (55)	93 (57)
ΔmTSS ≤0.5[c]	16 (94)	54 (82)	70 (84)	132 (87)	12 (60)	41 (68)	53 (66)	111 (69)
PASI50[d]	14 (82)	42 (64)	56 (68)	N/A	3 (15)	8 (13)	11 (14)	N/A
PASI75[d]	8 (47)	35 (53)	43 (52)	N/A	1 (5)	3 (5)	4 (5)	N/A
PASI90[d]	7 (41)	24 (36)	31 (37)	N/A	1 (5)	2 (3)	3 (4)	N/A

All analyses are non-responder imputation, unless otherwise noted.
[a]Severe psoriasis defined as psoriasis activity and severity index (PASI) ≥12 OR body surface area (BSA) ≥10%; [b]mild-to-moderate psoriasis defined as PASI <12 AND BSA <10%; [c]imputation using ranks of total Sharp score and 75th percentile; [d]PASI responses were only collected for patients with psoriasis involving >3% BSA at baseline; ADA: adalimumab; eow: every other week; PBO: placebo; Ps:psoriasis; MDA:minimal disease activity; DAPSA:disease activity index for psoriatic arthritis; HAQ-DI: health assessment questionnaire disability index; ΔHAQ-DI:change from baseline in HAQ-DI; ΔmTSS:change from baseline in modified total Sharp score.

Methods: Pts with baseline PASI and BSA available from ADEPT, a phase 3, randomized, double-blind, PBO-controlled trial of ADA 40 mg every other week, were included in this post hoc analysis.[2] Pts were sub-grouped based on baseline PsO severity (severe PsO: PASI ≥12 OR BSA ≥10%; mild-to-moderate PsO: PASI <12 AND BSA <10%), relative to overall study population. Clinical outcomes at wk 24 were assessed by attainment of minimal disease activity (MDA), remission and low disease activity (LDA) by disease activity index for psoriatic arthritis (DAPSA), and PASI50/75/90; function and structural progression were assessed by the% of pts experiencing HAQ-DI normative values (≤0.25) and improvement from baseline ≥0.22 (MCID), and the% of pts having change from baseline in mTSS ≤0 and ≤0.5 in the modified total Sharp score (mTSS) respectively. A logistic model with treatment group baseline PASI/BSA and PASI/BSA by treatment interaction was fit for each outcome variable. *P*-values for interaction term and baseline BSA/PASI were calculated. Non-responder imputation was used for missing clinical and functional endpoints. 75th percentiles were imputed for missing radiographic data. Treatment-emergent adverse events (TEAEs) were monitored throughout.

Results: Of the 163 pts enrolled in the study with baseline PASI and BSA, only 23% (n=37; ADA: 17; PBO: 20) were classified as having severe PsO and had similar characteristics to those with mild-to-moderate PsO, except for numerically higher physician's global assessment, dactylitis, and enthesitis scores. Following 24 wks of treatment, 41% of ADA-treated pts achieved MDA and 45% achieved DAPSA LDA or better, a finding consistent irrespective of baseline PsO severity (**Table**). 72% of ADA-treated pts with baseline PsO did not exhibit any structural progression by mTSS (≤0) through 24 wks as compared to 55% receiving PBO. Logistic regression analyses confirmed limited role that PsO severity played across examined outcomes. DAPSA remission was more likely at wk 24 among pts with higher baseline PASI scores, and this effect was less apparent with ADA treatment. TEAEs appeared comparable between ADA and PBO groups; fewer infectious AEs occurred in the ADA severe PsO group vs the mild-to-moderate PsO group.

Conclusion: Prevalence of severe PsO in this population of PsA pts was consistent with previous observations.[3] Treatment with ADA was associated with better PsA outcomes as compared to PBO irrespective of the degree of PsO severity at baseline.

REFERENCES

[1] Singh, et al. *Arthritis Rheumatol*, 2018;71:2-29.
[2] Mease, et al. *Arthritis Rheumatol*, 2005;52:3279-89.
[3] Alinaghi, et.al. *J. Am. Acad. Der,* 2019;80(1):251-265.e219.

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AB0766 EVOLUTION OF BONE MINERAL DENSITYIN PATIENTS WITH PSORIASTIC ARTHROPATHY

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Background: Some studies indicate that psoriatic arthritis (PsA) patients have increased bone loss due to chronic inflammation, but data in the Spanish population is scarce.

Objectives: To study the evolution over time of bone mineral density (BMD) in patients with PsA and to investigate the factors related to these changes.

Methods: We included PsA patients with peripheral joint involvement. They were treated at the Doctor Peset University Hospital and a 3-year follow-up was carried out.

All patients underwent a bone densitometry and history of fracture was collected by conventional radiology at baseline and at 3 years. Phosphocalcic metabolism was also analyzed. We collected demographic and clinical variables [disease duration, DAS28, body mass index (BMI), smoking]. We considered 25OHD as deficient if <20 ng/ml, low bone mass as T or Z scale <-1 SD and osteoporosis as scale T <-2.5 DE or Z <-2 SD. Statistical analysis were performed with SPSS 22.0 program.

Results: We included 91 patients (67,2% women), with a mean age of 56,4 (SD 1,2) years. The mean of disease duration was 104,9 (SD 11,8) months. The BMI mean was 27,6 (SD 0,5) and 36,3% of patients were smokers. 25OHD mean was 27.7 (SD 1.3) ng/ml and 33,3% of patients had a deficient 25OHD. More than half of the patients (53.8%) had low bone mass and 14.3% had osteoporosis, measured by densitometry. Twelve patients had history of fractures [6 distal forearm, 5 vertebral fractures (VF) and 1 of femur]. Thirteen patients received antiresorptive treatment [9 bisphosphonates, 3 denosumab and 1 selective estrogen receptor modulator (SERM)], and 39.6% of patients received 25OHD supplements. We did not observe any significant correlation between the 25OHD values and the activity parameters of the PsA. However, we observed lower levels of 25OHD in obese patients. At 3 years, the BMD remained stable in the majority of patients (68.1%) receiving antiresorptive treatment, and it worsened in 2 patients despite treatment with bisphosphonates. We registered new fractures in 7 patients (4 VF, 1 femur fracture and two patients had more than one fracture). New fractures were not correlated with age, 25OHD deficiency or with previous osteoporotic treatment. We observed greater progression of BMD in patients exposed to tobacco.

Conclusion: More than half of patients with PsA have a low BMD (53.8%) and 33,3% deficient levels of 25OHD. Our study confirms results found in general population: classic risk factors, such as smoking, are related to BMI progression. It is important to evaluate BMD in these patients and intervene early.

Disclosure of Interests: None declared

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AB0767 MULTI-SYMPTOM IMPACT ON THE EQ-5D INDEX IN BIO-NAÏVE ACTIVE PSORIATIC ARTHRITIS PATIENTS: AN ANALYSIS THROUGH WEEK 24 OF THE GO-VIBRANT STUDY

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by peripheral arthritis, axial inflammation, dactylitis, enthesitis and skin and nail psoriasis. The impact of skin and joint components of the disease on patient health-related quality of life has been described in

previous research (1,2) but the impact of other major clinical manifestations has not been similarly characterized.

Objectives: To quantify the impact of the major clinical manifestations of PsA on patient reported health related quality of life, as estimated by disease state preference (utility) derived from the EQ-5D index in a randomized clinical trial.

Methods: This analysis used data from a multicenter, randomized, double-blind, placebo-controlled trial of intravenous (IV) Golimumab in biologic naïve patients with active psoriatic arthritis (GO-VIBRANT study). Patient baseline characteristics of the GO-VIBRANT study population have been previously described (3). Core outcome measures recommended by OMERACT (Outcome Measures in Rheumatology Clinical Trials) and guideline on utility mapping by ISPOR (International Society for Pharmacoeconomics and Outcome Research) were used to guide initial attribute selection. Utility was derived from patient responses to the EQ-5D index, which assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and was completed at weeks 0, 8, 14, and 24 in the trial (placebo-controlled period). EQ-5D index is used as a measure of overall health and is an outcome commonly used in health economic analyses. Multivariate analysis was performed using a Mixed-Effect Repeated Measures model based on observed data until week 24 in pooled patient population.

Results: Based on univariate analyses and evaluation of collinearity between variables, the following attributes were included in the multivariate models: age, gender, region, PsA disease duration, PASI score, enthesitis, dactylitis, tender joint count (TJC), swollen joint count (SJC), C-reactive protein (CRP mg/L) and Health Assessment Questionnaire-Disability Index (HAQ-DI). In the final model, PASI score (β=-0.00126, p=0.0006), enthesitis (β=-0.01237, p=0.03), TJC (β=-0.00112, p<0.0001), CRP (β=-0.00079, p<0.0001) and HAQ-DI (β=-0.1664, p<0.0001) were all statistically significantly associated with the EQ-5D index. A sensitivity analysis among a subgroup of patients who had spondylitis with peripheral joint arthritis as their primary arthritic presentation of PsA showed that spinal pain (β=0.0101, p<0.0001), as measured by question #2 of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), was also statistically significantly associated with the EQ-5D index in the multivariate model.

Conclusion: Multiple PsA clinical manifestations including psoriasis, enthesitis, TJC, spinal pain, CRP, and physical function were statistically significantly associated with utility among PsA patients as derived from the EQ-5D index. These findings indicate that consideration of multiple clinical manifestations of PsA is warranted when evaluating the impact of PsA on patients.

REFERENCES

[1] Borman P, et al. Clin Rheumatol. 2007;26(3):330–4.
[2] de Vlam K, et al. *Rheumatol Ther.* 2018;5(2):423–36.
[3] Kavanaugh A, et al. *Arthritis Rheumatol.* 2017 Nov;69(11):2151-2161.

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AB0768

BASELINE PAIN SEVERITY AS A PREDICTOR OF PAIN IMPROVEMENT FOLLOWING TREATMENT WITH TOFACITINIB IN PSORIATIC ARTHRITIS

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Background: Pain is a core domain of psoriatic arthritis (PsA).[1] Rapid, sustained pain reduction is a priority for patients (pts) and physicians when choosing treatment. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA.

Objectives: This post hoc analysis aimed to estimate time to clinically meaningful pain improvement with tofacitinib.

Methods: Data were analysed from 2 Phase 3 studies of tofacitinib in pts with active PsA and an inadequate response to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD) (OPAL Broaden; NCT01877668; 12-month study), or to ≥1 tumour necrosis factor inhibitor (OPAL Beyond; NCT01882439; 6-month study). Pts treated with tofacitinib 5 mg twice daily (BID) and placebo (PBO) advanced to tofacitinib 5 mg BID at Month 3 (PBO-tofacitinib), in combination with csDMARDs, were included in this analysis. Current arthritis pain severity was reported by pts using a 100 mm visual analogue scale, where higher scores indicated greater severity of pain. Pain improvement was defined as the first post-baseline improvement of ≥30% (meaningful change), ≥50% (substantial change) or ≥70% relative to baseline.[2] Time-to-event analyses were performed using a Kaplan-Meier (KM) method on pooled data. Descriptive analyses of the rate of improvements by study were performed.

Results: Overall, 354 pts were available for analysis. Rates of pain improvement over time with tofacitinib 5 mg BID were approximately the same in both studies (Figure). By Month 1, ≥40% of pts experienced ≥30% pain improvement, and by Month 2, approximately 55% of pts experienced ≥30% pain improvement (Figure). KM analyses showed that pts receiving tofacitinib 5 mg BID achieved improvements in pain severity of 30–70% significantly faster compared with pts in the PBO-tofacitinib group (Table). The median time to ≥30% pain improvement was 55 days in the tofacitinib 5 mg BID group and 106 days in the PBO-tofacitinib group (pts switched to tofacitinib 5 mg BID at Month 3; p=0.0132). Similar trends between treatment groups were observed across other pain improvement thresholds.

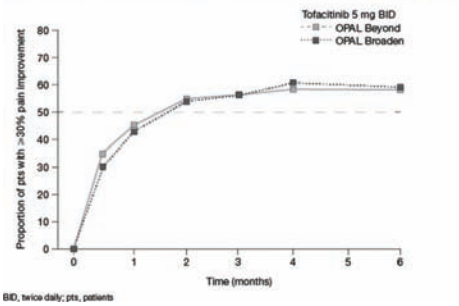
Table. Median time (days) to clinically meaningful pain improvement by improvement threshold in pts with PsA

VAS pain improvement threshold	Median time (days) to pain improvement		Test of equality between groups
	Tofacitinib 5 mg BID	PBO switching to tofacitinib 5 mg BID at Month 3	Log-rank test, p value
≥30%	55	106	0.0132
≥50%	85	169	0.0068
≥70%	184	337	0.0033

Derived using non-parametric KM (nonparametric) models for time to event

BID, twice daily; KM, Kaplan-Meier; PBO, placebo; PsA, psoriatic arthritis; pts, patients; VAS, visual analogue scale

Figure. Proportion of pts receiving tofacitinib 5 mg BID with ≥30% improvement in pain, by study



BID, twice daily; pts, patients

Conclusion: In pts with active PsA, faster, clinically meaningful pain improvements were reported in pts receiving tofacitinib 5 mg BID vs pts receiving PBO who switched to tofacitinib 5 mg BID at Month 3. After switch from PBO to active treatment, pain improvement was observed in line with pts receiving active treatment from Day 0. To achieve pain improvement at greater thresholds, longer duration of active treatment was required.

REFERENCES

[1] Orbai AM, et al. Ann Rheum Dis 2017;76:673-80.
[2] Dworkin RH, et al. J Pain 2008;9:105-21.

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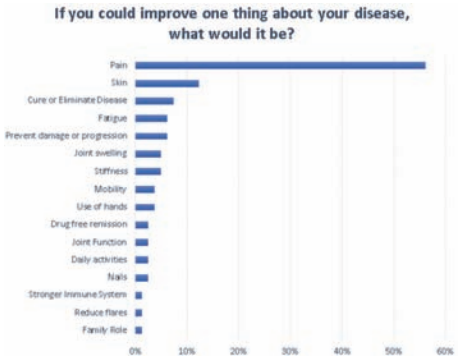
AB0769 PATIENT IDENTIFIED TREATMENT GOALS IN PSORIATIC ARTHRITIS: DECREASING PAIN AND INCREASING ACTIVITY LEVEL ARE HIGH PRIORITIES

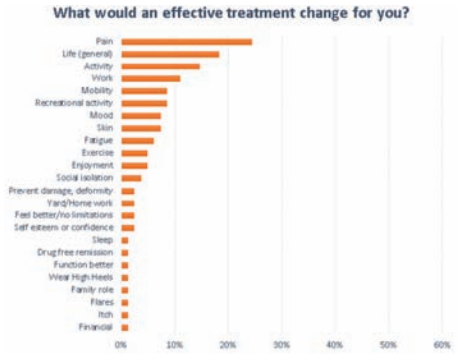
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Background: Treatment goals for physicians are primarily focused on improving musculoskeletal and cutaneous signs and symptoms of psoriatic disease. Studies have reported that perceptions of psoriatic arthritis (PsA) disease control are often divergent between patients and physicians. Moreover, specific patient goals are uncommonly discussed or elicited in routine clinical practice.

Objectives: To examine patient reported treatment goals through direct questioning on what they most want to improve about their disease and how an effective treatment would improve their lives.

Methods: Patients in the Psoriatic Arthritis Research Consortium (PARC) completed standardized assessments between 2017-2018. PARC is a longitudinal observational cohort study conducted at four institutions in the United States: University of Pennsylvania, Cleveland Clinic, New York University, and University of Utah that includes a range of patient and physician disease measures. Answers to two open-ended questions (questions included on figures) were qualitatively categorized into response categories and descriptively reported in this cross-sectional study. While patients were encouraged to provide the one best answer, many listed multiple themes. We also examined differences in responses by gender, self-identified race (Caucasian vs not Caucasian), and whether a change in disease modifying anti-rheumatic drug was recommended (yes/no) on the date the questionnaire was completed.





Results: Among 82 patients with PsA enrolled, mean age was 48.3 (SD 13.2), 38 (46%) were female, and 57 (70%) of patients were changing therapy. The mean swollen (0-66) and tender (0-68) joint counts were 4.3 (SD 6.0) and 8.5 (12.2) respectively, mean psoriasis body surface area was 3.2% (SD 10.0), and mean physician and patient global assessments were 4.6 (SD 2.0) and 4.7 (2.6) respectively. Patient answers to the two questions are shown in the Figures. Decreasing pain was the most commonly cited goal for improvement (56%) with skin improvement the second most commonly reported goal for improvement (12%). Goals for successful therapy were more diverse. Decreasing pain was still most common (24%) but general improvement in life (18%), the ability to be more active (15%), participate in recreational activities (9%), function at work (11%) and exercise (5%) were common responses. There were no significant differences in responses according to race, or therapy change. However, all patients reporting fatigue or enjoyment as important outcomes for improvement were women.

Conclusion: In order to inform goals of care for patients with PsA, both physician and patient treatment goals should be defined to achieve optimal treatment success. In this study, while the majority of patients reported pain and activity as the most important outcomes for improvement, patient goals were heterogeneous. This underscores the importance of eliciting patient treatment goals on a regular basis to best individualize management in PsA.

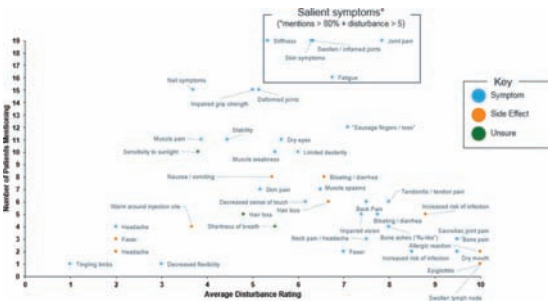
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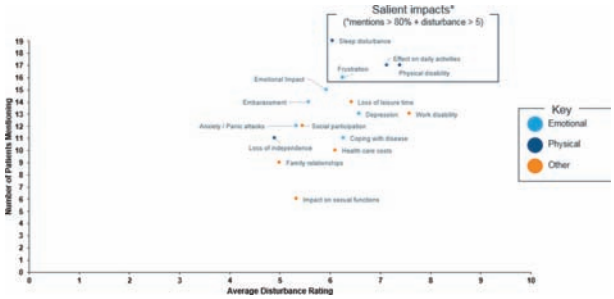
AB0770 SYMPTOMS AND IMPACTS IN PSORIATIC ARTHRITIS: FINDINGS FROM QUALITATIVE PATIENT INTERVIEWS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease resulting in significant symptom burden.[1] Over time and without adequate treatment, PsA can lead to disability and reduced patient quality of life.[2] Fatigue is among the most common symptoms,[1] but is complex and difficult to measure. The most burdensome symptoms that impact PsA patients need to be better understood in order to select patient reported outcomes (PRO) tools that adequately capture these concepts.
Objectives: 1.) Identify the signs and symptoms of PsA experienced by patients, with a focus on fatigue, and how the disease and its treatment (s) impact patients' lives. 2.) Assess the content validity of select PRO instruments and items to measure fatigue.
Methods: Qualitative interviews were conducted among patients with PsA recruited through the FORWARD databank. The most frequently experienced symptoms and impacts of PsA and the degree to which they disturbed patients' lives, were tabulated. Disturbance was evaluated on a scale from 0 (not at all) to 10 (greatly disturbs). Patients reporting fatigue were probed to describe the experience in their own words, and descriptors were recorded. Interviews were conducted and assessed on a rolling basis and recruitment continued until concept saturation was achieved.
Results: Nineteen PsA patients were interviewed for this study. A core set of PsA symptoms were identified by nearly all patients and with moderate to high average disturbance ratings (Figure 1): joint pain, skin symptoms, stiffness, swollen/inflamed joints, and fatigue. The most salient impacts (Figure 2) were sleep disturbance, physical disability, effects on daily activities, and feelings of frustration. Most common descriptors of fatigue included "fatigue," "tiredness," "lack of energy," "mental fatigue," and "exhaustion."
Conclusion: Salient symptoms were consistent with those previously reported, along with a broader range of symptoms and impacts, which included fatigue. In addition to physical disability, others such as sleep disturbance, frustration, and effect of daily activities were common high impact themes that emerged.



***Abstract AB0770 Figure 1.**. Salient Symptoms Reported by Patients in Qualitative Interviews (n=19)*



Abstract AB0770 Figure 2.. Salient Impacts Reported by Patients in Qualitative Interviews (n=19)

REFERENCES

[1] Dures, E., et al. (August 2017). Important treatment outcomes for patients with psoriatic arthritis: a multisite qualitative study. Patient (10). Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/28229377
[2] Orbai, A., et al. (April 2017). International patient and physician consensus on a psoriatic arthritis core outcome set for clinical trials. *Annals of Rheumatic Disorders*, 76(4). Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/27613807

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AB0771 IMPROVEMENT IN MORNING STIFFNESS IN SUBJECTS WITH PSORIATIC ARTHRITIS IS ASSOCIATED WITH IMPROVEMENTS IN PAIN, PHYSICAL FUNCTION AND PATIENT GLOBAL RESPONSE TO TREATMENT

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Background: Stiffness is an important component of inflammatory arthritis and plays a role in psoriatic arthritis (PsA) flare. Patients with inflammatory arthritis report difficulty with activities, "slowing down" due to stiffness and reduced quality of life. Stiffness is hard to quantify because it cannot be measured directly.
Objectives: We examined morning stiffness in PsA patients treated with apremilast (APR) for 16 weeks in the ACTIVE study and explored the relationship between improvements in morning stiffness and pain, physical function and Patient's Global Assessment of Disease Activity (PtGA).
Methods: Subjects who met CASPAR criteria for PsA, were biologic-naïve and had prior exposure to ≤1 conventional disease-modifying anti-rheumatic drug (DMARD) were randomized (1:1) to APR 30 mg twice daily or placebo (PBO) for 24 weeks. Subjects initially randomized to PBO

were switched to APR at Week 16 (early escape) or Week 24. Duration of morning stiffness and severity, assessed by subjects' reported categories of stiffness (none, mild, moderate, moderately severe, severe), was reported. In the post hoc analysis, changes in morning stiffness severity and effect on pain, physical function and PtGA from baseline to Week 16 were compared between treatment arms. An analysis of covariance model adjusting the baseline value was used in the analysis, where missing values were imputed using the last-observation-carried-forward approach.

Results: A total of 219 subjects were randomized (APR: n=110; PBO: n=109), and 192 remained in the study through Week 16. APR and PBO groups were balanced with respect to baseline tender joint count (mean [SD]: 17 [13] vs. 18 [14]), swollen joint count (mean [SD]: 9 [5] vs. 10 [6]), and severity of morning stiffness (moderate to very severe: 87% vs. 80%), as well as previous use of DMARD (67% vs. 72%), baseline use of non-steroidal anti-inflammatory drug (69% vs. 68%) and oral corticosteroid use (12% vs. 13%). Mean [SD] duration of morning stiffness at baseline was shorter with APR vs. PBO (48 [49] vs. 72 [127] minutes). Baseline PtGA (mean [SD]: 5.9 [2.1] vs. 6.1 [2.0]), Patient's Pain Numeric Rating Scale (NRS; mean [SD]: 6.1 [1.9] vs. 5.8 [2.2]), Health Assessment Questionnaire-Disability Index (HAQ-DI; mean [SD]: 1.3 (0.6) vs. 1.2 [0.6]), Short-Form Health Survey version 2 (SF-36v2) Physical Component Summary (mean [SD]: 32.4 [9.2] vs. 33.9 [8.3]), SF-36v2 Physical Functioning subscale (mean [SD]: 33.2 [11.2] vs. 34.2 [10.1]) and SF-36v2 Bodily Pain domain (mean [SD]: 35.4 [7.6] vs. 37.4 [7.8]) scores were similar in the APR and PBO groups, respectively. As early as Week 2, a significantly greater proportion of APR vs. PBO subjects experienced morning stiffness severity improvements (≥1 category improvement) (43% vs. 21%; *P*=0.0007). Significant improvements in morning stiffness severity were sustained through Week 16 in APR vs. PBO subjects (46% vs. 26%; *P*=0.0015). Subjects with improvements in morning stiffness severity in the APR and PBO groups showed consistent improvements in pain, physical function and PtGA at Week 16 (Table). In patients with unchanged stiffness severity, greater improvements were observed across outcome measures in the APR vs. PBO group, although the change from baseline was less than the improved stiffness group. Worsened morning stiffness was associated with lack of improvement in other patient-reported outcome measures.

Conclusion: In biologic-naïve PsA subjects treated with APR for 16 weeks, improvement in morning stiffness severity was evident as early as Week 2 and associated with improvements in pain, physical function and PtGA response.

Stiffness Dynamics With APR Treatment and PBO and Improvement in Pain, Physical Function and PtGA Response From Baseline to Week 16

Change in Stiffness Severity*	Improved			No Change			Worsened		
Outcomes, Least-Squares Mean Change (SD)	APR n=58	PBO n=30	*P* Value	APR n=37	PBO n=57	*P* Value	APR n=14	PBO n=22	*P* Value
HAQ-DI score†	−0.37 (0.06)	−0.35 (0.09)	0.876	−0.14 (0.05)	0.01 (0.04)	0.018	0.40 (0.12)	0.16 (0.1)	0.126
PtGA score‡	−1.99 (0.27)	−1.61 (0.38)	0.414	−0.69 (0.29)	−0.12 (0.24)	0.132	1.06 (0.61)	1.15 (0.48)	0.911
Patient's Pain NRS score¶	−2.11 (0.25)	−1.76 (0.35)	0.425	−0.93 (0.30)	0.01 (0.24)	0.016	1.30 (0.47)	1.40 (0.37)	0.875
SF-36v2 Physical Component Summary score	6.14 (1.00)	4.55 (1.39)	0.356	3.11 (1.07)	−0.79 (0.85)	0.005	−3.86 (1.82)	−5.38 (1.45)	0.516
SF-36v2 Physical Functioning subscale score	4.71 (1.10)	3.73 (1.52)	0.605	2.95 (1.08)	−0.58 (0.87)	0.013	−6.13 (2.18)	−5.57 (1.74)	0.841
SF-36v2 Bodily Pain subscale score	8.29 (0.93)	7.01 (1.30)	0.428	3.27 (1.01)	0.25 (0.82)	0.022	−2.86 (1.72)	−5.79 (1.37)	0.193

The n reflects the number of subjects randomized to the group; actual number of subjects having data available for each parameter may vary. *Improved and worsened are defined as a shift by at least 1 stiffness severity category (none, mild, moderate, moderately severe, very severe); subjects with baseline value and at least 1 post-baseline value are included. †Range of 0 to 3. ‡0 indicates not active, 10 indicates very active. ¶0 indicates no pain, 10 indicates most severe pain. The lower the scores, the better for HAQ-DI, PtGA, Patient's Pain scores. The higher the scores the better for SF-36v2 scores.

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AB0772

EFFICACY OF GUSELKUMAB IN PSORIASIS PATIENTS WITH SELF-REPORTED PSORIATIC ARTHRITIS WITH INVOLVEMENT OF THE SCALP, NAILS, HANDS, AND FEET: A POOLED ANALYSIS FROM 2 PIVOTAL PHASE 3 PSORIASIS STUDIES

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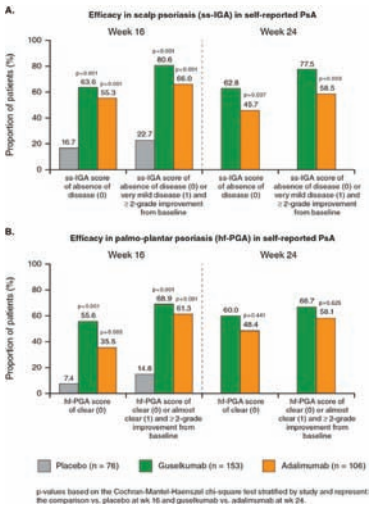
Background: VOYAGE 1 & 2 were the pivotal Ph3 GUS trials for plaque psoriasis (PsO).[1,2]

Objectives: Here we compare efficacy of GUS vs PBO & vs adalimumab (ADA) on PsO involving scalp, nail & palmoplantar (palmoplantar pustular PsO excluded per protocol) in a a subgroup of pts with self-reported psoriatic arthritis (PsA), given the association between these distinct PsO phenotypes & PsA.

Methods: VOYAGE 1(n=837) & VOYAGE 2(n=992) enrolled adult pts who had plaque PsO for ≥6 months, an Investigator Global Assessment (IGA) score ≥3, PASI score ≥12, ≥10% BSA involvement at baseline (BL), & were candidates for phototherapy or systemic treatment for PsO. Pts were randomized to GUS, PBO or ADA at BL, w/PBO crossover to GUS at wk16. This post-hoc analysis used observed pooled efficacy data for scalp-specific Investigator Global Assessment (ss-IGA), Physician's Global Assessment (PGA) of Hands &/or Feet (hf-PGA), fingernail PGA (f-PGA), & Nail Psoriasis Area & Severity Index (NAPSI) in subset of pts self-reporting PsA.

Results: In VOYAGE 1 & 2 combined, 335 (18.3%) PsO pts self-reported PsA (PBO 76, GUS 153, ADA 106). Baseline demographics were generally comparable across all 3 treatment grps, with history of methotrexate use: PBO 64.5%, GUS 70.6%, ADA 61.3%. A significantly greater proportion of GUS-treated pts achieved a ss-IGA score of 0/1 (absent/very mild) at wk16 vs PBO, & at wk24 vs ADA (Figure A). Significantly higher proportions of GUS-treated pts achieved a hf-PGA score of 0/1 (clear/almost clear) vs PBO at wk16 with numerically greater differences at wk24 vs ADA (Figure B). At wk16, proportions of pts achieving a f-PGA score of 0/1 (clear/minimal) were 47.6% for GUS vs 17.0% for PBO (p<0.001). The proportions of pts achieving an f-PGA score of 0/1 for GUS vs ADA were comparable at wk16 (47.6% vs 46.4%) & wk24 (67.0% vs 60.9%), but were higher for GUS by wk48 (82.5% vs 57.5%, Table). Mean (SD)% improvement from BL in NAPSI score was significantly higher for GUS vs PBO [39.5 (48.9) vs 6.5(47.5), p<0.001] at wk16 & was comparable for GUS vs ADA at wk24 [58.0 (51.3) vs 59.9 (40.4)]. By wk48, mean% improvement from BL in NAPSI score was higher for GUS vs ADA (70.8% vs 61.3%, Table).

Conclusion: GUS-treated PsO pts with self-reported PsA showed clinically meaningful improvements vs ADA in ss-IGA & hf-PGA scores at wks16 & 24. Although improvements in f-PGA & NAPSI were similar in pts treated with GUS vs. ADA at earlier timepoints, numerically greater differences were observed with GUS by wk48, likely requiring the additional duration to discriminate between treatments in this slow-growing cutaneous appendage.



REFERENCES

[1] Blauvelt A, et al. J Am Acad Dermatol. 2017 Mar;76(3):405-417

[2] Reich K, et al. J Am Acad Dermatol.2017 June;76(6): 1226

Table. Fingernail (f)-PGA score of clear (0) or minimal (1) in Psoriasis Patients with Self-Reported PsA at Wk 48*

	Guselkumab	Adalimumab
PsO Patients randomized at Week 0, n	329	334
PsO Patients with Self-reported PsA, n	64	62
Patients with f-PGA score >2 at baseline	40	40
f-PGA score of clear (0)	20 (50.0%)	16 (40.0%)
f-PGA score of clear (0) or minimal (1)	33 (82.5%)	23 (57.5%)

Percent improvement from baseline in NAPSI Scores in Psoriasis Patients with Self-Reported PsA at Wk 48*

	Guselkumab	Adalimumab
PsO Patients randomized at Week 0, n	825	582
PsO Patients with Self-reported PsA, n	153	106
NAPSI (N)	111	74
Mean (SD)	70.84 (40.49)	61.25 (42.43)
Median	100.00	70.85
Range	(-100.0; 100.0)	(-50.0; 100.0)
IQ range	50.00; 100.00)	(33.30; 100.00)

*–Post-hoc analyses based on Voyage 1 only

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AB0773

PSORIATIC ARTHRITIS IMPACT OF DISEASE QUESTIONNAIRE SCORES ARE CORRELATED WITH DISEASE ACTIVITY, AS MEASURED BY CDAPSA, IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: LAPIS-PsA is an ongoing, national, 52-week, multicenter, prospective, non-interventional study assessing long-term treatment with apremilast (APR) in adult patients with active psoriatic arthritis (PsA) in routine clinical practice in Germany.

Objectives: The current interim analysis assesses the clinical effectiveness of APR, as measured with the Clinical Disease Activity Index for PsA (cDAPSA) and its core components, as well as PsA health-related quality of life (HRQoL), measured with the 9-domain PsA Impact of Disease Questionnaire (PsAID9). In addition, correlations between cDAPSA and PsAID9 were assessed.

Methods: The interim analysis included data obtained at baseline (BL), Visit 1 (V1; ≥1 month), Visit 2 (V2; ≥4 months) and Visit 3 (V3; ≥7 months); all available data for patients treated with APR 30 mg twice daily were included in the analysis. A subgroup analysis was performed among patients categorized by cDAPSA disease activity scores at BL. Clinical characteristics and disease assessments at BL and V1-3 were assessed. Mean PsAID9 scores and proportions of patients meeting the PsAID Patient-Acceptable Symptom State (PASS), defined as a PsAID9 score of 4, were assessed by cDAPSA category at BL. Analyses are based on data as observed at each visit. Pearson's correlations were calculated between cDAPSA and PsAID9 at BL, V1, V2 and V3.

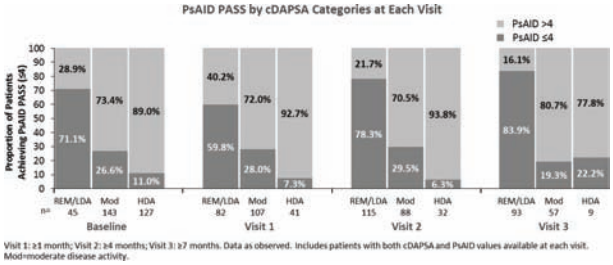
Results: A total of 394 patients were included in the analysis population (mean age: 55.1 years; female: 55.1%; previous biologic use: 25.4%). At BL, patients had a mean PsAID9 score of 5.3 and a mean cDAPSA score of 26.6. Continuous improvements in swollen/tender joint counts and patient-reported pain and disease activity were observed with continued APR treatment (Table). Patients reported incrementally reduced mean cDAPSA scores and consistent improvements in PsAID9 scores from BL to V3. Patients with low disease activity (cDAPSA >4 to ≤13) at BL had a mean (SD) PsAID9 score of 3.4 (1.7) with 71.1% in PsAID PASS (Figure). Those with moderate (cDAPSA >13 to ≤27) and high (cDAPSA >27) disease activity had mean (SD) PsAID9 scores of 5.3 (1.9) and 6.1 (1.8), with 26.6% and 11% showing PsAID PASS, respectively. At follow-up visits, greater proportions of patients achieving cDAPSA low disease activity or remission also achieved PsAID PASS (Figure). Significant moderate to high correlations were observed between cDAPSA and PsAID9 at BL (Pearson's coefficient r=0.43), V1 (r=0.51; P<0.0001), V2 (r=0.64; P<0.0001) and V3 (r=0.64; P<0.0001).

Conclusion: Results from this observational PsA study of APR demonstrate a significant correlation between disease activity, as assessed by cDAPSA, and PsA-specific life impact/HRQoL, as measured by PsAID9. More patients met the PsAID PASS cutoff while achieving remission or lower disease activity, and improvements in PsA disease activity are associated with the PsAID PASS from a life impact perspective.

Clinical Characteristics and Disease Assessments at Visits

	V0 (BL) N=394*		V1 (≥1 Month) N=313*		V2 (≥4 Months) N=359*		V3 (≥7 Months) N=265*	
	n§	Mean (SD)	n§	Mean (SD)	n§	Mean (SD)	n§	Mean (SD)
SJC (0-66)	337	4.7 (4.5)	249	2.9 (3.7)	262	2.7 (4.8)	184	1.2 (2.2)
TJC (0-68)	363	10.4 (10.6)	274	7.0 (9.8)	289	5.8 (9.0)	203	4.3 (8.1)
Pain (VAS 0-100 mm)	389	52.7 (22.9)	295	46.2 (23.3)	320	40.2 (25.1)	222	37.2 (25.8)
PtGA (VAS 0-100 mm)	387	55.7 (22.5)	287	45.0 (24.0)	317	38.2 (26.5)	223	36.1 (26.0)
cDAPSA (0-154)	323	26.6 (14.8)	230	19.2 (13.8)	232	15.7 (13.3)	157	12.2 (10.7)
PsAID9 (0-9)	378	5.3 (2.0)	278	4.7 (2.1)	299	4.0 (2.2)	212	3.7 (2.2)

Data as observed. *Number of patients evaluated at each visit. §Number of patients with data for the given assessment at both BL and post-BL (V1, V2 and V3). SJC=swollen joint count; TJC=tender joint count; VAS=visual analog scale; PtGA Patient's Global Assessment of Disease Activity.



Visit 1: ≥1 month; Visit 2: ≥4 months; Visit 3: ≥7 months. Data as observed. Includes patients with both cDAPSA and PsAID values available at each visit. Mod=moderate disease activity.

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AB0774

PREDICTORS OF SWITCHING IN A RETROSPECTIVE ITALIAN COHORT OF PSORIATIC ARTHRITIS PATIENTS RECEIVING BIOTECHNOLOGICAL DRUGS FOR AT LEAST 3 YEARS

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Background: Psoriatic Arthritis (PsA) is a chronic inflammatory disease typically treated, in its moderate-severe form, with biologic disease-modifying antirheumatic drugs (bDMARDs). However, refractory patients are not infrequent, and they are commonly managed by switching from one bDMARD to another. Since the chance of observing a good clinical response decreases according to line of treatment, it would be important

to recognize from the beginning patient prone to switching, in order to adopt tight-control strategies to optimize treatment.
Objectives: Our aim was to compare characteristics of patients who could maintain the same bDMARD over time (non-switchers) with those of refractory patients in whom bDMARD switch was necessary (switchers), and to evaluate predictors of switching.
Methods: PsA patients attending the Rheumatology Unit of University of Padova, classified according to CASPAR criteria and starting a first line bDMARD, were enrolled in the present retrospective study. We only included patients who maintained a bDMARD regimen (with or without switching) for at least 3 years, to ensure more complete follow-up data. Demographic data, comorbidities, clinimetric and anthropometric indexes, collected at baseline and once a year for every follow-up year and registered in the patient's records, were used. Disease activity was evaluated through Disease Activity in PSoriatic Arthritis (DAPSA), Leeds Enthesitis Index (LEI), Psoriasis Area and Severity Index (PASI). An overall Body Mass Index (BMI) category, summarizing data from the whole follow-up, was assigned to each patient, according to the BMI category which recurred more frequently in the patient's record. Then the variable was treated as categorical grouping underweight and normal-weight patients (base category), overweight and class I obesity (2° category), and class II and III obesity (3°categoy). Baseline characteristics for switchers and non-switchers were compared through chi-square or Fisher exact test, for categorical variable and t-test or Mann-Whitney test, for continuous variable, as appropriate. Logistic regression analysis was conducted to assess predictors of therapeutic switch. All variables associated to the outcome with a p<0.2 at univariate analysis were included in the initial multivariable model. Backward selection was applied to select the most significant predictors.
Results: One-hundred-eighty-nine PsA patients were enrolled with a mean follow-up time of 7.0±3.5 years. Their characteristics at the beginning of bDMARDs therapy are outlined in Table 1. Among the patients, 51 became switchers and 138 remained non-switchers. Their baseline features did not differ significantly, with the only exception of LEI, higher in switchers (0.5 ± 1.0 vs 0.2 ± 0.6, p=0.05). When predictors of switch were evaluated, the independent variables positively associated to the outcome at univariate analysis with p<0.2 were: male sex (OR 1.57; 95% CI 0.82, 2.99), BMI (OR 1.58; 95%CI 0.08, 3.08 for the II and III class obesity together with respect to normal-weight patients), inflammatory bowel disease (OR 5.59; 95%CI 0.49, 63.04), baseline PASI (OR 1.10; 95%CI 0.96, 1.26), baseline LEI (OR 1.45; 95%CI 0.98, 2.14), baseline DAPSA (OR 1.01; 95%CI 0.99, 1.03). In the multivariable model, only BMI (5.03; 95%CI 1.10, 22.89 for the II and III class obesity together with respect to normal-weight patients) and LEI (OR 1.46; 95%CI 1.00, 2.18) were able to independently predict the odds of switching.
Conclusion: Obesity and entheseal involvement, as expressed by LEI, seem to be the most useful predictor in order to identify patients who are more likely to switch, in line with data from literature that highlight a lower response of bDMARDs in obese patients.

REFERENCES

[1] Merola JF, et al. Semin Arthritis Rheum. 2017 Aug;47(1):29-37.

Disclosure of Interests: None declared
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AB0775 EFFECTIVENESS AND SAFETY OF USTEKINUMAB 90 IN PATIENTS WITH PSORIATIC ARTHRITIS.REAL WORLD EVIDENCE STUDY

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Background: Ustekinumab (UST) is a drug with proven efficacy in two randomized clinical trials in psoriatic arthritis -PsA- (PSUMMIT I and II). The data from these trials suggest that the 90 mg dose may be better than the 45 mg dose. Studies real world evidence (RWE) show that UST is effective and safe, nevertheless most of the evidence is base on the 45mg dose.[1]
Objectives: Our objective has been to check the effectiveness and safety of UST 90 mg in patients with PsA in RWE conditions.
Methods: An observational study in RWE conditions was driven. We included 58 patients (37 women, 21 men, age 55 ± 8.7 years) with PsA from a single university hospital. All patients met CASPAR criteria. The observation period was from July 2017 to the present. All patients received the 90 mg dose from the beginning. The average BMI was 29.9 ± 4.41. 50% of patients were obese. To measure the disease activity, the DAPSA index was used. A descriptive statistic was performed and the McNemar test was used to analyse the mean change of the DAPSA (final-basal). A bivariate analysis was performed to identify associated factors with a DAPSA remission/low activity.
Results: The duration of psoriasis was 14.8 ± 12.8 years, and 6.3 ± 6.5 years for the arthritis. 34.5% were oligoarticular forms, 13.8% polyarticular forms, and the remaining 51.7% were mixed forms. The distal interphalangeal joints synovitis was present in 38% of the patients and dactylitis in 24%. 17 patients were naive to biologic drugs (29.3%), UST was second line in 25.9%, third in 32.8%, fourth in 10.3% and fifth in 1.7% of patients. Half of the patients were treated with MTX. In the baseline situation, 9.4% had low activity, 75% had moderate activity, and 15.6% had high activity by DAPSA index. At the end of the analysis, 12.5% were in remission, 59.4% in low activity, and 28.1% in moderate activity, according to the DAPSA index. There were no patients in high activity. That is, 72% were in DAPSA remission/low activity. The average reduction of DAPSA was 9.53 ± 5.52 (McNemar's p <0.0005). The only factor associated with remission/low DAPSA activity was baseline DAPSA, OR 1.51 (1.02-2.22), p = 0.044. In 6 patients, the drug was discontinued (4 due to lack of efficacy and 2 due to poor tolerance or adverse effects).

Table 1. Baseline demographic and clinical characteristics of patients

Age (years), mean ± SD	54.6 ± 11.8
Male sex, n (%)	108 (57.1)
Disease duration (years), mean ± SD	16.2 ± 8.8
Family history of psoriasis, n (%)	168 (88.9)
Family history of arthritis, n (%)	181 (95.8)
IBD, n (%)	3 (1.6)
Uveitis, n (%)	3 (1.6)
Dactylitis, n (%)	15 (8.0)
LEI (0-6), mean ± SD	0.4 ± 0.8
PASI (0-72), mean ± SD	1.9 ± 2.2
HAQ (0-3), mean ± SD	0.8 ± 0.7
PCR (mg/L), mean ± SD	8.8 ± 11
DAPSA, mean ± SD	28.6 ± 18.2
BMI, mean ± SD	25.6 ± 4.6
CCI, mean ± SD	1.5 ± 1.4

IBD, Inflammatory Bowel Disease; LEI, Leeds Enthesitis Index; PASI, Psoriasis Area and Severity Index; HAQ, Health Assessment Questionnaire; CRP, C Reactive Protein; DAPSA, Disease Activity in PSoriatic Arthritis; BMI, Body Mass Index; Charlson Comorbidity Index

Conclusion: In this RWE series, UST 90 mg was effective and safe in 75% of our patients probability of achieving a remission/low activity state by DAPSA.

REFERENCES

[1] Ustekinumab in psoriatic arthritis: need for studies from real-world evidence.
Queiro R, Coto-Segura P.
Expert Opin Biol Ther. **2018** Sep;18(9):931-935.
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AB0776 RATES OF MYOCARDIAL INFARCTION, STROKE AND REVASCULARIZATION AMONG PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH APREMILAST, BIOLOGICS, DMARDS AND CORTICOSTEROIDS IN THE US MARKETSCAN DATABASE

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Background: Patients with psoriatic arthritis (PsA) are at increased risk for cardiovascular events, but different treatment options may not have the same rates of cardiovascular events.[1,2]
Objectives: To compare rates of myocardial infarction (MI), stroke and revascularization by treatment type in patients with PsA.
Methods: We conducted a population-based cohort study of treated PsA patients in the MarketScan database in 2014-2016. The cohort entry was the date of the first prescription for a study drug (apremilast only or in combination with ≥1 other study drugs, anti-TNF-α biologics only, other

biologics and DMARDs [OBDs] only, corticosteroids only, OBDs + corticosteroids and anti-TNF-α biologics with OBDs and/or corticosteroids) after March 21, 2014, the date on which apremilast was approved. Patients were followed from cohort entry through censor date, defined as the first of the following: index date (date patient became a case), end of record or end of study period (December 31, 2016). MI and stroke cases required 1 inpatient diagnosis plus 2 additional diagnoses on separate days; revascularization required a procedure code for revascularization without MI or stroke; all ≥7 days after cohort entry. A patient was considered currently exposed from the prescription date through the prescription duration + 30 days. We calculated incidence rates (IRs) and 95% confidence intervals (CIs) for each outcome per 100 patient-years among the entire population and in the subgroup of patients with no history of serious cardiovascular disease (CVD).

Results: The study population included 51,971 patients (median age: 52 years, 52% female, 4.0% serious CVD history). IRs were low for all outcomes, and differences between treatments did not reach statistical significance (95% CIs for IRs were overlapping). Among the 187 MI cases, IRs (95% CIs) were as follows: for apremilast only, 0.10 (0.01, 0.35); anti-TNF-α biologics only, 0.13 (0.09, 0.19); anti-TNF-α biologics with OBDs and/or corticosteroids, 0.31 (0.22, 0.43); OBDs only, 0.32 (0.23, 0.44); corticosteroids only, 0.44 (0.27, 0.68); OBDs + corticosteroids, 0.45 (0.24, 0.76); and apremilast in combination, 0.49 (0.20, 1.02). Among the 79 stroke cases, IRs (95% CIs) were as follows: for corticosteroids only, 0.08 (0.02, 0.22); anti-TNF-α biologics only, 0.09 (0.06, 0.13); for OBDs only, 0.10 (0.05, 0.17); anti-TNF-α biologics with OBDs and/or corticosteroids, 0.12 (0.06, 0.20); apremilast only, 0.15 (0.03, 0.43), or in combination, 0.14 (0.02, 0.51); and OBDs + corticosteroids, 0.21 (0.08, 0.45). Among the 292 revascularization cases, IRs (95% CIs) were as follows: for apremilast only, 0.25 (0.08, 0.57), anti-TNF-α biologics only, 0.36 (0.29, 0.44); anti-TNF-α biologics with OBDs and/or corticosteroids, 0.37 (0.27, 0.50); OBDs + corticosteroids, 0.38 (0.19, 0.68); apremilast in combination, 0.42 (0.15, 0.92); OBDs only, 0.48 (0.36, 0.61); and corticosteroids only, 0.49 (0.31, 0.73). Among patients with no serious CVD history, IRs were generally lower but results were not materially different from the main analyses.

Conclusion: Rates of MI, stroke and revascularization were low for treated PsA patients and were similar across treatments.

REFERENCES

[1] Jamnitski A, et al. *Ann Rheum Dis.* 2013;72:211-6. 2. Ogdie A, et al. Curr Opin Rheumatol. 2015;27:118-26.

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AB0777 PSA PATIENTS REACHING MINIMAL DISEASE ACTIVITY5/7 IMPROVE IN ALL FIELDS OF PSAID

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Background: Patients with psoriatic arthritis (PsA) show impact on physical and psychological aspect of the disease and it can be measured with the PsA Impact of Disease (PsAID) questionnaire. Impact of disease should improve if patient reach a minimal disease activity (MDA).

Objectives: To assess the association between MDA and PsAID questionnaire in patients with PsA from daily clinical practice.

Methods: A cross-sectional study was carried out in consecutive patients who fulfilled CASPAR criteria and who were treated according to routine clinical practice (EULAR/GRAPPA recommendations). Patients were considered in MDA if they met at least 5/7 of the MDA criteria. PsAID was also recorded. Continuous variables were reported as median (Q1-Q3). Categorical variables were reported as percentages and frequencies. All analyses were performed using SPSS software. Differences were considered statistically significant if p<0.05 (two tailed).

Results: Seventy-two patients were included, 40 males (55.6%), median of age 53.5 years old (47.0-62.7) and disease duration 5 years (3-10). Obesity was 29.6% and C-RP level was 0.31mgr/dl (0.10-0.97). Patient treatments were: NSAID 22.2%, corticosteroids 31.9%, csDMARD 55.6% and biological therapy 20.8%. DAPSA was 9.0 (2.2-19.4) being in VLDA (0-4) 37.5%, LDA (5-14) 22.2%, MDA (15-28) 30.6% and HAD (>28) 9.7%. Patients in MDA 5/7 state were 36 (50%) and median of total score of PsAID was 4.70 (0.85-9.40). All fields of PsAID improved if they reached MDA 5/7 (p <0.01). MDA 5/7 was also related to age, duration of the disease, CRP and DAPSA (see table).

	MDA5/7 n=36	No MDA5/7 n=36	p
Age, years	60.5 (49.2-70.0)	52.0 (45.2-57.0)	0.027
Gender, n% male	21 (58.3)	15 (41.7)	0.635
Years from diagnoses	7.0 (4.0-13.0)	4.0 (0.2-8.0)	0.02
Obesity, n (%)	8 (22.9)	13 (36.1)	0.221
scDMARD, n (%)	24 (66.7)	16 (44.4)	0.058
bDMARD, n (%)	10 (27.8)	5 (13.9%)	0.147
CRP, mgr/dl	0.16 (0.08-0.40)	0.49 (0.27-1.75)	0.001
DAPSA	3 (0.3-4.2)	19.3 (15.5-25.8)	<0.001
Total PsAID	1.20 (0.05-4.32)	8.75 (5.60-12.0)	<0.001

Conclusion: Fifty percent of PsA patients achieve MDA in daily clinical practice. MDA patients had a significantly lower impact of the disease according to PsAID.

REFERENCES

[1] Queiro R, et al. Arthritis Res Ther. 2017 Mar 29;19(1):72.

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AB0778 IMPACT OF DISEASE IN A SPANISH POPULATION WITH PSORIATIC ARTHRITIS

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Background: Patients with psoriatic arthritis (PsA) experience significant disability and reduced quality of life, resulting from the emotional distress and functional impairment associated with psoriatic skin lesions, as well as joint disease. Patient reported outcomes are important to evaluate healthcare interventions and to reflect the impact of PsA on patients' lives.

Objectives: The aims of the present study were to describe disease characteristics of PsA patients with an acceptable symptoms state (PsAID score<4) as well as to analyze predictive factors for PsAID<4.

Methods: Post-hoc analysis of data from a cross-sectional observational, multicenter study, aimed at evaluating the prevalence of MDA in a Spanish population with PsA, to describe their characteristics and to evaluate the association between MDA and the impact of the disease as assessed by the PsAID questionnaire. The original study included 227 adult patients of both genders diagnosed with PsA according to CASPAR criteria with at least one year of disease evolution and on treatment with biological and/or conventional synthetic disease modifying anti-rheumatic drugs (cDMARD). The PsAID questionnaire reflects the effect of PsA from the patient's perspective. It is composed of 12 physical and psychological domains. PsAID score < 4 identified patient-acceptable symptoms state.

Results: 122 patients with a PsAID score <4 were included. Demographic and clinical characteristics of the study population are shown in Table 1. Overall, 53/102 (52.0%) and 83/122 (68.0%) patients presented articular or skin remission, respectively. 76/122 (62.3%) of patients were in MDA state; the majority presented a low disability state according to HAQ (85.2%).

A moderate relationship between HAQ<0.5 and PsAID<4 (k=0.5325) and fair between MDA and PsAID<4 (k=0.3594) were observed. Multivariate logistic regression analysis showed that patients with distal interphalangeal joint (DIP) involvement (odds ratio (OR) [95%CI], 0.402 [0.203-0.799]; p=0.009), family history of PsA (OR: 0.252 [0.089-0.716]; p=0.010) and

increased CRP (OR: 0.922 [0.854–0.995; P = 0.036] were significantly less likely to reach a PsAID score<4.

Abstract AB0778 Table 1.. Demographic and clinical characteristics of PsA patients with PsAID <4

	Total N (122)
Male, n (%)	70 (57.4)
Age, mean (SD), yr	54.5 (12.7)
BMI, mean (SD) (kg/m^2)	27.1 (3.9)
CRP (mg/L), mean (SD)	2.8 (3.3)
Comorbidities, n (%)	
Dyslipidemia	40 (32.8)
HBP	33 (27.0)
Obesity	30 (24.6)
DM	12 (9.8)
PsA clinical patterns, n (%)	
Axial	3 (2.5)
Peripheral	107 (87.7)
Mixed	12 (9.8)
DIP disease	45 (36.9)
Familial history, n (%)	
Psoriasis	60 (49.2)
PsA	11 (9.0)
Ankylosing spondylitis	2 (1.6)
PsA duration, mean (SD), yrs.	9.6 (7.9)
Skin symptoms duration, mean (SD), yrs.	21.6 (14.5)
Articular symptoms duration, mean (SD), yrs.	11.9 (8.7)
Radiologic findings	
Erosions in hands, n (%)	40 (32.8)
Erosions in feet, n (%)	33 (27.0)
PASI, mean (SD)	1.2 (3.8)
HAQ, mean (SD)	0.2 (0.3)
HAQ ≤ 0.5, n (%)	104 (85.2)
MDA, n (%)	76 (62.3)
Kappa [CI$_{95\%}$] HAQ ≤ 0.5 vs. PsAID <4	0.5325[0.4212-0.6438]
Kappa [CI$_{95\%}$] MDA vs. PsAID <4	0.3594 [0,2393-0,4795]

MDA; Minimal disease activity; SD: Standard deviation; BMI: Body mass Index. CRP: C-Reactive Protein; HBP: High blood pressure; DIP: distal interphalangeal joint disease. DM: Diabetes mellitus; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; PsAID: Psoriatic Arthritis Impact of Disease. CI : confidence intervals

Conclusion: There are discrepancies between the treatment goals (MDA) and the impact of disease as assessed by PsAID. Clinical characteristics such as DIP involvement, inflammatory load (PCR) and genetic factors (familial history) seem to be associated with a lower probability of being in an acceptable symptoms state in PsA patients.

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AB0779 TOWARDS A GLOBAL MANAGEMENT OF PSORIATIC ARTHRITIS: ESTIMATION OF THE CARDIOVASCULAR RISK AND THE ACTIVITY OF THE DISEASE IN CLINICAL PRACTICE

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Background: Psoriatic arthritis (PsA) patients usually have a high prevalence of cardiovascular risk factors (CVRF) and cardiovascular events, which makes the routine estimation of cardiovascular risk (CVR) highly advisable. Currently, this risk is estimated through classic risk scores (SCORE, Framinghan), however, the values of these scores may underestimate the real CVR of these patients.

On the other hand, in clinical decision making and when evaluating the therapeutic response, it is advisable the use of some composite activity index. The heterogeneity of PsA makes it difficult to estimate the real activity and the remission state, so it is important to assess which of these composite index is more suitable for these purposes in clinical practice.

Objectives: We aimed to analyze whether carotid ultrasound is a useful tool for estimating CVR in patients with PsA, and if it is capable of correcting the estimated risk using classical tables. We also analyzed the usefulness of the MDA criteria and the DAPSA categories for clinical decision making in real practice.

Methods: A cross-sectional study was conducted with 136 consecutive patients with PsA (CASPAR criteria). Sociodemographic and anthropometric data, CVRF, disease activity according to DAPSA categories, HAQ, MDA, and CVR measured by SCORE chart, was collected. An IMT> 800 μm and/or the presence of carotid plaque (Mannheim consensus), defined a high CVR by ultrasound. We analyzed the concordance (kappa) between the MDA response and the low activity and remission categories according to the DAPSA. Clinical variables of PsA associated with a high CVR were evaluated by multivariateanalyses.

Results: Intima-media thickness values correlated well with CVR categories according to SCORE (p< 0.0001). 40% of patients included in the low and moderate risk categories according to the SCORE risk chart were reclassified as high CVR after the ultrasound examination.

	High cardiovascular risk (ultrasound)		
	No n (%)	**Yes n (%)**	**p value**
SCORE risk chart	51 (87.9)	7 (12.1)	<0.0005
Low	35 (71.4)	14 (28.6)	
Moderate	11 (39.3)	17 (60.7)	
High			

In the multivariate analysis, some characteristics of the disease were independently associated with a high CVR.

	OR (95% CI)	**p value**
Age	1.08 (1.03-1.13)	0.00
HAQ	1.94 (0.68-5.56)	0.22
DM	1.65 (0.42-6.40)	0.47
AHT	0.75 (0.24-2.31)	0.62
DL	2.61 (0.91-7.48)	0.07
Tobacco	4.26 (1.44-12.65)	0.01
Enthesitis	3.76 (1.36-10.40)	0.01
Erosions	5.23 (1.33-20.53)	0.02

This reveals that patients with enthesitis and/or structural damage are those who tend to have a high CVR.

When comparing DAPSA and MDA criteria, we found a moderate correlation between the MDA response and the DAPSA low activity (κ = 0.52, p <0.0001) and between MDA and DAPSA remission (κ = 0.47; p <0.0001).

Conclusion: A high percentage of patients with low-moderate risk according to the SCORE risk chart are reclassified as patients with high CVR after the ultrasound examination.

The high CVR in our population is related not only to classical CVRF, but also to the inflammatory load (enthesitis) and structural damage (erosions) of PsA.

DAPSA is an appropriate instrument for clinical decision making in routine practice because it correlates reasonably well with stringent therapeutic goals such as MDA.

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AB0780 PERSISTENCE OF MOLL AND WRIGHT CLASSIFICATION CRITERIA OVER TIME

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Background: In 1973 Moll and Wright published the first paper on the classification criteria for Psoriatic Arthritis (PsA) which included several phenotypes of PsA: Oligoarticular, Polyarticular, Axial, DIP, and Mutilans. Whether these subtypes change over time or are related to treatment response is not known. The hypothesis of this study is that with some exceptions, the Moll and Wright subtype classification criteria are stable over time and the pattern may have important therapeutic implications.

Objectives: The objective of this study was to evaluate the persistence of the Moll and Wright classification criteria in PsA patients.

Methods: This study is a retrospective chart review of PsA patients seen at a single center between January 1, 2013 and December 31, 2016. The patients in this study were identified using the ICD-9 or ICD-10 codes for PsA and were then classified using the CASPAR classification criteria for psoriatic arthritis. Patients who met CASPAR classification

criteria were subsequently sub-classified using the Moll and Wright classification criteria based on the manifestations of PsA at their index outpatient visit. This subtype was then compared to their Moll and Wright subtype at the last outpatient visit prior to January 3, 2019. While it was possible for patients to display more than one subtype simultaneously, the classification made at baseline and at latest visit reflected the predominant Moll and Wright subtype of the patient, in the opinion of the expert treating rheumatologist.

Results: 76 patients were identified as meeting entry criteria, with none being in remission at the index visit. Mean age of patients at the latest visit was 60.2 ± 12.6 years, and 47.4% were male. Median time between the index visit and latest visit was 7 years [IQR: 5 to 8 years]. 42.1% of patients had the same Moll and Wright subtype at both visits. Table 1 presents the distribution of Moll and Wright subtypes present at index visit and latest visit. Table 2 reports the changes, or lack thereof, in subtype between visits. 22/76 patients (28.9%) were in remission at the latest visit. Of the patients in remission, 12 (54.5%) were being treated with a biologic, DMARD, and/or steroid.

Abstract AB0780 Table 1.. Distribution of Moll and Wright subtypes at index visit and latest visit.

Moll and Wright subtype (N=76 patients)	Index visit (N)	Latest visit (N)
Polyarticular	19	8
Oligoarticular	42	36
Distal interphalangeal joint predominant	2	1
Spondylitis predominant	12	7
Arthritis mutilans	1	2

Abstract AB0780 Table 2.. Persistence of Moll and Wright subtype.

Description of change from index visit to latest visit[1]	N = 76
No change	32 (42.1%)
Polyarticular	5
Oligoarticular	20
Distal interphalangeal joint predominant	1
Spondylitis predominant	5
Mutilans	1
Polyarticular → oligoarticular	11 (14.5%)
Spondylitis predominant → oligoarticular	4 (5.3%)
Distal interphalangeal joint predominant → oligoarticular	1 (1.3%)
Oligoarticular → polyarticular	3 (3.9%)
Oligoarticular → spondylitis predominant	2 (2.6%)
Polyarticular → mutilans	1 (1.3%)
Oligoarticular → remission	17 (22.4%)
Polyarticular → remission	2 (2.6%)
Spondylitis predominant → remission	3 (3.9%)

[1] Arrow (→) indicates change from index visit to latest visit.

Conclusion: In this retrospective analysis there was a persistence of Moll and Wright subtype in 42.1% of psoriatic arthritis patients over the median time of 7 years. Whether patients who maintain Moll and Wright subtypes respond differently to targeted therapy for PsA should be evaluated in prospective trials.

REFERENCES

[1] Moll J. M. H., Wright V. Psoriatic Arthritis. Semin Arthritis Rheum. 1973; 3 (1): 55-78.

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AB0781 ASSOCIATION OF MICA POLYMORPHISM AND SERUM LEVELS WITH PREDISPOSITION TO PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a multifactorial chronic inflammatory disease manifested by joint inflammation and cutaneous psoriasis. The precise etiology of PsA remains unknown, however both genetic and environmental factors contribute to development of this immune-mediated disease.

Objectives: This present study aimed to assess whether polymorphism within gene coding for major histocompatibility complex (MHC) class I chain-related A (MICA) proteins could be a prognostic factor of PsA.

Methods: For this purpose 77 PsA patients and 234 controls were enrolled to the study on MICA polymorphic variants. Genotyping for MICA rs1051792 (Met/Val; G>A) was performed using a LightSNiP assay. In addition the MICA serum levels were studied in 66 patients and 99 controls employing Luminex assay.

Results: Interestingly, MICA polymorphism was found to affect the susceptibility to PsA. The presence of the A (Val) variant was found to increase the risk of PsA (OR= 1.932, p=0.022).

No significant differences were detected between MICA serum levels in patients and controls. However, patients carrying this risk variant (A allele) characterized with lower MICA serum levels as compared GG homozygotes (p=0.018)

Conclusion: These results imply that MICA polymorphism may constitute a risk factor of PsA and be associated with MICA serum levels in PsA patients.

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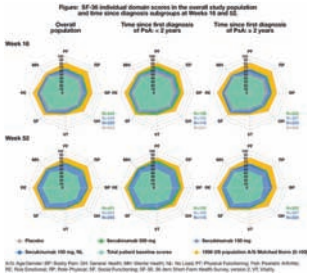
AB0782 SECUKINUMAB PROVIDES IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PSORIATIC ARTHRITIS, REGARDLESS OF THE TIME SINCE DIAGNOSIS: POOLED RESULTS FROM THE SECUKINUMAB PHASE 3 TRIAL PROGRAM

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Background: Psoriatic arthritis (PsA) can have a profound impact on health-related quality of life (HRQoL). Secukinumab (SEC), a fully-human IL-17A inhibitor, has been shown to improve symptoms and HRQoL in patients (pts) with PsA.[1]

Objectives: To evaluate the impact of SEC on HRQoL, assessed using the Short Form-36 Health Survey (SF-36), in pts with PsA stratified by time since first diagnosis (<2 or ≥2 yrs).

Methods: Pts were randomized to either subcutaneous placebo (PBO) or SEC 150 mg (FUTURE 2, 3, 4, 5), 150 mg no load (NL; FUTURE 4, 5), or 300 mg (FUTURE 2, 3, 5). Doses were administered at baseline (BL) and Wks 1–4, followed by every 4 wks (or every 4 wks from BL in NL groups). Pts on PBO were re-randomized to SEC at Wk 16 or 24. Mixed-models for repeated measures were used to assess changes from BL to Wk 16; observed data are presented at Wk 52. The proportion of pts reporting improvements ≥ minimum clinically important differences (MCID) in SF-36 physical (PCS responders), mental component summary (MCS responders), and individual SF-36 domains was also assessed. Non-responder imputation was employed for missing values in responder analyses. Fisher's exact test was used to compare the proportion of responders.



Results: A total of 2049 pts were included: 681, 461, 572, and 335 in the PBO, SEC 300 mg, 150 mg, and 150 mg NL groups, respectively. Of these, 34%, 30%, 32%, and 33%, were classified as <2 yrs since PsA diagnosis (overall: 32%). Mean times since diagnosis were 0.8–0.9 yrs across treatment groups in the <2 yrs subgroup, and 8.6–10.1 yrs in the ≥2 yrs subgroup. The least squares mean (LSM) changes from BL to Wk 16 in PCS and MCS were significantly improved with all doses of SEC vs PBO in both <2 yrs (PCS: PBO = 0.8 vs 6.5 [p<0.0001], 4.8 [p<0.0001], 3.6 [p<0.01] for the 300 mg, 150 mg, and 150 mg NL groups, respectively; MCS: PBO = 1.3 vs 4.0 [p<0.01], 4.4 [p<0.01], 3.8 [p<0.05]) and ≥2 yrs since diagnosis (PCS: PBO = 1.9 vs 6.9 [p<0.0001], 5.3 [p<0.0001], 5.5 [p<0.0001]; MCS: PBO = 0.9 vs 3.6 [p<0.01], 2.8 [p<0.01], 3.0 [p<0.01]) groups. Improvements in individual SF-36 domains were reported with SEC vs PBO in the overall population and both subgroups (Figure). At Wk 16, the proportion of PCS responders was significantly higher with SEC vs PBO, in both <2 yrs (PBO: 38.5% vs 300 mg: 69.1% [p<0.0001]; 150 mg: 59.5% [p<0.01]; 150 mg NL: 53.6% [p<0.05]) and ≥2 yrs (PBO: 43.8%; 300 mg: 64.6% [p<0.0001]; 150 mg: 59.4% [p<0.01]; 150 mg NL: 65.8% [p<0.0001]) groups. Overall, improvements in SF-36 scores and MCID responses were generally more prominent with SEC 300 mg vs SEC 150 mg and in those <2 yrs vs ≥2 yrs from diagnosis. Improvements in PCS, MCS, individual domains, and MCID responses with SEC were sustained to Wk 52.

Conclusion: SEC offered significant, clinically meaningful and sustained improvements in HRQoL (SF-36) in pts with PsA, regardless of time since diagnosis.

REFERENCES

[1] Mease PJ, et al. Ann Rheum Dis. 2018;77:890–7

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AB0783

RELATIVE IMPACT OF JOINT AND SKIN SYMPTOMS ON QUALITY OF LIFE AND WORK PRODUCTIVITY IN PSORIATIC ARTHRITIS (PSA) PATIENTS

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Background: PsA is a chronic inflammatory arthritis with heterogeneous clinical manifestations. Disease burden and quality of life (QoL) is affected by both joint and skin aspects of the disease (1,2). Given variability among patients of the extent and severity of joint and skin symptoms, the relative impact of each aspect on overall burden to the patient has not been well quantified.

Objectives: Describe the relative impact of joint and skin symptoms in PsA in a real-world population through an assessment of patient perception of symptom importance, QoL, and work productivity.

Methods: Cross-sectional survey of rheumatologists and dermatologists and their PsA patients in Australia, Canada, France, Germany, Italy, Japan, Spain, UK, and US. Physicians provided data on patient Body Surface Area (BSA) psoriasis coverage at the time of survey. Patient self-reported data included perceptions of symptom importance, EQ-5D, Psoriatic Arthritis Impact of Disease (*PsAID12*), and Work Productivity and Activity Impairment (WPAI: SHP) Index. Patients were compared according to BSA (BSA=0 vs. BSA>0), using parametric and non-parametric tests as appropriate.

Results: Data were collected for 3200 patients with PsA by 454 rheumatologists and 238 dermatologists. 556 patient self-completed questionnaires were also collected. Mean age was 49 years, 46% female, 69% had a BSA>0. Patients with BSA>0 had mean tender joint count (TJC) of 5.2 and mean swollen joint count (SJC) of 4.8. Patients with BSA=0 had mean TJC and SJC of 2.0 and 1.5, respectively.

Across all patients, when asked to prioritize the burden of symptoms, 62% of patients prioritized joints and 38% prioritized skin. In patients with BSA=0, 35% still prioritized skin as most important. 41% indicated they experienced anxiety/depression as a result of their PsA, with 62% indicating both joint and skin symptoms were the cause (28% joint alone, 9% skin alone).

Patients with BSA >0 reported significantly worse QoL and work productivity and activity impairment than BSA=0 (EQ5D index 0.79 vs. 0.85, p<0.0001; EQ5D VAS 71.98 vs. 77.68, p<0.0001; PsAID 2.91 vs. 1.66, p<0.0001; WPAI overall 25.61 vs. 16.32, p<0.0001).

Conclusion: The majority of PsA patients prioritise joint symptoms over skin. Patients with any joint/skin involvement likely have worse quality of life than in the general population (3). PsA patients report that both joints and skin have an impact on their QoL and work productivity with significantly greater impact in those who have skin involvement. Treatment goals focusing on both components of PsA would optimize patient outcomes.

REFERENCES

[1] Mease PJ. Biologic Therapy for Psoriatic Arthritis. Rheum Dis Clin North Am. 2015;41(4):723–38.
[2] Sokoll KB, Helliwell PS. Comparison of disability and quality of life in rheumatoid and psoriatic arthritis. J Rheumatol. 2001 Aug 1;28(8):1842 LP-1846.
[3] Hanmer J, et al. Report of Nationally Representative Values for the Noninstitutionalized US Adult Population for 7 Health-Related Quality-of-Life Scores. Med Decis Mak. 2006 Jul 1;26(4):391–400.

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Hexal, Sanofi, and USB; advisory board: AbbVie, Bio Skin, Bristol-Myers Squibb, Celgene, Dignity, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen Cilag, Leo Pharma, Morphosis, Novartis, Pfizer, Sandoz, Sanofi, and UCB, Nicola Booth Employee of: Adelphi Real World, Steve Lobosco Employee of: Adelphi Real World, Gary Milligan Employee of: Adelphi Real World, Matthew Hufford Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Julie Birt Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Wolf-Henning Boehncke Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, Elizabeth Holdsworth Employee of: Adelphi Real World

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AB0784 SUBCLINICAL MYOCARDIAL INVOLVEMENT IN PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) is a systemic inflammatory disease affecting 15-30% of patients with psoriasis[1]. Patients with PsA present 43% higher risk of cardiovascular disease, involving myocardial infarction, heart failure and cerebrovascular events compared with the general population[2]. The common underlying pathophysiologic basis of these clinical events is early atherosclerosis. Myocardial fibrosis in the context of systemic inflammation[3] seems to play a significant role in the cardiac manifestations of the disease as well. However, only a few trials have evaluated the possibility of recognition of myocardial involvement in its subclinical phase, which might be of value in reducing the morbidity and mortality of the disease.

Objectives: Our goal was to evaluate the systolic and diastolic myocardial function in asymptomatic patients with PsA and no cardiac comorbidities and emphasize the value of speckle tracking echocardiography in this condition.

Methods: Sixty patients (29 males) and 34 healthy controls (18 males) participated in the study. The patients' mean age was 52.5 (s.d = 11.29) and the controls' mean age was 50.7 years (s.d. = 17.42). They were all subjected to 2D transthoracic echocardiography, tissue Doppler imaging, and speckle tracking echocardiography, in order to evaluate left ventricular systolic function with conventional indices such as ejection fraction (EF), and with novel indices such as global longitudinal strain (GLS). Diastolic dysfunction was also assessed in both groups. Blood tests including CRP and ESR were conducted. Disease duration and severity scores, PASI and DAS 28, were also recorded. The statistical analysis was conducted with SPSS v.23.0.

Results: Linear regression analysis showed statistically significantly impaired left ventricular systolic function (p<0,001), as assessed with global longitudinal strain (GLS), in PsA patients (mean =-19.79, s.d. =4.54) compared to the controls (mean =-23.67, s.d. =3.27). The results were adjusted for age and gender. Ejection fraction, on the contrary, did not show any statistically significant difference between the two groups (p=0,535). Left ventricular diastolic function did not present significant difference between the two groups. GLS showed no association with disease duration, severity scores or the blood tests.

Conclusion: PsA patients present a higher risk of left ventricular systolic dysfunction compared to controls. GLS measured by speckle tracking echocardiography is a useful tool in revealing this subclinical myocardial impairment.

REFERENCES

[1] Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis 2005;64 Suppl 2:ii14–7

[2] Polachek A, Touma Z, Anderson M, Eder L. Risk of Cardiovascular Morbidity in Patients With Psoriatic Arthritis: A Meta-Analysis of Observational Studies. Arthritis Care & Research Vol. 69, No. 1, January 2017, pp 67–74

[3] Kania G, Blyszczuk P, Eriksson U. Mechanisms of cardiac fibrosis in inflammatory heart disease. Trends Cardiovasc Med 2009; 19: 247-252

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AB0785 DRUG SURVIVAL OF SECUKINUMAB FOR PSORIATIC ARTHRITIS IN A REAL-WORLD SETTING

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Background: Secukinumab is a newly introduced biologic therapy against IL-17 which has been approved for Psoriatic Arthritis and has showed efficacy in clinical trials, but real world data is still lacking.

Objectives: This study aims to analize secukinumab drug survival for psoriatic arthritis in a real world environment.

Methods: Multicentric observational, longitudinal retrospective study conducted at 4 tertiary hospitals in Madrid region. Patients with clinical diagnosis of psoriatic arthritis which had received at least one dose of secukinumab between january 2016 and october 2018 were included. with follow up period till December 31, 2018. Medical records were reviewed to collect data about psoriatic arthritis involvement, comorbidities, previos DMARD and bDMARD therapies and its reasons for discontinuation, duration of secukinumab therapy, reasons for discontinuating secukinumab therapy and adverse events. Statistical analysis was performed including bivariate analisys (considering withdrawal of drug during study period or not) and survival analysis with Kaplan-Meier and Cox regression.

Results: 177 patients that initiated secukinumab therapy in the recruitment period were included. 123 pacients were on 150 mg dose and 54 on 300 mg dose. Average follow up period was 13 months (SD 8,28; range 1-34) In the bivariate analysis, a higher proportion of biologic-naïve patients was found among the group without secukinumab withdrawal during the study (40% vs 23%, p 0.07). No other differences were observed between both groups regarding demographic characteristics nor comorbidities (tobacco exposure, hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease or malignancy). Median survival time for secukinumab in the Kaplan-Meier analysis was 21.2 months (IC 95%: 14.3 - 22.2), with an average of 19,9 months. One event was censored due to lost to follow-up. Secukinumab treatment was withdrawn in 79 patients (44.6%). Reasons for discontinuation were lack of effectiveness (37%), either primary (40 patients) or secondary (26 patients), adverse events (9 patients, 0,5%), elective surgery in one patient and latex allergy in other. The only variable associated to higher drug survival in Cox regression analysis was biologic-naïve status. No differences in drug survival were found in all other variables studied (gender, age, secukinumab dosage, illness duration, clinical features, tobacco exposure and rest of comorbidities).

Conclusion: As secukinumab was marketed in 2016, real-word setting studies lack long term data. The mean follow up period in our study was 13 months. Most of withdrawals were to lack of effectiveness. Median survival was 21.2 months, significatively higher in biologic-naïve patients. No other differences were found in all other variables studied. Probably real-world data differ from those of clinical trials.

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AB0786 HIGH TREATMENT SATISFACTION OF THERAPY WITH USTEKINUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS DUE TO EARLY AND LONG-TERM TREATMENT RESPONSE AND HIGH TOLERABILITY – RESULTS OF THE NON-INTERVENTIONAL STUDY SUSTAIN

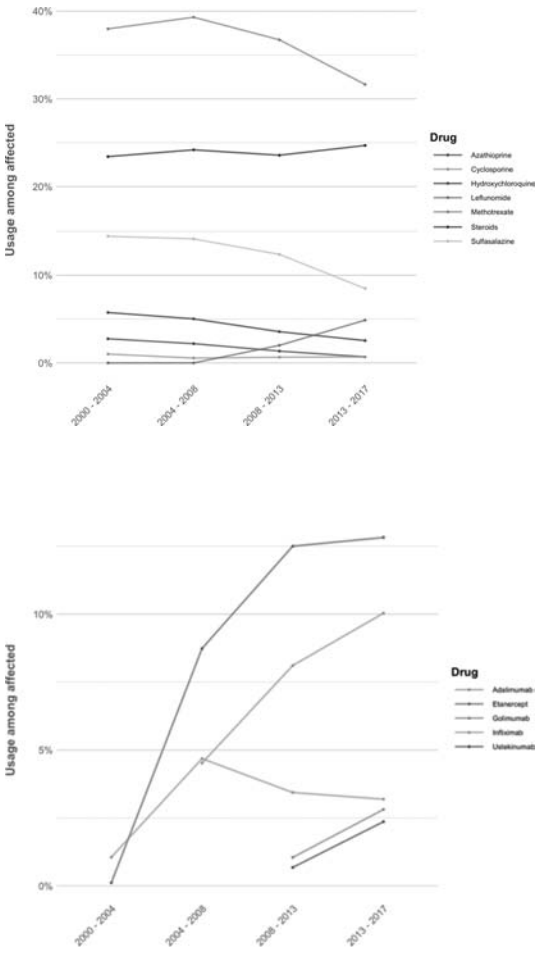
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Background: SUSTAIN is a prospective, multi-center non-interventional study in Germany.
Objectives: The objectives are to observe long term efficacy and safety, quality of life and further patient reported outcomes in patients with active psoriatic arthritis (PsA) under treatment with ustekinumab in routine clinical care.
Methods: In this study nearly 400 patients were planned to be included at 75 centers for 160 weeks with documentation intervals at week 0 and 4 and then every 12 weeks. The treatment with ustekinumab is according to the label. Besides demographic data, the following data will be documented: Number of swollen and tender joints, tender entheses, amount of skin psoriasis (BSA and PASI), patient reported outcome concerning disease activity of PsA and pain, Health Assessment Questionnaire (HAQ), quality of life (SF-12), sleep quality (VAS), satisfaction with therapy of patient and physician, safety (adverse events/serious adverse events), pharmacoeconomic aspects, number of patients with "Minimal Disease Activity" (MDA), number of patients with MDA at week 28 und 52. For the present interim analysis baseline data of 336 patients and results of the documented visits up to week 112 were analyzed.
Results: For the present analysis 336 patients (57% women) at 75 centers were observed. The number of documented patients was 310 at week 4, 318 at week 16, 278 at week 28, 160 at week 76 and 108 at week 112. At time of inclusion into the study, patients had arthritis at small (73.2%) and/or large (52.4%) joints, spinal involvement (17%) and enthesitis (13.1%). For 30.1% of patients, the medical history revealed structural bone damage and 2.1% had uveitis present at time of inclusion. Mean age was 54 years (22-85), mean BMI 30 kg/m² (19-52). The mean ustekinumab dose was 0.7 mg/kg body weight (0.2-1.3). 54.5% of the patients had as prior medication at least one TNF inhibitor and 44% used MTX as concomitant medication.
The data extension of the present interim analysis demonstrated relevant improvements with high treatment satisfaction and good safety and tolerability after 4 weeks and up to 112 weeks. The data show the maintenance of these treatment results up to week 112, i.e. reduction in the number of tender joints from a mean of 10.0 (CI 95% 8.6/11.3) at baseline to 1.8 (1.1/2.5) at week 112. The number of swollen joints improved from 4.1 (3.4/4.9) at baseline to 0.7 (0.3/1.0) at week 112. In the same period, skin symptoms (PASI) declined from 8.4 to 1.0 and pain assessment (VAS) declined from 56.0 to 34.3. Of the 96 patients who completed the week 112, 30.2% reached MDA at week 28 and 29.2% reached MDA at week 52.
Efficacy of the therapy with ustekinumab was assessed as "very good" or "good" by 91.1% of the treating physicians and by 89.9% of the patients at week 112. Until data cut off point (45 months after study start), 105 SAEs have been documented, of which only 14 were related to ustekinumab as assessed by physician of treatment center. 3.9% of patients discontinued treatment with ustekinumab (N=121), mainly due to an adverse event. Safety of therapy with ustekinumab was assessed as "very good" or "good" by 100% of the treating physicians and by 100% of the patients at week 112.
Conclusion: The present interim analysis of the prospective non-interventional study SUSTAIN confirmed relevant improvements with high treatment satisfaction and good safety in patients with active psoriatic arthritis treated with ustekinumab after 4 weeks and demonstrated that these effects were maintained at least up to 112 weeks in routine care.
Disclosure of Interests: Joerg Wendler Consultant for: Roche Pharma AG, AbbVie, Jannssen Cilag, Novartis, Speakers bureau: Roche Pharma AG, AbbVie, Jannssen Cilag, Novartis, Peter Wagener: None declared, Frank Hamann: None declared, Nils Damann: None declared, Evgenia Movshovich: None declared, Frank Behrens Grant/research support from: AbbVie, Pfizer, Roche, Chugai, Prophylix, Bioline, Novartis, Consultant for: AbbVie, Pfizer, Roche, Chugai, UCB, Bristol-Myers Squibb, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Eli Lilly, Speakers bureau: Ad board: AbbVie, Pfizer, Roche, Chugai, UCB, Bristol-Myers Squibb, Celgene, Novartis, Biotest, Janssen, Genzyme, Eli Lilly
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AB0787 **TREATMENT TRENDS IN PSORIATIC ARTHRITIS IN A REAL-WORLD SETTING; RESULTS FROM A HEALTH PROVIDER DATABASE OF THE PSORIATIC ARTHRITIS PATIENTS**

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Background: Emerging Psoriatic Arthritis (PsA) treatments have had a great impact on treatment strategies and healthcare costs in PsA disease management. Therefore, investigating changes in therapy is important to patients, healthcare providers, and healthcare payers alike.
Objectives: To describe changes in treatment strategies and management of PsA patients in a real-world setting over the years 2000-2017 since the introduction of diverse novel biologic disease modifying anti-rheumatic drugs (bDMARDS).
Methods: A retrospective study was performed using the previously-tested and validated database of Clalit Health Services, the database of the largest healthcare provider in Israel. The database includes continuous real-time input from pharmaceutical and medical digital systems regarding prescribed and dispensed medications. In this study, data on all conventional DMARDs (cDMARDs) and bDMARDs dispensed to the PsA patient cohort from 2000-2017 was retrieved. In Israel, all patients are eligible for bDMARDS following treatment failure of at least 2 cDMARDS with bDMARDs used in different sequences and/or combinations based on patient and physician preference. Of note, Etanercept and Infliximab are available on the Israeli market since 2000, Adalimumab since 2002, Golimumab since 2006 and Ustekinumab since 2014. Descriptive statistics, including means (standard deviations) for continuous variables and frequencies (%) for categorical variables, were used.



Results: The study included 5062 PsA patients. Data showed an increase in use of bDMARDs in recent years (Fig 1). The trend in increasing use of bDMARDS was not affected by age, sex, and ethnicity. Etanercept was the most commonly used bDMARD (10.1%) over time, whereas, methotrexate was the most commonly used cDMARD (25.9%). A decrease in use of infliximab was noted along with the introduction of adimumab, golimumab and ustekinumab. Notably, a decrease in the utilization of cDMARDs, but not corticosteroid use, was seen with the advent of bDMARDs (Fig 2). However, this decrease in cDMARD use was not observed in patients treated with infliximab [Correlation Coefficient 2.69% (-47.5%, 51.6%), P=0.921].**Conclusion:** More PsA patients are using bDMARDs in recent years in lieu of cDMRADS. This change in PsA management highlights a need for further research on the relative safety efficacy and cost of biologic agents to better guide evidence-based treatment decisions.

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AB0788 LUPUS CO-MORBIDITY IN PATIENTS WITH PSORIATIC ARTHRITIS: A POPULATION-BASED CASE-CONTROLLED STUDY

Danielle Korkus[1], Tal Gazitt[2], Ilan Feldhamer[3], Idit Lavi[4], Amir Haddad[2], Erez Batat[3], Sari Greenberg-Dotan[3], Arnon Cohen[3,5], [1,2]Devy Zisman*. *[1]The Ruth and Bruce Rappaport Faculty of Medicine Technion, Haifa, Israel*; *[2]Carmel Medical Center, Rheumatology Unit, Haifa, Israel*; *[3]Central Headquarters, Clalit Health Services, Chief Physician's Office, Tel Aviv, Israel*; *[4]Carmel Medical Center, Department of Community Medicine and Epidemiology, Haifa, Israel*; *[5]Faculty of Health Sciences, Ben-Gurion University of the Negev, Siaal Research Center for Family Medicine and Primary Care, Beer-Sheva, Israel*

Background: Patients with psoriasis and psoriatic arthritis (PsA) can develop a variety of comorbidities including metabolic syndrome, diabetes, hypertension, cardiovascular diseases and depression. Comorbidities, in turn, may influence the therapeutic regimen and affect treatment results. Previous studies show a high incidence of coexistence of psoriasis and systemic lupus erythematosus (SLE). Unlike psoriasis, the coexistence of PsA and SLE has been reported only in case reports.

Objectives: To assess the prevalence of SLE in a PsA patient cohort and to compare it to the general population using the database of a large health care provider.

Methods: The study, which was conducted from 2002-2017, is a retrospective study on a PsA cohort consisting of 4,836 PsA patients matched for age and sex with 24,180 randomly selected control patients. Data on this cohort was derived from the database of more than 4.3 million people enrolled in the largest health care provider in Israel, Clalit Health Services. The database was used to extract demographic data, such as age, sex, ethnicity and socioeconomic status; clinical and laboratory manifestations of SLE; medication dispensed and SLE-inducing medications. T-test was used to compare continuous variables and a Chi-square test was used for categorical variables. All tests were 2-sided; p values of <0.05 were considered statistically significant.

Results: The PsA study group consisted of 4,836 subjects, at a median age of 56+/-15, 2603 (53.8%) of whom were females. The control group consisted of 24,180 subjects matched for age and sex. 18 patients (0.37%) in the PsA study group, and 39 patients (0.16%) in the control group where diagnosed with SLE (p=0.002). SLE patients without co-existing PsA had higher anti-double stranded DNA (anti-dsDNA) positivity (92.3% vs 66.7%, p=0.022) and positive anti-cardiolipin (ACL) antibodies (46.2% vs 16.7%, p=0.041). No other significant differences were observed between the two groups in terms of clinical and laboratory manifestations of SLE. PsA patients with concomitant SLE compare to PsA patients without SLE were more often female (100% vs 53.7%, p<0.0001), had more osteoporosis (38.9% vs 12.8%, p=0.005) and were more likely to be treated with beta blockers (27.8% vs 9.8% p=0.027). Usage of medications with known potential to induce SLE prior to diagnosis of SLE was higher in the study group of PsA patients (11 out of 18 patients) than in the control group, but there was no difference in SLE manifestations between these two groups. Culprit medications associated with later onset of SLE included proton pump inhibitors (PPI) [0.27% in the PsA cohort vs 0.1% in the control group (p=0.004)], beta blockers [0.33% vs 0.16% (p=0.011)], angiotensin converting enzyme inhibitors (ACE-I) [0.35% vs 0.13% (p=0.001)], thiazide diuretics [0.35% vs 0.1% (p=0.001)], anti- tumor necrosis factor (anti-TNF) agents [0.4% vs 0.2% (p=0.002)].

Conclusion: A 2.3 fold increase in the prevalence of SLE in PsA patients than in the control group was found in our study population. There were no significant differences in the clinical and laboratory manifestations of SLE between these two groups. The positive correlates between SLE and PsA may point to common underlying pathogenetic pathways and may affect treatment choices and medication development. More research is needed for a better understanding of this diseases association.

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AB0788B RECOMENDATIONS FOR DISEASE ACTIVITY ASSESSMENT AND DEFINITION OF CLINICAL REMISSION IN PSORIATIC ARTHTITIS: A DELPHI-BASED EXPERT CONSENSUS

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Background: Patients with psoriasis arthritis (PsA) have heterogeneous clinical presentations, with diverse articular and dermatological features and varied disease courses and outcomes, so the assessment of disease activity implies important difficulties. Although the goal of treatment of PsA is to achieve remission, there is no a universally accepted definition.

Objectives: The purpose of this study was to assess agreement by experts on recommended disease activity assessment in PsA patients and to develop a consensus definition of clinical remission.

Methods: A modified Delphi approach was used as a consensus method. A scientific committee of experts provided 86 statements that were submitted in 2 rounds to a panel of 130 Spanish experts in PsA (in September and October 2018, respectively), addressing issues regarding the current assessment of remission, variables that should be included in the minimal assessment of PsA patients and the definition of remission, and the use of disease activity scores.

Results: The expert panel reached agreement for 53 proposed statements (61.6%). There was consensus that the definition of remission in PsA should include: the absence of signs and symptoms, physical well-being, the absence of impact of the disease, the absence of inflammation and progression in imaging tests (radiography and magnetic resonance) and the absence of inflammation measured by biomarkers (ESR, CRP). It is recommended to use some index designed specifically for the assessment of disease activity and the variables that should include the minimal assessment of PsA patients are: painful/swollen joints, enthesitis, dactylitis, axial involvement, skin and nail involvement, physical function, quality of life, structural damage assessed by imaging techniques, CRP, both patient and physician global assessment, both patient and physician skin assessment and extra-articular manifestations. The use of a treat-to-target (T2T) strategy should be considered in PsA patients, especially in those

with a high risk of progression of structural damage. Although the ideal therapeutic goal is remission, there is consensus that low disease activity (LDA) is an acceptable goal. The most recommended tool to assess the disease activity in the clinic is DAPSA, with cut-off values of ≤ 4 for remission and > 4 to 14 for LDA. In patients who have reached the minimum activity of the disease, there was agreement in which the most suitable index was the MDA (Minimal Disease Activity), with cut-off values of 5 to 7. ASDAS (or alternatively BASDAI) may be used in cases with axial involvement. There was also consensus to include the Psoriatic Arthritis Impact of Disease questionnaire (PsAID) for the assessment of patients' quality of life in follow-up consultations. The proposed definition of clinical remission in PsA is the absence of disease activity assessed using DAPSA or MDA (and/or ASDAS in patients with axial involvement), and the absence of later radiological progression.
Conclusion: On the basis of the available evidence and expert consensus, recommendations have been made for disease activity assessment in PsA and a proposal for definition of clinical remission was made that may be useful in the management of PsA patients
Disclosure of Interests: None declared
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AB0788C **PSORIASTIC ARTHRITIS IN PATIENTS DIAGNOSED WITH PSORIASIS ASSISTING DERMATOLOGY CONSULTATION IN A COHORT OF THE DOMINICAN REPUBLIC**

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Background: Psoriatic arthritis (PsA) is a disease of an inflammatory, heterogeneous nature that involves skin, nails, peripheral and axial joints, as well as the entheses. Due to its systemic involvement, it makes diagnosis and therapy a challenge in clinical practice. (1) It has been estimated that around 6% to 41% of patients with Psoriasis (Pso) will develop PsA, finding an accumulated incidence of 1.7% at 5 years of diagnosis of Psoriasis, 3.1% at 10 years and 5.1% at 20 years (2). In the Dominican Republic we do not have studies that characterize this pathology, so it would be interesting to be able to specify the clinical course, as well as the risk factors and associated prognoses for the development of this entity.
Objectives: To determine the factors associated with psoriatic arthritis in patients diagnosed with psoriasis attending the Dermatology service.
Methods: A multicenter, descriptive study of primary and secondary source data collection was conducted at the Psoriasis clinic of the Regional University Hospital José María Cabral and Báez, Cibao Regional Dermatological Institute and the Foundation to support patients with psoriasis and psoriatic arthritis (FUNAPAPSO), in the period of August-December 2018, the universe consisted of 304 patients, 103 patients met inclusion criteria. After signing informed consent, a form was completed that included general, clinical, serological and image data. Analysis of the variables was performed and Chi 2 was used, considering statistical significance p <0.05.
Results: Of a total of 103 patients with psoriasis, the mean age was 40 ± 13 years, 63.1% male, 36.9% female. The prevalence of psoriatic arthritis by CASPAR criteria was 36.89%. The presentation of arthritis was asymmetric oligoarthritis in 56.52%, symmetric polyarthritis 21.74% and distal interphalangeal arthritis 13.04%, radiographic findings were present in 7.77% (p: 0.00) of patients with PsA. The forms of presentation of Pso that were most associated with arthritis were plaques 48.57% (p: 0.000) and drop 12.5% (p: 0.01). The quality of life was average in 39.47% and poor in 18.42%. Psoriasic onychopathy was present in 40.23% (p: 0.048) of patients with arthritis. 39% of patients had some type of comorbidity, and of these arterial hypertension obtained 34% (n = 13), obesity 26% (n = 10) and diabetes mellitus 21% (n = 8).
Conclusion: The presence of psoriatic arthritis in the population with psoriasis in our environment is high. This is related to the presence of psoriatic onicopathy, radiographic findings and deterioration in the quality of life of patients.

REFERENCES

[1] S Raychaudhuri, RW, AS, SR, EM. Management of psoriatic arthritis: Early diagnosis, monitoring of disease severity and cutting edge therapies. Journal of Autoimmunity. 2016 Octubre.
[2] A Ogdie P. The Epidemiology of Psoriatic Arthritis. Rheum Dis Clin N Am. 2015
[3] P Helliwel. Natural history, prognosis and socioeconomic aspects of Psoriatic Arthrits. Rheum Dis Clin N Am. 2015
[4] M. Boutet, AGC. Role of the IL-23/IL-17 axis in Psoriasis and Psoriatic Arthritis: the clinic importance of its divergence in skin and joints. Int J Molc Sci 2018; 19(2):p.530
[5] L. Sakkas. Are psoriasis and psoriatic arthritis the same disease? Autoimmunity Review. 2017 Enero; 16(1): p10-15
[6] J Torre. Utilidad y aplicación en la práctica clínica de los criterios CASPAR. Reumatol Clin 2010; 6(1):p 18-21
[7] L Gossec, LM, AS, PC, DJ. Management of psoriatic arthritis in 2016: a comparison of EULAR and GRAPPA recommendations. Nature Reviews Rheumatology. 2016

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Osteoarthritis

AB0789 **AN EHEALTH TOOL TO PREPARE A FIRST ORTHOPAEDIC CONSULTATIONS: A USE AND USABILITY STUDY**

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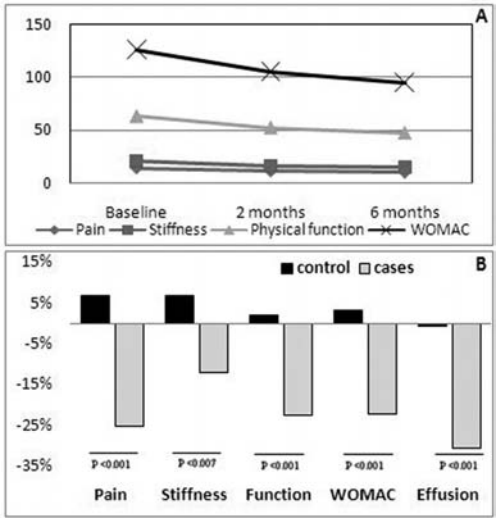
Background: The use of eHealth technology to prepare first orthopaedic consultations for patients with hip or knee osteoarthritis seems promising. Exploration of data on use and usability of an educational eHealth tool can reveal potential modifications that may increase engagement and effectiveness.
Objectives: 1) to identify use and usability of a standalone educational eHealth tool for patients with suspected hip or knee osteoarthritis (OA), 2) to explore if recorded questions in the eHealth tool were in line with an existing widely used question prompt list, and 3) to investigate if user characteristics are related to use and usability.
Methods: We used data of 144 patients who used the educational eHealth tool to prepare an upcoming first orthopaedic consultation. We defined 'users' and 'non-users' based on opening the tool at least once or not. 'Users' were specified as 'active' and 'passive'. Recorded questions in preparation for the upcoming consultation were categorized into 3 themes: 'What are my options?', 'What are the possible benefits and harms of those options?' and 'How likely are each of the benefits and harms to happen to me?', or in a 'remaining' category. Usability was measured using the System Usability Scale (SUS, 0-100). We collected data on demographic and clinical characteristics, knowledge on OA and internet and smartphone usage in daily life. Characteristics associated with 'users' and 'non-users' were analysed using multivariable logistic regression analysis.
Results: A total of 116 (81%) participants used the educational eHealth tool, of whom 87 (75%) were 'active users'. Out of 3 components ('Information', 'My consultation' and 'Medication), 'Medication' was least used (34%). Based on the recorded questions of users a fourth predefined question could be proposed, i.e. "What is my situation at this moment?". Mean (SD) SUS score was 64.8 (16.0). No difference was found in SUS scores between superficial and active users (mean difference (95% CI): 0.04 (-7.69, 7.77)). Participants with higher baseline knowledge on OA (OR (95% CI): 1.2 (1.0, 1.4)), who used the internet less frequent in daily life (OR (95% CI): 0.6 (0.5, 0.9)) were more likely to use the educational eHealth tool. We found no differences in demographic and clinical characteristics between superficial and active users.
Conclusion: Based on the results of this study it can be concluded that the use of an educational eHealth tool to prepare a first orthopaedic consultation in patients with hip and knee OA is feasible. Results provide points for improvements to the content of the tool to improve usability. No clear practical implications were found in this study to support implementation of the educational eHealth tool in specific subgroups.
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AB0790

EVALUATING THE EFFECTIVENESS OF INTRA-ARTICULAR KNEE INJECTION USING ALLOGENIC PLATELET DERIVED LYOPHILIZED GROWTH FACTORS IN EGYPTIAN PATIENTS WITH SYMPTOMATIC PRIMARY KNEE OSTEOARTHRITIS

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Background: Using intra-articular injections of autologous platelet-rich plasma (PRP) has showen promising results in treatment of knee osteoarthritis (KOA). Its regenerative properties depends on the amount of growth factors (GF) released after platelets activation. Using large-volume of blood for obtaining allogenic PRP can provide higher concentrations of platelet and GF. However once prepared, PRP is stable for only 8-hours. Freeze drying (lyophilization) can be used to stabilize the biological materials for prolonged storage without causing their damage (1).
Objectives: Investigating the effectiveness of intra-articular allogenic lyophilized growth factors (L-GF) injection in patients with symptomatic KOA using clinical and knee ultrasonography assessment.
Methods: 30-patients with symtomatic primary KOA, diagnosed according to revised criteria of the ACR (2), were enrolled. Local ethical approval was obtained. All patients had given a written informed consent. The study group was equally randomized into intervention and control groups. Both was subjected to baseline functional assessment using WOMAC score; evaluating pain, stiffness, and physical function (3), and ultrasonography (US) assessment of knee effusion. The patients in control group were kept on their medications without intervention. The intervention group was recieved two doses of L-GF; at baseline and after 2-months. L-GF was prepared from platelets derived from individual whole blood donations. Each unit of platelets was tested in and found to be non-reactive for HBsAg, HIV I & II antibodies, HIV p-24 antigen, HCV antibodies and antibodies to Treponema Palidum, by licensed assay methods. Seronegative plasma were further examined by Nuclear Acid Testing. Further viral inactivation by UV-radiation and Riboflavin by the Mirasol system was done. The platelets in the buffy coat layer were activated using $CaCl_2$ to release their GF. Excess water, cellular elements and fibrinogen were removed and the remaining GF were “ultraconcentrated.” Lyophilization of the obtained GF was then processed. The L-GF was supplied as powder in tightly sealed container and was stored at 2° to 8° C. Prior to use, reconstitution of the product was done using 1-ml saline and 1-ml lignocaine then the mixture was kept at ambient temperature for 5-min. to ensure complete protein re-hydration. After 6-months the WOMAC score and knee US were repeated for all particepients. Then percent of improvement of WOMAC and US detected effusion were calculated for all patients.



Results: The patients in the intervention group was significantly older (56 ±9 years) and had heigher BMI (38±5.3 kg/m^2) in comparison to control (44±11 years, 33±5.6 kg/m^2). Both groups showed statistically insignificant difference regarding the baseline total WOMAC score and radiographic assessment. Post injection pain was reported by all patients in intervention group, it lasted only for 2.4±0.83 hours and was graded as mild. The mean of total WOMAC score and its 3-compenents in addition to knee effusion were decreased significantly in the intervention group after 2 months and 6 months of follow-up (figuer-A). After 6-months, the intervention group showed statistically significant persentage of improvement regarding WOMAC scores and effusion in comparison to the control (figuer-B).
Conclusion: Allogenic L-GF was well tolerated and showed encouraging results in patients with symptomatic KOA, regarding improvement of pain, stiffness and function in addition to decreasing knee effsuion.

REFERENCES

[1] Pan L, et al. Aesth Plast Surg. 2016;40: 157.
[2] Altman R, et al. Arthritis Rheum 29:1039, 1986.
[3] Bellamy N, et al. J Rheumatol 1988; 15:1833-40.

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AB0791

ONE VERSUS TWO INJECTIONS OF INTRA-ARTICULAR HIGHLY CROSS-LINKED HYALURONAN YEARLY IN PATIENTS WITH KNEE OSTEOARTHRITIS: INSIGHTS FROM ROUTINE CLINICAL PRACTICE

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Background: Hyaluronic acid (HA) is a natural polysaccharide, which is an important structural component of synovial fluid and cartilage. There are different injectable forms of HA used for clinical application. Highly cross-linked/high-molecular-weight hyaluronans (HMWHA) provide additional stability and improve functionality [1], resulting in longer bioavailability in the knee joint and promoting viscoinduction [2]. A direct comparison between the two most common injection protocols of HMWHA in our routine practice is of great practical interest, since viscosupplementation is among the most commonly used treatment modalities for patients with knee osteoarthritis (KOA) in Bulgaria [3].
Objectives: Our aim was to compare the clinical effectiveness of two different regimens for injecting intra-articular HMWHA in KOA patients under ‘real-world’ conditions in routine clinical practice.
Methods: This prospective, open-label, observational study included 50 patients with KOA who were followed for a period of 1 year. They were divided into two therapeutic arms according to their preselected treatment regimen: patients injected once with HMWHA (n = 25; group 1) at baseline and patients injected twice 6 months apart with HMWHA (n = 25; group 2). A 100-mm visual analogue scale (VAS) for pain, disease-specific (Western Ontario & McMaster Universities Osteoarthritis Index [WOMAC]) and generic (health assessment questionnaire – disability index [HAQ-DI]) questionnaires were used to evaluate patients at baseline, three months, six months, and one year later. Standardized radiographs were obtained at baseline and after one year. The response to the treatment was determined using the OMERACT-OARSI set of responder criteria [4].
Results: A single injection of HMWHA resulted in a statistically significant improvement in pain even at 12 months (ΔVAS = 10.12 ± 14.5 mm, $p < 0.05$), although the effect progressively decreased after the third month when ΔVAS was 18 ± 14.31 mm, $p < 0.05$ (Figure 1). If the two regimens of HA injections were directly compared, the mean difference of pain improvement for the year of follow-up was about 9 mm in favor of group 2, but this result was not “statistically” significant (10.12 vs 19.16 mm, $p > 0.05$). Physical function was statistically improved in both

groups ($p < 0.05$) without any statistically significant difference. Responders in the first group in the end of the year were 40% (10/25) and 60% (15/25) in group 1 and group 2, respectively ($p > 0.05$). In the end of the follow-up period HAQ-DI did only statistically improve among patients in group 2.

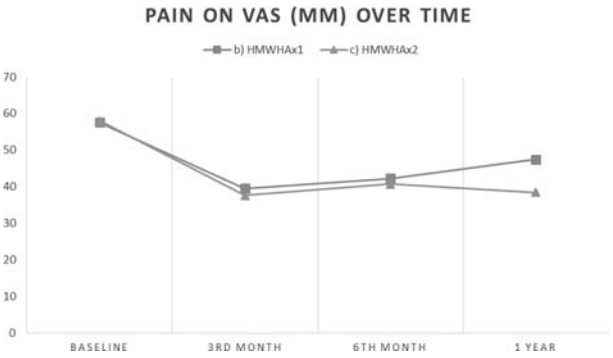


Fig.1. Mean change in 100-mm VAS values for pain over time in both groups

Conclusion: If maximal symptomatic relief is our primary goal, it would be logical to choose a two-injection regimen. However, if we take into account the financial aspect, we may be satisfied with a single injection of highly cross-linked HA over a year.

REFERENCES

[1] Bowman S, Awad ME, Hamrick MW, Hunter M, Fulzele S. Recent advances in hyaluronic acid based therapy for osteoarthritis. Clinical and translational medicine. 2018 Dec;7(1):6. doi: 10.1186/s40169-017-0180-3
[2] Divine JG, Zazulak BT, Hewett TE. Viscosupplementation for knee osteoarthritis: a systematic review. Clin Orthop Relat Res. 2007;455:113–122.
[3] Georgiev T, Stoilov R. Bulgarian rheumatology: science and practice in a cost-constrained environment. Rheumatology International. 2018 Nov 9:1-3. doi: 10.1007/s00296-018-4202-2
[4] Pham T, van der Heijde DM, Altman RD, Anderson JJ, Bellamy N, Hochberg M, Simon L, Strand V, Woodworth T, Dougados M. OMERACT-OARSI initiative: Osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited. Osteoarthritis and Cartilage. 2004 May 1;12(5):389-99.

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AB0792 CURCUMIN IN OSTEOARTHRITIS TREATMENT: THE PRESENT STATE OF EVIDENCE

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Background: Osteoarthritis (OA) is a degenerative disease of the joint occurring in elderly population. According to World Health Organization, its worldwide prevalence ranges from 11,8% to 12,7%. Since it is known that OA has an inflammatory cause, with IL-1β and TNF-α being the key cytokines that drive the production of inflammatory mediators and matrix-degrading enzymes, the compounds with anti-inflammatory properties are targeted as therapeutic options for osteoarthritis treatment. Curcumin is a plant-derived compound extracted from the rhizomes of turmeric (*Curcuma longa*). It has been demonstrated as an effective anti-inflammatory and antioxidative agent. In vitro studies have shown that curcumin can block the activation of NF-κB system in the chondrocytes. Therefore, it prevents the apoptosis of chondrocytes, suppress the release of proteoglycans and metal metalloproteases and expression of cyclooxygenase, prostaglandin E-2, and inflammatory cytokines in chondrocytes. Besides its influence on inflammatory markers, clinical trials also demonstrated curcumin's effects in pain and function in patients with osteoarthritis.
Objectives: The purpose of this paper is to critically review evidences regarding the role of curcumin in osteoarthritis treatment.
Methods: PubMed/MEDLINE, Lilacs, and SCIELO databases were searched using the terms "curcumin" AND "osteoarthritis" without imposing time limitations. The search was limited to humans and to the English and Portuguese languages. Studies that met the following inclusion criteria were included in the review: 1) clinical trials that evaluated the effects of curcumin on osteoarthritis. The selection phase involved a review of abstracts and an examination of the full text based on the eligibility criteria and the last search was conducted on January 2019.
Results: Overall, 9 clinical trials involving a total of 797 patients met the inclusion criteria. The studies have a degree of heterogeneity concerning the dosage, treatment duration, objectives and endpoints, but the main objectives were to evaluate the efficacy and safety of curcumin in osteoarthritis treatment. All studies have shown a beneficial effect of curcumin supplementation in the treatment of osteoarthritis, mainly in reduction of pain, stiffness, improvement of physical function, decrease the use of NSAIDs and other painkillers. Results also showed a decrease on inflammatory markers
Conclusion: The studies demonstrated that curcumin is clinically effective as a long term adjuvant treatment of osteoarthritis further to an excellent tolerability. However, large and well-designed randomized controlled trials are warranted to confirm the use of curcumin in osteoarthritis treatment.

REFERENCES

[1] BELCARO, G. et al. Efficacy and Safety od Meriva, a Curcumin-phosphatidylcholine Complex, during extended administration in osteoarthritis patients. Altern Med Rev, v. 15, n. 4, 2010.
[2] CHIN, K.Y. The spice for joint inflammation: anti-inflammatory role of curcumin in treating osteoarthritis. Drug Des Devel Ther, v. 10, p. 3029-3042, 2016.
[3] MIRZAEI, H. et al. Phytosomal curcumin: a review of pharmacokinetic, experimental and clinical studies. Biomedicine & Pharmacotherapy, p. 102-112, p. 85, 2017.
[4] MOBASHERI, A. et al. Scientific evidence and rationale for the development of curcumin and resveratrol as nutraceuticals for joint health. Int J Mol Sci, v. 13, p. 4202-4232, 2012.
ONAKPOYA, I.J. et al. Effectiveness of curcuminoids in the treatment of knee osteoarthritis: a systematic review and meta-analysis of randomized clinical trials. Int J Rheum Dis, v. 20, n. 4, p. 420-433, 2017.
Disclosure of Interests: Maria Goulart Employee of: Ache Laboratories, Daniela Partar Employee of: Ache Laboratories, Luis Cunha Employee of: Ache Laboratories, Stevin Zung Employee of: Ache Laboratories
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AB0793 LONG-TERM USE OF AMTOLMETIN GUACIL IN PATIENTS WITH OSTEOARTHRITIS, RHEUMATOID ARTHRITISAND ANKYLOSING SPONDYLITIS

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Background: Long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs) is used to control of chronic pain in osteoarthritis (OA), rheumatoid arthritis (RA) and to prevent the progression of ankylosing spondyloarthritis (AS). Amtolmetin guacil (AMG), which has a low risk of gastrointestinal complications, may have advantages for long-term use.
Objectives: To evaluate the effect and safety of long-term use of AMG.
Methods: AMG 600-1800 mg/day was prescribed to 442 patients with OA (60.6 + 10.2 years, women 88.7%), 126 with RA (55.0 + 14.0 years, women 84.2%) and 73 with the AS (47.0 + 12.0 years, women 30.0%). The primary end point was the dynamics of pain on a numerical rating scale (NRS), additional for OA - WOMAC pain and HAQ, for RA - DAS28-CRP, for AS - BASDAI, BASFI and ASDAS-CRP. The result of treatment was evaluated on 3 consecutive visits after 3 months (9 months of treatment).
Results: After 9 months 65.2% of OA patients, 75.3% of RA patients, and 82.2% of AS patients continued to take AMG. In end of study, the median of pain decreased with OA from 5.6 [4.1–6.9] to 3.4 [1.7–5.1], with RA from 5.8 [4.0–7.5] to 3.4 [2.0-4.8], with AS from 5.8 [4.2-7.5] to 3.1 [1.5-5.0] NRS ($p <0.001$). In OA WOMAC pain decreased from 127 [24-159] to 13.7 [14-40], $p <0.001$, HAQ from 0.54 ± 0.44 to 0.34 ± 0.26, $p <0.001$. With RA, the average value of DAS28 decreased from 4.81 + 1.18 to 4.30 + 1.24, $p <0.05$. In AS, the median BASDAI index decreased from 4.5 [1.0–8.0] to 3.0 [0–8.0], $p <0.001$. The number of AS patients with high activity on the ASDAS-CRP index (> 3.5) decreased from 76.9% to 25.8%, $p <0.001$. The BASFI index has not changed. 77.9% of patients with OA, 77.0% of patients with RA, and 74.5% of patients with AS were satisfied with the results of AMG treatment.

AMG tolerability was good. 15-25% patients had mild dyspepsia. Discontinuation of therapy due to side effects was only in 6 patients (0.93%). The development or worsening of arterial hypertension, as well as other cardiovascular complications, was not observed.
Conclusion: AMG is an effective, well-tolerated NSAID, which is appropriate for long-term treatment of OA, RA and AS.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.6102

AB0794 PATIENTS GENOTYPE AND OA TREATMENT EFFICACY

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Background: it is known that some genes (FDPS, LCT, VDR) which determine the calcium, vitamin D and lactate metabolism may have impact on osteoarthritis (OA) development and course, and thus, has a possible influence on OA treatment efficacy.
Objectives: To determine the influence of genetic factors (genotyping of FDPS, LCT, VDR) on the efficacy of standard and modified treatment (with use of the platelet autologous plasma (PAP) in the early stages of knee OA.
Methods: WOMAC index and the frequency of genotype variants for the FDPS, LCT, and VDR genes were studied in 96 patients (57 women, 38 men, 41.7 ± 1.2 years old) with primary knee OA (X-ray stage I-II). All patients had OA exacerbation with no clinical evidence of synovitis. Enrolled patients were divided into 2 groups: the first group consisted of 49 patients (27 women, 22 men, mean age 41.7 ± 1.2 years) who agreed to receive standard OA treatment (NSAID, exercises, orthopedic devises – as needed) and 3 intra-articular PAP injections (2 courses in 12 month, plasma volume 12-15ml/course, total platelet count per injection 1260,24 ± 22,1x10^9). The second group - 47 patients with OA who received standard treatment. Both groups were comparable by age, gender, body mass index and initial WOMAC. Genetic parameters and its influence on OA course and treatment efficacy was analyzed during 12 months.
Results: The earliest age (37.2 ± 2.01 years) of clinical manifestation of knee OA was connected to homozygous genotype variants: LCT (relative risk 6.3:1), FDPS (relative risk 6.5:1) and VDR (relative risk 6.8:1). The best positive WOMAC changes was determined in patients with the CC genotype of LCT both in first and second groups. The WOMAC changes showed lower treatment efficacy in patients with CC genotype of FDPS and VDR in both groups, but results of patients who received PAP were better and their remission was longer (in 1.7 times) than in the standard treatment group.
Conclusion: age of knee OA clinical manifestation and the treatment efficacy (both standard and with the use of platelet autologous plasma) has genetic predisposition.
Disclosure of Interests: None declared
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AB0795 IMPACT OF PRIMARY HAND OSTEOARTHRITIS ON MICROSTRUCTURE AND BIOMECHANICS IN FINGER JOINTS

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Background: Primary hand osteoarthritis (HOA) is a heterogeneous disease that is associated with erosive and osteoproliferative changes of the finger joints and progressive functional impairment. Despite these severe changes the effect of HOA on bone mass, microstructure and biomechanics in the affected skeletal regions is largely unknown.
Objectives: To study the effect of HOA on bone microstructure, density and biomechanical properties using high-resolution peripheral quantitative computed tomography (HR-pQCT) of the finger joints and radius.
Methods: HOA patients and healthy controls (HC) underwent HR-pQCT scans of the distal radius and 2nd metacarpal (MCP 2) head. Total, trabecular and cortical volumetric bone mineral densities (vBMD) as well as microstructural and biomechanical properties (failure load) were determined. Failure load and scaled multivariate outcome matrices from distal radius and 2nd metacarpal (MCP 2) head measurements were analyzed using multiple linear regression adjusting for age, sex and functional status and reported as adjusted z score differences for total and direct effects.
Results: 105 subjects were included (76 HC/29 HOA). After adjustment, HOA was associated with significant changes in the multivariate outcome matrix of the MCP 2 head ($p < 0.001$) explained by an increase in cortical vBMD ($\Delta z = -1.07$, $p = 0.02$) and reduction in the trabecular vBMD ($\Delta z = 0.7$, $p = 0.09$) Distal radius analysis did not show an overall effect of HOA however there was a gender-study group interaction explained by reduced trabecular vBMD in males ($\Delta z = 1.23$, $p = 0.02$). HOA was associated with lower failure load [-514 N (95%CI:-1025,-2), p=0.05].
Conclusion: HOA is associated with reduced trabecular and increased cortical bone mineral density and a reduction in radial bone strength. Impaired mobility might be an explanation for this reduction. These results underline the clinical importance of HOA-related functional impairment and indicate that HOA patients should be treated with awareness of increased fracture risk and antiosteoporotic treatment.
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AB0796 DIFFERENCES AND SIMILARITIES OF THE BONE-CARTILAGE UNIT IN PATIENTS WITH PRIMARY OSTEOARTHRITIS AND SECONDARY OSTEOARTHRITIS CAUSED BY RHEUMATOID ARTHRITIS

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Background: Despite distinct aetiologies of joint diseases, the osteoarthritic end-stage of primary osteoarthritis and rheumatoid arthritis are described using similar radiological features. However, primary and secondary osteoarthritis may be different at the bone-cartilage unit depending on the pathogenesis.
Objectives: The main purpose was to investigate the histological differences in the bone-cartilage unit of the hip joint in patients with primary osteoarthritis and patients with secondary osteoarthritis due to rheumatoid arthritis.
Methods: Femoral heads were obtained during arthroplasty from 12 patients with primary osteoarthritis and six patients with secondary osteoarthritis due to rheumatoid arthritis. Twelve femoral heads from healthy age- and sex-matched subjects were obtained post-mortem. Femoral heads were investigated, using stereological methods to provide unbiased quantitative data. The femoral head, articular cartilage, calcified cartilage, subchondral bone, and osteophytes were measured.

Table 1:. Volume and thickness of the bone-cartilage unit, femoral head volume and osteophyte area in healthy subjects (HS), osteoarthritis (OA) and rheumatoid Arthritis (RA) patients.

	Healthy subjects (n = 12)	Osteoarthritis (n = 12)	Rheumatoid Arthritis (n = 6)	ANOVA	OA vs RA	HS vs RA	HS vs OA
		Mean [95%CI]			P - value		
Age (years)	62[60;65]	62 [59;65]	63[60;65]	*0.984*	—	—	—
Gender (M:F)	6:6	6:6	3:3	*1.000*	—	—	—
Femoral head volume (cm^3)	52.0[39.6;64.3]	43.6[37.3;50.0]	41.1[33.6;48.7]	0.233	—	—	—
Articular cartilage volume (cm^3)	7.4[5.9;8.9]	5.1[4.0;6.1]	2.9[1.6;4.3]	**<0.001**	**0.012**	**<0.001**	**0.021**
Articular cartilage thickness (μm)	1413 [1244;1582]	1134 [931;1338]	721[403;1040]	**<0.001**	**0.029**	**<0.001**	0.086
Subchondral bone thickness (μm)	227[172;282]	406[285;527]	409[186;632]	**0.021**	1.000	0.099	**0.034**
Calcified cartilage thickness (μm)	108[81.1;143]	119[94.1;151]	56.6[25.3;127]	**0.016**†	**0.017**	**0.046**	1.000
Osteophyte area (mm^2)	8.8[2.2;35.7]	70.9[41.4;121]	49.2[4.7;513]	**0.008**†	1.000	0.073	**0.006**

Data are presented as mean [95%CI], Statistical significance was found using one-way ANOVA. The Post-hoc Bonferroni test was used to identify intergroup differences. †Data not normally distributed was log-transformed and presented as geometric mean [95%CI].

Conclusion: Patients with secondary osteoarthritis due to rheumatoid arthritis had thinner articular cartilage and calcified cartilage but were otherwise not significantly different from patients with primary osteoarthritis. Thus, the inflammatory joint in rheumatoid arthritis was associated with a more pronounced loss of cartilage than the degenerative joint disease in primary osteoarthritis. The thicker calcified cartilage in primary osteoarthritis has been attributed to endochondral ossification; this does not seem to be the case in rheumatoid arthritis.

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AB0797 GRANULYSIN MEDIATED CYTOTOXICITY AND ITS SERUM CONCENTRATION IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: In OA joint, synovial membrane contain immunocompetent cells (1-4), which produce predominantly pro-inflammatory cytokines (2,5), justifying the name "osteoarthritis" and directing the development of disease towords mild systemic inflammatory condition (6). Granulysin (GNLY) is mediator of cellular immunity expressed in T and NK cells in 15 kDa precursor and 9 kDa cytotoxic forms (2). It is regulated by interleukin 15. We investigated GNLY expression in perifperal blood lymphocytes and GNLY mediated apoptosis *in vitro*, serum concentration of IL-15 and the correlation of GNLY expression with intensity of the pain in the knee of OA patients and with 6-minute walk distance.

Objectives: Women with knee OA (20), and healthy control (17) were medically examined, and their blood samples tested. All of them signed informed consent before medical sampling of peripheral blood (PB).

Methods: Visual analogue scale (VAS) of pain and results of 6-minute walk test were noticed in all participants. Peripheral blood mononuclear cells were isolated by gradient density centrifugation and intracellular GNLY labeling in CD3-CD56+NK cells, CD3+CD56- T cells and CD3 +CD56+ NKT cells was performed and analyzed by flow cytometry. NK cells' apoptotic activity against NK sensitive K-562 cells was measured in 18-hour PKH-26 (red) cytotoxicity assay with evaluation of propidium iodide-/annexin V+ target cells by flow cytometry. In some samples anti-GNLY and/or anti-perforin antibodies were added. IL-15concentration was measured by ELISA. Nonparametric Kruskal-Wallis and Mann-Whitney U-test, as well as Spearman correlation test were used for statistical evaluation.

Results: In lymphocytes of OA patients GNLY expression and NK cell-mediated apoptosis of K-562 cells did not differ significantly from the healthy control. In OA patients only, RC8 antibody against cytotoxic GNLY molecule significantly decreased apoptosis of K-562 cells. RF10 anti-15 kDa GNLY did not show such effect. Anti-perforin antibody completely abolished apoptosis in both groups tested and the effects of additionally added RC8 or RF10 anti-GNLY antibodies were not observed. Serum IL-15 concentration in healthy controls and OA patients was low and did not show statistically significant difference. GNLY expression in lymphocytes, and particularly in NK subset, positively correlated with VAS of pain and 6-minutes walking distance.

Conclusion: In OA patients, GNLY mediated apoptosis is involved in apoptosis of NK sensitive K-562 cells *in vitro* and might be involved in the killing of damaged joint cells *in vivo* after direct contact.

REFERENCES

[1] Lindblad S, Hedfors E. Arthritis Rheum. 1987;30(10):1081-8.
[2] Wojdasiewicz P, et al. Mediators Inflamm. 2014;561459.
[3] Leheita O, et al. Egypt J Immunol 2005;12:113-24.
[4] Huss RS, et al.. Arthritis Rheum. 2010;62:3799-805.
[5] Imamura M, et al. Int J Inflam. 2015;2015:329792.
[6] Maldonado M, Nam J. Biomed Res Int. 2013;2013:284873.

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AB0798 GENDER DIFFERENCES IN DURATION OF SYMPTOMS AND PREOPERATIVE EXPECTATIONS IN TOTAL KNEE ARTHROPLASTY PATIENTS

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Background: The literature suggests that women with knee osteoarthritis (OA) perceive greater disability and a lower functional level before total

knee arthroplasty (TKA) and undergo surgery at a later stage of the disease than men, which could lead to worse postoperative outcomes (1). These differences have been attributed to differences in the interpretation of symptoms between men and women (2), yet little is known about expectations of the postoperative outcomes of TKA.

Objectives: To compare the duration of symptoms before TKA and the preoperative expectations of postoperative outcomes of TKA between men and woman.

Methods: Preoperative data from a multicenter cohort study on outcomes of primary TKA were used. Preoperatively, patients were asked to indicate the duration of symptoms to TKA (<1 year, 1-5 years, 5-10 years and >10 years). The Hospital for Special Surgery (HSS) Knee Replacement Expectations Survey was used to obtain information on expectations regarding postoperative pain relief, mobility and daily activities and improvement of quality of life (score range 0-100), with lower scores indicating higher expectations. In addition, the Knee injury and Osteoarthritis Outcome Score (KOOS), pain (Numeric Rating Scale, NRS), comorbidities and work-status were gathered. Differences between men and women regarding the duration of symptoms and preoperative expectations were examined by the means of the Chi-Square test and independent t-test and difference with the 95% Confidence Interval (CI) respectively.

Results: A total of 1543 patients, 556 men (mean age 71 (SD 8), 32.3% paid employment) and 987 women (mean age 71 (SD 9), 20.3% paid employment) were included. Women had more pain preoperatively than men, 5.3 (SD 3) versus 4.3 (SD 3) at rest and 7.1 (SD 2) versus 6.2 (SD 3) during activity, respectively. Furthermore, men scored better on each KOOS subscale compared to women. Overall the duration of symptoms was longer in men than women: <1 year: 11.3% versus 9.6%, 1-5 years: 38.8% versus 49.7%, 5-10 years: 18.3% versus 20.0% and > 10 years: 31.5% versus 20.7%. Finally, women had significantly higher expectations of postoperative TKA outcomes than men, 67.4 (SD 19) and 70.2 (SD 19), respectively (Mean Difference; 2.79, 95% CI 0.84-4.75).

Conclusion: Preoperatively, men reported a longer duration of symptoms and had lower expectations of TKA outcomes than women. However, men seemed to perceive less symptoms and restrictions in daily activities despite a longer duration of symptoms.

REFERENCES

[1] Katz JN, Wright EA, Guadagnoli E, Liang MH, Karlson EW, Cleary PD. Differences between men and women undergoing major orthopedic surgery for degenerative arthritis. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 1994;37(5):687-94.

[2] Parsley BS, Bertolusso R, Harrington M, Brekke A, Noble PC. Influence of gender on age of treatment with TKA and functional outcome. Clinical Orthopaedics and Related Research®. 2010;468(7):1759-64.

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AB0799 ART- QUALIVIE: ASSESSMENT OF THE QUALITY OF LIFE OF PATIENTS WITH KNEE OSTEOARTHRITIS SIX MONTHS AFTER TREATMENT WITH THREE INTRA-ARTICULAR INJECTIONS OF ARTHRUM H 2%

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Background: Knee osteoarthritis (KOA) is a chronic condition affecting mainly the elderly and considered as the leading cause of disability after cardiovascular disease. KOA is characterized by functional discomfort and deformities, leading to a deterioration in the quality of life (QoL) of patients.

Objectives: The main objective was to demonstrate that 3 intra-articular injections of ARTHRUM H 2% improves the physical QoL of patients over a 6-month period.

Methods: A French observational, prospective, multi-centre study was conducted between 02/2016 and 07/2017 in patients over 40 suffering from Kellgren and Lawrence (KL) grade I, II or III primary KOA and treated with 3 intra-articular injections of ARTHRUM H 2%. The variables included a questionnaire completed by a physician and the validated 12 items Short Form Health Survey (SF-12), completed by patients at baseline (right before the injections), and then at 90 and 180 days. The primary endpoint was the change in physical summary score from baseline to 180 days (paired Student t-tests). Logistic regression analyses were used to identify the mains drivers of significant increase of physical summary score, adjusted for sociodemographic and health covariates.

Results: Of the 134 patients treated with ARTHRUM H 2% included in the study, 115 were evaluable for the primary outcome (non-exploitable data for 19 patients).

The baseline characteristics of the analysable population were as follows: mean age of 66.4 years (±10.7); majority female (66.4%); mean BMI of 28.7 (±5.3) kg/m^2 (43.3% overweight and 35.1% obese); KL grade KOA grade: I 13.6%, II 40.2%, III 46.2%; localization: uni-compartmental 53.0% (78.6% medial, 15.7% lateral, 5.7% patellofemoral), bi-compartmental 40.2% and tri-compartmental 6.8%. Regarding management history, respectively 6.7% and 44.8% of patients had previously received physical therapy or rehabilitation, and a visco-supplementation (2.2 treatments on average). Comorbidities observed in 73.9% of patients were metabolic-related in 54.5%, cardiovascular-related in 46.3%, gastrointestinal-related in 20.9%, and neurological-related in 8%.

A clinically and statistically significant improvement in the QoL of patients was observed with an increase from 40.0 at baseline to 44.8 at 6 months ($p<0.001$). A significant improvement was achieved during the 3 months following visco-supplementation (D0: 40.0 vs. D90: 44.8) and maintained from three to 6 months from baseline (D90: 44.8 vs. D180: 44.9).

The factors significantly associated with an improvement in QoL were: grade III KOA (OR=5.254, p=0.032), grade II KOA (OR=3.507, p=0.100), lateral femorotibial osteoarthritis (OR=3.175, p=0.029) and a single history of visco-supplementation (OR=2.936, p=0.044).

Conclusion: ART-QUALIVIE is a French study providing real-world data on the evolution of QoL of visco-supplemented KOA patients. It has demonstrated the positive impact of ARTHRUM H 2% on the QoL of patients over the 3 months following injections maintained until 6 months after treatment.

REFERENCES

[1] Maheu E, Zaim M, Appelboom T, et al. Comparative efficacy and safety of two different molecular weight (MW) hyaluronans F60027 and Hylan G-F 20 in the symptomatic osteoarthritis of the knee (KOA). Results of a non-inferiority, prospective, randomised, controlled trial. Clin Exp Rheumatol 2011; 29:527-535.

[2] Gandek B, Ware JE, Aaronson NK, et al. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: Results from the IQOLA Project. International Quality of Life Assessment, J Clin Epidemiol 1998;51(11):1171-1178.

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AB0800 ESTABLISHMENT OF TECHNICAL PERFORMANCE CRITERIA AND REFERENCE INTERVALS FOR OSTEOARTHRITIS-RELATED SOLUBLE BIOMARKERS: THE APPROACH CONSORTIUM

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Background: Disease modifying therapy of osteoarthritis (OA) represents an unmet clinical need, and appropriate outcome measures are required that can robustly identify patients with different OA phenotypes who may benefit from specific and more targeted therapies. APPROACH is an exploratory, 5-centre, 2-year prospective follow-up European cohort study. It entails extensive clinical, imaging, biomechanical and biochemical parameters, in a cohort recruited using machine learning models based on retrospective patient data to display a high likelihood of radiographic joint space width loss, MRI changes and/or knee pain over the course of the study. Biochemical markers (biomarkers) can be used to understand

pathogenesis, drug mode of action and as prognostic tools, as well as finding the right treatment for the right patients.

Objectives: Different biomarkers were selected to be measured in APPROACH patient samples for prospective predictive and prognostic analyses. Here we describe the biological rational, reference ranges and technical performance of the selected biomarker.

Methods: The APPRAOCH cohort includes 300 OA patients recruited based on the APPROACH enrichment model (www.approach.eu), in the period from 2017 and 2019. Serum and urine will be collected at baseline, 6, 12 and 24 months, as well as pain, radiographic and MRI assessments.

Results: Eighteen exploratory and technically validated biomarkers reflecting joint tissue (i.e. cartilage, bone, synovium) turnover were chosen based on following characteristics; i) has shown association with OA pathogenesis (published data such as OAI[1]); ii) has shown diagnostic or prognostic potential [2]; iii) GLP or GMP certified assay production with acceptable technical performance (e.g. precision and linearity data, table); iv) readily availability of the kits from consortium partner or from third party vendor. The markers will be tested asking following research questions: Can the markers alone or in combination subgroup patients into different phenotypes which display different progression rates, or with different pain and radiographic profiles. Also, we will test whether a change in markers are correlated with change in the clinical assessments scores. Results from these analyses may provide insight to the potential usage of the biomarkers in drug development.

Biomarker	Description	Analysis method	Reported donor range in Serum and Urine (n>30)	Technical performance with in the dynamic range of the assay • Precision (Intra/Inter-assay CV %) • Serum/urine linearity within the measurement range (relative error %)
S-ARGS-aggrecan [3]	Aggrecan degradation	Electro-chemiluminescence	0.010 – 0.200 pmol/mL	2.8% (mean)/10% (mean) -15.3 to 21.4%
		Chemiluminescence	132 – 1844 U/mL[b]	<3.1% /<15.2 (max) -10.1 to 4.9 %
S-C1M [4]	Type I collagen degradation	Colorimetric	28.7 – 66.8 ng/mL	<17.7% / <11.6 % (max) -7.8 to 2.4 %
S-C2M [5]	Type II collagen degradation	Colorimetric	0.162 – 0.938 ng/mL	<17.7% / <11.6 % (max) -8.8 to 15.4 %
S-C3M [4]	Type III collagen degradation	Colorimetric	13.1 – 31.1 ng/mL	<13.5% / <14.5 % (max) -9.5 to 12.8%
S-C-Colneo (C10C) [6]	Type X collagen degradation	Colorimetric	600 – 1800 umol/L	<7.6% / <11.6 % (max) -9.4 to 9.5%
S-ColII2-1 [7]	Type II collagen degradation	Colorimetric	160 – 224 nmol/L	<9% / <20% (max) -6.2 % to 8.6%
S-ColII2-1-NO2 [7]	Nitrated form of colI2-1	Colorimetric	ND [a]	<12% / <13% (max) -10.3 % to 9.4 %
S-COMP [1]	Cartilage oligomeric protein	Colorimetric	ND [a]	ND [a]
S-CRPM [5]	C-reactive protein degradation	Colorimetric	4.4 – 11.7 ng/ml	<11.1 / <20.8 % (max) -12.2 to 8.6 %
S-CTX-I [1]	Type I Collagen C-terminal Telopeptide (cross-linked)	Chemiluminescence	16 – 1008 pg/mL	ND [a]
S-F3F [8]	Fibulin-3	Colorimetric	ND [a]	<10%/<11% -13.4 to 12.5%
S-HA [1]	Hyaluronan	Colorimetric	20 – 196 ng/mL	<7.2 / <16.2 % (max) -5.8 to 7.6 %
S-hsCRP [1]	High sensitive C-reactive protein	Chemiluminescence (automatic)	ND [a]	<5 / <5 % (max) <±20%
S-hsPRO-C2 [9]	Type IIB Collagen synthesis	Electro-chemiluminescence	1.1 – 4.9 ng/mL	<15.9 / <13.3 % -15.1 to 12.2%
S-NMID [1]	Osteocalcin	Chemiluminescence (automatic)	11 – 46 ng/mL	<2.8 / <4.6 % (max) -4.0 to 8.1 %
S-PIIANP [1]	Type IIA Collagen Synthesis	Colorimetric	1236 – 4475 ng/mL	<10.8 / <16.6 % (max) -8.0 to 19.8 %
U-ALPHACTX-I [1]	Type I Collagen C-terminal Telopeptide	Colorimetric	ND [a]	<3.4/ <6.0 % <±20%
U-CTX-II [1]	Type II Collagen C-terminal Telopeptide	Colorimetric	ND [a]	<7.8 / <12.2 % -12.3 to 7.4 %

[a] ND; not determined by the consortium members, but reference can be found elsewhere. [b] U; units, ADAMTS5 cleavage units, corresponding. S- and U-; Serum and Urinary

Conclusion: The APPROACH consortium is the first European study that attempts to establish robust technical performance criteria and reference intervals for osteoarthritis-related soluble biomarkers in an effort to develop biomarker panels that can identify patients with different OA phenotypes.

REFERENCES

[1] Kraus VB et al. *OAC* 2015. 2) Bauer DC et al. OAC 2006. 3) Larsson S et al. OAC. 2014. 4) Wang SX et al. OAC 2017. 5) Bay-Jensen A-C et al. *Drug Discov Today* 2018. 6) He Y et al. OAC 2019. 7) Y. H, T. C, M. D, et al. *OAC* 2011. 8) Runhaar J et al. OAC *Cartil.* 2016. 9) Luo Yet al. *Int J Mol Sci*. 2018

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AB0801 RELIABILITY OF A NOVEL ULTRASONOGRAPHIC SCALE FOR ACTIVITY OF KNEE OSTEOARTHRITIS

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Background: Knee osteoarthritis
Objectives: To assess the reliability of a novel ultrasonographic scale of activity in knee osteoarthritis (OA)
Methods: A cross-sectional observational study included 110 patients with knee pain who fulfilled the American College of Rheumatology (ACR) criteria for knee osteoarthritis (OA). All patients were subjected to clinical assessment WOMAC scale (Western Ontario and McMaster Universities Index of Osteoarthritis and global visual analog scale) and functional assessment using health assessment questionnaire (HAQ). Ultrasonographic assessment of activity was done By 3 rheumatologists with different levels of experience in musculoskeletal Ultrasonography (1-12 years). Ultrasonographic assessments were done according to (MOAKA scale) that was proposed by the first author (table 1).

Abstract AB0801 Table 1. Mortada OsteoaArthritis Knee Activity score (MOAKA score)

Domain	Description	Score
Severity of knee OA	6 grades according to severity scale published by Mortada et al 2016 (1)	Grade 0: 0 Grade 1: 1 Grade2a: 2 Grade 2b: 3 Grade 3: 4 Grade 4: 5
Effusion	4 grades Grade 0:no effusion Grade 1: Mild effusion Grade 2: moderate effusion Grade 3: severe effusion	Grade 0: 0 Grade 1: 1 Grade 2: 2 Grade 3: 3
Synovitis	4 grades using the combined EULAR/OMERACT score of grey scale synovitis and Doppler activity	Grade 0: 0 Grade 1: 1 Grade 2: 2 Grade 3: 3
Pes Anserine tendonitis/bursitis	3 grades Grade 0:normal, Grade 1: mild inflammation Grade 2: severe inflammation	Grade 0: 0 Grade 1: 1 Grade 2: 2
Backer cyst	3 grades; Grade 0: normal no cyst, Grade 1: small and simple cyst Grade 2: large and/or complicated cyst	Grade 0: 0 Grade 1: 1 Grade 2: 2
Total scores	Sum of scores of all domains	0 - 15

Results: There were high kappa values both in intraobserver and interobserver evaluation of activity of knee OA using the proposed (MOAKA) ultrasonographic scale (0.85 and 0.75 respectively).
There were positive correlations between MOAKA score and all WOMAC subscales (pain, stiffness and function) (r=0.4, P=0.02, r=0.35, P=0.001 and r=0.4, P=0.01) respectively.
Also there were a strong positive correlation between MOAKA scale and both (VAS and HAQ) (r=0.86, P=0.001 and r=0.71, P=0.001)
Conclusion: US can reliably detect the activity of Knee OA. Good agreement was found between the proposed US grading scale and WOMAC & HAQ scores. MOAKA US scale is simple and reliable.
Disclosure of Interests: None declared
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AB0802 CYTOKINE PROFILE IN SYNOVIAL FLUID FROM PATIENTS WITH OSTEOARTHRITIS WITH OR WITHOUT CALCIUM CRYSTALS

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Background: The most important pathogenetic calcium crystals that can be found in synovial fluid (SF) are calcium pyrophosphate (CPP) and basic calcium phosphate (BCP) crystals. We and others have demonstrated that a good portion of patients with osteoarthritis (OA) have these type of crystals in their SF and that they are associated with a higher inflammatory state independently from the disease severity [1].
Objectives: The aim of this study was to investigate the levels of IL-1b, IL-8, IL-6, IL-10, CCL2 and OSMr in the SF of patients affected with OA considering the presence of CPP crystals and the positivity to the alizarin red test (a non-specific test for BCP crystals). A sub-analysis has been conducted subdividing patients according to their Kellgren-Lawrence (K-L) radiographic score.
Methods: Synovial fluid was collected from 69 OA consecutive patients diagnosed according to the EULAR criteria. Forty patients were negative to (CPP-) and 29 positive to (CPP+) CPP crystals. A standard analysis was performed for each sample including, white blood cell (WBC) count, differential cell count, crystal search under polarized light microscopy and alizarin red test. The cytokines were measured after appropriate dilutions by ELISA (Thermofisher) and expressed as pg/ml. The Mann-Whitney test was used to investigate differences between the groups of patients positive and negative to CPP; the Spearman rank test was used for correlations, while the Kruskal-Wallis to compare the groups according to the K-L score.
Results: With respect to the group of CPP-, the group of CPP+ patients had higher levels of WBC count (251.7±199.3 vs 176.3±161.8 cells/mm3; p=0.004), PMN% (5±7.1 vs 0.44±1.54; p<0.0001), IL-1b (8.92±6.29 vs 4.63±12.2; p<0.0001) and IL-8 (53.73±45.83 vs 26.20±35.94; p=0.0003). No differences were instead observed for the other cytokines considered. We did not find any differences subdividing patients according to the SF positivity to the alizarin red staining. Some correlations were observed in the whole group of patients between IL-1 and IL-8 (p=0.004), IL-1 and PMN (p=0.0006), IL-8 and WBC (p=0.001), IL-8 and PMN (p<0.0001), IL-10 and IL-8 (p=0.04),IL-10 and WBC (p=0.014), CCL2 and IL-6 (0.006).
Although no differences have been found analysing the variables in the groups subdivided by the K-L scores, all the cytokines showed higher levels in patients with a K-L score equal to 2.
Conclusion: Although associated with higher inflammatory SF indices and IL-1 and IL-8 levels, calcium crystals still play an undefined role in OA. More studies are warranted to evaluate if patients with calcium crystals in their SF might need a more specific treatment.

REFERENCE

[1] Frallonardo P, Ramonda R, Peruzzo L, Scanu A, Galozzi P, Tauro L, et al. Basic calcium phosphate and pyrophosphate crystals in early and late osteoarthritis: relationship with clinical indices and inflammation. Clin Rheumatol. 2018 Jun 7.

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AB0803 SYNOVIAL INTERLEUKIN-8 LEVELS ARE ASSOCIATED TO RADIOGRAPHIC SEVERITY OF KNEE OSTEOARTHRITIS. A CROSS-SECTIONAL STUDY

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Background: Radiographic severity is used in routine clinical practice to evaluate knee osteoarthritis (KOA) structural damage. There are no conclusive studies on the associations between synovial inflammatory markers and the different features of radiographic damage in KOA.

Objectives: To evaluate the association between inflammatory markers in synovial fluid with the different features of radiographic severity in patients with KOA.
Methods: Cross-sectional study of 114 female patients aged 50-85 with symptomatic primary KOA with significant joint effusion (>4 mm at midline patellar line) confirmed by ultrasound. The following information was collected: age, KOA symptoms duration, body mass index; plain standing knee Rx in semi-flexion were evaluated for radiographic severity by modified OARSI atlas evaluating separately osteophytes (OPH) and joint space narrowing (JSN). The OPH score was obtained searching for marginal osteophytes in both medial and external femoral condyles and tibial plateaus, scoring 0 to 3 in each quadrant, for a total score ranging from 0-12. Due to the high number of different scores obtained, and sometimes with a low number of patients, we grouped osteophytes scores 1-2 as mild, 3-6 as moderate and seven or more as severe osteophyte count. The JSN score was calculated in both medial and lateral knee compartments, grading the joint space 0 to 3 in each one, for a total score ranging from 0 to 6. A JSN score of 0 was considered as normal, 1-2 as moderate and 3 or more as high JSN severity. Five inflammatory markers: TNF alpha, high sensitivity C-reactive protein (hsCRP), interleukin 6 (IL-6), interleukin 8 (IL-8) and calprotectin were measured by ELISA following manufacturer recommendations for synovial fluid dilutions. A comparison between medians of the three groups was carried out and a multivariate analysis controlled by age, symptom duration, BMI and all five inflammatory markers were performed.
Results: A significant association for symptom duration and synovial IL8 was observed for osteophytes ($p<0.0001$ and $p<0.05$, respectively), which remained after adjustment ($p=0.002$ and $p=0.037$, respectively). Regarding symptom duration, the differences were related to high severity osteophyte index, compared to moderate or low stages ($p= 0.0005$ and $p=0.002$, respectively), while for IL-8 the differences were associated to a low OPH severity index compared with a moderate osteophyte score ($p=0.011$), with IL-8 levels approximately 33% less than the moderate OPH score ($p=0.011$).
For JSN, in the adjusted analysis, patients with a high JSN score had synovial IL-8 levels of 40% more than those with JSN 0 ($p=0.035$), while no differences were found between the moderate JSN score and the other two degrees. Regarding hsCRP, 30% higher levels were found in patients with a JSN moderate degree compared with JSN 0 ($p=0.033$), while no significant differences were observed between severe and the other two degrees.
Conclusion: Interleukin-8 IL 8 was the inflammatory marker associated to radiographic severity as evaluated by osteophyte count and joint space narrowing score on plain radiography in patients with knee osteoarthritis.
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AB0804 OSTEOARTHRITIS (OA) PATIENTS WITH LOW BASELINE MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE/ROUTINE ASSESSMENT OF PATIENT INDEX DATA (MDHAQ/RAPID3) SCORES FOR PAIN, PATIENT GLOBAL ASSESSMENT AND MORNING STIFFNESS ARE SIGNIFICANTLY MORE LIKELY TO IMPROVE OVER THE NEXT 6 MONTHS

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Background: The course of osteoarthritis (OA) is highly variable; up to 50% of patients show little progression over many years, while other patients show rapid progression. Relatively little is known about the clinical variables that might affect prognosis for progression.
Objectives: To analyze OA patient status in routine care at baseline according to baseline candidate prognostic multidimensional health assessment questionnaire (MDHAQ) variables, and 6 months later as improved, worsened or similar according to the same variables.
Methods: All patients complete an MDHAQ/RAPID3 (routine assessment of patient index data) at all visits prior to seeing the rheumatologist at an academic site. The 2-page MDHAQ/RAPID3 includes 0-10 scores for physical function (FN), and visual analog scales (VAS) for pain (PN) and patient global assessment (PATGL), compiled into a 0-30 RAPID3, as well as a 0-10 fatigue VAS, 0-48 self-report painful joint count, 0-60 symptom checklist, and minutes of morning stiffness. OA patients were classified into 3 groups, based on change in RAPID3 $\geq$3.8, the minimal clinically important improvement (MCII), from baseline to 6-month follow-up (range 3-9 months), as >3.8, <3.8, or within 3.8 units. Statistical significance was studied with one-way analysis of variance (ANOVA) and chi square.
Results: Among 173 OA patients, 22 (13%) were improved, 95 (55%) unchanged, and 56 (32%) worsened 6 months later. The 3 groups did not differ significantly in age, gender, ethnicity, educational level or BMI (Table). Patients who improved compared to those who were unchanged or worsened had significantly lower baseline RAPID3, pain and patient global VAS, and morning stiffness. The patients who improved also had lower, but not statistically significant, physical function score and fatigue VAS. No differences were seen among the 3 groups in numbers of symptoms or self-report painful joint counts (Table).

Abstract AB0804 Table 1. MDHAQ demographic and clinical variables at baseline of 173 osteoarthritis (OA) patients according to level of improvement 6-months later

	Groups according to RAPID3 difference from baseline to 6 m			
	WORSE (diff. <-3.8)	**SAME (diff. -3.8 to 3.8)**	**IMPROVED (diff. >3.8)**	**P**
N (%)	56 (32%)	95 (55%)	22 (13%)	
Demographics				
Age (years), mean (SD)	66.3 (10.4)	65.6 (10.3)	67.4 (13.1)	0.77
Female,%	96%	93%	79%	0.06
BMI, mean (SD)	33.6 (7.3)	32.7 (8.5)	32.5 (5.6)	0.88
Obese,%	65%	61%	54%	0.40
% Black	48%	44%	42%	0.18
Education (years),mean(SD)	13.4 (3.8)	13.9 (3.8)	13.2 (4.1)	0.76
Clinical Variables mean (SD)				
Function (0-10)	3.3 (1.9)	2.9 (1.9)	2.3 (1.7)	0.10
Pain VAS (0-10)	7.6 (1.7)	6.9 (2.3)	5.1 (2.8)	**<0.001**
Patient global VAS (0-10)	6.9 (2.2)	5.7 (2.6)	3.7 (2.9)	**<0.001**
RAPID3 (0-30)	17.4 (5.5)	15.2 (7.0)	10.2 (5.7)	**0.004**
Fatigue VAS (0-10)	5.6 (3.5)	4.9 (3.3)	4.8 (3.6)	0.59
Symptom checklist (0-60)	10 (8)	13 (8)	12 (10)	0.20
Self-report painful joint count (0-48)	13 (11)	12 (9)	12 (12)	0.92
Morning Stiffness, minutes	32.7 (37.5)	53.1 (50.5)	14 (15.1)	**0.010**

Abbreviations: VAS= visual analog scale; RAPID3= routine assessment of patient index data; BMI= body mass index; statistically significant in bold.

Conclusion: OA patients who were improved over 6 months according to RAPID3 had significantly lower baseline scores for RAPID3, pain, patient global assessment, and morning stiffness. It may be of value to stratify patients in clinical trials, other clinical research, and routine clinical care according to these variables.
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AB0805 WHAT FACTORS AFFECT THE RESULT OF LONG-TERM ANALGESIC THERAPY FOR OSTEOARTHRITIS? DATA FROM A MULTICENTER OPEN STUDY OF ORAL AVOCADO/SOYBEAN UNSAPONFABLES EFFECTIVENESS

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Background: Symptomatic slow-acting drugs for OA (SYSADOAs) and oral nonsteroidal anti-inflammatory drugs (NSAIDs) play a central role in the pharmacological management of osteoarthritis (OA). Factors affecting the effectiveness of OA therapy should be taken into account.
Objectives: to identify factors affecting the effectiveness of long-term analgesic therapy in patients with OA.
Methods: the study included 6448 patients with knee OA (mean age 57.8 ± 10.2 years, 70,9% women), with pain level $\geq$40 mm VAS. All patients received oral avocado/soybean unsaponfables (ASU) 300 mg/day within 3 months and ketoprofen lysine salt (KLS) 320 mg/day within 2 weeks at the beginning of the study. A 100 mm visual analog scale (VAS) was used to assess pain intensity. The result of treatment was evaluated on a scale of 0-5 points, where 0 – no effect, 5 - excellent effect. The criteria for a "good response" to therapy were: pain reduction $\geq$50% and treatment result $\geq$ 4 points. The value of the studied factors was determined using odds ratio; 95% confidence interval (OR; 95% CI).
Results: After 3 months of therapy the pain level decreased from 63.7 ± 12.0 mm to 14.2 ± 11.7 mm. A good response to treatment was noted in 87.4% of patients. Sex, body mass index $\geq$ 30 kg/m², type 2 diabetes, poor effect of NSAIDs and SYSADOAs in history did not affect the

result. The effectiveness of treatment was less in patients >65 years (OR 0.418; 95% CI 0.342-0.509, p<0.001), OA stage ≥ 2 by Kelgren-Lawrence (OR 0.556; 95% CI 0.298-0.738, p<0.001), with rest pain (OR 0.690; 95% CI 0.596 - 0.800, p<0.001), synovitis (OR 0.780; 95% CI 0.673-0.900, p=0.001), and sensory symptoms such as burning, pain cold, electric shocks (OR 0.530; 95% CI 0.458-0.613, p<0.001).
Conclusion: the ASU and KLS combination allows to achieve successful pain control in OA. A number of factors: age >65 years, OA stage ≥ 2 by Kelgren-Lawrence, rest pain, synovitis, and sensory symptoms are associated with the worst result of treatment.
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AB0806 EFFICACY MANAGEMENT AND ADHERENCE EVALUATION OF DICLOFENAC IN THE TREATMENT OF KNEE OSTEOARTHRITIS PAIN

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Background: The incidence of knee osteoarthritis is increasing day by day. The accompanying pain has seriously affected people's quality of life. No relevant researches have studied the relationship between pain relief and adherence after taking NSAIDS in outpatients.
Objectives: To investigate the effect of diclofenac on pain control of knee osteoarthritis and the relationship between pain relief and medicine adherence. To evaluate the pain relief rate of patients with different initial pain.
Methods: 120 patients with knee osteoarthritis were recruited from the outpatient department of osteoarthritis, Peking University People's Hospital. The population was randomly divided into the experimental and control group. The baseline and follow-up contents were interviews including socio-demographic factors, evaluation of knee pain, WOMAC and MMAS-8 questionnaire. The experimental group was given regular follow-up and medication advice, while the control group was only given observational records at the middle and late stages. SPSS25.0 nonparametric T test and one way ANOVA were used to evaluate the efficacy of diclofenac in relieving knee osteoarthritis pain and the relationship between pain relief and adherence.
Results: A total of 120 patients with knee osteoarthritis at baseline were randomly enrolled and 108 patients were followed up. 55 patients in the experimental group and 53 patients in the control group (1) The 2-week adherence of test group/control group was 86.38%/64.78%(P<0.01), the 6-week adherence of test group/control group was 75.24%/35.22%(P<0.01). The 2-week and 6-week adherence of test group and control group were significantly different (P=0.015 and P<0.01). (2) The pain relief rate at 2 and 6 weeks in the experimental group was 67.56% and 69.41%, respectively, the pain relief rate was significantly higher than baseline (P<0.01), but there was no significant difference between the two groups (P=0.739).The pain relief rates at 2 and 6 weeks in the control group were 46.51% and 29.03% and was significantly higher than baseline (P<0.01), there was a significant difference between the two groups (P < 0.01). In the evaluation of 2 and 6 weeks, the pain relief rates in the experimental group were significantly different from those in the control group (P<0.01). (3) The initial pain scores of different degrees did not affect the adherence and pain relief rates in the experimental group. In the control group, the 2-week adherence of severe pain patients was higher than that of mild and moderate pain patients (P<0.01), but the 6-week follow-up adherence shows no significant difference in patients with different degrees of initial pain (P=0.073), the 6-week adherence of patients with moderate/severe pain (38.07%/42.6%) was significantly different from the 2-week adherence (68.34%/84.77%) (P<0.01),the 6-week pain relief rate (18.46%/29.72%) in patients with mild/moderate pain was lower than the 2-week pain relief rate (48.72%/47.44%) (P=0.052/P<0.01). (4) The patients with better adherence have the higher pain relief rate (P < 0.01).
Conclusion: For patients suffering from knee osteoarthritis pain, diclofenac 150 mg/day for 6-week is recommended. Regular follow-up can improve adherence significantly, increased adherence can improve the pain relief rate significantly, the pain relief rate may not be related to the patient's initial pain score. It is suggested that clinical workers should supervise the medication of patients with knee osteoarthritis and make regularly follow up.

REFERENCES

[1] da Costa BR, Reichenbach S, Keller N, et al. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. Lancet 2016;387:2093-105

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AB0807 FOLLOW-UP OF PATIENTSWITH HIP OSTEOARTHRITIS WHO RECEIVED VISCOSUPPLEMENTATION: HOW NEW TECHNOLOGIES CAN HELP

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Background: Digital health innovations have opened up several opportunities to help patients with rheumatologic conditions and their treating clinicians in improving routine healthcare.
Objectives: To evaluate the applicability of a wearable smartwatch for monitoring patients with hip osteoarthritis who received viscosupplementation. Samsung Electronics Italia and MDApp srl supported the present study.
Methods: Consecutive patients with hip osteoarthritis who received viscosupplementation with jaluronic acid between November 2017 and May 2018 were enrolled in this observational study. All patients gave their informed consent. A Samsung Gear smartwatch was given to each patient and was worn during the day for measuring daily steps, walking distance, and mean velocity. Patients were asked to wear the smartwatch starting from one week before infiltration (T0), until two weeks before (T1). Patients were assessed with Lequesne index and WOMAC score at T0 and T1.
Results: Overall, 24 patients (7 male and 17 female, mean age 44 years-old) were enrolled. Of these, 70% has worn the smartwatch for most of the time (range 90-100%). An improvement of velocity (45%), an increase of daily steps (29%), and walking distance (25%) were seen. Similarly, Lequesne index and WOMAC score were consistent with subjective improvement. Most of the patients (95%) declared to be satisfied with this digital health study.
Conclusion: Samsung smartwatches proved to be an effective tool for tracking and recording medical parameters linked with perceived general health. Health technologies are more than an accessories and could be useful in chronic musculo-skeletal diseases because they allow to ease remote diagnosis and to monitor patients' symptoms and clinical response. Telemedicine could fill the gap between patients and healthcare, with a reproducible and objective tool, enhancing patients' engagement with the treatment plan. The high patients' satisfaction further support the use of digital health technology.

REFERENCE

[1] Kataria S, Digital Health: a new dimension in rheumatology patient care. Rheumatol Int. 2018

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AB0808

COMBINATION OF ORAL PARACETAMOL AND TOPICAL NSAIDS FOR OSTEOARTHRITIS PAIN: A SYSTEMATIC SCOPING REVIEW OF THE LITERATURE

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Background: Topical NSAIDs and paracetamol (APAP) are frequently used for osteoarthritis (OA) pain.[1,2] In real-world settings, combination treatment is common,[3,4] with more than one-quarter of patients using topical NSAIDs with oral non-opioid analgesics such as APAP.[4]
Objectives: We conducted a systematic scoping review to: understand current recommendations on concomitant use of topical NSAIDs and APAP for OA pain; evaluate the extent of supporting evidence for this practice; and identify literature gaps.
Methods: We searched PubMed and the Cochrane Library for clinical studies (database inception to January 2019) of topical NSAIDs in OA in which APAP was given concomitantly, either regularly (combination treatment) or as needed (rescue treatment). Grey literature searches were conducted to identify clinical practice guidelines for management of OA from leading organizations.
Results: After removing duplicates, the literature searches returned 375 articles, of which 66 were clinical studies of topical NSAIDs in OA and were reviewed further. Of these, we identified 1 randomized controlled trial (RCT) evaluating efficacy and safety of combination treatment with APAP and a topical NSAID, in which 43 patients with knee OA currently treated with APAP were randomly assigned to double-blind treatment with ketoprofen plaster or placebo for 4 weeks.[5] Results showed that the combination of APAP/topical ketoprofen was statistically significantly more effective in pain reduction (P=0.03) and physician's global assessments (P=0.01) compared with APAP/placebo. Of the remaining 65 topical NSAID studies, another 37 (57%) allowed rescue treatment with APAP during the treatment period (including 34 RCTs; 1 open-label extension of 2 RCTs; 1 patient preference study; and 1 single-arm open clinical trial). Because none of these studies randomly assigned patients to the combination, it was not possible to evaluate efficacy or safety of the combination based on these data. Review of OA guidelines identified 3 major organizations—EULAR, NICE, and ESCEO—that recommend or allow concomitant use of topical NSAIDs and APAP for specific joints.[6-8]
Conclusion: In clinical practice, drug combinations are frequently used to manage OA pain, and some OA treatment guidelines allow the use of topical NSAIDs concomitantly with APAP. Very limited supporting data are available, with only a single small RCT demonstrating the efficacy and safety of the combination. However, it may be inferred from the fact that more than half of the topical NSAID studies identified allowed APAP rescue therapy that this combination is generally perceived to be efficacious and well tolerated. Additional, larger RCTs are needed to confirm the benefit of this commonly used analgesic combination in managing OA pain.

REFERENCES

[1] Conaghan PG, et al. *Clin Rheumatol*. 2015;34:1581-8.
[2] Jackson H, et al. BMJ Open. 2017;7:e019694.
[3] Gupta R, et al. Int J Res Med Sci. 2018;6:985-9.
[4] Wilson N, et al. Rheumatology. 2015;54:860-7.
[5] Yoo B, et al. J Korean Rheum Assoc. 1996;3:70-5.
[6] Bruyere O, et al. Semin Arthritis Rheum. 2014;44:253-63.
[7] Geenen R, et al. Ann Rheum Dis. 2018;77:797-807.
[8] NICE. Guideline CG177. 2014.

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AB0809

A STUDY TO COMPARE ARTICULAR CARTILAGE VOLUME IN HEALTHY AND OSTEOARTHRITIC KNEE AND ITS CORRELATION WITH CLINICO – RADIOLOGICAL SEVERITY

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Background: Knee Osteoarthritis (KOA) is a persistent debilitating disease characterized by loss of articular cartilage. Known to be a disease of elderly, it may not be necessarily so, as the loss in articular cartilage volume (ACV) begins early but detected very late on X-rays and by that time no therapy works and joint replacement is the only answer.
Objectives: To determine the role of ACV in early diagnosis of KOA, which may not only monitor disease progression from a very early stage, it may also open a gateway to slow down or stop the structural changes involved in KOA.
Methods: 60 Cases and equal number of age, sex matched controls were recruited. Each subject had MRI of the reference knee. ACV was measured manually by means of image processing on an independent workstation using semi-automated machine GE Signa. VAS for knee pain and WOMAC for pain, stiffness and disability were recorded for clinical severity and X-rays for radiological severity by KL grading.
Results: With age, a statistically significant inverse correlation of ACV was found in both healthy and osteoarthritis knees. Height, weight and BMI were independent of ACV in healthy knee. In KOA, a significant positive correlation of ACV was observed with height, a significant inverse correlation with WOMAC scores and significant difference with sub- scales of WOMAC index (pain, stiffness and physical function). The statistical difference in ACV between the two categories of WOMAC scores (<32 and >32) was significant.
Conclusion: This study concluded that ACV is significantly lower in osteoarthritis knee as compared to healthy adult knee. This study also found that KOA in females occurs at an early age and progresses slowly whereas in males occurs late and progresses rapidly. ACV may become one of the most promising tools for early diagnosis of KOA and in monitoring disease progression.

REFERENCE

[1] Beary JF III. Joint structure modification in osteoarthritis: development of SMOAD drugs. CurrRheumatol Rep 2001;3:506-512.

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AB0810

INTRA-ARTICULAR CNTX-4975 FOR PAINFUL KNEE OSTEOARTHRITIS: ASSESSMENT OF COOLING METHODS FOR REDUCING PROCEDURAL PAIN

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Background: CNTX-4975 is a long-acting, *trans*-capsaicin injection in phase 3 trials for treatment of moderate to severe pain associated with knee osteoarthritis (OA). Intra-articular (IA) CNTX-4975 injection produces short-lived procedural pain that can be ameliorated with joint cooling. A prior analysis (Cohort 2) demonstrated that a circumferential circulating ice water wrap (CCIWW) more effectively lowered IA knee temperature and reduced procedural pain than an ice pack on top of the knee (3.4 vs 7.3, respectively, on a numeric pain rating scale [NPRS] 10 minutes post-CNTX-4975).
Objectives: Subjects were enrolled in 2 separate cohorts (C3/C4) to: compare effects of 2 circumferential cooling methods on IA and skin knee temperature and procedural pain (C3); and assess procedural pain with an abbreviated cooling schedule and with vs without post-CNTX-4975 cooling (C4).
Methods: Eligible subjects were adults aged 45–75 yrs with ≥3 months of bilateral moderate to severe OA knee pain. All subjects received each

cooling device on opposite knees; IA CNTX-4975 injections and other procedures on the left and right knees were separated by 7 (±2) days. See **Figure** for study design. IA and skin temperatures were recorded throughout the procedures. Subjects rated procedural pain at prespecified times using NPRS (0=no pain; 10=worst possible pain).

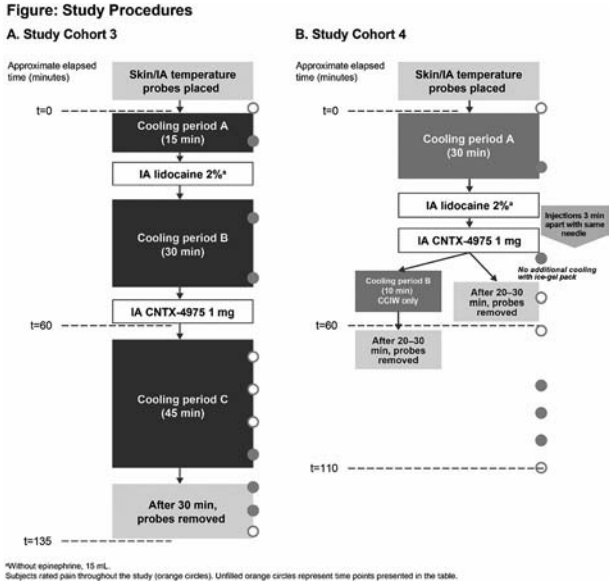
Results: Five subjects enrolled in and completed each cohort (mean age, yrs: C3, 57.6; C4, 59.6; each 80% male). In C3, mean IA temperatures decreased with both methods; mean temperatures at baseline and 105 minutes were 33.7°C and 26.7°C for ice-gel pack cooling and 32.4°C and 28.2°C for CCIWW. Skin temperature reductions between cohorts were similar; mean temperatures were 28.8°C and 14.3°C (ice-gel pack) and 28.7°C and 15.2°C (CCIWW). Mean IA temperatures in C4 at baseline and 55 minutes (15 minutes post-CNTX-4975 and/or end of last cooling period [CCIWW only]) were 33.6°C and 29.0°C for ice-gel pack cooling and 32.1°C and 27.7°C for CCIWW. Mean skin temperatures were 28.5°C and 22.8°C for ice-gel pack and 27.8°C and 18.8°C for CCIWW. Pain levels before CNTX-4975 were low. Procedural pain peaked 10–20 minutes after CNTX-4975 injection in both cohorts. While mean pain levels were similar across cohorts (**Table**), pain was reduced more effectively by CCIWW in C3 and ice-gel pack in C4. Procedural pain was not increased in the absence of post-injection cooling in C4.

Conclusion: The ice-gel pack and CCIWW effectively reduced IA knee joint temperatures and procedural pain in both cohorts. Shorter cooling time and low pain levels observed with IA CNTX-4975 and ice-gel pack cooling in C4 suggest that this strategy may be feasible in clinical practice.

Procedural Pain Over Time (min), Mean±SE[a]	Cohort 3		Cohort 4	
	Ice-gel pack	CCIWW	Ice-gel pack	CCIWW
Baseline	0.8±0.37	0.4±0.24	0.4±0.24	0.2±0.20
10[b]	4.2±1.36	2.2±1.46	2.4±1.29	4.2±1.20
20[b]	3.6±1.33	2.2±1.20	3.0±1.22	2.6±1.25
30[b]	2.6±0.81	2.2±0.97	2.0±1.05	1.8±1.11
Last assessment[c]	2.4±0.81	1.4±0.40	1.6±1.03	2.4±1.60

Cohort 3: Comparison of 2 circumferential cooling methods; Cohort 4: Shortened cooling and with/without post-CNTX-4975 cooling.
[a]Lower scores=less pain; [b]Post-CNTX-4975 injection; [c]Approximately 70 min post-injection for C3; 60 min for C4.

Figure: Study Procedures



Disclosure of Interests: Randall Stevens Shareholder of: Centrexion Therapeutics Corp, Employee of: Centrexion Therapeutics Corp, Kimberly Guedes Employee of: Centrexion Therapeutics Corp, Nilam Mistry Employee of: Centrexion Therapeutics Corp, Duncan Lascelles Consultant for: Centrexion Therapeutics Corp, David Ball: None declared

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AB0811

MULTICENTER PROSPECTIVE STUDY TO ASSESS EFFICACY AND SAFETY OF INTRA-ARTICULAR INJECTIONS OF A SOLUTION COMBINING HYALURONIC ACID AND CHONDROITIN SULPHATE IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background:

Objectives: To assess efficacy and safety of a single intra-articular injection of a solution combining hyaluronic acid (HA) 60 mg and chondroitin sulphate (CS) 90 mg in 3 mL on patients with knee osteoarthritis (OA) in a multicenter prospective study.

Methods: 79 outpatients (predominantly females - 81,0%) from 5 RF constituent territories with primary tibiofemoral Kellgren-Lawrence score grade II or III knee OA, ≤40 mm pain intensity during walking on visual analogue scale (VAS), requiring NSAIDs intake (for at least 30 days during 3 months prior to enrollment) were included into the study after signing the informed consent form. Mean age was 60,3 ± 8,7 years, mean BMI – 29,2 ± 4,7 kg/m^2, disease duration – 6 (3 - 10) years. Grade II OA was documented in 68,4% of patients, Grade III - in 31,6%. The study lasted for 6 months. Efficacy and safety evaluations were made based on VAS pain assessment, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) - (WOMAC pain (0-500), WOMAC function (0-1700), WOMAC stiffness (0-200)), VAS patients' health status, EQ-5D-based assessment of patients' quality of life, global physician's and patient's efficacy assessment, and daily NSAIDs requirements.

Results: Obtained results demonstrate statistically significant VAS pain reduction during walking already in 1 week after intra-articular injection of the combination (respectively, 62 (55-72) and 41 (32-51) mm, p<0,0001). Moreover, pain continued to subside during all 3 months of follow up (in 1 month – 28 (20-42), in 3 months – 22 (14-37) mm). A significant pain reduction achieved at Mo 3 persisted until Mo 6 - 20 (14-42) mm, without documented pain increase (Fig. 1). Similar trends were observed with total WOMAC score (1125 (899-1540) – at baseline, and 552 (309-837) mm – by the end of the study, p<0,0001), and all WOMAC sub-scores (268 (189-312) – baseline WOMAC pain, 91 (48-171) mm – by the end of the study p<0,0001 (Fig. 2); stiffness – 101 (59-130) and 40 (20-61) mm, p<0,0001; function – 802 (647-1095) and 402 (191-638) mm, p<0,0001, respectively). Median time to the onset of therapeutic effect was 7 (5-18) days. Statistically significant improvement of patients' quality of life by EQ-5D and general health status was observed during all follow up period (respectively, 0,52 (-0,02-0,59) and 0,69 (0,59-0,80), p<0,0001; 48 (30-60) and 72 (60-80) mm, p<0,0001). One injection of the drug resulted in dose reduction or discontinuation of NSAIDs therapy: at baseline 76 patients (96,2%) were taking NSAIDs, in one week 31 (39,2%) patients discontinued NSAIDs, in 1 month – 72,2%, in 3 months – 73,4%, and by the end of the study at Mo 6 – 54,4% were not taking NSAIDs. These data were consistent with physician's and patient's global assessment of the efficacy of treatment, who stated «significant improvement» and «improvement» in the majority of cases, with only few "no effect" or "worsening" cases documented in analyzed population. Adverse events, such as worsening of pain and/or swelling of the joint, were documented in 8 patients (10,1%); they resolved spontaneously or following NSAIDs intake.

Fig.1. VAS pain, mm

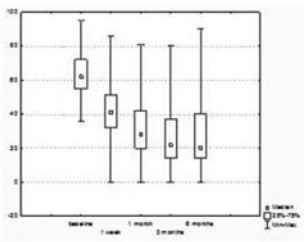
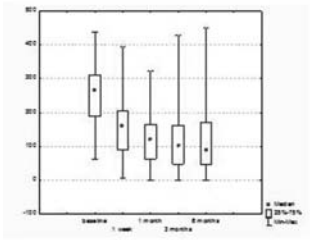


Fig.2. WOMAC pain



Conclusion: These results suggest that intra-articular injections of hyaluronic acid plus chondroitin sulfate in patients with knee OA are efficient and safe. A single injection of the drug resulted in statistically significant reduction of pain and stiffness, reduction in NSAIDs intake, as well as improvement in patients' quality of life and function:

Disclosure of Interests: Elena Taskina Speakers bureau: Bayer, Sandoz, Boeringer-ingelheim, Ludmila Alekseeva Speakers bureau: Bayer, Boeringer-ingelheim, Gedeon-Richter, Servier, Natalia Kashevarova: None declared, Evgenia Sharapova: None declared, Ekaterina Strebkova: None declared, Sergey Anikin: None declared, Lena Zonova Speakers bureau: Sandoz, Pfizer, Abbvie, Novartis, Bayer, Tatiana Raskina: None declared, Elvira Otteva Speakers bureau: Pfizer, Abbvie, Novartis, Aleksandr Lila Speakers bureau: Sandoz, Pfizer, Abbvie, Novartis, Bayer

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AB0812

PAIN CATASTROPHIZING SCORE AND GAIT, TOGETHER WITH WOMAC, ARE ALTERED IN KNEE OSTEOARTHRITIC PATIENTS UNDERGOING ARTHROPLASTY SURGERY, COMPARED WITH PATIENTS FOLLOWING CONSERVATIVE TREATMENT. PRELIMINARY RESULTS FROM HOLOA PROJECT

Laura Tío[1], Francisco Castro[1,2], Simone Tassani[3], Santos Martinez[1,4], Raul Torres[1,4], Raquel Arredondo[1], Miguel Ángel Gónzález-Ballester[3,5], Joan Carles Monllau[1,4], Jérôme Noailly[3], Jordi Monfort[1,2]. *[1]IMIM, Barcelona, Spain*; *[2]Hospital del Mar, Rheumatology service, Barcelona, Spain*; *[3]Pompeu Fabra University, BCN MedTech, DTIC, Barcelona, Spain*; *[4]Hospital del Mar, Orthopedic Surgery and Traumatogy service, Barcelona, Spain*; *[5]ICREA, Barcelona, Spain*

Background: Osteoarthritis (OA) is a pathology that includes several disorders that produce the same symptomatology: pain, functional impotence and inflammation. It lacks therapies that act over the physiopathology of the disease, rather than over the symptoms [1]. Patients' phenotyping is essential to describe the disorders underlying the OA symptoms, and would allow applying treatments to the altered conditions, in a personalized medicine approach.

Objectives: The HOLOA project aims to design a multivariate model that allows classifying knee OA patients according their characteristics in 3 areas: pain, clinical/morphological characteristics and articular defects. The present work is a preliminary study with the aim to describe the clinical and gait dynamics differences between OA patients classified by treatment: conservative (CNS) vs arthroplasty surgery (ART).

Methods: Prospective study of OA patients graded 2-3 in KL scale and classify by treatment. Both groups are paired by genre, age, and BMI. The studied variables are: WOMAC index (Pain (Wp), Stiffness (Wst) and Function (Wf), Hospital Anxiety and Depression Scale (HADS), London Chest Activity of Daily Living scale, Modified Baecke Physical Activity Questionnaire, Pain Catastrophizing Score(PCS), pain threshold (according to the extended peripatelar map of Arent-Nielsen) pain sensitization at the tibia anterior surface, pain temporal summation (these 3 parameters are measured with the use of an algometer [2]), ultrasound measurement of synovial hypertrophy and effusion, and gait analysis (with Helen Hayes marker protocol. Inverse dynamic analysis was performed to compute the reaction forces and torques of the OA and control leg [3]). Multivariate analysis of variance was performed for the treatment, genre, age and BMI.

Results: This study was performed with the data of the 70 patients recruited to date. They are classified as shown in Table 1.

Variable	Category	N
Gender	Male	28
	Female	42
Age	60-67	29
	68-75	41
BMI	25.5-29.9	30
	>30	40
Treatment	CNS	44
	ART	26

Only treatment factor related differences are reported.

ART group present significant higher values in Wst (p=0.012), Wf (p=0.018), and PCS (p=0.018), than CNS group (Figure 1).Differences in PCS values show interaction with BMI (p=0.007) (Figure 2). Regarding the joint, number of painful sites depend on treatment and BMI group (p=0.032)(Figure 3). Finally, gait study show no direct effect of the treatment, interactions are observed in the reaction forces and torques when comparing control vs OA leg, in ART and CNS group (p=0.004 and p=0.002, respectively) (Figure 4).

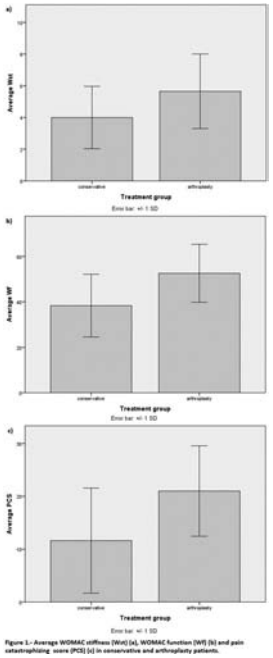


Figure 1.- Average WOMAC stiffness (Wst) (a), WOMAC function (Wf) (b) and pain catastrophizing score (PCS) (c) in conservative and arthroplasty patients.

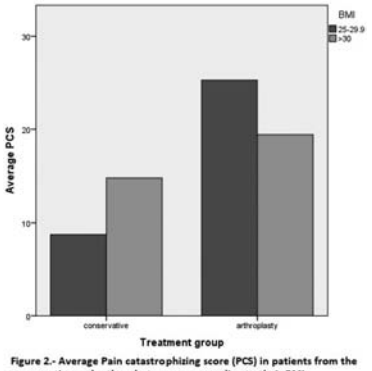


Figure 2.- Average Pain catastrophizing score (PCS) in patients from the conservative and arthroplasty group, according to their BMI.

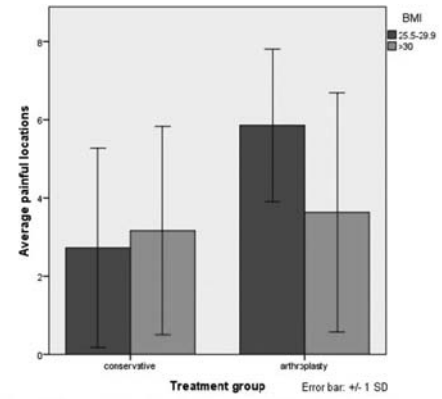


Figure 3.- Average of number of reported painful knee locations after pressure of <4Kg/cm2.

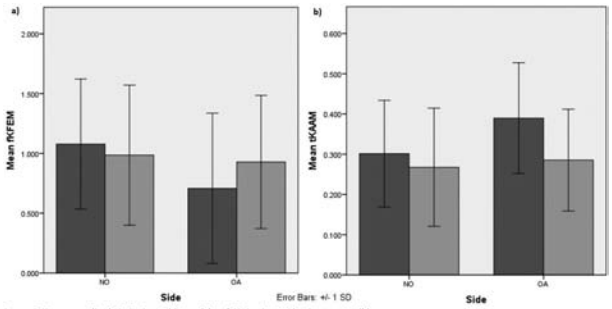


Figure 4.-Knee normalized Medio-Lateral forces (a) and Abduction-Adduction torques (b)

Conclusion: Although both treatment groups present the same OA radiologic grade, ART group presents significant higher stiffness and functional disability. That may affect to the gait of these ART patients, altering the forces distribution and torques between both legs. Although no differences in knee pain in life situation (Wp) between treatment group are reported, ART group present more painful sites in the knee with pressure stimuli. Emotional component may be playing a role in the pain and illness perception, influencing the patient decision to undergo ART surgery

REFERENCES

[1] Grazina, R, Adv Exp Med Biol.1059 111-135, 2018
[2] Pujol, J et al, Pain. 158(9) 1831-1838, 2017.
[3] R.B. Davis, Hum. Mov. Sci. 10 575–587, 1991.

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Procare Health

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AB0813

AN EXPERT CONSENSUS ON THE APPROPRIATE USE OF ORAL SYSADOAS FOR THE TREATMENT OF THE OSTEOARTHRITIC PATIENT IN PRIMARY HEALTH CARE: A DELPHI STUDY

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Background: Clinical studies have demonstrated that osteoarthritic pain is linked to disability and quality of life (QoL). The therapeutic modalities in the treatment of osteoarthritis (OA) are numerous and despite the availability of evidence-based guidelines for OA management, agreement on treatments is lacking[1]. Symptomatic Slow-Acting Drugs for OA (SYSADOA), are natural compounds, used in OA treatment. Thus, there is disagreement about SYSADOAs use in clinical practice.

Objectives: Our objective was to prepare a consensus document on the appropriate use of oral SYSADOAs: chondroitin sulphate (CS), glucosamine(G), diacerein(D) and the combination of CS plus G for OA management in primary health care.

Methods: A two-round Delphi study was carried out to assess expert consensus on the appropriate use of SYSADOAS in primary care. The questionnaire validated by the expert committee (3 rheumatologists, 2PC physicians, 1 clinical pharmacologist) included 24 questions The Delphi panel was composed of 15 experts (10 PC physicians, 1 rheumatologist, 1 traumatologist, 1 rehabilitator, 1 gynaecologist and 1 clinical pharmacologist) with extensive experience in the treatment of OA and the use of oral SYSADOAs which were identify by clinical coordinator, a methodological coordinator, and four members of the Scientific Committee. Participants were asked 24 questions on SYSADOAs use. Items that reached consensus by at least 80% across both panels were included in the guidelines. The fieldwork of the study was developed for approximately 4.5 months. This study was promoted by the International Osteoarthritis Foundation (OAFI) with the support of the Spanish Ministry of Health, Social Services and Equality.

Results: Consensus statements emerged: (1)patient phenotypes affects SYSADOAs action; (2)SYSADOAs are effective in primary and secondary OA, in the three first grade of Knee OA, hand and hip; there is no evidence for erosive hands, shoulder, spine, and ankle OA; (3)CS, G and association can reduce pain, inflammation, improve QoL and functional capacity and have a chondroprotective effect; (4)CS and D can reduce synovial membrane inflammation, all oral SYSADOAs, except D, can decrease cell death and the enzymes responsible for cartilage destruction; (5) The maximum therapeutic efficacy is reached after 3 to 6 months; (6) SYSADOAs con be prescript to patients having comorbidities: cardiovascular risk or disease, digestive disease, hypertension, dyslipidemia, peripheral vascular disease, type 2 diabetes, and oesophageal reflux. There is disagreement in the prescription of oral SYSADOA in patients with liver and kidney disease.

Conclusion: This study sheds light on the appropriate use of oral SYSADOAs in primary health care by providing added value to published evidence. Results based on literature evidence on efficacy and safety, the clinical experience of the panellist experts in OA treatment and the fact that OA patient is a chronic, elderly, with multiple diseases and polymedicated person. The diffusion of our results among primary health practitioners will contribute to improving OA patient management protocols to ensure a personalized treatment to OA patients and to ameliorate their QoL.

REFERENCES

[1] Ethgen O, Reginster JY. Degenerative musculoskeletal disease. Ann Rheum Dis 2004;63:1-3.

Disclosure of Interests: Jordi Monfort Speakers bureau: Bioibérica Procare Health, Benjamín Abarca: None declared, Xavi Carné: None declared, Sergio Giménez: None declared, Ingrid Möller: None declared, Montserrat Romera: None declared, Marco Bibas: None declared, Marianna Vitaloni: None declared, Josep Verges: None declared

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AB0814

INDIVIDUAL AND SOCIAL FACTOR CAN INFLUENCE THE QUALITY OF LIFE OF KNEE OA PATIENTS: A SYSTEMATIC REVIEW

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Background: Knee OA (KOA) is the most common form of chronic joint disease and bears more responsibility than any other disease for disability[1]. It associates with remarkable functional restrictions due to pain. The limitations in activity caused by KOA seriously affect social relationships, emotional well-being, reducing the quality of life (QoL) of patients.

The identification of therapies and factors that affects and improve QoL in KOA patients may mitigate the clinical, economic, and social burden of this disease[2]. Thus, the assessment of QoL in KOA is becoming increasingly common in both research and clinical practice[3]. Still a general recompilation of the factors of interest as demographic features, lifestyle characteristics and comorbidity are missing.

Objectives: Our aim was to recapitulate the existing information on QoL in KOA patients as an international tool to raise awareness on their condition and guide future actions for patient's management

Methods: We conducted a systematic review examining the breadth of the literature regarding the QoL in patients with KOA (up to 2017). We identify articles using MEDLINE, EMBASE, Cochrane, and PsycINFO using relevant keywords as KOA, QoL and well-being and their short forms. All articles were reviewed for inclusion by 3 independent reviewers. QoL domains and items relevant to patients with KOA were extracted. Only original articles were included when containing information on QoL of patients with KOA. Inclusion criteria were QoL compared to one or more demographic factors (e.g., age, gender), lifestyle factor (e.g., functional independence), or comorbidity factor (e.g., diabetes, obesity) or a control group. The quality of included studies was assessed using a quality appraisal tool.

Results: We retrieved 610 articles, of which 62 articles fulfilled inclusion criteria for review. Most of the studies were carried out in Europe, American Continent and Asia. The mean of participants in these 62 studies was 561 patients and the majority of them were female, the mean age was 63 years. All the studies described a worse QoL in KOA patients when compared to a control group having women a worst QoL perception than men.

A higher BMI, a lower level of physical activity and higher energy expenditure were one of the main factors that correlated with worse QoL. Educational level and higher total mindfulness were shown to improve QoL while poverty, physiological distress, depression and having severely dysfunctional families reduce it. The delivery of a knee self-management program by health care professionals was proven to improve QoL. Finally, surgical KOA interventions generally resulted in good outcomes these results were influenced by individual factors as age, weight, and depression

Conclusion: This is the first review pertaining to QoL in KOA patients. KOA has a strong impact on QoL. Individual factors (sex, weight, exercise, mental health, education) can influence QoL. These factors affect treatment outcomes and should be considered for a better patient's management. These data are a valuable tool for health professionals, to better understand the disease and to implement more adequate standard of care.

Disclosure of Interests: Josep Verges: None declared, Marianna Vitaloni: None declared, Marco Bibas: None declared, Rosa Sciortino: None declared, Maritza Quintero: None declared, Jordi Monfort Speakers bureau: Bioibérica

Procare Health, Francisco de Abajo: None declared, Patrick du Souich: None declared, Ingrid Möller: None declared, Elizabeth Oswald: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS; MSD, Janssen, Guy Eakin: None declared, Angie Botto-van Bemden: None declared

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AB0815 THE INFLUENCE OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON INFLAMMATORY SONOGRAPHIC FEATURES IN EROSIVE HAND OSTEOARTHRITIS

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Background: Erosive hand osteoarthritis (HOA) is a subtype of hand osteoarthritis affecting the interphalangeal (IP) finger joints, characterized by a more inflammatory burden. Hitherto, pharmacologic treatment options are restricted to symptomatic therapy like paracetamol and/or non-steroidal anti-inflammatory drugs (NSAIDs)(1). The latter may affect the presence of inflammatory features on ultrasound (US). Hence, assessment of the disease activity could be influenced by this treatment.

Objectives: To examine whether inflammatory US features (i.e. synovial proliferation (SP), effusion (EFF) and Power Doppler (PD) signal) in erosive HOA patients change when discontinuing NSAIDs intake for two weeks before the US assessment.

Methods: Ninety-nine patients with erosive HOA, according to American College of Rheumatology criteria (2) were enrolled. Presence of central erosions on conventional radiographs and any clinical sign of inflammatory activity (soft tissue swelling) in at least one proximal or distal IP finger joint were present. The patients were allocated to the NSAIDs or control group according to their intake before baseline (if no NSAIDs use = control group; if intake of NSAIDs on a regular base = NSAIDs group). At baseline (T0), 16 IP finger joints were examined by US. Patients in the NSAIDs group were asked to discontinue all NSAIDs intake for two weeks, when another US was performed (T1). The inflammatory features were scored at T0 and T1 using a semi-quantitative scale ranging from 0-3 (3).

Binomial mixed models with logit function were fitted for ultrasound scores SP (score>2), EFF (score>2), and PD (score>1) with a random intercept for patient and with age (in years), sex (female vs. male), duration of illness (in years), joint, side (left vs. right), anatomical phase group (N, S, J vs. E/R, R, E, F), NSAID group (NSAIDs withdrawal vs. No NSAIDs), time (t1 vs. t0), and a two-way interaction between NSAIDs group * time as fixed factors. The Odds ratios (OR, 95% confidence interval (CI)) of having an ultrasound score of at least '2' versus at most '1' for SP and EFF, and '0' vs. '$\geq$1' for PD are shown.

Results: Forty seven patients were included in the NSAIDs group and 52 in the control group. Both groups were comparable at baseline for VAS pain, disease duration, number of radiographic affected joints and body mass index, but not for age (p=0.005). The US baseline data were comparable between both groups (all p>0.05). At T1, in the NSAIDs withdrawal group, more SP and PD was seen compared to baseline (p = 0.018 and 0.031, respectively). However, the interaction term time*NSAIDs was not found significant for any variable (table 1).

Abstract AB0815 Table 1. Association (Odds ratio (OR), 95% confidence interval (CI)) and comparison between T1 and T0 sonographic inflammatory features between groups

Variable	Group	OR*	95% CI	P-value
SP	No Nsaids	1.304	0.958 - 1.775	0.091
	Nsaids withdrawal	**1.552**	**1.079 - 2.232**	**0.018**
	Interaction term time*Nsaids	-	-	0.470
EFF	No Nsaids	1.027	0.761 - 1.387	0.860
	Nsaids withdrawal	1.164	0.872 - 1.554	0.303
	Interaction term time*Nsaids	-	-	0.560
PD	No Nsaids	1.016	0.715 - 1.444	0.929
	Nsaids withdrawal	**1.480**	**1.036 - 2.116**	**0.031**
	Interaction term time*Nsaids	-	-	0.140

*Odds of showing a score of at least 2 versus at most 1 for synovial proliferation and effusion, and Odds of showing a score of at least 1 versus 0 for Power Doppler signal (PD)

Conclusion: No significant changes in inflammatory US features were seen in erosive HOA patients after withdrawal of NSAIDs for two weeks. This study suggests that an NSAIDs free period is not necessary before assessing inflammatory disease activity in erosive HOA patients.

REFERENCES

[1] Kloppenburg M, et al. Ann Rheum Dis. 2019 Jan;78(1):16-24.
[2] Altman R, et al. Arthritis Rheum 1990;33:1601–10.
[3] Mathiesen A, et al. Arthritis Rheumatology. 2017;69(S10).

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AB0816 **QUALITY OF LIFE AND TREATMENT SATISFACTION IN CHINESE PATIENTS WITH CHRONIC KNEE OSTEOARTHRITIS PAIN: A CROSS-SECTIONAL STUDY**

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Background: Joint pain is one of the most common symptoms of osteoarthritis (OA) and affects the physical function and quality of life of patients.
Objectives: To understand the impact of chronic pain due to knee OA on health-related quality of life (HRQoL) and evaluate treatment satisfaction of current medications among Chinese patients.
Methods: A cross-sectional survey was conducted in orthopedics, rheumatology and pain departments in five first-class hospitals in China from March to October 2018. Eligible patients were ≥40 years old, with diagnosed knee OA, experiencing joint pain for at least 3 months and receiving oral medications during the past 12 months. Socio-demographics, disease characteristics, Brief Pain Inventory (BPI), treatment information, Treatment Satisfaction Questionnaire for Medication (TSQM-1.4), and HRQoL (EQ-5D-5L) were assessed. Descriptive analysis and t-test were used for statistical analysis.
Results: A total of 601 patients were included and 75.2% of them were female. The mean (SD) age was 61.77 (9.53) years. More than half (55.1%) had at least 1 comorbidity. The most common comorbidities were hypertension (39.8%), diabetes (15.3%), gastritis (14.3%) and coronary heart disease (12.5%). The mean (SD) age at first diagnosis of knee OA was 58.13 (9.62) years. The most commonly used current treatments for knee OA were oral medication (78.0%), followed by patch or ointment (45.1%) and intra-artlar hyaluronic acid injection (31.5%). The mean (SD) of BPI-Severity and BPI-Interference ratings were 3.78 (1.62) and 2.97 (1.70), respectively. More than half (52.9%) of patients rated BPI-average pain ≥4. Around 37.1% of patients reported ≥4 days per week of work or housework loss due to OA pain. Overall, the mean (SD) score of EQ-5D-5L is 0.72 (0.21). Patients with BPI-average pain ≥4 reported significantly lower EQ-5D-5L score than those with BPI-average pain <4 (0.62 vs 0.84, p<0.0001). The mean (SD) scores of TSQM effectiveness, side effects, convenience and global satisfaction were 54.19 (14.13), 96.00 (10.93), 62.30 (10.42) and 58.97 (15.43), respectively. The scores in all of the four dimensions of TSQM were lower in patients with BPI-average pain ≥4 than in those with BPI-average pain <4 (effectiveness: 51.01 vs 57.81, p<0.0001; side effects: 94.91 vs 97.24, p=0.0099; convenience: 60.18 vs 64.71, p<0.0001; global satisfaction: 57.74 vs 60.35, p=0.0402).
Conclusion: Chronic pain due to knee OA, especially moderate to severe pain, has significant impact on patients' HRQoL and work productivity. Patients were not satisfied with current treatments. There are unmet needs for better pain management including more drug choices in China to improve the treatment satisfaction.
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Osteoporosis

AB0817 **CAN STATINES IMPROVE BONE QUALITY IN POSMENOPAUSAL OSTEOPOROSIS?**

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Background: Osteoporosis (OP) is the most frequent metabolic bone disease. It has low bone mass and microarchitectural deterioration, which increases the risk of fractures. The most commonly used drugs are bisphosphonates, however statins (ST) have pleiotropic properties, and some researchers suggested their use in OP.
Objectives: To determine the effect of ST on bone mineral density (BMD) in postmenopausal osteoporotic women.
Methods: A cross-sectional study, control case where postmenopausal women with hypercholesterolemia treated with ST for a period not less than 6 months were studied for two years. The control group was postmenopausal population that did not receive statins. Exclusion criteria: Diabetes, previous treatment with estrogen, calcitonin, anabolic, steroids, bisphosphonates or vitamin D during a period of 6 months prior to enter to the study or with amenorrhea less than 12 months. We evaluated age, weight, height, BMI, personal and first degree family members' history of fracture, use of corticosteroids, smoking, alcoholism, daily calcium intake, sedentary lifestyle, phosphocalcic metabolism laboratory and Vitamin D. All patients were performed Bone Densitometry by dual-energy X-ray absorptiometry (DXA) with an Hologic equipment in right hip and lumbar spine, staging them according to WHO. The statistical analysis was performed using the Student's test and the Fisher test for categorical variables. Values of p less than 0.05 were considered significant.
Results: 202 patients were enrolled in the ST group and 203 in the control group. Age, weight, height and BMI were 62.54; 69.6; 1.60 and 27.1 in the ST group and 58.5; 65.7; 1.59 and 26.83 in the control group respectively (p = 0.000, p = 0.001 p = 0.79, p = 0.38). There were no significant differences in risk factors for OP between groups. The average lumbar BMD was -0.87 for the ST group and -1.76 for the control group (p = 0.000), the average femur neck BMD was -1.15 for the ST group and -1.56 for control (p = 0.000), the total hip BMD was -0.32 for the ST group and -0.74 for the control group (p = 0.001), vitamin D was 25.57 for the ST group and 27.71 (p = 0.120).
Conclusion: ST can improve Bone Mineral Density in postmenopausal women, more studies are needed to confirm these results.

REFERENCES

[1] Pacheco-Pantoja EL, Alvarez-Nemegyei J. Statins and osteoporosis: a latent promise. Reumatol Clin. 2014 Jul-Aug;10(4):201-3. doi: 10.1016/j.reuma.2014.04.005.
[2] An T[1], Hao J[2], Sun S[1], Li R[1], Yang M[1], Cheng G[3], Zou M[4]. Efficacy of statins for osteoporosis: a systematic review and meta-analysis. Osteoporos Int. 2017 Jan;28(1):47-57. doi: 10.1007/s00198-016-3844-8.
[3] Kaleağasıoğlu F, Olcay E, Onur R. Statins as potential agents for the prevention and treatment of osteoporosis. Endocrine. 2018 Oct;62(1):269. doi: 10.1007/s12020-018-1650-0. Epub 2018 Jun 17.
[4] Horiuchi N, Maeda T. Statins and bone metabolism. Oral Dis. 2006 Mar;12 (2):85-101. Review.

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AB0818 **INCIDENCE OF FRACTURES AND ASSOCIATED RISK FACTORS DURING THE DRUG HOLIDAYS PERIOD WITH BISPHOSPHONATES**

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Background: Biphophosnates are the most widely used treatment for osteoporosis. The optimal treatment duration, however, remains unclear. The occurrence of adverse effects, such as osteonecrosis of the jaw (ONJ) and atypical femoral fractures (AFF), has raised the issue of bisphosphonate discontinuation ("drug holiday") after a certain treatment period.
Objectives: To assess the incidence of fractures in patients during the drug holidays period with bisphosphonates, as well as to determine the risk factors are associated to it.
Methods: Analytical, observational, longitudinal, and ambispective study of a cohort of patients with postmenopausal osteoporosis or men over 50 years of age treated with oral bisphosphonates (at least for 5 years) or intravenous (at least for 3 years) and who had been at least for one year in a drug holidays period, from 01/01/2012 to 12/31/17. Patients treated with corticosteroids and/or with diseases with effects on bone

metabolism were excluded. Statystical analysis included a descriptive study of the variables to assess the association between the incidence of fractures and various risk factors, as well as univariate and multivariate Cox regression analysis.
Results: 128 patients with osteoporosis were studied, of wich 19 (14.7%) suffered an osteoporotic fracture during the follow-up. Bivariate analysis showed in the group of patients with fractures a higher proportion of smoking patients (p = 0.004), osteopening treatment (p = 0.005) and a femoral neck t score lower at the beginning of the drug holidays period -2.07 (0.68) vs - 1.58 (0.63), p = 0.008.
In addition, there was a higher proportion of patients with fracture with moderate risk before the start of the drug holidays period (p = 0.007). The fracture survival curves were lower in patients older than 75 years (p = 0.04). When applying the same treatment, for each year increase, the risk of fracture was increased by 6% (p = 0.04), while, for the same age, this risk was increased 4.33 times in patients who were treated with Risedronate versus those with Alendronate (p = 0.05).
The multiple regression analysis showed that vertebral fracture was independently associated with Tabaco (HR 4,28 p=0,047).
Conclusion: Based on our results, it would be useful to follow closely those patients during drugs holidays period who are smokers, older than 75 years, with osteopening treatment, who present a low femoral neck tscore and/or have been previously treated with Risedronate.

REFERENCES

[1] Silverman SL, et al. Osteoporos Int. 2016;27 (3):849-852.
[2] Bindon B, et al. Endocr Pract. 2018;24(2):163-169.
[3] Mignot MA, et al. Osteoporos Int. 2017;28(12):3431-3438.

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AB0819 HANDGRIP STRENGTH PREDICTS HIGH FRACTURE RISK IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background: Accumulating evidence has revealed that the risk of osteoporosis related fractures is significantly increased in type 2 diabetes mellitus (T2DM) patients in comparison with healthy controls. Dual X-ray Absorptiometry (DXA) derived bone mineral density (BMD) is not completely useful to discriminate at risk patients.
Objectives: To find a valuable clinical tool that is helpful to identify T2DM subjects with poor bone health, finally preventing fragility fractures.
Methods: In a setting of Caucasian subjects with T2DM, anthropometric data and information about metabolic control and diabetic complications were recorded. Handgrip strength by dynamometer, FRAX derived 10-years probability of major osteoporotic fractures and hip fractures were also assessed. Bone evaluation was performed by a dual-energy X-ray absorptiometry (DXA) densitometer at the lumbar spine (L1-L4) and at the femoral neck; based on specific software, the trabecular bone score (TBS) was calculated. Lateral scan of thoracic and lumbar spine was assessed to investigate morphometric vertebral fractures (Vfx).
Results: 29 patients (female 65%) [median age 67 (60 to 70)] with T2DM were considered. Morphometric vertebral fractures were detected by DXA in 17% of patients without any gender differences (males vs. females, p=0.6). The median ten years probability of fractures was 8.1% and 2.3% as for major osteoporotic or hip fracture respectively. Median femoral neck T-score value [-1.1 SD (-1.8 to -0.5)] was indicative of a slight osteopenia while lumbar spine T-score was even in the normal range [-0.8 SD (-1.5 to -0.1)]. The median TBS value was 1.28 (1.2 to 1.31) and TBS was positively associated with BMD at lumbar spine and femoral neck. Median handgrip strength value was 22.3 kg (18.9 to 31.3). At multiple regression analysis, handgrip strength predicted both lumbar (β= 0.009, SE 0.0034, p=0.01) and femoral neck BMD values (β= 0.006, SE 0.002, p=0.01). Age (β= -0.008, SE 0.002, p=0.007) and handgrip strength (β= 0.01, SE 0.002, p=0.0001) were also independently associated with TBS score, after correcting for mean HbA1c values and time since T2DM diagnosis.
Conclusion: Handgrip strength may be a reliable tool to screen for bone fragility in T2DM.

REFERENCES

[1] Napoli N, Chandran M, Pierroz DD et al. Mechanisms of diabetes mellitus-induced bone fragility. Nat Rev Endocrinol 2017; 13(4):208–219.
[2] Russo GT, Giandalia A, Romeo EL, Nunziata M, Muscianisi M, Ruffo MC, Catalano A, Cucinotta D. Fracture Risk in Type 2 Diabetes: Current Perspectives and Gender Differences. Int J Endocrinol. 2016;2016:1615735.
[3] Li YZ, Zhuang HF, Cai SQ, Lin CK, Wang PW, Yan LS, Lin JK, Yu HM. Low Grip Strength is a Strong Risk Factor of Osteoporosis in Postmenopausal Women. Orthop Surg. 2018 Feb;10(1):17-22.

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AB0820 COGNITIVE IMPULSIVITY CORRELATES WITH BONE MINERAL DENSITY

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Background: Cognitive impairment is known to be associated with low bone mineral density (BMD) and low levels of BMD have been associated with increased rates of progression from mild cognitive impairment to Alzheimer's disease and with the onset of episodic verbal learning deficit.
Objectives: The potential involvement of executive functions impairment on BMD is still unclear. The aim of this study was to investigate the correlations between cognitive impulsivity, BMD and fall risk.
Methods: Cognitive impulsivity was measured by Stroop Color and Word Test (SCWT) administration in a setting of 40 consecutively recruited postmenopausal women referring to a outpatients clinic for the evaluation of fracture risk. SCWT is a neuropsychological test able to assess the ability to inhibit cognitive interference: during the administration, women were required to quickly read three different tables of which two represented the "congruous condition" in which participants were invited to read names of colors printed in black ink and name different color patches. In the third table, named "incongruous condition", color-words were printed in inconsistent color ink (e.g. the word "red" is printed in green ink) and participants were required to name the color of the ink instead of reading the word. Women with Mini Mental State Examination (MMSE) score < 24, known neurologic or psychiatric disorders, history of significant hearing or visual impairment, or significant physical disability, history of uncontrolled diabetes and abnormal thyroid function, cancer, heart, respiratory, kidney or liver failure were excluded. BMD was measured at lumbar spine and femoral site by a DXA densitometer (Hologic Discovery). History of falls in the previous 12 months was recorded
Results: Cognitive impulsivity, as highlighted by making errors at the SCWT, was significantly associated with lumbar spine and femoral neck T-score (r= -0.39, p= 0.01 and r= -0.43, p= 0.008; respectively). MMSE score was not associated with T-score values, neither at lumbar spine (r= 0.09, p= 0.5) nor at femoral neck (r= 0.2, p= 0.21); differently MMSE score was significantly associated both with Stroop test error (r= -0.34, p= 0.02) and time interferences (r= -0.39, p= 0.01). Furthermore, time interference was positively associated with the self-reported history of falls (r= 0.342; p= 0.031).
Conclusion: Cognitive impulsivity was significantly associated with BMD values and higher prevalence of falls in postmenopausal women. It could be considered as a possible clinical risk factor for osteoporotic fractures.

REFERENCES

[1] J.R. Stroop, Studies of interference in serial verbal reactions. J. Exp. Psychol 18 (1935) 643–662.
[2] P. Caffarra, G. Vezzadini, F. Dieci, F. Zonato, A. Venneri. A short version of the Stroop test: Normative data in an Italian population sample. Nuova Rivista di Neurologia 12 (4) (2002) 111-115.
[3] A. Mirelman, T. Herman, M. Brozgol, M. Dorfman, E. Sprecher, A. Schweiger, N. Giladi, J.M. Hausdorff. Executive function and falls in older adults: new findings from a five-year prospective study link fall risk to cognition. PLoS One 7 (6) (2012).
[4] B. Abrahamsen, D. Brask-Lindemann, K.H. Rubin, P. Schwarz. A review of lifestyle, smoking and other modifiable risk factors for osteoporotic fractures. Bonekey Rep 3 (2014) 574. Bonekey Rep. 2014 Sep 3;3:574.

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AB0821 APPRECIATION OF OSTEOPOROTIC TREATMENT COMPLIANCE WITH ALENDRONATE 70MG ORALLY

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Background: Patients suffering from osteoporosis (OP) dont have the opportunity to enjoy from an accurate and concrete parameters response to OP treatment. They therefore have no palpable evidence of the favorable effect generated by anti- osteoporotic treatment (AOT), given the silent nature of the pathology. That is way we see the non-compliance with treatment in some patients.
Objectives: It was essential to estimate the extent of the lack of compliance with AOT in order to deduce the factors related to this deficiency in order to reduce the size of the problem.
Methods: Its a Descriptive cross study performed in all patients over 38 years for both sexes and that exhibit post menopausal or corticosteroid-induced OP justifying AOT orally (alendronate 70mg oraly per week) observed over a period of at least 6months.
Results: We collected data of 153 patients, in 9 out of 10 cases this was a woman, the mean age was 59.3 ± 8.1 years, the average duration of gain of treatment was 32.2 ± 18.2 months, 3 of 5 patients believe that treatment is for musculoskeletal pains, 1/3 of respondents confess not to take their weekly treatment regularly, regular physical activity was performed by only 21% of patients, the factors related to non-compliance were : lack of education (p = 0, 032) and sedentary lifestyle (p = 0, 044).
Conclusion: OP is unfortunately underestimated by both patients and physicians, and its short- and long- term repercussions are often minimized. Our study has shown that the various measures required in its management are poorly followed by patients despite their proven effectiveness in reducing fractures.One in three patients in ours ample do not follow their treatment properly.Therapeutic education seems to be the answer to overcome this lack of adhesion.
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AB0822 VITAMIN D (25OHD) IN PATIENTS WITH CHRONIC RHEUMATIC DISEASESRECEIVING TREATMENT WITH ADALIMUMAB. DESCRIPTIVE STUDY OF A COHORT

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Background: Patients with chronic rheumatic diseases (CRD) have lower levels of 25OHD, inverse correlation has been describe and greater severity between the different CRD with 25OHD deficit. Most scientific societies recommend levels> 30 ng/mL. Patients with refractary disease to conventional therapy have a higher inflammatory load, require optimal levels of 25OHD and often needs biological disease-modifying antirheumatic drugs (bDMARD) in order to prevent structural damage.
Objectives: The aim of this study was to describe the epidemiological, clinical and therapeutic characteristics of patients receiving Adalimumab (ADL) in which 25OHD levels were determined in 2018.
Methods: Transversal, retrospective study in a hospital setting. We analyzed data from patients included in a study to determine levels of ADL, in whom the serum level of 25OHD was determined at least once during the last year. Among 104 patients, 74 with 25OHD determination were included.
Results: Seventy-four patients selected, 45.9% were men and 54.1% women. The mean age was 54.9 years (SD ± 13.6). 41.9% (31) had Rheumatoid Arthritis, 36.5% (27) Spondyloartrhitis, 17.6% (13) Psoriatic Arthritis and 4.1% (3) Juvenile Idiopathic Arthritis. 35.1% (26) had deficit (<20 ng/mL) of 25OHD, 31.1% (23) insufficiency (20-30 ng/mL) and only 33.8% (25) optimal levels (>30 ng/mL). The 62.2% (46) of the patients received oral supplementation, of these 67.4% maintained levels >20 ng/mL and 32.6% <20 ng/mL. 37.8% (28) did not receive supplementation, despite this 60.7% within this group had levels >20 ng/mL. No statistical differences were found regarding vitamin D deficit and oral supplementation (p> 0.05).
13.5% (10) of the patients also had Osteoporosis (OP); in this group 6 had deficit of 25OHD, 1 insufficiency and only 3 optimal levels, all of them received 25OHD supplementation. No differences between the groups in relation to the DMARD treatment.
Conclusion: Vitamin D levels were determined in 71.2% of patients and not in all of them as it would be advisable. Among the patients with 25OHD determination, 62.2% received oral supplementation, however only 33.8% of the patients reached optimal levels (> 30 ng/mL) without statistical differences regarding supplementation. 13.5% of the patients who received supplementation also had OP.
Despite the weakness of the study in terms of design and sample, most patients did not reached optimal levels of 25OHD; we can assume that it is necessary to obtain levels of 25OHD >30 ng/mL in all patients, with adequate supplementation if necessary due to the positive effects known in CRD.

REFERENCES

[1] Fernandes S1, Etcheto A2, van der Heijde D3, Landewé R4, van den Bosch F5, Dougados M2, Moltó A2. Vitamin D status in spondyloarthritis: results of the ASAS-COMOSPA international study. Clin Exp Rheumatol. 2018 Mar-Apr;36(2):210-214
[2] Lin J1, Liu J1, Davies ML2, Chen W1. Serum Vitamin D Level and Rheumatoid Arthritis Disease Activity: Review and Meta-Analysis. PLoS One. 2016 Jan 11;11(1):e0146351
[3] Dawson-Hughes B1, Mithal A, Bonjour JP, Boonen S, Burckhardt P, Fuleihan GE, Josse RG, Lips P, Morales-Torres J, Yoshimura N. IOF position statement: vitamin D recommendations for older adults. Osteoporos Int. 2010 Jul;21(7):1151-4.
[4] Bischoff-Ferrari HA1, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr. 2006 Jul;84(1):18-28.

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AB0823 TRABECULAR BONE SCORE AT LUMBAR SPINE IS ASSOCIATED WITH QUANTITATIVE ULTRASOUND MEASUREMENTS AT PHALANGEAL SITE IN BREAST CANCER SURVIVORS RECEIVING AROMATASE INHIBITORS

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Background: In breast cancer (BC) survivors, the age-related reduction in bone mineral density is exacerbated by aromatase inhibitors (AIs) treatment. AIs disrupt also bone quality and enhance fracture risk in aging women. Consequently, bone health evaluation is mandatory in BC women receiving AIs.
Objectives: Quantitative ultrasound of bone (QUS) and trabecular bone score (TBS) are recognized tools to explore bone health beyond bone mineral density (BMD). The aim of our research was to explore the association of TBS with QUS measurements at phalangeal site in a setting of postmenopausal women taking aromatase inhibitors (AIs).
Methods: BMD at lumbar spine, femoral neck and TBS were evaluated by a DXA densitometer (Hologic Discovery). Amplitude Dependent Speed of Sound (AD-SoS), Bone Transmission Time (BTT) and Ultrasound Bone Profile Index (UBPI) were detected at phalangeal site by Bone Profiler (Igea).
Results: In 102 postmenopausal women (mean age 61.64 ± 8.33 yr.) (60 AIs treated and 42 controls), at baseline examination, TBS was negatively associated with age (r=-0.39, p<0.001) and positively related with T-score values at lumbar spine and femoral neck. After 18 months, AD-SoS, UBPI and BTT values were significantly decreased in BC women receiving AIs (-3.7%, -6.45%, -8.5%, respectively, p<0.001 for all), but not in controls (-0.7%, -3.53%, -2.97%, respectively). Change of BMD at lumbar spine was significantly different between AIs treated women and controls (-2.94% vs. -0.69%, p=0.001) and the same result was observed as for BMD at femoral neck (-2.5% vs. -0.39%, p=0.01). Percent change of TBS was significantly greater in AIs treated women in comparison with controls (-2.2% vs. -0.4%, respectively, p=0.02). In AIs treated women, but not in controls, CTX levels significantly increased after 18 months [0.47 (0.36 to 0.62) vs. 0.66 (0.43 to 0.77), p=0.0004] and the same trend was observed as for BSAP levels [14 (13.01 to 15.57) vs. 15 (13.75 to 16.75), p=0.003]. At a multiple regression analysis, change of TBS was independently predicted by change of AD-SoS, after correcting

for BMD change at lumbar spine and femoral neck and for modification of CTX and BSAP levels (β= 0.37, SE= 2.44, p<0.001).
Conclusion: TBS variation was independently predicted by phalangeal QUS measurement in AIs treated BC women. Phalangeal QUS may represent an alternative tool to evaluate bone health also in this setting of patients.

REFERENCES

[1] Catalano A, Morabito N, Agostino RM, Basile G, Gaudio A, Atteritano M, Natale G, Xourafa A, Morini E, Adamo V, Lasco A. Bone health assessment by quantitative ultrasound and dual-energy x-ray absorptiometry in postmenopausal women withbreast cancer receiving aromatase inhibitors. Menopause. 2017 Jan;24(1):85-91.
[2] Catalano A, Morabito N, Basile G, Fusco S, Castagna G, Reitano F, Albanese RC, Lasco A. Fracture risk assessment in postmenopausal women referred to an Italian center for osteoporosis: a single day experience in Messina. Clin Cases MinerBone Metab. 2013 Sep;10(3):191-4.
[3] Martineau P, Leslie WD. Trabecular bone score (TBS): Method and applications. Bone. 2017 Nov;104:66-72.

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AB0824 THE EFFECTS OF CEMENT VOLUME DISTRIBUTION OF PERCUTANEOUS KYPHOPLASTY IN OSTEOPOROTIC VERTEBRAL FRACTURE

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Background: Osteoporotic vertebral compression fractures (OVCF) account for 45% of osteoporotic fractures. It cause severe back pain, unable walk or even stand Percutaneous kyphoplasty (PKP) is commonly used to treat painful OVCF, effective relieve pain and walking ability. But there have been few clinical studies that have specifically explored the relationship of the cement volume distribution rate and clinical outcomes.
Objectives: To access the effect of the cement volume distribution pattern in percutaneous kyphoplasty.
Methods: We retrospectively reviewed 126 cases of osteoporotic compression fractures treated with percutaneous kyphoplasty from Jan 2005 to May 2015. The cement volume distribution (CVD) was measured with X-ray and CT scan. 126 thoracolumbar vertebrae were divided into two groups based on CVD ratio: 51 vertebrae in group A with CVD ratio<=2; 15 in group B with CVD ratio>2. The relationships of the cement volume distribution and clinical outcomes of pain, vertebral height and kyphotic angle change between the two groups were compared
Results: The mean duration of follow-up was 25 months (range 11~76), and the mean age was 68.2±8.7 years. Correlation of volume of cement distribution measured by CT scan and X-ray is 89.3% (P<0.001). The VAS improvement after kyphoplasty was no statistically significant (P = 0.651). Statistically greater height gain was observed in group B at the anterior border (4.42±2.42 VS 1.83±1.5, P = 0.035) and at the center (4.64±1.73 VS 3.01±0.41, P = 0.044). Subsequent fracture was 7 cases in group A and 4 case in group B.
Conclusion: Larger volume of cement distribution, greater correction of kyphosis. The greater distribution of the cement without leakage would be suggested when the limited volume of cement is injected.

REFERENCES

[1] Rebolledo B J, Gladnick B P, Unnanuntana A, et al. Comparison of unipedicular and bipedicular balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures A prospective randomised study[J]. Bone Joint J, 2013, 11(3):401-406.
[2] Lian-Hua L I, Tian-Sheng S, Zhi L, et al. Comparison of unipedicular and bipedicular percutaneous kyphoplasty for treating osteoporotic vertebral compression fractures: a meta-analysis[J]. Chin Med J (Eng), 2013, 126 (20).
[3] Song B K, Eun J P, Oh Y M. Clinical and radiological comparison of unipedicular versus bipedicular balloon kyphoplasty for the treatment of vertebral compression fractures[J]. Osteoporosis International, 2009, 20(10):1717-1723.

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AB0825 IMPACT OF AROMATASE INHIBITOR TREATMENT ON BONE MINERAL DENSITY AND PREVALENT VERTEBRAL FRACTURE

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Background: In recent years, despite the growing incidence of breast cancer, a reduction in mortality has been observed. Adjuvant therapy with aromatase inhibitors (AI) has contributed to a longer disease free survival. However these molecules induce a hyper bone remodeling, modifying the bone architecture and thus increasing the fracture risk. The new guidelines indicate extension of treatment duration up to 10 years. So special precautions must be established in order to avoid bone mineral density (BMD) decrease and to reduce fracture risk.
Objectives: The aim of this study was to evaluate the impact of AI treatment on BMD and to screen vertebral fracture (VF) in post menopausal women with breast cancer.
Methods: A clinical cross sectional study was carried between August 2018 and December 2018, including post-menopausal women with non-metastatic breast cancer. Each woman had an extensive medical history and physical examination. BMD was measured using dual energy X absorptiometry DeXa at femoral neck, total hip and at lumbar spine. We used the WHO criteria for the diagnosis of osteoporosis and osteopenia. Vertebral fractures were screened by performing a vertebral fracture (VFA) image. VF grade 1 were excluded.
Results: Thirty-six post-menopausal women were examined in our rheumatology department. The mean age was 59.5±10.38 years with an average body mass index (BMI) of 30.7 kg/m^2 [15.81-38.28].The average age of menopause was 45.5±5.25 years.The mean length of menopause was 14 years [2.1-31]. The mean duration of breast cancer follow-up was 71.7 months. 22 patients underwent chemotherapy and radiotherapy.Mean femoral neck BMD was 0.805 g/cm^3 [0.647-1.049 g/cm^3] and the vertebral BMD was 1.003 g/cm^3 [0.739-1.314g/cm^3].According to the WHO classification, 12 women (34.6%) had osteoporosis, 15 (42.3%) had osteopenia and 9 (19.2%) had normal BMD. 9 patients showed signs of osteoporosis at femoral neck and 8 had osteoporosis at lumbar spine. 10 subjects (27.8%) had VF identified by VFA, which were grade 2 and 3 in respectively 8 and 2 vertebra. No multiple VF were assessed. No statistically significant difference was found between women with and without VF for age, BMD value, and duration of follow-up or previous fragility fracture. We did not find a significant correlation between treatment length and BMD at either site: femoral neck (p=0.42), total hip (p=0.783) and lumbar spine (p=0.357).
Conclusion: This data has shown that approximately one-third of patients receiving AI treatment have at least one vertebral fracture, and 40% had osteoporosis. Therefore we need to screen bone mineral density and fracture in women under AI therapy.
Disclosure of Interests: None declared
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AB0826 OSTEODENSITOMETRIC PROFILE DURING JUVENILE CELIAC DISEASE

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Background: Bone mineralization abnormalities are often seen in children with chronic gastrointestinal disease.
Among these pathologies, celiac disease (CD) is the most likely source of abnormalities of bone mineral density. These disorders are of multifactorial origin involving malabsorption, nutritional status, decreased physical activity and chronic inflammation.
Objectives: The purpose of this study was to determine the frequency and factors associated with lower bone mineral density in children with CD.
Methods: This is a retrospective study, over a period of 4 years (from January 2014 to December 2017) including children followed for CD who had a measurement of bone mineral density (BMD) by DEXA. Clinical, anthropometric and densitometry data (BMD at the femoral and vertebral site) were recorded.
Results: Thirty-six children were collected. Among them 29 were girls and 7 were boys. The average age was 11.94 years old.
The average size was 137.8 cm. The average weight was 35.3 kg. The average body mass index (BMI) was 17.69 kg/m² [13.05-21.69 kg/m²].
The average vertebral BMD was 0.891 g/cm3. The average z-score was -1.08. BMD was normal in 26 cases. A decrease in bone mineral density

with respect to chronological age was observed in 10 cases. A very significant correlation was observed between BMI and vertebral BMD (r = 0.75, p = 0.000).

Conclusion: The frequency and severity of the decline in BMD in children with CD requires regular monitoring. It seems to be favored by a low BMI, which is common during CD in relation with the associated malabsorption.

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AB0827 IS DENOSUMAB SAFE IN HIV PATIENTS?

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Background: The survival of the infected patients by the human immunodeficiency virus (HIV) has increased in the last years, increasing the incidental comorbilities, being osteoporosis (OP) one of them, caused by traditional risk factors, by the ones associated to the infection itself and due to the specific treatments used. The denosumab is a human monoclonal antibody that acts against the link of the receptor that activates the nuclear kappa B (RANK-L), and among its secondary effects most commonly described, there are the infections, reason why its indication in HIV patients requires special caution.

Objectives: To analize efficacy, security and compliance to denosumab in HIV patients.

Methods: Retrospective longitudinal observational study. There were included all HIV patients with OP diagnosed by bone mineral density measured by dual-energy X-ray densitometry (DEXA) or fragility fractures treated with denosumab at Infectious Diseases Unit of our Hospital from August 2014 until December 2018. There were collected clinical data, immunological status, antiretroviral therapies, fragility fractures and duration, adverse events, tolerance and compliance to denosumab treatment.

Results: There were included 14 patients, 8 females and 6 males, with a mean age of 58.35 (50-73) years old, and a mean HIV evolution of 23,78 (± 9.56) years, with a mean denosumab treatment duration of 27.07 (9-58) months. They presented a DEXA mean T-score values of -2.39 for femoral neck and -2.96 for spine. There were collected a patient with múltiple vertebral fractures, and an other patient with a single vertebral fractures before started denosumab treatment and 1 distal radius fracture 9 months on denosumab treatment. There were reported adverse events in 5 of the 14 patients: 2 mild infections of the upper respiratory track, 1 injection site rash that lead to the interruption of the treatment, and 2 exitus but none of them with a direct relationship with denosumab treatment: a patient with refractory small cell lung cancer history, deceased of pneumonia, and a 77 year old woman with Alzheimer disease deceased of respiratory infection. Compliance was not met in three patients, 1 because lost of follow-up, 1 caused by bad general compliance and another because indication of odontological surgery, these two last ones are waiting for re-introduction. There have not been collected jaw osteonecrosis neither atypical fractures cases. There have not been collected viral loads or CD4 changes during the follow-up period that involved a switch for the OP treatment. The antiretroviral treatment changes have been caused by intolerances to previous treatments and treatment simplifications in order to improve the compliance, but never because denosumab concomitant therapy.

Conclusion: Denosumab treatment in the HIV patients of our series is well tolerated, has adequate adherence and seems safe although perhaps it should be used with greater caution in patients with comorbidities.

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AB0828 RHEUMATIC PATHOLOGY AFTER SOLID ORGAN TRANSPLANTATION

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Background: Organ transplantation has become as effective therapy for end-stage renal, hepatic, cardiac and pulmonary diseases within the past 2 decades. Osteoporosis, low level of vitamin D and hyperuricemia have emerged as frequent and sometimes devastating complications of organ solid transplantation process.

Objectives: The objective of the study was to detect the prevalence of osteoporosis, low level of vitamin D and hyperuricemia in *liver* and lung *transplant patients*.

Methods: We evaluated a cohort of 48 patients who underwent liver and lung transplantation in a single Romanian center between July 2014 and January 2019. 44 pts undergone liver transplantation and 4 undergone lung transplantation. We have measured the level of the 25-hydroxyvitamin D and serum urate before and after the transplantation in all patients.

Results: The average age of the patients was 53.7 ± 10 years (range 32–69) with a sex ratio 1:1. 32 (66%) of patients came from urban area. 8 (16.6%) patients were excluded from this study due to recurrent HCV infection with hepatic failure in the first few months after transplantation. The final group consisted of 40 patients.

The indications of the orthotopic liver transplantation in these patients were: cirrhosis secondary chronic hepatitis B, C, D virus infection in 24 (60%) cases, autoimmune hepatitis in 7 (17.5%) patients, alcoholic liver disease in 2 (5%) patients, hepatocellular carcinoma in 1 (2.5%) patient, polycystic liver disease in 1 (2.5%) patient and nonalcoholic fatty liver disease in 1 (2.5%) patient.

In all 4 cases with lung transplantation, the reason for of the lung transplantation was chronic obstructive pulmonary disease (COPD).

36 (91%) patients were receiving combination immunosuppressant therapy (tacrolimus and) and only 4 (9%) patients were receiving cyclosporine; in this situation, the association between tacrolimus and mycophenolate mofetil was preferred versus cyclosporine because of the negative *effect of cyclosporine on the bone*.

Post-transplant, hyperurcemia (according to local *laboratory* reference values >6.5 mg/dL) was presented in 28 (70%) transplant recipients but none of the hyperuricemic patients developed gout. Despite this fact, all of them were treated with allopurinol.

Vitamin D deficiency was reported in 22 (55%) transplant recipients. Also, *a DXA scan* of the lumbar spine and femoral neck *measuring T-score and bone mineral density (*BMD) *was routinely performed after a mean interval of 4-6 months post-transplant*. From this group of patients, 10 (25%) patients had decreased bone mineral density (<2.5 SD) and 8 (20%) of them who complained of back pain in the early posttransplantation period, presented on x-rays *vertebral fragility fractures* at different sites (most frequently in the thoracic spine). The mean T-score was -2.7 and the mean BMD was 27.4 kg/m².

Conclusion: The standard care of liver and lung transplant recipients must includes, besides other lab tests, a measurement of 25-hydroxyvitamin D and serum urate. For patients with low levels of 25-hydroxyvitamin D, evaluation for osteoporosis (risk factors, x-ray, DXA scan) should be mandatory.

REFERENCES

[1] P. R. Ebeling, "Approach to the patient with transplantation-related bone loss," The Journal of Clinical Endocrinology & Metabolism, vol. 94, no. 5, pp. 1483–1490, 2009.

[2] Sullivan PM, William A, tichy EM, *"Hyperuricemia and gout in solid-organ transplant: update in pharmacological management,"* Prog Transplant. 2015 Sep;25(3):263-70. doi: 10.7182/pit2015322.

[3] Mazzali M, *"Uric acid and transplantation"*, Semin Nephrol. 2005 Jan;25 (1):50-5.

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AB0829 **OSTEOGENESIS IMPERFECTA : EVOLUTION OF THE BONE MINERAL DENSITY AND EVALUATION OF FRACTURE RISK UNDER BISPHOSPHONATES**

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Background: Osteogenesis imperfecta (OI), or Lobstein's disease, also known as 'Glass bone disease' is a rare genetic disorder predisposing to low bone mass with impaired bone microarchitecture and abnormal quality of bone material, causing fracture susceptibility and bone deformities.
Objectives: The main objective of our work was to study the clinical and para-clinical characteristics, and global management, of adult patients and children with OI in a rheumatology departement by comparing them with data from the littérature.
The secondary objectives were to study the evolution of the bone mineral density and to evaluate the fracture incidence under treatement by Bisphosphonates.
Methods: This is a cross-sectional, observational, descriptive, analytical and monocentric study of subject with OI followed at Fattouma Bourguiba University Hospital in Monastir, Tunisia
Results: We collected 13 patients with OI, including 5 children and 8 adults. Seven patients were female and 6 were male, including 12 patients with type IB and one with type IIIB. Three adult patients had a family history of OI. For children, it was sporadic and the genetic survey did not reveal similar cases in the family. The mean age of clinical onset of the disease was 9 years and 3 months [0-33 years] with a mea nage at diagnosis of 15 years and 7 months [14 months- 40 years]. The clinical manifestations were dominated by osteo-articular symptoms. Chronic mechanical bone pain related to fractures was present in eight patients. Twelve patients had a history of fracture. These were repeated fractures without trauma or minimal traumain the majority of cases mainly in the lower limbs. The first fracture site was the femur associated with other fracture sites (there were no fractures in the pelvis, hands and skull). Deformities were observed in 7 patients, mainly in the limbs (6 patients), in the spine (2 patients) and in the thorax (1 patient).
In our study the frequency of osteoporosis and/or osteopenia regardless of the mesured site and using the T-score value for women≤-2,5 and the Z-score≤-2 for children and men was 84,62%. All patients received Aredia treatment according to Glorieux's protocol with calcium and vitamin D supplementation. The treatment was also multidisciplinary. Bisphosphonate treatment was well tolerated for the majority of patients. There was a decrease in the number of fractures and also a densitometric gain objectivised for the majority of patients.
Conclusion: Our results confirm the efficacy of BP in patients with OI regardless of age group. Short-term adverse are rare and transient.

REFERENCE

[1] R. Morello, Osteogenesis imperfecta and therapeutics, Matrix Biol. (2018). doi:10.1016/j.matbio.2018.03.010.

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AB0830 **CG AND DMARDS INDUCED BMD CHANGES IN PRE-, POSTMENOPAUSAL WOMEN AND MAN WITH RHEUMATOID ARTHRITIS (RA)**

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Background: Risk factors for GC-induced fracture include low bone strength at the beginning of GC treatment and the rate of decline in bone mass during treatment, which is largely determined by the dose and duration of GC use [1]. The absolute risk of future fracture in an individual is substantially influenced by demographic and other characteristics (age, race, sex, and concomitant OP risk factors). For these reasons, it is important to identify differences in BMD changing depends on sex and reproductive status.
Objectives: To compare the BMD changes in man, pre- and postmenopausal women with RA depends on different treatment regiments.
Methods: The study was performed on 145 patients: 117 women (mean age 45.4±13.0 years, mean disease duration 9.7±7.7 years, 41% (n=48) postmenopausal) and 28 man (mean age 45.5±17.5 years, mean disease duration 5.7±4.8 years) with RA. Female patients were divided in two groups by menopause: premenopausal (PreM) in mean age 36.9±9.3 years and postmenopausal (PM) in the mean age 57.6±5.9 years. 68.4% women and 64.3% man received prednisolon ≤10 mg/day during 5.67 ±4.82 and 3.5±5.9 years respectively. 60.7% of men received MTX, 50% in combination with CGs. Among the women group 87% PreM patients received MTX, 58.3% in combination with GCs and 46.4% with biologics. 85.4% PM women took MTX, 68.8% in combination with GCs and 33.3% - with biologics. BMD was measured in 3 part of the skeleton: hip (total and neck), lumbar spine, distal part of forearm.
Results: BMD was decreased in 44.5% of women and 42.9% of man. BMD of hip, lumbar spine, distal part of forearm were respectively decreased in 26.1%, 26.1%, 18.8% PreM women and 66.7%, 70.8%, 79.2% PM women. 39.3% of man had decrease BMD in the hip and 42.8% - in the lumbar spine. According to logistic regression in all women group the fact of CG intake was strong associated with BMD decrease in the hip (total and neck) and lumbar spine ($r=-0.25$, $p<0.05$), in man no association with the fact of CG intake was found. The effect of CGs on BMD in man was cumulative dose dependent, negative correlation between treatment duration and low hip neck ($r=-0.44$, $p<0.05$) and lumbar spine BMD ($r=-0.5$, $p<0.05$) was detected. In PreM women only association between CG therapy and decreased total and neck hip BMD ($r=-0.33$, $p<0.05$) was detected, any relationship with cumulative dose and treatment duration wasn't found. Only in PM patients BMD decreasing depends on average cumulative dose and treatment duration. MTX intake was negatively correlated with BMD only in PM women in total hip and lumbar spine ($r=-0.37$, $p<0.05$) and in men in the distal part of forearm ($Z=-2.46$, $p<0.05$). In PM women BMD in total hip and distal part of forearm was significantly higher in MTX+CG+biologics group than without biologics ($r=0.38$, $p<0.05$). The level of PTG was significantly higher in PM patients on GCs and was negatively correlation with cumulative dose ($r=-0.77$, $p<0.05$). In PreM women GCs intake was negatively correlated with C-TP level ($r=-0.37$, $p<0.05$) and positively with RANKL level ($r=0.35$, $p<0.05$).
Conclusion: A sexual differences in BMD changes during different treatment regiments was observed in different parts of the skeleton. In man BMD lost in hip and lumbar spine depends on GCs treatment duration and on in the distal part of forearm on MTX intake. In PM women BMD decreasing was strong associated with GC and MTX cumulative dose and treatment duration.

REFERENCE

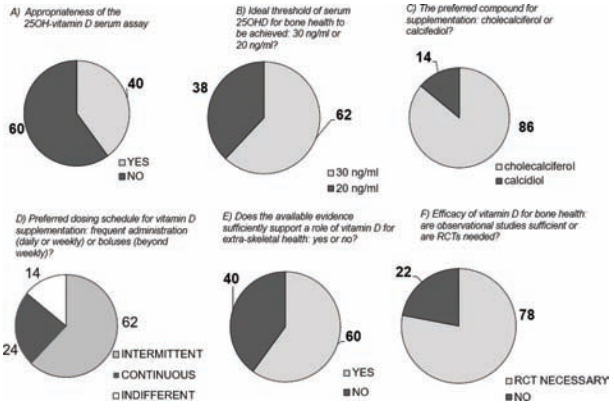
[1] Lenore Buckley, Gordon Guyatt, Howard A. Fink, et al. 2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis Arthritis Rheum Vol. 69, No. 8, August 2017, pp 1521–1537.

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AB0831 **PERSPECTIVE ON THE CLINICAL PRACTICE MANAGEMENT OF HYPOVITAMINOSIS D FROM A MEETING OF ITALIAN EXPERTS**

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Background: Scientific interest in the clinical aspects surrounding vitamin D has increased exponentially in recent years. Unfortunately, this interest is not currently associated with a proportional level of consensus. Indeed, the large number of studies in this field, which are often of low quality and secondary importance has confused even experts and driven them towards controversial positions.
Objectives: To shed light on this topic, we arranged a meeting with the aim of collecting the opinions of 50 experts in different specialties ("D.. Battito Group"), including internists, endocrinologists, rheumatologists, pediatricians, geriatricians, dermatologists, gynecologists and nephrologists. This meeting dealt with specific questions regarding the management of hypovitaminosis D and aimed to investigate the opinions of Italian experts on this topic. Six key questions were addressed in the meeting.
Methods: After a short lecture and a 30 minutes discussion, all the experts expressed their opinions, which were recorded together with any specific commentary.
Results: The results of the meeting demonstrated the presence of insufficient agreement on many key questions regarding the management of vitamin D deficiency, even among clinical experts.



Conclusion: We hope that the various scientific societies will recognize and analyze the inconsistencies in their own positions and reach adequate consensus, especially on the tenets required for conducting proper and useful investigations on the topic, and that the results of these future new studies will be able to shed the needed light.
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AB0832 VERTEBRAL PAIN AND PHYSICAL PERFORMANCE INDICES IN POSTMENOPAUSAL WOMEN WITH VERTEBRAL FRACTURES DEPENDING ON PRESENCE OF OBESITY

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Background: Vertebral fractures (VFs) are important osteoporotic fractures which manifest increased morbidity and mortality; however, their clinical features usually differ. Obesity is one of the important parameters of risk of osteoporotic fractures and vertebral pain syndrome.
Objectives: The aim of the research was to study the indices of vertebral pain (VP) and physical performance (PP) in postmenopausal women with VFs depending on presence of obesity.
Methods: We examined 87 females aged 50-89 years old with VFs in thoracic and/or lumbar spine which were divided into 3 groups: I – patients with normal weight (NW), according to WHO criteria, n=32; II – women with overweight (OW), n=37; III – females with obesity (OB), n=18. The parameters of VP in thoracic and/or lumbar spine were measured by 11-component visual analog scale (VAS), the indices of PP using static and dynamic functional tests (Thomayer, Schober tests, chest excursion, lateral trunk lean, 3-, 4-, 15-meter tests, "stand up from the chair", static balancing). Bone mineral density (BMD) was measured by DXA (Lunar, Prodigy).
Results: We have found the significantly higher parameters of BMD of femoral neck and lumbar spine in women with VFs and OB compared to females with NW. However, we did not establish any reliable differences of VP neither in thoracic nor in lumbar spine depending on obesity presence. Also, we did not reveal the significant differences of most parameters of PP, except for the indices of chest excursion (mean parameter, of the inhalation and exhalation) which were reliably higher in patients with OB.
Conclusion: In conclusion, the indices of VP and PP do not differ in postmenopausal women depending on obesity presence, except for chest excursion that should be taken into account in rehabilitation programs for females with VFs.
Disclosure of Interests: None declared
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AB0833 BONE TURNOVER MARKERS – DO THEY HAVE A ROLE AS PREDICTORS OF MORTALITY AND NEW FRACTURE IN PATIENTS WITH FRAGILITY HIP FRACTURE?

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Background: In Osteoporosis (OP), bone turnover markers (BTM) are potential monitors of drug adherence/efficacy as well as predictors of bone loss and fracture risk. However, without solid evidence, international guidelines still do not recommend their systematic measurement to assist treatment decision and follow-up.
Objectives: To evaluate the predictive value of baseline BTM (beta crosslaps – bCL; osteocalcin – OC) in the outcome (death and/or new fracture) of patients that suffered a fragility hip fracture (FHF).
Methods: Patients referred to a Fracture Liaison Service from March 2015 until March 2017 with a FHF were considered for this study. Clinical/demographic variables were collected, including: age at time of fracture, sex, serum OC and serum bCL at baseline and outcome (death, new fracture, lost to follow-up) until January 2018. Cox regression analysis was used to calculate hazard ratios (HR) for values of OC and bCL; p<=0.05 was considered statistically significant.
Results: From a total of 522 patients, 218 presented a baseline measurement of OC and/or bCL and were included for analysis. Table 1 summarizes clinical and demographic characteristics of the sample. Twenty seven patients died (median days until death=457, min 160, max 1049) and 18 had a new fracture (median days until refracture 343.5, min 30, max 835); 129 patients maintained follow-up. Median serum bCL was

0.71 ng/ml (0.12-3.28, n=217) and median OC was 28.2 ng/ml (6.80-198.60, n=215). Through univariate analysis, higher bCL values predicted worse survival outcome (HR=3.09; 95% CI=1.14-8.39;p=0.026), even after adjustment for age/sex (HR=4.28; 95% CI=1.48-12.29;p=0.007); however, it did not predict higher risk of new fracture (HR=3.00;95%CI=0.85-10.68; p=0.089). Serum OC levels showed no statistically significant results, neither for mortality (HR=1.01; 95% CI=0.99-1.03;p=0.341) nor new fracture (HR=1.01;95%CI=0.99-1.04;p=0.057).

Abstract AB0833 Table 1

Total (N)	215
Age at admission, y (median, min-max)	82 (65-99)
Sex, female (n,%)	172, 78.9
BMI (N)	195
Underweight (n,%)	4, 2.1
Normal (n,%)	90, 46.2
Overweight (n,%)	66, 33.8
Obesity class I (n,%)	29, 14.9
Obesity class II (n,%)	5, 2.6
Obesity class III (n,%)	1, 0.5
Degree of dependence (N)	205
Totally dependent (n,%)	10, 4.9
Partially dependent (n,%)	53, 25.9
Autonomous (n,%)	142, 69.3
Type of fracture (N)	217
Transtrochanteric (n,%)	111, 51.2
Femoral neck (n,%)	90, 41.5
Subtrochanteric (n,%)	16, 7.4
Vertebral fracture (N)	213
0 (n,%)	92, 43.2
1 fracture (n,%)	53, 24.9
$\geq$ 2 fractures (n,%)	68, 31.9
Femur neck BMD, g/cm^2 (mean, SD, N)	0.66, +-0.12, 198
Femur neck T score (mean, SD, N)	-2.79, +-1.1, 198
>2.5 (n,%)	62, 31.3
≤2.5 (n,%)	136, 68.7
vitD, ng/ml (median, min-max, N)	23.24, 3-97

Conclusion: In this cohort, increased serum levels of bCL predicted higher mortality risk. These results support the value of BTM in OP, strengthening their potential as prognostic markers, besides treatment monitors.

REFERENCE

[1] Glendenning P, Chubb SAP, Vasikaran S. Clin Chim Acta. 2018 Jun;481:161-170.

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AB0834 FREQUENCY OF OSTEOPOROTIC HIP FRACTURE IN AN ALGERIAN HOSPITAL

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Background: The hip fracture is the most serious complication of osteoporosis. It is a public health issue in elderly because of its frequency, severity and economic impact. We report the result of an 18 months investigation.
Objectives: The aim of this study was to determine the frequency of osteoporotic hip fractures and identify the risk factors of osteoporosis and falls leading to these fractures.
Methods: Cross-sectional, prospective, descriptive study. Were included patients with spontaneous or secondary low trauma hip fractures during 18 months, who consulted at trauma unit, Mohamed Lamine Debaghine hospital. Have been collected: patient characteristics, risk factors for osteoporosis and falls, type of treatment and length of hospital stay.
Results: 115 cases of hip fractures were recorded out of a total of 486 fractures, with a frequency of 16.8%, from all the fractures operated, it represents 22.7%. We noted a female predominance (62.6%) with a sex ratio of 0.60, the average age is 76.44 +/- 11.71 years. The associated comorbidities are: cardiovascular (55.7%), diabetes (33%), dysthyroidism (11.4%), asthma (10.4%), chronic renal failure (5.2%) prostate adenoma (4.5%). The fracture mechanism is dominated by the fall (92%), it is most often a domestic accident: slipping (30%), stumbling (26%), ablution (11%), falling on the stairs (7%).%). The risk factors for osteoporosis identified are: age more than 70 years (72.8%), female sex (62.6%), low BMI (18%), sedentary lifestyle (15.3%), corticosteroid therapy 7.2%, smoking (6.3%), history of rheumatoid arthritis in 3.4% and early menopause in 2.1% of patients. The risk factors of fracture: visual disturbances (40%) neuromuscular disorders in 11, 9%, poor health (more than 3 chronic diseases) in 9% of patients, mother's history of hip fracture (1.7%). A personal history of osteoporotic fracture was noted in 17.4%, 7 patients presented a contralateral hip fracture. The average duration of hospitalization is 5.2 +/- 2.5 days. The treatment is surgical in 81.6% (40.8% prostheses).
Conclusion: Through this study, we found that osteoporotic hip fracture is frequent. The osteoporosis risk factors identified were female sex, advanced age, corticosteroid therapy and sedentary lifestyle. Fall risk factors were dominated by visual disturbances and neuromuscular disorders.

REFERENCES

[1] Charles M. Court-Brown, Ben Caesar. Epidemiology of adult fractures: A review. Injury 2006.
[2] Desmond Curran. Épidémiologie des fractures liées à l'ostéoporose en France : revue de la littérature. Revue du rhumatisme 77 (2010) 579–585.
[3] Denise Grolimund Berset. Traumatologie de la personne âgée: une urgence nutritionnelle? Nutrition clinique et métabolisme 23 (2009) 129–132
[4] Margaret stevens.preventing falls in older peoples: impact of an interventionto reduce environmental hazards in home. J Am Geratr Soc 2001; 49: 1442-7.

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AB0835 BONE MINERAL LOSS DURING ULCERATIVE COLITIS : PREVALENCE AND RISK FACTORS

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Background: Patients with ulcerative colitis (UC) are at increased risk of bone mineral loss, leading to osteoporosis and osteopenia. Etiopathogenetic factors may be divided into factors specific to the underlying inflammatory process, and factors resulting from the disease process, such as, malabsorption of nutrients vitamins and minerals,decreases in weight,and the use of bone toxic medications.
Objectives: to evaluate the prevalence and possible risk factors for bone mineral density disorders in patients with UC.
Methods: A retrospective study from January 2000 to December 2018, including all patients with UC followerd in our department. Bone mineral density was determined by dual energy X-ray absorptiometry.
Results: Seventy eight patients were included in our study (36 men, 26 premenopausal, and 17 postmenopausal women) with an average age of 47.5 years. Forty osteodensitometries (DXA) were performed : 17 were normal (42.5%), 13 patients had osteopenia (32.5%) and 10 suffered from osteoporosis (25%). Among the 23 patients having a bone mineral loss, the average Z-score were (-0.8 SD) in the femoral neck and (-1.78 SD) in the lumbar (L2-L4) spine whereas the average T-score were (-1.23 SD) in the femoral neck and (-2.15 SD) in the lumbar (L2-L4) spine. Osteoporotic patients included 12 men, 5 premenopausal, and 6 postmenopausal women with an average age of 53.04 years. The research of risk factors has shown that 14 patients with bone mineral loss (60.86%) underwent systemic corticosteroid treatment with an average duration of 6 months. Tobacco intoxication has been mentioned in 8 cases (34.78%) and alcoholism in 6 cases (26.08%). Otherwise, patients with bone mineral loss showed a lower body mass index (average BMI =19.46) than patients with normal bone density (average BMI = 23.64). Anemia has been reported in 11 cases with low bone density (47.82%) and low level of albumin as noted In 8 cases (34.78%). No osteoporotic fractures has been reported. Pan-ulcerative Colitis was reported in 11 cases (47.82%) and acute severe ulcerative colitis in 10 cases (43.47%).
Conclusion: Our study shows that more than half of our patients having ulcerative colitis (UC) who had an osteodensitometry presented bone demineralization (osteoporosis or osteopenia). It seems to be associated with a low BMI, an extended and severe form of UC,and the cumulative corticoid doses.

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AB0836 THE INVESTIGATION OF BONE METABOLIC MARKERS ACCORDING TO THE FUNCTIONAL DISORDERS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is one of the causes of secondary osteoporosis, and steroids are often used in combination, therefore osteoporosis is highly associated with RA. Furthermore, joint disorders due to RA cause various degrees of dysfunction and ADL declines. The Steinbrocker classification is often used as the degree of dysfunction. Immobilization progresses with the progress of dysfunction, possibly causing severe osteoporosis.
Objectives: Of the 2238 cases in Akita Orthopedic Group omn Rheumatoid Arthrotis (AORA) registry 2017, 101 cases simultaneously measuring bone metabolism markers (TARCP-5b, NTX, urinary DPD, BAP, total P1NP) and pentosidine were involved.
Methods: Patients were divided by Steinbrocker classification into class 1,2 (group A 84 cases) and clss 3, 4 (group B 17 cases). we examined whether there is a difference in bone metabolism markers in each group according to Steinbrocker classification.
Results: The average age in group B (75.9) was significantly higher than group A (66.9) ($p = 0.01$). DAS 28 ESR was significantly higher in group B ($p < 0.01$). There was no difference in eGFR representing renal function between the two groups. The urinary DPD (nM/mM · Cr) and pentosidine (μg/ml) in group B was significantly higher than group A ($p < 0.01$). No difference was observed between the two groups in other bone metabolism markers.
Conclusion: Immobilization by long-term bed rest is known to enhance bone resorption. In 2002, Wakae reported DPD in urine showed a higher value in the group of not going out in femoral neck fracture cases. Based on the results of this study, urinary DPD showed a high value in RA group with high degree of dysfunction, which possibly reflected immobilization due to progress of functional disorder. Moreover, it is known that pentosidine will be higher in cases with high disease activity, severe osteoporosis will be occurred in the group with progressive functional disorder which is difficult to tight control.
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AB0837 INFLUENCE OF AUTO-IMMUNE HEPATOPATHIES ON BONE MINERAL DENSITY

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Background: Osteoporosis is a common complication of chronic liver diseases especially associated with Primary biliary cholangitis (PBC). Its occurrence during others autoiummune hepatopathies such us autoimmune hepatitis, primary sclerosing cholangitis has been described.
Objectives: The aim of our study was to assess the prevalence of osteoporosis in patients with autoimmune hepatopathies.
Methods: We carried out a retrospective study from January 1996 to December 2018, including all patients with auto-immune hepatopathy [autoimmune hepatitis/Primary biliary cholangitis (PBC)/Primary sclerosing cholangitis (PSC)/overlap syndrome]. Only patients who had bone mineral density (BMD) were selected.
Results: During the study period, 124 patients were included. The mean age of our patients was 55 years [18-87]. BMD has been realised in 51 patient [32 PBC/5AIH/3PSC/11 overlap Syndrome]. It was normal in 18 cases (35%), whereas 9 patients had osteopenia (18%) and 24 had osteoporosis (47%)[15PBC/2AIH/5overlap/2PSC].
The mean values of L2-L4 T-scores and femur total T-scores were -3.27 and -1.97, respectively., Osteoporotic patients had an average age of 58 years: 1 men, 3 premenopausal, and 20 postmenopausal women. The study of risk factors of osteoporosis has shown that 5patients underwent systemic corticosteroid. A tobacco intoxication has been noted in 1patient. Biochemical analysis indicated a high level of cytolysis (superior to twice normal value) in 14 patient. Cholestasis was noted in 10 patients. The mean values of bilirubin was 23mg/l. Among the 24 patients with osteoporosis, 10 had positif antinuclear antibodies, 17 had positif anti-mitochondrial antibodies and 5 had positif anti-smooth muscle antibodies. Eight of patients were at an advanced stages of liver fibrosis at the moment of diagnosis.
Conclusion: Our study has shown that autoimmune liver diseases has an influence on bone mineral density as a bone nineral loss was noted in more than half of the cases. It should be considered for all patients with auto immune hepatopathy especially with long duration of corticosteroid treatment.
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AB0838 COMPARISON OF THE CHARACTERISTICS OF THE OSTEOPOROTIC PATIENTS WITH AND WITHOUT RHEUMATOID ARTHRITIS THROUGH RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY

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Background: Osteoporosis is a common bone disease characterized by reduction in bone mass accompanied by microarchitectural changes, resulting in brittle bones and in an increased risk of fractures. Rheumatoid arthritis is a well-known risk factor for the development of osteoporosis. With the introduction of radiofrequency echographic multi spectrometry (REMS), easily evaluation of the lumbar spine bone mineral density (BMD) ultrasound (BMDus) and hip BMDus is possible for early diagnosis of osteoporosis.
Objectives: The aim of this study is to compare the characteristics of the osteoporotic patients with and without rheumatoid arthritis through radiofrequency echographic multi spectrometry.
Methods: A total of 70 patients with osteoporosis were included in the study. 43% of them (30/70) had RA and 57% (40/70) were without RA. Patients were diagnosed with rheumatoid arthritis if they had a score of 6/10 or higher based on 2010 ACR/EULAR classification criteria for RA. Age, body mass index (BMI), lumbar spine BMDus, as well as total hip BMDus and fracture risk score (FRAX) were assessed.
Results: Patients with RA were significantly younger (69.3 ± 6.5 years) than those without RA (76.4 ± 5.0 years) ($p = 0.002$). BMI values did not differ significantly between the two groups (25.76 ± 4.82 kg/m^2 for patients with RA and 27.57 ± 5.37 kg/m^2 for patients without RA). Patients with and without RA did not show any significantly differences between BMDus values of L1-L4 (0.629/0.607 g/cm^2 for L1, 0.692/0.688 g/cm^2 for L2, 0.761/0.743 g/cm^2 for L3 and 0.789/0.769 g/cm^2 for L4). Patients with RA had higher total lumbar spine T-score (-2.6 ± 0.8 standard deviations) compared to those without RA (-3.1 ± 0.5 standard deviations), but this difference was not significant ($p > 0.05$). Femoral neck BMDus, trochanteric BMDus and total hip BMDus were similar in the groups with and without RA (0.550/0.548 g/cm^2 for femoral neck, 0.710/0.693 g/cm^2 for trochanter, 0.688/0.678 g/cm^2 for total hip). FRAX score of the patients with RA was significantly higher (32.89% for 10-year probability of major osteoporotic fracture and 14.29% for 10-year probability of hip fracture) compared to the patients without RA (22.36% for 10-year probability of major osteoporotic fracture and 8.75% 10-year probability of hip fracture).
Conclusion: Although there were no significant differences in lumbar spine BMDus values and total hip BMDus values between the patients with and without RA, patients with RA showed higher 10-year probability of major osteoporotic fracture and hip fracture.

REFERENCES

[1] Conversano F, Franchini R, Greco A, Soloperto G, Chiriacò F, Casciaro E, Aventaggiato M, Renna MD, Pisani P, Di Paola M, Grimaldi A, Quarta L, Quarta E, Muratore M, Laugier P, Casciaro S (2015) A novel ultrasound methodology for estimating spine mineral density. Ultrasound Med Biol 41:281–300
[2] Casciaro S, Peccarisi M, Pisani P, Franchini R, Greco A, De Marco T, Grimaldi A, Quarta L, Quarta E, Muratore M, Conversano F (2016) An advanced quantitative echosound methodology for femoral neck densitometry. Ultrasound Med Biol 42:1337–1356
[3] Casciaro S, Conversano F, Pisani P, Muratore M (2015) New perspectives in echographic diagnosis of osteoporosis on hip and spine. Clin Cases Miner Bone Metab 12:143–151

[4] Heidari B, Hassanjani Roushan MR. Rheumatoid arthritis and osteoporosis. *Caspian J Intern Med*. 2012;3(3):445-6.
[5] Sözen T, Özışık L, Başaran NÇ. An overview and management of osteoporosis. *Eur J Rheumatol*. 2016;4(1):46-56

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AB0839 ASSOCIATION BETWEEN BODY FAT AND BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN THROUGH RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY

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Background: Osteoporosis is characterized by reduced bone mineral density (BMD) and increased fracture risk. Age, concomitant diseases, body mass index (BMI), body composition, etc. are important risk factors that could reflect on bone density and on the increased risk of fractures. Although obesity has been associated with increased bone mineral density (BMD) in the most studies, the relationship between body fat and BMD remains contradictive.
Objectives: The aim of this study is to determine if there is any association between body fat distribution and bone mineral density in postmenopausal women through novel ultrasound technique applicable on both-lumbar spine and femoral neck.
Methods: A total of 98 women with mean age 62 ± 11 years underwent radiofrequency echographic multi spectrometry (REMS). Bioelectrical impedance analysis (BIA) software was used to assess body fat percentage. Patients were divided into two groups-with body fat $\geq$ 32% and body fat < 32%. Age, BMI, lumbar spine BMD, total hip BMD and fracture risk score (FRAX) were compared between the patients with normal body fat and those with high body fat.
Results: The mean age of the women with normal body fat was 61.1 ±14.6 years and the mean age of the women with high body fat was 63.3±9.5 years. BMI of the women with body fat < 32% was significantly lower (22.5 kg/cm^2) compared to the BMI of the women with body fat $\geq$ 32% (30.2 kg/cm^2) (p = 0.000). Bone mineral density of L1-L4 and total lumbar spine BMD did not differ between the women with normal body fat and high body fat. Femoral neck BMD, trochanteric BMD and total hip BMD of the patients with normal body fat (0.604 g/cm^2, 0.737 g/cm^2 and 0.736 g/cm^2 respectively) were significantly lower than those patients with high body fat (0.682 g/cm^2, 0.864 g/cm^2 and 0.838 g/cm^2 respectively) (p = 0.000 for femoral neck BMD and trochanteric BMD, and p = 0.001 for total hip BMD). FRAX score for 10-year probability of major osteoporotic fracture did not differ significantly between the two groups (20.8% for women with normal body fat and 16.6% for women with high body fat). FRAX score for 10-year probability of hip fracture was also not significant between the two groups, but there was a trend to statistical significance (p = 0.059) (9% for women with normal fat and 4.9% for women with high fat).
Conclusion: Postmenopausal women with body fat $\geq$ 32% showed higher femoral neck BMD compared to those with body fat < 32%, but there was no significant difference in the lumbar spine BMD values between the groups. Women with high body fat did not show significantly lower FRAX score than the women with normal body fat.

REFERENCES

[1] Paola Pisani, Francesco Conversano, FernandaChiriacò, Eugenio Quarta, Laura Quarta, MaurizioMuratore, Aimè Lay-Ekuakille, Sergio Casciaro. Estimation of femoral neck bone mineral density by ultrasound scanning: Preliminary results and feasibility. Measurement, Volume 94, 2016, pp. 480-486
[2] Shapses SA, Sukumar D. Bone metabolism in obesity and weight loss. Annu Rev Nutr. 2012;32:287-309.
[3] SILVA, Ana Carolina Veiga, et al. Factors associated with osteopenia and osteoporosis in women undergoing bone mineral density test. Rev. Bras. Reumatol. [online]. 2015, vol.55
[4] Zhao LJ, Jiang H, Papasian CJ, et al. Correlation of obesity and osteoporosis: effect of fat mass on the determination of osteoporosis. J Bone Miner Res. 2007;23(1):17-29.

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AB0840 SCREENING FOR OSTEOPOROSIS IN AN AMBULATORY AND HOSPITALIZED POPULATION: A 6-YEAR EXPERIENCE IN A UNIVERSITY HOSPITAL

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Background: Osteoporosis (OP) is a serious and prevalent disease identified by Dual Energy X-ray Absorptiometry (DEXA) that can be performed in an ambulatory or an hospitalized population.
Objectives: Aims are: (1) to characterize patients who had DEXA in a university department of rheumatology to study its diagnostic efficacy; (2) to look after risk factors specific to our population; (3) to evaluate the efficiency of a non-systematic and opportunistic intra-hospital OP screening by comparing results for ambulatory and hospitalized patients in the different departments of the hospital.
Methods: From 2007 to 2012, 6406 initial DEXA from consecutive patients were prospectively encoded (1494 in 2007, 1158 in 2008, 1079 in 2009, 945 in 2010, 868 in 2011 and 862 in 2012) (identical DEXA).
Results: Cohort characteristics are the following: women 74.4%, mean age (± 1 standard deviation) 60.5 years (± 14.3), mean BMI 25.1 (± 5.1), history of corticotherapy in 30.5%, previous fracture in 29% and current hospitalization in 28.8% of cases. OP (at one of the 3 sites) was diagnosed in 22.3%, a stable value over the years, with, as a repartition, lumbar spine, femoral neck and total hip OP in 13.7%, 13.6% and 9.2% respectively. In 3.9%, OP was diagnosed at all the 3 sites. In univariate analysis, OP risk factors were age, history of fracture and low BMI (for all 3 sites), corticotherapy (lumbar spine and femoral neck) and male gender (lumbar spine). In multivariate analysis, regardless of site, age, fracture history, low BMI, and male gender increased the OP risk.
Intra-hospital screening identified OP (at any of the 3 sites) in 31.8% (*vs* 18.5%, p<0.001 for ambulatory screening) and OP at 3 sites simultaneously in 7.9% (vs 2.3%, p <0.0001). This better efficiency was stable and present for each year analyzed. The intra-hospital population tested was older [64.2 years (13.2) vs 59 (13.2), p<0.0001], with more men (35.2% vs 21.7, p<0.0001), more history of fracture (39% vs 24, p<0.0001) and with a slightly higher BMI [25.4 (5.8) vs 25.1 (4.8), p=0.028], with no difference in corticosteroid use. In addition to T-scores analyzes, Z-scores were also compared and showed similar differences with lower Z-scores in the hospitalized population.
Conclusion:
(1) One in five DEXA identified OP at one of the three sites in the ambulatory population but only one in three in the hospitalized patients. Hospital screening is therefore essential and more efficient than the ambulatory one. Hospital time seems to be an opportunity to fill the gaps in ambulatory screening.
(2) Intra–hospital screening targeted an older and more masculine population with more fracture history, which may explain its better performance, which does not decline over the years. Z–score differences revealed that the efficiency difference was not only due to an older age of the hospitalized population but could be secondary to more internistical co–morbidities or treatment deleterious for bones.
(3) In addition to conventional ones, the male gender is a risk factor for OP, recalling the importance of screening for all and not only in the female population (which represents $^3/_4$ of the cohort).

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AB0841 PROSPECTIVE STUDY OF BONE METABOLISM AND FRACTURE INCIDENCE IN SPINAL CORD INJURY PATIENTS DURING A PERIOD OF 24 MONTHS

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Background: Spinal Cord Injury (SCI) produces a wide variety of changes in systemic physiology that can lead to several complications,

such as Osteopenia or even Osteoporosis. It has been reported in several studies, an incidence of fracture between 30-40% in this population.
Objectives: To evaluate the evolution of bone turnover biomarkers before and after treatment (according to 2015 NOF guidelines) and to describe the incidence of fracture after a SCI.
Methods: A prospective study was conducted, including 48 SCI patients followed during an observation period of 24 months, with visits every six months. Thirty two patients concluded the study. In each visit patients were enquired about fractures. A blood test was also performed. In addition a dual-energy x-ray absorptiometry (DEXA) and simple x-ray of hip and spine was requested annually. Patients were also educated in lifestyle measures, such as an adequate calcium and vitamin D dietary intake. Oral supplementation was initiated in cases of low intake or deficit, respectively. In patients with bone mineral density (BMD) measured by DEXA in range of Osteoporosis, pharmacological therapy was initiated (bisphosphonate or Denosumab). Statistics had been performed with mixed linear regression models.
Results: Our sample was 56.25% men with an average age of 56.08 ± 13.82 years old. In 32 patients (68.09%) low Vitamin D levels were detected. At baseline in 12 cases (25%) DEXA showed a BMD in osteoporosis range; in 12 (25%) osteopenia, plus 6 fractures (2.6 fractures per 100 years/patient). Afterwards, until the end of the study only a fracture of the tibia was observed (however, it was after a high impact accident), so the fracture rate was 1.2 fractures per 100 year/patient.
The evolution of the variables can be seen on the next table.

	Month-0 N=48 *Mean (SD)*	Month-6 N=32 *Mean (SD)*	Month-12 N=36 *Mean (SD)*	Month-18 N=37 *Mean (SD)*	Month 24 N=32 *Mean (SD)*
CALCIUM (mg/dl)	9.1 (0.59)	9.53 (0.4)	9.37 (0.54)	9.46 (0.41)	9.55 (0.44)
PHOSPHOR (mg/dl)	3.63 (0.7)	3.42 (0.44)	3.32 (0.52)	3.33 (0.55)	3.25 (0.45)
VIT D (UI)	16.42 (9.95)	42.28 (18.93)	35.88 (13.53)	35.77 (18.08)	37.55 (15.06)
PTH (ng/mL)	38.15 (25.55)	36.09 (17.89)	38.33 (21.2)	40.1 (17.27)	43.35 (25.08)
PINP (ng/mL)	79.25 (80.9)	68.15 (35.77)	53.05 (45.76)	42.82 (24.26)	40.67 (25.17)
bCTX (ng/mL)	0.82 (0.49)	1.23 (4.22)	0.34 (0.35)	0.28 (0.21)	0.51 (1.36)
T-SCORE SPINE	-0.49 (1.9)		-0.61 (1.26)		-0.24 (1.34)
T-SCORE NECK	-0.95 (1.53)		-1.29 (1.41)		-1.53 (1.16)
T-SCORE HIP TOTAL	-1.02 (1.58)		-1.38 (1.58)		-1.42 (1.33)
CALCIUM SUPP	29 (60.42%)	20 (62.5%)	26 (72.22%)	27 (72.97%)	22 (68.75%)
VIT D SUPP	46 (95.83%)	2 (6.25%)	35 (97.22%)	36 (97.3%)	32 (100%)
BIPHOSPHONATE	4 (8.33%)	5 (15.62%)	3 (8.33%)	5 (13.51%)	6 (18.75%)
DENOSUMAB	7 (14.58%)	7 (21.87%)	7 (19.44%)	7 (18.91%)	7 (21.87%)

On multivariate analysis an inverse relationship between vitamin D and CTX levels was detected ($p \leq 0.05$). DEXA hip measures tend to become stabilized after Bisphosphonate treatment.
Conclusion: On our cohort, bone resorption biomarkers decrease after Vitamin D restoring. Antiresorptive therapy in high risk patients stopped bone loss, especially in hip. After two years follow up, with the treatment algorithm applied, fracture incidence was lower than other series published.

REFERENCE

[1] *J Musculoskelet Neuronal Interact 2011: 11(3):257-265

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AB0842 POTENTIAL RISKS FOR OSTEOPOROSIS AND SARCOPENIA IN ALCOHOLIC WOMEN

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Background: Recent statistics indicated an accumulating number of patients with alcohol dependency in Japan. In particular, there had been a considerable increase in the number of alcoholic women, reaching up to 130,000 patients. Because alcoholic women often have insufficient dietary intake and physical inactivity, they may be at risk for low bone mineral density and decreased muscle power. However, these points may not be widely recognized, and the current program for the rehabilitation of alcoholism may not be sufficient to address this issue.
Objectives: To assess the risk for osteoporosis and sarcopenia in alcoholic women from a nutritional viewpoint
Methods: Thirty-two women (mean age: 42.9 ± 7.49 years) who were admitted to the Alcoholics Rehabilitation Program (ARP) for alcoholism, which was diagnosed according to International Classification of Diseases (ICD)-10, were enrolled in the study. The patients were subjected to self-answered questionnaire, nutritional assessment by expert dietitians, and measurement of body composition and grip strength.
Results: Of the 32 patients, 14 (44.0%) had a history of eating disorder, mostly anorexia. All 32 patients had elevated levels of transaminases at the time of admission. History of bone fracture was present in eight of the 32 (25.0%) patients; among them, at least three (9.4%) cases were considered to be due to a fragility fracture. The mean body mass index (BMI) was 20.4 kg/m2; 10 (31.3%) patients had BMI < 18. The average energy intake was low at 1,474.5 ± 324.3 kcal. Twenty-one (65.6%) patients were taking dietary calcium of <650 mg/day, which is the level recommended for adult women. The mean grip strength was 23.8 ± 6.5 kg, and 8 (25%) patients had grip strength of only <18 kg, which is the definition of sarcopenia in the Asian elderly.
Conclusion: Young to middle-aged alcoholic women should be treated as having high risks for osteoporosis and sarcopenia. ARP should include multidisciplinary assessment and interventions to prevent future locomotive disabilities.
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AB0843 HYPOVITAMINOSIS D IN A MARFAN POPULATION

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Background: Marfan syndrome is an autosomal dominant disorder of connective tissue caused by mutations in FBN1 gene on the long arm of chromosome 15. Information is often lacking regarding an increased risk of fractures and its management and prevention in patients with Marfan syndrome. In these patients reduced bone mineral density was rarely reported. A pivotal role in bone mineralization is played by Vitamin D.
Objectives: This study evaluates whether the reduction of the values of Vitamin D is present in Marfan patients.
Methods: 60 patients (pts) (28 M/32 F; age 15-75 mean age 46,2) with Marfan syndrome were studied. The patients were followed from the clinical and research regional Marfan Center in Florence, Italy. All pts met new Ghent criteria that identified ectopia lentis, thoracic aorta dilatation with Z score = or > 2 and a large group of systemic clinical features represented by cardiovascular, musculoskeletal, central nervous system (dural ectasia) pulmonary, cutaneous and ocular clinical manifestations (systemic features) reaching a score = or > 7 as major clinical criterion. Familiarity and the detection of a gene mutation (in MFS FBN1 gene displays a mutation in about 90% of patients) are also considered criteria necessary for Marfan diagnosis.
Results: 11/60 pts (18,3%) (5M/6F age 15-75 mean age 44,9) showed reduced values of Vitamin D. 6/11 pts (45,4%) (3M/3F age 15-56, mean age 34,1) showed very poor Vitamin D values (range 8.7 ng/ml – 13,17 ng/ml).
Conclusion: Our results suggests that Vitamin D may play an important role in bone metabolism in Marfan patients. These results need confirmation since further data are missing in literature.

REFERENCES

[1] Trifirò G, Marelli S, Viecca M, Mora S, Pini A. Areal bone mineral density in children and adolescents with Marfan syndrome: evidence of an evolving problem.
[2] Bone. 2015 Apr;73:176-80. doi: 10.1016/j.bone.2014.12.006. Epub 2014 Dec 13.

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AB0844

THE ENIGMA OF FRAGILITY FRACTURE WITH NORMAL BONE MASS; EXPERIENCE OF A LIAISON SERVICE FRACTURE UNIT

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Background: The enigma of fragility fracture with normal bone mass; Experience of a Liaison Service Fracture Unit
Objectives: To describe the characteristics of patients with fragility fracture and normal DXA treated in an FLS unit.
Methods: Prospective 6-year observational study of a FLS fracture unit. Demographic variables, FRAX items, DXA and TBS were collected. The characteristics of patients with normal and abnormal DXA are described. The statistical analysis was performed by means of a descriptive, comparing the normal DXA/osteopenia/osteoporosis groups by means of contingency tables, Fisher's exact test, Student's t test or ANOVA, as appropriate, as well as regression analysis.
Results: 1,631 patients were included, 205 with normal DXA (12.5%), 747 with osteopenia (45.8%) and 680 with osteoporosis (41.6%). Patients with normal DXA were characterized by a higher percentage of males, a younger age and a higher BMI. Hip fracture was less frequent in patients with normal DXA, while the frequency of other fractures was higher. The frequency of previous fracture, history of hip fracture of the parents and secondary osteoporosis was lower in patients with normal DXA. The TBS and FRAX values were higher in the cases of normal DXA compared to osteopenia and osteoporosis. In the multiple regression analysis, excluding TBS, remained significant associated with abnormal DXA age (OR 1.04; 1.03-1.06), sex (OR 2.48; 1.71-3.58), BMI (OR 0.91; 0.89-0.94),) and parent hip fracture (OR 1.99; 1.11-3.58). Including TBS <1,230 as a dichotomous variable (N = 451 cases) remained significant age (OR 1.03; 1.00-1.06), sex (OR 3.58; 1.81-7.10) and TBS (OR 5.23; 1.55-17.68).

	Bone densitometry		
	Normal	**Osteopenia**	**Osteoporosis**
N	205	747	680
Sex (male), N (%)**	54 (26)	140 (19)	84 (12)
Age in years, mean (DE)**	68.8 (10)	71.3 (9)	74.2 (10)
BMI, mean (DE)**	31.4 (10)	29.4 (5)	27.1 (7)
Type of fracture, **N (%)**			
Forearm**	75 (36)	284 (38)	206 (30)
Hip**	21 (10)	188 (25)	148 (22)
Humerus**	44 (21)	111 (15)	168 (25)
Spine*	14 (7)	61 (8)	79 (11)
Others**	51 (25)	102 (13)	76 (11)
FRAX items, N (%)			
Previous fracture**	18 (8)	111 (14)	145 (21)
Parent's hip fracture**	14 (7)	73 (10)	98 (14)
Smoking	23 (11)	92 (12)	80 (13)
Corticoids	14 (7)	51 (7)	42 (6)
Rheumatoid arthritis	3 (1)	16 (2)	16 (2)
Secondary osteoporosis**	24 (12)	117 (15)	150 (22)
Alcohol	10 (5)	40 (5)	28 (4)
>1 fall in the last year, N (%)$	65 (43)	211 (40)	200 (41)
TBS, mean (DE) **	1.220 (469)	1.166 (426)	1.115 (435)
Degraded TBS, N (%)**&	3 (5)	38 (18)	47 (25)
FRAX, mean (DE)			
Major fracture**	5 (3)	9 (5)	18 (10)
Hip fracture**	1 (1)	3 (3)	9 (8)

*P<0.05; **P<0,01; $ analyzed in 1,161 patients; & analyzed in 451 patients

Conclusion: Patients with fragility fracture and normal DXA are younger, with more frequent males and with BMI and higher TBS values.**Acknowledgement:** Fabiola Santana y Carmen Alonso
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AB0845

EFFECTIVENESS AND SAFETY OF BISPHOSPHONATES IN THE TREATMENT OF SECONDARY OSTEOPOROSISIN CHILDREN

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Background: Prevalence of secondary osteoporosis (SO) in children is an ongoing challenge, due to the rise in life expectancy of chronic diseases and the bone toxicity medication usage. Bisphosphonates (BF) has been stated as an alternative therapy, although studies targeted children are few.
Objectives: The goal was to establish the effectiveness and safety of bisphosphonate therapy in children with SO.
Methods: A retrospective study of BF treatment in children (≤16 years) with SO at a Pediatric Reumathology Unit from 2015 to 2018.
Descriptive statistics were performed to examine anthropometric measurements, clinical features, diagnoses and treatment received. We measured bone mineral density by dual-energy x-ray absorptiometry and we expressed the results as adjusted for height-for-age Z-score (HAZ).
We assessed the treatment outcome by the change of HAZ after a year treatment and the decreasing fractures rate per year.
Afterwards we made a bivariate analysis to identify related factors with effectiveness and safety of bisphosphonates. Values of p<0,1 were considered statistically significant.
Results: In our study 12 patients were treated with BF, three of them with two different type. Table 1 shows the descriptive data.
The HAZ and the fracture rate per year after a year of treatment were significantly lower [(-2,22±1,46) vs (-1,06±1,27); p=0,04, and (1 (0,5-2) vs 0 (0-0); p< 0,01), respectively].

Table 1. Descriptive analysis

Demographic features and anthropometric measurements (n=12)	
Males, n (%)	9 (75)
Age (years), mean (±SD)	9,8 (±1,87)
BMI SD, mean (±SD)	1.03 (±2,36)
Clinical features of the patients, (n=12)	
Secondary osteoporosis cause, n (%)	
Neurologic	6 (50)
Hematologic	5 (41,7)
Before treatment fractures, mean (±SD)	1.41 (±1,16)
Vertebral fractures (Yes), n (%)	7 (58,3)
Z score* before treatment, mean (±SD)	-2.40 (±1,31)
Age at first fracture (years), mean (±SD)	8,2 (± 3,4)
Bisphosphonates treatment features of the patients (n=15)	
Drug administration via (iv), n (%)	8 (53,3)
Bisphosphonate type, n (%)	
Pamidronate	1 (6,7)
Alendronate	6 (40)
Zoledronate	7 (46,7)
Risendronate	1 (6,7)
Treatment duration (months), median (Range)	19 (11-63)
Treatment ending, n (%)	8 (53,3)
Cause of treatment ending, n (%)	
HAZ > -2 and lack of fractures after a year	5 (62.5)
Adverse effects	1 (12,5)
Exitus*[†]	2 (25,5)
Adverse effects, n (%)	
Flu-like syndrome	2 (13,3)
Asymptomatic hypocalcemia	1 (6,7)
Gastrointestinal intolerance	1 (6,7)

*[†] Due to underlying disease complications

The change at HAZ and the before treatment fractures rate per year (r:0,57; p=0,07) were directly proportional. Also, the change at HAZ was inversely proportional to the before treatment Z-score (r: -0,53; p=0,09) and the BF starting age (r: -0,53; p: 0,09).
The decrement of fractures rate per year showed a statistical significant relationship with BMI percentile (r:0,48; p=0,08), the treatment starting age (r:-0,537; p=0,05) and before treatment fractures rate per year (r:0,941; p<0,001).
Three patients experienced adverse effects (20%). Three related to zoledronate use: two of them showed flu-like syndrome after first infusion and the other asymptomatic hypocalcemia. In another patient the treatment with alendronate was ended due to gastrointestinal intolerance.
There was not significant relationship between adverse effects and our study variables.
Two patients died during the treatment due to their underlying disease complications.
Conclusion: BF are an effective medication for SO. The treatment outcome exhibits to be better with a good nutritional status, younger age and at more severe forms of the disease. Additionally, they are safe showing just minor adverse effects but often.

REFERENCES

[1] Galindo Zavala R, Núñez Cuadros E, Díaz Cordovés-Rego G., Urda Cardona, AL. Advances in the treatment of secondary osteoporosis. An Pediatr (Barc). 2014; 81(6): 399.e1-399.e7.
[2] Zemel BS, et al. Height adjustment in assessing dual energy x-ray absorptiometry measurements of bone mass and density in children. J Clin Endocrinol Metab.2010; 95(3): 1265–73.
[3] Gordon CM, Leonard MB, Zemel BS. 2013 pediatric position development conference: Executive summary and reflections. J Clin Densitom. *2014;*17 (2): 219–24.

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AB0846 OSTEOPOROSIS IN MEN

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Background: Careful attention to postmenopausal osteoporosis (OP) leads to an underestimation of this problem in men.
Objectives: To assess the frequency of bone mineral density reduction (BMD) in men referred for examination, analysis of bone mineralization disorders in men at different age periods, the main reasons for referral for examination.
Methods: During the year, a two-energy X-ray absorption osteodensitometry (LUNAR XP, USA) was examined by 2,731 patients according to a standard program.
Results: Among the 2731 patients referred for examination, the proportion of men is 5%, men over 60 years old are 2%, male children and teenagers are 0.29%. Normal BMD was detected in 31.88%, low bone mass (LBM) - in 39.86%, OP - in 28.26%.
60.14% (83 people) - men of young and middle age, NCM was detected in 33 men, OP - in 14. In 8 - severe form. Reduced BMD patients revealed the presence of serious underlying disease (ankylosing spondylitis, rheumatoid arthritis (RA), systemic lupus erythematosus, diabetes mellitus I type, diffuse toxic goiter disease operated stomach, ulcerative colitis, chronic autoimmune hepatitis and alimentary toxic hepatitis with outcome in cirrhosis of the liver, bronchial asthma (BA), alveolitis.
Elderly and senile men among the surveyed were 55 people (39.86%), LBM - in 22 of them, OP - in 25. Low traumatic fractures in the anamnesis in this group of patients were detected in 13 of 55. In 6 - multiple vertebral fractures, in 2 - multiple repeated fractures of tubular bones. Secondary causes of a decrease in BMD were detected only in 5 out of 55 (9.09%) men aged 60 years and older (RA, BA, idiopathic alveolitis, liver cirrhosis; all currently or with a history of glucocorticoid therapy).
Normal BMD was detected in 44 men. Up to 59, their number was 36 people (81.8%), 60 years and older - only 8 (18.2%). The majority of men with normal BMD indices were sent for examination by dentists, endocrinologists, orthopedic traumatologists. 5 adolescents with BMD in accordance with normal age criteria BMD had repeated traumatic bone fractures in history (fractures during sports (wrestling, football)).
Conclusion: Unlike women, men do not pay enough attention to the prevention of OP, often use dairy products in limited quantities, do not take calcium preparations for prophylactic purposes. A high percentage of the population is characterized by low physical activity. Men more often than women abuse alcohol and smoking.
OP occurs without obvious clinical manifestations until the moment of fracture of the skeleton bones, primary care physicians and hospitals have low alertness for the detection of OP in men. FRAX (fracture risk assessment tool) makes it easy to calculate the probability of a 10-year risk of fractures and identify men at high risk for further examination. The urgency of the problem is due to the increase in the average life expectancy of a modern person.

REFERENCES

[1] Problemy diagnostiki nizkotravmatichnyh perelomov pozvonkov u lic starshego vozrasta. Pisareva V., Mihajlov M., Poljakov V.[et al]. Russian Journal of Pain. 2018. V.56.(2).P.90-1.
[2] Issledovanie rasprostranennosti osteoporoza, ego oslozhnenij i znachimosti faktorov riska/Zavodovskij B., Sivordova L., Poljakova Ju.[et al]. Palliative medicine and rehabilitation. 2015. 2. P.9–12.
[3] Osteoporosis in men: current issues. Simakova E., Seewordova L.[et al]. Uspekhi Gerontologii. 2015. V28(1). P 77-9.

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AB0847 INCIDENCE RATES OF OSTEOPOROSIS(OP) RISK FACTORS IN A LARGE URBAN LONDON BOROUGH

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Background: Identification of osteoporosis risk factors(OPRFs) is a necessary part of assessing fracture risk and treating patients with OP. Incidence rates of OPRFs are variably reported in the literature. Patients seen in OP clinics tend to have a higher risk of fractures compared to those managed in primary-care hence the need for closer scrutiny of their OPRFs. In some instances, managing modifiable OPRFs may form the principle part of the patient's management plan.
Objectives: We examined the rates of OPRFs in patients attending the Bone Health Clinic at Croydon Health Services NHS Trust.
Methods: Retrospective review of OP patients seen between February-June 2018 at Purley Memorial Hospital and assessed for presence of OPRFs including: demographics,BMI,early menopause,late menarche,nulliparity,secondary medical conditions,medicines,family history of OP/parental hip fracture,recurrent falls,previous fragility fractures(FFs) and lifestyle OPRFs(smoking,alcohol,low calcium intake,sedentary).
Results: 201 patients were included. Mean age was 70-years-old (range:37-96), with approximately 9:1 female:male ratio. Mean BMI was 23(normal) with approximately 20% being <18.5(underweight). 25.5%(46/180-females) experienced an early menopause(<45-years) but only 8.3% (15/180) had late menarche(>16years). Of the 25.5% with early menopause, only 13%(6/46) had been offered HRT. 17% of women were nulliparous. Of the medical conditions, thyroid disease was the most commonly reported(18%) with a third of these being newly diagnosed in clinic. Coeliac was identified in 7.5% with 5% newly diagnosed. 2% had newly diagnosed haematological disorders (MGUS,Myeloma,Lymphoma). Only 8 patients had 2-or-more diagnoses at the same time. Almost 40% had a family history of OP, 19% history of parental hip fracture and 15% had both. The majority 66.7%(134/201) had experienced a previous FF with 36% having suffered 2 or more. 16%(32/201) had experienced

recurrent falls. 19% were living sedentarily, 11% currently smoking, 10% drinking 3 or more units of alcohol-per-day and 31% having poor dietary calcium, with 22% having 2 or more of these lifestyle OPRFs. Of the medicines, steroids and PPIs were the most commonly seen. Overall, 73%(147/201) of subjects had at least one modifiable OPRF with over half having 2 or more OPRFs.

Conclusion: This study identified numerous OPRFs and their incidences. Low BMI(<18.5) was common in 1/5 patients requiring input from the dietetics team as part of their treatment plan. Early menopause was seen in a quarter of female patients with just over 10% of these being offered HRT; undoubtedly more could have benefited from intervention at menapause. Many medical conditions associated with OP were identified with several patients being newly diagnosed (coeliac/hypothyroidism/haematological disorders especially). Therefore, global health assessments are needed to identify undetected disease and review and optimise control of established disease. Just under 50% had at least one lifestyle OPRF. Therefore, focus on implementing lifestyle alterations is clearly essential in the management of these patients. Given the high number of patients with at least one modifiable OPRF, it is crucial that OP services are organized accordingly to identify OPRFs to intervene and modify these factors as part of the overarching management plan.

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AB0848 BMD AND MUSCLE MASS IN PATIENTS WITH ISCHEMIC HEART DISEASE

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Background: Mounting biological and epidemiological evidence supports a link between the ischemic heart disease (IHD) and osteoporosis (OP), but the studies investigating muscle mass and its relationship with OP in patients with IHD are limited.

Objectives: The aim of this study is to investigate the relationship between OP and muscle mass in patients with IHD.

Methods: The study included 45 patients with IHD (36 males/9 females, mean age 63,16±6,71 years) verified by coronary angiography. BMD was measured by DXA in the the lumbar spine L1-L4, total hip and femoral neck. BMD was evaluated as: normal BMD (T-score ≥-1), osteopenia (T-score between -1 and -2.5) and osteoporosis (T-score of <-2.5). Muscle mass was assessed using computed tomography of total psoas area (TPA) (cm2) and calculating L3 muscle index (LMI) (<52,4 cm2/m2 in men; <38,5 cm2/m2 in women).

Results: The results of densitometry patients were distributed as follows: 30 patients (66,6%) with normal BMD, 12 (26,6%) with osteopenia and 3 (0.66%) with osteoporosis. Patients was divided into 2 groups: 1) nonosteopenia-nonOP and 2) osteopenia/OP. Mean femoral neck BMD was 1,024±0,09 g/cm2 and 0,809±0,06 g/cm2, respectively. L1-L4 BMD was 1,260±0,14 g/cm2 for normal BMD group and 1,154±0,16 for osteopenic/OP group. Patients with osteopenia/OP had statistically significant lower LMI (45,57±4,66 cm2/m2 vs. 52,78±10,24 cm2/m2, p=0,01 for low femoral neck BMD; 46,33±6,97 cm2/m2 vs. 52,76±6,74 cm2/m2, p=0,02 for low L1-L4 BMD, respectively). According to the correlation analysis a positive relationship between L1-L4 BMD and LMI was revealed (r=0,373, p<0,05). There was no correlation between femoral neck BMD and LMI (r=0,272, p=0,274).

Conclusion: The decline in BMD in IHD patients is associated with low muscle mass and correlated with severity of BMD dissension in the lumbar spine, but not in the neck of the femur. The obtained results confirm high probability of existence of common pathogenetic links between OP and sarcopenia.

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AB0849 CAUSES OF EARLY MORTALITY IN PATIENTS WITH OSTEOPOROTIC HIP FRACTURES

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Background: Osteoporosis (OP) is a skeletal disorder characterized by compromised bone strength, which predisposes the individual to an increased risk of fractures of the hip, spine, and other skeletal sites. OP, a major public health problem, is becoming increasingly prevalent with the world population and occupies a leading place in the structure of morbidity and mortality.

Objectives: To study the causes of mortality in patients with hip osteoporotic fractures during 6 months after injury.

Methods: 432 patients with osteoporotic hip fractures were under observation. During the study, mortality rates were assessed both in hospital and during the first 6 months after the fracture. The main causes of mortality were tracked by ICD-10 classes. Information about fractures and their outcomes was obtained from data from the archives of the trauma departments of Kemerovo, city registry offices, telephone interviews of patients and their relatives.

Results: In the first 6 months after injury, 95 out of 432 patients died. Overall mortality was 22.0%. In the group of deceased patients, females prevailed: 73 women (16.5%) and 22 men (5.1%) (χ^2 = 4.4; p <0.0001). It was established that 6 months after a hip fracture in 63 (66.3%) patients, death occurred from cardiovascular system diseases: in men - 13 (59.0%) cases and in women - 50 (68.4%) (p = 0.9). Respiratory diseases, as the cause of death, were detected in 18 (18.9%) patients (in men - 5 (22.9%) cases and in women - 13 (17.8%) (p = 0.1)), oncological diseases - in 10 (10.5%) men and women: 2 (9.1%) and 8 (10.9%) cases, respectively (p = 0.5). Diseases of the digestive system accounted for a small percentage of the total number of deaths (3.2%), without statistically significant differences by gender (1 (4.5%) case for men and 2 (2.9%) cases for women (p = 0.75)). Among the dead men, 1 (1.1%) death was caused by an infectious disease.

Conclusion: During all periods of observation, most of the deceased men and women had cardiovascular and respiratory diseases.

REFERENCE

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AB0850 THE LIPID SPECTRUM OF BLOOD, DEPENDING OF BONE MINERAL DENSITY (BMD) IN MEN WITH CORONARY HEART DISEASE (CHD)

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Background The problem of the relationship between osteoporosis in men and risk factors for atherosclerosis is insufficiently studied.

Objectives The aim was to assess the lipid profile of the blood depending on the BMD in men with CHD.

Methods 93 men older than 50 years (mean age – 60.8±6.9 years) with coronary artery disease verified by coronary angiography were examined. The concentration of total cholesterol (OHS), triglycerides (TG), high and low density lipoprotein cholesterol (HDL and LDL cholesterol) in serum was determined by spectrophotometric method. T-criterion of the femoral neck and lumbar spine was used for the assessment of BMD, which was investigated by the method of two-energy absorptiometry (densitometer Excel XR-46, NORLAND, USA). According to the T-criterion, patients were divided into 3 groups: I – 30 patients with osteoporosis (T-criterion ≤-2.5), II – 44 patients with osteopenia (T-criterion from -1 to -2.5) and III – 19 men with normal BMD (T-criterion ≥-1).

Results Most men with established CHD dyslipidemia (95.7% of patients): hypercholesterolemia – 76.3%, elevated level of LDL cholesterol – 81.7% of the patients, hypertriglyceridemia in 49.5%, a decrease in the concentration of HDL cholesterol – 44.1% of cases. In all three groups of patients hypercholesterolemia (80, 75 and 73.7% of patients in groups I, II and III, p>0.05) and increased LDL-C concentration (83.3, 84.1 and 73.7% of men in groups I, II and III, p>0.05) were revealed. Reduction of HDL cholesterol level was determined in 46.7% of cases in group I, 43.2% in group II and 42.1% in group III (p>0.05). Hypertriglyceridemia was registered in 60% of patients with osteoporosis, 43.2% - with osteopenia and 47.4% – with normal BMD (p>0.05). Correlation analysis of the relationship of lipid metabolism with the T-criterion in all patients included in the study did not reveal significant relationships (p>0.05).

Conclusion The results of the study indicate the presence of severe dyslipidemia and the absence of dependence of lipid parameters on the state of BMD in men with CHD.

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AB0851 OBESITY AND RISK OF FRACTURE: DEPENDS ON THE BODY MASS INDEX AND TYPE OF FRACTURE

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Objectives: To know the impact of obesity on the risk of fracture.
Methods: Observational study, during 2010-2018, of patients referred for bone densitometry (BMD), to the Bone Densitometry Unit of Rheumatology.
BMD performed by Rheumatology nursing, collect several data (age, gender); osteoporosis (OP) risk factors: age of menopause, smoking and current alcohol intake, hip fracture parents, body mass index (BMI), diseases-drugs that reduce bone mass, fractures, treatment; BMD in lumbar spine (LS), femoral neck (FN); FRAX with BMD. BMI result was as WHO recommendations in kg/m^2: Normal: 18.5-24.99; Obesity: ≥30; type I: 30-34.99, type II: 35.39.99, type III: ≥40.
Results: A first BMD in 6.943 postmenopausal women was done. 2.196 (32%) had normal BMI, low weight (BMI <18.5 kg/m^2) 103 (1.5%) patients, overweight (BMI 25-29.99 kg/m^2) 2.643 (38%) and obesity 2.001 (29%).
Obesity (BMI ≥30 kg/m^2) vs normal BMI, are older (65±13 vs 61±13, p=0.005), lower current smokers (12% vs 27%) P <0.0001), more treated for OP (37% vs 29%, p=0.002), higher percentage of fractures (44% vs 29%), especially distal radius (DR) (30% vs 11%), p<0.001) and vertebral (19% vs 7%, p=0.002), lower mean T score in LS (-1.1±1.5 vs 1.8±1.5, p <0.0001) and FN (-1.1±1.5 vs -1.6 ± 1.5, p<0.0001) and lower mean FRAX hip fracture with BMD (1.9±3.6 vs 2.4±3.6, p <0.0001). In table, obesity groups are compared with normal BMI.
Conclusion: In postmenopausal women referred for BMD, obese women vs normal BMI are 1. Older. 2. Overall, with higher percentage of fractures. 3. But, women with BMI≥ 40 kg/m^2 do not have a higher overall percentage of fracture, except in DR.

References:

	IMC Normal 18.5-24.9 N: 2.196	IMC Obesity I 30-34.99 N: 1.403	P Normal vs Obesity I	IMC Obesity II 35-39.99 N: 421	P Normal vs Obesity II	IMC Obesity III ≥40 N: 177	P Normal vs Obesity III
Age years, mean (SD)	61.4 (13.1)	65.6 (13.1)	**0.0001**	65.7 (13.1)	**0.0001**	63.5 (13.1)	**0.04**
BMI, mean (SD)	22.7 (5.2)	32.1 (5.2)	**0.0001**	36.8 (5.2)	**0.0001**	43.4 (5.2)	**0.0001**
Menopause age, mean (SS)	47.3 (5.5)	47.6 (5.5)	0.11	47.8 (5.4)	0.08	48.3 (5.5)	**0.02**
Current smoker, n (%)	587 (27)	176 (13)	**0.0001**	40 (10)	**0.02**	19 (11)	0.23
Hip fracture in mother, n (%)	254 (12)	144 (10)	0.54	36 (9)	0.59	16 (9)	0.71
Current treatment, n (%)	645 (29)	516 (37)	**0.004**	147 (35)	0.15	58 (33)	0.52
Corticosteroids, n (%)	156 (7)	94 (7)	1	32 (8)	0.84	18 (10)	0.64
Fracture, n (%)	645 (29)	520 (37)	**0.004**	168 (40)	**0.006**	60 (34)	0.41
Colles	235 (11)	160 (30)	**0.0001**	58 (32)	**0.0001**	20 (32)	**0.007**
Vertebral	145 (7)	101 (19)	**0.004**	32 (18)	**0.049**	7 (11)	0.68
Hip	66 (3)	32 (6)	0.47	11 (6)	0.61	4 (6)	0.74
Humerus	22 (1)	53 (10)	0.17	14 (8)	0.28	8 (12)	0.17
Other	194 (29)	193 (36%)	0.14	66 (36%)	0.28	23 (37)	0.42
Lumbar BMD, mean (SD)	-1.78 (1.5)	-1.14 (1.5)	**0.0001**	-1.1 (1.5)	**0.0001**	-0.25 (1.5)	**0.0001**
Normal, %	572 (27)	591 (43)	**0.0001**	230 (57)	**0.0001**	116 (68)	**0.0001**
Osteopenia, %	923 (43)	557 (41)	0.45	132 (33)	**0.03**	47 (27)	**0.03**
Osteoporosis, %	657 (31)	216 (16)	**0.0001**	40 (10)	**0.005**	8 (5)	0.11
Femoral neck BMD, mean (SD)	-1.58 (1.1)	-1.1 (1.1)	**0.0001**	-0.94 (1.1)	**0.0001**	-0.79 (1.1)	**0.0001**
Normal, n (%)	586 (27)	617 (45)	**0.0001**	195 (47)	**0.0001**	104 (60)	**0.0001**
Osteopenia, n	1218	674 (49)	**0.001**	187 (48)	**0.02**	58 (33)	**0.0001**

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AB0852 DOES INADEQUATE RESPONSE TO DENOSUMAB TREATMENT EXIST?

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Background: Denosumab (Dmab), an anti-receptor activator of nuclear factor kappa-B ligand (RANKL) monoclonal antibody, has been shown to increase bone mineral density (BMD) at lumbar spine and proximal femur up to 21.6% and 9.1% respectively at 10 years of treatment. Additionally, Dmab has shown a marked decrease of vertebral, nonvertebral and femoral fractures during treatment. Nowadays, the existence of inadequate response to Dmab treatment remains unknown.
Objectives: to describe the clinical, analytical and densitometric characteristics of patients with an inadequate response (IR) to Dmab treatment. IR was defined as the presence of a new fragility fracture during Dmab treatment or a significant decrease in BMD (≥5% at lumbar spine or ≥4% at proximal femur) within at least 12 months of therapy.
Methods: retrospective study including patients with osteoporosis with an IR to Dmab. Therapeutic compliance was checked by clinical anamnesis and the electronic prescription. Risk factors for osteoporosis, history of fragility fractures, previous anti-osteoporotic treatment, densitometric and analytical data were collected before and at the moment when IR was diagnosed.
Results: Fourteen patients were included (12 women and 2 men) with mean age of 75 ± 9 years. The causes of osteoporosis were: postmenopausal (n=8, 57.14%), induced by glucocorticoids (n=3, 21.43%), alcoholic (n = 1, 7.14%) and multifactorial (n=2; 14.28%). Nine patients (64.28%) had been previously treated with oral or intravenous bisphosphonates for a mean of 5.8 ± 2.76 years. Nine patients (64.28%) had previous vertebral fractures (median 2, range 1-8), 2 of them had also presented a femoral fracture. During Dmab treatment, 7 patients (50%) presented a decrease in BMD (mean loss: proximal femur -3.5%, p=0.09; lumbar spine - 5.8%, p=0.046;) and 7 had incidental fractures: 5 vertebral (median 1, range 1-4), 1 humerus and 1 femur. The duration of treatment with Dmab was 3.82 ± 1.85 years in patients who sustained fragility fractures and 2.39 ± 1.4 years in patients with a BMD decrease. A multiple myeloma was diagnosed in a patient with vertebral fractures during Dmab treatment. After The identification of Dmab RI most patients mantained same treatment. Of the patients with incidental fragility fractures, 2 started combined treatment with teriparatide and Dmab, 1 changed to teriparatide and 2 maintained the same treatment. Of the 7 patients with BMD only 1 changed to zoledronic acid.
Conclusion: Most patients with IR to Dmab treatment had previous fragility fractures and had been previously treated with bisphosphonates for a mean duration of 5 years. The patients with a significant decrease in BMD had lesser duration of Dmab treatment than those who sustained fractures during Dmab treatment. Only one patient had a clinical cause for the IR development.
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AB0853 BONE DENSITOMETRY IN CROHN'S DISEASE: RISK FACTORS FOR OSTEOPENIA AND OSTEOPOROSIS

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Background: Osteoporosis and osteopenia are common situations in chronic inflammatory bowel disease (IBD), particularly in crohn's disease.

Objectives: The objective of our study was to determine the prevalence of these affections during crohn's disease and to identify the risk factors for osteopenia and osteoporosis.
Methods: We conducted a descriptive monocentric retrospective study of consecutive patients with crohn's disease who were hospitalized between January 2016 and December 2018.
Results: We included 100 patients (64 female and 36 male) with an average age of 37 years [17-68 years]. Among these patients 21% were smokers and among women 20% were in menopause. Bone densitometry was performed in 39 patients. It was found to be pathological in 53.8% of cases. The rate of osteoporosis was 17.9% (7 patients) and the rate of osteopenia was 35.9% (14 patients). Tobacco and a BMI of less than 18 had a statistically significant association with osteopenia (p=0.046; p=0.038 respectively). The presence of a family history of IBD had a statistically significant influence on a pathological bone densitometric investigation (p=0.036). An albuminemia rate of less than 35g/dl had an association at the limit of significance with bone pathology in BMD (p=0.059).
Conclusion: Osteoporosis and osteopenia are frequent during crohn's disease. They are in the majority of cases asymptomatic. This makes bone densitometry essential, especially in the presence of a family history of IBD, smoking and malnutrition (BMI less than 18) in order to act early and avoid complications such as fractures.
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AB0854 PERSPECTIVES OF WOMEN WITH EXPERIENCE OF A FRAGILITY FRACTURE IN EUROPE: ATTITUDES TOWARDS FUTURE FRACTURE RISK, OSTEOPOROSIS AND PHARMACOTHERAPY

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Background: Fragility fractures (FF) are common in women >50 years (yrs), with 1 in 3 experiencing a fracture (Fx).[1] However, the cause of these Fx is poorly recognised and measures taken to prevent future Fx are often inadequate. Recent US patient (pt) survey data suggest that awareness of osteoporosis (OP) and its contribution to Fx risk, appreciation of the benefits of OP pharmacotherapy (Rx), and discussion about OP with healthcare professionals (HCPs) are limited.[2]
Objectives: This study gained insight into the attitudes and experiences of post-FF women in Europe regarding future Fx risk management.
Methods: Women ≥51 yrs from Germany (DE), Spain (ES), UK, France (FR) and Italy (IT) (EU5) with self-reported experience of a FF completed a 30–min online survey (AplusA; 13–20 Feb 2018). Data are reported for EU5 pts who had their first Fx at ≥50 yrs; pts whose first Fx was a hand/finger or ankle/foot/toe Fx were excluded.
Results: 199 women participated (DE: 38; ES: 36; UK: 41; FR: 34; IT:50). The most commonly experienced Fx was of the lower arm/wrist (43%). 43% reported >1 Fx (any type). Most women discussed bone health with an HCP within 6 months (mo) (70%; 42% with a GP) and HCPs were their primary source of information on OP (85%). Around a third reported taking a DEXA test within 6 mo of their first FF (37%). Advice from HCPs to prevent Fx focused on calcium/vitamin D supplements (74%) and diet/exercise changes (54%); 46% were prescribed OP-Rx. After having a FF, around half worried about future Fx (51%) and 39% voiced concerns about their general health (Figure). A third of pts thought that OP had caused their Fx (33%), most were likely to attribute it to a fall (67%). Only 18% felt empowered to manage their bone health; 61% did not think OP-Rx reduces risk of Fx or were unsure. 97% had never joined a support group.
Conclusion: These results indicate that pts discuss future Fx risk with an HCP soon after having a FF and are concerned about future Fx. However, low levels of DEXA testing and OP-Rx, and poor awareness of the link between OP and Fx risk remain. Better education to empower women at risk of FF is critical.

REFERENCE

[1] Hernlund E. Arch Osteoporos 2013;8:136; 2. Boudreau D. J Am Geriatr Soc 2017;65:1829–35.

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AB0855 FACTORS ASSOCIATED WITH ADHERENCE TO OSTEOPOROSIS TREATMENT IN PATIENTS WITH RHEUMATIC DISEASES

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Background: Patients with rheumatic diseases (RD) have an increased risk of developing osteoporosis (OP) and fractures compared with healthy population due to chronic inflammation, low physical activity and using some kind of medications. Persistence and adherence to OP therapy are important factors in achieving successful outcomes in fracture reduction.
Objectives: To identify the factors affecting persistence and adherence to OP therapy in patients with RD
Methods: We conducted observational study of 196 RD (150 - with rheumatoid arthritis and 46 - with systemic sclerosis) patients aged 50 years and older (96% women, mean age 61±9 years) with OP. Persistence and adherence were assessed 3 years after OP therapy initiation. The patients kept a diary on osteoporosis therapy. The information was collected during the visits to the doctor or from telephone contact with the patient every year.
Results: During 3 years 32% of patients received zoledronic acid, 27% - alendronate, 16% - denosumab, 12%- ibandronate, 5% - alfacalcidol, 3% - strontium ranelate, 1% - teriparatide, 3% - calcium and vitamin D. 45 (23%) persons were switched from one antiosteoporotic medication to another due to physician's recommendation. 123 patients (63%) were persistent with OP therapy, including 78% of those who received zoledronic acid, 75% - denosumab, 60% - oral bisphosphonates, 53% - among those, who switched OP therapy during follow up period. The most common reason for interruption or discontinuation of OP treatment was poor tolerance (33%). Persistence in patients with RD was associated with determination of vitamin D level (OR =3.84, 95%CI 1.91-7.72, p=0.0001), 10 years fracture risk assessment (FRAX®) (OR=3.9, 95%CI 1.4-10.9 p=0.006), annual BMD measurement (OR=2.19, 95%CI 1.08-4.42, p=0.028), quantity of biochemical blood tests (p=0.0043) and visits to the doctor (p=0.003). Age, education, marital status, income level, duration of disease, educational brochures and lectures on OP, previous fractures, hip fractures in parents, the number of comorbidities, the total number of taken medications did not affect adherence and persistence to OP treatment.
Conclusion: 63% of patients with RD and OP received antiosteoporotic medication during 3 years. Assessment of serum vitamin D level and FRAX score, monitoring of OP therapy with annual DEXA, blood biochemical markers and regular visits to the rheumatologist associated with increased persistence with OP treatment in RD patients.
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AB0856 RISK FACTORS OF CIRRHOSIS- RELATED OSTEOPOROSIS

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Background: Osteoporosis, that may lead to a high risk of fractures and compromises quality of life, is the main bone disturbance among cirrhotic patients. Despite that, it tends to be under-diagnosed.
Objectives: To determine frequency of osteoporosis and identify risk factors associated among cirrhotic patients.
Methods: We performed a retrospective analysis of data from consecutive cirrhotic patients recruited from **January 2010 to December 2017** and who had at least one bone mineral density measurement (BMD). By definition from the World Health Organization, osteoporosis is defined by bone densitometry as a T score < -2.5 and osteopenia as a T score between -1 and -2.5.
Results: 227 patients with an average age of 65.5 years [24-90] were included. Thirty one had a BMD: ten patients with HCV-related cirrhosis (HCV), seven patients with HBV-related cirrhosis (HBV) and 14 patients with autoimmune liver disease (eight cases of primary biliary cholangitis (PBC), two cases of primary sclerosing cholangitis (PSC), two cases of autoimmune hepatitis (AIH) and two cases of overlap syndrome (PBC +AIH)).. Osteopenia was observed in seven patients (22.5%): three cases of HCV, two cases of PSC and two cases of overlap syndrome. 17

patients had an osteoporosis (54.8%): six cases of HCV, three cases of HBV, five cases of PBC, two cases of AIH and one case of PSC. Osteoporosis is most common in postmenopausal women with significant correlation (p<0,001). Hyperbilirubinaemia and increased Gamma Glutamyl Transferase (GGT) were significantly correlated with osteoporosis (p<0.05). However, there was no significant correlation between osteoporosis and body mass index or the Child-Pugh score.

Conclusion: In our study, 54.8% of cirrhotic patients who have had a BMD, had an osteoporosis. It was more frequent among postmenopausal women with hyperbilirubinaemia and increased GGT. The systematic realization of BMD in these patients could contribute to better management.

Disclosure of Interests: None declared

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AB0857 DENSITOMETRY VALUES CHANGE WHEN STOPPING DENOSUMAB

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Background: Denosumab (DMAB) withdrawal without subsequent bisphosphonate treatment seems to be related to a rebound effect: a rapid decrease in mineral density in bone densitometry (DEXA). However, evidence is scarce.

Objectives: To analyze DEXA values in patients who have stopped DMAB without subsequent treatment and to detect possible factors associated.

Methods: Unicentric observational study. We included patients with osteoporosis (OP) who attended our rheumatology clinic from May 2017 to December 2018, who had stopped DMAB without any further treatment. Demographic data, risk factors for OP (smoking, age of menopause, previous fractures, chronic corticotherapy), data related to calcium and vitamin D analogues supplementation, previous OP treatment and durantion of active treatment with DMAB were collected; as well as DEXA data (last DEXA while on DMAB and inmmmediate DEXA after its withdrawal, no more than 3 years later). For the statistical analysis, means, standard deviations, frequencies and percentages are reported accordingly. Paired Student's T test has been used to analyze medias in both DEXAs, and chi square for comparisons when appropriate.

Results: 39 patients (38 women) age 70.17±.4, menopause at 46±4.07 years, 37(94%) never used tobacco, 25 (64%) suffered some fracture before treatment with DMAB, 17(43%) received previous bisphosphonates, 5 (13%) teriparatide and 7(18%) strontium ranelate. The average duration of DMAB use was 2 ±0.86 years, onset at 61 ±7.34 years. Standard deviations (T score) of DEXA values worsened significantly (p <0.001) in all the locations: femur -0.28 (IC95% -0.36 to -0.19), columnL1 -0.43 (IC95% -0.30 a - 0.56), columnL2 -0.44 (IC95% -0.25 to -0.62) columnL3 -0.40 (IC95% -0.22 to -0.59) columnL4 -0.52 (IC95% -0, 33 to -0.72) columnL1-L4 -0.48 (IC95% -0.33 to -0.64) (table 1). We analyzed the decrease in T-scores alongside the other variables, obtaining a proportionally inverse relation between duration of DMAB use and this reduction (table 2). Given that DMAB use in one patient was several standard deviations above the mean (12 yrs), her data where excluded for analysis.

Conclusion: DMAB withdrawal without subsequent antiresorptive treatment produces a rapid decrease in DEXA values in our patients. This phenomenon appears to diminish in patients who have received DMAB for a longer period.

Abstract AB0857 Table 1. Comparison T-score DEXA previous to DMAB withdrawal (1st DEXA) and afterwards (2nd DEXA)

	Mean T-score ± SD+ 1st DEXA	T-score Media ± SD+ 2nd DEXA	Media difference between 1st and 2nd DEXA
Total Femur	-1.46 ± 0.85	-1.74 ± 0.87	-0.28*
Column L1	-2.16 ± 0.82	-2.59 ± 0.75	-0.43*
Column L2	-2.42 ± 0.81	-2.87 ± 0.75	-0.44*
Column L3	-2.01 ± 0.82	-2.42 ± 0.89	-0.40*
Column L4	-2.04 ± 1.10	-2.57 ± 1.06	-0.52*
Column L1-L4	-2.12 ± 0.76	-2.61 ± 0.71	-0.48*

*p<0.001 +SD: Standard deviation

Abstract AB0857 Table 2

YEARS ON DMAB DIVIDED INTO TERTILES * COLUMN L1 L4 SD DIFFERENCE IN TERTILES Crosstabulation

			Difference L1 L4 in tertiles			Total
-0.60 and more	-0.59 to -0.30	-0.29 and less				
YEARS ON DMAB DIVIDED INTO TERTILES	0-1.95	Count	7	5	1	13
		% within Difference L1 L4 in tertiles	46.7%	50.0%	10.0%	37.1%
	1.96-2.38	Count	3	5	3	11
		% within Difference L1 L4 in tertiles	20.0%	50.0%	30.0%	31.4%
	2.39 or more	Count	5	0	6	11
		% within Difference L1 L4 in tertiles	33.3%	0.0%	60.0%	31.4%
Total		Count	15	10	10	35
		% within Difference L1 L4 in tertiles	100.0%	100.0%	100.0%	100.0%

Disclosure of Interests: None declared

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AB0858 MAINLY MEN, AND OLDER PEOPLE, WITH FRAGILITY HIP FRACTURE DO NOT RECEIVE ANTIOSTEOPOROTIC TREATMENT

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Background: Osteoporotic hip fractures have a profound impact on the physical health and psychosocial wellbeing of patients, with considerable economic implications. More than 20% of individuals experience a subsequent hip fracture in the following year (1,2). Although there are effective treatments in the prevention of fractures, the proportion of patients who start treatment after a fragility fracture is low, having decreased in recent years (3).

Objectives: The aim of the study is to know the percentage of patients who received medical treatment for osteoporosis after a fragility hip fracture in our health department. Secondary, we want to know the mortality and re-fracture rates two years after the fracture.

Methods: Cross-sectional retrospective observational study. Patients discharged during 2015 with diagnosis of "Fragility Hip Fracture" were reviewed, data collected through electronic medical record. Variables: sex; age; age and date of death; treatment (calcium, vitamin D or antiosteoporotic drugs) before and after discharge; Fragility fracture before and after hospital discharge. Statistical methods: absolute and relative frequencies for qualitative variables, means and standard deviations for quantitative. Associations between variables were studied using Chi square and T-student test.

REFERENCES

[1] M. B. Zanchetta, J. Boailchuk,F. Massari,F. Silveira,C. Bogado and J. R. Zanchetta. Significant bone loss after stopping long-term denosumab treatment: a post FREEDOM study. Osteoporos Int(2018) 29:41–47

[2] Olivier Lamy, Delphine Stoll, Bérengère Aubry-Rozier, Elena Gonzalez Rodriguez. Stopping Denosumab. Current Osteoporosis Reports. Published online Jan. 2019

[3] Chapurlat R, Effects and Management of Denosumab Discontinuation, Joint Bone Spine (2018).

Results: A total of 320 patients were obtained, 17 discarded (3 other fracture locations, 1 duplicate, 6 high energy trauma fractures and 8 had other pathologies than osteoporosis that justified the fracture). Mean age was 83.3 ± 7,9 years, 223 (73.6%) women. Prior to admission, 43 patients (14%) took calcium and/or vitamin D, 10 (3%) some antiosteoporotic drug and 20 (7%) both. 230 patients (76%) did not receive treatment. 102 exitus (33.7%) occurred in the 2 years after the fracture. In the post-discharge analysis, 30 patients were discarded (17 died during admission and 13 in the subsequent month), since it was not possible for them to be treated. After discharge, 49 patients (18%) receive Calcium and/or Vitamin D, 15 (5%) some antiosteoporotic drug and 37 (14%) both, leaving 172 patients (63%) without treatment. There were 12 new hip fractures (4.0%). There is a greater proportion of deaths in men (43.8% vs. 30% in women, p = 0.026) and in patients not treated before the fracture (33.2% vs 11.6% calcium-Vit D, p <0.001, 30.5% vs 9.4%, antiosteoporotic treatment p = 0.002). The multivariate analysis found lower probability of having received treatment in men (RR 0.34 IC 95% (0.16-0.72), p = 0.005) and with more age (RR 0.95 IC 95% (0.92-0.98), p = 0.004). After correcting with age: the risk of death in men is 83% higher than in women (p = 0.035). The probability of exitus increases by 10% for each additional year of life. Treatment with calcium and/or vitamin D after discharge is a protective factor against mortality from any cause (p = 0.037).
Conclusion: Percentage of patients receiving drug treatment after suffering an osteoporotic hip fracture is very low. This is accentuated in males, and at an older age, populations that also have higher mortality rates in the two years after the fracture.

REFERENCE

[1] Weaver J, et al. Prevalence and Cost of Subsequent Fractures Among U. S. Patients with an Incident Fracture. J Manag Care Spec Pharm 2017; 23:461-71.
[2] León-Vázquez F, et al. Prevención de fractura osteoporótica en España: uso de fármacos antes y después de una fractura de cadera. Rev Osteoporos Metab Miner 2015; 7:54- 23
[3] Van der Velde R.Y., et al. Trends in oral anti-osteoporosis drug prescription in the United Kingdom between 1990 and 2012: variation by age, sex, geographic lication and ethnicity. Bone. 2017; 94: 50-55.

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AB0859 THE SERUM CREATININE TO CYSTATIN C RATIO; A POSSIBLE NEW SURROGATE MARKER FOR BONE MINERAL DENSITY

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Background: Bone mineral density (BMD) measured using dual-energy X-ray absorptiometry (DEXA) is one of the most important markers for osteoporosis diagnosis. The serum creatinine-to-cystatin C ratio (Cr/CysC) is in focus as a sarcopenia marker because it represents total muscle volume. Recently, Cr/CysC was suggested to have correlation with bone fragility fracture risk [1].
Objectives: This study aimed to assess whether Cr/CysC is correlated with BMD.
Methods: BMD at the lumbar spine (LS) and femoral neck (FN) were measured in women diagnosed with postmenopausal osteoporosis. Steroid induced osteoporosis patients were eliminated. Cr/CysC was assessed at the time. Clinical factors, such as age, concurrent rheumatoid arthritis treatment (RA), concomitant biological drug administration (BIO), body mass index (BMI), concurrent dementia treatment (dementia), number of comorbidities other than dementia (N.Com), frailty score (FS), bone fragility fracture (BFF), and drug intervention for osteoporosis (DI), were evaluated. Multivariate linear regression (MLR) was used to assess the correlation of these factors with BMD at each part. The relationships between Cr/CysC and other parameters were statistically evaluated using MLR. Additionally, the relationships between the BMD change at each part and parameters were evaluated in the same manner.
Results: The study enrolled 207 subjects. BMD at the LS was significantly correlated with BMI and N.Com ($p<0.01$), whereas BMD at the FN was significantly negatively correlated with age and was positively correlated with BMI, BFF, Cr/CysC, and DI ($p<0.01$). Cr/CysC was significantly correlated with age, RA, BIO, dementia, FS, and BFF ($p<0.01$).
After effect of age was corrected, BMD at the FN demonstrated significant positive correlation with Cr/CysC ($p<0.01$), whereas no statistical correlation demonstrated between BMD at the LS and Cr/CysC, Both BMD at the LS and the FN demonstrated significant positive correlation with BMI ($p<0.05$). No parameter significantly correlated with the BMD change at both the LS and FN ($p<0.01$).
Conclusion: Cr/CysC represents BMD at the FN and is a candidate for BMD substitution.

REFERENCES

[1] Komorita Y, et al. Diabetes Res Clin Pract 2018;146:202-10.
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AB0860 RECURRENCE OF VERTEBRAL FRACTURE IN PATIENTS WITH OSTEOPOROTIC VERTEBRAL FRACTURES: RETROSPECTIVE REVIEW IN MONCLOA UNIVERSITY HOSPITAL. PRELIMINARY RESULTS

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Background Current drugs for patients who suffer from stablished osteoporosis (OP) with osteoporotic vertebral fracture (VF) have demonstrated their efficacy with different levels of evidence for secondary prevention of fractures1. In fact, this level of efficacy can be limited in real clinical practice, with pluripathological and previously polimedicated patients.
Objectives Main objective of this study is to describe the percentage of patients with VF in which the therapeutic goal of avoiding new VF during their follow-up has been achieved. As a secondary objective, clinical and therapeutic differences will be analyzed among distinct groups arisen from achieving or not the therapeutic goal.
Methods Retrospective, observational, longitudinal, descriptive study of patients from Rheumatology Departament in Moncloa University Hospital who have suffered a osteoporotic VF.
Results 133 cases have been reviewed, 115 (86.5%) females and 18 males (13.5%). Average age is 72 years (+/- 7) and average follow-up time is 2.68 years (+/- 2.3). 25 cases (18.5%) were smokers, 9 (6.8%) oncologic patients, 33 (24%) with chronic corticotherapy and 28 (21%) with immune-mediated diseases. 81 patients (60.9%) had previous VF (0.933 fracture /patient) and 14 (10.5%) non-vertebral fracture (NVF). The average VF was 1.967/patient and 0.133/patient for NVF. 52 patients (39.1%) had received prior treatment for OP (36 Biphosphonate, 23 Denosumab, 5 SERM, 2 strontium ranelate and 1 teriparatide) and in 39 cases (29.3%) a cementoplasty was performed. Initial treatments prescribed by Rheumatology Departament were Biphosphonates (48%),Denosumab (31%) and Teriparatide (21%). 35 patients received sequencial-treatment (26.9%). 86.5 % of patients haven´t presented new VF. 18 cases (13.5%) have been registered with new VF. This group is composed by 13 females and 5 males; the average age was 75 years (+/-7.5) and the average follow-up time 2.8 years (+/- 2.46); 14 (77.8 %) patients presented previous VF and 3 (16.7 %) previous NVF. The average number of previous VF was 2.0/patient and 0.33/patient for NVF. 14 cases (78.8%) of new VF ocurred during the first year of follow-up. The treatment they were receiving at the time of the new VF was in 8 cases with Denosumab (44%), 4 with Teriparatide (22%), 2 Alendronate (11%), 3 Riserdronate (16%) and 1 case without treatment.
Conclusion These are preliminary data from a register for prognosis evaluation of patients who suffer VF in Moncloa University Hospital. A larger sample size is necessary to developed a strategic conclusion in this patients, pluripathological, with previous osteoporotic fractures and treatment.78 % of new VF ocurred during the first year of the follow-up, 44% of them were receiving Denosumab, 77% (vs. 58% of the patients without new VF) had previous VF and 44% (vs. 37% patients without new VF) had received previous OP treatment.

Table: Results of multivariate linear regression analysis for relationship between BMD in each part and parameters

	univariate mode				multivariate mode			
parameters	Coefficient	LCL	UCL	p-value	Coefficient	LCL	UCL	p-value
age	-0.002	-0.005	$2.0x10^{-3}$	0.078				
RA	0.065	0.017	0.114	$9.00x10^{-4}$	0.034	-0.017	0.084	0.19
BIO	0.036	-0.037	0.109	0.338				
BMI	0.018	0.012	0.024	$3.54x10^{-8}$	0.019	0.013	0.025	$2.60x10^{-9}$
N.Com	0.008	0.012	0.345	$6.70x10^{-6}$	0.01	0.053	0.014	$3.00x10^{-5}$
Dementia	-0.009	-0.062	0.046	0.757				
Frailty score	-0.015	-0.031	$9.0x10^{-3}$	0.065				
bone fragility fracture	-0.051	-0.108	0.005	0.073				
Cr/CysC	0.203	0.006	2.028	0.044	0.086	-0.11	0.283	0.39
Drug intervention	-0.042	-0.103	0.019	0.18				
age	-0.004	-0.006	-5.641	$5.72x10^{-8}$	-0.003	-0.001	-3.213	$1.55x10^{-3}$
RA	0.065	0.034	0.095	$4.00x10^{-6}$	0.025	-0.01	0.059	0.16
BIO	0.059	0.014	0.105	0.011	0.001	-0.049	0.051	0.98
BMI	0.004	$3.0x10^{-4}$	0.008	0.048	0.004	$2.0x10^{-3}$	0.008	0.037
N.Com	0.002	0.005	1.13	0.26				
Dementia	-0.049	-0.083	-0.015	$4.78x10^{-3}$	0.008	-0.029	0.044	0.69
Frailty score	-0.019	-0.028	-0.009	$2.60x10^{-5}$	0.005	-0.007	0.017	0.44
bone fragility fracture	-0.068	-0.103	-0.033	$1.50x10^{-4}$	-0.036	-0.071	-0.001	0.046
Cr/CysC	0.248	0.126	0.37	$8.00x10^{-6}$	0.132	0.007	0.256	0.038
Drug intervention	-0.079	-0.116	0.041	$5.00X10^{-6}$	-0.057	-0.093	-0.021	$1.88x10^{-3}$

REFERENCES

[1] T. Saito, J. M. Sterbenz et al. Effectiveness of anti-osteoporotic drugs to prevent secondary fragility fractures: systematic review and metaanalysis. OsteoporosInt (2017) 28:3289–3300

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Crystal diseases, metabolic bone diseases other than osteoporosis

AB0861

METHODS TO EFFICIENTLY RECRUIT MINORITY PATIENTS WITH GOUT FOR CLINIC-BASED REGISTRIES

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Background: Gout is frequently misdiagnosed and/or miscoded, making approaches to identifying eligible patients for observational and interventional studies more challenging. Ethnic and racial minorities are under-represented in many gout studies. Methods to better identify minorities and confirm gout diagnosis are essential to ensure studies have both validity and generalizability.

Objectives: To define efficient methods for identifying African Americans (AA) interested in participating in a gout registry and who satisfy the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) gout classification criteria.

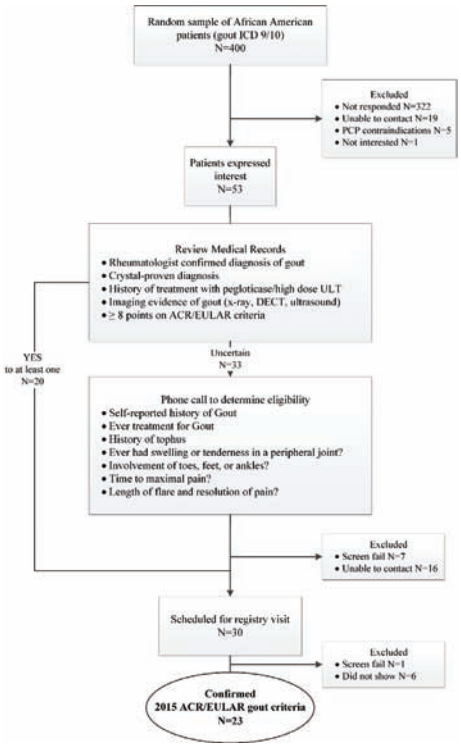
Methods: We identified all AA patients seen at University of Alabama at Birmingham 01/09/2017 and 31/08/2018 with an ICD 9/10 code for gout. Patients not "opted out" by their primary care provider (PCP) were invited to participate. Those interested underwent detailed medical record review followed by phone contact to determine eligibility. Those with a high likelihood of meeting diagnostic criteria for gout were invited for an in person visit to confirm diagnosis (**Abstract AB0861 Figure 1**).. We compared descriptive characteristic of participants enrolled in the registry and the larger potential gout populations

Results: From 3,032 AA patients with an ICD 9/10 gout diagnosis we generated a random sample of 400 patients. 5 patients were excluded by their PCPs, thus 395 patients were preliminarily eligible and invited via e-mail (N=176) and/or letter (N=375). 1 patient (< 1%) communicated lack of interest, 19 (4.8%) were unreachable, 322 (81.5%) did not respond to the invitation, and 53 (13.4%) expressed preliminary interest and underwent medical record review. We successfully scheduled 30 subjects for a registry visit, 24 completed the visit, and 23 (6% of initial sample) satisfied 2015 ACR/EULAR gout classification criteria (see **Table 1**). We found no significant difference in age, sex, and the number of medical encounters in the last year between enrolled patients and the remaining population.

Conclusion: We present a strategy for identifying and recruiting AA patients with ACR/EULAR classified gout into a population-based registry. Among a randomly selected cohort of AAs with an initial ICD 9/10 diagnosis code of presumed gout, slightly under 15% expressed interest and 6% satisfied the 2015 ACR/EULAR criteria and successfully enrolled in the registry. Our experience emphasizes a potential approach as well as some challenges in creating a generalizable gout registry.

Abstract AB0861 Table 1. Characteristics of African Americans (n = 24) who completed in person visit for a gout registry

Gender	
Men (%)	12 (50%)
Women (%)	12 (50%)
Age years, mean (SD)	62.7 (8.3)
2015 ACR/EULAR criteria ≥8 (%)	23 (96%)
2015 ACR/EULAR criteria, mean (SD)	9.5 (0.9)
Sufficient criteria (%): MSU crystals present	0 (0%)
Joint/bursa involvement (%)	
Ankle or midfoot	1 (4%)
First metatarsophalangeal joint	23 (96%)
Characteristics of episode(s) ever (%)	
One	0 (0%)
Two	2 (8%)
Three	22 (92%)
Time course of episode(s) ever (%)	
One	0 (0%)
Recurrent	24 (100%)
Clinical evidence of tophus(i) (%)	0 (0%)
Serum urate (uricase method) (%)	
<4 mg/dl	0 (0%)
4-6	2 (8%)
6-8	9 (37.5%)
8-	10 (42%)
≥10	3 (12.5%)
Synovial fluid analysis (%)	
Negative	1 (4%)
Not done	23 (96%)
Imaging evidence of urate	0 (0%)
Imaging evidence of damage	1 (4%)
Gout medication	
Allopurinol	
Current (%)	15 (63%)
Past (%)	2 (8%)
Colchicine	
Current (%)	10 (42%)
Past (%)	2 (8%)
Gout flare history	
Last year (%)	18 (75%)
Number of flares last year, mean (SD)	3 (6.0)
Age at diagnosis, mean (SD)	52.7 (11.9)
Positive family history (%)	10 (42%)
Gout attack at screening visit (%)	3 (13%)



Abstract AB0861 Figure 1. Sequential steps employed to recruit African Americans to gout to a registry

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AB0862 EFFICACY AND SAFETY OF US-GUIDED INJECTIONS OF THE KNEES WITH HYALURONIC ACID IN PATIENTS AFFECTED BY OSTEOARTHRITIS ASSOCIATED TO CALCIUM PYROPHOSPHATE DEPOSITION DISEASE: PRELIMINARY RESULTS

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Background: Calcium pyrophosphate deposition disease (CPPD) and Osteoarthritis (OA) are often associated (1). However, is still controversial how calcium pyrophosphate (CPP) deposits coul d affect OA features (1) and, eventually, the response to the OA treatments.
Objectives: To evaluate the efficacy and the safety of Ultrasound (US)-guided injections of the knees with Hyaluronic Acid (HA) in patients with OA and CPPD, compared to OA.
Methods: Consecutive patients, referred to the outpatient clinic with a clinical and radiological knee OA required intra-articular (IA) treatment with high molecular weight (HMW) HA and without any clinical inflammatory signs, were enrolled. No limits about OA score [Kellgreen-Lawrence (K-L) score] were used. Patients with diagnosis or suspicion of other chronic inflammatory rheumatic diseases were excluded. For each patients, were recorded age, sex, Body Mass Index (BMI) and K-L score. The presence of CPP deposits were evaluated by US at level of menisci and knee hyaline cartilage, using the OMERACT criteria (2). All the patients were submitted to three IA injections with HA, performed every week. Before each injection, the synovial fluid (SF) was aspirated and its amount recorded. All SF aspiration and injections were US-guided. At baseline and before each injection, the Western Ontario and Mc Master Universities Osteoarthritis Index (WOMAC) was submitted to the patients.
The data were analyzed using a Wilcoxon test for independent samples and a regressive logistic model, including age, sex, BMI, K-L, SF and CPPD presence.
Results: We enrolled 23 patients (12 woman [52,17%]) with a mean age of 67,65 yo (SD±11,93), a mean BMI of 27,43 (SD±4,82) and a median K-L score of 3 (range 2-3). 10/23 (43,88%) patients were identified as affected by CPPD at US [6 woman, mean age 67,39 yo (SD±12,1), BMI 27,14 (SD±4,4), median K-L of 3 (range 2,75-3,25)]. No differences about age, BMI and K-L score were observed. Regard the baseline WOMAC, the CPPD group mean [955,89 (SD±416,5)] was significantly higher ($p<0,01$) than OA [379,5 (SD±225,21)].
Considering the short term effect, the WOMAC score improved in both groups after the first injection, but it was significantly higher in the CPPD group ($p<0,01$) and the regressive model analysis, showed that only the CPPD is correlate to the WOMAC change.
After the second injection, the improvement continues but without differences. The regressive model showed that no variables correlate with WOMAC. The data from the long term follow up are not still available.
Regarding the SF amount, no differences statistically significant were observed between the two groups at every time.
Conclusion: The US-guided injections with HMWHA at knees appear effective and safe in patients with OA associated to CPPD. Particularly the presence of CPP does not appear a risk factor for the development of inflammation. However, these results are preliminary and should be confirmed in a larger cohort and for a longer follow-up.

REFERENCES

[1] Abhishek A, et al. Evidence of a systemic predisposition to CC and association between CC and OA at distant joints: a cross-sectional study. Arthritis Care Res (Hoboken). 2013 Jul;65(7):1052-8.
[2] Filippou G, et al. Definition and Reliability Assessment of Elementary US Findings in CPPD: A Study by the OMERACT CPPD Ultrasound Subtask Force. J Rheumatol. 2017 Nov;44(11):1744-1749

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AB0863 AN AUDIT OF MANAGEMENT OF GOUT ACCORDING TO THE BRITISH SOCIETY FOR RHEUMATOLOGY GUIDELINES,2017 IN A TEACHING HOSPITAL RHEUMATOLOGY UNIT

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Background: Gout is the most common form of inflammatory arthritis worldwide. Its prevalence is 2.49% in UK general practice. In spite of the availability of effective treatments in the UK, the incidence of gout has increased in the last decade, the reasons for which are many.There is also evidence that gout is being sub-optimally treated in primary and secondary care. (1)
Fewer than 50% of patients receive urate lowering therapy (ULT), and many patients on ULT do not achieve the target serum urate level of 300 μmol/l or lower. which is essential to prevent further attacks of gout. This target has been proposed by the British Society for Rheumatology (BSR), in the latest guideline from 2017. (2)
Objectives: To asess the compliance of gout management with the BSR 2017 guideline in our unit (a teaching hospital rheumatology department):
a) Urate lowering therapy should be discussed with all patients diagnosed with Gout.
b)ULT is strongly advised in patients with recurrent attacks (>2 over 12 months), chronic gouty arthritis, tophi, renal impairment (eGFR <60), patients on diuretics and primary gout at an early age.
c)Aim of urate lowering to reduce serum urate to <300μmol/l. (2)
Methods: Inclusion criteria:
All patients being treated for gout in the department of rheumatology, between 1st October 2016 to 31st September 2017, were included in this retrospective study. Demographics, treatment details obtained from electronic patient records. Adherence to the BSR guidelines was expressed as percentage.

Results: Total number of patients with gout was 113. Among these, 83 patients remain under rheumatology follow up, 30 were discharged within the 1 year period. 113 were considered were audit standard 1 and 2, and 83 were considered for standard 3.

Audit standard	Expected	Achieved
Urate lowering therapy should be discussed with all patients diagnosed with Gout.	100%	100% (113/113)
Strongly advised in patients with recurrent attacks (>2 over 12 months), chronic gouty arthritis, tophi, renal impairment (eGFR <60), patients on diuretics and primary gout at an early age	90%	92.9% (105/113)
Aim of urate lowering to reduce serum urate to <300µmol/l	80%	36% (30/83)

Among the 113 patients being followed up in Rheumatology, 83% were on Allopurinol, 19 were on Febuxostat, 1 patient was on Benzbromarone. 10 patients were not on Urate lowering therapy. However, 2 among them had first attack of gout without any sign of chronicity, organ damage or tophi, so not started on ULT.

- Median Allopurinol dose was 300mg. (IQR 200mg–700mg).
- 25 patients among the 113 had topheaceous gout, and 5 of them achieved BSR treatment target
- 22/83 (26.5%) patients on Allopurinol achieved BSR treatment target of <300µmol/l. 7/19 (37%) patients on Febuxostat achieved BSR treatment target of <300µmol/l

Conclusion: It is clear that a "treat to target" approach have not been adopted for x% of the patients. Gout has been shown to have better outcomes with treat to target approach. (3)
Adequate escalation of ULT is essential to achieve target serum urate level, where as the median dose of Allopurinol here is 300mg.
Gout remains inadequately treated, even in secondary care

- A consistent "Treat to target "approach needed for treatment of gout.
- Annual gout review clinic may be an effective strategy and is now being implemented as a result of this audit.

REFERENCES

[1] Kuo C, Grainge MJ, Mallen C, Zhang W, Doherty M. Eligibility for and Prescription of Urate-Lowering Treatment in Patients With Incident Gout in England. JAMA 2014 Dec 24,;312(24):2684-2686.
[2] Hui M, Carr A, Cameron S, Davenport G, Doherty M, Forrester H, et al. The British Society for Rheumatology Guideline for the Management of Gout. Rheumatology (Oxford, England) 2017 Jul 1,;56(7):e20.
[3] Perez-Ruiz F, Moreno-Lledó A, Urionagüena I, Dickson AJ. Treat to target in gout. Rheumatology (Oxford, England) 2018 Jan 1,;57(suppl_1):i26..

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AB0864 THE EFFECT OF ZOLEDRONIC ACID ON CHARCOT NEUROARTHROPATHY

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Background: The Charcot foot syndrome is a serious neuroarthropathy that may threaten the functional prognosis of diabetic patient. Some studies had emphasized the beneficial effect of bisphosphonates such as pamidronate and alendronate on the reduction in bone turnover markers in this disease. Though, the use of Zoledronic acid in the treatment of Charcot foot was only evaluated in two clinical trials and its efficacy remains controversial (1, 2).
Objectives: The aim of this study was to investigate the clinical and radiological efficacy of Zoledronic acid in patients with diabetes and acute Charcot neuroarthropathy.
Methods: A prospective 2-year follow-up study was carried out on eight patient with type 2 diabetic and acute Charcot neuroarthropathy. All our patients had a physical examination and podiatry exam. The stage of the neuroarthropathy has been assessed according to the clinical and the radiographic findings (Eichenholtz Classification). All patients were assigned to intravenous infusions of 4 mg Zoledronic acid.
Results: The mean age of the study group was 61.4 +/- 4.5 years. The mean age of the onset of foot pain was 18.3 +/- 1.5 years. The midfoot involvement was bilateral in 6 patients and unilateral in the other two. A biological inflammatory syndrome was found in 3 patients with a mean erythrocyte sedimentation rate (ESR) level at 43 mm after one hour. Foot X-rays were abnormal at all cases. The clinical outcomes at one month after Zoledronic acid infusions were the complete disappearance of acute symptoms in 6 patients and the improvement of the pain in one patient with a decreased Visual Analogue Scale (VAS) for pain by 30%. One patient had a persistence of the pain (VAS for pain at 5mm). A radiological Control was performed after 6 months for 5 patients. All of them had bone consolidation and remineralization.
Conclusion: Our study showed that the Zoledronic acid, given as a single dose, had a beneficial effect on clinical and radiological features in diabetic patients with acute Charcot neuroarthropathy.Despite our encouraging outcomes, further prospective and randomized studies are needed to confirm our preliminary results.

REFERENCES

[1] Pakarinien TK, Laine HJ, Mäenpää H, et al. the effect of zoledronic acid on the Clinical Resolution of Charcot Neuroarthropathy. Diabetes Care. 2011;34:1514-16.
[2] Bharath R, Bal A, Shanmuga S, et al. A comparative study of zoledronic acid and once weekly Alendronate in the management of acute Charcot arthropathy of foot in patients with diabetes mellitus.Indian J Endocrinol Metab. 2013 Jan-Feb; 17(1): 110–116

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AB0865 GOUT IN HOSPITALISED PATIENTS FOR CARDIOVASCULAR DISEASES: PREVALENCE AND MANAGEMENT STATUS

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Background: Gout is an independent risk factor for cardiovascular diseases (CVDs), where the urate crystal-led inflammatory state likely has a key role. Crystal dissolution may carry with cardiovascular benefits, so optimal management of gout patients is essential, especially in high-risk individuals, such as those hospitalised for CVDs. Although the prevalence of gout in Western country adults is about 2-4% [1], the rate and characteristics in inpatients with CVDs remains to be defined.
Objectives: To determine the prevalence of gout, characteristics and management in a hospitalised population for CVDs.
Methods: Observational, descriptive, cross-sectional study. Patients admitted for CVDs in the Cardiology, Neurology and Vascular Surgery units of a tertiary centre were recruited following a non-consecutive, systematic sampling up to reaching the estimated minimum sample size. A face-to-face interview and a review of electronic health records were performed, in order to collect clinical, laboratory and management data regarding CVD and gout. Gout diagnosis was established in the interview using ACR/EULAR 2015 criteria. In addition, prior clinical or crystal-proven diagnoses at records were also registered. 95% confidence intervals (95%CI) were calculated for primary variable (gout prevalence), and comparisons were performed by Student's t, chi-squared and Fisher's exact tests.
Results: 299 patients were interviewed, 33 were excluded, and the final study sample was 266 participants. They were predominantly males (69.9%) and Caucasians (96.6%) with a mean age of 68 years (SD±12). The CVDs leading to admission were acute coronary syndrome (18.8%; n=50), heart failure (13.2%; n=35), stroke or transient ischemic attack (20.7%; n=55) and peripheral artery disease (47.4%; n=126).
Gout was identified in 40 individuals (prevalence 15.0%; 95%CI 10.9-19.2). Prior gout diagnosis in records was found in only two-thirds of them, mostly clinical (Table).
Patients with gout were older (72±9 vs 68±13 years, p=0.026) and showed higher rates of chronic kidney disease (55.0% vs 23.0%, p<0.001) and use of diuretics (55.0% vs 38.5%, p=0.05), with no differences in other variables.
The disease was long-standing though low numbers of flares and involved joints were referred (Table). Tophi were seen in about 8%. The serum urate levels were not properly controlled, both at the time of the CVD and as a median of the previous five years, and only one-third of the patients were on target (<6 mg/dl). Despite 70% of patients having been treated with urate-lowering agents at some point, at admission only half remained treated (38.5% of them were on target). Nearly a quarter of patients used prophylactic colchicine.

Abstract AB0865 Table 1. Clinical & management of gout in inpatients for CVDs.

	Gout (n=40)
Prior diagnosis at records	14 (35.0)
-No	20 (50.0)
-Clinical diagnosis	6 (15.0)
-Proven by crystals	
Serum urate levels (mg/dl) at admission, mean (SD)	7.1 (±2.6)
Median serum urate levels in the previous 5 years (mg/dl), mean (SD)	6.8 (±1.6)
Current serum urate <6 mg/dl	8 (33.3)
Years since the first flare, median (IQR)	15 (10-30)
Number of flares, median (IQR)	3 (1-9)
Number of involved joints, median (IQR)	2 (1-3)
Presence of tophi	3 (7.7)
Urate-lowering agents at some point	28 (70.0)
Current use of urate-lowering agents	20 (50.0)
Use of prophylactic colchicine	5 (23.8)

Data shown as n (%), unless otherwise specified.

Conclusion: Gout is prevalent in hospitalised patients for CVDs, affecting one in seven cases. The management of gout in these patients appears suboptimal, with serum uric acid levels above recommended targets and a significant percentage of no urate-lowering treatment.

REFERENCE

[1] Kuo, NNR 2015.

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AB0866 METABOLIC SYNDROME IN PATIENTS WITH GOUT ATTENDED IN A SPECIALIZED OUTPATIENT UNIT IN SPAIN. COMPARISON WITH GENERAL POPULATION AND CARDIOVASCULAR IMPLICATIONS

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Background: Metabolic syndrome (MS) is a cluster of interrelated components: central adiposity or higher waist circumference (WC), high values of triglycerides (TG), elevated blood pressure (BP), impaired fasting glucose and decreased HDL-cholesterol (HDL-c). It is associated with a higher incidence of developing diabetes (DM), as well as with other cardiovascular diseases (CVD). A direct relationship between serum uric acid (sUA) and the risk of develop MS has been reported in several studies of patients with hyperuricemia and gout.

Objectives: To study the prevalence of MS and associated CVD in patients with gout attended in a specialized outpatient unit, comparing with other local and national studies.

Methods: Retrospective observational study with consecutive patients diagnosed with gout according to EULAR/ACR criteria between August and December 2018. We analyzed the presence of MS according to the 2015 International Diabetes Federation criteria (central obesity as BMI ≥30 kg/m2 or WC ≥94 cm (≥80 in women), with ≥2 of the following: TG ≥1.71 mmol/l, HDL-c <1.04 mmol/l (<1.3mmol/l in women), hyperglycemia ≥5'55 mmol/l (or T2DM previously diagnosed or hypoglycaemic treatment), hypertension (HT; ≥130/85 mmHg or use of antihypertensive drugs). Treatments received and family history (FH) of gout an CVD were recorded. Demographic, anthropometric, clinical and analytical variables were analyzed. All data were compared with those obtained in three Spanish studies of the general population: DARIOS, ENRICA, SIMETAP.

Results: 57 patients with gout were included. Average age 62 years (39-90), 48 years (18-90) at the time of gout onset. 94.7% males. 40.3% with FH of gout, tophi in 52.6%. Clinical pattern: monoarticular 15.8%, oligoarticular 56.1%, polyarticular 28.1%. 68.4% received urate-lowering therapy: 45.6% Allopurinol, 22.8% Febuxostat. SUA at the time of inclusion 6.7 mg/dl (2.6-11.3). Total cholesterol 186 mg/dl (4.84 mmol/l; 96-350 mg/dl/2.5-9.1 mmol/l). TG 185 mg/dl (2.11 mmol/l; 68-742 mg/dl/0.78-8.46 mmol/l). BMI 31.8 kg/m2 (24-58.1). MS was found in 66.7% and premorbid metabolic syndrome (pMS; excluding patients with previously diagnosed CVD or DM) in 26.3%. Obesity 57.9% and overweight 38.6%. HT 80.7%; 10.5% diagnosed in our unit. DM 22.8%. Dyslipidemia (DL: hypercholesterolemia or high levels of TG) 64.9%; 14% diagnosed in our unit. 29.8% smokers, 49.1% formers. Alcohol consumers 54.4%. Chronic kidney disease (CKD) 42.1%; 12.3% diagnosed in our unit. Ischemic heart disease (IHD) 14%. Stroke 24.6%. FH of CVD 24.6%. Comparing with the general population the prevalence of MS and pMS was higher (DARIOS: 31% and 24%, respectively; ENRICA: 22.7% and 16.9%; SIMETAP: 41% and 25%), as well as with the presence of CKD (11.5% in SIMETAP) and CVD (SIMETAP: HT 38%, T2DM 16%, obesity 28%, IHD 4.8% and stroke 3.8%).

Conclusion: There is a very significant percentage of MS and pMS in patients with gout compared to the general population, with important presence of CKD and CVD, sometimes underdiagnosed. Nursing guidelines were established with healthy lifestyle and periodic controls directed at all patients, with special emphasis on those newly diagnosed of HT or DL, as well as those of higher cardiovascular risk.

REFERENCES

[1] Fernández-Bergés D, et al. Metabolic syndrome in Spain: prevalence and coronary risk associated with harmonized definition and WHO proposal. DARIOS study. Rev Esp Cardiol. 2012;65(3):241-8

[2] Guallar-Castillón P, et al. Magnitude and management of metabolic syndrome in Spain in 2008-2010: the ENRICA study

[3] Ruiz-García A, et al. Population and methodology of the SIMETAP study: Prevalence of cardiovascular risk factors, cardiovascular diseases, and related metabolic diseases. Clin Investig Arterioscler. 2018;30(5):197-208

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AB0867 DEPRESSIVE SYMPTOMS INFLUENCE SUCCESS OF ALLOPURINOL AS URATE LOWERING THERAPY

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Background: Elevated levels of serum urate (sUA) is the known precursor of gout and urate lowering therapies (ULT) are the backbone of successful gout treatment. However, less is known about factors that influence the effectiveness of ULTs. Depression has shown strong relationships with treatment noncompliance, which may translate into reduced effectiveness of treatment with allopurinol. Little is known about any effects depression may produce on the observed serum urate lowering efficacy of ULTs (e.g.; allopurinol).

Objectives: To evaluate the role of depressive symptoms in the efficacy of allopurinol for lowering sUA in the context of a clinical trial.

Methods: Within a larger cross-over clinical trial of 300 daily mg of allopurinol vs. placebo for urate lowering and its effect in ambulatory blood pressure (1), 67 patients had complete data for depressive symptoms at the beginning of each treatment period, as well as sUA before and after a 4-week treatment period with allopurinol and a 4-week placebo period (order of conditions was randomized). Depressive symptoms were assessed with the Center for Epidemiologic Studies Depression Scale-10 (CESD-10) (2). Paired samples t-test evaluated change in sUA from pre- to post-treatment during active treatment and placebo. Then, linear regressions predicted change in sUA over each treatment period from pre-treatment depressive symptoms, adjusting for sex and race which were associated with baseline sUA levels.

Results: The 67 patients had average age 27.01 years (SD=6.5, range 18-40), 39% were African-American, and 64% were males. Over the 4-week active treatment period, sUA levels decreased from average 5.8 mg/dL (SD=1.2) (345.7 μmol/L) to 4.4 mg/dL (SD=1.2) (261.7 μmol/L), p<.001. However, sUA did not change during the 4-week placebo condition (both 5.8 mg/dL (345.7 μmol/L), SD=1.1 and 1.3, p=0.71). Pre-treatment depressive symptoms ranged from "no symptoms" (0) to "severe symptoms" (16 or 20), with mean in the "no to mild" range (M=4.6, SD=4.1 before active treatment; M=6.1, SD=4.8 before placebo). After adjusting for pre-treatment sUA, sex and race, pre-treatment depressive scores predicted higher levels of sUA at the end of the active treatment period (b=.07, beta=.25, p=.028) but not at the end of the placebo period (b=.03, beta=.11, p=.102). After 4 weeks of allopurinol, the estimated difference in sUA between individuals with pre-treatment depressive scores of 0 vs. 16 was 1.12 mg/dL (66.6 μmol/L), which was similar to the average treatment effect of 1.4 mg/dL (88.3 μmol/L).

Conclusion: Even in the absence of clinical diagnosis of depression, depressive symptoms are associated with reduced efficacy of urate-

lowering with allopurinol. This could have important implications for gout treatment, as it would suggest that screening for depressive symptoms might be indicated for treatment success. Additional analyses will address whether this effect can be explained by treatment noncompliance.

REFERENCES

[1] Saddekni MB, Saag KG, Dudenbostel T, et al. Contemp Clin Trials. 2016:238-44.

[2] Björgvinsson, T., Kertz, S.J., Bigda-Peyton, J.S., McCoy, K.L., Aderka, I.M. Assessment. 2013. 20, 429-436.

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AB0868 ULTRASOUND MONOSODIUM URATE CRYSTAL DEPOSITS IN THE JOINTS OF GOUT PATIENTS CORRELATE WITH THE WORSENING OF THE HEART SYSTOLIC FUNCTION

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Background: The connection between gout and cardiovascular (CV) complications has been investigated a lot. Recent studies demonstrate that higher body urate load is an indicator of increased CV risk.

Objectives: To determine whether ultrasound deposits of monosodium urate (MSU) crystals in the joints of gout patients (pts) correlate with the worsening of the heart systolic function and left ventricular hypertrophy.

Methods: This was a single-center cross-sectional study including 56 consecutive gout pts, 40 males and 16 females, in a mean age 58.9±13.2 years with disease duration 6.42±6.93 years. All of them underwent transthoracic echocardiography and ultrasound examination of the joints of the hands, elbows, knees, ankles and feet. By transthoracic echocardiography, conducted with 2.5 MHz transducer phased array working with pulse Doppler frequency of 2.5 MHz, were measured parameters which are independent predictors of CV risk: left ventricular mass index (LVMi), ejection fraction (EF), fractional shortening (FS) and systolic motion of the myocardium (Sm). Ultrasound studies of the joints were performed with a high-frequency, linear transducer, 4-15 MHz. The existence of double contour sign, tendon MSU deposits, snow storm, tophi and tophi with erosions or a combination of these ultrasound features was assessed. Examinations were done in accordance with the latest published guidelines. Data were analyzed by Kolmogorov-Smirnov, Mann-Whitney, t-test, Kruskal Wallis test and Spearman correlation.

Results: 49(87.5%) of the pts had ultrasound evidence of crystal deposits. Serum uric acid levels were equal in pts with and without MSU deposits in the joints, (p=0.569). Among individuals without ultrasound MSU deposits, pts with MSU findings in one joint area and in those with crystal deposits in two or more joint areas we did not find a difference in the mean values of LVMi (mean±SD; 126.86±21.95 g/m² vs 120.09 ±31.50 g/m² vs 128.68±35.19 g/m², p=0.761), FS (mean±SD; 37.73 ±4.62% vs 38.25±3.51% vs 35.40±6.57%, p=0.205) and Sm (mean±SD; 0.27±0.35 m/s vs 0.11±0.02 m/s vs 0.10±0.02 m/s, p=0.266). A tendency of lower EF without reaching significance was detected in subjects with crystal deposits in two or more joints, (p=0.071). The values of LVMi (p=0.295), EF (p=0.396), FS (p=0.566) and Sm (p=0.154) were similar in pts without MSU findings, subjects who had a double contour sign, those with tendon MSU deposits, pts with snow storm, individuals with tophi and in pts with tophi and erosions. However, pts with crystal deposits in the knees and in the tibiotalar joints had lower EF (p=0.047; p=0.049, respectively) and lower FS (p=0.036; p=0.016, respectively) compared to those who had no crystal deposits in these joint areas. Further a weak negative correlation was detected between the number of joints with crystal deposits and EF (r= -0.294, p=0.029) and FS (r= -0.292, p=0.030). Regarding LVMi and Sm no correlation was established with the presence of crystal deposits in the joints (r=0.079, p=0.568 and r= -0.242, p=0.076).

Conclusion: Despite the lack of difference in serum uric acid between pts with and without MSU deposits in the joints, those with MSU findings in the knees and in the tibiotalar joints had more deteriorated systolic function of the heart in comparison to pts without crystal deposits in these joint areas. A negative correlation existed between the number of joints with crystal deposits and functional pumping indices of the heart. On the other hand, MSU deposits in the knees and in the tibiotalar joints are associated with higher urate load than deposits in the small joints. We suggest that the higher urate load is connected to the worsened pumping function of the heart.

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AB0869 SERUM LEVELS OF ROS PRODUCTS, NO AND ASCORBATE RADICALS IN GOUT PATIENTS ARE NOT ASSOCIATED WITH ARTERIOSCLEROTIC COMMON CAROTID ARTERIES CHANGES AND USE OF XANTHINE OXIDASE INHIBITORS

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Background: Oxidative stress along with chronic inflammation and hyperuricemia links gout to arteriosclerotic vascular changes. Studies examining the connection between the level of oxidative stress and arteriosclerotic carotid arteries changes in gout patients (pts) are not enough.

Objectives: To establish the association between the serum levels of reactive oxygen species (ROS) products, nitric oxide (NO) radicals and ascorbate radicals with intima-media thickness (IMT) and common carotid artery resistive index (CCARI) in gout pts, and to find out whether the connection is more pronounced when tophi are present.

Methods: This was a cross-sectional study including 71 gout pts in a mean age 56.86±11.95 years, 61 males and 10 females (45 without tophi pts and 26 gouty tophi pts). Serum levels of ROS products, NO radicals and ascorbate radicals were determined by ex vivo electron paramagnetic resonance (EPR) study. All EPR measurements were performed on an X-band EMXmicro, spectrometer Bruker, Germany, equipped with Standard Resonator. Spectral processing was done by using Bruker WIN-EPR and Sinfonia software. By applying ultrasound of the common carotid arteries, conducted with 10 MHz linear transducer working with pulse Doppler frequency of 5 MHz, were measured IMT and CCARI. Statistical analyses were done by One-Sample Kolmogorov-Smirnov, Chi-Square, Fisher's exact test, Mann-Whitney, t-test and Pearson correlation.

Results: Gouty arthritis without tophi and gouty tophi pts were age-matched, (p=0.309). The mean values of serum uric acid (p=0.569) and distribution of the subjects with gout attack (p=0.173), smoking (p=0.828), arterial hypertension (p=0.735), dyslipidemia (p=0.646), chronic renal failure (p=0.233) and obesity (p=0.623) was equal in the groups. In the tophi group CRP and the number of pts who had suffered a cardiovascular event were higher (p=0.048; p=0.031). Serum levels of ROS products, NO radicals and ascorbate radicals were comparable in gouty arthritis without tophi and in gouty tophi pts (p=0.783; p=0.521; p=0.651). In the groups no difference was registered in CCARI (p=0.273) but intima-media was thicker in the presence of tophi, (p=0.027). No correlation existed between ROS products, NO radicals and ascorbate radicals with IMT (r= -0.100, p=0.405; r= -0.186, p=0.121; r=0.154, p=0.201). ROS products, NO radicals and ascorbate radicals did not correlate with CCARI (r= -0.110, p=0.359; r= -0.066, p=0.587; r=0.094, p=0.436). Among treated and untreated with Allopurinol pts no difference was found in the mean values of ROS products (p=0.169), NO radicals (p=0.167), ascorbate radicals (p=0.460), IMT (p=0.873) and CCARI (p=0.930). Among treated and untreated with Febuxostat pts the mean values of ROS products (p=0.546), ascorbate radicals (p=0.309), IMT (p=0.842) and CCARI (p=0.100) were similar. A tendency of higher serum NO radicals was established in pts taking Febuxostat in comparison to those not treated with it (p=0.076).

Conclusion: Although between the earlier and the later stage of the disease there was no difference in the level of oxidative stress, the level of chronic inflammation was higher in gouty tophi pts. No connection was found between serum ROS products, NO radicals and ascorbate radicals with arteriosclerotic changes of the carotid arteries and use of xanthine oxidase inhibitors. We suggest that in gout pts chronic inflammation has an important role in the process of atherogenesis.

Abstract AB0870 Table 1. Number of discharges with a principal diagnosis of stroke, by age group and sex, reported to HIPE, 2007-2017

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Age Group											
0-29 years	191	193	112	93	136	118	90	94	92	97	89
30-34 Years	62	53	62	65	57	65	56	54	59	56	57
35-39 Years	93	107	119	68	82	75	82	63	98	93	81
40-44 Years	141	153	134	162	152	163	125	123	131	144	158
45-49 Years	215	169	170	205	232	214	198	193	176	249	201
50-54 Years	315	293	277	284	279	299	254	307	289	309	295
55-59 Years	338	386	395	417	393	345	372	415	386	398	413
60-64 Years	467	560	523	508	500	504	492	489	559	565	505
65-69 Years	566	578	585	600	631	643	662	657	667	677	766
70-74 Years	730	709	763	677	712	682	749	782	821	838	778
75-79 Years	886	890	935	937	889	926	845	867	909	862	915
80-84 Years	967	902	975	924	860	959	878	944	912	935	927
85-89 Years	648	695	728	699	703	717	705	695	666	697	702
90 Years and over	278	315	325	363	342	388	354	352	401	411	412
Sex											
Male	2,988	3,066	3,107	3,087	3,071	3,174	3,032	3,198	3,368	3,413	3,499
Female	2,909	2,937	2,996	2,915	2,897	2,924	2,830	2,837	2,798	2,918	2,800
Total	**5,897**	**5,897**	**5,897**	**5,897**	**5,897**	**5,897**	**5,897**	**5,897**	**5,897**	**5,897**	**5,897**

Disclosure of Interests: Rada Gancheva: None declared, Atanas Kundurdjiev: None declared, Galina Nikolova: None declared, Mariana Ivanova Goycheva Speakers bureau: Abbvie, Pfizer, UCB, Novartis, Todor Kundurzhiev: None declared, Zlatimir Kolarov: None declared, Veselina Gadjeva: None declared

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AB0870 IS THE INCIDENCE OF GOUT SIMILAR TO OTHER RISK FACTORS IN PATIENTS PRESENTING WITH STROKE OR MYOCARDIAL INFARCTION?

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Background: Gout is a common form of inflammatory arthritis. The prevalence of gout in Europe is between 0.9-2.5% with rates as high as 4% reported in Ireland.1 Studies have suggested gout as a risk factor in patients presenting with myocardial infarction (MI) and stroke (CVA).However the incidence gout in patients presenting to hospital with MI or CVA in Ireland has not previously been assessed.

Objectives: The aim of this study was to assess the incidence of gout in patients presenting with CVA and MI in Ireland. A further objective was to explore if the incidence of gout is similar to other risk factors such as hypertension, diabetes mellitus and dyslipidemia in Irish patients presenting with CVA and MI.

Methods: The Hospital In-Patient Enquiry Scheme (HIPE) was used to identify patients admitted with stroke or myocardial infarction from 62 acute public hospitals in Ireland from January 2007 until December 2017. HIPE is a national database which records coded hospital admission and demographic, clinical and administrative data on discharges from, and deaths in, acute public hospitals nationally.2 Discharges are coded using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM), Australian Classification of Health interventions (ACHI), Australian Coding Standards (ACS), 8th Edition. Age, gender and number of patient admissions with MI or CVA with gout, diabetes, hypertension, peripheral vascular disease (PVD) and hyperlipidemia were recorded.

Results: From 2007 until 2017, 64,867 were admitted with a diagnosis of CVA in Ireland. The age and gender of patients admitted with a principal diagnosis of CVA are outlined in Table 1. 70,628 patients were admitted with MI.

In the CVA population,14.5% of patients had diabetes. Incidence of gout in patients with CVA(0.7%) was similar to patient with the risk factors of hyperlipidemia (0.91%) and PVD (0.94%).

The incidence of gout in the MI group (0.5%) was lower when compared to the stroke group (0.77%). The presence of diabetes as a risk factor (6.7%)was significantly higher compared to gout (0.5%)in patients admitted with myocardial infarction. Chart one outlines the incidence of each risk factor in patients discharge with a primary diagnosis of MI in Ireland between 2007 and 2017

Conclusion: The incidence of gout in patients presenting with CVA or MI in Ireland was low compared to other risk factors including diabetes. In patients presenting with MI then incidence of gout is lower than in patients presenting with CVA.

REFERENCES

[1] Richette P et al, 2016 updated EULAR evidence-based recommendations for the management of gout, Ann Rheum Dis 2017;76:29-42.

[2] Moloney ED, et l Do consultants differ? Inferences drawn from hospital inpatient enquiry (HIPE) discharge coding at an Irish teaching hospital Postgraduate Medical Journal 2005;81:327-332.

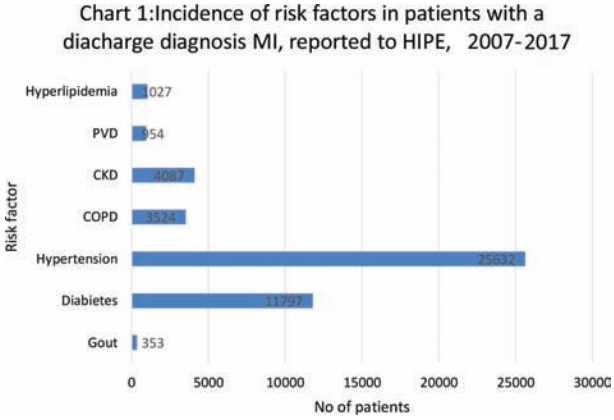


Figure 1

Disclosure of Interests: None declared

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AB0871 ASSESSMENT OF THE KIDNEYS AND URINARY TRACT DYSFUNCTIONS THAT INCREASE THE RISK OF DEVELOPING CHRONIC KIDNEY DISEASE IN PATIENTS WITH GOUT BASED ON COMPLEX RENAL SCINTIGRAPHY

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Background: In 40% of cases patients with gout can develop gouty nephropathy, the "kidney mask" of gout. The newest version of the technology for systemic examination of nephrourological status based on complex renal scintigraphy (SENS-CRS) has been developed at the «N.N. Blokhin National Medical Research Center of Oncology». SENS-CRS at the lowest doses of radiation (0.6 mSv per adult) allows for an in-depth differential analysis of dysfunctions of the renal parenchyma, upper and lower urinary tract which increase the risk of chronic kidney disease (CKD) development.

Objectives: To assess early signs of CKD risk development in patients with gout by SENS-CRS technology.
Methods: We examined 66 patinets with gout. 95% were men (average age 54±9 years). Duration of gout was 8 [4; 11] years. All patients had chronic gouty arthritis, 30% of patients had tophuses. SENS-CRS was carried out on a 2-detector γ-camera with simultaneous recording in 2 projections. In studies of the urinary system domestic radiopharmaceutical (RP) 99mTc-technefor with glomerulo- and 10-15% tubulotropic properties was used. The CRS study consisted of: 1) a basic 21-min functional study; 2) a delayed 21-min study (without the injection of RP) with a preliminary diuresis forcing to identify persistent urodynamic dysfunction.
Results: 16 patients with gout with serum creatinine level of more than 125 μmol/l had established diagnosis of chronic pyelonephritis, glomerulonephritis, urolithiasis, etc. and were allocated into a separate subgroup. In the comparative analysis of these 16 patients and other 50 patients with gout there was reliable distinction only for one indicator D (%), the rate of RP removal from a kidney parenchyma ($p < 0,05$). There was no significant distinctions for glomerular filtration rate by Reberg, the nuclear indicator (G_{ren}) of renal parenchyma concentration function, and other indicators. Renocortical parameter D (%) is one of the earliest highly sensitive markers of intrarenal developments of stagnation at development of serious morphofunctional violations in a parenchyma. In the subgroup of 16 patients the indicator accounted on average D = 48% ± 7% (range 38-55%); in subgroup of 50 patients D = 63% ± 10% (47-89%).
According to the CKD-EPI formula and SENS-CRS technology in the subgroup of 16 patients CKD stage II-III was evaluated. In addition to the sign of broken rate of RP removal from a parenchyma (D) when comparing the 2 phases of CRS there was observed a steady sign of stagnation in a parenchyma and groups of upper and/or lower cups: ID = $G_{calc}/GC < 1$. Based on the water test which accelerates diuresis there was a sufficient regulation of urostasis in the renal pelvis revealed at the basic test (IP = $G_{pelv}/GP > 1,0$). This indicated that the functional reserve of the outflow regulation from the kidneys was preserved at these patients.
Conclusion: This functional diagnostics allows one-time control of hemodynamics and concentration function of the parenchyma of each kidney, quantitative and qualitative signs of urodynamic delays in the intra- and post-renal urinary tract. Differentiated analysis SENS-CRS contributes to the timely therapeutic correction as well as referral for consultation to specialists (urologists, nephrologists, gynecologists, etc.).
Disclosure of Interests: Margarita Gromova Speakers bureau: Speaker during conferences in Russian Federation, Vladimir Tsurko Speakers bureau: Speaker during conferences in Russian Federation, Anna Kashkadayeva: None declared, Svetlana Averinova: None declared, Andrey Aliokhin: None declared
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AB0872 OXIDATIVE STRESS MARKER ALLANTOIN IS NOT ASSOCIATED WITH THE CHANGE OF SERUM URIC ACID LEVEL IN PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES AFTER ABROGATION OF SYSTEMIC INFLAMMATION BY TNF INHIBITION

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Background: In patients with gout, the serum uric acid (SUA) is usually lower during acute gouty attacks than during intercritical periods. In a previous study, we have shown that abrogation of systemic inflammation by TNF inhibitors (TNFi) results in an increase in the levels of SUA in patients with systemic rheumatic diseases. We have not found any correlation between the magnitude of change of SUA and CRP or pro-inflammatory cytokines (MCP-1, IFN-α2, IFN-γ, Il-1β, IL-6, IL-8, IL-10, IL-12, IL-17a, IL-18, IL-23, IL-33, TNF-α).[1] Another possible mechanism for the lowering of SUA during inflammation may be consumption of circulating SUA in free radical reactions generated during systemic inflammation. Allantoin has been validated as a stable biomarker of oxidative stress in humans.[2]
Objectives: We aimed to investigate whether the magnitude of change of SUA after starting therapy with TNFi is associated with the change of oxidative stress marker – allantoin in patients with systemic autoimmune rheumatic diseases: rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and juvenile idiopathic arthritis (JIA).
Methods: A cohort of 94 patients with clinically active chronic inflammatory rheumatic diseases (31 with RA, 33 with AS, 18 with PsA, 12 with JIA) and CRP > 10 mg/L was recruited in the Institute of Rheumatology, Prague. SUA, CRP and allantoin were measured before and after 3 months of treatment with TNFi. Assessment of allantoin in plasma samples was carried out on the Agilent Infinity 1290 system coupled with a Triple Quad 6460 tandem mass spectrometer. For the statistical analysis the ratio between the values at the baseline and values after 3 months of therapy with TNFi were used. We retrieved demographic data and disease characteristics.
Results: The levels of SUA have significantly increased after 3 months of treatment with TNFi (270.5 [78.8] vs. 303.0 [101.5] μmol/l, $p < 0.0001$), while CRP (29.4 [27.7] vs. 2.0 [3.8] mg/l, $p < 0.0001$) has decreased. There was no significant change of allantoin before and after 3 months of treatment with TNFi. In the linear regression model, CRP or allantoin had no effect on the magnitude of change of SUA.
Conclusion: The abrogation of systemic inflammation by TNFi results in an increase in the levels of SUA in patients with systemic rheumatic diseases, but the mechanism remains elusive. We have not observed any correlation between the magnitude of change of SUA and CRP or oxidative stress marker allantoin.

REFERENCES

[1] Petru L, Hulejova H, Mahajan A, et al. SAT0366 Serum uric acid increases after abrogation of systemic inflammation by TNF inhibition. Annals of the Rheumatic Diseases 2018;77:1047
[2] Marrocco I, Altieri F, Peluso I. Measurement and Clinical Significance of Biomarkers of Oxidative Stress in Humans. Oxidative medicine and cellular longevity 2017;2017:6501046

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AB0873 ENDOTHELIAL DYSFUNCTIONIN PATIENTS WITH GOUT. RELATIONSHIP BETWEEN CARDIOVASCULAR RISK FACTORS

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Background: Patients with gout have a high risk of developing cardiovascular disease based on atherosclerosis. An early marker, and at the same time a risk factor of cardiovascular disease, is a violation of the vasoregulating endothelial activity.
Objectives: To identify the relationship between cardiovascular risk factors and endothelial dysfunction (ED) in patients with gout.
Methods: The study included 80 pts with gout. The criteria for inclusion were 1.Male
2.Age >55 years 3.Interictal period of arthritis 4.Absence of clinical signs of coronary artery disease 5.Absence of drug therapy. Vasoregulating endothelial activity was evaluated in all pts, 52 of them determined the carotid intima-media thickness (C-IMT). Flow-mediated (endothelium-dependent) dilatations (FMD), nitroglycerin-induced (endothelium - independent) dilatation (EID) were assessed by highresolution ultrasonography (D. Celermajer). A non-invasive ultrasound technique was used to measure C-IMT. All patients were diagnosed with serum total cholesterol (CHOL), subtypes (LDL-C, HDL-C), glucose (GLU), uric acid (SUA), hsCRP. Cardiovascular risk (CVR) was calculated. Statistical analysis was conducted using the applied programs package of descriptive statistics STATISTICA 12.0 (StatSoft.Inc.,USA).
Results: It was found that 41 (51.25%) pts had FMD less than 8%. A correlation was found between FMD and CVR ($r= -0.28$, $p <0.05$), age ($r= -0.37$, $p<0.001$), Body mass index (BMI)

(r= -0.23, p<0.05). The links between FMD and LDL, GLU, SUA and with parameters reflecting the severity of gout were not revealed (p>0.05). C-IMT in pts was 0.7 (0.6-0.8) mm. 7 (14,4%) pts had > 1.0 mm. A direct correlation was found between the C-IMT and the FMD (p <0.01), CVR (p <0.001), age (p <0.001), duration of gout (p <0.001), the number of joints affected for all time (p <0.005) and the frequency of arthritis in the last year (p <0.05). Correlation between C-IMT and LDL, GLU, SUA, hsCRB was not revealed (p>0.05).

Conclusion: The ED, reflecting the risk of atherosclerosis, was found in 51.3% of patients with gout under the age of 55 years without clinical signs of coronary artery disease. The ED is associated with an increase in the CVR. C-IMT correlates with an increase in CVR and with parameters reflecting the severity of gout.

REFERENCES

[1] Celermajer D.S, Sorensen K.E., Gooch V.M. et al. Non-invasive detection of endothelial dysfunction in children and adults at risk atherosclerosis// Lancet.- 1992. - Vol.340. - P.1111-1115.

[2] Corretti M.C., Anderson T.J., Benjamin E.J. et al. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of brachial artery//Jam. Coll. Cardiol. – 2002. - Vol.39. – P.257-265.

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AB0874 ANALYSIS OF LIFESTYLE AND CLINICAL FEATURES OF THE PATIENTS WITH GOUT IN MEIZHOU, GUANGDONG, CHINA

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Background: Gout is one of the most common metabolic diseases caused by purine metabolic disorder, leading to joint destruction and kidney impairment. With the improvement of living conditions, the incidence of gout is increasing year by year, especially in the developed coastal areas of China. Previous studies found that the management of gout was unsatisfied [1]. Besides, the development of rheumatology in Meizhou, Guangdong province is extremely slow. There are only ten rheumatologists, and the general public has a limited understanding of gout.

Objectives: Our aim was to explore the lifestyle, clinical features and risk factors of recurrent gout attacks in patients with gout in Meizhou, Guangdong province.

Methods: Demographic data, lifestyle and clinical data of 188 patients with gout in Meizhou were collected. Demographic variables included age, gender, marital status, education, BMI, smoking status, drinking status, diet, daily water intake, work style, exercise habit, late sleeping habit. Smoking status includes never smoking, ever-smoking or current smoking, and pack-year of smoking. The diet includes loving sweet food, beverage, seafood, fried food, and disliking vegetables and fruits. Amount of daily water intake is divided into 500-999ml, 1000-1499ml, 1500-1999ml and 2000ml and above. Working styles include long time of sitting, standing, walking, etc. Exercise habits include not exercising, exercising at least 1 hour a day, exercising at least 1 hour a week, and exercising at least 1 hour a month. Clinical characteristics include first time and cause of gout attack, blood uric acid value, the position of gout attack, pain score, duration, alleviating methods, treatment, patients' self-reported gout episodes (below 5 times, 5-10 times, 11-20 times, more than 20 times), tophi, family history and comordities. Multiple regression analysis was used to analyze the factors of the numbers of gout attacks.

Results: of the 188 cases, 171 (91.0%) were males and 17 (9.0%) were females. The average age was 55±16 years. 94 (50%) of the patients were drinking alcohol, and 58 (30.9%) were fond of seafood and other high-purine food. 149 (79.3%) patients had less than 1000ml of water per day, and the vast majority of patients had no exercise habit (136 (72.3%)). The interval between the first gout attack and the first uric acid increasing was -0.4 (S=2.5) years. The first gout attack occurred in the first metatarsophalangeal joint in 57 (30.3%) cases, followed by ankle jointa in 40 (21.3%) cases, knee jointa in 23 (12.2%) cases, and dorsal foot joints in 23 (12.2%) cases. The first gout attack occurred in 87 (46.3%) cases on the right side of the body. 25 (13.3%) patients' first gout attack occurs in more than one joint. The number of tophus is 0~21 per person. 64 (38.1%) patients had more than 20 gout attacks. Up to 70 (40.7%) patients never visited the hospital. 14 people were hospitalized due to gout. Colchicine was the most commonly used drug in treatment in 59 (31.4%) cases, followed by allopurinol in 49 (26.1%) cases. Gout was positively correlated with age (B=0.313, *P*=0.007) and uric acid (B=0.04, *P*=0.018).

Conclusion: Gout patients in Meizhou, Guangdong are mainly male, and have bad living habits such as drinking, loving hyper purine food and lack of drinking water and doing exercises. The first gout attack is more likely to involve a unilateral lower extremity, especially first metatarsophalangeal joints. Meizhou patients with gout have earlier occurrence of tophi, and fail to see a doctor and have medication regularly. Therefore, gout patients should develop good living habits and receive regular medical education.

REFERENCE

[1] Li XM, Chen ZN, Gu JR. The current situation of hyperuricemia cannot be ignored [J]. New medicine,2016(03): 137-141 (in Chinese).

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AB0875 GOUT, NOT JUST A DISEASE OF THE FOOT. LITERATURE REVIEW OF SYSTEMIC DEPOSITION OF URATE

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Background: Gout is the most common adult inflammatory arthropathy in the US. Although tophi in the extremities is a known source of the inflammatory cascade, urate deposition in organs throughout the body is not as well recognized. Patients with gout often have associated co-morbidities including renal disease, cardiovascular disease and metabolic syndrome, however, a casual role has not been established. Direct urate deposition in these organ systems may be of interest to link the causality of these systemic disorders.

Objectives: Perform a literature review including clinical exam, autopsy, pathology, and radiology imaging results demonstrating systemic deposition of urate exclusive of the extremities.

Methods: PUBMED from 1920 to 2018 was searched to identify reports of non-extremity urate deposition. Key words included: extra-articular gout, systemic deposition of urate, ocular gout, gout nephropathy, renal tophi, gouty heart, cardiac valves and urate, urate deposition in the arteries, prostate and urate, autopsy findings in gout, cutaneous urate deposits, gouty panniculitis, auricular gout, breast and urate, gastrointestinal gout, pancreas and tophus, laryngeal tophus, and spinal gout. The reference lists from these publications were also used to identify additional articles. The literature was reviewed for organ system involvement and documented based on sites of urate deposition within an organ system.

Results: There were 249 case reports documenting non-extremity urate deposition confirmed by autopsy, biopsy, surgery, clinical exam and/or radiology imaging. Urate deposition was reported in multiple organ systems (*Table 1)* including the spine, integumentary, ocular, renal, cardiovascular, gastrointestinal, larynx, breast, middle ear, pancreas, nasal, prostate gland, liver, pulmonary, penis, nailbed, and pelvis.

Conclusion: Numerous case reports document systemic deposition of urate based on autopsy, pathology, imaging and clinical exam. Urate crystal deposition with the formation of tophi and micro-tophi involve multiple organ systems including cardiovascular, renal, spine, integumentary, prostate, bowel, pancreas, eyes, pelvic, breast, lungs, middle ear, larynx, liver, penis, nailbed, and nose. Given the strong association of gout with various comorbidities, this demonstrates a need for further studies to determine the clinical significance of systemic urate deposition with respect to ongoing subclinical inflammation and potential end-organ damage.

REFERENCES

[1] Park, J. et al. BMJ Open. 2014; 4:e005308.

[2] Nickeleit, V, et al. Nephrol Dial Transplant. 1997; 12:1832-1838.

[3] Ao, J, et al. *Clinical and Experimental Ophthalmology*. 2017; 45: 73–80

[4] Forbess LJ, et al. Semin Arthritis Rheum. 2012; 42:146–54.

[5] Elgafy, H, et al. World J Orthop. 2016; 7(11): 766–775.

Abstract AB0875 Table 1

Organ System	# of Case Reports N= 249	Diagnostics (Autopsy, biopsy, clinical exam, surgery, imaging)

Spine: Lumbar, thoracic, cervical facet joints, intervertebral discs, interlaminar space	102	Autopsy, biopsy, surgery, imaging
Integumentary: Dermis, hypodermis	40	Clinical exam, biopsy, autopsy
Ocular: Periocular soft tissues, conjunctiva, sclera, episclera, cornea, uvea, lens, orbit, retina, optic disc, vitreous body	33	Biopsy, clinical exam, imaging
Renal: Renal parenchyma (nephrolithiasis was excluded)	25	Autopsy, biopsy imaging
Cardiovascular: Valves (mitral, pulmonic, aortic), myocardium, conduction pathway, arterial wall, atherosclerotic plaque	12	Autopsy, biopsy, surgery, imaging
Gastrointestinal: Small intestine, colon	6	Autopsy, biopsy, imaging
Larynx	6	Clinical exam, biopsy
Breast	5	Biopsy, imaging
Middle Ear	4	Clinical exam, biopsy, imaging
Pancreas	4	Biopsy, imaging
Nasal	4	Clinical exam, biopsy
Prostate Gland	2	Biopsy
Liver	2	Biopsy, imaging
Pulmonary: Bronchus	1	Bronchoscopy, biopsy, imaging
Penis	1	Clinical exam, surgery
Nailbed	1	Clinical exam, biopsy
Pelvis	1	Biopsy, imaging

Disclosure of Interests: Ada Kumar Shareholder of: I am an employee of Horizon Pharma and own shares in the company., Consultant for: I have worked as a paid consultant for Horizon Pharma., Employee of: I am currently employed by Horizon Pharma., Puja Khanna Grant/research support from: AstraZeneca, SOBI, Ironwood, Horizon, Consultant for: SOBI
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AB0876 GOUT CAUSING URATE CARDIAC VEGETATIONS: SUMMARY OF PUBLISHED CASES

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Background: Gout is a progressive inflammatory disease that is both widely prevalent and widely undertreated. In gout patients, urate deposition occurs in peripheral joints, the spine, and organs including the prostate, kidneys, and in atherosclerotic plaques as well as heart valves. Due to the concern of bacterial endocarditis and associated sequelae, cardiac valve vegetations are generally thoroughly evaluated even without systemic symptoms. Gout causing cardiac valvular vegetations is believed to be rare, though to date a number of case reports on this topic have been published.
Objectives: This project sought to compile and synthesize the existing published cases of proven cardiac valve urate deposition in gout patients.
Methods: Medline and google were used to search for all available published cases involving gout associated with or causing cardiac valve vegetations. The references of each publication were additionally completely examined to find any other cases that may not have been identified on previous searches. The case reports were obtained and patient, disease, and valve factors were compiled and synthesized.
Results: Eight publications were found from 1954 to 2012 reporting 9 cases of urate deposition on cardiac valves. All cases had known tophaceous gout, mean age 60.9, and 89% were male. The mean uric acid level was 10.2 mg/dL, 4/9 (44%) reported a heart murmur, and in only one (11%) of the nine cases was infective endocarditis suspected. The diagnosis of gouty valvular involvement came from autopsy in 4 patients (44%), pathological report in 3 patients (33%), and was a diagnosis of exclusion after transthoracic echocardiogram in two patients (22%). The mitral valve was the most commonly involved heart valve, with 6 of the 9 gout patients (66%) with urate valvular deposits having them on the mitral valve. One patient had aortic and another had pulmonic valve involvement, while no patients were found to have tricuspid urate deposits from gout.
Conclusion: Though gout generally causes urate deposition in peripheral joints, urate deposits have been found in organs including the prostate, heart, kidneys, and eyes. Urate deposits from gout in heart valves are quite rarely reported, and this project describes 9 cases of urate valvular deposition associated with gout from 8 case report publications dating back to 1954. Based on these findings, urate deposition from gout on a cardiac valve will primarily remain a rare diagnosis of exclusion, but should be considered in patients with known longstanding visibly tophaceous gout, hyperuricemia, mitral valve involvement, and a lack of systemic signs or symptoms of infective endocarditis.

REFERENCES

[1] Traut, EF, et al, "Specific vascular changes in gout", JAMA, 1954,156 (6):591-593
[2] Dennstedt, FE, et al, "Tophaceous mitral valve: Report of a case", *Am J of Surg Path*, 1982;6(1):79-81
[3] Curtiss, EI, et al, "Pulmonic regurgitation due to valvular tophi", Circulation, 1983;67(3):699-701
[4] Jaworski. RC, et al, "Tophaceous aortic valve: a case report", Pathology, 1983(15):197-9
[5] Scalpino, JN, et al, "Case report: mitral stenosis associated with valvular tophi", Mayo Clin Proc, 1984;59:509-512
[6] Gawoski, JM, et al, "Aortic valvular tophus: identification by X-ray diffraction of urate and calcium phosphates", J Clin Pathol, 1985;38:873-876
[7] Iacobellis, G, et al, "A rare and asymptomatic case of mitral valve tophus associated with severe gouty tophaceous arthritis", J Endocrinol Invest, 2004;27:965-966
[8] Rohani, A, et al, "A case of mitral valve tophus in a patient with severe gout tophaceous arthritis", J Clin Imaging Sci, 2012;2:68

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AB0877 OXIDIZED LOW DENSITY LIPOPROTEIN IS CORRELATED WITH INFLAMMATORY STATUS IN GOUTY ARTHRITIS

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Background: Lipid peroxidation and oxidized LDL (oxLDL) are hallmarks in the development of various metabolic, cardiovascular and other inflammatory diseases. Cholesterol crystals and oxLDL, which are considerably present in atherosclerotic plaques, can activate inflammasomes. The concentration of plasma ox-LDL was also closely associated with the high incidence of atherosclerotic diseases in patients with gout might be closely related to increased ox-LDL levels. However, the study about the relationship between the level of ox-LDL and the inflammatory status in gout patients are rare.
Objectives: We aimed to the relationships between ox-LDL level, inflammatory markers and uric acid lowering agents in gout patients.
Methods: One hundred seventy four gout patients were included from the 3 institutions from 2014 to 2017. Details of demographic and clinical features along with laboratory parameters, ESR, CRP, lipid profiles, oxLDL and disease status were noted in patients with gout. We classified inflammatory status as acute, subacute chronic tophaceous and well controlled status. The level of ox-LDL was measured using the latex enhanced immune transmission turbidimetric method. We analyzed the comparison between dermographics, inflammatory markers, lipid profiles and disease subset.
Results: The primary objective of this study was to assess the oxLDL according to inflammatory status in gouty arthritis. Mean age was 50.4 year-old, 85.7% was woman, 98.9% were male, mean BMI was 25.86 and mean disease duration was 48 months. Among 174 gout patients, 61 patients (35.1%) were acute flare-up, 38 patients (21.8%) were subacute, 67 patients (38.5%) were chronic tophaceous, and 7 patients (4%) were well controlled stable status.
Age, sex, BMI, and accompanying disease were not statistically different in the 4 groups according to inflammatory status. However, it showed statistically significant differences in the use of glucocorticoid and uric acid lowering agents. There was no significant difference in uric acid in laboratory tests, but there was a significant difference between ESR and CRP in each disease group. Especially, oxLDL showed difference according to inflammatory state of disease.

Laboratory features	Acute	Subacute	Chronic tophaceous	Well controlled	*p-value*
Uric acid	7.22 ± 2.07	6.77 ± 2.40	6.94 ± 2.20	7.24 ± 1.65	0.780
ESR	36.36 ± 32.52	18.87 ± 18.98	16.85 ± 18.30	8.29 ± 7.67	**0.000****
CRP	1.45 ± 2.31	0.45 ± 1.12	1.33 ± 4.58	0.12 ± 0.08	**0.008****
Lipid profiles					
Total cholesterol	193.9 ± 46.06	208.39 ± 47.77	185.21 ± 49.08	163.14 ± 44.93	**0.042***
HDL	46.10 ± 11.96	43.28 ± 9.51	43.58 ± 12.98	42.57 ± 8.76	0.539
Triglyceride	216.85 ± 171.69	221.55 ± 117.9	207.05 ± 108.78	180.57 ± 125.70	0.645
LDL	126.81 ± 55.04	126.05 ± 41.27	119.98 ± 38.95	111.4 ± 25.68	0.825
Oxidized LDL	785.38 ± 369.14	775.5 ± 272.80	653.23 ± 430.99	366 ± 173.43	**0.001****

Conclusion: The levels of oxLDL in gout patients were significantly different according to inflammatory status. The oxLDL may be associated with inflammation process in gout patients.
Disclosure of Interests: None declared
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AB0878 CARDIOVASCULAR GOUT

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Background: Gout is characterized by clinical heterogeneity and associated with multicomorbidity. In clinical practice, we can highlight a group of patients suffering from cardiovascular diseases (CVD) and requiring constant medication, in which the gout joins later.
Objectives: To study the group of patients with gout developing on the basis of pre-existing CVD at the gout onset.
Methods: 240 patients from our Center database with confirmed gout were included in our study. Comorbidities were registered before the gout onset, at its appearance. The study group consisted of 140 patients with CVD: hypertension with duration for 5 years and treated by medication, CHD, atrial fibrillation, CHF and stroke. The comparison group consisted of patients with gout, but without CVD (n=100).
Results: Among patients with pre-existing CVD, the gout debuted later, at the age of 60 (55-65) years (p 0.001). The most frequent comorbidity was HTN – 83.6% (n=117) (OR=7.63; 95%CI 5.33-10.93; $\chi 2$ = 48.9, p 0.001). Diabetes mellitus (OR=4.47; 95%CI 3.65-5.48; F = 0.035, p = 0.005) also dominated in this group. At the same time, BMI $\geq$ 25 kg/m^2 was prevalent in comparison group (OR=19.46; 95%CI 2.84-133.2; $\chi 2$ =15.4, p 0.001). Alcohol abuse was considerably lower – 37.1% (n=52) (OR=54.72;95%CI 17.87-167.44; $\chi 2$ =88.8, p 0.001), but medication use was higher – diuretics in 16.4% (n=23) (OR=6.36; 95%CI 5.28-7.64; F=0.045, p 0.001) and low-dose aspirin in 35.0% (n=49) of patients (OR=17.41; 95%CI 14.80-20.47; F=0.147, p 0.001). In the study group, the urolithiasis was evidenced more often (OR=4.13; 95%CI 3.42-4.98; $\chi 2$ = 12.1, p 0.001), and the presence of CKD with GFR 60 ml/min/1.73 m^2 was observed in 15.0% (n=21) of patients (F=0.069, p 0.001), but not found in the comparison group. The percentage of patients with metabolic syndrome (3 components according to ATP III) did not differ between the groups (p 0.05).
The number of patients having a concentration of uric acid (UA) in blood 360 mkmol/l and 480 mkmol/l was similar in the both study and comparison groups (p 0.05). At the same time, the cases of UA 600 mkmol/l were higher in study group by 13.1% (OR=1.86; 95%CI 1.50-2.38; $\chi 2$= 5.94, p = 0.015).
Conclusion: Among our patients, the gout developing on the basis of pre-existing CVD is one of the variant of a debuting gout. The group of patients with so called "cardiovascular gout" is characterized by later gout onset, comorbidities typical for CVD, prevalence of medication (low-dose aspirin, diuretic) and renal mechanisms-triggers of gout. In these patients, the maximal concentration of UA in blood (600 mkmol/l) was registered more frequently than in patients with primary gout.
Disclosure of Interests: None declared
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AB0879 INTRATENDINOUS TOPHI IN PATIENTS WITH GOUT: PERSISTENCE IN SPITE OF CLINICAL CONTROL AND SCOPE OF URICEMIA THERAPEUTIC TARGET

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Background: The tendon affectation of the gout consists of the deposit of uric acid in territories habitually perientésicos causing its accumulation in the substance of the body of the tendon or occupying part of it and protruding towards zones of extension. Their presence is usually not clinically accounted for except when they obstruct tendon displacement and therefore their role as part of the clinical picture of patients with gout is often underrepresented.
Objectives: The purpose of this study is to determine the ultrasound response of these tophi once the clinical activity has been controlled and the serum uricemia therapeutic target of 6.0mg/dL has been reached.
Methods: Quasi-experimental study type before after. We include 19 patients with tophaceous gout diagnosed between 2012 and 2014 and followed regularly in three rheumatology consultations through clinical, analytical and ultrasound controls. We compared the ultrasound records of static images of your Achilles, patellar and tricipital tendons at the time of diagnosis and in your last review. The longitudinal measurements of the tophi obtained were compared. The independent variable was the evaluation time (before and after) and the dependent variables were the quantification of tophi and their measurements in the longitudinal axis.
Results: All the patients were male. Mean age of 58 SD 6.8 years (Range 29-76). Mean basal uric acid 11.3mg/dL. Mean follow-up time to reach therapeutic objective 18 SD 10 months (Range 9-61). Median number of intratendinous tophi (counting one for each tendon of 6 possible tendons): 2. Fashion 2 (Range 1-4). Mean longitudinal diameters: Achilles (8 cases) 18.3 SD 4.2 mm; Rotulian (11 cases) 15.3 SD 3.1 mm; Tricipital (6 cases) 9.8 SD 5.1mm. Hypouricemiant treatment administered: Alopurinol 12; Alopurinol followed by Febuxostat 7; Febuxostat only 0. In the ultrasound study, once the therapeutic objective was reached, the accounting of the intratendinous tophi Achilles and patellar tophi remained identical. One tricipital tofo disappeared completely and the rest were maintained. The longitudinal measurements of tophi that did not disappear were as follows: Achilles 18.0 SD 3.2mm (P=0.805); Rotulian 14.9 SD 3.2 (P=0.803); Tricipital 7.9 SD 3.2 (N=5, P=0.489). No differences were detected when comparing the two hypouricemiant treatment sequences.
Conclusion: Although this is a small retrospective cohort, our results show a poor ultrasound response of reduction of intratendinous tophi reaching the serum uricemia target of 6.0mg/dL. This observation raises two reflections: (1) On the one hand, and as already proposed, the therapeutic target of uricemia in our patients could require an even stricter adjustment and (2) on the other hand, it would be necessary to consider whether the inclusion of regulated ultrasound scans of certain tendons would have clinical value if they were routinely incorporated into the study of our patients with gout.

DISCLOSURE OF INTERESTS
None declared
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AB0880 ACUTE GOUTY ARTHRITIS RELATED EMERGENCY DEPARTMENT VISITS AMONG US VETERANS: CHARACTERISTICS, PREDICTORS AND AREAS OF IMPROVEMENT

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Background: Gout is quite prevalent among United States veterans and many do not achieve optimal levels of uric acid (< 6 mg/dl).[1] This suggests that there are large number of veterans who are at risk for gout flare, leading to utilization of health care resources such as emergency department (ED) and outpatient office visits. We investigated the ED visit patterns among veterans with history of gout and the factors contributing to ED visits.
Objectives: The objectives of the study were to identify the risk factors for ED visits by veterans for gout flare up. Future remediation of the risk factors would reduce utilization of health care resources.
Methods: This was a retrospective chart review of veterans diagnosed with gout in the ED at VA Medical Center Memphis TN between January 1st, 2011 and December 31st, 2016 using ICD-9 codes. A rheumatologist reviewed all cases and only confirmed cases of gout were included in the study. There were 2516 veterans seen for acute gout during the

study period and of these, random selection of 10% i.e. 250 subjects were considered for the study. Baseline demographics, medical comorbidities, serum uric acid level, medication history, and information whether they were followed by rheumatologist or primary care physician (PCP) were extracted from electronic health record.

We used Stat view Version 5.01 (SAS Institute Inc. Cary, NC) for analysis. We described data with frequency terms, continuous data by mean ± standard deviation, and categorical data by percent. Univariate analysis identified predictors of interest that were later incorporated in the best fit model with logistic regression. A p value of ≤ 0.05 was considered statistically significant.

Results: The mean age of subjects was 61 +/-11 years, mean BMI was 32 +/- 7 kg/m2, 98% were males and 80% were African Americans. 26% of subjects had history of alcohol use, 89% had hypertension and 88% had chronic kidney disease (CKD stage ≥2). 86% of the subjects were followed by primary care physician (PCP), and 5% of them were followed by rheumatology and rest of the 9% were non- compliant. 30% of subjects were receiving urate-lowering therapy and 23% of patients were on gout prophylactic therapy. 21% of patients had multiple (≥ 2) visits to the ED. The mean uric acid level was 8.5 ± 2.1 mg/dl for subjects with single visit compared to 9.04± 2.1 mg/dl for multiple visits to the ED (P = 0.09).

In the univariate analysis, CKD (stage ≥ 2) and higher uric acid level were associated with increased ED visits (P = 0.09) and not being on urate lowering therapy was also associated with increased frequency of ED visits (P = 0.02). On logistic regression analysis, irrespective of the type of physician follow up (PCP vs rheumatologists), being on urate-lowering therapy was associated with reduced frequency of ED visits. (P=0.02).

Conclusion: Urate-lowering therapy (ULT) was associated with reduced ED visit irrespective of follow up care provided by PCP or rheumatologist. Given that only one third of our patients were on ULT, improving ULT dispensing by the physician and patient compliance with ULT can decrease health care utilization.

REFERENCE

[1] Hughes JC, Wallace JL, Bryant CL, et al. Monitoring of urate lowering therapy among US veterans. Annals of Pharmacotherapy.2017 Apr;51(4):301-306

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AB0881 DESCRIPTIVE ANALYSIS OF PATIENTS WITH OSTEOGENESIS IMPERFECTA IN A TERCIARY HOSPITAL IN MADRID

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Background: Osteogenesis imperfecta (OI) is an inherited connective tissue disorder with an incidence of 1 per 20,000 births. It is also called "brittle bone disease" and is most commonly caused by mutations in genes encoding type I collagen or proteins involved in its posttranslational modification. Most patients have an autosomal dominant mutation in *COL1A1* or *COL1A2.* The severity of the clinical presentation depends upon the effect of the mutation that occurs, having many different phenotypic presentations. In the most severe forms, patients suffer multiple fractures with minimal or no trauma whereas mild forms may only manifest with premature osteoporosis. Attending to the clinical presentation, radiographic findings and the mutation that occurs, 11 different types have been described, with type I and III being the most prevalent. Many treatments have been studied, but none has been found to be curative. The most frecuently used are biphosphonates which try to prevent bone fragility and reduce the number of fractures but none have been approved specifically for use in either children or adults with OI.

Objectives: The aim of the study is to analyse the clinical characteristics of osteogenesis imperfecta (OI) patients followed in our hospital and to evaluate the different treatments used in their management.

Methods: A retrospective study was conducted. All patients diagnosed with OI and seen in the different departments of our hospital were included and analyzed. A database was created, including both clinical and epidemiological data and a descriptive analysis was carried out.

Results: 25 patients with OI are currently being followed up in our hospital and were included. Although most patients were beeing followed in both the Rheumatology (9) and Orthopedic units (9), 4 were being followed by pediatrics, 1 by endocrinology, 1 by internal medicine and 1 by geriatrics. 72% were female (18) with a mean age at diagnosis of 17 years (range: 1 month to 67 years). All of them had had previous fractures before the diagnosis. The number of fractures during their follow-up varied according to the different types of OI, with an average of 6 fractures (range 3-24) per patient and an average of at least 4.16 orthopedic surgeries each. 12/25 patients were diagnosed in the first ten years of life, being the ones that accumulated the highest number of fractures (96 vs. 54). Only 3 patients had family background of OI, all of them beeing type I. Although only 9/25 patients had undergone genetic study, all 3 cases of type III, which is the most severe, debuted in the first decade of life. Phenotipically 14/25 (56%) had short stature and 18/25 (72%) had blue sclerae, being these less frequent in those patients with debut after 20 years of age, of which 57% (4/7) had normal sclerotics. Only 4 patients suffered from dentinogenesis imperfecta (16%) and 3 from otosclerosis and had hearing problems (12%). Regarding the treatment received, 60% of the patients (15/25) were on current treatment with oral calcium and 64% (16/25) with oral vitamin D supplements. On the other hand only 60% of the patients received biphosphonates (4 were beeing treated with risedronate, 7 with pamidronate, and 4 had received both zoledronic and pamidronate during their lives).

Conclusion: Although a rare disease, OI has an important morbimortality in most patients. Severe cases suffer multiple fractures and undergo several orthopedic surgeries during their lifes. Given the high cost of genetic analysis, this is reserved for the most severe cases which tend to debut at younger ages and are mostly type III. Treatment for this condition is not standardized and is generally reserved for type III OI patients, which is one of the most severe types. Biphosphonates, calcium and vitamin D are usually used in order to try to prevent new fragility fractures but in most cases fracture rates remain high despite treatment.

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AB0882 ACROMEGALY DO NOT INCREASE THE RISK OF VERTEBRAL FRACTURES : A RETROSPECTIVE AND PROSPECTIVE STUDY ON 50 PATIENTS

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Background: Patients with acromegaly appear to be at an increased risk of vertebral fractures (VFs) despite normal bone mineral density (BMD)[1]. However, these patients could have several endocrine deficits as hypogonadism known to increase the fracture risk risk independently of the GH effects. The physiopathology of GH excess on bone is unclear. In addirion, patients with acromegaly have radiological deformations of the spine, called Erdheim's syndrome, which can overestimate the radiological vertebral fractures.

Objectives: Investigate the prevalence of VFs in our cohort of patients with acromegaly.

Methods: It was a monocentric, retrospective and prospective study. The rheumatologic evaluation was less than 3 years for all patients. For 40% of patients, this evaluation was prospective after the begin of the sudy. Acromegaly patients younger than 80 and followed at the Nantes University hospital in January 2018 were included. Patients were excluded if they had a rheumatologic or endocrinologic disease interfering with the results. The prevalence of radiological vertebral fractures was evaluated on conventional lombar and thoracic spine radiographs using Genant's semi-quantitative assessment. We also assessed qualitative abnormalities of the spine using 3 criteria : osteophytes, disc space narrowing and cuneiform aspect of vertebrae. The X-rays were read by two rheumatologists independently. We analyzed BMD at lumbar spine and total hip, endocrine status and quality of life through 3 questionnaires (AcroQol, specific of acromegaly; Oswestry evaluating the functional impact of pain; HAQ evaluating the functional capacity).

Results: We included 56 patients. 6 patients were excluded : 3 declined, 1 had bone metastasis and 2 had another endocrinologic disease (adrenocortical and panhypopituitarism). We analyzed the prevalence of VFs in 50 patients (19 females, 31 males, median age 53, range 28-79). The average of time between the diagnosis of acromegaly and the last rheumatologic evaluation was 9.1 years. 3 patients (6.1%) had a VF : 1 grade 1 and 2 grade 2 of Genant's assessment. 28% patients were osteopenic and 12% were osteoporotic. Among fractured patients, 2 were osteoporotic and 1 osteopenic. 26% were hypogonadal (100% substituted), 16% had central adrenal insufficiency (100% substituted). 14 women were menopaused (74% of women). Thoracic spine was deformed in 31 patients (61%) and lombar spine in 21 patients (43%), for at leat

one of the 3 criteria. Patients with spine deformation were older (p=0.043), with higher BMI (p=0.004) and had a trend to be more hypogonadal (p=0.06). Concerning quality of life, AcroQoL's average was 70.9% (score 0 to 100, maximal quality of life =100, range 32-98), HAQ's average was 0.18 (score 0 to 3, maximal quality of life 0, range 0-1.38) and Oswestry's average was 9.8 (score 0 to 100, maximal quality of life 0, range 0-44).

Conclusion: This study shows fort the first time that acromegaly patients are not at an increased risk of vertebral fractures. This result differs from the literature that reported more than 30% of VF in this population. Our study bring several points of explanation. First, the vertebral abnormalities were frequent in our patients and can overestimate the VFs without a qualitative analysis of the X-ray. Secondly, the right endocrine balance plays an important role in osteoporosis. Our patients were well supplemented, it can reduce the risk of osteoporosis. More studies are needed to confirm this new hypothesis.

REFERENCE

[1] Claessen and al. 2016. « Bone and Joint Disorders in Acromegaly ». Neuroendocrinology 103 (1):86–95.

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AB0883 SYSTEMIC INFLAMMATION AND ATHEROSCLEROSIS IN PATIENTS WITH GOUT. RESULTS FROM THE NOR-GOUT STUDY

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Background: The association between gout and cardiovascular disease (CVD) is well known,[1] whereas mechanisms behind this association are poorly understood.

Objectives: This study aimed to evaluate factors associated with asymptomatic carotid atherosclerosis in patients with gout.

Methods: In this prospective study patients with crystal-proven gout were included after a recent diseaseflare, if the serum urate level was >360 µmol/L (>6 mg/dl). We analysed baseline data in patients without established CVD who were referred to a CVD risk evaluation, including ultrasound of the carotid arteries, blood pressure measurement and laboratory tests. Carotid atherosclerotic plaques were defined in the longitudinal view as protrusions into the lumen of ≥1.5 mm or at least 2 times the adjacent intima-media thickness according to the Mannheim criteria.

Results: Of the 79 gout patients included, approximately 10% were females, and mean (SD) age was
52.1±13.1 years. Thirty-two (40.5%) had carotid plaques (Table). Only 9.3% were current smokers, while mean (SD) body mass index was high (29.1±4.7 kg/m^2). Lipids were in the normal range, with a mean (SD) total cholesterol at 5.3±1.09 mmol/L and low density lipoprotein cholesterol 3.12±0.95 mmol/L. Systolic blood pressure was in the normal range 134.0±15.1 mmHg, although 29.1% of the patients were treated with antihypertensive agents. In univariate analyses, higher age, hypertension and higher erythrocyte sedimentation rate (as a marker of systemic inflammation) were significantly associated with the presence of carotid plaques (p=0.01 and p=0.04, respectively) (Figure). Serum urate levels or disease duration were not associated with carotid plaques (p=0.27 and p=0.44, respectively).

Table. Patient characteristics

Number n (%)	79 (100.0)	32 (40.5)	47 (59.5)	-
Age (years) mean±SD	52.1±13.1	60.0±10.4	46.7±12.1	
Sex male/female n (%)	72/7 (91.1)/ (8.9)	28/4 (87.5)/ (12.5)	44/3 (93.6)/(6.4)	0.43
Disease duration (median IQR)	6.0 (3.0-12.0)	6.0 (3.8-14.3)	5.0 (2.0-10.0)	0.44
CV risk factors				
Smoking n (%)	7 (9.3)	2 (2.7)	5 (6.7)	0.69
BMI mean±SD	29.1±4.7	28.5±4.2	29.5±5.0	0.35
TC (mmol/L) mean±SD	5.3±1.09	5.21±1.18	5.39±1.02	0.48
LDL-c (mmol/L) mean±SD	3.12±0.95	3.24±1.07	3.04±0.84	0.41
BP systolic (mm Hg) mean±SD	134.0±15.1	138.0±16.2	131.3±13.9	0.06
BP diastolic (mm Hg) mean±SD	82.8±8.0	83.6±6.9	82.3±8.8	0.46
Co-morbidities n (%)				
Hypertension	36 (45.6)	21 (26.6)	15 (19.0)	0.01
Diabetes	4 (5.1)	3 (3.8)	1 (1.3)	0.30
*Biomarkers*mean±SD				
S-urate (µmol/L)	495.6±84.0	481.8±97.5	504.9±73.2	0.27
ESR (mm/h)	12.9±13.9	17.3±17.6	9.8±9.7	0.04
CRP (mg/L) median (IQR)	3.5 (2.0-7.8)	5.0 (2.0-13.5)	3.0 (1.0-6.0)	0.09

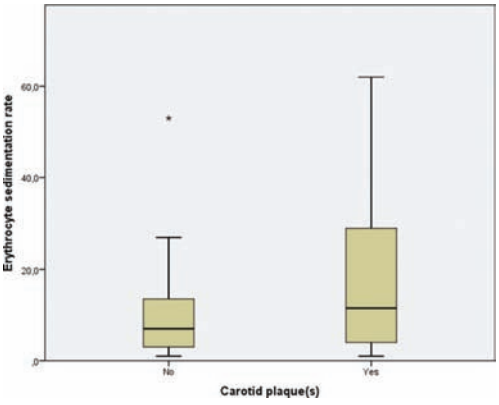


Figure. Association of carotid plaques and systemic inflammation

Conclusion: Our results indicate an association between systemic inflammation and atherosclerosis in patients with gout. To be able to efficiently prevent CVD in this patient group, prospective studies with larger sample sizes are needed to elucidate the mechanisms behind the increased risk of CVD in gout patients.

REFERENCES

[1] Choi HK, Curhan G. Independent impact of gout on mortality and risk of coronary heart disease. Circulation 2007;116:894-900.

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AB0884 CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH OCHRONOTIC ARTHROPATHY

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Background: Alkaptonuria (AKU) is a metabolic disorder that causes accumulation of oxidized homogentisic acid (HGA) in the connective tissues. The excessive deposition of HGA and its metabolites can cause

joint destruction and skeletal abnormalities which the entity is clinically referred as ochronotic arthropathy (OA) [1].

Objectives: To assess clinical, demographic features and radiographic findings in patients with OA.

Methods: Adult AKU patients registered in the database were included in the study. All patients investigated for the presence of OA and inflammatory symptoms. Patients with musculoskeletal symptoms (MSK) underwent conventional X-rays and routine laboratory evaluation. In cases suggestive of inflammatory disease additional work-up such as autoantibodies, HLA-B27 and MRI with inflammatory protocol were performed.

Results: Six out of 15 patients had symptoms compatible with OA (40%; 4 male [M], 2 female [F], median age 56 [51-62] years). The median duration of MSK symptoms were 7 (2-19) years. None of the patients had family history of rheumatologic disease. Baseline CRP were normal in all patients. The HLA-B27 test was negative in all cases. One patient had high titers of rheumatoid factor along with positive anti-CCP that were accompanying erosive arthritis on MCP joints by X-rays. Two patient had positive ANA. All patients had chronic back pain and had changes compatible with OA in their spines (narrowing of the intervertebral spaces, vacuum phenomenon and intervertebral disc calcification). Two patient had inflammatory type of pain character (IBP). Radiographic sacroiliitis according to modified New York criteria was present in 2 cases. Inflammatory spine and SIJ lesions were detected by MRI in 1 patient. Extra-articular involvement including enthesitis (1 patient), interstitial lung disease (1 patient) and scleritis (1 patient) was also noted. The clinical and demographic characteristics of the OA are given in Table 1.

Conclusion: There was a high prevalence of inflammatory arthritis (2 axSpA; 1 RA) in OA (50%) which contradicts with the common concept that OA is a degenerative disorder. According to our results, inflammatory disease should be carefully screened in OA patients as accumulated metabolic products may trigger inflammatory pathways.

Table-1

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age (yr), Sex	55, F	56,M	51,M	56,M	59,F	62,M
Symptom duration/year	7	19	17	6	2	7
Structural changes documented by X-rays						
Cervical	+	+	+	+	+	+
Dorsal	+	+	+	+	+	+
Lumbar	+	+	+	+	+	+
SIJ (Right/Left)	2/3	0/1	2/3	1/1	1/1	0/0
Shoulder	-	+	+	+	+	+
Hip	-	+	+	+	-	+
Knee	+	+	-	+	-	+
Wrist	+	-	-	-	-	-
Total joint replacement	Bilateral knee	-	-	Right hip	-	Bilateral hip
Inflammatory manifestations	IBP, inflammatory SIJ and spine lesions by MRI	IBP, Scleritis, enthesitis, structural changes in SIJs by MRI	ILD, erosive arthritis, SIJ MRI was suggestive of crystal deposition	-	-	-
Laboratory findings			ANA, RF, CCP positivity		ANA,RF positivity	

REFERENCES

[1] Phornphutkul, C., et al., *Natural history of alkaptonuria*. New England journal of medicine, 2002. 347(26): p. 2111-2121.

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AB0885 THE RELATIONSHIP BETWEEN METABOLIC SYNDROME SEVERITY AND THE RISK OF MORTALITY IN GOUT PATIENTS: A POPULATION-BASED STUDY

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Background: Metabolic syndrome (MetS) is common amongst gout patients. The MetS is diagnosed when a patient has at least 3 of the following 5 conditions of hyperglycemia, hypertension, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol or abdominal obesity.

Little is known about the relationship between the cumulative effects of all five metabolic syndrome conditions and the risk of mortality among adult patients with gout. Metabolic Syndrome Severity Score (MetSSS) is a new clinical prediction score that employs available components (sex, age, race, systolic blood pressure, waistline circumference, high-density lipoprotein, triglycerides and fasting blood glucose). MetSSS is a validated summary score that accounts for the combined effects of all 5 metabolic features. MetSSS allows examination of associations between MetS severity and the risk of mortality.

Objectives: to use the MetSSS to examine the overall associations between MetS severity and the risk of mortality related to all-causes, cardiovascular disease and diabetes amongst United States (US) gout patients.

Methods: Mortality-linked data for 12,101 adults aged 18 to 90 years who participated in the Third National Health and Nutrition Examination Survey (NHANES) III (1988-1994) was analyzed. Data from NHANES III were linked to national mortality records for all participants up to time of death or end of study (i.e. 23 years following initial recruitment). All 5 metabolic features were used to calculate gender-race/ethnicity specific MetSSS Z-scores in gout patients. The Z-score is the number of standard deviations from the mean a data point is and allows a continuous representation of all MetS conditions while accounting for gender-race/ethnicity disparities.

Results: A total of 3,381 deaths were observed, of whom 215 had gout. The prevalence of gout amongst adults was 2.59% (95% CI; 2.13%-3.05%). Moderate to high MetS severity was significantly prevalent among gout patients (47.33% vs. 21.16% no gout; P-value <0.0001). The mean MetSSS Z-score for gout patients was significantly higher than those without gout (0.71 vs. -0.04 no gout; P-value <0.0001). For gout patients, a one-unit increase in MetSSS score was associated with a significant increase in the risk of all-cause mortality Adjusted Hazard Ratio (aHR) 1.46 (95% CI; 1.13, 1.87).

In a disease-specific survival model, a one-unit increase in MetSSS score was associated with a aHR 1.62 (95% CI; 1.21, 2.15) increase in heart disease related mortality among gout patients. Amongst those with gout, a one-unit increase in MetSSS score was associated with increased risks of diabetes- and hypertension- related mortalities aHR 2.53 (95% CI; 1.43, 4.62), aHR 1.73 (95% CI; 1.07, 2.79), respectively.

Conclusion: The Z score calculation in our study allowed a quantification of increased diabetes- and hypertension- related mortalities, all- cause and cardiovascular mortality in patients with gout.

Use of the MetSSS can provide an opportunity to identify patients at highest risk influencing patients to change their lifestyle and better comply with treatment.

REFERENCES

[1] Wiley JF, Carrington MJ. A metabolic syndrome severity score: A tool to quantify cardio-metabolic risk factors. Prev Med 2016;88:189-195.

[2] Thottam GE, Krasnokutsky S, Pillinger MH. Gout and metabolic syndrome: a tangled web. Curr Rheumatol Rep 2017;19:60.

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AB0886 IS THE SENSE OF SMELL IMPAIRED IN GOUT PATIENTS?

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Background: The sense of smell is sensitive to hundreds of thousands of odorants. Smell disorders significantly compromise the quality of life. A National Health and Nutrition Examination Survey (NHANES) 2013-2014 survey among US population aged 40 years of age and older years found smell dysfunction in ~ 20.5 million (13.5%) of Americans (1). Prevalence increased with age. Other factors influencing the sense of smell include ethnicity, smoking, medications, head trauma, chronic sinusitis, upper respiratory tract infections, alcoholism and neurological disorders.

The University of Pennsylvania Smell Identification Test (UPSIT) (2) is a well-validated test of olfactory function that correlates with odor detection and other quantitative measures of olfaction. This test has become the 'gold standard' for olfactory testing and is comprised of four test booklets, each containing 10 microencapsulated (scratch & sniff) odors.

Patients with gout, the most common inflammatory arthritis, frequently have multiple associated comorbidities, affecting many organs and aspects of one's health.

Objectives: To determine whether gout patients have an impaired sense of smell.
Methods: This was a cross-sectional prospective study of gout patients seen in our rheumatology clinic. The first 30 clinic patients were recruited during the period 7/15/17-5/25/18. Each patient was administered the 40-item UPSIT. UPSIT scores were compared to age- and sex-matched controls from a normative database maintained at the University of Pennsylvania Smell and Taste Center using a paired t-test.
Results: Gout patients ranged in age from 31 - 86 years (mean: 59 years); 26 (87%) of patients were $\geq$ 40 years old and included 26 men and 4 women. The duration of gout ranged from 1- 43 years (mean: 9 years), with 19 having gout for >5 years. Visible tophi were observed in 6 patients (33%). C-reactive protein was within normal range except in one gout patient. Serum urate levels ranged from 5.1-12 mg/dL (mean: 6.29 mg/dL). Two patients were current smokers; both have microsomia. No patients had head trauma, chronic sinusitis, upper respiratory tract infections, alcoholism or neurological disorders.
The mean UPSIT scores of the two groups did not differ significantly [respective patient and control means (SDs) = 31.40 (5.79) and 31.80 (4.37); t_{29} = -0.342, p = 0.74].
Conclusion: This is the first study to quantitatively assess smell function in patients with gout. Despite being a systemic inflammatory disease, with multiple assocaited comorbidities, we did not find a statistically significant effect of gout on smell function using a well validated olfactory test.

REFERENCES

[1] Liu G, Zong G, Doty RL, Sun Q. Prevalence and risk factors of taste and smell impairment in a nationwide representative sample of the US population: a cross-sectional study. BMJ Open 2016;6:e013246.
[2] Doty RL, Shaman P, Dann M. Development of the University of Pennsylvania Smell Identification Test: a standardized microencapsulated test of olfactory function. Physiol Behav 1984;32:489-502.

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AB0887 A SURVEY FOR DIAGNOSIS AND TREATMENT OF PATIENTS WITH GOUT IN KOREA

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Background: The prevalence and incidence of gout has risen over the past few decades and the socioeconomic costs of gout have been increasing accordingly, but it is unclear whether proper medical care is provided for patients with gout.
Objectives: This study aims to investigate the actual status and adequacy of diagnosis and management of gout patients.
Methods: The patients with gout who visited between November 2017 and February 2018 were consecutively enrolled. Data were collected using a pre-designed questionnaire and reviews of medical records. The collected data included diagnosis and management of gout before starting a steady treatment in our clinic, and disease status at first visit to our clinic.
Results: In total, 172 gout patients were enrolled. The average age of the patients was 55 (interquartile range (IQR): 45-66) years, and 94.2% were men. The average disease duration was 8 (IQR: 4-13) years. The average age of first gout symptoms was 45 (IQR: 36-53) years. The first symptom started in the feet for 93.4% of patients. The patients in which the first symptom region was around large joints were 35.1%, and 17.3% of patients developed first gout symptoms around multiple joints. Several patients (64%) visited the hospital directly after their first acute gout attack. The first physicians to examine gout patients were orthopedic surgeons (38.2%), emergency doctors (23.6%), and rheumatologist (16%). Upon initial medical examination, 67% of patients were clinically diagnosed or suspected with gout. Monosodium urate crystals in synovial fluid or tophi were confirmed in 10.5%. Furthermore, 31% of patients had a history of pharmacology urate lowering therapy (ULT) after acute gout attack, and 84.4% were indicated for pharmacologic ULT upon first visit to our clinic. Additionally, 47.6% of patients showed symptoms of chronic kidney disease, past urolithiasis, or tophi, and 52.4% suffered from $\geq$ 2 gout attacks/year. However, only 11.3% of patients were receiving continuous ULT before visiting our clinic.
Conclusion: Most patients were clinically diagnosed without appropriate tests for gout diagnosis, such as joint aspiration, and only a very small number of patients were receiving adequate pharmacologic ULT. The management of gout seems to be inadequate in many respects.

REFERENCES

[1] Roddy E, Choi HK: Epidemiology of gout. Rheumatic diseases clinics of North America 2014, 40(2):155-175.
[2] Singh JA, Hodges JS, Toscano JP, Asch SM: Quality of care for gout in the US needs improvement. Arthritis and rheumatism 2007, 57(5):822-829.
[3] Young-Il S, Kyeong Min S, Young Ok J, In Je K, Kyung Lee K, Young Deok B, Hyun Ah K: Survey of Current Trends for Diagnosis and Treatment in Korean Gout Patients. *J Rheum Dis* 2011, 18(3):187-192.
[4] Doherty M, Bardin T, Pascual E: International survey on the diagnosis and management of gout. Annals of the rheumatic diseases 2007, 66 (12):1685-1686.

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AB0888 ULTRASOUND FEATURES IN GOUT: A COMPARATIVE ANALYSIS WITH MATCHED CONTROL

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Background: Gout is a frequent inflammatory disease characterized by deposition of monosodium urate crystals in joints and tissues in the presence of hyperuricemia (1). Ultrasound (US) is a simple imaging technique that has gained interest in the assessment of individuals with gout due to its ability to identify inflammation and joint damage, as well as crystal deposition. The most characteristic gout US findings are the presence of intra-articular aggregates and the double contour (DC) signal, included in the 2015 ACR/EULAR classification criteria.
Objectives: To identify potential differentiating US findings between individuals with gout and matched controls.
Methods: A cross-sectional study was conducted, including 57 gout adult patients and 32 adult individuals with a normal uricemia, matched by age and gender. Sociodemographic, clinical and analytical data were collected. Bilateral US grey scale evaluation of the 1st metatarsophalangeal joint (MTP1), 2nd metacarpophalangeal (MCP2) and knee was performed in all participants. The following findings were assessed: intra-articular effusion, synovial hypertrophy, bone erosion, DC signal and intra-articular deposits. None of the participants presented with clinical signs of arthritis at the time of the evaluation.
Results: The mean age of gout patients and healthy individuals was 63.3 ±12.6 and 63.8±10.5 years, respectively. The majority of the gout patients were male (87.7%), 77.2% had previous history of podagra and 26.3% had tophi. Mean disease duration was 4.3 years. Mean uricemia was 6.7 ±2.0 mg/dl in gout patients and 4.9±0.9 mg/dl in the control group. At the time of the study, 31 patients (54.4%) were treated with allopurinol, 9 (15.8%) with febuxostat, 1 (1.8%) with both allopurinol and febuxostat and 16 (28%) were not on urate lowering therapy.
Comparatively to the control group, in the MTP1, patients with gout presented more frequently with synovial hypertrophy (26 vs 0, p<0.001), bone erosion (19 vs 0, p<0.001), DC signal (7 vs 0, p<0.05) and intra-articular aggregates (8 vs 0, p<0.05). At the knee, patients showed more often effusion (19 vs 2, p<0.001), synovial hypertrophy (26 vs 1, p<0001) and DC signal (8 vs 0, p<0.05). At the MCP2, only the presence of erosion was significantly more common in the gout group (8 vs 0, p<0.05).
DC signal was found in 17 patients and in none of the healthy subjects (p<0.001); this finding was more frequently observed at the knee.
There was an association between previous gout crisis in the MTP1 and the presence of erosion in this joint (p=0.04). An association was found between the presence of tophi and erosion (p<0.001), DC signal (p<0.05) and intra-articular aggregates (p=0.006). There was no association between uricemia levels, disease duration and the different US findings.

Conclusion: In this study, the presence of synovial hypertrophy, erosions, DC signal and intra-articular deposits were the most frequent US findings in patients with gout. Moreover, these findings at the MTP1 joint allowed to distinguish between gout patients and matched control subjects.
US seems to be useful to demonstrate evocative signs of crystal accumulation, inflammation or joint damage, even in the absence of overt arthritis.

REFERENCES

[1] Stewart S. et al. Ultrasound features of the first metatarsophalangeal joint in gout and asymptomatic hyperuricaemia: comparison with normouricaemic individuals. Arthritis Care (Hoboken) 2017 Jun; 69(6):875-883.
[2] Neogi T. et al. Gout Classification Criteria: Na American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheumatol 2015; 67:2557-68.

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AB0889 NEURAL NETWORKS IN PREDICTION OF KIDNEY DISEASE IN GOUT PATIENTS WITH OBESITY

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Background: Nowadays, in addition to correctly verified diagnosis and effective therapy of gouty nephropathy in obese patients, there is a problem to predict the development of kidney disease in this cohort of patients. Gouty nephropathy may have subclinical course for years, that's why, with what probability it can occur? To solve such kind of problem we used neural networks or "artificial intellect".
Objectives: To predict gouty nephropathy.
Methods: A one-center cohort prospective study was conducted that included 117 patients with gouty arthritis, who were on scheduled inpatient treatment at the Rheumatologic Department of Ternopil University Hospital during 2015-2018 years. All patients had no history of any kidney disease. Statistical analysis was performed with STATISTICA software.
Results: To create a neural network, as input information, it is necessary to select data that have the greatest correlation with gouty nephropathy. Significant correlations between gouty nephropathy and hyperuricemia (r=0,85), uricosuria (r=-0,79), hypercholesterolemia (r=0,44), hypertriglyceridemia (r=0,84), an increase of low density lipoproteins (r=0,80), concomitant arterial hypertension (r=0,81), diabetes mellitus (r = 0,59) were established. Age of the patients, the number of involved joints and the duration of the disease were also included.
Then the probability of development of gouty nephropathy can be calculated by the formula:

$$P(I) = \frac{1}{1+e^{-5\,D*W}}$$

P(I) – probability (III) of having gouty nephropathy in a patient. Accepts values from 0 to 1. 0 – absolutely (100%) healthy patient, 1 – absolutely (100%) ill patient;

W – weight, vector of weights of synaptic arches of artificial neuron;

D – patient's data scaled at intervals of 0 to 1, in such a way that the minimum possible value corresponds to 0, and to the maximum possible – 1;

e – Euler's number.

To facilitate mathematical calculations, a peculiar "calculator" for predicting kidney damage in obese gout patients has been developed. This formula was written in Microsoft Office Excel and automatically calculates the probability of development of gouty nephropathy in%. Approval of this method indicated that 15.6% of the patients without gouty nephropathy may have development of kidney disease in the range of 55.1 - 98.8%.
Conclusion: Consequently, having input data (levels of uric acid in the blood, uric acid in the urine, cholesterol, triglycerides, low density lipoproteins, the presence of concomitant hypertension, diabetes mellitus, the number of affected joints and the duration of the disease), it is easy to predict the probability of kidney disease in patients with gout and obesity using the proposed formula.

REFERENCES

[1] Qeethara Al-Shayea. Artificial Neural Networks in Medical Diagnosis. IJCSI International Journal of Computer Science Issues, Vol. 8, Issue 2, 2011, P.150;
[2] Sarfaraz Ahmed. Medical Diagnosis using Neural Networks. International Journal of Engineering Development and Research. 2014. P.201.

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AB0890 EFFECT OF DIFFERENT TYPES OF URIC ACID-LOWERING DRUGS ON GOUT ATTACK

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Background: Gout is an inflammatory arthritis associated with hyperuricemia which is caused by purine metabolism disorders. General uric acid lowering treatment sometimes causes the onset of gout, but the specific cause is not clear. Our group has found that adenine nucleoside triphosphate (ATP) plays an important role in the pathogenesis of gout. It synergizes with MSU to stimulate the secretion of IL-1β, leading to the onset of gout.[1,2] The xanthine oxidase inhibitors promote the production of ATP, while the drugs that promotes the excretion of uric acid does not affect ATP production. Therefore, we speculate that gout attacks induced by allopurinol and febuxostat are related to the role that ATP plays in the pathogenesis of gout.
Objectives: To compare the effects of drugs that inhibit uric acid production and promote uric acid excretion on gout.
Methods: A case-control study was used to compare the changes in serum uric acid concentration and observe whether the patients would suffer gouty arthritis within one month. The gout patients complied with the standard that the number of gout attacks did not exceed three times, as well as more than one time within the past six months, were selected. And patients with other chronic inflammatory and infectious diseases were excluded.
Results: A total of 148 patients with gout in the Department of Rheumatology and Immunology of Anhui Provincial Hospital were collected, all of whom were male. According to the patients taking uric acid-lowering drugs, they were divided into four groups: group A: control group (no uric acid-lowering treatment, n=35); group B: febuxostat group (40 mg Qd, n=66); group C: allopurinol group (0.1 g Bid, n=11); group D: benzbromarone group (50mg Qd, n=36). The statistical results are as follows: (1) The levels of serum uric acid in group B, C and D were significantly decreased after uric acid-lowering treatment compared with those before treatment (B: 389.6±88.9 vs 547.5±93.0, C:363.3±28.6 vs 504.0±38.3, D: 376.2±108.5 vs 557.3±101.8) within one month, and there was no significant difference in the level of uric acid before uric acid-lowering treatment among the three groups. (2). Comparison of gouty arthritis recurrence rates: The recurrence rate of gout patients in group B was 33.3%, and was 18.2% in group C, which was significantly higher than that in group D (11.1%), the difference was statistically significant (P<0.05); the recurrence rate of gout patients in group A was 14.3%, and there was no significant difference compared with group D (P>0.05); the recurrence rate of gout patients treated by drugs that inhibited uric acid production (B+C group) was 31.2%, which was significantly higher than patients treated by drugs that promoted uric acid excretion (D group) 11.1%, the difference was statistically significant (P<0.05).
Conclusion: Under the same uric acid-lowering intensity, the drugs that inhibit uric acid production can induce gout attacks during the process of uric acid lowering, while the drugs that promote uric acid excretion has less effect on the recurrence of gouty arthritis.

REFERENCES

[1] Tao JH, et al. P2X7R: A potential key regulator of acute gouty arthritis. Semin Arthritis Rheum. 2013; 43(3): 376-380.
[2] Tao JH, et al. Single nucleotide polymorphisms associated with P2X7R function regulate the onset of gouty arthritis. PLoS One. 2017 Aug 10;12 (8):e0181685.

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AB0891 **HYPERURICEMIA AND GOUT IN PATIENTS WITH PAGET´S DISEASE OF BONE**

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Background: Hyperuricemia and gout has been described as metabolic complications in patients with more extensive Paget's disease, with a very variable prevalence. However, there is no data about fluctuations of uric acid levels asociated with its treatment and its correlation with alkaline phosphatase variations during gout attacks.
Objectives: To analyze the frequency of hyperuricemia and gout in patients with a diagnosis of Paget's disease of bone (PD) and to establish the correlation between the activity of Paget's disease and its treatment in the fluctuations of uric acid levels.
Methods: Patients with Paget's disease and with scintigraphic uptake suggestive of activity were included. A database was created including demographic information, the presence of symptoms associated with PD, its type (monostotic or polyostotic), alkaline phosphatase (AP) and uric acid (UA) levels at diagnosis and the treatment received. AP and UA levels after treatment were also collected as well as the presence of possible hyperuricemic risk factors (HRF), history of gout and levels of AP and UA during gout attacks, if any. Finally data was analyzed using SPSS v21.
Results: A total of 95 patients were included with a mean age of 70.59 years (range 45-89), with 56% of them being women. The mean values of AP and UA at diagnosis were 178.05± 82.81 mg/dL and 5.84±1.74 mg/dL respectively. 58.9% of the patients had monostotic involvement (56/95) and only 53.12% had associated symptoms (51/95), whereas in the rest of the patients PD was an incidental finding. 70.83% did not present HRF and 56 patients (58.9%) had received treatment for their PD (41% of them with zoledronic acid). Pearson correlation between PA and UA levels was found moderatly positive (0.710 with $p<0.0005$) and 50.52% of the patients (48/95) had UA levels above 6mg/dL at the time of diagnosis, with a mean of 7.10 mg/dl ±1.74. In 93.5% of the cases there was a decrease in UA levels after the treatment for PD, with a mean decrease of 0.78±1.3 mg/dL over the baseline value at one year of follow-up. Only 11.57% of the patients in our cohort presented gout symptoms during their follow-up, with an increase in AP levels at the time of the attack in 63.63% of the cases.
Conclusion: In our cohort, there was a moderate positive correlation between the elevation of AP and UA in patients with active Paget's disease. Treatment for PD produced a decrease in UA levels from baseline in most patients. Similarly, during gout attacks, an increase in AP levels could be.

REFERENCE

[1] Lluberas-Acosta G, Hansell JR, Schumacher HR Jr. Paget's disease of bone in patients with gout. Arch Intern Med 1986 Dec; 146 (12):2389-92.

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AB0892 **ACUTE POLYARTICULAR GOUT WITH SYSTEMIC INFLAMMATORY RESPONSE – A SINGLE TERTIARY CENTRE COHORT**

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Background: Gout is a common, inflammatory, crystal-induced disease with increasing prevalence and incidence. Typical monoarticular involvement can be quite easily and effectively treated. In recent years, we have observed more frequently gout cases with severe polyarticular manifestation and with systemic inflammatory response syndrome (SIRS). In clinical practice such a complicated gout attack used to be identified with delay and therapy is not adequate.
Objectives: To assess clinical and laboratory parameters of systemic inflammatory polyarticular gout and to identify risk factors and convenient therapeutic strategy.
Methods: Retrospective analysis of 133 consecutive new patients (14 females) with gout (according to the classification criteria ACR/EULAR 2015) on the presence of acute polyarticular involvement ($\geq$ 4 joints) and fullfilling criteria for SIRS.
Results: Seventeen (12.8%) of 133 gout patients had polyarticular manifestation and met SIRS criteria; 2 females and 15 males, average age 73.2±11.3 years, BMI 29.9±3.8. All these patients had to be admitted to inpatient department because of gout severity. Mean CRP was 204±113 mg/l, leucocytes 15.2±6.8 10^9/l, serum uric acid 401±140 μmol/l. Procalcitonin was slightly positive in 2 patients (with concurrent respiratory infection). Mean 6 joints were affected, 13 (76,5%) patients had involvement of both upper and lower limbs, tophi were present in 7 of 17 patients. Synovial fluid analysis was performed with proving urate crystals and leukocyte count 24.4±17.3 10^9/l. Typical gout features were found in 70.6% patients on joint X-ray and in 52.9% ones on musculoskeletal ultrasound. Risk factors for systemic inflammatory polyarticular manifestation were preceding renal function impairment, long-term diuretic therapy and alcohol above-average consumption. Monotherapy was not effective in any patients, combination of NSAID with colchicin or systemic glucocorticoids was used with success.
Conclusion: Acute polyarticular gout with systemic inflammatory response mimics septic status and mostly requires hospitalization. Complex management with combination therapy should be guided by an experienced rheumatologist.

REFERENCE

[1] Schäfer VS, Krause A, Trauzeddel RF, Schmidt WA. Systemic Inflammatory Polyarticular Gout Syndrome – Description of a Previously Neglected Entity. JSM Arthritis 2017; 2: 1024.

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AB0893 **WHAT IS THE CHANCE IN AN INDIVIDUAL GOUTY PATIENTTHAT DISEASE WILL BE STILL ACTIVE IN A YEAR? PREDICTIVE MODELLING MIGHT COME TO AID**

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Background: The treat-to-target concept is currently applied to gout [1] and a composite outcome to measure disease activity may serve as a target in clinical practice. Strategies for achieving the target are still not individualized and the ability to adjust the treatment on an individual basis using prognostic information from predictive models might help practitioners to identify patients with a high or low probability of remission or disease inactivity.
Objectives: To develop a prediction model for disease inactivity in gouty patients.
Methods: Data were retrieved from the Kick-off of the Italian Network for Gout (KING) observational cohort multicentre study on behalf of the Italian Society for Rheumatology. The gout activity score (GAS) [2,3] was used as validated outcome to define inactive disease (cut off <2.5) at 12 months in gouty patients with active disease at baseline and receiving the standard of care in two visits 6 months apart. Logistic regression analyses and backwards elimination of baseline predictors with bootstrap resampling were used to develop parsimonious models. Performance and correction for optimism were assessed. Missing data were handled through multiple imputation by chained equations (50 completed datasets).
Results: Out of 446 patients enrolled from 30 rheumatology centres, 265 (59%) had active disease at baseline (mean age 63±11 years, male 91%, median disease duration 7 years, tophi 23%, urate lowering therapy 82%, mean serum urate [sUA] levels 6.7±1.6 mg/dl) and a 12-month visit. In 34% (65/206) gout was inactive at 12 months. From 20 candidate predictors (complete cases n=150) disease duration, use of nonsteroidal anti-inflammatory drugs (NSAIDs), number of flares in the previous 12 months, presence of tophi, sUA <6 mg/dl, visual analogue scale (VAS) global patient, and baseline GAS were selected. The performance of the four developed models is shown in table. In the completed case analysis (n = 258) the c-statistics (95% confidence interval [CI]) of

models 1 to 4 were 0.79(0.73-0.85), 0.78(0.72-0.84), 0.76(0.70-0.82), and 0.74(0.68-0.81), respectively.

MODEL	1		2		3		4	
PREDICTORS	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Disease duration	-0.07	-0.11,-0.02	-0.06	-0.11, -0.02	-0.06	-0.11, -0.02	-0.08	-0.12, -0.03
Current NSAIDs	-1.14	-2.24,-0.05	-0.96	-2.02, -0.10	-1.09	-2.12, -0.05	-0.85	-1.87, 0.18
Last 12 months flares	-0.42	-0.70, -0.13	-0.23	-0.41, -0.06	-0.25	-0.05, -0.06	-	-
sUA <6 mg/dl	1.68	0.38, 2.98	0.82	0.00, 1.65	0.76	-0.06, 1.57	-	-
Tophi	-1.66	-3.18, -0.14	-0.68	-1.65, 0.29	-0.73	-1.79, 0.32	-	-
VAS patient disease	-0.64	-1.28, 0.00	-0.09	-0.24, 0.06	-	-	-	-
Baseline GAS	1.59	-0.20, 3.38	-	-	-	-	-0.47	-0.83, -0.12
Intercept	-3.50	-8.36, 1.34	0.76	0.00, 1.52	0.60	-0.10, 1.31	2.03	0.64, 3.43
PERFORMANCE								
C-statistic	0.81	0.73, 0.88	0.81	0.73, 0.88	0.80	0.73, 0.87	0.77	0.69, 0.85
Optimism-corrected	0.77		0.78		0.78		0.77	
Hosmer–Lemeshow test	0.64		0.37		0.38		0.49	

Conclusion: These preliminary prediction models for inactive disease showed good performance in gouty patients from a real-life secondary setting. External validation in ad-hoc studies is required to identify the best model and to search for additional predictors and increase its predictive performance.

REFERENCES

[1] Kiltz U, et al. Ann Rheum Dis 2017
[2] Sciré CA, et al. Arthritis Care Res (Hoboken) 2016
[3] La-Crette J, et al. Joint Bone Spine 2018

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AB0894 CHANGE OF ULTRASONOGRAPHIC SIGNS DURING URATE LOWERING THERAPY IN PATIENTS WITH GOUT

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Background: US is widely used in clinical practise in gout diagnosis and follow up. However, the crystal resolution time is not widely studied in gout patients by ultrasonography.
Objectives: To explore related factors of changes in gouty patients by ultrasonography after initiation of uric acid lowering therapy.
Methods: There were 72 gout patients enrolled who admitted to First hospital of Peking University from December 2012 to June 2017. All the patients had clinical and ultrasound examination at both knees, ankles and feet joints at the baseline. Regular uric acid lowering therapy started for one year. The endpoint was the last time who repeat the ultrasound examination during the follow up. According with uric acid level and its measuring time, the area under the curve was calculated to reflect the uric acid burden.
Results: In the 216 joint regions of 72 patients, double contour sign were detectable in 112/216(;51.85% , tophi were detectable in 71/216 (;32.87% . Among MTP Joints, DCS was detected in 32/144 (22.22%), and tophi in 47/144 (32.64%). Among Knee joints, DCS was detected in 33/144 (22.92%), tophi in 4/144 (2.78%). Among ankle joints, DCS was detected in 47/144(;32.64% , tophi in 20/144(;13.89% . DCS disappearance occurred in 38/55 (69.09%) joints positive for DCS at baseline.Time-to-disappearance was 148 days (63-985 days . Tophi disappeared completely in 18/45 joints (40%). Time-to-disappearance was 382.5 days(;397.25 686 days . There was no significant difference in age, BMI, duration of disease and complications between DCS persisted group and DCS disappearance group. SUA in the DCS disappeared group at baseline, second, third, fourth and ninth months of follow-up was significantly lower than that of the non-disappeared group. SUA load in the DCS group was significantly lower than the non-disappeared group. Post hoc tests showed that SUA levels fell significantly from baseline through fourth month of follow-up in DCS disappeared group, and SUA of the sixth months was the lowest.
Conclusion: To screen for specific features of gout such as DCS or tophi by US at initiation of ULT and during follow-up is a useful, and effective modality to detect the lowering and often disappearance of burden of urate load in gouty joints.

REFERENCES

[1] Kiltz U, Smolen J, Bardin T, et al. Treat-to-target (T2T) recommendations for gout[J]. Annals of the Rheumatic Diseases,2017,76(4):632-638.
[2] Pascual E, Sivera F. Time required for disappearance of urate crystals from synovial fluid after successful hypouricaemic treatment relates to the duration of gout[J]. Ann Rheum Dis,2007,66(8):1056-1058.
[3] Neogi T, Jansen T L T A, Dalbeth N, et al. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative[J]. Annals of the Rheumatic Diseases,2015,74(10):1789-1798.
[4] Gutierrez M, Schmidt WA, Thiele RG, et al. OMERACT Ultrasound Gout Task Force group. International Consensus for ultrasound lesions in gout: results of Delphi process and webreliability exercise[J]. Rheumatology (Oxford), 2015, 54(10): 1797 1805.
[5] Peiteado D, Villalba A, Martín-Mola E, et al. Ultrasound sensitivity to changes in gout: a longitudinal study after two years of treatment. Clin Exp Rheumatol. 2017 Sep-Oct;35(5):746-751.
[6] Ebstein E, Forien M, Norkuviene E, et al. Ultrasound evaluation in follow-up of urate-lowering therapy in gout: the USEFUL study. Rheumatology (Oxford). 2018 Oct 4. doi: 10.1093/rheumatology/key303. [Epub ahead of print]

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AB0895 EFICACY AND SAFETY OF ALLOPURINOL WHILE TITRATING HYPERURICAEMIA IN GOUTY PATIENTS

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Background: according to EULAR 2016 recommendations (1), a drug of choice for gout treatment in patients with normal kidney function is Allopurinol, which should be started at 100 mg daily and titrated up to 600-900 mg daily (raised up for 100 mg every 2-4 weeks) in order to reach the target serum uric acid (SUA) level of < 6 mg/dL (360 μmol/L). However, this advice is mostly not followed in daily clinical practice, mainly because of the adverse events precaution.
Objectives: to monitor the eficacy and safety of different dose regimens of Allopurinol while treating hyperuricaemia in gouty patients.
Methods: in a prospective study gouty patients were included consequetly, as they have entered the Rheumatology Institute in Belgrade, classified as either chronic or newly-diagnosed. Allopurinol was titrated monthly up to the recommended SUA level or the severe adverse events occurence (following hypersensitive drug reactions, liver and kidney function tests and the number of blood cells). Patients were followed-up for 6 months.
Results: study enrolled 61 patients (92,1% male) aged 59,2 (9,6) years. Their mean (SD) SUA level was 454,8 (99,3), 362,7 (60,9) and 388,2 (74,4) μmol/L at 1,2 or 3 months of therapy, respectively. At three months of therapy, target SUA level was reached by 45 (73,8%) of patients treated with Allopurinol up to 300 mg daily. For non-responders, Allopurinol was raised to 400-600 mg daily and additional 12 (19,6%) of patients reached the target SUA level (mean 353,6 (36,2) μmol/L), whereas only 6,6% of patients did not reach the therapeutic goal. Gouty flares were identified in 11/61 (18%) of patients, gastrointestinal symptoms were reported by 6/61 (9,8%), 5/61 pts (8,2%) have evolved

hepatotoxicity with minor liver function abnormalities and Allopurinol induced mild skin rash was seen in 7/61 (11%) of patients. All adverse events were mild and the therapy was not changed.
Conclusion: Allopurinol increasing dose regime was efficient in hyperuricaemia treatment, and the target goal was reached by 93,4% of patients. All adverse reactions were mild and did not influence dose regimen at the end of the 6 months period of follow-up.

REFERENCE

[1] Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castañeda-Sanabria J,Coyfish M, Guillo S, Jansen TL, Janssens H, Lioté F, Mallen C, Nuki G, Perez-Ruiz F, Pimentao J, Punzi L, Pywell T, So A, Tausche AK, Uhlig T, Zavada J, Zhang W, Tubach F, Bardin T. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2017 Jan;76(1):29-42

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Infection-related rheumatic diseases

AB0896 REINFECTION OF PROSTHETIC JOINT WITH A DIFFERENT MICROORGANISM: A PROSPECTIVE COHORT STUDY

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Background: Treatment failure of prosthetic joint infection (PJI) may be due to relapsing infection (with the same microorganism) or a new infection (with a different microorganism). Data on new prosthetic joint infections (NPJI) are scarce, although they represent a devastating complication and a therapeutic challenge of joint arthroplasty.
Objectives: The aim of this study was to describe epidemiological, clinical and microbiological characteristics of NPJI, their treatment and outcome.
Methods: This observational single-center cohort study was conducted in a French referral center for bone and joint infections. All patients admitted between January 2000 and December 2015 with a documented hip or knee PJIs and at least 2 years of follow-up, were identified. Among those, all patients treated in our center for at least two successive PJIs, involving the same joint and due to different microorganisms, were included. We compared these patients with a random selection of 124 "single"-PJIs (72 knee and 52 hip prostheses) treated in our center and followed at least 2 years.
Results: Among 909 PJIs treated during the study period, 62 patients with 70 NPJIs were included (7.7%) NPJIs developed more frequently in knee (15.7%) than in hip prostheses (4.4%) (p<0.001). Median [range] age was 70 [66-80] years old and median [range] body mass index was 28.7 [25-33] kg/m^2. Median [range] duration from the first to the NPJI was 16 months [0-98]. Hematogenous spread of the infection was quite higher in NPJIs compared to single-PJIs (92% versus 31% (p=0.0001). NPJIs were predominantly monomicrobial (82%), due to *S. aureus* (29%), *Streptococcus* sp. (29%) *Gram-negative bacilli* (11%) or others (31%).
A curative strategy was applied to 71% of the patients with a NPJI: DAIR (31%), 1-stage exchange arthroplasty (24%), 2-stage exchange arthroplasty (5%) and other strategies (11%). For the other patients, prolonged suppressive antibiotic therapy was prescribed (29%), combined with surgery in 10% of patients. Eight patients had a second NPJI, 6 were an acute hematogenous PJI.
Four risk factors for NPJI were identified by multivariate analysis : chronic dermatitis (odds ratio [OR] 11.49; 95% CI,2.40,55.01; p=0.002), 2-stage exchange arthroplasty during the first PJI (OR 6.99; 95% CI,2.83, 17.27; p=0.0001), high blood pressure (OR 3.17; 95% CI,1.39, 7.20; p=0.006) and male gender (OR 2.99;95% CI,1.35, 6.60; p=0.007).
Conclusion: NPJIs are complex PJI affecting more frequently the knee prostheses. They occur predominantly via hematogenous spread from a distant infectious focus, especially the skin. In these complex settings, management by multi-disciplinary teams, should be adapted to each clinical situation.
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AB0897 ABSCESSES DURING OSTEOARTICULAR BRUCELLOSIS: A STUDY OF 26 CASES

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Background: Brucellosis remains an important economic and public health problem in developing countries. The osteoarticular involvement is one of it serious complication mainly due to abscess formation.
Objectives: The aim of our study was to identify the frequency and radiological features of abscesses during osteoarticular brucellosis.
Methods: We conducted a retrospective study including 26 patients who have been hospitalized for osteoarticular brucellosis from 1998 to 2018. The diagnosis of brucellosis was made on the basis of clinical symptoms, imaging finding (CT scan or MRI) and isolation of brucella species in blood or tissue specimens and/or a positive Wright agglutination test.
Results: Twenty six patients were included. 15 patients were male. The mean age was 52 years [21-77].the geographical origin of the patients was rural in 80% of the cases. The average duration of symptoms progression was 4.76 months [1-12]. Prominent clinical symptoms were inflammatory pain (all cases), fever (in 21 cases) and sweating (in 17 cases). Weight loss was found in 11 cases (42.8%) and hepatomegaly was found in 1 patient. The physical examination revealed a paresis of the two lower limbs in 2 cases. Brucella agglutination test was $\geq$1/160 in all cases (mean 1/760). Blood cultures were negative in all cases. Erythrocyte sedimentation rate (ESR) and serum C-reactive protein level were ranged 2-108 mm (mean 41.37 mm) and 0-125 mg/l (mean 30 mg/l) respectively. Leucopenia was found in only 1 case and leukocytosis in 6 cases. The most frequent osteoarticular involvement was spondylodiscitis in 20 cases (76.9%) affecting the lumbar dorsal and cervical spine in respectively 12, 6 and 2 cases. Sacroiliitis was found in 4 cases (15.4%) and septic arthritis in 2 cases (7.7%). Biopsy was performed in 8 cases, but bacteriological examination was contributory to the diagnosis in 2 cases. The radiological findings showed that 14 patients (53.8%) had abscesses. Soft tissue abscesses were detected in 7 cases with mean size of 1.3 cm [0-9cm]. Bilateral psoas abscess was recorded in one case. Epidural collection was revealed in 3 cases with an average size of 0.3 cm [0-5cm].Paravertebral and peri-vertebral abscesses were detected in 5 cases. Intradiscal abscesses were observed in 3 cases. Cord compression and involvement of root nerve were noted in respectively 6 and 1 cases.Compared to the group without abscesses, subjects with abscesses had higher ESR and the difference was statistically significant (mean ESR 26.83 vs 55.9 mm) (p=0.016). There was no statistically significant link between duration of symptoms or duration of hospitalization and the presence of abscesses. All patients had antibiotic treatment (cyclins and rifampicin). The evolution was favorable in all cases. Surgical intervention was required in one case (evacuation of an epidural abscess).
Conclusion: Our study showed that abscesses are frequent in osteoarticular brucellosis.In spite of the low risk of complication, we have to screen it using a cross sectional imaging.
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AB0898 HIV AND RHEUMATOLOGICAL DISEASES. MISDIAGNOSIS OR CONSEQUENCE!

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Background: Human immunodeficiency virus (HIV) infection is pandemic nowadays, more than 35 million people are infected with HIV, with two-thirds being resident in Africa.(1) The incidence of rheumatic manifestations in HIV infection was reported in about 4 to 71.3% cases in different studies depending on the stage of the disease and musculoskeletal involvements.(2,3)
Objectives: The aim of these study to scope the light on HIV associated rheumatic syndromes. Rheumatic disease were a misdiagnosis or not?
Methods: Cross sectional study of patients admitted to rheumatology unit in Alexandria University with a previous diagnosis of autoimmune rheumatic diseases, resistant to treatment, were screened for HIV.
Results: Three patients found to be HIV positive with low CD4+ less than 200 cells mm^3 among 130 screened patients. Two patients were diagnosed as behcet disease due to recurrent oral and genital ulcers.

The first one, also had recurrent skin infections associated with bilateral anterior and posterior uveitis. The second one admitted by recurrent oral and genital ulcerations associated with severe oral candidiasis, arthritis, erythema nodsum and positive pethargy test. The third one diagnosed as peripheral spondyloarthritis admitted with low-grade fever, palmoplantar psoriasis as well as acute extensive anterior and posterior uveitis in left eye and chronic anterior and posterior uveitis in right eye with CMV positive.

Conclusion: HIV infection might be misdiagnosed as a rheumatic disease. It is important to screen patients with inflammatory autoimmune rheumatic manifestations for HIV infection for its implications in the diagnosis and management.

REFERENCES

[1] Global AIDS Update 2016. Geneva, Switzerland: Joint United Nations Programme on HIV/AIDS. Accessed August 5, 2018.

[2] Calabrese LH. Human immunodeficiency virus (HIV) infection and arthritis. Rheum Dis Clin North Am. 1993;19:477–88.

[3] Fox C, Walker-Bone K. Evolving spectrum of HIV-associated rheumatic syndromes. Best Practice & Research Clinical Rheumatology. 2015 Apr 1;29(2):244-58.

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AB0899 COMPUTER TOMOGRAPHY GUIDED BIOPSY YIELD IN PYOGENIC VERTEBRAL OSTEOMYELITIS. AN EXAMINATION OF INFLUENCING FACTORS

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Background: Vertebral Osteomyelitis (VO) is an infectious disease that could involve intervertebral space (discitis), which it is avascular in adults. VO and discitis may occur together or independently. Both are frequently the result of a spreading of a distant focus, such as infectious endocarditis or soft tissue infection. Due to the lack of direct blood supply, reliability of blood cultures is low, so biopsy is highly encouraged by current guidelines. Treatment includes long term antibiotic (ATB), that should be initiated after biopsy (if possible) and sometimes, further surgery is needed.

Objectives: To analyze which factors influence the result of a CT-guided biopsy in patients with VO.

Methods: Retrospective observational study including adult patients diagnosed of VO based on the combination of clinical presentation with either a definitive bacteriologic diagnosis or pathological and/or imaging studies, who underwent CT-guided biopsy from January 2010 to January 2019. Demographic features, concurrent diseases, clinical history (length of pain and fever prior to admission), laboratory findings, microbiological diagnosis and radiological data were compiled. Days until biopsy from admission, prior antibiotic exposure was also collected. We considered as immunosuppressed patients those who had rheumatic or inflammatory bowel disease undertaking immunomodulatory drugs, solid organ transplantation receptors, and patients with an active malignancy or Human Immunodeficiency Virus (HIV) infected. Clinical and radiological history of lumbar stenosis or disc herniation was considered as prior spine pathology. Spinal infections after surgery, Fungal and tuberculous disease were excluded. We considered deaths attributive to PVO those which were directly caused by the infectious picture and/or its complications during the next year after diagnosis.

Results: Seventy-two of 109 patients with VO underwent biopsy (66.06%). Thirty-nine brought a positive culture (54.2%). Basal demographic and clinical features are exposed in table 1. Positive cultures included 33 cases (84.61%) of Gram+ infection (23 *Staphylococcus* and 6 *Streptococcus*) and 6 (15.39%) by Gram- bacilli (3 cases of *Pseudomona aeruginosa*, 2 *Escherichia coli* and 1 *Brevundimona spp*).

	CULTURE +		CULTURE -	
	N= 39 (54.2%)		N= 33 (45.8%)	
Male sex	26	66.67%	22	66.67%
Age	62.66 (mean)	sd:15.25	61.84 (mean)	sd:11.81
High blood pressure	20	51.28%	18	54.55%
Diabetes	12	30.77%	6	18.18%
Chronic Kidney Disease III-V	7	17.95%	6	18.18%
Immunosuppressed	8	20.51%	6	18.18%
Prior Spine Pathology	22	56.41%	23	69.69%
Liver cirrhosis	5	12.82%	9	27.27%

Conclusion: In our population, it has been observed that not a single variable collected showed influence on culture result, although a negative tendency is observed in cases of prior antibiotic exposure, with no signification. Since CT guided biopsy is a safe technique, offering an acceptable reliability, our results support its use even in those cases that empirical antibiotic had been already initiated.

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AB0900 ACUTE PARAPARESIS AS CLINICAL PRESENTATION OF VERTEBRAL OSTEOMYELITIS

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Background: Vertebral Osteomyelitis (VO) is an infectious disease that could produces neurologic complications such as paresthesia, limb weakness or even acute paraparesis (AP)[1].

Objectives: To analyze the clinical characteristics of patients with VO with AP as clinical presentation.

Methods: Single center retrospective observational study including adult patients diagnosed of VO based on the combination of clinical presentation with either a definitive bacteriologic diagnosis and/or imaging studies, who had a clinical examination at diagnosis compatible with AP, from January 2010 to January 2019. ASIA score (American Spinal Injury Association) was registered at diagnosis and one year after. Clinical and radiological history of lumbar stenosis or disc herniation was considered as prior spine pathology. We considered deaths attributive to PVO those which were directly caused by the infectious picture and/or its complications during the next year after diagnosis.

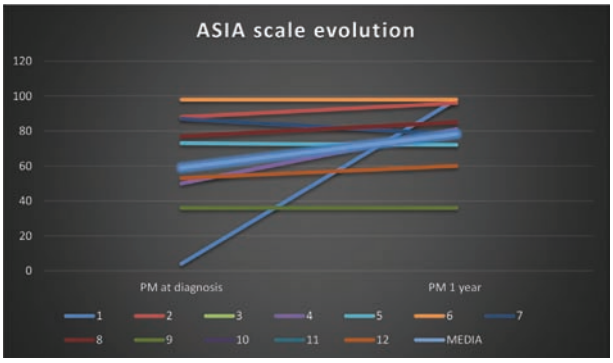


Figure 1

Results: In 15 of 122 patients with VO (18.30%), AP was described on physical examination at admission. Basal demographic and clinical features are exposed in table 1. ASIA scores at diagnosis and 1 year after are showed in chart 1. Duration of pain prior to diagnosis had a median of 24 days (7.5, 55). C reactive protein showed a median value of

153mg/L (83.2, 217.57), higher results than in no AP group [85.5 (37, 144.9), p=0.05]. The region most frequently affected was dorsal spine (73.33%). Epidural abscess was detected in all the patients (100%) significative higher than in no AP patients (56.07%, p<0.01). Similar results concerning vertebral destruction were observed (100% in AP group against 44.86% in non AP, p<0.01) and cord compression (93.33% versus 23.36% respectively, p<0.01). Eleven patients underwent CT guided biopsy (73.33%), culture positive in 33.33 of cases, with prior antibiotic exposure in five of them. Median exposure was 1.5 days (0, 4.25). In 6 patients, the picture was attributed to Gram+ (50%), in other 4 cases Gram- (33.33) and 2 cases of tuberculosis (16.67). Nine patients (60%) required further surgery and 3 patients (20%) died, slightly greater than in non AP group (10.28%) with no statistical signification, p=0.06.

	Acute paraparesis		No Acute Paraparesis	
	N=15		N=107	
Male sex	9	60%	73	68.22%
Age	70.2 (mean)	sd:8.36	62.03 (mean)	sd:15.28
High blood pressure	10	66,67%	56	52.34%
Diabetes	5	33.33%	22	20.56%
Chronic Kidney Disease III-V	1	6.67%	19	17.76%
Immunosuppressed	2	13.33%	16	14.95%
Prior Spine Pathology	11	73.33%	61	57.01%
Prior spine procedure	3	20%	19	17.76%
Infectious Endocarditis	1	6.67%	15	14.02%

Conclusion: Despite of being a well-known condition, VO is still an issue since 1-2 out 10 patients have a serious complication at diagnosis, such as AP. None of the basal characteristics analyzed acted as a risk factor, though AP group showed more proportion of prior spine pathology. No delay in diagnosis was noted on AP patients, but higher CRP value at diagnosis has been observed and predilection towards dorsal spine. Almost all patients tend to improve their ASIA scale, but in every case, some physical damage remain. More than a half required surgical procedure after diagnosis and mortality seems to be higher in this group.

REFERENCE

[1] Berbari EF, et al. 2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults. Clin Infect Dis. 2015.

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AB0901 TWO TYPES OF SYSTEMIC AMYLOIDOSIS IN A SINGLE PATIENT

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Background: The systemic amyloidoses are a group of rare diseases, in which extracellular deposition of a variety of proteins in an abnormal fibrillar confirmation results in life-threatening organ dysfunction. Acquired and hereditary amyloidoses differ in their precursor proteins and predilection for specific organ involvement.
Objectives: To describe the history of two types of amyloidosis developing consecutively in a single individual.
Methods: Targeted biopsies were used to confirm the presence of amyloid by Congo red staining viewed under polarized light, while immunohistochemistry and mass spectrometry were used to characterize the amyloid fibril type. I^{123}labeled serum amyloid P component (SAP) scintigraphy was performed to map the distribution of amyloid deposits.
Results: We report a woman of Sudanese origin who presented aged 31 with dysuria and haematuria. She was found to have an estimated Glomerular Filtration Rate of 38 ml/min and no proteinuria, and a renal biopsy demonstrated AA amyloid deposition. An I-123 labelled SAP scan demonstrated a small amount of amyloid confined to the kidneys. She had no overt underlying inflammatory disease, an infectious diseases work up, including blood borne viruses, was negative and serial measurement of serum amyloid A protein showed no significant elevation with a median of 5 mg/L. Management was blood pressure control only, and her inflammatory markers and renal function remained stable until she was lost to follow up 3 years later. Thirteen years after her renal biopsy she represented in end stage renal failure with a history of weight loss, deranged liver function tests and marked easy bleeding. Further investigation demonstrated well controlled C reactive and serum amyloid A proteins, and an IgG lambda M-band with no serum free light chain bias. A bone marrow demonstrated 7% neoplastic plasma cells and was complicated by a retroperitoneal bleed. An SAP scan now showed a large amyloid load with amyloid deposition in the liver and spleen obscuring the kidneys. Review of the bone marrow and a duodenal biopsy demonstrated amyloid deposition which was AL (lambda) type by both immunohistochemistry and proteomic analysis after laser dissection and mass spectroscopy. Review of the original biopsy confirmed AA type amyloid by both immunohistochemistry and proteomics. Six-cycle chemotherapy for AL amyloidosis was administered with complete clonal response. She remained on dialysis and died four years later of a cerebrovascular accident.
Conclusion: This is the first reported case of two types of amyloidosis in a single patient. The underlying inflammatory driver of her AA amyloidosis was never identified and given that she had migrated some years earlier from Africa, previous chronic infection that has resolved or responded to non-disclosed prior treatment was thought to be the most likely cause. Whether the subsequent development of AL amyloidosis was pure chance remains unclear. Theoretically chronic inflammation/infection may drive generation of oligoclonal bands with the potential for monoclonal breakthrough. Whether her AA amyloid deposits played a role by providing a template for deposition of subsequent AL amyloidosis derived from an entirely separate precursor protein is also unknown although this theoretically possible and has been shown in reverse in mice models.

REFERENCES

[1] Varga J, Flinn MSM, Shirahama T, Rodgers OG, Cohen AS. The induction of accelerated murine amyloid with human splenic extract. Virchows Archiv B. 1986;51(1):177-85.

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AB0902 RHEUMATIC LYME DISEASE SYMPTOMS BASED ON EPIDEMIOLOGICAL DATA IN HIGH ENDEMIC EUROPE AREA

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Background: Lyme disease is a tick born infectious disease caused by different genospecies of Borrelia bacteria (B. burgdorferi sensu strictu (ss), B. afzelii and B. garinii). The signs and symptoms of Lyme disease vary, they usually appear in stages, but the stages can overlap. In early stage skin rash (erythema migrans) appears, which may be accompanied by fever, chills, fatigue, body aches, headache, neck stiffness, and swollen lymph nodes. Later signs and symptoms can be these: joint pain and inflammation, neurological problems or other less common syndromes - heart problems, eye inflammation, and liver inflammation. Lyme disease is very common disease in the world, approximately 300,000 people get Lyme disease each year in the United States (Centers for disease control and prevention US), in Lithuania disease frequency is 101.6 cases per 100 000 population (Center for Communicable Diseases and AIDS, Lithuania, 2016 year).
Objectives: To investigate the frequency of rheumatic symptoms between Lyme diagnosed persons in Lithuania, based on epidemiological data.

Methods: We have analyzed data of Center for Communicable Diseases and Aids of Lithuania about Lyme diagnosed patients from 2014 to 2016 years.
Results: Total number of cases was 7425. 2791 males, 4633 females, age range 1 - 91 years, median age 52 years. 996 patients found out as symptomatic. The rest were either asymptomatic either information about clinical disease manifestation was not known. Among symptomatic patients two rheumatic symptoms were observed: arthralgia (220 cases, 22,1%), 140 females, 80 males, age range 12 – 84 years, median age 58 years, and myalgia (78 cases, 7,8%), 44 females, 34 males, age range 15-80, median age 56. Other symptoms were erythema migrans (75.6%), headache (15.2%), general weakness (12.4%), fever (10, 1%), and head dizziness (6.4%).
Conclusion: In total, almost 30 percentages (29, 91%) of symptoms were rheumatic. To conclude, joint pain and/or muscle pain can lead not only to systemic rheumatic diseases, but to infection diseases as well (for example: Lyme disease).

REFERENCES

[1] Sergamumo užkrečiamomis ligomis Lietuvoje apžvalga 2016. Užkrečiamų ligų ir AIDS centras. 96-98 pages. http://www.ulac.lt/uploads/downloads/leidiniai/Sergamumo_apzvalga_2016.pdf
[2] Franc Strle, Gary P. Wormser, Linden T. Hu, John A. Branda, Joppe W. R. Hovius, Xin Li, and Paul S. Mead. Lyme borreliosis. Nat Rev Dis Primers. 2017 Aug 3;3:17062. doi: 10.1038/nrdp.2017.62.
[3] Lyme disease: summary of NICE guidance. BMJ 2018;361:k1261.
[4] Clinical spectrum of Lyme disease. Cardenas-de la Garza, J.A., De la Cruz-Valadez, E., Ocampo-Candiani, J. et al. Eur J Clin Microbiol Infect Dis (2018). https://doi.org/10.1007/s10096-018-3417-1

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AB0903 LYME ARTHRITIS IN HIGH LYME DISEASE ENDEMIC EUROPE ZONE

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Background: Lyme disease is a tick born infectious disease caused by different genospecies of Borrelia bacteria (B. burgdorferi sensu strictu, B. afzelii and B. garinii). Disease clinical manifestation varies and belongs on the variety of Borrelia bacteria genospieces. In America Lyme arthritis dominates, which is caused by B.burgdorferi, while in Europe Lyme disease is caused by Borrelia afzelli or Borrelia garinii (less commonly by Borrelia burgdorferi) leading to usual disease manifestation as erythema migrans or neuroborreliosis. Lyme disease is very common disease in the world, approximately 300,000 people get Lyme disease each year in the United States (Centers for disease control and prevention US), in Lithuania disease frequency is 101.6 cases per 100 000 population (Center for Communicable Diseases and AIDS, Lithuania, 2016 year).
Objectives: To investigate the frequency of Lyme arthritis in high disease endemic European country Lithuania. To find out with joint was most frequently affected.
Methods: A retrospective, single center study was performed. We have analyzed the medical documents of adult patients, who were hospitalized to Infectious disease center (Vilnius, Lithuania), due to severe Lyme disease clinical manifestation, in 2014-2017 years.
Results: 88 patients were enrolled (57 females, 31 males, age range 18-90 years, median age 57 years). Patients were divided into four groups according disease clinical manifestation: erythema migrans, neuroborreliosis, Lyme arthritis and carditis (atrioventricular block). The most frequently erythema migrans was observed (53 cases, 62, 35 percentages (%)), than neuroborreliosis (27 cases, 31, 76 percentages), following by Lyme arthritis (3 cases, 3, 53 percentages) and Lyme carditis (2 cases, 2, 35 percentages). Between Lyme arthritis patients inflamed joints were these: knee (one case), ankle (one case) and both - knee and ankle (one case). In two cases high laboratory markers (ESR 116; 23 mm/h, CRP 125; 50 mg/l) and high body temperature (38, 2; 39, 5 0 t) was documented.
Conclusion: 2.35% of hospitalized Lyme infected patients reveal as Lyme arthritis. Inflamed joint were knee (50%) and ankle (50%). Despite the fact that it is used to think that Lyme arthritis occurs only (mostly) in America we can find it in Europe too, though its incidence is low

REFERENCES

[1] Sergamumo užkrečiamomis ligomis Lietuvoje apžvalga 2016. Užkrečiamų ligų ir AIDS centras. 96-98 pages. http://www.ulac.lt/uploads/downloads/leidiniai/Sergamumo_apzvalga_2016.pdf
[2] Franc Strle, Gary P. Wormser, Linden T. Hu, John A. Branda, Joppe W. R. Hovius, Xin Li, and Paul S. Mead. Lyme borreliosis. Nat Rev Dis Primers 2, Article number: 16090 (2016).
[3] Cardenas-de la Garza, J.A., De la Cruz-Valadez, E., Ocampo-Candiani, J. et al. Eur J Clin Microbiol Infect Dis (2018). https://doi.org/10.1007/s10096-018-3417-1

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AB0904 EFFECTIVENESS AND SAFETY OF RITUXIMAB IN SYSTEMIC AUTOIMMUNE DISEASES: A CASE SERIES DESCRIBING THE EXPERIENCE OF AN AUTOIMMUNE DISEASES UNIT IN A 3-YEAR PERIOD

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Background: Rituximab (RTX) is a drug composed of chimeric monoclonal antibodies against the CD20 protein, producing a depletion of B lymphocytes. Nowadays, it is used to treat severe and refractory systemic autoimmune diseases (SAD).
Objectives: Analysing the effectiveness and safety of RTX in patients with SAD in clinical practice.
Methods: We conducted a retrospective analysis of patients with SAD treated at least once with RTX in the autoimmune diseases unit of our hospital in the last 3 years. We evaluated demographic, clinical and serological variables as well as the presence of adverse events (AE).
Results: Twenty two patients have been included (13 women and 9 men, mean age 63 ±15 years). The diagnosis were ANCA-associated vasculitis (31,8%), cryoglobulinemic vasculitis (18,2%), autoimmune hemolytic anemia (13,6%), systemic lupus erythematosus (9,1%), immune thrombocytopenia in antiphospholipid syndrome (9,1%) and one each of: Felty syndrome, IgG4-related disease, necrotizing myopathy and systemic sclerosis. Indications for treatment were renal disease in 36,4% of the cases, haematological manifestations in 27,3%, skin involvement in 13,6%, neurologic manifestations in 9,1% and other different reasons in the remaining 13,6%. RTX was used after therapeutic failure with previous treatments in 81.8% and as first line treatment in only 18.1% of the cases. RTX dose was 375 mg/m2 once weekly for 4 doses (54,5%) and 1000 mg on days 1 and 15 (45,5%). After rituximab, 77,3% of patients had complete response, 9,1% partial response, and 13,7% non-responding. There were 14 AE reported in 10 of the 22 patients (45,5%) (See table). Three severe infections were found: were 2 patients with invasive pulmonary aspergillosis and 1 patient with invasive cryptococcosis. All of them died within the next month after beginning RTX. One of those who were diagnosed of arpegillosis had never received steroids. The other two were treated with high dose of steroids for several months. One patient had a nonischemic cardiomyopathy (NIC) with systolic dysfunction that resolved 4 months after RTX discontinuation.
Conclusion: As far as we are concern, RTX is a useful and pretty safe biological agent in the treatment of refractory SAD. However, we must be aware of rare adverse effects such as NIC. In addition, given the potential severity of the infections found (although not totally attributable to RTX), we must closely follow up these patients for early diagnosis, treatment and even starting profilaxis in high risk patients.

N	Age	Sex	SAD	GFR	CDose	Mild AE	Moderate AE	Severe AE
1	48	W	CV	>90	1020	Increased liver enzymes Thrombocytopenia		
2	57	M	CV	66	700	Hypertension Diarrhea		
3	67	W	AAV	>90	1000		Pneumonia	
4	60	M	AAV	70	1000			NIC
5	39	W	AAV	8	2000			IPA
6	74	W	AAV	16	2000		PA	
7	52	M	AAV	9	1000			IC
8	77	M	AIHA	47	2175		Pneumonia	
9	76	M	APS	50	1000		Pneumonia	IPA
10	40	M	AAV	>90	900		Bronchospasm Rash	

C: Cumulative dose; W: Woman, M: Man; SAD: Systemic autoimmune disease; GFR: Glomerular filtration rate; AE: adverse event; CV: cryoglobulinemic vasculitis; AAV: ANCA associated vasculitis; APS: Antiphospholipid syndrome; AIHA: Autoimmune haemolytic anemia; NIC: nonischemic cardiomyopathy; IPA: Invasive pulmonary aspergilolosis; IC: Invasive cryptococcosis.

REFERENCES

[1] Cheungpasitporn W, Kopecky SL, Specks US, Bharucha K. Non-ischemic cardiomyopathy after rituximab treatment for membranous nephropathy. J Renal Inj Prev. 2017;6(1):18-25. Doi: 10.15171/jrip.2017.04

[2] Fianchi L, Rossi E, Murri R, De Stefano V, Pagano L.. Severe infectious complications in a patient treated with Rituximab for idiopathic thrombocytopenic purpura. Ann Hematol. 2007 86;225-226. DOI: 10.10.1007/s00277-006

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Fibromyalgia

AB0905 MAY CHRONIC CONSTIPATION-INDUCED CHRONIC INFLAMMATION AFFECT THE ONSET AND SEVERITY OF FIBROMYALGIA SYMPTOMS?

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Background: Up to 70% of fibromyalgia patients have functional bowel disorders as irritable bowel syndrome (IBS), constipation and diarrhea. Patients with chronic constipation may feature changes in microflora of large bowel, which are characterized by a relative decrease in obligate bacteria and a parallel increase in potentially pathogenic microorganisms and fungi. This condition causes chronic low-grade inflammation. It has been reported that as a result of chronic constipation, altered microbiota and intestinal permeability may be related to neurological diseases such as autism and Parkinson's disease.
Objectives: As you know, the etiology of fibromyalgia is related to both central nervous system and peripheral causes. So the aim of this study was to evaluate the relationship between chronic constipation and duration and severity of the disease in fibromyalgia.
Methods: The cross-sectional study was designed as two groups: fibromyalgia patients, who is diagnosed according to the ACR 2016 revised classification criteria, and healthy population. All study participants were 18 years and older. Subjects were excluded if they had systemic disease, neurological disease, cognitive problems and secondary fibromyalgia. The Fibromyalgia Impact Questionnaire (FIQ) was applied to fibromyalgia patient. All subjects were questioned in terms of IBS, functional constipation and functional diarrhea according to Roma IV criteria. The Patient Assessment of Constipation Quality of Life questionnaire (PACQLQ) and the Constipation Severity Instrument (CSI) were applied to patients with constipation.
Results: The study was completed with 40 patients in both groups. No difference was found between the fibromyalgia group and the control group in terms of age, body mass index and educational status ($p > 0.05$). While 10% constipation (n = 4), 0% IBS (n = 0) and 25% gastritis (n = 10) were observed in the control group; 45% constipation (n = 18), 22.5% IBS (n = 9), 67.5% gastritis (n = 27) were found in fibromyalgia group ($p < 0.01$). In fibromyalgia patients with constipation, the mean duration of constipation was 20.1 ± 8.9 and the mean duration of fibromyalgia symptoms was 16.0 ± 10.2 years. Fibromyalgia symptoms started in 16 of 18 patients after constipation (Mean year: 4.1 ± 5.3). Compared with constipated and non-constipated fibromyalgia patients, symptom duration and FIQ were significantly higher in constipated fibromyalgia patients ($p < 0.01$). The duration of constipation was correlated with duration of fibromyalgia symptom ($r^2 = 0.85$, $p = 0.000$), PACQLQ ($r^2 = 0.71$, $p = 0.001$) and CSI ($r^2 = 0.59$, $p = 0.01$). There was a correlation between FIQ and CSI ($r^2 = 0.96$, $p = 0.00$) and PACQLQ ($r^2 = 0.62$, $p = 0.006$).
Conclusion: The frequency of gastrointestinal symptoms increased in patients with fibromyalgia. As the severity of constipation increases, the symptoms of fibromyalgia are exacerbated. The presence of constipation findings before fibromyalgia suggests that low-grade chronic inflammation caused by constipation may have an effect on the onset of fibromyalgia. There is a need for a prospective cohort study to clarify this cause and effect relationship.

REFERENCES

[1] Nair AT, Ramachandran V, Joghee NM, Antony S, Ramalingam G. Gut Microbiota Dysfunction as Reliable Non-invasive Early Diagnostic Biomarkers in the Pathophysiology of Parkinson's Disease: A Critical Review. J Neurogastroenterol Motil. 2018 Jan 30;24(1):30-42.

[2] Goebel A, Buhner S, Schedel R, Lochs H, Sprotte G. Altered intestinal permeability in patients with primary fibromyalgia and in patients with complex regional pain syndrome. Rheumatology (Oxford). 2008 Aug;47 (8):1223-7.

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AB0906 RELATİONSHİP BETWEEN FİBROMYALGİA AND TRUNK MUSCLE PERFORMANCE

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Background: Muscle performance is adversely affected by pain, fatigue and low aerobic capacity in fibromyalgia syndrome(FMS).
Objectives: We compared trunk muscle performance of women with FMS and healthy individuals who have similar age and body mass index (BMI).
Methods: A total of 37 women with FMS and 32 healthy women were included this study. The demographic and clinical characteristics of the participants such as age, height, weight, body mass index (BMI), occupations, exercise habits were recorded. In semi-standing position with isokinetic dynamometer (BIODEX) at 60 ° -90 ° -120 °/second (s) angular velocities, trunk flexor and extensor muscle performances were evaluated. Flexor (flex) peak torque (PT), extensor (ext) PT values and flex/ext PT ratio (%) were noted.
Results: The mean age was 43.9 ± 8.1 years in FMS group and 43,7 ± 6,7 in control group. The mean BMI was 27.5 ± 4.19 in FMS group and 26.4 ± 4.08 in control group. There was no significant difference between the groups in terms of age and BMI ($p > 0.05$). As a result of isokinetic measurements of trunk muscles, extensor PT values were found significantly lower in women with FMS than C group at all three angular velocities ($p < 0.05$). The flexor PT values also were lower in FMS group but no statistically significance in flexor PT values between the groups ($p > 0.05$). When flexor/extensor PT ratio was compared, it was seen that this ratio increased in the FMS group.
Conclusion: There are many studies in the literature assessing upper and lower extremity muscle performances in FMS (1-2). To our knowledge, we first evaluated trunk muscle performances of patients with FMS and we found that trunk muscles, especially extensors, were significantly weaker in FMS group. As a result, in treatment of FMS, there is a need for more comprehensive randomized controlled studies showing the importance of strengthening exercises to improve trunk muscle performance.

REFERENCES

[1] Yetişgin A, Tiftik T, Kara M, Karabay İ, Akkuş S, Ersöz M. Isokinetic muscle performance of the hip and ankle muscles in women with fibromyalgia.Int J Rheum Dis 2016; 19 (6): 551-6.

[2] Güler H, Yıldızgören MT, Üstün N, Paksoy H, Turhanoğlu AD. Isokinetic Assessment of the Wrist Muscles in Females With Fibromyalgia. Arch of Rheumatol 2016; 31(3): 215-20.

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AB0907

AUTONOMIC AND INFLAMMATORY CHANGES IN FM AND ME/CFS AND THE CONTRIBUTION TO SIGNS AND SYMPTOMS

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Background: Dysautonomia describes a group of conditions associated with a malfunction of the autonomic nervous system. Symptoms of dysautonomia and inflammation have been described in Fibromyalgia (FM) and Myalgic encephalomyelitis (ME)/Chronic Fatigue Syndrome (CFS) [1–4]. Symptoms include increased disabling fatigue, pain, dizziness and digestive problems.
Objectives: This ongoing study investigates, for the first time, how a sympathetically mediated challenge and induced systemic inflammatory state impact on mood, pain, fatigue, and autonomic function.
Methods: In a randomized, double-blind, placebo-controlled study, 25 participants with FM and/or ME/CFS underwent an autonomic- and inflammatory challenge during three visits. Outcome measures included a range of questionnaires including the Profile of Mood States (POMS), Pain visual analogue scales (VAS), measures of heart rate (HR), Pressure Pain Threshold (PPT), alongside subjective pain and fatigue measures. Autonomic function was assessed using a passive non-invasive tilt-test (upright tilt of 60°) and active-stand (AS) with beat-to-beat HR and blood pressure monitoring. Remaining visits involved an inflammatory challenge using intramuscular typhoid- and saline (placebo) injection.
Results: Tilt-table test was positive in 20% participants and AS in 92% participants indicated by HR rise >30 bpm or a sustained HR of 120 bpm. Overall fatigue correlated with peak HR during tilt (r=.465, p=.025, n=23). There was a positive correlation between the average HR during AS under typhoid after controlling for placebo and average HR during tilt (r=.517, p=.049, n=15). Scores on the Wide Spread Pain Index (WPI) at screening correlated with the change in POMS pre-and post-typhoid after controlling for placebo (r=.479, p=.045, n=18). Scores on the Fibromyalgia Severity Scale correlated with the change in physical fatigue pre-and post-typhoid after controlling for placebo (r=.633, p=.015, n=14). Pain at screening correlated with change in physical fatigue pre-and post-tilt (r=.405, p=.044, n=25). Scores on the pain severity scale at baseline correlated with change in pain measured on a visual analogue scale pre and post tilt (r=.517, p=.049, n=15). Mean change in heart rate pre-post active stand correlated with a change in pain VAS pre-and post-typhoid after controlling for placebo (r=.582, p=.047, n=12).
Conclusion: Preliminary findings suggest that dysautonomia and induced inflammation significantly impacts on pain, fatigue, and autonomic function in FM and ME/CFS. On-going data collection of 100 participants (25 controls) will allow extended analyses to test how autonomic function and inflammation affect symptom domains that impact on quality of life.

REFERENCES

[1] McIntosh DN, Miller LJ, Shyu V, Hagerman RJ. Sensory-modulation disruption, electrodermal responses, and functional behaviors. Dev Med Child Neurol. 2007 Feb 13;41(9):608–15.
[2] López-Solà M, Woo CW, Pujol J, Deus J, Harrison BJ, Monfort J, et al. Towards a neurophysiological signature for fibromyalgia. Pain. 2017;158 (1):34–47.
[3] Solano C, Martinez A, Becerril L, Vargas A, Figueroa J, Navarro C, et al. Autonomic dysfunction in fibromyalgia assessed by the Composite Autonomic Symptoms Scale (COMPASS). J Clin Rheumatol. 2009;15(4):172–6.
[4] Maia MM, Gualano B, S??-Pinto AL, Sallum AME, Pereira RMR, Len CA, et al. Juvenile fibromyalgia syndrome: Blunted heart rate response and cardiac autonomic dysfunction at diagnosis. Semin Arthritis Rheum. 2016;46(3):338–43.

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AB0908

ARE CHRONIC PAIN SYNDROMES BEHIND STATIN-ASSOCIATED MUSCLE PAIN?

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Background: Statin myalgia, defined as muscle pain or weakness without elevation of CPK levels, is a common complaint among statin users. Chronic pain syndromes affect a high percentage of the population[1], therefore it is likely that such syndromes may confound reports of statin myalgia.
Objectives: The objective of this study was to compare the occurence of chronic pain between patients taking statins who later developed myalgia with those who did not.
Methods: This study included 112 statin-treated patients at the Lipid Center in Tel Hashomer - 56 of whom were diagnosed with Statin Asocciated Muscle Symptoms [SAMS] and 56 patients who were not. Questionnaires were used to assess diagnoses of fibromyalgia, pain intensity, functional impairment, anxiety and depression in the study population.
Results: Patients with statin myalgia were more likely to fulfill the diagnostic criteria for fibromyalgia than patients without stating myalgia (11 vs. 0, respectively). Patients in the SAMS group also exhibited higher levels of anxiety and depression in comparison with the control group. Female sex, scoring in Brief Pain Inventory pain intensity, and a Hamilton level indicative of an anxiety disorder were found to be significant predictors for fibromyalgia in patients suffering from stating myalgia.
Conclusion: A significant percentage of patients who were thought to suffer from statin myalgia fulfill the criteria for fibromyalgia, depression or anxiety. Detection of these patients and treatment of their priamry pain or psychiatric illness may prevent cessation of effective statin therapy.

Table 1 - Univariate analysis of myalgia cases *versus* controls.

Variable	*Controls*	*Myalgia cases*	*Statistical significance*
Age	49.71±12.91	54.07±10.25	0.075
Gender			0.033
Male	40 (71.4%)	28 (50.0%)	
Female	16 (28.6%)	28 (50.0%)	
BMI	25.66±3.29	27.06±4.71	0.070
Current smoking status	9 (16.1%)	8 (14.3%)	1.000
Psychiatric disorders	6 (10.7%)	4 (7.1%)	0.742
CPK (IU/L)	213.16±554.44	310.63±715.67	0.066
Prevention purpose			0.538
Primary prevention	41 (73.2%)	37 (66.1%)	
Secondary prevention	15 (26.8%)	19 (33.9%)	
Disease length	11.05±8.41	13.34±8.39	0.070
WPI	0.43±1.02	3.29±3.31	<0.0001
Hamilton Depression scale	3.89±4.20	6.46±4.82	<0.0001
Hamilton Anxiety scale	5.48±4.94	9.71±6.23	<0.0001
Fullfilling FM criteria	0 (0.0%)	11 (19.6%)	0.001

REFERENCE
[1] Cho L, Rocco M, Colquhoun D, et al. Clinical Profile of Statin Intolerance in the Phase 3 GAUSS-2 Study. Cardiovasc Drugs Ther 2016;30(3):297–304.

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Back pain, mechanical musculoskeletal problems, local soft tissue disorders

AB0909 EFFICACY AND SAFETY OF ULTRASOUND GUIDED ASPIRATION AND INTRA_LESIONAL CORTICOSTEROIDS INJECTION OF RUPTURED BAKER'S CYST

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Background: Baker's cyst is the most common mass in the popliteal fossa and results from fluid distension of the gastrocnemio-semimembranosus bursa. The most common complication of Baker's cyst is the rupture or dissection of fluid into the adjacent proximal gastrocnemius muscle belly, which results in a pseudothrombophlebitis syndrome mimicking symptoms of DVT.
Treatment of ruptured Baker cysts ranged from conservative management to surgical resection.
Ultrasonographic guided aspiration and corticosteroids injection may be an effective and easy method of management of these cases.
Up to the best of our knowledge, this is the first study to detect the efficacy and safety of ultrasonographic guided aspiration and injections of ruptured Baker cysts.
Objectives: To evaluate the efficacy and safety of ultrasonographic guided aspiration and local corticosteroids of ruptured Baker cysts based on follow-up clinical and sonographic results.
Methods: A retrospective study was conducted on 42 patients (12 males and 30 females, mean age 36 +/- 10 SD years) affected by a ruptured Baker cysts associated to knee joint disorders in the period between January 2013 to January 2019.The diagnosis was done by clinical presentation of acute calf pain, swelling, tenderness at the calf muscles and ultrasonographic evidences of ruptured backer cysts in the form of free fluid collection in the calf connected to a well defined cyst at the back of knee.
All cases were treated by ultrasonographic guided aspiration and intra_lesional injection of corticosteroids once or twice one week a part. Follow up were done on a weekly basis until complete resolution of symptoms then 3 months later. Visual analogue scale (VAS) for calf pain and Rauschning-Lindgren and Lysholm Knee Scoring Scales were used to assess pre/post-injection knee functions.
Results: The primary diagnoses to patients presented with ruptured Baker cyst in this study were as follow: 18 (42.8%) cases with rheumatoid arthritis, 15 (37.5%) cases with osteoarthritis and 9 (21.4%) cases with psoriatic arthritis.
Clinical parameters (VAS for calf pain and Rauschning-Lindgren score) improved significantly in all patients at both post injection evaluation visits.
Rauschning-Lindgren score was significantly lower after US guided injections (mean, 0; range, 0-1) than at baseline (mean, 2; range, 1–2); $p < 0.001$ (table1).
VAS for calf pain also significantly lower after US guided injections (mean,0.5; range, 0-1) than at baseline (mean, 9.5; range, 0-10); $p < 0.001$.
Ultrasonographic features improved significantly with complete disappearance of free fluid at the calf in 35 (83.3%) cases one week after the injection.
As regards Baker cyst only 5 (11%) cases showed complete disappearance of the backer cyst and in the majority of cases 37 (88%) there were persistent Baker cysts.
No side effects were reported in all cases.

Abstract AB0909 Table 1. Clinical results of Baker cyst excision (Rauschning and Lindgren scale and VAS for calf pain)

	Pre injection	1 week later	3 months later
grade 0	0	30	39
Grade 1	0	8	3
Grade 2	6	4	0
Grade3	36	0	0
VAS for calf pain	9.5	1.5	0.5

VAS; visual analogue scale
Conclusion: Ultrasonographic guided aspiration and intra_lesional corticosteroids injection is an effective and safe method in management of ruptured Baker cysts.

REFERENCE
[1] Nigerian Journal of Orthopaedics and Trauma June 2009: 8 (1): 31-32

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AB0910 EFFECTIVE RESTORING MOTION AND EFFECTIVE TREATMENT OF MYOFASCIAL AND NEUROPATHIC LOW BACK PAIN BY TARGATED DRY NEEDLING USING ULTRASOUND GUIDANCE

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Background: Low back pain (LBP) involves both myofascial and neuropathic components of pain. Neuropathic pain is a widespread problem, require continuous consumption of medications. Muscle spasticity might evoke nerve compression, dry needling (DN) of myofascial trigger points (MTrP) under ultrasound (US) guidance is effective method for treatment myofascial pain [1,2] restoring posture [3] and can be effective for neuropathic pain.
Objectives: The aim was to evaluate efficacy of dry needling under US guidance for treatment myofascial and neuropathic components of LBP.
Methods: We included 52 patients, 37 females, aged 18-84 years (the average was 55 years) with clinically diagnosed chronic low back pain with neuropathic component with clinically diagnosed low back pain over 3 month with neuropathic component and reduced motility in spine, pelvis and lower extremity. All patients had symptoms over 3 month, underwent general exam, including MRI, laboratory, neurologic, orthopedic tests. We conducted precise physical tests and neuromuscular ultrasound using M-mode and evaluated nerves and motion in intervetrebral spaces, pelvis, intrinsic foot and leg muscles. We conducted ultrasound survey at the levels of predicted nerve injury. Patients received DN of MTrP under US guidance according to approach by R.Bubnov [1,2], considering nerve entrapment area. Visual analogue scale (VAS, 0-10) and Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scores were measured before, immediately after, 24 hours, and 7 days after intervention.
Results: After 7 days, VAS scores showed pain improvement from 7.4 to 2.2; LANSS scores improved from 16 to 4. In diabetic and postherpetic neuropathy cases we obtained similar results as in rest of patients ($p < 0.05$). US demonstrated improvement nerve structure, increasing motility, contractility (muscle contracted/rested thickness) on M-mode during functional tests and walking in all levels. Improvement of neuropathy signs as decrease of fascicles diameter from 2 to 0.9 mm measured on US in sciatic nerve, both in tibial, peroneal portions, data correlated with self-assessment pain decrease ($r > 0.8$). Preferably MTrP were identification in supinator muscle (wrist pain); rotator muscles (infraspinatus, supraspinatus, subscapular and teres minor muscles); scalene muscles; obliquus capitis muscles, and also in fascial tissue.
Conclusion: Dry needling under US guidance guidance effectively reduce myofascial pain, ameliorate symptoms of neuropathy and local muscle hypomotility in low back pain. Further research needed for development US patterns and study causation in chain spasticity-contractility- motion-neuropathic pain.

REFERENCES

[1] Bubnov RV: The use of trigger point "dry" needling under ultrasound guidance for the treatment of myofascial pain (technological innovation and literature review). Lik Sprava 2010, 5-6:56-64.

[2] Bubnov RV: Evidence-based pain management: is the concept of integrative medicine applicable? EPMA J 2012, 3(1):13.

[3] Bubnov R, Kalika L, Babenko L. AB1199 Dynamic ultrasound for multilevel evaluation of motion and posture in lower extremity and spine. Annals of the Rheumatic Diseases 2018;77:1699. http://dx.doi.org/10.1136/annrheumdis-2018-eular.3949

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AB0911 REFRACTORY LOW BACK PAIN AND LUMBAR CT-GUIDED STEROID INFILTRATION. STUDY OF 582 PROCEDURES FROM THE SAME CENTER

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Background: Mechanical low back pain which is refractory to analgesic and rehabilitative treatment is an important cause of disability. The primary objective of corticosteroid (CS) lumbar infiltratation is to accelerate the recovery process and to avoid surgery. However, its use is not without controversy.

Objectives: To review the indications, efficacy and complications of lumbar computed tomography (CT)-guided CS infiltration.

Methods: Retrospective study (January 2012 - April 2018) of lumbar CT-guided CS infiltrations performed in a single center. The epidemiological variables, underlying pathologies, approach of injection, used CS (dexamethasone during the whole period and triamcinolone until February 2015), efficacy after 1 and after 3 months and complications were registered. In addition, a comparative study of the efficacy according to indication, type of CS and approach of injection was performed.

Frequencies and percentages were used in qualitative variables, mean ±SD in quantitative and for the comparison between groups Chi2 test or Fisher test was used in categorical variables and Student T test or U of Mann-Whitney in quantitative. Statistical analysis was performed with IBM SPSS v.23.

Results: 582 procedures were performed in 445 patients (1 infiltration in 445 patients, 2 in 106, 3 in 23, 4 in 7 and 5 in 1). The mean age±SD was 58.6±14.8 years with a male/female ratio of 224/221. Traumatology was the service with highest demand (88.8%) followed by rheumatology (4.8%). The indications were disc herniation (43.1%), lumbar spinal stenosis(36.4%), postoperative fibrosis (14.8%), spondyloarthrosis (2.7%) and other [listhesis, synovial cyst and facet joint syndrome] (2.8%). Posterior epidural access was performed in 27.1% of the procedures, foraminal in 17.9% and lateral recess in 55%. The used CS were dexamethasone (66.3%) and triamcinolone (33.7%). In 86% of patients the oral analgesic treatment had been ineffective.

Improvement was observed in 68% of patients at the first month (table) regardless of the indication, approach of injection and CS used and in 63.2% at 3 months.

Only 124 patients (21.3%) required surgery due to the persistence of pain, mostly within the first year after infiltration (66.9%).

Clinical efficacy showed no statistically significant differences regarding to the indication of the procedure. On the other hand, we observed a significantly higher improvement of the pain through the foraminal and lateral recess than through the epidural at 3 months (p= 0.002). Regarding the CS used, the improvement was significantly greater with triamcinolone compared to dexamethasone in the first and third months (p= <0.001).

Concerning safety, there were 16 cases (2.7%) of local complications (5 punctures of the thecal sac, 4 extravasations of the contrast and 7 transient pain in lower extremities) and 5 (0.9%) systemic complications (3 allergic reactions and 2 syncope due to low blood pressure), without clinical relevance and they were not associated with the indication, approach of injection and CS used.

Conclusion: In our series disc herniation, lumbar stenosis and postoperative fibrosis were the most common indications. Improvement was observed in 68% and in 63.2% of the patients in the first and third months respectively.

TABLE. Clinical evolution of pain at the first month according to indication, approach of injection and used steroid.

	Total response, n (%)	Partial response, n (%)	No response, n (%)	Worsening, n (%)	TOTAL, n (%)
INDICATION					
-Disc herniation	12 (4.8%)	167 (66.5%)	66 (26.3%)	6 (2.4%)	251 (43.1%)
-Lumbar spinal stenosis	5 (2.3%)	131 (61.8%)	75 (35.4%)	1 (0.5%)	212 (36.4%)
-Postoperative fibrosis	1 (1.2%)	56 (65.1%)	29 (33.7%)	0 (0%)	86 (14.8%)
-Spondyloarthrosis	1 (6.2%)	11 (68.8%)	4 (25%)	0 (0%)	16 (2.8%)
-Other (listhesis, synovial cyst and facet joint syndrome)	1 (5.9%)	11 (64.7%)	5 (29.4%)	0 (0%)	17 (2.9%)
APPROACH					
-Lateral recess	14 (4.4%)	207 (64.7%)	94 (29.4%)	5 (1.5%)	320 (55%)
-Epidural	3 (1.9%)	94 (59.5%)	60 (38%)	1 (0.6%)	158 (27.1%)
-Foraminal	3 (2.9%)	75 (72.1%)	25 (24%)	1 (1%)	104 (17.9%)
STEROID					
-Dexamethasone	8 (2.1%)	234 (60.6%)	140 (36.3%)	4 (1%)	386 (66.3%)
-Triamcinolone	12 (6.1%)	142 (72.5%)	39 (19.9%)	3 (1.5%)	196 (33.7%)
TOTAL n=582	20 (3.4%)	376 (64.6%)	179 (30.8%)	7 (1.2%)	582 (100%)

Figure 1

Only 21% required surgery. Triamcinolone (although its use is currently discouraged because it is a particulate CS), foraminal infiltration and lateral recess proved to be more effective for pain control.

In this study, lumbar CT-guided CS infiltration in patients with refractory low back pain is an accessible, minimally invasive, safe and effective procedure in long term.

Disclosure of Interests: None declared

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AB0912 EXTRACORPOREAL SHOCKWAVE VERSUS MUSCULOSKELETAL MESOTHERAPY FOR ACHILLES TENDINOPATHY IN ATHLETES

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Background: Achilles tendinopathy (AT) is considered as one of the common tendon pathologies, which occurs mainly in athletes. Different conservative treatment options have been introduced and used for symptoms relief of At but with short-term effect.1 Extracorporeal shockwave treatment (ESWT) provides longer effects and could be used in cases fail to respond to conservative treatments.2 Mesotherapy is widely practiced in sports medicine as multiple injections, often of anti-inflammatory medications into the subcutaneous fat overlying a region of musculoskeletal pain. The effect appears unclear but may be due to localized tissue uptake of anti-inflammatory medication which may provide symptomatic relief especially in insertional Achilles tendinopathy 3

Objectives: In this study, we aimed to evaluate the effect of extracorporeal shockwave treatment
(ESWT)and mesotherapy on chronic Achilles tendinopathy in athletes

Methods: 40 patients with chronic AT were diagnosed clinically & using high resolution ultrasound (US) according to the Eular guide lines and randomly allocated in two groups, first receive ESWT, other group underwent mesotherapy (MT) one session once a week for 4 weeks to the 2 groups. Pain, ankle-hindfoot scale of the American Orthopedic Foot and Ankle Society (AOFAS) 4 & US were recorded at baseline, 4 and 12 weeks after intervention

Results: Both groups improved during the treatment and follow-up period. The mean VAS score decreased from 7.55 to 3 in the ESWT group and from 7.70 to 4.30 in MT group. There was no significant difference in terms of AOFAS and VAS scores between both groups at 4 weeks follow up while Mean AOFAS & VAS scores were significantly different between ESWT and MT groups at 12 weeks of follow-up (P = 0.013) (P = 0.47). US assessment significantly improved after 12 weeks in ESWT group as regards tendon thickness, calcifications(figure1,2) and doppler signal.

Conclusion: ESWT showed improvement of pain and inflammation of AT than MT injections which was documented by the decreased VAS, increased AOFAS scores as well as US improved findings shortly after the treatment as well as on late follow up.

REFERENCES

[1] Diehl P, Gollwitzer H, Schauwecker J, Tischer T, Gerdesmeyer L. Conservative treatment of chronic tendinopathies. Orthopade. 2014;43:183–93.

[2] Moayednia A, Haghdani S, Khosrawi S, Yousefi E, Vahdatpour B. Long-term effect of extracorporeal shock wave therapy on the treatment of chronic pelvic pain syndrome due to non bacterial prostatitis. J Res Med Sci. 2014;19:293–6

[3] Paoloni J. Current Strategy in the Treatment of Achilles Tendinopathy. In: Čretnik Andrej., editor. Achilles'tendon. InTech Rijeka; Croatia: 2012

[4] Madeley NJ, Wing KJ, Topliss C et al. Responsiveness and validity of the SF-36, Ankle Osteoarthritis Scale, AOFAS Ankle Hindfoot Score, and Foot Function Index in end stage ankle arthritis. Foot Ankle Int 2012;33:57–63

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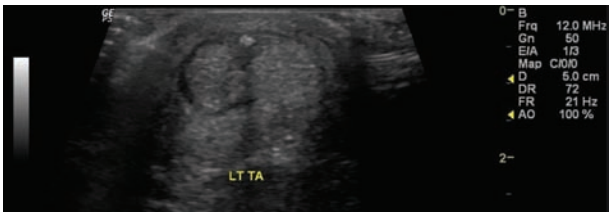
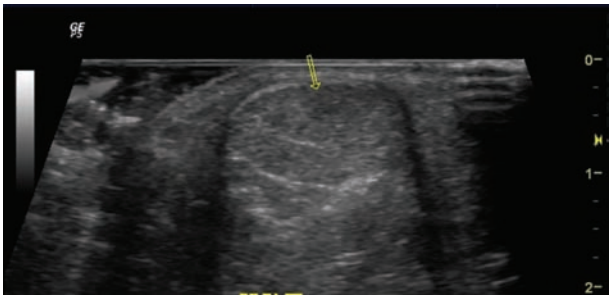


Fig (1) Ultrasound Transverse scan over left TA of male 25 squash player shows hyperechoic dot of calcification inside the tendon with acoustic shadowing before treatment.

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Fig(2) same patient, after 3 months of treatment with ESWT shows disappearance of calcification

Disclosure of Interests: None declared
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AB0913 **THE ROLE OF BISPHOSPHONATES IN THE MANAGEMENT OF SPONTANEOUS OSTEONECROSIS OF THE KNEE (SONK)**

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Background: Spontaneous osteonecrosis of the knee (SONK) was first described by Ahlbäck, Bauer and Bohnein in 1968 when they identified 39 patients with radiolucent lesions of subchondral bone in the medial femoral condyle which represented a manifestation of osteonecrosis. The aetiology and pathogenesis of SONK remains unclear with possibilities including microvascular compromise, reduced bone mineral density, and mechanical disruption within the knee. The treatment compromises of conservative, medical and surgical options depending on the severity of osteonecrosis identified on imaging. Lai *et al* (2005) demonstrated the beneficial effect of alendronate in the prevention of early collapse of the femoral head in patients with nontraumatic osteonecrosis. However, the role of bisphosphonates in the treatment of SONK is debated and the evidence is based upon a few studies.
Objectives: To assess the evidence for the use of bisphosphonates in SONK.
Methods: A literature search was conducted to identify studies reporting the effect of bisphosphonates in the treatment of SONK and the usefulness and validity of their conclusions was subsequently assessed.
Results: We have identified one randomised controlled trial and four case series investigating the use of a bisphosphate on the clinical and radiological outcome in patients with osteonecrosis of the knee. All four case series showed improvements with bisphosphonates on patient visual analogue scale (VAS) and radiological outcome. However, the sole randomised controlled trial reported that bisphosphonates had no additional benefit over conservative measures and anti-inflammatory medications after 24 or 48 weeks both functionally and radiographically. These studies had a small number of participants and the size of the osteonecrotic lesion was either small, which traditionally is managed conservatively, or not interpreted in the context of the results.
Conclusion: The role of bisphosphonates in the treatment of SONK remains unclear. Further randomised controlled trials would be beneficial in these patients with emphasis on the symptom duration and the size of the osteonecrotic lesion.

REFERENCES

[1] Agarwala, S., Sharoff, L. and Jagani, N., 2018. Effect of zoledronic-acid and alendronate on bone oedema and pain in spontaneous osteonecrosis of the knee: a new paradigm in medical management. Revista Brasileira de Ortopedia (English Edition). Accessed via: https://www.sciencedirect.com/science/article/pii/S2255497118300089 on 31st December 2018.
[2] Breer, S., Oheim, R., Krause, M., Marshall, R.P., Amling, M. and Barvencik, F., 2013. Spontaneous osteonecrosis of the knee (SONK). Knee Surgery, Sports Traumatology, Arthroscopy, 21(2), pp.340-345.
[3] Jureus, J., Lindstrand, A., Geijer, M., Roberts, D. and Tägil, M., 2012. Treatment of spontaneous osteonecrosis of the knee (SPONK) by a bisphosphonate: A prospective case series with 17 patients. Acta orthopaedica, 83(5), pp.511-514.
[4] Kraenzlin, M.E., Graf, C., Meier, C., Kraenzlin, C. and Friedrich, N.F., 2010. Possible beneficial effect of bisphosphonates in osteonecrosis of the knee. Knee surgery, sports traumatology, arthroscopy, 18(12), pp.1638-1644.
[5] Lai, K.A., Shen, W.J., Yang, C.Y., Shao, C.J., Hsu, J.T. and Lin, R.M., 2005. The use of alendronate to prevent early collapse of the femoral head in patients with nontraumatic osteonecrosis: a randomized clinical study. JBJS, 87(10), pp.2155-2159.
[6] Meier, C., Kraenzlin, C., Friederich, N.F., Wischer, T., Grize, L., Meier, C. R. and Kraenzlin, M.E., 2014. Effect of ibandronate on spontaneous osteonecrosis of the knee: a randomized, double-blind, placebo-controlled trial. Osteoporosis international, 25(1), pp.359-366.

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AB0914 **EFFECT OF VITAMIN D SERUM CONCENTRATION ON ARTRALGIA INDUCED BY ADJUVANT THERAPHY WITH AROMATASE INIBITORS IN NON METASTATIC BREAST CANCERS SURVIOVORS**

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Background: Hand arthralgia is often reported by breast cancer patients treated with adjuvant hormonal therapy. Aromatase inhibitors (AIs) improve survival in postmenopausal women with hormone-sensitive breast cancer, but can cause joint pain and stiffness (2). Low concentration of vitamin D in adults can cause musculoskeletal pain and joint discomfort (1). No data are available to date, on serum concentrations of (25-hydroxyvitamin D) [25 (OH) D_3] vitamin D in AI-treated patients and possible relationship with arthralgia.
Objectives: To evaluate possible correlation between different 25 (OH) D_3 serum concentrations and hand arthralgia in patients with breast cancer treated with AIs.
Methods: All patients that during the AIs therapy develop arthralgia referred to the rheumatologist; they reported the pain following the VAS (visual analogic scale) and contemporary performed a sample blood for dosage of vitamin D as well as biomarkers for inflammation and autoimmunity to exclude concomitant immune/inflammatory rheumatic musculoskeletal causes.
Results: In a group of 63 women taking AIs (mean age 62.3±9.8years; disease duration from first assumption of AIS 10.6±3.2 months) 81% reported hand arthralgia and stiffness within the first year of follow-up; the most prevalent site of pain localization was bilateral hands (85%). Symptom was associated with minimal increase of serum parameters of inflammation (the mean value of C-reactive protein was 7.1±3.0 mg(L (normal value 0-5) but negative autoimmune profile (negative rheumatoid factors and anticitrullinated protein antibodies). The mean 25(OH)D_3 serum concentration was 18.4± 8.5 ng/ml. Only 9% of women had an adequate ($\geq$ 30 ng/ml) [25 (OH) D_3] vitamin D serum levels, 70% were insufficient (> 10 < 20 ng/mL), and 21% were severely deficient (< 10 ng/mL). 55% of patients started AIs after chemotherapy. From the group that received AIs after chemotherapy 77% patients with arthralgia were found during the first years of hormonal therapy, in the group that previously did not take chemotherapy 88% of patients referred arthralgia. There was any

difference on vitamin D serum levels between patients previously treated or not treated with chemotherapy (17.8± 7.8vs 19.3± 9.7 p=0.6). After subdivision of patients that referred hand arthralgia according to the different type of AIs used: 22% have been treated with tamoxifen, 30%, anastrozole and 48% letrozole. Therefore, the baseline serum vitamin D concentrations did not significantly predict arthralgia in the overall group (P = 0.70) or separately in the single AIs group (anastrozole (P = 0.60) or tamoxifene(P=0.30) or letrozole (P = 0.60, respectively).

Conclusion: Vitamin D serum concentrations in women treated with AIs are at lowest ranges in the majority of the patients analysed, but no apparent interference with musculoskeletal symptoms was found related to the different concentrations; the cause of arthralgia might be better related to estrogen deficiency induced by AIs their self.

REFERENCES

[1] Kathryn R, et al. 2017 Ther Adv Musculoskelet Dis.9(6):131-135
[2] Hsieh KP, et al. 2014. PLoS One, 9, e87027.

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AB0915 ЭФФЕКТИВНОСТЬ АКУПУНКТУРЫ ПРИ ТЕРАПЕВТИЧЕСКИХ УПРАЖНЕНИЯХ ПРИ ЛЕЧЕНИИ МИОФАСЦИАЛЬНОЙ БОЛИ В НИЖНЕЙ ЧАСТИ СПИНЫ

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Background: Myofascial pain syndrome in the lower back is one of the most common diseases. At the current time, there are no ideal ways to treat this disease. Pharmacological treatments are not suitable for many patients. Regular use of painkillers and NSAIDs is associated with the risk of serious adverse reactions in patients. Using only pharmacotherapy without using non-pharmacological treatment methods is not a rational approach to treating such patients.

Acupuncture has a wide range of effective methods of combating combat syndrome that can have a quick positive effect, and, unlike drugs, this method remains safe. Therapeutic exercise is a treatment method that is able to raise the general threshold of pain sensitivity by including non-specific adaptation mechanisms [1]. This effect develops slowly, but it acts for a very long time.

Objectives: The purpose of this study is to compare the effectiveness of acupuncture with massage in the treatment of myofascial pain in the lower back with complex treatment, including exercise.

Methods: A prospective clinical study was conducted with patients suffering from myofascial pain syndrome in the lower back, which were randomly divided into one of two groups: patients (60 cases) who received combined treatment including massage, acupuncture and exercise therapy, and patients (30 cases) of group 2 (G2) who received only massage procedures and acupuncture without medical gymnastics. They were assigned to group 1 (G1). The age composition of the G1 group of patients from 31 to 70 years. Gender composition - 22 (37%) - women, and 38 (63%) - men.

All patients received treatment 5 times a week (from Monday to Friday, excluding Saturday and Sunday), the total duration of the rehabilitation course is 10 days. The therapeutic program included the following non-drug methods of exposure: for G1, 30 minutes - an acupuncture session, 20 minutes a back massage session, and at least 45 minutes of exercises in the gymnastics hall with an instructor in physical therapy. G2 patients received similar non-drug therapy with the exception of classes in the gymnastics room. The visual-analogue scale (VAS) was used as a method of performance evaluation, which was evaluated at the beginning of the study, at the fifth, ninth and last visit to the clinic.

Results: The average time between the onset of clinical symptoms and the first day of treatment was 34.6 days. In 80% of patients, a history of pain lasted for more than 3 months. 89 patients (98%) completed the protocol: 60 (100%) in G1 and 29 (97%) in G2. The average VAS score in G1 was 6.9 at the beginning of the study and after the tenth session it dropped to 2, 6. A significant decrease in pain was registered in the G2 group (from 6.9 at the beginning of the study to 3.3 after the tenth session). A statistically significant difference (p <0. 05) between different sessions was noted.

In order to assess the period of time during which the effect of treatment is maintained, all patients were asked to send a subjective assessment on the VAS scale to the attending physician after completion of treatment monthly for 12 months. When analyzing these data, it was established that the inclusion of physiotherapy exercises preserves a clear effect of therapy for 3.1 months longer than without the use of therapeutic gymnastics.

Conclusion: The results indicate high efficiency acupuncture in the treatment of myofascial pain syndrome, however, its combination with therapeutic exercises allows to better consolidate the effect and contributes to a longer remission of pain syndrome. It is necessary to establish clear criteria for inclusion in the treatment of exercise

REFERENCE

[1] Krysyuk O.B., Lutkov V.F., Smirnov G.I., Shadrin D.I. Physiotherapy and massage in the complex rehabilitation of athlete. Ministry of Sport of the Russian Federation, PF Lesgaft National State University of Physical Education, Sport and Health, St. Petersburg. St. Petersburg, 2014.

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AB0916 INVESTIGATION OF PAIN AND DEPRESSION IN CANCER OUTPATIENTS RECEIVING CHEMOTHERAPY

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Background: Cancer treatments such as chemotherapy contribute to the development of depression and pain (1). Prevalence of pain ranges from 14% to 100% and depressed symptoms occur 1-42% in cancer patients (2). The empirical evidence indicates that pain is often untreated and may induce depression in cancer patients (1,2) and depression affects the management of symptoms such as pain (3). Therefore, depression and pain have interrelated effects with each other. Pain and depression in cancer patients lead to discontinuation of therapy, difficulties in controlling symptoms and negative treatment compliance (4). Studies report the need for more research on pain and depression associated with cancer treatment (2).

Objectives: The objectives of this study are to: 1) compare the depression levels of painful and painless cancer patients who received outpatient chemotherapy; and 2) investigate the relationship between pain and depression in these patients.

Methods: This study was carried out in outpatient chemotherapy unit of Hacettepe Oncology Hospital based in Ankara, the capital city of Turkey. The visual analog scale (VAS) was used to investigate if the patients may have had pain. The Brief Pain Inventory (BPI) was of help to assess the pain severity and pain interference on the function of patients while the Beck Depression Inventory (BDI) was applied to evaluate depression.

Results: The study findings are based on the outcomes of 27 cancer outpatients receiving chemotherapy. Their mean age was 56.89±11.08 years (age range; 31–73). Almost half of the of patients had pain (48.15%). There was a difference between the depression scores of the patients who had pain and the other patients without pain but this is not statistically significant (p=.07). The depression scores of painful patients and non-painful patients were 13 and 6, respectively. There was a moderate association between scores of pain severity and depression (r=0.4, p=0.04). Moreover, there was a high association between the score of depression and pain interference on function (r=0.61, p=.016).

Conclusion: This study shows that pain is related with depression in cancer outpatients receiving chemotherapy. Depression may occur more frequently in patients who have experienced pain than in patients with no pain and also depression is likely to increase pain in cancer patients. Therefore, the addition of emotional and psychosocial components for treatment procedures and effective pain management may have positive effects on the treatment of cancer outpatients receiving chemotherapy.

REFERENCES

[1] Kelly, Debra Lynch, et al. "Relationships Among Fatigue, Anxiety, Depression, and Pain and Health-Promoting Lifestyle Behaviors in Women With Early-Stage Breast Cancer." Cancer nursing (2019).
[2] Patrick, D. L., et al. "National Institutes of Health State-of-the-Science Conference Statement: symptom management in cancer: pain, depression, and fatigue, July 15-17, 2002." Journal of the National Cancer Institute 95.15 (2003): 1110-1117.
[3] Mercadante, Sebastiano, et al. "Symptom hyper-expression in advanced cancer patients with anxiety and depression admitted to an acute supportive/palliative care unit." Supportive Care in Cancer (2019): 1-8.

[4] Güleç, Gülcan, et al. "Anxiety, depression and coping behaviors with pain in cancer patients who are aware or unaware of their cancer." Ağrı-The Journal of The Turkish Society of Algology 29.3 (2017): 109-116.

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AB0917 PATTERN OF SERUM CHOLECALCIFEROL (VITAMIN D3) LEVEL AMONG THE FEMALE IN RELATION TO CLOTHING'S

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Background: Both clinical and subclinical low level vitamin D is common[1]. Various kinds of health hazard including musculoskletal symptoms are frequently seen among the Vitamin D deficients. It is also not uncommon even in a sunny country. Lack of sun exposure, particularly female using veil may be an important cause.
Objectives: To assess the relationship between using veil and serum vitamin D_3 (cholecalciferol) level
Methods: This prospective cross-sectional descriptive study was conducted during July 2017 to June 2018. Patients with common complaints related to lack of Vitamin D (muscle cramp, myalgia, fatigue, bone pain, generalized weakness, difficulty in getting up, climbing stairs and pain in weight bearing joints) were enrolled. Patient having other disease were excluded from study. Serum cholecalciferol was measured for each patient. Race, occupation, educational status, skin complexion, body mass index, sunlight exposure, covering of body with clothing's and use of sunscreen were taken under consideration in final analysis. Correlation of serum cholecalciferol level with different types of veils (Burkha, halve sleeve, full sleeve, quarter sleeve and Hijab) of individual's was analyzed.
Results: A total 79 female patients were enrolled after screening 108. All of them were of multi-ethnic Asian origin. Age distribution of them is 17 to 39 years 34.2%, 40 to 50 years 38%, 51 to 70 years 26.6% and above 70 years 1.3%. Maximum (93.7%) of them were house wife, 91.1% had no adequate sun exposure and 81% had no skin exposure to sunlight. Among clothing 79.7% used Burkha, 5.1% halve sleeve, 2.5% full sleeve and 12.7% quarter sleeve. Among Burkha 28.6% (18), 55.6% (35) & 15.9% (10) and among quarter sleeve 50% (5), 40% (4) & 10% (1) had deficient, insufficient & sufficient vitamin D level respectively while 2 (100%) female with full sleeve and 4 (100%) female with halve sleeve had deficient and insufficient vitamin D level respectively. The cholecalciferol level among the users of veil is shown in Table-1. There was no significant difference between different types of clothing's (Table: 2).

Abstract AB0917 Table 1. Weight, height and Vitamin D level in different types of clothing's.

Type of clothing		Wt in Kg	Ht in cm	Vit D level (range) in ng/ml
Burkha	Mean	68.63	150.43	(8-40) 23.921
	N	63	63	63
	Std. Deviation	11.706	6.574	6.3074
Halve sleeve	Mean	70.75	150.50	(25-30) 27.000
	N	4	4	4
	Std. Deviation	17.500	1.000	2.4495
Full sleeve	Mean	64.00	145.50	(15-19) 17.000
	N	2	2	2
	Std. Deviation	8.485	13.435	2.8284
Quarter sleeve	Mean	63.40	150.10	(16-38) 23.350
	N	10	10	10
	Std. Deviation	10.834	6.437	6.7497
Total	Mean	67.96	150.27	(8-40) 23.829
	N	79	79	79
	Std. Deviation	11.790	6.488	6.2418

Abstract AB0917 Table 2. Difference of Vitamin D level in relation to clothing's (ANOVA)

Gender		Sum of Squares	df	Mean Square	F	P value
Female	Between Groups	136.315	3	45.438	1.174	0.325
	Within Groups	2902.568	75	38.701		
Total	3038.883	78				

Conclusion: Main source of Vitamin D is sunlight. Proper exposure to sunlight is essential for adequate vitamin D level even in a sunny country. Regarding in vitamin D absorption from sunlight, there may be no difference between Burkha and other covered dressings. Further study needed to have a conclusion.

REFERENCE

[1] Jones AN, Hansen KE. Recognizing the musculoskeletal manifestations of vitamin D deficiency.J Musculoskelet Med. 2009; 26(10): 389 – 96.

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AB0918 CERVICAL INSTABILITY AND VISUAL PATHWAYS COMPROMISE IN PATIENTS WITH JOINT LAXITY

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Background: Cervical spine stability is to a great extent dependent on the capsular ligaments, laxity of which would lead to extensive movements of the vertebrae. This instability of the cervical spine, particularly in the upper segments (C0-C2) would be a major source of vertebrobasilar insufficiency. The resultant brain posterior circulation compromise would then make the foundation of white matter changes and cause many neurological signs and symptoms. Occipital lobe and visual pathways are certainly in danger in these circumstances. How and to what extent could the visual pathways be involved in patients with joint laxity is not well studied yet.
Objectives: This study was designed to find whether the visual evoked potential parameters (latency and amplitude) of the patients with generalized joint laxity differs from that of the normal population.
Methods: In this corss-sectional comparative study, 90 consecutive patients with generalized lax joints and 90 normal individuals were enrolled and underwent the visual evoked potential test by pattern reversal. The latency and amplitude of P100 were determind for all the particiipants and data from the 2 groups were compared statistically.
Results: The results demonstrated that although none of the VEP parameters fell in the abnormal range, there was significant difference between P100 latency in patients with generalized lax joints (mean:110.23 ms) versus normal population (100.18 ms) ($P<0.001$) with longer latency in patients with generalized lax joints. But the amplitude was not significantly differed across the groups ($P > 0.05$).
Conclusion: It can be concluded from this study that although the VEP parameters of the patients with generalized joint laxity don't exceed the normal range limits, P100 latency in these patients is significantly more prolonged than in normal population. This finding is valuable from two points of view, first P100 latency at the verge of abnormality (upper limit of normal range) in these patients is a warning sign implying the visual pathway involvement, and second VEP could be invaluable in diferentiating the signs and symptomes that are produced by vertebrobasilar insuficiancy secondary to the joint laxity from multiple sclerosis, which can be mimicd both clinically and in MRI findings by many vascular problems but shows a great percent of VEP abnormality as a particular fiture.

REFERENCES

[1] Steilen D, Hauser R, Woldin B, Sawyer S. Chronic neck pain: making the connection between capsular ligament laxity and cervical instability. The open orthopaedics journal. 2014;8:326-45.
[2] Jaumard NV, Welch WC, Winkelstein BA. Spinal facet joint biomechanics and mechanotransduction in normal, injury and degenerative conditions. Journal of biomechanical engineering. 2011;133:071010.
[3] Siva A. Common Clinical and Imaging Conditions Misdiagnosed as Multiple Sclerosis: A Current Approach to the Differential Diagnosis of Multiple Sclerosis. Neurologic clinics. 2018;36:69-117.
[4] Lin P-C, Chang F-C, Huang H-C, Tsai J-Y, Lin Y-Y, Chung C-P. Greater periventricular white matter hyperintensity severity in basilar artery branch atheromatous disease. BMC neurology. 2017;17:135-.
[5] Kose Ozlece H, Ilik F, Huseyinoglu N. Coexistence of Ehlers-Danlos syndrome and multiple sclerosis. Iranian journal of neurology. 2015;14:116-7. .
[6] Pajak M, Majos MA, Szubert W, Stefanczyk L, Majos A. Acute brain ischemia as a complication of the Ehlers-Danlos syndrome, the case series. Vascular. 2014;22:341-5
[7] EL-Cart AK, Mahammoud A, Mahgoub EH. Hypermobility among egyptian childern: prevalence and features. J Rheum 1998; 25(5): 3-5.

[8] Mishra MB, Ryan P, Atkinson P, et al. Extra-articular features of benign joint hypermobility syndrome. Br J Rheumatol. 1996; 35(9):861-6.

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AB0919 EFFECTS OF ALEXITHYMIA ON ACTIVITY PAIN, UPPER EXTREMITY FUNCTION, SYMPTOM AND DEPRESSION LEVELS IN PATIENTS WITH THORACIC OUTLET SYNDROME

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Background: Presentation of the most common changes in the thoracic outlet syndrome causing functional disorders of the upper limb (1). The majority of the studies published on TOS highlight physiotherapy strengthening exercises and postural reducational drills as being the mainstay of any conservative management programme for TOS (2). However, in the literature, the effect of emotional state on progression in treatment programs has not been investigated. Alexithymia, which refers to deficiencies in the self-awareness of emotional states, has been reported to be associated with poor ability in various aspects of social cognition (3). The ability of TOS patients to express themselves and their emotions will affect the success of the treatment.
Objectives: The aim of this study was to investigate the effect of alexithymia on upper extremity functions, symptoms, pain level, depression and anxiety in patient with Thoracic Outlet Syndrome.
Methods: Forty-three TOS patients (36.67±13.99 years; 38 women, 5 men) were enrolled to the study. Alexithymia was assessed with Toronto Alexithymia Scale (TAS-20). The patients were divided into two groups as non-alexithymia group and alexithymia group according to 51 points TAS -20 cut-off score. Pain levels at rest and activity were assessed with visual analogue scale; upper extremity function was assessed with Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire, and upper extremity symptom was assessed with using Servical Brachial Symptom Questionnaire. Mann-Whitney U test was used for data analyses.
Results: Activity pain level and depression in alexithymia group was higher than the non-alexithymia group, p=0,008 and p=0,007, respectively. Also, functional level and symptoms were worst in alexithymia paitents, p=0,041 and p=0,05, respectively. No difference was found between groups in anxiety and resting pain level (p>0,05).
Conclusion: Thoracic outlet syndrome patients who have alexithymia show worse pain, symptoms, function, and depression. Emotion should be considered in physiotherapy programs. Because the progression of alexithmia patients are worst than non-alexithmia patients.

REFERENCES

[1] Laulan, J., Fouquet, B., Rodaix, C., Jauffret, P., Roquelaure, Y., & Descatha, A. (2011). Thoracic outlet syndrome: definition, aetiological factors, diagnosis, management and occupational impact. Journal of occupational rehabilitation, 21(3), 366-373.
[2] Watson, L. A., Pizzari, T.,Balster, S. (2010). Thoracic outlet syndrome part 2: conservative management of thoracic outlet. Manual therapy, 15(4), 305-314.
[3] Moriguchi, Y., Ohnishi, T., Decety, J., Hirakata, M., Maeda, M., Matsuda, H., & Komaki, G. (2009). The human mirror neuron system in a population with deficient self awareness: An fMRI study in alexithymia. *Human brain mapping*, *30*(7), 2063-2076.

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AB0920 THE EFFECT OF TIBIALIS POSTERIOR MUSCLE FATIQUE PROTOCOL ON THE STATIC AND DYNAMIC FOOT PARAMETERS

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Background: The tibialis posterior has a important key role as an invertor of the rearfoot. Also providing dynamic support across the midfoot. The value of the tibialis posterior shown by biomechanical research conducted on patients with posterior tibialis tendon dysfunction. One method of assessing a muscle's contribution to a specific movement pattern is via fatigue-inducing exercise of that muscle. Consequently, to realize the role of tibialis posterior fatigue on foot mechanics it seems prudent to use an exercise that more selectively activates this muscle (1,2).
Objectives: The purpose of this study is to investigate dynamic and static foot parametres changed by tibialis posterior muscle fatique protocol.
Methods: Thirty patients were participated in this study. Socio-dermographic and descriptive characteristics of the participants were recorded. The changes on the dynamic and static parametres of foot were measured by pedobarography. The two exercises selected for the fatigue protocol are: 1-Unilateral heel raise 2-Close chain resisted foot adduction. Fatigue level was measured by Borg scale. Static and dynamic parameters obtained before and after fatigue protocol were compared.
Results: The mean age of the patients was 24,88 ± 4,39 years, mean height was 171 ± 7,89 cm and mean weight was 68,7 ± 14,5 kg. We found significiant increase in the maximum pressure measurement of mid foot (p= 0,004). In the total contact area during the static position, there were no significant changes (p>0.05). Participants' maximal pressure in the middle standing phase was changed from 19,78 ± 10,71 N/cm^2 to 22.89 ± 13.03 N/cm2 after fatigue protocol in medial of middle foot (p=0.03).
Conclusion: According to the results, there was a correlation between the fatique of tibialis posterior and the static and dynamic parameters of foot. The increase in the middle foot peak pressure distributions after the fatigue protocol of the tibialis posterior muscle can be explained as the increase of the angular amount of pronation and prolongation of the time with the middle standing phase. Increase in pressure forces of the middle foot and increase in percentages of the area cause increase of the weight in the front foot during the gait cycle. Thus, fatigue protocol causes similar effects as tibialis posterior muscle dysfunction.

REFERENCES

[1] Bubra, P. S., Keighley, G., Rateesh, S., & Carmody, D. (2015). Posterior tibial tendon dysfunction: an overlooked cause of foot deformity. *Journal of family medicine and primary care*, 4(1), 26.
[2] Pohl, M. B., Rabbito, M., & Ferber, R. (2010). The role of tibialis posterior fatigue on foot kinematics during walking. Journal of foot and ankle research, 3(1), 6.

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Paediatric rheumatology

AB0921 JUVENILE-ONSET LUPUS WITH SECONDARY CMV-INDUCED MACROPHAGE ACTIVATION SYNDROME (CASE REPORT)

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Background: Juvenile-onset lupus (JSLE) is a complex illness with an aggressive course and higher chances of morbidities and mortality. JSLE is extremely rare before the age of 5 years. A sole disease criterion may precede long time before others,making diagnosis rather challenging
Objectives: Identifying JSLE and its subsequent complications
Methods: A three and half years old female patient presented with an established diagnosis of idiopathic thrombocytopenia (ITP) of one year duration.One month ago,the patient developed an acute onset of high grade persistent fever, bilateral knee swelling and significant weight loss.
Results: On physical examination, patient was emaciated and pale with multiple ecchymotic patches allover her body. Vital data showed normal blood pressure and apical heart rate ranges for age. Systemic examination revealed multiple oral ulcers, hepatosplenomegaly,bilateral knee arthritis and bilateral below knee painless pitting lower limb edema. Neurological examination was free. Laboratory evaluation showed a CBC with TLC 1.800/mm^3 NE 0.5/mm^3, HB 7.9 gm/dl, PLT 79 x10^3/µL.ESR 120 mm/1st hr and CRP 96 mg/dl. Routine chemistry showed elevated liver enzymes (ALT 137 IU/L & AST 280 IU/L), LDH 960 U/L, serum albumin 2.5 g/dl, normal renal functions. The history of chronic ITP together with evolution of other autoimmune manifestations raised the suspicion of an underlying Connective tissue disorder. Immunological profile showed positive immune markers (ANA 1/320 speckled and positive Anti-DNA), positive lupus anticoagulant and anticardiolipin IgM,C3 was consumed(49 mg/dl). Secondary Macrophage activation syndrome (MAS)

was suspected and markers revealed serum ferritin 30.000 ng/ml, fibrinogen 250 mg/dl,Triglycerides 350 mg/dl and soluble CD25 12.000U/ml. Bone marrow aspiration confirmed the diagnosis.Cytomegalovirus (CMV) IgM and PCR were significantly high.With regard to all the previous clinical and laboratory features,a CMV-induced secondary MAS in JSLE was confirmed.Patient was managed according to HLH-2004 treatment protocol (pulsed methylprednisolone 30mg/kg/day,cyclosporine A 6mg/kg/day, IV etoposide 150mg/m²)and IVIG.Ganciclovir was also added (5mg/kg IV q12h x7 days). Patient showed marked clinical improvement together with significant diminution of the MAS laboratory markers to normal.Two weeks post discharge on oral dexamethasone and cyclosporine A, the patient showed a severe clinical and laboratory MAS relapse (serum ferritin 50.000 ng/ml). The previous treatment protocol was restarted together with adding Rituximab 375mg/m² x 3 doses two weeks apart.Patient showed marked clinical and laboratory improvement and was maintained on full dose oral prednisone and oral Cyclosporine A. Tight gradual withdrawal of oral steroids was done with close clinical and laboratory follow up.

Conclusion: JSLE is a major diagnostic conundrum in pediatrics owing to its extremely variable clinical manifestations which can mimic many common pediatric conditions(e.g.malignant disease,other auto-inflammatory conditions,malignancy and any specific organ associated disease).Compared to adults JSLE has a more severe disease presentation.MAS is a life threatening condition that requires high index of suspicion and prompt management.In our case, controlling JSLE activity using Rituximab was significantly beneficial in arresting HLH evolution.

REFERENCES

[1] Amol P.etal : Juvenile systemic lupus erythematosus: A diagnostic dilemma.J Nat Sci Biol Med. 2011 Jul-Dec; 2(2): 229–231.
[2] Henter JI etal : diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer (2007) 48:124–31.

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AB0922 UPDATES ON THE EVIDENCE BASED INTERDISCIPLINARY GUIDELINES FOR HENOCH-SCHÖNLEIN PURPURA

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Background: Henoch-Schönlein purpura (HSP) is the most common childhood vasculitis, it is characterized by inflammation of small vessels leading to non-thrombocytopenic purpura, arthritis/arthralgia, GI hemorrhage and glomerulonephritis[1]. There is a very poor evidence base to guide the management of HSP, particularly for those with the severe forms of HSP nephritis, Up till now there are no EULAR or ACR recommendations for management of HSP.

Objectives: To set an updated interdisciplinary recommendations for the management of HSP

Methods: Interdisciplinary guidelines were developed with representative from PRINTO Egypt for pediatric rheumatology as well as patients' group. A systemic literature analysis in MEDLINE was performed, evidence and recommendations were graded, an algorithm for treatment and final statements were discussed in a consensus meeting (Nominal Group Technique). A preliminary draft was fine tuned and discussed thereafter by all participants (Delphi Procedure).

Results: Consensus was reached on recommendations, including a standardized treatment strategy according to the HSP severity state in the individual patient. In this updated interdisciplinary guideline for HSP; treatment was tailored to the patient's pathology and its severity (figure 1). Criteria for admission were identified as: severe arthritis or arthralgia limiting ability to weight bearing and mobilization, severe abdominal pain, GI hemorrhage, evidence of nephritis/nephritic syndrome or renal impairment, evidence of neurological symptoms. Criteria for early referral to pediatric nephrologist were also identified including: hypertension, abnormal renal function, macroscopic hematuria for 5-days, nephrotic syndrome, acute nephritic syndrome, as well as persistent proteinuria.

Conclusion: A total of seven evidence based interdisciplinary recommendations for management of HSP have been formulated, that provide an up-to-date guidance of HSP management.



Figure 1: recommendations for management of HSP

Figure 1

REFERENCE

[1] Hetland LE, Susrud KS, Lindahl KH, Bygum A. Henoch-Schönlein Purpura: A Literature Review. Acta Derm Venereol. 2017 Nov 15;97(10):1160-1166. doi: 10.2340/00015555-2733.

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AB0923 EFFECTS OF EXON 10 MUTATIONS VS NON-EXON 10 MUTATIONS ON FMF PHENOTYPE AND RESPONSE TO TREATMENT

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Background: Familial Mediterranean fever (FMF) is the most common monogenic periodic fever syndrome. The MEFV gene mutation encoding the pyrin protein results in an uncontrolled increase in interleukin-1. Today, more than 333 MEFV mutations have been identified; however, exon 10 mutations are still seem to be best correlated with clinical findings.

Objectives: In this study, we aim to investigate the role of exon 10 mutations vs non-exon 10 mutations on clinical features and response to treatment in patients with FMF.

Methods: Data charts of children (n=935) with FMF from Dokuz Eylul University childrens' hospital and Dr.B.Uz childrens' hospital were reviewed. Patients were divided into two groups with regard to having

exon 10 mutation or non-exon 10 mutations. Genotype-phenotype features and response to treatment were compared.

Results: There were exon 10 mutations in 631 (67.5%) patients and non-exon 10 mutations in 304 (32.5) patients. The follow-up period was 50 (26-83.2) months. The age of symptoms onset was significantly lower in group with exon 10 positive than compared group with non-exon 10 mutation. There was no difference between the age of diagnosis and colchicine onset and the diagnosis delay time. The symptoms of fever, chest pain, and arthritis were significantly higher in the exon 10 mutation group than compared other group. Biological agent need was statiscally higher in exon 10 mutation group (4.8%) than group with non-exon 10 mutation (1.3%) (Table 1).

Conclusion: In our study, it was observed that cases with exon 10 mutation have early symptoms of disease. Fever, chest pain and joint findings were more prominent in cases with exon 10 mutation than cases with non-exon 10 mutation. Additionally, colchicine resistance should be kept in mind in cases with exon 10 mutation.

REFERENCES

[1] Wang DQH, Bonfrate L, de Bari O, Wang TY, Portincasa P (2014) Familial Mediterranean fever: from pathogenesis to treatment. J Genet Syndr Gene Ther 5:248.

[2] Ozen S, Demirkaya E, Amaryan G, et all. Results from a multicentre international registry of familial Mediterranean fever: impact of environment on the expression of a monogenic disease in children. Ann Rheum Dis. 2014 Apr;73(4):662-7

Abstract AB0923 Table 1. Comparison of patients with exon 10 and non-exon 10 mutations

	Exon 10 (+)	Exon 10 (-)	p
n (%) = 935 (100)	631 (67.5)	304 (32.5)	
Female/Male (n) =445/490	303/328	142/162	0.707
Median age of symptoms onset (months)	**48 (24-86.5)**	**60 (26-109)**	**0.009**
Median age of diagnosis (months)	80 (47-127)	87 (54-136)	0.106
Median diagnosis delay time (months)	17 (6-38)	15 (7-36)	0.484
Symptoms n (%)			
Fever	**442 (70.3)**	**193 (64.1)**	**0.050**
Abdominal pain	458 (72.8)	206 (68.7)	0.191
Chest pain	**65 (10.3)**	**18 (6)**	**0.029**
Erysipelas like rash	11 (1.7)	10 (3.3)	0.127
Arthralgia	231(36.8)	110 (36.8)	0.999
Arthritis	**137(21.8)**	**46 (15.3)**	**0.019**
Myalgia	78 (12.5)	26 (8.6)	0.083
Emesis	12 (2)	12 (4)	0.061
Use of biologic agent	**30 (4.8)**	**4 (1.3)**	**0.009**

Disclosure of Interests: Hatice Adiguzel Dundar: None declared, ozge altug gucenmez Speakers bureau: Novartis, Abbvie, Ceyhun Acari: None declared, Serkan Turkucar: None declared, Balahan Makay Speakers bureau: Enzyvant, Novartis, Roche, Abbvie, Erbil Unsal Grant/research support from: Novartis, AbbVie, Roche, Koçak Pharma, Speakers bureau: Novartis, AbbVie, Roche, Koçak Pharma

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AB0924 EVALUATION OF PERIPHERAL NERVOUS SYSTEM INVOLVEMENT IN PATIENTS WITH JUVENILE SYSTEMIC SCLEROSIS AND JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Juvenile systemic sclerosis (JSS) and juvenile systemic lupus erythematosus (JSLE) are rare connective tissue disorder characterized by multisystemic involvement, including gastrointestinal, cardiovascular, respiratory and nervous system complications. According to data from literature, peripheric nervous system (PNS) involvement is seen in 10-86.7% of adult patients with systemic sclerosis. Frequency of PNS disorders is reported as 10-86.7% in adult patients. Data on PNS involvement in patients with JSS and JSLE are scarce.

Objectives: We aimed to evaluate PNS involvement in patients with JSS and JSLE. Consequently, we sought to detect patients with PNS disorders, in order to enable early diagnosis and timely intervention.

Methods: Patients with JSS and JSLE were included in a cross-sectional study. Demographic and clinical data of patients were recorded during clinical visits. All of patients were evaluated and examined for sings of PNS involvement. In order to examine mononeuropathy, polyneuropathy and trigemino-facial involvement, all patients underwent routine nerve conduction studies (NCS), blink reflex (BR) and sympathetic skin responses (SSR) evaluation.

Results: Twenty JSS (15 (75%) female) and 18 (15 (83%) female) JSLE patients were initially included. All of JSS and JSLE patients had normal neurologic examination. NCS was normal in all JSS (20/20) and JSLE (18/18) patients. SSR was not recorded in 1 (5%) JSS and in 3 (16.67%) JSLE patients. BR was recorded in all JSLE (18/18) patients and in majority of JSS patients (19/20, 95%). According to SSR, mean latency of hand and foot was similar in both patients' groups. Amplitude of foot response was lower in JSS patients, comparing to JSLE (Table 1). Among JSLE patients, amplitude of hand response was lower than amplitudes of foot response.

Abstract AB0924 Table 1. Sympathetic skin responses

SSR	JSS mean latency	JSS mean amplitude	JSLE mean latency	JSLE mean amplitude
HAND	1424,63	0,75	1353,26	0,9
FOOT	1935,26	0,55	2011,6	**2,6**

According to BR, R1, R2, R2K duration and latency were not different between right and left eyes in both patients' groups. R3 was absent in 2 (10%) bilaterally and in 1 (5%) JSS patients unilaterally (right). R3 was absent in 4 (22.2%) bilaterally and in 2 (11%) JSLE patients unilaterally. Absence of R3 was more prominenet in JSLE patients, comparing to JSS. (Table 2)

Abstract AB0924 Table 2. Blink reflex responses

	JSS-right	JSS-left	JSLE-right	JSLE-left
R1 duration	5,9	5,8	6,7	6,5
R1 latency	10,3	10,3	10,3	10,2
R2 duration	33,5	33,7	32,7	29,1
R2 latency	30,3	29,8	29,6	30,5
R2K duration	34,4	29,4	34,7	32,2
R2K latency	32,5	33,3	31,9	33,1
R3 presence	**3/19**	**2/19**	**4/18**	**6/18**

Conclusion: BR could be considered as a potential indicator of neuropathy in JSLE and JSS patients. Data on SSR need to be evaluated in studies with higher number of patients with juvenile-onset connective tissue disorders.

REFERENCES

[1] Adrovic A, Şahin S, Barut K, Kasapçopur Ö. Juvenile Scleroderma: A Referral Center Experience. Arch Rheumatol. 2018;33(3):344-351.

[2] Sahin S, Adrovic A, Barut K, Canpolat N, Ozluk Y, Kilicaslan I, Caliskan S, Sever L, Kasapcopur O (2018) Juvenile systemic lupus erythematosus in Turkey: demographic, clinical and laboratory features with disease activity and outcome. Lupus. 27:514-519.

[3] Spirin NN, Bulanova VA, Pizova NV, Shilkina NP. Peripheral nervous system lesion syndromes and the mechanisms of their formation in connective tissue diseases. Neurosci Behav Physiol. 2007;37(1):1-6.

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AB0925

TOCILIZUMAB AS A TREATMENT OPTION FOR PATIENTS WITH JUVENILE SYSTEMIC SCLEROSIS

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Background: Juvenile systemic sclerosis (JSS) is a rare autoimmune disease characterized by skin stiffness and fibrosis of internal organs (eg. lung, hearth, gastrointestinal system). The efficacy and safety of tocilizumab (TCZ), an interleukin 6 receptor-α inhibitor, in adult patients have been studied in a few recent studies. Reports on its efficacy among children have been reported among patients with localized disease form. This is a first report on treatment of JSS patients with TCZ.
Objectives: We aimed to evaluate efficacy of tocilizumab as a treatment option for patients with juvenile systemic sclerosis. Consequently, we sought to explore its influences on internal organ involvement, skin stiffness and patient global assessment score.
Methods: We retrospectively evaluated patients diagnosed with JSS according to EULAR criteria. Among 30 patients diagnosed with JSS, 7 (23%) were treated with TCZ. Demographic data are taken from patients' charts. Data on clinical characteristics and treatment outcome are recorded during the patients' last visit.
Results: Seven patients treated with TCZ were analyzed: 6 (85.71%) girls, one boy. Median age of patients was 17.5 years (range:11-12 years), at disease onset 10 years (range 6-15 years) and at diagnosis 11 years (range 7.5-17 years). Median disease duration was 8 years (min. 3-max.11 years). Median duration of TCZ treatment was 10 months (min. 1-max. 21 months). One (14.28%) patient had gastro-intestinal involvement, 4 (57.14%) patients had lung involvement and 2 (28.57%) patients had both gastro-intestinal and lung involvement. Improvement in mRSS was detected in 5 (71.43%) patients. DLCO improved in 4 (57.14%) patients. Four (57.14%) patients had radiologically confirmed improvement in lung findings. Data on radiological findings of one patient treated with TCZ for 6 moths were nor available. Five patients (71.43%) reported improvement in patient global assessment (PGA) score after the TCZ treatment. PGA score of two remaining patients were not applicable due to short treatment duration (Table 1). None of 7 patients had recorded adverse effect of TCZ treatment.

Abstract AB0925 Table 1. Clinic characteristics of juvenile systemic sclerosis patients patients treated with tocilizumab

Lung involvement	GIS involvement	Treatment duration (months)	TCZ treatment duration (months)	Radiological improvement in thorax HRCT	Pre-/ Post-treatment DLCO (%)	Pre-/Post-treatment mRSS	Pre-/ treat P
+	+	78	12	+	52/52	21/19	5
-	+	90	6	NA	93/95	33/22	2
+	+	108	21	+	65/71	32/22	4
+	-	96	11	+	54/62	28/16	3
+	-	66	10	+	107/125	28/24	4/
+	-	30	1	NA	51/NA	12/NA	3/
+	-	12	1	NA	NA/NA	32/NA	5/

Conclusion: JSS is rare condition characterized with internal organ involvement. Tocilizumab represents an efficacy treatment options for patients unresponsive to standard treatment. Long-term prospective studies with higher number of patients are needed to provide more relevant data.

REFERENCES

[1] Adrovic A, Şahin S, Barut K, Kasapçopur Ö. Juvenile Scleroderma: A Referral Center Experience. Arch Rheumatol. 2018;33(3):344-351.
[2] Adrovic A, Sahin S, Barut K, Kasapcopur O. Juvenile Scleroderma-What has Changed in the Meantime? Curr Rheumatol Rev. 2018;14:219-225.
[3] Arnold MB, Khanna D, Denton CP, et al. Patient acceptable symptom state in scleroderma: results from the tocilizumab compared with placebo trial in active diffuse cutaneous systemic sclerosis. Rheumatology (Oxford). 2018;57(1):152-157.
[4] Khanna D, Denton CP, Lin CJF, et al. Safety and efficacy of subcutaneous tocilizumab in systemic sclerosis: results from the open-label period of a phase II randomized controlled trial (faSScinate). Ann Rheum Dis. 2018;77 (2):212-220.

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AB0926

JUVENILE SYSTEMIC SCLEROSIS AND MUCINOUS ADENOCARCINOMA OF THE LUNG IN PATIENT WITH CYSTIC ADENOID MALFORMATION-PARANEOPLASTIC SYNDROME OR JUST A COINCIDENCE?

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Background: Juvenile systemic sclerosis (JSS) is a rare auto-immune condition characterized by the skin stiffness and internal organ fibrosis. In adult patients, systemic sclerosis has been related to an increased risk of malignancy with lung cancer being most prevalent. Up-to-date, we haven't found any report on lung cancer in patient with JSS.
Objectives: Herein, we aimed to present a case with juvenile systemic sclerosis and coincidentally detected cystic adenoid malformation complicated by the mucinous adenocarcinoma of the lung.
Methods: Data on disease history are taken from patient's chart. Clinical and laboratory findings are recorded during the last visit at our outpatient department.
Results: A 14 years old previously healthy female patient, admitted to our outpatient department due to puffy fingers, Raynaud's phenomenon and stiffness of the skin proximally to metacarpophalangeal joints. Her anti-nuclear antibody was positive (1/80) but the other auto-antibodies (including Anti Scl 70, anti-centromere antibody) were negative. Patient was diagnosed as progressive systemic sclerosis and the prednisolone, methotrexate and nifedipine were started. Routinely performed echocardiography was normal. Respiratory function tests were appropriate for the age and hemoglobin level: FVC 80%, DLCO 92%. Surprisingly, thorax HRCT revealed cystic adenoid malformation on the left lower lobe of the lung so pediatric surgery department has been consulted. The decision for surgical intervention has been made and the lesion has been removed. Tissue sample has been sent to the pathological investigation and the result was consistent with mucinous adenocarcinoma of the lung. There were 2 focus (0.4 cm in diameter) of the adenocarcinoma in the cystic adenoid malformation without invasion to the local perineural, lymphatic or vascular tissues, with positive KRAS (KRAS12-612C, 612S) mutation. Cranial MRI and PET-CT show no residual, relapse nor the metastatic lesions. Clinical follow-up has been suggested, without need for further oncological treatment.

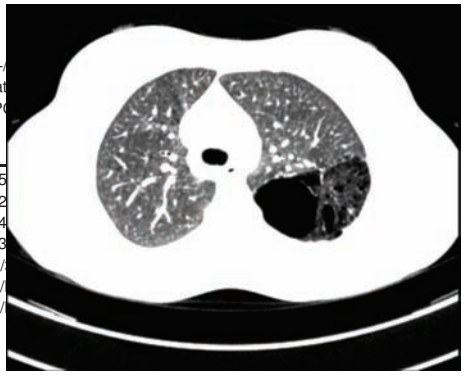


Figure 1. Thorax HRCT of patient

Conclusion: Juvenile systemic sclerosis is a rare disease characterized with multiorgan involvement. The paraneoplastic syndrome with clinical presentation of systemic sclerosis should be kept on mind among adolescents, especially those with negative autoantibodies.

REFERENCES

[1] Adrovic A, Şahin S, Barut K, Kasapçopur Ö. Juvenile Scleroderma: A Referral Center Experience. Arch Rheumatol. 2018;33:344-351.
[2] Bento J, Fernandes G, Barbosa MA, Magalhães A, Santos AR, Hespanhol V. Lung adenocarcinoma associated with systemic sclerosis: a case report. Rev Port Pneumol. 2009;15:93-9.
[3] Yoshimi R, Takeno M, Yamanaka S, et al. Systemic sclerosis and pseudomesotheliomatous adenocarcinoma of the lung. Mod Rheumatol. 2006;16:165-8.

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AB0927 SUPERB MICROVASCULAR IMAGING COMPARED WITH POWER DOPPLER ULTRASOUND IN ASSESSING SYNOVITIS OF THE KNEE IN JUVENILE IDIOPATHIC ARTHRITIS: A PRELIMINARY STUDY

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Background: Juvenile idiopathic arthritis (JIA) is a complex entity and is the most common rheumatologic disease of the children with the knee being the most frequently affected joint. Extensive proliferation of the synovial cells, synovial thickening and inflammation are the hallmark pathological processes ongoing in the affected joints. The traditional methods in assessing the disease activity involve investigating tenderness, pain, and swelling of the relevant joint on psychical examination in addition to biochemical markers; however, the psychical examination may yield equivocal results in some patients. Sonographic modalities are being increasingly used as a complementary method in the assessment of the joints in JIA and Power Doppler ulltrasound (PDUS) is the current reference sonographic method in assessing the inflammation by measuring the vascularity in the synovium. SMI is a novel Doppler technique using advanced filtering algorithms with an ability to detect even subtle and slow blood flow signals.

Objectives: we aimed to investigate the efficiency of Superb Microvascular imaging (SMI) in assessing inflammation of synovium in the knee of patients with JIA compared with PDUS.

Methods: Both knees of the patients with a diagnosis of clinically active JIA were examined using gray-scale US. The knees with positive US and physical examination findings included in group A while the knees with positive US findings despite negative physical examination findings included in group B. The observers calculated vascularity index (VI) by manually drawing a region of interest (ROI) onto the thickest part of the synovium using PDUS and SMI.

Results: A total of 41 knees with both clinical and sonographic positive findings constituted group A and 14 knees with sonographic positive findings and normal physical examination categorized as group B in the final cohort. The median SMI-VI (observer 1= 4.9%, IQR 3.6; observer 2= 4.1%, IQR 4.6) was exceeded the median PDUS-VI (observer 1= 1.5%, IQR 1.8; observer 2= 1.5, IQR 1.9) (P<0.0001). In group B, the median SMI-VI (observer 1= 2.85%, IQR 8; observer 2= 3.1%, IQR 6.3) were exceeded the median VI PDUS-VI (observer 1= 0.5%, IQR 2; observer 2= 0.55, IQR 2.3) (P=0.002 and P=0.001 for observer 1 and observer 2, respectively). No significant differences were observed between groups concerning PDUS-VI and SMI-VI (P>0.05). In all of the patients in group A, SMI was able to identify the presence of vascularity for both observers while no blood flow was detected (VI=0%) using PDUS in 6 patients (14.6%) for observer 1 and 7 patients (17.1%) for observer 2. In all of the patients in group B, SMI was also able to identify the presence of vascularity for both observers while no blood flow was detected (VI=0%) using PDUS in 5 patients (%35.7) for each observers.

Conclusion: SMI-VI obtained from the hypertrophied synovium of both clinically active and inactive knee joints were substantially higher compared with PDUS-VI in JIA patients. Furthermore, SMI detected the presence of blood flow in patients in whom PDUS could not be able to identify any blood flow. The findings of the present work indicate that SMI seems to a promising tool and a valuable adjunct to conventional US in assessing the inflammation of the synovial tissue in JIA patients.

REFERENCES

[1] Giancane G, et al. Juvenile Idiopathic Arthritis: Diagnosis and Treatment. Rheumatol Ther 2016;3:187-207

[2] Strunk J, et al. A new approach to studying angiogenesis in rheumatoid arthritis by means of power Doppler ultrasonography and measurement of serum vascular endothelial growth factor. Rheumatology 2004;43:1480–1483

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AB0928 CORONARY ARTERY LESIONS AT PRESENTATION IN KAWASAKI DISEASE: A MARKER OF IVIG RESISTANCE?A RETROSPECTIVE STUDY FROM NORTH INDIA

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Background: Kawasaki disease has been well described from all around the world.This has been well described from our country. We recently changed our practice with regards to addition of corticosteroids and undertook this study.

Objectives: To study the clinical profile of children with Kawasaki disease presenting to our unit.

To study the response of therapy in children with Kawasaki disease

To study the efficacy of addition of upfront steroids in children with coronary artery lesions (z score>2.5)

Methods: All children with Kawasaki disease seen in the last 5 years were included and data collected on prefilled proforma. IVIG 2gm/kg as a single dose over 18-24 hours was given to all children. Aspirin in dose of 30-80mg/kg/day was given to all children along with IVIG. Response was defined as defervescence within 36 hours of completion of IVIG. Fever beyond 36 hours of completion of IVIG was considered as no response/resistance to 1st dose of IVIG.

Results: 60 children diagnosed with Kawasaki disease were included. Median age at diagnosis of disease was 3.12 years(0.3-15 years).33 children had complete Kawasaki disease, 26 children had incomplete disease and one child had atypical Kawasaki disease36 children were diagnosed within first 10 days of disease onset and 24 children were diagnosed after day 10 of illness.18 children had history of infections prior to onset of Kawasaki disease.29 children(48%) had coronary artery lesions at the time of presentation.48 children(80%) were given1st dose of IVIG without any corticosteroids.36 children (75%)responded to first dose of IVIG, one child was not given IVIG as he was diagnosed retrospectively and had self limiting disease. 14 children(29%) did not respond to 1st dose of IVIG. 9 children were given intravenous methylprednisolone 2mg/kg/day in four divided doses along with IVIG. All of these responded to the first dose of IVIG. The size of coronary artery lesion also plays an important role. In children with z score >2.5 the response to 1st dose of IVIG was 61.5% whereas it was 94%in those who had z scores<2.5(p value 0.03)

Abstract AB0928 Table 1. Response of therapy in children with and without coronary artery lesions

Group	No.	%
No coronary artery lesion	27/30	90
Coronary artery lesion present, no steroids used	11/20	55
Coronary artery lesion present, steroid given upfront	9/9	100

Response rate was significantly higher in patients with no coronary artery lesions (p value0.007).In children with coronary artery lesions at presentation, the response rate was significantly higher in children who were given steroids upfront (p value 0.027).

Conclusion: We see many children with coronary artery lesions at presentation. This seems to be an indicator of resistance to IVIG. It is beneficial to add steroids upfront along with IVIG to children with coronary artery lesions more than 2.5 z score.

REFERENCE

[1] Dallaire F, Dahdah N. New equations and a critical appraisal of coronary artery Z scores in healthy children. J Am Soc Echocardiogr. 2011 Jan;24 (1):60-74.

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AB0929 **ACUTE RHEUMATIC FEVER: IS PROLONGED CORTICOSTEROID TEATMENT ASSOCIATED TO A BETTER CARDIAC OUTCOME?**

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Background: Acute rheumatic fever (ARF) is a nonsuppurative sequaela that can occur two to four weeks after group A beta-hemolytic Streptococcus pharyngitis. Despite its decline in incidence in modern countries, ARF still represents worldwide a serious healthcare concern. The most common manifestations are arthritis and carditis, followed by chorea, erythema marginatum, and subcutaneous nodules. The diagnosis of ARF is clinical and requires satisfaction of revised Jones criteria as well as evidence of a recent streptococcal infection.

Carditis and chorea both need systemic corticosteroid treatment (prednisone, 1 mg/kg) but with different treatment courses: 2-3 weeks prednisone treatment course in carditis is generally undertaken compared to a longer prednisone treatment period in chorea (at least 2 months).

Objectives: The aim of this study was to investigate if the longer corticosteroid treatment used for patients with chorea and carditis is related to a better regression of cardiac damage compared to the shorter course of corticosteroid treatment in patients with only carditis.

Methods: Data regard 14 patients were retrospectively revised (8 males, 6 females): 7 ARF patients with both cardiac and neurological involvement treated with systemic prednisone for 2 months; 7 ARF patients with only cardiac involvement treated with systemic prednisone for 2 weeks. The regression of cardiac damage in the two different groups was evaluated in relation to the different duration of corticosteroid treatment comparing ultrasound echocardiography (cardiac-US) performed at ARF onset and during a 2-3 year follow-up. The trend of the grade of aortic and mitral valves insufficiencies was chosen as indicator of the ARF cardiac damage evolution.

Patients with a similar grade of cardiac damage at disease onset were identified; then pairs were created according to the presence of chorea (so one patient was affected only by carditis and the other one of the same pair, according to the similar cardiac damage, had both carditis and chorea). Cardiac-US damage regression of the 7 pairs was assessed in order to evaluate if the grade of regressione was higher in the patients with only carditis compared with the ones with both carditis and chorea.

Results: in 3 pairs a better regression of the cardiac damage was evident in the patients with only carditis; in other 3 a better regression was noticed in the patients with both carditis and chorea; finally no difference was detected in the last pair. No significant cardiac-US difference according to patient pairs appeared in relation to the steroid time treatment course (2-3 weeks vs 2-3 months); however in 85% of the cases (12 patients) steroid therapy did achieve regression on ARF cardiac damage.

Conclusion: This retrospective study does not reveal any significant difference between steroid duration therapies in ARF complicated by carditis; limits of the study are the size sample as well as the intra/inter observer variation during cardiac-US (all exams were achieved in a high level experience paediatric cardiac service); this study underlines the established importance of the use of corticosteroid in ARF carditis.

Disclosure of Interests: None declared

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AB0930 **EFFICACY OF TOCILIZUMAB IN TREATMENT OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME**

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Background: Macrophage activation syndrome (MAS) is a rare and severe complication of juvenile idiopathic arthritis (JIA) that most typically develops in patients with its systemic form (sJIA). Tocilizumab proved to be efficacious for treatment of both systemic JIA and polyarthritis. Nevertheless, the question regarding the effect of MAS on efficacy of TOC therapy in patients with sJIA is still to be solved.

Objectives: To evaluate the efficacy of tocilizumab therapy in patients having sJIA and MAS versus the patients without MAS.

Methods: Throughout the period between 2009 and 2018, 251 children with the acute phase of sJIA started to be treated with TOC at the Rheumatology Department of the National Medical Research Center of Children's Health (Moscow, Russia). Of those, 69 patients had active MAS at initiation of TOC therapy. Patients were diagnosed with MAS according to the preliminary diagnostic guidelines for MAS complicating sJIA [1]. Treatment efficacy was evaluated according to the dynamics of clinical and laboratory signs using the ACRPedi criteria. The Wallace criteria were used to evaluate whether or not remission had been achieved.

Results: At initiation of TOC therapy, patients with and without MAS were comparable in terms of their sex and age characteristics, as well as the overall severity of arthritis (the percentage of women, 56.6% (intergroup p=0.396); the median age, 7.83 (4.39-11.3) years (intergroup p=0.640); and JADAS-71, 17.4 (13.7-22.8) (intergroup p=0.055)). Nevertheless, patients differed in terms of intensity of certain clinical manifestations and prior history of the disease. The group with MAS was characterized by such parameters as shorter disease duration, shorter duration morning stiffness, and smaller number of affected joints but higher activity and severity score (Patient/Parent and Physician VAS score).

After treatment initiation, TOC was discontinued after treatment for 4-12 weeks only in 2 out of 69 (2.9%) patients because of persistent MAS or MAS flare. The patients successfully achieved remission after therapy switching. No intergroup differences were observed for the rate of treatment discontinuation within the first year of therapy: the drug was discontinued in 5 (7.2%) patients in the MAS+sJIA group (2 MAS flares + 3 cases of poor efficacy) and in 25 (13.7%) patients in the sJIA group (4 SAEs + 21 cases of poor efficacy).

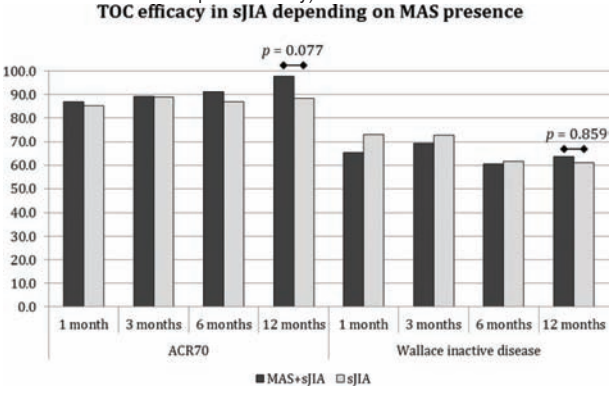


Figure 1

One-year treatment with TOC proved that this drug is highly efficacious to treat sJIA regardless of whether or not patients had MAS at treatment initiation (Figure).

No deaths were reported throughout the entire treatment period. We attributed this to early diagnosis and high efficacy of treatment of JIA patients.

Conclusion: Tocilizumab therapy in patients with sJIA in the presence of MAS is as efficacious as in patients without MAS and does not aggravate the course of MAS.

REFERENCE

[1] Ravelli A, Magni-Manzoni S, Pistorio A, Besana C, Foti T, Ruperto N, Viola S, Martini A. Preliminary diagnostic guidelines for macrophage activation syndrome complicating systemic juvenile idiopathic arthritis. J Pediatr. 2005;146(5):598-604.

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AB0931

TRANSLATION AND VALIDATION OF THE MTX INTOLERANCE SEVERITY SCORE QUESTIONNAIRE FOR PORTUGUESE VERSION IN BRAZIL IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Methotrexate (MTX) is the first-choice disease-modifying antirheumatic drug (DMARD) for the treatment of juvenile idiopathic arthritis (JIA). During therapy, there are frequent reports of discontinuation of MTX, either by physicians or patient's own conduct. Through the MTX Intolerance Severity Score questionnaire (MISS), we determined the prevalence of MTX intolerance.
Objectives: Translate and validate the MTX Intolerance Severity Score questionnaire (MISS) to Portuguese.
Methods: The MISS was translated into Portuguese following the "Guidelines for the process of cross-cultural adaptation of self-report measures". The MISS consists of 4 domains: stomachache, nausea, vomiting, and behavioral complaints. Each domain includes three to four items, and for every item, four answers are possible: no complaints (0), mild complaints (1 point), moderate complaints (2 points), and severe complaints (3 points). The points are summed to give a total score from 0 to 36. Statically analysis was performed on the SPSS®, version 21. The psychometric properties were analyzed according to the Consensus based Standards for the Selection of Health Measurement Instruments (COSMIN), analyzing acceptability for each item; internal consistency using Cronbach's alpha coefficient and reproducibility assessed by Kappa. We plot the ROC curve to evaluate the discriminant validity of the MISS compared to gold standard (clinical interview) and cut-off score was determined.
Results: We included 220 subjects, 144 patients with JIA in use for least 3 months of MTX and 76 parents. The median age of patients were 18.3 SD±8.7 years. Seventy-three (73%) patients were females and the JIA subtype most frequently observed was polyarticular. Routes of administration of MTX were subcutaneous (81%) and oral (19%). All the subjects answered the MISS with less than 5 minutes. The internal consistency of MISS had a Cronbach's alpha = 0.851 (patients) and 0.805 (parents), considered good ($\geq$0.8). The reproducibility between the test (40 patients) and the retest done after 15 days (36 patients) was almost perfect (kappa> 0.8). Reliability between patients and parents was almost perfect (kappa> 0.8), except stomachache (anticipatory with kappa = 0.30); considered weak (κ = 0.2 - 0.4) and stomachache by association (κ = 0.54); considered moderate (κ = 0.4 - 0.6). A cut-off scores of 3 showed the best sensitivity (93%) and specificity (71%). Using this cut-off we observed 78 (54.2%) patients intolerant
Conclusion: MISS is a good tool for physicians, because it can not only measure the intolerance, but also explore the different forms in which it manifests. Although MTX has a great therapeutic index, the adverse reactions are still seen as a major form of abandonment of this pharmacological treatment. Therefore a careful history is essential to identify side effects and adequate treatment to increase adherence.

REFERENCES

[1] Bulatovic M, et al. Arthritis&Rheumatism. 2011; 63: 2007-2013.
[2] Chausset A, et al. Clin Rheumatol. 2017; 36:1281-1288.
[3] Beaton D, et al. Spine.2000; 24:3186-3191.
[4] Terwee C, et al. J Clin Epidemiol.2007; 60:34-42.

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AB0932

PREDICTORS OF FLARE FOLLOWING ETANERCEPT WITHDRAWAL IN PATIENTS WITH RHEUMATOID FACTOR NEGATIVE JUVENILE IDIOPATHIC ARTHRITIS DURING 48 MONTHS OF FOLLOW-UP

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Background: Little is known about the risk of flare after etanercept (ETN) withdrawal in children with Juvenile Idiopathic Arthritis (JIA). Recently we conducted a retrospective chart review of 110 patients with JIA who discontinued ETN due to persistent clinically inactive disease (CID) on medication and were followed up to 12 months after ETN withdrawal. We showed that 60% of patients flared with arthritis. Male gender, presence of ANA and elevated CRP at baseline were associated with higher risk of flare.
Objectives: To evaluate frequency and timing of flares during 48 months of follow-up after withdrawal of ETN first course in patients with JIA who attained clinical remission on medication and to identify predictors of early flares (<12 months after withdrawal of ETN first course) and predictors of repeated flares ($\geq$2).
Methods: The 110 patients enrolled in the previous study with oligo (o-JIA) and RF-negative polyarticular JIA (p-JIA) who received a first course of ETN for at least 18 months and maintained clinically inactive disease (CID) for at least 6 months on treatment, were followed for 48 months after withdrawal of first course of ETN. We excluded patients that switched or swapped to other biologics or with limited follow-up. Demographic and clinical features at onset, at baseline (initiation of ETN) and at time of disease flares were collected.
Results: Among the cohort of the study, 10 patients (9%) were lost to follow-up and 18 (16%) switched/swapped to other biologics during 48 months of follow-up after withdrawal of ETN first course. Of the 82 patients included in the analysis, 55 (67%) were treated with only one course of ETN, while 27 (33%) received more than one course of ETN. The median age at disease onset was 3.6 years (IQR 1.9-8.5) and 72% of patients were female, ANA positive patients had a younger age at onset and were more frequently o-JIA. After withdrawal of ETN first course, 70 of the 82 (85%) patients enrolled flared with arthritis, without evident differences between o-JIA and p-JIA. Disease duration at diagnosis and at ETN start, total number of joints involved and total MTX treatment duration were not associated with flare. Patients who flared were more frequently males (p=0.017) and ANA positive (p=0.026), presented with higher levels of CRP (p=0.029) at baseline and had longer total ETN treatment duration (p=0.0046). Higher values of CRP were associated with a higher risk of repeated flares (p=0.0094). No predictors of early flares were identified in this group.
When we analysed the 55 patients treated with one course of ETN, 48 (87%) flared during follow-up. Patients who flared were more frequently ANA positive (p=0.015), presented higher CRP levels (p=0.042) at baseline and concomitant MTX at ETN withdrawal (p=0.009). Higher levels of CRP was also associated with higher numbers of repeated flares (p=0.049). No predictors of early flares were identified in this subgroup.
Conclusion: Our results show that almost 90% of patients with JIA experience at least one flare after ETN withdrawal during 48 months of follow-up. Our findings confirmed that male gender, positive ANA and elevated CRP at baseline are associated with a higher risk of flare. Higher CRP levels at baseline resulted also associated with a higher risk of repeated flares.

REFERENCES

[1] Predictors of Flare Following Etanercept Withdrawal in Patients with Rheumatoid Factor-negative Juvenile Idiopathic Arthritis Who Reached Remission while Taking Medication.
[2] Aquilani A, Marafon DP, Marasco E, Nicolai R, Messia V, Perfetti F, Magni-Manzoni S. J Rheumatol. 2018;45:956-961

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AB0933

ANALYSIS OF THE STATE OF IMMUNITY IN PATIENTS WITH JIA IN TREATMENT

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Background: The correct indication of the suspension of treatment with FAMES and biological therapy in pediatric patients, in the presence of a mild infectious disease or vaccination is a common problem in children's rheumatology. In patients with juvenile idiopathic arthritis (JIA), joint or extra-articular clinical reactivation during these "pauses" is not uncommon,

however, there are not enough studies in the pediatric population to show the influence of treatments on the immune system., and therefore, that justify this clinical practice.
Objectives: To analyze the levels of T, B and NK lymphocyte subpopulations in patients diagnosed with JIA treated with FAMES and biological therapy.
Methods: A descriptive and cross-sectional study in which 39 patients from the Pediatric Rheumatology Unit of the Reina Sofía University Hospital were recruited, diagnosed with JIA according to the ILAR 2001 criteria. The patients were divided into four groups: 8 controls in clinical remission without treatment, 17 in treatment with DMARD in monotherapy, 7 in biological treatment in monotherapy and 7 in treatment with DMARD-biological. Patients with systemic JIA were excluded because they had a pathogenic mechanism different from the rest of the JIA categories. By flow cytometry, the levels of CD3, CD4, CD8 and CD19 cells were measured for acquired immunity and from NK for innate, the CD4/CD8 index was also calculated.
Results: The mean age of the 39 patients was 10 ± 5.7 years, 29 were girls (74.3%), 4 patients had arthritis related to enthesitis, 16 patients had oligoarticular involvement ANA +, 6 subjects polyarticular involvement FR- and 13 they were psoriatic arthritis. Although no statistically significant differences were found when contracting cellular levels among the 4 groups evaluated, it was observed that the group treated with DMARD monotherapy had the highest percentage of children with alterations in cellular levels CD3, CD4, CD8 and CD19 (41.17% of the patients of the group); the group treated in monotherapy with biological treatment (28%) presented alteration in the levels of CD8 and CD19 and the group treated in combination of DMARD and biological (14.28%) in CD19. On the other hand, the NK cells and the CD4/CD8 index were not altered in any of the groups. Only 6 cases of serious infections were registered in patients in combination therapy (DMARD-biologic) who had received corticosteroids by clinical activity. There were no statistical differences between patients who had received corticosteroids and those who did not.
Conclusion: Patients in treatment with DMARD monotherapy had a tendency to decrease cellular levels. On the other hand, alterations in innate immunity or CD4/CD8 index were not observed.
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AB0934 IL-6 AND ALLELIC POLYMORPHISM OF ITS GENE IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: The development and maintenance of inflammation in juvenile idiopathic arthritis (JIA) is mediated by cytokine imbalance; interleukin 6(IL6) plays a leading role among pro-inflammatory cytokines. Its pathological synthesis has a negative impact on all organs and system. It is not excluded that its effector ability depends on genetic structures of IL6 gene. It has not been studied whether the allelic polymorphism of the IL6-174CG gene affects the effectiveness of targeted biological therapy.
Objectives: to assess the IL6 dynamics level in serum of patients with ineffective JIA-treatment.
Methods: The level of IL6 in the serum of JIA patients 1-18y.o. was determined using ECLIA method, debut of the disease (54) and treatment failure (36: 6 oJIA, 14 pJIA, 10 enthJIA, 6 sJIA). In patients with JIA, allelic polymorphism of the IL6-174CG gene was studied by PCR-method using allele-specific primers. A correlation analysis of clinical and laboratory parameters was made.
Results: Among patients with ineffective treatment of JIA, the duration of the disease was 39.5±35.8 months, 62.9% were girls. 27 patients received GC (<1mg/kg), 30-MTX(10-15mg/m2), 3-leflunomide, 1-AZA, 10-TZ, 16–ADA/ETA, 1-TFC, 5 were switched from antiTNF for antiIL6. The level of IL6 in the serum of JIA patients with treatment ineffectiveness was higher than at the beginning of disease (sJIA 52.40±73.84vs24.4±4.7 ($p < 0.05$); pJIA 36.19±58.6vs2.3±0.25($p < 0.05$); oJIA 8.69±5.27vs1±0.1; enthJIA 90.55±63.33vs .4±0.9pg/ml). There was no increase in IL6-level in patients with an unfavorable course of the RFpos-pJIA (8.4±7.35pg/ml) and with uveitis (5.59±4.94pg/ml) (norm.1.5–7pg/ml). In 57.1% of cases of RFneg-pJIA IL6 was elevated, in 3 children it was the highest (79.77-218.7pg/ml), they had anemia and osteoporosis. A high (51-484.6pg/ml) level was observed in 4 patients with enthJIA, in 1-inadequate therapy was performed, in 3 patients there was a fever, a lag in physical development, the highest CRP (up to 300 mg/ml). The correlation between the level of IL6 in the blood of children with JIA and the presence of lymphadenopathy in the debut of the disease (r=0.53), the child's age at the debut of the disease (r=0.63), examination (r=0.74), and the patient's weight (r=0.87), the duration from the onset of the disease to the initiation of biological therapy (r=0.44), the number of exacerbations in the first years of the disease (r=0.66-0.69), the formation of contractures and the limitation of movement in the joints (r=0.75), radiological progression in the 1st year from the debut (r=0.54), ESR (r=0.48), CRP (r=0.40), doctor's estimate of disease activity (r=0.79), ALT (r=0.69), AST (r=0.99), LDH (r=0.73) was found. There was no correlation with the number of affected joints (r=0.28), heart rate (r=0.48), metabolic abnormalities on the ECG (r=0.39). In children with an adverse course of JIA, IL6 correlated backward with TNF (r=-1), which was not observed in children at the onset of the disease (r=0.19).
Analysis of the results of genetic examination showed that among children with treatment failure 50% had GC-allele of the IL-6-174GC gene, 27,3% had GG allele, and 23,7% had CC allele.
Conclusion: Treatment of JIA leads to changes in cytokine profile. The IL6-174CG gene is associated with a high level of IL6 in the blood. The longer the duration of the disease and the time before the start of treatment with biological DMARDs, the greater the likelihood of an increase of IL-6-level in serum. In cases of even short-term enzymemia in JIA, subclinical activity with IL-6 can be suggested. In case of presence of some signs (hyperthermia, osteoporosis, anemia) in patients with antiTNF, it is advisable to determine the level of IL-6 in blood serum.
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AB0935 ANTI-TIF-1 G-ANTIBODIES IN JUVENILE DERMATOMYOSITIS ARE ASSOCIATED WITH VARIOUS CLINICAL PHENOTYPES

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Background: Juvenile dermatomyositis (JDM) is a rare heterogeneous autoimmune disease. The identification of myositis specific antibodies (MSAs) has allowed the characterization of subgroups of JDM patients who each have specific phenotypes. Antibody (Ab) against transcriptional intermediary factor-1-γ (TIF-1-γ or p155/140) is the most common MSA in JDM [1]. In the American and English JDM cohorts, anti-TIF-1-γ associated JDM is classically associated with a larger proportion of caucasians, mild or moderate severity with typical cutaneous manifestations (Gottron's papules, and/or heliotrope rash, photosensitivity), and a chronic disease course with a low mortality. The frequency of skin ulcerations and lipodystrophy differs between the two cohorts
Objectives: To report the clinical and muscle histology associations of anti-TIF-1-γ Ab in a series of patients with JDM followed in the French referral center for rare pediatric systemic autoimmune diseases.
Methods: Retrospective study of patients with JDM (according to the EULAR/ACR criteria) associated with anti-TIF-1-γ autoantibodies and included in our CEMARA database approved by the French National Committee on Informatics and Liberty.
Results: Thirteen patients were included (males: 5, females: 8; Caucasians: 6, Black Africans: 2, North Africans: 5). Age at diagnosis ranged from 1.5 to 11 years. Serum creatine kinase was elevated in 12 patients (range: 180-43 000 IU/L). Three different phenotypes were identified according to the severity and course. In group 1 (n=4), 3 patients had a moderate JDM: classical cutaneous manifestations and moderate muscle involvement; relapsing course, which remitted under methotrexate/corticosteroids; an additional 2-year-old girl had an amyopathic JDM. In group 2 (n=7), patients had a severe JDM : ulcerating skin lesions, severe muscle involvement, dysphagia, gastrointestinal vasculitis and/or requirement to an intensive care unit, and required more than two lines of treatment. In this group, 2/7 patients died from refractory JDM, comparing to a mortality rate of 2% in the remaining JDM patients tested for MSA and negative for anti-TIF-1-γ. Only 2/5 patients achieved a complete remission under treatment. Group 3 comprised two patients with severe muscle atrophy, calcinosis and lipodystrophy and a chronic course; one of them had a very-early-onset JDM at 1.5 year-old and the other an inherited neurological involvement, potentially suggestive of a genetic predisposing condition to JDM. None of the patients developed lung involvement or malignancy. Six patients underwent a muscle biopsy which was

scored using the JDM severity score tool. The histo-pathologists' overall severity score (VAS) varied from to 1 to 9/10; the highest scores were observed in the two patients who died.
Conclusion: In the present series of patients with JDM, TIF-1-γ Ab-associated-clinical phenotypes and ethnicities are more heterogeneous than previously reported. TIF-1-γ Ab is associated with a high mortality rate in a subset of patients.

REFERENCES

[1] Rider LG, Nistala K. The juvenile idiopathic inflammatory myopathies: pathogenesis, clinical and autoantibody phenotypes, and outcomes. J Intern Med. 2016;280(1):24-38

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AB0936 A NATIONAL SURVEY OF CLINICAL PRACTICE OF CORTICOSTEROID USE IN NEWLY DIAGNOSED OR FLARING CASES OF JUVENILE IDIOPATHIC ARTHRITIS ACROSS THE UK

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Background: Corticosteroids (CS) are widely used for rapid-action or induction treatment in children and young people (CYP) with juvenile idiopathic arthritis (JIA). Given a lack of evidence base on CS induction regimen for CYP with JIA, and since criteria for choosing CS are based on healthcare professional (HCP) preference, further research is needed (1).
Objectives: To establish the opinions of HCPs current practice regarding the clinical criteria for commencing CS treatment
Methods: A national electronic survey was undertaken among HCPs across the UK as part of the Steroid Induction Regimen for Juvenile Idiopathic Arthritis (SIRJIA) study.
Results: A total of 39 (24%) responses were received from 162 HCPs. These included 22 (56%) NHS consultants, five (13%) grid trainees, eight (21%) clinical nurse specialists and four other HCPs (10%).
The most common treatments in CYPs with newly diagnosed JIA or a disease flare were intra-articular (IA) CS or a combination of DMARDs and IAS (except for systemic JIA and oligoarticular JIA). The majority of HCPs 17 would treat new and flaring CYP the same in terms of a CS remission induction regime, with 53% choosing a different regime or not answering.
The key criteria that HCPs used for commencing CS and choosing the route of administration were rapid induction of remission (31 (89%)), high disease activity (31 (89%)), severity of systemic JIA (30 (86%)) and level of inflammation (28 (80%)) Table 1. The number one determinant of route of administration of CS was disease severity followed by disease subtype.
The majority of HCPs (52-72% depending on role) would consider entering CYP with JIA into a trial randomising to the various modes of administration.

Table 1:

Reasons of CS Choice	Number N=39	Percentage%
High Disease Activity	35	89.7
Rapid induction of remission	34	87.2
Severity of Systemic JIA	34	87.2
Level of inflammation	32	82.5
Severe Uveitis	30	76.9
JIA subtype	27	68.2
Targeting Specific Joints	26	66.7
Level of Disability	18	46.2
Level of pain	16	41.0
Long-standing Disease	11	28.1
Patient reluctance to take DMARDS	8	20.5

Conclusion: The results from this national survey of clinical practice showed varying practices in the management of new CYP with JIA and those that are flaring. The majority of HCPs who completed this survey, indicated that they would be prepared to consider entering CYP into a trial that randomised to the four CS delivery methods.

REFERENCES

[1] Deepak, et al. 2017 Literature review on the use of corticosteroids in juvenile idiopathic arthritis (JIA) Rheumatology 56(Suppl7)

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AB0937 IDENTIFYING THE PRIMARY OUTCOME MEASURE AND PROTOCOL COMPONENTS FOR A PROSPECTIVE FEASIBILITY STUDY OF CORTICOSTEROID REGIMENS FOR CHILDREN AND YOUNG PEOPLE WITH JUVENILE IDIOPATHIC ARTHRITIS USING CONSENSUS METHODS WITH YOUNG PEOPLE, FAMILIES AND PROFESSIONALS

Simon Stones[1], Heather Bagley[2], Ashley Jones[2], Flora Mcerlane[3], Tracy Moitt[2], Gloria Nkhoma[2], Frances Sherratt[4], Bridget Young[4], Michael Beresford[2,5], Eileen Baildam[5], SIRJIA Trial Management Group. *[1]University of Leeds, School of Healthcare, Leeds, United Kingdom*; *[2]University of Liverpool, Institute of Translational Medicine, Liverpool, United Kingdom*; *[3]Newcastle Hospitals NHS Foundation Trust, Great North Children's Hospital, Newcastle upon Tyne, United Kingdom*; *[4]University of Liverpool, Institute of Population Health Sciences, Liverpool, United Kingdom*; *[5]Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom*

Background: Juvenile idiopathic arthritis (JIA) is an umbrella term for seven relapsing-remitting inflammatory conditions in children and young people (CYP). Early, intensive treatment can prevent long-term damage; however, established drugs exhibit a delayed response, prompting the need for rapid-onset treatment in the form of corticosteroids. Given a lack of consensus as to which corticosteroid induction regimen should be used for CYP with JIA, a feasibility trial of different regimens is needed.

Objectives: The aim was to achieve consensus among CYP, families, and healthcare professionals (HCPs) about the primary outcome measures and protocol components to include in a prospective feasibility study.
Methods: A modified Nominal Group Technique was used to achieve consensus on the most appropriate primary outcome measure to be included in a prospective feasibility study, in addition to other protocol components such as inclusion/exclusion criteria. Fifteen participants participated in the process, including a combination of CYP with JIA, families (n=9) and HCPs (n=6).
Results: In the first vote, participants agreed that 'Juvenile Arthritis Disease Activity Score (JADAS)' and 'Physician Global Assessment Score' were most meaningful. During sub-group discussions, the need for a composite score which captured the voice of CYP and families was emphasised. In the second vote, 'JADAS' and the 'JIA Core Set' were identified as the most important. Further discussions led to the results of the third vote, agreeing 'JADAS' as the primary outcome measure of choice being measured at 6 weeks after commencement of treatment. The majority of HCPs, CYP and families voted for all JIA sub-types to be included in a prospective feasibility study, with some queries about the inclusion of systemic JIA given its unique presentation. Participants also identified the need for more frequent data collection time points to capture the rapid onset of corticosteroid action, while CYP and families opted for accessible mechanisms for participation, such as digital follow-up strategies.
Conclusion: It is feasible to include CYP, families and HCPs in synthesising complex concepts to agree by consensus the design components of clinical research. The primary outcome measure for inclusion in a prospective feasibility study of corticosteroid regimens in CYP with JIA was co-prioritised, with CYP and families taking a leading role in the ultimate selection of an appropriate outcome measure and other study protocol components. Using consensus methods with CYP, families and HCPs is a systematic and rigorous way in which to select outcome measures that are both meaningful and relevant to everyone involved in the care and treatment of CYP with JIA.

REFERENCES

[1] Sherratt F, et al. Family perspectives on the feasibility of a corticosteroid induction regimen trial in juvenile idiopathic arthritis. In: International Clinical Trials Methodology Conference: 2017; Liverpool, UK: Trials; 2017

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AB0938

EFFICACY AND SAFETY OF BIOLOGICAL THERAPY WITH ETANERCEPT IN A CASE OF SEVERE POLIARTHRITIS ASSOCIATED TO HARLEQUIN ICHTIOSIS

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Background: Harlequin Ichthiosis (HI) is a rare autosomical recessive congenital disease, due to mutations of gene ABCA12.The estimated incidence is approximately 1 in 300,000 births, and approximately 200 cases have been reported worldwide. Typical manifestations of the disease at birth are the presence of hyperkeratotic plates with erythematous fissures, ectropion (eversion of the lower eyelids) and eclabium (eversion of the lips), rudimentary ears and nasal hypoplasia, and articular contractures. Babies who survive into infancy tend to loose hyperkeratotic plaques in favour of generalized scaling and erythroderma. Mental retardation is present in about 2/3 of cases.The association between HI and inflammatory joint involvement has been reported only in few patients since now.
Objectives: We are describing the case of a 6 years old kid with HI that at the age of 4 developed arthritis with severe impact on his quality of life.
Methods: We report clinical and laboratory findings, treatment choices and outcomes of young boy with HI who developed polyarthritis.
Results: A 6 years old kid with HI (the genetic test showed homozigous mutation of ABCA12) came to our attention with an history of chronic arthritis.
Since he was 4, he developed bilateral knee arthritis. At first, he was treated with antimicrobial drugs, without improvement, in suspect of septic arthritis. In the following two years, he developed severe chronic poliarthritis.At the first visit in our center, he showed the classical clinical feature of HI (severe ectropion, contracture and generalized erythroderma), and had history of multiple severe infections and sepsis. Arthritis affected both hips, knees, ankles, wrists, elbows, shoulders and all the feet joints. He lost the ability to walk since the onset of arthritis.
Laboratorial features showed negative anti nuclear antibodies (ANA) and anti. extractable nuclear antigen antibodies (ENA), anti ciclic citrullinated peptide and rheumatoid factor. No signs of uveitis were present at ophtalmological evaluation.
The patient was treated with intraarticular corticosteroid injections (IACI) into knees, wrists, elbows and ankles, and then oral methotrexate (MTX) was started.
The clinical response was initially good, with partial recovery of deambulation in the 4 months following the intrarticular injection treatment. After 7 months ankles and wrists showed swelling and tenderness, and IACI were repeated, with clinical improvement.



Figure 1



Figure 1



Figure 1



Figure 1

Nonetheless, two months later, due to the persisting arthitis activity, anti TNF therapy was started. Etanercept at the dose of 0,8 mcg/week was found to be effective and safe, allowing the patient to walk again. Since the therapy onset, no severe adverse reaction was observed.

Conclusion: This is the first case of a kid with HI and poliarthritis treated with IACI and anti-TNF agent in combination with MTX. This clinical case shows the efficacy of IACI as a safe and powerful mean, with fast clinical response, in the treatment of arthritis in those patients. Furthermore, we observate the efficacy and safety of anti-TNF agents as baseline therapy for arthritis in patients with HI.

REFERENCES

[1] Raghuvanshi S, et al. Harlequin Ichthyosis and Inflammatory Arthritis: Case Reports of a very Rare Combination. Rheumatology 2015; 54, suppl_1, i55

[2] Clement S A, et al. Harlequin ichthyosis and juvenile idiopathic arthritis: a rare combination. Clin Rheumatol 2007; 26: 460–462.

[3] Chan YC, et al. Harlequin Ichthyosis in Association with Hypothyroidism and Juvenile Rheumatoid Arthritis. Pediatr Dermatol 2003; 20: 421–426.

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AB0939 NAILFOLD CAPILLAROSCOPY IN JUVENILE DERMATOMYOSITIS. DESCRIPTION OF ABNORMALITIES IN A SERIES OF PATIENTS

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Background: Juvenile dermatomyositis (JDM) is characterized by the presence of microangiopathy which can be assesed by nailfold capillaroscopy (NFC), a simple and noninvasive imaging technique. Morphological abnormalities in scleroderma NFC are well described, but it is known that they may be present in other autoimmune diseases, such as JDM.

Objectives: To describe the capillary morphological abnormalities assessed by NFC in a series of patients diagnosed with JDM in contrast with patients diagnosed with juvenile idiopathic arthritis (JIA).

Methods: A cross-sectional descriptive study in which 34 patients were recruited sequentially and randomly, 15 with JDM and 19 with JIA, from the Rheumatology department of Niño Jesus Hospital between September-November (2018). Demographic, clinical, analytical data, presence and subtype of calcinosis, active treatment, HAQ, patient and physician global assessment (PGA), cutaneous assessment tool (CAT) and manual muscle testing (MMT8) validated for JDM were collected. One observer performed blindly, both for clinic and diagnosis, a NFC initially using a videodermatoscope in order to obtain a wide view of the vascular bed and then with a videocapillaroscope (x500), which recorded 2-4 images per finger (except thumbs) to be analyzed far ahead. The presence of a decreased nailfold capillary density (NCD, capillary n°/mm≤6), architectural derangement (disorganization), neoangiogenesis, giant capillaries (ø>50μm, pathological if ≥1), enlarged loops (ø20-50μm) and microhaemorrhages, both pathological present in ≥2 fingers were evaluated. Neovascular pattern was defined as the sum of NCD, disorganization and neoangiogenesis with frequent haemorrhages and giants (active and late scleroderma pattern).

Results: The descriptive analysis of the main variables is shown in *table1*. Patients with **JIA:** all received active treatment, 95% MTX (33% concomitant with anti-TNF, 1 TCZ and 16% CE) and 1 anti-TNF. 26% active uveitis. Two patients presented morphological abnormalities: 1 neoangiogenesis and another enlarged loops. Patients with **JDM**: 73% received MTX (18% concomitant with CE, 73%Igs and 1 RTX). Three patients had active calcinosis: 2 mixed (circumscribed and cutis) and 1 calcinosis cutis. 2 had previous calcinosis (both circumscribed). 87% presented for the first-time weakness but none had current weakness (MMT8 40). 67% presented morphological abnormalities: NCD 33%, disorganization 40%, neoangiogenesis 53%, enlarged loops 27%, giants 20% and microhaemorrhages 13%. All patients with calcinosis (active or previous) presented disorganization and neoangiogenesis, NCD 80%, giants 60%, enlarged loops and microhaemorrhages 40%. 50% of patients with JDM had a neovascular pattern, of which 80% had a previous or current history of calcinosis.

Conclusion: Patients with JDM presented more abnomalities in NFC compared to patients with JIA. Neovascular pattern was observed in half of patients, who have previous or current history of calcinosis. Consequently, NFC could be a useful imaging technique in routine clinical practice to evaluate skin activity in patients with JDM.

REFERENCES

[1] Wu Q. Juvenile dermatomyositis: Latest advances Best Pract Res Clin Rheumatol.2017 Aug;31(4):535-557. **2.**Barth Z. Assesment of microvascular abnormalities by Nailfold Capillaroscopy in Juvenile Dermatomyosistis after medium to long-term follow up. Arthritis Care Res (Hoboken). 2018 May;70(5):768-776.

Abstract AB0939 TABLE 1. DEMOGRAPHIC, CLINICAL AND ANALYTICAL CHARACTERISTICS

Sex%	♀63 ♂38
Age (yr)	11
Disease duration (mn)	57
ESR/CRP	7/0.3
Patient/physician global assessment (PGA)	0/2
HAQ	0.14
Initial/current CAT BM	3/0
CPK	101
LDH	261
Initial/current MMT8	35/40

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AB0940 OBESITY AND NUMBER OF ACTIVE JOINTS AT TUMOR NECROSIS FACTOR-INHIBITOR START ARE ASSOCIATED WITH SHORTER REMISSION DURATION AFTER WITHDRAWAL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: PRELIMINARY RESULTS FROM A MONOCENTRIC COHORT

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Background: No recommendations on appropriate withdrawal of tumor necrosis factor-inhibitors (TNFi), once remission status has been achieved

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Gender	Male	Male	Male	Male	Female	Female
Age of onset of symptoms (years)	4	4	5	2	4	2
Age of diagnosis (years)	5	5	5	3	4	3
Time elapsed for diagnosis (months)	13	12	3	11	4	6
Initial manifestation	-Fever -Thrombocytopenia	-Arthritis	-Convulsive crisis	-Cutaneous vasculitis -Arthritis	-Cutaneous vasculitis -Arthritis	-Deep cutaneous lupus -Autoimmune hepatitis
Number of ACR criteria (1997)	4	6	6	5	4	4
Renal disease	LN Class IV, A:6/24 C:0/12)	LN Class III, A:2/24 C:2/12	LN Class IV A:7/24 C:3/12	LN Class III, A:5/24 C:1/12)	No	No

* LN: lupus nephritis. A: activity score. C: chronicity score.

in patients with juvenile idiopathic arthritis (JIA), are currently available[1]. With regards to possible predictors of flare, the role of obesity has not been investigated yet.

Objectives: To investigate to role of obesity at start of TNFi therapy on remission duration and flare rate after TNFi withdrawal in JIA patients.

Methods: The charts of JIA patients followed at the study center and treated with TNFi as first biologic from 2009 to 2015, who reached remission and with at least one year of follow up after withdrawal, were retrospectively reviewed. Exclusion criteria were: systemic JIA and pJIA RF-positive. Demographic and clinical features were registered, including: ILAR JIA subtype, occurrence of uveitis, ANA status, number of active joints at TNFi start and at flare onset, BMI (z-score and percentile at time of biologic withdrawal for determining obesity, overweight and underweight), concomitant DMARDs. For each patient we registered the remission duration and the occurrence of flare after 12 months from TNFi withdrawal. For comparison of continuous and categorical variables we respectively used the Mann-Whitney and Fisher's exact probability test. Spearman's test was used for correlation analysis. Data were expressed as median and interquartile range (IQR 25-75) and analyzed with SPSS 25.0. P values < 0.05 were considered significant. Variables with significant association with remission duration were included in the multivariable linear regression model.

Results: 57 JIA patients were included: 34 of them (59.6%) flared within 12 months after TNFi withdrawal with a median of 5 months (IQR 3-8). Obesity was found in 6 patients (10.5%), overweight in 7 (12.2%) and underweight in 6 (10.5%). No statistically significant difference in the aforementioned factors was found in patients who flared, if compared with patients who did not flare. In obese patients we observed a shorter remission duration (p = 0.04). In addition, remission duration was inversely correlated with the number of active joints at TNFi start (r = -0.40 p = 0.03). A multiple linear regression analysis was performed with remission duration as dependant variable and active joints at TNFi start (p = 0.007; B = -0.47) and obesity (p = 0.05 B = 0.31) as explanatory variables.

Conclusion: In our cohort the number of active joints at TNFi start and obesity were both associated to shorter remission duration after anti-TNF withdrawal. In particular obesity, a modifiable factor involved in several pathological conditions, should be handled more carefully in order to optimize JIA management. Larger studies need to confirm our preliminary data.

REFERENCES

[1] Shoop-Worrall SJW, Kearsley-Fleet L, Thomson W, Verstappen SMM, Hyrich KL. How common is remission in juvenile idiopathic arthritis: A systematic review. Semin Arthritis Rheum. 2017 Dec;47(3):331-337.

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AB0941

SYSTEMIC LUPUS ERYTHEMATOSUS IN CHILDREN UNDER 6 YEARS OF AGE, EXPERIENCE IN A TERTIARY CENTER

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Background: Systemic lupus erythematosus (SLE) is a rare entity in patients under 5 years old, depending on the ethnic group it has a prevalence of 3.3 to 24 per 100 000 children. Before puberty no difference in prevalence associated with gender was observed. In the pediatric age, SLE has a more aggressive course.[1]

Objectives: To describe the demographic and clinical characteristics of 6 patients under 6 years old diagnosed with SLE.

Methods: To describe the demographic and clinical characteristics of 6 patients under 6 years old with a diagnosis of SLE based on the 1997 ACR criteria at the Federico Gomez Children's Hospital of Mexico from June 2017 to January 2019.

Table N°1. Demographic and clinical characteristics of patients under 6 years of age diagnosed with SLE.

Results: The diagnosis of SLE in patients under 5 years old is rare, the literature describes that in these patients there is greater renal, hematological and neuropsychiatric manifestations; We present the demographic and clinical characteristics of 6 patients under 6 years of age with a diagnosis of SLE based on criteria of ACR 1997; 4 of the patients presenting are male, in three of the cases the initial manifestation was non-erosive arthritis and skin manifestations (in two purpura and in one deep cutaneous lupus), in four of the cases lupus nephritis was presented; the average time between the onset of symptoms and the diagnosis was 8 months (range between 3 and 13 months).

Conclusion: The diagnosis of SLE in patients under 6 years old is rare, the initial manifestations may be nonspecific, which causes greater complexity to establish an opportune diagnosis. It is described that in lupus cases in pediatric patients there are clinical manifestations of greater severity and early diagnosis modifies the prognosis. The initial manifestations of SLE in patients younger than 6 years old in our series are similar to those described in the literature: arthritis and seizures, as well as the presentation associated with gender, with no difference in preschool age. [2] It has been described that the time elapsed from the onset of symptoms to the diagnosis is shorter at younger age of patient, however in our series the time of diagnosis was an average of 8 months, probably related to the low prevalence of the disease in this age group.

REFERENCES

[1] Malattia C., Martinni A. (2013 Jun). Paediatric-onset systemic lupus erythematosus. Best Pract Res Clin Rheumatol;27(3):351-62.

[2] Jia Zhu., Fengqi Wu., Xiaolan Huang. (2013 Jan). Age-related differences in the clinical characteristics of systemic lupus erythematosus in children. Rheumatol Int 33:111–115.

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AB0942 RADIOLOGICAL SACROILIITIS AFTER 18 YEARS OF FOLLOW-UP IN THE POPULATION-BASED NORDIC JUVENILE IDIOPATHIC ARTHRITIS (JIA) COHORT

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Background: A challenge with the present classification of JIA is the evolution of the disease over time. One category that is especially difficult to classify is enthesitis-related JIA (ERA).
Objectives: To longitudinally study radiologically diagnosed sacroiliitis (SI) developed during the first 18 years in an aim to gain knowledge about classification challenges posed by the proposed, new classification (Martini A. et al. J Rheumatol. 2018 Oct; Epub ahead of print).
Methods: 510 consecutive cases of JIA with disease onset 1997 to 2000 were prospectively included in a Nordic, longitudinal, close to population-based 18-year follow-up study, and 434 (85%) had at least two follow-up visits during disease course. At the 18-year follow-up visit; 329 (76%) attended a clinical visit, and 105 (24%) a telephone interview. The follow-up period was 17.5 ± 1.7 years (mean ± SD) after onset. Mean age of the study participants was 24.0 ± 4.4 years. Clinical data, collected at one, eight and 18 years after disease onset, were evaluated regarding variables for enthesitis/spondylitis-related arthritis compared to the other JIA categories.
Results: In 376 participants evaluated for SI, radiology was performed on clinical suspicion, 26 (16 males, 10 females) developed radiologically verified sacroiliitis (rad-SI) during the first 18 years of disease. Age at onset was significantly higher in this group compared to the other participants, median 9.9 (IQR 6.4-12.0) vs. 5.6 (IQR 2.6-9.5) years, (p=0.001). Only 3/26 had rad-SI at eight-year follow-up.
Using the ILAR criteria 12/26 with rad-SI were classified as ERA after median 7 (IQR 6-10.2) months, 1/26 as juvenile psoriatic arthritis, 5/26 as undifferentiated JIA because of psoriasis-related variables, the remaining had oligo- or polyarticular arthritis. At 18-year follow-up, 18/26 fulfilled criteria for ERA, 2/26 juvenile psoriatic arthritis, and 3/26 the undifferentiated category because of psoriasis-related variables, 3/26 had polyarticular RF negative or oligoarticular extended disease. Enthesitis, inflammatory back pain and SI joint tenderness were more common with rad-SI (p<0.001; p<0.001; p<0.001), also HLA-B27, 18/26 vs. 62/351 (p<0.001), but not 1st degree heredity for ankylosing spondylitis. Uveitis developed in 10/26 (38.5%). Two participants developed IBD.
Conclusion: The majority of variables involved in the new proposed classification of enthesitis/spondylitis-related JIA were significantly more common during the first 18 years of disease in those that developed rad-SI. Psoriasis-related variables, no longer exclusion criteria for ERA, should be further evaluated as possible inclusion criteria, as well as higher age at onset.
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AB0943 CLINICAL AND LABORATORY PRESENTATION OF JUVENILE SJÖGREN'S SYNDROME IN A COHORT OF 30 PATIENTS

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Background: Sjögren´s Syndrome (SS) is a chronic autoimmune disease, rare in childhood and adolescence, characterized mainly by xerostomia and xerophthalmia, which compromises exocrine glands causing inflammatory response that leads to glandular hyposecretion. SS is probably underdiagnosed in pediatric range due to differences in presentation regarding adults with this condition, causing low recognition of the disease in children.
Objectives: The authors describe demographic, clinical, laboratory and therapeutic profiles of a cohort of children with primary SS attended at a university center.
Methods: Retrospective analysis of 30 selected patients' medical records between 2005 and 2017 allowed collection of various data. Laboratory and additional investigations included documentation of ocular dryness (Schirmer test, Rose-Bengal stain); evidence of parotid involvement (scintiscan, sialometry); and histological evidence of lymphocytic infiltration of the minor salivary glands or other organs.
Results: 30 patients diagnosed with juvenile SS were selected: 22 girls (73%) and 8 boys (27%) with an average age of 11 years. The clinical characteristics were: parotid enlargement as the initial manifestation of the disease in 11 patients (37%), and recurrent episode in 4 patients (13,3%). 12 patients (40%) had xerostomia and 17 (57%) xerophthalmia. One patient (3,3%) presented with leukocytoclastic vasculitis in lower limbs as first manifestation of the disease in association to recurrent parotid swelling. Two (6,6%) patients presented neurological symptoms (1 peripheric sensory neuropathy and 1 with dysautonomic manifestations). Positive Schirmer test was observed in 11 patients (37%), Rose Bengal stain in 10 (33%). 76% of patients had abnormal salivary glands scintigraphy. In 8 patients (30%) the salivary gland biopsy revealed compatible with Sjogren syndrome. 9 patients (30%) presented positive RF, 14 patients (46%) anti-Ro/SSA, 10 patients (33%) anti-La/SSB, 28 patients (93%) had +ve ANA. 50% received glucocorticoid. Hydroxychloroquine was the drug most often used in 25 patients (83%), followed by methotrexate in 12 patients (40%), azathioprine in 4 patients (13%) and cyclophosphamide in 3 patients (10%). Only one patient required the use of human immunoglobulin and one leflunomide (3.3%). Two patients (6.6%) received rituximab.
Conclusion: The present study demonstrated the demographic, clinical aspects and laboratory and treatment in a series of patients with primary juvenile Sjögren's syndrome, a relatively rare condition, presenting an overview of this population in our hospital.

REFERENCES

[1] Primary Sjogren syndrome in the paediatric age: a multicentre survey. Rolando Cimaz, Annachiara Casadei, Carlos Rose, et al. Eur J Pediatr (2003) 162: 661–665.
[2] Primary Sjögren's syndrome in children and adolescents: Proposal for diagnostic criteria. J. Bartunková, A. Sedivá, J. Vencovsky, V. Tesar. Clinical and Experimental Rheumatology 1999; 17: 381-386
[3] Primary Sjo¨gren syndrome in childhood: Report of a case and review of the literature. Nikolaos G. Nikitakis, Helen Rivera, Carmela Lariccia, John C. Papadimitriou, and John J. Sauk. Oral Surgery Oral Medicine Oral Pathology Radiol Endod 2003;96:42-7.

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AB0944 SJÖGREN'S SYNDROME IN CHILDREN: A CASE SERIES

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Background: The symptoms of pediatric Sjögren's syndrome (SS) are different than in adults. There are currently no validated pediatric diagnostic criteria or treatment guidelines for SS. In most cases adult criteria are used, but they apply poorly to children.
Objectives: To present pediatric patients with primary SS who were treated at University Children's Hospital (UCH) Ljubljana in the past 10 years.
Methods: Eight children with primary SS were identified. Demographic data, clinical and laboratory findings and therapy were analysed by retrospective review of medical records at UCH Ljubljana.
Results: Six girls and 2 boys were evaluated. The mean age at disease onset was 12.3 years (range 6.5 – 17) and mean age at diagnosis was 13.8 years (range 7.5 – 17.5). The mean follow-up duration was 2.8 years (range 0.5 – 8.5). Four patients presented with recurrent bilateral parotitis, two with rash, one with arthralgia and fatigue and one with acute central nervous system vasculitis. The latter patient presented with rheumatic fever at the same time. During disease course arthritis and/or

arthralgia was present in 5/8, parotitis in 4/8, oral symptoms in 4/8, rash in 4/8, fatigue in 3/8 and ocular symptoms in 2/8 patients. One patient developed calcinations on fingers. All patients had high titer of antinuclear antibodies, 7/8 were positive for anti-Ro and 5/8 for anti-La antibodies. Three patients were tested for rheumatoid factor and all were positive. 6/8 patients had elevated ESR and hypergammaglobulinemia. 4/8 patients had elevated serum amylase.

Biopsy of salivary glands was performed in 5 patients and foci of lymphocytic infiltration were shown in all of them. Further two patients had salivary gland changes on MRI and/or US. On ophthalmologic evaluation 3 patients had positive Schirmer test and one had unstable tear film. One patient had CNS vasculitis and two decreased diffusing capacity of the lungs. Other patients showed no signs of internal organ involvement.

4/8 patients were treated with NSAIDs, 7/8 patients with hydroxychloroquine, 2/8 also received corticosteroids and one patient MMF. At this point the patient with CNS vasculitis has stable changes on head MRI without clinical symptoms. Other patients have no signs of internal organ damage. Calcinations that appeared on fingers in one patient are not progressing.

Conclusion: Most common symptoms in our cohort were arthritis and/or arthralgia, parotitis, oral symptoms and rash. Half of the children presented with recurrent parotitis. One child developed calcinations on fingers, which have not yet been described in patients with SS. Pediatric SS differs from adult SS and specific pediatric diagnostic criteria would improve management of these patients.

REFERENCES

[1] Yokogawa N, Lieberman SM, Sherry DD, Vivino FB. Features of childhood Sjogren's syndrome in comparison to adult Sjogren's syndrome: considerations in establishing child-specific diagnostic criteria. Clin Exp Rheumatol 2017; 34(2): 343–351.

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AB0945 CO-MORBID AFFECTIONS FORMATION IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: In children with systemic lupus erythematosus (SLE) due to the cascade of immune-inflammatory reactions there is a development of systemic vascular endothelium lesion, which causes not only clinical manifestations of the main process, but also leads to the damage of vital organs and systems, the development of metabolic disorders. Extensive damage aggravates more the course of the disease, worsens its prognosis, complicates the response to therapy and reduces the quality of life of patients.

Objectives: The aim of study was to determine the frequency and variants of comorbid conditions in children depending on the duration and activity of the disease and feathers of the therapeutic complex.

Methods: A survey was conducted on 41 patients with SLE: 37 girls (90.2%), 4 boys (9.8%); the duration of the disease is up to 3 years in 20 patients (48.8%)and more than 3 years in 21 (51,2%). Presence of comorbid conditions determinates as the cardiovascular system, kidney, liver and lungs functions changes. General clinical trials included autoantibodies, disease activity and drugs assessment. Total cholesterol, triglycerides, high density lipoprotein cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, ApoA-I and lipoprotein-α were evaluated. The state of the blood coagulation system was also studied: fibrinogen of the blood, prothrombin index, thrombin time, active partial thrombin time, D-dimer, international normalized ratio. Bone mineral density was determined.

Results: In 74.3% of children with SLE, the presence of comorbid conditions characterized by pathology of the cardiovascular system, kidneys, liver, the organ of vision, pulmonary system is established. Besides, atherogenic dislipoproteinemia has been detected in 60,0%, disorders in the hemostasis system were in 25,0% of patients and 43,0% persons have osteopenia. Children with SLE and the presence of comorbid conditions, especially with the involvement of the liver and kidneys and the long-term preservation of the disease activity (SRP, ANA, anti-DNA), are more likely to develop atherogenic dislipoproteinemia and hypercoagulation (increase in the prothrombin index, fibrinogen and D- dimer). The values of the comorbidity index in patients with SLE increased while maintaining the activity of the process and using high doses of glucocorticosteroids (GCS) including pulse therapy. Comorbidity index was 2.9 ± 0.5 points in the patients who received the GCS pulse therapy; 2.5 ± 0.3 in the cases of treatment by combination GCS + azathioprine; 2,0 ± 0,6 in the children without GCS; $p<0,05$). ANA-positivity was also accompanied by higher values of the comorbidity index (2.8 ± 0.3 vs. 1.4±0.5, $p<0.05$).

Conclusion: Children with SLE in the long-term course of the disease and while maintaining the activity of the pathologic process (ANA, DNA antibodies high level) have a formation of lesions of systems and organs, the lipids metabolism disorders, prolonged hypercoagulation and the development of osteopenia. Aggressive therapy for reducing the activity of the autoimmune process helps to prevent the formation of comorbid states and persistent metabolic disorders.

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AB0946 QUALITY IMPROVEMENT IN PEDIATRIC RHEUMATOLOGY: A NEW APPROACH TO CARE IN QATAR

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Background: Quality improvement (QI) projects have been established in many pediatric and adult rheumatology centers around the world to enable real time improvement of health delivery and outcomes. QI has been driven by the Institute of Medicine, patients, professional organizations and the providers. Notably, another driver is the discrepancy between the availability of better and targeted therapies and poor disease outcomes.[1] QI allows for healthcare teams to decide on improvement goals to address gaps in care and implement these goals in sustainable ways, evaluate the impact and start a new cycle of improvement. In so doing, teams collaborate, learn from each other, and improve variability in a short time frame. In small practices with limited resources, effective QI projects allows for understanding the gaps in the processes, data collection and several process improvements to be done by different team members, in short cycles that allow for real time data evaluation and fine tuning processes.

Objectives: We describe the chosen quality measures, implementation of processes and first 6 months of data at a newly opened Children's Hospital in Doha, Qatar.

Methods: We chose quality measures that have been proposed in the literature and have been implemented in large learning collaboratives. [1] We worked with the informatics team to build measures that are accurately captured and retrievable from the electronic medical record. Additionally we worked with our Ophthalmology clinic to ensure a smooth referral pathway that is coordinated by nursing staff. Our EMR measures were 1) the screening for drug toxicity among patients receiving methotrexate or leflunomide within 3-4 month of receiving Methotrexate 2) the time between referral to and visit in Ophthalmology, to screen for toxicity among patients receiving hydroxychloroquine 3) time between referral to and visit in Ophthalmology, to screen for uveitis in children diagnosed with juvenile idiopathic arthritis.

Our nursing teams developed a manual joint injection log 1) to capture whether the time between referral for procedure and procedure date occurred within 2 weeks, and monitor side effects.

We examined data between June to December 2018 from the pediatric rheumatology patient population of 420 unique patients.

Results: 96% of children receiving methotrexate or leflunomide were screened for methotrexate toxicity within 3-4 months of the medicine being dispensed.

50% of children receiving hydroxychloroquine were seen by Ophthalmology within 4 months of the referral.

71% of children with JIA were seen by Ophthalmology within 1 month of the referral.

100% of children had joint injections performed within 14 days of the referral.

Conclusion: We described the development, implementation and results of our pediatric rheumatology QI projects. To our knowledge it is the first of a kind in Qatar and in the area. For our growing practice of 600 patient visits our data shows areas of great performance and poor performance, specifically in eye care for our patients. Barriers included education of teams about QI measures and processes, collaborating with other services on negotiating best patient practices.

Successful implementation in our processes underlines the need for further data collection and additional improvement cycles. Additionally, in resource poor areas, it is essential to make good use of the EMR and

work in collaborative teams to ensure participation and sustainability of processes. Next steps would be to add additional quality and disease outcome measures.

REFERENCES

[1] Harris, J. et al. Improving Care Delivery Outcomes in Pediatric Rheumatic Diseases. Curr Opin Rheumatol. 2016 March; 28(2): 110–116.

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AB0947 TREATMENT WITH SIMULTANEOUS BIOLOGICAL AGENTS IN JUVENILE IDIOPATHIC ARTHRITIS: SINGLE-CENTER CASE SERIES AND REVIEW OF LITERATURE

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Background: Several therapeutic choices are currently available for juvenile idiopathic arthritis (JIA) patients. The classical first line therapies are NSAIDs and corticosteroids (CTCs) and the second line encompasses synthetical and biological DMARDs. The clinical efficacy of DMARDs (alone or in combination) has been well demonstrated in RCTs and the treatment is often tailored on an individual basis. Combination of bDMARDs has not been formally evaluated in rheumatology and few publications are available concerning the combination of bDMARDs in patients with severe active forms of JIA, mainly systemic [SoJIA] and polyarticular [PA] categories. (1)
Objectives: To describe efficacy and safety of JIA patients resistant to MTX and bDMARDs requiring a simultaneous bDMARDs treatment.
Methods: Retrospective analysis of 7 (4.7 ± 2.1 years, male sex 75%) patients with JIA of a single tertiary center. A systematic review of literature was made to search observational studies from MEDLINE database (January 1946 to January 2019).
Results: All patients in the Paediatric Rheumatology Department (Lyon University Hospital) receiving combination therapy with bDMARDs were eligible. Seven patients with JIA diagnosis (4 SoJIA and 3 PA) were included. Genetic studies were performed in three patients, with positive LACC1 mutation in one. The exposure to the bDMARDs of the whole cohort was 79 patient-years (PY), including 16.5 PY of combination with simultaneous bDMARDs. The delay between the date of diagnosis and the first prescription of a combination of simultaneous bDMARDs treatment was 8.3 ± 4.8 years. Nine bDMARDs drugs were prescribed: anti-TNFs, tocilizumab and rituximab (nine times each). Ten co-prescriptions of the bDMARDs were administrated with 5 possible types of combinations between them, the most frequent associating tocilizumab/rituximab. Rituximab was used most frequently in combination with another bDMARD. The rituximab schedule was different between patients. Disease activity decreased for all patients, primarily at the biological level without reaching complete clinical remission.
In general, the clinical tolerance to the co-prescription of bDMARDs was acceptable. One patient (P2) experienced a severe hepatitis event in adulthood attributed to the treatment (tocilizumab), dropping the bDMARDs combination. During the exposure time, the most frequent adverse events were infections: repeated otitis media (P1), persisting vaginitis and fungal urinary infection (P3) not requiring hospitalization. One patient (P6) had 2 episodes of purpuric rash on the days of the canakinumab injection requiring oral CTC treatment. No severe acute reactions were found and no patients died.
The systematic review found a publication: retrospective series of 4 patients (SoJIA) combining abatacept and canakinumab (2).
Conclusion: Severe forms of JIA that are refractory to the current therapeutic options available could benefit from the combination of bDMARDs. The combination of bDMARDs may be an alternative therapy to explore in this group of patients.

REFERENCES

[1] Cimaz R, Marino A, Martini A. How I treat juvenile idiopathic arthritis: A state of the art review. Autoimmun Rev. 2017 Oct;16(10):1008–15.
[2] Record JL, Beukelman T, Cron RQ. Combination Therapy of Abatacept and Anakinra in Children with Refractory Systemic Juvenile Idiopathic Arthritis: A Retrospective Case Series. J Rheumatol. 2011 Jan;38(1): 180–1.

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AB0948 PARADOXICAL TINEA AMIANTACEA IN A PATIENT WITH JUVENILE IDIOPATHIC ARTHRITIS RECEIVING ADALIMUMAB

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Background: Tinea amiantacea is a papulo-squamous condition of the scalp that can lead to scalp fibrosis and subsequent permanent hair loss. It is thought to represent a reaction pattern to inflammatory skin disease as psoriasis or seborrheic dermatitis (1).
Objectives: To highlight an adverse reaction which involved the skin in the disease course of a young JIA (juvenile idiopathic arthritis) patient, during treatment with adalimumab.
Methods: A 16-month-old female patient presented to our clinic with a 4-week history of knee swelling, associated with functional limitation and morning stiffness. Family history was unremarkable, while past medical history revealed atopic dermatitis in the first year of life. The baby was initially treated with NSAIDs, but one month later, due the persistence of arthritis and the appearance of uveitis, subcutaneous methotrexate was started (15 mg/m^2/weekly). However 5 months later, given the persistence of uveitis and the onset of a severe hypertransaminasemia, methotrexate was interrupted and adalimumab (24 mg/m^2 every 2 weeks) was introduced with a prompt and stable control of ocular and articular disease and a gradual normalization of transaminases. One year later the patient developed dry, itchy, red and cracked skin behind her ears, with fissuring in the lower attachment of the ear lobe, and presented right parietal yellowish scalp lesions which were pruriginous, thick, and scaly, attached both to the scalp and to the proximal hair shafts. A first diagnosis of pityriasis amiantacea secondary to atopic dermatitis was made. A paradoxical cutaneous reaction to the anti-TNF therapy was later hypothesized (2), and 7 months later adalimumab was interrupted with quick resolution of the dermatologic lesions. However, both arthritis and uveitis rapidly recurred, showing an inadequate response to a six month cycle of abatacept treatment (10 mg/kg/month). Adalimumab was than reintroduced with a rapid improvement.
Results: Currently, after 16 months of adalimumab treatment, the patient still shows complete disease control, without any new dermatologic lesions up to now.
Conclusion: TNF antagonist-induced tinea amiantacea is a rare adverse reaction that may require the drug discontinuation. Although the exact pathogenetic mechanism is unclear, an imbalance in the cytokine milieu with a selective overexpression of type I interferon has been hypothesized.

REFERENCES

[1] F. Osório, F. Magro, C. Lisboa, S. Lopes, G. Macedo, H. Bettencourt, F. Azevedo, S. Magina, Anti-TNF-Alpha induced psoriasiform eruptions with severe scalp involvement and alopecia: report of five cases and review of the literature. Dermatology. 2012;225(2):163-7. doi: 10.1159/000342503
[2] J. Ettler, D.A. Wetter, M.R. Pittelkow. Pityriasis amiantacea: a distinctive presentation of psoriasis associated with tumour necrosis factor-α inhibitor therapy. Clin Exp Dermatol. 2012 Aug;37(6):639-41. doi: 10.1111/j.1365-2230.2011.04286.x.

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AB0949 IS PEDIATRIC ONSET LUPUS MORE SEVERE IN BOYS? OUR EXPERIENCE AT A TERTIARY CARE CENTER IN NORTH-WEST INDIA

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Background: There is diversity in clinical presentation of pediatric onset SLE (pSLE) and the manifestations are more severe as compared to

adults. Males comprise 4-22% of all SLE patients. Gender distribution of pSLE is 4.5-5: 1 (female-to-male) as opposed to 9-10: 1 (female-to-male) in the adult population. However male patients have been known to have a more severe disease with higher morbidity, especially due to renal causes.

Objectives: To evaluate clinical and immunological profile and outcomes in a follow up series of males with pediatric onset SLE

Methods: We analyzed the clinical and immunological profile and outcome of male patients diagnosed with SLE at less than 16 years of age. These children were followed-up in Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Postgraduate Institute of Medical education and research, Chandigarh, India. Details on demographic data, clinical presentation, laboratory findings, immunological profile, treatment regimens and outcomes of these children were retrieved from clinic files.

Results: Forty-three boys were diagnosed to have SLE between January 1998 to December 2018. Mean age at presentation was 9.7 years (range: 9 months-12 years). Total patient years of follow up was 192 years. The most common clinical presentation was fever in 38 (88%) patients; rash in 27(63%); pallor in 21(49%); edema with urinary abnormalities in 17(40%) and photosensitivity in 16 (37%). A diagnosis of lupus nephritis was made in 25 (58%) patients out of which 17 (39.5%) had nephritis at presentation. Renal biopsies were performed in 18 patients; 11 had class IV disease, 2 had class 5 disease, 2 had class IV/V. Neuropsychiatric manifestations were seen in 11 (26%) patients- 7 of these had symptoms at presentation. Seizures were the predominant manifestation in 9 patients (21%)-6 of these had MRI changes consistent with posterior reversible encephalopathy syndrome while 3 had cerebral infarcts. Other central nervous system abnormalities included psychosis (1 patient) and chorea (1 patient). We also noted a family history of lupus like illness in 4 patients and 3 (6.9%) were found to have early complement deficiencies. Antiphospholipid antibodies (aPLA) were detected in 8 (18.6%)patients - anticardiolipin antibody was positive in 8 and lupus anticoagulant was positive in 6. Dual aPLA positive was seen in 6(13.9%) and triple positive was positive in none. Infections were seen in 16 (37%) patients during follow-up. All patients received steroids in gradually tapering doses along with hydroxychloroquine following a diagnosis of SLE. Cyclophosphamide was given for induction in 13 patients who had severe forms of lupus nephritis. Remission was maintained through azathioprine in 8 patients and 8 required Mycophenolate mofetil. Ten patients (23%) had a relapse on therapy -1 had CNS relapse, 3 had renal relapse, 2 had muco-cutaneous relapse and 4 had hematological relapse. Six fatalities (14%) were recorded during follow-up -1 with severe disease activity and neuropsychiatric manifestations, 1 had disseminated tuberculosis, 1 had CNS flare with status epilepticus, 4 had sepsis.

Conclusion: This is one of the largest series on boys with pediatric onset SLE from a developing country. It appears that while the severity of lupus nephritis in boys is no different from that in girls, neurological disease is more severe in the former. Further, boys appeared to have earlier onset of neuropsychiatric lupus as compared to girls. The incidence of complement deficiency lupus was also more in boys. Mortality in boys with SLE appears to be comparable to our previously published mortality data on pSLE(1).

REFERENCES

[1] Abujam B, Gupta A, Suri D, Rawat A, Singh S. Trends and predictors of mortality in childhood onset lupus in a single North-Indian centre over 23 years: a retrospective study. Clin Exp Rheumatol. 2016;34(3):554–9.

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AB0950 CORRELATION OF QUANTITATIVE MAGNETIC RESONANCE IMAGING BIOMARKERS AND AXIAL PAIN IN ENTHESITIS-RELATED ARTHRITIS PATIENTS

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Background: Magnetic resonance imaging is increasingly used to diagnose, stratify and monitor inflammation in patients with spondyloarthritis, including young patients with enthesitis-related arthritis (ERA). Recently, there has been interest in the use of quantitative magnetic resonance imaging (qMRI) as an objective method of assessing disease. For example, diffusion-weighted imaging (DWI) and fat fraction (FF) mapping have emerged as biomarkers of oedema and structural damage, respectively, in inflamed bone[1]. However, as yet there are limited data to tie these biomarkers to underlying immunopathology.

Objectives: To analyse the relationships between quantitative imaging biomarkers (QIBs), axial pain and serum biomarkers – including 'inflammatory' biomarkers and those reflecting bone turnover - in a cohort of ERA patients.

Methods: 28 patients with ERA were prospectively recruited. The hips, sacroiliac joints and lumbar spine were assessed with chemical shift-encoded MRI and diffusion weighted imaging. Quantitative MRI parameters, such as the apparent diffusion coefficient (ADC) and fat fraction (FF) were measured in the sacroiliac joints. Visual scores for inflammation and fat metaplasia were also reported. BASDAI questionnaires were completed. Serum cytokines and bone markers were measured via multiplex bead-based immunoassays (Luminex) and results were available for 14 patients with ERA.

Results: The mean visual analogue score for spinal and hip pain (BASDAI Q2) was 3.9 (Table 1). There was a correlation between ADCmean and spinal and hip pain (rs=0.393, P=0.043). There was also a negative correlation between FFmean and the above pain score (rs = -0.378, P=0.047). There was a positive correlation between matrix metalloproteinase-3 (MMP-3) levels and FFmean (n=14, rs=0.698, P=0.006). However, the correlation did not reach statistical significance when corrected for multiple testing.

Conclusion: The correlation of ADCmean, which increases with increased tissue water/inflammation, with spinal and hip pain suggests that BASDAI Q2 relates to pain of active inflammation. Similarly the inverse correlation of FFmean, which increases with bone healing and reduced inflammation, and BASDAI Q2, would also support this relationship.

REFERENCES

[1] Bray TJP, Bainbridge A, Punwani S, Ioannou Y, Hall-Craggs MA. Simultaneous Quantification of Bone Edema/Adiposity and Structure in Inflamed Bone using Chemical-Shift Encoded MRI in Spondyloarthritis. Magnetic Resonance in Medicine 2018 Feb;79(2):1031-1042

Abstract AB0950 Table 1

Baseline Characteristics of ERA patients	
Number, n	28
Age (years), mean	17.96 (12-22)
Disease duration (years)	5.64 (0-16)
Sex	
Male, n (%)	19 (67.9%)
Female, n (%)	9 (32.1%)
Biologic monotherapy, n (%)	1 (3.6%), (Etanercept)
csDMARD monotherapy, n (5)	7 (25%), (4 Methotrexate, 3 Sulfasalazine)
Biologic and csDMARD, n (%)	12 (42.9%)
NSAIDS only, n (%)	2 (7.1%)
No treatment, n (%)	6 (21.4%)
BASDAI (mean)	3.41 (0-8)
Spinal and Hip pain (BASDAI Q2, 0-10)	3.89 (0-10)
HLA-B27 positive, n (%)	12 (42%)
CRP (mean, mg/dl), n=23	4.07 (0.5-22)
Sacroiliitis on MRI, n (%)	21 (75%)

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AB0951 MULTICENTRIC CARPOTARSAL OSTEOLYSIS SYNDROME – A RARE BUT IMPORTANT DIFFERENTIAL OF JUVENILE IDIOPATHIC ARTHRITIS. CASE REPORT OF TWO BROTHERS WITH AN IDENTICAL MAFB MUTATION

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Background: Carpotarsal osteolysis is observed in a rare group of 'vanishing bone' skeletal dysplasias. Diagnosis requires a high index of suspicion combined with clinical and radiological signs. Inheritance varies amongst subtypes.

Multicentric carpotarsal osteolysis syndrome (MCTO) is characterised by aggressive osteolysis in early childhood predominantly in the carpal and tarsal bones. It is associated with kidney disease in >50% which can progress rapidly to end stage renal failure. Prediction of renal impairment is not currently possible. MCTO shows an autosomal dominant inheritance pattern with heterozygous mutations in the *MAFB* gene.

Objectives: Describe two brothers affected by MCTO highlighting the importance of a genetic diagnosis.
Methods: B1 (20 years) presented age 3 years with swollen painful feet and restricted movement in his fingers and wrists and was diagnosed with polyarticular juvenile idiopathic arthritis (JIA). After no response to steroid treatment he developed rapid onset fixed flexion deformity of both elbows. He had mild learning difficulties. Based on clinical and radiological findings he was diagnosed with carpotarsal osteolyisis age 4 years. Bisphosphonates and vitamin D replacement did not halt progressive bony destruction. Consistent with the literature osteolysis stabilised in the teenage years. Renal function remains normal.
B2 (5 years) is a dizygotic twin and younger sibling of B1. All other family members: parents (non-consanguineous), twin sister, sister, brother and half-brother are healthy. B2 presented aged 21 months with bilateral painful swollen wrists and reduced range of movement. His development was normal and comparable to his twin. Clinical presentation was similar to B1 who was yet to receive a genetic diagnosis. Plain films were not diagnostic as carpi unossified. Regular monitoring of renal function was advised although it was noted the nephropathy associated with MCTO does not normally manifest until the second decade.
At genetic review an autosomal recessive form of carpotarsal osteolysis was considered most likely. The elbow contractures in B1 were consistent with this phenotype although subcutaneous nodules were absent. Genetic testing for *MAFB* gene alterations identified an identical mutation in B1 and B2 (*MFAB* – c176c>Tp(Pro59leu) confirming the autosomal dominant MCTO. B2 developed hypertension, heavy proteinuria and hypoalbuminemia at 3 years, responding to tacrolimus.
Results: Two brothers with clinical features of MCTO and identical mutations in *MAFB* gene are described. The phenotype varied significantly with early renal disease in one and mild learning difficulties in the other.
Inheritance of this autosomal dominant condition in these two brothers with unaffected parents could result from either gonadal mosaicism or incomplete penetrance. There is a case of incomplete penetrance in MCTO described in the literature. [2]
Conclusion: Individually skeletal dysplasias are rare yet as a group they represent an important differential to JIA requiring different management.
Pursuing a genetic diagnosis in carpotarsal osteolysis is important not only for prediction of recurrence risk. It allows a definitive diagnosis to be made earlier than is possible clinically/radiologically.
Significantly different phenotypes yet the same genetic mutation lends weight to the possibility of modifier genes or other epigenetic mechanisms/environmental factors affecting disease penetrance as proposed by Dworschak et al [2]. A greater understanding of these may enable prediction of renal involvement and aid development and stratification of new therapies.

REFERENCES

[1] Zankl, et al. Multicentric Carpotarsal Osteolysis Is Caused by Mutations Clustering in the Amino-Terminal Transcriptional Activation Domain of MAFB Am J Hum Genet 2012 9;90(3)494-501
[2] Dworschak, et al. An incompletely penetrant novel MAFB (p.Ser56Phe) variant in autosomal dominant multicentric carpotarsal osteolysis syndrome *International Journal Molecular Medicine* 2013 174-178

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AB0952 RETROSPECTIVE STUDY OF PROCEDURAL PAIN ANALYSIS DURING JOINT INFILTRATION IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Idiopathic Arthritis (JIA) is the rheumatic disease more common in childhood. Intra-articular corticosteroid injections (IAC) are a mainstay in the treatment of this disease, unfortunately it is often associated with pain and anxiety, for this reason is extremely important to pay attention both to procedural analgesia and to the reduction of anticipatory anxiety.
Objectives: The primary aim was evaluate the impact of the our analgesic procedure on the perception of infiltration pain; the secondary aims were stratify the results according to the demographic characteristics, number of joints infiltrated for each patient.
Methods: 40 patients (pt) studied between august 2016 and august 2017 (1 year) received a IAC [F/M=25/15, age 8.63 ± 3.41 yrs, weight 32.1 ± 13.9 kg; monoarticular JIA 7 pt (17.5%), oligoarticular 19 (47.5%), polyarticular 14 (35%). 27/40 (67.5%) pt infiltrated in one joint, 13/40 (22.5%) in two or more joints].
One hour earlier of the procedure for each pt was applied 1% prilocaine cream and 30 minuts before administered Midazolam orally at a dose of 0.5 mg/kg (maximum 15 mg), 50% nitrogen protoxide mixture dispensed with a mask, in spontaneous breathing and continuous flow. In 25/40 (62,5%) pt distraction techniques were performed during IAC and in 24/40 (60%) was also applied ice spray before IAC. To monitor pain, before and after IAC, appropriate scales have been used, stratified by age: CHIPPS scale (pt ≤ 5 yrs), Wong-Baker scale for ages 5 to 8, numerical scale analog visual VAS (pt ≥8 yrs). CHIPPS and VAS scales <4: indicative of mild pain. For each pt pain assessment was performed before and after IAC.
Results: VAS before IAC = 0.90 ± 1.67/Median (M) = 0, after IAC = 1.07 ± 1.56/M = 0; CHIPPS before IAC = 0.82 ± 1.88/M = 0, during IAC = 2.75 ± 3.01/M = 2. No significant correlation between VAS scale scores and after IAC and of CHIPPS both before and during IAC and respectively of age, weight, sex, application of ice spray, application of distraction techniques before the execution of the procedure, number of infiltrated joints. Significant correlation between VAS before and after IAC (RHO Spearman 0.397, p = 0.018), CHIPPS before and during IAC (RHO Spearman 0.599, p ≤ 0.0001). Highly significant correlation coefficient between VAS and CHIPPS before IAC (RHO Spearman 0.6, p = 0.0001) and between CHIPPS during IAC and VAS after IAC (RHO Spearman 0.403, p <0.05). Significant difference between CHIPPS before and after IAC (Wilcoxon Ranks Signed Test, R = 8.5, p <0.0001), not between VAS before and after IAC (R = 83, p = 0.62).
Conclusion: In our study the intensity of pain would seem exclusively subjective, in fact it does not depend: on age, number of IAC, on the application of distraction techniques and application of ice spray. Anyway the protocol that we used seems to be effective on pain control (VAS and CHIPPS scale respectively after and during IAC: m ± sd and M. <4 points) and it can be performed on outpatients safely without an anesthetic procedure. Our results encourage to expand the series with a future prospective trial.

REFERENCES

[1] Oren-Ziv, et al. Sedation methods for intra-articular corticosteroid injections in Juvenile Idiopathic Arthritis: a review. Ped Rheumatol (2015);
[2] Nicole M. et al. Systematic Review: Predisposing, Precipitating, Perpetuating, and Present Factors Predicting Anticipatory Distress to Painful Medical Procedures in Children Journal of Pediatric Psychology (2016)

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AB0953 EAR INVOLVEMENT IN PATIENTS AFFECTED BY JUVENILE IDIOPATHIC ARTHRITIS

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Background: Few clinical studies in pediatric patients have shown a possible link between hearing loss and Juvenile idiopathic arthritis (JIA). It could be related to the involvement of the joints of the ossicular chain as a result of the autoimmune inflammatory process in the middle and inner ear
Objectives: The aim of this study was to assess the frequency of hearing impairment in patients affected by JIA versus a healthy control group.
Methods: We studied 64 ears of 32 JIA patients (25 girls and 7 boys, mean age 15 years, age range 8-19 years) from June to December 2018. The mean disease duration was 7 years (+/- 4 DS). Polyarticular JIA was diagnosed in 6 patients, oligoarthritis JIA in 19; 5 patients had psoriatic arthritis and 2 spondyloarthritis. The control group consisted of 60 ears of 30 healthy children, sex-and age-matched. Patients with previous otitis media at least 3 months and/or ear surgery were excluded. The study was approved by the local ethics committee and parents and/or patients signed their informed consent. All subjects underwent

audiological examination involving otomicroscopy, audiometry, tympanometry and stapedius reflex. Rheumatologic evaluation included joint examination with application of a measure of functional ability (disability) using the Childhood Health Assessment Questionnaire (CHAQ). The investigators were blinded about JIA type, severity, duration, and treatments of the patients.

Results: 11/32 (34%) JIA patients had abnormal audiological exam. Hypoacusia was significatively more frequent (p<0,05) in JIA patients (15/64 ears=23%) respect to the control group. In particular, hypoacusia was associated to psoriasic arthritis (6/15 ears). Conductive hearing loss was detected in 12/15 involved ears, while sensorineural type in 3/15. In the JIA group, according to the Jerger classification for tympanometry, abnormal findings were observed in 7 ears. The stapedius reflexes were absent in only one patient (3%). JIA patients with hypoacusia had a greater CHAQ (0.4+/-0.3) than JIA patients with normal audiometry (0.18 +/-0.29).

Conclusion: The presence of hearing impairment and/or abnormal tympanogram suggests early involvement of the tympanic-ossicular complex, especially in patients with psoriatic arthritis. These findings could be a marker of the JIA activity. Therefore, it is advisable that JIA patients perform periodic audiological examination to early detect eventual hearing impairment, in order to prevent hearing loss in adult age.

REFERENCES

[1] M.EG Amani: Acta Oto-Laryngolica 2016
[2] A.I.C. Cruz: Reumatologia Clinica 2017
[3] F Borgia: Acta Derm Venerreol 2018

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AB0954 PEDIATRIC RHUPUS A RARE OVERLAP SYNDROME: CASE SERIES OF MEXICAN CHILDREN'S HOSPITAL FEDERICO GOMEZ

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Background: Rhupus is an overlap syndrome of rheumatoid arthritis and systemic lupus erythematous (SLE) in adult patients. Its pediatric presentation is very rare, the presentation of both juvenile idiopathic arthritis (JIA) and SLE as a clinical manifestation of the same patient has aroused different theories being the most accepted a true overlap between SLE and JIA. To diagnosis a patient with Rhupus present with clinical symptoms of SLE with positive ANA, antiDNA or antiSm, associated with clinical symptoms of JIA

Objectives: Describe clinical and serological findings of pediatric patients diagnosed with Rhupus of Mexican Children's Hospital Federico Gomez

Methods: We present a case series of 4 patients diagnosed with Rhupus. We describe the demographic characteristics, clinical presentation, serological finding, the criteria for the diagnosis of SLE (ACR 1997) and JIA (ILAR 2001) and the treatment installed

Results: We describe four patients with Rhupus, the medium age at diagnosis was 12.5 years, and it was more common in female 3:1. Three presented joints manifestations, integrating an initial JIA diagnosis. The evolution to an overlap syndrome took an average time of 19 months. The main symptom at diagnosis was erosive arthritis, poliarticular, morning stiffness and decreased joint range of motion. Three patients met 6 classification ACR 1997 criteria for SLE. All of the patients met ILAR 2001 criteria for JIA diagnosis. The four patients were treated with multitarget therapy. Joint manifestations were treated with methotrexate, and kidney and neurological manifestations with MFM and IV CFM. One patient required etanercept therapy for persistent joint disease

Abstract AB0954 Table 1. Demographic and clinical characteristics

	CASE 1	CASE 2	CASE 3	CASE 4
AGE AT DIAGNOSIS	15	11	11	13
SEX	F	M	F	F
FIRST DIAGNOSIS	SLE	JIA	JIA	JIA
TIME TO OVERLAP months	Simultaneous	18	15	36
SLE ACR 1997	7	6	6	6
JIA ILAR 2001	Si	Si	Si	Si
TYPE AIJ	Oligoarticular	Polyarticular	Polyarticular	Polyarticular
TREATMENT	MTX 3 months CFM MFM (kidney disease) HCQ steroids	MTX 3 months MTX sulfasalazine 6 months MFM 6 months Etanercept HCQ steroids	MTX 3 months MTX sulfasalazine present HCQ steroids	MTX 6 months CFM MFM (neurological condition) HCQ steroids

All of the patients presented with elevated acute phase reactants, positive ANA, antiDNA and antiCCP. Two patients had positive antiSm antibody and three presented with positive RF

Abstract AB0954 Table 2. Serological features

	CASE 1	CASE 2	CASE 3	CASE 4
ANA	PH1:1280	PH1:5120	PH1:640	PH1:1280
ANTI DNA	+	+	+	+
ANTI SM	+	-	+	-
VSG/ PCR	+	+	+	+
FR	-	+	+	+
ANTI CCP	+	+	+	+
ANTI RO	-	-	+	-
AFLS	+	-	+	+

Conclusion: The coexistence of two or more connective tissue disease in the same patient is a very uncommon finding. The overlap of SLE and RA has been estimated between 0.01-2%. There are no reliable data about the overlap of SLE and JIA. Patients with JIA and positive antinuclear antibodies should have a thorough follow up taking into account the possibility of developing a juvenile Rhupus, evaluating cutaneous, renal, neuropsychiatric or hematologic manifestations in each visit. Its manifestations can be very devastating, increasing the morbidity and mortality of children. Previous findings showed that positive antiCCP antibodies are very specific for Rhupus diagnosis (96-98%). The clinical response to conventional therapy as not as than seen in patients with JIA, requiring of a multitarget treatment and biological agents to achieve a respond. Severe organ specific manifestations such as lupic glomerulonephritis and neuropsychiatric disease, are common. It is very important to recognize the Rhupus in order to make a prompt diagnosis and intervention that assures a better outcome for patients

REFERENCES

[1] Fernández A, et al. Lupus arthropathy: A case series of patients with rhupus.ClinRheumatol. 2006; 164-7
[2] Mondal R, et al. Childhood lupus: Experience from Eastern India. IndianJPediatr. 2010; 77: 889-91

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AB0955 TRANSITIONAL CARE: A SINGLE CENTER ITALIAN EXPERIENCE

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Background: Transitional care from paediatrics to adults is an important step in the growth of the adolescent patients. One of the final goals is to guarantee the continuity of health care, increasing compliance in treatment and visits.

Objectives: To describe disease features and adherence to the follow-up in rheumatic patients that were transferred from Paediatric Clinic to our adult department.

Methods: From May 2016 to May 2018 the transition has been performed with a visit in presence of both specialists and 28 patients were evaluated. For juvenile Idiopathic Arthritis (JIA) we registered: category of

arthritis, extra-articular involvement, treatment (during paediatric follow-up and at the time of the first evaluation) and disease activity (using JADAS10-CRP and DAS28-CRP; table 1). Finally, to assess the efficacy of this transition-model, we compared the rate of losses at follow-up with those occurred until 2016, when transition was performed only with a Clinical Report sent by paediatrician.

Table 1 Cutoff of disease activity: JADAS10* and DAS28-CRP**

	Cutoff
JADAS10 (for Oligoarthritis)	
Inactive disease	≤1
Low activity	≤1.5
Moderate activity	1.51-4
High activity	>4
JADAS10 (for Polyarthritis)	
Inactive disease	≤1
Low activity	≤2.5
Moderate activity	2.51-8.5
High activity	>8.5
DAS28-CRP	
Inactive disease	≤2.6
Low activity	>2.6-3.2
Moderate activity	>3.2-5.1
High activity	>5.1

**Modified from Consolaro A. et al., Ann Pediatr Rheum 2014*
*** Modified from Prevoo ML et al., Arthritis Rheum 1995*

Figure 1

Results: Between May 2016 and May 2018, 28 patients were enrolled (6 male, 22 female); mean age at diagnosis was 8.1 years (range 1-6 years); mean age at transition was 18.5 years (range 17-21 years). Twenty patients had a diagnosis of JIA, 3 of Undifferentiated Connective Tissue Disease, 1 Dermatomyositis, 1 Systemic Lupus Erythematosus, 1 Takayasu Arteritis, 1 Morphea, 1 Raynaud's phenomenon.
Among JIA, 6 (30%) were Persistent Oligoarthritis, 4 (20%) Extended Oligoarthritis, 8 (40%) Polyarthritis (RF negative), 1 (5%) Psoriatic Arthritis, 1(5%) Enthesitis Related Arthritis. Five patients (25%) had history of uveitis. Treatment during the paediatric follow-up period are summarized in table 2. At the time of first evaluation in adult department, 2 patients (10%) were on treatment with systemic steroids (5mg/day), 6 (30%) with methotrexate, 2 (10%) sulfasalazine, 1 (5%) with hydroxychloroquine, 1 (5%) leflunomide; 10 patients (50%) were on treatment with bDMARDs (6 adalimumab, 3 etanercept, 1 infliximab). Mean JADAS10-CRP was 3.8 (range 0-17, SD 5.8) as mean DAS28-CRP was 1.65 (range 0.96-3.44, SD 0.72). In 7 patients, disease activity assessed with JADAS10 was moderate-high as it resulted low-absent using DAS28-CRP. The rate of patients classified as having moderate-high activity was significantly different using the two index (35% using JADAS10 vs 5% using DAS28-CRP, pvalue 0.044).
Until 2016, 6 of 44 (11%) patients were lost to follow-up while in the period between May 2016 and May 2018 no patients were lost (11% vs 0; pvalue 0.042)
Conclusion: Disease activity seems to be underestimated using DAS28-CRP as compared with JADAS10-CRP. This could be due to the more frequent involvement of ankles and feet (that are not included in DAS28-CRP) in JIA. The adherence to follow up was greater in patients whose transition was performed in presence of the two Specialists.

Abstract AB0955 Table 1. Cutoff of disease activity: JADAS10* and DAS28-CRP**

Table 1 Cutoff of disease activity: JADAS10* and DAS28-CRP**

	Cutoff
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JADAS10 (for Polyarthritis)	
Inactive disease	≤1
Low activity	≤2.5
Moderate activity	2.51-8.5
High activity	>8.5
DAS28-CRP	
Inactive disease	≤2.6
Low activity	>2.6-3.2
Moderate activity	>3.2-5.1
High activity	>5.1

**Modified from Consolaro A. et al., Ann Pediatr Rheum 2014*
*** Modified from Prevoo ML et al., Arthritis Rheum 1995*

Abstract AB0955 Table 2. treatment during paediatric follow-up

TERAPIA	N (%)
Intrarticular infiltrations	13 (65%)
Systemic Steroids	11 (55%)
Methotrexate	15 (75%)
Hydroxychloroquine	1 (5%)
Leflunomide	1 (5%)
Sulfasalazine	4 (20%)
Cyclosporin A	2 (10%)
Biologic DMARDs	11 (55%)

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AB0956

JIA ASSOCIATED TO CHROMOSOME 18 SHORT ARM DELETION: A CASE REPORT

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Background: Monosomy 18p is a rare chromosomal disease resulting from complete or partial deletion of chromosome 18 short arm. It is associated with a variable phenotypic spectrum. Most reported patients have holoprosencephaly, developmental delay, short stature and distinctive facial features while autoimmune diseases are rarely seen. Manifestations of this syndrome vary depending on the extent of deletions.
Objectives: We report the case of a child with juvenile arthritis and uveitis associated to 18p deletion syndrome.
Methods: A 5-year-old girl diagnosed with 18p deletion presented for pain and swollen joints since more than a year.

She is the first born of a 51-year-old father and 40-year-old mother, non-consanguineous parents, at full term, and has a history of early hypotonia, psychomotor developmental delay and failure to thrive.
Physical exam revealed arthritis of both ankles, the right knee and the MCP joint of the left thumb. We noted loose joints, high-arched palate and facial dysmorphism (hypertelorism, large protruding ears, flat nose and short philtrum). Body weight and height were at -3SD. Intellectual disability was mild.
Laboratory tests showed slightly increased ESR (35mm at first hour) with positive ANA (>1/1000) and negative RF and anti-CCP. Karyotype is 46XX with deletion of the short arm of chromosome 18. Both parents had normal Karyotypes. MRI of the brain showed cortical atrophy and periventricular leucomalacia.
Ophthalmic screening detected bilateral anterior uveitis.
The patient was treated by AINS and methotrexate along with topical ophthalmic steroids. 6 months after treatment, the child had complete regression of uveitis and arthritis.
Results: This case of de-novo 18p deletion is associated to oligoarticular JIA with uveitis. According to our knowledge, there have only been 2 published cases of juvenile inflammatory arthritis with 18p deletion although 5 other cases were reported in association to other chromosome 18 abnormalities (deletion of long arm and ring). Few reports of adult-onset arthritis with monosomy 18p are available.
The exact explanation of this association is still unclear. As gene loss is a major factor in the pathogenesis of inflammation, this presentation might be related to deletion of PTPN2, a gene that has been associated to rheumatoid arthritis. PTPN2 encodes Protein Tyrosine Phosphatase Non-receptor type 2 and is located in the short arm of chromosome 18. PTPN2-deficiency stimulates T follicular helper cell and B cell responses thus promoting autoimmune reaction. Of the 67 genes in 18p, only around 12 (of which PTPN-2) are responsible of a phenotype when hemizygous. Further genetic studies are needed to better elucidate the role of deleted genes in the pathogenesis of inflammation in monosomy 18p.
Conclusion: In addition to skeletal deformities such as kyphosis and feet deformities, children with 18p deletion should be screened for inflammatory arthritis.

REFERENCES

[1] M.Hasi-Zogaj,C.Sebold,P. Heard,E.Carter,B.Soileau,D. Rupert and al. A review of 18p deletions. American journal of medical genetics. Part C, seminars in medical genetics. 2015 Sep;169(3):251-64.
[2] A.Chau, KH. Ramesh,AD. Jagannath, S. Arora. Rheumatoid arthritis in an adult patient with mosaic distal 18q-, 18p- and ring chromosome 18.F1000 research. 2018;6:1940.
[3] C.Ciccacci, P.Conigliaro,C.Perricone,S.Rufini,P.Triggianese and al. Polymorphisms in STAT-4, IL-10, PSORS1C1, PTPN2 and MIR146 Agenes are associated differently with prognostic factors in Italian patients affected by rheumatoid arthritis. Clinical and experimental immunology.2016;186:157-163.
[4] F.Wiede,F.Sacirbegovic,Y.A.Leong,D.Yu,T.Tiganis. PTPN2 deficiency exacerbates T follicular helper and B cell responses and promotes the development of autoimmunity. The journal of immunology.2017;76:85-100.

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AB0957 ATYPICAL PRESENTATION AND EARLY RECURRENCE OF KAWASAKI DISEASE IN A FEMALE INFANT: CASE REPORT

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Background: Kawasaki Disease (KD) is the second most common vasculitis in the pediatric population and the leading cause for pediatric acquired heart disease in developed countries. It is commonly diagnosed in the Mexican pediatric population, epidemiology in this country is not established, since cases are not usually reported to the healthcare system. The clinical features are quite variable, but diagnosis and prompt treatment will decrease morbidity and mortality. Coronary artery aneurysms are the most common complication, which represent the leading cause of acute coronary syndrome before 40 years of age. Recurrence of KD is estimated to be around 3% in Japanese patients and 1% in the United States, nevertheless, this data in Latin-American children is unknown. It usually affects patients before reaching 3 years old and within 2 years of the initial attack, presenting with an abrupt onset and higher complication rates, requiring aggressive workup, treatment and follow-up.
Objectives: To review an atypical presentation of KD and early recurrence in a 7-month-old female.
Methods: We present a 7-month-old female diagnosed with KD at 48 days old. She presented to the emergency unit with irritability, high and persistent fever and acholia. During workup, she was found with cholestasis and gallbladder hydrops. Negative CSF, blood and urine cultures were documented during hospitalization, and fulfilled the KD criteria. The cardiac ultrasound revealed coronary abnormalities: a RCA of 2.8mm (Z-Score +4.79), LCA of 3.3mm (Z-Score +5.69) and LAD of 2.4mm (Z-SCORE +4.25), which fit into classification 3 and 4, as small and medium aneurysms, according to AHA 2017. Immunoglobulin (2g/kg) and aspirin (80mg/kg) were administered and she was discharged 36 hours after the IVIg infusion, afebrile and with ambulatory follow-up, 30 days later the coronary abnormalities showed RCA of 2.0mm (Z-Score +2.3), LCA of 3.0mm (Z-Score +6), LAD 2.3mm (Z-Score +2.9). Six months later, she presented fever for 6 days, irritability and polymorphous rash. On physical exam BCGitis, non-suppurative conjunctivitis and pallor in hands and feet, elevated CRP and ESR, leukocytosis, thrombocytosis and sterile leukocyturia. Echocardiography reported RCA od 2.4mm (Z-Score +4.8), LCA of 3.1 (Z-Score +4.2) and LAD of 2.3mm (Z-Score +3.2), diagnosing KD recurrence, admitting the patient for IVIg and aspirin administration.
Results: The patient was treated with IVIg and aspirin. Follow-up by Cardiology determined improvement of Z-Scores. Recurrence occurred with worsening of the cardiac abnormalities. Cardiac prognosis is importantly affected due to the atypical age, vascular abnormalities and repeated vasculitic process. Rheumatologic consult should be considered since disease like Takayasu Arteritis, Polyarteritis Nosa and ADA2 deficiency need to be ruled out.
Conclusion: KD needs prompt diagnosis and treatment due to the potential consequences when delayed. Clinical suspicion is important due to the possible atypical presentation. As with this patient, age, gender and presentation are not exclusive. Despite adequate treatment, recurrence and worsening of the cardiac abnormalities occurred. Both KD events before 1 year old and with atypical presentations. Rheumatologic and cardiac follow-up need to be stringent through lifetime, to determine pharmacologic treatment, as ell as physical activity and reproductive counseling.

REFERENCES

[1] McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, Treatment and Long-term Management of Kawasaki Disease: A scientific Statement for Health Professionals From the American Heart Association. Circulation 2017;135(17):e927-e99.

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AB0958 PEDIATRIC BEHCET'S DISEASE WITH SINUS VENOUS THROMBOSIS: THREE CENTER EXPERIENCE FROM TURKEY

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Background: Behçet's disease (BD) is an autoinflammatory disorder which may present with multi-systemic involvements including the vascular, cutaneous, articular, gastrointestinal, and/or central nervous systems (CNS). CNS involvement appears in two main groups: parenchymal or non-parenchymal. Neurological symptoms in children and adolescents can be confused with many other disorders and may be the initial symptom of BD.
Objectives: To report our experiences of the juvenile Behçet's Disease patients with cerebral venous sinus thrombosis (CVST) and to review previous studies reporting the clinical characteristics and outcomes of Juvenile Behçet's Disease with CVST.
Methods: The patients who met Pediatric Behçet's Disease (PEDBD) classification criteria for juvenile Behçet's Disease from 3 referral centers in Turkey were reviewed retrospectively. Disease activity was assessed by BD current activity form (BDCAF). A systematic review of literature of all published data was conducted.

Results: The study group consisted of 12 juvenile BD patients with CVST. At the time of CVST diagnosis, the most common symptom was headache (%100), followed by vomiting (25%), blurred vision (16.6-7%), and disturbances in eye movements (16.7%). Six (50%) patients presented with sinus venous thrombosis as an initial symptom. Transverse sinus was the most frequently affected sinus (9/12, 75%) followed by superior sagittal sinus (8/12, 66.6%) and sigmoid sinus (1/12, 8.3%). The median (minimum-maximum) BDCAF was 6 (5-8). Four children (33.3%) had another venous thrombosis apart from CVST. All patients received pulse methylprednisolone for three consecutive days continued with oral prednisolone. Steroid treatment was tapered and discontinued minimum in six months. Eleven patients received azathioprine concomitant to steroid treatment at the time of CVST. All the patients received anticoagulant therapy concomitantly. Only one patient had relapse. Median (min-max) follow-up period was 4 years (1-10). In the literature review, we identified nine articles, describing 35 pediatric CVST patients associated with BD. Thirty patients achieved remission, while five patients had residual neurologic deficit.

Conclusion: Further multicenter studies with more patients and prospective follow-up may help us to understand the whole spectrum in these patients.

REFERENCES

[1] Behcet, H., Über rezidivierende, aphtöse, durch ein Virus verursachte Geschwüre am Mund, am Auge und an den Genitalien. Dermatologische Wochenschrift, 1937(105): p. 1152-63.

[2] Metreau-Vastel, J., et al., *Neurological involvement in paediatric Behcet's disease*. Neuropediatrics, 2010. 41(5): p. 228-34.

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AB0959 EXCELLENT RESPONSE TO TOCILIZUMAB IN PEDIATRIC ONSET REFRACTORY TAKAYASU ARTERITIS: CASE SERIES OF THREE PATIENT

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Background: Takayasu arteritis (TA) is a idiopathic and rarely seen chronic systemic vasculitis that affect the aorta and its major branches. Stenosis, occlusion and aneurysms may develop in large arteries in the setting of granulomatous panarteritis (1). The first purpose in patients with TA after diagnosis is to prevent the progression of vascular lesions with medical treatment. Used as a first choise in medical treatment, steroids and steroid-sparing immunosuppressive agents, may sometimes fail to prevent to progression of the disease. Interleukin (IL)-6, which synthesize from activated dendritic cells, is one of the main cytokine in the development of panarteritis in TA. Tocilizumab (TCZ), an anti-IL-6 receptor antibody, has been shown to be used as an effective treatment in many refractory adult TA patients (2).

Objectives: We have presented our experience with TCZ treatment in three children with refractory TA.

Methods: We reviewed three cases of childhood TA diagnosed between 2016-2018. These patients were successfully treated with TCZ that started due to the refractory disease.

Results: The first patient, 15 year-old girl, presented with fever, headache and abdominal pain. Physical examination showed systolic murmur in interscapular area and abdominal tenderness. The C-reactive protein (CRP) level was 4.7 mg/dL (n: <0.5 mg/dL) and the erythrocyte sedimentation rate (ESR) was 78 mm/h (n: <20 mm/h). Doppler ultrasound imaging showed wall thickening in bilateral carotid arteries. The angio-CT imaging revealed that 70% stenosis in the bilaterally renal arteries and partial stenosis in the mesenteric artery. Methylprednisolone treatment was started (30 mg/kg/d x 3 days). Maintenance treatment consisted of prednisone (1 mg/kg/d), methotrexate and azathioprine. Her complaints improved rapidly and the acute phase reactants decreased. However, the patient relapsed while tapering the corticosteroid.

The second patient was diagnosed with TA in 2012 after the complaint of chest pain and finding of hypertension. MRI angiography revealed wall irregularities and stenosis in the descending aorta and dilatation in the ascending aorta. CRP and ESR levels found high. The patient was followed up with glucocorticoid and azathioprine treatment. After four years of follow-up, relapse of the disease was observed with symptoms of fever, chest and back pain.

The third patient presented with fever, abdominal pain, arthralgia in the left elbow and arthritis of the left knee, and was diagnosed with TA two years ago. His CRP and ESR levels were found elevated. The angio-CT imaging revealed that 70% stenosis in the 4 cm segment of the abdominal aorta, 70% stenosis in the right renal artery, 50% stenosis in the left renal artery and 90% stenosis in the origin of celiac trunk and superior mesenteric artery. Despite the given bolus methylprednisolone and methotrexate therapy, there had not seen any improvement in disease activity.

Tocilizumab was started at 8 mg/kg monthly in all three patient and they achieved complete clinical and laboratory remission.

Conclusion: These cases demonstrate that the TCZ treatment has been shown to be a successful option in TA patients resistant to conventional immunosuppressive therapies.

Disclosures: The authors have declared no conflicts of interest.

Informed consent form was obtained from patients and their legal guardians

REFERENCES

[1] Mathew AJ, Goel R, Kumar S, Danda D. Childhood onset Takayasu arteritis: an update. Int J Rheum Dis. 2016;19:116 26.

[2] Goel R, Danda D, Kumar S, et al. Rapid control of disease activity by tocilizumab in 10 'difficult-to-treat' cases of takayasu arteritis. Int J Rheum Dis 2013;16:754–61.

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AB0960 THE HELIOS (HACETTEPE UNIVERSITY ELECTRONIC RESEARCH FORMS) REGISTRY: USE OF BIOLOGIC DRUGS IN AUTOINFLAMMATORY DISEASES

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Background: Autoinflammatory diseases (AID) are characterized by a dysregulation of innate immunity leading to uncontrolled inflammation. The treatment in AID is critical to control the disease activity, to prevent complications, and to improve the health-related quality of life. Biologic drugs have revolutionized the treatment and outcomes in AID.

Objectives: Herein we aim to present the clinical characteristics of children to whom biologic drug therapy was initiated for the management of AID.

Methods: A web-based registry called the Helios Registry (**Hacettepe univErsity eLectronIc research fOrmS) has been formed to evaluate the data of all children on biologic treatment. We have been enrolling patients since August 2018 retrospectively and prospectively. We have analyzed the data about the general characteristics of the patients, treatment, the biologic drug used, and adverse effects. Only the patients with the following diagnoses were included: systemic juvenile idiopathic arthritis (SJIA), familial Mediterranean fever (FMF),** cryopyrin associated periodic syndrome (CAPS), and chronic recurrent multifocal osteomyelitis (CRMO).

Results: Of 60 patients included, 19 had FMF (31.7%), 24 had sJIA (40%), 10 had CAPS, (16.7%), and 7 had CRMO (11.7%). Their median age was 10.7 (2-20) years old and disease duration was 2.8 (0-6) years, at the time of biologic drug initiation. 58.3% were currently on canakinumab, 20% anakinra, 10% tocilizumab, 10% etanercept, and 1.7% adalimumab. 63.3% of our patients had previously used at least one other biologic drug. The rate of glucocorticoid use before biologic treatment was 56.6%. The median duration of glucocorticoid treatment after initiating biologic drugs was 7.4 months. 56 (93%) patients achieved remission on biologic therapy. There were 15 patients (25%) who received tuberculosis prophylaxis due to positive tuberculin skin test (diameter$\geq$10 mm) and there was no Quantiferon test positivity. Thirteen adverse events (AE) had been noted. 2 of them were serious events as anaphylaxis due to tocilizumab infusions. The rest of the adverse events were mild thrombocytopenia (n=2), varicella infection (n=1), and local side effects (n=8). The median number of the infections per year was one and there were no death or malignancy.

Conclusion: The most commonly prescribed biologic drugs were IL-1 inhibitors especially for patients with IL-1-mediated AID (FMF, CAPS, and SJIA). The biologic treatment in AID is effective and there were no serious side effects.

REFERENCES

[1] Ozen S, Bilginer Y. A clinical guide to autoinflammatory diseases: familial Mediterranean fever and next-of-kin. Nat Rev Rheumatol. 2014 Mar;10 (3):135-47. doi:10.1038/nrrheum.2013.174

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AB0961 ADVERSE EVENTS ASSOCIATED WITH ANTI-TNF-ALPHA THERAPY IN PEDIATRIC RHEUMATIC DISEASES

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Background: In recent years, the biologic drugs has led to a dramatic change in the management of rheumatic diseases. The most commonly used molecules are TNF-α antagonists among biologic treatments in pediatric age (1). The anti-TNF-α agents used in childhood are; etanercept (a fusion protein of the TNF-α receptor), infliximab (a chimeric monoclonal antibody) and adalimumab (completely human monoclonal antibody). As a result of the increasing use of anti-TNF-α agents in recent years, adverse events reports have also increased (2). We assessed the prevalence of adverse events (AEs) in a single pediatric referral center for chronic rheumatic diseases.
Objectives: The aim of this study was to evaluate the adverse events that associated with anti-TNF-α therapy in children with rheumatic disease.
Methods: This was cross-sectional study conducted University of Health Sciences, Umraniye Training and Research Hospital, Department of Pediatric Rheumatology, in Turkey. We retrospectively reviewed the patients with a diagnosis any of pediatric rheumatic disease whom treated at least 3 months with an anti-TNF-alpha agents (etanercept, infliximab, adalimumab), between June 2016 and January 2019. Adverse events that develop after anti-TNF-α treatment were recorded. AEs were categorized and graded based on the Common Terminology criteria for AEs (CTCAE). Grades 3-5 were considered severe AEs.
Results: We evaluated 131 patients who were treated with anti-TNF-a drugs; 110 with juvenile idiopathic arthritis (JIA)(27 of with uveitis) 83%, 10 with idiopathic uveitis 7%, 5 with Behçet's uveitis%4, 4 with adenosine deaminase deficiency%3, and 2 with juvenile sarcoidosis%2.
The study included 74 females and 57 males (F/M: 1.29/1) and the mean age of the patients was 12.8 years. Of the patients, 106 had used only 1, 21 had two different and 4 had 3 different anti-TNF-alpha biologic treatments. A total of 160 different anti-TNF-alpha experiences had in 131 patients.
A total of 333.4 patient-years (PYs) were included: 136 PYs-63 patients for etanercept (2.15 patient/year), 134 PYs-68 patients for adalimumab (1.97 p/y) and 63.4 PYs- 29 patients for infliximab (2.18 p/y). During follow-up, 44 patients (33.5%) experienced at least one AEs. 14 of them (10%) were recorded as SAEs. 17 of the AEs were show up after adalimumab, 16 were etanercept and 11 were infliximab. The most common AEs were found; local reactions, increased infection frequency and PPD positivity in follow up, respectively. The SAEs that observed were; anaphylactoid reactions (n=5), uveitis (n=3), pneumonia (n=3), TAILS (n = 2) and vasculitis (n=1).
Conclusion: Here in, we presented safety data of anti-TNF-alpha drugs in pediatric patients. Although the high prevalence of AEs was observed, when anti-TNF-a discontinuation, AEs were mostly not persistent and not mortal.

REFERENCES

[1] Vanoni F, Minoia F, Malattia C. Biologics in juvenile idiopathic arthritis: a narrative review. Eur J Pediatr. 2017;176:1147-53.
[2] Pastore S, Naviglio S, Canuto A, Lepore L, Martelossi S, Ventura A, Taddio A. Serious Adverse Events Associated with Anti-Tumor Necrosis Factor Alpha Agents in Pediatric-Onset Inflammatory Bowel Disease and Juvenile Idiopathic Arthritis in A Real-Life Setting. Paediatr Drugs. 2018;20:165-71.

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AB0962 UPDATE FOR THE CLINICAL PRACTICE: INTEGRATED, EVIDENCE-BASED APPROACH FOR THE MANAGEMENT OF JUVENILE SPONDYLOARTHRITIS

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Background: Juvenile onset spondyloarthritis (SpA) is a heterogeneous group of human leukocyte antigen (HLA) -B27 associated inflammatory syndromes that affect children and adolescents under the age of 16 years No specific recommendations for the treatment of juvenile spondyloarthritis have been established. Important differences exist between spondyloarthritis in children and adults, supporting the need for pediatric-specific recommendations.
Objectives: To set recommendations for the management of children and adolescents with spondyloarthritis.
Methods: Searching Medline for Juvenile spondyloarthritis management was done. A systematic literature search was conducted to collect the existing recommendations, guidelines involved line of treatment for Juvenile SpA & adult SpA. These included 2011 ACR recommendations for the treatment of JIA and the 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis.
Results: NSAIDs have been shown to improve symptoms, reduce inflammatory lesions and may slow spinal radiographs progression with continuous use. Glucocorticoid injections directed to the local site of musculoskeletal inflammation may be considered. Sulfasalazine may be considered in patients with peripheral arthritis. Initiation of a (tumor necrosis factor inhibitor (TNFi) was recommended for patients with active sacroiliac arthritis who have received an adequate trial of NSAIDs. Also, it should be initiated to those who fail to respond to synthetic disease modifying anti-rheumatic drugs (sDMARD). If TNFi therapy fails, switching to another TNFi should be done. If a patient is in sustained remission, tapering of a biological DMARD can be considered.
Conclusion: These guidelines provide up-to-date guidance on the management of patients with juvenile SpA, based on combining evidence and expert opinion.

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AB0963 ROLE OF THYROID HORMONES IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: The frequency of autoimmune thyroid disease have been reported in adults with systemic autoimmune diseases. However, little is

known about the association between those diseases and rheumatic disorders during childhood, such as juvenile idiopathic arthritis (JIA).
Objectives: Our objective was to evaluate the correlation between the thyroid function and the clinical presentation in children with juvenile idiopathic arthritis.
Methods: Ninety-seven children (56 female, 41 male, median age 9.57 years, range 1.1–17.5 years) with juvenile idiopathic arthritis were evaluated. All patients underwent thyroid function tests (TSH, free T_4 and free T_3), antithyroglobulin (TgA) and antiperoxidase (TPOA) antibodies. All patients had a thyroid high-resolution sonography examination. Patients with nodules on US examination, low-TSH level and/or high thyroid hormone levels or positive TPOA and/or TgA values were referred to thyroid scintigraphy. The gained data was correlated with disease activity indices. Thyroid autoimmunity was evaluated by fluorescence enzymatic immunoassays of TgA and TPOA antibodies, considering TgA >50 IU/ml and TPOA>100 IU/ml as positive values.
Results: Fifty-one of the cases were classified as oligoarticular, thirty-one as seronegative polyarticular, two as seropositive polyarticular, eleven as systemic, and two as enthesitis related- juvenile idiopathic arthritis.
No cases of overt clinical and biochemical hypothyroidism were found among children with juvenile idiopathic arthritis. On opposite, mean thyroid free T3 levels were higher in 36.4% of cases and free T4 in 29,7% cases. Anti-TPO antibodies were found in 5 of 97 patients (5.15%) and anti-TG antibodies were found in 2 patients (2.06%). All patients with thyroid antibodies positives were females. The ultrasound examination of thyroidal gland revealed abnormalities in 41% cases, most of them cystic changes (33.7%) and hypo-echogenicity (28,57%). In those patients with thyroid nodules on US examination, the thyroid scintigraphy did not revealed pathological activity or other processes. Although, 2 patients presented mean thyroid volume above 2SDS according their age reference values. An increased vascular flow patter on Doppler examination of thyroidal gland was found in 26% cases. Correlation and regression analysis showed low age at diagnosis and longer duration of the disease to be predictors for those thyroid disorders.
Conclusion: These data seem to suggest careful monitoring of thyroid function and thyroid autoantibodies just in children with juvenile idiopathic arthritis presenting clinical symptoms of thyroid involvement.

REFERENCES

[1] Fröhlich E., Wahl R., Thyroid Autoimmunity: Role of anti-thyroid antibodies in thyroid and extra-thyroidal diseases, Front. Immunol. 8:521. doi: 10.3389/fimmu.2017.00521
[2] Stagi S. et all., Thyroid function, autoimmune thyroiditis and coeliac disease in juvenile idiopathic arthritis, Rheumatology 2005;44:517–520, doi:10.1093/rheumatology/keh531

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AB0964 DIAGNOSIS OF CROHN`S DISEASE IN PATIENTS WITH PRIMARY RHEUMATOLOGICAL MANIFESTATIONS

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Background: Sometimes Crohn's disease (CD) manifests initially with rheumatological symptoms. Therefore, there's an important for a rheumatologist to recognize this pathology correctly and timely.
Objectives: To present cases of CD, referred to V.A. Nasonova Research Institute of Rheumatology.
Methods: Case series of 7 pts (5 boys, 2 girls) with initial rheumatological condition who developed CD. All pts were subjected to standard rheumatological examination. CD diagnosis was suggested by a rheumatologist and confirmed in gastroenterology hospital.
Results: Mean age at CD onset was 12,7±3,98 yrs, varying from 5 to 17 yrs. In 4 pts gastrointestinal (GIT) symptoms manifested simultaneously with rheumatological, in 2 pts GIT symptoms were delayed for 4 and 5 years. The time-interval from the onset of first symptoms until establishing CD diagnosis varied from 2 months till 6 years, averaging to 96± 38 months. The list of initial rheumatological diagnoses included the following entities: juvenile idiopathic arthritis (JIA) with oligoarticular onset – in 5 pts, and systemic onset JIA – in 2 pts. In all cases arthritis manifested initially as an oligo-involvement of a lower limb joints. High active sacroiliitis with deep bone oedema was detected by MRI in 5 pts. Fever was present in 5 pts, uveitis – in 1, cutaneous psoriasis – in 1. Other documented symptoms included: weight loss (3), hepatosplenomegaly (1), lymphadenopathy (1), aphthouse stomatitis (1), nodular erythema (1), erythematous rash (1). HLA B27-antigen positivity was established in 3 pts out of 5 examined. All pts had significant increase in CRP and ESR levels and WBC counts; (additionally 3 examined for calprotectin cases demonstrated significant increase of its' concentration (>1000 μg/g).
Conclusion: IBD, including CD, should not be missed and ruled out in all pts with oligoarticular and systemic JIA onset. Fecal calprotectin should be checked in suspected CD cases among individuals with rheumatologic symptoms. Special attention should be given to cases manifesting during puberty, accompanied by weight loss, fever, GIT symptoms, increased levels of acute phase inflammatory markers. MRI stir lesion may be as suspected of IBD especial CD.
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AB0965 PAEDIATRIC SARCOIDOSIS: A PROFESSIONAL IMITATOR

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Background: Sterile granulomatous inflammation is a hallmark of disorders covered by the term ‚paediatric sarcoidosis", a rare disease classified among autoinflammatory conditions. While the classical triad of arthritis, uveitis and dermatitis associated with the NOD2 gene mutation is typical for Early-onset sarcoidosis (EOS), mutation-negative disease has extremely variable phenotype in children and can mimic various other conditions.
Objectives: To illustrate variability of clinical presentation of sarcoidosis in a cohort of children from 2 collaborating paediatric rheumatology units
Methods: Retrospective case analysis.
Results: Seven Caucasian patients (2 boys) followed for a median of 1 (0.2-12) year were identified (Table). Patients 1 and 3 presented with typical rash (with biopsy-proven granuloma), polyarthritis and severe, treatment-resistant uveitis which has never been fully controlled. Patient 2 presented with recurrent self-limited febrile episodes and was investigated for periodic fever syndrome. Within 3 months she developed erythema nodosum-like rash, granulomatous uveitis and arthritis. In 4 patients with disease onset after 10 years of age two major organ systems were affected: renal and gastrointestinal (GIT). In patients 4 and 5 renal biopsy performed for insufficiency showed tubulointerstitial nephritis with granulomas. Patients 6 and 7 had been initially treated for "atypical inflammatory bowel disease" with granulomas on biopsy. In both of them finding of granulomatous uveitis eventually lead to the diagnosis of sarcoidosis. Additional symptoms are listed in the Table. Presence of granulomatous inflammation was confirmed in all patients. Chronic uveitis was present in 6/7 patients and was an important diagnostic clue in EOS as well as adult-type of sarcoidosis while respiratory tract was affected subclinically in 2 older patients only. Apart from combinations of clinical symptoms elevation of chitotriosidase significantly aided diagnostic process and when available, it also reflected disease activity. (1)
Pt – patient, F – female, M – male, Dx – diagnosis, CS – corticosteroids, MTX – Methotrexate, ADA – Adalimumab, MMF – Mycophenolate mophetil

Pt	Sex	Age (yrs) at Onset/ Dx	NOD2 gene mutation	Manifestations	Chitotriosidase N 4.4-89 nmol/ ml/h	Therapy
1	F	0,25/4	R334Q	Rash, fever, uveitis, arthritis, meningitis	299	MTX, MMF, ADA,
2	F	0,6/1	Negative	Rash, fever, uveitis, arthritis, panniculitis	433	MTX, ADA, CS
3	F	1/3	Variants S178S, V955I, N289S	Rash, fever, panuveitis, arthritis, liver granuloma	N/A	CS,MTX, ADA, Infliximab
4	M	4/15	Pending	Fever,arthralgia, lymphadenopathy, granulomatous nephritis	N/A	CS, MMF
5	F	13/13	Negative	Uveitis, granulomatous nephritis, hearing loss	604	CS, MTX, ADA

6	M	6/15	Negative	Uveitis, granulomatous colitis, pneumonitis, splenomegaly	512	MTX
7	F	10/10	Pending	Uveitis, granulomatous gastroenterocolitis and bronchitis	N/A	CS, ADA

Conclusion: Manifestations of sarcoidosis vary significantly across the paediatric age spectrum. While EOS is a known juvenile idiopathic arthritis mimic, nephritis and GIT inflammation may lead to a non-rheumatologic misdiagnosis. Apart from specific infections other childhood diseases may also present with granuloma formation: Crohn's disease, chronic granulomatous disease (and other primary immunodeficiencies), granulomatosis with polyangiitis. Our small series reflects disease heterogeneity and diagnostic difficulties that prolonged the diagnosis by years in 4/7 patients.

REFERENCES

[1] Popevic S. et al. Verifying Sarcoidosis Activity: Chitotriosidase versus ACE in Sarcoidosis – A Case-control Study. J Med Biochem. 2016 Nov 2;35 (4):390-400

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AB0966 PROPOSAL OF OUTCOME MEASURES TO BE USED ON A 12-MONTH OPEN LABEL DRUG TRIAL IN JUVENILE SYSTEMIC SCLEROSIS. RESULTS OF THE 3RD CONSENSUS MEETING IN HAMBURG DECEMBER 2018

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Background: Juvenile systemic sclerosis (jSSc) is an orphan disease, associated with high morbidity and mortality. New treatment strategies are much needed. To develop an open label drug trial for the treatment of jSSc patients, it is necessary to clearly define how to evaluate outcomes in this disease, which are currently not existing. A group of experts in jSSc has met annually and worked to develop an index to evaluate outcomes in this disease.
Objectives: The aim of our third consensus meeting was to establish the domains and the items that should be assessed in a clinical drug trial in jSSc.
Methods: In the consensus meeting 26 jSSc international experts with various specialties participated (22 voted). In a nominal group technic, moderated by DEF, was used to develop the outcome measures. Agreement was defined if 80% or more of the participants approved an item.
Results: Domains and items suggested in the 2017 consensus meeting were reconsidered and selected or rejected during the 2018 meeting, as were additional domains/items (Table).

Domain	Item	voted for - yes/nominator
Global Disease Activity	Physician global of disease activity	22/22
	Change in HAQ/CHAQ- DI	22/22
	Scleroderma HAQ	22/22
Skin	Change in Modified Rodnan Skin Score	22/22
Raynaud Phenomenon	Scleroderma HAQ question regarding Raynaud	22/22
Digital ulcerations	DUCAS Score	22/22
Musculoskeletal System	Juvenile Idiopathic Arthritis Definition of active joint	22/22
Cardiac Involvement	Left ventricular ejection fraction	22/22
	Development of clinically significant arrhythmia as a sign of non-response	22/22
Pulmonary Involvement	FVC	22/22
	age- defined DLCO in all trials	20/22
Renal	New occurrence of renal crisis	22/22
Gastrointestinal Involvement	Body Mass Index	22/22
	Scleroderma HAQ- Gastrointestinal section	22/22
Global health/Health related Quality of Life (QOL)	QOL instrument should be used	18/18

Conclusion: We reached consensus on domains and items which should be assessed in an open label 1 year clinical jSSc trial. We also listed research items which should be assessed but should not currently be included as an outcome in such a trial.
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AB0967 IS THERE A DIFFERENCE IN PRESENTATION OF FEMALE AND MALE PATIENTS WITH JUVENILE SYSTEMIC SCLERODERMA. AN UPDATE FROM THE JUVENILE SYSTEMIC SCLERODERMA INCEPTION COHORT. WWW.JUVENILE-SCLERODERMA.COM

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Background: Juvenile systemic scleroderma (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children (1). There are limited data published regarding the differences in clinical presentation of male and female patients with jSSc. The Juvenile Systemic Scleroderma Inception Cohort (JSSIC) is a multinational cohort with a prospective standardized assessment of the patients. The data regarding the difference in clinical characteristics at time of inclusion in the cohort are presented.
Objectives: Evaluation of the differences in clinical presentation of male and female jSSc patients at the time of inclusion in the JSSIC.
Methods: The JSSIC is a prospective multicentre registry of patients with jSSc, who fulfil the adult classification criteria (2), and presented the first non-Raynaud symptoms before 16 years old and were younger than 18 years old at the time of inclusion in the cohort. Patients characteristics at time of inclusion in the cohort were evaluated.
Results: As of 15th of December 2018 120 patients are included in JSSIC. The great majority are female (80%). There were more female patients with CK elevation (29% vs 22%) and more female patients with Gottron papulae (25% vs 12%). The mean modified skin score was higher in males (18.6 vs 13.9).
Sclerodactyly was more frequent in males (90% vs 76%). Active ulceration was present in 33% of males compared to 14% of females (p=0.026). FVC<80% occurred more often in males with 47% compared with 24% in females (p=0.018). Pulmonary hypertension was more

common in females with 7% compared to 4% in males. Urine sediment changes were more common in males (8% vs 4%). Gastrointestinal involvement was more common in females (37% vs 29%). Contractures occurred more often in males with 62% compared with 46% in females. Tendon friction rub was observed in 21% of males and 3% of females (p=0.001). Physician global scores of disease activity and damage were higher in males with 48 for both assessments compared to 36 and 30 in females.

Conclusion: Male patients with jSSc have a higher severity of disease, as it has been reported in adults.

REFERENCES

[1] Beukelman T, Xie F, Foeldvari I. Assessing the prevalence of juvenile systemic sclerosis in childhood using administrative claims data from the United States. Journal of Scleroderma and Related Disorders. 2018;3 (2):189-90.

[2] van den Hoogen F, Khanna D, Fransen J, Johnson SR, Baron M, Tyndall A, et al. 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European

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AB0968 INTEGRATED RHEUMATOLOGY AND OPHTHALMOLOGY CARE IN PEDIATRIC AUTOIMUNE UVEITIS – OUTCOME AND EFFECTIVENESS

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Background: Uveitis is an ocular inflammatory disease that may lead to irreversible blindness if not treated early and properly. May be induced by infectious and non-infectious diseases (autoimmune diseases, especially juvenile idiopathic arthritis), or "masquerade" causes. Some uveitis are termed "idiopathic" although autoinflammatory evidence. Treatment effectiveness depends on the accuracy of the ophthalmologic evaluation and the appropriate management, especially when immunosuppressive medications are necessary. [1, 2]

Objectives: To describe the first year experience of the Integrated Ophthalmology and Pediatric Rheumatology Outpatient Clinic in the management of pediatric patients with autoimmune uveitis.

Methods: Retrospective chart review study of twenty-four patients followed up from June 2017 to October 2018. The patients clinical evolution at 0, 3, 6, 9 and 12 months was analyzed.

Results: In this group, 62% were female, and mean age at first appointment and at symptoms onset were 11.7 (2.9 to 17. 5) and 7.3 (1.1 to 12.6) years, respectively. Anterior uveitis was present in 70.8% of the cases, and in 65.6% it was bilateral; cataract or glaucoma was observed in 20.5%. The identified diagnosis during follow-up were: idiopathic autoimmune uveitis in 45.8%, juvenile idiopathic arthritis in 41.6% (20.8% oligoarticular, 16.6% polyarticular, 4.1% associated with enthesitis) and juvenile systemic lupus erythematosus, Kawasaki Disease and Vogt-Koyanagi-Harada syndrome one case of each. Antinuclear antibodies were present in 41% and inflammatory markers in 28.7% patients. At first appointment, 20.5% presented ocular inflammatory activity and 53.3% had sequelae when examined in slit lamp or indirect ophthalmoscopy. Medications used were: topical corticosteroids (61.6%), topical mydriatic (49.2%), oral corticosteroid (41%), methotrexate (41%), etanercept (12.3%), adalimumab (28.7%) and periocular injections of triamcinolone, cyclosporin, tocilizumab, azathioprine (4.1% each). The comparison of the data at inclusion and during follow-up is reported in Table:

Table –Uveitis activity and medication use at the beginning and during follow-up

	At inclusion	3 months	6 months	9 months	12 months
Ocular inflammation(%)	20.5	24.6	12.3	12.3	12.3
Topical Corticosteroid(%)	61.6	32.8	16.4	8.2	20.5
Topical Mydriatic (%)	41	24.6	28.7	20.5	20.5
Oral Corticosteroid (%)	73.8	20.5	12.3	12.3	20.5
Metotrexate (%)	12.3	53.3	49.2	36.9	28.7
Etanercept (%)	12.3	4.1	4.1	4.1	4.1
Adalimumab (%)	20.5	20.5	16.4	16.4	16,4
Others (%)	12.3	4.1	4.1	4.1	4,1
No medication (%)	4.1	8.2	8.2	8.2	4,1

At the end of 12 months, only 12.3% of the patients still had active uveitis. We have also observed a reducing in 66.6% of topical corticosteroids and 72.2% of oral corticosteroids use during the treatment of uveitis over 12 months

Conclusion: Considering that before the inclusion, patients were followed independently in each clinic, there was optimization of the treatment and reduction in number of medical appointments after the creation of the integrated outpatient clinic. The interprofessional management teams should be the standard of care for pediatric patients with autoimmune uveitis.

REFERENCES

[1] Angeles-Han ST, Rabinovich CE. Uveitis in children. Curr Opin Rheumatol. 2016;28(5):544-9.

[2] Jabs DA, Nussenblatt RB, Rosenbaum JT, Standardization of Uveitis Nomenclature Working G. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol. 2005;140(3):509-16.

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AB0969 COMPARISON AMONG ACR1997, SLICC AND THE NEW EULAR/ACR CLASSIFICATION CRITERIA IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: To date there are no specific classification criteria for childhood-onset systemic lupus erythematosus (cSLE).

Objectives: This study aims to compare the performance among the American College of Rheumatology (ACR) 1997, the Systemic Lupus International Collaborating Clinics criteria (SLICC) and the new European League Against Rheumatism (EULAR)/ACR criteria, in a cSLE cohort.

Methods: Data were retrospectively collected from medical charts of cSLE cases and controls with defined rheumatic diseases, both ANA positive, to establish each ACR1997, SLICC and EULAR/ACR criterion fulfilled, at first visit and 1-year-follow-up.

Results: 122 cSLE cases and 89 controls were included. At first visit, SLICC criteria had greater sensitivity than ACR 1997 (89.3% versus 70.5%, $p < 0.001$), but similar specificity (80.9% versus 83.2%, $p = 0.791$), however performance was not statistically different at 1-year-follow-up. SLICC performed better in specificity compared to EULAR/ACR score $\geq$ 10 at first visit (80.9% versus 67.4%, $p = 0.008$) and 1-year

(76.4% versus 58.4%, p = 0.001), although sensitivities were similar at both times. EULAR/ACR criteria score ≥10 exhibited greater sensitivity than ACR 1997 (87.7% versus 70.5%, p < 0.001) at first visit, but comparable at 1-year, whereas specificity was lower at first visit (67.4% versus 83.2%, p = 0.004) and 1-year (58.4% versus 76.4%, p = 0.002). A EULAR/ACR score ≥13 against a score ≥10, resulted in higher specificity, positive predictive value, and cut-off point accuracy. Compared to SLICC, a EULAR/ACR score ≥ 13 resulted in lower sensitivity at first visit (76.2% versus 89.3%, p < 0.001) and 1-year (91% versus 97.5%, p = 0.008), but similar specificities at both periods. When compared to ACR 1997, a EULAR/ACR total score ≥ 13, resulted in no differences in sensitivity and specificity at both times.

Conclusion: In this cSLE population, SLICC criteria performed best at first visit and 1-year-follow-up. The adoption of a EULAR/ACR total score ≥ 13, against the initially proposed ≥10 score, was most appropriate to classify cSLE in our study. Further studies are necessary to address if SLICC might allow cSLE classification earlier in disease course and be more inclusive of cSLE subjects for clinical studies.

REFERENCES

[1] Tedeschi SK, Johnson SR, Boumpas DA, Daikh D, Dörner T, Jayne D, et al. Developing and Refining New Candidate Criteria for SLE Classification: An International Collaboration. Arthritis Care Res (Hoboken) 2018; 70:571-581.

[2] Leuchten N, Hoyer A, Brinks R, Schoels M, Schneider M, Smolen J, et al. Performance of Anti-nuclear Antibodies for Classifying Systemic Lupus Erythematosus: a Systematic Literature Review and Meta-regression of Diagnostic Data. Arthritis Care Res (Hoboken) 2018; 70:428-438.

[3] Aringer M, Costenbader KH, Brinks R, Boumpas D, Daikh D, Jayne D, et al. Validation of New Systemic Lupus Erythematosus Classification Criteria. In: 2018 ACR/AHRP Annual Meeting; Chicago, Illinois, 20-24 October 2018. https://acrabstracts.org. Accessed 24 Oct 2018.

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AB0970 LONG-TERM FOLLOW-UP OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN A MEXICAN CENTER

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Background: JIA comprises an heterogeneous group of diseases characterized by chronic arthritis, of unknown etiology, and onset age before 16. (1)

Juvenile Idiopathic Arthritis(1) is the most common chronic rheumatic disease in children, being an important cause of disability, affecting quality of life (2).

There are several subtypes of the disease, despite oligoarticular course has been described as the most frequently seen, up to 50% of JIA cases presented a polyarticular disease (4 3).

Data suggest that patients who receive early therapeutic intervention are more likely to reach clinical remission. In a systematic review, Wallace's criteria were used to determine drug remission and inactive disease. They reported 7% and 47% of patients reached remission at 1.5 and 10 years, respectively. Oligoarticular patients had a shorter time to remission, while polyarticular positive rheumatoid factor were the least likely to achieve it (5).

Mexico belongs to a group of developing countries where there is limited information about incidence, prevalence, clinical features, age and time to diagnosis, treatment, and remission of JIA patients.

Objectives: The aim of the study is to describe demographics, clinical data and long-term follow-up of a cohort of juvenile idiopathic arthritis patients in a Mexican center.

Methods: The study design was observational with no intervention, ambispective, among patients with JIA, according to ILAR criteria of pediatric rheumatology clinic from University Hospital "Dr. José Eleuterio González" over a 2-year period (2016-2018). Medical records of patients were retrospectively reviewed and collected information as demographics, age at diagnosis, disease activity, joints involved, treatment, adverse events, clinical inactivity and remission.

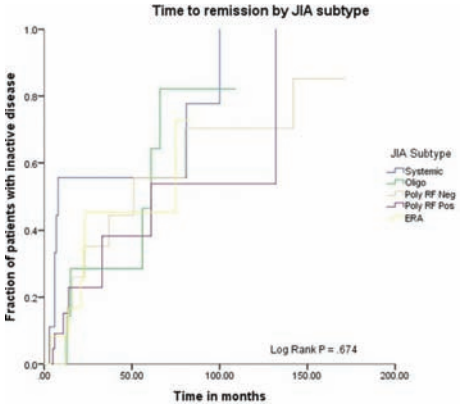


Figure 1

Statistical analysis was descriptive with measure of central tendency. For continuous variables, mean, median, interquartile range and standard deviation were used to present data.

Results: We enrolled 70 patients with JIA, 52 (74%) female, with a median age at diagnosis of 11.7 years. The most frequent subtype was polyarticular positive rheumatoid factor (25, 36%). Eighty adverse events were reported; 45 of special interest.

The median time to remission observed was 61 months (95% CI 43.3-78.6); 33 (47%) patients reached inactive disease (Figure 1).

Conclusion: The rates of adverse events was low, demonstrating a good safety profile of the treatment, however time to remission is greater than reported in literature.

REFERENCES

[1] Ravelli A, Martini A. Juvenile idiopathic arthritis. Lancet. 2007;369 (9563):767–78.

[2] Ruperto N, Ravelli A, Levinson JE, Shear ES, Murray K, Link Tague B, et al. Long-term health outcomes and quality of life in American and Italian inception cohorts of patients with juvenile rheumatoid arthritis. II. Early predictors of outcome. J Rheumatol [Internet]. 1997;24(5):952–8. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=9150088

[3] Thierry S, Fautrel B, Lemelle I, Guillemin F. Prevalence and incidence of juvenile idiopathic arthritis: A systematic review. Vol. 81, Joint Bone Spine. 2014. p. 112–7.

[4] Minden K, Horneff G, Niewerth M, Seipelt E, Aringer M, Aries P, et al. The time of DMARD start in Juvenile Idiopathic Arthritis determines the likelihood of a drug-free remission in young adulthood. Arthritis Care Res (Hoboken) [Internet]. 2018; Available from:

[5] Shoop-Worrall SJW, Kearsley-Fleet L, Thomson W, Verstappen SMM, Hyrich KL. How common is remission in juvenile idiopathic arthritis: A systematic review. Vol. 47, Seminars in Arthritis and Rheumatism. 2017. p. 331–7.

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AB0971 A CASE OF PEDIATRIC IDIOPATHIC CALCINOSIS

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Background: Calcinosis includes a rare group of disorders characterized by abnormal intracutaneous, subcutaneous, fascial or intramuscular calcium deposits. Idiopathic calcinosis is diagnosed after the exclusion of secondary forms related to trauma, abnormal calcium/phosphorus metabolic disorders, inflammatory processes, neoplasms, connective tissue diseases or renal insufficiency. There are very few cases reported, especially in childhood.

Objectives: We report the case of idiopathic calcinosis cutis in a young girl.

Methods: A 15-year-old female presented an abrupt onset of 2 painful swollen lesions on the left trochanteric region and over the posterior side

of her right elbow. The patient denied any trauma or associated symptoms such as muscle weakness or joint stiffness. On physical examination, a large hard mass was present over her left trochanteric region, with hyperemic skin, and a similar one was palpable over her right elbow.

Results: Radiographs of the two sites showed well-defined calcified masses, one (9x5 cm) over the trochanteric region, and the other (3x2) cm over the posterior aspect of the distal end of the humerus extending up to the elbow. MRI confirmed the presence of calcified intramuscular lesions (Figure 1). Serologic evaluation showed increased levels of CRP and ESR, while autoimmune screening was negative. Calcium/phosphorus metabolism, creatinine kinase, aldolase and ferritin levels were within the normal limits. Therefore, a clinical diagnosis of idiopathic calcinosis was made. After 3 months, the lesion on the elbow had spontaneously reabsorbed, while the other one kept on growing, with 3-4 episodes per month of febrile painful swelling. A CT-guided biopsy was then performed, confirming the diagnosis of calcinosis. No infectious causes were detected. One year later, since there was no local amelioration, the lesion was surgically removed with apparent complete local remission. No other new lesions were detected during the 3 months follow-up period.

Conclusion: Idiopathic calcinosis is very rare and no specific medical therapies are available. In our patient no causative factors were identified and thus the diagnosis of idiopathic calcinosis was made. Prognosis seems to be variable, since one lesion risolved spontaneously while the other needed surgical excision.

REFERENCES

[1] Alabaz D, Mungan N, Turgut M, Dalay C: Unusual Idiopathic Calcinosis Cutis Universalis in a Child. Case Rep Dermatol 2009;1:16-22. doi: 10.1159/000227285

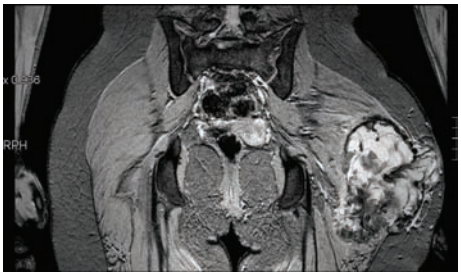
[2] N. Reiter, L. El-Shabrawi, B. Leinweber, A. Berghold, and E. Aberer, "Calcinosis cutis. Part I: diagnostic pathway," Journal of the American Academy of Dermatology, vol. 65, no. 1, pp. 1–12, 2011.

[3]

[3] Hwang ZA, Suh KJ, Chen D, Chan WP, Wu JS. Imaging Features of Soft-Tissue Calcifications and Related Diseases: A Systematic Approach. Korean J Radiol. 2018 Nov-Dec;19(6):1147-1160.

[5] S. K. Venkatesh Gupta, Ramana Rao Balaga, and Suman Kumar Banik, "Idiopathic Calcinosis Cutis over Elbow in a 12-Year Old Child," Case Reports in Orthopedics, vol. 2013, Article ID 241891, 4 pages, 2013.

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Abstract AB0971 Figure 1. MRI of the trocanteric region showing calcified intramuscolar lesion.

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AB0972 ARTEFACTUAL SKIN LESIONS: A TRAP FOR RHEUMATOLOGISTS

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Background: Dermatitis artefacta (DA) refers to deliberate and conscious self-inflicted skin lesions to satisfy an unconscious psychological or emotional need. It is an unusual condition often described in women, and rarely reported in children. The disorder is often misdiagnosed and needs to be distinguished from organic illness, Munchausen's by proxy syndrome, and from illicit, nontherapeutic drugs or overdose of medications.

Objectives: We report three paediatric cases with a long medical hystory characterized by many laboratory and radiological exams, and mistaken etiologies.

Methods: *Case 1.* An 11-year-old female was referred to our Rheumatology Department for a second opinion about a suspicion of Behcet's disease based on her cutaneous manifestations. Clinical examination was unremarkable except for bluish ecchymoses, and linear cutaneous abrasions and scars located in accessible areas of her skin (Figure 1, Figure 2 and Figure 3). Extensive laboratory tests and radiological exams were normal.

Case 2. A 14-year-old female was admitted to our pediatric hospital for a 1 month history of fever, malaise and multiple purpuric lesions. The patient referred a 3 year history of similar recurrent episodes characterized by abrupt onset of fever, arthralgia and purpuric lesions for which she already received the diagnosis of urticarial vasculitis. The girl was in good general conditions, without fever. Violaceous ecchymotic lesions were evident on her left forearm. Exhaustive laboratory tests, chest X-ray, and abdomen ultrasound were within normal limits.

Case 3. A 14-year-old female was referred to our Pediatric Rheumatology department for a 6 month history of musculoskeletal pain, recurrent shoulder and hip dislocations, and spontaneous ecchymosis on her neck and face. Except for joint hypermobility (Beighton score 7/9), physical examination was normal. At a careful orthopedic evaluation and after shoulder and hip imaging the history of dislocations appeared to be inconsistent. Blood and radiologic tests, cardiological and genetic evaluations for Elher-Danlos syndrome were negative.

Results: In *Case 1,* dermatitis artefacta was suspected and the patient was referred to our mental health colleagues that confermed a severe psychological stress in a basal condition of psychiatric disorder. In *Case 2,* an in-depth psychological evaluation highlighted a depressive status for personal and familiar suffering. The patient was therefore referred to our mental health department for assessment and management. In *Case 3*, eventually a psychiatric interview oriented the diagnosis to a major depressive disorder.

Conclusion: DA is a rare condition that should be evaluated in the differential diagnosis, in the presence of unexplained cutaneous lesions without an apparent identifiable cause. Association with various psychological disturbances is the mainstay for this diagnosis, and a careful psychiatric history represents the essential diagnostic key to identify this disorder.

REFERENCES

[1] Alcántara Luna S, et al. Dermatitis Artefacta in childhood: a retrospective analysis of 44 patients, 1976-2006. Pediatr Dermatol 2015;32:604-8.

[2] Ring HC, et al. Artefactual skin lesions in children and adolescents: review of the literature and two cases of factitious purpura. Int J Dermatol 2015, 54, e27–e32.

[3] Finore ED, et al. Dermatitis artefacta in a child. Pediatr Dermatol 2007;24: E51-6.



Abstract AB0972 Figure 1



Abstract AB0972 Figure 2

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Abstract AB0972 Figure 3

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AB0973 ATYPICAL KAWASAKI DISEASE SHOCK SYNDROME CASE REPORT: NOT ALL SHOCKS ARE SEPTIC OR TOXIC

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Background: Kawasaki disease (KD) is an acute, self-limited vasculitis of unknown etiology with peak incidence at 9-12 months of age. The term Kawasaki Disease Shock Syndrome (KDSS) was introduced in 2009 after reports of hemodynamic instability during the acute phase of the illness.
Objectives: Present and discuss a rare case of KDSS in an adolescent patient.
Methods: Review of patient's clinical records and scientific literature.
Results: A 12 year-old boy was admitted in the pediatric intensive care unit (ICU) with a 5-day history of high persistent fever, abdominal pain, vomiting and headaches. On examination, he looked ill, was tachycardic and hypotensive with delayed capillary refill, had non-exsudative oropharyngeal erythema, cracked lips, terminal nuchal rigidity, jaundice and small palpable supraclavicular lymph nodes. On day 3 a generalized morbiliform rash and diffuse swelling of the hands became apparent. Blood gas showed metabolic acidosis. He had decreased platelet count of 72,000/mm3, AST 122 U/l, ALT 192 U/l, LDH 366 U/L, triglycerides 207 mg/dl, total bilirubin 85,5 µmol/l (direct 68,4). Renal function, urinalysis and fibrinogen were normal. ESR was 42 mm/h, CRP was markedly high (268 mg/l) and ferritin 544 ng/ml. Lumbar puncture revealed mild sterile pleocytosis. Due to progressive hemodynamic instability he required fluid resuscitation, inotropic drugs and mechanical ventilation. Broad-spectrum antibiotherapy was started due to suspected septic shock/streptococcal toxic shock syndrome. IVIG was empirically started 24h later due to non-response. Viral screening, all blood and urine cultures and ASO titers were negative. Myelogram revealed no signs of hemophagocytosis, neoplastic changes or growth of microorganisms in culture. Fine needle biopsy of a supraclavicular lymph node showed nonspecific inflammatory changes. Thoracoabdominal scan revealed moderate bilateral pleural effusion, mild hepatoesplenomegaly, retroperitoneal/mesenteric lymphadenopathy. Brain MRI and echocardiogram were normal as well as ophtalmologic evaluation. In the presence of prolonged fevers, mucosal changes, extremity edema and non-specific rash in a severely-ill adolescent with no response to broad spectrum antibiotics and negative cultures, the possibility of KD was raised.
Due to ongoing fevers and inflammation after 36h of first IVIG, he received a second IVIG dose 2g/Kg, methylprednisolone IV pulses for 3 days and aspirin, with rapid clinical and laboratorial improvement. Within 24h the patient was off inoptropic support, 48h off mechanical ventilation and 3 days later he was discharged from the ICU. His general condition continued to improve gradually, with increased platelet counts, normalization of liver function and CRP. In this phase, skin desquamation (buttocks/perineal region) was noted. At follow-up, thoracoabdominal angioMRI and serial ecocardiograms were normal. He was weaned off corticosteroids and aspirin without recurrence of symptoms.
Conclusion: In this case, despite the atypical age and lack of some classical signs/symptoms, broad-spectrum antibiotic refractoriness and the described clinical presentation raised the hypothesis of KSSD. Diagnosis can be difficult, especially if shock occurs in incomplete forms of KD, but must be suspected early and treatment promptly started in order to ensure a good prognosis. Clinicians should be aware that thrombocytopenia and hepatitis are risk factors for refractory severe KD. MAS must always be excluded in cases of hemodinamic instability.

REFERENCES

[1] Kanegaye, *et al.*
[2] Recognition of a Kawasaki disease shock syndrome. Pediatrics 123:e783–e789.

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AB0974 A CASE OF ADENOSINE DEAMINASE 2 DEFICIENCY (DADA2) WITH AN UNCOMMON CLINICAL PRESENTATION AND RESPONSE TO IV IG

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Background: DADA2 is an autoinflammatory disease with autosomal recessive inheritance characterized by a heterogeneous clinical phenotype ranging from multisystemic inflammation (fever, polyarteritis nodosa, cerebral stroke, livedo reticularis etc.) to immune-dysregulation and immunodeficiency.
Objectives: To extend the clinical spectrum of DADA2 reporting a case of isolated nonspecific systemic inflammatory syndrome associated with signs of immune-dysregulation in a patient with a novel ADA2 mutation.
Methods: In a patient with nonspecific inflammatory phenotype associated to susceptibility to viral infections, Next Generation Sequencing (NGS) panel was performed; mutations detected were confirmed by Sanger analysis. ADA2 enzymatic activity was analyzed in monocyte isolated from the patient and incubated with adenosine and an ADA1 inhibitor.
Results: The girl, adopted and of Asian origin, began to suffer from nonspecific systemic inflammatory symptoms (persistent fever and arthralgias) at the age of 6. In past history recurrent respiratory infections and impaired immunological response to viruses (CMV related hepatitis, measles after vaccination) were reported. After few months the patient developed clinical and laboratory findings of HLH (Hemophagocytic Lympho-Histocytosis), confirmed on bone marrow samples; treatment with intravenous (IV) high dose (HD) steroids was started, with prompt response. During steroids tapering fever and systemic inflammation reappeared; anti-IL1 treatment (anakinra) was not effective. Immunologic assessment demonstrated mild hypogammaglobulinemia and moderate NK deficiency on lymphocyte subsets. HD IV Immunoglobulins (IG) (2 g/kg every month) allowed to achieve a complete control of the clinical picture; the frequency of administration was progressively reduced to every 4 months due to persistent wellbeing. At the age of 9, after switching IG to the

substitutive dosage, the patient experienced Herpes Zoster virus reactivation (requiring prolonged antiviral treatment), followed by the reappearance of the inflammatory phenotype complicated by HLH with neurological involvement (irritability and lethargy), responsive to HD steroids and IG. A later cerebral MRI evidenced a small gliotic area in left Centrum Ovale. After steroids suspension, monthly HD IV IG administrations maintained clinical remission. Further immunological studies confirmed a reduction of NK cells with normal function. Hereditary HLH, Autoimmune Lympho-Proliferative Syndrome (ALPS) and main primary immunodeficiencies were ruled out. Given the clinical picture, a large NGS diagnostic panel (courtesy by K. Botzug, Vienna) for autoinflammatory diseases and immunodeficiencies was performed revealing the homozygous LEU141PRO ADA2 mutation, confirmed by Sanger analysis. Being this mutation novel, an ADA2 enzymatic activity test was performed revealing a complete loss of ADA2 activity. The parents refused anti-TNF treatment and the patient is still on monthly HD IG with a complete wellbeing after 3 years of follow-up.

Conclusion: The current report enlarges the clinical spectrum associated with DADA2 to a persistent unspecific inflammatory syndrome, complicated by HLH. This case further emphasizes the possibility that NGS could unravel unusual phenotypes of already known inflammatory syndromes. Even if further reports are required, the response to HD IG observed in the present case it is of interest. Even if anti-TNF is the treatment of choice HD IG could be a possible treatment in DADA2, especially during the acute phase.

REFERENCES

[1] Caorsi R, et al. Ann Rheum Dis. 2017 76(10):1648-1656

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AB0975 INITIAL BIOLOGICAL THERAPY RESPONSE IN PATIENTS WITH SUSPECTED AUTOINFLAMAMTORY DISEASE

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Background: The choice of the initial biological therapy for patients with suspected autoinflammatory diseases and not conclusive genetic test remains challenging.

Objectives: To assess the clinical response to the initial biological therapy in pediatric patients with suspected autoinflammatory disease with no genetic diagnosis.

Methods: We retrospectively reviewed the clinical charts of patients followed in our clinic who started empirical biological therapy after being diagnosed with suspected autoinflammatory disease(sAID) due to the intensity of their symptoms and no response to colchicin or FAMEs. Next generation sequencing using an immune deficiency/dysregulation(115 genes) and autoinflammatory panel(12 genes) was negative/inconclusive in all patients.

	Mean	SD	Median	IQR	Min	Max
PCR max mg/L	199.4	134	181	190	39	440
VSG 1h max	89.7	29.6	86	32	44	140
Leukocytes/ul	25942	9950	25105	9450	11670	45200
Neuthrophils/ul	16132	6692	16250	9450	6500	25300
Lymphocytes/ul	1518	1050	1275	1350	200	3300
Haemoglobin (g/dl)	9.6	2.1	10	2.75	6.2	12.8
Platelets/ul (max)	603375	225317	560000	198000	25000	100300
Platelets/ul (min)	182875	104840	160500	145000	74000	368000
Amyloid(mg/L)	Data in 5 patients: 1 patient 3.7 ; 2 patients >8					

Results: We identified 9 patients:6/9 were male, median age at fever onset 1.33 years old IQR(0.46-4), age at diagnosis of sAID 3.8 years old IQR(1.75-7). Clinical presentation included fever(9/9), abdominal pain and arthromyalgia(7/9), aphthous(6/9), headache, rash and adenopathy(5/9), delayed growth(4/9), tonsillitis and pericarditis(3/9) as well as diarrhea and pleuritis(2/9). One patient presented with stroke, cutaneous lesions, vasculopathy and haemolytic uraemic syndrome and 1 patient with amyloidosis and secondary hepatosplenomegaly. None of the children suffered from uveitis or meningitis. The flares lasted a median of 14 days(IQR 8-20). Two patients had persistent symptoms. Their mean/median lab values are shown at table. 4/9 patients had homozygous mutations with uncertain significance, heterozygous mutations or polymorphism but their symptoms or familiar study was not suggestive of the corresponding AID. One patient had an heterozygous mutation in MEFv (p.P3696,p.R408q) and also a CECR1 heterozygous mutation with uncertain significance, one patient had pR92Q heterozygous mutation in TNFRSF1A, one patient had MEFv pR202Q homozygous mutation, other patient had a NOD-2 heterozygous mutation and the patient with amyloidosis had
INO80 deficiency and a NOD2 mutation (p.A918D). All patients responded to steroid therapy; subsequently 8/9 received anti IL-1Receptor kineret as first biological therapy and 1/9 with suspected vasculopathy received anti-TNF. Response to IL-1R antagonist was complete in 3/8 and partial in 4/8 children;1/8 showed no response. 2/8 patients were switched to anti-TNF: One each to etanercept and Infliximab with good response. The patient with amyloidosis was changed to anti IL-6R with incomplete response but clear improvement compared to anti Il-1R response. The patient with suspected vasculopathy and initial anti-TNF treatment had partial response with no recurrent stroke but persistent skin lesions.

Conclusion: An important group of patients with sAID lack genetic confirmation. Empirical use of IL-1R antagonist is promising but not effective in all patients as it was observed in our case series,where 5/8 children showed partial or no response,3/5 needing a second biologic treatment in form of anti-TNF due to persistent moderate-severe symptoms.

A model to predict the response to different therapeutic strategies, based on clinical features and immunological profile (including inflammatory cytokines) might help to choose the most appropriate immunomodulatory treatment.

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AB0976 PSYCHIATRIC DISORDERSDURING TRANSITION CARE IN ADOLESCENTS WITH RHEUMATIC DISEASES

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Background: Chronic rheumatic diseases (CRD) have a strong impact on psychosocial development of pediatric patients. There are several factors associated with psychiatric disorders (PD) in these children; physical disability, complex treatments, long-term follow-up, and flares, are the most cited in literature.

Juvenile Idiopathic Arthritis (JIA) is the first cause of disability in children with CRD, on the other hand, Major Depressive Disorder (MDD) and Dysthymia are the third cause. Some PD, mostly MDD, appear as a consequence of disability caused by CRD, but immune pathways might be implicated in pathogenesis as well.

Adolescents with CRD need to transition to an adult-centered care while deal with emotional and physical changes. This implies a difficult situation in which patients could be in higher risk for develop PD. There are a lack of information on how this process affects emotional health in this population.

Objectives: The aim of the study is to calculate the prevalence of PD in adolescents with CRD during transitional care and their relationship with clinical and social factors.

Methods: Patients older than 16 years with an established CRD, who were in transitional care during the period between July 2017 and January 2019 were included in this transversal study.

We used MINI KID assessment tool to characterize PD in our patients. Each patient performs an interview with both a clinical psychologist and

a pediatric psychiatrist to confirm psychiatric/emotional diagnosis. Clinical, social and demographic data were collected from medical records.
Descriptive statistics with frequencies or measures of central tendency and dispersion, depending on variable characteristics were used. Comparisons and correlations were performed with parametric and non-parametric tests as appropriate.
Results: Forty patients were recruited during study period, aged 18 (IQR 16 - 19) years old, 31 female, and most diagnosed with JIA (22, 55%) and Systemic Lupus Erythematosus (SLE, 7, 17.5%). Time since diagnosis were 5.5 (IQR 0.5 - 13) years and half of the patients presented with an active disease.
After psychiatric evaluations, 24 (60%) patients presented a PD, 7 (17.5%) were identified with MDD, while minor disorders (specific phobia and anxiety) were notice in 11 (27.5%). Two patients presented alcohol dependence, and 11 (27.5%) were diagnosed with more than one PD.
PD were more frequently in patients with SLE (71%) and in those with active disease regardless underlying diagnosis (54% vs 45%, P = .490). Other significant factors related with more prevalence of PD were female gender (66% vs 44%, P < .001), having a couple (90% vs 57%, P < .001), have a single parent (83% vs 60%, P = .005), and sex activity (71% vs 61%, P = .002).
Conclusion: We found a higher prevalence of PD in adolescents during transitional care, especially in those with active disease. It is priority to involve a multidisciplinary team to transition adolescents from pediatric to adulthood care to prevent and detect PD in this population.

REFERENCES

[1] Ravelli A, Martini A. Juvenile idiopathic arthritis. Lancet. 2007;369 (9563):767–78.
[2] Vos, Theo, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for. Lancet. 2017;390.
[3] Nerurkar L, Siebert S, McInnes IB, Cavanagh J. Rheumatoid arthritis and depression: an inflammatory perspective. The Lancet Psychiatry. 2018;

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AB0977 ULTRASOUND MEASUREMENT OF JOINT CARTILAGE THICKNESS IN HEALTHY ASIAN SCHOOL-AGED CHILDREN

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Background: Degeneration of the osteocartilaginous structures due to synovial inflammatory process is a feature of juvenile idiopathic arthritis (JIA)[1]. While anthropometry difference has been reported between Asian and Caucasian[2,] Asian specific age- and gender-related normal standard reference values should be established before ultrasound (US) measurement of cartilage thickness (Cth) becomes standard procedure in the clinic.
Objectives: The standard cartilage thickness in Asian children population
Methods: A cross-sectional study was performed in 100 healthy Asian children (including 48 girls and 52 boys, age between 5 to 12 years-old). Bilateral knees, ankles, wrists, second metacarpophalangeals (MCPs) and proximal interphalangeals (PIPs) were measured using US. Children's body weight and body height were also recorded for later adjustment.
Results: We observed no difference in the Cth between right and left knees, ankles and wrists but MCPs and PIPs. Cartilage thickness in the large joints such as ankles and knees differed between sexes ($p<0.001$), and the boys had thicker cartilage than those of the girls. Cartilage thickness decreases with increasing age after weight, height and BMI adjustment. A formula for calculating sex-specific cartilage thickness at different ages in childhood is suggested.
Conclusion: Cartilage thickness measurement with US in small joints may be biased. A standard reference of Cth for Asians in the knee, ankle and wrist joints between age 5- to 12 have been proposed.

REFERENCES

[1] Naredo, E. et al. Longitudinal power Doppler ultrasonographic assessment of joint inflammatory activity in early rheumatoid arthritis: predictive value in disease activity and radiologic progression. Arthritis Rheum 57, 116-124, doi:10.1002/art.22461 (2007).
[2] Yue, B. et al. Differences of knee anthropometry between Chinese and white men and women. J Arthroplasty 26, 124-130, doi:10.1016/j.arth.2009.11.020 (2011).

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AB0978 NEUROLOGICAL MANIFESTATIONS OF PEDIATRIC SYSTEMIC LUPUS ERYTHEMTOSUS IN EGYPTION PATIENTS

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Background: SLE is a complex autoimmune disorder, characterized by multisystem involvement including the nervous system, juvenile onset SLE has more aggressive clinical course in comparison with adult-onset SLE.
Objectives: To study the neuropsychiatric manifestations of SLE in Egyptian children.
Methods: We reviewed the charts of all children and adolescents who were diagnosed with SLE and evidence of neuropsychiatric manifestations was defined by full neuropsychiatric history and examination.
Results: Out of 54 children with SLE, 30 (55.6%) had neuropsychiatric (NP) manifestations, the mean age at onset of the disease was 13.6 years. The mean period between onset of SLE and NP manifestations 15.5 months. NP manifestations was the presenting feature in 3 patients. Headache was the initial symptom of central nervous system (CNS) involvement in 35% of patients seizures was the most frequent CNS finding seen in 7(23.3%) patients, 6 (20%) patients had congnifive impairment, 6(20%) patient had cognitive impairment, 6(20%) patients had CVA, 2(6.7%) had chorea, 2(6.7%) had psychosis, 2(6.7%) had depression, 1 (3.3) had cerebritis, 1(3.3%) had peripheral neuropathy. Lupus anticoagulant was high in patients with chorea, seizures or cerebrovascular accidents (CVA). Electroencephalogram (EEG) was abnormal in 30% of patients presented by seizures and rarely helpful in patients with diffuse NP symptoms. Magnetic resonance imaging (MRI) was abnormal in 13 cases, long term outcome was good, 3 patients had significant persistent CNS deficits, the majority of patients (90%) had excellent recovery from neuropsychiatric SLE.
Conclusion: NPSLE is one of the most common serious complications of pediatric SLE, so early recognition and management are of paramount importance. CNS involvement was observed in 55% of our pediatric patients with SLE, 76% of whom developed symptoms during the first year of onset of the disease Headache and seizures were the most common neurological manifestations of pediatric SLE, followed by CVA and intellectual disability. Psychosis, depression and chorea were less frequent in our study group, while peripheral neuropathy and cerebritis were rare.

REFERENCES

[1] Smith PP and Gordon C (2010): Systemic lupus erythematosus: clinical presentations. Autoimmunity Reviews, 10(1): 43–45.
[2] Khajezadeh M (2016): The prevalance of neurologic manifestation of children diagnosed by systemic lupus erythematous refer to the children medical center since during 10 years. in MD (speciality of Pediatrics) disertation, Tehran University of Medical Sciences, In Persian.
[3] Fernandes M, Trevisani V, Castro AA, Ferreira Neves Neto J, Atallah AAN (2013): Cyclophosphamide versus methylprednisolone for treating neuropsychiatric involvement in systemic lupus erythematosus. Cochrane Database Syst Rev., (2):CD002265.
[4] Zambrano YC, Ramos JD, Vargas NE, Ramirez DC, Rodriguez SM, Niño AC, Bello ÁH (2014): Risk factors for neuropsychiatric manifestations in children with systemic lupus erythematosus: case-control study. Pediatric Neurology, 51(3):403-9.
[5] Bader-Meunier B, Armengaud JB, Haddad E, Salomon R, Deschênes G, Koné-Paut I, Leblanc T, Loirat C, Niaudet P, Piette JC, Prieur AM (2005):

Initial presentation of childhood-onset systemic lupus erythematosus: a French multicenter study. The Journal of Pediatrics, 146(5):648-53.
[6] Singh S, Gupta MK, Ahluwalia J, Singh P, Malhi P (2009): Neuropsychiatric manifestations and antiphospholipid antibodies in pediatric onset lupus: 14 years of experience from a tertiary center of North India. Rheumatology International, 29(12):1455-61

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AB0979 CORTICOSTEROID TREATMENT IN PEDIATRIC RHEUMATIC DISEASES AND SUPPRESSION OF THE HYPOTHALAMIC-PITUITARY AXIS

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Background: Corticosteroids are the mainstay in the treatment of several chronic inflammatory diseases. Long-term treatment may lead to suppression of hypothalamic-pituitary-adrenal axis, which in turn can be dangerous in stress situations such as after surgical interventions. Oral replacement therapy may be needed in some cases. Data on pediatric populations are scanty.
Objectives: The aim of our study has been to evaluate hypothalamic-pituitary-adrenal function during corticosteroid tapering by measuring serum cortisol.
Methods: During long term corticosteroid treatment, serum cortisol levels were evaluated when oral prednisone dose was decreased to 7.5 mg/day and also after 4-6 weeks, and if below range ACTH levels were also determined.
All patients aged < 18 years seen in our center during the last 6 months who were on corticosteroid treatment for > 1 month were included. Serum cortisol levels were considered normal if in the range of 5-25 μg/dL in a morning fasting blood drawing, while ACTH levels were considered normal in between 6 and 55 ng/L (with chemiluminescent method). Clinical and demographic data were recorded from clinical charts in a customized database.
Results: We have included in this preliminary study 12 patients (7F, 5M) affected by uveitis (n=4), JIA (n=4), scleroderma (n=3), lupus (n=1). The mean age (at the time of sampling) was 11.5 years, with a median of 10 and a range of 8-17. Prednisone starting dose was 1 mg/kg/day.
Four out of 12 patients had decreased cortisol levels. Characteristics of these four patients (none of whom had additional steroid pulses) are detailed in the table.
Conclusion: One third of our patients had decreased cortisol levels, after three months of prednisone treatment. In one case, who showed persistent low levels, oral supplementation with hydrocortisone 20 mg/day for two months was needed. Our study is ongoing and results could help in identifying patients at risk for adrenal crisis.

REFERENCES

[1] Gangadharan A, McCoy P, Phyo A, McGuigan MP, Dharmaraj P, Ramakrishnan R, McNamara PS, Blair J, "Recovery of hypothalamo-pituitary-adrenal axis suppression during treatment with inhaled corticosteroids for childhood asthma", J Asthma Allergy. 2017 Dec 15;
[2] Sidoroff M, Kolho KL, "Screening for adrenal suppression in children with inflammatory bowel disease discontinuing glucocorticoid therapy", BMC Gastroenterol. 2014 Mar 24;
[3] Ahmet A, Brienza V, Tran A, Lemieux J, Aglipay M, Barrowman N, Duffy C, Roth J, Jurencak R, "Frequency and Duration of Adrenal Suppression Following Glucocorticoid Therapy in ChildrenWith Rheumatic Diseases"; Arthritis Care Res (Hoboken). 2017 Aug;

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AB0980 EFFICACY OF ETANERCEPT TREATMENT FOR CHILDREN WITH KAWASAKI DISEASE INTRACTABLE TO INTRAVENOUS IMMUNOGLOBULIN THERAPY IN RUSSIAN CHILDREN

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Background: Kawasaki disease (KD) is recognized in developed countries as a fundamental reason of acquired heart diseases in children nowadays. The main treatment is infusion of intravenous immunoglobulin (IVIG) at a dose of 2 g/kg. However for about 10-30% of children is reported the development of resistance to standard therapy: continuance of fever (≥38,0 °C) or recurrency of fever after 36 hours afebrile period (T<37,5 °C), but not later than on the 7th day after completion of the IVIG infusion at a dose of 2 g/kg. Until now there are no unified recommendations for treatment of such patients. As alternative therapy researchers empirically apply second infusion of IVIG (77%), high doses of glucocorticoids (18%), blockers of tumor necrosis factor α (3%) and interleukin-1, cyclosporine and other cytostatic drugs.
Objectives: Efficacy evaluation of therapy by inhibitor of TNF-alpha (Etanercept) in treatment of KD immunoglobulin -resistant forms according to the data from Morozovskaya Children's City Clinical Hospital,Moscow.
Methods: There were examined 152 patients (boys:girls – 2:1, median age Me = 21 months [10;36]) with KD hospitalized in Morozovskaya Children's City Clinical Hospital in 2014-2018. The frequency of complete form of KD was 80,6%. All children had a standard therapy –IVIG. Efficacy evaluation was based on normalization of body temperature, decrease of neutrocytosis, decrease of C-reactive protein (CRP) level. In case of ineffectiveness of therapy the second infusion of IVIG, pulse-therapy and inhibitor of TNF-alpha (Etanercept) were used
Results: The resistance to standard IVIG therapy was revealed in 16 children (10,5%), mostly in boys (4,3:1) at the age of Me = 21,5 months [9,5; 34]. Complete form of KD was diagnosed in 11 patients (68,8%), incomplete form - in 5 children (31,2%). Cardiovascular lesions were noted in 14 children (87,5%): pericarditis - in 2 (12,2%), coronary arteries (CA) lesions – in 12 (75%), with formation of aneurysms in 8 (50%), including the giant ones in 3 children (18,8%); peripheral arteries damages were noted in 2 children (12,5%), thrombosis and thromboembolism – in 4 children (25%).
To all of children was made the second IVIG infusion, 13 of those children (81,2%) had a positive effect:11 children with complete form of KD, 2 children with incomplete form of KD. For 3 children (18,7%) with incomplete form of KD and significant cardiovascular changes (pericarditis, giant aneurysm of coronary and peripheral arteries,thrombosis and thromboembolism) it was needed an additional therapy. As a second-line therapy the methylprednisolone pulse-therapy was used in 2 children(12,5%) at a dose of 10 mg/kg, without sufficient effect. For these three patients (3) as a third-line therapy was applied Etanercept at a dose of 0,8 mg/kg/a week subcutaneously. In all children normalization of body temperature, decrease of leukocytosis by factor of 1,5-3 and decrease of CRP by factor of 10-15 occurred after three injections of Etanercept. However, for 1 child it was needed the additional fourth injection of Etanercept because of repeated fever, increased laboratory parameters, development of thrombosis of the left coronary artery after 2 weeks upon discharge.
Conclusion: The frequency of immunoglobulin-resistant forms was 10, 5%. The first-line therapy of resistance (second IVIG-infusion) was efficient in 13 children (81,2%). Methylprednisolone pulse therapy was ineffective. The use of 3 subcutaneous injections of Etanercept at a dose of 0,8 mg/kg/ a week resulted in decrease of intensity of inflammatory changes and in fever relief, but it did not prevent the development of relapse and thrombosis of coronary arteries.
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Patient	Gender	Age	Disease	PDN initial dose [mg/Kg/die]	PDN duration of therapy up to 7.5mg/day	Cortisolemia (1) [mcg/dl]	Cortisolemia (2) [mcg/dl]	ACTH [ng/L]
1	M	17	Uveitis	0.9	3 months	4,37	N/A	N/A
2	F	13	Scleroderma	1	3 months	2,87	5,22	15,90
3	F	8	JIA	1.4	4 months	0.20	2.68	7.98
4	M	10	Uveitis	1.3	3 months	4.3	N/A	25.01

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AB0981 10-YEARS EXPERIENCE OF ETANERCEPT USE IN TREATMENT OF JUVENILE IDIOPATHIC ATRTRITIS IN CHELYABINSK REGIONAL PEDIATRIC HOSPITAL

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Background: Juvenile idiopathic arthritis (JIA) in recent decades has changed its course, thanks to the use of genetically engineered biological drugs. If therapy with methotrexane is inefficient etanercept is the drug of choice for JIA treatment. Etanercept has been used in Chelyabinsk regional pediatric hospital during 10 years.
Objectives: Performance and safety assessment of etanercept in patients with JIA in Chelyabinsk regional pediatric hospital.
Methods: 51 children aged from 3 to 17 (mean age 10,0 years) diagnosed with JIA were under monitoring (12 boys, 39 girls). Disease duration was from 2 to 15 years (mean duration 5,4 years). JIA was diagnosed based on ILAR diagnostic criteria. Oligo arthritis was diagnosed in 9 children, sero-negative polyarthritis was diagnosed in 34 children. 3 patients had systemic JIA (without active systemic presentations), 5 children had enthesitic JIA. X-ray stage 1-2 was observed in 45 children and stage 3-4 in five. Enhancement antigens HLA B 27 were found in 11 children. In all children methotrexate was ineffective in dose of 15 mg/m^2 during 6-12 months. Etanercept was introduced in dose of 0.8 mg QW. Therapy duration was from 3 months to 8 years (mean duration 29 months). Assessment of disease activity and therapy efficiency was conducted in accordance with ACR pedi criteria. Nonparametric statistical methods were used to compare results.
Results: Prior to etanercept use high disease activity was observed in all children. Mean number of joints with active arthritis was 8 [4, 10] (Me[25;75%]). Mean number of joints with functional impairments – 4 [2;10]. Mean ESR (according to Panchenkov) – 23 [10;35] mm/h, CRP 12,0 [5,7;32] g/L. Assessment of functional activity according to CHAQ questionnaire – 1,25 [1;2]. Activity assessment according to VAS by doctor – 70 [60;70]. Assessment of parents/patients according to VAS 70 [60;80]. No active systemic presentations and eye lesions were found in children under monitoring.
On the background of etanercept therapy a decrease in disease activity was observed in 50 patients. Mean number of joints with active arthritis was 0 [0;2] (Me[25;75%]) (P≤0.0001). Mean number of joints with functional impairments – 0 [0;.2] (P≤0.0001). Mean ESR was 5 [3,6] mm/h (P≤0.0001), CRP 3 [2;4] g/L (P≤0.0001). Assessment of functional activity according to CHAQ questionnaire was 0,125 [0;0,5] (P≤0.0001). Activity assessment according to VAS by doctor – 10 [5;20] (P≤0.0001). Assessment of parents according to VAS 10 [5;20] (P≤0.0001).
Clinical disease remission (according to ACR pedi criteria ≥90%) was observed in 32 patients after 6-12 months of treatment. Remission duration up to now is from 1 to 7 years. Efficiency according to ACR pedi criteria is 70% in 11 children, 50% in 5, 30% in 2.
Etanercept was well-tolerated. Drug was cancelled in 9 patients. 6 patient (11,8%) developed bilateral uveitis, one patient had an allergic reaction (rash), one - systemic manifestations, one - urinary tract infection. There were no cases of tuberculosis.
Conclusion: Etanercept therapy was highly effective and safe in patients with JIA. Clinical remission was achieved in 62,7% children. Decrease in disease activity was observed in 98% of children. 11,8% patient developed uveitis, on average, after a year of using etanercept.

REFERENCES

[1] Lovell D. J., Reiff A., Jones O. Y., Schneider R. et al. Long-term safety and efficacy of etanercept in children with polyarticular-course juvenile rheumatoid arthritis//Arthritis Rheum. 2006; 54: 1987–1994.

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AB0982 CENTRAL NERVOUS SYSTEM ANGIITIS: THE EXPERIENCE OF A TERTIARY PEDIATRIC RHEUMATOLOGY BRAZILIAN CENTER

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Background: Central nervous system (CNS) angiitis is a severe and rare inflammatory brain disease whose course varies from patient to patient. May be associated with infections, malignances, metabolic diseases or systemic collagen vascular disorders. It is classified as primary or idiopathic in the absence of associated systemic diseases. The exact incidence is still undetermined.
Objectives: To describe the clinical and laboratory data, the response to therapy and outcome of patients with CNS angiitis seen at a Tertiary Pediatric Rheumatology Center.
Methods: This is a retrospective, single-center chart review study of pediatric patients with clinical diagnoses of CNS angiitis, followed up in a Tertiary Pediatric Rheumatology Center, from January 2009 to December 2018. Diagnosis was confirmed by magnetic resonance angiography (MRA) or after exhaustive exclusion of other causes.
Results: Nine patients (4 girls) were enrolled in this study. Mean age at inclusion and at diagnosis was 11.5 years (7.8 to 19.9) and 8 years (3,5 to 12,5), respectively. Among the 9 patients, 4(44%) were diagnosed with primary CNS angiitis. Polyarteritis nodosa (n=4) and Behçet disease (n=1) were the aetiologies of secondary CNS angiitis. Main clinical features were sudden onset of seizures (67%) and headache (55%). Other important symptoms were: decreased level of consciousness, hemiparesis and neurocognitive dysfunction. In the cerebral spinal fluid, protein was elevated in 22% of patients. The pattern of lesions was bilateral in 67% and multifocal in 55%, being suggestive of ischemic lesions by CNS magnetic resonance in 78% of the cases. The MRA was conclusive in all cases of secondary and normal in only one case of primary CNS angiitis. Increased erythrocyte sedimentation rate, C-reactive protein and leukocyte count were more frequently observed in patients with secondary CNS angiitis as compared to patients with primary angiitis. In one case of primary CNS angiitis with negative vascular study, the Von Willebrand factor antigen was positive, being useful in the differential diagnosis. Steroids were administered in 100% of patients, associated with immunosuppressants in 7/9 cases. Induction therapy with intravenous cyclophosphamide was used in 78% of the cases and in the maintenance phase, azathioprine in 78% of them. No relapses occurred. The most commonly clinical sequel observed was residual epilepsy (55%).
Conclusion: In this study, seizures were the most frequently symptom found. Steroids plus immunosuppressants were effective in the disease control. MRA was positive in all cases of secondary CNS angiitis, being effective in the diagnosis of this condition. Recognition of findings and adequate diagnosis guides the treatment, which should be specific to the underlying cause, aiming to provide a good neurologic outcome.

REFERENCES

[1] TWILT M, BENSELER S. Central Nervous System vasculitis in adults and children. Handbook of Clinical Neurology, 2016;133: 283-300.
[2] DEMIR S, SAG E, DEDEOGLU F, et al. Vasculitis in Systemic Autoinflammatory Diseases. Frontiers in Pediatrics 2018; 6:377.

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AB0983 PENTRAXIN 3 AS A MARKER OF DISEASE ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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Background: Pentraxin-3 (PTX3) is a secretory acute phase protein which is produced and expressed in many immune cells especially macrophages, fibroblasts and endothelial cells at different inflammatory sites [1].

PTX3 is known to have an interesting role in regulation of innate immunity and it is a key player in regulation of many inflammatory reactions [2].

Objectives: This study aimed to measure serum and synovial fluid (SF) levels of PTX3 in juvenile idiopathic arthritis (JIA) patients and to correlate them with different clinical, laboratory and musculoskeletal ultrasound parameters of disease activity.

Methods: We measured PTX3 in the serum (n=57) and SF samples (n=18) from 57 JIA patients and in the serum from twenty healthy control. Disease activity was calculated using the Juvenile Arthritis Disease Activity Score in 27 joints (JDAS27) and musculoskeletal ultrasound examination (MSUS) was performed using grey scale (GS) and power Doppler (PD) 10-joint score (bilateral knee, ankle, wrist, elbow and the 2nd metacarpophalangeal (MCP) joints)[3]; Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, serum ferritin, rheumatoid factor (RF) titre were measured and the Juvenile arthritis multidimensional assessment report (JAMAR) was documented.

Results: Serum PTX3 level was significantly higher in JIA patients (3.59± 2.38 ng/mL) compared to serum level in the healthy controls (1.5 ± 0.9 ng/mL) ($p<0.001$). There was no significant difference between SF PTX3 level (4.73 ± 2.62 ng/mL) and its level in paired serum samples(4.23± 2.93 ng/mL) ($p=0.59$). JIA patients with systemic onset subtype (n=13) had higher PTX3 serum levels (5.57± 2.52 ng/mL) compared to serum level in the oligoartiular (n=25) and polyarticular (n=19) subtypes (2.88± 2.13 ng/mL and 3.18 ±11.92 ng/mL respectively) ($p=0.001$ and 0.005 respectively). In JIA patients, serum PTX3 level significantly correlated with JDAS27 ($r=0.52$, $p<0.05$), CRP titres ($r=0.46$, $p<0.05$) and serum ferritin ($r=0.48$, $p<0.05$). Both serum and SF PTX3 levels significantly correlated with PD score ($r=0.51$ and 0.48 respectively, $p<0.05$). SF PTX3 ($p=0.001$) was shown to be superior to serum PTX3($p=0.02$), ESR ($p=0.07$) and comparable to CRP ($p=0.001$) at predicting PD synovitis score.

Conclusion: JIA patients have significantly increased serum and synovial fluid levels of Pentraxin 3 that remarkably correlated with the JDAS27 and MSUS parameters of inflammations suggesting that it could be a useful marker to reflect JIA disease activity.

REFERENCES

[1] Liu S, Qu X, Liu F, Wang C. Pentraxin 3 as a Prognostic Biomarker in Patients with Systemic Inflammation or Infection. Mediators Inflamm; 2014:421-429.
[2] Mantovani A, Garlanda C, Doni A, Bottazzi B. Pentraxins in innate immunity: from C-reactive protein to the long pentraxin PTX3. J Clin Immunol. 2008 Jan;28(1):1-13.
[3] Collado P, Naredo E, Calvo C, Gamir ML, Calvo I, García ML, et al. Reduced joint assessment vs comprehensive assessment for ultrasound detection of synovitis in juvenile idiopathic arthritis. Rheumatology (Oxford). 2013 Aug; 52(8):1477-84.

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AB0984 **INTERSTITIAL LUNG DISEASE IN CHINESE JIA PATIENTS**

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Background: Rheumatic diseases and or medications (for example methotrexate) used to treat the underlying condition are associated with the development of interstitial lung disease (ILD). Development of ILD in subjects with juvenile idiopathic arthritis (JIA) is assumed to be rare, however, severe respiratory complications are increasingly reported in JIA patients.

Objectives: To describe the prevalence of respiratory diagnoses and ILD in a group of Chinese JIA patients at a tertiary center.

Methods: Retrospective chart review of JIA patients attending rheumatology clinic during 2012 to 2019

Results: Fifty-eight cases of JIA were identified. Thirty-three (57%) received DMARDs, majority were on methotrexate (MTx, 24, 73%) and sulphasalazine (SSZ, 14, 42%). Eleven (19%) were currently or previously on biologics (adalimumab 5, etanercept 5, anakinra 1, previous exposure: infliximab 1, etanercept and anakinra 1).

Respiratory diagnosis was made in 11 (19%) patients. There were 2 (3.4%) cases of ILD diagnosed during the study period (see below). The rest were asthmatics. Among them, 9 were on DMARDs [MTx 8(89%), SSZ 4(44%), leflunomide 2(LEF), hydroxychloroquine 1(HCQ)] or biologics [Etanercept 3(33%), adalimumab 1, tocilizumab and anakinra 1(sequential use)]. Four subjects were on combination DMARDs [MTx&SSZ in 2, 1 each for MTx+LEF+HCQ+SSZ (sequential combination)& MTx+LEF]. Three received combination DMARDs and biologics (1 each for MTx+adalimumab, MTx+etanercept & MTx+anakinra).

Cases of ILD

One was a SJIA patient diagnosed at 2 years old. She failed methotrexate, etanercept & tocilizumab (infusion reaction). She was on low dose prednisolone, methotrexate and anakinra when she presented to us with acute right heart failure requiring ICU care 3 years after diagnosis. Advanced clubbing was noted (fig 1). HRCT thorax on presentation showed severe interstitial lung disease with marked fibrosis and traction bronchiectasis (fig 2). She was diagnosed acute on chronic cor pulmonale and pulmonary hypertension secondary to ILD.

The other was an oligoarticular JIA patient, diagnosed at 2 years old. She was refractory to intra-articular steroid injections and combination DMARDs including MTx, SSZ, LEF & HCQ. Arthritis was controlled by Etanercept. At 12 years of age, she started to have chest pain. Lung function test showed restrictive lung pattern. HRCT thorax showed pulmonary fibrosis.

Conclusion: From this Chinese cohort we identified 2 cases of ILD. They did not present with any symptoms until advanced stage or when complications set in. Both were very young at diagnosis and were difficult to control, as evidenced by the use of multiple DMARDs and biologics including methotrexate, IL6 and IL1 blockade. The causes of ILD are believed to be multifactorial. For severe case, prognosis is poor[1]. Although rare, methotrexate induced pneumonitis do occur.

Symptoms of ILD may not be obvious until late stage. Clinical examination alone is not sensitive enough to detect disease progression. Asthma is common, as in this cohort, and may further complicated the assessment. It is recommended in the recent SHARE initiative on JSLE to screen for lung disease[2]. We believe it should be performed in JIA patients as well. 6 minute walk test is a noninvasive way to assess cardiopulmonary functional status and is validated in children[3]. Patients with unexplained chest symptoms or impaired lung function should be referred to pulmonologist for further assessment.

REFERENCES

[1] Kimura Y, et al. Pulmonary Hypertension and other potentially fatal pulmonary complications in systemic juvenile idiopathic arthritis. Arthritis Care Res 2013;65(5):856-52
[2] Groot N, et al. European evidence-based recommendations for diagnosis and treatment of childhood-onset systemic lupus erythematosus: the SHARE initiative. Ann Rheum Dis 2017;76:1788-96
[3] Li AM, et al. The six-minute walk test in healthy children: reliability and validity. Eur Respir J 2005;25:1057-60



Figure 1

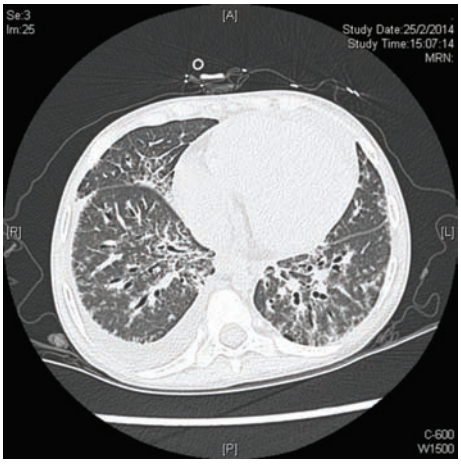


Figure 2

Disclosure of Interests: None declared
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AB0985 EVALUATION OF SERUM CALPROTECTIN (MRP-8/MRP-14) LEVEL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Evaluation of inflammatory activity is an important element in the management of patients with juvenile idiopathic arthritis (JIA), for which C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are traditionally used. However, they might be uninformative in case of subclinical inflammation. The serum level of calprotectin MRP-8/MRP-14 (sCal) correlates well with arthritis activity, as it is produced by activated cells directly in synovia.
Objectives: We evaluate the level of sCal in patients with JIA depending on the type of therapy in order to assess comprehensively the disease activity for further treatment correction.
Methods: 74 patients with JIA were examined, 18 of them had oligoarticular disease subtype, 39 – polyarticular, 17 – systemic. The mean age was 11.3 ± 0.4 years; the disease duration was 5.2 ± 0.4 years. Among them, there were 49 (66%) females and 25 (34%) males. All patients were divided into 2 groups depending on the therapy type. Group I consisted of 33 children treated with methotrexate, while 11 of them were in a state of clinical remission. Group II included 41 children treated with biologic DMARDs (adalimumab, etanercept, tocilizumab), while 14 of them achieved clinical remission. All children had normal levels of CRP and ESR. Quantitative indicators distribution is given as a median [5th; 95th percentile], the calculations were carried out using the Mann-Whitney U test.
Results: Level of sCal in the active disease stage in children of Group I was 8,750 ng/ml [3,700; 17,100], while sCal level in Group II was 2,900 ng/ml [1,200; 24,900]; sCal level in children of Group I which achieved clinical remission – 3,400 ng/ml [1,200; 6,000], and the same indicator in Group II – 1,000 ng/ml [100; 2,800]. sCal level was significantly higher in the group of patients who did not receive biologic DMARDs, both in the active stage of disease ($p = 0.000006$, $U = 71.5$) and in the stage of clinical remission ($p = 0.00034$, $U = 11$). sCal level is 5,800 ng/ml less in patients with active stage of disease and 2,400 ng/ml less in patients with clinical remission, both treated with biologic DMARDs. In addition, the level of sCal is 5.5 times higher in our patients (3,300 ng/ml) compared with healthy children (600 ng/ml) ($p = 0.015$). The moderate positive correlation of sCal and JADAS-27 activity index (r-Spearman's = 0.58) was credibly established.
Conclusion: The level of sCal can reflects the degree of inflammatory activity in JIA, it is significantly higher in the group of patients who did not receive biologic DMARDs in the treatment regimen, both in the active disease stage ($p = 0.000006$, $U = 71.5$) and in the stage of clinical remission ($p = 0.00034$, $U = 11$), which indicates the effectiveness of biologic DMARDs in the treatment of JIA. We assume that it would be appropriate to estimate the serum calprotectin level in the comprehensive analysis of clinical status in JIA patients for the further correction of therapy.
Disclosure of Interests: None declared
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AB0986 VITAMIN D LEVEL AND BONE MINERAL DENSITY IN PATIENTS WITH JUVENILE RHEUMATOID ARTHRITIS

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Background: An impaired bone metabolism is observed in patients with juvenile idiopathic arthritis (JIA), associated both with the activation of pro-inflammatory cytokines and use of steroid medications. The majority of children with JIA have low vitamin D level, which may complicate the disease course. We regard the monitoring of bone mineral density (BMD) in patients with juvenile rheumatoid arthritis (JRA) should be complemented with an additional assessment of calcidiol (25(OH)D) serum level as an indicator of BMD and a criterion of successful therapy.
Objectives: To evaluate the bone densitometry data and calcidiol level in patients with JRA in order to estimate the osteopenic syndrome and the advisability of prescribing the vitamin D additional doses.
Methods: The calcidiol level and BMD data in 65 patients with JIA were assessed (41 girls and 24 boys). All children were divided into 2 groups, depending on the therapy type. Group I consisted of patients who received methotrexate (n = 37), Group II – patients who received the biological DMARDs (n = 28), namely tocilizumab (6 patients), adalimumab (20 patients) and etanercept (2 patients). At the time of the study, 14 children of the Group II were prescribed the biological DMARDs only, while the 12 patients were in the state of clinical remission unlike the 7 patients of Group I. It should be mentioned that the majority of children in the Group II had high disease activity degrees before the start of treatment with biological DMARDs. In order to show the correlation between BMD and disease activity, cJADAS-27 score result for the last 6 months was estimated. The data were processed using Pearson's chi-squared test and Spearman's Rank correlation coefficient.
Results: The study revealed, 60 children (92% of all patients) showed vitamin D insufficiency, that mainly manifested by decreased calcidiol level (from 21 to 29 ng/ml), only 8 children (12%) showed calcidiol level deficiency (<20 ng/ml). A significant difference was found in the BMD results depending on the therapy type ($\chi 2 = 10.05$; $p < 0.01$) using Pearson's chi-squared test. As a result, children who received biological DMARDs, demonstrated significantly better results according to BMD assessment data. A direct association of moderate strength was found (the correlation coefficient (r-Spearman's) is 0,39). The strong negative association (r-Spearman's was -0,72) was observed between BMD assessment data and cJADAS-27 score result, which confirmed our statement – high disease activity affects the bone tissue mineralization. There was a weak negative association between 25(OH)D level and cJADAS-27 score result (r-Spearman's was -0,15).
Conclusion: There was a paucity of vitamin D level in 92% of patients with JRA, in 60% secondary osteopenic syndrome. It was revealed that patients, who receive biological DMARDs in integrated treatment, demonstrate significantly better results according to BMD assessment data. Calcidiol level has a moderate effect on BMD, while BMD strongly depends on disease activity degree according to the Spearman's Rank correlation coefficient.
Disclosure of Interests: None declared
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AB0987 CHOICE AND SWITCH BETWEEN BIOLOGICAL AGENTS IN NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: Over the past few decades, biologic therapy has significantly improved the prognosis in children with JIA. The issue of optimal and personalised biologics prescription and the problem of switching between drugs are relevant questions of modern paediatric rheumatology.

Objectives: The aim of our retrospective observation was to describe trends in the biologics prescription in first and subsequent lines for the treatment of non-systemic JIA.
Methods: We recruited 252 patients with non-systemic JIA, who received medical treatment with biologics at the Department of Paediatric Rheumatology of Sechenov University from January 2015 to December 2017. 18% of them (n=46) had chronic anterior uveitis at the moment of biologic therapy initiation. Eye involvement influenced treatment decisions in these patients, and therefore they were excluded from the analysis. 206 children with non-systemic JIA and without uveitis were included in a study group.
Patients' characteristics: 128 girls and 78 boys (1,6/1). Mean age 13,5 ± 3,8 years, age of disease onset 7,8 ± 4,2 years; mean disease duration before biologic therapy initiation 3,3 ± 3,4 years. JIA categories: 135 (65,5%) had polyarticular RF-, 29 (14,1%) – oligoarticular, 26 (12,6%) – enthesitis-related, 9 (4,4%) – polyarticular RF+, and 7 (3,4%) – psoriatic subtype. At baseline, 204 patients (99,0%) received concomitant therapy with conventional DMARDs: 175 children (85,0%) received Methotrexate (MTX), 3 (1,5%) – combination of MTX and sulfasalazin (SSZ), 9 (4,4%) – SSZ, 9 (4,4%) – leflunomid, 4 (1,9%) – combination of MTX and leflunomid, 4 (1,9%) – cyclosporine A. Two children (1,0%) received biologics as monotherapy.
Results: As a first biologic abatacept was used in 26 patients, adalimumab in 14, tocilizumab in 6 and infliximab in 4. Etanercept was prescribed to 156 patients (75,7%± 3,5) with non-systemic JIA, which was significantly more frequently than other biologics together – 50 (24,3%± 6,2) (t=7,1; P>99,7%). Later 24 children (11,7%) were switched from a first to a second biologic agent. The main reason for switching (n=14) was inefficacy of the first-line drug. When etanercept was ineffective, abatacept (n=3) and adalimumab (n=5) were prescribed as second-line biologics. Etanercept was used as a second-line biologic in 6 children, who were initially treated with other biologic agents. The other reason for switching was the appearance of chronic anterior uveitis (n=7): 6 of these children were initially treated with etanercept, 1 with abatacept; they were switched to adalimumab (n=6) and abatacept (n=1). In 2 cases adverse events were observed – one episode of intrathoracic lymphatic nodes tuberculosis in a patient receiving etanercept, and one allergic reaction (rush, asphyxia) after the infliximab injection. At the end of our observation etanercept was chosen as treatment for 148 (71,8%) patients with non-systemic JIA.
Conclusion: Thus, etanercept was preferred biologic agent in the treatment of non-systemic JIA. The presence of uveitis requires a different treatment approach.

REFERENCES

[1] Kearsley-Fleet, et al. Factors associated with choice of biologic among children with JIA: results from two UK paediatric biologic registers. Rheumatology (Oxford).2016;55:1556-1565

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AB0988 THE ASSOCIATION BETWEEN CLINICAL FEATURES AND ANALYSIS OF MEFV GENE IN 20 JAPANESE PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF)

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Background: FMF is recessive systemic auto inflammatory disorder characterized by recurrent fever, peritonitis, pleuritis, pericarditis and arthritis accompanied with skin rash. Mutation of MEFV gene encoding pyrin resulted in inflammasome activation and the uncontrolled production of IL-1β. Overview of pathogenesis, clinical features and management in Japanese patients with FMF had been reported[1]. However, the differences of clinical features between mutated and non-mutated of MEFV still remain unclear.
Objectives: We have analyzed 20 Japanese patients with FMF to clarify the association between various clinical features and mutation of *MEFV*.
Methods: Genomic DNA were purified from white blood cells in 20 FMF patients, and mutated MEFV has been explored. We have analyzed *MEFV, TNFRSF1A, MVK and NLRP3 genes* in 20 patients with FMF. Therefore, we excluded another autoinflammatory diseases such as TNF receptor-associated syndrome (TRAPS), mevalonate kinase deficiency and cryopyrin-associated periodic syndrome. Clinical symptoms and laboratory data were analyzed around onset time. Each patient had been treated with colchicine (0.5-2 mg).
Results: Characteristics of Patients with FMF (13 female/7 male) were as follows; Onset time were 0-53 years old (17.5 ±12.2), and teen aged patients were most. Frequencies of clinical symptoms such as periodic fever, headache, arthralgia, abdominal pain, chest pain, myalgia, and cervical lymph nodes swelling were 20/20, 7/20, 6/20, 5/20,4/20,2/20 and 1/20, respectively (double symptoms were observed). Patients with FMF were divided to 3 groups as follows; Patients with typical compound heterozygous mutations of MEFV (E148Q/M694I) which indicated exon 10 mutation, were 3 cases (group 1). Patients with atypical mutations, except for mutations in exon 10, such as exon 1 (E84K, L110P), 2 (E148Q), 3 (P369S, R408Q), 5(S503C) and 9(I591M) were 8 cases (group 2). Patients with no mutations in MEFV gene were 9 cases (group 3). There were no significant differences of age at first visiting hospital (FV), onset age of fever attack (O), duration of fever attack (D) and frequency of fever attack (FF) between group 1, group2 and group 3 (FV: 22.3 ± 4.5, 26.8 ± 14.6 years old (yo) and 29.5 ± 8.7 yo, O: 11.6 ± 2.4 yo, 18.5 ± 13.8 yo and 18.5 ± 12.0 D: 3.0 ± 1.4 hrs, 6.3 ± 3.2 hrs, and 8.1 ± 8.5 hrs, FF: 1.2 ± 0.2/month (M), 1.2 ± 1.1/M, and 1.1 ± 0.2/M), respectively. Laboratory examinations such as WBC, CRP and serum amyloid A (SAA) were not significantly different between 3 groups. All of those patients were effective for colchicine treatment except for 2 patients in group 1 because of severe diarrhea and alopecia. Finally, 2 patients in group 1 received canakinumab treatment. Mutations of E148Q were found in 9 patients (45%).
Conclusion: We have examined association between clinical features and mutations of MEFV in 20 Japanese patients, suggesting no positive findings in Japanese patients with FMF. Mutations of E148Q in exon 2 were observed in 16-23 % of normal Japanese patients[1], indicating that E148Q is the polymorphism or accelerating factor.

REFERENCES

[1] K. Migita et al, Familial Mediterranean fever : overview of pathogenesis, clinical features and management. Immunological Medicine 41:2, 55-61, 2018

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DOI: 10.1136/annrheumdis-2019-eular.1327

AB0989 PATIENTS' AND CAREGIVERS' ASSESSMENT OF A DEDICATED OUTPATIENT SERVICE FOR INTRAARTICULAR GLUCOCORTICOID INJECTIONS IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Patients with juvenile idiopathic arthritis (JIA) may require several hospital admissions over the disease course, due to flares or persistently active arthritis, with a negative impact on the patients' and family's daily life. To provide timely intervention and support the patients' and families' quality of life, in 2018 an afternoon outpatient service for intraarticular glucocorticoid injections (IAGI) in JIA has been created at the study center.
Objectives: To evaluate the patients' and caregivers' assessment of the outpatient service for IAGI in JIA; to investigate demographic and clinical features of patients entering the service.
Methods: All consecutive JIA patients and their caregivers seen at the IAGI outpatient service from February 2018 to January 2019 completed a satisfactory questionnaire just after the IAGI procedure. The patient's part included: satisfaction on the overall service and on dedicated personnel (yes/no, why), procedure pain assessment (VAS 0-10, 0=none; 10 worst); whereas the caregiver's part: satisfaction on the overall service (yes/no, why), facilitation of family burden (yes/no, why). Demographic and clinical data of patients, including previous hospitalization for IAGI under general sedation or local anesthesia and geographical provenance, were registered during the questionnaire completion. Descriptive analysis was performed on data. Open answers were synthetized in items.

Results: All of the 46 JIA patients seen at the IAGI outpatient service and their caregivers completed the questionnaire. Patients were mostly females (78%) with early disease onset (median 4.8 years) and positive ANA status (61%). The majority (52%) had persistent oligo-JIA, followed by extended oligo-JIA (26%), RF-negative polyarthritis (17%), ERA and systemic JIA (2%, respectively). The median age at IAGI was 14.7 years (IQ 11.3-19.5). Forthy patients (87%) had previous hospitalization for IAGI, mostly under general sedation (64%). All patients, except a 12 year old girl (0.02%) with uncontrolled needle phobia and previous IAGI in general sedation, (99.98%) and all caregivers (100%) were satisfied with the IAGI outpatient service. In Table 1 reasons of satisfaction are detailed in items. Procedural pain was median rated 3 (IQ 2-6). Most of the families came from the city or province of the study center (76%); 17% from other provinces of the same geographical region; 7% from other regions.

Abstract AB0989 Table 1. Frequency of specific reasons of satisfaction on the IAGI outpatient service, synthesized in items, during the 56 procedures of the study.

Items	Patients, n (%)	Parents, n (%)
Time saving	45 (80)	30 (54)
Stress saving	5 (9)	-
Reduction of absence from school/work	27 (48)	23 (41)
Less negative impact on personal commitments	-	26 (46)
Improvement of family burden organization	-	54 (96)
High quality of dedicated Staff	55 (98)	19 (34)

Figure 1. Proportion of specific sites injected in the 46 JIA patients in the 56 procedures performed at the outpatient dedicated service during the study

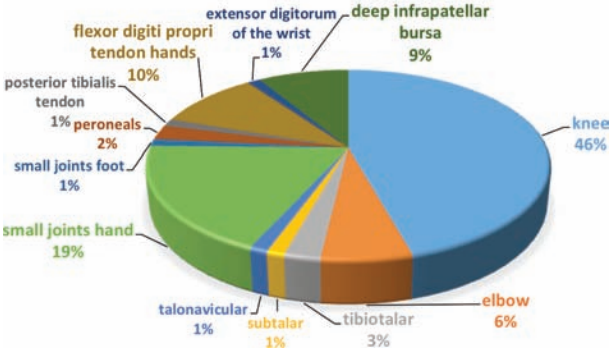


Figure 1

Figure 2. Proportion of procedures with one or multiple injected sites at the IAGI outpatient service during the study

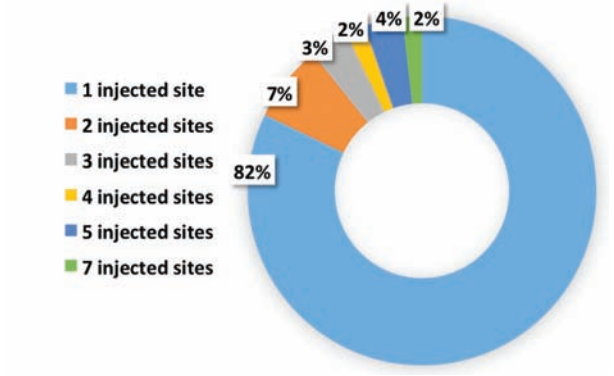


Figure 1

Conclusion: The results outline the afternoon IAGI outpatient service foster the management of flares or persistently active arthritis in JIA patients, particularly at older ages, with high rate of satisfaction and lower impact on patients' and family burden compared to hospital admission and, of note, despite moderate pain rating and multiple site injections. This supports the development of Diagnostic Therapeutic Care Pathways for JIA patients, in the view of improving patients' quality of life and also towards resource optimization.

REFERENCES

[1] Minden K. What are the costs of childhood-onset rheumatic disease? Best Pract Res Clin Rheumatol 2006;20:223-40.
[2] Cavazzana L, Fornili M, Filocamo G, Agostoni C, Auxilia F, Castaldi S. Hospital clinical pathways for children affected by juvenile idiopathic arthritis. Ital J Pediatr 2018;44:139.

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AB0990 FINAL DIAGNOSIS OF THE PATIENTS WITH MUSCULOSKELETAL COMPLAINTS: PRELIMINARY RESULTS OF ONE-YEAR STUDY

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Background: Musculoskeletal (MS) complaints are one of the most common reason for administration to outpatient clinics.
Objectives: The study aimed to summarize the final diagnosis of the patients who suffered from musculoskeletal (MS) findings.
Methods: We prospectively evaluated the patients who were referred with the complaints of MS systems in a year period.
Results: A total of 940 patients with the complaint of musculoskeletal systems were examined. Among them, 577 patients suffered from arthralgia, 234 had arthritis, 39 had low-back pain, 26 had limping, and 64 had other symptoms such as myalgia, heel pain, hip and neck pain. A diagnosis of rheumatic disease was made in 430 of patients, while 510 had non-rheumatic conditions. Final rheumatological disease diagnoses were as follows: juvenile idiopathic arthritis (n=195), familial Mediterranean fever (n=101), reactive arthritis (n=46), acute rheumatic fever (n=39), toxic synovitis (n=17), psoriasis (n=8), Raynaud's phenomenon (n=6), chronic recurrent multifocal osteomyelitis (n=5), vasculitis (n=5), systemic lupus erythematosus (n=4), juvenile dermatomyositis (n=2) and juvenile scleroderma (n=1). Among patients with non-rheumatic conditions, most of them had vitamin D deficiency, infections, mechanic-orthopedic conditions, and growing pains.
Conclusion: Evaluation of a child presenting with MS findings requires a comprehensive, multidisciplinary, and systematic approach. As a busy pediatric rheumatology center, we demonstrated the final diagnosis of referred patients with MS symptoms and only less than half of the patients were diagnosed as a rheumatological condition. Whilst pediatric rheumatology centers are limited in number, our results put forth the need of formulating recommendations for clinicians in order to prevent unnecessary referrals

REFERENCES

[1] Cavkaytar O, Duzova A, Tekşam O, et al. Final diagnosis of children and adolescents with musculoskeletal complaints. Minevra Pediatr. 2017; 69:50-58
[2] Hashkes PJ, Profile of a pediatric rheumatology practice in Israel, Clin Exp Rheumatol. 2003 Jan-Feb;21(1):123-8.

Disclosure of Interests: None declared
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AB0991 PRELIMINARY RESULTS OF REFERRALS TO A TERTIARY PEDIATRIC RHEUMATOLOGY OUTPATIENT CLINIC: A YEAR IN REVIEW

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Background: Previously, the profile of pediatric rheumatology practice was demonstrated from several countries(1,2). However, there is not a

documented data about the pediatric rheumatology clinic population in our country.

Objectives: To evaluate and define the patient population referred to a tertiary pediatric rheumatology outpatient clinic in Turkey

Methods: We prospectively evaluated the patients who were initially referred to our department with suspicion of rheumatic diseases in a year period. These findings cover only ten months results as a preliminary study.

Results: A total of 2317 new patients(1142 male/1175 female) were seen. Among them, most of patients(n=1455) were referred from pediatric outpatient clinics, pediatric emergency units(n=168) and orthopedic surgeons(n:91). Of these 48.9% had a final diagnosis of a rheumatic disease, 37.9% had non-rheumatic conditions, and 13.2% had no definitive diagnosis yet. Most of them were periodic fever syndromes(n=553), juvenile idiopathic arthritis(n=207) and vasculitis(n=160)(Table 1). Other than rheumatological diseases, non-rheumatic conditions were mostly vitamin d deficiency, infections, mechanic-orthopedic conditions, and growing pains (Table 2).

Abstract AB0991 Table 1. Distribution of the patients who were diagnosed with a rheumatic disease

Diseases	n (%)
Periodic fever syndrome	553 (48.9)
• Familial Mediterranean fever	444 (80.2)
• Periodic fever with aphthous stomatitis, pharyngitis, and adenitis	43 (7.8)
• Cryopyrin-associated periodic fever syndromes	2 (0.4)
• Hyper-immunoglobulin D syndrome	1 (0.2)
• Un-defined (genetic analyzes are still in progress)	63 (11.4)
Juvenile idiopathic arthritis (JIA)	207 (18.3)
• Oligoarticular JIA	97 (46.9)
• Enthesitis related arthritis	76 (36,8)
• Polyarticular JIA	15 (7.3)
• Psoriatic arthritis	10 (4.8)
• Systemic JIA	8 (3.8)
• Unclassified	1 (0.4)
Vasculitis	160 (14.2)
• Henoch-Schönlein purpura	127 (79.5)
• Kawasaki disease	16 (10)
• Behçet's disease	11 (6.8)
• Takayasu arteritis	1 (0.6)
• Adenosine deaminase 2 deficiency	1 (0.6)
• Other (drug or infection induced)	4 (2.5)
Reactive arthritis and toxic synovitis	68 (6)
Acute rheumatic fever	46 (4)
Raynoud's phenomena	42 (3.8)
Uveitis	15 (1.3)
Juvenile systemic lupus erythematosus	14 (1.2)
Psoriasis	13 (1.1)
Juvenile scleroderma	6 (0.6)
Others	6 (0.6)

Abstract AB0991 Table 2. Distribution of the patients who had non-rheumatic conditions

Non-rheumatic conditions	n (%)
Vitamin D deficiency	148 (16.8)
Infections	102 (11.6)
Orthopedic disorders	73 (8.3)
Growing pains	57 (6.4)
Dermatological disorders	52 (5.9)
Gastrointestinal disorders	42 (4.8)
Hypermobility	41 (4.7)
Recurrent oral aphthous ulcers	34 (3.9)
Mechanical problems	24 (2.7)
Benign or malign lesions of the bone	11 (1.3)
Hematologic disorders	7 (0.8)
Pain amplification syndrome or fibromyalgia	7 (0.8)
Others	281 (32)

Conclusion: Both in our country and all over the world, there are limited number of pediatric rheumatology centers and experienced pediatric rheumatologists, and it is clearly known that diagnosing a rheumatic disease requires a careful evaluation and a high index of suspicion. As our study implies, a vast majority of referrals are composed of non-rheumatic conditions, so specifying the algorithms before referring the patients to pediatric rheumatology centers will be cost-effective and time for evaluation of patients with rheumatic diseases will be satisfactory.

REFERENCES

[1] Hashkes PJ, Profile of a pediatric rheumatology practice in Israel, Clin Exp Rheumatol. 2003 Jan-Feb;21(1):123-8.

[2] Rosenberg AM, Analysis of a pediatric rheumatology clinic population. J Rheumatol. 1990 Jun;17(6):827-30.

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AB0992 HEPATITIS A VIRUSVACCINATION IN AUTOINFLAMMATORY DISEASES UNDER CANAKINUMAB AND TOCILIZUMAB TREATMENT

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Background: Autoimmune, autoinflammatory mechanism and drugs used in treatment increase the risk of liver disease in patients with chronic rheumatic diseases. Hepatitis A vaccine is a highly effective vaccine that prevents both the formation and spread of clinical hepatitis. The risk of various infections increases with the immunosuppressive effect of both the disease and the drugs. Therefore, vaccination of these diseases is of high importance for the prevention of infectious diseases. Systemic juvenile idiopathic (SJİA) arthritis is a juvenile idiopathic arthritis (JİA) subtype with autoinflammatory pathogenesis. Steroid, methotrexate and anti-interleukin 1 and 6 are used for the SJİA treatment. Anti-interleukin 1 treatments are also used in the treatment of Cryopyrin-associated periodic syndromes (CAPS), which is also characterized with autoinflammatory pathogenesis.

Objectives: The aim of this study was to investigate the efficacy and safety of hepatitis A vaccine in patients with autoinflammatory disease on anti-interleukin 1 and 6 treatment.

Methods: In this study a total of 39 patients with autoinflammatory diseases on anti IL-1 and IL-6 therapy were initially evaluated but 25 of them were excluded due to anti-HAV IgG positivity. At the end, 24 patients with autoinflammatory diseases on anti IL-1, anti IL-6 therapy and 39 healthy participants who were seronegative for hepatitis A received two doses of the hepatitis A vaccine in a 0 and 6 month schedule. Hepatitis A virus (HAV) IgG antibodies were measured before vaccination and one month after last dose of the vaccine. Anti-HAV IgG titer as S/CO;1.1, IU/L was considered positive and protective.

Results: Total 24 patients with autoinflammatory condition (13 females, 11 males) and 39 healthy controls (18 female, 21 male) were included in the study. Among patients with diagnosis of autoinflammatory disease, 19 were SJİA and 5 were CAPS patients. The mean age was 14.1±3.7 and 12.2±3.3 years respectively. Canakinumab was used in 15 (62.5%) and tocilizumab in 9 (37.5%) all patients. Among all SJİA patients, 10 (52.6%) were treated with canakinumab and 9(47.4%) were treated with tocilizumab. All patients with CAPS (n: 5) were using canakinumab. Among SJIA cases, 15(75%) were also using methotrexate and 14(70%) prednisolone. Anti-HAV IgG concentrations were measured one month after the last dose of hepatitis A vaccine. There was statistically significant difference between patients with autoinflammatory condition and healthy controls regarding the anti-HAV IgG titer (mean 5.3±1.5 IU/L) versus (10.5±7 IU/L) $p<0.05$. The rate of anti-HAV IgG seropositivity (cut-off 1.1 IU/L) in autoinflammatory disease (24/24 (100%) was significantly different comparing to healthy controls (33/39, 84.6%) (p=0.04). There was no disease flare of disease nor the adverse event detected in any patients after vaccination.

Conclusion: Anti-HAV IgG seroconversion was detected in patients with autoinflammatory disease on anti-IL1 and anti - IL6 therapy 1 month after the last dose of hepatitis A vaccine. The response to vaccine did not differ between healthy children and patients with autoinflammatory disease under canakinumab and tocilizumab. In this study hepatitis A vaccine was found to be safe in autoinflammatory diseases with canakinumab and tocilizumab treatment.

REFERENCES

[1] Mertoglu S, S Sahin S, Beser OF, et al. Hepatitis A virus vaccination in childhood-onset systemic lupus erythematosus. Lupus: 2018; 1–7

[2] Erguven M, Kaya B, Hamzah OY, et al. Evaluation of immune response to hepatitis A vaccination and vaccine safety in juvenile idiopathic arthritis. J Chin Med Assoc 2011; 74: 205–208.

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AB0993 COMORBIDITIES IN FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is a periodic fever syndrome, characterized by recurrent episodes of fever and serosal inflammation accompanied with high acute phase reactants.The analysis of possible comorbidities is important to understand the impact of these conditions on clinical care and whether they share a common etiological pathway.
Objectives: We aimed to evaluate the comorbidities associated with FMF patients in a large genetically diagnosed cohort.
Methods: We retrospectively evaluated the medical records of FMF patients who were followed up at Department of Pediatric Rheumatology in Hacettepe University between 2000 and 2015. This study was approved by the Research Ethics Committee and was conducted in accordance with the Declaration of Helsinki. The diagnosis of FMF was made according to Tel Hashomer diagnosis criteria for patients who applied prior to April 2009 and to the Turkish FMF pediatric diagnosis criteria after April 2009. The FMF patients who had homozygous or compound heterozygous mutations were included in the study. Comorbidities associated with FMF were divided into three groups; associated with increased inflammation, associated with FMF and incidental.
Results: A total of 1999 patients were enrolled in the study. Of all 1999 FMF patients, 636 were children (31.8%), 1029 were males (51.4%), with a mean age of 31.60±16.01 years. The mean follow up time was 4.50 ±3.99 years (median:3.84 range from 0.21-29.4 years). 880 of 1999 (44%) FMF patients had homozygous MEFV gene mutation, the most common mutation was M694V homozygous. The remaining were compound heterozygous. 656 patients (32.8%) had one or more than one comorbidity associated with FMF. Ankylosing spondylitis was the most common comorbidity associated with increased inflammation while the most common comorbidity in FMF related comorbidities was renal amyloidosis. The frequency of ankylosing spondylitis, henoch schonlein purpura, juvenile idiopathic arthritis, polyarteritis nodosa (PAN), multiple sclerosis (MS) and Behçet's disease were increased in patients with FMF when compared to those in the literature. Systemic lupus erythematosus was observed less frequently in the patients with FMF than in the population. While the increase in the frequency of MS was 3.3 times, the frequency of PAN was increased 110 times.
Conclusion: This study shows that FMF is a hereditary disease associated with significant comorbidity. We also confirm that inflamatory and rheumatic diseases are more common in FMF.
Disclosure of Interests: Ummusen Kaya Akca: None declared, Banu Balci Peynircioglu: None declared, Zehra Serap Arici: None declared, Edibe Avci: None declared, Zulfiye Yeliz Akkaya Ulum: None declared, Engin Yilmaz: None declared, Yelda Bilginer: None declared, Seza Özen Consultant for: Seza Ozen is receiving consultancy fees from Novartis, Speakers bureau: Roche
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AB0994 VITAMIN D STATUS IN CHILDREN WITH JIA DEPENDING ON THE SEASON

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Background: Plenty of studies demonstrated the relationship between vitamin D and Juvenile idiopathic arthritis (JIA) disease activity [1,2].Others reported no relationship between 25(OH)D and disease activity [3,4]. The main source of vitamin D is endogenous vitamin D synthesis induced by sunlight exposure.
Objectives: The aim of this study was to examine the status of vitamin D in children with JIA depending on the peculiarities of the disease and the season.
Methods: 92 patients with JIA were examined. The median age of them was 10,5±1,7 years, from 1,8 to 17,6 years (55 female, 37 male). The serum level of vitamin D was measured through blood test by chemiluminescence method. The relationship between the level of vitamin D and disease activity was analyzed based on juvenile arthritis disease activity score (JADAS27).
Results: The average level of vitamin D was 22,75±1,97ng/ml (corresponded to an insufficient level). It was not found relationship between the frequency of vitamin D deficiency and gender. Vitamin D status changed throughout the year from lowest value 19,52±1,61 ng/ml (in May) till the greatest value 29,62±2,49 ng/ml (in September). Significantly higher level of vitamin D was in September compared to most months (January, p=0,04; February, p=0,04; March, p=0,01; April, p=0,02; May, p=0,01; October, p=0,03; November, p=0,03; December, p=0,01).
The geographical location of Kharkiv (Ukraine) is at 50° latitude. It was proved that UVB radiation above the 33° latitude is not intense enough for the synthesis of vitamin D during the whole year [5].
At the same time there was no significant relationship between the low level of vitamin D in serum and disease activity.
Conclusion: A decrease of vitamin D status were observed throughout the year. Despite the fact that in September was the highest level of vitamin D, the normal concentration was not reached. Seasons should be taken into account, but patients with JIA need supplementation of vitamin D all around the year.

REFERENCES

[1] Szymańska-Kałuża J. Biernacka-ZielińskaM, Stańczyk J, Smolewska E. Vitamin D level in children with juvenile idiopathic arthritis and its correlation with clinical picture of the disease. Reumatologia. 2013;51:271–6. doi: 10.5114/reum.2013.37250.
[2] Çomak E, Doğan ÇS, Uslu-gökçeoğlu A, Akbaş H, Özdem S. Association between vitamin D deficiency and disease activity in juvenile idiopathic arthritis. Turk J Pediatr. 2014;56:626–631.
[3] Dağdeviren-çakır A, Arvas A, Barut K, Gür E, Kasapçopur Ö. Serum vitamin D levels during activation and remission periods of patients with juvenile idiopathic arthritis and familial Mediterranean fever. Turk J Pediatr. 2016;58:125–31. doi: 10.24953/turkjped.2016.02.001.
[4] Bouaddi I, Rostom S, El Badri D, Hassani A, Chkirate B, Abouqal R, et al. Vitamin D concentrations and disease activity in Moroccan children with juvenile idiopathic arthritis. BMC Musculoskelet Disord. 2014;15:115. doi: 10.1186/1471-2474-15-115.
[5] Wacker M, Holick MF. Sunlight and vitamin D: a global perspective for health. Dermatoendocrinol. 2013;5:51–108. doi: 10.4161/derm.24494.

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AB0995 EXPLORING UVEITIS IN EARLY ONSET ANA POSITIVE JIA

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Background: Juvenile idiopathic arthritis (JIA) is the most frequent childhood systemic disease affiliated with uveitis, where uveitis occurs in 10-13% of the patients, frequently causing long lasting consequences when unrecognized, untimely or incorrectly treated.
Objectives: To explore correlations between age, gender, ANA, RF titer in patients with JIA, occurrence of ocular manifestations and its complications. To examine similarities and differences between patients with different subtypes of JIA and uveitis.
Methods: The retrospective study included 31 children treated for JIA and uveitis in the period 2009-2017 at the Department of Paediatrics, UHC Zagreb. The SUN working group classification and grading system were used to evaluate ocular manifestations. Data analysis was executed using R programming language.
Results: We followed 31 patients (81% female) suffering from JIA with ocular manifestations. Median age at JIA onset in girls was 2.5 (1-14) years and in boys 8.6 (1-14.5) years, while girls had median age 4.25 (1-14) years at first ocular manifestation and boys 8.25 (4 -13.5) years. All patients were RF negative. 61% of patients was ANA positive, out of

which 88% had onset of JIA before the age of 6 (all girls). Complete remission of uveitis was achieved in two patients treated with topical corticosteroids, with non-steroid anti-inflammatory medication and methotrexate used in one of the patients. Inactive uveitis was most frequently achieved with a combined therapy which included biologics. A patient suffering from uveitis and JIA was found to be significantly more likely to suffer from oligoarthritic subtype (64.5%, CI 45.4-80.8%, p<0.001). We determined that a positive ANA titer occurred statistically significantly more frequent in females (OR inf., CI 3.18-inf., p=0.001). No significant statistical difference in ANA titer was found between groups of patients who were diagnosed with rheumatologic or ocular disease before and after the age of 6 (OR 1.85, CI 0.12-29.57, p=0.6111) nor between different subtypes of JIA. There was no difference in time passed between the occurrence of rheumatologic and ocular manifestations (median difference =1.75 years, W=131, p=0.2597), nor between ANA titer (OR 0.57, CI 0.09-3.12, p=0.4775) between groups with and without ocular complications. Patients who first presented with ocular manifestations did not have a greater likelihood to develop ocular complications (OR 5.59, CI 0.51-299.98, p=0.175).
Conclusion: A group of female patients suffering from RF negative subtypes of JIA and uveitis, with onset occurring before the age of 6 and positive ANA was prominent. These patients were traditionally classified as different subtypes of JIA, but together, they are best described as "early onset ANA positive JIA", concurring the need for reclassification of JIA. Limited by a small number of patients, this was partly confirmed with significant statistical findings, a recurrent positive ANA titer in females with JIA and uveitis and a more frequent occurrence of uveitis in oligoarthritis. The occurrence of ocular complications was not dependent upon ANA titer, nor upon the time difference between rheumatic and ocular symptoms or their order of appearance.

REFERENCE

[1] Martini A., Ravelli A., Avcin T. el al. Toward New Classification Criteria for Juvenile Idiopathic Arthritis: First Steps, Pediatric Rheumatology International Trials Organization International Consensus. J Rheumatol. 2018;Oct 1.

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AB0996 APPLICATION OF YAMAGUCHI CRITERIA FOR CLASSIFICATION OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: The ILAR criteria require the presence of arthritis to classify a patient as having sJIA. The sJIA patients prior to the onset of arthritis (suspected sJIA) appeared clinically similar to patients fulfilling the ILAR criteria for sJIA.
Objectives: Children with sJIA may have a delayed onset of arthritis and it fail to fulfill the ILAR criteria for sJIA. This study was undertaken to determine whether the Yamaguchi criteria is useful in classification of child with sJIA particularly in pre-arthritic phase of illness.
Methods: Retrospective chart review all patients with a diagnosis of sJIA in Hallym University Medical Center from Feb. 2002 through April 2016.
Results: Total 73 patients were diagnosed by ILAR classification criteria. 38 boys and 35 girls formed the study cohort. There are only 20 patients who are fulfilled of ILAR criteria in sJIA.
Characteristics sJIA (n=20) suspected (n=53) Total (n=73)
Evanescent Rash 19 24
Sore throat 1 5
Lymphadenopathy 2 11
Hepatomegaly 1 11
Splenomegaly 4 10
37 patients were diagnosed with suspected sJIA due to have not an arthritis. 36 patients were presented the arthritis at the onset of sJIA. The Yamaguchi criteria was fulfilled in a higher number of patients in the study (n=44) as compared to the ILAR criteria (n=20). Among the patients with the absence of arthritis (n=37), 25 patients fulfilled the Yamaguchi criteria. (67.5%).
ILAR criteria Yamaguchi criteria
Yamaguchi criteria fulfilled 16 28
Yamaguchi critieria not fulfilled 4 25
Total cohort 20 53
Conclusion: Overall the Yamaguchi criteria was fulfilled in a higher number of patients in the study (60.2%) as compared to the ILAR criteria (27.3%). The failure of ILAR criteria was mainly due to the absence of arthritis. The Yamaguchi criteria is more helpful to diagnosis of sJIA. The Yamaguchi criteria may be useful on early diagnosis and treatment for patient with delayed onset arthritis at onset of disease.

REFERENCE

[1] Kumar S., Junhiraman D.S. and Jajam L. et al: Application of the Yamaguchi criteria for classification of "suspected" systemic juvenile idiopathic arthritis (sJIA). Pediatric Rheumatology 2012, 10:40.

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AB0997 MATCHED CONTROLLED SURVEILLANCE OF TOCILIZUMAB TREATMENT FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS–AN INTERIM ANALYSIS

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Background: Tocilizumab (TOC) is approved for treatment of polyarticular juvenile idiopathic arthritis (poly-JIA). Real world data are limited.
Objectives: Long-term surveillance of patients newly initiating tocilizumab treatment for at least five years compared to a cohort of patients newly initiating a comparator biologic using the BIKER–registry.
Methods: Baseline demographics, clinical characteristics and disease activity parameters as well as efficacy and safety parameters were compared between patients using TOC and a control cohort using alternative biologics. The cohorts were matched for region and date of therapy start. Efficacy outcome variables were JADAS10 and joint counts. Functional status was determined with the Childhood Health Assessment Questionnaire disability-index (CHAQ-DI). Safety assessments were based on adverse events (AE) reports.
Results: Patients starting on TOC had a longer disease duration (5.2y vs. 2.9 y; p= 0.0001) and had TOC significantly more often as second line biologic than patients in the comparator group (80% vs 14%, p< 0.0001). No differences could be observed regarding disease activity parameters (JADAS 10 14.7 +/- 6.4 vs 15.8 +/- 6.0) or disability (CHAQ DI 0.65 +/- 0.63 vs 0.66 +/- 0.66) at baseline. Patients treated with TOC showed a substantial response to treatment with a significant reduction in JADAS 10 from 14.7 to 5.4 (p<0.0001). After 6 months of TOC treatment, 40% of patients had reached JADAS minimal disease activity (MDA), 22% of patients had reached JADAS remission. Tolerability was comparable between the two cohorts, with 31 in the TOC versus 34 patients in the control cohort experiencing AE; serious AE (SAE) were documented in 3 patients in the TOC and one patient in the control cohort. The SAE in the TOC cohort were medication intoxication with suicidal intent, JIA flare, gastrointestinal infection and abdominal pain in 1 patient each. In the control cohort there were JIA flare in 2 patients and gastrointestinal infection in 1 patient. No significant differences regarding infectious AEs, cytopenias or elevated transaminases were observed. No other AE were reported more than once; no deaths occurred.
Conclusion: Comparability of efficacy was limited due to the fact that patients in the TOC cohort had longer disease duration and were more often second line biologic users. Tolerability was comparable in both cohorts. Long-term observation is ongoing.

Abstract AB0997 Table 1. Comparison of TOC patients and matched controls. Baseline parameters and adverse events are listed. *Number and rate of patients are given. # t-test or χ2-test as appropriate

	TOC cohort N=88	Matched controls N=88	P-value#
Baseline Parameters			
Gender female, n (%)	73 (82.9)	67 (76)	0.35
Age onset, mean (SD), years	7.5 (4.6)	7.5 (4.7)	0.89
Disease duration, mean (SD), years	5.2 (4.4)	2.9 (2.8)	**0.0001**
RF neg. poly-JIA, n (%)	57 (64.8)	62 (70.5)	0.52
RF pos. poly-JIA, n (%)	10 (11.4)	10 (11.4)	1.0
Extended Oligo-JIA, n (%)	21(23.9)	16 (18.2)	0.46
Pre-treatment with biologics, n (%)	70 (79.5)	12 (13.6)	**<0.0001**
Active joint count, mean (SD)	7.3 (7.4)	7.4 (5.9)	0.92
CHAQ DI, mean (SD)	0.65 (0.63)	0.66 (0.66)	0.92
CRP, mg/l, mean (SD)	8.9 (18.9)	9.4 (18.6)	0.86
JADAS10, mean (SD)	14.7 (6.4)	15.8 (6.0)	0.24
Adverse Events			
Patients with AE, n (%)*	31 (35.2)	34 (38.6)	0.75
Patients with SAE, n (%)	3 (3.4)	1 (1.1)	0.62
Patients with infectious AE, n (%)	19 (21.6)	20 (22.7)	1.0
Patients with medically important infections, n (%)	1 (1.1)	3 (3.4)	0.62
Patients with increased transaminases, n (%)	4 (4.5)	3 (3.4)	1.0
Patients with hyperbilirubinemia, n (%)	3 (3.4)	-	0.25
Patients with neutro-/leukopenia, n (%)	3 (3.4)	1(1.1)	0.62

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AB0998 SEVERE IGA VASCULITIS: CYCLOPHOSPHAMIDE IN QUESTION

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Background: Cyclophosphamide (CYC) has been a mainstay in the treatment of severe childhood primary systemic vasculitis. Although major organ involvement is rare in IgA vasculitis (IgAV), CYC is among therapeutic options in moderate and severe IgAV nephritis.(1) No specific recommendations are available for cerebral vasculitis of IgAV.
Objectives: To describe disease course and treatment response in 2 patients with severe IgAV with CNS and renal involvement.
Methods: Case reports with disease assessments using Paediatric Vasculitis Activity Score (PVAS).(2)
Results: Both children were Caucasian boys with unremarkable previous history aged 4 (Patient 1) and 8 (Patient 2) years. In both cases the initial typical presentation included purpura and abdominal pain in both, arthritis in Patient 1 and haematuria in Patient 2. After 2 weeks of prednisone therapy for severe gastrointestinal (GIT) symptoms Patient 1 was admitted for right-sided weakness and facial palsy. His brain MRI revealed an ischaemic lesion. His PVAS reached 21/63 for skin, abdominal, renal (haematuria) and CNS systems. When Patient 2 was admitted for abdominal symptoms he developed a focal epileptic paroxysm. His brain MRI was compatible with cerebral vasculitis. His nephritic-nephrotic syndrome prompted renal biopsy showing mesangioproliferative nephritis with IgA deposits. His PVAS was 27/63 for skin, abdominal, renal (hypertension, haematuria, proteinuria) and CNS systems. Both patients received 3 doses of intravenous methylprednisolone 30 mg/kg followed by oral prednisone 1 mg/kg with subsequent tapering and 3 doses of CYC 500mg/m^2(monthly i.v.). At follow-up 3 months after the 1st CYC dose both patients fully recovered neurologically. Patient 2 was on prednisone (0.2 mg/kg) and ACE inhibitor and his urine was negative for the first time, PVAS=0. Patient 1 had been developing significant proteinuria during prednisone withdrawal and his PVAS counted 10/63 for renal disease. Prednisone was re-instituted and ACE inhibitor added while renal biopsy has been pending.
Conclusion: In both cases therapy with corticosteroids and CYC led to the full recovery of CNS disease but did not prevent progression of nephritis in Patient 1. Response of Patient 2 nephritis to CYC appeared satisfactory at 3 months visit but would require confirmation after full prednisone withdrawal. Although generally benign, when IgAV presents with major organ involvement its treatment is challenging. Further research is needed in order to gather better evidence to support treatment recommendations.

REFERENCES

[1] Özen S, et al. Europen consensus-based recommendations for diagnosis and treatment of IgA vasculitis – the SHARE initiative. Rheumatology (Oxford) 2019, in print
[2] Doležalová P, et al. Disease activity assessment in childhood vasculitis: development and preliminary validation of the Paediatric Vasculitis Activity Score (PVAS). Ann Rheum Dis 2013 72(10):1628-33

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AB0999 TREATMENT FOLLOW UP AFTER TRANSITION FROM PAEDIATRIC TO ADULT RHEUMATOLOGY CARE

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Background: Many juvenile onset rheumatic diseases continue to have activity in adulthood. Therefore, a continuous uninterrupted healthcare of these patients is needed.
Objectives: To determine whether and how therapy has changed in patients after transition from paediatric to adult rheumatology service in our medical centre.
Methods: A retrospective single centre study was performed. Patients seen at least once at both paediatric and adult rheumatology outpatient service were enrolled. Data was collected from patients medical records.
Results: A total of 50 patients were included. Most of them were female (82%). Average age at transition was 19,6 years (range 18- 27 years). Mean time of follow up was 44 months (range 2- 119 months). Juvenile idiopathic arthritis (JIA) was the most common juvenile onset chronic rheumatic disease. The medications used either as monotherapy or in combination before transition at last visit at paediatric rheumatology

outpatient unit were nonsteroidal anti-inflammatory drugs (NSAIDs) (14%), corticosteroids (6%), synthetic disease modifying antirheumatic drugs (DMARDs) (18%), biologic DMARDs (2%).
After transition 34% of patients used NSAIDs, 16% corticosteroids, 24% synthetic DMARDs, 8% biologic DMARDs.
Without any medication before and after transition were 66% and 48% of patients, respectively.
After transition 36% of patients had their therapy changed. 30% needed escalation of therapy because their disease was still active or they experienced exacerbation.
Most changes in therapy occurred in the first year after transition.
Conclusion: We confirmed that many patients with juvenile onset rheumatic disease had changes in their therapy after transition, especially escalations of therapy. Most changes occurred in the first year after transition which is a vulnerable period in a young adult life.

REFERENCES

[1] Foster H, et al. EULAR/PReS standards and recommendations for the transitional care of young people with juvenile- onset rheumatic diseases. Ann Rheum Dis 2017;76:639-46.
[2] Jensen PT, et al. Quantitative evaluation of a pediatric rheumatology transition program. Pediatric Rheumatology 2015; 13:17.
[3] Kanakoudi-Tsakalidou F. The art of transitioning pediatric patients with rheumatic diseases to adult rheumatologists. Mediterr J Rheumatol 2016;27(2):55-8.
[4] Luque Ramos A. Transition to adult rheumatology care is necessary to maintain DMARD therapy in young people with juvenile idiopathic arthritis. Semin Arthritis Rheum 2017;47(2):269-75.

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AB1000 THE SURVIVAL OF METHOTREXATE IN JUVENILE IDIOPATHIC ARTHRITISCHILDREN AFTER DURING FIRST BIOLOGIC TREATMENT

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Background: Methotrexate (MTX) is a gold standard for treatment of juvenile idiopathic arthritis (JIA) patients. The main adverse events (AE) related to the MTX are intolerance, increased rate of infections, elevation of the liver enzymes, hematological abnormalities and stomatitis, which required to stop the MTX therapy [1]. In children without remission who tolerated MTX often the second-line treatment is the biologics, which may use alone or in the combination with MTX.
Objectives: The aim of our study was to evaluate the main reasons of MTX discontinuation in JIA children who started first biologic.
Methods: In the study were included 173 non-systemic JIA patients, whom biologic therapy was prescribed firstly to previous MTX treatment. We evaluate the main reasons of MTX discontinuation after the starting of the biologic treatment, duration of MTX treatment (all and after biologic start), achievement the remission, according C. Wallace criteria and time to remission, flare of JIA. We compared two groups: i) patients with biologics with ongoing methotrexate and ii) patients with biologics alone, whom MTX was discontinued or not prescribed.
Results: During the trial MTX discontinued 40 (23.1%) patients: due to intolerance (n=11), other adverse events (AE) (n=10), except intolerance (mainly, frequent infection and transaminitis) and remission of JIA (n=19). Patients with onset age of JIA <4.4 years were in the risk of developing MTX intolerance (LogRank test, p=0.000001), but the younger patients usually developed other AE. Compare of the three subgroups of patients, who discontinued MTX we have not yet found any differences, except the onset age and frequency of remission, which was higher in patients who discontinued MTX due to other AE than due to intolerance.
Conclusion: The main factor, associated with MTX discontinuation in JIA patients, who received first biologic was the disease onset age. Eldest age was related to higher risk of developing the MTX intolerance.

REFERENCES

[1] van Dijkhuizen EH, Pouw JN, Scheuern A, Hügle B, Hardt S, Ganser G, Kümmerle-Deschner JB, Horneff G, Holzinger D, Bulatović Ćalasan M, Wulffraat NM. Methotrexate intolerance in oral and subcutaneous administration in patients with juvenile idiopathic arthritis: a cross-sectional, observational study. Clin Exp Rheumatol. 2016;34(1):148-54.

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Parameter	Still ongoing MTX (n=133)	Intolerance (n=11)	Other AE (n=10)	Remission (n=19)	p	p for 3 groups of MTX discontinuation
Sex, females, n (%)	87 (66)	7 (64)	7 (70)	13 (68)	0.99	0.95
Uveitis, n (%)	27 (20)	1 (9)	0 (0)	5 (26)	0.28	0.12
ANA positivity, n (%)	37/85 (44)	3/8 (38)	2/4 (50)	1/9 (11)	0.29	0.28
Onset age, years	4.8 (2.3-10.2)	10.2 (5.6; 12.7)	2.1 (1.5; 3.2)	7.2 (3.0; 9.2)	0.012	0.005
CRP	1.5 (0.4; 9.2)	3.3 (2.4; 4.7)	0.9 (0.3; 1.7)	3.8 (1.0; 9.1)	0.22	0.06
Active joints, n	3.0 (2.0; 7.0)	2.0 (2.0; 5.0)	2.5 (1.0; 9.0)	3.0 (1.0; 5.0)	0.63	0.97
Time before biologics, years	2.7 (1.1; 6.0)	3.1 (1.4; 4.3)	2.1 (1.5; 7.9)	1.6 (0.9; 2.8)	0.51	0.35
Time before MTX, mo	12.2 (3.6; 37.5)	27.3 (3.6; 43.6)	12.3 (5.1; 30.7)	6.1 (2.0; 19.3)	0.39	0.41
MTX duration, all, mo	65.9 (42.9; 91.3)	27.6 (6.8; 37.6)	30.9 (6.0; 35.5)	25.4 (14.6; 39.5)	0.00001	0.97
MTX duration after biologics, mo	54.2 (32.1; 65.8)	12.3 (7.8; 16.2)	11.3 (5.8; 12.5)	14.7 (5.3; 25.9)	0.00001	0.74
Remission, n (%)	82/130 (63)	7 (64)	9 (90)	19 (100)	0.006	0.015
Remission duration, mo	14.6 (6.3; 36.3)	16.1 (9.6; 45.1)	9.8 (3.9; 20.2)	10.5 (4.8; 39.6)	0.43	0.41
Flare, n (%)	55/129 (43)	5 (46)	0 (0)	7 (37)	0.06	0.04

AB1001 **ARE ANY DIFFERENCES IN THE LOCATION OF BONE LESIONS BETWEEN BONE MALIGNANT TUMORS AND INFLAMMATORY OSTEOPATHIES?**

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Background: Different pediatric bone destructive diseases may have similar radiological findings but have their typical localizations [1].
Objectives: The aim of our study was to differences in the bone lesions location in various pediatric bone destructive diseases.
Methods: Our cohort (n=204) consists of four main subtypes: i) chronic non-bacterial osteomyelitis (CNO, n=91), ii) hematogenous osteomyelitis (HO, n=47); iii) tuberculosis osteomyelitis (TBO, n=33), and iv) malignant bone tumors (MBT, n=33) - osteosarcoma and Ewing's sarcoma.
Results: Al bone destructive diseases have the similar frequency of femur and humerus involvement. MBT patients compare to others had the highest onset age, and higher frequency of pelvic involvent, and comparatively rare the involvement of spine, tibia, foot bones, sternum, the bones of forearm and hand (table).
Conclusion: Patients with bone destructive process with femur, humerus and pelvic involvement have to be under high level of consideration about all type of osteopathy, especially MBT.
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REFERENCES

[1] McCarville MB. The child with bone pain: malignancies and mimickers. Cancer Imaging. 2009;9 Spec No A:S115-21.

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AB1002 **IMMUNOGLOBULIN G4 RELATED DISEASE IN A 10 YEAR-OLD GIRL WITH MULTISYSTEM INVOLVEMENT**

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Background: IgG4-related disease (IgG4RD) is an immune-mediated fibroinflammatory condition characterized by the infiltration of IgG4-carrying plasma cells and storiform fibrosis in most of the tissues. The condition is reported to cause multisystem involvement, however salivary gland is the most commonly affected organ with IgG4-related sialadenitis. Raised IgG4 concentrations in the serum and prominent infiltration by plasmacytes expressing IgG4 in the lacrimal and salivary glands have been confirmed
Objectives: IgG4-RD has mostly been decribed in adult population and therefore generally not well-known among paediatricians. To the best of our knowledge, this patient is one of the rare paediatric cases in literature diagnosed with IgG4-RD. We intended to emphasize that IgG4RD should be kept in mind for differential diagnosis of the patients presenting with enlarged parotid, lacrimal and submandibular glands and sicca symptoms.
Methods: We extracted patient's clinical, laboratory and imaging data from our database and reviewed literature to reveal different manifestations of the IgG4RD.
Results: 10 year-old-girl presented with lacrimal and salivary gland swelling, sicca symptoms and fatigue. Ultrasound scan (USS) neck revealed multiple small lymph nodes and enlargement of both submandibular glands. Salivary glands also appeared bulky and heterogenous with multiple small hypoechoic focci. Appearances were likely to represent sialoadenitis and there was no convincing evidence of malignancy or lymphoma. USS abdomen showed no abnormality. Full blood count, routine biochemistry and urine microscopy were normal. Autoantibodies came back as negative (ANA:Negative, ANCA: negative, Anti-Ro and Anti-La: negative, RF:negative, thyroid autoantibodies:negative). Anti-Cardiolipin IgG was weakly positive on the first visit, however repeated analyses were negative. IgG level was elevated in repeated samples. IgA, IgM and IgE levels remained normal. IgG subgroups were performed which revealed significantly elevated IgG4 levels (21.49 Normal range: 0-1.1) IgG1, IgG2 and IgG3 levels were slightly elevated. The biopsy of salivary gland showed chronic inflammation with IgG4 staining and was suggestive of IgG4 related disorder. The patient was diagnosed with IgG4 related disease and treatment was started with intravenous methylprednisolone followed by Anti-CD20 (Rituximab) therapy and a weaning plan for steroids was given. Mycophenolate mofetil was commenced for the maintenance therapy. Patient has been in remission on maintenance therapy.
Conclusion: IgG4RD is a rare condition which can cause multisystem involvement with the infiltration of IgG4-bearing plasma cells in the tissues. We wanted to emphasize that this condition could also be seen in the paediatric population. Steroids are the cornerstone of the treatment, however Anti-CD20 medication (Rituximab) and steroid sparing agents such as mycophenolate mofetil could be the choice for maintenance therapy.

REFERENCES

[1] IgG4 related Disease: A disease Entity Developed in the 21st Century. Mimori T. Mod Rheumatol. 2019 Jan 24:1-2
[2] Major salivary gland enlargement in IgG4 related disease is associated with multiorgan involvement and higher basal disease activity. Martín-Nares E, Ángeles A, Hernandez-Molina G. Mod Rheumatol. 2019 Jan 24:1-15

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Parameter	NBO	HO	TBO	MBT	P
Onset age, years	7.3 (2.5-10.6)	10.9 (6.2-12.9)	1.7 (1.4-3.4)	12.0 (10.0-16.0)	0.00001
Number of foci, n (%)	3.0 (1.0-6.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	0.0001
Gender, males	47 (51.7)	23 (61.7)	27 (81.8)	20 (60.6)	0.026
Monofocal involvement, n (%)	26 (28.6)	47 (100.0)	33 (100.0)	32 (97.0)	0.000001
Spine involvement, n (%)	29 (31.9)	2 (4.3)	1 (3.0)	1 (3.0)	0.000001
Femur involvement, n (%)	37 (40.7)	7 (14.9)	14 (42.4)	12 (36.4)	0.015
Tibia involvement, n (%)	33 (36.3)	12 (25.5)	6 (18.2)	4 (12.2)	0.029
Fibula involvement, n (%)	12 (13.2)	8 (17.0)	1 (3.0)	2 (6.0)	0.17
Foot involvement, n (%)	36 (39.6)	9 (19.2)	3 (9.1)	0 (0.0)	0.000005
Pelvis involvement, n (%)	17 (18.7)	3 (6.4)	1 (3.0)	6 (18.8)	0.047
Sternum involvement, n (%)	11 (12.1)	0 (0.0)			
Clavicula involvement, n (%)	10 (11.0)	1 (2.1)	0 (0.0)	1 (3.0)	0.045
Ribs involvement, n (%)	6 (6.7)	0 (0.0)	0 (0.0)	3 (9.1)	0.09
Humerus involvement, n (%)	10 (11.0)	4 (8.5)	7 (21.2)	4 (12.1)	0.36
Maxilla involvement, n (%)	2 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0.47
Radius involvement, n (%)	3 (3.3)	0 (0.0)	2 (6.1)	1 (3.0)	0.46
Ulna involvement, n (%)	3 (3.3)	1 (2.1)	2 (6.1)	0 (0.0)	0.52
Hand involvement, n (%)	4 (4.4)	1 (2.1)	0 (0.0)	0 (0.0)	0.37
Scapula involvement, n (%)	1 (1.1)	0 (0.0)	0 (0.0)	1 (3.0)	0.53

AB1003

DELAY IN DIAGNOSIS OF KAWASAKI DISEASE IS THE COMMONEST PROXIMATE REASON FOR DEVELOPMENT OF GIANT CORONARY ARTERY ANEURYSMS- OUR EXPERIENCE AT CHANDIGARH, NORTH INDIA

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Background: Long-term effects of Kawasaki disease (KD) depend primarily on development of coronary artery abnormalities. Giant coronary aneurysm (GCA) is the one of the most severe sequelae in KD. Regression of giant aneurysm is rare. Data from Indian subcontinent is limited. Herein, we review patients with KD who had GCA.
Objectives: To describe the profile of patients with KD who developed GCA from a cohort of KD patients at Advanced Pediatric Centre, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh.
Methods: Records of all children diagnosed to have KD during 1994-2017 were analysed. Out of the 680 patients with KD, clinical details of 17 (2.5%) children with GCA were retrieved.
Results: Diagnosis of GCA was based on coronary artery diameter $\geq$8 mm or $\geq$+10 z score. Six of 17 children (boys 13; girls 4) with GCA had incomplete KD. Diagnosis of KD was made at a mean of 17.2±12.2 days of fever. Eight (47%) children were <1 year. Median age of diagnosis was 18 months (range 1.5 months-12 years). Left anterior descending (LAD) coronary artery was affected in 82% followed by right coronary artery (RCA) in 59%. Multiple GCA >1) were seen in 65% patients. All patients had received first line therapy as IVIg. Median day of IVIg administration was 15.5 days. Twelve had received additional therapy with infliximab. Thromboses developed in 4 (23.5%) and most common coronary affected was LAD. All patients were started on anticoagulation therapy and there were no significant complications related to anticoagulation.
Conclusion: Results of this study suggest that GCA develop more commonly in infants and young children. Delay in diagnosis and consequent administration of IVIg appears to be the commonest proximate cause of development of GCA.

REFERENCES

[1] Fukazawa R, Kobayashi T, Mikami M, et al. Nationwide Survey of Patients With Giant Coronary Aneurysm Secondary to Kawasaki Disease 1999-2010 in Japan. Circ J. 2017;25;82(1):239-246
[2] Gupta A, Singh S, Rohit M, et al. Giant coronary aneurysms in Kawasaki Disease. Indian J Pediatr. 2014;81(4):401-2.
[3] Tsuda E, Hamaoka K,et al. A survey of the 3-decade outcome for patients with giant aneurysms caused by Kawasaki disease. Am Heart J. 2014;167 (2):249-58.

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AB1004

LUPUS LIKE SYNDROME ASSOCIATED WITH INFLIXIMAB TREATMENT IN CHILDHOOD: CASE SERIES OF TWO PATIENT

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Background: Drug-induced lupus (DIL) caused by medication is a form of lupus erythematosus. When the medication is stopped, disease symptoms generally disappears in in days or months. Infliximab is an anti-TNF chimeric antibody widely used and approved for the treatment of many diseases. TNF-α antagonist induced lupus-like syndrome (TAILS) is among the uncommon side effects of infliximab. TAILS is a clinical syndrome with features similar to SLE, but with some differences in laboratory and clinical findings.
Objectives: We have presented our experience with lupus like syndrome emerge after infliximab treatment in two children.
Methods: We evaluated the clinical properties of 2 patients who were monitored with diagnoses of juvenile idiopathic arthritis and uveitis symptoms and developed TAILS after infliximab treatment.
Results: First patient applied to our pediatric rheumatology outpatient clinic with a complaint of swelling in the left knee continuing for 1 month. During the physical examination, we found arthritis on the left knee. During the eye examination, it was discovered that he had bilateral pars planitis. Anti-nuclear antibodies were found positive at 1/320 titration, and anti-dsDNA was negative. Following JIA and accompanying uveitis diagnoses, methylprednisolone and methotrexate treatment was started for the patient. After treatment, the patient whose joint and eye symptoms started to regress, was subjected to lesser dose of methylprednisolone, but the uveitis attack of the patient started to occur again. We added infliximab treatment to its treatment that was resistant to uveitis. At the 6-month of infliximab treatment, there was no uveitis attack observed. During remission, after 6. dose of infliximab treatment, there were complaints of tiredness and polyarthralgia. It was observed that the patient had arthritis in several joints. After the re-studied laboratory tests, there was anti-dsDNA antibody positivity. We thought the patient developed TAILS, and stopped the infliximab treatment. After stopping the treatment, complaints of tiredness and polyarthralgia, as well as arthritis symptoms were improved, and anti-dsDNA antibody levels returned back to normal.
The second, 15-year-old patient was being monitored by pediatric rheumatology outpatient clinic with oligoarticular JIA diagnosis since the age of 1. The patient had also uveitis on the right eye since the age of 6. During methylprednisolone, methotrexate, and azathioprine treatment, there were uveitis attacks that developed at different periods. We started infliximab treatment for uveitis of the patient. After 2. dose of infliximab, the patient started to complain about migraine style headaches that occurred once or twice a week. In redone laboratory tests, ANA (at 1/320 titration), anti-cardiolipin antibody, and anti-beta2 glyco-protein antibody were found positive. There was also low levels of C3 and C4 detected. The infliximab treatment was stopped for the patient who was diagnosed with TAILS. After stopping treatment, the headache complaints regressed, and auto-antibody positivity's turned back to normal.
Conclusion: Although the development of ANA anti-dsDNA antibodies during infliximab therapy is common, TAILS is rare, especially in the pediatric population. In patients develop SLE findings under infliximab infusion, TAILS must be considered and the drug should be discontinued.

REFERENCES

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AB1005

THE UNUSUAL ADVERSE EVENTS INCLUDING MULTIPLE SCLEROSIS DEVELOPED UNDER ABATACEPT THERAPY IN A PATIENT WITH JIA

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Background: Biological therapy in patients with pediatric rheumatology disease may be associated with adverse events up to demyelinative lesion of CNS including multiple sclerosis (MS). It is a rare condition in the pediatric practice.
Objectives: to describe the clinical case of newly diagnosed psoriasis and subsequently developing of multiple sclerosis in pediatric patient revealed in JIA who has been followed-up in Pediatric department of V. A. Nasonova Research Institute of Rheumatology for 8 years.
Methods: Description of clinical case of 13 y.o. male Caucasian pts presented with polyarthritis variant of juvenile idiopathic arthritis (JIA) since 2006.
Results: The first symptoms (at the age of 1,5) were polyarthritis with fever, morning stiffness and inflammatory activity in laboratory tests in chronological link of DTP – re-vaccination. The patient admitted to the regional hospital where JIA was diagnosed and he received traditional therapy including NSAIDS, methotrexate, numerous of intraarticular injections, methylprednisolone pulse therapy with initial response. By the 2012 the child deteriorated with progressive polyarthritis, deformation of wrist joints, bilateral camptodactylia with progressive destruction on X-ray. Under the administration of abatacept therapy in our clinic in 2012 the significant improvement (70-90% ACR response) was achieved. 2 years later the plaque psoriasis developed. The cutaneous changes were impaired by the regular local application of GC so infusions of abatacept were continued. In 4th years of regular therapy (in the age of 13) sudden neurological symptoms such as headache, loss of sensitivity, ataxia, visual field defect appeared. He was admitted to neurological clinic. Multiple sclerosis was diagnosed based on the presenting signs and symptoms supporting cranial MRI – multiple focal areas of demyelination.
Conclusion: We presented a patient with JIA who developed two different immunological related adverse events under long-term abatacept using:

psoriasis "de novo" appeared as a native origin of juvenile arthritis and CNS – multiple sclerosis. This is the first case of developing MS under the abatacept therapy among the 1118 pts (2002-2018) who receive biological therapy in our clinic.

Disclosure of Interests: None declared

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AB1006 THE CLINICAL SPECTRUM OF TWO HETEROZYGOUS MUTATIONS IN THE MVK GENE CONFIRMING HYPERIMMUNOGLOBULIN D SYNDROME

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Background: Autoinflammatory syndromes represent the wide spectrum of rare diseases (associated with genetic disturbances) characterized by the presence of chronic or recurrent systemic inflammation with diverse clinical presentation.

Objectives: We report a case report of child with confirmed two heterozygous mutations in the MVK gene with clinical features associated hyperimmunoglobulin D syndrome.

Results: We present girl with clinical symptoms starting just after birth when in the first days of life she was examined at gastroenterology department in Belgrade due to elevated parameters of inflammation, anemia, direct hyperbilirubinaemia, abdominal bloating and hepatosplenomegalia. Breastfeeding was discontinued due to galactosuria and lactose free diet was advised. Due to the maintenance of hepatomegaly, a detailed hematological, virusological and gastroenterological diagnostic testing was performed. Since liver biopsy has showed portal and lobular hepatitis with cholestasis without fibrosis she was on ursofalk treatment with partial response. At five months of age she started to have recurrent episodes of fever every month for few days with no associated infection, but always followed with digestive symptomatology (abdominal pain and abdominal flatulence) and elevation of inflammatory parameters. Despite antibiotics, episodes of fever continued to repeat twice monthly with accompanying occurrence of hypersalivation, small ulcers in the mouth, skin rash, cervical lymphadenopathy, hepatosplenomegaly, abdominal pain and abdominal bloating with elevated inflammatory markers. One year later she was admitted for the first time at our department and detailed differential diagnostic testing was performed. Clinical spectrum of presenting symptoms with specific phenotypic aspect (hypertelorismus and frontal bossing) were enough to suspect on autoinflammatory disease background (hyper IgD syndrome), but without IgG increase. Genetic testing have revealed presence of two heterozygous mutations (heterozygous variant c.790del p.(Leu264Serfs*2) and heterozygous variant c.1129G>A p.(Val377Ile) in the mevalonate kinase deficiency gene (MVK gene) confirming hyperimmunoglobulin D syndrome. Introduction of nonsteroidal antiinflammatory drug and corticosteroids have led to complete or partial remission during a fever episodes. As fever episodes continued on every two weeks we are about to start with donated fully-humanized protein (canakinumab), highly efficacious in fever episodes resolution by blocking interleukin-1 beta cytokine.

Conclusion: Diverse clinical manifestations of some patients with autoinflammatory diseases can provoke differential diagnostic and treatment dilemmas. Genetic testing is of great importance for establishing the final diagnosis and starting accurate treatment in order to prevent potential serious complications seen in these patients.

Disclosure of Interests: None declared

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AB1007 PREVALENCE AND CHARACTERISTICS OF TEMPOROMANDIBULAR JOINT (TMJ) INVOLVEMENT IN A COHORT OF YOUNG ADULT PATIENTS WITH DIAGNOSIS OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) AND NON-JIA CHRONIC INFLAMMATORY ARTHROPATIES

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Background: TMJ is involved in about 50% of JIA cases, often bilateral and asymptomatic in up to 71% of cases[1]. Adult patients with JIA have been shown to have, compared to healthy individuals, higher rate of dysfunction and anatomical abnormalities[2]. Clinical examination has been shown to have high specificity but low sensitivity in revealing TMJ inflammation[3]. To date MRI is the gold standard to assess TMJ involvement [4]

Objectives: To investigate the prevalence of TMJ involvement in young adults with JIA and young adults with non-JIA inflammatory rheumatisms.

Methods: Patients were recruited prospectively in 2 clinical centers. Inclusion criteria were: patients <35 years diagnosed with JIA who had undergone transition from the pediatric to the adult rheumatologist, and patients diagnosed with non-JIA inflammatory arthropathies. All patients were assessed for joint count, clinical examination for TMJs (tenderness to palpation, swelling, signs of damage such as joint crepitations, lateral deviation, retrognathia and decreased mouth opening), evaluation of global disease activity with composite indexes and underwent MRI of the TMJs to detect inflammation (bone marrow edema, effusion, synovial thickening) or damage (condylar flattening, erosions, disk abnormalities); MRIs with either inflammation or damage were considered pathological. Demographic and clinical characteristics were described using frequency or median and interquartile range (IQR), depending on the distribution of the variable. Differences between groups were analyzed using the Mann-Whitney U test and the χ^2 test when appropriate. The significance was set at p-value $\leq$ 0.05.

Results: 19 patients were included in the JIA group and 8 patients in the non-JIA group. Patients' demographic and disease characteristics were reported in Table 1.

	JIA n 19	**Non-JIA** n 8
Sex F, n (%)	16 (84.2%)	4 (50%)
Age (ys) at diagnosis, median (IQR)	8 (4-12.5)	23 (20.5-25.5)
Current age (ys), median (IQR)	22.5 (20.2 – 27.1)	29.5 (28.1-32.5)
Disease duration (ys), median (IQR)	16 (13-17)	6 (5.8-8.5)
Global disease activity, n (%)		
Remission	12 (63.1%)	4 (50%)
Low	1 (5.3%)	2 (25%)
Moderate	5 (26.3%)	1 (12.5%)
High	1 (5.3%)	1 (12.5%)
TMJs tenderness, n (%)	4 (21.1%)	2 (25%)
TMJs swelling, n (%)	0 (0%)	0 (0%)
TMJ damage, n (%)	13 (68.4%)	4 (50%)

Abstract AB1007 Table 1

MRI results are collected in Table 2.

	JIA TMJs n 38	**Non-JIA** TMJs n 16
Inflammation on MRI, n (%)	14 (36.8%)	5 (31.2%)
Joint damage on MRI, n (%)	26 (68.4%)	11 (68.8%)
Pathological MRI, n (%)	26 (68.4%)	11 (68.8%)
TMJ involvement, n patients (%)		
Monolateral	2 (10.5%)	1 (12.5%)
Bilateral	12 (63.2%)	5 (62.5%)

Abstract AB1007 Table 2

There are no statistically significant differences between groups for the presence of inflammation on MRI, while damage (in particular, disk abnormalities) is more likely in JIA rather than non-JIA patients (p= 0.02). Joint effusion is more likely to be mild rather than moderate/severe in JIA patients (p = 0.04).

Conclusion: It was found that it is more likely to find damage on MRI in patients of both groups rather than inflammation. Both groups show the same frequency of TMJ involvement, suggesting that TMJ involvement must be sought by the adult rheumatologist as it not only affects JIA patients, but also those with adult-onset inflammatory arthropathies.

REFERENCES

[1] Billiau AD, et al. J Rheumatol. 2007 Sep;34(9):1925–33
[2] Arvidsson LZ, et al. Radiology 2010 Jul;256(1):191–200
[3] Koos B, et al. J Rheumatol. 2014 Sep;41(9):1871–7
[4] Hemke R, et al. Eur Radiol. 2014 Feb;24(2):327–34.

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AB1008 AGE DEPENDENT SAFETY AND EFFICACY OF COLCHICINE TREATMENT FOR FAMILIAL MEDITERRANEAN FEVER IN CHILDREN

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Background: Colchicine has been found to be highly effective for the treatment of familial Mediterranean fever (FMF). However, it is FDA-approved only for children older than 4 years owing to the lack of studies in younger children.

Objectives: Our tertiary pediatric rheumatology department routinely uses colchicine even in very young children with FMF. The aim of the study was to evaluate its safety and efficacy in children with FMF <4 years old.

Methods: The departmental database was searched for all children diagnosed with FMF between 2010-2018. Those who started treatment with colchicine before age 4 years were identified and matched by MEFV variant to children who started treatment at age 4-8 years. Drug efficacy was assessed by the improvement in the frequency and duration of attacks. Adverse events were assessed according to the Rheumatology Common Toxicity Criteria ver. 2.0.

Results: The cohort included 89 patients with FMF: 41 first treated before age 4 years, and 48 first treated at age 4-8 years. Rates of complete response to colchicine were 61% in the younger group and 60.4% in the older group. Corresponding rates of partial remission were 24.4% and 29.2% (p=0.77). The most frequent adverse event was diarrhea, with a prevalence of 24.4% in the younger group and22. 9% in the older group (p=0.87). There were no significant between-group differences in other adverse events.

Conclusion: Colchicine is equally effective and safe for use in patients with FMF under 4 years old, with no difference in response from older pediatric patients.

Abstract AB1008 Table 1. Clinical parameters at disease onset in younger and older patients with FMF

Clinical parameter	Age <4 yr (n=41)	Age 4-8 yr (n=48)	P value
Age at symptom onset (yr), mean±SD	1.70 ±0.86	3.45 ±1.40	**<0.001**
Fever*	39 (95.1%)	42 (87.5%)	0.27
Erysipelas-like rash	5 (12.2%)	7 (14.6%)	0.74
Arthralgia	20 (48.8%)	36(75.0%)	**0.011**
Arthritis	6 (14.6%)	7 (14.6%)	0.99
Abdominal pain	27(65.9%)	35 (72.9%)	0.47
Chest pain	5 (12.2%)	8 (16.7%)	0.55
Orchitis	1(2.4%)	1 (2.1%)	1.00
Protracted febrile myalgia	0 (0%)	2 (4.2%)	0.49
Frequency of attacks (per month), median (IQR)	2.0 (1.00-4.00)	1.00 (1.00-2.00)†	**0.041**
Duration of attacks (days), median (IQR)	2.0 (1.5-3.00)‡	2.0 (1.0-3.0)§	0.39
Initial colchicine dose (mg/kg), median (IQR)	0.038 (0.034-0.046)	0.036 (0.031-0.050)	0.60

*Defined as >38°C rectally or >37.5°C orally
†Data available for 45 patients.
‡Data available for 38 patients.
§Data available for 43 patients.
IQR-interquartile range
Values are n(%) unless otherwise indicated.

Abstract AB1008 Table 2. Safety of colchicine in younger and older children with FMF

Variable	Age <4 yr (n=41)	Age 4-8 yr (n=48)	P value
Durable colchicine dose (mg/kg)	0.053 (0.039-0.066)	0.050 (0.040-0.060)	0.33
Primary outcome			
No AEs	30(73.2%) 7(17.1%)	33(68.8%) 5(10.0%)	0.24§
RCTC score,%	4(9.8%)	9(16.0%)	
1	0	1(4.0%)	
2	0	0	
3			
4			
Secondary outcomes			
Lowered dose due to AEs	5(12.2%)	8(16.7%)	0.55
Colchicine failure due to AEs	1(2.4%)	0(0.0%)	0.46
Reported adverse events			
Diarrhea	10(24.4%)	11(22.9%)	0.87
Abdominal pain	3(7.3%)	2(4.2%)	0.65
Anorexia/nausea	0 (0%)	1(2.1%)	1.00
Elevated transaminase levels	4 (11.8%)†	10(23.3%)‡	0.19
Leukopenia	0 (0%)	2 (4.4%)	0.50
Total	14(34%)	19(39.6%)	0.59

AEs – adverse events
* RCTC- Rheumatology Common Toxicity Criteria, version 2.0 for AE severity:0-no, 1– mild, 2 – moderate, 3 – severe, 4 – life-threatening
Values are n (%) unless otherwise indicated.
§ Due to statistical limitations, Statistic analysis (Fisher's exact test) was performed between No AEs & RCTC score 1 and RCTC score 2-4 in the respected age groups.
†Data available for 34 patients.
‡Data available for 43 patients.

Disclosure of Interests: None declared
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AB1009 CLINICAL FEATURES PREDICTIVE OF RENAL AND GASTROINTESTINAL INVOLVEMENT IN PATIENTS WITH HENOCH-SCHÖNLEIN PURPURA

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Background: Henoch-Schönlein purpura (HSP), the most common form of vasculitis in children, predominantly involves the small vessels of the skin, the gastrointestinal (GI) tract, joints, and kidneys. GI involvement is the most severe short-term complication, in contrast, renal disease is the most troublesome long-term complication. Meanwhile, although the disease course of HSP is usually benign in children, recurrence still occurs in a subset of patients. Studies documenting the incidence and predictive factors of recurrent HSP, and biomarkers of the various manifestations of HSP are limited.

Objectives: We aimed to delineate characteristics and biomarkers of HSP patients with GI or renal involvement, and hoped to clarify the incidence and predictive markers of recurrent HSP

Methods: We retrospectively reviewed the medical records of 40 patients admitted in one tertiary medical center in Taipei, Taiwan over a 5-year period with a diagnosis of Henoch-Schönlein purpura. Incidence and risk factors for GI involvement, renal involvement, and recurrent HSP were analyzed. The Mann-Whitney U test and Fisher exact test were utilized for statistical assessment.

Results: From January 1, 2005 to December 31, 2010, 40 HSP patients aged < 18 years were identified. The mean onset age was 8.35±3.3 years. Among them, 45%(18/40) of the patients were male. Ten patients had more than 2 HSP episodes (recurrence rate 25%). Renal involvement was noted in 17.5% (7/40) of the patients, and it was found to occur more frequently in children with later onset age (with renal involvement: 11.43±4.33 years; without renal involvement: 7.73±2.72 years; p=0.03). Recurrent HSP was found to occur more frequently in patients with renal involvement, though without statistical significance (odds ratio: 6; 95% confidence interval; 1.05-34.14; p=0.051). Renal involvement was not associated with GI involvement (p=0.69). GI involvement was noted in 47.5% (19/40) of the patients, and it was found to occur more frequently in patients with higher segmented neutrophil percentage as assessed by complete blood count (with GI involvement: 74.16±13.31%; without GI involvement: 63.14±11.11%; p=0.0056). GI involvement was not associated with relapse of HSP. Fourteen patiens(35%) had arthritis or arthralgia, and it was found to occur more frequently in children with earlier onset age (with arthralgia/arthritis: 7.26±2.55 years; without arthralgia/arthritis: 10.39±3.63 years; p=0.01).

Conclusion: HSP patients with GI involvement had higher segmented neutrophil percentage, consistent with previous studies proposing neutrophil-lymphocyte ratio as a biomarker for GI involvement. Patients with renal involvement had a later age of onset, and the relapse rate was higher in this subpopulation but not statistically significant.

Table 1. Clinical manifestations

	Hb	Nt	Pla	Crea	Brb	AST	ALT	Fe	Tg	Fb	INR
sJIA	10.1	2.736	116930	0.85	2.77	141.8	257.9	9508.7	297.7	237.9	1.24
SLE	7.4	1.403	59983	1.53	9.77	274.3	133.2	5736	433	192.3	2.06

Table 2. Analytical measures. Hb=haemoglobin(g/dl), Nt=neutrophils (10^3/mm^2), Pla=platelets (10^3/mm^2), Cr=creatinine (mg/dl), Brb=bilirubin (mg/dl), AST (UI/L), ALT (UI/L), Fe=ferritine (ng/ml), Tg=triglycerides (mg/dl), Fb=fibrinogen (mg/dl), INR (International Normalizated Ratio).

	Hypotension	Fever	Rash	Adenopathy	Splenomegaly	Hepatomegaly	Haemorrhage
sJIA	1 (10%)	7 (70%)	7 (70%)	3 (30%)	4 (40%)	1 (10%)	0
SLE	0	4 (66.7%)	1 (16.7%)	3 (50%)	5 (83.3%)	4 (66.7%)	3 (50%)

REFERENCES

[1] Hong, S. H., C. J. Kim and E. M. Yang (2018). "Neutrophil-to-lymphocyte ratio to predict gastrointestinal bleeding in Henoch: Schonlein purpura." Pediatr Int 60(9): 791-795.

[2] Lei, W. T., P. L. Tsai, S. H. Chu, Y. H. Kao, C. Y. Lin, L. C. Fang, S. D. Shyur, Y. W. Lin and S. I. Wu (2018). "Incidence and risk factors for recurrent Henoch-Schonlein purpura in children from a 16-year nationwide database." Pediatr Rheumatol Online J **16**(1): 25.

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AB1010 MACROPHAGE ACTIVATION SYNDROME: A CASE SERIES OF 16 PATIENTS

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Background: Macrophage activation syndrome (MAS) is a severe complication of several rheumatologic diseases, being of special relevance systemic lupus erythematosus (SLE) and systemic juvenile idiopathic arthritis (sJIA). Its characterized by an excessive activation of the immune system due to various mechanisms, including hyperactivation of macrophages and a failure in downregulation activity by NK and cytotoxic lymphocytes. There are various criteria for its diagnosis, highlighting secondary lymphohistiocytosis syndrome (HLH) criteria from 2004 and provisional secondary MAS criteria for JIA proposed by Ravelli in 2016[1].
Objectives: To describe a case series of patients with MAS.
Methods: This is a retrospective case series of 16 patients with MAS secondary to systemic autoimmune diseases diagnosed in Ramón y Cajal University Hospital between April 2009 and September 2018.
Results: The baseline pathology was sJIA in 8 patients (2 cases with 2 episodes) and SLE in the other 6 patients. Mean age at diagnosis was 17.44 years for sJIA and 37.5 years for SLE. Mean time from diagnosis of the baseline disease to MAS episode was 11.31 years, with 3 cases being the initial manifestation of their systemic disease. 43.8% of patients were treated with corticosteroids previously to MAS episode, and 50% were being treated with DMARDS/biologic agents (SLE: 3 patients with hydroxychloroquine and 1 patient with mycophenolate and hydroxychloroquine; sJIA: 2 patients with Anakinra, 1 patient with tocilizumab and 1 patient with etanercept). Clinical and analytical characteristics of the patients are presented in table 1 and table 2, respectively. In SLE group, only 2 patients (33.3%) had high anti-DNA titers during the MAS episode, 5 patients (83.3%) had increased C3 consumption and 4 patients (66.6%) had increased C4 consumption. As severe manifestations, 4 SLE patients presented neurologic abnormalities and 3 patients presented external hemorrhage. Infection was confirmed as a trigger in 3 patients with SLE (50%) and 4 patients with JIA (40%). Prednisone at high doses was prescribed to all patients, cyclosporine in 4 patients (66.6%) with SLE and 9 patients (90%) with sJIA. Additionally, anakinra was prescribed in 4 patients (40%) with sJIA. 4 patients (66.6%) with SLE met secondary HLH criteria and 9 patients (90%) with sJIA met secondary MAS criteria. Bone marrow biopsy was performed in all patients with SLE and in 9 patients with sJIA, demonstrating hemophagocytosis in 5 patients (83.3%) with LES and 5 (50%) patients with sJIA. Only 2 patients in the SLE group died because of MAS.

Abstract AB1010 Table 2. Analytical measures. Hb=haemoglobin(g/dl), Nt=neutrophils (10^3/mm^2), Pla=platelets (10^3/mm^2), Cr=creatinine (mg/dl), Brb=bilirubin (mg/dl), AST (UI/L), ALT (UI/L), Fe=ferritine (ng/ml), Tg=triglycerides (mg/dl), Fb=fibrinogen (mg/dl), INR (International Normalizated Ratio).

Conclusion: In our case series rash and fever were more frequent among sJIA patients, the rest of the clinical manifestations were more common in SLE group. Analytical measures were more altered in SLE group except for ferritin and ALT. Mortality was 33.33% in SLE group vs 0% in sJIA group, probably due to early diagnosis and treatment in these patients.

REFERENCES

[1] Ravelli A, Minoia F, Davì S, Horne A, Bovis F, Pistorio A, et al. 2016 Classification Criteria for Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis. Ann Rheum Dis. 2016 Mar 10;75 (3):481–9.

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AB1011 APPLICATION OF AUTOINFLAMMATORY DISEASE DAMAGE INDEX (ADDI) TO AUTOINFLAMMATORY DISEASES IN A TERTIARY REFERRAL HOSPITAL

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Background: Autoinflammatory diseases (AIDs) cause chronic systemic inflammation that can damage multiple organs. Recently, the autoinflammatory disease damage index (ADDI) has been developed and validated in the four most common monogenic AIDs, Cryopyrin-associated Periodic Syndrome (CAPS), Familial Mediterranean Fever (FMF), Mevalonate Kinase Deficiency (MKD) and Tumor Necrosis Factor Receptor-associated Periodic Fever Syndrome (TRAPS). The use of ADDI index could also be of great value in other AIDs.
Objectives: The aim of this study is to assess the application of ADDI in patients with the four most common monogenic diseases and other AIDs. To accomplish this objective a detailed cohort of patients with different AIDs is presented.
Methods: All patients with AIDs followed in the Pediatric Rheumatology Unit comprising the Transitional Care and specialized AIDs outpatient clinics from Hospital Universitari Vall d'Hebron were identified. A cross- sectional, descriptive study was performed applying ADDI by two pediatric rheumatologists (EM, ML). Laboratory test including C-reactive protein (CRP) mg/dl, amyloid protein (AP) mg/L, erythrocyte sedimentation rate (ESR) mm/h and protein/creatinine rate (mg/g Cr) were performed at the moment ADDI was applied. Variables related with disease duration, current treatment and accumulated corticosteroids treatment were assessed. The continuous variables are presented as mean and standard deviation (mean ± SD) and categorical variables are presented by percentages.
Results: A total of 41 patients with AIDs were included, 61% were female, with a median age of 20 ± 11.9 years at inclusion. Disease duration was 11 ± 8.2 years. AIDs included were 11 patients with FMF (26.8%), TRAPS n=4 (9.8%), MKD n=3 (7.3%), CAPS n= 2 (4,9%), Blau

syndrome n= 7 (17.1%), SAVI syndrome n=3 (7.3%), CRMO n=4 (9.8%), PFAPA n=2 (4.9%), APLAID n=1 (2.4%), Stickler syndrome n=1 (2.4%), and 3 unknown AIDs with genetic test negative n=3 (7.3%). Current treatment is variable among patients, 6 (15.8%) are taking disease-modifying antirheumatic drugs (DMARDs), 9 (23.7%) Colchicine, 8 (21.1%) Anakinra, 13 anti-TNF therapy (34.2%), 1 (2.6%) Ruxolitinib and 1 (2.6%) Abatacept. Only 6 patients were receiving corticoids with mean prednisone dose of 7.5 mg/day. The global ADDI mean score was 2.3 ± 2.2. Regarding the eight different items included in the item, musculoskeletal domain shown the highest score with 1.02, followed by the ocular domain with 0.42. The patient with APLAID syndrome had the highest score of 6 followed by BLAU syndrome with 4.71. FMF has the lowest score with 0.83. Laboratory test results were mean ESR 27.2 ± 26.7mm/h, CRP 0.7 ± 1.3 mg/dl, AP 13.9 ± 18.6mg/L. Proteinuria was present in 2 patients with mean 286.5 ± 246.1mg/g. EM and ML applied ADDI in 5-10 minutes average.

Conclusion: ADDI is a feasible index suitable to measure damage in a single patient. Despite it was performed to the four most common AIDs it could be applied to other diseases. In our cohort the mean ADDI index was low and musculoskeletal item has the highest score. This result could be explained by the tight control of the disease and successful targeted therapy. Laboratory tests also support this finding. Nevertheless, some organ systems are not assessed like respiratory, cardiovascular or cutaneous damage, important in some syndromes. Knowing the difficulties of applying an unified index for all diseases, ADDI may be supportive in other AIDs and longitudinal cohorts.

REFERENCES

[1] Ter Haar NM, van Delft ALJ, et al. In silico validation of the Autoinflammatory Disease Damage Index. Ann Rheum Dis. 2018 Nov;77(11):1599-1605.

[2] Ter Haar NM, Annink KV, et al. Development of the autoinflammatory disease damage index (ADDI). Ann Rheum Dis. 2017 May;76(5):821-830.

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AB1012 HENOCH-SCHÖNLEIN PURPURA AND UVEITIS, AN UNUSUAL ASSOCIATION

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Background: Henoch-Schönlein purpura (HSP) is the most common childhood vasculitis characterized by cutaneous palpable purpura predominantly located in the lower limbs, arthralgia/arthritis, renal and bowel involvement. To our knowledge only 4 cases of HSP with ocular involvement have been reported so far.

Objectives: We describe a 6-year-old female patient who presented HSP and panuveitis.

Methods: Describe a case report.

Results: A 6-year-old female, previously in good health, received the diagnosis of HSP for cutaneous palpable purpura on her lower limbs, bilateral ankle arthritis and haematuria. Two weeks later the girl was admitted to our Emergency Department due to monolateral ocular pain with red eye. At ophthalmological assessment there was evidence of anterior uveitis with and edema of the optic disc. Blood tests showed increased values of CRP (1.92 mg/dl) and ESR (69 mm/h) with normal values of complement levels and complete blood count. Urinalysis displayed mild hematuria and proteinuria. Immunoglobulin levels were slightly increased: IgG (1850 mg/dl, n.v. 540-1330 mg/dl), IgA 244 mg/dl (n.v. 50-240 mg/dl) and IgM 72 mg/dl (n. v. 50-180 mg/dl) An extensive infectious work-up for viral, bacterial and parasitic infections was negative. ANA, ANCA, ASCA, LAC, HLA B27 and B51 were all negative. Chest X ray, abdominal ultrasound and echocardiography were negative. A brain MRI with contrast revealed an iris inflammation and excluded CNS involvement. Systemic therapy was started with i.v. methylprednisolone (30mg/kg/d for three consecutive days) and continued with oral prednisone (2 mg/kg/day), with a progressive improvement of the ocular, skin, nephrological and articular involvement. Prednisone was then gradually tapered over 2 months without disease recurrence.

Conclusion: In our literature search we were able to find an association between HSP and uveitis only in two adults and in an 11-year-old child. All these patients showed cutaneous and articular involvement and 3/4 nephrological involvement. Uveitis was observed in the first week of vasculitis onset. Although rare, the presence of ocular involvement can occur during HSP.

REFERENCES

[1] Ozen S, et al. EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. Ann Rheum Dis. 2010 May;69(5):798-806.

[2] Kaur S. et al. Henoch–Schonlein purpura with uveitis: an unusual case and review of literature. Rheumatol Int (2012) 32:4057–4059

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AB1013 CHILDREN IN RISK OF LOW BONE MASS HAVE MORE THAN 2 RISK FACTORS

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Background: Low Bone Mass (LBM)/Infantile Osteoporosis (IOP) require an active evaluation for its diagnosis and prevention. Therefore, its incidence is unknown and could be undertreated. The systematic collection of risk factors associated with LBM/IOP could help identify the population at risk of presenting it

Objectives: To assess the prevalence and number of risk factors (RF) in the pediatric population at risk of developing LBM/IOP. Assess its influence on Bone Mineral Density

Methods: Demographic and clinical data were prospectively collected from patients from 2 to 20 years of age, who had at least one risk factor for LBM/IOP, among them: chronic diseases, treatment with immunosuppressants and/or corticosteroids and insufficient calcium intake. Calcemia, calciuria, and Vitamin D were determined in blood samples, and whole body and lumbar DXA were performed. The calcium intake, the number of previous fractures and other RF were collected

Results: Data were collected from 103 patients, with an average age of 9'8 years, 52'4% women, and 80%Caucasians. Of these, 9 were preschoolers (2-3 years old), 33 schoolchildren (4-9y), 55 teenagers (10-17th) and 6 young people (18-20th)

The most frequent diagnoses were: Malabsorption/Food allergies: 46.6%, JIA: 17.5%, Nephropathies: 17.8%, Hematological diseases: 6.8%, and Vasculitis and connective tissue diseases: 3.9% each

The frequency of RFs can be observed inTable 1

	%
Insufficient calcium intake in the diet	84.5
Association of a second chronic diagnosis	4.9
Hypovitaminosis D in blood (<30 nmol/L)	8.1
Sedentary lifestyle (PAQ test <2)	13.6
History of long bone or vertebral fractures	12.6
24-hour urine hypercalciuria	3.1
Proteinuria $\geq$ 0.20 g/L in 24-hour urine	17
Drugs with osteopening potential (non-corticosteroid immunosuppressants)	31.1
Corticosteroids at the time of inclusion	19.4
Corticosteroids prior to inclusion in the study	18.4

The average dose of current corticoids was 0.21 mg/kg/day of prednisone with a total cumulative average dose of: 7 gr, with an exposure of 1 to 144 months

4'3% of the sample had an isolated RF, 38% had 2 RF, 31% 3, 15% 4, and 12% 5 or more

8'7% of the sample presented a LBM and 4.8% met criteria for Opi for vertebral fractures, 3 of them asymptomatic and discovered by morphometry

In the multiple linear regression analysis: age, latin ethnicity, gender, and hypovitaminosis D were the main RFs related to lumbar BMD. Likewise,

age, latin ethnicity and sedentary lifestyle were the RF related to the BMD of the whole body without head (BMDwbwh)
In lumbar BMD, these 4 FR explained up to 85% of the BMD variation, where the age adds 0'032 per year gained, the male sex subtracts 0'061, the hypovitaminosis D sum 0'077 and the latin ethnicity subtracts 0'070
Up to a 90'8% variation of BMDwbwh is explained by these 3 RF: age adds 0'036 per year gained, sedentary life subtracts 0'084 and latin ethnicity subtracts 0'055.
Conclusion: The child population at risk of LBM/IOp associates 2 or more risk factors
8.7% of children with risk factors have LBM and 4.8% IOP
The RFs related to changes in BMD are: age, sex, sedentary lifestyle and ethnicity. Hypovitaminosis D correlated positively with lumbar BMD
Disclosure of Interests: None declared
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AB1014 USE OF ETANERCEPT BIOSIMILAR IN JIA: PRELIMINARY EXPERIENCE USING REAL WORLD DATA

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Background: Biosimilars are biological medical drugs that are almost an identical copy of an original drug, manufactured by a different company. Since last year regional regulations have imposed a non-medical switch from reference etanercept (ETN) originator to biosimilar (SB4). We compared treatment survival on SB4 to reference etanercept, assessing efficacy and safety data in our cohort of patients with JIA.
Objectives: To review clinical charts of JIA patients, including efficacy and safety of ETN biosimilars after transition from originator. Compliance was also assessed.
Methods: This was a retrospective observational study of patients with JIA who switched from reference etanercept to SB4 starting during 2018 in our Pediatric Reumatology Department. Clinical and demographic data were collected from charts and inserted into a dedicated database. relevant data included: age at disease onset, age at first administration and duration of treatment, if patients had remission of disease with etanercept therapy or if there were any relapses, ESR and CRP values before and after etanercept therapy, ESR and CRP values before switch to SB4 and after SB4 onset, any adverse effects or relapses of disease after biosimilar.
Results: A total of 14 patients (13F, 1M) were identified. Age at diagnosis ranged from 1 to 12 years. Before ETN, all had received methotrexate. ETN was added for disease activity persistence, and induced remission in all cases but one. SB4 treatment duration ranged from 1 to 11 months. After switch to SB4 no disease recurrence was observed. CRP levels, initially elevated in 8/14 cases, normalized during reference etanercept treatment and remained within normal values in all cases during SB4 treatment. ESR median value initially was 40 mm/h (elevated), normalized during reference etanercept treatment (ESR median value 7 mm/h) and remained within normal values (ESR median value 8 mm/h), in all cases during SB4 except one. No side effects were seen, and all families accepted willingly the new prescription.
Conclusion: Our preliminary experience shows that a switch from originator to a biosimilar did not lead to loss of efficacy or new safety signals. Our preliminary results suggest that transitioning from reference etanercept to SB4 is associated with sustained efficacy and no change in the adverse event profile. In conclusion SB4 may provide therapeutically equivalent alternative in pediatric patients with JIA.
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AB1015 CENTRAL NERVOUS SYSTEM VASCULITIS PRECEDING A HENOCH-SCHÖNLEIN PURPURA:. *[1]CASE REPORT OF A UNCOMMON ASSOCIATION edoardo marrani**; *[2]Gabriele Simonini*; *[1]Eleonora Fusco*; *[1]Ilaria Maccora*; *[2]Anna Rosati*; *[2]Rolando Cimaz, Teresa Giani[2 3]*

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Background: Henoch-Schönlein purpura (HSP) is a systemic small vessel vasculitis and represent the most common cause of non-thrombocytopenic purpura in children; vasculitis very rarely can involve internal organs. Central nervous system (CNS) is exceptional.
Objectives: We report the case of a patient with CNS vasculitis who presented HSP 4 months after the stroke and during corticosteroid withdrawal.
Methods: Case report
Results: A 9-year-old Caucasian boy was admitted to our hospital due to sudden onset of severe headache and left faciobrachial hemiparesis associated with facial palsy and dysarthria. Brain MRI revealed hyperintense signal changes in amygdala, putamen, and internal capsule, suggestive of recent cerebral ischemic lesion. Magnetic resonance *angiography showed* asymmetry of internal carotid arteries and middle cerebral artery stenosis, suggestive for a vasculitic-inflammatory nature. He received high dose intravenous methylprednisolone, followed by oral corticosteroids with nearly complete recovery. He was discharged on oral prednisone and low-dose aspirin. In the following months a slow tapering of prednisone was attempted. Four months after the stroke, while receiving prednisolone 0.5 mg/kg/day, he presented with sudden onset of purpuric rash on extensor surfaces of the lower extremities, buttocks and arthralgia of the upper and lower extremities. Painful scrotal swelling and abdominal pain were also present. Serial urinalyses were normal. The patient underwent a second MRI of the brain, which ruled out new-onset inflammatory lesions. Therefore, he received intravenous high dose steroids, with complete remission. Sequencing of adenosine deaminase 2 (ADA2) gene ruled out ADA2 deficiency.
Conclusion: We report a case of CNS vasculitis preceding HSP by several months; intriguingly, HSP developed while the patient was under corticosteroid treatment. The exact nature of the association needs to be clarified, to determine if the association was determined by a common pathogenic mechanism or by chance.

REFERENCES

[1] Akçaboy M, Fidan K, Kandur Y, et al. Cerebral Vasculitis in Henoch-Schönlein Purpura: A Case Report. Arch Rheumatol. 2017. Mar 24;32 (3):264-267.
[2] Bérubé MD, Blais N, Lanthier S. Neurologic manifestations of Henoch-Schönlein purpura. Handb Clin Neurol. 2014;120:1101-11.
[3] Suh JS, Hahn WH, Cho BS, Kim SD, Hong IK. A rare case of cerebral vasculitis in Henoch-Schönlein purpura with emphasis on the diagnostic value of magnetic resonance angiography (MRA) and single-photon emission computed tomography (SPECT) given normal magnetic resonance imaging (MRI). Int J Dermatol. 2010 Jul;49(7):803-5.

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AB1016 OUTCOME OF TRANSITION OF CARE IN YOUNG ADULTS WITH JUVENILE ONSET CHRONIC RHEUMATIC DISEASES

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Background: The transition process of adolescent care from a paediatric to an adult medical environment may affect the compliance with the management plan. Paediatric care is family oriented and relies on significant parental involvement in decision making. On the contrary, adult care is patient-specific and requires autonomy and independent skills.
Objectives: The aim of this study was to evaluate the transition of care at our centre, namely the adherence to clinical appointments, modification of disease activity and patient satisfaction.
Methods: All consecutive patients with juvenile onset of rheumatic chronic diseases followed in a young adult clinic were included. Disease activity was evaluated at the last appointment in the paediatric unit and up to 2 years after transition of care, according to validated scores for each rheumatic disease. Dropout was defined as not attending the clinic for 2 consecutive visits. Global assessment of patient satisfaction with the clinical

appointments before and after transition of care was evaluated in a scale of 0 to 10. Variables were analysed as means, medians and frequencies as appropriate. Univariate analysis was performed with student t-test and Qui-square.

Results: 126 patients were included. Of these, 77 (61.1%) had juvenile idiopathic arthritis (JIA, see table I for list of diagnosis), 78 (61%) were female with a mean age of 23.1±3.2 years and a mean disease duration of 12.7±5.3 years. During the transition of care, 92 patients were treated with conventional disease modifying antirheumatic drugs (73%) and 35 with biologic therapy (27.8%). 69 patients (54.7%) missed at least one clinical appointment with a dropout rate of 9%. This was associated with longer disease duration (15.9 vs 12.3 years, p=0.024). 11 patients (8.7%) had worsened clinical activity: 5 patients with polyarticular JIA with arthritis flare (ΔDAS28 2.14 ± 0.83); 4 patients with oligoarticular JIA with new onset uveitis and 2 patients with juvenile systemic lupus erythematosus with a SLEDAI increase from 5 to 16 points. 4 patients abandoned DMARDs. Regarding patient satisfaction questionnaire, paediatric rheumatology appointments had a median evaluation of 9 (7-10), adult rheumatology appointments of 8 (5-10) and the transition process had an evaluation of 8 (5-10). The majority of patients reported the longer appointment waiting time as the major negative aspect after transition.

Conclusion: In our centre the transition of care had a small percentage of dropping out from the clinic, which was associated with longer disease duration, a slight worsening of disease activity and a 10% decrease in patient satisfaction.

REFERENCES

[1] Foster H, et al. EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases. Annals of the Rheumatic Diseases 2018; 77 960-960 Published Online First: 10 May 2018.

Abstract AB1016 Table 1. Descriptive analyses of diagnosis. SLE - systemic lupus erythematosus.*Mixed connective tissue disease, Systemic sclerosis, Raynaud phenomenon, Overlap syndrome, Osteoporosis, Osteogenesis Imperfecta, Spondyloarthriti

Diagnosis	N (%)
JIA	77 (61.1)
Persistent Oligoarthritis	22 (17.5)
Enthesitis related arthritis	22 (17.5)
Rheumatoid factor - polyarthritis	11 (8.7)
Extended Oligoarthritis	9 (7.1)
Systemic	6 (4.8)
Psoriatic Arthritis	4 (3.2)
Rheumatoid factor + polyarthritis	3 (2.4)
Systemic lupus erythematosus	14 (11.1)
Vasculitis	9 (7.1)
Autoinflammatory syndrome	5 (4)
Dermatomyositis	3 (2.4)
Other diagnosis*	19 (15.1)

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AB1017 WHAT IS THE CURRENT SITUATION OF THE PAEDIATRIC RHEUMATOLOGY TRANSITION CARE UNITS?

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Background: Switching from paediatric rheumatology to the adult rheumatology care units has a negative impact on disease control and adherence in young patients with juvenile idiopathic arthritis (JIA) but also in other chronic diseases. Transitional care services provide the opportunity of being followed-up by an adult rheumatology specialized in juvenile rheumatic diseases.

Objectives: In our study we report the current situation of a rheumatology transition care unit (RTCU).

Methods: We set up an observational and retrospective study of patients followed in our unit between September 2015 and December 2018. We included those patients with a disease beginning at 16 years or younger and those patients who were attended on RTCU for the first time before age 25. Clinical and demographic data and all treatments received by the patients before and after de first visit in the transition care unit were also collected.

Results: 119 patients were attended in our RTCU. After applying the exclusion criteria, 110 patients remained: 78 female/32 male (70.9/29.1%) with a median age of 18.5 [17.9-19.8] years at the first visit. No significant differences in age at the first visit were found between the first (September-2015 to September-2017) and the second stage (October-2017 to December-2018), 18.7 (17.8-20.2) vs. 18.2 (17.9-18.6) years respectively. The most frequent diagnoses are included in the **table 1**.

Of the 75 patients with JIA, 54 were women (72%) with a median age at the disease onset of 6.88 [2.3-12.7] and 21.3% of patients had chronic anterior uveitis. 22 patients (29.3%) presented joint or ocular inflammatory activity or flare at the time of transition first visit but only 1 patient maintained inflammatory activity during the 3 years of follow-up.

A total of 64 patients (85.3%) with JIA diagnosis were under treatment with synthetic DMARD, mostly methotrexate (61) or leflunomide (7). In addition, 43 patients (57.3%) required biological DMARD in the past, and 8 of them (10.7%) required more than one. The most frequently used drugs were: etanercept (ETN) (29 patients) and adalimumab (ADA) (19 patients). Tocilizumab (TCZ) (4), abatacept (1) and infliximab (1) were also used.

Of these patients, at the time of the first visit on RTCU, 24 (32%) had no treatment, 42 patients (56%) had synthetic DMARD and 34 patients (45.3%) had biologic therapy in monotherapy or combined with DMARDs (19 ETN, 12 ADA, and 3 TCZ).

Table 1.

	Patients RTCU (N=110)
Baseline demographic data	
Years at the time of transition, median [IQR]	18.5 [17.9-19.8]
Sex, n (%)	78F/32M (70.9/29.1%)
ANA +, n (%)	42 (38.2)
RF +, n (%)	1 (0.9)
Most frequent disease, n (%)	
- JIA	75 (68.2)
o JIA (Persistent oligoarthritis)	27 (36)
o JIA (Extended oligoarthritis)	11 (14.7)
o JIA (RF - polyarthritis)	18 (24)
o JIA (RF + polyarthritis)	1 (1.3)
o Enthesitis-related arthritis	9 (12)
o Systemic JIA	4 (5.3)
o Psoriatic JIA	5 (6.7)
- Collagenosis	11 (10)
- Others	24 (21.8)
Previous treatment (JIA patients)	
- Oral glucocorticoids, n patients (%)	40 (36.4)
o *Maximum dose (mg/d), mean±SD*	*21.5±11.7*
- Synthetic DMARD, n patients (%)	64 (85.3)
o Methotrexate, n	61
o Leflunomide, n	7
- Biological DMARD, n patients (%)	43 (57.3)
o Etanercept, n	29
o Adalimumab, n	19
o Infliximab, n	1
o Tocilizumab, n	4
o Abatacept, n	1
Treatment at first visit RTCU (JIA patients)	
- Synthetic DMARD, n patients (%)	42 (38.2)
o Methotrexate, n	38
o Leflunomide, n	5
- Biological DMARD, n patients (%)	34 (31)
o Etanercept, n	19
o Adalimumab, n	12
o Infliximab, n	3
RTCU Follow-up (years) mean±SD	2.2±1.1

Conclusion: RTCU assessed mainly patients with JIA and connective tissue diseases. Most patients were inactive during the transfer to the adult unit, but the existence of patients that were still active and/or needed treatment with synthetic and/or biological DMARD reaffirms the need for close control in this period.

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AB1018 CONE BEAM CT IN JUVENILE IDIOPATHIC ARTHRITIS: ROLE OF IMAGING DIAGNOSTIC TOOL WITH MINIMAL X-RAY EXPOSURE IN THE FREQUENT, SUBTLE AND INDOLENT TEMPOROMANDIBULAR JOINT INVOLVEMENT

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Background: The prevalence of the temporomandibular joint (TMJ) involvement in patients affected by juvenile idiopathic arthritis (JIA) ranges from 17% to 87% depending on population. TMJ is frequently the first and unique joint involved in the arthritic process. Unfortunately detection of TMJ arthritis in children with JIA is difficult as early signs and symptoms are missing in most patients. Therefore failure to diagnose and treat TMJ arthritis may have severe consequences on masticatory function, like

pain at biting, chewing and yawning and moreover mandibular growth can be impaired and facial asymmetries may develop. Although Magnetic Resonance Imaging (MRI) is the gold standard to identify TMJ involvement, it is affected by lack of informations about bone components. Cone beam CT (CBCT), an imagine diagnostic tool with minimal xray exposure, thanks to its 3D studies provides an accurate image of anatomical bone alteration.

Objectives: Provide a screening imaging tool for TMJ involvement in JIA patients so TMJ dysfunction can be detected and managed at an early stage.

Methods: Eighteen patients affected by JIA from 2 to 16 yeas of age were included in this prospective study (M/F, 3/15); they were all admitted to a Pediatric Rheumathology and Maxillofacial Surgery Integrated out-patient ambulatory, where an experienced surgeon focused on evaluation of TMJs. All symptomatic patients (uni or bilateral TMJ's pain) performed MRI: anomalous imaging such as increased joint enhancement or intra-articular effusion, was treated with intra-articular corticosteroid injections (IACI). After about two month from intra-articular treatment CBCT was performed in all the enrolled patients (symptomatic and not).

Results: CBCT is a useful tool to improve the diagnostic and therapeutic iter of TMJ involvement in JIA; in fact on one hand it highlights the unsuccessful and palliative role of IACI and on the other hand it can reveal significant impairment of the joint bone components in frequent asymptomatic patients; systemic therapy from the early phase of TMJ involvement could prevents the irreversible modification of the mandibular growth process of undertreated inflammation

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REFERENCES

[1] Farronato G. et all "Craniofacial Growth in Children Affected by Juvenile Idiopathic Arthritis Involving the Temporomandibular Joint: Functional Therapy Management". The Journal of Clinical Pediatric Dentistry 33(4):351–358, 200

[2] Keller H., et all." Is early TMJ involvement in children with juvenile idiopathic arthritis clinically detectable? Clinical examination of the TMJ in comparison with contrast enhanced MRI in patients with juvenile idiopathic arthritis". Pediatric Rheumatology (2015) 13:56

[3] Silvia Caruso, et all. "Temporomandibular Joint Anatomy Assessed by CBCT Images". BioMed Research International.2017:2916953.

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AB1019 THE EFFECT OF TREATMENT REGIMEN ON HEALTH-RELATED QUALITY OF LIFE AND FUNCTIONING IN CHILDREN WITH UVEITIS

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Background: Pediatric non-infectious uveitis can lead to ocular complications and blindness. Complex treatment regimens are often needed and consist of frequent topical treatments (glucocorticoids, mydriatics, glaucoma medications) and systemic immunosuppression.

Objectives: To examine the impact of topical and systemic treatment on health-related quality of life (HRQOL), mental health, and uveitis-related quality of life (QOL) of children with uveitis.

Methods: We reviewed records of 40 children with uveitis (22 JIA-associated uveitis (JIA-U), 18 other uveitis types). Parents and patients completed questionnaires on general QOL (Pediatric Quality of Life Inventory-PedsQL), depression and anxiety (Revised Children's Anxiety and Depression Scale- RCADs), physical functioning (Childhood Health Assessment Questionnaire- CHAQ), and visual function and uveitis-related QOL (Effect of Youngsters' Eyesight on QOL-EYE-Q). We used ANOVA and T-Test to compare treatment groups: 1) topical only vs. systemic only vs. combined topical and systemic treatment; 2) topical vs. no topical treatment.

Results: Of 40 children most were non-Hispanic (98%), Caucasian (80%), and female (70%). Most had bilateral (73%), anterior disease (83%), with minimal disease activity (93% inactive uveitis) and normal vision (100% visual acuity 20/40 or better).

When comparing by treatment group, there were worse EYE-Q Parent and Child uveitis-related QOL scores among the children of the topical treatment only group compared to those on systemic treatment only or the combined treatment group, however they were not statistically significant. (Parent: 1.57 vs. 1.83 vs. 1.6, p=0.13)(Child: 1.68 vs. 1.9 vs. 1.7, p=0.20).

However, when comparing children by use of topical treatment, children on topical treatment had worse EYE-Q total scores compared to those who were not on topical treatment for Parent reports (1.75 vs. 1.93, p=0.01) (Table 1). They also had worse EYE-Q visual function scores (1.82 vs. 1.96, p=0.02) and uveitis-related QOL scores (1.59 vs. 1.83, p=0.04). For child reports, EYE-Q total score and subscores were lower in the topical treatment group but were not statistically significant.

Children with uveitis had similar Parent and Child reports of PedsQL, RCADS, and CHAQ regardless of treatment group.

Table 1. Vision-Specific Outcome Measures by Treatment Regimen in Children with Uveitis

Measure	No Topical Rx (n =11)	Topical Rx (n = 24)	P Value
EYE-Q Parent Total	1.93 (0.07)	1.75 (0.26)	**0.006***
Visual Function	1.96 (0.06)	1.82 (0.26)	**0.021***
Uveitis-related QOL	1.83 (0.19)	1.59 (0.33)	**0.041***
EYE-Q Child Total	1.87 (0.18)	1.71 (0.3)	0.12
Visual Function	1.86 (0.23)	1.73 (0.34)	0.254
Uveitis-related QOL	1.9 (0.19)	1.69 (0.34)	0.07

*p<0.05

Conclusion: The parents of children with uveitis who need topical treatments as part of their therapy regimen report worse uveitis-related QOL. This is likely secondary to parental responsibility for instilling topical therapy. Additionally, visual function scores were also lower in the topical treatment group and could reflect disease activity or use of mydriatics which can affect vision. Other measures including the PedsQL, CHAQ, and RCADS did not appreciate differences based on treatment regimen. Our findings demonstrate the importance of including uveitis-specific disease measures in the assessment of the impact of uveitis. The burden of medication use, specifically eye drops, that can sting, require frequent application, or affect vision, needs further study as this can affect medication adherence and patient outcomes.

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AB1020 DISEASE ACTIVITY INDEX IS ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is considered an independent risk factor for cardiovascular events in association with traditional risk factors. Therefore, it is important to recognize and to identify the specific risk factors for atherosclerotic disease in these patients for the prevention and early treatment of cardiovascular diseases, aiming to provide a better quality of life with long-term morbidity reduction.

Objectives: To determine the prevalence of subclinical atherosclerosis by the measurement of carotid intima-media thickness (CIMT) in patients with childhood-onset systemic lupus erythematosus (cSLE) younger than 21 years. To check for associations between sex, age, race, body mass

index, medications in use, cumulative dose of corticosteroid, traditional and nontraditional risk factors for atherosclerosis, laboratory tests, including plasma cytokine levels, clinical disease activity score (SLE Disease Activity Index - SLEDAI-2K) and cumulative damage index (Cumulative Organ Damage of the SLE International Collaborating Clinics - SLICC/ACR damage index) with CIMT.

Methods: This was a cross-sectional study. Clinical and laboratory data were collected based on chart review and laboratory testing; present clinical and nutritional evaluation were performed during interviews and CIMT was evaluated by ultrasound carried out by an expert radiologist. Associations were estimated using univariate analysis (Fisher and Wilcoxon-Mann-Whitney tests) and multivariate analysis (linear and log binomial regression).

Results: Twenty-eight patients, aged 13.9 ± 3 years, were enrolled in the study. The prevalence of subclinical atherosclerosis was 32.14% (95% CI: 14.8, 49.4) and the mean carotid intima-media thickness (CIMT) was 0.43 ± 0.035 mm. Most common traditional risk factors observed were dyslipidemia in 89,3%; uncontrolled hypertension in 66,6%; overweight or obesity in 32% and poor diet in 78,6%. Nontraditional risk factors observed were duration of disease of 2.4 ± 2.12 years; mean SLEDAI-2K of 7.8 ± 6.0; SLICC/ACR damage index scored $\geq$ 1 in 25%; high levels of ultrasensitive C-reactive protein in 25% and nephritis and neuropsychiatric involvement in 75% and 28.5% of the patients, respectively. Cumulative dose of corticosteroids was 0.48 ± 0.83 mg/kg/day and 60.7% of patients were using immunosuppressive drugs. Univariate analysis showed that uncontrolled hypertension, proteinuria, estimated glomerular filtration rate < 75ml/min/1.73 m^2 and SLEDAI-2K > 5 were associated with subclinical atherosclerosis. The association of CIMT with SLEDAI-2K > 5 was maintained after adjusting for control variables (cumulative corticosteroid dose, duration of disease, levels of cholesterol fractions,hypertension and renal disease).

Conclusion: This study demonstrated that subclinical atherosclerosis was frequently observed in cSLE, mainly in patients with moderate to severe activity disease (SLEDAI-2K greater than 5)

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AB1021 CURRENT COURSE OF JUVENILE ARTHRITIS AND ASSESSMENT OF PHYSICAL DEVELOPMENT OF CHILDREN

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Background: Appointment of modern methods of treatment led to a modification of the course of juvenile idiopathic arthritis (JIA). In Ukraine, the basic preparations were prescribed at JIA since 1984, then the biological registered only in 2011

Objectives: To evaluate the effect of treatment changes on activity indicators, functional disorders and physical development of patients with JIA.

Methods: retrospective analysis of medical records of 67 patients in 2018 and compared with the data of the clinical registry of the department in 1997-2010 (231 children). The diagnosis of JIA is based on the PRINTO criteria, the evaluation of the activity was performed for JADAS27, the JADI functional disturbances, the linear growth delay was estimated for SD, the BMI calculation using the Kettl formula was performed.

Results: The analysis showed that the structure of sub-variants of JIA during the 20 yrs. did not significantly change (10.6% sJIA, 31.9% oJIA, 8.5% RF+pJIA, 29.8% RF-pJIA, 12.8% of the eA). Compared to the historical control group, there was a decrease in the total no. of affected joints, which increased with age (from 4.92±0.7 in 1-6 yrs. to 7.7±1.8 in adolescents now compared with 5.33±0.8 & 14,3±1,02 in the past). The max. no. of injured joints was at RF+pJIA (17.0±2.9), and 38.3% of the limbs were deformed. In recent years, JIA did not show visceral lesions (12.8% in past). JADAS27 was generally low, the max. for sJIA 7,1±5,0, eA 6,7±0,79, and RF-pJIA 6,5±1,04. The greater activity of the disease was observed on average in children aged 10-14 y, 5,8±0,9 (3,3±0,9 at 6-10 & 5.0±1.3 in 1-6 y). The race was the best in oJIA: an acceptable state of symptoms was 27%, a lack of activity of 27%, while with pJIA in 40% - high activity of the disease. Indicator JADAS27 did not significantly depend on serological features: ANA+ 3.9+0.6 (r=-0.06), RF+ 4.5 ±1.0 (r=-0.2), HLA B27 7.2±0.8 (r=0.05), sero-neg. 4.9±0.6 (r=-0.6). In cases of relapse or persistence of active inflammation in patients with $\geq$5 y, JADAS27 was lower when DMARDS was administered before 3 mo. from the debut of the disease (1.8±1.2 vs. 3.5±0.7). In patients with high disease activity, the combination of DMARDS and sCS was worse in the first 6 mo. from the debut (JADAS 6.6±1.2- 5.5±1.7) than DMARDS + ADA (4.0± 2.3 - 0,0) and DMARDS + TOCY (5,2±1,2 - 3,6 ±1,3). The max. JADI were in RF-pJIA (2,0±1,3), in general, JADI increased with age (<6y 0.55±0.3; >10y 1.7±0.9). JADI didn`t depend on the onset age (r=-0.12), disease duration (r=0.16), ANA detection (1.8 ±1.1; r=0.18), the RF (1.2±0.5; r=0.07); HLA B27 0.5±0.3 (r=-0.1); seronegative (1.02±0.4; r=0.07). In patients last years of FI II-III cen. marked with a higher frequency of 35.9%. A smaller proportion of patients with growth retardation was observed than in previous yrs. (10.4 vs 49%). The delay in linear growth with JIA is -1.37±0.06SD now, the degree of growth retardation depends on the duration of the disease (up to 3y -1.2 ±0.1, 8-13y 1.6±0.07) and the variant of the course (the max. growth retardation rate observed in sJIA (78% to -1.2SD; 11% -3SD). The DMARDS+sCS+TZ in high activity JIA and growth retardation was better for normalizing the growth (-0.94±0.04SD after 2y) compared to DMARDS +sCS+ADA (-1.3±0,4). On average, BMI at JIA did not differ from the age norm (17.8±0.7; 48% cases with overweight in last). DMARDS in higher doses was better for the normalization of BMI (MTX 15 mg/m^2 17.1±1.2; 10 mg/m^2 19.2±1.9). The use of ADA in patients with malnutrition resulted in 6 mo. to normalization of the BMI (18,55±1,5) in contrast to the use of ETA (16,52±0,1).

Conclusion: The results obtained show that the overall activity of JIA is significantly reduced today. Improvement of the course of JIA and the degree of functional impairment is explained by the introduction of modern methods of pathogenetic therapy into the clinical practice.

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AB1022 UVEITIS AND ANTI-DFS70 ANTIBODIES IN JUVENIL IDIOPATHIC ARTHRITIS: AN OBSERVATIONAL RETROSPECTIVE STUDY

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in childhood and uveitis is one its major extra-articular manifestation. Children with JIA and a positive antinuclear antibodies (ANA) are known to be at risk to develop severe uveitis, which is usually asymptomatic and can lead to blindness if misdiagnosed. To date the finding of markers of uveitis is still a challenge. In adults anti-DFS70, ANA which have indirect immunofluorescence pattern described as dense fine speckles (DFS pattern) and bind a 70kDa protein in immunoblot or chemioluminescence, are reported to be a marker of otherwise healthy individuals among asymptomatic ANA positive patients (in the absence of anti-Extractable Nuclear Antigens antibodies). The role of anti-DFS70 in children is yet not established even though but it has also been reported with a remarkably high frequency in unhealthy children (localized scleroderma, juvenile dermatomyositis and uveitis); it has also been detected in 2.1% of healthy children.

Objectives: The aim of our observational study is to evaluate the correlation between uveitis and anti-DFS70 antibodies in children with JIA.

Methods: 36 paediatric patients (24 females, 12 males) affected by JIA admitted to the Rheumatology Unit of Verona were evaluated. For each patient the following data were analysed: JIA subtype, ANA positivity, anti-DFS positivity, presence of uveitis diagnosed by a pediatric ophthalmologist.

Results: In our series oligoarticular ANA + JIA was the predominant subtype (25 cases, 70% of total JIA cases), followed by oligoarticular ANA – subtype (6 cases, 16.5% of total), poliarticular ANA – subtype (3 cases, 8% of total) and poliarticular ANA + (2 cases, 5.5% of total).

All 6 patients (16.5%), who developed mono- or bilateral uveitis, were affected by oligoarticular ANA + JIA and presented DFS ANA pattern, confirming the evidence that DFS ANA pattern is the most common pattern associated with uveitis. Only one patient presented anti-ENA antibodies encompassing anti-DFS70 positivity. None of the other five patients presented antibodies anti-DFS70, regardless of the clinical history of uveitis.

Conclusion: DSF ANA pattern remains the most common pattern seen in JIA patients and seems to be an hallmark of uveitis. In our series we found that neither JIA nor the risk of uveitis in JIA correlates with anti-DFS70 isolated positivity. The role of these antibodies in children remains unclear. Further studies are necessary to identify a reliable biomarker to

guide ophthalmologic screening in JIA patients in order to identify children likely to develop uveitis.

REFERENCES

[1] Conrad K, et al. The Clinical Relevance of Anti-DFS70 Autoantibodies. Clinic Rev Allerg Immunol. 2017; 52: 202.
[2] Malyavantham K, et al. Analysis of DFS70 pattern and impact on ANA screening using a novel HEp-2 ELITE/DFS70 knockout substrate. Auto Immun highlights 2017; 8: 3
[3] Mariz, et al. Pattern on the antinuclear antibody-HEp-2 is a critical parameter for discriminating antinuclear antibody-positive healthy individuals and patients with autoimmune rheumatic diseases. Arthritis Rheum 2011; 63: 191.
[4] Mahler M, et al. Anti-DFS70/LEDGF antibodies are more prevalent in healthy individuals compared to patients with systemic autoimmune rheumatic diseases. J Rheumatol 2012; 39: 2104.

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AB1023 PHYSICAL ACTIVITY LEVEL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITISIN THE GERMAN NATIONAL PAEDIATRIC RHEUMATOLOGIC DATABASE: A COMPARISON WITH THE GENERAL POPULATION

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Background: Insights in pathogenesis and the availability of new biologic drugs have created requirements and an increasing interest for encouragement of physical activity (PA) as long-term treatment option in patients with juvenile idiopathic arthritis (JIA). A low level of PA in healthy individuals is related to a higher incidence of overweight and hypertension in later life. This low level of PA might even be more dangerous for children with JIA, as they also have elevated inflammatory parameters, perhaps increasing the risk of future cardiovascular diseases.
Objectives: Since children and adolescents with physical disabilities may have an increased risk for developing a sedentary lifestyle, the objective was to investigate if encouragement of PA in most German medical care settings has led to PA levels in JIA similar to that of healthy counterparts.
Methods: Data from children and adolescents with JIA recorded in the German National Paediatric Rheumatologic Database (NPRD) in the year 2017 were considered for the analyses. In accordance with the methodology used in the general population survey [1], the achievement of the WHO recommendations on PA for health was determined on the basis of self-reported outcomes in individuals aged 3 to 17 years. Patients met the WHO criteria if they stated to be physically active for at least 60 minutes per day.
Results: In 2017, the data from 5.918 patients (mean age 11.2 ± 4.1 years, female 67%, disease duration 4.6 ± 3.7 years, persistent oligoarthritis 42%) were available for evaluation. Almost 35% of patients aged 3 to 17 years met the recommended physical activity level (72% aged 3 to 6; 47% aged 7 to 10; 27% aged 11 to 13; 16% aged 14 to 17). In the general population, 26% fulfilled the WHO recommendations on PA (46% aged 3 to 6; 27% aged 7 to 10; 38% aged 11 to 13; 12% aged 14 to 17). In multivariable analyses, increasing age (OR 1.27; 95%CI: 1.24-1.29), psoriatic arthritis (OR 1.49; 95%CI: 1.06-2.11), overweight (OR 1.33; 95%CI: 1.04-1.71), functional disability (OR 0.83; 95%CI: 0.69-0.98), and worse patient-reported overall well-being (OR 1.10; 95%CI: 1.03-1.17) were associated with non-achieving the recommended PA amount.
Conclusion: Encouraging PA in most German medical care settings and the growing attention of the importance of regular PA for pleasure and health benefits may have led to a similar or even higher amount of PA compared to healthy counterparts. However, since a large proportion does not meet the global recommendations on PA, further research should address especially patients with inactive or minimal active disease who have previously largely refrained from PA. In order to derive adequate strategies, future work is warranted to comprehensively and objectively measure PA behavior in this population.

REFERENCES

[1] Finger JD, et al. Körperliche Aktivität von Kindern und Jugendlichen in Deutschland - Querschnittergebnisse aus KiGGS Welle 2 und Trends. Journal of Health Monitoring 2018;3:24–31.

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AB1024 USE,EFFICACY AND LONG TERM SAFETY OF RITUXIMAB IN PEDIATRIC RHEUMATIC DISEASES: SINGLE CENTER EXPERIENCE FROM NORTH INDIA

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Background: Rituximab(RTX) is used in pediatric rheumatic diseases as an off label indication.There is paucity of data on safety and long term efficacy in countries with high burden of infectious diseases.
Objectives:
- 1. To study the use and safety of RTX in pediatric rheumatic diseases
- 2. To assess the long term efficacy of RTX in pediatric systemic lupus erythematosus(pSLE).

Methods: Data of all children who received RTX was collected on standardized collection forms.This data set was reviewed.Children with pSLE who were given RTX were included for efficacy analysis.Screening, use and safety were evaluated for all patients.
Results: USE: Rituximab was given to 4 children with polyarticular juvenile idiopathic arthritis(PJIA)(4/145=2.7%) and 17 children with pSLE(17/225=7.5%).In children with PJIA, RTX was used as third line treatment, who failed methotrexate and TNF inhibitor therapy. In pSLE, lupus nephritis was the primary indication for RTX(56%), vasculitis(17%), neuropsychiatric SLE and refractory cytopenias(12% each) and aggressive polyarthritis with steroid dependence(5%).
SAFETY: Pre-biologic screen for HIV, Hepatitis B and C and tuberculosis was negative. Total immunoglobulinG level was assayed prior to RTX for all children. CMV PCR was done in 11/17 pSLE patients. No immediate or delayed anaphylaxis was noted. No child had reactivation of herpes zoster.There was no mortality in this cohort.
EFFICACY: Studied in 17 children with pSLE over 21 episodes of RTX(2 received 3 cycles of RTX over 5 years).Median age at RTX use was 13.66 years(range 6.58-21.66 years).Median duration of follow up was 48 months(range 3-120 months).During long term follow up 14 patients didnot have any disease flare. Three(17.6%) flared and required cyclophosphamide/second cycle of RTX. Mean dose of prednisolone prior to RTX was 0.7mg/kg/day while that at 1 year post RTX was 0.065mg/kg/day(p value 0.001) and at 2 years was 0.05mg/kg/day(p value 0.003). Mean SLE disease activity index 2K(SLEDAI-2K) prior to RTX was 16.25 while that at 1 year post RTX was 1.25(p value 0.004), at 2 years was 2(p value 0.004) and at 3 years was 0.85(p value 0.028).

Abstract AB1024 Table 1. Therapy prior and post RTX in patients with pSLE

Medication	Prior to RTX (n=17)	At 1 year (n=14)	At 2 year (n=12)	At 3 year (n=7)
Prednisolone	17(100%)	7(50%)	4(33%)	3(43%)
Hydroxychloroquine	17(100%)	14(100%)	12(100%)	7(100%)
Mycophenolate mofetil	7(41%)	12(86%)	10(83%)	7(100%)
Cyclophosphamide	6(35%)	1(7%)	0(0%)	0(0%)
Methotrexate	2(12%)	1(7%)	1(8%)	0(0%)
Tacrolimus	1(6%)	1(7%)	1(8%)	1(14%)
Cyclosporin	1(6%)	0(0%)	0(0%)	0(0%)
Intravenous immunoglobulin	1(6%)	0(0%)	0(0%)	0(0%)
Azathioprine	0(0%)	1(7%)	1(8%)	0(0%)

Conclusion: We conclude that RTX is efficacious for use in severe spectrum of pSLE and is relatively safe to use even in a developing country like ours with huge infectious disease burden.

REFERENCES

[1] Gladman DD, Ibanez D, Urowitz MB (2002) Systemic lupus erythematosus disease activity index 2000. J Rheumatol 29:288–291

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AB1025 HARMONIZING JAPANESE VERSION OF THE CHILDHOOD HEALTH ASSESSMENT QUESTIONNAIRE (CHAQ) WITH CHAQ

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Background: Juvenile idiopathic arthritis (JIA) is one of the most common rheumatic diseases of childhood. The Childhood Health Assessment Questionnaire (CHAQ) is one of the most widely-used self-report questionnaires to measure patient disability and discomfort (1). The American English version of the CHAQ was previously translated into Japanese, cross-culturally adapted and validated in a cohort of healthy Japanese children and Japanese patients with JIA (2).

Objectives: To revise the Japanese version of the CHAQ (JCAHQ) to meet requirements of clinical international trials that pool data from various centers in different countries which need the same number of questions in each functional area of the CHAQ and to validate the harmonized JCHAQ with JIA patients.

Methods: The questionnaire in the JCHAQ consisted of 36 items, measuring eight functional areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activities, was changed to 30 items of questionnaire as each functional area has same number of questions as the original American English version after a conference among pediatric rheumatologists in US and Japan. The revised version was professionally translated from English to Japanese and reviewed by the rheumatologists for accuracy. Then, it was validated with Japanese JIA patients.

Results: A total of 42 JIA patients were enrolled in the validation: 7 systemic, 30 polyarticular/oligoarticular and 5 enthesis related. Most patients were well controlled and the median disability index (DI) scores was 0.0, however, significant correlation was seen with VAS (Visual Analog Scale) of pain, VAS overall well-being, physician VAS, DAS (Disease Activity Score)28-ESR, and JADAS (Juvenile Arthritis Disease Activity Score)-27. All variables in the questionnaire were shown to be significant ($P<0.001$). In comparison of two groups of disease activity, remission/mild vs. moderate/severe, both DAS28-ESR and JADAS27 showed significant correlation with DI.

Conclusion: The Harmonized JCHAQ was a reliable and valid tool for the functional assessment of children with JIA. It is more suitable for international comparison.

REFERENCES

[1] Singh G, et al. Measurement of health status in children with juvenile rheumatoid arthritis. Arthritis Rheum. 1994;37:1761–9.

[2] Miyamae T, et al. Cross-cultural adaptation and validation of the Japanese version of the Childhood Health Assessment Questionnaire (CHAQ). Mod Rheumatol. 2008;18:336-43. Erratum in: Mod Rheumatol. 2008;18:344.

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AB1026 CLINICAL PRACTICE GUIDANCE FOR THE TRANSITIONAL CARE OF YOUNG PEOPLE WITH JUVENILE-ONSET RHEUMATIC DISORDERS IN JAPAN

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Background: The transition from pediatric to adult healthcare systems has recently received worldwide attention, and it is "the purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented healthcare systems." In Japan, 1,000 patients with childhood-onset chronic disease reach adulthood every year, and many of them survive without serious sequelae or disabilities. The Japan Pediatric Society convened a committee of healthcare transition, summarized their statements, and the working group launched its activities in 2013.

Objectives: A clinical practice guidance for the transitional care of young people with childhood-onset rheumatic disorders has been established in Japan.

Methods: The guidance was designed to support pediatric and non-pediatric rheumatologic health care professionals make decisions about appropriate transitional health care for childhood-onset rheumatic disorders. It offered statements and recommendations addressing key clinical questions regarding transitional care proposed by leading pediatric and non-pediatric rheumatology medical experts and consisted of general core and disease-specific guidance.

Results: Category of clinical questions in the general core guidance involved the following: (1) initial statement of transitional care in rheumatology; (2) management of social life environment and public funded health care; (3) issues specific to adolescence; (4) risk management in childhood-onset rheumatic disorders; and (5) decision-making, privacy and consent, access to information, adherence to care, and preferred methods of communication, including attending to health literacy needs. In the disease-specific guidance, issues focused on each rheumatic disorder such as juvenile idiopathic arthritis, childhood-onset systemic lupus erythematosus, juvenile dermatomyositis, and Sjögren's syndrome were brought up.

Conclusion: The guidance informs policy and strategies to reach optimal outcomes in transitional care for both pediatric and non-pediatric rheumatologists based on available evidence and expert opinion.

REFERENCES

[1] Miyamae T, et al. Survey of attitudes of non-pediatric rheumatologists among councilors of the Japan College of Rheumatology regarding transitional care. Mod Rheumatol. 2017;27(6):1047-1050.

[2] Matsui T, et al. Survey of the awareness of adult rheumatologists regarding transitional care for patients with juvenile idiopathic arthritis in Japan. Mod Rheumatol. 2018;28(6):981-985.

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AB1027 DEVELOPMENT OF A NOVEL DIAGNOSTIC METHOD FOR ATYPICAL AND TREATMENT-REFRACTORY KAWASAKI DISEASE USING NEWLY IDENTIFIED PROTEINS AS BIOMARKERS

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Background: Kawasaki disease (KD) is a representative acute inflammatory disease of the children mainly under 4 years old. There were more than 15,000 onset cases per year in Japan. KD without proper treatment can lead to cardiovascular complications such as coronary artery lesions (CALs). We are still missing about an etiology and the onset mechanism of KD. Therefore, the diagnosis of KD depends on its clinical features. There are also no specific biomarkers for therapy effectiveness in clinical settings. By using proteomic analysis, we found that the serum expression of lipopolysaccharide binding protein (LBP) and leucine rich α 2 -glycoprotein 1(LRG1) at the acute phase of KD were significantly high, compared with that of healthy control or patients with autoimmune disease and these two proteins could diagnose KD efficiently. We also found the usefulness of LBP and LRG1 values as KD-related biomarkers for therapy effectiveness.

Objectives: To develop a novel objective and quick diagnostic method using LBP and LRG1 for "atypical case" that cause a CALs without presenting symptoms of typical KD, or "treatment-refractory case" that is none-effective for immunoglobulin therapy.

Methods: The research strategy is composed of clinical phenotype subgrouping of KD patients using clustering analysis based on clinical features and biomarkers such as LRG1 and LBP. This study contains more than 350 KD patients' data sets including clinical characteristics and laboratory parameters including those of Biomarkers.

Results: According to these results of study, we can objectively diagnose KD without depending on only clinical manifestations.

Conclusion: These two biomarkers may be added in a new KD diagnostic criteria, resulting in quality enhancement of KD treatment and may have the potential of proper clinical examination for KD without consequence of CALs.

REFERENCES

[1] Kimura Y, Yanagimachi M, Mori M, et al. Scientific Reports 2017;7:43732. (PMID:28262744)

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AB1028 MYOCARDITIS IN PEDIATRIC LUPUS: A CLINICAL CONUNDRUM

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Background: Myocarditis in pediatric lupus is uncommon but carry a significant morbidity and mortality.

Objectives: To study the clinical profile and outcome of children with lupus myocarditis

Methods: We reviewed our cohort of children with lupus registered between January 1993 to November 2018. Of the 140 lupus patients that were diagnosed during this time, 3 had myocarditis.

Results: Patient 1 was an 11-year-old girl who presented with fever, rash and generalized body swelling for 3 months. Physical examinations revealed heart rate 148/min, respiratory rate 30/min, and blood pressure (BP) 100/80 mmHg. She had pallor, malar rash, hepatomegaly and gallop rhythm. Investigations are detailed in the table. She received intravenous immunoglobulin and initiated on pulse methylprednisolone and followed by pulse intravenous cyclophosphamide. She was discharged on oral prednisolone and subsequently tapered. Patient 2 was a 9-year-old girl presented with fever and rash for 3 months with lethargy for 1 day. She had pallor, malar rash, hepatomegaly. Physical examinations revealed heart rate 132/min, respiratory rate 32/min, feeble peripheral pulses and BP 100/80 mmHg. She received intravenous cyclophosphamide monthly for 6 months along with oral prednisolone in tapering dose. Patient 3 was a 12-year-old girl, who was known to have SLE for 2 months, presented with fever, malar rash, and photosensitivity. She had stopped taking steroids for 2 weeks. On examination, she had heart rate 122/min, respiratory rate 28/min and BP 100/72 mmHg. She had pallor, alopecia, oral ulcers, malar rash, gallop rhythm and tender hepatomegaly. She was given pulse methylprednisolone and furosemide therapy followed by oral prednisolone in gradually tapering dose.

Conclusion: Myocarditis in lupus is uncommon but carries a significant morbidities. The presence of global hypokinesia with a low ejection fraction on two dimensional echocardiography (2DE) is a strong pointer towards the diagnosis. Immunosuppressant drugs with supportive therapy remain the preferred treatment. Early diagnosis and prompt treatment may be very rewarding.

REFERENCES

[1] Chang JC, Xiao R, Mercer-Rosa L, Knight AM, Weiss PF. Child-onset systemic lupus erythematosus is associated with a higher incidence of myopericardial manifestations compared to adult-onset disease. Lupus. 2018 Nov;27(13):2146–54.

Table: Laboratory investigations:

Investigation	Case 1	Case 2	Case 3
Haemoglobin (g/L)	94g/L	92 g/L	80 g/L
White cell counts	6.7 10^9/L	7.2 10^9/L	6.5 10^9/L
Lymphocyte count	1.15x 10^9/L	1.91 X 10^9/L	1.65X10^9/L
Platelets	130×10^9/L	150 ×10^9/L	220 x 10^9/L
Urine routine Urine protein (mg/m^2/hour)	No RBC, No albumin	No RBC, No albumin	No RBC, No albumin
C3 (Normal 50-150 mg/dL)	27 mg/dl	28 mg/dL	31 mg/dl
C4 (Normal 20-50 mg/dL)	4 mg/dl	3 mg/dL	10 mg/dl
ANA	4+ diffuse	3 + diffuse	3+ diffuse
Anti dsDNA (N: <25 IU/mL)	59	583	112
Antiphospholipid antibodies: a) Lupus anticoagulant b) Anticardiolipin antibody (IgG and IgM) c) Anti ß2 Glycoprotein -1 antibody (IgG & IgM)	Positive Negative Negative	Negative Negative Negative	Negative Negative Negative
2Dimensional Echocardiography	Mild pericardial effusion, dilated left ventricle, ejection fraction (EF) 30%	Mild pericardial effusion, EF 25%	Mild pericardial effusion, moderate mitral regurgitation, mild tricuspid regurgitation, global hypokinesia, EF 56%

Disclosure of Interests: None declared

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AB1029 FIBRODYSPLASIA OSSIFICANS PROGRESSIVA: A CHALLENGE TO DIAGNOSE AND TO TREAT

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Background: Fibrodysplasia ossificans progressiva (FOP) caused by mutations in the ACVR1 gene, which codes for activin receptor IA, a type I receptor of the bone morphogenetic protein (BMP) pathway. FOP is a very rare disease which usually begins in the first decade of life and characterized by congenital bilateral hallux valgus in combination with progressive heterotopic ossification in specific anatomical patterns preceded by inflammatory responses and soft tissue swelling.
Objectives: Our objective is to expand the differential diagnosis of recurrent swelling without trauma by presenting a case of Infant suffering from recurrent swellings and diagnosed to have FOP.
Methods: We used standard laboratory assessment and ultrasound to exclude other diseases. To confirm the diagnosis we used next generation sequencing to identify ACVR1 variants.
Results: A full-term male infant from non-consanguine parents delivered spontaneously after uncomplicated pregnancy. Initially bilateral hallux valgus, as well as limited motility in the metacarpophalangeal joint of D1 of the right hand was noted. At the age of 1.5 months, a severe swelling appeared on the left head without trauma. The further investigation showed no signs of retinal hemorrhage or intracranial injury. The swelling resolved spontaneously, but he readmitted to the hospital due to swellings of different localization in the head area. At the beginning a child abuse had been discussed with the family, although there was no concrete evidence.
At the age of 7 months he presented to our center with renewed swelling in the area of the forehead. Due to the characteristic symptom constellation, a genetic analysis was performed on ACVR1, which confirmed a de novo mutation c.617G> A, p.R206H.
We started a combined therapy with Montelukast 4 mg oral daily for specific inhibition of mast cell activation, Neridronat (Bisphosphonate) 2 mg/kg as i.v. every 3 months for the modification of secondary ossification. As well as Prednisolone for 3 days 20 mg/kg i.v. in the flare up.
At the beginning there were a significant reduction in the frequency and severity of new swellings, however after 9 Months he had frequent flare up with limitation of head movement. At that point we decided to start an off-label therapy with Imatinib. He responded well to the current therapy and the medication is well tolerated.
Conclusion: FOP is a very rare and important differential diagnosis of child abuse. With the characteristic symptom of congenital bilateral hallux valgus and unclear swellings, the diagnosis can be genetically secured. An early specific treatment concept for the avoidance of trauma as well as drug-based anti-inflammatory therapy are crucial for the clinical course and subsequent impairment of the patient. New targeted treatment approaches offer a promising option for the long-term improvement of disease progression and associated quality of life like Imatinib, which is a tyrosine kinase inhibitor used in the treatment of chronic myeloid leukemia in adult and children. A recent article showed that it decreased the flare up in 6 out of 7 patients with FOP.

REFERENCES

[1] Pignolo RJ, Shore EM, Kaplan FS. Fibrodysplasia ossificans progressiva: clinical and genetic aspects. Orphanet J Rare Dis. 2011;6:80.
[2] Hatsell SJ, Idone V, Wolken DM, Huang L, Kim HJ, Wang L, et al. ACVR1R206H receptor mutation causes fibrodysplasia ossificans progressiva by imparting responsiveness to activin A. Sci Transl Med. 2015;7 (303):303ra137.
[3] Luo Y, Alsamarah A, Zhang K, Hao J. Development of New Therapeutic Agents for Fibrodysplasia Ossificans Progressiva. Curr Mol Med. 2016;16 (1):4-11.
[4] Kaplan FS, Andolina JR, Adamson PC, Teachey DT, Finklestein JZ, Ebb DH, Whitehead B, Jacobs B, Siegel DM, Keen R, Hsiao E, Pignolo RJ. Early clinical observations on the use of imatinib mesylate in FOP: A report of seven cases: Bone. 2018 Apr;109:276-280.

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AB1030 NEUROPSYCHIATRIC MANIFESTATIONS IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: RETROSPECTIVE STUDY IN ONE SINGLE CENTER

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Background: Systemic lupus erythematosus is a complex autoimmune disorder characterized by multisystem involvement, including the nervous system, which elevate damage and mortality. The investigation of neuropsychiatric involvement in childhood-onset SLE (cSLE) is important in real clinical practice to improve the prognosis.
Objectives: The aim of this study was to assess neuropsychiatric manifestations (NM) in cSLE in one single center.
Methods: The study included all pts with cSLE who undergoing in-patient treatment in our center from 1992 to 2017 yy. Diagnosis of SLE was reviewed based on 2012 SLICC criteria. Data including sex, age at the time of onset, age at the time of diagnosis, physical examination, laboratory review, and neuropsychiatric inventory were extracted from our database. Classification of NM of cSLE was according to the 1999 American College of Rheumatology (ACR) neuropsychiatric manifestations of SLE case definitions.
Results: We included 218 consecutive pts with cSLE, of which 45 pts (20.6%) had neuropsychiatric involvement at the time of diagnosis (Tab.1).

Abstract AB1030 Table 1. Clinical and demographic characteristics of patients.

Characteristics	Patients without NM of cSLE (173)	Patients with NM of cSLE (45)
Girls/boys (girls to boys ratio)	154/19 (8.1:1)	36/9 (4:1)
The average age at onset, years	12.8±3.52	13.0±2.84
The median of disease duration at the time of cSLE verification, months	6.0 (2.0;15.0)	5.0 (3.0;11.0)
The average of disease activity by SLEDAI at the time of cSLE	12.9±6.5	22.0±9.5

Neurolupus was significantly more frequently detected during the acute development of SLE (46.7% of patients, p = 0.003). Among immunological disorders, patients with NM often had antibodies to RNP (p = 0.073) in the absence of any differences in other immunological parameters. Of the clinical manifestations in patients with NM, chronic skin lesions were recorded more often (p = 0.076), while arthritis was detected relatively less frequently (p = 0.028). Serositis and nephritis were diagnosed significantly more often in the group of patients with NM (p = 0.003, 0.003, respectively). Of the hematological disorders, NM was relatively more frequently accompanied by leuco/lymphopenia (p = 0.087) and thrombocytopenia (p = 0.077). In general, the group of patients with NM was characterized by a higher degree of multiorgan involvment (the number of clinical manifestations was on average 5.6 and 3.7, respectively, p <0.0001), but both groups were comparable for number of immunological disorders (p = 0.49).
As early signs of NM, all patients had mood disorders and impaired school adaptation. In the structure of NM, central nervous system involvement prevailed (89%). 15 pts (33.3%) had experienced more than one NM. Headaches, cognitive dysfunction and cerebrovascular disease were the most common (28.9%, 28.9% and 24.4%, respectively). Other NM included distal polyneuropathy - 20%, episyndrom – 15.5%, acute confusional state – 11.1%, anxiety disorder – 11.1%, psychosis – 8.9%, paresis – 6.7%, chorea – 4.4%.
Conclusion: Acute onset, multiorgan lesions, mood disorders, impairment of school adaptation in a patient with suspected SLE should prompt investigations into diagnosis of the primary nervous system involvement. Patients with neuropsychiatric disorders require earlier complex aggressive therapy due to greater disease activity and poor prognosis.

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AB1031 ETANERCEPT-INDUCED LUPUS-LIKE SYNDROME IN THE BOY WITH IDIOPATHIC DERMATOMYOSITIS OR DELAYED MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS?

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Background: Treatment of juvenile onset rheumatic diseases (RD) is an ongoing problem because of the more aggressive disease course and more various clinical manifestations than adult-onset RD. Since the main clinical symptoms may overlap between well-known various RD, in some cases the path to diagnosis and the search for optimal therapy takes longer, especially in patients of pre-adolescence and adolescence.
Objectives: We described a rare case of one boy with RD who presented initially with severe dermatomyositis with sequential evolution to systemic lupus erythematosus.
Methods: Case report.
Results: A 8 yo male patient with normal physical, psychosocial and cognitive development experienced muscle weakness, periorbital erythema, Gottron symptom, dysphagia in September 2015 y, which developed after insolation. When he was admitted to hospital, increased levels of muscle-derived enzymes and positivity of ANA 1:640 were found. He was diagnosed as having juvenile dermatomyositis and was treated with prednisolone (Pr) for 3 years (IV courses repeated and per os constantly, max dose 1.5 mg/kg/day, min dose 0.5 mg/g/day), IVIG courses repeated and sequentially methotrexate, hydroxychloroquine, cyclosporine with short time of remission. Muscle weakness disappeared after the treatment, but in October 2015 y he experienced new eruptions on his face, heavy aphtosis stomatitis, lymphadenopathy, distal polyneuropathy, weight loss without strong effect after increase the dose of Pr, IVIG courses repeated, cyclosporine and added of abatacept during 6 months. Because the response to this treatment was low, etanercept was started in June 2016 y, but after two injections he had flare of disease: bright rash on the face, scalp and legs, hard aphthosis stomatitis, cheilitis, cognitive disorders, diffuse alopecia. He received IV course of Pr without significant stable effect. We reviewed diagnosis as systemic lupus erythematosus and changed therapy in November of 2016. Because he had steroid's osteoporosis with spondylopathy, this combination that made us initiate treatment with mycophenolate mofetil and repeating courses of rituximab (3 courses in total) without increased dose of Pr. Clinical features gradually improved and now he feel goog and receive mycophenolate mofetil and Pr 5 mg/day.
Conclusion: This clinical observation can be considered as a course of overlap-syndrome with a successive phase change that could be triggered by anti-TNF therapy, or as an unusual course of SLE in a male patient with a predominance of myositis at onset. Treatment strategy, including of Pr, mycophenolate mofetil and rituximab in a young patient proved successful for treatment and seems to be justified in similar cases.
Disclosure of Interests: None declared
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AB1032 FACTORS TO AID IN EARLY DIAGNOSIS OF KIKUCHI'S DISEASE IN ASIAN CHILDREN

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Background: The diagnosis of Kikuchi's Disease (KD), also known as histiocytic necrotizing lymphadenitis, is often delayed as patients often undergo multiple investigations to exclude other causes of cervical lymphadenopathy, such as infection and malignancy[1].
Objectives: To describe the clinical features and treatment response of pediatric patients diagnosed with KD in our institution to aid early recognition.
Methods: A retrospective study was conducted on patients < 18 years old diagnosed with KD in National University Hospital, Singapore, from Jan 2006 – Dec 2018. Demographics, clinical characteristics and treatment information were collected.
Results: 14 patients were diagnosed with KD. All were Asian and majority were Chinese (64.2%). 57.1% were male and the age of presentation ranged between 2.8 to 17.9 years old. Fever duration at diagnosis ranged between 8 - 50 days. Median height of temperature was 39.8 (IQR: 39.4 – 40.0) deg C. This was frequently associated with neck pain and swelling (57.1%) and constitutional symptoms (71.4%) such as anorexia and weight loss. Other symptoms include abdominal symptoms of pain, vomiting or diarrhea (57.1%), rash (35.7%) and oral ulcers (28.6%).
All patients had cervical lymphadenopathy either in the anterior cervical triangle or both anterior and posterior triangles, but not in the posterior triangle alone. This was usually multiple (92.9%), measuring ≥2cm in diameter (100%), tender (85.7%), and tended to be unilateral (64.3%); none had overlying warmth or skin changes. 14.3% had isolated hepatomegaly while 14.3% had hepatosplenomegaly.
Common lab abnormalities included cytopaenias (50% bicytopaenia, 28.6% leucopaenia, 7.1% anaemia), elevated inflammatory markers C-reactive protein (CRP) (range: 12 – 117 mg/L), erythrocyte sedimentation rate (ESR) (range 15 – 116 mm/h) and lactate dehydrogenase (range: 480-1514 U/L). Only 3/14 had mild transaminitis. Interestingly, almost half had low alkaline phosphatase (ALP). All patients had normal to high complements and were negative for anti-dsDNA antibodies. Ultrasound of the neck typically revealed non-specific findings of reactive lymphadenopathy while 1 showed suspicious features of thickened cortex and loss of fatty hilum. 10/14 patients underwent excision biopsy which confirmed the diagnosis of Kikuchi Disease on histology. 3/14 did not have excision biopsy as they responded promptly to non-steroidal anti-inflammatory drugs (NSAIDs), one declined excision biopsy.
All patients had received empiric antibiotics with no response. 64.3% required treatment with NSAIDs for an average of 2-4 weeks. Of the 4 patients who required steroid therapy, one was started at the diagnosis of KD, while the other 3 received steroids upon failure of NSAIDs. Response to either NSAIDs or prednisolone, if effective, was usually prompt, within 24 hours.
Conclusion: Prolonged high grade fever with multiple tender cervical lymphadenopathy ≥ 2cm without warmth or redness and non-response to antibiotics, should raise concerns for KD. The presence of cytopaenia with moderately elevated inflammatory markers and LDH, coupled with low ALP, may be considered supporting biochemical features of KD. Prompt response to a trial of NSAIDs can help with the diagnosis of KD and potentially avoid excision biopsy of the lymph node.
More research needs to be done to determine a clinical and biochemical diagnostic criteria for Kikuchi's Disease so as to aid early diagnosis and potentially avoid invasive excision biopsy of the lymph nodes.

REFERENCES

[1] Lin HC, et al. Kikuchi's disease in Asian children. Pediatrics. 2005 Jan;115 (1):e92-6.
[2] Chen CK, et al. Kikuchi disease in Asian children. J Paediatr Child Health. 2006 Mar;42(3):104-7.

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AB1033 MEASUREMENT OF DISEASE ACTIVITY LEVEL OVER TIME IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS UNDER BIOLOGIC TREATMENT, USING THE JUVENILE DISEASE ACTIVITY SCORE HUNGARIAN DATA FROM THE JUVENILE IDIOPATHIC ARTHRITIS REGISTRY OF THE NATIONAL INSTITUTE OF RHEUMATOLOGY AND PHYSIOTHERAPY

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Background: A wide variety of measures are currently available to monitor the disease course over time in children with JIA.The Juvenile Disease Activity Score JADAS71 version was validated for 71 joints, global score for the JADAS71 is: 0-101.
Objectives: To report the changes of disease activity in JIA patients under biological treatment at age 18, using the JADAS 71 score for the extended oligoarticular and seropositive/seronegative polyarticular form of JIA.
Methods: The Hungarian Biologics JIA Registry of National Institute of Rheumatology and Physiotherapy, Budapest is a longitudinal, unicenter, observational study, that has been maintained since 2002. JIA-ILAR criteria were used for the diagnosis.Patients with polyarticular course, who failed to respond or did not tolerate methotrexate and were treated with biological agents at the Paediatric Rheumatologic Centre of the National Institute of Rheumatology and Physiotherapy, Budapest, Hungary from 2002 to 25th January,019, were enrolled in an open label observational study and have been monitored prospectively in the registry. At baseline patients and disease characteristics were registered such as, patients'

history, demographic characteristics, and previous DMARDs treatments. Adverse events(AEs), reason for the discontinuation of the biologic treatment, or switch to another biological treatment were documented. The study was approved by the Institutional Review Board. Written informed consent was obtained from parents of the patients and the study was conducted in accordance with the Declaration of Helsinki.

Results: In this study 64, 18-year-old Caucasian JIA patients were evaluated from the day of entrance into the registry, who had JADAS 71 results at age 18, from the 347 patients treated with biologics at the submission.

Demographic data and disease related variables by descriptive statistics:

Gender: Female: N(%): 49(77%).

Subtypes of JIA: Extended oligoarticular form: 11 patients, Polyarticular form: 53 patients (5 RF positive,48 negative)

Median age: 8 (range:4-17) years.

Mean disease duration: 3352 days.

Mean time on biological treatment:1030 days.

The first JADAS 71 summation at the entry into the registry: Median: 18,65 (range:14,4-55,4).

The age 18 JADAS71 summation: Median:3,75 (range: 2,1-38).

All patients were under biologic treatment (etanercept: 56, adalimumab: 29, tocilizumab: 12, abatacept: 4 patients).

Disease activity states and responses to treatments:

JIA extended oligoarticular subtype	Cutoffs for disease activity states JADAS10/71	Number of patients at the entry into the study	Number of patients at age 18
Inactive disease	≤1		1
Low disease activity	1.1 –2	1	
Moderate disease activity	2.1 –4.2		2
High disease activity	>4.2	10	8
JIA Polyarticular RF (negative+positive) subtype			
Inactive disease	≤1		10
Low disease activity	1.1 –3.8	3	20
Moderate disease activity	3.9 –10.5	3	9
High disease activity	>105	47	14

Conclusion: It appears from our study that at age 18, 72,3% JIA patients with extended oligoarticular subtype and 26,4% with polyarticular subtypes report a JADAS71 high disease activity sum, so, these young adults will need transitional care.

REFERENCES

[1] Consolaro A et.al. Arthritis Rheum. 2009;61:658–66.

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AB1034 NO DIFFERENCES IN HEPATITIS B ANTIBODY POSITIVITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS ON BIOLOGICAL THERAPY

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Background: Biologic disease-modifying antirheumatic drugs (DMARDs) are frequently used in the treatment of juvenile idiopathic arthritis (JIA) resistant to nonbiologic DMARDs recently. There is a concern for their reducing the effectiveness of vaccines due to immunosuppresive effects.

Objectives: To evaluate hepatitis B antibody (anti-HBs) positivity and antibody titers between JIA patients on biologic DMARDs therapy and healthy conrols.

Methods: Anti-HBs antibody positivity and titers were compared between 88 patients with JIA on biologic DMARDs therapy followed in our clinic and 91 healthy controls aged 2-19 years. All participants were vaccinated according to the routine vaccination schedule in our country.

Results: Eighty-eight JIA patients included and fifty five (62,5%) patients were female. The median age of patients was 13,31 (4,07-18,08) years. The JIA subtypes were systemic JIA (10,2%), oligoarticular JIA (33%), poliarticular JIA (25%), entesitis related arthritis (26,1%), psoriatic JIA (3,4%), and undifferantiated JIA (2,3%). The median duration of biologic DMARDs was 31,995 (1,33-115) months. 54 patients were treated only with one anti-TNF (34 etanercept, 17 adalimumab), 16 patients were treated more than one TNF-alfa inhibitor. 18 patients were treated with more than one different group biologic DMARDs, and 7 of them had more than two biologic DMARD due to disease activity. Anti-HBs positivity was 67% in the JIA group and 54,9% in the control group, and no significant difference detected between the two groups (p=0,097). The anti-HBs titer was 12,95 (min-max: 2-1000) in the controls and 22,44 (2-1000) in the biological DMARDs.

Conclusion: Patients with JIA on biologic DMARDs had not lower anti-HBs positivity than healthy controls in our study. Further studies are required to understand the effects of biologic DMARDs on protective anti-HBs antibody levels.

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AB1035 MAFB-VARIANTS IN MULTICENTRIC CARPOTARSAL OSTEOLYSIS WITH NEPHROPATHY DO NOT SEEM TO AFFECT SERUM C1Q CONCENTRATION

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Background: Multicentric carpotarsal osteolysis syndrome (MCTO)-associated progressive nephropathy is an orphan disease associated with well-known structural kidney damage that usually requires kidney transplantation in adulthood. Although ACE-inhibitors could potentially slow down the progression of kidney dysfunction, other treatments would be welcome. Furthermore, a slight proteinuria reduction in a patient with MCTO treated with cyclosporine has been reported. MafB-deficient mice develop systemic lupus erythematous-like autoimmune disease by inhibited C1q production and efferocytosis. In the human, monoallelic mutations in MafB result in MCTO.

Objectives: To investigate whether C1q levels in patients with MCTO are reduced and might contribute to the development of renal disease.

Methods: In three individuals with clinical and radiographic signs of MCTO, the *MAFB* gene was sequenced. The serum C1q concentration was determined with a commercial laboratory kit.

Results: Three patients with MCTO were enrolled (table 1). Patient A presented recurrent urinary tract infections since 18 months of life for a third-degree vesicoureteral reflux. Despite correction surgery, he displayed proteinuria after one year, and kidney biopsy did not reveal significant lesions. After two years, he displayed bilateral tarsal malformations requiring orthopedic surgery. At the age of 6, a pathological fracture of the right wrist occurred, and local X-ray revealed osteolysis of carpal bones. - Because of a suspected juvenile idiopathic arthritis of the right wrist, patient B was treated with intra-articular steroid injection and subcutaneous methotrexate for one year without benefit. After one year, he developed proteinuria and kidney biopsy revealed focal segmental glomerular lesions with tubular fibrosis and renal vasa sub-intimal delamination. C3 and C4 positive mesangial deposits were also present. - Patient C was referred to us for suspected juvenile idiopathic arthritis of the right wrist. No inflammatory signs were present at the ultrasound examination. Sequencing of the *MAFB* gene revealed in all the patients a novel heterozygous mutation. Although specific variants have not been reported before, the nature and position of the variants associated with the clinical features of the patients strongly argued in favor of their pathogenic role. The serum C1q concentration was normal in all the patients.

Abstract AB1035 Table 1. Main features of three patients with MCTO.

Patient	A	B	C
Age (years); gender; country of origin	14; M; Croatia	16; M; Italy	11; F; Russia
MAFB mutation	c.184A>G, p.Thr62Ala	c.172A>G, p. Thr58Ala	c.208T>C, p. Ser70Pro
Bone lesions onset (age; years)	5	8	8
Presentation	Bilateral	Monolateral	Monolateral
Site	Tarsus	Carpus	Carpus
Current state (except carpotarsal joints)	Elbows and knees contractures	Knees contractures	None

Nephropathy onset (age; years)	3	9	None
Current state	Proteinuria (720mg/ 24h)	Proteinuria (1.3g/24h)	Normal kidney function
Serum C1q concentration	174 mg/l	312 mg/l	176 mg/l

Conclusion: C1q plasma levels in our patients were normal, suggesting that MCTO-associated genetic variants do not play a role in MafB-dependent regulation of complement component C1q production in humans. Further studies are necessary to exclude a role of complement system in the progressive nephropathy of patients with MCTO.

REFERENCES

[1] Tran MTN, et al. MafB is a critical regulator of complement component C1q. Nat Commun. 2017;8:1700.

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AB1036 AN UNSOLVED CASE: IS THIS A CANDLE-LIKE SYNDROME?

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Background: Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature (CANDLE) syndrome is a complex autoinflammatory disorders arising from inborn defects in immunoproteasome. Several genes can be involved and cases with digenic inheritance have been described. However, many cases remain without the identification of a specific genetic defect. A positive interferon signature is typically found in patients and may serve as a diagnostic clue.
Objectives: To describe clinical and genetic features in a girl with CANDLE and in her relatives with a variety of different rheumatologic complaints.
Methods: We performed Whole Exome Sequencing (WES) on 10 family members. Moreover, we assessed RNA-seq on three sample from the proband, collected during acute phases of disease (samples positive to class I interferon signature (IS)) (1), and her parents. Results of RNA sequencing (RNA-seq) were compared with specimens from healthy controls.
Differentially expressed genes (DEGs) were filtered by fold change > 2 and padj < 0.05. DEGs enrichment were performed using different R packages, such as pathfindR.
Results: We describe the case of a 20 years old girl with clinical and biological data supportive of CANDLE syndrome. At the age of 3 years, she started presenting a clinical picture reminiscent of amyopathic dermatomyositis, with skin rash, lipodystrophy, subcutaneous panniculitis nodules, and more recently with chilblains, skin ulcerations, polyarticular arthritis and alopecia.
Her pedigree includes several relatives with rheumatic disorders, but none has a clinical picture as complex and severe as our patient. This girl was found to have a strongly positive class I IS in peripheral blood cells. After several unsuccessful therapeutic attempts with antirheumatic drugs and biologics, the girl showed a dramatic clinical response to the JAK inhibitors tofacitinbib.
IS resulted positive also in 4 of her relatives, three of whom presented also rheumatologic symptoms. Conversely, one uncle of the girl was affected with rheumatologic symptoms but had negative IS. The pedigree may suggest a complex pattern of inheritance, likely with a major dominant disorder, whose expression can be modulated by multigenic and/or environmental factors.
WES failed to detect significant genetic variants in proteasome components. However, RNA-seq revealed a profile of differentially expressed IFN-regulated genes similar to that reported by Anja Brehm et al. in subjects with CANDLE/PRAAS (2).
Conclusion: Our results suggest that our family may present a multigenic form of CANDLE, with a complete clinical picture only in the proband, whilst other relatives may only present partial or incomplete forms of the disease.

REFERENCES

[1] Rice GI, et al. Assessment of Type I Interferon Signaling in Pediatric Inflammatory Disease. J Clin Immunol. 2017 Feb;37(2):123- 132. doi: 10.1007/s10875-016-0359-1. Epub 2016 Dec 9.
[2] Brehm A, et al. Additive loss-of- function proteasome subunit mutations in patients with CANDLE/PRAAS promote type I IFN production. J Clin Invest. 2016 Feb;126(2):795. doi: 10.1172/JCI86020. Epub 2016 Feb 1.

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AB1037 SEROLOGICAL PHENOTYPES, UVEITIS AND DISEASE ACTIVITY INTO ADULTHOOD: LONG TERM OUTCOME IN A COHORT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Deepening the long-term study in adulthood of Juvenile Idiopathic Arthritis (JIA) is fundamental in order to expand knowledge of the pathogenesis, optimize the therapeutic choices, favour a more active communication between paediatric and adult care specialists.
Objectives: The present project deals with adult patients affected by JIA. The main objectives were those of: analyse the serological profile (rheumatoid factor –RF- IgM, ACPA IgG, ANA) of such patients to investigate possible seroconversions in adulthood compared to the diagnosis in paediatric age; investigate whether correlations between antibodies (Ab) and diagnostic subgroups subsist in adulthood; evaluate the association between Ab and disease activity; investigate the association between the presence of uveitis in the medical history and specific Ab, diagnostic subgroups and disease activity.
Methods: 68 patients were selected. Data were collected from medical records, a sample was taken to search for ANA, RF and ACPA; clinical data were collected on the evaluation of disease activity, using JADAS27 and SDAI as clinical scores (fig.1)
Results: The data obtained were significant for the negativization of ANA in adulthood: at the diagnosis 45.6% of patients had ANA positivity, while in adulthood 13.2%. The difference was statistically significant. The Ab picture of both RF and ACPA remains unchanged in adulthood, therefore there was neither a significant positivization nor negativization. The concomitant positivity for RF and ACPA was found to exist, demonstrating statistical significance for both the diagnosis and the adulthood (p 0.05). A higher incidence of uveitis was not correlated either with the presence of ANA in paediatric age, nor in adulthood, but is instead associated with the diagnosis of oligoarticular JIA (p = 0.002). Analyses of the positivity for RF and ACPA (in relation to disease activity calculated with clinimetric indices such as JADAS27, SDAI and CDAI) detected the negative prognostic role of the two Ab as they correlated with higher disease activity in the population of the patients in the study (fig.2)
Conclusion: In a rheumatological scenario enriched of great improvements in the diagnostic and therapeutic field during the last decades, a far from negligible portion of patients with JIA requires the continuation of rheumatological care in adulthood. The analyses of the present study report a significant negativization of ANA, thus suggesting the need to confirm the presence of these Ab in adulthood, and the difficulty in recognizing the classifying role of such Ab. The serological profile of RF and ACPA remains unchanged in adulthood, their correlation with the polyarticular subgroup is maintained even in the long term and both correlate with greater disease activity in adulthood.

REFERENCES

[1] Oliveira-Ramos F, Eusébio M, et al. Juvenile idiopathic arthritis in adulthood: fulfilment of classification criteria for adult rheumatic diseases, long-term outcomes and predictors of inactive disease, functional status and damage. RMD Open.2016; (2)
[2] Coulson EJ, Hanson HJM, et al. What does an adult rheumatologist need to know about juvenile idiopathic arthritis? Rheumatology. 2014;53(12).
[3] Selvaag AM, Aulie HA, et al. Disease progression into adulthood and predictors of long-term active disease in juvenile idiopathic arthritis. Ann Rheum Dis. 2016;75(1)

Fig.1 *Demographic, clinical and serological characteristics of patients (n=68)*

Female n (%)	54 (79,4%)					
Age (±d.s.)	28 anni (±10)					
Disease duration (±d.s.)	17 anni (±10)					
Uveitis	12 (17,6%)					
Diagnostic subgroups	Sistemic JIA n=10 (14,7%)	Oligoarticular JIA n=28 (41,2%)	Poliarticular JIA n=20(29,4%)		Psoriasic JIA n=3 (4,4%)	Entesitic JIA n=7 (10,3%)
			RF Positiv n=9	RF Negativ n=11		
Female n (%)	6 (60%)	13 (46,4%)	9 (100%)	9 (81%)	2 (67%)	2 (28,5%)
Uveitis	0	8 (28,6%)	0	2 (18%)	0	2 (28,5%)

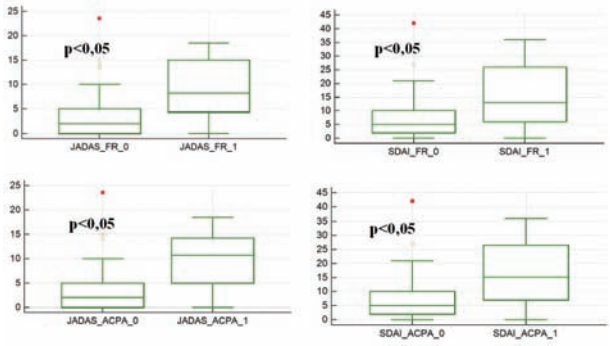


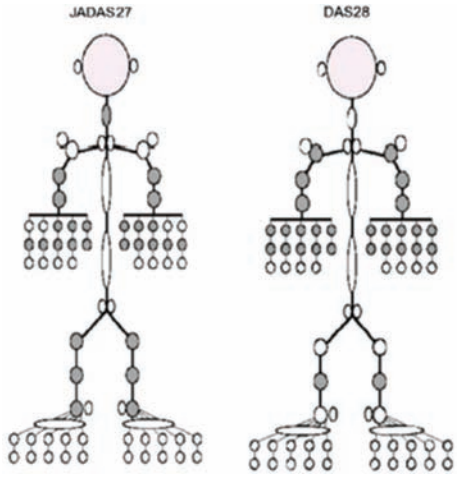
Figure 1

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AB1038 JUVENILE IDIOPATHIC ARTHRITIS INTO ADULTHOOD: HOW DO WE ASSESS DISEASE ACTIVITY?

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Background: Deepening the long-term study of Juvenile Idiopathic Arthritis (JIA) in adulthood is essential to increase the pathogenetic knowledge of the disease, to optimize the therapeutic choices accordingly, as well as to promote a more active communication between paediatric care and adult care specialists
Objectives: The present project, created as part of the "transition of care", aims to compare clinimetric scores of wide use for adult inflammatory rheumatisms of the adult (DAS28, CDAI and SDAI) with the JADAS27 score, which has been validated and widely used in order to quantify JIA's activities in the paediatric field. As of today, adult patients with JIA are usually evaluated with clinimetric scores developed for adult chronic rheumatic diseases (DAS28, CDAI, SDAI) and there is no consensus concerning which of these scores doctors should favour, so that the choice is quite autonomous and varies from centre to centre. It is therefore of interest to verify whether among these indices of purely rheumatological use of adults there is one that is more appropriate than JADAS27 which can be useful in monitoring adult patients with JIA.
Methods: The relevant clinical data were collected from 68 adult patients with JIA. A correlation analysis was performed between the clinimetric scores according to McNemar Test and Kappa by Cohen.
Results: The results obtained suggest that none of the clinimetric scale commonly used in the rheumatological clinical practice of adult patients can completely replace JADAS27. DAS28 is the score that goes further from an acceptable correlation with JADAS. Since both CDAI and SDAI are calculated with formulas that are similar to the one used for JADAS (algebraic sums of affected joints, subjective outcomes reported by the patient, clinical judgment of the physician), they happen to be a method of quantification of disease activity quite closer to JADAS itself. The analyses outlined a scenario in which a much larger portion of patients are classified in remission stages or in low disease activity when using CDAI and SDAI compared to JADAS27.



	Test di McNemar	Kappa di Cohen
JADAS-DAS28	p=0,00	0,08
JADAS-CDAI	p=0,00	0,11
JADAS-SDAI	p=0,00	0,20

Figure 1

Conclusion: This element inspired us to consider how in paediatric age a more "demanding" attitude towards the disease led to the validation of both a score and its very stringent cut-offs which are functional to a treat to target characterized by a complete remission whose main goal is to avoid long-term sequelae. SDAI was found to be the scale of common use in the adult care that more properly approaches the clinometry validated for the paediatric population (JADAS27). Although clinical common sense should not distract from assessing disease activity in this specific patient population from a global perspective, such a study could suggest using SDAI as clinimetric score of choice in adult patients with JIA. Further checks in larger population samples are obviously necessary.

REFERENCES

[1] Oliveira-Ramos F, Eusébio M, et al. Juvenile idiopathic arthritis in adulthood: fulfilment of classification criteria for adult rheumatic diseases, long-term outcomes and predictors of inactive disease, functional status and damage. RMD Open.2016; (2)
[2] Coulson EJ, Hanson HJM, et al. What does an adult rheumatologist need to know about juvenile idiopathic arthritis? Rheumatology. 2014;53(12).
[3] Selvaag AM, Aulie HA, et al. Disease progression into adulthood and predictors of long-term active disease in juvenile idiopathic arthritis. Ann Rheum Dis. 2016;75(1)

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Actelion
Amgen
Biogen
BMS
Celgene
Grunenthal
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Janssen
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UCB
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AB1039 ADA2 DEFICIENCY PRESENTING AS INFANTILE POLYARTERITIS NODOSA

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Background: Polyarteritis nodosa (PAN) is a rare form of primary systemic vasculitis with heterogeneous presentations, treatments and disease course. There have been improvements in understanding of certain causes of PAN such as the association of the monogenic disorder Deficiency of Adenosine Deaminase 2 (DADA2) with a PAN phenotype. This described autoinflammatory disease is caused by loss-of-function homozygous or compound heterozygous mutations in CECR1 and can be characterised by an early onset vasculopathy with clinical and histopathological features of PAN associated with haemorrhagic and ischaemic strokes.
Objectives: We report a case of a 14 year-old boy, with a prenatal diagnosis of Klinefelter syndrome, whose parents are first cousins.
Methods: Review of patient´s clinical records and scientific literature.
Results: During his first two years of age, he suffered two small strokes, was investigated in another Hospital and no diagnosis was made. At 4 years of age he was admitted to another hospital for prolonged fever and arthralgia. At age 5 he was admitted to our hospital for fever, arthralgia and myalgia. He later developed a medular stroke and arterial hypertension. Due to suspected PAN he underwent a renal angiogram which confirmed our suspicion.
He completed induction treatment with IV cyclophosphamide (6 months), steroids, acetylsalicylic acid (ASA), warfarin and ramipril, followed by maintenance with azathioprine (AZA).
While on remission, 2 weeks after after stopping warfarine he suffered a transient ischemic attack; brain-MRI showed a small *de novo thalamic* lesion.
CECR1 testing revealed c.1226C>A variant in homozygosity, his parents are both carriers. ADA2 enzymatic activity was then tested and was absent, which confirms the diagnosis. IgM levels are low. He started adalimumab and stopped warfarin, aspirin and AZA. He mantains follow-up, with no sequelae to his strokes and apparent clinical remission.
Conclusion: The age of onset and clinical manifestations of DADA2 vary widely and are not clearly related to the genotype. Although this variant in CECR1 was of uncertain pathological significance, the absence of ADA2 enzymatic activity confirms the diagnosis.
Timely diagnosis and treatment with anti-TNF drugs are thought to be crucial to prevent severe complications. Also, these patients should not be treated with ASA or anticoagulants which are frequently used in PAN patients. Low IgM levels can be a clue to raise the suspicion.
Lack of long term outcome data in children with DADA2 makes the prognosis uncertain and underlines the need to maintain a lifelong follow-up.

REFERENCES

[1] Zhou Q et al. Early-onset stroke and vasculopathy associated with mutations in ADA2. N Engl J Med. 2014 Mar 6;370(10):911-20
[2] Navon E et al. Mutant adenosine deaminase 2 in a polyarteritis nodosa vasculopathy. N Engl J Med. 2014 Mar 6;370(10):921-31.

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AB1040 PEDIATRIC SJÖGREN SYNDROME: A MONOCENTER CASE SERIES

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Background: Sjögren syndrome (SS) is a chronic autoimmune disorder characterized by inflammation of the lacrimal and salivary glands leading to oral and ocular dryness. Childhood SS is rare and poorly defined and underdiagnosed owing to the lack of child-specific diagnostic or classification criteria [1].
Objectives: The purpose of this study is to describe five cases with pediatric SS in order to better clarify the characteristics of the disease in the childhood.
Methods: We retrospectively reviewed medical records of patients with pediatric SS referring to our center (ASST-PINI-CTO, University of Milan) from November 2008 to December 2018. No adequate childhood SS-specific criteria exist. Therefore we select our pts according to a combination of clinical, serological, histopatological findings. For the assessment of systemic disease activity we applied ESSDAI (EULAR Sjögren's syndrome disease activity index). We calculated ESSDAI at diagnosis, at the peak disease activity and at the last follow up visit.
Results: We collected data on 5 pts (4 females). The mean of age at onset is 8.4 yrs (range 4.8-11.2). The mean of age at diagnosis is 10.8 (range 6.5-13.3). The follow up period varied from 1.2 to 9.3 yrs (mean 6.3). The most common manifestations were parotid/salivary glands swelling (5/5 pts) and articular involvement (5/5 pts) with arthritis in 2 pts and arthralgia in the others. Nobody of our pts presented dryness of eyes. Xerostomia was found in 2/5 pts. Fever and fatigue occurred in 2/5 and 3/5 pts respectively. We also recorded 2 cases of abdominal pain, 1 case of glomerular proteinuria, 2 cases of purpura and 1 case of erythema nodosum. ANA, anti-SSA, anti-SSB, RF, elevation of ERS and hypergammaglobulinemia (1.6 – 8.04 g/dl) were present in all cases. Minor salivary gland biopsy was performed in 4 pts resulting in histological evidence of focal lymphocytic sialadenitis (one of them showed chronic sialadenitis with a focus score <1/4mm2). Ultrasound studies of salivary glands were positive in 5/5 cases. Mean ESSDAI scores at diagnosis, peak activity and the last follow up visit were 8 (range 5-11), 13.2 (9-20), 4.8 (0-9). The most frequently involved domains at the peak activity were biological (5/5), parotid/salivary glands swelling (5/5) and articular (5/5). No major complications have been observed. With regard to treatment, all patient received corticosteroids and DMARDs (5/5 hydroxychloroquine, 3/5 methotrexate, 1/5 azathioprine, 1/5 leflunomide); one patient needed plasmapheresis and immunosuppressive therapy with cyclophosphamide. Biological therapy was administered to 2 patients: 1 received belimumab and then rituximab, while the other patient received rituximab.
Conclusion: Xerostomia and keratoconjunctivitis sicca are not a common features in children, on the other hand juvenile SS has higher incidence of recurrent parotid swellings than adults [2, 3]. All pts had laboratory abnormalities. The long-term prognosis of pediatric SS is unknown, in our series only 2 patients were inactive (ESSDAI score <5, according to the definition by EULAR) at last evaluation, 3 were moderately active with a minimal clinically important improvement (MCII) observed in all of them [4].

REFERENCES

[1] Lieberman SM. Curr Opin Rheumatol, 2013.
[2] Kobayashi I et al, Modern Rheumatology, 2018.
[3] Cimaz R et al, Eur J Pediatr, 2003
[4] Seror R et al, RMD Open, 2015.

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AB1041 PREVALENCE OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) SUBGROUPS AND JIA-ASSOCIATED UVEITIS AMONG JIA PATIENTS ADMITTED TO REFERRAL PEDIATRIC RHEUMATOLOGY CLINICS IN TURKEY: A RETROSPECTIVE STUDY, JUPITER

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Background: Juvenile Idiopathic Arthritis (JIA) is a chronic childhood arthritis with onset before age of 16 and has a significant degree of morbidity that negatively affects quality of life. Uveitis, which is defined as the inflammation of the iris, ciliary body and choroid, is the most common cause of morbidity of JIA. This study was planned to collect data from a Turkish cohort to provide the initial national prevalence data of patients with JIA.
Objectives: The objective of this study was to determine the frequency of JIA subtypes in Turkey. We also aimed to assess the frequency and characteristics of eye involvement in JIA.
Methods: This national, non-interventional, multicenter, observational study was conducted in a retrospective manner in four study centers which were main referral pediatric rheumatology clinics across Turkey. Data on patient demography, medical history, JIA disease characteristics, laboratory data, cases of JIA-associated uveitis, JIA treatment history and data on other comorbidities were collected from a cohort of 500 patients.
Results: Oligoarthritis (n=194, 38.8%) was the most common JIA disease characteristic in this study cohort. The frequency of the subgroups was as follows: Enthesitis-Related Arthritis (ERA) in 23.2% (n=116), polyarthritis in 15.6% (n=78), systemic arthritis in 12.2% (n=61), psoriatic arthritis in 5.2% (n=26), idiopathic arthritis in 2.8% (n=14) and polyarthritis (RF+) in 2.2% (n=11) of patients were identified. The most frequently prescribed treatment for JIA was methotrexate (n=384, 76.8%). A total of 85 comorbidities were reported, and the most frequently reported comorbidity was Familial Mediterranean Fever (FMF) (n=63, 12.6%).
The number of patients with JIA-associated uveitis diagnosis was 34 (6.8%), and the mean duration of uveitis was 3.2 (±2.3) years. The mean duration between the initial JIA diagnosis and diagnosis of uveitis was 1.8 (±1.9) years. Among 34 patients with uveitis, 45 eye involvements were identified; left eye, right eye and both eyes were affected in 5, 8 and 16 patients, respectively. Five patients (14.7%) had uveitis-related complications that required surgical intervention.
Conclusion: The main difference from the European Caucasian population is the lower frequency of oligoarticular JIA and higher frequency of ERA in Turkish JIA patients. Uveitis was also somewhat lower than expected. Geographic and ethnic factors, that may affect these differences, need further investigation.

REFERENCES

[1] Barut K, Adrovic A, Şahin S and Kasapçopur Ö. Juvenile Idiopathic Arthritis. Balkan Med J. 2017;34:90-101.
[2] Demirkaya E, Ozen S, Bilginer Y, et al. The distribution of juvenile idiopathic arthritis in the eastern Mediterranean: results from the registry of the Turkish Paediatric Rheumatology Association. Clin Exp Rheumatol. 2011;29:111-6

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AB1042 THE EFFECT OF INTRA-ARTICULAR STEROID INJECTION ON THE CARTILAGE THICKNESS IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Intra-articular corticosteroid injection is a choice in the treatment of juvenile idiopathic arthritis (JIA), especially in large and few joints involvement. Intra-articular steroid injection provides relief in active synovitis but its effects on cartilage are controversial.
Objectives: The aim of this study is to evaluate the effect of intra-articular steroid injection on distal femoral cartilage thickness in patients with JIA by ultrasonography.
Methods: Distal femoral cartilage thicknesses were measured before the procedure and 6 months later by ultrasonography in the patients that were injected an intra-articular steroid to the knee.
Results: The mean age of the patients was 12.1±4,8 years. Nine of patients were girls and 2 were boys. The mean disease duration was 5,1±4,2 years. Ten patients had oligoarticular JIA and one patient had enthesitis-related arthritis. The number of patients injected to the right knee was 3, the left knee was 5 and both the knee was 3. The femoral cartilage thickness before the procedure was 3.0 mm [min-max 2.0-3.65 mm], 6 months after the procedure was 2.95 mm [min-max 2.0-3.55 mm] and there was no statistical difference (p>0,05).
Conclusion: In this study, no effect of intra-articular steroid treatment on cartilage was observed. However, the number of patients is lack. Therefore, we planned a comprehensive study with more patients.

REFERENCES

[1] Huppertz HI, Tschammler A, Horwitz AE, Schwab KO. Intraarticular corticosteroids for chronic arthritis in children: efficacy and effects on cartilage and growth, J Pediatr. 1995;127(2):317-21.
[2] Pradsgaard DØ, Hørlyck A, Spannow AH, Heuck C, Herlin T. A Comparison of Radiographic Joint Space Width Measurements Versus Ultrasonographic Assessment of Cartilage Thickness in Children with Juvenile Idiopathic Arthritis, JRheum 2019; 46:doi:10.3899/jrheum.170571.

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AB1043 CLINICAL OUTCOMES OF ANTI-NUCLEAR ANTIBODY POSITIVENESS IN THE 0-18 AGE GROUP: SINGLE-CENTER REAL-WORLD EXPERIENCE

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Background: Anti-nuclear antibody (ANA) assay is important in the diagnosis of autoimmune diseases. However, it has a poor positive predictive value and is detected positive in 10% of general population. In this study, the children that ANA assay was performed in a tertiary pediatric clinic, was evaluated and was aimed to investigate the clinical outcomes in positives.
Objectives: In this study, the children that ANA assay was performed in a tertiary pediatric clinic, was evaluated and was aimed to investigate the clinical outcomes in positives.
Methods: 0-18 age group patients that ANA assay was requested in the various clinics of Erciyes University were included. The patients with positive ANA assay and access to hospital records were retrospectively examined. Patients with and without autoimmune disease were identified as group 1 and group 2, respectively.
Results: The number of patients who required ANA assay in pediatric clinics was 3812. There was a positive ANA assay in 1010 of these patients. The medical records of 909 patients were reached. There were 345 (38%) patients in group 1 and 564 (62%) in group 2. In group 1, female gender was higher compared to group 2 ($p < 0.05$).

Musculoskeletal, hematologic, enterohepatic, and ocular findings as initial findings were significantly high in group 1 ($p < 0.05$). Pediatric Rheumatology, general pediatrics and pediatric neurology are the three clinics which the assay was requested most common. The patients who were examined in pediatric rheumatology, pediatric hematology-oncology, pediatric gastroenterology departments had a higher incidence of autoimmune disease ($p < 0.05$). In patients with autoimmune disease, $\geq$1/1000 ANA titer and homogenous staining were frequent ($p < 0.05$).
Conclusion: In our center, which is a tertiary health center, the autoimmune disease was not detected in most of the patients whose ANA assay was positive. The proportion of patients with autoimmune disease was low in most of the commonly requested departments. The ANA assay should be requested after the patient's clinical findings are evaluated in detail.

REFERENCES

[1] Abeles AM, Abeles M. The clinical utility of a positive antinuclear antibody test result. Am J Med. 2013 Apr;126(4):342-8. doi: 10.1016/j.amjmed.2012.09.014.

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AB1044 CYTOKINE PROFILE OF MACROPHAGE ACTIVATION SYNDROME ASSOCIATED WITH KAWASAKI DISEASE

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Background: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening complication of childhood systemic inflammatory disorders. MAS occurs most often in children with systemic juvenile idiopathic arthritis and less commonly in children with Kawasaki disease (KD).
Objectives: Our study aimed to assess the kinetics of cytokine release and compare the accuracy of serum biomarkers for diagnosis of MAS, including neopterin, IL-18, IL-6 and soluble TNF receptor type I (sTNFR-I) and sTNFR-II levels, we analysed these levels in patients with KD, including those with MAS, and compared them to the clinical features of KD and MAS.
Methods: Serum neopterin, interleukin (IL)-18, IL-6 and soluble tumour necrosis factor receptor type I (sTNFR-I) and sTNFR-II levels were determined using enzyme-linked immunosorbent assay in 78 patients with KD, including five with MAS. Results were compared to the clinical features of MAS.
Results: Serum neopterin, IL-18, sTNFR-II levels and sTNFR-II/I ratio were significantly elevated in KD patients with MAS compared to those in the acute phase. Receiver operating characteristic curve analysis revealed areas under the curve and cutoff values of neopterin, IL-18, sTNFR-II levels and sTNFR-II/I ratio were 0.9750/30.0 nmol/L, 0.9813/1165 ng/mL, 0.9969/16,600 pg/mL and 0.9875/4.475, respectively. Serum sTNFR-II levels correlated positively with disease activity.
Conclusion: These findings indicate that interferon (IFN)–γ and tumour necrosis factor-α (TNF-α) are closely associated with the pathogenesis of MAS associated with KD. Serum sTNFR-II levels might be a useful marker to diagnose the transition to MAS.

REFERENCES

[1] García-Pavón S, et al. J Pediatr Hematol Oncol 2017;39:445-451.
[2] Shimizu M, et al. Cytokine 2018;108:168-172.

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AB1045 MULTICENTRIC CARPOTARSAL OSTEOLYSIS (MCTO) IN PRACTICE OF PEDIATRIC RHEUMATOLOGIST: DIFFERENTIAL DIAGNOSIS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Rare genetic pathologies involving the musculoskeletal system can be erroneously misdiagnosed as juvenile idiopathic arthritis (JIA). Idiopathic multicentric carpotarsal osteolysis (MCTO) is a congenital disease, liked to MAFB-gene mutation, described in 2012. MCTO is characterized by progressing osteolysis, mostly of carpal and tarsal bones, leading to articular deformities and functional impairment, with or without nephropathy. The incidence has not yet been established. And there is no available treatment as of today
Objectives: To share the experience of MCTO identification in pediatric rheumatologist practice at federal center.
Methods: Totally 2 MCTO cases were identified in boys 6 ad 13 years old during the period 2009 – 2018. Standard rheumatological examination was performed. Genetic testing (Sanger sequencing) in 1 patient identified MAFB-gene mutation.
Results: Both patients had pain and swelling in wrist and ankle joints, flexion contractures in elbow joints, and gait abnormalities. Disease duration at the time of MCTO verification was 4 and 11 years. Both patients went through erroneous polyarticular JIA diagnoses. During the follow up patients' ESR and CRP were normal, HLA B27 - negative, ANA and RF – negative. No visceral pathology, including kidneys, was found. Therapy included NSAIDs, glucocorticosteroids – in one case, MTX and Tocilizumab gave no effect in the second patient. Radiographic findings were severe osteolysis of wrist and feet bones. JIA diagnosis was ruled out and MCTO suspected, and later confirmed in both patients by a geneticist. Heterozygous MAFB gene c.206C>T (p.Ser69Leu) mutation was detected in one patient.
Conclusion: Specific phenotypical features and patient's articular status, osteolysis of the carpal and tarsal bones, absence of laboratory activity signs and of response to antirheumatic therapy is a sound motive to continue diagnostic elaboration in order not to miss rare genetically-linked conditions of the musculoskeletal system.
Disclosure of Interests: None declared
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AB1046 PHYSICAL ACTIVITY ASSESSMENT IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS COMPARED TO CONTROLS

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Background: Physical activity (PA), known to maintain optimal metabolic function and normal development could be impaired during Juvenile Idiopathic Arthritis (JIA).
Objectives: The aim of our study was to assess PA in children and adolescents with JIA compared to healthy peers using the physical activity questionnaire for children (cPAQ) and adolescents (aPAQ).
Methods: This is a cross-sectional study of measured level of PA in children and adolescents with JIA, compared to age and gender-matched healthy Tunisian schoolchildren. PA was estimated by cPAQ and aPAQ filled by the patient group and the reference group. If the child is unable or unsure to answer the questions we have helped with the parents' response. The PAQ scores 2 as "low activity," >2 and ≤ 3 as "moderate activity," and >3 as "high to vigorous activity".
Results: A total of 55 patients (38 boys and 17 girls) with JIA and 60 healthy control schoolchildren were included. No significant difference in demographic background was found between the two groups. The mean age was 8.5 ± 4.12 years in the JIA group and 9.2 ± 3.51 years in the control group. Thirty-one patients (53%) had persistant oligoarticular JIA, 15 (27%) had polyarticular JIA, 5 patients (9%) had systemic JIA, and 4 (7%) had enthesitis-related arthritis. The median disease duration was 3.2 ± 2.8 years. The mean cPAQ was 2.101 ± 0.722 in the JIA group and 4.112 ± 0.644 in the control group ($p=0.0001$). Children and adolescents with JIA had a significantly lower levels of PA compared with their healthy peers as assessed by cPAQ/aPAQ ($p=0.012$). The time spent in each cPAQ/aPAQ item was significantly lower in the JIA group compared to the healthy group: sports activities (3.4 ± 0.5 versus 4.7 ± 1.4 hours/week, $p=0.002$), leisure time activities (2.2 ± 0.3 versus 6.2 ±1.3 hours/week, $p=0.001$), activities at school (1.1 ± 0.3 versus 2.1 ± 0.5 hours/week, $p=0.001$), and after school activities (0.5 ± 0.5 versus 2.5 ± 0.8 hours/week, $p=0.001$). Seventy six percent of the JIA group spent the day on the two lowest PA categories: sleeping and sitting, which was significantly higher compared with the reference group ($p=0.001$ and $p=0.055$, respectively).
Conclusion: In our study, children and adolescents with JIA were less physically active than the healthy peers as assessed by the PAQ. More objective methods are needed to better evaluate and quantify the PA.
Disclosure of Interests: None declared
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AB1047 DYNAMICS OF GROWTH AND BONE AGE IN CHILDREN WITH JIA DURING BIOLOGICAL THERAPY

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Background: In children with severe juvenile idiopathic arthritis (JIA), growth impairment is often accompanied by retardation of bone age. Dynamics of growth and bone during biological therapy is an important criterion for the effectiveness of treatment.
Objectives: To assess the effect of biological therapy on growth and bone age in children with JIA.
Methods: The study included 45 patients with JIA and (30 boys and 15 girls, mean age 12.2 ± 2.7 years; disease duration before the start of biological therapy 6.5 ± 3.3 years, 18 children with systemic JIA and 27 with polyarticular JIA). All children due to the ineffectiveness of standard therapy were transferred to biological therapy with TNF-α and IL-6 inhibitors. The study assessed growth SDS and bone age (according to x-ray imaging) before starting biological therapy (initialy) and after 24 months of therapy.
Results: Of the 45 children, the initial growth retardation marked in 13 children, all with systemic JIA (growth SDS -3.19 ± 0.36 (-6.67; -2.04)). All these children also showed a lag of bone age from the passport by 2.9 ± 0.5 years, which corresponded to growth retardation. During biological therapy, the growth retardation decreased within 24 months: growth SDS -2.73 ± 0.34 (-5.87; -1.17). The lag of bone age was maintained at 2.3 ± 1.5 years, which is comparable to the baseline (p = 0.053). In 32 children, the initial growth was within the normal range (growth SDS 0.12 ± 1.07 (-1.97; 1.76)); 8 children with sJIA, 24 with polyarticular JIA. In all these children, the lagging of bone age from the passport at the time of the start of biological therapy was not detected (deviation from the passport age at most 1 year). During biological therapy for 24 months, growth rates remained normal: growth SDS was 0.22 ± 0.99 (-1.58; 1.67). Indicators of bone age in all children were corresponding passport age.
Conclusion: In children with severe JIA and normal growth, the bone age is more likely to correspond to the passport age; during therapy with biological agents, there is no significant change in bone age in these children. In children with severe JIA, growth impairment and bone age may be observed, most likely in children with systemic JIA. During biological therapy, there is an improvement in growth, while the lagging of bone age from the passport remains, which indicates the preservation of growth potential and the possibility of achieving higher final growth.

REFERENCES

[1] Uettwiller F, Perlbarg J, Pinto G, Bader-Meunier B, Mouy R, Compeyrot-Lacassagne S, Melki I, Wouters C, Prieur AM, Landais P, Polak M, Quartier P. Effect of biologic treatments on growth in children with juvenile idiopathic arthritis.//J Rheumatol. 2014 Jan;41(1):128-35

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AB1048 SYSTEMIC LUPUS ERYTHEMATOUS WITH UNUSUAL PRESENTATION : SINGLE CENTRE EXPERIENCE FROM NORTH INDIA

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease.Presentation can range from constellation of non specific constitutional symptoms to definitive signs and symptoms.Systemic Lupus International Collaborating Clinics(SLICC) criteria help in making a diagnosis of SLE. SLE mimics many clinical entities and diagnosis may become difficult at times,especially if presentation is atypical.We describe children who presented with unusual manifestations and were finally diagnosed to have pediatric SLE.
Objectives: To highlight unusual presentation of pediatric SLE.
Methods: Retrospective case review of all children diagnosed as SLE from July 2017–November 2018 at a single tertiary care hospital in north India was done. We here describe 5 children who presented with unusual manifestations.
CASE 1: 8 years,girl, presented with fever for 1 month and bilateral pleural effusion. She had had 2 hospitalizations in the past. Once with fever, epistaxis and haemorrhagic shock and subsequently with fever, hepatosplenomegaly and bicytopenia and was managed as tropical infections at both times.She was evaluated this time and was diagnosed to have SLE and managed for the same.
CASE 2: 11 years,boy, presented with arthritis in multiple small and large joints of body.No other features of SLE were seen. On evaluation ANA and anti dsDNA was found to be positive and he fulfilled criteria for SLE. He was started on subcutaneous, weekly methotrexate and responded to treatment. However, he developed lupus nephritis during disease course after 6 months of diagnosis. Renal biopsy revealed ClassIII+V lupus nephritis. Intravenous Cyclophosphamide pulses were started for induction along with tapering doses of corticosteroids.
CASE 3: 8 years,girl, presented with early morning periorbital puffiness and abdominal distension. She also had a history of photosensitivity and Raynaud phenomenon. Urine routine examination revealed nephrotic range proteinuria with no hematuria. Clinical possibility of nephrotic syndrome secondary to SLE was kept.Renal biopsy revealed Class V Lupus nephritis. She was started on oral prednisolone and enalapril.
CASE 4: 15 years old, girl, presented with non-specific generalized body pains with n joint pains associated with low grade fever.There were no other complaints. Examination was unremarkable. Investigations, however, were suggestive of SLE.
CASE 5: 17 years old,girl,presented with high grade fever and pain in bilateral knee joints and malar rash. Investigation were suggestive of SLE with MAS(macrophage activation syndrome). Child was started on iv antibiotics and iv immunoglobulins but died during the disease process.
ANA positivity, hypocomplimentimia and Anti ds DNA positivity were seen in all the 5 cases.
Results: out of 11 children diagnosed to have SLE, 5 presented with unusual manifestations as described above.All patients were initiated on hydroxychloroquine and photoprotection other drugs used were prednisolone, naproxen, subcutaneous weekly methotrexate, cyclophosphamide and Azathioprine.
Conclusion: In this report we present unusual presentations as the predominant manifestation of SLE and emphasize the fact that early recognition and awareness of unusual presentation of SLE help institute timely initiation of appropriate treatment.

REFERENCES

[1] Iqbal S, Sher MR, Good RA, et al. Diversity in presenting manifestations of systemic lupus erythematosus in children. J Pediatr. 1999;135:500-505
[2] Bennarroch LMK, Sterba G, Bosque M. Macrophage activation syndrome as an early presentation of lupus erythematosus. J Allergy Clin Immunol 2006;117:s210.

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AB1049 CO-MORBIDITY INDEX IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Comorbid conditions in patients with rheumatic diseases (RD) aggravate the course of diseases, worsen the prognosis, impede the response to therapy, and reduce the quality of life of patients. Initial manifestations of comorbid lesions of organs and systems are already manifested in childhood and adolescence, and in the future are the causes of persistent morphologic and functional disorders, disability and mortality of patients.
Objectives: The purpose was to identify comorbid conditions in children with systemic lupus erythematosus (SLE), followed by an assessment of the comorbidity index (CI).
Methods: 41 patients with SLE aged 7-18 years were examined. The average duration of the disease at the time of the survey was 44.5± 2.9 months, 20 persons (48.78%) had a period of illness up to 3 years, 21 (51.22%) - over 3 years. Among the patients female subjects predominated - 37(90.24%). The comorbidity index (CI) was determined by the total score (points) of the disturbances in all systems of the organism without specific diagnoses.

Results: Pathological changes of the one or two systems were noted in 19.51% of patients, between three and four systems - in 24,4%, and in some cases - five (7.32%) and six systems (2.44%).
The mean values of CI among patients with SLE were 2.6±0.3 points and did not differ significantly depending on the duration of the disease (2.5±0.7 points before 3 years and 2.4±0.3 points after 3 years; p>0.05), as well as did not differ in female and male patients (2.6±0.3 and 2.8 ±0.5 respectively, p>0.05). The IC was higher in the cases of development of SLE before the age of 7 years than in older patients (3.6±0.5 vs 2.4±0.3 respectively, p<0.05).
The activity of the pathological process significantly influenced the indicators of the CI: 2.4±0.4 with its minimal activity; 2.7±0.4 with an average degree of activity and 3.0±0.6 with a high degree (p<0.05). The frequency of the smallest CI (0 or 1) turned out to be associated with the lowest activity of the disease.
The CI with ANA-positivity association was defined: 2.8±0.3 points among patients with ANA that has twice exceeded the CI of ANA-negative patients (1.4±0.5), p <0,05). Its highest level (like 4, 5 and 6 points) was registered only among the ANA-positive patients.
In patients with SLE with high CI, changes in the system of coagulation due to elevated fibrinogen levels predominated (3.7±0.4 g/l vs 2.8±0.3 g/l (p<0.05). Similar changes were recorded with the atherogenic coefficient increased (2.7±0.7 vs 1.3±0.5; p<0,05).
Conclusion: According to the research, it was found that in children and adolescents with SLE the formation of lesions of systems and organs occurs while maintaining the activity of the process, especially immunological (ANA-positivity). Disruption of lipid metabolism and blood coagulation were associated with the formation of comorbid states.
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AB1050 TOCILIZUMAB MODIFIES CLINICAL MANIFESTATIONS AND LABORATORY FEATURES OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED MACROPHAGE ACTIVATION SYNDROME

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Background: Previous studies including a systematic literature review revealed clinical manifestations and laboratory features of systemic juvenile idiopathic arthritis (s-JIA) associated macrophage activation syndrome (MAS) could be modified in patients treated with tocilizumab (TCZ) [1,2].
Objectives: To clarify whether TCZ modifies clinical manifestations and laboratory features of s-JIA associated MAS, and to assess performance of the 2016 MAS classification criteria for patients with s-JIA associated MAS while treated with TCZ in the real world.
Methods: A combination of expert consensus and analysis of real patient data was conducted by a panel of 15 pediatric rheumatologists. Clinical manifestations and laboratory features of s-JIA associated MAS at the MAS diagnosis in 12 patients while treated with TCZ and 18 patients not treated with TCZ were evaluated. Possible MAS was defined as having characteristic laboratory features but lack of clinical features of MAS, or atypical MAS, or early treatment that prevented fulminant MAS [3,4].
Results: Among 12 patients while treated with TCZ, only 2 patients were diagnosed with definite MAS, and other 10 patients were diagnosed with possible MAS. On the other hand, among 18 patients not treated with TCZ, 10 patients were diagnosed with definite MAS, and other 8 patients were diagnosed with possible MAS. MAS classification criteria could classify the patients diagnosed with definite MAS while treated with TCZ as having MAS as well as the patients not treated with TCZ (100% and 100%, respectively). However, this criteria were less likely to classify the patients diagnosed with possible MAS while treated with TCZ as well as the patients not treated with TCZ (60% and 75%, respectively). Furthermore, the patients with possible MAS while treated with TCZ were less likely febrile and significantly less often had rash, and had notably lower ferritin levels (587 versus 8518 ng/ml; P=0.0021), compared to the patients with possible MAS not treated with TCZ. Other laboratory features of MAS including lower platelet counts, lower fibrinogen were more pronounced in patients treated with TCZ.
Conclusion: These findings show TCZ could modify clinical manifestations and laboratory features of s-JIA associated MAS. When evaluating s-JIA patients while treated with TCZ, care must be taken to not underdiagnose MAS based on MAS classification criteria.

REFERENCES

[1] Shimizu M, et al. Cytokine 2012;58:287-294.
[2] Sculert GS, et al. Arthritis Care Res 2018;70:409-419
[3] Grom AA, et al. Arthritis Rheumatol 2016;68:218-228.
[4] Yokota S, et al. J Rheumatol 2015;42:712-722.

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AB1051 TRANSITION CARE IN A NEW PEDIATRIC RHEUMATOLOGY CENTER IN BRAZIL: CARING FOR ADOLESCENCE BEYOND RHEUMATISM

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Background: Transition care is the planned transfer of adolescents with chronic health conditions from children-centered to adult-oriented health systems. Its challenges include gaps in continuity of care, poor adherence, delays in adult services attendance, differences between pediatric and adult centers, difficulties in autonomy over care and unstable medical conditions. EULAR/PRES recently published recommendations, standards and quality indicators on transitional care for young people with rheumatic diseases, which serve as a guide for transitional outpatient clinics. In Brazil, few centers focus on transition from pediatric rheumatology. The Pediatric Rheumatology Unit of Hospital Geral de Fortaleza is a reference in North and Northeast of the country, intending to be pioneer in transitional medicine in region.
Objectives: To evaluate the adolescents and their families´ perception regarding follow-up and autonomy in health care, as well as to identify the main risks inherent to this age group.
Methods: A longitudinal and descriptive study was carried out through interviews, questionnaires and medical records analyzes. Adolescents between 15 and 18 years old, regularly followed, who had at least three planned visits/year were included. Patients with cognitive impairment or without definite diagnosis were excluded. Epidemiological and clinical data were collected; self-management and health care utilization skills were evaluated by Transitional Readiness Assessment Questionnaire (TRAQ), a self-administered questionnaire.
Results: Eighty two patients were recruited into the transitional service (61 female [74.4%]). Patients´ ages ranged from 15.0 to 18.7 years (median 16.9). Regarding religion, 41 patients (54.7%) were Catholic and 27 were Protestant (36%). Concerning to ethnicity, most of them declared themselves brown (61%) or white (22%). Fifty-nine adolescents (72%) considered themselves able to take care of their own follow-up, whereas 39 relatives (50%) considered the patient capable of doing so. The most frequent diseases were juvenile idiopathic arthritis (31.7%) and systemic lupus erythematosus (29.3%), of which 37 (45.1%) were in remission. Median disease duration and follow-up were 48.5 (5 - 180) and 34.5 (1 - 175) months, respectively. The median TRAQ value was 3.27 (1.61 - 4.55). There were 191 transitional visits (median 2.0 visits/patient). Fifty three patients had 2 or more visits, out of which 42 (79.2%) had at

least one risk identified. The most prevalent risks were: overweight or obesity (31.7%), sedentarism (26.4%), anxiety (22.6%), changes in family structure (22.6%), school problems (20.8%), depression (18.9%), suicidal ideation/self-mutilation (18.9%), low self-esteem (15.1%). Risks related to psychiatric diseases were identified in 23 patients (43.4%).
Conclusion: This is one of the first studies on transition care in Brazil focused on risks identification in adolescence. Transition care allows improvement survival and quality of life due to advances in preventive medicine and treatment of chronic rheumatological diseases. The identification of inherent risks, especially psychiatric disorders, plays a fundamental role in the long-term follow-up, making it possible to deliver multidisciplinary and rehabilitation of adolescents.

REFERENCES

[1] Ardoin SP. Transitions in Rheumatic Disease: Pediatric to Adult Care. Pediatr Clin North Am. 2018;65(4):867-883.
[2] Foster HE, et al. EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases. Ann Rheum Dis. 2017;76(4):639-646.
[3] Wood DL, et al. The Transition Readiness Assessment Questionnaire (TRAQ): its factor structure, reliability, and validity. Acad Pediatr. 2014;14 (4):415-22.

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AB1052 SYSTEMIC LUPUS ERYTHEMATOSUS IN CONTEXT OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION: A CLINICAL CONUNDRUM

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Background: Systemic lupus erythematosus (SLE) and Human immunodeficiency virus (HIV) infection can occasionally coexist in a patient (1). Also, in rare scenarios, the clinical symptomatology and laboratory tests of these diseases can masquerade each other (2).
Objectives: To describe diagnostic and therapeutic dilemmas of coexistent SLE and HIV
Methods: We analyzed case records of 2 patients with childhood SLE who had the clinical conundrum of HIV infection as well
Results: Case 1- An 11-year-boy presented with large joint arthralgia, fever and respiratory distress for 4 days. On examination he had pallor, oral thrush,and onycomycosis. A malar rash was also noted. Systemic examination revealed consolidation in right lung and hepatosplenomegaly. Investigations showed severe anemia and lymphopenia. HIV serology was strongly reactive and CD4 counts were low (49 cells/µl). In view of malar rash he was investigated for SLE and anti-nuclear antibody (ANA) by indirect immunoflorescence (IIF) was 4+ homogenous with rim enhancement. Anti double stranded DNA (dsDNA) antibody titer was 1200 IU/ml, serum complements were low (C3- <28 mg/dl; C4-10 mg/dl) and direct Coombs test for IgG was positive. Antiphospholipid antibody titers were elevated (Anticardiolipin antibody- Ig G: 695 U/L; anti b2 glycoprotein antibody Ig G: 3177 U/L). Blood culture grew Streptococcus pneumoniae. He was started on ceftriaxone and amphotericin, however, he had an acute neurological worsening (raised intracranial pressure) during hospital stay. A diagnosis of concomitant HIV infection and neuropsychiatric SLE was considered in this child. Pulse methylprednisolone was given, but he soon succumbed to the complications.
Case 2: An 8-year-old girl was admitted with fever for 6 months and cough and respiratory distress for 15 days. On examination she had anascarca, oral ulcers, hyperpigmented macules over face and crepitations in right lung fields. Her HIV ELISA was intermediate reactive. Considering a clinical possibility of secondary immunodeficiency due to HIV infection she was managed with broad spectrum antimicrobials while awaiting confirmatory tests for HIV infection. She went on to develop hypertension and nephritis. ANA was 4+ homogenous, low complements and elevated anti dsDNA. Further tests for confirmation of HIV infection showed CD4 counts - 421 cells/µl, negative HIV viral loads, negative HIV DNA PCR and p24 antigen was negative, so it was considered that the intermediate reactivity of HIV serology was false positive. Subsequently she was given immunosuppression (methylprednisolone pulse and cyclophosphamide) to which she transiently responded however she developed acute intracranial bleed during hospital stay and died.
Conclusion: These cases highlight the fact that serological tests can be difficult to interpret in patients with overlapping manifestations of HIV infection and SLE. However, early diagnosis and prompt therapy is imperative.

REFERENCES

[1] Burton J, Vera JH, Kapembwa M. HIV and systemic lupus erythematosus: the clinical and diagnostic dilemmas of having dual diagnosis. Int J STD AIDS. 2010 Dec;21(12):845–6.
[2] Carugati M, Franzetti M, Torre A, Giorgi R, Genderini A, Strambio de Castilla F, et al. Systemic lupus erythematosus and HIV infection: a whimsical relationship. Reports of two cases and review of the literature. Clin Rheumatol. 2013 Sep;32(9):1399–405.

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AB1053 MACROPHAGE ACTIVATION SYNDROME AS A PRESENTATION IN PEDIATRIC LUPUS: A RETROSPECTIVE STUDY OF 3 CASES

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Background: Macrophage activation syndrome (MAS) can, at times, be the presentation of pediatric lupus and diagnosis requires high index of suspicion.
Objectives: To report children who had MAS as a presenting manifestation in our cohort of childhood lupus
Methods: We retrospectively studied 140 pediatric lupus patients from January 1993- November 2018 and collected clinical and laboratory data of patients (3) who had MAS as presenting manifestation.
Results: Case 1 was 11-year-old girl with fever for 4 months associated with rash and generalized body swelling for 1 month. Examination revealed rash over malar area and ear lobules, anasarca, hepatomegaly, bilateral pleural and pericardial effusion. In view of multisystem involvement a possibility of lupus was considered which was confirmed by investigations (table 1). She had elevated ferritin and fasting triglyceride and low fibrinogen. A clinical possibility of lupus with associated MAS was considered. She received pulses of methylprednisolone, one dose of intravenous immunoglobulin following which she improved. In view of nephrotic range proteinuria she was started on induction regimen with cyclophosphamide and shifted to mycophenolate in maintenance. Her initial SLEDAI-2k was 32- this decreased to 4 at 3 year follow-up.
Case 2 was a 9-year-old girl with fever, rash, generalized body swelling for 1 month and altered sensorium for 4 days. Examination revealed pallor, oral ulcers and hepatomegaly. She was in shock at presentation. In view of multisystem involvement a possibility of lupus was considered which was confirmed by investigations (table 1). She had pericardial effusion and low ejection fraction (25%). A possibility of MAS was considered and investigations revealed hyperferritinemia, elevated triglyceride and hypofibrinoginemia. She was given methylprednisolone pulses and continued on oral prednisolone, mycophenolate and hydroxychloroquine. Her initial SLEDAI-2k was 17- this decreased to 0 at 3 year follow-up.
Case 3 was an 8-year-old girl who had fever, rash and body swelling for 15 days. On examination she had tachycardia, tachypnea, pallor, anasarca, subconjunctival bleed and frontal alopecia. She had pleural and pericardial effusion. In view of multisystem involvement a possibility of lupus was considered which was confirmed by investigations (table1). She had high ferritin and triglyceride. So a possibility of MAS was considered and she received pulse methyl prednisolone and intravenous immunoglobulin. She also had hematuria and proteinuria (renal biopsy could not be performed as she was sick and had thrombocytopenia) so was given pulse cyclophosphamide followed by mycophenolate. Her initial SLEDAI-2k was 25- this decreased to 0 at 2 year follow-up.
Conclusion: MAS can be the presenting manifestation of pediatric lupus and may contribute to disease severity and requires aggressive management.

REFERENCES

[1] Borgia RE, Gerstein M, Levy DM, Silverman ED, Hiraki LT. Features, Treatment, and Outcomes of Macrophage Activation Syndrome in

Childhood-Onset Systemic Lupus Erythematosus. Arthritis Rheumatol. 2018 Apr;70(4):616-624. doi: 10.1002/art.40417. Epub 2018 Mar 2.

Abstract AB1053 Table 1

Investigations	Case 1	Case 2	Case 3
Haemoglobin (g/L)	70	67	70
White cell counts (/L)	1.5 X10^6	2.5 X 10^6	3.5 X 10^6
Lymphocyte count (/L)	0.4 X 10^6	0.6 X 10^6	0.8 X 10^6
Platelet count (/L)	63 ×10^9	50 ×10^9	76 x 10^9
Urine protein (mg/m^2/hour)	74		
C3 (Normal 50-150 mg/dL)	< 27	< 27	< 27
C4 (Normal 20-50 mg/dL)	4	3	3
ANA (immunofluorescence method)	4+ diffuse	3 + diffuse	4+ diffuse
Anti dsDNA (N: <60 IU/mL)	707	583	1394
Serum ferritin (ng/ml)	3233	6767	1019
Fasting triglyceride (mg/dl)	442	504	328
Fibrinogen (mg/dl)	120	160	

Disclosure of Interests: None declared
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AB1054 HEPATIC INVOLVEMENT AS A PRESENTATION IN PEDIATRIC LUPUS: A RETROSPECTIVE STUDY OF 3 CASES

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Background: Though abnormal liver tests can be seen during the course of disease in lupus, liver involvement as a presenting manifestation is uncommon in children with lupus (1).
Objectives: We report on 3 children with lupus who had predominant liver involvement at presentation.
Methods: We retrospectively studied 140 pediatric lupus patients from January 1993- November 2018 and collected clinical and laboratory data of patients who had liver involvement as presenting manifestation.
Results: Case 1 was 13-year-old girl with fever and joint pain for 7 months associated with rash and yellow discoloration of eyes and body for 1 month. She also had altered behavior for 3 days. Examination revealed malar rash, pallor, jaundice, bilateral knee arthritis and hepatosplenomegaly. Investigations revealed (table 1) anemia, thrombocytopenia and lymphopenia. She had conjugated hyperbilirubinemia. Transaminases were elevated. Further investigations confirmed diagnosis of lupus (table 1). Markers for autoimmune hepatitis (SMA; LKM) were negative. She received pulse methylprednisolone followed by tapering doses of oral prednisolone. In view of neurological involvement she also received cyclophosphamide and shifted to azathioprine later. Her initial SLEDAI-2k was 22, that decreased to 4 at 2 year follow-up.
Case 2 was a 11-year-old boy with fever, rash and joint pain for 1 month. Examination revealed pallor, malar rash, oral ulcers, arthritis of bilateral elbow and knee and hepatomegaly. Investigations (table 1) revealed anemia; thrombocytopenia; leucopenia and lymphopenia. In view of multisystem involvement a possibility of lupus was considered which was confirmed by investigations (table 1). He had elevated transaminases. There was no coagulopathy. He was started on oral prednisolone. She also had class 3 lupus nephritis and received pulse cyclophosphamide followed by azathioprine in maintenance. Her transaminases decreased in follow-up. Her initial SLEDAI-2k was 18, that decreased to 2 at 2 year follow-up.
Case 3 was an 9-year-old girl who had rash and abdominal distention for 20 days and fever and altered sensorium for 6 days. On examination she had pallor, malar rash, ascitis and hepatosplenomegaly. Investigations revealed anemia; thrombocytopenia; leucopenia and lymphopenia. She had conjugated hyperbilirubinemia, elevated transaminases and coagulopathy. She also had deranged renal function tests. Ultrasonography reveals coarse echotexture, gross ascitis and splenomegaly. Possibility of lupus with acute on chronic liver decompensation was considered which was confirmed by investigations (Table 1). She was given methyl prednisolone. She had progressive azotemia so possibility of rapidly progressive renal failure was considered and cyclophosphamide was given. However, she developed refractory shock and eventually expired.
Conclusion: Hepatic involvement at presentation in lupus can be multifaceted and poses challenge in diagnosis.

REFERENCES

[1] Bessone F, Poles N, Roma MG. Challenge of liver disease in systemic lupus erythematosus: Clues for diagnosis and hints for pathogenesis. World J Hepatol 2014 Jun 27; 6(6): 394–409.

Abstract AB1054 Table 1

Investigation	Case 1	Case 2	Case 3
Haemoglobin (g/L)	93	96	75
White cell counts (/L)	9.5 X10^6	3.5 X 10^6	4.8 X 10^6
Lymphocyte count (/L)	1.9 X 10^6	1.2 X 10^6	0.3 X 10^6
Platelet count (/L)	145 ×10^9	147 ×10^9	37 x 10^9
Total serum bilirubin (mg/dl)	13.8		7.1
Conjugated bilirubin (mg/dl)	12		4
Aspartate aminotransferase (IU/L)	329	203	69
Alanine aminotransferase (IU/L)	96	156	57
Urine protein (mg/m^2/hour)		24 mg/m^2/hr	
C3 (Normal 50-150 mg/dL)	68	23	68
C4 (Normal 20-50 mg/dL)	4	4	3
ANA	3+ diffuse	3 + diffuse	4+ speckled
Anti dsDNA (N: <60 IU/mL)	733	1621	689

Disclosure of Interests: None declared
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AB1055 FINAL DIAGNOSES OF THE PATIENTS WHO WERE REFERRED TO A TERTIARY PEDIATRIC RHEUMATOLOGY OUTPATIENT CLINIC FOR LABORATORY ABNORMALITIES

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Background: Rheumatology laboratory tests are commonly ordered by clinicians to screen for rheumatic diseases.
Objectives: The study aimed to determine the frequency of use of common rheumatology tests and the final diagnosis of the patients who were referred to a tertiary pediatric rheumatology outpatient clinic for the presence of laboratory abnormalities.
Methods: We prospectively evaluated the patients who were referred due to the abnormal laboratory findings.
Results: A total of 216 patients were examined. Among them, 62 patients had anti-streptomycin O positivity, 47 patients had ANA positivity, 41 patients had elevated acute phase reactants, 16 patients had RF positivity, 9 patients had elevated creatine kinase levels, 2 had lupus anticoagulant positivity. Regarding patients were referred due to carrying *MEFV* variants (n=35). A diagnosis of rheumatic disease was made in 54 of patients, while the others had non-rheumatic conditions. Final rheumatological disease diagnoses were as follows: familial Mediterranean fever (n=29), juvenile idiopathic arthritis (n=12), systemic lupus erythematosus (n=4), reactive arthritis (n=3), Raynaud's phenomenon (n=3), chronic recurrent multifocal osteomyelitis (n=1), vasculitis (n=1), acute rheumatic fever (n=1).
Conclusion: Diagnosing a rheumatic disease mainly base upon clinical findings rather than laboratory test results. However, clinicians usually prefer to screen rheumatology laboratory tests when patients suffer from non-specific musculoskeletal findings or symptoms such as fatigue. As our study shows most of patients who were referred due to the abnormal laboratory findings, finally diagnosed as having a non-rheumatological condition. Therefore, systemic and careful approach may be needed to reduce unnecessary use of rheumatology laboratory tests.

REFERENCES

[1] Hashkes PJ, Profile of a pediatric rheumatology practice in Israel, Clin Exp Rheumatol. 2003 Jan-Feb;21(1):123-8.
[2] Rosenberg AM, Analysis of a pediatric rheumatology clinic population. J Rheumatol. 1990 Jun;17(6):827-30.

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AB1056 THE EXPERIENCES OF BIOLOGICAL THERAPIES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS, SINGLE CENTER STUDY

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Background: Juvenile idiopathic arthritis (JIA) is the most common systemic disease causing uveitis in childhood, with a prevalence of 10 per 100 000 persons. JIA-associated uveitis is estimated to have a poor prognosis and has a high rate of complications. JIA-associated uveitis can manifest in various forms, depending on the location and severity of the ocular inflammation, as well as on the type of arthritis. The most of JIA patients with uveitis have oligoarthritis. Therefore, other types of JIA are rarely accompanied by uveitis. Topical corticosteroids are the first line therapy, and disease conventional and biologic modifying anti-rheumatic drugs (DMARDs) are used.

Objectives: The purpose of the present study was to report on the clinical characteristics, ocular complications, treatment, and visual outcome in children with JIA-associated uveitis who were examined in recent years at a single tertiary pediatric rheumatology and ophthalmology center in Turkey.

Methods: We retrospectively analyzed the data of 41 JIA patients (14 males, 27 females).

The duration between the initial evaluation and the final visit was recorded as follow-up time. Juvenile idiopathic arthritis was defined according to the International League of Associations for Rheumatology (ILAR) classification criteria. Uveitis was classified according to the SUN classification.

Two approaches were utilized to evaluate the change of visual acuity (VA) during the disease course: (i) VA was measured on Snellen chart. The equivalent logarithm of the minimum angle of resolution acuity (logMAR) was calculated and used for analysis.

Results: The study included 31 patients (57 eyes) of whom 22 (71%) were females. Mean age (±SD) at uveitis diagnosis was 8.42 (±4.13) years (median 8, range: 34 month–17 years) and there was no significant difference between genders. The mean age at jia diagnosis was 8.42 (±4.7), respectively. Nine patients were ≤ 7 years of age at the time of JIA diagnosis. Anterior uveitis (AU) was the most common type, diagnosed in 57 (76%) eyes. All patients had methotrexate, therefore biologic therapy was used in 29/31 patients (93.5%) at the follow up time (infliximab in 12, adalimumab in seventeen, and tocilizumab in three patients) and 9 children (31%) required ≥2 biologics over the follow up period. Thirteen patients switched between infliximab and adalimumab (10 patients switched from infliximab). The reason for treatment switch included treatment failure and treatment-related side-effects (n=3). Systemic and topical steroids treatment were gradually tapered and discontinued in all patients after initiation of biologics. Of the all affected eyes, posterior synechiae (n=24) was the predominant complication on presentation. During the follow-up period new complications were seen in 11 eyes (13%). Posterior synechiea (6 eyes, 7,5%) was the most frequent complication observed followed by cataract (3 eyes, 3,%) and glaucoma (2 eyes, 2,5%) Improvement or preservation of visual acuity (VA) was noted in 77 eyes (%94,3) at the last visit.

Conclusion: We report a large cohort of children with JIA uveitis managed in a Turkey tertiary unit. Low complication rates and favorable visual outcomes are found in the present study. The high rate of biologic use), and close monitoring of affected children with pediatric rheumatology and uveitis clinic may have contributed to our improved outcomes.

Disclosure of Interests: None declared

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AB1057 DIFFICULTIES IN THE DIAGNOSIS OF THE PFAPA SYNDROME IN THE REAL CLINICAL PEDIATRICIAN PRACTICE

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Background: Symptom complex of PFAPA syndrome is characterized by a rather diverse clinical picture, including recurrent fever, aphthous stomatitis, pharyngitis, adenitis. The annual incidence of PFAPA syndrome does not exceed 0,2‰ [1], but it is believed that this disease is much more common than diagnosed [2]. The absence of specific genetic and biochemical markers of this syndrome determine the complexity of timely diagnosis and treatment of this auto-inflammatory disease.

Objectives: The object is to identify objective reasons that impede timely diagnosis of PFAPA syndrome in the clinical practice of a pediatrician.

Methods: We conducted a follow-up analysis of the medical documentation of patients with verified PFAPA syndrome who were examined and treated at the hospital pediatrics department of the university clinic for the period from 2015 to 2019 year. A survey of pediatricians and pediatric otolaryngologists was carried out on the knowledge of diagnostic criteria, protocol for the management and treatment of patients with PFAPA syndrome.

Results: During this period, in the department of PFAPA syndrome was diagnosed in 7 patients. Among patients with a diagnosis of PFAPA syndrome, there were 4 boys and 3 girls, the average age of children at the time of diagnosis was 3,4 ± 0,7 years. Before the diagnosis was verified, all patients were observed by a pediatrician or otorhinolaryngologist regarding repeated manifestations of tonsillitis and received antibacterial therapy at each episode of exacerbation of the disease. The average period from the first manifestations of the disease to the verification of the diagnosis was 1,4 ± 0,5 years. Diagnostic algorithm for verification of the diagnosis was completed by setting prednisolone test. According to the results of this test, in 100% of cases it was possible to completely arrest the phenomena of the inflammatory process (fever, tonsillitis, pharyngitis, stomatitis) and to normalize biochemical markers of inflammation (CRP) without the use of antibacterial therapy. With further observation, two of 7 patients recorded a decrease in the effectiveness of glucocorticoid therapy, which required a tonsilectomy, and one of them noted the temporary effectiveness of colchicine.

According to the results of a questionnaire survey of pediatricians and children's otorhinolaryngologists of the outpatient service, a low level of knowledge was revealed on the issues of the clinic, diagnosis and therapy of auto-inflammatory diseases. Only 40% of respondents were able to specify the diagnostic criteria for setting PFAPA syndrome and determine the further routing of these patients. It should be noted that more than half of the respondents (57%) had a clear idea about the methods of rational therapy of patients with PFAPA syndrome.

Conclusion: Thus, the complexity of the primary diagnosis of PFAPA syndrome is associated both with the clinical features of the disease and the insufficient level of knowledge of primary outpatient specialists on this issue, which is largely due to the low incidence of PFAPA syndrome. This conclusion was the reason for the inclusion of additional topics in the educational course of pediatricians.

REFERENCES

[1] Forsvoll J., Kristoffersen E.K., Oymar K. Incidence, clinical characteristics and outcome in Norwegian children with periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis syndrome; a population-based study. Acta Paediatrica. 2013; 102: 187–192.

[2] Schindera F., Niederhoff H., Schindera S. et al. Periodisches Fieber, aphthose Stomatitis, Pharyngitis, zervikale Adenitis. Das PFAPA-Syndrome. Monatssch. Kinderheilkunde.2000; 148 (6):596-599.

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AB1058 CO-DESIGNING A COMPARATIVE RANDOMISED CONTROLLED CLINICAL TRIAL OF CORTICOSTEROID REGIMENS WITH CHILDREN, YOUNG PEOPLE AND PARENTS LIVING WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Previous research has identified the need for a randomised controlled trial (RCT) evaluating the most appropriate corticosteroid induction regimen to be used for children and young people (CYP) with juvenile idiopathic arthritis (JIA) (1). A recent qualitative study found that parents and CYP understood trial concepts and were able to identify potential flaws in a proposed RCT. This confirms the need to involve parents and CYP in co-designing RCTs to best meet the needs of future trial participants (2).

Objectives: To co-design components of an RCT of corticosteroid regimens with CYP and parents living with JIA.
Methods: A focus group was conducted with CYP with JIA and parents as part of a wider consensus and discussion group meeting within the Steroid Induction Regimen for Juvenile Idiopathic Arthritis (SIRJIA) study in December 2018. The discussion focused on two components of the RCT design: i) Discussing the most appropriate treatment protocols; and ii) Addressing practicalities associated with an RCT.
Results: Two RCT protocol options, chosen through an online survey by a clear majority out of a possible eight protocols, were discussed and critiqued: i) Protocol A (intravenous vs intraarticular corticosteroid delivery); and ii) Protocol B (intravenous vs intraarticular vs intramuscular vs oral corticosteroid delivery). Several issues pertaining to both protocols were raised, related to the influence of age and past experience, routes of administration and concerns over randomisation. Participants emphasised the importance of clinicians/researchers discussing all of the potential risks with them. Participants also wanted enough information to make an informed choice. Participants emphasised the usefulness of combining trial visits with regular follow-up appointments to minimise the burden of taking part in an RCT and had a preference for their usual hospital being the site they visited. Some participants remarked that videos could be a useful way of conveying information beyond traditional participant information sheets. Some also felt that awareness of research opportunities is not equally accessible to them either, depending on where they lived in the country. Participants would want to be kept regularly updated about the progress of the RCT and felt that incentives were a good way of keeping people engaged, although some were trepidatious to hear negative treatment results. With regards to dissemination, participants felt that study results should be readily available to them in an accessible format, should they wish to view them.
Conclusion: CYP and parents have a considerable amount of knowledge and experience which can shape the design of RCTs. With adequate support, complex concepts such as treatment protocols can be discussed and critiqued. Involving CYP and parents at the design stage of an RCT has been shown to eliminate some potential challenges in the future.

REFERENCES

[1] Deepak, et al. (2017). Literature review on the use of corticosteroids in juvenile idiopathic arthritis (JIA). Rheumatology 56(Suppl7).
[2] Sherratt FC, et al. (2018). Protective parents and permissive children: what qualitative interviews with parents and children can tell us about the feasibility of juvenile idiopathic arthritis trials. Pediatric Rheumatology 16:76.

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Disclosure of Interests: Simon Stones Consultant for: SS has provided consultancy services to Envision Pharma Group, though this is not related to the contents of this abstract., Speakers bureau: SS has undertaken speaking engagements for Actelion, eyeforpharma, Four Health, Janssen and Roche, though these are not related to the contents of this abstract., Heather Bagley: None declared, Frances Sherratt: None declared, Louise Roper: None declared, Eileen Baildam Consultant for: EB has received one paid consultancy for Pfizer in the last 12 months, but this was not related to this study.
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AB1059 CLINICAL MANIFESTATIONS OF CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PRESENTING WITH CYTOPENIA

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Background: Childhood-onset Systemic Lupus Erythematosus is a rare disease, with more than 50% of patients presenting with cytopenia of a decrease in at least one cell line.
Objectives: The purpose of this study was to evaluate whether clinical characteristics differed according to hematologic manifestation.
Methods: We retrospectively reviewed the presenting clinical and laboratory manifestations for 40 pediatric SLE patients (mean age 13.4 years, range 0-18 years), with leukopenia (n=12) and thrombocytopenia (n=15). Variables including age, inflammatory markers (ESR and CRP), prothrombin time, complement system (C3, C4 and CH50), immunoglobulin (IgG, IgA and IgM), Lupus anticoagulant ratio, antinuclear antibody, anti-phospholipid antibody, anti-platelet antibodies, anti β2-glycoprotein antibody, anti-cardiolipin antibody, anti-smith antibody and anti-dsDNA antibody levels were compared according to grouping by presence of leukopenia ($<4000/mm^3$) or thrombocytopenia ($<100,000/mm^3$).
Results: Patients with cytopenia showed younger age at diagnosis than without (mean 13.1 vs. 15.2 years, p=0.0031 for leukopenia and 12.8 vs. 15.2 years, p=0.014 for thrombocytopenia), although the onset of puberty might not contribute to cytopenia. Patients with leukopenia showed lower C3 level than without (mean 44.7 vs. 73.7, p=0.013). Patients with thrombocytopenia showed lower anti-dsDNA titer than without (mean 94.1 vs. 259.8, p=0.038), and was more often negative for anti-platelet antibody (Ib/IX). There were no statistical differences among other variables. Also, there was no significant difference in one cell line decrement compared with both.
Conclusion: Pediatric SLE patients with leukopenia and thrombocytopenia in our study may independently decrease the levels of C3 and anti-dsDNA/anti-platelet (Ib/IX) antibody, suggesting respective pathologic pathways that do not affect each other.

DISCLOSURE OF INTERESTS

None declared
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AB1060 BONE MARROW FOOT OEDEMA IN CHILDREN: THE ROLE OF VITAMIN D

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Background: Bone marrow oedema (BMO) in children is a rare clinical condition characterized by joint and bone extremity pain, out of proportion to the clinical findings, exacerbated by weight bearing, in the absence of a known etiologic cause. It is associated with typical increased signal intensity on T2-weighted MRI. Management is still under debate. Treatment has mostly been reported in adult case series encompassing analgesic drugs, a variety of pharmacological treatments (corticosteroids, bisphosphonates, vasodilators), physiotherapy, reduction of weight-bearing, or core decompression. No treatment guidelines for children are to date available.
Objectives: Recently it has become evident that BMO is associated by an increase in bone turnover, in which vitamin D plays a pivotal role. In literature association between hypovitaminosis D and BMO of the foot and ankle in adult patients is reported. No data are reported in cohorts of children. The purpose of this study is to investigate the incidence of hypovitaminosis D in a paediatric population with primary bone BMO of the feet and the role of a vitamin D supplementation therapy.
Methods: A retrospective study involving 12 paediatric patients (range age 8-14 years) referred to our Rheumatologic Paediatric Clinic of Verona University in the period 2015-2018 with persistent foot pain and MRI compatible with BMO of the foot has been performed. They had all been misdiagnosed in other institutions as affected by algodystrophy or complex regional pain syndrome. Data collection included sex, age, medical and surgical history, recent or remote trauma history, symptoms at presentation, clinical examination, laboratory bone turnover markers, vitamin D levels, MRI, treatment and outcome.
Results: 2/12 patients are male and 10/12 female (male to female ratio: 1:5). 2/12 had a previous diagnosis of juvenile idiopathic arthritis ANA + with the disease in remission at the moment of evaluation. 10/12 were previously healthy.
In all cases history of minor ankle strain or recurrent microtraumas of feet prior to symptom onset had been reported. Joint hypermobility was observed in 75% of cases. One child had been previously treated with bisphosphonates and 5 with limb immobilization, without any improvement.

Physical examination revealed weight bearing pain of foot or ankle in all patients. No other sensory, vasomotor, trophic ore neurological signs and symptoms were detected. Vitamin D deficiency was found in all cases (range 10 to 22 ng/ml). All patients were thus treated with adequate vitamin D daily intake. Pain relief was achieved with paracetamol, low dose ibuprofen, or a short course of oral prednisone. Rest from intense physical activity and physical therapy, avoiding detrimental feet and ankle immobilization were recommended. All children (100%) fully recovered in 3-month lag period.

Conclusion: BMO in children is a cause of disability and it is often misdiagnosed and incorrectly treated. Environmental factors, such as underestimated articular or bone microtraumatisms, as well as joint hyper mobility, typical of paediatric age, in a bone turnover milieu of vitamin D deficiency could be the cause of the clinical conditions. Adequate vitamin D supplementation, associated with physical and analgesic therapy, are crucial in the management of BMO. We highlight the importance of supplementing vitamin D as recommended in the current guidelines, in order to avoid its deficiency and prevent invalidating clinical complaints.

REFERENCES

[1] Horas K. High prevalence of vitamin D deficiency in patients with bone marrow edema syndrome of the foot and ankle. Foot & Ankle International 2017.

[2] Patel. Primary bone marrow oedema syndrome. Rheumatology 2014; 53:785-792

[3] Mirghasemi SA. Bone marrow edema syndrome in the foot and ankle. Foot & Ankle International 2016.

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AB1061 SHORT TERM FOLLOW-UP RESULTS OF CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER AFTER CESSATION OF COLCHICINE: IS IT POSSIBLE TO QUIT?

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Background Familial Mediterranean Fever (FMF) is considered as the prototype of autoinflammatory diseases, and colchicine is the main treatment option for FMF. However, the data on cessation of colchicine treatment in FMF patients is limited

Objectives To define the characteristics of children with familial Mediterranean fever (FMF) whose colchicine treatment was discontinued and then to compare these features of the patients whose colchicine was restarted with the ones not restarted.

Methods Sixty-four out of 1786 children with FMF whom colchicine was stopped by the physician or patients/parents own decision were enrolled. These patients were grouped into two as: group 1; children whose colchicine was re-started and group 2; children whose colchicine was not re-started. The demographic, clinical and genetic data were collected and compared between group1 and group 2.

Results Colchicine was stopped in 59.4% (38/64) by the physician and 40.6% (26/64) of them had stopped colchicine by patients/parents will. Colchicine was ceased at a median of 10.6 (2.120.5) years of age, and attack- and inflammation-free periods of 18.2 (6-148) months. The median follow-up of 64 patients after colchicine cessation was 37.4 (6.4-154.7) months. It was re-started in seventeen patients due to attacks (n=11) or elevated acute phase reactants (n=6), while remaining 47 patients did not require colchicine. The age at cessation of the colchicine was lower (p= 0.04) and duration of colchicine treatment until its cessation was shorter (p= 0.007) in group 1 than group 2.

Conclusion Even though the results of our study are not satisfactory enough to endorse the hypothesis that colchicine may be discontinued by close follow-up; older age and long duration of colchicine treatment before cessation may be two important features that should be considered in the future studies.

REFERENCES

[1] Sonmez HE, Batu ED, Bilginer Y, Ozen S. Discontinuing colchicine in symptomatic carriers for MEFV (Mediterranean FeVer) variants. Clin Rheumatol. 2017;36(2):421-5.

[2] Ben-Zvi I, Krichely-Vachdi T, Feld O, Lidar M, Kivity S, Livneh A. Colchicine-free remission in familial Mediterranean fever: featuring a unique subset of the disease-a case control study. Orphanet J Rare Dis. 2014;9:3.

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AB1062 INTER-LABORATORY COMPARISON OF TYPE I INTERFERON SIGNATURE ANALYSES: PAVING THE WAY TO SHARE RECOMMENDATIONS.

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Background Interferon (IFN) signature analysis is experimentally used to classify pathological conditions characterized by a type I IFN dysregulation (i.e. monogenic interferonopathies, dermatomyositis, systemic lupus erythematosus), and to formulate targeted therapy approaches.Indeed, IFN signature is used to differentiate patients with IFN-related inflammation from conditions predominantly mediated by other cytokines (e.g. JIA and periodic fevers), through the calculation of an IFN score (IS). However, at the moment, there is not a shared threshold able to discriminate among different inflammatory conditions.

Objectives To characterize the IS in different inflammatory diseases and evaluate the concordance of IFN signature results among the laboratories of the three Italian Hospitals.

Methods Assessment of the expression in peripheral blood of six IFN-induced genes (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1) in Real Time PCR, referring to a calibrator sample (healthy controls). Calculation of the "interferon score" (IS) for each patient using the median fold change of the six relative quantifications.

50 patients with different inflammatory disorders considered not related to IFN (e.g. Crohn, JIA, hereditary periodic fevers) were compared with established type I IFN-related diseases (SLE, monogenic interferonopathies, dermatomyositis). We analysed the concordance of the clinical classification of different inflammatory diseases and the IS results.To assess the inter-laboratory variability, twenty patients with different degree of type I IFN inflammation were analysed at three different laboratories.

Results Despite the IFN signature showed a similar and comparable trend, the IS was not consistent between different laboratories, in particular for samples with higher IS score. Thus, the concordance between clinical classification and IS could be assessed only separately for each laboratory. Although in each series IFN-related disorders showed a IS significantly higher than other kind of inflammatory disorders, preliminary results suggest there is no clear threshold able to differentiate among these groups.

Conclusion Analysis of type I IFN activation in peripheral blood showed a relevant inter-laboratory variability between our three centers, limiting the possibility of identifying a shared defined threshold to differentiate inflammatory syndromes, and suggesting the need to determine reproducible calibrator samples. Cooperation between different institutes could facilitate the collection of clinical and laboratory data in a common database, to exchange expertise in type I IFN-mediated diseases, and provide practical advices for IFN signature assessment and interpretation in the clinical practice.

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AB1063 INTERSTITIAL LUNG DISEASE IN A NEWBORN AFFECTED BY MEVALONIC ACIDURIA

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Background: Mevalonic aciduria (MA) is the most severe phenotype of mevalonate-kinase deficiency (MKD), with early onset and poor prognosis. Given its rarity and its unspecific symptoms, MA diagnosis may be

challenging in the newborn. To our knowledge, interstial lung involvement has never been described as onset feature in MKD.
Objectives: We report the case of a newborn affected by MKD characterized by interstitial lung disease.
Methods: The patient underwent laboratory and radiology evaluation as clinically indicated. Direct Sanger sequencing was used to screen the 10 exons of the MVK gene.
Results: A female neonate born at term from consanguineous parents was referred to our hospital at 16 days of life (DOL) for mild hypotonia and persistent raised inflammatory markers despite antibiotic therapy. Infectious work-up was negative. Chest x-ray revealed bilateral perihilar peribronchial thickening. Electroencephalography reported moderate diffuse anomalies of background activity without major abnormalities. On DOL 20 the first episode of fever was recorded. Due to worsening tachypnea and persistent abnormal chest x-ray, a pulmonary CT scan was performed and showed diffuse groundglass bilateral infiltrates consistent with alveolar-interstitial lung disease. On DOL 22 a maculo-papular skin rash appeared on feet and hands, vanishing spontaneously 24 hours later. Bone marrow examination and levels of perforins, neuron-specific enolase and urinary catabolites of catecholamines were normal. A total body MRI was normal except for a mild cerebellar hypoplasia and the known interstitial lung disease. The patient kept presenting hypotonia, relapsing episodes of fever and skin rashes, developed severe anemia and failure to thrive. Type-I IFN signature was negative. A genetic test was requested, as well as quantification of urinary levels of mevalonic acid, which were markedly elevated. Direct Sanger sequencing allowed to detect a homozygous c.709A>T missense mutation in the exon 8 of the MVK gene, coding for a protein substitution p.T237S, classified as pathogenic in the INFEVERS database and therefore consistent with the diagnosis of MKD. Both parents and her sister were heterozygous carriers of the same mutation. On DOL 38 treatment with anakinra was started, with prompt regression of fever and skin rash, decrease in inflammatory markers, increase in reticulocytes count and weight gain. Hypotonia improved but persisted. The patient was discharged from hospital on DOL 56 in good clinical conditions, with acute phase reactants within the normal range and mild hypotonia. She is now 4 months old, still on anakinra treatment without adverse events.
Conclusion: Autoinflammatory diseases in the neonatal period are a diagnostic challenge. Clinical suspicion is crucial in order to perform specific laboratory and genetic testing and start appropriate treatment. Interstitial lung involvement may be present in MKD and, together with increased inflammatory markers, could be the first manifestation of the disease.

REFERENCES

[1] Ter Haar NM, et al. The Phenotype and Genotype of Mevalonate Kinase Deficiency: A Series of 114 Cases From the Eurofever Registry. Arthritis Rheumatol. 2016;68:2795-805.
[2] Papa R, et al. A web-based collection of genotype-phenotype associations in hereditary recurrent fevers from the Eurofever registry. Orphanet J Rare Dis. 2017;12:167.

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AB1064 LONG-TERM SAFETY AND EFFICACY OF ADALIMUMAB IN GREEK ADULTS WITH JIA OR NON-INFECTIOUS UVEITIS AT THE TRANSITION PERIOD

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Background: Our previous publication on Juvenile Idiopathic Arthritis (JIA) revealed that half of the pts had flares in adulthood, despite previous administration of several anti-TNFs.
Objectives: a. To describe the long-term outcome of adults with JIA or non-infectious uveitis (NIU), exposed to Adalimumab (ADA) as the single or last biologic during the transition period. b. To evaluate our model of transition in a subgroup of refractory to conventional DMARDs JIA or NIU pts, in the 1st Greek Transition Clinic for Pediatric Rheumatic Diseases.
Methods: Retrospective cohort analysis of Greek adults with JIA or NIU between 2004 and 2018. The JIA activity state was assessed by 2 quantitative tools: the Juvenile Arthritis Disease Activity Score-10 (JADAS-10, Clinical Remission [CR], Low, Moderate and High Disease Activity [LDA, MDA, HDA], respectively) and Wallace criteria (CR on/off ADA). Baseline was defined as the 1st ADA dose
Results: 28 pts were enrolled: 24 JIA pts (female 18), aged 20.6±3.1 yrs, for a f/u of 6.5±3 years (Group-A) and 4 female pts with active uveitis (2 with JIA-associated and 2 with NIU, mean aged: 18.9 yrs, f/u: 2.3 yrs) (Group-B). The age at baseline was 14.1±3.2 yrs in Group-A and 16.7 yrs in Group-B. The lag time from JIA onset to baseline was 6.3±3.8 yrs and the JIA subtypes were: 37.5% polyarthritis RF neg, 33.3% extended oligoarthritis, 20.8% enthesitis-related arthritis, 4.2% persistent oligoarthritis, 4.2% psoriatic arthritis. 11/24 (45.8%) pts (Group-A) and 3/4 pts (Group-B) were ANA positive, 5/24 JIA-pts had a history of uveitis (20.8%). Naïve to anti-TNF drugs were 18 pts (75%) of Group-A and 4/4 from Group-B. The baseline JADAS-10 was 13.9±5.9. The ADA yr-administration was 5.3±2.3 in Group-A and 2 in Group-B. Compliance to ADA had 17/24 (70.8%) pts in Group-A and all from Group-B. Regarding safety, 4/28 patients (14.3%) experienced Events of Special Interest (1/33.6 patient-years), herpes zoster (n=1), anorexia nervosa (n=1), breast fibroadenoma (n=1) and uveitis (n=1). Among the Group-A pts: 4/24 (16.7%) discontinued ADA due to inefficacy and 1/24 due to pregnancy planning. 6/24 pts (25%) achieved CR and discontinued ADA after 5.3 ±1.6 yrs. CR off ADA lasted 15.5±9.8 mo. The rest 13/24 continued ADA at the last f/u. In Group-B, 3/4 were still on ADA and 1 pt discontinued ADA due to NIU remission after 4.2 yrs and sustained CR 16 mo off ADA. The median% of CR remission on ADA total administration period was 75% in Group-A and 100% in Group-B. Among the ongoing receivers: a) the JIA activity state at the last assessment was: CR 84.6%, LDA 7.7% MDA 7.7% (median JADAS: 0, Group-A), b) 100% were in remission in Group-B.
Conclusion: 86% of adult pts with JIA or NIU tolerate ADA well. Pts exposed to ADA achieved CR on/off medication in 75% and 25%, respectively.

REFERENCES

[1] Dimopoulou D, et al. Rheumatology (Oxford) 2017
*: Despoina Dimopoulou and Maria Trachana contributed equally
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AB1065 THE UTILISATION OF S100 PROTEINS TESTING IN PEDIATRIC RHEUMATOLOGY PATIENTS IN A TERTIARY CARE INSTITUTION AND IMPLICATIONS FOR CARE

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Background: S100 proteins are calcium-binding proteins of increasing value as biomarkers in various inflammatory conditions. The two highly studied members in this family, S100A8/9 and S100A12 have been considered sensitive biomarkers of disease activity in rheumatologic disorders as rheumatoid arthritis (1) and juvenile idiopathic arthritis (JIA) (2). They are considered more accurate than conventional inflammatory indices such as the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) (3).
Objectives: To evaluate the utilization of S100 proteins in the clinical setting as supportive diagnostic tools as well as their performance in evaluating disease activity.
Methods: Patients seen at the hospital's specialty clinics who had S100 proteins tested during their care from April 2017 to August 2018. A retrospective chart review was performed to collect data on serum S100 protein levels, other inflammatory markers as CRP and disease activity measured as active joint count (AJC) in JIA patients and the presence of systemic symptoms in systemic JIA (sJIA) patients.
Graphpad Prism Version 7.05 was used for data analyses. Descriptive statistics were calculated for all variables. Comparisons were done by the Mann-Whitney U test and the Kruskal-Wallis test. Spearman correlation were calculated to assess association between S100 proteins and other numerical variables.

Results: A total of 164 patients were included. All 164 patients had S100A8/9 collected but only 151 had S100A12 samples. Patients with sJIA had higher levels of S100A8/9 and S100A12 compared to patients with non-systemic JIA (nsJIA) and periodic fever syndrome (PFS). CRP levels were not statistically different among diagnosis while S100 proteins were. Both S100A8/9 and S100A12 showed a good ability to differentiate sJIA from PFS (AUC=0.76 for both) compared to AUC=0.6 for CRP. At a cut-off value of 164 ng/ml, S100A12 was 71% sensitive and 73% specific in differentiating between sJIA and PFS (Figure 1). In JIA there was no correlation between S100 protein levels and AJC, either sJIA or nsJIA patients. S100A8/9 and S100A12 were significantly elevated in active sJIA patients compared to inactive ones while CRP levels were not different. S100 proteins levels where significantly higher during a flare of PFS compared to inactive disease, as well as CRP. There was no difference in S100 proteins and CRP in patients with or without tocilizumab treatment (small number on tocilizumab).
Conclusion: S100A8/9 and S100A12 are particularly elevated in sJIA compared to nsJIA and PFS. They are useful in distinguishing sJIA from other diagnoses with similar presentations, such as PFS. S100 proteins were significantly higher in active disease status of patients with sJIA and PFS compared to inactive status and their levels were closer associated with sJIA disease activity than CRP. The S100 proteins could provide valuable data in the work-up of patients with autoinflammatory conditions and monitoring disease activity in sJIA and PFS patients.

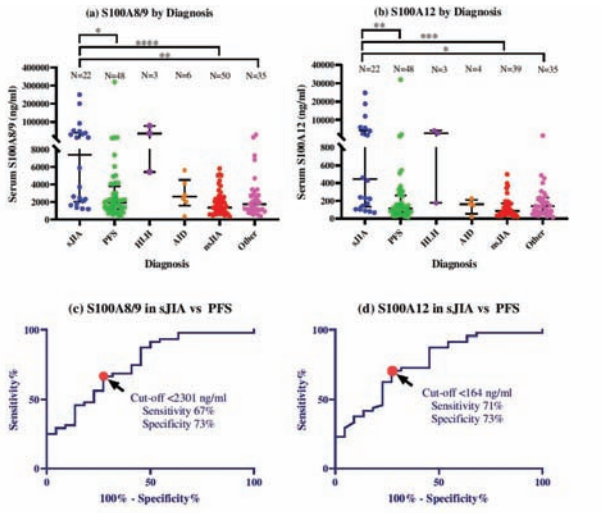


Figure 1. Panels (a) and (b) show serum levels of S100A8/9 (a) and S100A12 (b) across diagnoses. Values represent median and IQR (error bars). Comparison between diagnoses are done by Kruskal-Wallis test. Panels (c) and (d) show receiver operating charachteristic (ROC) curves for S100A8/9 (c) and S100A12 (d) in differentiating systemic juvenile idiopathic arthritis (sJIA) vs. periodic fever syndrome (PFS). The area under the curve (AUC) for both S100A8/9 and S100A12 is 0.76. Sensitivities and specificties for the cut-off values are outlined.

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$

Figure 1

REFERENCES

[1] Choi IY, Gerlag DM, Herenius MJ, Thurlings RM, Wijbrandts CA, Foell D, et al. MRP8/14 serum levels as a strong predictor of response to biological treatments in patients with rheumatoid arthritis. Annals of the Rheumatic Diseases. 2015;74:499-505.
[2] Foell D, Wittkowski H, Hammerschmidt I, Wulffraat N, Schmeling H, Frosch M, et al. Monitoring Neutrophil Activation in Juvenile Rheumatoid Arthritis by S100A12 Serum Concentrations. Arthritis and Rheumatism. 2004.
[3] Frosch M, Ahlmann M, Vogl T, Wittkowski H, Wulffraat N, Foell D, et al. The myeloid-related proteins 8 and 14 complex, a novel ligand of toll-like receptor 4, and interleukin-1β form a positive feedback mechanism in systemic-onset juvenile idiopathic arthritis. Arthritis and Rheumatism. 2009.

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AB1066

DEFICIENCY OF ADENOSINE DEAMINASE 2: THE IMPORTANCE OF A DIAGNOSIS BEFORE IRREVERSIBLE DAMAGE

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Background: In 2014, two independent groups, Zhou et al.(1) and Navon-Elkan et al.(2), described the first 34 patients with disease-associated mutations in adenosine deaminase 2 (ADA2*).*
Objectives: To describe a new case of ADA2 deficiency (DADA2) in a 15 years old girl presenting with acute lower limb flaccid paralysis.
Methods:
Results: A 15 years old girl presented with acute lower limb flaccid paralysis. Neurologic exam showed peripheral deficit of the VII cranial nerve, absent motor activity at lower limbs with sensitive deficit. At physical examination she had marked and diffuse livedo reticularis. She underwent a brain and spinal magnetic resonance imaging (MRI) revealing multiple areas of signal abnormalities (T2 hyperintensity) in both thalamus and basal ganglia, small area in the spinal cord at C2-C3, at D10-D11 and L1 levels; these images were related to vascular damage. Blood exams showed high blood counts and inflammatory markers (C-reactive protein 16.76 mg/dl). Coagulation was normal, antiphospholipid and antinuclear antibodies were negative, immunological work-up showed normal immunoglobulins level, T and B phenotype. She received intravenous steroid and high-dose intravenous immunoglobulin. The constellation of findings led to clinical suspicion for DADA2, which was confirmed by low plasma ADA2 activity. For the presence of microhematuria, worsening proteinuria and hypertension, vascular ultrasound was performed with no evidence of renal artery stenosis. She underwent renal biopsy negative for glomerulonephritis, renal vasculitis and amyloidosis. Following the diagnosis of DADA2, she was initiated on etanercept 50 mg once weekly and she was able to taper steroid with normalization of inflammatory markers and improvement of skin rash.
The girl is the second of 3 children, born from consanguineous parents of Italian origin. By the age of 1 she started suffering from fever, arthritis, pericarditis with elevated inflammatory markers and was diagnosed with systemic juvenile idiopathic arthritis (sJIA) and chronic disease anemia. At that time, she already presented livedo reticularis. She was treated with short term oral steroid and methotrexate with remission of fever and articular symptoms. At the age of 2 she had a convulsive crisis, polysomnography and brain MRI were negative. One year later she presented a convulsive status epilepticus, brain MRI was repeated and resulted negative. She was started on topiramate with no further crisis, treatment was stopped 2 years later. When she was 9, she was admitted for pancytopenia and she was diagnosed of Leishmania infection. The two siblings of the girl were tested for plasma ADA2 activity and both resulted deficient. The boy is 12 years old with mild development delay and a previous diagnosis of sJIA when he was 5. He was treated with steroid and Methotrexate with remission. The older sister is now 19 years old and she had an episode of erythema nodosum. Genetic test of all family members is still pending.
Conclusion: Given the important morbidity, especially in consanguineous families, a high index of suspicion is needed for early diagnosis and precocious intervention, before persistent neurologic damage has been established. Our report describes for the first time a new neurological presentation as acute transverse myelitis in a patient with DADA2.

REFERENCES

[1] Zhou Q, Yang D, Ombrello AK, Zavialov A V., Toro C, Zavialov A V., et al. Early-Onset Stroke and Vasculopathy Associated with Mutations in ADA2. N Engl J Med. 2014;
[2] Navon Elkan P, Pierce SB, Segel R, Walsh T, Barash J, Padeh S, et al. Mutant Adenosine Deaminase 2 in a Polyarteritis Nodosa Vasculopathy. N Engl J Med. 2014.

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AB1067 **THE IMPACT OF ACUTE RHEUMATIC FEVER IN A PROVINCE OF CENTRAL-NORTH ITALY**

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Background: Acute rheumatic fever (ARF) is a multisystem complication of group A streptococcal (GAS) infection. The incidence of ARF varies greatly in different geographic areas, with the highest incidence in Asia, Eastern Europe, and Australia (10-350 out of 100 000 per year) (1) and lowest (0.5-3 out of 100 000) in the US and Western Europe.
In 2015 the latest version of Jones Criteria has been published (2), incidence less than 2 out of 100.000 per year was established to define low-risk (LR) population. Due to the lack of nationwide epidemiologic data in Italy, it is difficult to define the correct population Jones criteria's category to use.
Objectives: To estimate the incidence of ARF in a metropolitan area of Central-North Italy and to study the clinical characteristics of the disease in a developed country.
Methods: We retrospectively analyzed the data of all patients with ARF aged 5-14 years old, diagnosed according to the classical and now LR Jones criteria (2), referred to Sant'Orsola-Malpighi Hospital of Bologna from January 2012 to December 2017 living in the province of Bologna.
Results: We identified a total of 24 patients diagnosed by ARF. In the province of Bologna, the inhabitants between 5 and 14 years of age varied from 82.967 in 2012 to 89.699 in 2017. Every year the annual incidence of ARF was above 2 out of 100.000. The highest incidence was reported in 2013 with 8 new diagnosis (incidence of 9.3 out of 100 000 per year). Carditis was present in 20 patients (83.3% of cases), chorea in 8 children (33.3%). Only 3 patients presented polyarthritis at diagnosis while 9 had polyartralgia and 3 presented with monoarthritis. In 6 patients the diagnosis followed the onset of chorea and no joint involvement was recorded. In 5 patients the diagnosis of ARF was made after the detection of classical cardiac findings without other major criteria. Cardiac involvement was characterized by mitral regurgitation in 17 cases and aortic regurgitation in 10 (8 patients with mitral aortic involvement). Five patients presented with fever ($\geq$38.5°C), 11 children had elevated inflammatory markers as erythrocyte sedimentation rate (ESR) $\geq$ 60 mm/h and/or C-reactive protein (CRP) $\geq$3.0 mg/dL. Only 5 patients had positive swab for GAS. Twelve patients (50%) were treated with steroid. Fourteen patients received secondary prophylaxis every 28 days, two of them switched to every 21 days.
Conclusion: Our study confirms the previous published data of Breda *et al.* (3) and Licciardi *et al.* (4) in other Italian areas supporting the evidence for high risk (HR) in our region. Furthermore, this study shows that in our population only few patients had the classical polyarthritis presentation. It is important to consider the new HR criteria for arthritis in order not to miss diagnosis. A careful clinical history is needed because the demonstration of GAS infection is often difficult. These data may strengthen the hypothesis to consider our whole country as a HR area for ARF. A nationwide study is mandatory.

REFERENCES

[1] Carapetis J, McDonald M, Wilson N. Acute rheumatic fever. Lancet 2005;366:155-68.
[2] Gewitz H, Baltimore R, Lloyd T, Craig S, Stanford S, Carapetis J. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. Circulation 2015;131:1806-18.
[3] Breda L, Marzetti V, Gaspari S, Del Torto M, Chiarelli F, Altobelli E. Population-based study of incidence and clinical characteristics of rheumatic fever in Abruzzo, central Italy, 2000-2009. J Pediatr. 2012 May;160(5):832-6.e1.
[4] Licciardi F, Scaioli G, Mulatero R, Marolda A, Delle Piane M, Martino S, Montin D, Tovo PA. Epidemiologic Impact of the New Guidelines for the Diagnosis of Acute Rheumatic Fever. J Pediatr. 2018 Jul;198:25-28.e1.

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AB1068 **CLINICAL FEATURES IN TURKISH CHILDREN WITH CHRONIC NON-BACTERIAL OSTEOMYELITIS**

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Background: Chronic non-bacterial osteomyelitis (CNO) is a rare bone disease of autoinflammatory origin. CNO patients present with bone, joint pain and swelling. Other autoinflammatory disorders such as palmoplantar pustulosis, psoriasis and inflammatory bowel disease may accompany CNO.
Objectives: Our aim is to determine demographic, clinical and radiological characteristics of Turkish children with CNO.
Methods: Clinical, laboratory features and imaging findings were retrospectively analyzed in 28 CNO Turkish patients from three pediatric rheumatology centers. Clinical findings, radiological data, treatments and outcome were evaluated.
Results: Of the 28 CNO patients, 10 (35.7%) female and 18 (64.3%) were male. Mean age at diagnosis was 9.54 (3-16.5) year. The lag time between symptoms and diagnosis was 6.5 (0-60) months. The median follow-up time was 18.5 (1-107) months. At the time of admission, symptoms were arthralgia (75.0%), bone pain (64.3%), limping (32.1%), swelling (28.6%), weakness (10.7%), and fever (3.6%). Two patients had inflammatory bowel disease (IBD) and six had familial Mediterranean fever (FMF). The bone lesions were mostly multifocal (%96.4),%3.6 was unifocal. The most frequently involved bones were femur (67.9%), tibia (53.6%) and pelvic bones (32.2%). (Table I) The patients had mildly elevated CRP and ESH levels. HLA B27 association was 25%. ANA was positive in 5%. All patients were RF negative. Six patients had mutations in the MEFV gene, all of them had M694V allele. The most common finding in Histopathological examination (n=9) demonstrated sterile mixed cell infiltration composed of lymphocyte and neutrophils. MRI results were mostly defined as bone marrow edema, and bone scan findings showed increased osteoblastic activity. All of patients received NSAIDs. Other drugs were methotrexate (46.4%) sulfasalazine (39%), steroids (25%), anti-TNF drugs (32%), and pamidronate (25%). Response to treatment was partial in 32.1%, whereas 39.3% patients had complete remission. There was no response in 8 patients (28.6%).
Conclusion: CNO was first described by Giedion in 1972 as multifocal bone lesions of inflammatory origin.[1] There are 500 CNO patients reported in the literature as individual or case series.[2] The laboratory findings are nonspecific and the diagnosis is mostly clinical and radiological. MRI and bone scan are the most commonly used imaging modalities. Histopathological results are non-specific, and may be necessary to exclude infection and malignancy. NSAIDs, sulfasalazine and methotrexate are mostly used in the treatment. Steroids, biological drugs and pamidronate are other options. There is still need for further treatment options, because there are significant number of resistant patients.

REFERENCES

[1] - Taddio A, Ferrara G, Insalaco A, Pardeo M, Gregori M, Finetti M, Pastore S, Tommasini A, Ventura A, Gattorno M. Dealing with Chronic Non-Bacterial Osteomyelitis: a practical approach Pediatric Rheumatology (2017) 15:87
[2] - Marion R. Roderick, Ethan S. Sen and Athimalaipet V. Ramanan Chronic recurrent multifocal osteomyelitis in children and adults: current understanding and areas for development *Rheumatology*, Volume 57, Issue 1, 1 January 2018, Pages 41–48 doi:10.1093/rheumatology/kex066

Affected bones	***n***	***%***
Femur	19	67.9
Tibia	15	53.6
Pelvic bones	9	32.1
Calcaneus-talus	6	21.4
Clavicula	4	14.3
Mandible	3	10.7
Vertebra	2	7.1
Metatars	2	7.1
Sacrum	1	3.6
Cranium	1	3.6
Localisation	***n***	***%***
Metaphysis	17	60.7
Metaphysis-epiphysis	6	21.4
Metaphysis-diaphysis	4	14.3
Diaphysis	1	3.6

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AB1069 HYPERZINCAEMIA AND HYPERCALPROTECTINEMIA SYNDROME: MORE THAN JUST AUTOINFLAMMATION?

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Background: Hyperzincaemia and hypercalprotectinemia (HandH) syndrome has been described as a new rare entity characterized by recurrent infections, dermatological involvement, increased inflammatory markers, hepatosplenomegalia and anemia. Little is known about its heterogeneous presentation, pathophysiology and treatment.
Objectives: To describe three cases with HandH syndrome
Methods: Serum calprotectin (MRP8/14) was measured according to Buehlmann assay (ELISA) and plasmatic zinc by atomic absorption spectrometry
Results: Three patients were referred to our centre because an history characterized by recurrent episodes of skin rash, severe oral aphtosis and increased level of serum amyloid A (SAA). Patient 1 presented, since the age of ten years, with recurrent episodes of fever and rash; skin biopsy showed a picture consistent with a lymphocytic lichenoid vasculitis resembling erythema multiforme. Patient 2 presented at birth, with hemolitic anemia and thrombocytopenia. At the age of 5 she was admitted to another hospital due to EBV related hemophagocytic limphohystiocytosis (HLH). At the age of 8, she was first seen at our center because of a persistent desquamant erythematous rash with recurrent abdominal pain and recurrent arthritis. Intestinal biopsy showed small intestine inflammation (erosions in the digiunum). Patient 3 presented with recurrent episodes of fever, rash, two episodes of transient hip synovitis and muscoloskeletal pain. A bone scintigraphy was performed resulting normal. Patients 1 and 2 suffered from recurrent infections (pneumonia, otitis, skin abscesses). Immunological studies revealed in patient 2 a reduction of memory B cells and a reduced response to Toll like receptor 9 agonist. Of note, all the patients presented in their medical history at least one episode of vasculitis: patients 1 and 3 suffered from Schonlein-Henoch's purpura at the age of 11 and 3 respectively and patient 2 had at the age of 2 years an undefined vasculitis (evaluated elsewhere). Laboratory tests showed in all patients elevated inflammatory markers, zinchemia and serum calprotectin (table)

	Patient 1	Patient 2	Patient 3
Age at 1st evaluation (years)	14.3	7.8	4.9
Sex	F	F	M
Clinical features	Recurrent fever, recurrent infection, vasculitis, skin rash, musculoskeletal pain	Hemolitic anemia, thrombocytopenia, HLH, vasculitis, recurrent infections, recurrent fever, arthritis, skin rash, gastrointestinal involvement	Recurrent fever, skin rash, vasculitis, arthritis, musculoskeletal pain
SAA	13-23	27,5-76,4	20
Zinchemia (mcg/dl) (n.v. 80-125)	132-143	102-233	147
Serum MRP8/14 (ng/ml) (n.v. < 2900)	22431	10383	10363

Figure 1

Conclusion: We report three patients with high serum levels of calprotectinemia and zinch presenting with a clinical phenotype consistent with previously reported cases. The presence of vasculitis in all of the patients suggest that it may represent the first symptom of this condition. Vasculitis could lead to an increase of serum calprotectin already proposed as a marker of vascular impairment. Moreover, considering the immunological defect detected in one of our patient, we speculate that recurrent infections described in this syndrome may underline an immune-dysregulation process in which the role of zinc metabolism needs to be assessed
Disclosure of Interests:: Andrea Uva: None declared, Claudia Bracaglia: None declared, Silvia Federici: None declared, Camilla Celani: None declared, Manuela Pardeo: None declared, christoph kessel: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer, Antonella Insalaco: None declared
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AB1070 MICROVASCULAR NAILFOLD ALTERATIONS BY VIDEOCAPILLAROSCOPY IN PATIENTS WITH RHEUMATOLOGICAL SYMPTOMS WITH JUVENILE INFLAMMATORY BOWEL DISEASE

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Background: Juvenile Inflammatory Bowel Disease (jIBD) is a chronic relapsing inflammatory condition of the gastrointestinal system that includes Crohn's disease (CD) and Ulcerative Colitis (UC) and develops during childhood or adolescence in up to 25% of patients and affects the patients and parent s quality of life. Endothelial dysfunction is considered one of the etiological factors of jIBD. Nailfold videocapillaroscopy is one of the best and safest diagnostic non-invasive imaging techniques to analyze microvascular abnormalities. Previous studies describe the involvement of the microvasculature in the pathogenesis of this diseases, suggested that chronic mesenteric vasculitis is a pathogenetic mechanism in CD. Nailfold abnormalities founded are similar to those observed in some systemic vasculitidies. Subpapillary venous plexus dropout and low vessel density were previously reported.
Objectives: In this abstract we describe nailfold videocapillaroscopy findings in patients with jIBD and their correlation with disease activity.
Methods: This is a prospective and analytical study thad recruited pediatric patients between 2 and 18 years with jIBD. A single cross-sectional 8-finger nailfold videocapillaroscopy was performed using a 200x optical probe videocapillaroscope. The images were collected, encoded and stored using the Optipix® software. Qualitative, quantitative and semi-quantitative assessment for architecture were scored following the international definitions for the capillary abnormalities Blood chemistry, C-reactive Protein, erythrocyte sedimentation rate, antineutrophil cytoplasmic antibody, and calprotectin were performed. Sociodemographic data, clinical eva- luation, confirmation of IBD criteria, disease history, and activity evaluation were collected from patients clinical records. Statistics were performed using Spearman test to evaluate the correlation coefficient between the variables under study.
Results: 10 patients with jIBD were included 60% male, 50% Ulcerative Colitis and 50% Crohn s Disease. 20% had severe disease according the Pediatric Ulcerative Colitis Activity index, Pediatric Crohon s Disease activity index showed mild activity in just one patient. Rheumatological manifestations were found in 40%,4 had arthritis, systemic vasculitidies in 2 and 10% hematological manifestations. Abnormal endoscopy in 60% showing pancolitis. Normal microvasculature pattern were only found in 3 patients (25%), microangiopathy was found in 75%, edema of the nailfold bed was present in n=6 patients, a low capillary density was found in 100% of the patients with disease activity. A statistical negative correlation between the number of capillarities per millimeter and disease activity was found (coefficient -0.936, p=0.001).
Conclusion: Previous data showed that low capillary density was find in patients with jIBD, the data in this pilot study are consistent with those findings. The assessment of the microvasculature through the use of videcapillaroscopy could be useful in this diseases.

REFERENCES

1. Deban et al. Multiple Pathogenic Roles of Microvasculature in Inflammatory Bowel Disease: A Jack of All Trades. AJP June 2008, Vol. 172, No. 6 1457-1466

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AB1071 AUTO-IMMUNE AND INFLAMMATORY DISEASES IN CHILDREN WITH SICKLE CELL DISEASE: DIAGNOSTIC AND THERAPEUTIC ISSUES

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Background: Coexistent auto-immune and inflammatory diseases (AIID) and sickle cell disease (SCD) have been recently described in adults and children, however its frequency and physiopathology remain unclear (1–6).
Objectives: The aim of this study is the analysis of clinical and biological characteristics at AIID diagnosis and the evolution under treatment in children with SCD
Methods: Between May 1991 and March 2018, 35 of 3,800 SCD children diagnosed with AID in seven hospitals in Paris and suburb were analyzed in a retrospective survey.
Results: Thirty-five patients reported 44 AIID: auto-immune liver disease (AILD, n=13), inflammatory bowel disease (IBD, n=7), juvenile idiopathic arthritis (JIA, n=6), systemic lupus erythematosus (n=5), autoimmune hemolytic anemia (n=3), Sjögren's syndrome (n=2), histiocytic necrotizing lymphadenitis (n=2), vasculitis (n=2), myasthenia gravis (n=2), sarcoidosis (n=2), inflammatory uveitis (n=1), sclerodermia/juvenile dermatomyositis (n=1). Median age at diagnosis was 10 [2 – 18] years. The mean delay between first symptom and diagnosis was 15.5 (± 29) months. The time of diagnostic was significantly longer for patients with JIA compared to other AID (63 versus 10 days, p=0.004). Sixteen patients (45.7%) had hypergammaglobulinemia > 20 g/L at diagnosis. AILD had a hypergammaglobulinemia at the time of diagnosis (30.0g/L), with a statically significant decrease at the end of follow-up (18.2g/L, p=0,0048). Among 21 patients (60%) treated with systemic steroids, it triggered vaso-occlusive crisis in 14 (66.7%), one acute chest syndrome, one transient ischemic attack. Thirteen of 35 patients (37.1%) were managed with biotherapy for AIID, well tolerated. Three patients (8.6%) underwent stem cell transplantation, one died of a cortico-resistant and multipolar graft versus host reaction, two were cured of both AIID and SCD. Nine severe infections were reported, four under steroids, five under biotherapy.
Conclusion: Diagnosis and therapeutic care of coexistent auto-immune and inflammatory diseases are difficult and challenging in children with SCD. Annual monitoring of inflammatory markers could be recommended to detect AIID earlier and prevent diagnostic delay in case of high ascension in SCD patients.

REFERENCES

[1] Li-Thiao-Te V, Uettwiller F, Quartier P, et al. Coexistent sickle-cell anemia and autoimmune disease in eight children: pitfalls and challenges. Pediatr Rheumatol Online J. 17 janv 2018;16(1):5.
[2] Cherner M, Isenberg D. The overlap of systemic lupus erythematosus and sickle cell disease: report of two cases and a review of the literature. Lupus. juin 2010;19(7):875–83.
[3] Adelowo O, Edunjobi AS. Juvenile idiopathic arthritis coexisting with sickle cell disease: two case reports. BMJ Case Rep. 1 déc 2011;2011.
[4] Michel M, Habibi A, Godeau B, Bachir D, Lahary A, Galacteros F, et al. Characteristics and outcome of connective tissue diseases in patients with sickle-cell disease: report of 30 cases. Semin Arthritis Rheum. déc 2008;38(3):228–40.
[5] Galmiche S, Amiot X, Georgin-Lavialle S, et al. Maladies inflammatoires chroniques de l'intestin chez des patients atteints de syndrome drépanocytaire majeur : à propos de 6 cas. Disponible sur: http://www.em-premium.com.frodon.univ-paris5.fr/article/1122766/resultatrecherche/34
[6] Jitraruch S, Fitzpatrick E, Deheragoda M, et al. Autoimmune Liver Disease in Children with Sickle Cell Disease. J Pediatr. oct 2017;189:79-85.e2.

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AB1072 UVEITIS IN PEDIATRIC RHEUMATOLOGY: TERTIARY CENTER EXPERIENCE IN TURKEY

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Background: Since pediatric uveitis is generally asymptomatic, the diagnosis and treatment may be mostly delayed. Severe complications and visual loss may be observed even at the initial visit. Pediatric uveitis is tend to be chronic, persistent, recurrent, and the management may be complex (1).
Objectives: The aim of this study is to report epidemiology, etiology, clinical features, management and the outcomes of non infectious pediatric uveitis at a tertiary pediatric rheumatology center in Turkey.
Methods: The clinical records of the patients with non infectious uveitis who were followed up by department of pediatric rheumatology and ophtalmology were reviewed, from January 2013 to June 2018, retrospectively. The inclusion criteria were as follows being age ≤ 16 years, following up at least 6 months in both the ophtalmology and pediatric rheumatology clinics. Uveitis was categorized anatomically according to the Standardization of Uveitis Nomenclature criteria (2).
Results: Of 37 patients (67 eyes), 45,9% were female. Mean age of onset was 8, 5 ± 4, 4 years (1,6 - 15,6), mean follow-up was 60 ± 42 months (6 - 191). The general features of uveitis were anterior, idiopathic and bilateral in this study similar to literature (Table 1).The most common systemic diseases associated with uveitis were juvenile idiopathic arthritis (JIA).Two patients improved with local medications, while the remaining 35 patients required systemic treatments such as short-time (oral/iv) corticosteroids (CS) in 94.5% of them, methotrexate (MTX) in 86.4%, azathioprine (AZA) in 5.4%, adalimumab (ADA) in 67.5%, tocilizumab (TCB) in 2.7%. In 26.1% of patients receiving ADA who did not respond to standard dose of ADA, we had to shorten the dosage intervals of ADA from every 2 weeks to every week. At least 1 ocular complication was observed in 83.7% of the patients, such as cataract, glaucoma, band keratopathy, synechiae, macular edema and retinal detachment. Four (10.8%) patients had moderate visual loss and 6 (16.2%) patients severe visual loss (3). The prevalence of surgery in our study was 18.9% for cataract and glaucoma treatment.
Conclusion: Diagnosis and management of uveitis in childhood is complicated. Despite the new medication options, the advancements in diagnosis and surgical techniques, the complications are still high. Usage of shorter dose interval of ADA may be an alternative to control of the disease in patients with unresponsive to standard dosage of ADA. However large-scale clinical trials are required to assess the efficacy and safety of this treatment.

REFERENCES

[1] Tugal-Tutkun I. Pediatric uveitis. J Ophthalmic Vis Res 2011; 6: 259-269.
[2] Jabs DA, Nussenblatt RB, Rosenbaum JT, et al. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol 2005; 140:509–16.
[3] World Health Organisation. Report of WHO/IAPB scientific meeting, Hyderabad, India 13-47. Childhood Blindness Prevention. WHO/PBL/87. 1999.

Abstract AB1072 Table 1. Clinical features of patients according to the anatomical classification of uveitis.

		Anterioruveitis 21 cases (56.8%)	Intermediateuveitis 12 cases (32.4%)	Posterioruveitis 1 case (2.7%)	Panuveitis 3 cases (8.1%)	Total 37 cases (100%)
Gender	**Female**	9(24.3%)	6 (16.2%)	1(2.7%)	1(2.7%)	17(45.9%)
	Male	12(32.4%)	6(16.2%)	0	2 (5.4%)	20 (54%)
Ocular involvement	**Unilateral**	3 (8.1%)	3(8.1%)	0	1(2.7%)	7 (18.9%)
	Bilateral	18 (48.6%)	9 (24.3%)	1(2.7%)	2(5.4%)	30 (81%)
Etiology	**Idiopathic**	13 (35.1%)	11(29.7%)	0	2(5.4%)	26 (70.2%)
	JIA	5 (13.5%)	0	0	0	5(13.5%)
	BehcetDisease	0	1(2.7%)	0	1(2.7%)	2(5.4%)
	Sarcoidosis	1(2.7%)	0	1(2.7%)	0	2(5.4%)
	TINU	2(5.4%)	0	0	0	2(5.4%)

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AB1072B THE CONSEQUENCES OF THE PROVISIONAL PAEDIATRIC RHEUMATOLOGY INTERNATIONAL TRIALS ORGANISATION JUVENILE IDIOPATHIC ARTHRITIS CLASSIFICATION CRITERIA

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Background Last year the International League of Associations for Rheumatology (ILAR) classification criteria for juvenile idiopathic arthritis (JIA), [1] were challenged by the provisional Paediatric Rheumatology International Trials Organisation (PRINTO) classification criteria.[2] Four disorders were proposed: (a) systemic JIA; (b) rheumatoid factor (RF)-positive JIA; (c) enthesitis/spondylitis-related JIA; and (d) early-onset antinuclear antibody (ANA)-positive JIA. Early-onset ANA-positive JIA is defined by: arthritis for ≥ 6 weeks, and early-onset (≤ 6 yrs), and presence of 2 positive ANA tests with a titer ≥ 1/160 at least 3 months apart with the exclusions of having systemic JIA, RF-positive arthritis, or enthesitis/spondylitis-related JIA.
Objectives To evaluate the shifts from the original subtypes of JIA in the new disorder of early-onset ANA–positive JIA.
Methods This study used data from the international PRINTO based registry regarding pharmacovigilance in JIA called Pharmachild.[3] For this analysis we used the data of 4,165 patients completely categorized following the ILAR 'oligoarthritis', 'RF-negative polyarthritis', 'psoriatic arthritis' and 'undifferentiated JIA' (UJIA) subtypes and with complete determination of ANA status. These patients were if possible reclassified in the early-onset ANA–positive JIA according to the provisional PRINTO classification criteria.
Results Table 1 shows the characteristics of all 4,165 patients according to the ILAR criteria. Of this final set of 4165 patients, 1279 (30.7%) were ANA-positive and 957 (74.8%) classified into the PRINTO 'early onset ANA-positive JIA' category. Of these 957, 2 patients were RF-positive, which is an exclusion criterion for the 'early onset ANA-positive JIA' category and therefore were not categorized as early onset ANA-positive JIA. The female proportion was higher than in any ILAR subtype being 83.0% (793/955). The origin (ILAR categories) of the 955 patients in the 'early onset ANA-positive JIA' category consisted of 33.7% patients with persistent oligoarthritis (322/955), 24.7% (236/955) with extended oligoarthritis, 28.0% with RF-negative polyarthritis (267/955), 4.2% with psoriatic arthritis (40/955) and 9.4% with UJIA (90/955).

	Persistent OJIA	Extended OJIA	RF negative PJIA	Psoriatic arthritis	UJIA
Total number of patients, n (%)	1283 (30.8%)	663 (15.9%)	1665 (40.0%)	210 (5.0%)	344 (8.3%)
Age of disease onset, years (IQR)	4.5 (2.5-8.3)	3.7 (2.3-1.7)	6.7 (2.9-11.3)	8.6 (3.4-13.3)	5.7 (2.6-10.8)
Female, n (%)	968 (77.6%)	541 (81.6%)	1283 (77.1%)	145 (69.0%)	228 (66.3%)
ANA positive, n (%)	424 (33.0%)	293 (44.2%)	384 (23.1%)	51 (24.3%)	127 (26.9%)

Table 1. Patient characteristics (4165 patients) divided in ILAR 2001 categories; correctly determined (taking all exclusion criteria into account).
OJIA= oligoarticular JIA, PJIA= polyarticular JIA

Conclusion This study shows that of all ANA-positive JIA patients belonging to the 'oligoarthritis', 'RF-negative polyarthritis', 'psoriatic arthritis' and 'UJIA' ILAR subtypes, 74.8% met the criteria for the PRINTO 'early onset ANA-positive' category. The female proportion was higher than in any ILAR subtype being 83.0%. This new category consists largely of 3 ILAR subtypes: persistent oligoarthritis (34%), extended oligoarthritis (25%) and RF negative polyarthritis (28%). Further studies on these provisional criteria are ongoing.

REFERENCES

[1] Petty RE, Southwood TR, Manners P et al. International League of Associations for Rheumatology Classification of Juvenile Idiopathic Arthritis: Second Revision, Edmonton, 2001. J Rheumatol. 2014
[2] Martini A, Ravelli A, Avcin T et al. Toward New Classification Criteria for Juvenile Idiopathic Arthritis: First Steps, PRINTO International Consensus. J Rheumatol. 2018 Oct 1
[3] Swart J, Giancane G, Horneff G et al. Pharmacovigilance in juvenile idiopathic arthritis patients treated with biologic or synthetic drugs: combined data of more than 15,000 patients from Pharmachild and national registries. Arthritis Res Ther. 2018 Dec 27

Disclosure of Interests Vera Mars: None declared, Joost F. Swart: None declared, Gabriella Giancane: None declared, Sytze De Roock: None declared, Anne Estmann: None declared, Marija Jelusic: None declared, Estefania Moreno Ruzafa: None declared, Jaime de Inocencio: None declared, Jelena Vojinovic: None declared, Agustin Remesal: None declared, M Laday: None declared, Rolando Cimaz: None declared, A V Cochino: None declared, Inmaculada Calvo Grant/research support from: received research grants from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK, Consultant for: Advisory boards: Novartis, AbbVie, Speakers bureau: AbbVie, Roche, Novartis, SOBI, M Harjacek: None declared, Nico Wulffraat: None declared, Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda.
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AB1072C CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS THE CORRELATION BETWEEN CAROTID INTIMA-MEDIA THICKNESS AND MARKERS OF INFLAMATION TO DETERMINE PRE-CLINICAL ATHEROSCLEROSIS

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. JIA is a heterogeneous group of disorders with different disease progression and prognosis. Cardiovascular

morbidity and mortality are becoming major health concerns for children with inflammatory rheumatic diseases. Inflammation has been suggested to play an important role in the pathogenesis of both atherosclerosis and JIA.
Objectives: objective of this study was to determine carotid intima-media thickness (cIMT) in children with JIA and their correlation with JIA subtype and markers of inflammation.
Methods: We included 112 patients (50 boys and 62 girls) with diagnosis of JIA for at least 6 mouths and 54 healthy control subjects (32 girls and 22 males).These all children were had normal body mass index, blood pressure, lipids and blood glucose levels to exclude conventional risk factors.
Carotid ultrasound for evaluation of cIMT was performed by same radiologist who was blinded to the participants' clinical and laboratory data. Patients datas were collected. We compared all cMIT values of patients and controls and investigated the relationship between inflammatory markers, disease status,periods and therapies.
Results: Our study showed that children with JIA had more increased cIMT values than controls. There was no correlation between disease subgroups, activity status, ANA, HLA-B27, RF positivity, WBC, ESR and CRP with cIMT. The cIMT values were not differences between patients used steroid, DMARD and biologic agents and non used. An increased active disease and total disease periods, decreased in mean platelet volüme were determined as independent risk factors at increased of cIMT.
Conclusion: The study showed that the patients with JIA had more risks than healthy controls for cardiovascular diseases.
Disclosure of Interests: None declared
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Other orphan diseases

AB1073 A RETROSPECTIVE COHORT STUDY OF IGG-4 RELATED DISEASE IN IRISH PATIENTS

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Background: Immunoglobulin (Ig) G4-related disease (IgG4RD) is a novel clinical entity characterized by elevated serum IgG4 concentration and tumefaction or tissue infiltration by IgG4-positive plasma cells.
Objectives: To describe the clinical presentations, laboratory features, imaging manifestations, histopathologic characteristics and treatments in a cohort of 38 patients with IgG4RD.
Methods: A retrospective study was performed at St. Vincent's University Hospital. Clinical, laboratory, imaging and histopathologic data was retrieved from electronic records. All data were assessed using SPSS 24.0.
Results: Median age was 59 years with M:F ratio= 2.2:1. 24 (63.2%) patients were between 25-65 years), 14 (36.8%) were >65 years. 23 (60.5%) patients fulfilled the Comprehensive Diagnostic Criteria for IgG4RD as 'definite', whereas 5 (13.2%) patients fulfilled 'probable' diagnoses and 10 (26.3%) patients fall in 'possible' category. GI manifestations (followed by pancreatic) were the most frequent clinical presentation. 23 (60.5%) patients presented with single organ involvement; pancreas was the most frequently involved organ (17/38, (44.7%)). 55.3% had a serum IgG4 level above 135mg/dL. Lymphoplasmacytic infiltration was the commonest histopathologic pattern reported in 29 (76.3%) specimens. 25 (65.8%) patients had received steroid therapy and 19 (50.0%) had a good response. 11 (28.9%) patients received immunomodulatory agents including Rituximab (n=4), Azathioprine (n=7), and Mycophenolate mofetil (n=4). Overall, 28 (73.7%) patients had complete remission with treatment.
Conclusion: IgG4RD is a rare entity in Ireland and an inadequately understood condition overall. Further research is required to better understand the pathophysiology, clinical course and optimal treatment for IgG4RD.

REFERENCES

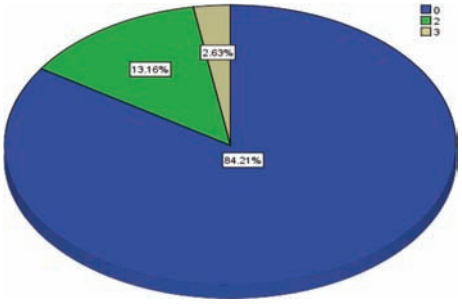
[1] Umehara H, Okazaki K, Masaki Y, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. Mod Rheumatol. 2012;22 (1):21–30.
[2] Okazaki K, Kawa S, Kamisawa T, Naruse S, Tanaka S, Nishimoril, et al. Clinical diagnostic criteria of autoimmune pancreatitis: revised proposal. J Gastroenterol. 2006;41(7):626–31.
[3] Hisanori Umehara et al, A novel clinical entity, IgG4-related disease (IgG4RD): general concept and details. Mod Rheumatol (2012) 22:1–14
[4] Inoue D, Yoshida K, Yoneda N, et al. IgG4-related disease: dataset of 235 consecutive patients. Medicine (Baltimore). 2015;94(15):e680.

Abstract AB1073 Table 1. Organ involvement in 38 patients with IgG4RD

Organ involved	Number of patients (%)
Pancreas	17 (44.7%)
Bile ducts (Biliary tract)	13 (34.2%)
Retroperitoneal mass	7 (18.4%)
Retro-orbital mass (Orbit adnexa)	4 (10.5%)
Lacrimal glands	3 (7.9%)
Salivary glands	2 (5.2%)
Lungs	2 (5.2%)
Lymph nodes	1 (2.6%)
Thyroid	1 (2.6%)
Testicles	1 (2.6%)
Kidney	1 (2.6%)

Abstract AB1073 Table 2. Histopathologic patterns in 38 patients with IgG4RD

Histopathologic pattern	Number of patients (%)
Lymphoplasmacytic infiltration	29 (76.3%)
Oblitrative phlebitis	2 (5.3%)
Lymphoplasmacytic infiltration + Increased esinophils number	1 (2.6%)
Lymphoplasmacytic infiltration + Storiform fibrosis + Oblitrative phlebitis	1 (2.6%)
Lymphoplasmacytic infiltration + Storiform fibrosis + Phlebitis without obliteration	1 (2.6%)



Abstract AB1073 Figure 1. IGG-4 Responder Index score in 38 patients with IgG4RD

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AB1074 AUTOIMMUNE/INFLAMMATORY SYNDROME INDUCED BY ADJUVANTS—ASIA—RELATED TO BIOMATERIALS: ANALYSIS OF 50 CASES

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Background: Systemic autoimmune or granulomatous disorders related to biomaterials of human use have rarely been described
Objectives: The aim of this study was to report cases of autoimmune/inflammatory syndrome induced by adjuvants (ASIA) related to biomaterial injections and prostheses, mainly silicone, hyaluronic acid, acrylamides and methacrylate compounds in a Spanish patient cohort.
Methods: This study is a retrospective analysis of clinical, laboratory, histopathological and follow-up data of 50 cases of patients suffering from late-onset, non-infectious inflammatory/autoimmune disorders related to bioimplants. Late onset was defined as 3 months or more post injection. Data were obtained through a further non-systematic but comprehensive review of the literature. Fifty cases of late-onset adverse reactions related to biomaterial injections or prostheses were reviewed.
Results: All cases had systemic complaints that could be categorised as ASIA. In all but five patients, inflammatory features at the implantation

site preceded distant or systemic manifestations. Abnormal blood tests were common. Localised inflammatory nodules and panniculitis in 88.88% evolved into a variety of disorders, viz., primary biliary cirrhosis, Sjögren's syndrome, sarcoidosis, human adjuvant disease, vasculitis, inflammatory bowel syndrome and inflammatory polyradiculopathy. 11.11% cases presented primarily with systemic autoimmune disorders.
Conclusion: Biomaterials and prostheses can provoke late-onset systemic autoimmune disorders fulfilling ASIA criteria, or present primarily local/regional inflammatory reactions that may eventually evolve into systemic autoimmune and/or granulomatous disorders which fall under ASIA

REFERENCES

[1] Hanke CW, Rohrich RJ, Busso M, Carruthers A, Carruthers J, Fagien S, et al. Facial soft-tissue fillers: assessing the state of the science conference proceedings report. J Am Acad Dermatol. 2011;64(4 Suppl):S53–65.
[2] Ellis DA, Makdessian AS, Brown DJ. Survey of future injectables. Facial Plast Surg Clin North Am. 2001;9:405–11.
[3] American Society of Plastic Surgery. Statistics of 2010, http://www.surgery.org/site/default/stats2010_1.pdf (2010, Accessed 01 Aug 2011).

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AB1075 IDIOPATHIC ORBITAL PSEUDOTUMOUR: A CASE SERIES AND LITERATURE REVIEW

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Background: Idiopathic orbital pseudotumour (IOP), also known as idiopathic orbital inflammatory syndrome is a benign, non-infective, inflammatory condition of the orbit without identifiable local or systemic causes. After Grave's disease and lymphoproliferative disorders, orbital pseudotumor is the 3rd most common ophthalmologic disease of the orbit and account for approximately 8-11% of all the orbital tumors.Pathogenesis of orbital pseudotumor remains elusive but several lines of evidence point to immune-mediated processes as the likely underlying ocular mechanism. The etiology of orbital pseudotumor is unknown, but infection, autoimmune disorder, and aberrant wound healings have been put forward as possibilities. The ocular manifestations of orbital pseudotumor may include periorbital edema, erythema, proptosis, ptosis, diplopia and pain with eye movements.
Objectives: Describe clinical and demographic characteristics, most frequent diagnoses, immunological serology and treatments in patients with Orbital Pseudotumor.
Methods: We performed a retrospective cohort study of adult and pediatric patients with orbital pseudotumor diagnosis referred to the Department of Rheumatology of the Fray Antonio Alcalde Civil Hospital in Guadalajara Jalisco, Mexico, from 2012-2018. We collected data that included demographic data of the patient, symptoms, laboratory data that included antibodies, management plans and results.
Results: A total of 20 patients diagnosed with orbital pseudotumor, with a mean age of 42±18.5 years, 3 pediatric patients and 65% women.
Clinical manifestations were: 90% unilateral, 90% lacrimal gland involvement, 75% ptosis/proptosis, 40% conjunctival hyperemia, 35% ocular pain, 20% decreased visual acuity, 15% headache and no optic nerve involvement. The findings were similar between adults and children.
The most common diagnoses were: 40% idiopathic, 10% orbital cellulitis, 10% granulomatosis with polyangiitis and 5% each of the following: systemic lupus erythematosus, Sjögren's syndrome, dacryoadenitis and myositis due to IgG4, Kimura's disease, Mikulicz, meningioma and cavernous sinus aneurysm.
All patients underwent excisional biopsy, and the histopathological report showed the following findings: 40% non-specific chronic inflammation, 30% non-specific chronic dacryoadenitis, 5% granulomatous inflammation/vasculitis, 10% chronic sclerosing inflammation-IgG4 and 15% others.
Only 9 of the 20 patients underwent immunological serology, finding positivity in:15% for c-ANCA, 10% PR3, 5% p-ANCA, 10% MPO, 5% ANAs and 10% elevated blood levels of IgG4.
Regarding treatment, 100% received glucocorticoids, and received immunomodulatory therapy: 20% received azathioprine, 5% mycophenolate mofetil, 20% methotrexate, 15% cyclophosphamide IV, 15% rituximab and 25% received no other medication.
Conclusion: The orbital pseudotumor might be the first manifestation of an autoimmune or autoinflammatory disease, the early and correct diagnosis is necessary to avoid permanent sequelae.

REFERENCES

[1] Yuen SJ, et al. Idiopathic orbital Inflamation: Ocular mechanism and clinicopathology. Ophthalmol Clin North Am 2002;15:121-6.
[2] Grouteau E, et al. Acute orbital myositis and idiopathic inflammatory pseudotumor in children: cases. Arch Pediatr 1998;5:153-158.
[3] Chaudhry IA, et al. Orbital pseudotumor: Distinct diagnostic features and management. Middle East Afr J Ophthalmol 2008;15:17-27

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AB1076 TREATMENT REVIEW OF ADULT-ONSET STILL'S DISEASE IN A TERTIARY HOSPITAL

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Background: Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder of unknown aetiology, and approximately 60% or 70% of the patients can develop a chronic poliphasic form of the disease or a chronic polyarthritis. Due to the rarity of this disease, the treatment of AOSD is not based on a controlled study, but in the experience based on real cases.
Objectives: Describe the different treatments employed in a patient cohort diagnosed with adult-onset Still's disease (AOSD).
Methods: Descriptive, restrospective study of patients treated in our Hospital (2008-2018), diagnosed with AOSD according to the classification criteria of Yamaguchi. The data were achieved by the review of the clinical records.
Results: Twenty-four patients (15 women), average age of 41±13 years, were included. Two women, with presentation on the symptoms at 8 and 3 years old, first diagnosed with systemic juvenile idiopathic arthritis (S-JIA), and then with AOSD.
The initial treatment was based in non-steroidal anti-inflammatory drugs (96%) and glucocorticoids (0,5-1 mg/kg/day) (96%) for symptom control, with the necessity to add oral or subcutaneous methotrexate at a dose of 15 mg per week in 13 patients (54%).
Only two patients used acetyl salicylic acid as initial treatment, with no improvement.

Previous treatment		Current treatment	
Drug	**n (%)**	**Drug**	**n (%)**
NSAIDs	23 (96%)	NSAIDs	2 (8%)
Glucocorticoids	23 (96%)	Glucocorticoids	3 (12%)
DMARDs	15 (62%)	DMARDs	3 (12%)
• Methotrexate	13 (86%)	• Methotrexate	2 (8%)
• Leflunomide	5 (33%)	• Hydroxychloroquine	1 (4%)
• Hydroxychloroquine	8 (53%)		
• Sulfasalazine	2 (13%)		
Biological treatments	5 (21%)	Biological treatments	3 (12%)
• Etanercept	3 (60%)	• Sarilumab	1 (33%)
• Adalimumab	1 (20%)		
• Infliximab	4 (80%)	• Tofacitinib	2 (66%)
• Tocilizumab	2 (40%)		
• Sarilumab	1 (20%)		
• Rituximab	2 (40%)		
• Baricitinib	2 (40%)		
• Tofacitinib	1 (20%)		
Immunosupresores	4 (17%)	DMARDs + Biological treatments	0
• Azathioprine	2 (50%)		
• Mycophenolate Mofetil	1 (25%)		
• Cyclophosphamide	1 (25%)		
		Without treatment	11 (46%)

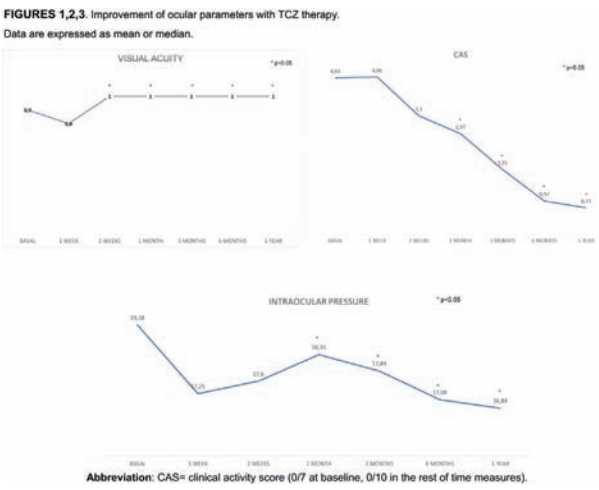
Five patients used also biological treatments with a standard doses, with the neccesity of various drugs to achieve their clinical remission. Nowadays, all patients have their clinical remission. Patient 1: Infliximab, rituximab, tocilizumab and baricitinib. Patient 2: Etanercept and rituximab. Patient 3: Etanercept, adalimumab and infliximab. Patient 4: Etanercept, infliximab and tofacitinib. Patient 5: Infliximab, tocilizumab, baricitinib and sarilumab (great responde to a anti-IL6, tocilizumab were removed because of a local reaction in the injection's spot, althought it had a good response too). Two patients with clinical remission with JAK-kinase

inhibitors (baricitinib and tofacitinib, respectively), one patients with anti-TNF (infliximab) and another one with anti-CD20 (rituximab).
Conclusion: In general, our results match with what it is published in the literature.
For the treatment of AOSD has been used high doses of ASA (4g/day) or NSAID. However, the required doses (with their respective adverse effects), its limited responses and the frequent relapses after its suppression make difficult to maintain it. Nowadays, the systemic glucocorticoids are our first choice (0,5 to 1 mg/kg/day). A high average of our patients have a positive response with it, but in a 54% of the cases were neccesary to add methotrexate or others DMARDs because of a partial response with steroids.
In the physiopathology of the AOSD there is an increase of pro-inflammatory cytokines, as the tumor necrosis factor, IL-1 e IL-6. The use of therapies that inhibit these molecules (anti-TNF, anakinra or canakinumab as anti-IL1 or tocilizumab or sarilumab as anti IL-6) is being a progress. The inhibitors of IL-1 can be more efficient for systemic manifestations, while the inhibitors of IL-6 are for articular and systemic affectation. The TNF inhibitors should being used for the articular affectation only. In our patient cohort there is no patient with anti-IL1, a patient in clinical remission with anti-TNF and another one with anti-IL-6. Prospective studies with a higher number of patients is neccesary to define better the AOSD treatment.
Disclosure of Interests: None declared
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AB1077 ANTI-IL6-RECEPTOR TOCILIZUMAB IN GRAVES' ORBITOPATHY. MULTICENTER STUDY OF 46 PATIENTS IN CLINICAL PRACTICE

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Background: Graves' orbitopathy (GO) is the most common and important extrathyroidal manifestation of Graves' disease. Corticostereoids and conventional immunosuppressors are not always effective or well tolerated. The IL-6 receptor antibody tocilizumab (TCZ) has demonstrated efficacy in the treatment of this pathology.
Objectives: To assess the efficacy of TCZ in refractory thyroid associated orbitopathy (TAO) due to Grave's disease.
Methods: Multicenter study of 46 patients with TAO refractory to conventional immunosuppressive therapy.
Results: We studied 46 patients (85 eyes) (37 women/9 men); mean age at diagnosis 49.2±11.8 years. Besides oral corticosteroids, before the onset of TCZ patients had been treated with pulses of iv methylprednisolone (42), radioactive iodine (4), methotrexate (2) and other drugs (selenium in 11 cases, methimazole in 8, leflunomide in 1 and azathioprine in 1). 7 patients underwent ocular urgent decompressive surgery.
According to the classification of severity of the EUGOGO group (European Group on Graves' Orbitopathy) using the clinical activity score (CAS), before TCZ onset patients whose data were available had severe (27 eyes) or moderate (34 eyes) disease. Moreover, patients presented exophthalmos (53 eyes), strabismus (37 eyes), muscle fibrosis (38 eyes) and dysthyroid optic neuropathy (10 eyes).
TCZ was used in monotherapy (43) or combined with methotrexate (2) or azathioprine (1) at 8 mg/kg/iv/4 w (41) or 162 mg/sc/w (5). TCZ yielded rapid and maintained improvement in all ocular parameters as shown in Figures.



FIGURES 1,2,3. Improvement of ocular parameters with TCZ therapy.
Data are expressed as mean or median.
Abbreviation: CAS= clinical activity score (0/7 at baseline, 0/10 in the rest of time measures).

Figure 1

After a mean of 7.42±6.41 months using TCZ and a mean follow-up of 16.47±11.99 months, all patients experienced ocular improvement, with TCZ withdrawal in 28 cases due to complete remission (10), improvement (12) or stability of ocular inflammation (3), inefficacy (2) and total thyroidectomy (1). Only 5 relevant adverse effects were observed (neutropenia, external otitis, otitis media, costal osteitis and gingival hyperplasia, 1 each).
Conclusion: TCZ appears to be a useful and secure option in GO treatment.

REFERENCES

[1] Bartalena L, et al. Consensus statement of the European group on Graves' orbitopathy (EUGOGO) on management of Graves' orbitopathy. Thyroid. 2008; 18 (3:333-346).
[2] Russell DJ, et al. Tocilizumab as a steroid sparing agent for the treatment of Graves' orbitopathy. Am J Ophthalmol Case Rep. 2017 Jul 8;7:146-148.

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AB1078 RED CELL DISTRIBUTION WIDTH (RDW) – A NEW POSSIBLE DISEASE ACTIVITY PREDICTOR IN RELAPSING POLYCHONDRITIS

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Background: Relapsing polychondritis (RP) is a rare condition defined by recurrent inflammation of cartilaginous tissue and systemic manifestations. Biomarkers for RP diagnosis and assessment of disease activity, damage and prognostic in clinical practice are currently lacking. Red blood cell distribution width (RDW) is an index of erythrocyte size variation depicting

anizocytosis. RDW is routinely assessed, is not influenced by infections and its standard deviation (RDW-SD) does not depend on medium corpuscular volume. Recent studies showed an increased RDW in various autoimmune diseases (systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, systemic vasculitis), correlating with inflammatory markers and disease activity. Also, the RDW seen in solid tumors and hematological cancers has prognostic value.
Objectives: To asses the RDW-SD in RP patients, its relation with the disease activity and with the presence of neoplasia
Methods: We performed a retrospective study on the patients diagnosed with RP in a tertiary Rheumatology department between January 2017 and January 2019, using the Atlasmed data management system of the institution. The concomitant diseases and the inflammation parameters were recorded. The RP activity was measured using RPDAI (relapsing polychondritis disease activity index). The correlation between variables were calculated using GraphPad Prism.
Results: We identified 20 patients, median age 59.04 years (range 38-81), with a male-to-female ratio of 1: 5.66. An associated autoimune disease (Sjogren syndrome, Hashimoto thyroiditis, systemic lupus erythematosus, rheumatoid arthritis, psoriatic arthritis) was found in 85% of pacients. Moreover, 40% of the pacients had various types of solid or hematologic neoplasia, including myelodysplastic syndrome. An elevated RDW-SD was seen in 90% of RP patients. The average RPDAI was 10.6 points. RDW-SD significantly correlated to RPDAI (p=0.0012). Of the inflammatory parameters, RDW-SD was not found to be related to ESR and CRP. RDW-SD increased with age, but no correlation was found between RPDAI and age. All pacients with neoplasia had abnormally high RDW-SD. Nevertheless, RDW-SD was not significantly different in RP patients with or without neoplasia (Mann-Whitney test, p=0.56).
Conclusion: RP was frequently associated with other autoimune diseases, but also with neoplasia.The positive correlation of RDW-SD and RPDAI in RP suggests a possible new, clinically employable, biomarker of disease activity.

REFERENCES

[1] Arnaud L et al, Autoimmun Rev 2012; 12(2):204-9. doi:10.1016/j.autrev.2012.06.005.
[2] Hu ZD, JLPM 2016, doi: 10.21037/jlpm.2016.10.02

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AB1079 **CHECKPOINT INHIBITOR-ASSOCIATED ARTHRITIS: PHENOTYPES AND CYTOKINE ASSOCIATIONS**

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Background: Immune checkpoint inhibitors (CI) have revolutionized cancer management, but can also cause immune-related adverse events. Five percent of CI-treated patients develop inflammatory arthritis, but it is poorly defined phenotypically and immunologically.
Objectives: To characterize phenotypes of CI-associated arthritis, and compare cytokine levels in these patients to rheumatoid arthritis (RA) and osteoarthritis (OA) controls.
Methods: Patients referred for CI-associated arthralgia or arthritis were prospectively enrolled in an institutional registry. Serum was collected when patients underwent phlebotomy for a clinical indication. We used a Luminex Human Magnetic Assay to measure levels of IL-1β, IL-2, IL-6, IL-8, IL-10, IL-12, IL-17, IL-22, TNF, IFN-γ, PD-L1, CCL2, CXCL2, CXCL13, OSM, CCL20, GM-CSF, CXCL-11 in CI-treated patients, and in stored serum from 7 RA patients (matched for medication, age, sex, CDAI) and 4 OA patients (age, sex matched). All comparisons were planned a priori.
Results: Thirty-six patients were enrolled 5/1/18-1/25/19. Median [IQR] age was 67[58-78], 18(50%) were female, 14(39%) were smokers and 13 (36%) had melanoma. Twenty-two (61%) were on anti-PD1 or PD-L1 monotherapy, and the remainder were on combination CI. Phenotypes included 1. Small joint involvement in 17(47%), 2. Exclusively large joint involvement in 6(17%), 3. Arthralgia without arthritis in 9(25%), and 4. Polymyalgia rheumatica in 4(11%). In all, 7(19%) had concomitant tenosynovitis or enthesitis, mostly accompanying large joint arthritis or arthralgia (6/7). Median CDAI at entry was 11[7-23] and median ESR 29[18-44]. The majority (58%) of patients with the small joint phenotype were RF and/or CCP positive and one had erosive disease, compared to none with the large joint phenotype. ANA positivity was common (74%) and did not vary across phenotypes. Median time of symptom onset was 4 [0.8-12] months after CI initiation. Median follow up was 7[3-22] months but only 5(14%) had resolution of arthritis off medication during that period. 22(61%) required CI discontinuation, 5(14%) due to arthritis. 29 (81%) required steroids including 15(42%) who required >20mg prednisone. 19(53%) required a synthetic DMARD and 5(14%) required a biologic DMARD. Of 33 patients with known cancer status, 15(45%) had a complete response, 5(15%) a partial response, 5(15%) "stable" disease, 6 (18%) progression, and 2(6%) died. Cytokines were measured in 22 patients, who were similar to the cohort as a whole except for more CCP positivity (p=0.02). CI patients with the small joint phenotype had higher levels of IL-6 than RA controls (p=0.04) (Figure 1) and IL-6 levels trended higher in the small joint vs. exclusively large joint phenotype (Figure 2). The B cell chemoattractant CXCL13, a factor produced by T peripheral helper cells in RA synovium[1], trended higher in the serum of CI patients (Figure 3). Other cytokine levels did not differ significantly in patients with the small joint vs. exclusively large joint phenotype, or in CI-arthritis patients vs. controls.
Conclusion: Half of patients with CI-arthritis present with an RA-like phenotype with small joint involvement and frequent seropositivity, and have elevated levels of IL-6 compared to RA patients. This small joint phenotype may represent an accelerated form of RA.

REFERENCES

[1] Rao DA, et al. Nature 2017: 542(7639):110-114

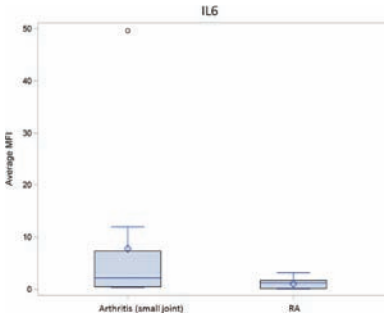


Figure 1. MFI=mean fluorescent intensity

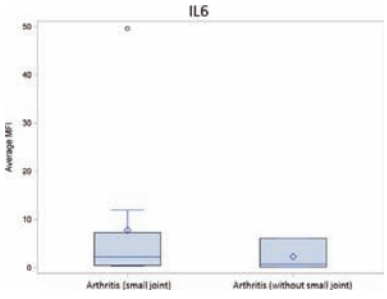


Figure 2

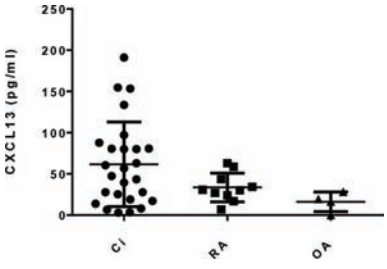


Figure 3

Disclosure of Interests: Karmela Kim Chan Grant/research support from: Roche: sponsored research agreement on stromal cells, Consultant for: GSK: consultant. (I am part of their immunology network, a group of about 8 immunologists who advise them regularly and broadly in the areas of inflammation and infection)., Gregory Vitone: None declared, Sara Shanaj: None declared, Aidan Tirpack: None declared, Jackie Finik: None declared, Laura Donlin: None declared, Deepak Rao Grant/research support from: Merck - Sponsored research project funding support, Consultant for: Janssen - Consultant
Scipher Medicine - Consultant
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Patent submitted on Tph cells, Caroline Benson: None declared, Vivian Bykerk Grant/research support from: Mallinckrodt, BMS, Crescendo Biosciences, Sanofi/Regeneron., Consultant for: Amgen, Pfizer, UCB, Scipher, Sanofi/Genzyme/Regeneron, Dana Orange Consultant for: Astra Zeneca and Pfizer., Michael Brenner Grant/research support from: Roche: sponsored research agreement on stromal cells (but has nothing to do with checkpoint related disease), Consultant for: GSK: consultant. (I am part of their immunology network, a group of about 8 immunologists who advise them regularly and broadly in the areas of inflammation and infection)., Susan Goodman Grant/research support from: Novartis: research support, Consultant for: Novartis, UCB, Pfizer: consulting, Anne Bass: None declared
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AB1080 TOCILIZUMAB FOR REFRACTORY DYSTHYROÏD MYOPATHY (RDM) : A MONOCENTER OBSERVATIONAL STUDY OF 8 PATIENTS

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Background: Dysthyroïd myopathy (DM) refers to Graves' ophthalmopathy (GO) in 90% of the cases but can also be observed with hypothyroidism, and is responsible for orbital fat and muscles inflammation. In those patients with euthyroidism and no thyroid receptor antibody, a strong argument for DM can be the aspect of the extra ocular muscles. In myositis of other causes, muscle insertions are increased in size. In DM, the insertions are respected and not increased in volume in magnetic resonance imaging. This was the case of our eight patients.
Objectives: To describe the efficacy of Tocilizumab (TCZ) in RDM in 8 patients
Methods: We conducted a monocenter study of 8 patients with RDM refractory to conventional treatment scheme
All patients have been treated following the EUGOGO (European Group on Graves' Orbitopathy) scheme, which consists in weekly infusions of 500 mg prednisolone (4 to 6) followed by weekly infusions of 250 g (4 to 6). One patient had received before oral prednisolone, which is known to be less effective and no other immunosuppressive therapy.
The aim was to reduce the clinical activity score (CAS) of the disease to a score of 1 (score composed of 7 items)
Results: We studied 8 female patients (16 eyes); mean age at diagnosis 64,37±9,37 years.
All patients had normal thyroid function at diagnosis.Three patients had a previous history of hashimoto's thyroiditis and the other 5 had no immunological abnormalities.
The duration of orbitopathy between first supposed manifestations and therapy onset was 5,7 months +/- 2,3. TCZ was introduced at the end of the steroid pulses, or before, during steroid therapy, in 2 patients who did not improve at all their ocular status after 3 steroid infusions. TCZ was used intravenously as a monotherapy, at the classical dosage of 8 mg/kg per infusion, with no other immunosuppressives.
According to the classification of severity of the EUGOGO group using the CAS [1], before TCZ, 1 had severe (n=2 eyes) or moderate (n= 14 eyes) disease. Moreover, patients presented exophthalmos (n=16 eyes), strabismus (n=16 eyes), muscle inflammation and volume increase at MRI and severe optic neuropathy (n=1).
After a mean of 4 pulses (extremes 1 to 7), all patients experienced improvement with TCZ withdrawal in all due to complete remission in 3 and regression in ocular inflammation in 5. Unfortunately, one patient relapsed two months after the 6th TCZ infusion, despite of initial complete remission and was treated with 4 weekly infusions of rituximab at 375 mg/m 2 with a very good response three months later. Only one patient experienced a severe anal abcess after the first TCZ infusion leading to treatment interruption, but with a good improvement of DM.
Improvement of ocular parameters with TCZ therapy. Data are expressed as mean±SD or median [IQR]. (VA : visual acuity; IOP : intra ocular pressure; CAS : clinical activity score)
Before tocilizumab after tocilizumab
VA 0,7 (0,3-1) 0,9 (0,7-1)
IOP 26,5 +/-7,7 21,1+/-13
CAS 4,25 +/- 1,28 1
Conclusion: TCZ seems to be effective in RDM, as previously reported. In case of ineffectiveness or relapse, rituximab may be effective as well. This questions us about a new treatment scheme, which patients could benefit from biotherapies alone for a better and quicker efficiency?

REFERENCES

[1] - Dolman PJ. Grading Severity and Activity in Thyroid Eye Disease. Ophthalmic Plast Reconstr Surg. 2018;34(4S Suppl 1):S34-S40

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AB1081 A COMPARATIVE STUDY ON THE FEATURES OF THE SPINAL INVOLVEMENT IN SAPHO SYNDROME

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Background: SAPHO syndrome is a rare disease with the typical involvement of the anterior chest wall. The spinal involvement is more often than we thought and less understood by us.
Objectives: To assess the clinical and imaging features of the spinal involvement in SAPHO syndrome.
Methods: Patients diagnosed with SAPHO syndrome in Peking University Third Hospital from 2006 to 2018 were recruited. Patients were divided into spinal involvement group and non-spinal involvement group. Patients with AS (ankylosing spondylitis) were recruited as control group. Their clinical data, laboratory data and imaging data (CT, MRI and radionuclide imaging) were collected and were conpared. All the patients with SAPHO syndrome were followed up regularly.
Results: Totally 46 SAPHO patients were included (17 male and 29 female) and 34 patients (73.9%) had spinal involvement. The mean age was 50.2±10.9 years and the mean disease duration was 5.4±6.4 years. 50 patients with AS were also included.
Compared with non-spinal involvement group, the age at disease onset in spinal involvement group was older, the disease duration was longer,t; he CRP elevation was more often and the anterior chest wall involvement was less often (table 1).
In spinal involvement group, the thoracic spine was most commonly involved and the vertebral inflammatory changes including bone marrow edema were often seen. These patients were more likely to suffer from cervical spine involvement, endplate inflammation and spondyldiscitis (table 2).

Abstract AB1081 Table 1. characteristics of SAPHO syndrome patients with and without spinal involvement

characteristics	Spinal involvement (n=34)	Non-spinal involvement (n=12)	P value
Sex, female	21(61.8%)	8(36.7%)	NS
Age at diagnosis yrs	52.2±10.3	44.6±10.6	0.033*
Disease duration yrs	6.1±7.1	3.1±2.4	0.048*
Dermatological disorders	19(55.9%)	10(83.3%)	NS
CRP elevated	21 (4.6±12.1	4 (3.0±4.3	0.047*
ESR elevated	16 (31.2±24.0	6 (32.2±27.2	NS
TNF-αelevated	12 (58.6±55.9)	13 (45.3±22.7)	NS
IL-6 elevated	18 (320.5±343.9)	42 (48.6±328.2)	NS
sternoclavicular	18	12	0.003*
Clavicle	6	2	NS
First rib	8	5	NS
Sternocostal joint	6	2	NS
Sternum corner	1	3	0.02*
Manubrium	6	0	NS
Sacroiliac joint	6	5	NS

Abstract AB1081 Table 2. characteristics of SAPHO syndrome and AS patients with spinal involvement

characteristics	SAPHO (n=34)	AS (n=50)	P value
Sex, female	21(61.8%)	17(34.0%)	0.012*
Age at onset, yrs	52.2±10.3	35.4±12.0	0.0008*
Disease duration, yrs	6.1±7.1	7.4±7.3	NS
CRP elevated	16(4.6±12.1)	26 (2.11 ±2.52)	NS
ESR elevated	16 (31.2±24.0)	18 (28.4 ±24.6)	NS
HLA-B27 positive	1(2.9%)	48(96.0%)	0.000*
Cervical vertebra	17(50.0%)	13(26.0%)	0.024*
Thoracic vertebra	22(64.7%)	33(66.0%)	NS
Lumbar vertebra	17(50%)	34(68.0%)	NS
Contiguous/multiple vertebra involvement	28(82.4%)	50(100%)	0.002*
Vertebral inflammation	34(100%)	48(96.0%)	NS
Endplate inflammation	8(23.5%)	3(6.0%)	0.019*
Spondylodiscitis	16(47.1%)	4(8.0%)	0.001*
Vertebral body corner involvement	11(32.4%)	13(26.0%)	NS
Paravertebral ossification	4(11.8%)	5(10.0%)	NS

All the SAPHO patients with spinal involvement were followed up. 30 patients received NSAIDs plus DMARDS/biologics and the symptoms improved. Reexamined imaging data of 10 patients were available and the spinal involvement became better.

Conclusion: 73.9% of SAPHO patients had spinal involvement and they were more likely to suffer from cervical spine involvement, endplate inflammation and spondyldiscitis. The combination of NSAIDS and biologics/DMARDs were helpful to improve the symptoms.

REFERENCES

[1] Mcgauvran A M, Kotsenas A L, Diehn F E, et al. SAPHO Syndrome: Imaging Findings of Vertebral Involvement.[J]. Ajnr Am J Neuroradiol, 2016, 37 (8).

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AB1082 IATROGENIC INFECTIOUS SPONDYLODISCITIS: 6 CASES

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Background: The increasing proportion of iatrogenic spondylodiscitis (SD) is a prominent feature of infectious DS in recent decades

Objectives: To describe iatrogenic clinical, aetiological and evolutive SD features.

Methods: We report 6 cases of iatrogenic DS collected in our department in 2001-2012 period.

Results: All patients were male. The average age was of 49 (35 to 68 years). Four cases of SD were caused by direct inoculation (surgical in 3 cases, chemonucleolysis in 1 case) and 2 cases of hematogenous SD from an initial outbreak. The seat of infection is lumbar in all cases. Spinal pain is almost constant. The admission examination noted apyrexia in 5 cases. A biological inflammatory syndrome was present in 5 cases and hyperleucocytosis in 2 cases. The bacteriological investigation was able to isolate a methicillin-sensitive Staphylococcus aureus (SAMS) and a proteus mirabilis in one patient and SAMS in another. The radiological assessment made it possible to objectify a para vertebral abscess in 5 cases and an epilepitis in 1 case. The evolution was favorable in all cases under antibiotherapy of average duration of 4.5 months and immobilization of the spine by corset.

Conclusion: The detection of an anaerobic germ causing infectious spondylodiscitis should search for an iatrogenic portal chronologically and anatomically close to the vertebral disc infection.

Disclosure of Interests: None declared

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AB1083 IN A FAMILIAL MEDITERRANEAN FEVER PREVALENT REGION, ARE FAMILIAL MEDITERRANEAN FEVER AND BEHÇET'S DISEASE ASSOCIATED?

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Background: The co-existence of Familial Mediterranean Fever (FMF) and Behçet's Disease (BD) has been questioned. There have been a variety of claims on a common pathogenesis.

Objectives: We intended to report the prevalence of Familial Mediterranean Fever (FMF) and Behçet's disease (BD) and comorbidity ratio of these two diseases in Sivas, Turkey, a city where FMF is known to be very high.

Methods: Seventy-two primary schools in the center of Sivas participated in the study. A total of 14881 randomized sample children from 6th, 7th, and 8th grades, and also 985 of them with their parents (n: 978) were interviewed. During these interviews, the family tree up to second degree relatives was drawn. The presence of a diagnosis of FMF or BD was questioned. The ones who have a diagnosis were confirmed by contacting the medical centers. The ones who were suspected of a disease were further investigated at Sivas Cumhuriyet University Medical Faculty, Family Medicine Outpatient unit. For each disease a disease related history, physical examination, eye examination and pathergy test for BD were performed when needed.

Results: 985 students, 978 mothers, 953 fathers and 1876 relatives (4792 in total) were included in the study. Only 30 (0.6%) of the sample was diagnosed with FMF, and 3 (%0.06) was diagnosed with BD. One of them had concomitant FMF diagnosis.

Table. FMF symptoms within the last year

Symptoms	N	%
Abdominal Pain	20	66.7
Fever	23	76.7
Joint Pain	8	26.7
Chest Pain	10	33.3
Muscle Pain	7	23.3
Erysipelas like erythema	5	16.7

Conclusion: The prevalence of FMF in Sivas is higher than Turkey's prevalence; however, BD prevalence was found very low. According to these findings, it is not easy to conclude that these two diseases share a similar background of pathogenesis.

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AB1084 PECULIARITIES OF ERYTHEMA NODOSUM ASSOCIATED WITH SARCOIDOSIS AND BACTERIAL-VIRAL INFECTION IN RHEUMATOLOGIST PRACTICE

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Background: Erythema nodosum (EN) is a nonspecific immune inflammatory syndrome, which is a septal panniculitis without vasculitis. Often EN acts as one of the symptoms of systemic pathology, which can cause late diagnosis and, accordingly, the appointment of adequate therapy.

Objectives: to study clinical, laboratory and radiological data in EN in the acute form of sarcoidosis (SAR) and EN associated with bacterial and viral infection in patients sent to the rheumatology center.

Methods: The study included 312 patients (61 men and 251 women, age 35.4 ± 8.2 years) who applied to the clinic with a referral diagnosis of EN in 2007-2017. The median duration of the disease was 1.6 [0.3;4.7] months. All patients underwent a comprehensive clinical examination and laboratory and instrumental examination of biochemical, serological (ASL-O, antibodies against chlamydia and Mycoplasma of 2 classes, ureaplasmas, herpes viruses of type I and II, cytomegalovirus, Epstein-Barr virus, hepatitis B/C, Yersinia, HIV, etc.) and immunological parameters, radiography or computed tomography (CT) of the chest organs.

Results: 145 patients (46.4%) were diagnosed with SAR (34 men and 111 women). EN associated with bacterial-viral infection was detected in 167 patients (53.5%). Serological examination of these patients showed an increase of ≥3 times the levels of antibodies to Herpesviridae (79 people), M. pneumonie (15), CL. Pneumonia (11), Y. enterocolitica (11), Chl. trachomatis (9), M. hominis (6), increase of ASL-O (57). EN with SAR is characterized by: the duration of the disease up to 6 months (odds ratio (OR) 7,320, 95% confidence interval (CI) 2,297– 23,329, p<0.005), multiple diffuse lesions on the legs and single diffuse lesions on the thighs and/or forearms (OR 15,500, 95% CI 1,983–121,132; p<0.005), lesions of ankle joints (OSH 35,905, 95% CI 9,523–135,365; p<0.005), high CRP level (OR 5,429 95% CI: 2,164–13,618; p<0.005). Predictors of the formation of the CT phenomenon of "frosted glass" in ATS were male sex (OR 6.5; DI 1.2–35; p = 0.026) and the presence of conglomerates of nodes (OR 4.8; DI 1.4–16.1; p = 0.01). Postinfectious EN was characterized by its development typically before the age of 30 (OR 0.825, 95% CI 0.328-2.077, p<0.005), the symptom of "blooming" bruise (OR 0.028, 95% CI 0.009–0.092, p<0.005), an increase in antistreptolysin-O (OR 0.035, 95% CI 0.006–0.207, p<0.005). Within 1 year of follow-up, 72% of patients with SAR EN did not relapse, and the joint syndrome almost completely regressed. Postinfectious EN recurred within 1 year in 38 people due to: exacerbation of chronic tonsillitis (14), ARVI/hypothermia (10), stress (5), violation and ineffectiveness of prescribed therapy (9).
Conclusion: Post-infectious EN is somewhat more common than EN in SAR. The latter is characterized by greater severity of clinical parameters and high parameters of inflammatory activity. These features should be borne in mind when carrying out differential diagnosis in patients with EN.
Disclosure of Interests: None declared
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AB1085 OSTEO-ARTICULAR MANIFESTATIONS OF SARCOIDOSIS: ABOUT 13 CASES

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Background: Sarcoidosis is a systemic disorder of unknown etiology, affecting the respiratory tract and the lymphatic system with predilection. It is an ubiquitous condition whose clinical phenotype is very diverse.
Objectives: To detail the epidemiological, clinico-biological, therapeutic and evolutionary features of osteoarticular forms of sarcoidosis.
Methods: This is a monocentric, descriptive retrospective study conducted over a 17-years period [2002-2018] involving 13 patients diagnosed with sarcoidosis with osteoarticular manifestations at the department of Rheumatology at Farhat Hached University Hospital in Sousse.
Results: 13 patients with osteoarticular manifestations were studied; this was indicative of the disease in 8 cases (61.5%). The sex ratio was 0.23 with a mean age of 42.38 years and a diagnostic delay of 12 months. In 77% of cases, inflammatory arthralgia was noted, Löfgren syndrome (30.7%), chronic polyarthritis (30.7%), phalanges cystoid osteitis (15.4%) and no cases of monoarthritis. The extra articular manifestations found were; Adenomegaly (92.3%), lung (77%), cutaneous (38.5%) (including 80% erythema nodosum), neurological (30.7%) (Aseptic meningitis and convulsion), ocular (23%) (chorioretinitis, keratoconjunctivitis and retro-bulbar optic neuritis), cardiac (15.4%), and biological hepatitis (7.7%). In the biology, a biological inflammatory syndrome was found in 30.7% with a mean sedimentation rate of 31.07 in the 1st hour, an average CRP of 9 mg/L, cholestasis and cytolysis found in 15.4% and 7.7%, respectively. No Hypercalcemia was noted. The value of the conversion enzyme was high in 5 out of 6 patients who were dosed with an average of 71 µg/L. In imaging, sarcoidosis was destructive in 4 cases; A multifocal osteonecrosis, Algodystrophy of the two hips and two cases of bullous cystoid osteitis of phalanges.
Conclusion: The osteo-articular involvement of sarcoidosis is polymorphic, which can reveal the disease or enamel its evolution.
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AB1086 ADULT ONSET STILL'S DISEASE: EXPERIENCE OF THE RHEUMATOLOGY DEPARTMENT OF THE UNIVERSITY HOSPITAL OF CASABLANCA

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Background: Adult onset Still's disease (AOSD) is a rare condition characterized by four cardinal signs: fever, arthralgia/arthritis, rash, and neutrophilic leukocytosis. The absence of specific criteria is currently compensated by pathophysiological advances, leading to the introduction of a promising new therapeutic arsenal represented by biotherapies.
Objectives: The aim of this study was to compare the profiles of this disease in our latitudes with data from foreign literature; and to study the most recent data concerning the pathophysiology and treatment of this disease.
Methods: We conducted a retrospective study of hospital files from January 1993 to October 2018. The diagnosis is retained according to Yamaguchi criteria. Analysis was performed using IPSS.
Results: 17 patients were selected. The sex ratio was 0.54, and the average age was 31.5 years. At the time of diagnosis, fever was found in 94% of cases, arthralgia/arthritis in 100% of cases, and rash in 65% of cases. Concerning rheumatic features, the most frequently affected joints were: wrists (87%), knees (73%), shoulders (67%), proximal interphalangeal (62%), elbows and ankles (60%), hips (47%). The involvement of the hands is dominated by the proximal interphalangeal and metacarpophalangeal (45%). Distal interphalangeal involvement is observed in 23% of cases. Cervical spine involvement is noted in 50% of cases. Biologically, 88% of patients had neutrophilic leukocytosis. Ferritinemia was increased in 79% of patients. The glycosylated fraction of ferritin was measured at diagnosis in 47% of patients, of whom 63% had a fraction ≤ 20%. Elevated transaminases were found in 47% of cases. Therapeutically, 100% of patients received corticosteroids; 65% methotrexate; and 29% biotherapies (tocilizumab, anakinra, infliximab, adalimumab). The evolutionary profile was exploitable in 13 patients, of whom 10 were in complete remission.
Conclusion: Our data are consistent with those in the literature. Some peculiarities emerge concerning the articular features. From 3 series of literature and ours, totaling 135 cases, it appears that the most frequent locations are: wrist (82%), knees (70%), elbows (46%), ankles (45%), proximal interphalangeal (44%), shoulders (42%) and metacarpophalangeal (42%). The pathogenesis of AOSD seems to lie at the crossroads between auto-inflammatory diseases and lymphohistiocyte activation, resulting from a multifactorial predisposition. The central role of innate immunity, the clinical presentation, and the efficacy of blocking the IL-1 pathway comparable to that observed in "monogenic inflammasomopathies" justify the reclassification of AOSD among polygenic auto-inflammatory syndromes.

REFERENCES

[1] Georgin-Lavialle S, et al. [Clinical overview of auto-inflammatory diseases]. Rev Med Interne. 2018;39(4):214-32.
[2] Gerfaud-Valentin M, et al. Adult-onset still disease: manifestations, treatment, outcome, and prognostic factors in 57 patients. Medicine (Baltimore). 2014;93(2):91-9.
[3] Wouters JM, et al. Adult-onset Still's disease; clinical and laboratory features, treatment and progress of 45 cases. Q J Med. 1986;61(235):1055-65.
[4] Pouchot J, et al. Adult Still's disease: manifestations, disease course, and outcome in 62 patients. Medicine (Baltimore). 1991;70(2):118-36.
[5] Ben Taarit C, et al.[Adult Still's disease: study of a series of 11 cases]. J Mal Vasc. 2002;27(1):31-5.

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AB1087 THE RELATIONSHIP BETWEEN FEMORAL CARTILAGE THICKNESS AND AMYLOIDOSIS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: PRELIMINARY STUDY

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Background: Familial Mediterranean fever (FMF) is the most common hereditary inflammatory disease characterized by recurrent attacks of fever and serositis. The most devastating complication of FMF is amyloidosis, leading to chronic renal failure (CRF). The amyloid protein may accumulate in many tissues including the cartilage, particularly in the kidneys. Sonographic femoral cartilage thicknesses (FCT) was evaluated in many chronic rheumatic diseases and was shown to be thinner than healthy individuals.
Objectives: The aim of this study was to determine FCT in FMF patients and healthy individuals and to assess the relationship of FCT with the development of amyloidosis and clinical features.
Methods: Patients diagnosed with FMF according to the Tel-Hashomer criteria were included in the study. Patients with trauma and other inflammatory disease and patients with a history of knee operation were excluded. Femoral cartilage thickness of both knees was measured with a 7-12 MHz linear probe in maximum knee flexion. Three mid-point measurement were obtained from each knees: lateral femoral condyle (LFC), intercondylar area (ICA) and medial femoral condyle (MFC). Clinic characteristics of the patients including disease duration, medications, comorbid conditions, amyloidosis, CRF, FMF gene mutation, arthritis, sacroiliitis, PRAS score and physical activity scores were recorded. Descriptive analysis was performed for all parameters. The Mann-Whitney U-test and Spearman's correlation coefficient were used in statistical analysis. $P<0.05$ was considered statistically significant.
Results: A total of 45 patients with FMF (35 women, 10 men) and 20 age-sex-BMI matched controls (14 women, 6 men) were enrolled in this study. The mean age of the patients and controls were 38.2 (SD:12.2) and 37.5 (SD:8.5) years, respectivelly. Amyloidosis occurred in 7 patients (15.6%), CRF in 3 (6.7%), sacroilitis in 10 (22.2%) and arthritis in 16 (35.6%). Disease activity was mild in 48.9%, moderate in 20% and severe 22.2% of the patients. The mean FCT in centimeters values in the FMF and control groups were as follows: on the right side LFC 0.19 (SD:0.03) and 0.22 (SD:0.05), ICA 0.23 (SD:0.05) and 0.24 (SD:0.06), MFC 0.20 (SD:0.04) and 0.24 (SD:0.06); on the left side LFC 0.19 (SD:0.03) and 0.21 (SD:0.03), ICA 0.22 (SD:0.05) and 0.24 (SD:0.06), MFC 0.19 (SD:0.03) and 0.22 (SD:0.04). Patients with FMF had decreased cartilage thickness at the lateral condyle of both knees ($p<0.05$) and medial condyle of the left knee ($p<0.05$) compared with controls. FCT measurements were similar in patients with or without arthritis, sacroiliitis, amyloidosis and CRF. Physical activity scores were significantly correlated with the left LFC ($r=0.309$). Total protein in 24-hour urine showed a highly negative correlation with left LFC ($r=-0.718$).
Conclusion: These findings suggest that patients with FMF have decreased FCT compared with controls. There is no significant relationship between the FCT and amyloidosis, it has significant relation with proteinuria level.

REFERENCES

[1] Ozcakar, L., et al., Femoral cartilage thickness measurements in healthy individuals: learning, practicing and publishing with TURK-MUSCULUS. J Back Musculoskelet Rehabil, 2014. 27: p. 117-24.
[2] Mitrovic, D.R., et al., Amyloid deposits in human knee and hip joints. J Rheumatology International. 1985. 5(2): p. 83-89.

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AB1088 HEMOGRAM PARAMETER CHANGES DURING THE ATTACK AND THE REMISSION IN FAMILIAL MEDITERRANEAN FEVER PATIENTS

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Background: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease. Disease-specific symptoms are fever and polyserositis attacks (1). The most important complication in the long term is amyloidosis (2). Many cytokines and acute phase reactants have been studied in patients with familial Mediterranean fever. Erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), serum amyloid A (SAA) and fibrinogen levels increase during attack and return to normal values after the attack (3,4). Biomarkers that are useful on the course of the disease and the development of amyloidosis are still needed.
Objectives: In this study, we aimed to observe the changes reflected in the hemogram parameter values during the remission and attack periods of FMF patients.
Methods: Study included 67 patients who met the FMF Tel-Hashomer criteria. The patients with available results of both remission and attack periods were included in the study.Since the distribution of all continuous variables used in the study as a statistical method was not suitable for normal distribution, Wilcoxon T test was used to investigate the difference in hematological variables during remission and attack periods
Results: 21 of the patients were male and 46 were female. The mean age of the male patients was 41.57 ± 11.08 and the female patients were 35.84 ± 11.75. The mean age of all patients was 38.18 ± 11.20 years. There was a statistically significant difference between neutrophils in the comparisons of hematological variables between remission and episode periods of familial Mediterranean Fever patients ($p<0.001$). No significant difference was found in terms of other variables (Table 1).
Conclusion: Our study does not support that neutrophil/lymphocyte ratio, MPV and PDW values may be helpful in the attack. Significant differences in neutrophil counts suggest that further studies are needed to show neutrophil cell morphology, number, and function in FMF patients.

REFERENCES

[1] Özen S, Batu ED, Demir S. Familial Mediterranean Fever: Recent Developments in Pathogenesis and New Recommendations for Management. Front Immunol. 2017 23;8:253.
[2] Sönmez HE, Batu ED, Özen S. Familial Mediterranean fever: current perspectives.J Inflamm Res. 2016 17;9:13-20.
[3] Özer S, Yılmaz R, Sönmezgöz E, Karaaslan E, Taşkın S, Bütün İ, Demir O. Simple markers for subclinical inflammation in patients with Familial Mediterranean Fever.Med Sci Monit. 2015 23;21:298-303.
[4] Tunca M, Kirkali G, Soyturk M, et al. Acute phase response and evolution of familial Mediterranean fever. Lancet. 1999;353:1415.

Abstract AB1088 Table 1. Distribution of hematological parameter characteristics of patients with remission and attack episodes

	n	Remission	Attack	p
CRP(mg/L)	54	3.23 [3.03-4.20]	27.90 [17.60-51.10]	**<0.001**
RDW(%)	54	16.10 [15.20-17.30]	16.00 [14.80-17.00]	0.157
MPV(fL)	54	7.52 [7.02-8.20]	7.50 [6.85-8.29]	0.054
PDW(%)	54	17.70 [17.30-18.30]	17.70 [17.20-18.20]	0.185
Neutrophil(μL)	54	3815.00 [2980.00-4660.00]	4740.00 [3330.00-6180.00]	**0.047**
Lymphocyte(μL)	54	2035.00 [1700.00-2400.00]	1900.00 [1500.00-2210.00]	0.060
Neutrophil/Lymphocyte Ratio	54	0.79 [0.57-1.47]	1.14 [0.90-1.25]	0.137

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AB1089 CLINICAL FEATURES OF FAMILIAL MEDITERRANEAN FEVER PATIENTS IN NORTH-WESTERN PART OF TURKEY: ANALYSIS OF 139 PATIENTS

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Background: Familial Mediterranean fever (FMF) is known the most common monogenic autoinflammatory disease. Its prevalence is reported high from the eastern Mediterranean areas (1) The disease is characterized by episodes of fever, serositis, arthritis,renal complications and other different clinical manifestations (2)
Objectives: Here, we aimed to present our data of our 139 FMF patients for demonstrating the demographic and clinical features of the study group,from North-western part of Turkey.
Methods: A total of 139 FMF patients who were diagnosed and treated in the department of Internal medicine/Rheumatology, Sakarya University (North-western area of Turkey) were included in the study and the demographic and clinical characteristics of the patients were examined.
Results: The mean age of the patients was 39.02 ± 11.3. Male gender was 42 (30.2%) and female gender was 97 (69.8%).107 (77%) of patients had fever and 32 (23%) had no history of fever. 127 (91.4%) patients complained about peritonitis, 27 (%19.4) patients had pleuritic pain, 19 (13.7%) patients had erysipelas like erythema and 53 (38.1%) patients had arthritis attack. 34 (24.5%) patients also had sacroiliitis. The ratio of resistance of treatment response to colchicine drugs that can be available in Turkey (Colchicum dispert ®), 6 (4.3%) was determined. Interestingly these patients responded to the colchicine drugs available from some other countries from Europe (as Colchicine-opocalcium® and Colchicina-lirca®) None of our patients needed anti-IL1 therapies. The rate of amyloidosis was 5 (3.6%).
Conclusion: FMF is a disease with high morbidity and mortality, 95.7% of the patients in our region have response to colchicine drugs which is available in our country. The remaining patients have also response to colchicine available from some other countries. None of our patients had anti-IL1 therapies.

REFERENCES

[1] Özen S, Batu ED, Demir S. Familial Mediterranean Fever: Recent Developments in Pathogenesis and New Recommendations for Management. Front Immunol. 2017 23;8:253.
[2] Alghamdi M. Familial Mediterranean fever, review of the literature Clin Rheumatol. 2017;36:1707-1713.

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AB1090 CECR1/ADA2 MUTATION IN A BRAZILIAN FAMILY

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Background: Deficiency of adenosine deaminase 2 (DADA2) is a recently identified disease caused by mutations in the CECR1/ADA2 gene, encoding for adenosine deaminase 2 protein. Clinical presentation is variable and includes early-onset polyarteritis nodosa, hemorrhagic and ischemic strokes, hypogammaglobulinemia and cytopenia
Objectives: To present the clinical cases of two Brazilian siblings with early stroke episodes carrying a homozygous CECR1/ADA2 mutation.
Methods: Chart review of clinical data, laboratory tests and mutation analysis
Results: The index case is a 7-year-old boy who presented to the emergency unit with right lower limb weakness, rhyme deviation and palpebral ptosis, associated with recurrent and intermittent fever, mood change and hypertension. The physical exam revealed drowsiness, lateral and vertical ocular paresis, diplopia, facial palsy, and bilateral ataxia. The brain MRI showed acute left mesencephalic small vessel lacunar stroke, previous right mesencephalic subacute stroke, and cerebellar cavity related with anterior cerebellar artery segmental narrowing. Laboratory tests revealed increased inflammatory markers and anemia. Autoantibodies and viral screening were negative. Renal ultrasound showed a pattern of low resistance in the intrarenal arteries bilaterally. At this time, he was diagnosed as polyarteritis nodosa (PAN). Despite of adequate treatment (cyclosphosphamide and corticosteroids), two new stroke episode occurred at left head of caudate and right thalamus. His brother, a 9-year-old healthy boy at that time, had a previous history of ischemic stroke when he was 4 years old, after receiving a vaccine, with complete recover. Considering this family history and the fact that parents are consanguineous, mutation analysis of CECR1/ADA2 gene was performed and showed homozygosity for the p.Y453C mutation in exon 9 in both siblings and heterozygosity for the same mutation in both parents. Although the eldest boy remained asymptomatic for 5 years without any specific treatment, shortly after the identification of the gene mutation, he presented recurrent fever episodes, myalgia, livedo reticularis and increased inflammatory markers. Anti-TNF treatment was initiated for both patients with good disease control.
Conclusion: DADA2 should be suspected in patients with PAN-like phenotype and history suggestive of an inherited disease (eg.: affected siblings and consanguineous parents) or resistance to conventional treatment.

REFERENCES

[1] Fayand A, Sarraby G, Belot A, et al. Multiple facets of ADA2 deficiency: Vasculitis, auto-inflammatory disease and immunodeficiency: A literature review of 135 cases from literature Rev. Med Interne 2018 39:297
[2] Caorsi R, Penco F, Grossi, et al. ADA2 deficiency (DADA2) as an unrecognised cause of early onset polyarteritis nodosa and stroke: a multicentre national study. Ann Rheum Dis 2017; 76:

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AB1091 THE RELATIONSHIP BETWEEN NAILFOLD CAPILLAROSCOPY FINDINGS IN BEHÇET'S PATIENTS AND COURSE OF THE DISEASE

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Background: Behçet's disease is a chronic, recurrent and systemic vasculitis that may affect veins and arteries at all diameters. Small vessel involvement is responsible for most of its pathological signs.
Objectives: We aimed to compare the nailfold capillaroscopy findings of patients with Behçet's disease to a healthy control group and examine the relationships, as well as revealing the relationships with the sub-type, activity and other characteristics of Behçet's disease.
Methods: We conducted a cross-sectional analysis of 153 patients with Behçet's disease and 165 healthy volunteers in a single center. The capillaroscopic findings of the 2nd-5th fingers of both hands of the participants in the Behçet's patients and control groups were included in the analysis. Capillaroscopic findings were evaluated by two different experts who were experienced in this field by using the scoring at Atlas of Capillaroscopy in Rheumatic diseases by Maurizio Cutolo (1).
Results: There was no statistically significant difference between the two groups in terms of age or sex (respectively p=0.189 and p=0.585). There was no difference between the Behçet's patients and healthy volunteers in the qualitative analysis on capillary density, capillary visibility, aneurism, capillary tortuosity, capillary enlargement and presence of avascular areas (p values respectively: 0.610, 0.147, 0.481, 0.057, 0.514 and 0.110). In the Behçet's patients, bushy capillaries (24.2%, 37/153), capillary dilatation (32%, 49/153) and microhemorrhage (39.2%, (60/153) rates were significantly higher than those in the healthy control group (p<0.001). In the quantitative analysis, total capillaroscopy score was significantly higher in the Behçet's patients than those in the healthy control group (p<0.001) (Table 1). No statistically significant relationship was found between the presence of clinical signs and capillaroscopy scores, except for erythema nodosum.
Conclusion: the Behçet's patients had significantly higher total capillaroscopy scores in comparison to those in the healthy control group. Based on these data, we believe that the capillaroscopic changes found in Behçet's patients, though unspecific, may support clinical diagnosis in uncertain cases where Behçet's disease is considered as a probability. There is a need for well-planned prospective studies to support this our thought.

REFERENCES
[1] Cutolo M. Atlas of Capillaroscopy in Rheumatic Diseases. Elsevier, Milan 2010, 77-86

Abstract AB1091 Table 1. The results of the quantitative evaluation of nailfold capillaroscopic findings

	Behçet's patients N=153	Healthy controls N=165	*p*
Irregularly enlarged capillary score*	0 (0-0.44)	0 (0-0.25)	***<0.001***
Giant capillary score*	0 (0-0.13)	0 (0-0.13)	0.517
Microhemorrhage score *	0 (0-0.63)	0 (0-0.19)	***<0.001***
Capillary number score *	0 (0-0.88)	0 (0-0.25)	***<0.001***
Capillary ramification score *	0 (0-0.75)	0 (0-0.25)	0.224
Disorganize capillary score*	0 (0-0.44)	0 (0-0.25)	***<0.001***
Total capillaroscopy score*	0.16 (0-1.75)	0 (0-0.50)	***<0.001***

*Data were given as median (minimum - maximum)

Abstract AB1091 Table 2. The relationship between clinical findings and total capillaroscopy scores

	Total Capillaroscopy Score		p
	Present	Absent	
Vasculer involvement (n=54/99) *	0.19 (0-1,48)	0.13 (0-1,75)	0.814
Oculer involvement (n=64/89) *	0.19 (0-1,48)	0.13 (0-1,75)	0.358
Neurological involvement (n=12/141) *	0.19 (0,6-1,48)	0.13 (0-1,75)	0.222
Genital ulcer (n=131/22) *	0.19 (0-1.75)	0.13 (0-1.48)	0.121
Erythema nodosum (99/54) *	0.13 (0-1.75)	0.19 (0-1.48)	**0.026**
Papulopustular eruption (n=119/34) *	0.19 (0-1.75)	0.13 (0-1.2)	0.238

N, number of patients, *Data were given as median (minimum - maximum)
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AB1093 INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES: A SINGLE CENTER EXPERIENCE AND THE IMPORTANCE OF A MULTIDISCIPLINARY APPROACH

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Background: Interstitial lung disease (ILD) remains a significant cause of morbidity and mortality in patients with connective tissue diseases (CTD). Interstitial pneumonia with autoimmune features (IPAF) is a subset of ILD with clinical features suggestive of but do not definitive for a CTD. IPAF is a new concept relatively unknown to rheumatologists. A multidisciplinary approach to diagnosis and management of IPAF patients is essential, involving close interaction between pulmonologists, rheumatologists, radiologists and pathologists.
Objectives: Revision of ILD patients followed at a specialized tertiary hospital's ILD department and description of their clinical characteristics and multidisciplinary approach.
Methods: The study was conducted according to the declaration of Helsinki. All patients who met the Fischer criteria for IPAF in 2000-2018 were identified. Clinical characteristics, comorbidities, ILD subtype, pulmonary function tests, baseline serologies and treatment strategies were collected. The consents from a multidisciplinary meeting and Rheumatology referral and evaluation were also recorded.
Results: We identified 8 cases fulfilling classification criteria for IPAF (4 [50%] female); mean age 64.9 years (range 34-83); past smoking was referred in 5 (62.5%) patients with an average of 54.15 smoking pack years. Overall, 4 (50%) patients were exposed to organic dusts and 2 (25%) to inorganic dusts. Arterial hypertension was the most frequently recorded comorbidity (50%). Among the 8 patients, 6 (75%) had at least 1 feature from the serologic and morphologic domains, 1 patient had at least 1 feature from clinical and serologic domains and 1 patient had at least 1 feature from all 3 domains. From those meeting "suggestive radiology pattern based on high resolution chest CT (HRCT)", 2 had nonspecific interstitial pneumonia (NSIP) and 1 had organizing pneumonia (OP). Biopsy (3 transbronchial cryobiopsies and 1 transthoracic biopsy) were conclusive in 4 patients (2 NSIP, 1 lymphoid interstitial pneumonia and 1 OP). Usual interstitial pneumonia (UIP) pattern was observed in two patients. Antinuclear antibodies were positive in 5 (62.5%) patients. Overall, 5 (62.5%) clinical cases were discussed in a multidisciplinary meeting including revision of imaging and biopsies. A Rheumatology appointment was requested in 5 patients to investigate a possible CTD diagnosis. Six (75%) patients had pulmonary function tests (PFT) and diffusing capacity of the lung for carbon monoxide (DLCO) results recorded at baseline: 4 patients had a DLCO below 70% (33.8 – 61.8%), 3 patients had normal PFT, 1 had restriction pattern and 2 had small airways obstruction. During a median of 2.7 years of follow-up, none of the patients progressed to a definitive diagnosis of CTD. Pharmacological treatment was prescribed in 6 patients, including corticosteroids (5), DMARDs (3), antifibrotic therapy (2) and azithromycin (2).
Conclusion: IPAF is a relatively new and developing concept. Rheumatologists and pulmonologists should share their experience to uniformize terms and classifications, recognize relevant clinical patterns and optimize management of those affected with CTDs and ILD and IPAF.

REFERENCES
[1] Eur Respir J 2015; 46; 976-987

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AB1094 ARTERIOSCLEROSIS MAY AFFECT PERIAORTIC/ PERIARTERIAL LESIONS AND THEIR ANEURYSMAL CHANGES IN PATIENTS WITH IGG4-RELATED PERIAORTITIS/PERIARTERITIS

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Background: IgG4-related periaortitis/periarteritis (IgG4-PA) is a major organ manifestation of IgG4-related disease (IgG4-RD) [1]. In the affected aorta/artery, arteriosclerotic changes are frequently observed [2]. However, the influence of arteriosclerosis on IgG4-PA and aneurysmal changes of the affected lesions has not been well evaluated.
Objectives: This study aimed to clarify the relationship of arteriosclerosis with periaortic/periarterial lesions and their aneurysmal changes.
Methods: We retrospectively investigated the medical data, including the presence of IgG4-PA at diagnosis, new development of IgG4-PA during the clinical course, arteriosclerotic and aneurysmal changes of the affected lesions, and classic risk factors for arteriosclerosis in 130 patients with IgG4-RD at a single center in Japan. The relationship of arteriosclerosis with the periaortic/periarterial lesions and their aneurysmal changes was statistically analyzed.
Results: Of the 130 patients with IgG4-RD, 44 comprising 39 men and 5 women (mean age 67.4 years) were diagnosed with IgG4-PA. The mean follow-up period was 72.8 months, and the mean serum IgG4 level at diagnosis was 851 mg/dL. The proportions of males (88.6% vs. 55.8%, $P<0.001$), positive smoking history (81.4% vs. 47.6%, $P<0.001$), and history of malignancy (36.4% vs. 14.0%, $P=0.006$) were significantly higher in the 44 patients with IgG4-PA than in the 86 without it. Arterial wall calcification and/or mural thrombus in the affected lesions were detected in 86.0% of the IgG4-PA patients, some of whom had had these arteriosclerotic changes before the development of periaortic/periarterial lesions. Of the 44 with IgG4-PA, 9 had aneurysmal changes of the affected lesions at the time of the first diagnosis of IgG4-RD. Notably, these 9 patients with aneurysmal changes had a significantly higher incidence of hypertension (77.8% vs. 34.3%, $P=0.027$) and mural thrombus in the affected lesions (100% vs. 64.7%, $P=0.044$) than the remaining 35 without aneurysmal changes. However, diabetes mellitus, dyslipidemia, smoking history, C-reactive protein level elevation, or arterial wall calcification of the affected lesions did not differ significantly between the two groups.
Conclusion: The present study suggests that arteriosclerotic changes and the classic risk factors for arteriosclerosis may be related to periaortic/periarterial lesions and their aneurysmal changes in IgG4-PA.

REFERENCES
[1] Stone JH, et al. IgG4-related disease. N Engl J Med. 2012 Feb 9;366 (6):539-51.
[2] Inoue D, et al. Immunoglobulin G4-related periaortitis and periarteritis: CT findings in 17 patients. Radiology. 2011 Nov;261(2):625-33.

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AB1095 THE GENETIC CHAMELEON IN RHEUMATOLOGY'S BACK GARDEN: A 2-CASE PRESENTATION

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Background: Adult Refsum disease is an autosomal recessive disorder, in which phytanic acid cannot be metabolized and it accumulates in plasma and lipid-containing tissues (1). Although its common clinical features are known, patients are displaying symptoms that can mimic an autoimmune pathology, making this disease a diagnostic dilemma.
Objectives: To highlight the overlap between the clinical and serological features of adult Refsum disease with those of a connective tissue disease, in order to achieve the correct diagnosis and make appropriate therapeutic decisions.
Methods: Clinical and laboratory data were evaluated for 2 patients with adult Refsum disease in a rheumatology tertiary department. The data was retrieved from patients' files.
Results: Both patients were females in their 50s with undiagnosed adult Refsum disease. A medical history revealed that both reported progressive nyctalopia, anosmia, ageusia, peripheral vision loss. In addition to these clinical features one of them reported muscle weakness, weight loss and fatigue, displaying periorbital oedema, heliotrope rash, periungual capillary changes. Her muscular enzymes were elevated (creatin-kinase was 3 times elevated and lactat dehydrogenase was 9 times above normal range), along with C-reactive protein (CRP = 2.4mg/dl). Due to clinical features, increased serum enzymes and a recently diagnosed myocarditis, a high suspicion of dermatomyositis was raised, but was disregarded after extensive investigations (immunology tests, muscular biopsy). The other patient had, in addition, sicca features (dry mouth, eyes, skin) with a Schirmer test of 4mm and an elevated CRP (3.23mg/dl). She was referred to the rheumatology department with a high suspicion of Sjogren's syndrome. Immunology and minor salivary gland biopsy were negative. Interestingly, physical examination showed bilateral brachymetacarpia and brachymetatarsia in both patients, suggesting pseudopseudohypoparathyroidism but, after investigations, the diagnosis was excluded.
Both patients underwent ophthalmological examination to further investigate progressive nyctalopia and peripheral vision loss. Specific changes for pigmentary retinopathy were described, which, together with the above neurological changes and skeletal deformities, were highly suggestive of adult Refsum disease (2). Plasma phytanic acid was 41 and 42 times above normal range respectively, confirming the diagnosis.
After dietary restrictions which excluded phytanic acid containing foods, there was an improvement concerning both clinical and serological manifestations. All connective tissue disease relating symptoms, slowly and gradually started to subside. Muscular enzymes and CRP values returned within normal range (3).
Conclusion: High levels of phytanic acid have triggered a series of uncommon symptoms and serological changes resembling a connective tissue disease, making the diagnosis of adult Refusm disease a very tangled, costly and lengthy process. Although this disease affects many body systems, a case of myositis or sicca syndrome hasn't yet been acknowledged in relation to this condition.

REFERENCES
[1] Wierzbicki A.S., Lloyd M.D, et al. Refsum's disease: a peroxisomal disorder affecting phytanic acid alpha-oxidation. Journal of Neurochemistry, 2002, 80, 727-735.
[2] Gibberd F.B., et al. Heredopathia atactica polyneuritiformis: Refsum's disease. Acta Neurol Scand 1985;72:1-17.
[3] Baldwin E., Gibberd FB, et al. The effectiveness of long term dietary therapy in the treatment of adult Refsum disease. J Neurol Neurosurg Psychiatry 2010;81:954-957.

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AB1096 CLINICAL SPECTRUM AND TREATMENT OF THE RELAPSING POLYCHONDRITIS: A SERIES OF 12 CASES

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Background: Relapsing polychondritis (RP) is a systemic autoimmune disease characterized by inflammation of the cartilaginous tissues associated with the appearance of symptoms caused by the involvement of other non-cartilaginous tissues and the presence of systemic symptoms.
Objectives: To describe the clinical characteristics and treatment of patients diagnosed with RP in a third level university hospital.
Methods: Data from RP patients were obtained from the computerized medical history of our center, including demographics, disease phenotype, treatment, laboratory and imaging studies.
Results: A total of 12 patients were included; 66.7% were women, age at diagnosis was 36 [34-52.5] years (median [p25-p75]). The main manifestation observed was auricular involvement (75%) followed by nasal (66.7%), joint (66.7%), and laryngo-tracheo-bronchial disease (50%). All patients were on DMARD's treatment and two thirds of the patients were receiving biological therapy at the time of analysis. Infliximab was the first biological line in all the cases (100%). Other biological therapies used, in order of frequency, were: adalimumab (25%), rituximab (25%) and tocilizumab (12.5%). 50% of the patients associated another autoimmune disease diagnosed before or during RP follow-up: Crohn's disease, epidermolysis bullosa, primary biliary cholangitis, autoimmune hypothyroidism, systemic lupus erythematosus, granulomatosis with polyangiitis and ulcerative colitis. Only one patient (8.33%) associated hematologic disease (myelodysplastic syndrome) and another one died during follow-up.
Conclusion: RP is a rare disease with a broad spectrum of clinical expression, which often requires intensive management to control its manifestations, potentially serious when there is involvement of the tracheobronchial tree or is associated with other autoimmune diseases. A large part of our patients require biological therapy at some point in their evolution.

REFERENCES
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AB1097 RETROPERITONEAL FIBROSIS- A SINGLE CENTER EXPERIENCE

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Background: Idiopathic retroperitoneal fibrosis (iRPF) is a rare, chronic, progressive disorder of unknown etiology and characterized by the presence of inflammatory and fibrous retroperitoneal tissue that often encompasses the ureters or abdominal organs.

Objectives: We evaluated iRPF cases of a single institution cohort to describe the features of patients (pts) with iRPF.
Methods: Twenty-eight iRPF patients who were being followed in our outpatient clinic between 2009 and 2018 were reviewed retrospectively. The demographic characteristics, clinical and radiologic findings, medical and interventional therapies were retrospectively collected and reported.
Results: We evaluated the data of 28 patients (17M/11F). The mean age at the time of diagnosis was 53±10,57, median follow up was 46 (IQR:23-67) months. Fifteen (%50) patients were presented with abdominal-pain which was the most common initial complaint; 9 (32%) flank pain, 1 anuria, 1 nocturia, and 2 had nausea. Twenty-one patients had hydronephrosis (11 bilateral hydronephrosis, 5 right and 5 left hydronephrosis) at initial visit and one patient diagnosed while on temporary hemodialysis therapy. Laboratory tests showed that ESR was elevated in 15 of 23 cases in which it was available (65.2%), with a median value of 39 mm/h (IQR:17-88); CRP was elevated in 19 of 28 patients (68%), with median value 11 (IQR:5,5-46,5). Mean serum creatinine level was 1,14 mg/dl IQR (0,83-1,9). Tissue involvement was detected with computed tomography in 25 (89%) patients. The remaining 3 patients' Involvement was located with ^{18} F-fluorodeoxyglucose positron emission tomography (^{18} F-FDG-PET). ^{18} F-FDG-PET has been performed in 19 patients and 16 of them (84%) revealed tissue involvement of iRPF. Histopathological samples were available for further analysis in 8 cases and 5pts' findings were consistent with iRPF (storiform fibrosis and dense lymphoplasmacytic infiltration were observed) and of these 5 pts, 2 of them were classified as IgG4-related subtype. The remaining 3 pts were diagnosed with positive radiologic findings. Medical and interventional therapies are presented in Table 1. The mean initial oral prednisone dose was 45,5±13,8 mg/day. Prednisone was discontinued in 4 patients after remission and for the remaining 23 pts; 12 pts' prednisone was tapered <5 mg/day at mean 9 (IQR:6,7-22,5) months. One patient diagnosed AML-M2 during the follow-up and had allogenic stem cell transplantation. Final median values of ESR and CRP were 10 mm/h (IQR:4,7-17,7) and 4,4 mg/l (1,9-7,7), respectively (p= 0.001 and p=0.002). Final median serum creatinine level was 1,03 (IQR:0,78-1,28) (p=0,2). Thirteen pts (% 46) were treated successfully with Rituximab who were not responded initial prednisone therapy. Twenty-one pts had ureteral stents and 11 of them are stent free at the final visit. Two pts had ureteroysis but the procedure was failed in one patient. None of the pts was deceased on the follow-up.
Conclusion: Steroids are the mainstay treatment for iRPF and steroid resistant cases could be treated with rituximab rescue therapy. Prompt interventional approaches are valuable bridging therapies for pts who presented with hydronephrosis. Imaging modalities add great value on the diagnose of iRPF.

. Types of medical and interventional therapy

Types of medical therapy	**n, (%)**
Glucocorticoid	27(96,5)
Glucocorticoid only	3 (10,5)
Tamoxifen	8 (28)
Azathioprine	8 (28)
Cyclophosphamide	1 (3,5)
Methotrexate	10(35)
Rituximab	13(46)
Mycofenolate Mofetil	1 (3,5)
Types of interventional therapy	n, (%)
Left ureteral stents	15(53,5)
Right ureteral stents	16(57)
Right nephrostomy	4 (14)
Left nephrostomy	2 (7)
Ureterolysis	2 (7)
Temporary Hemodialysis	1 (3,5)

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AB1098 COMPARISON OF THE PERFORMANCE OF CLASSIFICATION/DIAGNOSTIC CRITERIA FOR POLYMYALGIA RHEUMATICA. SINGLE CENTERSTUDY OF 100 PATIENTS

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Background: Polymyalgia rheumatica (PMR) diagnosis is based on the combination of shoulder and pelvic girdle pain associated with elevated acute phase reactants. Traditionally, Bird et al. [1] and Chuang et al.[2] criteria have been used for establishing PMR diagnosis. In 2012 an international working group developed new European League Against Rheumatism (EULAR)/American Collegue of Rheumatology (ACR) classification criteria for PMR.[3]
Objectives: a) To compare the performance of Bird et al., Chuang et al. and 2012 EULAR/ACR classification criteria for PMR in a single-center study. b) To describe the characteristics of the patients excluded by these criteria.
Methods: We included 100 patients with new-onset PMR who were consecutively diagnosed over a 7-year period by experienced rheumatologists from a single center. PMR diagnosis was confirmed during a prospective 24-months follow-up after excluding other mimicking conditions. Rheumatoid factor (RF) and anticitrullinated protein antibodies (ACPA) were determined in all patients. Subjects were classified by each of the three different criteria.

TABLE 1. 2012 ACR/EULAR CLASSIFICATION CRITERIA

Age at onset ≥ 50 years (required)	94/100	94%
Bilateral shoulder aching (required)	89/100	89%
Abnormal CRP and/or ESR (required)	96/100	96%
Morning stiffness duration > 45 min (2 points)	54/100	54%
Hip pain or limited range of motion (1 point)	90/100	90%
Absence of RF or ACPA (2 points)	100/100	100%
Absence of other joint involvement (1 point)	95/100	95%
Required for classification: score of 4 or more	**84/100**	**84%**

TABLE 2. CHUANG ET AL. CRITERIA (1982)

Age at onset ≥ 50 years (required)	94/100	94%
ESR ≥ 40 mm/hr	96/100	96%
Bilateral aching for ≥ 1 month involving two of the following areas:		
- Neck	47/100	47%
- Shoulders or proximal regions of the arms	89/100	89%
- Hips or proximal aspects of the thighs	90/100	90%
Exclusion of all other diagnosis of mimicking entities	100/100	100%
All criteria are required for classification	**94/100**	**94%**

TABLE 3. BIRD/WOOD CRITERIA (1979)

Age at onset > 65 years	59/100	59%
ESR > 40 mm/hr	96/100	96%
Bilateral shoulder pain/stiffness	89/100	89%
Duration onset < 2 weeks	77/100	77%
Stiffness > 1 h	54/100	54%
Depression and/or weight loss	16/100	16%
Bilateral upper arm tenderness	89/100	89%
Probable: 3 or more	**96/100**	**96%**

Results: We studied 100 patients (61 women/39 men); mean age 67.1 ± 10.2 years. 96% of the patients fulfilled Bird et. al criteria, 94% fulfilled Chuang et al. criteria and 84% of the patients fulfilled 2012 EULAR/ACR criteria (TABLE 1, 2 and 3). We assessed the characteristics of the 16 patients who did not fulfilled 2012 EULAR/ACR criteria: 6 of them were under 50 years of age (range age 43-48 years). Another 10 patients did not complain of pain/stiffness in the shoulder girdle at any time. However, they had typical inflammatory pain involving the pelvic girdle and elevated acute phase reactants.
Conclusion: In our single-center experience we found that 2012 EULAR/ACR criteria classified most of our patients. However, patients who presented predominant pelvic girdle affection and those who were under 50 years old despite showing all the rest of clinical and analytical required criteria were excluded. Some of these patients did fulfill Bird and/or Chuang criteria.

REFERENCES

[1] Bird HA, et al. Ann Rheum Dis.1979;38:434-9
[2] Chuang T, et al. Ann Intern Med. 1982; 97:672-80
[3] Dasgupta B, et al. Ann Rheum Dis. 2012; 71:484-92

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AB1099 CHAGAS DISEASE REACTIVATION IN THE RHEUMATOLOGIC IMMUNOSUPPRESSED PATIENT. IS IT NO LONGER AN ORPHAN DISEASE?

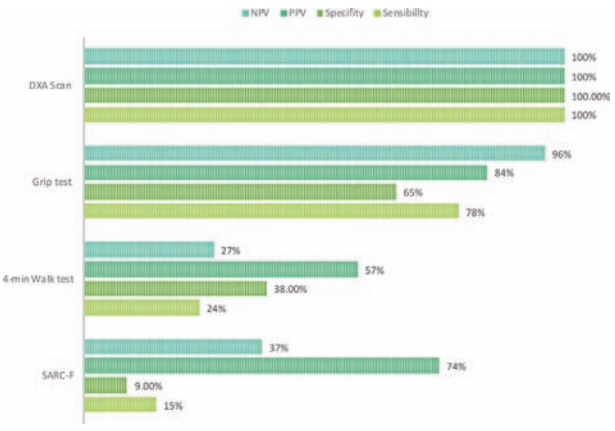
Ariana Ringer[1], Juan Pablo Ruffino[1], Nadia Cuadranti[1], Florencia Martinez[1], Cecilia Argento[1], Ignacio Rolla[1], Juan Manuel Vandale[1], Carla Achilli[1], Mariano Palatnik[1], Noel Cortese[1], Mariana Lagrutta[2], Rodolfo Leiva[3], Damian Aguila[4], Laura Cordoba[5], Milagros Zafra[5], T Gambande[5], Patricia Sciarratta[6], M Svetaz[6], F Gonzalez[7], F Pacini[7], Silvina Villar[7], Ana Rosa Perez[7], Oscar Bottasso[7], Marcelo Abdala[1]. *[1]Reumatología, Hospital Provincial del Centenario, Universidad Nacional de Rosario, Rosario, Argentina*; *[2]Clínica Médica, Hospital Provincial del Centenario, Rosario, Argentina*; *[3]Cardiología, Hospital Provincial del Centenario, Rosario, Argentina*; *[4]Infectología, Hospital Provincial del Centenario, Rosario, Argentina*; *[5]Microbiología, Universidad Nacional de Rosario, Rosario, Argentina*; *[6]Laboratorio Central, Facultad de Ciencias Bioquímicas y Farmaceúticas, UNR, Rosario, Argentina*; *[7]Instituto de Inmunología Clínica y Experimental de Rosario (IDICER, CONICET, UNR), Rosario, Argentina*

Background: Chagas´ disease (CD) is an endemic and neglected infection in Latin America. Due to international human migration, it has become a worldwide issue. Scarce evidence is published regarding its behavior in rheumatic diseases (RD) with rheumatologic treatments (RT).
Objectives: To screen and follow up patients with CD under RT. To detect clinical and serological reactivation.
Methods: A systematic screening was conducted between January 2018 and January 2019 in a third-level Hospital in Argentina. Patients with CD and concomitant RD under RT were included. Assessments were done before and after RT. A direct (Strout) and indirect method (Polymerase chain reaction-PCR) were performed in order to detect parasitemia, levels of antibodies were evaluated by three techniques. Clinical, infectological and cardiological features were examined. Everything was assessed in, at least, two opportunities, separated by a minimum of one month. If treatment was modified or clinical condition changed, all the evaluations were repeated as before. In case of reactivation, specific treatment was indicated and follow up controls were stricter.
Results: 38 patients were identified. RD: Rheumatoid Arthritis: 22 (57,9%), Systemic lupus erythematosus: 4 (10,5%), Systemic Sclerosis: 3 (7,9%), Vasculitis: 2 (5,3%), Psoriatic Arthritis: 1 (2,6%), others: 6 (15,8%). RT: classic, synthetic and biological disease-modifying antirheumatic drugs, cyclophosphamide and corticosteroids.
Two reactivations were detected with both direct and indirect methods, with a significant title antibody increment and consistent clinical signs and symptoms. Cardiological abnormalities were found. A 64-years old lady with Microscopic Polyangiitis, under prednisone 60 mg/day and a 57-years old lady with Systemic Lupus Erythematosus under hydroxychloroquine and prednisone 40 mg/day, who happen to be sisters. They did not have other treatments. Both of them developed high fever, myalgias, arthralgias and asthenia. Other infections were ruled out. They received Benznidazole and Nifurtimox respectively. After one-week treatment, Strout and PCR became negative and antibodies decreased, with remarkable clinical improvement.
Conclusion: Two patients with parasitemia and concomitant symptoms were detected, after high doses of corticosteroids. Because they were sisters, a genetic background would also play a role. Parasite´s screening before starting immunosuppression and its follow-up during treatment in search of reactivation should be integrated to rheumatology daily practice in endemic countries. It should also be taken into account in patients from non-endemic countries that have an epidemiological nexus. CD specific antibodies determination, Strout and PCR are economic and practical techniques, although they require qualified personnel and equipment. In areas with high prevalence of CD, the benefits of this measures would outweigh costs. A more advanced study should be performed to extend our knowledge.
Disclosure of Interests: None declared
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AB1100 PREVALENCE OF SARCOPENIA IN ECUADORIAN POPULATION BASED ON SCREENING AND DIAGNOSTIC TOOLS

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Background: Sarcopenia is defined as an abnormal loss of muscle mass associated with aging. It has been validated that sarcopenia can predict functional deterioration.
Objectives: The purpose of this study is to determine the diagnosis of sarcopenia by conventional methods and gold standard.
Methods: Prospective observational study of patients attending a rheumatology center, to whom anthropometric and densitometric measurements were taken in order to determine sarcopenia.
Results: A total of 110 patients were studied, from which 91% were women and 9% men. 66% presented sarcopenia by means of the gold standard test (DXA). The mean age was 65.80±9.84 [44-89]. The mean age for women was 66.2±9.9 [44-86] and the average age of menopause was 46.08±8.53 and 63% were found to have sarcopenia. In men, the mean age was 73.3±13.8 [63-89] and 30% had sarcopenia.
Anthropometric measures were determined. The mean body mass index was 26.58±4.67, which corresponds to overweight. Three tests were performed in addition to the gold standard. The average gait speed test was 1.12±0.74 seconds and 45% were positive for sarcopenia. The mean of the muscle strength test (dynamometer) was 19.33± 9.52 and 63% had sarcopenia. The mean of the SARC-F screening questionnaire was 3.02±2.24 and 22% were positive for sarcopenia. According to the measurement of muscle mass by DXA, the mean appendicular skeletal muscle mass (ASMM) was 16.08±3.52, ASMM index 6.77±1.12 and the total skeletal muscle was 21.39±4.68. Men presented a higher muscle mass index compared to women [7.82±1.93 vs. 6.66±0.95]. When grouping patients by BMI, sarcopenia was present in all of the patients with low weight, 88% in the ideal weight group, 67% in the overweight group and 25% in the obesity group. A statistically significant relationship was found between sarcopenia and sex [0.01], weight and height [<0.001], gait test [0.04], muscle strength test [<0.001] and DXA [<0.001]. In addition, the sensitivity and specificity of the tests were determined. SARC-F had a 15% sensitivity and a 9% specificity, with a positive predictive value of 74% and a negative predictive value of 37%. The gait speed test 24% sensitivity and 38% specificity, with a positive predictive value of 57% and negative predictive value of 27%. The muscle strength test had a 78% sensitivity and 65% specificity, with a positive predictive value of 84% and negative predictive value of 96% (Figure 1).



Abstract AB1100 Figure 1. Statistical measures of sarcopenia's diagnostic tools.

Conclusion: This is the first study of determination of Sarcopenia in a Rheumatology Center in the city of Guayaquil. 66% of the studied population presented sarcopenia. It is evident that conventional methods may determine a diagnosis, however, a definitive diagnosis can be established by DEXA. Because Sarcopenia is a multidisciplinary entity, more studies are needed to determine the usefulness of the conventional methods.
Disclosure of Interests: None declared
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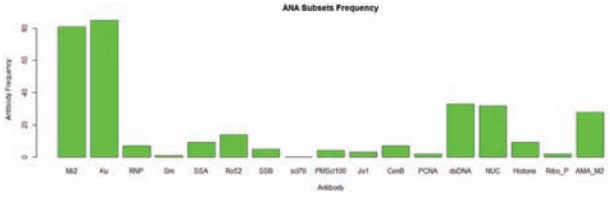
AB1101 ANA SUBSETS ANTIBODY PROFILE OF EARLY UNDIFFERENTIATED ARTHRITIS (UA) IN PAKISTAN

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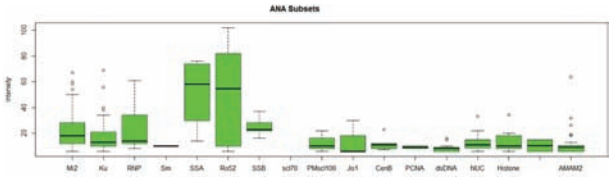
Background: Undifferentiated Arthritis (UA) is a group of inflammatory disorders where early synovitis (duration less than 12 months) is present, however patients do not meet criteria for established rheumatologic disorders such as Rheumatoid arthritis, Lupus or Spondyloarthritis (1). On long term follow up, a subpopulation of UA patients converge into definitive Rheumatologic disorders. Up to 50% of early arthritis in European cohorts has been reported to be UA (1, 2).
Objectives: Identify Anti-nuclear antibody (ANA) Subset antibodies in patients presenting with early UA.
Methods: Over a 1-year period (2017-18) patients with early UA were prospectively evaluated. This included clinical exam, routine laboratory investigations including ESR and CRP, RF and anti-CCP as well as Musculoskeletal ultrasound (MSKUS) (3). These patients underwent further testing for ANA Subset antibodies. ANA subsets (17 antibodies) were performed using standard immunoblot assays (EUROIMMUN) at our clinical laboratory (4).
Results: 110 UA patients were found to have positive ANA subsets. The most frequent antibodies were Ku (77.3%) and Mi2 (73.6%) followed by dsDNA (30%) and Nucleosome antibody (29%) (Figure 1). Low frequency antibodies included Sm (n=1), Ribosomal-P and PCNA (n=2 each), Jo-1 (n=3), PM-Scl100 (n=4) and SSB (n=5), whereas Scl70 antibodies were absent. SSA (n=9) and Ro-52 (n=14) together constituted 21% frequency. These antibodies had high signal intensities (mean ± SD SSA = 52±35 and Ro-52 = 46±25). Ku (17±11) and Mi2 (22±15) had modest signal intensities (Figure 2). Clinically 42 patients were classified as RA (RF+ = 33%; anti-CCP+ = 14%) and 41 patients met ACR criteria for SLE while 2 patients met criteria for both and were classified as Rhupus. ANA subset antibody frequencies did not statistically differ between the RA and SLE groups signifying that the clinically classified RA patients in fact had early Rhupus which did not meet ACR criteria for SLE.
Conclusion: Early UA is difficult to categorize clinically, sometimes even after long term follow up, though a substantial portion converge into RA. This study shows that there is a significant portion of early Rhupus in the RA group whose steroid discontinuation leads to a disease flare. ANA Subset antibody profile in such patients may help in their more accurate diagnoses and treatment.

REFERENCES

[1] van Aken J, van Bilsen JH, Allaart CF, Huizinga TW, Breedveld FC. The Leiden Early Arthritis Clinic. Clin Exp Rheumatol. 2003 Sep-Oct;21(5 Suppl 31):S100-5. PMID: 14969059.
[2] Hülsemann JL, Zeidler H. Undifferentiated arthritis in an early synovitis out-patient clinic. Clin Exp Rheumatol. 1995 Jan-Feb;13(1):37-43. PubMed PMID: 7774101.
[3] Horton SC, Tan AL, Wakefield RJ, Freeston JE, Buch MH, Emery P. Ultrasound-detectable grey scale synovitis predicts future fulfilment of the 2010 ACR/EULAR RA classification criteria in patients with new-onset undifferentiated arthritis. RMD Open. 2017;3(1):e000394. PMID: 28469936.
[4] Op De Beéck K, Vermeersch P, Verschueren P, Westhovens R, Mariën G, Blockmans D, Bossuyt X. Antinuclear antibody detection by automated multiplex immunoassay in untreated patients at the time of diagnosis. Autoimmun Rev. 2012;12(2):137-43. PMID: 22387973.5.



Abstract AB1101 Figure 1. ANA Subsets Antibody Frequency



Abstract AB1101 Figure 2. ANA Subsets Antibody Intensity

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AB1102 SCHNITZLER SYNDROME IN THE CLINICAL PRACTICE OF A RHEUMATOLOGIST

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Background: Schnitzler syndrome (SchS) is a rare autoinflammatory multifactorial disease, manifested by urticaria, monoclonal immunoglobulin (usually IgM) secretion, bone pain, and clinical and laboratory signs of systemic inflammation (fever, leukocytosis, and CRP increase) [1]. SchS is included in the differential diagnosis of the adult Still's disease, autoinflammatory diseases, and Waldenstrom macroglobulinemia. Interleukin 1 (IL-1) inhibitors (anakinra and canakinumab) have been shown to the efficient pathogenetic therapy of SchS [2,3].
Objectives: To provide clinical and laboratory characteristics and the results of IL-1 inhibitors therapy in the SchS patients from 2015 to 2018 observed in the V.A. Nasonova Research Institute of Rheumatology (Moscow, Russia).
Methods: The study included 4 patients (1 female, 3 males) aged from 32 to 56 years. Patients with suspected SchS were studied with electrophoresis of serum and urine proteins, histological and cytological examination of the bone marrow (in 3 of 4 patients), and testing of mutations in *NLRP3* and *TNFRSF1A* genes (in 3 of 4 patients).
Results: SchS was diagnosed 3 to 22 years (median 3,5 years) after the onset of clinical manifestations. Three patients had a fever. All patients showed chronic urticaria and musculoskeletal manifestations (arthralgia and leg bone pain). Two patients showed fluid collections in serous cavities. Pericarditis was observed in one patient, and pleurisy in another patient. To our knowledge, serositis was not described in SchS previously. Three patients had leukocytosis from 16.0 to 23.6 $x10^9$/L. In all patients, ESR (from 31 to 140 mm/h) and CRP level (from 29 to 192 g/L) increased. In all patients, secretion of monoclonal IgM was detected, not exceeding 7.8 g/L. In three cases, IgM included kappa chain, and in one patient biclonal secretion was found (IgM kappa and IgM lambda). Mutations in *NLRP3* and *TNFRSF1A* genes were not identified. None of the patients showed lymphoplasmacytic infiltration of bone marrow. All patients before the diagnosis were prescribed with glucocorticosteroids with a temporary positive response and relapse of the disease after the dose reduction or withdrawal. Two patients received canakinumab 150 mg subcutaneously once every 8 weeks for 1.5-3.5 years, with a complete response. In one, the interval between injections was increased during the last year to 5 months, with the preservation of clinical and laboratory remission of SchS. Against the background of canakinumab therapy, one patient became a farther of a healthy baby. One patient received anakinra 100 mg subcutaneously of daily, with the complete clinical and laboratory response after 2 weeks of therapy. During the use of the IL-1 inhibitors, we have observed none clinically significant side effects.
Conclusion: To diagnose SchS in adult patients with chronic urticaria, fever, and acute phase signs of inflammation, one should perform serum proteins electrophoresis. SchS can manifest with serositis. IL-1 inhibitors in SchS patients are the efficient by and safe therapy.

REFERENCES

[1] Simon A, Asli B, Braun-Falco M, et al. (2013). Schnitzler Syndrome: diagnosis, treatment, and follow-up. Allergy. 68:562-568

[2] Neel A., Henry B., Barbarot S. et al. Long-term effectiveness and safety of interleukin-1 receptor antagonist (anakinra) in Schnitzler syndrome: a french multicenter study Autoimmunity. Reviews. 2014;13:1035-1041
[3] Krause K., Tsianakas A.,Wagner N. et al. Efficacy and safety of canakinubab in Schnitzler syndrome: a multicenter randomized placebo-controlled study. 2017; J Allergy Clin Immunol 2017;139:1311-20.

Disclosure of Interests: None declared
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AB1103 NEUROLOGICAL IMPAIRMENT DURING SARCOIDOSIS

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Background:
Objectives: To describe neurological impairment characteristics in sarcoidosis.
Methods: This was a descriptive and retrospective study including 65 patients with sarcoidosis, followed in the departments of internal medicine and neurology at the Military Hospital of Tunis over a period of 20 years from 1997 to 2017.
Results: A total of 65 patient files have been selected, of which 38 have neurological involvement.
Thirty-eight patients met the inclusion criteria for Neurosarcoidosis. According to Zajicek's criteria, the diagnosis of neurosarcoidosis was certain in 2 cases, probable in 18 cases and possible in 18 cases.
Neurological disorders were symptomatic in 58.5% of the studied population. Neurological signs were inaugural in 9 patients (14% of cases). A central neurological involvement was demonstrated in 33 patients (86.8%), the peripheral nervous system was affected in 5 patients (13.1%), and cranial nerve involvement was found in 10 patients (26.3%).%). Ten patients have had both central and peripheral impairement.
Neurological involvement was significantly associated with cardiac, renal extra-thoracic, ophthalmologic, articular and cutaneous involvement ($p < 0.05$)
Genotyping of the conversion enzyme and HLA typing did not show any particular pattern of neurosarcoidosis in comparison with patients without neurological signs.
Conclusion: Neurological impairement was frequently observed in our series. It was also significantly associated with multivisceral involvement without particular genetic pattern.
Disclosure of Interests: None declared
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AB1104 GENETIC ASPECTS OF SARCOIDOSIS IN A TUNISIAN POPULATION

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Background:
Objectives: To determine the frequencies of the HLA alleles and genotypes of the ACE gene.
Methods: This is a cross sectional study of 65 patients with sarcoidosis, followed in the departments of internal medicine and neurology at the Military Hospital of Tunis.The genetic study involved only 50 patients. DNA extraction was performed to determine the frequencies of the HLA alleles and genotypes of the ACE gene.
Results: 1. HLA typing
The analysis of HLA typing allowed us to estimate the different frequencies of alleles in patients. The calculation of the allelic frequency found that the most frequent alleles are HLA-DRB1 * 1501 alleles with a frequency of 38% and HLA-DRB1 * 0301 of 28%. Other alleles are at lower frequencies (Table1).

HLA N=50	N	%
HLA-DRB1*1501	19	38%
HLA-DRB1*0301	14	28%
HLA-DRB1*1106	9	18%
HLA-DRB1*0401	8	16%

2. Genotyping of the ECA gene
Genotyping of the polymorphism of the angiotensin converting enzyme (ACE) involved 50 patients. Genotypic frequencies (II, ID and DD) and allele frequencies (I and D) were estimated in order to evaluate the frequencies of each genotype and the 2 alleles for this pathology. The genotypic and allelic frequency results were summarized in Table 2.

Genotypes	N	%
II	11	22%
ID	24	48%
DD	15	30%
Alleles		
I	46	46%
D	54	54%

Conclusion: The most frequent alleles in Tunisian patients with sarcoidosis are HLA-DRB1 * 1501 alleles with a frequency of 38% and HLA-DRB1 * 0301 of 28%. The genotypic and allelic results showed that genotype ID was the most frequent with 48% with a predominance of the D allele in 54%.
References:

DISCLOSURE OF INTERESTS
None declared
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AB1105 A NOVEL AUTOINFLAMMATORY AND LYMPHOPROLIFERATIVE SYNDROME ASSOCIATED WITH PIM1 MUTATIONS

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Background: Whole exome sequencing can allow genetic diagnosis in subjects with long lasting clinical stories not supporting any well-defined disorder.
A 35-year-old man was referred to ophthalmologist's evaluation for blurry vision in his left eye. The fundus examination showed choroidal lesions in both eyes. His past medical history was relevant for celiac disease, recurrent episodes of fever and skin rashes with leukocytoclastic vasculitis, inflammatory lesions of the osteoarticular and muscular system, one episode of aseptic meningitis, an intracranial granuloma and two episodes of anterior uveitis. He had also splenomegaly with non-caseating granulomas. Brain TC founded multiple lytic and sclerotic skull lesions. He was diagnosed with atypical sarcoidosis and treated with oral steroid and methotrexate.
Laboratory data always showed elevated erythrocyte sedimentation rate, strong positive C-reactive protein and polyclonal gammopathy.
Objectives: To describe functional and genetic data supporting the role of a PIM1 mutation in the multisystemic inflammation and lymphoproliferation of the patient.
Methods: Whole exome sequencing (WES) analysis. Flow-cytometry to evaluate Pim1 expression, Bad phosphorylation (target of Pim1 kinase) and the effect of PIM inhibitor on peripheral blood mononuclear cell (PBMC) viability. RNAseq was on primary fibroblasts from the patient and

from healthy donors. Cloning of the mutated gene in a vector for further functional studies.

Results: WES analysis revealed the de novo heterozygous missense variation c.C1132A (p.H378N) in *PIM1* gene. This variation was never described in on-line database and was predicted as damaging by various bioinformatic tools. Preliminary functional investigations in fibroblasts showed normal expression of Pim1, but higher phosphorylation of BAD protein was measured in cells from the patient. Moreover, PBMC from the patient displayed a lower sensitivity to the PIM inhibitor PIM447. RNAseq showed an altered expression profile in genes involved in the extracellular matrix organization.

Conclusion: PIM1 is an oncogene that encodes a protein kinase and, indeed, somatic gain of function mutations can be found in cancers. Preliminary data obtained from our patient suggest a gain of function effect of the p.H378N variant. The lymphoproliferative disorder may be sustained by the anti-apoptotic action of phosphorylated BAD. Recent data correlated hyperactive PIM1 in tumors with high degree of inflammatory infiltration accompanied by NFAT and mTOR activation and IL6 expression. A role of this cytokine also in our patient was coherent with a good clinical response to a treatment with tocilizumab, targeting IL-6.

Although these results are supportive of a role of mutated PIM1 in the observed phenotype, we cannot still claim that this is causative of a novel syndrome. The detection of further cases and functional studies on cells transfected with mutated PIM1 will help shedding more light on this inflammatory and lymphoproliferative disorder.

Disclosure of Interests: None declared

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AB1106

PREVALENCE AND EPIDEMIOLOGY OF FAMILIAL MEDITERRANEAN FEVER AND TUMOR NECROSIS FACTORRECEPTOR-ASSOCIATED PERIODIC SYNDROME: RESULTS FROM AN ITALIAN CENTER

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Background: Familial Mediterranean fever (FMF) and tumor necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) represent two forms of periodic monogenic autoinflammatory diseases, characterized by recurrent and auto-limiting attacks of fever and systemic inflammation. Both the diseases are due to the aberrant activation of inflammasome platforms. Several variants in the *Mediterranean Fever (MEFV)* gene and *TNF Receptor Superfamily Member 1A (TNFRS1A)* gene are respectively at the basis of FMF and TRAPS.

Objectives: The aim of this study is to report the genotype and phenotype prevalence of a cohort of patients referring to our laboratory with a suspicious diagnosis of FMF or TRAPS.

Methods: We retrospectively collected genetic and demographic data of patients undergoing *MEFV* (NM_000243) and *TNFRS1A* (NM_001065) genetic test at our laboratory. Both genes were analysed by direct sequencing on both strands. Data were statistically analysed for descriptive and inferential purposes.

Results: A total of 168 cases were collected, most of which were Caucasian subjects (88.0%). The most common clinical manifestation was periodic fever, occurring in 121 cases, with musculoskeletal, intestinal and cutaneous symptoms, polyserositis and lymphadenopathy occurring at variable rates. Demographic and clinical characteristics are resumed in *tab.*1.

MEFV genotyping, performed in 159 patients, identified 8 different pathogenic variants (p.Phe479Leu, p.Met680Ile, p.Met694Val, p.Met694Ile, p. Lys695Arg, p.Val726Ala, p.Ala744Ser, p. Arg761His), associated with different geographic provenience and symptoms (*tab.*2, 4).

Analysis of *TNFRS1A* gene in 80 subjects revealed the presence of the pathogenic variant p.Cys102Tyr in 3 patients (3.75%); *tab.*3, 5.

According to Eurofever scoring system, the *MEFV* variant p.Ala744Ser was significantly associated to the likelihood of having FMF and to the severity of the disease. A higher prevalence of *MEFV* pathogenic variants was observed in Egyptians and patients living in Southern Italy.

Patients n. 168	
Age, years (mean±SD)	39.9 ± 18.0
Age at disease onset, years (mean±SD)	25.8 ± 16.3
Gender [females/males; n.(%)]	94(56.0%)/74(44.0%)
Periodic fever, n.(%)	121 (72.0%)
Musculoskeletal symptoms, n.(%)	72 (42.9%)
Cutaneous rash, n.(%)	14 (8.3%)
Eye involvement, n.(%)	4 (2.4%)
Oral aphtosis, n.(%)	19 (11.3%)
Spleen enlargement, n.(%)	4 (2.4%)
Hepatomegaly, n.(%)	6 (3.6%)
Lymphoadenopathy, n.(%)	34 (20.2%)
Intestinal symptoms, n.(%)	77 (45.8%)
Pericarditis, n.(%)	39 (23.2%)
Peritonitis, n.(%)	10 (6.0%)
Pleuritis, n.(%)	22 (13.1%)
Pharyngodynia, n.(%)	23 (13.7%)
Familial history, n.(%)	22 (13.1%)
NSAIDs, n.(%)	27 (16.1%)
Steroids, n.(%)	36 (21.4%)
Colchicine, n.(%)	35 (20.8%)
Immunosuppressants, n.(%)	12 (7.1%)

Table 1. Demographic characteristics of the whole cohort of patients examined.

Variant	Amino acid Change	rs Code	Exon	Clinical Significance	Wild Type Patients, n. (%)	Heterozygous Carriers, n. (%)	Homozygous Carriers, n. (%)	Missing Subjects, n. (%)
c.306T>C	p.Asp102=	rs224225*	2	Benign	52 (33.1%)	49 (31.2%)	25 (15.9%)	31 (19.7%)
c.414A>G or T	p.Gly138=	rs224224 *	2	Benign	53 (33.8%)	48 (30.6%)	25 (15.9%)	31 (19.7%)
c.442G>C	p.Glu148Gln	rs3743930	2	Uncertain	147 (93.6%)	10 (6.4%)	0 (0%)	0 (0%)
c.495C>A	p.Ala165=	rs224223*	2	Benign	49 (31.2%)	52 (33.1%)	25 (15.9%)	31 (19.7%)
c.605G>	p.Arg202Gln	rs224222*	2	Benign	82 (52.2%)	38 (24.2%)	7 (4.5%)	30 (19.1%)
c.808A>G	p.Asn270Asp	/	2	Other	155 (98.7%)	2 (1.3%)	0 (0%)	0 (0%)
c.866C>T	p.Ala289Val	rs104895132	2	Uncertain significance	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.942C>T	p.Arg314=	rs224213*	3	Benign	31 (19.7%)	61 (38.9%)	34 (21.7%)	31 (19.7%)
c.1105C>T	p.Pro369Ser	rs11466023	3	Other	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.1322G>A	p.Arg441Gln	/	4	/	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.1422G>A	p.Glu474=	rs224208*	5	Benign	34 (21.7%)	55 (35.0%)	37 (23.6%)	31 (19.7%)
c.1428A>G	p.Gln476=	rs224207*	5	Benign	34 (21.7%)	55 (35.0%)	37 (23.6%)	31 (19.7%)
c.1437 C>G or A	p.Phe479Leu	rs104895083	5	Pathogenic	150 (95.5%)	2 (1.3%)	0 (0%)	0 (0%)
c.1503C>T	p.Arg501=	rs76464258	5	Benign	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.1518 C>T	p.Ile506=	rs104895099	5	Likely benign	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.1530T>C	p.Asp510=	rs224206*	5	Benign	36 (22.9%)	54 (34.4%)	36 (22.9%)	31 (19.7%)
c.1764G>A	p.Pro588=	rs12311122*	9	Benign	40 (25.5%)	58 (36.9%)	29 (18.5%)	30 (19.1%)
c.1772T>C	p.Ile591Thr	rs11466045	9	Other	154 (98.1%)	3 (1.9%)	0 (0%)	0 (0%)
c.1818C>G or T	p.Thr606=	rs10489521	10	Untested	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.2040G>A	p.Met680Ile	rs28940580	10	Pathogenic	149 (94.9%)	7 (4.5%)	1 (0.6%)	0 (0%)
c.2080A>G	p. Met694Val	rs61752717	10	Pathogenic	149 (94.9%)	8 (5.1%)	0 (0%)	0 (0%)
c.2082G>A	p.Met694Ile	rs28940578	10	Pathogenic	151 (96.2%)	6 (3.8%)	0 (0%)	0 (0%)
c.2084A>G	p.Lys695Arg	rs104895094	10	Pathogenic	154 (98.1%)	3 (1.9%)	0 (0%)	0 (0%)
c.2118G>A	p.Pro706=	rs2234939	10	Likely benign	155 (98.7%)	2 (1.3%)	0 (0%)	0 (0%)
c.2177T>C	p.Val726Ala	rs28940579	10	Pathogenic	150 (95.5%)	7 (4.5%)	0 (0%)	0 (0%)
c.2230G>T	p.Ala744Ser	rs61752874	10	Pathogenic	154 (98.1%)	3 (1.9%)	0 (0%)	0 (0%)
c.2282G>A	p.Arg761His	rs104895097	10	Pathogenic	155 (98.7%)	2 (1.3%)	0 (0%)	0 (0%)

Table 2. Variants identified in *MEFV* gene (NM_000243).

Variant	Amino acid Change	rs Code	Exon	Clinical Significance	Wild Type Patients, n. (%)	Heterozygous Carriers, n. (%)	Homozygous Carriers, n. (%)	Missing Subjects, n. (%)
c.36A>G	p.Pro12=	rs76745*	1	Benign	17 (20.5%)	38 (45.8%)	15 (18.1%)	13 (15.7%)
c.305 G>A	p.Cys102Tyr	/	3	Likely pathogenic	82 (98.8%)	1 (1.2%)	0 (0%)	0 (0%)
c.362G>A	p.Arg121Gln	rs4149584	4	Uncertain	81 (97.6%)	2 (2.4%)	0 (0%)	0 (0%)
c.369C>T	p.Thr123=	rs1048 95260	4	Uncertain	82 (98.8%)	1 (1.2%)	0 (0%)	0 (0%)

Table 3. Variants identified in *TNFRSF1A* gene (NM_001065).

Variant	Amino acid Change	rs Code	Significant associations	p
c.442G>C	p.Glu148Gln	rs3743930	Provenience from Egypt	0.006
			Provenience from Sicily	0.008
c.808A>G	p.Asn270Asp	/	Provenience from Sicily	0.001
c.866C>T	p.Ala289Val	rs104895132	Provenience from Campania	<0.001
c.1105C>T	p.Pro369Ser	rs11466023	Provenience from Abruzzo	<0.001
c.1322G>A	p.Arg441Gln		Provenience from Abruzzo	<0.001
c.1437 C>G or A	p.Phe479Leu	rs104895083	Provenience from Sicily	<0.001
c.1503C>T	p.Arg501=	rs76464258	Provenience from Abruzzo	<0.001
c.1518 C>T	p.Ile506=	rs104895099	Pleural effusion	<0.001
			Provenience from Lombardy	0.002
c.1772T>C	p.Ile591Thr	rs11466045	Pericardial effusion	0.03
c.1818C>G or T	p.Thr606=	rs10489521	Provenience from Emilia Romagna	<0.001
c.2040G>A	p.Met680Ile	rs28940580	Provenience from Sicily	<0.001
			Provenience from Egypt	<0.001
c.2080A>G	p. Met694Val	rs61752717	Provenience from North Africa	0.02
			Provenience from Lombardy	0.02
			Eye involvement	0.03
c.2082G>A	p.Met694Ile	rs28940578	Provenience from Egypt	<0.001
			Provenience from Calabria	<0.001
c.2177T>C	p.Val726Ala	rs28940579	Provenience from Egypt	0.003
			Provenience from Sicily	<0.001
			Abdominal pain	0.003
c.2230G>T	p.Ala744Ser	rs61732874	Provenience from Trentino Alto Adige	0.002
			Provenience from Campania	<0.001
c.2282G>A	p.Arg761His	rs104895097	Provenience from Egypt	<0.001

Table 4. Significant associations between pathogenic or uncertain significance variants and geographical provenience and clinical data of *MEFV* gene-tested patients.

Variant (nucleotide)	Amino acid Change	rs Code	Clinical significance	p
c.305 G>A	p.C102Y	/	Peritoneal effusion	<0.001
			Lymphoadenopathy	0.01
c.362G>A	p.R121Q	rs4149584	Provenience from Emilia Romagna	<0.001
			Provenience from Campania	<0.001
c.369C>T	p.T123=	rs104895260	Provenience from Campania	<0.001
			Buccal aphtosis	0.01

Table 5. Significant associations between pathogenic or uncertain significance variants and geographical provenience and clinical data of *TNFRSF1A* gene-tested patients.

Conclusion: Our data report *MEFV* and *TNFRS1A* genotypes identified in a cohort of patients referring to an Italian center, affected by periodic fever and other systemic symptoms. Only the *MEFV* variant p.Ala744Ser appeared to be significantly correlated with the Eurofever classification score.

REFERENCES

[1] Vitale A, Rigante D, Lucherini OM, De Palma A, Orlando I, Gentileschi S, Sota J, Simpatico A, Fabiani C, Galeazzi M, Frediani B, Cantarini L. The diagnostic evaluation of patients with a suspected hereditary periodic fever syndrome: experience from a referral center in Italy. Intern Emerg Med. 2017;12(5):605-611.

[2] Federici S, Sormani MP, Ozen S, Lachmann HJ, Amaryan G, Woo P, Koné-Paut I, Dewarrat N, Cantarini L, Insalaco A, Uziel Y, Rigante D, Quartier P, Demirkaya E, Herlin T, Meini A, Fabio G, Kallinich T, Martino S, Butbul AY, Olivieri A, Kuemmerle-Deschner J, Neven B, Simon A, Ozdogan H, Touitou I, Frenkel J, Hofer M, Martini A, Ruperto N, Gattorno M; Paediatric Rheumatology International Trials Organisation (PRINTO) and Eurofever Project. Evidence-based provisional clinical classification criteria for autoinflammatory periodic fevers. Ann Rheum Dis. 2015;74 (5):799-805.

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AB1107 COMPLEMENTARY AND ALTERNATIVE MEDICINE USAGE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is the most common hereditary, chronic autoinflammatory disease. Colchicine is the mainstay of the treatment, which reduces frequency of attacks and amyloidosis risk. Complementary and alternative medicine (CAM) therapies can be a non-mainstream treatment choice in chronic diseases. Frequency of use of CAM therapies among patients with FMF is not established yet.

Objectives: In the current study we aimed to identify the prevalence of the patients using CAM therapies and the factors associated with CAM usage among the patients with FMF.

Methods: One hundred and sixty-five patients were included in the study. Data regarding demographic, social and clinical characteristics were obtained from the patients. The patients were asked whether they were using any type of CAM and if they had suffered harm and/or benefit. The treatment adherence of the patients was assessed using by Morisky Green Levine Scale (MGLS). The Beliefs About Medicines Questionnaire (BMQ-T) was used to assess patient's beliefs about medicines.

Results: Fifty-six (33.9%) patients declared to use at least one CAM. The mean age of the patients was 34.1 ±12.7 years and the mean disease duration was 16.8±10.8 years. The mean dose of colchicine was 1.4±0.4 mg/day. Patients with concomitant disease and positive history of FMF in relatives had higher rates of using of CAM (p=0.011 and p=0.014 respectively). There was no statistically significance between age, sex, marital, socioeconomic and working status, difficulty of access to the treatment center, dose of colchicine, adverse events related to colchicine, attack frequency and disease severity of the patients and frequency of CAM using (p>0.05). The most frequently chosen types of CAM modalities were massage therapy (12.1%), imagining (9.7%), relaxation techniques (9.1%), cupping (9.1%) and natural products (9.1%). It is found that 42 (75.0%) of patients reported that they have suffered benefit from CAM. The mean duration of the using of CAM was 7.9 ±6.4 years.
According to the BMQ-T, there was higher rate of concern about colchicine among patients that were using CAM (p=0.035) (Table 1). There was no statistically significance between compliance with colchicine treatment and using of CAM (p=0.313).

Abstract AB1107 Table 1. Comparison of Beliefs about Medicines Questionnaire Scale of patients according to the use of CAM

Variable	CAM user (n=56)	CAM non-user (n=109)	test	p
	Median (25th–75th percentile)	Median (25th–75th percentile)		
BMQ-T-Specific Necessity	4.0 (3.6-4.6)	4.0 (3.3-4.6)	-0.410[a]	0.682
BMQ-T-Specific Concerns	3.2 (2.6-3.8)	2.8 (2.4-3.6)	-2.110[a]	**0.035**
BMQ-T-General Overuse	2.5 (2.3-3.3)	2.5 (2.0-3.1)	-0.675[a]	0.500
BMQ-T-General Harm	2.4 (2.0-3.0)	2.3 (2.0-3.0)	-0.858[a]	0.391

CAM complementary and alternative medicine, *BMQ-T*Beliefs about Medicines Questionnaire Turkish translation, a Mann-Whitney U test:

Conclusion: Colchicine is the gold standard of treatment because of the known effect of colchicine treatment on the severity and frequency of FMF attacks and the risk of development of amyloidosis. Approximately one third of patients with FMF were using at least one of the CAM modalities in the current study. Concerns about colchicine treatment may have increased the tendency to use CAM therapies. On the other hand, patients should be informed that CAM therapies should not be an alternative to colchicine.

Disclosure of Interests: None declared
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AB1108 COEXISTENCE OF SARCOIDOSIS AND CHRONIC INFLAMMATORY RHEUMATIC DISEASES

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Background: Sarcoidosis is a systemic granulomatous disease of unknown etiology, mediated by Th1 lymphocytes, characterized by bilateral hilar adenopathies, pulmonary infiltrates, ocular, articular and cutaneous involvement and histologically by noncaseating granulomas. Sarcoidosis can simulate many chronic rheumatic diseases but can also coexist with them, so there are doubts about whether there is a true association or is incidental. Likewise, the occurrence of sarcoidosis has been described as a paradoxical effect during treatment with biological drugs, especially with tumor necrosis factor antagonists possibly due to a dysregulation in the compensatory proinflammatory cascade related of TNF blockade.The association between sarcoidosis and Sjögren's syndrome, systemic lupus

erythematosus, polymyositis, spondyloarthritis, systemic sclerosis (ES) or rheumatoid arthritis (RA) has been reported.
Objectives: To describe the clinical characteristics of 15 patients with sarcoidosis and chronic inflammatory rheumatic diseases in 6 hospitals of Catalonia.
Methods: Retrospective descriptive study of patients affected by sarcoidosis and chronic inflammatory rheumatic diseases. The following data were recorded: sex, age, date of diagnosis and clinical characteristics, treatment and evolution of both pathologies. As well as the results of the pulmonary CT, the angiotensin converting enzyme (ACE) and the biopsy results.
Results: We described 15 patients with sarcoidosis, 6 men and 9 women, median age 58 years (39-84). Five patients had seropositive RA (rheumatoid factor and citrullinated antipeptide antibodies), 2 ankylosing spondylitis, 2 psoriasic arthritis, 3 systemic sclerosis, 2 Sjögren's syndrome and 1 dermatomyositis and primary biliary cirrhosis. The diagnosis of sarcoidosis preceded that of rheumatic disease in 5 patients with a mean time of 11.2 years (2-27). It was found to be concomitant in 3 cases and later in 7 patients with an average time difference of 7 years (2-19). At the time of diagnosis of sarcoidosis, 3 patients received treatment with biologic drugs (etanercept, abatacept and golimumab). Fifteen patients presented adenopathies (14 mediastinal and 1 retroperitoneal), 8 lung involvement (micronodullillar interstitial pattern in 4, pulmonary nodules in 2 and unspecified 2), 1 pleural effusion, 8 cutaneous manifestations (2 erythema nodosum, 5 cutaneous sarcoidosis and 1 scar sarcoidosis), 1 muscular pattern with muscle enzymes elevation, 2 lower limb arthritis, 1 meningitis, 1 hepatosplenomegaly, 1 panuveitis and 1 posterior uveitis. The ACE values were high in 8 cases. The histopathological diagnosis of sarcoidosis was made by lung biopsy in 6 patients, ganglionar in 5, cutaneous in 3 and muscular in 1. Ten patients received systemic glucocorticoid treatment with improvement of clinical manifestations and imaging tests. One patient who presented pulmonary involvement also received mycophenolate and another with joint involvement received methotrexate and leflunomide.
Conclusion: A diagnosis of sarcoidosis is often challenging. We must not forget to include it in the differential diagnosis of lung affectation of our patients with chronic inflammatory rheumatic diseases and in particular in those who receive treatment with biological drugs.
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AB1109 CHARACTERIZATION OF PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES (IPAF) AND ITS COMPARISON WITH PATIENTS WITH SCLERODERMA-RELATED INTERSTITIAL LUNG DISEASE AND WITH IDIOPATHIC FIBROSIS

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Background: Diffuse parenchymal pulmonary diseases, called interstitial lung diseases, are a heterogeneous group of disorders that are classified together due to clinical, radiographic, physiological or similar pathological manifestations[1].The diagnosis of idiopathic interstitial pneumonias requires the exclusion of known causes of interstitial pneumonia. Identifying an underlying etiology is important for clinical perspectives because it impacts prognosis and treatment[2]. A recent number of studies has shown that many patients diagnosed as idiopathic interstitial pneumonia have clinical elements that suggest an underlying autoimmune process without meeting established diagnostic criteria for connective tissue disease[3,4].
Objectives: Our objectives were characterize the clinical findings of patients who meet the IPAF criteria and compare them with the clinical characteristics of patients with scleroderma-related interstitial lung disease and patients with idiopathic pulmonary fibrosis.
Methods: We retrospectively reviewed 254 patients hospitalized at the Hospital Clínico de La Universidad de Chile between January 2012 and June 2018 who had ICD-10 diagnosis of J.84 (Other respiratory diseases principally affecting the interstitium) and J99.1 (Respiratory disorders in other diffuse connective tissue disorders). The electronic medical record was reviewed retrospectively to extract pertinent data. We applied IPAF criteria to this 254 patients. We then characterized the clinical, serological and morphological features of the IPAF cohort and compared outcomes to other ILD cohorts: scleroderma-related interstitial lung disease and idiopathic pulmonary fibrosis (IPF).

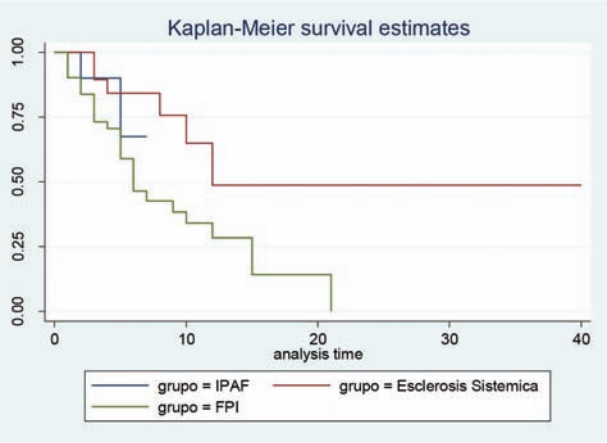


Figure 1

Results: Of 254 patients screened, 17 patients met the IPAF criteria. Mean age was 60 years with a female predominance. The most frequent pattern by high-resolution computed tomography was NSIP present in 46.7%. The median of Forced Vital Capacity was 82%, and median of DLCO was 50%. 14 patients (82%) were treated with corticosteroids. 11 Patients (64%) used other immunosuppressant: 6 patients azathioprine, 4 mycophenolate and 1 patient used cyclophosphamide. One patient received a lung transplant in IPAF cohort. We identified 2 deaths in IPAF cohort, 6 in sclerosis systemic and 30 in IPF cohort. IPAF cohort survival was worse than Scleroderma cohort and better than the IPF cohort.
Conclusion: Our IPAF cohort is similar to the cohorts described in other studies, in relation to the age of diagnostic, female predominance and High-resolution Computed Tomograph pattern. Also the trend in survival was similar to others previously described. Our study have limitations, the first one is related to the retrospective nature of the reviewed cohorts. Further prospective studies should be conducted for a more comprehensive evaluation of the evolution of these diseases and the impact of the treatments used.

REFERENCES

[1] Travis, W. (2002). American Thoracic Society/European Respiratory Society Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. Am J Respir Crit Care Med, 165, 277–304.
[2] Park, J. (2007). Prognosis of fibrotic interstitial pneumonia: idiopathic versus collagen vascular disease-related subtypes. Am J Respir Crit Care Med; 175: 705–711.
[3] Corte, T. 2012. Significance of connective tissue disease features in idiopathic interstitial pneumonia. Eur Respir J 2012; 39: 661–668.
[4] Vij, R. (2011). Autoimmune-featured interstitial lung disease: A distinct entity. Chest; 140:1292–1299.

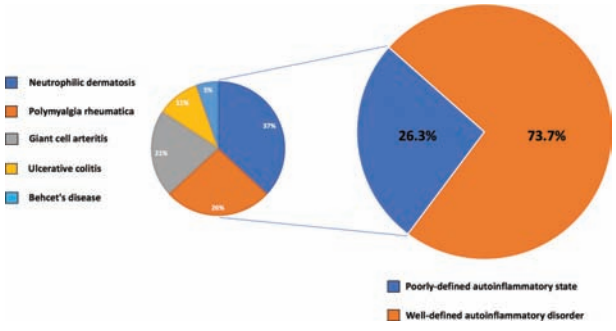
Disclosure of Interests: Karen Vergara: None declared, Silvana Saavedra: None declared, Felipe Reyes: None declared, Annelise Goecke Consultant for: Roche, abbvie, novartis, Phizer, Paid instructor for: Roche, Speakers bureau: Roche, Novartis, Abbvie, pfizer, Caterina Chesta: None declared, Sebastian Chavez: None declared
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AB1110

AUTOINFLAMMATORY DISORDERS ARE COMMON IN PATIENTS WITH MYELODYSPLASTIC SYNDROME AND LINKED TO KARYOTYPE ABNORMALITY AND SOMATIC MUTATIONS STATUS AND A WORSE PROGNOSIS

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Background: Many autoinflammatory diseases are associated with mutations in myeloid lineage cells including neutrophils and macrophages. Myelodysplastic syndrome (MDS) is clinically linked to autoinflammatory diseases e.g. Sweets syndrome and NLRP3 inflammasome activation, is an intrinsic feature of some MDS cases.
Objectives: We tested the hypothesis that autoinflammatory disease is common in MDS cohorts and we further theorised that MDS with somatic mutations and karyotypic abnormalities were associated with autoinflammation.
Methods: 140 MDS patients referred to St. James's University Hospital in Leeds during the period 2012-2018 were systematically and retrospectively recruited with karyotypes and somatic mutations status being performed. Patients with autoinflammation were classified as well-defined autoinflammatory disease or poorly defined "autoinflammatory state" (non-infection related elevated CRP over 10.0 mg/L in 5 consecutive times, taken at separate occasions) based on their final diagnosis and compared in terms of demographic, clinical, laboratory, cytogenetics charts, and outcomes.
Results: The average age was 77.08±11 years (median 79 years), with (n=91, 65.0%) male. 72 (51%) patients had an autoinflammatory state and were younger (75.15±11.23 *versus* 79.15±11.92, p<0.05), and had more frequent arthritis (n=25, 34.7%, *versus* n=12, 17.6%, p=0.0225), arthralgia (n=32, 44.4%, *versus* n=18, 26.5%, p=0.0271), skin rash (n=22, 30.6%, *versus* n=10, 14.7%, p=0.0261), pleuritis (16, 22.2%, *versus* n=3, 4.4%, p=0.0022). 26.3% of MDS patients with autoinflammatory state had a well-defined autoinflammatory disorder (neutrophilic dermatosis, and polymyalgia rheumatic being the commonest). Mutations affecting the transcription factors pathway (NPM1, RUNX1, BCOR, WTI, TP53, MYD88) (OR 3.15 [95%CI 1.04-9.56], p=0.0426) and deletion of chromosome 5 (OR 3.37 [95%CI 1.01-11.22], p=0.0479) were associated with autoinflammation. Stratifying autoinflammatory state, deletion of chromosome 7 and chromosome 5 were found independent predictors for well-defined autoinflammatory disorder and poorly-defined autoinflammatory state, respectively. Furthermore, acute leukaemia transformation was more frequently in MDS patients with autoinflammatory status (n=25, 34.7%, *versus* n=8, 11.8%, p=0.0002).
Conclusion: Both well-defined and poorly defined autoinflammatory diseases are common in MDS. Transcription factors pathway somatic mutations and abnormal karyotype are associated with the risk of autoinflammation. Autoinflammation is linked to a worse prognosis which may be linked to the higher risk of malignant transformation.



Abstract Figure 1. Autoinflammatory state stratified to well-defined and poorly-defined autoinflammatory disorder in MDS patients

Abstract Table 1. Predictors of overall, well-defined or poorly-defined autoinflammatory conditions.

Predictor	OR [95%CI]	p-value
Overall autoinflammation		
Genes mutated	2.28 [95%CI 1.08 to 4.78]	0.0296
Abnormal karyotype	2.67 [95%CI 1.27 to 5.64]	0.0097
Transcription factors pathway	3.15 [95%CI 1.04 to 9.56]	0.0426
Deletion chromosome 5	3.37 [95%CI 1.01 to 11.22]	0.0479
Well-defined autoinflammatory disease		
Genes mutated	3.09 [95%CI 1.01 to 9.46]	0.0486
Abnormal karyotype	3.13 [95%CI 1.03 to 9.48]	0.0439
Transcription factors pathway	4.50 [95%CI 1.04 to 19.47]	0.0441
Deletion chromosome 7	6.13 [95%CI 1.16 to 32.33]	0.0325
Number of mutations	3.39 [95%CI 1.08 to 10.66]	0.0441
Poorly-defined autoinflammatory state		
Abnormal karyotype	2.64 [95%CI 1.82 to 5.88]	0.0179
Deletion chromosome 5	3.57 [95%CI 1.02 to 12.48]	0.0465

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AB1111

RELATIONSHIP BETWEEN SERUM ADENOSINE DEAMINASE LEVELS AND DISEASE ACTIVITY IN AUTOIMMUNE HEPATITIS

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Background: Autoimmune hepatitis(AIH)[1] is a chronic liver inflammation mediated by autoimmune response, characterized by serum autoantibodies, high immunoglobulin G(IgG), and interface hepatitis histology, which can develop into cirrhosis and liver failure. Adenosine deaminase(ADA) is an enzyme involved in purine metabolism, which can catalyze the irreversible conversion from deoxyadenosine to deoxyinosine. As adenosine is an important immunoregulatory factor in the physiological microenvironment, ADA plays an important role in regulating the balance of the human immune system. Previous studies have reported the associations between ADA and disease activity in a variety of autoimmune diseases, such as systemic lupus erythematosus[2], rheumatoid arthritis[3]and juvenile idiopathic arthritis[4].
Objectives: To investigate the relationship between serum adenosine deaminase levels and disease activity in patients with autoimmune hepatitis.
Methods: Thirty patients with autoimmune hepatitis and 30 healthy individuals were included in the study. We enrolled 30 patients who met the simplified criteria suggested by the International Autoimmune Hepatitis Group. All of the cases had been diagnosed with AIH between 2013-2018 at Northern Jiangsu People's Hospital, Department of Gastroenterology or Rheumatology, and the diagnosis was confirmd by liver biopsy. Serum adenosine deaminase levels were measured by enzyme-coupled assay, and >25U/L were determined to be high level 25U/L.
Results: The mean serum ADA levels were prominently higher in AIH patients than those in healthy controls (29.13 ± 8.70 U/L vs 14.50 ± 4.63 U/L, P < 0.001). Serum ADA levels were > 25 U/L in 70% AIH patients and in 0% healthy controls(P < 0.001). Mean serum ADA levels were significantly increased in each stage of disease activity: 26.32 ± 8.78 U/L for mild patients, 31.33 ± 4.23 U/L for moderate patients and

37.20 ± 7.36 U/L for severe patients(P = 0.03). Correlation analysis showed that there was a positive association between serum ADA levels and disease activity (r = 0.43, P = 0.02). Receiver operating characteristic analysis showed that 38.5 U/L was the optimum cut-off point of ADA level for severe disease activity (sensitivity 60%, specificity 92%, area under the curve: 0.81).

Conclusion: The evaluation of serum adenosine deaminse level in patients with autoimmune hepatitis should be considered a useful biomarker in the monitoring of their disease activity.

REFERENCES

[1] Hennes, E.M., et al., *Simplified criteria for the diagnosis of autoimmune hepatitis*. Hepatology, 2008. 48(1): p. 169-76.
[2] Gao, Z.W., et al., *Serum adenosine deaminase activity is increased in systemic lupus erythematosus patients and correlated with disease activity*. Immunol Res, 2018. 66(2): p. 299-304.
[3] Zamani, B., R. Jamali, and A. Jamali, *Serum adenosine deaminase may predict disease activity in rheumatoid arthritis*. Rheumatol Int, 2012. 32(7): p. 1967-75.
[4] Doudkani-Fard, M., et al., *Sensitivity and specificity of adenosine deaminase in diagnosis of juvenile idiopathic arthritis*. Med J Islam Repub Iran, 2014. 28: p. 113.

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AB1112 DIAGNOSTIC DELAY AND DAMAGE OF POLISH ADULT PATIENTS AFFECTED BY HEREDITARY AUTOINFLAMMATORY SYNDROMES

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Background: Autoinflammatory diseases (AIDs) cover a spectrum of diseases, which lead to chronic or recurrent inflammation caused by activation of the innate immune system, typically in the absence of high titre autoantibodies.[1] The most common monogenic AIDs are cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF) and tumour necrosis factor receptor-associated periodic fever syndrome (TRAPS). In hereditary AIDs, chronic and recurrent inflammation can lead to both acute disease and irreversible damage.[2]

Objectives: To describe irreversible damage and diagnostic delay of AID in Polish adult patients (age≥18).

Methods: We rewieved the records of 11 Caucasian (2 women, 9 men) and one female patient with Middle Eastern ancestry followed in our center from Aug 2012 to Jan 2019. We analysed demographic features, diagnostic delay, previous diagnosis and organ damage[3].

Results: Eleven patients had documented variant mutation and AID diagnosis (6-TRAPS, 4-CAPS, 1-FMF). One patient with AA amyloidosis had negative genetic results. The mean age of the patients at the time of disease onset was 9,1 years (0,1- 37) and 33 years (16-62) at diagnosis, In all Caucasian patients diagnosis was established after the age of 18. Previous diagnosis was: JIA (2), AOSD (2), UCTD (4), vasculitis (1), seronegative RA (1), FMF (3 finaly confirmed TRAPS) and allergy (3). Prior treatment included GCS (12/12), cDMARDS (7), antimalarials (6), colchcine (4), bDMARDS: tocilizumab-1, etanercept-2, adalimumab-1, CYC (2).After diagnosis 11 patients received IL-1 inhibitor, ankinra, Only one, 62 year old woman with TRAPS, did not need biological treatment. Only 3 TRAPS patients were free from damage accrual. We documented following damage categories: renal/amyloidosis (5 male cases), developmental (3 growth retardation), ear (severe hearing loss -3 CAPS cases). CINCA male patient at age 29 had multiple organ damage: neurological (epilepsy), severe hearing loss, severe ocular involvement (including optic nerve athrophy), joint restriction and deformity leading to complete physical disability. One FMF woman was adviced elective abortion, one MWS had miscarriage. Two of 3 women had history of malignancy (one: breast cancer and ovarian cancer, and another thyroid cancer). No any mental retardation occured. During follow up 2 male patients with extensive amyloidosis died despite anakinra treatment.

Conclusion: AID are misdiagnosed and have high risk of damage. We advocate the need for efforts in order to increase awarness of AID to reduce the diagnostic delay. The frequency of malignancy in AID should be addressed in future international collaborative studies.

REFERENCES

[1] Masters SL, et al. Horror autoinflammaticus: the molecular pathophysiology of autoinflammatory disease. Annu Rev Immunol 2009;27:621–68.
[2] Federici S, et al. Evidence-based provisional clinical classification criteria for autoinflammatory periodic fevers. Ann Rheumatic Dis 2015;74:799–805.
[3] ter Haar NM, et al. Development of the autoinfammatory disease damage index. Ann Rheum Dis 2017;76:821–830

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Diagnostics and imaging procedures

AB1113 RELATION BETWEEN RESTRICTIVE PULMONARY FUNCTION TESTS AND ULTRASONOGRAPHIC CHANGES OF ASYMPTOMATIC ANTERIOR CHEST WALL JOINTS IN RHEUMATOID ARTHRITISPATIENTS

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Background: Ultrasonography can detect different changes in anterior chest wall (ACW) joints in patients with Rheumatoid Arthritis (RA) even before being clinically manifested.(1) Pulmonary functions may be affected during the course of RA due to interstitial lung problem or chest wall problem.(2)

All studies usually demonstrate the interstitial pulmonary affection in RA but the chest wall joints is usually underestimated by the rheumatology community. Up to the best of our knowledge, there are no previous studies about the relationship between ultrasound detected subclinical changes in ACW and the pulmonary functions in RA patients.

Objectives: To detect the relation between ultrasonographic changes of asymptomatic ACW joints and pulmonary function tests (PFTs) in patients with RA.

Methods: The study included 44 subjects (22 RA and 22 control) in whom 88 sternoclavicular joints (SCJ) and 44 manibrusternal joints (MSJ) were studied. None of the participants had a history of respiratory complaints such as dyspnea, chronic cough, or chest pain. High resolution Computed Tomography (HRCT) was done on the chest to exclude interstitial lung problem that may affect chest expansion and PFTs. Ultrasound (US) assessments were performed to detect synovitis, erosions, ankylosis, osteophytes, or Doppler signals. Chest expansion was measured. PFTs was done and included measurement of the forced expiratory volume in1 s (FEV1), forced vital capacity (FVC), and the ratio of forced expiratory volume in 1 s to the forced vital capacity(FEV1/FVC). In RA group, DAS28 and Health Assessment Questionnaire Disability Index (HAQDI) were recorded.

Results: US detected subclinical changes of ACW joints in (74.2%) of RA patient with significant difference between total US changes in RA (74.2%) and control (21.2%) (p<0.001). MSJ ankylosing and erosions were highly associated with limited chest expansion in RA group(P <0.001). PFTs were found to be restrictive in 13 RA patient (59.1%) with mean of FVC (65.5*±5)%, FEV1 (70.4±9.1)%, FEV1/FVC (80.1±2.6)* with significant difference to control with mean of FVC (93.6*±7.2)%, FEV1 (94.3±4.5)%, FEV1/FVC (95.1±2.4)*. These restrictive PFTs were associated with SCJ synovitis (p=0.04),SCJ PD activity (p =0.04), SCJ erosions (0.02) and highly associated with MSJ ankylosing and erosions (p< 0.001). All RA patients (100%) with MS ankylosing and erosions and SCJ PD activity by US had limited chest expansion and restrictive PFTs. Restrictive PFTs were associated also with limited chest expansion with mean of (*2.3±0.5) with significant difference* (p< 0.001) *to non-restrictive PFTs in RA with mean of (5.2±1.4).*

In RA group, ultrasonographic changes and restrictive PFTs were found to be higher with smoking, longer disease duration and high DAS28.

Conclusion: Our study demonstrated that ultrasonographic subclinical changes in ACW joints is associated with restrictive pattern of PFTs and limited chest expansion in RA patients.

REFERENCES
[1] -Abdelrahman F, Mortada M, Abdul_Sattar A, et al; Annals of the Rheumatic Diseases 2017;76:733.
[2] - Kalyani Praba P, Thamarai Selvi K, Vijay Anand B, Saravanan A. Evaluation of lung function tests in rheumatoid arthritis patients. Natl J Physiol Pharm Pharmacol 2017;7(7):693-696.

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AB1114 CALPROTECTIN IN SERUM AND SYNOVIAL FLUID AS A BIOMARKER IN ACUTE ARTHRITIS

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Background: There are increasingly data about the usefulness of calprotectin levels in chronic inflammatory arthritis and its relationship with prognostic factors. However, few data are available on its role in the diagnosis of acute arthritis.
Objectives: To evaluate the possible usefulness of testing plasma and synovial fluid (SF) calprotectin levels as a predictor of the final diagnosis behind an acute mono or oligoarthritis.
Methods: Longitudinal observational study. We included non-consecutive patients referred to the rheumatology emergency department with suspected mono or acute oligoarthritis for a period of 23 months. Patients with a previous diagnosis of inflammatory, infectious or neoplastic disease were excluded. All of them underwent diagnostic arthrocentesis and blood extraction simultaneously. The SF was evaluated under optical microscopy immediately for the study of microcrystals. Samples of SF were also routinely sent to microbiological culture, and calprotectin levels (SFC) and cell count were determined. In blood, the calprotectin level (SC), CRP and ESR were determined. The calprotectin level in plasma was determined by an automated fluoroenzyme-immunoassay technique on an ImmunoCAP250 analyzer (Thermo Fisher). All patients were followed until diagnostic confirmation. The statistical analysis was performed with the SPSS 22.0 program.
Results: 41 patients were collected, 28 men (68.3%) and 13 women (31.7%) with a mean age of 56.2 years (SD 17.6). The patients presented an average of 6.5 days of symptoms duration (SD 7), manifested as monoarthritis in 80.5% of the cases, with the knee being the most frequently affected joint (92.5%).
In all patients, SF culture was negative. The most frequent diagnosis was microcrystalline arthritis in 21 patients (13 gout and 8 pseudogout), followed by the forms of onset of different chronic inflammatory arthropathies (9). Another 8 patients presented a mechanical joint effusion, in 1 patient the final diagnosis was not collected and there were 2 patients who presented other diagnoses (viral oligoarthritis, pigmented villonodular synovitis).
Calprotectin values were higher in SF than in serum (mean 73,058 vs 824.75 µg/g). A high positive correlation was found between the SC and the CRP ($p<0.05$, $r=0.7$) whereas the correlation with the number of leukocytes in SF ($p<0.05$, $r=0.47$) and with the ESR (<0.05, $r=0.5$) was moderate. The SFC was correlated with the CRP ($p<0.05$, $r=0.45$) and with the cell count in SF ($p <0.05$, $r = 0.6$), but not with the ESR. Regarding the different diagnoses, SC was numerically higher in microcrystalline arthritis (1157 µg/g) compared to non-microcrystalline arthritis (862 µg/g), although these differences were not significant due to the low number of patients in each group.
Conclusion: Our preliminary results suggest that the analysis of SC could complement the information provided by a conventional analysis in the differential diagnosis of acute arthritis in situations in which an arthrocentesis is not possible. Studies with a greater number of patients and that include patients with septic arthritis are necessary.
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AB1115 OBESITY AND FLAT VERTEBRAE

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Background: Spine is a mechanical structure, in a young and healthy individual, under a radiological focus, disposes their vertebral bodies in harmony with their stature, and progressively increasing in magnitude from the cervical to the lumbar spine, in a range of vertical growth that it can exceed the horizontal (1).
It is postulated that the important obesity in the early stages of life, could modify the vertebral parameters by skeletal overloads, but the problem is that the current vertebral indexes do not measure a relation of the person height with his vertebra (2).
Objectives: Thus, to check whether the childhood obesity could modify the vertebral parameters, or it is accepted that it entails a loss of equivalent stature, and in this case would be necessary a study comparative of average height, or whether the harmony of the individual is accepted, it would be necessary to create an index that combine these variables to objectify if its value is a constant, and thus, eliminate the ambiguity of the observer.

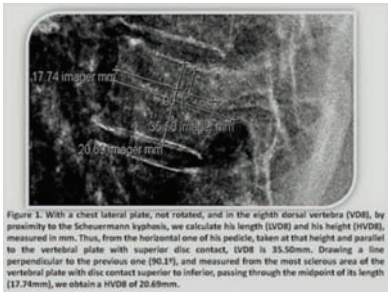


Figure 1. With a chest lateral plate, not rotated, and in the eighth dorsal vertebra (VD8), by proximity to the Scheuermann kyphosis, we calculate his length (LVD8) and his height (HVD8), measured in mm. Thus, from the horizontal one of his pedicle, taken at that height and parallel to the vertebral plate with superior disc contact, LVD8 is 35.50mm. Drawing a line perpendicular to the previous one (90.1º), and measured from the most sclerous area of the vertebral plate with disc contact superior to inferior, passing through the midpoint of its length (17.74mm), we obtain a HVD8 of 20.69mm.

Methods: We selected a population of obese (BMI≥35), both sex, between 20 and 55 years old, in bariatric surgery protocol, with a significant obesity in their development. Was excluded any cause that could produce vertebral flattening. As a control group, was included any patient that went to outpatient visit of rheumatology, and which met the inclusion and exclusion criteria above, except obesity.

As variables, sex, age, body mass index (BMI), and with a chest lateral plate, not rotated, and in the eighth dorsal vertebra, we calculate his length (LVD8) and his height (HVD8), measured in mm. Figure 1.
Finally, we applied a comparative study of average of height and vertebral index (VI) results: VI = 10 x LVD8/(HVD8 x stature)
Results: 90 patients were analyzed. 20 patients in the study group (22.2%): 48.1% female, 48.6 years old, 38.2 BMI, and VI 11.6 Meters-1 And 70 patients in the control group (77.8%): 51.1% females 45.15 yers old, 26.2 BMI, and VI 11.2 Meters-1
The comparative analysis of averages does not show any significant differences in the index or in the stature of these patients.
Conclusion: It is a small study, and according to height or the created index, it does not seem that obesity in development modifies the overall height or the vertebral parameters. In addition, the index gives a stable value regarding the sex of both populations in the eighth dorsal vertebra.

REFERENCES
[1] White AA, Panjabi MM. Clinical Biomechanics of the Spine. 2nd ed, Lippincott Williams & Wilkins, 1990.
[2] Gooding CA, Neuhause EBD (1965) Growth and developedment of the vertebral body in the presence and absence of normal stress. AJR 93:388.
[3] Veiga C RM. Vértebra plana. Revisión de concepto y aproximación diagnóstica. Semin Fund Esp Reumatol. 2009;10(2):56-63.

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AB1116 CORRELATION BETWEEN SERUM RESISTIN AND CAROTID INTIMA-MEDIA THICKNESS AS A MARKER OF SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Although SLE management has improved markedly in the last few decades, cardiovascular disease (CVD) is still one of the most important leading cause of death. Subclinical atherosclerosis is increased in patients with SLE and it is not fully explained by traditional cardiovascular risk factors. Evidences suggest that resistin is involved in pathological processes leading to CVD including; inflammation, endothelial dysfunction, thrombosis, angiogenesis and smooth muscle cell dysfunction. Objectives: to determine the relation between serum resistin level and carotid intima-media thickness by doppler technique as a marker of premature or subclinical atherosclerosis in SLE patients.
Methods: this is a cross-sectional study, carried on thirty Egyptian SLE patients who fulfilled the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria. All patients had metabolic syndrome were excluded. Twenty healthy individuals, non smokers, matched for age and sex as controls. All patients were subjected to detailed history taking, a complete clinical examination. Laboratory investigations were done included serum resistin and HOMA was calculated, also the SLE disease activity index (SLEDAI 2K) and SLE disease damage index (SLEDDI) were applied and the scores were estimated. The carotid intima media thickness (CIMT) was assessed by carotid doppler ultrasonography.
Results: There was no statistically significant difference in serum resistin between SLE patients and healthy individuals (p=0.804). As regards the correlation with disease parameters Serum resistin show statistically significant correlation correlation with hs-CRP (p=0.027), HDL (p<0.001), and ANA titre (p=0.013), but no significant correlation with HOMA, SLEDAI, SLEDDI, CIMT and different clinical activities. There was a statistically significant difference in CIMT between SLE patients and the controls (P= 0.006).
Conclusion: Although serum resistin is correlated with two of cardiovascular risk factors (HDL, hs-CRP), it doesn't correlate significantly with CIMT in SLE patients. Resistin is correlated to inflammation more than subclinical atherosclerosis. Moreover, SLE patients have higher CIMT than healthy population so SLE is considered a CVD risk factor.

REFERENCES

[1] Gisterå A, Hansson GK. The immunology of atherosclerosis. Nature Reviews Nephrology. 2017 Jun;13(6):368.
[2] Stanic AK, Stein CM, Morgan AC, Fazio S, Linton MF, Wakeland EK, Olsen NJ, Major AS. Immune dysregulation accelerates atherosclerosis and modulates plaque composition in systemic lupus erythematosus. Proceedings of the National Academy of Sciences. 2006 May 2;103(18):7018-23.
[3] Chu S, Ding W, Li K, Pang Y, Tang C. Plasma resistin associated with myocardium injury in patients with acute coronary syndrome. Circulation Journal. 2008;72(8):1249-53.

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AB1117 DIAGNOSTIC VALUE OF ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODIES FOR JUVENILE IDIOPATHIC ARTHRITIS IN KOREA

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Background: Anti-cyclic citrullinated peptide(CCP) antibodies are considered to have specificity for rheumatoid arthritis(RA). However, the diagnostic value of anti-CCP antibody has not been proved in juvenile idiopathic arthritis(JIA).
Objectives: The purpose of this study was to access the prevalence of anti-CCP antibodies in Korean children with JIA, and to investigate the diagnostic accuracy of anti-CCP antibodies according to JIA subgroup.
Methods: JIA patients were recruited from Severance Children's Hospital, Seoul, Korea from 2004 to 2018. Diagnosis of JIA was made by pediatricians according to the International League of Associations for Rheumatology (ILAR) classification. Control group consisted of healthy children with anti-CCP antibodies test, who had visited the outpatient clinic of the hospital for JIA suspected symptoms, but diagnosed as not JIA. Enzyme-linked immunosorbent assay (ELISA) was used for detection and quantification of anti-CCP antibodies.
Results: Study subjects included 295 JIA patients and 165 controls. Among the JIA children, 14 (8.6%) patients were found to be positive for anti-CCP antibodies. 1 (0.6%) of the control group was positive for anti-CCP antibodies. The positive rates of anti-CCP were highest in rheumatoid factor (RF)-positive polyarticular JIA (n=8, 66.7%), followed by systemic JIA (n=3, 3.4%) and oligoarticular JIA (n=3, 2.2%). The sensitivity and specificity of anti-CCP antibodies in all JIA patients was 4.7% and 99.4%.
Conclusion: Anti-CCP antibodies have high specificity for JIA, but its sensitivity is low. Therefore, it can provide additional help for diagnosis of JIA with its high specificity. In particular, anti-CCP antibodies have the highest sensitivity in RF-positive polyarticular JIA than other subgroups, so it can be a more effective diagnostic tool in the subtype.

REFERENCES

[1] Ferucci ED, Majka DS, Parrish LA, et al. Antibodies against cyclic citrullinated peptide are associated with HLA-DR4 in simplex and multiplex polyarticular-onset juvenile rheumatoid arthritis. Arthritis Rheum 2005; 52:239.
[2] Hamooda M, Fouad H, Galal N, et al. Anti-cyclic citrullinated peptide antibodies in children with Juvenile Idiopathic Arthritis. Electron Physician 2016; 8:2897.
[3] Petty RE, Laxer RM, Wedderburn LR. Juvenile idiopathic arthritis. In : Petty RE, Laxer RM, Lindsley CB, Wedderburn LR. Textbook of Pediatric Rheumatology. 7th ed. Phliladelphia: W.B Saunders, 2016:188-204.

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AB1118 THE ROLE OF ANGIOPOETHIN-LIKE PROTEIN 4 TYPE IN PROGRESSION OF INFLAMMATORY CHANGES IN RHEUMATOID ARTHRITIS

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Background: Angiopoietin-like protein 4 (ANGPTL4) is actively involved in the processes associated with inflammation, angiogenesis and lipid metabolism in rheumatoid arthritis (RA).
Objectives: To study of the effect of ANGPTL4 on the features of the inflammatory process in RA.
Methods: The study included 36 RA patients (aged from 33 to 64 years old). A control group (12 people) comprised healthy individuals aged 28 to 52 years old, 28 patients with osteoarthritis (OA) aged 48 to 70 years and 14 people with ankylosing spondylitis (AS) aged 39 to 62 years. Levels of ANGPTL4 in serum were determined by the enzyme immunoassay using the commercial test systems «Human Angiopoietin-like Protein 4 ELISA» from «Bio Vendor» (Czech Republic). Serum C-reactive protein (CRP) levels, erythrocyte sedimentation rates (ESR), rheumatoid factor (RF) titers, and anti-cyclic citrullinated peptide antibody (anti-CCP) were also measured in patients with RA.
Results: The following results were obtained: the level of ANGPTL4 was significantly higher in patients with RA than in patients with OA, AS, and healthy individuals ($p = 0.04$, $p = 0.021$, $p = 0.038$, respectively). A strong positive correlation was found between the level of ANGPTL4 and the activity of RA according to DAS28 ($r = 0.71$, $p = 0.002$). There is no reliable association between ANGPTL4 and anti-CCP ($p > 0.05$). The ANGPTL4 level in the serum was correlated with levels of ESR ($r = 0.42$, $p = 0.019$), CRP ($r = 0.49$, $p = 0.007$) and the Sharp score of radiologic change ($r = 0.39$, $p = 0.045$) in RA. Hypervascularization rates were significantly correlated with ANGPTL4 in patients with RA ($r = 0.38$, $p = 0.002$) according to Doppler data. ANGPTL4 can activate proliferation processes in the synovial membrane by binding to integrin-$\alpha v\beta 3$. Besides,

the concentration of mast cells is increased in the synovium of affected joints. Mast cells significantly influence angiogenesis through the production of proangiogenic cytokines, including ANGPTL4.
Conclusion: Changes of the level of ANGPTL4 in the serum of patients with RA may be a potential biomarker of disease activity, severity of neovascularization, inflammation and development of bone erosion.
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AB1119 THE PRESENCE OF SYNOVITIS IS THE MAIN FACTOR INFLUENCING THE DEVELOPMENT OF PAIN SYNDROME IN ARTHRITIS OF THE KNEE JOINT

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Background: Dysfunctions and pain syndrome in lesions of the knee joint can significantly discomfort a sick person and lead to a persistent decrease in physical activity and disability. Often pain syndrome precedes radiographic appearance of the structural changes in the joint and is accompanied by an increase in number of different changes in the synovium according to ultrasound investigation.
Objectives: To investigate the clinical significance of ultrasound criteria of changes in the synovial membrane of the knee joint cavity and its role in the assessment of pain in gonarthrosis.
Methods: 30 people aged 30 to 50 years with osteoarthritis of the knee joint were under observation; assessment of the severity of pain in the knee when walking was at least 40 mm on a visual analogue scale (VAS). Ultrasound examination of the knee joint was carried out according to standard procedure using a linear sensor with a frequency of 05.12 MHz in an ultrasonic diagnosis system Accuvix V10 (Samsung Medison, Korea).
Results: The evaluation of ultrasound changes was performed in the upper inversion of the knee joint according to the following criteria: the severity of intraarticular effusion (1), synovial proliferation (2), local vascularization of the synovial membrane by power doppler (3). All patients were divided into three groups, according to the severity of pain in the knee joint: group I (12 people) - 41–59 mm, group II (10 people) - 60–79 mm, group III (8 people) - 80-100 mm on the VAS scale. By comparing changes in the knee joint by ultrasound data in patients of different groups, the following results were obtained: group I: severity of intraarticular effusion - 10 people (minimal changes in 60%, moderate in 20%, expressed in 20%), synovial proliferation - 4 people (moderate changes in 50%, expressed in 50%), local vascularization of synovium - 6 people (minimal changes in 66.7%, moderate in 16.7%, expressed in 16.6%); Group II: severity of intraarticular effusion - 9 people (55.6%, 22.2% and 22.2%), synovial proliferation - 3 people (0%, 33.3% and 66.7%,), local vascularization of the synovial membrane - 4 people (25%, 25% and 50%, respectively); group III: severity of intraarticular effusion - 8 people (62.5%, 12.5% and 25%), synovial proliferation - 5 people (20%, 40% and 40%), local vascularization of the synovial membrane - 3 people (per 33.3%, respectively).
Conclusion: The use of ultrasound in the diagnosis of diseases of the knee joints allows to reliably determine the structural and functional changes in all components of the knee joint. The severity of pain in gonarthrosis is most associated with the presence of synovitis in the joint.
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AB1120 DIAGNOSTIC ROLE OF NEUROMUSCULAR ULTRASOUND IN CUBITAL TUNNEL SYNDROME

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Background: Cubital tunnel syndrome (CuTS) is the second most common compressive neuropathy of the upper limb following carpal tunnel syndrome and is the most common site for entrapment for the ulnar nerve
Objectives: Our aim is to evaluate the role of ultrasonography (US) as a diagnostic tool for Cubital tunnel syndrome (CuTS) in comparison with nerve conduction study (NCS).
Methods: twenty elbows with CuTS and twenty asymptomatic controls were assessed by NCS and underwent ultrasonography of elbows. Data from patients and controls were compared to determine the diagnostic relations in patients with CuTS and the grade of severity
Results: There was a high degree of correlation between NCS of the ulnar nerve, clinical parameters and variable US measurements. The CSA of the ulnar nerve was the most sensitive parameter and a cut-off point of 9.5 mm^2 behind medial epicondyle was found to be 100% sensitive and 80% specific. The ulnar nerve ratios (UNR) had a diagnostic accuracy of 95% with 85% specificity.
Conclusion: Ultrasonographic measurements of the ulnar nerve CSA and UNR have a comparable diagnostic value as a non-invasive and an alternative modality for the evaluation of CuTS

REFERENCES

[1] Simon N, Ralph J, Poncelet A, Engstrom J, Chin C, Kliot M. A comparison of ultrasonographic and electrophysiologic 'inching'in ulnar neuropathy at the elbow. Clin Neurophysiol. 2015;126(2):391-398.
[2] Omejec G, Podnar S. Normative values for short segment nerve conduction studies and ultrasonography of the ulnar nerve at the elbow. Muscle nerve. 2015;51(3):370-377.
[3] Yoon J, Walker F, Cartwright M. Ultrasonographic swelling ratio in the diagnosis of ulnar neuropathy at the elbow. Muscle nerve. 2008;38 (4):1231-1235.
[4] Bayrak A, Bayrak I, Turker H, Elmali M, Nural M. Ultrasonography in patients with ulnar neuropathy at the elbow: Comparison of cross sectional area and swelling ratio with electrophysiological severity. Muscle nerve. 2010;41(5):661-666.

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AB1121 EFFICACY AND SAFETY OF ULTRASOUND GUIDED ASPIRATION AND INTRA_LESIONAL CORTICOSTEROIDS INJECTION OF RUPTURED BAKER'SCYST

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Background: Baker's cyst is the most common mass in the popliteal fossa and results from fluid distension of the gastrocnemio-semimembranosus bursa. The most common complication of Baker's cyst is the rupture or dissection of fluid into the adjacent proximal gastrocnemius muscle belly, which results in a pseudothrombophlebitis syndrome mimicking symptoms of DVT.
Treatment of ruptured Baker cysts ranged from conservative management to surgical resection.
Ultrasonographic guided aspiration and corticosteroids injection may be an effective and easy method of management of these cases.
Up to the best of our knowledge, this is the first study to detect the efficacy and safety of ultrasonographic guided aspiration and injections of ruptured Baker cysts.
Objectives: To evaluate the efficacy and safety of ultrasonographic guided aspiration and local corticosteroids of ruptured Baker cysts based on follow-up clinical and sonographic results.
Methods: A retrospective study was conducted on 42 patients (12 males and 30 females, mean age 36 +/- 10 SD years) affected by a ruptured Baker cysts associated to knee joint disorders in the period between January 2013 to January 2019.The diagnosis was done by clinical presentation of acute calf pain, swelling, tenderness at the calf muscles and ultrasonographic evidences of ruptured backer cysts in the form of free fluid collection in the calf connected to a well defined cyst at the back of knee.
All cases were treated by ultrasonographic guided aspiration and intra_lesional injection of corticosteroids once or twice one week a part. Follow up were done on a weekly basis until complete resolution of symptoms then 3 months later. Visual analogue scale (VAS) for calf pain and Rauschning-Lindgren and Lysholm Knee Scoring Scales were used to assess pre/post-injection knee functions.
Results: The primary diagnoses to patients presented with ruptured Baker cyst in this study were as follow: 18 (42.8%) cases with rheumatoid

arthritis, 15 (37.5%) cases with osteoarthritis and 9 (21.4%) cases with psoriatic arthritis.
Clinical parameters (VAS for calf pain and Rauschning-Lindgren score) improved significantly in all patients at both post injection evaluation visits.
Rauschning-Lindgren score was significantly lower after US guided injections (mean, 0; range, 0-1) than at baseline (mean, 2; range, 1–2); $p < 0.001$ (table1).
VAS for calf pain also significantly lower after US guided injections (mean,0.5; range, 0-1) than at baseline (mean, 9.5; range, 0-10); $p < 0.001$.
Ultrasonographic features improved significantly with complete disappearance of free fluid at the calf in 35 (83.3%) cases one week after the injection.
As regards Baker cyst only 5 (11%) cases showed complete disappearance of the backer cyst and in the majority of cases 37 (88%) there were persistent Baker cysts.
No side effects were reported in all cases.

Abstract AB1121 Table 1. Clinical results of Baker cyst excision (Rauschning and Lindgren scale and VAS for calf pain)

	Pre injection	1 week later	3 months later
grade 0	0	30	39
Grade 1	0	8	3
Grade 2	6	4	0
Grade3	36	0	0
VAS for calf pain	9.5	1.5	0.5

VAS; visual analogue scale
Conclusion: Ultrasonographic guided aspiration and intra_lesional corticosteroids injection is an effective and safe method in management of ruptured Baker cysts.

REFERENCES

[1] Nigerian Journal of Orthopaedics and Trauma June 2009: 8 (1): 31-32

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AB1122 PREDICTION OF THE UTILITY OF ULTRASOUND EVALUATION IN RHEUMATOID ARTHRITIS BY THE CLINICAL FACTORS

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Background: It is known that ultrasound detects synovitis with higher sensitivity than physical examination in rheumatoid arthritis (RA), and the residual inflammation detected by ultrasound even in the patient achieving clinically remission well correlates with progression of erosion.[1] However, It is impossible to perform ultrasound evaluation on all the joints in all the patients in terms of time and human resource.
Therefore, ultrasound use in RA should be more focused on situations when the physical findings and ultrasound findings likely to dissociate. Hirata et al showed the concordance between swelling or tenderness joint and ultrasound-detected synovitis are low in the PIP, MCP, and wrist joint.[2]
Objectives: To investigate the factors that can predict dissociation between clinical and ultrasound-detected synovitis in the patient with rheumatoid arthritis.
Methods: Patients aged 18 years or older who satisfied ACR/EULAR 2010 criteria who visited St. Luke's International Hospital from June 1, 2018 to November 9, 2018 and were performed ultrasound on PIP, MCP, and wrist joints were eligible for this study. We retrospectively reviewed the electronic medical chart and ultrasound data, and analyzed the dissociation of clinical synovitis defined as existence of swelling or tenderness and ultrasound-detected synovitis defined as both of power doppler grade and gray scale grade 1 or gray scale grade 2. Clinical evaluation was done by the attending physician who ordered the ultrasound evaluation. Ultrasound evaluation was done using standard scan technic[3] by the sonographers who are blinded to the clinical evaluation.
The correlation between patient's characteristics and dissociation was analyzed using χ^2 test, Mann-Whitney U test and logistic regression analysis.
Results: 51 joints in 32 patients (4 males, 28 females) were included in the study. Among the 32 patients, 18 was classified in the dissociation group (DG) and 14 in the non-dissociated group (NDG). No significant difference was observed in the patient's characteristics of DG and NDG. In the univariate analysis, the absence of swelling in the target joint had tendency to be the risk of dissociation. The same tendency was preserved in the multivariate analysis with the presence of tenderness in the target joint assigned as a covariate (OR 3.68, 95% CI = 0.85 - 15.90, p = .08).
Conclusion: There was a numerical tendency that no swelling on the joint is a risk factor for the dissociation between clinical synovitis and ultrasound-detected synovitis. Future study with increased number of participants may identify more sensitive risk factors for dissociation, and enable to make an effective indication of ultrasound evaluation in the care of RA.

REFERENCES

[1] Kawashiri S, et al. Rheumatology 53.3, 2013: 562-569.
[2] Hirata A, et al. Arthritis Care & Research Vol. 69, No. 6, June 2017: 801–806
[3] Naredo E, et al. Annals of the rheumatic diseases 64.3, 2005: 375-381.

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AB1123 SHOULDER PAIN: ARE THERE PREDICTIVE FACTORS OF RESPONSE TO TREATMENT AND OF ULTRASOUND FINDINGS?

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Background: Shoulder pain is a common cause of consultation in Primary Health Care, and may correspond to up to 30% of the reasons for consultation. Pathology of the rotator cuff is the most common cause of pain. Ultrasound is a valuable diagnostic tool in assessing shoulder disorders; it can be as effective as magnetic resonance imaging.
Objectives: To determine the predictive factors of response to treatment and ultrasound findings in shoulder pain.
Methods: We performed an analysis of the patients' cases sent to the rheumatology consultation with shoulder pain, every patients had an echography shoulder evaluation, and the rheumatologist decided treatment based on the guidelines for the treatment of shoulder tendinopathies. The use of nonsteroidal anti-inflammatory drug (NSAIDs) and muscle relaxant medications as well as the following techniques: corticosteroids local injection, barbotage, capsular distension and physiotherapy programs were some of the variables assessed. Posteriorly, the patients were clinically assessed in a follow-up visit.
Results: A total of 119 patients were evaluated. Men presented a higher risk of distension of the subscapular bursa. There was a statistically significant relationship between the time from the beginning of the symptomatology and treatment response. Diabetes *mellitus*, arterial hypertension and dyslipidaemia were statistically significantly associated with some rotator cuff lesions and distention of the subscapular bursa.
Conclusion: In patients with shoulder pain, early intervention positively influences the response to treatment. Thus, it is important that these patients are evaluated more promptly.
Some comorbidities seem to be associated with a higher risk of specific rotator cuff lesions.
No relationship was found between response to treatment and age, sex, occupation, previous treatments or type of therapy selected. The associations found in this study seem to have clinical implications. Prevention of rotator cuff disease is a matter of major relevance as well as early institution of treatment.

REFERENCES
[1] Greenberg D.L. 2014
[2] Rechardt M. et al. 2010
[3] Teunis T, et al. 2014
[4] Armstrong A. 2014
[5] Lenza M, et al. 2013
[6] Middelton WD, et al. 2004
[7] Mathias R, et al. 2018
[8] Gatt DL, et al. 2014
[9] Booker S, et al. 2015
[10] Alfahad N, et al. 2015
[11] Le Goff B. et al. 2010
[12] Lansdown DA, et al. 2012
[13] Mantone JK, et al. 2000
[14] Gialanella B, et al. 2013
[15] Titchener AG, et al. 2014
[16] Namdari S, et al. 2014
[17] Boissonnault WG, et al. 2007
[18] Abboud JA, et al. 2010
[19] Lui PPY, et al. 2017
[20] Gumina S, et al. 2013

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AB1124 PREDICTIVE VALUE OF MRI FOR CT-GUIDED POSITIVE BIOPSY IN SUSPECTED INFECTIOUS SPONDYLODISCITIS

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Background: Spondylodiscitis is a potentially life-threatening infection burdened by high morbidity rates. MRI remains the key examination in the diagnosis of infectious spondylodiscitis. The microbiological diagnosis is the main predictive factor for successful treatment.
Objectives: To evaluate the MRI characteristics associated with the detection of microbial pathogens by computed tomography (CT) guided biopsy in case of suspicion of infectious spondylodiscitis.
Methods: Retrospective study including all patients hospitalized in our department between 1999 and 2019 and who underwent MRI and CT-guided biopsy for suspicion of septic spondylodiscitis.The diagnosis was based on clinical, biological, radiological and bacteriological data. We divided the patients into two groups: patients with a non-contributory CT guided biopsy (group 1) and patients with a contributory biopsy (Group 2).
Results: We included 82 patients including 37 women and 45 men with a mean age of 56 years old [16 - 86]. The median delay of consultation was 3 months. Inflammatory back pain was reported in 78% of cases. Neurologic deficiency was noticed in 19.5% of cases. The lumbar spine was involved more than 50% of cases. Spinal MRI was performed to all patients and showed paravertebral abscess in 64.6%, epiduritis in 62.1%, intra-discal abscess in 3.6%, spinal cord compression 10.9%, and vertebral ostelysis in 6.09% of cases.The causative microorganism was mycobacterium tuberculosis in 53.6%, brucella in 24.3%, and pyogenic germs in 15.8% of cases. Disco vertebral biopsy was performed in 55 patients and was contributory in 45.4% of cases.
The presence of spinal cord compression, intra-discal abscess and vertebral osteolysis was more frequent in group 2, but with no statistically significant difference (p = 0.65, 1 and 0.58; respectively). In addition, there was no significant difference in the presence of paravertebral abscess and epiduritis (p = 0.41 and 0.53; respectively).
Conclusion: Spondylodiscitis is an emergency which must be diagnosed on time to avoid life threatening complications, neurological sequelae and spinal deformities.

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AB1125 LESS SEVERE SYNOVITIS IN PATIENTS WITH KNEE OSTEOARTHRITIS IS ASSOCIATED WITH HIGHER SELF-REPORTED PAIN INTENSITY 12 MONTHS AFTER TOTAL KNEE ARTHROPLASTY – AN EXPLORATORY COHORT STUDY

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Background: Synovitis is a pain generator in patients with osteoarthritis and associated with upregulation of pro-inflammatory cytokines, which have been found to lead to pain sensitivity and worse self-reported pain (1).
Objectives: This study aimed to investigate the association between pre- and perioperative synovitis from imaging and histology and self-reported pain 12 months after total knee arthroplasty (TKA).
Methods: Preoperative synovitis was assessed from MRI data of the knee by 11 point synovitis score a.m Guermazi (2) using contrast enhanced MRI (CE-synovitis) and heuristic time intensity curve analysis of the dynamic contrast enhanced MRI (DCE-MRI) data using the DYNAMIKA® software (Image Analysis group, London) providing Dynamic Enhanced MR Quantification (DEMRIQ) Indices (3). Perioperative synovitis was also assessed from biopsies of the synovium in 6 predefined places graded histologically a.m Krenn (4). Worst pain within the last 24-hours (visual analog scale, VAS, 0-100) was assessed before and 12 months after TKA. Patients were divided into a low-pain (VAS≤30) and a high-pain (VAS>30) group based on 12-months postoperative VAS.
Results: Twenty-six patients had full pre- and postoperative data and were analysed. The high-pain group had significantly lower CE-synovitis (P=0.03), DCE-MRI inflammation indices (DEMRIQ-inflammation) (P<0.03) and a trend towards lower histologically assessed synovitis grades (P=0.077) compared to the low-pain group at baseline. Preoperative synovitis scores were also inversely correlated with pain 12-months after TKA, CE-synovitis (R = - 0.455, P = 0.022) and DCE-MRI inflammation (R = - 0.528, P = 0.007), indicating that more severe preoperative synovitis is associated with less severe pain at 12-months.
Conclusion: Higher preoperative synovitis scores are associated with less postoperative pain 12-months after TKA. Further, correlation analysis revealed that less severe preoperative synovitis was associated with worse pain 12-months after TKA, suggesting that CE and DCE-MRI synovitis quantification could be used as imaging markers for prediction of good surgical outcomes.

REFERENCES
[1] Schaible HG. Nociceptive neurons detect cytokines in arthritis. Arthritis Res. Ther. 2014:470.
[2] Guermazi A, et al. Assessment of synovitis with contrast-enhanced MRI using a whole-joint semiquantitative scoring system in people with, or at high risk of, knee osteoarthritisAnn. Rheum. Dis. 2011
[3] Riis RGC, et al. The association between histological, macroscopic and magnetic resonance imaging assessed synovitis in end-stage knee osteoarthritis Osteoarthr. Cartil. 2017;
[4] Krenn V, et al. Grading of chronic synovitis-a histopathological grading system for molecular and diagnostic pathology. Pathol. Res. Pract. 2002

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AB1126 ULTRASOUND CHANGES IN PATIENTS WITH CALCIFICATIONS IN THE SUPERSPINATUS TENDON BEFORE AND AFTER THE DEVELOPMENT OF A SUBACROMIAL PAINFUL SYNDROME

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Background: The relationship between subacromial syndrome (SS) and the presence of calcifications in the thickness of the superspinatus tendon is complex. It is undeniable that the presence of a solid body hinders the movement of the rotator cuff through the subacromial space and to some extent contributes to the trapping that conditions pain and functional limitation, but, on the other hand, calcifications in the thickness of the supraspinatus tendon are incidental findings that have no clinical significance or whose presence precedes the painful syndrome in months or years. We understand that in a SS related to calcification, it contributes as an irreducible agent that conditions an inflammatory response of the tendon when it attempts to cross the subacromial space, however, there are no studies available that explain this relationship from a sonoanatomic perspective.
Objectives: To determine the extent to which the disposition and characteristics of a calcification of the supraspinatus tendon, or of the tendon itself, are modified when an SS is triggered.
Methods: A quasi-experimental, "before-after" study was conducted with individuals who presented a SS and in whom incidental calcification in the TSE had been previously diagnosed in an ultrasound study. Demographic data and static images from the ultrasound studies of each patient were compared. The explanatory variable was time (before-after) and the response variables in image were: (1) Increased tendon thickness measured at 30mm from the deep edge of the acromion (GROSORB), (2) Increased tendon thickness measured at the height of the middle of the longitudinal axis of the calcification (GROSORC), (3) Longitudinal axis of the calcification (LONGC), (4) Thickness or height of the calcification, when this was measurable (ALTC), and (5) Distance between the calcification and the deep end of the acromion (DISTC). In addition, two indices were determined: (a) Increased tendon thickness in the calcification zone (GROSORC/GROSORB) and (b) proportion of tendon thickness occupied by calcification (ALTC/GROSORC). The measurements were carried out using the software of the equipment in which the original and subsequent study was made (GE Logiq e; Toshiba Nemio XG).

Variables measured by ultrasound assessment	Before measurements	After measurements	T Student (paired data)
ALTC (N=20) mm	5.075 DE 1.055	5.160 DE 0.994	0.0073
LONGC mm	6.184 DE 2.414	6.236 DE 2.446	0.1066
GROSORB mm	6.348 DE 0.691	6.436 DE 0.674	0.1285
GROSORC mm	6.845 DE 0.718	7.263 DE 0.872	0.0003
GROSORC/GROSORB	1.082 DE 0.085	1.129 DE 0.069	0.0072
ALTC/GROSORC	0.748 DE 0.164	0.716 DE 0.130	0.0611

Results: The "before" ultrasounds were performed between 2012 and 2016 and the "after" ultrasounds between 2015 and 2018. The time fashion between the two ultrasounds for each patient was 2 years. Thirty-three subjects were included, with an average age of 47.5 SD 7.6 years. Proportion of women 66.6%. Proportion of dominant shoulders (51.1%).
As shown in table 1, the most significant changes were the thickness of the tendon measured at the height of the middle of the longitudinal axis of calcification and the increase of this measure with respect to the thickness measured at 30mm from the deepest region of acromion (GROSORC/GROSORB). Although the calcification height also showed a statistically significant increase, it could only be measeured in 20 of the 33 subjects.
In the correlation tests, the GROSORC/GROSORB index increase correlated strongly with the DISTC (Coef. Pearson 0.686, P<0.01) and with the longitudinal diameter of the calcification (LONGC) (Coef. Pearson 0.797, P<0.01).

Conclusion: The most important factor that explains the development of an SS associated with calcification is the increase in tendon thickness at the height of the calcification itself and, at the same time, this measure increases when the calcification is more lateralized and the more elongated its longitudinal diameter. These modifications could have implications when deciding the therapeutic management of these processes.
Disclosure of Interests: None declared
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AB1127 ULTRASOUND INTER-READER RELIABILITY OF INFLAMMATORY FINDINGS IN PATIENTS WITH POLYARTHRITIS

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Background: Ultrasonography is an imaging technique that allows rheumatologists to visualise structural and inflammatory changes within a joint.
Objectives: The objective of this study was to assess the inter-reader reliability of interpretation of inflammatory and destructive changes in a wide range of joints in patients with polyarthritis.
Methods: This study was divided in two parts: 1) consensus process and 2) reliability exercise. For the first part, a written questionnaire was sent by email to 6 sonographers from 3 portuguese hospitals with the highest level of competence (EULAR competency assessment level 2). The questionnaire included 17 questions divided in two groups: 1) elementary components in B-mode and Doppler assessment (effusion, synovial hypertrophy (SH), power Doppler (PD), erosions and synovitis definition) and 2) approach at the joint level (the definition of which plan and recess will be assessed in each joint). The participants were asked to rate their level of agreement/disagreement for each statement using a 1-5 Likert scale (1=strongly disagree to 5-strongly agree). For the reliability exercise, video clips of US examinations of 40 joints (wrist, metacarpophalangeal (MCP) from 1 to 5, proximal interphalangeal (PIP) from 1 to 5, knee, tibiotarsal (TT) and metatarsophalangeal (MTP) joints from 1 to 5, elbow and shoulder) from each of 15 patients were collected (showing a multiplanar bilateral ultrasound approach). Each joint in each video was scored by individual ultrasonographers for the presence/absence of elementary components: effusion (Yes/No), SH (No/Grade 1 to 3), PD (No/Grade 1 to 3) and erosions (Yes/No). Inter-reader agreement analysis was assessed through Fleiss' kappa coefficient and classified according to Landis and Koch[8]: κ values 0 were considered poor, 0-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 good and 0.81-1.00 excellent. Statistical significance was defined as p<0.05. Statistical analysis was performed using STATA V.14.
Results: Thirty seven joints of the 600 joints were excluded due to dislocation of the joint or presence of objects (rings/catheters) and the videos of a total of 563 joints were analysed by the 6 ultrasound experts. Inter-reader agreement was superior for TT joints and inferior for wrist; the identification of the erosions had the better agreement in the elementary components (Table 1).

Table 1. Inter-observer agreement for each elementary component and for anatomical region

Elementary component	κ	Joint	κ	Joint	κ
Effusion	0.6044	**Wrist**	0.6767	**Shoulder**	0.7271
Synovial hypertrophy	0.6291	**MCP**	0.6866	**Knee**	0.7192
Power doppler	0.7195	**PIP**	0.7107	**TT**	0.8043
Erosions	0.7314	**Elbow**	0.7291	**MTP**	0.7040

MCP - Metacarpophalangeal joints, MTP – Metatarsophalangeal joints, PIP - Proximal interphalangeal joints, TT-Tibiotarsal joint. All p<0.001

Conclusion: The reliability of interpretation of inflammatory and destructive changes using video clips was in general good to excellent and it was better for erosions and tibiotarsal joint (regarding elementary component and anatomical region, respectively).
Disclosure of Interests: None declared

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AB1128 SENSITIVITY AND SPECIFICITY OF THE AUTOMATED SQUEEZE TEST (GAENSLEN'S MANEUVER) FOR IDENTIFYING METACARPOPHALANGEAL SYNOVITIS BY MAGNETIC RESONANCE IMAGING

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Background: It is well known that an early diagnosis and treatment for Rheumatoid Arthritis (RA) prevents its complications, therefore there are many efforts to identify individuals at risk to develop RA. The Squeeze test has been used to detect synovitis in metacarpophalangeal joints, even though it is used in daily practice, there is a great variability in their performance among rheumatologists. [2]
Objectives: The aim of this study is to determine the diagnostic performance of the automated squeeze test (AST) on the metacarpophalangeal (MCP) joints to detect the presence of synovitis, edema, or erosions by magnetic resonance imaging (MRI) using the rheumatoid arthritis magnetic resonance imaging score (RAMRIS) in first-degree relatives (FDR) of RA patients, of whom clinically suspect arthralgia (CSA) in hands was suspected, as well as in RA patients.
Methods: It is an observational and cross-sectional study for a diagnostic test. A total of 60 patients, older than 18 years, were included and divided in three groups: CSA group: 22 with less than 1 year with arthralgia and required to be FDR of RA patients; early RA group: 22 patients who met ACR/EULAR 2010 Classification Criteria with less than 1 year with the disease; and late RA group: 16 patients who met ACR/EULAR 2010 Classification Criteria, with more than 1 year with the disease. The AST was performed in the 60 participants' dominant hand. The device was evaluated by MRI, which examined the same hand in the 60 patients.
Results: A total of 240 MCP joints were evaluated. The AUC for the total RAMRIS score >10 was [0.480 (95% CI 0.301-0.617) *P*=0.597], for synovitis RAMRIS score > 7 was [0.459 (95% CI 0.331-0.669) *P*=0.791], and for the presence of any synovitis by RAMRIS was [0.575 (95% CI 0.428-0.723) *P*=0.331]. For the RAMRIS synovitis score, the most sensitive and specific cut-off of the force by AST was 4.645 kg with a 66.7% sensitivity and 50% specificity.

Abstract AB1128 Table 1. Baseline characteristics

	TOTAL	CSA n=22	ERA n=22	LRA n=16
Age mean (SD)	44.7 (13.7)	37.6 (10.9)	49.05 (11.9)	47.5 (16.2)
Female n (%)	50 (83.3)	18 (81.8)	18 (81.8)	14 (87.5)
TJC median (IQR)	4 (12)	0.5 (4)	5 (13)	10 (11)
SJC median (IQR)	3 (8)	0 (3)	5 (12)	7.5 (9)
DAS28-ESR median (IQR)			4.8 (1.5)	5.4 (1.4)
HAQ median (IQR)			0.64 (0.75)	1.47 (0.94)
CDAI median (IQR)			18.07(16.8)	23.8 (15.5)
Married n (%)	41 (68.3)	12 (54.5)	15 (71.4)	14 (93.3)
Smoker n (%)	19 (31.7)	2 (22.7)	10 (45.5)	4 (25)
Morning stiffness n (%)	31 (51.7)	4 (18.2)	16 (72.7)	11 (68.8)
RF IgM positivity n (%)	46 (76.7)	9 (40.9)	12 (70.6)	4 (25)
ACPA positivity n (%)	25 (41.7)	19 (86.4)	20 (90.9)	7 (43.8)

Clinically suspect arthralgia, **CSA**; Early Rheumatoid Arthritis, **ERA**; Late Rheumatoid Arthritis, **LRA**; Tender Joint Count, **TJC**; Swollen Joint Count, **SJC**; Disease Activity Score – Erythrocyte Sedimentation Rate, **DAS28-ESR**; Health Activity Questionnaire, **HAQ**; Clinical Disease Activity Index, **CDAI**; Rheumatoid Factor, **RF**; Anti-citrullinated peptides antibodies, **ACPA**.

Figure 1

Conclusion: The application of AST with a force of 4.645 kg, to exert pain in the dominant hand, is a sensitive and specific technique to establish MCP joint inflammation, compared with other automated methods that had been recently tested.

REFERENCES

[1] van Steenbergen HW, Aletaha D, Beaart-van de Voorde LJ, et al. EULAR definition of arthralgia suspicious for progression to rheumatoid arthritis. Ann Rheum Dis 2017;76:491-6.

[2] Vega-Morales D, Esquivel-Valerio JA, Arana-Guajardo AC. Automated squeeze test (Gaenslen's manoeuvre) to identify patients with arthralgia suspicious for progression to RA: improving time delay to rheumatology consultation. Ann Rheum Dis 2017;76:e40.

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AB1129 ULTRASOUND MEASUREMENT OF MUSCLE THICKNESS AT THE PROXIMAL FOREARM: VALIDITY ISSUES

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Background: The term *sarcopenia* defines the muscle strenght loss and muscle mass loss due to aging, and it is one out of three criteria for the diagnose of frailty in the elderly. A number of studies have related the handgrip strength with muscle thickness (MT) in the forearm measured by ultrasound (US)[1], but a standardized scanning protocol has not been described and its interobserver reliability has not been investigated yet.
Objectives: The aims of this study were to provide detailed description of the scanning protocol to measure the MT in the forearm and to test its feasibility and interobserver reliability.
Methods: A total of 27 consecutive subjects were enrolled at Ospedale "Carlo Urbani", in Jesi (Ancona, Italy): 2 healthy volunteers recruited from among our staff, and 25 patients referred to the Rheumatology Department affected by rheumatoid arthritis (5), psoriatic arthritis (4), spondyloarthritis (3), polymyalgia rheumatica (2), systemic lupus erythematosus (1), systemic sclerosis (1), overlap SLE/SSc (1), Sjögren syndrome (1), antisynthetase syndrome (1), undifferentiated connective tissue disease (1), osteoporosis (1), small vessels vasculitides (2) and fibromyalgia (2). The female to male ratio was 19/27, the mean age was 52.1 years (SD ±13.7), and the mean Body Mass Index was 27.4 Kg/m² (SD ±4.2). Four rheumatologists (SC, EC, GS, EF) trained in musculoeskeletal US, with a different degree of experience, performed the examinations using a MyLab ClassC (Esaote SpA) equipped with a broadband linear probe (frequency range 4-13 MHz). All subjects sat in front of the sonographer with their hands supinated and the forearm resting on the examining table. First, the coronoid process was imaged according to the "longitudinal scan of the coronoid recess" as indicated by the 2017 EULAR US guidelines. Then the probe was moved distally following bony cortex until the ulnar tuberosity was identified. Immediately distally to the ulnar tuberosity the bone turns flat and hyperechoic and this was taken as the anatomical reference for the measurement. Afterwards the probe orientation was changed to obtain a transverse view. During the rotation, the proximal third of the diaphysis of the radius was imaged. Two MT were measured, the ulnar MT (UMT) and the radial MT (RMT), between the subcutaneous tissue-muscle interface and the muscle-bone interface of each bone respectively. The measurement of UMT and RMT of both arms were registered, as well as the scanning time of all the examiners.
Results: We found an excellent interobserver reliability of this scanning protocol, with and interclass correlation coefficient (ICC) among the four sonographers of 0.975 (CI 0.955 - 0.987) for the right UMT, an ICC of 0.968 (CI 0.942 - 0.984) for the left UMT, an ICC of 0.932 (CI 0.878 - 0.966) for the right RMT and an ICC of 0.949 (CI 0.908 - 0.974) for the left RMT. The mean time required to acquire all measurements in each subject was less than five minutes (SC 4.4 min; EC 4 min; GS 4.2 min; EF 4.5 min).
Conclusion: The results of this study provide evidence in favour of both feasibility and interoberver reliability of US measurement of the forearm MT.

REFERENCES

[1] Abe T, Thiebaus R S, Loenneke J P, Ogawa M and Mitsukawa N. Association between forearm muscle thickness and age-related loss of skeletal muscle mass, handgrip and knee extension strength and walking performance in old men and women: a pilot study. Ultrasound in Med. & Biol., Vol. 40, No. 9, pp 2069-2075, 2014.

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AB1130 RELIABILITY OF ULTRASOUND MEASUREMENT OF HYALINE CARTILAGE THICKNESS IN RHEUAMTOID ARTHRITIS

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Background: Only few studies investigated the role of ultrasound (US) in the assessment of hyaline cartilage in rheumatoid arthritis (RA).
Recently, a positive correlation was found between the US measurement of the metacarpal head cartilage thickness (MCT) and both the anatomical MCT and the radiographic joint space width[1].
Objectives: To evaluate inter- and intra-observer reliability in the assessment of MCT in RA patients and healthy subjects; to compare the agreement of the sonographers in the assessment of the MCT using different methods (i.e. semiquantitative and quantitative); to determine the inter-observer smallest detectable difference (SDD) of MCT measured by US.
Methods: US assessment was performed by two rheumatologists on 160 metacarpophalangeal (MCP) joints of 10 healthy subjects and 10 patients with RA (according to 2010 ACR/EULAR classification criteria) using a MyLab Twice (Esaote Biomedica, Genoa, Italy) equipped with a linear very high frequency probe (i.e. 10-22 MHz)
To assess inter-observer reliability, the hyaline cartilage of metacarpal head from II to V digits of both hands were examined independently on the same day by two rheumatologists (an experienced musculoskeletal sonographer and an investigator with limited US training).
To assess intra-observer reliability, all the subjects were re-scanned using the same scanning protocol and the same US setting by one sonographer after a week.
Hands were scanned with the MCP joints in maximal flexion (approximately 90°). The hyaline cartilage of all the metacarpal heads was scanned in longitudinal and transverse views in the central portion of the metacarpal head. Particular attention was paid on maintaining the probe in a position providing an angle of 90° between the direction of the US beam and the cartilage surface[2].
MCT was scored both semi-quantitatively (using a five-grade scoring system[3]) and quantitatively (using the average value of the longitudinal and transverse measures).
The inter- and intra-observer agreements for assessing the MCT with the semiquantitative scoring system were calculated using Cohen's kappa and interpreted according to Landis and Koch.
The inter- and intra-observer agreements for assessing the MCT with the quantitative scoring system were calculated using intraclass correlation coefficients (ICC) and their 95% confident intervals (95%CI).
The SDD was determined using Bland-Altman 95% limits of agreement method.
Results: The inter- and intra-observer agreements for the semiquantitative assessment of the MCT were moderate [k=0.59 (95%CI 0.35-0.83) and k=0.63 (95%CI 0.39-0.87), respectively].
Considering all the measurements, a substantial inter-observer [ICC= 0.88 (95%CI 0.82-0.92)] and intra-observer [ICC= 0.88 (95%CI 0.87-0.94)] agreements for the quantitative assessment of MCT were found.
The SDD of the MCT measurement was: 0.11 mm for both longitudinal and transverse scans and 0.09 mm for the average of the two measures.
Conclusion: This study provides evidence in favor of the reliability of semiquantitative and quantitative US methods for assessing MCT in RA. Further studies are required to determine standard reference values of MCT by US in healthy subjects.

REFERENCES

[1] Mandl P, Supp G, Baksa G, et al. Relationship between radiographic joint space narrowing, sonographic cartilage thickness and anatomy in rheumatoid arthritis and control joints. Ann Rheum Dis. 2015;74:2022:7.
[2] Torp-Pedersen S, Bartels EM, Wilhjelm J, Bliddal H. Articular cartilage thickness measured with US is not as easy as it appears: a systematic review of measurement techniques and image interpretation. Ultraschall Med. 2011;32:54-61.
[3] Filippucci E, da Luz KR, Di Geso L, et al. Interobserver reliability of ultrasonography in the assessment of cartilage damage in rheumatoid arthritis. Ann Rheum Dis. 2010;69:1845-8.

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AB1131 HIGH-RESOLUTION ULTRASOUND ASSESSMENT OF CARTILAGE THINNING IN RHEUMATOID ARTHRITIS

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Background: Conventional radiography is the standard imaging modality to detect joint damage in rheumatoid arthritis (RA). Ultrasound (US) allows for a direct visualization of hyaline cartilage. To date, only few studies investigated the role of US in the assessment of cartilage damage in RA.
Objectives: To compare US qualitative and quantitative assessments of cartilage thinning at metacarpal head (MH) in RA patients and in an age-, sex- and height-matched healthy controls (H). To correlate cartilage damage and clinical parameters in RA.
Methods: US examination was performed on 318 metacarpophalangeal (MCP) joints of 40 consecutive RA patients and on 320 MCP joints of 40 age-, height- and sex-matched H using a MyLab Twice (Esaote Biomedica, Genoa, Italy), equipped with a high frequency linear probe (up to 22 MHz).
RA patients were enrolled according to the 2010 RA classification criteria. The hyaline cartilage of MH from II to V digits of both hands was examined with the MCP joints in maximal flexion.
Each MH was scanned in longitudinal and transverse views. Particular attention was paid on maintaining the probe in a position providing an angle of 90° between the direction of the US beam and the cartilage surface[1].
Cartilage thickness (CT) was assessed both semi-quantitatively (using a reliable qualitative five-grade scoring system[2]) and quantitatively (using the mean value of longitudinal and transverse measurements of the CT). Finally, association between cartilage damage and clinical parameters was assessed.
Results:
Semiquantitative score: Cartilage thinning (grade 2, 3 and 4) was found in at least one MH in 23 RA patients (57.5%) and in 4 H (10.0%) (p<0.01). A significantly higher prevalence of cartilage damage (grade 2, 3 and 4) at joint level was found in RA patients (86 MCP joints, 27.0%) in comparison with H (13 MCP joints, 4.1%) (p<0.01).
Quantitative assessment: CT of the MH ranged from 0.0 to 1.10 mm (0.60±0.26 mm, mean±SD) in RA patients and from 0.41 to 1.08 mm (0.67±0.12 mm, mean±SD) in H. Male had a thicker hyaline cartilage than female, both in RA patients (p<0.01) and in H (p<0.01). No significant difference was found between left and right side, both for RA patients (p=0.48) and healthy subjects (p=0.94).
Detailed quantitative measurements of CT of MH are reported in table 2.

Abstract AB1131 Table 2. US cartilage thickness measurement for each digit in RA patients and healthy controls.

	RA patients (n=39)	Healthy subjects (n=40)	Mean difference, 95% CI (mm)	P value
	Mean (mm)	Mean (mm)		
II MH	0.62	0.75	0.13; 0.06-0.21	**<0.01**
III MH	0.57	0.64	0.07; 0.02-0.13	**0.01**
IV MH	0.61	0.64	0.03; -0.03-0.09	0.35
V MH	0.62	0.65	0.03; -0.02-0.09	0.20
Sum	2.43	2.68	0.25; 0.03-0.46	**0.02**

95%CI: 95% confidence interval; **L**: left; **MH**: metacarpal head; **R**: right; **RA**: rheumatoid arthritis; **SD**: standard deviation; **US**: ultrasound.
A significant association was found between the CT value and age (r=-0.528, p<0.001), disease duration (r=-0.376, p=0.005) and grade of the semiquantitative scoring system (r=-0.80, p<0.001). No association was found between CT and BMI, weight, ACPA positivity and RF positivity.
Conclusion: This study demonstrated that a significantly higher prevalence of cartilage damage was found in RA patients using both the semiquantitative score and the quantitative assessment. In particular, in RA patients the hyaline cartilage of II and III MH is thinner in comparison with H. Finally, a significant association was found between the CT values and disease duration and age.

REFERENCES

[1] Torp-Pedersen S, Bartels EM, Wilhjelm J, Bliddal H. Articular cartilage thickness measured with US is not as easy as it appears: a systematic review of measurement techniques and image interpretation. Ultraschall Med. 2011;32:54-61.

[2] Filippucci E, da Luz KR, Di Geso L, et al. Interobserver reliability of ultrasonography in the assessment of cartilage damage in rheumatoid arthritis. Ann Rheum Dis. 2010;69:1845-8.

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AB1132 THE ROLE OF PET/CT IN THE MANAGEMENT OF GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a large vessel vasculitis that affects the aorta and/or its major branches including the superficial temporal artery. Together to cranial symptoms such as headache and visual disturbances, extra cranial manifestations have been widely reported, sometimes as unique clinical presentation. Several imaging modalities are available to evaluate aortic involvement including fluorodeoxyglucose (FDG) positron emission tomography (PET), however there are few reports that analyzed the impact of the findings of this advanced imaging in predicting outcomes of the disease.
Objectives: To assess the utility of PET in disease extension assessment to predict, together to clinical manifestations, the disease evolution.
Methods: We retrospectively reviewed all the clinical records of patients receiving a diagnosis of large vessel vasculitis from 1st January 2010 to 1st January 2016 at a tertiary immunorheumatology clinic of a university Hospital, who underwent a PET. Clinical, laboratory, and imaging data were collected. Non-parametric analysis was performed.
Results: We recruited 19 patients (10 females, 52.6%). The median age was 74.0 [65.5-76.0]; at the diagnosis, the median erythrocyte sedimentation rate (ESR) was 65.5 [49.0-86.0], while C-reactive protein (CRP) was 8.5 [5.5-14.0]. 12 patients showed a typical cranial GCA (63.2%), while 7 (36.8%) were diagnosed with extracranial GCA. The two groups were comparable at diagnosis for age, gender, median ESR and CRP. Interestingly, the PET was significative for aortitis not only in the 7 patients with extracranial involvement, but also in 7/12 patients with cranial GCA (58.3%). Along a median follow-up of 15 months [4.5-26.5], 4 relapses were reported. Notably, all the relapsers were males and showed both aortic and cranial involvement. In a multivariate model, male gender was the only predictor of relapse (p=0.02), while age at onset, clinical subset (cranial vs. extracranial) and steroid dose did not fit the model
Conclusion: The use of PET in GCA is relevant in the assessment of extension of disease since a significative number of patients without cranial symptoms in the end resulted to have large vessel involvement. In addition, PET is useful in identifying patients with cranial involvement that have also aortic inflammation since they seems to have worse prognosis.
Disclosure of Interests: None declared
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AB1133 AUTOMATED ASSESSMENT (AUTOCAPI) OF NAILFOLD CAPILLARY NUMBER VERSUS MANUAL COUNTING IN SYSTEMIC SCLEROSISPATIENTS WITH DIFFERENT CAPILLAROSCOPIC PATTERNS

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Background: The nailfold videocapillaroscopy (NVC) analysis allows microvascular detection of possible markers of severity and progression in systemic sclerosis (SSc), as reduced capillary number, which has been associated with a high risk of developing disease complications (i.e. digital ulcers over time) (1-2). A recent study validated an automated counting system (AUTOCAPI) for the absolute nailfold capillary number in SSc patients by analysing the capillaroscopic images (3).
Objectives: To evaluate the performance of this automated software for absolute nailfold capillary number counting, in SSc patients with different NVC patterns of microangiopathy.
Methods: 183 random SSc patients collected at both Genova and Ghent Divisions of Rheumatology were enrolled (LeRoy 2001 or ACR 2013 criteria, mean age 55±13 year, mean disease duration 5.5±6.8 years) and classified by NVC in the following patterns: 28 "not specific", 37 "early", 89 "active", 29 "late"). 8 fingers for each patient were analysed, counting the number of nailfold capillaries manually and by the AUTOCAPI software (DS Medica, Italy) along a millimetre in each finger image. The mean capillary number value of the eight finger images was calculated. The software reliability was assessed through calculation of the intraclass correlation coefficient (ICC) between automatic and manual counting.
Results: The mean number of capillaries assessed by manual vs automatic counting was as follows: 5.23±1.7 vs 5.47±1.3 in the total group of SSc patients, 5.91±1.2 vs 6.87±1.2 in the "not specific", 7.23±1.4 vs 5.67 ±1.1 in the "early", 4.67±1.1 vs 5.16±1.2 in the "active" and 3.72±1.5 vs 4.85±1.1 in the "late" pattern of microangiopathy. The higher standard deviation observed for automatic counting was 1.23 in the "not specific" group. The following ICC's were obtained respectively for total patients, "not specific", "early", "active", and "late" NVC patterns: 0.53, 0.51, 0.48, 0.50 and 0.66. The mean values for the manual versus automatic capillary counting assessed by the two centres in all SSc patients were respectively: 5.92±1.8 and 5.02±1.1 for Genova centre, and 4.71±1.5 and 5.83±1.4 for Ghent centre. The automatic counting confirmed that capillary number progressively reduces from "early" to "active" to "late" NVC pattern of microangiopathy in SSc.
Conclusion: This study reports for the first time the good reliability of AUTOCAPI software in nailfold capillary number counting in SSc patients with different patterns of microangiopathy. The use of automated counting software need to standardize nailfold capillary assessment among different Rheumatological centres.

REFERENCES

[1] Smith V, et al. J Rheumatol. 2013;40:2023-8. 2. Cutolo M, et al. Arthritis Rheumatol. 2016;68:2527-39. 3. Cutolo M, et al. Microcirculation. 2018;25: e12447.

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AB1134 IMPROVING THE STANDARDISATION OF DIAGNOSTIC LABORATORY TESTS FOR RF AND ACPA THROUGH THE ESTABLISHMENT OF A NEW INTERNATIONAL REFERENCE MATERIAL

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Background: Rheumatoid arthritis is a debilitating chronic inflammatory disease. Its laboratory diagnosis relies mainly on testing for the presence of two groups of autoantibodies in patient's serum: rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA). Most RF assays are standardised against W1066, the WHO international standard rheumatoid arthritis serum established in 1968, or 64/002, the British Standard rheumatoid arthritis serum, which is the same material. Stocks of W1066 are becoming exhausted which triggered a decision by NIBSC and WHO to prepare a new standard preparation intended to replace W1066.
Objectives: Primarily, we have a responsibility to ensure the continuity of W1066 as a calibrator in RF agglutination-based assays. However, science has progressed and ACPA are now recognised as equally important to RF in the diagnosis of rheumatoid arthritis which is reflected in the ACR/EULAR 2010 classification guidelines. Therefore, we intend to assign the new standard values in international units to both RF and ACPA. In addition, some assays look at isotype-specific RF, so we will assess whether we can establish nominal values for the most common isotypes, IgM-RF and IgA-RF.
Methods: A pool of rheumatoid arthritis serum was prepared and dispensed into ampoules, lyophilised and sealed under an inert nitrogen atmosphere. An international collaborative study was organised with expert laboratories, including commercial kit manufacturers and medical

laboratories, to assess the suitability of the new candidate standard and calibrate it against W1066.
Results: The results of the collaborative study will be used to propose a unitage to the new candidate standard in RF and ACPA for consideration at the WHO Expert Committee for Biological Standardisation.
Conclusion: Standardisation of diagnostic laboratory tests involves the development of a physical sample for each analyte. The use of these international reference standards as primary calibrants promotes the harmonisation of test results between different assays. Because the assays use a similar scale, their results are easily understood, which ultimately increases the impact of published research and clinical findings on our knowledge of the disease.

REFERENCES

[1] WHO Expert Committee on Biological Standardization, sixty-seventh report. Geneva: World Health Organization; 2017 (WHO Technical Report Series; no. 1004). 2017

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AB1135 THE MANAGEMENT OF INTERSTITIAL LUNG DISEASES: THE IMPORTANCE OF THE RHEUMATOLOGIC EXPERTISE IN MULTIDISCIPLINARY MEETINGS

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Background: Multidisciplinary Team (MDT) meetings are the current "gold standard" in interstitial lung disease (ILD) diagnosis. Requisite participants are respiratory physicians, radiologists and pathologists. A rheumatologist physician is not routinary involved in MDT even if up to 20% of ILD are related to connective tissue disease, rheumatoid arthritis or systemic vasculitis.
Objectives: The aim of this study is to evaluate the prevalence and predictors of systemic rheumatological diseases in a cohort of patients with ILD, evaluated by a rheumatology specialist on the advice of MDT in a university hospital.
Methods: Thirty-two patients with ILD, evaluated at dedicated MDT were referred to a rheumatologist in 2018, usually for autoantibodies positivity or clinical history suspected for a rheumatological disorder. Rheumatologic evaluation included physical examination, routinary blood and urine tests, serum levels of C3 and C4, ANA, Rheumatoid Factor (RF), ANCAs, anti-Sm, anti-RNP, anti-Ro/SSA, anti-La/SSB, anti-Sm, anti-Jo1, anti-dsDNA and anti-CCP antibodies. Family history of autoimmune diseases, presence of rheumatologic red flags (Raynaud's phenomenon, photosensitivity, inflammatory skin manifestations, sicca syndrome, recurrent fever, inflammatory arthralgias, paresthesias, oral or genital aphthosis, thrombosis and recurrent miscarriages), respiratory symptoms and pulmonary function test were also evaluated. When indicated, capillaroscopy, joint imaging and salivary gland biopsy were performed.
Results: Twenty-one patients (65.6%) were female. At the time of rheumatological evaluation, the patients had a mean age of 64.4±12.6 years with a mean period of 21.1±39.6 months since the first identification of ILD on a CT scan. Twenty-five (78.1%) and 18 (56.3%) patients respectively complained exertional dyspnea and cough, 6 patients (18.8%) were on oxygen therapy and 13 (40.6%) had a FVC<80%. The pattern on CT scan suggested a UIP, NSIP and OP respectively in 18 (56.3%), 6 (18.8%) and 2 (6.3%) patients. Ten patients (31.3%) were diagnosed with a defined rheumatological condition (4 with Sjogren Syndrome, 3 with scleroderma, 1 with Rheumatoid Arthritis, 1 with Mixed Connective Tissue Disease and 1 with Granulomatosis with Polyangiitis); 7 (21.9%) were diagnosed with Interstitial Pneumonia with autoimmune feature (IPAF). A rheumatological diagnosis was not statistically associated with any specific rheumatologic red flag, routine laboratory abnormalities or family history of systemic autoimmune disease. Three out of 13 capillaroscopies and 3 out of 9 salivary glands biopsies performed had diagnostic findings. The only immunologic abnormalities associated to a rheumatologic diagnosis were RF positivity (20.0%vs54.5%, p=0.024) and p-ANCA positivity (10.0%vs40.9%, p=0.042), both with low specificity (respectively 15.0% and 5.0%) and sensitivity (respectively 55.6% and 42.9.0%). After diagnosis, 11 patients (34.4%) started immunosuppressive therapy and 7 (21.9%) started antifibrotic therapy.
Conclusion: Single clinical or laboratory abnormalities are not strongly associated to a rheumatological diagnosis in patients with ILD, suggesting that only a comprehensive rheumatological evaluation allows correct classification of the disease associated with ILD and is mandatory to make or exclude a diagnosis. In this study, we evaluated only preselected patients by ILD-MDT, but the results indirectly suggest that direct participation of rheumatologist to MDT is advisable to increase accuracy and reduce delay in diagnosis and treatment.
Disclosure of Interests:: Enrico De Lorenzis: None declared, Gerlando Natalello: None declared, Lucrezia Verardi: None declared, Silvia Laura Bosello: None declared, Elisa Gremese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer
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AB1136 CD26: A POTENTIAL NOVEL HISTOLOGICAL MARKER OF IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of acquired skeletal muscle disorders including polymyositis (PM), dermatomyositis (DM), inclusion body myositis (IBM) and immune-mediated necrotizing myopathy (IMNM), characterized by immune-mediated muscle damage[1]. Activated T cells are the predominant inflammatory infiltrates in muscle biopsies of PM and DM patients and the lack of T regulatory cells (T_{regs}) has been implicated in the persistence of muscle damage. CD26 is an intrinsic membrane glycoprotein and a serine exopeptidase involved in the activation of T lymphocytes and amplification of inflammatory cytokines production. The enzymatically active form of CD26 is selectively expressed by activated T cells and has been described as a negative selection marker for human T_{regs}[2-5].
Objectives: The aims of this study were to evaluate the expression of CD26 in muscle biopsies of IIM patients and to correlate it with patients' clinical and histological features.
Methods: Immunofluorescence was used to evaluate CD26 expression and co-localization with CD3 and CD31, markers of T cells and endothelial cells respectively, in muscle biopsies of 6 DM, 6 PM, 3 IBM and 3 IMNM patients and of 6 healthy controls.
Results: We found that CD26 is preferentially expressed in muscle biopsies of IIM patients with respect to controls and that its level of expression is higher in DM patients. In muscle biopsies of IIM patients, CD26 is distributed not only in the extracellular matrix surrounding myofibers and infiltrating leukocytes, but also at the level of T cell membranes and endothelial cells. Specifically, CD26 co-localization with CD31 is more prominent in DM muscle biopsies. We could not find any association between vessel morphology in terms of size and shape and CD26 endothelial expression, suggesting that CD26 is expressed at the perivascular level independently of the degree of vessel dysfunction. With regard to clinical features, we found that CD26 is more expressed in patients presenting the typical DM rash. Moreover, CD26 expression was found not to be significantly associated with the degree of muscle weakness nor with the presence of interstitial lung disease, dysphagia, myalgias or mechanic's hands. As for histological data, higher levels of CD26 expression were found in biopsies with perivascular inflammatory infiltrates, especially T lymphocytes and macrophages.
Conclusion: Our data suggest that CD26 may represent a suitable marker for the diagnosis of IIM and a potential novel target for selective immune-therapies.

REFERENCES

[1] Dalakas, M. C. (2015). "Inflammatory Muscle Diseases." N Engl J Med 373(4): 393-394.
[2] Goebels N, Michaelis D, Engelhardt M, et al. Differential expression of perforin in muscle-infiltrating T cells in polymyositis and dermatomyositis. J Clin Invest 1996;97:2905–10.
[3] Waumans Y, Baerts L, Kehoe K, Lambeir A M, De Meester I. The dipeptidyl peptidase family, prolyl oligopeptidase, and prolyl carboxypeptidase in the immune system and inflammatory disease, including atherosclerosis. Front Immunol 2015; 6:387.

[4] Bengsch B, Seigel B, Flecken T, Wolanski J, Blum HE, Thimme R. Human Th17 cells express high levels of enzymatically active dipeptidylpeptidase IV (CD26). J Immunol 2012; 188:5438–47.
[5] Salgado FJ, Pérez Díaz A, Villanueva NM, Lamas O, Arias P, Nogueira M. CD26: a negative selection marker for human Treg cells. Cytometry A 2012; 81:843–55.

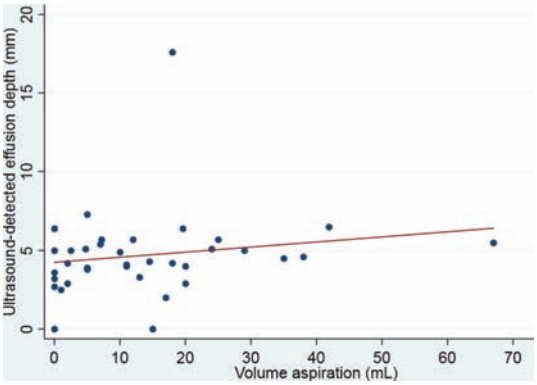
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AB1137 QUANTIFYING KNEE JOINT EFFUSIONS WITH CLINICAL TESTS, MUSCULOSKELETAL ULTRASOUND AND SYNOVIAL FLUID ASPIRATION: A PROSPECTIVE COHORT STUDY

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Background: Aspiration of knee joint effusions is an integral diagnostic and therapeutic intervention in many rheumatologic diseases. Clinical examination has traditionally involved tests including the “patella tap” or “bulge test”. The accuracy of these tests for determining effusion presence and size is not well established. Musculoskeletal ultrasound (MUS) is considered better for identification and quantification of knee effusions.
Objectives: To investigate the correlation between both clinical examination and MUS to aspirated knee effusion volume.
Methods: We performed a prospective cohort study of 37 osteoarthritis patients with symptomatic knee effusions. Clinical assessment with patella tap, bulge test and knee circumference measurement were carried out. MUS was used to measure effusion depth in the suprapatellar, lateral and medial parapatellar views. All knee effusion aspirations were performed by the same experienced clinician using a consistent, lateral approach. Linear regression analysis was used to assess correlations between clinical tests, MUS and aspiration volume.
Results: In patients with >3ml of fluid aspirated, patella tap and bulge test were positive in 67% and 80% respectively. The positive predictive value for bulge test was 80%. Where larger volumes were aspirated (i.e. >10ml), patella tap and bulge test were only positive in 52% and 65% respectively. There was a significant correlation between the measured circumference of the index and non-index knee and aspiration of fluid (coefficient=5.6, p=0.007). The relationship between fluid depth on MUS and aspirated volume showed a trend towards statistical significance, with a depth of 1mm equating to 1.57 ml of fluid (coefficient=1.57, p=0.06).

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Abstract AB1137 Figure 1. Relationship between aspirated volume and USS detected knee effusion depth

Conclusion: This pilot study demonstrates that a positive patella tap or bulge test is moderately predictive of knee effusion volume. However, this association is weaker when larger knee effusions are present. MUS showed promise at accurately predicting knee effusion volume. A larger study is underway to assess this relationship further.
Disclosure of Interests:: Thilinie De Silva: None declared, Chris Pham: None declared, Adam Rischin: None declared, Kim Le Marshall: None declared, Sara Vogrin: None declared, Albert Leung: None declared, Keith Lim Consultant for: Advisor for role of hepatitis and TB in Cimzia, UCB, Speakers bureau: Role of biological in pregnancy UCB
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AB1138 BONE SARCOIDOSIS: USEFULNESS OF 18F-FDG PET/CT

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Background: Bone sarcoidosis: usefulness of ^{18}F-FDG PET/CT
Objectives: Bone sarcoidosis is usually rare but more sensitive imaging procedures such as ^{18}F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (^{18}F-FDG PET/CT) allow a better characterization of such lesions. We aimed to describe bone sarcoidosis involvement using ^{18}F-FDG PET/CT.
Methods: We performed an observational retrospective study of patients with pulmonary sarcoidosis having a ^{18}F-FDG PET/CT. As stated by ATS/ERS/WASOG criteria, diagnosis of sarcoidosis was established on the presence of clinical symptoms and/or imaging features of sarcoidosis, and evidence of non-caseating epithelioid granuloma in a biopsy sample after exclusion of other known etiology of granuloma. We assessed clinical and ^{18}F-FDG PET/CT characteristics.
Results: A total of 85 patients (56.5% of female, median age 47 years) with sarcoidosis were analyzed. The median of disease follow-up was 4 years. Sarcoidosis occurred in more than three organs among 66% of cases. Using ATS/ERS/WASOG criteria, bone sarcoidosis was diagnosed in 12 (14%) patients. Spine was the most commonly affected bone (92%), followed by pelvis (67%), sternum (33%), humerus (25%) and fingers (17%). Only peripheral adenopathy was associated with bone lesions (p=0.04). Seven patients have benefited from a follow-up ^{18}F-FDG PET/CT, which in 100% of cases showed an improvement of lesions.
Conclusion: Bone sarcoidosis occurred in 14% of patients, affecting multiple bones and mostly the axial skeleton. ^{18}F-FDG PET/CT appears to be a sensitive imaging for diagnosis and follow-up of bone sarcoidosis.

REFERENCES

[1] Aberg C, *and al.* AJR Am J Roentgenol. avr 2004
[2] Baldini S, *and al.* Br. J. Haematol. nov 2008
[3] Bechman K, *and al.* Rheumatology 1 mai 2018
[4] Clarençon F, *and al.* Spine. 15 sept 2007
[5] Conte G, *and al.* Ecancermedicalscience. 7 mai 2015
[6] Costabel U, *and al.* European Respiratory Society. World Association for Sarcoidosis and Other
[7] Granulomatous Disorders. European Respiratory Journal. 1 oct 1999
[8] Glaudemans AWJM, *and al.* Journal of Immunology Research. 2013
[9] Grozdic Milojevic I, *and al.* Sarcoidosis Vasc Diffuse Lung Dis. 29 mars 2016
[10] James DG, *and al.* Ann. N. Y. Acad. Sci. 1976
[11] Judson MA, *and al.* Sarcoidosis Vasc Diffuse Lung Dis. 18 avr 2014
[12] Kaira K, *and al.* Chest. avr 2007
[13] Lefere M, *and al.* Clin Nucl Med. mars 2003
[14] Mostard RL, *and al.* Clin Nucl Med. janv 2012
[15] Prost N de, *and al.* RES. 2010
[16] Sparks JA, *and al.* Seminars in Arthritis and Rheumatism. 1 déc 2014
[17] Thelier N, *and al.*J. Rheumatol. août 2008
[18] Wilcox A, *and al.* Current Opinion in Rheumatology. juill 2000 [
[19] Zhou Y, *and al.* Seminars in Arthritis and Rheumatism. 1 févr 2017
[20] Zisman DA, *and al.* Semin Respir Crit Care Med. déc 2002

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AB1139 CONTRIBUTION OF CERVICAL SPINE IMAGING IN RHEUMATOID ARTHRITIS

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Background: Cervical involvement in rheumatoid arthritis (RA) ranks third after erosive lesions of the hands and feet. The evolution is unpredictable and imposes regular radio-clinical surveillance because of the frequency of asymptomatic forms and of its seriousness, especially the neurological involvement could threaten functional and vital prognosis.
Objectives: To specify the contribution of imaging means in the diagnosis of rheumatoid cervical involvement and perform a comparison of these different imaging means to establish an exploration strategy.
Methods: This is a cross-sectional and descriptive retrospective study of 55 patients with RA which evolves since more than two years. All patients were explored by standard radiographs. CT and/or cervical MRI were performed according to the radiological findings.
Results: The mean age of the patients was 57.55 ± 13.59 years with a female predominance (72.7%). Functional signs were dominated by neck pain (87.3%). The stiffness of the cervical spine was the most recovered physical sign (69.1%). In imaging, cervical involvement was dominated by atloido-axoidal subluxations (AAS) in 50.9% and pannus of C1-C2 (14.54%). Among AAS, anterior AAS was the most common (40%) followed by vertical AAS (7.27%) then lateral and rotary (both in 1.81%). Subaxial subluxation was found in 14.54% of cases. Standard radiographs detected 38.2% of previous AAS versus 20% on MRI. CT allowed a better study of rotatory and lateral subluxations. MRI detected pannus of C1-C2 and assessed the neurological impact of the various cervical rheumatoid lesions.
Conclusion: Clinical examination alone remains insufficient in the evaluation of the rheumatoid cervical spine. Imaging has thus emerged as a key examination in exploration and therapeutic orientation. The standard radiography with its different incidences is the first-line examination. CT and MRI will be discussed as second-line. CT essentially detects atypical subluxations and bone lesions. MRI is the exam of choice for the study of pannus and neurological repercussions.

REFERENCES

[1] Currier B, Coblyn J. Cervical subluxation in rheumatoid arthritis. Available at:https://www.uptodate.com/contents/cervical-subluxation-in-rheumatoid-arthritis. Accessed March 23, 2018

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AB1140 ROLE OF ULTRASOUND IN ASSESSMENT OF JOINT PAIN AMONG HEMO DIALYSIS PATIENTS

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Background: Few studies including limited number of patients assessed the rheumatologic effects of hemodialysis (HD) on joints using ultrasonography.
Joint ultrasound has been emerged as a cheap noninvasive tool for assessment of joint pain among HD patients. This was the aim of our study to make use of such tool in such life quality threatening complaints
Objectives: to determine the role of ultrasound in evaluation of joint pain and its causes among patients on regular HD
Methods: One hundred and four patients with end stage renal disease (ESRD) who were regular on HD three sessions per week four hours per session were subjected to history taking, complete physical examination stressing on musculoskeletal examination and ultrasonography of painful joints.
Results: Dialysis related arthropathy (DRA) was not the only cause of joint pain among HD patients but there were diverse causes in different joints. As regard affected joints, knee was the most affected one then came wrist, shoulder, ankle and elbow respectively.
As regard causes of joint pain, DRA was the commonest one then came osteoarthritis,
Nonspecific ultrasonographic findings and few cases showed normal ultrasonographic studies.
Conclusion: This study confirmed that joint pain in HD patients has diverse causes not DRA by necessity but other causes must be considered as well as multifactorial etiologies.

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AB1141 A SIMPLE CLINICAL SCORING TOOL CAN BE USED TO IMPROVE PATIENT SELECTION FOR ULTRASOUND IN DIAGNOSING EARLY INFLAMMATORY ARTHRITIS

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Background: Ultrasonography has been shown to be more sensitive than clinical examination in detecting clinical/subclinical synovitis and improving diagnostic certainty in early inflammatory arthritis (EIA). Local audit suggests increasing demand on ultrasound clinics to aid diagnosis in patients with suspected EIA therefore increasing waiting times. There is limited research to identify the patients most likely to benefit from an early ultrasound.
Objectives:
- (i) To evaluate the proportion of patients in whom an ultrasound resulted in a change in the pre– to post–scan diagnosis.
- (ii) To devise a simple scoring tool to predict patients where an ultrasound may alter the diagnosis/outcome
- (iii) To assess if such a scoring tool can be used prospectively in the clinical setting

Methods: We conducted a retrospective analysis of the electronic records of patients attending the rheumatology-led musculoskeletal ultrasound clinic for a diagnostic scan between January and September 2017. Data on pre-test diagnosis, ultrasound findings and post-scan diagnosis was obtained. Clinical data was used to devise a scoring tool to predict variation in pre and post-scan diagnosis. Prospective data was then collected to confirm the validity of this scoring tool.
Results: 200 patient records were reviewed. In 102 patients (51%), the post ultrasound scan diagnosis differed from the pre-scan diagnosis. Patients referred with polyarthralgia of uncertain cause (n=92) were the largest group in whom the post-scan diagnosis differed (64, 69.6%) as the scan was able to identify a diagnosis. Patients with a pre-scan diagnosis of osteoarthritis or fibromyalgia (n=48) were more likely to have no difference in post-scan diagnosis (40, 83.3%).
We generated a score for each patient with one point given to: duration (>6 weeks), (any)tender joints, (any)swollen joints, rheumatoid factor positive, anti-citrulinated protein antibody positive, C-reactive protein(>5mg/L), erythrocyte sedimentation(>age adjusted value), early morning stiffness(>30 minutes), or radiographic erosions. 39 patients scored 0–1, and 4 patients scored 7–9. In none of these categories did the ultrasound alter the diagnosis. Among patients with a score 2–6, the ultrasound altered overall diagnosis in 26% (n=157). Scores 5 and 6 demonstrated most variation between pre and post-scan diagnoses (45%).
We applied the score set prospectively and preliminary data indicates a similar distribution of results (data collection in progress).
Conclusion:
- 1. Ultrasound contributed to the overall diagnosis in over 50% of patients under investigation for EIA.
- 2. A simple clinical scoring tool can predict which patients the scan will make no difference to overall diagnosis.
- 3. Patients with scores in the middle range should be prioritised over those with very low or high scores.
- 4. This can be applied to improve patient selection and maximise the utility of ultrasound in EIA clinics.

REFERENCES

[1] Naredo E, Bonilla G, Gamero F, Uson J, Carmona L, Laffon A. Assessment of inflammatory activity in rheumatoid arthritis: a comparative study of clinical evaluation with grey scale and power Doppler ultrasonography. Ann Rheum Dis 2005;64(3):375-81
[2] Wakefield RJ, Green MJ, Marzo-Ortega H, Conaghan PG, Gibbon WW, McGonagle D, et al. Should oligoarthritis be reclassified? Ultrasound reveals a high prevalence of subclinical disease. Ann Rheum Dis 2004;63 (4):382-5.

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AB1142 **PROGNOSTIC VALUE OF 18F-FLUORODEOXYGLUCOSE PET-CT SCORE AT BASELINE ON THE THERAPEUTIC RESPONSE TO PREDNISONE IN PATIENTS WITH POLYMYALGIA RHEUMATICA**

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Background: Polymyalgia rheumatica (PMR) is one of the most common inflammatory rheumatic diseases. To date, there is no imaging procedure that can be used as a prognostic factor for good or poor response to corticosteroid therapy
Objectives: To evaluate the prognostic value of 18F-fluorodeoxyglucose PET-CT (FDG-PET/CT) score at baseline, on the therapeutic response to prednisone, in patients with polymyalgia rheumatica (PMR).
Methods: This is a monocentric retrospective study realized at the university hospital of Besancon. We included patients with a diagnosis of PMR meeting the 2012 ACR/EULAR criteria, who had performed a FDG-PET/CT at baseline, between december 2012 and december 2017. Patients were treated with an initial prednisone dose of 0.3mg/kg a day, progressively decreased following a standardized tapering dose protocol (10%/month). We excluded patients who received corticosteroids before the FDG-PET/CT, or without baseline FDG-PET/CT. Seventeen specifics previously described hotspots were visually analyzed (1). We realized a semi-quantitative analysis of FDG uptake (4-point score from 0 to 3), following Goerres scoring system (2). Hotspot with 0 indicating no uptake (same as bone); 1, slight uptake; 2, moderate uptake (same as liver); and 3, uptake higher than the liver, with a global range score of 0 to 51. Then we defined two groups of patients according to their resistance to prednisone at 12 months, defined as the reoccurrence of symptoms and/or an increase of systemic inflammation twice during the prednisone tapering.
Results: 33 patients where included: 14 (42%) in the group "resistant "and 19 (58%) in the group "sensitive". There were 57.6% of women, with a mean age of 67.57 ± 11,63 years. The mean CRP at baseline was 45.02 ± 39.59 mg/L. The mean FDG-PET/CT score at baseline was 18/51. The FDG-PET/CT score at baseline was significantly lower in the resistant group (13.1 vs 22.8/51, p =0.019). Resistant patients were younger (61.1 vs 72.4 years, p <0.01), and mostly men (66.5% vs 22%, p<0.02). ROC curve showed a threshold of 9.5/51 with a sensitivity of 61.54% and a specificity of 84.21% [AUC 0.76 (+/- 0.089), p= 0.014]. There was no statistically significant difference concerning CRP at baseline (48.6mg/l vs 44.8mg/l; p= 0.58), and no correlation between CRP and PET/CT score (r =0.25, p=0.15). The prevalence of synovitis (21% vs 37%, p=0.46), and neoplasia (0% vs 15.79%, p=0.79) were similar between the two groups.
Conclusion: Our results suggest that in patients with PMR, a baseline FGD-PET/CT score over 9.5/51 score is predictive of a good response to prednisone.

REFERENCES

[1] Sondag.M, et al. Utility of 18F-fluoro-dexoxyglucose positron emission tomography for the diagnosis of polymyalgia rheumatica: a controlled stud. Rheumatology 2016 Aug;55(8):1452-7.
[2] Goerres GW, Forster A, Uebelhart D, et al. F-18 FDG whole-body PET for the assessment of disease activity in patients with rheumatoid arthritis. Clin Nucl Med 2006;31:386-90.

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AB1143 **SUBCLINICAL MICROVASCULAR INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS**

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Background: Peripheral microcirculation is well studied in primary Raynaud's phenomenon (RP), but poorly investigated in systemic lupus erythematosus (SLE) (1-3).
Objectives: To investigate morphological and functional aspects of microcirculation in different skin areas of the hands in SLE patients in comparison with primary RP (PRP) patients and healthy subjects (CNT).
Methods: 15 SLE patients without RP (ACR 2013 criteria) (mean age 52 ±13 SD years, mean disease duration 6±3 years), 15 PRP patients (LeRoy 2001 criteria) (mean age 52±16 years, mean RP duration 6±4 years) and 15 sex-matched controls (CNT) (mean age 51±16 years) were enrolled during the winter period. Nailfold videocapillaroscopy (NVC) and laser speckle contrast analysis (LASCA) have been performed in the three groups of patients. The absolute nailfold capillary number (CN) per linear millimeter at first distal row was assessed by NVC (4). Blood perfusion (BP) was detected by LASCA at the level of fingertips, periungual areas, dorsum and palm of both hands (2). Patients were not taking vasoactive drugs since at least one month before study entry. Statistical analysis was performed by non parametric tests.
Results: SLE patients showed a statistically significant lower nailfold absolute CN than both PRP and CNT (median 9.2 vs 10.2 vs 11.1, respectively, p<0.0006). Conversely, no statistically significant difference of nailfold CN was observed between PRP and CNT. PRP patients showed a statistically significant lower BP than SLE and CNT, and SLE than CNT, at the level of fingertips (median 90, 113, 186 PU, respectively; p<0.0001), periungual (median 75, 100, 142 PU, respectively, p<0.0001), dorsal (median 63, 73, 126 PU, respectively, p<0.0001), and palm areas (median 76, 95, 124 PU, respectively, p<0.0001). A positive correlation between nailfold CN and BP was observed in all areas of hands in SLE patients (p<0.0001). On the contrary, no statistically significant correlation was observed in both PRP and CNT, between nailfold CN and BP in all examined areas (p=0.74 and p=0.23, respectively).
Conclusion: SLE patients, without RP, show a subclinical microvascular impairment, having lower nailfold CN and lower BP than CNT. Conversely, PRP patients show only a functional dysfunction, having lower peripheral skin BP than both SLE patients and CNT. A correlation between morphological and functional microvascular features was also found in SLE patients. These findings seem to suggest interesting microvascular insights in active SLE patients.

REFERENCES

[1] Ruaro B, et al. Ann Rheum Dis 2014;73:1181-5. **2.** Cutolo M, et al. J Rheumatol 2010;37:1174-80. **3.** Cutolo M, et al. Autoimmun Rev. 2018;17:344-352. **4.** Cutolo M, et al. Arthritis Rheumatol. 2016;68:2527-39.

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AB1144 **ULTRA HIGH FIELD MRI MICROARCHITECTURE ANALYSIS IMPROVES THE PREDICTION OF PROXIMAL FEMUR FRACTURE: A COMBINED STUDY WITH EX VIVO BIOMECHANICAL TESTS**

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Background: The purpose of this study was to assess cadaveric proximal femurs from the points of view of bone microarchitecture using ultra-high field (UHF) 7 Tesla magnetic resonance imaging (MRI), bone strength using biomechanical tests and bone mineral density (BMD) using Dual-energy X-ray absorptiometry (DXA).
Objectives: We aimed at determining whether bone microarchitecture parameters were related to bone strength and BMD and whether UHF MRI can provide additional information regarding bone strength.
Methods: BMD of ten proximal femurs from five cadavers were investigated using DXA and the bone volume fraction (BVF), trabecular thickness (Tb.Th), and trabecular spacing (Tb.Sp), fractal dimension (FD), Euler characteristics (Euler Ch.), Connectivity density (Conn. D) and Degree of anisotropy (DA) of each femur was quantified using UHF MRI. The whole set of specimens underwent mechanical compression tests to failure.
Results: BMD and all the microarchitecture parameters except ConnD were significantly correlated with failure load (p < 0.05). The

microarchitecture parameters were correlated to each other but not correlated with BMD. Multiple regression analysis demonstrated that the combination of the microarchitecture parameters and BMD improved the prediction of the failure load with for example an improved fracture risk prediction from R^2 = 0.418 to 0.688 when combining BMD and Euler Ch. Overall, femur bone microarchitecture assessed with UHF MRI was significantly correlated with biomechanical parameters. The multimodal assessment of BMD and trabecular bone microarchitecture using UHF MRI improved the fracture risk prediction of femoral bone and might be of interest for the future investigation of selected osteoporotic patients.

Conclusion: We demonstrated that femur bone microarchitecture assessed with UHF MRI was significantly correlated with biomechanical parameters. The multimodal assessment of bone mineral density and trabecular bone microarchitecture using UHF MRI improved the fracture risk prediction of femoral bone and might be of interest for the future investigation of selected osteoporotic patients.

Disclosure of Interests: None declared

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AB1145 FULLY CONVOLUTIONAL NEURAL NETWORK-BASED SEGMENTATION OF INDIVIDUAL MUSCLES IN MR IMAGES USING MUSCLES AND BORDERS PARCELLATIONS

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Background: Segmentation of individual muscles in MR images is challenging considering the poor contrast between muscles and the large variability between and within subjects.

Objectives: The segmentation performance of the Bayesian SegNet network was assessed for the four individual muscles of the quadriceps group. In addition to the classes corresponding to each muscle, we analyzed the effect of adding four additional classes corresponding to muscle borders. We also investigated the network performance taking into account each muscle individually or the whole set of muscles. The corresponding results were compared with those obtained using a conventional multi-atlas method.

Methods: For the training phase, a dataset of 500 images was used while the testing phase was performed for two other datasets with 140 images each. Four different variants of the same network were assayed considering simultaneous segmentation of individual muscles (On5), separate segmentation of individual muscles (Fn2) and the use of additional classes related to muscle borders in both cases (On9 and Fn3).

Results: All approaches largely outperformed the results of a multi-atlas strategy. The higher DSI values i.e. 0.96 ± 0.01 for the *rectus femoris* muscle, 0.93 ± 0.01 for the *vastus intermedius* muscle, 0.94 ± 0.03 for the *vastus lateralis* muscle and 0.96 ± 0.01 for the *vastus medialis* muscle were obtained with the On9 and Fn3 networks i.e. taking into account the muscle borders labels in addition to the muscle labels.

Conclusion: Deep-learning based methods are optimal for the segmentation of thigh muscles and the corresponding efficiency can be improved when considering labels for muscles together with borders.

Disclosure of Interests: None declared

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AB1146 PREVALENCE OF STRUCTURAL CHANGES AT THE POSTERIOR PART OF THE SPINE IN AXIAL SPONDYLOARTHRITIS EVALUATED WITH MR

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Background: In clinical trials radiographic damage is frequently quantified by conventional x-ray but neither the thoracic spine nor the posterior parts of the vertebral column including the intervertebral joints, the vertebral arch and the spinous process can be evaluated reliably with this instrument. Bone inflammation and areas of enthesitis can easily be detected by magnetic tomography imaging (MRI) and the introduction of high-resolution 3-tesla MRI allows analysis of bone structures more precisely than with x-ray without radiation exposure [1].

Patients with axial SpA frequently present with reduced spinal mobility and functional impairment, but radiographic signs of ankylosis are missing on plain radiographs. These particular clinical findings are reinforced by data in the literature showing, that the relation between radiographic damage, spinal mobility and function is low. Radiographic damage to the posterior parts of the vertebral column may be responsible for the discrepancy found between clinical and radiographic results as suggested by a Dutch group [2].

Objectives: To evaluate the localisation and incidence of new bone formation in the posterior part of the vertebral bodies with MRI.

Methods: In a cohort of 56 patients with diagnosed axial SpA (mean age 50.29y, mean disease duration 14.4y, 76.4% men, 88.7% HLA-B27 positive) we performed a MRI (*3 Tesla scanner Skyra, Siemens Healthcare, Erlangen, Germany).* The whole spine was scanned with T1 weighted and Turbo-Inversion Recovery Magnitude (TIRM) sequences in sagittal planes and each segment of the vertebral column was divided into four areas (ventral and posterior part of the vertebral bodies, intervertebral joints andspinous processes) to assess osseous changes like sclerosis, erosion, syndesmophytes, ankylosis, (partial) fusion of intervertebral joints and fibroostosis of spinous processes.

Results: Syndesmophytes and ankylosis of the ventral segments were present from C7/Th1 down to L5/S1 with a maximum in Th5/6 (62.5%). In the posterior segments of the vertebral bodies we detected a contrary accumulation inside the cervical and lumbar spine with a max. in C5/6 (55.4%) respectively L2/3 (66.1%). Erosions were mainly found at the ventral edges with an accumulation in middle cervical, lower thoracic and the whole lumbar spine (max. Th9/10 24.5%)

Ankylosis of the intervertebral joints was present over the whole spine with a preference of the cervical (max. C5/6 27.7%) and lumbar column (max. L2/3 47.3%). Fibroostosis of the spinous processeswere rarely found in the middle and lower thoracic spine (Th5-11, each 2.7%).

In up to 57.10% of the cervical spine (54.78% for lumbar, 32.18% for thoracic spine) with detectable new bone formation of the posterior segments we found no changes of the ventral part.

Conclusion: With high resolution MRI we were able to detect structural in the dorsal part of the spine, which can hardly be assessed by conventional radiographs. These findings may explain functional disability in patients with non-corresponding findings in x-ray.

REFERENCES

[1] Lee CH, et al. (2015) Correlation of structural abnormalities of the wrist and metacarpophalangeal joints evaluated by high-resolution peripheral quantitative computed tomography, 3 Tesla magnetic resonance imaging and conventional radiographs in rheumatoid arthritis. International journal of rheumatic diseases

[2] Maas F, et al. (2015) Comparison of radiographic damage of the zygapophyseal joints and the vertebral bodies of the cervical spine in patients with ankylosing spondylitis before and after 4 years of TNF-alpha blocking therapy. Annals of the rheumatic diseases

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AB1147 VERTEBRAL FRACTURE ASSESSMENT : A SIMPLE TOOL TO DETECT VERTEBRAL FRACTURE IN THE OSTEOPOROSIS ASSESSMENT OF PATIENTS WITH TYPE2 DIABETES MELLITUS

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Background: Vertebral fracture assessment (VFA) has several benefits, including substantially lower radiation dose, lower cost, higher patient convenience, and less operator-dependent variance,VFA can be directly assessed during bone mineral density (BMD) measurement

Objectives: evaluate the accuracy of VFA performed in the supine position by using conventional visual radiography of the spine as the reference standard in patients with type 2 diabetes mellitus

Methods: A total of 207 patients with type 2 diabetes mellitus (mean age, 46,59 ±7,53years; range, 21–60 years) consisting of 102 women

and 105 men,who were suspected of having osteoporosis and who underwent VFA in the supine position and radiography of the spine were evaluated. VFA was analyzed by using a six-marker point method to describe the shape and deformity of each vertebra. Visual radiography of the lateral spine was performed by an experienced radiologist. The agreement between VFA and visual radiography, was assessed by using weighted statistics.

Results: Visual radiography helped identify 51 (24.6%) patients with at least one vertebral fracture versus 49(23,67%) with VFA. Most fractures were present in T7, T12, and L1. Excellent agreement was found between VFA and visual radiography, with 97. 3% concordance and 0.89. Sensitivity, specificity, and positive and negative predictive values calculated by lesion level for VFA compared with visual assessment were 90.2%, 98.08%, 93.88%, and 96.84%, respectively.

Conclusion: VFA performed with patients with type 2 diabetes, in the supine position, is an accurate method to help detect vertebral fractures when compared with conventional spine radiography. VFA permits combination of fracture assessment with bone mineral density measurement in a single session

REFERENCES

[1] -Jacobs-Kosmin D, Sandorfi N, Murray H, Abruzzo JL. Vertebral deformities identified by vertebral fracture assessment: associations with clinical characteristics and bone mineral density. J Clin Densitom 2005;8: 267–272.

[2] -Binkley N, Krueger D, Gangnon R, Genant HK, Drezner MK. Lateral vertebral assessment: a valuable technique to detect clinically significant vertebral fractures. Osteoporos Int 2005;16:1513–1518.

[3] -Schousboe JT, DeBold CR. Reliability and accuracy of vertebral fracture assessment with densitometry compared to radiography in clinical practice. Osteoporos Int 2006;17: 281–289

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AB1148 THE RELATION ANALYSIS OF BONE MICROARCHITECTURE EVALUATED BY HR-PQCT, AND SYNOVITIS, BONE DESTRUCTION, SYSTEMIC OSTEOPOROSIS IN RHEUMATOID ARTHRITIS

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Background: Periarticular osteoporosis is one of hallmark of rheumatoid arthritis (RA). However, until now the periarticular bone structure including bone mineral density have not been fully elucidated. High-resolution peripheral quantitative computed tomography (HR-pQCT) is a new technique with high spatial resolution that enables us to assess microarchitecture of cancellous and cortical bones that cannot be assessed by conventional X-ray examinations. Recently, few studies using HR-pQCT revealed that bone microarchitecture such as trabecular volumetric densities (Tb.vBMD) were different between RA and non-RA[1], but these study had not compared findings of HR-pQCT with synovitis assessed by ultrasonography(US) or systemic osteoporosis.

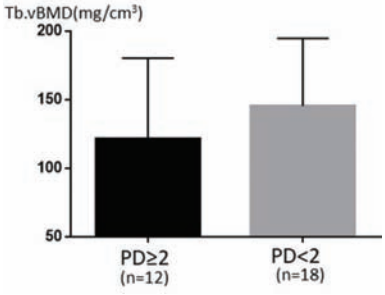
Objectives: To investigate bone microarchitecture evaluated by HR-pQCT in RA.

Methods: This study included 21 RA patient. HR-pQCT imaging analyses quantified bone microarchitecture in 2,3 Metacarpal Head. We measured the bone mineral density (BMD) of lumber spine and femoral neck using Dual-Energy X-ray Absorptiometry (DXA). Synovitis and bone destruction were assessed by US and X-ray, respectively.

Results: Disease duration, age and disease activity were not correlated with bone microarchitecture. BMD of femoral neck was correlated with Tb.vBMD (r=0.84,p<0.01). The joints with US-proven active synovitis [power doppler score (PD)≥2)] showed less Tb.vBMD, trabecular number (Tb.N) and trabecular thickness (Tb.Th) as compared with the patients with US-PD<2 synovitis (Tb.vBMD:121.5 mg/cm^3 vs 145.3 mg/cm^3, Figure 1). These tendencies were also shown in deferent Metacarpal Heads in the same patient (the mean difference of Tb.vBMD, PD≥2 – PD<2: -11.9 mg/cm^3). Moreover, the joints with progressive joint destruction as classified by more than steinbrocker stage 3 showed less Tb.vBMD (122.1 mg/cm^3 vs 150.0 mg/cm^3). The longitudinal analysis of 10 patients revealed that Tb.vBMD and TB.N were improved along with improvement of disease activity (DAS -2.80: from baseline to 12 months after new treatment initiated , but Tb.Th was not improved.

Conclusion: This study revealed that bone destruction and synovitis were associated with bone microarchitecture and, the difference of treatment response by parameter of bone microarchitecture. However, this study was mainly transverse analysis and small samples, we need longitudinal analysis using larger samples.

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Abstract AB1148 Figure 1

REFERENCES

[1] Feehan LM, Li LL, McKay HA. Micro-structural bone changes in early rheumatoid arthritis persist over 1-year despite use of disease modifying anti-rheumatic drug therapy. BMC Musculoskelet Disord 2017; 18(1): 521.

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AB1149 CHARACTERIZATION OF SALIVARY PROTEINS IDENTIFIED AS POTENTIAL BIOMARKERS FOR SYSTEMIC LUPUS ERYTHEMATOSUS THROUGH PROTEOMIC ANALYSIS

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by pathogenic autoantibodies and uncontrolled inflammatory response. There are few reliable biomarkers available for diagnosis and monitoring the disease.

Objectives: We tried to find and characterize specific protein components in saliva of patients with SLE for their use as biomarkers in future.

Methods: Salivary proteins were prepared from 11 samples from patients with SLE and healthy controls (HC), and were subjected to 2-dimensional gel electrophoresis (2-DE). The spots with greater than 2 fold change in intensity were identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometer (MS) analysis. The relative and absolute amounts of the several candidate proteins in saliva of patients with SLE and rheumatoid arthritis (RA), and HC were analyzed using western blotting, and enzyme-linked immunosorbent assay.

Results: Proteomic analysis using 2-DE and MS identified 20 differentially expressed protein spots in the saliva of SLE patients compared in that of HC. Among them, proteins with more than two-fold differences in expression were found as immunoglobulin gamma-3 chain C (IGHG3), immunoglobulin alpha-1 chain C region, protein S100, lactotransferrin, leukemia-associated protein 7, and 8-oxoguanine DNA glycosylase (OGG1). salivary IGHG3 levels were increased in SLE (3.9 ± 2.2 pg/mL) compared to those in RA (1.8 ± 1.0 pg/mL, p < 0.001) or HC (2.1 ± 1.6 pg/mL, p < 0.001), and salivary lactotransferrin levels were increased in SLE (5.0 ± 1.7 pg/mL) compared to those in RA (3.1 ± 1.6 pg/mL, p < 0.001) or HC (2.3 ± 1.7 pg/mL, p < 0.001). The patients with nephritis had higher salivary IGHG3 (4.7 ± 1.9 pg/mL) than those not (3.6 ± 2.2

pg/mL, p = 0.007). The follow up study, the patient with increased salivary IGHG3 had significantly different in changes of hemoglobin (-0.85 ± 0.87 vs 0.42 ± 0.99/μL, p = 0.02), and changes of complement 3 (-7.67 ± 14.15 vs +7.0 ± 9.34, p = 0.02) compared to those not. In addition, the patients with increased salivary lactotransferrin had significantly different in changes of ESR (-2.0 ± 4.6 vs 8.4 ± 9.56, p = 0.02) compared to those not, and salivary lactotransferrin levels negatively correlated with complement 3 levels (r = -0.5, p= 0.02).
Conclusion: Salivary IGHG3 and lactotransferrin levels were significantly increased in patients with SLE compared to those in patients with RA or HC, and could be used as potential biomarkers of SLE.

REFERENCES

[1] Baldini C, Giusti L, Ciregia F, Da Valle Y, Giacomelli C, Donadio E, Sernissi F, Bazzichi L, Giannaccini G, Bombardieri S, Lucacchini A: Proteomic analysis of saliva: a unique tool to distinguish primary Sjogren's syndrome from secondary Sjogren's syndrome and other sicca syndromes. Arthritis Res Ther 13: R194, 2011
[2] Lamy E, Mau M: Saliva proteomics as an emerging, non-invasive tool to study livestock physiology, nutrition and diseases. J Proteomics 75: 4251-4258, 2012

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AB1150 IMPLICATIONS OF CORONARY ARTERY CALCIUM AND ITS PROGRESSION AS MARKERS OF PLAQUE VULNERABILITY AND PATIENT RISK IN RHEUMATOID ARTHRITIS

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Background: Atherosclerotic plaque calcification represents a stabilizing physiologic process; calcified coronary plaques (CP) are less prone to rupture and yield lower risk of cardiovascular events (CVE) compared to non-calcified (NCP) or mixed- partially calcified- plaques (MP). Interestingly, higher coronary artery calcium score (CACS) and its progression associate with higher event risk in general patients. We, likewise, reported that CACS predicted cardiac events in rheumatoid arthritis (RA) patients independently of risk factors or cardiac risk scores.
Objectives: To address this paradox, we evaluated the contribution of vulnerable MP burden to CACS as well the influence of change in MP burden on CACS progression in RA patients who underwent coronary anatomy evaluation with computed tomography angiography (CCTA).
Methods: One hundred-one patients underwent a repeat CCTA within 83 ±3.6 months from baseline. Total number of segments with plaque (segment involvement score-SIS) and cumulative stenosis severity rendered by plaque over all evaluable segments (segment stenosis score-SSS) were computed for all participants. Coronary lesions were defined as non-calcified (NCP), mixed (MP) or calcified (CP). Generalized Linear Models predicted the contribution of MP and CP plaque burden to the baseline and follow-up CACS as well as the influence of change in the burden of the respective lesions on CACS progression.
Results: Mixed and CP burden (SSS-MP and SSS-CP respectively) strongly correlated with CACS at both baseline (r_{mp}= 0.75 and r_{cp}= 0.77, p<0.001) and follow-up (r_{mp}= 0.57 and r_{cp}= 0.68, p<0.0001), whereas non-calcified plaque did not (r_{ncp}= -0.03, p=0.85 and -0.16, p=0.30 respectively). Both MP and CP burden comparably and significantly contributed to CACS magnitude at both times (table 1); MP accounted for 36.5% and 38.5% of explainable variance in CACS while CP accounted for 63.5% and 61.5% of it at baseline and follow-up respectively (all p<0.001). Likewise, change in MP and CP burden from baseline to follow-up significantly contributed to and justified 27% and 73% of explainable CACS change variance.
Conclusion: The vulnerable MP and the more stable CP burden and their change significantly and collectively contributed to CACS at any time as well as its progression respectively in RA. Therefore, the MP burden and its change embody the vulnerability components within the higher baseline and progressing CACS scores explaining the higher CVE risk observed.

Abstract AB1150 Table 1. Impact of MP and CP burden and their change on CACS and its progression in RA

CCTA	Model	predictor	Beta	p-value	Raw RW (95% CI)	Rescaled RW
Baseline	*Model 1*	SSS-MP	.564	*.000*	0.258 (0.085-0.472)	36.5%
		SSS-CP	.532	*.000*	0.450 (0.232-0.662)	63.5%
	Model 2	SSS-MP	.548	*.000*		
		SSS-CP	.518	*.000*		
		Age	.062	.092		
		Gender	-.007	.83		
Follow-up	*Model 1*	SSS-MP	.416	*.000*	0.250 (0.112-0.399)	38.5%
		SSS-CP	.634	*.000*	0.399 (0.235-0.554)	61.5%
	Model 2	SSS-MP	.399	*.000*		
		SSS-CP	.610	*.000*		
		Age	.086	.070		
		Gender	-.030	.48		
Change (follow-up - baseline)	*Model 1*	SSS-MP	.388	*.003*	0.106 (0.017-0.251)	27%
		SSS-CP	.585	*.000*	0.288 (0.115-0.483)	73%
	Model 2	SSS-MP	.314	*.010*		
		SSS-CP	.538	*.000*		
		Age	.341	*.005*		
		Gender	-.063	.58		

Model 1: unadjusted, Model 2: age and gender adjusted, RW: Relative Weight
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AB1151 APPLICATION OF ULTRASOUND TO DISTINGUISHING PMR FROM POLYARTHRALGIA

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Background: Japan is the world's most aged country. The number of patients with polymyalgia rheumatica (PMR) is expected to increase more. Classification criteria including ultrasound findings were published in 2012, but the ability to differentiate PMR from rheumatoid arthritis (RA) was not significant. We will clarify whether recently reported ultrasound findings (1, 2) which could be characteristic in PMR are helpful for distinguishing from other diseases and treatment outcome in suspected PMR patients.
Objectives: Patients who were clinically suspected of PMR and underwent ultrasound examination from March 2015 to July 2018.
Methods: Recorded ultrasound images were retrospectively interpreted by the ultrasound expert, who was blind for clinical information. They were classified into three groups of PMR, RA, others/no inflammation. Initial dose of glucocorticoid (GC), therapeutic response, presence or absence of relapse, and concomitant medications were collected and compared among the 3 groups. Cases in which steroids had already been used before ultrasound examination were excluded from the analysis.
Results: The number of subjects was 81, and the number of ultrasound examination was 88. The ultrasound expert classified 29 PMR, 20 RA, 3 other/no inflammation. 18.5% (15/81) of the subjects were improved with no GC and relapse. The average prednisolone (PSL) dose was 15.3 mg in the PMR group, and 9.7 mg in the RA group. Concomitant medications were introduced in 31% (9/29) of PMR group, in 65% (13/20) of RA group.
Conclusion: Ultrasound is useful for distinguishing PMR from seronegative RA and other arthralgia. These findings showed that ultrasound is useful for the proper use of GC and concomitant medications.

REFERENCES
[1] Suzuki T, Yoshida R, Hidaka Y, Seri Y. Proliferative Synovitis of the Shoulder Bursae is a Key Feature for Discriminating Elderly Onset Rheumatoid Arthritis Mimicking Polymyalgia Rheumatica From Polymyalgia Rheumatica. Clin Med Insights Arthritis Musculoskelet Disord 2017;10: 1179544117745851.
[2] Suzuki T, Yoshida R, Okamoto A, Seri Y. Semiquantitative Evaluation of Extrasynovial Soft Tissue Inflammation in the Shoulders of Patients with Polymyalgia Rheumatica and Elderly-Onset Rheumatoid Arthritis by Power Doppler Ultrasound. Biomed Res Int 2017;2017: 4272560.

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AB1152 CORRELATING SERUM RESISTIN LEVEL TO ULTRASONOGRAPHIC FINDINGS OF OSTEOARTHRITIC KNEES AFTER INTRA-ARTICULAR GLUCOCORTICOID INJECTION

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Background: Osteoarthritis (OA) is one of the ten disabling diseases affecting 9.6% of men and 18% of women aged over 60 worldwide (1). OA characterized by articular cartilage loss, subchondral bone remodeling, soft tissue damage and low grade synovitis It is the most common form of arthritis and major cause of disability in the adult population (2). The main source of resistin in humans is mononuclear cells(3). Evidence has shown that higher serum levels of resistin in patients with severe OA compared to controls with no OA and resistin are detected in both serum and synovial fluid, proving its systematical and local involvement in inflammatory changes of OA (4).
Objectives: The aim of this work is to study the effect of local GC intra articular injection on the level of serum resistin in OA knees and to study the relation between different serum levels of resistin and US findings of the knee.
Methods: Thirty patients with primary knee OA Grade 2-3 Kellgren Lawrence score (5) in acute flare according to ACR criteria with or without effusion will be recruited for the study from the Physical medicine, Rheumatology and Rehabilitation Outpatient Clinic of Al-Azhar University Hospitals starting from November 2017 till may 2018.
Patients with secondary OA. All systemic autoimmune diseases. Previous local GC injection within 3 months preoperative evaluation were excluded. Twenty healthy individuals matched for age, sex and BMI with patients were also enrolled in this study as a control group.
Serum Resistin level was measured and Musculoskeletal ultrasound examination of the knee before and three months after steroid injection was done by TOSHIBA APILO 400. linear probe frequency 12L5. Effusion and Synovitis were assessed.
Results: Serum resistin showed significant difference (p-value < 0.05) before and after injection. It was 7.6 ng/ml in patients before injection and 5.1 ng/ml in patients after injection.

Groups Variables		Before (N = 30)	After (N = 27)	p-value
Resistin (ng/ml)	Mean	7.6	6.9	0.3
±SD	2.8	2.6		

US showed significant difference (p-value < 0.001) before and after injection as regard effusion level.

Groups Variables		Before (N = 30)	After (N = 27)	p-value
U/S	No effusion	0 (0%)	14 (52%)	< 0.001*
	Mild effusion	11 (37%)	10 (37%)	
Moderate efusin	19 (63%)	3 (11%)		

Conclusion: Resistin could be considered as an important severity marker of knee OA. Serum resistin level is markedly decreased after intra articular steroid injection into OA knee joint The longer the duration of illness the higher the resistin level. The older the age the higher the resistin level. The longer the duration of illness, the higher the radiological grade..

REFERENCES
[1] Hardcastle SA, Gregson CL, Deere KC, Smith GD (2013): High bone mass is associated with an increased prevalence of joint replacement: a case –control study. Rheumatology, 52 (6): 1042-51.
[2] Karvonen-Gutierrez CA, Harlow SD, Mancuso P, Jacobson J (2013): Association of leptin levels with radiographic knee osteoarthritis among a cohort of midlife women, Arthritis Care and Research, 65 (6): 936-44.
[3] Lazar MA (2007): Resistin and Obesity associated metabolic diseases. Horm Metab Res., 39:710-6.
[4] Perruccio V, Mahomed N, Chandran V, Gandhi R (2014): Plasma adipokine levels and their association with overall burden of painful joints among individuals with hip and knee osteoarthritis. Journal of Rheumatology, 41 (2): 334–337.
[5] Kellgren J and Lawrence J (1957): Radiological assessment of osteoarthritis. Ann Rheum Dis.,16 (4):494-502.
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AB1153 EVALUATION OF DIAGNOSTIC DISCREPANCY USING THE ASAS CRITERIA AND F-18 NAF PET/CT IN PATIENTS WITH SUSPECTED AS

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Background: The latest ASAS diagnostic criteria allow early diagnosis of ankylosing spondylitis by using MRI. Nuclear imaging techniques may detect increased bone turnover not only during inflammation, but probably also paralleling postinflammatory reparative changes at starting point of new bone formation.
Objectives: We focus on diagnostic discrepancy to evaluate AS between fluorine-18 sodium fluoride (F-18 NaF) PET/CT and assessment of spondyloarthritis international society (ASAS) criteria in patients with chronic low back pain suspected ankylosing spondylitis
Methods: Sixty-eight patients with chronic lower back back pain over 3 months and limited lumbar movement were included. Among them, 49 patients who fulfilled ASAS diagnostic criteria were included as AS groups and 19 others were controlled. For clinical assessment, ESR, CRP, BASDAI, and BASFI scores were measured. For imaging assessment, conventional radiography for sacroillitis and F-18 NaF PET/CT were performed. We defined AS-positive lesions on PET/CT as uptake of sacroiliac joint, syndesmophyte, enthesitis lesions and facet joint.
Results: No significant differences were observed in the baseline demographic evaluation between two groups in terms of age, sex. follow-up period and clinical parameters including BASDAI, BASFI, ESR level. However, there were significant differences in terms of HLA-B27 positive value, CRP level and standard uptake value ratio (SUVR) of sacroiliac joint in patients fulfilled ASAS criteria.
Conclusion: In diagnosing AS, F-18 NaF PET/CT showed 79.59% sensitivity, 84.21% specificity and 80.88% accuracy. This shows the diagnostic value of the F-18 NaF PET/CT, which can be a good alternative to the diagnosis of early ankylosing spondylitis, and can evaluate whole body lesions in a single session.
Disclosure of Interests: None declared
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AB1154 CLINICAL SIGNIFICANCE OF MONOSPECIFIC ANTI-DFS70 IN ANTINUCLEOLAR ANTIBODY (ANA)-POSITIVE PATIENTS

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Background: The most commonly used method for ANA detection is the indirect immunofluorescence test (IFI) on HEp-2 cells. Among ANA, antidense fine speckled (DFS) 70 antibodies produce a pattern (nuclear dense fine speckled) that can be confused with homogeneus or fine speckled pattern (typical of ANA-associated rheumatic disease, AARD). The presence of anti-DFS70 have been reported in a variety of clinical

conditions. Isolated anti-DFS70 could be used as a differential marker for AARD.

Objectives: To analyse the clinical significance of isolated anti-DFS70 antibodies.

Methods: All the serum samples obtained in our hospital between January 2017 to December 2018 that were positive for ANA testing and negative for anti-extractable nuclear antigen (ENA) antibodies panel, were tested for anti-DFS70 (HEp-2/DFS70 knock-out IFA, A.MENARINI diagnostics). Demographic and clinical data were collected from anti-DFS70 positive adult patients.

Results: From 145 samples tested 68 were found positive for monoespecific anti-DFS70: 82.4% were women and the median age was 55.4±14.4 years. The ANA titer was greater than 1/320 in all of cases and 26.5% of patients had two positive determinations DFS70 separated 15.4±9.2 months. The reasons for requesting ANA were diverse (arthralgias in 33.8% of the cases), and most of them were ordered from primary care. Clinical follow-up was performed in 66.1% of the patients for a mean of 2.9 years (between 2 months and 7 years). Only 3 patients (4.1%) had a defined AARD: 2 systemic lupus erythematosus and 1 antiphospholipid syndrome, diagnosed years before. There were 5 patients with rheumatoid arthritis (7.3%) and one had sarcoidosis. Nineteen patients (27.9%) had an organ-specific autoimmune disease: 14 autoimmune hypothyroidism, 2 autoimmune hepatitis, 2 primary biliary cholangitis and 1 immune thrombocytopenia. Six patients (8.8%) were followed up because of undifferentiated connective tissue disease (they did not meet criteria for AARD). Other clinical associations found were obesity (13.2%), depression (8.8%), sleep disorders (8.8%), fibromyalgia 5,8%, cancer, asthma and psoriasis (2.9% each one of them). Thirty-nine patients (57.3%) did not have any autoimmune disease (systemic or localized).

Conclusion: In our experience, patients with monospecific anti-DFS70 ANA rarely present AARD, even though 42.7% of subjects showed autoimmune features. Rheumatoid arthritis patients occasionally had an isolated anti-DFS70 ANA. Therefore isolated anti-DFS70 may be potentially considered as marker of benign autoimmunity.

REFERENCES

[1] Michael Mahler, Luis E. Andrade, Carlos A. Casiano, Kishore Malyavantham & Marvin J. Fritzler (2019): Anti-DFS70 antibodies: an update on our current understanding and their clinical usefulness, Expert Review of Clinical Immunology, DOI: 10.1080/1744666X.2019.1562903.

[2] Bonroy C, Schouwers S, Berth M, Stubbe M, Piette Y, Hoffman I, et al.: The importance of detecting anti-DFS70 in routine clinical practice: comparison of different care settings. Clin Chem Lab Med 2018; 56:1090-9.

[3] Shovman O, Gilburd B, Chayat C, Amital H, Langevitz P, Watad A, et al.: Prevalence of anti- DFS70 antibodies in patients with and without systemic autoimmune rheumatic diseases. Clin Exp Rheumatol 2017; 36:121-6.

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AB1155 CORRELATION BETWEEN NAILFOLD VIDEOCAPILLAROSCOPY PATTERNS, LEFT VENTRICLE DYSFUNCTION AND PULMONARY DISEASE IN SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis (SSc) is a multisystem connective disease characterized by a microvascular damage, which leads to systemic fibrosis, immune dysregulation and progressive involvement of internal organs [1].

According to the classification of the morphological aspects, into the scleroderma pattern proposed by Cutolo et al. are described the early, active and late patterns.

Objectives: The aim of our study is thus to report a correlation between specific nailfold videocapillaroscopy pattern and internal organ involvement.

Methods: All enrolled patients were diagnosed for SSc, according to the American College of Rheumatology criteria and underwent an echocardiographic examination and a nailfold videocapillaroscopy.

Myocardial function parameters considered were: global contractility (computed with the Simpson method), linear contractility (computed through the MAPSE) [2], diastolic dysfunction (through the analysis of the transmitral flow) [3]; whilst those of lung damage were: PAPs and the evaluation of the right ventricle contractility through the TAPSE [4].

Statistics were performed with SPSS 20 software, by using the Mann Whitney U Test and the Fisher Test.

Results: We enrolled 27 patients, of which 16 showing "active pattern" and 11 "early pattern", compared to a group of 21 healthy controls.

Of the 11 patients belonging to the "early" group, 1 resulted affected by diastolic dysfunction, whilst 3 had pulmonary hypertension, defined by PAPs $\geq$40 mmHg [4] (early vs controls; p=0.03). In the 16 patients of the "active" group. instead, 5 were found to have a diastolic dysfunction (active vs controls; p=0.01) and 6 pulmonary hypertension (active vs controls; p=0.003). In the group with "active" pattern we also observed a reduction in TAPSE compared to the control group (2,0 ± 0,2 vs 2,2 ± 0,2; p=0,025) and compared to the group with early pattern (2,0 ± 0,2 vs 2,2 ± 0,3; p=0,07).

No presence of modifications in the global contractility emerged; however, we observed a progressive reduction of the MAPSE (controls 1.76 ± 0,08; early 1.57 ± 0,04; active 1.49 ± 0,12), which resulted statistically significant among the different comparisons (controls vs early p=0.001; controls vs active p=0.0001; early vs active p=0.04).

Conclusion: The analyses showed a strict correlation between the severity of the microvascoular alterations, reported by nailfold videocapilloroscopy, and the severity of the cardiopulmonary damage, expressed by an increase in the percentage of pulmonary hypertension, diastolic dysfunction and a progressive reduction of MAPSE and TAPSE.

Abstract AB1155 Table 1. early vs controls

	EARLY	CONTROLS	P
PAPs	**32,3 ± 5,4**	**22,6 ± 6,7**	**0,0001**
TAPSE	**2,2 ± 0,3**	**2,2 ± 0,2**	**NS**
MAPSE	**1,57 ± 0,04**	**1,76 ± 0,08**	**0,0001**
EF	**65 ± 4**	**64 ± 2,7**	**NS**
E/A	**1,34 ± 0,2**	**1,38 ± 0,19**	**NS**
DECT	**148 ± 23**	**163 ± 27**	**NS**
Diastolic dysfunction	**1(11)**	**0(21)**	**0,3**
Pulmonary hypertension	**3(11)**	**0(21)**	**0,03**

Abstract AB1155 Table 2. active vs controls

	ACTIVE	CONTROLS	P
PAPs	**34 ± 7,8**	**22,6 ± 6,7**	**0,0001**
TAPSE	**2,0 ± 0,2**	**2,2 ± 0,2**	**0,025**
MAPSE	**1,49 ± 0,12**	**1,76 ± 0,08**	**0,0001**
EF	**65 ± 4**	**64 ± 2,7**	**NS**
E/A	**1,34 ± 0,4**	**1,38 ± 0,19**	**NS**
DECT	**157 ± 24**	**163 ± 27**	**NS**
Diastolic dysfunction	**5(16)**	**0(21)**	**0,01**
Pulmonary hypertension	**6(16)**	**0(21)**	**0,003**

REFERENCES

[1] LeRoy EC. Systemic sclerosis. A vascular perspective. Rheum Dis Clin North Am.

[2] Ibadete Bytci, Left atrial change in early stages of heart failure with preserved ejection fraction. Echocardiography

[3] Sherif F. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography. Journal of the American Society of Echocardiography

[4] Luke S. Howard, Echocardiographic assessment of pulmonary hypertension: standard operating procedure. European Respiratory Review

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AB1156 DEFINITION OF TWO NEW ULTRASOUND ENTHESOPHYTES SCORES: APPLICATION IN A CONSECUTIVE SERIES OF IBD PATIENTS

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Background: Recent studies have developped criteria for US definition of entheseal abnomalities [1] however no actual scores are available to

determine the extension and severity of enthesophyte growth in clinical practice.
Objectives: To **evaluate** the faseability of two new scores to quantifie enthesophytes occurence and its dimensional changes with time.
Methods: We have evaluated 816 enthesis two years apart in a consecutive series of 68 IBD patients for the presence and size of enthesopytes. Images were collected at baseline and after 24 months using an Esaote MyLabClass, 18-6 MHz linear multifrequence transducer both in B-mode and PD-mode. The following sites were evaluated bilaterally: lateral epicondyle of the humerus, distal quadricipital insertion at the patella, superior and inferior pole of the patella, Achilles tendon insertion, and plantar aponeurosis insertion. The presence of enthesophyte was scored dichotomously as present (=1) or absent (=0) for each site and summed up to generate the ARE score (ARES). Enthesophytes was also scored semiquantitatively in a 0-3 scale (0 = absent, 1 = minimal, 2 = discrete, 3 = massive) according to Aydin SZ et al. [2] for each site and summed up to generate RES score (RESS). All the stored images were then reviewed and scored by 4 rheumatologists (FM, GC, PM, NG) well trained in US examination of enthesis. ICC inter- and intra-observers was done for each site and for the ARES and RESS.
Results: ICC was exellent for presence or absence of enthsophytes both intra and inter examinator for all the sites. ICC of the ARE score was excellent (Cronbach alfa = 0.930, 95%CI 0.72-0.98). ICC was excellent also for the semiquantitative RESS at all the examined sites and only moderate at the plantar fascia level (Cronbach alfa = 0.571, 95%CI - 0.72-0.89). The total RESS have an exellent ICC (Cronbach alfa = 0.963, 95%CI 0.85-0.99).
Conclusion: The two scores are easily feasible and have high reliability and and exellent intra- and inter-obeserver reproducibility.

REFERENCES

1. Balint PV, et al. *Reliability of a consensus-based ultrasound definition and scoring for enthesitis in spondyloarthritis and psoriatic arthritis: an OMERACT US initiative.* Ann Rheum Dis. 2018 Dec;77(12):1730-1735.
2. Aydin SZ, et al. *A relationship between spinal new bone formation in ankylosing spondylitis and the sonographically determined Achilles tendon enthesophytes.* Rheumatol Int 2016 Mar;36(3):397-404.

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AB1157 VALIDATION OF VECTOR (VELCRO CRACKLES DETECTOR) FOR THE DIAGNOSIS OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH CONNECTIVE TISSUE DISEASES

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Background: Interstitial lung disease (ILD) represents one of the most frequent pulmonary manifestations in connective tissue diseases (CTD) and it is characterized by severe implications in morbility and overall prognosis. However, a routinely assessment of ILD is not so common in all CTDs. Velcro-type crackles are typical of lung fibrosis and have been proposed for the early diagnosis of the disease.
Recently, we validated the algorithm VECTOR (VElcro Crackles detecTOR), developed to detect the presence of velcro-crackles in pulmonary sounds recorded by an electronic stethoscope (ES) in RA-ILD patients as screening for the diagnosis of interstitial lung involvement, showing a diagnostic accuracy, a sensitivity and a specificity of 83.9%, 93.2% and 76.9%, respectively.
Objectives: The aim of the present study was to evaluate the diagnostic accuracy of VECTOR in a population of CTDs, compared with the reference standard of high-resolution computed tomography (HRCT), in a monocentric study.
Methods: CTDs patients who underwent HRCT in the last 12 months were enrolled. They were auscultated with an ES (Littmann 3200TM 3M, USA), bilaterally, at dorsal level, in at least 3 pulmonary fields (apical, medium and basal). All tracks recorded were analyzed by suitably developed software (VECTOR) capable of recognizing pathological crackles in lung sounds. Results were compared with HRCT findings detected in a blind manner by an expert radiologist.
Results: Ninty CTDs patients were enrolled, namely 27.8% systemic sclerosis (SSc), 31.1% primary Sjögren's syndrome (pSS), systemic lupus erythematosus 11.1%, 7.8% polymyositis, 6.6% dermatomyositis, and 15.5% undifferentiated CTD (UCTD). Male/female ratio was 1/3.1 and a mean age of 63.9±12.7 years; among them 45 (50%) showed ILD at HRCT.
The algorithm correctly classified 73/90 patients, with a sensitivity and specificity of 93.3% and 68.9%, respectively, and a diagnostic accuracy of 81.1% (figure 1).

Figure 1. Contingency table of diagnostic accuracy of VECTOR (Velcro-Sounds Detector)

	ILD -	ILD +	
Velcro -	31 34.4%	3 3.3%	91.2%
Velcro +	14 20.9%	42 46.7%	75%
	68.9% Specificity	93.3% Sensitivity	81.1% Diagnostic accuracy

Conclusion: These data confirm the diagnostic accuracy of VECTOR in detection of ILD in CTDs patients, as previously described also for RA-ILD. In some CTDs such as SSc, a careful evaluation of lung involvement is quite diffused, while for other CTDs, for example pSS or UCTD, ILD remains often underestimated, with a delay in diagnosis and treatment. Since lung complications represent one of the most serious and frequent cause of poor prognosis for all CTDs patients, the search for a simple, repeatable and radiation-free tool for the screening of these patients is mandatory. The routinely employment of an ES and VECTOR, combined to clinical findings (cough, dyspnea) and respiratory lung function tests, could increase our ability to early identify ILD in CTD patients.

REFERENCES

[1] Kelly C, Iqbal K, Iman-Gutierrez L, Evans P, Manchegowda K. Lung involvement in inflammatory rheumatic Diseases. Best Pract Res Clin Rheumatol 2016; 30:870-888.
[2] Pancaldi F, Sebastiani M, Cassone G, Luppi F, Cerri S, Della Casa G, Manfredi A. Analysis of pulmonary sounds for the diagnosis of interstitial lung diseases secondary to rheumatoid arthritis. Comput Biol Med. 2018; 96:91-7

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AB1158 CLINICAL AND VISUAL US PARAMETERS IN SYMPTOMATIC KNEE OSTEOARTHRITIS AND ASYMPTOMATIC PATIENTS

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Background Sonography is widely used because of its easy accessibility, relatively low cost. Sonography provides distinct information that bridges the gap between clinical and radiologic evaluation. There has been a growing interest in determining the sources of pain with ultrasound (US) findings in patients with knee osteoarthritis.
Objectives The aim of this study was to determine the relationships between clinical parameters and features of US of the knee.
Methods This was a cross-sectional study, recruiting 47 consecutive patients aged 47 (36- 54), 60,42% (n=29) were female. Those with recent trauma, rheumatic diseases were excluded from the study. Patients underwent assessment for knee pain (Visual Analog Scale (VAS)), US examination of the knee joints according to the 4-point scale (synovial proliferation, joint effusion, power Doppler signal (PD), patellofemoral joint cartilage (PFJ), medial femoral cartilage (MF), medial (MM) and lateral meniscus (LM), osteophytes, Baker cysts). US staging of knee OA was also performed.
Results Patients were divided into 2 groups: those with knee pain (n=28) and asymptomatic patients (n=19). Pathological US features were found in both groups (Table). In 5 out of 19asymptomatic patients, degenerative changes of different degree of the joint structures were identified (PFJ, MF, osteophytes, MM,

LM), in 4 patients – joint effusion. Prevalence of PFJ, MF, MM, LM changes, osteophytes and Baker cysts didn't differ between groupsG. roups differed in PD signal expression in the synovia (p=0,07). Functional association between VAS score and PD expression (R=1,0, p<0,05) was revealed$ moderate correlation between VAS score and joint effusion (R=0,47, p<0,05), PFJ (R=0,58, p<0,05), osteophytes (R=0,66, p<0,001) was observed.

Conclusion In the patients under study, degenerative and inflammatory findings were common in the symptomatic group, but were also identified in the asymptomatic patients. Clinical parameters were more strongly associated with active inflammation (as verified by US) rather than with degenerative changes.

Disclosure of Interests None declared

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AB1159 INTER-READER RELIABILITY AND COMPARISON OF FLUORESCENCE OPTICAL IMAGING ENHANCEMENT IN PATIENTS WITH EROSIVE HAND OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

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Background: Fluorescence Optical Imaging (FOI) is an imaging technique demonstrating indocyanine (ICG)-enhanced microcirculation in wrist and finger joints, as a sign of inflammation. A reliable scoring method is essential in the assessment of these images.

Objectives: To assess inter-reader reliability of three FOI scoring methods from Berlin, Stockholm, and Copenhagen, and to compare the amount of enhancement in joint groups of both hands in patients with erosive hand osteoarthritis (OA) and rheumatoid arthritis (RA).

Methods: Patients with erosive hand OA (n=13) and with RA (n=13) underwent FOI of both hands. Five readers blinded for clinical diagnoses scored all finger and wrist joints bilaterally on semi-quantitative 0-3 scales using three different FOI scoring methods. In the Berlin method, FOI enhancement was evaluated on three different images, defined as different phases based on the enhancement in the fingertips. A composite image (Prima Vista Mode, PVM) of the 240 first images was also assessed. The Copenhagen method assumed that inflamed tissues will demonstrate a more rapid FOI enhancement than the surrounding tissues, defining inflammation as sharply marginated enhancement over a joint area with clear delineation from surrounding tissues lasting $\geq$3 sec. The Stockholm method was evaluated in PVM format of 240 and 120 images in 'temperature' palette setting, with additional scrolling through the image sequence to detect ambiguous signals. To evaluate inter-reader reliability, we calculated the intraclass correlation coefficients (ICC) of the sum scores on patient level and weighted kappa values and prevalence and bias adjusted kappa values for ordinal scales (Pabak-OS) on joint level. Finally, we compared the averaged sum scores in the different joint groups in patients with erosive hand OA vs. RA using the Mann-Whitney test.

Results: The ICC of the sum scores was very good for the Stockholm method (0.83), and for Berlin PVM (0.93) and Phase 2 (0.83), while the Copenhagen method (0.65) and Berlin phase 3(0.73) showed good reliability. Berlin phase 1 showed fair reliability (0.30). On joint level we found moderate to good agreement with pabak-OS for all methods (table). Patients with erosive hand OA had significantly more enhancement in DIP joints across all methods, while PIP enhancement was more common in erosive hand OA for the Berlin PVM and Stockholm methods only. Enhancement in the 1st CMC was not detected in any of the methods, and no consistent differences were observed for the wrist (data not shown).

Conclusion: We found moderate to very good inter-reader reliability on patient level for all methods except for Berlin phase 1 and moderate to good agreement on joint level for all methods. FOI showed different enhancement patterns between erosive hand OA and RA, with more enhancement in the DIP joints in the OA patients across all methods, supporting its validity.

Disclosure of Interests: Øystein Maugesten: None declared, Sarah Ohrndorf: None declared, Daniel Glinatsi: None declared, Mads Ammitzbøll-Danielsen: None declared, Yogan Kisten: None declared, Mikkel Østergaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Lene Terslev Speakers bureau: Speakers fee from : Roche, Novartis, Pfizer, MSD, BMS, Celgene, Till Uhlig: None declared, Tore K. Kvien Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB., Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB, Ida Kristin Haugen Grant/research support from: ADVANCE research grant from Pfizer, Consultant for: Advisory board Abbvie

Weighted kappa and prevalence and bias adjusted kappa for ordinal scales (Pabak-OS) for different joint groups

	All joints		DIP 2 - 4		PIP 2 - 4		MCP 1 - 5		Wrist	
	W. kappa	Pabak OS	W. kappa	Pabak OS	W. kappa	Pabak OS	W. kappa	Pabak OS	W. kappa	Pabak OS
Berlin PVM	0.51	0.78	0.47	0.74	0.58	0.72	0.53	0.84	0.45	0.79
Berlin P1	0.44	0.69	0.26	0.69	0.30	0.56	0.60	0.83	0.61	0.81
Berlin P2	0.44	0.50	0.43	0.56	0.51	0.58	0.37	0.38	0.45	0.51
Berlin P3	0.37	0.62	0.36	0.77	0.40	0.57	0.30	0.56	0.40	0.62
Stockholm	0.40	0.63	0.41	0.61	0.39	0.47	0.45	0.74	0.34	0.71
Copenhagen	0.39	0.56	0.39	0.65	0.30	0.35	0.52	0.70	0.36	0.48

Table 1

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AB1160 INVOLVEMENT OF ANKLE JOINTS AND TENDONS IN SYSTEMIC LUPUS ERYTHEMATOSUS: AN ULTRASOUND STUDY

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with heterogeneous clinical manifestations. The musculoskeletal involvement is among commonest and earliest symptoms occurring in 95% of patients. The clinical examination of the ankle joints may underestimate the type and distribution of pathological changes. Musculoskeletal ultrasound (US) is a useful diagnostic tool for evaluation of joints and tendons in the majority of inflammatory rheumatic diseases.

Objectives: The aim of this study is to assess the ankle joints and tendons involvement in SLE patients using US and to correlate the findings with the physical examination, laboratory tests and disease activity scores.

Methods: Forty consecutive SLE patients were enrolled in the study and underwent clinical evaluation, laboratory tests and bilateral high-resolution US on the same day. Grey-scale and power Doppler (PD) US of the talocrural (TC), subtalar joints (ST), ankle tendons, second and third MCP joints, second and third PIP joints, wrists and second and third MTP joints were performed.

Results: A total of 720 joints and 800 tendons were examined. US detected inflammatory joint abnormalities were present in 35/40 (87,5%) patients while tenosynovitis was present in 7/40 (17,5%) patients. The most frequently affected were MTP joints (67,5%) followed by MCP(42,5%) and TC joints (40%), wrists (27,5%) and PIP joints (7,5%). The most prevalent pathological US finding was joint effusion.Synovial hypertrophy and positive PD signal were less frequently observed. Effusion in TC joints was present in 40%, synovial hypertrophy in 20% and positive PD in 2,5% of the patients. Only two patients had bony erosions detected.Six out of forty patients (15%) reported pain or swelling in ankle joints and two(33%) of them didn't have any US abnormalities.As many as 47% of patients without inflammatory joint symptoms had pathological US findings in ankle joints. The most commonly affected tendon was tibialis anterior (7,5% of patients), followed by extensor halluces longus tendon (5% of patients).

Conclusion: Results of this study show a high prevalence of US verified inflammatory joint changes in SLE patients, while tendon changes were extremely rare. Foot joints were most commonly affected, followed by wrists and ankle joints. It is important to stress that a great number of asymptomatic patients had pathological US findings in ankle joints. From this and previous studies it is clear that US should be used more in the periodical assessment of the musculoskeletal system in patients with SLE.

REFERENCES

[1] Iagnocco A, Ceccarelli F, Rizzo C, Truglia S, Massaro L, Spinelli FR, et al. Ultrasound evaluation of hand, wrist and foot joint synovitis in systemic lupus erythematosus. Rheumatology. 2014;53(3):465–72.

[2] DelleSedie A, Riente L, Scire CA, Iagnocco A, Filippucci E, Meenagh G, et al. Ultrasound imaging for the rheumatologist XXIV. Sonographic evaluation of wrist and hand joint and tendon involvement in systemic lupus erythematosus. ClinExpRheumatol. 2009;27(6):897–901.

[3] Iagnocco A, Epis O, DelleSedie A, Meenagh G, Filippucci E, Riente L, et al. Ultrasound imaging for the rheumatologist. XVII. Role of colour Doppler and power Doppler. ClinExpRheumatol. 2008 Oct;26(5):759–62.

[4] Porta F, Radunovic G, Vlad V, Micu MC, Nestorova R, Petranova T, et al. The role of Doppler ultrasound in rheumatic diseases. Rheumatology. 2012;51(6):976–82.

Disclosure of Interests: Ljiljana Smiljanic Tomicevic Speakers bureau: Novartis, Sandoz, Abbvie, Pfizer, Alvogen, Darija Cubelic Speakers bureau: Merck Sharp & Dohme, Abbot, Krka, Astrazeneca, Pliva, Boehringer Ingelheim, Berlin-Chemie Menarini, Goran Sukara Speakers bureau: Novartis, Sandoz, Abbvie, Pfizer, Alvogen, Roche, Branimir Anic Speakers bureau: Novartis, Sandoz, Abbvie, Pfizer, Alvogen, Roche, MSD, Octapharma, Miroslav Mayer Speakers bureau: Novartis, Sandoz, Abbvie, Pfizer, Alvogen, Roche, MSD, Octapharma
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AB1161 ULTRASOUND IMAGING IN EVALUATION OF ENTHESITIS: STATUS AND PERSPECTIVES

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Background: The high-frequency ultrasound is a reliable method to identify enthesitis, including subclinical and early diagnosis, in patients with psoriasis (Pso) and psoriatic arthritis (PsA)[1].
Objectives: To establish an epidemiological profile of patients with Pso and/or subclinical and clinical PsA; to establish the ultrasound (US) profile with gray scale and Doppler in entheses in these groups.
Methods: A case control study conducted in the period from December 2015 to December 2016, at Hospital das Clínicas/UFG. It was performed in 144 patients with Pso and/or PsA and 24 healthy controls. Patients with and without arthritis/enthesitis were submitted to the US. The US findings were according to the MASEI (the Madrid sonography enthesitis index). The entheses were studied bilaterally: plantar fascia, distal calcaneal tendon, distal and proximal ligament of the patella, distal quadriceps and tendons of the brachial triceps. In addition to the US in the 2nd and 3rd distal interfalanges. The interobserver reliability was calculated in 24 patients - kappa index (k).
Results: In the case group the mean age was 50.13 years, BMI of 28.14; duration of illness of 16 years; **Mean±SD PASI: 5.34±6,03; PEST:2,21±1,66 and DLQI:4.39±5,16**. Of the total 90.3% of the patients presented Pso; 39.8% APs already diagnosed and 77.8% with signs of US enthesopathy. Of the total of the 1728 entheses evaluated in the case group and the control group of 288 structures evaluated. The most common sign in both groups was the thickening, being more seen in the calcaneus tendon (table). The MASEI score was significantly higher in patients with Pso and PsA than in the control group and had correlation with **PEST: r= 0,397, p<0,001 and IMC: r=0,208, p= 0,012**. Of the 288 nail insertion of the 2nd and 3rd distal interphalangeal, presented some type of enthesopathy to the US, like thickening **(34,7%, p=0,036 to 0,003)** or loss of the trilaminar pattern **(31,6%, p= 0,027 to 0,004)** and the most common change was positive PD **(61,1%, p<0,001)**. Of the total nails evaluated only 17.5% had clinic injury. And the κ values weighted for the US findings showed excellent agreement **(0.930 and 1)** for PD and erosions, respectively. The epidemiological profile of patients with Pso and/or subclinical and clinical PsA were overweight. As for the US profile, the majority presented signs of enthesopathy, where the most frequent occurrence was the calcaneal tendon, and the Doppler was the most affected topography of the triceps tendon.
Conclusion: The ultrasonography shows an important perspective in assessing entheses these patients.

REFERENCES

[1] Kaeley, G. S., Eder, L., Aydin, S. Z., Gutierrez, M., & Bakewell, C. *Enthesitis: A hallmark of psoriatic arthritis*. Seminars in Arthritis and Rheumatism., 2018; 48(1), 35–43.

Table: MASEI score:

Ultrasound Findings	Case (n=144)	Control (n=24)	p
Number of entheses changed	**1728**	**288**	
Structure (n (%))	472 (27,3)	16 (5,6)	< 0,001
Thickening (n (%))	503 (29,1)	37 (12,8)	< 0,001
Bursitis (n (%))*	95 (16,5)	05 (1,73)	0,004
Erosion n (%))	48 (2,8)	02 (0,7)	0,035
Calcification (n (%))	373 (21,6)	34 (11,8)	< 0,001
PD(n (%))	124 (7,2)	08 (2,8)	0,005

Test: Chi-Square; (PD: power Doppler).
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.3836

AB1162 ARE SONOGRAPHIC FINDINGS CORRELATED WITH DISEASE ACTIVITY SCORE IN RHEUMATOID ARTHRITIS REMITTED PATIENTS?

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Background: Obtaining remission is the ultimate and now attainable goal of treatment in rheumatoid arthritis (RA). However, the definition of remission kept changing over the last decade. Several composite scores and indices are now validated to assess remitting RA such as the Disease Activity Index 28 joints (DAS28), and more recently, the Simplified Disease Index (SDAI) and the Clinical Disease Index (CDAI). Despite more stringent definition criteria, progressive radiographic damages still occur in RA patients who reached remission. Defining other criteria for remission including ultrasound (US) might help preventing such evolution.
Objectives: The aim of this study was to compare US findings and composite score results in RA patients that achieved a status of remission according to DAS28.
Methods: Thirty Tunisian patients followed up for RA with DAS28 ≤2,6 for at least three months were enrolled. Among them, we identified patients in remission according to the SDAI (≤3,3) and the CDAI (≤2,8). US (Esaote MyLab 60 machine and a 13-18 MHz linear array transducer) was performed by an experienced rheumatologist blinded to clinical and laboratory data. For each patient, 22 joints were scanned (wrists, metacarpo-phalangeal, and proximal interphalangeal joints) using a semi-quantitative score.
Results: Over the 26 patients in CDAI remission, ultrasonographic synovitis in B-mode were noted in 81% of patients. The average ultrasound score per patient was 4.58. In PD mode, US abnormalities were noted in 58% of patients. The average PD score per patient was 2.6.
Neither correlation between CDAI and B-mode US score (r = 0.104; p = 0.319) nor between CDAI and DP US score (r = 0.251; p = 0.217) was noted.

	US findings	Grade 0	Grade 1	Grade 2	Grade 3
Patients in CDAI remission	Synovial hypertrophy	491	48	28	5
	PD positive	535	14	15	8
Patients in SDAI remission	Synovial hypertrophy	365	34	16	3
	PD positive	396	6	9	7

B-mode examination of the 19 patients in SDAI remission detected synovitis in 79% of patients. The average ultrasound score per patient was 3.95. PD signal was positive in 53% of patients. The average PD-US score per patient was 2.3. Likewise, no correlation with SDAI was found neither with B-mode US score (r = 0.99; p = 0.687) nor with DP US score (r=-0,036; p=0,884).
Conclusion: Thanks to the therapeutic armory we dispose of and the treat-to-target approach, remission is now a reachable goal. However, defining this goal is no easy task. Including US parameters in definition criteria of remission might help to detect subclinical evolving RA and adjust treatment in such cases.

REFERENCES

[1] Olmez MO, Gunal EK, Ureyen SB, Keskin H, Ozturk AB, Yeter G, Cobanoglu E, Aydin SZ. Comparison of composite indices with global synovitis score on ultrasound for detecting remission. Clin Rheumatol. 2018 Apr;37 (4):1111-1114.

[2] E Naredo,L Valor,I De la Torre,J Martínez Barrio, M Hinojosa F Aramburu et al,Ultrasound Joint Inflammation in Rheumatoid Arthritis in Clinical Remission: How Many and Which Joints Should Be Assessed?.Rheumatoid Arthritis Vol65, Issue4 Apr 2013: 512-517

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AB1163 CAN A MUSCULOSKELETAL ULTRASOUND REPORT CHANGE A RHEUMATOLOGIST'S OPINION?

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Background: The era of musculoskeletal ultrasound (MSUS) is becoming enormous, but the extent to which MSUS has influenced management plans for patients with different musculoskeletal symptomsremains questionable.
Objectives: To assess the changes in the provisional diagnosis and treatment decisions made by rheumatologistsafter receiving MSUS reportsfor their patients.
Methods: This study has been carried out at Rheumatology & Rehabilitation outpatient clinicsin Zagazig University Hospitals in Egypt. This is anobservational study on 101 patients with musculoskeletal complaints who have been referredby rheumatologists for a MSUS scan atZagazig University MSUS Unit in the same department.The patients' mean age was 41.5 ± 15.67, including 70 females (69.3%) and 31 males (30.7%). Patients included 29 patients with hand/wrist complaints (28.7%), 2 patients with elbow pain (2%), 36 patients with shoulder pain (35.6%), 7 patients with ankle/foot pain (6.9%), 10 patients with knee pain (9.9%), and 17 patients with polyarticular pain (16.8%). The rheumatologists were asked to set a provisional diagnosis and treatment planbefore the MSUS scan and toreconsider their own plan for any adjustments afterwards.
Results: Regarding all 101 patients, the diagnosis & treatment decisions were changed in 37%and 65% respectively after the MSUS scan as shown in figure (1). Fifty percent of the changes in treatment were classified as minor in the form of adding/changing the type of NSAIDs, adding/changing the dose of steroids, changing the dose of DMARDS and adding/modifying physiotherapy while the other 50%were major in the form of initiating/adding DMARDs, interventional treatmentor referral to surgery.Ten patients out of 29 with hand/wristcomplaints encountered change in diagnosis (34.5%), 1 patient out of 2 with elbow pain (50%) and 11 patients out of 36 with shoulder pain (30.6%). In patients with knee pain and ankle/foot pain, changes occurred with 4 patients for each representing 40% and 42.9% respectively. Regarding patients with polyarticular complaints 8 patients representing 47.1% were categorized to different disease entities. Treatment decisions were much more frequently changedas more pathological details were clarified by MSUS. Treatment decision changes occurred in 83.3% of patients with shoulder pain 70% of which were minor mainly due to better evaluation of rotator cuff syndromes grading tears and detecting bursitis. While for knee pain 50% of treatment decisions were changed of which 60% were major as in knee osteoarthritis detection of significant synovitis&Baker's cysts lead to interventionaltreatment.Regarding patients with hand/wrist &polyarticularcomplaints, 44.8% and 68.8% of treatment decisions were changed respectively of which 75% and 90.8% were major owing mainly to changes in diagnosis &detectingsubclinical activity. Finally regarding ankle/foot pain, treatment changes happened in 71.4%of which 80% were minor.

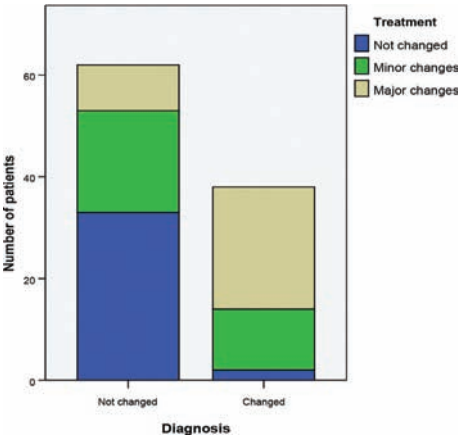


Figure 1

Conclusion: MSUS scanshave a great impact on rheumatologists' decisions in clinical practice. Remarkable changes in diagnosis with subsequent significant major changes in treatment plans were due to the ability of MSUS to differentiate between different disease entities.Changes in treatment decisions were very frequent even without changing the diagnosis owing to a more detailed look into the diseased joint and surrounding structures.
Disclosure of Interests: None declared
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AB1164 EDUCATION ON PEDIATRIC MUSCULOSKELETAL ULTRASOUND: A SYSTEMATIC LITERATURE AND EVENTS REVIEW

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Background: Recently some Pediatric musculoskeletal ultrasound (PedMSUS) courses have been held on national and international ground. Nonetheless, content, conduct and format of PedMSUS courses have never been investigated and shared.
Objectives: To perform a systematic literature and events review on PedMSUS educational initiatives.
Methods: Educational material/events on PedMSUS were extensively searched on websites/networks (PubMed, Cochrane, Embase, ERIC, Medline, CINAHL complete, Google, Yahoo, Ask, Baidu, Bing, Lycos, Duckduckgo). The keywords were: "musculoskeletal", "ultrasound", "sonography", "course", "education", "training", "children", "paediatrics", "pediatrics". Only courses/events, articles and books in English were considered. Descriptive analysis was performed on the documentation retrieved.
Results: No articles neither books on educational recommendations for PedMSUS courses were found. A total of 13 PedMSUS courses were identified. Two online courses and three residential ones were not consistent with the purpose and were excluded. Eight courses were finally included for the analysis (Figure 1). Seven were endorsed by EULAR and followed the recommendations for the content and conduct of EULAR MSUS courses. No requirements/skills should be fulfilled for registration; only one level of competency was proposed. The courses were residential of 2-3 days and included theorical and practical lessons. Lectures were on MSUS examination techniques, physiological musculoskeletal (MSK) anatomy and basic pathology in pediatric rheumatology. Hands-on scanning of healty models/patients with pediatric rheumatic diseases was generally organized in groups supervised by tutors, and included optimization of the machine settings, identification of pediatric MSK sonoanatomy, correct acquisition of images, and identification of basic pathological findings in children. A competency assessment was performed at the end of only three courses.

Abstract AB1164 Table 1. Main features of the 8 PedMSUS courses analysed.

n	PedMSUS course	Duration, days	n max Attendees	n Faculties	n Tutors	Theory, hours (%)	Practice, hours (%)	Fee, €
1	Paediatric musculoskeletal ultrasound course, Madrid – Spain, 2012	3	50	14	14	9 (56)	7 (44)	NS
2	4th musculoskeletal sonography course for rheumatologists - basic level pediatric course, Belgrade – Serbia, 2013	3	40	18	13	9 (56)	7 (44)	800*, 600#
3	5th musculoskeletal sonography course - basic level paediatric rheumatology, Belgrade – Serbia, 2015	3	40	12	9	9 (56)	7 (44)	800*, 600#
4	Musculoskeletal ultrasound course basic pediatric, Bucharest – Romania, 2016	3	36	10	13	9 (56)	7 (44)	850*
5	EULAR ultrasound course - PReS paediatric musculoskeletal course, Madrid – Spain, 2017	3	50	10	14	9 (56)	7 (44)	1600*
6	Musculoskeletal ultrasound in pediatric patients, Aarhus – Denmark, 2018	2	20	3	4	8 (57)	6 (43)	SS
7	Paediatric musculoskeletal ultrasound course, Antalya – Turkey, 2018	3	60	11	11	7 (50)	7 (50)	950*
8	Paediatric musculoskeletal basic ultrasound course, Lisbon – Portugal, 2018	3	50	11	17	9 (56)	7 (44)	1100*, 800#@

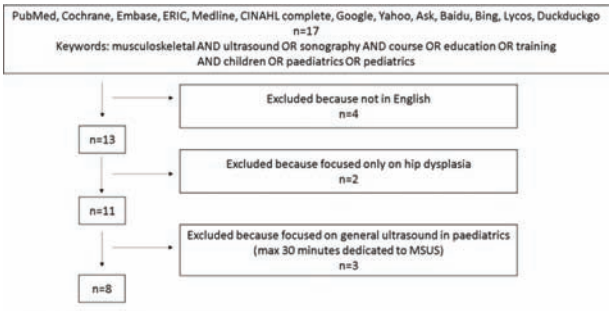


Figure 1

Legend: NS, not specified; EULAR, European League Against Rheumatism; PReS, Paediatric Rheumatology European Society. *,accommodation, meals and coffee breaks included; #, accommodation excluded; SS, supported by Sponsors; @, dinners excluded.

Conclusion: Almost all PedMSUS courses held were under EULAR endorsement. Slightly variable features were found among courses, apart being all at only one level of competency. An international initiative is deserved for identifying shared recommendations on the best suited content, conduct and format of future PedMSUS courses.

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AB1165 FLUORESCENCE OPTICAL IMAGING XIRALITE® IS HELPFUL IN THE DECISION FOR RITUXIMAB RE-THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rituximab (RTX) is an effective and well-tolerated therapeutic option in rheumatoid arthritis (RA) patients with insufficient response to TNFα inhibitors. However, the exact time point of RTX re-therapy often varies and objective parameters (e.g. imaging, such as MRI and/or musculoskeletal ultrasound [US]) are not yet included in the RA treatment strategy [1].

Objectives: The aim of this study was to evaluate the ability of the fluorescence optical imaging Xiralite® (FOI) to predict RTX re-therapy in RA patients - in comparison to clinical, laboratory and US.

Methods: In this study, n=31 patients with established RA were included and prospectively followed over one year by DAS28, patient's global VAS (0-100 mm), CRP/ESR, US7 score (for synovitis and tenosynovitis in greyscale and power Doppler of the clinically dominant hand/foot; [2]), and by FOI (phases 1-3 and PrimaVistaMode [PVM]) at baseline (before RTX), and after 3,6, and 12 months. The need for RTX re-therapy was defined according to DAS28 response criteria by EULAR [3].

Results: Of the included 31 patients (female 77.4%, mean age 60.1 ±11.4, mean disease duration 14.9±7.1 years), n=14 (45.2%) received RTX re-therapy within 12 months: n=3 after 6months (mths), n=4 after 7mths, n=5 after 9mths, and n=2 after 10mths. In the group with RTX re-therapy, FOI in PVM mode was the only parameter that presented significant increase (beta 0.40, CI 0.08-0.71; p=0.013) – compared to the group without re-therapy. In the prediction model via receiver operating characteristic (ROC) analysis, FOI in PVM reached the highest values of all imaging parameters (phases 1-3, US) at baseline for the prediction of re-therapy over one year with an area under the curve (AUC) of 0.64 (OR 0.9, CI 0.79-1.03), however, without significance (p=0.117). Patient's VAS and CRP had similar predictive power with AUC of 0.66 each (each p=ns).

Conclusion: The FOI Xiralite® in PVM is able to discriminate between groups with and without need for RTX re-therapy better than other included imaging parameters. It is able to predict the need for RTX re-therapy with comparable predictive power to patient's VAS and CRP. At the same time, FOI is a more objective tool, while patient's VAS and CRP can also depend on other influence (i.e. psychological, infectious) factors.

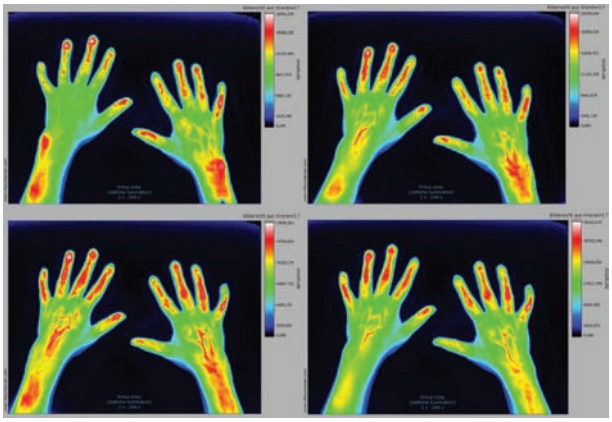


Figure:

Left image above shows FOI in PVM of both hands at baseline (before RTX). Right image above shows FOI in PVM of the same patient at 3months follow-up. Left image below shows FOI in PVM of the same patient at 6months follow-up. Right image below shows FOI in PVM of the same patient at 12months follow-up. This patient received re-therapy with RTX after 9 months

Legend: FOI: fluorescence optical imaging; PVM: PrimaVista Mode; RTX: rituximab

REFERENCES

[1] Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun;76 (6):960-977.

[2] Backhaus M, Ohrndorf S, Kellner H, et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. Arthritis Rheum. 2009;61(9):1194-201.

[3] https://www.das-score.nl/das28/en/difference-between-the-das-and-das28/importance-of-das28-and-tight-control/eular-response-criteria.html

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AB1166 SUBCLINICAL ENTHESEAL INVOLVEMENT IN LOWER LIMBS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: AN ULTRASOUND STUDY

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Background: Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia, which results from defects in insulin secretion, insulin action, or both (1).
DM impacts the connective tissue and causes various changes in periarticular and articular structures.An increase in enthesopathic complications in diabetic patients such as patellar tendinitis bursitis, achilles tendinopathy and plantar fasciitis, was observed In many studies.
Objectives: This study aims to detect subclinical lower limb enthesitis in type 2 DM by musculoskeletal ultrasonography & its relation to poor glycemic control & disease duration
Methods: This study was carried out on 80 persons. Diabatic group forty patients diagnosed as diabetes according to ADA diagnostic criteria. Control group Forty apparent healthy volunteers both groups was matched at age and sex.Sonographic evaluations and scoring were performed according to Glasgow Ultrasound Enthesitis Scoring System(GUESS) on the enthses of both lower limbs.
Results: At the diabetic group the Musculoskeletal Ultrasound findings was as following. The Quariceps tendon enthesitis in 30 patients (75%), proximal patellar enthesitis was in 28 patients (70%), Distal patellar enthesitis in 22 patients (55%), Achilles enthesitis in 27 patients (67.5) & planter aponeurosis enthesitis in 25 patients (55%).There is a statistically significant difference between age and Ultrasound findings p. value <0.05.There is a statistically significant correlation between disease duration and (proximal patellar ligament,Achilles tendon, quadriceps tendon and plantar fascia) thickness p. value<0.05.
Conclusion: Entheseal abnormalities can be documented by ultrasonography in clinically asymptomatic patients with Diabetes. These findings could be related to a subclinical entheseal inflammation.

REFERENCES

[1] Okur SC, YaseminPekinDogan, Murat Mert, OzgeAksu, OzerBurnaz, Nil SayinerCaglar(2017): Ultrasonographic Evaluation of Lower Extremity Entheseal Sites in Diabetic Patients Using Glasgow Ultrasound Enthesitis Scoring System Score, Journal of Medical Ultrasound (2017), http://dx.doi.org/10.1016/j.jmu..03.011
[2] SMITH, L., BURNET, S. & MCNEIL, J. (2003): Musculoskeletal manifestations of diabetes mellitus. British journal of sports medicine, 37, 30-35.

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AB1167 RELIABILITY AND VALIDITY OF ULTRASOUND PATHOLOGIES IN KNEE OSTEOARTHRITIS FOR SEMI-QUANTITATIVE AND QUANTITATIVE METHODS WITH MRI AS A REFERENCE

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Background: Ultrasound can visualize both structural and inflammatory changes of osteoarthritis (OA) with greater accessibility. Therefore, the Outcome Measures in Rheumatology (OMERACT) Ultrasound Task Force recently proposed a semi-quantitative knee ultrasound scoring system[1] which requires further validation.
Objectives: To investigate inter-rater reliability (IRR) of ultrasound pathologies between three raters with varying experiences and examine construct validity of these features against magnetic resonance imaging (MRI) using OMERACT semi-quantitative ultrasound image atlas and quantitative ultrasound measures.
Methods: According to standardized OMERACT scanning protocol, 20 participants with symptomatic and radiographic knee OA were scanned dynamically with a multi-frequency linear transducer (6-18MHz) of Aplio Platinum 500 machine, Toshiba, Japan.
Following an initial calibration of ultrasound scores using the image atlas, three raters with varying experience (a physician operator certified with RhMSUS, a musculoskeletal ultrasonographer and a medical student) independently obtained semi-quantitative scores (0-3) for synovitis and power Doppler activity in suprapatellar recess, medial osteophytes and medial meniscal extrusion, as well as quantitative measurements (mm) of synovitis, effusion, synovial hypertrophy, medial osteophyte and meniscal extrusion (maximal measures).
Semi-quantitative MRI Osteoarthritis Knee Score (MOAKS) scores of effusion-synovitis, osteophyte and meniscal extrusion were independently calculated by an experienced researcher. 3-T Sagittal proton-density (PD) weighted fat-suppressed turbo spin-echo (TSE) non-contrast MRI sequences were used for quantitative effusion-synovitis, and coronal plane for osteophyte and meniscal extrusion.
Weighted kappa coefficient (Kw) or intra-class correlation coefficient (ICC) were calculated for IRR, Spearman's rank (rs) and Pearson (rp) correlation coefficients for construct validity and Bland-Altman plots for extent of agreement between ultrasound and MRI.

Table 1. Inter-rater reliability of three operators of ultrasound pathologies in OA

Weighted Kappa (95% CI)	Meniscal Extrusion grade	Osteophyte grade	Power Doppler grade	Synovitis grade	Intra-class Correlation Coefficient (95% CI)	Effusion (mm)	Meniscal extrusion (mm)	Osteophyte (mm)	SH (mm)	Synovitis-effusion (mm)
PO vs MU	0.55 (0.25 to 0.84)	0.88 (0.72 to 1.00)	0.52 (0.17 to 0.87)	0.55 (0.36 to 0.75)		0.85 (0.15 to 0.95)	0.90 (0.39 to 0.97)	0.96 (0.84 to 0.98)	0.84 (0.59 to 0.93)	0.86 (0.18 to 0.96)
PO vs MS	0.27 (0.06 to 0.49)	0.73 (0.50 to 0.96)	0.14 (-0.36 to 0.63)	0.42 (0.21 to 0.64)		0.85 (0.16 to 0.96)	0.93 (0.83 to 0.97)	0.90 (0.55 to 0.97)	0.72 (0.25 to 0.89)	0.88 (0.31 to 0.97)
MU vs MS	0.28 (-0.01 to 0.56)	0.75 (0.56 to 0.94)	-0.11 (-0.21 to -0.01)	0.66 (0.43 to 0.90)		0.89 (0.73 to 0.96)	0.90 (0.75 to 0.96)	0.95 (0.88 to 0.98)	0.68 (0.22 to 0.87)	0.86 (0.66 to 0.95)

MU=Musculoskeletal Ultrasonographer; MS=Medical Student; PO=Physician operator; SH=Synovial Hypertrophy; mm=Millimeter

Value of K	Strength of agreement
< 0.20	Poor
0.21 - 0.40	Fair
0.41 - 0.60	Moderate
0.61 - 0.80	Good
0.81 - 1.00	Excellent

Figure 1

Table 2. Correlation of ultrasound pathologies with MRI for semi-quantitative and quantitative methods

Ultrasound vs MRI (correlation)	Synovitis grade	Meniscal extrusion Grade	Osteophyte Grade	Synovitis (mm)	Meniscal extrusion (mm)	Osteophyte (mm)
Spearman (rs)	**0.48 P=0.03**	0.27 P=0.26	0.36 P=0.12			
Pearson (rp)				**0.51 P=0.02**	**0.67 P=.001**	**0.54 P=.02**

Significant test is denoted in bold.

Figure 1

Figure 1 Bland–Altman plots to illustrate the agreement between ultrasound and MRI quantitative measures (a) osteophyte, (b) Synovitis-effusion, (c) Meniscal extrusion

The solid line represents the mean difference and the dashed lines represent the 95% limits of agreement.

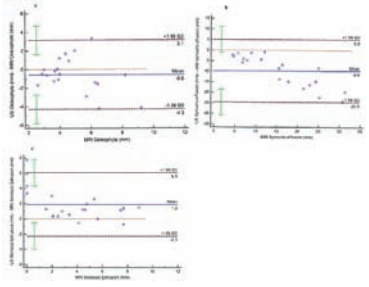


Figure 1

Results: Demographics were 60.2±8.3 years of age, 65% female, BMI of 28.6±4.5 of kg/m2; 60% with Kellgren and Lawrence (KL) grade 2 and 40% with a KL grade 3. Semi-quantitative OMERACT ultrasound scores (**Table.1**) revealed good to excellent IRR (Kw=0.73 -0.88) for osteophyte, and moderate to good IRR (Kw=0.42-0.66) for synovitis. Conversely, quantitative measures of ultrasound pathologies had excellent IRR (ICC= 0.84-0.95) except for synovial hypertrophy (ICC=0.67-0.72).
A significant association was found between semi-quantitative ultrasound synovitis and MRI effusion-synovitis (rs= 0.48, p=0.03). All three quantitative ultrasound measurements were significantly associated with quantitative scores of MRI (**Table. 2**).
In Bland–Altman plots for quantitative measurements, there were systemic offsets of 0.6 mm, 1.9 mm and 9.8 mm for osteophyte and meniscal extrusion and synovitis respectively (**Fig. 1**).
Conclusion: These is moderate to good IRR between operators with varying experience using the OMERACT knee scoring image atlas for osteophyte and synovitis. While quantitative ultrasound measurements showed excellent IRR and significant association with MRI quantitative outcomes, the absolute feature-specific agreement is called into question.

REFERENCES

[1] Bruyn, G.A.W., et al., An OMERACT reliability exercise of inflammatory and structural abnormalities in patients with knee osteoarthritis using ultrasound assessment. Annals of the Rheumatic Diseases, 2016. 75(5): p. 842-846.

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AB1168 SIGLEC1/CD169 IS A SENSITIVE MARKER FOR MONOGENIC INTERFERONOPATHIES

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Background: Monogenic Interferonopathies are a rare group of inflammatory diseases that are difficult to diagnose in the onset phase given the lack of well-defined disease-markers.[1]A correlation with interferon-stimulated genes (ISG) has been reported for *SIGLEC1* (syn. CD169), in systemic lupus erythematodes (SLE).[2] Furthermore, expression of *SIGLEC1* on monocytes is the second highest ISG in SLE.[3]
Objectives: To study the relevance of *SIGLEC1* as a putative diagnostic marker for early detection of interferonopathies.
Methods: Clinical data, classical inflammatory markers, blood count values and genetic information were obtained from the medical files of eight patients with genetically confirmed monogenic interferonopathies. *SIGLEC1* expression was measured by flow cytometry with a highly standardized quantitative assay with a reference range in healthy controls less than 2500 *SIGLEC1* molecules/monocyte. Additionally, transcriptional level of *SIGLEC1, IFI44L, IFI27, ISG15* and *RSAD2* as type I Interferon stimulated genes were assessed by real-time PCR.
Results: All eight patients with interferonopathies carried mutations in the genes *TREX*-1 (n=3), *IFIH*-1 (n=2), *SAMDH1* (n=2) and *RNASE2HB* (n=1). Mean age of patients was 12 years (range 6 months to 49 years). Six of eight patients showed neurological symptoms consistent with Aicardi-Goutieres-Syndrome presenting developmental delay and microcephaly. Five patients showed abnormalities on cranial MRI including periventricular calcifications and corpus callosum thinning. Two patients were diagnosed with Singleton-Merten-Syndrome presenting abnormal ossification of extremities and dental anomalies. One patient with homozygous *TREX1* mutation presented with postnatal glaucoma, microcephaly, sensorimotor polyneuropathia and recurrent fever with persistent chilblain lesions. All patients had elevated *SIGLEC1* levels (mean molecules/monocyte +/- SD: 10272 +/- 3746) without high levels of standard inflammatory markers. In six patients, elevated *SIGLEC1* expression showed dysregulation of the type 1 interferon pathway prior to genetic testing. The relative expression (ΔCt) of all ISG´s was significantly elevated in comparison to healthy controls (*SIGLEC1* p= 0,0167, *ISG15* p=0,0015, *RSAD2* p=0,0067, *IFIL44* p=0,0001, *IFI27* p=0,0056).
Conclusion: We report high expression of *SIGLEC1* in monogenic interferonopathies like Aicardi-Goutières-Syndrome.
Therefore, *SIGLEC1* qualifies as an easy accessible and cheap diagnostic marker to screen patients with suspected interferonopathy.

REFERENCES

[1] Crow, Y.J., *Type I interferonopathies: mendelian type I interferon up-regulation*. Curr Opin Immunol, 2015. 32: p. 7-12.
[2] Rose, T., et al., *Are interferon-related biomarkers advantageous for monitoring disease activity in systemic lupus erythematosus? A longitudinal benchmark study*. Rheumatology (Oxford), 2017. 56(9): p. 1618-1626.
[3] Biesen, R., et al., *Sialic acid-binding Ig-like lectin 1 expression in inflammatory and resident monocytes is a potential biomarker for monitoring disease activity and success of therapy in systemic lupus erythematosus*. Arthritis Rheum, 2008. 58(4): p. 1136-45.

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AB1169 ASSOCIATION OF ANXIETY, DEPRESSION WITH ULTRASONOGRAPHIC EVALUATION OF THE JOINTS, DISEASE ACTIVITY, FUNCTIONAL DISABILITY AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATIC DISEASES:

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Objectives: The aim of this study is to evaluate anxiety and depression disorders and to study their correlation with disease activity, ultrasonographic (US) finding indicative of synovitis, functional status and quality of life in patients (pts) with rheumatic diseases.
Methods: 39 pts (F/M–29/10) with rheumatoid arthritis (RA, n=17), ankylosing spondylitis (AS, n=10), psoriatic arthritis (PsA, n=12) were included. All RA pts fulfilled the ACR/EULAR 2010, AS pts - the ASAS, PsA pts - the CASPAR criteria. 20 pts (8 RA, 6 AS, 6 PsA) were performed US examinations (Mindray DC-N6 (China), C5-2, L10-13 MHz probes) included bilateral of the hip and knee joints. Each joint was scored according to the OMERACT definitions of pathology. Functional status (BASFI), disease activity indices (DAS28-CRP, ASDAS-CRP, DAPSA), anxiety and depression levels (Hads-A, Hads-D) and quality of life (RAPID3, EQ-5D) were assessed. The Mann-Whitney U-test was applied for intergroup comparison and correlation was evaluated using a Spearman's Rank two-tailed test (*R* value is shown).
Results: Median age of 39 pts - 52 (44;61) years and the body mass index – 28 (23;30). Mean anxiety index was 6.7±3.4, depression index - 6.6±3.3. Anxiety disorders were detected in 13/39 pts (33.3%), depression disorders in 17/39 pts (43.5%). Pts with Hads-D $\geq$8 (n=17) had higher score ASDAS-CRP (4.6 (4.2;5.0) vs 3.1 (2.7;3.9), p<0.01), BASFI (7.2 (6;7.3) vs 4.2 (3;5.5), p<0.05), EQ-5D index (9.8 ±1.2 vs 8.5±1.6, p<0.01) and the same tendency to US score and DAS28-CRP compared pts without depression. But pts with Hads-A $\geq$8 (n=13) had only higher EQ-5D (10 ±1.2 vs 8.7±1.6, p<0.005) and RAPID3 (17.1 ±5.8 vs 15.6 ±1.6, p<0.05). However, US – synovitis of the hip joints was positively correlated with Hads-D (r=0.713, p<0.05) and Hads-A (r=0.587, p<0.05).
Conclusion: Anxiety and depression more common in patients with active rheumatic diseases. Psychological disorders are associated with disease activity, US- finding of synovitis and the severity of functional disability.
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AB1170

A PHASE IV, MULTICENTER, SINGLE-ARM, OPEN-LABEL STUDY TO EVALUATE THE IMPACT OF APREMILAST ON HAND AND WHOLE-BODY MRI OUTCOMES IN PATIENTS WITH PSORIATIC ARTHRITIS (MOSAIC): RATIONALE, DESIGN AND METHODS

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Background: Phase III clinical trials have shown apremilast (APR) reduced PsA signs/symptoms and improved physical function,[1-3] but no study has addressed its impact on structural disease progression. MRI is a highly sensitive, validated tool to assess inflammatory and structural changes, as it can detect soft tissue inflammation, bone marrow edema (BME) lesions, bone erosion and proliferation in peripheral joints and axial skeleton. Whole-body (WB)-MRI, a relatively novel technique in musculoskeletal studies, allows assessment of all peripheral/axial joints and entheses in 1 examination.[4] Recent, consensus-based and semi-quantitative scoring methods were developed and validated. This study is the first to systematically use new state-of-the-art MRI scoring methodologies to assess PsA inflammatory and structural changes in a global clinical trial.
Objectives: To assess APR efficacy on inflammatory indices and imaging outcome measures associated with PsA structural progression by conventional static MRI and dynamic contrast-enhanced (DCE)-MRI of the most affected hand and WB-MRI.
Methods: The study aims to enroll 120 biologic-naïve adults with PsA for ≥3 mos to ≤5 yrs and prior treatment with ≤2 conventional DMARDs. Subjects must have ≥3 swollen and ≥3 tender joints, hand involvement (≥1 swollen joint or ≥1 dactylitis) and ≥1 active enthesitis site. After 4-wk screening, all eligible patients will receive APR 30 mg twice daily (titrated during the first 5 days) as monotherapy or in combination with methotrexate for 48 wks, with a 4-wk observational follow-up. Conventional MRI and optional DCE-MRI of the most affected hand and WB-MRI of the entire body will be performed at Wks 0, 24 and 48. The primary endpoint is change from BL to Wk 24 in OMERACT PsA MRI (PsAMRIS) composite score of BME + synovitis + tenosynovitis. Other imaging endpoints include change from BL to Wk 48 in PsAMRIS composite score (BME + synovitis + tenosynovitis) and change from BL to Wks 24 and 48 in PsAMRIS composite score (BME + synovitis), PsAMRIS composite inflammation score (BME + synovitis + tenosynovitis + periarticular inflammation), PsAMRIS total damage score (erosion + bone proliferation), WB-MRI indices (including peripheral joint inflammation index and peripheral enthesis inflammation index), hip and knee inflammation MRI scores (HIMRISS, KIMRISS), OMERACT heel enthesitis MRI indices, axial inflammation indices (SPARCC, CanDen), DEMRIQ-Volume and DEMRIQ-Inflammation and other DCE-MRI–derived parameters. Clinical parameters will include SJC/TJC, cDAPSA, SPARCC Enthesitis Index, Leeds Enthesitis Index, Leeds Dactylitis Index, PASDAS, PtGA, PhGA, Patient's Assessment of Pain, HAQ-DI, and BASDAI and impact of disease (PsAID12). Safety and tolerability also will be assessed.
Results: The study protocol was approved by an independent ethics committee and is now enrolling in the USA. Selected countries in Europe and Russia will also participate. MRI, clinical and patient-reported outcomes will be analyzed.
Conclusion: This study will provide important evidence of APR's impact on inflammatory/structural changes by assessing all PsA musculoskeletal domains (peripheral arthritis, enthesitis, dactylitis and axial disease). Furthermore, it will yield information on use of conventional MRI–, WB-MRI– and DCE-MRI–driven outcome measures in PsA clinical trials.

REFERENCES

[1] Kavanaugh 2014. 2. Cutolo 2016. 3. Edwards 2016. 4. Østergaard 2017.

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AB1171

COMPUTER-BASED EVALUATION OF JOINT SPACE NARROWING IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH WITH CERTOLIZUMAB PEGOL

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Background: The reduction of finger joint space width in patients with rheumatoid arthritis (RA) is associated with joint destruction. Anti-TNF treatment with certolizumab pegol is an effective therapy in RA-patients. The computer-assisted joint space analysis is a new computer based technique to measure joint space width on hand radiographs.
Objectives: The aim of this post-hoc analysis of the data set used in the RAPID 1 trial was to quantify finger joint space width of RA patients treated with Certolizumab pegol.
Methods: The post-hoc analysis includes 328 patients. These patients were divided into three groups: methotrexate plus placebo, certolizumab pegol 200 mg (every two weeks) plus methotrexate, and certolizumab pegol 400 mg (every two weeks) plus methotrexate. All patients underwent x-rays of the hand at baseline and week 52 as well as the quantification of finger joint space width of the metacarpal-phalangeal articulations (MCP) using the computer-assisted joint space analysis (Version 1.3.6; Sectra; Sweden). The joint space distance is expressed as mean joint space width of the MCP joints I to V (JSD-MCP total).
Results: The methotrexate group presented a significant joint space reduction with -4.8% for JSD-MCP total from 0.151 ± 0.028 cm (baseline) to 0.144 ± 0.033 cm (week 52). For the patients treated with certolizumab pegol 400 mg a non-significant change (0.6%) of JSD-MCP total from 0.146 ± 0.034 cm (baseline) to 0.147 ± 0.036 cm (week 52) was observed. A similar result was evaluated for the certolizumab pegol 200 mg group (JSD-MCP total: 0.147 ± 0.035 cm [baseline] to 0.147 ± 0.036 cm [week 52]).
Conclusion: The study highlights that patients treated with certolizumab pegol plus methotrexat show no change of joint space width of the metacarpal-phalangeal articulations in comparison to patients with methotrexate plus placebo estimated by computer-assisted joint space analysis. Consequently, the automatic quantification of finger joint space is a sensitive technique for the quantification of joint space reduction and treatment monitoring.

REFERENCES

[1] Keystone E, Heijde Dv, Mason D Jr, et al. Certolizumab pegol plus methotrexate is significantly more effective than placebo plus methotrexate in active rheumatoid arthritis: findings of a fifty-two-week, phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. Arthritis Rheum 2008;58:3319-29.

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AB1172 **ARE CIRCULATING BLOOD BIOMARKERS FOR INFLAMMATORY RHEUMATIC DISEASES GENDER-DEPENDENT? – SYSTEMATIC REVIEW BASED ON OMICS DATA**

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Background: Inflammatory rheumatic diseases (IRDs) are thought to be multifactorial diseases. Female-male ratio in IRDs differs according to the disease[1]. In Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) female prevalence is higher opposing to Ankylosing Spondylitis (AS)[2,3].Until recently, differences on gender-bias observed in predisposition to IRDs, and to their pathophysiologies have been understudied and neglected. Recent research using omics approaches shows that gender-bias is outspread in a diversity of pathologies. The integration of omics results, spite the extremely complex crosstalk among the several biomolecules involved, places these methods at the lead of medical research, overcoming limitations and increasing the forecasts of targeted methodologies[4–6].
Objectives: The purpose of this systematic review is to aggregate existing omics results on biomarkers for RA, SLE and AS to raise awareness about whether gender can actually play a role on their profiles.
Methods: Two searches were conducted on PUBMED database (22nd November 2018) with a final output of 81268 articles. Both searches were sorted by best matches and for the second thousandth articles ranked no relevance was found for the aim of this review. The first 1000 articles were further analyzed based on the title, abstract and content. Three articles having relevant results were selected from the first thousand publications. Ten more were identified from the cross-references of both searches. The PICO (P, population; I, intervention; C, comparison; O, outcome) concept was used to perform the analysis according to: Patients: adults (>18 years old) with RA, SLE or AS (SpA); Intervention: any –omic study; Comparison: gender information regarding results; Outcomes: identified genes, proteins or metabolites.
Results: *Dectin-2*, *MCP-1* and *DC-SIGN* polymorphisms where proposed as possible accounts for gender-associated differences in susceptibility to RA[7]. Sex-differentiated and sex-interaction analyses of a GWA study revealed strong evidence of association in both sexes, highlighting links with RA only in one of the genders[8]. Several transcriptomic studies pointed to gender differences on biomarkers profiles for the three diseases. For instance, different expression levels of TNFα, IL-6, IL-17, IL-18, IFNα as well as X or Y chromosome-linked genes were found in SLE and/or AS[9–11]. In AS, male patients with syndesmophytes showed higher levels of TNFα and men without syndesmophytes presented higher levels of VEGF, IL-6, TNFα and IL-18 both compared to females-matched[12]. In RA patients, microRNAs 222, 532, 98, and 92a were found significantly down regulated in PBMC of female versus male[13]. Six genes displayed a gender-biased expression among male and female SLE patients[14].
Conclusion: Blood biomarkers signatures for the IRDs analyzed in this study have been shown gender-biased. These will contribute for a better understanding of these diseases pathophysiology and probably to different gender approaches regarding diagnosis, monitoring and therapeutic approach.

REFERENCES

[1] Amur S, et al. (2012),38,J254;Nussinovith U, Shoenfeld Y(2012),11,6; van Vollenhoven RF(2009),7,1;
[2] Effler SW, et al. (2013),39,101;
[3] Russell C et al(2013),4,395;
[4] Song X, Lin Q(2017),37,1257;
[5] Cáliz R, et al. (2013),8,e72732;
[6] Zhuang JJ,Morris AP(2009),3,Suppl 7:S90;
[7] Gracey E et al(2016),68,679;
[8] Hui-Yuen J et al(2016),45,394;
[9] Wang XB et al(2017),18,184;
[10] Huang WN et al(2012),15,163;
[11] Khalifa Oet al(2016),17;
[12] Martin AR et al(2018),1

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AB1173 **ENDOCARDIAL LESIONS IN PATIENTS WITH RHEUMATIC DISEASES: CASE REVIEW**

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Background: The infection of a native or prosthetic heart valve usually occurs in patients with structural valvular anomalies that predispose to turbulent flows. Manifestations such as arthralgia, arthritis or back pain appear in up to 40% of patients, which acts as a confounding factor when this infection occurs in patients with rheumatic diseases. On the other hand, in the latter patients, noninfectious endocarditis has been described, which adds even more complexity to the diagnosis.
Objectives: To describe the characteristics of endocardial lesions in patients with rheumatic diseases.
Methods: Patients attending clinics at the Department of Rheumatology were analyzed to determine how many of them required hospitalization for causes directly related to endocardial lesion, from January 2015 until December 2018. The following information was recorded: age, sex, type of rheumatic disease, duration of the disease, immunosuppressive treatment, characteristics of endocardial lesions, complications of endocardial lesions, and cardiovascular risk factors.
Results: All patients were identified from an electronic database. Results regarding to demographic and clinical data are as follows:
Conclusion: The spectrum of endocardial involvement in patients with rheumatic diseases is variable. In this case review, we found lesions of different origin: infectious, thrombotic and tumoral. The appearance of fever of unknown origin in patients with rheumatic diseases, requires ruling out an endocarditis, needing transesophageal echocardiography in case the transthoracic study, which is less sensitive, is negative. It is striking the case of patient 3, a systemic sclerosis with calcinosis in limbs, whose endocardial wart, was studied histologically, revealing in its composition mainly calcium and fibrin. We have not found a bibliographic reference of calcium endocarditis in systemic sclerosis.
In conclusion, patients with rheumatic diseases can develop infectious endocarditis, but also thrombotic valvular vegetations, as well as myxomas whose consequences, from their clinical debut, may pose life-threatening situations for the patient. The presence of fever, stroke or embolic events in these patients should put us on the track of an underlying endocardial involvement.

REFERENCES

[1] Am J Med (2007) 120, e1-e2
[2] World J Cardiol 2014 September 26; 6(9): 993-1005
[3] Rev Esp Enferm Metab Óseas 2002;11(2): 50-58

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	Age	Sex	Rheumatic disease	Baseline Treatment	Endocardial lesions clinical debut	Blood culture	Endocardial lesions	**C**omplications	Clinical evolution
1° case	27	Male	Dermatomyositis	Methotrexate + glucocorticoids	Digital ulcers + Febrile syndrome	Staph. Aureus	Infectious endocarditis	Mitral valve perforation	Resolution after cardiac surgery
2° case	64	Male	Rachialgia	NSAIDS	Febrile syndrome	Strept. Gallolyticus	Infectious endocarditis	-	-
3° case	53	Female	Systemic Sclerosis	Tocilizumab + glucocorticoids	Febrile syndrome	-	Nonbacterial thrombotic endocarditis	Acute ischaemia right lower limb	Resolution after embolectomy
4° case	13	Female	Autoinmune hemolytic anemia	Glucocorticoids, splenectomy	Ischaemic stroke	-	Auricular myxoma	-	Systemic lupus ANA and anti-DNA +
5° case	48	Female	Autoinmune thrombocytopenia	Glucocorticoids	Iliac artery embolism	-	Auricular myxoma	-	Immunologic síndrome secondary to myxoma

declared, Jose Luis Marenco Speakers bureau: abbie, pfizer, novartis, janmsen

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AB1174 IS MONITORING SYNOVITIS IN THE HANDS BY ULTRASOUND ENOUGH TO ASSESS TREATMENT EFFECT IN PATIENTS WITH RA IN CLINICAL PRACTICE?

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Background: The use of ultrasound (US) as a tool for assessing disease activity in patients with rheumatoid arthritis (RA) has increased in recent years and its value is supported by studies showing that US provides more accurate assessment of joint inflammation than clinical examination at time of diagnosis and in clinical state of remission.

Various scoring systems have been proposed for monitoring of synovitis. Among these are the novel consensus-based Global OMERACT-EULAR Synovitis Score (GLOESS) was developed applying the highest score of grey-scale (GS) or Doppler as the final score for the joint.

Different joint sets have been proposed for optimal and feasible evaluation of patients with inflammatory arthritis but currently there is no agreement on a specific reduced set of joints that should be evaluated by US to acquire the best information about clinical and subclinical activity when monitoring patients with RA.

Objectives: To evaluate if synovitis assessment of hands only is enough (testing GS, Doppler and GLOESS sum scores) for assessing changes during treatment in order to increase clinical feasibility of US in daily clinical practice.

Methods: US and clinical assessment for tender/swollen joint count (TJC/SJC) were performed in 19 patients fulfilling ACR 1987 criteria for RA initiating treatment with TNF inhibitor (TNFi) (week 0), and after 6 and 16 weeks of follow up.

Forty-six joints were evaluated by US (sternoclavicular, acromioclavicular, glenohumeral, elbow, wrist, MCP1-5, PIP1-5, hip, knee, ankle and MTP 1-5 bilaterally) using a GE Logiq E9 machine with a linear array transducer. Joint inflammation was graded 0-3 on GS and Colour Doppler (CD) and synovitis was defined as a GS score ≥1 with or without Doppler score ≥1. Doppler settings for slow flow was applied according to guidelines.

Table 1. Correlation coefficients between GS sum score, CD sum score and GLOESS with the 46 joint set in different joint combinations

	Baseline, *rho*	Median	IQR	Week 6, *rho*	Median	IQR	Week 16, *rho*	Median	IQR
GS 28-joint	0.94	8	2-18	0.88	4	1.2-15.7	0.95	6	1-16.5
CD 28-joint	0.94	2	0-6.5	0.93	0	0-6.5	0.95	0	0-4
28-GLOESS	0.93	8	2-8	0.87	4	1.2-18.5	0.89	6	1-17.5
GS hands	0.90	5	1-10	0.78	3	1-10.7	0.87	5	0.5-9.5
CD hands	0.92	1	0-4	0.91	0	0-5	0.95	0	0-3.5
Hands GLOESS	0.88	6	1-11	0.78	3	1-10.7	0.81	5	0.50-11
GS 9-joints	0.51	3	0-10	0.54	0	0-4	0.30	3	0-3
CD 9-joints	0.81	5	1-10.2	0.73	0	0-5	0.83	5	0-9
9-GLOESS	0.95	5	2-14	0.94	4	1.2-10.5	0.86	3	0-9

Spearman's rho correlation between the 46- joint set and different joint sets GS, CD sum scores and GLOESS at baseline and 16 weeks.
GS grey-scale, CD colour Doppler, GLOESS Global OMERACT-EULAR Synovitis Score, IQR interquartile range

Table 1

GS, CD and GLOESS sum scores were obtained for the total joint set and different joint subsets: hands as joint set (wrist, 1-5 MCP, 1-5 PIP bilaterally), 28 conventional joints evaluated for DAS and the 9-joint set suggested for the GLOESS (shoulder, elbow, wrist, MCP1 and 4, PIP2, MTP 3 and 5, knee). Data from the different joint sets were analyzed applying Spearman's correlation coefficient.

Results: Mean change in GS sum score between week 0 and 16 was of 2.58, 1.35, 1.47 and 1.11 for 46-joint set, hands, 28-joint set and 9-joint set, respectively. Compared to the 46 joint set the GS and CD sums core had a high correlation coefficient (≥0.78) for 28 joint set and the hand as joint set for all time points - table 1. The 9 joint set GS sum score had low correlation when compared to the 46 joint set at baseline and during follow up – table 1. GLOESS for the hands performed equally well with a correlation coefficient (≥0.70) for all joint sets at all time points – table 1. DAS28-CRP did not correlate with the total joint set or the different joint subsets.

Conclusion: The present study of patients with RA shows that the US examination of both hands only for assessing disease activity is highly correlated for with the 46-joint evaluation at all time points, both regarding GS and Doppler sum scores. Using hands as a reduced joint set US assessment of inflammation could be an option to increase the feasibility of US in routine clinical practice.

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AB1175 FACET JOINTS INVOLVEMENT IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY

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Background: Even it is accepted among rheumatologists that rheumatoid arthritis (RA) does not involve the facet joints (FJs) of the spine, the issue is still under debate. Studies that described a prevalence of the FJs in rheumatoid arthritis patients are scarce.

Objectives: To compare the prevalence of FJs changes between patients with RA and age and sex-matched peers.

Methods: We compared computed tomography (CT) scans of 34 patients with RA, who suffered from low back pain, and 70 age and sex-matched controls-people without RA, with low back pain.

The changes in FJs were evaluated according to the score proposed by Kalichman et al: joint space narrowing, marginal osteophytes, articular process hypertrophy, subchondral sclerosis, inter-joint vacuum phenomenon, and subchondral cysts. The characteristic joint changes of RA were also evaluated.

Disease activity characteristics, duration of RA, age, and gender were taken from patients' clinical charts.

Results: Prevalence of facet joints changes in patients with RA and group of age and sex-matched controls were not significantly different at any spinal level or in total L5-S1 score. Marginal erosions, that are characteristic feature of joint change in RA, were not found in any subject with RA in our sample. In subjects with RA, individuals with affected FJs and without affected FJs have no difference in any disease parameters and markers (Tables 1 and 2).

Conclusion: In our samples of CT scans we did not find a difference in facet joints changes between the subject with RA and control group. The occurrence of FJs changes among subjects with RA had no correlation with disease duration and activity. According to the findings, we may assume, that facet joints of the lumbar spine are not involved in the inflammatory process of RA, and patients' low back pain is not due to inflammation in this region of the spine.

Abstract AB1175 Table 1. Prevalence of FJ degenerative changes in patients with RA and age and sex-matched controls.

Segment	RA patients	Controls	Comparison (χ^2-test)
L1-L2 Left	1 (3.0%)	1 (1.8%)	χ^2=0.157, d.f.=1, p=0.692
L1-L2 Right	0 (0.0%)	0 (0.0%)	-
L2-L3 Left	0 (0.0%)	1 (1.7%)	χ^2=0.575, d.f.=1, p=0.448
L2-L3 Right	1 (3.0%)	1 (1.8%)	χ^2=0.157, d.f.=1, p=0.692
L3-L4 Left	2 (6.1%)	2 (3.4%)	χ^2=0.363, d.f.=1, p=0.547
L3-L4 Right	1 (3.0%)	4 (6.9%)	χ^2=0.605, d.f.=1, p=0.436
L4-L5 Left	2 (6.1%)	2 (3.4%)	χ^2=0.342, d.f.=1, p=0.559
L4-L5 Right	4 (12.1%)	3 (5.3%)	χ^2=1.370, d.f.=1, p=0.242
L5-S1 Left	4 (12.1%)	5 (8.9%)	χ^2=0.233, d.f.=1, p=0.629
L5-S1 Right	0 (0.0%)	5 (8.8%)	χ^2=3.065, d.f.=1, p=0.080
Total L1-S1 score	9 (27.3%)	11 (19.0%)	χ^2=0.846, d.f.=1, p=0.358

Abstract AB1175 Table 2. Association between changes in FJs and disease markers in RA patients (results if one-way ANOVA).

Markers	No FJ changes	Affected FJ	Comparison
Age (years)	57.67±9.91	60.00±10.45	F=0.353, p=0.557
Years of rheumatoid arthritis	7.00±4.45	7.56±3.50	F=0.113, p=0.739
CRP (mg/l)	5.39±4.81	6.22±2.22	F=0.247, p=0.623
ESR (mm/hour)	17.64±10.87	28.60±18.69	F=2.244, p=0.156
DAS-CRP	2.34±0.97	2.56±0.96	F=0.333, p=0.568
DAS-ESR	2.51±0.98	2.81±0.84	F=0.328, p=0.577
CDAI	7.27±5.14	8.11±6.55	F=0.152, p=0.699
SDAI	7.84±5.24	8.73±6.80	F=0.163, p=0.690

CRP– C-reactive protein; ESR – Erythrocyte sedimentation rate; DAS-Disease Activity Score; CDAI – Clinical Disease Activity Index; SDAI – Simple Disease Activity Index.

REFERENCES

[1] Kalichman L, Li L, Kim DH, Guermazi A, et al. 2008. Facet Joint Osteoarthritis and Low Back Pain in the Community-Based Population. Spine 33:2560-2565.
[2] van der Heijde D, Dankert T, Nieman F, et al. 1999. Reliability and sensitivity to change of a simplification of the Sharp/van der Heijde radiological assessment in rheumatoid arthritis. Rheumatology (Oxford) 38:941-947.

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AB1176 CORRELATION OF THE FINDINGS OF ULTRASOUND EXAMINATION OF THE LUNGS AND INTERSTITIAL LUNG FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Interstitial lung disease is one of the most severe complications in patients with systemic sclerosis (SSc), especially in those with diffuse form of this disease. Carbon monoxide diffusion capacity (DLCO) measurement is an important diagnostic method for assessing lung fibrosis. In recent years, ultrasound (US) lung examination has been used to evaluate the presence of interstitial changes (B lines) in the lungs.
Objectives: Determine whether there is a statistically significant difference in positive US findings on the lungs between the groups of subjects with a diffuse SSc and limited SSc, and whether there is a statistically significant difference in the presence of pulmonary fibrosis between these two groups of subjects. Then determine whether there is a correlation between the presence of B lines on the US examination of the lungs and the finding of lung fibrosis in patients with diffuse and limited SSc.
Methods: The study included 55 patients of both sexes with SSc from the Institute of Rheumatology (28 with diffuse and 27 with limited SSc), aged between 43 and 79 years. Data on the presence of pulmonary fibrosis were based on clinical findings and reduced lung diffusion parameters (DLCO less than 75%). An US examination of the lungs was performed for all patients and the number of B lines in all lung segments was determined. Positive US finding was the finding of 3 or more B lines in at least two adjacent fields of US scanning or more than 5 B lines in any single field of ultrasound scanning.
Results: There was a statistically significant difference in positive US findings on the lungs between the groups of subjects with diffuse SSc and limited SSc (85.7% versus 44.4%, p <0.001). A statistically significant difference was observed in the presence of pulmonary fibrosis between the groups of subjects with diffuse SSc and limited SSc (85.7% versus 55.6%, p <0.05). It has also been shown that there is a highly statistically significant correlation between the presence of B lines on US examination of the lungs and findings of lung fibrosis in patients with diffuse and limited SSc (t = 0,700, p <0.001).
Conclusion: The conducted study confirmed that there is a highly statistically significant correlation between the presence of B lines in the US examination of the lungs and the findings of lung fibrosis in patients with diffuse and limited form of SSc. The study also found that patients with diffuse SSc had significantly more frequent positive US findings on the lungs, as well as a more frequent presence of pulmonary fibrosis compared to the patients with limited SSc. Introducing US into a routine protocol for monitoring patients with SSc diagnosis would provide a simple, inexpensive, fast and accurate orientation to the development of fibrotic changes in the lungs.

REFERENCES

[1] Shahin AA. Pulmonary involment in systemic sclerosis. Treat Respir Med 2006;5:429-36.
[2] Doveri M, Frassi F, et al. Ultrasound lung comets: new echographic sign of lung interstitial fibrosis in systemic sclerosis. Reumatismo. 2008 Jul-Sep;60(3):180-4.
[3] Barskova T, Gargani L, et al. Lung ultrasound for the screening of interstitial lung disease in very early systemic sclerosis. Ann Rheum Dis 2013; 72: 390-395.

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AB1177 HOW TO DEFINE RHUPUS SYNDROME: SYSTEMATIC REVIEW OF THE CURRENT LITERATURE

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by the presence of multi-systemic manifestations in patients with immunologic anomalies. While joint involvement is present in up to 90% of patients with SLE [1], only a small subset of patients develops erosive arthritis. The term rhupus refers to the coexistence of erosive symmetrical polyarthritis, typical manifestation of rheumatoid arthritis (RA), and clinical signs of SLE in the presence of anti double-stranded DNA (anti-dsDNA) and/or anti-Smith antibodies (anti-Sm) [2]. However, to date, no consensus exists on how to define the rhupus syndrome.
Objectives: In this study we aim to investigate the definition of rhupus by systematically reviewing the current literature.
Methods: A detailed literature research has been developed a priori to identify articles that reported findings from rhupus patients. The search strategy was applied to Ovid MEDLINE In-Process and Other Non-Indexed Citation 2000 to present. Studies that included rhupus patients were systematically analyzed by two independent reviewers (ER and SGF). Disagreements were resolved by consensus; if consensus could not be achieved, a third party (MR) would provide an assessment of eligibility.

Table 1.

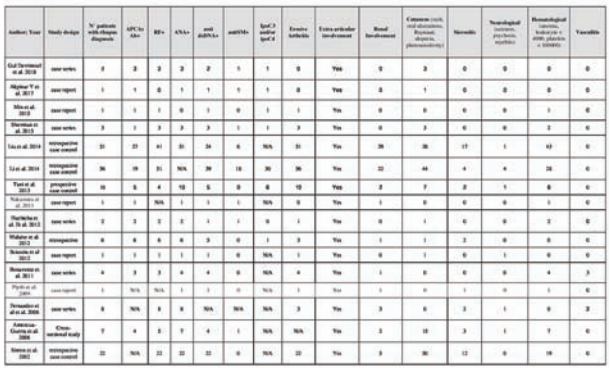


Table 1

Results: We analyzed clinical and serological data of 176 patients with diagnosis of rhupus derived from a total of 16 studies. All works considered the presence of autoantibodies specific for SLE by including antinuclear antibodies (ANA), anti-dsDNA, and anti-Sm antibodies. Only 67% of patients had ANA positivity (119/176), 64% showed anti-dsDNA in serum (113/176) and 17% were positive for anti-Sm antibodies. No heterogeneous data were available on pattern or title of these autoantibodies. Only two studies did not assay ANA or anti-dsDNA. Twelve out of 16 studies tested the occurrence of anti-citrullinated peptide antibodies (ACPAs) that have been reported in 73 patients (41%), rheumatoid factor (RF) was detected in 149 patients (84%) resulting from 13 out of 16 studies. Among clinical criteria of rhupus, an erosive arthritis has been observed in 155 patients (88%), only one study did not take into account the joint erosion. Hematological and cutaneous disorders (64% and 86%,

respectively) were the most frequent extra-articular manifestations of SLE. Few patients experienced main systemic signs such as renal (67 patients, 38%) and neurological (9 patients, 5%) disorders, vasculitis (6 patients, 3%), and sierositis (43 patients, 24%).
The studies included in the present analysis are displayed in Table 1.
Conclusion: We observed a strong heterogeneity in the elements taken into account to establish the presence of rhupus, reflecting the lack of consensus and validated criteria to define the disease. Rhupus can represent an aggressive and disabling condition, and a harmonization in the classification criteria might represent the first step to improve the management of these patients.

REFERENCES

[1] Ceccarelli F, et al. The role of disease activity score 28 in the evaluation of articular involvement in systemic lupus erythematosus. ScientificWorldJournal. 2014; 2014: 236842.
[2] Lozada-Navarro, et al. An imbalance in the T-helper phenotypes displayed by senescent CD4 CD28null T cells is associated with erosive arthritis (rhupus syndrome) in systemic lupus erythematosus. Lupus. 2018 Nov;27 (13):2155-2160.

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AB1178 PLANTOGRAPHIC ASSESSMENT OF FOOT DEFORMITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In almost one third of the patients with rheumatoid arthritis (RA) the disease begins with involvement of the small joints of the feet with high risk for developing significant foot deformities with disease progression. Irreversible structural changes occur as a result of synovitis combined with mechanical stress. The pain and the impaired static cause functional disability in these patients and the orthotic correction is often limited and with no evidence for effectiveness.
Objectives: To assess the foot structure and determine the incidence of foot deformities in patients with RA with different disease duration ranging from 3 months to more than 10 years.
Methods: Forty two RA patients (32 women and 10 men) underwent assessment of the foot structure under an axial load and while walking on a pressure measuring plate as well as a 3D scan of the feet.
Results: The most common foot deformities found in the study group included hallux valgus deformity in 73,81%, flattening of the medial longitudinal arch in 64,29% and valgus deformity of the calcaneus in 35,71% of the patients.
Conclusion: The introduction of the plantography in the clinical practice offers the opportunity for early diagnosis of foot deformities in patients with RA and indicates the necessity of correction through orthotics or surgery.
Disclosure of Interests: None declared
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AB1179 TYPES OF JOINT LESIONS IN REACTIVE ARTHROPATHY

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Background: Differential diagnosis of ReA has certain difficulties, especially at an early stage in the absence of confirmation of trigger infection. Radiographic signs of joint damage when the response are not specific and appear not earlier than 3-6 months from the onset of the disease; enthesitis this method is not visualized, making it difficult to timely diagnosis of ReA [1]. To determine the tactics of patient management and selection of adequate therapy is no less important to determine the duration and characteristics of the course of ReA.
Objectives: To study the ultrasonic features of joint lesions in reactive arthropathy depending on the course of the disease.
Methods: We examined 66 patients with Rea who met the preliminary international criteria were examined (4th International Workshop on Reactive Arthritis, Berlin 1999). Women were 26 (39%), men - 40 (61%), median age - 34 years (31-42), median duration of ReA- 1 year (0.3-3.25). Among the patients there were 40 (61%) people with acute ReA and 26 (39%) people with chronic ReA. All patients had confirmed chlamydial infection (PCR and IFA). Patients underwent a comprehensive clinical and laboratory examination, MRI and ultrasound of the knee joints. Statistical processing of the information package.
Results: The MRI of the affected joints clearly visualized inflamed entheses and the presence of local osteitis with an erosive defect of the closing plate of the bone (Fig.1).



Figure 1

In patients with acute ReA were visualized: thickening of entheses more than 3 mm (98%), hypo-, anechogenic areas in the projection of the tendon-ligamentous apparatus and places of its fixation (74%), the formation of a bone defect under them with a contour of reduced echogenicity (erosion of acute inflammation - 66,8%) and uneven edges, pronounced effusion (75%), lack of strengthening of local blood flow in the projection of synovia and joint structures (Fig.2).

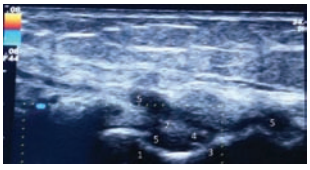


Figure 2

In patients with chronic ReA, the following were visualized: thickening of entheses to 3 mm (65%), hyperechogenic inclusions in the projection of the tendon-ligamentous apparatus and its fixation sites (53%), the formation of a bone defect under them with a contour of increased echogenicity (erosion of chronic inflammation – 46,9%) and uneven edges, slight effusion (28%), the absence of strengthening of local blood flow in the projection of synovia and joint structures (Fig.3).

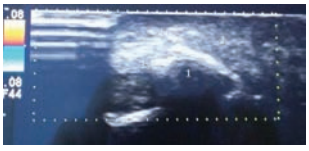


Figure 3

All patients with ReA were found to have a positive "pain test" in palpation of the affected entheses under the control of ultrasound entesopathy.
Conclusion: Based on the results we have made the following conclusions:

- 1.Ultrasound of joints allows to identify and assess the nature of joint lesions depending on the duration of the ReA.
- 2.Ultrasound criteria of acute ReA: enthesitis, erosion acute inflammation under affected entheses, enthesopathy expressed by secondary synovitis.
- 3. Ultrasound criteria for the chronic course of ReA: enthesitis, erosion of chronic inflammation under the affected entheses, enthesopathy, minor secondary synovitis, calcinates.

REFERENCES

[1] 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative/D. Aletaha [et al.]//Ann. Rheum. Dis. – 2010. – Vol. 69. – P. 1580-1588.

[2] Sirotka, V. Clinico-tool differential diagnostics erosive lesions of joints at patients with rhematoid and reactive arthritis/V. Sirotka, A. Litvyakov// VEDECKY PRUMYSL EVROPSKENO KONTINENTU-2013: materialy IX mezinarodni vedecko-prakticka conference, Praha, 27 listopadu - 05 prosincu 2013 rocu/Praha Publishing House «Education and Science». – Praha, –2013. –P. 23-24.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.2610

AB1180 ULTRASOUND SEMIOTICS OF DEFEATS OF THE JOINTS IN REACTIVE ARTHRITIS AND OSTEOARTHRITIS

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Background: The most common cause of knee joint damage in people of working age is osteoarthritis. However, in recent years, cases of reactive arthropathy, which often takes a chronic course, have become more frequent [1]. Given the current possible ultrasonic equipment, relevant is the study to study the ultrasonic features of defeat of joints with ReA and OA.
Objectives: To study the ultrasonic features of joint lesions at osteoarthritis and reactive arthritis.
Methods: We studied 55 patients with ReA and 22 patients with OA. Among patients with ReA were 25 women and 20 men, median age was 31 years (18 to 47), the median duration of the current Imple - of 2.86 (0,07-29,0) months. Among patients with OA were examined in 15 women and 7 men, median age was 56.5 years (43-61), the median duration of flow OA - 139 months (12-360 months). All patients with ReA at the time of the study or in history had confirmed genital chlamydial infection. All patients were multiplescale dynamic study of the knee by the ultrasonic device expert class using a sensor with a frequency of 12 MHz.
Results: As a result of the ultrasound examination of the 110 joints with ReA, we have identified: pronounced synovitis in 69 (62.7%) joints, but the absence of pathological vascularization in the projection of the synovia; narrowing of the joint space 73 (66,4%) joint; heterogeneous structure of the ligament in 82 (75%) joints, tenosynovitis in 20 (18%) joints, thickening entheses in 89 (80.9%) joints, hypoechoic entheses in 72 (65.5%) joints, hyperechogenic inclusions in projection entheses in 39 (36%) joints; local osteolysis of cortical layer of bone in the fixation entheses with the formation of erosive lesions in 77 (70%) joints, osteitis 26 (23,6%) joints; swelling parenthetically in 81 (74%) joint effusion parenthetically 49 (44,5%) joints (Fig. 1 a,b,c).
a. b. c.

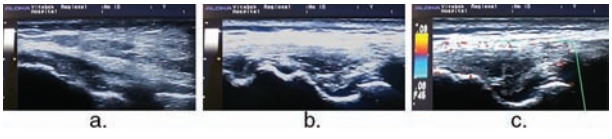


Fig.1(a,b,c) Ultrasound examination of knee joints in a patient with ReA

As a result of the ultrasound examination of the 44 joints with osteoarthritis, we have identified: a decrease in the thickness of the cartilage and narrowing of the joint space of degree 1 in 14 (31,8%) joints, reducing the thickness of the cartilage and narrowing of the joint space of 2 degrees in 22 (50%) of the joints, reducing the thickness of the cartilage and narrowing of the joint space grade 3 in 20 (45,6%) joints; subchondral osteosclerosis and cysts rebuilding bone was detected in 42 (95,5%) joints, the heterogeneity of the cords in 15 (of 34.10%) joints, thickened ligaments in 1 (2,30%) joint; single marginal osteophytes in 26 (59.1%) joint; multiple osteophytes in 20 (45,50%) joints; 29 (65,9%) joints detected a moderate effusion (Fig.2 a,b,c).
b. b. c.

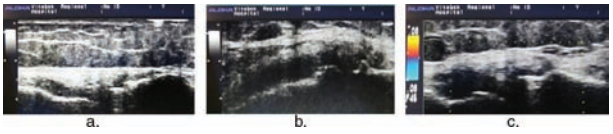


Fig.2 (a,b,c) Ultrasound examination of knee joints in a patient with OA

Conclusion: Ultrasound criteria of joint damage in ReA are: no hypervascularization synovia; pronounced synovitis; narrowing of the joint space; thickening entheses with hypo-anechoic areas; local osteitis with osteolysis of the cortical layer of bone in the fixation entheses and the formation of erosive lesions; parenthetically swelling.
Ultrasound criteria of lesions of the joints in OA are: narrowing of the joint space; thinning hrase; hyperechogenic zones of subchondral osteosclerosis; cysts rebuilding of the subchondral bone; hyperechoic marginal osteophytes.

REFERENCES

[1] Kumar, P. Reactive arthritis and research/P. Kumar, D. S. Bhakuni, S. Rastogi//J. Infect. Dev. Countries. – 2014. – Vol.8, №5. – P. 648 – 654.

Disclosure of Interests: None declared
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AB1181 ULTRASOUND PATHOLOGICAL PATTERNS AT CARPAL TUNNEL LEVEL IN RHEUMATOID ARTHRITIS AND IDIOPATHIC CARPAL TUNNEL SYNDROME

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Background: High-frequency ultrasound (US) has proven to be a useful imaging tool for the evaluation of carpal tunnel pathology. US impact in the assessment of idiopathic carpal tunnel syndrome (CTS) has been widely investigated, but only few studies have been carried out with the aim of revealing the pathologic conditions responsible for CTS in rheumatoid arthritis (RA) patients[1].
Objectives: The aim of this study is to evaluate US findings at carpal tunnel level in a cohort of patients with RA, focusing on those with a clinical diagnosis of CTS, and to compare these findings with those observed in a cohort of patients with idiopathic CTS (without RA).
Methods: Fifty-six patients with RA fulfilling the ACR/EULAR 2010 classification criteria were consecutively enrolled. CTS was diagnosed according to the American Academy of Neurology practice parameter for CTS. We also enrolled 19 patients with idiopathic CTS and evaluated 24 symptomatic wrists, excluding those already surgically decompressed. The US assessment was performed using a MyLab ClassC (Esaote SpA) US system, working with a 6-18 MHz linear probe. The power Doppler (PD) frequency was set at 9.1 MHz. The following grey scale (GS) US pathologic findings were assessed at the carpal tunnel level: cross-sectional area (CSA) of the median nerve at the carpal tunnel inlet (at the level of the pisiform and scaphoid bones), presence of finger flexor tenosynovitis and palmar radio-carpal synovitis (both in GS and PD), and marked bone profile irregularities. The median nerve was considered enlarged if its CSA was more than 12 mm^2. We evaluated the presence of intra-neural PD signals at the carpal inlet and scored its entity (0=no PD signal, 1=one single vessel within median nerve, 2=two or three single or two confluent vessels and 3=more than three single or more than two confluent vessels).
Results: CTS was diagnosed in 21 out of 112 wrists (18.75%) and in 14 out of 56 RA patients (25%).
Enlarged median nerve was found in 4 out of 21 wrists with RA and CTS (19%), in 6 out of 84 wrists of patients without CTS (7.1%) and in 22 out of 24 wrists of patients with idiopathic CTS (91.7%). Flexor tenosynovitis was found in 6 out of 21 wrists with RA and CTS (28.6%), in 8 out of 84 wrists of patients without CTS (8.2%) and in 4 out of 24 wrists with idiopathic CTS (16.7%). Palmar radio-carpal synovitis was found in 4 out of 21 wrists with CTS (19%), in 10 out of 84 wrists of patients without CTS (11.9%) and in 1 out of 24 wrists with idiopathic CTS (4.2%). Marked bone profile irregularities were detected in 3 out of 21 wrists with CTS (14.3%), in 22 out of 84 wrists without CTS (26.2%) and in none of the patients without RA. In RA patients, positive intraneural PD signal was found in 9 out of 21 wrists with CTS (42.8%) and

in 12 out of 84 wrists without CTS (14.3%). In idiopathic CTS, PD signal was found in 15 out of 24 wrists (62.5%).
Conclusion: US allowed a detailed identification of the pathological findings at carpal tunnel in both RA and idiopathic CTS patients. When CTS was diagnosed, different US patterns were distinguished being median nerve less frequently enlarged and synovitis more frequently detected in RA patients. Finally, a positive association was found between the presence of intra-neural PD signal and clinical diagnosis of CTS independently of the diagnosis of RA.

REFERENCES

[1] Hammer HB, Hovden IA, Haavardsholm EA, Kvien TK. Ultrasonography shows increased cross-sectional area of the median nerve in patients with arthritis and carpal tunnel syndrome. Rheumatology (Oxford) 2006; 45 (5):584-8.

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AB1182 THE CORRELATION BETWEEN THE ULTRASOUND-DETECTED SYNOVITIS OF SMALL JOINTS AND THE DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In patients with rheumatoid arthritis (RA), small joints, especially metacarpophalangeal (MCP), and interphalangeal (PIP) joints are frequently affected. Ultrasound (US) is a sensitive method for detecting joint inflammation in patients with RA. So far, what degree does the synovitis of every small joint contribute to the disease activity in RA was not clear.
Objectives: The purpose of the present study was to compare the correlation between the ultrasound-detected synovitis of small joints and the disease activity in RA.
Methods: 211 RA patients with DAS28-ESR >2.6 were included in this study. Thirty joints, including bilateral metacarpophalangeal (MCP) 1-5, proximal interphalangeal (PIP) 1-5 and metatarsophalangeal (MTP) 1-5 joints, were evaluated by ultrasound scan in all patients. Disease activity was assessed by DAS28-ESR, DAS28-CRP, CDAI, SDAI. Synovitis was detected by using semi-quantitative scoring systems (0-3) for grey scale (GS) and power Doppler (PD). All correlations among US variables and clinical variables were assessed using Spearman's rank correlation test.
Results: Their median age was 51.82 years, median disease duration was 60 months, with 84.3% females. The mean (SD) DAS28-ESR and DS28-CRP were 4.59±1.51 and 4.18±1.39, respectively. The whole GS scores of MCPs (MCP1-5 joints) showed highest correlation with the disease activity (r=0.403-0.452, p<0.01), including DAS28-ESR, DS28-CRP, CDAI and SDAI, followed by PIPs (r=0.318-0.331, p<0.01) and MTPs (r=0.277-0.301, p<0.01). Similarly, the whole PD scores of MCPs also showed highest correlation with the disease activity (r=0.332-0.396, p<0.01), followed by PIPs (r=0.211-0.242, p<0.01), and then the least MTPs (r=0.198-0.222, p<0.01). In individual joint, GS score showed better correlation with disease activity than PD score. In 30 joints, MCP3 joint exhibited the highest correlation between GS score and DAS28-ESR (r=0.411, p<0.01), DAS28-CRP (r=0.459, p<0.01), SDAI (r=0.444, p<0.01). MCP2 joint exhibited the highest correlation between GS score and CDAI (r=0.421, p<0.01). While MCP5 joint exhibited the highest correlation between PD score and DAS28-ESR (r=0.353, p<0.01), DAS28-CRP (r=0.399, p<0.01), CDAI (r=0.368, p<0.01), SDAI (r=0.377, p<0.01). In 30 joints, PIP1 showed lowest correlation between GS (r=0.166-0.199, p<0.01)/PD (r=0.134-0.143, p<0.01) score and disease activity.
Conclusion: In small joints of RA patients, the ultrasound-detected synovitis of MCPs had best correlation with disease activity, compared with PIPs and MTPs. In individual joint, MCP2, MCP3, and MCP5 joint had the best correlation between ultrasound-detected synovitis and disease activity, while PIP1 joint showed lowest correlation.

REFERENCES

[1] Targońska-Stępniak B, Piotrowski M, Zwolak R, Majdan M. [Clinical and ultrasound assessment of the disease activity in patients with rheumatoid arthritis]. Wiad Lek. 2016;69(4):616-620.

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Disclosure of Interests: None declared
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AB1183 ULTRASOUND POWER DOPPLER AND GREY-SCALE JOINT INFLAMMATION: WHAT DO THEY REVEAL ABOUT RHEUMATOID ARTHRITIS?

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Background: Grey-scale (GS) and Power Doppler (PD) imaging are routinely performed when assessing rheumatoid arthritis (RA) joint inflammation using ultrasound (US). While PD vascularity is often regarded as an US feature of more active joint inflammation, the true clinical significance of GS joint inflammation in RA is less understood.
Objectives: To gain further insight into US PD and GS joint Inflammation through studying their relationship with two distinct, yet important outcome measures: (i) DAS28 – a disease activity measure and (ii) US-detected erosion - a structural joint damage measure.
Methods: In this cross sectional study, US PD and GS joint inflammation were graded semi-quantitatively (0-3), while bone erosion(s) was scored dichotomously (1=yes/0=no) at each joint recess. At the patient level, PD and GS scores were correlated with DAS28 and US erosion scores respectively using Pearson's correlation coefficient, while linear regression was used to characterize the relationship between variables.
Results: 1080 joints and 1800 joint recesses from bilateral elbows, wrists, MCPJs, thumbs' IPJs, PIPJs, ankles and MTPJs were scanned in 30 adult RA patients (baseline characteristics: 76.7% Chinese; 93.3% female; mean (SD) DAS28, 3.58 (1.20); mean (SD) disease duration, 70.3 (61.2) months). PD scores were correlated (r=0.46, P<0.0104) with DAS28 but not with US erosion scores. GS scores were correlated (r= 0.64, P<0.0001) with US erosion scores but not with DAS28 (table 1). Scatter plots for these variables are presented in Figure 1. Results of simple linear regressions showing PD as a predictor of DAS28 (coefficient (95% CI), 0.167 (0.048, 0.286); P=0.0104) and GS as a predictor of US erosion (coefficient (95% CI), 0.223 (0.125, 0.322); P=0.0001) are summarized in table 2.

Figure 1: Scatter plots for the ultrasound and clinical variables

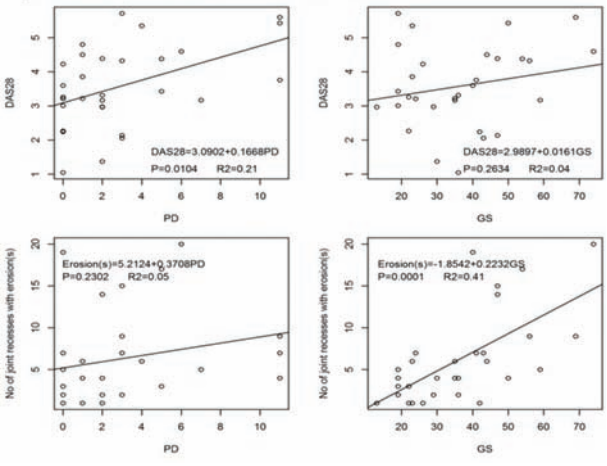


Figure 1

Conclusion: US PD and GS joint inflammation in RA were characterized using disease activity and structural joint damage outcome measures. PD joint inflammation is associated with disease activity and has moderate

correlation with DAS28. In contrast, GS joint inflammation is associated with structural joint damage and has strong correlation with US-detected erosion.

REFERENCES

[1] Backhaus M, et al. Guidelines for musculoskeletal ultrasound in rheumatology. Ann Rheum Dis 2001;60:641–9.

[2] Backhaus M, et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. Arthritis Rheum 2009;61:1194-201.

[3] Hammer HB, et al. Examination of intra and interrater reliability with a new ultrasonographic reference atlas for scoring of synovitis in patients with rheumatoid arthritis. Ann Rheum Dis 2011;70:1995–8.

[4] Wakefield RJ, et al. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. Journal of Rheumatology 2005;32(12):2485–7.

Abstract AB1183 Table 1. Pearson's correlation for the ultrasound and clinical variables

Variables	Correlation coefficient	P-value
Correlation with DAS28		
PD score	0.46	**0.0104***
GS score	0.21	0.2634
Correlation with number of joint recesses with ultrasound-detected erosion(s)		
PD score	0.23	0.2302
GS score	0.64	**0.0001*****

Statistically significant: * p<0.05; *** p<0.001

Abstract AB1183 Table 2. Linear regression for the ultrasound and clinical variables

Variables	Coefficient (95% CI)	P-value
Prediction of DAS28		
PD score	0.167 (0.048, 0.286)	**0.0104***
GS score	0.016 (-0.012, 0.044)	0.2634
Prediction of number of joint recesses with ultrasound-detected erosion(s)		
PD score	0.371 (-0.222, 0.963)	0.2302
GS score	0.223 (0.125, 0.322)	**0.0001*****

Statistically significant: * p<0.05; *** p<0.001

Disclosure of Interests: None declared

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AB1184 BONE MINERAL DENSITY, TRABECULAR BONE SCORE AND 3D-DXA ASSESSMENT IN ADULT PATIENTSWITH A POSITIVE AND NEGATIVE GENETICAL TESTING FOR HYPOPHOSPHATASIA

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Background: *Scarce evidence exists on the assessment of bone mineral density (BMD) in adult Hypophosphatasia (HPP). Recent studies suggest that* dual-energy X-ray absorptiometry *(DXA) could not* appropriately *predict their fracture risk and note the importance on further explore bone microstructure.*

Objectives: To evaluate BMD at the lumbar spine (LS) and proximal femur (PF) assessed by DXA, the trabecular bone score (TBS) at the LS and the fracture risk assessment (FRAX and adjusted by TBS, T-FRAX) in patients with persistent low alkaline phosphatase levels (ALP) and HPP genetically confirmed (HPP TG +) compared with a group of subjects with the same biochemical abnormality and a negative HPP genetic test (HPP TG-). As a secondary objective, to assess the cortical and trabecular bone at the PF using DXA-based 3D modeling.

Methods: Seventy-three subjects with persistent low ALP levels - at least two values < 35 IU/L and none > 45 IU/L - and a genetic test for HPP performed were included. Individuals were distributed into 2 groups according to their genetic status. BMD was measured using GE-LUNAR iDXA and TBS. The 3D-SHAPER software was employed in a subgroup of 52 subjects matched by age, gender and body mass index. A clinical questionnaire and a battery of lab measures to assess risk factors for Osteoporosis were also performed.

	HPP - GT	HPP + GT	P-VALUE
DEMOGRAPHICS			
Age (years ± SD)	48,2 ± 10,1	50,1 ± 14,1	0,516
Gender (Female, n/N, %)	29/35 (82,9%)	26/38 (68,4%)	0,182
Weight (kg ± SD)	63,15 ± 15,15	72,00 ± 13,62	0,016
Height (cm ± SD)	161,94 ± 8,67	164,37 ± 7,236	0,210
BMI (kg/m2 ± SD)	23,90±4,39	26,57 ± 4,08	0,011
BIOCHEMICAL DATA			
Alkaline phosphatase (UI/L)	33,2 ± 8,8	24,9 ± 6,9	0,0004
Serum calcium (mg/dl)	9,48 ± 0,39	9,49± 0,460	0,928
Urinary calcium (mg/24h)	145,15 ± 72,28	178,25 ± 69,6	0,053
Serum phosphate (mg/dl)	3,54 ± 0,5	3,886 ± 0,64	0,010
Urinary phosphate (mg/24h)	669,57 ± 181,65	752,66 ± 203,7	0,075
Vitamine D	23,11 ± 11,9	20,38 ± 9,65	0,285
PTH	47,8 ± 17,3	42,8 ± 22,04	0,296
DUAL X-RAY ABSORTIOMETRY			
Lumbar spine aBMD (g/cm2 ± DE)	1,157 ± 0,147	1,115± 0,148	0,233
Femoral neck aBMD (g/cm2 ± DE)	0,948 ± 0,155	0,864 ± 0,18	0,014
Wards aBMD (g/cm2 ± SD)	0,781 ± 0,161	0,695 ± 0,140	0,021
Trochanter aBMD (g/cm2 ± SD)	0,771± 0,147	0,750 ± 0,095	0,494
Diaphysis aBMD (g/cm2 ± SD)	1,174 ± 0,146	1,108 ±0,150	0,076
Total aBMD (g/cm2 ± SD)	0,981± 0,142	0,93±0,112	0,106
TRABECULAR BONE SCORE (TBS)			
Lumbar spine TBS	1,396 ± 0,094	1,363 ± 0,126	0,261
FRAX INDEX			
Major FRAX (%)	2,136 ± 1,84	3,058 ± 1,62	0,05
HIP FRAX (%)	,346 ± 0,87	0,84 ± 0,94	0,049
Major T-FRAX (%)	1,846 ± 0,947	3,496 ± 2,199	0,002
Hip T-FRAX (%)	0,15 ± 0,25	0,82 ±0,883	0,001
3D-SHAPER * * performed in a subgroup of 52 subjects (26 per subgroup) with no differences in gender, sex and BMI			
Total cortical vBMD (mg/cm2 ± DE)	167,3 ± 25,3	155,8 ± 19	0,070
Cortical vBMD (mg/cm3 ± DE)	873,6 ± 84,4	819,4 ±-95,3	0,035
Trabecular vBMD total (mg/cm3 ± DE)	179,1 ± 39,2	161,6 ± 39,9	0,117
Integral total vBMD (mg/cm3 ± DE)	340,9 ± 51,1	313 ± 58,9	0,074

Figure 1

Results: Demographic, densitometric, TBS and 3D-DXA parameters are shown in table 1. Of the 73 subjects included, 38 (52%) had pathogenic mutations in ALPL. Between postmenopausal women and men above 50 years, 9 subjects (29%) with ALPL mutations had osteopenia and 4 (13%), osteoporosis whereas 4 (13%) and 2 (6,5%) were detected in the HPP-GT group, respectively (p>0,05). Between premenopausal women and men under age 50, only 2 (5%) showed low BMD (Z-score < -2). BMD at femoral neck was significantly lower in the HPP + GT group compared to the HPP- GT group (0.864 ± 0.18 vs 0.948 ± 0.16 (p=0.014), similar findings were found for Wards area (0.695 ± 0.14 and 0.781 ± 0.16, p=0.021) and a trend was observed at the femoral diaphysis (p=0,076). BMD at the LS and TBS assessment did not show differences. Major, hip FRAX and T-FRAX were superior in the HPP + GT group. In terms of the parameters of bone metabolism, ALP levels were lower in the HPP + GT (p= 0.0004), serum phosphate levels were higher in this group (p=0.01) and the rest did not show differences. The 3D-SHAPER software was applied in a subgroup of 52 subjects: volumetric BMD at the PF was lower in the HPP + GT (873,6 ± 84,4 g/cm^3 vs 819,4 ± 95,3 g/cm^3; p = 0.035) with no differences in trabecular vBMD (p=0.117).

Conclusion: HPP + GT group showed less BMD at femoral neck and wards area and this trend was also observed at the diaphysis. At the femur, vBMD was also lower in this group. No differences in BMD at the lumbar spine and in TBS were found. These findings and its value for predicting the risk of fractures, specially in atypical femoral fractures, must be elucidated.

Disclosure of Interests:: Carolina Tornero: None declared, Monica Coronado: None declared, Ludovic Humbert: None declared, Sara García-Carazo: None declared, Carmen Lancha: None declared, Domenico Monachello: None declared, Luis Dominguez-Gadea: None declared, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Pilar Aguado: None declared

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AB1185 RADIOLOGICAL INDEX IN THE FLAT VERTEBRAE

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Background: Spine is a mechanical structure, which disposes their vertebral bodies in harmony with their stature, and progressively increasing in magnitude from the cervical to the lumbar spine (1). Defects in type II collagen gene are described, and in these cases, flat vertebra can be found, defined with flattening of the vertebral body, with irregular surface

or with nodules of Schmorl, in isolation or in a maximum of two vertebral bodies, to distinguish it from Scheuermann's disease (2). Image 1.
Objectives: Current vertebral indexes, don´t measure a relation between a person height and his vertebra, and if the harmony of the individual is accepted, an index that combines these variables must be created in order to guaranteeing the objectivity of the resultant value.



Image 1: MRI of the spine with two dorsal flat vertebrae (7th and 8th) in which their vertebral bodies do not get larger farther down the colum, showing disproportion in relation to immediately above and below vertebrae.

Figure 1

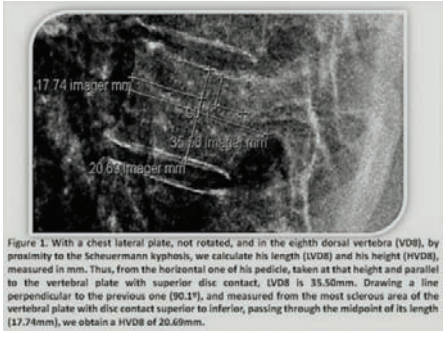


Figure 1. With a chest lateral plate, not rotated, and in the eighth dorsal vertebra (VD8), by proximity to the Scheuermann kyphosis, we calculate his length (LVD8) and his height (HVD8), measured in mm. Thus, from the horizontal one of his pedicle, taken at that height and parallel to the vertebral plate with superior disc contact, LVD8 is 35.50mm. Drawing a line perpendicular to the previous one (90.1º), and measured from the most sclerous area of the vertebral plate with disc contact superior to inferior, passing through the midpoint of its length (17.74mm), we obtain a HVD8 of 20.69mm.

Figure 2

Methods: Patients attending physician since 1994, both sexes, 20-55 years old, in whom Type II collagen disease or vertebral dysplasia was suspected, were selected for the study. A control group was created from patients that didn´t fulfill the last inclusion criteria. Their medical histories were taken. Eighth dorsal flat vertebra in a lateral chest radiograph were assessed by tripleobserver (two rheumatologists and one radiologist) according to the defined criteria. In all selected patients, a DEXA osteoporosis screening was performed, being chest trauma exclusion criteria.
Finally, a descriptive study was carried out and a comparative study of average of vertebral index of the eight dorsal vertebra (VIDV8) results was applied: VIDV8 = 10 x LVD8/(HVD8 x stature). Image 2.
Results: 174 subjects were analyzed, 84 in the study group and 90 in the control one, both homogeneous and without statistically significant differences in sex, age and height, with an average value in the study group of 47.15 years old, 48.8% women, 80.5 kg and 1,64 m. In control group: 44.5 years old, 52.2% women, 78.5 kg and 1,65 m. The VIDV8 value, did not show any significant difference compared to the previous variables, except for patient cohort, with an average value of 10.1 Meters-1 in control group, and 12.5 Meters-1 in pathological one ($p < 0.001$). To a value of 11,108 Meters-1 the sensitivity is 90.5% and specificity 92.2%.
Conclusion: The VIDV8 is stable for the variables sex, age, height, and weight. To an outcome of 11,108 Meters-1, it discriminates both groups with sensitivity of 90.5% and specificity of 92.2%, in order to avoid the ambiguity of the explorer.

REFERENCES

[1] .White AA, Panjabi MM. Clinical Biomechanics of the Spine. 2nd ed, Lippincott Williams & Wilkins, 1990.
[2] Rimoin DL, Lachman RS; The condrodysplasias, Practise of Medical Genetics. Edited by AEH Emery, DL Rimoin. New York, Churchill Livingston, 1990.

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AB1186 **PELVIC CT CONTRIBUTIONS FOR EARLY DIAGNOSIS OF INFECTIOUS SACRO ILIITIS**

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Background: The sacroiliac joint is a rare localization of septic arthritis whose diagnosis is often delayed due to a heterogeneous and non-specific clinical presentation. The gold standard for diagnosis in osteo-articular infections is MRI, but its emergency access is sometimes difficult and the acquisition time of this imaging mode is long.
Objectives: To look for early CT scan signs suggestive of infectious sacro iliitis.
Methods: In a monocentric retrospective study at the Besançon University Hospital between January 2013 and March 2018, we analyzed the cases of septic arthritis of the sacroiliac joints in subjects over 18 years of age. We studied the clinical, biological and imaging data of each patient.
Results: 7 cases of infectious sacro-iliitis were collected. The characteristics of the patients were: 57% male, average age 44.1 years, left sacroiliac in 4 cases, fever in 57%, average CRP 184mg/l, average leucocytes 12500/ml. 3 patients were immunocompromised, 1 patient was postpartum. In 5 cases, bacteriological documentation was found (1 multisensitive aureus staphylococcus, 2 streptococci, 2 Gram negative bacilli). In the last 2 cases, no germ could be detected due to antibiotic therapy initiated before their hospitalization, but the clinical presentation, biology, imaging and evolution under antibiotics were in favour of an infectious etiology. The 7 patients underwent a pelvic CT scan during their hospitalization, on average 6 days after the beginning of their symptoms. 4 early signs in favour of the diagnosis of infectious sacro iliitis could be identified: fat infiltration in front of the sacroiliac joint in 86% of cases, bulging and elevation of the anterior part of the joint capsule in 43%, swelling of the piriform (71%) and iliac (71%) muscles on the sacroiliac side. All patients had at least 1 positive sign out of 4, 86% had at least 2. In 1 case, signs of osteitis were present. In 4 out of 7 cases, the injection of iodized contrast medium did not provide any additional element compared to the non-injected sequences. 5 patients underwent an MRI after the scan, which confirmed the signs in favour of the infectious nature of sacroiliitis. MRI detected in one case an aspect of osteomyelitis of the sacrum and iliac bone, but also a hypersignal of the joint space on the T2 sequences (80%) and a better visualization of abscesses.
In the literature, there is data on the interest of the CT scan for the diagnosis of infectious sacro iliitis (1) but there is no precise description of the early signs suggestive apart from the signs of osteitis, which appear later. Hermet et al (2) advised to be careful if the scan is performed within 3 days after the onset of symptoms, but our short series shows that some signs are positive even if the pelvic scan is performed very early. The interest of the scanner, in addition to its rapid access and acquisition, allows on the injected sequences to rule out differential infectious diagnoses of abdominal-pelvic or gynaecological origin, the clinic being sometimes put in defect.
Conclusion: Despite its radiant nature, the scanner can be a preferred accessible alternative to MRI for the diagnosis of infectious sacro iliitis with the detection of 4 signs of early onset.

REFERENCES

[1] Matt M,et al. Med Mal Infect 2018; pii: S0399-077X(16)30754-5.
[2] Hermet M, et al. BMC Infect Dis 2012;12:305.

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AB1187 **IMPACT OF IN-CLINIC ULTRASOUND ON AGE AND GENDER OF PATIENTS SCANNED AND DETECTION OF SYNOVITIS – RESULTS FROM A QUALITY IMPROVEMENT PROJECT**

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Background: Inflammatory arthritis is more common in women, and the majority of patients have onset before the 6th decade. Synovitis can be difficult to diagnose clinically in the early stages, and can be especially easy to miss where the index of suspicion is low, such as men and the elderly. Ultrasound (US) can confirm synovitis and other conditions in Rheumatology, particularly where examination features are not very obvious. US has traditionally been offered via Radiology services in our hospital as a separate appointment following referral from the

Rheumatology clinic, with variable waiting times causing potential delay in starting treatment such as DMARDs. There is also a cost implication with respect to commissioning of the Radiology scan appointments. In Bolton, an US system was installed in Rheumatology from 2016 to perform in-clinic US, for improving access and reducing referrals to Radiology.

Objectives: We aimed to assess the US usage pattern before and after the new Rheumatology US was installed, with respect to access based on age and gender, the pattern of scanning in-clinic, and rate of synovitis diagnsosis, using a quality improvement framework.

Methods: US referral data from the Radiology department from October 2015 to March 2016 were collated as baseline on a MS Access database. Two Consultant Rheumatologists performed US in-clinic. From May to October 2016 Rheumatology in-clinic data, and also Radiology referral data were collated on the database for comparison. Patient demographics and diagnoses were collated from clinic letters. Descriptive statistics were processed in MS Excel 2010.

Results: Between October 2015 and March 2016, 68 patients (median age 52 yrs; 28% male) had scans in Radiology. Between May and October 2016, 59 patients (median age 60 yrs; 21% male) had scans in Radiology, and 78 patients (median age 59yrs; 35% male) had scans in Rheumatology clinic. There was no significant difference in scanned areas amongst the three cohorts with the most common overall being hand/wrist area (n=57, 54 and 61 respectively; total 84%), followed by foot/ankle (n=6, 4 and 4 respectively; total 7%). Between the two time periods, there was an increased trend in final working diagnoses of inflammatory arthritis (28 [41%] vs 36 [61%] and 39 [50%] in the 3 cohorts respectively); and a decreasing trend in the final working diagnoses of non-inflammatory conditions (OA, FM, other non-inflammatory pain: 36 [53%] vs 22 [37.3%] and 28 [35.9%] in the 3 cohorts respectively).

Conclusion: The availability of Rheumatology US was associated with increased propensity for scanning older patients and a greater proportion of men compared to previously, a qualitative improvement as synovitis diagnosis could be delayed in these groups. The introduction of Rheumatology US was also associated with a trend towards higher proportion of inflammatory diagnoses, suggesting potentially increased appropriate clinical use due to availabiltiy in-clinic. This is supported by the majority being hand/wrist scans, suggesting Rheumatology use is mainly aimed at diagnosing synovitis. Although there was a modest reduction of 13% in Radiology referrals between the two time periods, there was an overall increase of scans performed by 101% following introduction of the Rheumatology US service. We therefore recommend Rheumatology in-clinic US provision, as in addtion to obvious improvement in time to diagnosis, it is likely to increase the range of patients able to access US eg older patients and men, and also likely to increase the pick-up rate of synovitis by improving patient selection.

Disclosure of Interests: None declared

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AB1188 AUDIT: IMPACT OF MUSCULOSKELETAL ULTRASOUND USE IN RHEUMATOLOGY CLINICS

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Background: Musculoskeletal ultrasound (MSUS) has assumed a prominent role in rheumatological practice as both a diagnostic and monitoring tool.[1] It has utility in excluding and quantifying active synovitis and can be used to guide adjustments of therapies.[2,3]

Objectives: We aimed to observe impacts on clinical practice of utilising ultrasound (US) scanners in outpatient clinics in a district general rheumatology service. We were particularly interested to see if this affected treatment choices, follow-up plans and referrals for radiological investigations.

Methods: US scanners were obtained and used by 2 rheumatology consultants with previous ultrasound training. Scanning was performed during standard 20 minute appointments within general rheumatology outpatient clinics. No extra time was allocated. Over 8 weeks, we completed questionnaires for each scan and assessed the impact on management decisions.

Results: Over 8 weeks, data was collected for 36 consecutive patients scanned. Commonly imaged joints were hands (81%,n=29), wrists (75%, n=27), feet (19%, n=7), and ankles (14%, n=5).

Most common patient diagnoses were osteoarthritis (n=13, 36%), rheumatoid arthritis (n=10, 28%) and psoriatic arthropathy (n=6, 17%). The remaining patients had diagnostic labels including undifferentiated inflammatory arthritis or no formal diagnosis. Abnormalities suggesting active inflammation were seen in 42%. In 33% osteoarthritic changes were observed, erosions were seen in 5%. 20% scans were normal.

US altered the management in 58% (n=21/36) of cases. These alterations to management included: drug added(n=5), drug stopped(n=3), dose increase (n=1), joint injection (n=3), intramuscular injection (n=2). Of the medications added, 3 were DMARDs, 1 was a biologic therapy and one case was not specified. The medications stopped were all DMARDS.

US use in clinic prevented radiological investigation in 72% (26/36) of cases. These were radiology ultrasound (n=23) and MRI (n=3). Hands and wrists scans accounted for 86% of these.

US altered the follow up in 56% (20/36) of cases. Of these, 40% (8/20) were reviewed earlier, and 40% (8/20) of patients were discharged based on ultrasound information.

In 16/36 patients, US did not alter management. The average time taken to scan in clinic was 7 minutes per patient. The median time was 5 minutes, with the average skewed due to a few prolonged scans of multiple anatomical areas.

Conclusion: This audit has demonstrated that US use has impacted on our clinical practice. We identified patients to be seen earlier and altered management based on US findings.

US use also prevented radiological investigations in 72% of cases. This has positive impacts on staffing, finances, radiology department capacity and patient convenience. Furthermore, we were able to discharge 40% of patients who otherwise would have been recalled.

Overall, we believe this audit shows positive impacts of MSUS on patient care. Challenges include time pressures of scanning in clinic, time and cost implications of ultrasound training and the need to standardise and record ultrasound methods and findings consistently. Costs are offset by savings to radiology resources and increased discharges. We plan to expand ultrasound usage and train our colleagues to employ ultrasound for our patients.

REFERENCES

[1] Möller I, Janta I, Backhaus M, et al. The 2017 EULAR standardised procedures for ultrasound imaging in rheumatology Annals of the Rheumatic Diseases 2017;76:1974-1979.

[2] Alivernini S, et al. Tapering and discontinuation of TNF-alpha blockers without disease relapse using ultrasonography as a tool to identify patients with rheumatoid arthritis in clinical and histological remission. Arthritis Res Ther18:39.

[3] Bawa S, Todd M, France J SAT0203 Optimization of biologic tapering using ultrasound in ra patients *Annals of the Rheumatic Diseases* 2018;77:962.

Disclosure of Interests: Andrew Wilkinson: None declared, Mike Reed Speakers bureau: Paid to speak at meeting by Novartis, Sara Else Consultant for: Contributed to advisory boards for: Abbvie, Norartis, Roche and Chungai Pharma., Speakers bureau: Paid to organise and chair meetings, and speak at educational events by following companies: BMS, Celegene, Grifols, Jansess, MSD, Novartis, UCB.

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AB1189 THE IMPORTANCE OF POSITRON EMISSION TOMOGRAPHY-COMPUTED TOMOGRAPHY (PET -CT) IN FEVER OF UNKNOWN ORIGIN (FUO) AND INFLAMMATION OF UNKNOWN ORIGIN (IUO)

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Background: Fever of unknown origin (FUO) and inflammation of unknown origin (IUO) are rare clinical problems but diagnostically challenging for clinicians. Patients are exposed to extensive and expensive medical examinations for the identification of the FUO/IUO. FDG PET-CT can help to identify the underlying disease in these patients.

Objectives: The aim of this study was to evaluate the role of PET-CT in patients with FUO/IUO and to identfy FDG uptake sites and patterns

Methods: Total of 286 patients who were performed 18F FDG-PET-CT between Jan 2014 and Dec 2017 were evaluated, retrospectively. There were a total 62 patients scanned by PET-CT for FUO/IUO. Definitive diagnosis, PET-CT patterns, organ involvement and SUVmax values in these patients were reevaluated

Results: Rheumatic disease in 27 patients (43.5%), 20 malignancy (32.3%) and 6 infectious diseases (9.7%) were diagnosed in the FUO/IUO patients performed PET-CT scan. Systemic vasculitis were the most frequently diagnosed rheumatic disease. 11 patients of the 62 patients (17.7%) were diagnosed large vessel vasculitis (9 Takayasu arteritis, 2

Temporal arteritis). Significant vascular FDG involvement was detected (77.7%) in these patients. 4 of 7 patients diagnosed Takayasu arteritis were not seen any pathological finding in the other imaging modalities.
Vascular FDG uptake ($p < 0.001$) was statistical significantly higher in the patients diagnosed with rheumatic disease whereas lymph node ($p = 0.013$) and bone ($p = 0.005$) FDG uptake were significantly higher in patients with malignancy. Patients with malignancy had the highest SUV-max mean value ($p < 0.001$).
Conclusion: Our findings reveal that PET-CT is a useful imaging modality in the FUO/IUO patients. Inflammatory diseases, especially large vessel vasculitis, should be considered in addition to malignancies in these patients, and subclinical inflammation in the blood vessel can be visualised by PET -CT
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7085

AB1190 EXTENDED POLY-DIMENSIONAL IMMUNOME CHARACTERIZATION (EPIC): A WEB-BASED IMMUNE REFERENCE ATLAS OF THE HEALTHY HUMAN IMMUNOME AND A TOOL FOR TRANSLATIONAL MEDICINE

Joo Guan Yeo[1,2], Lu Pan[1], Martin Wasser[1], Pavanish Kumar[1], Thaschawee Arkachaisri[2,3], Su LI Poh[1], Fauziah Ally[1], Jing Yao Leong[1], Kee Thai Yeo[1,2], Liyun Lai[1], Angela Yun June Tan[2], Salvatore Albani[1,2]. *[1]Translational Immunology Institute, SingHealth/Duke-NUS Academic Medical Centre, Singapore, Singapore*; *[2]KK Women's and Children's Hospital, Singapore, Singapore*; *[3]Duke-NUS Medical School, Singapore, Singapore*

Background: An atlas of the developing immune system will not only improve our understanding of normal immune ontogenesis but more importantly, aid in our identification of disease-associated cell subsets. However, such a resource is still unavailable despite accessibility to technologies like mass cytometry due to the general focus on specific cell subsets or ages. There is a critical unmet need for standardized datasets depicting at single cell level and with high dimensionality the entire developmental gradient of the healthy immune system from the neonatal to adult age.
Objectives: We aim to provide a detailed depiction of the architecture of the human healthy Immunome across an entire age gradient.
Methods: We have created a high dimensional atlas of the healthy human immunome (EPIC: Extended Poly-dimensional Immunome Characterization) by interrogating the peripheral blood mononuclear cells (PBMC) of over 200 healthy subjects, ranging from cord blood to adult age, with 63 unique mechanistic and phenotypic markers per cell by mass cytometry (CyTOF). The EPIC analytical and visualization pipeline is based on an open source web-based R Shiny bioinformatics toolkit that allows it to be easily accessible to the research community.
Results: EPIC can be mined in various ways, for instance to follow developmental changes of any given cell subset or to depict the architecture of the Immunome at any given age range. For example, transition developmental milestones were observed in the TNFα+ CD4+ T cells where the size of its memory subset would exceed its naive subset at 8 year old. There was a significant reduction and increase in the frequency of the naive and memory TNFα+ CD4+ T cells with a Spearman's correlation coefficient, rho, of -0.4662 and 0.4164 respectively. More importantly, we have built and will keep developing datasets from various immune mediated diseases using the same approach. Consequently, by providing the healthy standard, EPIC enables the depiction and dissection of disease-dependent perturbations of the Immunome architecture.
Conclusion: EPIC provides a transformational conceptual advance in Translational Immunology from individual subset focused to immune architecture based approach for the understating of physiology and pathogenesis of immune mediated mechanisms. We intend to make EPIC available to the entire community in its full capacity.

REFERENCES

None

Disclosure of Interests: Joo Guan Yeo: None declared, Lu Pan: None declared, Martin Wasser: None declared, Pavanish Kumar: None declared, Thaschawee Arkachaisri Speakers bureau: Abbvie Pte, Ltd, Su Li Poh: None declared, Fauziah Ally: None declared, Jing yao Leong: None declared, Kee Thai Yeo: None declared, Liyun Lai: None declared, Angela Yun June Tan: None declared, Salvatore Albani: None declared
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AB1191 DIFFERENTIAL DIAGNOSIS OF SERONEGATIVE ARTHRITIS: DIAGNOSIS ONE YEAR FOLLOW UP AFTER FIRST DIAGNOSIS

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Background: The ACR/EULAR classification criteria (AECC) for rheumatoid arthritis (RA) is well known criteria for early diagnosis of RA with high sensitivity. However, the criteria weigh three points for seropositive, thus automatically subtracted 3 points for seronegative arthritis. Recently, elderly onset RA is increasing, that has relatively higher ratio of seronegative than young onset RA.
Objectives: To compare diagnosis of seronegative arthritis between initial and second diagnosis after one year follow up.
Methods: Arthritis patient who are sustained for more than one year since first refer despite his/her ACPA or Rheumatoid Factor were negative, were collected. From these patients, difference from initial diagnosis to second after one year follow up was evaluated statistically with chi square test. Mean EACC score and mean involved joint count for large and small joint (LJC and SJC) at initial diagnosis were compared with each of second diagnosis statistically with Mann Whitney U test (MWU).
Clinical course evaluated with 28-joints disease activity score (DAS28) and Health Assessment Questionnaire Disability Index (HAQ-DI) for each diagnosis was compared at every other 3 months with MWU. Comparison between 475 seropositive RA patients treated in the same institute and seronegative RA in the study was also evaluated in a same manner.
These patients' sensitivity and specificity (Sens & Specs) in according with 1987 ACR diagnosis criteria (1987ACR) was also evaluated and compared with Sens & Specs of AECC.
Results: Ninety-six patients were enrolled. In these, RA was diagnosed to 18 patients and 78 were unclassified arthritis as first diagnosis. Second diagnosis of these patients were RA for 41, spondyloarthritis (SpA) for 22, other collagen disease (CD) for 5, osteoarthritis (OA) for 9, hypothyroidism (HTh) for 2, non-tuberculotic mycobacterium (NTM) for 1, and unclassified arthritis (UA) for 16. Mean EACC score and range for each second diagnosis was 5.2 and 2 to 7, 4.4 and 3 to 7, 4.4 and 3 to 5, 5.0 and 4 to 6, 4.0 and 4, 4.0, and 4.25 and 3 to 5, for RA, SpA, CD, OA, HTh, NTM, and UA, respectively. There is no significant difference between any pair of second diagnoses. LJC and SJC of each second diagnosis was 3.2 and 9.8, 5.7 and 4.8, 2.4 and 4.8, 2.4 and 8.1, 2.0 and 6, 2 and 2, and 1.8 and 5.9, for RA, SpA, CD, OA, HTh, NTM, and UA, respectively. There is also no significant difference between any pair of second diagnoses (Table).
In clinical course, there is no significant difference between the second diagnoses, and also no significant difference between seropositive and seronegative RA.
In these seronegative arthritis patients, Sens & Specs of RA in accordance with 1987ACR were 75.0% and 43.4%, while 83.3% and 66.7% in accordance with AECC.
Conclusion: Diagnosis of seronegative RA is not uncomplicated, whereas rheumatologist's diagnostic skill is questioned.

Table: Comparison between second diagnosis

Second diagnosis	First diagnosis	N	AECC	Joint point	LJC	SJC
RA	RA(15), UA(26)	41	5.2	3.7	3.2	9.8
SpA	RA(1), UA(21)	22	4.4	3.0	1.9	5.7
CD	UA(5)	5	4.4	2.8	2.4	4.8
OA	RA(2) OA or UA (7)	9	5.0	3.4	2.4	8.1
HTh	UA(2)	2	4.0	3.0	2.0	6.0
NTM	UA(1)	1	4.0	2.0	2.0	2.0
UA	UA(16)	16	4.25	3.0	1.8	5.9

Disclosure of Interests: None declared
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AB1192 **CLINICAL APPLICATION OF 18F-FDG PET/CT IN RHEUMATIC DISEASES**

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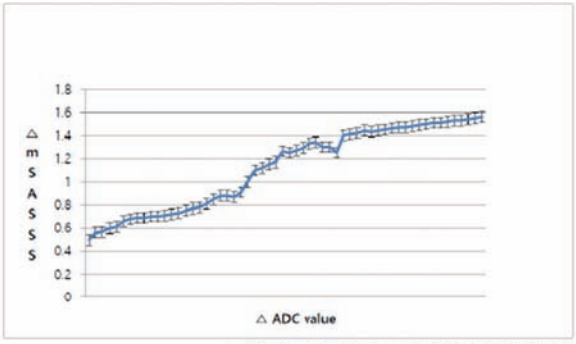
Background: ^{18}F-Flurodeoxyglucose Positron Emission Tomography/Computed Tomography (^{18}F-FDG PET/CT) is widely used in diagosing malignant diseases. It is also useful applying to autoimmune diseases.
Objectives: To investigate the clinical application and significance of ^{18}F-Flurodeoxyglucose Positron Emission Tomography/Computed Tomography (^{18}F-FDG PET/CT) in rheumatic diseases.
Methods: Patients who underwent ^{18}F-FDG PET/CT in the Department of Rheumatology and Immunology, Peking University People's Hospital from January 2012 to July 2018 were retrospectively analyzed for clinical application and imaging characteristics of ^{18}F-FDG PET/CT in rheumatic diseases.
Results: 1. From 2012 to 2018, 459 patients underwent ^{18}F-FDG PET/CT examination in the Department of Rheumatology and Immunology, accounting for 5.79% of the total number of PET/CT examinations in the hospital. Further analysis of 415 patients with complete data, including 158 males (38.07%) and 257 females (61.93%), male to female ratio of 1:1.6, average age of patients are (57 ± 16.2) years old. The highest proportion group of patients is from 45 to 65 years old (201/415, 48.43%). The total number of PET-CT examinations in the whole hospital increased year by year. Compared with 2012, the number has increased nearly 10 times in 2017 among patients in the Department of Rheumatology and Immunology. 2. In patients with rheumatic diseases, major purpose of PET/CT examination included exclusion of tumors, diagnosis, and assessment of the disease activity. 3. Of all the 459 patients, 315 cases may indicate the differential diagnosis of the disease, of which 269 (85.4%) were highly suggestive of rheumatic clinical diagnosis, including 55 cases of vasculitis (17.46%), 54 cases of myositis (17.14%), 34 cases of rheumatoid arthritis (10.79%), 30 cases of Sjogren's syndrome (9.52%), 27 cases of adult still's disease (8.57%), 25 cases of systemic lupus erythematosus (7.94%), 25 cases of IgG4-related diseases (7.94%), 10 cases of rheumatic polymyalgia (3.17%) and 6 cases of systemic sclerosis (1.9%); the remaining 46 cases (14.6%) only suggested the possibility of autoimmune diseases.
Conclusion: Rheumatic diseases are complex and diverse, and it is difficult to diagnose. The application of ^{18}F-FDG PET/CT in the diagnosis of diseases is increasingly widespread. The results of this study suggest that ^{18}F-FDG PET/CT to some extent has significance in the classification and diagnosis of rheumatic diseases, especially for the exclusion of malignant tumors.
Disclosure of Interests: None declared
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AB1192B **DIFFUSE WEIGHT IMAGE IS A POTENTIAL MAGNETIC RESONANCE SEQUENCE IN THE PREDICTION OF SPINAL SYNDESMOPHYTE IN YOUNG PATIENT WITH ANKYLOISNG SPONDYLITIS**

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Background: Diffusion-weighted imaging (DWI) is an MRI sequence and has been shown to have advantages over standard MRI sequences in some clinical settings, such as early diagnosis of ischemic stroke and in staging some type of cancers. Different measures of diffusion have been proposed, with the apparent diffusion coefficient (ADC) measure the most widely used. Severe Inflammation leads to higher ADC values through increased water in extracellular, less constrained, spaces. Several studies have investigated the clinical utility of DWI in AS, with suggestive evidence that this sequence has valuable discriminatory capacity between AS and non-inflammatory back pain by inflammation degree on sacroiliac joint (SIJ).

Table 1. Scatterplots of the correlation between ADC value by MR DWI and the radiographic spinal progression over 4 years.



mSASSS: modified Stoke Ankylosing Spondylitis Spine Score.

Table 2. The univariate and multivariate analysis of affecting factor for new spinal syndesmophyte

variate	Univariated anylysis		Multivariated analysis	
	OR (95%)	p-value	OR (95%)	p-value
ADC value	3.88 (0.76-4.25)	0.03	2.02 (0.89-3.56)	0.01
AS-DAS	2.01 (0.52-2.28)	0.04	1.01 (0.56-2.65)	0.09
BASDAI	0.89 (0.78-1.02)	0.03	0.67 (0.34-1.78)	0.08
BASMI	0.58 (0.52-1.22)	0.09	0.88 (0.59-1.88)	0.34
BASFI	0.31 (0.11-0.68)	0.13	0.34 (0.12-0.78)	0.12

Table 1

Objectives: This study was tested the potential capacity of ADC value estimated by DWI on SIJ as the predictor of new spinal syndesmophyte in young patients with ankylosing spondylitis (AS).
Methods: The 58 patients who fulfilled the ASAS axSpA criteria were enrolled and their age was 18-23 years old. All subjects underwent MRI on SIJ with oblique coronal images parallel to the long axis of the sacrum (fast spin-echo T1WI and STIR) at diagnosis and lumbar spine radiograph at diagnosis, 2 and 4 years sequentially. The ADC value on SIJ measured by DW-MRI at diagnosis and spinal radiographs were scored using the stoke AS Spinal Score (SASSS) at diagnosis, 2 and 4 years continuously. All patients were underwent a detailed clinical evaluation, including the serum erythrocyte sedimentation rate, C-reactive protein, BASDAI, BASMI and BASFI. The univariate and multivariate logistic regression analysis was performed to identify that ADC value on SIJ had an important influence on spinal syndesmophyte growth.
Results: The ADC value on SIJ showed a positive association with inflammatory marker such as, ESR and CRP, but no association with BASDAI, BASMI and BASFI. However, AS-DAS showed a positive association with ADC value. The high ADC value showed more strongly associated with high SASSS over 2 and 4 years continuously. The univariate logistics analysis showed ADC value and AS-DAS were significant predictors for new spinal syndesmophyte. However, multivariate logistics analysis showed the high ADC value had the highest risk of developing new syndesmophytes in spine.
Conclusion: This study showed that the inflammation of AS patient was a positive association with ADC value on SIJ by DW-MRI and the measured the ADC value on SIJ by DW-MRI was the modest discriminating capacity method for predicting development of new spinal syndesmophyte in young AS patients.

REFERENCES

[1] Sequence in the Diagnosis of Ankylosing Spondylitis Diffusion-weighted Imaging Is a Sensitive and Specific Magnetic Resonance Robinson, Nivene Saad, Kim-Anh Lê Cao and Matthew A. Brown Linda A. Bradbury, Kelly A. Hollis, Benoît Gautier, Sateesh Shankaranarayana, Philip C. J Rheumatol 2018;45;771-778

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Public health, health services research, and health economics

AB1193 OBSERVATIONAL PROSPECTIVE COHORT STUDY TO EVALUATE EFFICACY AND SAFETY OF TAPENTADOL IN PATIENTS WITH RESPIRATORY DISEASE

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Background: Chronic pain analgesia is a concern in clinical practice in rheumatic patients, especially when the intensity is severe. In this case opioids are indicated but also contraindicated in cases of important respiratory depression and, therefore, must be administered with caution to patients with respiratory disease (1). Many of our patients are not in the condition of severe respiratory depression although they present plurypathologies, which could be triggered at the use of certain doses (2). For this reason, it is important the existence of a study that shows that tapentadol is safe in pluripathological patients when used at regular doses in clinical daily practice in Reumathology (3).
Objectives: Single site, non-postmarketing observational study. The main objective is to evaluate the safety of tapentadol prolonged release (TPR) 50 mg/12h, measured as tolerance ("good", "bad" or "not too bad") and by the comparative analysis of gradients between both groups of the study (control group and pathological group), the basal oxygen saturation, and after the dose of TPR (basal pulse oximetry minus the mean of the oxygen saturation after 30 days of study).
Methods: Inclusions criteria arepatients with severe chronic pain (Visual Analogical Scale, VAS>4) diagnosed from mild to severe chronic obstructive pulmonary disease (COPD) (spirometry after bronchodilatation with forced expiratory volume (FEV)/forced vital capacity (FVC)< 70% and FEV1=50%), and/or obesity, and/or controlled asthma and/or other conditions likely to produce respiratory depression with opioids (pathological group). Exclusion criteria consists in basal oxigen saturation measured by the pulse oximeter inferior to 92%. A descriptive analysis of variables and a comparison of the means were performed.
Results: 29 patients; 12 in control group and 17 pathological group (obesity: 9, controlled asthma: 3; mild to moderate COPD: 7; other pathologies: 7). Overall, the type of pain was nociceptive 59%, neuropathic 21% and mixed 20%; mainly women (67%), caucasic race (92%), median age 60 years old, and with 93% good tolerability and 97% good treatment adherence. Concerning results per groups, at control group, VAS mean, arterial pressure (AP), oxygen saturation (SO2) and heart rate (HR) before and after treatment. 8,3 vs 5,8; 127/74 vs 124/73 (mmHg); 95,6 vs 95,7 (%); 76 vs 73 (bpm). In the pathological group: 7,5 vs 5,6; 131/82 vs 127/78 (mmHg); 96 vs 95,5 (%); 75 vs 76 bpm. Regarding the results as per gradients between groups, no statistically significant differences were found, except for VAS, (p=0,00008). There were no cases of decrease of the oxygen saturation below 92% along the study.
Conclusion: The results support the safety of tapentadol from the respiratory point of view, measured by oxygen saturation, since no statistically significant differences were found between both groups, and, due to the excellent tolerability, as no clinical data showed signs of hypercapnia. No statistically significant differences were found in the oxygen saturation between both groups with the intake of TPR, with excellent tolerability and treatment adherence. There were no cases of decrease of the oxygen saturation below 92% along the study.

REFERENCES

[1] Carr DB, How prevalent is chronic pain?. Pain clinical updates 2003; (11) 2:1-4
[2] Breivik H, ColletB, Ventafridda V, Cohen R, Gallacher, D. Survey of chronic pain in Europa: Prevalence, impact on daily life, and treatment. Eur J Pain 2006; 10 (4) 287-333
[3] Ficha Tecnica Palexia® Retard.

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AB1194 KNOWLEDGE AND PERCEPTIONS OF PORTUGUESE FAMILY PHYSICIANS TOWARDS ANKYLOSING SPONDYLITIS: RESULTS FROM THE ASSESSMENT OF RESULTS IN ANKYLOSING SPONDYLITIS(AREA) STUDY

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Background: Ankylosing spondylitis (AS) patients have a significant delay between symptom onset and disease diagnosis, reaching on average 7 to 10 years in developed countries. Understanding the reasons behind this delay is essential to reduce the individual and socio-economic burden of the disease.
Objectives: To assess knowledge and perceptions of Portuguese family physicians (FP) towards AS and determine whether these contribute to the diagnostic delay at the primary care level.
Methods: The Assessment of REsults in Ankylosing spondylitis (arEA) study was developed by the NOVA-Information Management School (Lisbon) in collaboration with the Portuguese Society of Rheumatology, the Portuguese Association of Family Physicians (APMGF), the National Association of Primary Care Units (USF-AN), the National Association of AS Patients and the Portuguese League Against Rheumatic Diseases. The arEA aimed at assessing reasons for delayed diagnosis of AS, as well as disease impact in patients' lives, global health and work. A comprehensive online survey was developed and sent to FP associated with APMGF and USF-AN, collecting data on demographics, global knowledge and diagnostic and treatment attitudes towards AS.
Results: 91 FP responded the survey, 51.6% female, more frequently from the 25-44 year-old age group, half of which with <5 years of clinical experience. Most FP (70%) did not consider AS to be a relevant disease in everyday clinical practice but recognized (90%) there was a delay in diagnosis (5 years on average). Nevertheless, knowledge over AS was adequate. On average, prevalence was considered to be 56 cases per 1000 persons (close to the actual prevalence of 47 cases per 1000 persons reported in the epidemiological study EpiReumaPt). When assessing a patient with suspicious AS, the most valued symptoms/signs were inflammatory back/buttock pain, extra-articular manifestations (uveitis, enthesitis, dactylitis, psoriasis) and sacroiliitis on imaging (4.1, 3.9 and 3.9 on a 1-6 scale, respectively); 92.5% of FP refer the patient to a hospital consultation, rheumatology in 88.5% of cases; 37.5% of FP initiate treatment, with NSAIDs in 81% of cases. A mean delay of 9 months between patient referral and first hospital consultation was also reported (>1 year in 22%). In 73.4% of cases, no specific referral protocol exists for AS or other rheumatic inflammatory conditions; 33.8% of FP felt that the development of such protocol would improve access, while 36.8% considered that a rheumatologist acting as consultant in primary care units would facilitate identification and referral of inflammatory conditions.
Conclusion: Portuguese FP reported significant delay in hospital consultation after referral of suspicious AS cases. They apparently had good knowledge of AS, though responses may have been influenced by a younger, more updated and willing-to-participate physician population (selection and response bias).

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AB1195 PREGNANCIES IN AUTOIMMNUNE DISEASES: EXPERIENCE OF TWO CENTERS IN CALI, COLOMBIA: 2011- 2018

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Background: The outcome in pregnancy varies according to the rheumatic disease.
Objectives: To describe the pregnancies outcomes of women with rheumatic diseases at two reference centers in Cali, Colombia.
Methods: Descriptive study. Records of pregnant patients attended from August 2011 to December 2018 were reviewed. Thirty-nine patients were found, 11 without a defined rheumatic entity (10 with positive ANA only,

and 1 with incomplete criteria for antiphospholipid syndrome), and 28 with an autoimmune rheumatic disease. A total of 41 pregnancies occurred (2 women with 2 pregnancies) and were chosen for the final analysis (Table).

Results: The mean gestational age at the first rheumatology visit was 16,8 ± 8,9. The mean age at the end of pregnancy was 29,5 ± 5,7 years. Only nine pregnancies were planned (34,6%). Among the patients with a defined autoimmune disease the diagnoses were: systemic lupus erythematosus (SLE) (12), rheumatoid arthritis (RA) (5), antiphospholipid syndrome (APS) (2), autoimmune hemolytic anemia (AHA) (2), juvenile idiopathic arthritis (JIA) (2), overlap syndrome (OS) (3: 2 SLE/SSc; 1 SLE/Sjögren´s) mixed connective tissue disease (MCTD) (1) and undifferentiated connective tissue disease (UCTD) (1). There were 8 pregnancies exposed to teratogenic drugs (MTX 5, LEF 1, MMF 1, CYC 1): 2 ended in fetal loss and 1 had a congenital pneumonia. There were 27 full-term births, 37-40 weeks (wk); 8 preterm births, 23-36 wk (4 twins); 1 stillbirth, 26 wk; and 3 abortions (2 in the same mother). Seven patients had an active disease before pregnancy, 13 during pregnancy (7 SLE, 3 RA, 2 AIHA, 1 MCTD) and 13 during the puerperium (7 SLE, 4 AR, 1 AIJ, 1 EMTC). No maternal deaths, neonatal lupus or congenital heart block were documented in this series. Four patients did not require any medication. One woman received treatment for pulmonary tuberculosis, and other was on anti-retroviral treatment for HIV infection. At the last follow-up, 2 patients were still pregnant.

Conclusion: The outcome of rheumatic disease during pregnancy remains variable. It seems that SLE patients tend to be more active and flare more commonly than other patients. The documented complications were similar to those reported in the literature.

REFERENCES

[1] Davutoğlu EA, Ozel A, Yılmaz N, Madazli R. Pregnancy outcome in 162 women with rheumatic diseases: experience of a university hospital in Turkey. Arch Gynecol Obstet. 2017 Dec;296(6):1079-1084.

Table. Main clinical findings and outcomes

Variables	SLE (n=15)*	Non-SLE (n=13)**
Gestational age at first rheumatology follow up, mean (standard deviation, SD)	11,6 (5,9)	18 (9)
Treatment during prenangcy, n (%)		
Antimalarial	11 (73,3%)	6 (46,2%)
Steroids	10 (66,6%)	7 (53,8%)
Azathioprine	5 (33,3%)	1 (7,7%)
Laboratory fidings, n (%)		
Anti-Ro antibodies	6/9 (66,7%)	0/9 (0%)
Lupus anticoagulant	1 (8,3%)	1 (14,3)
Anticardiolipin antibodies, IgM	1 (8,3%)	0
Anticardiolipin antibodies, IgG	1 (8,3%)	1 (14,3)
Relapses during pregnancy, n (%)	7 (46,7%)	8 (61,5%)
Maternal outcome, n (%)		
Preeclampsia	3 (20%)	1 (9,1)
HELLP syndrome	1 (6,7%)	0
Fetal outcome, n (%)		
Preterm newborn	6 (40%)	2 (18,2%)
Abortion	2 (13,3%)	0
Stillbirth	1 (6,7%)	0

SLE: systemic lupus erythematosus. * Two gemelar pregnancies ** Two patients with primary antiphospholipid syndrome.

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AB1196 A REVIEW OF ELECTRONIC RHEUMATOLOGY REFERRALS AT THE QUEEN ELIZABETH UNIVERSITY HOSPITAL (GLASGOW, UK) AND HOW THIS HAS LED TO SERVICE IMPROVEMENTS

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Background: Our department provides a service for inpatient Rheumatology reviews Monday to Friday, 9am to 4pm, with a guaranteed review timeframe of 48-72 hours. We work predominantly on the QEUH site, which comprises 1677 acute inpatient beds. We launched an electronic referral system for inpatient Rheumatology reviews in February 2018.

Interspeciality referrals are an essential part of most inpatient stays. In a time of increasing service demand within the NHS it is important that we have an effective system to manage our time and resources[1,2]. Electronic referrals allow us to audit our workload, our efficiency at reviewing patients and allow for accountability of both the referrer and reviewer, therefore improving patient safety[3]. Using a set proforma allows us to improve communication, the quality of the referral and triage effectively[4].

Objectives: We performed a baseline review of the new system.

Methods: We reviewed all electronic referrals between 8.2.18 and 13.8.18. We collected data on demographics, timing, reasons for referral and outcomes.

Results: There were 346 referrals (58.4% female, mean age 64 years). Most (78%) were made from medical wards; the mean number of referrals per month was 49.4. Referrals were most frequently made on Fridays (23%). Most were in-hours (81%).

The most common reason for referral was: a request for review (212; 61.3%); phone advice (70; 20.2%); procedural requests (50; 14.5%). 207 referrals (59.8%) were made for new patients, 91 (26.3%) for patients known to Rheumatology prior to admission, and 48 (13.9%) for patients already seen during the current admission.

50% of procedures were performed on knees and 50% on other joints.

82% of patients were seen within 72 hours.

Acute hot swollen joint was the commonest reason for referral of new patients (38%), followed by vasculitis (6%). Questions regarding pre-existing disease management (59%) or DMARD questions (24%) predominated amongst referrals for patients known to Rheumatology prior to this admission.

Conclusion: The use of the electronic referrals system has made it simple to review the workload of our Rheumatology on-call service.

We have used the data on 'reason for referral' to guide the topics for our educational meetings to improve patient management.

We actively contribute to the procedural teaching on knee joint aspiration both in junior doctor's formal training sessions, and opportunistically on wards following referral. This is a core procedure required for training completion for medical trainees in the UK and should help reduce referrals and manage patients in a more time efficient and cost-effective manner.

We have also improved documentation by recording the time, date and name of the reviewer in our electronic entry

We intend to collect data in the same period this year, to assess changes in referral pattern in the 12 months since the system was initiated and the impact of our interventions.

REFERENCES

[1] Rheumatology in Scotland: The state of Play, BSR and SSR
[2] Oliver O'Sullivan, James Bateman, Paresh Jobanputra; 172 Acute Rheumatology Referrals are Increasing: A Service Evaluation of more than 1000 Consecutive Acute Inpatient Referrals from a Tertiary Centre, Rheumatology, Volume 55, Issue suppl_1, 1 April 2016, Pages i131–i132
[3] Shephard E, Stockdale C, May F, et al. E-referrals: improving the routine interspecialty inpatient referral system. BMJ Open Quality 2018;7:e000249. doi:10.1136/bmjoq-2017-000249
[4] Scheibe eat al. Efficiency gains for Rheumatology Consultation using a novel electronic referral system in a safety-net health setting. Arthritis Care and Research 2015;Vol.67 pp.1158-1163

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AB1197 EFFECTS AND SAFETY OF THE YELLOW FEVER VACCINE 17DD IN PATIENTS WITH IMMUNOMEDIATED RHEUMATIC DISEASES

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Background: The yellow fever is an acute infectious disease caused by the amarilic virus. It is present in tropical areas of South America and

Africa and is transmitted to humans through the bites of the infected female mosquitos, found in the endemic forest zones. The vaccine is produced with attenuated viruses and represents an essential prevention method. It confers prolonged immune protection and is considered to be safe in the general population. For the immunosuppressed condition under which many patients with immunomediated rheumatic diseases (IMRD) are submitted, little is known about its efficacy and safety in this group.
Objectives: The aim of this study is to analyse the effects of the vaccine in patients with IMRD.
Methods: The methodology of this research consisted of the application of a form-based interview, the analyses of the vaccine card and medical records, if existent. The requirement to take part as a volunteer was to be an IMRD patient that was vaccinated against yellow fever.
Results: 60 ambulatorial patients, unadvisedly vaccinated or not, were evaluated. Of those, 40 (66.7%) were female and 20 (33.3%) were male, with an age range varying from 8 to 48 years. It was observed that 52 (86.7%) presented no adverse effects from the vaccine, while 7 (11.7%) presented at least one side effect and 1 (1.7%) exhibited a severe reactivation of the underlying rheumatic disease. In the group of 7 patients that registered any side effects, it was described 1 case of bilateral optic neuritis with temporary vision loss, initiated three weeks after the vaccination. The other side effects registered were mild and included: 3 occurrences of headache and 1 record of each of the following: fever, local pain, arthralgia, myalgia, nausea, coryza and diarrhea.
Conclusion: Our data suggested that the vaccine exhibits a relative degree of safety in these patients. The benefits of the immunization should be evaluated by the rheumatologist, taking in account the risk of infection and lethality of yellow fever in patients who live or are visiting the endemic areas. The recommendations are that the vaccination in this group must always be planned, done under medical orientation and order. It should preferably be applied in patients under disease remission, without immunosuppression treatment or in those who, under immunosuppressors, it is possible to temporarily suspend this treatment in order to the vaccine to be administered.

REFERENCES

[1] J. ERIN STAPLES, MD1; JOSEPH A. BOCCHINI JR., MD2,3; LORRY RUBIN, MD2,4; MARC FISCHER, MD. Yellow Fever Vaccine Booster Doses: Recommendations of the Advisory Committee on Immunization Practices, 2015 Morbidity and Mortality Weekly Report MMWR/June 19, 2015/Vol. 64/No. 23
[2] TANRIÖVER M.D. da. et al. Vaccination recommendations for adult patients with rheumatic diseases European Journal of Rheumatology. 2016; 3: 29-35

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AB1198 EVALUATION OF THE WAITING TIME AND QUALITY OF RHEUMATOLOGY REFERRAL AT A TERTIARY CARE CENTER OF PORTO ALEGRE – RS, BRAZIL

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Background: To improve waiting time for a first consultation with a rheumatologist has become an important challenge in many countries [1, 2]. In 2008, a previous survey [3] evaluating the referrals to our Service, we observed long waiting times (median 3.8 months, interquartile range (IQR) =1.5-10.0, ranging from 3 days to 8 years) and that only 31% of consultations were related to hypothesis of systemic inflammatory rheumatic diseases (SIRD), which should be properly managed at a resourceful tertiary care center. In 2015, a new process of triage for referrals (based on a protocol recording relevant information and judgment by a rheumatologist) was introduced in our state health system aiming to improve quality of referrals and reduce waiting lists [4]. However, this system is applied only for patients from cities other than the capital (Porto Alegre, RS).
Objectives: To evaluate the waiting time and quality of referral for first Rheumatology consultations at a tertiary care center of South Brazil, comparing the present results with those obtained 10 years ago in a similar survey [3].
Methods: In a cross-sectional study, information regarding all first consultations at the Rheumatology Service of Hospital Nossa Senhora da Conceição were prospectively collected from Oct 2017 to Mar 2018. Referred patients were characterized in terms of demographic features, diagnostic hypothesis formulated by the rheumatologist and time from initial referral. For analytical purposes, patients with adequate referrals were considered to be those that presented high probability of SIRD, needing assistance at secondary or tertiary level of care. The results were compared with data collected in the same way in 2008 [3]. Chi-square test was used for statistical analysis.
Results: Of 444 appointments for scheduled for new patients, 87 (19%) did not attend. The features of the remaining 357 patients were: female=85%, mean (SD) age= 53 (15) years. The waiting time for consultation ranged from 7 days to 63,8 months (median 12.7, IQR= 4.4-14.1). Diagnostic suspicion of SIRD occurred in 186 (52%). Among SIRD, rheumatoid arthritis (23,5%) was the most frequent, while among non-SIRD, osteoarthritis (21,0%) and fibromyalgia (20.7%) were the most common diagnostic hypotheses. A SIRD was the main hypothesis in 75/193 (38.9%) patients from the capital, comparing with 111/174 (67,7%) among those from other cities (P<0,001), indicating better selection of the latter group of patients. A reanalysis of data colleted in 2008 revealed that, at that time, the prevalence of suspected SIRD was not significantly different between patients from capital (76/262, 29.0%) and those from other cities (74/225, 32,9%; P=0.354).
Conclusion: We observed improvement in the quality of referrals from other cities comparing to those from the capital of our state, suggesting a better selection process in the former [4]. Despite the efforts to reduce the waiting time for Rheumatology consultations, we observed an increase when compared to 2008. We believe that the delay is secondary to an increase of the demand without a proportional increase in the number of rheumatologist in the public health system. The elaboration of guidelines with standardized information required for referral and triage process seems to be promising to improve access to consultations in Rheumatology.

REFERENCES

[1] Widdifield J, et al. Arthritis Care Res (Hoboken) 2017;69:104-114.
[2] Villeneuve E, et al. Annals Rheum Dis 2013;72: 13-22.
[3] Simon, et al. Revista Amrigs 52(4):303-308
[4] Harzheim E, et al. TelessaúdeRS-UFRGS, 2016. Available at: https://www.ufrgs.br/telessauders/documentos/protocolos_resumos/protocolos_encaminhamento_reumatologia_TSRS_20160324.pdf

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AB1199 BARRIERS AND FACILITATORS TO THE IMPLEMENTATION OF A STRATIFIED MODEL OF CARE FOR LOW BACK PAIN PATIENTS IN PRIMARY CARE IN PORTUGAL

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Background: The results of a recent study have suggested that the current clinical practice is not in line with clinical guideline recommendations and may not be delivering the best outcomes to Low Back Pain (LBP) Portuguese patients. Since the stratified primary care approach has demonstrated clinical and cost-effectiveness in the UK and other countries, the SPLIT project aimed to introduce a similar approach that involves general practitioners (GPs) and physiotherapists (PTs) in the triage and targeted treatment for LBP patients, in Portugal. In order to facilitate the implementation of this project a training program for GPs and PTs was delivered by rheumatologists and PTs. Considering the specific organization of the Portuguese primary care, it was important to explore the perceptions of the GPs and PTs, who attended to the training, regarding the implementation of the SPLIT stratified model of care in the Portuguese context.
Objectives: Identify and understand the potential barriers and facilitators to the implementation of the SPLIT stratified model of care.
Methods: After obtaining ethical approval, two focus groups (one for each professional group) were carried out. The focus groups were based on a semi-structured interview schedule, audio-recorded and transcribed verbatim. A thematic analysis was conducted. Firstly, two researchers independently coded the transcripts. Secondly, these researchers discussed the codes and examined their scope and relevance. Thirdly, the researchers developed a coding scheme that included the main themes and subthemes, as well as the connections among them.

Results: The potential barriers were identified and explored by both professional groups. The introduction of change into the routine delivery care was identified as one of the most important barriers. According to the GPs` perspective, the possibility of inadequate referral was considered as an issue. The PTs highlighted the challenges inherent to the psychosocial informed physiotherapy treatment of patients classified with high risk of developing persistent and disabling pain. More specifically, they emphasised the need to receive mentoring sessions in clinical practice, in order to develop competences for the management of psychosocial issues.
In what concerns to the potential facilitators to the implementation of the model, the participants` personal motivation was considered as one of the most important factors. The alignment of the SPLIT model with the mission and goals of the health care units where the project was going to be piloted was also identified as an important facilitator. Finally, both professionals groups considered that the SPLIT model may facilitate the interdisciplinary approach to the management of this condition, as it clarifies the specific contribution of GPs and PTs in the approach to LBP patients
Conclusion: The knowledge about the potential barriers and facilitators to the implementation of the SPLIT stratified model of care may contribute to the successful implementation of stratified care for LBP patients in Portugal.

REFERENCES

[1] Foster, N., et al. (2018) Prevention and treatment of low back pain: evidence, challenges, and promising directions. Lancet. 10137(391): 2368-2383.
[2] Gouveia, N., et al. (2016) Prevalence and social burden of active chronic low back pain in the adult Portuguese population: results from a national survey. Rheumatology International. 36(2): 183-97.

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AB1200

IMPROVEMENT IN THE QUANTITY AND QUALITY OF OBSERVATIONAL DATA COLLECTED FOR US VETERANS ENROLLED IN THE VETERANS AFFAIRS RHEUMATOID ARTHRITIS REGISTRY USING AN ELECTRONIC AUDIT, FEEDBACK, AND DATA CORRECTION SYSTEM

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Background: The Veterans Affairs (VA) Rheumatoid Arthritis (RA) (VARA) registry is an observational cohort study of US Veterans with RA at 11 VA Medical Centers. VARA investigators capture clinical and laboratory disease activity measures (DAMs) during clinic visits via standardized templates in the electronic health record (EHR). Six clinical (tender/swollen joints, patient/provider global, MD-HAQ, pain) and 2 laboratory (ESR, CRP) DAMs are extracted post-visit using natural language processing (NLP).
Objectives: This analysis determined the impact of an audit, feedback and data correction system on the quantity and quality of DAMs collected in the VARA registry.
Methods: After September 2017, VARA site investigators were provided monthly feedback reports of incomplete/missing DAMs for the prior month to allow sites to correct data entry errors. Updated and/or corrected data were entered into the EHR via note addendums and then automatically re-extracted by NLP to complete the capture of DAM data. DAMs from October 1, 2016 to September 30, 2017 (pre-feedback implementation – Pre-IMP) was compared to October 1, 2017 to September 30, 2018 (post-feedback implementation – Post-IMP).

Patients and Notes	Pre-IMP	Post-IMP		Increase (%) †
Unique patients	1,116	1,208		92 (8.2%)
Total Notes	2,411	2,873		460 (19.1%)
Average notes per patient	2.2±1.1	2.4±1.1		0.2 (10.1%)
		Impact of Feedback/Corrections		
Disease Activity Measure (DAMs)		Before	After	
Total DAMs	15,709	20,688	21,064	5,355 (34.1%)
Number Clinical DAMs per note	4.9±1.5	5.5±1.2	5.6±1.1	0.7 (14.6%)
Notes with 6 Clinical DAMs	1,267 (52.5%)*	2,195 (76.4%)‡	2,332 (81.1%)‡	1,065 (84.1%)
Notes with 4 DAMs for DAS28	1,526 (63.3%)*	2,038 (70.9%)‡	2,873 (74.5%)‡	615 (40.3%)
Notes will 6 clinical and 2 lab DAMs	1,055 (43.8%)*	1,794 (63.4%)‡	1,857(64.7%)‡	802 (76.0%)

* Percent of total notes during the pre-implementation period.
‡ Percent of total notes during the post-implementation period.
† Percent change from pre-implementation baseline to post-implementation after corrections.

VARA registry goal is to collect the following Disease Activity Measures (DAMs) at each visit.

Six Clinical DAMs
Joint Tender Count of 28 joints
Joint Swelling Count of 28 joints
Patient Global Assessment of Disease Activity
Physician Global Assessment of Disease Activity
Modified Health Assessment Questionnaire
Patient Pain Score

Two Laboratory DAMs
Westergren Erythrocyte Sedimentation Rate
C-Reactive Protein

Composite DAM
Disease Activity Score for 28 joint count (DAS28)

Table 1

Results: During the pre-IMP period, there were 2,411 notes with DAMs collected on 1,116 unique patients compared to 2,873 notes on 1,208 unique patients in the post-IMP period - an increase of 92 (8.2%) unique patients and 460 (19.1%) notes. Enrollment in the VARA registry only increased by 121 (6.5%) during post-IMP period. During post-IMP period, there were 541 notes identified with deficiencies in clinical DAMs and monthly audit and feedback reports were provided to VARA sites to allow corrections. Individual site review resulted in 376 additional DAMs in 225 notes, with complete resolution of all error in 137 (25.3%) notes. The quantity of DAMs collected increased from 15,709 to 21,064, a 34.1% increase with the average number of DAMs collected per note rising from 4.9 to 5.6. The quality of data improved as demonstrated by the proportion of notes with all 6 clinical DAMs increasing from 52.5% to 81.1% and other improvements in quality/completeness as noted in table.
Conclusion: An audit, feedback, and efficient data collection system improved both the quantity and quality of DAMs collected. The improvement in the collection of DAMs in RA patients will further enhance epidemiologic and outcomes studies of RA and provide higher quality longitudinal data to enhance the care of RA patients.

REFERENCES

[1] Fed Pract 2015; 32(5):24-29

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AB1201 MANAGEMENT OF COMORBIDITY IN INFLAMMATORY ARTHRITIS: GECOAI PROJECT

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Background: The impact of comorbidity on the diagnosis, prognosis, and treatment of rheumatic diseases could be very high. However, several studies have depicted a sub-optimal assessment of comorbidity in these diseases.
Objectives: To generate common, simple and practical support materials (checklists, questionnaires and other complementary materials) for rheumatologists, health professionals and patients, in order to: 1) Assess comorbidity; 2) Identify and implement preventive procedures; 3) Define referral criteria to other health professionals, in patients with rheumatoid arthritis (RA), axial spondylitis (axSpA), and psoriatic arthritis (PsA).
Methods: This project was promoted by CONARTRITIS (Association of patients with arthritis), OPENREUMA (Multidisciplinary association of professionals dealing with patients with rheumatic diseases) and SORCOM (Rheumatology Society of the Madrid Region). A multidisciplinary team specialized in comorbidity in inflammatory arthritis was established (6 rheumatologists, 2 primary care physicians, 2 nurses, 1 internist, 1 psychologist). A qualitative study was performed following these phases: 1) Review of the GECOAR[1], GECOAX[2] and GECOAP[3] projects, that were focus on the evaluation of comorbidity in RA, axSpA and PsA, as well as an exhaustive bibliographic search in Medline; 2) Generation of preliminary checklists (different versions and formats) to be used by health professionals and patients for the identification, management and prevention of comorbidity; 3) Patient focus group in which the preliminary patients checklist was evaluated and discussed; 4) Nominal group meeting in which the selected health professionals analyzed all the checklists and modified them taking into account the opinion of the patients; 5) External evaluation of the modified checklists by patients, health professionals and rheumatologists, all of them outside the project; 6) Generation of the final checklists based on everything collected in the previous phases.
Results: Three checklists for clinical practice were designed, two for health professionals (one to identify comorbidity, another on prevention/health promotion), one for patients. The comorbidity checklist includes, for example, the evaluation of cardiovascular risk factors, depression and anxiety, allergies or infections. The prevention checklist includes life style issues (smoking, diet, exercise), social life, sexuality, sleep, or oral hygiene. The checklists also specify the evaluation method (questions, specific questionnaire, etc.).
Conclusion: The use of specific checklists for the identification, management and prevention of comorbidity inpatients with RA, axSpA and PsA might contribute positively in their prognosis.

REFERENCES

[1] Loza E, et al. Rheumatol Int. 2015 Mar;35(3):445-58.
[2] González C, et al. Reumatol Clin. 2018 Nov - Dec;14(6):346-359.
[3] Torre-Alonso JC, et al. Rheumatol Int. 2017 Aug;37(8):1239-1248.

Disclosure of Interests: Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Carlos M. González: None declared, María del Carmen Castro Villegas Paid instructor for: MSD, Abbvie, Pfizer, Janssen, Lilly, Roche, Silvia García-Díaz: None declared, Juan Carlos Hermosa: None declared, Cristina Lajas: None declared, Leticia León: None declared, Juan Carlos Obaya: None declared, María Rodero: None declared, Carmen Suarez: None declared, Virginia Villaverde: None declared, Juan Carlos Torre-Alonso: None declared
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AB1202 SWITCHING OF ETANERCEPT IN A MONOGRAPHIC CONSULTATION OF BIOSIMILAR CLINICAL PRACTICE AND ECONOMIC COST

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Background: The recent appearance of biosimilars by the European Medicines Agency in January 2015 allows a quality treatment in rheumatic diseases with a lower cost. We present our initial experience in a specific biosimilar consultation with the introduction of biosimilar Etanercept (BE).
Objectives: To describe the switching experience from original etanercept (OE) to BE and to evaluate the economic impact of this strategy.
Methods: Retrospective study carried out in a tertary level hospital. We included patients treated with OE which were evaluated in the Specific Biosimilar Consultation where a rheumatology and a nurse proposed them switching to BE. Demographic, clinical and pharmacotherapeutic variables of all patients were collected. The outcome evaluated was the drug switch as well the reasons why the change was not made. To analyze the economic impact, the estimated savings in the use of BE vs OE was calculated, [costs according to the net prices of our center (PVL - discount)+VAT].
Results: The registry included of 133 patients treated with OE from the Rheumatology Department of our center, only 56 patients were evaluated in a period of 3 months in the specific biosimilar consultation: 73% were women over 53 years (17-75 years). Regarding the diagnosis: 45% rheumatoid arthritis, 46% psoriatic arthropathy and 9% ankylosing spondylitis.
All patients chosen to switch from OE to BE should have stable base disease (defined as low activity according to the specific scale for each pathology), approval of the change by a evaluating physician and patient, signing the informed consent.
Finally, the switch from OE to BE was performed in 31/56 patients (55%). In the 25 patients who did not change: 3 patients (12%) had moderate or high disease activity, in 8 patients (32%) the change was not accepted by the patient or by the evaluating physician and 14 patients (56%) were in remission of the disease.
The patients chosen were in a dosage regimen of 50 mg/week, so the annual costs per patient are 9143.16€ with OE and 6095.44€ with BE. The switching to BE represent annual savings of 3047.72€ per patient and 94479.32€ total.
Conclusion: The experience with the implementation of a specific biosimilar consultation in our center has been positive. In the first 3 months of its operation, the switching from OE to BE have been made in 55% of patients allowing savings allowing savings of 3047.72€ per patient/year.

REFERENCES

[1] Brites L, Costa F, Freitas J, Luis M, Coutinho M, Santiago M, et al. Impact of Block Switch to Biosimilar Etanercept in Practice, Accross Different Rheumatic Disease [abstract]. *Arthritis Rheumatol.* 2018;70 (suppl 10).
[2] Di Giuseppe D, Frisell T, Ernestam S, Forsblad-D'Elia H, Lindqvist E, Lindström U et al; ARTIS group. Uptake of rheumatology biosimilars in the absence of forced switching. Expert Opin Biol Ther. 2018 May;18(5):499-504.
[3] Glintborg B, Loft AG, Omerovic E, Hendricks O, Linauskas A, Espesen J, et al. To switch or not to switch: results of a nationwide guideline of mandatory switching from originator to biosimilar etanercept. One-year treatment outcomes in 2061 patients with inflammatory arthritis from the DANBIO registry. Ann Rheum Dis. 2019 Feb;78(2):192-200.
[4] Tweehuysen L, Huiskes VJB, van den Bemt BJF, Vriezekolk JE, Teerenstra S, van den Hoogen FHJ, et al. Open-Label, Non-Mandatory Transitioning From Originator Etanercept to Biosimilar SB4: Six-Month Results From a Controlled Cohort Study. Arthritis Rheumatol. 2018 Sep;70 (9):1408-1418.

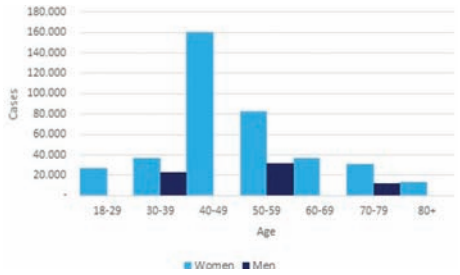
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7911

AB1203

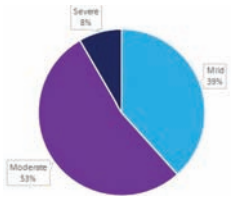
BURDEN DISEASE OF RHEUMATOID ARTHRITIS IN COLOMBIA, 2015

Francy Cuervo[1], Ana María Santos[1], Ignacio Angarita[1], Juan Camilo Rueda[1], Rodrigo Giraldo[1], Jesús G. Ballesteros[2], Ingris Peláez-Ballestas[3], Diana Díaz-Jiménez[4], Pedro Santos-Moreno[5], Diana Padilla-Ortiz[1], Viviana Reyes[1], Carlos Castañeda-Orjuela[4], John Londono[1]. *[1]Universidad de La Sabana, Chía, Colombia*; *[2]Central Military Hospital, Bogotá, Colombia*; *[3]Universidad Nacional Autonoma de México, Faculty of Medicine, Ciudad de México, Mexico*; *[4]National Institute of Health, Colombian National Health Observatory, Bogotá, Colombia*; *[5]Biomab, Bogotá, Colombia*

Background: The prevalence of rheumatoid arthritis (RA) in Colombia according to the COPCORD study was 1.49%. The disease burden data available in our country are based on the results of the Global Burden Disease study (GBD) of 2016. However, the GBD study takes reference data from non-Colombian residents that was extrapolated to our population, given the absence of demographic data at that moment.
Objectives: To estimate the disease burden of RA for 2015
Methods: A descriptive study was developed. The reference data of the population was taken by DANE (Departamento Administrativo Nacional de Estadistica) and the WHO (World Health Organization). The GBD disability definitions were adapted from individual questions of functionality and quality of life questionnaires of the COPCORD study in Colombia (1). A Markov model was developed to calculate the years of life lost due to premature mortality (YLL), years lived with disability (YLD) and Disability-Adjusted Life Year (DALY).
Results:
The distribution of cases by age and severity levels of RA are shown in figure 1 and 2 respectively.



Abstract AB1203 Figure 1. Distribution of cases by age and sex



Abstract AB1203 Figure 2. Distribution of severity levels of RA

Since direct death due to RA were not registered according to the search of the ICD-10 codes in DANE, the YLL was 0. The YLDs in total were 118,358. The DALYs were 118,358 for a rate of 361.54 per 100,000, which is higher than the GBD 2016 results (60 per 100.000).
Conclusion: The burden disease of rheumatoid arthritis is higher than that referred by GBD. Holistic approaches are required to reduce these parameters of impact on the public health of Colombians. Our data on DALYs usefulness lies in the urgent need for an early diagnosis, to reduce disability and thereby improve the quality of life of patients. Even though, RA was not the registered primary cause of death, it is necessary to explore mortality-associated conditions due to this rheumatic disease.

REFERENCES

[1] Londono J, Peláez I, Cuervo F, et al. Prevalencia de la enfermedad reumática en Colombia, según estrategia COPCORD-Asociación Colombiana de Reumatología. Estudio de prevalencia de enfermedad reumática en población colombiana mayor de 18 años. Rev Colomb Reum [Internet]. 2018;1–12. Available from: https://doi.org/10.1016/j.rcreu.2018.08.003

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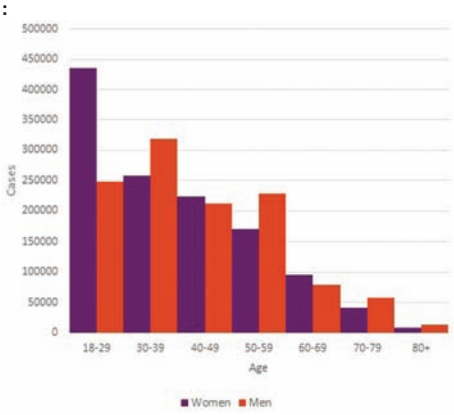
AB1204

BURDEN DISEASE OF LOW BACK PAIN IN COLOMBIA, 2015

Francy Cuervo[1], Juan Camilo Rueda[1], Ana María Santos[1], Eugenia-Lucia Saldarriaga[1], Ignacio Angarita[1], Rodrigo Giraldo[1], Ingris Peláez-Ballestas[2], Diana Díaz-Jiménez[3], Jesús G. Ballesteros[4], Pedro Santos-Moreno[5], Diana Padilla-Ortiz[1], Viviana Reyes[1], Carlos Castañeda-Orjuela[3], John Londono[1]. *[1]Universidad de La Sabana, Rheumatology, Chía, Colombia*; *[2]Universidad Nacional Autonoma de México, Faculty of Medicine, Ciudad de México, Mexico*; *[3]National Institute of Health, Colombian National Health Observatory, Bogotá, Colombia*; *[4]Central Military Hospital, Bogotá, Colombia*; *[5]Biomab, Bogotá, Colombia*

Background: Low back pain (LBP) is the second most frequent rheumatic disease in Colombia. According to the COPCORD study, LBP prevalence was 7.24% (CI 95% 6.28-8.34%) (1).
Objectives: To estimate the disease burden of LBP for 2015.
Methods: A descriptive study was conducted. A Markov model was developed based on cases with LBP, distribution of disability and mortality according to DANE (Departamento Administrativo Nacional de Estadistica) and the WHO (World Health Organization) reference data. The results are shown in terms of the years of life lost due to premature mortality (YLL), years lived with disability (YLD) and finally as Disability-Adjusted Life Year (DALY).
Results: The distribution of cases by age of LBP are shown in figure 1.

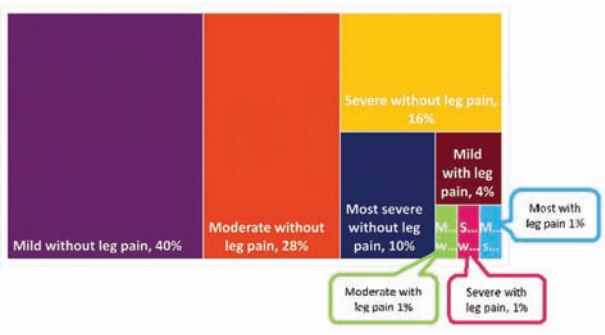
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Abstract AB1204 Figure 1. Distribution of cases by age and sex

An algorithm was designed to determine the distribution in percentages of severity levels, according to the GBD definitions (figure 2).

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Abstract AB1204 Figure 2. Distribution of severity levels of rheumatoid arthritis

According to ICD-10 codes, 9 deaths were reported, so the YLL were 124. The YLDs were 264,658.
Finally, the DALYs were 264,782 for a rate of 808.82 per 100,000, which is higher than the
GBD 2016 results (647 per 100,000).
Conclusion: The main cause of burden disease of rheumatic disease in Colombia is due to LBP. The burden is because of the YLD, related to the frequency of cases in people younger than 50 years of age. It is necessary for an early detection and development of intervention strategies.

REFERENCES

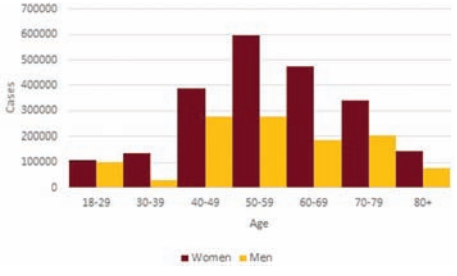
[1] Londono J, Peláez I, Cuervo F, et al. Prevalencia de la enfermedad reumática en Colombia, según estrategia COPCORD-Asociación Colombiana de Reumatología. Estudio de prevalencia de enfermedad reumática en población colombiana mayor de 18 años. Rev Colomb Reum [Internet]. 2018;1–12. Available from: https://doi.org/10.1016/j.rcreu.2018.08.003

Disclosure of Interests: Francy Cuervo: None declared, Juan Camilo Rueda: None declared, Ana María Santos: None declared, Eugenia-Lucia Saldarriaga: None declared, Ignacio Angarita: None declared, Rodrigo Giraldo: None declared, Ingris Peláez-Ballestas: None declared, Diana Díaz-Jiménez: None declared, Jesús G Ballesteros: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Padilla-Ortiz: None declared, Viviana Reyes: None declared, Carlos Castañeda-Orjuela: None declared, John Londono: None declared
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AB1205 BURDEN DISEASE OF OSTEOARTHRITIS IN COLOMBIA, 2015

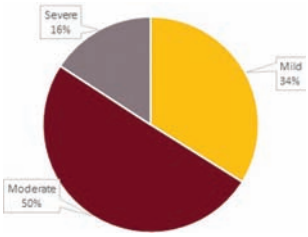
Francy Cuervo[1], Ignacio Angarita[1], Ana María Santos[1], Eugenia-Lucia Saldarriaga[1], Juan Camilo Rueda[1], Jesús G. Ballesteros[2], Rodrigo Giraldo[1], Ingris Peláez-Ballestas[3], Diana Díaz-Jiménez[4], Pedro Santos-Moreno[5], Diana Padilla-Ortiz[1], Viviana Reyes[1], Carlos Castañeda-Orjuela[4], John Londono[1]. *[1]Universidad de La Sabana, Rheumatology, Chía, Colombia*; *[2]Central Military Hospital, Rheumatology, Bogotá, Colombia*; *[3]Universidad Nacional Autonoma de México, Faculty of Medicine, Ciudad de México, Mexico*; *[4]National Institute of Health, Colombian National Health Observatory, Bogotá, Colombia*; *[5]Biomab, Rheumatology, Bogotá, Colombia*

Background: Osteoarthritis (OA) is the most prevalent rheumatic disease in Colombia, as reported by the COPCORD 2015 study. The prevalence is 10.81% (IC 95, 9.68-12.06) (1).
Objectives: To estimate the disease burden of OA for 2015
Methods: A descriptive study was developed. The reference data of the population was taken by DANE (Departamento Administrativo Nacional de Estadística) and the WHO (World Health Organization). It was necessary to develop an algorithm to determine the distribution in percentages of severity levels, according to the GBD definitions. A Markov model was elaborated to calculate the years of life lost due to premature mortality (YLL), years lived with disability (YLD) and Disability-Adjusted Life Year (DALY).
Results: Figure 1 shows the distribution of cases by age of OA, with the highest frequency of cases over 50 years in both sexes.



Abstract AB1205 Figure 1. Distribution of cases by age and sex

Figure 2 describes the distribution of the severity levels of the disease, with most cases being moderately severe.



Abstract AB1205 Figure 2. Distribution of severity levels of rheumatoid arthritis

The YLLs were 781 and the YLDs were 245,626. Finally, the DALYs calculated were 246,408 for a rate of 752.69 per 100,000.
When compared with that reported data by the GBD 2016, the burden of disease for OA was 204 (IC95% 143-278). The results of the present study show that the burden of the disease is higher, and the conditional factor is the YLDs.
Conclusion: Osteoarthritis is a frequent and disabling rheumatic disease that confers a large burden of rheumatic disease affecting people over 50 years of age. The treatment of OA should be focused on reducing disability and holistic intervention strategies to promote good quality of life.

REFERENCES

[1] Londono J, Peláez I, Cuervo F, et al. Prevalencia de la enfermedad reumática en Colombia, según estrategia COPCORD-Asociación Colombiana de Reumatología. Estudio de prevalencia de enfermedad reumática en población colombiana mayor de 18 años. Rev Colomb Reum [Internet]. 2018;1–12. Available from: https://doi.org/10.1016/j.rcreu.2018.08.003

Disclosure of Interests: Francy Cuervo: None declared, Ignacio Angarita: None declared, Ana María Santos: None declared, Eugenia-Lucia Saldarriaga: None declared, Juan Camilo Rueda: None declared, Jesús G Ballesteros: None declared, Rodrigo Giraldo: None declared, Ingris Peláez-Ballestas: None declared, Diana Díaz-Jiménez: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Padilla-Ortiz: None declared, Viviana Reyes: None declared, Carlos Castañeda-Orjuela: None declared, John Londono: None declared
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AB1206 SELF-REPORT OF FRACTURE HISTORY COMPARED TO FRACTURE CODES FROM AN ELECTRONIC HEALTH RECORD DATASET

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Background: Self-reported fracture history data is frequently used in epidemiological studies of osteoporosis. Self-reported fracture data may differ from fracture history coded in electronic health records (EHR) due to imperfect patient recall, incomplete communication with clinicians, or lack of a universal EHR. Because both self-reported fracture history and EHR data can define phenotypes for clinical research studies, it is important to understand how these 2 data sources compare.
Objectives: To compare self-reported fracture history using survey data with fracture codes from an available EHR dataset.
Methods: Self-reported fracture data was derived from the Activating Patients at Risk for OsteoPOroSis (APROPOS) trial, which recruited participants from the Global Longitudinal study of Osteoporosis in Women (GLOW) cohort. Prior fracture data was collected using a survey deployed June - August 2015. Women were asked if they ever had a fracture and for each fracture type the date of the most recent one. Data on fractures recorded in the EHR September 2011 - June 2015 was obtained from Kaiser Permanente Washington Health Research Institute. We excluded skull, toes and fingers fractures. We defined concordance between the EHR and self-reported data if the location of a fracture was reported to be the same and if the reported dates were within 1 year of each other. Kappa (κ) statistic described the concordance between the 2 sources of fracture history. Descriptive statistics

evaluated potential factors associated with discordance between the self-reported and EHR-coded fracture history.
Results: A total of 133 fractures from 360 women (91% white, mean [SD)] age 74.5(7.5) years, 82% had some college education) were included. There were 35 fractures reported on the survey but not in the EHR and 39 fractures coded in the EHR but not in the survey. Agreement between self-reported and EHR fractures was κ 0.48. Of the discordant fractures, we were more likely to find claims for fractures in EHR referent to self-report among whites (OR=5.5, 95%CI 1.1-27.9), for major osteoporotic fractures (OR=2.8, 95%CI 1.1-7.1), and for fragility fractures that typically require hospitalization (vertebral, hip, femur, pelvis) (OR=3.8, 95%CI 1.3-10.7). Discordance between EHR codes and self-reported fractures did not vary by age, formal education, or health literacy.
Conclusion: There was only modest correlation between self-reported fracture history and EHR fracture codes. This discrepancy may have implications for clinical and epidemiological studies of fractures suggesting that combining both types of data may be optimal.
Disclosure of Interests:: Maria Danila Grant/research support from: Pfizer, Inc., Consultant for: Sanofi Genzyme & Regeneron, Amy Mudano: None declared, Elizabeth Rahn: None declared, Andrea LaCroix: None declared, Jeffrey Curtis: None declared, Kenneth Saag Grant/research support from: Amgen, Ironwood/AstraZeneca, Horizon, SOBI, Takeda, Consultant for: Abbvie, Amgen, Ironwood/AstraZeneca, Bayer, Gilead, Horizon, Kowa, Radius, Roche/Genentech, SOBI, Takeda, Teijin
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AB1207 **ASSESSMENT OF RHEUMATIC DISEASES PATIENTS EXPERIENCE WITH THEIR HEALTHCARE USING IEXPAC. FACTORS ASSOCIATED AND AREAS OF IMPROVEMENT:**

Javier de Toro-Santos[1], L María. García Vivar[2], Lucía Pantoja[3], Cristina Lerín Lozano[4], Silvia García-Díaz[5], Yvonne Mestre[6], Sabela Fernández[6], Luis Cea-Calvo[6]. [1]*Hospital Universitario A Coruña, A Coruña, Spain*; [2]*Hospital Universitario de Basurto, Bilbao, Spain*; [3]*Hospital del Bierzo, Ponferrada, Spain*; [4]*Hospital de Manacor, Manacor, Spain*; [5]*Hospital de Sant Joan Despí Moisès Broggi, Barcelona, Spain*; [6]*Merck Sharp and Dohme, Madrid, Spain*

Background: The experience of patients with healthcare has been associated to important outcomes.
Objectives: We describe the experience with healthcare of patients with rheumatic diseases from Spain self-reported through IEXPAC, a validated questionnaire, and the influence of demographic and health care-related factors.
Methods: The IEXPAC scale *("Instrument to Evaluate the EXperience of PAtients with Chronic diseases"*, http://www.iemac.es/iexpac/) was developed and validated in Spain by health care professional and social organizations, experts in quality of healthcare and chronic patients (1). It consists of 12 items with Likert responses from "always" to "never" and yields an overall score from 0 (worst) to 10 (best experience). Three factors with sub-scores derive from the scale: Factor 1 (productive interactions, average of items 1, 2, 5 and 9, on patient-health care professionals relationship), Factor 2 (new relational model, average of items 3, 7 and 11, on the use of new technologies and contact with other patients) and Factor 3 (self-management, patients' ability to self-care, average of items 4, 6, 8 and 10). Data were obtained through an anonymous survey to patients from 25 Spanish hospitals. Bivariate comparisons and a multivariate analysis were made to explore the association between scores and demographic and health care-related characteristics.
Results: 625 patients received the survey, 359 (57.4%) returned it (mean age 55 years, 67% women). The percentage of patients who responded "always" or "nearly always" to the different statements is displayed in table 1. Mean overall IEXPAC score was 5.5 (SD 2.0), sub-scores were: productive interactions: 7.5 (2.5); new relational model: 1.7 (2.1); self-care: 6.5 (2.5). Overall score was higher (better experience) in men (p= 0.022), in those needing follow-up in a different region (p= 0.004), seen by a lower number of physicians (p= 0.025), seen by the same physician each time (p< 0.001), treated with lower number of medicines (p= 0.039) or with subcutaneous or intravenous (SC/IV) drugs (p= 0.083). Multiple linear regression models (table 2) showed that being followed up by the same physician, being seen by lower number of specialists, and being treated with SC/IV drugs were associated to better overall experience scores. Associations were similar for the productive interactions and self-management factors.
Conclusion: Through IEXPAC, patients with rheumatic diseases identified areas of improvement in healthcare, especially those related with access to reliable information and services, interaction with other patients and continuity of health care after hospital discharge. Better experience was associated to being seen by lower number of specialists or being followed-up by the same physician each time, and also with treatment with SC/IV drugs, maybe in relation to the more personalized care these patients receive.

Table 1. Word-for-word IEXPAC items. Percentage of patients who responded "mostly" or "always" to each item

IEXPAC item	Percentage (%) who responded "mostly" or "always"
1.They respect my lifestyle The professionals who care of me listen to me and ask me about my needs, habits and preferences to adapt my treatment and care plan	76.5
2. They are coordinated to offer good health care to me Health and social care services are coordinated to improve my wellbeing and quality of life in my environment (family, neighbourhood, town).	60.6
3. They help me to get information from the Internet The professionals who care for me inform me about trustful webpages and internet forums that I can consult to better know my disease, its treatment and the consequences they may have on my life.	12.8
4. Now I can take care of me better I feel that my confidence in my ability to take care of myself, manage my health problems and keep my autonomy has improved.	74.3
5. They ask me and help me to follow my treatment plan I regularly review the adherence to my treatment and care plan with the professionals who care for me.	73.5
6. We set goals for a healthy life and better control my illness I've been able to agree with the professionals who care for me on specific objectives regarding diet, physical exercise and medication to get better control of my health problems.	63.4
7. I can use Internet and my mobile phone to consult my medical records I can consult my clinical record, tests results, programmed visits and access to other services through the internet or the mobile app of my health service.	7.3
8. They make sure that I take medication correctly The professionals who care for me review with me all of the medication I take, how I take it and how it suits me.	72.4
9. They worry about my welfare	79.1
The professionals who care for me are concerned with my quality of life and I feel they are committed to my wellbeing	
10. I have been informed on the health and social resources that can help me The professionals who care for me inform me about the health and social resources available in my neighbourhood or town that I can use to improve my health problems and take better care of myself.	33.8
11.They encourage me to talk to other patients The professionals who care for me invite me to participate in patients groups to share information and experiences on how to care for ourselves and improve our health.	10.3
Respond to the following statement only if you have been admitted to the hospital in the last 3 years, **12. They care about me when I come home after being in the hospital** After hospital discharge, they have called or visited me at home to see how I was and what care did I need.	25.7

Abstract Table 2. Multivariate analysis. Variables associated to IEXPAC experience scores. Beta coeff. (SD): Beta coefficient (standard deviation). Positive coefficients indicate higher IEXPAC experience scores (better experience). SC: subcutaneous; IV: intravenous.

Parameter	Overall experience score		Productive Interactions (Factor 1)		New Relational Model (Factor 2)		Patient Self-management (Factor 3)	
	Beta coeff.	*P*	Beta coeff.	*P*	Beta coeff.	*P*	Beta coeff.	*P*
Sex (women *vs.* men)	-0.43 (0.28)	0.132	-0.65 (0.36)	0.073	-0.13 (0.30)	0.663	-0.46 (0.35)	0.189
Age (per year of increment)	0.00 (0.01)	0.715	0.01 (0.01)	0.682	-0.00 (0.01)	0.886	0.01 (0.01)	0.659
Educational level achieved (university or further)	-0.02 (0.19)	0.933	-0.28 (0.24)	0.251	0.32 (0.20)	0.112	-0.03 (0.23)	0.886
Follow-up in a region different from home region (*vs.* same region)	0.62 (0.54)	0.252	0.09 (0.68)	0.896	1.11 (0.57)	0.053	0.78 (0.67)	0.243
Barthel Index >80	0.28 (0.37)	0.45	0.26 (0.47)	0.578	0.48 (0.39)	0.226	0.27 (0.46)	0.554
Number of specialists visited in the last year (per unit of increment)	-0.11 (0.06)	0.080	-0.14 (0.08)	0.082	-0.05 (0.07)	0.447	-0.12 (0.08)	0.122
Follow-up by the same physician (*vs.* different)	0.84 (0.26)	0.001	1.17 (0.33)	<0.001	0.08 (0.27)	0.773	1.15 (0.32)	<0.001
Follow-up by a nurse (*vs.* no nurse follow- up)	0.10 (0.29)	0.738	-0.08 (0.37)	0.822	0.43 (0.31)	0.167	-0.04 (0.36)	0.914
Having help from others for care (*vs.* only self-care)	0.30 (0.30)	0.308	0.09 (0.38)	0.809	0.42 (0.32)	0.189	0.49 (0.36)	0.178
Number of different medicines (per unit of increment)	-0.03 (0.06)	0.580	-0.05 (0.07)	0.454	0.01 (0.06)	0.927	0.00 (0.07)	0.958
Being treated with SC/IV drugs (*vs.* no SC/IV treatment)	0.64 (0.27)	0.021	0.87 (0.35)	0.013	0.32 (0.29)	0.275	0.69 (0.33)	0.040

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AB1208 POINT PREVALENCE OF UVEITIS AND ARTHRITIS AMONG SCHOOL CHILDREN IN A DEVELOPING COUNTRY

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Background: Sight-threatening uveitis associated with pediatric rheumatologic diseases, especially juvenile idiopathi arthritis, often remains asymptomatic till late. On the other hand, children with indolent asymptomatic uveitis may later on develop the characteristic arthritis of juvenle idiopathic arthritis, especially the oligoarticular rheumatoid factor negative type. A multidiscipliary screening of children at the peak age of developing these potentially handicappinng manifestations, allows active case findng and facilitates a comprehensive ophthalmic-rheumatolgic management plan.

Objectives: A point prevalence study aiming at active case finding and describng the prevalence of uveitis and arthritis among school children between the ages of 4 and 9 years in 10 screened schools in Egypt.

Methods: All children between the ages of 4 and 9 years in 10 schools were screened for the clinical evidence of uveitis and/or arthritis. The children discovered to be suffering from uveitis and/or arthritis, were referred to the appropriate tertiary clinics for detailed evaluation and management

Results: A total of 6372 children were screened, 3418 of them were females (53.6%) and 2954 were males (46.4%). Thirty four children were found to have uveitis (0.5%). Of these, 26 children were females (76.5%) and 8 children were males (23.5%). Two female children were known uveitis patients and were on treatment. A hundred and eleven children had arthralgia. Of these, 56 children had clinically evident arthritis at the time of screening. Twenty eight children with arthritis were females (50%) and the other twenty eight children were males (50%). Three girls were previously known to be arthritis patients (2 with juvenile idiopathc arthritis and one with psoriasis). Sixteen children had both uveitis and arthritis. All cases detected to have uveitis, arthralgia, or arthritis, in the study were referred to tertiary clinics for further management.

Conclusion: Screening of school children for uveitis and joint manifestations in developing countries with a modest socioeconomic status, is a method of active case finding that helps an, as early as possible, implementation of the proper plan of mangement.

REFERENCES

[1] Kanski JJ, Shun-Shin A. Systematic uveitis syndromes in childhood; an analysis of 340 cases. Ophthalmology 1984; 91: 1247–1252.
[2] Chang JH-M, Wakefield D. Uveitis: a global perspective. Ocul Immunol Inflamm. 2002; 10: 263–279:
[3] O'Brien JM, Albert DM. Therapeutic approaches for ophthalmic problems in juvenile arthritis. Rheumatol Dis Clin N Amer 1989; 15: 413–22.
[4] Tsirouki T, Dastiridou A, Symeonidis C, et al. A focus on the epidemiology of Uveitis. Ocul Immunol Inflamm 2016; 1–15.
[5] Dollfus H. Eye involvement in children's rheumatic diseases. Baillere's Clin Rheumatol 1998; 5: 197–202
[6] Soylu M, Ozdemir G, Anli A. Pediatric uveitis in southern Turkey. Ocul Immunol Inflamm 1997; 5:197–202
[7] Hamade IH, Al Shamsi HN, Al Dhibi H, et al. Uveitis survey in children. Br J Ophthalmol 2009; 93:569–572

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AB1209 THE RHEUMA-BUS-TOUR: TWO WEEK OPEN-ACCESS SCREENING FOR EARLY RHEUMATIC DISEASES

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Background: Early diagnosis is crucial for patients with rheumatic diseases. Studies show that early stage patients already show reduced mental and physical health [2, 3]. However, early diagnosis is often delayed due to the severe lack of rheumatologists in Germany.

Objectives: The cross-sectional study compares data on physical and mental health of known and suspected early rheumatic patients, collected from participants of the bus tour.

Methods: The Rheuma-Bus-Tour is an annual, two week open-access screening event in three states (Rhineland-Palatine, Saarland, Lower Saxony) that raises awareness for rheumatic diseases and identifies people with potential early cases of RA, SpA and PsA.

All participants, regardless of their diagnosis status, completed a screening questionnaire about early symptoms, sociodemographic as well as physical and mental health parameters: Habitual Physical Activity Questionnaire (HPA) [1], Hannover Functional Ability Questionnaire (FFbh-R), Patient Health Questionnaire (PHQ-9), Well-Being Index (WHO-5).

Additionally, a CRP on-site test and a medical consultation were offered.

Results: In total, 853 participants completed the questionnaire, 214 with a known rheumatic diagnosis and 626 without one. Of 533 conducted CRP tests, 107 were positive. After the consultation, 58 patients were referred for an immediate rheumatologist appointment through the Rheuma-VOR network, 16 of which were diagnosed with RA, SpA, or PsA. Tables 1 and 2 present the group differences between the already diagnosed and the not diagnosed groups, split by CRP results.

Abstract AB1209 Table 1. Basic characteristics of the participants

	Rheumatic disease (N=214)		No Diagnoses+CRP neg (N=426)		No Diagnoses+CRP pos (N=107)	
	Mean	SD	Mean	SD	Mean	SD
BMI	27.6	5.5	27.2	5.0	29.0	6.6
HPA Work Index	2.5	1.0	2.7	0.9	2.6	1.1
HPA Sports Index	2.4	0.9	2.4	0.8	2.2	0.9
HPA Leisure Time Index	3.0	0.8	3.1	0.8	3.1	0.9
HPA Index	7.9	1.9	8.2	1.7	7.9	2.0
FFbH-R	69.2	21.4	80.9	18.4	66.4	88.0
PHQ-9	17.3	6.7	16.3	5.5	15.6	6.6
WHO-5	16.9	7.4	15.9	6.1	15.2	7.2

Abstract AB1209 Table 2. Group differences of physical and mental health parameters

	Rheumatic disease vs. No Diagnoses+CRP neg	Rheumatic disease vs. No Diagnoses+CRP pos	No Diagnoses+CRP neg vs. No Diagnoses+CRP pos
BMI	0.374	0.087	0.012*
HPA Work Index	0.223	0.630	0.687
HPA Sports Index	0.817	0.194	0.141
HPA Leisure Time Index	0.184	0.442	0.889
HPA Index	0.121	0.867	0.300
FFbH-R	0.000*	0.014*	0.007*
PHQ-9	0.029*	0.023*	0.317
WHO-5	0.017*	0.034*	0.581

* Significant at $p \leq 0.05$.

Average age for all three groups falls in the 50-59 year range. Differences were found between PHQ-9, WHO-5 and FFbH-R, whereas none were found for HPA.

Conclusion: As expected, a difference in mental health parameters was found for the "known diagnosis" and "no diagnosis+CRP negative" groups. The results also show differences for daily functional tasks between all three groups. However, the lowest scores were found for the group "no diagnosis+CRP pos", i.e. people with strong indications for an early rheumatic disease. This further supports evidence of reduced functionality for early stage patients and the need for early diagnosis and therapy. The lack of significant differences for HPA patterns could be caused by generally very low physical activity for all three groups.

REFERENCES

[1] Baecke JA, Burema J, Frijters JE (1982) A short questionnaire for the measurement of habitual physical activity in epidemiological studies. Am J Clin Nutr 36:936-942.

[2] Branco JC, Rodrigues AM, Gouveia N, et al. (2016) Prevalence of rheumatic and musculoskeletal diseases and their impact on health-related quality of life, physical function and mental health in Portugal: results from EpiReumaPt- a national health survey. RMD Open 2:e000166.

[3] Triantafyllias K, Leiß R, Dreher M, et al. (2019) Depressive Symptomatik bei früher rheumatoider Arthritis. Zeitschrift für Rheumatologie (in press).

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AB1210 SOCIAL MEDIA USE IN RHEUMATOLOGY PATIENTS

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Background: The impact of social media on individual or institutional communication and knowledge acquisition is non-negligible. Whether patients (patients) with rheumatic diseases share information about their health on social media is unknown.

Objectives: We aimed to investigate how often and to what extent patients with a rheumatic condition use social media. We also wanted to know whether they communicate with their doctors through social media and what their expectations are.

Methods: Consecutive patients with diverse diagnoses attending a rheumatology outpatient clinic were studied. Patients completed a self-administered questionnaire (1) which was modified. Information on demographic features, educational status and diagnosis was also recorded.

Results: 397 patients completed the questionnaire (Table). 329 patients with devices, 40 (12%) of these patients were not using social media. 68 patients without devices, thus social media users reached 73% (289/397). While, Facebook users and non-users were similar according to age, gender or educational status, Twitter users were more likely to be male and more educated (Figure). 96% were willing to communicate with their doctors through one of the social media sources. 75% desired to be friends with their rheumatologist on the Facebook. When we asked, "why would you like to communicate with your rheumatologist?"; The majority (39%) responded that it would be easier to understand each other;% 32 thought that they would feel more connected,% 27 thought that their rheumatologist would be more responsible 21% thought that their disease will get better.

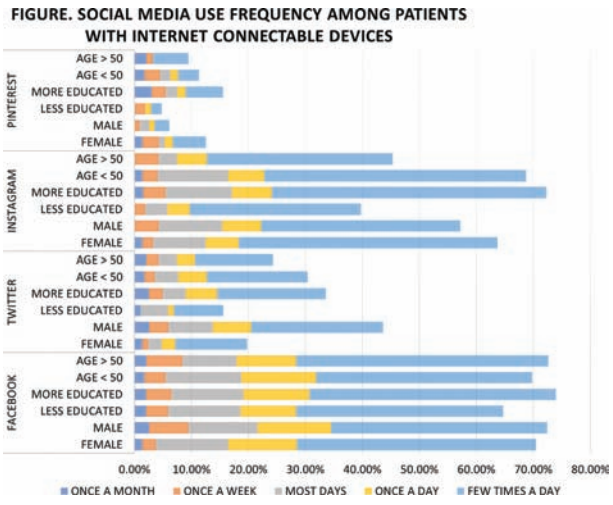
Conclusion: This survey showed that younger and more educated patients had significantly more communication devices. Facebook was the most preferred social media website. More educated patients prefer using Twitter, Instagram and Pinterest and younger patients Instagram and Pinterest. The majority thought that social media was a useful information source about health. While only 23% had an actual connection with their rheumatologist through social media, 75% desired to be friends on the Facebook.

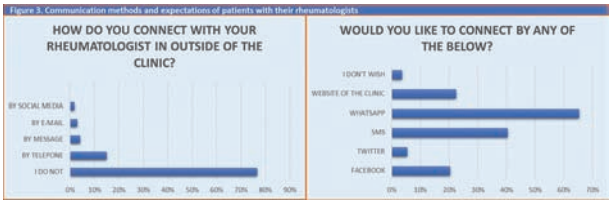
REFERENCES

[1] Hausmann, Jonathan S., et al. "Adolescent and young adult use of social media for health and its implications." *Journal of Adolescent Health* 60.6 (2017): 714-719.

Table. General Features of Patients

Median Age [IQR]	45[34-56]
Female/Male Ratio	1.9
Diagnosis of the patients, n (%)	
Rheumatoid Arthritis	99 (25)
Spondyloarthritis	67 (17)
Connective Tissue Disease	60 (15)
Behçet's Syndrome	74 (19)
Familial Mediterranean Fever	57 (14)
Others*	9 (2)
Unknown	31 (8)
Education Status, n (%)	
Elementary School	171 (43)
High School	143 (36)
College	83 (21)
Having an internet connectable device, n (%)	
Smart phone	301 (77)
Laptop	105 (27)
Desktop	72 (18)
Tablet	68 (17)
None	68 (17)
Use Frequencies, n(%)	
Facebook	234 (81)
Instagram	202 (70)
Twitter	92 (32)
Pinterest	38 (13)





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AB1211 A RETROSPECTIVE ANALYSIS OF LABORATORY ABNORMALITIES FOUND DURING METHOTREXATE MONITORING AND THE COST IMPLICATIONS

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Background: Methotrexate (MTX) remains the first line treatment in majority of cases of inflammatory arthritis. The current British Society of Rheumatology (BSR) Guidelines suggest checking Full blood Count (FBC), ALT/AST, Albumin, Creatinine at 0,2,4,6,10,14, 18 weeks and then 12 weekly. Despite this close monitoring recommendation, MTX is generally considered a safe drug by Rheumatologists and its use has grown significantly over last two decades.
Objectives: To evaluate the incidence of liver, renal and haematological toxicities during Methotrexate treatment and calculate the cost implications.
Methods: 101 patients (30 males 71 females) (Age 40-89 year Mean 66.5 year) prescribed MTX were randomly selected and retrospective analysis was performed. 91 Rheumatoid arthritis, 8 Psoriatic arthritis and 2 patients had Undifferentiated Inflammatory Arthritis. 20 patients had Early Inflammatory Arthritis (<1 year) and 81 had established disease. 24 patients were on MTX for <1 year. Average dose of MTX in our cohort was 15mg once weekly (Min 7.5mg Max 25mg). All patients were on folate supplementation. Blood investigations over last 1 year were reviewed individually for all patients. Severe Liver toxicity (LS) was defined as ALT/AST >100 U/l; unexplained reduction in albumin <30 g/l and mild liver toxicity (LM) was between normal and LS values. Severe haematological toxicity (HS) was defined as WCC $<3.5 \times 10^9$/l, MCV >105 fL, Neut $<1.6 \times 10^9$/l, PLT $<140 \times 10^9$/l unexplained eosinophilia $>0.5 \times 10^9$/l and mild haematological toxicity (HM) was between normal and HS. Severe renal toxicity (RS) was defined as Creatinine increase >30% over 12 months and/or calculated GFR <60 ml/min. Mild renal toxicity (RM) was between normal and RS.
Results: Over 1 year, 101 patients had total of 609 blood tests for MTX monitoring (Min 1 Max 17). FBC, Liver Function Test, Urea & Electrolytes, CRP and ESR each cost £8.54. LS was found in 4 patients, LM in 15, HM in 3 and RM in 2 patients. MTX was stopped in all 4 patients with LS. Mild toxicities (LM, HM and RM) recovered after close monitoring or reduction in dose. 5 patients with mild toxicities were on MTX for <1 year. Rest of the patients were on stable dose of MTX for >1 year. All patients with severe and mild toxicities did not have any significant comorbidities compared to rest of the patients. It was calculated that detecting one LS cost (609x8.54)/4 = £1300.2. Similarly one LM cost £346.7, one HM £1733.6 and one RM £2600.43. These costs does not include travel expenses, parking charges and time off work for appointments in phlebotomy.
Conclusion: Our cohort shows that mild liver toxicity is the most commonly found abnormality during MTX monitoring and patients on stable doses still need monitoring for liver toxicity. Haematological and renal toxicities are much less common and a more relaxed monitoring schedule may be acceptable for these parameters. Regular monitoring for inflammatory markers (CRP, ESR) causes an extra cost burden. The direct cost for identifying each abnormality is considerable.

REFERENCES

[1] Ledingham J, Gullick N, Irving K, Gorodkin R, Aris M, Burke J, et al. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. Rheumatology. 2017 Feb 27;56 (6):865-868. kew479.

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AB1212 POLYPHARMACY AND OUTPATIENT HEALTHCARE USE IN RHEUMATOID ARTHRITIS: PATTERNS AND ASSOCIATIONS

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Background: Polypharmacy is a considerable problem in people with rheumatic diseases, including rheumatoid arthritis (RA), related amongst others to worse disease outcomes and increased cost for the health-system (1).
Objectives: To assess polypharmacy in RA and usage of the health-care system (outpatient clinics) in a real-world setting.
Methods: Medical records of 170 consecutive RA patients from a large outpatient service of a central hospital were retrospectively reviewed. Demographic characteristics, treatment for RA and comorbidities as well as frequency and type of visits to any outpatient services were recorded. The latter included rheumatologists, "medical specialties" doctors (general physicians, cardiologists, respiratory physicians, oncologists, dermatologists, gastroenterologists, hematologists, nephrologists and neurologists) and "surgical specialties" (general surgery, orthopedics, neurosurgery, urology, ophthalmology, ENT, maxillofacial and vascular surgery). Disease duration was defined as the time between RA diagnosis and the end of the study (May 2018). Univariable and multivariable analyses were performed (Table).
Results: Data from 170 RA patients (77.1% female) with a mean±SD age of: 62.1 ± 13.7 years and disease duration: 87.8 ± 22.0 months, were recorded. The median number of non-rheumatic drugs receieved througouht disease duration was 3. Only 7% of the patients were not receiving any additional drugs, while 15.3%, 40.6% and 56.4% had received 1, 2 and 3 non-rheumatic drugs, respectively. The most commonly used non-rheumatic drugs were, anti-hypertensive, anti-osteoporotic and lipid-lowering drugs. Higher total number of drugs correlated with age of the patient and longer disease duration. Methotrexate (MTX) experienced or biologic-naïve patinets, had received a larger number of non-rheumatic drugs compared to those who had not received methotrexate or were biologic-experienced. Multivariable analysis confirmed age and exposure to methotrexate/biologics to be positively and negatively association respectively, with the number of non-rheumatic drugs received (Table).
Number of visits to rheumatologists/year were: median (range) 2.9 (0.5 – 13.6). The number of visits was correlated with age of the patients, disease duration and number of non-rheumatic drugs received. Multivariable analysis, identified, disease duration, number of non-rheumatic drugs received and being MTX-naive as predictors of number of rheumatology visits (Table).
Number of visits to non-rheumatologists/year were: median (range) 1.8 (0.0 – 13.7). Visits to "internal medicine" doctors were more common than in "surgical specialties" doctors (p<0.0001). Number of visits to non-rheumatologists was correlated with age, disease duration, and with the number of non-rheumatic drugs received. Multivariable analysis confirmed only the association with the total number of drugs but revealed also that being MTX-naive was also associated with more frequent visits to non-rheumatologists.
Conclusion: The majority of RA patients received more than 3 (non-RA related) drugs. This increased with older age and associated with more frequent visits to rheumatology and other specialties.

Feature	Total number of non-rheumatic drugs	
	Univariable	Multivariable
Age	p<0.0001, r=0.383	p<0.0001, beta: 0.351
Disease duration*	p=0.03, r=0.171	
MTX-experienced	p=0.002	p=0.02, beta: 0.71
Exposure to Biologics	p=0.02	p=0.09, beta: - 0.124
	Total number of visits to rheumatologists	
	Univariable	Multivariable
Age	p=0.04, r=0.160	
Disease duration	p<0.0001, r=0.340	p<0.0001, beta= 0.310
Number of non-rheumatic drugs	p=0.02, r=0.182	p=0.02, beta= 0.194
MTX-naive		p=0.04, beta= -0.161
	Total number of visits to non-rheumatologists	
	Univariable	Multivariable
Age	p<0.0001, r=0.321	
Disease duration	p=0.03, r=0.169	
Number of non-rheumatic drugs	p<0.0001, r=0.428	p<0.001, beta= 0.455
MTX-naive		p=0.03, beta= -0.163

Table: Univariable and multivariable analysis, (backward stepwise regression model) were performed having: the number of non-rheumatic drugs or total number of visits to rheumatologists or total number of visits in non-rheumatologists as the dependent variables. Pre-defined epidemiological, clinical and laboratory features were tested as independent variables. MTX: methotrexate, * for definition please see text

Table 1

REFERENCES

[1] Filkova M, et al. J Rheumatol. 2017 Dec;44:1786-1793

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AB1213

PATIENTS' PERSPECTIVES OF OUTCOMES AFTER TOTAL KNEE AND TOTAL HIP ARTHROPLASTY: A NOMINAL GROUP STUDY

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Background: Utilization rates of total joint replacements (TJR) are high and rising to treat advanced symptomatic arthritis, but there is little qualitative research to define the most important outcomes from the patient perspective.
Objectives: To assess the most important outcomes of TJR from the patients' perspective using nominal group technique (NGT).
Methods: Recruited patients were ≥18 and had received total hip (THR) or total knee replacements (TKR). Participants completed a questionnaire including demographics and pain and function measures, and answered "What result/results matter the most to a patient undergoing/having a knee or hip replacement?". Outcomes were independently selected, listed in a round robin, and ranked by the group using NGT.
Results: 36 patients participated in 6 nominal groups in January 2019. 42% were men **(Table 1)**. For THR, 94% reported no/mild pain. For TKR, 81% reported no/mild pain pivoting or on stairs, 1 patient reported severe pain. Satisfaction was high, 97% reported very/somewhat satisfied with pain relief. Of 216 total votes, A) pain received 98 votes, B) function 52; C) quality of life 40; D) adverse events 16 votes and E) revision 2 votes, the remainder 8 votes were distributed to post-op concerns including access to rehabilitation or education **(Table 2)**.
Conclusion: Pain, function, quality of life, and adverse events are the outcomes ranked highest by patients, supporting their inclusion in TJR clinical trials.

Abstract AB1213 Table 1. Baseline Characteristics

Age (mean, years)	75.7±8.2	65.9±8.1	66.3±5.4	71.1±9.3
Men, n(%)	6 (31.6)	8 (57.1)	1 (33.3)	15 (41.7)
Black, n(%)	3 (15.8)	3 (21.4)	-	6 (16.7)
Asian, n(%)	-	-	1 (33.3)	1 (2.8)
Multi-race, n(%)	1 (5.3)	1 (7.1)		2 (5.6)
Education				
High school, n(%)	-	1(7.1)	-	1 (2.8)
Some college, n(%)	1(5.3)	3(21.4)		4 (11.1)
College or above, n(%)	18 (94.7)	10 (71.4)	3 (100)	31 (86.1)
Employment				
Employed for wages, n(%)	3 (15.8)	9 (64.3)	3(100)	15 (41.7)
Self-employed, n(%)	4 (21.1)	3(21.4)	-	7 (19.4)
Out of work but not looking for work, n(%)	1(5.3)	-	-	1 (2.8)
Retired, n(%)	11 (57.9)	2 (14.3)	-	13 (36.1)
Reason for surgery				
Osteoarthritis, n(%)	13 (68.4)	12 (85.7)	3(100)	28 (77.8)
Rheumatoid arthritis, n(%)	2 (10.5)	1(7.1)	-	3 (8.3)
Other arthritis, n(%)	3 (15.8)	1(7.1)	-	4 (11.1)
Avascular necrosis of the bone, n(%)	1(5.3)	-	-	1 (2.8)

Abstract AB1213 Table 2. Theme: What result/results matter the most to a patient undergoing a hip or knee replacement?

NG1-6, 36 people, 14 Male, 22 Female; 8 African-American, 26 White, 2 Asian; 216 votes*	
A. Pain: No more pain/to be pain free • "Goes beyond physical pain, isolates you, not living the way you're used to living" • "You're a slave to the joint"	98
B. Function: Regaining range of motion/mobility/able to carry out ADL (activities of daily living) • "Has some emotional impact – when I was able to put my socks on without pain for the first time I had tears in my eyes"	52
C. Quality of life: Ability to have a normal life • "Before captive to the pain and immobility, now have an ability to be participating in life"	40
D. Adverse events: Not feeling the fear of infection or set back/long term good outcomes • "It's a horrible thing (infection), it's a sin that happens"	16
E. Revision: Longevity, no repeated replacement of joint in my lifetime • "The useful life of the replacement"	2
F. Optimization of post-operative care: having a short recovery period • "Prepared for a lengthy recovery – was not an issue, expected a year"	6
G. Education: What to expect with healing • "Know what to expect after surgery"	2
***combined votes; NG= nominal group**	

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AB1214

PRELIMINAR STUDY OF THERAPY ADHERENCE CONTROLLED BY PRESCRIPTION OF MEDICATION AND SELF-PERCEPTION ADHERENCE OF INFLAMMATORY CHRONIC DISEASE PATIENTS

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Background: The absence of therapy adherence is a public health problem and leads to negative consequences in inflammatory chronic diseases. The measurement of therapy adherence has demonstrated effectiveness on the improvement of compliance, but it is difficult to estimate because it is based on indirect measurements. With high probability there will be discrepancies between different measurements.
Objectives: To estimate the discrepancies between therapy adherence controlled by prescription of medication, Morisky-Green test and self-perception adherence patients under biological subcutaneous treatment or under JAKinhibs oral treatment.
Methods: Observational study including inflammatory chronic disease patients under biological subcutaneous treatment or under JAKinhibs oral treatment, selected consecutively. We performed a preliminary stage where patients were contacted by telephone and after that the questionnarie was sent to the email address they provided. The questionnaire included Morisky-Green test and a self-perception adherence scale (0-10). Data about dispensation of medication was collected from the pharmacy service. We defined as "adherent patient" a dispensation rate over 80%.
Results: 54 patients were contacted, and 37 of them full-filled the questionnaire. 28 full-filled the online questionnaire but the other 9 preferred the paper format. The patients from the online format questionnaire had a mean age of 50.86 years (range 22-74), and patients of paper format questionnaire had a mean age of 61.38 years (38-71).
We observed a high proportion of patients with university studies among those who preferred the online format.
21 of the patients surveyed had rheumatoid arthritis, 7 psoriatic arthritis, 7 ankylosing spondylitis and 1 juvenile idiopathic arthritis. 21 were under subcutaneous biological therapies and 16 under oral JAKinhibitor therapies. From the 37 patients, 64.8% took 2 or more pills daily.
among the 37 surveyed patients a discrepancy between therapy adherence controlled by dispensation of medication and adherence by Morisky-Green was observed (94.6% vs 72.97%, P<0.005). Moreover, 72.97% of patients considered easy or very easy to follow the prescribed therapy, and in the self-perception adherence scale the 54.05% of them scored 10, the 21.62% scored 9, the 21.62% scored 8 and the 2.7% scored 6.
among the analyzed factors which may affect the therapy adherence, the oral route of administration showed more adherence rate controlled by dispensation of medication (P=0.019) and with Morisky-Green adherence rate (P=0.016). No other association with other factors as age, gender or time of disease evolution was observed.
Conclusion: Younger patients and those with university studies preferred to full-fill the online questionnaire. A discrepancy between therapy adherence controlled by dispensation of medication and adherence by Morisky-Green was observed. Moreover oral route of treatment showed more therapy adherence than subcutaneous route of treatment.
Even if the patients are no self-considered as 100% adherents (Morisky-Green), a tendency of collect the medication on a regular basis was observed. This seems to indicate that instead of the controlled dispensation of medication by Pharmacy, patients with lower therapy adherence will collect all the medication.

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AB1215 **CURRENT PRACTICE OF HYDROXYCHLOROQUINE PRESCRIPTION AND MONITORING IN INDIA -A NATIONAL SURVEY**

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Background: Hydroxychloroquine was introduced as an antimalarial during World War 2 and since then has found numerous indications for usage as an immonomodulator. Research is ongoing for new uses of the drug. Hydroxychloroquine is generally considered to be safe and monitored less rigorously than other DMARDS that have strict bloods monitoring regimes. Emerging evidence of increased risk of retinal toxicity possibly due to widespread usage in a population with diverse co-morbidity has prompted updates to prescription and monitoring guidelines worldwide.

Objectives:

- 1. Evaluate current practice of Hydroxychloroquine prescription and monitoring in secondary care.
- 2. Understand awareness of cross specialty guidelines.
- 3. Explore barriers to evidence based monitoring.

Methods: Questionnaire based survey shared to practicing clinicians(consultant rheumatologists, Immunologists, postgraduate trainees, other clinicians with interest in rheumatology) who prescribe Hydroxychloroquine. Results analyzed through excel spreadsheet and charts.

Results: We received 61 responses from clinicians nationally.88.5% were consultant rheumatologists,6.6% consultant immunologists and others included clinicians with interest in rheumatology. Special interest was CTD for 47.5% and 36% inflammatory arthritis. All respondents worked in urban areas and average experience in specialty was 9 years. Majority saw in excess of 500 patients month.

61 clinicians saw in excess of 24,700 patients per month and on average started more than 2481 patients on Hydroxychloroquine. Approximate prescription rate was 41 patients per clinician per month. Indications included connective tissue disease and inflammatory arthritis mainly. Other indications include antiphospholipid syndrome, osteoarthritis, post viral arthropathy, dermatomyosistis and diabetic arthropathy.

Pretreatment tests as per international guidelines were recommended by 35% clinicians only which includes baseline Optical coherence tomography 25% or eye evaluation by ophthalmologist 10%. 54% clinicians advised OCT after 5 years (47.5%) or formal ophthalmology monitoring(6.5%) in line with published international guidance. Barriers to following required pretreatment tests and monitoring we noted from this survey include lack of awareness or disagreement with guidelines (lack of conclusive data), doubtful cost effectiveness and nonadherence by patients due to cost implications.

Conclusion: There is need to improve awareness of existing evidence based guidelines on prescription and monitoring of Hydroxychloroquine by international ophthalmology and rheumatology organizations There is more data needed to prove effectiveness of current guidelines beyond doubt. We also need to better counsel and educate patients on the drug so adherence can be improved.

REFERENCES

[1] https://www.rcophth.ac.uk/wp-content/uploads/2018/07/Hydroxychloroquine-and-Chloroquine-Retinopathy-Screening-Guideline-Recommendations.pdf

[2] Ledingham J, Gullick N, et al.BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs; Rheumatology 2017; 56: 865–868

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AB1216 **CHECKING IN WITH IMMUNE CHECKPOINT INHIBITORS: RESULTS FROM A NEEDS ASSESSMENT SURVEY OF CANADIAN RHEUMATOLOGISTS**

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Background: Immune checkpoint inhibitors (ICI) have revolutionized the treatment of cancer. However, enhanced immune activation from ICI has been associated with immune-related adverse events (irAE), including autoimmune rheumatologic diseases such as inflammatory arthritis, spondyloarthritis, polymyalgia rheumatica-like syndrome and inflammatory myositis, among many others. This emerging field represents a challenge given that experience with these conditions is limited and evidence-based recommendations do not yet exist.

Objectives: The Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO) is an emerging network of rheumatologists interested in rheumatic irAE (rh-irAE). CanRIO undertook a needs assessment survey to understand the need for education and recommendations for the management of rh-irAE in the rheumatology community in Canada. The primary objective was to recognize the knowledge gaps, if any, and understand current patterns of practice in this newly emerging area.

Methods: A 25-item electronic survey was developed by the CanRIO investigators. The survey, which was available in both French and English, was distributed via electronic mail to 574 members of the Canadian Rheumatology Association (CRA). Responses were collected over a period of 14 days. Results were summarized using descriptive statistics.

Results: Of the 574 CRA members who were invited to participate, 83 responded (response rate of 14.5%). Half of the respondents were adult rheumatologists from academic centres and 25% from the community. Over 25% of the respondents were not familiar with ICI and irAE. Half of the respondents had not seen or managed patients with irAE, and among the remaining, the majority had seen less than 5 patients with irAE. Inflammatory arthritis was the most common rh-irAE encountered. Other rh-irAE included sicca, myositis, sarcoid and vasculitis. Prednisone and methotrexate were the most common treatment strategies. Almost half of the respondents (43.6%) had been asked for advice from oncologists regarding discontinuation of ICI for irAE, and of these, almost half (48.7%) reported that they were either 'slightly confident' or 'not confident at all' in providing advice. Over half of the respondents had not yet been asked to provide advice concerning ICI for patients with pre-existing auto-immune diseases. The vast majority (87.2%) agreed that there was a need for clinical practice guidelines for the management of rh-irAE.

Conclusion: The survey highlighted the important knowledge gaps in the emerging field of rh-irAE. Given the increasing use of ICI in a growing number of cancer types and stages, referrals for rh-irAE are likely to increase. There is strong rationale to develop educational programs and clinical practice guidelines to support Canadian rheumatologists who will be increasingly responsible for managing rh-irAE.

REFERENCE

[1] Ye, Carrie; Jamal, Shahin; Hudson, Marie. CRAJ 2018. Volume 28, Number 3, pages 24-25. "Rheumatic Immune-related Adverse Events Associated with Immune Checkpoint Inhibitors for Cancer: Coming Soon to a Clinic Near You!"

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AB1217 **WHY DO PATIENTS CLAIM? ANALYSIS OF THE CLAIMS MADE BY PATIENTS THROUGH CUSTOMER SERVICE**

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Background: Analysis of the claims made by patients could be an indicator of quality and show strengths and aspects of improvement in the organization of a rheumatology department

Objectives: The aims of the present study are to evaluate these claims, describe the sociodemographic and clinical characteristics of claiming patients and to determine the association between medical history and types of complaints.

Methods: cross-sectional study. Claims made by patients treated by a Rheumatology department between 04/2016 and 12/2017 were analyzed. A descriptive analysis of these claims was carried out followed by a multivariate logistic regression model to determine the effect of the diagnosis of Fibromyalgia (FM)/Chronic Widespread Pain (CWP) on the type of claim and its association with clinical variables. A $p < 0.05$ was considered significant.

Results: One hundred and nine patients (mean age 54.7 ± 18.5 years, 78% women and 50.5% residents in rural areas) made 113 claims. The main reasons for claiming were: *"advance medical evaluation and/or tests"* (45.1%), *"request for evaluation by a specific physician"* (24.8%) and *"rejection of evaluation by specific physician"* (13, 3%). 67% of the claims were satisfied. The least satisfied claims were *"request for evaluation by specific doctor"* (39.3%) while claims for *"cancellation of evaluation"* were satisfied in 88% of the cases.

Median time between claim and previous medical visit was 99 [34-203] days and between claim and the subsequent medical consultation was 44 [28-82] days. Patients whose claims were due to *"unpleasant attendance"* were the first to complaint (median 28 [2-72] days) but waited for the longest time to be attended (median 103 [46-147] days). "*Cancellation of evaluation*" was attended after a median of 31.5 [28-33] days.

The main reasons for medical evaluation were: inflammatory/systemic disease in 25 patients (22.15%), neck and low back pain in 23 patients (20.35%) and FM/CWP also in 20.35% of patients. As personal medical history, Psychiatric Disorders were present in 20.5% of patients and multiple comorbidities in 19.6% of patients. Twenty patients had no medical history of interest.

Regarding the type of claims, differences were observed related to the diagnosis and the patient´s medical history. The logistic regression model (FM as dependent variable) adjusted for sex, age, rural area, time to/after the claim and medical history showed that patients with FM/CWP requested more frequently to "*be evaluated by other physician*" (OR of 23.92 (95% CI, 1.4-409.06) and "*reject to be evaluated by a specific physician*" (OR of 8.48 (95% CI, 1.2-60.09) than rest of the patients and also presented more frequently with psychiatric history (OR of 22.39 (95% CI, 1.15-437.23)

Conclusion: the present study reflects main reasons for claiming of patients treated in a rheumatology department. Reasons of claiming and comorbidities of patients with FM/CWP differ from those of the rest of patients. These findings may be of interest for the organization of resources in rheumatology departments.

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AB1218 ANALYSIS OF REFERRAL TRENDS TO A SECONDARY CARE RHEUMATOLOGY SERVICE FROM GENERAL PRACTICE,OVER A TEN- YEAR PERIOD

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Background: The practice of Rheumatology in the UK has undergone significant change in the past decade. These have been driven by developments in our understanding of the diseases; early arthritis clinics; changing population demographics; changes in the health services (NHS) all of which have influenced referral patterns to rheumatology.

Objectives: To analyse referral data from primary care three time points of a month at a time, over a decade – from 2006 to 2016 to assess changing trends, if any, of patients attending Rheumatology.

Methods: We analysed referrals from the primary care in the months of Feb '06 (n=89), Aug'12 (n=50) and Feb'16 (n=100). We looked at the following: reason for referral and our response, referral to out-patient review interval; outcome and final diagnosis.

We also analysed between first appointment and DMARD initiation in inflammatory arthritis.

Results: Referrals were grouped as demonstrated in the table below.

Diagnostic category	2006 (n=89)	2010 (n=50)	2016 (n=100)
non inflammatory/inflammatory arthritis	82% (n=73)	68% (n=34)	73% (n=73)
Abnormal investigations results for opinion	2.5% (n=2)	6% (n=3)	10% (n=10)
Back pain	11.3% (n=10)	10% (n=5)	5% (n=5)
Myalgia	1.1% (n=1)	10% (n=5)	3% (n=3)
Suspected connective tissue disease	1.1% (n=1)	4% (n=2)	6% (n=6)
Soft tissue conditions/others	2.2% (n=2)	2% (n=1)	3% (n=3)

The mean interval from Referral to patient review was 11.5 weeks in Feb 2006, 7.15 weeks in August 2012 and 6.6 weeks in Feb 2016. In patients with the diagnosis of inflammatory arthritis we also looked at mean timeframe from 1st review to initiation of DMARDs which is demonstrated in the chart below.

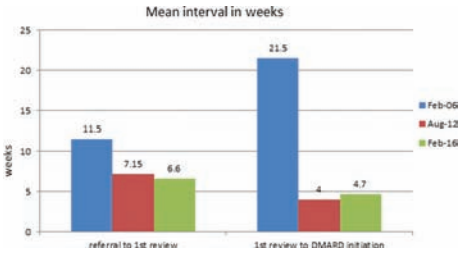


Figure 1

Conclusion:
- Mean interval between primary care referral to first outpatient review has improved significantly over the period of 10 years
- Mean interval for DMARD initiation in inflammatory arthritis patients has also improved in the 10 years' time

Disclosure of Interests: None declared

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AB1219 EFFECTS OF A WORKPLACE-CENTERED COUNSELING OF INDIVIDUALS WITH MUSCULOSKELETAL COMPLAINTS: A PROSPECTIVE COHORT STUDY

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Background: Employed people with musculoskeletal complaints often seek medical advice when symptoms are chronic and lead to loss of workability.

Objectives: A brief examination was offered in the workplace setting to detect and to counsel individuals with symptoms of Rheumatic and musculoskeletal diseases(RMDs).

Methods: Employees received a questionnaire regarding musculoskeletal problems. In case of a positive screening, consultation by RMD specialists was offered. If necessary, participants were referred to a clinic specialized in RMDs. Employees' work was categorized into physically-highly-demanding(HD) and less-demanding(LD).

Following data were acquired: demographics, known pre-existing RMD, pain intensity, affected region(s), current treatment, number of sick-leave-days due to musculoskeletal complaints, and out of pocket costs for treatments during the preceding year. General wellbeing and depression were measured by Euroquol-5d. Follow-up information about data mentioned above was collected by telephone-interview.

Results: 6170 employees were invited. 413 participated in the counselling program, 344 were enrolled in the study. 56.6% of the participants had no previously diagnosed RMD, after the specialists' assessment, this percentage decreased to 35.7%. Men with LD-workload had significantly higher wellbeing (EQ-5d scale) compared to women with both LD (p=0.034) and HD (p=0.001). LD and HD differed significantly regarding percentage with painful upper (p=0.006) and lower (p=0.016) limbs. Back pain was distributed equally among all groups. HD women reported significantly higher use of NSAIDs (p=0.001).

235 individuals participated in telephone follow-up. There was significant improvement in wellbeing(p=0.006) and in rating of RMD pain (p=0.001). Participants who were suspected to suffer from RMDs had significantly increased out of pocket costs after one year (p=0.026). Use of NSAIDs decreased significantly from 29.1 to 17.4% (p=0.02). Rates of use of physiotherapy (p=0.001), gymnastics (p=0.001), physical therapy (p=0.027) and complementary/alternative methods (p=0.003) were significantly increased.

Conclusion: We found most physical/psychological problems related to RMDs in HD-working women. After one year, participants reported improved quality of life, reduction of RMD pain, higher utilization of medical services and of gymnastics, less use of NSAIDs, and, if suspected to suffer from RMDs, higher out of pocket costs. Thus, this workplace-centered intervention appears to have beneficial effects on both subjective well-being and physical/physiological health.

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Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, MedImmune, MSD, Novartis, Pfizer, Roche, Samsun, Sanofi, UDB, Speakers bureau: AbbVie, Amgen, Astra-Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, MedImmune, MSD, Novartis, Pfizer, Roche, Samsun, Sanofi, UDB, Klaus Machold Grant/ research support from: Abbvie

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AB1220 DISTRIBUTION OF RHEUMATOLOGISTS AND YOUNG RHEUMATOLOGISTS' ORGANIZATIONS ACROSS THE WORLD: STILL ROOM FOR IMPROVEMENT

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Background: Rheumatology is a rapidly advancing specialty. The increasing understanding of autoimmune mechanisms and advanced therapies have improved care for patients with chronic inflammatory conditions immensely. National and international collaborations are growing and are key to scientific developments. Still, the number and geographical distribution of rheumatology organizations globally, is not known.

Objectives: To gain further insights into the distribution of established and young rheumatologists' organizations beyond Europe. Furthermore, we intended to explore correlations between presence of rheumatology organizations and demographic and socio-economic parameters.

Methods: A systematic online search was performed independently by three investigators (AN, SS, JS). Keywords used in the search related to three main themes (i) Rheumatology (rheumatology or rheumatologist(s) or rheumatism), (ii) Organizations (associations or young organization or society or group or association or league or federation) and (iii) country's name. All identified rheumatology organizations worldwide were reported. Countries were grouped in eight regions according to their geographic location. General demographic information (including population, area, pop. density, net migration, infant mortality, GDP, literacy, phones, arable, crops, climate, birth-rate, death rate) was retrieved from World Bank Open Data by one extractor (SS). Descriptive statistics and quartile distribution for each analysed variable were performed using Excel[R] (Microsoft Office) and SPSSR software [R], using the total number of countries per region as the denominator.

Figure 1. Overview of the percentage of national rheumatology societies

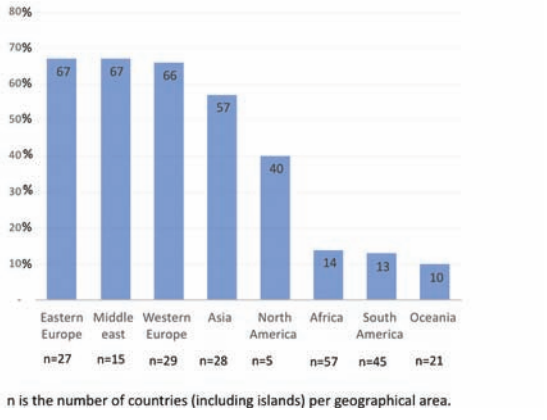


Figure 1

Results: Four international societies and three junior international organizations (EMEUNET, PANLAR joven, ALPAR Young rheumatologists) were identified. Out of the 227 countries assessed, 89 national rheumatology societies (39%) and seven junior national organizations were identified (n=4, 2%). Rheumatology societies were more frequent in Eastern Europe (n=18/27, 67%), Middle east (n=10/15, 67%) and Western Europe (n=19/ 29, 66%) (Figure 1). Rheumatology societies were more frequently found in countries in the upper quartiles (Q1) of population density, gross domestic product and literacy when compared to Q2-4 (as assessed for each variable, $p<0.05$). Conversely, it was significantly less frequent in countries with high migration and infant mortality (Q1 Vs Q2-3, $p=0.043$ and $p=0.039$, respectively).

Conclusion: National rheumatology societies were identified in less than half the countries across the globe and were unequally distributed. We only found 7 national young organizations. Such organizations are needed, as trainees can highly benefit from educational and networking offers. Further steps will include the exploration of the impact and the reasons for lack of such establishments in some countries.

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AB1221 VIEWS OF PRIMARY CARE PHYSICIANS AND RHEUMATOLOGISTS REGARDING SCREENING FOR HYPERLIPIDEMIA AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Screening of hyperlipidemia in rheumatoid arthritis (RA) is suboptimal, despite RA patients' high risk for cardiovascular disease (CVD) mortality.

Objectives: To identify barriers to screening for hyperlipidemia among patients with RA from the viewpoint of primary care physicians (PCPs) and rheumatologists.

Methods: We recruited rheumatologists and PCPs nationally to participate in separate moderated structured group teleconference discussions using the nominal group technique. Participants in each group generated lists of barriers to screening for hyperlipidemia in patients with RA, then each selected the three most important barriers from this list.

Results: Twenty-six rheumatologists participated in 3 groups and 20 PCPs participated in groups. The resulting barriers were organized into physician-, patient- and system-level barriers. Rheumatologists prioritized physician level barriers (e.g. 'ownership' of hyperlipidemia screening), whereas PCPs prioritized patient-level barriers (e.g. complexity of RA itself). See table 1 for details.

Conclusion: These rheumatologists were conflicted about whether screening of CVD risk among patients with RA should fall within the role of the rheumatologist or PCPs. On the other hand, participating PCPs were concerned about the overall effect of RA and RA treatments in the context of screening hyperlipidemia.

Table 1221. Screening for hyperlipidemia: List of themes and sub-themes of barriers for rheumatologists and primary care physicians (PCPs) to screen patients with RA, with their respective priority votes

Category	*Subcategory*	*Rheumatologist* (% votes) *Total Votes N=162*	*PCP* (% votes) *Total Votes N=120*
Physician Level	**Total Votes**	**83.0**	**42.5**
	Lack of time	34.0	1.7
	Conflict regarding ownership of hyperlipidemia screening	25.9	10.8
	Lack of training and knowledge of hyperlipidemia guidelines or RA itself	17.9	20.0
	Focus only in RA	4.9	–
	Physician prioritization of RA symptomology over preventive measures	–	10.0
Patient Level	**Total Votes**	**7.5**	**44.2**
	Effect of RA and its treatment	2.5	9.2
	Patient prioritization of RA symptomology over preventive measures	2.5	9.2
	Patient expectations	1.9	–
	Patient already on multiple medications	0.6	0.0
	Multiple blood draws	0.0	8.3
	Side effects of statins and drug interactions with statins	0.0	5.0
	Poor patient compliance with medical care	0.0	9.2

	Patients' lack of awareness of CVD risk	–	3.3
System Level	**Total Votes**	**9.9**	**13.4**
	Lack of care coordination	6.8	11.7
	Financial barriers (limited insurance coverage, cost of repeating labs)	3.1	–
	Lack of financial incentive for screening	–	1.7

Note: RA = rheumatoid arthritis; CVD = cardiovascular disease; 0% = that sub-theme emerged during the brainstorming session but did not receive votes; " – " = the sub-theme did not emerge in the respective group.

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AB1222 PATIENT PREFERENCES FOR THE USE OF DIGITAL TOOLS AND SOCIAL MEDIA IN DIET AND EXERCISE INTERVENTIONS

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Background: Healthy behavior changes such as improving diet/exercise are important to improve outcomes in rheumatic and musculoskeletal disease (RMD) patients. These changes require incentives, whether internal or external motivation or social support.

Objectives: To assess feasibility of using digital symptom tracking and social media peer support to conduct diet/exercise health behavior change interventions among adults with inflammatory arthritis (IA) and osteoarthritis (OA).

Methods: A 37-item cross-sectional survey was developed and administered online and via mobile app in the ArthritisPower research registry. Participants (pts) were eligible if they were $\geq$ 19 years of age, resided in the US, and reported physician diagnosis of IA or OA. Pts reported on use of technology and social media, experience with exercise and weight loss programs, and interest in various program features. We descriptively reported differences between respondents with IA (RA, PsA, AS) and OA.

Results: 418 pts completed the survey. A majority were female (89.5%) and white (89.5%); mean age was 56 (10.5). The proportion of pts who were obese (BMI >30) was higher among OA than IA pts (67.7% and 50.0%, respectively; p<0.001). Most pts were willing to provide blood samples remotely and use WiFi-enabled digital scale and blood pressure monitor for a trial (Table). Interest in social media for peer support and apps differed between IA vs. OA pts: more IA pts used an app to help them exercise (35.1% vs. 19.2% of OA pts, p=0.001) and were interested in using an app to track diet and exercise in the context of peer support on Facebook (72.2% vs. 62.3% of OA pts, p=0.04). The most commonly used social media platform overall was Facebook (93.3% of pts) followed by Twitter (51.9%) and Instagram (41.9%). Pts cited pain/difficulty moving (57.4%) and sedentary behavior, such as watching TV, (47.6%), as their biggest weight loss challenges. OA pts reported depression (46.9%, p=0.01) and disliking exercise (34.6%, p=0.003) as bigger challenges to weight loss than did pts with IA (34.0% and 20.8% respectively). Motivations to exercise also differed between groups: more IA than OA pts said building muscle was a top motivation (54.5% and 43.1%, respectively; p=0.03).

Table: Interest in program features by arthritis type

	n (%)	Inflammatory Arthritis (n=288)	Osteoarthritis (n=130)	p-value
Regularly using WiFi-enabled digital scale to measure weight and blood pressure monitor automatically linked to study	332 (79.4)	236 (81.9)	96 (73.9)	0.12
Providing blood samples for study by going to nearby Quest or other lab	320 (76.6)	222 (77.1)	98 (75.4)	0.88
Participating in study that would provide an activity tracker (e.g. Fitbit) and resources to increase daily steps	313 (74.9)	224 (77.8)	89 (68.5)	0.03*
Participating in peer support (via Facebook private group), with other arthritis patients	299 (71.5)	207 (71.9)	92 (70.8)	0.82
Participating in peer support (via Facebook private group), that includes patients without arthritis	40 (9.6)	27 (9.4)	13 (10.0)	0.84
Using a mobile app to track my diet and exercise	289 (69.1)	208 (72.2)	81 (62.3)	0.04*
Participating in group facilitated by professional weight loss counselor	274 (65.6)	189 (65.6)	85 (65.4)	0.96
Using wireless scale that automatically sends my weight to the counselor	270 (64.6)	187 (64.9)	83 (63.9)	0.83
Sharing my banking information so study could provide compensation	222 (53.1)	161 (55.9)	61 (46.9)	0.23

*Statistically significant at alpha=0.05

Conclusion: Program focus and format may need to be tailored depending on arthritis type, but pts with both IA and OA are interested in social media peer support and digital symptom tracking to motivate achievement of health behavior change goals.

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AB1223 A SYSTEMATIC REVIEW OF STUDIES INVESTIGATING THE EFFECTIVENESS OF ADALIMUMAB PATIENT SUPPORT PROGRAMMES

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Background: Adalimumab patient support programmes (A-PSPs) are offered to patients with chronic inflammatory indications creating the need to study how such A-PSPs assist patients and other stakeholders in improving health outcomes. A deeper understanding of the effects of A-PSPs can improve treatment outcomes and experience of patients being treated with adalimumab.

Objectives: To review current studies evaluating A-PSPs, summarize their general characteristics and methodology, and recommend future research work in the area of A-PSPs.

Methods: Studies were identified through Web of Science and were cross-checked by searching through PubMed and MEDLINE databases, following PRISMA guidelines. Full-text papers and conference proceedings identified by the database search were reviewed for relevance.

Results: 17 studies evaluating the impacts of A-PSPs on patient outcomes were identified – 6 full-text articles and 11 meeting abstracts. Most research was done at the international level or in North America [1-3]. In only 5 reviewed studies a prospective study design was applied. Indications most commonly investigated were rheumatoid arthritis and inflammatory bowel disease. 12 studies evaluated the impact of all interventions of A-PSPs while others assessed the impact of Coach Care Calls or phone calls. Patient outcomes most commonly measured were persistence, adherence and low disease activity or remission. Overall, patients using any of the interventions of A-PSPs experienced significantly better improvements in all studied patient outcomes at different follow-up assessments compared to those not enrolled into any of the programme's interventions. Study population sizes and ratios between assigned users and non-users of interventions differed between studies. The most frequent follow-up assessments were after 12 and 24 months of treatment with adalimumab. Data for analysis was mostly obtained by linking a patient support database and claims administrative database, and in 5 cases by applying patient and physician reported surveys. Methodology for assessing the differences between users and non-users of interventions of A-PSPs consisted of univariate and multivariate methods, where the causal relationships between the impact of patient support program and patient outcomes were estimated by regression modelling adjusted for multiple confounders.

Conclusion: Interventions of A-PSPs have been shown to have a positive impact on all investigated patient outcomes. Main recommendations for

future studies are to design a prospective study, include persistence and adherence measures in the study design, and to assess patient outcomes with additional measures such as patient outcomes based on a patient-centric approach and adverse effects.
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REFERENCES

[1] Van den Bosch F, Ostor AJK, Wassenberg S, Chen NJ, Wang C, Garg V, Kalabic J. 2017. Impact of participation in the adalimumab (Humira) patient support program on rheumatoid arthritis treatment course: results from the PASSION study. *Rheumatol Ther*, 4(1): 85-96
[2] Marshall JK, Bessette L, Thorne C, Shear NH, Lebovic G, Gerega SK, Millson B, Oraichi D, Gaetano T, Gazel S, Latour MG, Laliberté MC. 2018. Impact of the adalimumab patient support program's care coach calls on persistence and adherence in Canada: an observational retrospective cohort study. Clin Ther, 40(3): 415-429
[3] Rubin DT, Mittal M, Davis M, Johnson S, Chao J, Skup M. 2017. Impact of a patient support program on patient adherence to adalimumab and direct medical costs in Crohn's disease, ulcerative colitis, rheumatoid arthritis, psoriasis, psoriatic arthritis, and ankylosing spondylitis. *J Manag Care Spec Pharm*, 23(8): 859-867

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AB1224 IS THERE A NEED TO OPTIMIZE REFERRAL DIAGNOSIS TO A RHEUMATOLOGY DEPARTMENT?:

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Background: The initial visitation of patient suffering from rheumatic disease related symptoms often occurs in absence of a rheumatologist.
Objectives: This study evaluated the following questions: I. Which medical specialists referral patients to a rheumatology department? II. To quantify the accordance of the presumptive diagnosis and the finial diagnosis of a rheumatologist.
Methods: 1151 patients (355 men and 796 women) were admitted to a hospital for rheumatological diagnostic. The referral medical specialists were identified. Kappa-Analysis was performed to evaluate the presumptive diagnosis and the finial diagnosis by the rheumatologists.
Results: 73.0% of the referrals were performed by general practitioner. The other referrals were: 7.7% rheumatologist, 4.8% specialist in internal medicine (excluding rheumatology), 4.3% orthopaedic surgeon, 1.0% orhter surgeon and 9.2% other specialists.
The highest accordance of the presumptive diagnosis and the finial diagnosis was κ=0,534 for rheumatologists and κ=0,400 for specialist in internal medicine (excluding rheumatology). Lower kappa values were evaluated for general practitioner (κ=0,345), orthopaedic surgeon (κ=0,310) and other specialists (κ=0,252).
Conclusion: The referrals were frequently realized by general practitioners. In this context the presumptive diagnosis of a general practitioner presents a low accordance with the finial diagnosis. In this context, general practitioners should achieve a detailed education in the assessment of rheumatic-related symptoms to optimize the dedicated referral to rheumatological departments.
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AB1225 POSSIBLE EARLY DETECTION OF ADVERSE EVENTS USING REMOTE SYSTEMATIC WEEKLY ELECTRONIC MDHAQ

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Background: Adverse events of medications are reported to account for 5% of hospital admissions in the USA, including 10% in the elderly. Warnings from doctors and pharmacies concerning adverse events are given at initiation of new medications, but adverse events occur between visits and reporting depends primarily on communication between a patient and a health professional, which may be variable. Therefore, recognition and reporting of adverse events remain relatively haphazard. Several reports present strategies for systematic monitoring for adverse events, primarily involving telephone contacts from nurses to patients. A far less expensive systematic approach based on patient self-report using a remote electronic multidimensional health assessment questionnaire

Date	19 Jan 2018	25 Jan 2018	11 May 2018	2 Aug 2018	15-29 Aug 2018	24 Sep 2018	26 Sep 2018	4 Oct 2018	9 Oct 2018	9 Nov 2018	25 Nov 2018	28 Dec 2018
Site of MDHAQ	Clinic	Clinic	Clinic	Clinic	None	Home	Home	Home	Home	Home	Home	Home
RAPID3 (0-30)*	14.0	10.2	5.7	3.5	?	19.5	10.2	6.7	6.5	4.8	6.0	4.2
Fatigue VAS (0-10)	6	4.5	2.0	2.0		9.0	4.5	4.0	3.5	1.0	1.0	1.0
Medications												
Prednisone mg/ day	B 40	↓20	↓7	↓6	D/C 0	R 10	5	5	5	5	5	5
Methotrexate mg/w			B 10	20	D/C 0	0	0	0	0	R 10	10	10
pirfenidone					B3-9/d	9/d	D/C	0	0	3/D	D/C	0
#Symptoms (0-60)	10	5	6	6		15	15	13	13	6	8	6
Weight loss	+	+				+	+	+	+			
Feeling sickly	+											
Unusual fatigue	+					+	+	+	+	+	+	
Bruising/bleeding	+			+							+	
Other skin problem				+								
Loss of appetite						+	+	+	+	+	+	
Other eye problems			+									
Stuffy nose	+		+	+		+	+	+	+	+	+	+
Dry mouth	+	+	+			+	+	+	+	+	+	+
Problems with smell/taste				+		+	+	+	+			
Cough	+	+	+	+		+	+	+	+	+	+	+
Dyspnea	+	+	+	+		+	+	+	+	+	+	+
Heartburn/gas	+					+	+	+	+			
Dizziness	+											
Muscle weakness		+				+	+	+	+		+	+
Swelling of hands						+	+	+	+			
Swell-other joints						+	+	+	+			
Joint pain						+	+	+	+			+
Back pain						+	+					
Anxiety			+									
Sleep problems						+	+					

(MDHAQ) 60-symptom checklist may recognize most adverse events of medications.

Objectives: To document recognition of adverse events using a remote weekly electronic MDHAQ completed by patients at home, as a cost-effective approach to reduce their morbidity, costs, and mortality

Methods: The MDHAQ includes 0-10 scales for physical function, pain, and patient global assessment, compiled into a 0-30 RAPID3, fatigue and painful joint count, to assess treatment efficacy. The MDHAQ also includes a 60-symptom checklist to recognize comorbidities, review of systems, and symptom reduction; this checklist also recognizes adverse events associated with medications. Weekly remote completion of an electronic MDHAQ at home can monitor both efficacy and adverse events.

Results: A flowsheet from a patient with pulmonary fibrosis monitored over 2018 illustrates remote electronic MDHAQ use. At a first visit of 19 Jan, a routine clinic-based MDHAQ indicated RAPID3 of 14/30, fatigue 6/10, and 10 symptoms (Flowsheet). Treatment with low-dose methotrexate and prednisone led to clinical improvement from 19 Jan to 2 Aug, RAPID3 to 3.5, fatigue 2, and 6 symptoms. On 15 Aug, a pulmonologist discontinued prednisone and methotrexate and prescribed pirfenidone, an anti-fibrosis agent. A telephone call from the patient on 24 Sep indicated distress. A home-completed remote MDHAQ indicated RAPID3 19.5, fatigue 9, 15 symptoms - 7 not reported on 2 Aug were among 16 adverse events listed for pirfenidone. Discontinuation of pirfenidone and resumption of prednisone and methotrexate led to improvement of RAPID3 to 4.2, fatigue to 1.0, and resolution of pirfenidone-specific symptoms by 24 Dec, documented with weekly remote electronic MDHAQ (Flowsheet). A brief retrial of pirfenidone indicated an increase of RAPID3 to 6.0, which was discontinued in a timely manner.

78-year-old man monitored over 2018–all data from self-report on MDHAQ – pirfenidone highlighted (many entries deleted for space considerations)

Conclusion: Weekly remote electronic MHDAQ monitoring of a high-risk medication for treatment response and adverse events may provide a cost-effective approach to reduce the morbidity and mortality of adverse events, involving about 10 minutes/weekly or 2 hours of patient time over 12 weeks.

Disclosure of Interests: None declared

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AB1226 ONE YEAR´S RESULTS OF A PROTOCOLIZED HIGH RESOLUTION RHEUMATOLOGY CLINIC

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Background: Mechanical musculoskeletal pathologies put high demands on the Public Health Service, as they affect a significant percentage of the population, and cause both temporary and permanent disabilities.

The specialised High Resolution Rheumatology Clinic (CAR in Spanish) at our centre started up in October 2017, and focuses on the diagnosis and treatment of pathologies which are fundamentally of a mechanical ethology. The centre covers a population of approximately 328,868 inhabitants (Álava 2018 census).

The aim of our study, carried out at the unit over one year, is to determine the patients' epidemiological features.

Objectives:
- •To provide the Primary Care Centres with a "fast–track" and immediate care system in order to guide, diagnose, and treat patients who have worsening acute or chronic mechanical afflictions to the musculoskeletal system.
- •Diagnosis confirmation, request for non–accessible tests, adaptation of treatments mainly for the primary care doctor.
- •To speed up and reduce waiting lists, for both inflammatory rheumatic pathologies and mechanical rheumatic pathologies, by establishing new referral guidelines.
- •To draw up protocols in agreement with primary care doctors and related specialists.
- •To act as a support for other medical services.

Methods: The main services available are those offered mainly to primary care level. There are 3 clinics a week, attending to approximately 30 new patients per week. 1330 patients are included in the study, seen at the High Resolution Rheumatology Clinic (CAR) over 12 consecutive months (November 2017 – 2018), with non-complex regional pathologies and/or soft tissue rheumatism, which are able to be resolved with one or two visits.

Results: 1330 patients were seen, with an average age of 58 ±15.6 years, 64.64% female and 35.36% male, mainly for musculoskeletal ailments. In order of frequency, the visits were for shoulder (25.79%), hip (16.10%), axial skeleton (15.13%), ankle/foot (13.06%), wrist/hand (12.08%), knee (11.21%), and elbow (6.63%).

61.95% of the patients were discharged after the first visit, and one year later, this figure rose to 90.15% of all the patients discharged; only 2.78% made a return visit after being discharges. 22.26% were referred to other services, mainly Traumatology and Orthopaedics (10.53%); Rehabilitation and Physiotherapy (8.72%); and the Pain Management Unit (1.65%). The 3.68% were referred to the usual Rheumatology department. For 52.33% of the patients seen, there was no need to request more than one diagnostic tests, even though 12.41% visited for reasons other than the main one. Moreover, 63.08% received some kind of infiltration injection. The negative point was that 7.89% of the referrals had been made from Primary Care to several specialists at the same time; and 7.98% were consultations regarding traumatic injuries.

Conclusion: Systematising a clinic for mechanical musculoskeletal pathologies which have a high chance of being resolved in the short term, means that the quality of the care given, the waiting times, and the demand on the health service can be improved. Developing these can have important repercussions on waiting lists for other related services, and even for the Rheumatology service itself, allowing more serious cases to be seen earlier. Creating multi-disciplinary units should be encouraged, in order to improve care quality and prevent the various medical services involved from all carrying out fragmented courses of action. New guidelines could be considered, to optimise the care and management of new resources and/or links to other services, as the most prevalent pathologies can be identified.

Most of the patients seen represent the economically active part of the population; there are therefore, repercussions as far as sick leave, disability leave, etc. is concerned.

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AB1227 PREFERRED REFERRAL PROTOCOL FOR RECENT ONSET ARTHRITIS IN ADULTS FROM PRIMARY CARE TO RHEUMATOLOGY

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Background: The time of rheumatoid arthritis (RA) evolution until treatment begins is key to controlling the disease. Many studies have shown that a prolonged duration of symptoms at the onset of treatment is associated with a more severe course of RA. The time from symptoms onset to first DMARD prescription is >12 weeks in Spain, because of diagnostic delay due to either patient-related factors (delay in consultation), Primary Care Physician (PCP) (delay in citation/referral) or rheumatologist (delay in citation).

Objectives: To evaluate the usefulness of teleconsulting as a preferred referral tool from PCP to Rheumatology for early detection, diagnosis and treatment of inflammatory joint disease in adults, in the health area of a tertiary hospital.

Methods: A preferential referral circuit was established between the PCP and the Rheumatology Service of a tertiary hospital, defining the referral criteria as "patient suspected of recent onset arthritis (ROA)": arthritis or inflammatory arthralgia in >1 peripheral joint for >2 weeks with neither traumatic cause nor previous diagnosis of rheumatic disease. PCP performed first assessment, the request for initial tests (blood test including acute phase reactants, rheumatoid factor ± ANA, elemental urine and hands radiography) as well as the referral to Rheumatology with "ROA suspicion" motive. These consultation requests were cited from the Rheumatology Service within <15 days of receipt.

Before the protocol was established, its functioning was communicated as a face-to-face clinical session: by 2 rheumatologists in a Health Centre (HC) and by 1 PCP in the rest of the HC in the area. A poster was

edited and published, exposing criteria and referral method for PCP´s offices.
Results: During the first 6 months 33 patients were correctly referred. 78.8% were women and the average age was 49 years old. 48.8% (16 patients) were diagnosed with some inflammatory arthropathy: 31.5% were RA (5 cases); other diagnoses were arthropathy due to microcrystals deposit (2), overlap SLE/RA (1), MCTD(1), psoriatic arthritis (1), spondyloarthritis associated with IBD (1) or inflammatory arthralgia associated with retroperitoneal fibrosis (1). 12% (4 patients) were diagnosed with hands incipient osteoarthritis and 33.8% (12 patients) with arthralgias without data on inflammatory pathology. One patient missed her follow-up. The median time from symptom onset to Rheumatology assessment was 90 days in all patients; in the inflammatory pathologies subgroup, 68.8% was assessed in <12 weeks, with a median of 60 days and a mean of 96 days, starting treatment in this subgroup in the first assessment by Rheumatology.
Conclusion: In our experience, the establishment of a specific protocol in collaboration with Primary Care for the preferential referral of patients with suspected recent onset arthritis, obtained diagnoses not only for patients with rheumatoid arthritis, but also for other systemic autoimmune diseases in early stages, as well as early treatment initiation (<12 weeks) in most of these patients. In addition, it turned out to be an effective and comfortable referral route for PCP with suspected connective and/or inflammatory arthritis.
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AB1228 ACCESS TO RHEUMATOLOGIC TREATMENTS AND AUTOIMMUNE CONDITIONS IN LATIN AMERICA

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Background:
Objectives: To know the availability of treatment for rheumatologic and autoimmune conditions in Latin America, according to rheumatologists in the region.
Methods: A digital survey was created using Google Forms, it was approved and endorsed by the scientific committee of PANLAR, and later sent to the different Rheumatology associations of the region. The data was analyzed in the statistical program SPSS v.23.
Results: 456 surveys were filled by rheumatologists from 23 countries. The majority were females (54%). The mean age was 47.18 ± 11.79 [25-78] years. 91% reported access to DMARDs, methotrexate 95%, azathioprine 94%, cyclophosphamide 92%, hydroxychloroquine 92%, leflunomide 90%, mycophenolate mofetil 90%, sulfazalasin 88%, cyclosporine 80%, tacrolimus 64%, chloroquine 60%. 85% have access to biological therapy: adalimumab (78%), etarnercept (83%), rituximab (81%), infliximab (74%), tocilizumab (73%), abatacept (67%), golimumab (63%), certolizumab (59%), secukinumab (55%), ustekinumab (44%), certolizumab (59%), belimumab (47%), canakinumab (22%), sarilumab (15%), ixekizumab (12%), anakinra (10%) and rilonacept (3%). 58% have access to biosimilar drugs: rituximab (27%), infliximab (24%), etanercept (18%) and adalimumab (4%). 61% have access to small molecules such as: tofacitinib 62%, baricitinib 18% and ruxolutinib 1%. Regarding the survey by each country 95% reported access to DMARDs: between 80-100% (Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, Dominican Republic). 70% of the countries reported access to biological therapy between 80-100% (Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Panama, Paraguay, Puerto Rico, Uruguay.) 15% did not have access to biosimilar therapy (Cuba, Honduras and Uruguay). 30% have access to therapy with small molecules between 80 -100% (Argentina, Guatemala, Honduras, Panama, Paraguay and Dominican Republic), 25% did not have access to small molecules (Cuba, Uruguay and Venezuela).
Conclusion: It is evident that most Latin American countries have access to drugs focused on rheumatic diseases, however, there are substantial differences in countries that do not have access to all therapies. In addition, newer treatment as small molecules are less accessible to the region.
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AB1229 RHEUMATIC DISEASES REMISSION DURING PREGNANCY: MYTH OR REALITY? FACT OR HOPE?

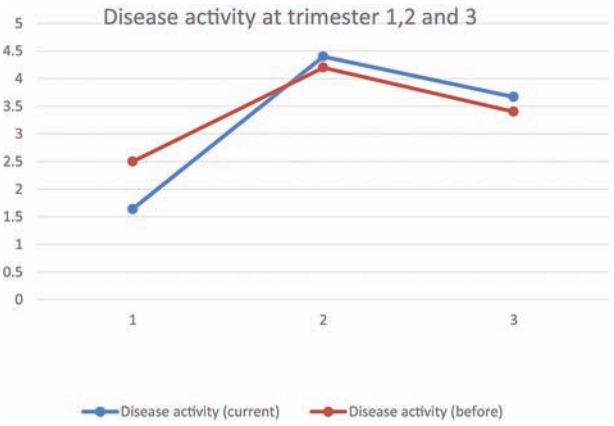
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Background: A Rheumatology Obstetric Combined Clinic (ROCC) has been running in our trust since 2013 for patients with any musculoskeletal (Msk) rheumatological disease. Observing pregnant ladies in this clinic it became noticeable that patients with msk diseases do not always go into remission during pregnancy.
Objectives: To register their perception of disease activity during pregnancy and from their memory of that disease activity before pregnancy. A secondary aim was to assess whether the remission (or flare) during pregnancy was disease specific or trimester specific.
Methods: Patients with Msk disorders attending ROCC were given 2 different 10 cm visual analogue scales (VAS) asking them to grade the current (at the time of the assessment in ROCC) disease activity and their perceived disease activity prior to pregnancy. The recorded diseases were: (1) Lupus and other Connective Tissue Diseases= 18 [(33.3%) of whom 13 were having Lupus and 5 Sjogren's syndrome, (2)SPAs =16 [(28.6%) of whom 4 had Ankylosing Spondylitis (AS) and 12 Psoriatic arthritis (PsA)], (3) Rheumatoid Arthritis (RA) =9 (16.7), Antiphospholipid Syndrome (APS) =7 (13%) and other =4 (7.4%). In the "other" group there was 1 patients with sarcoidosis, 1 with Adult Onset Still's disease, 1 JIA which progressed to CREST, 1 knee pain. The last group was excluded from the analysis. SPSS was used for statistical analysis and chi square to assess the difference between the 2 groups
Results: We analyzed data from 50 patients who attended the ROCC. At the time of presentation mean age (±sd) was 33.4 years (± 4.29) range 22-43y while age of disease presentation was 25.5 (±8.06). The weeks (w) of pregnancy during the time of assessment were (mean) 22.2 (±8.6) range 8-37 w. ESR (mean in mmHg) was 27 (± 21.7), CRP 13.6 (±14.18). Disease activity at presentation on a VAS was 4.24 (± 2.8) while reported disease activity prior to pregnancy was exactly the same of 4.24 (± 3.07).
Looking at groups of diseases RA and SpA patients showed reduction in the reported disease activity during pregnancy while CTDs and APS showed an increase, both of which however was not statistically significant (ss (table1)

Diseases (nr of patients)	Disease activity during pregnancy [mean (± sd)]	Disease activity before pregnancy [mean (+sd)]	Statistical significance
CTDs (18)	4.5 (2.6)	3.93 (2.4	0.6
SpAs (16)	4.6 (2.8)	5.8 (3.9)	0.8
RA (9)	4.13 (2.5)	4.75 (2.5)	0.9
APS (7)	2.2 (3.1)	1 (1.7)	0.4

Looking at DA according to trimester, it was in the 1st trimester (up to week 13) that patients were reported remision. (table 2 and figure 1).

Trimester (n= number of patients)	ESR	CRP	Disease activity (current)	Disease activity (before)	Ss (chi square)
1st (n=14)	6 (6.9)	20 (30)	**1.64 (2.09)**	**2.5 (2.7)**	**0.02**
2nd (n=19)	30.2 (35.5)	16.8 (SD +13.5)	4.4 (3.6)	4.2 (3.5)	0.2
3rd (n=18)	17.3 (20.3)	3.9 (sd +5.5)	3.67 (2.56)	3.4 (3.14)	0.4



Abstract AB1229 Figure 1. shows DA according to trimester before and during pregancy

Conclusion: In our group of pregnant patients with Msk diseases the overall disease activity is the same during pregnancy and before as measured by a VAS. Looking at the diseases patients with RA and SpA showed some reduction and patients with CTDs and APS showed an increase both not statistically significant.
Looking at reported VAS according to trimester of pregnancy, it is in the 1st trimester that pregnant patients report reduced activity.
Acknowledgement: Thanks to pregnant women filling the questionnaire
Disclosure of Interests: None declared
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AB1230 DISEASE ACTIVITY OF RHEUMATIC DISEASES DURING PREGNANCY COMPARED TO REPORTED DISEASE ACTIVITYPRIOR TO PREGNANCY AS OBTAINED FROM AN ANTENATAL RHEUMATOLOGY OBSTETRIC COMBINED CLINIC AND MODE OF DELIVERY

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Background: A Rheumatology Obstetrics Care Clinic (ROCC) was established at our ante natal unit to ensure specialist care for women with complex rheumatological conditions (RC).
Although patients are often counselled about a likely improvement in their RC in pregnancy, this was not the experience of our patients' group from the ROCC.
Objectives: To obtain pregnant women with RC disease activity (DA) scores during and prior to pregnancy. To assess modes of delivery (MoD) and compare them to our general non arthritic population MoD.
Methods: Patients suffering from any RC attending a dedicated highly specialized antenatal ROCC were given 2 separate 10cm visual analogue scales (VAS) asking them to grade on each one of them the current (at ROCC) DA and their perceived DA prior to pregnancy. Electronic delivery records were used to collect obstetric and foetal outcomes. SPSS was used for statistical analysis and chi square to assess the difference between the 2 groups.
Results: Data from 54 patients who attended the ROCC included of whom 50 were analyzed. At the time of presentation mean age (±sd) was 33.4 years (± 4.29) range 22-43y while age of disease presentation was 25.5 (±8.06). The weeks (w) of pregnancy during ROCC were (mean) 22.2 (±8.6) range 8-37 w. ESR (mean) was 27 mmHg (± 21.7), CRP 13.6 mg/L(±14.18). DA at presentation on VAS was 4.24cm (± 2.8) and prior to pregnancy was 4.24cm (± 3.07).
The recorded diseases were: Connective Tissue Diseases (CTD)=n= 18 (33.3%) Spondylo-arthropathies (SpA) n=16 (29.6%),Rheumatoid Arthritis (RA)n =9 (16.7%), Antiphospholipid Syndrome (APS) n=7 (13%) and other n=4 (7%) The group of other (Still's disease 1, Juvenile idiopathic arthritis 1, fibromyalgia 1 and knee pain 1) were excluded from analysis.
Looking at the disease groups RA and SpA patients' showed a reduction in the reported DA during pregnancy while CTDs and APS showed an increase; neither was statistically significant (ss).
Delivery outcomes available on 35 patients revealed that 25 of 35 RC patients (71.4%) achieved a vaginal delivery with 5 of 25 (20%) requiring assisted delivery and 10 of 35 (28.5%) had a Caesarean section (CS). These percentages are comparable with non arthritic patients.
Conclusion: In our group of pregnant patients with RC the overall DA is the same during pregnancy and prior to conception. DA according to diseases showed that women with RA and SpA had a reduction in DA and those with CTDs and APS had an increase.
The MoD showed similar percentages in vaginal and CS delivery rates as per healthy population suggesting that MoD is not impacted by RC.
Acknowledgement: Patients for filling the ROCC questionnaire
Disclosure of Interests: None declared
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AB1231 INCIDENCE OF TUBERCULOSIS IN PATIENTS WITH RHEUMATIC DISEASES USING TNF INHIBITORS: A SYSTEMATIC REVIEW

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Background: The TNF inhibitors (anti-TNF) are indicated for the treatment of several rheumatic diseases, but their use is associated with an increased risk of tuberculosis. Many measures of preventive measures have been adopted, but some groups of patients appear to be at greater risk of developing infection.
Objectives: The primary objective is to estimate the incidence of tuberculosis in patients with rheumatologic diseases exposed to anti-TNF. The secondary objectives are to evaluate the incidence of tuberculosis by region and subgroups of diseases, to assess the presentation of tuberculosis in these patients and the time elapsed between onset of anti-TNF and the development of active granulomatous disease.
Methods: A systematic review of the literature was conducted in Medline (Pubmed, Embase), Cochrane Library and Lilacs with inclusion of observational studies. The selection of articles was performed by two independent reviewers and the disagreements were resolved by consensus. The primary endpoint was described in measure of incidence and secondary outcomes through subgroup analyzes and means comparisons.
Results: We included 54 observational studies with a total of 98,483 patients exposed to anti-TNF. Among the exposed patients, 947 cases of tuberculosis were documented (pulmonary form in 62.2% of cases), with a cumulative incidence of 9.62 cases per 1,000 patients exposed [CI: 9.01 - 10.23]. Regarding TB incidence considering the different continents, we found the following distribution: South America with 11.75 per 1,000 patients exposed [CI: 7.17 - 16.33], North America with 4.34 per 1,000 patients exposed [CI: 3.31-5.38], Europe with 6.28 per 1,000 patients exposed [CI: 5.34 - 7.14] and Asia with 13.47 patients per 1,000 exposed [CI: 12.44 - 14.49]. There were no significant differences in TB incidence among the described diseases (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis). The mean time of use of the medication until the endpoint was 14.49 months.
Conclusion: The overall incidence of TB in individuals with rheumatic diseases using anti-TNF was 9.62 cases/103 patient-years, being higher in South America and Asia compared to North America and Europe. Most cases occurred in the first XX months of use and the predominant form was pulmonary. There were no differences in incidence between diseases.

REFERENCES

[1] Pérez-Sola MJ, Torre-Cisneros J, Pérez-Zafrilla B, Carmona L, Descalzo MA, Gómez-Reino JJ. Infections in patients treated with tumor necrosis factor antagonists: incidence, etiology and mortality in the BIOBADASER registry. Med Clin (Barc). 2011;
[2] Yonekura CL, Oliveira RDR, Titton DC, et al. Incidência de tuberculose em pacientes com artrite reumatoide em uso de bloqueadores do TNF no Brasil: dados do Registro Brasileiro de Monitoração de Terapias Biológicas BiobadaBrasil. Rev Bras Reumatol. 2017;
[3] Dixon WG, Hyrich KL, Watson KD, et al. Drug-specific risk of tuberculosis in patients with rheumatoid arthritis treated with anti-TNF therapy: Results from the British Society for Rheumatology Biologics Register (BSRBR). Ann Rheum Dis. 2010;
[4] Askling J, Fored CM, Brandt L, et al. Risk and case characteristics of tuberculosis in rheumatoid arthritis associated with tumor necrosis factor antagonists in Sweden. Arthritis Rheum. 2005;
[5] Lee SK, Kim SY, Kim EY, et al. Mycobacterial infections in patients treated with tumor necrosis factor antagonists in South Korea. Lung. 2013.

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AB1232 RHEUMA-VOR: A PROOF-OF-CONCEPT NETWORK STUDY FOR THE IMPROVEMENT OF RHEUMATOLOGICAL HEALTH CARE THROUGH COORDINATED COOPERATION

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Background: Rheumatoid arthritis (RA), psoriasis arthritis (PsA) and spondyloarthritis (SpA) are the most common chronic autoimmune rheumatic diseases. For all 3, the so-called "window of opportunity" [1-3] has been identified as the decisive factor affecting the outcome.
Objectives: The aim of the prospective study is to improve early diagnosis of RA, PsA and SpA and thus positively impact the quality of care for patients with the help of coordinating centers. The primary endpoint is the number of cases with an actual indication for immediate referral to a specialist in proportion to all reported cases.
Methods: The project establishes a network of the University Medical Center Mainz, the Medical School Hannover, the Center for Rheumatology Lower Saxony e.V., the University Medical Center Saarland, the ACURA Center of Rheumatology Rhineland-Palatinate, the Leibniz University Hannover and the University Medical Center Freiburg, local rheumatology specialists, the associations of statutory health insurance physicians and general practitioners and the 3 regional associations of the Deutsche Rheuma-Liga e.V. Covering 3 federal states, the network reaches approximately 13 million inhabitants.
Primary care providers are given access to screening questionnaires to document potential early cases of RA, PsA, and SpA, based on characteristic symptoms. These are evaluated by multidisciplinary teams at the regional coordinating centers. If they fulfill the criteria for referral, patients get an appointment at a cooperating rheumatology specialist within weeks. If a rheumatic disease is diagnosed, physicians and patients receive questionnaires on sociodemographic data, quality of life, functionality, medication, diagnosis and psychological aspects. After 12 months, the questionnaires are completed a second time. The collected data is compared with a matched reference group of the German Rheumatism Research Center. It is planned to screen up to 8.700 people within the 30-month survey phase that started in October 2017.
Results: Preliminary data will be presented at the conference. Currently, 2.400 patients have been screened, of which 400 patients were included in the study and 15 already underwent their follow-up screening.
Conclusion: Previous studies have shown positive results of coordinated cooperation among the relevant care providers. For example, 75 percent of the patients diagnosed with early RA within the ADAPTHERA network were in remission after 2 years (DAS28<2.6) [4]. Corresponding developments are expected in all clinical pictures for participants in Rheuma-VOR.

REFERENCES

[1] O'Dell, J.R., Treating rheumatoid arthritis early: a window of opportunity? Arthritis Rheum, 2002. 46(2): p. 283-5.
[2] Boehncke, W.H. and A. Menter, Burden of disease: psoriasis and psoriatic arthritis. Am J Clin Dermatol, 2013. 14(5): p. 377-88.
[3] Claudepierre, P., Spondyloarthritis: a window of opportunity? Joint Bone Spine, 2014. 81(3): p. 197-9.
[4] Lauter, A., et al. ADAPTHERA - Landesweit transsektorales Versorgungsnetzwerk für Patienten mit früher rheumatoider Arthritis zeigt anhaltende Remissionen in der Regelversorgung. Wunder Punkt: Die Triage. (2018). Manuscript.

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AB1233 PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES CONNECT AND LEARN ABOUT HEALTH-RELATED ISSUES USING SOCIAL MEDIA

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Background: Smartphone applications and social media (SM) are increasingly used, transforming the way in which people communicate. Peer interaction, remote information access and community building are just some of the uses of SM, presenting novel opportunities and challenges, especially for people with chronic conditions such as rheumatic and musculoskeletal diseases (RMDs).
Objectives: To explore the perspectives of people with RMDs on using SM for health-related purposes.
Methods: A questionnaire-based survey, co-designed in English by rheumatologists and patient research partners and translated into German, Italian, Spanish, Russian, French and Portuguese, was issued between May and December 2018, distributed via patient organizations and SM platforms. We report on the main quantitative exploratory analyses.
Results: A total of 992 participants started the survey; 853 (86%) participants reached at least 25 of 31 questions and were subsequently included in analyses. Participants were from 56 countries, with 50% from the UK, Germany, Portugal and Spain; 11% were outside of Europe. 60% of participants reported a good or very good experience in the use of SM. More than half (56%) were between 35 and 54 years, 90% were female, 37% had >1 RMD and 62% were multimorbid.
The use of smartphones, SM, SM for health-related purposes was affirmed by 93%, 95% and 76%, respectively. They started this in particular to connect with other people living with the same condition (58%). In general, 50% use SM to seek medical information, treatment options and to exchange experiences. Facebook (58%), Google+ (17%) and YouTube (17%) were the top three used platforms for health-related purposes; while Facebook (88%), YouTube (50%) and Instagram (47%) were most popular for general use. Platforms, that are usually used are not always the preferred one for health-related purposes, since only 16% of Instagram, 28% of YouTube and 67% of Facebook users prefer the same for health-related purposes. The greatest advantage of SM is to acquire different experiences and exchange knowledge with peers. More than half voiced concerns regarding confidentiality and 21% were hesitant of disclosing their condition. Virtual appointments are still novel, since only 4% reported experience.
SM use and education were comparable between groups with different levels of multimorbidity, although health was poorer (p=0.001) and they were older (p=0.001). Participants more frequently considered that information provided by primary care physicians was inadequate (p=0.014) and wanted to make their voice heard (p=0.006), but at the same time were more skeptical about reliability of information on SM (p=0.036).
Conclusion: The use of SM for health-related purposes is widespread among people with RMDs, mainly as a means to connect and exchange knowledge and experience, thus empowering individuals to better self-manage their health. The strong concerns about confidentiality and better guidance of patients may improve health literacy and the relationship between the patient and the health care team, addressing new avenues and challenges in healthcare.
Acknowledgement: We would like to thank PARE in their support distributing this survey study.
Disclosure of Interests: Paul Studenic: None declared, Simon Stones Consultant for: SS has provided consultancy services to Envision Pharma Group, though this is not related to the contents of this abstract., Speakers bureau: SS has undertaken speaking engagements for Actelion, eyeforpharma, Four Health, Janssen and Roche, though these are not related to the contents of this abstract., Alessia Alunno: None declared, Valentin Ritschl: None declared, Elena Nikiphorou: None declared
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AB1234 **OUTCOME OF EDUCATION WITH REGARD TO INFLUENZA AND PNEUMOCCOCAL VACCINATIONS IN INFLAMMATORY ARTHRITIS PATIENTS ON DMARDS**

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Background: Inflammatory arthritis (IA) patients on immunosuppressant disease modifying drugs (DMARDs) are at an increased risk of infections. Influenza and pneumococcal vaccines are recommended as part of the BSR and EULAR guidelines for the clinical management of these patients. Prior to commencing DMARDS, the patients are reviewed by the nurse specialist, who discusses the benefits versus risks of DMARDS, necessary monitoring and recommends the pneumococcal and influenza vaccines.
Objectives: The aim of this audit is to assess the uptake of the pneumococcal and the influenza vaccine in IA patients prior to starting biologic or synthetic DMARDs as advised by the nurse specialist during the education visit with the patient.
Methods: The study sample included 139 patients with various types of IA, including rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, who attended the rheumatology nurse education sessions prior to starting DMARDs in a secondary care hospital in 2017. Verbal advice supported by a vaccination leaflet developed in 2016 was given by the rheumatology nurse. Data was compiled by means of a telephone questionnaire.
Results: One hundred and twenty six (90.6%) participants recalled being given advice on vaccinations. Seventy eight (62%) of these patients received the influenza vaccine. The rest (28%) did not receive the vaccine for various reasons including fear of side effects, fear of developing a worse infection, belief of inefficacy and fear of injections.
A significant improvement (p=0.0084) in the influenza vaccination rates was noted since a previous audit in 2016, where following verbal education by a rheumatologist, only 41.4% received the influenza vaccine.
A significant improvement in uptake was also noted in the pneumococcal vaccination rates since only 17.2% of the patients received the pneumococcal vaccine in 2016 compared to 62.7% in 2017 (p<0.0001). Various reasons including fear of side effects, belief of inefficacy, fear of injections and financial implications were given by patients who did not receive the pneumococcal vaccine.
Overall, 62% of the patients received both vaccines after education given by the rheumatology specialist nurse and receiving the vaccination leaflet.
Conclusion: This audit showed a significant progress in the uptake of the influenza and pneumococcal vaccinations in patients with inflammatory arthritis following verbal advice by the specialist rheumatology nurse and the introduction of a vaccinations' educational leaflet.
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AB1235 **COST-SAVING FOR HEALTH SERVICES DETECTING THE MISDIAGNOSIS OF RHEUMATOID ARTHRITIS USING IMAGING IN THE PROCESS OF DIAGNOSIS: EVIDENCE FROM REAL-WORLD**

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Background: The diagnosis of rheumatoid arthritis (RA) using EULAR criteria through conventional assessments remains controversial, especially for those with seronegative results, many of patients without other diagnostic aids as imaging, could be wrong diagnosed followed by expensive treatments (1-3).
Objectives: To evidence through real-world data how the use of imaging within a screening process of diagnosis of RA can saving future costs for unnecessary treatments in patients with misdiagnosis of RA.
Methods: A retrospective real-world data (RWD) analysis was developed from medical records of patients with presumptive RA diagnosis reportedly seronegative for both rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (ACPA), and who met ACR/EULAR 2010 classification criteria, in the period between July 2016 and June of 2017; patients were assessed by imagenology (X-ray, ultrasound (US) or magnetic resonance imaging (MRI) according to the screening diagnosis protocol in a center of integral attention for rheumatoid arthritis (CIA-RA) in order to confirm diagnosis of RA, or classify patients in an alternative proper diagnosis. Direct costs of diagnosis was estimated in two scenarios: the conventional diagnosis and the screening process of diagnosis in the CIA-RA. To quantify the cost-savings for this process we also estimated the cost of treatment for the first year after diagnosis for patients with RA and patients with the most common diagnosis found after screening.
Results: 440 patients were referred to our center with presumptive diagnosis of RA in the period, who were assessed for ACPA and RF obtaining a seronegative result for both. After screening process just 115 patients were classified as RA, 99 as SRA and 16 as Nonspecific RA; 12.2% were identified by X-Ray, 67.7% were identified by US and 20% by MRI. The most frequently misdiagnosis found was Osteoarthritis in the 72.5% of patients assessed by the screening process. In that way, the conventional diagnosis cost $54.4, while the CIA-RA screening diagnosis cost was $247.1 per patient, however there was found a potential cost-saving from using the CIA-RA screening process of diagnosis of $1,440,494 per year due to the pharmacological cost saving of 325 patients who requires treatment for OA and not for RA.
Conclusion: According with our findings the use of imaging within a diagnostic screening process combining conventional criteria is a useful tool to discard false positive diagnosis of RA. Despite the fact that at first sight, the cost of screening process of diagnosis is more expensive than conventional diagnosis, after one year of treatment it can be assumed potential cost-savings using the proposed approach.

REFERENCES

[1] Hu H, Luan L, Yang K, Li S-C. Burden of rheumatoid arthritis from a societal perspective: A prevalence-based study on cost of illness for patients with rheumatoid arthritis in China. Int J Rheum Dis [Internet]. 2017 Feb 17 [cited 2017 Mar 1]; Available from: http://www.ncbi.nlm.nih.gov/pubmed/28211251
[2] Cross M, Smith E, Hoy D, Carmona L, Wolfe F, Vos T, et al. The global burden of rheumatoid arthritis: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014;73(6).
[3] Østergaard M, Pedersen SJ, Døhn UM. Imaging in rheumatoid arthritis - status and recent advances for magnetic resonance imaging, ultrasonography, computed tomography and conventional radiography. Best Pract Res Clin Rheumatol [Internet]. 2008;22(6):1019–44. Available from: http://dx.doi.org/10.1016/j.berh.2008.09.014

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AB1236 **IMPROVING CLINICAL OUTCOME AND REDUCING COST FOR PATIENTS WITH RHEUMATIC DISEASES VIA ONLINE INTERACTION WITH RHEUMATOLOGISTS BASED ON SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOL**

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Background: Without efficient primary medical care and follow-up system in China, patients can choose any hospitals or doctors they like in seeking care. As a result, most patients rush to large hospitals. Once patients left those clinics, no follow up data is available. Surveys show that over 40% of the rheumatic patients don't need to go to a hospital, only need advice from rheumatologists. SSDM is a series of applications for chronic diseases management, which strengthens the interaction between doctors and patients based on valuable clinical data. Our previous study showed that patients can master the SSDM and perform self-management after training, including evaluations on disease activity and health assessment questionnaire (HAQ), as well as medication and lab test data entries.

Objectives: To evaluate the feasibility and benefit of improving medical economics and disease activity outcomes in rheumatic patients through online consultation based on SSDM by rheumatologist.
Methods: The rheumatologists implemented the education and training programs on patients in using SSDM and assist the patients in downloading the SSDM mobile application. The SSDM includes doctors' and patients' interfaces. The patients' terminal includes serial self-assessments (DAS28, SLEDAI, HAQ), medication management, adverse events management and lab records. After data entry, data synchronizes to the mobile of the authorized doctor. On the basis of these data, the rheumatologists can accept the request from their follow-up patients and practice consultation through SSDM in the form of text or voice.
Results: From Feb 2015 to Jan 2019, 679 rheumatologists supplied 7,405 patients (RA 35%, SLE 23%, AS 9.5%, gout 8.8%, Sjogren syndrome 3.8%, OA 3.4% and other 16.5%) with 10,527 consultations. The consulting fee ranged from RMB 0 to 500 yuan (USD: RMB =1: 6.81) each in average of 78.10 ± 45.12 yuan, which match the registration fee in hospital. The total fee for consultations was 822,169 yuan RMB. 37% patients receiving online consultation lived in different cities from the rheumatologists. If the patients seek medical care in hospital, in addition to the registration fees and medical expenses, the mean cost of transportation, accommodation, and lost wages was 577.48 ± 505.21 (200 - 2,800) yuan. The total of cost for all patients would have been 6,079,135.00 yuan RMB, which is 7.39 times more compared with the cost of online. Among 2,611 RA and 1,671 SLE patients with repeat self-evaluations who were followed up for over 90 days, the treat-to-target rate improved from 28% to 45% (DAS28<=3.2) and from 41% to 70% (SLEDAI<=4), respectively. Survey shows that satisfaction rate with the consultations is 100%.
Conclusion: Through online disease management and consultations using SSDM, Chinese patients with rheumatic diseases enjoy good quality of care at lower cost with high satisfaction. Armed with data science, SSDM may supply the rest world with an option for reshaping the healthcare system.
Disclosure of Interests: None declared
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AB1237 COST OF ILLNESS AND QUALITY OF LIFE IN ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH ADALIMUMAB IN CHINA

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease which may lead to limited physical function, impaired quality of life and increased economic burden for society. There were many studies about the superior effects of biologic agents on symptom release, disease activity and functional remission in AS patients. However, studies on the economic burden and health-related quality of life of AS patients in China were spark.
Objectives: To access the cost of illness, work limitation and quality of life in active ankylosing spondylitis (AS) patients using adalimumab in China.
Methods: A prospective study was performed in 91 patients with active AS in China. Adult patients (aged $\geq$ 18 years) fulfilled the 1984 New York modified criteria of AS with the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) $\geq$ 4 and C reactive protein (CRP) 6 were enrolled from rheumatology center from Jan 2017 to Aug 2017. All participants received adalimumab (40mg per 2 weeks) therapy and completed questionnaires about disease characteristics, quality of life, direct and indirect costs. Only patients with pay-work completed the Work Limitation Questionnaire (WLQ) to accesses the impact of chronic health conditions on job performance and productivity. Quality of life was measured using the Ankylosing Spondylitis Quality of life (ASQoL) and EuroQol-5 Dimensions (EQ-5D).
Results: A total of 91 patients with mean age of 30 years old (87.8% males) and mean disease duration of 10 years received adalimumab treatment for 24 weeks. 78.02% of patients have a paid job with average work productivity loss of 28% measured by WLQ. The annual estimated costs of each patient were $35238.8 while the direct cost accounted for 90.2% and the cost of medication accounted for 78.6%. There were significant differences in change of ASQoL (change, 3.89 [95%CI, 3.06 to 4.71]; P<0.0001) and EQ-5D (change, -0.19 [95%CI, -0.24 to -0.31]; P<0.0001) scores from baseline and 24 weeks, with more improvements after therapy compared with baseline. Cost of illness was estimated as $21927.38 per quality-adjusted life year and $15728.16 per BASDAI unit, respectively.
Conclusion: The cost of AS patients treated with adalimumab therapy was high in China and symptoms and QoL improved significantly after therapy.
Disclosure of Interests: None declared
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AB1238 PATIENTS' PERCEPTIONS OF SUPPORT PROGRAMS FOR THE TREATMENT OF CHRONIC INFLAMMATORY DISEASES

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Background: Adherence to therapy in chronic diseases such as inflammatory rheumatic diseases (CIRD), inflammatory bowel diseases (IBD) and psoriasis (Pso) is a major condition to achieve positive outcomes. Patient support programs (PSPs) were developed to improve the quality of care and enhance adherence to therapy.
Objectives: To evaluate the perception of patients treated for inflammatory chronic diseases towards PSPs.
Methods: All available PSPs were identified at the national level, and their services were classified into categories: financial, logistic, educational, and emotional support. Consecutive adult patients with CIRD, IBD and Pso, enrolled in a PSP for more than 3 months, were interviewed by a trained medical student. Demographic data, disease and treatment characteristics were collected at the physician's clinic. Global satisfaction was estimated using a 5-points Likert scale, adherence to treatment was measured by the Compliance Questionnaire for Rheumatology (CQR), PSPs services were classified according to their importance to the patient using a 5-points Likert scale. An open questionnaire identified the patients' perceptions qualitatively. Predictive factors of satisfaction were identified.
Results: Forty-seven patients were included in the study, 53% were males, with a mean age of 49.8 years (SD 15.2) (Patients' characteristics in Table 1). The majority declared that the PSP was very useful (95.7%) and were highly satisfied with the programs (97.9%). Higher attributes were assigned, by decreasing order, to: financial (copay program, providing of free samples), logistic (hotline, refrigerating box), educational (educational material) and emotional support. Nursing services and telephone reminders were rated as least important (Figure 1). Most open comments gave higher appreciation to financial support (54%), followed by education (38%) and logistics (8%). High appreciation of education was associated with lower age, type of treatment and PSP. Shorter treatment duration was associated with appreciation of educational material, emotional support and telephone reminders.
Conclusion: Patients were highly satisfied with PSP programs, and ranked the financial support as the most important followed by logistics, whereas education, nursing services and telephone reminders were found less important. Lower age and shorter treatment duration were associated with higher appreciation of education and support.

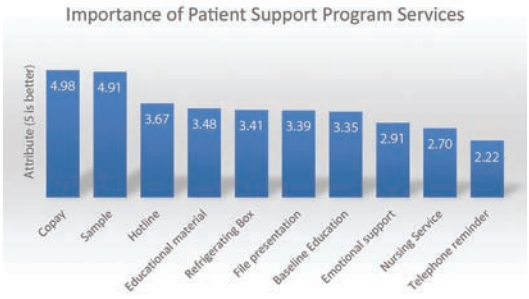
REFERENCES

[1] Rubin D, Mittal M, Davis M, et al. Impact of a Patient Support Program on Patient Adherence to Adalimumab and Direct Medical Costs in Crohn's Disease, Ulcerative Colitis, Rheumatoid Arthritis, Psoriasis, Psoriatic Arthritis, and Ankylosing Spondylitis. J Manag Care Spec Pharm. 2017;23 (8):859-67.
[2] Gangi A, Clewell J, Shillington A. The impact of patient support programs on adherence, clinical, humanistic, and economic patient outcomes: a targeted systematic review. Patient Preference and Adherence 2016:10 711–725.
[3] Van den Bosch F, Ostor A, Wassenberg S, et al. Impact of Participation in the Adalimumab (Humira) Patient Support Program on Rheumatoid Arthritis Treatment Course: Results from the PASSION Study. Rheumatol Ther (2017) 4:85–96.

Table 1. Patients characteristics:

N	47 patients
Disease, N (some patients have multiple diseases)	18
- Inflammatory Bowel Disease	17
- Axial Spondyloarthritis	17
- Peripheral Spondyloarthritis	13
- Rheumatoid Arthritis	13
- Psoriasis	
Age, mean (SD)	49.8 (15.2)

Male gender, N (%)	25 (53%)
Current treatment, N (%)	31 (66%)
- Anti-TNF alpha	9 (19%)
- Jak-Inhibitor	3 (6%)
- Anti-Integrin	2 (4%)
- Anti-IL12-23	2 (4%)
- Anti-IL17	
Biologic treatment rank	23 (49%)
- 1	14 (30%)
- 2	5 (11%)
- 3	4 (8%)
- 4	1 (2%)
- 5	
Disease duration, years (SD)	11.6 (9.6)
Current treatment duration, years (SD)	1.6 (1.9)
Use of previous PSP, N (%)	15 (32%)
CQR score, mean (SD)	86.9 (6.8)



Abstract AB1238 Figure 1. Patient Support Program: Importance Assigned by the Patients to the different Services.

Disclosure of Interests: None declared
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Epidemiology, risk factors for disease or disease progression

AB1239 GENDER DIFFERENCE IN PULMONARY ARTERIAL HYPERTENSION, ASSOCIATED WITH CONNECTIVE TISSUE DISEASES

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Background: Pulmonary arterial hypertension (PAH) is a progressive fatal disease with a known gender dimorphism. However, data on gender differences at patients with pulmonary arterial hypertension, associated with connective tissue diseases (PAH-CTD), currently not enough.
Objectives: Therefore, this study aimed to investigate the role of gender in clinical future, hemodynamic data and survival PAH-CTD.
Methods: We examined the long-term prognosis of 97 consecutive PAH-CTD patients, mean age 49 years (7 males and 90 females) diagnosed in our Institute from January 2009 to December 2018. The primary outcome was death. We used nonparametric analysis, Cox regression and the Kaplan-Meier method to assess variables obtained at baseline. All patients received PAH-specific therapy according to the current recommendations.

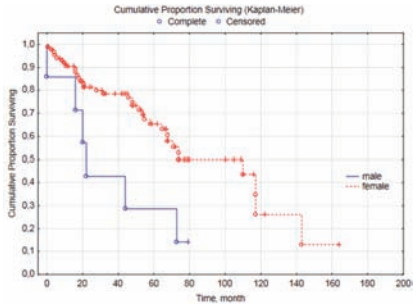


Figure 1

Results: We found that male patients had differences in diagnosis duration, level of creatinine, uric acid, RAP. We did not reveal differences in age, a functional class, a risk scale, and the majority clinical, tool and hemodynamic indicators. However, there were significant differences in survival. So, in male group survival was 21 [12; 51] months, in comparison in female group 74 [48; 119] months, p<0,02. Thus, the male sex was an independent predictor of poor prognosis (HR 2.92 [95%CI 1.21; 7.03], p = 0.018) of PAH-CTD.
Conclusion: These results indicate that female PAH-CTD patients have better long-term prognosis than male, despite lack of many distinctions. It needs to be considered at outcome assessment.
Disclosure of Interests: Alexander Volkov : None declared, Natalia Yudkina: None declared, Ekaterina Nikolaeva: None declared, Evgeny Nasonov Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc.
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AB1240 CAUSES AND ASSOCIATION OF DEATH IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN A TERTIARY REFERRAL UNIVERSITY HOSPITAL IN EGYPT

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with heterogeneous, multisystem involvements which can sometimes be severe and life threatening. Different causes of mortality have been described over different decades in SLE patients[(1)].
Objectives: To describe and analyze the causes of death in SLE patients and to identify the associated risk factors in Egypt.
Methods: A retrospective study was conducted on the SLE patients who died in the period from January 2014 to November 2019 in the Zagazig University hospitals. We collected demographic and laboratory data for all patients including; age of onset of SLE, age at death, disease duration, systems affected, last reported disease activity using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), treatment received immunosuppressive regimen (dose and duration) and the cause of death.
Results: 41 SLE patients (33 female and 8 males) had died during period from January 2014 to November 2019 with mean age at onset (26.1±8.1), mean age at death (37.4±13.3), mean SLE duration (11.2 ±6.7) and mean SLEDAI (15.4±6.8). Majority of the dyed patients had lupus nephritis (87.8%), (26.8%) had neurophsycatric lupus, (14.6%) had SLE vasculitis. (31.7%) had APS, (29.2%) had ILD, (14.6%) had pneumonitis, (19.5%) had carditis, and (14.6%) had PAH. All these patients were on a median dose of prednisolone 10 (2.5-20) mg daily with median of 10 (4-24) years of steroids. 11 of these patients (26.8%) had a family history of SLE. 21(51.2%) of them had received intravenous cyclophosphamide during their with mean cumulative dose of (6.7±4.6) gm, 16 (39%) had received MMF, 5 (12.3%) had received cyclosporine and 9 (22%) had received azathioprine. As regard causes of death, serious infection particularly pulmonary infection was the most common cause of death in 16 patients (39%), followed by stroke in 8(19.5%) patients, renal failure in 7 (17.1%), pneumonitis in 3(7.3%),cancer in 3 (7.3%), Disseminated Intravascular Coagulation (DIC) in 1 (2.4%), Macrophage Activating Syndrome (MAC) in 1 (2.4%), pancytopenia in 1 (2.4%) and one (2.4%) pregnant patient died from eclampsia in her third trimester with her fetus. The risk of death from serious pulmonary infections is higher in patients with ILD and pneumonitis (p<0.000). The risk of stroke is higher in SLE patients with APS (P=0.03) and neurophsycatric lupus (p= 0.002).
Conclusion: pulmonary infections was the most common cause of death in SLE patients in a tertiary university hospital in Egypt.

REFERENCES

[1] Wu, X., Yang, M., Xie, Y. et al. Clin Rheumatol (2019) 38: 107. https://doi.org/10.1007/s10067-018-4259-z.

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AB1241 MOST PREVALENT COMORBIDITIES IN PRIMARY SJÖGREN'S SYNDROME IN A HISPANIC POPULATION

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Background: Comorbidities are an important issue to consider in patients with rheumatic diseases (RD), as well as the clinical assessment of the autoimmune disease. Looking for concomitant diseases is a necessary step for a global approach of the rheumatic patient, knowingly that some diseases are more frequent in patients with RD than in the general population and could influence the course of RD and achievement of treatment goals[1]. Despite this, there is a need of new evidence about primary Sjögren's Syndrome (pSS) comorbidities and their association with clinical outcomes.

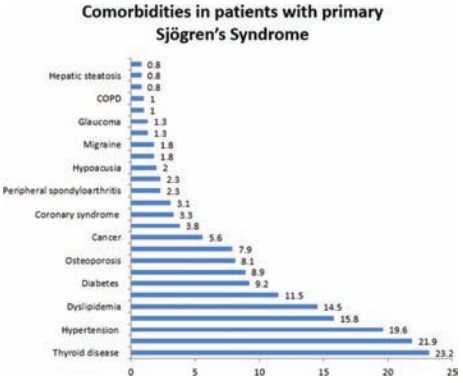


Figure 1

Objectives: To determine the prevalence of comorbidities in patients with pSS in mexican population.
Methods: This was a national, multicenter, cross-sectional, and observational study. We included 393 patients with pSS, diagnosed according to the American-European Consensus Group (AECG) criteria 2002 or ACR/EULAR 2012 criteria. Comorbidities, serological profile of autoantibodies, Schirmer's test, sialometry and histopathological assessment from minor salivary gland biopsies reported in the medical records were evaluated by a rheumatologist. The comparisons between the study groups were carried out using the two-tailed Student's t test, $\chi 2$ test, and unidirectional. A value of $p<0.05$ was considered statistically significant.
Results: At least one comorbidity were reported in 310 (78.9%) patients, 2 to 4 comorbidities were reported in 183 (46.6%), and only 18 (4.6%) had a least 5 comorbidities. Thyroid disease was the most frequent comorbidity, observed in 91 (23.2%) subjects, being hypothyroidism the main cause. Smoking (21.9%) and hypertension (19.6%) were in second and third place. Psychiatric disease was present in 62 (15.8%) patients being depression and anxiety disorders the most frequent, appearing in 49 (79%) and 12 (19.35%) patients respectively. Regarding malignancy, we documented 10 (2.5%) patients with lymphoma, and 4 (1%) patients with breast cancer. The rest of comorbidities are shown at Figure 1 and Table 1. There was no significant difference for each variable measured between the groups except for the mean age (p= 0.001).

Table 1. Demographic and clinical variables. *n=393:*

Variable	***Comorbidities***	***No comorbidities***	
	n= 310	***n=83***	*P*
Age years, mean(SD)	*58.52 (13.12)*	*48.57 (12.52)*	*0.001***
Female gender, n (%)	*297 (95.8)*	*80 (96.4)*	*0.812*
(+) Anti-Ro/SSA, n (%)	*194 (62.6)*	*59 (71.1)*	*0.139*
(+) Anti-La/SSB, n (%)	*139 (44.8)*	*38 (45.8)*	*0.867*
(+) Schirmer test, n (%)	*210 (67.7)*	*50 (60.2)*	*0.102*
Abnormal sialometry,n (%)	*180 (58.1)*	*47 (56.6)*	*0.946*
(+) GSM biopsy, n (%)	*228 (73.5)*	*66 (79.5)*	*0.140*
Use of corticosteroids, n (%)	*113 (36.5)*	*27 (32.5)*	*0.430*

GSM; Minor salivary gland. P; asymptotic significance,** statistical significance
Conclusion: The systematic evaluation of comorbidities in patients with pSS is essential for an integral management. Physicians should be aware that these conditions might directly impact quality of life, prognosis, treatment response and healthcare costs. We encourage further research for the identification of new approaches in benefit of the patients.

REFERENCES

[1] Yurkovich, et al. (2014). Overall and Cause-Specific Mortality in Patients With Systemic Lupus Erythematosus: A Meta-Analysis of Observational Studies. Arthritis Care & Research, 66(4), 608–616. https://doi.org/10.1002/acr.22173.

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AB1242 COLCHICINE USE DURING PREGNANCY: CASE REPORTS

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Background: If used during pregnancy it is known that colchicine passes through the placenta to the fetus[1]. Although it has been shown to increase the risk of congenital malformations in animal studies, there is no increase in undesirable results in humans[2]. The guidelines indicate that the use of colchicine in pregnancy and lactation is appropriate[3,4]. However, data from clinical studies and case reports for the use of colchicine during pregnancy are not sufficient.
Objectives: The aim of this study was to evaluate pregnant and/or nursing patients who were consulted to our teratology information center for colchicine use.
Methods: Colchicine treated patients during pregnancy was included in this study. Patients consulted to our information service between 2012-2018 were evaluated for risk assessment of colchicine. Information regarding pregnancy outomes was recorded by telephone interviews with patients.
Results: Indications for colchicine use in 34 cases (33 patients; one of them had pregnancy twice) were familial Mediterranean fever (n=21), Behcet's disease (n=9), systemic lupus erythematosus (n=1), ankylosing spondylitis (n=1) and vasculitis (n=1). Of the cases, 22 used the drug in pregnancy and lactation, 12 used only in pregnancy period. Of the 34 pregnancies, three had elective termination of pregnancy (the reason in one case was cytomegalovirus infection, the other is unplanned-unwanted and the other was unknown) and three had spontaneous abortion.Twenty eight had given birth, 19 of them were term and 9 of them were preterm. Delivery mode of 18 were caesarean and 10 of them were vaginal birth. A total of 30 live birth infant (two twins) exposed to colchicine due to their mother's treatment. Twenty three infant was healthy and the remaining 7 had different problems. Four of them cardiac [minor cardiac septal defect which not needs operation (n=2), pink tetralogy of fallot (n=1), heart valve stenosis (n=1)], nephrolithiasis, inguinal hernia and death (respiratory distress after birth) (table 1).
Conclusion: Currently, systematic review and meta-analysis driven data suggests that colchicine does not significantly increase the incidence of foetal malformations or miscarriage and colchicine for FMF should not be withheld on this basis during pregnancy. Although the causality between colchicine use and the above reported mostly cardiac and rare problems such as tetralogy of fallot is not proven, the contribution of colchicine cannot be ruled out totally and should be beard in mind in cases of colchicine use for indications other than FMF or Behçet's disease.

Table 1. List of unhealthy infant of colchicine exposure in pregnancy (TO: Through pregnancy)

Problems	Diagnosis	Exposure time	Colchicinedetails mg/d	Delivery mode, time w	Gender/ Birth weight g	Concomitant medication
Nonopere cardiac septal defect	BD	first 8 week	1	Vaginal,40	M 3400	-
Nonopere cardiac septal defect	Vasculitis	first 20 week	1	C/S, 31	Unknown	Corticosteroid
Heart valve stenosis	BD	TO	1-1.5	Unknown	Unknown	-
Pink tetralogy of fallot (opere)	FMF	TO	3-4	C/S, 38	M 3200	-
Inguinal hernia	FMF	TO	2	C/S, 33	M 1370	Corticosteroid
Nephrolithiasis	BD	TO	0.5-1	C/S, 38	M 3640	Azathioprine, Corticosteroid
Death	AS	first 8 week	Unknown	C/S, 34	Unknown	Sulfadiazine

REFERENCES:
[1] Indraratna PL, et al. Use of colchicine in pregnancy: a systematic review and meta-analysis. Rheumatology (Oxford). 2018 Feb 1;57(2):382-387.
[2] reprotox.org
[3] Götestam Skorpen C, et al. The EULAR points to consider for use of anti-rheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis. 2016 May;75(5):795-810.
[4] .Breastfeeding and Maternal Medication. World Health Organization, Geneva, Switzerland,1995
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AB1243 OBESITY, METABOLIC SYNDROME AND OTHER COMORBIDITIES: INFLUENCE ON RHEUMATOID ARTHRITISAND PSORIATIC ARTHRITIS ACTIVITY AND QUALITY OF LIFE

Soraia Azevedo[1], Daniela Faria[1], Joana Silva[1], Joana Rodrigues[1], Joana Neves[2], Daniela Peixoto[1], José Tavares-Costa[1], Sérgio Alcino[1], Carmo Afonso[1], Filipa Teixeira[1]. *[1]Unidade Local de Saúde do Alto Minho, Rheumatology department, Ponte de Lima, Portugal; [2]Hospital de Braga, Rheumatology department, Braga, Portugal*

Background: Patients with rheumatic inflammatory conditions have an increased risk of premature death due to cardiovascular causes. It can be explained by the unfavourable interaction between the inflammatory process and the traditional cardiovascular risk factors. In obesity, especially if visceral, and in rheumatic diseases, there is production of pro-inflammatory cytokines, which contributes to an increase in cardiovascular risk. The influence of body mass index (BMI) on the evolution, activity and quality of life in rheumatoid arthritis (RA) and in psoriatic arthritis (PsA) has been proven. However, studies evaluating the influence of the abdominal circumference (AC) and metabolic syndrome (MS) are meagre.
Objectives: To assess the influence of BMI, AC and MS, on disease activity and quality of life in RA and PA, using parameters of inflammatory activity (sedimentation rate (SR) and C-reactive protein (CRP), Activity Score (DAS28), Visual Analogue Pain Scale (VAS) and Health Assessment Questionnaire (HAQ) and to compare patients with RA and PA.
Methods: A cross-sectional study, including 150 patients with RA, diagnosed according to the ACR/EULAR criteria and 75 patients with PsA (CASPAR criteria). Assessment of weight, height, AC, SR and CRP of all patients, clinical and demographic data collection. The presence of MS was assessed according to WHO definition. Participants completed HAQ and disease activity was measured by DAS28. SPSS was used for the statistical analysis, significance level was 2-sided $p<0.050$.
Results: Age, duration of illness, schooling and professional class were similar in RA and PsA. In RA there was a predominance of females (78.7%), while in PsA a predominance of males (53.3%). There were no differences between the quality of life (by HAQ), or in the disease activity (by DAS28 or by inflammatory parameters). PsA patients had significantly higher BMI and AC. The number of comorbidities was higher in cases of PsA. Dyslipidaemia and hyperuricemia were significantly more frequent in this group of patients. Independently the underlying pathology (RA or PsA), the number of comorbidities correlated positively with DAS28, with HAQ, CRP and SR.
In RA group, there was a positive correlation of both BMI and AC with HAQ, also MS associated the highest HAQ values. Overweight/obesity ($BMI \geq 25 kg/m^2$) were associated with at least one painful joint. Still, the risk of having at least one swollen joint was 3.4 times higher in patients with increased AC (95% CI: 1.08-10.39). There was an association between the BMI and AC and the CRP value. Patients with $BMI \geq 25$ kg/m^2 and with increased AC had DAS28 values significantly higher. MS was associated with significantly higher SR.
In PsA group Patients with MS had higher CRP values, more joint pain and higher disease activity according to DAS28. Patients with $BMI \geq 25 kg/m^2$ also had more painful joints and higher CRP values. None of the patients with normal BMI had swollen joints, however 20.4% of overweight patients had at least one swollen joint. There was no association between the disease phenotype and BMI, AC or MS.
Conclusion: In this study there was a higher prevalence of classic cardiovascular risk factors in patients with PsA. The number of comorbidities showed to influence inflammatory parameters, disease activity and quality of life. We found that BMI, AC and MS are associated with disease activity, which may be improved by weight reduction and control of comorbidities. Therefore they should be considered in the treatment of rheumatologic diseases.

REFERENCES
[1] Avina-Zubieta J. A. et al
[2] Ursini, F. et al.
[3] Wei S. T et al.
[4] Azfar RS et al.
[5] Eder L. et al.
[6] Souza CS et al.
[7] Clavelab G. et al.
[8] George MD et al.
[9] Vidal C. T. et al.
[10] Frazier-Mironer A.

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AB1244 TUBERCULOUS SPONDYLODISCITIS : A CASE SERIES ANALYSIS

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Background: Spinal tuberculosis or Pott's disease is one of the many manifestations of active tuberculosis and is still common in Mediterranean countries such as Tunisia with high endemicity. Definitive diagnosis of tuberculous spondylodiscitis requires the identification of Mycobacterium tuberculosis.
Objectives: We aimed to describe clinical, laboratory, diagnostic and therapeutic features of spinal tuberculosis.
Methods: Retrospective study including 64 patients followed up in our department between 1999 and 2019. Clinical, biological and radiological data were collected. Therapeutic outcome was studied.
Results: We studied 64 patients included 35 women and 17 men with a mean age of 56 years old [16 - 86]. Seven patients had a contact with Mycobacterium Tuberculosis Bacilli and 3 patients had a history of pulmonary tuberculosis. The median delay of consultation was 6 months. Inflammatory back pain was found in 79%. Other clinical symptoms: 27.4% fever, 40.3% night sweats, 74.1% impaired general condition. Neurologic deficiency was noticed in 16.1% of cases. 7 patients had another localization of tuberculosis. The inflammatory biological syndrome was found in 92% of cases. The lumbar spine was involved in 58% of patients, followed by the dorsal spine (41.9%) and cervical spine (9.67%). The spondylitis was multifocal and multi-stage in 24.19% of cases. Plain

radiographs revealed narrowing of disc spaces in 67.7% of cases and vertebral erosion, vertebral fracture and a paravertebral spindle in 14.51%.
Computed tomography and Spinal magnetic resonance imaging was performed respectively in 62.9% and 70.9% of cases. They showed paravertebral abscess in 66.1%, epiduritis in 56.4%, intra-discal abscess in 3.22%, spinal cord compression in 8.06%, and vertebral ostelysis in 9.67% of cases. Tuberculin Skin Test was performed in 57 (92%) patients and it revealed a positive result in 29 (47%) patients. Disco vertebral biopsy was performed in 45 patients and was contributive in 32.2% of cases revealing caseating granulomas.
A four-drug therapy including isoniazid (INH), rifampin (RMP), pyrazinamide (PZA) and ethambutol (EMB) were administered to 59 (95.16%) patients for the initial two months. Three patients received initial three-drug combination therapy. Following the initial 4-drug regimen, most patients continued to receive a two-drug regimen with RMP and INH for a mean duration of nine months. Over 80% of patients had an immobilisation.
Adverse effects of anti-TB therapy were noted in 17.7% of the patients; [nausea-vomiting: 1.6%, hepatotoxicity: 9.6%, rash: 3.2%, hyperuricemia: 3.2%]. A surgery was needed for 6.4% of patients. Neurological complication occurred in 4 cases, sepsis occurred in 2 other cases and 2 patients were dead.
Conclusion: Spinal tuberculosis results in a significant rate of morbidity due to its insidious course and delayed diagnosis. Early establishment of definitive etiologic diagnosis and appropriate treatment is of paramount importance to prevent development of sequelae.
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AB1245 COMPARATIVE ANALYSIS OF SPONTANEOUS INFECTIOUS SPONDYLITIS: PYOGENIC VERSUS BRUCELLA

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Background: Infectious spondylitis is an infectious disease of the spine or paraspinal structures that can be caused by various microorganisms. Without adequate chemotherapy, the outcome can be fatal or result in severe neurologic damage. Therefore, differentiating the etiology of spondylitis is very important.
Objectives: To compare the clinical features, laboratory and radiological aspects, treatment and outcome data of patients diagnosed as brucellar spondylitis (BSP) and pyogenic spondylitis (PSP).
Methods: Retrospective study including 45 (22 BSP and 23 PSP) spondylodiscitis hospitalized in our department between 1999 and 2019. The diagnosis was based on clinical, biological, radiological and bacteriological data.
Results: The patients' mean age was 54 years. There were 31 men (68.8%) and 14 women (31.2%). There was no difference in mean age and sex between the two groups (p=0.8 and p=0.4; respectively).
The pyogenic group had a relatively higher proportion of Predisposing factors especially diabeties (p=0.04). PSD patients suffered an impaired general condition more frequently than BSD patients (p=0.01) while BSD patients complained of night sweats more frequently compared to PSD cases (p=0.026).
The peak CRP value was higher in the pyogenic group than in the brucella group (87 mg/L and 37 mg/L, respectively, p=0.027), whereas the ESR was not significantly different between the groups (71 mm/h and 67 mm/h, respectively, p=0.7). We found no statistically significant difference regarding the seat of the spondylitis. Whereas, multifocal involvement was higher in PSD (p=0.049). Radiologically, the frequency of prevertebral, paravertebral, epidural, and psoas abscess formations and spinal cord compression was similar in both groups (p=0.8)
Surgical interventions and percutaneous sampling and/or abscess drainage were applied more frequently in PSD but with no significant difference (p<0.23). Favourable clinical outcome rate was 60% in PSD and it was 72% in BSD group (p=0.39).
Conclusion: The clinical and radiological manifestations of spontaneous spondylitis differ based on the causative organism. Pyogenic spondylitis patients tend to have a more severe clinical course and a higher CRP level. However, there was no significant difference regarding the presence of abscess and epiduritis or the occurrence of complications between brucella and pyogenic spondilitis.
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AB1246 PREDICTORS OF IMPAIRED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC DISEASES

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Background: Systemic diseases are heterogeneous diseases that represent one of the leading causes of disability in the industrialized world and can even reduce life. They are associated with high rates of disability, premature mortality, and significant social costs.
Objectives: The objectives of our study were to evaluate the quality of life (QoL) of patients with systemic disease and a comparison between these patients, to search for factors predicting the impairment of quality of life during systemic diseases, and to evaluate work disability of those patients.
Methods: We conducted a cross-sectional study at the Internal Medicine Department of the Farhat Hached Hospital in Sousse between July 2017 and September 2017. We investigated patients with systemic rheumatic, thrust or remission who were present as outpatients or were admitted to the ward during this period. The outcomes were baseline Short Form Health Survey physical (PCS) and mental (MCS) component summary scores QoL. Work disability was evaluated by the work productivity assessment impairment (WPAI) questionnaire. Correlations were calculated by the test t student or Anova factor test and comparison with chi2 test.
Results: Two hundred thirty five patients were included, 183 females and 52 males. The average age was 48,3 years with extremes between 15 and 90 years old. Forty seven per cent of the population had work during the study. The most frequent diseases were: Systemic lupus erythematosus (SLE) in 66 patients, Behçet syndrome in 33 patients and Sjogren primary syndrome (SPS) in 27 patients. Mean PCS were 52.55 ± 17.3 and MCS scores were 47.74 ±14.8. For the predictors related to patients: the age ((PCS: r=-0.250, p=0.000), (MCS: r=-0.160, p=0.014)), the presence of comorbidities (PCS p=0.003) and the low level of education (p=0.001) were significantly correlated with impaired QoL, the presence of profession was not significantly correlated with QoL. For the predictors related to the disease; inflammatory myositis influences most the QoL. Pulmonary manifestations (PCS: p=0.021, MCS: p=0.006) were the most correlated with impaired QoL. Disease index of activity was calculated in 3 diseases and it was significantly correlated with impaired QoL; SLE ((PCS; r=-0.581, p=0.000),(MCS; r=-0.494,p=0.000)),SSP ((PCS; r=-0.500,p=0.007), (MCS; r=0.522, p=0.005)), Systemic sclerosis ((PCS; r=0.698, p=0.012), (MCS; r=0.710,p=0.01)). Work disability was evaluated in working patients: absenteeism was at 31.16±24, productivity impairment at 48.77 and systemic sclerosis was the most disease predictive of absenteeism and work disability (p=0.011).
Conclusion: QoL may be severely impaired in patients suffering from systemic diseases. We studied for the first time the predictors of impaired QoL for all patients followed in our department. Our study concord with literature (1), beside the objective criteria resulting from clinical examination and biological investigations, it seems essential to take into account the individuality of each patient. This measure aims to further humanize medical practice and maintain the quality of life of patients.

REFERENCES

[1] Anyfanti P, Triantafyllou A, Panagopoulos P, Triantafyllou G, Pyrpasopoulou A,Chatzimichailidou S, et al. Predictors of impaired quality of life in patients with rheumatic diseases. Clin Rheumatol 2016;35(7):1705:11.

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AB1247 RISK FACTORS FOR ADVERSE CLINICAL OUTCOME IN SEPTIC SPONDYLODISCITIS

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Background: Spondylodiscitis is defined as a serious infection of the intervertebral disc and/or adjacent vertebrae. It can lead to neurological sequelae and put life-threatening ones into play.

Objectives: To describe the clinical features and outcomes of septic spondylodiscitis and to identify factors associated with an unfavourable clinical outcome.
Methods: Retrospective study including 107 patients followed up in our department between 1999 and 2019. Clinical, radiological and microbiological data were collected.
We divided patients into two groups: patients with unfavourable clinical outcome (defined as death, drug toxicity, neurological complication, sepsis or persistent pain) (group 1) and patients with a favourable one (Group 2).
Results: We included 107 patients (49 women and 58 men), with a mean age of 55 years old [16 - 86]. The median delay of consultation was 3 months. Predisposing factors were found in 59 patients (55.1%). Inflammatory back pain was seen in 78.5% of cases. Neurologic deficiency was noticed in 16.82% of cases: motor deficit in 1.8% of cases, spinal cord compression in 1.8% of cases and Cauda equina s*yndrome in 2.8% of cases*. An inflammatory biological syndrome was found in 90.6% of cases. The lumbar spine was involved in 55%. The spondylitis was multifocal in 19.6% and multi-stage in 15.8% of cases. CT and Spinal MRI was performed respectively in 60% and 78.8% of cases and showed paravertebral abscess in 63.5%, epiduritis in 54.2%, intra-discal abscess in 4.67%, spinal cord compression 9.3%, and vertebral ostelysis in 8.4% of cases. The causative microorganism was mycobacterium tuberculosis in 59.8%, brucella in 20.56%, and pyogenic germs in 16.8% of cases. 34.5% of patients had an unfavourable clinical outcome: persistent pain was noticed in 18.7%,drug toxicity occurred in 13% of cases, neurological complication occurred in 10.2% of cases, sepsis occurred 3.7% of cases and 3.7% of patients were dead.
In the group1 the frequency of diabetes, impairment of the general state and clinical evidence of neurological impairment at presentation was higher, but with no statistically significant difference. Similarly, the presence of paravertebral abscess, epiduritis or spinal cord compression was slightly more frequent, with no significant difference.
There was no statically significant difference in the age (p=0.15), the localisation and the causative microorganism (p=0.68).
Conclusion: Spondylodiscitis is a rare but serious condition that leads to significant long-term morbidity. In our study, unfavourable clinical outcomes was found in the presence of diabetes, neurological impairement at presentation and the presence of paravertebral abscess, epiduritis or spinal cord compression in MRI but with no statically significant difference.
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AB1248 MALHEUR PROJECT CONFIRMS SPECIFIC CHARACTERISTICS OF MALIGNANCIES IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Both rheumatic and musculoskeletal diseases (RMDs) and malignancies are frequent in the population and the probability of simultaneous occurrence in one individual is accordingly high. However, the interrelation of malignancies in patients with RMDs is still a blind spot in rheumatology. Since both disorders present two extremes of a dysregulated immune response, their interdependencies are undoubtedly complex. There is very little reliable data on cancer and relapse risk due to a certain disease entity as well as particular disease modifying therapies.
Objectives: The MalheuR project is a registry-based study that has been initiated at the university hospital Heidelberg, Germany to close this gap.
Methods: In three subregistries, we address the specific situation of patients suffering from concomitant RMD and malignancy (RheuMal registry), paraneoplastic rheumatic disorders due to a malignancy (ParaRheuMa registry) and rheumatic immune-related adverse events (irAE) due to cancer immunotherapy (TRheuma registry). Herein, we present first data from RheuMal registry.
Results: We analyzed 55 patients with concomitant RMDs and malignancies. The mean onset of the RMD was 58.9 years in females (n=33) and 54.2 years in males (n=22), the mean onset of the malignancy was 59.9 years and 56.3 years respectively. In patients first suffering from a RMD (n=38), the average time to malignancy diagnosis was 10.3 years [1-33 years]. Only 13 patients were diagnosed with a malignancy before RMD. 4 were diagnosed for both disorders simultaneously. Solid tumors were present in 54%, hematologic neoplasms in 17%, non-melanoma skin cancer in 21% and melanoma in 8%. 13 patients suffered from more than one neoplasm with 1 patient showing a secondary neoplasm, 4 patients with recurring skin cancer and 4 with additional benign neoplasms. Out of 6 patients pre-treated with cyclophosphamide, lymphoma, bladder and prostate cancer were diagnosed in one case each. 16 patients were pre-treated with TNFa-inhibitors, 2 cases of melanoma, 4 cases of non-melanoma skin cancer and 2 cases of hematologic neoplasms occurred. Among 7 patients with azathioprine intake, two developed non-melanoma skin cancer, but no melanoma was diagnosed.
A comparison with the German cancer registry of the Robert Koch Institute suggests an earlier onset of gender specific cancers in our patients with mean onset of breast cancer (n=5) 5.2 years and prostate cancer (n=8) 7.0 years earlier. Furthermore, in males with RMDs melanoma occurred 8.4 years earlier (n=5), but squamous cell skin cancer was diagnosed 12.2 years later than in the reference cohort.
Conclusion: Overall, our data show specific characteristics of malignancies in RMD patients suggesting a different cancer epidemiology compared to overall population.
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AB1249 HOSPITAL ADMISSIONS IN PATIENTS WITH CHRONIC RHEUMATIC DISEASESRECEIVING ADALIMUMAB. DESCRIPTIVE STUDY OF A COHORT

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Background: Patients with chronic rheumatic diseases (CRD) treated with biological DMARDs may increase the risk of complications and hospitalizations for serious adverse reactions (SAR). Concomitant treatment with conventional DMARDs and corticosteroids may increase the risk of complications.
Objectives: To describe the prevalence and characteristics of hospital admissions among patients with CRD who are currently receiving Adalimumab (ADL) in a hospital setting.
Methods: Cross-sectional, retrospective, unicentric study. Data obtained from a cross-sectional study to determine levels of ADL and antidrug antibodies in patients currently receiving ADL. We clustered the income in SAR and income not related to bDMARD, describe the clinical and therapeutic data. Groups were compared using Student's t-test and Chi-squared test.
Results: We included 103 patients on ADL treatment, 54.4% (56) men, 45.6% (47) women. The mean age was 54.6 years (SD ± 13.04). 38.8% diagnosed of rheumatoid arthritis, 42.7% spondyloarthritis, 15.5% psoriatic arthritis and 2.9% juvenile idiopathic arthritis.
33% (34) had at least one income, mean 2.29 SD ± 2.93 (1-17). Within this group, the mean age was 62.3 years (SD ± 9.93), the mean time of exposure to ADL was 98.9 months SD ± 43.68 (3.48-151.49). 44.1% (15) had a standard dose of ADL and 55.9% (19) had a minimum effective dose. 55.9% (19) also received scDMARD and 47.1% (16) oral corticosteroids with a mean dose of prednisone of 3.4 mg (SD ± 4.6). 78 incomes were produced, 7 (9%) by SAR and 71 (91%) not related to bDMARD. The average income per SAR was 0.50 SD ± 1.48.
The mean time of exposure to ADL in the group of patients with SAR was 101.97 months SD ± 33.8, in contrast to patients without hospital admissions that was 65.02 months SD ± 50.17 ($p < 0.01$). Patients without incomes received a mean daily dose of prednisone of 2.45 mg/day SD ± 3.71 while those with SAR admission of 4.58 mg/day SD ± 4.00 ($p < 0.05$).
Conclusion: 33% (34) of patients had at least one admission, they were older (62.3 years SD ± 9.93) than those without incomes. The mean of income was 2.29 SD ± 2.93 (1-17). 55.9% of patients also had a scDMARD prescribed and 47.1% oral corticosteroids. 9% of the admissions were by SAR with an average ADL exposure of 101.97 months SD ± 33.8 compared to patients without hospital admissions, mean 65.02 months SD ± 50.17 with statistically differences ($p < 0.01$). In addition, differences were found regarding the dose of prednisone, patients with admissions by SAR received 4.58 mg/day SD ± 4.00 unlike those without incomes who received 2.45 mg/day SD ± 3.71 ($p > 0.05$).
Weakness of the study is a selection bias since we include the data of patients with current ADL treatment, losing information of those in whom

ADL was suspended. These results suggest a direct relationship between the time of exposure to ADL and concomitant use with DMARDs and corticosteroids at dose >2.5 mg, similar findings are also described in other studies.

REFERENCES

[1] Duquenne L, Gul H, Emery P. Safety evaluation of adalimumab in immune-mediated inflammatory disorders: a rheumatological point of view. Expert Opin Drug Saf. 2018 Nov 16:1-9.
[2] Fleischmann R, Mysler E, Hall S, et al. Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy): a phase 3b/4, double-blind, head-to-head, randomised controlled trial. Lancet. 2017 Jul 29;390(10093):457-468.
[3] Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun;76 (6):960-977.

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AB1250 SLE AND SEXUAL FUNCTION: ARE WE FORGETTING MEN?

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Background: Whereas SLE is uncommon in men, the disease is usually more severe and requires more aggressive immunosuppression in male patients. There are multiple studies regarding sexual aspects in women with SLE, but information about sexual function in male patients is quite scant.
Objectives: To determine the relationship between SLE and sexual function alterations in men, through the application of validated questionnaires.
Methods: We performed a longitudinal study in a third-level referral center in Mexico City. We included men aged ≥16 years who fulfilled ACR criteria for SLE and who were sexually active. All subjects answered the International Index of Erectile Function-15 (IIEF-15), the SF-36 and the HAQ in two visits. Other clinical, serological and demographic variables were measured. Oxidized LDL was quantified by ELISA.
Results: We included 108 male SLE patients. Mean age was 37.2±1.1 years and most patients (87%) were taking immunosuppressive therapy. Comorbidities were present in 58% of subjects, with dyslipidemia and hypertension being the most prevalent (34% and 28%, respectively).
The prevalence of sexual dysfunction (SD) was 53%. In the basal visit, the only significant differences between the patients with SD and those without SD were a lower education degree (p=0.007) and persistent lymphopenia (p=0.01). There was a positive correlation between global IIEF-15 score and SF-36 score (r=0.46, p=0.001). The physical function domain had the highest correlation (r=0.50, p=0.001). Likewise, there was a weak negative correlation between IIEF-15 and HAQ score (r=-0.25, p=0.012). Also, the IIEF-15 had a weak correlation with the absolute lymphocyte count (r=0.27, p=0.005) and oxidized LDL (r=0.31, p=0.04).
In the follow-up visit the only significant differences between the patients with SD when compared with subjects without SD was a low absolute lymphocyte count (1031±89 vs 1458±119, p=0.005); the correlations mentioned in the baseline visit remained significant. Regarding erectile function, 44% of the subjects had some degree of dysfunction. The rest of the variables are shown in Table 1.

Abstract AB1250 Table 1. Demographic, clinical and laboratory features

Variable	Mean ± SEM
Demographic	
Age (years)	37.2 ± 1.1
Body mass index (kg/m^2)	26.5 ± 0.4
Less than 10 years of schooling (n,%)	21/108 (19.4)
Time since SLE diagnosis (years)	9.1 ± 0.6
Clinical Features	
Total score IIEF-15	58.7 ± 1.3
Erectile function	23.9 ± 0.6
Intercourse satisfaction	10.9 ± 0.3
Orgasmic function	8.1 ± 0.2
Sexual desire	7.5 ± 0.1
Overall satisfaction	8.1 ± 0.1
Total score SF-36	69.2 ± 1.3
Secondary antiphospholipid syndrome (n,%)	16/108 (14.8)
SLEDAI score (points)	4.2 ± 0.4
Others comorbidities (n,%)	63/108 (58.3)
Laboratory features	
Hemoglobin (mg/dl)	15.3 ± 0.2
Leukocytes (mm^3) (x10^3)	5.9 ± 0.2
Absolute lymphocyte count (mm^3)	1362.6 ± 76.0
Serum creatinine (mg/dl)	1.4 ± 0.1
C3 levels	104.1 ± 3.2
C4 levels	19.7 ± 1.2
Anti-dsDNA antibodies	208.2 ± 70.4
Use of immunosuppressive treatment (n,%)	95/108 (87.9)
Prednisone (n,%)	58/108 (53.7)
Azathioprine (n,%)	31/108 (28.7)
Antimalarial (n,%)	73/108 (67.5)
Mycophenolate mofetil (n,%)	42/108 (38.8)
Cyclophosphamide exposure previous 6 months (n,%)	7/108 (6.4)
Anticoagulation (n,%)	18/108 (16.6)
Non-immunosuppressive treatment (n,%)	85/108 (78.7)

Conclusion: Sexual function is affected in men with lupus, regardless of comorbidities and treatment. Interestingly, lymphopenia is persistently associated with an impaired sexual function, which could be related to the role it plays in endothelial dysfunction and atherosclerosis. The patients' disease perception, which is influenced by their academic level and physical role in their daily activities, seems to affect their sexual performance and quality of life.
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AB1251 ASSOCIATION BETWEEN VITAMIN D DEFICIENCY AND A HIGHER RATE OF DISEASE ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Spondyloarthritis is a group of chronic inflammatory diseases with involvement of the axial skeleton (mainly), and also of peripheral joints. Patients with spondyloarthritis have a significant prevalence of vitamin D levels below normal and that would correlate with the degree of activity of the disease.
Objectives: To determine the association between vitamin D deficiency and the degree of activity of the disease (inflammatory activity) in a cohort of patients with spondyloarthritis.
Methods: Observational, extensive and transversal study. We propose a retrospective review of the database of patients with spondyloarthritis who were treated in the outpatient clinics of the Rheumatology Service of the General University Hospital of Ciudad Real during September 2016 to September 2018. Patients with the data will be selected. necessary for the analysis of the variables under study. The variables evaluated will be described using measures of frequency and measures of central tendency/dispersion as appropriate. To assess the association between vitamin D deficit and activity index, the odds ratio (OR) will be calculated. All analyzes were performed with a confidence level of 95% using SPSS 21.0.
Results: The first advances of the results of the study are presented. 101 patients were analyzed, of which 58 were men and 43 women, with an average age of 46.33 years (+/- 13.05 DE). 15 (14.85%) were non-radiographic axial spondyloarthritis, 48 (47.52%) ankylosing spondylitis, 24 (23.76%) psoriatic arthropathy, 3 (2.97%) spondyloarthropathy associated with inflammatory bowel disease, and 11 (10, 89%) were other types of spondyloarthritis. The average of the activity was a BASDAI of 4.355 (+/- 2.376 SD), 64 patients were in activity (BASDAI> or = 4) and 31 patients (30.69%) with an elevation of acute phase reactants. Vitamin D levels were 24.52 (+/- 9.21 SD). 77 patients (76.24%) presented figures

of vitamin D deficiency or insufficiency. When performing the association analysis, the vitamin D deficit/insufficiency presented an OR 12.46 (95% CI: 4.07-38.08)., p = <0.0001) with the degree of activity measured with BASDAI. Regarding the comparative analysis of means between vitamin D deficiency/insufficiency and BASDAI it is +2,253 (95% CI: 1,241 to 3,266, p <0.0001).

Conclusion: In our study, patients with spondyloarthritis who have a vitamin D deficit correlate with presenting disease activity (BASDAI> or = 4). Therefore, inflammation along with increased bone turnover and low levels of vitamin D could be related to the pathophysiology of osteoporosis related to spondyloarthritis, and may adversely affect the patient's functional status and quality of life.

Disclosure of Interests: None declared

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AB1252 FUNCTIONAL STATUS CHANGES ASSOCIATED WITH INFLAMMATORY ARTHRITIS IN REPUBLIC OF MOLDOVA

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Background: Inflammatory joint disease is a burden to the patient and society, due to medical costs and the impact it has on the health-related quality of life. Functional status plays a significant role in quality of life impairment.

Objectives: To study and compare functional status changes between different inflammatory joint diseases and degenerative joint disease.

Methods: 1500 patients with inflammatory joint disease and 400 patients with degenerative joint disease were included in this study. In the first group, 645 (43.0%) were diagnosed with rheumatoid arthritis, 330 (22.0%) - psoriatic arthritis, 100 (6.7%) - ankylosing spondylitis, 200 (13.3%) - axial spondyloarthritis, 135 (9.0%) - gout, 20 (1.3%) - other crystal arthritis, 45 (3.0%) - early arthritis and 25 (1.7%) with other arthritis. Physical exam with functional status was assessment were performed. Descriptive statistics and Mann-Whitney U tests were used to compare the study groups, as well as the subgroups within the inflammatory disease group.

Results: Both groups were comparable according to sex, with a predominance of female sex (χ^2 = 86.4 and 30.74 respectively, p<0.001), and no difference in sex distribution (mean ranks of U test – 950.98 and 967.44, p = 0.524). Mean age was significantly lower in the inflammatory joint disease group (44.76 vs 60.19, p<0.001). The Mann-Whitney U test showed a significantly greater mean rank in the inflammatory disease group (999.07 vs 790.66, p<0.001), suggesting an overall higher functional class, and thus worse functional status in the inflammatory joint disease group. Further analysis using the same method, between subgroups in the inflammatory joint disease group, showed a higher mean rank (worse functional status) in patients with rheumatoid arthritis, when compared with psoriatic arthritis (501.95 vs 460.73, p<0.05) and early arthritis (352.24 and 248.83, p<0.001). Psoriatic arthritis showed a higher mean rank, compared to axial spondyloarthritis (282.88 vs 254.97 p<0.05) and early arthritis (193.34 vs 148.83, p<0.01). Gout patients showed a higher mean rank (worse functional status), when compared to rheumatoid arthritis (453.65 vs 377.28, p<0.001), psoriatic arthritis (281.33 vs 213.23, p<0.001), ankylosing spondylitis (127.07 vs 105.75, p<0.05), axial spondyloarthritis (184.67 vs 156.75, p<0.01) and early arthritis (101.70 vs 56.89, p<0.001), thus making it the subgroup associated with the poorest functional status. Ankylosing spondylitis showed a higher mean rank, when compared to psoriatic arthritis (238.13 vs 208.64, p<0.05), axial spondyloarthritis (151.75 vs 129.88, p<0.05) and early arthritis (81.63 vs 53.83, p<0.001). Axial spondyloarthritis and other crystalline arthritis subgroups both showed higher mean ranks compared to early arthritis (130.0 vs 91.89 and 43.2 vs 28.56 respectively, p<0.01), making early arthritis the subgroup associated with the best functional status. No significant differences were found when comparing rheumatoid arthritis with ankylosing spondylitis, axial spondyloarthritis and other crystalline arthritis.

Conclusion: This is the first study conducted on a national scale to assess the impact of inflammatory joint disease on functional status. Inflammatory joint disease involved a younger age group, when compared to degenerative joint disease, with a higher impact on the functional status. Interestingly, gout was associated with one of the poorest functional status, suggesting the need for a more aggressive approach toward this disease. After gout, a significantly impaired functional status was associated with rheumatoid arthritis, ankylosing spondylitis and axial spondyloarthritis, whereas early arthritis was generally associated with a better functional status, when compared to other inflammatory diseases.

Disclosure of Interests: None declared

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AB1253 DETERMINATION OF RISK FACTORS OF DEVELOPMENT OF HYPERURICEMIA IN PROFESSIONAL ATHLETES IN SOME SPORTS

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Background: Prevalence of hyperuricemia worldwide has been steadily increasing over the past decades and becomes higher with age.

The number of studies on the prevalence of hyperuricemia and its role in development of diseases in some social groups is low, yet there is data on its high frequency in professional athletes.

Objectives: to assess impact of certain factors upon the risk of development of hyperuricemia in professional athletes in some sports.

Methods: the study was performed as retrospective. Out of 753 athletes in six sports, 267 athletes who met the study criteria were selected.

The inclusion criteria: professional athletes aged 18-40, serum uric acid level <360 μmol/l, according to screening tests. The exclusion criterion was refusal to undergo a thorough medical examination.

Out of 753 athletes, 228 (30.3%) showed high uric acid level in their screening test, 258 (34.3%) athletes refused to undergo a medical examination. 267 people were included in the study, 130 men (48.7%) and 137 women (51.3%), with the mean age of 24.4±5.2 years and the average observation period of 3.0±0.3 years.

Parameters under investigation: anthropometric measurements, laboratory tests (serum levels of lactate, creatinine, crude protein, triglycerides, thyroid-stimulating hormone (TSH), AST, ALT, myoglobin, testosterone, uric acid (UA)), glomerular filtration rate (GFR) (using the MDRD formula) with subsequent statistical analysis.

Hyperuricemia was defined as SUA level >360 μmol/L. Hypercholesterinemia - as serum cholesterol level >5.0 μmol/L, hypertriglyceridemia - as serum TG level >1.7 mmol/L. High serum creatinine level as >100 μmol/L.

Statistical analysis was conducted using the applied programs package of descriptive statistics STATISTICA 12.0 (StatSoft.Inc., USA).

Results: Hyperuricemia developed in 60 athletes (22.5%), including 51 (39.2%) men and 9 (6.6%) women.

The frequency of risk factor detection was the following: hypercholesterinemia was detected in 91 (34%) professional athletes, hypertriglyceridemia - in 10 (3.7%), reduction in GFR <100mL/min - in 46 (17.2%), BMI >25 kg/m^2 - in 65 (24.3%), BMI >30 kg/m^2 - in 3 (1.1%), arterial hypertension in 0 (0%) professional athletes.

The univariate analysis showed that out of all the factors under investigation, the following factors were significantly associated with the development of hyperuricemia: male sex (OR 9.181, 95% CI (4.285;19.674 p<0.001), hypertriglyceridemia (OR – 4.857, 95% CI (1.056;22.339) p=0.042), BMI >25 kg/m^2 (OR – 2.470, 95% CI (1.243;4.909) p=0.01), increased level of CPK (OR – 2.247, 95% CI (1.230;4.105) p=0.008). Age >25 years was associated with lower risk of development of hyperuricemia.

According to the multifactor analysis, development of hyperuricemia is associated with male sex (OR – 13.4, 95% CI (3.6;49.6) p=0.00012) and BMI >25 kg/m^2 (OR – 2.4, 95% CI (1.02;5.69) p=0.04).

Conclusion: hyperuricemia developed in professional athletes in 22.5% cases in 3.0 years. This study confirms high risk of development of hyperuricemia in professional athletes (22.5% cases in the 3-year observation period) along with low frequency of many traditional risk factors (obesity, hypercholesterinemia, hypertriglyceridemia, chronic kidney disease), which can be linked to the peculiarities of diet. This fact calls for a detailed investigation of the dietary intake of athletes with the purpose of its optimization.

Disclosure of Interests: Maria Chikina: None declared, Maxim Eliseev : None declared, Olga Sheliabina Speakers bureau: Berlin Chemie Menarini, Svetlana Glukhova: None declared, Irina Kruglova: None declared, Evgeny Nasonov Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc., Alexander Lila Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc.

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AB1254 LOW-BACK PAIN CHRONICITY IN A PRIMARY CARE SETTING IS ASSOCIATED WITH MALADAPTIVE PSYCHOSOCIAL FACTORS, OTHER CHRONIC PAIN CONDITION AND HIGH LEVELS OF PAIN AT BASELINE

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Background: Low back pain (LBP) is the leading cause of disability in Portugal and worldwide. The majority of the patients use primary health care services but the treatment outcomes are unknown. Findings of prognostic studies indicate that a marked reduction in mean pain and disability is expected in the first 6-8 weeks, for acute or persistent LBP. Beyond that time frame period, improvement slows and thereafter the probability to develop a persistent disabling back pain condition improves. Therefore, it seems important to measure the patients' outcomes at this time-point to better assess the effectiveness of the care provided.
Objectives: This study aims to describe the short-term outcomes for LBP patients treated in a primary health care centre in Portugal and to identify the prognostic factors for non-recovery and poor health related quality of live (HRQoL).
Methods: 116 patients with LBP were consecutively recruited from 7 different primary care units in Portugal. Baseline assessment includes sociodemographic and clinical data, psychosocial factors, pain, disability, and HRQoL. Pain, disability and HRQoL were then assessed at 8-weeks follow-up. A Global Rating of Change Scale to assess patient perception of improvement with treatment was added in the follow-up reassessment. Recovery criteria were determined according to the Minimal Clinically Important Difference established for pain and disability (reduction of ≥30% from baseline). The EQ-5D,3L index was dichotomised into 'poor' HRQoL (<0.6) and 'good' HRQoL (≥ 0.6), based on a proposed cut-off for having sufficient capacity to be able to work for a population with LBP. The relationship between variables on baseline and non-recovery/'poor' HRQoL was modulated through logistic regression.
Results: Of the 116 participants enrolled, 110 completed the 8-weeks follow-up. (mean age of 48,06±11,41). Approximately half of the participants (53.4%) were acute presentations of LBP. The main treatment strategy was medication (83.5%), with only 8.3% of patients having been referred for physiotherapy. At 8 weeks follow-up, there were statistically significant improvements on pain, disability and HRQoL (p≤ 0.05). However, 38% of the patients reported they felt the same or worse, 76.4% had a poor HRQoL, and only half of the patients reached the established recovery criteria (49% in disability and 50% in pain). In the adjusted model, the probability of non-recovery (p≤0.05) was associated with the presence of maladaptive psychosocial factors (OR: 1.65, 95% CI 1.13-2.40, for pain; OR: 1.61, 95% CI 1.15-2.24, for disability), a chronic pain condition (OR: 1.71, 95% CI 1.33-1.88, for pain; OR: 1.76, 95%CI 1.43-1.89, for disability), and high levels of pain at baseline for pain (OR: 1.26, 95%CI 1.09-1.39). Poor HRQoL was associated to the female gender (OR: 1.88, 95%CI 1.61-1.96), chronic pain condition (OR: 1.68, 95%CI 1.03-1.89) and high levels of pain intensity at baseline (OR: 1.36, 95%CI 1.11-1.67).
Conclusion: These results suggest there is a room for improvement in the healthcare delivered to LBP patients in the Portuguese primary healthcare setting.
Disclosure of Interests: None declared
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AB1255 SELF-PERCEPTION OF CARDIOVASCULAR RISK IN RHEUMATOLOGIC DISEASES; CASE-CONTROL STUDY

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Background: Several immune-inflammatory diseases are associated with an increased prevalence of cardiovascular diseases. Risk reduction through improved control of traditional cardiovascular risk (CVR) factors and the adoption of healthy lifestyle behaviors are critically important to reduce the CVR, although the general population must be aware of their CVR to make healthy sound decisions. Individuals who perceive an increased risk are more likely to adopt behaviors to reduce it, such as smoking cessation, exercise, weight loss, and medication compliance.
Objectives: The aim of this study is to assess the awareness of the CVR in patients with/without rheumatic diseases (RD).
Methods: Observational, cross-sectional study was design. Subjects with RD attending an outpatient clinic were consecutively recruited (RA, SLE, PsA OA, Sjögren syndrome, fibromyalgia, scleroderma, osteoporosis and osteopenia). A complete clinical history was made and a self-applied questionnaire (Precaution Adoption Process Model) was used to assess the awareness of the CVR in patients with RD. Comparisons were made to controls without RD. Frequencies (%), media and median values (q25-q75) were used for descriptive analysis and Chi Square test for comparisons.



Figure 1

Results: 250 patients were included with 76 controls and 174 cases. Demographic characteristics shown in table 1. The majority of the patients located themselves in stage 1 of their CVR perception 31.6% in cases vs. 30.3% in controls (p>0.05), other results are shown in figure 2. In the case group, 69.5% have not made any changes to reduce their CVR and the same was seen in controls. Most of the individuals are unaware of their higher CVR even though they have traditional CVR factors. Only 30.5% of the group of RD have received information from a health care provider about their CVR.

Abstract AB1255 Table 1. Demographic Characteristics

	Rheumatic Diseases (n=167)	Controls (n=60)	*p*
Age, n (%)	58 (47-60)	51.5 (34-65)	**0.001**
Female, n (%)	156 (89.7)	51 (67.1)	**0.000**
Family history CVD, n (%)	79 (45.4)	29 (38.2)	NS
Hypertension, n (%)	43 (24.7)	16 (21.1)	NS
T2DM, n (%)	16 (9.2)	13 (17.1)	NS
Dyslipidemia, n (%)	52 (29.9)	26 (34.2)	NS
Myocardial infarction, n (%)	3 (1.7)	2 (2.6)	NS
Stroke, n (%)	5 (2.3)	0	NS
Kidney disease, n (%)	6 (3.4)	4 (6.6)	NS
Active smoking, n (%)	12 (6.9)	8 (10.5)	NS
Inactive lifestyle, n (%)	92 (52.9)	36 (47.4)	NS

Abstract AB1255 Table 2. Source of Information of Cardiovascular Risk

	Rheumatic diseases (n=167)	Controls (n=60)	*p*
None, n (%)	62 (35.6)	24 (31.6)	NS
Health care provider, n (%)	53 (30.5)	19 (25)	
Television, n (%)	18 (10.3)	8 (10.5)	
Magazine, n (%)	4 (2.3)	2 (2.6)	
Internet, n (%)	14 (8)	14 (18.4)	
Books, n (%)	0	1 (1.3)	
More than 1, n (%)	11 (7.7)	5 (5.3)	
No answer, n (%)	12 (6.8)	3 (3.9)	

Conclusion: Even though patients with RD have and increased CVR, most of the individuals perceived it the same as the control group. The majority of the individuals (69.5%) haven't made any changes to reduce their CVR and many of them didn't have any source of information about their CVR, and according to EULAR recommendations the rheumatologist is the one responsible. Therefore, they should commit to give a better education to their patients.

REFERENCES

[1] Lynch EB, et al. Cardiovascular disease risk factor knowledge in young adults and 10-year change in risk factors: The Coronary Artery Risk Development in Young Adults (CARDIA) study. Am J Epidemiol. 2006;164:1171Y1179.

[2] Elmer PJ, et al. Effects of comprehensive lifestyle modification on diet, weight, physical fitness and blood pressure control: 18 months results of a randomized trial. Ann Intern Med. 2006;144:485Y495.

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AB1256 HIGH PREVALENCE OF DEPRESSION IN RHEUMATIC DISEASES: CASE-CONTROL STUDY

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Background: Prevalence of depression is higher in subjects with rheumatic diseases (RD) when compared to other general medical conditions. It's associated with chronic pain and long-term medical treatment. The Patient Health Questionnaire 9 (PHQ-9) is an extensively validated screening tool, with a negative predictive value of 99%; it has several advantages, like being self-applied and able to be used by any clinician. Currently there are no trials using this screening tool in Mexican rheumatic patients.
Objectives: To determine the prevalence of depression in a group of rheumatic subjects and compare it to non-rheumatic controls.
Methods: An observational, cross-sectional study was designed. Subjects with RD attending an outpatient clinic were consecutively recruited. A complete clinical history with information about exercise history, and the PHQ-9 screening tool were performed to every subject. Subjects without RD were recruited as controls. Descriptive analysis was done using frequencies (%) and median (q25-q75). Comparisons were done using Chi-square and Mann-U Whitney's test, considering only $p<0.05$ as significant.
Results: A total of 269 subjects were included. Demographic characteristics are shown in Table 1. In the RD group, a higher percentage were female ($p<0.001$) and had a higher median age ($p<0.001$). A higher prevalence of depression was found in the RD group ($p<0.002$). Regarding exercise history, subjects with an inactive lifestyle had a higher prevalence of depression ($p<0.001$). This remained significant after evaluating only subjects with RD ($p<0.007$) and controls ($p<0.003$).

Abstract AB1256 Table 1. Demographic Characteristics

	Rheumatic diseases (n=195)	Controls (n=74)	*p*
Female, n (%)	175 (89.7)	52 (70.3)	**<0.001**
Age, n (%)	58 (47-65)	46 (30-60)	**<0.001**
Hypertension, n (%)	46 (24.3)	18 (24.7)	NS
T2DM, n (%)	22 (11.7)	13 (17.8)	NS
Dyslipidemia, n (%)	59 (31.7)	23 (32.4)	NS
Active smoking, n (%)	11 (5.9)	8 (11.1)	NS
Inactive Lifestyle, n (%)	103 (55.1)	33 (48.5)	NS
RA, n (%)	106 (54.3)	-	-
OA, n (%)	32 (16.4)	-	-
LES, n (%)	7 (3.5)	-	-
Sjogren Syndrome, n (%)	7 (3.5)	-	-
Fibromyalgia, n (%)	9 (4.6)	-	-
Ankylosis spondylitis, n (%)	5 (1.9)	-	-
PsA, n (%)	3 (1.1)	-	-
Scleroderma, n (%)	4 (2)	-	-
Other RD, n (%)	22 (11.2)	-	-

Abstract AB1256 Table 2. Patient Health Questionnaire (PHQ-9)

Classification Cut-off point	Rheumatic diseases N=195	Controls N=74	*p*
Normal 0-5, n (%)	84 (43.1)	49 (66.2)	**0.003**
Mild 6-9, n (%)	41 (21)	11 (14.9)	
Major Depression ≥10, n (%)	70 (35.9)	14 (18.6)	

Conclusion: Patients with RD have a higher prevalence of depression than non-rheumatic controls ($p<0.001$). An inactive lifestyle was associated with a higher prevalence of depression in our cohort, both in RD subjects and in controls ($p<0.001$). This is the first study that evaluates the PHQ-9 screening tool in Mexican patients with RD. The physicians should be aware of it and use screening tools to detect depression disorders and provide an adequate treatment.

REFERENCES

[1] O'Malley PG, Jackson JL, Kroenke K, Yoon IK, Hornstein E, Dennis GJ. The value of screening for psychiatric disorders in rheumatology referrals. Arch Intern Med 1998;158:2357-62.

[2] Ohayon MM, Schatzberg AF. Using chronic pain to predict depressive morbidity in the general population. Arch of Gen Psychiatry 2003;60:39-47.

[3] Anyfanti, P., et al. Depression, anxiety, and quality of life in a large cohort of patients with rheumatic diseases: common, yet undertreated. Clin Rheumatol DOI 10.1007/s10067-014-2677-0

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AB1257 CARDIOVASCULAR RISK FACTORS IN GOUT COMPARED TO AS, PSA AND RA – RESULTS FROM A QUESTIONNAIRE STUDY

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Background: Increased risk for cardiovascular disease (CVD) is a hallmark for many rheumatic diseases including gout, ankylosing spondylitis (AS), psoriatic arthritis (PsA) and rheumatoid arthritis (RA). This is likely explained by a combination of increased occurrence of CVD risk factors (CVDRF) and chronic inflammation and in gout possibly by increased serum urate levels.
Objectives: To compare the prevalence of CVRFs and CVD in gout, AS, PsA and RA.
Methods: All individuals aged ≥18 years with at least one ICD-10 diagnosis of gout (M10), AS (M459), PsA (M073) and RA (M059/M060) recorded by a physician during a two year period (Jan 2015 through Feb 2017) were identified at 12 primary care centers and three rheumatology units in the Western Sweden Health Care Region. A total of 1589 gout, 1095 AS, 1200 PsA and 1246 RA subjects were sent a questionnaire which included questions on demographics, CVRFs (smoking, alcohol consumption, physical activity (PA)) and comorbidities (diabetes (DM), hypertension (HT), dyslipidemia (DL), acute coronary syndrome (ACS) and stroke). High alcohol intake was defined as >4 std drinks/week. Low PA was defined as ≤3 hours of moderate PA/week. Primary non-responders received a second mailing of the questionnaire. All prevalences were indirectly age standardized (IAS) to the population of Sweden 2017, due to the differences in age distribution between the diseases. Chi square test with significance level .05 was performed. IAS prevalences for BMI, PA, DM and HT for the general population (GP) was retrieved from the National public health survey from 2015 which was sent to more than 100 000 randomly selected citizens in Sweden aged 16-84.
Results: Response rates ranged from 53.6% (AS) to 59.6% (RA) and after excluding subjects who had not provided complete information on the evaluated variables we included 2437 individuals. The gout and RA

patients were older (mean age 71 (SD 12) and 66 (SD 13) years respectively) compared to AS and PsA (mean age 50 (SD 14) and 55 (SD 13) years respectively). When adjusting for these differences by IAS by sex, both prevalent CVD (stroke, ACS) and all traditional risk factors were more common in gout compared to RA, AS or PsA (Table 1+2), except for alcohol intake in women, where highest exposure was seen in PsA (Table 2). The male AS patients displayed the highest PA level and the lowest prevalence of stroke (table 1). Smoking was least common in male PsA and female AS and RA patients (table 1+2).

Males	Gout, n= 582, prevalence %	AS, n= 273, prevalence %	PsA, n= 268, prevalence %	RA, n= 315, prevalence %	p-value*	GP, n= 23177, prevalence %
BMI ≥25	85.3	51.5	59.0	65.9	< 0.0001	56.2
PA, low	61.9	44.0	54.8	58.0	0.0001	42.5
Alcohol, high	43.3	20.0	28.3	16.5	< 0.0001	N/A
Smoking, ever	48.5	53.4	35.9	46.6	0.0003	N/A
DM	14.2	4.8	8.4	8.7	0.0001	6.0
HT	49.2	23.9	32.9	29.2	< 0.0001	18.7
DL	25.3	9.6	11.2	13.1	< 0.0001	N/A
Stroke	7.7	0.9	4.1	4.9	0.0005	N/A
ACS	7.7	3.1	6.1	6.4	0.6	N/A

Age-standardized prevalences of CVD riskfactors and outcomes in males, *Chi-square comparing gout, AS, PsA and RA

Females	Gout, n= 134, prevalence %	AS, n= 215, prevalence %	PsA, n= 305, prevalence %	RA, n= 345, prevalence %	p-value*	GP, n= 26714, prevalence %
BMI ≥25	87.3	40.8	60.0	45.9	< 0.0001	43.1
PA, low	74.8	48.3	54.3	52.6	<0.0001	46.5
Alcohol, high	7.0	6.4	14.2	6.9	0.003	N/A
Smoking, ever	56.7	37.8	56.8	38.0	< 0.0001	N/A
DM	14.9	2.3	4.9	4.2	< 0.0001	4.4
HT	56.8	20.3	27.5	24.4	< 0.0001	17.6
DL	26.7	7.4	10.5	9.7	< 0.0001	N/A
Stroke	3.7	0.8	0.6	1.7	0.09	N/A
ACS	3.6	0.0	1.8	2.5	0.2	N/A

Age-standardized prevalences of CVD riskfactors and outcomes in females, *Chi-square comparing gout, AS, PsA and RA

Conclusion: Gout patients display the highest prevalence of CVRFs in both men and women compared to AS, PsA and RA. Thus, addressing CVDRFs is of particular importance in patients with gout.

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AB1258 THE 10 YEAREXPERIENCE OF IDENTIFYING AND MONITORING INDIVIDUALS AT RISK OF RA IN AN ARTHRITIS PREVENTION CLINIC

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Background: Anti-cyclic citrullinated protein antibodies (anti-CCP) are highly specific for rheumatoid arthritis (RA) and may appear more than 10years before the disease. As the test has become more accessible, many patients without clinical synovitis are being globally tested.

Objectives: We have developed in Leeds a prevention study clinic for referrals from individuals identified through our primary care research network alongside the patients from secondary care referrals, aiming for an early identification of inflammatory arthritis (IA)[1].

Methods: From June 2008 to December 2018, individuals from our primary care network with new musculo-squeletal symptoms were invited to be tested. All anti-CCP tests were performed centrally in our Rheumatology Department in Leeds (LIRMM), using a standard Anti-CCP2 assay (immunocap method, Phadia assay). Individuals from primary or secondary care who were tested positive for anti-CCP antibodies (CCP positive) were invited to Leeds and followed prospectively in a research, observational study until progression to IA.

Results: As shown in figure 1, the number of patients referred to our study from either primary or secondary care has been increasing gradually. Over the last year, the overall referrals reached 2368 participants, 115 of them from secondary care and 2253 from primary care.

Of the 901 CCP positive individuals, 479 met the inclusion criteria and accepted to participate to the study (Table 1). Actually, the mean follow-up time of the overall cohort is 98.5weeks (SD 105.55) with a cumulative time of follow-up of over 50 000 weeks. There is a female predominance of 72.1% and a mean age of 50.3 years (SD 13.51) at baseline. Of the 165 participants that have been withdrawn from the study, 134 developed IA after a mean time of 83.8 weeks (28.0% of the overall cohort). Currently, 353 anti-CCP positive patients are still being followed. Age and sex of the patients who progressed are similar to the ones still in the study (respectively p=0.798 and p=0.326).

Conclusion: Leeds Teaching Hospital and LIRMM have now been following patients at risk of progressing to IA for more than 10 years. The steady increase in recruitment from both primary care and secondary care centres confers a viable base for recruitment. As prevention is a key aspect in global Health management, our study is a sustainable model for identifying at-risk subjects of progression, a necessary step towards prevention. This increase in overall referrals correlates with a need of recommendation regarding management of patients, especially those at high risk.

REFERENCES

[1] Hunt, L. and P. Emery, *Defining populations at risk of rheumatoid arthritis: the first steps to prevention*. Nat Rev Rheumatol, 2014. 10(9): p. 521-30.

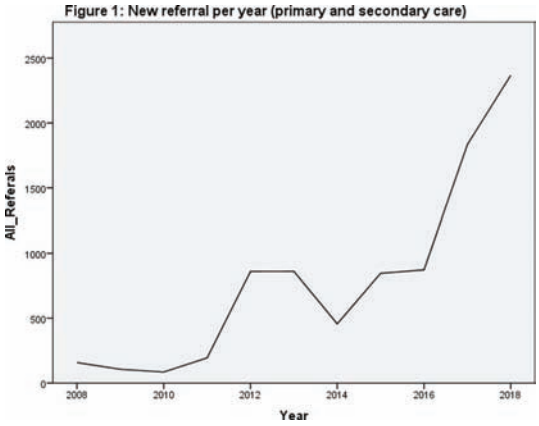


Figure 1

Table 1. Demographics

	Overall cohort	Progressors (84% of total withdrawn (n=165))	Ongoing follow-up
N	479	136 (26.1%)	314
Mean follow-up (weeks)	98.5 (SD 105.55)	83.83 (SD 90.87)	105.72 (SD111.65)
CCP titre	High: 59.9% (n=288) Low: 36.4% (n=175) Neg: 3.11% (n=15)*	High: 89.7% (n=122) Low: 9.6% (n=13) RF control: 0.7% (n=1)	High: 49.4% (n=155) Low: 49.4% (n=155) Neg: 1.3% (n=4)
Gender	F 72.1% (n=347) M 27.9% (n=134)	F 68.4% (n=93) M 31.6% (n=43)	F 72.9% (n=229) M 27.1% (n=85)
Age	50.34 (SD13.51)	52.8 (SD 13.05)	49.84 (SD13.56)

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AB1259 EVALUATION OF ENALAPRIL ON ARTERIAL STIFFNESS IN RHEUMATOID ARTHRITIS IN A RANDOMISED CLINICAL TRIAL

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Background: This is the first study where suboptimal doses of enalapril proved to be successful for the reduction of arterial stiffness in in a clinical trial of rheumatoid arthritis (RA) patients.
Objectives: The aim of this study was to analyze the effect of enalapril on arterials stiffness through the evaluation of subclinical parameters in RA patients without traditional cardiovascular risk factors or previous comorbidities.
Methods: Fifty three patients were enrolled in a clinical, randomized, closed-label trial. The subjects were randomly assigned into two groups: One receiving 5 mg of enalapril (27) and 5 mg of placebo (26), both twice a day. Clinical assessment included a structured questionnaire to gather demographic and clinical variables, including disease duration, treatment, disease activity, laboratory, anthropometric measurements and determination of cardiovascular parameters [carotid femoral pulse wave velocity (cfPWV) (1), cardio-ankle vascular index (CAVI) (2), carotid intima media thickness (cIMT), carotid artery distensibility (3), Young´s incremental elastic modulus (Einc)]. The whole set of evaluations were analyzed at the baseline and at the end of 12 weeks of intervention.
Results: A significant reduction in delta CAVI of 0.21 in the enalapril intervention group was found. In contrast, an increase of 0.39 was observed in the placebo group. The delta CAVI reduction was not influenced by age or peripheral systolic blood pressure (pSBP).
Conclusion: Enalapril seems to be effective in CAVI reduction in RA patients. The effect of enalapril intervention on arterial stiffness translated to the clinical context, might be interpreted as a reduction of 6.4 years of arterial aging.

REFERENCES

[1] Vazquez-Del Mercado, M., et al., *Disease duration of rheumatoid arthritis is a predictor of vascular stiffness: a cross-sectional study in patients without known cardiovascular comorbidities: A STROBE-compliant article*. Medicine (Baltimore), 2017. 96(33): p. e7862.
[2] Saiki, A., et al., *The Role of a Novel Arterial Stiffness Parameter, Cardio-Ankle Vascular Index (CAVI), as a Surrogate Marker for Cardiovascular Diseases*. J Atheroscler Thromb, 2016. 23(2): p. 155-68.
[3] Vazquez-Del Mercado, M., et al., *Subclinical parameters of arterial stiffness and arteriosclerosis correlate with QRISK3 in systemic lupus erythematosus*. PLoS One, 2018. 13(12): p. e0207520.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8241

AB1260 CHARACTERISTICS OF METABOLIC SYNDROME IN AN ASIAN COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Metabolic syndrome (MS), the concurrence of hypertension, abdominal obesity, dyslipidemia and glucose intolerance, is an important risk factor for type II diabetes mellitus (T2DM) and cardiovascular disease (CVD). CVD is a leading cause of morbidity and mortality in patients with rheumatoid arthritis (RA). Studies in RA suggest that inflammation and glucocorticoid use predispose to MS, and that MS is associated with active disease.
Objectives: To investigate the prevalence and characteristics of MS in our cohort of RA patients.
Methods: A total of 409 patients who fulfilled the 1987 ACR criteria for RA and with complete data for classification of MS were included. MS was defined according to the Adult Treatment Panel III report of the National Cholesterol Education Programme (NCEP/ATP III). Information related to demographics, disease onset, serologies, disease activity and treatment was collected. Independent t-test or Mann-Whitney U test was used to compare continuous quantitative data, while Pearson Chi-square or Fisher Exact test for categorical data. Logistic regression was used to identify factors associated with of MS. All the statistical tests were two sided, and p value <0.05 was considered as statistically significant.
Results: Fifty-two patients (12.7%) fulfilled the criteria for MS. Most of the patients in the cohort were female (85.3%) and non-smokers (84.6%). The mean age was 60.5±11.09 years and mean BMI 23.67±5.06. The patients with MS were significantly older (age 64.21±8.63 vs 59.96±11.32, p=0.010). The mean disease duration was 14.09±9.74 years. Rheumatoid factor and anti-cyclic citrullinated peptide antibody were present in 80.0% and 95.1% respectively. 4.4% of them had a history of CVD or stroke/ transient ischaemic attack but the prevalence was the same in patients with and without MS. Comparing the two groups, there was no significant difference in the history of ever-smoking (15.4% vs 15.4%, p=0.699), disease duration (16.44±10.11 vs 13.72±9.66 years, p=0.060), cumulative glucocorticoid use (p=0.649), DAS28 score (2.12±1.09 vs 2.11±1.24, p=0.458) and HAQ score (0.13 vs 0.13, p=0.767). There was also no significant difference in the use of methotrexate, leflunomide or biologics. The commonest MS criteria fulfilled were hypertension (88.5%) and dyslipidaemia (84.6%). 46.2% of the patients with MS had T2DM. Males were less likely to have MS than females [adj. OR (95%CI): 0.039 (0.005, 0.292), p=0.002].
Conclusion: MS is found in 12.7% of our RA patients and they were significantly older than those without MS. In our study, MS does not have a significant association with RA disease activity, disease duration, glucocorticoid usage or disease modifying anti-rheumatic treatment.

REFERENCES

[1] Rostom S, et al. Metabolic syndrome in rheumatoid arthritis: case control study. BMC Musculoskeletal Disorders. 2013 Apr 26;14:147.
[2] Tantayakom P, et al. Metabolic syndrome is associated with disease activity in patients with rheumatoid arthritis. Joint Bone Spine. 2016 Oct;83 (5):563

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AB1261 CADMIUM TOXICITY AS A PROBABLE CAUSE OF OSTEOPENIA IN ADOLESCENTS AND ITS RELATION TO BAD DIETARY HABITS

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Background: Cadmium is a naturally occurring minor element; it has been recognized as an occupational health hazard for many decades. Water and food are the main source of environmental cadmium exposure in non-smokers in most parts of the world. Cadmium accumulates gradually in the human body, where it gives rise to a number of adverse health effects and especially to kidney and bone. Several studies have addressed a possible association between long-term low-level environmental cadmium exposure and osteoporosis. Osteoporosis is a large and escalating public health problem.
Objectives: This study was conducted to assess the bone mineral status in secondary school students in Egypt and to measure cadmium level in their blood and urine and possible relationship between cadmium retention and bone mineral abnormalities as well as its consumption from some food and drinks commonly utilized by those students.
Methods: Two hundred secondary school students from different secondary schools in Egypt were included in this study(100 males, and 100 females). Bone mineral status was assessed in the 200 students by Quantitative Ultrasonography (QUS) of the calcaneus using the ultrasound bone densitometer unit PEGASUS PRESTIGE, OSTEOMED, FRANCE. Students with abnormal bone mineral status (T score < -1) were considered osteopenic, data obtained from this osteopenic group were compared

to those from a group of apparently healthy students with normal T score (T score $\geq$ -1).
Results: Osteopenic group were 52 students (26%); 16 males and 36 females, their mean age was 15.46 ± 0.40 years. Cadmium level in blood and urine was significantly higher in osteopenic group. Interpretation of dietary habits in the osteopenic and control groups revealed that carbonated beverages, potatoes chips, corn snacks intake were significantly increased in osteopenic group, whereas no significant difference was detected in milk, tea, and coffee intake. T score was negatively correlated with blood cadmium, urine cadmium, as well as carbonated beverages, potatoes chips, corn snacks. Cadmium concentrations in tap water as well as in commercial mineral water were negligible, but its concentration in carbonated beverages, potatoes chips, corn snacks was relatively high.
Conclusion: Osteopenia and osteoporosis are not uncommon problem among secondary school students in Egypt. Cadmium exposure, evident by high blood and urinary levels, is a risk factor for development of low BMD. Fault dietary habits, including increased carbonated beverages, potatoes chips, and corn snacks intake, contributes to the occurrence of osteopenia.

REFERENCES

[1] Abdel-Haleem AS, Sroor A, El-Bahi SM, et al.: Heavy metals and rare earth elements in phosphate fertilizer components using instrumental neutron activation analysis. Appl Radiat Isot 55:569-573; 2001.
[2] Abdel-Sabour MF: Cadmium status in Egypt. J Environ Sci (China) 13:351–360; 2001
[3] Abou-Arab AA and Abou Donia MA: Heavy metals in Egyptian spices and medicinal plants and the effect of processing on their levels. J Agric Food Chem 48:2300–2304; 2000.
[4] Åkesson A, Bjellerup P, LundhT, et al.,: Cadmium-Induced Effects on Bone in a Population-Based Study of Women. Environmental Health Perspectives 116 (6): 830-834; 2006.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.731

AB1262 THE RELATIONSHIP BETWEEN HYPERURICEMIA AND HEART RATE IRREGULARITY, USING DATA FROM THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2016

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Background: Hyperuricemia is one of the well-known cardiovascular risk factors. In recent studies, hyperuricemia has been shown to be an independent risk factor for atrial fibrillation, which may be associated with oxidative stress or inflammation. There is still a lack of data on the association of hyperuricemia and arrhythmia other than atrial fibrillation.
Objectives: In this study, we investigated the relationship between hyperuricemia and heart rate (HR) irregularity using representative sample data of adult Korean.
Methods: The study included 5870 subjects aged 19 years or older who completed the uric acid measurement in the Korean National Health and Nutrition Examination Survey conducted in 2016. Logistic regression was used to analyze the association between hyperuricemia and HR irregularity identified by the examiner at the time of the survey.
Results: Subjects with HR irregularity were older, had more smoking and drinking, had a higher prevalence of HTN, and had lower glomerular filtration rate than those with regular heartbeat. In the presence of hyperuricemia, the HR irregularity was three times higher than in the absence (HR 3.65, 95% CI 1.77-7.53, *P* = 0.0005). The association of HR irregularity and hyperuricemia was significant in most subjects, especially in those older than 65 years, with diabetes and hypertension.
Conclusion: Hyperuricemia was highly correlated with HR irregularity in adult Korean representative sample data, especially in subjects with conventional cardiovascular risk factors such as old age, hypertension, diabetes mellitus. This study included all subjects who showed HR irregularity at the time of examination, not just atrial fibrillation. Therefore, it is suggested that hyperuricemia may be associated with other arrhythmia as well as atrial fibrillation. Further researches are warranted to clarify the relationship between hyperuricemia and arrhythmia and its mechanism.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7783

AB1263 C-REACTIVE PROTEIN LEVEL AS A MARKER FOR DYSLIPIDEMIA, DIABETES, AND METABOLIC SYNDROME: RESULTS FROM THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY:

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Background: High sensitivity C-reactive protein (hsCRP) C-reactive protein (CRP) is a marker of inflammation and increased hsCRP is reported in many diseases including cardiovascular disease, diabetes, metabolic syndrome, arthritis, and malignancies.
Objectives: This study evaluated the association between hsCRP and comorbidities.
Methods: A total of 5,887 (weighted n = 40,251,868) participants age 19 or older from the 2016 Korean National Health and Nutrition Examination Survey were included for analysis. Weighted prevalence and odds ratio (OR) of comorbidities were analyzed according to the continuous variable of log hsCRP levels.
Results: Mean age was 46.7 and mean hsCRP levels were 1.23mg/L. Mean hsCRP levels were higher in participants with cardiovascular diseases and cardiovascular risk factors, osteoarthritis, rheumatoid arthritis, pulmonary tuberculosis, and several cancers of gastric, colon, breast, and cervix than the general population. In multivariable analysis, hsCRP concentration was associated with increased prevalence of hypertriglyceridemia (OR 1.15, 95% CI 1.04-1.28, p = 0.007), diabetes (OR 1.20, 95% CI 1.05-1.37, p = 0.005), and metabolic syndrome (OR 1.22, 95% CI 1.11-1.35, p < 0.001) after adjustment for socioeconomic and lifestyle characteristics. There was no significant association between hsCRP level and cancers.
Conclusion: hsCRP was associated with increased risk of dyslipidemia, diabetes, and metabolic syndrome in the general population.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.5244

AB1264 THE RELATIONSHIP BETWEEN SERUM URIC ACID AND PULMONARY FUNCTION IN KOREAN ADULT POPULATION: DATA FROM THE KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY:

Hyemin Jeong[1], Yeoung Hee Eun[2], In-Young Kim[3], Eun-Jung Park[4], Hyungjin Kim[2], Jaejoon Lee[2], Chan Hong Jeon[1]. *[1]Soonchunhyang University Hospital, Bucheon, Bucheon, Korea, Rep. of (South Korea)*; *[2]Samsung Medical Center, Seoul, Korea, Rep. of (South Korea)*; *[3]National Police Hospital, Seoul, Korea, Rep. of (South Korea)*; *[4]National Medical Center, Seoul, Korea, Rep. of (South Korea)*

Background: Hyperuricemia is associated with several comorbidities. The association between uric acid and pulmonary function is still controversial.
Objectives: The aim of this study was to evaluate the relationship between serum uric acid and pulmonary function in Korean adult population.
Methods: A total of 3,177 (weighted n = 19,770,902) participants aged 40 years or older from the 2016 Korean National Health and Nutrition Examination Survey were included and performed cross-sectional study.
Results: Participant with hyperuricemia was older than participants with normouricemia in females. Body mass index, Mean arterial pressure, and hemoglobin A1c, and estimated glomerular filtration rate (eGFR) were significantly associated with uric acid levels in both sex. Hyperuricemia was significantly associated with decreased FEV1 and FVC in females after adjustment for age, income, region, education, marital status, alcohol consumption, smoking, body mass index, mean arterial pressure, hemoglobin A1c, and eGFR (β = -0.143, P-value = 0.002 and β = -0.159, P-value = 0.001, respectively). There was no significant association between uric acid levels and lung function in males. After additional adjustment for respiratory disease including pulmonary tuberculosis, asthma, and lung cancer, hyperuricemia was associated with decreased FEV1 and FVC in females (β = -0.142, P-value = 0.001 and β = -0.161, P-value < 0.001, respectively)
Conclusion: Hyperuricemia was associated with decreased FVE1 and FVC in female general population.

Disclosure of Interests: None declared
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AB1265 EVALUATION OF ADHERENCE TO TREATMENT IN PATIENTS OF RHEUMATIC DISEASES

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Background: Patient adherence to treatment is one of the most important factors influencing the effectiveness of therapy, the course of the disease and the prognosis of the patient's life. In addition to understanding the degree of adherence, it is important to study the factors that reduce patient adherence. In 2008, the Russian questionnaire for evaluation of adherence to treatment was developed, assessing adherence to drug therapy, to medical care, to lifestyle modification and general adherence to treatment. The questionnaire showed good sensitivity (93%) and specificity (78%).
Objectives: Using the questionnaire, assess the level of adherence to treatment, to drug therapy, medical care and to to lifestyle modification of patients with rheumatic diseases.
Methods: The study included 130 patients (30 men and 100 women) with rheumatic diseases observed in the hospital (63.1%) or outpatient (36.9%). The average age of patients was 53.1 ± 11.72 years (from 27 to 81). 69 patients (53%) suffered with rheumatoid arthritis, with ankylosing spondylarthritis 21 (16.2%), with osteoarthritis 13 (10%), with psoriatic arthritis and systemic vasculitis in 7 patients (5.4%), the remaining 10% were other rheumatic diseases. The average disease duration is 12.3 years. Patients received NSAIDs (83.8%), glucocorticoids (62.3%), methotrexate (39.2%), immunosuppressive specialty drugs (23%), cyclophosphamide (3.8%), hydroxychloroquine (3%), sulfasalazine (2, 3%), leflunomide (1.5%), azathioprine (0.8%). Based on the data obtained in points and comparing them with theoretically possible, the level of adherence was assessed as high (76% or more), medium (51-75%) and low (50% or less).
Results: The high level of adherence was observed only in 12 people (9.2%), in 66 patients (50.8%) - medium and in 52 people (40%) - low. Men had a higher level of adherence (57.6%) than women (55.4%). Among those using non-traditional methods of treatment (33.1%), adherence to treatment was 54.5%, for non-applicants (66.9%) the level of adherence was higher - 56%.
The average level of adherence to drug therapy was 61%, to medical care - 65%, to lifestyle modification - only 48.8%. The degree of adherence to lifestyle changes was slightly higher among women - 48.3% than among men - 47.6%. Patients suffering from rheumatic diseases from 5 to 10 years - 53.4% had a higher level of adherence to lifestyle changes than patients suffering from less than 5 years (48.2%) and more than 10 years (45.2%). Patients with osteoarthritis have a higher level of adherence to treatment (58%) than patients with rheumatoid arthritis (55.8%), ankylosing spondyloarthritis (56%), and psoriatic arthritis (56.1%).
Conclusion: In patients with rheumatic diseases, 40% showed a low level of adherence to treatment, 50.8% - an average level, which indicates a lack of adherence. The lowest level of adherence is noted for modifying the lifestyle - 48.8%, which depended on the sex and duration of the disease.

REFERENCES

All these factors must be considered when discussing the strategy and tactics of treatment with each patient in real clinical practice.

Disclosure of Interests: None declared
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AB1266 THE CORRELATION BETWEEN SMOKING AND DISEASE ACTIVITY AND MRI INFLAMMATION IN EARLY AXIAL SPONDYLOARTHRITIS IN AN EGYPTIAN COHORT

fatma fayed, Abeer Abdelati. *Alexandria, rheumatology and immunology unit, Alexandria, Egypt*

Background: literature suggests that smoking is one of the crucial triggering factors of rheumatological diseases.[1] In axial Spondyloarthritis (axSpA), classified into radiographic SpA (AS) and non-radiographic SpA (nrSpA), smoking associated with disease activity and extra-articular manifestation. [2] The relationship between smoking and HLAB-27 as well as MRI inflammation in axSpA patients and the difference between nrSpA and AS regarding smoking have not been studied to date in details.
Objectives: to investigate the influence of smoking on disease activity and MRI inflammation in axSpA patients (AS and nrSpA).
Methods: sixty Egyptian patients (42 males and 18 females) with the mean age (31.33 ± 7.02), with early active axial spondyloarthritis (49 AS and 11 non-radiographic SpA) within two years disease duration, diagnosed based on ASAS classification criteria. All clinical indices (BASDI, BASFI, BASMI, ASDAS-CRP) were applied to all patients. HLA-B27 and the inflammatory markers (ESR, CRP) was done. MRI of sacroiliac joints was performed in a standard protocol using short tau inversion recovery and T1 sequences (slice thickness 3-4mm, both semi-coronal and semi-axial orientations), and scored by the Berlin method. Smoking use assessed by smoking pack-year index.
Results: of all 60 patients, 38 smokers and 22 non-smokers. No significant difference regarding smoking packs index between nrSpA and AS. (p=0.822) There was a robust correlation between smoking packing index and the Berlin score of MRI in all axSpA patients (r_s=0.631) (p=<0.001). Moreover, there was a significant correlation between smoking and C-reactive protein (r_s=0.952) as well as HLA-B27. (r_s=0.340) (p<0.001) Furthermore, a significant relationship between smoking and activity indices (BASDI (r_s=0.961) and ASDAS-CRP (r_s=0.938)). Otherwise, no significant correlation among smoking, BASMI, and BASFI as well as ESR.

Table (1): Correlation between smoking pack index and different parameters

Disease activity	Smoking pack index					
	Non radiographic SpA (n = 11)		Radiographic SpA (n = 49)		Total (n = 60)	
	r_s	p	r_s	p	r_s	p
BASDI	0.986*	<0.001*	0.224	<0.001*	0.204	<0.001*
ASDAS-CRP	0.981*	<0.001*	0.969*	<0.001*	0.938*	<0.001*

r_s: Spearman coefficient*: Statistically significant at $p \leq 0.05$

Table (2): Correlation between smoking pack index and HLAB27, inflammatory marker (CRP) and Berlin score of MRI

	Smoking pack index					
	Non radiographic SPA (n = 11)		Radiographic SPA (n = 49)		Total (n = 60)	
	r_s	P	r_s	p	r_s	p
HLAB27	0.602*	0.049*	0.293*	0.041*	0.340*	0.008*
Berlin score of MRI	0.687*	0.020*	0.742*	<0.001*	0.631*	<0.001*
CRP	0.991*	<0.001*	0.970*	<0.001*	0.952*	<0.001*

r_s: Spearman coefficient
*: Statistically significant at $p \leq 0.05$

Conclusion: Smoking has no significant difference between AS and nrSpA. Smoking has a significant association with HLA-B27, the inflammatory lesions of MRI, and clinical indices (BASDI, ASDAS-CRP) as well as C reactive protein in AS and non-radiographic SpA patients while it has no association with the other clinical indices in term of BASMI and BASFI as well as the Erythrocyte sedimentation rate (ESR).

REFERENCES

[1] Belbasis L, Dosis V, Evangelou E. elucidating the environmental risk factors for rheumatic diseases: An umbrella review of meta analyses. International journal of rheumatic diseases. 2018;21(8):1514-24.
[2] Zhao S, Jones GT, Macfarlane GJ, et al. Associations between smoking and extra-axial manifestations and disease severity in axial spondyloarthritis: results from the BSR Biologics Register for Ankylosing Spondylitis (BSRBR-AS). Rheumatology2018.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7771

AB1267 THE PREVALENCE OF RHUPUS SYNDROME IN A MONOCENTRIC TERTIARY REFERRAL COHORT

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Background: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are two systemic chronic autoimmune diseases characterised by a wide spectrum of clinical and immune-pathological features. In clinical practice, the concept of *Overlap Syndrome* is defined when the two diseases coexist in the same patient. Rhupus syndrome is a rare clinical condition, characterized by overlap of SLE and RA. However, it is still subject to debate whether the syndrome should be considered a distinctive entity or an aggressive form of SLE. To date, the estimated prevalence of rhupus is unknown.
Objectives: To evaluate the prevalence of patients with rhupus syndrome in our tertiary care center.
Methods: We chart-reviewed all patients with a diagnosis of SLE[1] or RA[2], based on the current ACR classification criteria, who presented to our outpatient clinic rheumatology unit. Clinical and laboratory data were retrospectively collected from patient notes. Diagnosis were systematically analyzed by two independent reviewers (SGF and ER). Disagreements were resolved by consensus; if consensus could not be achieved, a third party (SS) would provide an assessment of eligibility.
Results: One-hundred eighty-two patients with a diagnosis of SLE and 253 patients of RA, were identified. Out of 182 SLE and 253 RA cases analysed, only 2 patients fulfilled rhupus criteria. The estimated prevalence in our cohort was 0.46% (2/437).
In Figure 1 are illustrated the clinical manifestations of SLE (Panel A; Malar rash) and RA (radiograph-documented erosive polyarthritis) of the two patients.



Figure 1

Additionally, we identified 7 patients (1.61% of the total cohort) that only partially fulfilled both criteria for SLE and RA. In detail, 1 patient (0.23%) manifested with an overlap of clinical manifestations of SLE and RA, while 1 patient had an overlap of both laboratory criteria. Two patients (0.46%) presented with clinical criteria of RA and laboratory criteria for SLE and RA and 3 patients (0.69%) with clinical criteria of SLE and laboratory criteria for SLE and RA.
Patient's selection is resumed in Figure 2.

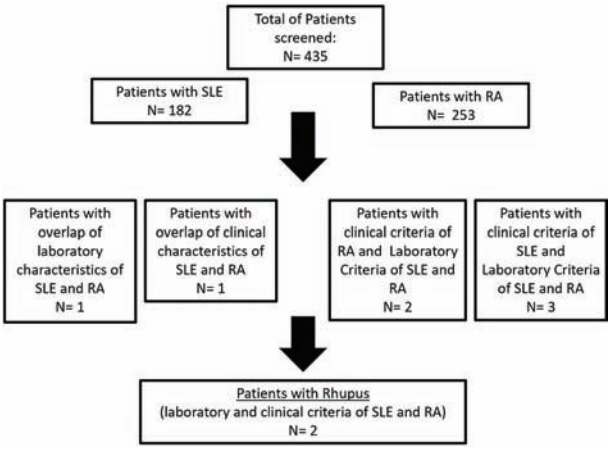


Figure 1

Conclusion: The prevalence of rhupus observed in our study was relatively low (0.46%). However, we identified up to 1.6% of patients partially fulfilling a diagnosis of rhupus. Rhupus syndrome is a rare and aggressive clinical condition and further prospective studies and an harmonization of classification criteria are highly needed.

REFERENCES

[1] Hochberg MC. Updating the ACR revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997 Sep;40(9):1725.
[2] Aletaha D, et al. 2010 rheumatoid arthritis classification criteria: an ACR/EULAR collaborative initiative. Ann Rheum Dis. 2010 Sep 1;69(9):1580–8.

Disclosure of Interests: None declared
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AB1268 VASCULAR INVOLVEMENT IN BEHÇET'S DISEASE : ABOUT 87 CASES

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Background: Behçet's disease (BD) is a systemic vasculitis which ethiopathogenesis still poorly understood.
Vascular involvement is one of the major causes of mortality and morbidity in this disease.
It occupies a special place in the cardiovascular pathologies because of its venous and arterial tropism all confounded caliber but also because of its pejorative prognosis as well on the functional level as vital.
Objectives: Our goal was to present the various venous and arterial manifestations of BD, their epidemiological, clinical, evolutionary and therapeutic characteristics.
Methods: This is a retrospective study over a period of 9 years [2009-2018] that enrolled 87 patients who met the international criteria for Behçet's disease. The characteristics of vascular involvement were studied.
Results: Twenty-two patients had vascular involvement (25%). There are 17 men and 5 women (sex ratio H/F=3,4), mean age at diagnosis of angina Behçet 39 years [22 years-63 years].
The vascular lesions were indicative of the disease in 17 cases (77%), and for the other 5 patients, the mean time to onset of vascular disease compared with the diagnosis of BD was 2 years.

Patients' fulfilling the diagnosis of rhupus is resumed in Table 1.

	ANA	anti-dsDNA	RF (U/ml)	anti-APCAs (U/ml)	Articular involvement	SLE extra-articular manifestations	Immunosuppressive treatment undergone
Patient 1	1:320 Homogeneous pattern	Positive (IFI)	219	63	Erosions of MTF and ulnar deviation of the wrists	leukopenia, malar rash	hydroxychloroquine, methotrexate, leflunomide, sulfasalazine, ciclosporin, azathioprine, abatacept, rituximab, tocilizumab
Patient 2	1:160 Granular pattern	Positive (IFI)	55	47.95	Loss of ICs, CMCs and MCPs joint space and bilateral MCP joint erosions (2nd-4th)	Myelitis, leukopenia, malar rash, oral ulcers	hydroxychloroquine, methotrexate, azathioprine, mycophenolate, tocilizumab

Venous thrombosis involved 20 patients (90%). They were deep in 16 patients, superficial in one patient and superficial and deep in 3 patients. It was recurrent in 14 patients.
The most common site of deep vein thrombosis was the lower limbs (n=17). The others had unusual sites: inferior vena cava thrombosis (n = 3), superior vena cava thrombosis (n = 2), sus-hepatic vein (n=1) and upper limb thrombosis (n = 1). Pulmonary embolism was noted in one case.
Arterial damage involved 4 patients (20%) divided into arterial aneurysms (3 cases) and arterial thromboses (2 cases). The locations were divided as follows: lower extremity arteries in 2 cases, upper limb arteries in one case, pulmonary artery in 2 cases and abdominal aorta in one case.
Lower limb ischemia had occurred in one patient.
Two patients (10%) had mixed vascular, arterial and venous involvement, confirming the multiple and ubiquitous nature of angio-Behçet.
The treatment was based on colchicine, anticoagulants and corticosteroids in venous thromboses. Immunosuppressive therapy was started in 4 patients in front of the unusual site.
In arterial cases, corticosteroids in combination with immunosuppressant were prescribed. Flattening of the aneurysm was indicated in 2 cases with simple operative follow-up.
Conclusion: Behçet disease (BD) is very common in the Mediterranean basin, mainly affects the 30-year-old man. This systemic disease is characterized by oral aphthosis, genital ulcers and systemic involvement including occular, gastrointestinal, neurological, and vessels that make the severity of the disease.
All types of vessels, regardless of size and seat, may be affected, with venous tropism.
Our study has just supported current literature data regarding the extensive and recurrent venous thrombosis during MB. The seriousness of this venous involvement lies in the involvement of the cavernous veins and in pulmonary embolism.
Arterial damage, such as thrombosis and/or aneurysm, is rare but maybe life-threatening.
Early diagnosis, intensive and appropriate treatment, regular follow-up and the involvement of a multidisciplinary team including internists, vascular surgeons and radiologists are key to better management of patients with angio -Behçet.
Our study illustrates the frequency and significance of vascular involvement in BD.
Disclosure of Interests: None declared
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AB1269 RISK FACTORS ASSOCIATED WITH PERIPHERAL NEUROPATHY (PN) IN ANCA-ASSOCIATED VASCULITIS (AAV):

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Background: Few studies have reported on the risk factors associated with PN in AAV. Vasculitic PN in AAV has been associated with male sex, arthritis, cutaneous, mucous membranes, and ENT manifestations of vasculitis[1,2,3]. PN can lead to life quality impairment, as only 35% of the patients with PN have complete symptoms resolution within 6 months[1].
Objectives: Along with describing the prevalence of incidence of PN in our cohort, we undertook this study to identify the risk factors associated with PN in AAV.
Methods: From 153 AAV patients (defined according to the EMA algorithm), 97 were eligible (complete data and no exclusion criteria -diabetes mellitus, axial disc disease, malignancies, herpetic neuralgia, other comorbidities). Clinical, electromyographic (EMG) and histopathological data were recorded. According to the presence (cases) or absence (controls) of clinical data for PN descriptive analysis is reported as means ± SD or medians (interquartile range-IQR). Categorical variables are reported as percentages. Student t-test and Mann-Whitney U-test were used for continuous variables, two-tailed Fisher exact test to compare proportions differences. To estimate PN predictors, bivariate and multivariate models to establish hazard ratios [HR] were built and analysed with Cox regression.
Results: Thirty-two (33%) patients (19-GPA, 9-MPA, 4-EGPA; 17 prevalent, 15 incident) had PN. Mean age±SD was 47.2±13.0 at vasculitis diagnosis. The median follow-up was 55 months (IQR 37-79) until PN diagnosis. Main symptoms: paresthesias 97%, hypoesthesia 72%, hyporeflexia 53%, burning pain and weakness 47%, mononeuritis multiplex 44%. Diagnostic EMG support in 60%. The estimated incidence rate of PN was of 4/100 persons-year. Differences between cases (n-32) and controls (n-65) were smoking history (p=0.03), drug abuse (p=0.04), and a higher mean BVAS (p<0.001) at AAV diagnosis. The table shows the factors associated with a higher risk for the development of PN. After adjustment for covariates and in a multivariate analysis, a higher BVAS at baseline conferred risk for the presence of PN (HR=1.1, 95% CI 1.03-1.25, p=0.01).

Table. Risk factors for development of PN in AAV expressed as hazard ratios after Cox regression analysis.

Variable	HR (95% CI)	*p* value
Drug abuse history	4.34 (1.2-15.6)	0.025
Arthritis	2.98 (1.01-8.7)	0.04
BVAS at AAV diagnosis	1.13 (1.03-1.23)	0.005

Conclusion: The risk for development of PN is related to overall higher disease activity when AAV is diagnosed. However, it may not be present after many years of its appearance. We had almost the same amount of incident cases than prevalent ones at diagnosis. Therefore, patients with a highly active disease need to be followed up specifically in order to detect PN during the disease course, probably with specialised neurological evaluation.

REFERENCES

[1] - Suppiah R, Hadden RDM, Batra R, et al. Peripheral neuropathy in ANCA-associated vasculitis: outcomes from the European Vasculitis Study Group trials. Rheumatology. 2011;50:2214-22.
[2] - de Groot K, Schimdt DK, Arlt AC, et al. Standarized Neurologic Evaluations of 128 Patients With Wegener Granulomatosis. Arch Neurol. 2001;58:1215-21.
[3] - Nishino H, Rubino FA, DeRemee RA, et al. Neurological involvement in Wegener's granulomatosis: an analysis of 324 consecutive patients at the Mayo Clinic. Ann Neurol 1993;33:4-9.

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AB1270 EVALUATIONS OF ANTIRHEUMATIC DRUGS AT PRECONCEPTIONAL, PREGNANCY AND POSTPARTUM PERIODS OF RA PATIENTS' IN A UNIVERSITY HOSPITAL; PRELIMINARY RESULTS

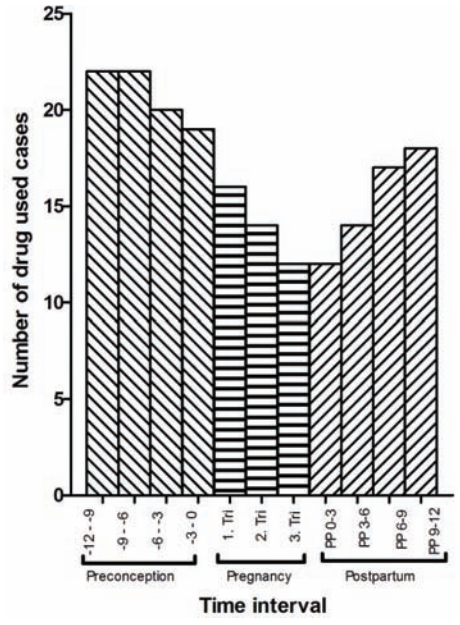
Nesrin Caglayan Duman[1], Atila Karaalp[1], Nevsun Inanc[2]. *[1]Marmara University, School of Medicine, Department of Pharmacology, Istanbul, Turkey*; *[2]Marmara University, School of Medicine, Division of Rheumatology, Department of Internal Medicine, Istanbul, Turkey*

Background: Rheumatoid arthritis (RA) spontaneously improves during pregnancy and disease activity decreases in approximately two-thirds of pregnant but this decrease does not last long and postpartum exacerbation can be seen[1].Conversely discontinuation of antirheumatic drug (ARD) during pregnancy may be a risk factor for exacerbation of RA[2]. In case of preconceptional, pregnancy and postpartum (P&P&P) situations during RA treatment, current options are discontinuation of inappropriate medications and switching to appropriate ones. With the latest BSR and EULAR guidelines on prescribing drugs in P&P&P, treatment options expanded with some of the biologic drugs[3,4].
Objectives: The aim of this study is to analyse alterations of ARD use (discontinuation, increasing or switching) at P&P&P periods of RA patients' retrospectively between 2002-2018.
Methods: In our records there are 25 cases of 19 female RA patients who having at least one pregnancy experienced out of 140 RA patients. The data were collected by telephone calls and patient file. Female patients that had no pregnancies after the RA diagnosis were not included. Preconception period was defined as 1 year before estimated last menstrual date. Postpartum period was defined as 1 year after infants' birth.
Results: RA patients participating in our study of 140 female (age median 55 (26-87)), 121 of them (86%) did not give birth after the RA diagnosis. 19 of them (age median 39 (26-61)) had been pregnant after the RA diagnosis (%14) and 14 of them gave birth 1, 4 of them gave birth to 2, one of them gave birth to 3. Twelve out of 140 (9%) patients had postnatal diagnosis. Each of the pregnancies counted as one case so some female patients represented in our data more than ones. While 22 of cases used the ARD before pregnancy (88%), it decreased 18 of

cases (72%) after giving birth. Drug use rate (n=12, 48%) was most lowest particularly 3. trimester and first 3 months after birth (Figure 1). While there was a change such as discontinuation, increasing or switching in the treatment of 15 patients (60%) compared to before and after pregnancy and 6 of them (24%) continued to increase treatment (added drug to preconception treatment). More than half of the patients used steroids and nonsteroidal antiinflammatory drug in all periods (Figure 2).

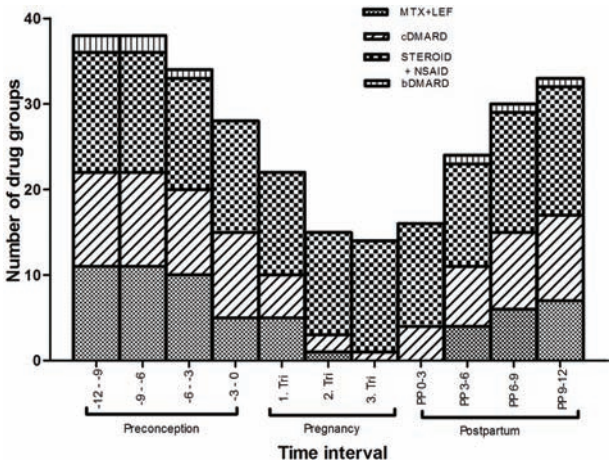
Conclusion: In conclusion the present study suggests that RA patients and doctors avoid the use of ARDs other than steroids and NSAIDs in P&P&P periods. The fact that 60% of the patients undergoing postpartum drug change were showed that pregnancy affected the RA treatment regimen. The need for steroid and NSAID in a high proportion of patients during P&P&P periods indicates the continuation of RA disease activity and the necessity of strong RA treatments during all these periods.

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Abstract AB1270 Figure 1. Number of ARD use cases and P&P&P periods (none drug user preconception period, n=3)

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Abstract AB1270 Figure 2. Number of ARD groups and P&P&P periods

REFERENCES

[1] Hazes JM, et al. Rheumatoid arthritis and pregnancy: evolution of disease activity and pathophysiological considerations for drug use. Rheumatology (Oxford). 2011 Nov;50(11):1955-68.

[2] van den Brandt S, et al. Risk factors for flare and treatment of disease flares during pregnancy in rheumatoid arthritis and axial spondyloarthritis patients. Arthritis Res Ther. 2017 Mar 20;19(1):64.

[3] Flint J, et al. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding-Part I: standard and biologic disease modifying antirheumatic drugs and corticosteroids. Rheumatology (Oxford). 2016 Sep;55 (9):1693-7.

[4] Götestam Skorpen C, et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. Ann Rheum Dis. 2016 May;75(5):795-810.

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AB1271 **DESCRIPTION OF A COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS AND ANTINEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA)**

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Background: The presence of antineutrophil cytoplasmic antibodies (ANCA) in systemic sclerosis (SSc) has been described rarely. The series published in the literature are scarce[1] Its role in the evolution on the disease is unknown

Objectives: To describe the epidemiological and clinical characteristics of ANCA positive patients from a cohort of patients with SSc

Methods: Retrospective observational descriptive study in a cohort of 312 SSc. We analyzed those patients who were positive for ANCA, collecting variables: gender, race, age, age at diagnosis of SSc, at onset of symptoms, type and immunological profile, clinical manifestations of SSc, association with other systemic autoimmune diseases (SAD), capillaroscopic findings, and treatment. Regarding the ANCA profile, pattern, specificity and titration, as the time of evolution of SSc until the appearance of ANCA

Results: Four of 312 patients with SSc had ANCA (prevalence = 1.28%). All were women and 2 had perinuclear pattern. The reason to request ANCA was kidney failure with proteinuria in 2 cases. One patient developed anti-myeloperoxidase (MPO) renal vasculitis and biopsy showed segmental glomerular necrosis and extracapillary proliferation. Other had proteinuria with hematuria without renal failure and biopsy with glomeruli in wafer. Regarding clinical manifestations all ANCA had some degree pulmonary disease 3 interstitial lung disease (ILD)1 pulmonary arterial hypertension (PAH) confirmed by right heart catheterization (KT). Three had SAD associated

Characteristics of the sample in table 1

	1	2	3	4
Sex	F	F	F	F
Raynaud's debut/Diagnosis SSc (years)	No/67	72/74	40/41	72/73
Ethnic group	Caucasian	Latin american	Caucasian	Caucasian
Subtype SSc	Diffuse	Limited	Diffuse	Limited
Pattern specificity titration ANCA	N/A	Perinuclear MPO 102.69	Cytoplasmic	Perinuclear PR3 8.0
ANCA diagnosis (years)	1	3	27	1
Antibodies	ANA nucleolar 1/1280 ANTIKU/ RNAPOL 1	ANA speckled 1/640 ACA	ANA nucleolar 1/ 320 ANTIFIBRILARINA/ SRP	ANA speckled 1/1280 ANTIKU/RO52
Autoinmune disease	Graves	Sjögren Primary biliary cirrhosis	Antisintetase	Idiopathic inflammatory myopathy
Kidney		Renal vasculitis Prot 0.52g/L	Membranous nephropathy Microhematuria Prot 0.14g/L	Prot 0.24g/L
Creatinine and GFR pre/post ANCA (mg/dl)	0.72/0.66 >60	0.86/2.13 65/37	0.88/0.7 >60	0.96/0.76 >60
Gastrointestinal		Gastroesophageal reflux	Gastroesophageal reflux	Gastrointestinal Sepsis
Pulmonary	**HAP/NSIP** sPAP 39.2 TAPSE 2.0 cm KT PCP8 TPG35 TDG 15	**No HAP/LIP**	**No HAP/UIP**	No HAP/No ILD sPAP 58 TAPSE 1.4 cm TRV(cm/s)333

Skin	Sclerodactyly mRSS 11/51 Telangiectasia	Sclerodactyly Telangiectasia Leukocytoclastic Vasculitis	Sclerodactyly mRSS 2/51 Acroosteolysis Digital ulcers Telangiectasia	Digital ulcers Telangiectasia
Acute-phase reactant			ESR y CPR	ESR
Capillaroscopy	ACTIVE	NONSPECIFIC (irregular enlargement Ramified dilated)	LATE	LATE (moderate avascular, disorganisation)
Treatment	MMF/	MMF CYC/	NO/	Sulfasalazine
Pre/Post-ANCA	Macitentan	MMF CYC	CS AZA	HCQ/CS

sPAP systolic pulmonary artery pressure/mmHg TAPSE tricuspid annular plane systolic excursion PCP pulmonary capillary pressure TPG transpulmonarypressure gradient TDG transpulmonary dyastolic pressure NSIP Nonspecific interstitial pneumonia LIP Lymphocytic interstitial pneumonia UIP usual interstitial pneumonia TRV Tricuspid regurgitation peak velocity AZA Azatioprine

Conclusion: In our cohort the presence of positive ANCA was associated with renal vasculitis in one case. All patients with ANCA had vascular or interstitial pulmonary involvement, as well as other associated SADs. Further studies are needed to characterize the clinical associations of the presence of ANCA in SSc

REFERENCES

[1] J Rheumatol 21:864–870
[2] Rheumatol Int (2006) 26: 369–375

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AB1272 TREATMENT OF RHEUMATOID ARTHRITIS WITH EXTENSION OF THE ANTI-TNF INTERDOSE INTERVALS. A MONOCENTRIC OFF-LABEL STUDY.

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Background: Since the advent of anti-TNFs a revolution has been established in the treatment of Rheumatoid Arthritis (RA).
Objectives: To evaluate the ability to safely extend the interdose intervals of the anti-TNFs in RA patients.
Methods: Eighty-six patients with early RA fulfilling the ACR/EULAR classification criteria were included and followed-up at predefined times. All patients were on conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) plus an anti-TNF. At every visit, the disease activity score using the 28-joint count (DAS-28) as well as all the drug-related laboratory parameters were recorded. Clinical remission was defined as DAS-28 <2.6 for ≥12 months. RA patients in clinical remission had the possibility to extend interdose intervals.
Results: A total number of 57 females and 29 males (mean age: 62.7 ±4.1 years; disease duration: 14.9±2.4 months) were included. 76 patients were in clinical remission, while 10 were in low disease activity. From those in clinical remission, 40 patients received adalimumab (ADA), 23 etanercept (ETN) and 13 golimumab (GOL). Regarding the extension of the interdose intervals, 29 patients were on ADA every 21 days, 11 every 30 days. Regarding the extension of the interdose intervals in patients receiving ETN: 15 patients were on ETN every 10 days, 8 every 15 days. Finally, 6 patients were on GOL at a dose interval of 35 days, 4 every 40 days, 3 every 45 days. Young, female and seronegative patients treated early with an anti-TNF had more chances of extending the interdose interval.
Conclusion: We found that the extension of the interdose intervals of the anti-TNFs is a feasible option in early RA patients and it reflects not only significant clinical benefits for the patient but also economic benefits for the healthcare systems.
Disclosure of Interests: None declared

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AB1273 ESTABLISHMENT OF A PROSPECTIVE COHORT FOR RHEUMATOID ARTHRITIS PATIENTS WITH INTERSTITIAL LUNG DISEASE: COMPARISON OF BASELINE CHARACTERISTICS BETWEEN RHEUMATOID ARTHRITIS PATIENT WITH OR WITHOUT INTERSTITIAL LUNG DISEASE

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Background: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) has a clinical significance of high mortality rate in patients with RA. Hence, we established a multidisciplinary prospective single center cohort for RA-ILD patients with multidisciplinary collaboration called the HUMANISM. Patients with RA who have checked a chest computed tomography (CT) scan within previous 2 years were eligible for the enrollment, and they were classified according to the presence of ILD by expert radiologists. All RA patients were assessed with various outcomes of RA, and reviewed for treatment pattern of medications annually.
Objectives: To introduce a prospective, non-interventional cohort of RA-ILD patients, HUMANISM cohort and to compare baseline characteristics and treatment patterns between RA patients according to the presence of ILD using the enrollment data of this prospective cohort.
Methods: We compared the baseline characteristics between RA patients with and without ILD using the Chi-square test and Student's t-test. For RA-ILD patients, we described the ILD patterns that could be identified in high-resolution CT (HRCT) to determine their dominant radiological characteristics.

Figure 1. Patient selection flow of HUMANISM cohort

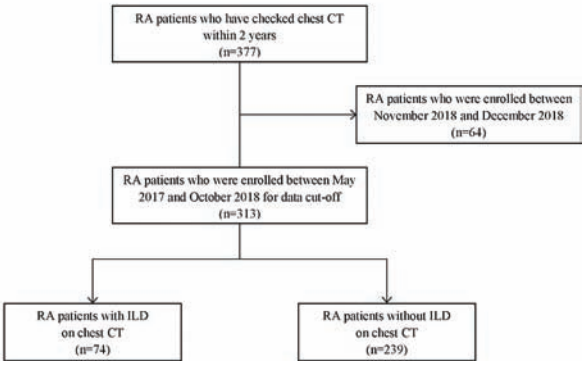


Figure 1

Results: A total of 74 RA-ILD patients and 239 RA patients without ILD were consecutively enrolled between May 2017 and October 2018. At the baseline, RA-ILD patients showed higher proportion of male patients and older age compared to RA patients without ILD. They also showed higher RF positivity than those without ILD. RA-ILD patients also have higher disease activity measured with DAS28. In the treatment, oral glucocorticoids (OC) are used in higher rate and higher doses in RA-ILD patients than those without ILD. Methotrexate (MTX) use rate was higher in RA without ILD patients compared to RA-ILD patients, but there was no difference in the prevalence of biological DMARDs. In HRCT findings of RA-ILD patients, usual interstitial pneumonia (UIP) and non-specific interstitial pneumonia (NSIP) dominant patterns were common, followed by organizing pneumonia (OP), and overlapping patterns combined with NSIP or UIP.
Conclusion: We found that RA-ILD patients showed higher disease activity, male predominance and older age than those without ILD. Treatment patterns were different in the use of MTX or OCs. In our HUMANISM cohort, common HRCT findings of RA-ILD patients were UIP and NSIP.

Abstract AB1273 Table 1. Baseline characteristics of RA patients with and without ILD in HUMANISM cohort

Variables	RA-ILD (n=74)		RA without ILD (n=239)		*P*
Sex (female)	46	(62.2)	202	(84.5)	<0.001
Age	65.4	± 10.9	58.9	± 10.3	<0.001
Disease duration	8.7	± 7.6	11.3	± 7.8	0.011
DAS28-ESR	3.7	± 1.4	3.3	± 1.2	0.021
DAS28-CRP	2.6	± 1.1	2.3	± 0.9	0.041
RF (+)	67	(90.5)	191	(79.9)	0.036
ACPA (+)	66	(89.2)	213	(89.1)	0.189
Medications					
MTX	39	(52.7)	193	(80.8)	<0.001
Biologic DMARDs	12	(16.2)	50	(20.9)	0.302
OC	43	(58.1)	68	(28.5)	<0.001
OC dose[a], mg/day	4.2	± 2.7	2.6	± 1.7	<0.001
HRCT findings					
UIP	29	(39.2)			
NSIP	29	(39.2)			
OP	7	(9.5)			
Overlapping of HRCT patterns	6	(8.1)			
Others	3	(4.0)			

[a] Prescriptions of regular oral glucocorticoids were considered in the calculation and the prednisone-equivalent dose was presented

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AB1274 OF 60 PUBLICATIONS REFERRING TO BIG DATA IN RHEUMATIC AND MUSCULOSKELETAL DISEASES, 33 APPLIED ARTIFICIAL INTELLIGENCE STATISTICAL TECHNIQUES: A SYSTEMATIC LITERATURE REVIEW INFORMING A EULAR TASKFORCE

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Background: Big data are defined as data sets that are too large or complex for traditional data-processing application software to adequately deal with. Artificial Intelligence (AI) includes various statistical techniques which can deal with big data. The current use of these concepts in publications related to RMDs is unknown.
Objectives: To assess the current use of big data and AI in the field of RMDs.
Methods: A systematic literature review (SLR) was performed in PubMed MEDLINE in November 2018, with key words referring to ("big data"[All Fields] *OR* "Artificial Intelligence"[Majr]) and RMDs. All original reports published in English and referring to big data in RMDs were analyzed. We collected general information on the paper (including year of publication and impact factor of the journal, and country of the first author), and information on the rheumatic disease, the number of data analyzed and the statistical methods used. The analysis was descriptive.
Results: Of 648 articles, 60 met the inclusion criteria. Among them, 34 (57%) were observational studies including 22 (37%) cohort studies, 3 (5%) were experimental studies, 7 (12%) were literature reviews or literature data mining and 16 (27%) were general reviews which provided no original data. Among the 44 original papers, the mean year of publication was 2015 (SD=5.0, range 1991-2018), with 38 articles (86%) published during the last 5 years. The mean impact factor was 5.1 (SD=8.5, range 1.6-41.9). The mean number of data was 1.4 million (SD=4.6 million, range 212 MRIs – 25 million units of observation). Many articles were written by European (N=16, 36%) or US (N=15, 34%) authors. Most papers were on inflammatory joint diseases (N=17, 37%) (Figure 1); 7 (16%) were applied to -omics and 9 (20%) to imaging. Statistical methods were based on AI in 33 papers (75% of 44), specifically Machine Learning (N=28 articles, 64%) (Figure 2), with varied methods applied (mostly different kinds of Artificial Neural Networks, N=17).
Conclusion: Big data is an emergent area in the field of RMDs, and we found 60 papers on various diseases and with diverse applications of "big data". Most of these papers were published very recently, and some in high impact factor journals, indicating the interest of researchers for this field. Overall, 33 publications mentioned AI techniques to deal with big data, whereas 11 used usual statistical methods. The heterogeneity of methods used indicates the need for further research in this area, and for collaboration with data scientist specialized in big data, particularly to determine which statistical methods (traditional or AI) should be used. These findings will inform a EULAR taskforce on big data in RMDs.

Figure 1: Description of the RMDs

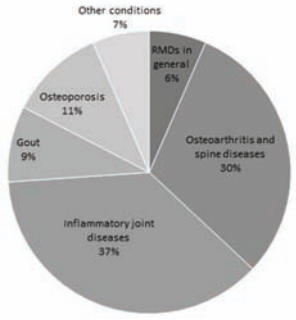
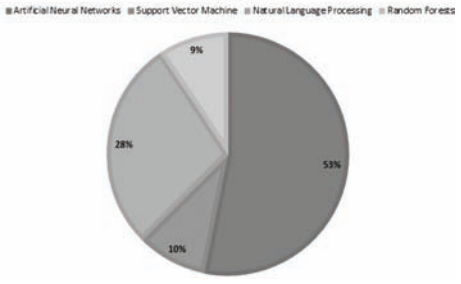


FIGURE 2: DESCRIPTION OF THE MACHINE LEARNING TECHNIQUES



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AB1275 COMPARATIVE ANALYSIS OF LOCAL COMPLICATIONS OF HIP AND KNEE ARTHROPLASTY IN PATIENTS WITH RHEUMATOID ARTHRITISAND OSTEOARTHRITIS

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Background: Surgical treatment of patients with rheumatoid arthritis (RA) is associated with an increased risk of complications. It can be caused by: an inflammatory process, the osteoporosis, the reduced physical activity, the severity of functional impairment, long-term glucocorticoid therapy, biologic and disease-modifying antirheumatic drugs. All of the above reasons provide elongated wound healing period, the development of infectious complications, increased risk of periprosthetic fractures.
Objectives: to provide a comparative analysis of local complications of hip and knee arthroplasty in RA and osteoarthritis (OA) patients.
Methods: We analyzed 2142 operations: hip (n = 1177) and knee (n = 965) replacement, which were performed to patients with RA and OA between 1998 and 2018.

Abstract AB1276 Table 1. Incidents rates of diabetes mellitus in patients with JIA compared to healthy population and asthma patients

	Healthy			Asthma			JIA		
	Cases	Person-years	IR (95% CI)	Cases	Person-years	IR (95% CI)	Cases	Person-years	IR (95% CI)
Type 1 DM	62	276,695	0.22 (0.17-0.28)	68	237,919	0.29 (0.23-0.37)	18	39,943	0.45 (0.28-0.71)
Type 2 DM	134	276,573	0.48 (0.41-0.57)	138	237,781	0.58 (0.49-0.69)	27	39,930	0.68 (0.47-0.99)
Composite DM	147	276,540	0.53 (0.45-0.62)	150	237,755	0.63 (0.54-0.74)	34	39,907	0.85 (0.61-1.19)

Results: There were 2142 hip and knee arthroplasty performed, including 1118 operations on patients with RA and 1024 operations on patients with OA. The number of local complications after total hip replacement was 155 (7.24%): 96 (8.59%) of them were patients with RA and 59 (5.76%) patients with OA.

There were 1177 hip arthroplasty performed, including 467 operations on patients with RA and 710 operations on patients with OA. The number of local complications after total hip replacement was 85 (7.22%): 48 (10.28%) of them were patients with RA and 37 (5.21%) patients with OA. There were 965 knee arthroplasty performed, including 651 operations with RA patients and 314 operations in patients with OA were performed. The number of local complications after total knee replacement was 70 (7,25%): 48 (7.37%) of them were patients with RA and 22 (7.00%) patients with OA.

We revealed a significantly greater number of complications in patients with RA ($p<0.005$).

Conclusion: Local complications after hip and knee arthroplasty with RA patients (8.59%) more than in OA patients (5.76%) in 1.5 times. It shows us that the operative treatment of patients with RA requires a special approach and more gentle management of patients with RA in co-operation with rheumatologist and careful treatment of the bone with surrounding tissues during the surgery.

Disclosure of Interests: None declared

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AB1276 THE RISK OF DIABETES MELLITUS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: A COHORT STUDY

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Background: Few studies have suggested higher prevalence of type 1 diabetes mellitus (DM) in juvenile idiopathic arthritis (JIA). To date, the risk of type 1 or 2 DM among patients with JIA patients has not been fully understood.

Objectives: To examine the incidence rate (IR) of DM in JIA patients compared to patients with asthma and healthy children.

Methods: We conducted a cohort study using a U.S. claims data from Truven MarketScan (2005-2016). We identified individuals between age 6 and 18 with $\geq$2 diagnoses of JIA with International Classification of Diseases (ICD)-9 and 10 diagnostic codes followed by one dispensing of JIA-treatment medication. For comparison, we selected 1) children with asthma and 2) healthy individuals. Each JIA patient was matched by age, sex and index date to 5 asthma patients and 5 healthy children. The primary outcome was DM, identified with 1 ICD diagnostic code followed by one dispensing of an antidiabetic drug. We assessed type 1 DM and type 2 DM separately, and composite endpoint of type 1 or 2 DM. IR and hazard ratio (HR) of DM in JIA patients versus patients with asthma and healthy subjects was calculated along with stratification by age (6 to 12 versus 13 to 18).

Results: After 1:5 matching, there were 74,385 healthy children, 74,385 asthma patients, and 14,877 JIA patients. The mean age in all cohorts was 13.9 years and 66.9% were female. During a mean follow up of 3.72 years, the composite IR of DM in the JIA group was 0.85 per 1,000 person-years (95% Confidence Interval [CI], 0.61-1.19) compared to 0.63 (0.54-0.74) per 1,000 person-years in the asthma population and 0.53 (0.45-0.62) per 1,000 person-years in the healthy population (Table 1). The multivariable adjusted HR (95% CI) associated with DM in JIA was 1.27 (0.77-2.07) compared to the asthma group and 1.47 (0.90-2.42) compared to the healthy population (Table 2). Age-stratified analyses also showed numerically increased risk of DM in JIA patients.

Conclusion: In our cohort of 163,647 children with 14,877 JIA patients, JIA was associated with a numerically higher, albeit not statistically significant, risk of type 1 or 2 DM compared to asthma patients or healthy children.

REFERENCES

[1] Schenck S, et al. Comorbidity of Type 1 Diabetes Mellitus in Patients with Juvenile Idiopathic Arthritis. The Journal of pediatrics. Jan 2018;192:196-203.

† The study cohorts were age-, sex-, and index date-matched. IR is per 1,000 person-years

Abstract AB1276 Table 2. Hazard ratio of diabetes mellitus in patients with JIA compared to healthy population and asthma patients

	JIA vs Asthma		JIA vs Healthy Children	
	Unadjusted HR (95% CI)	Multivariable HR (95% CI)	Unadjusted HR (95% CI)	Multivariable HR (95% CI)
Type 1 DM	1.54 (0.91-2.58)	1.51 (0.76-3.03)	1.93 (1.14-3.27)	1.62 (0.80-3.25)
Type 2 DM	1.20 (0.79-1.81)	1.10 (0.64-1.89)	1.41 (0.93-2.14)	1.30 (0.74-2.26)
Composite DM	1.37 (0.94-1.98)	1.27 (0.77-2.07)	1.59 (1.09-2.31)	1.47 (0.90-2.42)

† The full model includs age, demographics, comorbidities, medications, and health care utilization factors

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AB1277 PREVALENCE OF THE DIFFERENT ANTI-CARBAMYLATED PROTEIN ANTIBODIES ISOFORMS IN FIRST-DEGREE RELATIVES OF PATIENTS WITH RHEUMATOID ARTHRITIS IN A LATIN POPULATION

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Background: Rheumatoid arthritis (RA) affects approximately 1.5% of the population worldwide and 0.5-3.3% of the Mexican population[1]. Anti-carbamylated proteins (anti-CarP) antibodies are identified in RA patients with a prevalence up to 44%[2], early arthritis, first-degree relatives (FDR) of patients with RA with a prevalence of 18%, and healthy controls with a prevalence of 4.7%. There is no evidence regarding the prevalence of the three different isoforms of anti-CarP antibodies worldwide.

Objectives: Establish the prevalence of the different isoforms of anti-CarP antibodies (IgA, IgM, IgG) in FDRs of patients with RA.

Methods: It is an observational descriptive cohort. Subjects underwent a complete physical examination, made by a certificated rheumatologist, which included clinical and serological measurements. The serological measurements included anti-citrullinated peptides antibodies (ACPA), RF, and anti-CarP detected by ELISA using carbamylated fetal calf serum, according to Shin J et al with some modifications. The cut-offs for the

anti-CarP IgA isoform was >125 U/mL, for the IgG isoform was >90 U/mL, and for the IgM isoform was >300 U/mL. The FDRs were classified as: suspicious arthralgia for progression according to Van Steenvergen criteria; undifferentiated arthritis (UA) and RA according to ACR/EULAR 2010; and soft tissue rheumatic diseases.

Results: A total of 144 FDRs from 99 RA patients were enrolled. The demographic characteristics are shown in Table 1. The prevalence (Table 2) for anti-CarP was 2.8% for IgA, 4.2% for IgG, whereas IgM was not detected. The serologic association was for RF/ACPA 4.48%, RF/anti-CarP 2.7%, FR 64.5%, ACPA 1.3%, ACPA/anti-CarP 0.69%, anti-CarP 3.4%, and no RF/ACPA/anti-Carp was observed.

The group of suspicious arthralgia for progression had to 2 subjects positive for IgG anti-CarP, the group of UA had 1 subject positive for IgA anti-CarP, albeit no anti-CarP for the RA group was present. Soft tissue rheumatic diseases group had 5 subjects positive for IgG anti-CarP, while the asymptomatic group had 2 subjects positive for IgA anti-CarP.

Table 1

Population, n (%)	144 (100%)
Age (years), median (IQR)	45.25 (18-76)
Weight (kg), median (IQR)	70 (42-117)
Height (meters), median (IQR)	1.61 (1.44-1.88)
BMI, median (IQR)	26.19 (16.7-47.3)
Female, n (%)	119 (82%)
HAQ, median (IQR)	0.29 (0-2.15)

IQR: interquartile range, Kg: kilograms; BMI: body mass index, HAQ: Health Assesment Questionare

Abstract AB1277 Table 2

	POSITIVE, n (%)	MIN/MAX	MEDIAN
CRP, mg/dL	19 (13%)	0.0-2.27	0.36
ESR, mm/H; mean (SD)	37 (25.3%)	1-72	13.0 (11.95)
Anti-CarP, U/mL			
IgA	4 (2.8%)	0.0-818	2.0
IgM	0 (0.0%)	0.0-56	5.45
IgG	6 (4.2%)	0.0-187	8.0
Rheumatoid Factor, U/mL			
IgA	31 (21.5%)	1-219	6.96
IgM	64 (44.4%)	1-205	15
IgG	14 (9.7%)	1-160	3.04
ACPA-IgG, U/mL	10 (7%)	1-200	1.21

CRP: C Reactive Protein; ESR: erythrocyte Sedimentation Rato; anti-CarP: Anti-Carbamylated Protein; SD: Standard Deviation; ACPA: anti-Citrullinated Peptides Antibodies.

Conclusion: Even though we used the 3 isoforms of anti-CarP antibodies, the prevalence of these antibodies in our cohort showed less positivity than other cohorts, who only detected the IgG isoform, worldwide.

REFERENCES

[1] Ingris Pelaez-Ballestas, et al. Epidemiology of the Rheumatic Diseases in Mexico. A Study of 5 Regions Based on the COPCORD Methodology. J Rheumatol 2011; 38 Suppl 86:3–6.

[2] Jing Shi, et al. The specificity of anti-carbamylated protein antibodies for rheumatoid arthritis in a setting of early arthritis. Arthritis Research & Therapy (2015) 17:339.

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AB1278 ANNOUNCEMENT OF CHRONIC RHEUMATIC INFLAMMATORY DISEASE: THE RHEUMATOLOGIST'S POINT OF VIEW

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Background: The onset of a chronic rheumatic inflammatory disease (CRD) is a turmoil in a patient's life. The announcement, first step of information (a legal and ethical necessity), will leave a lasting impression in a patient's history.

Objectives: Determine the rheumatologist's methods to reveal a potentially disabling disease with an uncertain prognosis. Compare, in the discussion chapter, the rheumatologist's vision and the patient's experience at the time of the announcement.

Methods: 39 private practice rheumatologists from the CREER group. 52% women, mean age 59 years. 222 CRD including 56% rheumatoid arthritis (RA), 27% spondyloarthritis (SPA), 17% others. Survey including 31 questions. Direct eye contact 89%, gesture 56%, modulated tone 49%, silence 36%, compassional approach 26%. Gaining confidence by : availability, listening to, explanations, empathy, frankness.

The rheumatologist thinks that he is reassuring and comforting 100%, empathic 98%, transparent 72%. He calms 42%, supports, is optimistic because he is sensitive to the patient's reactions 61%, but sometimes destabilized by a treatment refusal. He mentions life quality 51%, invites him to question it 58%, encourages him on a mutual management of the CRD 92% and insists on treatment compliance. He gives few documents, rarely mentions patient organizations, speaks about chronic disorder status, informs the treating physician and is always available.

Results: The announcement is different depending on : the type of CRD (59%), its presentation, the prognosis (29%), the induced emotion, the patient's profile, 82% (intellect 41%, personality 22%, age 16%), the information to provide (course, treatment).

Duration of consultation : long 51%, doubled 64%. Time given to assimilate the information 93%, to discuss 90%. Explanations given 100%, rephrased 32%, repeated 27%, verified 9%.

Announcement unchanged if patient alone or accompanied; handling adapted to its degree of worry. If patient is anxious, depressive, rebelious or denying : see him again 29%, re-explain 22%, listen to him, adapt.

When comparing the rheumatologist's and the patient's assessment about the announcement, there is globally an agreement, but it's less affirmative for all the items. However, the patient thinks his rheumatologist more frank than he really is. Indeed, he announces with feeling and spends time on it, but not enough for the patient. He is less comforting, reassuring and explaining what he believes. He mentions the treatment inconveniences and life quality, which is well perceived. But he should guide more to annex treatments. For all the suggested items, the SPA patients are less optimistic then the RA patients.

Conclusion: the announcement takes into account above all the patient's profile, the type and the seriousness of the CRD. The rheumatologist dedicates a lot of time on the announcement, which is made step by step, but still too fast for the patient. He explains, listens to, reassures, comforts by using human methods to gain the patient's confidence. He supprts him and helps him to manage his disease. He involves the patient and stays available. The patient feels well informed and taken care of in his entirety with empathy.

REFERENCES

[1] CREER group

Disclosure of Interests: None declared
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AB1279 PHYSICAL ACTIVITY LEVELS AND ATTITUDES IN PATIENTS WITH AXIAL AND PERIPHERAL SPONDYLOARTHRITIS

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Background: Spondylarthritis is one of the common inflammatory rheumatic diseases in adults, with an overall prevalence of 0.5 to 1%. Based on clinical manifestations and the Assessment in Spondylarthrosis International Society (ASAS) criteria, spondyloarthritis can be distinguished as predominately axial or peripheral. Despite the health-related benefits of regular physical activity, patients with spondyloarthritis, are generally less active than those without disease. Studies evaluating the differences in physical activity levels and attitudes towards exercise of patients with axial and peripheral spondyloarthritis are limited.

Objectives: To characterize and compare self-reported physical activity and attitudes towards exercise among patients with axial and peripheral spondyloarthritis.

Methods: We used baseline information from an on-going, longitudinal, single-site, prospective cohort study consisting of 244 patients with spondyloarthritis including psoriatic arthritis, ankylosing spondylitis, and other spondyloarthropathies. Attitudes and beliefs towards exercise were assessed from 5 domains including: 1) general attitude towards exercise; 2) support from other people; 3) benefits in exercise/physically active; 4) concerns about being active; and 5) exercise/physical activity behavior. A continuous scale (range: 0 -100) was used to evaluate attitudes and beliefs towards exercise. High scores indicated that the individual found exercise to be beneficial and/or liked engaging in physical activity. Physical activity was evaluated using the Nurses' Health Study physical activity questionnaire II (NHSPAQ II). Physical activity levels were assessed using

the total metabolic equivalent (MET) to incorporate the frequency, duration and intensity by different type of activities. Minutes spent in each level of activity (e.g., sedentary, light, moderate, and vigorous) were then summed for each week. Adjusted multivariable linear models estimated the relationship between physical activity levels and disease status.

Results: Overall, nearly 80% of the study sample had predominantly peripheral spondyloarthritis. The average age for participants with peripheral disease was 53.2 (standard deviation (SD):12.9) and for those with axial disease was 44.2 (SD: 12.4). Most of the study participants were men, white, non-Hispanic, married, and had attended at least some college, regardless of predominant joint distribution (peripheral versus axial). While the median for general attitude towards regular exercise in participants with peripheral disease was 88.5, the median score was 81.0 in participants with axial disease. The median score regarding benefits of exercise/physical activity to improve general function was 97.0 among participants with peripheral disease and 95.5 among those with axial disease; the median score for pain relief was 67.0 in participants with peripheral disease and 66.5 for those with axial disease. Regardless of predominant joint distribution, walking, bicycling, and swimming were the most common types of exercise. Compared to participants with predominately peripheral disease, participants with axial disease spent more time per week engaging in light physical activities (adjusted β: 13.0 hrs/week; 95% confidence interval: 0.4 to 25.6 hrs/week) after adjusting for sociodemographic and clinical factors.

Conclusion: Patients with spondyloarthritis have positive attitudes towards physical activity/exercise, regardless of their predominant joint distribution, and believe that these activities improve general function and, to a lesser extent, relieve pain. However, patients with axial disease spend more time per week engaging in light physical activities than do those with peripheral disease.

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AB1280 EPIDEMIOLOGICAL PROFILE OF PATIENTS WITH FIBROMYALGIA IN A SPECIALIZED INSTITUTE IN MEDELLÍN, COLOMBIA 2010–2016

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Background: Fibromyalgia is a common cause of chronic musculoskeletal pain in the world, with diverse clinical manifestations and with a ruinous effect on the quality of life of patients. The estimations of prevalence in the general population are very variable (0.2% - 6.4%) as well as the clinical presentation.

Objectives: This study aims to describe the sociodemographic and clinical characteristics of patients with fibromyalgia treated in a specialized institution between 2010 and 2016, in Medellín, Colombia.

Methods: We performed a retrospective, descriptive, secondary source study of patients diagnosed with fibromyalgia from a specialized institution between 2010 and 2016. Descriptive statistics and period prevalence tools were applied for the variables studied, among which was evaluated the use of the diagnostic criteria (1990 or 2010) of the American College of Rheumatology.

Results: We evaluated 1106 records of patients diagnosed with fibromyalgia. The median age was 54 years (IQR 16), the age of greatest presentation is between 40 and 65 years for both sexes, 95.1% were women and a 51.1% were married or living with their partner. 23.6% of the patients had a basic and middle level education (secondary and technological level), 93% of the population came from the department of Antioquia (for a prevalence for this institution in the period 2010 to 2016 of 0.017%), and 54% resided in the city of Medellín. The proportion of people with low and medium low socioeconomic status was 26.3%, while 41.4% reported being active in a job. The symptoms most frequently presented among the patients were myalgia (70.2%), sleep disturbances (59.9%), chronic fatigue (48.5%), headache (47.3%) and muscular weakness (40.5%). When analyzing by sex, headaches were more frequent in women (48.8%) than in men (24.1%). The most commonly reported comorbidities were psychiatric disorders (31.1%, where depression was the most recorded with 24.1%), migraine (30.9%) and hypertension (27.9%). The most used criteria to make the diagnosis of fibromyalgia were those of 1990 with 62.2%. Regarding treatment, the most used were serotonin reuptake inhibitors and dual inhibitors (52.6%), along with acetaminophen (41.2%) and pregabalin (39%); only 8.2% of patients received non-pharmacological interventions (physical and psychological therapy).

Conclusion: Fibromyalgia is an important pathology in specialized medical consultation, accompanied by myalgia, sleep disturbances, chronic fatigue, headaches and muscle weakness. Psychiatric pathologies are the most frequently associated comorbidities and the 2010 criteria of the American College of Rheumatology are not yet widely applied. The treatment of fibromyalgia is complex and probably more effective with a transdisciplinary approach involving both pharmacological and non-pharmacological interventions.

REFERENCES

[1] Wolfe F, Walitt B, Perrot S, Rasker JJ, Häuser W. Fibromyalgia diagnosis and biased assessment: Sex, prevalence and bias. PLoS One [Internet]. Public Library of Science; 2018 Sep 13; 13(9): e0203755.
[2] Marques AP, Santo AdSdE, Berssaneti AA, Matsutani LA, Yuan SLK. Prevalence of fibromyalgia: literature review update. Revista Brasileira de Reumatologia (English Edition). 2017;57(4):356-63.
[3] Häuser W, Ablin J, Fitzcharles M-A, Littlejohn G, Luciano JV, Usui C, et al. Fibromyalgia. Nature Reviews Disease Primers. 2015;1:15022.
[4] Queiroz LP. Worldwide epidemiology of fibromyalgia. Current pain and headache reports. 2013;17(8):356.

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Disclosure of Interests: None declared

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AB1281 USAGE OF PROOF-BP TO PREDICT HYPERTENSION IN MEXICAN-MESTIZO RHEUMATIC PATIENTS

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Background: Subjects with rheumatic diseases have an increased risk of cardiovascular morbimortality. Hypertension (HTN) is a key modifiable risk factor for cardiovascular events (1). A recently published and validated prediction model (Predicting Out-of-Office Blood Pressure, PROOF-BP) has been proposed as a tool to improve diagnosis of HTN, and detection of out-of-office HTN in subjects with a previous diagnosis, with a *c*-statistic (AUC) of 0.86 in non-rheumatic subjects (2). This model has not been explored in rheumatic patients.

Objectives: To evaluate the diagnostic performance of the PROOF-BP algorithm for the prediction of HTN in subjects with/without rheumatic diseases.

Methods: A cross-sectional, observational trial was designed. Subjects were recruited at a rheumatology outpatient clinic in northeastern Mexico. Subjects with/without rheumatologic conditions were recruited. Complete clinical history with somatometry of each subject was registered. BP was measured by a physician 3 times to each participant using current recommendations, with an OMRON HEM-7121 BP monitor. Calculations using the PROOF-BP online site were done, and risk categories were assigned to each subject using their predicted out-of-office BP: low (<130/80 mmHg), medium (130/80-145/90 mmHg) and high risk (>145/90 mmHg). Subjects in the medium and high risk strata were then asked to return for further evaluation and additional BP measurement, to define each diagnosis of HTN. We used frequencies (%) and median (q25-q75) for descriptive analysis. Diagnostic accuracy of each category was determined using 2 x 2 tables.

Results: A total of 217 subjects were included. Baseline characteristics are shown in Table 1. The most frequent rheumatic disease was RA (n=78, 35.9%). Using PROOF-BP, 84 (38.7%) subjects were stratified as medium or high risk. Of these, only 36 (42.8%) returned for evaluation. A final diagnosis of HTN was attained in 14 (38.8%) of those who returned. Diagnostic performances of the low and high risk categories are shown in Table 2. In 21 (67.7%) cases of the medium risk category the

diagnosis of HTN was finally discarded, and in the remaining 10 (32.2%) diagnosis of HTN was finally ascertained. The high risk category had a specificity of 95% and a PPV of 80% for the diagnosis of HTN.

Abstract USAGE Table 1. Clinical characteristics.

	Number of patients, n (%) N= 217
Female	188 (86.6)
Hypertension	51 (23.5)
T2DM	24 (11.1)
Dyslipidemia	68 (31.3)
Active smoking	13 (6.0)
No rheumatic disease	65 (30.0)
RA	78 (35.9)
SLE	6 (2.8)
Sjögren syndrome	5 (2.3)
OA	29 (13.4)
Other	34 (15.6)
PROOF-BP class:	
Low risk	133 (61.3)
Medium risk	71 (33.6)
High risk	11 (5.1)
New diagnosis of hypertension	14 (38.9)

Abstract USAGE Table 2. Diagnostic performances.

	Sensitivity (%)	Specificity (%)	PPV (%)	NVP (%)
Low risk	100	55	58	100
High risk	29	95	80	68

PPV: Positive predictive value; NPV: Negative predictive value.

Conclusion: In a cohort of Mexican-mestizo subjects with rheumatic diseases, 38.7% were classified as medium or high-risk for HTN. Only 42.8% of patients that required further evaluation followed medical recommendations. More than 30% of patients in the medium-risk category had a final diagnosis of HTN. Using the PROOF-BP algorithm, none of the patients in the low-risk stratum had a final diagnosis of HTN (sensitivity= 100%); the high-risk category had a high specificity (95%) for the diagnosis of HTN.

REFERENCES

[1] Lewington S, et al. Lancet. 2002;360:1903–1913.
[2] Sheppard JP, et al. Hypertension. 2016;67:941–950.

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AB1282

A BIG-DATA APPROACH TO ELECTRONIC HEALTH RECORD DATA – USING DIMENSIONALITY REDUCTION AND CLUSTERING TECHNIQUES TO STUDY LONGITUDINAL RELATIONSHIPS BETWEEN DISEASES

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Background: Hypothesis-free, longitudinal collection of patient health data in the form of Electronic Health Records (EHR) offers a wealth of valuable information on complex, slow-developing diseases in regard to aetiology and comorbidities. Conventional analytical methods are ill suited for the highly dimensional, sparse data contained within EHR, highlighting a need for more sophisticated, high-throughput tools. As t-Distributed Stochastic Neighbour Embedding (t-SNE)[1] and Density-Based Spatial Clustering of Applications with Noise (DBScan)[2] are designed to identify patterns in high-dimensional data with possible non-linear relationships, we hypothesized that these methods can aid identification of associations in diseases with multiple aetiologies.

Objectives: Proof of principle showcasing the value of t-SNE and DBScan in detecting longitudinal relationships between diseases in EHR data.

Methods: The Partners HealthCare Biobank from Boston, Massachusetts, includes 64,819 patients with longitudinal visit data from hospitals and general practitioners between June 1987 and June 2017. Each visit and procedure (N = 24,377,442) is coupled to an ICD code (International Classification of Disease) describing a disease or examination. We randomly split the data into two datasets of 32,424 and 32,395 individuals: set 1 to optimise t-SNE and DBScan and set 2 for replication. To trim the overly detailed hierarchy of ICDs, we translated them to Phenotype Codes (PheCodes).[3] t-SNE further reduced dimensionality and indicated groups of patients based on their PheCodes and separated patients based on PheCode patterns rather than singular codes. Subsequently DBScan identified clusters of patients in t-SNE space, by grouping patients based on relative Euclidean distance. Finally transition-probability matrices were constructed for all codes in each cluster, from which probabilistic sequences could be constructed.

We defined replication as an overlap in ≥25% of the PheCodes between a cluster of set 1 and 2. Similarity was further assessed by calculating the absolute dissimilarity in transition probabilities for codes shared by matched clusters.

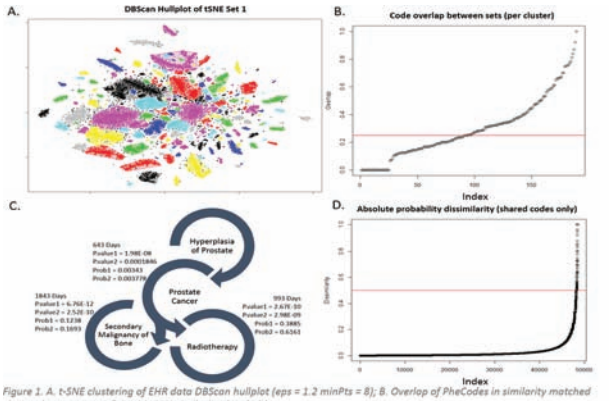


Figure 1. A. t-SNE clustering of EHR data DBScan hullplot (eps = 1.2 minPts = 8); B. Overlap of PheCodes in similarity matched clusters between set 1 & 2 with 25% similarity threshold;
C. Example of longitudinal flow within a single cluster, reproduced in both sets (both probabilities are shown along with averaged days between codes and the associated p.value calculated using a Student's t-test); D. Plot of the absolute dissimilarity in transition probabilities within the examale clusters visualised in C.

Figure 1

Results: The average (range) number of codes per individual was 376.3 (1 – 8,419) and 375.9 (1 – 10,315) spread over 4106 (1 - 10,781) and 4153 (1 – 10,746) days for set 1 and 2 respectively. Even though our input data was a sparse, high-dimensional (1,865) matrix of PheCodes, t-SNE and DBScan could clearly separate various unique patient groups with 284 and 295 clusters in set 1 and 2. Clusters consisted of patients with PheCodes of well-defined disease entities such as cardiovascular diseases and neurological disorders with objectively meaningful disease sequences. 34.5% of the clusters identified in set 1 were replicated in set 2 based on our replication criteria. Figure 1 shows the results of each step.

Conclusion: Our proof of principle supports the use of unsupervised techniques such as dimensionality reduction and data clustering to identify longitudinal associations between medical events. These methods could proof useful in our quest to identify medical risk factors for incompletely understood diseases.

REFERENCES

[1] L.J.P. v.d. Maaten, et al. Journal of Machine Learning Research 9 (Nov):2579-2605, 2008.
[2] M. Ester, et al. Proceedings of the Second International Conference on Knowledge Discovery and Data Mining: 226-231, 1996.
[3] Denny JC, et al. Bioinformatics. 2010;26(9):1205–10

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AB1283 **WHEN SHOULD WE EVALUATE CYTOMEGALOVIRUS INFECTION IN IMMUNOSUPPRESSED PATIENTS WITH CONNECTIVE TISSUE DISEASES?**

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Background: Cytomegalovirus (CMV) infection is an opportunistic and often problematic infection in patients with connective tissue diseases (CTD patients) who undergoes immunosuppressive therapy. However, in immunosuppressed CTD patients, CMV infection tends to be overdiagnosed, because it manifests with various symptoms and shows organ involvement. Little is known about when to suspect CMV infection and when to conduct CMV pp65 antigenemia assay in immunosuppressed CTD patients.
Objectives: To investigate the characteristics of patients who underwent CMV antigenemia assay and identify contributing factors of CMV infection in immunosuppressed CTD patients in a single center of Japan.
Methods: Medical records of hospitalized CTD patients who underwent CMV antigenemia assays between April 2015 and July 2018 were retrospectively reviewed. Patients were divided into groups with/without CMV antigenemia. Clinical features, basal immunosuppressive therapies, and laboratory data were analyzed.
Results: Overall, 108 patients were enrolled into the study; of these, the positive (group A) and negative (group B) CMV antigenemia groups had 49 and 59 patients, respectively. The underlying CTDs included systemic lupus erythematosus (n=27), anti-neutrophil cytoplasmic antibody-associated vasculitis (n=26), rheumatoid arthritis (n=22), polymyositis/dermatomyositis (n=13), and others (n=20). Glucocorticoid was used in 101 (93.5%) patients, and mean prednisolone dose was 27.1±18.3 mg/day. Pulse glucocorticoid therapy and intravenous cyclophosphamide (IVCY) therapy was administered in 14 (13.0%) and 22 (20.4%) patients, respectively.
Group A patients had a significantly higher rate of Charlson Comorbidity Index (CCI) $\geq$3 (69.4% vs. 30.5%, p<0.001). Mean prednisolone dose was significantly higher in Group A (32.9±15.5 mg/day vs. 22.3±19.0 mg/day, p=0.001). Pulse glucocorticoid therapy (26.5% vs. 1.7%, p<0.001) and IVCY (36.7% vs. 6.8%, p<0.001) were administered significantly more often to Group A patients. Myelosuppression was seen significantly more often in Group A (61.2% vs 39.0%, p=0.035). Laboratory data, including serum lymphocyte counts (1016±1136/μl vs. 1218±718/μl), hemoglobin level (10.5±2.6 g/dL vs. 11.5±2.1 g/dL), and platelet counts (14.5±9.7 $\times 10^6$/μl vs. 24.1±12.9 $\times 10^6$/μl) were significantly lower in Group A (p<0.05).
Multivariate logistic regression analysis revealed CCI$\geq$3 (odds ratio (OR) =3.21, 95% CI 1.13-9.16) and IVCY therapy (OR=8.89, 95% CI 1.99-39.7) as independent risk factors of CMV antigenemia. The result suggested that pulse glucocorticoid therapy could relate to CMV antigenemia (OR = 9.07, 95% CI 0.96-85.7).
Based on the prediction criteria for CMV antigenemia defined as the existence of one or more contributing factors including CCI$\geq$3, pulse glucocorticoid therapy, IVCY, and myelosuppression; sensitivity and specificity were 89.8% (95% CI 81.3-98.3) and 44.1% (95% CI 31.4-56.8), respectively. With contributing factors limited to CCI$\geq$3 and IVCY, sensitivity and specificity became 75.5% (95% CI 63.5-87.5) and 64.4% (95% CI 52.2-76.6), respectively.
Conclusion: Having multiple comorbidities and being on intensive immunosuppressive therapy, such as pulse glucocorticoid therapy and IVCY, were related to CMV antigenemia in CTD patients. The prediction criteria, including CCI$\geq$3, pulse glucocorticoid therapy, IVCY, and myelosuppression are helpful to clinically rule out CMV infection.
Disclosure of Interests: None declared
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AB1284 **THE PATIENT EXPERIENCE: A PROCESS EVALUATION OF A PILOT PRAGMATIC USING REMOTE MONITORING OF SYMPTOMS**

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Background: Traditional randomized controlled trials (RCTs) are important for testing drug efficacy but this study design is burdensome for patients (pts) and clinicians. Pragmatic trials addressing real world comparative effectivness are equally important but challenging to conduct. We piloted a trial platform aspiring to optimize the patient experience and minimize patient and physician burden. The trial (NCT02912221) tests an incentive strategy informed by behavioral economics to increase physial activity in pts with rheumatoid arthritis (RA) and psoriatic arthritis (PsA).
Objectives: To understand patient experiences using mobile applications (apps) and wearable activity devices (WAD) in a pilot pragmatic trial
Methods: Pts had RA or PsA with active disease defined by a Routine Assessment of Patient Index Data (RAPID3) score>3 (range 0-30). After screening and informed consent, pts received a WAD (FitBit™) and were assisted in setting up the device and an ArthritisPower account, a research registry where pts track patient-reported outcomes (PRO). A web-based platform, WayToHealth, was used to collect WAD data and deliver incentives. After a two-week baseline period, pts selected a daily step goal and were randomized to a financial loss-aversion incentive arm or control. Pts in both arms received weekly text messages reporting the number of days the step goal was met. In-person assessments were conducted at baseline and 14 weeks; pts completed weekly PROs (RAPID3, PROMIS Fatigue, PROMIS Sleep Disturbance and adverse event assessment) via mobile app or a web link. At 14 weeks, pts underwent a semi-structured interview to assess the patient experience in the trial. Content analysis was used to evaluate the responses
Results: To date, 27 pts completed the 14-week follow-up interview. Mean age was 48 (SD 14), 85% were women, 17 (63%) had PsA and 10 (37%) had RA. Mean disease duration was 9 years, mean swollen joint count (0-66) was 6.2 (SD 5.6) and tender joint count (0-68) was 8.1 (SD 9.1). The mean RAPID3 was 10.3 (SD 4.6). Overall pts enjoyed participation in the study and provided useful feedback for improvement (Table). Weekly PRO capture was acceptable to most but PROs need to be streamlined to remove repetitive questions. Pts frequently set goals they were not able to achieve and suggested the ability to change their goal in future studies
Conclusion: In this pilot pragmatic trial, only two in-office visits were conducted and all other data captured remotely. Pts enjoyed the experience and found the digital platform easy to use. Such trial designs will become increasingly important in conducting real-world comparative effectiveness and adjunct therapy trials

Table: Lessons learned from patient perspective in pragmatic trial

Trial Format
Pt enjoyed tracking progress
Weekly surveys were ok; 2 pts recommended EOW;
Weekly check ins kept pts accountable
Most pts completed surveys via a text link (over App or web portal)
Time to complete surveys was 5 min
Pt requested a text box to record reasons for not feeling well (e.g., injury, illness)
PROs
Repetitive questions in the PROMIS measures annoyed pts
MDHAQ questions were not always relevant
Tracking sleep helped understand level of fatigue
Emotional wellbeing questions were appreciated
Desire to track individual PRO goals
Wearable Activity Device
Served as a reminder to move
Annoyed by need to charge
Creating teams and self-competition was motivating and fun
Finger arthritis directed type of bracelet
Some exercise not captured (e.g., swimming, biking)
Physical activity
Goals frequently set too high; allow for a goal change
Weekly goals may be better than daily goals
Weather influenced physical activity; being accountable encouraged exercise indoors
Overexertion sometimes lead to pain and stiffness
Some reported knee/foot pain with increasing steps

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AB1285

IGA RF IS ASSOCIATED WITH HIGH AGE OF RHEUMATOID ARTHRITIS ONSET

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Background: IgM RF and anti-CCP2 have been shown to associate with young age at RA diagnosis [1, 2]. By contrast, little is known about the association between other RF isotypes and age at onset, or sex.

Objectives: To examine the association between individual RA autoantibodies, sex and age at RA onset.

Methods: Anti-CCP2, IgA-, IgG- and IgM-RF were analysed centrally in baseline sera from 1600 Epidemiological Investigations in RA (EIRA) patients aged 18-70 years and classified according to the 1987 ACR criteria within one year of first symptoms. Cut-offs for RF isotypes were determined at the 98th percentile based on the EIRA RA-free controls, close to the 98.4% anti-CCP2 specificity.

Results: Anti-CCP2, IgA-, IgG- and IgM RF were found in 1020 (64%), 692 (43%), 529 (33%), and 916 (57%), of the patients, respectively. Mean (median) age at diagnosis among men was 54 (57) year, higher than 51 (54) years among women (p<0.0001). The figure shows the autoantibody distribution in relation to sex and age tertiles. In univariate analysis, anti-CCP2 and IgM RF were both associated with lower age at RA diagnosis (table). When occurrence of all four autoantibodies were compared simultaneously as independent variables and with age at diagnosis as dependent variable in multiple regression, a strong association between IgA RF and higher age at RA diagnosis appeared, and the association between IgM RF and low age at RA diagnosis weakened (table). IgA RF and IgG RF associated with male sex, but IgM RF with female sex. No sex-difference was seen for anti-CCP2 (table). When the multiple regression was adjusted for sex, the association between IgM RF and age disappeared, whereas the strong associations between IgA RF and high age and between anti-CCP2 and low age at diagnosis persisted (table).

Conclusion: On average, IgA RF positive (vs. negative) RA patients are almost four years older at the time of diagnosis; the opposite was found for anti-CCP2 and IgM RF. Whereas sex-differences explain the age-association for IgM RF, this is not the case for anti-CCP2 and for IgA RF.

REFERENCES

[1] Diaz FJ, et al. Joint Bone Spine 2011;78:175.

[2] Jacobsen S. Clin Rheumatol 2004;23:121.

	Anti-CCP2 Pos/ Neg	P	IgA RF Pos/ Neg	P	IgG RF Pos/ Neg	P	IgM RF Pos/ Neg	P
N	1020/ 580		692/ 908		529/ 1071		916/ 684	
Age (mean) univariate	51/54	**<0.0001**	53/52	0.08	52/52	0.98	51/53	**0.0042**
Age (least squares mean multivariate)	51/55	**<0.0001**	55/51	**<0.0001**	53/53	0.7170	52/54	**0.0401**
Age multivariate (corr. sex)	52/55	**<0.0001**	55/52	**<0.0001**	54/53	0.9378	53/54	0.1128
Females n(%)	727/ 400 (71)/ (69)	0.3315	462/ 665 (67)/ (73)	0.0050	350/ 777 (66)/ (73)	0.0089	665/ 462 (73)/ (68)	0.0287

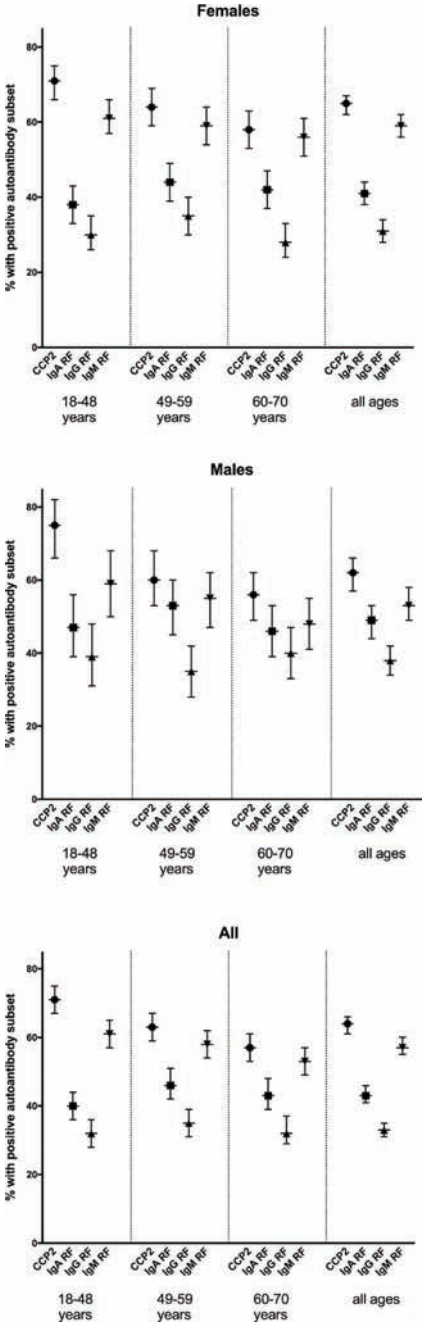


Figure. Distribution of individual autoantibodies in relation to sex and age tertiles.

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AB1286 **EVALUATION OF CARDIOVASCULAR RISK FACTORS AND PREVALENCE OF METABOLIC SYNDROME IN PATIENTSWITH DIAGNOSIS OF ANKYLOSING SPONDYLITIS:**

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Background: Cardiovascular events are the main causes of mortality in patients with Ankylosing Spondylitis. In addition, a higher prevalence of Metabolic Syndrome is reported in this group. With immunobiological therapy, much progress has been made in controlling the inflammatory process, but the cardiovascular risk remains high.
Objectives: To evaluate the prevalence of cardiovascular risk factors and Metabolic Syndrome in patients with Ankylosing Spondylitis at the Rheumatology Outpatient Clinic of HC-UFG and to correlate them with epidemiological, clinical, laboratory and radiographic characteristics of the disease.
Methods: Data from 59 patients were collected in medical records between July and August 2018. Clinical characteristics, cardiovascular risk factors and metabolic components were analyzed. Descriptive analyzes of the data were made, prevalences and their reasons were calculated. The associations between variables were assessed by chi-square test and Fisher's exact test.
Results: 81.4% were male, 67.8% self-denominated non-whites, average age 46.7 years. Isolated axial joint involvement was the most frequently observed (54.2%). Enthesopathic lesions were identified in 30.51% of the cases. Uveitis had a higher prevalence (22.02%), 4.2 times higher in the subgroup with HLA-B27 positive (p=0.0002). HLA-B27 was present in 67.8%. Advanced sacroiliitis (grades 3 and 4) and syndesmophytosis were identified in 61.1% and 49.2%, respectively, but didn't presented significant correlation with the presence of HLA-B27. 64,4% were using anti-TNF alone or in combination. The majority of the patients (72.9%) were sedentary. Clinical comorbidities were reported in 66.1% of the cases, with dyslipidemia (45.8%), systemic arterial hypertension (37.6%) and diabetes mellitus (13.6%) being the most common. Metabolic Syndrome was diagnosed in 23.7% of the samples. Normal levels of triglycerides and fasting glycemia and lower prevalence of Metabolic Syndrome had a statistically significant association with the presence of HLA-B27 (p=0.006; 0.026 and 0.014, respectively). Patients with HLA-B27 present had 61% lower frequency of Metabolic Syndrome. There was no association between the syndrome and its components with anti-TNF therapy; BASDAI; BASFI; metric evaluation; uveitis; degree of sacroiliitis and syndesmophytosis.
Conclusion: The prevalence of Metabolic Syndrome was below that is described in other populations. The presence of HLA-B27 was considered a protective factor for Metabolic Syndrome, triglyceride levels and fasting glycemia. This finding may be related to the presence of several HLA-B27 alleles, usually non-subtyped, and to the great ethnic miscegenation of the Brazilian population. Our observation suggests that spondylitics should be routinely evaluated for cardiovascular risk factors.

REFERENCES

[1] Maia, DG, et al. Metabolic Syndrome in patients with ankylosing spondylitis receiving anti-TNF alfa therapy: association with predictors of cardiovascular risk. Clin Rheumatology 2011;36(10):2371-76.
[2] Fiorillo, MT, et al. CD8+ T-cell autoreactivity to an HLA-B27–restricted self-epitope correlates with ankylosing spondylitis. The Journal of Clinical Investigation 2000;106(1):47-53.

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AB1287 **DISEASE EVOLUTION OF PRIMARY SJOGREN'S SYNDROME – A LONGITUDINAL STUDY**

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Background: The natural history of primary Sjogren's syndrome (pSS) remains poorly understood. It has been suggested that the initial presentations may predict the course of disease (1), with gradual reduction of biological activity as measured by serum Immunoglobulins levels (2), while symptoms such as fatigue remaining stable over time(3).
Objectives: To evaluate how pSS progresses over time using ESSDAI (Eular Sjögren's Syndrome Disease Activity Index) and the ESSPRI (Eular Sjögren's Syndrome Patient Index), EQ5D-Time trade off (TTO) and Visual Analogue Scale (VAS) of health states.
Methods: Routine clinical data from a large single centre cohort in the UK were analysed on patients with $\geq$3 clinical visits, including up to the 10th visit. Outcomes (ESSDAI/ESSPRI and their component scores, EQ5D-3L and VAS) were analyzed by a random effects linear regression using STATA 14.
Results: 346 patients out of 858 included, with a female preponderance of 89%, and median age of 63 years. The median follow up time was 4.9 years, and median disease duration of 12 years. Anti-Ro was positive in 61% and anti-La in 42% of the patients.
ESSDAI score decreased 0.1 point per visit (p=0.006). Anti-Ro and anti-La positive patients exhibiting a lower score (p=0.012 and 0.031), and patients with MALT at presentation had a score up to 6 points higher (p= 0.002). Regarding the ESSDAI domains, the constitutional and haematological domains showed increased activity (p-value<0.0001 and 0.018), with Anti-Ro and/or Anti-La patients having higher scores (p <0.0001 and 0.001). In contrast, the glandular, articular and peripheral nervous system domains showed decreases over time (p-values 0.003, 0.006 and <0.0001).
ESSPRI score increased 0.05 point/visit (p<0.0001). While Dryness scores remained relatively constant, Pain and Fatigue components of the ESSPRI increased over time (both p<0.0001). Dryness scores were higher in female patients (p=0.04).
EQ5D-TTO worsened by 0.03 point/visit (p<0.0001), but the VAS health states remained stable.
Conclusion: Our data suggest that symptoms of fatigue and pain as well as health utility worsen over time, whereas different ESSDAI domains showed different trends over time. Longer term follow-up to further understand the natural history of pSS is warranted.

REFERENCES

[1] Skopouli FN, Dafni U, Ioannidis JPA, Moutsopoulos HM. Clinical evolution, and morbidity and mortality of primary Sjogren's syndrome. Semin Arthritis Rheum. 2000;29(5):296–304.
[2] Pertovaara M, Pukkala E, Laippala P, Miettinen A, Pasternack A. A longitudinal cohort study of Finnish patients with primary Sjögren's syndrome: Clinical, immunological, and epidemiological aspects. Ann Rheum Dis. 2001;60(5):467–72.
[3] Haldorsen K, Bjelland I, Bolstad AI, Jonsson R, Gorgas Brun J. A five-year prospective study of fatigue in primary Sjögren's syndrome. Arthritis Res Ther. 2011;13.

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AB1288 **PREVENTION OF VENOUS THROMBOEMBOLISM AND THE RISK OF POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER TOTAL HIP ARTHROPLASTY:**

Alexey Rybnikov[1], Evgenij Bialik[2], Tatiana Reshetnyak[2], Sergey Makarov[2], Alexander Khramov[2], Sergey Maglevaniy[2]. [1]*Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*; [1]*Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: According to the administrative data, confirmed by several meta-analyses, patients with rheumatoid arthritis (RA) in comparison with the General population shows an increased risk of venous thromboembolic complications more than twice. Drug prevention can reduce the risk of venous thromboembolism (VTE) in patients with rheumatic diseases.
Objectives: The aim of this study was to analyze frequency of VTE, risk of bleeding and complications of the postoperative wound in patients with RA and osteoarthritis (OA) after total hip arthroplasty (THA).
Methods: **S**tudy included 486 patients (212 - with RA and 274 - with OA) who underwent primary THA. Each group of patients was divided into 3 subgroups by type of drug therapy (1-nadroparin calcium; 2-dabigatran etexilate; 3-nadroparin calcium with transfer to dabigatran etexilate). Intra-and postoperative blood loss and the wound healing process were assessed during the first 7 days after surgery.
Results: Postoperative VTE were reported in 36 (7.4%) of 486 patients. VTE in patients with RA were detected significantly less frequently than in OA (1.2% and 6.1%, p = 0.0013). Bleeding that required transfusion

of blood in RA were found significantly more often than in OA (respectively 14.4% and 5.7% of cases; P<0.001). The number of cases requiring cancellation of anticoagulant therapy in patients with RA was significantly higher compared with the OA group (6.6% and 1.4%, respectively). Slow wound healing in RA was more common (n = 56; 26.4%) than in OA (n = 14; 5.1%). In patients who underwent monotherapy with calcium nadroparin VTE occurred more often than when using combination therapy (p<0.0001) and more often than in the group of dabigatran etexilate (p=0.054).

Conclusion: The frequency of VTE, the risk of bleeding and complications of postoperative wound in patients with RA and OA after THA were analyzed. So, our study determined the dependence of VTE complications and bleeding risk according to the patient's underlying nosology. Also the advantage of combined postoperative therapy over others was evaluated.

Disclosure of Interests: None declared

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AB1289 TESTING DIFFERENT ITEMS INCLUDED IN THE DEFINITION OF REMISSION IN A MULTICENTRE SLE COHORT

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Background: Remission is the most desirable target in the treatment systemic lupus erythematosus (SLE) however, a universally accepted definition of remission in SLE is still missing.

Objectives: To test the contribution of the different items included into the currently used definitions of remission in SLE.

Methods: We studied 646 Caucasian patients from a multicentre lupus cohort followed for at least 5-years: female 585 (90.6%), mean age at baseline 40.59±12.14 years, mean disease duration 9.18±6.86 years. Disease activity was assessed by clinical SLE Disease Activity Index 2000 (cSLEDAI) and SELENA-SLEDAI physician global assessment (PGA), and damage by Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI). To test the performance of the different items included in the definitions of SLE remission [1, 2] we identify 7 subtypes of remission: (1) PGA (0-3)<0.5; (2) cSLEDAI=0; (3) prednisone (PDN)≤5mg/day; (4) PGA<0.5 and PDN≤5mg/day; (5) cSLEDAI=0 and PGA<0.5; (6) cSLEDAI=0 and PDN≤5mg/day; (7) cSLEDAI=0 and PDN≤5mg/day and PGA<0.5. The effect of remission on SDI was evaluated by Poisson regression analysis.

Results: The number of patients achieving remission according to the different definitions is show in Figure 1. The proportion of patients who maintained prolonged remission (5-consecutive years) was: PGA<0.5 13.0%; cSLEDAI=0 18.4%; PDN≤5mg/day 34.4%; PGA<0.5 and PDN≤5mg/day 12.5%; cSLEDAI=0 and PGA<0.5 12.7%; cSLEDAI=0 and PDN≤5mg/day 16.6%; cSLEDAI=0 and PDN≤5mg/day and PGA<0.5 12.4%.

Figure 1. Number of patients in remission according to the 3 single items (prednisone≤5 mg/day; PGA<0.5; cSLEDAI=0) and their overlap during a follow-up period of 5 years for all the patients. **A)** Patients achieving at least 1-year remission. **B)** Patients achieving prolonged remission (5-consecutive years).

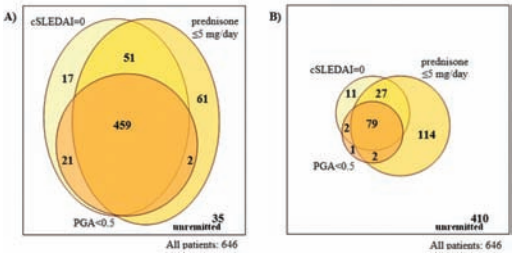


Figure 1

Table 1. Performance of 7 different remission subtypes in defining the risk of damage accrual (upper part) and the goodness-of-fit of the model (lower part).

	cSLEDAI=0	PGA<0.5	PDN ≤5mg/day	PGA<0.5 and PDN ≤5 mg/day	cSLEDAI=0 and PGA<0.5	cSLEDAI=0 and PDN ≤5 mg/day	cSLEDAI=0 and PDN ≤5mg/day and PGA<0.5
	OR(CI95%)*						
1-year remission pts vs unremitted	0.766 (0.548-1.072)	0.808 (0.590-1.108)	0.952 (0.610-1.485)	0.764 (0.554-1.054)	0.857 (0.629-1.167)	0.894 (0.646-1.236)	0.800 (0.583-1.098)
2-year remission pts vs unremitted	**0.454 (0.318-0.647)**	**0.560 (0.395-0.794)**	0.858 (0.566-1.301)	**0.495 (0.341-0.718)**	**0.514 (0.359-0.737)**	**0.501 (0.347-0.722)**	**0.479 (0.327-0.702)**
3-year remission pts vs unremitted	**0.512 (0.342-0.768)**	**0.427 (0.280-0.650)**	0.912 (0.600-1.387)	**0.480 (0.278-0.665)**	**0.459 (0.3015-0.698)**	**0.559 (0.370-0.845)**	**0.488 (0.283-0.677)**
4-year remission pts vs unremitted	**0.173 (0.105-0.286)**	**0.226 (0.130-0.395)**	**0.391 (0.245-0.626)**	**0.294 (0.177-0.488)**	**0.243 (0.140-0.425)**	**0.253 (0.156-0.408)**	**0.296 (0.176-0.497)**
5-year remission pts vs unremitted	**0.382 (0.260-0.561)**	**0.377 (0.238-0.595)**	**0.620 (0.430-0.895)**	**0.363 (0.226-0.581)**	**0.397 (0.251-0.626)**	**0.413 (0.276-0.618)**	**0.374 (0.234-0.560)**
	Goodness-of-fit of the model						
AIC	1082.90	1100.62	1132.83	1105.87	1103.96	1101.13	1106.59
BIC	1109.72	1127.44	1159.66	1132.70	1130.78	1127.96	1133.42
p Value	*<0.0001*	*<0.0001*	*0.0003*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*

pts: patients; PDN: prednisone; OR: Odds ratio; CI: confidence interval.
*Significative values are given in bold (p<0.001).

Figure 1

When PGA<0.5 was added to cSLEDAI, 198 (30.7%) patients lost 353 years in remission (1.8 years/patient): among them 195 (98.5%) showed a 0.5≤PGA≤1 suggesting a low disease activity state (LDA). When, PGA<0.5 was added to cSLEDAI =0 and PDN ≤5mg/day, 151 (23.5%) patients lost 254 years in remission (1.7 years/patient): among them 149 (98.0%) showed a 0.5≤PGA≤1 suggesting again LDA. All remission subtypes were protective against damage (p<0.001), however cSLEDAI=0 showed the best performance (lower AIC) (Table 1). At multivariate analysis all remission subtypes lasting ≥2 consecutive years were protective against damage (p<0.001), except PDN≤5mg/day which was protective after 4 consecutive years.

Conclusion: The prevalence and extent of damage significantly decreased as the time spent in remission increased, irrespective of the remission subtype. The addition of PGA<0.5 to cSLEDAI=0 or to cSLEDAI=0 and PDN≤5mg/day results in a decrease in the time spent in remission without significant difference in damage accrual.

REFERENCES

[1] van Vollenhoven R, et al. 2014
[2] Zen M, et al. 2015

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AB1290 VITAMIN D AND PAIN SYNDROME IN BREAST CANCER PATIENTS TREATED WITH ADJUVANT LETROZOLE

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Background: The third-generation aromatase inhibitors (AIs) have shown a favorable overall risk–benefit profile in the upfront adjuvant therapy of postmenopausal estrogen receptor–positive breast cancer. Breast cancer patients treated with long term AIs experience arthralgias and musculoskeletal aching often described as bone pain, musculoskeletal disorder, arthralgia.

Objectives: The purpose of this study was to investigate clinical, serological and anamnestic features associated to the joint pain syndrome in non-metastatic breast cancer patients treated with adjuvant AIs.

Methods: Between June 2017 and December 2017 patients with early stage estrogen receptor–positive breast carcinomas treated with adjuvant letrozole, attending our Rheumatologic clinic to undergo osteoporosis screening, were included. Pre-existing symptoms and clinical, serological and imaging features were evaluated to assess the type of musculoskeletal disorder.

Results: Among 64 patients included a musculoskeletal syndrome was detected in 46 patients (71.8%), whereas diffuse muscle pain was observed in 42 (65.6%) patients, and 83.3% of them had associated arthritis. Serological, imaging and clinical findings suggested more frequently a seronegative arthritis, whereas few patients developed rheumatoid arthritis and arthritis secondary to a connective tissue disease. A direct correlation between pre-existing autoimmune disease and pain symptoms before cancer diagnosis and risk of developing arthritis under AI therapy was observed. Mean vitamin D levels were significantly lower in patients with diffuse myalgia compared to patients with no diffuse myalgia (11.2±5.8 versus 29.5±10.8 ng/ml; t-test $p < 0.0001$), suggesting a potential involvement of vitamin D deficiency in diffuse muscle pain.
Conclusion: The etiology of AI-associated pain syndrome remain unknown, but clinical, serological, imaging data may be useful to identify the true origin of the musculoskeletal syndrome, as well as a detailed anamnestic history may be useful to identify autoimmune predisposing factors. Myalgias and generalized weakness are likely associated with hypovitaminosis D and might be misdiagnosed as fibromyalgia. The management of these patients should become a multispecialistic task.

REFERENCES

[1] Beckwée D, Leysen L. Prevalence of aromatase inhibitor-induced arthralgia in breast cancer: a systematic review and meta-analysis. Support Care Cancer 2017 May;25(5):1673-1686.
[2] Borrie AE,Kim RB. Molecular basis of aromatase inhibitor associated arthralgia: known and potential candidate genes and associated biomarkers. Expert Opin Drug Metb Toxicol. 2017 Feb;13(2):149-156.

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AB1291 ASSOCIATION OF CCL2 GENE POLYMORPHISMS AND THEIR SERUM LEVELS WITH SUSCEPTIBILITY TO KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is one of the most depleting chronic disorders and its pathogenesis is yet to be unfold. It is characterized by pain, swelling, stiffness, decreased ability to move and, sometimes, the formation of bone spurs. Knee Osteoarthritis (KOA) is multifactorial and remains largely understudied at molecular level. The available literature suggested that the development, onset and progression of OA is significantly affected by genetic factors. Chemokines are small, secreted proteins that released from chondrocytes and/or synovial fibroblasts of KOA patients. In this case control study, we investigated the possible association between promoter polymorphisms rs1024611 and the polymorphism rs4586 in exon 2 of the chemokine (C–C motif) ligand 2 (CCL2) gene and knee OA.
Objectives: To investigate the possible association between promoter polymorphisms rs1024611 and the polymorphism rs4586 in exon 2 of the CCL2 gene and KOA.
Methods: DNA was obtained from 300 primary knee OA patients and 300 healthy controls. CCL2 genomic variants (rs1024611 and rs4586 polymorphisms) were detected by polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP). In additional, the effect of serum levels of rs1024611 and rs4586 on cases and controls were examined by enzyme-linked immunosorbent assay (ELISA).
Results: The rs1024611 A/G promoter polymorphism was associated with KOA [genotype frequency, p= 0.007; allele frequency, p= 0.01]. Significant association was observed between the G carrier of the rs1024611 A/G promoter polymorphism and primary knee OA patients (p=0.01). However, no significant difference was found in the rs4586 polymorphism. Haplotype frequency analysis revealed a significant difference (x^2= 8.01, p= 0.02). The CCL2 serum level of subjects with the G carrier (285.0 ± 86.5 pg/mL) of the rs1024611 A/G promoter polymorphism was statistically higher than that of subjects with the non-G carrier (160.5±47.8 pg/mL). Further in relation with clinical severity of KOA, we observed signification association of the G carrier of the rs1024611 A/G promoter polymorphism with both Visual analogue scale (VAS) ($p<0.01$) and Western Ontario and McMaster Universities (WOMAC) score ($p<0.05$).
Conclusion: The G carrier of the rs1024611 A/G promoter polymorphism was found to be associated with primary knee OA, and could be a susceptibility factor in the development of primary knee OA in the North Indian population.

REFERENCES

[1] Hulin-Curtis SL, Bidwell JL & Perry MJ. Association between CCL2 haplotypes and knee osteoarthritis. International journal of Immunogenetics.2015
[2] Park HJ, Yoon SH, Zheng LT, Lee KH, Kim JW, Chung JH, Lee YA, Hong SJ: Association of the 22510A/G chemokine (C–C motif) ligand 2 polymorphism with knee osteoarthritis in a Korean population. Scand J Rheumatol 2007;36:299–306

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AB1292 PREVALENCE OF VITAMIN D DEFICIENCY AND ITS ASSOCIATED FACTORS AMONG RHEUMATOID ARTHRITIS PATIENTS MANAGED IN A RHEUMATOLOGY UNIT OF A TERTIARY CARE HOSPITAL IN SRI LANKA

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Background: Prevalence of unrecognized vitamin D deficiency can be high among Rheumatoid Arthritis (RA) patients. Lack of mobility among of these patients prevent them receiving adequate sun exposure. Low levels of vitamin D could potentially cause a higher disease burden and disease activity.
Objectives: To determine the prevalence of vitamin D deficiency and its associated factors among RA patients managed in a rheumatology unit of National Hospital of Sri Lanka (NHSL).
Methods: A descriptive cross-sectional study was done among patients with RA with a calculated sample size of 137. Being diagnosed according to ACR – EULAR criteria and availability of serum vitamin D level were among the inclusion criteria. Patients with disability due to causes other than RA were excluded. All patients satisfying the eligibility criteria were invited to be recruited. A data extraction sheet was utilized. Data was collected by investigators. The associations were evaluated with Chi square test and Spearman correlation coefficient at a significance level of 5%. Ethics approval was obtained from ethics committee of NHSL.
Results: The response rate was 92%. The median (IQR) age of participants' were 56.5 (49.0 to 64.25). Among participants, majority (n=117, 92.9%) was females. Only 11.1% (n=14) had normal vitamin D levels. The insufficient and deficient categories comprised of 38.1% (n=48) and 50.8% (n=64). The commonest symptoms included; joint pain (n=101,80.2%), fatigue (n=84,66.7%) and muscle pain (n=78,61.9%). Deficiency or insufficiency was lowest in the occupation category of "agricultural and labourer" (37.5%) while 100% in many indoor-occupied categories and among Muslims. "Deficiency or insufficiency" was significantly associated with muscle pain (p=0.001) but not with CDAI (p=0.896), fatigue (p=0.549), joint pain (p=0.735).
Conclusion: Vitamin D "deficiency or insufficiency" is common among patients with RA and commoner in the sub-categories with muscle pain and with restricted sun-exposure. More research must be promoted in this regard.

REFERENCES

[1] Imboden J.B., Hellmann D.B., Stone J.H. 2013. Current treatments and diagnosis rheumatology 3rd edition. New York : McGraw-Hill Medical
[2] Baker JF, Baker DG, Toedter G, Shults J, Von Feldt JM, Leonard MB (2012) Associations between vitamin D, disease activity, and clinical response to therapy in rheumatoid arthritis. Clin Exp Rheumatol 30:658–664 2.
[3] Braun-Moscovici Y, Toledano K, Markovits D, Rozin A, Nahir AM, Balbir-Gurman A (2011) Vitamin D level: is it related to disease activity in inflammatory joint disease? Rheumatol Int 31:493–499
[4] Craig SM, Yu F, Curtis JR, Alarcon GS, Conn DL, Jonas B, Callahan LF, Smith EA, Moreland LW, Bridges SL Jr, Mikuls TR (2010) Vitamin D status

and its associations with disease activity and severity in African Americans with recent-onset rheumatoid arthritis. J Rheumatol 37:275–2812)

[5] Haque UJ, Bartlett SJ (2010) Relationships among vitamin D, disease activity, pain and disability in rheumatoid arthritis. Clin Exp Rheumatol 28:745–747 5.

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AB1293 SMAD3 GENE POLYMORPHISMS AND EXPRESSION IN SERUM AND CARTILAGE INFLUENCE THE RISK OF KNEE OSTEOARTHRITIS

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Background: Knee Osteoarthritis (KOA) is the most common degenerative arthritis, a type of arthritis that is caused by breakdown of articular cartilage with eventual loss of the cartilage of the joints. Smad3 is a key intracellular messenger in the transforming growth factor β signaling pathway. Previous study suggested Smad3 gene mutation is a possible predisposing factor for human OA and found gene mutation in OA, providing insight into the function of SMAD3 mediated TGF-b signals in the development of OA and also suggested that Smad3 gene mutation may be a risk factor for genetic susceptibilities to OA. In this case control study, we investigated the possible correlation between the SNPs SmaI (C/T; rs6494629), FokI (A/C; rs2289263) in Smad3 gene and susceptibility to knee OA and validated in serum and cartilage.

Objectives: To investigate the possible association between SNPs (rs6494629 and rs2289263) of the Smad3 gene and KOA.

Methods: In this study cases consisted of men and women ≥40 years that fulfilled American College of Rheumatology (ACR) clinical and radiographic criteria for knee OA. Venous blood samples were obtained from all cases as well as controls for genetic analysis. Polymerase chain reactions were performed for SNP analysis using specific primer. Total protein was measured in serum by an enzyme linked immunosorbent assay according to the manufacturer's Protocol (ELISA) and in cartilage tissue done by western blot.

Results: A total of 200 cases that confirmed radiographic knee OA and equal number of age and sex matched healthy controls were enrolled. There was no significant difference in demographic characteristics between the cases and controls. A SNP (rs6494629 and rs2289263) mapping to intron 1 of SMAD3 was associated with knee OA ($P < 0.013$ and $P < 0.044$, respectively). Within the SNPs (rs6494629) of Smad3 gene, genotype CC and CT was found to be significantly ($p<0.013$) associated with knee OA as compared with the CC genotype and SNP rs2289263,genotype CC and CA was found to be significantly ($p<0.044$) associated with knee OA as compared with the AA genotype. In addition when alleles were compared, C allele of both the studied SNP was observed to be significantly associated with knee OA. Serum levels of Smad3 in KOA patients with rs6494629 TT, CT and CC genotypes were significantly higher than healthy subjects with the same rs6494629C/T genotypes (all $P < 0·0001$, $P < 0·0006$, $P < 0·017$ respectively). Increased serum levels of Smad3 were also observed in KOA patients with rs2289263 AA, CA and CC genotypes compared to controls (all $P < 0·006$, $P < 0·0006$, $P<0·004$). We performed Immunoblot analysis on cartilage tissue from 15 cases and 10 controls. The smad3 level in cases was significantly higher than controls ($P < 0.006$).

Conclusion: Our data indicate that genetic variation in the SMAD3 gene is involved in the risk of knee OA in North Indian populations, confirming the results from previous studies on the potential importance of this gene in the pathogenesis of OA. Further we also validated these genetic variations at protein level in both blood and tissue and found significant association.

REFERENCES

[1] Valdes AM, Spector TD, Tamm A, Kisand K, Doherty SA, Dennison EM. Genetic variation in the SMAD3 gene is associated with hip and knee osteoarthritis. Arthritis and rheumatism. 2010;10.1002/art.27530

[2] Su SL, Yang HY, Lee HS, Huang GS, Lee CH, Liu WS. Gene–gene interactions between TGF-b/Smad3 signalling pathway polymorphisms affect susceptibility to knee osteoarthritis. BMJ Open. 2015;5:e007931.

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AB1294 IMPACT OF INFERTILITY, PREGNANCY LOSS AND CHILDBEARING DECISION ON FAMILY SIZE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

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Background: Systemic lupus erythematosus (SLE) and Rheumatoid Arthritis (RA) often affects women in their reproductive years. These women are faced with a life-long illness that may have considerable impact not only on their physical health, but also on their reproductive potential. Fertility of these women may also be affected by the disease, treatment and/or organ damage.

Objectives: To determine the role of infertility, pregnancy loss and childbearing decision and patients concerns on family size in women with SLE and RA

Methods: A cross sectional study using a self-administered reproductive history questionnaire completed by woman with SLE/RA attending Rheumatology clinic follow up in Hospital Putrajaya, Hospital Tengku Ampuan Rahimah, and Hospital Raja Permaisuri Bainun, Malaysia from 1 January 2017 to 30 June 2017.

Within each disease cohort, women were identified into 3 groups, those with fewer children than planned (group A), those with same number of planned children (group B) and those with completed family or not interested in having any children (group C). Data on number of children, pregnancies, misscariges and self reported infertility were recorded.For group A, data on patient concerns and the factors that could impact family building were also obtained.

Results: Total of 110 women with SLE and 91 women with RA were surveyed. The mean age of women with SLE and RA were 37.6 years (+/- SD 7.4) and 45.37 years (+/- SD 11.7) respectively. Majority of women (48.8%) with SLE and RA were in group A with 59% (n=65) of women with SLE and 33% (n=33) of women with RA had fewer children than originally planned.

The average numbers of pregnancies were similar in both cohorts, but women with SLE had 1 less child and were more likely to report infertility and had higher rate of miscarriages (Table 1). SLE group A had a similar number of pregnancies, but 1 less child compared to SLE group B and C (Table 2). Similarly, among women with RA, group A had 1 less child with similar number pregnancies and miscarriage rate (Table 2). In both groups of women, concerns about inability to care for a child, damage from medications, and genetic transmission of their disease were associated with a lower pregnancy rate.

Table 1. Number of pregnancies, live births, miscarriages and rate of infertility among women with SLE and RA*

	SLE	RA	P
No. of pregnancies	2.28 ±1.626	2.60 ±1.949	0.128
No. of children	1.85 ±1.235	2.19 ±1.731	**0.019**
No. of miscarriages	0.46 ±0.809	0.36 ±0.659	**0.040**
No reporting infertility (%)	5 (4.5)	2 (2.2)	0.366

*values are the mean +/- SD unless otherwise indicated

Table 2. Pregnancy outcomes for women with SLE (n**=110) and RA (n=91)** *

	Fewer children than desired (group A)		Expected number of children (group B)		completed family (group C)	
	SLE	**RA**	**SLE**	**RA**	**SLE**	**RA**
No. of woman, n (%)	65 (59.1)	33 (36.3)	20 (18.2)	31 (34.1)	25 (22.7)	27 (29.7)
No. of pregnancies	2.11 ± 1.592	2.03 ± 1.723	2.3 ± 0.865	2.81 ± 2.12	2.72 ± 2.092	3.07 ± 1.9
No. of children	1.57 ± 1.212	1.55 ± 1.416	2.1 ± 0.553	2.39 ± 4.856	2.36 ± 1.497	2.74 ± 1.745
No. of miscarriages	0.51 ± 0.831	0.36 ± 0.603	0.25 ± 0.716	0.32 ± 0.653	0.52 ± 0.823	0.41 ± 0.747

*values are the mean +/- SD unless otherwise indicated

Conclusion: In this population, more than half of women with RA or SLE had fewer children than desired. Other than patient choice, infertility and miscarriage also play an important role on family size.

REFERENCES

[1] Clowse, et al. Effects of Infertility, Pregnancy Loss, and Patient Concerns on Family Size of Women With Rheumatoid Arthritis and Systemic Lupus Erythematosus. Arthritis Care & Research.2012; 64 (5):668–674

[2] Vinet at al. Systemic Lupus Erythematosus in Women: Impact on Family Size. Arthritis & Rheumatism (Arthritis Care & Research).2008; 59 (11);1656–1660

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AB1295 DISCREPANCIES BETWEEN THE RHEUMATOID ARTHRITIS PATIENT POPULATION IN RANDOMIZED CONTROLLED TRIALS OF BIOLOGICS AND THAT IN REAL-WORLD SETTINGS: A STUDY USING THE IORRA COHORT

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Background: Randomized controlled trials (RCTs), which are currently considered to provide the highest level of evidence, include patients with high disease activity and exclude those with comorbidities often seen in real-world settings. With the increasing recognition of the importance of real-world evidence, attention is being paid to discrepancies between RCT-based evidence and the patient population in routine clinical practice; however, few reports assessing these gaps in the context of rheumatoid arthritis (RA) are available.

Objectives: To evaluate the proportion of patients meeting the inclusion criteria in RCTs of biologics for the treatment of RA conducted in Japan using the real-world IORRA cohort.

Methods: The inclusion criteria used in Phase 2 or Phase 3 RCTs of the following biological DMARDs (bDMARDs) were extracted: infliximab (IFX), etanercept (ETN), adalimumab (ADA), golimumab (GLM), certolizumab (CZP), abatacept (ABT), tocilizumab (TCZ), and infliximab BS (IFX-BS). Patients participating in the IORRA study during the period when each RCT was conducted (Cohort A) and those who initiated treatment with each bDMARD at our institute in 2016 (Cohort B) were included in the analysis. The proportion of RA patients in Cohorts A and B who met the RCT inclusion criteria was assessed.

Results: A total of 19 RCTs were conducted in Japan (IFX, 2; ETN, 1; ADA, 2; GLM, 2; CZP, 3; ABT, 2; TCZ, 6; IFX-BS, 1). Key trial inclusion criteria were age, RA duration, tender joint count (TJC), swollen joint count (SJC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), methotrexate (MTX) use, corticosteroid use, and prior bDMARD therapy. The number of patients participating in the IORRA analysis during the period when each RCT was conducted ranged from 1,777 to 6,843 (mean: 5,470) (Cohort A). The median/average [range] proportion of RA patients meeting all RCT inclusion criteria was 0.6%/2.3% [range: 0.0%-16.2%]. The proportion by criterion was 93.9%/92.4% [59.7%-99.9%] for age, 68.9%/57.1% [9.0%-99.6%] for RA duration, 11.6%/16.0% [4.5%-33.0%] for SJC, 14.6%/17.2% [3.7%-33.9%] for TJC, 27.8%/32.1% [20.1%-49.8%] for CRP, 60.2%/58.7% [43.7%-66.8%] for ESR, 14.8%/40.6% [13.1%-73.9%] for MTX use, 99.5%/99.3% [98.5%-99.8] for prednisolone (PSL) use, and 91.9%/92.0% [85.6%-98.0%] for prior bDMARD use. In Cohort A, the proportion of RA patients meeting the RCT inclusion criteria was low, particularly with respect to SJC, TJC, and MTX use. Among 337 patients who initiated bDMARD therapy at our institute in 2016, a total of 139 biologic-naïve patients (IFX, 3; ETN, 33; ADA, 11; GLM, 21; CZP, 17; ABT, 25; TCZ, 28; IFX-BS, 1) were included in the analysis (Cohort B). In Cohort B, the median/average [range] proportion of RA patients meeting all RCT inclusion criteria was 0%/8.2% [0.0%-54.2%]. The proportion by criterion was 100%/99.1% [94.1%-100%] for age, 20.8%/26.5% [0.0%-57.1%] for SJC, 11.8%/17.0% [0.0%-50.0%] for TJC, 33.3%/34.9% [0.0%-66.7%] for CRP, 58.3%/57.3% [0.0%-75.0%] for ESR, 23.5%/35.5% [0.0%-100%] for MTX use, and 100%/100% [100%] for PSL use. As in Cohort A, the proportion of RA patients meeting the inclusion criteria was low in Cohort B, particularly with respect to SJC, TJC, and MTX use.

Conclusion: It is important to note that evidence from RCTs of bDMARDs is based on a limited RA population in real-world settings.

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AB1296 PREGNANCY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: MATERNAL AND FETAL COMPLICATIONS

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Background: Systemic lupus erythematosus is a chronic autoimmune disease often affecting women in fertile age. The physiological changes in T-helpers (Th1/Th2) activity balance during pregnancy can cause SLE flare. Women with SLE are at high risk for maternal and fetal complications. The high SLE activity is associated with higher risk of PE and lower birth weight, compared with population controls. Nevertheless, no detailed analysis of the relationship between clinical features/laboratory parameters and unfavorable pregnancy outcome in patients with SLE has been carried out in the recent studies.

Objectives: This study aimed to analyze influence of SLE activity, laboratory parameters and medications on risk of maternal and fetal complications.

Methods: A retrospective single-center cohort study 11/2014-12/2018: 43 pregnancies in 42 patients with proved SLE and > 20 weeks of gestation, mean age was 31,5 years. Renal function at conception and after delivery, pregnancy outcomes, clinical and laboratory parameters were collected. PE was diagnosed by the 2008 WHO criteria. The sFIT/PlGF ratio was used as the main differential marker to exclude lupus nephritis exacerbation in cases of increased proteinuria.

Age of the patients, SLE activity, hemoglobin and platelet levels, glomerular filtration rate, serum creatinine, AST, ALT, fibrinogen, D-dimer, aPTT, antinuclear factor and antiphospholipid antibodies concentrations, the using/non-use of glucocorticoids, hydroxychloroquine, low molecular weight heparins and aspirin were analyzed as potential risk factors of unfavorable pregnancy outcomes: PE, premature delivery, low birth weight, low Apgar score at 1 and 5 minutes after birth.

Results: In 12 cases (27.9%) there was no activity of SLE, in 16 cases (37.2%) there was low activity, in five (11.6%) – moderate, in three (7%) – high, in seven cases (16.3%) SLE activity was not assessed. SLE activity showed significant negative correlation with week at which labor occurred ($p = 0.003$, $R = –0.477$) and birth weight ($p = 0.005$, $R = –0.461$) and we found a significant fivefold increase in preeclampsia in patients with high activity of SLE ($p = 0.011$, OR = 4.95, 95% CI 1.449 to 16.931). Hemoglobin levels in third trimester correlated positively with birth weight ($p = 0.04$, $R = 0.322$). The dosage of glucocorticoids showed a significant correlation with week of delivery ($p = 0.011$, $R = -0.382$). Interestingly, the increase of aPTT in. the third trimester had an almost significant effect on the risk of developing PE ($p = 0.059$, OR = 1.237, 95% CI 0.958-1.596). Unfortunately, lupus anticoagulant (LA) at that moment was not measured. Other studied parameters were not associated with risk of PE.

Conclusion: High SLE activity significantly increases the risk of gestational complications and unfavorable pregnancy outcomes. We suggest that regular monitoring of antiphospholipid antibodies, especially LA, is needed. In this study, laboratory parameters did not significantly affect the risk of PE.

REFERENCES
[1] Zhang J.J. et al. A systematic review and meta-analysis of outcomes of pregnancy in CKD and CKD outcomes in pregnancy//Clin. J. Am. Soc. Nephrol. 2015. V. 10. № 11. P. 1964–1978.
[2] Skorpen C.G. et al. Influence of disease activity and medications on offspring birth weight, pre-eclampsia and preterm birth in systemic lupus erythematosus: A populationbased study//Ann. Rheum. Dis. 2018. V. 77. № 2. P. 264–269.
[3] Wu J. et al. Therapeutics and Clinical Risk Management Dovepress Management and outcomes of pregnancy with or without lupus nephritis: a systematic review and meta-analysis//Ther. Clin. Risk Manag. 2018. P. 14–885.
[4] Lightstone L., Hladunewich M.A. Lupus Nephritis and Pregnancy: Concerns and Management//Semin. Nephrol. 2017. V. 37. № 4. P. 347–353.

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AB1297 CARDIOVASCULAR EVENT AND RISK FACTORS IN PRIMARY SJÖGREN'S SYNDROME FROM LATIN-AMERICAN COHORT

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Background: Inflammation has been associated with higher cardiovascular risk in rheumatic autoimmune diseases. Primary Sjögren's syndrome (pSS) is associated with increased cardiovascular morbidity[1]. However, few and controversy data on the prevalence of cardiovascular events in patients with pSS have been reported[2,3] with no data regarding on Latin-American pSS patients.
Objectives: To assess the cardiovascular event and to evaluate its association with traditional and disease associated risk factors in pSS.
Methods: We included 455 patients with pSS according to AECG 2002 or ACR-EULAR 2016 classification criteria, attending tertiary referral centers from Brazil (n=183), Mexico (n=236) and Argentina (n=36). We retrospectively registered demographics, disease duration, cardiovascular event (CE) (coronary heart disease, cerebrovascular accident, peripheral arterial disease), smoking, and use of prednisone (PDN), immunosupressors and antimalarials. We evaluated traditional risk factors and scored the ESSDAI, ESSPRI and SSDDI at last follow-up.
Results: Most patients were female, miscigenous ethnicity, with median disease duration of 9.5 years. RF was positive in 48.5%, ANA in 85.6%, anti-Ro-SSA in 78.9% and anti-La-SSA in 43.1%. ESSDAI mean was 3.2 ±4.4, SSDDI 2.54±1.78 and ESSPRI 5.03±2.38. Fifty five percent used glucocorticoid in the past and 20% are currently using it, 33.4% are using immunosupressors, 44% antimalarials and 10.3% biological therapy. It was found 26 (5.7%, CI95% 3.73-8.37) CE. The prevalence of hypertension was 35.6%, diabetes 11.2%, dyslipidemia 27.7% and smoking 17.5%. In univariate regression analysis, aging, hypertension, diabetes, dyslipidemia and smoking were associated with CE. Beyond traditional risk factors, prednisone > 20mg/day, ESSDAI constitutional domain and ESSPRI fatigue were associated with CE. In multivariate analysis, aging OR= 1.037 (1.001-1.075, p= 0.043), hypertension OR=2.509 (1.028-6.128, p=0.043) and diabetes OR= 2.736 (1.059-7.070, 0.038) were independent risk for CE.
Conclusion: Traditional risk factors are independent risk for CE in pSS. Disease-associated factors, such as glucocorticoid, fatigue and disease activity seem to be associated and should be explored in larger samples.

REFERENCES
[1] Beltai A, et al. Cardiovascular morbidity and mortality in primary Sjögren syndrome: a systematic review and meta-analysis. Arthritis Care Res, 2018 (Epub ahead of print);
[2] Valim V, et al. Atherosclerosis in Sjögren's syndrome: evidence, possible mechanisms and knowledge gaps. Gerdts Clin Exp Rheumatol.34(1):133-42, 2016.
[3] Berardicurti O, et al. Cardiovascular Disease in Primary Sjögren's Syndrome. Rev Recent Clin Trial 13(3):164-169, 2018.

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AB1298 SAFETY AND EFFICACY OF PRIMARY YELLOW FEVER VACCINATION IN AUTOIMMUNE DISEASE: A PROSPECTIVE CONTROLLED STUDY

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Background: Alive vaccines should be used with caution in autoimmune diseases (AID).[1]
Objectives: To evaluate prospectively adverse events and efficacy of the Yellow Fever vaccine in patients with AID.
Methods: Prospective study, including 190 individuals, 47 with Rheumatoid Arthritis (RA), 36 primary Sjögren's Syndrome (SS), 48 Ankylosing Spondylitis (AS), 8 Systemic Sclerosis (SSc), 24 Systemic Lupus Erythematosous (SLE), and 29 Healthy Controls (HC). All individuals received 17DD (Biomanguinhos-FIOCRUZ) YF vaccine, for the first time during the 2017 Brazilian Campaign, aged ≥ 18 years, had no or low disease activity, low immunossupression. Exclusion Criteria: previous vaccination for yellow fever or PRNT > 1:50 at baseline, primary or secondary immunodeficiency, under treatment with cyclophosphamide, chlorambucil, mycophenolate mofetil, calcineurin inhibitors, azathioprine> 2mg/kg/day, prednisone ≥20mg/day, methotrexate >20mg/week or any immunobiological drug. Viremia (CRP) and plaque reduction neutralization test (PRNT; GeoMean title) were measured before (D0) and D3, D4, D5, D6, D7, D14, D28 after vaccine. Adverse events (AE) were registered through patient report diary and medical interview at D7, D14 and D28.
Results: Mean age was 52 years old for AID and 56 for HC. No serious adverse event was reported. However, mild local AE was more reported in AID as compared to HC (34.2% vs 3.4%, p=0.000). The frequency of AE was higher in AID compared to HC (34.1 vs. 3.4%). The Risk (Odds Ratio; 95%CI) for AE was 14.53 (1.9-109.7, p=0.000) and AID subgroups: RA=14.5 (1.8-116.2, p=0.0016), AS= 9.3 (1.1-76.2, p=0.0248), SS 25.1 (3.1-204.5, p<0.0001), SLE 9.3 (1.0-84.1, p=0.0377), SSc 56.0 (4.1-769.0, p=0.0014). The PRNT levels expressed in reverse of serum dilution was lower in AID 181 (144-228, p=0.04) as well in AS 112 (73-170, p<0.001), and in SLE 143 (61-332, p=0.01) as compared to HC 440 (291-665). The seropositivity rates were lower in AID after 28 days (78% vs. 96%, p=0.04) as well as in AS (73%, p=0.02) and SLE (73%, p=0.03) as compared to HC (Figure 1). Viremia peak was slightly late and low in AID (D6=5.8 x 10^3) compared to HC (D5= 8.3 x 10^3. Seropositivity was statistically lower at D14 in AID as compared HC (21% vs. 75%, p=0.04) and remained lower at D28 in AS and SLE subgroups.
Conclusion: Efficacy was lower in AID, especially in SLE and AS, in spite of viremia peak at D5-D6 similar to HC. Taking together, results suggest that YF vaccine is safe in AID with low disease activity and under low immunossupression, but probably a booster dose should be necessary.

REFERENCES
[1] Lopez A, Mariette X, Bachelez H, et al. Vaccination recommendations for the adult immunosuppressed patient: A systematic review and comprehensive field synopsis. Journal of Autoimmunity 2017;80:10-27

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AB1299 **AN ONGOING ANTICENTROMERE ANTIBODY RESPONSE ASSOCIATES WITH PROGRESSION TOWARDS SYSTEMIC SCLEROSIS**

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Background: Although some dated studies suggest a possible association between clinical characteristics and isotypes of anticentromere antibodies (ACA) in patients with systemic sclerosis (SSc), characteristics of ACA have not been described thoroughly in SSc.

Objectives:

1. Describe characteristics of anticentromere antibody (ACA) response in a large cohort of SSc patients.
2. Evaluate differences between ACA response between SSc patients fulfilling ACR 2013 criteria and those with very early diagnosis of SSc (VEDOSS).

Methods: ACA IgG, IgM and IgA levels were assessed in serum samples of patients visiting the Leiden SSc care pathway and who were IgG ACA+ at baseline. Patients had to fulfil either the ACR criteria or the VEDOSS criteria. Differences in isotype expression and levels between the two groups were evaluated, also with stratification for disease duration. Furthermore, in the SSc group we determined correlations between isotypes and disease duration and evaluated if isotype positivity was associated with clinical manifestations.

Results: ACA characteristics were measured in 167 ACA IgG+ patients. Thirty-five patients (21%) fulfilled the VEDOSS criteria and 132 (79%) the ACR criteria. ACA IgG+ patients displayed a broad isotype usage with 75% being ACA IgA+ and 68% being ACA IgM+ in serum. Patients within the SSc group showed higher ACA IgG levels and a higher percentage of ACA IgM positivity compared to the VEDOSS patients. Notably, these findings remained valid after stratification for disease duration, demonstrating that VEDOSS patients that did not progress to SSc within at least 5 years had lower ACA IgG levels and were less frequently positive for ACA IgM. In the SSc group, moderate correlations between isotypes were found; ACA IgM positivity was associated with occurrence of digital ulcers (p=0.02).

	Total group (n=167)	Very early SSc (n=35)	SSc (n=132)
Female, n(%)	150 (90)	34 (92)	116 (89)
Age, mean (SD)	58 (13)	55 (15)	58 (13)
Since RP, median(IQR)	12 (5-25)	10 (4-26)	13 (5-25)
Since non RP, median(IQR)	4 (1-11)	2 (1-5)	5 (1-12)
mRSS, median (IQR)	2 (0-4)	0 (0-0)	3 (0-5)
Teleangiectasia, n(%)	117 (70)	7 (20)	110 (83)
Digital ulcers, n(%)	33 (20)	0 (0)	33 (25)
ILD on HRCT, n(%)	13 (8)	0 (0)	13 (10)
PAH, n(%)	12 (7)	0 (0)	12 (9)
ACA characteristics			
IgA positivity, n(%)	125 (75)	26 (72)	99 (76)
IgA level [aU/mL], median (IQR)	73 (39-139)	76 (35-130)	73 (37-142)
IgM positivity, n(%)	114 (68)	**18 (50)**	**96 (73)***
IgM level [aU/mL]„ median (IQR)	64 (1-527)	21 (0-487)	65 (4-527)
IgG level [aU/mL]„ median (IQR)	361 (156-919)	**197 (94-530)**	**478 (183-1010)****

Table 1. Baseline characteristics IgG+ ACA patients. SSc= systemic sclerosis, ACA=anticentromere antibody, RP=Raynaud phenomenon, mRSS= modified Rodnan Skin Score, ILD= interstitial lung disease, HRCT= high resolution computed tomography, PAH= pulmonary arterial hypertension, Bonferroni correction applied * p= 0.03, ** p=0.03.

Figure 1

Conclusion: We observe a clear difference in the quality of the centromere-specific immune response between VEDOSS patients and SSc patients, also when stratifying for disease duration. The higher ACA IgG levels and presence of ACA IgM in SSc patients indicates that the ACA response in SSc is more pronounced showing signs of ongoing activity. These data indicate that the ACA B cell response is potentially relevant in disease development. In addition, ACA isotype expression and ACA IgG levels might contribute to better identify VEDOSS patients at risk for SSc development.

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AB1300 **AUTOIMMUNE/INFLAMMATORY SYNDROME INDUCED BY ADJUVANTS DUE TO SILICONE BREAST IMPLANT AND RHEUMATIC DISEASES:**

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Background: Silicone is considered biologically inert; thus it has been employed in many medical devices and nowadays is commonly used in plastic surgery for mammary prosthesis. The most common adverse reaction after silicone breast implant (SBI) is capsular contracture due to a foreign body reaction. Autoinmune Rheumatic Diseases (ARD) have been associated with SBI or siliconosis as part of the spectrum of Autoimmune/Inflammatory Syndrome Induced by Adjuvants (ASIA). Silicone is an adjuvant that may 'bleed' and subsequently may be a chronic stimulus to the immune.

Objectives: To determine the frequency of rheumatic diseases (ARD) and associated factors in patients with ASIA induced by SBI (ASIA-SBI).

Methods: This study was performed between 2012 to 2018 in a tertiary hospital from a cohort of 200 patients with ASIA (associated of oily substance, vaccines and siliconosis according to Shoenfeld criteria). We selected those patients with ASIA induced by SBI and clinical manifestations of any autoimmune disease. The clinical manifestations of ARD were evaluated and classified according to The American College of Rheumatology or EULAR criteria for some rheumatic diseases. We also investigated family history of autoimmune diseases, tobacco smoking coexisting allergies and comorbidities such as hypothyroidism, depression, anxiety and others. Main autoantibodies, histological findings were also evaluated. We used descriptive statistics for analysis.

Results: There were 30 women patients with mean age 48.5±16.3 46 years old, mean disease duration of disease 6±5.5 years. The mean time of appearance of clinical manifestations after SBI was 8 ±4.9 years. The rheumatic diseases (RD) or ARD were Systemic sclerosis (SSc) 7, Fibromyalgia (FM) 6, Systemic lupus erythematosus (SLE) 3, rheumatoid arthritis (RA) 6, overlap syndrome 2 (SSc plus SS and SLE plus SSc), Sjogren syndrome (SS) 1, Takayasu arteritis 1, Still disease 1, tunnel carpal syndrome 1, antiphospholipid syndrome 1 and angioedema and urticaria 1. We found family history of rheumatic disease in 40%, allergic history (food, drugs) in 40% and smoking in 50%. Hypothyroidism was observed in 30% and anxiety 30%. Patients were treated according to the rheumatic disease. Ten cases had their prostheses removed because extracapsular ruptured implants, with re-implantation of new prosthesis in 8 patients. Two patients experienced improvement of complaints after explantation of the implant.

Conclusion: We found a prevalence of ASIA associated to SBI of 15%. The main RD were SSc, FM and RA. We observed an association with family history, allergies and smoking in these patients.

Further studies are necessary to determine if SBI has a cause –effect relationship in the rheumatic disease manifestations.

REFERENCES

[1] Jara LJ, García-Collinot G, Medina G, Cruz-Dominguez MD, Vera-Lastra O, Carranza-Muleiro RA, Saavedra MA. Severe manifestations of autoimmune syndrome induced by adjuvants (Shoenfeld's syndrome). Immunol Res. 2016 Jul 13

[2] Colaris MJ, de Boer M,van der Hulst RR, Cohen Tervaert JW,Two hundreds cases of ASIA syndrome following silicone implants: a comparative study of 30 years and a review of current literature. Immunol Res. 2016 Jul 13.

[3] Watad A, Quaresma M, Brown S, Cohen Tervaert JW, Rodríguez-Pint I, Cervera R, Perricone C, Shoenfeld Y. Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome) - An update. Lupus. 2017 Jan 1:961203316686406.

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AB1301 IMMUNE REGULATION THERAPY PROMOTED THE RECANALIZATION OF CORONARY ARTERY IN A PATIENT WITH ANTIPHOSPHOLIPID SYNDROME: A CASE REPORT AND LITERATURE REVIEW

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Background: Thrombosis is considered as a major feature of antiphospholipid syndrome (APS). Once formed, thrombosis will threaten life and long-term oral anticoagulant therapy is required. In addition, some patients underwent percutaneous coronary intervention (PCI), but in-stent restenosis (ISR) is the most common complication of PCI. There is currently insufficient treatment for such patients. Because APS is an autoimmune disease, we developed a new therapy (Sirolimus based immunomodulatory) to treat a APS patients with ISR after PCI.
Objectives: Assess the degree of stenosis of the various branches of the coronary arteries, and to observe the changes in the number of regulatory T cells (Tregs) in the peripheral blood of patients.
Methods: An APS patient with coronary artery involvement was found in-stent restenosis after implantation of the stent. After sirolimus and other immunomodulatory treatments, coronary angiography and coronary CTA were performed to assess the degree of stenosis of the various branches of the coronary arteries, and to observe the changes in the number of regulatory T cells (Tregs) in the peripheral blood of patients.
Results: After 6 months of immunomodulation therapy, the patient did not have clinical symptoms such as chest tightness and tightness. Four consecutive coronary angiography and coronary CTA (dual source) showed disappearance of left main plaque. Stenosis, the degree of stenosis in the anterior descending stent was reduced from 90% to 66%; the degree of right coronary stenosis was reduced from 50% to 30%, new stenosis and new thrombosis did not occur in other branches. The absolute number of Treg cells in peripheral blood gradually increased from 34.41 to 50.83 cells/μL.
Conclusion: Sirolimus is an inhibitor of mTOR that is a serine/threonine kinase in two different complexes (mTORC1 and mTORC2) to promote cell proliferation and neovascularization. Antiphospholipid antibodies activate the mTOR pathway in endothelial cells in culture. When pretreated with mTOR inhibitors prevents this process from occurring. Sirolimus specifically inhibits the mTOR pathway and prevents neointimal hyperplasia and neovascularization in the coronary arteries. In ASP patients with coronary artery involvement, the reduction of Treg cells may also be an important cause of immune tolerance deficiency. Sirolimus also increased the number of Treg cells. If early use of immunomodulators such as sirolimus for prophylaxis, it may prevent re-stenosis after stenting. The successful treatment of this patient also provided us with new diagnostic and therapeutic ideas.

REFERENCES

[1] Chinese Medical Association Rheumatology Branch. Guidelines for the diagnosis and treatment of antiphospholipid syndrome. Chinese Journal of Rheumatology, June 2011, Vol. 15, No. 6.
[2] Nayak AK,Komatireddy G.Cardiac manifestations of the antiphospholipid antibody syndrome: a review. Mo Med.2002 Apr;99(4):171-8.
[3] Liu J, Liu Y, Jia K, et al. Clinical analysis of lectin-like oxidized low-density lipoprotein receptor-1 in patients with in-stent restenosis after percutaneous coronary intervention.Medicine (Baltimore).2018 Apr;97(17):e0366.
[4] Watanabe R, Wei L, Huang J. mTOR signaling, function, novel inhibitors, and therapeutic targets. J Nucl Med.2011 Apr;52(4):497-500.
[5] Van Laecke S, et al. Inhibition of the mTORC pathway in the antiphospholipid syndrome. N Engl J Med.2014 Jul 24;371(4):303-12.

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AB1302 SOCIAL MEDIA USE IN SYSTEMIC LUPUS ERYTHEMATOSUS IMPACT ON PREVALENCE OF ANXIETY AND DEPRESSION

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Background: The psychological problems of patients with Systemic lupus erythematosus (SLE) have been widely concerned. Studies found that the SLE patients showed a prevalence of depression in SLE cohorts ranging from 17% to 75%, and anxiety being 6%-52%[1, 2]. Factors contributing to mood disorders are various[3]. As a nontraditional form of media, social media has become increasingly popular worldwide[4]. Previous study has demonstrated that social media use (SMU) plays a significant role in adolescents' psychological functioning[5-8], whether SMU could impact the mental health of SLE patients, no previous finding of SMU on SLE patients is reported.
Objectives: We aimed to explore the potential association of the patterns of social media use (SMU) with anxiety and depression in patients with systemic lupus erythematosus (SLE).
Methods: The relevant data were collected from 402 SLE patients aged 18-60 years in the First Affiliated Hospital of Zhengzhou University between July 2018 and October 2018 for subsequent analysis. Demographic and clinical characteristics, the patterns of SMU, the reasons and barriers to SMU were recorded. Anxiety and depression were assessed using hospital anxiety and depression scale (HADS). Adjusted estimates of association were derived using logistic regression.
Results: The incidence of anxiety and depression were 41.1% and 28.4% respectively among SLE patients with a mean score of 6.71±3.65 and 5.45±3.86 in each subscale. Patients without social media were more likely than those with social media to develop anxiety or depression (P 0.05, P 0.01). A correlation was found between the frequency of SMU and the incidences of anxiety (P 0.05) and depression (P 0.001), besides, the presences of depression also had a association with the duration for SMU (P 0.05).
Conclusion: Depression and anxiety are prevalent in patients with SLE and high frequency of SMU may decline the risks of anxiety and depression, to educate patients use social media properly may result in alleviation of anxious and depressive symptoms in patients with SLE.

REFERENCES

[1] Macedo EA, Appenzeller S, Costallat LTL. Depression in systemic lupus erythematosus: gender differences in the performance of the Beck Depression Inventory (BDI), Center for Epidemiologic Studies Depression Scale (CES-D), and Hospital Anxiety and Depression Scale (HADS). Lupus 2018;27(2):179-89.
[2] Jolly M, Sequeira W, Block JA, et al. Sex Differences in Quality of Life in Patients With Systemic Lupus Erythematosus. Arthritis Care Res (Hoboken) 2018
[3] Tay SH, Cheung PP, Mak A. Active disease is independently associated with more severe anxiety rather than depressive symptoms in patients with systemic lupus erythematosus. Lupus 2015;24(13):1392-9.
[4] Nikiphorou E, Studenic P, Ammitzboll CG, et al. Social media use among young rheumatologists and basic scientists: results of an international survey by the Emerging EULAR Network (EMEUNET). Ann Rheum Dis 2017;76(4):712-15.
[5] Escobar-Viera CG, Shensa A, Bowman ND, et al. Passive and Active Social Media Use and Depressive Symptoms Among United States Adults. Cyberpsychol Behav Soc Netw 2018;21(7):437-43.
[6] Shensa A, Escobar-Viera CG, Sidani JE, et al. Problematic social media use and depressive symptoms among U.S. young adults: A nationally-representative study. Soc Sci Med 2017;182:150-57.
[7] Berryman C, Ferguson CJ, Negy C. Social Media Use and Mental Health among Young Adults. Psychiatr Q 2018;89(2):307-14.
[8] Griffiths S, Murray SB, Krug I, et al. The Contribution of Social Media to Body Dissatisfaction, Eating Disorder Symptoms, and Anabolic Steroid Use Among Sexual Minority Men. Cyberpsychol Behav Soc Netw 2018;21 (3):149-56.

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AB1302B CHRONIC KIDNEY DISEASE IN RHEUMATOID ARTHRITIS: PREVALENCE AND RISK FACTORS

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Background: The problem of chronic kidney diseases (CKD) in rheumatoid arthritis (RA) patients have not been fully studied. The role of biological therapy (BT) is poorly understood.
Objectives: Aim of the study was to examine the prevalence, risk factors and histological variants of CKD in RA, and impact of pharmacotherapy.
Methods: 135 patients with RA from 2013 to 2018 were enrolled in this study. Age, gender, duration of RA, drug therapy, ESR, CRP, DAS28, renal function, proteinuria (PU), histological variants were analyzed. Arterial hypertension, weight index, serum lipids and glucose levels were also assessed.
Results: The incidence of CKD in RA was 30.4% (41 from 135). CKD 3-4 stages with eGFR < 60ml/min/1.73m^2 was detected in 14.8%

patients. The duration of the disease, high ESR and DAS28 score, NSAIDs treatment and hyperlipidemia were risk factors for CKD in RA (Fig 1). We also found negative correlation between the DAS28 and eGFR (Fig. 2).

Amyloidosis was the most common histologic pattern (51.52%), followed by chronic glomerulonephritis (CGN) (24.24%) and tubulo-interstitial nephritis (24.24%). Among CGN mesangial glomerulonephritis was the most frequent (Table 1). Renal amyloidosis was associated with a duration of RA, presence of systemic symptoms and CRP level.

The levels of PU were lower, and eGFR levels were higher in patients treated with BT than in patients treated with synthetic disease-modifying anti-rheumatic drugs (DMARDs) (Fig 3).

Conclusion: CKD is often developed in patients with high RA activity. Treatment with biological agents is associated with a lower PU and higher GFR levels.

REFERENCES:

[1] Tokoroyama T, Ando M, Setoguchi K, Tsuchiya K, Nitta. K. Prevalence, incidence and prognosis of chronic kidney disease classified according to current guidelines: a large retrospective cohort study of rheumatoid arthritis patients. Nephrol Dial Transplant (2016) 0: 1–8 doi: 10.1093/ndt/gfw315

[2] Masako Kochi, Kentaro Kohagura, Yoshiki Shiohira,Kunitoshi Iseki, and Yusuke Ohya Inflammation as a Risk of Developing Chronic Kidney Disease in Rheumatoid Arthritis. PLoS One. 2016; 11(8): e0160225

[3] Kim HW, Lee CK, Cha HS, Choe JY, Park EJ, Kim J. Effect of anti-tumor necrosis factor alpha treatment of rheumatoid arthritis and chronic kidney disease. Rheumatol Int. 2015 Apr;35(4):727-34. doi: 10.1007/s00296-014-3146-4.

Abstract AB1302B Table 1. Renal histopathologic findings in RA patients (n=33)

Histological forms	n	%
Amyloidosis:	**21**	63.7
Chronic	**12**	36.3
glomerulonephritis:	7	21.2
- Mesangial GN:	4	12.1
IgA nephropathy	1	3.0
IgM nephropathy	2	6.0
Membranoproliferative	1	3.0
GN	1	3.0
- Minimal change disease	3	9.1
- Membranous nephropathy		
- Diffuse nephrosclerosis		

Figure 1. Laboratory data in RA patients

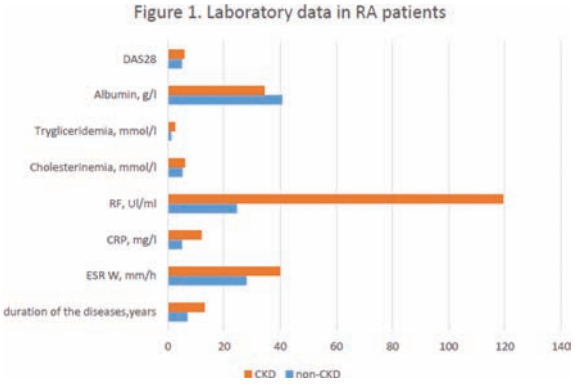


Figure 1

Figure 2. Correlation between eGFR and DSA28

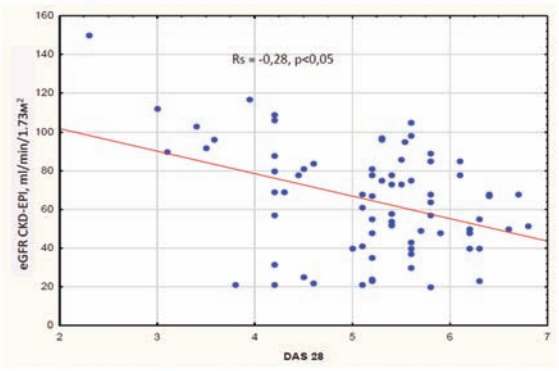


Figure 1

Figure 3. eGFR in RA patients treated with synthetic and biological DMARDs

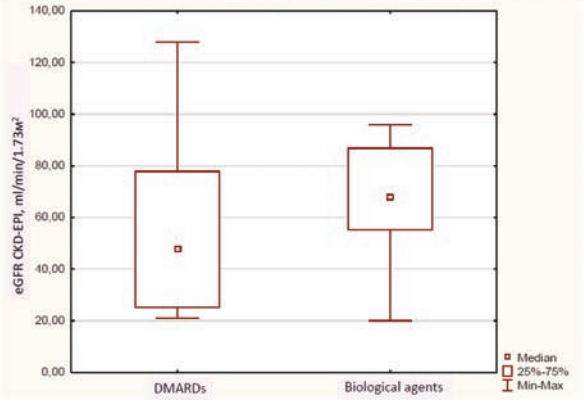


Figure 1

Disclosure of Interests: None declared

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AB1302C

SERUM IMMUNOGLOBIN G4 LEVEL IN DIFFERENT TYPES OF MALIGNANCY WITHOUT IMMUNOGLOBIN G4 RELATED DISEASE

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Background: High levels of serum immunoglobulin G4 (IgG4) would comprise a useful diagnostic tool in IgG4-related disease (IgG4-RD), but little information is available about IgG4 in conditions other than IgG4-RD such as malignancies. Previous studies indicate that IgG4-RD is a strong risk factor for malignancy development.

Objectives: The aim of this study is to evaluate the level of serum IgG4 in different malignancy without IgG4-RD.

Methods: 90 patients with malignancy were enrolled between March 1st and August 30th, which have been excluded with IgG4-RD. All samples were collected before treatment. Diagnosis of malignancy was determined by histological result. The levels of serum IgG4 were determined by

nephelometric assay. The cut-off value of serum IgG4 was 201 mg/dl. We compared the levels of serum IgG4 among patients with different types of malignancy.
Results: (1) Among the 90 patients, 18 patients were gallbladder carcinoma, 6 patients were lung carcinoma, 34 patients were liver carcinoma, 6 patients were gastrointestinal carcinoma, and 19 patients were pancreatic carcinoma. 68 (75.56%) patients were male and mean age was 52.8 ± 15.5 yrs. The mean value of serum IgG4 was 146.7±147.6 mg/dl, and 21 (23.3%) of patients have elevated serum IgG4. (2) Serum IgG4 level in gastrointestinal carcinoma is the highest (237.8±50.92 mg/dl), but the sample is too small. Serum IgG4 level in liver carcinoma was higher than other types of malignancy (180.5 ± 32.04 mg/dl. vs gallbladder carcinoma 114.4 ± 15.01 mg/dl, p<0.01. vs pancreatic carcinoma 91.63 ± 19.89 mg/dl, p<0.01. vs lung carcinoma 67.47 ± 11.75 mg/dl, P<0.01).
Conclusion: Elevated serum IgG4 level is common in patients with malignancies, while patients with liver carcinoma have significant higher serum IgG4 level than those with gallbladder carcinoma, pancreatic carcinoma and lung carcinoma. This suggests that IgG4 may have different role in different types of tumor.

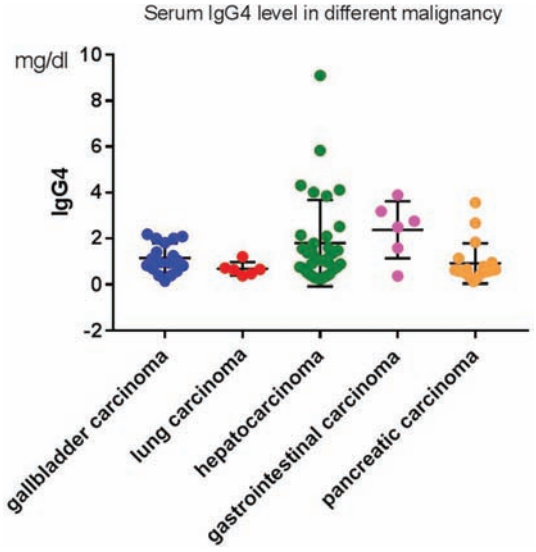


Figure 1

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.2807

Validation of outcome measures and biomarkers

AB1303 FUNCTIONAL AND PROFESSIONAL OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatism in adults. It affects the synovial membrane, evolves by outbreaks and can lead to joint destruction. It generates a physical disability that causes an impairment of quality of life and professional activity.
Objectives: To study the socio-demographic, clinical and professional characteristics of patients and to assess the impact of RA on quality of life and professional activity.
Methods: We conducted a retrospective, descriptive study on patients' files, followed at the rheumatology department of LA RABTA university hospital, for RA aver a period of ten years. The target population was patients having a professional activity at the time of the discovery of the disease. We assessed disease activity by the Disease Activity Score DAS28-CRP, work impact by the "Work Productivity and Activity Impairment" questionnaire (WPAI:RA) and quality of life by the Health Assessment Questionnaire (HAQ). The data was entered into an excel table and analyzed using SPSS software version 19.0. In all statistical tests, the significance level was set at 0.05.
Results: We collected 25 cases of RA. Mean age was 50.36 ± 8.28 years with a sex ratio of 1.08. The mean age of RA was 9.8 years and the mean age of onset was 40.56 ± 9.84 years. The study population occupied a manual job in 84% of cases. The average professional seniority was 21.76 ± 12.83 years. Patients reported having stopped work because of their illness in 44% of cases. The mean of DAS28-CRP was 4.32 ± 1.57, 72% of the study population had moderate to severe RA activity. The mean HAQ was 1.38 ± 0.69 with 76% of cases suffering from "moderate to severe" or "severe to very severe disability". The evaluation of the work productivity and activity impairment by the WPAI:RA questionnaire objectified an absenteeism of 30.7 ± 9.4%, a presenteeism of 46.7 ± 26.4%, a work productivity loss of 60.4 ± 33.8% and an activity impairment of 57.2 ± 25.4%. A positive and statistically significant correlation was noted between the results of WPAI and HAQ, between the results of WPAI (except absenteeism) and DAS286CRP and between HAQ and DAS28-CRP.
Conclusion: RA causes a significant functional disability that affects the professional activity and quality of life of patients. Early diagnosis and treatment of this disease can slow the progression o the disease. Occupational medicine plays an important role in the early detection and maintenance of employees with RA at work.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.7926

AB1304 THE RHEUMATOID ARTHRITIS FLARE QUESTIONNAIRE (RA-FQ) IS AN EASY TO ADMINISTER PATIENT-REPORTED OUTCOME MEASURE THAT TRACKS WELL WITH THE CLINICAL DISEASE ACTIVITY INDEX (CDAI) OVER TIME IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS (ERA) IN 2 DIFFERENT HEALTH SETTINGS

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Background: RA patients may cancel scheduled visits with their rheumatologist. In clinical practice, a validated patient-reported disease activity measure that tracks well with traditional clinical indices could address an important gap by providing real-time information on RA disease activity when a visit to the rheumatologist is not possible.
Objectives: To assess concordance between the 5-item patient-reported Rheumatoid Arthritis Flare Questionnaire (RA-FQ) ([1,2]) and the Clinical Disease Activity Index (CDAI) in patients with early RA (ERA) treated in rheumatology clinics in 2 countries with different health systems.
Methods: Data were analyzed from patients enrolled in the Canadian early ArThritis CoHort (CATCH) between Nov 2011 and March 2017 and in the Consortium of early ArThritis Cohorts- USA (CATCH-US) from Dec 2014 to Dec 2018. Both observational studies had a similar design; enrolled patients diagnosed with EIA (< 1 year of persistent symptoms) by a rheumatologist who completed similar regular protocolized clinical assessments, laboratory investigations and PROMs. The RA-FQ, designed to assess worsening of RA Inflammation, is a short composite PROM (total score 0-50) that sums 5 single items (NRS 0-10) querying pain, fatigue, stiffness, function and participation. The present analysis includes patients meeting ACR 1987 or 2010 ACR/EULAR criteria, with RA-FQ and CDAI at baseline and at least 1 other follow up (FU) over 12-months. We compared mean scores of the RA-FQ and CDAI over time and calculated intraclass correlation coefficients (ICC) to assess concordance between measures in the 2 cohorts.
Results: The study included 818 Canadian and 75 American early RA patients. Age, male sex, and disease activity was higher in the Canadian cohort, while post-secondary education was higher in the US cohort (Table1). RA-FQ and CDAI scores tracked closely with one another over time in both cohorts (Canada ICC: 0.76; US ICC: 0.80)
Conclusion: There was high concordance between the RA-FQ and CDAI measures over the 1st year of follow up in 2 early RA samples recruited in 2 countries. The RA-FQ may help patients and clinicians track patient disease activity between clinic visits.

Table: Patient and Disease Characteristics at Study Entry

Mean (SD) or%	CATCH (N=818)	CATCH-US (n=75)	p
Age, years	55 (15)	47 (16)	<0.001
Female,	72%	84%	0.028
Caucasian/White,	80%	76%	0.401
Education (High School or less)	42%	12%	<0.001
Symptom duration (months)	5.5 (2.9)	6.0 (3.3)	0.188
Seropositive (RF or ACPA),%	74%	77%	0.690
CDAI	28.0 (14.0)	14.4 (11.9)	<0.001
RA-FQ	26.7 (13.3)	16.0 (12.4)	<0.001

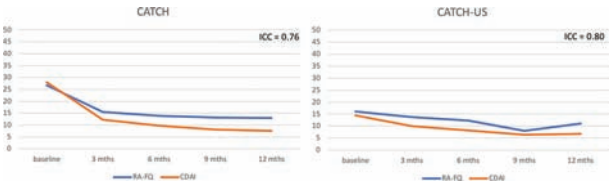


Figure 1. Mean RA-FQ and CDAI scores over 12-months Follow Up in Canadian and US Early Rheumatoid Arthritis Cohorts.

REFERENCES:

[1] Bykerk VP et al. RMD Open, 2016
[2] Bartlett SJ et al. J Rheumatol. 2017

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Disclosure of Interests: Vivian Bykerk Grant/research support from: Mallinckrodt, BMS, Crescendo Biosciences, Sanofi/Regeneron., Consultant for: Amgen, Pfizer, UCB, Scipher, Sanofi/Genzyme/Regeneron, Orit Schieir: None declared, Marie-France Valois: None declared, Glen Hazlewood : None declared, Gilles Boire Grant/research support from: Investigator-initiated studies: Amgen, Abbvie, BMS, Eli Lilly, Merck, Novartis, Pfizer, Consultant for: Advisory boards: Amgen, BMS, Celgene, Eli Lilly, Pfizer, Speakers bureau: Merck, BMS, Pfizer, CArol Hitchon Grant/research support from: Pfizer, UCB (unrelated studies), Louis Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant for: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Speakers bureau: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Carter Thorne Grant/research support from: Investigator-initiated studies: Amgen, Pfizer. RCTs: Abbvie, Celgene, CaREBiodam, Novartis, Pfizer, Consultant for: Advisory board: Abbvie, Amgen, Celgene, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi. Consultant: Abbvie, Centocor, Janssen, Lilly, Medexus/Medac, Pfizer, Speakers bureau: Medexus/Medac, Edward Keystone Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, Consultant for: AbbVie, Amgen, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Celltrion,
Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Gilead, Janssen Inc, Lilly
Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, UCB., Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Diane Tin: None declared, Caroline Benson: None declared, Janet Pope Consultant for: Eli Lilly and Company, Clifton Bingham Grant/research support from: BMS, Consultant for: AbbVie, BMS, Eli Lilly, Genentech/Roche, Janssen, Pfizer, Sanofi/Regeneron, Susan J. Bartlett Consultant for: Pfizer, UCB, Lilly, Novartis, Merck, Jansen, Abbvie

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AB1305

EVALUATION OF SERUM LEVELS OF ASC FOR THE DIAGNOSIS AND MONITORING OF CRYOPYRIN ASSOCIATED PERIODIC SYNDROMES (CAPS)

Fortunata Carbone[1], Teresa Micillo[2], Luca Cantarini[3], Maria Alessio[2], Alma Nunzia Olivieri[4], Maria Francesca Gicchino[4], Antonella Insalaco[5], Maria Cristina Maggio[6], Orso Maria Lucherini[3], Roberto Scarpioni[7], Matteo Piga[8], Maria Maddalena Angioni[8], Laura Obici[9], Antonella Simpatico[3], Pietro Leccese[10], Rita Consolini[11], Raffaele Manna[12], Paolo Sfriso[13], Sara Bindoli[13], Paola Galozzi[13], Ida Orlando[3], Sabrina Chiesa[14], Marco Gattorno[14], Giuseppe Matarese[1,15]. *[1]Istituto per l'Endocrinologia e l'Oncologia Sperimentale-Consiglio Nazionale delle Ricerche (IEOS-CNR), Napoli, Italy*; *[2]Università degli Studi di Napoli "Federico II", Napoli, Italy*; *[3]Università di Siena, Siena, Italy*; *[4]Università degli Studi della Campania "Luigi Vanvitelli", Napoli, Italy*; *[5]IRCCS Ospedale Bambino Gesù, Roma, Italy*; *[6]Ospedale dei Bambini "Di Cristina", Palermo, Italy*; *[7]Ospedale AUSL "Guglielmo da Saliceto", Piacenza, Italy*; *[8]Reumatologia, Policlinico Universitario, Cagliari, Italy*; *[9]Fondazione IRCCS Policlinico San Matteo, Pavia, Italy*; *[10]Ospedale San Carlo, Potenza, Italy*; *[11]Università di Pisa, Pisa, Italy*; *[12]Policlinico Gemelli Università Cattolica, Roma, Italy*; *[13]Department of Medicine, DIMED, University of Padova, Padova, Italy*; *[14]IRCCS Istituto Giannina Gaslini, Genova, Italy*; *[15]Università degli Studi di Napoli "Federico II", Dipartimento di Medicina Molecolare e Biotecnologie Mediche, Napoli, Italy*

Background: Dominantly gain-of-function mutations in the NLRP3 gene lead to Cryopyrin associated periodic syndromes (CAPS) characterized by constitutive activation of the inflammasome, increased secretion of interleukin (IL)-1beta and IL-18, and systemic inflammation. IL-1beta and active caspase-1 subunits are released in the serum together with the oligomeric particles of the adaptor ASC (apoptosis-associated Speck-like protein with a caspase-recruitment domain) after activation of the inflammosome complex and, as a consequence, patients with CAPS show an increased serum concentration of ASC^+ particles.

Objectives: Patients suffering from CAPS are characterized by clinical manifestation similar to other autoinflammatory diseases. This phenomenon together with the lack of specific laboratory tests makes difficult the diagnosis of CAPS. In this context the development of a test for the evaluation of serum ASC levels could provide novel biomarkers facilitating early disease diagnosis and able to monitor treatment responses.

Methods: We analysed, with a novel ELISA assay, the levels of ASC particles in serum and plasma of normal subjects, CAPS patients and patients with autoimmune disorders (Multiple Sclerosis (MS), Type 1 Diabetes (T1D) and juvenile idiopathic arthritis), to confirm that ASC presence in the serum is not due to other chronic inflammatory processes characterizing autoimmunity. To evaluate the specificity of this biomarker in CAPS patients and not in individuals suffering from others inflammatory disorders, we also analysed sera from TNF receptor–associated periodic syndrome (TRAPS) patients.

Results: ASC particles were higher **in** untreated CAPS patients with respect to healthy controls and patients suffering from MS and T1D. This tendency was also evident in patients with arthritis and TRAPS even if the difference was not statistically significant due to the small number of samples. In addition after pharmacological treatment there is a tendency to be confirmed through a reduction of ASC levels in CAPS patients.

Conclusion: These data suggest that ELISA quantitation of ASC protein could represent a novel and additional strategy for the diagnosis and monitoring of CAPS.

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AB1306 PILOT STUDY OF ADHERENCE IN PATIENTS WITH RHEUMATOLOGICAL DISEASES AUTOIMMUNE

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Background: Data on adherence in patients with autoimmune rheumatological diseases are limited.
Objectives: To analyze the adherence to treatment in patients with autoimmune rheumatological diseases.
Methods: A cross-sectional study was performed in patients from the Complexo Hospitalario Universitario de Pontevedra with diagnosis of systemic lupus erythematosus (SLE), Sjögren's Syndrome (SS) and Systemic Sclerosis (SE).
The patients filled an anonymous survey that included data about demographic, diagnosis and treatment. Adherence to treatment was assessed using the Spanish Compliance Questionnaire in Rheumatology (sCQR). [1] Likewise, a linear regression analysis was carried out in order to identify factors related to adherence to treatment. A significant value was considered as $p < 0.05$. Stata version 11.1 (Stata/IC 11.1 for Windows, StataCorp LP, College Station, TX) was used to perform all analyzes.
Results: A total of 44 patients participated in the study, although 90.9% of the surveys carried out could be used for the analysis. A total of 25 (62.5%) SLE, 9 (22.5%) SS and 6 (15.0%) SE patients participated. There were 82.5% of women and the mean age was 48.9 ± 12.8 (See Table 1). According to the sCQR 82.5% were compliant patients. None of the studied variables was associated with the adherence rate: sex ($p = 1.000$), age (0.134), time of evolution ($p = 1.000$), level of education ($p = 0.677$), marital status (0.392), illness ($p = 1.000$), number of drugs ingested per day ($p = 0.873$), treatment with steroids ($p = 0.679$) or antimalarials ($p = 1.000$).
Conclusion: The adherence rate in our cohort was 82.5% higher than previously reported in other studies. [2,3] The sCQR could be a useful and easy-to-apply tool for the study of adherence in these patients.

REFERENCES

[1] Salgado E, Maneiro Fernandez JR, Souto Vilas A, Gomez-Reino JJ. Correction to: Spanish transcultural adaptation and validation of the English version of the compliance questionnaire in rheumatology. Rheumatol Int 2018.
[2] Feldman CH, Yazdany J, Guan H, Solomon DH, Costenbader KH. Medication nonadherence is associated with increased subsequent acute care utilization among Medicaid beneficiaries with systemic lupus erythematosus. Arthritis Care Res 2015;67:1712–21.
[3] Alsowaida N, Alrasheed M, Mayet A, Alsuwaida A, Omair MA. Medication adherence, depression and disease activity among patients with systemic lupus erythematosus. Lupus. 2018 Feb;27(2):327-332. doi: 10.1177/0961203317725585. Epub 2017 Aug 21. PubMed PMID: 28825347.

Table 1. Clinical and sociodemographic characteristics of the patients

	N=40		N=40
Age (years), mean, n (%)	48.9 ±12.8	**Evolution, n (%)**	
Sex (women), n (%)	40 (82.5)	**• < 1 year**	2 (5.0)
Marital status, n (%)		**• 1-2 years**	3 (7.5)
• Single	14 (35.0)	**• 2-5 years**	8 (20.0)
• Married	25 (62.0)	**• > 5 years**	27 (67.5)
• Widows/Widower	1 (2.5)	**• Number of drugs ingested per day, n (%)**	
Education, n (%)		**• 1**	9 (22.5)
• None	3 (7.5)	**• 2**	5 (12.5)
• Primary	13 (32.5)	**• 3**	11 (27.5)
• Secondary	10 (25.0)	**• 4**	4 (10.0)
• Superior/University	1 (2.5)	**• 5**	2 (5.0)
Occupation, n (%)		**• >5**	9 (22.5)
• Student	1 (2.5)	**Treatments, n (%)**	
• Unemployed	2 (10.0)	**. Antimararial**	21 (52.5)
• Active	20 (50.0)	**. Steroids**	14 (35.0)
• Job loss	1 (2.5)	**. Methotrexate**	5 (12.5)
• Retirement	8 (20.0)	**. Azathioprine**	1 (2.5)
Diagnosis, n (%)		**. Rituximab**	1 (2.5)
• SLE	25 (62.5)		
• SS	9 (22.5)		
• SE	6 (15.0)		

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AB1307 STUDY OF CONCORDANCE AND EQUIVALENCE AMONG BARTHEL, LAWTON, HAQ AND BASFI QUESTIONNAIRES IN RHEUMATOID AND SPONDYLOARTHRITIS PATIENTS

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Background: Assessment of functional capacity of patients is usually performed using disease-specific questionnaires for rheumatoid arthritis (HAQ) and for axial spondyloarthropathies (BASFI). However, frequently non disease-specific, general indexes such as Barthel and Lawton-Brody (LB) are used to establish disability in legal environtments and in emergency rooms. Few studies have compared specific vs. generic questionnaires in rheumatic patients (1).
Objectives: To assess the equivalence between disability questionnaires of generic type, applicable to general population and various diseases (Barthel and LB), with specific questionnaires for rheumatic diseases (HAQ and BASFI).
Methods: A cross-sectional study was conducted in consecutive outpatients with inflammatory rheumatic diseases (rheumatoid arthritis, psoriatic arthritis, spondyloarthropathies) in usual daily clinical practice in a rheumatology clinic of a tertiary hospital.
The patients self-completed the questionnaires (Barthel, LB, HAQ, and BASFI) in a single session. HAQ was only filled by peripheral arthritis patients, while BASFI was only given to spondyloarthropathy subjects. Scores were also computed for SDAI, DAS28 and BASDAI in most patients. Intraclass correlation was used to measure concordance between questionnaires.
Results: A total of 214 patients where studied. There was good correlation between the scores of the indexes studied, especially between the two general questionnaires ($R = 0.45$ $p < 0.01$). We observed a high ceiling effect in the scores of both Barthel, (70% of patients obtained values> 95 over a maximum of 100) and Lawton-Brody (60% had values> 23 over a maximum of 24) tests. The disease-specific questionnaires showed a less skewed distribution. The agreement between Barthel's and Lawton's tests was significant when measured by the intraclass correlation ($R = 0.48$ $p < 0.01$). However, we could not find any significant correlation between the generic questionnaires and the HAQ questionnaire or the BASFI ($R < 0.3$).
Conclusion: The Barthel and Lawton-Brody indices show an important ceiling effect in rheumatic patients, and seem to evaluate dimensions of health other than rheumatic questionnaires such as HAQ and BASFI, and thus they are not interchangeable. This point must be taken into account when performing medicolegal or emergency room assessments. Our result is in line with other previous studies(1)

REFERENCE

[1] Zochling J, Stucki G, Grill E, Braun J. A comparative study of patient-reported functional outcomes in acute rheumatoid arthritis. J Rheumatol 2007;34(1):64–9.

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AB1308 FAILURE TO BIOLOGICAL THERAPY: WHEN TO EXPECT IT?

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Background: Using Biologic agents, has considerably improved the treatment of inflammatory diseases.But it is associated to thecapacity of inducing an immune response in patients that could result in unwanted adverse events or treatment failure.

Objectives: The aim of this work was to compare the clinical and biological response to biotherapy with the presence of ADA and the residual dose rate.
Methods: We analysed the medical records of 69 patients treated with biotherapy between September 2017 and October 2018.3 pathologies were considered: rheumatoid Arthritis (RA) diagnosed by ACR/EULAR 2009 criteria, Spondylarthritis (SPA) according to Assessment of Spondylarthritis international Society (ASAS) And crohn'sdisease (CD) classified upon the 2006' Montreal classification. We did search the presence of anti-bodyanti-drugs (ADA) and the residual dose for the following therapies: Etanercept (ETN),Infliximab (IFX), Adalimumab (Ada)or Rituximab (RTX).
Results: The mean age was 43.33 ± 11.4 year. The sexratio M/F was 1.57.
Regarding the RA: they were 13 patients. 10 had positive (ACPA) and seven positive (RF). All the patients had an initial treatment by conventional synthetic disease modifying antirheumatic drugs(csDMARDs) before moving to bDMARDs. 14 were in concomitant disease modifying therapy. The DAS28-ESR average was at 4.12 [2.67 à 5.79]. we found positive ADA in only one patient analysis. There were 8 responding versus five non-responding patients,according to the clinical and biological evaluation of disease activity.
28 patients were In the SPA group: 13 with an axial spondyloarthritis. 14% had the HLAB 27. It was an active disease in 15 cases. ASDAS-CRP average was 4,87 ± 0,17 [4.7; 5]. The received biotherapy was IFX 50%, ETN 28.6% and Ada 21.4%. 10 patients had a positive ADA and 8 of them had a rate superior to 100 UI. 19 patients were considered as non-Responding.
In the CD group, 28 patients were enrolled. All oft hem had a previous immunosupressor treatment. Same patients in association with biotherapy. It was positve ADA in 7 cases. And 7 patients were non-responding to the treatment.
The residual dose of drugs was calculated for each drug and it is explained in the following table :

	IFX		Ada		ETN		RTX	
	%	N	%	n	%	n	%	n
High Residual dose	60%	21	52.9%	9	90.9%	10	66.7%	4
Low residual dose	40)	14	47.1%	8	9.1%	1	33.3%	2

Positve ADA was associated with therapy failure in all type of biotherapy (p=0.001). A low residual dose was associate to therapy failure only in the case of IFX (p=0.005).
In multivariate analyses, the predictive factors associated with therapeutic failure were : positive ADA(p=0.008)and advanced age at diagnosis, bellow 30 years old age (p=0.020). Hosmer index=0.452.
Conclusion: Immune response induced in patients treated with biotherapy can be quantified now thanks to ADA dosage and the residual dose assessment.

REFERENCES

[1] Kristensen LE, Kapetanovic MC, Gülfe A, Söderlin M, Saxne T, Geborek P. Predictors of response to anti-TNF therapy according to ACR and EULAR criteria in patients with established RA: results from the South Swedish Arthritis Treatment Group Register. Rheumatology (Oxford). 2008;47:495-9.
[2] Lanfant-Weybel K, Lequerré T, Vittecoq O. Anti-TNF alpha dans le traitement de la polyarthrite rhumatoïde et de la spondylarthrite ankylosante. Presse Med. 2009;38:774-87.

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AB1309 QUANTIFICATION OF MINIMAL RESIDUAL DOSE ASSOCIATED WITH BIOLOGICAL THERAPEUTIC RESPONSE ANTI DRUG ANTI BODIES: ARE THEY ALL NEUTRALIZING?

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Background: The use of biological was associated to the capacity of inducing an immune response in patients that could neutralize the drug. The anti-body anti-drug (ADA) assay was a revolutionary tool to prevent treatment failure.
Objectives: The aim of this work was to asses if the presence of ADA in patients system is sufficient to preduct failure and indicates the switch of treatment.
Methods: We enrolled 69 patients treated with biotherapy between September 2017 and October 2018. 3 pathologies were considered: rheumatoid Arthritis (RA) diagnosed by ACR/EULAR 2009 criteria, Spondylarthritis (SPA) according to Assessment of Spondylarthritis international Society (ASAS) And crohn's disease (CD) classified upon the 2006'Montreal classification. We did search the presence of anti-body antidrugs (ADA) and the residual dose for the following therapies: Etanercept (ETN), Infliximab (IFX), Adalimumab (Ada) or Rituximab (RTX).
Results: The mean age was 43.33 ± 11.4 year. The sex ratio M/F was 1.57. there were 13 patients with RA, 28 SPA and 28 CD. The Majority of patients were receiving IFX 50.7%(n=35) with same doses. There were 20 responding versus 15 non-respondingpatients. 40% of them had a high residual dose. Regarding Ada 24.6% (n=17). There were 9 non-responding patients and low residual doses were found in 47.1%. 11 patients were using ETN. The ADA was positive in only one patient who was non-responding and having a low residual dose.
Concerning the RTX, it was used for 6 patients. The ADA was negative in all patients. Two non-responding cases having a low residual dose.
The following table explains the repartition of patients according to ADA rates:

		ADA Positifs	ADA Négatifs
IFX	Responding patients	4	16
	Non-responding	9	6
ETN	Responding patients	0	6
	Non-responding	1	4
Ada	Responding patients	0	8
	Non-responding	4	5
RTX	Responding patients	0	4
	Non-responding	0	2

Positive ADA was associated with therapy failure in all type of biotherapy (p=0.001). A low residual dose was associate to therapy failure only in the case of IFX (p=0.005).
Positive ADA was associated to a low rate of residual dose in the case of IFX and Ada.
This association couldn't be evaluated for RTX (none) and ETN (just one positive rate).
Conclusion: The ADA assay is a revolutionary tool allowing the evaluation of treatment response but it cannot be considered without the clinical assessment of patient. The evaluation residual dose should be concomitant to valorize and guide the therapeutic decision

REFERENCES

[1] Kristensen LE, Kapetanovic MC, Gülfe A, Söderlin M, Saxne T, Geborek P. Predictors of response to anti-TNF therapy according to ACR and EULAR criteria in patients with established RA: results from the South Swedish Arthritis Treatment Group Register. Rheumatology (Oxford). 2008;47:495-9.
[2] Lanfant-Weybel K, Lequerré T, Vittecoq O. Anti-TNF alpha dans le traitement de la polyarthrite rhumatoïde et de la spondylarthrite ankylosante. Presse Med. 2009;38:774-87.

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AB1310 PROSPECTIVE USE OF THE GLUCOCORTICOID TOXICITY INDEX (GTI) IN A COHORT OF VASCULITIS PATIENTS

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Background: The Charité Rh-GIOP is a prospective study of disease- & bone-related data from patients with chronic inflammatory diseases treated with glucocorticoids (GCs). The Glucocorticoid Toxicity Index app (GTI 2.0) measures changes in GC-associated morbidity. The GTI captures

improvement as well as worsening in GC toxicity, and consists of two subscores. With the Cumulative Worsening Score (CWS), only worsening toxicities are counted. The CWS is always a positive number or, if no toxicity has occurred, 0. With the Aggregate Improvement Score (AIS), both improvement and worsening are considered. If the overall GC toxicity has improved, the AIS is negative.

Objectives: To evaluate the GTI in a prospective cohort of GC-treated vasculitis patients.

Methods: Vasculitis patients were included if starting GC or having a flare requiring increased GC. Doses were calculated in prednisone (PRED) equivalents. Nearly all patients had received GC (often for years) baseline (V1). Data for the 9 GTI domains were collected at V1 and follow-up (V2). These included: medications for hypertension, hyperglycemia, and hyperlipidemia; body mass index; bone mineral density; and data pertaining to muscle strength, skin toxicity, neuropsychiatric effects, and infections. Data for the blood pressure, glucose control, and lipid domains were inferred from treatment changes. We used multivariate logistic regression models to examine the relationship of PRED dose to the likelihood of CWS worsening and AIS improvement.

Results: 37 patients (25F; 12M) of mean age 66.6 years (range: 40.5-81.7) were included. Diagnoses: GCA (n=7), PMR (14), AAV (10), EGPA (4), and PAN (2).

Table 1. Prednisone Dosing

Mean Cumulative PRED Dose V0 & V1 (mg)(range)	7888 (30-55,800)
Mean Cumulative PRED Dose V1 & V2 (mg)(range)	3762 (108-14,207)
Days Between V0 & V1 (range)	1095 (2-7,443)
Days Between V1 & V2 (range)	613 (335-1,111)
Mean Daily PRED Dose Before V1(mg)(standard deviation, SD)	6.1 (6.2)
Mean PRED dose V1 (mg)(SD)	34.2 (36.5)
Mean PRED dose V2 (mg)(SD)	3.1 (2.9)

Thirty-four (92%) patients had changes in GC toxicity between V1-V2. The mean CWS & AIS were 34.8 and 11.1, respectively. Twenty-eight patients (76%) had CWSs >0, indicating worsening toxicity. Twenty-one (57%) had AISs >0, also consistent with overall GC toxicity worsening. However, 13 (35%) had negative AISs, indicating improvements in GC toxicity. BMD measurements worsened by at least 3% in 16 (43%) patients and improved by at least 3% in 9 (24%). Cumulative PRED doses correlated strongly with the CWS. For every 1000mg of PRED between V1 & V2, the risk of CWS increase – worsening of GC toxicity – rose by 79% (Table 2).

Table 2. GTI Score Relationships to PRED Dose

PRED Dose	Total (n=37)	CWS		AIS	
		Did not worsen (n=9)	Worsened (n=28)	Improved (n=13)	Did not improve (n=24)
V1-V2 (mg/d)(SD)	6.3 (4.5)	4.8 (5.9)	6.9 (4.0)	5.5 (4.6)	6.8 (4.5)
Cumulative PRED V1&V2 (mg; SD)	3761 (2660)	2027 (2165)	4319 (2592)	3147 (2047)	4094 (2925)
			OR (95% CI)*		
	CWS			AIS	
Daily Mean Dose V1-V2** (per 1mg)	1.15 (0.92-1.43)			0.93 (0.78-1.11)	
Cumulative PRED V1&V2 (per 1000mg)**	1.79 (1.06-3.03)			0.85 (0.63-1.16)	

V0 = Date when PRED was started, before baseline (V1)
*OR for CWS refers to risk of worsening. OR for AIS refers to risk of improvement.
**Adjusted for age, sex.

Conclusion: The GTI captured changes in GC toxicity over time well, both improvement and worsening. Cumulative PRED dose correlated strongly with increase in the Cumulative Worsening Score.

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AB1311 NEUTROPHIL-, MONOCYTE-, EOSINOPHIL- AND BASOPHIL-LYMPHOCYTE RATIOS: ASSOCIATIONS WITH TRADITIONAL INFLAMMATORY MARKERS AND DISEASE ACTIVITY MEASURES AT BASELINE AND 6 MONTHS AFTER A BDMARD AMONG BIOLOGIC-NAÏVE RHEUMATOID ARTHRITISPATIENTS

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Background: Neutrophil-lymphocyte (NLR) and monocyte-lymphocyte (MLR) ratios have been not only suggested as systemic inflammatory markers, but also associated with disease activity in some inflammatory diseases. Eosinophil-lymphocyte (ELR) and basophil-lymphocyte (BLR) ratios have been studied to a lesser extent.

Objectives: To correlate NLR, MLR, ELR and BLR with inflammatory markers, other laboratory markers and disease activity measures in a portuguese sample of rheumatoid arthritis (RA) patients.

Methods: We conducted a retrospective study including all RA patients under the first bDMARD (*biological disease-modifying antirheumatic drug*), followed in a tertiary university hospital and registered in the Rheumatic Diseases Portuguese Register (*Reuma.pt*). Results of blood tests (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], serum amyloid A [SAA], rheumatoid factor [RF], anti-citrullinated protein autoantibodies [ACPA], haemoglobin, platelets, 25-hydroxide-vitamin D [25OHvitD]), leukocyte formula ratios (NLR, MLR, ELR, BLR) and disease activity and function measures (disease activity score 28 [DAS28 4V, 3V, 4V-CPR, 3V-CPR], clinician and simple disease activity scores [CDAI, SDAI], swollen and tender joint count [SJC, TJC], physician and patient visual analogical scale [VAS]) at baseline and at 6 months of bDMARD therapy were collected. Correlations between variables were evaluated by Spearman rank test (significance level at $p<0.05$), using SPSS 25.0 software.

Results: 435 patients were included: 81.2% female, mean age at baseline 53.3±11.4 years, mean disease duration 12.6±8.8 years, 72.2% RF positive, 77.1% ACPA positive, 52.5% erosive disease.

At baseline, NLR correlated positively with CRP (r=0.343; p<0.001), ESR (r=0.124; p=0.031), RF title (r=0.185; p=0.009), platelets count (r=0.137; p=0.018), DAS28(4V) (r=0.183; p=0.002), DAS28(3V) (r=0.159; p=0.007), DAS28(4V-CRP) (r=0.235; p<0.001), DAS28(3V-CRP) (r=0.222; p<0.001), SDAI (r=0.178; p=0.024), SJC (r=0.120; p=0.040), TJC (r=0.139; p=0.018) and patient VAS (r=0.133; p=0.026). At baseline, we also found a negative correlation between NLR and 25OHvitD levels (r=-0.286; p=0.012). Baseline MLR showed a positive correlation with baseline CRP (r=0.138; p=0.017), RF (r=0.156; p=0.027) and patient VAS (r=0.135; p=0.023). Similarly, at baseline, ELR correlated with CRP (r=0.115; p=0.048) haemoglobin levels (r=0.126; p=0.029) and DAS28(4V-CRP) (r=0.126; p=0.037); and BLR associated positively with DAS28(4V-CRP) (r=0.138; p=0.022), TJC (r=0.121; p=0.038) and patient VAS (r=0.131; p=0.028).

At six months of a bDMARD, NLR correlated positively with: CRP (r=0.340; p<0.001), ESR (r=0.140; p=0.018), SAA (r=0.350; p=0.008) and physician VAS (r=0.186; p=0.023). MLR also exhibited a positive association with CRP (r=0.161; p=0.007). Similarly, at six months, ELR correlated positively with CRP (r=0.120; p=0.043), RF (r=0.135; p=0.046), CDAI (r=0.180; p=0.027) and SDAI (r=0.183; p=0.025); and BLR correlated positively with platelets count (r=0.139; p=0.020).

Conclusion: Although weak to moderate in strength, we found significant correlations, between leukocyte formula ratios (NLR, MLR and ELR) and, not only, inflammatory markers but also disease activity measures, predominantly at baseline but also at 6 months of bDMARD. Interestingly, is of note the negative association between NLR and 25OHvitD at baseline. This study reinforced the suggested place of NLR and MLR (but also of ELR) as inflammatory markers and possible disease activity measures in RA. More studies are needed to validate this data.

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AB1312 TIME-COURSE CHANGE OF NEUTROPHIL-LYMPHOCYTE RATIO, MONOCYTE-LYMPHOCYTE RATIO AND PLATELET-LYMPHOCYTE RATIO IN PSORIATIC ARTHRITIS PATIENTS AND RESPONSE TO BIOLOGIC THERAPY

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Background: Recently, systemic inflammation has been shown to be a key determinant of prognosis. Neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), and platelet-lymphocyte ratio (PLR) has been related to inflammation status and suggested as additional markers of response to bDMARDs in patients with rheumatoid arthritis. However, few studies were yet developed about this subject in psoriatic arthritis (PsA).
Objectives: The aim of this study was to investigate the time-course change of NLR, MLR and PLR levels in PsA patients after 6 and 12 months of bDMARD therapy and to evaluate their clinical significance and utility in monitoring response to biologic agents.
Methods: An observational retrospective study was performed in patients with PsA under bDMARD, followed at our Rheumatology department until December 2018. Demographic and clinical data were collected from the national database. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and total blood count were consulted before and after 6 and 12 months of biologic treatment and NLR, MLR and PLR were calculated by dividing neutrophil, monocyte and platelet count by lymphocyte count, respectively. Disease activity was evaluated with DAS28 and ASDAS. The variation of each parameter was calculated as the difference between the levels registered at 6 and 12 months and the baseline and presented as Δ. Correlation between ΔNLR, ΔMLR and ΔPLR with ΔCRP and ΔESR levels, ΔDAS28 and ΔASDAS was calculated using the Spearman's test.
Results: A total of 83 patients were included. Forty-three were females (51.8%). The mean age at diagnosis was 41 years (±11.3) and the median disease duration at start of biological therapy was 6.9 years (min:1.4; max:32.4). In total, 67.5% of the patients had axial involvement (n=56), 91.6% articular involvement (n=76) and 43.4% enthesopathic involvement (n=36). Almost all patients fulfilled the CASPAR criteria for PsA (n=78; 94%). At the baseline, 25 patients (30.1%) had high disease activity and 45 patients (54.2%) very high disease activity according to ASDAS criteria. The most used bDMARD was etanercept (n=29; 35%), followed by golimumab (n=26; 31%), adalimumab (n=16; 19%) and infliximab (n=8; 10%). Certolizumab was administered to 2 patients and secukinumab to others 2 patients. Fifty-nine patients were concomitantly treated with csDMARDs. The median value of CPR was 1.5mg/dL [0.03-30], 0.26 [0.03-11] and 0.37 [0.02-19] at baseline, 6 and 12 months, respectively. The median value of ESR was 33mm/hr [4-98], 11 [2-75] and 10 [1-68] at baseline, 6 and 12 months, respectively. We realize that NLR, MLR and PLR decreased after 6 months of treatment and remained relatively stable at 12 months (NLR median: 2.6 [0.1-8.8], 1.6 [0.5-5.3], 1.6 [0.5-8]; MLR median: 0.32 [0.11-250], 0.23 [0-7.4], 0.25 [0.05-1]; PLR median: 132 [69.6-342.5], 97.6 [33.4-415.1], 98.6 [38.3-528.6] at baseline, 6 and 12 months, respectively). A significant positive correlation was found between ΔNLR and ΔCPR at 6 months (r=0.272; p=0.016) and also between ΔMLR and ΔCPR at 6 and 12 months (r=0.309, p=0.006; r=0.364, p=0.002). ΔPLR showed a statistically significant correlation only with ΔESR at 6 months (r=0.312; p=0.006). No correlation were found between ΔNLR, ΔMLR and ΔPLR with ΔDAS28 or between ΔNLR, ΔMLR and ΔPLR with ΔASDAS at evaluation of 6 and 12 months.
Conclusion: Our data showed that NLR, MLR decreased promptly in parallel with decrease of CRP and PLR with ESR for up 6 months of therapy with biologics. This results, in agreement with the literature, suggests that NLR, MLR and PLR may be seen as a useful marker for demonstrating systemic inflammation in PsA patients. Further studies are needed to better emphasize the importance of these parameters and to evaluate their utility to monitor the effectiveness of biologic therapy.
Disclosure of Interests: None declared
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AB1313 NMR SPECTROSCOPY REVEALS ALTERATIONS OF URINARY ACETATE AND CITRATE LEVELS FOLLOWING CYCLOPHOSPHAMIDE THERAPY IN PATIENTS WITH LUPUS NEPHRITIS

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Background: Metabolomics, the study of global alterations in small metabolites is a useful tool to look for novel biomarkers. Recently, we reported a reprogramming of the serum metabolomic profile on nuclear magnetic resonance(NMR) spectroscopy following treatment in Lupus Nephritis (LN) **[1]**.
Objectives: We explored urinary parameters using NMR Spectroscopy in patients with biopsy proven proliferative lupus nephritis. Change in parameters after 6 months Cyclophosphamide induction treatment and its correlation with disease activity was assessed.
Methods: Urine obtained from Lupus Nephritis (n=18, F=16,M=2) at diagnosis and following induction therapy with cyclophosphamide, and healthy controls (n=18, median age 35,all females) were stored at -80 °C. Metabolomic profiling was done using high resolution 800 MHz 1D 1H NMR spectroscopy. Urinary ratio of metabolites was calculated- (Metabolitex1000)/Creatinine. Disease activity was measured using SLEDAI. Metabolomic profiles were compared between groups and correlated with clinical parameters using SPSS.
Results: Urinary metabolomic fingerprint of LN patients differed from healthy controls by having significantly raised urinary acetate/creatinine (LN=41.84±100.6, HC=12.36±9.40, p=<0.002) and reduced urinary citrate/creatinine.(LN=34.22±54.8, HC=114.5±70.09, p=<0.0001). Urinary citrate (88.68±98.33) increased after 6 months of Cyclophosphamide, while urinary acetate showed a trend towards decrease(14.77±9.98). AUC for urinary citrate/creatinine and acetate/creatinine were 0.9136 and 0.8086. The urinary acetate levels correlated with SLEDAI (r=0.337,p=0.048). Urinary citrate levels correlated with C3 (r=0.362,p=0.03) and negatively correlated with uPCR (r=0.346, p=0.039).
Conclusion: The decreased urinary citrate mirrors the finding seen in serum of the patients done earlier which reflects dampened aerobic glycolysis and oxidative phosphorylation.(1) Raised urinary acetate levels possibly reflects proximal renal tubular injury leading to increased urinary excretion(2). Change in levels with treatment show that urinary metabolomics parameters are potential noninvasive biomarkers for diagnosis and monitoring treatment response in LN

REFERENCES

[1] Guleria A, et al. NMR based serum metabolomics reveals reprogramming of lipid dysregulation following Cyclophosphamide based induction therapy in lupus nephritis. J Proteome Res. 2018, 17 (7), 2440–2448.
[2] Gartland KP, Bonner FW, Nicholson JK. Investigations into the biochemical effects of region-specific nephrotoxins. Molecular Pharmacology. 1989 Feb 1;35(2):242-50.

Metabolite	SLEDAI		rSLEDAI		C3		C4		PCR	
	r	p	r	p	r	p	r	p	r	p
Acetate	**0.337**	**0.048**	0.22	0.205	-0.084	0.625	-0.097	0.573	0.003	0.988
Citrate	-0.314	0.066	-0.234	0.175	**0.362**	**0.03**	0.007	0.969	**-0.346**	**0.039**

Table 1. Showing correlation of urinary metabolites with clinical parameters

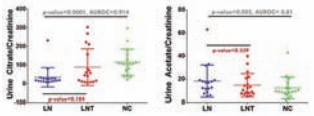


Figure: The box plot representation of Urinary Citrate/Cre and Acetate/Cre ratios obtained for different study groups: LN (in blue), LNT (in red) and NC (green). The significantly higher p-values and area under the ROC curve (AUROC) between LN and NC groups demonstrated the diagnostic potential of these urinary ratios. The table on the right side shows the correlation analysis parameters between urinary metabolic profiles and clinical parameters.

Disclosure of Interests: None declared
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AB1314 **ROLE OF NEUTROPHIL TO LYMPHOCYTE RATIO, MONOCYTE TO LYMPHOCYTE RATIO, PLATELET TO LYMPHOCYTE RATIO, EOSINOPHIL TO LYMPHOCYTE AND BASOPHILE TO LYMPHOCYTE RATIO IN ASSESSING DISEASE ACTIVITY IN SPONDYLOARTHRITIS**

Salomé Garcia, Bruno Miguel Fernandes, Sara Ganhão, Raquel Ferreira, Miguel Bernardes, Georgina Terroso, Lúcia Costa. *Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*

Background: Neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), platelet to lymphocyte ratio (PLR), eosinophil to lymphocyte ratio (ELR) and basophile to lymphocyte ratio (BLR) have been demonstrated to be promising systemic inflammation markers. NLR, MLR and PLR have been associated with disease activity in Spondyloarthritis (SpA) but the results remain conflicting.
Objectives: We aim to determine the role of NLR, MLR, PLR, ELR and BLR in assessing disease activity in SpA.
Methods: Observational retrospective study was performed including consecutive patients with the diagnosis of SpA (according to ASAS classification criteria) followed at our Rheumatology Department. Demographic, clinical (including BASDAI, BASFI, ASDAS ESR and ASDAS CRP indices) and laboratorial data were collected from our national database at baseline and 6 months after initiation of a tumour necrosis factor inhibitor (TNFi). Correlations between variables were studied using Spearman correlation analysis and comparison between groups was performed using Wilcoxon test.
Results: The mean age of patients (n=297) was 41 years old (± 12), 160 (53.9%) were males with median disease duration of 12.4 (IQR 14.8) years. Two hundred and seven patients (69.7%) had Ankylosing Spondylitis, 26 (8.8%) Inflammatory Bowel Disease related SPA and 36 (12.1%) Undifferentiated SpA. Seventy-three (24.7%) patients were taking glucocorticoids and regarding conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) use before starting the TNFi: 188 (63.3%) were not under any csDMARD and the remaining ones were under Sulfasalazine (70, 23.6%), Methotrexate (MTX) (21, 7.1%), Azathioprine (AZA) (5, 1,7%), Leflunomide (1, 0.3%) or associations between Sulfasalazine and AZA or MTX. Regarding the iTNF the majority of patients initiate Adalimumab (n=168, 28.6%), Golimumab (n= 61, 25.6%) or Infliximab (n= 57, 23.9%). The majority of patients had very high or high disease activity at baseline (59.6% and 31.3%, respectively); mean ASDAS CRP was 3.85 (± 0.99), mean ESR was 30.1 mm/h (± 21.9) and mean CRP was 36.9 mg/L (±113.9). The post-treatment mean ESR, CRP, ASDAS-CRP, ASDAS-ESR and BASDAI were significantly lower than mean baseline values, as they were also for NLR, MLR and PLR ($p<0.01$).
At the baseline evaluation, in anti-TNF naïve patients, NLR and MLR were positively correlated with the majority of parameters evaluated: ESR level ($r=0.322$; $r=0.203$, $p<0.01$ respectively), CRP level ($r= 0.475$; $r=0.221$, $p<0.01$ respectively), ASDAS-CRP ($r=0.255$; $r=0.192$, $p<0.01$ respectively), ASDAS-ESR ($r=0.257$; $r=0.206$, $p<0.01$ respectively) and BASMI ($r=0.288$; $r=0.150$, $p<0.01$ respectively). No correlations were found with BASDAI. PLR was positively correlated with ESR level ($r=0.379$, $p<0.01$), CRP level ($r= 0.331$, $p<0.01$), ASDAS-CRP (0.215, $p<0.01$) and ASDAS-ESR ($r=0.208$, $p<0.01$). No correlations were found between those parameters and ELR or BLR.
At the evaluation 6 months after introducing a TNFi, we found less and weaker correlations than in naïve patients: NLR and PLR correlate positively with CRP ($r=0.302$; 0.315, $p<0.01$ respectively) and, reaching lower statistical significance, PLR correlate also with ASDAS-ESR (0.156, $p<0.05$); NLR with BASMI (0.184, $p<0.05$) and ESR (0.179, $p<0.05$); MLR with CRP (0.173, $p<0.05$).
Conclusion: NLR, MLR and PLR may reflect disease activity and could represent future inexpensive potential parameters to evaluate disease activity or severity in SpA.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.2243

AB1315 **MIOSITIS AUTOANTIBODIES PROFILE: DIAGNOSTIC RELEVANCE**

Alicia García Dorta[1], Yvelise Barrios[2], Sonia Peña Montelongo[1], Hernández Díaz Marta[1], Andrea Monroy Calero[1], Beatriz Rodríguez Lozano[1], Andrés Franco[2], Sagrario Bustabad[1]. [1]*Hospital Universitario de Canarias, Reumatology, La Laguna, Spain*; [2]*Hospital Universitario de Canarias, Inmunology, La Laguna, Spain*

Background The idiopathic inflammatory myopathies (IIM) are autoimmune systemic diseases that can affect several organs, but with special impact in the muscular-skeletal system. Autoimmunity is believed to have a role in its pathogenesis, with the presence of Autoantibodies (Abs) in more than 50% of the patients. Those Abs have been classified into Myositis-Specific Autoantibodies (MSA), with the Anti-Jo being the most frequent1-2; and Myositis-Associated autoantibodies (MAA), also found in other connective tissue diseases. The availability of a multiplex analysis (Myositis Profile) has opened up new possibilities for the specific investigations of these Abs in the day-to-day clinical practice 1-2.
Objectives To describe the clinical spectrum and the Ab results obtained from the myositis profile in patients (hospital admissions and ambulatory) of a tertiary university hospital.
Methods Retrospective descriptive study (January to June 2018) of the results obtained on the myositis profile. The clinical characteristics of the sample is described in the context of the Abs results. We considered that applications of this Myostis Ab Profile were justified if they had EPID and/or if they had 2 or more clinical and/or analytical characteristics associated with MII. Myositis Profiles consisted in a solid phase ELISA from EuroLINE MII 16 Antigens (Mi2-alfa, Mi2-beta, TIF1gamma, MDA5, NXP2, SAE1, Ku, Pm-Scl100, Pm-Scl75, Jo-1, SRP, PL7, PL12, EJ, OJ, RO-52). Statistical analysis SPSS 17.0.
Results A total of 165 applications were studied, 47% requested by Reumatology, 30% by Neumology and 9% by Internal Medicine. Justifications were: ILD (n=49); osteomuscular (n=30), connective diseases (n=29), myositis (n=17), CK-NAC elevation (n=11), fibromyalgia (n=7) and others (n=22). 41% men and 59% women, Average Age 58 (+/- 15 years). We observe an increase of CKNAC, GOT, GPT y LDH in 21%, 12%, 19% y 24% respectively. They refer muscle weakness in 18%, Raynaud's phenomenon in 10%, arthritis in 15%, heliotrope eruption in 4%, Gottrons's papules in 1% and mechanics hand in 1%. Using the criteria specified in the method section, 52% of the applications were justified, being the 57% of them as ILD study. 32 (20%) of the 165 profiles were positive. 10 of the 49 patients with ILD had positive Abs (figure 1), 90% me. 8 of the 17 patients with myositis had positive Abs (figure 1), 63% women. 75% of them (6/8) were positive for MSA, the 65% were Anti-Jo1 (4/6). 1 patient with myositis associated with neoplasia (anti-OJ). 2 of 3 muscle biopsy were consistent with MII. 2 of 7 EMG were compatible. The 14 remaining patients had some positive Abs (figure 2): 7 connective tissue diseases studies, 4 osteomuscular pathology, 1 auto-inflammatory disease, 1 CK-NAC elevation and 1 with inflammatory bowel disease (IBD).

	Sex	Age	Diagnosis suspicion	Antibodies	ILD pattern
ILD	Man	73	Connective Tissue Diseases	PMSCL100	NSIP
	Woman	87	IPAF	PL-7	UIP
	Man	84	Scleropolimyositis	PMSCL100	NSIP
	Man	76	Systemic Lupus Erythematosus	SRP-B	NIU
				PMSC 100	
	Man	70	RA/SS	PL-12	NSIP
	Man	65	Myositis inflammatory amyopathic	SRP-B	UIP
	Man	74	UCTD/ Scleropolimyositis	PMSCL100	UIP
	Man	83	Connective Tissue Diseases	PMSCL100	UIP
	Man	74	Without Connective Tissue Diseases	PMSCL75	UIP
	Man	83	IPAF	MI2a	UIP
MYOSITIS	Man	62	Polimyositis	Kub	
	Woman	55	Dermatomyositis/ Anti-Synthetase syndrome	PL12	
	Man	71	Necrotizing myopathy	SRP-B	
	Man	74	Temporal Myositis	PL-7	
				JO-1	
	Woman	40	Myositis associated with neoplasia	OJ	
	Woman	52	Anti-Synthetase syndrome	Jo1	
	Woman	71	Scleropolimyositis	Jo1	
	Woman	56	Polimyositis	JO1	

Figure 1. ILD and Myositis patients and positive Abs

	Sex	Age	Diagnosis suspicion	Antibodies	ILD pattern
ILD	Man	73	Connective Tissue Diseases	PMSCL100	NSIP
	Woman	87	IPAF	PL-7	UIP
	Man	84	Scleropolimyositis	PMSCL100	NSIP
	Man	76	Systemic Lupus Erythematosus	SRP-B	NIU
				PMSC 100	
	Man	70	RA/SS	PL-12	NSIP
	Man	65	Myositis inflammatory amyopathic	SRP-B	UIP
	Man	74	UCTD/ Scleropolimyositis	PMSCL100	UIP
	Man	83	Connective Tissue Diseases	PMSCL100	UIP
	Man	74	Without Connective Tissue Diseases	PMSCL75	UIP
	Man	83	IPAF	MI2a	UIP
MYOSITIS	Man	62	Polimyositis	Kub	
	Woman	55	Dermatomyositis/ Anti-Synthetase syndrome	PL12	
	Man	71	Necrotizing myopathy	SRP-B	
	Man	74	Temporal Myositis	PL-7	
				JO-1	
	Woman	40	Myositis associated with neoplasia	OJ	
	Woman	52	Anti-Synthetase syndrome	Jo1	
	Woman	71	Scleropolimyositis	Jo1	
	Woman	56	Polimyositis	JO1	

Figure 1. ILD and Myositis patients and positive Abs

Conclusion The use of this Ab profile as a protocol for patients with ILD without myositis clinical features, allowed us to classify a group of patients with autoimmune diseases. In this group, the distribution by sex, 9 males and 1 woman is highlighted. We achieved the diagnosis on the 47% of patient with myositis clinical suspicion. The usefulness of myositis profile allowed us to detect antibodies which are not in other immunologic assays. Distribution by sex, 3 men and 5 women.

The implementation of this profile of auto-antibodies in patients without ILD and those without clinical and/or analytical characteristics associated with MII, did not provide any.

REFERENCES

[1] McHugh, Z. B. (2016). Myositis-specific autoantibodies: an important tool to. Journal of Internal Medicine, 280; 8–23.
[2] Protocolos de diagnóstico inmunológico en enfermedades autoinmune. (2014). Barcelona: Elsevier.

Disclosure of Interests None declared
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AB1316 AGREEMENT BETWEEN SUBJECTIVE AND OBJECTIVE DEFINITIONS OF INACTIVE DISEASE IN CHILDREN WITH JUVENILE IDIOPATHIC ARHRITIS

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Background: The choice of an appropriate definition of inactive disease (ID) is important because ID has been identified as the ideal therapeutic goal in the treat-to-target strategy in juvenile idiopathic arthritis (JIA).[1] Several criteria for ID in JIA have been proposed, including Wallace 2004 and 2011 criteria and JADAS10 and clinical JADAS10 (cJADAS10) criteria. However, a recent study[2] has shown that these criteria do not always identify the same group of patients. In addition, it is unknown whether and to what extent the formal definitions of ID agree with the subjective perception of disease remission by the physician and the parent.[3]
Objectives: To investigate the concordance between current criteria for ID and subjective judgment of disease remission by physicians and parents in children with JIA.
Methods: We evaluated the clinical data of the last visits made in 669 children with JIA from March 2007 to December 2010 to identify all visits in which the caring physician and a parent judged subjectively and independently the child's disease state as remission or non-remission and the parent declared whether he/she was satisfied or non-satisfied with current illness state (i.e. Parent Acceptable Symptom State, PASS).[4] All visits judged subjectively by the physician and the parent as remission or judged in PASS by the parent were examined to identify those which met the Wallace 2004 and 2011 criteria and the JADAS10 and cJADAS10 criteria for ID. Visits which met both subjective and objective definitions were defined as concordant.
Results: Of the 246 visits in which the physician judged subjectively the disease state as remission, 34.6% and 27.6% met the 2004 and 2011 Wallace criteria, respectively, and 38.6% and 54.5% met the JADAS10 and cJADAS10 criteria for ID, respectively.(Figure 1) Of the 338 visits in which the parent judged subjectively the disease state as remission, 19.8% and 18% met the 2004 and 2011 Wallace criteria, respectively, and 34.9% and 48.8% met the JADAS10 and cJADAS10 criteria for ID, respectively.(Figure 2) In 76.4% of visits judged as remission by the physician, the parent provided the same evaluation. In 55.6% of visits judged as remission by the parent, the physician provided the same evaluation.(Figure 1-2) Of 467 visits judged in PASS by the parent, 17.6% and 14.8% met the 2004 and 2011 Wallace criteria, respectively, and 26.6% and 37.5% met the JADAS10 and cJADAS10 criteria for ID, respectively.
Conclusion: The JADAS10 and cJADAS10 criteria for ID were more concordant with physician's and parent's subjective judgment of remission and with parent's satisfaction with current illness state than Wallace criteria. The cJADAS10, which lacks the acute phase reactant, revealed the best concordance with both physician's and parent's subjective assessments. Physician-parent agreement was greater for remission judged by the physician than for remission judged by the parent.

REFERENCES

[1] Ravelli A, et al. Ann Rheum Dis. 2018;77:819-828; 2. Shoop-Whorral SJW, et al. Ann Rheum Dis. 2017;76:1381-1388; 3. Giancane G, et al. Nat Rev Rheumatol. 2017;13:460-461. 4. Filocamo G, et al. J Rheumatol. 2012;39:856-63.

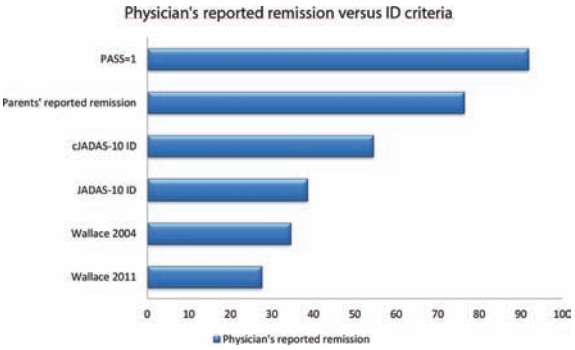


Figure 1. Physician-centered inactive disease state evaluation.

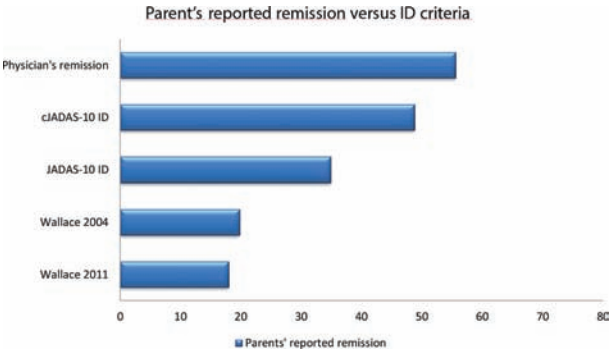


Figure 2. Parent-centered inactive disease state evaluation.

Disclosure of Interests: Gabriella Giancane: None declared, Maria Francesca Gicchino: None declared, Alessandra Alongi: None declared, Chiara Campone: None declared, Alessandro Consolaro Grant/research support from: AbbVie, Pfizer, Angelo Ravelli Grant/research support from: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benkiser, and Roche, Consultant for: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benkiser, and Roche, Speakers bureau: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benkiser, and Roche
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AB1317 WHAT IS A TOTAL KNEE OR TOTAL HIP ARTHROPLASTY FAILURE? A PATIENT PERSPECTIVE USING NOMINAL GROUPS

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Background: Total joint replacements (TJR) are commonly performed elective surgeries for people with end-stage arthritis. However, there is relative lack of qualitative research to define the patient perspective of what constitutes a failure of TJR
Objectives: To discover when a TJR is considered a failure from the patients' perspective using nominal group technique (NGT).
Methods: Patients who had undergone elective total hip (THR) and/or knee replacements (TKR) met in nominal groups to answer the question "When would you consider a knee or hip replacement to be a failure?". Patients competed questionnaires including demographics, pain, function, and satisfaction, independently listed their ideas and then ranked them with the group after clarification.

Results: Six groups with 35 patients were held, all of whom had undergone THR and/or TKR between 2016 and 2018. Of these, 42% were male, 17% black **(Table 1).** Overall pain and function scores were high; Hip Disability and Osteoarthritis Outcome Score (HOOS) JR 95.3 (SD+/-11) and Knee Injury and Osteoarthritis Outcome Score (KOOS) JR 83.7 (SD+/-12.8) (range 0-100, higher score=less pain/functional limitation), and 86.1% were very/somewhat satisfied with their quality of life. The concerns ranked highest by the patients equating a TJR failure were A) refractory index joint pain (67 votes); B) unable to resume normal activities or go back to work (38 votes); C) minimal or no improvement in quality of life (24 votes); D) post-operative adverse events (40 votes); E) early revision surgery (32 votes); F) death (7 votes); G) expectation-outcome mismatch (1 vote); continuing secondary depression (1 vote) **(Table 2).**

Conclusion: Poor results for pain, function, quality of life, or adverse events are the outcomes ranked highest by patients, defining TJR failure from the patients' perspective.

Table 1. Baseline Characteristics

	TKR N=19	THR N=13	Both TKR and THR N=3	Total N=35
Age (mean, SD)	75.7 ±8.2	65.3 ±8.0	66.3±5.4	71.1±9.4
Men, n(%)	6 (31.6)	8 (61.5)	1 (33.3)	15 (42.9)
Black, n(%)	3 (15.8)	3 (23.1)	-	6 (17.1)
Asian, n(%)	-	-	1 (33.3)	1 (2.9)
Multi-race, n(%)	1 (5.3)	1 (7.7)	-	2 (5.7)
Education				
High school, n(%)	-	1(7.7)	-	1 (2.9)
Some college, n(%)	1(5.3)	3(23.1)	-	4 (11.4)
College or above, n(%)	18 (94.7)	9 (69.2)	3 (100)	30 (85.7)
Employment				
Employed, n(%)	3 (15.8)	9 (69.2)	3(100)	15 (42.9)
Self-employed, n(%)	4 (21.1)	3(23.1)	-	7 (20.0)
Out of work, not looking for work, n (%)	1(5.3)	-	-	1 (2.9)
Retired, n(%)	11 (57.9)	1 (7.7)	-	12 (34.3)
Reason for surgery				
Osteoarthritis, n(%)	13 (68.4)	11 (84.6)	3(100)	27 (77.1)
Rheumatoid arthritis, n(%)	2 (10.5)	1(7.7)	-	3 (8.6)
Other arthritis, n(%)	3 (15.8)	1(7.7)	-	4 (11.4)
Avascular necrosis of the bone, n (%)	1(5.3)	-	-	1 (2.9)

Abstract AB1317 Table 2. Theme: When would you consider a hip or knee replacement a failure?

NG 1-6, 35 people, 14 Male, 21 Female; 8 African-American, 25 White, 2 Asian, 210 votes*	Score
A. Pain: Still in pain/remains unchanged/persists	67
• "Primary factor for getting surgery. Pain impacts every facet of life"	
B. **Activities:** Cannot regain normal function or activities/physical disability persisted	38
• "Can't reach a goal – goal is to reach the top of the stairs or room"	
C. Quality of life	24
• "Can't go back to work and can't walk. Purpose of surgery to get back life. Going to theater, cooking. Social, mental, physical, emotional."	
D. **Adverse Events:** Infection, implant rejection, bone damage, complications	40
• "Infection sets you back, psychological event, when does it get cured, do I have to go back for surgery. Start questioning everything."	
E. **Revision:** Having another surgery for the same problem	32
• "Did not want to go through it again"	
F. **Death:** infection leading to death, implant causing death, death during surgery	7
• "Friend died of infection, that's why I came here"	
G. **Other**	2
• "When outcomes don't meet expectations"	
***combined votes; NG= nominal group**	

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AB1318 VALUE OF NEW BIOMARKERS IN THE DIFFERENTIAL DIAGNOSIS OF SARCOIDOSIS AND TUBERCULOSIS

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Background: Due to multisystem involvement with almost similar presentation, tuberculosis (TB) and sarcoidosis poses a diagnostic challenge. As both of them show granulomatous inflammation in tissue, even histopathological examination is not helpful to differentiate the two. As a result of this difficulty, new biomarkers for differentiating the two are being investigated. Previous studies (1,2) done in other regional population attempted to show the efficacy and role of Neutrophil by lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) to differentiate sarcoidosis from TB, with inconsistent results. We attempt to see if these biomarkers can be used in our population to differentaite the two.

Objectives: The aim of our study was to investigate the value of neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) to differentiate TB from sarcoidosis. In addition, we also studied Neutrophil/lymphocyte/albumin/globulin ratio (NLR by A:G ratio) as a novel marker for differentiating the two.

Methods: Patients recruited for the study were selected retrospectively from hospital records during the period of September 2017 to December 2018:

1. 50 consecutive pulmonary TB patients diagnosed based on sputum acid–fast bacilli (AFB) positivity and/or culture–positivity
2. 39 consecutive patients diagnosed with sarcoidosis by an experienced Rheumatologist on clinical and histological grounds.
3. 50 consecutive healthy subjects who presented to general comprehensive check up on Monday of every week. Subjects who were having any autoimmune disease or infections were excluded.

We collected the information including clinical and biochemical parameters at the time of presentation, from the hospital records. NLR, NLR by A:G ratio and PLR were calculated. To test the statistical significance of continuous variables between sarcoid and tb student's t test/Mann Whitney U test was used. To find the cut off value of study variables, ROC curve was used. Diagnostic measures like sensitivity, specificity, predictive values and accuracy was computed.

Results: Though age was comparable, sex ratio varied between groups with more females in sarcoidosis group. Leukocyte count and neutrophil percentage, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), NLR, NLR by A:G and PLR were significantly higher in the TB group compared with sarcoidosis (for all parameters $P < 0.001$).

Table showing ROC analysis results and accuracy rates of NLR, NLR by A:G ratio and PLR in detection of tuberculosis among sarcoidosis and tuberculosis groups

Parameter	Cut - off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	Accuracy (%)	P value
NLR	3.58	92	73	82	88	0.86	84	<0.001
NLR by A:G ratio	4.48	82	83	87	77	0.88	83	<0.001
PLR	220	64	62	68	57	0.70	63	<0.001

Conclusion: TB vs sarcoidosis is a challenging diagnostic dilemma. Our retrospective study shows the role of NLR, NLR by A:G ratio and PLR in differentiating TB from sarcoidosis. These biomarkers can help to guide our clinical judgement in differentiating these two causes of granulomatous inflammation.

REFERENCES

[1] Iliaz S, Iliaz R, Ortakoylu G, Bahadir A, Bagci BA, Caglar E. Value of neutrophil/lymphocyte ratio in the differential diagnosis of sarcoidosis and tuberculosis. Annals of thoracic medicine. 2014 Oct;9(4):232.

[2] Ozdemir C, Sökücü SN, Önür ST. Can neutrophil/lymphocyte ratio and platelet/lymphocyte ratio be used in differential diagnosis of stage I sarcoidosis from tuberculosis lymphadenopathy?. Eurasian Journal of Pulmonology. 2018 Jan 1;20(1):22.

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AB1319 **EFFICACY AND SAFETY OF THE TREATMENT WITH JAK INHIBITORS IN PATIENTS WITH RA. RESULTS OF A CASE SERIES OF USUAL CLINICAL PRACTICE**

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Background: The JAK inhibitors, a new group of targeted synthetic DMARDs were marketed in Spain in 2018. These oral drugs are a good therapeutic alternative for patients with MTX failure. These are not biologic DMARDs and its place in clinical practice is not clear.
Objectives: To identify the clinical characteristics of the patients treated with JAK inhibitors in a Rheumatology service in the South of Spain. To know the efficacy and safety of these drugs used in usual clinical practice.
Methods: Setting: Rheumatology department in a 3rd level University Hospital.
Design: an observational and analytical case series.
From September 2018 to January 15, 2019 clinical data were collected of all patients with RA (ACR/EULAR 2010) treated with JAK inhibitors. The variables collected were demographics, clinical, related to RA, comorbidities, activity (DAS28ESR) and EULAR response. Safety variables included severe adverse events, and adverse events that caused the interruption of the treatment. The protocol was approved and conducted according to the local ethic committee regulations. The statistical analysis was done with descriptive and inferential non parametric tests. Data are shown as median (percentile 25 – percentile 75).
Results: In the study period, 33 patients were treated with JAK inhibitors. Two patients were excluded of this review due to lack of an evaluation of follow-up. Data of 31 RA patients are presented. They were female (74%) with RF+, ACPA+ and erosive disease en more of 90% of cases; 61% had at least one comorbidity. The Charlson comorbidity index was 3 (2-6). The median age at the time of the start of the JAK inhibitor was 63.3 (56.8 – 70.7) years. The disease duration at the time of the start of the JAK inhibitor was 14.7 (8.6 – 27.5) years. All the patients had received synthetic conventional DMARDs, the number of previous scDMARDs was 2 (2 – 6); 26% had been treated with biologic DMARDs. The number of previous bDMARDS was 2 (1 – 5); 26 (84%) patients were treated with baricitinib and 5 with tofacitinib, oh these 25 (77%) were treated with corticosteroids, the median daily dose of prednisone was 7.5 (5 – 15) mg/day, and 16 (52%) were treated with MTX, the mean weekly dose was 15 (10 – 25) mg/week. The baseline DAS28ESR was 4.9 (4.1 – 5.7) and the end DAS28ESR was of 2.6 (2.07 – 3.5), p<0.0001; the EULAR response was good in 15 (52%), Moderate in 11 (35%) and Poor in 5 (13%). At the last visit 15 (38%) were in remission (DAS28ESR ≤2.6), and the follow-up was of 11.1 (6.8 – 16.7) months. In 8 patients the treatment was stopped, one due to primary inefficacy, three due to secondary inefficacy and in five patients due to adverse events The most relevant adverse events were one case with septic arthritis of the knee after a intra articular injection; one case with a community acquired pneumonia; one case with pyometra, one breast cancer recurrence, one severe neutropenia and one with severe psoriasis flare. There were no thrombotic events. The only variable related with remission was the low baseline DAS.
Conclusion: The JAK inhibitors are tsDMARD with good profile of efficacy and safety in clinical practice. The patients treated with these drugs had a long and severe disease with failure to several drugs and poor prognostic variables, and a high comorbidity index, however these drugs show good response rates.
Disclosure of Interests: None declared
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AB1320 **NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO ARE ASSOCIATED WITH DISEASE ACTIVITY IN POLYMYALGIA RHEUMATICA**

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Background: Polymyalgia rheumatica (PMR) is a systemic inflammatory disorder, which develops inflammatory pain and stiffness of large joints. There is no specific serological marker or test to differentiate PMR.
Objectives: In this study, we compared the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) among patients with polymyalgia rheumatica (PMR) and rheumatoid arthritis (RA), and explored possible associations with clinical features, disease activity, and prognosis in PMR.
Methods: A total of 94 PMR and 242 RA patients who were initially diagnosed at the rheumatology clinic of a university-based tertiary hospital were enrolled. Symptoms, physical examination, and medical histories were collected with the results of laboratory tests.
Results: NLR (4.5 ± 3.3 vs. 2.8 ± 1.8), PLR (222.7 ± 115.5 vs. 159.7 ± 78.1), and MLR (0.4 ± 0.3 vs. 0.3 ± 0.2) were higher in patients with PMR compared with patients with RA (all $p < 0.001$). NLR, PLR, and MLR were correlated with specific serological values, including CRP and albumin, in patients with PMR. After disease activity resolved, NLR (2.95 ± 2.32, $p < 0.001$), PLR (137.5 ± 82.3, $p < 0.001$), and MLR (0.26 ± 0.16, $p < 0.001$) decreased significantly. By comparing patients according to the disease course, swollen joint counts were higher in the chronic course group compared with the remission group ($p = 0.03$), while NLR, PLR, and MLR levels were similar.
Conclusion: This study found that NLR, PLR, and MLR in patients with PMR were higher than in those with RA. Furthermore, NLR, PLR, and MLR levels were associated with disease activity and specific clinical features, although they could not predict prognosis in patients with PMR.

REFERENCES:

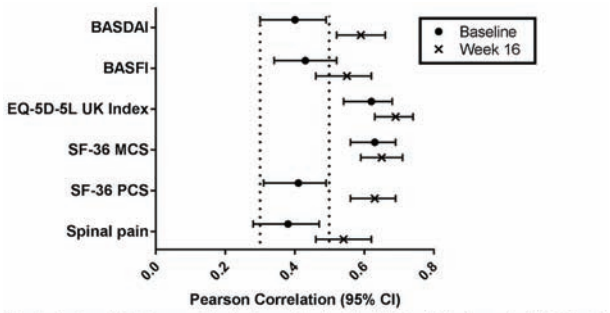
[1] van der Geest KS, Abdulahad WH, Rutgers A, Horst G, Bijzet J, Arends S, et al. Serum markers associated with disease activity in giant cell arteritis and polymyalgia rheumatica. Rheumatology (Oxford). 2015;54(8):1397-402.
[2] Erre GL, Paliogiannis P, Castagna F, Mangoni AA, Carru C, Passiu G, et al. Meta-analysis of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in rheumatoid arthritis. Eur J Clin Invest. 2018:e13037

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AB1321 **PSYCHOMETRIC PROPERTIES OF THE ASAS HEALTH INDEX IN PATIENTS WITH ACTIVE AS/RADIOGRAPHIC AXIAL SPA WHO HAVE PRIOR INADEQUATE RESPONSE/INTOLERANCE TO TNF INHIBITORS IN A PHASE 3 TRIAL**

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Background: The Assessment of SpondyloArthritis international Society Health Index (ASAS HI) assesses function, disability, and health in patients with ankylosing spondylitis/radiographic axial spondyloarthritis (AS/r-axSpA).
Objectives: To evaluate the psychometric properties of the ASAS HI in patients with active AS/r-axSpA in a placebo-controlled study of ixekizumab, a humanized IL-17A monoclonal antibody (COAST-W, NCT02696798).
Methods: The ASAS HI questionnaire consists of 17 dichotomous items that yield a total score ranging from 0 (good health) to 17 (poor health). The psychometric properties of the questionnaire, including test-retest reliability, convergent and discriminant validity, and responsiveness, were evaluated using pooled data from three exposure groups (placebo and ixekizumab 80 mg every 2 or 4 weeks). Adults enrolled fulfilled ASAS criteria (sacroiliitis defined centrally by modified New York Criteria and ≥1 SpA feature), had active disease (BASDAI ≥4, back pain ≥4), and either prior inadequate response or intolerance to 1 or 2 TNF inhibitors.
Results: Mean baseline ASAS HI score was 9.7 (SD=3.62, n=316). Intraclass correlation (0.78) indicated test-retest reliability of ASAS HI between screening and baseline. ASAS HI score was moderately correlated at baseline ($|r|>0.30$, Figure [circles]) and strongly correlated at Week (Wk) 16 ($|r|>0.50$; Figure [crosses]) with BASDAI, BASFI, SF-36 PCS, and spinal pain, and strongly correlated at both baseline and Wk 16 with EQ-5D-5L UK Population-based Index and SF-36 MCS. Greater improvements in disease activity were associated with greater improvements in ASAS HI scores at Wk 16 (Table).
Conclusion: The ASAS HI demonstrated reliability, validity, and responsiveness in adults with AS/r-axSpA, supporting its use in clinical trials.



Magnitude of correlation is presented without regard for directionality. Correlation for moderate (>0.3) and high (>0.5).*
Abbreviations: MCS=mental component summary; PCS = physical component summary; SF-36 = 36-item short-form health survey
*Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.). New Jersey: Lawrence Erlbaum.

Figure. Correlation between ASAS-HI and other health measures

Table. Association between ASAS HI Change from Baseline and Disease Activity at Wk 16 (Pooled Treatment Groups)

	ASAS20 Nonresponder	Patient Achieving ASAS20, but Not ASAS40	ASAS40 Responder
N	181	60	72
ASAS HI (LSM [SE])	-0.3 (0.21)	-1.9 (0.37)***	-4.2 (0.34)***,§
	ASDAS Improvement <1.1	**ASDAS Improvement ≥1.1 but <2.0 (clinically important improvement)**	**ASDAS Improvement ≥2.0 (major improvement)**
N	196	74	43
ASAS HI (LSM [SE])	-0.4 (0.20)	-2.8 (0.33)***	-4.6 (0.43)***,§
	BASDAI 50 Nonresponder	**BASDAI 50 Responder**	
N	255	58	
ASAS HI (LSM [SE])	-0.8 (0.18)	-4.6 (0.38)***	

ASDAS = AS Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; LSM = least squares mean
***p<.001 versus lowest response group; § p<.001 versus middle response group.

Note: An ANCOVA model with change in ASAS HI score as dependent variable and clinical outcome response and baseline ASAS HI as independent variables was applied. Post hoc comparison was conducted using Scheffé's correction.

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AB1322

DEPRESSION IN ESTABLISHED RHEUMATOID ARTHRITIS; MULTICENTER PROSPECTIVE COHORT STUDY FOR EVALUATION OF JOINT SURGERY ON PATIENT'S REPORTED OUTCOME

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Background: Loss of physical function is a clinical feature of RA. Total management including reconstructive joint surgery and rehabilitation should be needed for further improvements of physical function for established RA patients. In these days, it is very important to evaluate the effectiveness of joint surgery as well as drug therapy based on patient-reported outcome (PRO).

Objectives: The purpose of this study is to explore the relationship among depression, clinical variables and other PROs including physical function and improving of depressive status with joint surgery.

Methods: Multicenter prospective observational cohort study was conducted among patients who underwent elective joint surgery for RA from April 2012 to March 2016 (Study registration: UMIN000012649) (ref.1). In this study, we collected data at baseline and at 6 or 12 months after the surgery. These data were as follow; age, sex, disease duration, drug therapies, and disease activity (DAS28-CRP), and PRO measures [HAQ-DI, EQ-5D (QOL), pain VAS and BDI-II (depression)]. Correlation between BDI-II and other variables were determined using multiple liner regression analysis with forward stepwise.

Results: Totally, 346 patients before elective joint surgery were analyzed cross-sectionally. Mean age, disease duration, pain(VAS), DAS28, HAQ-DI, EQ-5D and BDI-II were 64.2 years, 17.0 years, 36.2 mm, 3.02, 1.111, 0.641 and 13.0, respectively. 52.6% of elective joint surgeries were in upper limbs and 47.4% were in lower limbs. Multiple liner regression analysis showed that HAQ-DI [β:-0.48, p<0.001] pain VAS(β:-0.26, p<0.001) and BDI-II (β:-0.19, p<0.001)were independent factors for EQ-5D. Furthermore, HAQ-DI (β: 0.31, p<0.001) and pain VAS (β: 0.17, p=0.002) had significant impact on BDI-II. Especially, walking (β: 0.12, p<0.001) and eating (β: 0.16, p=0.005) were independent factors for BDI-II in HAQ-DI categories. As longitudinal analyses (n=138), mean BDI-II was significantly improved from 12.1 at baseline to 10.5 at last observation (6 or 12 months) after joint surgery in lower limbs (paired t-test, p<0.001). Change in HAQ-DI (β: 0.23, p=0.031) had significant impact on that in BDI-II. The improving in walk category (β: 0.21, p=0.012) was a relevant factor for improving of BDI-II after the surgery.

Conclusion: Loss of physical function is an important factor for impairment of depressive status as well as QOL in established RA patients. Improving of physical function with joint surgery in lower limbs caused improving of depressive status. Rheumatologists should take the joint surgery into consideration as effective intervention for treatment of established RA patients.

REFERENCES

[1] Kojima T, et al. Int J Rheum Dis. 2018. doi: 10.1111/1756-185X.13394.

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AB1323 OSTEOPHYTOSIS PROCESS SUGGEST INVOLVEMENT OF MAST CELLS, REVEALED BY WHOLE TRANSCRIPTOME ANALYSIS OF OSTEOPHYTES FROM KNEE OSTEOARTHRITIS PATIENTS

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Background: Cartilage-loss is a central pathology of osteoarthritis while synovitis, sub-chondral bone sclerosis and osteophytes (OFs) formation are counted as integral phenomenon. Osteophytosis is a process of OFs formation, in which mesenchymal stem cells from periosteum and synovium, along with a number of cytokines, growth factors and biochemical factors gives out bony out-growth at margin of the affected joint. Although frequently associated, OFs are one of the less focused areas in OA research, particularly from the molecular mechanism point of view, involved in their formation. Also, it is a good ambiguity if OFs is a pathological condition linked with altered biochemical milieu or a functional adaptation for the joint instability.

Objectives: Accounting its importance in clinical OA and the obscure biochemical background, this study strives for a deeper comprehension of molecular mechanism and active pathways, involved in OF formation

Methods: We performed whole transcriptome analysis of OFs, collected from six knee OA patients during knee replacement surgery. Non-OF tissue from tibial plateau of the same patient was used as a control. After RNA isolation, RNA-seq was performed using SOLiD 5500W platform and fragment sequencing chemistry. For differential gene expression analysis, non- normalized raw counts were used for the EdgeR package. To find differential transcriptome between OF and control, we used group-wise comparisons where negative binomial fitting was followed by exact test. Finally, RT-PCR of significantly expressed genes was run for trascriptome validation.

Results: After cluster analysis, total 597 genes were significantly expressed between OFs and controls out of which, 323 genes were seen up-regulated (LogFC$\geq$ 2) while 274 were down-regulated (LogFC$\leq$ -2). Further, 88 genes showed marked increase (P<0.01); here CPA3, Selectin E, MS4A2, PLA2G2A and CSN1S1 were prominent. Similarly, 23 genes were with a noteworthy down-regulation (P<0.01) and APOB, CADM2, TNEFF2, GNAZ and GABRA2 remained as first five. GO analysis of the best extracted genes indicated significant involvement of ECM proteoglycan, GABA A receptor pathway (Reactome 2016 - homo sapiens_R-HSA-3000178 and R-HSA-977441, respectively), osteoblast and TNF-α signalling pathways (WikiPathways 2016 -homo sapiens WP322 and homo sapiens WP231 respectively). Finally, tracsriptome results were validated using RT-PCR of significantly expressed genes (CPA3, MMP-1, 3 and 13).

Conclusion: Significant expression of CXCL9, 10, 11 and PGR4 indicate chemotaxis and immune cells deployment; outstanding CPA3 and MS4A2 indicate active involvement of mast cells. Accounting a previous knowledge that 'mast cell products' are linked with increased osteoblastic and osteoclastic activity and impose pathological changes in articular and periarticular tissue, marked expressions of MC products or mediators here, enable us to propose an association between MCs and OF. Presence of E-selectin on endothelial cell surface is known to promote adhesion of neutrophils and further release of TNFα and IL1. Expression of PLA2G2A suggests increased prostaglandin synthesis and indicates activation of inflammatory cascade. In conclusion, this transcriptome analysis suggests a significant association of mast cells with osteophytosis. The genes involving chemotaxis, degranulation, cytokinin synthesis mark the initiation of OF. On the other hand, proteases metrixremodelling enzymes may indicate their growth. A host of different signalling molecules denotes involvement of canonical and non-cannonical pathways that warrants further investigations.

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AB1324 MEASUREMENT PROPERTIES OF THE 10-ITEM CONNOR-DAVIDSON RESILIENCE SCALE AMONG PATIENTS WITH TOTAL KNEE REPLACEMENT BASED ON ITEM RESPONSE THEORY

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Background: The number of older adults undergoing total knee arthroplasty (TKR) for knee osteoarthritis (OA) has been increasing. While psychological resilience may have a role in outcomes after TKR[1], no psychological resilience scale has been validated among patients with knee OA.

Objectives: To examine the measurement properties of the 10-item Connor-Davidson Resilience Scale (CD-RISC10) among older adults with knee OA.

Methods: Using data from 700 consecutive consented patients with knee OA enlisted for TKR, we examined four measurement properties of CD-RISC10. For **structural validity**, we fitted graded response model (grm) and examined standardized root-mean square residual (SRMR) for unidimensionality, Chi-square p-value for item fit, residual correlation for local independence and item-characteristic curves for monotonicity. For **internal consistency**, we examined Cronbach's alpha. For **construct validity**, we hypothesized that CD-RISC10 as a measure of psychological resilience would be moderately correlated (Pearson's R 0.30–0.50) with self-efficacy and mental well-being but weakly correlated (Pearson's R<0.30) with physical and social well-being (Table 1). For **measurement invariance**, we examined uniform and non-uniform differential item functioning (DIF) between gender, age group ($\leq$ median 66 vs >66 years), and language (English vs Chinese) and reported the McFadden's R^2. We used mirt and lordif packages on Rx64 v3.5.1 to examine grm and DIF respectively. We reported the findings based on COnsensus based Standards for the selection of health Measurement Instruments (COSMIN)[2].

Results: Of the 700 patients (age 65.5±6.9 years old), 70.6% were females, 83.9% Chinese, 55% responded questionnaire in Chinese. Mean CD-RISC10 score was 27.5±5.2, with minimal floor (0.1%) and ceiling effects (3.9%). CD-RISC10 demonstrated unidimensionality (SRMR=0.053), local independence (residual correlation=-0.025), monotonicity (adequate looking item characteristic curves) and internal consistency (Cronbach's alpha=0.91). Items 1 and 4 had potential misfit (Chi-square p>0.01). All a-priori hypotheses were met (Table 1). No item had significant DIF with age, gender and language, except item 4 had borderline non-uniform DIF across language (McFadden's R^2=0.03).

Conclusion: We demonstrated structure validity, internal consistency, construct validity and measurement invariance of CD-RISC10 in the measurement of psychological resilience among older adults with knee OA.

REFERENCES

[1] Rebagliati, et al. Funct Neurol, 2016. 31(3): 171-7.
[2] Mokkink, et al. COSMIN User Manual. 2018

Table 1. Hypothesized and actual correlations for convergent validity

	Hypothesized		Actual		Hypotheses Met
	Direction	R	R	p-value	
Internal resource					
Pain self-efficacy	+	0.30 – 0.50	0.48	0.000	Yes
Mental well-being					
HADS anxiety	-	-0.30 – -0.50	-0.37	0.000	Yes
HADS depression	-	-0.30 – -0.50	-0.31	0.000	Yes
SF-36 mental health	+	0.30 - 0.50	0.30	0.000	Yes
Physical well-being					
WOMAC physical function	-	> -0.30	-0.17	0.000	Yes
WOMAC pain	-	> -0.30	-0.16	0.000	Yes
WOMAC stiffness	-	> -0.30	-0.11	0.005	Yes
SF-36 physical functioning	+	< 0.30	0.15	0.000	Yes
Social well-being					
Lubben's social network score	+	< 0.30	0.22	0.000	Yes

HADS:Hospital Anxiety & Depression Scale; SF-36:Short-Form 36; WOMAC:Western Ontario & McMaster Universities Osteoarthritis Index

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AB1325 HAND FUNCTION IS IMPAIRED IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND PSORIASIS COMPARED TO HEALTHY CONTROLS

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Background: Inflammatory-rheumatic diseases affect hand joints with swelling and pain, leading to joint destruction. Even patients with psoriasis only may suffer subclinical inflammation in the hand joints, leading to changes of bone [1]. Finger joint involvement is different for rheumatoid arthritis (RA), psoriatic arthritis (PsA) and psoriasis (Pso) but hand function in these patients is not well characterized.

Objectives: To quantify and compare grip strength and hand function in patients with RA, PsA and Pso and to relate these outcomes to disease activity.

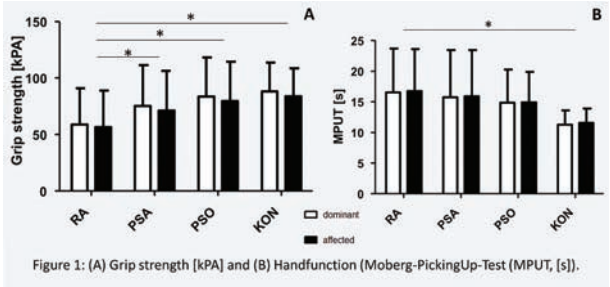


Figure 1: (A) Grip strength [kPA] and (B) Handfunction (Moberg-PickingUp-Test (MPUT, [s]).

Figure 1

Methods: Patient diagnosed with RA (ACR/EULAR 2010), PsA (Caspar) and Pso and 54 healthy individuals were included in the study after written informed consent. Maximal isometric grip strength (kPA) was measured with a hand dynamometer (Lafayette Instrument, Lafayette, IN, USA) as the highest value out of three measurements. Hand function was determined by way of the Moberg Picking-Up Test (MPUT) and the fastest (s) of two measurements was used. Disease activity was calculated as DAS28_ESR and TJC/SJC 78/76 was recorded. One-way Analysis of Variance (ANOVA), factorial ANOVA and Games-Howell post-hoc testing was performed ($p<0.05$).

Results: 101 RA (63 f; 38 m; age: 59.1±13.2 yrs), 92 PsA (48 f, 44 m; age 54.8±11.6 yrs) and 51 Pso patients (19 f, 32 m; age 47.3±14.1 yrs), as well as 54 healthy control subjects (30 f, 24 m; age 54.6± 16.5 yrs) participated in the study. Disease duration (yrs) was not different between groups (RA: 11.03±10.1, PsA: 9.1±9.75, Pso: 12.5±11.7; p=0.156) but Pso patients in our cohort were younger compared to RA and PsA patients. Mean DAS28_ESR was < 3.2 for all patient groups with control subjects (DAS28 1.6 ± 0.7) having lower scores compared to all patient groups and Pso patients presenting with lower DAS28 (2.3 ±1.3) compared to RA (3.0±1.3) and PsA (2.9±1.3). While TJC was higher for all patients compared to controls (RA: 5.2±6.8, PsA: 5.9±8.1 Pso: 3.2±6.4; CON: 0.5±1.4; p=0.00), SJC was higher for RA and PsA compared to Pso and CON (RA: 0.7±1.0, PsA: 0.9±2.2 Pso: 0.1±0.3; CON: 0.5±1.4; p=0.000). Grip strength of the dominant and/or affected hand of RA patients was lower compared to PsA, Pso and CON (Figure 1A). In contrast to this, hand function of the same hand in all tested patient groups was reduced compared to CON (Figure 1B). The results for grip strength and hand function were not different for the dominant and the affected hand and are independent of age differences between groups.

Conclusion: Overall, RA patients showed significantly lower grip strength compared to PsA and Pso patients as well as to the control group, whereas all three patient groups performed worse in the MPUT compared to the control cohort. This suggests that grip strength may be preserved longer than hand function in patients with inflammatory rheumatic disease. Further, it was surprizing that hand function was reduced in Pso patients without arthritic correlate compared to healthy subjects. This suggests that hand function may provide a potential parameter for discriminating Pso patients at risk for subclinical joint involvement.

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REFERENCES

[1] Faustini F, Simon D, et al. 2016, Ann Rheum Dis 75: 2068-2074.

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AB1326 INCREASED FIBRINOGEN TO ALBUMIN RATIO IN ANKYLOSING SPONDYLITIS: CORRELATION WITH DISEASE ACTIVITY

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Background: Fibrinogen to albumin ratio (FAR) has emerged as a new effective biomarker which can reflect the severity of chronic inflammation. However, none of study has focused on the role of FAR in ankylosing spondylitis (AS).

Objectives: The study aimed to investigate the association between FAR and the disease activity of AS.

Methods: The retrospective study included 117 AS patients and 165 age- and gender-matched healthy controls. AS patients were divided into remission group (Bath Ankylosing Spondylitis Disease Activity Index

(BASDAI) < 4) and active group(BASDAI ≥ 4). Remission group included 60 patients and active group included 57 patients. Fibrinogen, albumin, FAR, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were collected. Relationships between FAR and BASDAI as well as other biochemical indexes were assessed by the Sperman's correlations analysis. Receiver operation characteristic (ROC) curves were performed to discriminate AS patients from healthy subjects and active group from remission group. Furthermore, binary logistic regression analysis was conducted to evaluate the risk factors of AS disease activity.

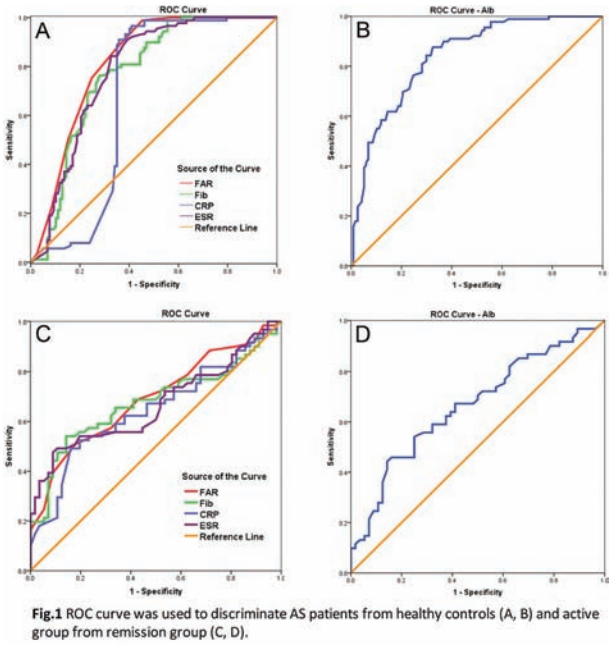


Fig.1 ROC curve was used to discriminate AS patients from healthy controls (A, B) and active group from remission group (C, D).

Figure 1

Results: FAR, fibrinogen, CRP and ESR were higher in AS patients compared with healthy controls (P < 0.05), while albumin was lower (P < 0.05). ROC results showed that area under curve (AUC) of FAR (0.818, 95%CI: 0.760 - 0.876) and albumin (0.841, 95%CI: 0.788 - 0.894) were higher than fibrinogen (0.772, 95%CI: 0.707-0.836), CRP (0.677, 95%CI: 0.598 - 0.756) and ESR (0.784, 95%CI: 0.721 - 0.847). Positive correlations were found between FAR and BASDAI (r = 0.488, P < 0.001), CRP (r = 0.858, P < 0.001) and ESR (r = 0.817, P < 0.001). Besides, FAR, fibrinogen, CRP and ESR in active group were higher than remission group (P < 0.05), while albumin was lower (P < 0.05). ROC results showed that AUC of FAR (0.691, 95%CI: 0.596-0.786) was higher than fibrinogen (0.676, 95%CI: 0.577 - 0.776), albumin (0.665, 95%CI: 0.567 - 0.763), CRP (0.646, 95%CI: 0.545 - 0.746) and ESR (0.667, 95%CI: 0.569 - 0.766). FAR was a risk factor of the disease activity in AS patients (OR: 1.354, 95%CI: 1.067 - 1.718, P = 0.013).
Conclusion: FAR was increased in AS patients compared with healthy controls and significantly correlated with the disease activity of AS. FAR might be a potential useful inflammatory biomarker to monitor disease activity of AS patients.

REFERENCES

[1] Karahan O, Acet H, Ertas F, et al. The relationship between fibrinogen to albumin ratio and severity of coronary artery disease in patients with STEMI[J]. Am J Emerg Med, 2016,34(6):1037-1042.
[2] Yang W M, Zhang W H, Ying H Q, et al. Two new inflammatory markers associated with disease activity score-28 in patients with rheumatoid arthritis: Albumin to fibrinogen ratio and C-reactive protein to albumin ratio[J]. Int Immunopharmacol, 2018,62:293-298.

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AB1327

SEROLOGICAL BIOMARKERS IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: CORRELATION WITH IMAGING AND DISEASE ACTIVITY IN 24-MONTHS FOLLOW UP (ITALIAN ARM OF SPACE STUDY)

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Background: Recently studies have focused on the role of new markers to diagnose early axial spondyloarthritis (axSpA), to evaluate disease activity (DA) and to predict patients (pts) at higher risk for a worse outcome.Common biomarkers, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are often ineffective in assessing DA.
Objectives: To evaluate biomarkers and their correlations with clinical and DA indices and imaging in pts with early axSpA.
Methods: Seventy-five patients with low back pain (≥3 months,≤2 years, onset ≤45 years) participating in the Italian arm of the SpondyloArthritis-Caught-Early SPACE study underwent a physical examination, questionnaires, laboratory tests, X-rays and MRI of the spine and sacroiliac joints (SIJ) at baseline (T0) and during a 24-months follow-up.Two expert rheumatologists formulated axSpA diagnosis and assessed fulfilment of Assessment of SpondyloArthritis International Society ASAS criteria.The DA and physical functioning were assessed using:Bath Ankylosing Spondylitis Metrology Index (BASMI);Maastricht Ankylosing enthesitis Spondilities Score (MASES); Bath Ankylosing Spondylitis Disease Activity Index (BASDAI);Bath Ankylosing Spondylitis Functional Index (BASFI);Ankylosing Spondylitis disease activity score (ASDAS);Visual Analogue Scale (VAS pain); VAS night pain;VAS disease activity;Bath Ankylosing Spondylitis Patient Global Score (BASG1); BASG2;Health Assessment Questionnaire (HAQ);ESR;serum ultrasensitive CRP(hs-CRP);matrix metalloproteinase (MMP3);interleukin (IL) IL-22, IL-17, IL-23.Positive spine and SIJ MRI images were scored independently by 2 readers using the Spondyloarthritis Research Consortium of Canada (SPARCC) method; the spine and SIJ X-rays images were scored using mSASSS and NY-criteria.After the X-rays and MRI images of all pts were read, they were classified in accordance ASAS criteria as: 21 patients classified according to axSpA imaging arm;29 patients classified according to axSpA clinical+/-imaging arm;25 patients not fulfilling ASAS criteria.

Table 1a: Correlations between MMP-3, IL-22 and clinical indices and imaging scores.

	MMP3	IL-22
ESR	0.26 (0.041)	ns
hsCRP	0.28 (0.029)	ns
mSASSS	0.31 (0.005)	ns
SPARCC-SIJ	ns	0.043
BASMI	ns	0.28 (0.040)
BASFI	ns	0.35 (0.008)
BASG1	ns	0.34 (0.008)
HAQ	ns	0.27 (0.040)
VAS pain	ns	0.26 (0.013)

Table 1b. Correlations between hsCRP, ESR and clinical indices and imaging scores.

	hsCRP	ESR
BASG1	ns	0.27 (0.028)
BASG2	ns	0.26 (0.041)
ASDAS	ns	0.29 (0.025)
SPARCC-SIJ	0.35 (0.047)	ns
mSASSS	ns	-0.12 (0.038)

P was calculated according to Spearman's correlation test. Data are expressed as correlation coefficient (p value).

Results: Significant differences were found in the prevalence of radiographic sacroiliitis, active sacroiliitis on MRI and SPARCC SIJ scores.At T0 biomarker levels were not significantly increased in any of the patient groups.It was observed instead a significant decrease of all functional and DA indices values from T0 to 24 months in the three groups: MASES (p=0.008),BASG1(p=0.02),BASG2 (p<0.0001),HAQ (p=0.0002),VAS-pain (p=0.01),VAS pain night(p=0.04),VAS disease activity(p=0.05), BASFI (p=0.02),BASDAI (p<0.0001),ASDAS(p<0.0001).There were no differences in the serological markers values during the 2 years follow up period.The correlation of IL-17 and IL-23 with other indices was not significant.On the other hand significant correlations were found between IL-22 and some clinical indices (BASFI,BASG1,HAQ,VAS pain);between mSASSS and MMP3 and between mSASSS and hsCRP (**Table 1a-b**).
Conclusion: Although not significantly higher in any of the three groups, IL-22, MMP3 and hsCRP values correlated with some disease activity indices and with mSASSS. ILs, MMP-3 and hsCRP values were not significantly increased in any of the study groups and were not related to radiographic SIJ involvement or to clinical and DA indices.The limitation

of the study was the small numbers of the patients in the single group and the early disease stage.Further studies are needed to analyze the validity and reproducibility of these biomarkers in early axSpA.
Disclosure of Interests: None declared
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AB1328 MEASUREMENT PROPERTIES OF THE BRIEF PAIN INVENTORY-SHORT FORM (BPI-SF) AND THE REVISED SHORT-FORM MCGILL PAIN QUESTIONNAIRE-VERSION-2 (SF-MPQ-2) IN PAIN-RELATED MUSCULOSKELETAL CONDITIONS: A SYSTEMATIC REVIEW

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Background: The Brief Pain Inventory (BPF-SF) and McGill Pain Questionnaire (SF-MPQ-2) are general-use, self-report, multidimensional pain assessment outcomes frequently used for pain assessment in musculoskeletal (MSK) conditions. Synthesizing knowledge on their measurement properties, as assessed in MSK conditions, should provide a deeper understanding of their strengths and limitations.
Objectives: To systematically locate, critically appraise, compare and summarize clinical measurement research about the BPI-SF and SF-MPQ-2 in pain-related musculoskeletal conditions
Methods: Four databases (Medline, CINAHL, EMBASE & SCOPUS) were systematically searched for relevant citations, each for the BPI-SF and SF-MPQ-2. We included articles that reported the psychometric properties (e.g. validity, reliability, responsiveness) and interpretability indices (e.g. minimal clinical important difference) of both tools, as assessed in mixed and specific MSK studies. Independently, two reviewers extracted data and assessed the quality of evidence with a structured quality assessment tool for measurement studies and according to the updated **CO**nsensus-based **S**tandards for the selection of health **M**easurement **IN**struments (COSMIN) guidelines.
Results: Twenty-five articles were included (BPI-SF, n=17; SF-MPQ-2, n=8). Both tools lack reporting on their cross-cultural validities and measurement error indices. High quality studies suggest that they are internally consistent (α = 0.83-0.96), and they associate modestly with similar outcome measures (r = 0.3-0.69). There is evidence that the BPI-SF conforms to its two-dimensional structure in MSK studies; the SF-MPQ-2 four-factor structure was not clearly established. In seven reports, high to moderate quality evidence was seen in supports of the BPI-SF known group validity (n=2) and responsiveness (n=5) but none was available for the SF-MPQ-2. Furthermore, the SF-MPQ-2 was more frequently associated with floor effects in MSK studies than the BPI-SF (SF-MPQ-2, 42% vs BPI-SF, 6%).
Conclusion: The SF-MPQ-2 has emeging evidence whereas the BPI-SF evidence is more mature. Both tools displayed high-quality evidence in support of their internal consistency and criterion-convergent validities. High to moderate quality evidence suggests the BPI-SF subscales have a better responsiveness, retest reliability, known group validity and structural validity than the SF-MPQ-2.

REFERENCES

[1] Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singapore. 1994;23(2):129-138. doi:10.1016/0029-7844(94)00457-O.
[2] Dworkin RH, Turk DC, Revicki DA, et al. Development and initial validation of an expanded and revised version of the Short-form McGill Pain Questionnaire (SF-MPQ-2). Pain. 2009;144(1):35-42. doi:10.1016/j.pain.2009.02.007.
[3] Dworkin RH, Turk DC, Trudeau JJ, et al. Validation of the Short-Form McGill Pain Questionnaire-2 (SF-MPQ-2) in Acute Low Back Pain. J Pain. 2015;16(4):357-366. doi:10.1016/j.jpain.2015.01.012.

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AB1329 THE PRELIMINARY VALIDATION OF LASER DOPPLER FLOWMETRY IN SYSTEMIC SCLEROSIS ACCORDING TO THE OMERACT FILTER: A SYSTEMATIC REVIEW

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Background: Systemic sclerosis (SSc) is characterised by a widespread vasculopathy. The vasculopathy comprises the skin microcirculation and results in features such as Raynaud's phenomenon (RP) and digital trofic lesions. The quantification of the skin blood perfusion at the level of the finger (FBP) is a major need in the assessment of SSc in clinical and research setting[1]. Up to now, laser doppler flowmetry (LDF) has been the most thoroughly investigated instrument to assess the FBP in SSc.
Objectives: To investigate the validation status of LDF in SSc according to the 'Outcome Measures in Rheumatologic Clinical Trials' (OMERACT) filter.
Methods: Literature was systematically reviewed to detect all reports in which the assessment of the FBP in SSc patients was described. The OMERACT filter, including the domains of truth, discrimination and feasibility was applied and a quality assessment was done by the Good Methods Checklist[2]. Comparison between studies was eased by grouping the results per dynamic test situation (basal circumstances, cold/heat challenge and occlusion).
Results: The systematic search resulted in 4340 hits. After title and abstract screening 228 hits remained and of these, 79 full texts described the assessment by LDF. Fifty studies were included for quality assessment of which 17 studies were retained for conclusion making (fig 1).

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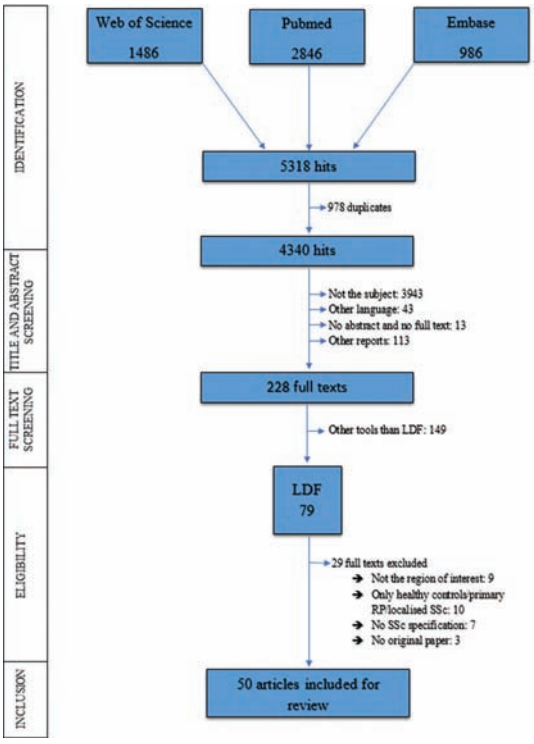


Figure 1. Flowchart of the systematic search

An overview of the validation status of LDF is given in table 1. Expert consensus is lacking on the face and content validity of LDF in SSc. The construct validity of LDF is partially validated (e.g. the correlation with laser speckle contrast imaging was attested in one study). Conflicting results exist on the discriminant capacity of LDF to distinguish healthy from diseased, primary from secondary RP and to differentiate between disease subsets. The addition of a heat challenge, as well as the evaluation of the post-occlusive hyperemic response to the LDF-measurement has the potential to elicit a difference between healthy and diseased. Lastly, there are no data on the feasibility of LDF in SSc.

Table 1. Validation of LDF according to the OMERACT filter

	TRUTH			DISCRIMINATION				FEASIBILITY
	Face	Content	Construct	Sensitivity in situations of change			Sensitivity in situations of no change	
				HC vs SSc	PRP vs SRP	LcSSc vs DcSSc	In clinical trials	
Basal	ND	NA	PV	PV	V	PV	PV	V	ND
Cold challenge	ND	V	ND	PV	V	ND	PV	ND	ND
Heat challenge	ND	V	PV	PV	V	PV	PV	ND	ND
PORH kinetics	ND	ND	ND	V	PV	V	ND	ND	ND
PORH amplitude	ND	ND	ND	PV	PV	UV	ND	ND	ND

Conclusion: This systematic review emphasizes the very preliminary validation status of LDF in the assessment of the FBP in SSc. No single application method has emerged as fully validated according to the OMERACT filter.

REFERENCES

[1] Herrick A, et al. ARD 1998; 57:70-78
[2] Boers M, et al. The OMERACT handbook. Ottowa, ON, Canada: OMERACT; 2017

Only those studies which were found of good quality according to the Good Methods Checklist were considered and only the results where p-values were given were considered in this table. OMERACT= Outcome Measures in Rheumatologic Clinical Trails; HC= healthy controls; PRP= primary Raynaud's phenomenon; SRP= secondary Raynaud's phenomenon due to systemic sclerosis; LcSSc: limited cutaneous disease; DcSSc: diffuse cutaneous disease; PORH= post-occlusive reactive hyperaemia; NA= not applicable; ND= no data; V= valid if agreement exists among studies; PV= partially valid if disagreement exists among studies; UV= unvalid if agreement about insignificant results exists.

Disclosure of Interests: None declared
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AB1330 SOLUBLE VASCULAR CELL ADHESION MOLECULE-1 AS AN INDEPENDENT MARKER FOR ENDOTHELIAL ACTIVATION IS ELEVATED IN ACTIVE RHEUMATIC DISEASES: A MULTIVARIATE ANALYSIS

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Background: CRP and/or ESR are often unreliable indicators of disease activity. Serum markers of endothelial activation may be promising alternatives. We have recently shown that soluble vascular cell adhesion molecule-1 (sVCAM-1) is elevated in patients with positive antinuclear antibodies [1]. We also have described similar findings in another cohort of patients with a variety of rheumatic diseases [2] and now report a multivariate analysis of these data.
Objectives: CRP, ESR, age, disease and gender were correlated to sVCAM-1.
Methods: Cross-sectional study with 230 patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and different vasculitides (VASC). Disease activities were determined using DAS28, BASDAI, BVAS, RF, ACPA, CRP or ESR. Treatment regimens were subgrouped for conventional DMARDs (cDMARDs) or sets of biologics (bDMARDs). sVCAM-1 (ng/ml) was determined in the serum by ELISA and data were compared to age- and gender-matched healthy controls (HC).
Results: Significant ($p < 0.05$) overexpression of sVCAM-1 as compared to HC were found in the following groups and subgroups (subgroup data not shown): **RA** (n=136): 1.26-fold and in subgroups with bDMARDs, female gender, age >50 years, and RF≥15 IU/ml. **AS** (n=34): 1.71-fold and in subgroups with bDMARDs, age ≤50 years, female gender, CRP <3 mg/dl, and ESR<20 mm/h. **VASC** (n=25): 2.52-fold and in subgroups with cDMARDs, BVAS ≤10 and >10, disease duration ≤120 months, age ≤50 years, female and male gender, CRP ≤3 mg/dl, and ESR ≤20 mm/h. **PsA** (n=35): no significant changes. Linear regression analysis showed that CRP and ESR but not sVCAM-1 were correlated to each other ($r=0.637$, $p<0.001$). In addition, multiple linear regression showed that sVCAM-1 was independently associated with age and disease (RA, AS, VASC). However, sVCAM-1 had no impact on CRP, ESR and gender.
Conclusion: sVCAM-1 is an objective disease marker in patients with RA, AS and VASC. sVCAM-1 is not correlated with CRP and ESR and may thus provide additional information of disease activity. Prospective studies are needed to establish sVCAM-1 as a marker of rheumatic diseases, especially in vasculitis.

REFERENCES

[1] Oleszowsky M, Seidel MF. Serum Soluble Vascular Cell Adhesion Molecule-1 Overexpression Is a Disease Marker in Patients with First-Time Diagnosed Antinuclear Antibodies: A Prospective, Observational Pilot Study. Biomed Res Int. 2018:8286067. doi: 10.1155/2018/8286067. eCollection 2018. 1;2018:8286067.
[2] Laaraj W, Seidel MF. Soluble vascular adhesion molecule-1 is overexpressed in patients with vasculitis, rheumatoid arthritis and ankylosing spondylitis. Ann Rheum Dis. 2018, 77(supp. 2018), A1185, DOI: 10.1136/annrheumdis-2018-eular.5850

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AB1331 URINE METABOLIC PROFILE IN RHEUMATOID ARTHRITIS DEVELOPMENT

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by increased mortality and associated with metabolic disorders including dyslipidaemia, insulin resistance and cachexia. Since the metabolomic profile is known to vary in response to different inflammatory conditions, metabolome analysis could substantially contribute to diagnosis and prognosis.
Objectives: To analyse the urine metabolic profile and assess its correlation with body composition parameters and disease activity of RA patients.
Methods: Seventy-nine RA patients, according to ACR/EULAR 2010 classification criteria, aged between 40 and 70 years, were recruited and followed for 12 months. Disease activity, body composition, fatigue and urine metabolome were measured. Body composition was assessed by total body dual-energy x-ray absorptiometry (DXA) for measurement of appendicular lean mass index (ALMI). Disease activity was assessed by Disease Activity Score-28 with erythrocyte sedimentation rate (DAS28-ESR). Fatigue as assessed by the Functional Assessment of Chronic Illness Therapy (FACIT). Nuclear Magnetic Resonance spectroscopy (NMR) measurements were performed to evaluate the profile of metabolic changes during the 12mo follow-up, resulting in the identification of 48 metabolites in urine collected at the baseline and after one year. Frequency analysis, Pearson Correlation and Multivariate data analysis with orthogonal projections to latent structures (OPLS) method were performed and a statistical significance was considered as $p<0.05$.
Results: The study population was characterized by the majority of women (86.7%), mean age 56 years old, mean disease duration of 8 years, around 80% with positive anti-CPP and RF. There was a significant increase of citric acid, creatinine, L-serine and urea during the follow-up, metabolites that are involved in the muscular-related metabolism. There was no substantial variation in the DAS28-ESR (baseline: 3,8, after

12 months: 4,0) and there was no significant correlation between changes in the metabolome pattern and DAS28-ESR score (p>0.05). Fatigue was negatively correlated with L-serine/creatinine (r: - 0,4, p<0.001). Appendicular lean mass index (ALMI) also showed a positive difference which correlated with the increase of urea and creatinine (r: 0,3, p<0.019).

Conclusion: This prospective metabolomic analysis indicated that the RA might be associated with amino acid metabolism alterations probably related to inflammation injury to muscle and fatigue. These findings suggest that urine metabolome analysis may be an interesting approach to study and monitor the systemic impact of RA.

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AB1332 COST EFFECTIVE BIOMARKER IN PREDICTING SLE IN DEVELOPING COUNTRIES – NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR), MPV

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Background: SLE is a disease which is easily missed in regular clinical practice. In developing countries due to lack of investigation modalities and rheumatologist, early identification of the diseases process is delayed. By the time the patient reaches a higher medical care centre there is a significant time loss and advancement of the disease. NLR, PLR, RDW and MPV can be calculated from a complete blood count which will be available at any grass route heath centre.

Objectives: To identify Cost effective biomarkers in predicting SLE in developing countries. Focussing on markers - Neutrophil Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR), MPV.

Methods: This is a retrospective hospital based observational study conducted screening patients admitted from January 2016- November 2018 in with a diagnosis of SLE. We identified 150 patients with SLE and their NLR, PLR, and MPV data were collected and were correlated with equal control group without SLE

Results: We found that NLR, PLR, and MPV were highly significant with a p-value of 0.001 to be used as bio marker and also when further analysis was done using ROC curve with an area under curve of 76%, 81% and 78% respectively when compared with the control group.

Conclusion: We conclude that NLR,PLR,and MPV is cost-effective bio marker which costs (< 1 Euro) in predicting SLE and also play a great in monitoring following up referring patient to higher centre for biopsy at a golden period which will aid in early management which will limit the mortality and morbidity associated with the disease

REFERENCES

[1] Qin B, Ma N, Tang Q, Wei T, Yang M, Fu H, Hu Z, Ling Y, Yang Z, Zhong R Neutrophil, to Lymphocyte ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. ModRhematol.2016;26(3):372-6. doi: 10.3109/14397595.2015.1091136. Epub 2016 Mar 4.

[2] Wu Y1, Chen Y1, Yang X2, Chen L1, Yang Y3 Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were associated with disease activity in patients with systemic lupus erythematosus.Int Immunopharmacol. 2016 Jul;36:94-99. doi: 10.1016/j.intimp.2016.04.006. Epub 2016 Apr 22.

[3] Soliman WM1, Sherif NM1, Ghanima IM1, El-Badawy MA2. Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratios in Systemic Lupus Erythematosus: Relation With Disease Activity and Lupus Nephritis.

[4] Reumatol Clin. 2018 Aug 27. pii: S1699-258X(18)30167-0. doi: 10.1016/j.reuma.2018.07.008. [Epub ahead of print]

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AB1333 CELL-FREE DNA AND BIOLOGICAL TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Cell free DNA (cfDNA) are DNA fragments released from the cell nucleus into extracellular compartment and is therefore detectible in plasma or serum. The most common reason for this release is tissue damage, cell death and inflammation of diverse origin. In regard to autoimmune diseases, increased levels of cfDNA has been found in plasma/serum in patients with systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and Sjögren´s syndrome. The results of some published works, appointing the correlation between levels of cfDNA and RA activity, are controversial, that´s why the position of cfDNA as a potential new biomarker remains unclear.

Objectives: The aim of our study was to describe the effect of biological therapy on the concentration of cfDNA and explore the correlation between therapeutic response DAS28 score and cfDNA levels. This potential correlation could define cfDNA as a new marker of treatment response and also potentially also clarify the role of cfDNA in the pathogenesis of RA.

Methods: Plasma samples of 40 patients with RA were collected before, as well as 3 and 12 months after starting treatment with tumor necrosis factor α- inhibitor (TNFα-inhibitor). Total cfDNA was quantified fluorometrically. Treatment response was evaluated by using DAS 28 scoring system and C-reactive protein.

Results: The treatment with TNFα-inhibitors showed statistically significant changes of DAS28 and cfDNA. According the EULAR treatment response defined by DAS28 changes, patients with good response showed statistically significant decrease of cfDNA in month 3 (p<0,005), but the improvement in month 12 was just on the border of statistical significance (p=0,059). There were also only slight changes in group with moderate DAS 28 response in month 12 (p=0,054). In the entire group there was found slight positive (r =0,44), statistically significant (p=0,0073) correlation between the levels of cfDNA and DAS 28 score after 12 month of treatment.

Conclusion: Even if treatment with TNFα-inhibitors decreases plasma cfDNA, there are other markers with better correlation with disease activity. We consider, that the changes in cfDNA levels after biological treatment could determine the role cfDNA more as a consequence of the inflammation, rather than the cause of inflammation in this autoimmune disease, but further research is needed.

REFERENCES

[1] 1. Zhong XY, von Mühlenen I, Li Y, et al. Increased Concentrations of Antibody-Bound Circulatory Cell-Free DNA in Rheumatoid Arthritis. Clin Chem 2007 53(9):1609-1614.

[2] Dunaeva M, Buddingh BC, Toes REM, et al. Decreased serum cell free DNA levels in rheumatoid arthritis. Auto Immun Highlights 2015 6(1-2): 23-30.

[3] Abdelal IT, Zakaria MA, Sharaf DM, et al. Levels of plasma cell-free DNA and its correlation with disease activity in rheumatoid arthritis and systematic lupus erythematosus patients. The Egyptian Rheumatologist 2016 38:295-300.

[4] Hashimoto T, Yoshida K, Hashimoto N, et al. Circulating Cell Free DNA: A Marker To Predict The Therapeutic Response for Biological Dmards in Rheumatoid Arthritis. Int J Rheum Dis 2017;20(6):722-730.

[5] Laukova L, Konečná B, Vlková B, et al. Anti-cytokine therapy and plasma DNA in patients with rheumatoid arthritis. Rhematol Int 2018;38 (8):1449-1454.

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AB1334 AN OPEN-SOURCE WEB-BASED ANALYTICS PLATFORM FOR THE HUMAN IMMUNE ATLAS

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Background: Mass cytometry (CyTOF) measures the expression of many proteins (currently up to 40) in single cells. TII applies CyTOF to characterise cellular diversity of the immune system in peripheral blood and other tissues. Using a growing collection of CyTOF data acquired from blood of clinically and demographically diverse human subjects, we have built our version of the immune atlas, called EPIC (Extended Poly-dimensional Immunome characterisation).
Objectives: We will discuss two main objectives of this project. To integrate CyTOF data, metadata, cell annotations or other inferred data into the immune atlas, we developed a novel data analytics pipeline. To provide a user-friendly gateway that helps researchers explore the immune atlas and gain new insights about their own CyTOF data, we implemented a web-based data analytics application using the R Shiny programming environment.
Methods: The core components of the atlas are 'immune maps', which comprise CyTOF data of samples labeled with identical antibody panels and grouped according to a common biological theme. Besides protein expression patterns, immune maps contain contain clinical and demographic metadata, as well as phenotypic information inferred from clustering and cell type annotation. To intuitively analyse these complex multi-dimensional data, we developed a Shiny/R web application that has two main objectives. First, clients can explore the immunome at different levels of details using a wide range of interactive visualisation methods, such as bar charts comparing the abundance of all or subsets of immune cell types in different age groups, or tSNE/UMAP scatter plots providing global perspectives of expression domains. Second, users can upload their own CyTOF data and, through pattern matching, obtain instant estimates about the abundance of selected immune cell populations in their own samples.
Results: We tested our system using immune maps constructed from healthy paediatric samples. Manually gated ground truth data along with interactive visualisation techniques were used to measure the accuracy of our pipeline in detecting and annotating homogenous cell populations. In addition, we will demonstrate how immune maps can be applied to classify uploaded CyTOF data.
Conclusion: Our interactive immune atlas platform promises to improve our understanding of the changing immunome landscape in response to disease, treatment and ageing.

REFERENCES

NA

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AB1335 AGE-RELATED MUSCULOSKELETAL STIFFNESS AMONGST HEALTHY SUBJECTS

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Background: A patient questionnaire for evaluating musculoskeletal stiffness (MSQ) has been developed for rheumatoid arthritis (RA) (Halls 2015) and also tested in chikungunya disease. Joint stiffness is associated with older age in adults.
Objectives: The aim of this study was to evaluate the variation in MSQ scores with age in a cohort of healthy adults.
Methods: Subjects ≥18 years old were enrolled at two sites. Subjects were engaged in, or had completed, tertiary education. Subjects with a diagnosis of joint disease, Parkinson's disease or multiple sclerosis were excluded. Each subject completed a 21-item questionnaire designed to evaluate the severity of musculoskeletal stiffness, its physical impact and psychosocial impact, and to provide an overall stiffness score. Results are expressed as a percentage of the maximum possible score.
Results: Two hundred and fifty-eight subjects were included, 120 males and 138 females. Subjects were >95% Caucasian. The mean age of subjects was 40±16 years. No differences were seen in the stiffness scores between males and females. The percentage of subjects reporting any stiffness was over 50% in every age group, and markedly higher in those aged ≥60 years (Table). The average overall MSQ scores and those of its three components were low and showed little variation between the three lower age cohorts, but scores increased in the upper age cohort (Table).

	18-30 years (n=97)	30-44 years (n=51)	45-59 years (n=77)	≥60 years (n=32)
Subjects (%) reporting any stiffness	71 (73)	30 (59)	54 (70)	30 (94)
Overall MSQ score: median% (IQR)	3.3 (0, 10.6)	4.2 (0, 9.6)	6.3 (0, 11.9)	12.0 (4.1, 22.4)
Stiffness severity: median% (IQR)	7.9 (0, 17.8)	6.9 (0, 15.1)	13.3 (0, 20.4)	18.9 (10.4, 31.9)
Physical impact: median% (IQR)	0 (0, 4.1)	0 (0, 4.1)	0 (0, 8.3)	8.3 (0, 16.5)
Psychosocial impact: median% (IQR)	0 (0, 13.2)	0 (0, 6.6)	0 (0, 13.2)	6.6 (0, 24.8)

Conclusion: The prevalence of musculoskeletal stiffness in healthy subjects as measured with this questionnaire is not negligible. Overall stiffness scores in this study were low in the subjects aged 18-59 years when compared to those in RA and chikungunya disease. However, the high frequency of stiffness and the higher average scores in the upper age cohort suggest that the background joint stiffness amongst older subjects should be considered when interpreting stiffness scores in patients.

REFERENCES

[1] Halls S, Dures E, Kirwan J, et al. AB1128-HPR Developing A New Rheumatoid Arthritis (RA) Stiffness Patient Reported Outcome Measure (PROM). Ann Rheum Dis 2016; 75: 1317

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AB1336 COMPARATIVE STUDY OF ANTI-CCP ANTIBODIES BY LATEX ENHANCED TURBIDIMETRIC IMMUNOASSAY AND ELISA

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Background: Some of the autoantibodies found in RA are primarily directed against these citrullinated protein epitopes and can be found even before the symptoms of arthritis appear [1]. So the detection of these antibodies can be used in clinical practice to help develop therapeutic strategies. The classic method for detecting anti-CCP antibodies in serum is ELISA. However, the traditional ELISA method still has some inevitable limitations, such as time-consuming, complicated process and low degree of automation, may not be able to provide clinicians with quick answers. Therefore, the purpose of our study was to determine whether the LETIA, which was faster than ELISA, can be used in routine experiments, and to explore the clinical application value of the LETIA in the detection of anti-CCP antibodies.
Objectives: The purpose of our study was to evaluate the consistency of Latex Enhanced Turbidimetric Immunoassay (LETIA) and ELISA in the detection of anti-cyclic citrullinated peptide antibodies (anti-CCP antibodies) in 139 patients, for the diagnosis of early rheumatoid arthritis (RA), and to determine that LETIA can be used in daily practice.
Methods: A total of 139 serum or plasma samples were collected from patients with or suspected of having RA. The anti-CCP antibodies of these samples were detected by LETIA and ELISA simultaneously, all tests were carried out in accordance with the manufacturer's standard procedures. Finally, we compared the technical performance and diagnostic accuracy, and assessed the clinical sensitivity and specificity of these two methods.
Results: The Kappa coefficient and consistency rate measured between LETIA and ELISA were greater than 0.91. The sensitivity and specificity values of LETIA were 83.33% and 95.6%, respectively. The positive predictive value and negative predictive value were 90.91% and 91.58%, respectively. The confidence interval of 95% positive coincidence rate was 78.97-82.75%, while the confidence interval of 95% negative

coincidence rate was 92.72%-94.79%. The sensitivity and specificity values of ELISA proposed by the manufacturer for clinical diagnosis RA were 82% and 95%. The two methods had the same detection effect.
Conclusion: The current commercially available methods for detecting anti-CCP antibodies were roughly the same, and the consistency between LETIA and ELISA were high. In general, the LETIA was more accurate and sensitive than the ELISA in the detection of anti-CCP antibodies in serum. Overall diagnostic performance of ELTIA can be compared. LETIA provided reliable information about antibody levels that made it useful in monitoring disease activity. Comparable to the classic ELISA, ELISA may even be replaced in the future.

REFERENCES
[1] Harich R, Roger C, Garnier L, et al. Comparison of anti-CCP autoantibodies measurement by ELISA and a bead-based assay in a large patient cohort.[J]. Clinical Biochemistry, 2014, 47(6):485-488.

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AB1336B **PERFORMANCE EVALUATION OF PARTICLE-ENHANCED TURBIDIMETRIC IMMUNOASSAY FOR ANTINUCLEAR ANTIBODIES DETECTION IN COMPARISON WITH LINE IMMUNOASSAY**

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Background: Detection of antinuclear antibodies (ANAs) supports the clinical diagnosis of ANA-associated rheumatic diseases, such as systemic sclerosis (SSc), systemic lupus erythematosus (SLE), primary sjogren's syndrome (SjS) and mixed connective tissue disease (MCTD) [1-3]. Throughout history, a number of autoantibody detection methods have emerged, for instance, indirect immunofluorescence (IIF), radioimmunoassay (RIA), enzyme-linked immunosorbent assay (ELISA) and line immunoassay (LIA) [4]. With the development of detection technology, new methods to detect ANAs were continuously developed by numerous manufacturers, for example, particle-enhanced turbidimetric immunoassay (PETIA). Therefore, in the current study, we evaluated for the first time the performance of PETIA in the detection of anti-nuclear antibody and compared it with commercial LIA.
Objectives: To evaluate the clinical performance of PETIA for the detection of ANAs in comparison to the currently commonly used LIA.
Methods: Total 606 serum samples from diseased and healthy controls were assayed to simultaneously determine SSA, Sm/RNP, SSB, Sm and U1-SnRNP antibodies by the PETIA and LIA. The sensitivity, specificity, consistency and area under curve (AUC) were analyzed for each antibody between PETIA and LIA.
Results: The positive rate and specificity of PETIA and LIA for ANA specific target antibodies were comparable. Compared with LIA, the sensitivity of SSA, SSB and Sm were 100.00%, 88.89% and 90.00%, while Sm/RNP and U1-SnRNP were 75.00%, 70.59%, respectively; Sm/RNP, SSB, Sm and U1-SnRNP have high specificity, respectively 97.87%, 98.90%, 97.80% and 94.68%, while SSA specificity is general, 81.52%. Under manufacturer's cut-off values, the consistent rates of SSA, Sm/RNP, SSB, Sm, and U1-SnRNP between PETIA and LIA were 87.22% (116/133), 92.06% (116/126), 96.61% (114/118), 97.03% (98/101) and 88.28 (113/128), respectively. Excellent consistencies were found between PETIA and LIA for the detection of Sm/RNP, SSB and Sm antibodies (kappa>0.75), and kappa coefficients were 0.776 ($p<0.001$), 0.901 ($p<0.001$) and 0.841 ($p<0.001$), while the coincidence for anti-SSA and U1-SnRNP detection were moderate (0.40<kappa<0.75), and Kappa coefficient was 0.731 ($p<0.001$) and 0.685 ($p<0.001$), respectively.
Conclusion: The performance of PETIA for the detection of antibodies to nuclear specific antigen was satisfying to correlate with that of LIA. With the additional benefits of short detection time, quantitative output and high universality. PETIA can better meet the requirements of quantitative detection of specific target antibodies.

REFERENCES
[1] Kapsogeorgou E K, Tzioufas A G. Autoantibodies in Autoimmune Diseases: Clinical and Critical Evaluation[J]. Israel Medical Association Journal, 2016, 18(9):519-524.
[2] Routsias J G, Tzioufas A G. B-cell epitopes of the intracellular autoantigens Ro/SSA and La/SSB: Tools to study the regulation of the autoimmune response[J]. Journal of Autoimmunity, 2010, 35(3):0-264.
[3] Suurmond J, Diamond B. Autoantibodies in systemic autoimmune diseases: specificity and pathogenicity[J]. Journal of Clinical Investigation, 2015, 125(6):2194-2202.
[4] Fritzler M, Fritzler M. The Emergence of Multiplexed Technologies as Diagnostic Platforms in Systemic Autoimmune Diseases[J]. Current Medicinal Chemistry, 2006, 13(21):2503-2512.

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Rehabilitation

AB1336C **COMPARISON OF NORMALIZED MUSCLE ACTIVATION EFFECTS OF THREE DIFFERENT EXERCISES ON SUPRAHYOID MUSCLES IN HEALTHY SUBJECTS**

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Background: The most important airway protection mechanism during swallowing is adequate laryngeal elevation. Suprahyoid muscles are responsible for laryngeal elevation. There are many treatment approaches to improve laryngeal elevation in swallowing rehabilitation. The most common methods are exercises including Shaker exercises, Chin-Tuck Against Resistance (CTAR) exercise, Neuromuscular Electrical Stimulation of suprahyoid muscles and Expiratory Muscle Strength Training (1-4).
Objectives: The aim of our study was to compare the effects of three different exercises including Shaker, CTAR and a new method Chin Tuck with TheraBand Exercises on suprahyoid muscles activity.
Methods: Forty-two healthy subjects with a mean age of 27.92±5.02 years (min=18, max=40), of which 50% were male were included. All individuals were divided into three groups; Chin Tuck Against Resistance (CTAR); Group 1, Shaker exercise; Group 2, Chin Tuck Exercise with Theraband; Group 3, with computerized randomization. Surface EMG evaluation was performed to determine electrical activity of the suprahyoid muscles during maximal voluntary isometric contraction (Figure1) and during performing CTAR, Shaker exercise and Chin Tuck with Theraband (Figure 2-4). Normalized suprahyoid muscle activations were calculated as: Recorded Maximum Electrical Activity During Exercise (mV)/ Recorded Maximum Electrical Activity During Maximum İsometric Contraction (mV).



Figure 1. *Evaluation of Maximum Isometric Suprahyoid Muscle Activity*



Figure 2. Chin Tuck Against Resistance Exercise (CTAR)

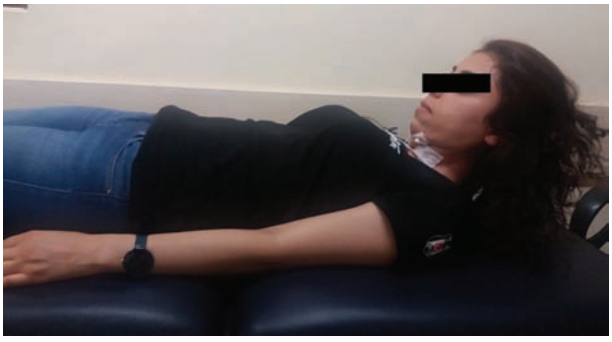


Figure 3. Shaker Exercise

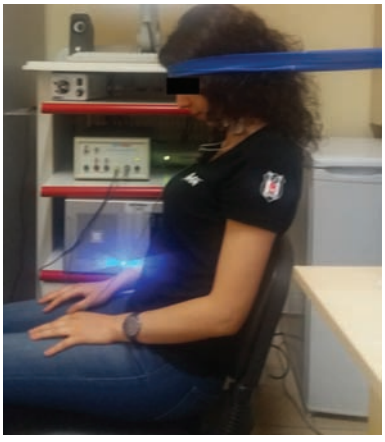


Figure 4. Chin Tuck Exercise with Theraband

Results: A statistically significant difference was found between three groups in terms of normalized suprahyoid muscle activity($p<0.001$) (Table 1). The difference between three groups was caused by the difference between Group 1 and Group 2 ($p<0.001$) and between Group1 and Group 3 ($p=0.040$) in favor of Group 1. No difference was found between Group 2 and Group3 ($p=0.104$) (Table 2-4).

Table 1. Comparison of Normalized Suprahyoid Muscle Activation between groups

	Group 1 (n:14) Mean ±SD	Group 2 (n:14) Mean ±SD	Group 3 (n:14) Mean ±SD	X^2	p
Normalized Suprahyoid Muscle activation (%)	0.791 ±0.380	0.306 ±0.116	0.472 ±0.284	15.760	*<0.001

*p<0.05

Table 2. Comparison of Normalized Suprahyoid Muscle Activation between Group 1 and Group 2

	Group 1 (n:14) Mean±SD	Group 2 (n:14) Mean±SD	p
Normalized Suprahyoid Muscle activation (%)	0.791 ±0.380	0.306 ±0.116	*<0.001

*p<0.05

Table 4. Comparison of Normalized Suprahyoid Muscle Activations of Group 2 and Group 3

	Group 1 Mean±SD (n:14)	Group 3 Mean±SD (n:14)	p
Normalized Suprahyoid Muscle activation (%)	0.791 ±0.380	0.472 ±0.284	*0.040

*p<0.05

Table 5. Comparison of Normalized Suprahyoid Muscle Activations of Group 2 and Group 3

	Group 2 Mean±SD (n:14)	Group 3 Mean±SD (n:14)	p
Normalized Suprahyoid Muscle activation (%)	0.306 ±0.116	0.472 ±0.284	0.107

*p<0,05

Conclusion: In conclusion, primarily CTAR exercise should be included in rehabilitation to increase the suprahyoid muscle activation. In addition, chin tuck exercise with Therband can also be considered as an alternative to CTAR.

REFERENCES

[1] Shaw GY, et al. Transcutaneous neuromuscular electrical stimulation (VitalStim) curative therapy for severe dysphagia: myth or reality? Annals of Otology, Rhinology & Laryngology. 2007;116(1): 36-44.
[2] Wheeler-Hegland KM, Rosenbek JC, Sapienza CM. Submental sEMG and hyoid movement during Mendelsohn maneuver, effortful swallow, and expiratory muscle strength training. J Speech Lang Hear Res. 2008;51 (5):1072-1087.
[3] Yoon WL, Khoo JK, Liow SJ. Chin tuck against resistance (CTAR): new method for enhancing suprahyoid muscle activity using a Shaker-type exercise. Dysphagia. 2014;29(2):243-248.

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Education

AB1337

A VIRTUAL BIOLOGIC PATHWAY TO IMPROVE CARE STANDARD, REDUCE TREATMENT DELAYS AND IMPROVE COST EFFICIENCY - THE WHIPPS CROSS VIRTUAL BIOLOGIC CLINIC EXPERIENCE

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Background Biologic therapies have become standardised as best practice for treatment of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Axial Spondyloarthopathies (AS) in the UK. There are more stringent criteria for access versus Europe and the USA. There is no agreed mechanism to choose a specific agent over and above locally agreed criteria that are disease specific. Most UK rheumatologists make an individual decision based on personal experience and guidelines as well as evidence. There are cost implications and inherent delays within locally agreed pathways that involve a pharmacist and a patient education process that may be nurse led. The overall process to initiate this treatment takes months. To this end a weekly one hour Virtual Biologic Clinic (VBC) has been set up: attended by the multi-disciplinary team of all consultants, clinical and research nurse specialists, lead pharmacist and an administrator.
Objectives We compared waiting time for biologic initiation before and after the VBC, assessed numbers whose treatment plan was altered and we attempted a cost analysis.
Methods All patients with RA, PsA, AS and a relevant connective tissue disease (CTD) attending VBC between Nov 2017 and Jun 2018 were included in this retrospective observation. All patients starting a biologic therapy one year earlier (Nov 2016-17) were compared. The time between decision to treat and prescription receipt by delivery company/day unit (for IV admin) was measured (by Mann-

Whitney U test) in both groups. In the VBC group time between decision to treat until funding approval obtained was measured and overall saving by all estimated drug cost was calculated.

Results 122 patients were discussed at VBC - 75 started a biologic (50 new, 25 switched) and 6 entered a clinical trial. The remaining 41 were agreed as unsuitable for a biologic table 1.

Table 1. Patient not suitable for biologics through VBC IFR: individual funding requests, cDMARDs: Conventional disease modifying ant rheumatic drugs.

Reasons for not receiving biologic	(n=41)	%
IFR application (rejected)	6	12.1%
Patient factor*	5	12.1%
Disease activity not meeting NICE criteria	22	53.60%
Alternative treatment offered (eg: cDMARDs)	6	14.60%
Other **	2	4.8%

*1 recurrent infection, 3 did not do their screening test, 1 did not do the recommended vaccination.

**1 relocated, 1 was referred to gastroenterology team

Comparing groups 69 patients (missing data = 6) waited an average of 35 days (median 27 days) to start a biologic vs 105 average days (median 85) pre VBC for 120 patients (U is 1033, p-value is < .00001 two tailed).

In the VBC group average delay occurred as follows: referral to VBC meet 14 days (n=74), discussion to funding approval 9 days (n=69), medication receipt by homecare 10 days (n=64) and first order 11 days (n=46).

We assume that in our clinic pre VC and, indeed, in the majority of UK Rheumatology Departments about 90% of patients recommended for a biologic by a specialist eventually ends up taking that medication and given that assumption potential costs savings with this model are estimated as equivalent to 35 patients (approx. £140K/yr. - drug costs savings calculated vs current cheapest option, SB4 (£4080/yr)).

Conclusion: Our study highlights that transforming biologic prescribing with a one-step virtual MDT clinic improves efficiency, significantly reduces patient access time and should ensure the most cost- effective treatment is agreed. Integration of the local research team in the VC allows eligible patients to be recruited for clinical trials where available offering further NHS cost savings. The VC creates a reliable, excellent training environment to maintain and enhance specialist knowledge and to deliver high standards of patient care.

Disclosure of Interests None declared

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AB1338 PATIENT EDUCATION IN PSORIATIC ARTHRITIS : ADDRESSING AN UNMET NEED

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Background: Patient education should be integral to the care of people with inflammatory arthritis [1]. Research suggests that the majority of patients with Psoriatic Arthritis (PsA) would like to receive education about their condition [2]. There are limited studies in PsA but randomised controlled trials in rheumatoid arthritis have demonstrated that patient education improves compliance to medication [3], disease specific knowledge [4] and coping mechanisms [5]. In our department, patient education in PsA was recognised as an unmet need.

Objectives: To pilot an educational session for PsA patients, to assess whether this improved patients' understanding of their condition, and to determine whether an education programme would be a useful adjunct to patient care.

Methods: Adult PsA patients attending their rheumatology clinic appointments were asked to complete a short survey on whether they would be interested in attending an education session and the aspects they would like to have covered. Those who expressed interest were invited to attend a 2.5 hour multidisciplinary team (MDT) session which covered 1) a general overview of PsA; 2) medications used in PsA; 3) the role of physiotherapy and occupational therapy; 4) flares and self management. Patients were asked to evaluate their knowledge or understanding before and after each topic covered, on the same day, using a series of 1-10 Likert scales. They were specifically asked whether they found the education session helpful; whether they would recommend it to other PsA patients; whether they would be interested in developing a PsA patient support group.

Results: 25 patients were invited to the session and 9 patients attended. There were 5 males and 4 females, across a wide range of age categories. There were statistically significant improvements in all topics covered, including a mean improvement of 120% in how well informed patients felt about PsA in general ($p<0.0001$); a mean improvement of 79% in confidence in accessing help from the MDT ($p<0.01$); a mean improvement of 211% in how well informed patients were about medications available ($p<0.0001$); a mean improvement of 86% in confidence in self-managing a flare ($p<0.0001$). All patients found the session helpful overall and all patients stated they would recommend it to others. Several patients expressed interest in developing a PsA patient support group.

Conclusion: All PsA patients demonstrated a greater awareness and understanding of their condition following a 2.5 hour education session. This study indicates that an education programme is a useful and important adjunct to patient care and supports extending this to the wider PsA patient population.

REFERENCES

[1] Zangi HA, Ndosi M, Adams J, Andersen L, Bode C, Bostrom C, et al. EULAR recommendations for patient education for people with inflammatory arthritis. Ann Rheum Dis. 2015; 74(6):954-62

[2] Dragoi RG, Ndosi M, Sadlonova M, Hill J, Duer M, Graninger W, et al. Patient education, disease activity and physical function: can we be more targeted? A cross sectional study among people with rheumatoid arthritis, psoriatic arthritis and hand osteoarthritis. Arthritis Res Ther. 2013;15(5): R156

[3] Ravindran V & Jadhav R. The effect of rheumatoid arthritis disease education on adherence to medications and follow up in Kerala, India. J Rheumatol. 2013;40(8):1460-61

[4] Lovisi Neto BE, Jennings F, Barros Ohashi C, Silva PG & Natour J. Evaluation of the efficacy of an educational programme for rheumatoid arthritis patients. Clin Exp Rheumatol. 2009;27(1):28-34

[5] Giraudet-Le Quintrec J, Mayoux-Benhamou A, Ravaud P, Champion K, Dernis E, Zerkak, et al. Effect of a collective educational program for patients with rheumatoid arthritis: a prospective 12-month randomized controlled trial. J Rheumatol. 2007;34(8):1684–91.

Disclosure of Interests: Keziah Austin: None declared, Nia Jones: None declared, Roopa Prasad Consultant for: Was on an Advisory Board for a pharmaceutical company meeting several years ago (unrelated to current abstract submission)., Speakers bureau: Speaker fees for a national psoriatic arthritis meeting in 2017 (unrelated to current abstract submission).

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AB1339 ONLINE CME IMPROVES ADOPTION OF JAK INHIBITORS IN CLINICAL PRACTICE BY RHEUMATOLOGISTS

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Background: The treatment landscape for RA is evolving rapidly. The JAK inhibitors are oral small molecules that have recently been approved for use in RA.

Objectives: This online CME-accredited educational activity was designed to address the challenges of integrating JAK inhibitors into clinical practice in RA and measure changes in practice

Methods: Non-US rheumatologists, dermatologists and primary care physicians (PCPs) participated in an online activity consisting of a 30-minute video roundtable discussion between 4 experts, with synchronized slides, posted online on August 25 2017. A Planned Change Assessment (PCA) survey (data collected through April 3 2018) with qualitative follow-up interviews was used to measure intent to change and actual change in clinical practice following participation in the activity.

A 2-question PCA survey in multiple choice format, which was administered immediately following the activity, asked:

What will you do differently in your practice as a result of participating in this activity?

What do you perceive as barriers to making the above selected changes in your practice?

A follow-up survey sent out approximately 8 weeks later included questions about completed changes and barriers to change. Finally, qualitative telephone interviews were conducted to ask learners why certain changes were selected, whether the changes were made and barriers to making the changes.

Results:

- 287 non–US physicians completed the initial PCA survey and 44 completed a follow–up assessment approximately 8 weeks later, resulting in a matched subset of 37 learners. Qualitative interviews were conducted with 13 learners

- 274 learners (96%) indicated that they intended to make a change as a result of participating in the activity with most learners selecting multiple changes
- The most common intended changes for rheumatologists were using a JAK inhibitor for the first time (65%) and selecting a JAK inhibitor when oral dosing is preferred (54%)
- Other than systems barriers such as reimbursement and lack of availability of JAK inhibitors, the most common anticipated barriers to change for rheumatologists related to lack of knowledge about MOA and safety, and lack of confidence in their use
- 44 learners completed the follow–up assessment: 42 (96%) reported making changes in their clinical practice
- o For rheumatologists, the most common actual changes were using a JAK inhibitor first–line (55%) and considering a JAK inhibitor when oral dosing is preferred (54%)
- At follow–up the key barriers reported by rheumatologists related to systems barriers/availability and lack of confidence in using JAK inhibitors

Conclusion: Learners in this activity reported increased knowledge about new treatment options for RA and the MOA of JAK inhibitors. The PCA assessment showed that the activity was most effective at prompting rheumatologists to more frequently consider using a JAK inhibitor as a first-line treatment in appropriate patients. Use of new therapeutics, however, may be challenging due to lack of availability of JAK inhibitors in many countries and financial burdens in others. Further education would help rheumatologists to gain confidence in using JAK inhibitors, overcome knowledge gaps, and meet challenges related to lack of access to JAK inhibitors.

Disclosure of Interests: None declared

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AB1340 IMPACT OF THERAPEUTIC PATIENT EDUCATION ON THE SAFETY OF PATIENTS ON BIOTHERAPY FOR CHRONIC INFLAMMATORY RHEUMATISM

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Background: Patients treated with biotherapy should be aware of the specific complications. The acquisition of safety skills is one of the objectives of therapeutic patient education programs in chronic inflammatory rheumatism.(1,2,4)

Objectives: Evaluation of the impact of the "EST-RIC" therapeutic patient education program on the safety skills of patients on biotherapy for chronic inflammatory rheumatism.

Methods: Descriptive cross-sectional study evaluating the impact of integration into a therapeutic patient education program on the skills of patients treated in a day hospital at the Constantine rheumatology department for chronic inflammatory rheumatism, using the validated "BioSecure" questionnaire (3)

Results: Of sixty patients, fifty-two patients (86.6%) completed the questionnaire. Forty-three patients have spondyloarthritis (83%) **(Tab1)**

The median Biosecure score was 62.90/100 (SD 10.83). Fifty-two percent of the patients had integrated the therapeutic education program. Their Biosecure score was significantly higher than that of naïve patients with therapeutic education (median score 69/100 in the ETP group versus 58/100, p <0.001) **(Fig 1).** The Bioscure score varied significantly with the lower level of education (p <0.0001), in the subgroup of patients with a professional activity (P = 0.008) and in patients whose treatment was introduced for less than one year (p <0.0001) and who had a pathology whose diagnosis was less than 5 years (p <0.008)

Conclusion: The integration of patients undergoing biotherapy into a specialized program of therapeutic patient education is correlated with a better mastery of theoretical safety skills.

REFERENCES

[1] Orefice D, Beauvais C, Gossec L, et al. Cross-sectional study of self-care safety skills in 677 patients on biodrugs for inflammatory joint disease. Joint BoneSpine Rev Rhum 2014;81:502–7.

[2] Claudepierre P, Flipo R-M, Sibilia J, et al. Patient's knowledge of their disease: a multicenter study in ankylosing spondylitis. Bone Spine2004; 71: 550-6.

[3] Gossec L, Fautrel B, Flipon E, et al. Tolerance of biotherapies: development and validation of a questionnaire evaluating self-management and patient safety skills: the Biosecure questionnaire. An initiative of the French Rheumatology Society, Therapeutic Education Section. Rev Rhum2013; 80: 479-85.

[4] Meesters JJL, Vliet Vlieland TPM, Hill J, et al. Measuring educational needsamong patients with rheumatoid arthritis using the Dutch version of the Needs Assessment Tool (DENAT). Clin Rheumatol 2009; 28: 1073-7.

Tab 1: Characteristics of the patient

Characteristics	Total population		Gpe ETP+		Gpe ETP -		P
Sex (N=52, NA=0)							
Women	24	46 %	11	46 %	13	54 %	P= 0,159
Men	28	54 %	16	57 %	12	43 %	
Age (years) (N=52, NA=0)							
<30	10	19 %	2	20%	8	80%	**P= 0,005**
30-50	32	62 %	17	53 %	15	46 %	
>50	10	19 %	8	80 %	2	20 %	
Family status (N=50, NA=2)							
Single	18	36 %	4	22 %	14	78 %	**P= 0,001**
No single	32	64 %	23	72 %	9	28 %	
school level (N=51, NA=1)							
BAC -	38	74,5 %	18	47 %	20	53 %	P= 0,105
BAC+	13	25,5 %	9	69 %	4	31 %	
Language mastery (N=50, NA=1)							
Non maitrisé	29	58 %	13	45 %	16	55 %	P= 0,033
Moyen	12	24 %	7	58 %	5	42 %	
Maitrisé	9	18 %	7	78 %	2	22 %	
professional status (N=50, NA=2)							
Active	30	60 %	18	60 %	12	40 %	P= 0,134
Non active	20	40 %	9	45 %	11	55 %	
Pathology (N=52, NA=0)							
RA	5	9,6 %	1	20 %	4	80 %	P= 0,263
PA	4	7,7 %	3	75 %	1	25 %	
Autres SA	43	82,7 %	23	53,5 %	20	46,5 %	
Duration of illness (N=47, NA=5)							
< 5 ans	10	21,3 %	5	50 %	5	50 %	P= 0,126
5 -10 ans	18	38,3 %	7	39 %	11	61 %	
> 10 ans	19	40,1 %	11	58 %	8	42 %	
Beginning of biotherapy (N=51)							
< 1 an	20	39 %	9	45 %	11	55 %	P= 0,068
1-2 ans	14	27,7 %	6	43 %	8	57 %	
>2 ans	17	33,3 %	11	65 %	6	35 %	
Adress (N=50, NA=2)							P= 0,228
Wilaya	42	84 %	22	52 %	20	48 %	
OUT of Wilaya	8	16 %	3	37,5 %	5	62,5 %	

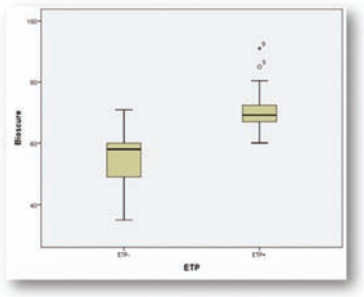


Figure 1:. The median Biosecure score

Disclosure of Interests: None declared

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AB1341 PUBLIC AWARENESS OF RHEUMATOID ARTHRITIS IN MONGOLIA

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Background: Rheumatoid arthritis (RA) is multifactorial, chronic, inflammatory disease which in the absence of early diagnosis can lead to joint destruction and disability. In the last decade, rheumatology has been developed as independent branch in Internal medicine in Mongolia, published rheumatological textbooks. The Mongolian Rheumatology Association has also introduced a RA guideline and conducted training that has led to the use of DMARDs in treatment and improves patient's quality of life is improving in Mongolia. Nevertheless, we have many patients with a late RA diagnosis in Mongolia. In some studies, poor public awareness of RA correlates with high level of disability.

Objectives: To develop understanding about current levels of public awareness of rheumatoid arthritis in patients coming to the outpatient department of the First central hospital in Ulaanbaatar, Mongolia

Methods: This was a cross-sectional descriptive study conducted in the outpatient department of the First central hospital of Ulaanbaatar in Mongolia for 3 days. The study population consisted of adults. Data collection was performed by using questionnaire of developed by the NRAS, addressed to assess awareness on RA.

Results: Total 376 persons stood for 3 days in outpatient clinic in First central hospital. 26 of them refused and 350 of them participated our study. The average age of the participants was 37.79. Participants responded, 22% of them know RA, 78% of whom do not know

rheumatoid arthritis. Understanding about the disease symptoms: 50,5% respondent answered they to do not know RA symptoms; 29% correctly identified joint swelling; 17.4% correctly identified morning stiffness; 12.6% correctly recognized extreme fatigue as a symptom; and only 6.5% correctly identified that crunching and grinding of the joints is not a symptom. Understanding about disease risk factors: 49.4% of participants responded they do not know the risk factor for RA, only 7% correctly identified genetics as a factor; 17% knew that women are more vulnerable than men; only 3% correctly stated that smoking can increase the risk of developing RA; and 34% stated that undertaking exercise and obesity is also a risk factor and 23% identified sore throat can increase RA. Understanding about disease impacts: 21.1% correctly recognized that RA affects a person's ability to walk short distances; 55% did not know how RA affects person`s quality of life, 40.3% correctly stated that RA affects a person's life expectancy; but only 11% knew that the disease affects the internal organs. In total, 12% of respondents saw information about the RA and 82% said public RA awareness needs to be improved.

Conclusion: In Mongolia, public awareness of rheumatoid arthritis was poor. Most of the participants responded to do not know. Other participants who have not responded to do not know that most of them misidentified disease symptoms, risk factors and impacts. The only good thing was most of the participants thought awareness of RA improvement certainly. A good awareness of RA can be one of the basic solutions for the early diagnosis of RA in Mongolia.

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AB1342 TRANSLATION AND ADJUSTING THE PATIENT GUIDE FOR OSTEOARTHRITIS INTO DUTCH. LESSONS LEARNED FROM THE JIGSAW-E PROJECT

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Background: In the UK a guidebook was co-developed with UK patients during a OA research study (1). Within the JIGSAW-E (Joint Implementation of Guidelines for Osteoarthritis in Western Europe) project the guidebook is disseminated and implemented in clinical practice in 5 countries: UK, The Netherlands, Norway, Denmark and Portugal. We translated and adapted the English guidebook for use in the Netherlands.

Objectives: To describe the process of translating and adjusting the guidebook into Dutch, and to summarize the key lessons learned.

Methods: Starting point was a paid translated version of the guidebook. The translation was reviewed by an interdisciplinary working group and distributed among stakeholder organizations. Data collections took place by reports of working group meetings, written feedback from stakeholder organizations and patients' interviews focusing on their information needs. Along the way a logbook of adaptations was kept. After triangulation of findings, adaptations were clustered in six preliminary categories and, together with lessons learned, agreed upon in a consensus meeting with the working group.

Results: The working group convened fifteen times. Ten patients were interviewed about the readability and usefulness of the OA guidebook. Eight out of thirteen stakeholder organizations provided feedback on the draft guidebook. Advice for adaptations related to the following preliminary categories: language; patients' needs; cross-cultural differences; health care system; scientific evidence; structure and layout (see Table 1 for examples). Lessons learned related to the low quality of the initial translation, selection of representative working group members, selection of stakeholder organizations, and required time for thorough deliberation during meetings.

Conclusion: Important ingredients for a successful translation and cross-cultural adaption of a guidebook (or other patient material) are: time, a professional translation (sufficient budget), relevant stakeholders, and patients who can be critical. Patients who were interviewed about the guidebook added valuable patients' information needs, relevant to the cross-cultural adaptation. A draft framework of categories for cross-cultural adaptation is proposed.

REFERENCES

[1] Osteoarthritis Cartilage. 2018;26:43-53

Categories	Examples
Language	Joint pain, osteoarthritis (OA) and arthritis are used interchangeably; explanation in Dutch is needed (gewrichtspijn, artrose, reuma, ontsteking); Translation of English expressions, such as 'no pain, no gain')
Patients' need	More practical tips for specific OA type (hand, knee, hip); 'people with OA' is preferred over 'patients'
Cross-cultural differences	Compared to what there is already in the Netherlands, the tone in the guidebook is much better, less paternalistic; Photographs of people cycling are needed
Health care system	The central role of the nurse in primary care OA management in the UK versus that of the physiotherapist in the Netherlands
Scientific evidence	Due to new scientific insights we deleted the part on insoles
Structure and layout	Photographs should be of younger people and other cultural backgrounds in the Netherlands; Shorter sentences and more subheadings

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AB1343 EFFECTIVENESSOF A RHEUMATOLOGY EDUCATIONAL PROGRAM TO IMPROVE METHOTREXATE PRESCRIBING PRACTICES FOR RHEUMATOID ARTHRITISIN THE SOLE PUBLIC ADULT RHEUMATOLOGY CLINIC IN ETHIOPIA

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Background: Treatment of recent onset Rheumatoid Arthritis (RA) is key to preventing deformities. Initial treatment with methotrexate (MTX) is standard of care. RA treatment in resource-limited countries is complicated by competing health priorities and a lack of rheumatologists. The sole public adult rheumatology clinic in Ethiopia, is at Tikur Anbessa Specialty hospital (TASH) (Addis Ababa). Due to the lack of rheumatologists, care is provided by internists with limited rheumatology training.

Objectives: To evaluate changes in RA management practice patterns following a series of educational activities provided by visiting rheumatologists.

Methods: With local faculty support, visiting rheumatologists conducted educational activities at TASH between July 2016 and December 2018 (2 continuing medical education workshops; 4 clinical preceptorships lasting 2-4 weeks each). Clinical charts of a convenience sample of RA patients seen in the TASH rheumatology clinic were reviewed in September 2016 (n=48) by a team of rheumatologists and a second set in December 2018 (n=78) by an internist. Socio-demographics, arthritis features, treatment patterns and drug safety monitoring were recorded when documented. Practice patterns were compared between 2016 and 2018 using univariate statistics.

Results: The patients were mainly female (90%) with a mean (standard deviation) age of 36(13) years, resided in Addis Ababa (61%) and received government funded health care (57%). When documented, (95/117; 81%) had polyarthritis and (42/55; 76%) clinical joint deformity (2016 vs 2018 p=NS). More patients were seropositive in 2016 compared to 2018 (32/43 vs 14/75 p<0.001) and more had radiographic damage (erosions, joint space narrowing, periarticular osteopenia) (21/27 vs 39/71 p<0.05). Between 2016 and 2018, prednisolone use remained common (92% in 2016 vs 99% in 2018 p=0.05) often in high doses (last visit daily dose 7.5mg (0-100) vs 5mg (0-100); p=NS; maximum daily dose 7.5 (0-100) vs 20 (0-100) p=NS) with continued documentation of steroid toxicity (45% vs 20%). The only available DMARDs prescribed were MTX (112/127; 97%) and chloroquine (50/125;40%). Median prescribed weekly MTX dose increased between 2016 and 2018 (starting dose 5 vs 7.5 mg/week p=0.01; maximum dose 7.5 vs 12.5 mg/week p<0.0001) and was co-prescribed with folate by 84% in 2016 vs 93% in 2018 (p=NS). Documentation of drug safety for those prescribed MTX improved with

adequate pre-MTX labs (hematology, renal and liver panel and or hepatitis serology) requested by 46% in 2016 to 90% in 2018 (p<0.0001). When documented, MTX use was often interupted (2016 17/24; 2018 14/43 p=0.003) and mainly due to limited drug availability.
Conclusion: An educational program conducted with support from the local medical community has potential to improve management of rheumatic disease in resource limited regions without adequate rheumatology capacity. However, interventions must be maintained over time and changes in practice measured to ensure that appropriate diagnosis and safe prescribing practices continue until local rheumatology expertise and capacity is available.
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AB1344 'CLINICAL ASSESSMENT OF THE MUSCULOSKELETAL SYSTEM' HANDBOOK AND ACCOMPANYING VIDEOS: 15 YEARS OF USE

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Background: 15 years ago, Arthritis Research UK (ARUK) produced the 'Clinical Assessment of the Musculoskeletal (MSK) System' handbook and a set of accompanying videos; 'Regional Examination of the Musculoskeletal System'.(1) There has been an evaluation of the use of this resource showing that they are widely used among medical students and healthcare professionals. Recently, ARUK has merged with Arthritis Care to create Versus Arthritis, and previous publications are due to be rebranded.
Objectives: This project aims to review how the handbook and videos are being used 15 years on. The secondary aim is to gain insight into any changes that may need to be made going forward as Versus Arthritis seeks to revise and update the original materials.
Methods: In September 2018, a clinical group was formed to review the current handbook's content and format. The project team was invited to take part in the surveys and disseminate them within their professional networks and across every UK medical school.
Results: 78 people took part in the survey; this included 61 users (students and trainees) and 17 medical school teachers.
User Survey: '*How to access the handbook?* respondents said online (36%), via an app (31%) or printed version (10%). 83% of respondents said they found the handbook very useful, 100% said it was easy to understand, 95% said it was well illustrated, and 75% said the video clips were very useful. 100% of respondents said the handbook did not contradict any previous teaching received.
When asked what would improve the handbook, the most popular response was case studies. When asked what the most useful thing was, most respondents commented on the structure and how clear and concise it was. When asked what the least useful thing was, respondents felt it lacked detail regarding the rationale behind the purpose of the examinations.
Teacher Survey: 17 medical school representatives completed the survey. 94% of respondents use the resource. Most provide their students with the online version of the handbook (64%). 88% thought the resource was very useful for their students. 94% said the resource maps well to the current MSK curriculum. When asked what would improve the handbook the most popular response was abnormal examination findings. The least popular response was patient exercise videos and sheets.
Content Review: Several comments were made suggesting the use of more appropriate language. Recommendations were made to introduce sections on physical activity, self-management and the multidisciplinary team involvement. A suggestion was made to include the patient's 'ideas, concerns and expectations' concept.
Conclusion: The consensus is that the resource is already very good and maps well to the MSK curriculum taught by the medical schools. It would benefit from adding new contents, e.g. examination clips of patients with pathology. We would need to be wary of overcomplicating the purpose of the new resource.
It was also highlighted that the resource would benefit from a refresh of the layout, including clear headings and more up to date images and diagrams. Several comments were made around the format to include an online resource that students could use to incorporate examination videos with experts explaining the findings.

REFERENCES

[1] Arthritis Research UK. 2018. Information for Health Professionals and Students. [Online] Available at: https://www.arthritisresearchuk.org/shop/products/publications/information-for-medical-professionals.aspx [Accessed 30 January 2019].

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AB1345 CONTEXTUAL FACTORS IMPACTING OSTEOARTHRITIS MANAGEMENT IN URBAN AND RURAL COMMUNITY-DWELLING SENIORS: AN ANALYSIS BASED ON THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING DISABILITY AND HEALTH

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Background: Living with arthritis requires lifelong management that can be influenced by person, place and context.
Objectives: The objectives of this study were to: (1) identify contextual factors that influence OA management in rural and urban-dwelling seniors, and (2) examine how contextual factors identified by rural and urban-dwelling seniors are explained in terms of the ICF framework
Methods: Semi-structured interviews were conducted with 20 community-dwelling seniors in Ontario, Canada.; purposivel inclding 11 seniors from an urban setting and 9 seniors from a rural setting, all over the age of 65, and previously diagnosed with OA. Broad questions on self-management and information weeking were explored. Interview concepts related to the environmental and contextual factors component were extracted from interview transcripts and organized into subthemes. Meaningful concepts were linked by 2 raters to ICF categories according to established linking rules. Descriptive analyses were performed.
Results: A total of 891 meaningful concepts were identified; 481 from interviews with 11 urban-dwelling seniors and were linked to 54 ICF categories: 24 Environmental Factors, 21 Activities and Participation, and 9 Body Functions and 410 meaningful concepts from interviews with 9 rural-dwelling seniors: 57 ICF categories: 27 Environmental Factors, 24 Activities and Participation, and 6 Body Functions. Within Activities and Participation component, "d839 Education" was the most code for both groups. From the Body Functions component, "b1800 Experiences of Self" followed by "b1301 Motivation" were most mentioned. Environmental factors represented 203 of 481 (42.2%) urban concepts and 253 of 410 (61.7%) rural concepts. The concepts linked to the Activities and Participation category were similar across urban and rural groups (17.3% and 17.1%). Personal Factors (e.g. "adapting to life with OA", "self-sufficiency", "pain tolerance", "age") or "nc - not covered" (e.g. "feeling old", "embarrassed by OA", "being a burden") were not coded. In 12.2% urban and 20.6% rural content was labeled as Personal Factors. Chapter e5 services, systems and policies was the chapter with the highest coverage overall. Within the environmental factors "e355 Health Professionals" was the most common code for both urban and rural groups, and mentioned in almost all interviews. Participants frequently discussed physician's attitudes and misconceptions towards patients with OA.
Conclusion: The complex interaction of personal and environmental factors impacting OA management in both urban and rural communities was illustrated. Rurality influences some aspects of ths complexity, but many common themes occur.

REFERENCES

[1] Weigl M, Cieza A, Harder M, et al. Linking osteoarthritis-specific health-status measures to the international classification of functioning, disability, and health (ICF). *Osteoarthr Cartil*. 2003;11(7):519-523. doi: S1063458403000864 [pii].

[2] Cieza A, Geyh S, Chatterji S, Kostanjsek N, Üstün B, Stucki G. ICF linking rules: An update based on lessons learned. J Rehabil Med. 2005;37 (4):212-218. doi:10.1080/16501970510040263.

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AB1346 PATIENTS' BELIEFS ABOUT MEDICINES PRESCRIBED FOR THEIR RHEUMATOID ARTHRITIS OR SPONDYLOARTHRITIS

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Background: Adherence to therapies is determined by multiple factors, some of which are patient's related and include economic resources, knowledge, attitudes, beliefs, perceptions and expectations about medication.
Objectives: To assess patients' beliefs about prescribed medication for their rheumatic disease (rheumatoid arthritis (RA) or spondyloarthritis (SpA), including psoriatic arthritis) and to determine the existence of any association between these beliefs and clinical and socio-demographic variables.
Methods: Observational cross-sectional study which included RA patients according to 1987 ACR and/or 2010 ACR/EULAR criteria and SpA patients according to 2009 ASAS classification criteria (CC) for axial SpA or to 2011 ASAS CC for peripheral SpA, on subcutaneous biological therapy, followed at our Center, able to complete questionnaires autonomously and who agreed to participate. Socio-demographic and clinical data, anxiety and depression through the Hospital Anxiety and Depression Scale (HADS) and fatigue using the Functional Assessment of Chronic Illness Therapy - Fatigue questionnaire (FACIT-F) were collected. To assess beliefs about medication, the cross-culturally adapted Portuguese version of the Beliefs about Medicines Questionnaire (BMQ)-Specific was used, asking patients to apply it considering only the prescribed medicines for AR or SpA. The BMQ-Specific comprises two subscales: a five-item Necessity scale (Specific-Necessity, SN) and a six-item Concerns scale (Specific-Concerns, SC). Each item is scored on a five-point Likert scale (from 1 = strongly disagree to 5 = strongly agree). Statistics: descriptive, Mann-Whitney and Kruskal-Wallis tests and Spearman correlation, p <0.05.

	RA patients	SpA patients
	Median (IQR)	Median (IQR)
Current age - years	60,0 (51,0-66,0)	47,0 (39,5-57,0)
Disease duration – years	14,5 (12,0-18,3)	13,0 (8,0-19,0)
Time on treatment with the current biologic therapy – months	31,0 (20,0-62,0)	37,0 (12,0-83,0)
PGA	32,0 (6,0-55,0)	29,0 (14,5-51,5)
VAS pain	41,0 (21.0-60.0)	-
PhGA	19,5 (6,5-33,8)	12,5 (5,0-23,5)
Nocturnal back pain VAS	-	17,0 (4,5-34,0)
Back pain VAS	-	18,0 (5.5-43,0)
VS – mm/H	15,0 (7,0-30,5)	7,0 (2,0-14,0)
CRP – mg/dL	0,2 (0,1-0,6)	0,3 (0,1-1,0)
DAS28_4V	3,2 (2,4-4,4)	-
BASDAI	-	2,8 (1,1-4,6)
ASDAS	-	1,8 (1,1-2,4)
BASMI	-	2,7 (2,1-4,0)
HAQ	0,8 (0,4-1,2)	-
BASFI	-	1,8 (0,7-3,7)
BMQ-SN	17,0 (15,0-18,0)	16,0 (15,0-18,0)
BMQ-SC	18,0 (15,0-22,0)	18,0 (13,5-22,0)

Abstract AB1346 Table 1. Descriptive statistics of the continuous variables of the RA and SpA patients

Results: We obtained data from 84 patients, 45 SpA (53.6%) and 39 (46.4%) RA patients. Table 1 presents the descriptive statistics of the continuous variables. In RA group, 92.3% were female, 84.6% under anti-TNF, 66.7% under their 1st biologic and we found an association between BMQ-SC score and HADS-anxiety (p=0.013) and positive correlations between BMQ-SC score and Patient Global Assessment (PGA) (p=0.031), VAS pain (p=0.004), Physician's Global Assessment (PhGA) (p=0.004), DAS28 (p=0.007), and HAQ (p <0.001). In SpA group, 62.2% were female, 86.7% under anti-TNF, 77.8% under their 1st biologic and BMQ-SN score was positively correlated with VAS nocturnal back pain (p=0.047), PhGA (p=0.045) and BASFI (p=0.003).
Conclusion: In RA patients, those with higher disability and a clinically more active disease presented higher levels of concern regarding the medication. In SpA, patients with a more aggressive disease, with nocturnal pain and worse function have a stronger conviction of the necessity and efficacy of the medication.

REFERENCES

[1] Salgado T, Marques A, Geraldes L, Benrimoj S. Horne R. Fernandes-Llimos F. Cross-cultural adaptation of the Beliefs about Medicines Questionnaire into Portuguese. Sao Paulo Med J. 2013; 131(2):88-94. doi:10.1590/S1516-31802013000100018.

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AB1347 ASSESSMENT OF PATIENTS' KNOWLEDGE ABOUT BIOLOGIC THERAPY AS A SELF-COMPLETION QUESTIONNAIRE. IS IT A GOOD WAY TO DO IT?

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Background: Lack of knowledge from a patient in his therapy may lead to a misuse process, increasing the probability of failure to achieve the therapeutic goal.
Objectives: To evaluate if the assessment of the RA and SpA patients' knowledge in their biologic therapy could be done as a self-completion questionnaire.
Methods: Observational cross-sectional study which included patients with RA according to 1987 ACR and/or 2010 ACR/EULAR criteria or SpA according to 2009 ASAS classification criteria (CC) for axial SpA or to 2011 ASAS CC for peripheral SpA (including patients with psoriatic arthritis), on subcutaneous biological therapy who agreed to participate. Patients' knowledge about their biologic therapy was assessed using the "*Conhecimento do doente sobre os seus medicamentos*" (CPM-PT-PT), meaning "Patient's knowledge about his medicines", intercultural adaptation for the Portuguese version of the original Spanish questionnaire, CPM-ES-ES. This questionnaire was created to be used as an interview, but we decided to give it to patients and ask them to complete it autonomously, reading the questions and writing their answers, considering only their biologic therapy. It consists of 11 questions, each with a score based on patient's answer: incorrect = -1, the patient doesn't know = 0, incomplete = 1 and correct = 2. The final score is calculated using the mathematical formula described by the authors, ranging from 0 (doesn't know the medicine) to 2 points (optimal knowledge). Statistics: descriptive, Mann-Whitney and Kruskal-Wallis tests and Spearman correlation, p <0.05.
Results: We included 84 patients, 45 of which with SpA (53.6%) and 39 (46.4%) with RA. In the RA group, 92.3% were female, 84.6% were under anti-TNFα, 66.7% were under their 1st biologic, the median age was 60.0 (51.0-66.0) years and the median time in treatment with current biologic was 31.0 (20.0-62.0) months. In the SpA group, 62.2% were female, 86.7% were under anti-TNF, 77.8% were under their 1st biologic, median age was 47.0 (39.5-57.0) years and median time in treatment with current biologic was 37.0 (12.0-83.0) months. Fifteen incomplete questionnaires were excluded. Sixty patients (87.0% of the 69 valid questionnaires) didn't meet the minimum criteria necessary to ensure correct use of medication (correct answer to the first 5 questions), thus obtaining a CPM score of 0. The mean CPM score was 0.2±0.5, the median 0 (0), the minimum 0 and the maximum 1,7. There were no differences in CPM according to age, time in treatment with the current biologic, disease duration, n° of previous biologics, gender, educational level, diagnosis, current biologic and n° of other concomitant drugs. Table 1

describes the scores obtained in each domain of the questionnaire. We noticed that if we ask the same questions orally, the patients knew more than what the questionnaire revealed.

Table 1. Scores obtained in the different domains of the questionnaire

Domains	Mean ±SD	Median (IQR)	Min.	Max.
Process of use [-8; 8]	5.6±2.0	6.0 (5.0-6.0)	-2	8
Therapeutic objective [-4;4]	3.5±1.1	4.0 (4.0-4.0)	0	4
Safety [-8;8]	1.3±1.5	1.0 (0-2.0)	-3	4
Conservation of the medicine [-2;2]	1.9±0.6	2.0 (2.0-.,0)	-1	2

Conclusion: The CPM-PT-PT underestimated the level of knowledge about biologic therapy in our population, suggesting the need to assess it during the clinical interview.

REFERENCES

[1] Salmerón Rubio J, García Delgado P, Iglésias Ferreira P, Mateus Santos H, Martinez-Martinez F. Validación del cuestionario de medidada del conocimiento del paciente sobre su medicamento adaptado al português. Ciência & Saúde colectiva. 2014;19(4): 1141-50.

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AB1348 PERSPECTIVES OF PATIENTS WITH INFLAMMATORY ARTHRITIS REGARDING CARDIOVASCULAR RISK: A QUALITATIVE STUDY

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Background: Cardiovascular disease (CVD) is the most common cause of death among patients with inflammatory arthritis (IA) such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis (AS).
Objectives: To elicit perspectives of patients with IA to inform the design of a patient-centered intervention for a CVD risk reduction intervention.
Methods: This was a qualitative study guided by Bandura's Social Cognitive Theory, placing special emphasis on knowledge about the relationship between arthritis and CVD as well as barriers and facilitators to receiving healthcare related to CVD risk such as screening and management for hyperlipidemia. We recruited patients from a single academic center with either RA, PsA, or AS to participate in focus groups. Data were analyzed thematically.
Results: We conducted three focus groups with a total of 17 participants (5 participants in two and 7 participants in one of the focus groups) of mean age 56 (SD+7.7) years; 15 were women; 3 were on a statin; and 1 previously had a stroke. Barrier Themes 1-2: 1) Need for more information about arthritis, prognosis, and IA medications; 2) Lack of knowledge about how IA increases cardiovascular disease (CVD) risk. Facilitator Themes 3-5: 3) Lifestyle changes to reduce overall CVD risk; 4) Potential roles for peer coaches; and 5) Improving doctor-patient communication about IA, medications, and CVD risk. Patients expressed that improving Themes 2 and 5 could facilitate CVD screening.
Conclusion: Education about increased CVD risk could help activate patients with IA engage in CVD risk reduction strategies. Peer coaches appears to be a reasonable tool towards that goal.
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Table 1. Themes and Key Points That Emerged From Focus Groups of Patients with Inflammatory Arthritis

Theme	Quotes from patients
Need for information about IA and medications	*"When I was first diagnosed, as far as the medications and the side effects and what I could expect. Like I said, everything I read was bad, and it didn't—I'm probably going to take it the rest of my life, and you have to get your blood tested every three months to make sure everything's looking good."*
Lack of understanding regarding the association between CVD risk and IA	*"I never even thought about it. Had no idea that it would even affect my heart like that. I'm still in shock [laughter] that that has to do with the arthritis."*
CVD risk reduction as an integrated lifestyle modification	*"They (doctors) know about the medicines and everything, so I'll ask them, "Is there something' I could do or take that would help it?" We've got to do our part, too. We've got to exercise. We got to watch what we eat. Stress. I know stress will cause a lot of stuff to come on."*
Possible uses for peer coaches around relevant CVD risk factor mitigation approaches	*"It would've been helpful if I would talk to somebody who, maybe, was on the medication and could tell me, "Well, I haven't had any problems with it," or, "Yeah, it does this." I'm sure it affects different people differently."* *"I guess if it would involve exercising takin' a walk, it'd be nice to do it with somebody if they've got the same (arthritis)—and do it together, that would be motivating."*
Improving doctor-patient communication about IA	*"The peer coach could go with you to your appointments and to help you to understand. I've thought about that, to completely understand and to help communicate."* *"If I'm at home, and all of a sudden, I'm like, 'Why didn't I ask her that? Let's write it down. Then when I go to my peer coach, maybe, with those questions, they can also help me to understand that."*

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AB1349 PATIENT INVOLVEMENT IN BASIC RHEUMATOLOGY RESEARCH IS CHALLENGING BUT FEASIBLE. A 3 YEAR'S RESPONSIVE EVALUATION OF ADDED VALUE, PITFALLS AND CONDITIONS FOR SUCCESS

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Background: Empirical evidence for effective patient-researcher collaboration in basic research is lacking.
Objectives: To explore the feasibility and impact of patient involvement in basic rheumatology research and to identify facilitators and barriers.
Methods: Responsive evaluation of three years' participatory research in which two formats were piloted: (1) patient participation in monthly team research meetings (first phase) and (2) patient-researcher partnerships in single research projects (second phase and follow-up). Data collection comprised surveys, interviews, training days, research team meeting reports and field notes. Regular reflective team meetings took place with active participant involvement. A qualitative analysis using thematic coding focused on impact, barriers and facilitators.
Results: In total 13 patient representatives (PRs) and 15 basic researchers participated. PRs experienced basic research as complex due to lack of understanding bio-molecular processes and the use of technical jargon. Their initial role was mostly listening, sometimes asking questions and sharing personal experiences. Informal communication was perceived as most beneficial. After three months the atmosphere relaxed and equal relationships emerged. Researchers' motivation increased by talking with PRs, resulting in better understanding of disease burden on daily life and the societal impact of their research. They started to speak in lay language, which enabled PRs to appreciate the value of scientific rigour and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved over a longer period. After 2 years, group-based consensus arose about the effectiveness of 1:1 patient-researcher contacts over patient participation in research team meetings. During follow-up, the number of partnerships increased from 2 to 11.

Facilitators of patient involvement related to a) education of principles of participatory research; b) training of patient-researcher collaboration; c) development of a common language level; d) open mind and respectful communication; e) professional support; and f) leadership commitment. Main barriers were the complexity of pathogenetic processes for patients and time commitment for researchers. All participants found the collaboration worthwhile.

Reported impact was divers. Having to look at their work from a helicopter view encouraged researchers to attain a holistic view of people with a rheumatic condition and skills to explain their research for a lay audience. Patients experienced personal satisfaction after sharing experiences and receiving recognition from others. For the research process, a few examples were reported where patients input led to new topics on the research agenda. One example was the grant application to explore determinants of fatigue in the laboratory, directly prompted by patients. More substantial benefits were experienced for the development of patient friendly educational materials and lay summaries of research protocols, dissemination of research findings through interviews and presentations, and even promotion of patient participation in national scientific societies of which the researchers are a member. Little impact was reported on the actual results of basic research.

Conclusion: Long term patient involvement in basic research is feasible and worthwhile. Despite the time investment, both patients and researchers experience valuable benefits that outweigh the lack of tangible impact on research findings.

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AB1350 HOW TO REDUCE THE NOCEBO EFFECT IN RHEUMATOLOGY? A SYSTEMATIC REVIEW OF RISK FACTORSAND INTERVENTION STRATEGIES

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Background: Nocebo effect (NE) defines any declared negative side effect of a drug that is non-specific, non-explained by its pharmacokinetic, and non-dose dependant. Recently, it has been pointed out as the main factor that reduces the retention rate of switches from a biologic originator (BO) to biosimilars (BS) in rheumatology.

Objectives: To identify the risk factors (RFs) and interventions strategies to reduce the NE in rheumatism and musculoskeletal diseases (RMDs), and more specifically in BS switches.

Methods: MEDLINE, Embase and Cochrane databases were systematically searched (inception to 15th November 2018) using relevant keywords: search1: “musculoskeletal diseases” and “nocebo” or “non-specific side effect” (NS-SE); search2: “biosimilars” and “nocebo” or “non-specific side effect”. Inclusion criteria were: studies on pharmacological treatments, studies investigating RFs for NE or NS-SEs, studies specifically describing an intervention aimed to reduce NE. Studies on non-RMDs and fibromyalgia were excluded.

Results: Of 212 and 639 references screened respectively in search1 and search2, 151 duplications were deleted, 32 mentioning NE or equivalent were read in full text by 2 independent investigators and consensually selected.

No study met inclusion criteria for NE risk factors: 6 studies investigated the RFs of discontinuation after switch to BS, 3 with etanercept (ETN), 3 with infliximab (IFX), one investigated risk factors of back switch (meaning return from BS ETN to BO ETN), one study analyzed a genetic factor of intolerance to methotrexate (MTX) in juvenile idiopathic arthritis (JIA) and one study assessed the RFs for overall discontinuation of biologics. Although contextual factors were mentioned, no study tested RFs on NE responders only. RFs for a negative outcome were low self-efficacy, small-size rheumatology department, early start of IFX BS after its introduction on the market.

Only 5 studies met the inclusion criteria for specific interventions to reduce NE. One was about countermeasures used to reduce MTX intolerance in children with JIA: including covert dosing and taste masking, with no significant results. The other four studies aimed to reduce NE related to a switch: by a shared decision-making method (ETN, one study), another by a structured communication strategy (ETN, one study) and two by a standardized information (ETN, one study; IFX, one study). Rate of NS-SE was mentioned in 3 studies, and the outcome (NS-SE rate compared to NE-SE rate of control group) was mentioned in only 2 studies. However, the assessment of intervention efficacy was not possible, since comparison was performed with historical cohorts.

Conclusion: Although nocebo effect is an important issue in rheumatology, especially as an explicative factor for limiting the retention rate when switching from biologic originators to biosimilars, its risk factors and intervention strategies to prevent it are poorly known. Our results encourage studies to better understand the risk factors associated with nocebo effect and the means to reduce it, particularly in the context of switches from bio-originators to biosimilars.

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AB1351 DO WE NEED A PATIENT PEER MENTOR PROGRAM IN DAILY PRACTICE FOR PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AND IF SO, HOW SHOULD THIS BE ORGANIZED?

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Background: Management and support by an interdisciplinary rheumatology team are essential for achieving optimal disease outcomes in rheumatoid arthritis (RA). Nevertheless, health professionals generally do not experience the disease themselves, and patients may have specific educational needs that can only be provided by other patients having gone through the same experience. Furthermore, patients with RA may benefit most from such additional care interventions in the early disease stage when they are particularly faced with threats to their normal life. Peer mentoring has been studied and successfully implemented in other chronic conditions, however, this is rather a new care concept in the field of rheumatology.

Objectives: Among four key stakeholders in the management of early RA, we aimed (1) to uncover the current experience with, need for and attitude towards implementing peer mentoring in the care for patients with early RA in Flanders; (2) to gather ideas for the content and format of a peer mentor program.

Methods: We conducted an explorative qualitative focus group study. In total, five focus groups were organized to capture the perspective of each of the following stakeholders: patients with early RA (n=10), representatives of patient organizations (n=5), rheumatologists (n=10) and rheumatology nurses (n=5). Data were analyzed using the constant comparison method as presented in the Qualitative Analysis Guide of Leuven. Two patient research partners helped to analyze and interpret the data.

Results: Most stakeholders perceived a potential need for peer mentoring in early RA. However, they underscored that this would be largely person and disease phase dependent suggesting that peer mentoring should be presented as an option to patients, rather than a standard of care. The additional value of peer mentors would be foremost situated in providing disease perspective and a sense of recognition to newly diagnosed patients. For some stakeholders, it was difficult to get a clear picture of such a program, which made it difficult for them to formulate an opinion on a specific format. The health professionals particularly mentioned the current lack of a formal framework for collaborating with patient experts, and the need for carefully selected and well-trained peer mentors. Stakeholders shared the view that the development of a peer mentor program and its integration within the current care context should ideally take place in co-operation with and under supervision of health professionals.

Conclusion: Our results underline that peer mentoring in early RA holds potential for certain patients under certain circumstances, yet a clear framework for all stakeholders is a prerequisite to ensure a chance for success of this complex intervention. Future research should thus focus on unfolding the facilitators and barriers of collaborating with patient experts in the daily care of patients with early rheumatoid arthritis.

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HPR Epidemiology and public health (including prevention)

AB1352-HPR INVESTIGATION OF EFFECT OF DISEASE AND RELATED FACTORS IN INDIVIDUALS WITH FIBROMYALGIA

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Background: Fibromiyalgia (FM), one of the most common rheumatologic disorders, is characterized by widespread pain in the body, sensitivity in the certain anatomical regions, fatigue, sleep disorders and reduced pain threshold, uncommon and extra-articular rheumatism disease (1). It has been reported that impairments in functional capacity and quality of life cause significant limitations in individuals with FM (2).
Objectives: The aim of this study was to examine the effect of disease and to investigate the factors associated with the disease in individuals with FM.
Methods: In our study, 334 voluntary individuals with FM (324 famele,10 male) who applied to Pamukkale University Department of Internal Medicine, Department of Rheumatology were diagnosed according to 2010 American College of Rheumatology criteria whom participated in the study with the mean age of 47,5510.46 (years). Fibromyalgia Impact Questionnaire (FIQ) was used to determine the effect of disease, Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) for emotional status and Pittsburgh Sleep Quality Index (PSQI) for sleep quality, right after demographic information and disease related data were recorded. Multiple regression analysis were used to examine the factors related to disease activity.
Results: High body mass index (B=.121, p=0.023), high tender point score (B=.427, p=0.000), high depression score (B=.350, p=0.00), high anxiety score (B=.258, p=0.000) and poor sleep quality (B=.157, p=0.002) corresponded to the higher FIQ score. However, age (B=-.019, p=0.716), level of education (B=.009, p=0.858) and disease duration (B=.054, p=0.331) did not significantly affect FIQ.
Conclusion: As a result of our study the progress of body mass index in individuals with FM, increase in number of tender points, poor sleep quality, depression and anxiety were among the factors affecting the disease. Therefore, these factors must be considered in order to reduce the severity of the disease in individuals with FM.

REFERENCES

[1] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristic of fibromyalgia in the general population. Arthritis Rheum 1995;38:19-28.
[2] Arnold LM, Crofford LJ, Mease PJ, et al. Patient perspectives on the impact of fibromyalgia. Patient Educ Couns 2008a;73:114-20.

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AB1353-HPR PREVALENCE OF PAIN MEDICATIONS PRESCRIPTIONS IN PATIENTS WITH RA

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Background: Pain is often disabling and can reduce the quality of life of a patient. Pain medications are drugs commonly prescribed for a variety of conditions one of them rheumatoid arthritis. The common molecules prescribed are paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioids.
Objectives: The goal of this study was to analyze the prevalence of pain medication prescription in patients with Rheumatoid Arthritis in a specialized center in Colombia.
Methods: We collected data from the medical charts in a specialized RA center conducted during 5 years, we performed a descriptive analysis, we collected sociodemographic information, DAS28, and the prevalence of prescription of analgesic medications divided in three groups non-opioid analgesics, opioid analgesics and NSAIDS. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We evaluated the relationship between DAS28 and the usage of pain medications.
Results: We reviewed the medical charts of 7076 patients diagnosed with rheumatoid arthritis, 82% were female and 17% were male. Median age was 60 years RIQ (51-69). The prevalence of usage of pain medications was 45%. Most of patients received paracetamol followed by a combination of paracetamol. See table 1. The prevalence of pain medications usage was not with associated disease activity.

Pain medication	n	%
Paracetamol	2407	34
Paracetamol + opioids	744	11
NSAID	63	1

Conclusion: As other studies have shown the prevalence of pain medications in patients with RA is high. The most prescribed medication was paracetamol or opioids, coinciding with other studies (1). This descriptive study is useful for further studies to develop in Colombia and Latin America. Additionally, it is important to consider other alternative therapies in order to approach in painful condition like RA.
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AB1354-HPR DESCRIPTION OF INDIVIDUALS WITH FIBROMYALGIA SYNDROME

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Background: Fibromyalgia (FM) affects negatively physical and mental health and reduces quality of life. The most common symptom is chronic widespread musculoskeletal pain in FMS.
Objectives: This study was planned to investigate comorbidities, number of medication and to determine the most painful body region in individuals with FM.
Methods: The study included 166 individuals (161 women, 5 men) who were diagnosed with FM, with a mean age of 47.5610.91 years. Comorbidities, number of medication which were used for FMS or other diseases of participants were recorded also painful body regions were assessed for 28 regions. The categorical variables were expressed in numbers and percentage.
Results: The results showed that a total of 42.8% (n=71) of individuals in this study had no comorbidities, 11.4% (n=19) of individuals had hypertension and 7.8% (n=13) of individuals had asthma. When the number of medication were examined, a total of 66.3% (n=110) of individuals did not use any medication, 25.8% (n=43) of individuals did use one type of medication with FM-related and 4.2% (n=7) of individuals did use two type of medications with FMSrelated. Painful body regions were reported by 74.1% (n=123) for neck, 66.3% (n=110) right shoulder, 68.7% (n=114) left shoulder,68.1% (n=113) right knee and 68.1% (n=113) left knee.
Conclusion: In general, there was no comorbidities with FMS. The study found that individuals with FMS usually did not use medication. Also neck were found the most painful body region in individuals with FMS.

REFERENCES

[1] Clauw DJ. Fibromyalgia: An overview. Am J Med 2009; 122(12 Suppl):S3-S13
[2] Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, et al. The Am College of Rheumatol 1990 criteria for the classification of Fibromyalgia: report of the multicenter criteria committee. Arthritis Rheum. 1990; 33:160-72.

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AB1355-HPR A SYSTEMATIC LITERATURE REVIEW (SLR) ON NURSING SENSITIVE OUTCOMES IN SYSTEMIC SCLEROSIS (SSC)

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Background: SSc affects significantly patients functionality and Quality of Life (QoL). Specific Nursing Sensitive Outcomes (**NSOs**) still need to be established in SSc.
Objectives: This SLR was aimed at identifying NSOs in SSc patients and the related screening tools.
Methods: Medline, CINHAL, EMBASE and PsycINFO were searched to identify relevant studies. Experimental and observational studies that reported nursing interventions and NSOs were included. All potentially eligible studies were read in full text and examined against the selection criteria previously listed. Quality assessment was carried out through *Critical Appraisal Skills Programme* tools; and, the *OMERACT* (*Outcome Measures in Rheumatology*) comprehensive conceptual framework for health was used to contextualise and summarize findings.
Results: 7015 records were screened for title and abstract, 39 full-text were identified and assessed. Eleven studies were included in this SLR. For the core area "*pathophysiological manifestations*" 4 domains (healths status, digital ulcers, clinical efficacy and fatigue), and, for the core area- "*impact on life*"- 5 domains were found (functionality, patient knowledge, patient satisfaction, psychological status and quality of life). Thus, NSOs identified were physical function and parameters, health events, upper limb functionality, patients knowledge of disease complications, degree of self-management, need for nursing instructions, self-efficacy, health efficacy, psychological state, depressive mood and QoL.

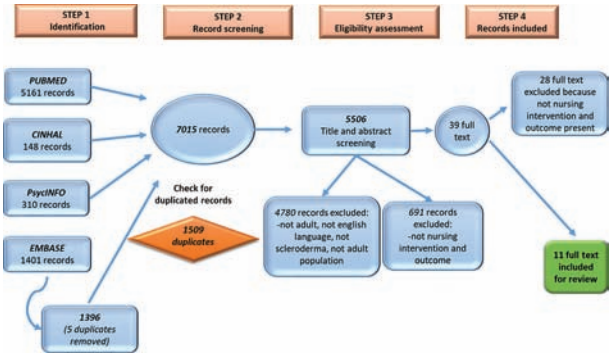


Figure 1

Conclusion: The results identify outcomes that may allow the structuring of a preliminary behavioural flow chart for nursing SSc case management. Further researches are warranted to examine the multidimensional and complex role of nursing in SSc management.
Flow chart of the SLR:

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AB1356-HPR PHYSICAL ACTIVITY BEFORE, DURING AND AFTER PREGNANCY IN WOMEN WITH SPONDYLOARTHRITIS – DATA FROM REVNATUS

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Background: There are no known studies on physical activity (PA) in pregnancy for women with spondyloarthritis (SpA).
PA is an essential and well-documented part of treatment for SpA [1]. The Norwegian Mother and Child Cohort Study (MoBa) found that established regular exercise routines pre-pregnancy was the strongest correlate of regular exercise during pregnancy [2].
A Swedish study of patients with SpA has shown that only 7 out of 10 patients with SpA meet the World Health Organization (WHO) recommendations of PA [3]. In MoBa 46.4% were regular exercisers (≥ 3 times a week) before pregnancy, while 25% were non-exercisers (≤ 3 times a month). At pregnancy week 17, 28% were regular exercisers, and 41% were non-exercisers.By pregnancy week 30, only 20% were still regular exercisers and 53% were non-exercisers [2].
Objectives: To describe the level of PA before, during and after pregnancy for Norwegian women with SpA.
Methods: Women with SpA (ICD-10 M45, M46.1, M46.8 and M46.9) enrolled in the Norwegian nationwide quality register RevNatus that have self-report their level of PA, are included. Data from seven time points are presented.
Results: BASDAI - Bath Ankylosing Spondylitis Disease Activity Index, BMI body mass index, VAS visual analogue scale
Conclusion: During pregnancy, the percentage of women with SpA in the non-exercising group are increasing. The percentage of regular exercisers is lower 12 months after delivery than pre-pregnancy. Throughout the seven time points, 68 91% of the women with SpA do not fulfil the WHO recommendations for PA.
PA should be an integral part of standard care throughout the course of disease for people with SpA and healthcare providers should take responsibility for promoting it and make necessary referrals to ensure that people with SPA receive appropriate PA-interventions [1].

REFERENCES

[1] Rausch Osthoff, A.K., et al., 2018 *EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis*. Ann Rheum Dis, 2018. 77(9): p. 1251-1260.
[2] Owe, K.M., W. Nystad, and K. Bo, *Correlates of regular exercise during pregnancy: the Norwegian Mother and Child Cohort Study*. Scand J Med Sci Sports, 2009. 19(5): p. 637-45.

Abstract AB1356HPR Table 1. Level of exercise, BASDAI, VAS pain, VAS fatigue and BMI presented with mean scores and standard deviation (SD)

		Before pregnancy N = 59 Mean (SD)	1st trimester N = 58 Mean (SD)	2nd trimester N = 79 Mean (SD)	3rd trimester N = 59 Mean (SD)	6 weeks postpartum N = 63 Mean (SD)	6 months postpartum N = 49 Mean (SD)	12 months postpartum N = 44 Mean (SD)
Regular exercisers ≥ 3 times a week		**32,2%**	**19%**	**20,3%**	**8,5%**	**9,5%**	**24,5%**	**13,6%**
	BASDAI	3,0 (2,6)	3,0 (2,5)	2,9 (2,2)	5,5 (1,8)	2,9 (2,5)	3,4 (2,9)	3,2 (2,3)
	VAS pain	26,2 (20,5)	56,8 (31,8)	33,4 (26,8)	45,4 (29,2)	28,5 (18,3)	29,9 (29,2)	24,8 (16,8)
	VAS fatigue	38,3 (3,8)	36,7 (32,9)	50,8 (24,5)	57,0 (36,4)	42,5 (32,6)	33,3 (37,4)	29,2 (27,1)
	BMI	25,3 (4,6)	24,5 (2,2)	26,1 (2,9)	26,0 (2,9)	25,0 (2,5)	25,8 (5,9)	27,7 (7,2)
Irregular exercisers ≤ 2 times a week		**40,7%**	**46,6%**	**38%**	**35,6%**	**25,4%**	**36,7%**	**34,1%**
	BASDAI	2,9 (2,4)	3,4 (2,2)	3,2 (2,6)	3,2 (2,3)	2,5 (1,9)	2,3 (2,1)	3,3 (2,6)
	VAS pain	28,1 (25,7)	35,4 (26,2)	38,8 (29,6)	29,4 (27,3)	27,4 (21,0)	24,7 (26,0)	31,8 (25,6)
	VAS fatigue	40,4 (33,5)	59,6 (31,3)	53,0 (33,5)	52,3 (33,8)	35,3 (30,3)	27,2 (33,5)	41,4 (32,5)
	BMI	26,5 (7,5)	25,5 (4,2)	26,9 (4,8)	28,2 (4,8)	25,2 (3,7)	24,7 (3,6)	25,1 (3,9)
Non-exercisers ≤ 3 times a month		**27,1%**	**34,4%**	**41,8%**	**55,9%**	**65%**	**38,7%**	**52,3%**
	BASDAI	4,0 (2,2)	3,6 (1,9)	2,8 (2,1)	3,9 (2,6)	3,4 (2,7)	4,0 (3,1)	3,8 (2,6)
	VAS pain	42,3 (26,7)	34,5 (27,4)	31,4 (24,5)	42,1 (29,8)	36,1 (31,0)	37,7 (25,3)	34,3 (28,3)
	VAS fatigue	48,7 (29,0)	55,6 (36,9)	46,2 (30,6)	54,1 (29,3)	43,9 (33,4)	52,3 (30,4)	48,5 (35,7)
	BMI	26,5 (5,1)	27,6 (5,8)	27,4 (3,9)	30,8 (6,1)	26,4 (5,2)	26,1 (4,9)	24,7 (5,7)

[3] Haglund, E., et al., *Differences in physical activity patterns in patients with spondylarthritis*. Arthritis Care Res (Hoboken), 2012. 64(12): p. 1886-94.

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AB1357-HPR PROSPECTIVE ANALYSIS OF IRREVERSIBLE ORGAN DAMAGE IN PATIENTS OF KYRGYZ NATIONALITY

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Background Special attention in recent decades has been paid to the accumulation of irreversible organ effects (SLICC) with systemic lupus erythematosus (SLE) in the form of most diseases, as well as therapy. Along with an increase in survival, the structure of lethal outcomes also changed: cardiovascular pathology, complications of drug therapy, malignant neoplasms, chronic renal and pulmonary insufficiency.
Objectives Study of irreversible organ damage in patients with SLE, prospective observation.
Methods The study included 150 (26.31%) Kyrgyz patients out of 570 with a reliable diagnosis of SLE, female (96%), young age (median - 34 [26; 44]), Kyrgyz nationality (89.33%), high - 61 (40.66%) and very high activity - 40 (26.67%), with the duration of SLE at 1 observation point from 7 months to 10 years, with dynamic observation from 1 year to 3 years. The development of irreversible organ damage was assessed on a scale of damage index (PI) developed by the International Cooperation Organization of SLE Clinics. The absence of damage was rated as 0 points, low PI - 1 point, average PI from 2 to 4 points, high PI more than 4 points.
Results In the Kyrgyz cohort at the initial visit, the absence of irreversible organ damage was observed in the overwhelming majority of patients - in 127 (84.67%) of 150. In 1 observation point with organ lesions there were 23 patients (15.33%) out of 150, of which with low PI values - 14 (60.87%), with average values - 9 (39.13%), there were no patients with high PI values, due to the small duration of the disease (median - 3 [0.7; 10] of the year). During the initial visit, irreversible organ damage was observed due to the administration of HA (8): aseptic necrosis of the femoral heads - in 2, spondylopathy - in 3, cataract - in 2 and diabetes - in 1. Second point of observation was damage to the respiratory organs - 7 patients: pulmonary fibrosis - in 3 and pulmonary arterial hypertension - in 4. The next in frequency were CNS lesions - in 6 patients: ischemic stroke - in 4 and cognitive impairment - in 2. By the final observation point, organ damage was observed already in 43 (28.67%) patients out of 150 without statically significant progression (p> 0.05), which in half of the cases were due to the administration of GC - in 24 (55.82%) as aseptic necrosis of the femoral heads - in 5, spondylopathy - in 7, cataracts - in 9 and diabetes - in 3. In second place were injuries of the respiratory organs - in 9 (20.93%) of 43: pulmonary fibrosis - in 5 and pulmonary arterial hypertension (PAH) - in 4. Next in frequency were CNS injuries - in 6 (13.95%) of 43: ischemic stroke at 4 and cognitive impairments - in the kidneys were observed 2. Damage - 4 (9.30%) of 43 patients: with a reduction in glomerular filtration rate (GFR) in the terminal 3 and the development of CRF 1 as starting severe lupus glomerulonephritis.
Conclusion Under dynamic observation, irreversible organ damage was detected in 28.67% of cases, which was 13.34% more compared to the initial state, without statically significant progression (p> 0.05), mainly due to the administration of GC (55, 82%).
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AB1358-HPR SUICIDAL BEHAVIORS IN PATIENTS WITH INTRAVENOUS BIOLOGIC THERAPIES

Amparo Lopez Esteban[1], Roberto Daniel Gonzalez Benitez[1], Aurora Alonso Amigo[2], Aurora Alonso Amigo[1], Juan Carlos Sanchez Zanotti[1], Florentina Garca Calle[1], Juan Carlos Nieto[1], Beln Serrano Benavente[1], Juan Ovalles[1], Tamara Del Ro Blasco[1], Alfonso Ariza[1], Carlos Gonzalez[1], Indalecio Monteagudo Sez[1]. *[1]Hospital General Universitario Gregorio Maran, Madrid, Spain*; *[2]Psicologa Isabel Pinillos, Madrid, Spain*

Background: In patients with rheumatic diseases, suicidal ideation (Si) and suicide attempt (Sa) have been observed more frequently than in the general population.
Objectives: 1. To determine the prevalence of Si and Sa in patients with biological therapies. 2. To evaluate possible factors associated with the Si.
Methods: Observational cross-sectional study in patients with intravenous BT from Day Hospital of a tertiary hospital in Madrid. Sociodemographic, disease features [weight, height, work disability (WD), diagnosis, treatment] and PRO (FiRST, FACIT-F, HAD, and GHQ-28) were collected. We defined the Si according to the answer at the 6th and 7th questions of section D of the GHQ-28. The Sa was registered according the patient`s clinical history. The categorical variables were analyzed with the Chi square test. A logistic regression analysis was performed to evaluate the possible factors associated with suicidal behavior (SB). To evaluate the variance of discrete quantitative variables between groups the Kruskal-Wallis test was used, with a post-hoc analysis with U-Mann Whitney, to determinate the difference between pairs.
Results: We included 321 patients, 65% women, with a mean age (range, SD) of 56 years (89-15, 14.1), and a mean disease duration (range, SD) of 16 years, DS (53-1, 9.7). The sociodemographic and clinical characteristics are described in Table 1 and 2. Of all patients, 4% had had 1 or more Sa and 11% had Si. 23% of patients had associated fibromyalgia (FiRST), 47% fatigue (FACIT-F), 27.4% anxiety (A-HAD), 16.2% depression (D-HAD) and a 48.6% a probable psychic disorder (GHQ-28). The final logistic regression model includes FACIT-F, IL, D-HAD, and first biological with Cox R^2 and Snell 20.1% and Nagelkerke 35.5%. The area under the curve was 0.849 with significance p <0.0001 [95% CI (0.786 - 0.912)]. Regarding the GHQ-28 score, a significant difference was observed among the diagnostic groups (p <0.001); in post-Hoc, a lower score was observed among patients with ankylosing spondylitis p <0.001. We also observed a significant difference among the treatment groups (p <0.001) for the GHQ-28 score. In the post-hoc analysis, the Abatacept group had a significantly higher mean p = 0.042 of GHQ-28 score, however, in the multivariate analysis no significant difference was observed p = 0.416.
Conclusion: There is a high prevalence of Si and Sa in patients with BT. Depression, fatigue, sleep disorders, fibromyalgia and work disability were associated with a higher prevalence of SB.

Table 1. Demographic characteristics No ideation/No attempt (273) Ideation (36) Attempt (12)

Table1. Demographic characteristics			
	No ideation/No attempt (273)	Ideation (36)	Attempt (12)
Gender, % females	171 (62,6)	28 (77,78)	9 (75)
Age [Media(DS)]	55,8 (14,41)	55,8 (11,48)	58,7 (16,45)
BMI (DS)	25,6 (4,62)	25,8 (4,97)	27,0 (4,67)
Work disability (%)	55 (20,14)	14 (38,88)	6 (50)
Difficulty to sleep (yes)	136 (49,81)	27 (75)	8 (66,67)
Disease duration Media (DS)	15,7 (9,89)	17,3 (8,81)	13,9 (9,15)

Table 2. Clinical characteristics

	No ideation/No attempt (273)	Ideation (36)	Attempt (12)
Diagnostic (%)			
Rheumatoid arthritis	125 (45,78)	20 (55,55)	5 (41,66)
Ankylosing spondylitis	94 (34,43)	6 (16.6)	3 (25)
Psoriatic arthritis	20 (7,3)	4 (11,11)	0 (0)
Others	34 (12,4)	6 (16,6)	4 (33,33)
Treatment (%)			
Infliximab	159 (58,24)	16 (44,44)	3 (25)
Tocilizumab	46 (16,84)	8 (22,2)	2 (16,67)
Abatacept	12 (4,3)	6 (16,67)	2 (16,67)
Rituximab	49 (17,94)	5 (13,88)	5 (41,67)
Others	7 (2,5)	1 (2,7)	0 (0)
Previous biologic (yes)	107 (39,19)	25 (69,44)	8 (66,67)
FiRST >5 (%)	49 (17,94)	15 (41,66)	9 (75)
FACIT-F < 34 (%)	109 (39,92)	31 (86,11)	11 (91,67)
GHQ-28 >5 (%)	114 (41,75)	34 (94,44)	8 (66,67)
CGHQ-28 >12 (%)	216 (79,12)	36 (100)	11 (91,67)
A-HAD >11 (%)	61 (22,34)	21 (58,33)	6 (50)
D-HAD >11 (%)	26 (9,5)	20 (55,55)	6 (50)

Disclosure of Interests: Amparo Lopez Esteban : None declared, Roberto Daniel Gonzalez Benitez: None declared, Aurora Alonso Amigo: None declared, Iustina Janta: None declared, Juan Carlos Sanchez Zanotti: None declared, Florentina Garca Calle: None declared, Juan Carlos Nieto: None declared, Beln Serrano Benavente: None declared, Juan Ovalles: None declared, Tamara Del Ro Blasco: None declared, Alfonso Ariza: None declared, Carlos Gonzalez Consultant for: Celgene, Gilead, Janssen, Merk, Novartis, Pfizer, Speakers bureau: Celgene, Roche, UCB, Indalecio Monteagudo Sez: None declared
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AB1359-HPR **THE COMBINED EFFECTS OF LIFESTYLE HABITS ON HEALTH-RELATED QUALITY OF LIFE, PHYSICAL AND MENTAL FUNCTIONS IN PATIENTS WITH SPONDYLOARTHRITIS**

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Background Earlier studies have found strong correlations between worse health and an unhealthy lifestyle, such as not meeting recommendations of moderate-to-vigorous physical activity, being overweight or obese and the use of tobacco in patients with spondyloarthritis (SpA). The impact of more than one unhealthy lifestyle habit (LsH) is however, scarcely described.
Objectives To study the combined effects of unhealthy LsHs on health-related quality of life (HRQoL) and physical and mental functions in patients with SpA. Differences between SpA subgroups and gender were also studied.
Methods Postal questionnaires were in 2009 and 2011 sent to all patients diagnosed with SpA and registered in the Skane Healthcare Register. This study included patients who at both time points responded to the survey, were ≥20 years, and had ankylosing spondylitits (AS), psoriatic arthritis (PsA) or undifferentiated spondyloarthritis (USpA). Cross-sectional data from the 2011 questionnaire were available for 1601 patients (AS n=455, PsA n=883, USpA n=263), with a mean age of 58 (13) years (52% women). Self-reported levels of weekly physical activity at moderate or vigorous intensity, (MVPA), use of tobacco (cigarettes and/or snuff) and BMI (overweight or obese) were dichotomized as "healthy" or "unhealthy". The number of unhealthy LsH were then summarized and stratified into four groups (scoring 0-3, 0=no unhealthy LsH). HRQoL was assessed with EQ-5D (0-1, worst-best), and physical function with BASFI. Disease activity (BASDAI), pain, fatigue (0-10, best-worst), anxiety, and depression (HADa/d) (0-21, no distress-maximum distress) were also measured. Statistical analyses were performed with Chi Square test and ANOVA.

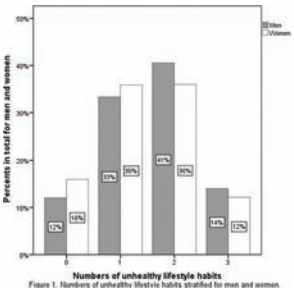


Figure 1. Numbers of unhealthy lifestyle habits stratified for men and women.

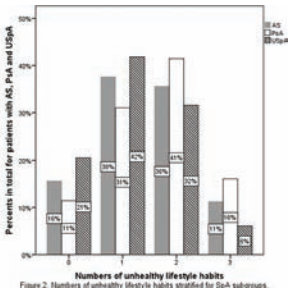


Figure 2. Numbers of unhealthy lifestyle habits stratified for SpA subgroups.

Results Fourteen percent (n=226) reported none of the studied unhealthy LsH, while 35% (n=555) reported one, 38% (n=611) two, and 13% (n=209) three unhealthy LsH. Reports of one and more unhealthy LsH had increasing negative impact on HRQoL (from mean 0.74 (SD 0.19) to 0.57 (0.30)), disease activity (from 3.2 (2.1) to 4.5 (2.3)), physical function (2.3 (2.1) to 4.4 (2.6)), VAS-pain (3.4 (2.3) to 4.8 (2.5)), VAS-fatigue (4.2 (2.7) to 5.5 (2.7)), anxiety (4.8 (4.2) to 5.6 (4.4)) and depression (3.3 (3.3) to 4.8 (3.8)) in patients with SpA (p=0.019-**Conclusion** Our findings support that the combined effect of unhealthy lifestyle habits have negative impact on many aspects of health. There is a need for interventions aiming at screening for not only one but several unhealthy lifestyle habits combined, and to offer coaching to increase behavioral change and promote better health.
Disclosure of Interests None declared
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AB1360-HPR **PREVALENCE OF TOBACCO AND ALCOHOL COMSUMPTION IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is a chronic, inflammatory arthritis leading to progressive joint and organ system damage and disability. It has been demonstrated that smoking and alcohol consumption is a risk factor for poor response to RA treatment.
Objectives: To describe the prevalence of smoking and alcohol consumption in patients with rheumatoid arthritis.
Methods: We conducted a retrospective study, patients were followed during 12 months. Smoking and alcohol consumption were assessed through yearly questionnaires. The disease activity and functional status were measured annually by the DAS28. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We estimated the prevalence smoking and alcohol consumption and explored if there was an association between DAS28 and smoking or alcohol consumption.
Results: We included 6491 patients. patients, 82% were female and 18% male; median age was 60 years RIQ (50-67), regarding disease activity, mean DAS28 was 2.59 1.08. The prevalence of alcohol consumptions was 2.26% while smoking 7.83%. We did no find an statistical association between smoking alcohol consumption and DAS28.
Conclusion: Our study showed a small prevalence of patients with rheumatoid arthritis who smoke or consume alcohol without any associations between smoking or alcohol consumption with disease activity. This could be attributed to a low prevalence in our study. Further research is needed in order to propose other methodological approaches to explore this association.
Disclosure of Interests:
Laura Villarreal: None declared, Michael Cabrera: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Buitrago-Garcia: None declared
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HPR Interventions (educational, physical, social and psychological)

AB1361-HPR **BENEFITS OF HYDROGINASTICA IN ELDERLY WITH OSTEOPOROSIS**

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Background: The aging of the population has repercussions in several social sectors, among them health, with a view to increasing the frequency of Chronic Non-Communicable Diseases. It is worth highlighting Osteoporosis, since it is associated with increased mortality and dependencies, becoming a growing public health problem. As a form of maintenance and prevention of osteoporosis it is indicated the performance of physical exercises, among them, the water gymnastics stands out.
Objectives: The study aimed to present and discuss studies on the benefits of water aerobics for the elderly with osteoporosis.
Methods: For the development of the present study a bibliographic research was carried out in the years 2010 to 2017 through searches in national and international journals indexed in PubMed, Scielo, Lilacs and Medline databases. The descriptors used were: Elderly, Aging Process, Hydrogeology, Aquatic Activity, Osteoporosis and Health Promotion in Portuguese, Spanish and English. The search period was between the months of February and March of 2017 and after selecting the articles, to extract the definitions about the theme, they were read.
Results: We can identify that water aerobics is a practice that addresses these benefits in the elderly with osteoporosis. Another aspect found in the studies is that water gymnastics provides the elderly with improved socio-affective relationships.
Even considering the natural losses due to aging on some physical characteristics, water aerobics is an important exercise practice option. The activities in the aquatic environment are indicated for a considerable gain of muscular mass and reduction of the loss of the same one, aiding in the tonification of the musculature, the loss of fat and the increase of the resistance. For the elderly with osteoporosis this modality is a preventive aid that contributes to improve their quality of life.
Among the studies found, one performed in Japan in the elderly with osteoporosis, found an increase in VO2max, flexibility and increased strength of hydrogymnastics participants; in Israel, the elderly women reduced the Muscle Mass Index and body fat. In Brazil, a study verified the improvement of functional capacity in elderly women practicing water aerobics.

Water aerobics for the elderly has been gaining momentum and growing numbers of fans, so much so that in the last 10 years the popularity of exercise in the aquatic environment has increased significantly.
Conclusion: With the present study it can be verified that the hydrogi-nastic presents numerous benefits for maintenance and prevention of osteoporosis in the elderly. Regular practice of water aerobics contributes to good body health, as well as providing physical and mental well-being and social interaction among its practitioners. This study may provide important health professionals with knowledge about the importance of encouraging and intensifying regular physical exercise, including hydrogymnastics, as one of the determinants of elderly health promotion.

REFERENCES

[1] Teixeira CS, Lemos FFC, Lopes LFD, Rossi AG, Mota CB. Corporal balance and physical exercises: an investigation in elderly women who practice different exercise modalities. **Acta Fisitrica**. 2008;15(3):156-159.
[2] Kemper, C., Oliveira, R. J. D., Bottaro, M., Moreno, R., Bezerra, L. M. A., Guido, M., & Frana, N. M. D. Effects of swimming and resistance training on bone mineral density of older women. Revista Brasileira de Medicina do Esporte. 2009;15(1):10-13.

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AB1362-HPR THE EFFECTS OF 4 WEEK REHABILITATION PROGRAM ON PATIENT OUTCOMES IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is the most common form of arthritis and a major cause of pain and disability in older adults (1). Older adults with knee OA report lower physical functioning and increased difficulty in performing activities of daily living compared with older adults without knee OA (2). Knee OA treatment aims to improve physical functions, quality of life, prevent disability, and decrease pain. Therapeutic exercises and physiotherapy treatment applications are recommended for the patients with knee OA (3).
Objectives: The purpose of this study was to examine the effects of 4 week physiotherapy and rehabilitation program on range of motion, balance, knee swelling, and activities of daily life, quality of life, and functional status in patients with knee osteoarthritis. It was hypothesized that 4 week rehabilitation program might provide improvements in measurements of the patient outcomes in patients with knee osteoarthritis.
Methods: Twenty-seven healthy subjects were participated in the study. Subjects had no surgery history of lower extremity. Range of motion, balance, knee swelling, activities of daily life, quality of life, and functional status were assessed by Goniometer, Berg Balance Test, Tape measure, Barthel Index, WHOQL Scale, WOMAC Scale, respectively. The physiotherapy and rehabilitation program started after the first assessment and was applied as 20 sessions for a total of four weeks, five sessions per week. All of the assessments procedures were performed again after the treatment.
Results: There were statistically significant improvements in measures of range of motion, balance, knee swelling, and functional status between pre- and post treatment ($p<0.05$). However, no significant difference was found in activities of daily life and quality of life after the 4-week rehabilitation program ($p>0.05$).
Conclusion: Based on our findings, short-term effects of physiotherapy and rehabilitation program may be beneficial on range of motion, balance, knee swelling, and functional status in patients with knee osteoarthritis. However, 4-week rehabilitation program has no effect on activities of daily life and quality of life in patients with knee osteoarthritis.

REFERENCES

[1] Huang L, Guo B, Xu F, Zhao J. Effects of quadriceps functional exercise with isometric contraction in the treatment of knee osteoarthritis. Int J Rheum Dis. 2018 May;21(5):952-959.
[2] Mihalko SL, Cox P, Beavers DP, et al. Effect of intensive diet and exercise on self-efficacy in overweight and obese adults with knee osteoarthritis: The IDEA randomized clinical trial. Transl Behav Med. 2018 Apr 4.
[3] 3Aydoğdu O, Sari Z, Yurdalan SU, Polat MG. Clinical outcomes of kinesio taping applied in patients with knee osteoarthritis: A randomized controlled trial. J Back Musculoskelet Rehabil. 2017 Sep 22;30(5):1045-1051.

Disclosure of Interests: None declared
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AB1363-HPR THE INVESTIGATION OF THE QUALITY OF LIFE AND FUNCTIONAL ABILITIES IN PATIENTS WITH JUVENILE SCLERODERMA

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Background: Juvenile scleroderma (JS) is a rarely seen chronic connective tissue disorder. There are two main disease forms: juvenile localized scleroderma (JLS) and juvenile systemic sclerosis (JSS). These conditions share common pathophysiologic features which are mainly characterized by inflammation and fibrosis of the skin. In JLS, fibrosis involves restricted areas of the skin, whereas in JSS it also affects the internal organs.
Objectives: There have been few studies of quality of life in pediatric scleroderma and these focused predominantly on self-perception and the influence of skin involvement. Our cross-sectional study aimed to describe the influence of juvenile scleroderma on functional ability and quality of life in relation to clinical and demographic measures.
Methods: 30 patients (26 girls, 4 boys) with JS between the ages of 6-18 years and 30 healthy controls (20 girls, 10 boys) with similar age and gender were included in our study. Patients with either localized scleroderma or systemic sclerosis (SSc) attending pediatric rheumatology clinics, together with their parents were asked to complete a set of 3 validated measures. Children completed their functional abilitiy status with Childhood Health Assessment Questionnaire (CHAQ) and Jebson Taylor Hand Function Test (JTHFT). The quality of life were evaluated with Scleroderma Health Assessment Questionnaire (SHAQ). Clinical and demographic data were provided by consultant pediatric rheumatologists and physiotherapists.
Results: The mean age of the JS group was 14.06 3.24 years (86% female, 14% male; while the%53 localized scleroderma,%47 SSc) and of the control group was 12.43 3.24 years. There were significantly differences between the two groups in functional ability scores (JTHFT), (CHAQ) and quality of life scores (SHAQ) ($p<0,05$). In JS grup, the total-CHAQ score was 0.470,63 (range 03, 0 indicating no impairment), the JTHFT-Total left hand and right hand scores were 44,059,83 and 41,497,42 second respectively, and the median SHAQ-Total score was 0,34 (range 06, 0 indicating no impairment)
Conclusion: Functional ability disabilities in JS patients cause limitations in daily living activity. Scleroderma had only a moderate effect on quality of life and functional abilites as measured by the 3 validated instruments. Although a small number of children reported greater impairment, this is an encouraging finding, given its potential disfiguring and debilitating effects.

REFERENCES

[1] Lam C, Young N, Marwaha J, McLimont M, Feldman BM. Revised versions of the Childhood Health Assessment Questionnaire (CHAQ) are more sensitive and suffer less from a ceiling effect. Arthritis Care Res. 2004; 51(6):881-9.
[2] Reedman SE, Beagley S, Sakzewski L, Boyd RN. The Jebsen Taylor Test of Hand Function: A Pilot Test-Retest Reliability Study in Typically Developing Children. Phys Occup Ther Pediatr. 2016; 36(3):292-304.
[3] Rocha, L. F., Marangoni, R. G., Sampaio-Barros, P. D., Levy-Neto, M., Yoshinari, N. H., Bonfa, E.,. .. & Kowalski, S. C. Cross-cultural adaptation and validation of the Brazilian version of the Scleroderma Health Assessment Questionnaire (SHAQ). Clinical rheumatology. 2014; 33(5):699-706.

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AB1364-HPR PRELIMINARY CASE REPORT ON SHARING PATIENT HISTORY IN CLINICAL TREATMENT OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic disease with periods of flare-ups and remissions, affecting daily life. Therefore, this disease requires lifelong management and support by the patients social circle and health professionals (HP).

Objectives: The aim of this study was to follow up the history of patients with RA, and demonstrate an improved understanding at each point in their disease trajectory, whilst encouraging them to cope, and enabling HP to optimize support provided.

Methods: We conducted two 30minute interviews with patients with RA. Interview questions included the patients perspective of their disease and disease information, effects on daily life, as well as psychological considerations using the Corbin and Strauss Chronic Illness Trajectory Framework approach [1].

This study was approved by the ethics committee of our hospital and informed consent was obtained.

Results: The first case; An unmarried 68 year old female living alone. The patients mother also suffered from RA. The patient was vaguely aware of the hereditary nature of RA (pretrajectory phase) and did not result in a big shock to her and she accepted her the diagnosis relatively smoothly (trajectory onset phase). She was prescribed initially prescribed methotrexate but this proved infective and infliximab was commenced. Remission was achieved and at that time she was satisfied with her relationship with her primary physician (stable phase).

Two years after beginning infliximab, she developed chest pain. However, her primary physician did not explore the problem and advised her that she had depression. She began to distrust him (unstable). She asked for infliximab to be stopped and requested her care be transferred to B university hospital where her mother was being treated. However, she was refused treatment due to the non-severity of her condition. She was unable to come to terms with refusal, and her physical and mental state deteriorated (downward phase).

Her mother advised the patient to go to D hospital, where she was put on Etanercept achieving remission with no complications (comeback phase). At D Hospital; (1) her condition and the need for treatment were clearly explained to her, and she was able to actively participate in shared decision making; and (2) she was given access to support from Health Professionals (HP) such as nurses, who offered a patient centered approach listening to her concerns and advising her appropriately whilst offering general psychological support.

A further 4 patients were interviewed. We will show the key phases of trajectories of their illnesses, the patients opinions about sharing their information with HP through interviewing, and the possibility of behavior change in the patients journeys.

Conclusion: This study shows that a patient centered approach taking into account the stages of the illness trajectory benefits patients perceptions of their disease and ability to cope with their condition. It also highlights the importance of having the support of ones social circle, particularly at challenging times.

Making a thorough record of the patients disease and QOL trajectory allows the patient to understand their disease process and associated life changes, and assist health professionals to provide the optimal support and resolve problems when they arise.

This preliminary study focuses on understanding the value of different phases of the trajectory of illness and sheds more light on the relationship between patients and HP and how the disease process and patients perspectives of their disease can facilitate mutual trust and smooth future treatment.

REFERENCES

[1] Corbin JM. Sch Inq Nurs Pract 1998;12: 341.

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AB1365-HPR INVESTIGATION OF THE ACUTE EFFECTS OF TAPING ON TISSUE TEMPARATURE, MUSCLE STRENGTH, FUNCTION AND BALANCE IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) mostly affects knee joint. It causes tissue temperature changes, muscle weakness, functional and balance impairments. Taping can be used to support knee joint. However, contradictory results presented in the literature (1-3).

Objectives: The aim of this study was to investigate the acute effects of taping on tissue temperature, muscle strength, function and balance in patients with knee OA.

Methods: Thirty-four patients with unilateral OA (34 females, age=60.118.29 years, height =159.765.27m; weight=80.1112.29 kg) were included. The patients were treated with a flexible kinesiology tape (Thera-Band Kinesiology tape, Cramer, USA). Supporting techniques for quadriceps muscle, patellar position and patellar tendon were applied. Before taping and after 30 min of application, tissue temperature with a thermal camera (Testo882, Germany), knee flexor and extensor muscle strength with a dynamometer (Lafayette, USA), function with timed up and go test and balance with computerized balance system (ProKin PK-254P, *Tecnobody*, Bergamo, Italy) were assessed. The paired samples t-test and Wilcoxon test used for analyses.

Results: The tissue temperature of the effected (34.661.16) and non-effected sides (34.871.08) of the cases were different (p=0.033). However, no significant difference was observed for tissue temperature before and after the taping (p=0,145). In the comparison of the effected side and non-effected side muscle strength, a significant difference was found for extensors (p=0.035). After taping the effected side, differences were found for extensor and flexor muscle strength (p=0.00; p=0.001) in comparison to before taping. While there was a significant difference in the time walking test before and after taping (p = 0.026), there was no difference for the balance scores (p> 0.05). The values of the cases before and after taping showed at Table 1.

Conclusion: It was observed that taping might not affect tissue temperature and balance. However, muscle strength and function could be affected positively with the acute supporting effect of taping.

REFERENCES

[1] Castrogiovanni P, Di Giunta A, Guglielmino C, Roggio F, Romeo D, Fidone F, Musumeci G. (2016). The effects of exercise and kinesio tape on physical limitations in patients with knee osteoarthritis. Journal of Functional Morphology and Kinesiology, 1(4), 355-368.

[2] Mutlu EK, Mustafaoglu R, Birinci T, Ozdincler AR. (2017). Does Kinesio taping of the knee improve pain and functionality in patients with knee osteoarthritis?: a randomized controlled clinical trial. American journal of physical medicine & rehabilitation, 96(1), 25-33.

[3] Wageck B, Nunes GS, Bohlen NB, Santos GM, de Noronha M. (2016). Kinesio Taping does not improve the symptoms or function of older people with knee osteoarthritis: a randomised trial. Journal of physiotherapy, 62 (3), 153-158.

Abstract AB1365HPR Table 1. The changes of the parameters before and after the tape application

Parameters	Before Taping	After Taping	p
Tissue temperature (degree)	34.661.16	34.430.90	0.145
Extensor muscle strength (Newton)	14.333.19	16.82.94	**0.000**
Flexor muscle strength (Newton)	10.071.89	11.032.5	**0.001**
Time up and go (seconds)	12.573.13	11.822.69	**0.026**
Eyes open balance*	158.56 (84.52/ 420.24)	183.20 (98.73/ 459.48)	0.091
Eyes close balance*	230.05 (111.91/ 567.97)	207.68 (128.08/ 412.56)	0.620
Limit of stability score*	64.29 (49.64/74.36)	64.62 (54.73/78.05)	0.673

* Wilcoxon test, Median (Percentiles%25-%75).

Disclosure of Interests: None declared

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AB1366-HPR **THE EFFECTS OF LAND AND WATER BASED MULTIDIMENSIONAL FUNCTIONAL MOBILITY EXERCISES ON PULMONARY FUNCTIONS IN ANKYLOSING SPONDYLITIS PATIENTS**

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Background: Pulmonary manifestations are common in ankylosing spondylitis (AS) yet there is not enough evidence about the results of different interventions on pulmonary functions.
Objectives: The aim of this study was to evaluate the pulmonary effects of land and water based multidimensional functional mobility exercises on pulmonary functions in AS patients.
Methods: This is a single-blinded, randomized and experimental study conducted in outpatient clinic and thermal center. A total of 38 patients with definite ankylosing spondylitis according to the modified New York criteria were recruited for the study Patients were randomly allocated to aquatic (AG) and land (LG) exercise group twice in a week for 8 weeks. Pulmonary Function Tests (PFT), maximal inspiratory mouth pressure (MIP), and maximal expiratory mouth pressure (MEP) were measured before and after the intervention.
Results: 3 patients from AG and 6 from LG missed 4 sessions consecutively. In AG, PEF (p=0.004), VC (p=0.025), MVV (p=0.006) and MIP (p=0.001) improved significantly on the other hand in LG FEV1/FVC (0.049), PEF (p=0.007) and MVV (p=0.004) significantly increased.
Conclusion: Performing multidimensional functional mobility exercises in water and on land could have different results. Exercising in water could have additional benefits such as increasing inspiratory muscle strength.

REFERENCES

[1] Berdal G, Halvorsen S, van der Heijde D, Mowe M, Dagfinrud H. Restrictive pulmonary function is more prevalent in patients with ankylosing spondylitis than in matched population controls and is associated with impaired spinal mobility: a comparative study. Arthritis research & therapy. 2012;14 (1):R19.
[2] Gyurcsik ZN, Andrs A, Bodnr N, Szekanecz Z, Sznt S. Improvement in pain intensity, spine stiffness, and mobility during a controlled individualized physiotherapy program in ankylosing spondylitis. Rheumatology International. 2012;32(12):3931-6.
[3] Altan L, Bingl, Aslan M, Yurtkuran M. The effect of balneotherapy on patients with ankylosing spondylitis. Scandinavian Journal of Rheumatology. 2006 2006/01/01;35(4):283-9.
[4] van Tubergen A, Hidding A. Spa and exercise treatment in ankylosing spondylitis: fact or fancy? Best Practice & Research Clinical Rheumatology. 2002 2002/09/01;16(4):653-66.
[5] Seckin U, Bolukbasi N, Gursel G, Eroz S, Sepici V, Ekim N. Relationship between pulmonary function and exercise tolerance in patients with ankylosing spondylitis. Clinical and experimental rheumatology. 2000;18(4):503-6.

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AB1367-HPR **EFFECTIVENESS OF THE HYPERBARIC TREATMENT ON THE PERCEIVED PAIN, FATIGUE AND FUNCTIONALITY OF WOMEN WITH FIBROMYALGIA**

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Background: Fibromyalgia (FM) is a chronic pain syndrome accompanied by other symptoms such as fatigue or altered functionality[1]. One of the most common non-pharmacologic treatment is physical exercise because of its known positive influence on pain as a consequence of the physical condition improvement. [2] However, they use to present a lack of adherence to this type of therapeutic programs may be attributable to post-exercise pain [3]. For this reason, alternative approaches that do not involve physical efforts, such as hyperbaric therapy, may be effective to reduce pain, fatigue or functionality in women with FM.[4]
Objectives: To compare the effectiveness of hyperbaric therapy and physical exercise on pain, fatigue and functionality in women with FM.
Methods: A randomized control trial was conducted. 28 women with FM were divided in two intervention groups: One group, composed of 14 women, received a low-intensity physical exercise program twice a week for 8 weeks (PEG). The other group received 40 sessions of hyperbaric treatment, 5 times per week (HBTG). To determine the effect of these therapeutic programs, the perceived pain was assessed with an analogue visual scale. Further, the fatigue was measured with the Borg scale and the covered walked distance with The Six minutes walk test. The measurements were conducted two times, before and one week after finishing the treatment. The effect of the treatments was statistically analyzed with a mixed factorial ANOVA with the between-subject factor called group (categories: PEG and HBTG) and with the within-subject factor called intervention (categories: pre and post-intervention).
Results: Our study shows that hyperbaric treatment significantly improved functionality and reduced the levels of pain and fatigue (Table 1). The physical exercise intervention improved functionality, but this program could not reduce the experienced intensity of pain nor the perceived fatigue (p>0.05).

Abstract AB1367HPR Table 1. Effect of the physical exercise program and hyperbaric therapy on pain, fatigue and functionality.

		Pre-intervention	Post-intervention
Pain	PEG	6.21 (2.29)	5.57 (2.24)
HBTG	7.43 (1.70)	5.07 (2.50)*	
Fatigue	PEG	6.86 (2.82)	7.21 (2.52)
	HBTG	7.79 (2.15)	6.5 (2.24)*
Distance	PEG	489.21 (76.39)	516.64 (71.58)*
	HBTG	507.14 (67.46)	566.79 (71.55)*

Data are shown as mean (SD). PEG: physical exercise group; HBTG: hyperbaric treatment group.
Conclusion: Both hyperbaric therapy and physical exercise achieved an improvement in the functionality. Nevertheless, only the hyperbaric therapy achieved a decrease in perceived pain and an improvement in the perceived fatigue.

REFERENCES

[1] Wolfe F, Clauw DJ, Fitzcharles M-A, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res. 2010;62(5):600610.
[2] Ambrose KR, Golightly YM. Physical exercise as non-pharmacological treatment of chronic pain: why and when. Best Pract Res Clin Rheumatol. 2015;29(1):120130.
[3] Dobkin PL, Sita A, Sewitch MJ. Predictors of adherence to treatment in women with fibromyalgia. Clin J Pain. 2006;22(3):286294.
[4] Wilson HD, Wilson JR, Fuchs PN. Hyperbaric oxygen treatment decreases inflammation and mechanical hypersensitivity in an animal model of inflammatory pain. Brain Res. 2006;1098(1):126128.

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AB1368-HPR **ENHANCED ROLE OF NURSES AND OTHER HEALTHCARE PROFESSIONALS (HCPS) IN THE CARE OF RHEUMATOID ARTHRITIS AND ASSOCIATED COMORBIDITIES**

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Background: Long-term morbidity and mortality in patients with rheumatoid arthritis (RA) are increased[(1)] due to the increased risk of comorbidities

including cardiovascular disease (40-70% incidence[2]; 5-12.9% prevalence[3]), diabetes (IR of 8.6 per 1000 person-years[4]; 20%[5]), interstitial lung disease (7.7%[6]; up to 60% (interstitial lung abnormalities in early RA)[7]) and depression (up to 200%[8]; 16.8%[9]). In addition to differing health care delivery systems throughout Europe, there is also variability in the roles and responsibilities of healthcare professionals (HCPs) across and within countries[10].

Objectives: This study aimed to identify good practices within the roles of HCPs in the care of RA and associated comorbidities and to understand how these practices may be implemented in other centres.

Methods: This study interviewed multidisciplinary teams at 12 selected specialist centres across Europe (1 centre per country) and examples of HCPs who had expanded roles and responsibilities were identified. Further, the questions whether these practices improved quality of care and could be implemented in other centres were addressed.

Results: This Europe-wide study identified good practice examples of enhanced roles and responsibilities for HCPs such as nurses, physiotherapists, occupational therapists and podiatrists that varied with different categories of patients and their corresponding needs. The scope and depth of extended roles also varied between different countries and health systems. Examples included:

Examples identified	Patient categories		
	suspected RA	newly diagnosed RA	established RA
Providing education on RA and comorbidities		x	x
Conducting history and joint examination	x	x	x
Coordinating care		x	x
Delivering preliminary comorbidity screening		x	
Providing treatment		x	x
Being first point-of-contact		x	x
Collaborating with community-based teams		x	x
Providing holistic support	x	x	x
Empowering self-management		x	x

Conclusion: Expanding the roles of HCP team members can help broaden perspectives on healthcare delivery, relieve the burden put on specialists and enable the provision of well-rounded, patient-centred holistic care that may improve quality of life for patients with RA, especially related to their associated comorbidities.

REFERENCES

[1] Dougados, et al. Ann Rheum Dis 2014;73:62-68
[2] Holmquist M, et al. Ann Rheum Dis 2017;76:1642-47
[3] Van Halm, et al. Ann Rheum Dis 2009; 68(9) :1395-1400
[4] Solomon D, et al. Ann Rheum Dis 2010; 69(12): 2114-7
[5] Albrecht K, et al. Rheum 2018; 57(2):329-336
[6] Bongartz, et al. Arthritis Rheum 2010; 62(6):1583-1591
[7] Reynisdottir, et al. Arthritis Rheum 2014; 66, 31-39
[8] Sheehy, et al. Rheum 2006; 45(11):1325-1327
[9] Matcham, et al. Rheumatology 2013; 52:2136-2148 1; 53(8):1491-1496

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AB1369-HPR THE EFFECTS OF CLINICAL PILATES TRAINING IN INDIVIDUALS WITH PRIMARY SJOGREN S SYNDROME

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Background: Primary Sjgrens syndrome (PSS), occurs in people with no other rheumatic disease, is a chronic, systemic, autoimmune disease characterized by lymphocytic infiltration of all exocrine glands, especially tears and salivary glands (1,2). Exercise training is commonly recommended in the approach of individuals with rheumatic disease and clinical pilates training have positive effects on endurance, functional mobility and quality of life. Nonetheless there is limited study related exercise training and no study which examined the efficacy of clinical pilates training in individuals with PSS in literature. Therefore, our study is very important.

Objectives: The aim of the study was to examine the effects of clinical pilates training on trunk and lower extremity endurance, functional mobility, emosyonel status, sleep quality, functional level and quality of life in individuals with PSS.

Methods: The study included 23 voluntary individuals (22 female,1 male; mean age: 50.529.38 years), with PSS who were diagnosed with primary Sjgrens syndrome according to 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria and according to Chisholm-Mason classification between grade 3 and 4 who applied to Pamukkale University Department of Internal Medicine, Department of Rheumatology. Anterior and lateral bridge was used to determine trunk endurance, 30-Second Chair Stand Test (30s-CST) and The Timed Up and Go (TUG) Test for lower extremity endurance, Lower Extremity Functional Scale (LEFS) for functional mobility, Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) for emotional status, Pittsburgh Sleep Quality Index (PSQI) for sleep quality, Health Assessment Questionnaire (HAQ) for functional level and Short Form 36 (SF-36) for quality of life, right after demographic information and disease related data were recorded. The all assessments were made before and after clinical pilates training. All participants attended 60-min exercises training (5-min warm up, 45-min clinical pilates exercises, 10-min cool down) three times a week for 8 weeks which was progressively challenged and applied by a Physiotherapist with 2 years of experience in this field. Wilcoxon test were used to examine the factors related to functional level.

Results: After training in all evaluations a statistically advanced level of significant improvement compared to pre-training values in individuals with PSS ($p<0.001$).

Conclusion: Muscular endurance and functional level and the associated with emosyonel status, sleep and quality of life are important for individuals with PSS. Exercise approaches for these parameters are recommended. This study showed that clinical pilates exercise programs have positive effects on trunk and lower extremity endurance, functional mobility, emosyonel status, sleep quality, functional level and quality of life in individuals with PSS.

REFERENCES

[1] Ramos-Casals M, Font J. Primary Sjogren's syndrome: current and emergent aetiopathogenic concepts. Rheumatology (Oxford) 2005; 44:1354-1367.
[2] Seror R, Theander E, Bootsma H, et al. Outcome measures for primary Sjogren's syndrome: a comprehensive review. J Autoimmun 2014; 51:51-56.

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AB1370-HPR COMPARISON OF SLEEP, FATIGUE AND SEXUAL PARAMETERS OF RHEUMATIC DISEASES

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Background: Chronic pain, sleep, and fatigue are common complaints in rheumatic disease (1). However, each rheumatic disease has different characteristics. So that it can be thought that individuals can be affected by different diseases in different ways (2).
Objectives: The aim of this study is to compare sleep, fatigue and sexual parameters in different rheumatic diseases.
Methods: Individuals diagnosed with Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS) and Fibromyalgia (FMS) who applied to the Rheumatology Department of the Medical Faculty of Hacettepe University were included in the study. After the demographic characteristics of the individuals were recorded; sexual function, sexual willingness, fatigue, and sleep features were assessed with 11th, 27th, 29th and 30th items of BETY-Biopsychosocial Questionnaire (BETY-BQ) which is developed in rheumatic patients (3).
Results: 160 RA, 108 AS, and 131 FMS patients were included in the study. The scores of individuals on scales are shown in Table 1. There was no statistically significant difference among the three groups in terms of BMI (p>0.05), while the mean age of RA patients was statistically different from the other two groups (p <0.05). The sleep, fatigue and sexual parameters (sexual function, sexual willingness) were examined with Kruskal Wallis analysis. When analyzed in terms of differences according to RA, AS and FMS, the responses to sleep (p=0.015) and sexual functioning (p=0.003) were found different according to the diseases. However, there was no significant difference in the sexual willingness (p=0.248) and fatigue (p=0.708) related to the disease. Mann-Whitney U test was performed to test the significance of a pairwise difference using Bonferroni correction to adjust for multiple comparisons revealed that the difference between the groups was due to RA patients (Table 2).

Abstract AB1370HPR Table 1. Comparison of three groups.

	RA (n=160)	AS (n=108)	FMS (n=131)
Age	51.440.83	41.751.19	43.600.78
BMI	28.650.88	27.490.52	28.641.59
Fatigue	3.020.10	3.090.10	3.170.87
Sexual function	1.200.11	1.640.15	1.750.13
Sexual willingness	1.500.12	1.720.15	1.770.13
Sleep	2.120.12	2.420.15	2.640.12

Abstract AB1370HPR Table 2. Mann-Whitney U test

	p	p
	No:27 Sexual function	No:30 Sleep
RA-AS	0.019	0.124
RA-FMS	**0.001**	**0.004**
AS-FMS	0.528	0.278

Conclusion: As a result, all the patients who participated in this study have sleep, fatigue and sexual problems. Although the mean age of RA patients is higher than other patients, it is quite interesting that they have less sleep and sexual function problems. On the other hand, it was expected that symptoms of RA and AS diseases due to their inflammatory nature would be worse than FMS. Moreover, it can be estimated that AS patients have spinal involvement and this situation may affect their sexual function, but FMS patients results in terms of these parameters were unclear. It was concluded that the psychosocial characteristics were taken into consideration especially in FMS patients sexual parameters, fatigue, and sleep features during the disease management.

REFERENCES

[1] Moldofsky, Harvey. "Rheumatic manifestations of sleep disorders." Current Opinion in Rheumatology 22.1 (2010): 59-63.
[2] Hurd, Kelle, and Cheryl Barnabe. "Systematic review of rheumatic disease phenotypes and outcomes in the Indigenous populations of Canada, the USA, Australia, and New Zealand." Rheumatology international 37.4 (2017): 503-521.
[3] Unal, Edibe, et al. "Effectiveness of a Biopsychosocial Exercise Approach in Rheumatic Diseases." Arthrıtıs & Rheumatology. Vol. 70. 111 Rıver St, Hoboken 07030-5774, Nj USA: Wıley, 2018.

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AB1371-HPR EFFECTS OF MORNING STIFFNESS ON THE PSYCHOSOCIAL AND FUNCTIONAL STATUS OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Idiopathic Arthritis (JIA) is a chronic childhood autoimmune disease that has significant implications on a childs physical health and psychosocial integration (1). Common symptoms of JIA include pain, joint stiffness, joint swelling, fatigue, and decreased physical function (2,3).
Objectives: The aim of this study is to investigate the effects of morning stiffness on the psychosocial and functional status of patients with JIA.
Methods: 387 JIA patients were included in this study. To determine the functional status of the patients functional subscale of The Juvenile Arthritis Biopsychosocial-Questionnaire (JAB-Q) and Childhood Health Assessment Questionnaire (CHAQ) were used. Psychosocial subscale of JAB-Q was used to assess psychosocial status. Finally, morning stiffness was measured as "less than 30 minutes", "between 30 minutes and 1 hour" and "more than 1 hour".
Results: A total of 162 boys and 225 girls participated in the study (Table 1). The effect of morning stiffness on functional and psychosocial status was examined with Kruskal Wallis analysis. There were statistically significant differences between the functional status (CHAQ Total, p=0,001; CHAQ General VAS, p=0.012; CHAQ Pain VAS, 0.001; Function JAB-Q, p<0.001) of the patients and the duration of morning stiffness. However, there was no significant difference between the duration of morning stiffness and psychosocial status. Mann-Whitney U test was performed to test the significance of a pairwise difference using Bonferroni correction to adjust for multiple comparisons revealed that the difference between the groups was due to the morning stiffness duration "less than 30 minutes" group (Table 2).

Abstract AB1371HPR Table 1. Descriptive statistics

	Mean SD
Age	12.503.67
BMI	19.934.34
Gender	
Female [n(%)]	225 (58.14)
Male [n(%)]	162 (41.86)

Abstract AB1371HPR Table 2. Mann-Whitney U test

	p	p	p	p
	CHAQ Total	CHAQ (General VAS)	CHAQ (Pain VAS)	Function
1-2	**0.004**	**0.003**	**0.001**	**0.002**
1-3	**0.004**	0.237	0.028	**<0.001**
2-3	0.393	0.517	0.943	0.038

1= <30 min morning stiffness, 2= 30 min-1 hour morning stiffness, 3= >1 hour morning stiffness
Conclusion: In our study, as a result psychosocial status was not affected by duration of morning stiffness. On the other hand, functionality of patients were getting worse as the duration of morning stiffness increases. It was concluded that psychosocial status should be dealt with independently of functional status, and children should be supported to participate in psychosocial environment such as school attendance, social activities.

REFERENCES

[1] Cassidy JT, Petty RE. Chronic arthritis in childhood. In Textbook of pediatric rheumatology. 5th edition. Edited by Cassidy JT, Petty RE, Laxer RM, Lindsley CB. Philadelphia, PA: Elsevier Saunders; 2005; 206-60
[2] Stanley LC, Ward-Smith P. The diagnosis and management of juvenile idiopathic arthritis. J Pediatr Health Care 2011;25:191-94.

[3] Johnson CJ, Reilly KM, Murray KM. Etanercept in juvenile rheumatoid arthritis. Annals of Pharmacotherapy 2001;35:464-71.

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AB1372-HPR THE INVESTIGATION OF THE RELATIONSHIP BETWEEN PSYCHOSOCIAL STATUS OF CHILDREN WITH JIA AND PARENTS

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Background: Juvenile idiopathic arthritis (JIA) is a heterogeneous group of diseases characterized by unknown origin arthritis that begins before the age of 16 years (1). Therefore, families are often affected by the disease of children. Parents and children often disagree with assessing different aspects of disease activity in JIA (2).
Objectives: The aim of this study is to investigate the relationship between children with JIA and their parents' psychosocial status.
Methods: A total of 345 children with JIA and their parents were included in the study (n = 690). Juvenile Arthritis Biopsychosocial Questionnaire (JAB-Q) was administered to the subjects (3). The psychosocial status of the individuals was evaluated by this questionnaires.
Results: The mean age of children included in the study (n = 345) was 12.32 3.76 years. While the median value of the Child Psychosocial score was 10 (min: 0 max: 38), the median value of the Parent Psychosocial score was 6 (min: 0 max: 20). Correlation coefficients and statistical significance were calculated by using the Pearson test. A positive low correlation was found between the psychosocial status of the child and parents (r = 0.273, p <0.001) (Table 1).
Table 1. Correlations:

JAB-Q	**Child Psychosocial**	r	1,00	**0,283**
		p		0,000
		n	345	345
	Parents Psychosocial	r	**0,283**	1,00
		p	0,000	
		n	345	345

Conclusion: It was observed that there was a low relationship between the psychosocial status of children and parents. It was concluded that child and parents psychosocial status may be affected by other variables such as high disease activity, school attendance. Further studies are needed in this area including different variables and interaction psychosocial status.

REFERENCES

[1] Prakken, B., Albani, S., & Martini, A. (2011). Juvenile idiopathic arthritis. The Lancet, 377(9783), 2138-2149.
[2] Garcia-Munitis P, Bandeira M, Pistorio A, Magni-Manzoni S, Ruperto N, Schivo A, et al. Level of agreement between children, parents, and physicians in rating pain intensity in juvenile idiopathic arthritis. Arthritis Rheum 2006;55:177-83.

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AB1373-HPR BIOPSYCHOSOCIAL CHARACTERISTICS OF INPATIENTS, OUTPATIENTS AND PATIENTS WHO ATTEND A GROUP EXERCISE SESSIONS REGULARLY

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Background: Studies show that patients' biopsychosocial characteristics may be affected by various factors such as inpatient, outpatients, exercise intervention regularly. [1]. No studies have been found to examine this situation in the literature.
Objectives: The aim of this study was to investigate the biopsychosocial characteristics of patients with rheumatic diseases who were inpatients, outpatients and participated in an exercise intervention regularly.
Methods: A total of 105 patients were included in the study (inpatient, outpatient, exercise intervention) (Table 1). For exercise intervention group, BETY as a biopsychosocial exercise model was applied 3 days a week for 3 months [2]. Biopsychosocial characteristics of the patients included in the study were evaluated by BETY- Biopsychosocial Questionnaire (BETY-BQ) [3]. In addition to the total score of BETY-BQ, the same time pain, functionality and fatigue, sexuality, emotional status and socialization subcategory of this questionnaire were evaluated on item basis among each patients.
Results: The demographics variables and BETY-BQ scores of the patients were shown in Table 1. There were a statistically significant differences among three groups. After post-hoc analysis, it was determined that there is no difference between the BETY-BQ scores of the outpatients and inpatients (p> 0.05), whereas the BETY-BQ scores of the patients who participated in the group exercise were lower (p 0.05). When the items were analyzed, it was found that pain (items 2, 3, 5, and 12), functionality and fatigue (items 6, 7, 11, 26, and 28), emotional status (items 16 and 17), and sleep (item 30) subcategory scores were also lower in patients who participated in BETY programme (p 0.05).

Abstract Table 1. Demographic statistics and BETY-BQ scores

		Inpatient (n=30)		Outpatient (n=44)		Exercise intervention (BETY) (n=31)	
		Female	**Male**	**Female**	**Male**	**Female**	**Male**
Gender (%)		61.3	37.8	87.2	12.8	53.7	7.4
		XSD		**XSD**		**XSD**	
Age (year)		46.3514.56		46.0613.26		48.67 11.89	
BMI (kg/m^2)		24.19 5.17		28.98 18.85		26.94 3.84	
BETY-BQ (0-120)	**p**	**XSD**		**XSD**		**XSD**	
	0.027	49.1017.94		45.6427.93		33.8121.73	

Conclusion: It is surprising that the biopsychosocial characteristics of the inpatients and outpatients were similar. According to this result, inpatients shouldnt be thought as worse than outpatients. On the other hand, the patients who participated in exercise intervention were improved in terms of biopsychosocial aspects. The positive effects of the BETY program on the biopsychosocial status of individuals have been demonstrated formerly [4]. It was concluded that inpatients should be supported to exercise in terms of their biopsychosocial needs during hospitalization period as well as rheumatic outpatients need.

REFERENCES

[1] Saketkoo, L.A. and J.D. Pauling, *Qualitative methods to advance care, diagnosis, and therapy in rheumatic diseases.* Rheumatic Disease Clinics of North America, 2018.
[2] Kisacik, P., et al., *Investigating the effects of a multidimensional exercise program on symptoms and antiinflammatory status in female patients with ankylosing spondylitis.* Complement Ther Clin Pract, 2016. 22: p. 38-43.
[3] NAL, E., et al., *Romatizmalı hastalar iin bir yaşam kalitesi leğinin geliştirilmesi: madde havuzunun oluşturulması.* Journal of Exercise Therapy and Rehabilitation, 2017. 4(2): p. 67-75.
[4] Unal, E., et al. *Effectiveness of a Biopsychosocial Exercise Approach in Rheumatic Diseases*. in *ARTHRITIS & RHEUMATOLOGY*. 2018. WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA.

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AB1374-HPR THE EFFECTIVENESS OF BIOPSYCHOSOCIAL EXERCISE PROGRAM ON PAIN COPING IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND FIBROMYALGIA

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Background: Ankylosing spondylitis (AS) and fibromyalgia (FM) are rheumatic diseases with a high incidence in the community. Although many studies have been done on pain in these patient groups, the studies on coping with pain are very limited (1, 2). Bilişsel Egzersiz Terapi Yaklaşımı (BETY) is an exercise approach that developed in rheumatic patients. This approach has its own Biopsychosocial Questionnaire

(BETY-BQ). This scale that assesses patients biopsychosocial status and includes the question about pain coping skill (3).
Objectives: The aim of this study is to the effectiveness of biopsychosocial exercise program on pain coping in with patients AS and FM.
Methods: Patients with AS and FM were included in the study and demographic data were recorded. Patients attended the BETY sessions for 8 weeks, 3 times a week for sixty minutes. BETY-BQ (3) was applied to individuals before and after 8 weeks. The answers to the question I don't know how to control my pain, which is the 5th question of the BETY-BQ scale, was recorded as 5-point Likert, ranging between yes-always to no-never.
Results: 47 women with AS (n = 30) and FM (n = 17) included in the study. The mean age was 41.83 11.24 and 43.35 8.86 and the body mass indexes were 26.385.15and 26.325.15 for the AS and FM patients, respectively. There was a statistically significant difference in the ability of AS subjects to cope with pain before and after the BETY intervention (p <0.05), there was no significant difference between individuals with FM before and after BETY intervention (p> 0.05) (Table 1).

Abstract AB1374HPR Table 1. Comparison of AS and FM patients before and after treatment

	AS (n=30)			FM (n=17)		
	Pre-treatment	Post-treatment		Pre-treatment	Post-treatment	
5th question (%)			p= 0.36			p= 0.314
Yes, always	33.3	10		23.5	17.6	
Yes, often	20	13.3		5.9	11.8	
Yes, sometimes	16.7	30		17.6	23.5	
Yes, rarely	10	13.3		41.2	11.8	
No, never	20	33.3		11.8	35.3	

Conclusion: Although both AS and FM are rheumatic diseases, it is known that FM patients experience more intense psychosocial stress. They are, therefore, resistant to change (4). We found that the positive change in pain coping skill seen in the AS group is not seen in FM group. It is concluded that FM patients regarding in pain coping strategies they need to attend exercise programs and need to be educated about pain coping skills for a longer period.

REFERENCES

[1] Dean, L.E., et al., Global prevalence of ankylosing spondylitis. Rheumatology (Oxford), 2014. 53(4): p. 650-7.
[2] Cabo-Meseguer, A., G. Cerda-Olmedo, and J.L. Trillo-Mata, Fibromyalgia: Prevalence, epidemiologic profiles and economic costs. Med Clin (Barc), 2017. 149(10): p. 441-448.
[3] NAL, E., et al., Romatizmalı hastalar iin bir yaşam kalitesi leğinin geliştirilmesi: madde havuzunun oluşturulması. Journal of Exercise Therapy and Rehabilitation, 2017. 4(2): p. 67-75.
[4] Clauw, D.J., Fibromyalgia and related conditions. Mayo Clin Proc, 2015. 90(5): p. 680-92.

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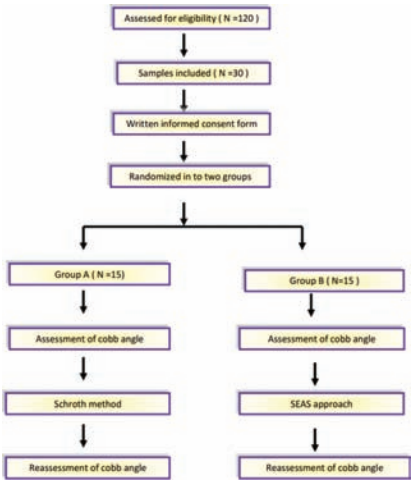
AB1375-HPR EFFECT OF SCHROTH METHOD AND SCIENTIFIC EXERCISE APPROACH TO SCOLIOSIS (SEAS) ON THE COBB ANGLE AMONG THE ADOLESCENT WITH IDIOPATHIC SCOLIOSIS A COMPARATIVE STUDY

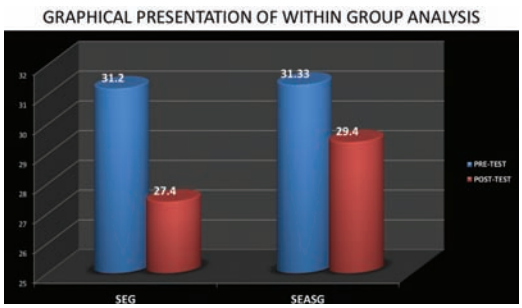
Jalpa Shah, T Padma Priya., Pahinian Arumugam, R Kousalya. *Sri Venkateshwaraa Medical College Hospital and Research Centre, physiotherapy, Puducherry, India*

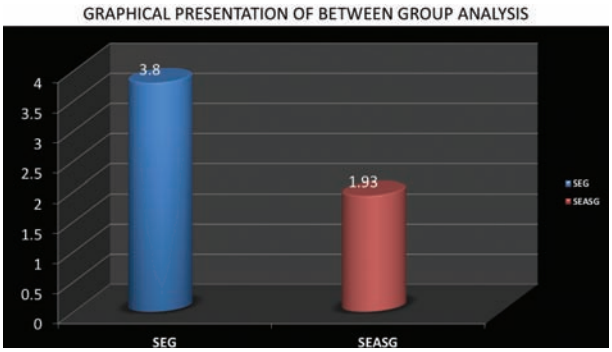
Background: Scoliosis is a three-dimensional deformity of the spine and trunk leading to physical and functional disability. Among adolescent, idiopathic scoliosis is the most common (80% - 89%) form of scoliosis with prevalence ranging between 0.47% and 5.2% in general population[1]. As the evidence on the comparative efficacy of various physical therapy in scoliosis is sparse, we conducted a comparative study assessing efficacy of Schroth method of exercise group (SEG)[2] and scientific exercise approach to scoliosis group (SEASG)[3] in adolescents with idiopathic scoliosis.
Objectives: To compare efficacy of schroth method and SEAS among adolescent with scoliosis.
Methods: Thirty subjects, both male and female of the age group of 10 to 18 years, with mild-moderate idiopathic scoliosis defined as the spinal radiographic Cobb angle in the range of 20 to 45 and riser sign of 0-2 were randomly allocated to Schroth method of exercise group (SEG, n=15) and scientific exercise approach to scoliosis group (SEASG, n=15). Subjects with diagnosis of spinal injury, previous spinal surgery, gibbus, limb deformity, infection and malignancy were excluded. The SEG and SEASG performed Schroth and scientific exercise respectively, 5 times a week for 7 weeks. To quantify the magnitude of spinal deformity, Cobb angle measurements were obtained by using radiograph to gain pre-post interventional differences. (Figure 1)
Results: SEG showed the significant changes in pre (mean sd 31.2 5.20) and post (mean sd 27.4 5.17) Cobb angle measurements. SEASG also showed the significant changes in pre (mean sd 31.33 5.26) and post (mean sd 29.4 5.9) Cobb angle measurements (Figure 2). Comparing both the groups by unpaired t test suggested SEG to be more efficacious than the SEASG with the t value (4.22) for change in Cobb angle (p <.0.0001) (Figure 3).
Conclusion: The study establishes the role of physical therapy in idiopathic scoliosis of mild to moderate degree among adolescents with.
Schroth method of exercise performs better compared to the SEAS in patients with mild to moderate scoliosis.

REFERENCES

[1] Negrini, Stefano & Fusco, Claudia & Minozzi, S & Atanasio, Salvatore & Zaina, Fabio & Romano, Michele. (2008). Exercises reduce the progression rate of adolescent idiopathic scoliosis: Results of a comprehensive systematic review of the literature. Disability and rehabilitation. 30. 772-85.
[2] Schreiber S, Parent EC, Moez EK, Hedden DM, Hill D, Moreau MJ, Lou E, Watkins EM, Southon SC. The effect of Schroth exercises added to the standard of care on the quality of life and muscle endurance in adolescents with idiopathic scoliosis-an assessor and statistician blinded randomized controlled trial:"SOSORT 2015 Award Winner". Scoliosis. 2015 Sep 18;10:24. doi:10.1186/s13013-015-0048-5
[3] Romano M, Negrini A, Parzini S, et al. SEAS (Scientific Exercises Approach to Scoliosis): a modern and effective evidence based approach to physiotherapic specific scoliosis exercises. Scoliosis. 2015;10:3. Published 2015 Feb 5.





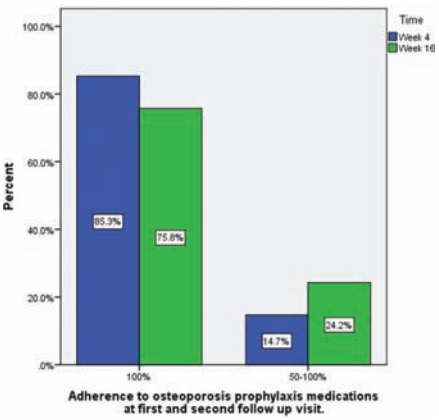


Disclosure of Interests: None declared
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AB1376-HPR ROLE OF NURSE-LED TELEPHONE FOLLOW UP TO ENHANCE AND SUBSEQUENTLY MAINTAIN HIGH LEVEL OF ADHERENCE TO OSTEOPOROSIS PROPHYLAXIS MEDICATIONS: A PROSPECTIVE COHORT STUDY OF PATIENTSWITH POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS

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Background: Poor adherence to the osteoporosis prophylaxis medications has been reported before, which may result in treatment failure.[1] However findings of previous studies are controversial.[1,2]
Objectives: To investigate the role of nurse-led telephone follow-up to increase the level of adherence to osteoporosis prophylaxis medications in patients with newly diagnosed Polymyalgia Rheumatica/Giant Cell Arteritis (PMR/GCA).
Methods: This is an ongoing 1-year prospective cohort study. 37 consecutive steroid treated patients with newly diagnosed PMR/GCA were included. Patients were seen by the physicians at baseline, 1st and 4th month, where they were interviewed about their compliance towards osteoporosis prophylaxis medications, i.e. Calcium/Vitamin D supplements and Bisphosphonates (if Tscore ≤ -1), using a standardized questionnaire. Patients were therefore categorized as 100%, 50-100%, <50% adherent or non-adherent to the prescribed drugs. Every individual patient were contacted by our nurses one week after treatment initiation, and subsequently one month after physician visit to evaluate the effect of treatment, compliance to the medications and possible drugs side effects.
Results: 85.3% and 75.8% of the patients were completely adherent to their osteoporosis medications at 1st and 4th months of treatment initiation, respectively. (figure 1) The difference between level of adherence to the osteoporosis medications at 1st (=week 4) and 4th month (=week 16) was not statistically significant. (P value:0.369). Decreased adherence in the patients was mainly due to forgetfulness.



Conclusion: Compared to the earlier findings we found a higher level of adherence in this group of patients. Nurse-led telephone follow up as well as educating the patients respecting the importance of the osteoporosis medications for preventing steroid related side effects, may enhance and subsequently maintain high level of adherence to the osteoporosis medications. Our findings are in line with our earlier study indicating a high level of adherence to the osteoporosis medications in PMR/GCA patients.[2]

REFERENCES

[1] Rossini M, et al. Determinants of adherence to osteoporosis treatment in clinical practice. Osteoporos Int. 2006;17:914-21.
[2] Emamifar A, et al. Level of Adherence to Prophylactic Osteoporosis Medication amongst Patients with Polymyalgia Rheumatica and Giant Cell Arteritis: A Cross-Sectional Study. International Journal of Rheumatology. 2015;2015:783709.

Disclosure of Interests: None declared
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AB1377-HPR PATIENT ACTIVATION MEASURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The Patient Activation Measure (PAM) is a 13-item measure that assesses patient knowledge, skill, and confidence for self-management. The measure was developed using Rasch analyses and is an interval level, unidimensional, Guttman-like measure. The current analysis is aimed at reducing the number of items in the measure while maintaining adequate precision(1). A Spanish adaptation of the scale was performed in 2017.
Objectives: To determine the level of activation, knowledge and skills for self-management in patients with Rheumatoid Arthritis
Methods: We performed a quantitative, observational, cross-sectional, and questionnaire-based study, convenience sampling was used. Participants were recruited in a specialized RA center, during a patients meeting. We applied the PAM-13 scale validated in Spanish. The scale has a score from 1 to 4 divided in four levels where level 1 represents a disengaged patient and suggests that the doctor is in charge of their health; level 2: the patient becomes aware but struggling; level 3: The patient is taking action and considers himself as a part of the healthcare team, and level 4 represents a patient that maintains behaviors and pushes forward. The maximum score is 52 points.
Results: 322 patients participated, 23 patients generated incomplete PAM scores (response rate 92%) and were excluded. From total 93% of patients were women. Mean age was 60 years 10; mean PAM-13 Was 19.83 6.16. In our study 68% of patients were in level 2 according to PAM-13 scale which means that they are becoming aware of their knowledge, skills and self-management but are still struggling. See table 1. In average 80% of patients answered each question to be in level 1 or 2, 15% in level 3 and only 5% in level 4.

LEVEL	n	%
Level 1	59	19.73
Level 2	204	68.23
Leve 3	34	11.37
Level 4	2	0,67

Conclusion: This is the first study in our country where the Patient Activation Measure is applied in patients with rheumatoid arthritis. Thus, it might be useful to implement patient activation monitoring, since the level of activation is low in patients with RA.
Disclosure of Interests: Laura Villarreal: None declared, Fernando Rodriguez: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Buitrago-Garcia: None declared
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AB1378-HPR EFFECT OF CLINICAL CHARACTERISTICS, HABITS, PHYSICAL ACTIVITY LEVELS AND FUNCTIONAL CAPACITY ON QUALITY OF LIFE IN SYSTEMIC SCLEROSIS PATIENTS

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Background: In patients with Systemic sclerosis (SSc), many factors such as inactivity, smoking, gastrointestinal system involvement are reported to have an adverse effect on overall health related quality of life, and quality of life is in line with the prognosis of the disease (1,2).
Objectives: The aim of this study was to investigate the effect of clinical characteristics, habits, physical activity levels and functional capacity of patients with SSc on quality of life.
Methods: Twenty-tree SSc patients were included in the study. The ages of patients, the amount of cigarette consumption, duration of diagnosis and body mass indexes (BMI) were questioned and recorded. Functional capacities of patients were measured by 6 Minute Walking Test (6MWT). Physical activity levels of patients were calculated using the International Physical Activity Questionnaire (IPAQ; using metabolic equivalent-MET). Quality of life was evaluated by the short form SF-36 quality of life questionnaire(SF-36 QoLQ). The SF-36 questionnaire was evaluated as two sub-scales, physical and mental.
Results: The mean age of the patients was 51.0011.10 years and the duration of diagnosis was 7.604.80 years, BMI was 26.606.37 kg/m^2 and amount of cigarette consumption was 6.023.30 packetyears. The mean physical activity levels (IPAQ) were 281.6860.45 MET, 6MWT distance were 435.3980.45 m, SF-36 QoLQ-physical were 32.4813.42 and SF-36 QoLQ-mental were 38.5611.42 score. It was found that there was a significant correlation between SF-36 QoLQ-physical and BMI (p =0.043, r =-0.426), 6DWT (p <0.001, r= 0.737) and IPAQ (p =0.001, r = 0.647). There was a significant correlation between the SF-36 QoLQ-mental and 6MWT (p=0.020, r = 0.483) and IPAQ (p =0.002, r = 0.614).
Conclusion: Reduced levels of physical activity in SSc patients affect functional capacity. Reduced physical activity level and functional capacity decrease the quality of life of patients related to both physical and mental health. Physical health related quality of life of patients is negatively affected by the increase in BMI. Functional capacity, clinical characteristics, habits and physical activity levels should be evaluated and improved in treatment programs aimed at improving the overall health-related quality of life of patients.

REFERENCES

[1] Turesson, C., & Matteson, E. L. (2007). Cardiovascular risk factors, fitness and physical activity in rheumatic diseases. Current Opinion in Rheumatology, 19(2), 190196.
[2] Hudson, M., Thombs, B. D., Steele, R., Panopalis, P., Newton, E., Baron, M., & Canadian Scleroderma Research Group (2009). Health related quality of life in systemic sclerosis: A systematicreview.ArthritisandRheumatism,61(8),11121120. https://doi.org/10.1002/art.24676

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AB1379-HPR EFFECTS OF DIFFERENT EXERCISE MODELS ON PAIN, FUNCTIONALITY, BALANCE, PROPRIOCEPTION AND COGNITION FEATURES OF PATIENTS DIAGNOSED WITH FIBROMYALGIA

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Background: Fibromyalgia syndrome (FMS) is a chronic disease characterized by diffuse pain, fatigue, sleep disturbance, cognitive impairment, and other physical symptoms that adversely affect physical and sensory functions and impair quality of life. Nowadays, in the treatment of FMS, low intensity aerobic exercises and exercise programs combined with other treatment methods are recommended.
Objectives: The aim of this study was to evaluate the effects of aerobic and balance-proprioception exercises on the symptoms of Fibromyalgia (FMS) and the superiority of the two exercise models.
Methods: 51 female patients who adhere to the inclusion criteria were divided into two groups randomly. Aerobic Exercise Group (AEG; n=26) and Balance-Proprioceptive Exercise Group (BPEG; n=25) was applied to the exercise laboratory under the supervision of physiotherapist in Istanbul Medical Faculty, Department of Sports Medicine 3 days a week for 6 weeks. Before and after the program Pain (VAS), functional status (FIQ), postural stability (Biodex balance system), knee joint proprioception (Cybex isokinetic dynamometer) were evaluated. Cognitive status was assessed by Standardized Mini Mental State Examination (SMMSE) only before program.
Results: There wasnt statistically significant difference between demographic (age, weigh, BMI etc.) and clinic (VAS, FIO, Biodex, Cybex, SMMSE) features of the groups at the beginning (p>0.05). Parameters measured in both groups after exercise programs showed progress compared to initial levels (p<0.05). There aren`t superiority between two exercise groups in terms of VAS, FIQ scores (p>0.05). Recovery is found to be superior at BPEG in balance parameters (eyes open overall stability index (EOOSI) and eyes open anterioposterior stability index (EOAPSI)) and some parameters that belongs to proprioception (p<0.05).
Conclusion: It is determined that aerobic exercise and balance-proprioception exercise programs at/in FMS are effective -in positive way- methods for functionality, pain, proprioception and balance parameter recovery of the patients. Except EOOSI and EOAPSI balance parameter values; according to other parameters it is found that aerobic exercise and balance-proprioception exercises are equal to each other. It is found out that balance-proprioception exercises are superior to aerobic exercises for improving EOOSI and EOAPSI. It is revealed that balance proprioception exercises are more effective for curing proprioception. It is observed that patients with FMS had deterioration in cognitive functions.

REFERENCES

[1] Duruturk N, Tuzun EH, Culhaoglu B. Is balance exercise training as effective as aerobic exercise training in fibromyalgia syndrome? Rheumatology international. 2015;35(5):845-54.
[2] Kibar S, Yıldız HE, Ay S, Evcik D, Ergin ES. New approach in fibromyalgia exercise program: a preliminary study regarding the effectiveness of balance training. Archives of physical medicine and rehabilitation. 2015;96 (9):1576-82.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.5682

AB1379B-HPR PATIENT SATISFACTION IS HIGH IN PATIENTS TRAINED TO SELF-INJECT WITH A BUTTON FREE AUTO-INJECTION USING VIDEO TRAINING

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Background: Once-weekly subcutaneous injection of methotrexate can optimize long-term treatment of rheumatic diseases such as rheumatoid arthritis.[1] However, available self-injection devices vary in terms of ease of use and level of operational dexterity required.
Objectives: This pilot study compared patient satisfaction with use of a methotrexate pre-filled, button-free, auto-injector pen (Nordic Pharma, UK) for subcutaneous injection with previous use of a button-activated pen device following the option to self-train via video.
Methods: Patients with rheumatoid arthritis currently administering subcutaneous methotrexate using a button-activated pen device were invited to change to a button-free auto-injector by letter. They were given the option to self-train using an online video or receive one-to-one instruction from a rheumatology nurse. Initial follow-up took place immediately after the first injection; invitation to participate in a 10-minute telephone questionnaire to evaluate their experience of using their new device took place after 3-4 weeks. Satisfaction with the device was assessed overall and according to 7 specific autoinjector attributes: ease of injection; experience of injection; comfort in hand; use with dexterity issues or during flare-ups; confidence in full dose being given; convenience of storage and disposal; and portability.
Results: Thirty-three patients were invited to change to an auto-injector: 22 patients responded (response rate: 64.7%), 19 of which made the switch and completed the survey. 79% of patients overall were satisfied or very satisfied with administering methotrexate using the auto-injector; 85% of patients were equally or more satisfied with the use of an auto-injector pen compared to their previous device. Patients were equally or

more satisfied with the new device across all 7 autoinjector attributes: convenience of storage and disposal (100.0%), portability (100.0%); comfort in the hand (94.1%); confidence in full dose being given (88.9%); use with dexterity issues or during flare-ups (85.7%); ease of injection (82.4%); experience of injection (68.4%). Self-training via video did not negatively affect satisfaction: 83.3% of those patients confident in their ability to perform self-injection correctly after viewing the video were satisfied or very satisfied with their new autoinjector device. Three patients discontinued with the new device: one switched to oral therapy for reasons unrelated to the device; two returned to their original device.

Conclusion: This pilot study showed that patients were more satisfied with use of a methotrexate button-free auto-injector device than with their previous auto-injector device across all 7 user attributes and that satisfaction was maintained with use of self-training. Patient views regarding acceptability and use of auto-injection devices should be considered when making device switches based on cost and nurse resource allocation to ensure continued adherence with injected medication.

REFERENCES

[1] Bianchi B, et al. Methotrexate and Rheumatoid Arthritis: Current Evidence Regarding Subcutaneous Versus Oral Routes of Administration. Adv Ther 2016;33:36978.

Disclosure of Interests: Dawn Homer Grant/research support from: This project was supported by an unrestricted educational grant from Nordic Pharma., Consultant for: Participation in an advisory board with Janssen-Cilag in 2018 and will be speaking for Roche-Chugai in March 2019.
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HPR Measuring health (development and measurement properties of PROs, tests, devices)

AB1380-HPR THE EFFECTS OF CERVICAL RANGE OF MOTION ON POSTURAL STABILITY IN PATIENTS WITH CHRONIC NECK PAIN

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Background: Neck pain is a common musculoskeletal problem within chronic pain and it effectuates up to 71% of adult population during their life time (1). Chronic neck pain is related to a series of disabilities: a range of reported pain, postural stability problems, and cognitive dysfunction (2). However, there is no report that investigate the relationship between range of motion and postural stability in patients with chronic neck pain.

Objectives: The purpose of this study was to investigate the effects of limitations in cervical range of motion on postural stability in patients with chronic neck pain. We hypothesized that the patients who have extension limitation might have postural stability deficit with flexion direction.

Methods: Thirty subjects of mean age 28.50 ± 10.95 years who admitted with chronic neck pain to a Private Physiotherapy Clinic were participated in this study. While goniometer was used for cervical range of motion, pedalo sensamove system was used for postural stability. In addition, pain and disability were measured with visual analogue scale, neck disability index, respectively.

Results: It was found that limitation of cervical range of motion was not correlated to postural stability deficits ($p>0.05$). The neck pain and disability status was not associated with level of postural stability ($p>0.05$).

Conclusion: The findings of this study showed that postural stability may not be affected by the limitation of cervical range of motion, and also neck pain intensity, neck disability status in patients with chronic neck pain. Further research with larger sample sizes is warranted.

REFERENCES

[1] Demirbüken İ, Özgül B, Kuru Çolak T, Aydoğdu O, Sarı Z, Yurdalan SU. Kinesiophobia in relation to physical activity in chronic neck pain. J Back Musculoskelet Rehabil. 2016;29(1):41-7.
[2] Nazari G, Bobos P, Billis E, MacDermid JC. Cervical flexor muscle training reduces pain, anxiety, and depression levels in patients with chronic neck pain by a clinically important amount: A prospective cohort study. Physiother Res Int. 2018 Jul;23(3):e1712.

Disclosure of Interests: None declared
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AB1381-HPR ADAPTABILITY, EFFECTIVENESS AND SAFETY OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Tofacitinib is a, selective JAK inhibitor that preferentially inhibits Janus kinase (JAK) 1 and JAK3. Oral tofacitinib 5 mg twice daily or 11 mg once daily is indicated for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant of, one or more DMARDs. Mainly, one of the strengths of Tofacitinib, is that it is a very suitable medicine for those patients who are afraid of applying a parenteral biological medicine, or who are of advanced age or are at high risk of adverse events, therefore It's easy to discontinue it.

Objectives: We aim to describe the tolerance and adaptability of patients to Tofacitinib, as well as the effectiveness and safety in patients with RA in a real-life setting in Bogot, Colombia.

Methods: During 2017 and 2018 we followed-up patients from a RA specialized center in Colombia receiving Tofacitinib. Patients were treated with therapeutic goals type T2T and a multidisciplinary approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3-5 weeks (DAS28 > 5.1), every 7-9 weeks (DAS28 $\geq$ 3.1 and $\leq$ 5.1), and every 11-13 weeks (DAS28 < 3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 > 3.2; We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) patients and one aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. On the other hand, we evaluated the tolerance and adaptability of patients to Tofacitinib. Adverse events were classified according the Common Terminology Criteria for Adverse Events (CTCAE) of the World Health Organization. Descriptive epidemiology for continuous variables, measure of central tendency and dispersion for qualitative and categorical variables through percentages and averages were calculated.

Results: We included 59 patients receiving tofacitinib, 92% were women and 8% men during last two years. Mean age was 60 11. From total, 70% of patients received anti-TNF drugs before tofacitinib and the other 30%. In reference to the adaptability, most of the patients up to 95% expressed to be happy with the oral intake and the suitable dosage of the medication. Regarding effectiveness, mean DAS28 at beginning was 4.6 0.83 and at the end 2.6 0.63; At the beginning of follow-up 57.6% of patients were in moderate disease activity according to DAS28 and 33.9% in severe disease activity, while at the end of follow up 64% of patients achieved remission and 16.9% low disease activity during the 12 months of follow-up. See table 1. Regarding safety 2 patients presented a dermatological adverse event (herpes zoster) with adverse event rate of 3.3%.

ACTIVITY LEVEL	BASELINE		24 MONTH FOLLOW-UP	
	n	%	n	%
REM			38	64.41
LDA	5	8.47	10	16.95
MDA	34	57.63	11	18.64
HDA	20	33.90	0	-

Abstract AB1381HPR Table 1. DAS28 in patients receiving tofacitinib.

Conclusion: Tofacitinib is a very suitable medicine in patients with RA and improved disease activity in impressive way; also proved to be very safe, except the occurrences of herpes zoster, which is an aspect to take into account in its prescription, but none of patients presented another serious adverse events.

Disclosure of Interests: Fernando Rodriguez: None declared, Anggie Aza: None declared, Michael Cabrera: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Buitrago-Garcia: None declared
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AB1382-HPR **COMPARISON OF EFFICACY OF DIFFERENT REHABILITATION APPROACHES IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS**

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Background: Osteoarthritis (OA) is the most common rheumatologic disease in the world, resulting primarily in progressive cartilage destruction. OA-induced changes are the main cause of disability and are mostly seen in the knee joint.
Objectives: To investigate the effects of different rehabilitation practices on the range of motion, muscle strength, pain, physical function and quality of life in patients with knee OA.
Methods: Thirty patients between the ages of 40-65 with knee OA were included in the study and divided into 3 groups. Transcutaneous Electrical Nerve Stimulation (TENS), ultrasound, hotpack/coldpack and home exercise program were given to the 1. group (n=10) for 15 days. 2. group (n=10) received three doses of Platelet-Rich Plasma (PRP) followed by home exercise program for 15 days. The control group (n=10) received only home exercise program for 15 days. All individuals were evaluated using 'Goniometer' for Range of Motion (ROM), 'Manual Muscle Test' for M. Quadriceps femoris muscle strength, 'Visual Analogue Scale' for pain, 'The Western Ontario and McMaster Universities Arthritis (WOMAC) Scale' for physical function and 'Short Form-12 Quality of Life Scale Mental (SF-12 - MC) and Physical Component (SF-12 - PC)' for quality of life at baseline and end of treatment.

Abstract AB1382HPR Table 1. Results before and after treatment

		1. Group			2. Group			Control Group		
		Pre Treatment	Post Treatment	p*	Pre Treatment	Post Treatment	p*	Pre Treatment	Post Treatment	p*
		Ave±SD	Ave±SD		Ave±SD	Ave±SD		Ave±SD	Ave±SD	
Quadriceps Femoris Muscle Strength	Right	4,50±0,52	4,55±0,49	0,317	4,30±0,53	4,45±0,55	0,083	4,45±0,36	4,60±0,45	0,083
	Left	4,35±0,62	4,40±0,61	0,317	4,35±0,52	4,45±0,55	0,157	4,50±0,52	4,60±0,39	0,157
Knee ROM	Right	91,5±28,5	98,0±26,4	**0,042**	99,0±10,7	101±9,06	**0,046**	111±9,73	113±8,23	0,083
	Left	94,0±24,0	105±10,9	**0,026**	94,0±13,2	97,5±13,5	**0,036**	106±14,3	109±13,6	0,063
VAS	Resting	3,00±2,53	1,40±2,06	0,067	1,50±3,17	0,80±1,75	0,180	1,00±1,05	0,40±0,69	**0,034**
	Activity	6,50±3,27	2,00±2,35	0,007	4,90±3,34	2,30±2,62	0,007	2,80±2,14	1,00±1,33	**0,011**
WOMAC		56,3±12,2	37,8±16,5	0,007	45,9±21,2	39,1±20,0	0,005	35,2±12,1	28,1±13,5	**0,009**
SF-12	PC	33,4±10,6	37,0±10,8	0,139	40,8±5,99	40,9±6,99	0,333	41,2±9,48	47,1±10,1	**0,037**
	MC	48,5±10,4	58,1±4,14	**0,022**	37,1±11,4	46,0±15,9	**0,028**	48,6±12,5	49,8±11,2	0,799

Abstract AB1382HPR Table 2. Comparison of pre- and post-treatment measurement results between groups

		Pre - Treatment				Post - Treatment			Between Groups
		1.Group n=10	2.Group n=10	Control Group n=10	p*	1.Group n=10	2.Group n=10	Control Group n=10	p*
		Ave±SD	Ave±SD	Ave±SD		Ave±SD	Ave±SD	Ave±SD	
Quadriceps Femoris Muscle Strength	Right	4,50±0,52	4,30±0,53	4,45±0,36	,652	4,55±0,49	4,45±0,55	4,60±0,45	0,487
	Left	4,35±0,62	4,35±0,52	4,50±0,52	,775	4,40±0,61	4,45±0,55	4,60±0,39	0,793
Knee ROM	Right	91,5±28,5	99,0±10,7	111±9,73	**,038**	98,0±26,4	101±9,06	113±8,23	0,322
	Left	94,0±24,0	94,0±13,2	106±14,3	,119	105±10,9	97,5±13,5	109±13,6	0,375
VAS	Resting	3,00±2,53	1,50±3,17	1,00±1,05	,061	1,40±2,06	0,80±1,75	0,40±0,69	0,175
	Activity	6,50±3,27	4,90±3,34	2,80±2,14	**,037**	2,00±2,35	2,30±2,62	1,00±1,33	**0,031**
WOMAC			40,8±5,99	41,2±9,48	,113	37,0±10,8	40,9±6,99	47,1±10,1	**0,013**
SF-12	PC	56,3±12,2	45,9±21,2	35,2±12,1	**,007**	37,8±16,5	39,1±20,0	28,1±13,5	0,173
	MC	48,5±10,4	37,1±11,4	48,6±12,5	,059	58,1±4,14	46,0±15,9	49,8±11,2	0,107

Results: Statistically significant difference was found at pain and WOMAC score at the time of activity in all groups (Table 1). Statistically significant difference was found at ROM and SF-12 MC score in group 1 and 2; at resting pain and SF-12 PC score in control group ($p < 0.05$) (Table 2).
Conclusion: In addition to electrotherapy treatment and PRP in knee OA treatment, it is thought that home exercise program can be used to relieve symptoms and improve quality of life in knee OA.

REFERENCES

[1] Huang GL, Hua S, Yang TM, et al. Platelet-rich plasma shows beneficial effects for patients with knee osteoarthritis by suppressing inflammatory factors. Exp Ther Med. 2018; doi: 10.3892/etm.2018.5794.
[2] Qiestad B, Juhl C, Eitzen I, et al. Knee extensor muscle weakness is a risk factor for development of knee osteoarthritis. A systematic review and meta-analysis. Osteoarthr Cartilage. 2015; 23:171-7.
[3] Reese NB, Bandy WD. Joint Range of Motion and Muscle Length Testing. Philadelphia: Elsevier Health Sciences; 2016.
[4] Huang L, Guo B, Xu F, et al. Effects of quadriceps functional exercise with isometric contraction in the treatment of knee osteoarthritis. Int J Rheum Dis. 2017; 21:952-959.
[5] Huang PH, Wang CJ, Chou WY, et al. Short-term clinical results of intra-articular PRP injections for early osteoarthritis of the knee. Int J Surg. 2017; 42:117-122.
[6] Martini LI, Via AG, Fossati C, et al. Single platelet-rich plasma ınjection for early stage of osteoarthritis of the knee. Joints. 2017; 5:2-6.
[7] Angoorani H, Mazaherinezhad A, Marjomaki O, et al. Treatment of knee osteoarthritis with platelet-rich plasma in comparison with transcutaneous electrical nerve stimulation plus exercise: a randomized clinical trial. Med J Islam Repub Iran. 2015; 27; 29:223.

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AB1383-HPR **THE VALIDITY AND RELIABILITY OF UNSUPPORTED UPPER LIMB EXERCISE TEST IN INDIVIDUALS WITH RHEUMATOID ARTHRITIS**

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Background: Rheumatoid arthritis (RA) is a systemic, inflammatory disease that causes pain, joint destruction and disability. RA affects the function of the hand and upper extremities; function deteriorates as the disease progresses and affects independence. Unsupported upper-limb exercise (UULEX) test was developed to evaluate upper extremity function and endurance in individuals with Chronic Obstructive Pulmonery Disease. It is suggested that this test can be used in other clinical cases with arm disabilities.
Objectives: The aim of this study was to examine whether the UULEX Test is valid and reliable in individuals with RA.
Methods: 71 individuals with RA (15 male, 56 female) with an average age of 52.15 10.11 were included in the study. The Intraclass Correlation Coefficient (ICC) was used to assess the reliability of the UULEX test. Each individual was assessed by one physiotherapists in two different sessions, a week apart. The correlations of the UULEX test with Disabilities Arm, Shoulder and Hand (DASH), Health Assessment Questionnare (HAQ), 30 sec Push Up Test and 6 Peg Board Ring Test were assessed for concurrent validity.
Results: Intrarater reliability of final level, final weight, duration of the UULEX Test were determined to be excellent (ICC= 0.922, 0.960, 0.958). A moderate to excellent correlation was found between UULEX Test and DASH, HAQ, 30 sec Push Up Test and 6 Peg Board Ring Test ($p<0.05$).
Conclusion: The results of this study showed that the UULEX test is a valid and reliable method in the assessment of upper extremity endurance in individuals with RA.

REFERENCES

[1] - Manning VL, Hurley MV, Scott DL, Coker B, Choy E. Bearne LM. Education, Self-Management, and Upper Extremity Exercise Training in People With Rheumatoid Arthritis: A Randomized Controlled Trial. Arthritis Care & Research 2014; 66, 2: 217227.
[2] - Hammond A, Prior Y, Tyson S. Linguistic validation, validity and reliability of the British English versions of the Disabilities of the Arm, Shoulder and

Hand (DASH) questionnaire and QuickDASH in people with rheumatoid arthritis BMC Musculoskeletal Disorders 2018; 19:118
[3] - Lima VP, Velloso M, Almeida FD, Carmona B, Ribeiro-Samora GA, Ferreira TJ. Testretest reliability of the unsupported upperlimb exercise test (UULEX) and 6-min peg board ring test (6PBRT) in healthy adult individuals.Physiotherapy Theory and Practice 2018; 34, 10:806812
[4] - Takahashi T, Jenkins SC, Strauss GR, Watson CP, Lake FR. A New Unsupported Upper Limb Exercise Test for Patients With Chronic Obstructive Pulmonary Disease. Journal of Cardiopulmonary Rehabilitation 2003;23:430-437.

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AB1384-HPR THE RELATIONSHIP BETWEEN QUALITY OF LIFE, PHYSICAL ACTIVITY LEVEL AND MENSTRUAL PAIN IN TURKISH WOMEN

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Background: Dysmenorrhea, defined as menstrual pain, is one of the common chronic pelvic pain problems associated with mussculoskeletal symptoms. [1] Dysmenorrhea is considered as a lower abdominal or pelvic pain appears just before and/or during menstruation and lasts about 2448 hours.[2] It is a common condition with prevalence rates between 50% and 91% in women. The daily life of women with menstrual pain can be adversely affected by pain and pain accompanying symptoms.[3] It is seen that these effects are mostly on the quality of life (QoL) of individuals. In addition, physical activity of individuals may be restricted due to menstrual pain.[4]
Objectives: The aim of this study was to determine the relationship between quality of life, physical activity level and the severity of menstrual pain in Turkish women.
Methods: 336 female cases aged over 18 years and with menstrual pain complaint in the majority of menstrual cycles were included in the present study. Menstrual pain severity was assessed by 0-10 point Visual Analogue Scale.[5] Physical activity level was assessed by the "International Physical Activity Questionnaire-Short Form" and the score was expressed in Metabolic Equivalent Task minutes per week. Total score of the short form included walking, moderate level activity and duration (minutes) and frequency (days) of sufficiently active. The quality of life of was assessed by the "Nottingham Health Profile". It consists of six parts: pain, physical activity, energy, sleep, social isolation and emotional reaction. The maximum score on any section is 100. The higher the score on any section the greater the number and severity of perceived problems in that area. Normality testing was performed on all data. Spearmans correlation was performed to identify correlation between menstrual pain score and other measures.
Results: The average age and body mass index of 336 participants were 223 years and 21,42,8 kg/m^2, respectively. There was a significant correlation between quality of life and menstrual pain severity (r=0.350; p:0.006). There was no significant correlation between physical activity level and menstrual pain severity (p>0.05).
Conclusion: Based on the results of the present study, quality of life seems to be related with menstrual pain. On the other hand, no relationship was identified between the physical activity level and menstrual pain. In order to determine the exact relationship, further studies with larger samples and with more varied levels of physical activity are needed.

REFERENCES

[1] Kaya, S., Hermans, L., Willems, T., Roussel, N., & Meeus, M. (2013). Central sensitization in urogynecological chronic pelvic pain: a systematic literature review. Pain Physician, 16(4), 291-308.
[2] Orhan, C., elenay, Ş. T., Demirtrk, F., zgl, S., zelpasacı, E., & Akbayrak, T. (2018). Effects of menstrual pain on the academic performance and participation in sports and social activities in Turkish university students with primary dysmenorrhea: A case control study. *Journal of Obstetrics and Gynaecology Research*, 44(11), 2101-2109.
[3] Hillen, T. I., Grbavac, S. L., Johnston, P. J., Straton, J. A., & Keogh, J. M. (1999). Primary dysmenorrhea in young Western Australian women: prevalence, impact, and knowledge of treatment. Journal of adolescent health, 25(1), 40-45.
[4] zgl S, zelpasacı E, Orhan C, Baran E, Beksa MS, Akbayrak T. Short-term effects of connective tissue manipulation in women with primary dysmenorrhea: A randomized controlled trial. Complementary Therapies in Clinical Practice. 2018;33:1-6.
[5] Wong C, Lai K, Tse H. Effects of SP6 acupressure on pain and menstrual distress in young women with dysmenorrhea. Complementary Therapies in Clinical Practice. 2010;16(2):64-9.

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AB1385-HPR TRUNK STRENGTH AND SPINAL MOBILITY IN SPONDYLOARTHRITIS PATIENTS

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Background: Spondyloartritis (SpA) can seriously affect spinal mobility and trunk strength. Even though exercise therapy is considered one of the keystones of non-pharmacological treatment[1], guidelines on exercise programs remain vague due to a lack of objective measurements of physical parameters such as trunk mobility and strength. Data on these parameters are scarce for both axial and peripheral SpA-patients (axSpA and perSpA pts).
Objectives: The aim of this study was to measure trunk strength and spinal mobility in SpA-pts and compare these parameters to healthy subjects matched for gender and age and to determine differences between the pts when grouped based on symptom duration and on presence of radiographic sacroiliitis.
Methods: SpA-pts of the Be-Giant cohort were consecutively asked to participate in the study. After informed consent, BASDAI, BASFI and BASMI were evaluated. To measure trunk and cervical strength, pts performed 2 repetitions of a maximal isometric contraction for flexion, extension, lateral flexion and rotation on the David Back devices (DBD) after measuring the spinal mobility in these directions. The maximum value of the 2 repetitions was kept for further analysis. For assessments of lateral flexion and rotation, measured with the DBD, the mean was calculated for right and left measurements. Spinal mobility and trunk strength were compared with a healthy reference population, matched for gender and age by means of Wilcoxon singed-rank tests. When comparing the perSpA with the r-axSpA and the nr-axSpA, a Kruskal Wallis test was used. A Mann-Whitney U test was used to check for differences between groups based on symptom duration.
Results: Thirty-one SpA-pts participated of which 18 were male (58%). Twenty-four (77%) were classified as axSpA and 7 (23%) as perSpA. Six (19%) of the axial pts had radiographic sacroiliitis and 18 (58%) were non-radiographic. Median time since diagnosis was 5 years and median symptom duration was 7.8 year. Mean age of the pts was 41 years (range: 21 58 years) and their BMI was on average 24 (range: 17-33). Averages for BASDAI, BASFI and BASMI were 2.6 (range 0.0-6.0), 1.7 (range 0-6.8) and 0.9 (range 0.6-4.4) respectively.
SpA-pts showed decreased mobility for cervical flexion (p<0.001), extension (p<0.001) and rotation (p<0.001) and trunk rotation (p=0.001) compared to the healthy population. Cervical and trunk muscle strength was significantly decreased in SpA-pts in all directions compared to the reference population (flexion: p=0.02, other directions: p<0.001).
When comparing mobility and strength based on groups by radiographic axial or peripheral involvement, no significant differences could be detected.
When grouped based on symptom duration, the pts with longer standing symptoms (>7.8 year) show a significant reduced mobility for cervical extension (p=0.004) and rotation (0.049) and lumbar rotation (p=0.033) and a trend toward significance for lumbar extension (p=0.066) compared to those with shorter symptom duration (<7.8 year). For strength no significant differences could be demonstrated between the groups.
Conclusion: Results of this study showed that SpA-pts have less mobility and decreased strength when compared with healthy gender- and age-matched controls.
When comparing within the patient group, based on radiographic involvement, there were no differences neither for mobility or strength. Only discrete differences were found for mobility and no differences for strength when grouped based on symptom duration.
Therefore, rehabilitation of all SpA-pts should focus not only on mobility but should include trunk strengthening exercises as well.

REFERENCES

[1] van der Heijde D. et al. 2016 Ann Rheum Dis 2017;76;978-991

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AB1386-HPR FORCE SENSE EVALUATION OF THE KNEE JOINT FOLLOWING MENISCECTOMY RELATED WITH DEGENERATIVE MENISCAL TEAR

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Background: Meniscal tears are associated with degenerative knee disease, which can range from mild chondral changes not visible on a radiograph to established knee osteoarthritis. Meniscectomy related with degenerative meniscal tear may affect the force sense of the knee joint which is defined as the ability to accurately reproduce a given force.
Objectives: The aim of this study was to compare the force sense of the knee joint of the patients with degenerative meniscal tear following meniscectomy with healthy peers.
Methods: Fifteen patients with meniscectomy and 18 healthy aged matched individuals were included in this study. Evaluation of force sense in the knee joint was measured with the use of a pressure biofeedback device, sphygmomanometer, (*Stabilizer, TM, Chattanooga Group Inc., Chattanooga, TN*). The pressure bag of this device was placed under the knee joint. All subjects were instructed to extend the knee via Maximal Voluntary Isometric Contraction (MVIC) for 5 s. Each measurement was repeated three times with 1-min rest intervals and the average constant errors observed on the pressure biofeedback device were recorded as mmHg. Subjects were instructed to obtain at 50% of MVIC. They were asked to maintain the contraction (reproduce the target force) for 5 s. The reproduction force was subtracted from the target force to create a trial error score. Higher error scores indicated lower force sense. *Mann Whitney U test* was used for group comparisons. Statistical significance was defined as a p value <0.05.
Results: There were no difference in terms of mean age, body mass index between patients (53.67.2 years, 26.21.8 kg/m^2) and healthy peers (53.47.09 years, 25.83.2 kg/m^2), respectively (p>0.05). Lower accuracy of the knee extensors during the 50% MVIC task was significantly seen in patients with meniscectomy (5.422.07 mmHg) compared to healthy group (1.881.1 mmHg) (p<0.001).
Conclusion: Results of this study demonstrated that higher force sense deficits are present in patients with meniscectomy related to degenerative meniscal tear compared to healthy peers. Thus, knee proprioceptive training focus on force sense might be developed to improve functional capabilities of knee joint especially following meniscectomy. It is also important to establish effective and feasible evaluation interventions for health professionals in clinical practice for assessing proprioception in terms of force sense in degenerative knees.

REFERENCES

[1] Sihvonen, R., Paavolah, M,D., Malmivaara, A., Itl, A., Joukainen, A., Nurmi, H., Halske, J., Jrvinen T.L.N. (2013). Arthroscopic Partial Meniscectomy versus Sham Surgery for a Degenerative Meniscal Tear. The new england journal o f medicine, 369:2515-2524.
[2] Jarraya, M., Roemer, F.W., Englund, M., Crema, M.D., Gale, H.I., Hayashi, D., Katz J,N,. Guermazi A. (2017). Meniscus morphology: Does tear type matter? A narrative review with focus on relevance for osteoarthritis research. Seminars in Arthritis and Rheumatism 46:552561.

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AB1387-HPR ASPECTS OF VALIDITY AND RELIABILITY OF THE SWEDISH VERSION OF PATIENT HEALTH QUESTIONNAIRE-8 IN INDIVIDUALS WITH SYSTEMIC SCLEROSIS

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Background: For assessing symptoms of depression in systemic sclerosis (SSc), the Patient Health Questionnaire-8 (PHQ-8) may be useful in clinical care as it is short and easy to administer. The English version of PHQ-8 has been found to be reliable and valid in SSc.
Objectives: To assess aspects of validity and reliability of PHQ-8 in Swedish (PHQ-8 Swe) for individuals with SSc.
Methods: Patients meeting the 2013 ACR/EULAR SSc criteria were recruited. The PHQ-8 Swe content validity was assessed via individual interviews (11 patients, 10 healthcare professionals, HPs) which was transcribed and analysed by content analysis. Patients ages, disease durations and symptoms of depression varied. The HPs had different occupational backgrounds and experiences in SSc care. Reliability was tested by internal consistency and test-retest reliability. Sixty-seven patients (median age 62 [minmax: 2887]) completed the PHQ-8 Swe on two different occasions.
Results: Content validity: The instruction, items, and response options were generally considered easy to understand; however, some clarifications were suggested. Among HPs, it was expressed that some items could be perceived as emotionally demanding for patients especially in recent onset disease. Further they experienced that PHQ-8 was problem- rather than possibility-based. Introducing the PHQ-8 to patients and the need for follow-ups of the answers to the questionnaire were stated as essential. It was further expressed that PHQ-8 covered key aspects of symptoms of depression in SSc nevertheless examples of items suggested to be included were purpose in life, thoughts about death, and loneliness. The items were overall experienced as important without redundancy, and that some items could reflect more general SSc-related symptoms.
Cultural adaption: Possible adjustments to the PHQ-8 translation were made. This version was back translated into English and compared with the original English version. Thereafter, minor changes were made. A final PHQ-8 Swe version was tested for reliability.
Reliability: Cronbachs alpha was 0.86 and the corrected item-to-total correlation range was 0.420.78. There were no significant differences between testretest for seven of the eight items. The median weighted kappa coefficient was 0.63. The median PHQ-8 Swe total score was 4 (020, no-severe depressive symptoms). There were no significant differences for total scores between test and retest and the ICC was 0.81.
Conclusion: Content validity of PHQ-8 Swe was satisfactory and a positive quality was indicated for aspects of reliability in individuals with SSc tested in this study. Although some items could be interpreted as covering more general SSc-related symptoms, the PHQ-8 could be valuable for detecting patients with symptoms of depression in need of discussing emotional issues, as reflected in our study. Further studies of the PHQ-8 Swes usefulness are currently being undertaken via evaluation of other psychometric aspects.

REFERENCES

[1] -Kroenke K, et al. The PHQ-8 as a measure of current depression in the general population. J Affect Disord. 2009; 114:163-73
[2] -Milette K, et al. Comparison of the PHQ-9 and CES-D depression scales in systemic sclerosis: internal consistency reliability, convergent validity and clinical correlates. Rheumatology. 2010; 49:789-96

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AB1388-HPR TREATMENT ADHERENCE AMONG PATIENTS WITH INFLAMMATORY ARTHRITIDES TREATED WITH BDMARDS: AN OBSERVATIONAL STUDY USING I-CQR5 QUESTIONNAIRE AND THE ADMINISTRATIVE CLAIMS DATABASE

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Background: Effective treatments have been introduced for inflammatory arthritides (IAs) in the last decades. However, adherence remains suboptimal.
Objectives: The aim of the study was to assess treatment adherence among patients with IAs treated with bDMARDs in a community hospital with the Italian 5-item Compliance Questionnaire for Rheumatology (I-CQR5) [1] and the hospital administrative claims database.
Methods: We conducted a monocentric, cross-sectional, observational study in IA patients (disease duration >1 year, undergoing treatment with self-administered bDMARDs, capable to complete the questionnaire unaided) recruited in a community hospital from February to October 2018. Treatment adherence was defined according to I-CQR5 and to the Medication Possession Ratio (MPR) obtained from the claims database. To investigate variables associated with adherence, demographic, social, and clinical characteristics were considered. I-CQR5 has 5 questions, with Likert-answering scale ranging from 1 to 4, an algorithm allows to classify the patient as poorly or highly adherent (i.e. likely to take >=80% of their medications correctly) [1]. MPR was obtained by dividing the number of dosage units withdrawn by patients by the prescribed number of dosage units. Agreement between the I-CQR5 and MPR definition of high adherence definitions was tested with McNemars test, while the association with patients characteristics with chi-square or Fishers exact test.
Results: A total 174 patients completed the I-CQR5 (median age 60 years, range 51-67; 37% males), affected by ankylosing spondylitis (16%), rheumatoid arthritis (RA) (62%), psoriatic arthritis (22%) with a median duration of 15 years (range 10-20). Etanercept (49%), adalimumab (20%), abatacept (8%) and tocilizumab (7.5%) were the most prescribed first-line biologics. Association with a conventional synthetic DMARDs was prescribed to 3.4% of subjects. High adherence rate, assessed with I-CQR5, was 83% overall, and 85% in RA patients. Significant differences were observed between highly and poorly adherent patients according to I-CQR5: lower educational status (lower primary or secondary school, and the use of cDMARDs were associated with poor adherence (both with $p<0.001$); while the use of bDMARDs was negatively associated with high adherence ($p<0.05$). High adherence rate measured with MPR was 72%. The agreement between high adherence, measured with I-CQR5 and MPR, was low $p=0.005$).
Conclusion: The study showed that IA patients treated with bDMARDs with a higher educational level are more adherent to physician prescription, as assessed by I-CQR5. I-CQR5 might overestimate adherence compared to MPR. In our study, the high adherence rate measured with I-CQR5 was higher compared with a report from a large outpatient clinic in the same area, which was limited to RA patients (85% vs 40,1%) [1] Our study may suggest that adherence benefits more from a close and stable relationship with the health care practitioner, such as in our centre, which is smaller than large outpatients clinics in which patients are followed by a health care professionals equipe rather than a single physician.

REFERENCES

[1] Ometto F, et al. Ann Rheum Dis 2018;77(Suppl): A1322.

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AB1389-HPR THE ASSOCIATION BETWEEN THE AMOUNT OF DIASTASIS RECTI ABDOMINIS AND THE STRENGTH OF ABDOMINAL MUSCLES IN PREGNANT WOMEN

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Background: Diastasis recti abdominis (DRA) is a common musculoskeletal problem, which is defined as a separation of the inter-recti distance between the two bellies of the rectus abdominis muscle at the linea alba.[1] Due to the hormonal, postural and musculoskeletal changes, and mechanical strain, the anterior abdominal wall becomes stretched and elongated during pregnancy. Studies have shown that DRA may occur between 27% and 100% in the second and third trimesters of pregnancy[2]. Although it has been reported that imbalance in the strength of the abdominal wall muscles altered with the facial tension, the role of abdominal muscle strength on DRA has not been clarified yet.
Objectives: The present study assessed the relation between the severity/amount of DRA and the degree of abdominal muscle (rectus abdominis (RA), external and internal oblique muscles) strength in pregnant women.
Methods: A total of 153 pregnant women between 14 and 35 weeks of a singleton pregnancy were included in the present study. The finger width method was used to measure the amount of DRA. The amount of separation was determined by the palpation of the medial sides of RA at three reference points: on the umbilicus, 4.5 cm above and 4.5 cm below of the umbilicus. After the subject contracts RA in hook lying position when her arms were in extended position, the size of the diastasis was measured by the number of finger.[3] The strength of abdominal muscles was assessed by the manual muscle test in supine hook lying position. The correlation between the amount of DRA and the degree of abdominal muscle strength was analyzed by the Spearmans correlation.
Results: The mean age was 28.40±3.69 years, mean Body Mass Index was 27.01±1.26 kg/m^2, and mean gestational age was 28.12±5.03 weeks. A negative correlation was found between the amount of the diastasis at 4.5 cm below of the umbilicus and the strength of the RA ($r=0.219$, $p=0.007$), right ($r=0.296$, $p=0.015$) and left external oblique muscles ($r=0.293$, $p=0.017$).
Conclusion: Based on the findings of the present study, the separation of RA on the lower level of umbilicus may be negatively associated with the strength of RA and oblique abdominal muscles. Therefore, to decrease the severity of DRA, abdominal strengthening programs should be provided to pregnant women.

REFERENCES

[1] Van de Water, A. T. M., & Benjamin, D. R. (2016). Measurement methods to assess diastasis of the rectus abdominis muscle (DRAM): a systematic review of their measurement properties and meta-analytic reliability generalisation. Manual therapy, 21, 41-53.
[2] B, K., Hilde, G., Tennfjord, M. K., Sperstad, J. B., & Engh, M. E. (2017). Pelvic floor muscle function, pelvic floor dysfunction and diastasis recti abdominis: prospective cohort study. Neurourology and urodynamics, 36 (3), 716-721.
[3] Michalska, A., Rokita, W., Wolder, D., Pogorzelska, J., & Kaczmarczyk, K. (2018). Diastasis recti abdominisa review of treatment methods. Ginekologia polska, 89(2), 97-101.

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HPR Patients perspectives, functioning and health (descriptive: qualitative or quantitative)

AB1391-HPR PASSIVE COPING STRATEGIES BUT NOT PHYSICAL FUNCTION ARE ASSOCIATED WITH WORSE MENTAL HEALTH, IN WOMEN WITH CHRONIC WIDESPREAD PAIN– A MIXED METHOD STUDY

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Background: Chronic widespread pain (CWP) is a common condition (approximately 10% prevalence), that affects women twice as often as men. There is a lack of knowledge in how different coping strategies relates to health status during CWP development in a general population.
Objectives: To explore different ways of coping with CWP and to relate the different coping strategies to health-related factors, before and after developing CWP.
Methods: A sequential explorative mixed methods study including 19 women 45-67 of age, who had reported CWP in a survey 2016, but not in 1995. Individual interviews were analysed with a phenomenographic approach, and resulted in four categories of coping strategies. These categories were further explored with regard to four dimensions of health status (physical function, bodily pain, vitality and mental health) as measured by SF-36 (0-100, a lower score indicates more disability) and sleep problems measured both in 1995, and 2016.
Results: The qualitative analysis revealed four categories representing different coping strategies, where each woman was labelled by the most dominant category; the mastering woman, the persistent woman, the compliant woman and the conquered woman. The first two categories emerged as being active coping strategies, and the latter two as passive. Women with passive strategies reported significantly lower vitality (median 57.5 vs 75, p=0.007) and worse mental health (median 54 vs 93, p=0.021) in 1995, before they had developed CWP compared with those with active coping strategies. No differences were seen between the groups on physical function, bodily pain or sleep.
In 2016, there were still a difference between the passive and active group regarding mental health (median 56 vs 80, p=0.022), but not for vitality (median 35 vs 40, p=0.707). No differences were seen between the groups on physical function or bodily pain. All eight women with passive strategies reported problems with sleep in 2016, as compared to 6 of the 11 women with active strategies (p=0.045).
Conclusion: Women that reported CWP in 2016, but not in 1995, described both active and passive coping strategies. The qualitative findings were associated with differences in vitality and mental health already in 1995, before they had developed CWP. Further, those with passive coping strategies reported worse health with regard to mental health and sleep problems in 2016. Interestingly, the groups did not differ in bodily pain or physical function neither in 1995 nor in 2016, which implicates the importance for the clinician to take the typical coping strategy into consideration, when meeting these patients in clinical settings.
Disclosure of Interests: None declared
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AB1392-HPR GO-BEYOND: A REAL-WORLD PERSISTENCE STUDY WITH GOLIMUMAB IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND RHEUMATOID ARTHRITIS IN TURKEY

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Background: Axial spondyloarthritis (ax-SpA) and rheumatoid arthritis (RA) are chronic inflammatory diseases and associated with substantial health and economic burden since these conditions affect individuals in their productive years[1,2]. Adherence to treatment is a major problem for inflammatory rheumatic diseases[3].
Objectives: In the present study, we aimed to evaluate rates of persistence with golimumab (GLM) therapy in ax-SpA and RA patients using real-world data.
Methods: This multicenter, non-interventional, retrospective study enrolled 329 patients diagnosed with ax-SpA (n=269) and RA (n=60) who currently receive or have received golimumab therapy for at least 3 months either as first-line treatment (biologic nave group) or as second-line treatment after failure to another anti-TNF or biologic agent (biologic-experienced group). In addition to the patients demographic and clinical characteristics, data on drug continuation and disease activity scores such as ASDAS/BASDAI and DAS-28 scores were retrieved from the patient records. A regression analysis was conducted to determine the factors associated with drug discontinuation including age, gender, smoking status, disease duration, presence of comorbidities, disease activity measures, concomitant csDMARD use.
Results: Only 28 (10.4%) axSpA and 7 (11.6%) RA patients were biologic-experienced. The changes in disease activity scores of RA and axSpA patients on therapy during 2-years of follow-up are presented in figure a and b.
Golimumab therapy provided good and long-term improvement in the disease activity scores in both RA and ax-SpA patients. At 6, 12 and 24 months treatment persistence rates were 86.4%, 74.5% and 65.5% for RA and 93.5%, 81.9% and 75.5% for axSpA patients, respectively. Persistence with GLM was similar between biologic-nave and -experienced patients. GLM persistence was also similar in RA and axSpA groups (figure c). Regression analysis revealed that smoking (HR 0.523; p= 0.006), presence of comorbidity (HR 2.731, p<0.001) and disease duration (HR 0.957, p=0.036) were significant predictors of drug persistence in GLM treated patients.
Conclusion: Our results show that GLM therapy is an effective treatment option with high drug retention rates in both RA and ax-SpA patients independent of previous biologic exposure. Smoking, co-morbidities and disease duration may affect the continuation of golimumab treatment in inflammatory rheumatic diseases.

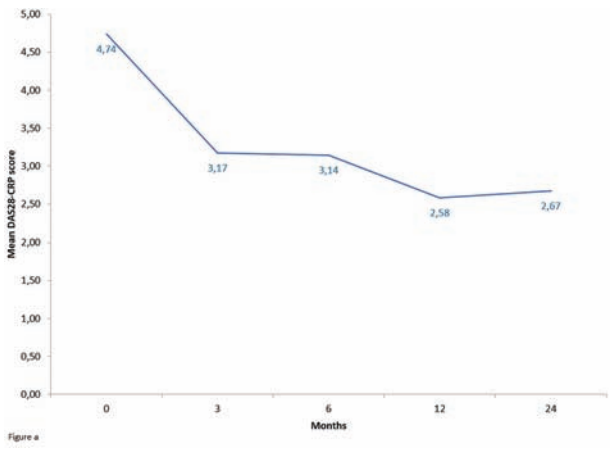


Figure a

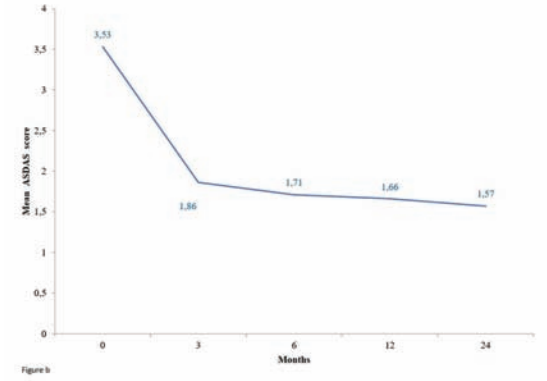


Figure b

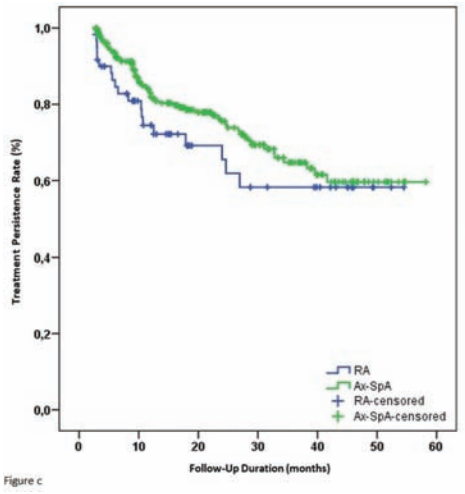


Figure c

REFERENCES

[1] Strand V, Singh JA. Patient Burden of Axial Spondyloarthritis. J Clin Rheumatol. 2017 Oct;23(7):383-391.

[2] Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. Lancet. 2010 Sep 25;376(9746):1094-108.

[3] Anghel LA, Farcaş AM, Oprean RN. Medication adherence and persistence in patients with autoimmune rheumatic diseases: a narrative review. Patient Prefer Adherence. 2018 Jul 3;12:1151-116

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AB1393-HPR COMPARISON OF THE QUALITY OF LIFE, FUNCTIONAL AND EMOTIONAL STATUS OF INPATIENTS AND OUTPATIENTS WITH RHEUMATIC DISEASES

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Background: Quality of life, function and emotional status of inpatients with rheumatic diseases may be estimated worse than outpatients. Previous studies had shown that there was a worsening in the emotional state of inpatients (1).

Objectives: The aim of this study is to compare the quality of life, functional and emotional status in inpatients and outpatients with rheumatic diseases.

Methods: The study included 78 patients (inpatient, n = 31; outpatient, n = 47) with rheumatic disease. The Health Assessment Questionnaire (HAQ) (2) and SF-36 (3) were used to evaluate the functionality and quality of life, and the Hospital Anxiety and Depression Scale (HADS) (4) was used to determine their emotional status. The variables were investigated using visual and analytical methods to determine whether or not they are normally disturbed. Since physical function, mental health and general health perception values of SF-36 and HADS-Anxiety were normally distributed, the Students T-test was used to compare these parameters between two groups. Physical role limitation, pain, social status, emotional difficulty, energy viability of SF-36, HAQ and HADS-Depression were not normally distributed. Thus, Mann-Whitney U test was used to compare these scores between two groups.

Results: The mean age of the subjects (n = 78) included in the study was 46.09 13.89 years and the mean BMI was 27.59 15.08. There was a significant difference in depression, anxiety and pain and social functioning sub-parameters of SF-36 (p <0.005) but there was no significant difference in other parameters (p> 0.005).

Abstract AB1393HPR Table 1. Comparison of the scores of inpatients and outpatients

	INPATIENTS (XSD)	OUTPATIENTS (XSD)	p
HAQ	0,930,82	0,890,68	0,152
HADS-Anxiety	9,873,8	8,215	0,022
HADS-Depression	9,935,02	7,474,34	0,006
SF-36 Physical Function	47,9428,42	48,3623,81	0,669
SF-36 Physical Role Limitation	27,533,7	27,6336,2	0,869
SF-36 Pain	33,6632,28	54,0721,42	0,011
SF-36 Social Status	39,5828,63	55,0627,09	0,032
SF-36 Mental Health	6121,8	62,7316,08	0,761
SF-36 Emotional Difficulty	31,1038,08	33,3243,83	0,717
SF-36 Energy Vitality	30,8320,63	43,2820,86	0,317
SF-36 General Health Perception	36,1621,68	47,4716,15	0,393

Conclusion: It was thought that during the period of admission to the hospital, inpatients should be supported in terms of pain management, social functioning and anxiety and, depression as well as taking medication. Besides, caregivers in hospitals should encourage inpatients with regard to maintaining physical activity.

REFERENCES

[1] Lambert, C. M., Hurst, N. P., Forbes, J. F., Lochhead, A., Macleod, M., & Nuki, G. (1998). Is day care equivalent to inpatient care for active rheumatoid arthritis? Randomised controlled clinical and economic evaluation. Bmj, 316(7136), 965-969.

[2] Fries JF, Spitz PW, Young DY: The dimensions of health outcomes: the Health Assessment Questionnaire, Disability and Pain Scales. J Rheumatol 9:789-793, 1982

[3] Brazier, J. E., Harper, R., Jones, N. M., O'cathain, A., Thomas, K. J., Usherwood, T., & Westlake, L. (1992). Validating the SF-36 health survey questionnaire: new outcome measure for primary care. Bmj, 305(6846), 160-164.

[4] Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. Acta psychiatrica scandinavica, 67(6), 361-370.

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AB1394-HPR CAN SUPPORT FROM SIGNIFICANT OTHERS RECUDE SICKNESS ABSENCE IN EARLY RHEUMATOID ARTHRITIS?

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Background: Persons with rheumatoid arthritis (RA) are at higher risk of sickness absence, and the probability of returning to work is lower compared to the general population [1]. In order for persons with RA to continue working, support from the social environment is claimed to be of importance [2]. However, this relation needs to be further investigated.

Objectives: To analyze how support from significant others affects the associations between disease related variables (medication, disease activity and activity limitations) at time for RA diagnosis and sickness absence one year after diagnosis.

Methods: Data were collected from 326 (71% women) patients in working age (18-63 years) included in the Swedish early RA cohort TIRA-2 [3] during 2006-2009. At time of inclusion, mean age was 50 years (SD=11), 89% were prescribed disease modifying anti-rheumatic drugs (DMARDs), mean disease activity score 28 joint count (DAS28) was 4.73 (SD=1.34), and mean score for activity limitation reported by Health Assessment Questionnaire (HAQ) was 0.91 (SD=0.60). The number of days with sickness absence during the first year after diagnosis and inclusion was retrieved from the Swedish Social Insurance Agency. Perceived support from significant others, family and friends separately, were self-reported

by VAS scales, zero indicating no support and 100 indicating full support. The associations of disease activity, activity limitation and DMARD use with sickness absence and how these associations were moderated by support from significant others, were analyzed using zero-inflated negative binomial regression.

Results: Higher activity limitation (HAQ) was associated with lower risk of sickness absence (p<.001) but more days with sickness absence (p=.001). Higher disease activity (DAS28) was associated with lower risk of sickness absence (p=.003). However, when including family support, this association was not significant (p=.117) and associated with higher risk of sickness absence, but the association was weaker with family support (p=.029). Disease activity was also associated with more days of sickness absence (p=.013). The use of DMARDs had no significant relation to sickness absence (p=.150) or number of days with sickness absence (p=.852). Although, when including support from friends, DMARD use was associated with higher risk of sickness absence (p=.041). However, this association decreased significantly with support from friends (p=.022).

Conclusion: Support from significant others has an impact on previously known relationships between disease activity, use of DMARDs and sickness absence. Hence, support from significant others has the possibility to help decrease sickness absence among persons with RA one year after diagnosis.

REFERENCES

[1] Hansen, SM., Hetland, ML., Pedersen, J., et al. Work ability in rheumatoid arthritis patients: a register study on the prospective risk of exclusion and probability of returning to work. Rheumatology. 2017;56(7):1135-1143.

[2] Feddersen, H., Kristiansen, TM., Andersen, PT., et al. Construction of meaningful identities in the context of rheumatoid arthritis, motherhood and paid work: a meta-ethnography. Journal of Clinical Nursing. 2017;26(23-24):4117-4128.

[3] Thyberg, I., Dahlstrm,., Bjrk, M., et al. Hand pains in women and men in early rheumatoid arthritis, a one year follow-up after diagnosis. The Swedish TIRA project. Disability and Rehabilitation. 2017;39(3):291-300.

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AB1395-HPR BURDEN IN CAREGIVERS OF PATIENTS WITH RHEUMATIC CONDITIONS

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Background: Rheumatoid arthritis (RA) is a chronic, disease that affects more than 1% of global population, it is a long term condition that causes pain and disability. Evidence had shown that most of the patients are moderately disabled, which brings the necessity of a caregiver to become the patients companion due to its chronic disease. The caregiving role can have an impact in the psychological and physical spheres of the caregivers life.

Objectives: The aim of this study was to explore demographical characteristics and caregiver burden through the Zarit Scale.

Methods: We conducted a cross sectional study in a meeting where caregivers in a rheumatoid arthritis specialized setting. We collected sociodemographic information, and applied the Zarit caregiver burden interview (ZBI) adapted to Spanish. The ZBI includes 22 questions which has 5 responses from 0 (never) to 4 (nearly always), where scores lower than 47 indicated little to no burden, 47 to 55 low burden and >55 intense burden. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates.

Results: We applied a survey to 132 caregivers. Mean age was 52 years SD 19 and 72% were women, 78% of them were taking care of a patient with rheumatoid arthritis, 12% osteoarthrosis 2% lupus, 2% osteoporosis the remaining 6% were caregivers of patients with ankylosing spondylitis, fibromyalgia, Sjogren syndrome. Regarding the time as caregiver 48% of them had been carrying the task for less than a year, 16% between two and three years, 18% for more than three years, and 13% for more than four years 5% of them were temporarily caregivers. In our study 85% of caregivers were a family member while15% was a nurse or a non-related person. Zarit mean score was 38.2913, additionally 35% had a score higher than 41 points. See table 1.

Variable	n	%
Zarit Score		
0-21 (little or no burden)	9	6.34
22 - 40 mild to moderate burden	82	57.75
41 - 60 moderate to severe burden	43	30.28
61-88 severe burden	8	5.63

Abstract AB1395HPR Table 1. Zarit scale classification

Conclusion: In our study 93% of our patients reported to have moderate to severe burden; thus, it is important to develop strategies and explore the factors related to burden in caregivers in patient with rheumatoid arthritis.

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AB1396-HPR SEXUAL SATISFACTION AND SEXUAL DYSFUNCTION IN PARTNER OF PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Sexual satisfaction is defined as a special experience with biological rules, value judgments and taboos and also is an important indicator of sexual satisfaction, social harmony and physical-mental well being. Sexual dysfunction or reluctance may be psychological, physiological or combination of both. Current studies showed that most of Ankylosing Spondylitis (AS) patients had sexual problems. They have not also severe joint deformities but also have painful intercourse. Therefore decrease in the range of motion of the hip joint due to AS complicates pelvic pain and sexual dysfunction.

Objectives: The aim of study was investigation of sexual satisfaction and sexual dysfunction in partner of patients with AS.

Methods: 50 individuals: 21 female partner of patients with AS with an average age of 40.38 5.31, 29 male patner of patients with AS with an average age of 52.37 5.84 were included in this study. The male partners were evaluated with the International Index of Erectile Function (IIEF) and the female partners were evaluated with the Female Sexual Function Index (FSFI).

Results: Total score of FSFI was 52.37 5.84 (Sexual desire:5.472.01, arousal:11.664.97, orgasm: 8.524.74, lubrication:12.005.06, satisfaction: 8.474.49, pain:8.044.17) in female partner. Erectile score of IIEF was 24.35 6.65, orgasm score was 8.85 3.28, sexual desire score was 7.271.70, sexual satisfaction score was 10.373.86 and general satisfaction score was 8.142.83 in male partner.

Conclusion: According to the results of the study, female partner had moderate sexual dysfunction, male partner had mild erectil function. This study showed that the sexual functions of female and male partners of patients with AS were affected negatively. Further studies need to assess their pelvic floor symptoms as well.

REFERENCES

[1] -Aguiar R, Ambrsio C, Cunha I, Barcelos A. Sexuality in spondyloarthritis the impact of the disease Acta Reumatol Port. 2014:39;152-157

[2] -Bal S, Bal K, Turan Y, Deniz G, Grgan A, Berkit IK, Sendur OF. Sexual functions in ankylosing spondylitis. Rheumatol Int 2011; 31:889-894.

[3] -Healey EL, Haywood KL, Jordan KP, Garratt AM, Ryan S, Packham JC. Ankylosing spondylitis and its impact on sexual relationships. Rheumatol 2009; 48(11):1378-1381. 12.

[4] -Demir SE, Rezvani A, Ok S. Assessment of sexual functions in female patients with ankylosing spondylitis compared with healthy controls. Rheumatol Int 2012; 33(1): 57-63. 13. 5-Ozkorumak E, Karkucak M, Civil F, Tiryaki A, Ozden G. Sexual function in male patients with ankylosing spondylitis. Int J Impot Res 2011; 23(6):262-267.

[6] -Basson R, Berman J, Burnett A, Derogatis L, Ferguson D, Fourcroy J, Goldstein I, Graziottin A, Heiman J, Laan E, Leiblum S, Padma-Nathan H, Rosen R, Segraves RT, Shabsigh R, Spski M, Wagner G, Whipple B. Report of the international consensus development conference on female sexual dysfunction:Definitions and classifications. J Sex Marital Ther. 2001; 27:83- 94.

[7] -Cayan S, Akbay E, Bozlu M, Canpolat B, Acar D, Ulusoy E. The prevalence of female sexual dysfunction and potential risk factors that may impair sexual function in Turkish woman. Urol Int 2004; 72(1): 52- 57.

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AB1397-HPR CLINICAL FEATURES IN COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN KAZAKHSTAN

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Background: Systemic lupus erythematosus (SLE) refers to socially significant diseases and the improvement of diagnosis, treatment of the disease belongs to the target indicators of the State Program in Kazakhstan.

Objectives: The aim of this study was to assess the demographic, clinical features, the degree of activity, damage to internal organs and therapy in patients with SLE.

Methods: The study involved 89 patients with a documented diagnosis of SLE (ACR, 1997) hospitalized for inpatient treatment in rheumatology centers. The register included an assessment of gender, age, Disease Activity Index (SLEDAI 2K), organ Damage Index (DI, SLICC, 2012), and therapy. For qualitative signs, absolute and relative values (n,%) are presented.

Results: In the studied cohort of patients with SLE prevailed women (98.8%), the mean age of patients was 33.610.47 years, 47% of them under 30 years old. The debut of the disease in the overwhelming majority (52%) patients is associated with stress, pregnancy and childbirth. By ethnicity: Kazakhs - 67 (75.2%), Russian - 7 (7.8%), Uighurs - 6 (6.7%), Korean - 5 (5.6%), other 5 (5.6%). 56% of patients had higher and secondary-special education. Only in a third of patients SLE was diagnosed in the first months of the disease, the rest had erroneous diagnoses, such as rheumatoid arthritis, reactive arthritis, and other systemic diseases. The disease activity (SLEDAI 2K) was very high in 9 (10.1%), high in 24 (26.9%), medium in 39 (43.9%), low in 15 (16.8%) patients and without activity were 2 (2.2%) patients.

Among SLE patients, 92% with mucocutaneous manifestations, 64% had photosensitivity, 56.2% had enanthema, 77.5% had arthritis and arthralgia, 28.1% with serositis, 55% had renal involvement, 25.8% had neurological and 58.4% had hematological disorders. Irreversible organ damages (SLICC) were detected in 67.4% of patients: low DI (1 point) - 26 (29.2%), moderate (2-4 points) - 33 (37.1%) and high (> 4 points) - in 3 (3.4%) patients. Medium and high DI were observed in patients with renal and neurological involvement.

Patients were predominantly in therapy: methylprednisolone (98%), cytostatics and mycophenolate mofetil (42.3%), hydroxychloroquine (39%). Biological therapy (rituximab, belimumab) was performed in patients with a high degree of activity, nephritis, and neurolupus and in 6 (6.7%) patients with good effect and the possibility of reducing glucocorticoids to minimal doses.

Conclusion: Creating a register and forming a cohort allows for a more complete assessment of activity, organ damage and therapy in patients with SLE.

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AB1398-HPR RHEUMATOID ARTHRITIS– BIOLOGICAL DMARDS EXPERIENCE IN TAWAM HOSPITAL, UAE. A 2-YEAR RETROSPECTIVE STUDY

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Background: Arthritis is the leading cause of disability in America, affecting 50 million adults. Although there is currently no cure for rheumatoid arthritis (RA), improved understanding of RA disease pathogenesis in recent years has led to the development of new treatments. Disease Modifying Anti-Rheumatic drugs (DMARDs) are added at early stages in the treatment of RA to suppress inflammation; they may be used as monotherapy or more commonly in combination. The treatment of RA, psoriatic arthritis (PSA) and ankylosing spondylitis (AS) is aimed at achieving the lowest disease activity and remission. Patient compliance is considered necessary for the success of treatment in chronic diseases.

Objectives: The objective of this study was to assess the patient adherence to their medications and clinic visits in addition to assessing the prescribing, screening and monitoring parameters of biological disease DMARDs according to the care pathway at Tawam Hospital and EULAR recommendations.

Methods: A retrospective observational review using data from the computer based system at Tawam hospital. All adult patients with RA, PSA and AS starting a biological DMARD during our study period; December 2016 to December 2018 were eligible.

Results: A total of 54 patients were included. Eighty percent were females. Sixty three percent RA patients, 24% PSA patients and 13% AS patients. Indication, dosing and blood monitoring criteria were met for 100% of the patients. Vaccination criteria was met in only 20%. Screening criteria was met by 57%. Ninety two percent of the RA and PSA patients were started on methotrexate for 3 months before biologics initiation as per guidelines. Forty three percent of AS patients used 2 non-steroidal anti-inflammatory drug before starting biological therapy.

Medication adherence was measure by; the duration of therapy, consistent clinic visits and regular medication refills. Eighty four percent of the total number of patients had a duration of therapy for 6 months or more. Twenty six percent were consistent with their monthly clinic visits. Sixty one percent were compliant with their monthly medication refills.

RA patients were further analysed as they made the majority of our patients. Ninety seven percent of the RA patients had a baseline DAS documented. Eighteen percent had a baseline of DAS28<2.6. Fifty percent had a baseline DAS28>3.2. Twenty nine percent had a baseline DAS28>5.1.Three percent of the patients started on a biologic with no baselines DAS. One hundred percent of the patients were started a biological DMARD including the 18% that had DAS28≤2.6; however the reasons were clearly stated (example of reasons, contemplating pregnancy, adverse reaction to previous treatment).

The DAS 28 was documented again at the end of the study period. Fifty nine percent of the patients had DAS28<2.6. Twenty six percent had DAS between 2.6-3.2, twelve percent had DAS28>3.2 and three percent of the patients had a DAS28>5.1. All the patients with DAS28>3.2 (15%) changed their treatment regimen.

Conclusion: This audit concluded 100% compliance with the care pathway at Tawam Hospital and EULAR recommendations in the treatment of RA, PSA and AS with regards to starting a biologic treatment, switching treatment, dosing and monitoring. Overall the patients adherence to their clinic visits and medication refills was satisfactory; however improving adherence to therapy could therefore dramatically improve the efficacy of drug therapy. However there was a gap in the vaccination and screening parameter which indicates a need to add a tool in computer system to aid the physicians in fulfilling this gap.

REFERENCES

[1] Mara Marengo, Mara Almazor. Improving treatment adherence in patients with rheumatoid arthritis:what are the options? Int J Clin Rheumtol. 2015

[2] American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care & Research 2015

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AB1399-HPR FOOT AND ANKLE ASSESSMENT IN PATIENTS WITH DIFFERENT GRADES OF KNEE OSTEOARTHRITIS

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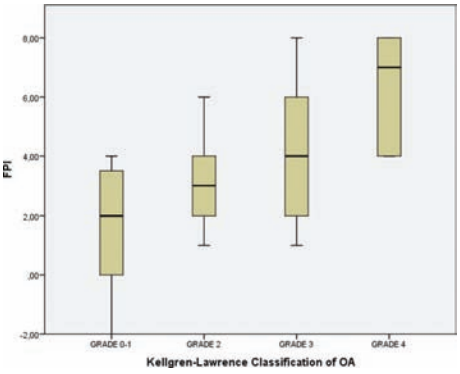
Background: Foot and ankle profile has long been considered to contribute to the development of knee osteoarthritis (OA). It may alter the mechanical alignment and dynamic function of the lower limb especially knee functions. It is important to determined compensatory changes in the foot and ankle posture in patients with different grades of knee osteoarthritis. Because it may help in understanding the role of foot orthoses, footwear modifications or treatment strategies on alignment and function of knee
Objectives: This present study was designed to assess the changes in foot and ankle profile among different grades of knee OA.
Methods: Patients were assessed with physical examination including foot and knee specifically and anteroposterior and lateral direct radiographies. All patients were divided into four groups for medial compartment OA severity by using the Kellgren-Lawrence grading system of knee OA on weight bearing knee radiographies. The Western Ontario and Mc Master University Osteoarthritis Index (WOMAC) questionnaire was performed to assess pain and the functional status of the patients. Structural foot profile was assessed by the Foot Posture Index (FPI) system and American Orthopaedic Foot and Ankle Society (AOFAS) anklehindfoot and midfoot scales.
Results: The study included forty-four patients with mean age 57.1212.2 years. In terms of severity of knee OA groups; percentages for grade 0-1,2,3 and 4 were 25%,22.7%,25%,27.2% respectively. In the grade 4 and 3 with knee OA; WOMAC total score, pain and function subscale scores were higher ($p < 0.001$). Besides, foot pronation was also increased as the severity of osteoarthritis increased. In the grade 0-1 and grade 2; AOFAS hindfoot and midfoot scores were higher ($p<0.001$) compere to severe OA (grade 3 and grade 4).
Conclusion: The study indicates that differences of the severity of OA have influence on the foot and ankle profile to different degrees. Therefore, it is clinically important to give appropriate orthotics advice or treatment to patients with different degrees of OA to correct the pronation of foot to different degrees.

REFERENCES

[1] Saito, I., Okada, K., Wakasa, M., Abe, H., & Saito, A. (2018). Foot pressure pattern, hindfoot deformities, and their associations with foot pain in individuals with advanced medial knee osteoarthritis. Gait & posture, 59, 83-88.

	K-L Scores				p value
Paremeter	0-1 (n: 11)	2 (n:10)	**3 (n: 11)**	**4 (n:12)**	
Age, years *	56.97.6	52.37.7	62.6 8.2	58.28.5	0.37
Female, n(%)	6(54.5)	6(60)	6(54.5)	7(58.3)	0.16
Height, (cm)*	164.70.7	165.40.11	162.20.08	163.4 1.1	0.25
Body weight (kg)*	80.310.3	82.216.9	70.711.1	78.9 15.1	0.14
Body mass index (kg/m^2)*	29.5 2.8	29.94.1	31.262	29.44.7	0.37
WOMAC **	12(7-15)	14(12.5-21))	31(14-40)	33(28-45)	0.001^{δ}
AOFAS-hindfoot**	80(74-88)	85(69-91.25)	55(48-74)	59.5(55-66)	0.001^{δ}
AOFAS-midfoot **	88(72-91)	85(79-87.75)	57(52-79)	59(54-66.5)	0.03^{δ}

*; Values are reported as mean SD
**;Values are reported as median(IQR)
$^{\delta}$; Significant at p<0.05



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AB1400-HPR EFFECT OF FOOT PAIN ON FUNCTION, FEAR OF FALLING AND QUALITY OF LIFE IN ELDERLY PEOPLE WITH KNEE OSTEOARTHRITIS

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Background: Knee osteoarthritis (OA) is a frequently seen disorder affecting approximately 30% of people over 65 years. Foot pain often defined as pain in the foot and/or ankle, is also very common among older people. This problem may effect on mobility, falling risk and quality of life in elderly patient with knee OA. But there is no study investigate to effect of foot pain on the function, fear of falling and quality of life in elderly people with knee OA.
Objectives: Concurrent foot pain in elderly people with knee OA may be the potential to further increase disability and immobility.
Methods: Fifty patients with radiographic and clinic evidence of tibiofemoral OA (Kellgren-Lawrence score 2) were included. The Western Ontario and Mc Master University Osteoarthritis Index (WOMAC) questionnaire was used to assess pain and the functional status of the all patients. Foot pain was measured with the Manchester-Oxford Foot Questionnaire (MOFQ) and 100 mm Visual Analog scale (VAS). Patients were divided into two groups (with foot pain and without foot pain) based on patient-reported pain using VAS and MOFQ. Two groups with knee OA were compared for difference in patient functional assessment quality of life and fear of falling. To evaluate physical function measured by using the Time up Go Test (TUG), health related quality of life (HRQOL) measured by using EuroQOL five dimensions (EQ-5D) questionnaire and fear of falling measured by using Tinetti Falls Efficacy Scale.
Results: Within our sample of older adults with knee OA, 52% had foot pain (26/50). VAS scores of patients with knee OA and without foot pain were zero. Compared to the group without foot pain of similar age (n = 24), those with foot pain had reduced quality of life and profound mobility limitations and more fear of falling (p< 0.001).
Conclusion: Older adults with knee OA and also foot pain have pronounced mobility limitations and increased fear of falling and also these are associated with a marked reduction in HRQOL. Future prospective research is required to build on this study.

REFERENCES

[1] Stubbs, B., Binnekade, T., Eggermont, L., Sepehry, A. A., Patchay, S., & Schofield, P. (2014). Pain and the risk for falls in community-dwelling older adults: systematic review and meta-analysis. Archives of physical medicine and rehabilitation, 95(1), 175-187
[2] Chen, J., Devine, A., Dick, I. M., Dhaliwal, S. S., & Prince, R. L. (2003). Prevalence of lower extremity pain and its association with functionality and quality of life in elderly women in Australia. The Journal of Rheumatology, 30(12), 2689-2693.

Variable	**1.Group with Foot Pain (n=26)**	**2.Group without Foot Pain (n=24)**	***p* value**
Age (years, SD)	74.4 (8.5)	76.3(7.8)	0.19
Female n(%)	16 (61.5)	16 (66.6)	0.24
Body Mass Index (kg/m^2,SD)	29.5(6.8)	29.9(7.1)	0.35
Number of comorbidities (SD)	3.8 (2.3)	3.1(1.2)	0.07
MOFQ (SD)	54.2(12.4)	4(1.2)	0.001*
Time Up Go Score (sec, SD)	32.84(19.3)	19.8(6.03)	0.001*
HRQOL (SD)	69.5(19.5)	43.2(13.7)	0.001*
Fear of Falling (SD)	76.1(17.8)	40.2(14.9)	0.040*

MOFQ; Manchester-Oxford Foot Questionnaire
HRQOL; Health Related Quality of Life
SD; Standard Deviation;
*Significant at p<0.05

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AB1401-HPR SELF-REPORTED PHYSICAL FUNCTION AND ASSOCIATED FACTORS IN INDIVIDUALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Physical activity and exercise have many positive effects in patients with Systemic Lupus Erythematosus (SLE) (1) and poor self-reported physical function has been reported to predict mortality (2). To facilitate and improve physical activity/function, it is thus important to investigate what factors are associated with good physical function. Few previous studies have addressed these issues (3).
Objectives: The aim of this study was to identify factors associated with good self-reported physical function, such as walking and running in individuals with SLE.
Methods: A total of 198 patients (mean age: 51.516.1 years; BMI: 24.74.7 kg/m^2) with SLE participated. The outcome, self-reported physical function was assessed with the question: How much do you think you can manage concerning walk, jog, and run? (From Physical Activity Questionnaire, PAQ). Disease activity was assessed using the SLAM-R and organ damage with SLICC/ACR-DI. The VAS part of EQ-5D, was used to assess self-reported health related quality of life (HRQL). Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety/depression levels. Self-reported exercise during the last year was assessed by questions from PAQ and sitting hours as well as physical activity level was determined from International Physical Activity Questionnaire Short Form (IPAQ-SF). Logistic regression analyses estimated the associations of the following independent variables: age, sex, BMI, disease activity, organ damage, HRQL and anxiety/depression levels, exercise last year, sitting hours and physical activity level, on the dependent variable self-reported physical function (PAQ-question). Statistical significance was defined as a p value <0.05.
Results: Median SLAM-R was 6 (IQR:6), SLICC-DI was 1 (IQR:3), EQ-5D VAS was 72.2 (IQR:22.1) and depression level 4 (IQR:5). Median Self-reported exercise during the last year (PAQ) was exercise irregularly. Median sitting hours a day (IPAQ-SF) was <5 hours. Median physical activity level was moderate (IPAQ-SF). Age (p<0.001; Odds ratio:6.40), SLICC-DI (p=0.002; Odds ratio:4.02) and EQ-5D VAS (p<0.001; Odds ratio:4.20) were significantly associated with better self-reported physical function (Nagelkerke R Square=0.437).
Conclusion: The results demonstrated that SLE-patients who report low physical function are older patients with more organ damage. However, patients who reported low HRQL also reported low physical function. Our results imply that patients with low self-reported HRQL are at risk for not being enough physically active. To break this vicious circle is a challenge for physicians and physical therapists that care for patients with SLE.

REFERENCES

[1] O'Dwyer T, Durcan L, Wilson F. Exercise and physical activity in systemic lupus erythematosus: A systematic review with meta-analyses. Semin Arthritis Rheum. 2017;47:204-215.
[2] Azizoddin DR, Jolly M, Arora S, Yelin E, Katz P. Patient Reported Outcomes Predict Mortality in Lupus. Arthritis Care Res (Hoboken). 2018 Aug 24. doi: 10.1002/acr.23734.
[3] Elera-Fitzcarrald C, Fuentes A, Gonzlez LA, Burgos PI, Alarcn GS, Ugarte-Gil MF. Factors affecting quality of life in patients with systemic lupus erythematosus: important considerations and potential interventions. Expert Rev Clin Immunol. 2018;14:915-931.

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AB1402-HPR CHILDRENS COMFORT COUNTS – CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITISEXPERIENCE OF USING ENTONOX AS AN ANALGESIC AGENT FOR INTRA-ARTICULAR JOINT INJECTIONS

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Background: Intra-articular corticosteroid injections (IACI) are frequently used in the medical management for children with juvenile idiopathic arthritis (JIA) as they allow treatment to be administered directly into a specific inflamed joint which may negate the requirement for further systemic medication or provide an adjuvant to them (1). However IACIs are often associated with significant pain and discomfort for children. Inhaled Entonox gas (50% nitrous oxide and 50% oxygen) is widely used as an analgesic and anxiolytic agent to reduce pain and anxiety for a variety of painful procedural in children. Evidence from a variety of different procedures has shown it to be an effective, safe and patient acceptable form of analgesia for both adults and children (2). It is widely acknowledged that patient satisfaction questionnaires allow clinicians to acquire meaningful and essential information that identifies gaps in care and facilitates the development of effective action plans for quality improvement in healthcare (3).
Objectives: The objective of this study was to assess children with JIA level of satisfaction and acceptability of using inhaled Entonox for IACI in a pediatric day-care unit.
Methods: Between the years 2017 and 2018, Entonox gas was administered to 48 children with JIA for Intra-articular corticosteroid injections in Temple Street Childrens University Hospital. Following this procedure children were invited to complete a modified version of a previously validated questionnaire (4).
Results: Of the 48 children approached, 32 completed the questionnaire (response rate =66.6%). The respondents ranged in age from 7-17 years and for 22 (69%) of the children it was their first time having an IACI. While 25% of respondents reported being nervous or scared before the procedure, 100% of the children who completed the questionnaire reported that if they required another IACI in the future they would like to use Entonox again.
Conclusion: Overall satisfaction was high with all children reporting that they would be willing to use Entonox again if required. Furthermore satisfaction with the care provided by the clinicians was also rated very highly.

REFERENCES

[1] Casado R, Lumbreras J, De Inocencio J, Remesal A, Merino R. Garcia-Cconsueqra. Sedation for intra-articular corticosteroid injections in juvenile idiopathic arthritis: the views of patients and their parents. Eur J Pediatrics. 2013; 172:14113.
[2] Young A, Ismail M, Papatsoris AG, Barua JM, Calleary JG, Masood J. Entonox inhalation to reduce pain in common diagnostic and therapeutic outpatient urological procedures: a review of the evidence. Ann R Coll Surg Engl. 2012; 94(1):81.
[3] Al-Abri R, Al-Balushi A. Patient satisfaction survey as a tool towards quality improvement. Oman Med J. 2014; 29(1):37.
[4] Lew, VK, Lalwani, K, Palermo, TM Factors affecting parental satisfaction following pediatric procedural sedation. J Clin Anesth. (2010). 22 2934.

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AB1403-HPR **INVESTIGATION OF SPINE POSTURE, MOBILITY AND POSTURAL COMPETENCY IN LOW BACK PAIN PATIENTS WITH MODERATE TO SEVERE DISABILITY: A CASE-CONTROL STUDY**

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Background: Low back pain (LBP) is the most common musculoskeletal complaint especially in women that causing disability and growing as a global burden (1,2). Changes in spine structures and alignment have been important in the occurrence of LBP (3,4).
Objectives: This study aimed to investigate spine posture, mobility and postural competency in women with and without LBP.
Methods: Thirty-four women with LBP having moderate to severe disability (age: 50.509.26 years; body mass index (BMI): 34.765.42 kg/m^2) and age-gender matched 37 asymptomatic healthy women (age: 48.948.99 years; BMI: 31.976.88 kg/m^2) were included. Oswetry Disability Index (ODI) was used for disability assessment (higher scores indicated more severe disability (0-50)). Overall spine posture, mobility, postural competency and spine check scores were evaluated using the Spinal Mouse (Idiag, Fehraltorf, Switzerland) device in standing position. The scores were evaluated between as poor "0" and "100" as perfect. T test was used for analysis.
Results: The mean score of ODI was 32.258.27 (moderate to severe disability). The scores of spine posture, mobility, postural competency and total spine check of women with LBP were found 24.7615.65; 25.1114.60; 36.6421.58; 30.2612.06, respectively; while, the scores of asymptomatic women were found 34.6716.27; 34.4521.47; 38.2115.18; 38.7215.06, respectively. Lower posture (p=0.011), mobility (p=0.037) and total spine check scores (p=0.011) were found in women with LBP compared to the controls; however, the postural competency was similar (p=0.722).
Conclusion: Women with LBP had poor spine posture, mobility and total spine check scores, but similar postural competency in comparison to controls. In the clinics, considering these parameters might be important while planning the optimal treatment for LBP.

REFERENCES

[1] Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, Woolf A, Vos T, Buchbinder R. A systematic review of the global prevalence of low back pain. Arthritis Rheum 2012;64:2028-2037.
[2] Buchbinder R, van Tulder M, berg B, Costa LM, Woolf A, Schoene M, Croft P; Lancet Low Back Pain Series Working Group. Low back pain: a call for action. Lancet. 2018 9;391(10137):2384-2388.
[3] Alricsson M, Bjrklund G, Cronholm M, Olsson O, Viklund P, Svantesson U. Spinal alignment, mobility of the hip and thoracic spine and prevalence of low back pain in young elite cross-country skiers. J Exerc Rehabil. 2016;12(1):21-8.
[4] Misir A, Kizkapan TB, Tas SK, Yildiz KI, Ozcamdalli M, Yetis M. Lumbar spine posture and spinopelvic parameters change in various standing and sitting postures. Eur Spine J. 2018 Nov 29. doi: 10.1007/s00586-018-5846-z.

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AB1404-HPR **JIA TEAMWORK FOR IMPROVING PATIENTS' ACCEPTANCE OF INTRAARTICULAR GLUCOCORTICOID INJECTIONS IN LOCAL ANESTHESIA IN OUTPATIENT DEDICATED SERVICE**

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Background: The discomfort and anxiety related to the medical care of patients with juvenile idiopathic arthritis (JIA), ampered by frequent and ongoing visits, diagnostic tests, medications and hospital stays, can negatively impact on the compliance during examinations and procedures, particularly intraarticular glucocorticoid injections (IAGI) in local anesthesia. A dedicated personnel for supporting patients and their caregivers may provide them relief, thus contributing also to a more serene environment for operators.
Objectives: To identify an appropriate approach for the relief of JIA patients most critical issues related to IAGI in local anesthesia. To provide preliminary validation of the approach identified.
Methods: In the first part of the study the nurse of the IAGI outpatient service at the study center had conversation with all consecutive JIA patients and caregivers seen at the service, while preparing them to IAGI in local anesthesia and while on discharge. In agreement with the patient, the nurse synthetized in keywords and registered each patients most relevant feelings with regard to the IAGI procedure. Patients and caregivers were also asked to suggest feasible tools for a better acceptance of the procedure. The results were discussed within the JIA team, who selected in a questionnaire the most frequently reported keywords and identified the most feasible among the proposed supportive tools. Secondly, all consecutive JIA patients seen at the service were asked to complete the feeling-status questionnaire after the IAGI. As the tools were available, the questionnaire was completed after IAGI procedures tool-supported. Statistics included descriptive analysis and Students t-test for comparison between feelings rating by patients with and without supportive tools (significance: p-value<0.05).
Results: From the list of keywords obtained by the first 10 patients with the nurse, the most reported -stress, anxiety, fear, and anger- were included in a feeling questionnaire composed of a VAS 0-10 (0=none, 10=worst) for each keyword. Among the suggested supportive tools the JIA team identified as feasible: colored drawings/pictures in the procedure room and the availability of favourite songs/videoclips/cartoons on tablet just prior and during IAGI. Forthy-one patients completed the questionnaire in a mean time of 22 seconds. Among them, 24 (59%) were supported by the selected tools, been meantime available, during IAGI procedure.

Abstract AB1404HPR Table 1. Mean of response to the feeling-questionnaire by JIA patients seen at the IAGI outpatient service without (A) and with (B) supportive tools

	Patients n.17 (A)	Patients n.24 (B)	P-value
Female/Male	16 (94)/1 (6)	20 (83)/ 4 (17)	
Age at IAGI, years, median (IQ range)	15,1 (12,8-20,5)	13,5 (9,7-17,8)	
Age at disease onset, years, median (IQ range)	4,9 (1,7 -11,2)	4,1 (1,9 -7,1)	
Stress*, mean (SD)	9 (1)	4 (2)	<0.005
Anxiety*, mean (SD)	9 (1)	4 (2)	<0.005
Fear*, mean (SD)	7 (4)	2 (2)	<0.005
Anger*, mean (SD)	5 (3)	1 (2)	<0.005

*VAS 0-10, 0=none, 10=worst
Conclusion: Our preliminary results highlight that a setting for IAGI more comfortable for patients provide an improvement in the JIA patients feelings rating undergoing injection procedures in local anesthesia. The nurses attitude to patients and the teamwork were fundamental in collecting the patients perspective and in adapting their suggestions to the IAGI outpatient service environment.
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AB1405-HPR **REDUCED HAND FUNCTION AFFECTS ACTIVITY PERFORMANCE AND QUALITY OF LIFE IN PERSONS WITH SIBM**

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Background: Reduced hand function is common in persons with (IBM) (1). Information regarding how hand function deficits affect activities of daily living and quality of life is limited (2,3). There is a need to improve treatment and increase knowledge on how to assess different aspects of sIBM.

Objectives: To investigate how hand function can influence activities of daily living and quality of life in persons with sIBM.
Methods: Data collection have been performed in both USA and in Sweden. In total 62 persons with IBM participated in this study (USA n= 36, Sweden n= 26), median age were (IQR) n=70 (66-75) years with a median disease duration (IQR) 6 (2-8) year. The majority were men n=39 (63%).
Hand strength was measured with the Jamar dynamometer and dexterity by the Purdue Pegboard. Activity limitation measured by the Disability of the Arm, Shoulder and Hand (DASH) and Myositis Activities Profile (MAP). Quality of life by SF-36.
Results: Hand strength and dexterity in IBM was reduced in both women and men ($p<0.001$). Percentage of reference values were (right hand/left hand) in Women 42%/25%, Men 30%/27%.
Persons with IBM had limitations in daily activities when compared to reference values ($p<0.001$). The most limited activities were: Activities of moving around (extremely difficult), Recreation (Very difficult), Movement (moderately difficult) and Household activities (moderately difficult)
Persons with IBM had reduced quality of life in SF-36 domains; Physical Function, Role Physical, General Health, Vitality, Social Function and Mental Health.
Hand strength correlated moderately with activity limitation measures by DASH ($p<0.001$) and MAP subscales; Movement, Activities of moving around, Personal hygiene, Housework, Social activities, Work/School and Recreation ($p<0.001$) and moderately to SF-36-dimension Physical Function ($p<0.001$).
Dexterity correlated moderately to DASH ($p<0.001$) and all subscales of MAP ($p<0.001$) and moderately to SF-36 dimensions Physical Function and Social Function ($p<0.001$).
Conclusion: Persons with IBM have reduced hand function and limitations in daily activities and quality of life. Suggesting the importance to include measures on both hand function, activity limitation and quality of life. The expertise on activity and occupational science of an occupational therapist may contribute to the assessment and treatment of persons with IBM.

REFERENCES

[1] Lindberg C, Oldfors A. Prognosis and prognostic factors in sporadic inclusion body myositis. Acta Neurol Scand. 2012;125(5):353-8.
[2] Eriksson M, Lindberg C. Hand function in 45 patients with sporadic inclusion body myositis. Occup Ther Int. 2012;19(2):108-16.
[3] Cox FM, Titulaer MJ, Sont JK, Wintzen AR, Verschuuren JJ, Badrising UA. A 12-year follow-up in sporadic inclusion body myositis: an end stage with major disabilities. Brain. 2011;134(Pt 11):3167-75.

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AB1406-HPR DIET AND LUPUS: WHAT DO THE PATIENTS THINK?

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Background: Cardiovascular disease (CVD) is the leading cause of mortality in patients with systemic lupus erythematosus (lupus). Therefore, using diet to control blood lipid levels and modify CVD risk could be a promising therapeutic strategy to control disease symptoms.
Objectives: The primary objective of this study was to learn about lupus patient experiences with diet including their opinion on considering diet as a therapeutic option. The secondary objective was to obtain this information in a cost and time effective manner.
Methods: A lay summary and a 15 question diet-based online survey was publicly available for 3 weeks. Social media was used to promote the survey through relevant charities, hospitals and research groups.
Results: 300 responses were received, 284 of whom had lupus. Patients reported that there was a lack of clinical counselling regarding diet with only 24% of patients stating that their doctor had spoken to them about diet. Despite this, 100% of patients stated that they would change their diet if they knew it would help their symptoms and 83% would take part in a future diet-based clinical trial. Text analysis of patient research suggestions identified a particular interest in using diet to treat fatigue and manage disease flares.
Conclusion: This project successfully gathered patient information regarding diet and lupus over a short timeframe using an anonymous social media platform. The survey provided evidence that patients support further research and potential diet intervention studies investigating the effect of diet on the symptoms of lupus.

REFERENCES

[1] Bernatsky S, Boivin JF, Joseph L, Manzi S, Ginzler E, Gladman DD, et al. Mortality in systemic lupus erythematosus. Arthritis & Rheumatism. 2006;54(8):2550-7.
[2] McDonnell TCR, Wincup C, Rahman A, Giles I. Going viral in rheumatology: a rapid, cost-effective method of obtaining patient opinion about mechanistic research in SLE and APSA. Rheumatology. 2018;57:1.

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AB1407-HPR NEUROLOGICAL MANIFESTATIONS DURING THE BEHCET DISEASE

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Background: behcet disease MB is a systemic inflammatory disease whose common histopathological substratum is a vasculitis that can reach all vessels. Neurological impairment is one of the diagnostic criteria for MB. A serious condition affects the functional and vital prognosis.
Objectives: The aim of our work was to study the epidemiological, clinical, therapeutic and evolutionary characteristics of patients with BD with neurological involvement.
Methods: This was a retrospective, monocentric, descriptive study of NB from the adult population collected from a population of 150 patients monitored for MB. The study was conducted in the Neurology and Internal Medicine departments over a period of 19 years, from January 1997 to December 2015. Patients meeting the criteria of the international Study Group of the MB of 1990, those of the criteria of the International Criteria for Behcet Disease (ICBD) and the diagnostic criteria of Neuro-behcet defined proposed by the international consensus of experts of 2014.
Results: We collect 35 patients. The gender ration was at 6 with 30 men for 5 women. The mean age of our population was 34+- 1.92 years. The neurological manifestations had inaugurated the MB in 55% of the cases. Ninety-four percent of patients had central nervous system involvement, while two patients had peripheral polyradiculoneuritis. Central involvement was parenchymal in 85% of cases, nonparenchymatous in 3% of cases and lixed in 6% of cases.
Cerebral imaging showed predominant demyelinating lesions in periventricular and brain stem in 15 patients, a peudo-tumor appearance in 3 patients, and vascular lesions with arterial aneurysm and cerebral thrombophlebitis in 2 patients. Therapeutically, all patients received corticosteroid therapy with immunosuppressive therapy for 15 patients. Three patients had received an immunomodulatory treatment of anti-TNF a Type. The evolution was by push in 60% of cases, primary progressive in 20% of cases and secondarily progressive in the rest of the cases. Three-quarters of patients with parenchymal brain injury had a favorable outcome. The Outcome was unfavorable in all patients with diffuse disease, brain stem damage, spinal cord injury, angio-behavior, polyradiculoneuropathy and mixed impairment. The change in visual impairment (NORB) was favorable in one case in two.
Conclusion: Neurological manifestations of MB are serious complications, and are typically poor prognosis both on a vital and functional level. Mortality remains high and neurological sequelae (motor and neuropsychological) are heavy. The prognosis in all the worse because the treatment is instituted late, hence the interest of an early and well conducted treatment

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AB1408-HPR INFLUENCE OF WEIGHT AND LIPID PROFILE IN RHEUMATIC PATIENTS WHO CHANGE FROM BIOLOGICAL THERAPY

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Background: The lack of efficacy of biological therapies in rheumatic patients causes a change of treatment, usually to another biological therapy. A significant number of studies have been published in relation to the reasons that cause this inefficacy, [1,2,3]; however, no studies have evaluated the involvement of the weight and lipid profile of patients in this process.
Objectives: To analyze the influence of weight and lipid profile in the relapse and change of biological therapy.
Methods: Retrospective-descriptive study. Rheumatic patients in treatment with biological therapies were recruited from January 2016 to December 2018. Sociodemographic data were collected (age and sex), along with anthropometric variables (weight, height, waist circumference and hip perimeter), toxic habits, comorbidities and variables related to the treatment. Associations between variables were analyzed using a Chi-square and T student. P-values < 0.05 were considered statistically significant. The spss v.19 program was used for data analysis.
Results: Two hundred and nine patients were enrolled, of which 80 (38.3%) were male and 129 (61.7%) were female. The mean age (SD) was 48.9 12.8 years. One hundred and twenty patients (57.4%) suffered rheumatoid arthritis, 35 (16.7%) spondylitis, 29 (13.9%) psoriatic arthritis and 10 (4.8%) spondyloarthritis. One hundred and fifty-three (73.2%) had not switches of biological therapy, 51 (24.4%) switched of biological therapy once and 5 (2.4%) three or more times. Statistically significant differences were found in the obese males who switched of biological therapy in relation to obese males who not switched (35.6% vs. 11.1%). Accordingly, the percentage of patients with hyperlipemia that switched of biological therapy was significantly higher than those who did not (29.4% vs. 13.1%).
The years of evolution and diagnosis we also involved, so that patients with more years of evolution and more years from the diagnosis had a higher percentage of switched (p = 0.006 IC 95% -17.22, - 0.96 and p = 0.042 -18, 32; -037 respectively).
Conclusion: Being obese male and with hyperlipidemia could be a risk factor that would condition the lack of response to a biological therapy and thus the need of switching to another.

REFERENCES

[1] Glintborg B1, stergaard M, Krogh NS, Tarp U, Manilo N, Loft AG, Hansen A, Schlemmer A, Fana V, Lindegaard HM, Nordin H, Rasmussen C, Ejstrup L, Jensen DV, Petersen PM, Hetland ML. Clinical response, drug survival and predictors thereof in 432 ankylosing spondylitis patients after switching tumour necrosis factor α inhibitor therapy: results from the Danish nationwide DANBIO registry. Ann Rheum Dis. 2013 Jul;72(7):1149-55. doi: 10.1136/annrheumdis-2012-201933. Epub 2012 Aug 31.
[2] Navarro-Compn V, Plasencia-Rodrguez C, de Miguel E, Diaz Del Campo P, Balsa A, Gratacs J. Switching biological disease-modifying antirheumatic drugs in patients with axial spondyloarthritis: results from a systematic literature review. RMD Open. 2017 Oct 10;3(2):e000524. doi: 10.1136/rmdopen-2017-000524. eCollection 2017.
[3] Ganzetti G, Campanati A, Bettacchi A, Brandozzi G, Brisigotti V, Bugatti L, Cataldi I, Filosa G, Giacchetti A, Lemme G, Morresi L, Nicolini M, Postacchini V, Ricotti G, Rosa L, Simonacci M, Offidani A. Switching from a biological therapy to another biologic agent in psoriatic patients: the experience of PsOMarche group. G Ital Dermatol Venereol. 2018 Feb;153 (1):5-10. doi: 10.23736/S0392-0488.16.05463-8. Epub 2016 Nov 15.

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AB1409-HPR INFLUENCE OF THE COMPANION ANIMALS IN THE PERCEPTION OF OUTBREAKS IN RHEUMATOLOGICAL DISEASES

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Background: Few papers analyze the health benefits of living with companion animals [1]. A significant number of studies have been published in relation to dog-assisted therapies for people with Alzheimer's or people with brain injuries, but all of them analyzed a reduced sample number [2] or did not show a good methodological structure [3]. Regarding the reduction of pain and quality of life, different studies showed positive results in the use of assisted therapies with dog [4]. However, this subject has not been evaluated yet in patients suffering Rheumatologic diseases.
Objectives: The main objective of this study is to evaluate the influence of companion animals on the perception of outbreaks in rheumatological diseases. Secondary objective: to analyze if having companion animals affected the general state of health or the degree of physical activity.
Methods: Prospective descriptive study. Consecutive patients attending rheumatology consultation were recruited during the month of October 2018. Sociodemographic data were collected (age, sex, cohabitation with companion animals, type of exercise performed) along with Beck questionnaires to assess depression, SF-12 to assess quality of life, and VREM (Spanish Short Version of the Minnesota Leisure Time Physical Activity Questionnaire) to assess the degree of physical activity. Associations between variables were analyzed using a Chi-square and T student. P-values < 0.05 were considered statistically significant. The main variables: dog, cat and other animals, were analyzed separately and then unified in a new variable called companion animals. The spss v.19 program was used for data analysis.
Results: Seventy one patients were enrolled, of which 30 (42.3%) were male and 41 (57.7%) were female. The mean age (SD) was 58.78 15.31 years. Thirty two patients (45.1%) suffered rheumatoid arthritis, 8 (11.3%) spondylitis, 8 (11.3%) osteoarthritis, and patients with fibromyalgia, becet, gout and scleroderma were present in a lower percentage. Regarding the coexistence with companion animals, 19 (26.8%) lived with dogs and 7 (9.9%) with cats.
The results of this study did not demonstrate any significant relationship between the duration of the outbreaks, the depressive state or the degree of physical activity and the coexistence with companion animals. However, statistically significant differences were found in the quality of live perceived by patients living with dogs in relation to patients without companion animals, so that we found higher scores in the mental SF-12 (56.5 vs 44), (p = 0.036, 95% CI - 24.41, - 0.80), the physical SF-12 (51.7 vs 39), (p = 0.042, 95% CI -25; -0.5) and total SF-12 (56.11 vs 43.8), (p = 0.018, 95% CI 22.4, -2.2).
Conclusion: Coexistence with dogs improves the perception of the quality of life of patients, both physically and mentally.

REFERENCES

[1] Saito T, Okada M, Ueji M, Kikuchi K, Kano K. [Relationship between keeping a companion animal and instrumental activity of daily living (IADL). A study of Japanese elderly living at home in Satomi Village. Nihon Koshu Eisei Zasshi. 2001 Jan;48(1):47-55.
[2] Folch A, Torrente M, Heredia L, Vicens P. Effectiveness of dog-assisted therapy in the elderly. A preliminary study. Rev Esp Geriatr y Gerontol. 2016 Jul-Aug;51(4):210-6. doi: 10.1016/j.regg.2015.12.001. Epub 2016 Feb 5
[3] Tabares Snchez, C, Castro, FV, Snchez Herrera, S, Gmez Acuas, M. Estado del arte sobre los efectos de la terapia asistida con perros en el tratamiento de enfermos de alzheimer. International Journal of Developmental and Educational Psychology [Internet]. 2013;1(2):271-281. Recuperado de: https://www.redalyc.org/articulo.oa?id=349852060025.
[4] Lust E, Ryan-Haddad A, Coover K, Snell J. Measuring clinical outcomes of animal-assisted therapy: Impact on resident medication usage. Consult Pharm J Am Soc Consult Pharm 2007;22(7):580-5.

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AB1410-HPR COPING WITH INFLAMMATORY RHEUMATIC DISEASE AND FATIGUE: PATIENTS PERCEPTIONS OF THEIR NEEDS

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Background: Fatigue is difficult to manage. In addition to pain, fatigue is the symptom reported to have the most negative impact on performance of daily activities by people living with rheumatoid arthritis (RA)[1]. At Haukeland University Hospital in Bergen, Norway, an activity pacing group is therefore offered as part of the rehabilitation program for people with inflammatory rheumatic diseases, to help them cope with fatigue in their everyday life.
Objectives: To explore patients experiences with the group and if there are unmet needs that should be addressed by health professionals.
Methods: Four to six months after attending rehabilitation, semi-structured interviews were conducted with two men and eight women of working age. Participants had a variety of inflammatory rheumatic diseases. The interviews were recorded and transcribed verbatim. Thematic analyses will be conducted.
Results: Preliminary findings indicate that persons living with rheumatic disease and fatigue have several needs to enhance their coping of everyday life, which can be described in three themes: *(1) A need for increased understanding of fatigue and recognition by health professionals:* Several informants reported feeling concerned, insecure and worried because they were unable to understand why they experienced overwhelming tiredness. Consequently, they wanted more knowledge concerning to which degree their fatigue was caused by their inflammatory rheumatic disease, or if it was caused by something else. They also wanted the rheumatologists to pay more attention to fatigue in persons with rheumatic diseases. *(2) A need for information sharing with peers:* Such sharing enhanced their understanding of fatigue, motivated them to consider trying out new strategies to manage their fatigue, and seemed to be the most important outcome of the activity pacing group. *(3) A need for practicing specific self-management strategies:* The informants valued that an occupational therapist led the group. They further described that the focus on activity balance and how to manage daily activities increased their awareness of what to do to manage their everyday life. Planning and prioritizing meaningful activities were the most frequently reported strategy. Despite gaining more knowledge, several of the informants seemed to struggle with changing their behavior and, thus, continued to exceed their energy reserves. Therefore, a few informants clearly expressed a need for follow-up over time and for practicing specific strategies, to be able to change their behavior.
Conclusion: The participants described seem to need information to increase their understanding of fatigue and how to manage their everyday life with fatigue. They also need rheumatologists to recognize fatigue experienced by persons with inflammatory rheumatic diseases. However, knowledge and increased awareness of self-management strategies alone do not seem to enable the participants to change their behavior. Therefore, there seems to be a need for follow-up allowing the participants to practice and evaluate goalsetting and the use of activity pacing strategies in their daily life.

REFERENCE

[1] Hewlett, S., et al., Patients' perceptions of fatigue in rheumatoid arthritis: overwhelming, uncontrollable, ignored. Arthritis Care & Research, 2005. 53 (5): p. 697-702.

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AB1411-HPR THE SELF- AND SHARED-MANAGEMENT OF PAEDIATRIC-ONSET RHEUMATIC AND MUSCULOSKELETAL DISEASES BY CHILDREN, YOUNG PEOPLE AND THEIR FAMILIES: INITIAL FINDINGS FROM A THEORY-GLEANING PROCESS WITH PATIENT ORGANISATION REPRESENTATIVES

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Background: Encouraging children and young people (CYP) with rheumatic and musculoskeletal diseases (RMDs) and their families to adopt self-management behaviours from the point of diagnosis is likely to positively influence the long-term health and wellbeing of CYP. However, there is limited evidence of such interventions targeted at CYP and families.
Objectives: Therefore, the aim of this study was to identify What works, for whom, in what circumstances, and why.
Methods: The study was based on the logic of realist evaluation and the Individual and Family Self-Management Theory. Realist evaluation is a recognised model of theory-driven evaluation which enables an in-depth appreciation of how complex health interventions may or may not work in real-world settings. In this study, a realist evaluation was undertaken using qualitative research methods to explore and refine theories regarding self- and shared-management interventions. The realist evaluation began with a set of initial programme theories, which were initially tested through interviews with one group of stakeholders involved in providing self- and shared-management support. Interviews were transcribed intelligent verbatim and data were analysed in NVivo using a realist logic of analysis to identify contextual influencers, interventions mechanisms and outcomes.
Results: In order to refine and consolidate theories about the self- and shared-management of RMDs by CYP and their families, theory was gleaned from patient organisation representatives with experience of supporting CYP and families. Contextual influencers discussed included the characteristics of: i) individual CYP living with RMDs; ii) the family dynamic; iii) peer and social interaction among both CYP and families; iv) the educational environment; and v) Organisational processes and structures. Patient organisation representatives highlighted the family dynamic and navigating organisation processes and structures as key influencers on CYPs willingness and ability to begin their self-management journey in an age- and developmentally-appropriate manner.
Conclusion: Concepts gleaned during the first phase of the study, particularly around the influence of family dynamic, will be further tested, refined, and consolidated with other groups of stakeholders, including: CYP with RMDs; families; healthcare professionals from the paediatric rheumatology multi-disciplinary team; school staff; and patient organisation representatives. In time, it is anticipated that the findings will form a programme specification detailing what works, for whom, in what circumstances, and why with regards to the self- and shared-management of paediatric-onset RMDs.

REFERENCES

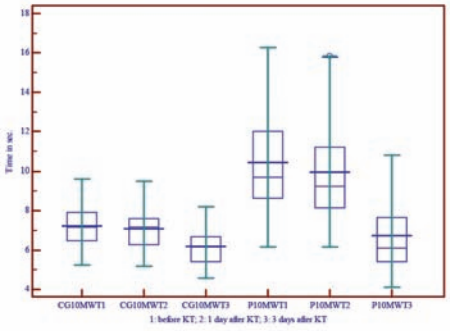
[1] Pawson, R. & Tilley, N. (1997). Realistic Evaluation. London: Sage.

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AB1412-HPR **CHANGES OF GAIT SPEED AND PAIN AFTER APPLYING KINESIOTAPE ON QUADRICEPS FEMORIS MUSCLE IN PATIENTS WITH KNEE OSTEOARTHRITIS**

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Background: Knee osteoarthritis is a chronic degenerative disease, known as the most common cause of difficulty walking in older adults and subsequently is associated with slow walking. Functional decline, increased risk of falls and presence of pain are, in many studies, related to the muscle weakness caused by osteoarthritis especially weakness of the quadriceps muscles. Pain is very noticeable while walking in rugged terrain, during ascent and descent of stairs, when changing from sitting to standing position as well as staying in one position for a long time. Many studies have shown that the strength of the quadriceps femoris muscle can affect gait, by improving or weakening it. Kinesio Tape is a physiotherapeutic technique, which reduces pain and increases muscular strength by irritating the skin receptors.
Objectives: The aims of this study was firstly to verify if the application of Kinesio Tape on quadriceps femoris muscle decreases time needed to accomplish the 10 meter walk test in patients with knee osteoarthritis and also in subjects without knee osteoarthritis. Secondly if applying Kinesio Tape on quadriceps femoris muscle reduces pain while walking only in patients with knee osteoarthritis.
Methods: In this study we observed the change of gait speed with the help of the 10-meter walk test before, one day and three days after the application of Kinesio Tape in quadriceps femoris muscle. We compared the results of the gait speed in two groups. In the first group, the Patients group, participated 102 out-patients with a clinical diagnosis of primary knee osteoarthritis, while in the second group, the Control group, participated 73 subjects with a main excluding criterion a clinical diagnosis of primary knee osteoarthritis. Secondly, we observed the change of pain, while walking for 10 meters at normal speed for the Patients group, before, one day and three days after the application, with the help of Numerical Pain Rating Scale - NRS.



Results: Our results indicated that there was a significant increase of gait speed in both groups while walking for 10 meters three days after application of Kinesio Tape on quadriceps femoris muscle. However there was not a significant change one day after the application of Kinesio Tape compared before its application in both groups. Also, there was a significant reduction of pain level 1 and 3 days after application of Kinesio Tape, compared to the level of pain before its application.
Graphic 1: Comparison of values of 10-meter walk test (10MWT) in the control group (CG) and in the patients group (PG), before Kinesio Tape (KT) application (1), 1 day after KT application (2) and 3 days after KT application (3)
Conclusion: Our results indicated that there was a significant decrease of time needed to accomplish the 10 meter walk test and also a significant decrease of pain while walking for 10 meters. Kinesio Tape is a technique that can be used especially when changing walking stereotypes is a long term goal of the treatment.

REFERENCES

[1] Sharma L. Proprioception in osteoarthritis. In: Brandt KD, Doherty M, Lohmander LS, editors. Osteoarthritis. 2nd ed. Oxford: Oxford University Press; 2003. pp. 1727.
[2] Ayis S, Ebrahim S, Williams S, Juni P, Dieppe P. Determinants of reduced walking speed in people with musculoskeletal pain. J Rheumatol. 2007;34 (9):190512. PMid:17696267.
[3] Zeni JA, Jr, Higginson JS. Differences in gait parameters between healthy subjects and persons with moderate and severe knee osteoarthritis: a result of altered walking speed? Clin Biomech (Bristol, Avon) 2009;24:3728. https://doi.org/10.1016/j.clinbiomech.2009.02.001. PMid:19285768. PMCid:PMC2715920.
[4] Vercelli S, Sartorio F, Foti C, Colletto L, Virton D, Ronconi G, et al. Immediate effects of kinesiotaping on quadriceps muscle strength: a single-blind, placebo-controlled crossover trial. Clin J Sport Med. 2012;22(4):31926. https://doi.org/10.1097/JSM.0b013e31824c835d. PMid:22450591.

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AB1413-HPR **FACTORS AFFECTING ACTIVITIES OF DAILY LIVING IN WOMEN INDIVIDUALS WITH SCLERODERMA**

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Background: Scleroderma is a multisystemic chronic disease with hand involvement in many patients and responsible for marked disability. Patients with scleroderma have reduced ability to perform activities of daily living (ADL) and several factors may be associated with difficulties in ADL and impairment of upper extremity functions.
Objectives: Aim of this study was to indicate the relationship among activities of daily living and pain, fatigue, disease severity, upper extremity strength and functional disability in patients with scleroderma and to identify the factors affecting activities of daily living in individuals with scleroderma.
Methods: Thirty five women individuals with scleroderma with mean age 56.46 10.45 were included into the present study. The activities of daily living was evaluated with Milliken ADL questionnaire, pain with visual analog scale (VAS), fatigue with fatigue severity scale (FSS), disease severity with modified Rodnan score (MRS), upper extremity strength with handgrip strength and functional disability with Health Assessment Questionnaire (HAQ). The relationships among the variables were analyzed by the Spearman correlation test. Correlation coefficients between Milliken ADL and other variables were determined by linear regression. The statistics were analyzed by SPPS 23.0 version.
Results: The Milliken ADL did not significantly correlated with MRS and VAS ($p > 0.05$), whereas Milliken ADL did significantly correlated with handgrip strength ($r = 0.680$, $p = 0.001$), FSS ($r = -0.729$, $p = 0.001$), HAQ ($r = -0.867$, $p = 0.001$). Additionally, handgrip strength, fatigue severity scale and HAQ were significant and independent determinants for activities of daily living, accounting for 95.0% of the variance in Milliken ADL in patients with scleroderma.
Conclusion: The findings of this study show that scleroderma patients daily life is affected by the disease at different levels. Impaired hand function and difficulties in the performance of ADL are common in scleroderma and may influence an individuals functional disability. Therefore, provide therapeutic interventions at the optimal time it is important to follow the development of these factors in the early stages of the disease.

REFERENCES

[1] G. Sandqvist, R. Hesselstrand & K. Eberhardt (2009) A longitudinal follow up of hand involvement and activities of daily living in early systemic sclerosis, Scandinavian Journal of Rheumatology, 38:4, 304-310, DOI: 10.1080/03009740802695466
[2] Kemal EROL, Kevser GOK, Gizem CENGIZ and Salih OZGOCMEN Hand functions in systemic sclerosis and rheumatoid arthritis and influence on clinical variables International Journal of Rheumatic Diseases 2018; 21: 249252

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AB1414-HPR PATIENTS' EXPERIENCES OF FATIGUE IN AXIAL-SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (ax-SpA) is a chronic inflammatory arthritis that predominantly affects the spine and the sacroiliac joints. Fatigue is recognised as a central ax-SpA symptom. Ax-SpA fatigue is under-explored and often not addressed. Attention in clinical practice seems to be focused on pain and disease activity.
Objectives: The objectives of this study were to explore the meaning, contributing factors and the impact of fatigue on the ax-SpA patients. Self-management and the role of clinicians were also explored.
Methods: A qualitative phenomenological approach was used. A purposive sample of 10 patients with ax-SpA, who were experiencing fatigue (

and attending a specialist rheumatology clinic were selected. The participants completed a demographic questionnaire, the Bath ankylosing spondylitis disease activity index (BASDAI) and the Bath ankylosing spondylitis functional index (BASFI) outcome measures.
Semi-structured interviews using open-ended questions lasted 30-60 minutes. Interviews were tape-recorded and transcribed verbatim. Data was analysed using Colaizzis framework. Two independent reviewers and 5 participants reviewed the data.
Results: Five males and five females were selected to participate in the study. The mean age was 46.6 years (29 - 69). Seven participants were working. The mean BASDAI was 5.4 and mean BASFI was 5. Most of the participants had disease duration of longer than 5 years.
The six themes that emerged from the data are:

- 1. The meaning of fatigue
- 2. Fatigue patterns
- 3. Factors that modulate fatigue
- 4. The impact of fatigue
- 5. Self–management of fatigue
- 6. Professional support.

Fatigue was defined as an unpredictable, extreme and persistent tiredness. Fatigue had a cognitive and physical component, which was not related to physical activity and did not resolve by rest or sleep. Fatigue was distinguished from tiredness. Tiredness was perceived as a normal feeling which occurred after physical activity and was resolved by rest or sleep.
The severity, duration and frequency of fatigue varied. Fatigue was described as having a multi-factorial aetiology. Fatigue had an overall negative impact upon participants lives affecting their quality of life, leading to psychological and emotional consequences. Participants struggled to self-manage fatigue, receiving no support from health care professionals.
Conclusion: This research has contributed to a better understanding of the patients experiences of ax-SpA fatigue. Fatigue was described as a huge burden and life-changing. Ax-SpA fatigue should be acknowledged in clinical practice. Ax-SpA patients should be asked about fatigue during their clinical consultation. Fatigue should be addressed in its own right and independently from pain and disease activity.
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AB1415-HPR PATIENTS PERSPECTIVES ON SELF-MANAGEMENT OF AXIAL SPONDYLOARTHRITIS FATIGUE

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Background: Axial spondyloathritis (ax-SpA) is a chronic inflammatory arthritis that mainly affects the axial skeleton and can lead to bony ankyloses. Pain, stiffness and fatigue are the most frequently ax-SpA-reported symptoms. Ax-SpA fatigue is multidimensional incorporating physical, psychological and social components, implying that self-management strategies are crucial.
Objectives: This study aimed to explore the self-management of ax-SpA fatigue. Patients perceptions of whether clinicians give importance to ax-SpA fatigue were also explored.
Methods: A qualitative phenomenological approach was used. A purposive sample of 10 patients with ax-SpA, who were experiencing fatigue (≥7cm on a 10cm VAS scale and attending a specialist rheumatology clinic were selected. The participants completed a demographic questionnaire, the Bath ankylosing spondylitis disease activity index (BASDAI) and the Bath ankylosing spondylitis functional index (BASFI) outcome measures.
Data was collected using semi-structured interviews that lasted about 30-60 minutes. Open-ended questions such as How do you manage fatigue?, How well do you think you are coping with fatigue?, What can be done to help address fatigue? and Is fatigue usually discussed when you attend clinic? were asked to the participants. Interviews were tape-recorded, transcribed verbatim and analysed using Colaizzis framework. Two independent reviewers and five participants reviewed the data.
Results: Ten ax-SpA patients (5 males) with a mean age of 46.6 years (29 - 69) participated in the study. The mean BASDAI was 5.4 and mean BASFI was 5. Most of the participants had disease duration of longer than 5 years.
Learning to self-manage fatigue was clearly a difficult process for the participants. Only four participants felt that they had learnt to cope with fatigue. They described how they overcame the initial feelings of anger and denial to cope with the fatigue and being told fatigue was part of the condition was helping in accepting the fatigue.
There was consensus that fatigue was not addressed in the clinical setting. Participants felt that they were not guided and supported enough to manage fatigue. More information was needed from health care professionals (HCP) on fatigue management. There was a feeling that HCP focused on the management of pain rather than fatigue.
Conclusion: This research highlighted a clear lack of knowledge about self-management skills to manage ax-SpA fatigue. Lack of adjustments and coping with fatigue was prominent even in patients who had long disease duration. Furthermore, fatigue was not addressed in clinical practice.
Understanding patients beliefs is an important step towards guiding them to self-manage fatigue. Patients should be guided in implementing self-management plans that would fit their goals, priorities and lifestyle. Self-management is important in improving health outcomes and quality of life.
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AB1416-HPR A REVIEW OF PUBLIC PATIENT INVOLVEMENT AND ENGAGEMENT (PPI/E) AT THE ARTHRITIS RESEARCH UK CENTRE FOR ADOLESCENT RHEUMATOLOGY AT UCL, UCLH AND GOSH

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Background: The adolescent and young adult (AYA) rheumatology clinical service has a well established culture of involving our users in shaping how services are delivered. Since its inception in 2012 the Arthritis Research UK Centre for Adolescent Rheumatology has worked to offer every patient within the clinical service the opportunity to participate in research
Objectives: This was achieved by 2015 and from 2014 we renewed our focus on an active involvementprogramme to promote the role of young people in prioritising and designing our research agenda and work-streams. We are currently developing our strategy for the next five years and reviewing our experience to date.
Methods: PPI/E activity records were searched for the period October 2014 to April 2018. This included number of patients involved, their age and diagnosis, and the type of activity along with the number of times they have been involved.
Results: 19 PPI/E activities were organised. From a total of 1554 adolescent and young adult patients 150 patients having been involved in PPI/E, the age range was 11-27 and 118 were female.
The activities consisted of focus groups (79%) and support days (11%) all but two of which were disease specific groups.
The disease specific PPI/E activities have been focused on JIA, JSLE, and JDM. The number of patients involved in these activities were 24.62% (n=99), 24% (n=17) and 66% (n=25) respectively. The mean instances of involvement per disease were 2.09 for JIA, 2.53 for JSLE and 3.56 for JDM.
Conclusion: Our results show that many of our patients have taken part in PPI/E activities (11.19%) with over 65% of of our JDM patients having taken part in either a focus group or support day. The focus on

inflammatory rheumatic disease is in keeping with the stated aims of our Centre. The mean instances of involvement ranging from 2.09 3.56 suggest that patients feel PPI/E is worthwhile. We aim to share our results with the young people who have driven this work and will consider how we might move forward. We aim to consult with the group of patients we serve who have not been part of this process to date.
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HPR Professional education, training and competencies

AB1417-HPR RHEUMATOLOGY NURSE PRACTICE: EDUCATION TO IMPROVE THE UNDERSTANDING OF RHEUMATIC DISEASES

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Background: *Rheumatology Nurse Practice* is an accredited educational initiative spearheaded by members of the Rheumatology Nurses Societys Board of Directors and Education Department that has been ongoing for the last 10 years. It involves a combination of print issues and live broadcasts geared toward rheumatology nurses, nurse practitioners, and physician assistants.
In 2017, nine evidence-based print issues were published along with nine corresponding case-based live broadcasts using the Google Hangouts On Air platform.
To gauge the impact of this education, a special cohort of 100 learners was recruited at the start of 2017 to provide in-depth feedback through the completion of detailed pre- and post- activity surveys. This abstract focuses on feedback from four issues of *Rheumatology Nurse Practice* that centered on the following topics:

- 1. New Insights into the Treatment of the Spondyloarthropathies
- 2. Looking at the Horizon: What Does the Future Hold in the Treatment of Rheumatoid Arthritis?
- 3. The Pathophysiology of Spondyloarthritis: Connecting and Differentiating Characteristics
- 4. The Pathophysiology of Systemic Lupus Erythematosus: A Nursing Primer

Objectives: To gauge improvements in learners knowledge, competence, and performance as a result of this education. Specific learning objectives were tied to each print issue of *Rheumatology Nurse Practice* and served as the basis for the pre- and post-activity surveys.
Methods: Each print issue contained a combination of evidence-based content related to the main theme, along with a series of individual essays written by activity faculty members. These essays all also linked to the main theme of the issue. Live broadcasts were intended to bring a real-life, case-based perspective to the education.
Results: Improvements of >25% in both knowledge and competence were noted between pre- vs. post-activity cohort surveys for all issues in this initiative. Learners also provided extensive feedback regarding specific areas of improvement within their day-to-day practice based on the education.
Conclusion: Print issues and online broadcasts within the Rheumatology Nurse Practice initiative are valued resources, dealing with sensitive and challenging issues faced by practicing rheumatology nurses and nurse practitioners in a clinically-meaningful manner
Survey cohort participants showed a substantial improvement in their understanding of a variety of rheumatic diseases and improved their ability to communicate with patients about disease diagnosis and treatment options.

REFERENCES

[1] Rheumatology Nurse Practice. New Insights into the Treatment of the Spondyloarthropathies. Volume 3, Issue 5.
[2] Rheumatology Nurse Practice. Looking at the Horizon: What Does the Future Hold in the Treatment of Rheumatoid Arthritis? Volume 3, Issue 6.
[3] Rheumatology Nurse Practice. The Pathophysiology of Spondyloarthritis: Connecting and Differentiating Characteristics. Volume 3, Issue 7.
[4] Rheumatology Nurse Practice. The Pathophysiology of Systemic Lupus Erythematosus: A Nursing Primer. Volume 3, Issue 8.

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HPR Service developments, innovation and economics in healthcare

AB1418-HPR MOBILE-PHONE-BASED HOME EXERCISE TRAINING PROGRAM IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Most rehabilitation programs are hospital-based and rely on regular supervision (1). However, mobile health technologies such as smartphone applications may provide lower-cost ways to monitor and train the patients (2). We have developed a mobile-phone application for monitoring and training the patients at home.
Objectives: The purpose of this study was to compare a mobile-phone-based home exercise training program along with supervised physiotherapy program to a brochure-based home exercise training program along with supervised physiotherapy program in patients with knee osteoarthritis. We hypothesized that the patients who received mobile-phone-based home exercise training program along with supervised physiotherapy program over 3 weeks would have better balance, quality of life and less pain and disability score versus the patients who received brochure-based home exercise training program along with supervised physiotherapy program.
Methods: This was a randomized, prospective, comparative clinical study. The study included 40 patients, aged 4565 years, who diagnosed with a grade 2-3 knee osteoarthritis. The patients were randomly divided into two groups. While one group (n=20) received a mobile-phone-based home exercise training program along with supervised physiotherapy program, the second group (n=20) received a brochure-based home exercise training program along with supervised physiotherapy program as 15 sessions for a total of three weeks, five sessions per week. Pain intensity, balance, disability, and quality of life were measured with Visual Analogue Scale, Berg Balance Scale, WOMAC, and SF-36, respectively. All of the assessments procedures were performed again after the treatment.
Results: There were statistically significant improvements in measures of pain intensity, balance, disability, and quality of life between pre- and post treatment in both groups ($p<0.05$). However, no significant differences were found in any of patient outcome variables between the groups ($p>0.05$).
Conclusion: We could report that mobile-phone-based home exercise training program is not superior to brochure-based home exercise training program in terms of patient outcomes over 3-week program.

REFERENCES

[1] Wang CH, Chou PC, Joa WC, et al. Mobile-phone-based home exercise training program decreases systemic inflammation in COPD: a pilot study. BMC Pulm Med. 2014 Aug 30;14:142.
[2] Persell SD, Karmali KN, Stein N, et al. Design of a randomized controlled trial comparing a mobile phone-based hypertension health coaching application to home blood pressure monitoring alone: The Smart Hypertension Control Study. Contemp Clin Trials. 2018 Oct;73:92-97.

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AB1419-HPR EFFICIENCY OF INDIVIDUAL STEEL ORTHESIS IN HEAVEN SPRAY

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Background: The most common cause of heel pain is the heel spur, which is 75% of patients with heel pain. The intensity of the pain does not depend on the size of the spur, as determined on the radiograph. Often sharp in shape and large in size, the spurs are a random X-ray finding. At the same time, severe pains in the heel region are possible with a normal radiograph [1]..
Objectives: The purpose of this study is to establish the effectiveness of the treatment of patients with pain syndrome in the heel spur, by affecting the main components of the pathogenesis of individually manufactured orthopedic insoles.
Methods: During the year, under our supervision there were 156 patients aged from 32 to 67 years. Gender composition - 123 (79%) - women, and 32 (21%) - men. The average time between the onset of clinical symptoms and the first day of treatment was 134 days. The average spur size was 4.3 mm. In 80% of patients, a history of pain lasted for more than 3 months. Patients were divided into 2 groups. The experimental group (G1) used individually manufactured insoles (78 people: 61 - women, 17 - men). The control group (G2) used factory insoles (78 people: 58 - women, 20 - men). 152 patients (98%) completed the protocol: 78 (100%) in G1 and 74 (96%) in G2. The criterion for inclusion in the study was the diagnosis of the heel spur. The diagnosis was made based on anamnesis, ultrasound of the plantar aponeurosis, and radiography of the heel region. The exclusion criteria were patients with heel spurs without heel pain, as well as systemic diseases: rheumatoid arthritis, diabetes mellitus, and severe vascular pathology.
The degree of longitudinal flat-footedness, stability of the foot, individual deformities of the feet were clinically evaluated using clinical and functional methods and the method of vacuum trace modeling [2].
Individual insoles were made based on frame materials in the projection of the arches of the foot. Dense materials maintain a constant tension of the plantar aponeurosis. G1 patients were made full contact insoles with a correction of the transverse arch, without adding relief elements under the heel.
The control group used factory-made insoles from different manufacturers, with soft elements under the heel. Measurement parameters: average pain intensity on a VAS scale; duration of pain throughout the day; distance traveled; subjective comfort when using insoles. The observation period is 12 calendar months.
Results: The average VAS score in G1 decreased from 5.4 0.3 at the beginning of the study to 1.01 in 62 patients (81%). 15 patients reported pain reduction, the average VAS score was 2.1 0.3.
Complete relief of G1 pain has been reported in patients with an osteophyte size of less than 5 mm. G1 patients regained their usual movement distance of 3.9 km per day. Cases of recurrence of heel pain is not recorded. No patients experienced discomfort from the use of insoles throughout the entire period of adaptation.
In G2, the average VAS score decreased from 5.6 0.3 at the beginning of the study to 2.9 0.3. Patients of the G2 group were able to increase the distance of movement to 1.2 km per day.
Conclusion: When using individual insoles, 93% of patients reported complete relief of pain. 7% of patients noted a significant reduction in pain. The use of individual insoles in the treatment of plantar fasciitis made it possible to reduce pain in a shorter time.

REFERENCES

[1] Kotelnikov G.G. Traumatology and Orthopedics. M.: GEOTAR-Med, 2018. 776 p.
[2] Joint pain/K. V. Kotenko (and others). M.: GEOTAR - Med, - 2018. 560 p.

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AB1420-HPR THE USE OF SUBCUTANEOUS METHOTREXATE IN INFLAMMATORY ARTHRITIS: TRANSLATING RESEARCH INTO PRACTICE USING QUALITY IMPROVEMENT METHODOLOGY.

Aicha Bouraoui[1]. [1]*Basildon University Hospital, Basildon, United Kingdom*

Background: Methotrexate (Mtx) is considered as the drug of choice in the management of inflammatory arthritis (IA). There is growing evidence of the benefit of sub-cutanous (s/c) methotrexate compared to the oral route. At the same dose, pharmacokinetic studies showed that s/c Mtx has better bioavailability. RCT studies showed that patients respond better to s/c mtx. Finally s./c Mtx has better tolerability with less risks of GI side effects.
Translating research into practice can be sometimes challenging due to a number of barriers including individual choices and variations as well as systems or organizational factors. Over the recent years there has been great focus on quality improvement in healthcare to make health care “safe, effective, patient centered timely efficient and equitable”.
Objectives: We aimed that within 6 months period, 100% of our patients with inflammatory arthritis should have trial of s/c methotrexate before starting biologics unless there is contraindication.
Methods: We reviewed the data of 50 patients to assess management of patients with IA using our biologic register. We used the 5 why strategy to have better understanding of the lack of prescribing of s/c mtx and vairiations in clinical practice. By applying improvement science we standardized our pathway, included methotrxate s/c trial prior to biologics. We also conducted a number of interventions including multidisciplinary educational events and one to one meetings, we mobilised and organised our resources in better way to meet our patients needs. We monitored our data over time and reviewed our practice accordingly.
Results: Baseline data showed that the majority of our patients had rheumatoid arthritis (RA) (74%) followed by Psoriatic arthritis in 24% of cases. Most patients had initial trial of methotrexate but only 32% were kept on oral methotrexate and 26% of patients had trial of s/c mtx before starting biologics. The main indication of starting s/c Mtx was oral methotrexate induced gastrointestinal side effects. Methotrexate was stopped all together in 34% of patients due to suspected major side effects(SE). SE mainly encountered with oral route with 10% suspected ILD, 14% had deranged LFTs. In order to have better understanding with issues related to the poor use of subcut Mtx the author conducted staff unstructured interviews to explore their experience with s/c Mtx. We also noticed variations between clinicians in their clinical practices.
Our theory of change included a number of interventions and results showed significant improvement in prescribing of s/c Mtx among IA patients. 3 months after starting the projects 1st cycle: 42 patients were switched to sub-cut Mtx with only 6 patients required subsequent biologics use.
There was reduction in the number of patients referred for biologics and among those started on biologics 50% of patients had trial of S/C methotrexate.
Conclusion: In summary, our baseline data showed poor use of s/c Mtx in patients with IA despite the growing evidence of its benefit. In order to translate research findings into practice we used 5 whys methodology to have better understanding of the barriers within our systems, we applied QI methodology and standardized our practice for better use of resources at lower cost.

REFERENCES

[1] Braun J, Kastner P, Flaxenberg P, et al. Comparison of the clinical efficacy and safety of subcutaneous versus oral administration of methotrexate in patients with active rheumatoid arthritis: results of a six-month, multicenter, randomized, double-blind, controlled, phase IV trial. Arthritis Rheum 2008;58:7381.
[2] Stamp LK, Barclay ML, ODonnell JL, et al. Effects of changing from oral to subcutaneous methotrexate on red blood cell methotrexate polyglutamate concentrations and disease activity in patients with rheumatoid arthritis. J Rheumatol 2011;38:25407.

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AB1421-HPR VIRTUAL CLINICS IN THE PRESENT- A PREDICTOR FOR THE FUTURE?

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Background: There is great interest in non face to face (F2F), internet or app based outpatient interact at the moment. As these become established, we look at the non F2F appointments already happening in telephone and virtual clinics in a busy urban rheumatology department. Here we look at the type of diagnoses dealt with in a non F2F environment and potential outcomes from these non F2F appointments.

Objectives: To assess the efficiency and utilisation of virtual and telephone clinics in a general rheumatology department.
Methods: Data was collected from electronic (Cerner) patient records on 240 patients who had a virtual appointment in May 2018. The data was analysed using Excel 2010.
Results: 240 patients had virtual appointments in one month. 121 (50.4%) were via telephone and 119 (49.6%) via patient letter. 34 (14.1%) patients had multiple virtual/telephone appointments. 129 (54%) were carried out by consultants, 78 (32%) by nurses and 33 (14%) by registrars. 37% had rheumatoid arthritis. 32 (13%) appointments lead to a prescription. Virtual appointments produced 44 referrals, including 18 to another specialty, 16 to physiotherapy, and the rest to hand therapy or podiatry. Most patients had a F2F appointment before and after their virtual appointment in May 2018, 1 patient had died before having a second face to face appointment and 13 (5%) were discharged from their virtual appointment.

	Mean Number of Days between appointments
From 1st Face to Face to Virtual Appointment	44
From Virtual Appointment to 2nd Face to Face	53
From 1st Face to Face to 2nd Face to Face	94

Abstract AB1421HPR Table 1. The mean number of days between each type of appointment.

Conclusion: Consultants undertook the bulk of virtual clinics, and these appointments resulted in the majority of referrals and prescriptions. Virtual appointments reduce the waiting times for contact with a healthcare professional between appointments. Many patients had several virtual appointments between face to face appointments and this cohort may benefit from more scrutiny. Current technology already imporves communication and leads to significant changes in patient care without requiring F2F appointments. Internet based and app based interaction should face the same scrutiny.
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AB1422-HPR MODERATE AND HIGH ADHERENCE TO A DISEASE MANAGEMENT MODEL IN PATIENTS WITH RHEUMATOID ARTHRITIS IMPROVES CLINICAL RESULTS IN A BIG UNICENTRIC COHORT

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Background: Rheumatoid arthritis (RA) is an inflammatory, chronic disease of unknown etiology. Usually it leads to deformity and destruction of joints through the erosion of cartilage and bone. Over 90% of patients with RA report to suffer symptoms in hands and joints, swelling, loss of motion, muscle weakness among others. These symptoms affect all aspects in a patients life. Therefore, management of a patient with RA should not only include evaluate outcomes related to the rheumatology specialty, on the contrary, aspects such as physical disability, nutrition, mental health, among others should be taken into account. Centers of excellence in rheumatoid arthritis have proposed a multidisciplinary model of care with an initial diagnosis, treatment prescription and follow-up with a rheumatologist, periodic consultations with a physiatrist, psychologist, physiotherapist, occupational therapy nutrition, and, a patient focused program. With a multidisciplinary model of care the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA.
Objectives: The aim of this research was to define adherence/attendance to a multidisciplinary model of care for patients with RA that attend to a RA specialized center in Colombia.
Methods: We implemented the center of excellence model program proposed by REAL-PANLAR group in 2015 (3). In order to define adherence to the multiapproach model the authors performed an informal expert consensus to propose a method to measure adherence to the model. The authors proposed three levels of adherence. We proposed three levels of adherence as follows: **High adherence:** For rheumatology patients had to attend between 6 and 12 consultations in one year. For physical therapy, physiatry, psychology, occupational therapy and nutrition patients had to attend to 3 or more consultations during one year per each specialty. **Moderate adherence:** For rheumatology patients had to attend between 3 and 5 consultations in one year. For physical therapy, physiatry, psychology, occupational therapy and nutrition patients had to attend between 2 or 4 consultations during one year per each specialty. **Low adherence:** For rheumatology patients had to attend between 1 and 2 consultations. For physical therapy, physiatry, psychology, occupational therapy and nutrition patients achieved only 1 consultation or less during one year per each specialty. We performed a descriptive analysis and compared the level of adherence and disease activity.
Results: During 2018 we reviewed the medical charts of 6851 patients diagnosed with rheumatoid arthritis; 82% were female and 18% were male. Mean age was 59 years 13 years old. Regarding disease activity mean DAS28 was 2.69 0.84. Most of patients that were considered as Moderate or High adherent achieve remission or LDA.
See table 1. Levels of Adherence in Patients with RA

DAS	LOW ADH		MODER ADH		HIGH ADH	
	n	%	n	%	n	%
REMISION	245	4%	2090	31%	1495	22%
LDA	121	2%	874	13%	589	9%
MDA	193	3%	699	10%	465	7%
SDA	27	0.4%	31	0.5%	22	0%

Conclusion: This is an initial approach in order to evaluate patients adherence and attendance to a new implemented multidisciplinary disease management model of attention for patients with RA in Colombia. Our descriptive study demonstrated that patients with moderate or high adherence can achieve better clinical outcomes compared to those who arent adherent to the model.
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AB1423-HPR ELICITING THE AGENDA OF PATIENTS WITH MUSCULOSKELETAL DISORDERS; THE PHYSIOTHERAPIST-PATIENT INTERACTION

Sercan Yilli[1], Serkan Kalmaz[1], Faruk Altay[2], Elif Turgut[2]. *[1]Hacettepe University, Ankara, Turkey*; *[2]Hacettepe University, Department of Physiotherapy and Rehabilitation, Ankara, Turkey*

Background: Eliciting main concerns via interviewing is important for patient-centered care and for planning individualized rehabilitation program (1, 2). Recently, it has been shown that clinicians often fail to elicit the patients agenda and, when they do, they interrupt the patients discourse (3). However, the prevalence of agenda setting in physiotherapist as a health care provider and the physiotherapist-patient interaction remains relatively unexplored.
Objectives: The aim of this study was to describe agenda elicitation in rehabilitation, to determine the frequency of encounters in which physiotherapists elicited the patients with musculoskeletal disorders agenda, the proportion and timing of interrupted answers.
Methods: An audio-recording analysis of 52 clinical encounters recorded during first physiotherapist-patient interaction were performed. The elicitation of the patient agenda characteristics as the time to interruption or to complete statement were analyzed.
Results: Physiotherapists elicited the patients agenda in all (96.1%) clinical encounters. Interestingly, in those encounters in which physiotherapists elicited patient concerns, the clinician interrupted the patient after a median of 15 seconds (interquartile range 6 to 22 seconds). In the uninterrupted encounters in which physiotherapists elicited patient concerns, the patients with musculoskeletal disorders was state their agenda in 2414.5 seconds.
Conclusion: Physiotherapist emphasize to elicit the patients agenda, however, they interrupt expression very sooner. Eventually, the failure to elicit the patients agenda inhibits the physiotherapists-patient communication and this would lead to failure to plan rehabilitation program based on the needs of each patient.

REFERENCES

[1] Dyche L, Swiderski DJJogim. The effect of physician solicitation approaches on ability to identify patient concerns. 2005;20(3):267-70.

[2] Marvel MK, Epstein RM, Flowers K, Beckman HBJJ. Soliciting the patient's agenda: have we improved? 1999;281(3):283-7.
[3] Ospina NS, Phillips KA, Rodriguez-Gutierrez R, Castaneda-Guarderas A, Gionfriddo MR, Branda ME, et al. Eliciting the patients agenda-secondary analysis of recorded clinical encounters. 2019;34(1):36-40.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8006

Arthritis research

AB1424-PARE EFFECTING A CHANGE AS A PATIENT INSIGHT PARTNER

Stephanie Skeffington[1], Emma Dorris[2]. [1]*University College Dublin, Patient Voice in Arthritis Research, Dublin, Ireland*; [2]*University College Dublin, Centre for Arthritis Research, Dublin, Ireland*

Background: In my patient advocacy work I had experience in every aspect except research. Through UCDs (University College Dublin) Centre of Arthritis Research (CAR) patient-research co-produced newsletter *News Rheum* I became aware of the Patient Voice initiative they had set up which is where I discovered the vasculitis research project I became involved with.
Objectives: My objectives to effect change were to be achieved by

- Sharing my knowledge
- Showing the value of patient involvement/engagement
- Learning how the research process works by being directly involved in the process

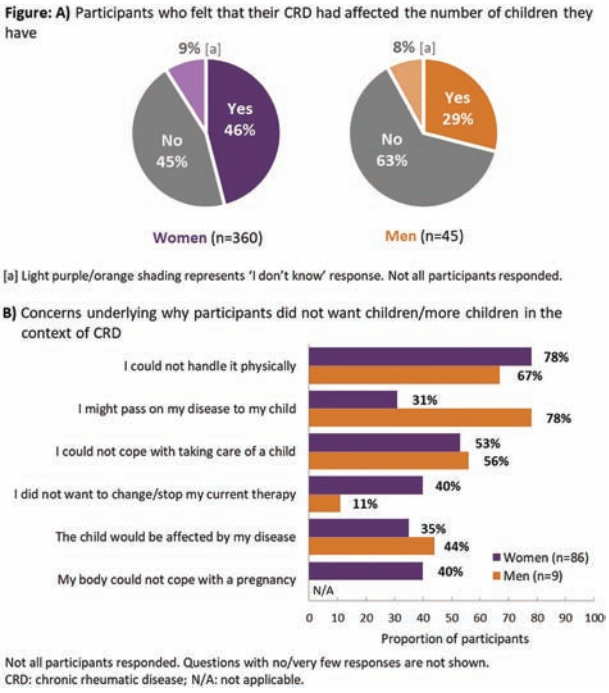
Methods: A personal perspective
Results: My formal involvement in this project started with my being invited to be a member of the interview panel choosing the postdoctoral researcher for the project. My remit was to ask the candidates about the impact of the project beyond just the science aspect, to try to figure out who just wanted a job, and who was interested and passionate about this project. I was not only choosing someone for the position but someone I was committing to work with for three years.
One of my first tasks was to act as a mentor in plain English to help the chosen researcher prepare a lay summary of the project. This helped both of us get to grips with the project and its objectives, as well as working out our working dynamic.
I work most closely with the project researcher, who has worked in rare disease but not in rheumatology. She has been very receptive and not only took an interest in learning more about the disease area but me as well.
I was introduced me to her first as a mentor, and second as a patient advocate. This helped us get to know each other and opened discussions including how PPI could aid her work and how invaluable it is from the patient perspective. This has given our relationship a great start and in a relatively short period we have built the great foundations for an excellent working relationship on a project we are both share a passion for.
For the researchers, to improve the process of PPI I would like some honest feedback on my performance as a patient insight partner. It may not be every patients ideal, but PPI is a knowledge exchange and we are all equal parties, I believe providing more robust feedback and sharing avenues for my improvement in a constructive way would be beneficial for my advocacy and future PPI work.
To prepare patient insight partners (PIPs) with no or limited experience of PPI there should be an opportunity to talk to another or former PIP about their experience or perhaps a leaflet detailing such experience which can be given to new PIPs. This is something not currently done within UCD, but, in response to my suggestion, Im working with UCD CAR to produce.
We are building the profile of our collaboration and showcasing the research by creating a blog together. The unique aspect of this blog is that it will represent both of our perspectives as researcher and patient advisor on specific topics. This is also an opportunity to inspire others involved in research projects to view other ways in which they can build on such collaboration, educate people about all aspects of the process and learn from each other even more along the way. The reciprocal learning nature of this blog is the number one reason for its creation.
Conclusion: Anyone thinking about being a PIP should be aware of how important it is to share their expert knowledge in such as setting and shouldnt let their fear or perceived lack of knowledge hold them back. They should be willing to be an equal and expect to be treated as such and be willing to contribute fully to the knowledge exchange process including giving honest constructive feedback
Despite this relationship still being quite new we have plans to grow and build my PPI within UCD CAR.
None declared
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Patient information and education

AB1425-PARE FAMILY PLANNING IN CHRONIC RHEUMATIC DISEASES: UNMET NEEDS OF WOMEN AND MEN IN SWEDEN

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Background: Family planning (FP) in the context of chronic rheumatic disease (CRD) can be challenging for both women and men, with additional requirements for information and support.[1] However, it is unclear whether the needs of this population are being met by current clinical practice in Sweden.
Objectives: To gain insight into the perspectives of women and men with different CRDs on FP, and to assess whether they feel adequately supported to make informed decisions.
Methods: A 10-minute survey focusing on participants experiences and current needs around FP was designed. The survey was distributed (24 Aug5 Sept 2018) via a web–based system to members of the Swedish Rheumatism Association; men and women aged 1847 years were included. Data are reported for participants with arthritic or systemic CRDs (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, juvenile idiopathic arthritis, systemic sclerosis, systemic lupus erythematosus, polymyositis, dermatomyositis). Participants with fibromyalgia, Ehlers-Danlos syndrome, other or no CRD were excluded.
Results: Of 944 participants, 542 (57%) women and 60 (6%) men with arthritic or systemic CRDs responded. Over a quarter of women (28%) who had/were expecting children felt their CRD had affected their ability to have children and more than half either believed that their CRD had influenced the number of children they had or were undecided (**Figure A**). Men were less affected by their CRD with respect to FP, with >60% reporting no impact on their ability to have children and/or how many. Of participants who did not want children/more children in the future, around a third attributed this to their CRD (women: 37% [n=86/232]; men: 30% [n=9/30]). Their biggest concerns were not being able to physically handle and/or cope with taking care of a child, and passing on their disease (**Figure B**). Womens concerns regarding disease activity after pregnancy were not unfounded, with 66% reporting disease worsening postpartum. The most common treatments reported by women with CRD while trying to conceive were DMARDs (20%), NSAIDs (18%), corticosteroids (14%) and anti-TNFs (13%). Of women on anti-TNF therapy (n=71), 68% discontinued treatment during pregnancy. Only around a third of women felt they had received adequate support and information about FP from their healthcare provider (HCP; 33%) and that this information was consistent between HCPs (28%). Men with CRD were even less satisfied with both the level of support (13%) and the consistency of information received around FP (13%).
Conclusion: The results of this survey suggest that in Sweden, CRD has a marked impact on FP for women, and to a lesser extent for men. Furthermore, the level of support and information on FP provided by HCPs to people with CRD, as well as the consistency of information received from different HCPs, were deemed inadequate. Providing better information on FP by HCPs, to both women and men with CRD, would help to support them on their journey to parenthood and overcome perceived obstacles to having children and continuing therapy.



REFERENCES

[1] Tincani A. Ann Rheum Dis 2018;77:866.

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Disclosure of Interests: Li Alemo Munters: None declared, Nathalie Holmen Employee of: Employee of UCB Pharma, Suzanna Jansson: None declared
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AB1426-PARE THE GLOBAL OSTEOARTHRITIS PATIENT PERCEPTION SURVEY (GOAPPS): A PILOT STUDY

Angie Botto-van Bemden[1], Guy Eakin[1], Rosa Sciortino[2], Maritza Quintero[2], Jordi Monfort[3], Patrick du Souich[4], Francisco de Abajo[5], Ingrid Mller[6], Elizabeth Oswald[7], Marco Matucci-Cerinic[8], Deborah Scotton[1], Marco Bibas[7], Marianna Vitaloni[7], Josep Verges[7]. *[1]ARTHRITIS FOUNDATION, Atlanta, United States of America*; *[2]Universidad de los Andes, Merida, Venezuela (Bolivarian Republic)*; *[3]Hospital del Mar, Barcelona, Spain*; *[4]University of Montreal, Montreal, Canada*; *[5]Alcala Universidad, Alcala de Henares, Spain*; *[6]Institut Poal de Reumatologia, Barcelona, Spain*; *[7]Osteoarthritis Foundation International, Barcelona, Spain*; *[8]University of Florence, Firenze, Italy*

Background: Globally, osteoarthritis (OA) is the third condition associated with disability. Science holds the key to finding better treatments and a cure. Still, it is essential to learn whats important to patients from the patients to implement the most effective global management of OA. The International Osteoarthritis Task Force, an initiative of the Osteoarthritis Foundation International (Barcelona, Spain) and the Arthritis Foundation (Atlanta, United States) with participation from member organizations in additional countries created the Global Osteoarthritis Patient Perception Survey (GOAPPS)-the first global survey to directly compare quality of life (QoL) & patient perceptions of care in the same OA patient survey across languages and cultures.
Objectives: The goal of the survey was to help all stakeholders in OA healthcare develop a better understanding of patients perceptions and how they may differ between cultures by collecting data on adult OA patient perceptions regarding their OA care. The survey will also collect data on patient demographics, OA symptomology, and impact of OA on daily functioning and QoL. Understanding patients needs and perceptions of care is the first step in optimizing global OA management.
Methods: Observational, cross-sectional study by online survey data collection translated into three languages. We collected data on patient demographics, symptomology, OA impact on daily activity and QoL to investigate the relationship between patient perceptions of their OA care, symptoms and impacts, and QoL. The questionnaire comprised of 4 sections: clinical characteristics, relationship with physicians and treatment, perception of attention, treatment and information received and auto-evaluation of QoL. Inclusion criteria included resident age 18 or older with an OA
Results: A total of 1485 surveys were completed from 7 countries. 1264 surveys were answered in English, 218 in Spanish and 3 in Italian; analysis of cultural differences was unable to be carried out in this pilot. Data show that the majority of the respondents were female (90%) and more than 55 years of age (82%). The majority (73%) of patients had knee OA, followed by hand (57%) and spine (54%). Comorbidities included hypertension (50%) and obesity (43%). Nearly all patients reported limitations related to physical activities (97%), followed by work activities (49%), social interaction (43%) and sex life (23%). 37% of patients experience emotional or mental health issue. The 58% says their doctor adequately explained their diagnosis and 55% understand the treatment options. Importantly, 41% of respondents are not satisfied with their OA treatment and 79% would like access to non-drug/non-surgical treatments. While 52% of respondents rate their QoL as good, 95% would rate it better if their OA was eliminated.
Conclusion: The results emphasize the significant impact of OA disease on patients daily activities and their desire to play an active role in managing their disease. Notably the majority asks for access to additional options for non-drug/non-surgical treatments stressing the need for an OA management improvement. This is a pilot survey and the results do not permit analysis of cultural differences. Continued survey distribution & analysis will determine differences in patient perception of QoL between OA patients living in different countries to further optimize global OA management.
Disclosure of Interests: Angie Botto-van Bemden: None declared, Guy Eakin: None declared, Rosa Sciortino: None declared, Maritza Quintero: None declared, Jordi Monfort Speakers bureau: Bioibrica
Procare Health, Patrick du Souich: None declared, Francisco de Abajo: None declared, Ingrid Mller: None declared, Elizabeth Oswald: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS; MSD, Janssen, Deborah Scotton: None declared, Marco Bibas: None declared, Marianna Vitaloni: None declared, Josep Verges: None declared
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AB1427-PARE PATIENTS AS RESEARCHERS OF TIETZES SYNDROME AND COSTOCHONDRITIS USING PARTICIPATORY NARRATIVE METHODS OF INQUIRY

Elke van Delft[1,2], Harold van Garderen[3], Rob Braamburg[1], Raymond Pieters[4]. *[1]Association of Tietze and costochondritis patients, Heukelum, Netherlands*; *[2]Maasstad Hospital, Rotterdam, Netherlands*; *[3]StoryConnect, Wageningen, Netherlands*; *[4]University of Applied Sciences Utrecht, Utrecht, Netherlands*

Background: Tietzes syndrome and costochondritis are rare, inflammatory rheumatic disorders characterised by chest pain. Pain is most commonly localised unilaterally at the costochondral junctions, with more than one junction generally affected (1). Whereas the conditions are considered self-limiting and in two third of the cases resolve within one year (2,3), they can last up to several years or be recurring (4), limiting the patients ability to function in occupational demands and activities of daily living. The exact cause is not known and therefore it remains a challenge to take on an effective treatment approach.
Objectives: This study aims to gain more insight into patients and medical professionals experiences with and handling of Tietzes syndrome and costochondritis.
Methods: It was noticed that hardly any research is done on Tietzes syndrome and costochondritis and hardly any medical professionals are specialised in these conditions. This sparked the idea to involve patients themselves as researchers of the conditions. To that end an online platform called a StoryPoint was designed, based on the Participatory Narrative Inquiry (PNI) approach (5). This StoryPoint allowed patients and medical professionals to anonymously share and do research on their personal experiences with the conditions.
This online assessment was followed by a live meeting with patients suffering from Tietzes syndrome or costochondritis. During this meeting the online gathered narratives were evaluated using group narrative evaluation methods (5).
Results: In total 53 experiences were retrieved. Approximately 60% of patients experienced complaints on a daily basis (figure 1). The reported limitations in daily living were inability to perform physical exercise, a lack of energy and incomprehension from the environment.

Treatments advised by specialists that relieved complaints were physical therapy, breathing techniques and NSAIDs. Relaxation, low impact movement and warmth were solutions that patients initiated themselves and were perceived helpful. Of all treatments advised by a medical professional 70% improved complaints, 22% had no effect at all, and 8% worsened the complaints (figure 2). Of the treatments that patients initiated themselves, 78% improved complaints and 22% had no effect (figure 2).
We are currently involving a wide variety of medical professionals and researchers for further evaluation of the narratives.

Conclusion: Tietzes syndrome and costochondritis can be very limiting conditions, especially when complaints become chronic. Treatments advised by medical professionals are hardly any more effective than treatments initiated by patients themselves. Since both conditions are rare and relatively unknown, medical specialists have difficulties recognising, diagnosing and treating these conditions. It is important that medical professionals become more familiar with Tietzes syndrome and costochondritis and become involved in this type of patient-driven research approaches.

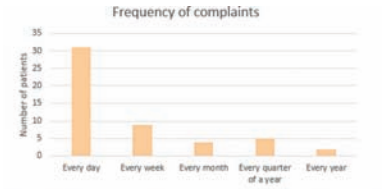


Figure 1: How often patients experience complaints from their Tietze's syndrome or costochondritis

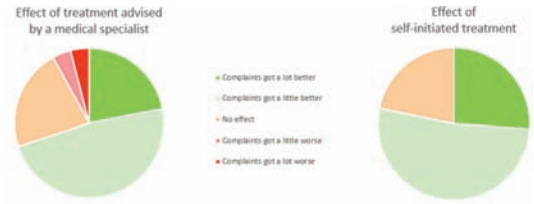


Figure 2: Comparison of the effect of treatment methods advised by a medical specialist or initiated by patients themselves

REFERENCES

[1] Proulx AM, Zryd TW. Costochondritis: diagnosis and treatment. Am Fam Physician. 2009;80(6):617-620.
[2] Disla E, Rhim HR, Reddy A, Karten I, Taranta A. Costochondritis. A prospective analysis in an emergency department setting. Arch Intern Med. 1994;154(21):2466-2469.
[3] Brown RT, Jamil K. Costochondritis in adolescents. A follow-up study. Clin Pediatr (Phila). 1993;32(8):499- 500.
[4] Freeston J, Karim Z, Lindsay K, Gough A. Can early diagnosis and management of costochondritis reduce acute chest pain admissions? J Rheumatol. 2004;31(11):2269-2271.
[5] Kurtz C. Working with Stories in Your Community or Organization: Participatory Narrative Inquiry (Third Edition). New York: Kurtz-Fernhout Publishing. 2014.

Disclosure of Interests: None declared
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AB1428-PARE FAMILY PLANNING IN CHRONIC RHEUMATIS DISEASES

Li Alemo Munters, Suzanna Jansson. *Stockholm, Stockholm, Sweden*

Background: Family planning (FP) in the context of chronic rheumatic disease (CRD) can be challenging for both women and men, with additional requirements for information and support.[1] However, it is unclear whether the needs of this population are being met by current clinical practice in Sweden.

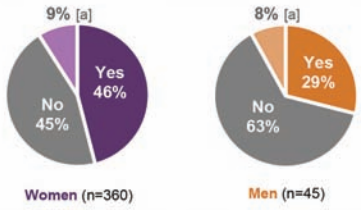
Objectives: To gain insight into the perspectives of men and women with different CRDs on FP, and to assess whether they feel adequately supported to make informed decisions.

Methods: A 10-minute survey focusing on participants experiences and current needs around FP was designed. The survey was distributed (24 Aug5 Sep 2018) via a web–based system to members of the Swedish Rheumatism Association; men and women aged 1847 years were included. Data are reported for participants with arthritic or systemic CRDs (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, juvenile idiopathic arthritis, systemic sclerosis, systemic lupus erythematosus, polymyositis, dermatomyositis). Participants with fibromyalgia, Ehlers-Danlos Syndrome, other or no CRD were excluded.

Results: Of 944 participants, 542 (57%) women and 60 (6%) men with arthritic or systemic CRDs responded. Over a quarter of women (28%) who had children/were expecting felt their CRD had affected their ability to have children and more than half either believed that their CRD had influenced the number of children they had or were undecided **(Figure A)**. Men were less affected by their CRD with respect to FP, with >60% reporting no impact on their ability to have children and/or how many. Of participants who did not want children/more children in the future, around a third attributed this to their CRD (women: 37% [n=86/232]; men: 30% [n=9/30]). Their biggest concerns were not being able to physically handle and/or cope with taking care of a child, and passing on their disease **(Figure B)**. Womens concerns regarding disease activity after pregnancy were not unfounded, with 66% reporting disease worsening postpartum. The most common treatments reported by women with CRD while trying to conceive were DMARDs (20%), NSAIDs (18%), corticosteroids (14%) and anti-TNFs (13%). Of women on anti-TNF therapy (n=71), 68% discontinued treatment during pregnancy. Only around a third of women felt they had received adequate support and information about FP from their healthcare provider (HCP; 33%) and that this information was consistent between HCPs (28%). Men with CRD were even less satisfied with both the level of support (13%) and the consistency of information received around FP (13%).

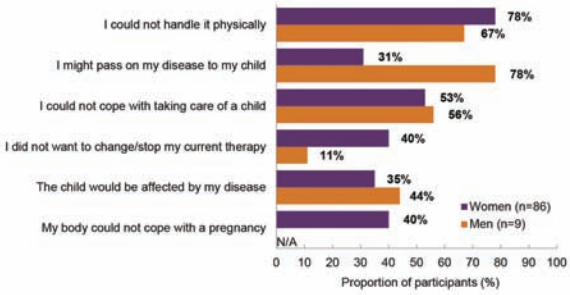
Conclusion: The results of this survey suggest that in Sweden, CRD has a marked impact on FP for women, and to a lesser extent for men. Furthermore, the level of support and information on FP provided by HCPs to people with CRD, as well as the consistency of information received from different HCPs, were deemed inadequate. Providing better information on FP by HCPs, to both women and men with CRD, would help to support them on their journey to parenthood and overcome perceived obstacles to having children and continuing therapy.

Figure: A) Participants felt that their CRD had affected the number of children they have



[a] Light purple/orange shading represents 'I don't know' response. Not all participants responded.

B) Concerns underlying why participants did not want children/more children in the context of CRD



Not all participants responded. Questions with no/very few responses are not shown.
CRD: chronic rheumatic disease; N/A: not applicable.

REFERENCES

[1] Tincani A. et al. ARD 2018; 77:866.

Acknowledgements: We thank the patients who participated. This study was funded by UCB Pharma and conducted by the Swedish Rheumatism Association. Editorial services were provided by Costello Medical.
LAM: None declared; **NH:** Employee of UCB Pharma; **SJ:** None declared.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.5255

Arthritis research

PARE0001 **CANNABIS-BASED PRODUCTS FOR MEDICINAL USE: EXPLORING THE VIEWS AND EXPERIENCES OF PEOPLE WITH FIBROMYALGIA**

Simon Stones[1,2,3], Des Quinn[2], Fibromyalgia Action United Kingdom. *[1]University of Leeds, School of Healthcare, Leeds, United Kingdom; [2]Fibromyalgia Action United Kingdom, Paisley, United Kingdom; [3]European Network of Fibromyalgia Associations, Heist-op-den-Berg, Belgium*

Background: A review by the Chief Medical Officer (CMO) of the United Kingdom (UK) in 2018 recommended moving cannabis-based products (CBP) from Schedule 1 of the Misuse of Drugs Regulations 2001 into Schedule 2, allowing CBP to be prescribed for medicinal purposes under controlled conditions by doctors on the Specialist Register of the General Medical Council. This prompted the National Institute for Health and Care Excellence (NICE) to develop guidance on prescribing CBP for medicinal use, which Fibromyalgia Action UK were invited to comment on. Anecdotally, we know that some people with fibromyalgia use CBP to help with pain relief; however, we wanted to explore these experiences further, while summarising people's thoughts of the draft scope guidelines.
Objectives: The aim of the survey was to understand experiences of CBP among people with fibromyalgia, including people's opinions of the NICE draft scope guidelines.
Methods: An online survey, hosted through Microsoft Forms, was disseminated via social media and Fibromyalgia Action UK's website between November and December 2018.
Results: A total of 69 people initially responded; with 66 eligible to participate. The average time to complete was 14:05 minutes. Over three-quarters (77%) reported using CBP. The types of CBP that people had used are shown in Fig 1. Over half reported using Cannabidiol (CBD)/ Hemp oil (55%), currently marketed as a food supplement. Around one quarter (26%) used herbal cannabis, with few reporting use of plant-derived/synthetic delta-9-tetrahydrocannabinol (THC) or THC/CBD sprays (3-5%). Of the 50 who responded, 52% reported using CBP for medicinal purposes on a daily basis; 28% stated they used CBP during a fibromyalgia flare. While some people did not report any benefits, one of the clear benefits reported by people was pain relief. People also reported improved sleep and mood, less fatigue, and reduced anxiety. When asked to score the current NICE draft scope guidelines, 48 people responded, with an average rating of 3.88 (1=very poor; 5 = excellent). Some felt that the scope was quite vague, difficult to digest, unclear as to who should and shouldn't be prescribed CBP, and lacked specific reference to conditions like fibromyalgia. There were also concerns in the time it takes to develop guidance. When asked about confusion among society distinguishing CBP for medicinal purposes from food supplements marketed as CBD/Hemp oil, of 63 respondents, 86% felt there was confusion which needs addressing. Individuals felt that alternative treatment options like CBP should be available to people with fibromyalgia, with additional research to identify the evidence for its potential benefit and safety.
Conclusion: The survey highlights that people with fibromyalgia are using CBP, but not necessarily those that are prescribed by a medical professional. There is an appetite among patients with fibromyalgia to explore the option of alternative treatment using CBP. There is widespread confusion among society distinguishing CBP from CBD/Hemp oil marketed as food supplements, which could be leaving certain individuals vulnerable. The development of national guidance is welcomed; however, investment in research to prove the efficacy and safety of CBP in people with fibromyalgia is also needed, to ensure that patients have appropriate access to safe treatments.

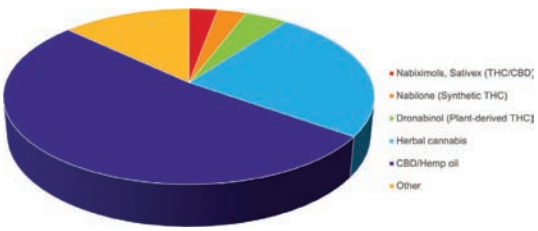


Fig 1. Types of CBP used by people with fibromyalgia in this survey.

REFERENCES

[1] Davies, S.C. "Cannabis Scheduling Review Part 1, The therapeutic and medicinal benefits of Cannabis based products – a review of recent evidence" London: Department of Health and Social Care (2018).

Acknowledgement: Thank you to those who took part in the survey.
Disclosure of Interests: Simon Stones Consultant for: SS has provided consultancy services to Envision Pharma Group, though this is not related to the contents of this abstract., Speakers bureau: SS has undertaken speaking engagements for Actelion, eyeforpharma, Four Health, Janssen and Roche, though these are not related to the contents of this abstract., Des Quinn: None declared
DOI: 10.1136/annrheumdis-2019-eular.8129

Best practice campaigning

PARE0002 **ME AND MY DILEMMA – A DANISH CAMPAIGN**

Connie Ziegler. *Gigtforeningen – Danish Rheumatism Association, Gentofte, Denmark*

Background: The Danish Rheumatism Association wanted to raise awareness on the challenges people face on a daily basis living with an invisible disease like some RMDs. In addition, the fact that many people living with a RMD experience that their surroundings have a lack of understanding the daily struggles they have living with a chronic disease.
Objectives: We wanted to increase the general awareness of RMDs and to show our presence in another context than expected. In addition, the campaign should open up for some difficult talks in an entertaining way giving people an occasion to continue the talks at home. Finally the campaign should show that RMDs are not only related to old people and that consist of a wide range of diseases.
Methods: Through Social Media and our website and magazine we called for daily dilemmas from people with RMDs and their relatives, colleagues or friends. Having enough dilemmas, we set up four dilemma shows in malls across Denmark and invited to a public show 'Me and My Dilemma'. Four famous people were brought in to constitute the panel and discuss the dilemmas. A journalist, who is also radio and tv-host was appointed moderator and through 1½ hour he took the panel through hard, funny and emotional dilemmas and involved the audience in the discussions as well.
Results: 'Me and my dilemma' had a very broad appeal; it was entertaining yet serious and eye opening to both the panel and the audience. It gave The Danish Rheumatism Association an opportunity to tell many different stories about living with RMDs. Just getting the word out about a disease that rarely receives a lot of focus in the public.
We received about 100 dilemmas, most of them we had to moderate a lot in order to be real dilemmas that could be discussed, have pros and cons and also to make sure that there was a variation in age, gender, diagnose and subject.
Between 200-300 people attended each show, which was less than we expected, however Denmark experienced one of the warmest months of May ever and since the shows were planned inside the malls that explained the limited attendance.
The people who did attend the shows were all in the target group, having either a RMD or were related to someone with a RMD.
Conclusion: It was quite a bit of work getting the shows ready, but they fulfilled their purpose in raising awareness to the public and still reach our target group in a new way and in a new context.
By recording all the shows we were able to make 5 great podcasts on different dilemmas, which people with RMD and their relatives can relate to and discuss.

REFERENCES

None
Disclosure of Interests: None declared
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Patient information and education

PARE0003 ESTABLISHING A PATIENT TRAINING CENTER OF RHEUMATOLOGY

Souzi Makri. *CYPLAR, Limassol, Cyprus*

Background: Patient education is considered of pivotal importance for the Organization. Patients should be informed, educated and well trained to acquire the necessary skills needed to deal with the challenges of living with a chronic disease. Equally important is the need of patients to acquire certain skills, necessary for advocating for their rights and representing their Organizations, both at the National but also at the European level. Realizing the above issues, the National Organization decided to create this training centre at its own premises, as it was noted that there was a lack of expertise in the above area, and that patients needed to be empowered to be equal partners in health decisions, but also effective Self managers of their condition.
Objectives: One main objective is to educate individual patients to Self manage their disease by accepting the new situation in their life, but also by learning how to effectively communicate with HPs, to be adherent to treatment, to cope with family work and social environments, and to regain self –confidence. The other objective is to train expert patients, enhance their knowledge and empower them for representing the Organization on all relevant Health committees and participate on all stages of the decision making process.
Methods: First step was to create a Brand name and acquire the relevant certificate of the establishment of the training centre. After the certification process had been finished, two volunteers from the Organization were trained by the National Authority of Human Resources and after successfully passing the 8-hour examination, they became certified trainers. A committee, under the two coordinators is now in the process of revising the modules of the first 5 courses which are offered initially, by restating the aims and objectives of each course as well as the training procedure, teaching techniques, methods and evaluation process. The courses are: The self-management (running), the expert patient (running) Self Diagnosis (running), Training for parents of Children with Rheumatic diseases (Coming before the end of Year), "Rebuilding the story of our life" –Systemic Sculpture method (Running from October 2019- April 2019)
The plans for the next steps include the creation of training course on building patient advocacy skills (Participation in Health committees, HTA, Advisory committees etc) and one on recruiting and training of volunteers.
Results: The experience from the implementation at the initial stage of the three training courses (Self-management, expert patient and self-diagnosis) shows that patients are happy to join, to share experiences and feelings and they successfully attempt to use the skills acquired in their everyday life. Some of the Organization's members have now become members on National Health committees. These include the Committee for Pricing of Medical products, National Health Insurance, ad hoc for updating the rights of patients, rare diseases, for digital Health etc. Success of the existing modules has led the Organization to decide on building an online portal for digital learning.
Conclusion: The creation of a rheumatology training centre for patients, although at its initial stage, has shown positive results for patients, by enhancing their ability to deal in an effective way with the chronic disease but also in improving their skills and knowledge to strive for effective advocacy and for being part of all in decisions that affect their rights in health.
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Best practice campaigning

PARE0004 EASY TO OPEN/EASY TO USE: ACCESSIBILITY FOR PEOPLE WITH REDUCED HAND FUNCTION

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Background: One fifth of Sweden's population, more than 1.5 million people, has reduced hand function.[1] For the European population, it would equal well over 60 million people.
People with reduced hand function, for example due to illness or age, are often unable to handle products or packaging without additional daily living aids. In addition to the 20 percent of the population with reduced hand function, often due to rheumatic disease, women on average have 40 percent lower hand strength than men. In other words, the market for inclusive design is huge and concerns a large portion of all consumers.
The Swedish Rheumatism Association, SRA, has for many years fought for accessibility of products and services for our members. The SRA has a history spanning over 15 years of activism for inclusive design. The highlight being the launch of the universal standard *SS-ISO 17480:2015 Packaging - Accessible design - Ease of opening*, of which the SRA was a big contributor. However, the aim for this abstract is not to put emphasis on previous successes but to describe current attempts to make the packaging industry adapt a more inclusive design for the many people with reduced hand function.
Every third year thousands of delegates visit Scanpack, Northern Europe's biggest packaging fair. Last year was the first time the SRA attended as an exhibitor, making the SRA the only non-profit organisation working for people with rheumatic diseases, to participate. 463 exhibitors from around 30 countries attended, with 16,500 delegates in total, of which 12,900 were visitors. The fair took place on October 23-26, 2018 in Gothenburg, Sweden.
Objectives: "Products that are functional and easy-to-use for people with reduced hand function, are suitable for everyone". This tagline defined our work for inclusive design. We focused on three objectives in order to make more visitors at the fair aware of the benefits with inclusive design on packages and products. We addressed the packaging industry, the pharmaceutical industry and those who produce products for the public environment. These were the objectives:

- Everyone should know that it is possible to measure manageability.
- Everyone should know that help is available. Tests apply to all types of products and packaging.
- Everyone should know that there is an "Easy to use" and "Easy to open" seal of approval available for packages.

Methods: At the fair, the SRA showed and told visitors how tests on manageability were done, and offered companies to do our small-scale tests of their products. We showed examples of packages that were approved with our certification method. The visitors were also encouraged to participate in our questionnaire.
The questions they had to answer were:

1. How many percent suffer from reduced hand function in Europe? 52 percent of the survey responses were correct. Correct answer: about 20 percent.
2. Women have weaker hand strength, compared to men. How much weaker? 56 percent of the survey responses were correct. Correct answer: 40 percent.

328 people participated in the survey.
Results: Representatives from leading packaging companies and visitors at Northern Europe's biggest packaging fair lack insight in the extent of reduced hand function in Sweden.
Half of the participants who visited the SRA's exhibition responded correctly to our questionnaire regarding reduced hand function, suggesting there is room for improvement in the packaging industry to adapt a more inclusive approach towards design that benefits people with rheumatic diseases.
Conclusion: Half of the participants who visited the SRA's exhibition responded correctly to our questionnaire regarding reduced hand function, suggesting there is room for improvement in the packaging industry to adapt a more inclusive approach towards design that benefits people with rheumatic diseases.

REFERENCE

[1] Lorentzen, L. (2018). Öppna dig! : Handbok i design av lätthanterliga förpackningar. Sweden : Sweden for All.

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Building patient led organisations

PARE0005 REFRESHING THE SOCIAL MEDIA STRATEGY OF FIBROMYALGIA ACTION UK: RESULTS OF A NATIONAL PATIENT ORGANISATION SURVEY

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Background: Patient organisations have traditionally provided support for patients. However, the method by which people seek support is increasingly desired across social media, particularly among certain populations within the fibromyalgia community who rely on social media as a key form of communication. In addition, the activity of patient organisations on social media is evolving to encompass greater advocacy and awareness activities with a growing target population of different stakeholders. To address this growing demand, Fibromyalgia Action UK conducted an online survey to inform the organisation's future social media strategy.
Objectives: The aim of the survey was to understand the preferences of people interacting with Fibromyalgia Action UK's social media platforms, in order to inform the organisation's evolving social media and wider communications strategy.
Methods: An online survey was disseminated via Facebook, Twitter and a post on Fibromyalgia Action UK's website over a one-month period, between October and November 2018. Questions focused on general demographics, social media branding, style and content.
Results: A total of 301 people responded to the survey, 89% of whom had been diagnosed with fibromyalgia and 5% of whom were a friend or relative. More than half of respondents (60%) were aged between 45 and 64 years, with only 13% of respondents aged under the age of 35 years. 91% of respondents felt happy with the organisation's current branding, with 78% rating the organisation's social media sites as 'Good' or 'Excellent'. While 92% of respondents were happy with the organisation's current social media content, around half (51%) suggested an increase in the amount of visual posts (such as infographics), and two thirds (66%) suggested an increase in news articles and patient/carer stories.
Conclusion: The survey highlights the need for more visual, engaging content to inform and educate people about fibromyalgia and related activities. Respondent demographics also highlighted a limited interaction on social media with younger people under the age of 35 years. Together, these findings have prompted the organisation to launch of a new campaign, titled #BecomeFibroAware, using visual content to inform, educate and empower the community, as well as an increased focus on engaging younger people with fibromyalgia.

REFERENCE

[1] Armstrong, S. Social networking for patients. BMJ 2016; 354 :i4201.

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Disclosure of Interests: Simon Stones Consultant for: SS has provided consultancy services to Envision Pharma Group, though this is not related to the contents of this abstract., Speakers bureau: SS has undertaken speaking engagements for Actelion, eyeforpharma, Four Health, Janssen and Roche, though these are not related to the contents of this abstract., Reece Henderson: None declared, Des Quinn: None declared
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PARE0006 LIVING WITH A RHEUMATIC DISEASE: A RESEARCH ABOUT QUALITY OF LIFE AND WORK CONDITIONS

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Background: There are 5 million people who suffer from rheumatic diseases in Italy with an annual expenditure of the health system, estimated for the chronic forms, around 4 billion euros. During the World Arthritis Day 2018 the Association of Persons with Rheumatic and Rare Diseases - Apmar Onlus presented the results of the survey "Living with a rheumatic disease" with the aim of raising public awareness by disseminating data useful to understand the quality of lives of people living with one of the 150 rheumatic diseases.
Objectives: The research investigated:

- The quality of life of people with a rheumatic disease
- The work problems and conditions experimented by people suffering from a rheumatic disease.

Methods: The survey was both qualitative and quantitative. The qualitative phase was held in Milan and was preparatory to the development of the questionnaire distributed at national level. In this first phase two groups of five people were interviewed for two hours. The people interviewed in the focus groups were women and men, age 25-55 years (50% 25-40; 50% 41-55) with at least one rheumatic disease, currently workers/laborers at least part-time.
In the quantitative phase, a questionnaire was administered throughout the national territory to a sample of 1,020 people, women and men, age 18-75 years with at least one rheumatic disease, currently workers/laborers at least part-time or who worked for a period following the diagnosis of rheumatic disease. The used methodology of on-line investigation was the Cawi (Computer Aided Web Interview).
Results:

- 89,1% of separated and/or divorced interviewed reported that the disease caused problems in the sexual relationship with the partner as to cause their divorce/separation;
- 61% of the sample had to reduce working activities significantly, in many cases abandoning the job completely;
- 26.3% of the sample stated that he prefers not to speak about his illness either with his work colleagues or with his boss and/or superiors.

Conclusion: Rheumatic diseases affect relationships and social life negatively. The research shows how the rheumatic disease can have a particularly critical effect in the relationship with the partner. The problems arising in the relationship of the couple are so meaningful, and cause of misunderstandings and psychological suffering to be considered among the main causes of divorce and separations.
Rheumatic diseases heavily affect the working life. From the research emerges that people with rheumatic diseases that have managed to preserve their work despite the disease, are often reluctant to talk about their health conditions at work. The main reason is the fear of worsening and/or compromising their relations with colleagues and superiors with consequent negative effects on work tasks and the risk of losing their workplace.
People suffering from rheumatic diseases in Italy declare that their condition of difficulty due to the pain, is often underestimated, this leads them to take a closing attitude for the fear of not being understood. The respondents also expressed the fear that in the highly competitive society we live in, there is no place for people to express their pain: they are afraid of being considered weak and in a certain way "to be put aside" and so they must therefore "show themselves strong".

REFERENCE

[1] A. Celano, President - APMAR Onlus; S. Mingolla, Journalist - APMAR Onlus, Matteo Santopietro - Managing Director - WeResearch – ricerche di marketing.

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PARE0007 RHEUMATISM CHALLENGE 2018 – "RHEUMATISM IN MOTION'' WE ARE GOING IN THAT TOGETHER!

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Background: Czech League Against Rheumatism plays an important role in promoting rheumatic patients in the Czech Republic. Its activity is aimed at:

- raising awareness about RA for early diagnosis and RA treatment
- improve an attitude of the Czech patients to the modern treatment, including the biological treatment
- co–operate on the change together with the professional community, regulatory authorities and Health Insurance Companies.
- striving to qualify the people with so called "moderate activity" of the disease for the biological treatment

- the struggle for full and equal life for people with rheumatic and musculoskeletal diseases
- the establishment of regional clubs and specific patient groups of Czech League Against Rheumatism

Objectives: Creating a campaign Rheumatism Challenge 2018 **- "Rheumatism in motion" We are going in that together!** The aim of this campaign is improving the health condition of people with RMDs. To motivate patients to move regularly and raising patient awareness about the importance of physical activity.
Methods: Walking as a means to reach a goal is the main content of this campaign. The aim of each participant in this campaign is to reach as much as possible steps and kilometers every months. Exiting challenges prompts patients to higher goals and giving them courage. Through walking Czech League Against Rheumatism wants to improve physical and mental health of people with RMDs. Wants to maintain a joint mobility and reduce a pain. Know and find the right kind of movement for each patient. Information about this campaign is published on the webpage, Facebook and Instagram of Czech League Against Rheumatism.
Results: This campaign managed to raise awareness about the importance of physical activity in patients with rheumatic and musculoskeletal diseases among the general public. Information about the campaign was in press and television. The campaign continues in 2019.
In response to the campaign has increased the number of members in Czech League Against Rheumatism, an increased number of visitors and fans of the Facebook page Czech League Against Rheumatism.
Conclusion: This campaign seems to be very useful in promoting how important physical activity is for patients with RMDs. This campaign can support patients be more healthy and physically active. Active approach to one another life can inspire other patients and their families and friends. Very important is also the support of this campaign from the professional community, medical doctors and health professionals.
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PARE0008 **UNDERSTANDING THE IMPACT OF ANKYLOSING SPONDYLITIS IN DAILY LIFE OF THE PORTUGUESE PATIENTS: RESULTS FROM THE ASSESSMENT OF RESULTS IN ANKYLOSING SPONDYLITIS (AREA) STUDY**

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Background: AS is known to have a significant burden upon the individual, family and society. It is essential to assess the impact of AS in patients' lives, to raise awareness and improve early referral, diagnosis and treatment, for a better quality of life.
Objectives: To assess the impact of AS in the life of Portuguese patients (work, daily activities, social life).
Methods: The Assessment of REsults in Ankylosing spondylitis (arEA) study was developed by the NOVA-IMS in cooperation with: Portuguese Society of Rheumatology, Portuguese Association of Family Physicians, National Association of Primary Care Units, National Association of AS Patients and the Portuguese League Against Rheumatic Diseases. The arEA aimed at assessing reasons for delayed referral of suspicious cases of AS to the rheumatologist, as well as disease impact in patients' lives, global health and work. A comprehensive online survey was developed with the collaboration of LPCDR and sent to AS patients. Data on demographics, lifestyle habits, daily life activities, working habits, disease indexes and healthcare utilization, health status/quality of life indicators, EQ-5D and BASDAI scales. A generalized linear model was adjusted in order to identify the factors impacting on quality of life of patients.
Results: 354 patients responded the survey, 42.1% female, most frequently from the 35-44 year-old age group. Mean age at disease onset was 27 years old, while the diagnosis was confirmed 7 years later. In the previous 12 months, the average of working days lost due to AS issues was 37 (including sick leaves). During that period, AS has affected work productivity in average around 73 days. Cumulatively, patients' relatives or friends had also lost about 13 days of work, to provide them assistance. Regarding limitations in daily life activities, house cleaning (55.5%), physical exercise (46.5%), getting in/out of bed (45.6%), using stairs (37.9%), shopping (37.4%) and tying shoes (35.2%) were reported as being highly limited by AS. As for the social life, family and friends' relationships were reported as not being affected by over 60% of AS patients. However, 19.8% of the respondents have reported a worse relationship with their partners after diagnosis, and 29.7% reported having decreased the frequency of sexual intercourse. Leisure activities, were only reported as not being affected by 34.6% and 40.5% of patients, while the practice of sports has much decreased in 40.7% of the respondents. Almost 80% had mobility issues during the last year, and over 65% had their usual activities/routines affected by AS. The average BASDAI score is 5.5 and the EQ visual analogue scale 55. Analyzing the impact of treatment, biologics and biosimilars were reported as having significantly improved patients' quality of life, except for physical or sexual activity.
Conclusion: AS has a major impact in the daily life of patients, work productivity, social relationships and leisure activities. Early diagnosis and treatment, along with physical rehabilitation/exercise plans, can reduce this impact and improve their quality of life.
Disclosure of Interests: None declared
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Best practice campaigning

PARE0009 **THE PHYSICAL AND EMOTIONAL BURDEN OF RHEUMATOID ARTHRITIS: DATA FROM RA MATTERS, A WEB-BASED SURVEY OF PATIENTS AND PHYSICIANS IN EUROPE AND CANADA**

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory disorder that negatively affects the patients' health-related quality of life (QOL).[1] Despite much progress in addressing the burden of RA, a gap exists in terms of understanding 'what really matters' to patients with RA, and balancing patients' QOL aspirations with clinical targets in key treatment decisions.
Objectives: This international survey investigated how RA affects the lives of patients according to the perceptions of both patients and healthcare providers (HCPs), in order to help health professionals attune their care on the domains that really matter to patients.
Methods: Data were collected from patients with RA, and rheumatologists or HCPs who treat RA in Canada, France, Germany, Italy, Netherlands, Spain, Sweden, and UK using a structured, closed-ended questionnaire in their local language. Respondents for the survey were recruited from survey panels of verified unique responses, as well as through social media. Data were summarized in terms of both frequency and percentages of patients to understand the experience of patients living with RA on daily activities, relationships, work, and aspirations.
Results: Overall, 5400 adult patients (81% female; mean age 52 years), and 808 rheumatologists or HCPs participated in the survey between November 2016 and February 2017. Of these, the highest proportion of patient and HCP respondents were from the UK (n=1250) and France (n=230), respectively. Overall, 52% of patients and 62% of HCPs believed that the emotional impact of RA is not well understood by people without the disease; whereas 46% of patients and 52% of HCPs had a similar belief with regards to the physical impact of the disease. Patients who felt that the impact of RA is less well understood by others expressed more negative feelings about every aspect of their life with RA. Important relationships with spouse or partner, children, family, friends, and colleagues were generally affected negatively. Almost half of the patients (48%) who participated in the survey reported that they were forced to take long-term leave/retirement or experienced slow career progress since being diagnosed with RA; more than 3 in 5 patients found exercising to be difficult; and almost 1 in 4 patients found difficulties in taking care of personal grooming. Aching/stiff joints, pain, and fatigue were the key physical barriers to activities for patients, and 65% of patients felt frustrated when they were unable to undertake or complete daily activities due to their disease. Two-thirds of patients wished to be able to accept their life with RA and do what they can to cope with it in the future. Over half of

the patients (52%) had a hope that the physical impact of RA will be better understood in the future.
Conclusion: Despite major advancements in the treatment of RA, the chronic disease continues to significantly affect many aspects of patients' lives, including relationships, career progression, daily activities, and ability to work. Both patients and HCPs felt that the physical and emotional impact of RA is not well understood by people without the disease. In line with a recently published study, pain, fatigue, and physical function remain primary barriers for patients to live a normal life and to participate fully.[2] In RA treatment decisions, patients' personal goals and patient-reported outcomes should be given greater consideration along with clinical targets.

REFERENCES

[1] Wysocka-Skurska I, et al. Clin Interv Aging. 2016;11:1741-50.
[2] Oude Voshaar MAH, et al. Arthritis Care Res (Hoboken). 2018 Oct 24. doi: 10.1002/acr.23799. [Epub ahead of print].

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PARE0010 INSIDE OUT – A PHOTO CAMPAIGN TO CREATE AWARENESS FOR YOUNG PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Inside Out is a photo campaign of Youth-R-Well.com, the organisation for young people (16-30 years) with rheumatic and musculoskeletal diseases (RMDs) in the Netherlands. The project was inspired by Unga Reumatiker, the youth organisation in Sweden and their campaign #doesntshowdoesntexist. The campaign of Unga Reumatiker showed that young people can suffer from rheumatic diseases, even though these diseases are invisible. Youth-R-Well.com recognized that the invisibility of an RMD can have a major impact on the lives of young people and wanted to create a similar photo campaign to show the invisible side of RMDs.
Objectives: The main objective of this project was to create more awareness for rheumatic and musculoskeletal diseases affecting young people. One of the hardest parts of living with an RMD is the invisibility of the disease in daily life. We wanted to show that even though you cannot see it, many young people have to deal with the consequences of having an RMD on a daily basis. We also wanted to show other young people who are in a similar situation, that they are not the only one.
Methods: To make the invisible side of an RMD visible for others, Youth-R-Well.com created Inside Out, an eight part photo campaign. Eight young people with different types of RMDs, took part in this project. From each individual, two photos were taken: one photo in daylight and one photo in the dark with their rheumatic-spots highlighted by blacklight paint. Next to the photos, the participants introduced themselves in a few sentences and ended with a life quote with a focus on the positive side of life. They were all telling very different and very personal stories. The general quote of the photo campaign was "Although you cannot see it from the outside, it is still there". The photo campaign was posted on Facebook and Instagram. The photo campaign was released the week before World Arthritis Day, in which the photos of one person were shared on each day. The final photo, a group photo with all the young people and their black light photos, was shared on World Arthritis Day 12 October 2018.
Results: It was a successful campaign, in which we reached almost 30.000 people on Facebook and 5.000 people on Instagram. The success of the project and all the shares and great comments it received were overwhelming. The power of two photos next to each other had a large impact on people who were not familiar with the fact that RMDs do exist among young people. As a result of the great comments, this photo campaign is going to be exhibited in Reade, the center for Rehabilitation and Rheumatology in Amsterdam, to reach more people and make them more aware of the invisibility of RMDs.
Conclusion: Based on inspiration from a youth organisation in Sweden, Youth-R-Well.com created the successful campaign Inside Out. We managed to create more awareness for young people with RMDs and the invisible side of having an RMD. We will continue to spread this campaign and show that young people with RMDs are not alone.
Acknowledgement: First of all, we want to thank all our brave participants who took part in this campaign. Secondly, we want to thank Unga Reumatiker, who inspired Youth-R-Well.com to launch this amazing photo campaign.
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Innovations in arthritis health care

PARE0011 PILOTING THE FIRST PATIENT PARTNERS PROGRAM FOR AXIAL SPONDYLOARTHRITIS: THE JOURNEY OF BELGIAN PATIENTSTO BECOME EXPERT TEACHERS IN RHEUMATOLOGY

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Background: Patients with axial spondyloarthritis (axSpA) were trained to deliver experience-based workshops to medical students, general practitioners, physiotherapists and other healthcare providers concerning axSpA. The most important aims of these workshops are to improve the early diagnosis and to increase awareness of axSpA in the medical sector. Taking an expert role as a patient however requires an extensive training.
Objectives: To describe the training program in detail and to illustrate both the less successful and the optimal implementation steps taken thus far.
Methods: In its first iteration, the training program was developed as a resource book including a curriculum, significant amounts of homework, without enough time for practical exercises. This resulted in a drop-out of a large portion of trainees. Thereafter, the training method has been adapted by copying successful parts of the approach of The Patient Partner® Program for Rheumatoid Arthritis (launched in 1999). Also, more concrete training opportunities via a DVD demonstrating the complete course and training materials, as well as offering hands-on trainings during a three day overnight stay were added. Besides creating opportunities for intensive practicing with each other, there was also more time for informal contacts and it allowed for proper group dynamics. So there is a lot of time for sharing among patients with a similar health background. A comfortable environment was created for the candidates, enabling them to go through a complete process and giving them sufficient time to train all the components of the program.
Results: On February 22nd 2018, five fresh SpA-patients started the training, all five of them successfully completed the training on June 2nd 2018. On a first evening of familiarization, trainers tried to know more about the motivation of the trainees, while in an individual interview a rheumatologist reassured that the candidates have the correct diagnosis, as their story should be consistent. The selected candidates received part 1 of the training manual by mail and they were invited to profoundly study the terminology and the anatomy, related to their disease.
During the first full day of the training, the trainers took time to explain this terminology and anatomy. Later on this constituted the building blocks of the course. The trainers closed this first day demonstrating the history taking and they asked the trainees to study at home their personal medical file.
On day 2, the homework of the previous day was first discussed, followed by related exercises. Day 2 finished with the demonstration of the clinical examination.
The training program was completed with three days with overnight stay. During these days a lot of practical exercises of the clinical examination were organized, followed by a discussion of the impact of the disease and the importance of active participation. The program ended with a general rehearsal and a written as well as an oral test to evaluate how each trainee had assimilated all this.

Conclusion: In the training program PPP SpA, the trainees learn to tell a uniform and academically correct story. This contains an accurate history taking and a correct clinical examination reinforced by the personal history of the Patient Partner. Moreover the whole process helps each Patient Partner to have a better insight in their own illness, a better capacity to cope and to develop more skills in the dialogue with medical practitioners. The experienced positive feedback of the trainees after every course is the best motivation to continue with this approach.
Disclosure of Interests: None declared
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Building patient led organisations

PARE0012 **INVOLVEMENT OF PATIENTS IN ERN RECONNET: A SUCCESSFUL INITIATIVE RAISING PATIENTS' LEADERSHIP AT EUROPEAN LEVEL**

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Background: European Reference Networks (ERNs) are virtual networks involving centres of expertise across EU Member States with the aim of tackling rare and complex diseases. The ERN ReCONNET involves currently 26 healthcare professionals (HCPs) from 8 countries and cover rare and complex connective tissue and musculoskeletal diseases (rCTDs). Patient participation and involvement, also through EURORDIS, is a key characteristic of ERNs.
Objectives: To demonstrate that patients' involvement and collaboration across disease and geographic borders via the ERN ReCONNET effectively brings better care for people living with rCTDs.
Methods: The European Patient Advocacy Groups (ePAGs) provide patients' opinion and input in all activities of the ERN. They relay the views of their wider communities, evaluate how the ERN acts on patients input, contribute to projects and research, develop and disseminate patients' information, ensure that patient rights and choices are taken into account in decision-making and identify national groups to work with the ERN's HCPs. To structure the patients' involvement, a Patients' Organizations Working Group led by a Senior and a Junior Coordinator, developed and approved its own Terms of Reference. Patients' Representative Disease Coordinator (PDR) have been identified for most diseases. They bring patient perspective, liaise with HCPs and their wider patient community. Three ePAGs are voting members of the Steering Committee.
Results: ePAGs have collaborated intensely in ERN activities, organising and participating to regular meetings, providing their input into projects. They co-designed and disseminated surveys on clinical practice guidelines and on patient education. In each disease area, they collected feedback from their community on topics such as unmet needs or therapeutic education, worked alongside HCPs on narrative reviews[2], abstracts, surveys and reviews of the literature[2]. Lay language versions of documentation enable the wider community to understand the efforts of ERN ReCONNET, of which the ePAGs form an essential part. ePAG's involvement in the ERN has brought perspective for the future, identifying common surveys for next year, providing input on therapeutic educational programs or preparing patient journey documentation. A project to certify websites information quality on ReCONNET diseases and disorders was approved during the last meeting. From 10 ePAGs invited at the EMA symposium on clinical trials, 2 were from ReCONNET.
Conclusion: The ERN ReCONNET is a great opportunity for patients' leadership, bridging from EULAR and its PRP program to ERN and other EU initiatives. It will make a tremendous impact on the EU diagnostic and treatment landscape bringing a better quality of life to people with rCTDs.

REFERENCES

[1] https://ec.europa.eu/health/ern_enTi
[2] https://rmdopen.bmj.com/content/4/Suppl_1

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Patient information and education

PARE0013 **EDUCATING PEOPLE WITH RMDS TO FOLLOW A CORRECT DIET: AN INNOVATIVE 3 STEPS PROJECT**

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Background: Patients associations in Italy as in all the European countries have a strong role not only in empowering people with Rheumatic and Muscle-skeletal Diseases (RMDs), but also in educating them to new healthier lifestyles, comprehending physical activity and diet.
In Italy, the special relationship between people and food make our job more difficult than in other countries and it needs to try new ways driving people with RMDs to a correct diet without feeling different from the healthy population
Objectives:

1. to make patients, their families & care givers and the society aware of how much important is to follow a correct diet to prevent some of the damages that may be related to rheumatic diseases;
2. to make patients and their families aware of the importance to rely on experts in setting up correct dietary regimes;
3. to educate people with RMDs to a correct diet and healthy lifestyle, showing them it is possible to eat meals appetizing, tasty and also appearing beautiful even if following an appropriate and healthy regimen.

Methods: STEP 1 - ANMAR published "RMDs and diet". The booklet written by dr. Annalisa Olivotti, biologist and nutritionist, contains all topics concerning diet and RMDs; the Rheumatologist position and some suggestions by patients are present too. The booklet has been sent to all people receiving the ANMAR magazine "Sinergia" and was available for free in all ANMAR events and on its website.
STEP 2 – Since September 2018, through the regional associations, ANMAR organized a series of events to educate all the population and especially patients, their families and care givers, to follow a healthy diet, as a first aid to the pharmacological therapies.
STEP 3 - To complete the educational pathway of each meeting, all participants can experience how fun may be eating in a healthy way, having a dinner cooked by local chefs who have previously received a complete list of the most suitable foods for proper nutrition for people with RMDs.
Results: The project is still ongoing: nowadays we can refer these data:

- 15.000 copies of the booklet "RMDs and Diet" were published and distributed
- 5 meetings were organized, directly approaching a total of 450 people
- All participant highly appreciated the healthy menu cooked in the dinners
- 54 new recipes have been sent to the regional Association of Piemonte, leader of the project
- Using a "free – offer" request to enjoy the dinner, the project may also become a good fundraising way for the regional association organizer.

Conclusion: Data collected seem to confirm this one may be a suitable way to overcome the Italian cultural gap which leads to live diet as a bad and depressing lifestyle, as in Italy eating is not only a way to feed on, but an enjoyable moment.
We hope further data will enforce this first impressions and definitely confirm it.
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PARE0014 **PATIENT VOICE IN GOUT – A EUROPEAN PATIENT SURVEY TO UNDERSTAND THE NEEDS OF PEOPLE LIVING WITH GOUT**

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Background: Gout is one of the most common form of inflammatory arthritis in Europe, but awareness of it is relatively low. There is limited information available about the impact of gout on patients, and more generally on society.
Objectives: To give gout patients a voice to better understand the impact that the disease has on their lives.
Methods: From June to September 2018, gout patients from 14 European countries were invited to complete a 15 minutes online survey. Adult (18+) patients diagnosed with gout who met the criteria and finished the survey were included in the analysis. The design and content of the survey has been developed together with several patient and clinical experts to ensure that the most relevant aspects of the disease were covered. The questionnaire was translated into 11 different languages and checked that patient-friendly language was used. Patients were recruited via patient associations, leaflets provided to doctors and consumer online market research panels to reach the targeted number of patients.
Results: 1,100 gout patients completed the survey, 78% of respondents were male and 22% female. The mean age of participating patients was 55 years, 56% were employed or studying. The mean age of patients at diagnosis was 45 years and 38% were diagnosed during their first flare. The patients had on average 2.9 flares per year and the length of their last flare was 5 days on average. 84% of patients experienced moderate to severe pain with their most recent flare, 63% had severe pain with their worst flare ever. Patients reported that gout has a significant impact on their daily activities: on their ability to walk (59%), changes in mood and mental well-being (43%) and difficulties relating to their partner (26%). 27% of patients reported that their self-esteem has dropped.
Inconvenience (53% of patients), agony (37%) and frustration (32%) were the words patients most often associated with gout. 10% of patients (or a family member) have retired or lost a job because of their gout.
Despite reporting these not-insignificant impacts of gout on their lives, 79% of patients said that they are satisfied with their current treatment. However, two-thirds (68%) of younger patients (18-35 years) reported that they are satisfied with their current treatment.
69% of gout patients felt they have an open and trusted relationship with their doctor. But 42% of patients told their doctor about <50% of their flares in the year. Over a quarter of gout patients who have had 5 or more flares feel they are wasting their doctor's time. 60% of patients said that they know nothing or very little about their condition, and 94% of the patients rated that there is no or very little knowledge amongst the general public about gout.
Conclusion: The results of this survey demonstrate that gout has a significant impact not only on patients, but also on their families and society. Gout seems to lead to stigma and many patients may feel guilty about their lifestyle choices. Actions need to be taken to manage dissatisfaction of patients and to encourage them to speak up to request better management of the disease. There seems to be an urgent need to educate both patients and the general public about the seriousness of gout and the burden on patients and their families. The results of this survey will be used for communication with healthcare professionals to better address patients' unmet needs.
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Psychosocial support

PARE0015 **EMOTIONAL HEALTH AND WELL-BEING MATTERS**

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Background: The most common co-morbidities amongst people with RA are mental health conditions, such as depression and anxiety, as evidenced by previous surveys and reports by the NRAS. NRAS also understands, through interaction with its membership across the UK, that mental health and well-being are important issues for people living with RA and JIA. NRAS therefore partnered with City University to undertake a survey exploring the impact of RA and adult JIA on mental health.
Objectives: To explore the psychological impact of Rheumatoid Arthritis (RA) and Juvenile Idiopathic Arthritis (JIA), along with any psychological support people may have received or would like to have access to, to help manage the anxiety, emotions and stresses that come with being diagnosed with and living with RA or JIA and its treatment.
Methods: Following a focus group held in Central London in early 2018 with a dozen NRAS members, NRAS and City University designed a survey to look at a range of aspects relating to emotional health and well-being, including validated questionnaires to compare data to existing research. The survey was open between May and July 2018, with participants recruited via NRAS newsletters, social media platforms, the NRAS HealthUnlocked forum and via healthcare professionals at rheumatology units. A total of 1,999 people participated in the survey and a final sample of 1,650 was used for analysis.
Results: The survey found that people with RA and adult JIA were less satisfied with their life, believed the things in their life were less worthwhile, and were less happy. The proportion of people who scored poorly on life satisfaction and life worth was over 7 times greater in those with RA and adult JIA than the national average. Despite this, the survey found that 2 in 5 people had never been asked by a health professional about their emotional and psychological well-being, and 1 in 3 people who had requested or been offered support had never received it. Positive experiences that respondents shared of psychological support, such as GPs and rheumatologists being very supportive, the importance of family, and services offered by NRAS, demonstrate the benefits of good and appropriate support being available. Negative experiences, such as lack of health professional understanding about mental health, lack of understanding of RA by counsellors, and lack of personalised care demonstrate the future work that must be done to help adequately support people with RA and adult JIA.
Conclusion: The survey has demonstrated the need to provide more effective self-management techniques of emotional as well as physical well-being, ultimately leading to overall improved health outcomes. In line with NICE guidelines, other additional support is needed, such as the availability of cognitive behavioural therapy and the implementation of mental health and well-being assessments at annual review. Further research is needed into specific areas, such as health inequalities and why people with severe mental health issues experience poorer disease activity, understanding why adults with JIA have poorer life quality than people with RA, and understanding the impact of psychological interventions for people with adult JIA.

REFERENCES

[1] Emotional Health and Well-being Matters, McBain, H., Bezzant, M., Bosworth, A., 2018.

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Work and rehabilitation

PARE0016 **IMPACT OF AXIAL SPONDYLOARTHRITIS ON PATIENTS' PROFESSIONAL LIFE: RESULTS FROM THE ONLINE SURVEY EMAS OF 638 FRENCH PATIENTS**

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Background: Axial spondyloarthritis (axSpA) can result in functional limitation and work disability. However, there are little data in the era of biologics.
Objectives: The aim of this analysis was to evaluate the impact of axSpA on professional life.
Methods: Between December 2017 and February 2018, patients followed for axSpA by their rheumatologists or affiliated to the French patients association AFLAR, and self-reporting axSpA, participated in the European Map of Axial Spondyloarthritis (EMAS) cross-sectional patient survey1. Socio-demographics (age, gender, relationship status, educational level, job status), disease activity (BASDAI) and the impact of axSpA on professional life (job choice, working hours, sick leave, unemployment and relationship with colleagues) were collected. The participants who were employed and working at the time of the survey were regrouped as "employed" and the ones employed or on temporary sick leave or students at the time of the survey as "active". No imputation of missing data was performed and the analyses were descriptive.
Results: In France, 638 persons (mean age 41.5 ± 11.1 years, 77% females, mean disease duration 6.9±8.2 years, mean BASDAI 5.9±1.7) participated to the survey. About half of them (51%) had a university degree. At the time of the survey, 54% were employed, 26% in temporary or permanent sick leave, 7% unemployed, 6% retired, 5% homemaker and 2% students. Overall, 176 (28%) received social compensation for handicap or disability due to their axSpA. Regarding the employed ones (n=331), 50% were unskilled workers, 15% had an intermediate profession and 23% a white-collar job. The majority (73%) reported working issues related to axSpA in the last 12 months, such as sick leave (60%), reducing or difficulties to fulfill working hours (62%) or missing working hours for health appointments (33%). Among patients on temporary sick leave (n=72), 92% reported that it was the consequence of their axSpA and the mean duration of their temporary sick leave in the last 12 months was 5.4±4.0 months. Considering active people (n=418), 39% declared that their relationships with their work colleagues were worse since their axSpA. AxSpA had also influenced 55% of them in their job choice and drove 44% to adapt their workplace and 34% to move to another job. Finally, 62% expressed their fear to lose their job because of axSpA.
Conclusion: In this survey of 638 young axSpA patients, 66% of participants were active; the impact of the disease on professional life was described as important and often had consequences including permanent sick leave or unemployment. These aspects of axSpA should be better assessed.

REFERENCE

[1] Gossec L, et al. Diagnostic Delay and Associated Factors in Axial Spondyloarthritis across Europe. Results from the European Map of Axial Spondyloarthritis Survey. Arthritis Rheumatol. 2018 Sep;70 Suppl 9:688

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Arthritis research

PARE0017 **EXPLORING DIFFERENCES IN THE AGE ON ONSET OF JIA BETWEEN MALES AND FEMALES: A PARENT-LED SURVEY**

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Background: The etiology of Juvenile Idiopathic Arthritis (JIA) remains unknown, despite a range of proposed mechanisms under investigation [1]. However, previous research has revealed biological differences depending on the age of onset of JIA, independent of the classification based on the number of joints involved [2].
Objectives: In this parent-led study, the age of onset of JIA by both disease subtype and sex of the child were explored, to identify whether there is a difference in age of onset of JIA between males and females.
Methods: An online survey was shared via social media, targeted at parents of children and young people (CYP) with JIA. Questions probed the age of symptom-onset and diagnosis (by single year of age), JIA subtype and Rheumatoid Factor (RF) status.
Results: Of the 409 CYP included, 296 had polyarticular (poly) or oligoarticular (oligo) JIA, including extended-oligo JIA (72% of all respondents). There were no differences between onset among these subtypes; therefore, they were grouped for further analysis, given comparable disease progression and genetic markers among these subtypes. There was no significant difference regarding age of symptom onset between RF-positive and RF-negative CYP. Amongst those with poly/oligo JIA, there was a clear peak of symptom-onset in the first few years of life, with over half experiencing symptoms before their third birthday, and 73% before the age of five years. Interestingly, the distribution of symptom-onset was significantly different in the poly/oligo JIA group between males and females (P=0.0093), with the onset of poly/oligo JIA appearing to occur earlier in females (Figure 1). Given that some CYP with older-onset JIA are sometimes reclassified as having enthesitis-related arthritis (ERA) when examined in adolescent services, the Mann-Whitney U Test was repeated with only those CYP with JIA onset before the age of seven years. In this case, there remained a significant difference in age of onset of poly/oligo JIA between males and females (P=0.0061).

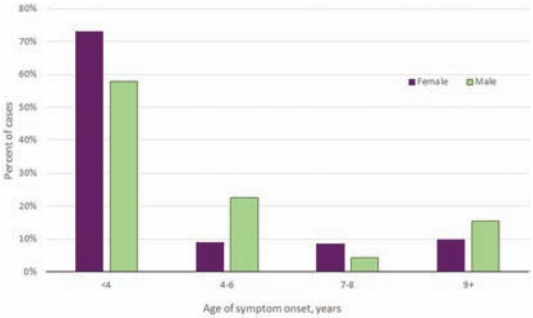


Figure 1. Grouped age of onset of polyarticular and oligoarticular JIA for females and males.

Conclusion: The age of symptom-onset among CYP with poly/oligo JIA differs between males and females, with females tending to exhibit symptoms earlier. This appears not to be attributable to misclassification of JIA subtype, and so this knowledge may assist future diagnoses of JIA. Further research is required to identify which temporal-associated factors may be critical in JIA onset and development.

REFERENCES

[1] Rigante, et al. The Etiology of Juvenile Idiopathic Arthritis. *Clinic Rev Allerg Immunol* 2015; 49:253.
[2] Barnes, et al. Biologic similarities based on age at onset in oligoarticular and polyarticular subtypes of juvenile idiopathic arthritis. *Arth Rheum* 2010; 62:3249-58.

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Building patient led organisations

PARE0018 ENABLING PATIENT-CENTRED CARE IN RHEUMATOID ARTHRITIS AND ASSOCIATED COMORBIDITIES

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Background: Patients with rheumatoid arthritis (RA) have an increased risk of comorbidities such as diabetes (IR of 8.6 per 1000 person-years[(1)]; 20% prevalence[(2)]), interstitial lung disease (7.7% incidence[(3)]; up to 60% (interstitial lung abnormalities in early RA)[(4)]), depression (up to 200%[(5)]; 16.8%[(6)]), and cardiovascular disease (40-70%[(7)]; 5-12.9%[(8)]) which contributes to increased long-term morbidity and mortality[(9)]. However, despite advances in treatment there are few established recommendations on the management of RA-related comorbidities.
Objectives: This study aimed to identify examples of good practice in the care of RA and associated comorbidities meeting standards of patient-centred care, and consider how these could be implemented in other European centres.
Methods: Following a literature review, multidisciplinary teams including specialists in rheumatology, cardiology and internal medicine, nurses, physiotherapists, psychologists, patient liaisons and care coordinators at 12 selected specialist centres across Europe (1 centre per country) were interviewed (approx. 180 interviews). The models identified were critically reviewed by a group of experts including a patient representative, and the degree to which the interventions impacted patient care and could be implemented in other centres was evaluated.
Results: Several care model interventions were identified which may improve quality and the patient's experience of care, e.g. fully integrated screening and diagnosis of comorbidities; coordination and sharing of care across different disciplines of comorbidity management; tailored individual education of patients and family members on lifestyle; enabling virtual engagement between patients on lifestyle management; and optimised convenience for patients having to attend multiple specialty appointments.
Conclusion: This study identified and evaluated interventions that may improve patient outcomes and quality of care in RA and associated comorbidities. The next steps will be to disseminate and implement these examples of good practices in a variety of European healthcare systems and settings.

REFERENCES

[1] Solomon D, et al. Ann Rheum Dis 2010; 69(12):2114-7
[2] Albrecht K, et al. Rheum 2018; 57(2):329-336
[3] Bongartz, et al. Arthritis Rheum 2010; 62(6):1583-1591
[4] Reynisdottir, et al. Arthritis Rheum 2014; 66(1):31-39
[5] Sheehy, et al. Rheum 2006; 45(11):1325-1327
[6] Matcham, et al. Rheumatology 2013; 52:2136-2148
[7] Holmquist M, et al. Ann Rheum Dis 2017;76:1642-47
[8] Van Halm, et al. Ann Rheum Dis 2009; 68(9):1395-1400
[9] Dougados, et al. Ann Rheum Dis 2014; 73(1):62-68

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Patient information and education

PARE0019 LIVING WITH SYSTEMIC SCLEROSIS: EXPLORING ITS IMPACT ON CAREGIVERS: A QUALITATIVE STUDY

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Background: Systemic sclerosis (SSc) is a rare, chronic and heterogenous disease with many possible outcomes and an uncertain horizon which presents difficulties not only for patients, but also for caregivers.
Objectives: To gain more insight in the experiences and unmet needs of caregivers for people with SSc in the Netherlands.
Methods: The study had a qualitative design. Participants were recruited by the Dutch patient organization (NVLE) using social media. One focus group and two individual interviews with a semi structured approach were held. Participants were asked to note down their associations with the disease, which lead on to a group conversation moderated by two researchers (MRS, CHE). The focus group was audiotaped and transcribed. Individual telephone interviews were summarized. All participants verified and approved the reports afterwards.
Results: Eight caregivers (4 males, 4 females: 4 partners, 2 widowers, 1 parent and 1 friend) of patients with SSc participated. Six attended the focus group session, two were interviewed over the phone. Several challenges were reported by the participants. The first challenge is coping with the chronic disease course, unawareness of treatment options and lack of information about limitations in treatment modalities. Furthermore, the witness of patients' ailing, changing bodies, decreasing mobility and poor energy levels without being able to provide a cure, was experienced as a huge burden by caregivers. Alongside this distress, caregivers personal lives are also affected; future opportunities are cut off, such as starting a family or continuing an active life style.
Caregivers addressed invalidation and the decrease in support from others due to misjudgment and misconceptions about severity, duration

and impact of the illness. Over time, this resulted in a dwindling network of social and emotional support, affecting family-life, relationships and mental health of both patient and caregiver.
Another strain was the complex mutual process of coping and the lack of frank communication about the condition between the partners, towards their social network and the medical staff. This is partly due to the indolent course of the disease, but also due to fear of what the future would hold and lack of insight in prognosis.
Caregivers reported that care provided at the hospital did not actively involve caregivers, nor provided them with the much-needed information with regard to prognosis, long-term treatment plans or daily care.
Conclusion: SSc has a major impact on the lives of caregivers, however, current care does not actively inform, include or support them to relieve some of this burden. Further research should focus on the modalities in which caregivers can be involved in the care and which information and support is required.



Figure 1. Word cloud/associations by participants, as part of the method used in focus group discussion.

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PARE0020 **EXERCISE FOR LUPUS PATIENTS**

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Background: Up to 80% of all Lupus patients experience fatigue and most of them report this as the most severe symptom. One of the major causes of morbidity in SLE patients is chronic, debilitating fatigue, decreasing quality of life, increasing risk of work disability with associated cumbersome healthcare costs.
Several research papers show that the only thing clinically proven to have an effect on Lupus fatigue is moderate exercise. If you tell this to a Lupus patient experiencing fatigue, however, you will find it very difficult to motivate them to exercise. The challenge is to make them realise that exercise does not necessarily mean running a marathon or going to the gym – a little movement goes a long way.
Objectives: To get lupus patients to exercise and thereby experience less fatigue/better manage their disease.
Methods: Develop an exercise program, that is approved by physiotherapists and leading lupologists, easy to do and inspires Lupus patients to keep active even when they feel exhausted.
Results: In collaboration with physical therapists Lupus Europe has developed an exercise program from our own experiences and had it approved by leading European lupologists. The program has five levels; from lying in bed up until being able to run and jump. All exercises can be done at home without training tools. In order to make it accessible we have planned to make five videos (with Lupus patients), shoving how to do each exercise and five connected pamphlets. We have already recorded the first three levels and are planning to finish the entire "package" in 2019. The materials will be made available to all Lupus patients on the Lupus Europe web site and YouTube channel free of charge.
Conclusion: We have already seen good results within the Lupus community, where people are finding the program easy to use and a help to keeping them active. Our hope is, that researchers will use our program to investigate its effectiveness on Lupus fatigue.

REFERENCES

[1] Piper BF. Pathophysiological Phenomena in Nursing: Human Responses to Illness. PA, USA: WB Saunders; 1993. pp. 279–302.
[2] Ramsey-Goldman R, Rothrock N. Fatigue in systemic lupus erythematosus and rheumatoid arthritis. PM R. 2010 May; 2(5):384–92.
[3] Da Costa D, Dritsa M, Bernatsky S, Pineau C, Ménard HA, Dasgupta K, Keschani A, Rippen N, Clarke AE. Dimensions of fatigue in systemic lupus erythematosus: relationship to disease status and behavioral and psychosocial factors. J Rheumatol. 2006 Jul; 33(7):1282-8.
[4] Wang C, Mayo NE, Fortin PR. The relationship between health related quality of life and disease activity and damage in systemic lupus erythematosus. J Rheumatol. 2001 Mar; 28(3):525-32.
[5] Al Dhanhani AM, Gignac MA, Su J, Fortin PR. Work disability in systemic lupus erythematosus. Arthritis Rheum. 2009 Mar 15; 61(3):378-85.
[6] Panopalis P, Yazdany J, Gillis JZ, Julian L, Trupin L, Hersh AO, Criswell LA, Katz P, Yelin E. Health care costs and costs associated with changes in work productivity among persons with systemic lupus erythematosus. Arthritis Rheum. 2008 Dec 15; 59(12):1788-95.
[7] Ramsey-Goldman R, Schilling EM, Dunlop D, Langman C, Greenland P, Thomas RJ, Chang RW. A pilot study on the effects of exercise in patients with systemic lupus erythematosus. Arthritis Care Res. 2000 Oct; 13 (5):262-9.

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